SUPPORTING INFORMATION FOR

Selective Heteroaryl *N*-Oxidation of Amine-Containing Molecules

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Table of Contents

I. General Information

All reagents were obtained commercially in the highest available purity and used without further purification. 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) were purchased from Oakwood Chemical Company. Anhydrous solvents were obtained from an aluminum oxide solvent purification system. Flash column chromatography was performed using silica gel or alumina gel (230 - 400 mesh) purchased from Fisher Scientific. Elution of compounds was monitored by UV. ^{1}H and ^{13}C NMR spectra were measured on a Varian Inova 600 (600 MHz) or Bruker Avance DRX 600 (600 MHz) or Bruker Avance III 800 (800 MHz) spectrometer and acquired at 300 K. Chemical shifts are reported in parts per million (ppm δ) referenced to the residual ^{1}H or ^{13}C resonance of the solvent. The following abbreviations are used singularly or in combination to indicate the multiplicity of signals: s - singlet, d - doublet, t - triplet, q - quartet, m - multiplet and br - broad. IR spectra were recorded on a Shimadzu IR Affinity-1S. HRMS data were obtained from the School of Chemical Sciences Mass Spectrometry Laboratory at the University of Illinois at Urbana-Champaign and are accurate to within 5 ppm.

II. Screening of Oxidant Conditions

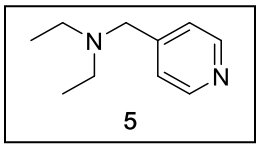
Reaction conditions and potential substrates were screened on a 0.1 mmol scale. A general procedure is as follows: the nicotine salt or nicotine was measured in a 2 dram vial with a stir bar,

followed by .5 mL of dichloromethane, HFIP (if included), and the acid additive (if necessary). The oxidant was then added and the vial capped and allowed to stir for 16 hrs. The organic layer was extracted with 5 mL of DCM 3x, dried with magnesium sulfate, and concentrated under vacuum. The sample was then analyzed by LC-MS or crude ^{1}H NMR.

II. Substrate Synthesis

General Procedure: Aldehyde (2.5 mmol, 1 eq.), amine (2.75 mmol, 1.1 eq.), were measured out into a 50 mL round bottom with a stir bar. Dichloroethane (20mL) was added and the suspension was gently mixed for 5 minutes. Sodium triacetoxyborohydride (3.5 mmol, 1.4 eq) was weighed out and then added to the mixture. The reaction stirred for 16 hrs or until complete by TLC. Upon reaction completion, the reaction mixture was basified with 1M NaOH (10mL). The layers were separated, and extracted with 5x15 mL EtOAc. The resulting organic layers were combined, dried with sodium sulfate, concentrated on a rotary evaporator, and purified by flash chromatography as noted.

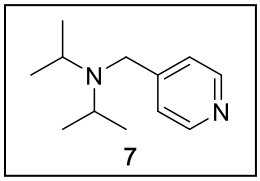
N-ethyl-N-(pyridin-4-ylmethyl)ethanamine (5)



5

N-ethyl-N-(pyridin-4-ylmethyl)ethanamine was synthesized using the general procedure on a 2.5 mmol scale relative to the aldehyde using isonicotinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (20% to 40% to 60% EtOAc/hexanes) to give product **5** as 0.0941 g of orange oil (0.573 mmol 22 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.51 (d, *J* = 6.0 Hz, 2H), 7.28 (d, *J* = 6.0 Hz, 2H), 3.55 (s, 2H), 2.51 (q, *J* = 7.1 Hz, 4H), 1.03 (t, *J* = 7.1 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 149.7, 123.8, 123.4, 59.3, 54.8, 23.5 ppm. **IR** (ATR) 2800.64, 1602.85, 1548.84, 1417.68, 1375.72, 1227.87, 1062.78, 1033.85 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{17}N_2$ 165.1392, found 165.1396

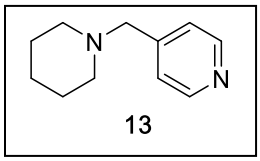
N-isopropyl-N-(pyridin-4-ylmethyl)propan-2-amine (7)



7

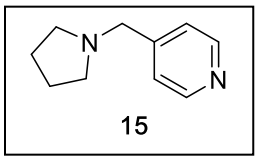
N-isopropyl-N-(pyridin-4-ylmethyl)propan-2-amine was synthesized using the general procedure on a 2.5 mmol scale relative to the aldehyde using isonicotinaldehyde and diisopropylamine. The reaction mixture was purified after workup using alumina flash chromatography (10% to 30% EtOAc/hexanes) to give product **7** as 23 mg of clear oil (0.119 mmol 4.7% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.48 (d, *J* = 6.0 Hz, 2H), 7.32 (d, *J* = 6.0 Hz, 2H), 3.63 (s, 2H), 3.00 (hept, *J* = 6.5 Hz, 2H), 1.01 (d, *J* = 6.6 Hz, 12H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 153.11, 149.36, 122.90, 48.44, 48.29, 20.71. ppm. **IR** (ATR) 2964.59, 1749.44, 1597.06, 1463.97, 1382.96, 1139.93, 1031.92 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{21}N_2$ 193.1705; Found 193.1710.

4-(piperidin-1-ylmethyl)pyridine (13)



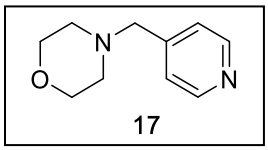
4-(piperidin-1-ylmethyl)pyridine was synthesized using the general procedure on a 5 mmol scale relative to the aldehyde using isonicotinaldehyde and piperidine. The reaction mixture was purified after workup using silica flash chromatography (1% NH_4OH/10% MeOH/89%DCM) to give product **13** as 0.5897 g of yellow oil (3.34 mmol 67%) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.51 (d, *J* = 6.0 Hz, 2H), 7.26 (d, *J* = 6.0 Hz, 2H), 3.46 (s, 2H), 2.44 – 2.30 (m, 4H), 1.58 (q, *J* = 11.8, 5.6 Hz, 2H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 149.6, 148.1, 123.9, 62.5, 54.6, 25.9, 24.1 ppm. **IR** (ATR) 2794.85, 2758.21, 1602.85, 1412.82, 993.34, 804.32 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{17}N_2$ 177.1392, found 177.1394

4-(pyrrolidin-1-ylmethyl)pyridine (15)



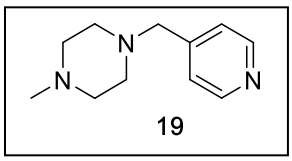
4-(pyrrolidin-1-ylmethyl)pyridine was synthesized using the general procedure on a 10 mmol scale relative to the aldehyde using isonicotinaldehyde and pyrrolidine. The reaction mixture was purified after workup using alumina flash chromatography (20% to 40% EtOAc/hexanes) to give **15** as 1.589 g of yellow oil (9.8 mmol 98% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.60 (d, *J* = 6.0 Hz, 2H), 7.35 (d, *J* = 6.0 Hz, 2H), 3.71 (s, 2H), 2.62 – 2.60 (m, 4H), 1.89 – 1.87 (m, 4H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 147.7, 148.3, 123.8, 59.4, 54.2, 23.52 ppm. **IR** (ATR) 2783.28, 2735.08, 1600.92, 1413.82, 933.34, 800.46 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{15}N_2$ 163.1235; Found 163.1235

4-(pyridin-4-ylmethyl)morpholine (17)



4-(pyridin-4-ylmethyl)morpholine was synthesized using the general procedure on a 2.25 mmol scale relative to the aldehyde using isonicotinaldehyde and morpholine. The reaction mixture was purified after workup using alumina flash chromatography (solvent gradient: 20% to 40% EtOAc/hexanes) to give product **17** as 0.3312 g of yellow-brown oil (1.858 mmol, 74% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.54 (d, *J* = 6.0 Hz, 2H), 7.28 (d, *J* = 6.0 Hz, 2H), 3.72 (t, *J* = 4.7 Hz, 4H), 3.49 (s, 2H), 2.48 – 2.45 (m, 4H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 149.8, 147.2, 123.9, 66.9. 62.1, 53.6 ppm. **IR** (ATR) 2854.65, 2808.36, 1602.85 1454.33, 1415.75, 1114.86, 1008.77, 866.04 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{15}N_2O$ 179.1184, found 179.1189

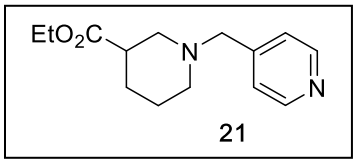
1-methyl-4-(pyridin-4-ylmethyl)piperazine (19)



1-methyl-4-(pyridin-4-ylmethyl)piperazine was synthesized using the general procedure on a 5 mmol scale relative to the aldehyde using isonicotinaldehyde and 1-methylpiperazine. The reaction mixture was purified after workup using alumina flash chromatography (80% EtOAc/hexanes to 100%) to give product as 0.535 g of yellow oil (2.8 mmol, 56% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.52 (d, J = 4.3 Hz, 2H), 7.26 (d, J = 4.4 Hz, 2H), 3.49 (s, 2H), 2.46 (s, 8H), 2.28 (s, 3H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 149.74, 147.60,

123.81, 61.67, 55.04, 53.16, 46.01 ppm. **IR** (ATR) 2792.93, 1602.85, 1560.41, 1456.26, 1413.92, 1290.38, 1165.00, 1139.93, 1012.63, 827.46, 794.67 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{18}N_3$ 192.1501, found 192.1500

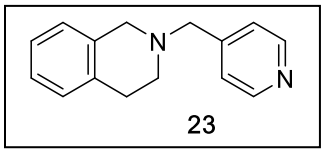
Ethyl 1-(pyridin-4-ylmethyl)piperidine-3-carboxylate (21)



21

Ethyl 1-(pyridin-4-ylmethyl)piperidine-3-carboxylate was synthesized using the general procedure on a 4 mmol scale relative to the aldehyde using isonicotinaldehyde and ethyl nipecotate. The reaction mixture was purified after workup using alumina flash chromatography (20% to 60% EtOAc/hexanes) to give product **21** as 45.3 mg of yellow oil (0.18 mmol, 4.5% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.48 (d, *J* = 6.1 Hz, 2H), 7.22 (d, *J* = 6.1 Hz, 2H), 4.12 – 4.01 (m, 2H), 3.46 (q, *J* = 14.3 Hz, 2H), 2.82 (d, *J* = 11.4 Hz, 1H), 2.62 (d, *J* = 11.0 Hz, 1H), 2.57 – 2.50 (m, 1H), 2.28 – 2.20 (m, 1H), 2.09 – 2.04 (m, 1H), 1.91 – 1.84 (m, 1H), 1.73 – 1.67 (m, 1H), 1.59 – 1.52 (m, 1H), 1.51 – 1.44 (m, 1H), 1.19 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 173.95, 149.64, 147.84, 123.65, 61.91, 60.28, 55.42, 53.78, 41.74, 26.64, 25.95, 24.41, 14.15 ppm. **IR** (ATR) 2805.50, 1726.29, 1600.92, 1413.82, 1367.53, 1180.55, 1028.06, 991.41 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{21}N_2O_2$ 249.1603, found 249.1602

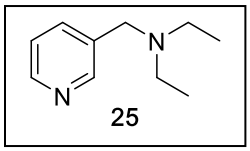
2-(pyridin-4-ylmethyl)-1,2,3,4-tetrahydroisoquinoline (23)



23

2-(pyridin-4-ylmethyl)-1,2,3,4-tetrahydroisoquinoline was synthesized using the general procedure on a 2 mmol scale relative to the aldehyde using isonicotinaldehyde and 1,2,3,4-tetrahydroisoquinoline. The reaction mixture was purified after workup using alumina flash chromatography (20% to 60% EtOAc/hexanes) to give product **23** as .205 g of yellow oil (0.91 mmol, 46% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.55 (d, *J* = 6.4 Hz, 2H), 7.31 (d, *J* = 6.4 Hz, 2H), 7.14 – 7.07 (m, 3H), 6.96 (d, *J* = 9.0 Hz, 1H), 3.63 (s, 2H), 3.61 (s, 2H), 2.89 (t, *J* = 6.2 Hz, 2H), 2.70 (t, *J* = 6.1 Hz, 2H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 149.35, 147.37, 134.02, 133.62, 128.25, 126.04, 125.79, 125.22, 123.26, 60.93, 55.65, 50.34, 28.68 ppm. **IR** (ATR) 2800.64, 1653.00, 1600.92, 1413.82, 794.67 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}N_2$ 225.1392, found 225.1391

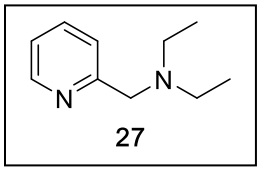
N-ethyl-N-(pyridin-3-ylmethyl)ethanamine (25)



25

N-ethyl-N-(pyridin-3-ylmethyl)ethanamine was synthesized using the general procedure on a 2 mmol scale relative to the aldehyde using nicotinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (20% to 30% to 40% EtOAc/hexanes) to give product **25** as 45 mg of white oil (0.33 mmol, 16.4% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.48 (s, 1H), 8.42 (d, *J* = 6.6 Hz, 1H), 7.62 (d, *J* = 7.1 Hz, 1H), 7.17 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.50 (s, 2H), 2.46 (q, *J* = 7.1 Hz, 4H), 0.98 (d, *J* = 7.3 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 150.17, 148.18, 136.35, 135.34, 123.15, 54.78, 46.67, 11.73. ppm**. IR** (ATR) 2804.50, 1575.84, 1423.47, 1028.06 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{17}N_2$ 165.1392, found 165.1396

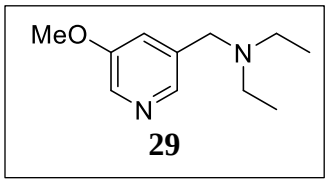
N-ethyl-N-(pyridin-2-ylmethyl)ethanamine (27)



27

N-ethyl-N-(pyridin-2-ylmethyl)ethanamine was synthesized using G the general procedure on a 2.5 mmol scale realtive to the aldehyde using picolinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (10% to 20% EtOAc/hexanes) to give product **27** as 0.276 g of brown oil (1.677 mmol 67% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.52 (d, *J* = 4.9 Hz, 1H), 7.62 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.13 – 7.10 (m, 1H), 3.71 (s, 2H), 2.57 (q, *J* = 7.1 Hz, 4H), 1.04 (t, *J* = 7.1 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 160.70, 148.91, 136.21, 122.81, 121.61, 59.58, 47.31, 11.8 ppm. **IR** (ATR) 2804.50, 1589.34, 1431.18, 991.41, 754.17 cm^{-1}. **HRMS** (ESI/QTOF) m/z: [M + H]+ Calcd for $C_{10}H_{17}N_2$ 165.1392, found 165.1395.

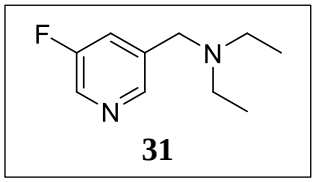
N-ethyl-N-((5-methoxypyridin-3-yl)methyl)ethanamine (29)



29

N-ethyl-N-((5-methoxypyridin-3-yl)methyl)ethanamine was synthesized using the general procedure on a 2.5 mmol scale relative to the aldehyde using 5-methoxynicotinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (90% Et_2O/MeOH) to give product as 0.3401 g of a chunky, clear oil (1.46 mmol, 49%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 8.08 (d, *J* = 2.9 Hz, 1H), 8.04 (d, *J* = 1.7 Hz, 1H), 7.15 (dd, *J* = 2.8, 1.8 Hz, 1H), 3.75 (s, 3H), 3.45 (s, 2H), 2.42 (q, *J* = 7.1 Hz, 4H), 0.94 (t, *J* = 7.2 Hz, 6H) ppm; **^{13}C NMR** (200 MHz, $CDCl_3$) δ 155.68, 142.24, 136.30, 136.08, 120.52, 55.38, 54.59, 46.72, 11.69 ppm; **IR** (ATR) 2968.45, 2802.57, 1587.42, 1463.97, 1425.40, 1282.66, 1157.29, 1041.56, 866.04, 707.88 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{19}N_2O$ 195.1497; Found 195.1493

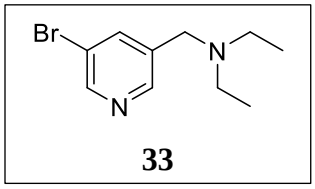
N-ethyl-N-((5-fluoropyridin-3-yl)methyl)ethanamine (31)



31

N-ethyl-N-((5-fluoropyridin-3-yl)methyl)ethanamine was synthesized using the general procedure on 2.5 mmol scale relative to the aldehyde using 5-fluoronicotinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (Et_2O) to give product as 0.1400 g of pale yellow oil (0.769 mmol, 31%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 8.30 (q, J = 2.0 Hz, 1H), 8.28 (p, J = 2.2, 1.6 Hz, 1H), 7.42 (d, J = 9.4 Hz, 1H), 3.53 (d, J = 2.6 Hz, 2H), 2.48 – 2.43 (m, 4H), 1.00 – 0.95 (m, 6H) ppm; **^{13}C NMR** (200 MHz, $CDCl_3$) δ 159.72 (d, J = 256.0 Hz), 145.65 (dd, J = 7.5, 3.9 Hz), 137.96 (d, J = 3.6 Hz), 136.48 (dd, J = 23.5, 8.2 Hz), 122.78 (dd, J = 18.4, 8.1 Hz), 54.21, 46.85, 11.81 (d, J = 4.9 Hz) ppm; **IR** (ATR) 2970.38, 2804.50, 1600.92, 1577.77, 1429.25, 1265.30, 1026.13, 875.68, 744.52, 700.16 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{16}FN_2$ 183.1298; Found 183.1304

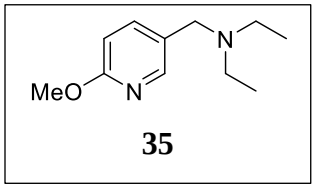
N-((5-bromopyridin-3-yl)methyl)-N-ethylethanamine (33)



33

N-((5-bromopyridin-3-yl)methyl)-N-ethylethanamine was synthesized using the general procedure on a 2.70 mmol scale relative to the aldehyde using 5-bromonicotinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (Et_2O) to give product as 0.1841 g of clear oil (0.757 mmol, 28%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 8.45 (d, J = 2.3 Hz, 1H), 8.37 (d, J = 1.8 Hz, 1H), 7.78 (t, J = 2.1 Hz, 1H), 3.45 (s, 1H), 2.43 (q, J = 7.1 Hz, 4H), 0.95 (t, 6H) ppm; **^{13}C NMR** (200 MHz, $CDCl_3$) δ 149.22, 148.05, 138.70, 137.72, 120.69, 54.28, 46.80, 11.79 ppm; **IR** (ATR) 2968.45, 2800.64, 1579.70, 1556.55, 1419.61, 1290.38, 1203.58, 1166.93, 1087.85, 1022.27, 860.25, 702.09, 678.94 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{16}BrN_2$ 243.0497; Found 243.0490

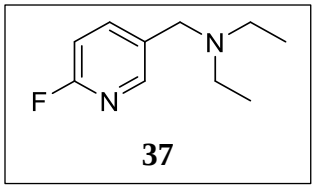
N-((5-bromopyridin-3-yl)methyl)-N-ethylethanamine (35)



35

N-ethyl-N-((6-methoxypyridin-3-yl)methyl)ethanamine was synthesized using the general procedure on a 3.65 mmol scale relative to the aldehyde using 6-methoxynicotinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (Et_2O) to give product as 0.3658 g of pale yellow oil (1.88 mmol, 52%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 8.00 (d, *J* = 2.5 Hz, 1H), 7.54 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 1H), 3.88 (s, 3H), 3.44 (s, 2H), 2.45 (q, *J* = 7.1 Hz, 4H), 0.99 (t, *J* = 7.2 Hz, 6H) ppm.**^{13}C NMR** (200 MHz, $CDCl_3$) δ 163.22, 146.43, 139.36, 127.60, 110.35, 53.94, 53.00, 46.29, 11.59 ppm; **IR** (ATR) 2986.45, 2800.64, 1608.63, 1573.91, 1490.97, 1458.18, 1392.61, 1355.96, 1307.74, 1288.45, 1259.52, 1199.72, 1166.93, 1116.78, 1058.92, 1026.13, 829.39, 775.38, 613.36 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{19}N_2O$ 195.1497; Found 195.1498

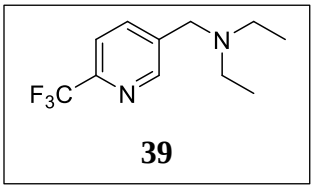
N-ethyl-N-((6-fluoropyridin-3-yl)methyl)ethanamine (37)



37

N-ethyl-N-((6-fluoropyridin-3-yl)methyl)ethanamine was synthesized using the general procedure on a 4.00 mmol scale relative to the aldehyde using 6-fluoronicotinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (Et_2O) to give product as 0.0989 g of pale yellow oil (0.543 mmol, 14%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 1.9 Hz, 1H), 7.73 (td, *J* = 8.1, 2.5 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.9 Hz, 1H), 3.47 (s, 2H), 2.43 (q, *J* = 7.1 Hz, 4H), 0.96 ppm (t, *J* = 7.2 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.77 (d, *J* = 237.5 Hz), 147.21 (d, *J* = 14.4 Hz), 141.60 (d, *J* = 7.7 Hz), 133.18 (d, *J* = 4.5 Hz), 108.91 (d, *J* = 37.4 Hz), 53.85 (d, *J* = 1.4 Hz), 46.59, 11.68 ppm; **IR** (ATR) 2968.45, 2935.66, 2873.94, 2810.28, 1595.13, 1481.33, 1382.96, 1288.45, 1242.16, 1201.65, 1166.93, 1114.86, 1060.85, 1024.20, 831.32, 775.38 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{15}FN_2$ 183.1298; Found 183.1304

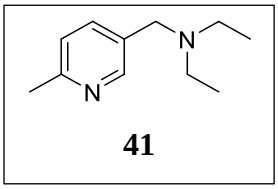
N-ethyl-N-((6-(trifluoromethyl)pyridin-3-yl)methyl)ethanamine (39)



39

N-ethyl-N-((6-(trifluoromethyl)pyridin-3-yl)methyl)ethanamine was synthesized using the general procedure on a 2.38 mmol scale relative to the aldehyde using 6-trifluoromethylnicotinaldehyde and diethylamine. The reaction mixture was purified after workup using silica flash chromatography (Et_2O) to give product as 0.4634 g of pale yellow oil (1.995 mmol, 84%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 8.55 (d, *J* = 1.7 Hz, 1H), 7.79 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.51 (d, *J* = 8.2 Hz, 1H), 3.54 (s, 2H), 2.42 (q, *J* = 7.1 Hz, 4H), 0.92 (d, *J* = 7.2 Hz, 6H) ppm; **^{13}C NMR** (200 MHz, $CDCl_3$) δ 150.06, 146.54 (q, *J* = 34.5 Hz), 139.26, 137.33, 121.64 (d, *J* = 273.9 Hz), 119.86 (q, *J* = 3.0 Hz), 54.45, 46.81, 11.58 ppm; **IR** (ATR) 2972.31, 2937.59, 2814.14, 1456.26, 1384.89, 1330.88, 1292.31, 1238.30, 1168.86, 1132.21, 1083.99, 1026.13, 850.61, 837.11, 752.24, 634.58, 592.15 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{15}F_3N_2$ 233.1266; Found 233.1270

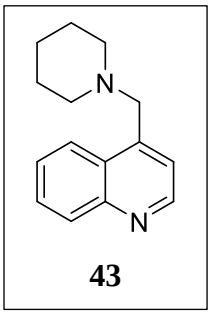
N-ethyl-N-((6-methylpyridin-3-yl)methyl)ethanamine (41)



41

N-ethyl-N-((6-methylpyridin-3-yl)methyl)ethanamine was synthesized using the general procedure on a 3.94 mmol scale relative to the aldehyde using 6-methylnicotinaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product as 0.2189 g of pale yellow solid (1.23 mmol, 31%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 8.39 (d, *J* = 2.3 Hz, 1H), 7.56 (dd, *J* = 7.9, 2.3 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 3.52 (s, 2H), 2.52 (s, 3H), 2.49 (q, *J* = 7.1 Hz, 4H), 1.02 (d, *J* = 7.2 Hz, 6H) ppm; **^{13}C NMR** (200 MHz, $CDCl_3$) δ 157.49, 149.33, 137.96, 128.88, 123.23, 53.55, 45.87, 23.63, 10.35 ppm; **IR** (ATR) 2972.31, 2569.18, 2497.82, 1604.77, 1568.13, 1490.97, 1381.03, 1296.16, 1267.23, 1172.72, 1028.06, 727.16, 578.64 cm^{-1}; **HRMS** (ESI/QTOF) m/z: [M + H]+ Calcd for $C_{11}H_{18}N_2$ 179.1548; Found 179.1551

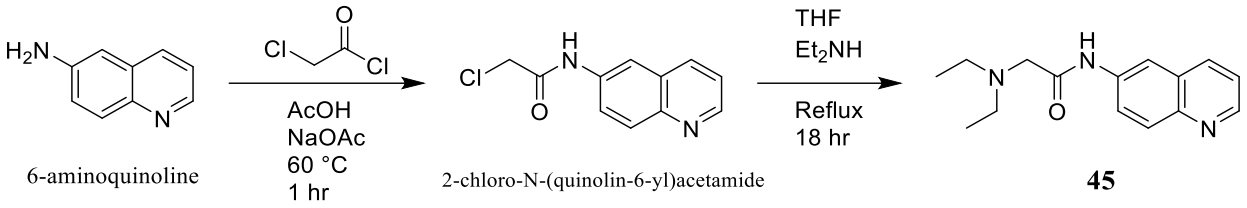
4-(piperidin-1-ylmethyl)quinoline (43)



43

4-(piperidin-1-ylmethyl)quinoline was synthesized using the general procedure on a 11.5 mmol scale relative to the aldehyde using 4-quinolinecarboxaldehyde and piperidine. The reaction mixture was purified after workup using alumina flash chromatography (Et_2O) to give product as 1.6923 g of greenish-yellow oil (7.48 mmol, 65%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.84 (d, J = 4.3 Hz, 1H), 8.23 (dd, J = 8.5, 1.3 Hz, 1H), 8.11 (dt, J = 8.3, 0.9 Hz, 1H), 7.69 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.53 (ddd, J = 8.3, 6.8, 1.3 Hz, 1H), 7.43 (d, J = 4.3 Hz, 1H), 3.86 (s, 2H), 1.59 (p, J = 5.6 Hz, 4H), 1.46 (p, J = 6.1 Hz, 2H) ppm; **^{13}C NMR** (150 MHz $CDCl_3$) δ 150.13, 148.32, 144.67, 129.91, 128.91, 127.74, 126.08, 124.14, 121.05, 60.21, 55.00, 26.05, 24.28 ppm; **IR** (ATR) 2931.80, 2850.79, 2798.71, 2756.28, 1591.27, 1568.13, 1508.33, 1344.38, 1296.16, 1236.37, 1107.14, 867.97, 842.89, 752.24 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{19}N_2$ 227.1548; Found 227.1559

2-(diethylamino)-N-(quinolin-6-yl)acetamide (45)

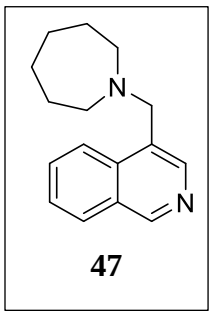


6-aminoquinoline — 2-chloro-N-(quinolin-6-yl)acetamide — **45**

2-chloro-N-(quinolin-6-yl)acetamide was prepared as follows. 6-aminoquinoline (1.19 g, 8.25 mmol) was dissolved in 35 mL of glacial acetic acid in a 100 mL round-bottom flask equipped with a stir bar. α-chloroacetylchloride (1.5 eq., 1.31 mL, 16.5 mmol) was added dropwise and reaction was heated to 60 °C for 10 min. Sodium acetate (6 g, 73.1 mmol in 45 mL of water) was added. After 1 hr reaction was brought to RT. 6 M NaOH (50 mL) added until product precipitated out. Collected by vacuum filtration to yield 0.1841 g of a brown, clay-like solid (7.04 mmol, 85%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 8.87 (dd, J = 4.2, 1.7 Hz, 1H), 8.48 (s, 1H), 8.35 (d, J = 2.3 Hz, 1H), 8.15 (d, J = 8.1 Hz, 1H), 8.09 (d, J = 8.9 Hz, 1H), 7.65 (dd, J = 9.0, 2.4 Hz, 1H), 7.41 (dd, J = 8.3, 4.2 Hz, 1H), 4.26 (s, 2H) ppm.

