

Supporting Information

Visible-light-induced C(sp³)-H functionalizations to 3,3-dichloro-2-hydroxy- piperidines with *N*-chlorosuccinimide

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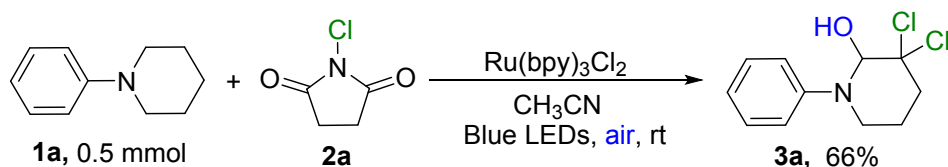
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1. General considerations

The ^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz Bruker FT-NMR spectrometer (400/100 MHz). All chemical shifts are given as δ value (ppm) with reference to tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet. The coupling constants, J , are reported in Hertz (Hz). High resolution mass spectroscopy data of the product were collected on an Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS (ESI). All the solvents and commercially available reagents were purchased from commercial suppliers. Products were purified by flash chromatography on 200–300 mesh silica gels, SiO_2 .

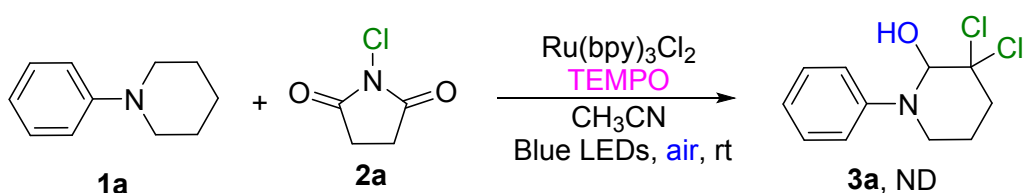
2. Representative procedure for the model reaction



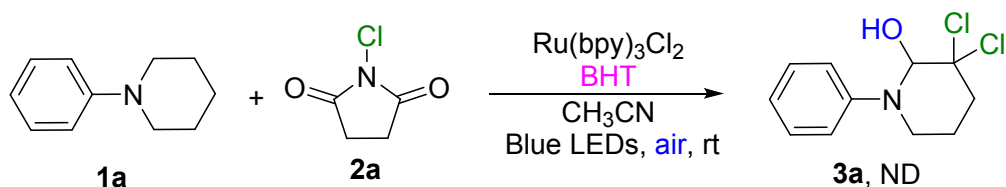
A 5 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with 1-phenylpiperidine (**1a**, 81 mg, 0.50 mmol), CH_3CN (2.0 mL), $\text{Ru}(\text{bpy})_3\text{Cl}_2$ (1.9 mg, 0.005 mmol) and *N*-chlorosuccinimide (NCS, **2a**, 133 mg, 1.0 mmol). The reaction vessel was exposed to blue LEDs (420–425 nm, 1.5 W) irradiation at room temperature in air with stirring for 12 h. Upon completion, it was quenched with water (3.0 mL), and then extracted with ethyl acetate (10 mL \times 3). The combined organic layer was washed with brine, dried over

anhydrous Na_2SO_4 , and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1) as the eluent to give **3a** in 66% yield.

3. Preliminary mechanistic investigation



(a) A 5 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with 1-phenylpiperidine (**1a**, 81 mg, 0.50 mmol), CH_3CN (2.0 mL), *N*-chlorosuccinimide (NCS, **2a**, 133 mg, 1.0 mmol) and TEMPO (156 mg, 1.0 mmol). The reaction vessel was exposed to blue LED (420–425 nm, 1.5 W) irradiation at room temperature in air with stirring for 12 h. TLC analysis of the resulting mixture showed that **3a** was not formed.



(b) A 5 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with 1-phenylpiperidine (**1a**, 81 mg, 0.50 mmol), CH_3CN (2.0 mL), $\text{Ru}(\text{bpy})_3\text{Cl}_2$ (1.9 mg, 0.005 mmol), *N*-chlorosuccinimide (NCS, **2a**, 133 mg, 1.0 mmol) and BHT (220 mg, 1.0

mmol). The reaction vessel was exposed to blue LEDs (420–425 nm, 1.5 W) irradiation at room temperature in air with stirring for 12 h. TLC analysis of the resulting mixture showed that **3a** was not formed. Meanwhile, enamine intermediate was observed in GC-MS analysis (Figure S1).

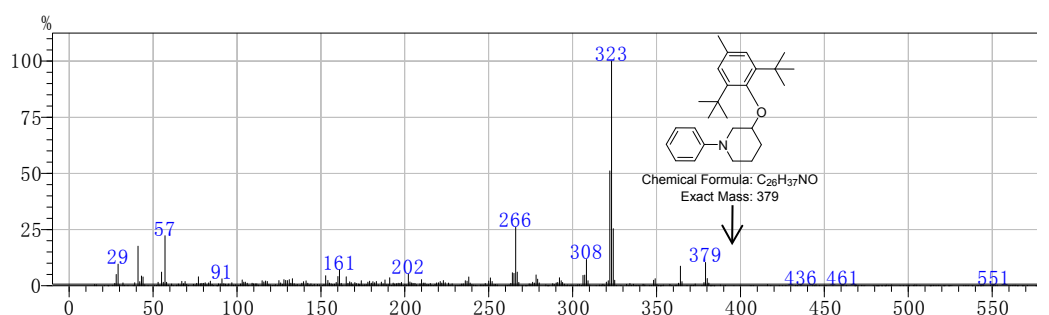
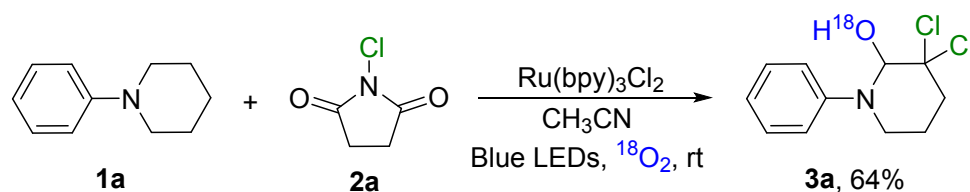


Figure S1. GC-MS analysis of enamine intermediate



(c) A 5 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with 1-phenylpiperidine (**1a**, 81 mg, 0.50 mmol), CH₃CN (2.0 mL), Ru(bpy)₃Cl₂ (1.9 mg, 0.005 mmol) and *N*-chlorosuccinimide (NCS, **2a**, 133 mg, 1.0 mmol). The reaction vessel was exposed to blue LEDs (420–425 nm, 1.5 W) irradiation at room temperature under molecular oxygen (¹⁸O₂) atmosphere at room temperature for 12 h. The ¹⁸O-labeling product (¹⁸O-**3a**) was isolated in 64% yield, and it was confirmed by GC-MS analysis (Figure S2).

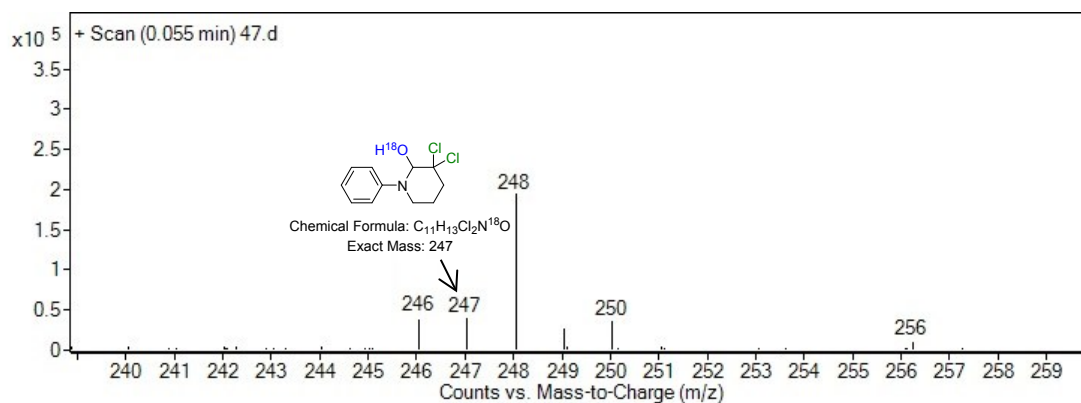
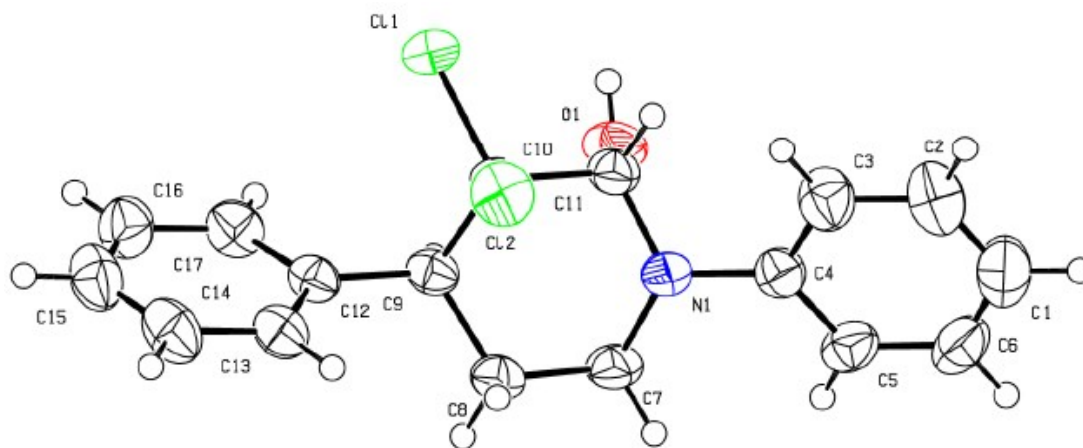


