

Supporting Information

A 5+1 Protic Acid-Assisted *aza*-Pummerer Approach for Synthesis of 4-Chloropiperidines From Homoallylic Amines

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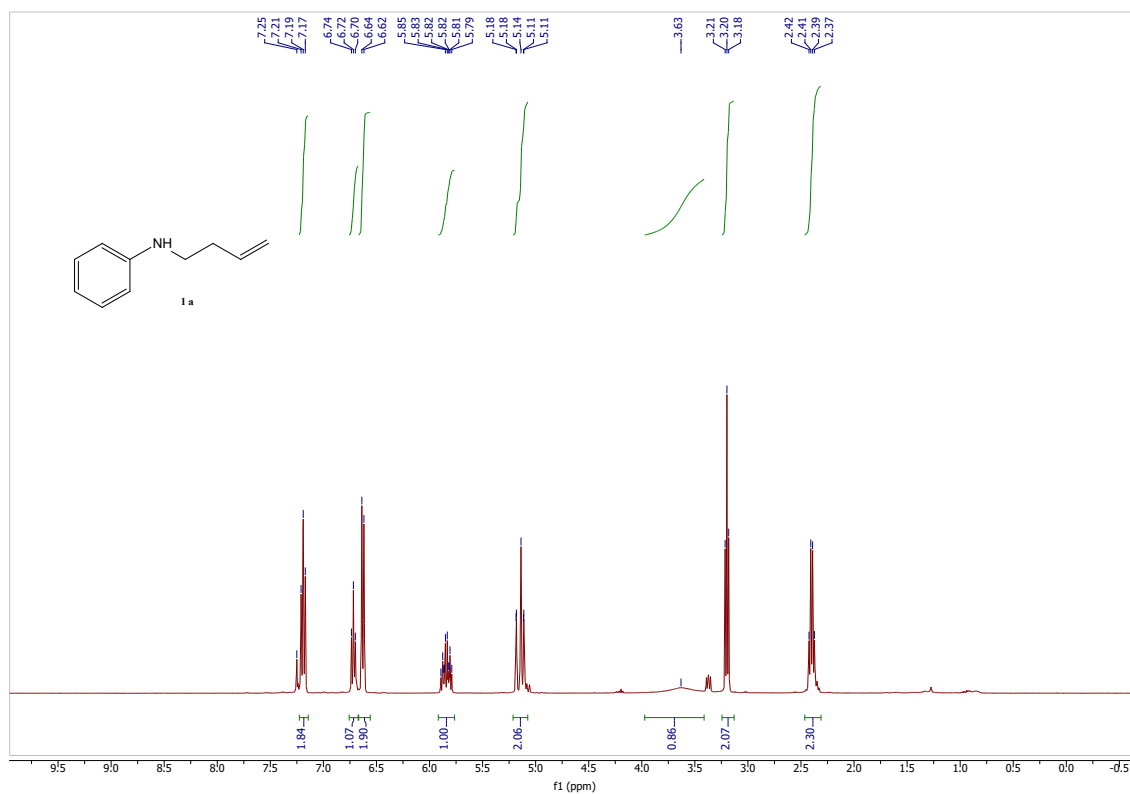
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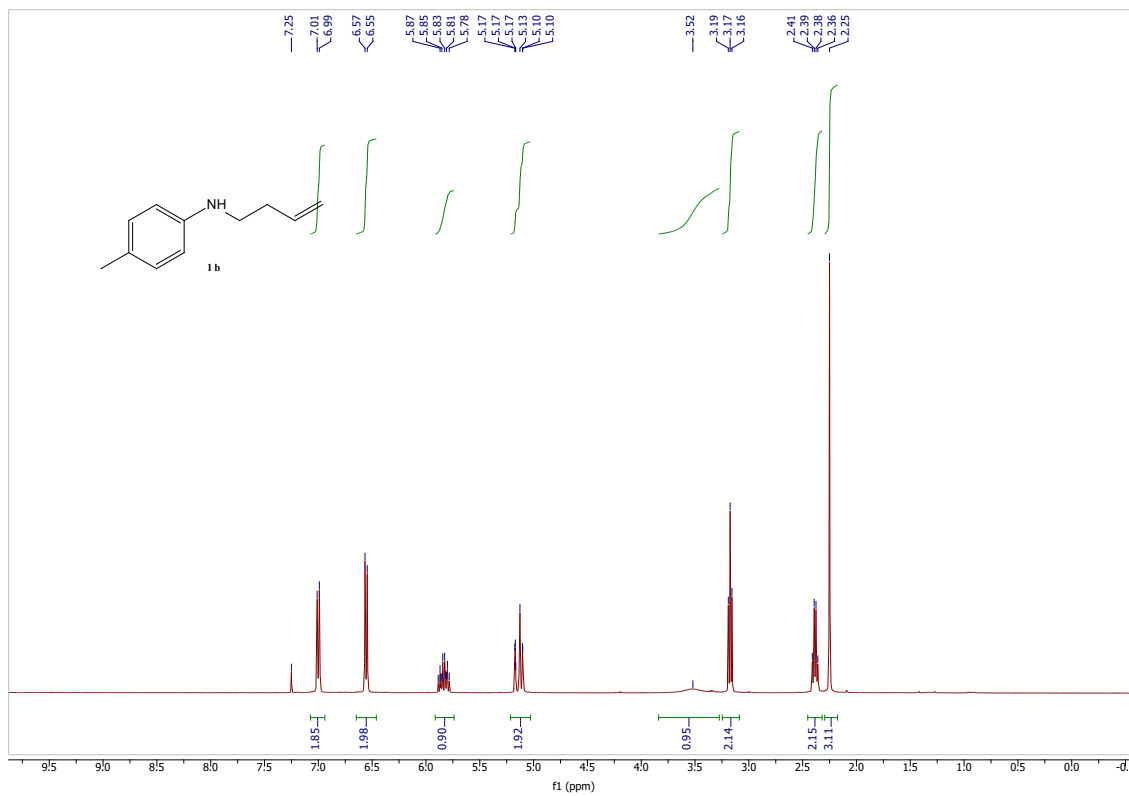
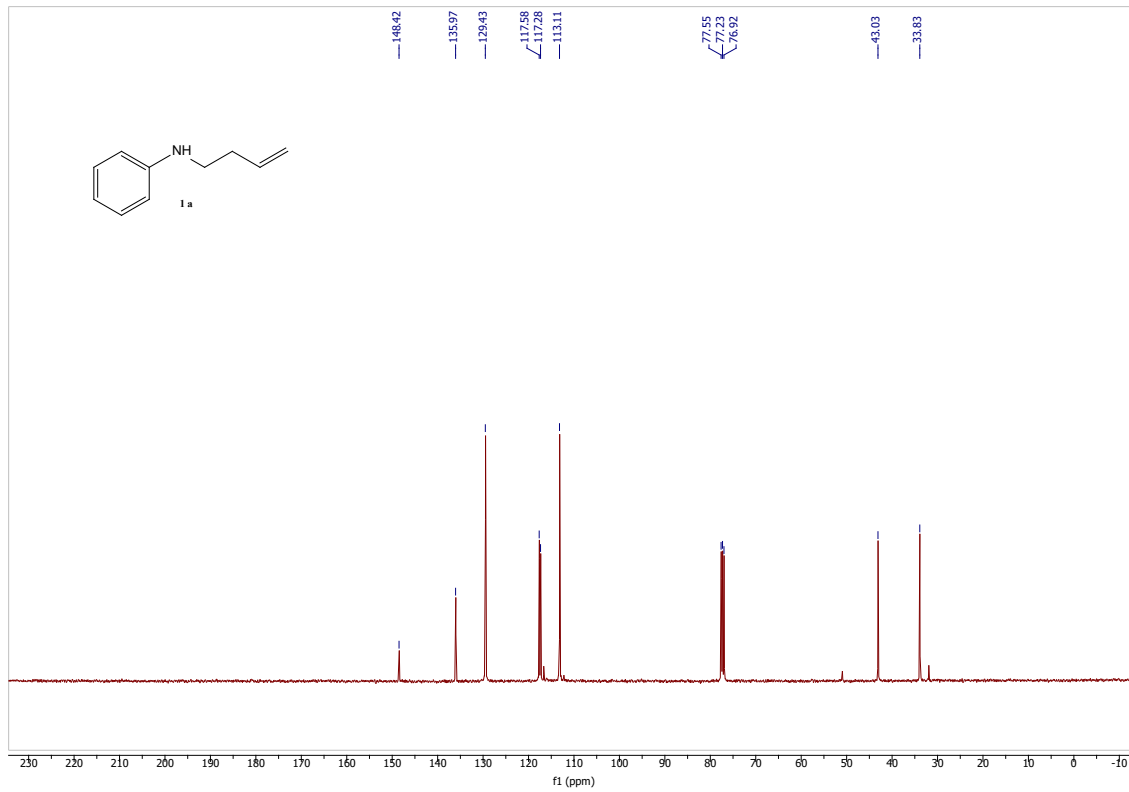
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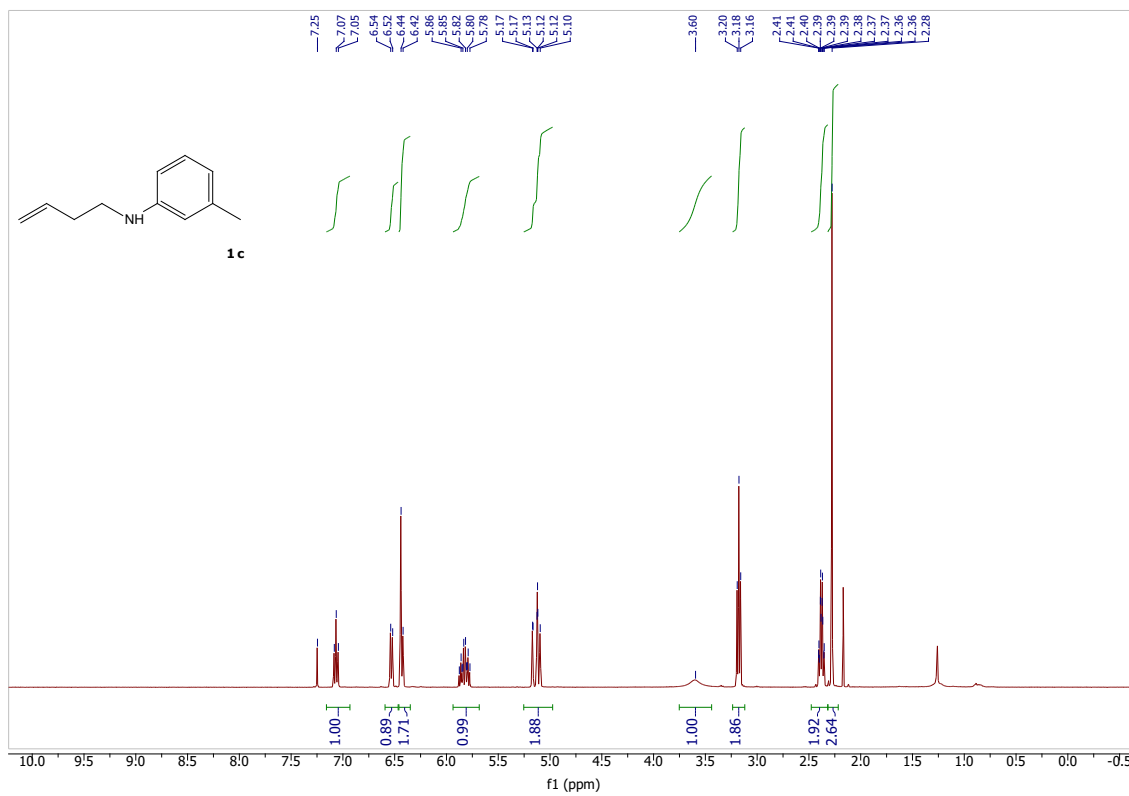
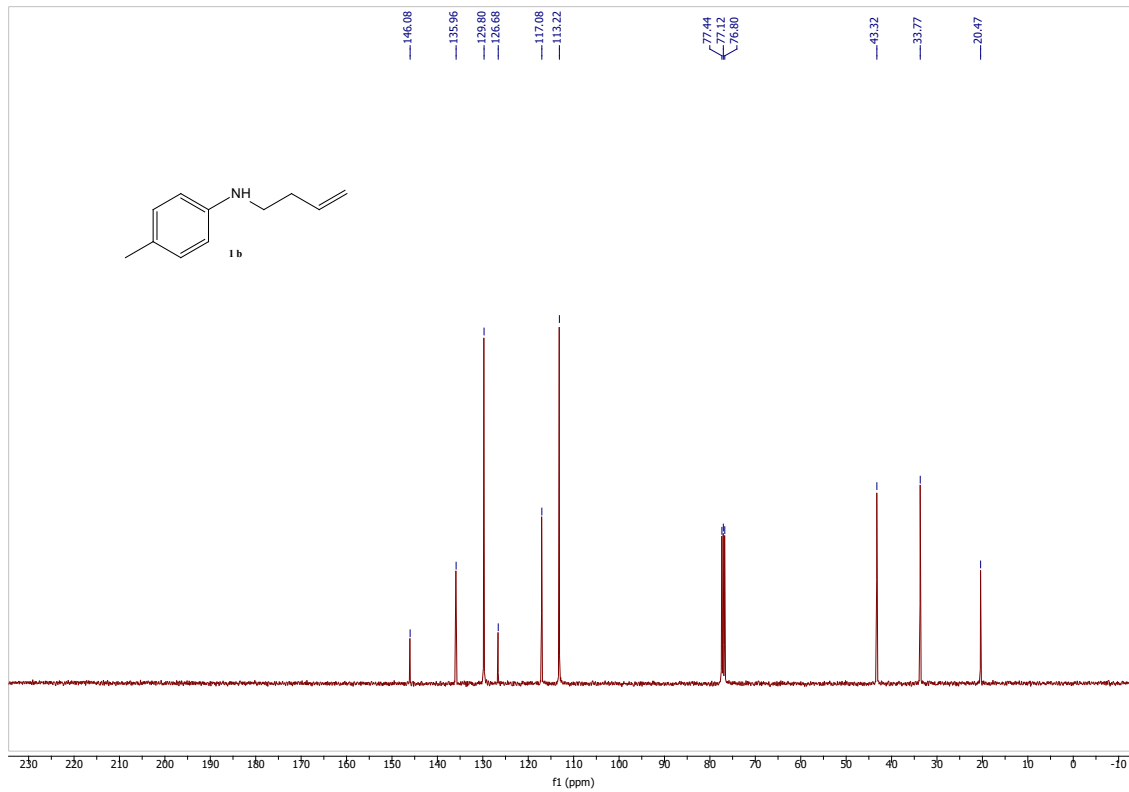
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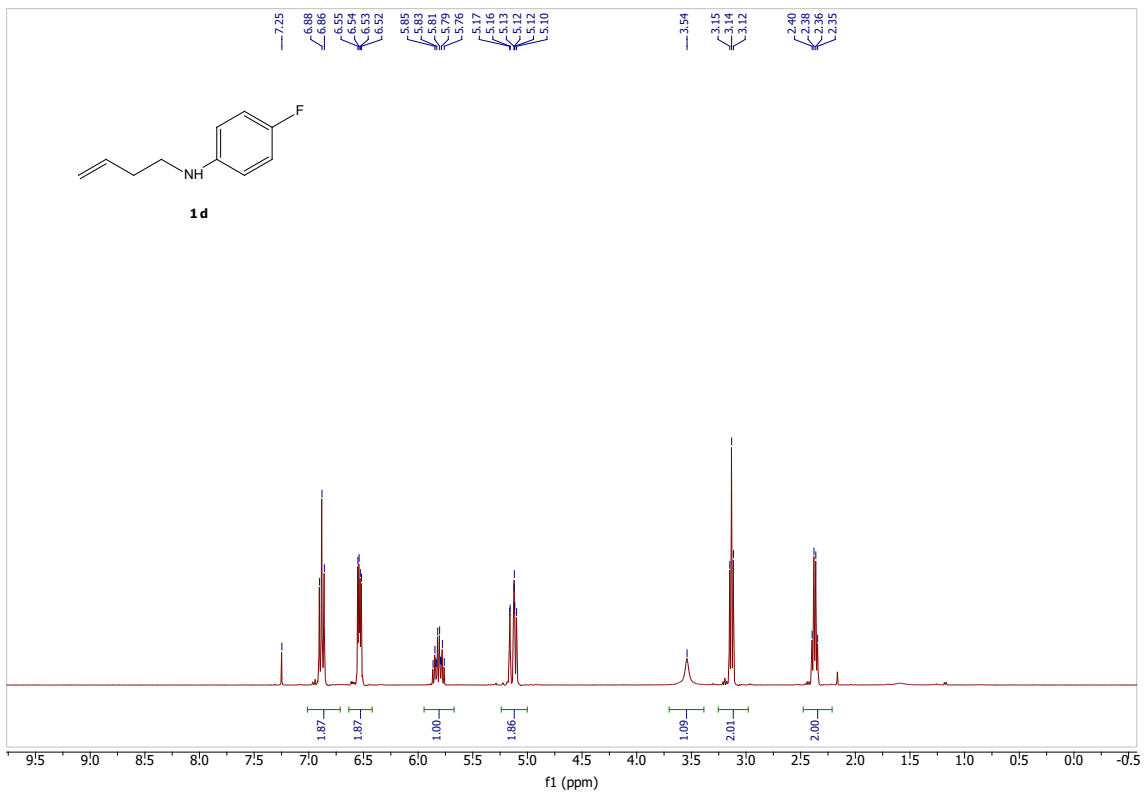
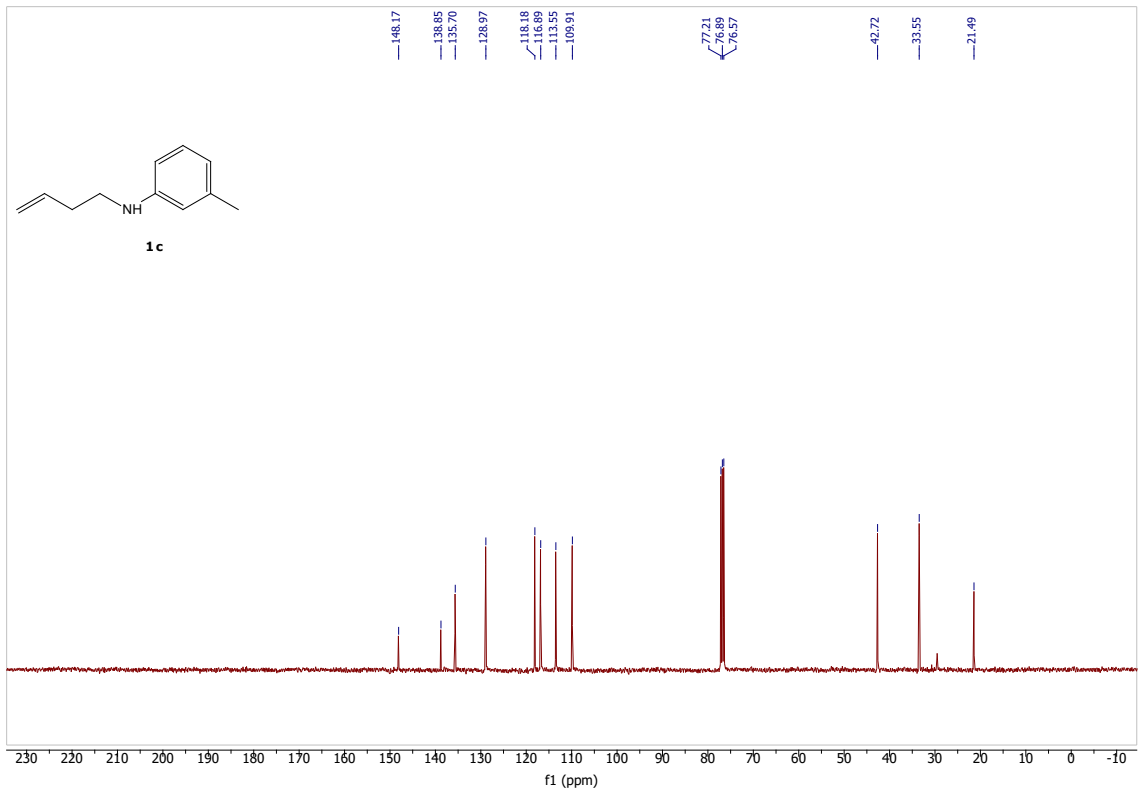
1. Copies of NMR spectra for compounds 1, 2, 3 and 4

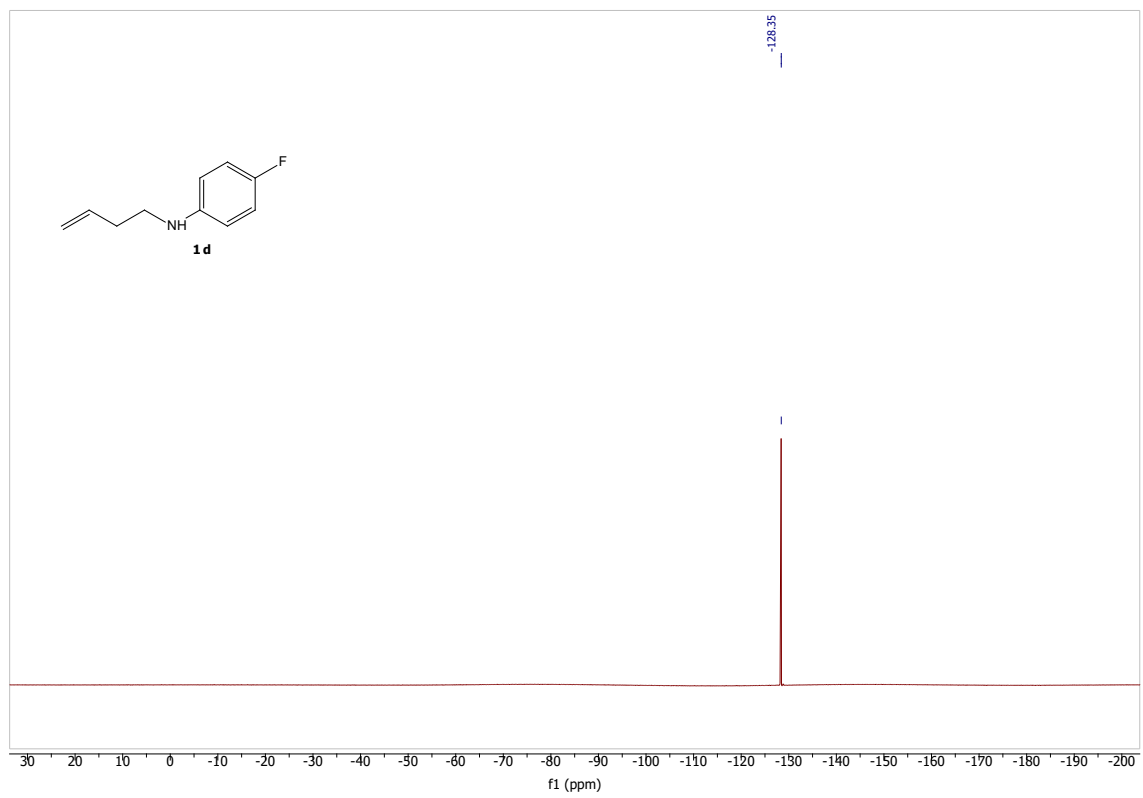
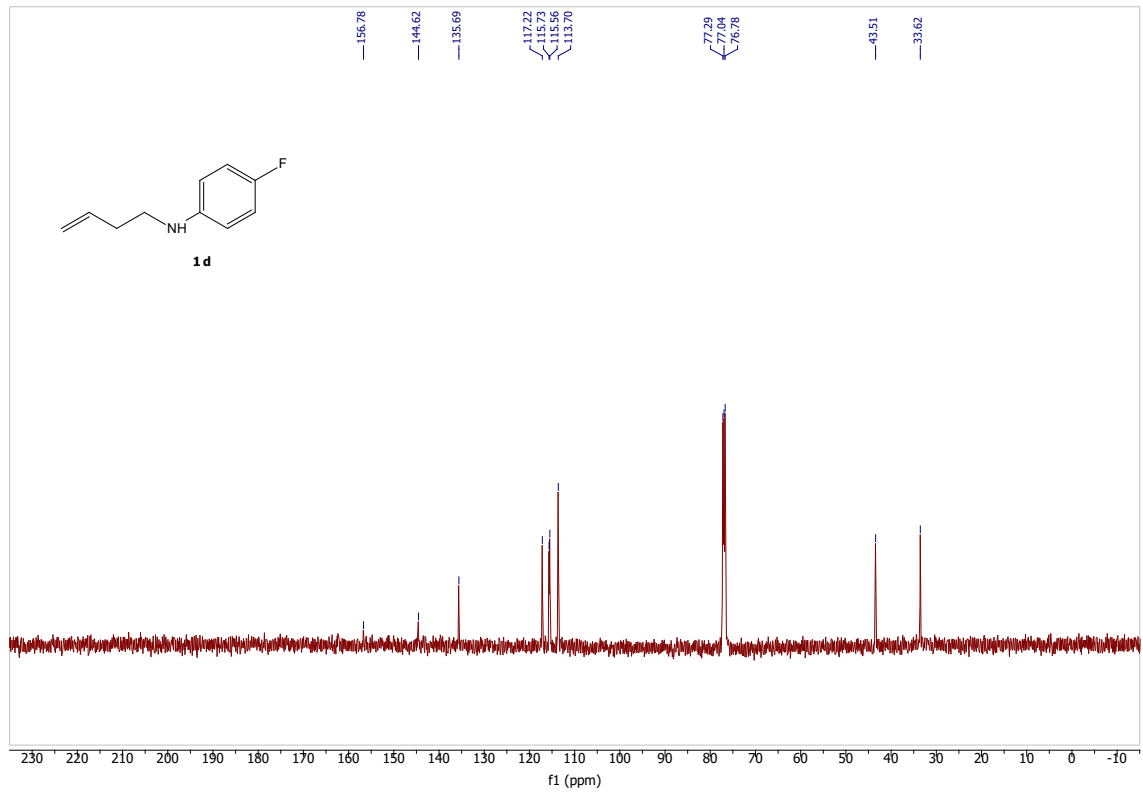
Some of the starting materials and products; **1a** and **1e**,¹ **1b**, **1c**, **1d** and **1f**,² **1e**,² **1k**, **1aa**, and **1ag**,³ **1ab**,⁴ **1ae**,⁵ **1ah**,⁶ **3a**,⁷ **3e**,⁸ **3f**,⁹ **2a**,¹⁰ **2aa**,¹¹ **2ae**,¹² **2ag**,¹³ are commercially available or reported compounds, their spectroscopic data agree well with the reported literature. Others are commercially available but do not have available spectral data. We report the HRMS data in the manuscript.

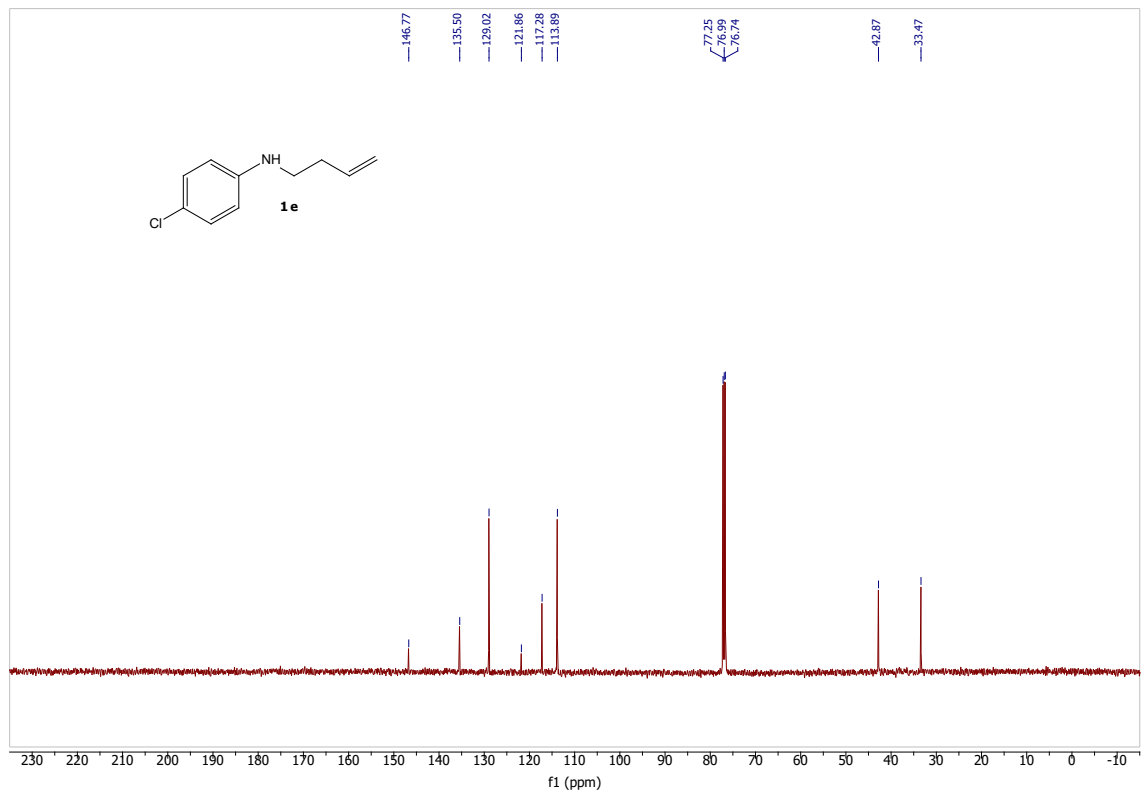
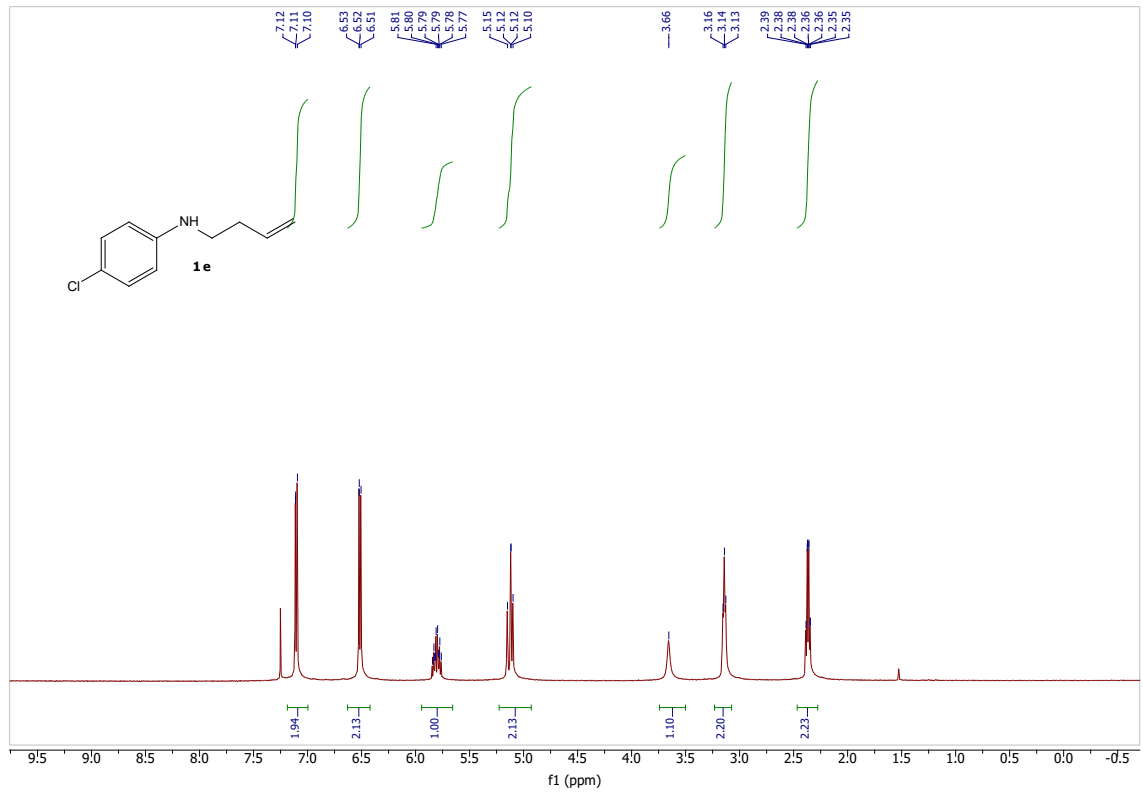


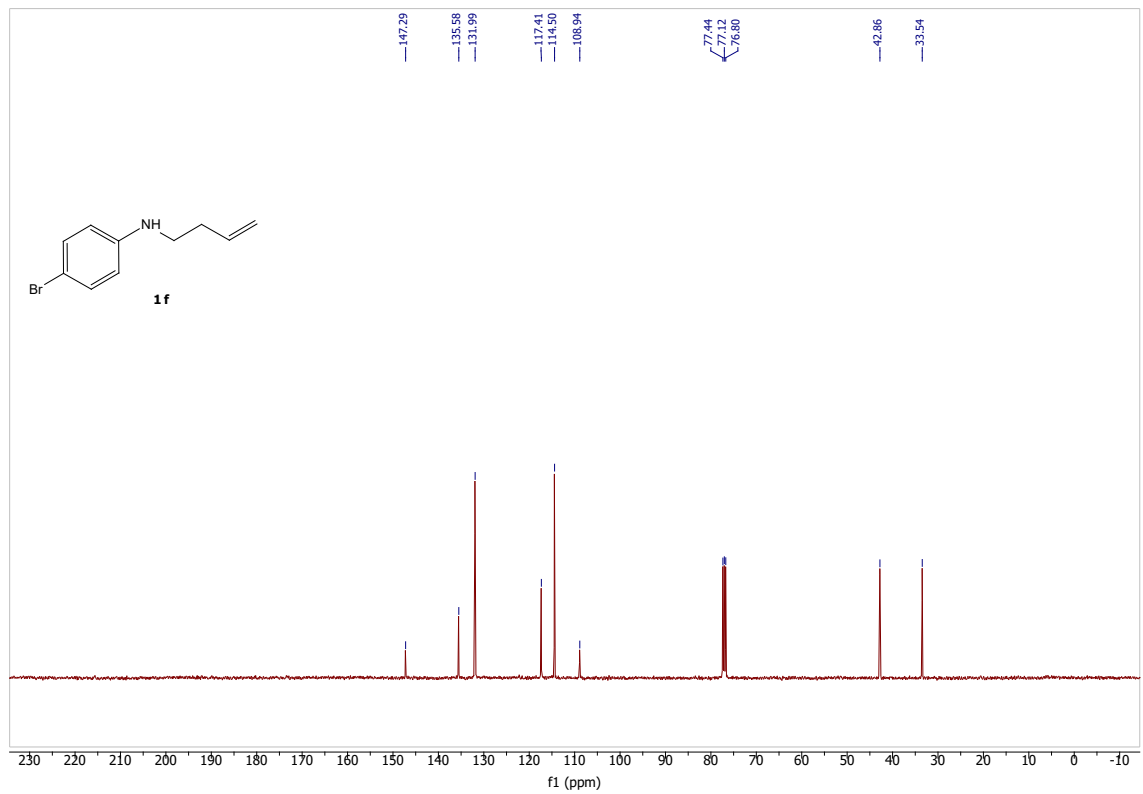
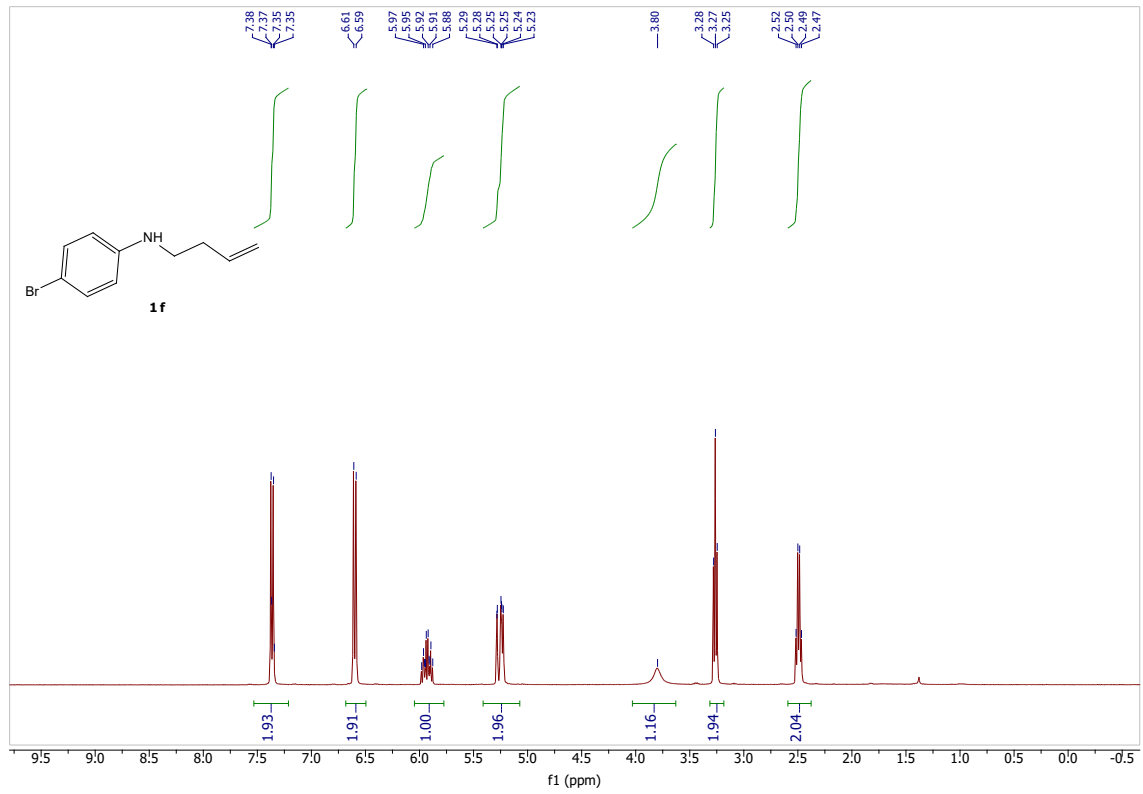


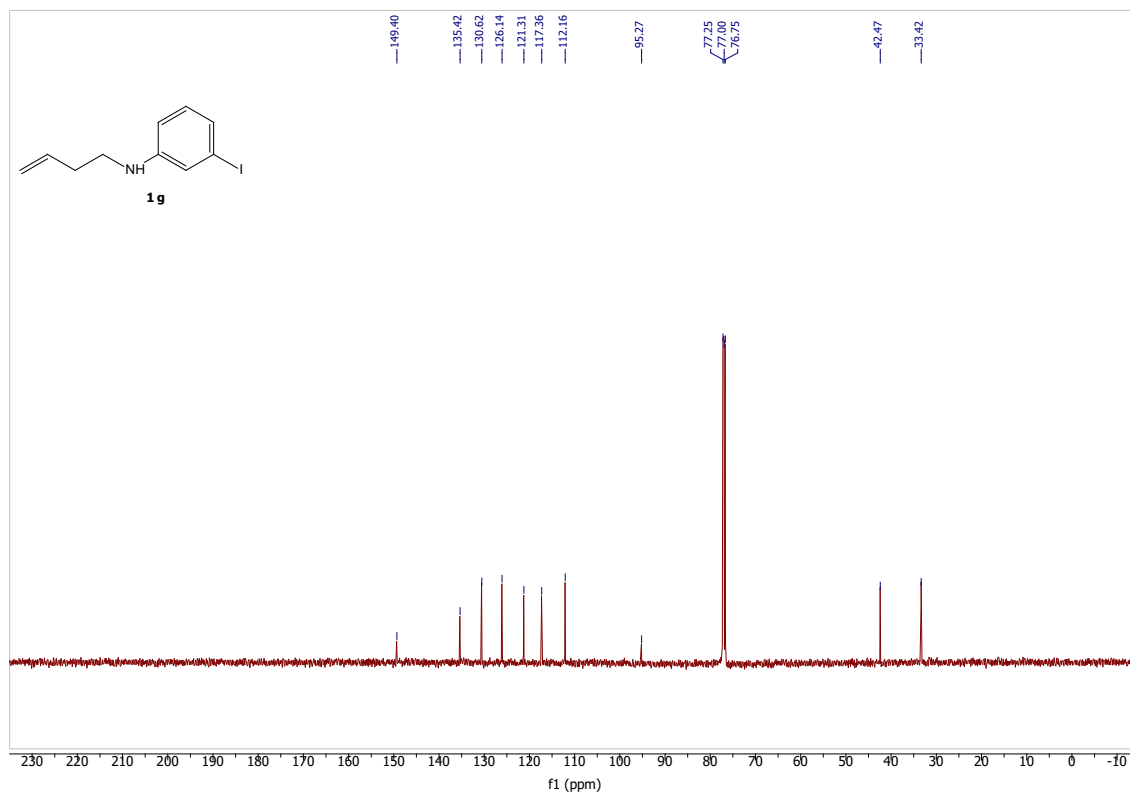
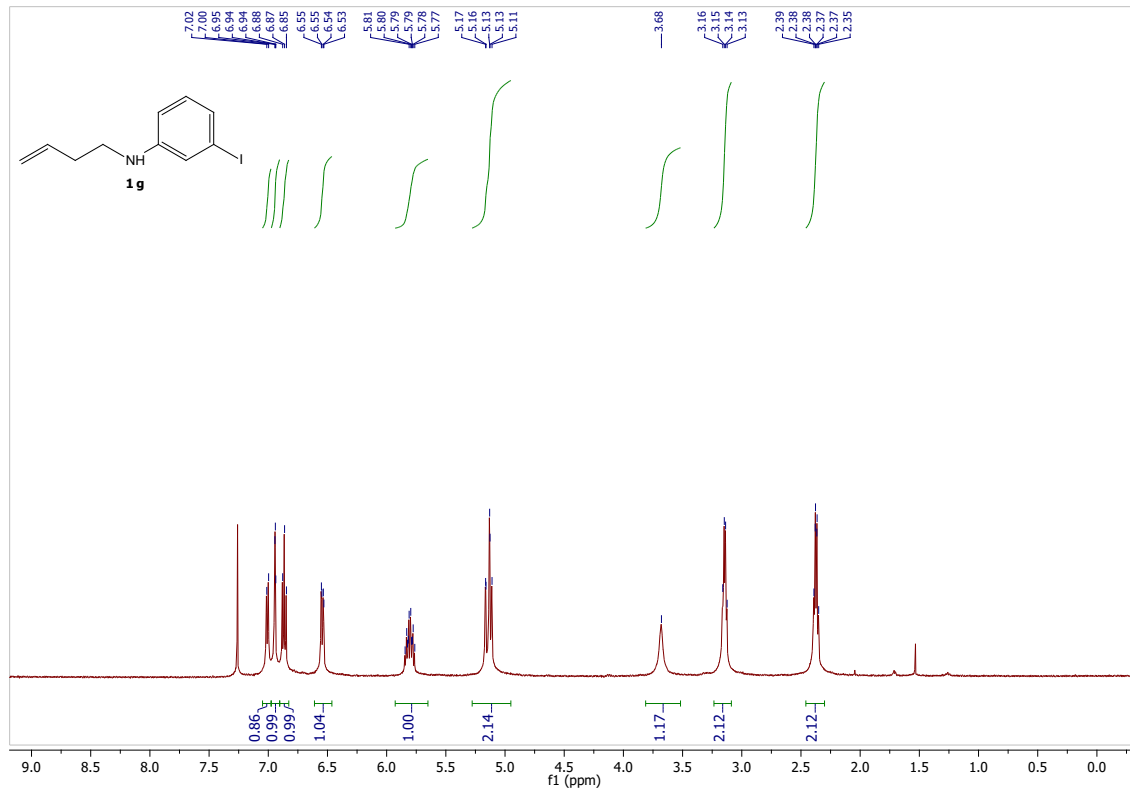


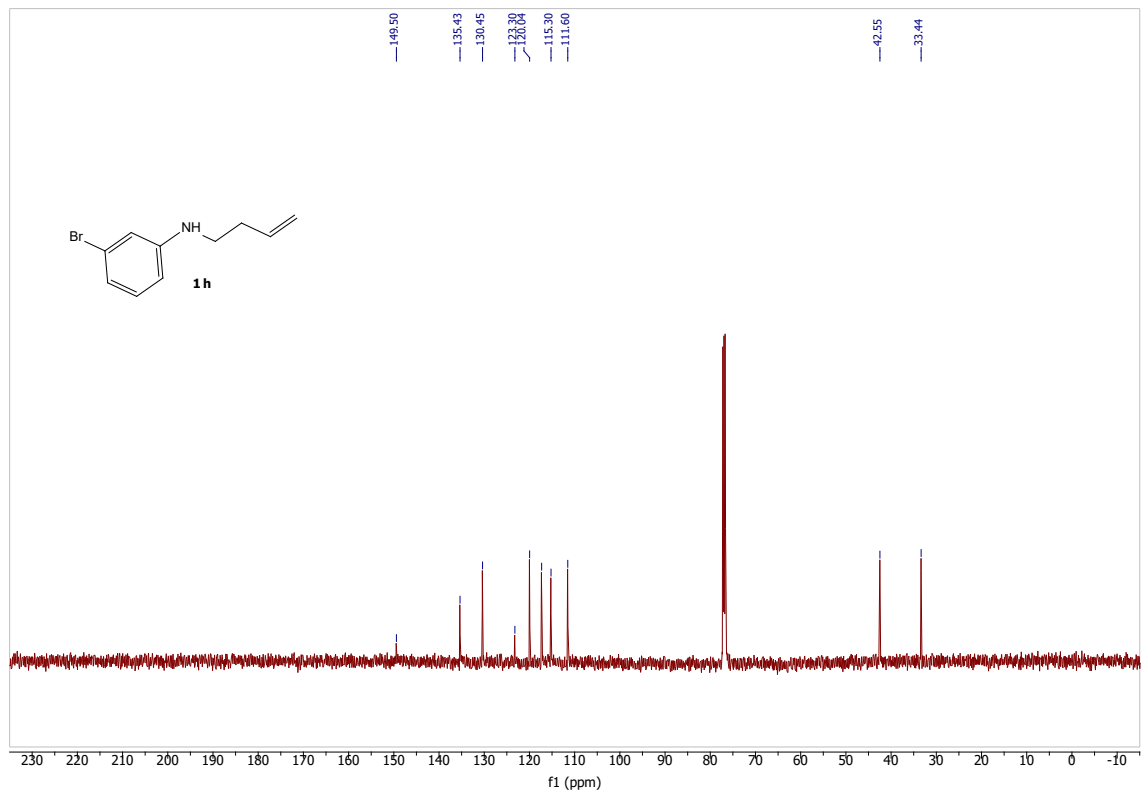
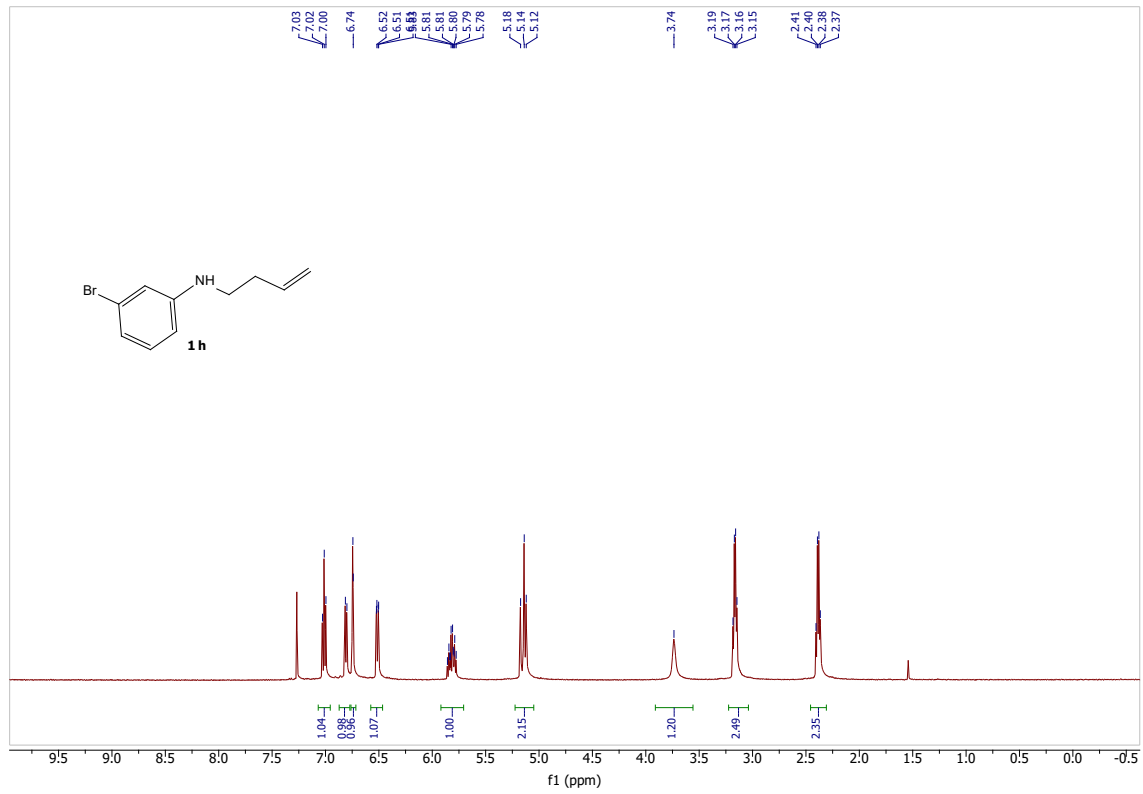


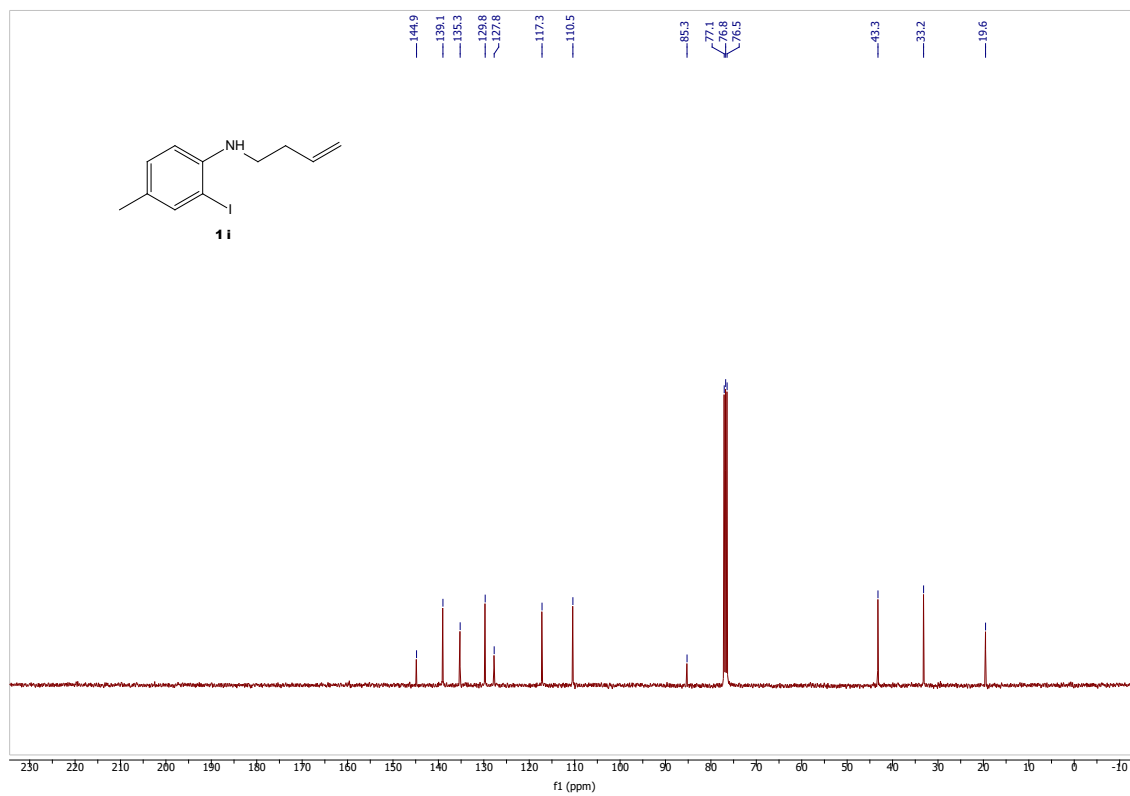
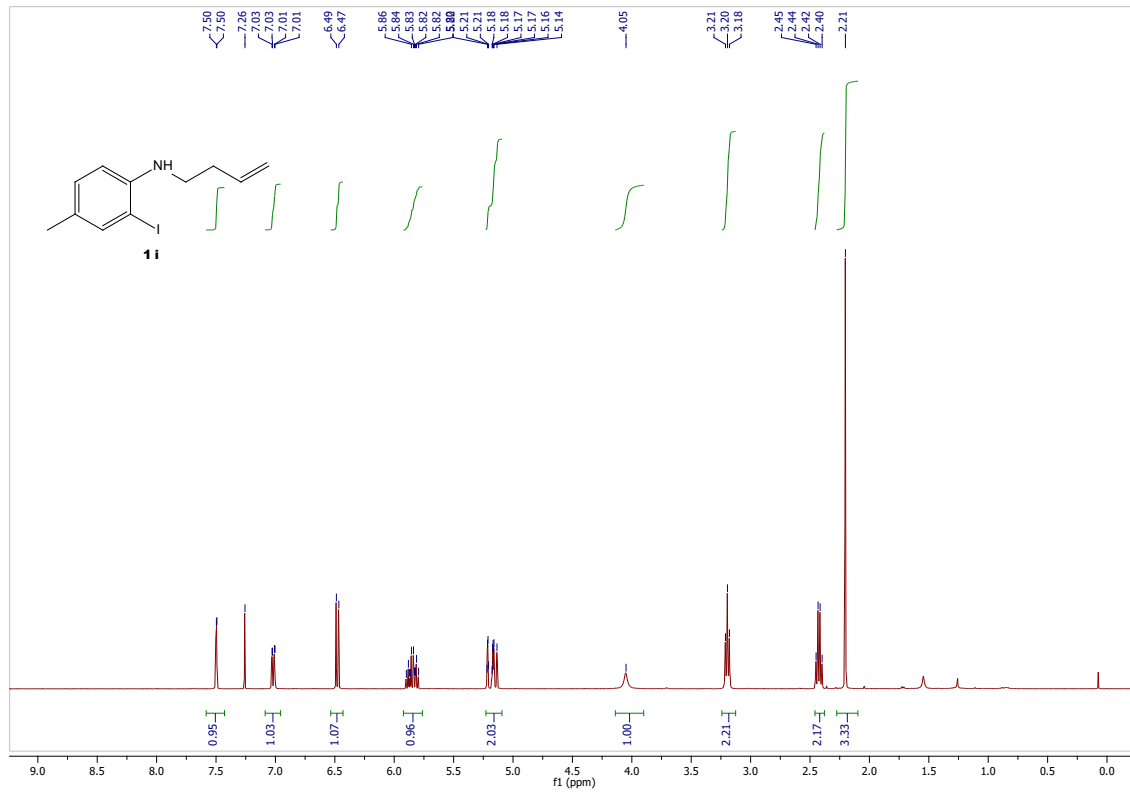


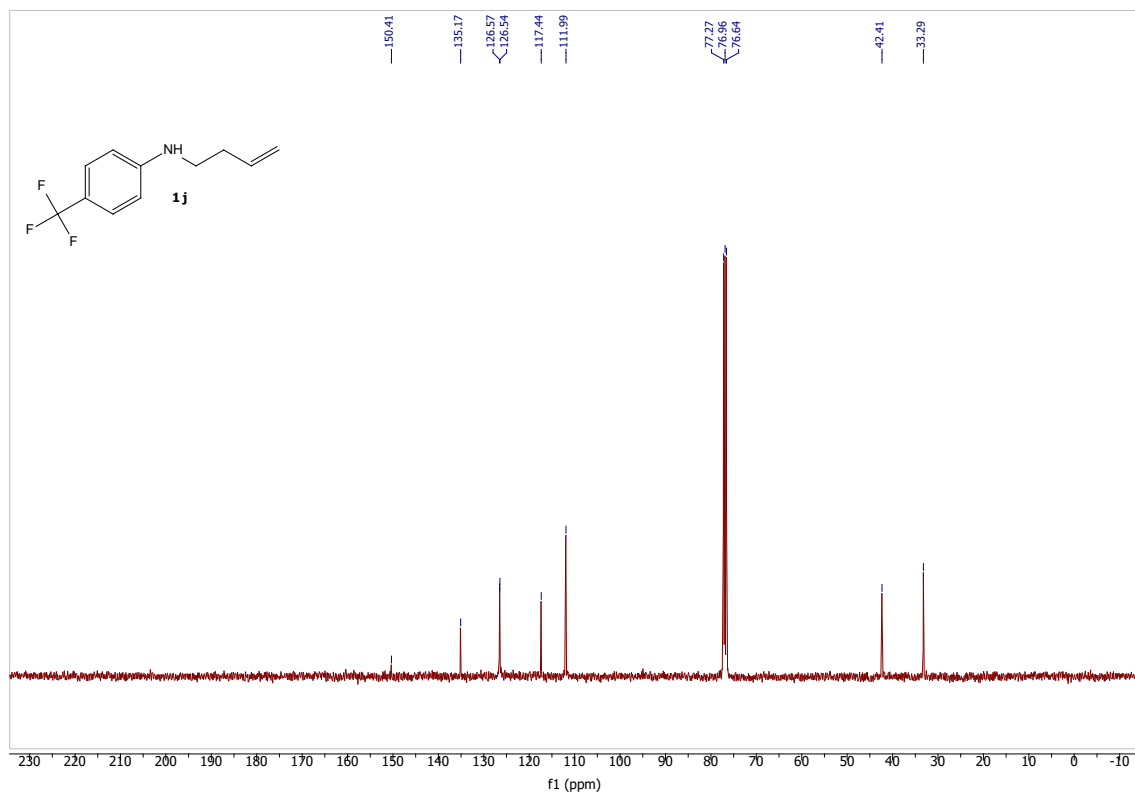
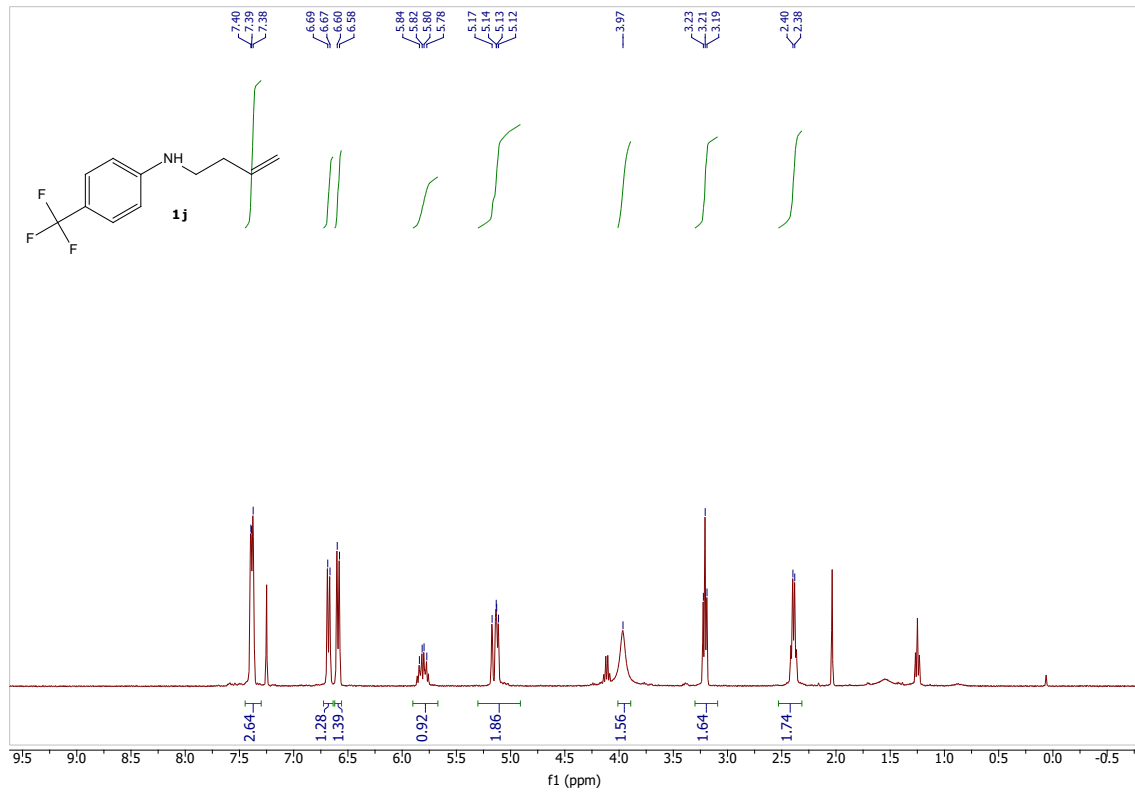