2-chloro-N-(quinolin-6-yl)acetamide (1.5635 g, 7.04 mmol) was dissolved in 150 mL dry THF in a 250 mL round-bottom flask equipped with a stir bar. Diethylamine (5 eq., 3.64 mL, 35.2 mmol) was added. Flask was equipped with a condenser and brought to reflux for 18 hr. Solvent evaporated and diluted with 20 mL EtOAc. Extracted with 3x 20 mL of 1 M HCl. Combined fractions basified with 15 mL of 6 M NaOH. Extracted with 5x 20 mL DCM. Combined fractions washed with brine and dried over Na_2SO_4 to give the title compound as 1.7199 g of brown powder (6.69 mmol, 95%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.65 (s, 1H), 8.81 – 8.79 (m, 1H), 8.37 (t, J = 2.5 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 8.9 Hz, 1H), 7.62 (dt, J = 8.9, 2.2 Hz, 1H), 7.35 (dd, J = 8.2, 4.1 Hz, 1H), 3.19 (s, 2H), 2.66 (q, J = 7.1 Hz, 4H), 1.10 (t, J = 7.1 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.43, 149.16, 145.39, 135.60, 135.40, 130.12, 128.75, 122.76, 121.46, 115.26, 58.03, 48.80, 12.35 ppm; **IR** (ATR) 3259.70, 2972.31, 2929.87, 2791.00, 1683.86, 1525.69, 1490.97, 1363.67, 1207.44, 1116.78, 877.61, 831.32, 792.74, 748.38, 611.43 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}N_3O$ 258.1606; Found 258.1604

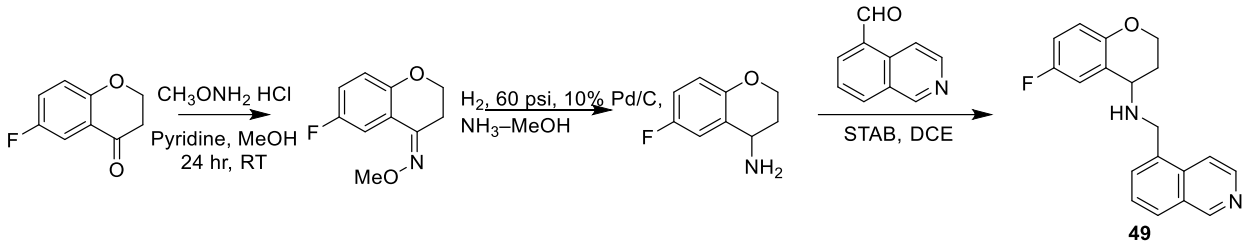
4-(azepan-1-ylmethyl)isoquinoline (47)



47

4-(azepan-1-ylmethyl)isoquinoline was synthesized using the general procedure on a 2.0 mmol scale relative to the aldehyde using 4-isoquinolinecarboxaldehyde and diethylamine. The reaction mixture was purified after workup using alumina flash chromatography (60% Et_2O/hexanes) to give product as 0.3299 g of orange oil (1.37 mmol, 69%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.42 (s, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 3.96 (s, 2H), 2.68 (m, 4H), 1.59 (m, 8H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 152.42, 143.33, 135.39, 129.85, 128.71, 128.46, 127.74, 126.79, 124.27, 58.15, 55.23, 28.26, 27.02; **IR** (ATR) 2922.16, 2850.79, 1622.13, 1583.56, 1500.62, 1450.47, 1355.96, 1220.94, 1147.65, 1078.21, 904.61,

887.26, 783.10, 748.38, 727.16, 626.87 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{21}N_2$ 241.1705; Found 241.1709

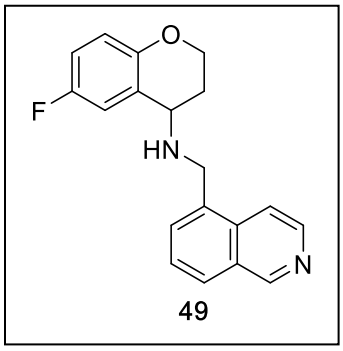


6-fluoro-N-(isoquinolin-5-ylmethyl)chroman-4-amine (49)[1]

6-fluoro-N-(isoquinolin-5-ylmethyl)chroman-4 amine was prepared as follows.

(·E)-6-fluorochroman-4-one O-methyl oxime was synthesized using 6-fluorochroman-4-one (0.253 g, 1.5 mmol), methoxyamine hydrochloride (0.124 g, 1.5 mmol), and pyridine (0.6 mL, 7.5 mmol). The reagents were combined together and allowed to stir for 24 hrs. The reaction mixture was reduced, 10 mL of 1M HCl was added, and the organic layer was extracted 3x with 10 mL DCM. The combined organics were dried with magnesium sulfate and reduced to give .2185 g (1.119 mmol, 80% yield) of product. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 9.4, 3.1 Hz, 1H), 6.95 (ddd, *J* = 9.1, 7.7, 3.1 Hz, 1H), 6.83 (dd, *J* = 9.0, 4.7 Hz, 1H), 4.18 (t, *J* = 6.2 Hz, 2H), 3.99 (s, 3H), 2.87 (t, *J* = 6.2 Hz, 2H) ppm. **^{13}C NMR** (200 MHz, $CDCl_3$) δ 157.49, 156.31, 150.35, 127.68, 117.78, 115.40, 114.38, 63.06, 45.42, 32.24 ppm. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}NO_2F$ 196.0774; Found 196.0778.

6-fluorochroman-4-amine was synthesized using (·E)-6-fluorochroman-4-one O-methyl oxime (0.822g, 4.21 mmol), 10% Pd/C (0.448g, 10 mol%), and MeOH-NH_2 (15 mL). The reagents were combined in a pressure reactor and pressurized with 60 psi H_2 for 48 hrs. Afterwards, the reaction mixture was filtered through celite, the filtrate was collected and reduced under pressure to give .3262 g (1.95 mmol, 46% yield) of product. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.03 (dd, *J* = 9.1, 3.1 Hz, 1H), 6.86 – 6.82 (m, 1H), 6.76 – 6.73 (m, 1H), 4.25 (ddd, *J* = 11.3, 8.4, 2.9 Hz, 1H), 4.19 (ddd, *J* = 11.2, 6.9, 3.1 Hz, 1H), 4.01 (t, *J* = 5.6 Hz, 1H), 2.18 – 2.12 (m, 1H), 1.86 – 1.80 (m, 1H), 1.59 (s, 2H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$) δ 157. 65, 156.08, 150.28 117.74 (d, *J* = 7.7 Hz), 115.25 (d, *J* = 23.3 Hz), 114.47 (d, *J* = 22.8 Hz), 63.05, 45.29, 32.23 ppm. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_9H_{11}NOF$ 168.0825; Found 168.0819.



6-fluoro-N-(isoquinolin-5-ylmethyl)chroman-4-amine was synthesized using the general procedure on a 1.95 mmol scale relative to the aldehyde using isoquinoline-5-carbaldehyde and 6-fluorochroman-4-amine. The reaction mixture was purified after workup using alumina flash chromatography (1% MeOH/99%DCM to 2% MeOH/98%DCM) to give product **49** as .3541 g of thick orange oil (1.14 mmol, 59% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.58 (d, J = 6.0 Hz, 1H), 7.94 (d, J = 5.9 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.75 (d, J = 7.1 Hz, 1H), 7.56 (dd, J = 8.2, 7.0 Hz, 1H), 6.97 (dd, J = 9.0, 3.1 Hz, 1H), 6.84 (dd, J = 8.9, 8.0, 3.1 Hz, 1H), 6.75 (dd, J = 9.0, 4.8 Hz, 1H), 4.40 – 4.27 (m, 3H), 4.23 – 4.19 (m, 1H), 3.90 (t, J = 4.8 Hz, 1H), 2.20 – 2.12

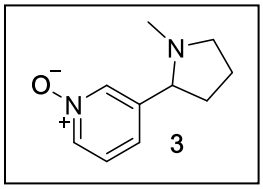
(m, 1H), 2.07 – 2.01 (m, 1H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$) δ 157.44, 155.87, 153.18, 150.82, 143.28, 135.10, 134.56, 130.06, 128.98, 127.39, 126.78, 125.27, 117.84, 116.85, 115.64, 115.15, 62.96, 51.33, 48.17, 27.66 ppm. **IR** (ATR) 1622.13, 1589.91, 1573.91, 1489.05, 1460.11, 1309.67, 1255.66, 873.75, 742.59, cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}N_2OF$ 309.1403, found 309.1400

III. Oxidation Reactions

General Procedure A: Substrate (0.5 mmol 1 eq) was measured out into a 2 dram screw top vial equipped with a stir bar. Dichloromethane (2.5 mL) was added and the suspension was gently mixed. 1M H_2SO_4 (1 eq) was added, followed by HFIP. Iminium catalyst (0.030g, 20 mol%) was weighed out and then added to the mixture. Finally 50% H_2O_2 (2 eq) was added to vial. The reaction stirred for 16 hrs. Upon reaction completion, the reaction mixture was basified with 6M NaOH (10mL). Brine (10 mL) was added to salt out N-oxide product. The layers were separated, and extracted with 3x10 mL DCM. The resulting organic layers were combined and dried with magnesium sulfate, concentrated on a rotary evaporator, and purified by flash chromatography as noted.

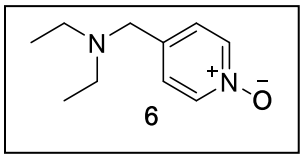
General Procedure B: Substrate (0.5 mmol 1 eq) was measured out into a 2 dram screw top vial equipped with a stir bar. Dichloromethane (2.5 mL) was added and the suspension was gently mixed. 50% Tetrafluoroboric acid diethyl ether complex (1 eq) was added, followed by HFIP. Iminium catalyst (0.015g, 10 mol%) was weighed out and then added to the mixture. Finally 50% H_2O_2 (2 eq) was added to vial. The reaction stirred for 16 hrs. Upon reaction completion, the reaction mixture was basified with 6M NaOH (10mL). Brine (10 mL) was added to salt out N-oxide product. The layers were separated, and extracted with 3x10 mL DCM. The resulting organic layers were combined and dried with magnesium sulfate, concentrated on a rotary evaporator, and purified by flash chromatography as noted.

3-(1-methylpyrrolidin-2-yl)pyridine 1-oxide (3)



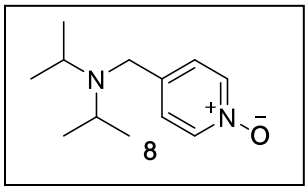
3-(1-methylpyrrolidin-2-yl)pyridine 1-oxide was synthesized from nicotine using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product **3** as 68.5 mg of clear oil (0.385 mmol, 77%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.10 (d, *J* = 6.3 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.24 – 7.20 (m, 1H), 3.21 (dd, *J* = 9.7, 7.9 Hz, 1H), 3.08 (t, *J* = 8.3 Hz, 1H), 2.32 (ddd, *J* = 9.4, 8.1 Hz, 1H), 2.26 – 2.20 (m, 1H), 2.19 (s, 3H), 1.96 – 1.88 (m, 1H), 1.85 – 1.76 (m, 1H), 1.66 (dddd, *J* = 12.9, 10.7, 8.4, 5.3 Hz, 1H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.87, 137.68, 125.66, 125.34, 67.93, 56.75, 40.38, 35.15, 22.77 ppm. **IR** (ATR) 2779.41, 1602.85, 1435.00, 1269.16, 1149.57, 1012.63, 794.67, 547.78, 486.06 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{15}N_2O$ 179.1184, Found 179.1184.

4-((diethylamino)methyl)pyridine 1-oxide (6)



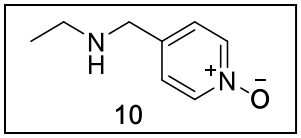
4-((diethylamino)methyl)pyridine 1-oxide was synthesized from compound **5** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% to 20% to 30% MeOH/Et_2O) to give product **6** as 70 mg of orange/yellow oil (0.387 mmol 77% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): 8.15 (d, J = 6.8 Hz, 2H), 7.29 (d, J = 6.3 Hz, 2H), 3.52 (s, 2H), 2.52 (q, J = 7.1 Hz, 4H), 1.03 (t, J = 7.1 Hz, 6H) δ ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) 141.08, 138.67, 125.64, 55.81, 47.08, 11.87 δ ppm. **IR** (ATR) 1483.26, 1232.51 1170.79, 786.96, cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{17}N_2O$ 181.1341, found 181.1344

4-((diisopropylamino)methyl)pyridine 1-oxide (8)



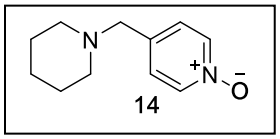
4-((diisopropylamino)methyl)pyridine 1-oxide was synthesized from compound **7** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% to 40% MeOH/Et_2O) to give product **8** as 64 mg of yellow oil (0.306 mmol 61% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.04 (d, 2H), 7.24 (d, 2H), 3.50 (s,2H), 2.89 (h, 2H), .90 (d, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.1, 138.4, 124.8, 48.5, 47.4, 20.6 ppm. **IR** (ATR) 1489.05, 1381.03, 1361.74, 1242.16, 1203.58, 1174.65, 947.05, 831.32, 790.81^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{21}N_2O$ 209.1654, found 209.1652

4-((ethylamino)methyl)pyridine 1-oxide (10)



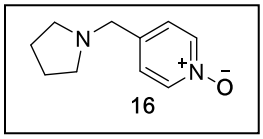
4-((ethylamino)methyl)pyridine 1-oxide was synthesized from compound **9** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% to 20% MeOH/Et_2O) to give product **10** as 61.3 mg of clear oil (0.403 mmol, 80% yield) **^{1}H NMR** (600 MHz,$CDCl_3$) δ 8.11 (d, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 6.9 Hz, 2H), 3.76 (s, 2H), 2.62 (q, *J* = 7.1 Hz, 2H), 1.09 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$) δ 141.11, 138.73, 125.19, 51.51, 43.64, 15.12 ppm. **IR** (ATR) 2966.52, 1483.26, 1284.59, 1176.55, 1099.34, 840.96 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_8H_{13}N_2O$ 153.1028; Found 153.1033.

4-(piperidin-1-ylmethyl)pyridine 1-oxide (14)



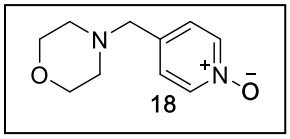
4-(piperidin-1-ylmethyl)pyridine 1-oxide was synthesized from compound **13** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product **14** as 60 mg of yellow oil (0.314 mmol 62% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.15 – 8.09 (m, 2H), 7.28 – 7.23 (m, 2H), 3.39 (s, 1H), 2.39 – 2.31 (m, 4H), 1.55 (p, *J* = 5.7, 5.2 Hz, 2H), 1.42 (s, 2H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 139.35, 138.75, 125.93, 61.38, 54.52, 25.86, 24.05 ppm; **IR** (ATR) 1483.26, 1446.61, 1234.44, 1172.72, 1037.00, 783.10 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{17}N_2O$ 193.1341; found 193.1343

4-(pyrrolidin-1-ylmethyl)pyridine 1-oxide (16)



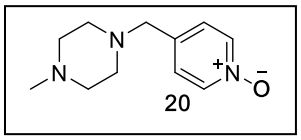
4-(pyrrolidin-1-ylmethyl)pyridine 1-oxide was synthesized from compound **15** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% to 40% MeOH/Et_2O) to give product **16** as 48.2 mg of yellow oil (0.271 mmol 54% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): δ δ 8.13 (d, *J* = 6.6 Hz, 2H), 7.26 (d, *J* = 6.5 Hz, 2H), 3.57 (s, 3H), 2.51 – 2.47 (m, 4H), 1.80 – 1.76 (m, 4H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 139.78, 138.75, 125.81, 58.30, 54.06, 23.48. ppm. **IR** (ATR) 2789.07, 1481.33, 1446.61, 1246.02, 1168.86, 1033.85, 786.96 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{15}N_2O$ 179.1184, found 179. 1188.

4-(morpholinomethyl)pyridine 1-oxide (18)



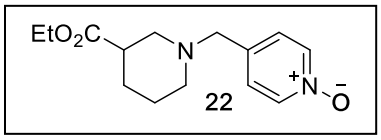
4-(morpholinomethyl)pyridine 1-oxide was synthesized from compound **17** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% to 30% MeOH/Et_2O) to give product **18** as 33.1 mg of white oil (0.206mmol, 34% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.20 (d, *J* = 7.0 Hz, 2H), 7.34 (d, *J* = 7.0 Hz, 2H), 3.76 – 3.73 (m, 4H), 3.50 (s, 2H), 2.54 – 2.42 (m, 4H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.8, 138.0, 126.0, 66.7, 60.8, 53.4 ppm. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{15}N_2O_2$ 195.1134, found 195.1131

4-((4-methylpiperazin-1-yl)methyl)pyridine 1-oxide (20)



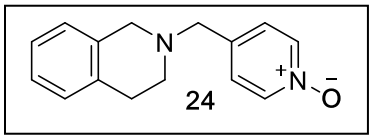
4-((4-methylpiperazin-1-yl)methyl)pyridine 1-oxide was synthesized from compound **19** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% to 30% MeOH/Et_2O) to give product **20** as 36.6 mg of clear oil (0.1765 mmol 50% yield). **^{1}H NMR** (600 MHz,$CDCl_3$) δ 8.14 (d, *J* = 7.0 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 2H), 3.48 (s, 2H), 2.59 – 2.37 (m, 4H), 2.28 (s, 3H) ppm. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.23, 138.80, 126.02, 60.37, 54.83, 52.63, 45.74 ppm. **IR** (ATR) 2796.78, 1483.26, 1456.26, 1282.66, 1213.23, 1138.00, 1099.43, 1010.70, 842.89 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{18}N_3O$ 208.1450; Found 208.1451.

4-((3-(ethoxycarbonyl)piperidin-1-yl)methyl)pyridine 1-oxide (22)



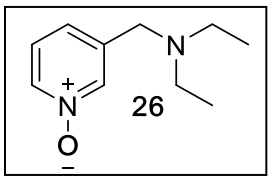
4-((3-(ethoxycarbonyl)piperidin-1-yl)methyl)pyridine 1-oxide was synthesized from compound **21** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% to 20% MeOH/Et_2O) to give product **22** as 39 mg of yellow oil (0.148 mmol 30% yield)) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.12 (d, J = 6.7 Hz, 2H), 7.24 (d, J = 6.8 Hz, 2H), 4.12 – 4.05 (m, 2H), 3.47 – 3.40 (m, 2H), 2.83 – 2.75 (m, 1H), 2.64 – 2.57 (m, 1H), 2.55 – 2.50 (m, 1H), 2.33 – 2.24 (m, 1H), 2.13 – 2.05 (m, 1H), 1.91 – 1.86 (m, 1H), 1.73 – 1.69 (m, 1H), 1.58 – 1.45 (m, 2H), 1.20 (t, J = 7.2 Hz, 3H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 173.7, 138.7, 138.6, 125.7, 60.8, 60.3, 55.2, 53.7, 41.6, 26.5, 24.3, 14.1 ppm **IR** (ATR) 1724.36, 1481.33, 1446.61, 1234.44, 1170.79, 1031.92 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{21}N_2O_3$ 265.1552; Found 265.1553.

4-((3,4-dihydroisoquinolin-2(1H)-yl)methyl)pyridine 1-oxide (24)



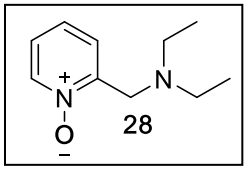
4-((3,4-dihydroisoquinolin-2(1H)-yl)methyl)pyridine 1-oxide was synthesized from compound **23** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% to 20% to 40% MeOH/Et_2O) to give product **24** as 50.8 mg of clear oil (0.199 mmol 40% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): 8.15 (d, *J* = 6.9 Hz, 2H), 7.32 (d, *J* = 6.9 Hz, 2H), 7.16 – 7.08 (m, 3H), 6.96 (d, *J* = 6.9 Hz, 1H), 3.63 (s, 2H), 3.61 (s, 2H), 2.90 (t, *J* = 5.9 Hz, 2H), 2.74 (t, *J* = 5.9 Hz, 2H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$): δ 138.94, 138.45, 134.12, 133.91, 128.71, 126.47, 126.35, 125.88, 125.74, 60.37, 55.96, 50.80, 29.04. ppm. **IR** (ATR) 1438.90, 1242.16, 1157.29, 974.05, 850.61 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}N_2O$ 241.1341, found 241.1343

3-((diethylamino)methyl)pyridine 1-oxide (26)



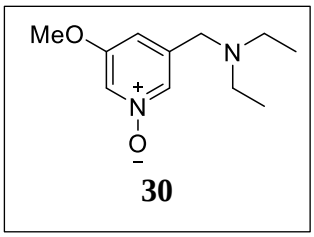
3-((diethylamino)methyl)pyridine 1-oxide was synthesized from compound **25** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product **26** as 60 mg of an oil (0.331 mmol 66% yield) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.26 (td, J = 1.7, 0.8 Hz, 1H), 8.09 (d, J = 6.7 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 7.20 (dd, J = 7.8, 6.3 Hz, 1H), 3.51 (s, 2H), 2.51 (q, J = 7.1 Hz, 4H), 1.02 (t, J = 7.1 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$): δ 140.20, 138.91, 137.30, 126.58, 125.20, 54.19, 46.76, 11.66. ppm. **IR** (ATR) 2804.50, 1602.85, 1431.19, 1273.02, 1147.65, 1012.63, 792.74, 759.95, 678.84 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{17}N_2O$ 181.1341, found 181.1346

2-((diethylamino)methyl)pyridine 1-oxide (28)



2-((diethylamino)methyl)pyridine 1-oxide was synthesized from compound **27** using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product **28** as 37 mg of yellow oil (0.206 mmol 41%) **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.17 (d, 1H), 7.65 (d, 1H), 7.24 (t, 1H), 7.10 (t, 1H), 3.80 (s, 2H), 2.57 (q, 4H), ppm 1.01 (t, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 152.1, 139.1, 125.9, 124.8, 123.0, 52.2, 48.1, 12.2 ppm. **IR** (ATR) 2968.45, 2810.28, 1487.12, 1431.18, 1228.66, 1186.22, 852.54, 767.67 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{17}N_2O$ 181.1341, found 181.1344

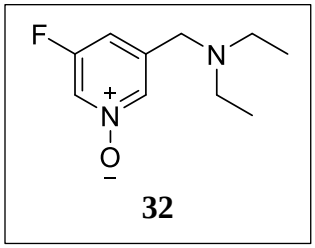
3-((diethylamino)methyl)-5-methoxypyridine 1-oxide (30)



30

3-((diethylamino)methyl)-5-methoxypyridine 1-oxide was synthesized from compound **29** using general procedure B. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product as 0.0712 g of a clear oil (0.339 mmol, 68%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 7.93 – 7.92 (m, 1H), 7.84 (t, J = 2.0 Hz, 1H), 6.89 (h, J = 2.1, 1.1 Hz, 1H), 3.82 (s, 3H), 3.46 (s, 2H), 2.49 (q, J = 7.1 Hz, 4H), 1.01 (t, J = 7.1 Hz, 6H) ppm.; **^{13}C NMR** (200 MHz, $CDCl_3$) δ 157.55, 140.13, 132.25, 125.98, 113.30, 56.07, 54.52, 46.96, 11.85 ppm; **IR** (ATR) 2968.45, 2810.28, 1573.91, 1469.76, 1425.40, 1327.03, 1286.52, 1263.37, 1228.66, 1193.94, 1159.22, 1058.92, 1004.91, 840.96, 667.37 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{19}N_2O_2$ 211.1447; Found 211.1440

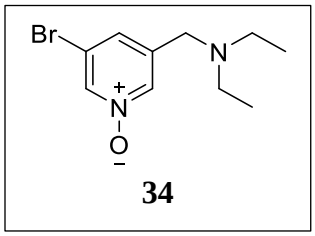
3-((diethylamino)methyl)-5-fluoropyridine 1-oxide (32)



32

3-((diethylamino)methyl)-5-fluoropyridine 1-oxide was synthesized from compound **31**using general procedure B. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product as 0.0963 g of a pale yellow oil (0.486 mmol, 97%) **^{1}H NMR** (800 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.97 (s, 1H), 7.10 (d, J = 7.7 Hz, 1H), 3.46 (d, J = 1.7 Hz, 2H), 2.46 (t, J = 7.3 Hz, 4H), 0.95 (d, J = 6.7 Hz, 6H) ppm; **^{13}C NMR** (200 MHz, $CDCl_3$) δ 160.15 (d, J = 252.9 Hz), 141.48 (d, J = 8.0 Hz), 135.54 (d, J = 4.4 Hz), 127.72 (d, J = 36.6 Hz), 114.65 (d, J = 20.2 Hz), 54.27, 47.05, 11.83 ppm; **IR** (ATR) 2970.38, 2810.28, 1614.42, 1573.91, 1431.18, 1327.03, 1286.52, 1213.23, 1157.29, 1010.70, 840.96 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{16}FN_2O$ 199.1247; Found 199.1268

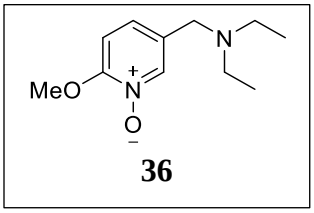
3-bromo-5-((diethylamino)methyl)pyridine 1-oxide (34)



34

3-bromo-5-((diethylamino)methyl)pyridine 1-oxide was synthesized from compound **33** using general procedure B. The reaction mixture was purified after workup using alumina flash chromatography (5% MeOH/Et_2O) to give product as 0.1196 g of a clear oil (0.462 mmol, 92%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.10 (s, 1H), 7.37 (s, 1H), 3.42 (s, 2H), 2.44 (q, J = 7.2 Hz, 4H), 0.94 (t, J = 7.2 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 141.09, 138.82, 137.78, 129.29, 119.84, 54.09, 46.99, 11.83 ppm. **IR** (ATR) 2966.52, 2931.80, 2804.50, 1589.34, 1541.12, 1454.33, 1408.04, 1284.59, 1201.65, 1153.43, 1118.71, 1064.71, 1002.98, 970.19, 840.96, 769.60, 669.30 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{16}BrN_2O$ 259.0446; Found 259.0443

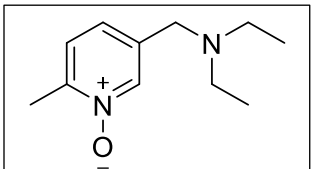
5-((diethylamino)methyl)-2-methoxypyridine 1-oxide (36)



36

5-((diethylamino)methyl)-2-methoxypyridine 1-oxide was synthesized from compound **35** using general procedure B. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product as 0.770 g of a pale yellow oil (0.366, mmol 73%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.29 (d, J = 1.2 Hz, 1H), 7.28 (ddd, J = 8.6, 2.1, 0.8 Hz, 1H), 6.83 (d, J = 8.6 Hz, 1H), 4.06 (s, 3H), 3.45 (s, 2H), 2.49 (q, J = 7.1 Hz, 4H), 1.01 (t, J = 7.2 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 156.97, 139.52, 131.03, 130.41, 107.67, 57.24, 53.60, 46.66, 11.67 ppm; **IR** (ATR) 2970.38, 1614.42, 1517.98, 1458.18, 1444.68, 1382.96, 1307.74, 1282.66, 1213.23, 1176.58, 1120.64, 1097.50, 1018.41, 891.11, 783.10, 734.88, 684.73, 613.36 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{19}N_2O_2$ 211.1447; Found 211.1452

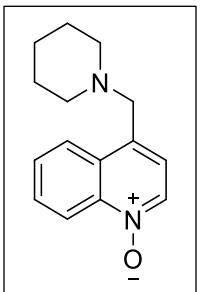
5-((diethylamino)methyl)-2-methylpyridine 1-oxide (42)