Figure S2. GC-MS analysis of $^{18}\text{O}_2$ -isotopic labeling product (^{18}O -**3a**)

4. X-Ray single crystal diffraction analysis of **3n**

3,3-Dichloro-1-(cyclohexa-1,3-dien-1-yl)-4-phenylpiperidin-2-ol

(**3n**, CCDC: 2081144)



checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 1

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

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	Calculated	Reported	
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Hall group	P 3 -2c	P 3 -2c	
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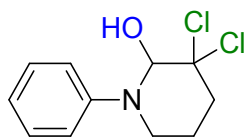
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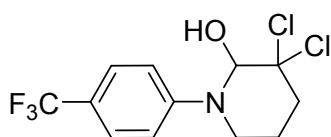
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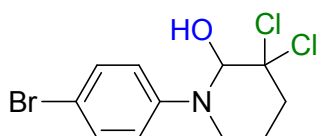
5. Characterization data for the products



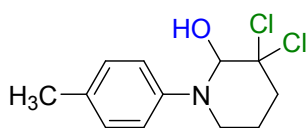
3,3-Dichloro-1-phenylpiperidin-2-ol (3a). Colorless oil (81 mg). ^1H NMR (400 MHz, CDCl_3) δ 1.74–1.81 (m, 1H), 2.09–2.21 (m, 1H), 2.43–2.48 (m, 1H), 2.65–2.71 (m, 1H), 2.72 (d, $J = 2.4$ Hz, 1H), 3.16–3.20 (m, 1H), 3.38–3.45 (m, 1H), 5.36 (s, 1H), 6.97 (t, $J = 7.6$ Hz, 1H), 7.05 (d, $J = 7.6$ Hz, 2H), 7.30 (dd, $J_1 = 8.4$ Hz, $J_2 = 7.6$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ : 23.3, 37.8, 41.1, 88.2, 90.8, 119.2, 121.8, 129.2, 149.7. HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{14}\text{Cl}_2\text{NO}$: 246.0447 $[\text{M}+\text{H}]^+$, found: 246.0428.



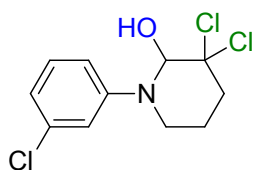
3,3-Dichloro-1-(4-(trifluoromethyl)phenyl)piperidin-2-ol (3b). Colorless oil (102 mg). ^1H NMR (400 MHz, CDCl_3) δ 1.78–1.82 (m, 1H), 2.13–2.19 (m, 1H), 2.46–2.49 (m, 1H), 2.66–2.74 (m, 1H), 2.92 (s, 1H), 3.25–3.32 (m, 1H), 3.38–3.45 (m, 1H), 5.44 (s, 1H), 7.08 (t, $J = 8.8$ Hz, 2H), 7.53 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ : 23.1, 25.4, 37.5, 40.9, 87.1, 90.5, 117.8, 126.5 (q, $^4J_{\text{C-F}} = 3.6$ Hz), 126.5 (q, $^2J_{\text{C-F}} = 10.9$ Hz), 152.3. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{13}\text{Cl}_2\text{F}_3\text{NO}^+$: 314.0321 $[\text{M}+\text{H}]^+$, found: 314.0326. ^{19}F NMR (376 MHz, CDCl_3) δ -61.7.



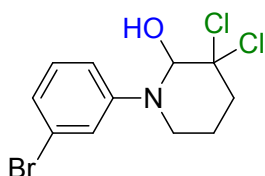
1-(4-Bromophenyl)-3,3-dichloropiperidin-2-ol (3c). Colorless oil (113 mg). ^1H NMR (400 MHz, CDCl_3) δ 1.75–1.80 (m, 1H), 2.10–2.18 (m, 1H), 2.44–2.47 (m, 1H), 2.64–2.69 (m, 1H), 2.77 (s, 1H), 3.11–3.15 (m, 1H), 3.36–3.41 (m, 1H), 5.29 (s, 1H), 6.93 (d, $J = 6.0$ Hz, 2H), 7.38 (d, $J = 6.0$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 23.2, 37.6, 41.3, 87.9, 90.6, 114.4, 120.8, 132.1, 148.9. HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{BrCl}_2\text{NO}$: 323.9552 $[\text{M}+\text{H}]^+$, found: 323.9548.



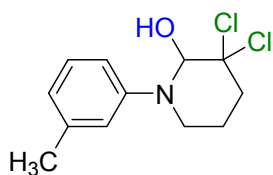
3,3-Dichloro-1-(*p*-tolyl)piperidin-2-ol (3d). Colorless oil (105 mg). ^1H NMR (400 MHz, CDCl_3) δ 1.74–1.78 (m, 1H), 2.10–2.18 (m, 1H), 2.29 (s, 3H), 2.43–2.46 (m, 1H), 2.64–2.69 (m, 1H), 2.71 (d, $J = 1.2$ Hz, 1H), 3.09–3.11 (m, 1H), 3.37–3.41 (m, 1H), 5.29 (s, 1H), 6.96 (d, $J = 5.2$ Hz, 2H), 7.10 (d, $J = 5.6$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 20.6, 23.4, 37.8, 41.4, 88.5, 90.8, 119.4, 129.8, 131.5, 147.3. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{16}\text{Cl}_2\text{NO}$: 260.0603 $[\text{M}+\text{H}]^+$, found: 260.0605.



3,3-Dichloro-1-(3-chlorophenyl)piperidin-2-ol (3e). Colorless oil (103 mg). ^1H NMR (400 MHz, CDCl_3) δ 1.77–1.79 (m, 1H), 2.10–2.19 (m, 1H), 2.45–2.47 (m, 1H), 2.65–2.70 (m, 1H), 2.76 (s, 1H), 3.17–3.20 (m, 1H), 3.37–3.41 (m, 1H), 5.35 (s, 1H), 6.92–6.94 (m, 2H), 7.02 (s, 1H), 7.20 (t, $J = 5.6$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 23.2, 37.6, 41.2, 87.7, 90.6, 117.0, 119.1, 121.7, 130.2, 134.9, 151.0. HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{Cl}_3\text{NO}$: 280.0057 $[\text{M}+\text{H}]^+$, found: 280.0059.

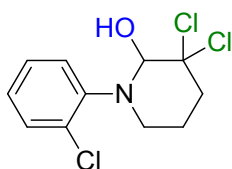


1-(3-Bromophenyl)-3,3-dichloropiperidin-2-ol (3f). Colorless oil (121 mg). ^1H NMR (400 MHz, CDCl_3) δ 1.77–1.79 (m, 1H), 2.10–2.18 (m, 1H), 2.44–2.47 (m, 1H), 2.65–2.70 (m, 1H), 2.79 (s, 1H), 3.17–3.19 (m, 1H), 3.37–3.41 (m, 1H), 5.33 (s, 1H), 6.96–6.98 (m, 1H), 7.08–7.09 (m, 1H), 7.15 (t, $J = 5.6$ Hz, 1H), 7.18 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 23.2, 37.6, 41.3, 87.7, 90.6, 117.6, 122.0, 123.1, 124.6, 130.5, 151.1. HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{BrCl}_2\text{NO}$: 323.9552 $[\text{M}+\text{H}]^+$, found: 323.9547.

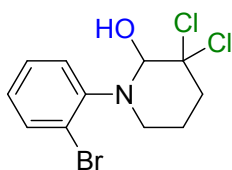


3,3-Dichloro-1-(*m*-tolyl)piperidin-2-ol (3g). Colorless oil (100 mg). ^1H NMR

(400 MHz, CDCl₃) δ 1.75–1.79 (m, 1H), 2.10–2.19 (m, 1H), 2.33 (s, 3H), 2.43–2.46 (m, 1H), 2.66–2.71 (m, 1H), 2.74 (s, 1H), 3.15–3.18 (m, 1H), 3.38–3.42 (m, 1H), 5.37 (s, 1H), 6.80 (d, $J = 5.2$ Hz, 1H), 6.85–6.87 (m, 2H), 7.18 (t, $J = 5.2$ Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 23.4, 37.8, 41.1, 88.2, 90.8, 116.2, 119.9, 122.7, 129.1, 139.1, 149.7. HRMS (ESI) calcd for C₁₂H₁₆Cl₂NO: 260.0603 [M+H]⁺, found: 260.0597.

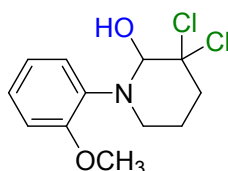


3,3-Dichloro-1-(2-chlorophenyl)piperidin-2-ol (3h). Colorless oil (87 mg). ¹H NMR (400 MHz, CDCl₃) δ 1.73–1.77 (m, 1H), 2.25–2.28 (m, 1H), 2.42–2.45 (m, 1H), 2.67–2.72 (m, 1H), 2.85 (s, 1H), 2.99–3.02 (m, 1H), 3.42–3.46 (m, 1H), 5.07 (s, 1H), 7.05 (t, $J = 5.2$ Hz, 1H), 7.22 (t, $J = 5.2$ Hz, 1H), 7.37 (d, $J = 5.2$ Hz, 1H), 7.41 (d, $J = 5.2$ Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 23.4, 38.5, 43.7, 87.5, 91.1, 124.6, 125.3, 127.5, 130.1, 130.6, 146.7. HRMS (ESI) calcd for C₁₁H₁₃Cl₃NO: 280.0057 [M+H]⁺, found: 280.0059.