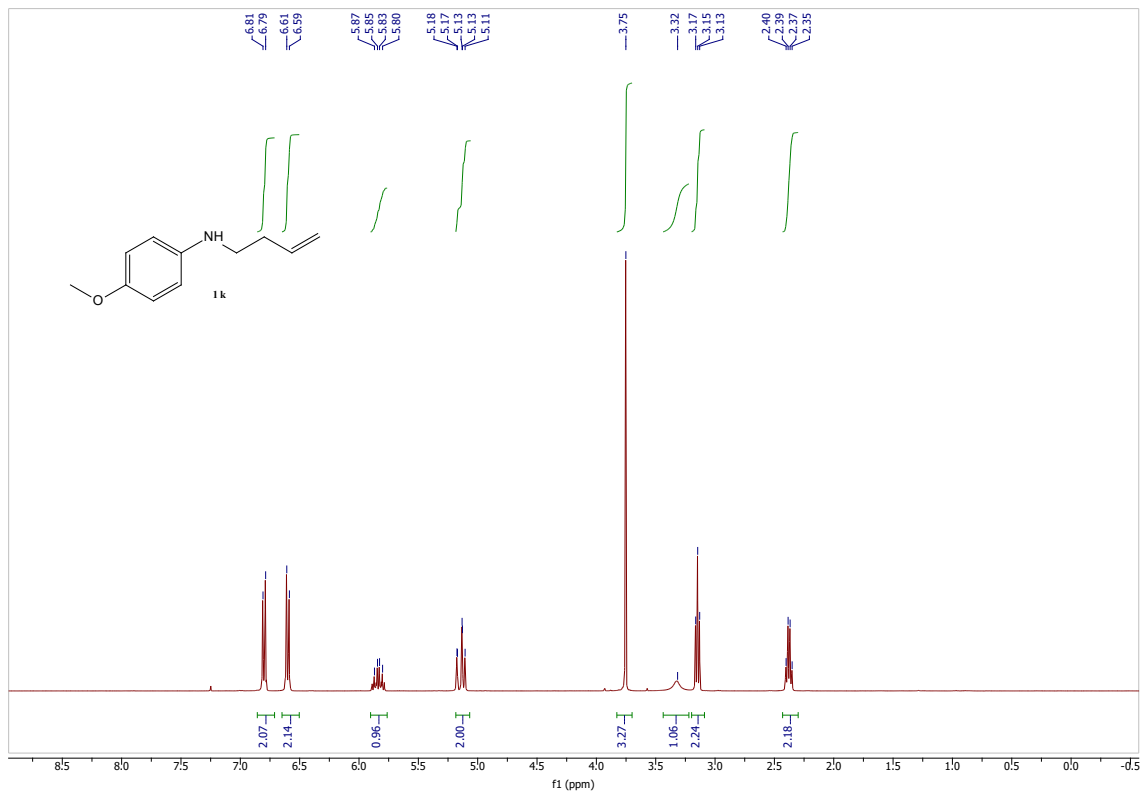
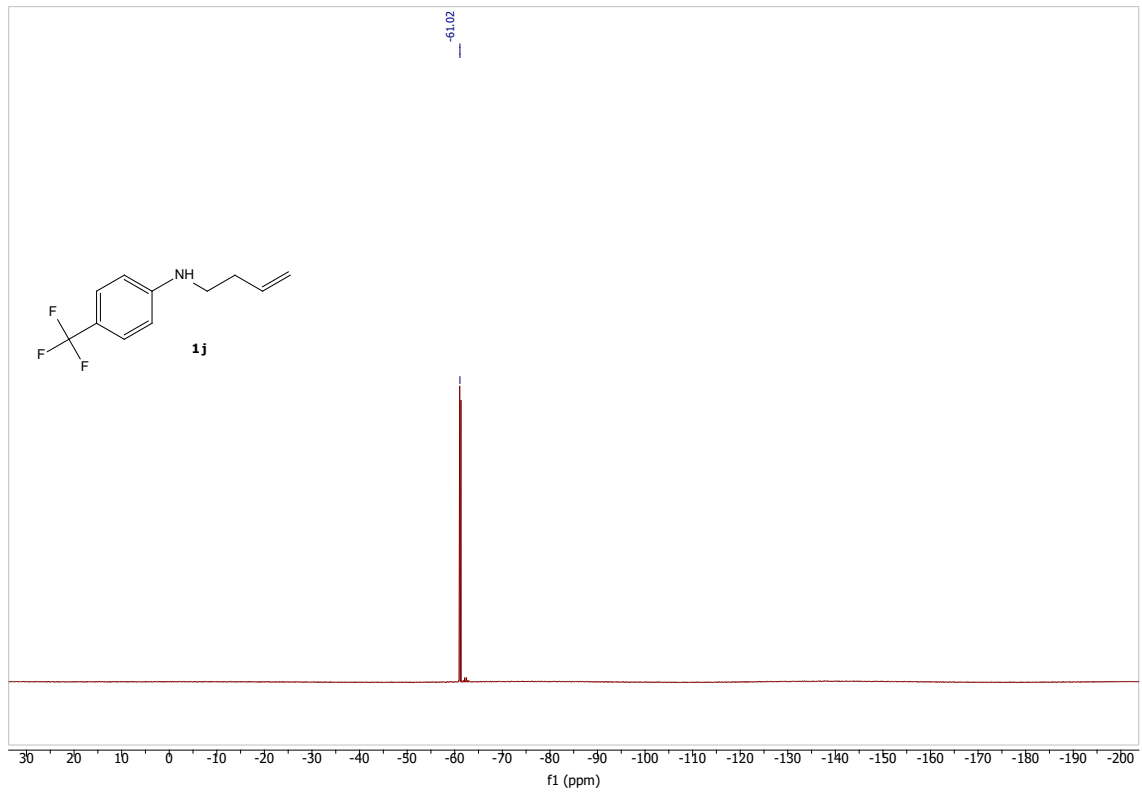


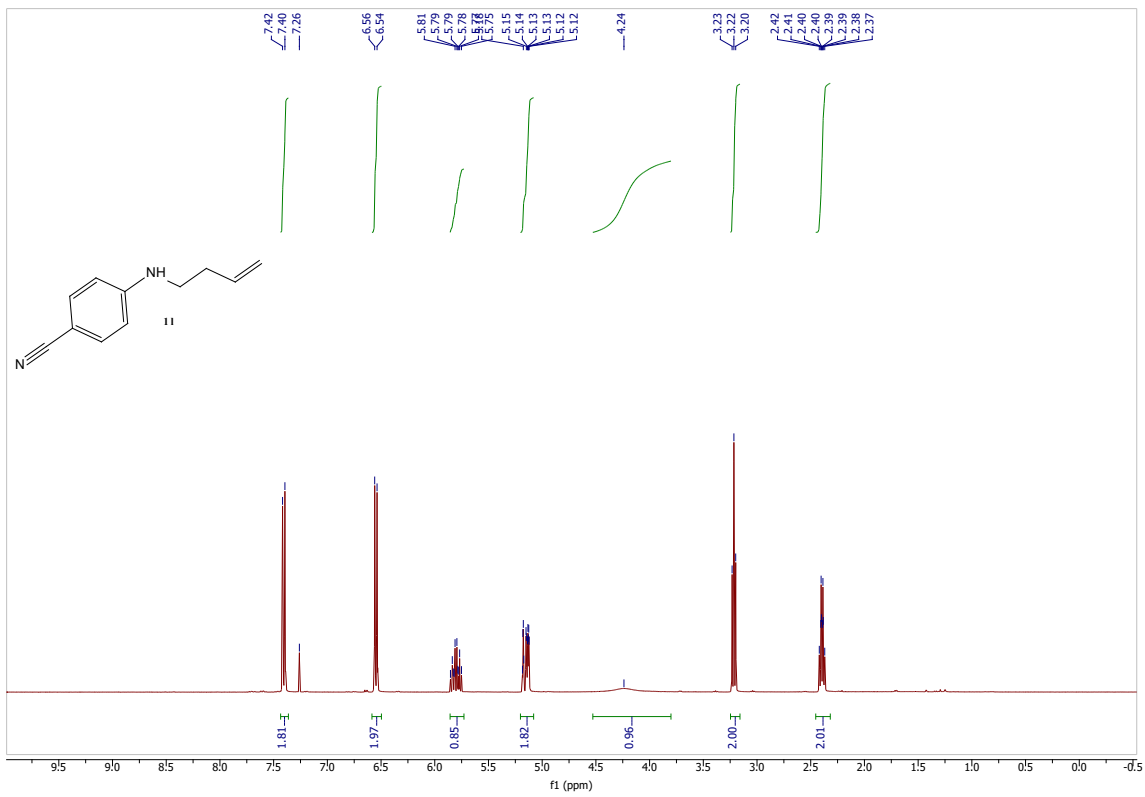
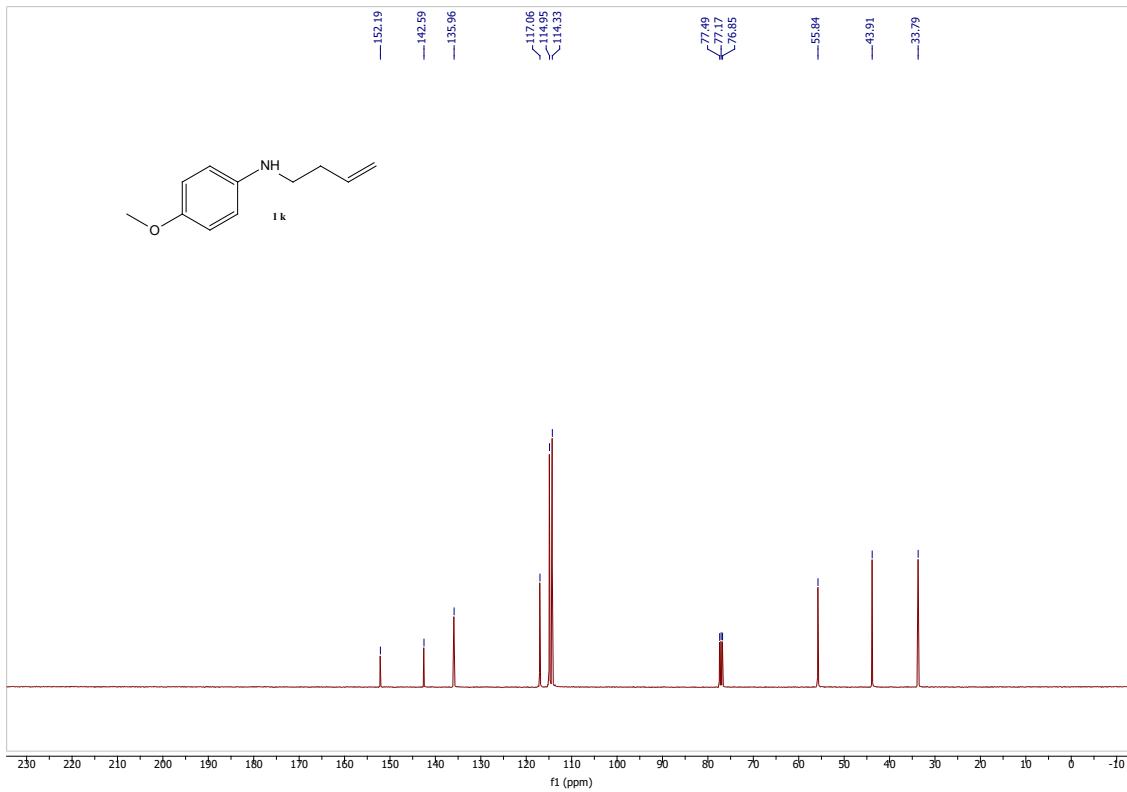


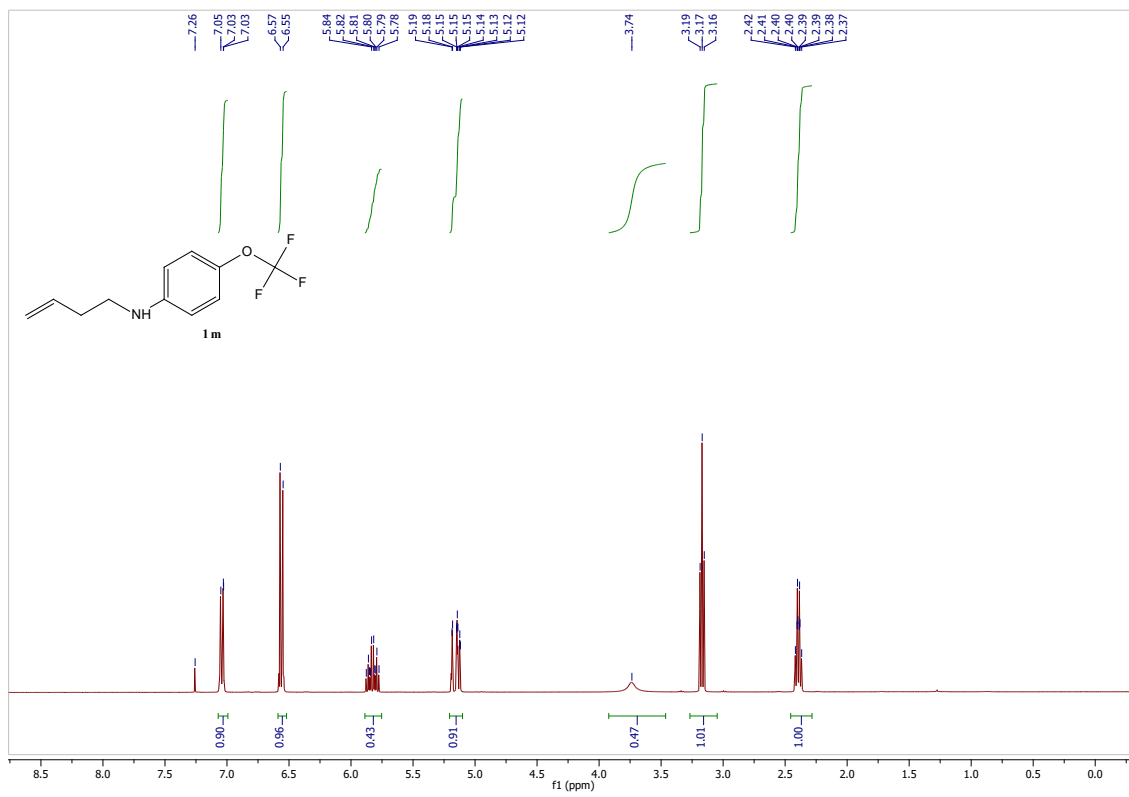
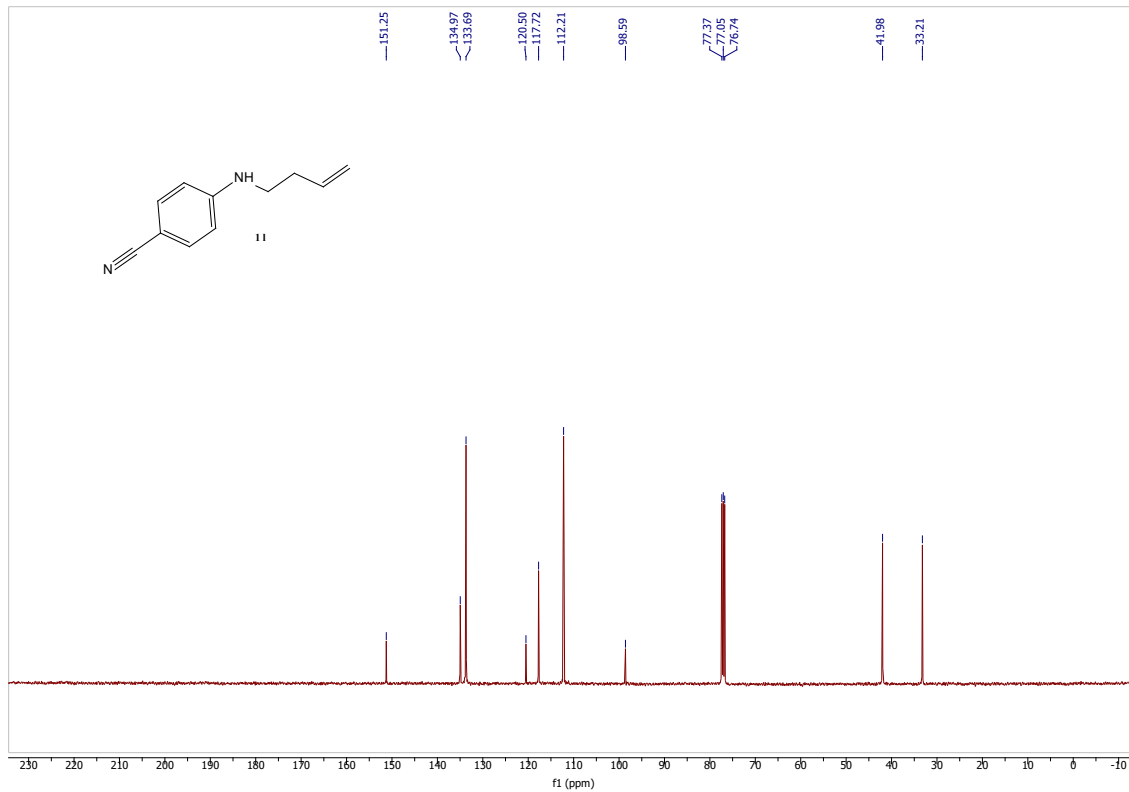


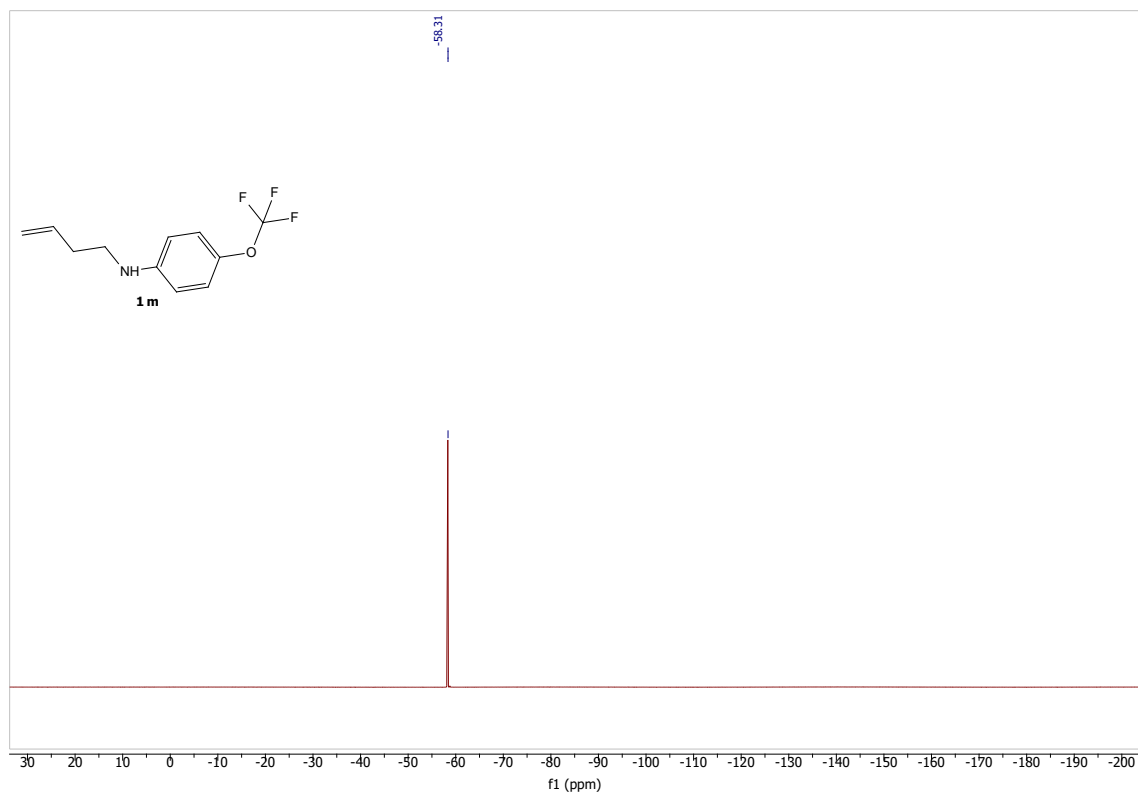
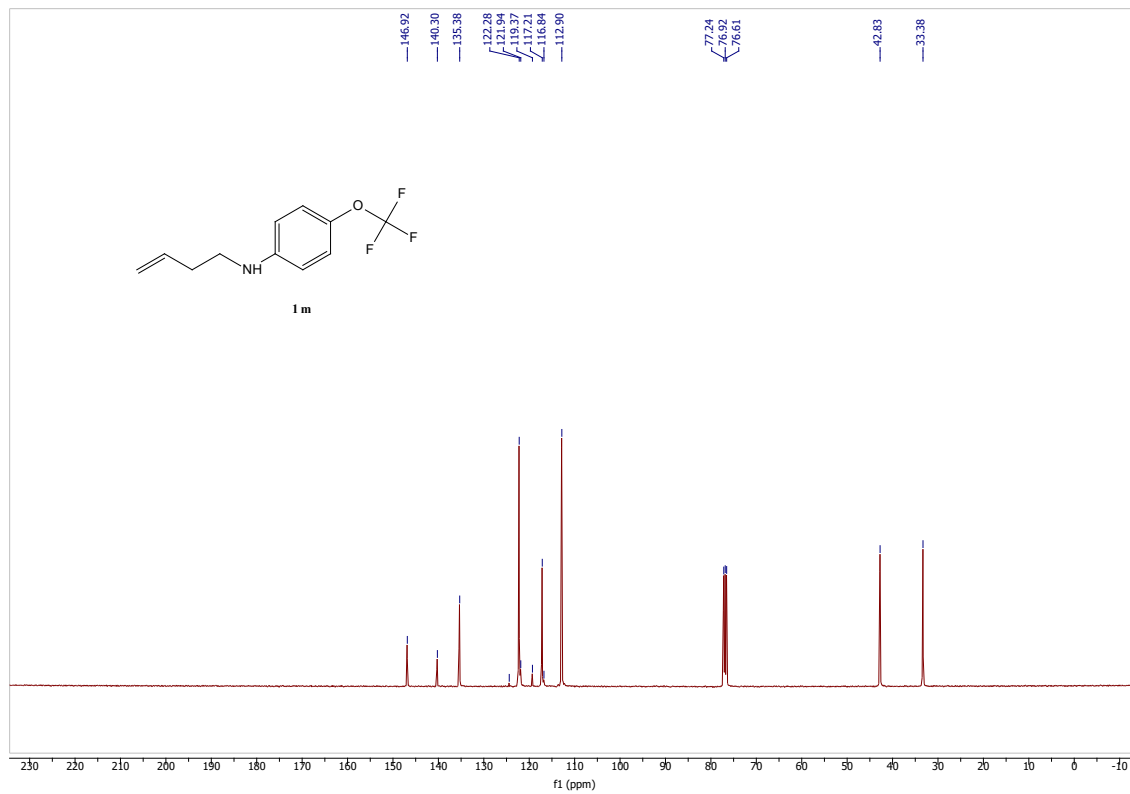


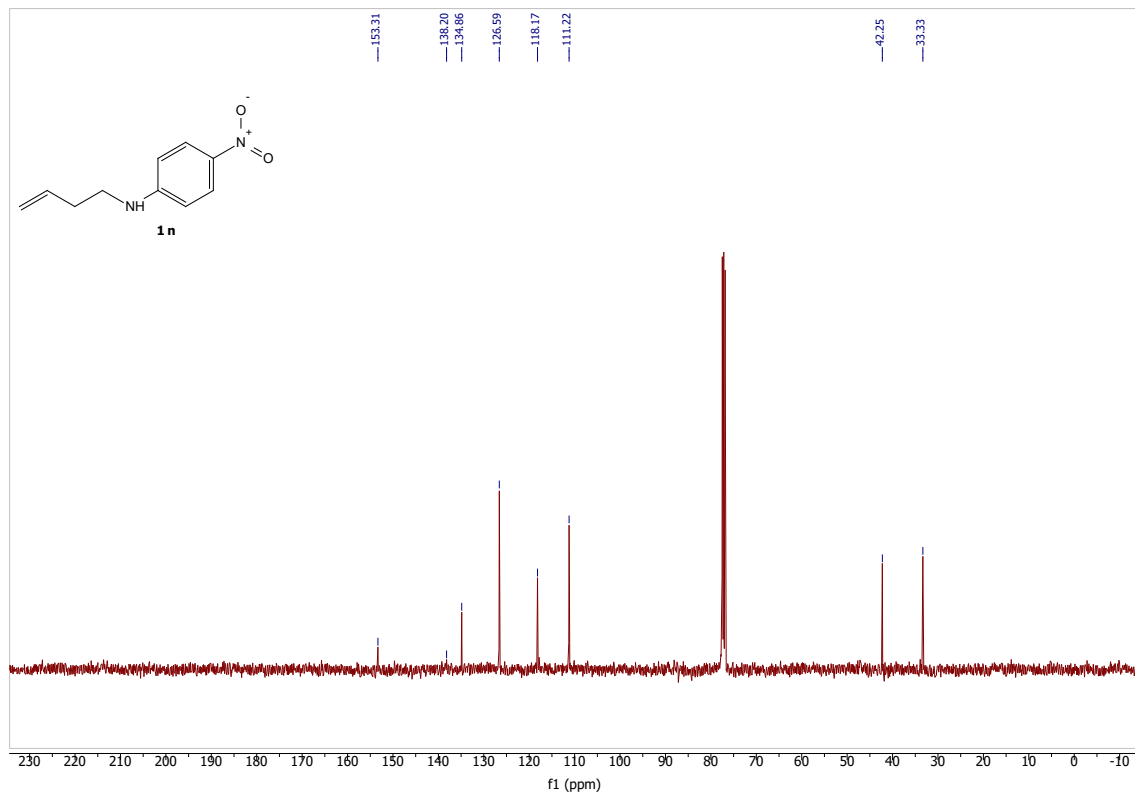
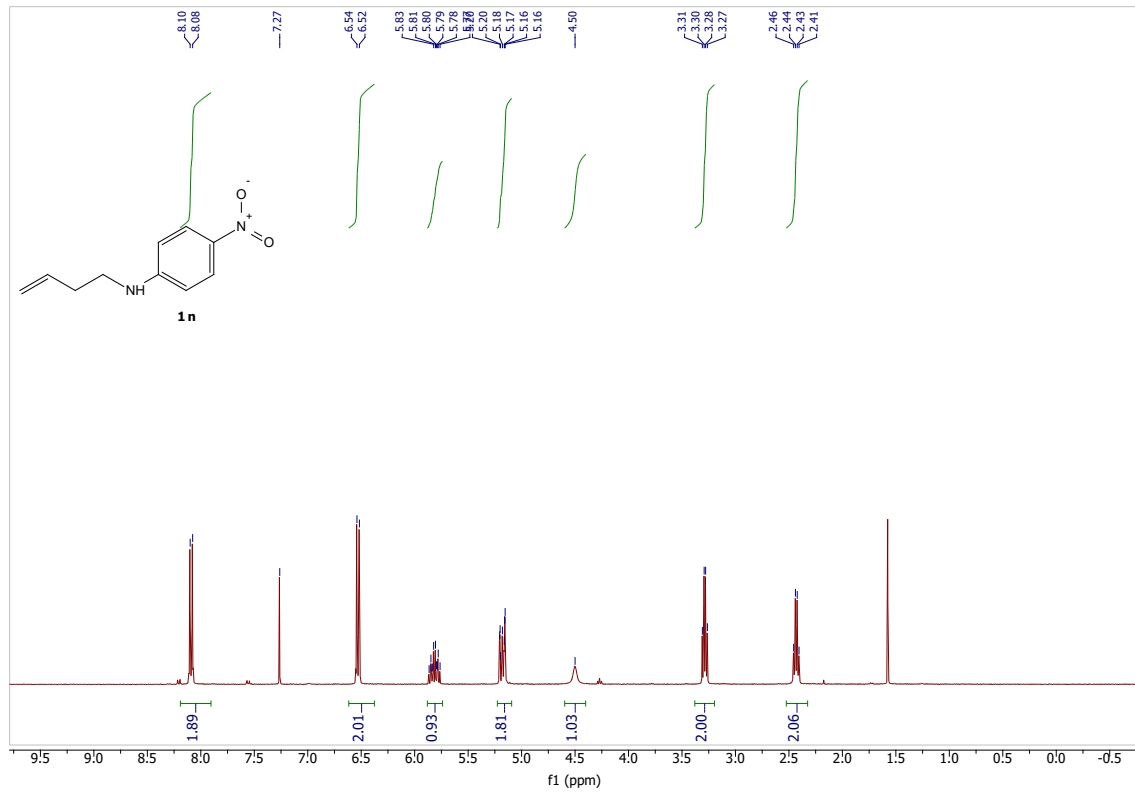


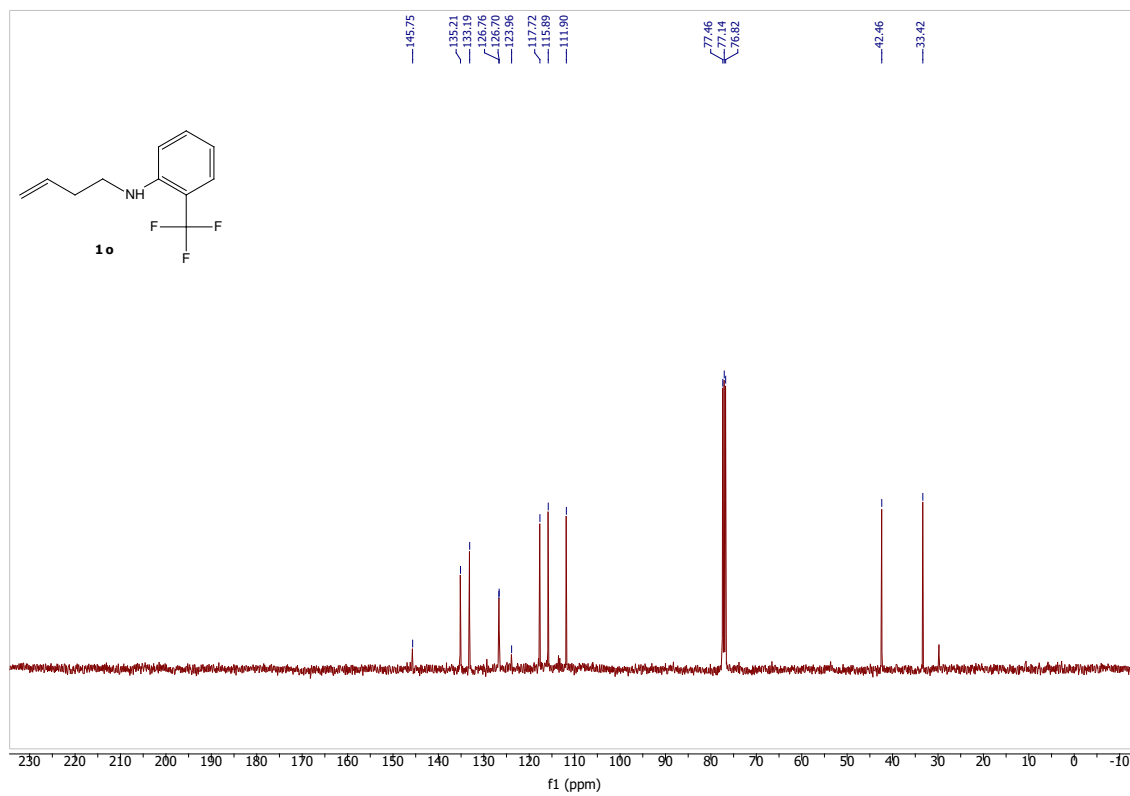
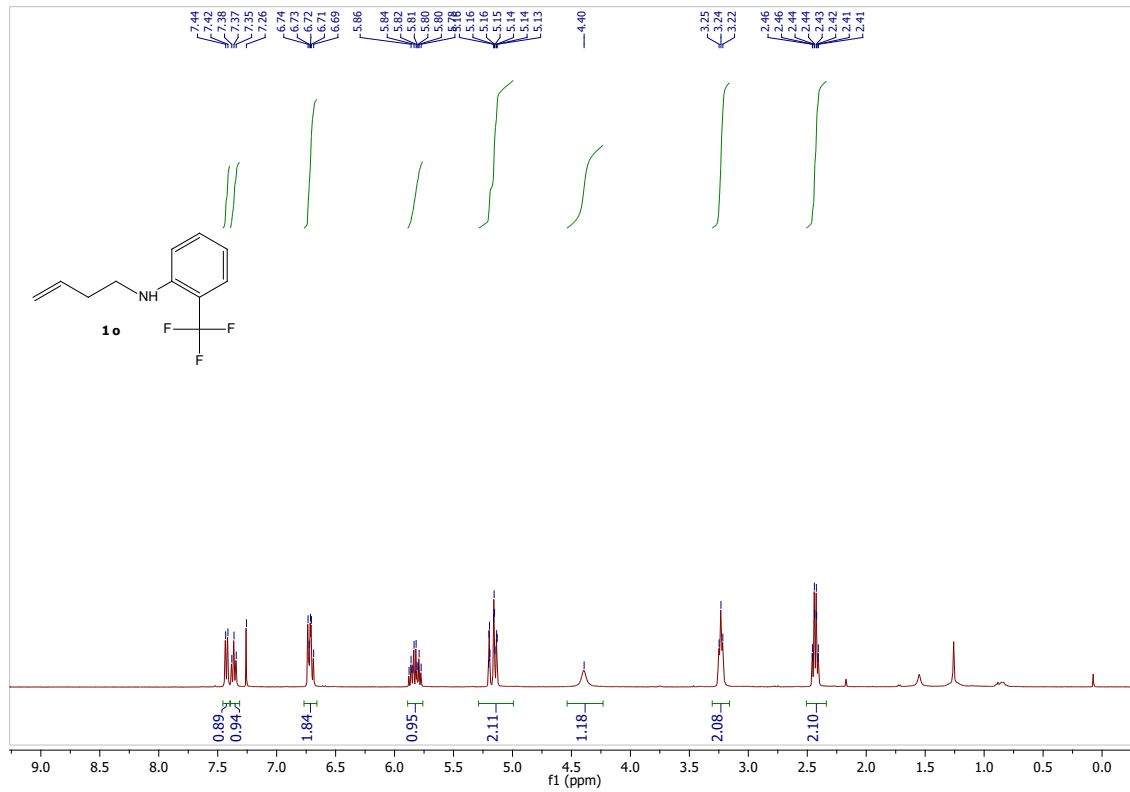


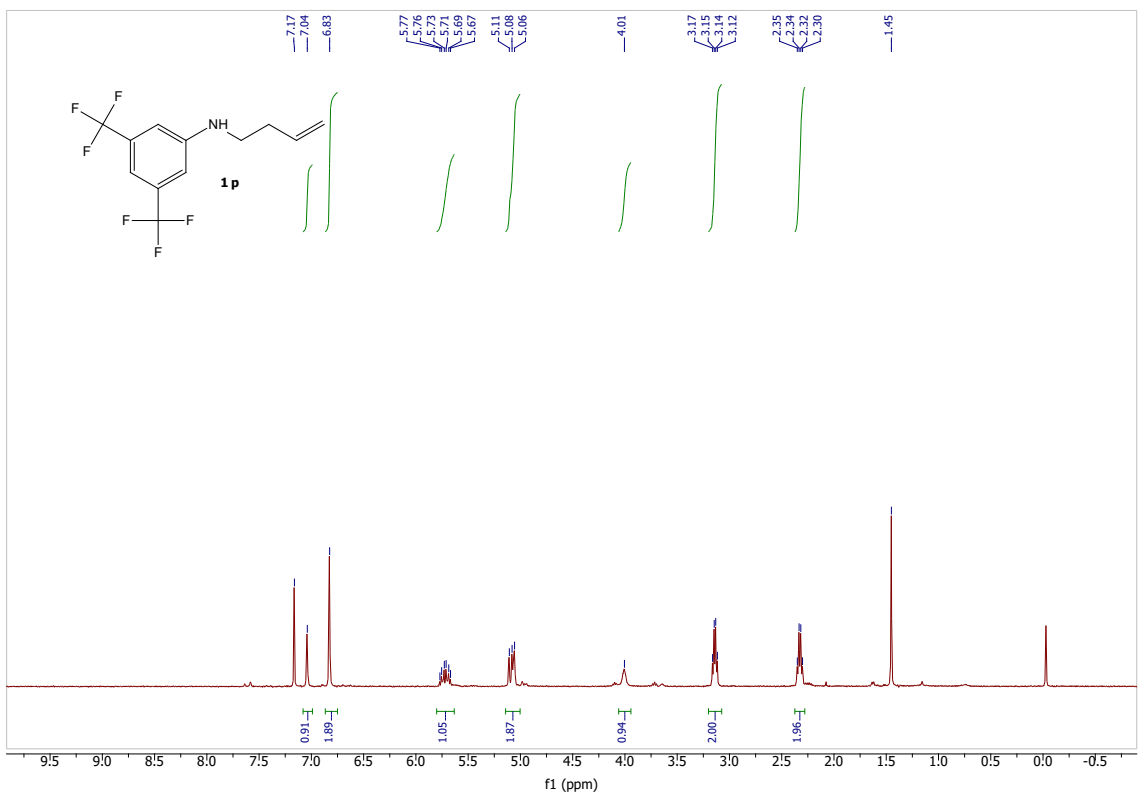
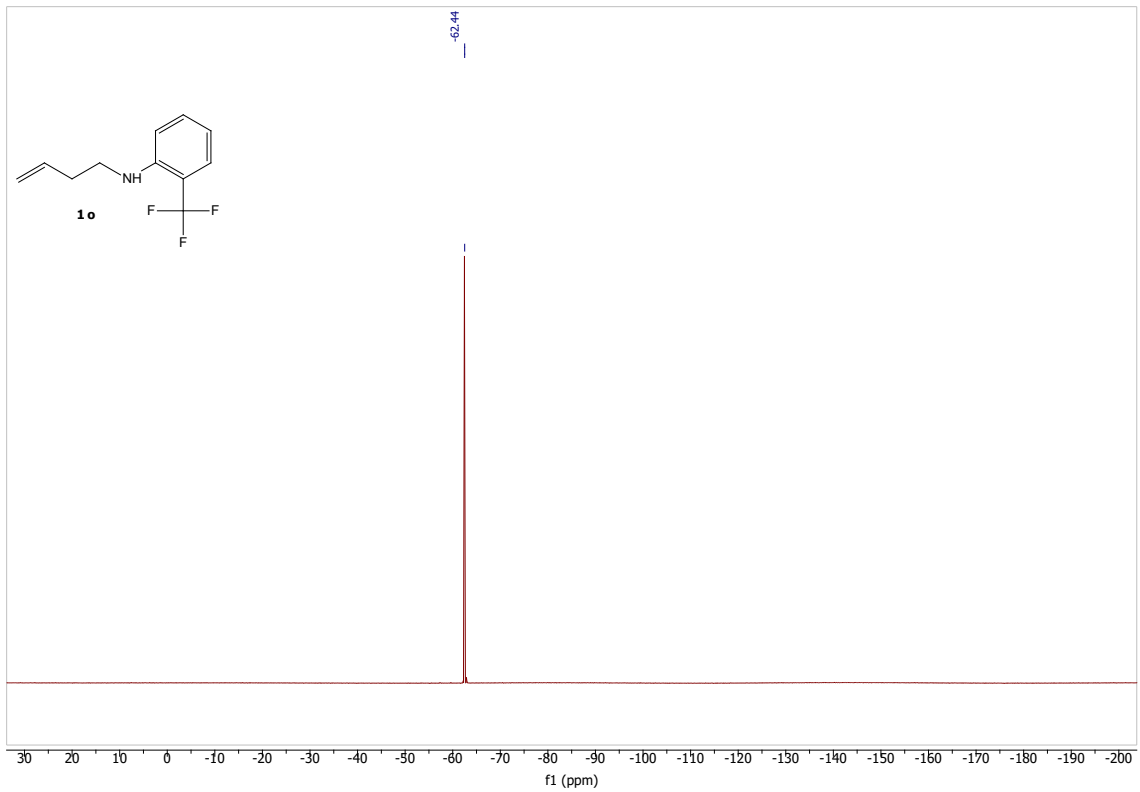


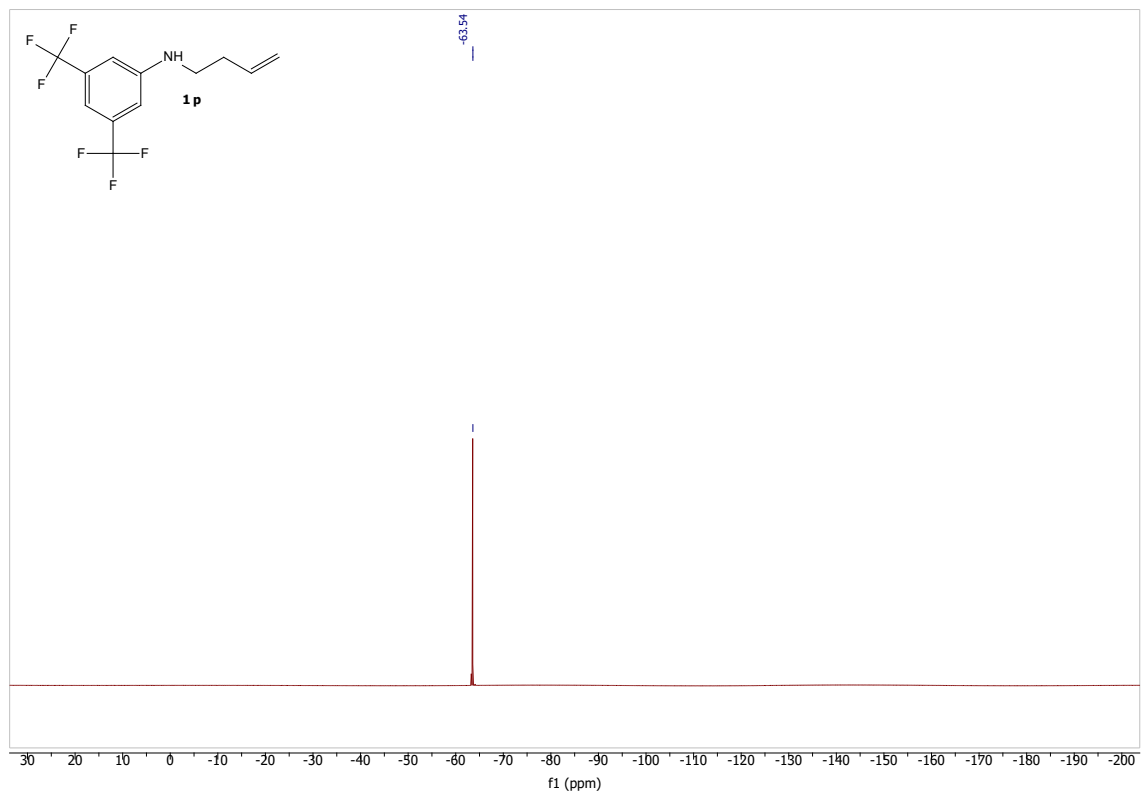
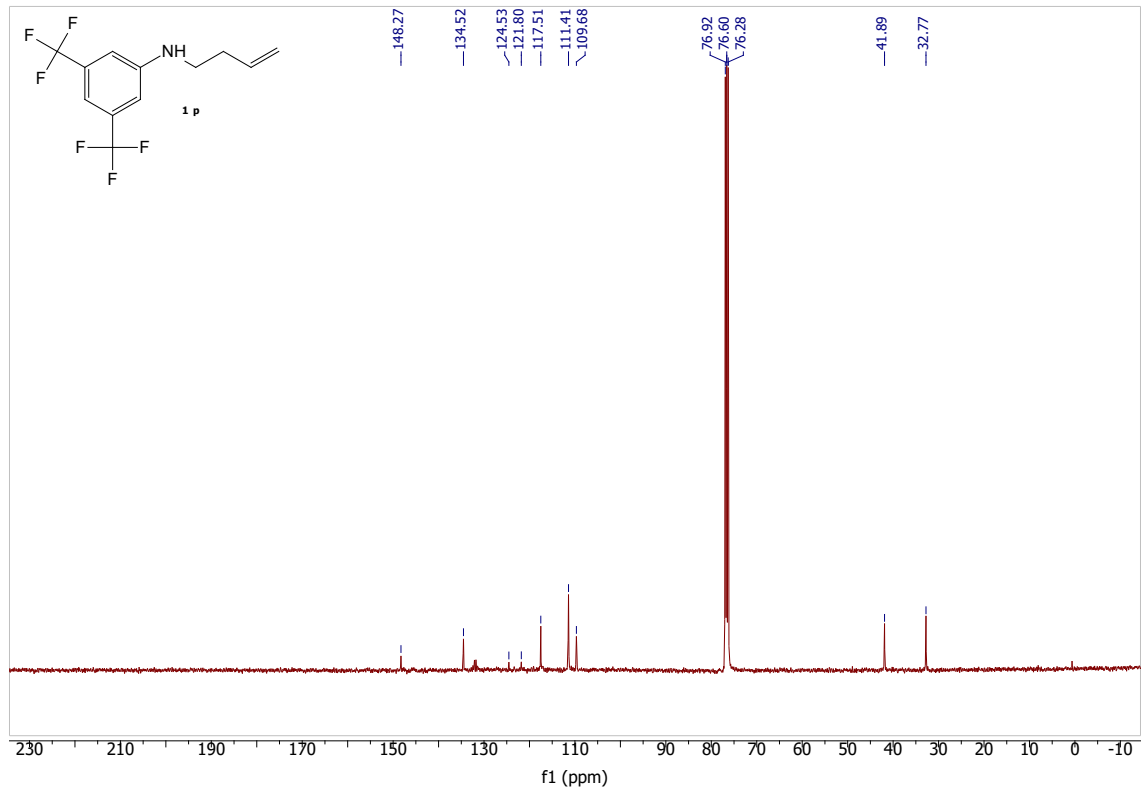


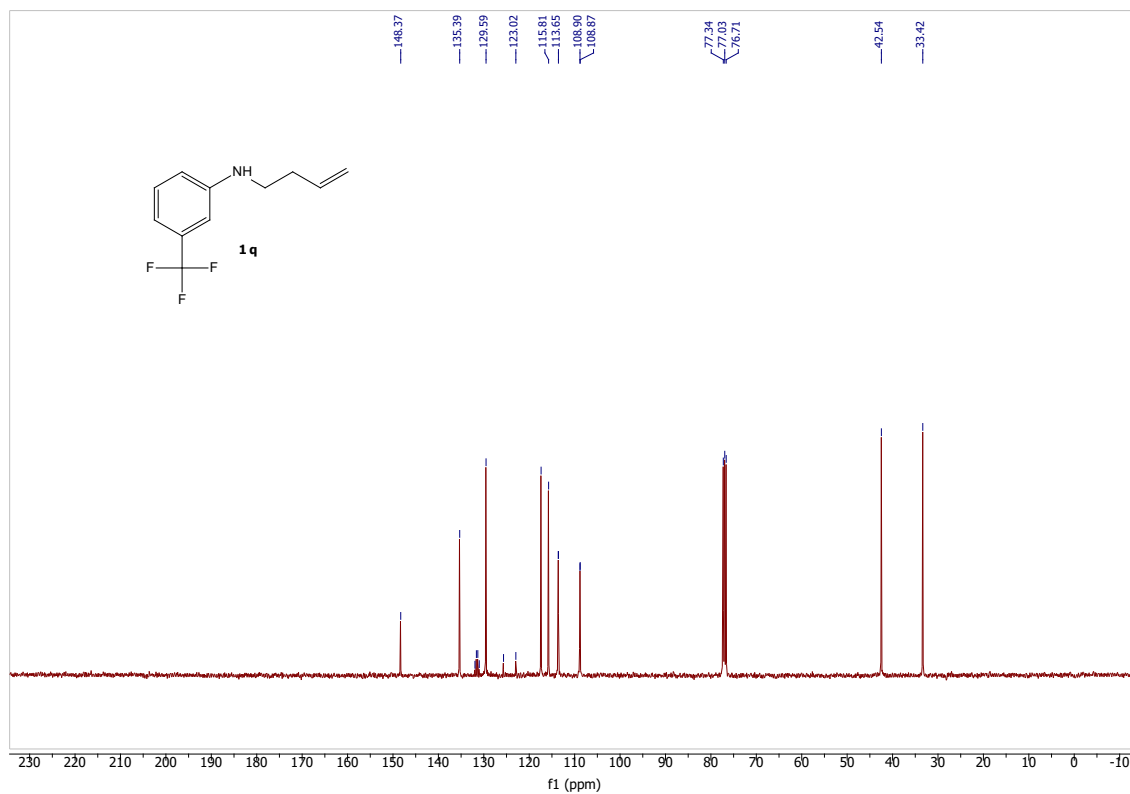
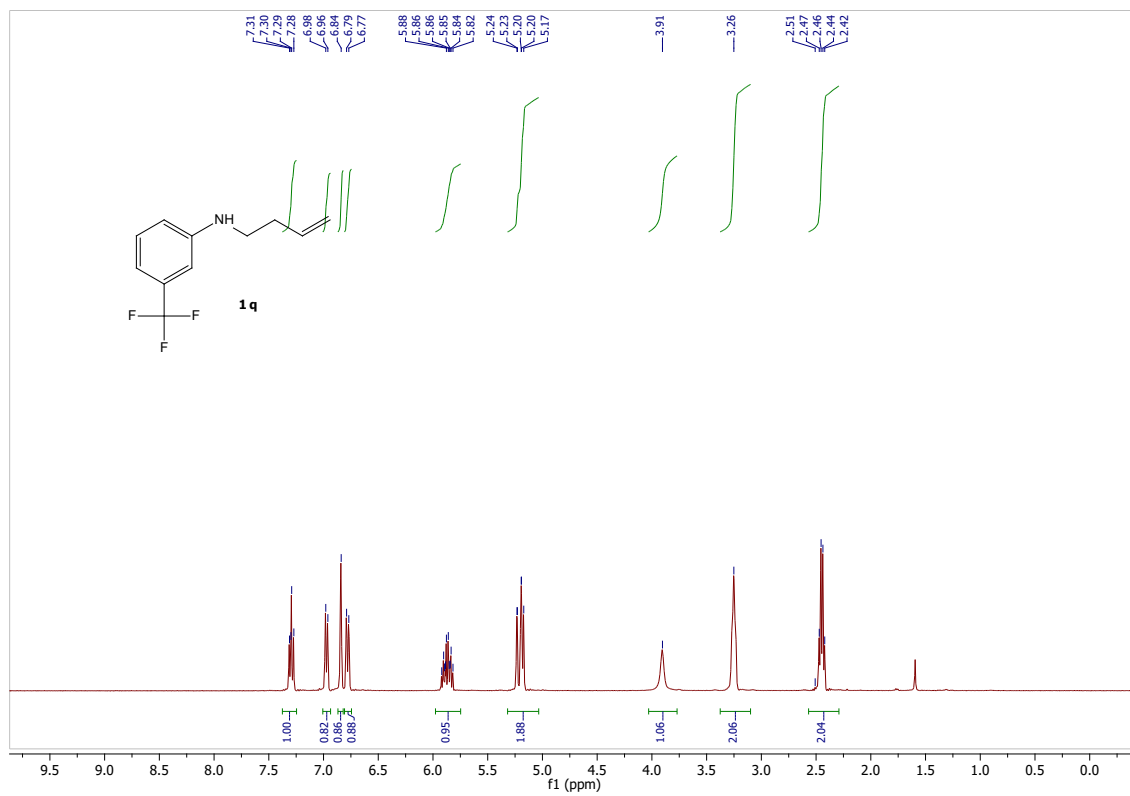


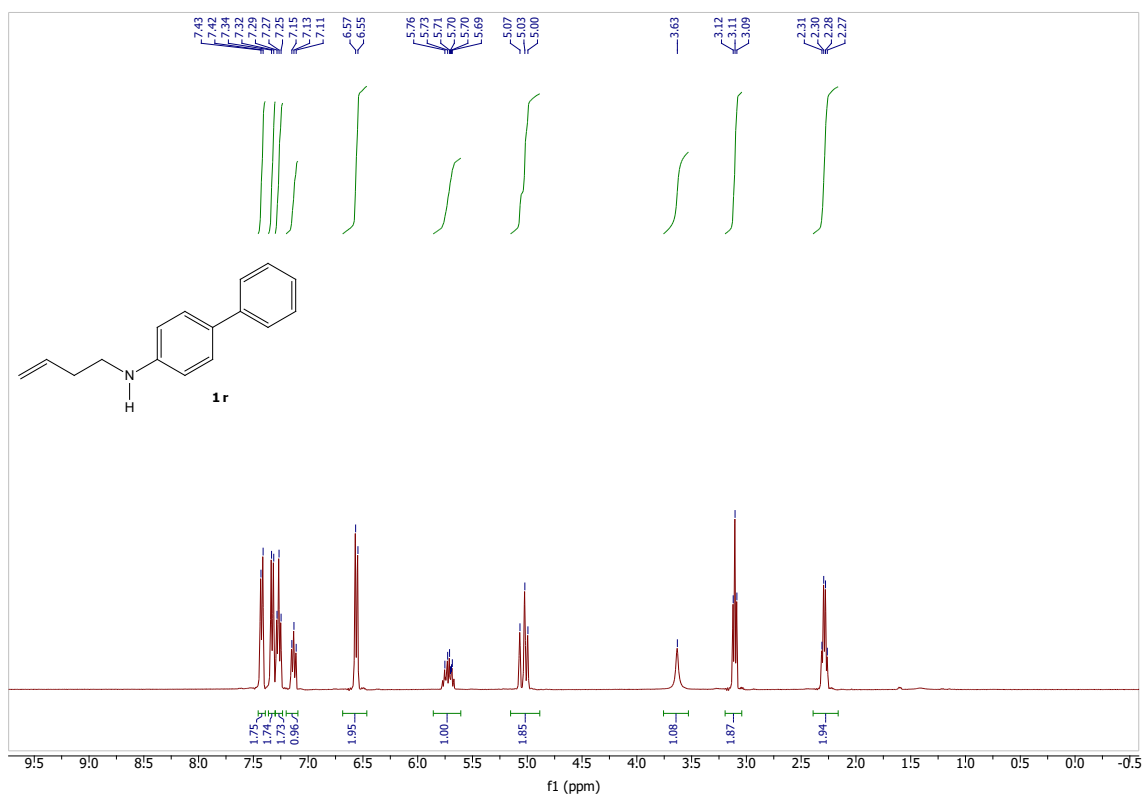
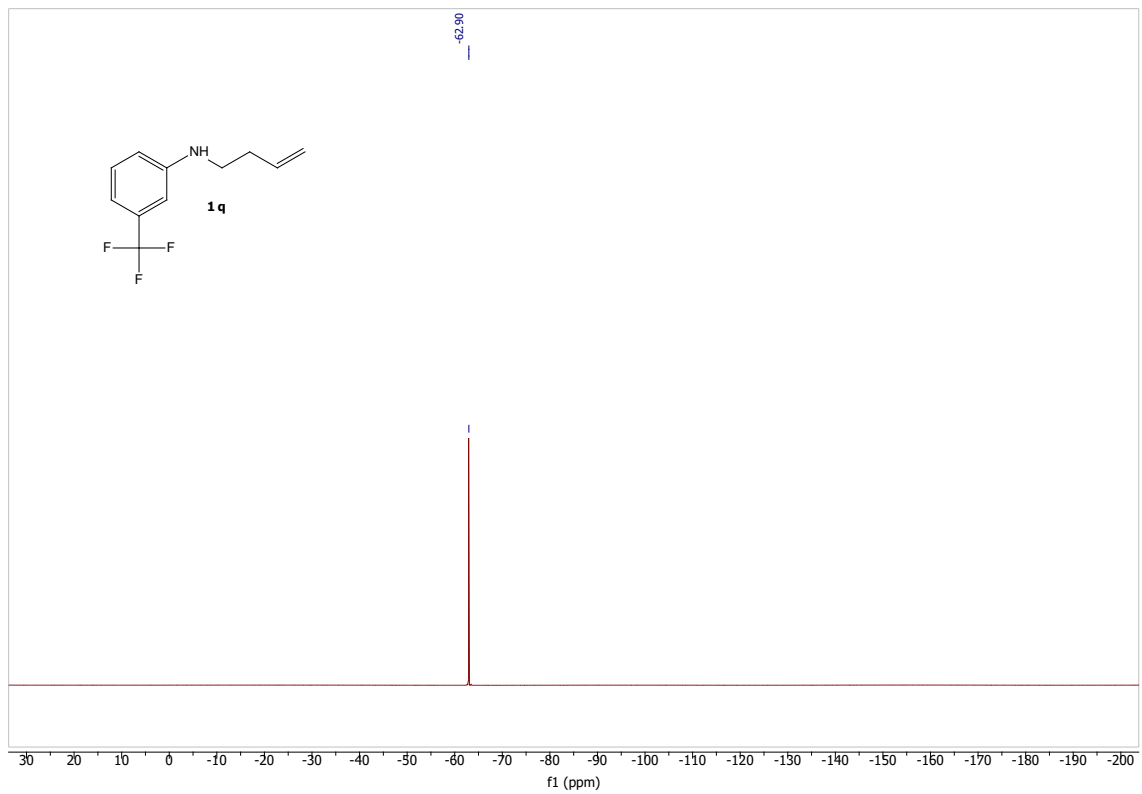