42

5-((diethylamino)methyl)-2-methylpyridine 1-oxide was synthesized from compound **41** using general procedure B on scale with 0.1 mmol of substrate. The reaction mixture was purified after workup using silica flash chromatography (10% MeOH/CH_2Cl_2) to give product as 0.0118 g of pale yellow oil (0.0607 mmol, 51%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.18 – 7.16 (m, 2H), 3.47 (s, 2H), 2.52 – 2.47 (m, 7H), 1.01 (t, *J* = 7.1 Hz, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 147.07, 139.25, 137.28, 126.25, 125.81, 54.17, 46.86, 17.52, 11.85 ppm; **IR** (ATR) 2966.52, 2926.01, 2808.36, 1616.35, 1506.41, 1448.54, 1375.25, 1354.03, 1265.30, 1217.08, 1163.08, 1116.78, 1062.78, 1002.98, 939.33, 810.10, 754.17, 586.36 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{18}N_2O$ 195.1497; Found 195.1500

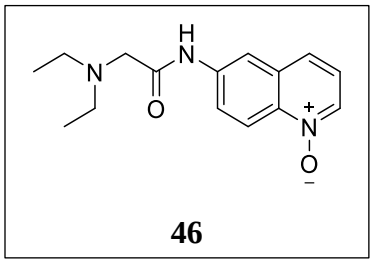
4-(piperidin-1-ylmethyl)quinoline 1-oxide (44)



44

4-(piperidin-1-ylmethyl)quinoline 1-oxide was synthesized from compound **43** using general procedure B. The reaction mixture was purified after workup using alumina flash chromatography (EtOAc) to give product as 0.0996 g of white solid (0.411 mmol, 82%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.76 (dt, J = 8.8, 1.2, 0.0 Hz, 1H), 8.45 (d, J = 6.1 Hz, 1H), 8.27 (ddd, J = 8.4, 1.4, 0.6 Hz, 1H), 7.75 (ddd, J = 8.8, 6.8, 1.3 Hz, 1H), 7.64 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.33 (dt, J = 6.2, 1.0 Hz, 1H), 3.80 (s, 2H), 2.44 (s, 4H), 1.57 (p, J = 5.6 Hz, 5H), 1.45 (d, J = 4.6 Hz, 2H) ppm.; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 150.98, 146.53, 137.74, 130.77, 129.67, 128.01, 127.34, 127.32, 126.73, 59.67, 54.70, 26.03, 24.21 ppm; **IR** (ATR) 3061.03, 2927.94, 2798.71, 2754.35, 1566.20, 1512.19, 1394.53, 1367.53, 1344.38, 1313.52, 1282.66, 1247.94, 1209.37, 1153.43, 1043.49, 842.89, 763.81 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{19}N_2O$ 243.1497; Found 253.1497

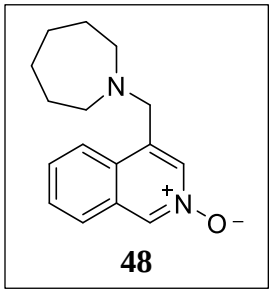
6-(2-(diethylamino)acetamido)quinoline 1-oxide (46)



46

6-(2-(diethylamino)acetamido)quinoline 1-oxide was synthesized from compound **45** using general procedure B on scale with 1.5 mmol of substrate. The reaction mixture was purified after workup using alumina flash chromatography (5% MeOH/Et_2O) to give product as 0.3079 g of white solid (1.13 mmol, 75%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.65 (d, *J* = 9.3 Hz, 1H), 8.51 (d, *J* = 2.3 Hz, 1H), 8.40 (dd, *J* = 6.0, 1.0 Hz, 1H), 7.71 (d, *J* = 8.9 Hz, 1H), 7.60 (dd, *J* = 9.3, 2.3 Hz, 1H), 7.26 (dd, *J* = 8.3, 6.1 Hz, 1H), 3.19 (s, 2H), 2.66 (q, *J* = 7.1 Hz, 4H), 1.09 (t, *J* = 7.2 Hz, 6H).; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 170.87, 138.28, 137.60, 134.59, 131.45, 126.13, 123.42, 121.56, 120.81, 115.37, 58.05, 48.91, 12.41; **IR** (ATR) 3269.34, 3051.39, 2966.52, 2927.54, 2854.65, 2791.00, 1670.35, 1575.84, 1523.76, 1489.05, 1367.53, 1271.09, 1203.58, 1182.36, 866.04, 823.60, 731.02 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}N_3O_2$ 274.1556; Found 274.1545

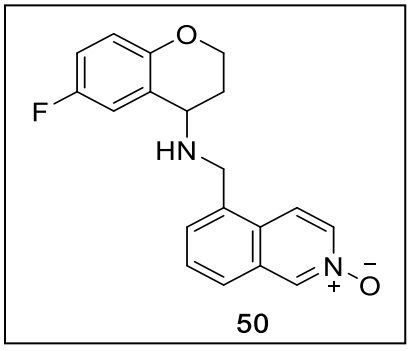
4-(azepan-1-ylmethyl)isoquinoline 2-oxide (48)



48

4-(azepan-1-ylmethyl)isoquinoline 2-oxide was synthesized from compound **47** using general procedure B. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product as 0.0768 g of white solid (0.300 mmol, 60%) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.21 – 8.17 (m, 2H), 7.73 – 7.69 (m, 1H), 7.62 – 7.58 (m, 2H), 3.94 (s, 2H), 2.70 (q, J = 4.3 Hz, 4H), 1.67 – 1.59 (m, 8H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 136.15, 135.16, 134.44, 129.67, 129.12, 128.66, 128.61, 125.37, 124.08, 57.40, 55.59, 28.29, 26.92 ppm; **IR** (ATR) 2918.30, 2831.50, 1624.06, 1600.92, 1560.41, 1454.33, 1438.90, 1388.75, 1346.31, 1336.67, 1305.81, 1280.73, 1246.02, 1222.87, 1172.72, 1155.36, 1122.57, 1105.21, 1083.99, 977.91, 966.34, 898.83, 856.39, 779.24, 761.88, 754.17, 731.02, 692.44, 634.58 cm^{-1}; **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{21}N_2O$ 257.1654; Found 257.1644

5-(((6-fluorochroman-4-yl)amino)methyl)isoquinoline 2-oxide (50)

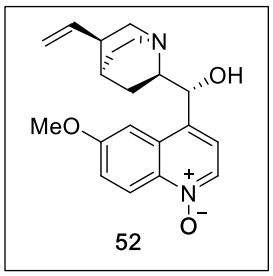


50

5-(((6-fluorochroman-4-yl)amino)methyl)isoquinoline 2-oxide was synthesized from compound **49** using general procedure A on a .660 mmol scale. The reaction mixture was purified after workup using alumina flash chromatography twice (1% MeOH/99%DCM and 10% MeOH/90% Et2O) to give 0.123 g of product **50** (.380 mmol, 57% yield) of white solid. **1H NMR** (600 MHz, $CDCl_3$) δ 8.79 (d, J = 1.9 Hz, 1H), 8.21 (dd, J = 7.3, 1.9 Hz, 1H), 8.15 (d, J = 7.3 Hz, 1H), 7.71 – 7.68 (m, 2H), 7.63 (dd, J = 8.2, 7.1 Hz, 1H), 7.06 – 7.03 (m, 1H), 6.91 (ddd, J = 9.0, 7.9, 3.1 Hz, 1H), 6.82 (dd, J = 9.0, 4.7 Hz, 1H), 4.42 – 4.37 (m, 2H), 4.32 (d, J = 13.2 Hz, 1H), 4.27 (ddd, J = 11.0, 6.0, 3.3 Hz, 1H), 3.95 (t, J = 5.0 Hz, 1H), 2.28 – 2.21 (m, 1H), 2.07 (dtd, J = 13.9, 5.6, 2.7 Hz, 1H), 1.65 (s, 1H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$) δ 157.24, 155.66, 150.65,

136.35, 135.99, 135.80, 129.97, 129.27, 127.92, 124.92, 124.78, 121.37, 117.74, 117.69, 115.53, 115.37, 114.96, 114.80, 62.83, 51.18, 50.25, 48.27, 27.49 ppm. **IR** (ATR) 2881.65, 1483.26, 1425.50, 1319.31, 1247.94, 1165.0, 1139.93, 1112.93, 1082.07, 933.55, 750.31, 729.09, 644.22 cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}N_2O_2F$ 325.1352, found 325.1343

4-((R)-hydroxy((1S,2R,4S,5R)-5-vinylquinuclidin-2-yl)methyl)-6-methoxyquinoline 1-oxide (52)



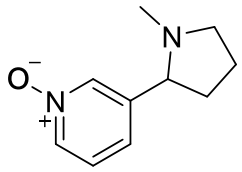
52

4-((R)-hydroxy((1S,2R,4S,5R)-5-vinylquinuclidin-2-yl)methyl)-6-methoxyquinoline 1-oxide was synthesized from quinine using general procedure A. The reaction mixture was purified after workup using alumina flash chromatography (10% MeOH/Et_2O) to give product **52** as 93 mg of white solid. (.274 mmol 54% yield) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.35 (d, *J* = 9.5 Hz, 1H), 7.85 (d, *J* = 6.3 Hz, 1H), 7.14 (d, *J* = 6.3 Hz, 1H), 7.11 (dd, *J* = 9.5, 2.6 Hz, 1H), 6.82 (d, *J* = 2.6 Hz, 1H), 6.20 (s, 1H), 5.67 (ddd, *J* = 17.1, 10.4, 7.6 Hz, 1H), 5.15 – 5.12 (m, 1H), 4.92 – 4.83 (m, 2H), 3.42 (s, 3H), 3.00 (dd, *J* = 13.8, 10.1 Hz, 1H), 2.78 (td, *J* = 10.1, 9.0, 4.5 Hz, 1H), 2.62 – 2.55 (m, 1H), 2.53 – 2.49 (m, 1H), 2.23 – 2.19 (m, 1H), 1.82 – 1.69 (m, 3H), 1.51 – 1.42 (m, 2H). 1.01 (t, 6H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 158.60, 142.14, 141.79, 135.02, 133.50, 128.40, 122.25, 120.86, 118.29, 113.99, 101.69, 70.90, 60.13, 56.76, 55.49, 42.76, 39.81, 30.10, 27.58, 22.29 ppm. **IR** (ATR) 3076.45, 2920.23, 1616.35, 1571.99, 1431.18, 1249.87, 1213.23, 1195.87, 1165.00, 1022.27, 829.39, cm^{-1}. **HRMS** (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{25}N_2O_3$ 341.1865, found 341.1863

IV. References

1. Schmidt, R. G., Bayburt, E. K., Latshaw, S. P., Koenig, J. R., Daanen, J. F., Mcdonald, H. A. Gomtsyan, A. (2011). Bioorganic & Medicinal Chemistry Letters Chroman and tetrahydroquinoline ureas as potent TRPV1 antagonists. Bioorganic & Medicinal Chemistry Letters, 21(5), 1338–1341.

V. Spectra



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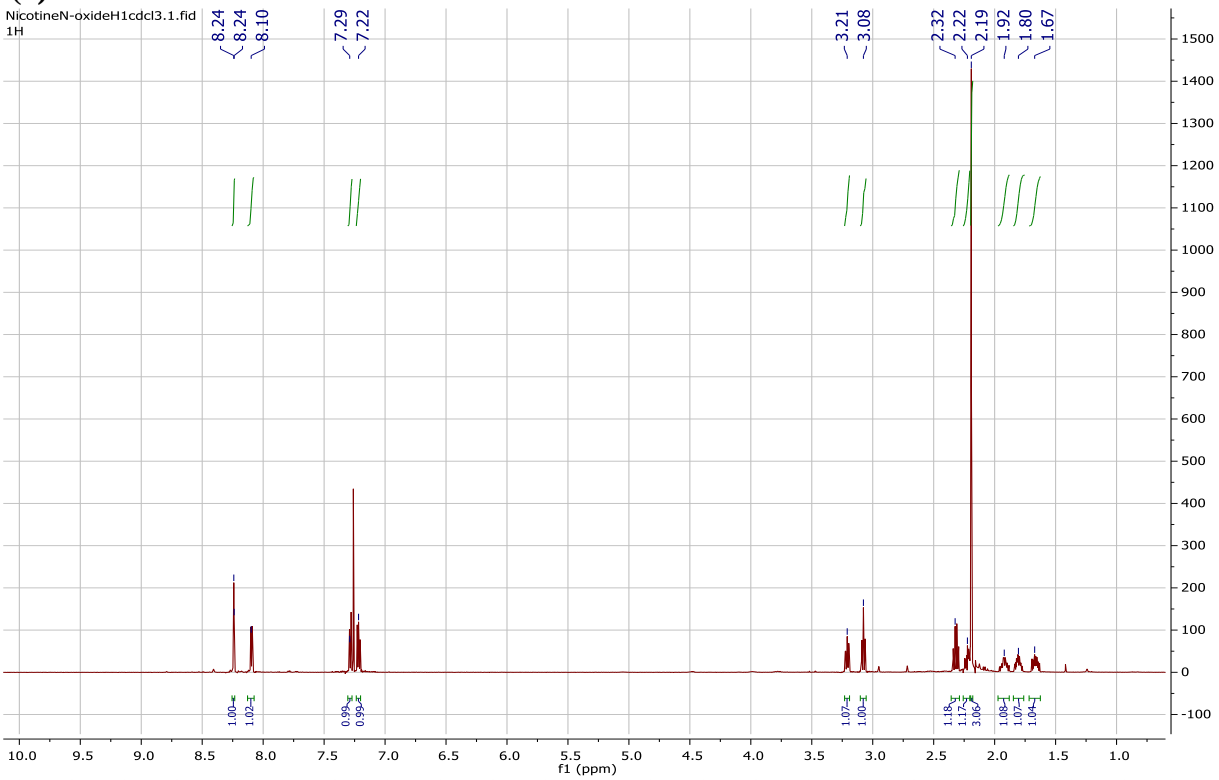
NicotineN-oxideH1cdcl3.1.fid
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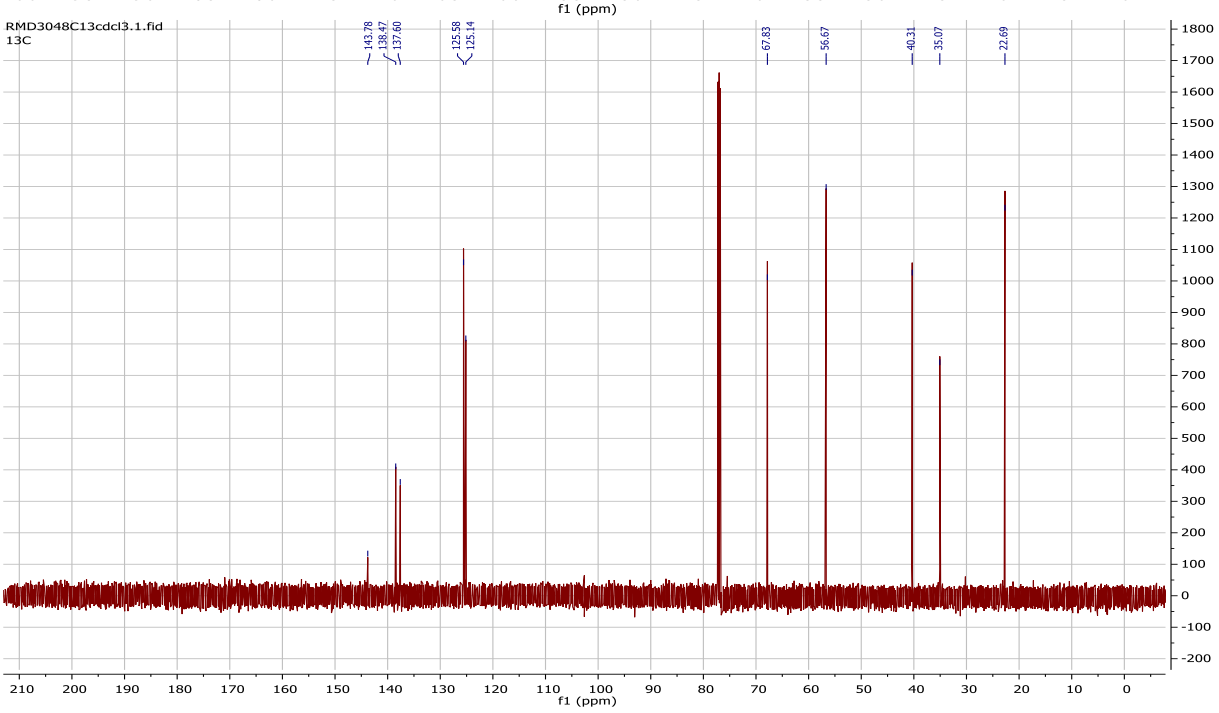
8.24
8.24
8.10
7.29
7.22
3.21
3.08
2.32
2.22
2.19
1.92
1.80
1.67
1.00
1.02
0.99
0.99
1.07
1.00
1.18
1.17
3.06
1.08
1.07
1.04
f1 (ppm)


RMD3048C13cdcl3.1.fid
13C
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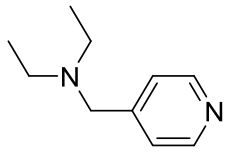
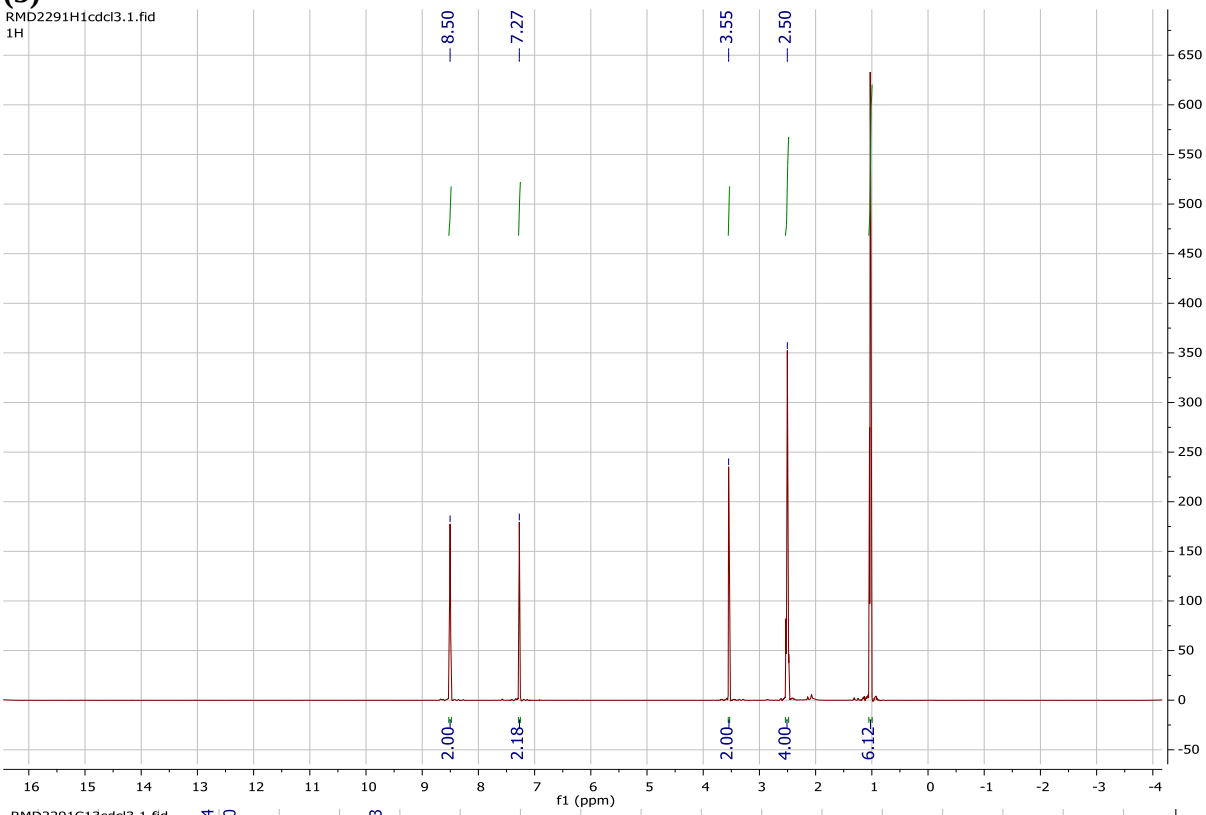
125.58
125.14
67.83
56.67
40.31
35.07
22.69
f1 (ppm)



(5)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7.27
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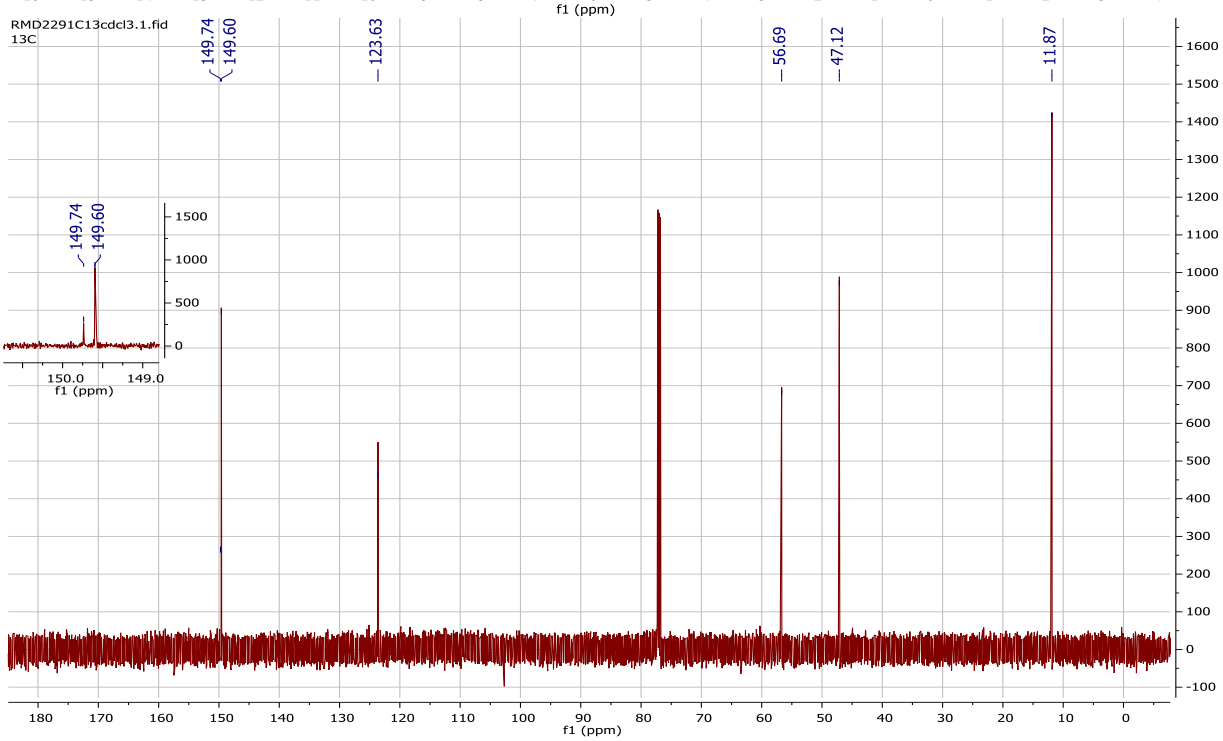
2.50
2.00
2.18
2.00
4.00
6.12
f1 (ppm)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13C
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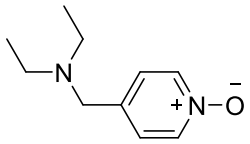
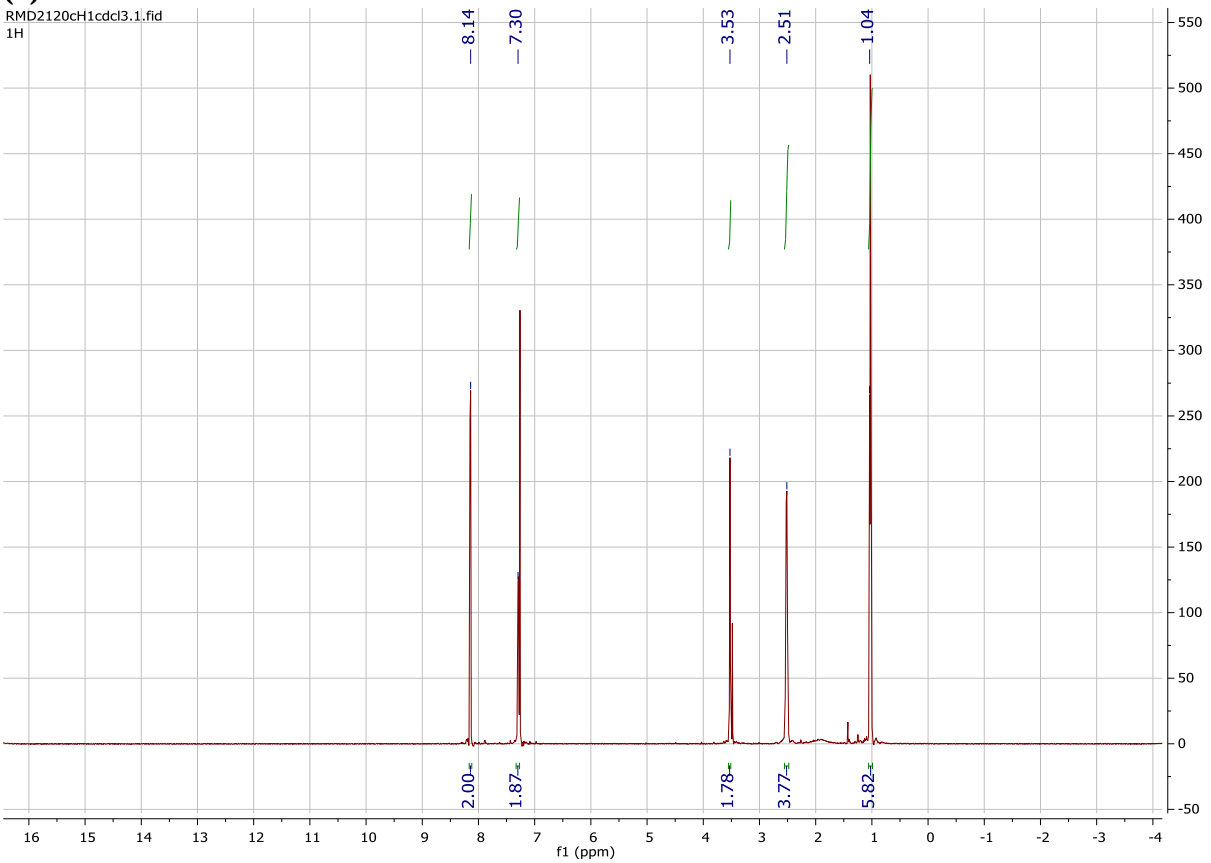
56.69
47.12
11.87
f1 (ppm)