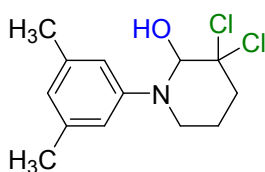


1-(2-Bromophenyl)-3,3-dichloropiperidin-2-ol (3i). Colorless oil (102 mg). ¹H

NMR (400 MHz, CDCl₃) δ 1.74–1.77(m, 1H), 2.24–2.32 (m, 1H), 2.44–2.48 (m, 1H), 2.68–2.73 (m, 1H), 2.89 (s, 1H), 2.99–3.02 (m, 1H), 3.38–3.42 (m, 1H), 5.00 (s, 1H), 6.99 (t, *J* = 5.2 Hz, 1H), 7.27 (t, *J* = 5.6 Hz, 1H), 7.48 (d, *J* = 5.2 Hz, 1H), 7.57 (d, *J* = 5.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 23.3, 38.7, 44.4, 87.7, 91.2, 121.1, 125.3, 125.9, 128.2, 133.8, 148.7. HRMS (ESI) calcd for C₁₁H₁₃BrCl₂NO: 323.9552 [M+H]⁺, found: 323.9547.

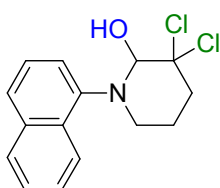


3,3-Dichloro-1-(2-methoxyphenyl)piperidin-2-ol (3j). Colorless oil (76 mg). ¹H NMR (400 MHz, CDCl₃) δ 1.73–1.77 (m, 1H), 2.17–2.25 (m, 1H), 2.42–2.45 (m, 1H), 2.68–2.73 (m, 1H), 2.95–2.98 (m, 1H), 3.48–3.53 (m, 1H), 3.87 (s, 3H), 5.17 (s, 1H), 6.88 (d, *J* = 5.6 Hz, 1H), 6.93 (t, *J* = 5.2 Hz, 1H), 7.07 (t, *J* = 5.6 Hz, 1H), 7.11–7.13 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 23.7, 38.4, 42.9, 55.8, 87.2, 90.7, 111.9, 121.3, 123.5, 124.7, 138.5, 153.2. HRMS (ESI) calcd for C₁₂H₁₆Cl₂NO₂: 276.0553 [M+H]⁺, found: 276.0556.

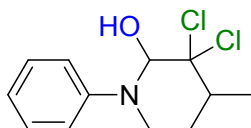


3,3-Dichloro-1-(3,5-dimethylphenyl)piperidin-2-ol (3k). Colorless oil (68 mg). ¹H

NMR (400 MHz, CDCl₃) δ 1.75–1.78 (m, 1H), 2.10–2.18 (m, 1H), 2.29 (s, 6H), 2.43–2.46 (m, 1H), 2.65–2.71 (m, 2H), 3.14–3.17 (m, 1H), 3.37–3.41 (m, 1H), 5.36 (s, 1H), 6.63 (s, 1H), 6.68 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 21.5, 23.4, 37.8, 41.2, 88.2, 90.8, 117.0, 123.7, 138.8, 149.7. HRMS (ESI) calcd for C₁₃H₁₈Cl₂NO: 274.0760 [M+H]⁺, found: 274.0761.

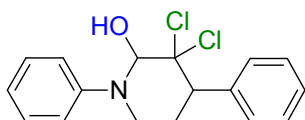


3,3-Dichloro-1-(naphthalen-1-yl)piperidin-2-ol (3l). White solid (84 mg), mp: 95–96 °C. ¹H NMR (400 MHz, CDCl₃) δ 1.78–1.80 (m, 1H), 2.37–2.39 (m, 1H), 2.50–2.53 (m, 1H), 2.75 (s, 1H), 2.93–2.95 (m, 1H), 3.60 (m, 1H), 5.09 (s, 1H), 7.41 (t, *J* = 5.2 Hz, 1H), 7.46–7.53 (m, 3H), 7.64 (d, *J* = 5.6 Hz, 1H), 7.83 (d, *J* = 5.6 Hz, 2H), 8.50 (d, *J* = 4.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 23.7, 38.1, 43.9, 88.3, 120.1, 123.7, 125.3, 125.7, 126.0, 126.1, 128.4, 134.8, 146.4. HRMS (ESI) calcd for C₁₅H₁₆Cl₂NO: 296.0603 [M+H]⁺, found: 296.0602.



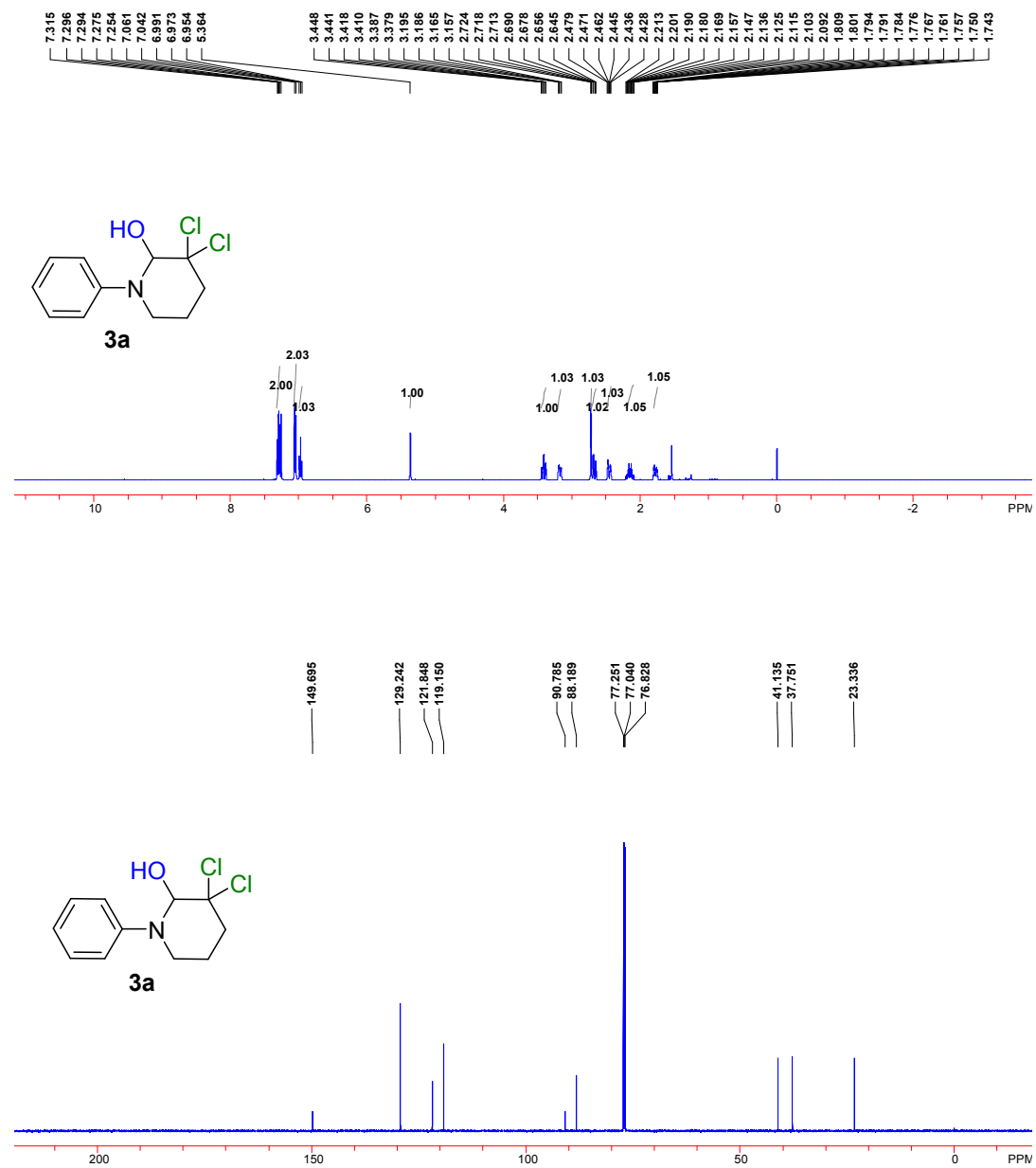
3,3-Dichloro-4-methyl-1-phenylpiperidin-2-ol (3m). Colorless oil (92 mg). ¹H NMR (400 MHz, CDCl₃) δ 1.28 (d, *J* = 4.4 Hz, 3H), 1.68–1.72 (m, 1H), 1.79–1.86 (m,