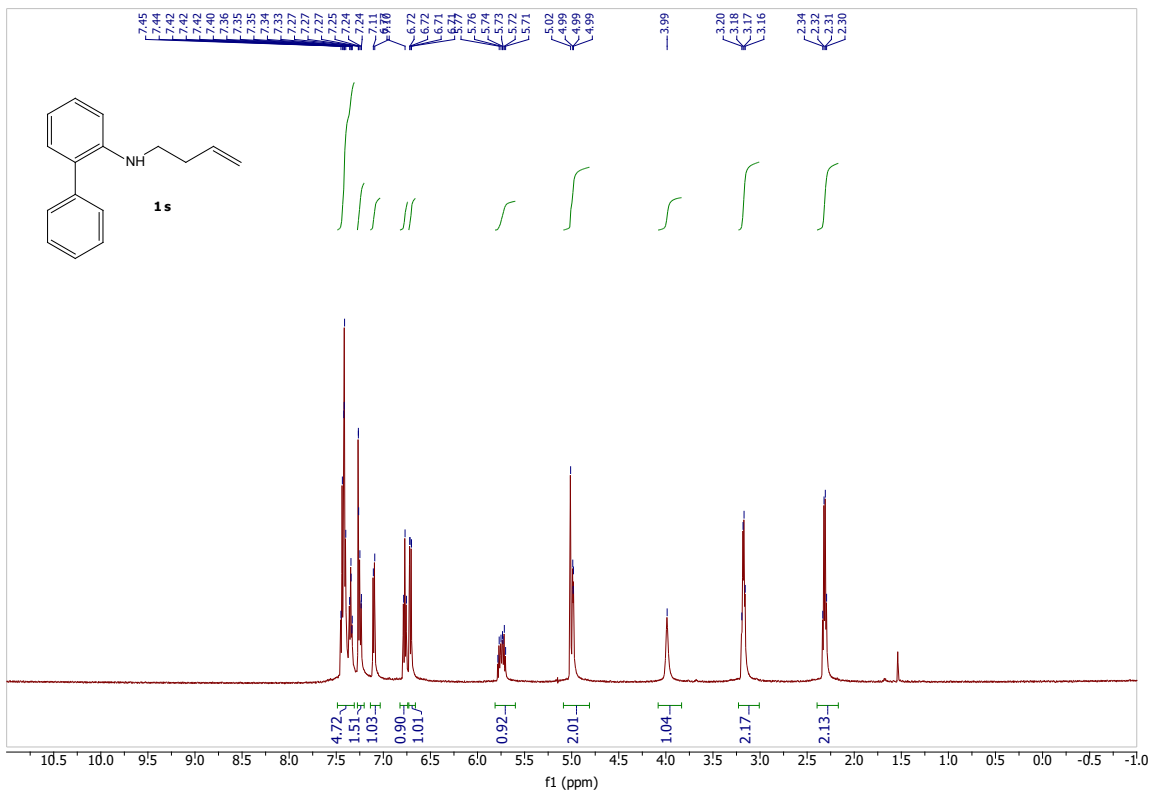
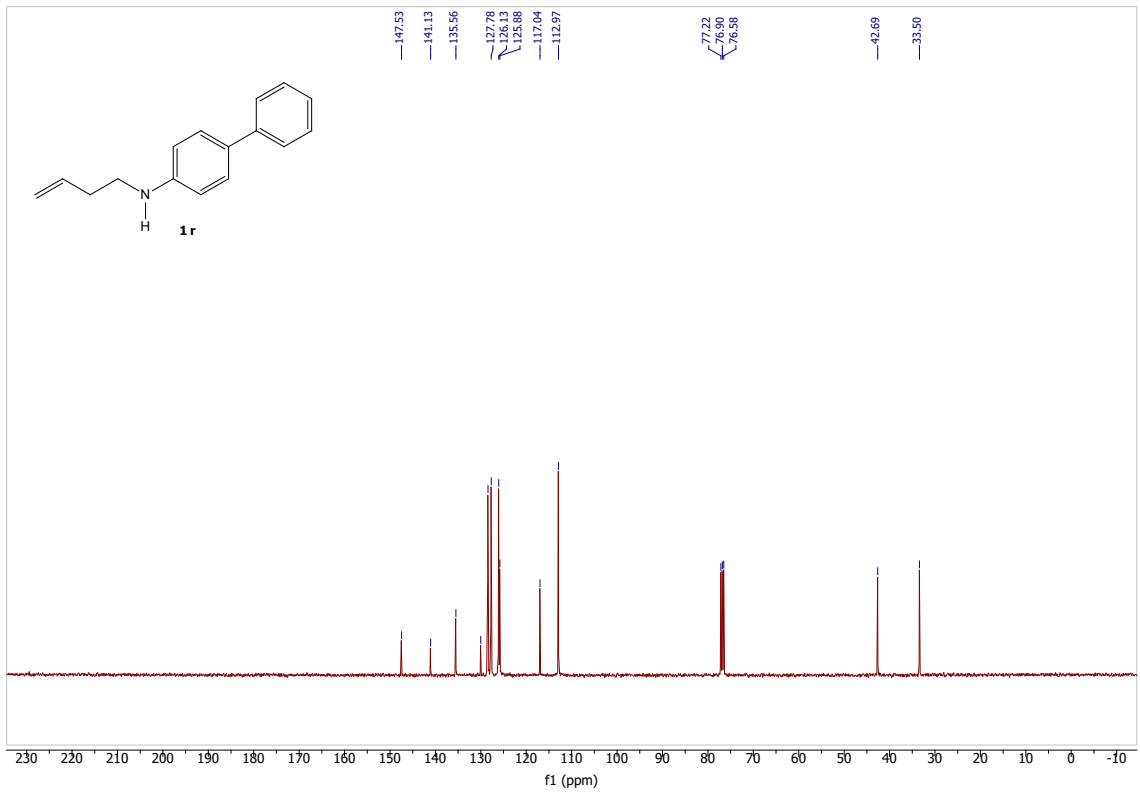


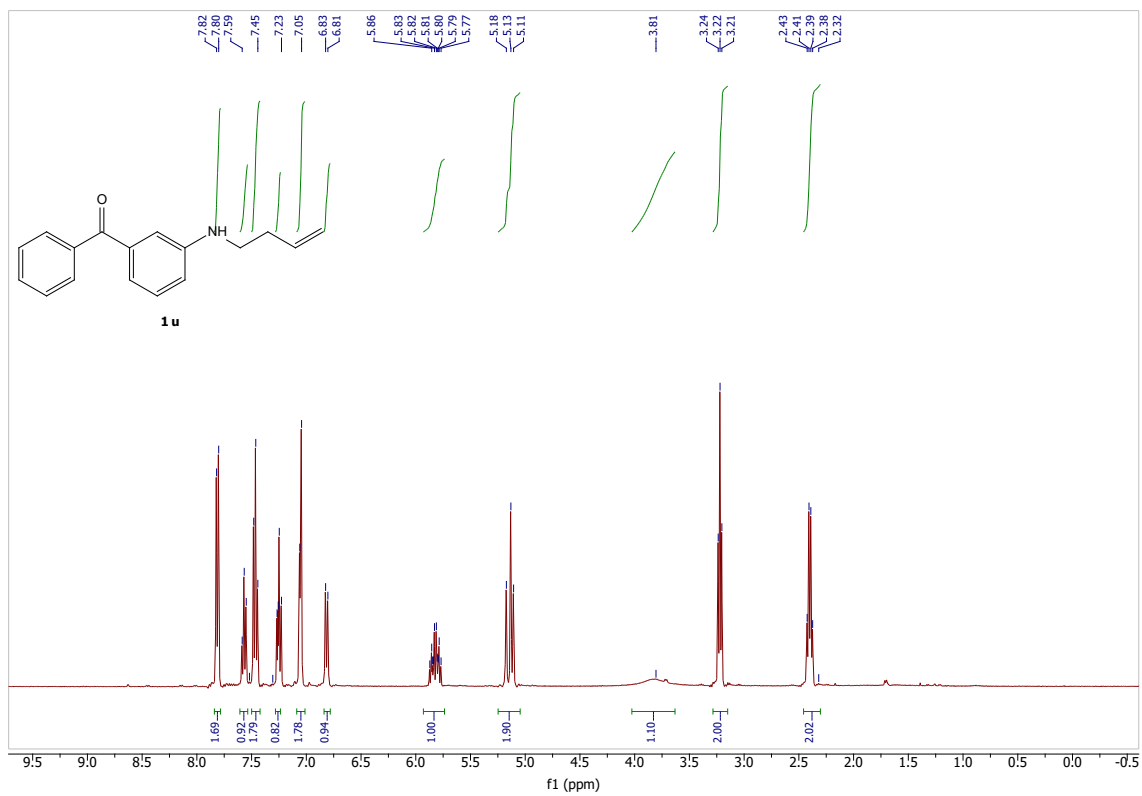
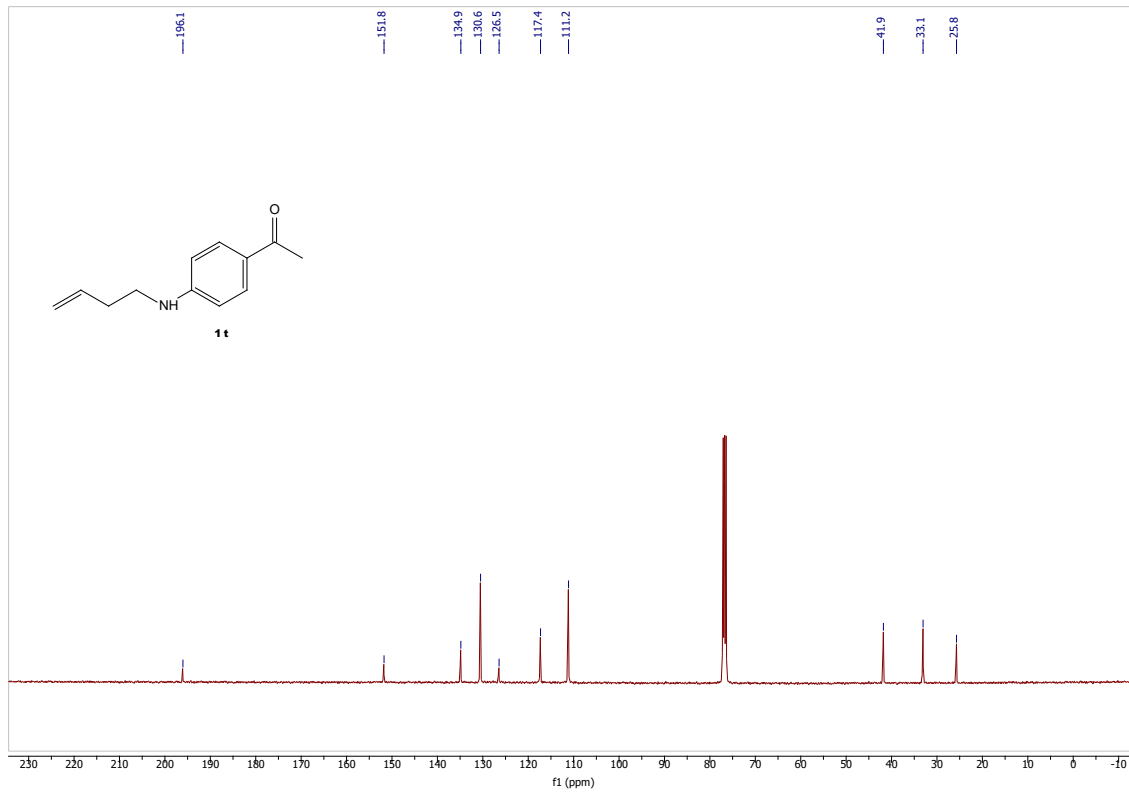


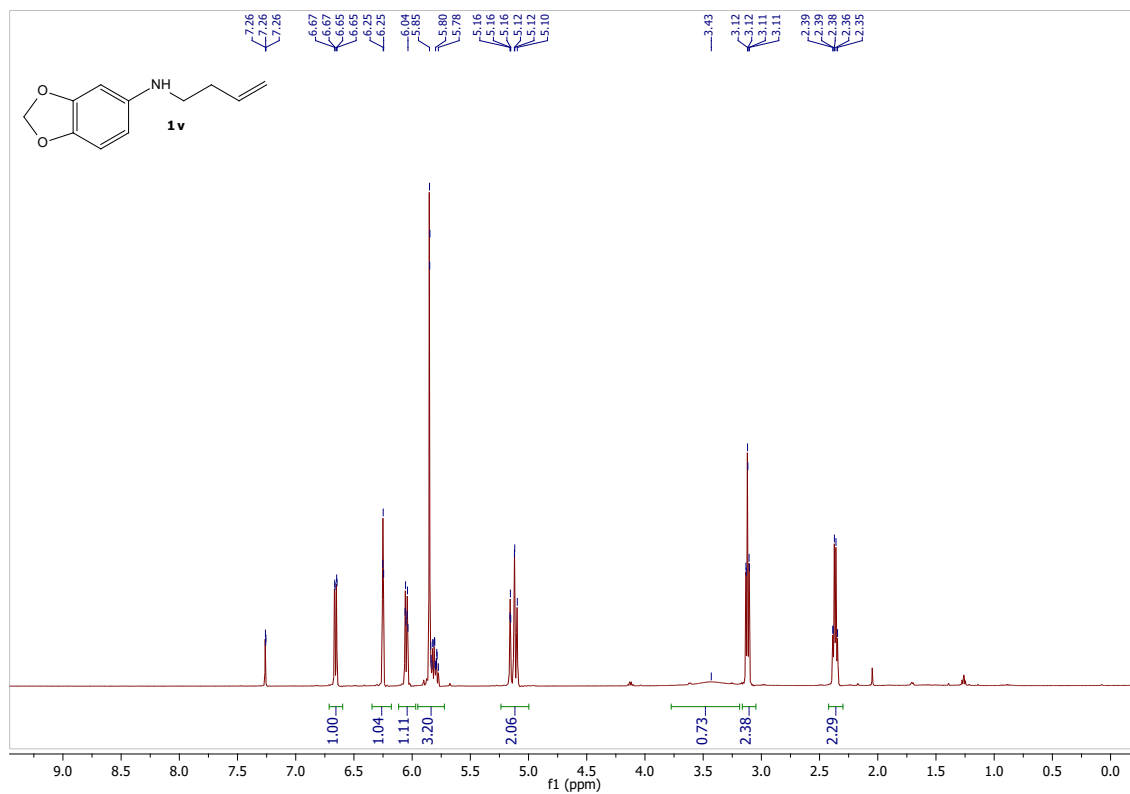
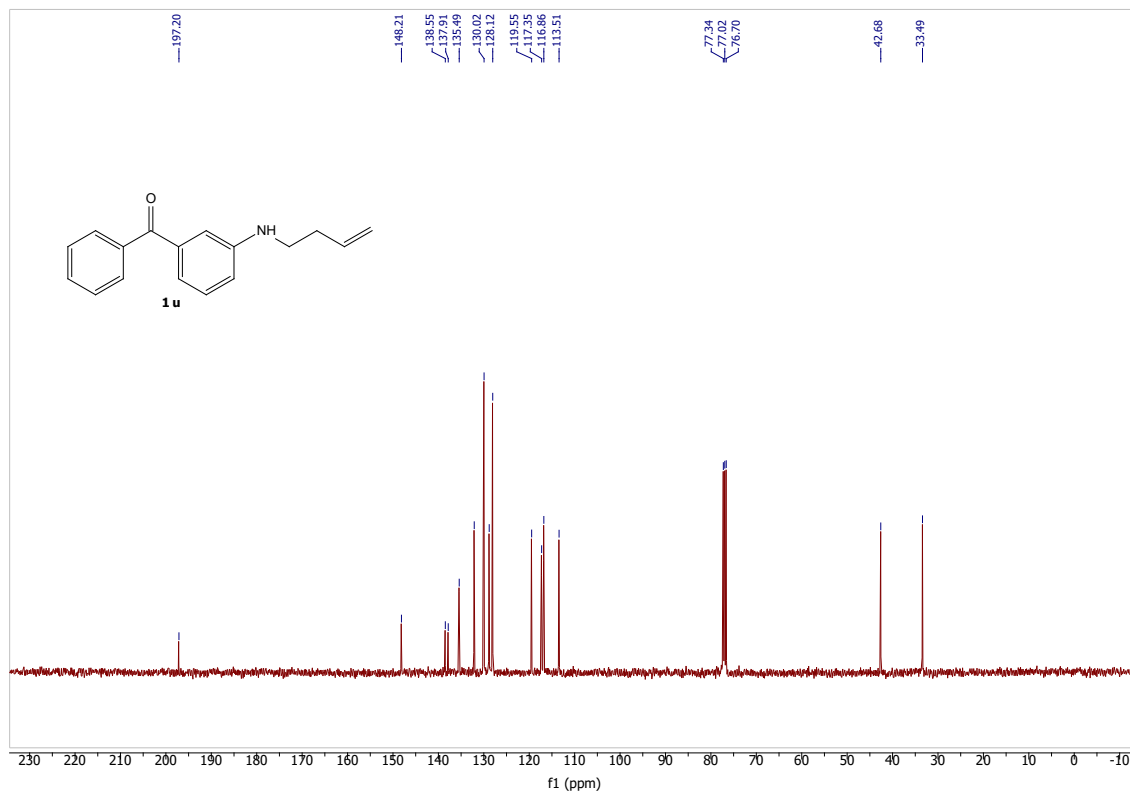


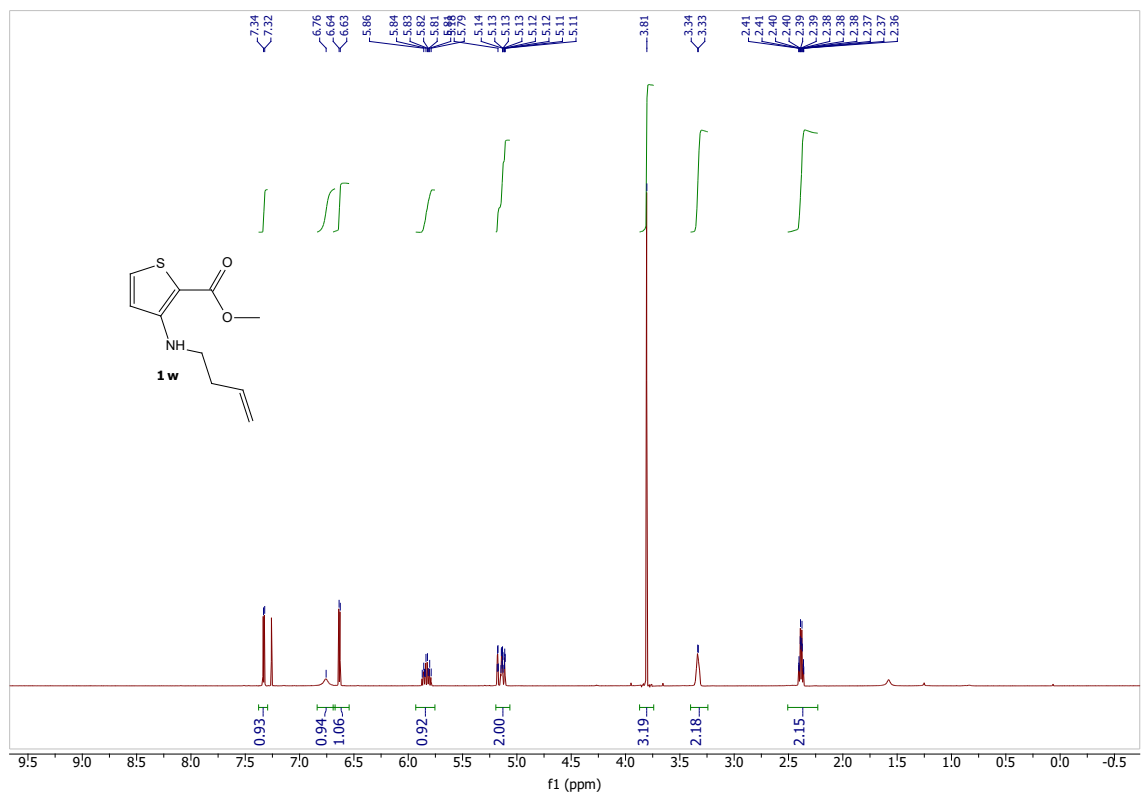
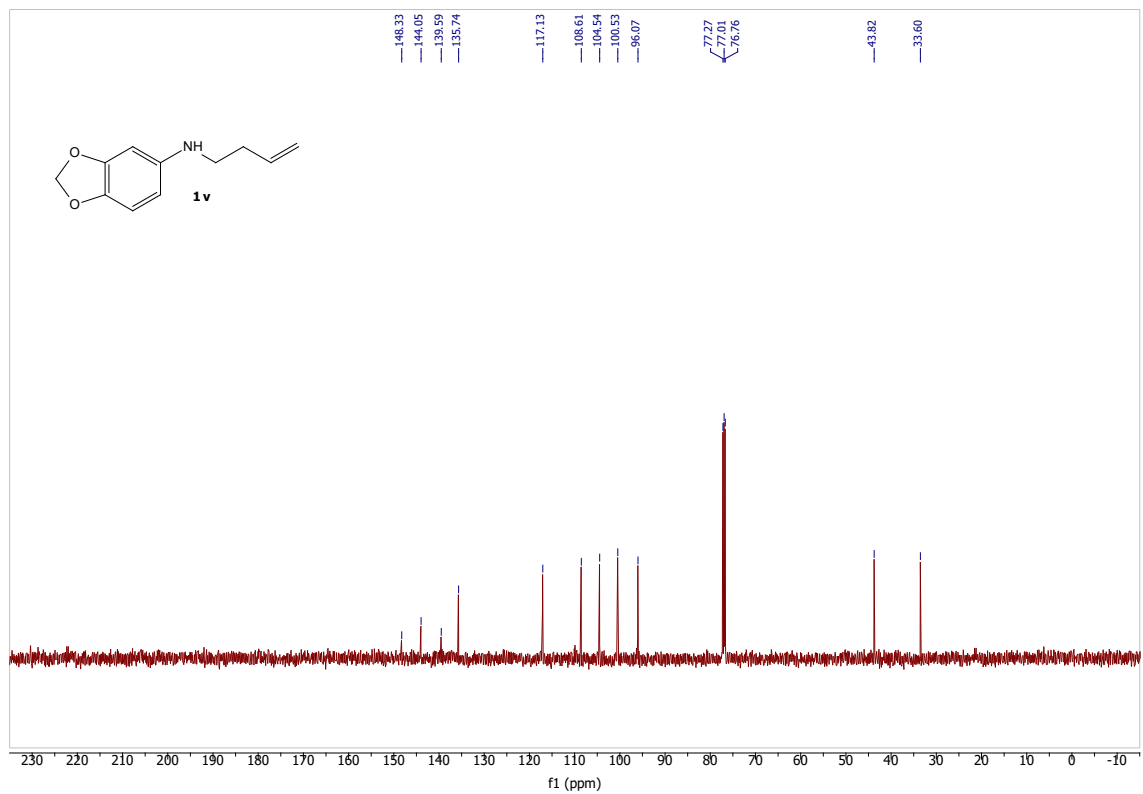


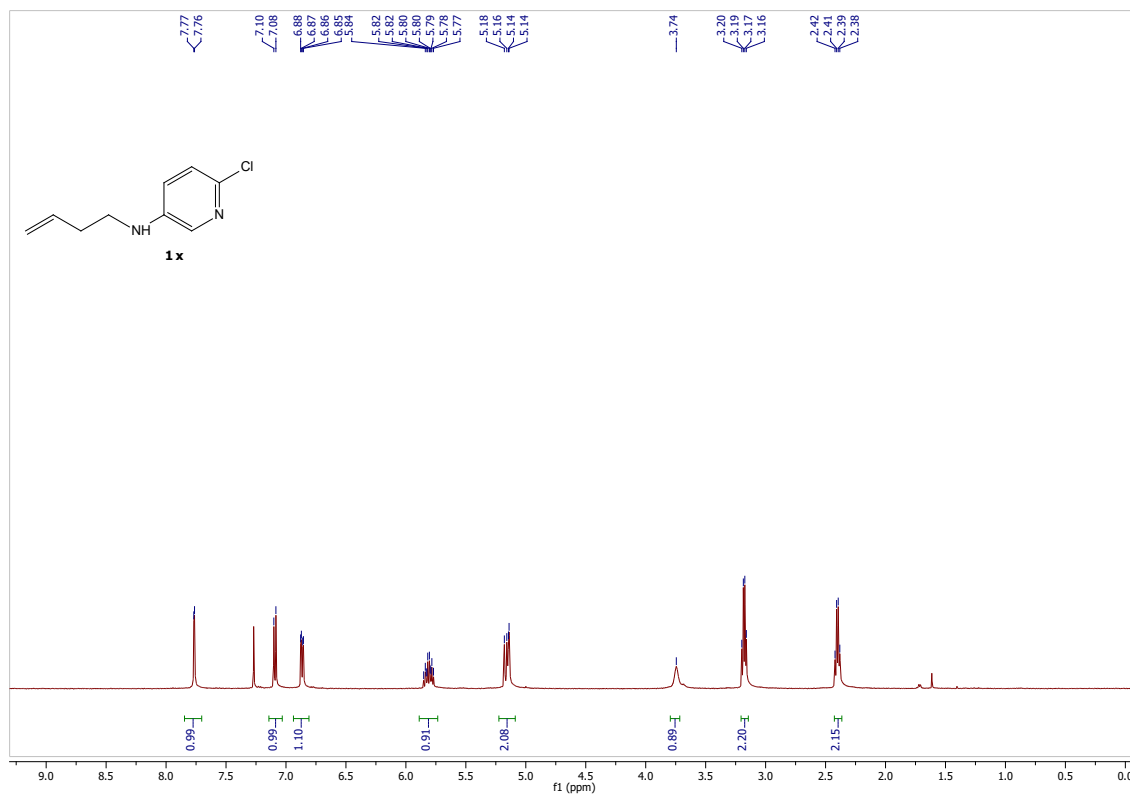
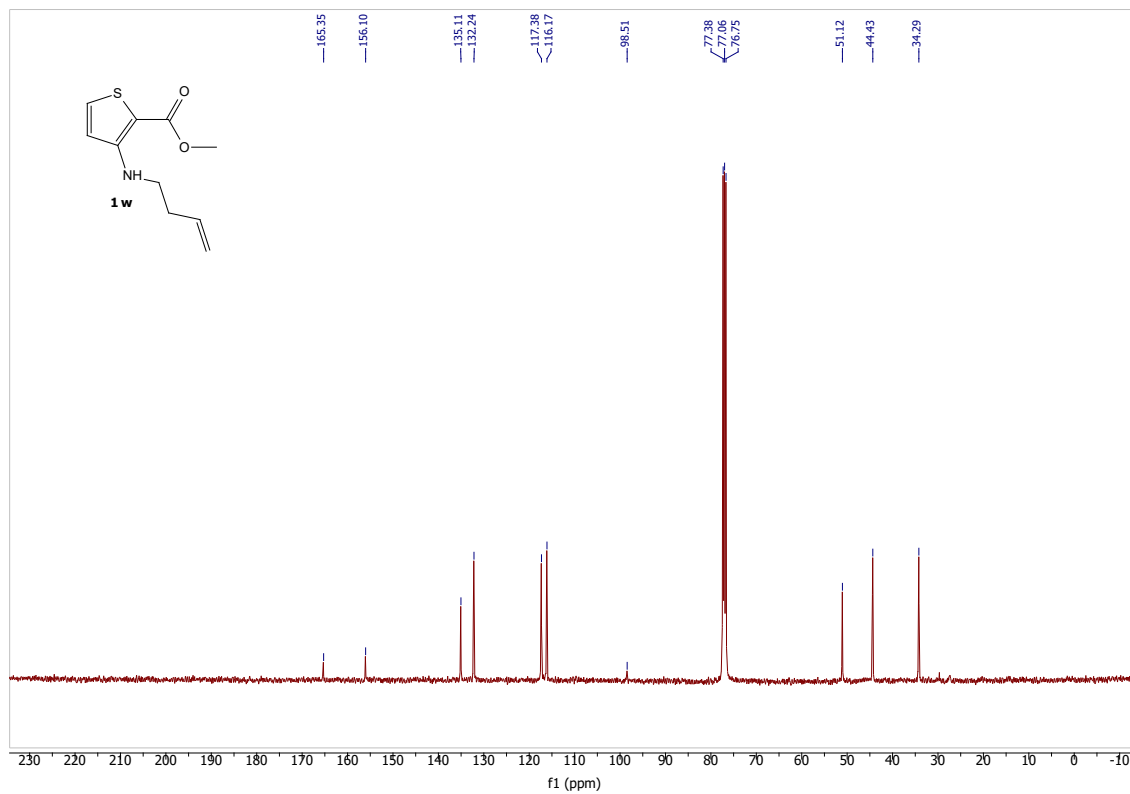


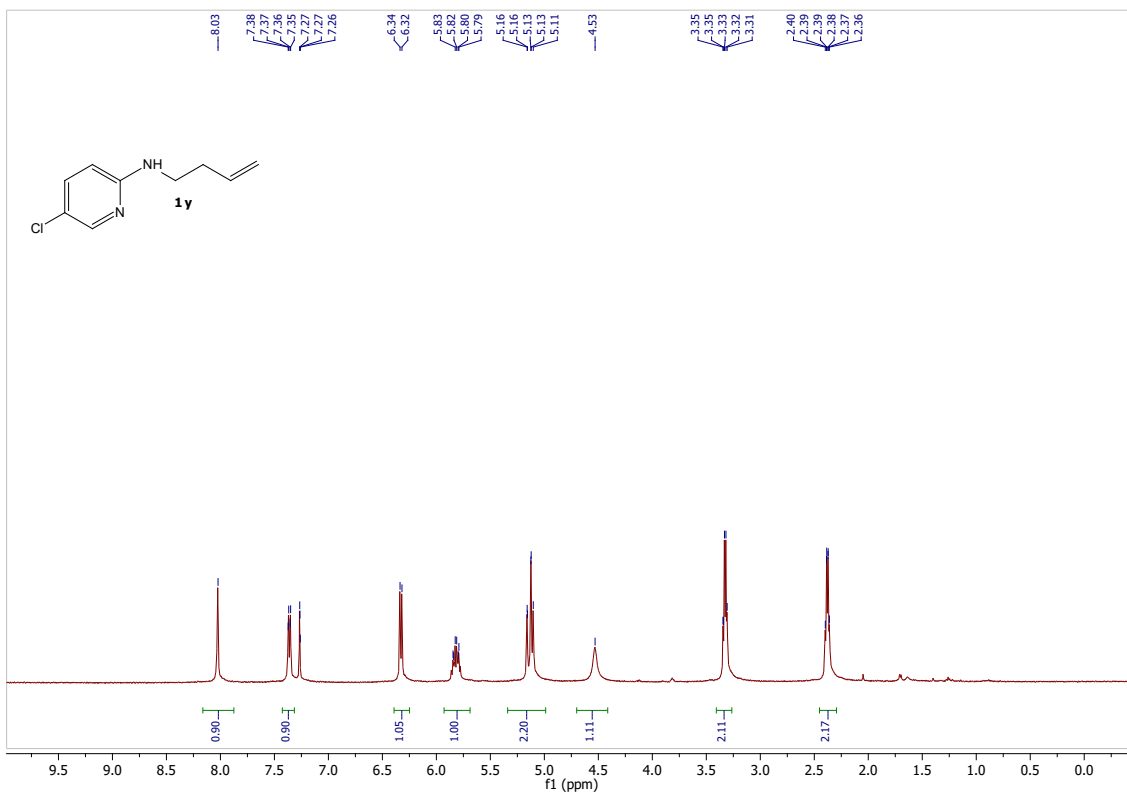
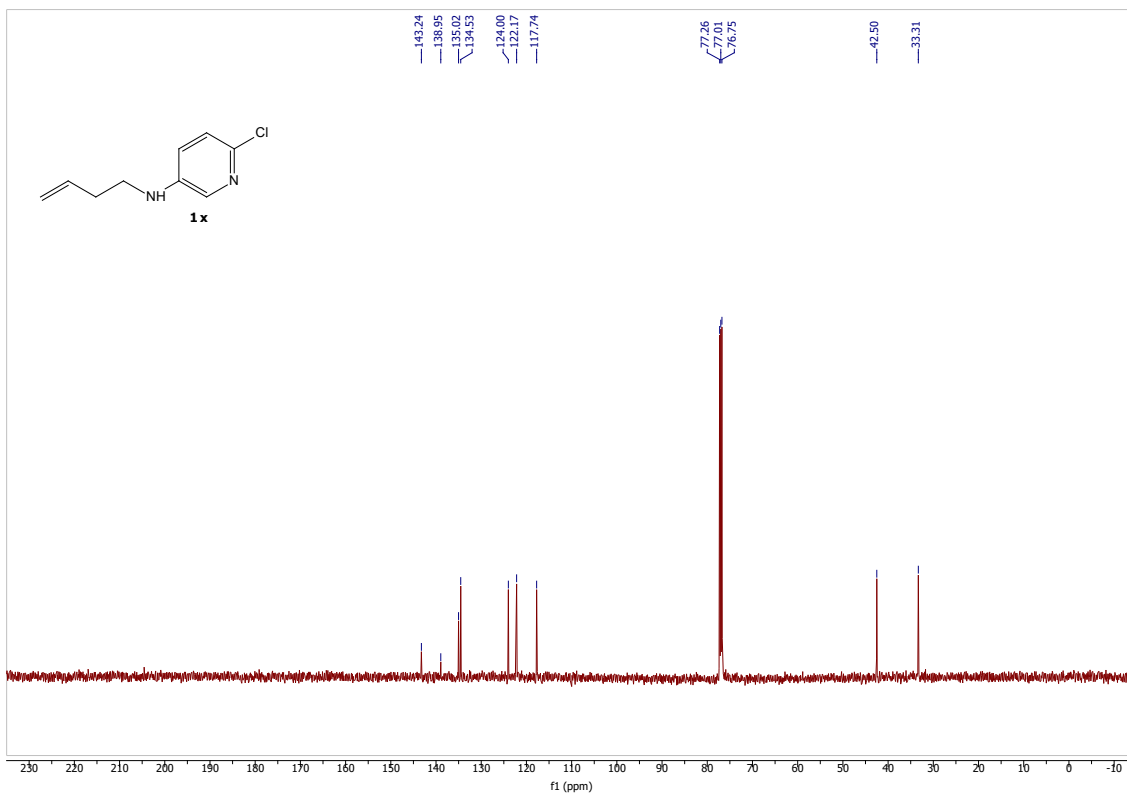


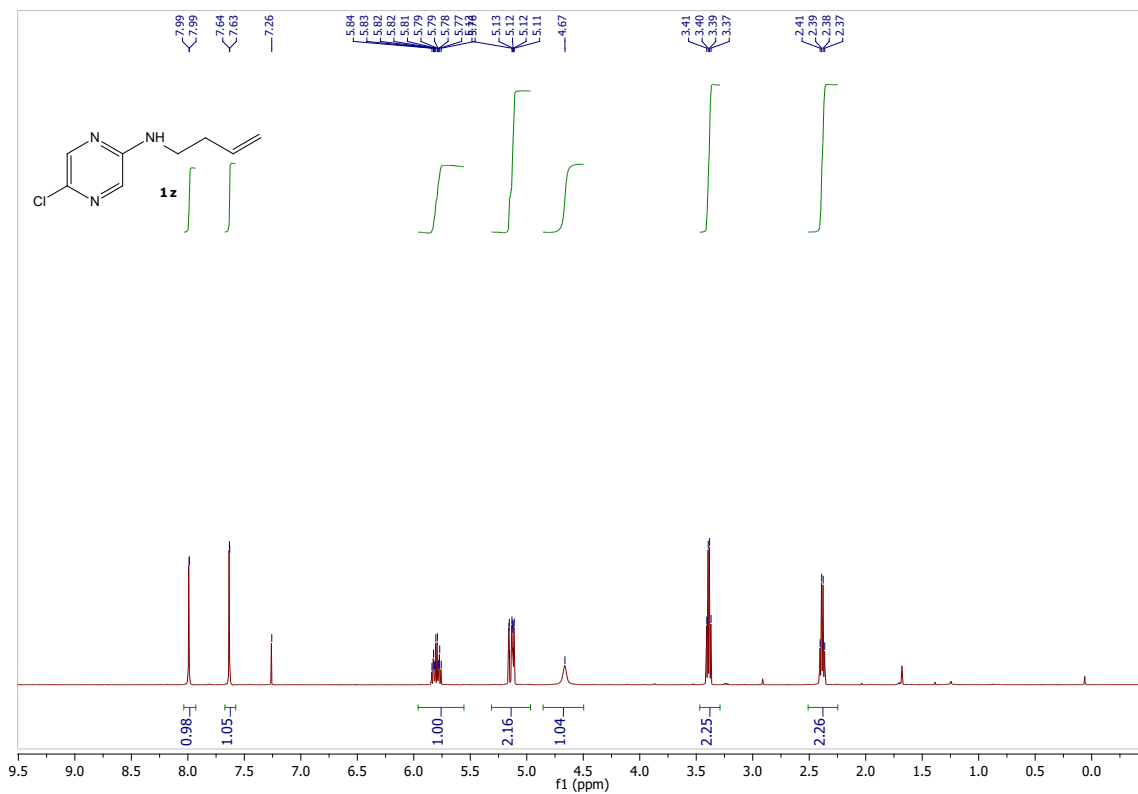
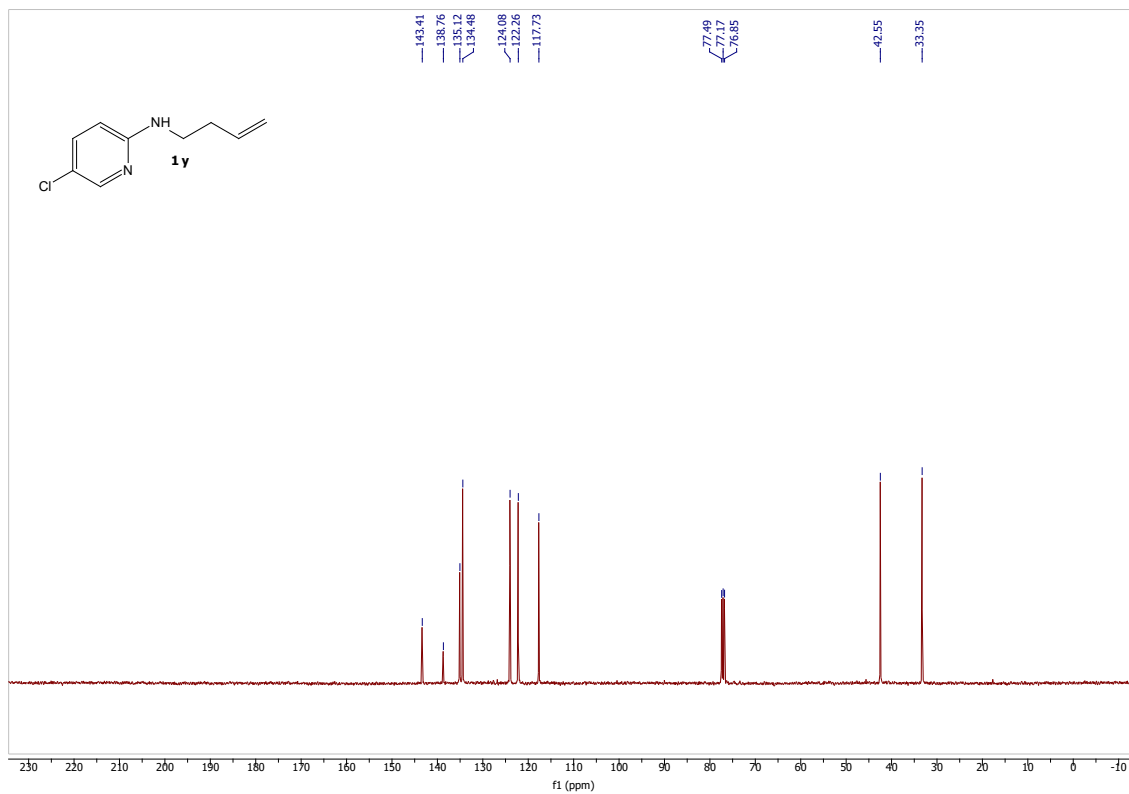


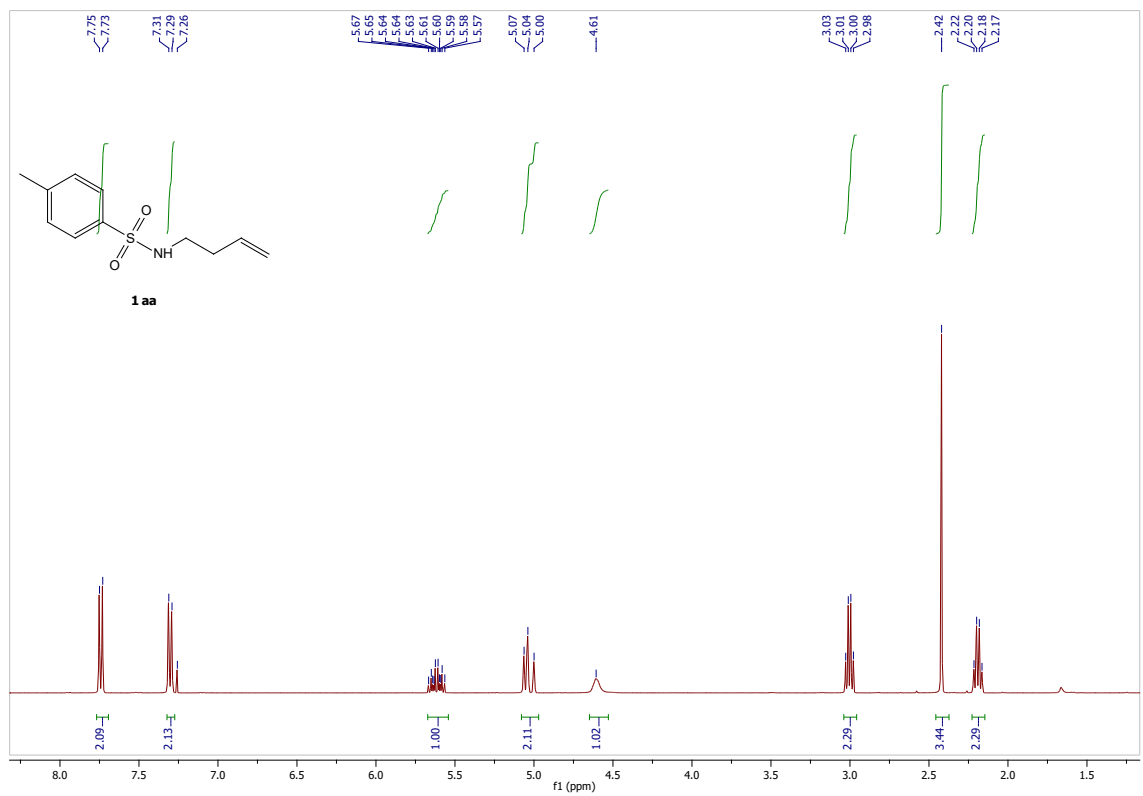
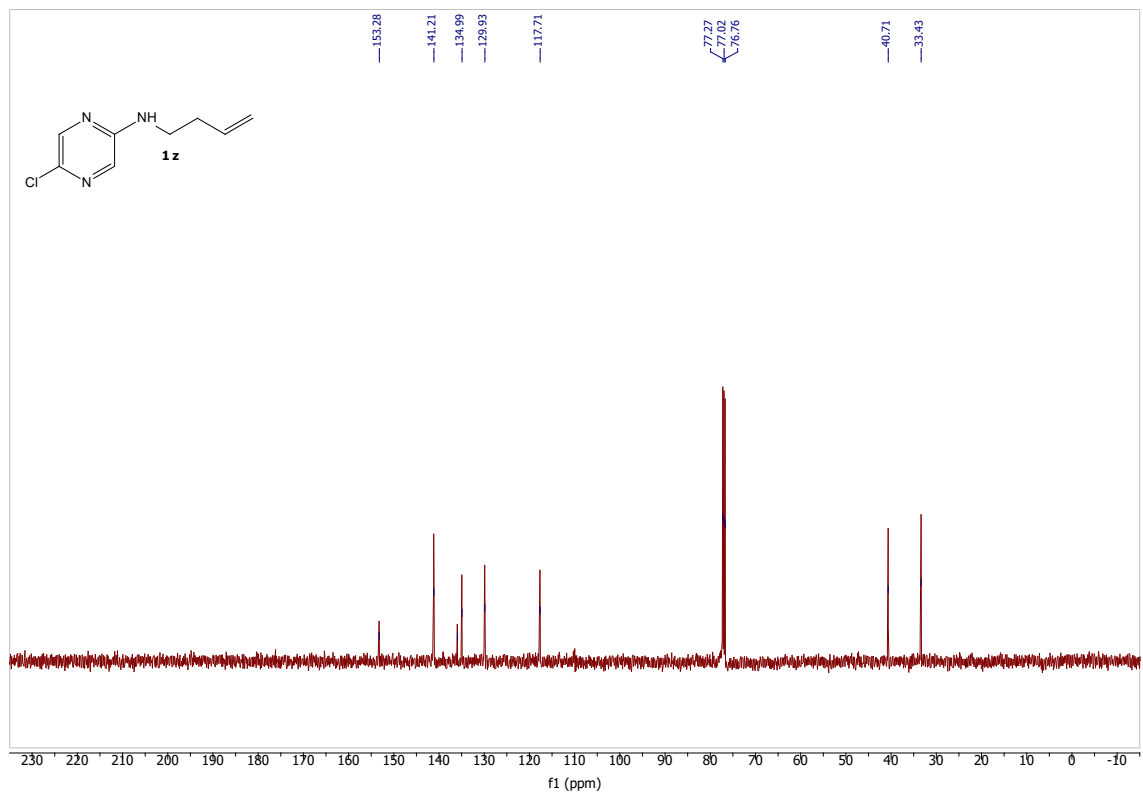


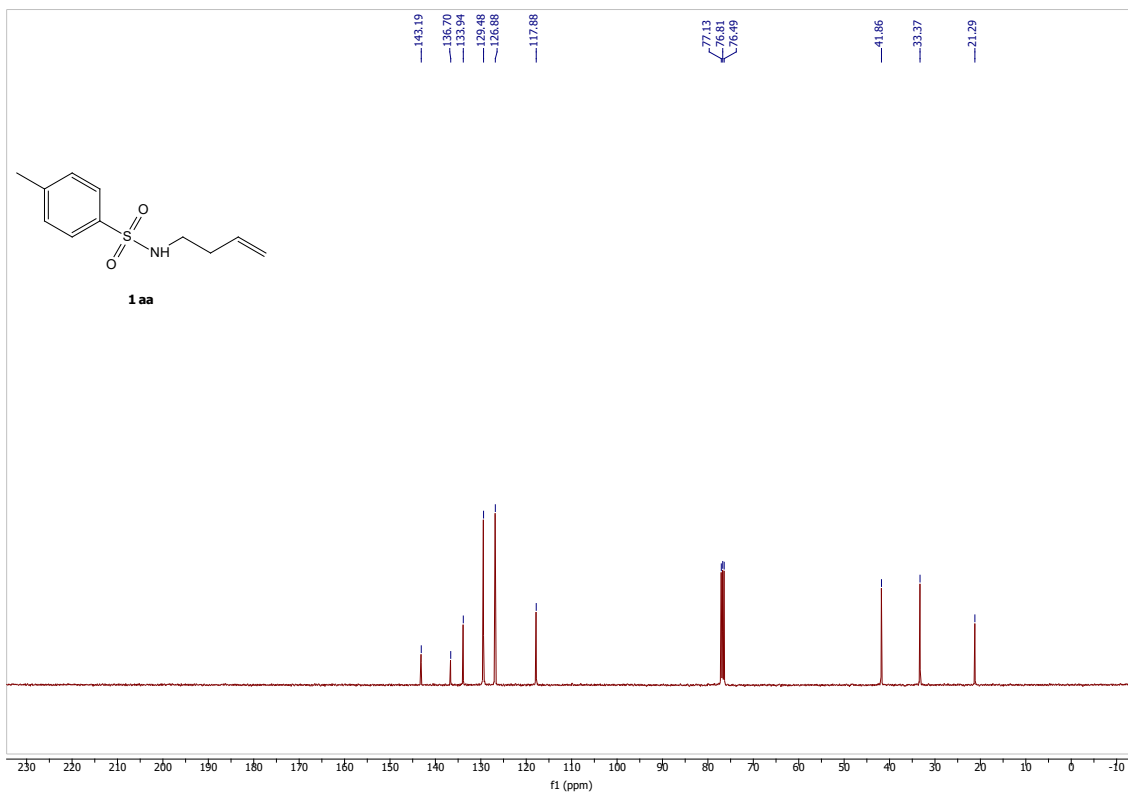


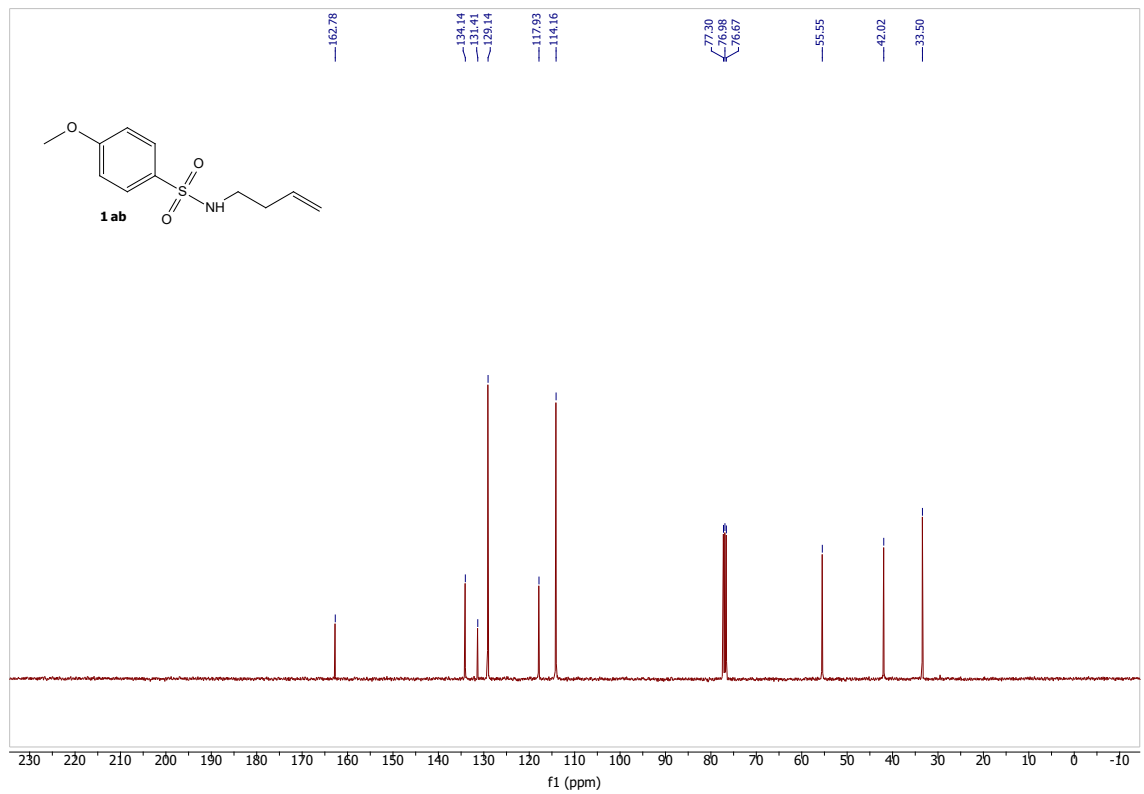
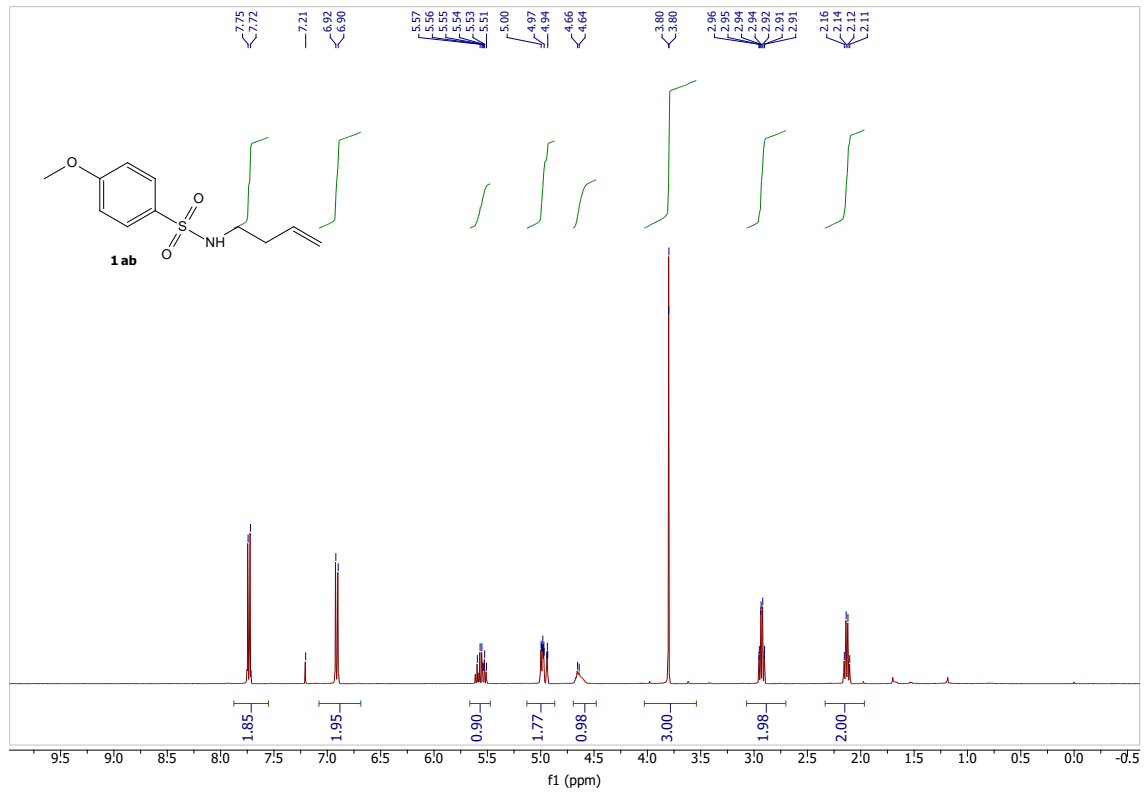


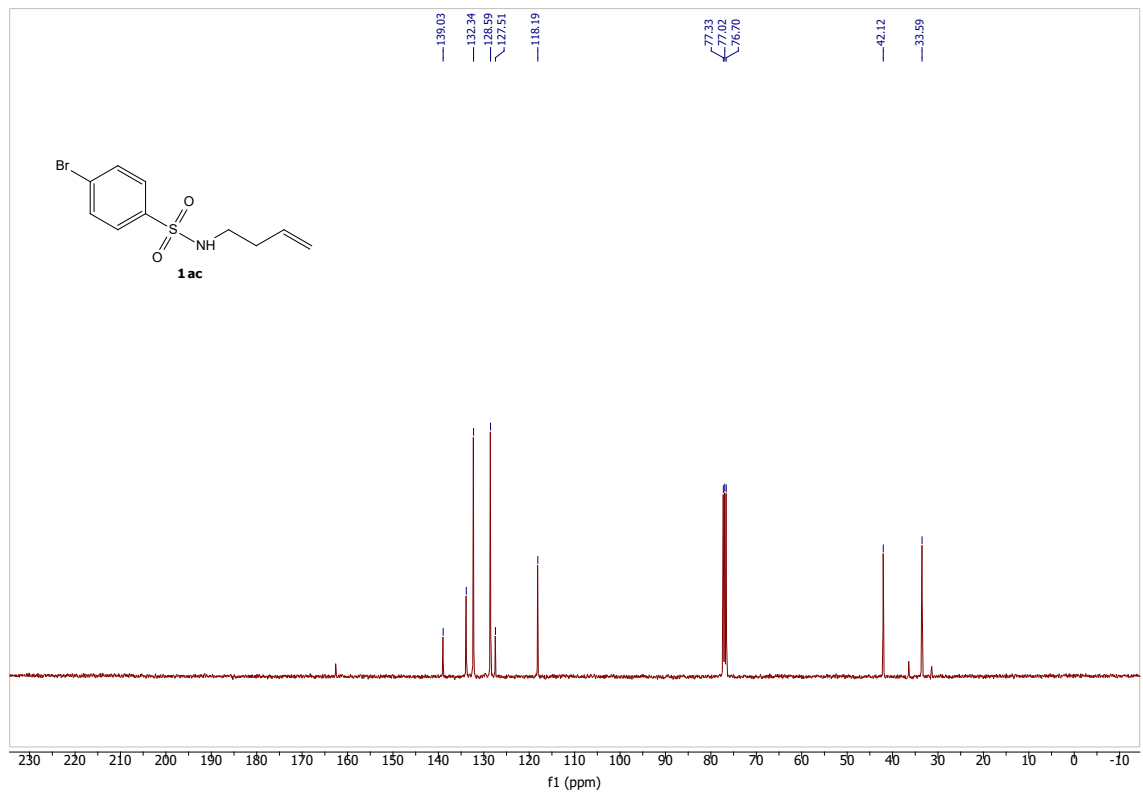
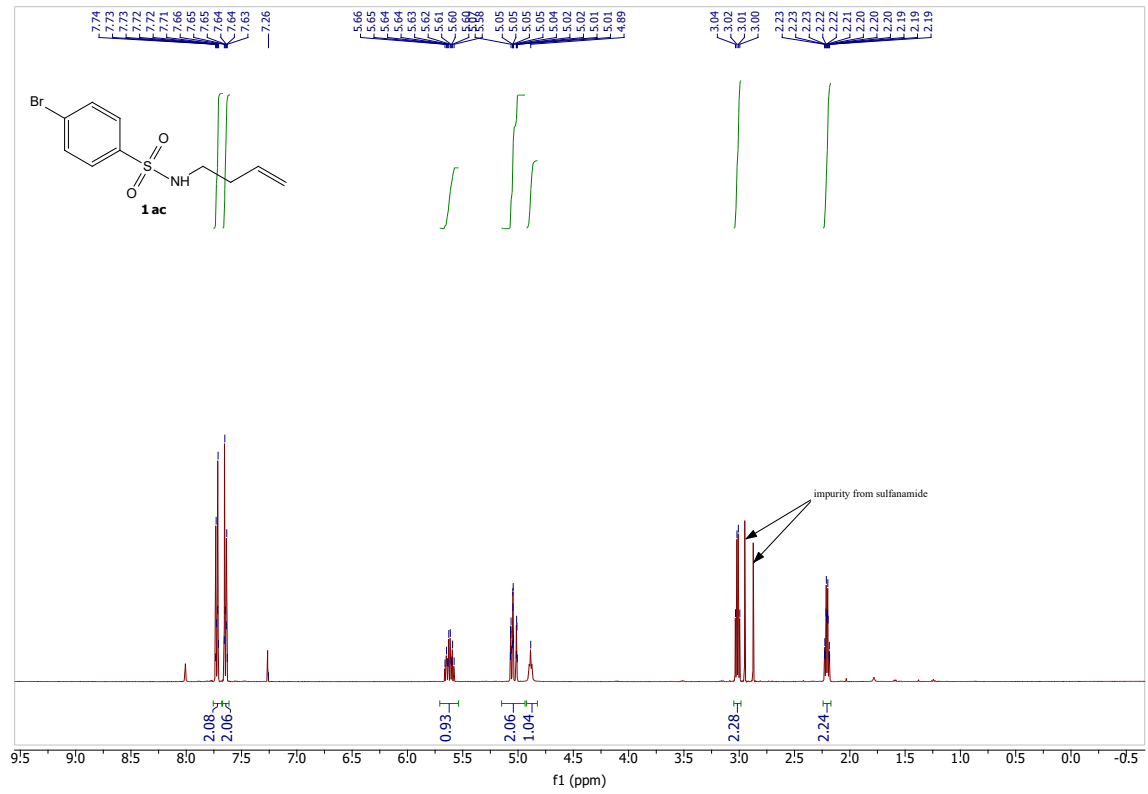