(6)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1H
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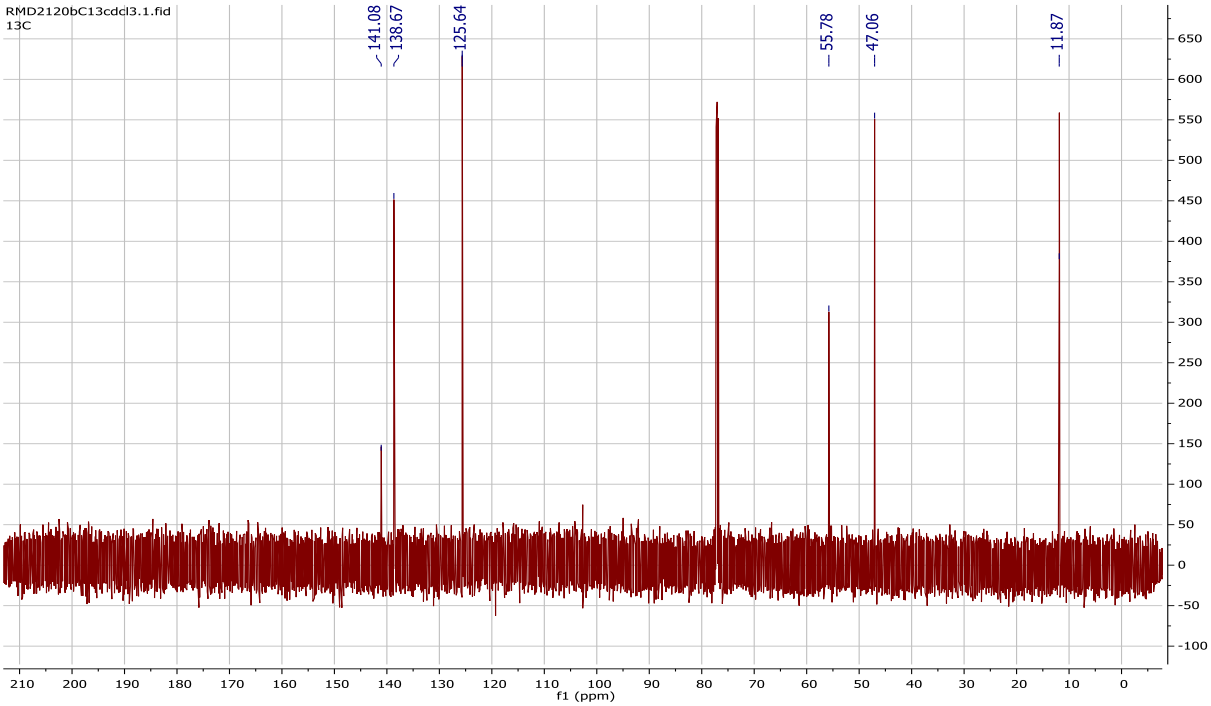
2.51
1.04
2.00
1.87
1.78
3.77
5.82
f1 (ppm)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55.78
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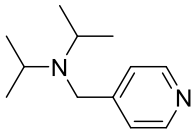
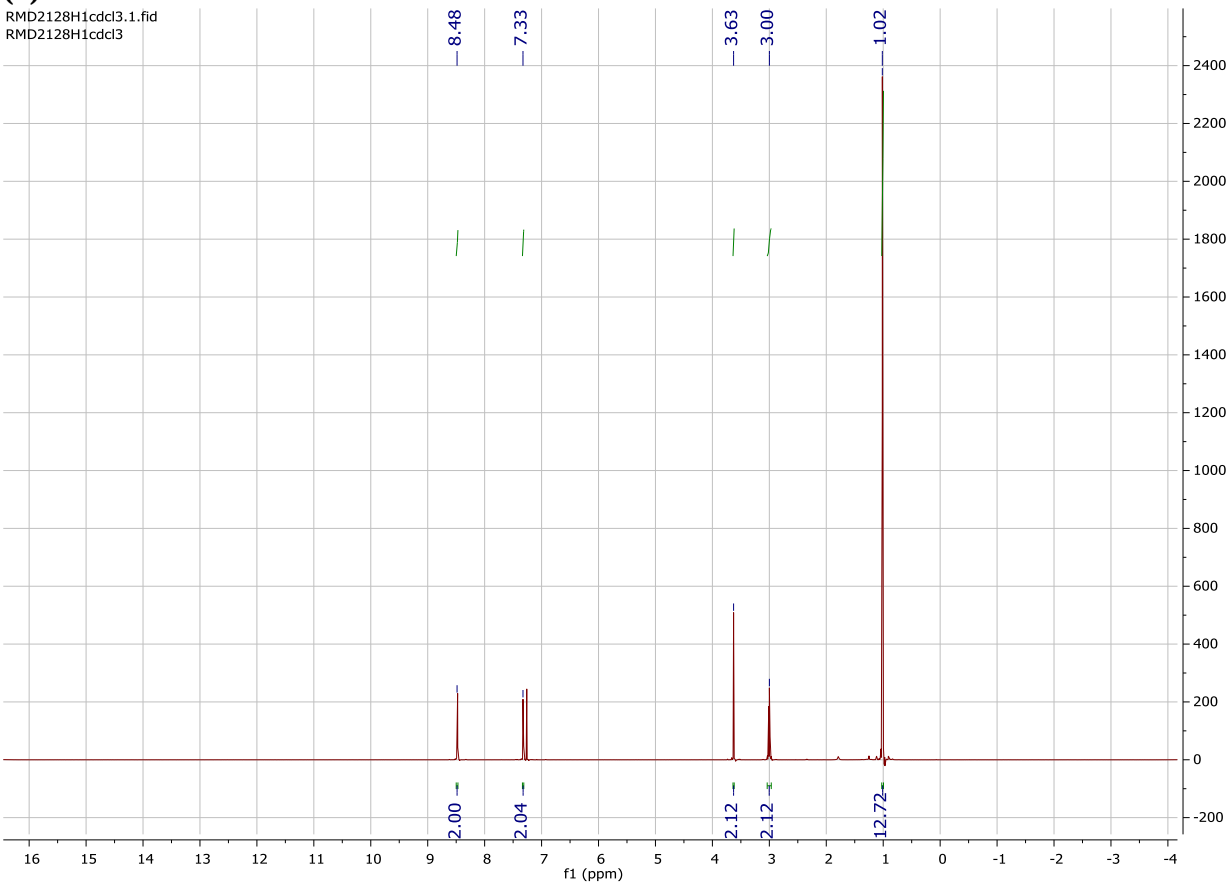
f1 (ppm)



(7)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RMD2128H1cdcl3
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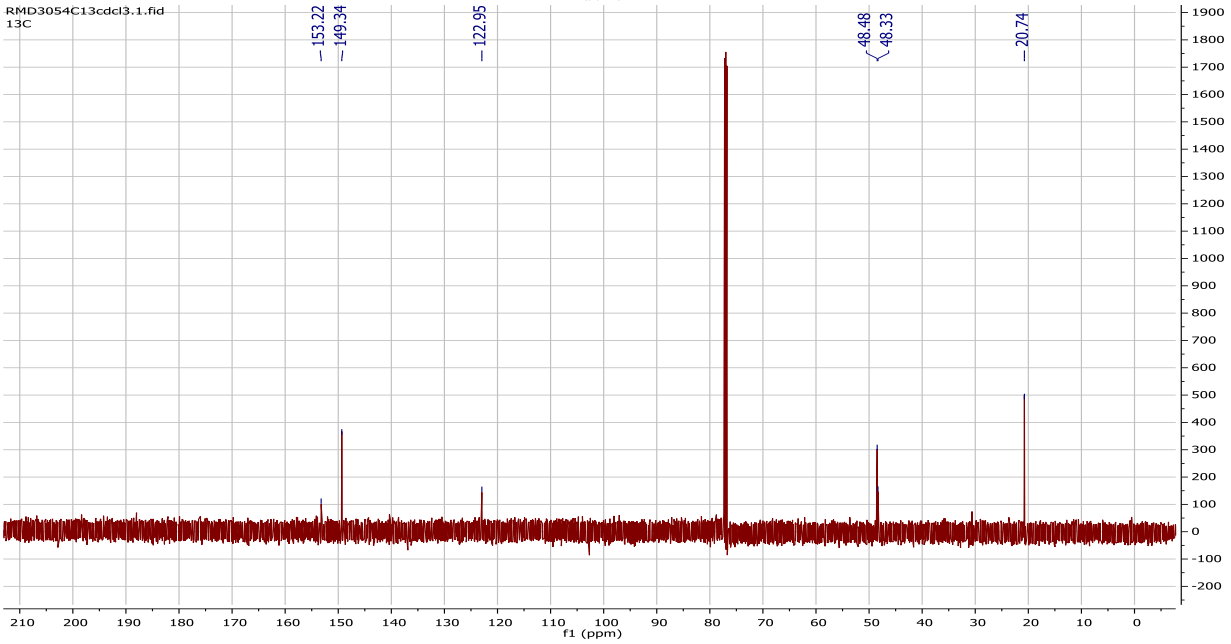
3.00
1.02
2.00
2.04
2.12
2.12
12.72
f1 (ppm)


RMD3054C13cdcl3.1.fid
13C
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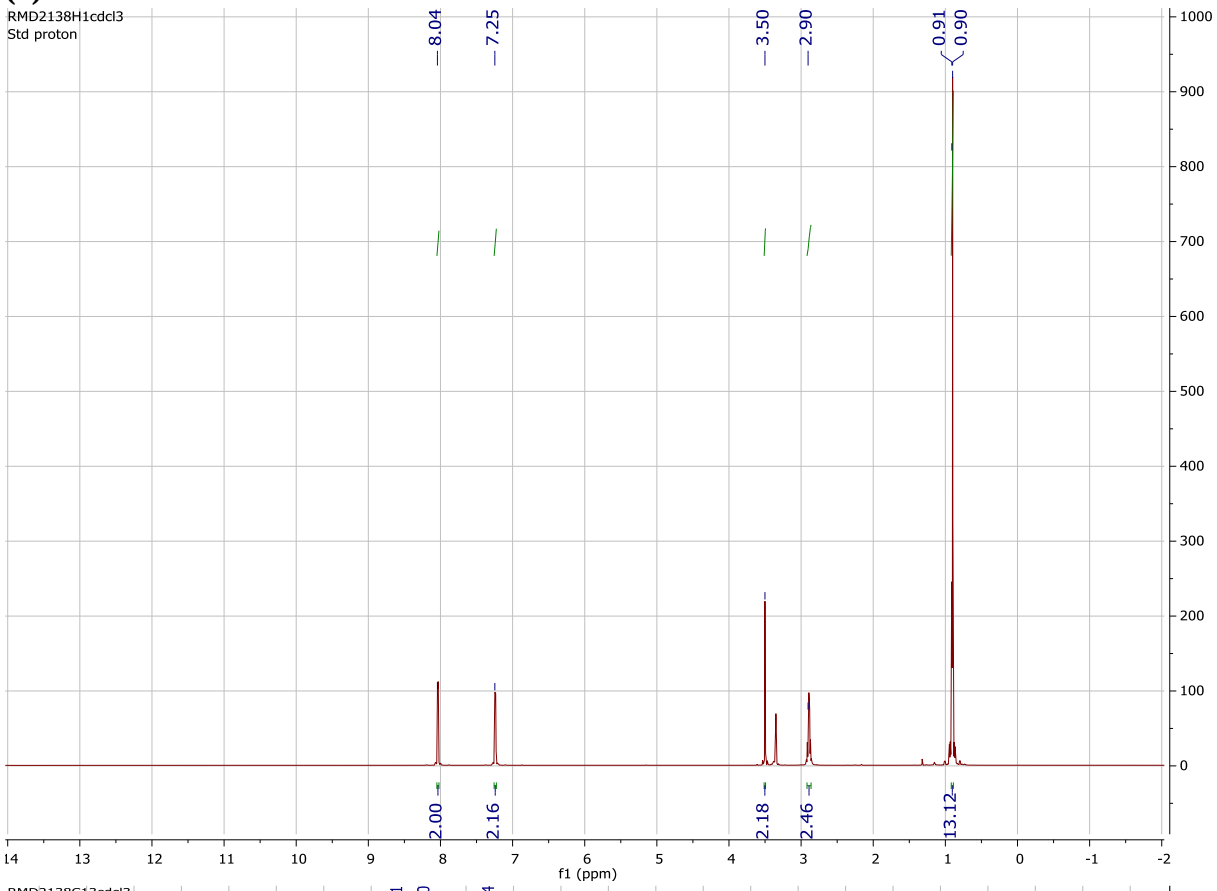
149.34
122.95
48.48
48.33
20.74
f1 (ppm)

(8)


RMD2138H1cdcl3
Std proton
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2.00
2.16
2.18
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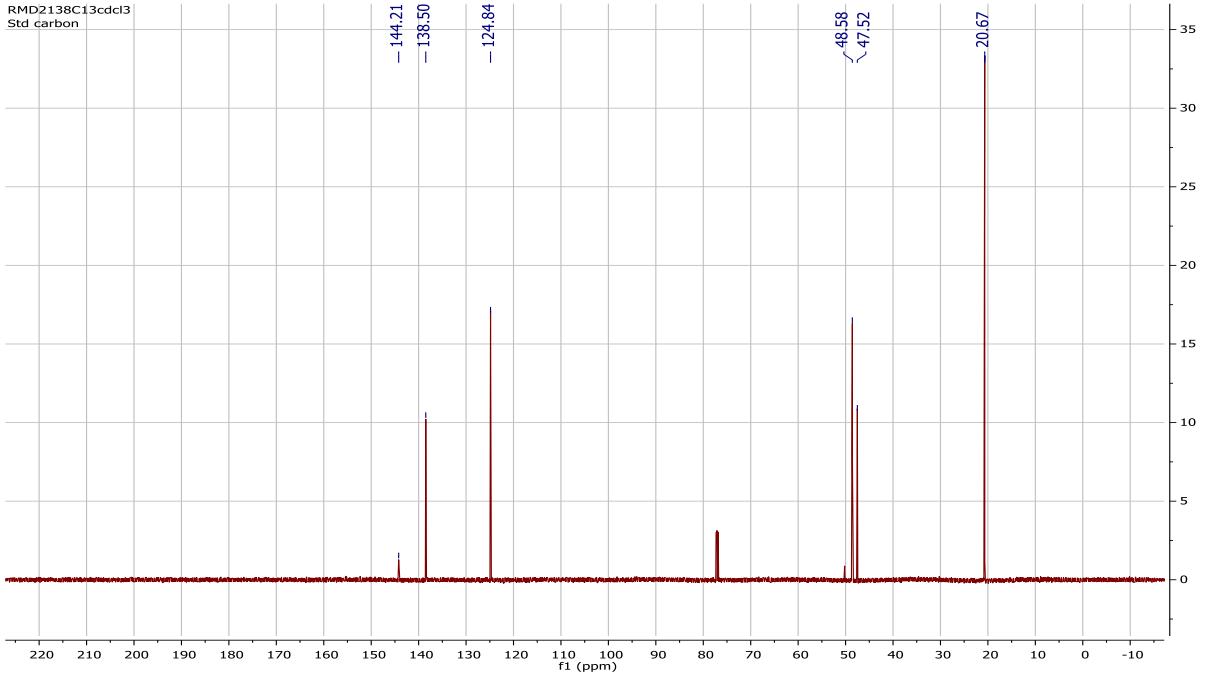
13.12
f1 (ppm)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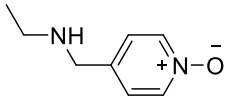
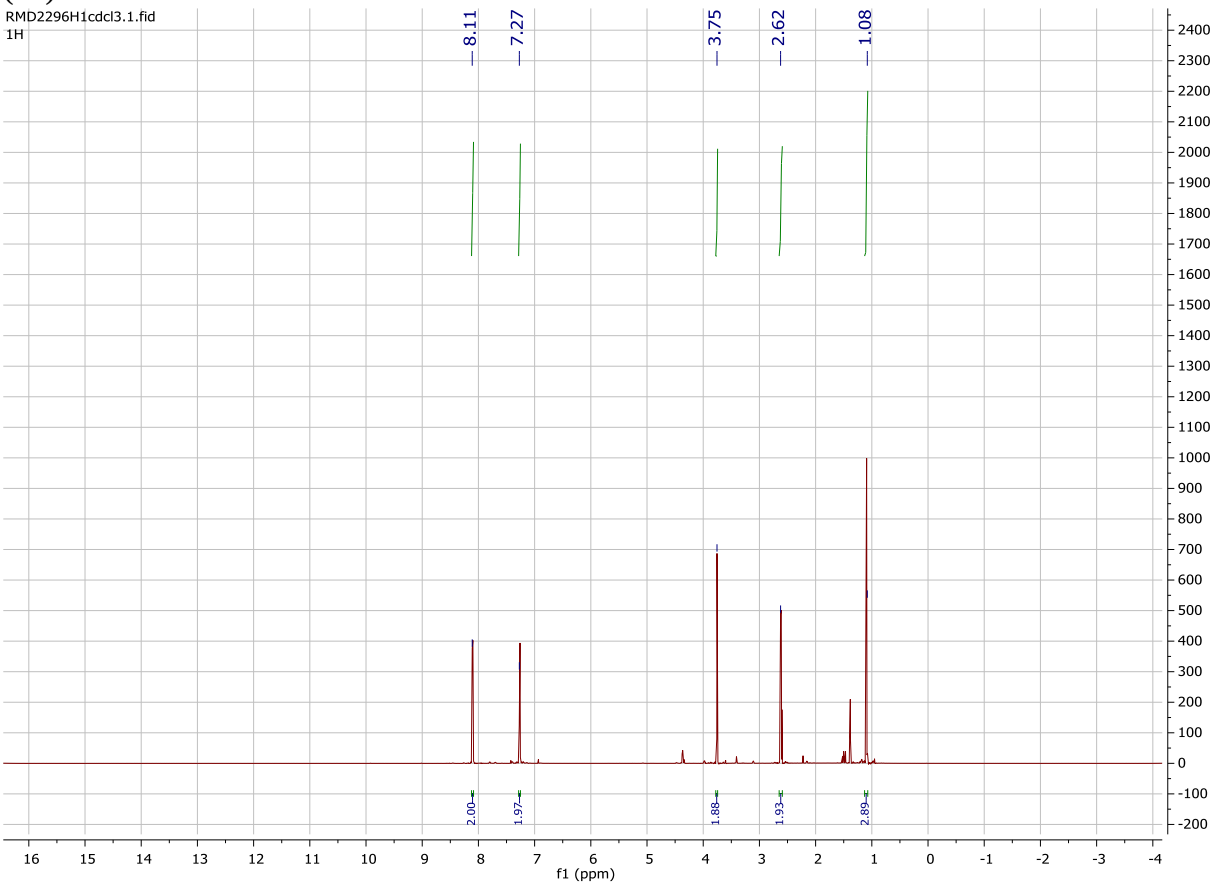

NH
+N−O
−

(10)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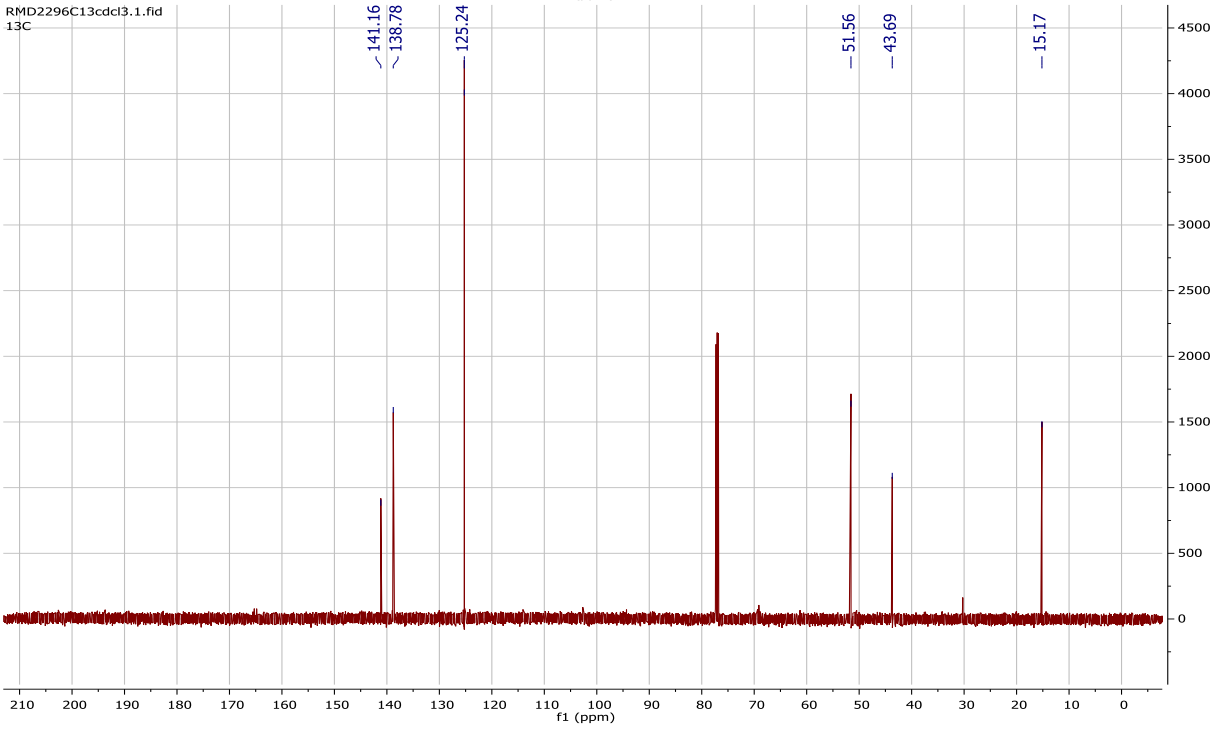
1.93
2.89
f1 (ppm)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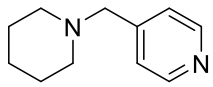
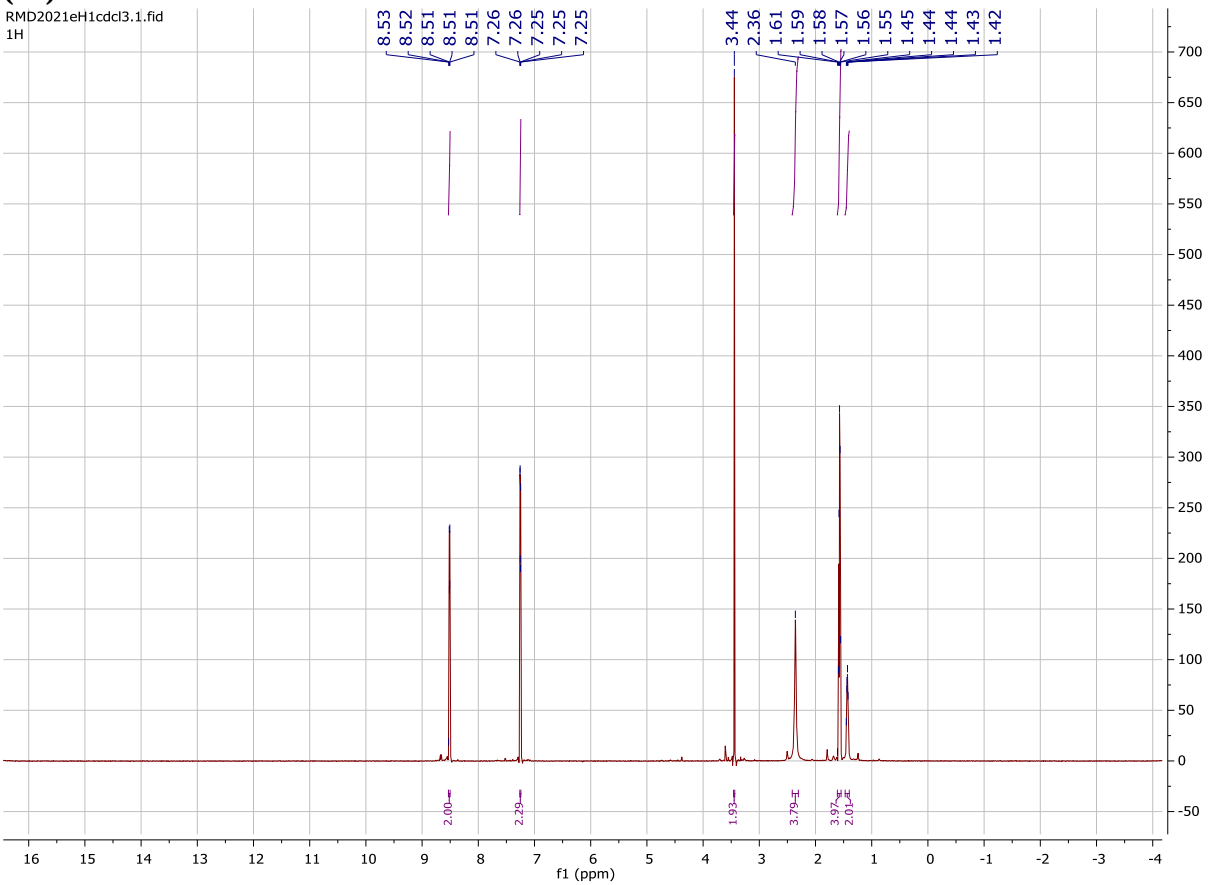
15.17
f1 (ppm)

(13)

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8.51
8.51
8.51
7.26
7.26
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7.25
3.44
2.36
1.61
1.59
1.58
1.57
1.56
1.55
1.45
1.44
1.44
1.43
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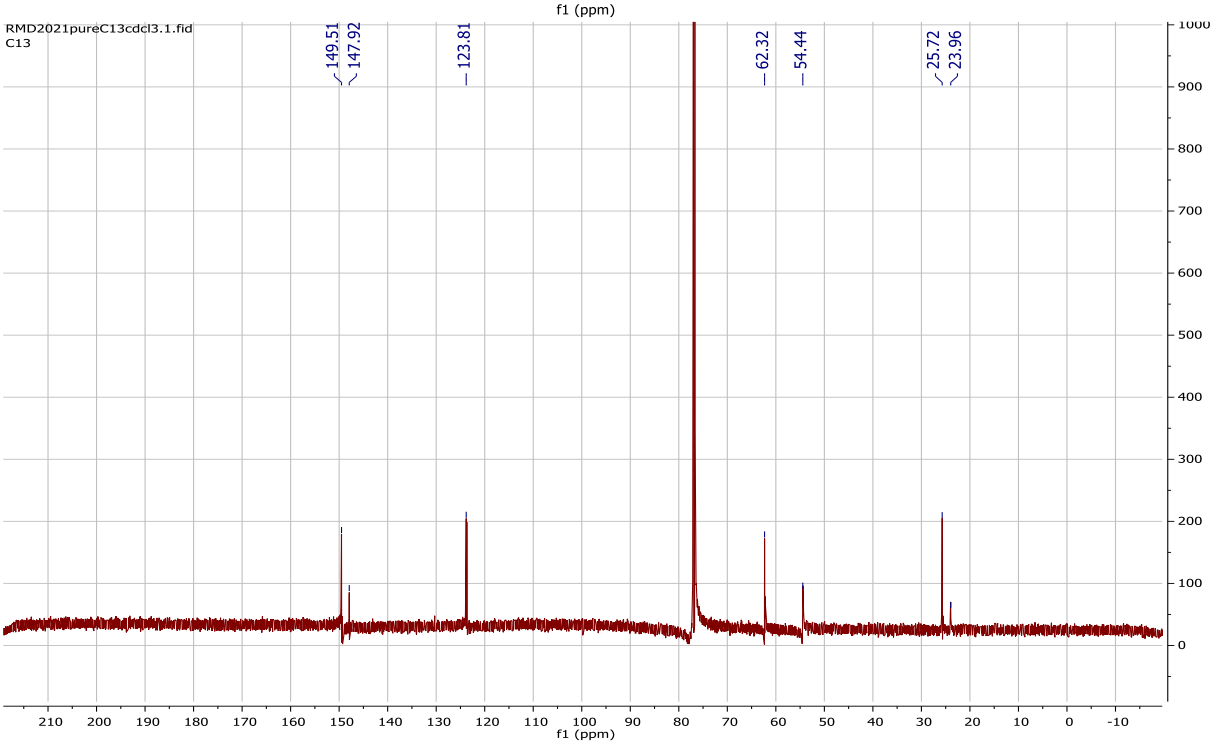
2.00
2.29
1.93
3.79
3.97
2.01
f1 (ppm)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62.32
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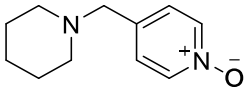
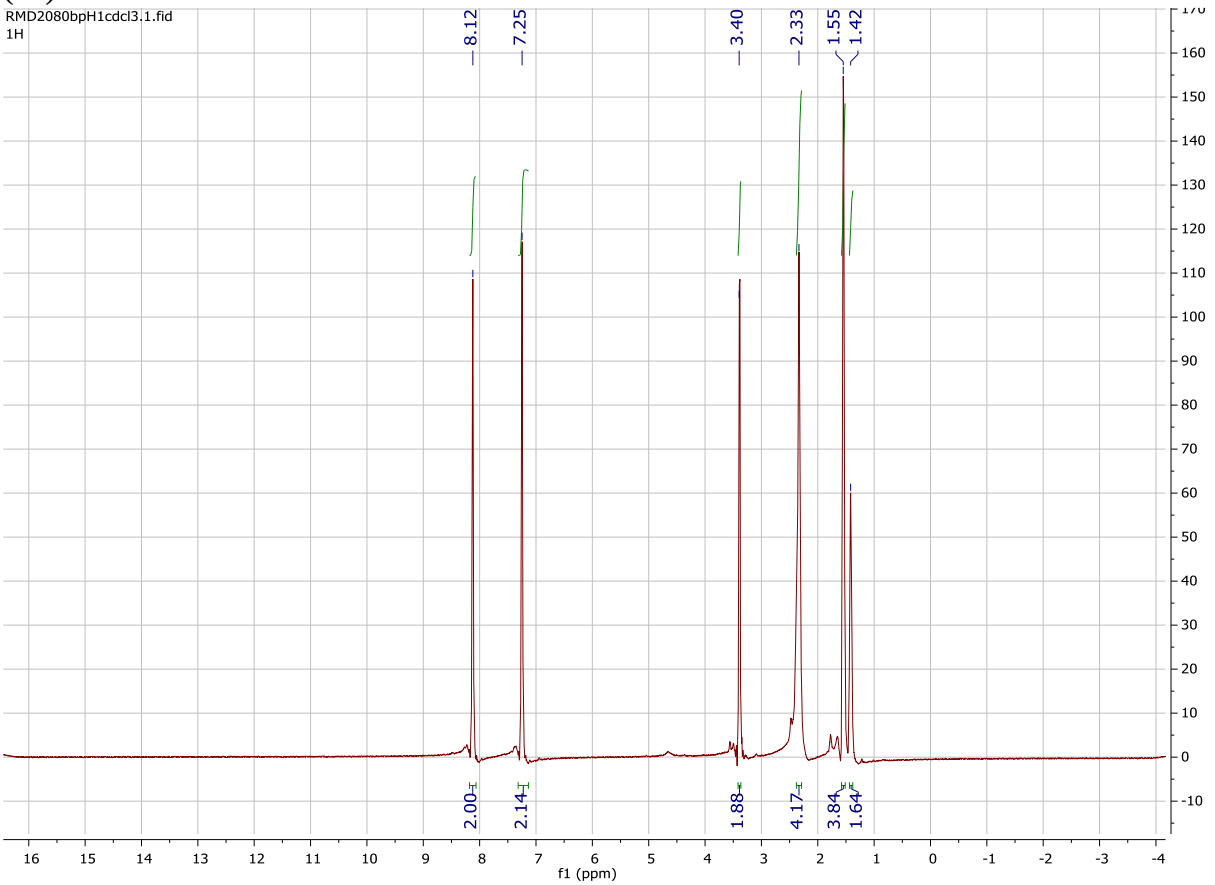
23.96
f1 (ppm)