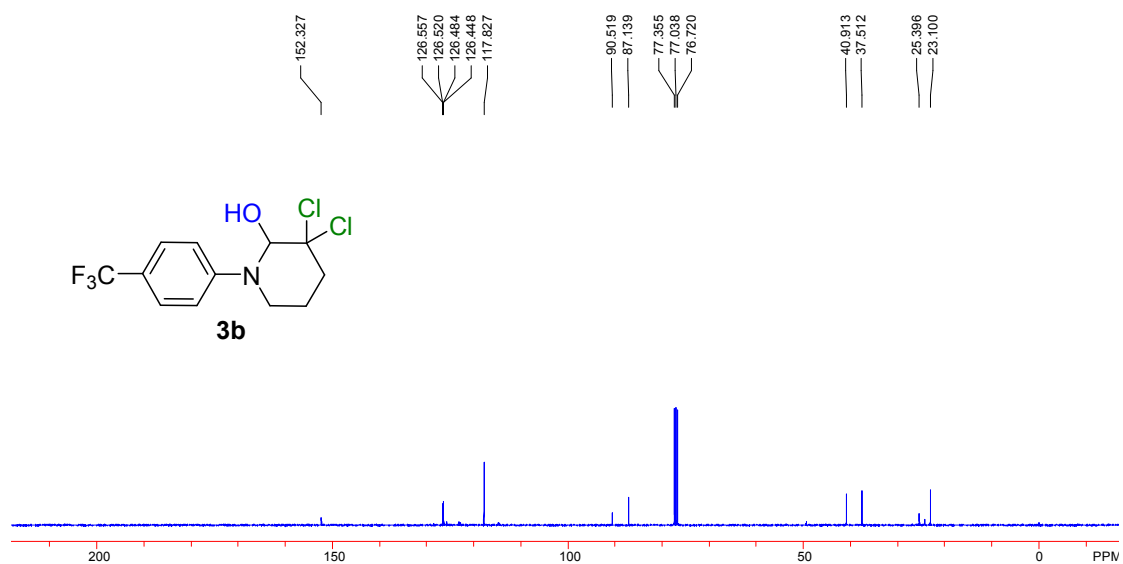
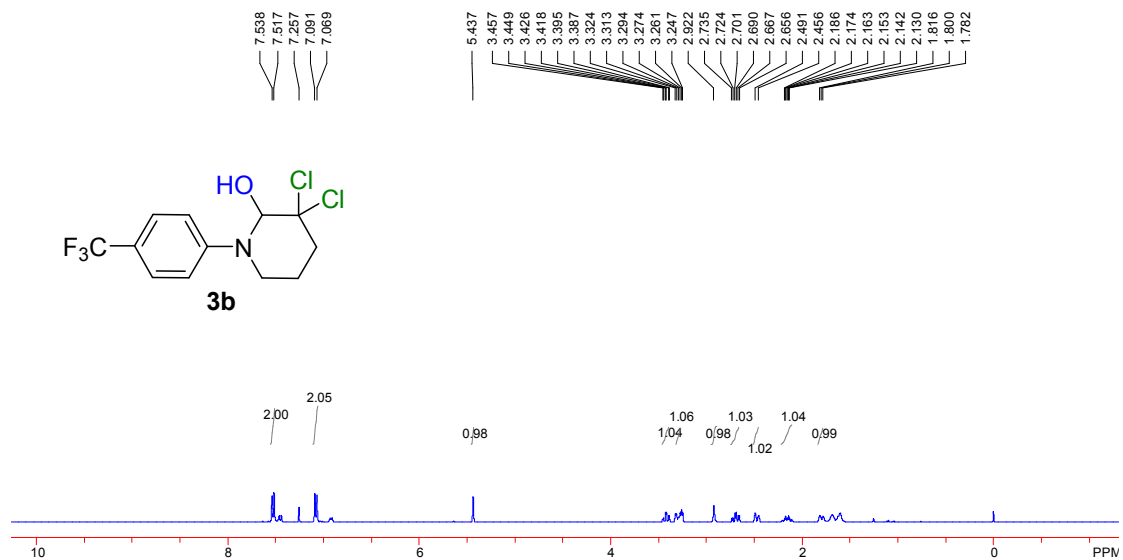
1H), 2.63–2.69 (m, 1H), 2.75 (s, 1H), 3.16–3.19 (m, 1H), 3.46–3.51 (m, 1H), 5.46 (s, 1H), 6.96 (t, $J = 5.2$ Hz, 1H), 7.05 (d, $J = 5.2$ Hz, 2H), 7.29 (t, $J = 5.2$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 16.0, 31.0, 38.6, 41.8, 88.9, 97.2, 118.9, 121.7, 129.2, 149.5. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{16}\text{Cl}_2\text{NO}$: 260.0603 $[\text{M}+\text{H}]^+$, found: 260.0607.

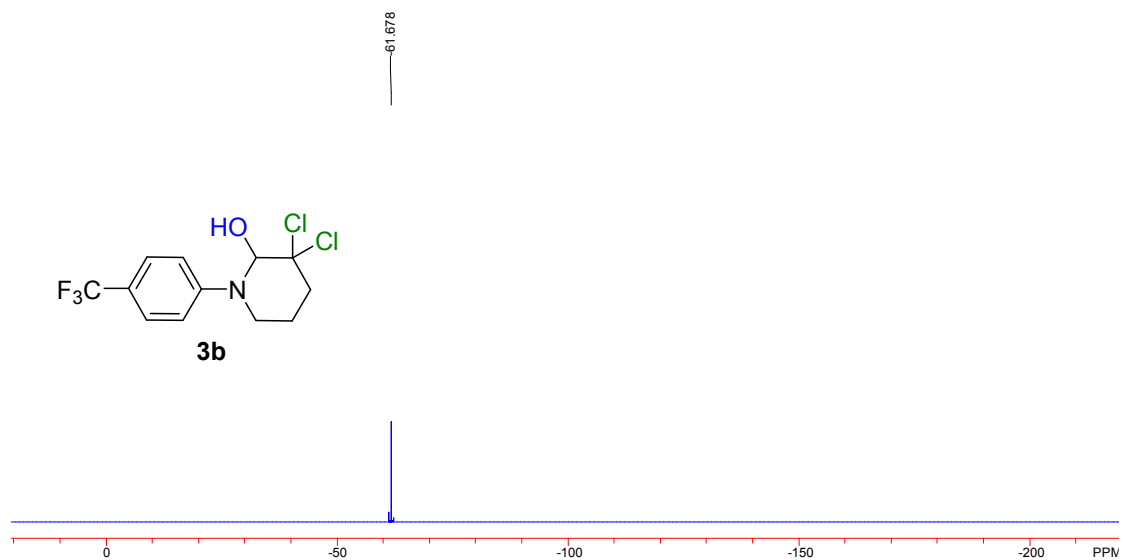


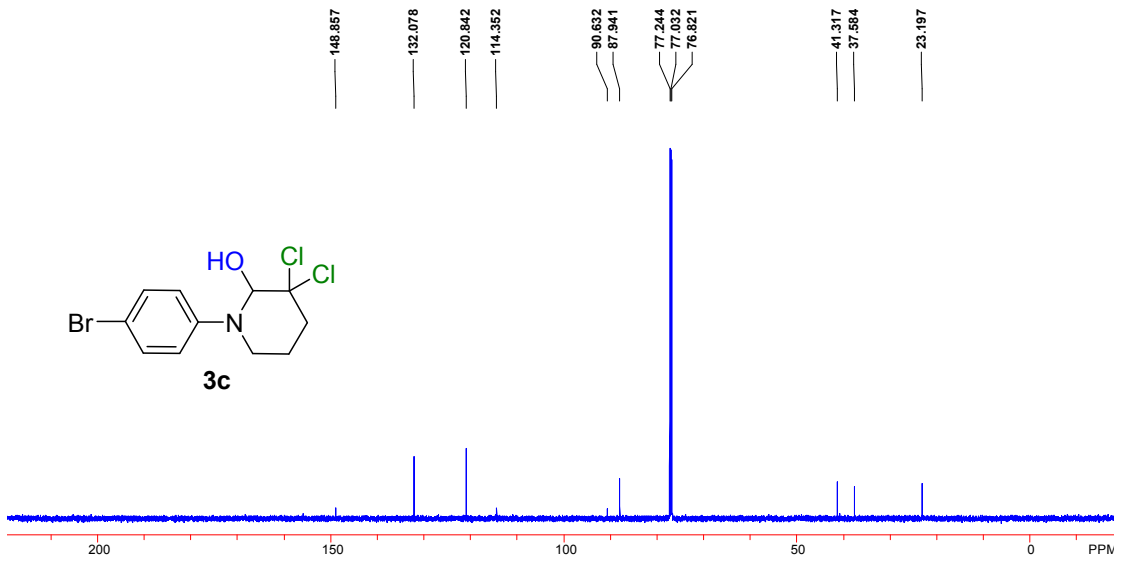
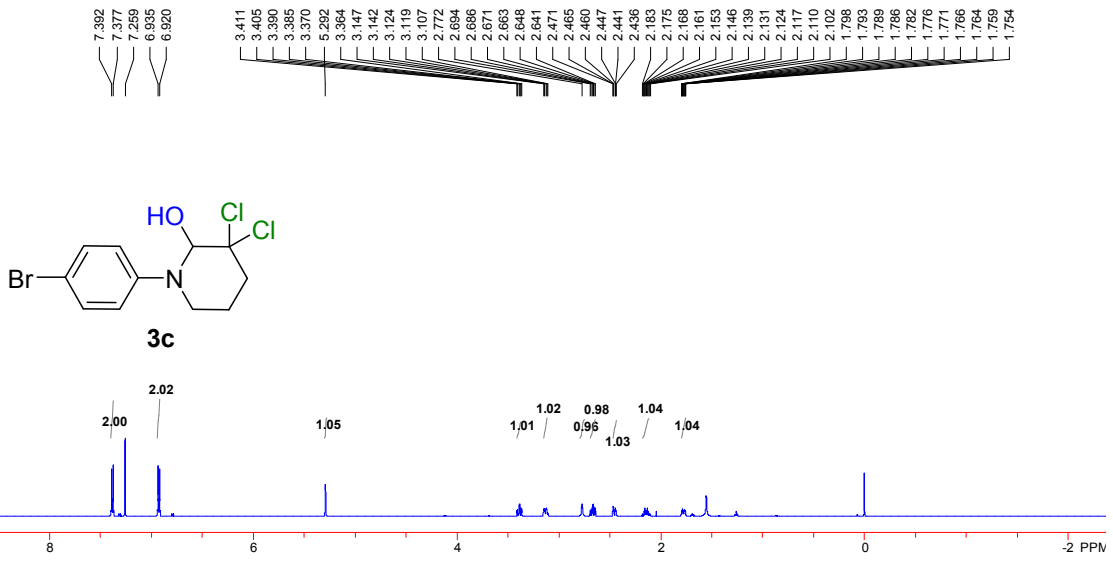
3,3-Dichloro-1,4-diphenylpiperidin-2-ol (3n). White solid (119 mg), mp: 85–86 °C. ^1H NMR (400 MHz, CDCl_3) δ 1.89–1.92 (m, 1H), 2.53–2.60 (m, 1H), 2.93 (s, 1H), 3.34–3.36 (m, 1H), 3.60–3.65 (m, 1H), 3.78–3.80 (m, 1H), 5.56 (s, 1H), 7.00 (t, $J = 5.2$ Hz, 1H), 7.10 (d, $J = 5.6$ Hz, 1H), 7.32 (t, $J = 5.2$ Hz, 2H), 7.35–7.39 (m, 1H), 7.46–7.47 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 29.3, 42.2, 48.9, 89.6, 94.6, 119.0, 121.9, 127.9, 128.0, 130.4, 137.8, 149.5. HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{18}\text{Cl}_2\text{NO}$: 322.0760 $[\text{M}+\text{H}]^+$, found: 322.0757.