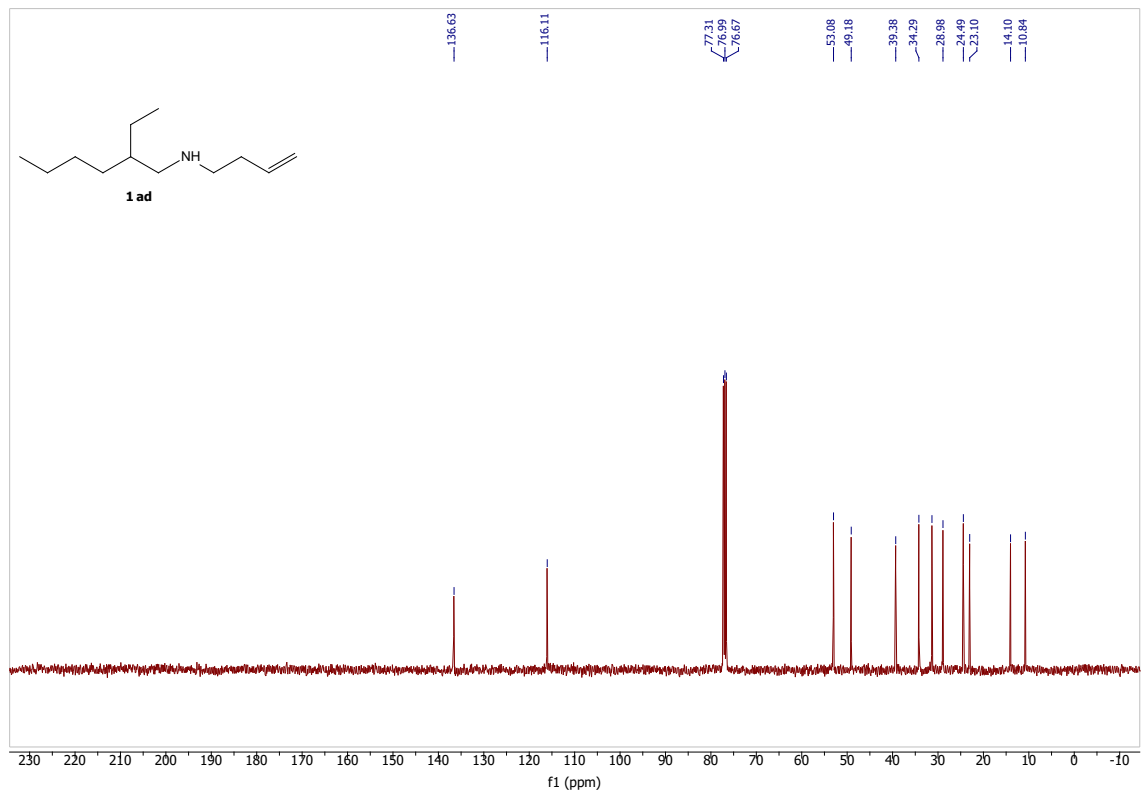
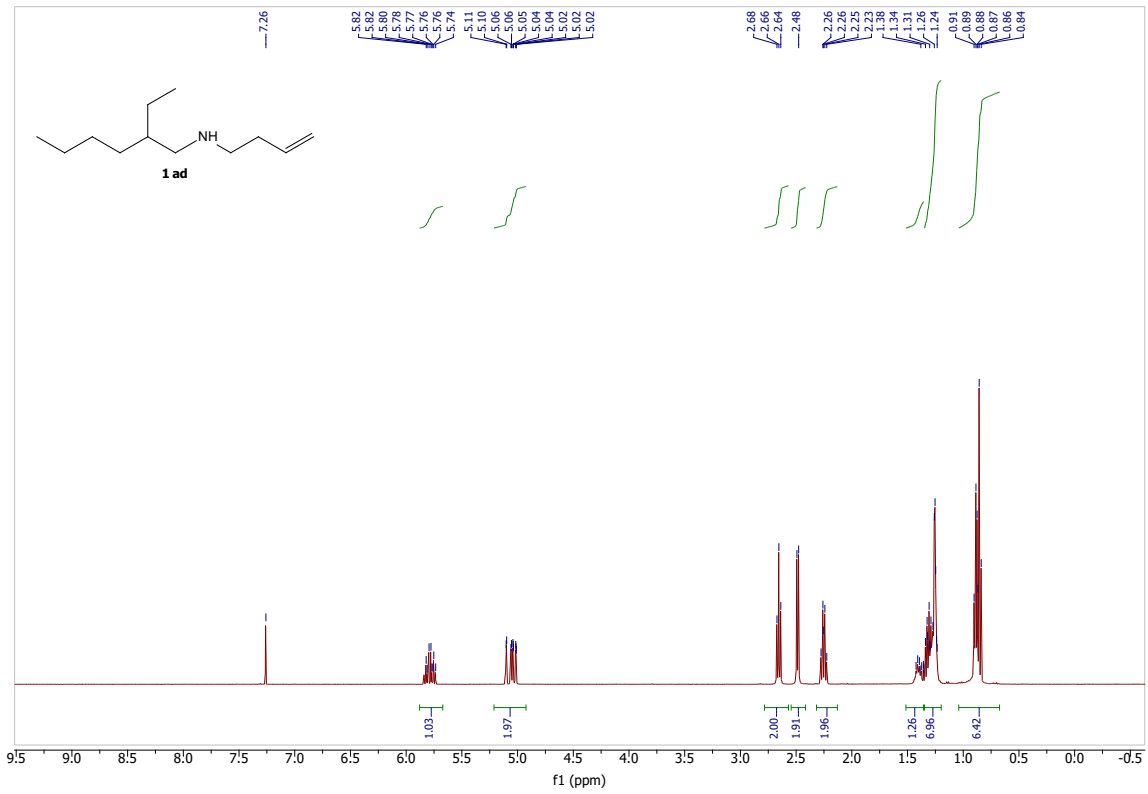


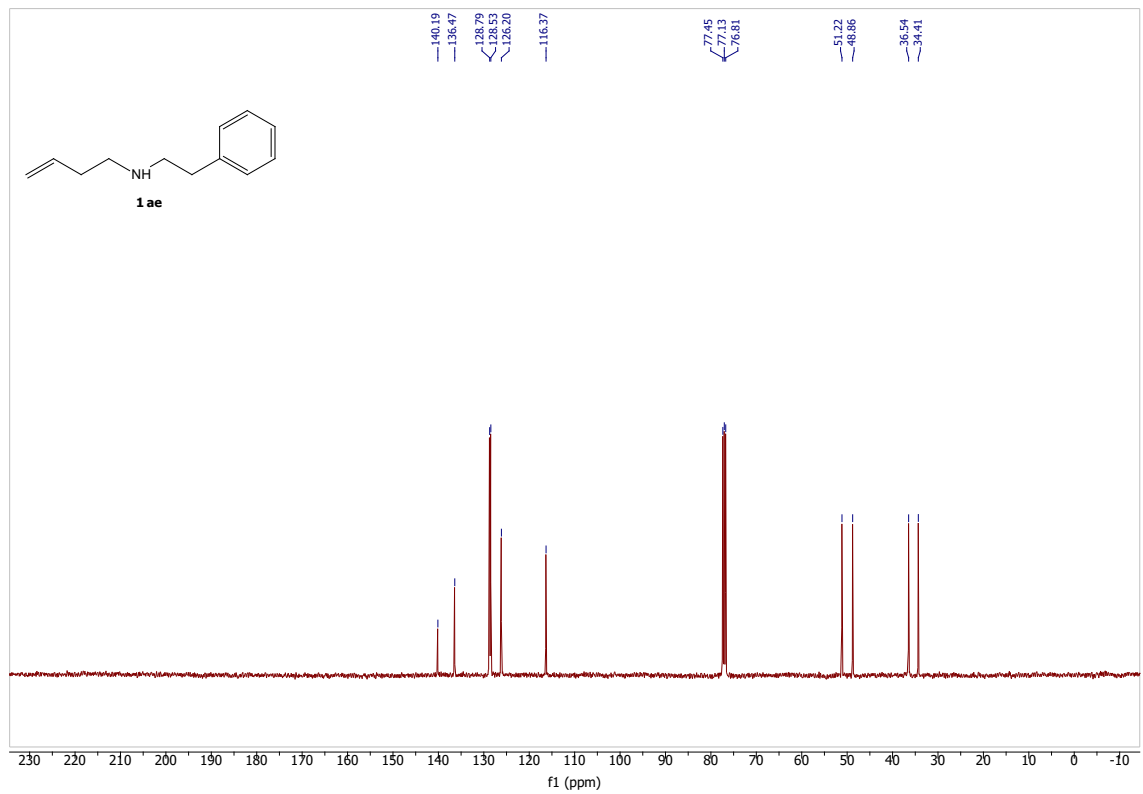
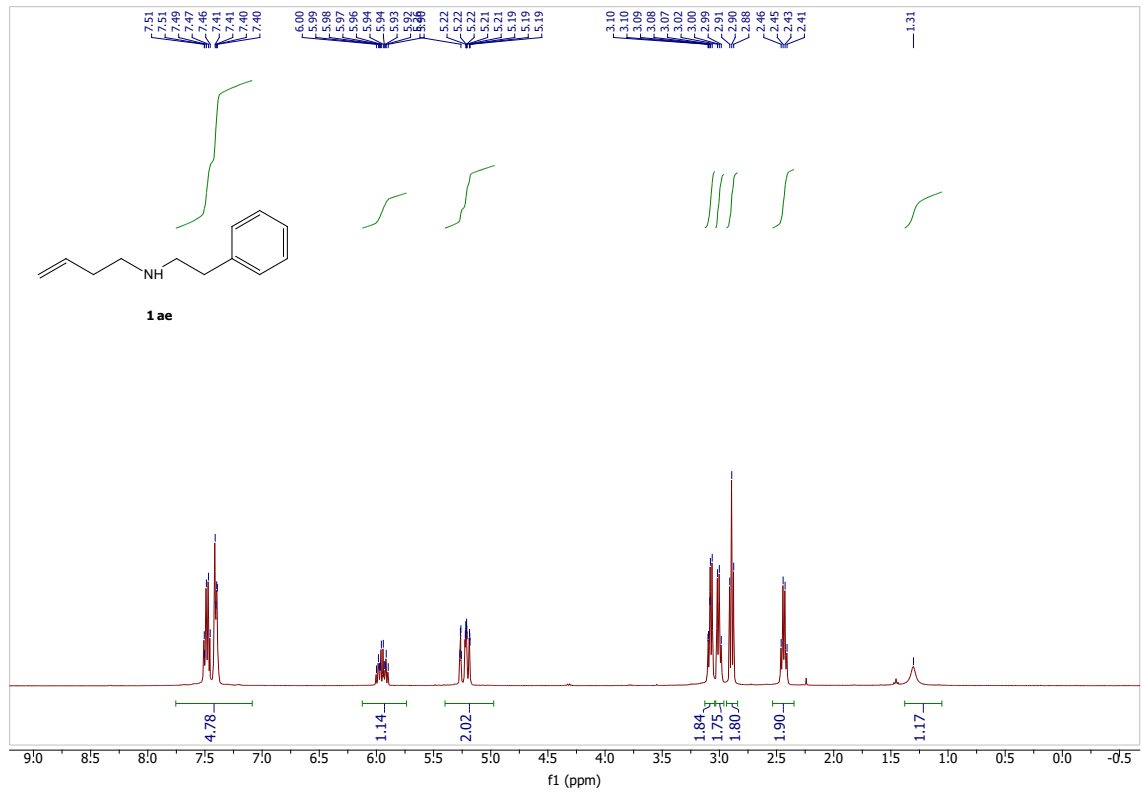


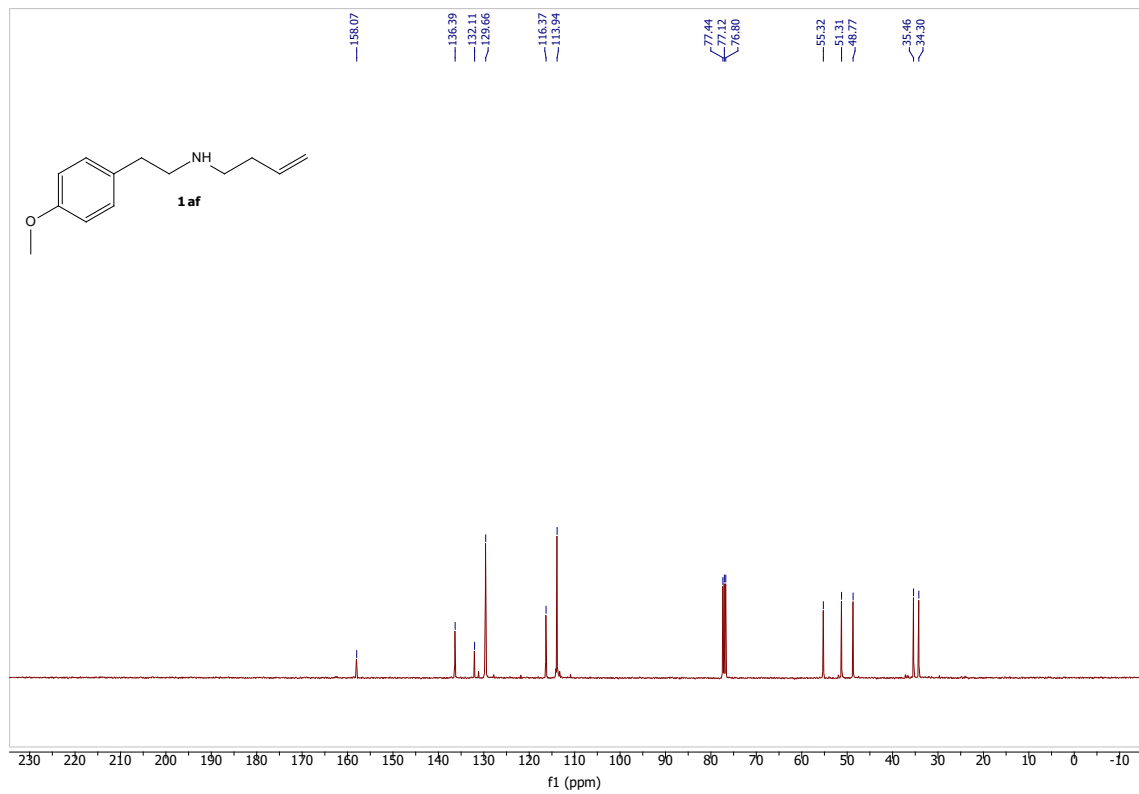
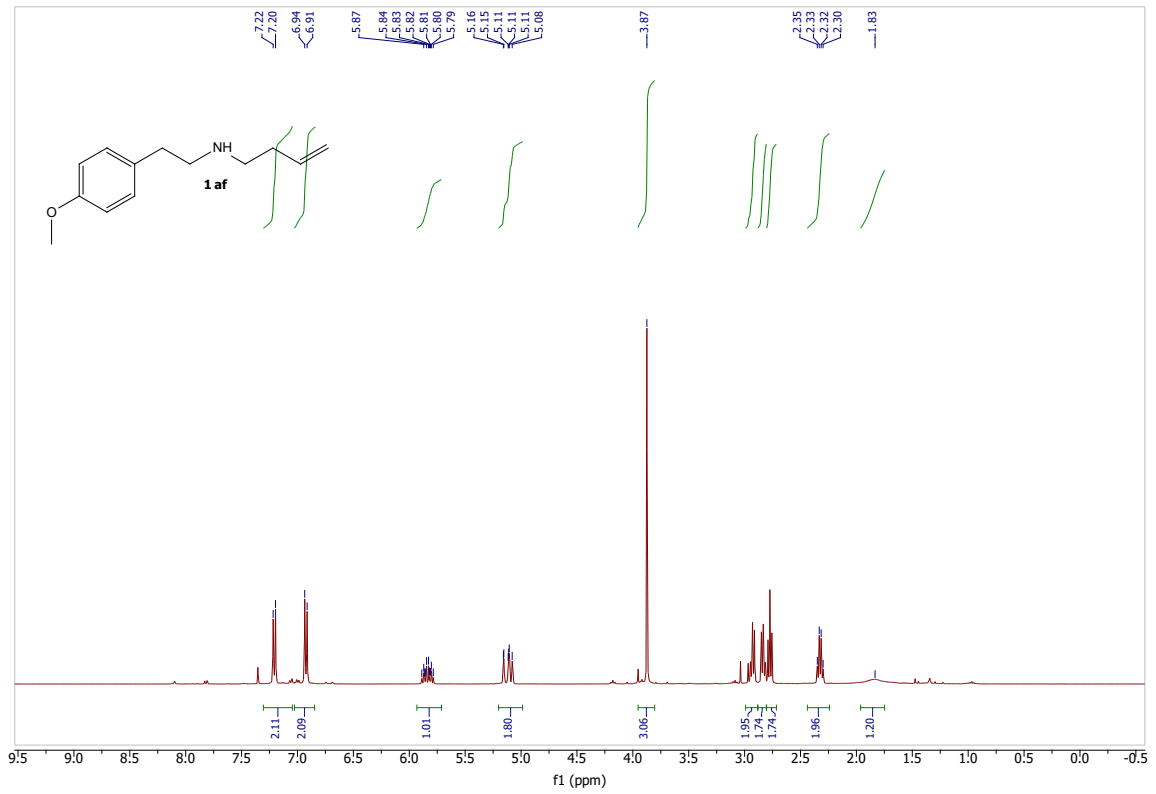


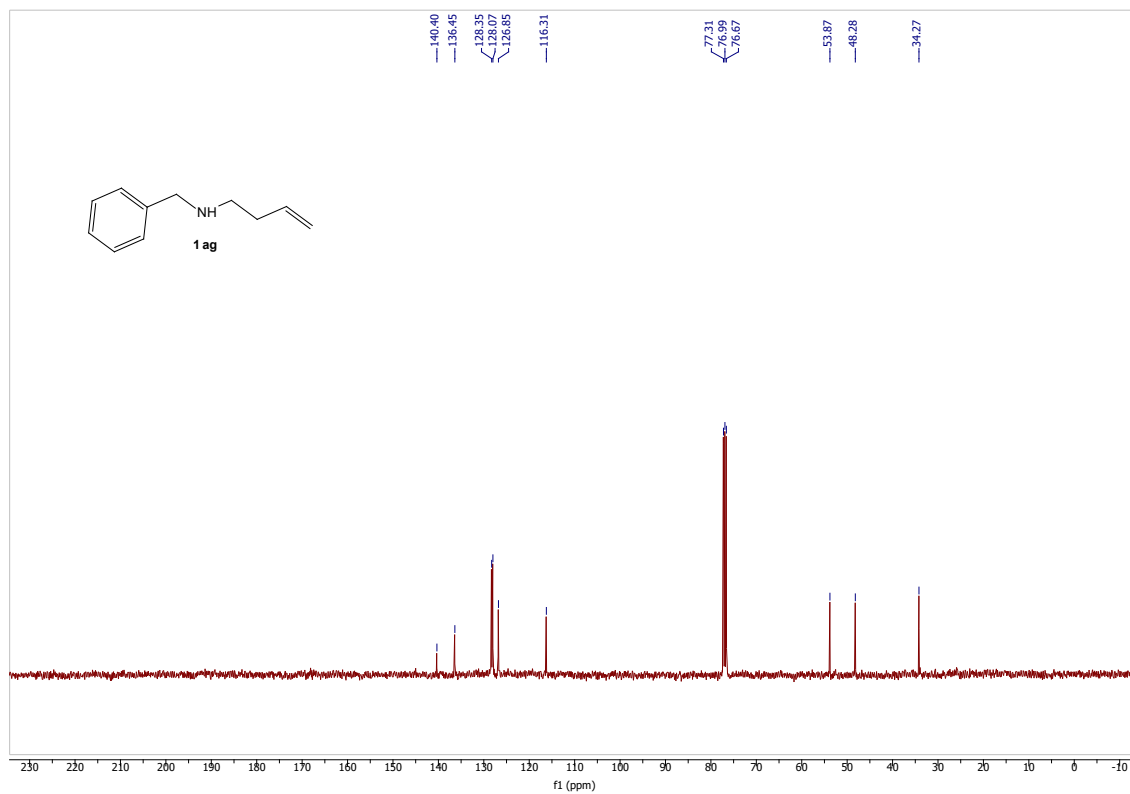
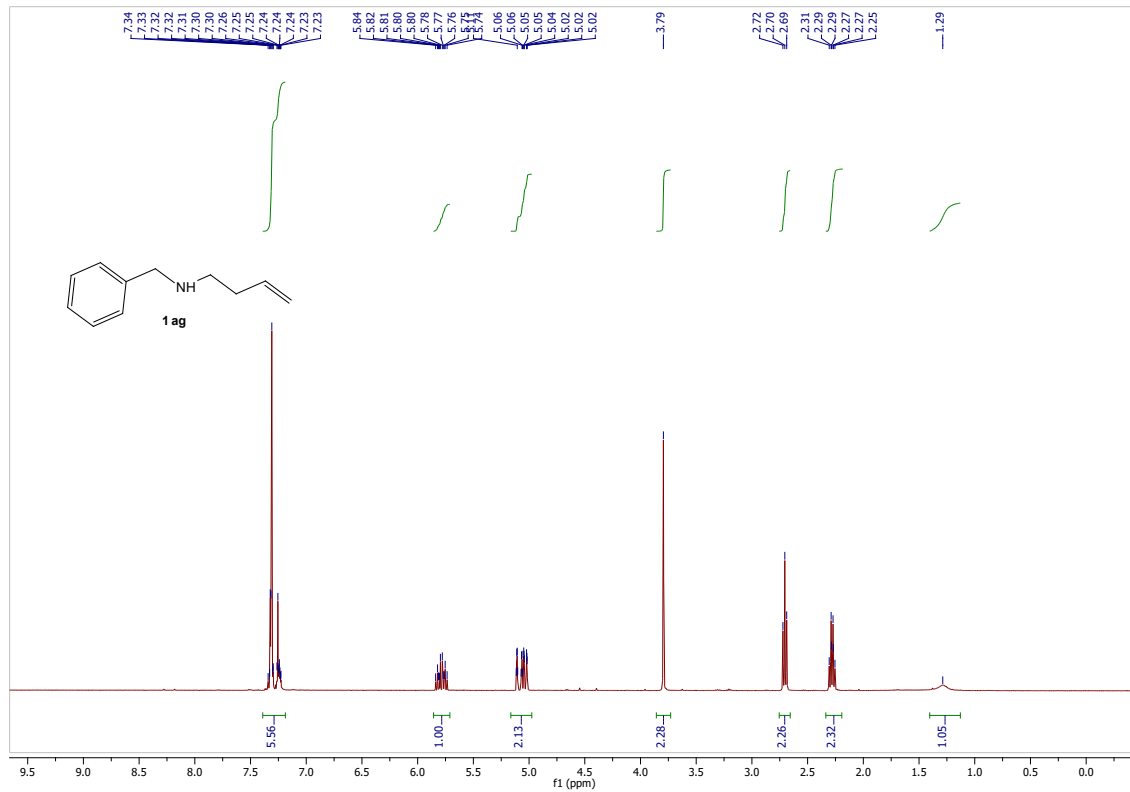


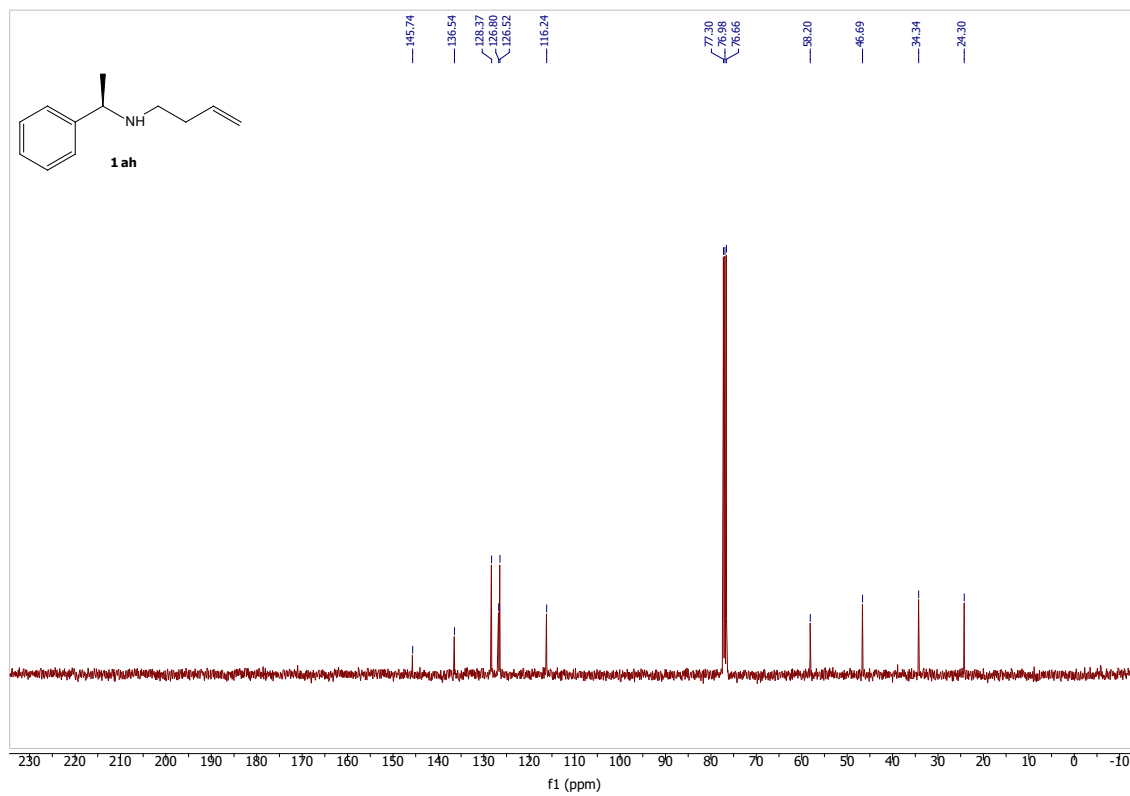
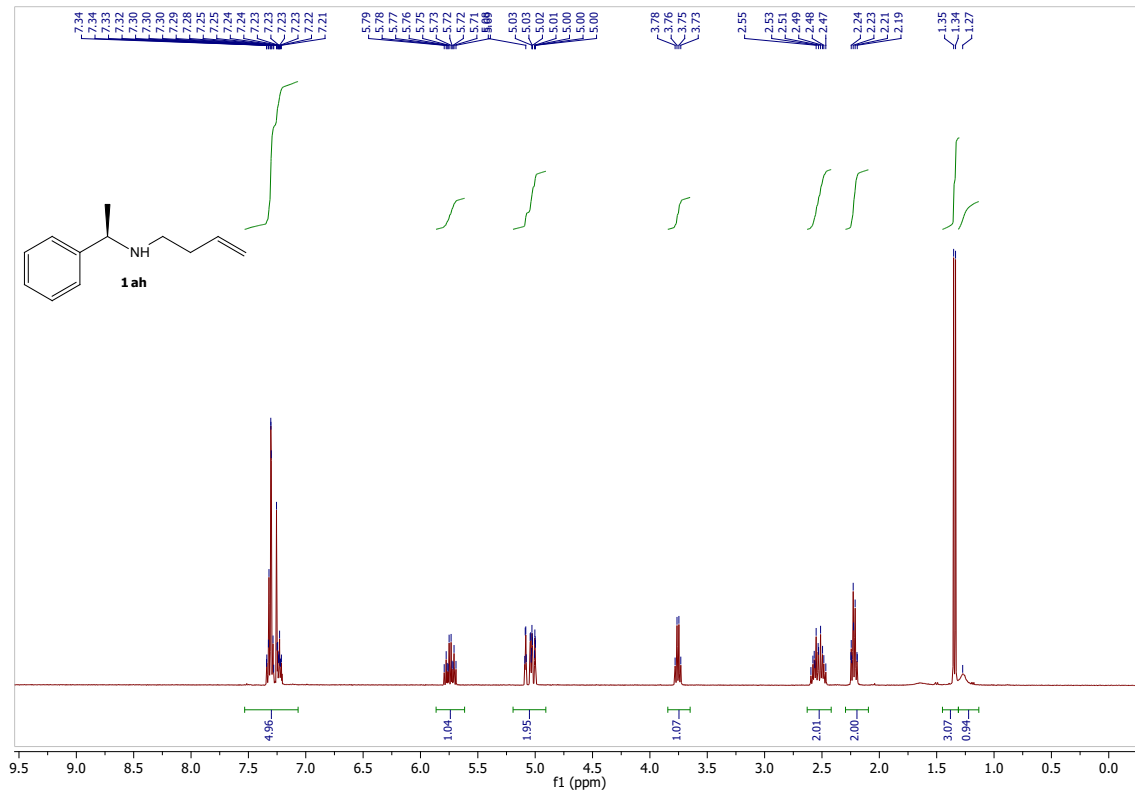


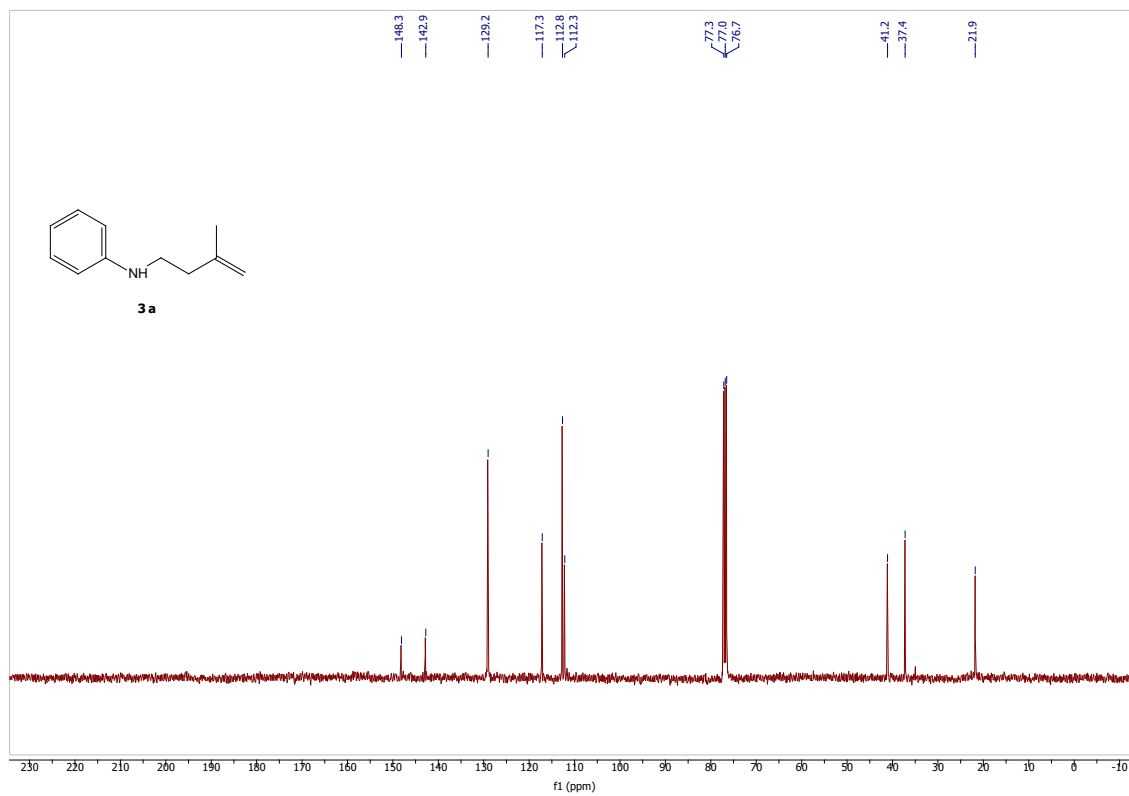
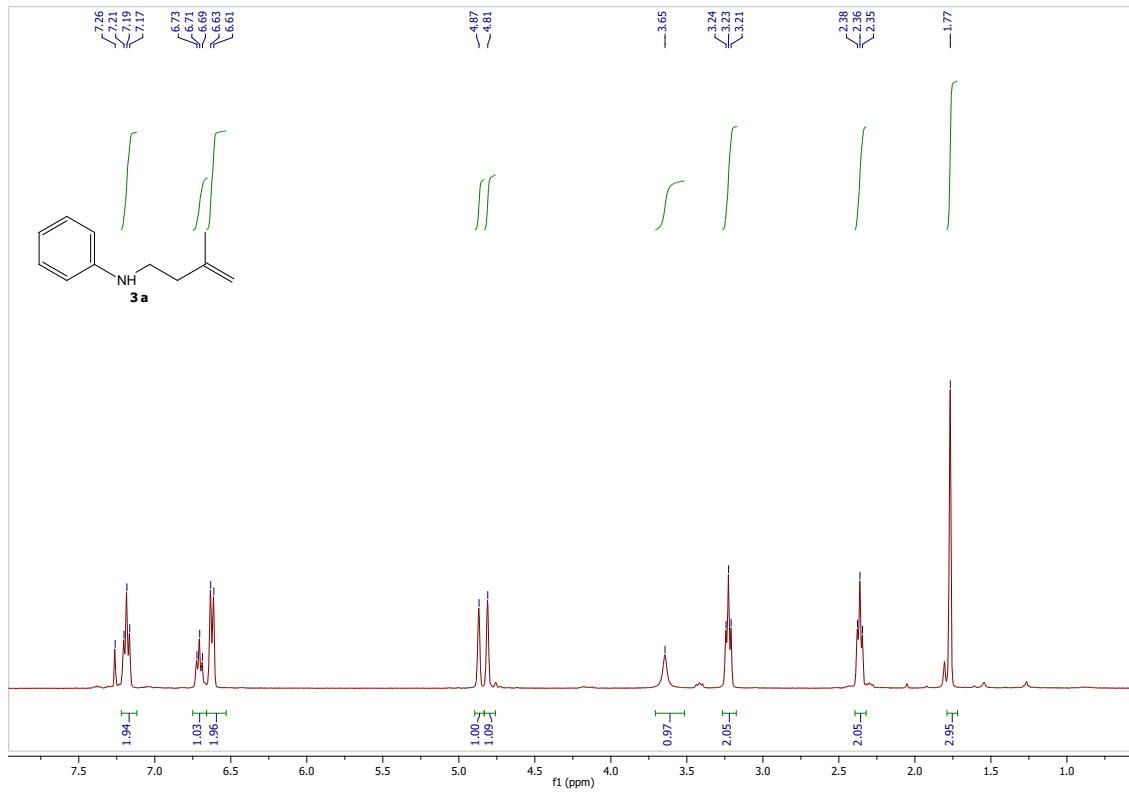


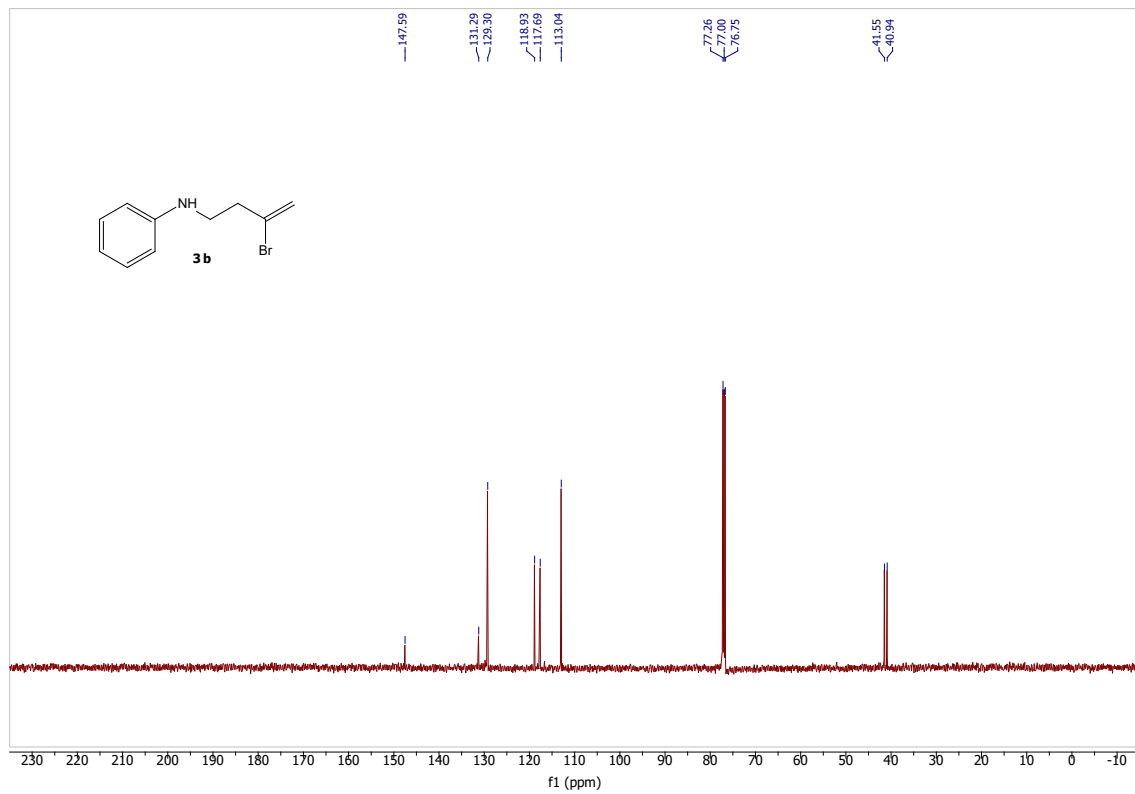
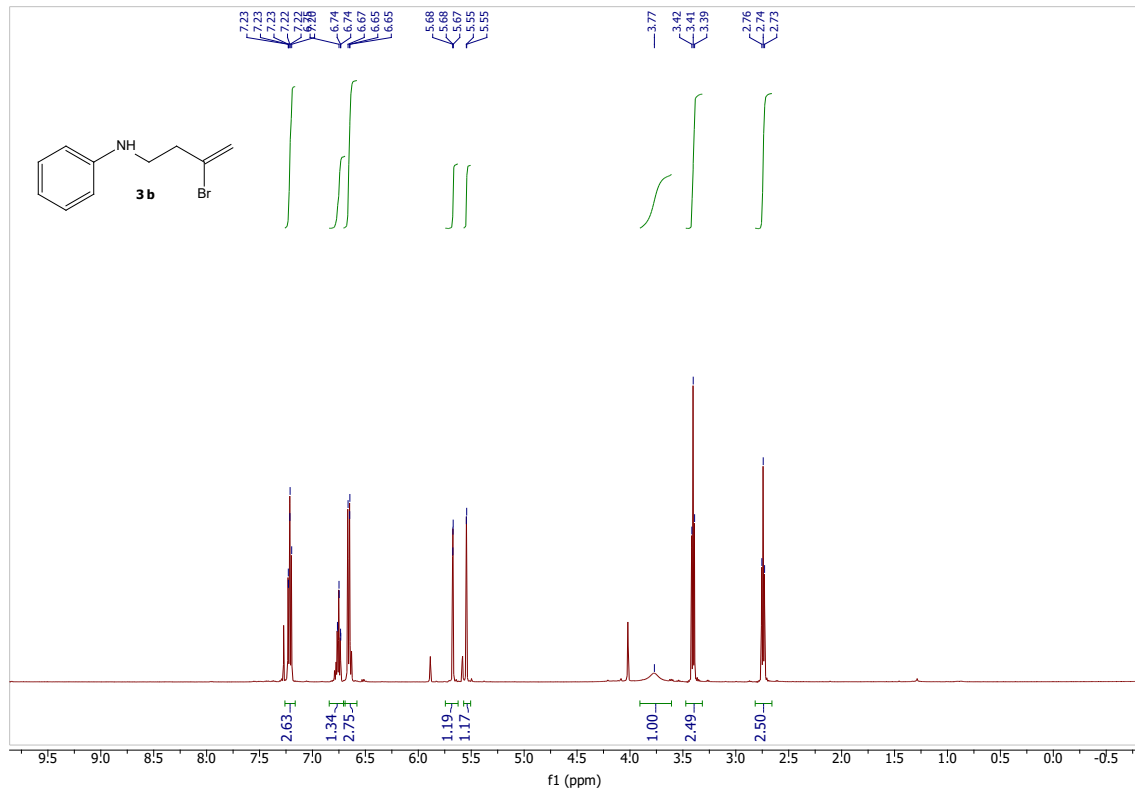


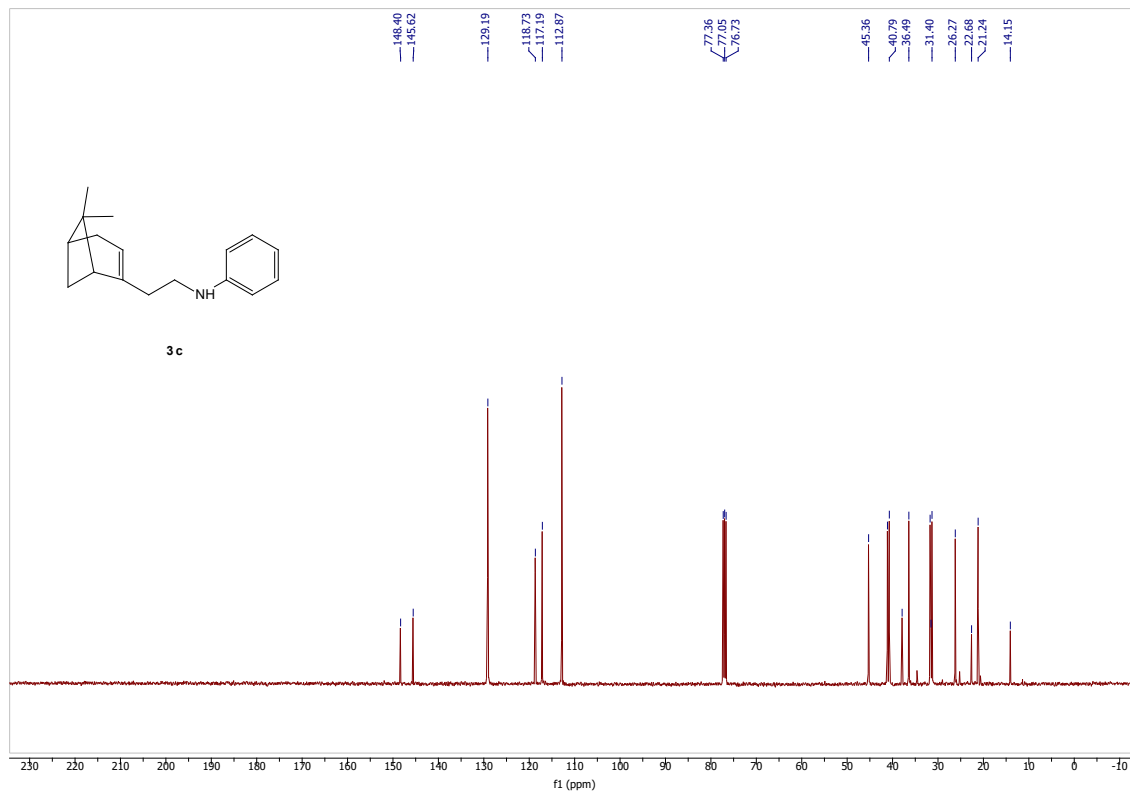
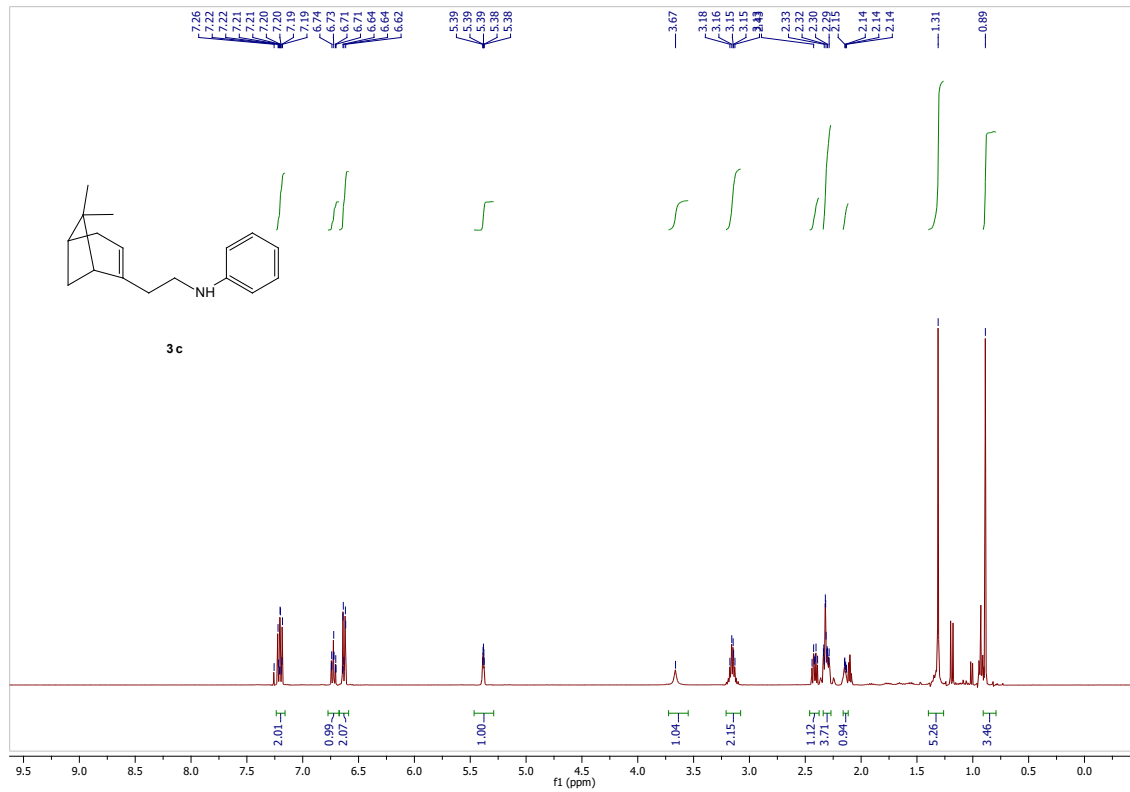


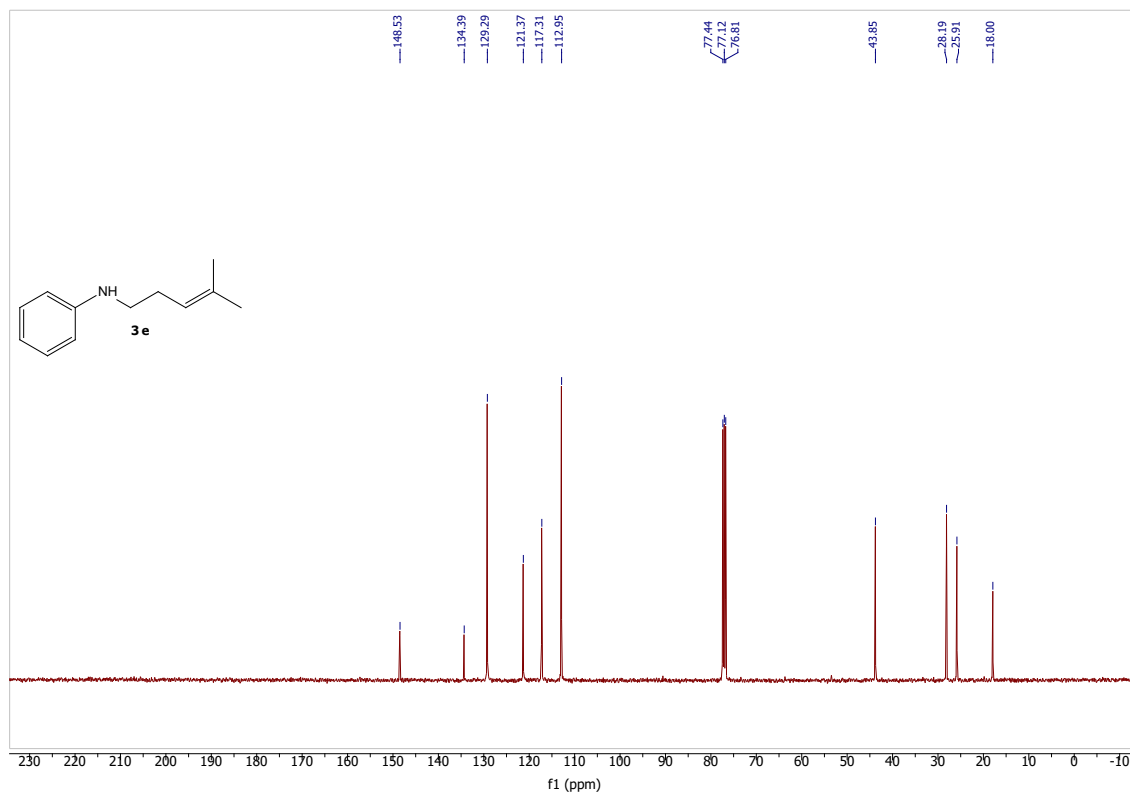
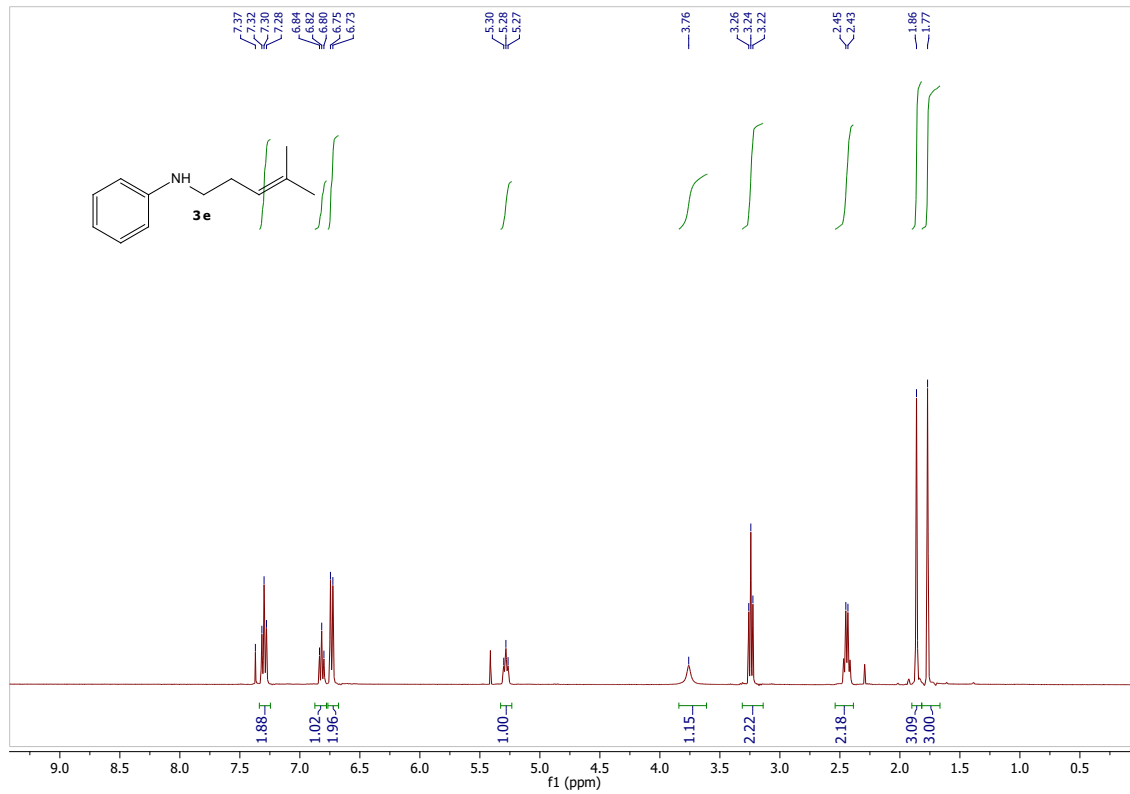


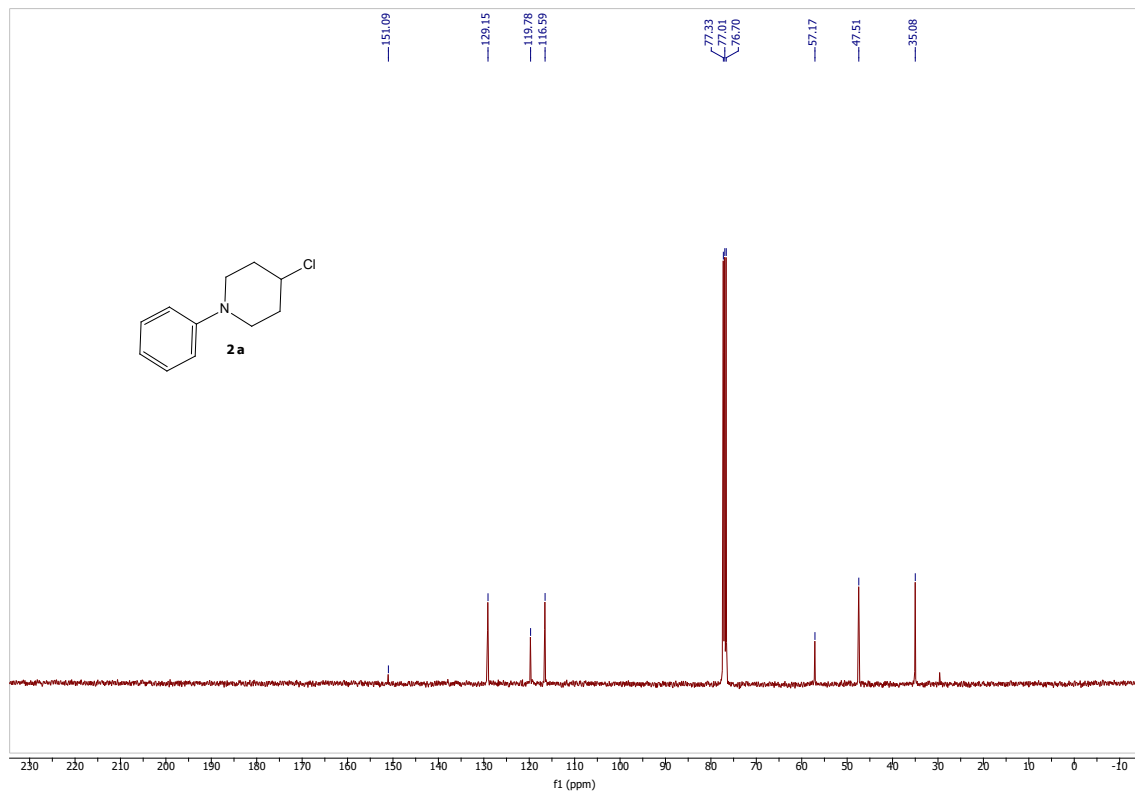
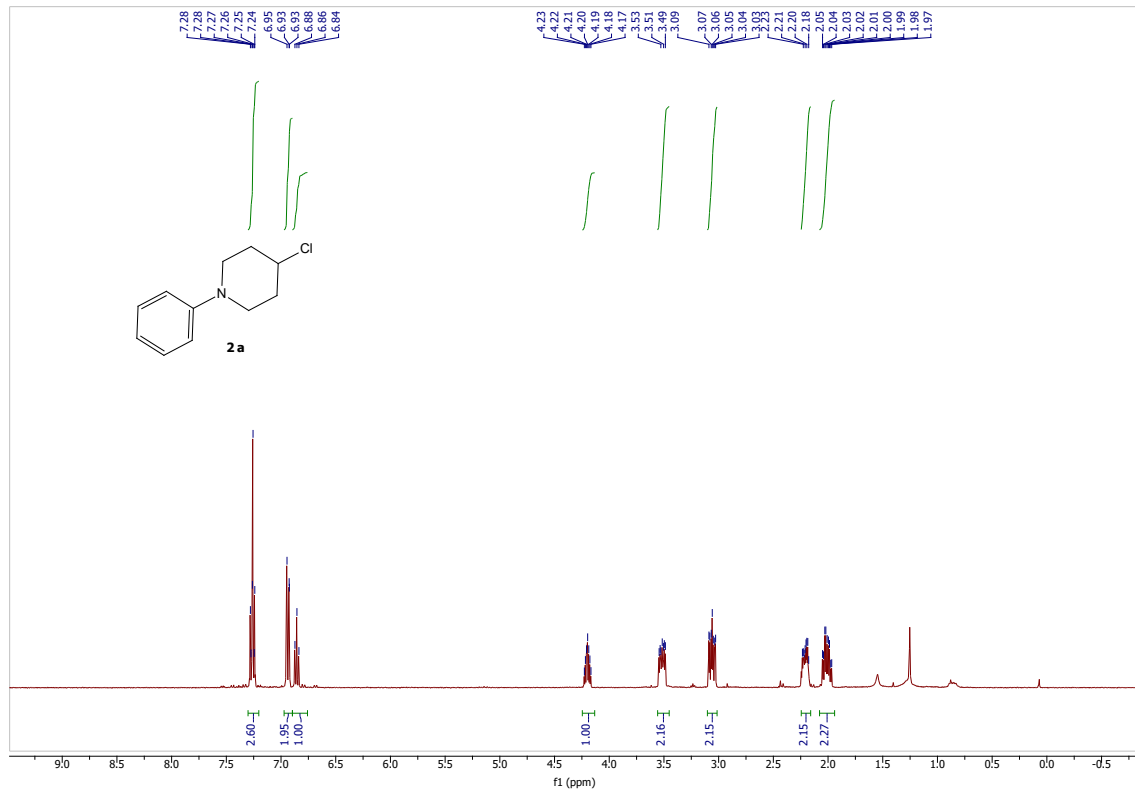