(14)

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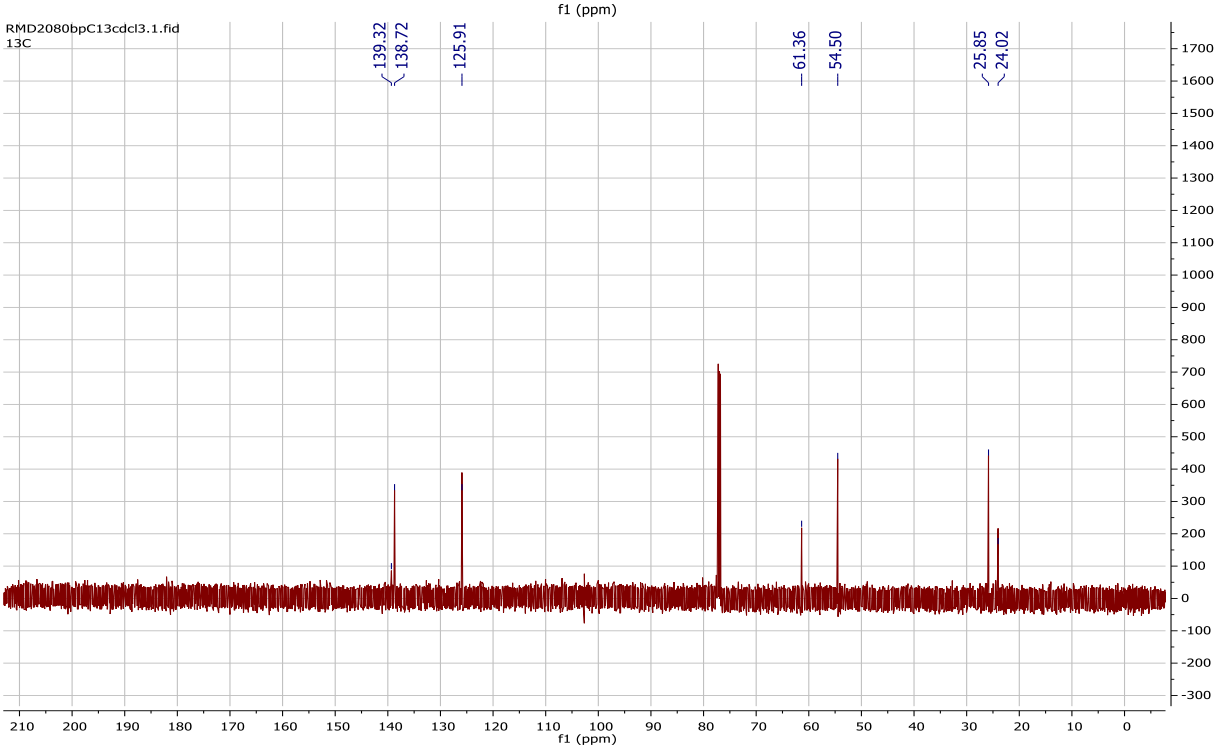
f1 (ppm)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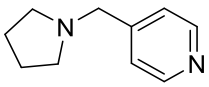
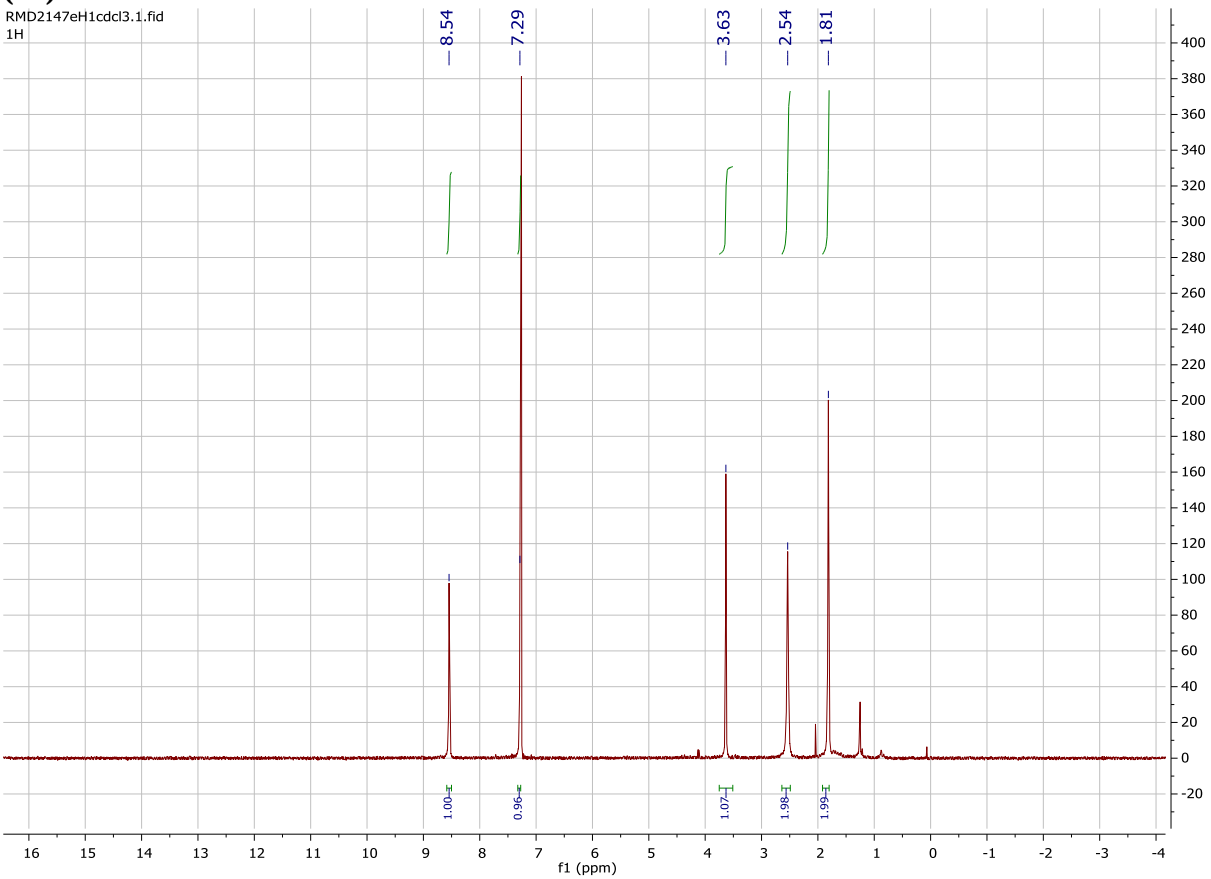
24.02
f1 (ppm)

(15)

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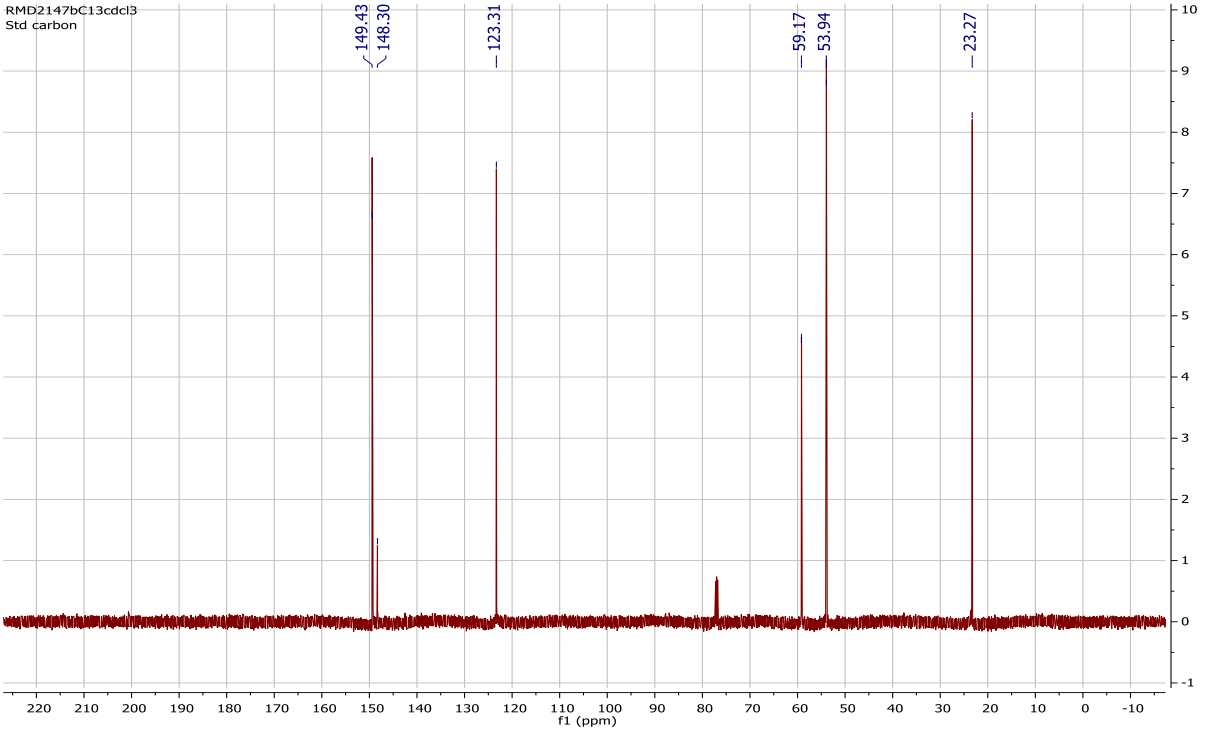
f1 (ppm)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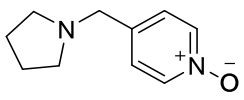
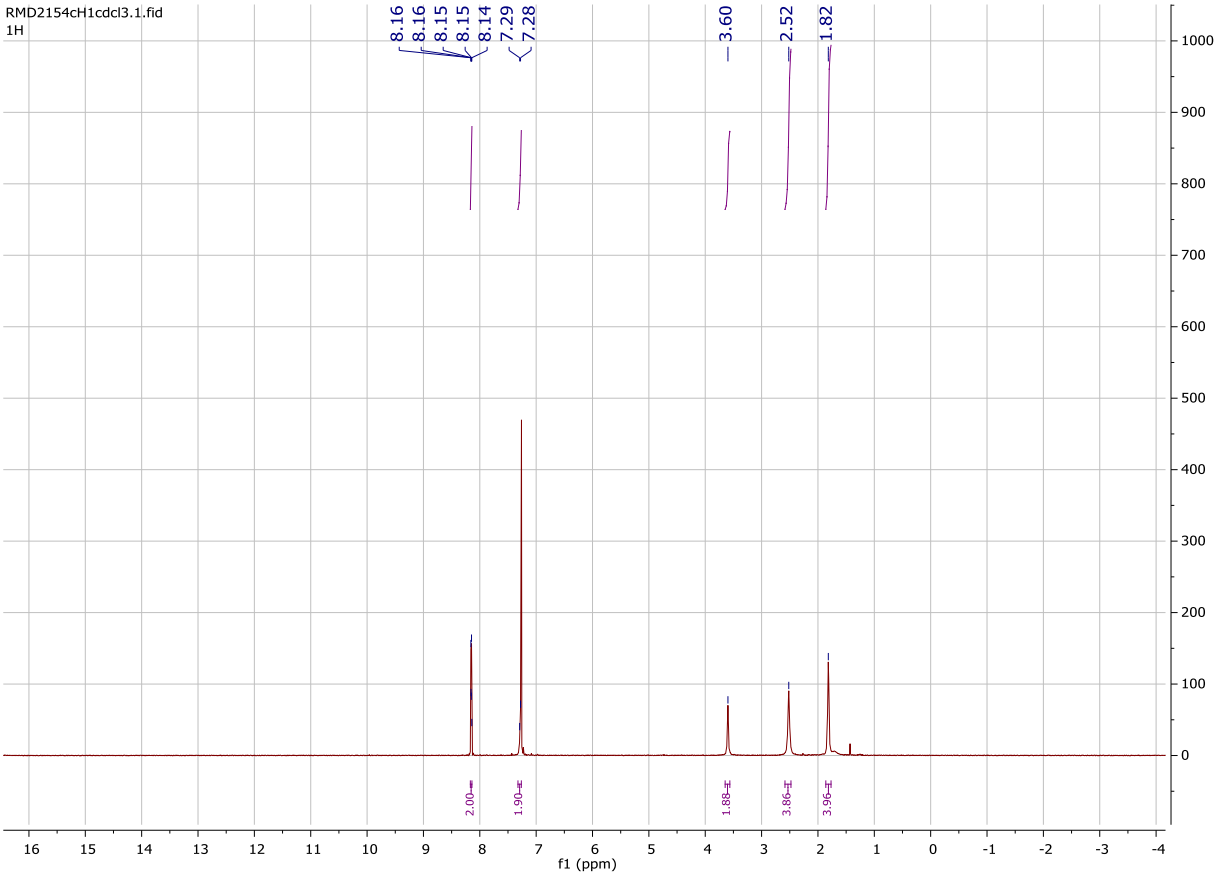
f1 (ppm)

(16)

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8.15
8.15
8.14
7.29
7.28
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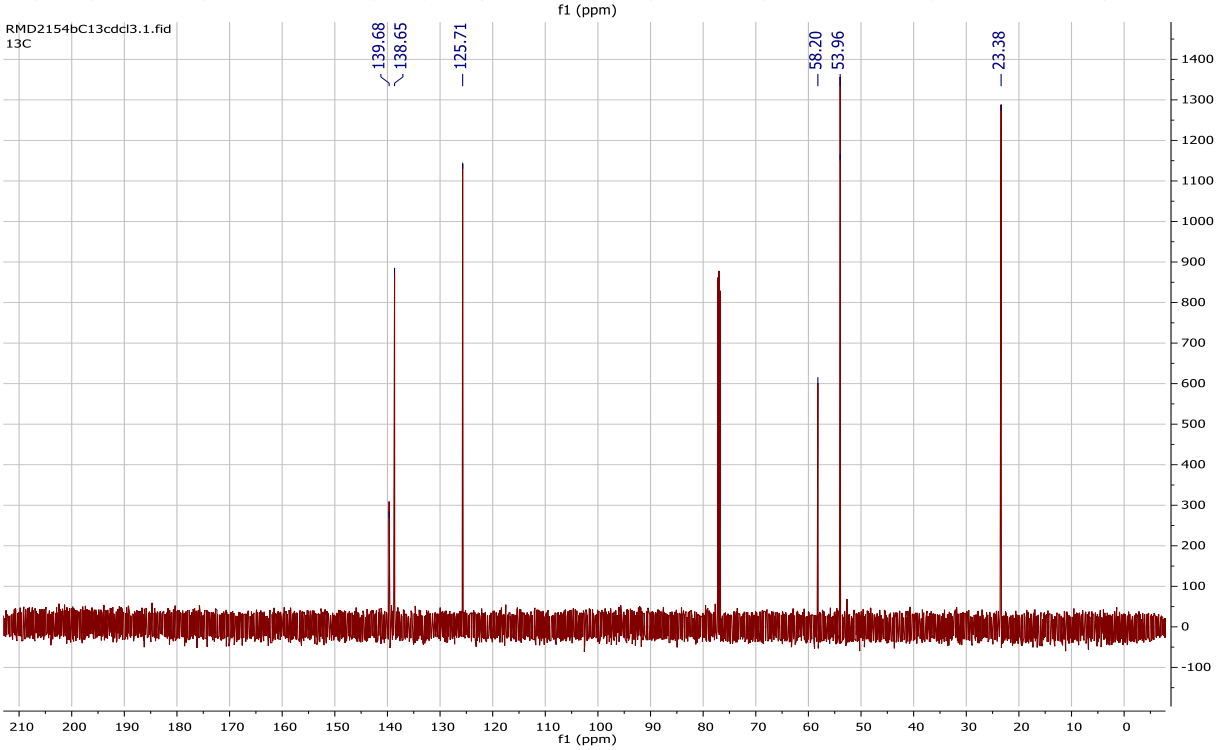
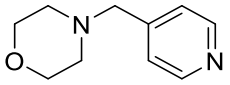
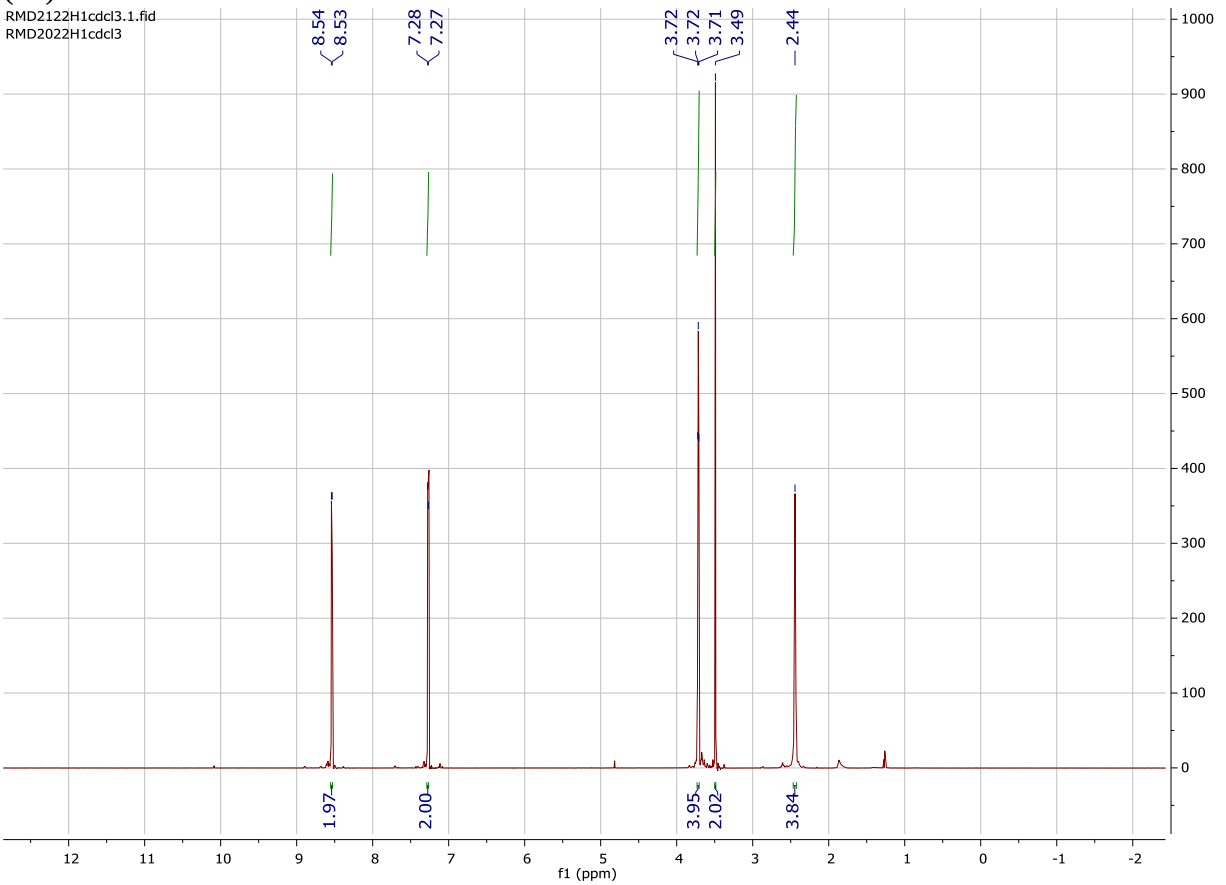
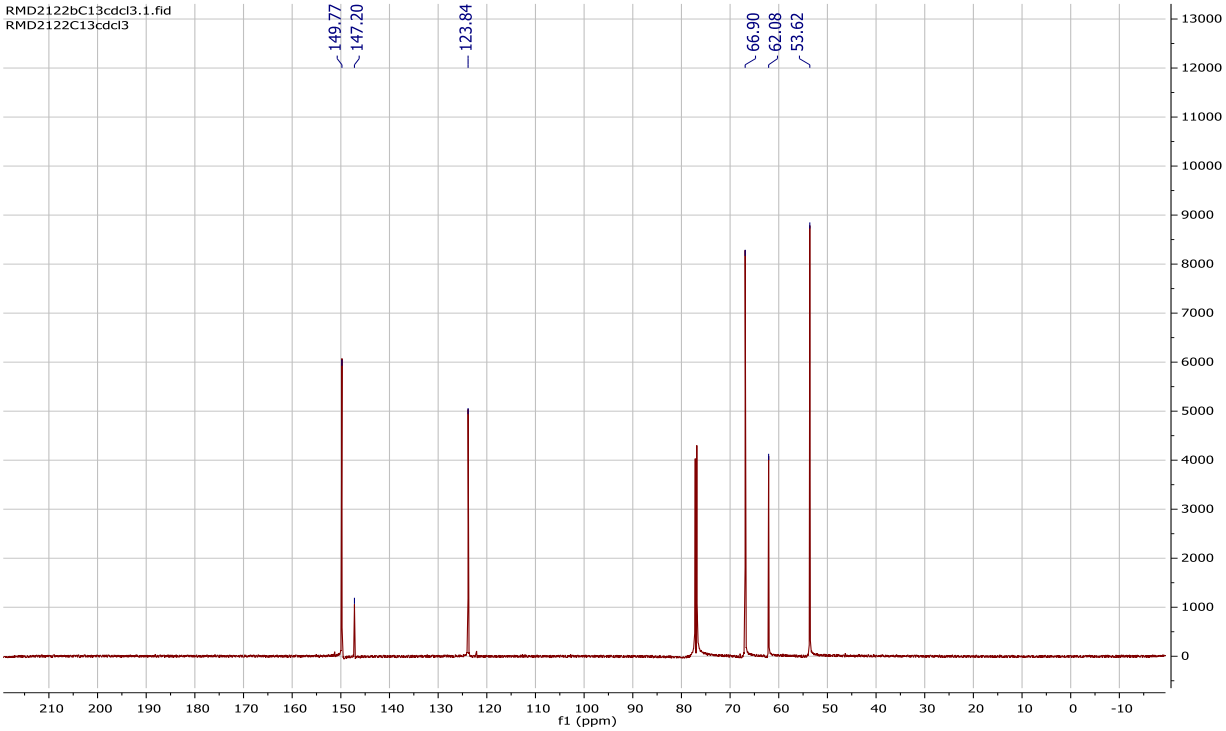
2.52
1.82
2.00
1.90
1.88
3.86
3.96
f1 (ppm)


RMD2154bC13cdcl3.1.fid
13C
139.68
138.65
125.71
58.20
53.96
23.38
f1 (ppm)

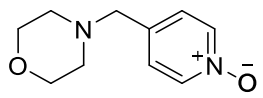
(17)

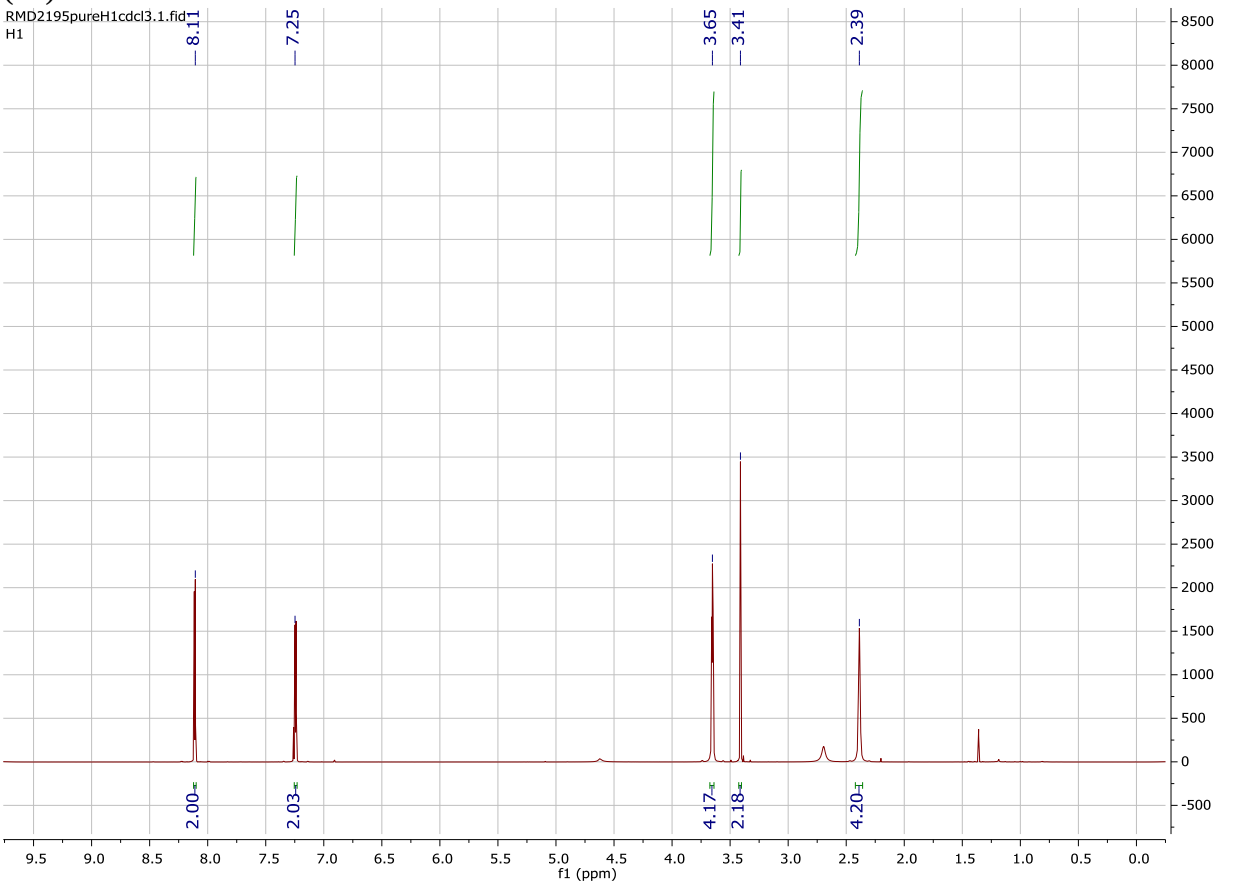


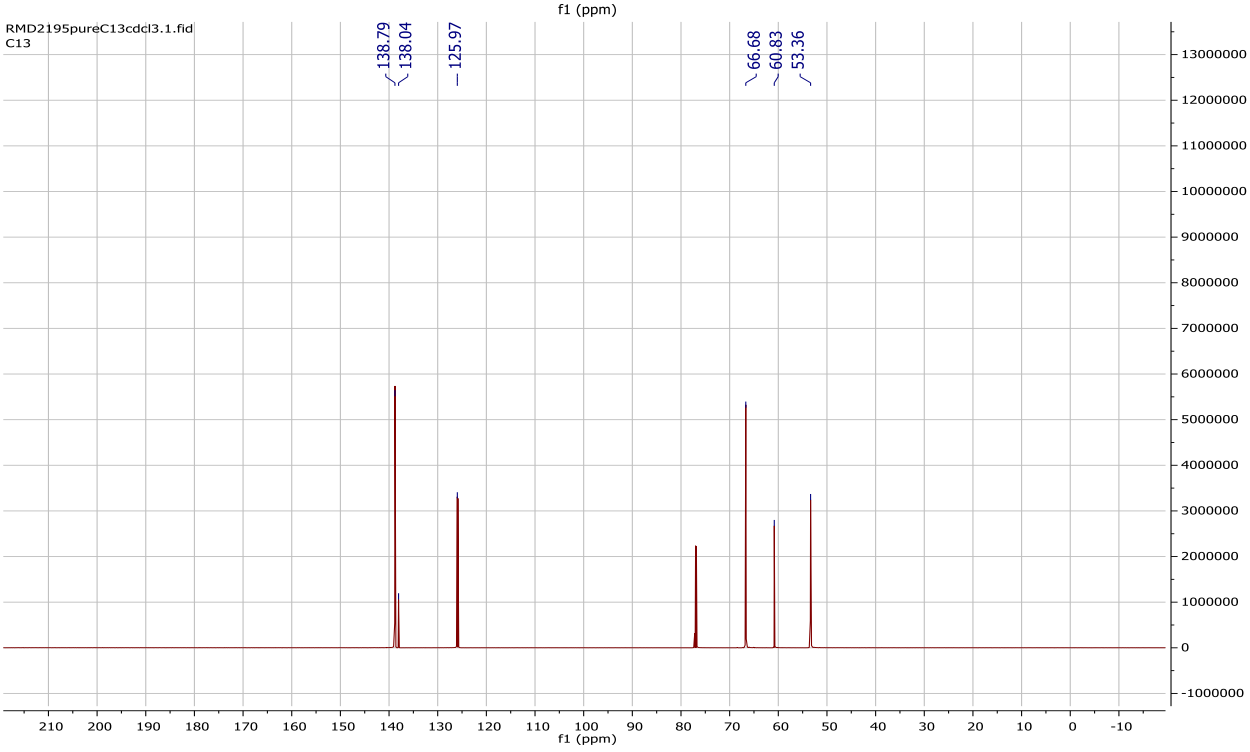

RMD2122H1cdcl3.1.fid
RMD2022H1cdcl3
8.54
8.53
7.28
7.27
3.72
3.72
3.71
3.49
2.44
1.97
2.00
3.95
2.02
3.84
f1 (ppm)