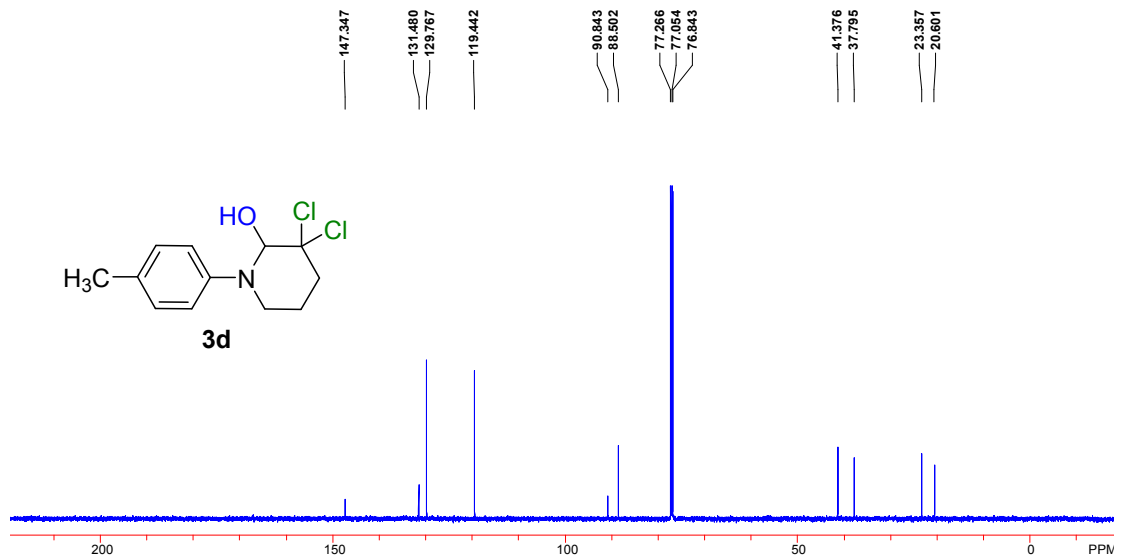
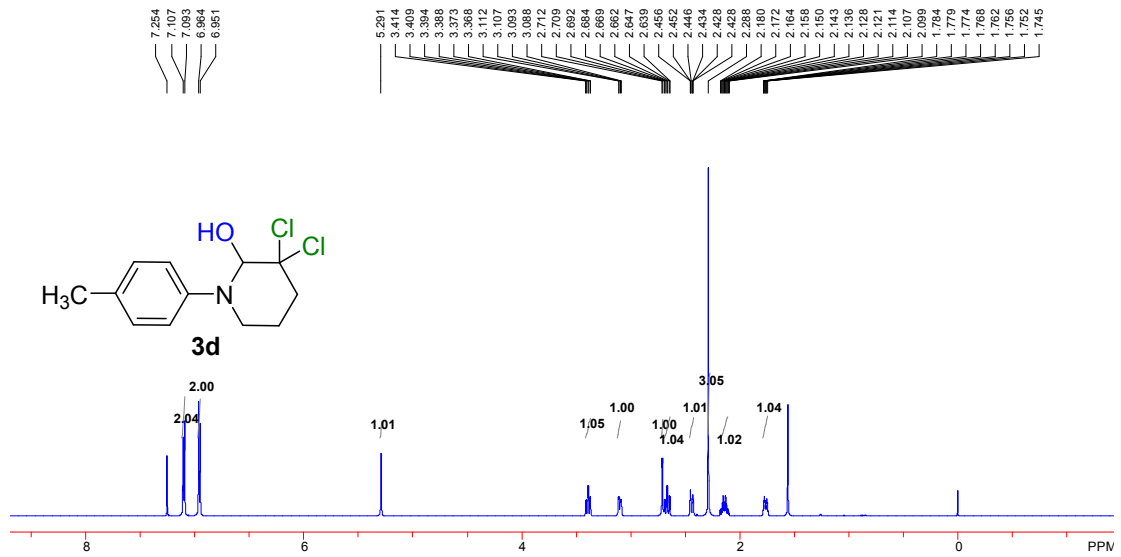
6. ^1H and ^{13}C NMR spectra of the products

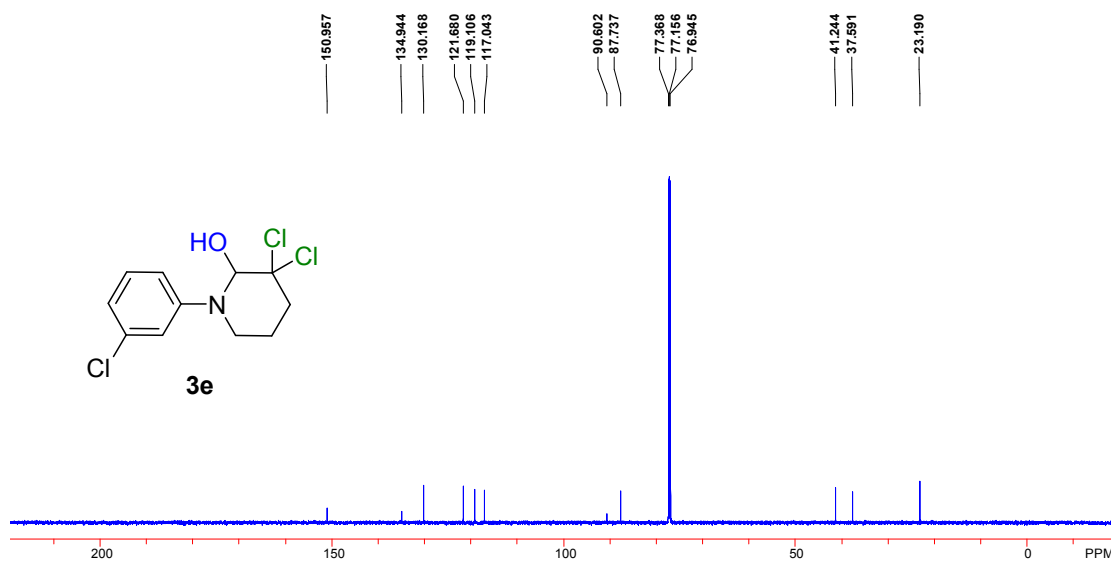
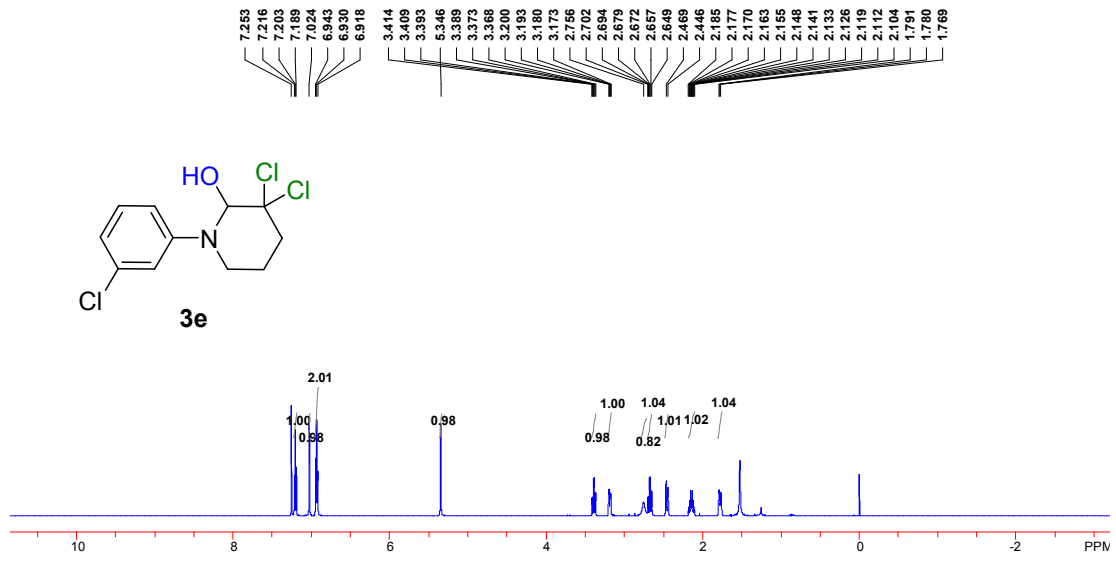
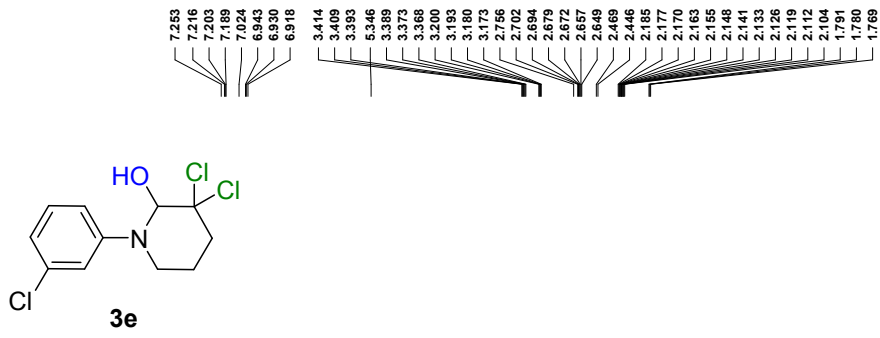