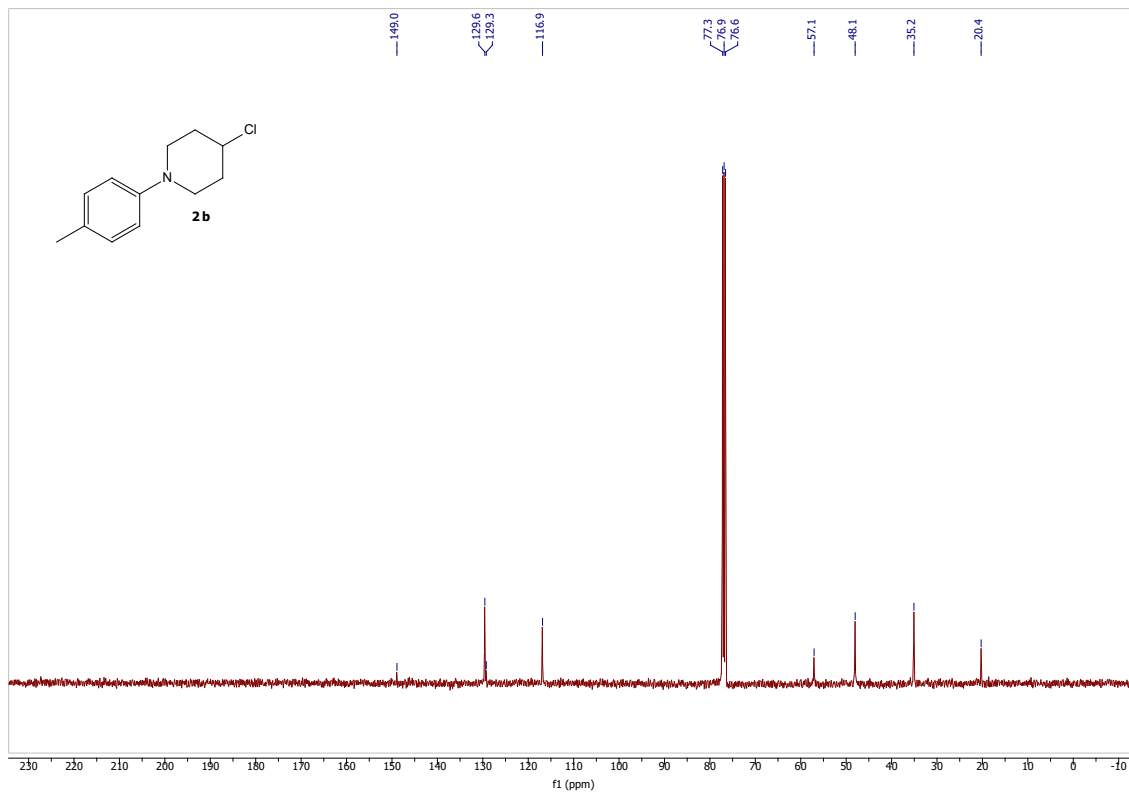
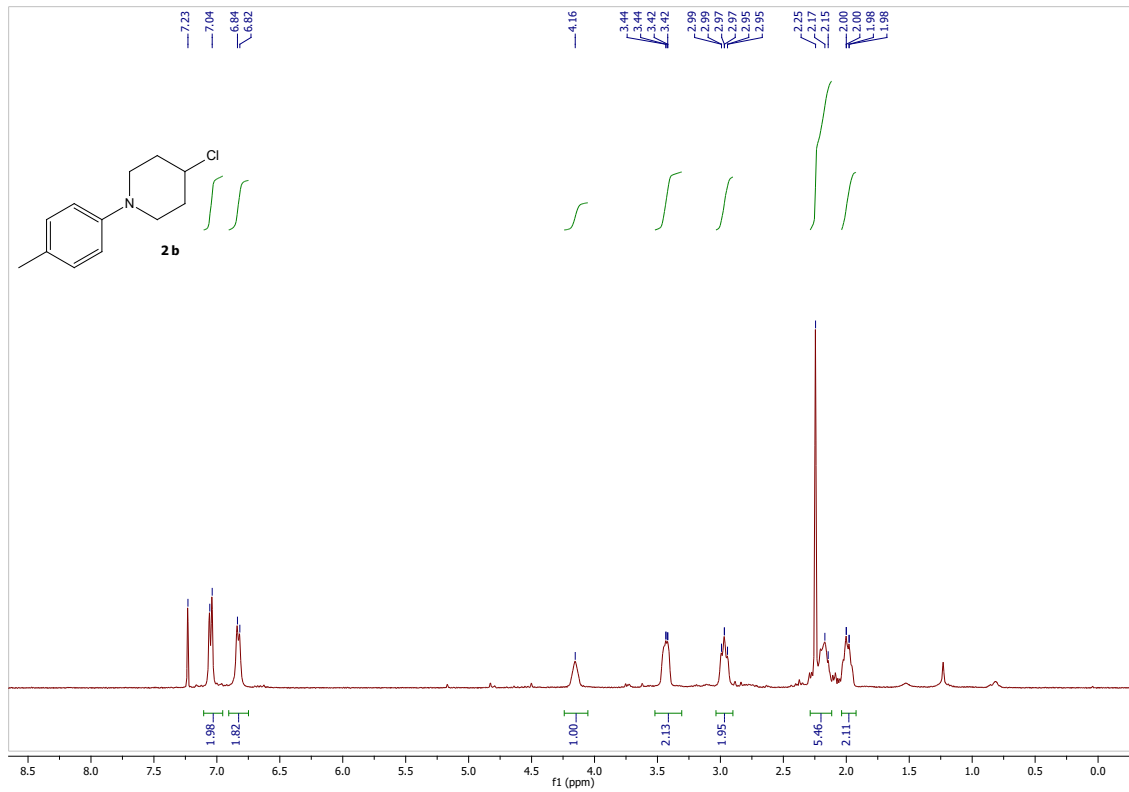


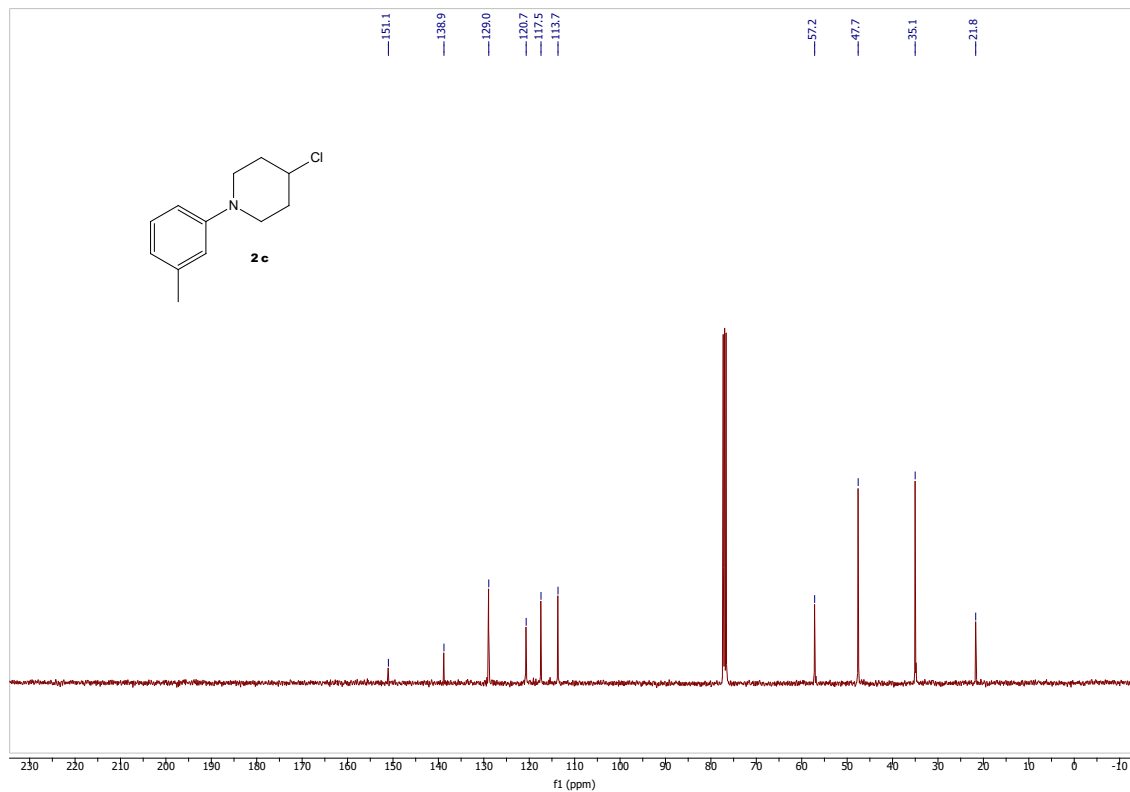
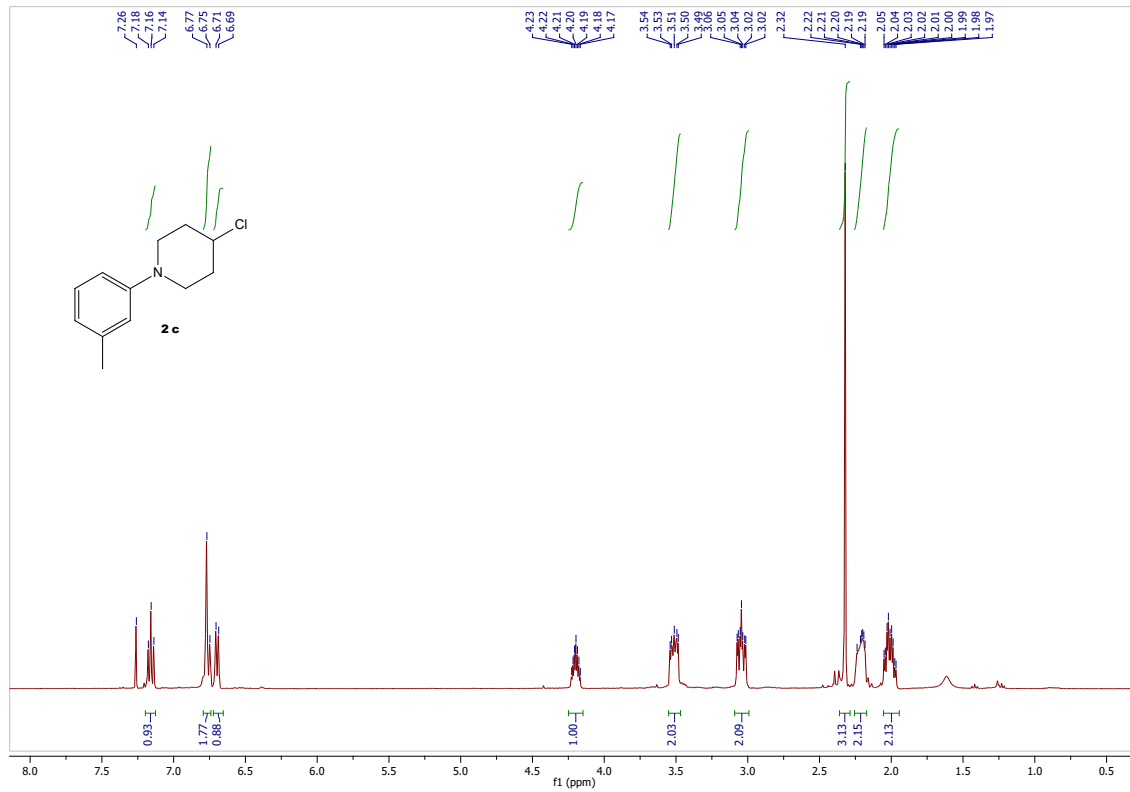


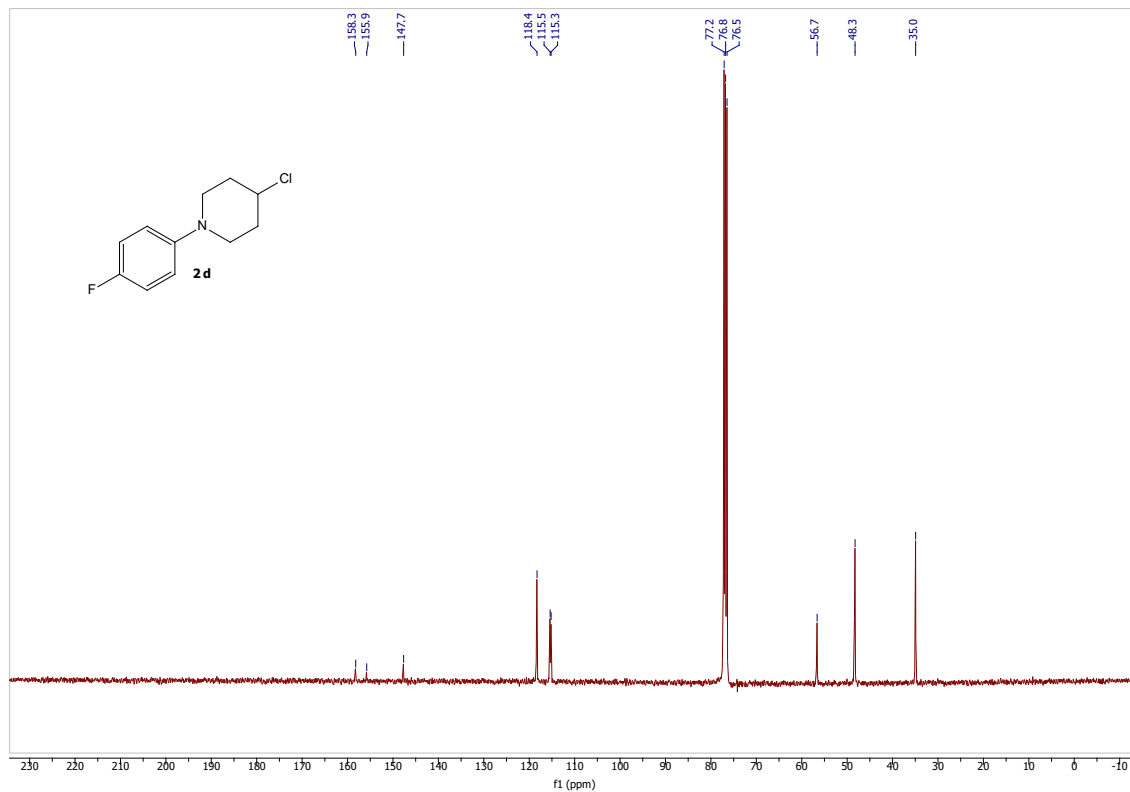
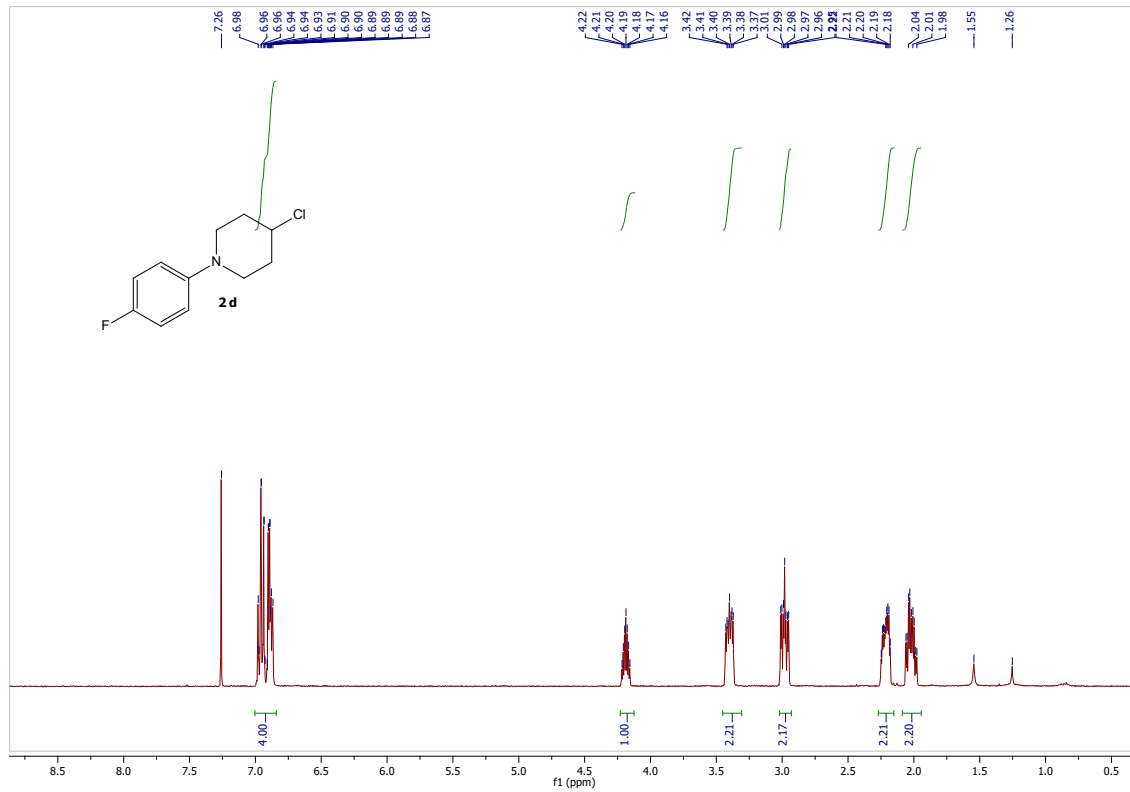


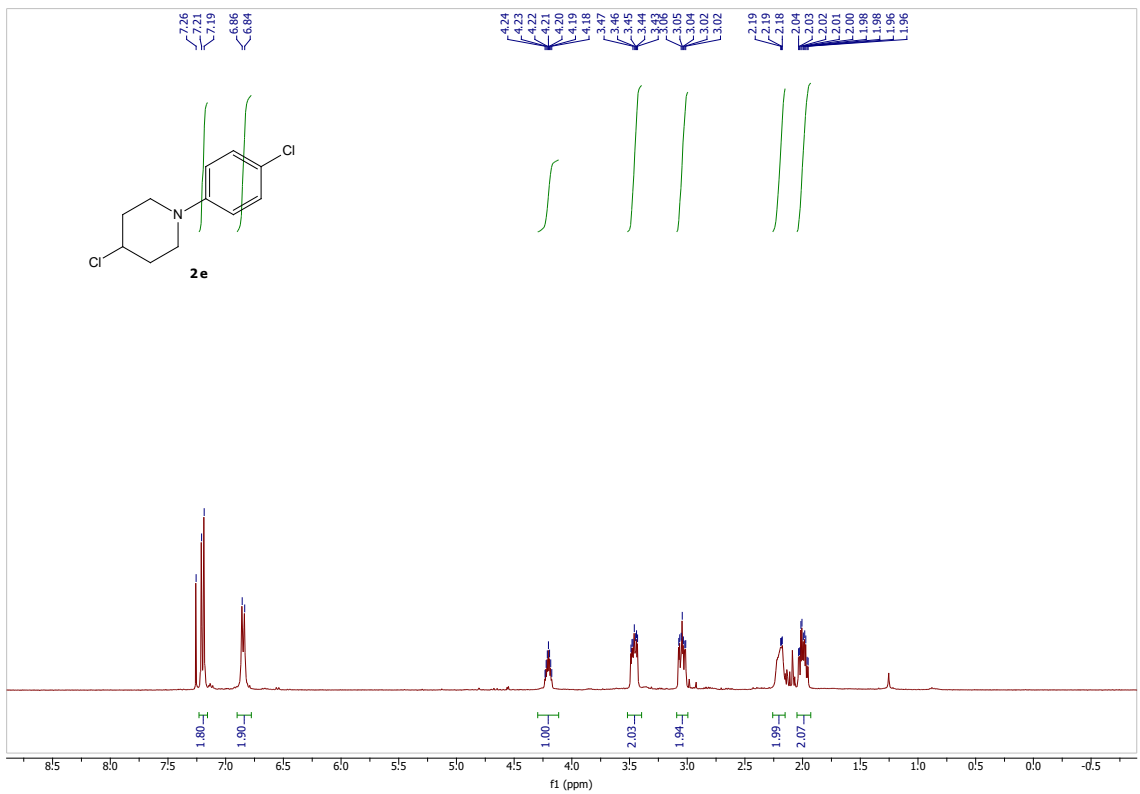
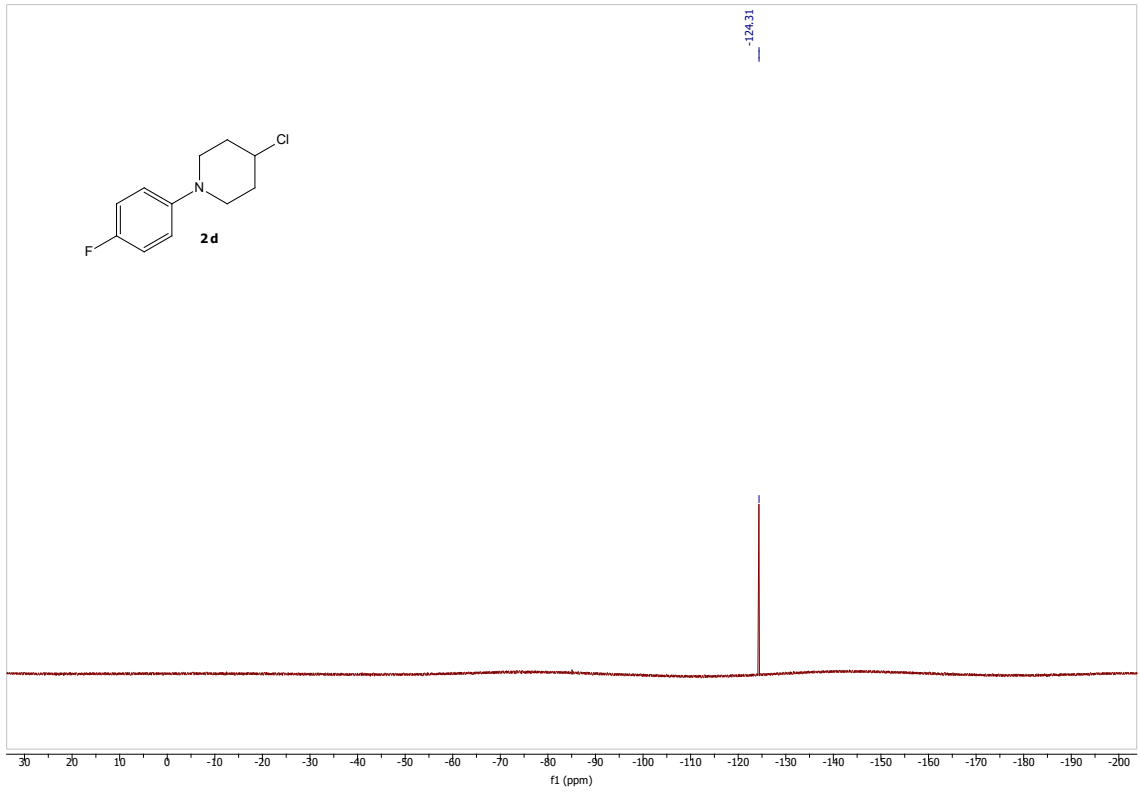


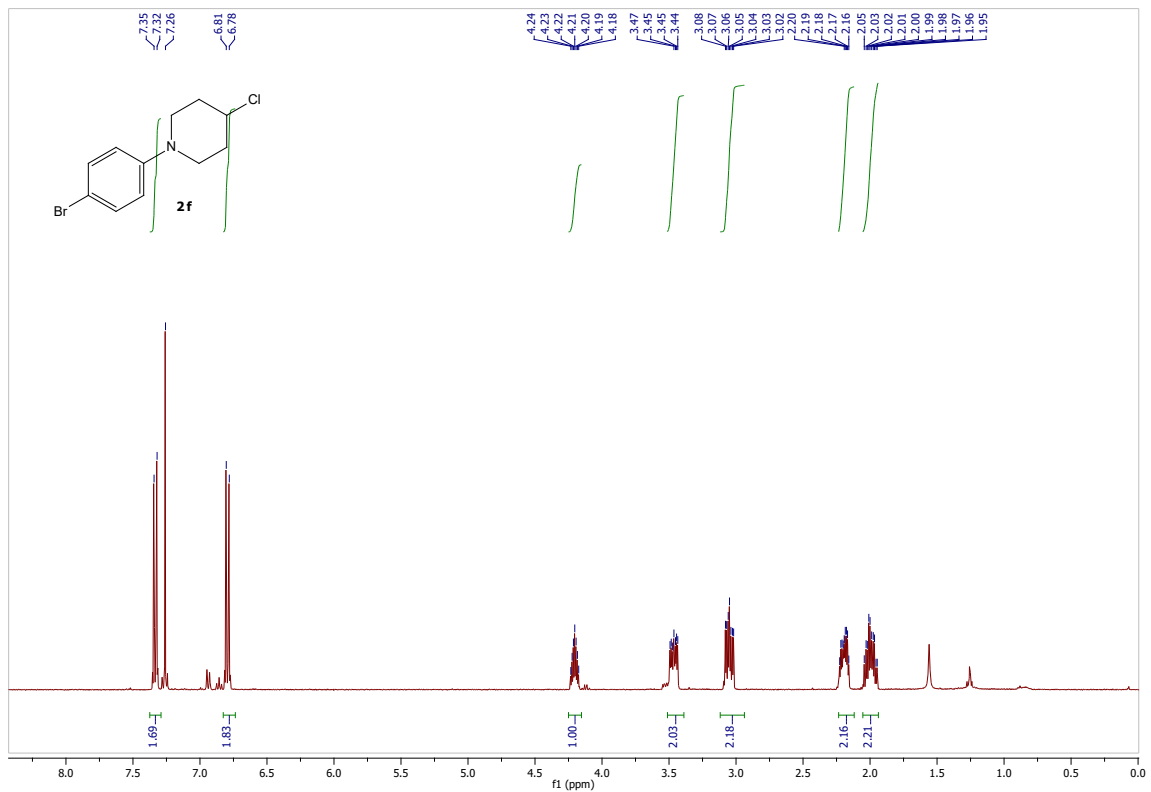
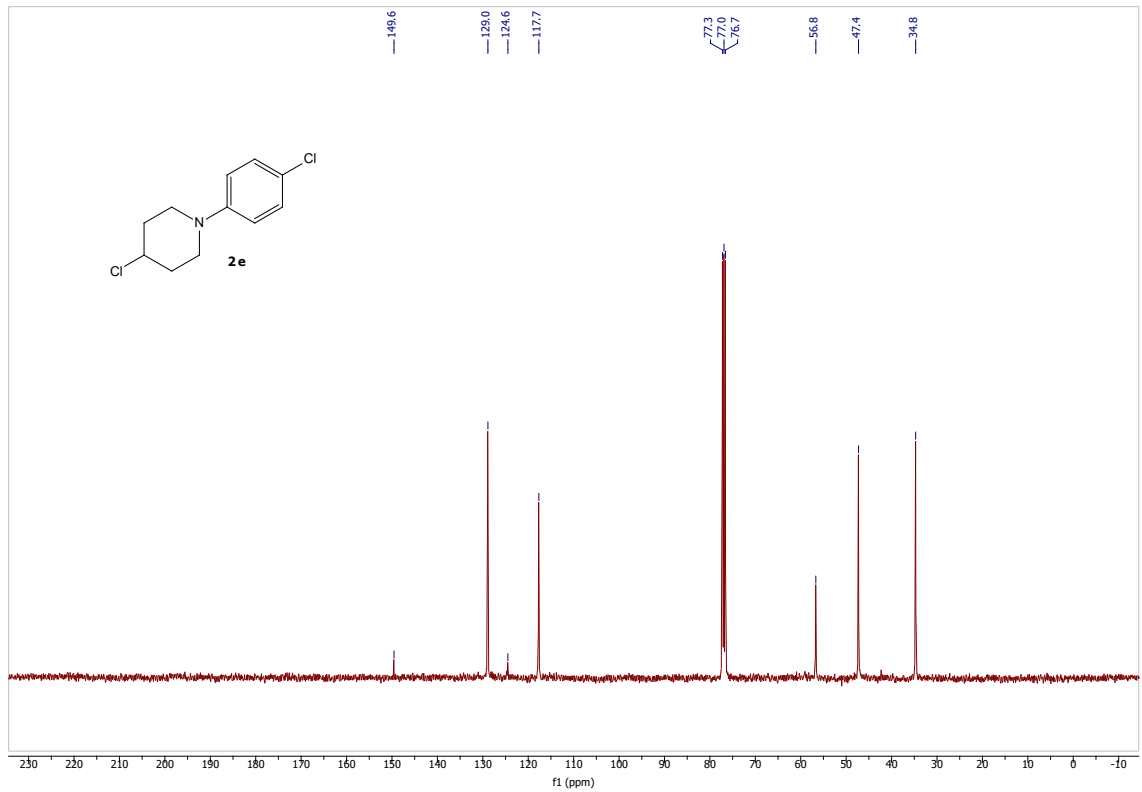


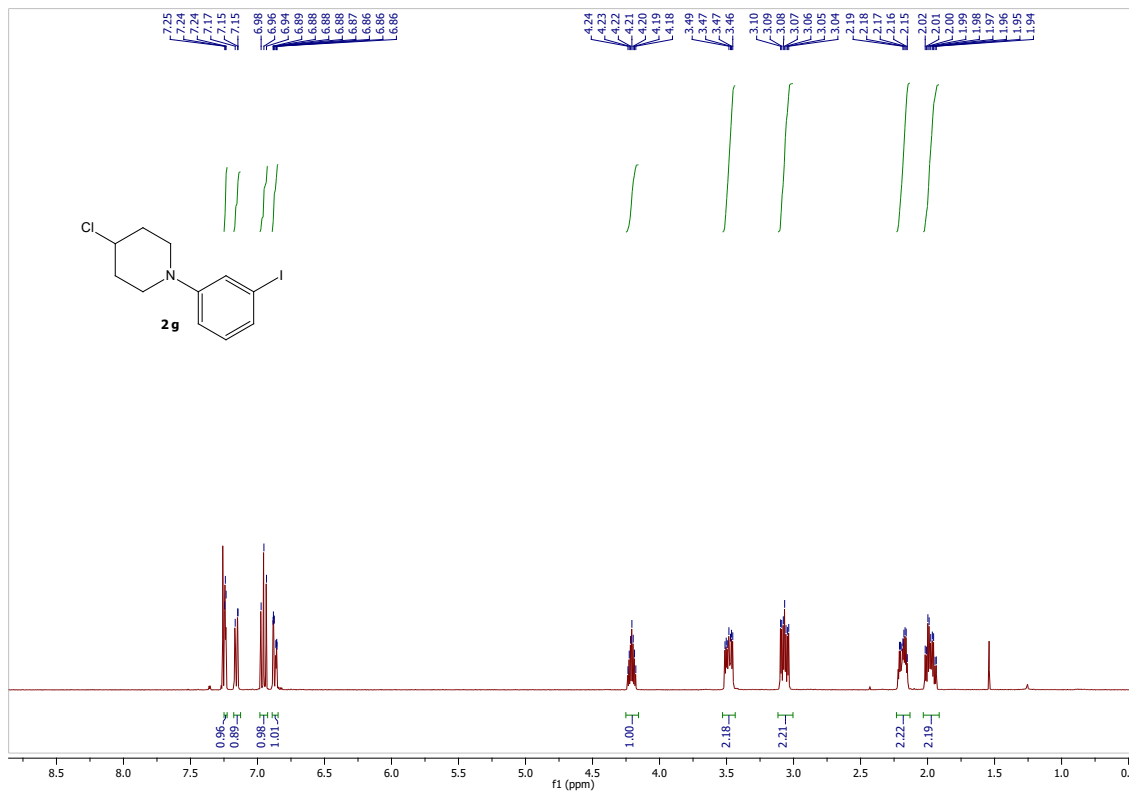
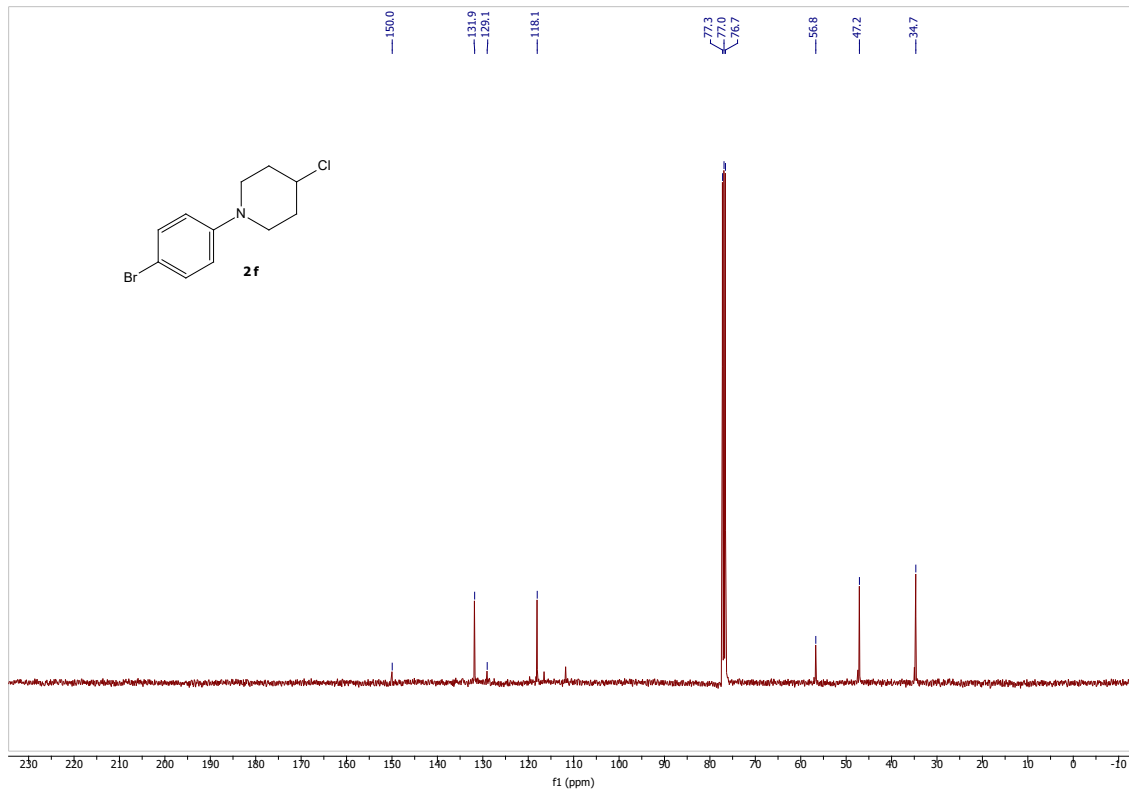


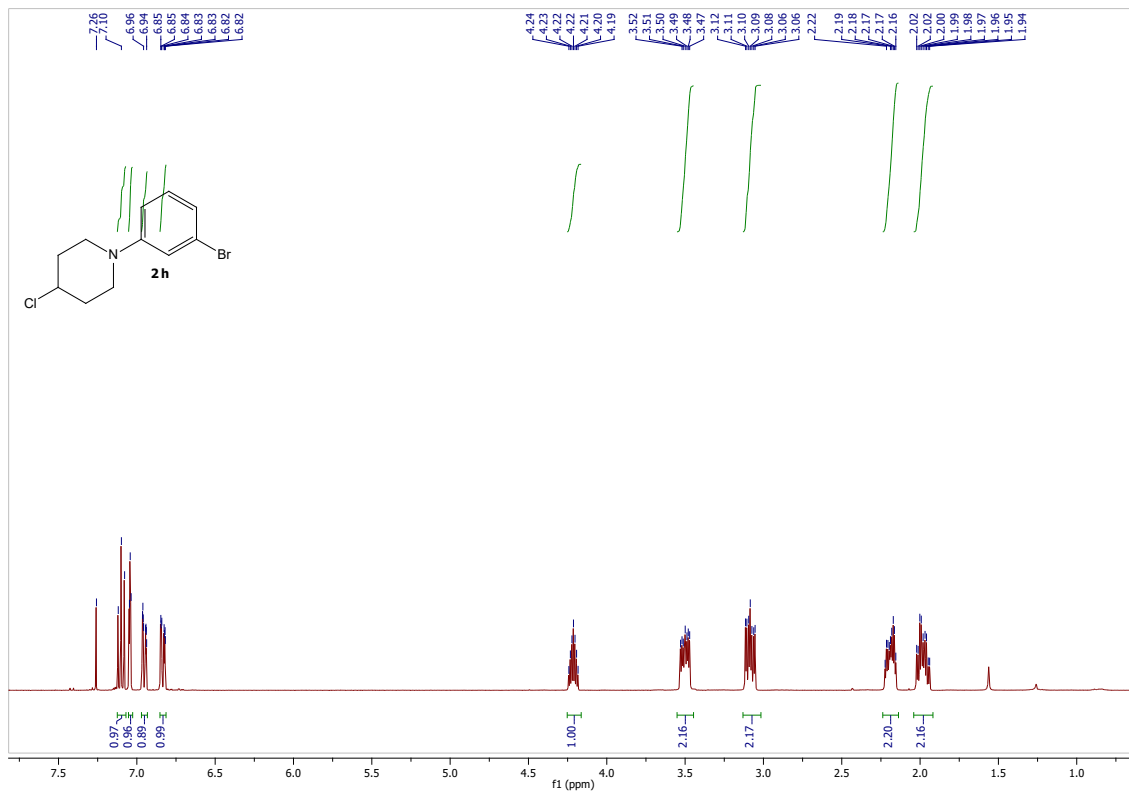
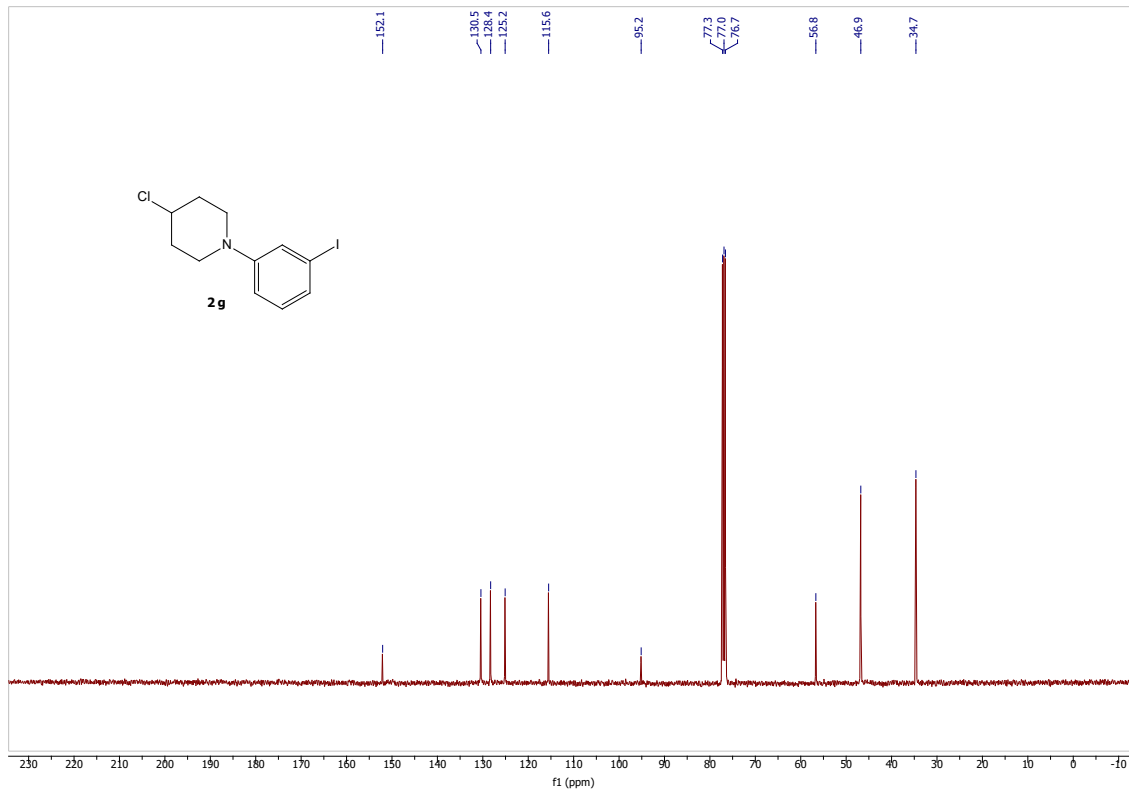


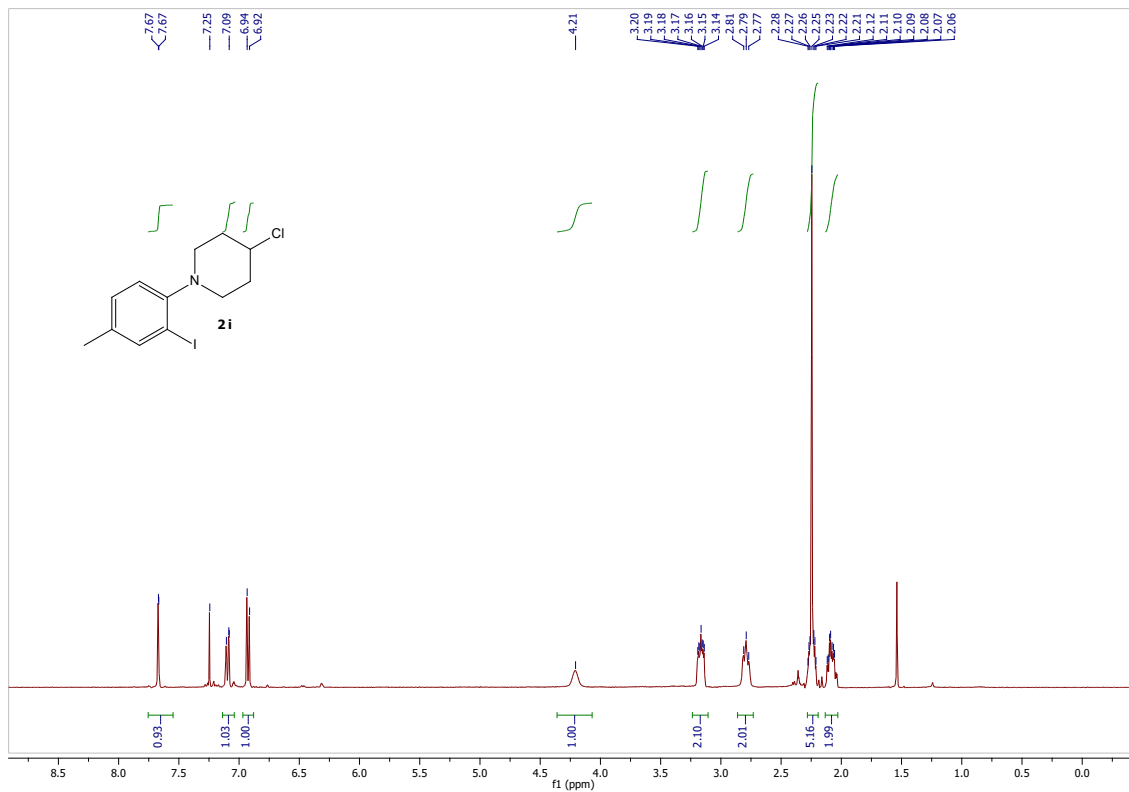
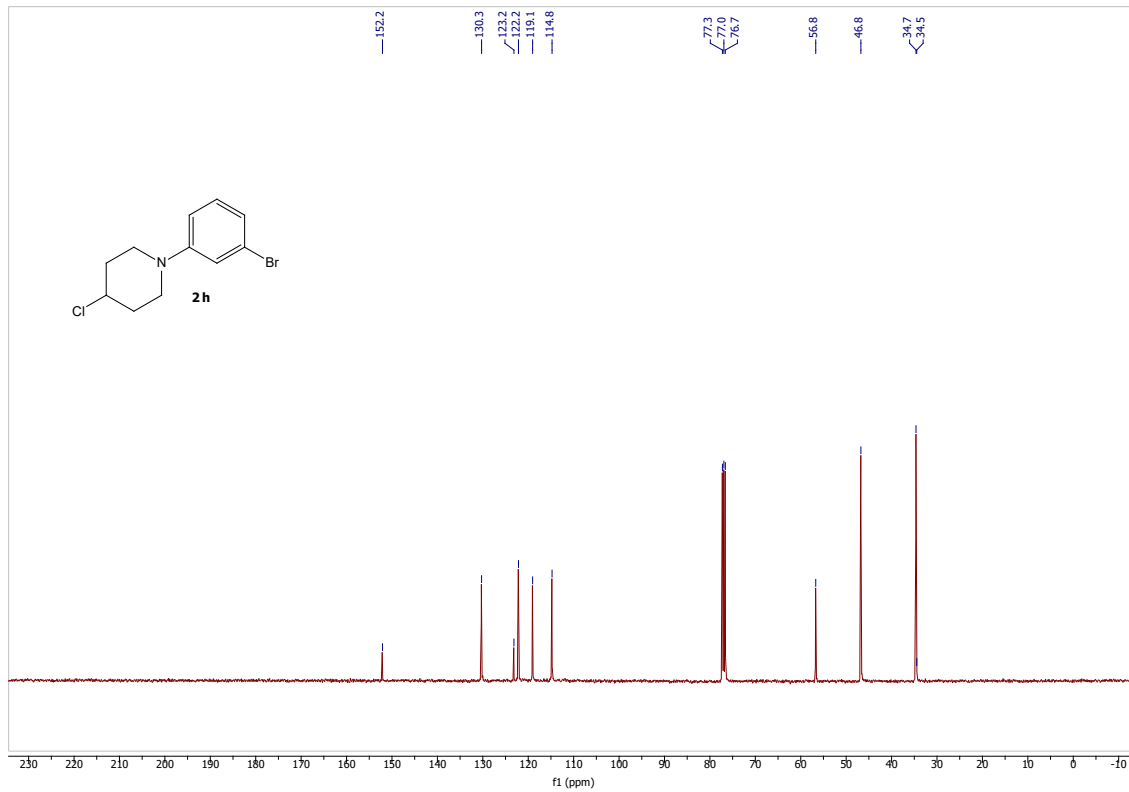


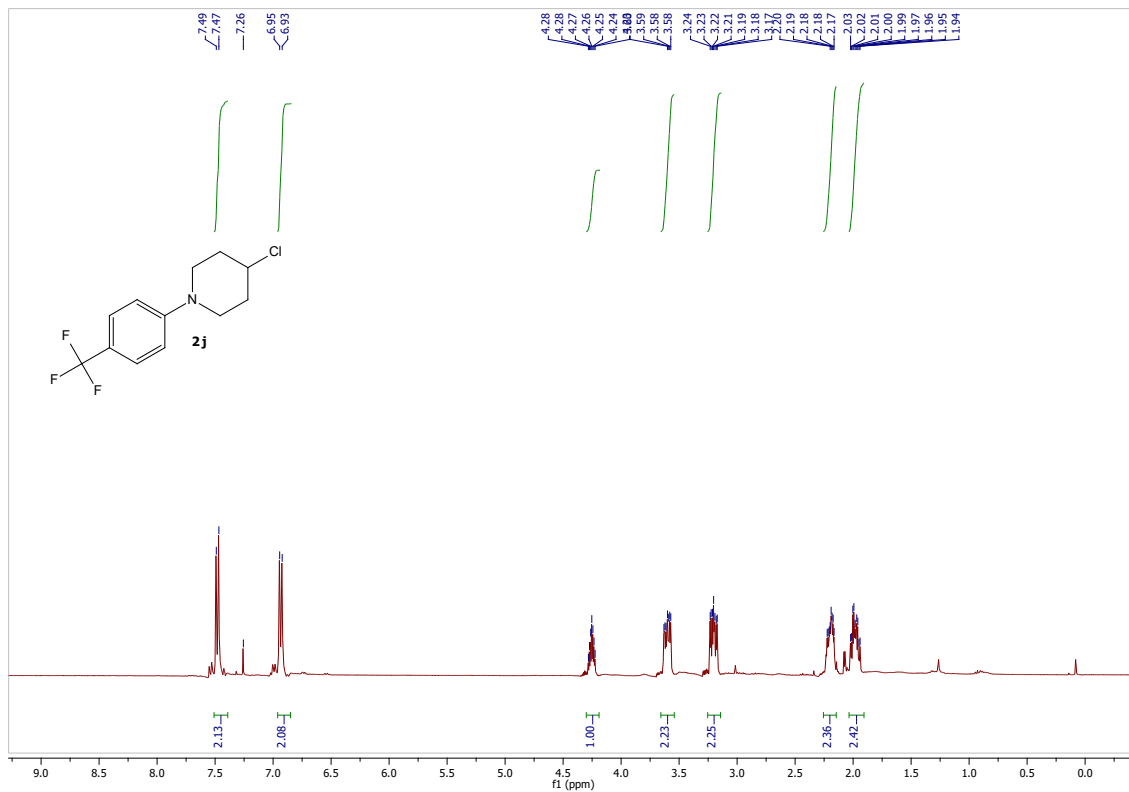
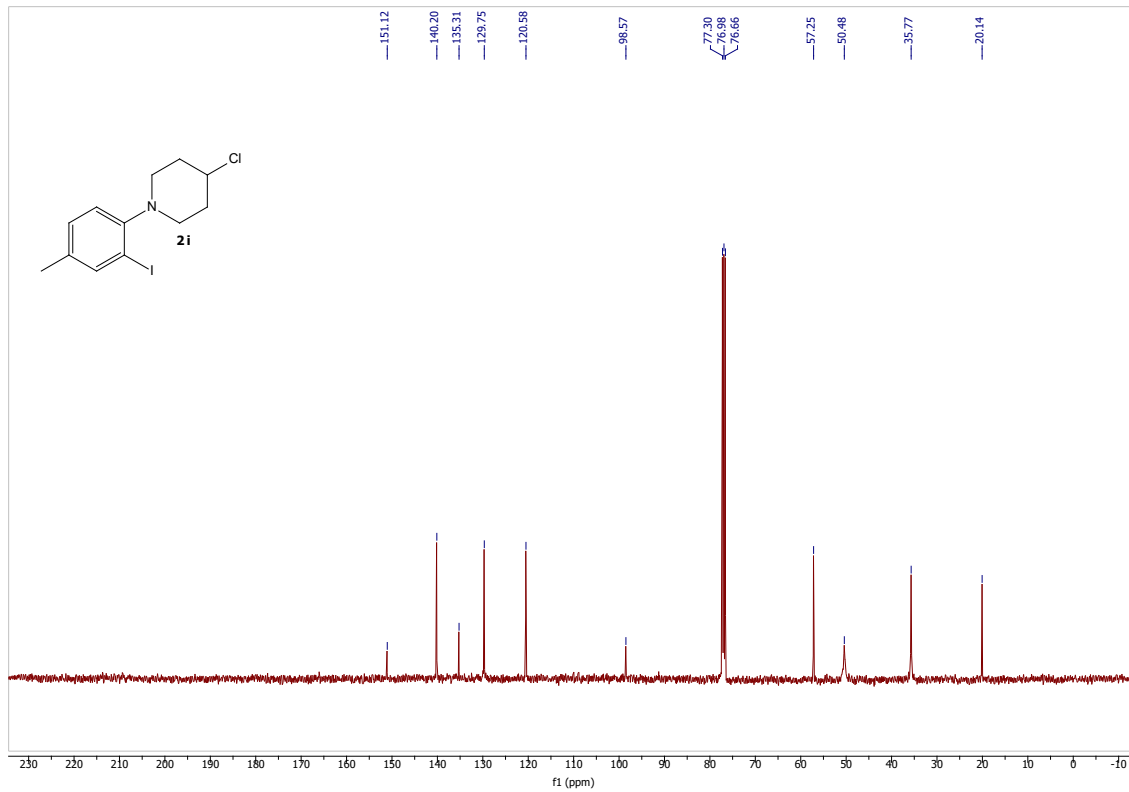


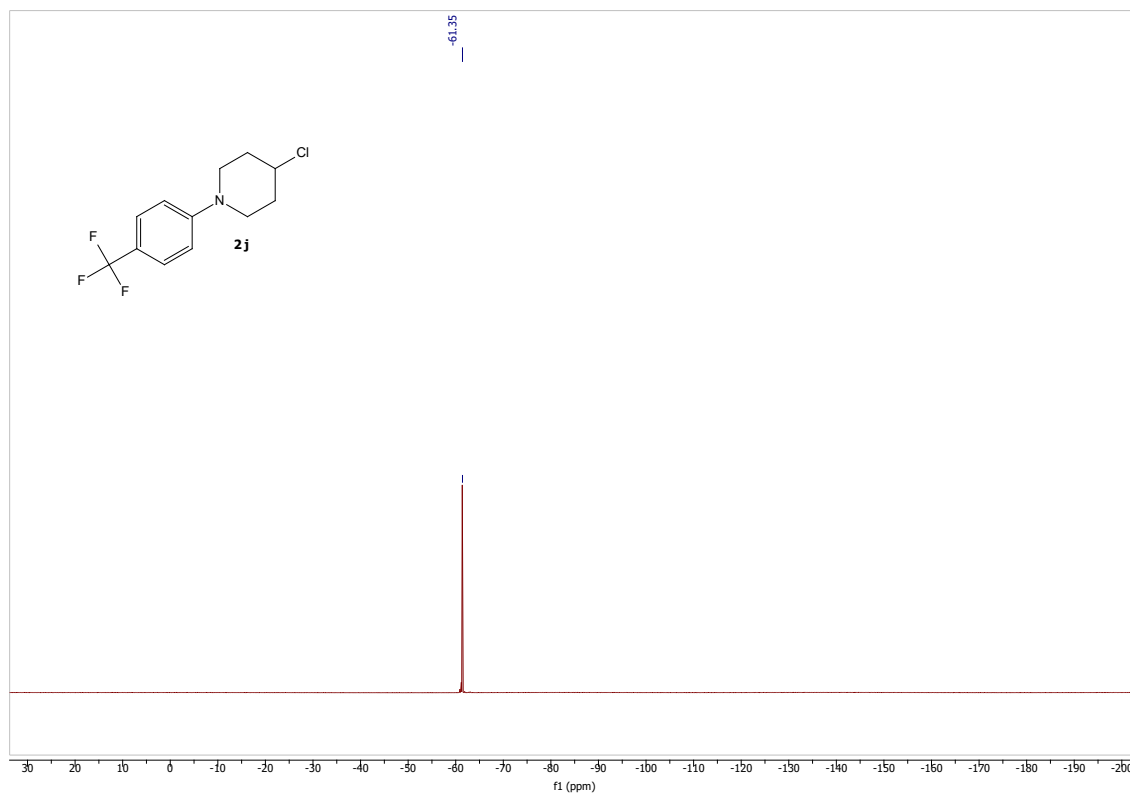
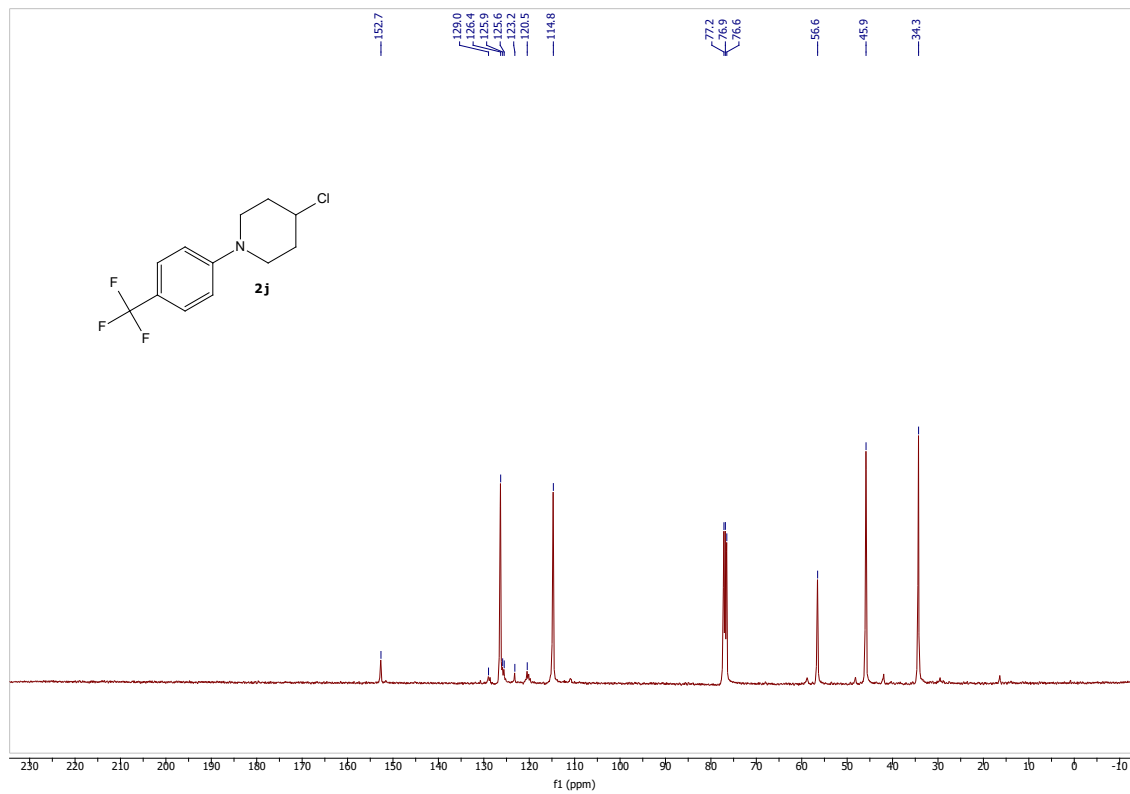


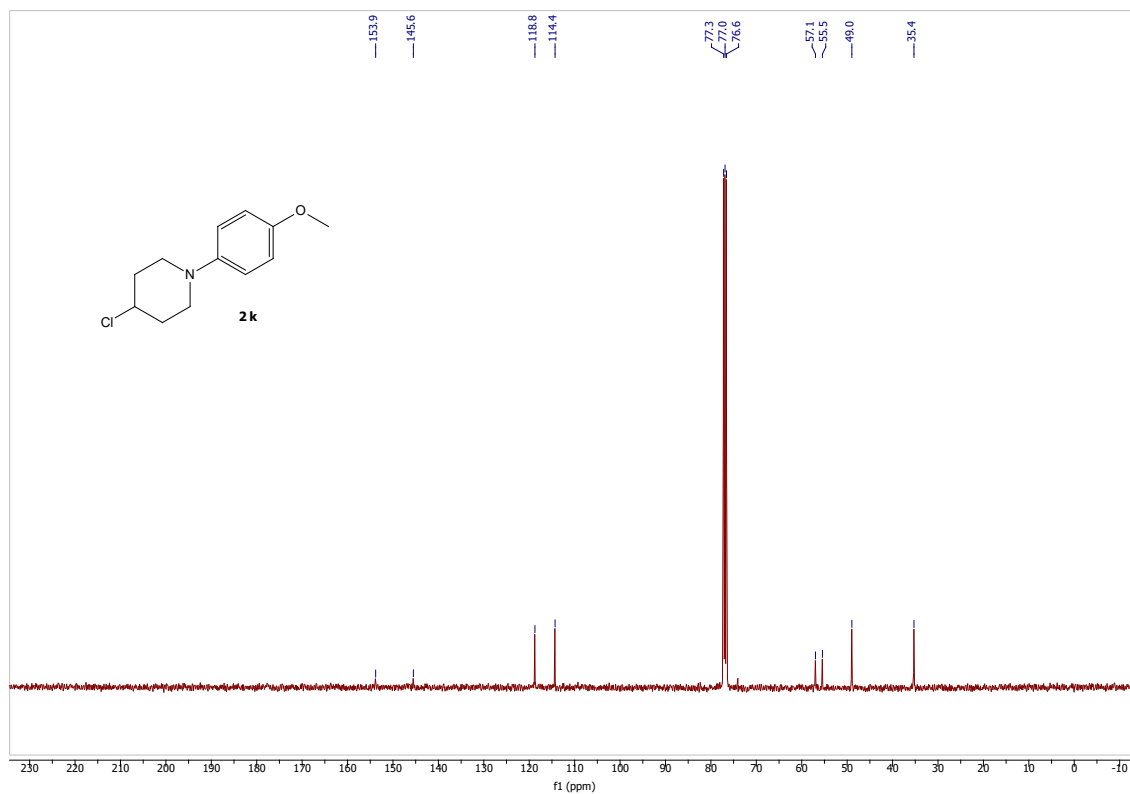
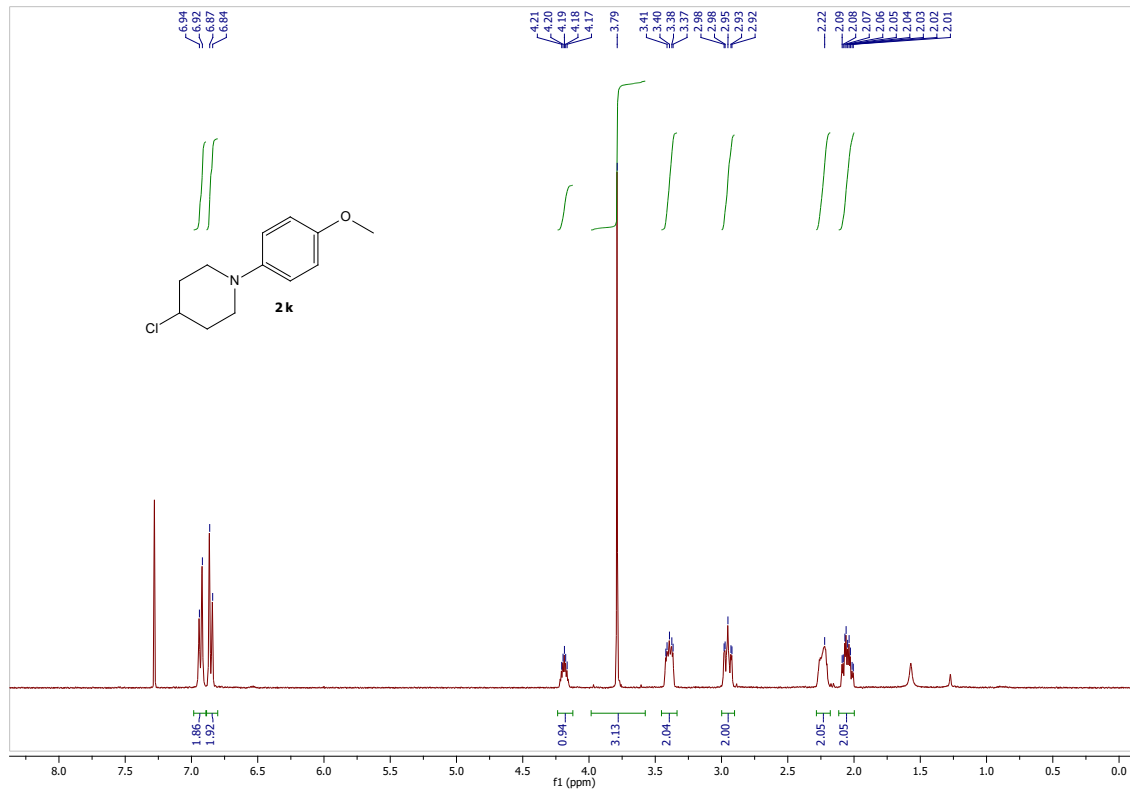