RMD2122bC13cdcl3.1.fid
RMD2122C13cdcl3
149.77
147.20
123.84
66.90
62.08
53.62
f1 (ppm)

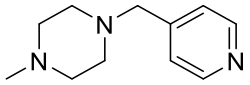
(18)

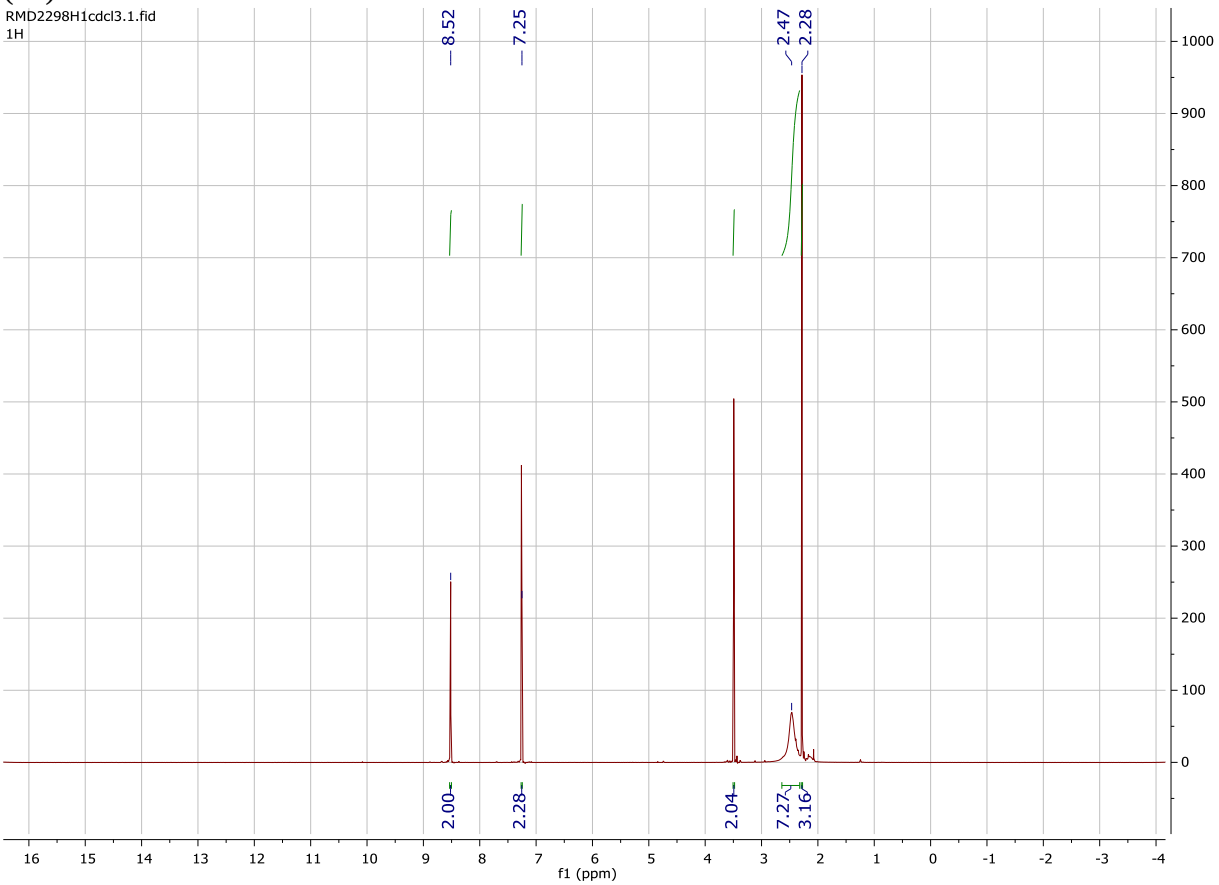


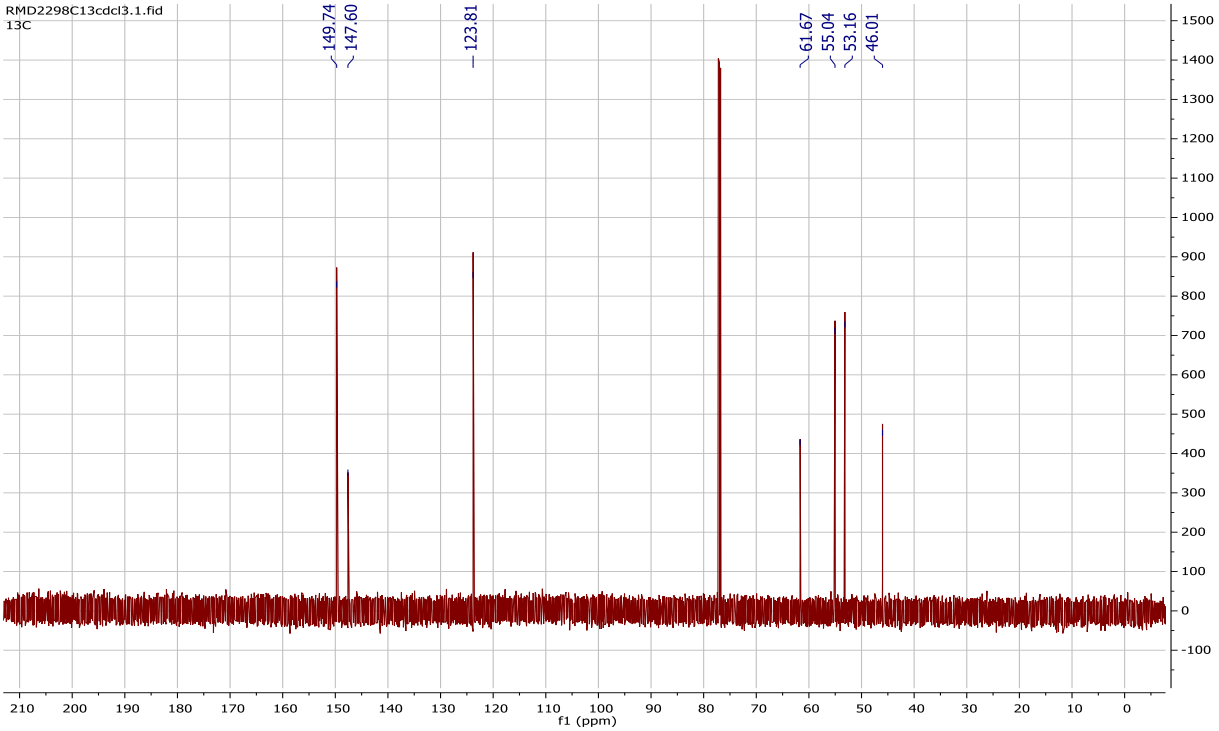

RMD2195pureH1cdcl3.1.fid
H1
8.11
7.25
3.65
3.41
2.39
2.00
2.03
4.17
2.18
4.20
f1 (ppm)


RMD2195pureC13cdcl3.1.fid
C13
138.79
138.04
125.97
66.68
60.83
53.36
f1 (ppm)

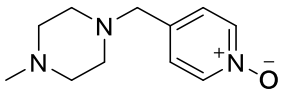
(19)

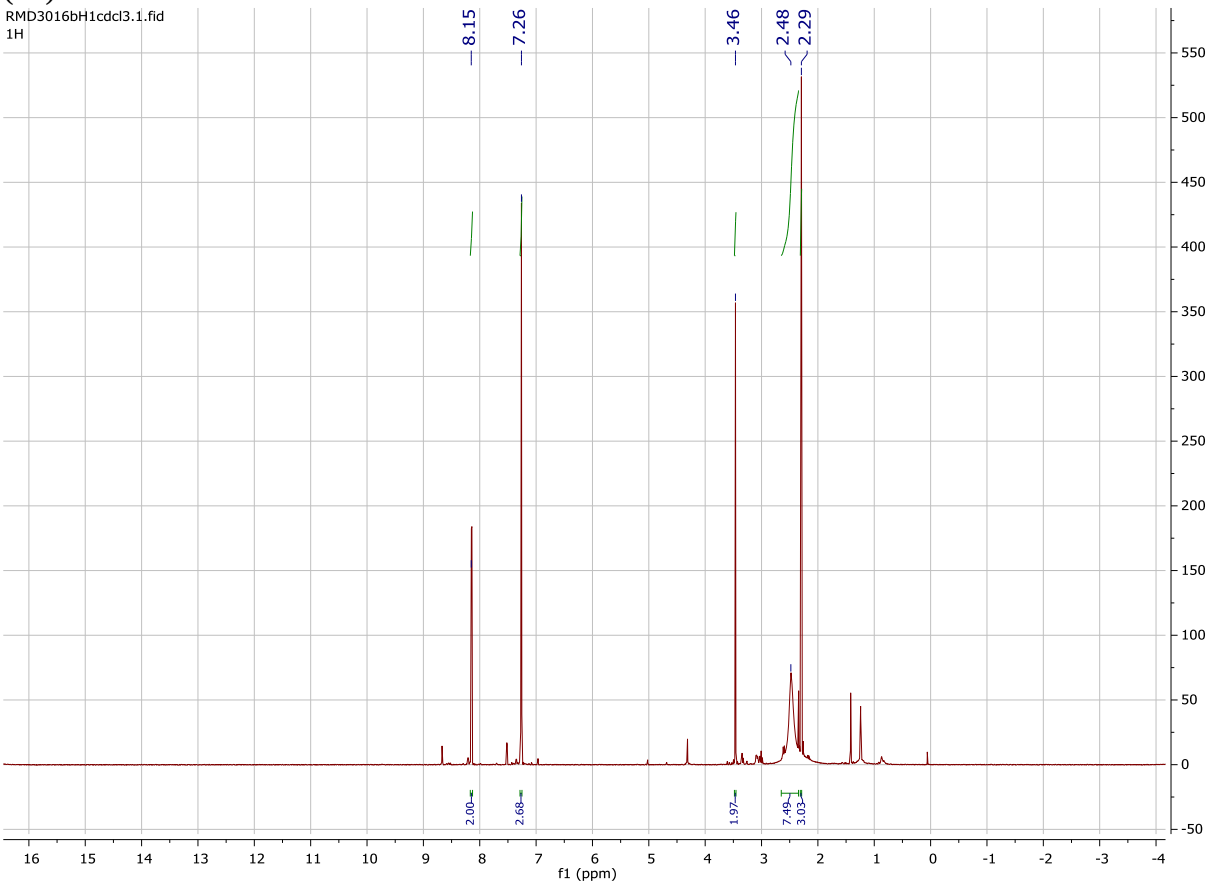


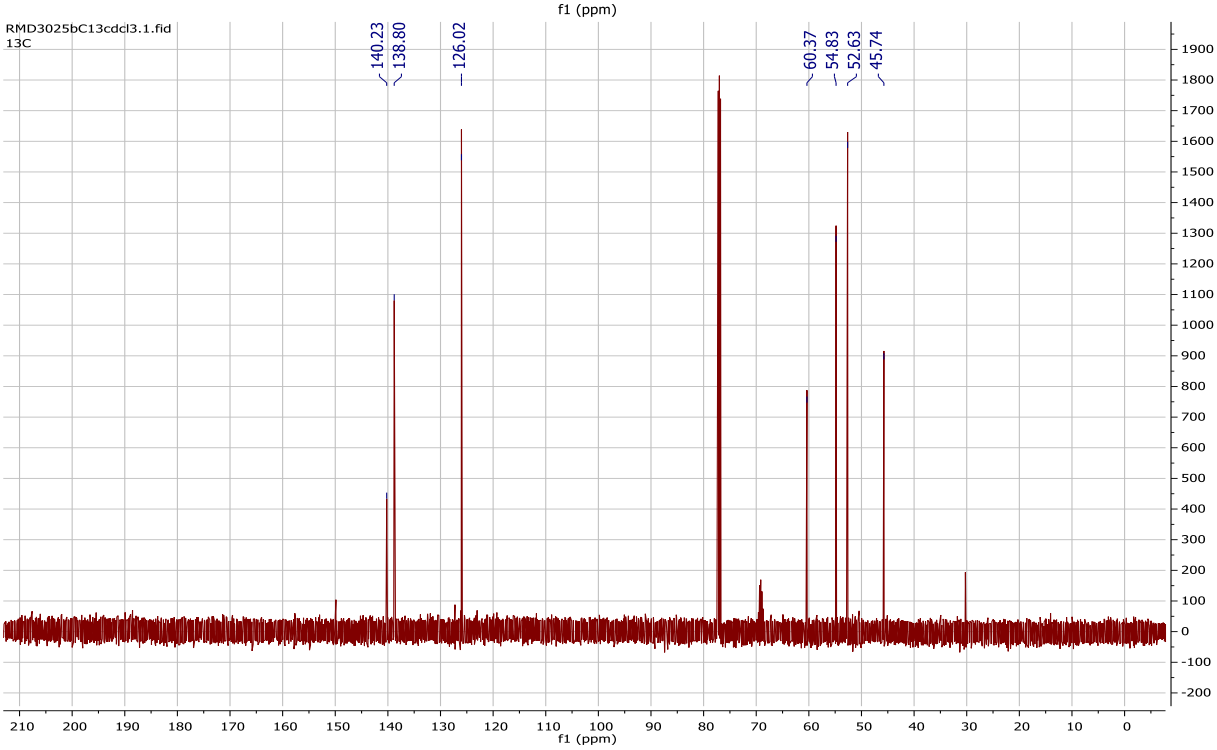

RMD2298H1cdcl3.1.fid
1H
8.52
7.25
2.47
2.28
2.00
2.28
2.04
7.27
3.16
f1 (ppm)


RMD2298C13cdcl3.1.fid
13C
149.74
147.60
123.81
61.67
55.04
53.16
46.01
f1 (ppm)

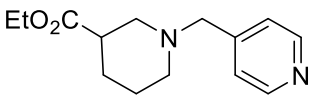
(20)

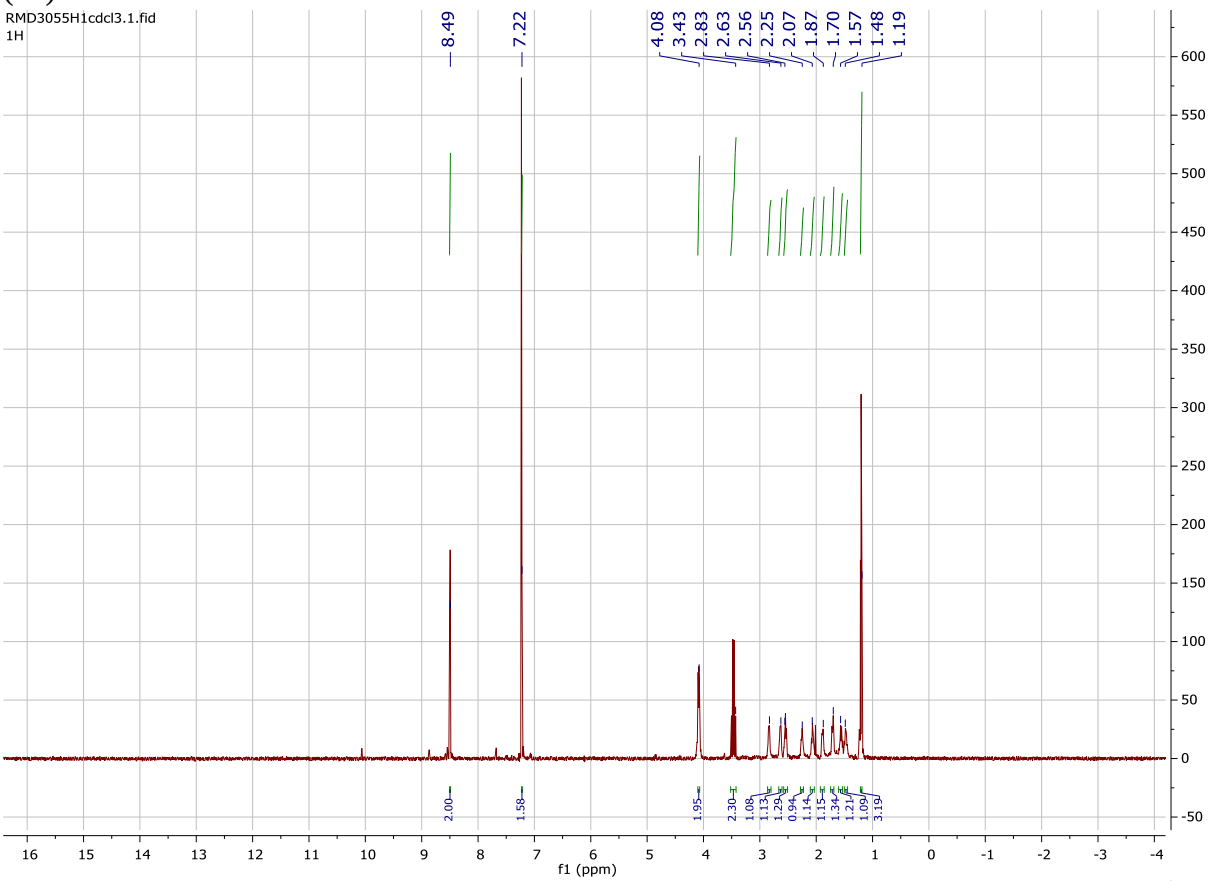


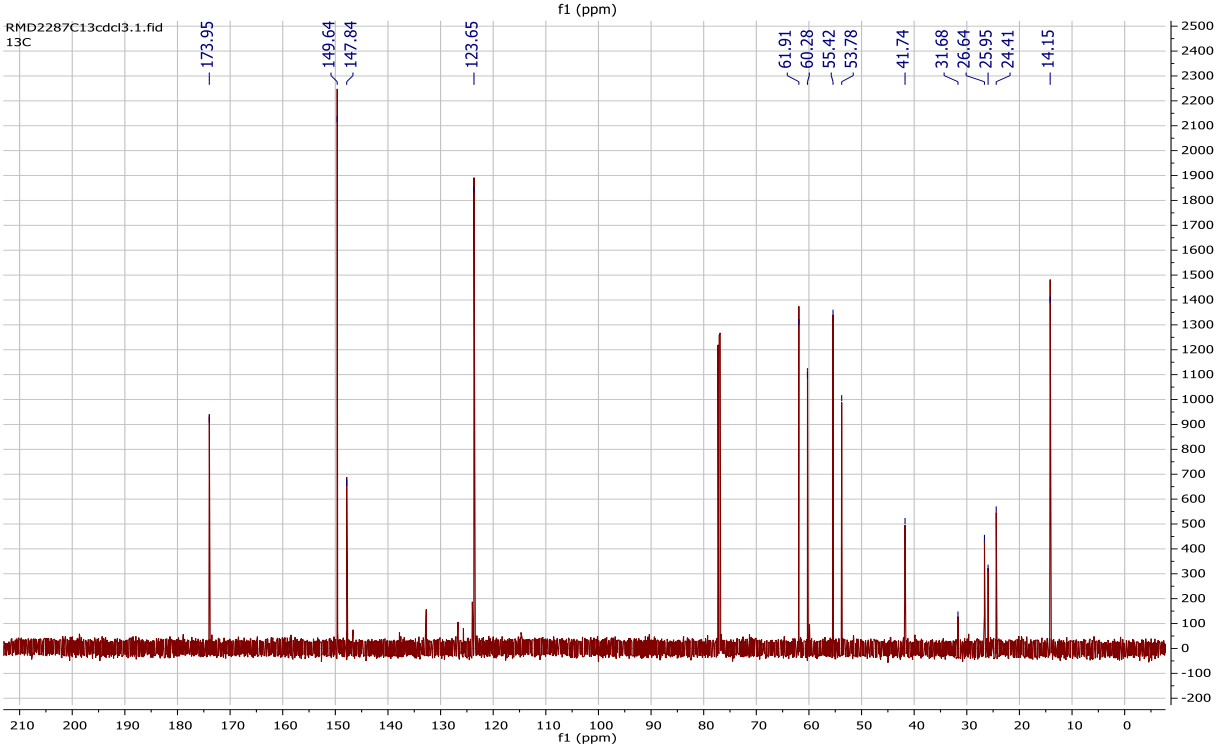

RMD3016bH1cdcl3.1.fid
1H
8.15
7.26
3.46
2.48
2.29
2.00
2.68
1.97
7.49
3.03
f1 (ppm)


RMD3025bC13cdcl3.1.fid
13C
140.23
138.80
126.02
60.37
54.83
52.63
45.74
f1 (ppm)

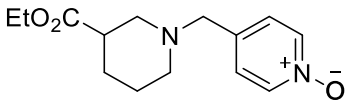
(21)

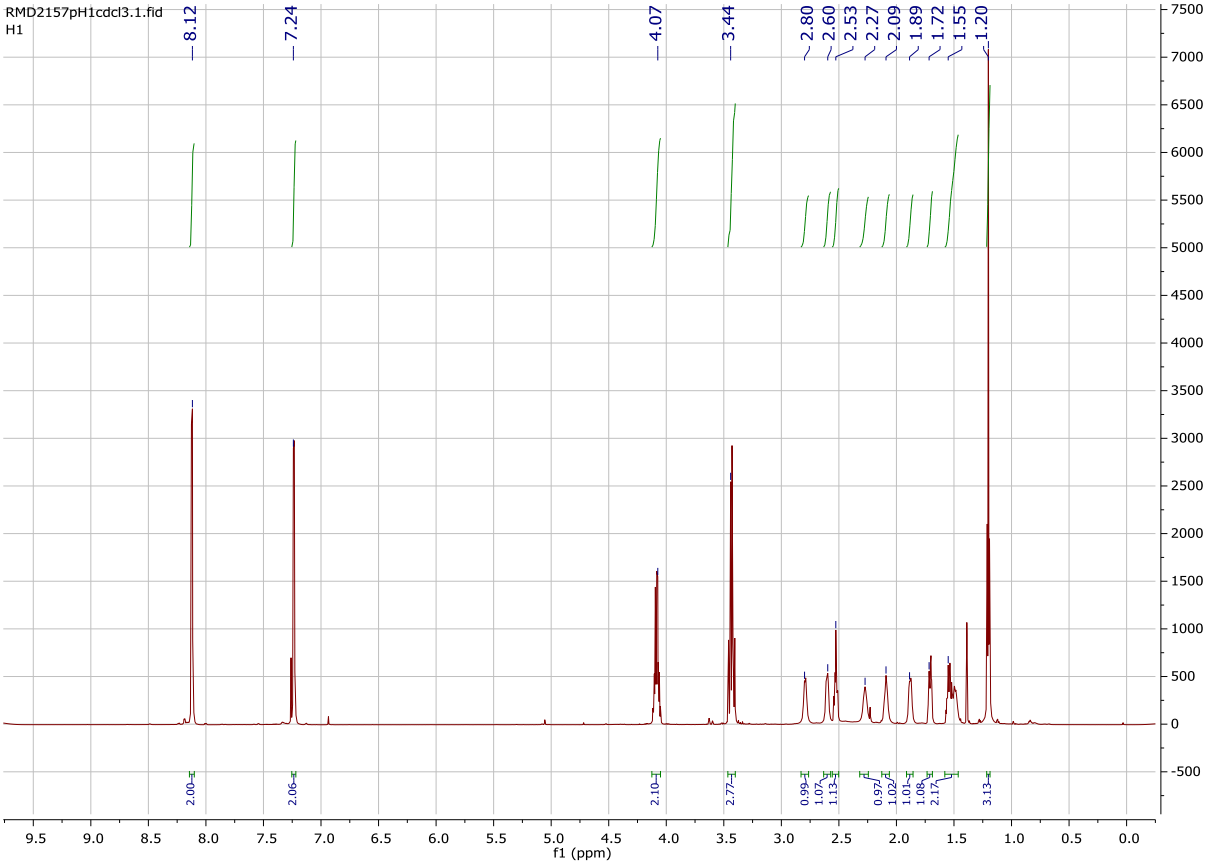

EtO2C
N
N

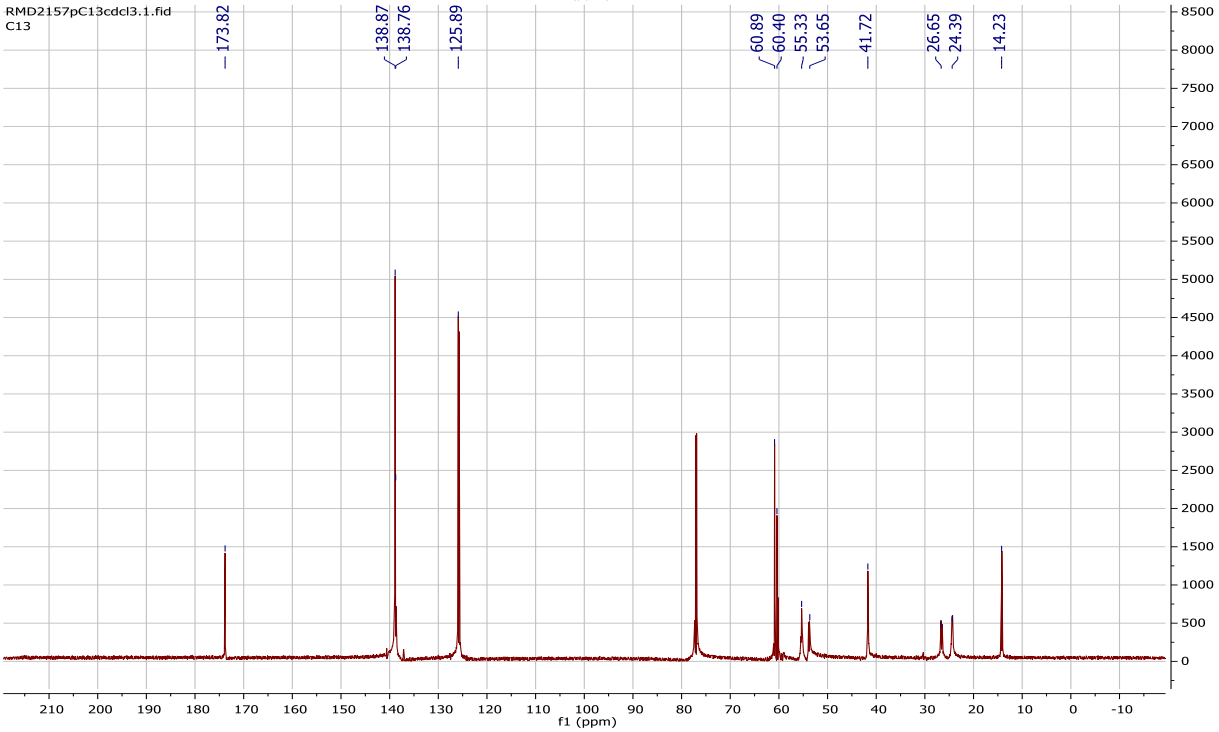

RMD3055H1cdcl3.1.fid
1H
8.49
7.22
4.08
3.43
2.83
2.63
2.56
2.25
2.07
1.87
1.70
1.57
1.48
1.19
2.00
1.58
1.95
2.30
1.08
1.15
1.29
0.94
1.14
1.15
1.34
1.21
1.09
3.19
f1 (ppm)