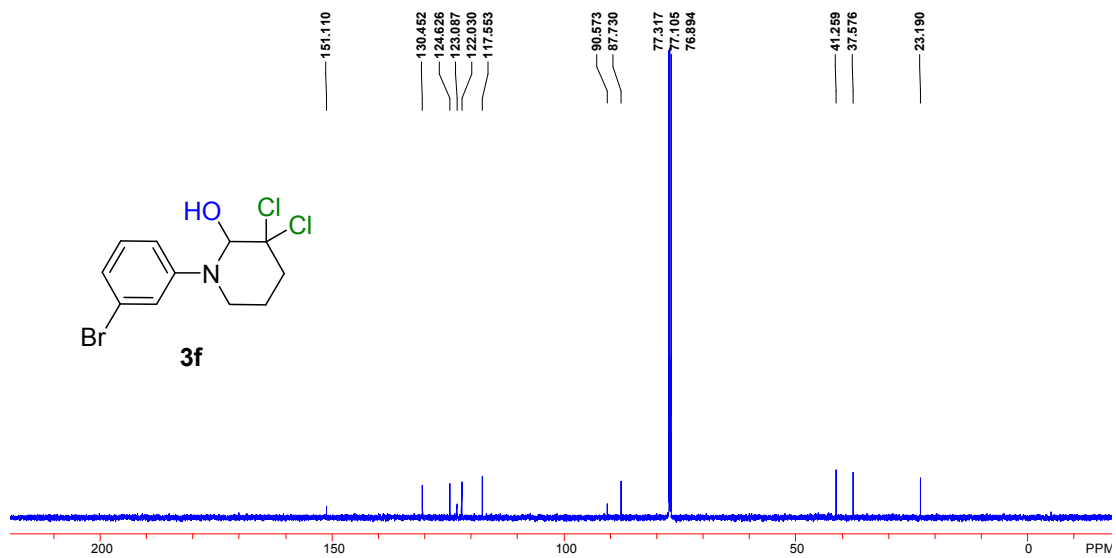
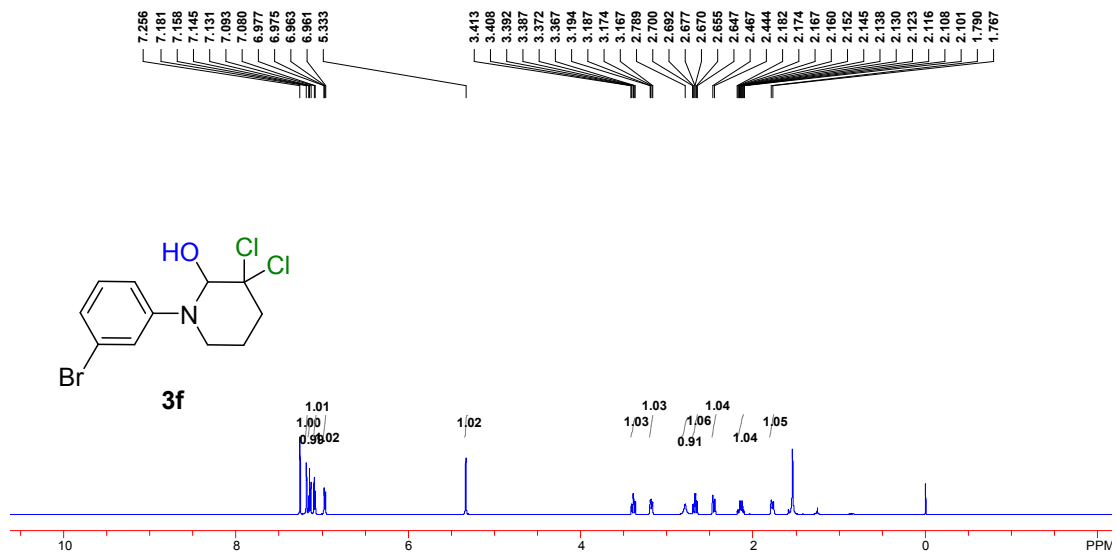


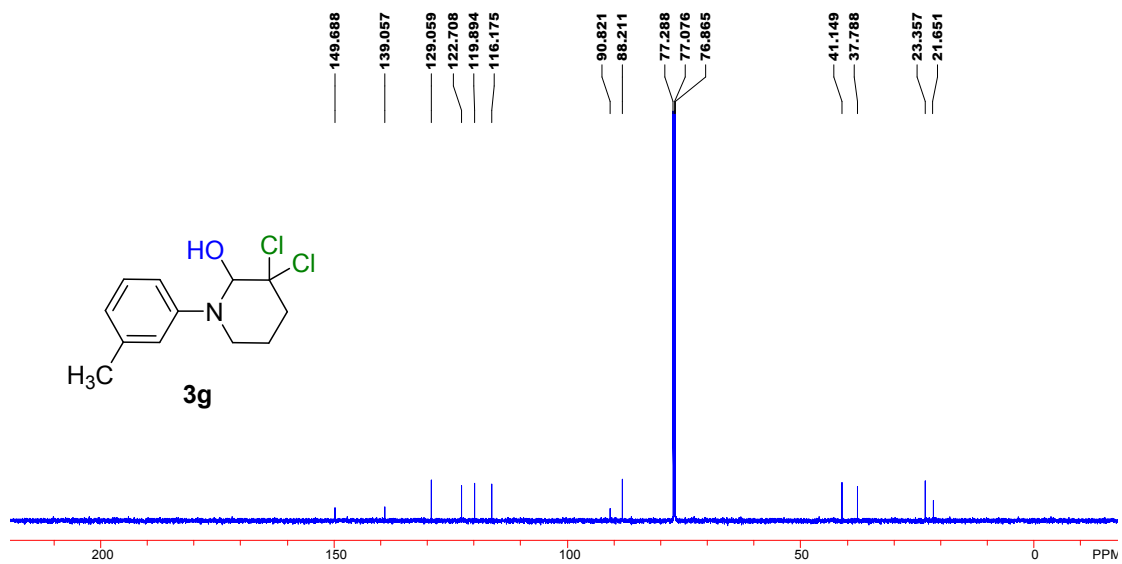
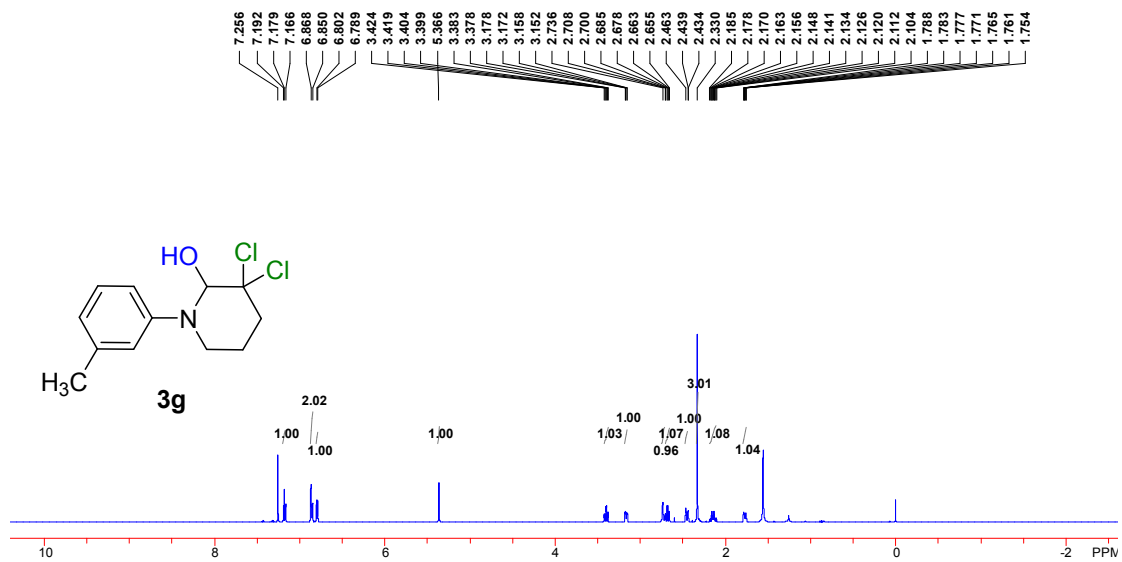