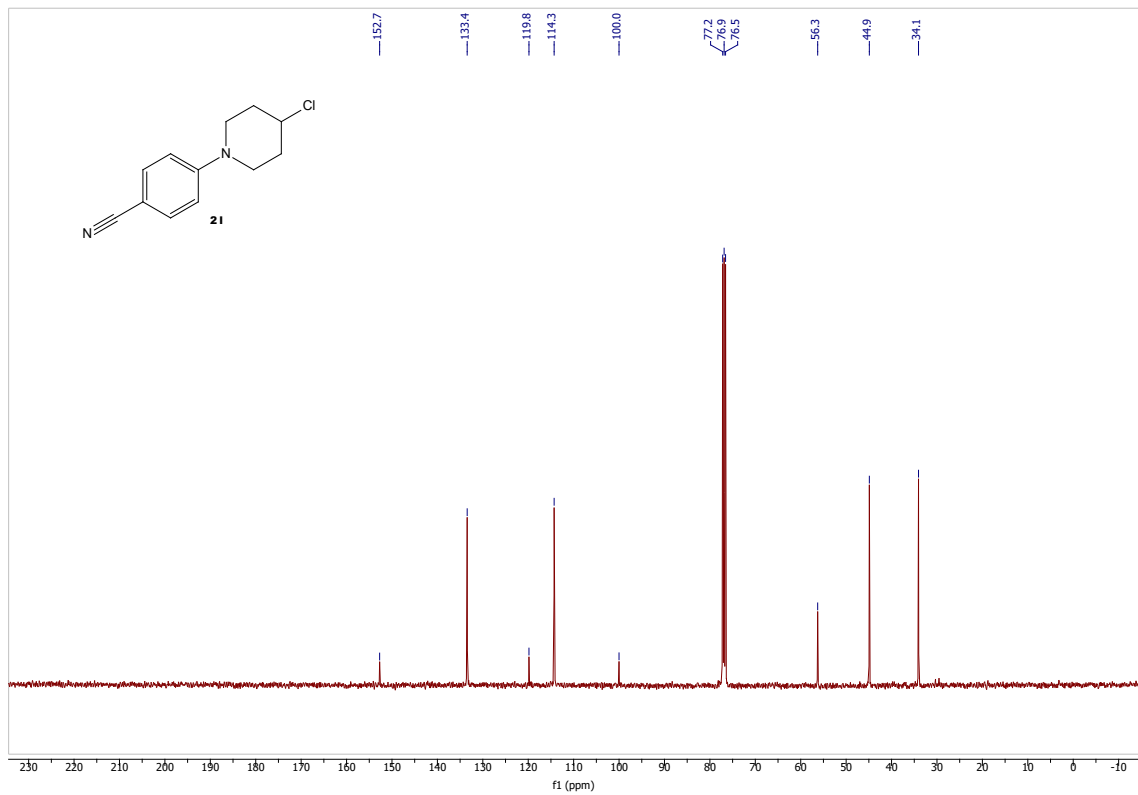
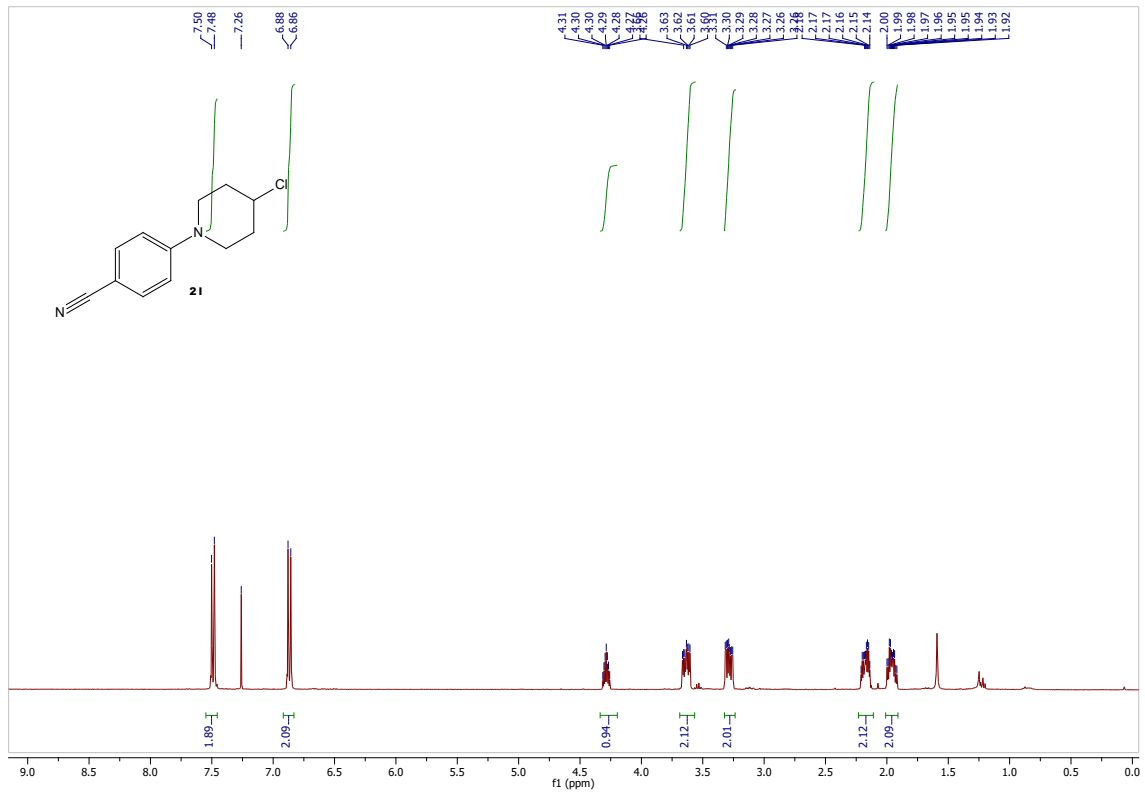


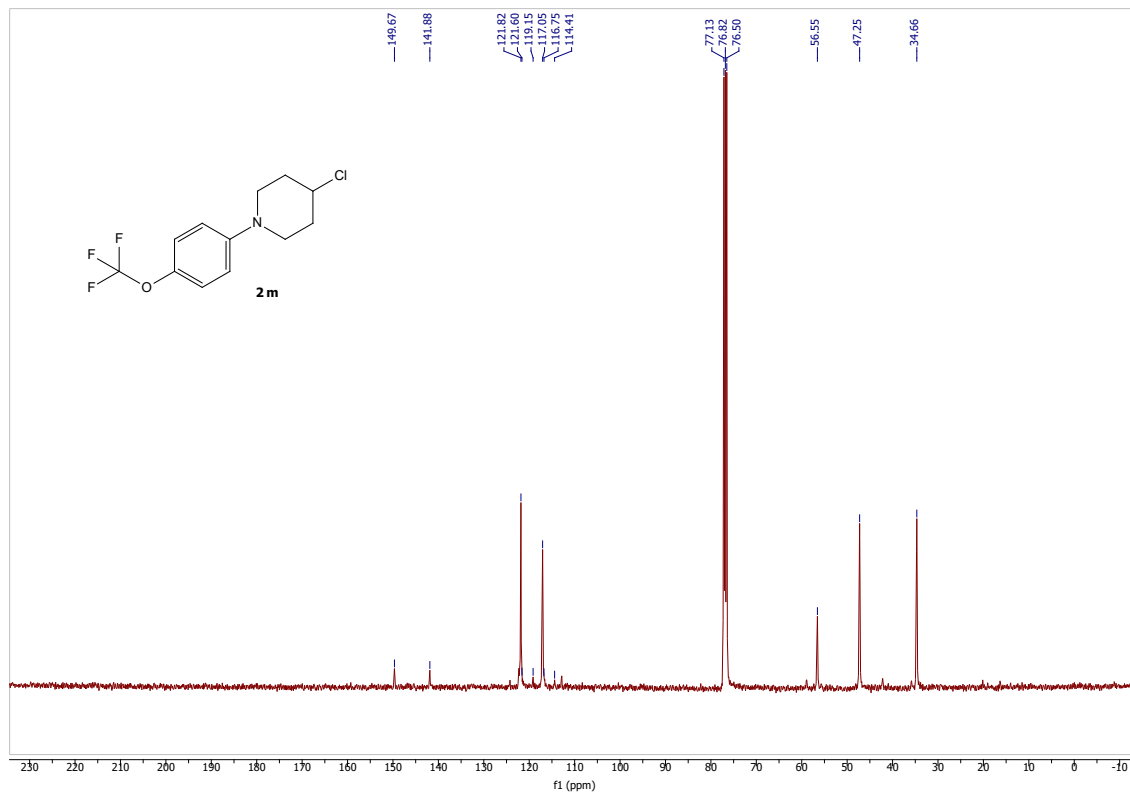
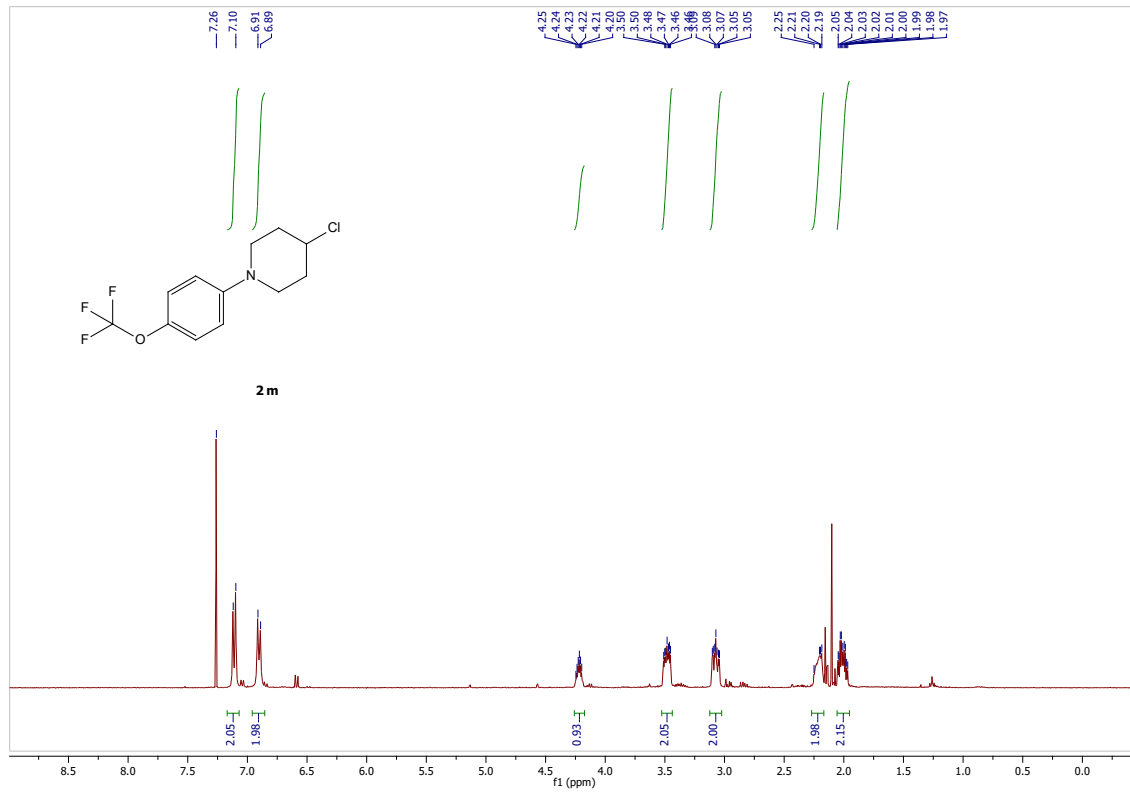


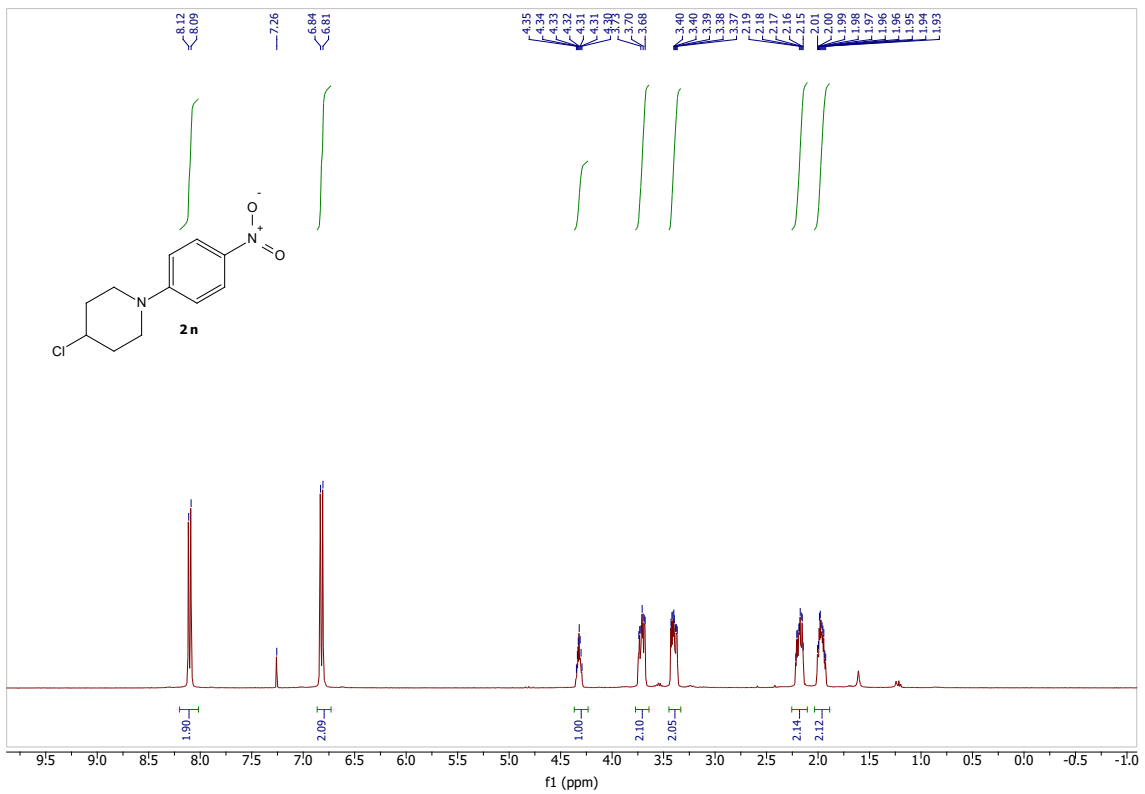
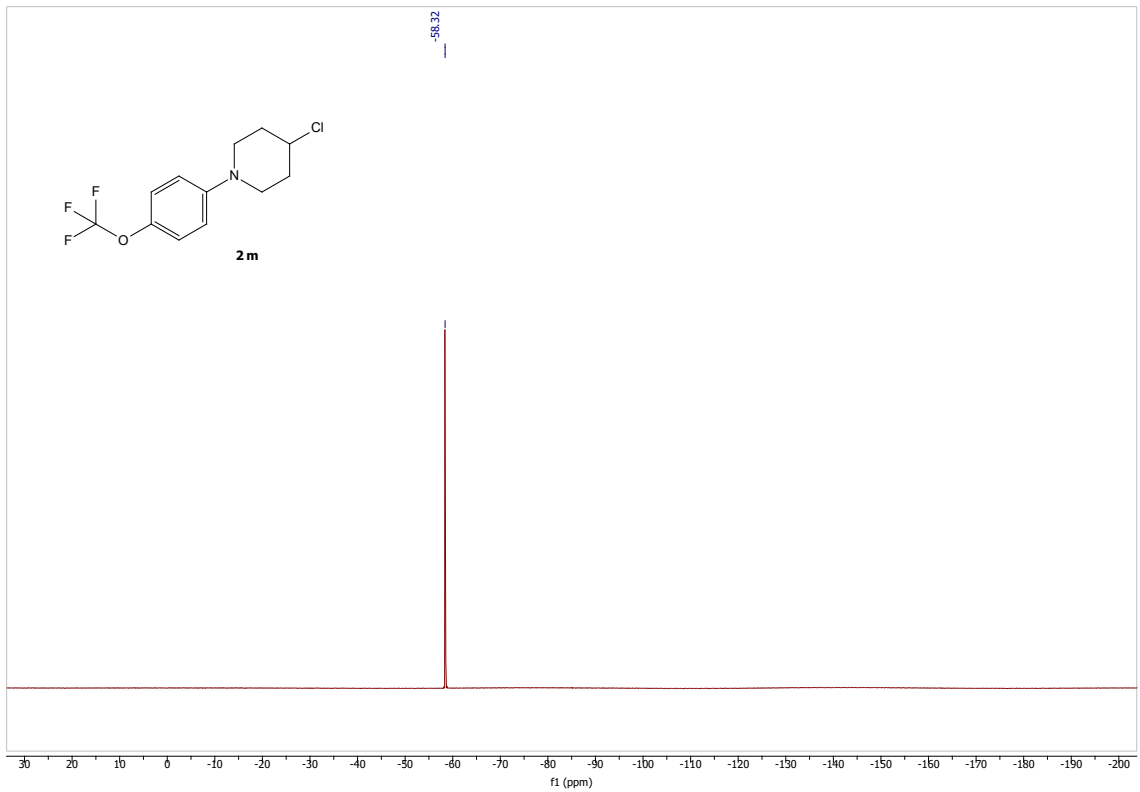


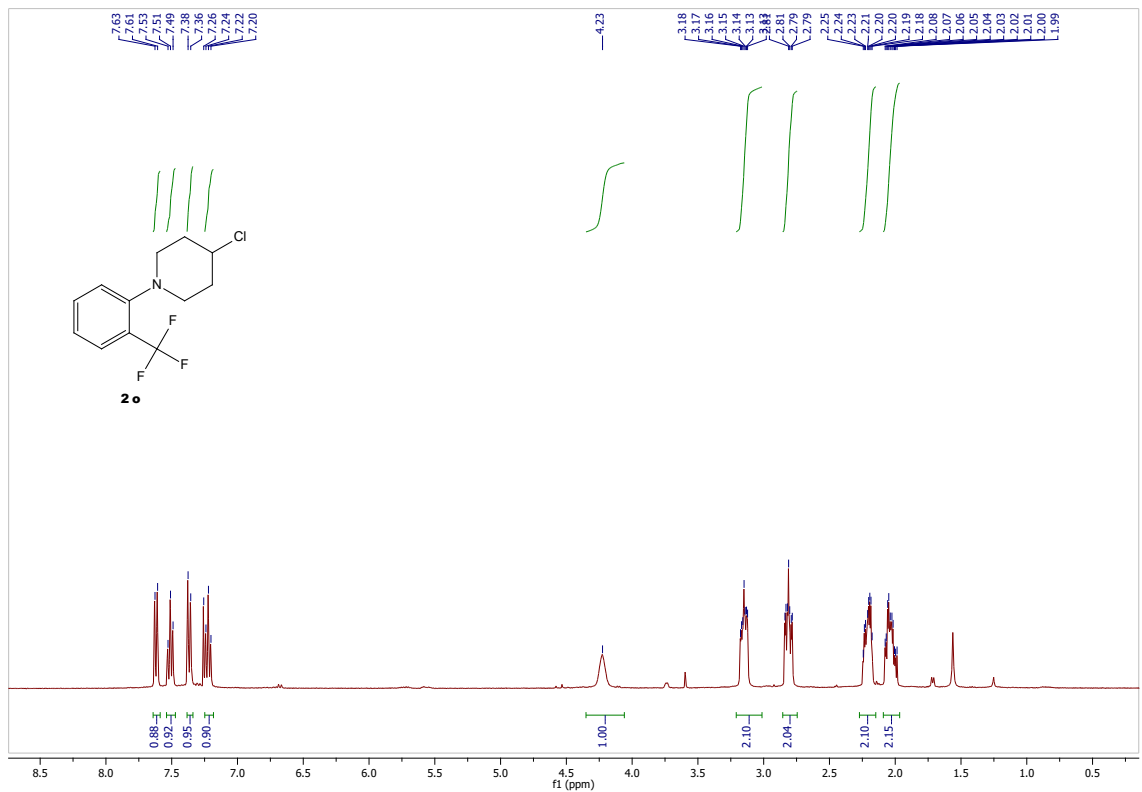
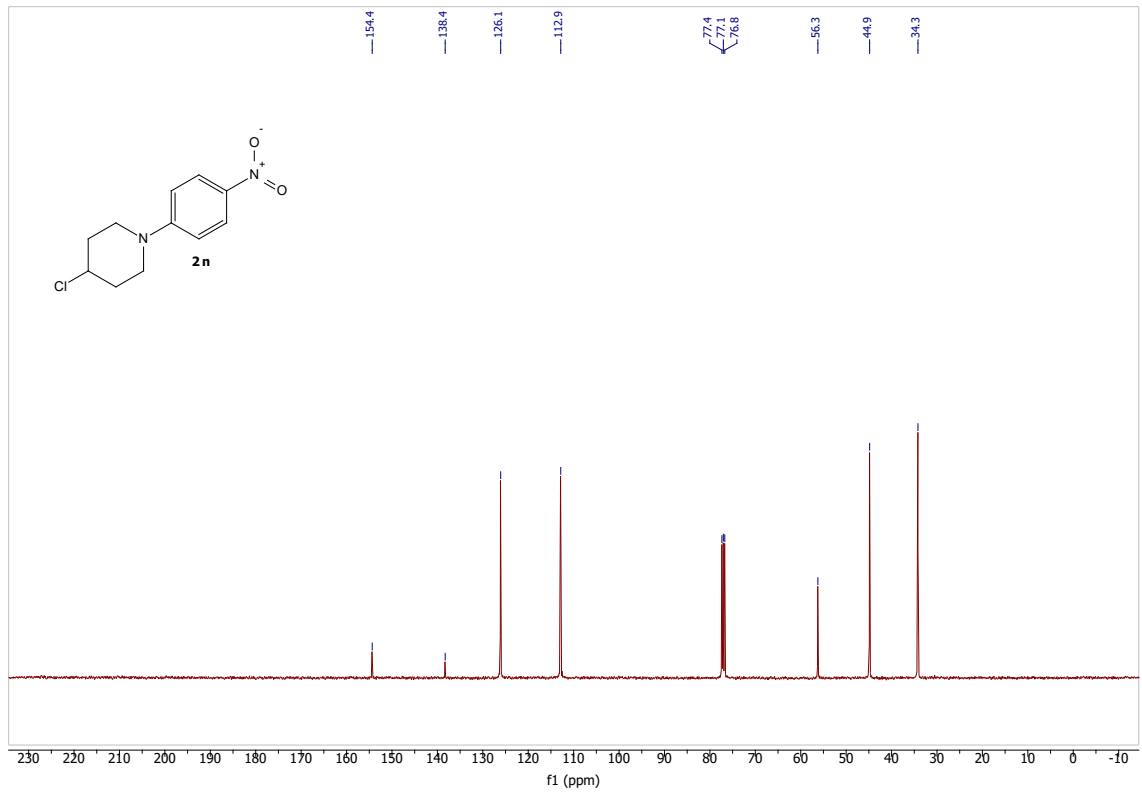


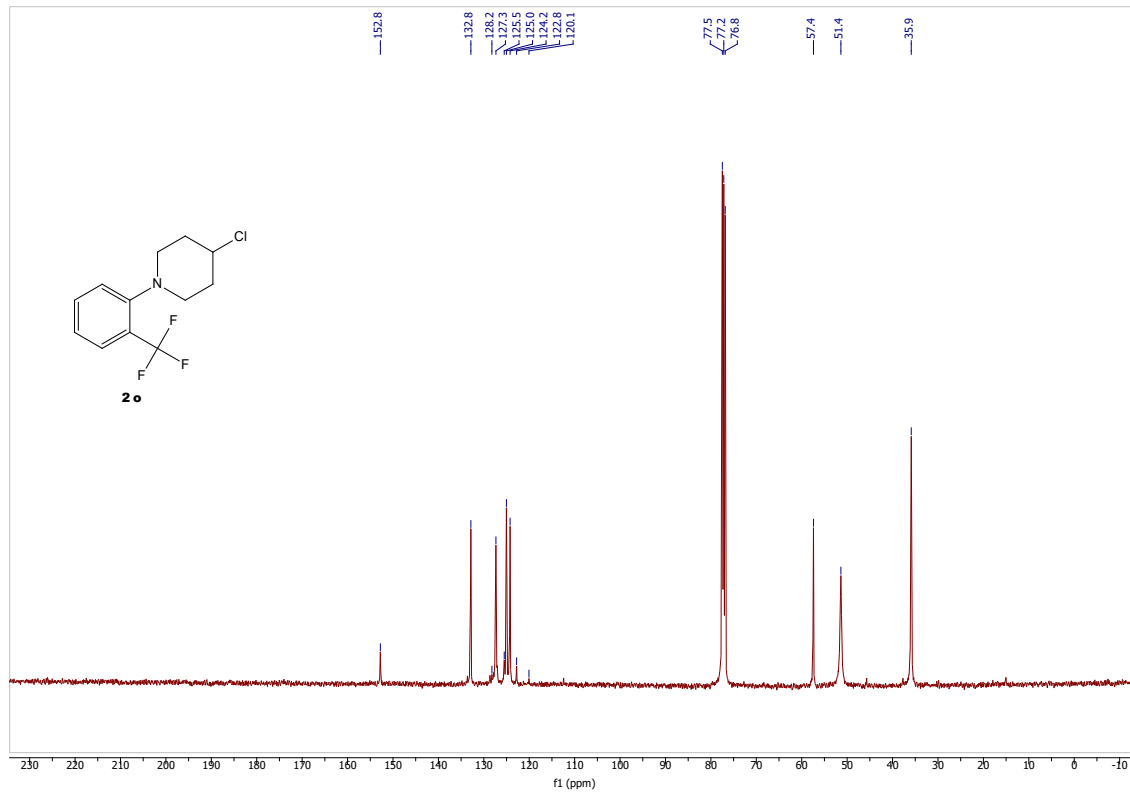


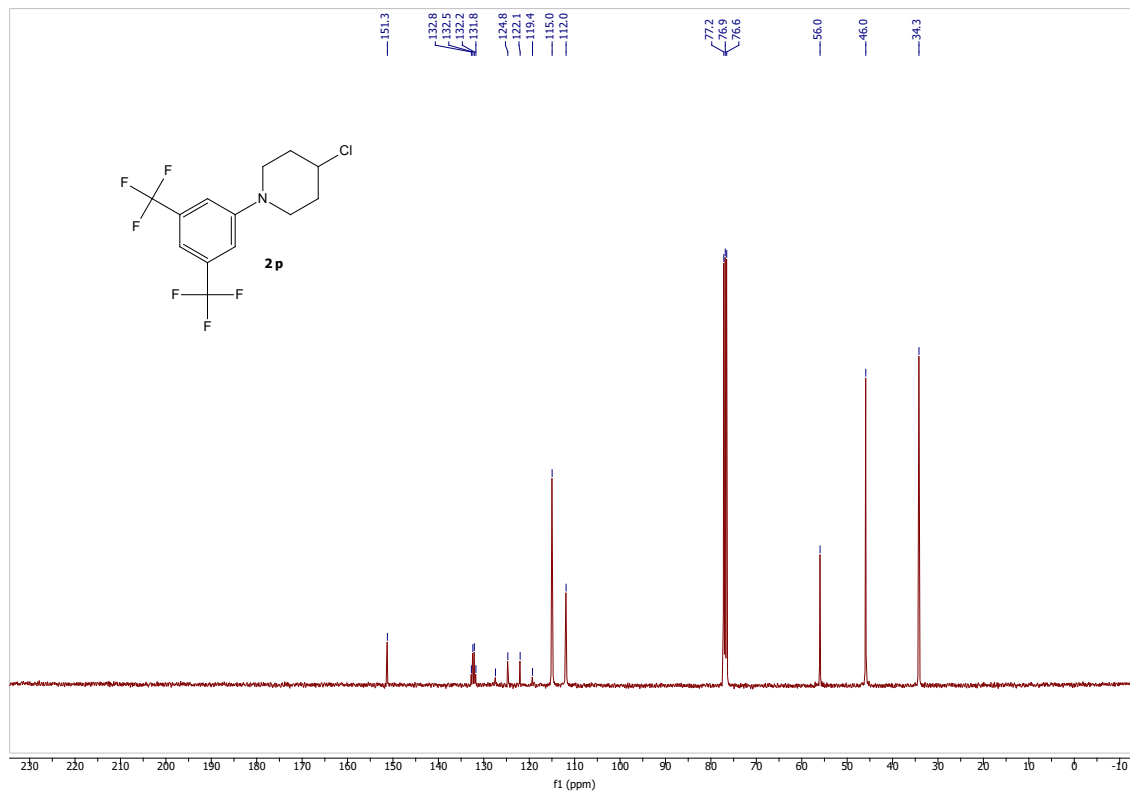
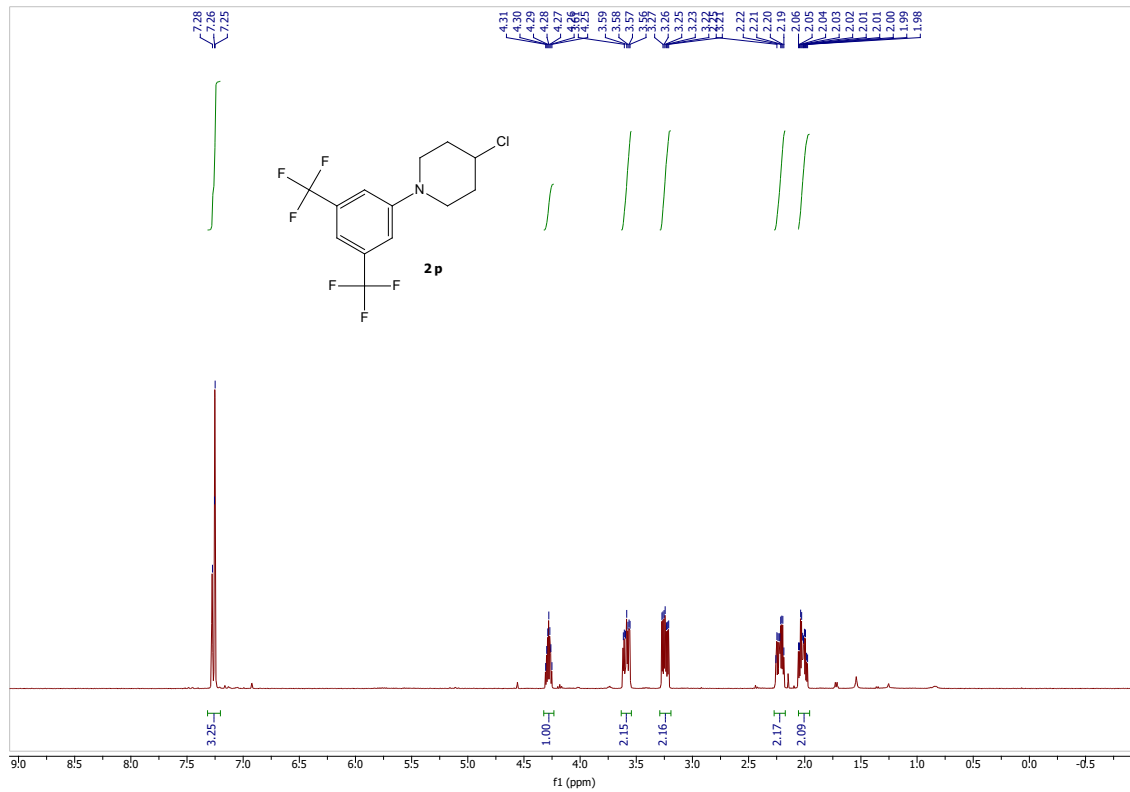


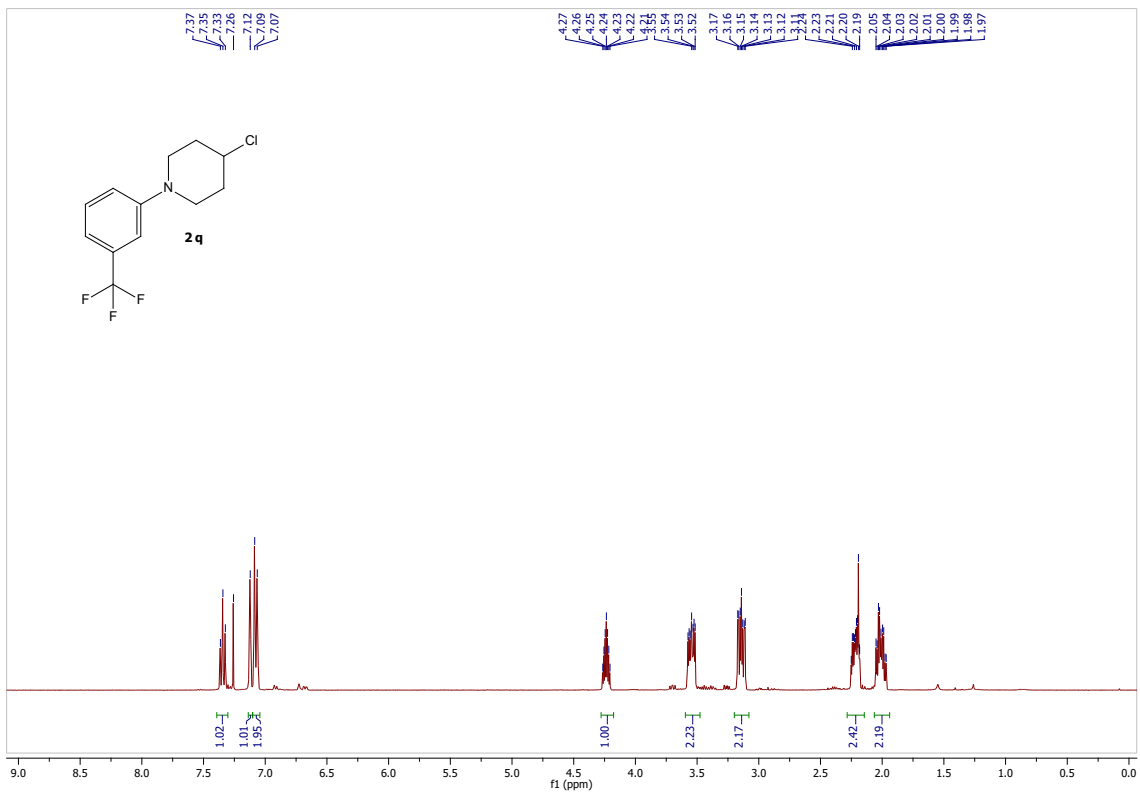
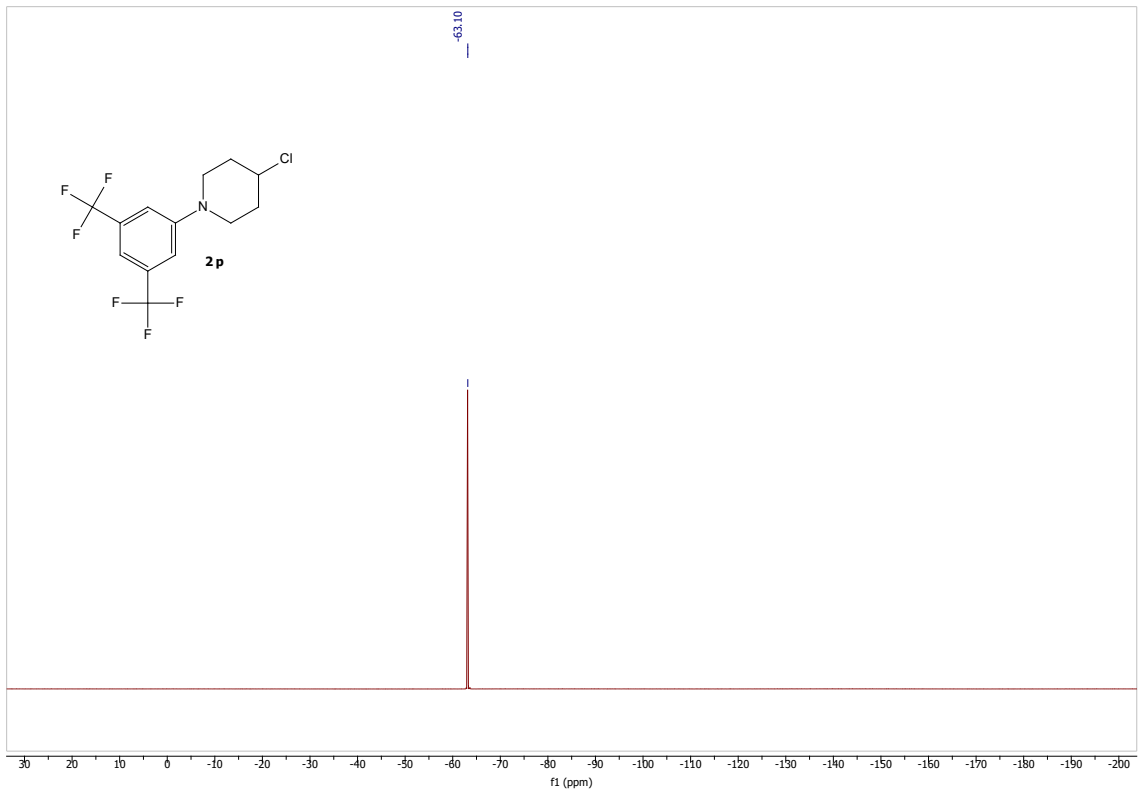


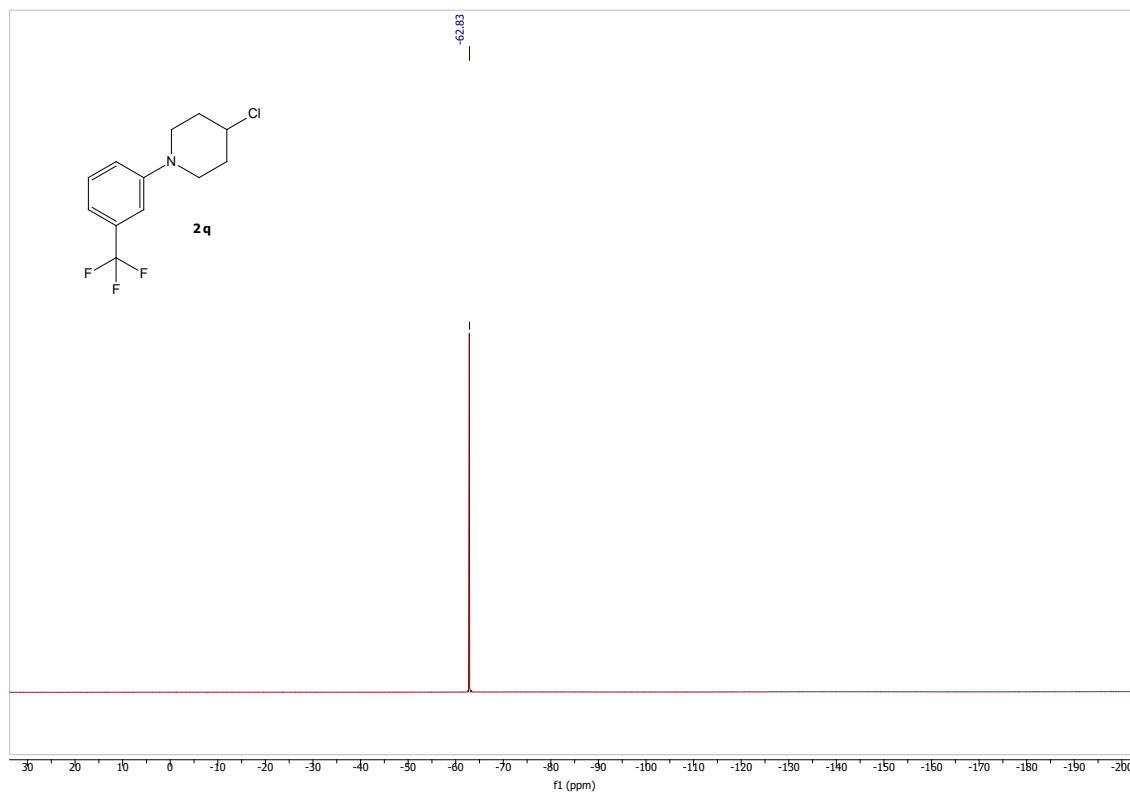
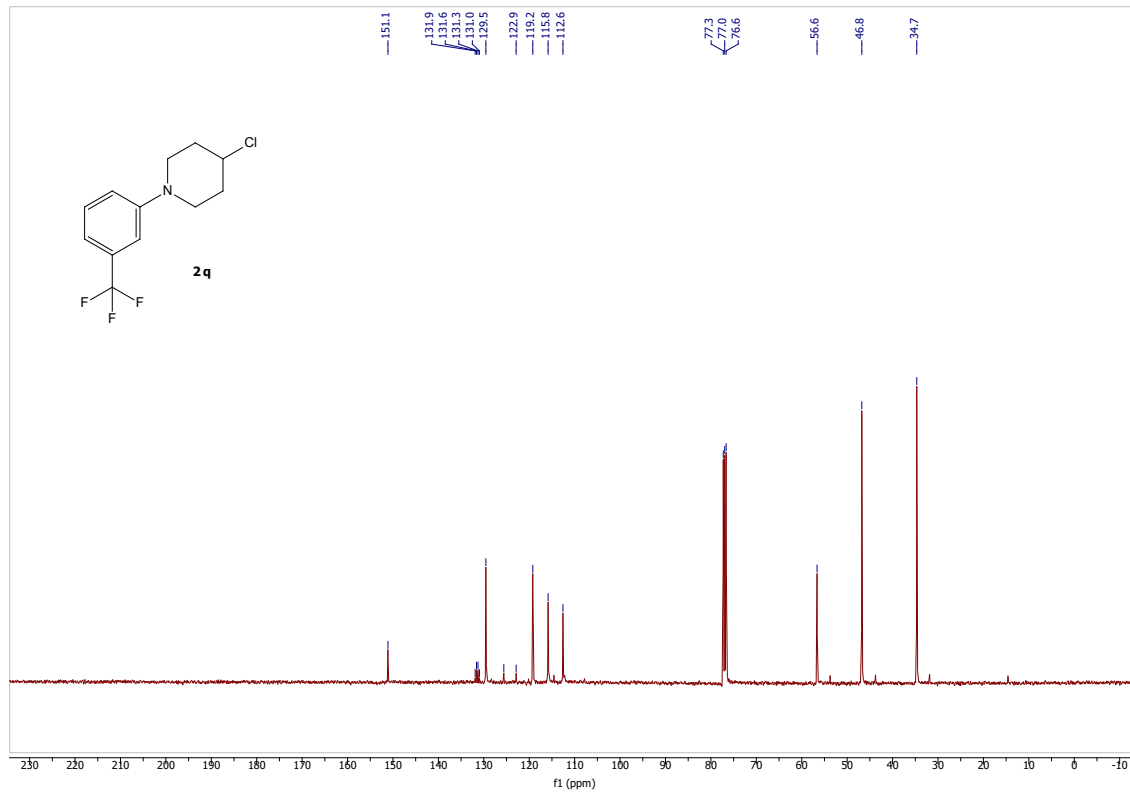


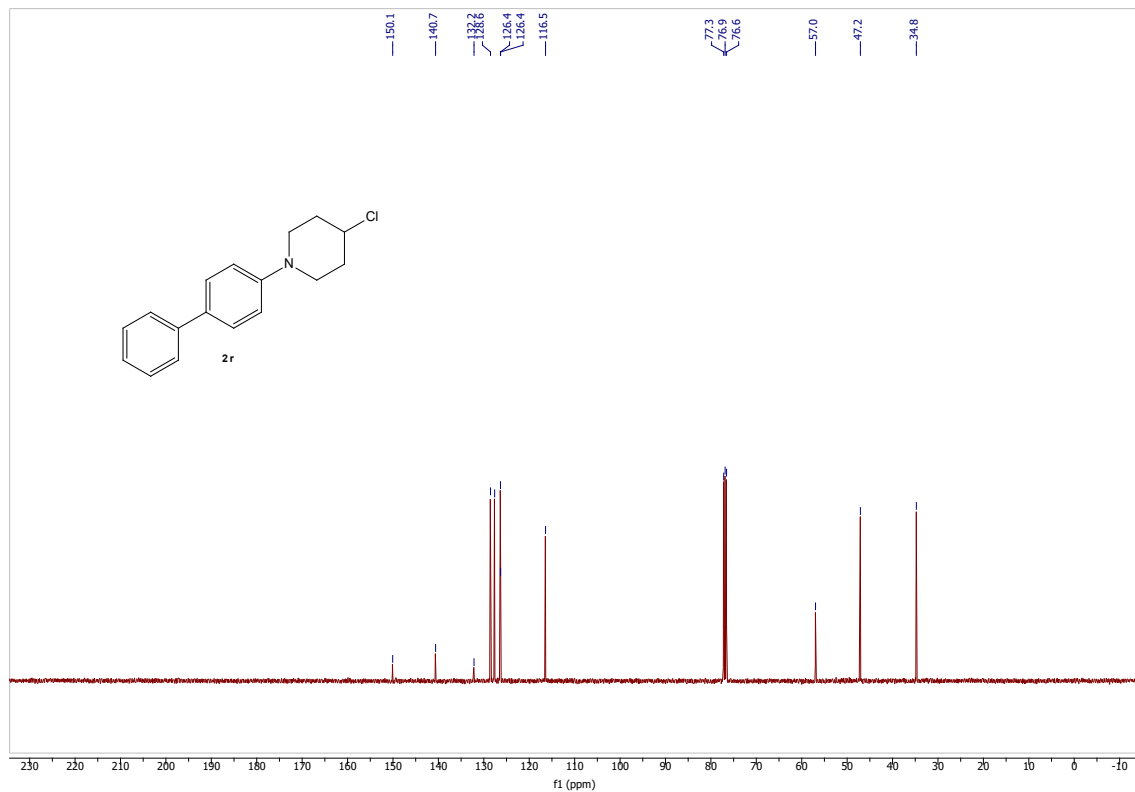
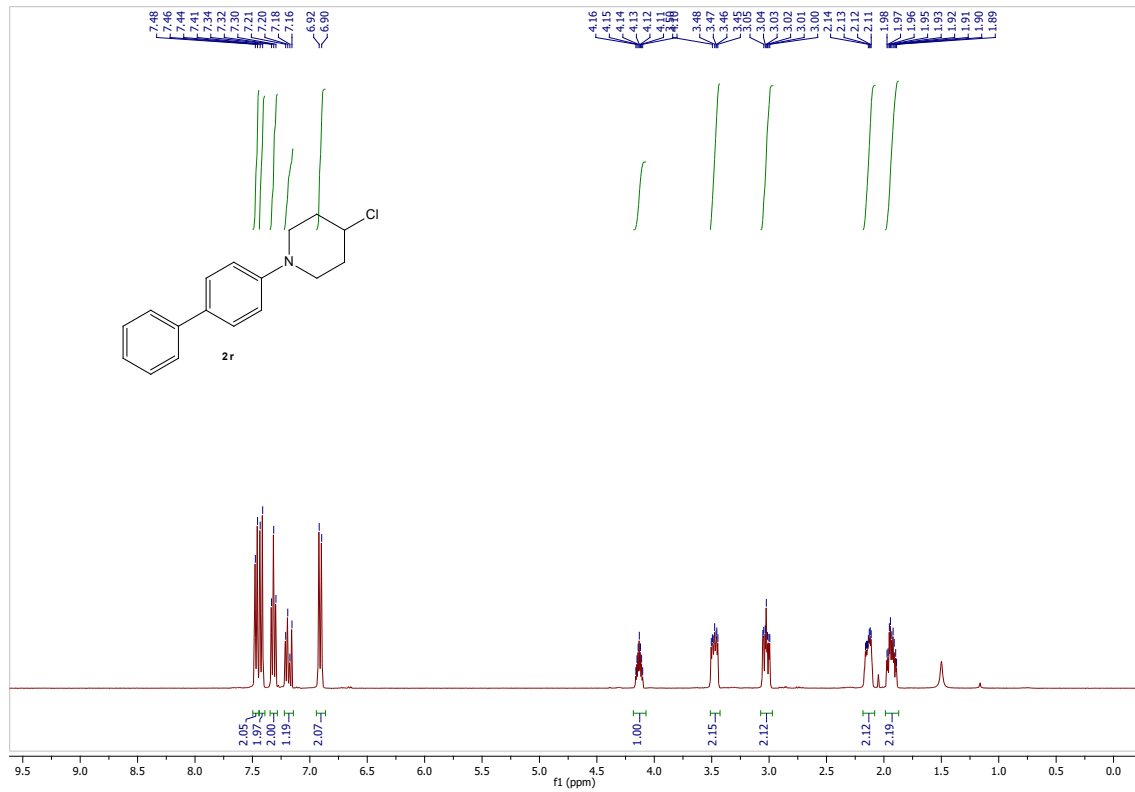


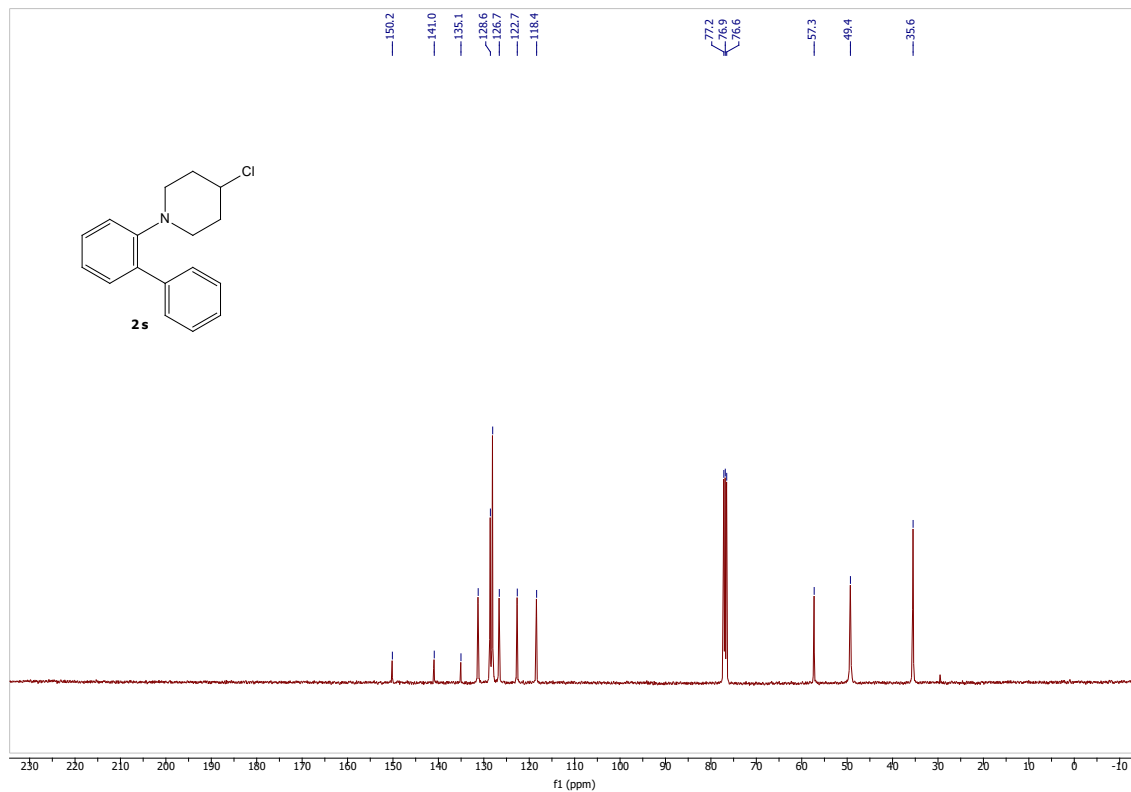
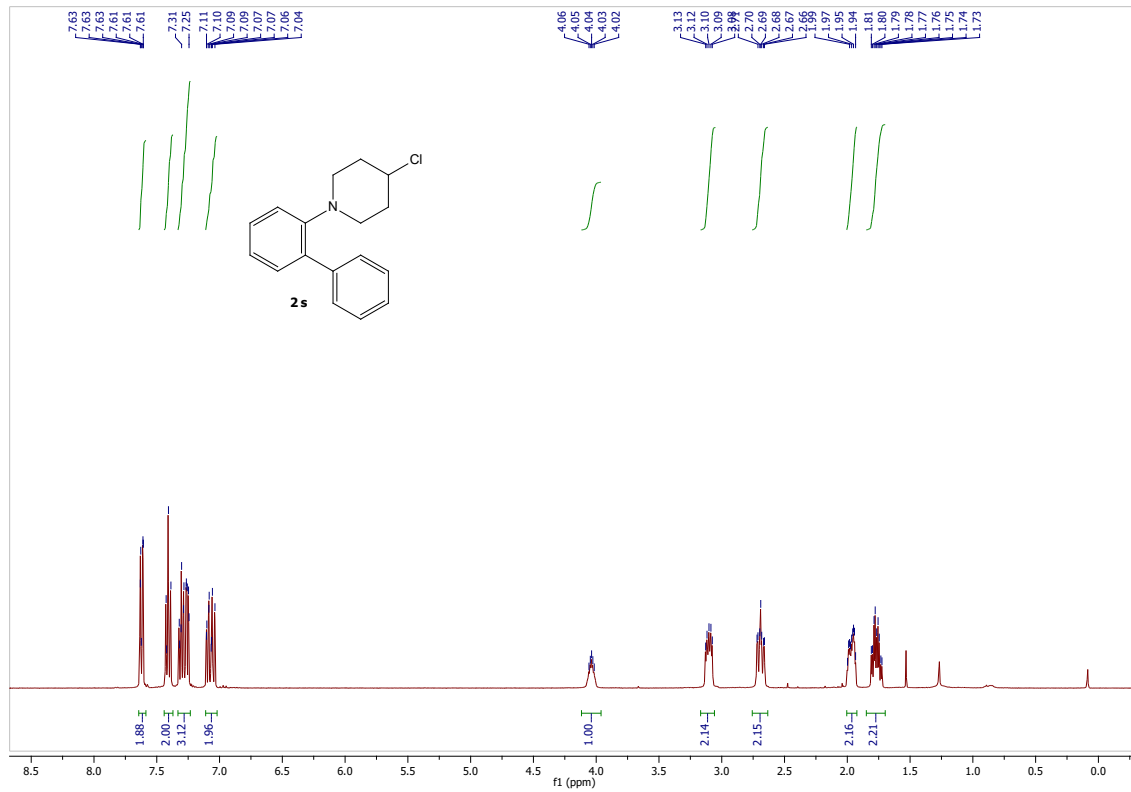


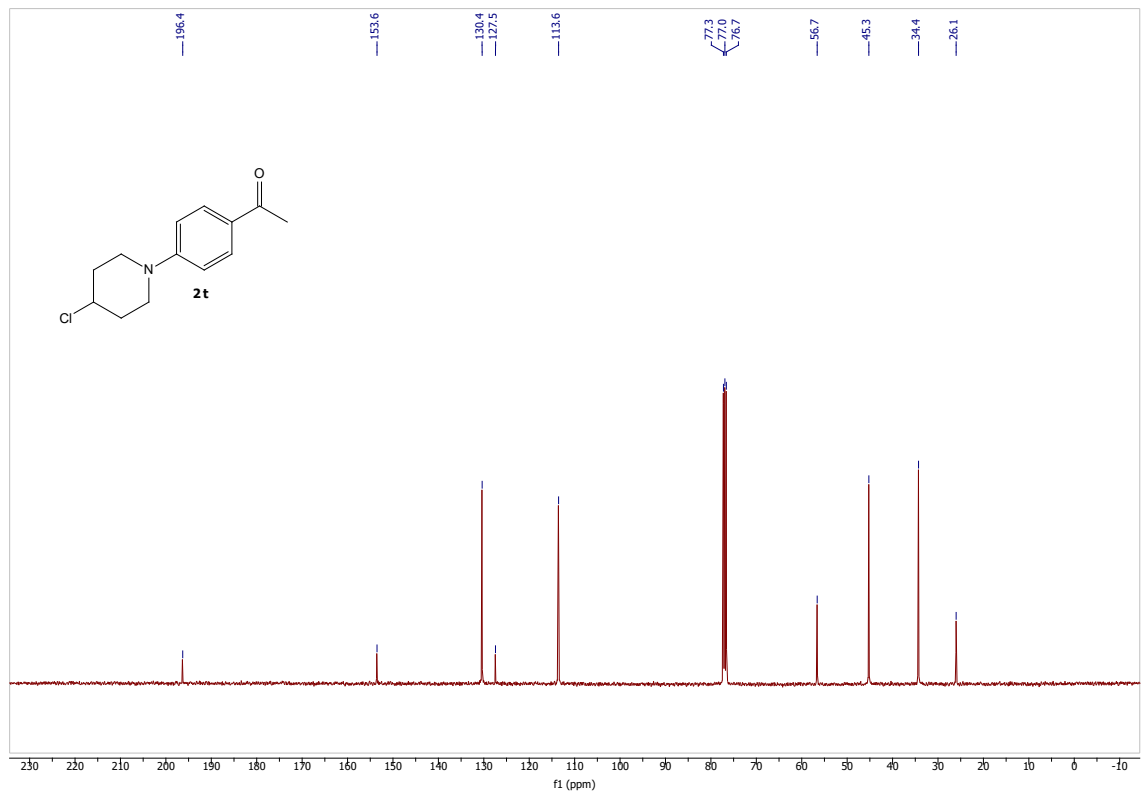
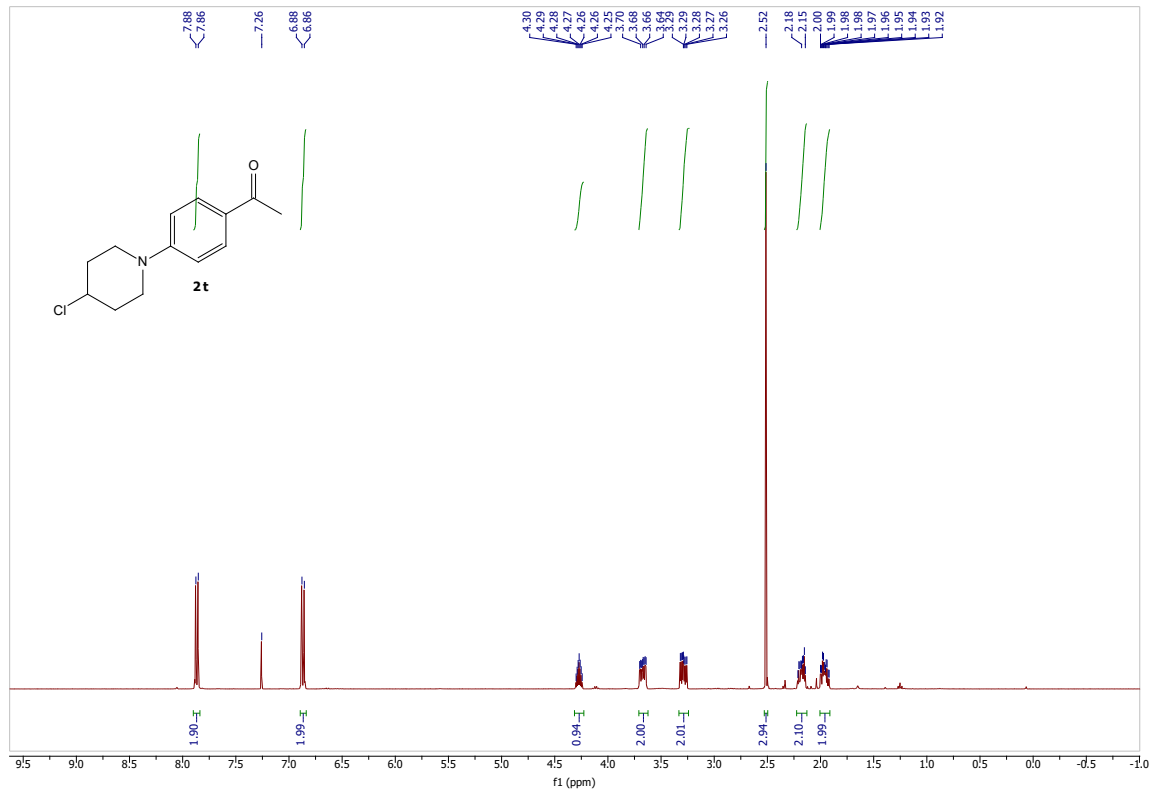