RMD2287C13cdcl3.1.fid
13C
173.95
149.64
147.84
123.65
61.91
60.28
55.42
53.78
41.74
31.68
26.64
25.95
24.41
14.15
f1 (ppm)

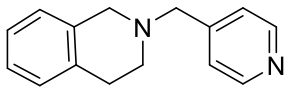
(**22**)

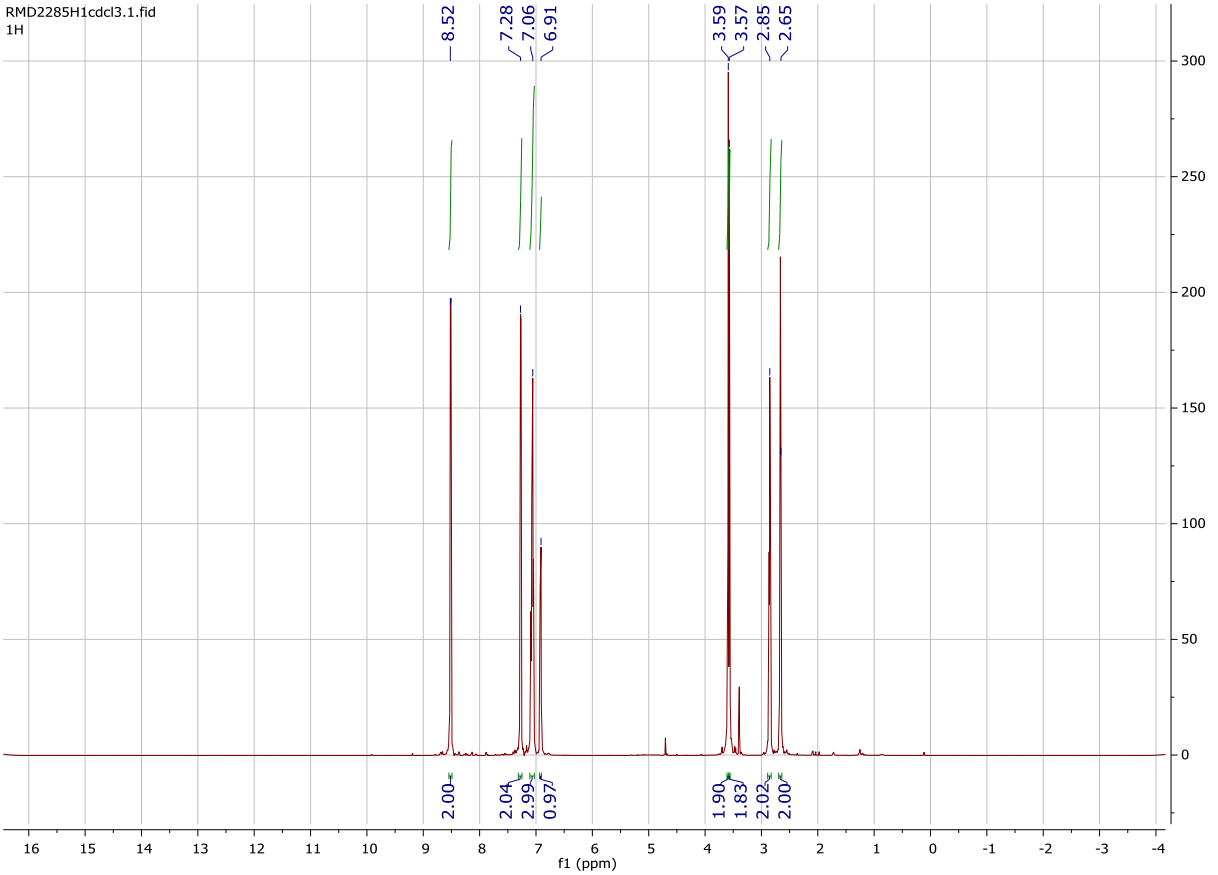

EtO2C
N
+N
O

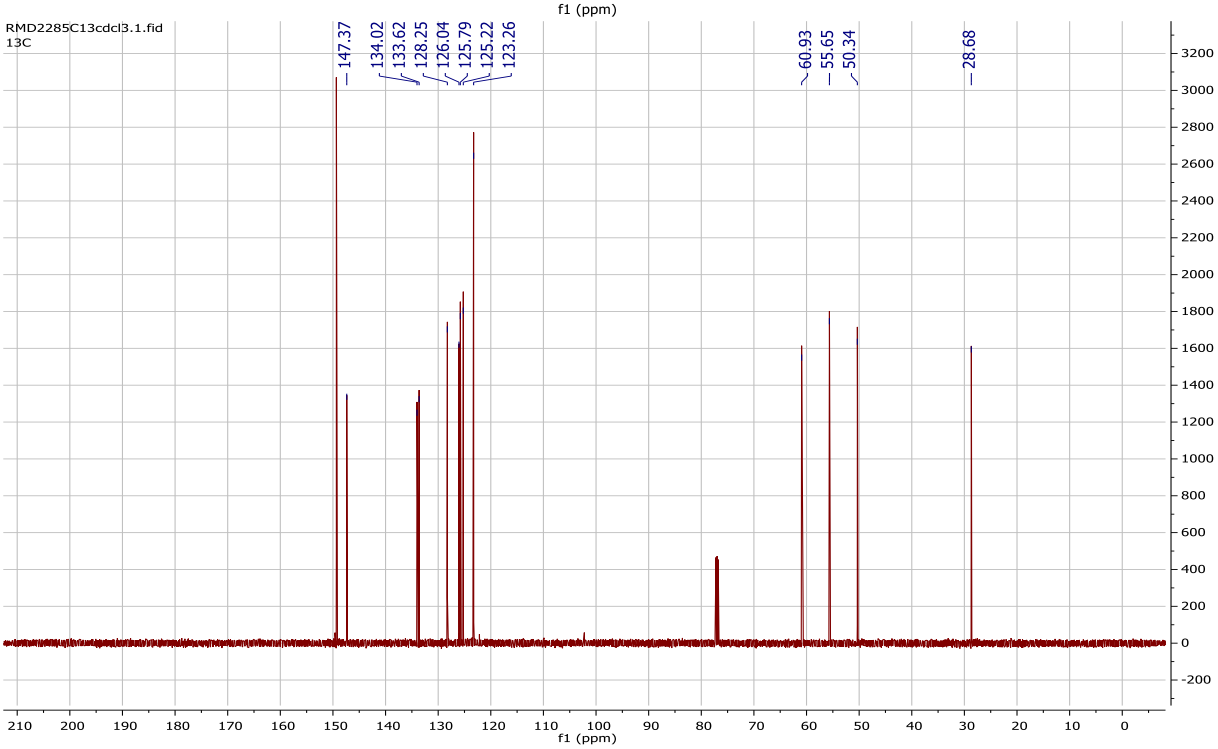

RMD2157pH1cdcl3.1.fid
H1
8.12
7.24
4.07
3.44
2.80
2.60
2.53
2.27
2.09
1.89
1.72
1.55
1.20
f1 (ppm)


RMD2157pC13cdcl3.1.fid
C13
173.82
138.87
138.76
125.89
60.89
60.40
55.33
53.65
41.72
26.65
24.39
14.23
f1 (ppm)

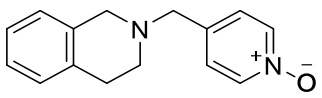
(23)

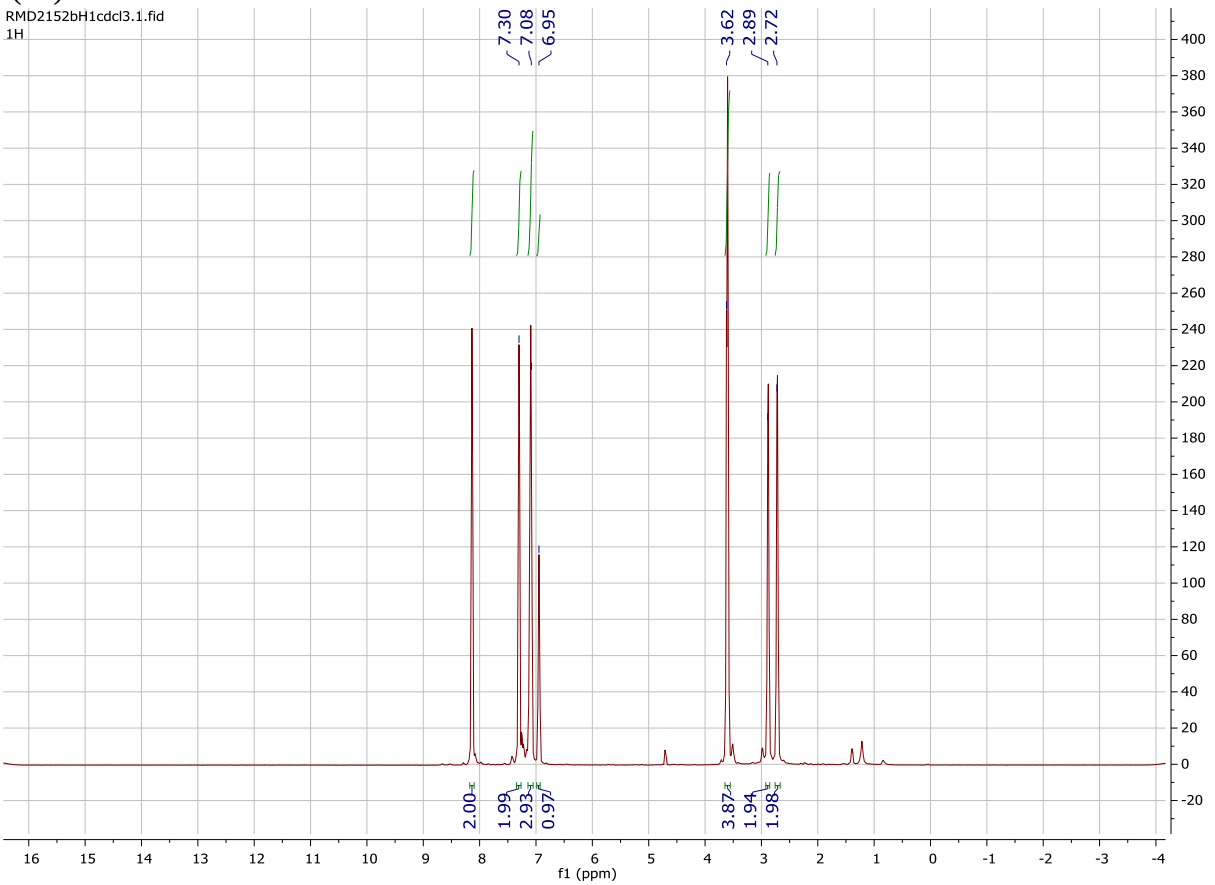


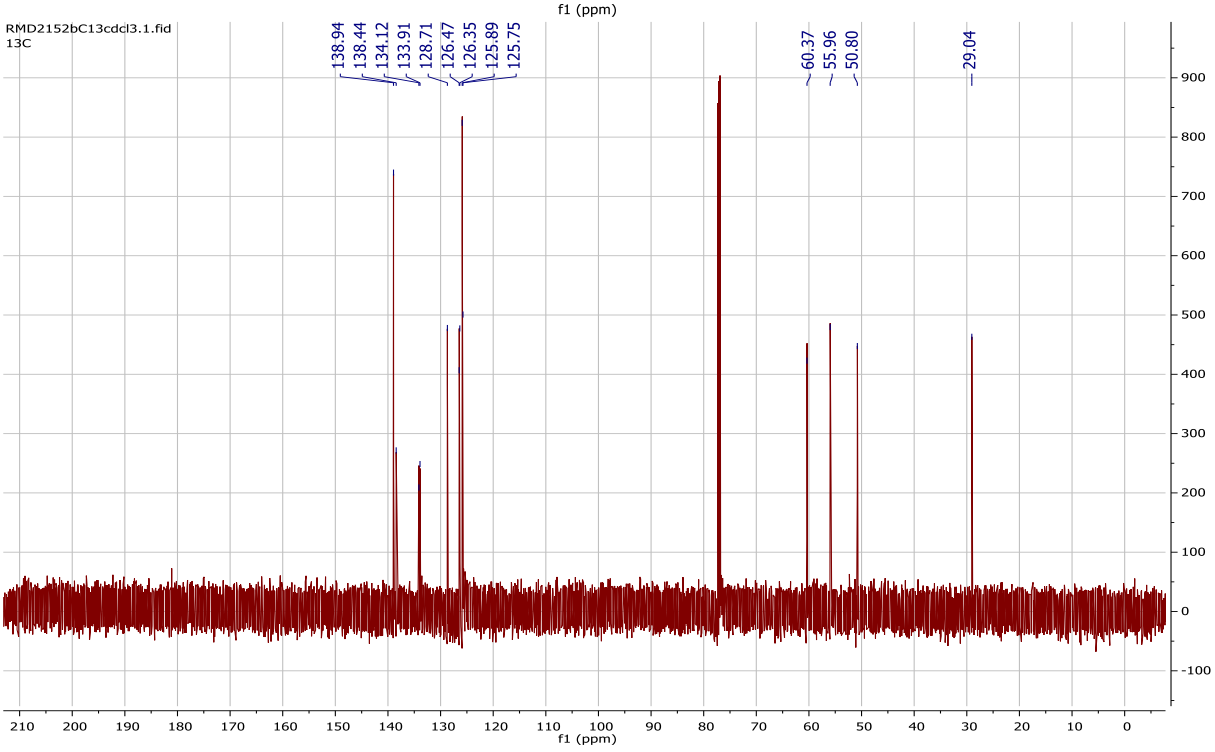

RMD2285H1cdcl3.1.fid
1H
8.52
7.28
7.06
6.91
3.59
3.57
2.85
2.65
2.00
2.04
2.99
0.97
1.90
1.83
2.02
2.00
f1 (ppm)


RMD2285C13cdcl3.1.fid
13C
147.37
134.02
133.62
128.25
126.04
125.79
125.22
123.26
60.93
55.65
50.34
28.68
f1 (ppm)

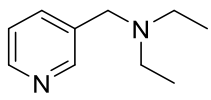
(24)

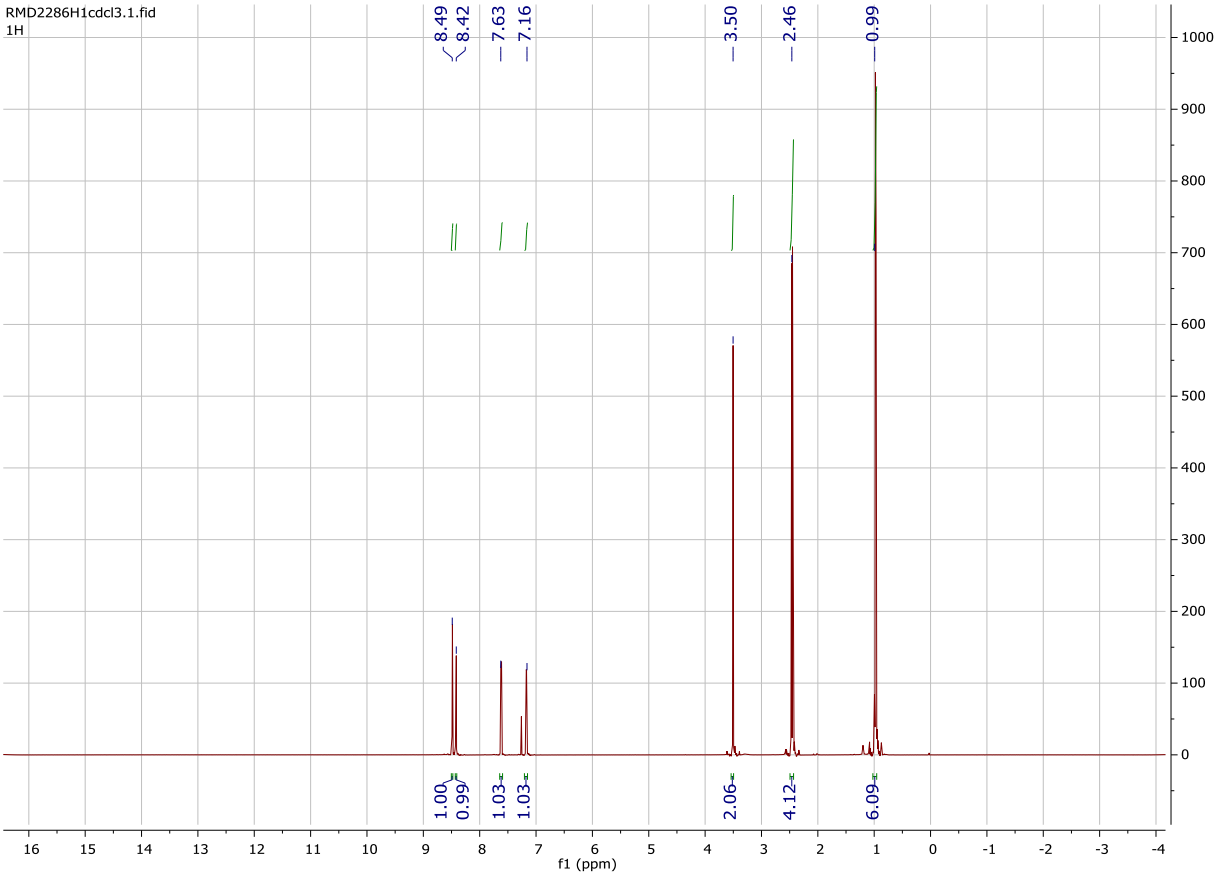


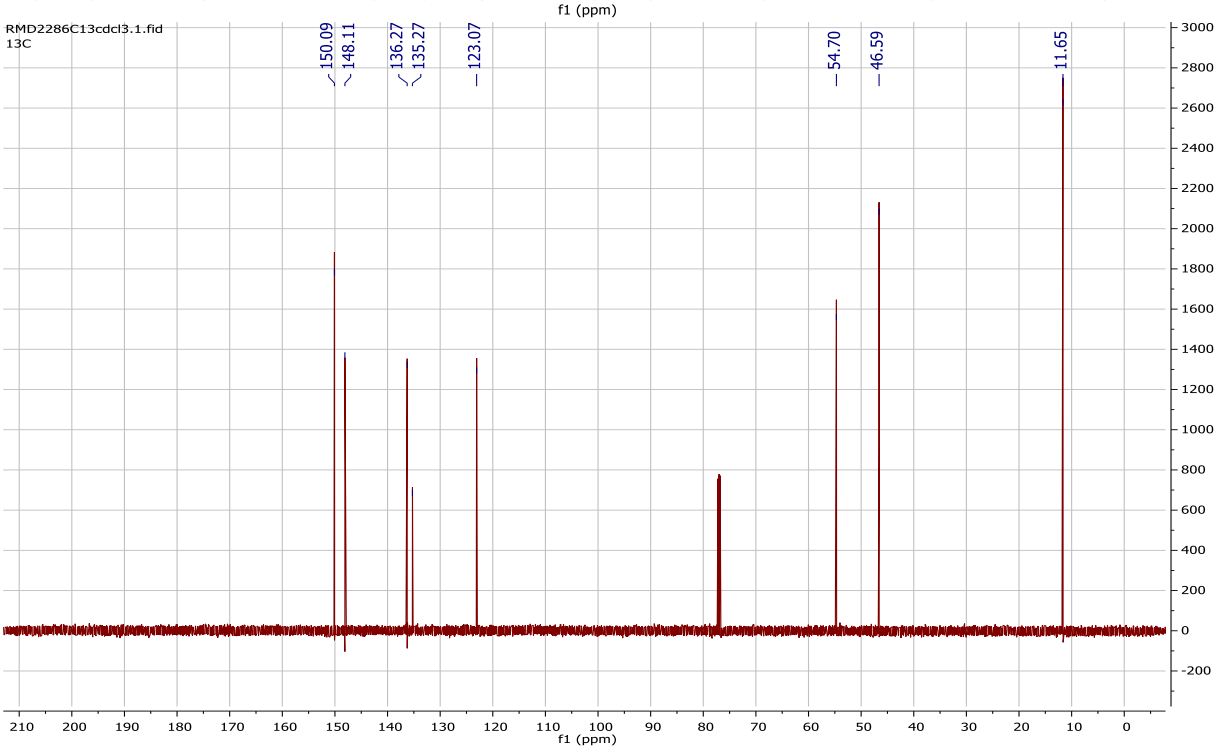

RMD2152bH1cdcl3.1.fid
1H
7.30
7.08
6.95
3.62
2.89
2.72
2.00
1.99
2.93
0.97
3.87
1.94
1.98
f1 (ppm)

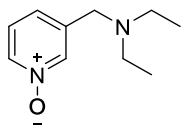

RMD2152bC13cdcl3.1.fid
13C
138.94
138.44
134.12
133.91
128.71
126.47
126.35
125.89
125.75
60.37
55.96
50.80
29.04
f1 (ppm)

(25)

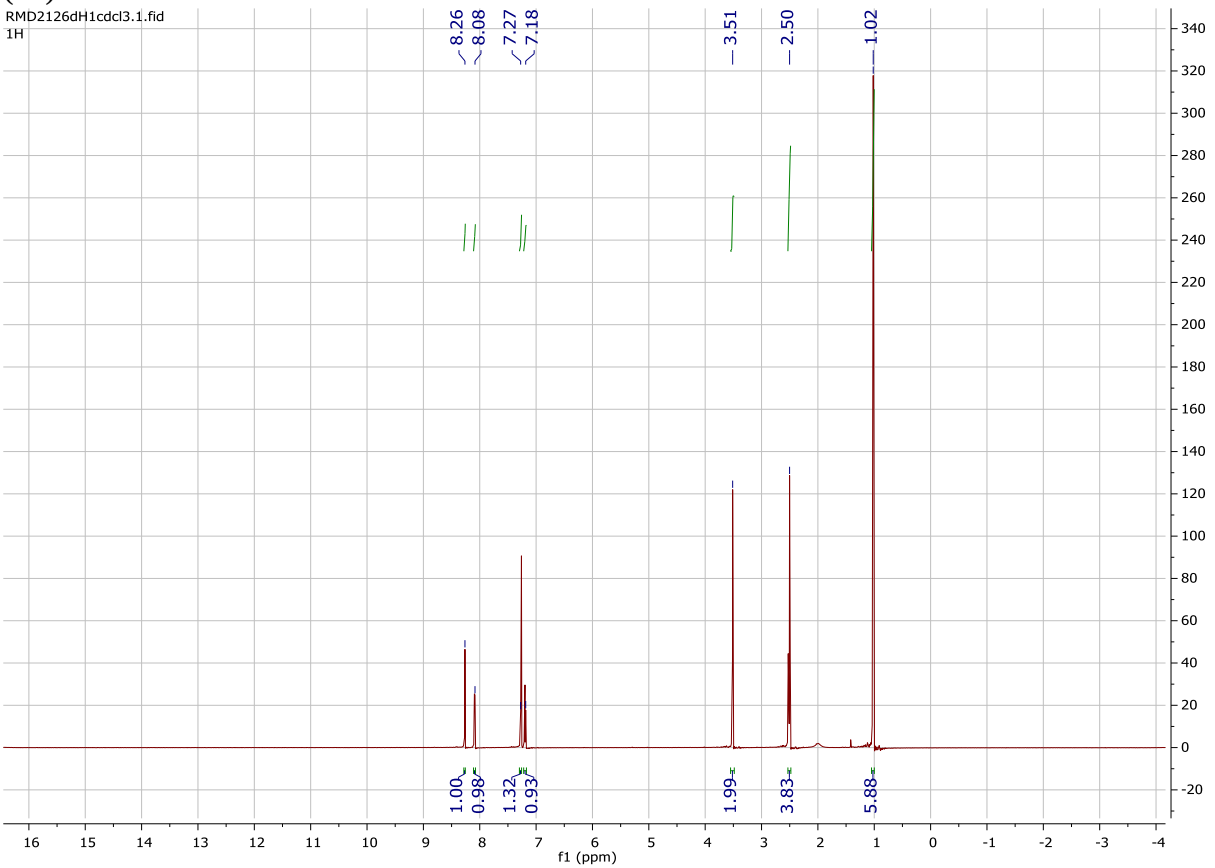


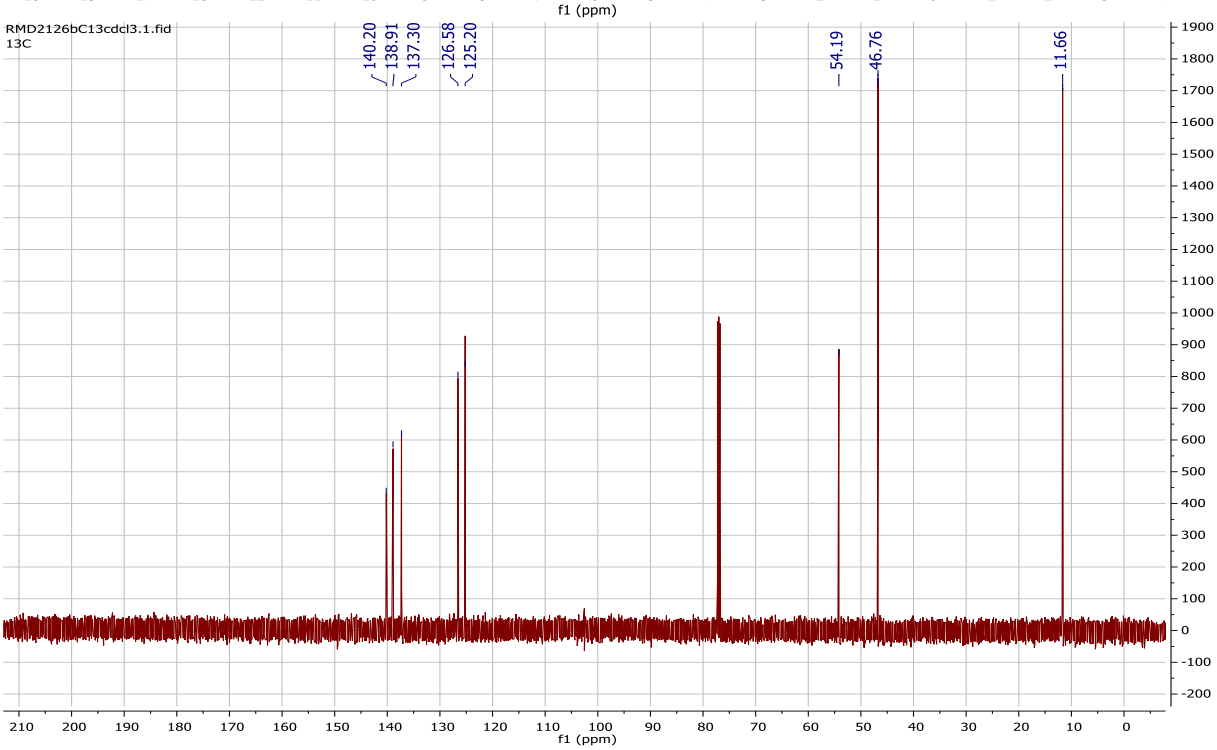

RMD2286H1cdcl3.1.fid
1H
8.49
8.42
7.63
7.16
3.50
2.46
0.99
1.00
0.99
1.03
1.03
2.06
4.12
6.09
f1 (ppm)