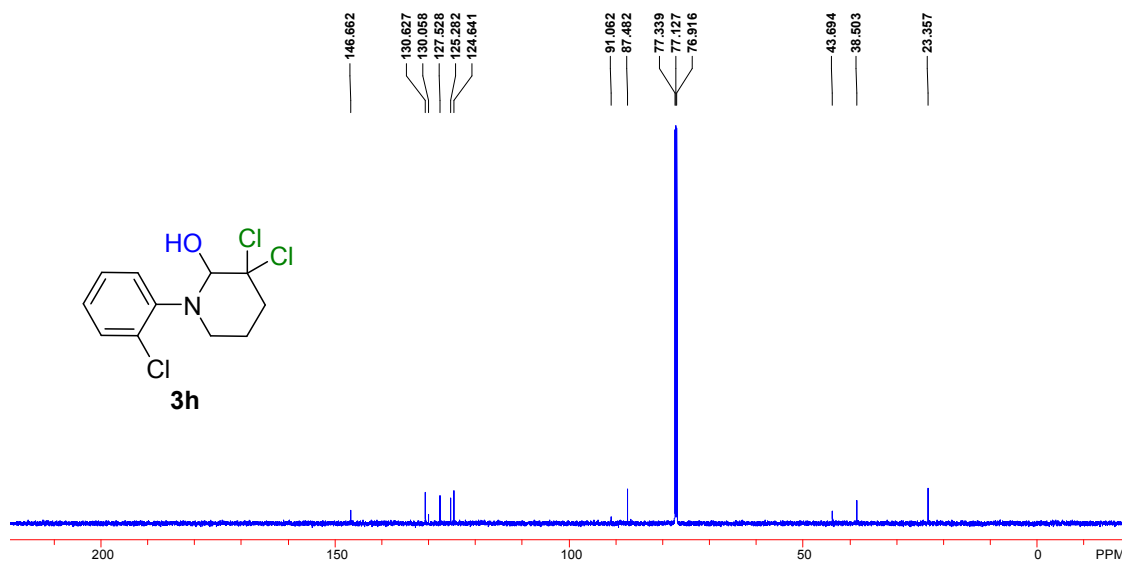
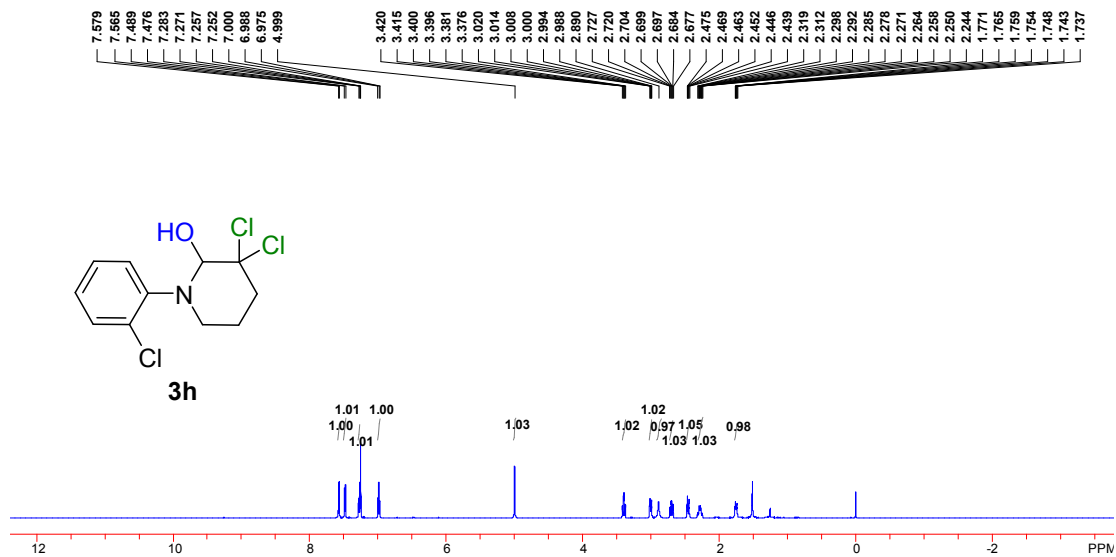


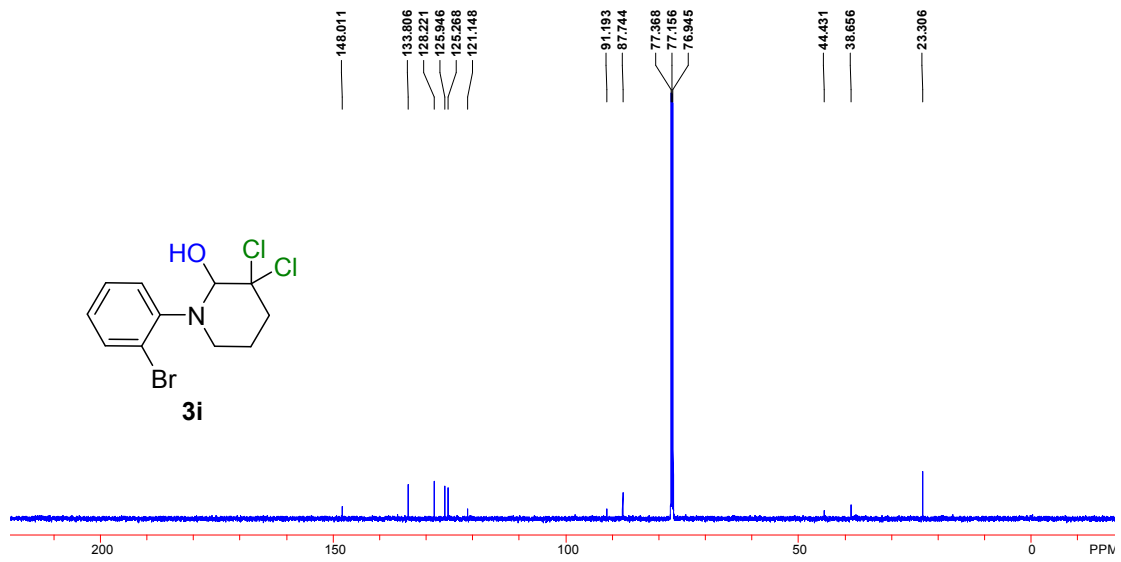
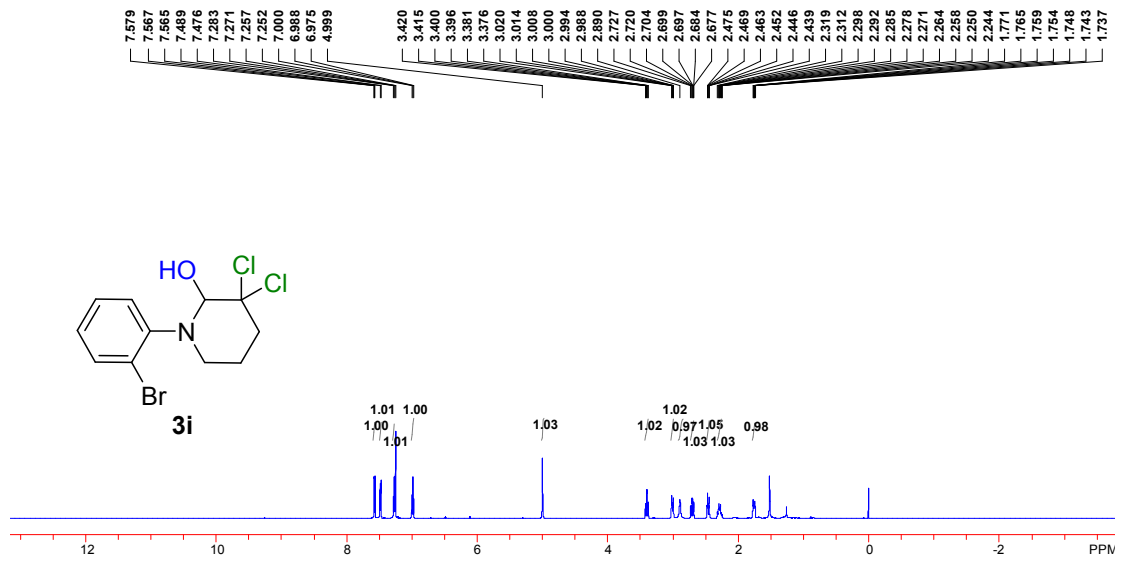