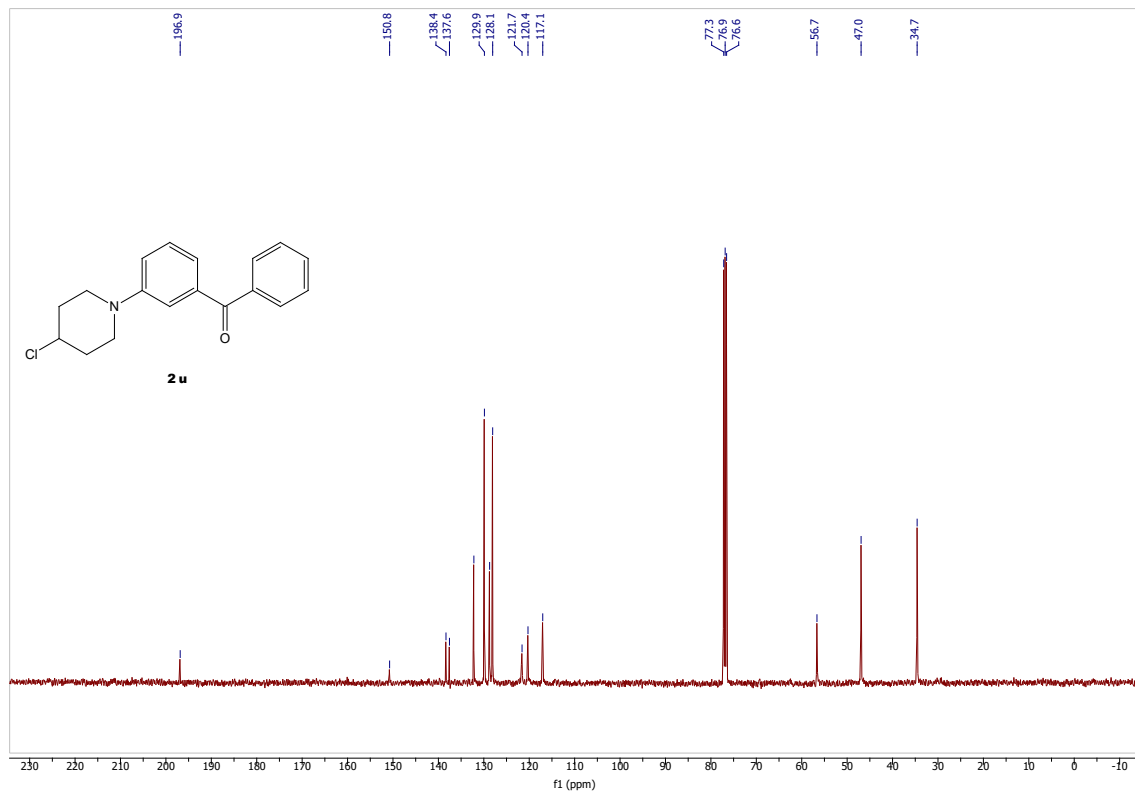
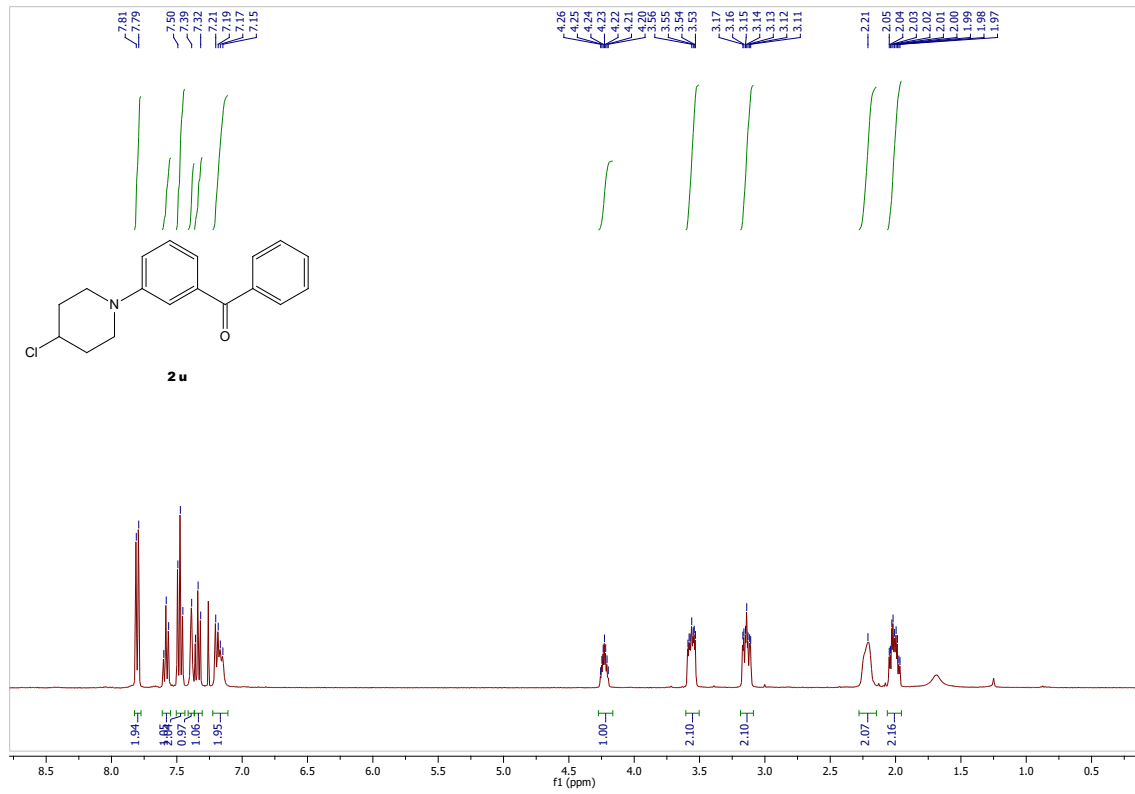


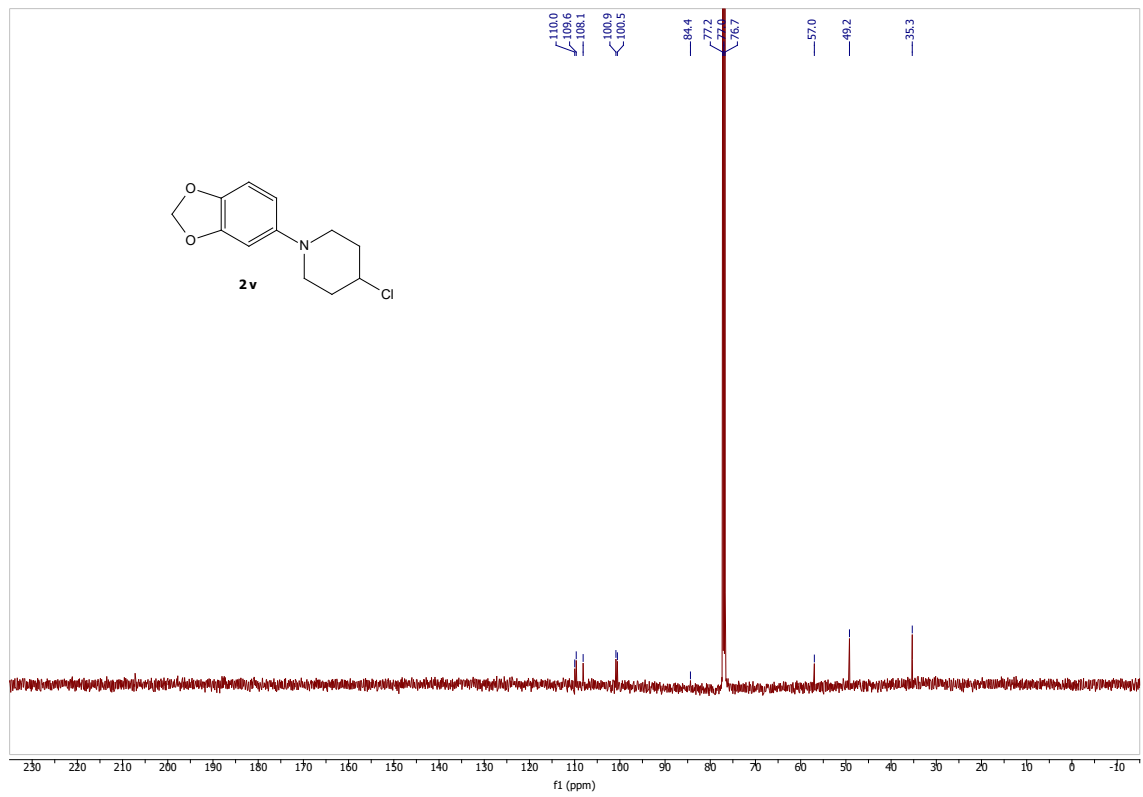
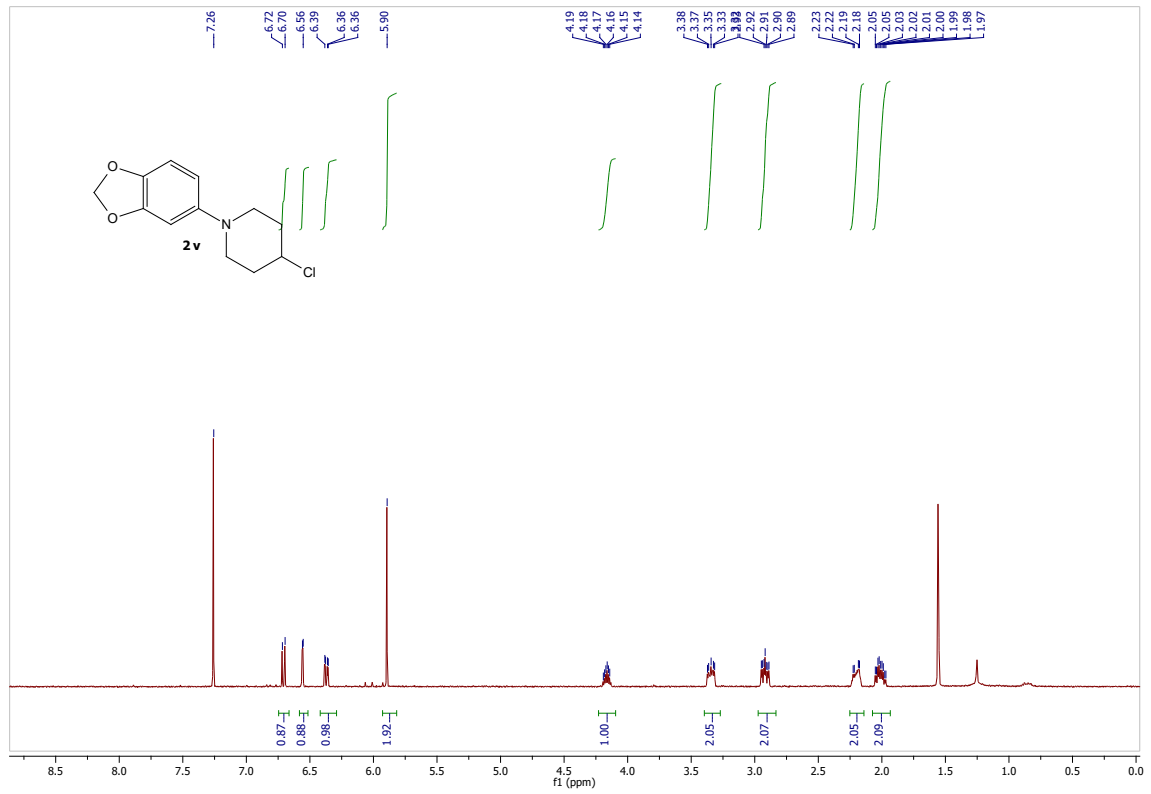


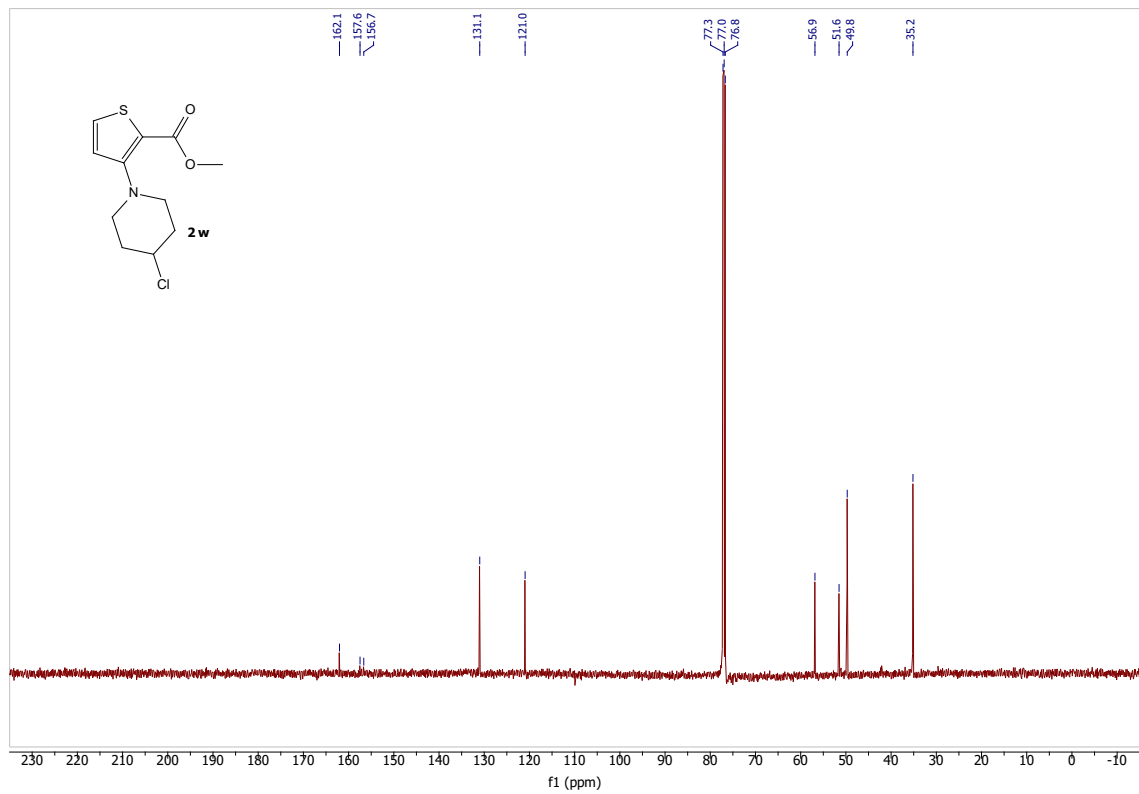
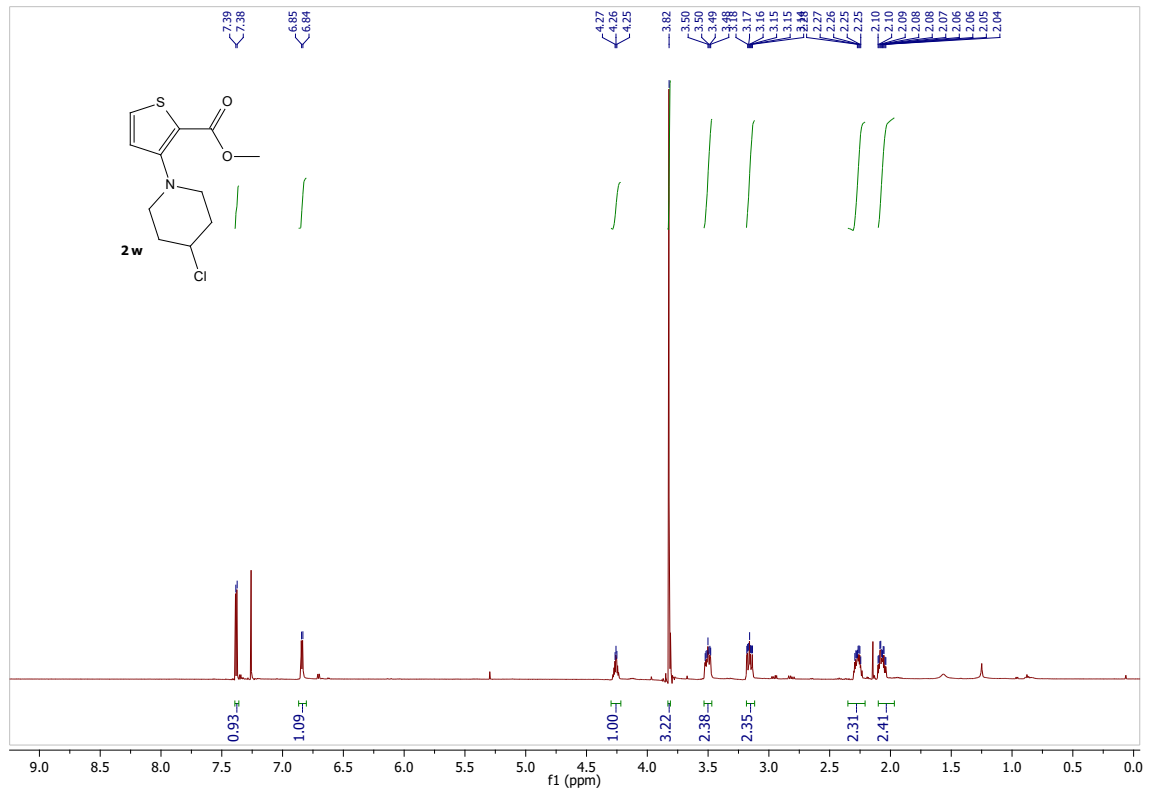


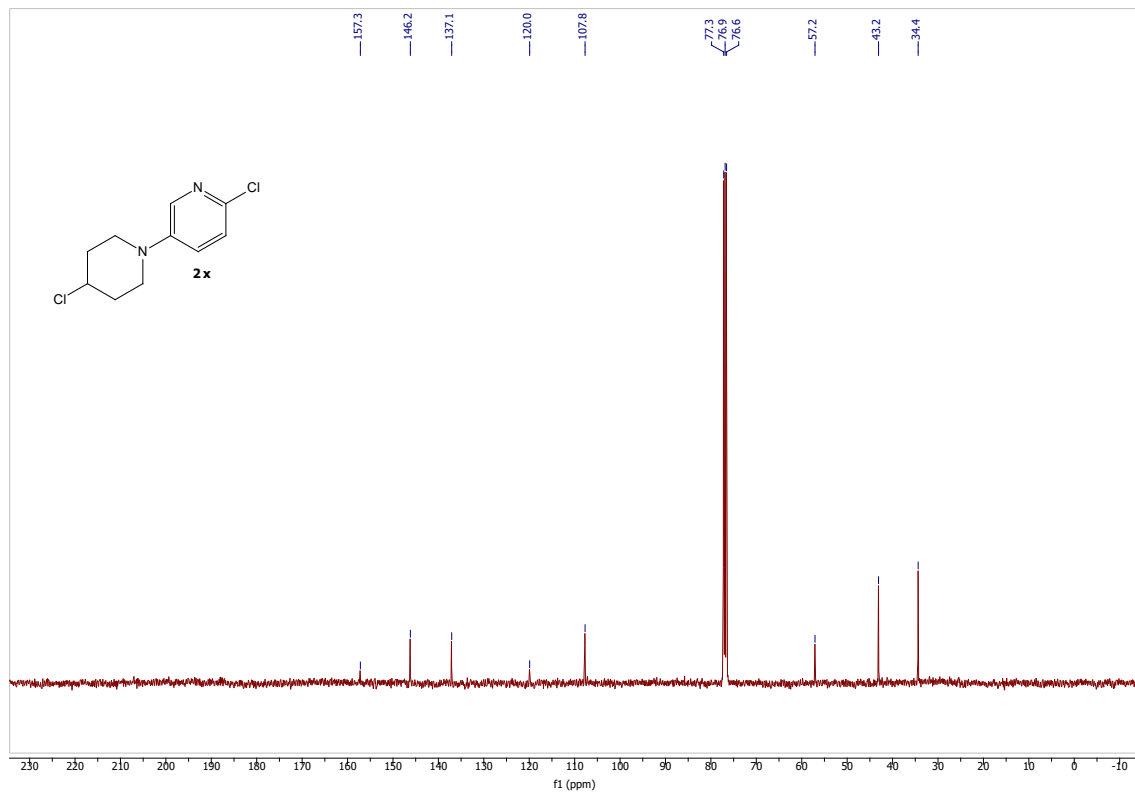
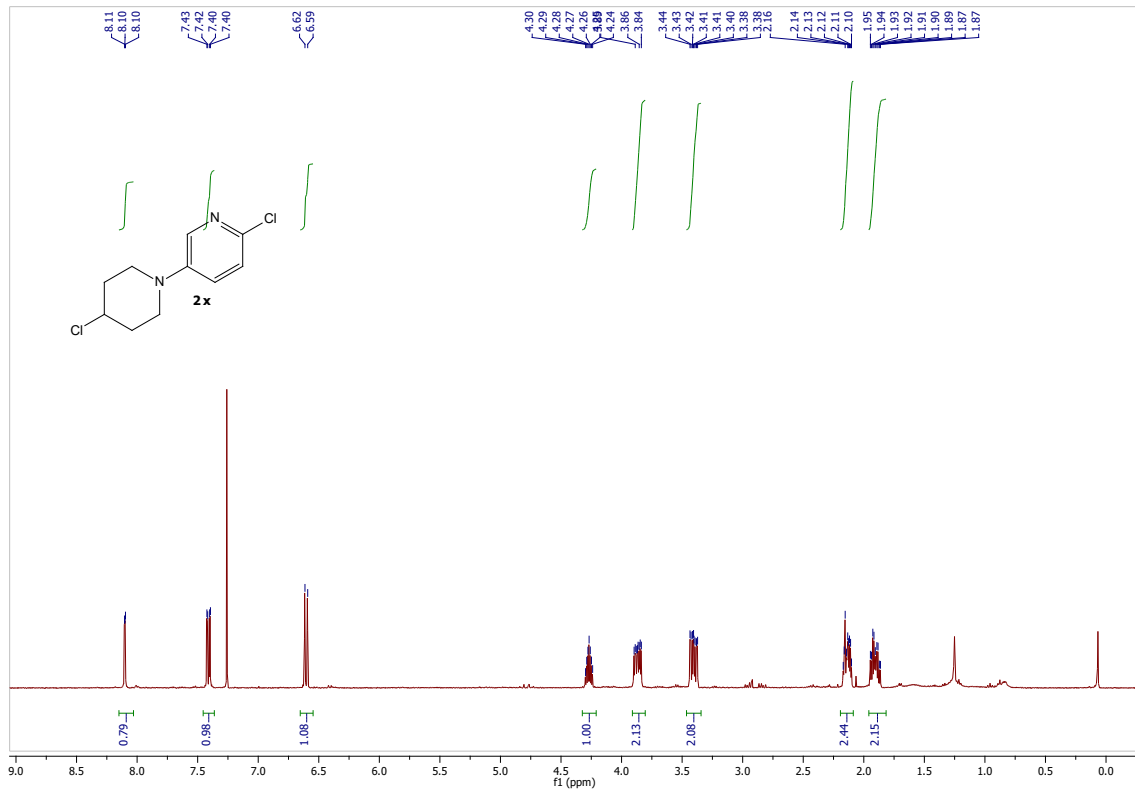


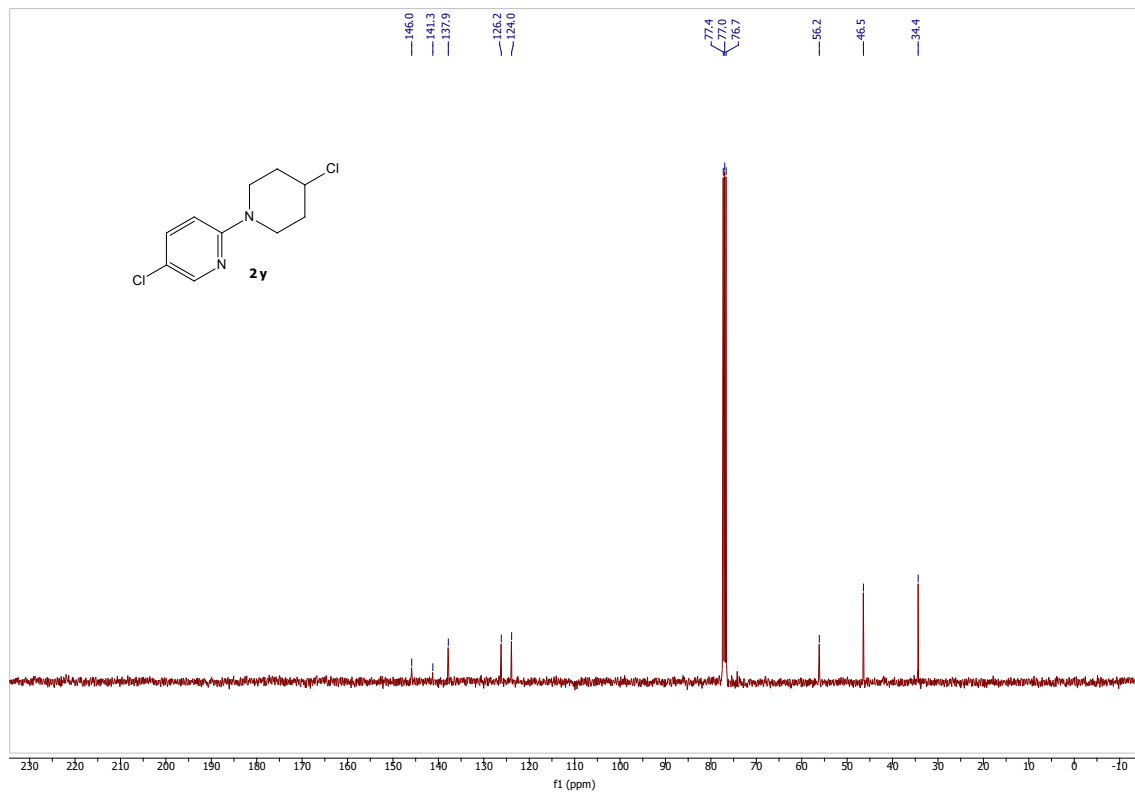
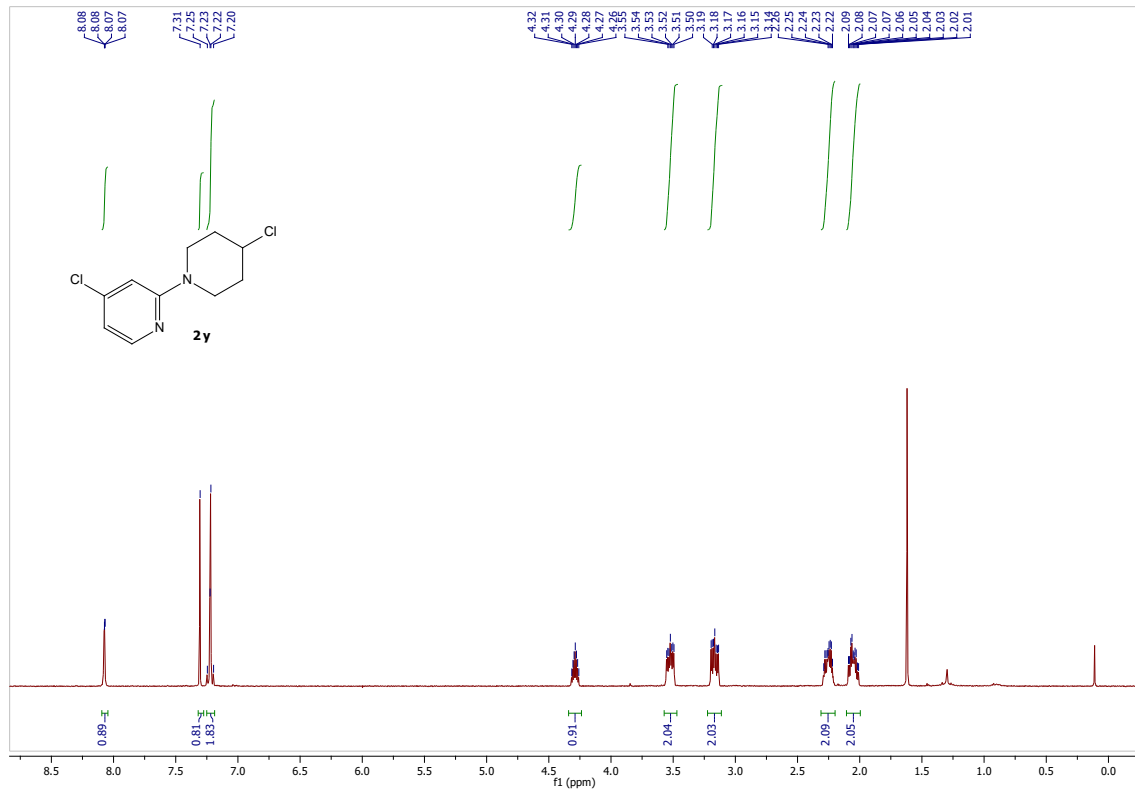


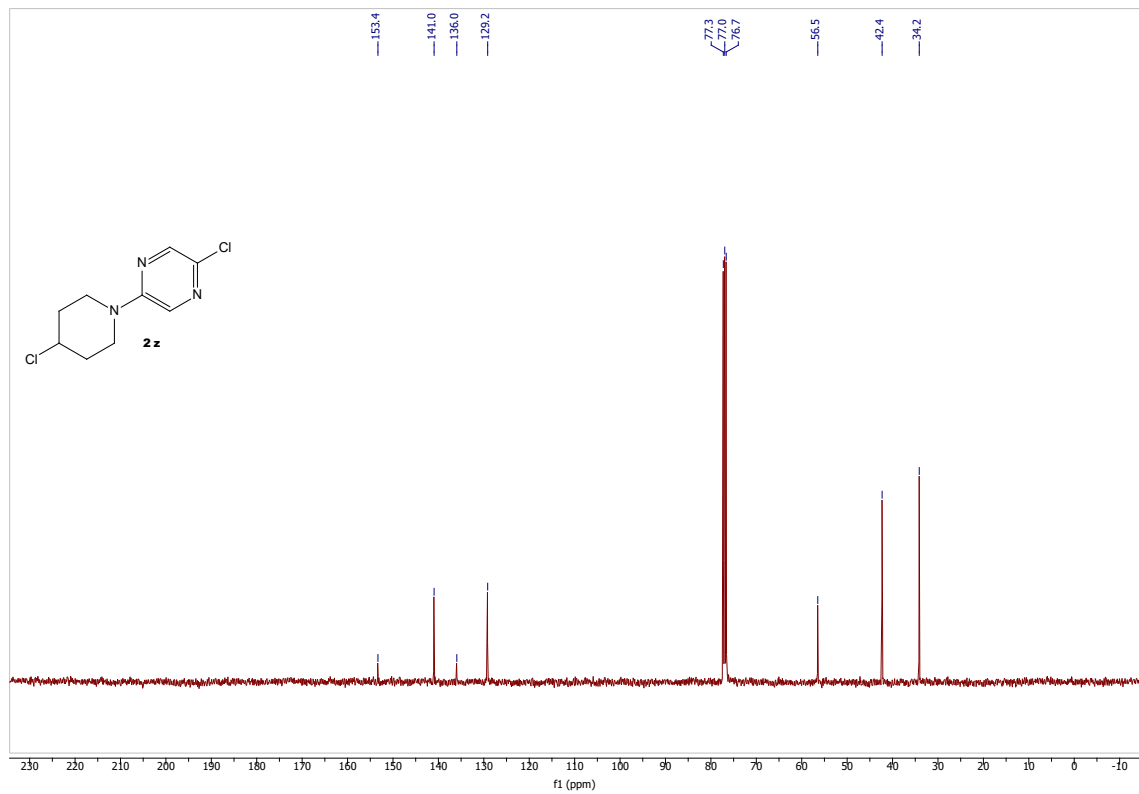
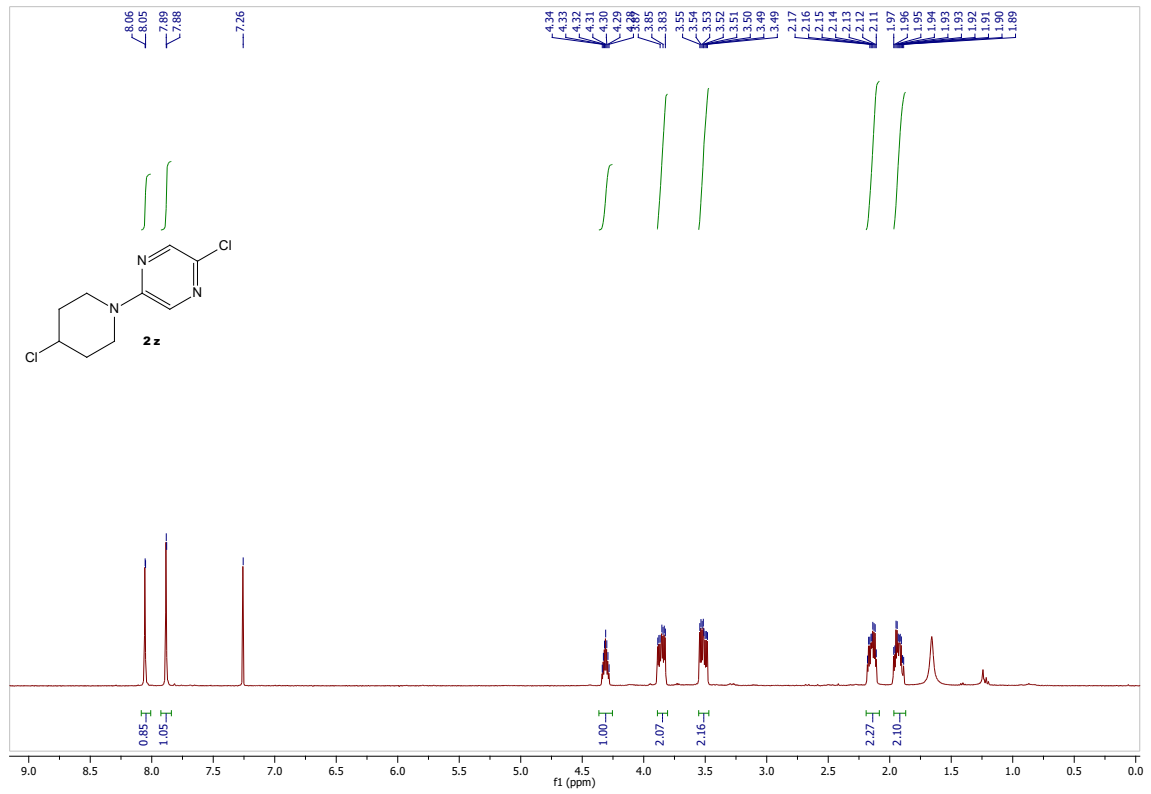


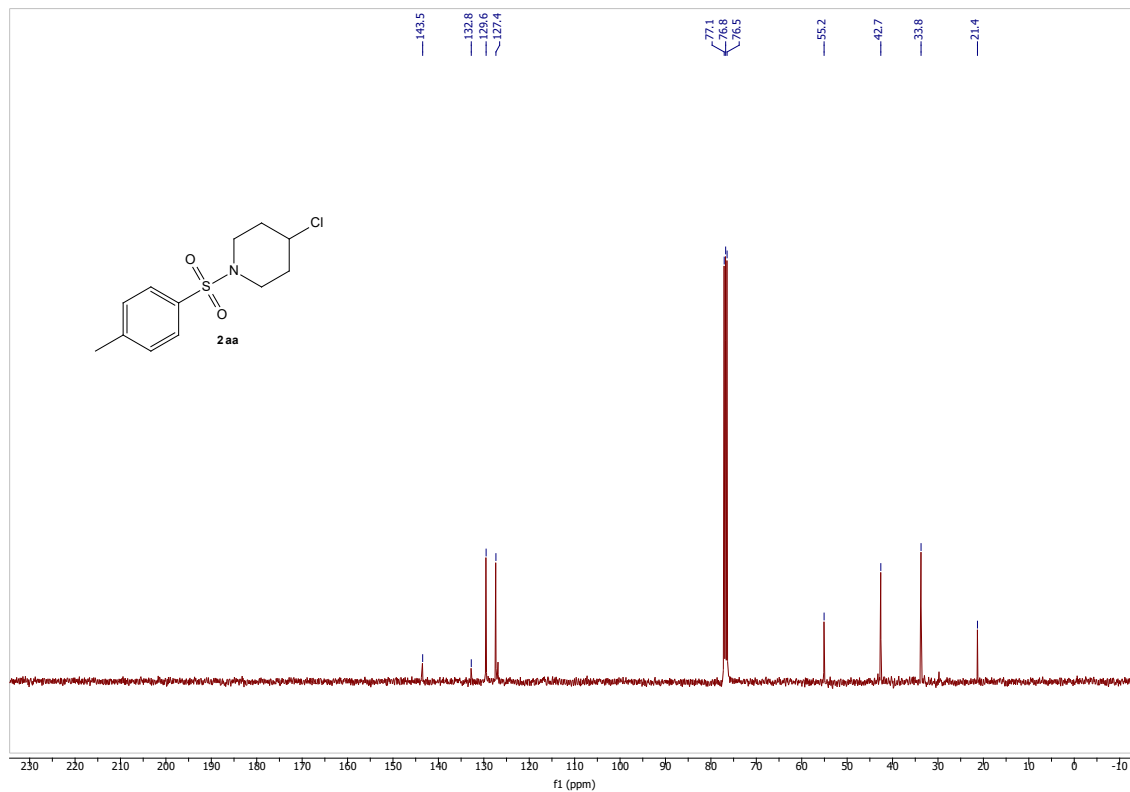
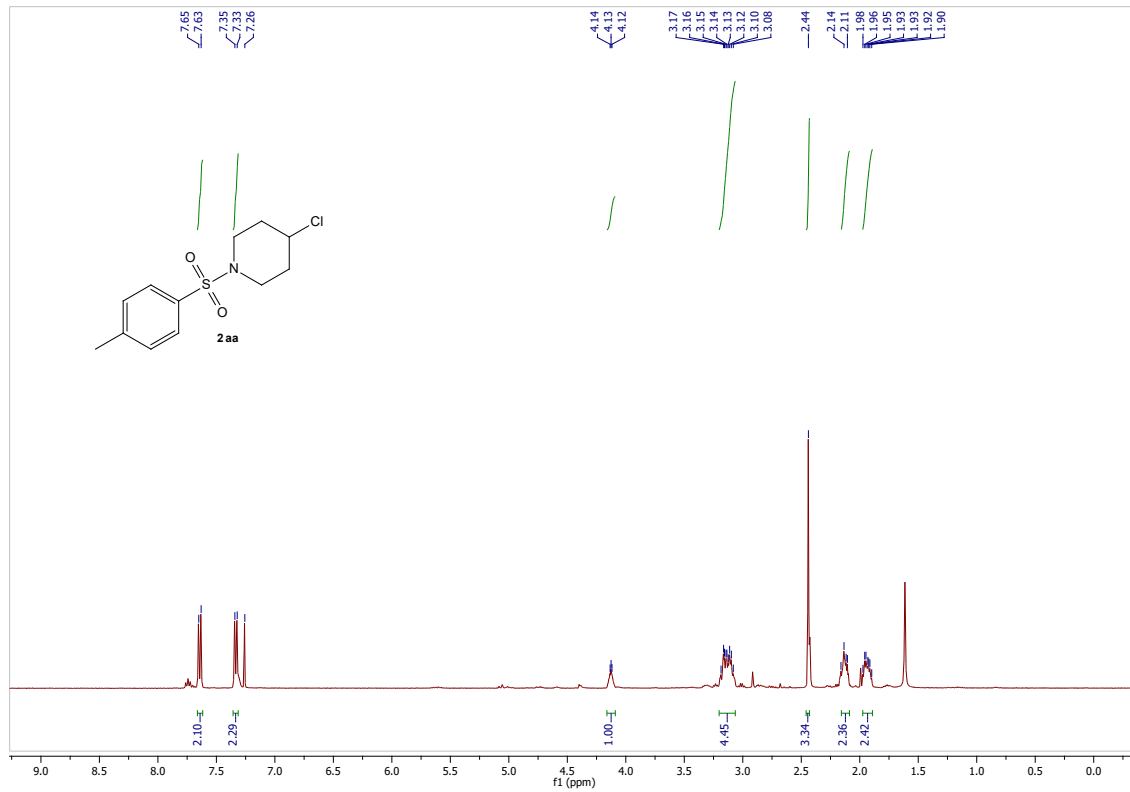


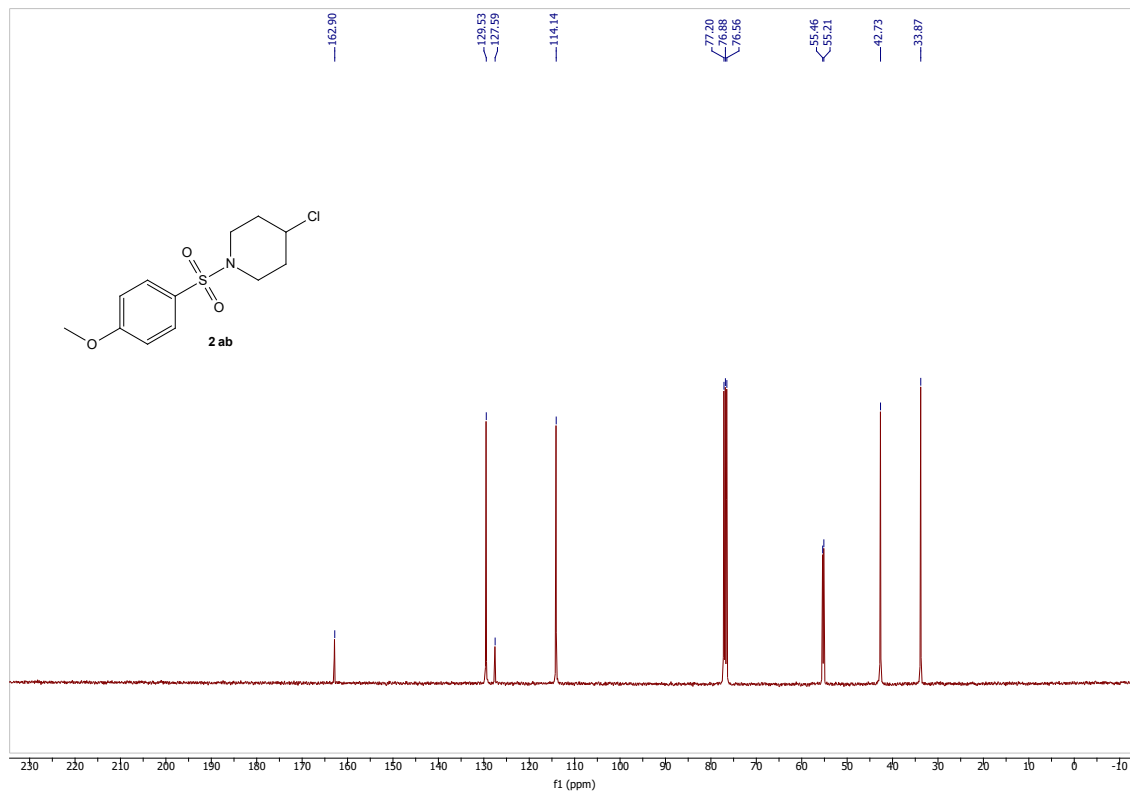
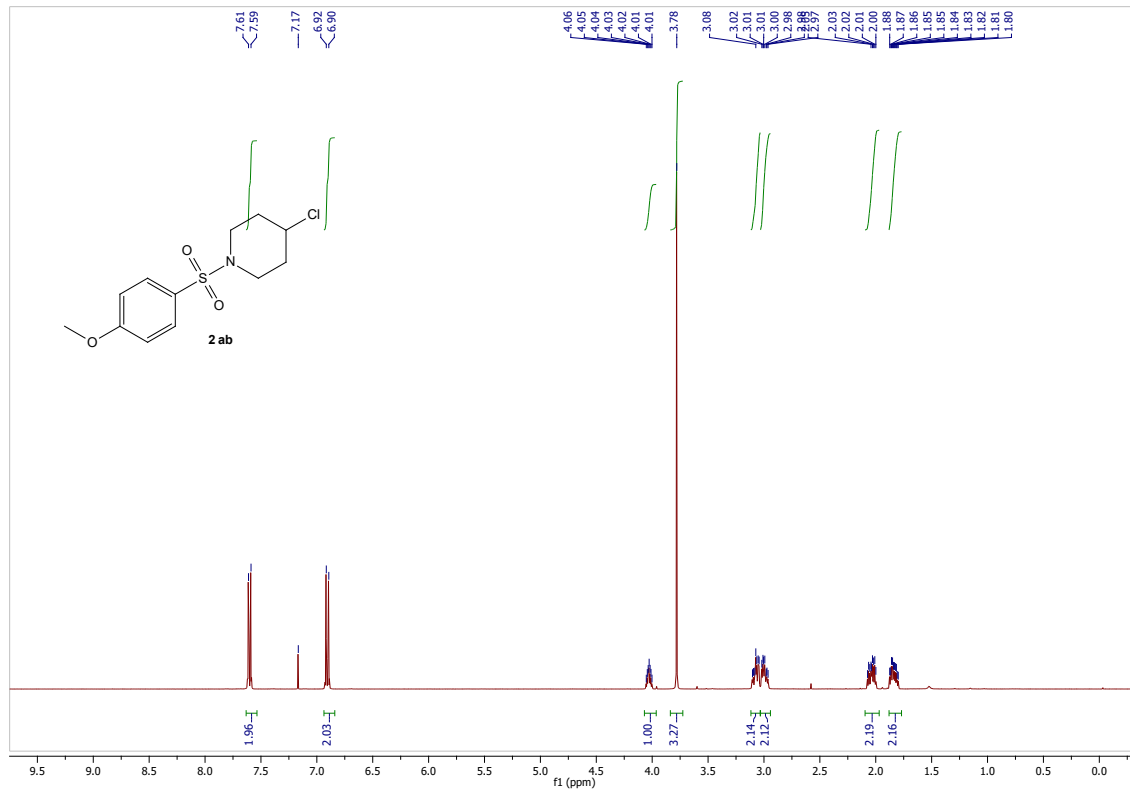


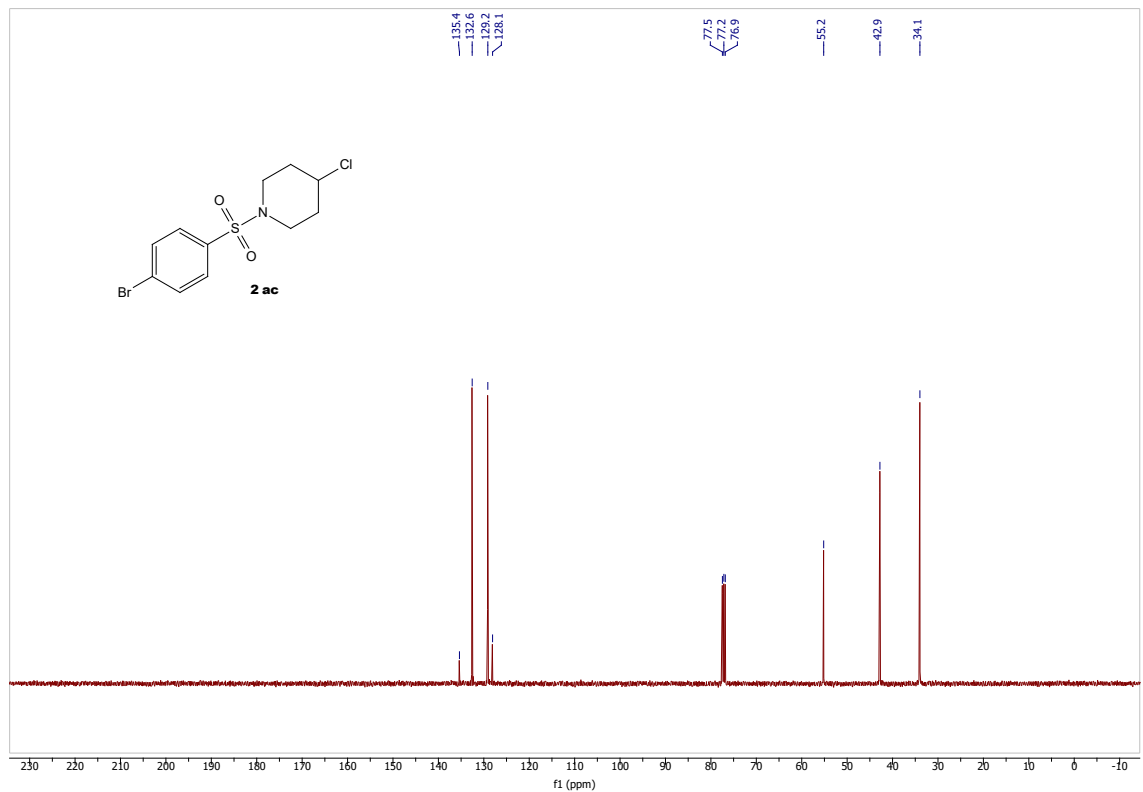
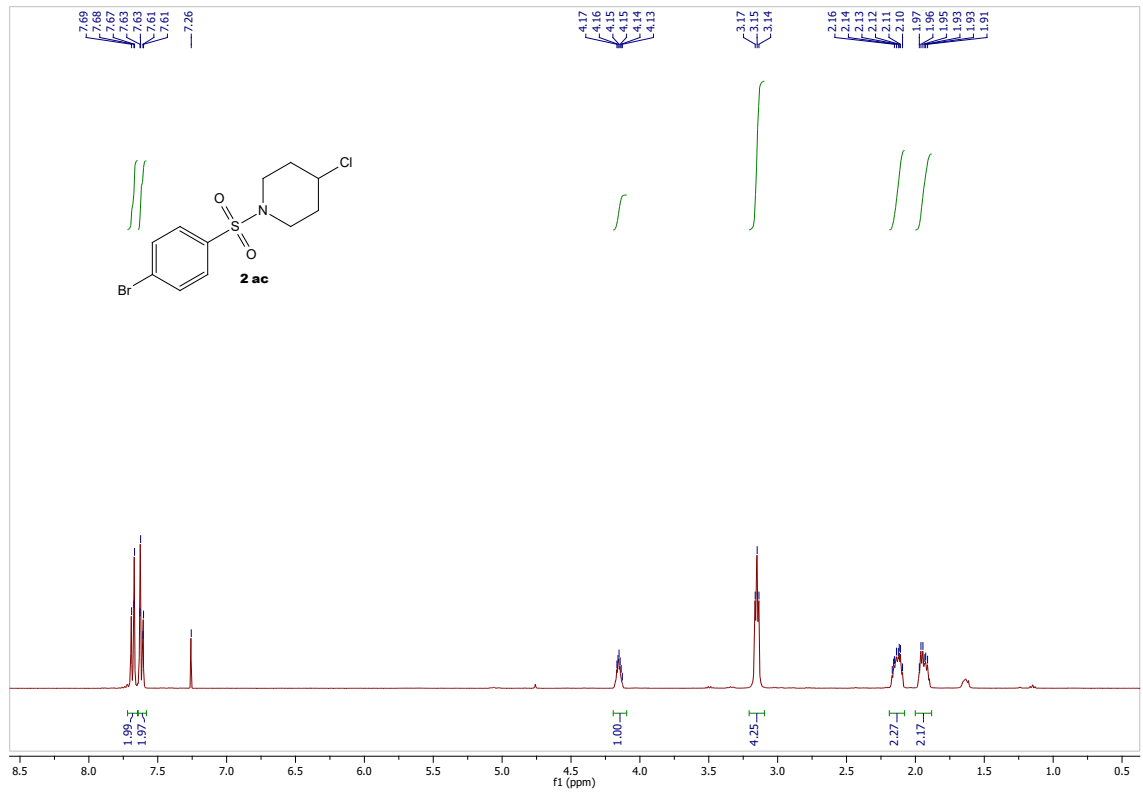


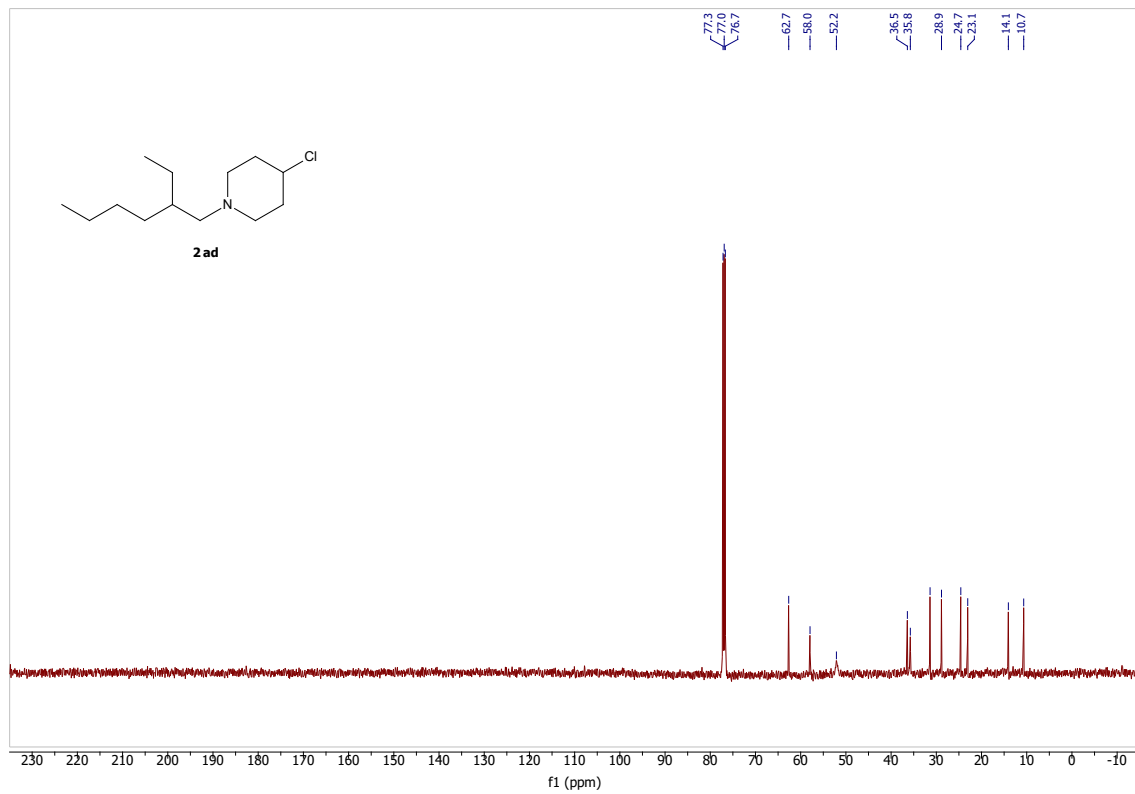
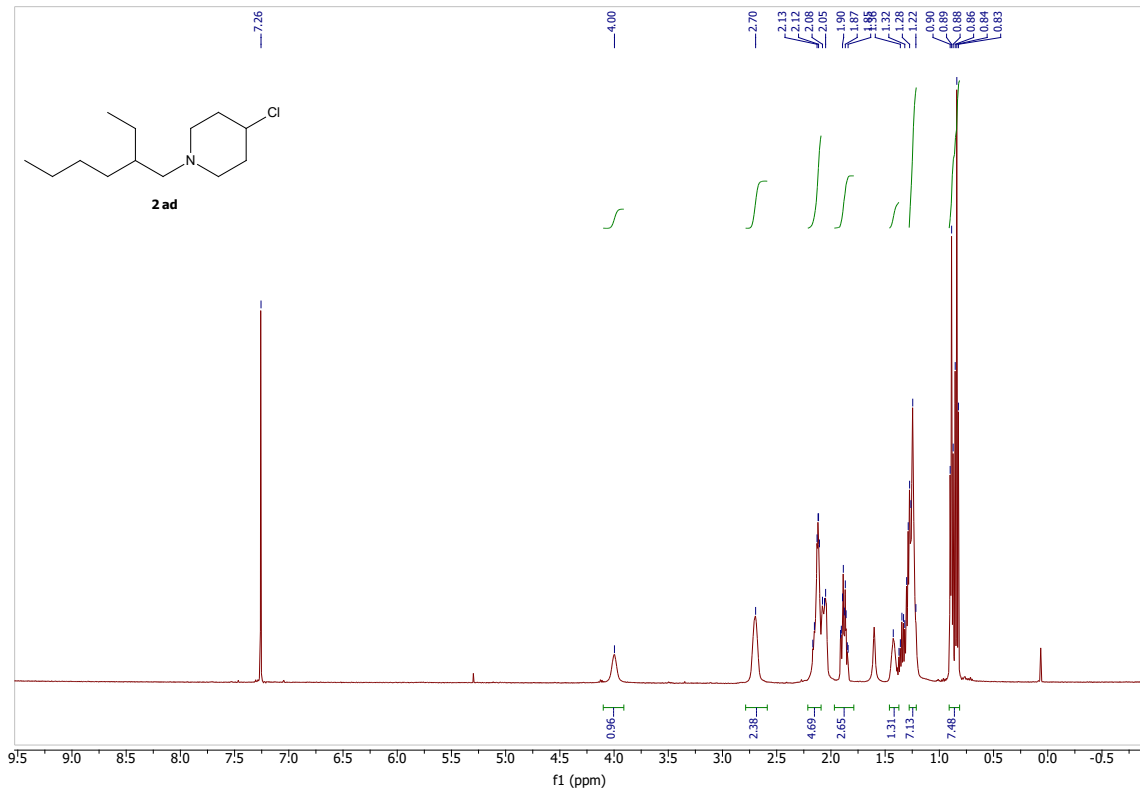


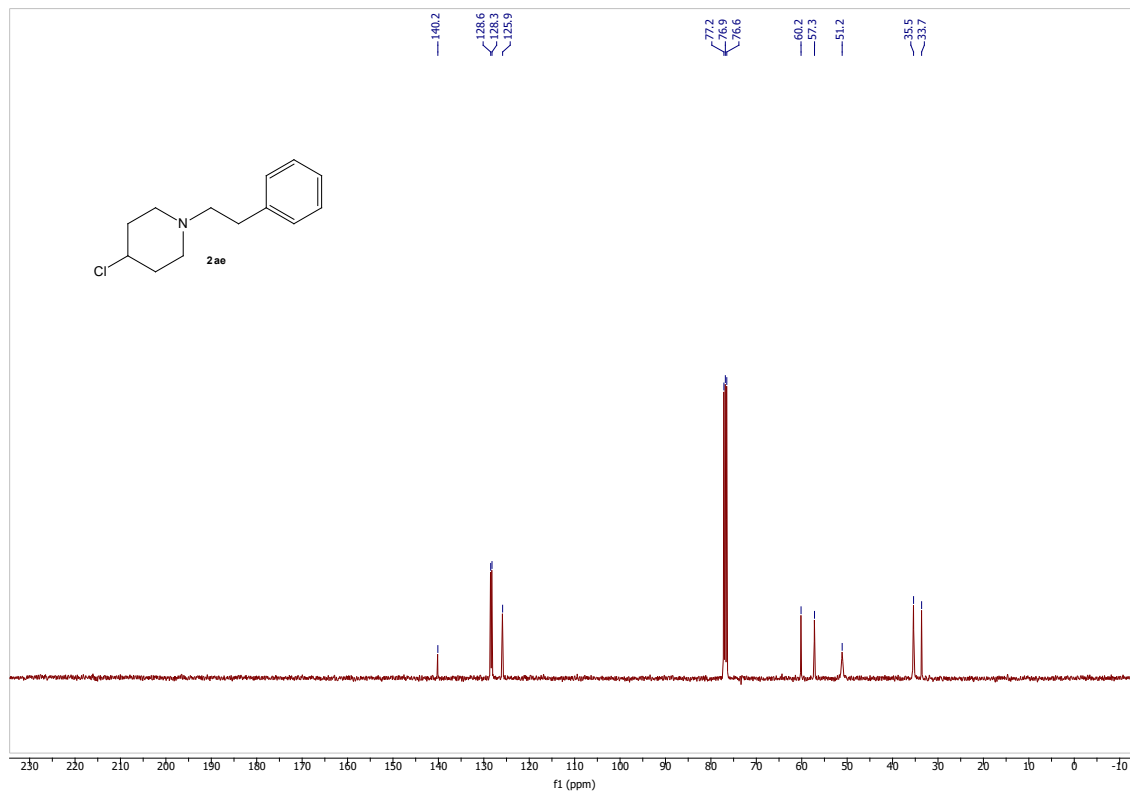
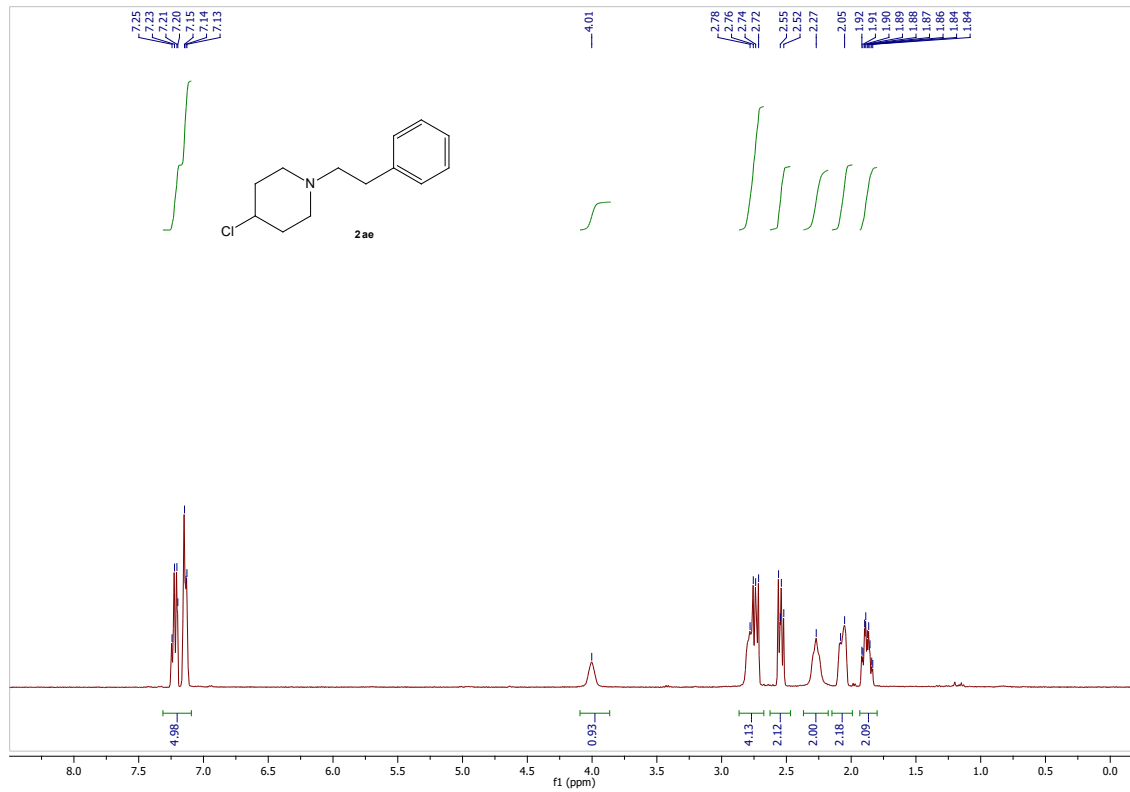


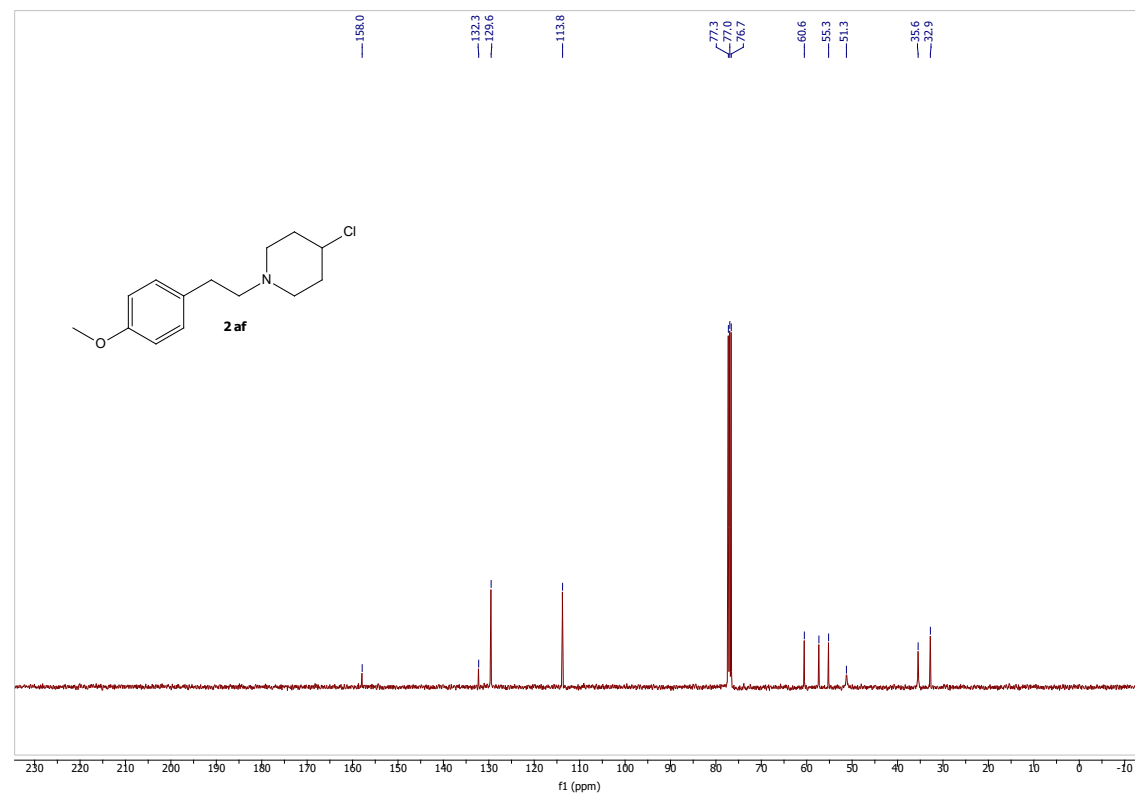
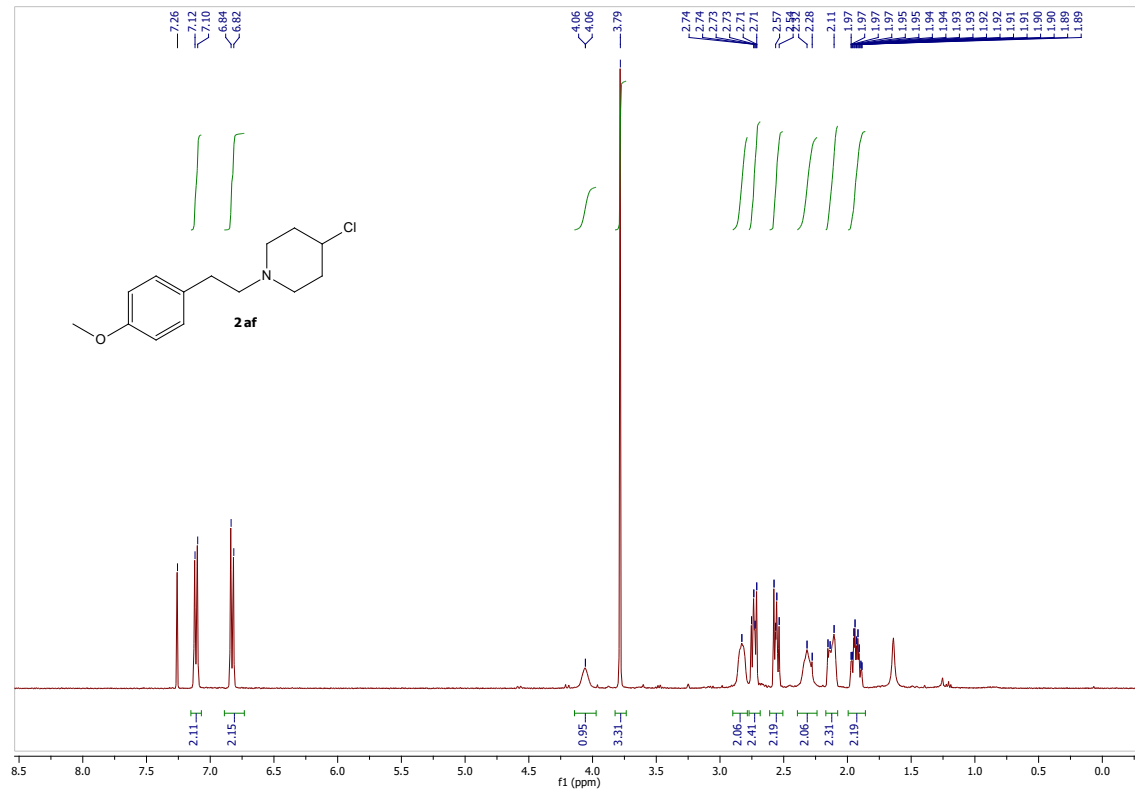


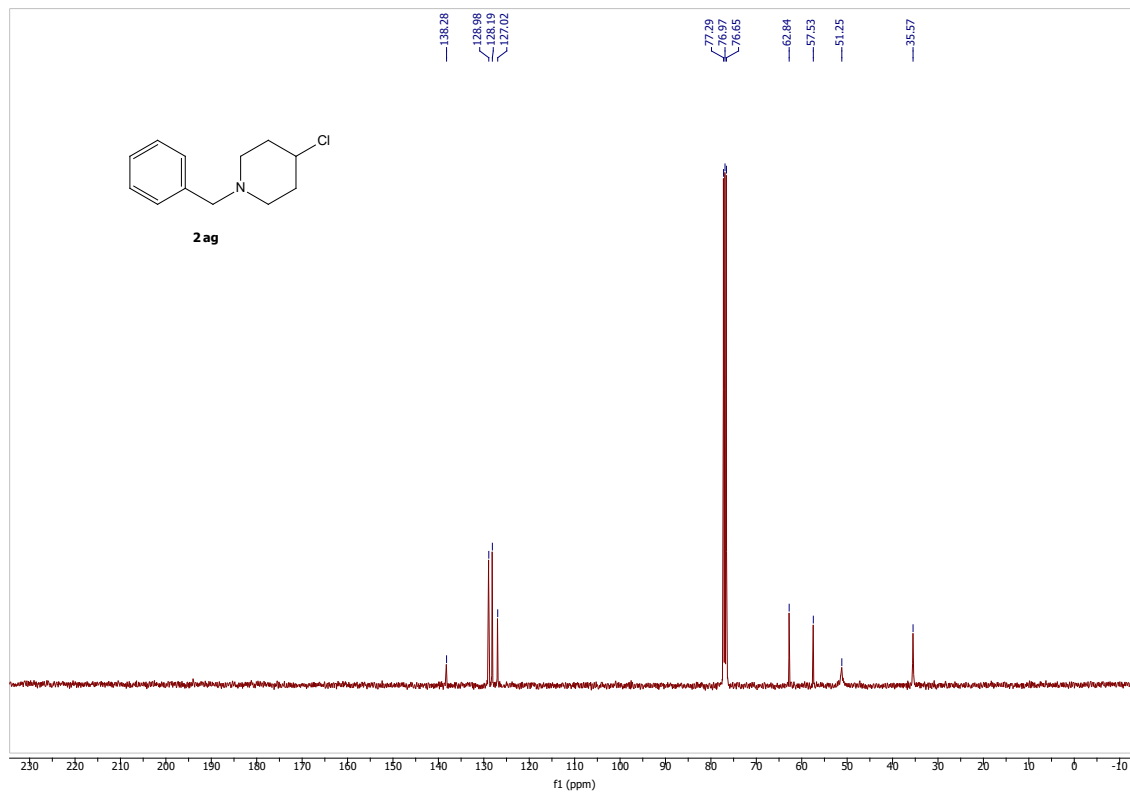
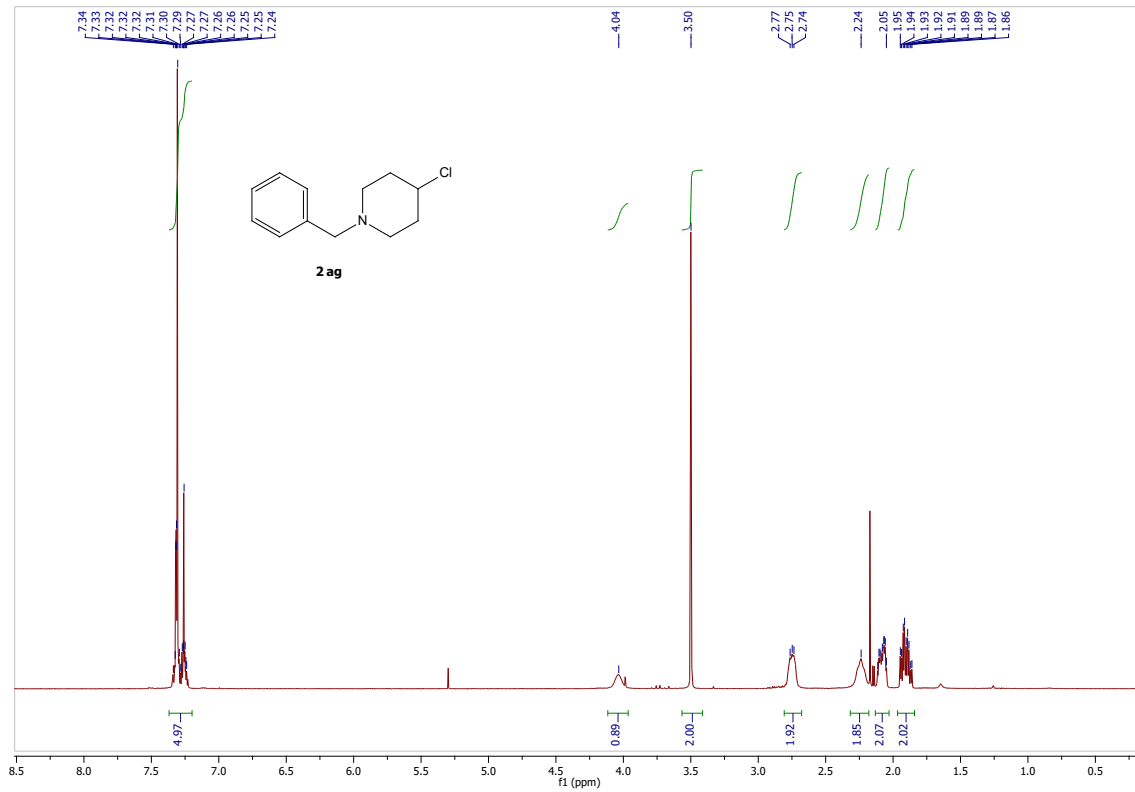


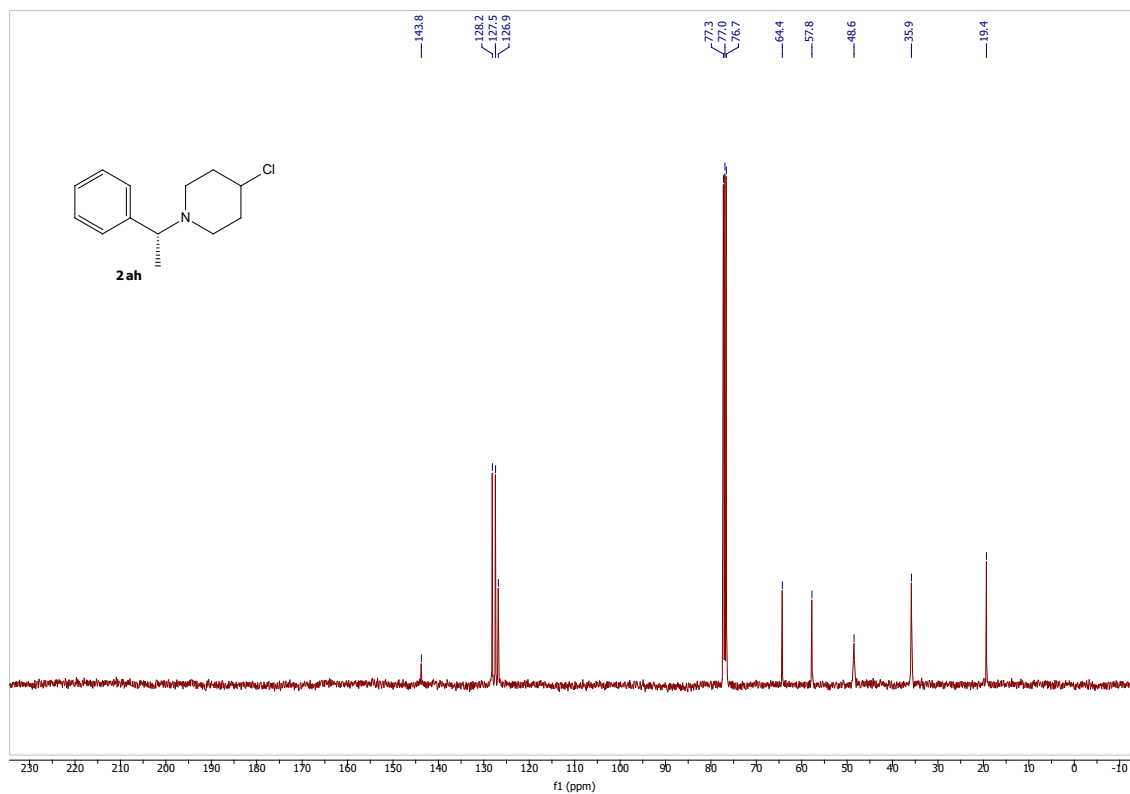
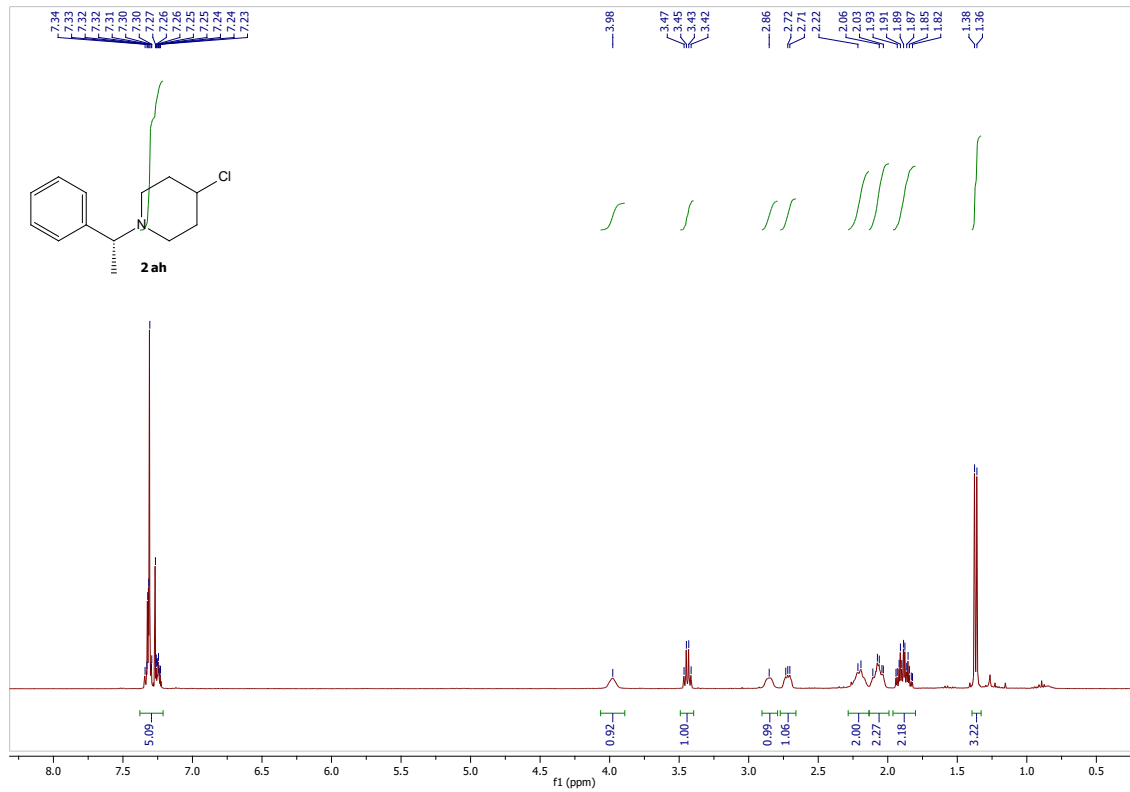


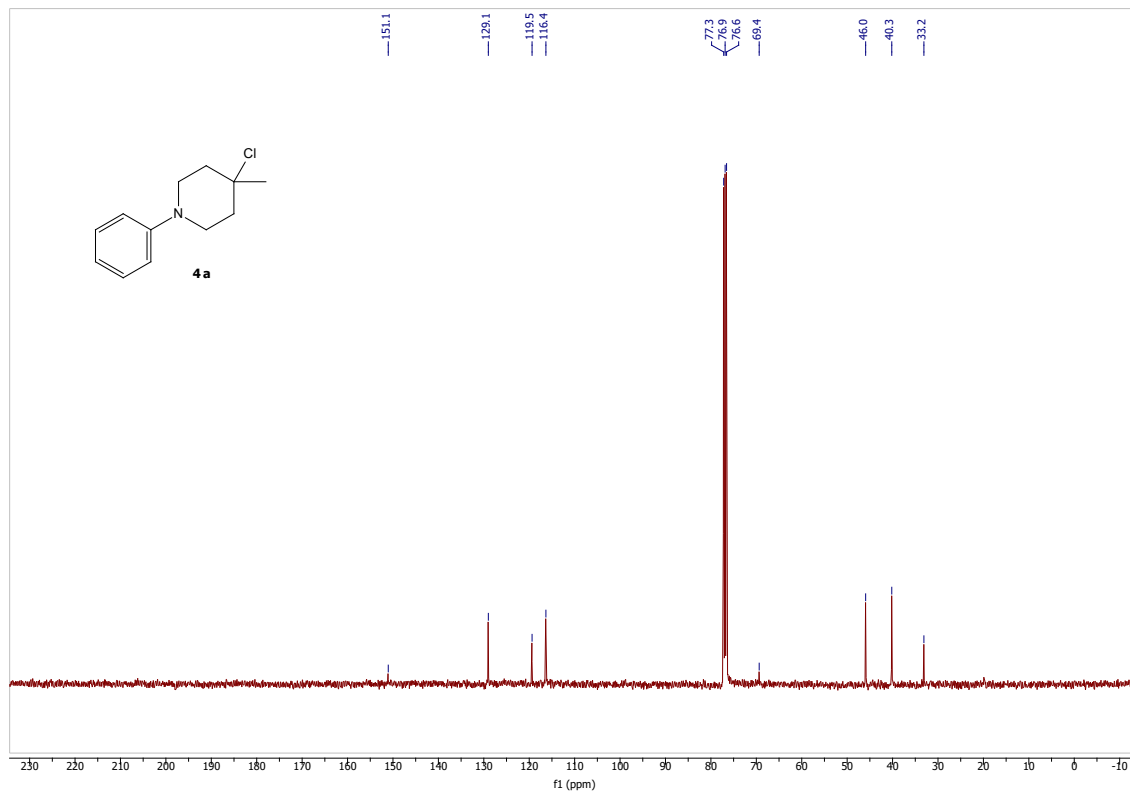
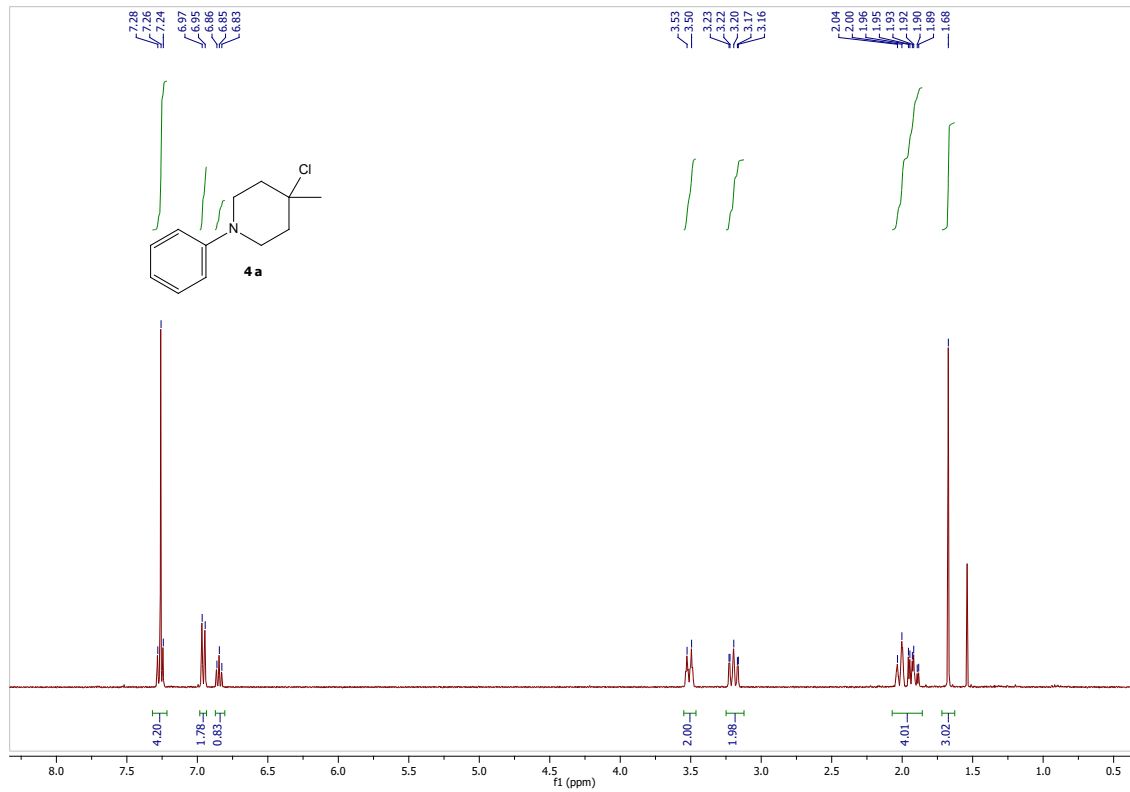


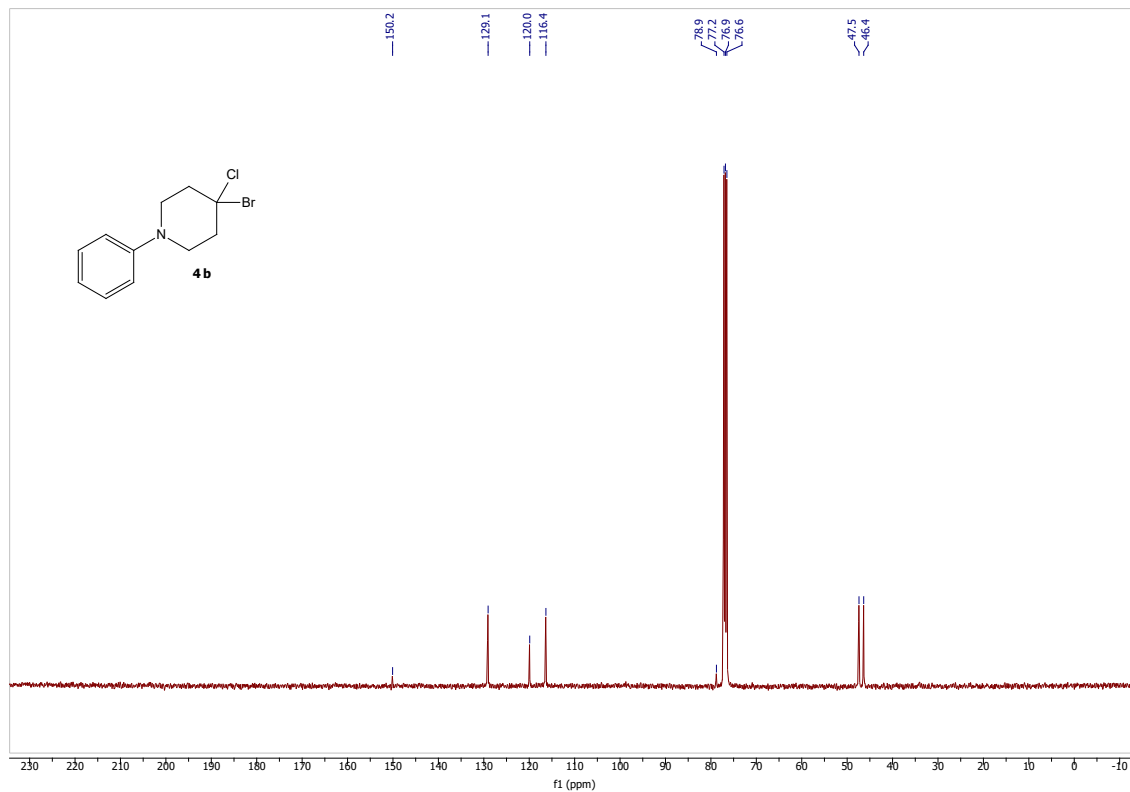
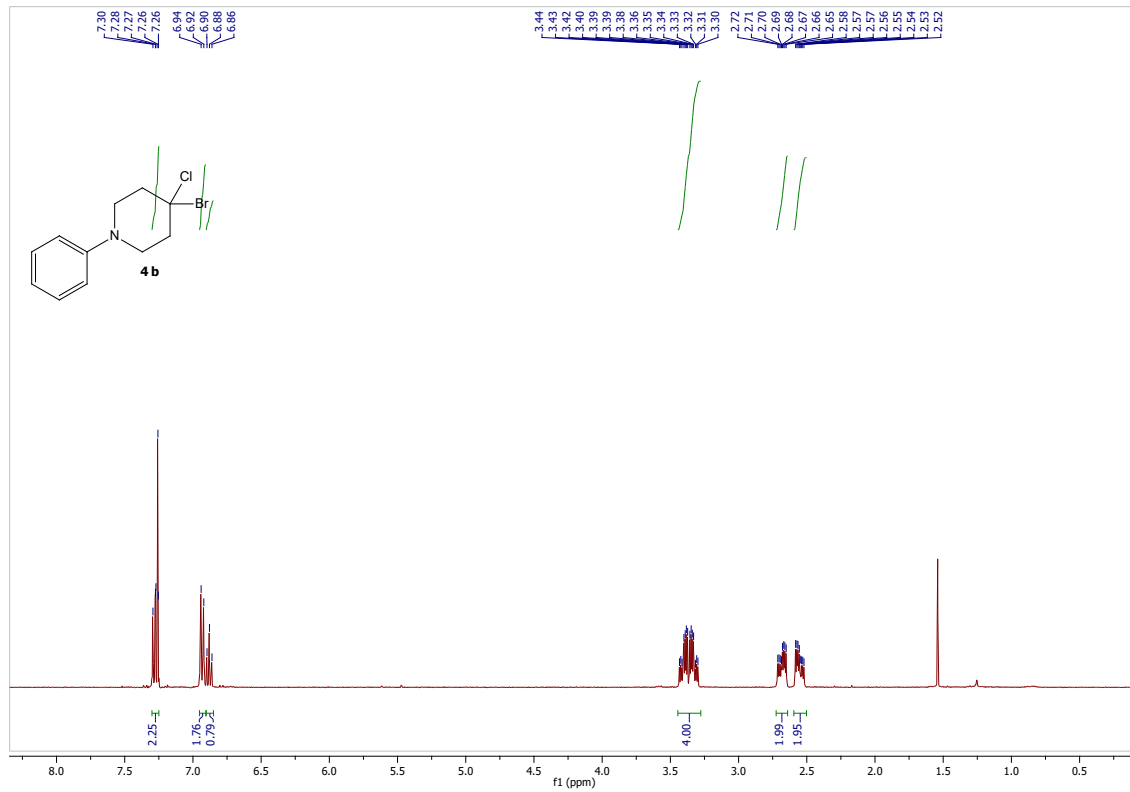


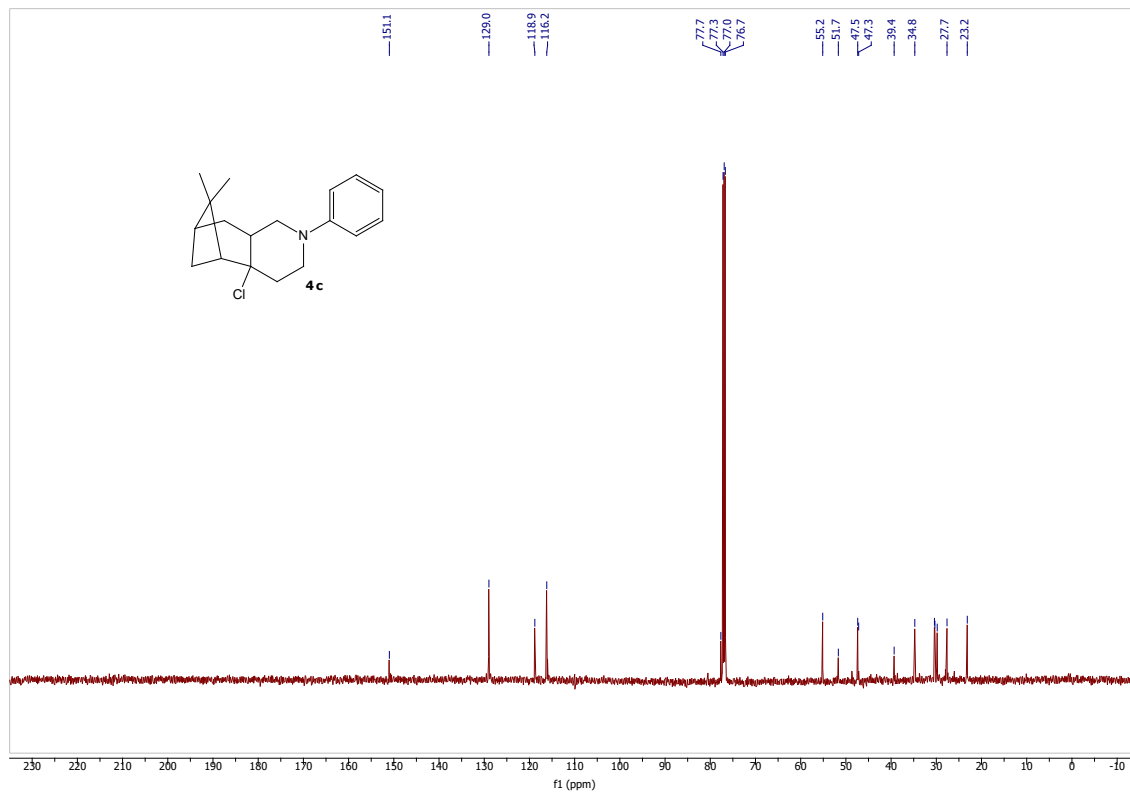
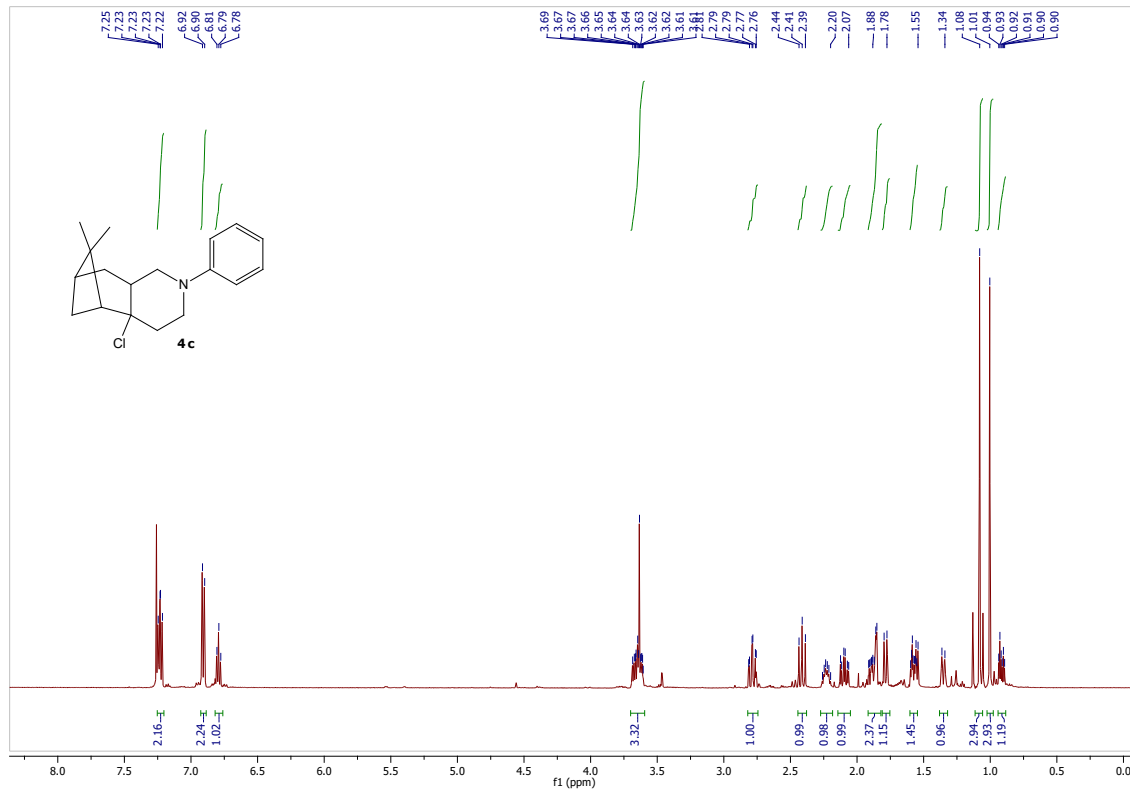


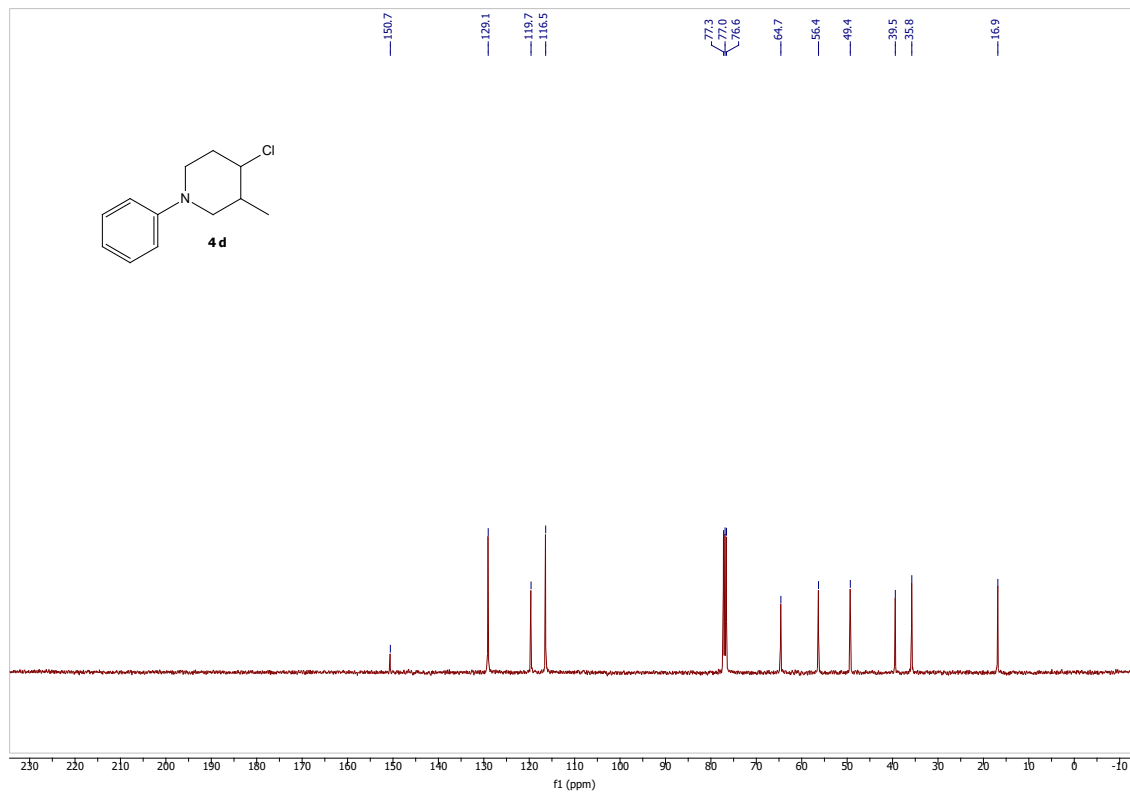
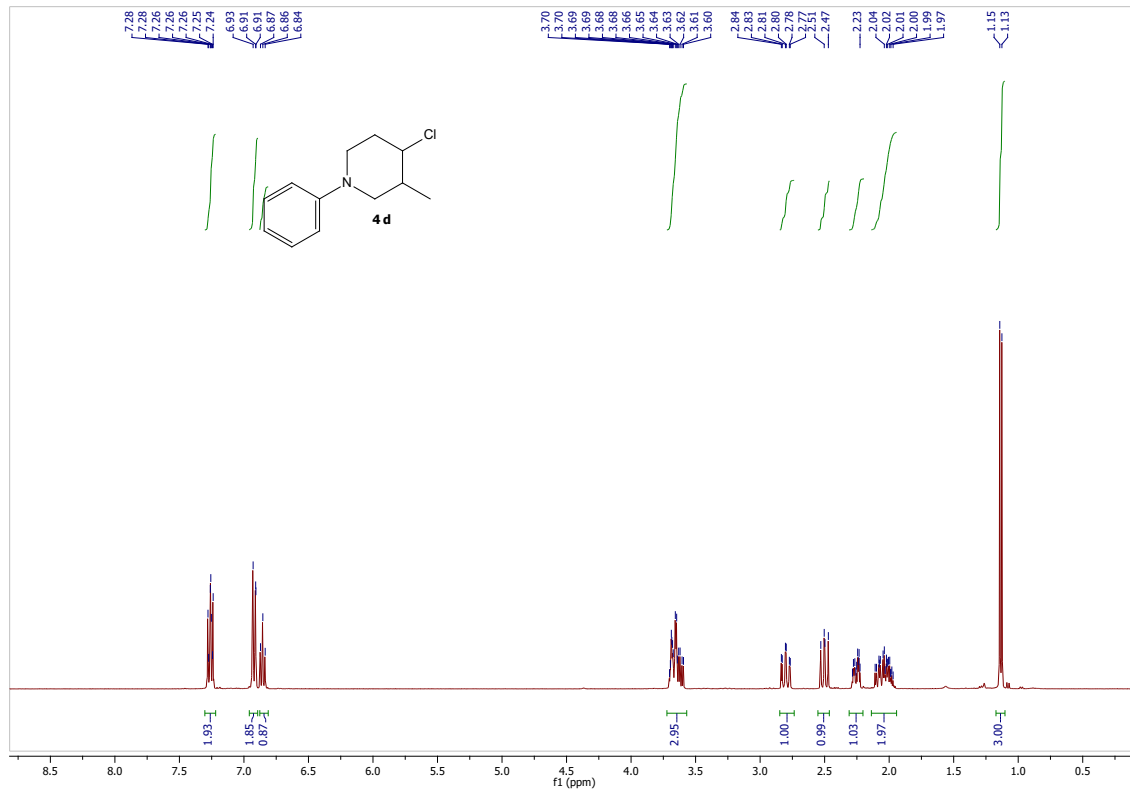


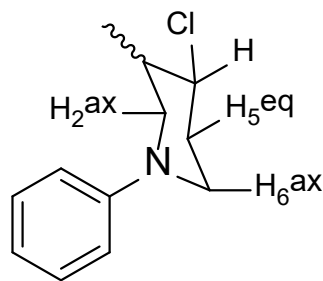
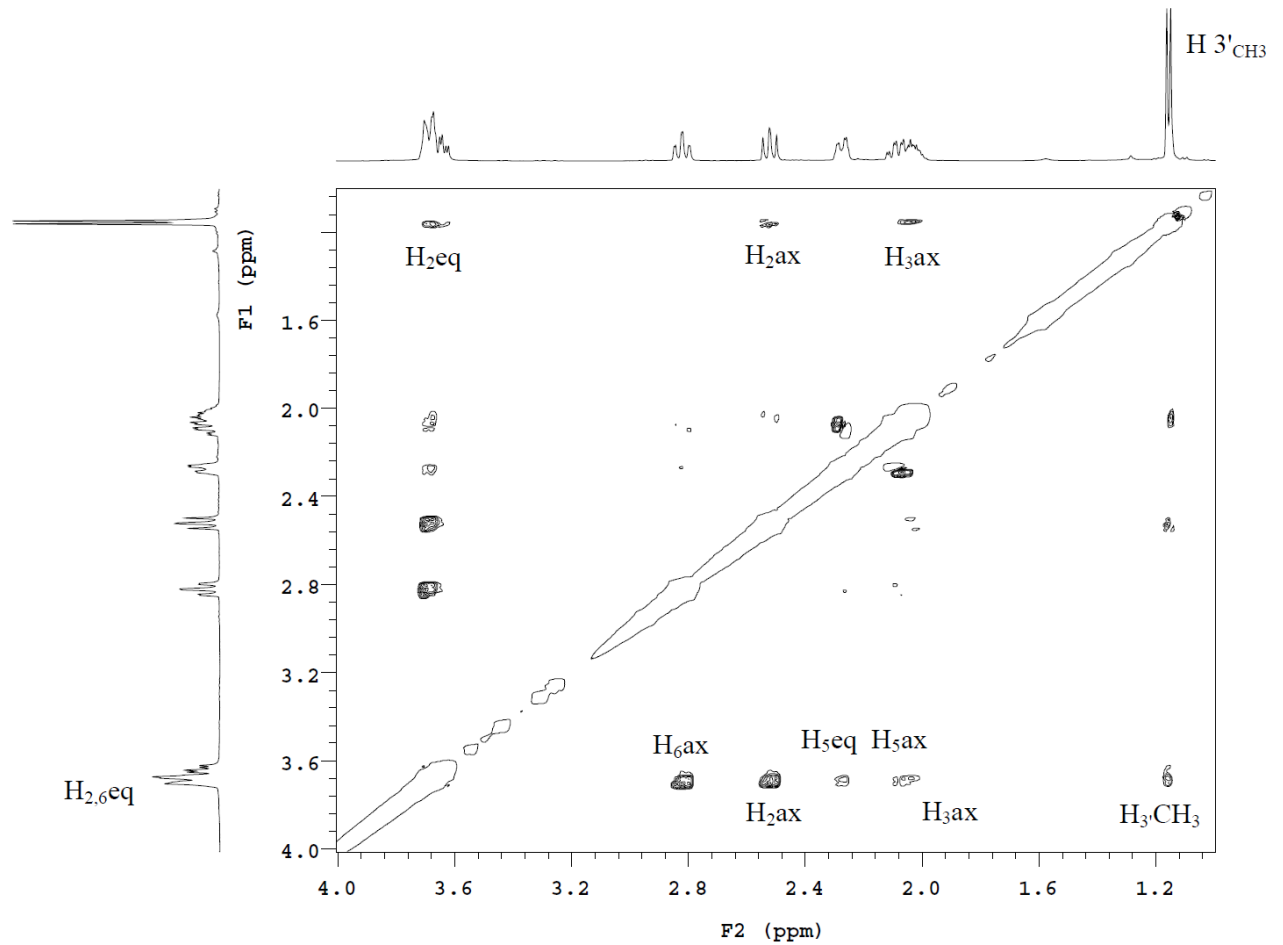












Note: Expected strong NOE between H_{2ax} and H_{6ax} is not observed for some reason. The CH₃ being equatorial should have NOE's to both H₂ protons as well as H₃ and H₄, although the later may or may not be there due to the limits of resolution of overlap between H₂, H₆ and H₄ around 3.65 ppm. One could argue however that lack of a CH₃ – H₄ NOE would be expected if they were both axial.

2. X-ray data for 2n

2.1 Sample preparation and crystal structure determination.

A yellow plate 0.39 x 0.38 x 0.05 mm³ crystal of (**2n**) grown from a solution of hot methanol was mounted on a glass fiber for collection of x-ray data on an Agilent Technologies/Oxford Diffraction Gemini CCD diffractometer. The CrysAlisPro CCD software package (v 1.171.36.32) was used to acquire a total of 779 thirty-second frame ω -scan exposures of data at 102K to a 2θ max = 66.24° using monochromated MoK α radiation (0.71073 Å) from a sealed tube. Frame data were processed using CrysAlisPro¹ RED to determine final unit cell parameters: $a = 17.2486(2)$ Å, $b = 10.17867(17)$ Å, $c = 6.17147(11)$ Å, $\alpha = \beta = \gamma = 90.00^\circ$, $V = 1083.51(3)$ Å³, $D_{\text{calc}} = 1.475$ Mg/m³, $Z = 4$ to produce raw hkl data that were then corrected for absorption (transmission min./max. = 0.906/1.000; $\mu = 0.338$ mm⁻¹) using SCALE 3 ABSPACK. The structure was solved by Direct methods in the orthorhombic space group Pnma using SHELXS and refined by least squares methods on F^2 using SHELXL. Non-hydrogen atoms were refined with anisotropic atomic displacement parameters. All methylene, methine and phenyl H's were located by difference maps and refined isotropically. For all 2160 unique reflections ($R(\text{int}) = 0.026$) the final anisotropic full matrix least-squares refinement on F^2 for 102 variables converged at $R1 = 0.036$ and $wR2 = 0.075$ with a GOF of 1.04.

2.2 ORTEP representation of (**2n**) with thermal ellipsoids shown at the 50% probability level.

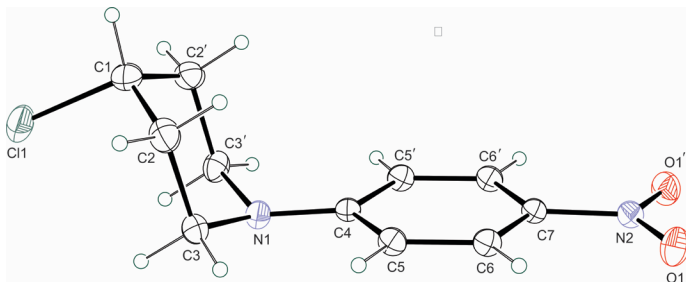


Table 1. Crystal data and structure refinement for 2n.

Identification code	2n	
Empirical formula	C11 H13 Cl N2 O2	
Formula weight	240.68	
Temperature	101.95(10) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P nma	
Unit cell dimensions	$a = 17.2486(2)$ Å	$\alpha = 90^\circ$.
	$b = 10.17867(17)$ Å	$\beta = 90^\circ$.
	$c = 6.17147(11)$ Å	$\gamma = 90^\circ$.
Volume	$1083.51(3)$ Å ³	

Z	4
Density (calculated)	1.475 Mg/m ³
Absorption coefficient	0.338 mm ⁻¹
F(000)	504
Crystal color, habit	yellow plate
Crystal size	0.39 x 0.38 x 0.05 mm ³
Theta range for data collection	3.51 to 33.12°
Index ranges	-26<=h<=25, -15<=k<=15, -9<=l<=9
Reflections collected	26127
Independent reflections	2160 [R(int) = 0.0265]
Completeness to theta = 33.12°	99.9 %
Absorption correction	SCALE 3 ABSPACK
Max. and min. transmission	1.000 and 0.906
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	2160 / 0 / 102
Goodness-of-fit on F ²	1.042
Final R indices [I>2sigma(I)]	R1 = 0.0320, wR2 = 0.0722
R indices (all data)	R1 = 0.0364, wR2 = 0.0746
Largest diff. peak and hole	0.489 and -0.344 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for 2n. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
Cl(1)	3167(1)	2500	6844(1)	33(1)
O(1)	-466(1)	1437(1)	-5484(1)	25(1)
N(1)	1383(1)	2500	3151(2)	18(1)
N(2)	-272(1)	2500	-4688(2)	18(1)
C(1)	3040(1)	2500	3903(2)	25(1)
C(2)	2604(1)	1265(1)	3244(2)	24(1)
C(3)	1761(1)	1318(1)	3992(2)	21(1)
C(4)	1019(1)	2500	1168(2)	15(1)
C(5)	810(1)	1313(1)	126(1)	17(1)
C(6)	394(1)	1313(1)	-1790(1)	17(1)
C(7)	182(1)	2500	-2727(2)	15(1)

Table 3. Bond lengths [Å] and angles [°] for 2n.

Cl(1)-C(1)	1.8285(14)
O(1)-N(2)	1.2347(8)
N(1)-C(4)	1.3753(15)
N(1)-C(3)#1	1.4632(11)
N(1)-C(3)	1.4632(11)
N(2)-O(1)#1	1.2347(8)
N(2)-C(7)	1.4417(15)
C(1)-C(2)#1	1.5206(13)
C(1)-C(2)	1.5206(13)
C(1)-H(1)	0.972(19)
C(2)-C(3)	1.5270(13)
C(2)-H(2A)	0.941(13)
C(2)-H(2B)	0.977(13)
C(3)-H(3A)	0.955(13)
C(3)-H(3B)	0.998(13)
C(4)-C(5)	1.4155(10)
C(4)-C(5)#1	1.4155(10)
C(5)-C(6)	1.3824(11)
C(5)-H(5)	0.936(12)
C(6)-C(7)	1.3886(10)
C(6)-H(6)	0.935(12)
C(7)-C(6)#1	1.3885(10)
C(4)-N(1)-C(3)#1	121.26(5)
C(4)-N(1)-C(3)	121.26(5)
C(3)#1-N(1)-C(3)	110.57(10)
O(1)-N(2)-O(1)#1	122.48(10)
O(1)-N(2)-C(7)	118.75(5)
O(1)#1-N(2)-C(7)	118.75(5)
C(2)#1-C(1)-C(2)	111.56(11)
C(2)#1-C(1)-Cl(1)	108.93(7)
C(2)-C(1)-Cl(1)	108.93(7)
C(2)#1-C(1)-H(1)	111.2(5)
C(2)-C(1)-H(1)	111.2(5)
Cl(1)-C(1)-H(1)	104.8(11)
C(1)-C(2)-C(3)	111.16(8)
C(1)-C(2)-H(2A)	111.1(8)
C(3)-C(2)-H(2A)	110.0(8)
C(1)-C(2)-H(2B)	107.1(8)
C(3)-C(2)-H(2B)	109.2(8)
H(2A)-C(2)-H(2B)	108.2(11)
N(1)-C(3)-C(2)	110.27(8)
N(1)-C(3)-H(3A)	111.6(8)
C(2)-C(3)-H(3A)	111.5(8)
N(1)-C(3)-H(3B)	108.1(8)
C(2)-C(3)-H(3B)	109.5(7)
H(3A)-C(3)-H(3B)	105.7(10)
N(1)-C(4)-C(5)	121.39(5)
N(1)-C(4)-C(5)#1	121.39(5)
C(5)-C(4)-C(5)#1	117.16(10)
C(6)-C(5)-C(4)	121.40(8)
C(6)-C(5)-H(5)	117.7(7)
C(4)-C(5)-H(5)	120.9(7)
C(5)-C(6)-C(7)	119.54(8)

C(5)-C(6)-H(6)	119.7(7)
C(7)-C(6)-H(6)	120.7(7)
C(6)#1-C(7)-C(6)	120.90(10)
C(6)#1-C(7)-N(2)	119.55(5)
C(6)-C(7)-N(2)	119.55(5)

Symmetry transformations used to generate equivalent atoms:

#1 $x, -y+1/2, z$

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for gbh40ltb. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl(1)	22(1)	50(1)	25(1)	0	-8(1)	0
O(1)	28(1)	22(1)	24(1)	-7(1)	-6(1)	0(1)
N(1)	18(1)	20(1)	17(1)	0	-2(1)	0
N(2)	17(1)	20(1)	16(1)	0	0(1)	0
C(1)	17(1)	37(1)	21(1)	0	3(1)	0
C(2)	23(1)	27(1)	21(1)	1(1)	1(1)	7(1)
C(3)	20(1)	23(1)	19(1)	5(1)	-3(1)	-1(1)
C(4)	13(1)	17(1)	15(1)	0	1(1)	0
C(5)	19(1)	14(1)	18(1)	1(1)	0(1)	1(1)
C(6)	18(1)	15(1)	17(1)	-1(1)	1(1)	-1(1)
C(7)	15(1)	16(1)	14(1)	0	0(1)	0

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for 2n.

	x	y	z	U(eq)
H(1)	3564(11)	2500	3320(30)	30
H(2A)	2846(7)	508(13)	3800(20)	28
H(2B)	2619(8)	1218(13)	1660(20)	28
H(3A)	1485(7)	541(13)	3590(20)	25
H(3B)	1742(7)	1354(13)	5610(20)	25
H(5)	941(7)	499(12)	727(19)	21
H(6)	262(7)	516(12)	-2440(20)	20

Table 6. Torsion angles [°] for 2n.

C(2)#1-C(1)-C(2)-C(3)	-50.40(13)
Cl(1)-C(1)-C(2)-C(3)	69.88(9)
C(4)-N(1)-C(3)-C(2)	88.96(11)
C(3)#1-N(1)-C(3)-C(2)	-62.21(12)
C(1)-C(2)-C(3)-N(1)	55.97(11)
C(3)#1-N(1)-C(4)-C(5)	165.40(9)
C(3)-N(1)-C(4)-C(5)	17.28(15)
C(3)#1-N(1)-C(4)-C(5)#1	-17.28(15)
C(3)-N(1)-C(4)-C(5)#1	-165.40(9)
N(1)-C(4)-C(5)-C(6)	175.18(9)
C(5)#1-C(4)-C(5)-C(6)	-2.25(15)
C(4)-C(5)-C(6)-C(7)	0.55(13)
C(5)-C(6)-C(7)-C(6)#1	1.26(16)
C(5)-C(6)-C(7)-N(2)	-178.08(9)
O(1)-N(2)-C(7)-C(6)#1	-178.93(9)
O(1)#1-N(2)-C(7)-C(6)#1	-0.42(15)
O(1)-N(2)-C(7)-C(6)	0.42(15)
O(1)#1-N(2)-C(7)-C(6)	178.93(9)

Symmetry transformations used to generate equivalent atoms:

#1 x,-y+1/2,z

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