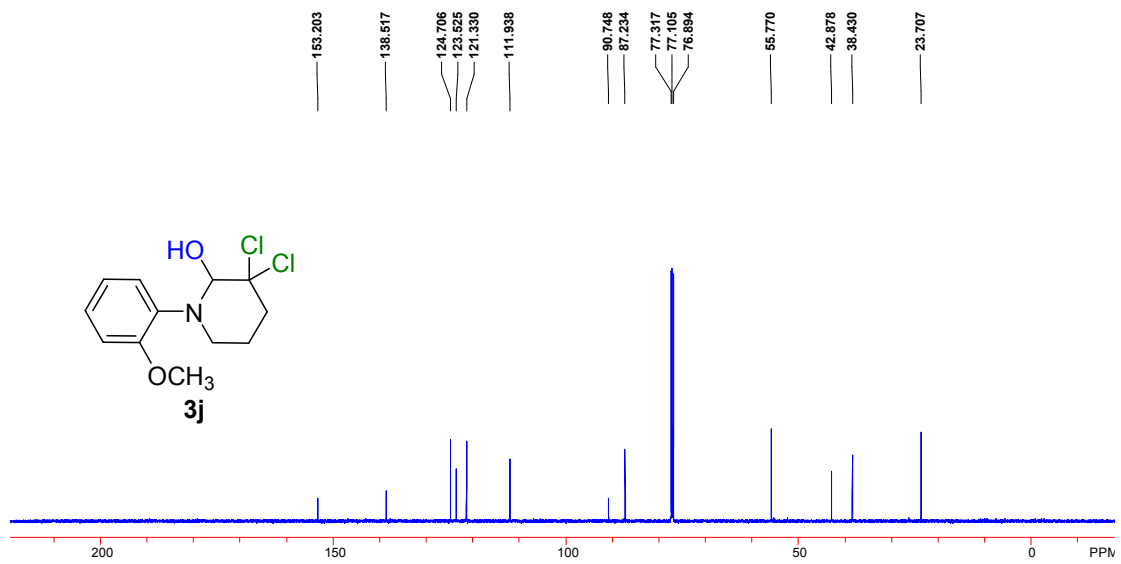
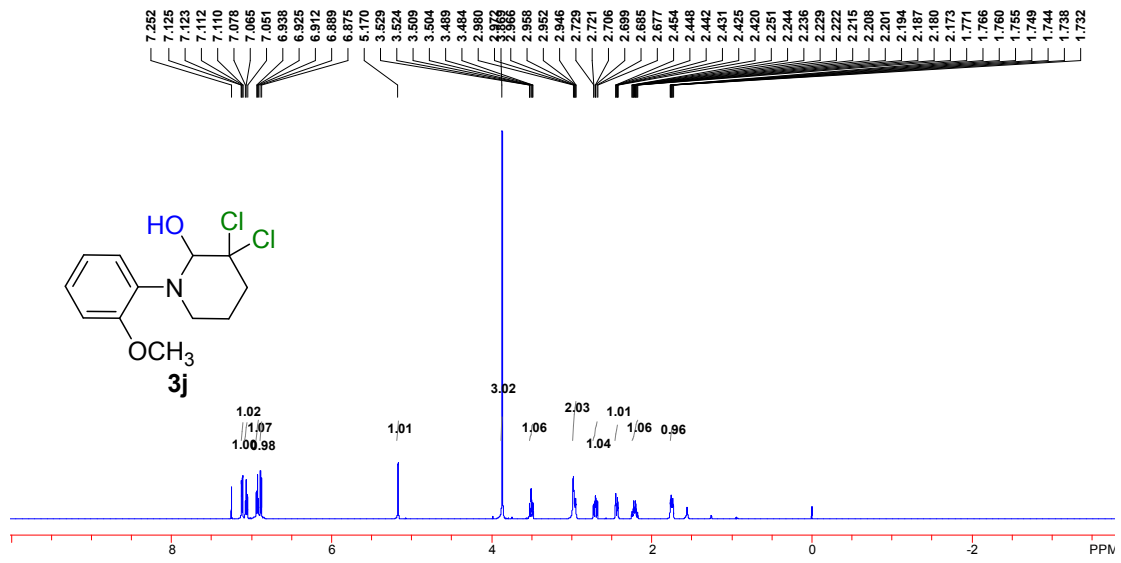


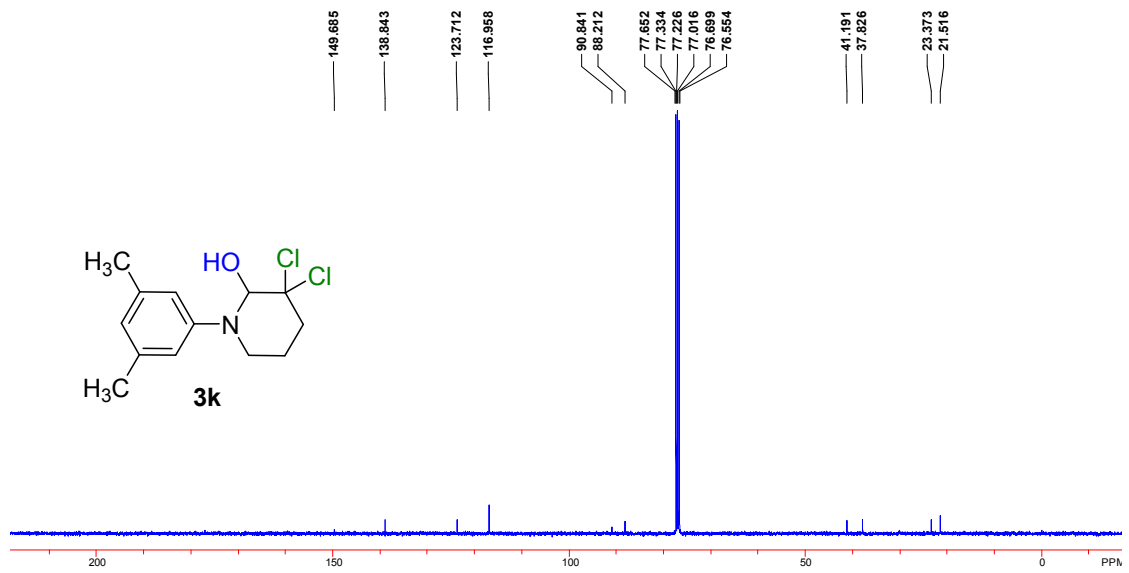
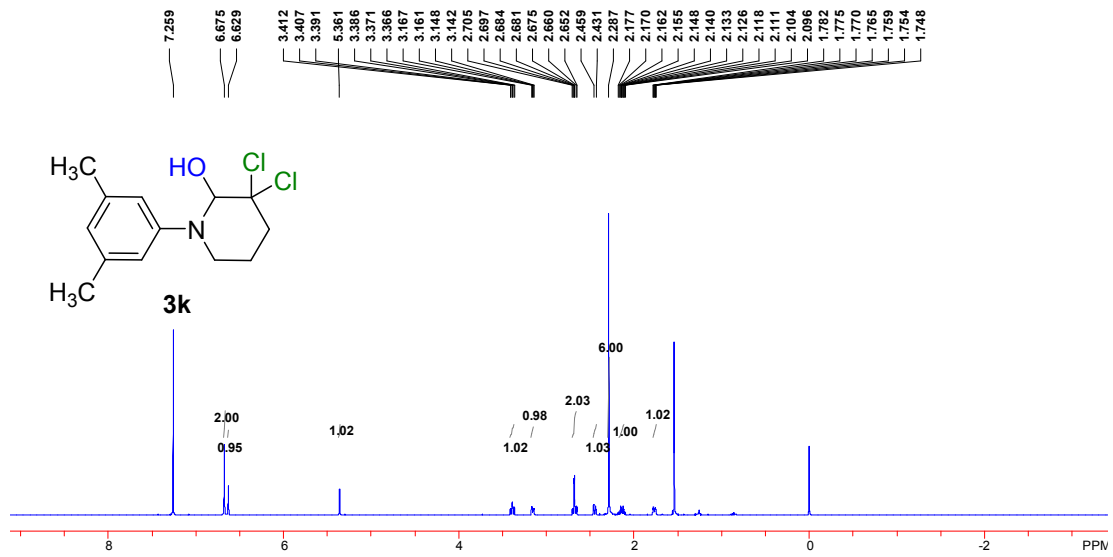


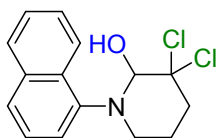
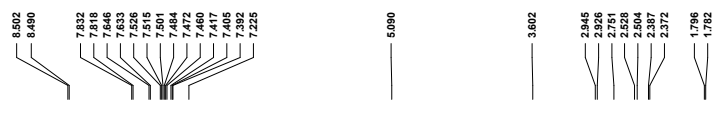




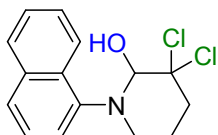
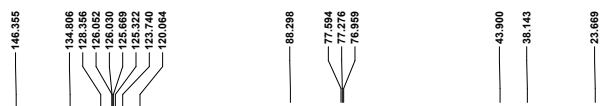
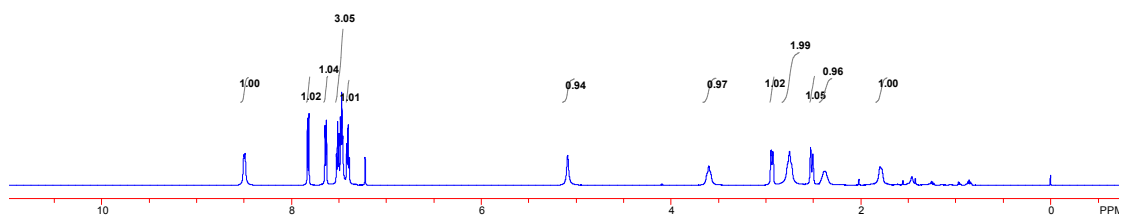




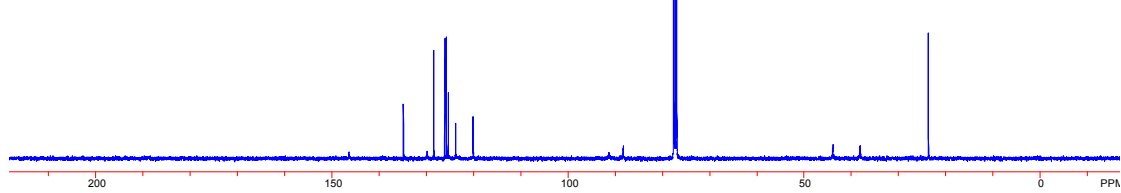




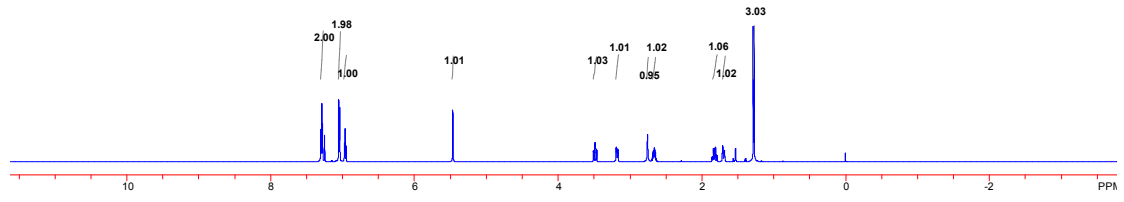
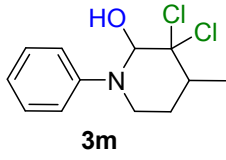
3I



3I



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7.289
7.274
7.248
7.052
7.039
6.975
6.962
6.946
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3.500
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1.692
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1.677
1.262
1.271



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15.955