RMD2286C13cdcl3.1.fid
13C
150.09
148.11
136.27
135.27
123.07
54.70
46.59
11.65
f1 (ppm)

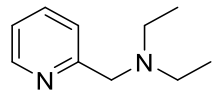


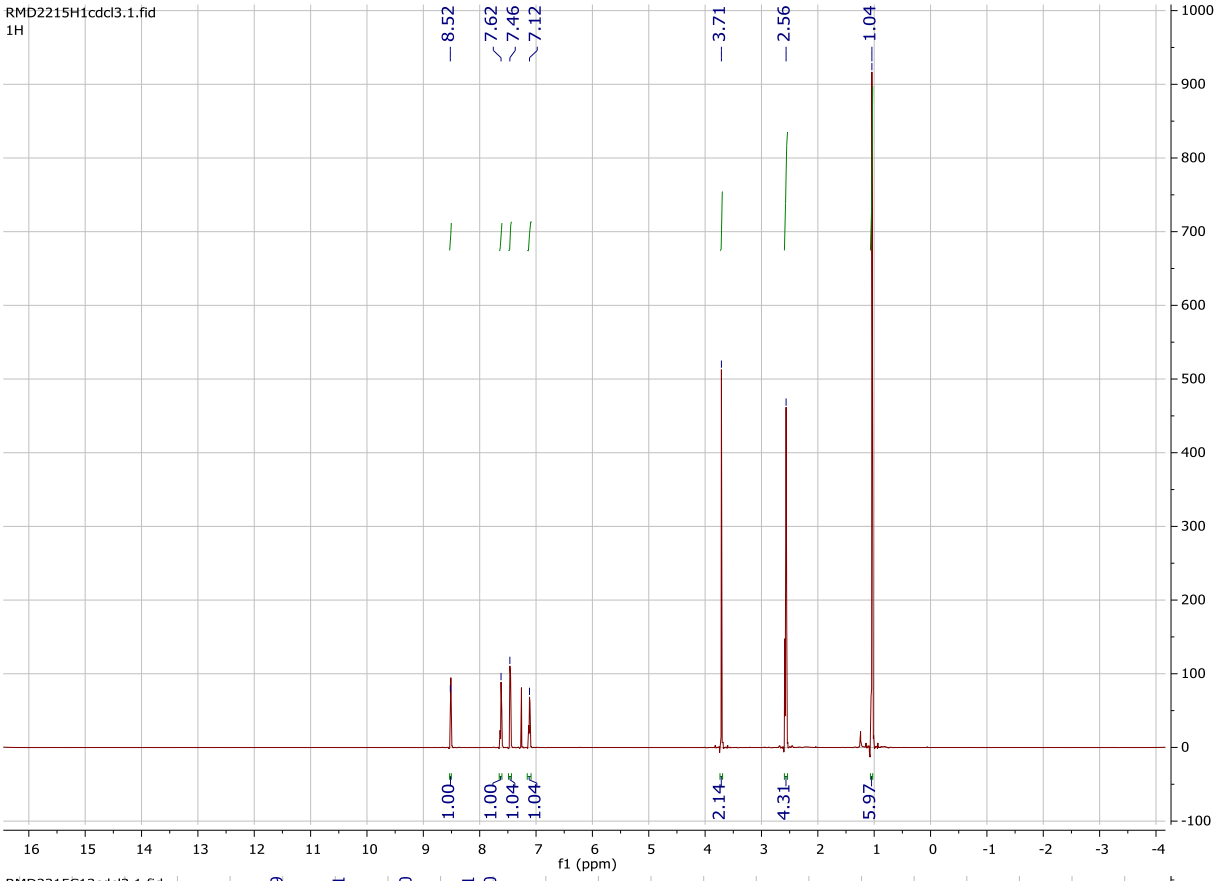
(26)

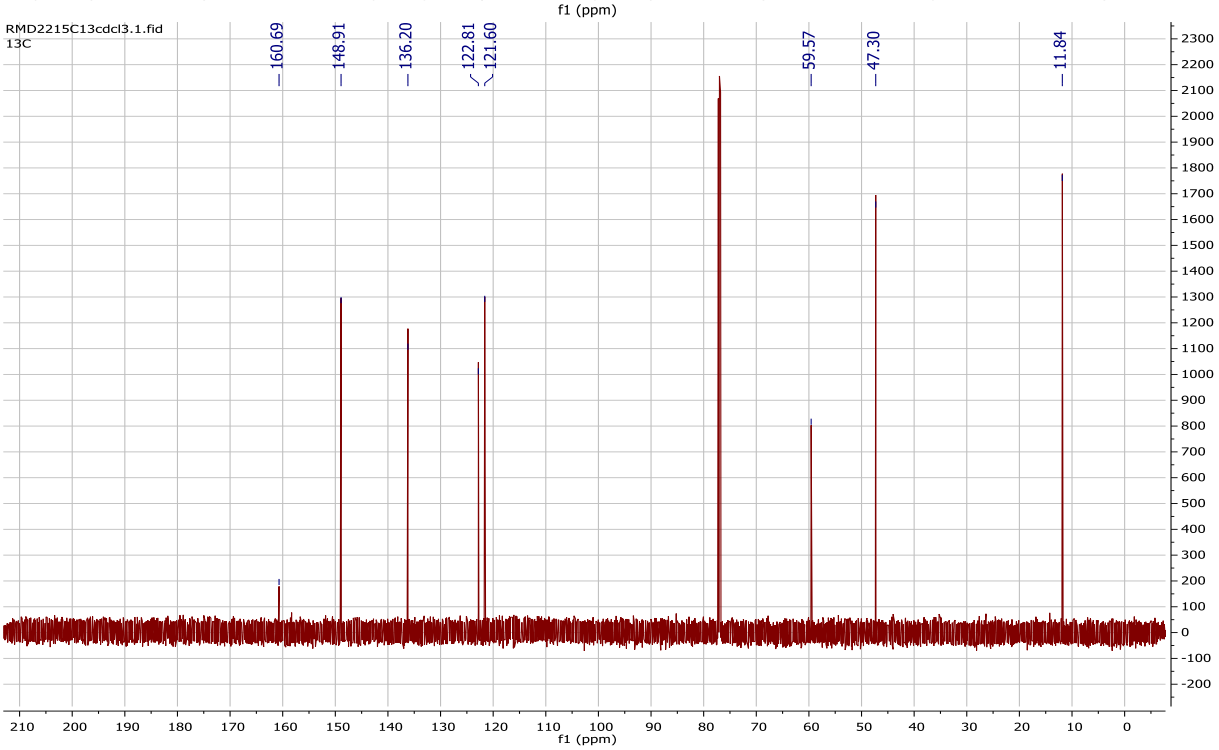

RMD2126dH1cdcl3.1.fid
1H
8.26
8.08
7.27
7.18
3.51
2.50
1.02
1.00
0.98
1.32
0.93
1.99
3.83
5.88
f1 (ppm)

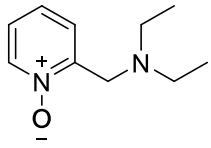

RMD2126bC13cdcl3.1.fid
13C
140.20
138.91
137.30
126.58
125.20
54.19
46.76
11.66
f1 (ppm)

(27)

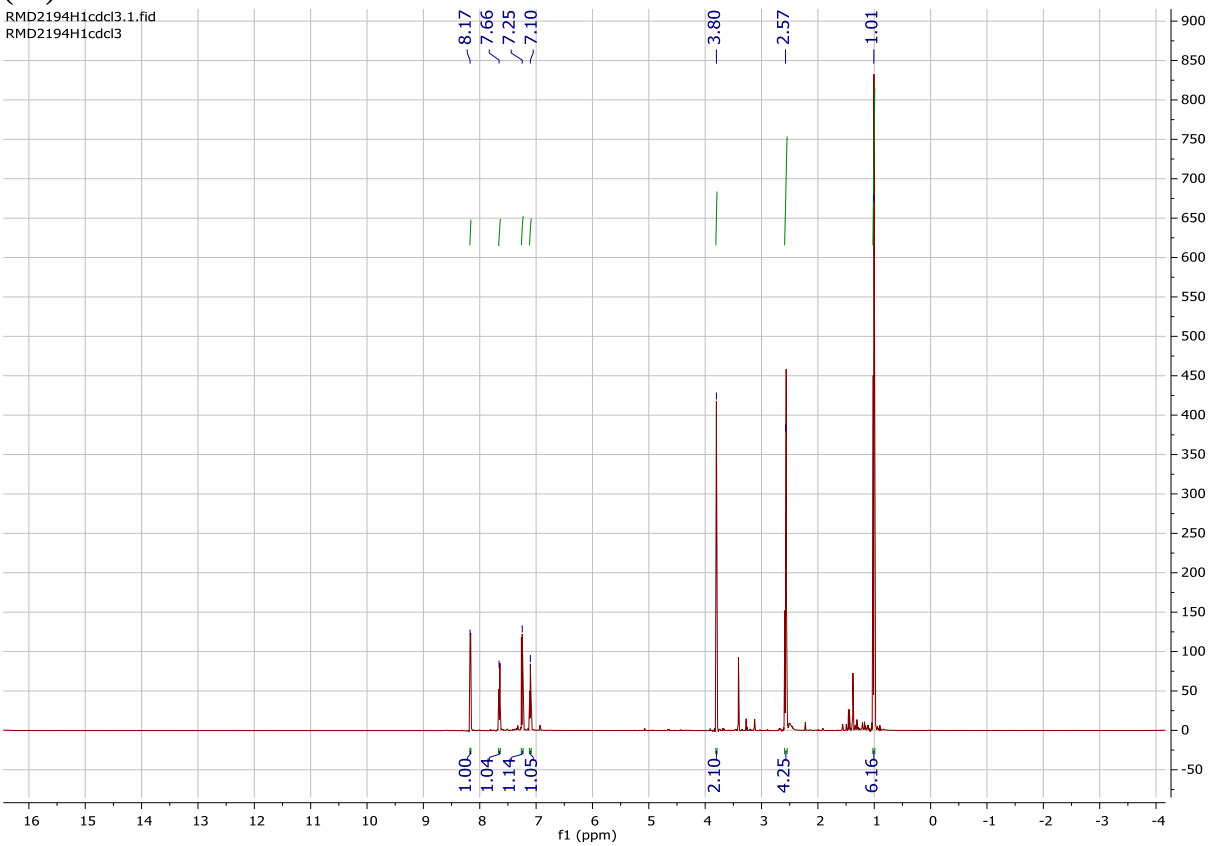


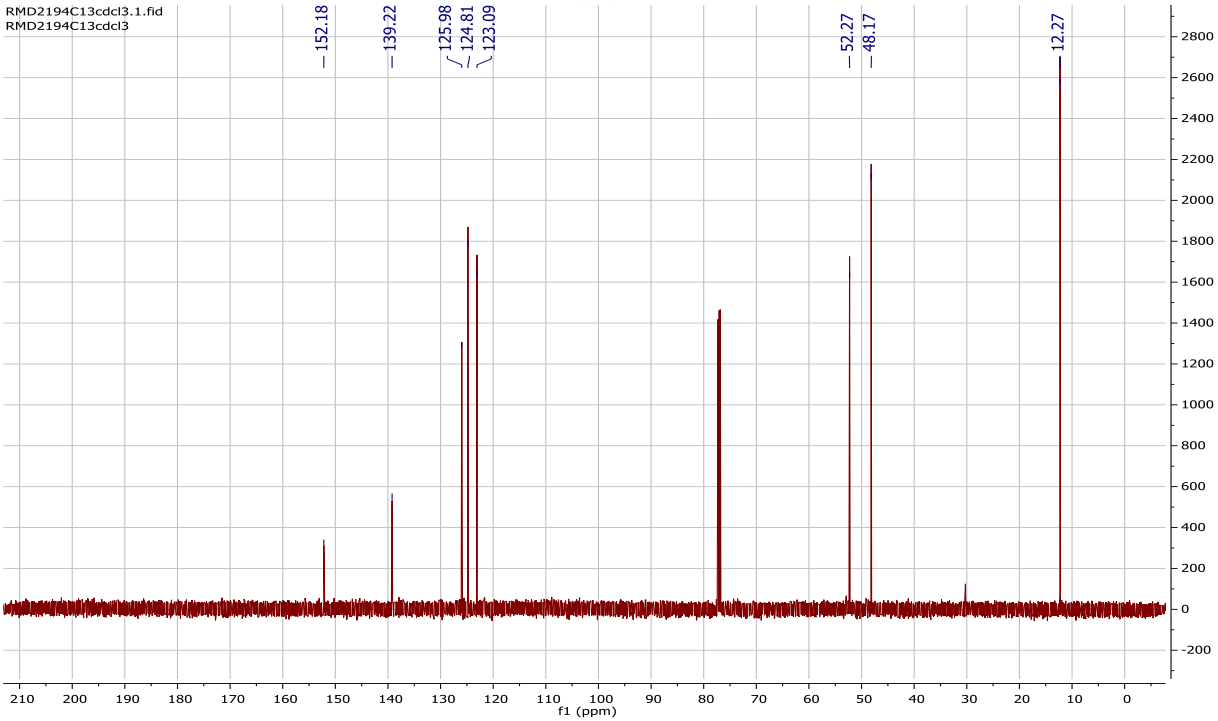

RMD2215H1cdcl3.1.fid
1H
8.52
7.62
7.46
7.12
3.71
2.56
1.04
1.00
1.00
1.04
1.04
2.14
4.31
5.97
f1 (ppm)

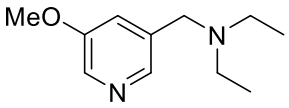

RMD2215C13cdcl3.1.fid
13C
160.69
148.91
136.20
122.81
121.60
59.57
47.30
11.84
f1 (ppm)



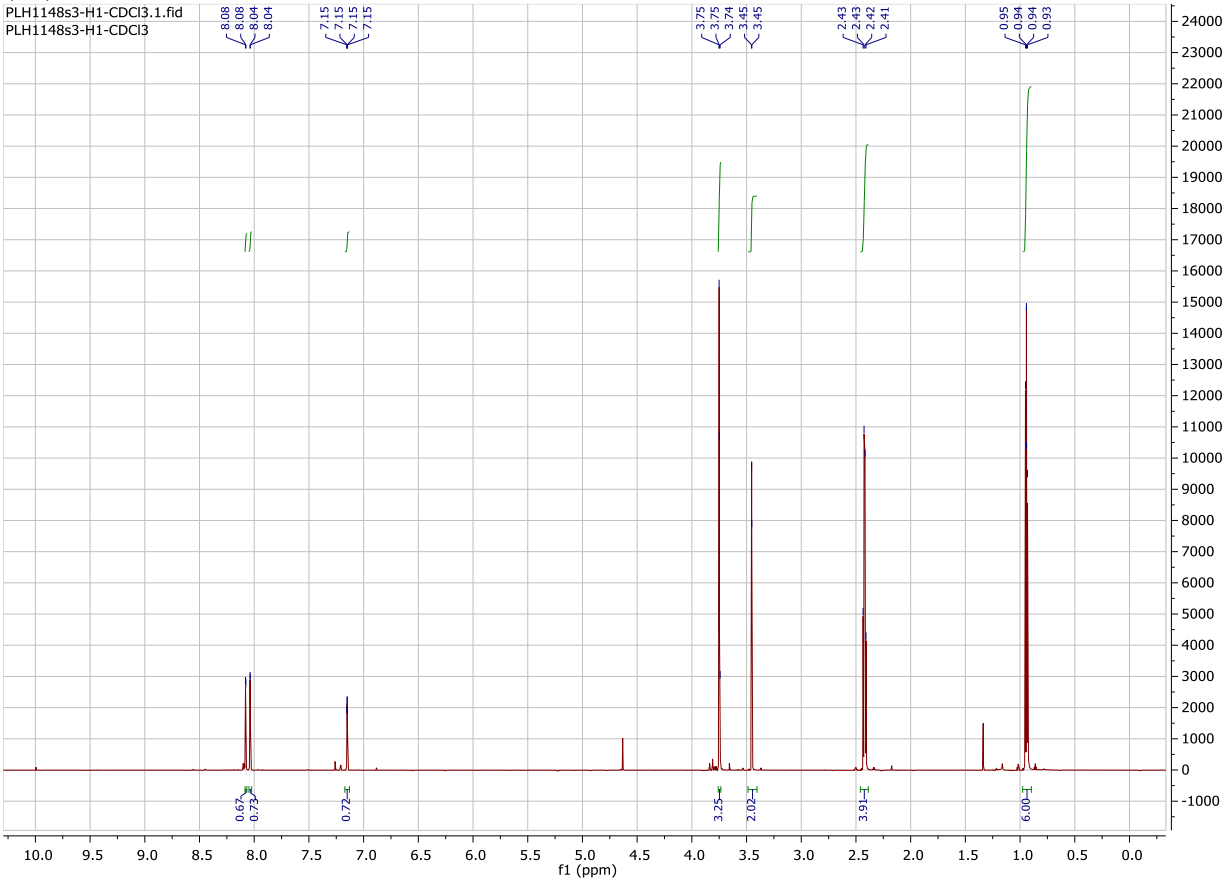
(28)

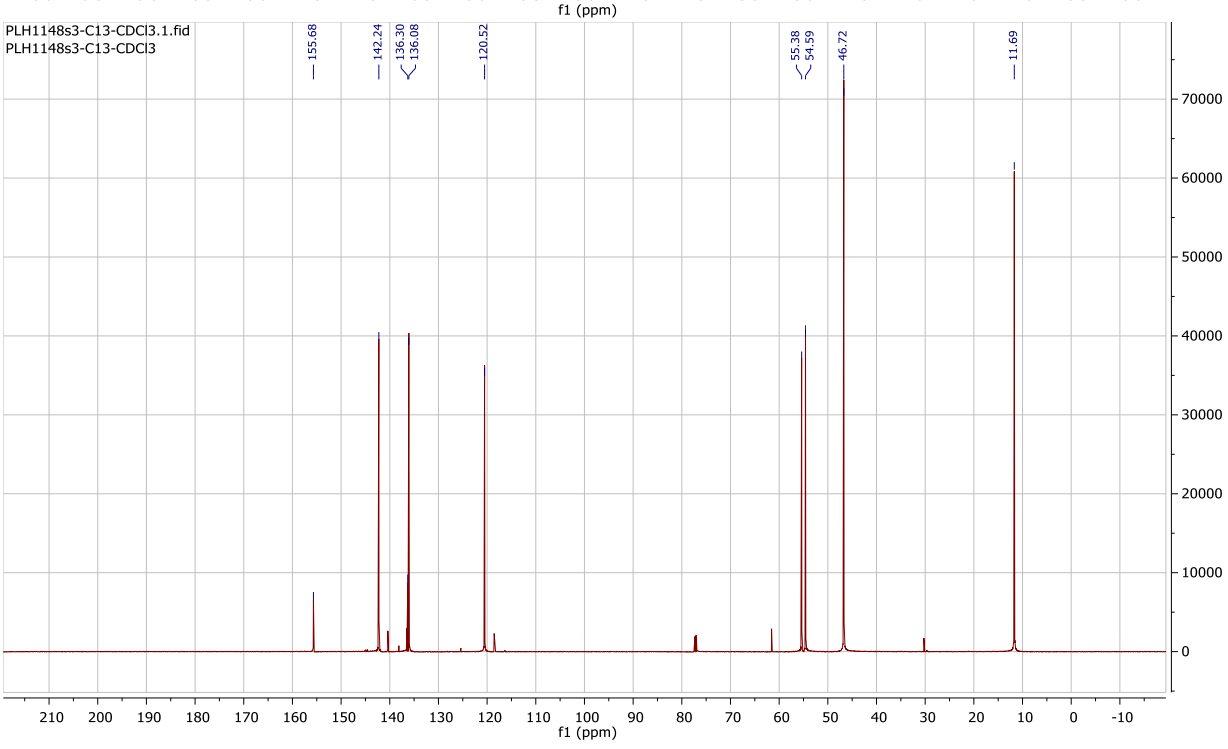

RMD2194H1cdcl3.1.fid
RMD2194H1cdcl3
8.17
7.66
7.25
7.10
3.80
2.57
1.01
1.00
1.04
1.14
1.05
2.10
4.25
6.16
f1 (ppm)

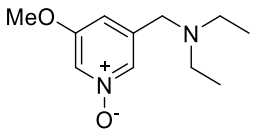

RMD2194C13cdcl3.1.fid
RMD2194C13cdcl3
152.18
139.22
125.98
124.81
123.09
52.27
48.17
12.27
f1 (ppm)


MeO
N
N

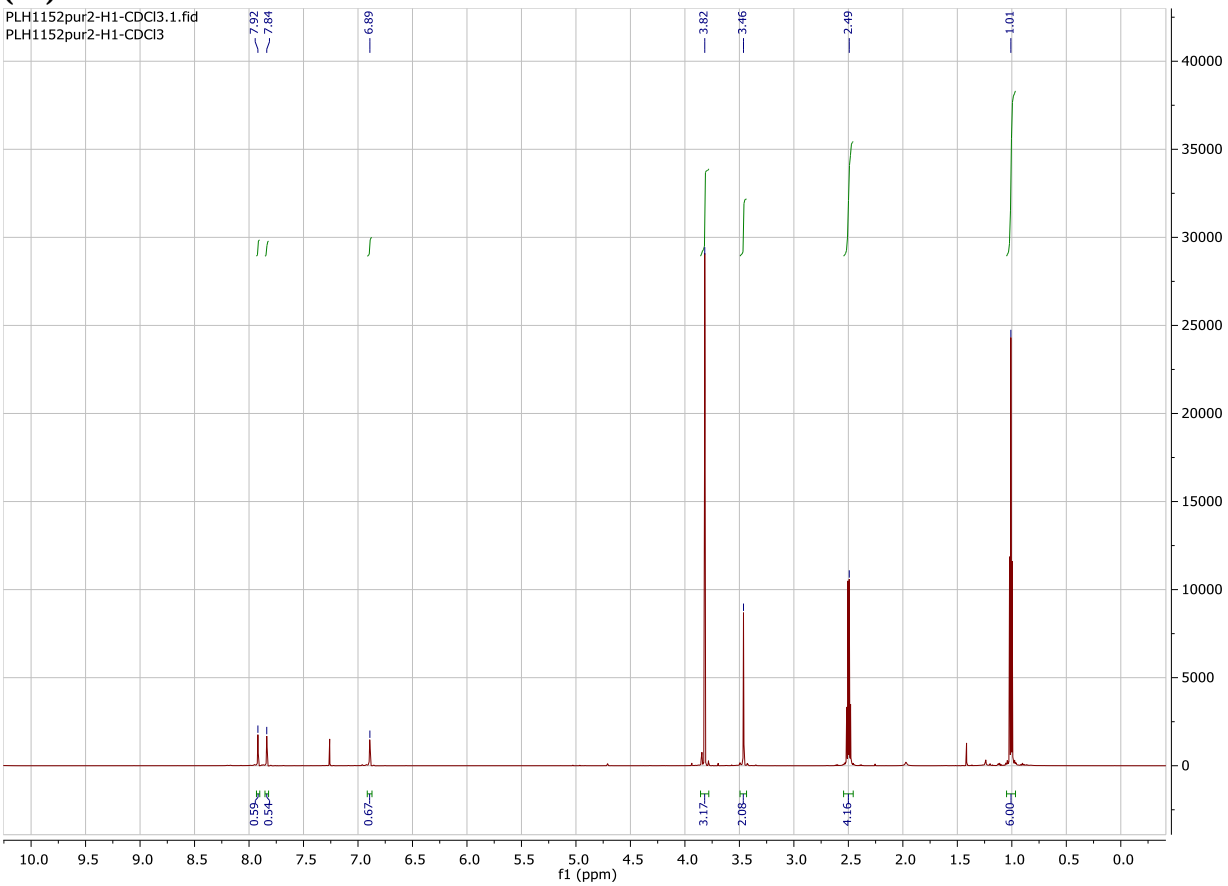
(29)

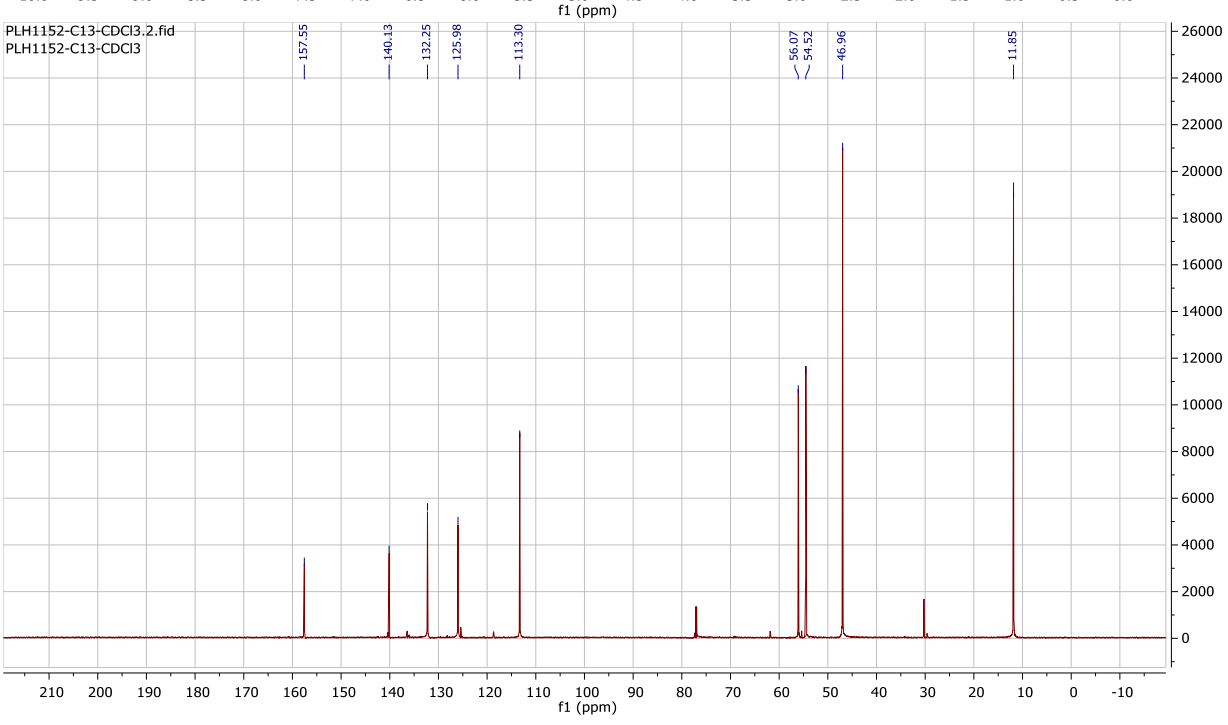

PLH1148s3-H1-CDCl3.1.fid
PLH1148s3-H1-CDCl3
8.08
8.08
8.04
8.04
7.15
7.15
7.15
7.15
3.75
3.75
3.74
3.45
3.45
2.43
2.43
2.42
2.41
0.95
0.94
0.94
0.93
0.67
0.73
0.72
3.25
2.02
3.91
6.00
f1 (ppm)


PLH1148s3-C13-CDCl3.1.fid
PLH1148s3-C13-CDCl3
155.68
142.24
136.30
136.08
120.52
55.38
54.59
46.72
11.69
f1 (ppm)

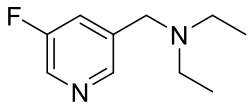

MeO
N
+
N
O-

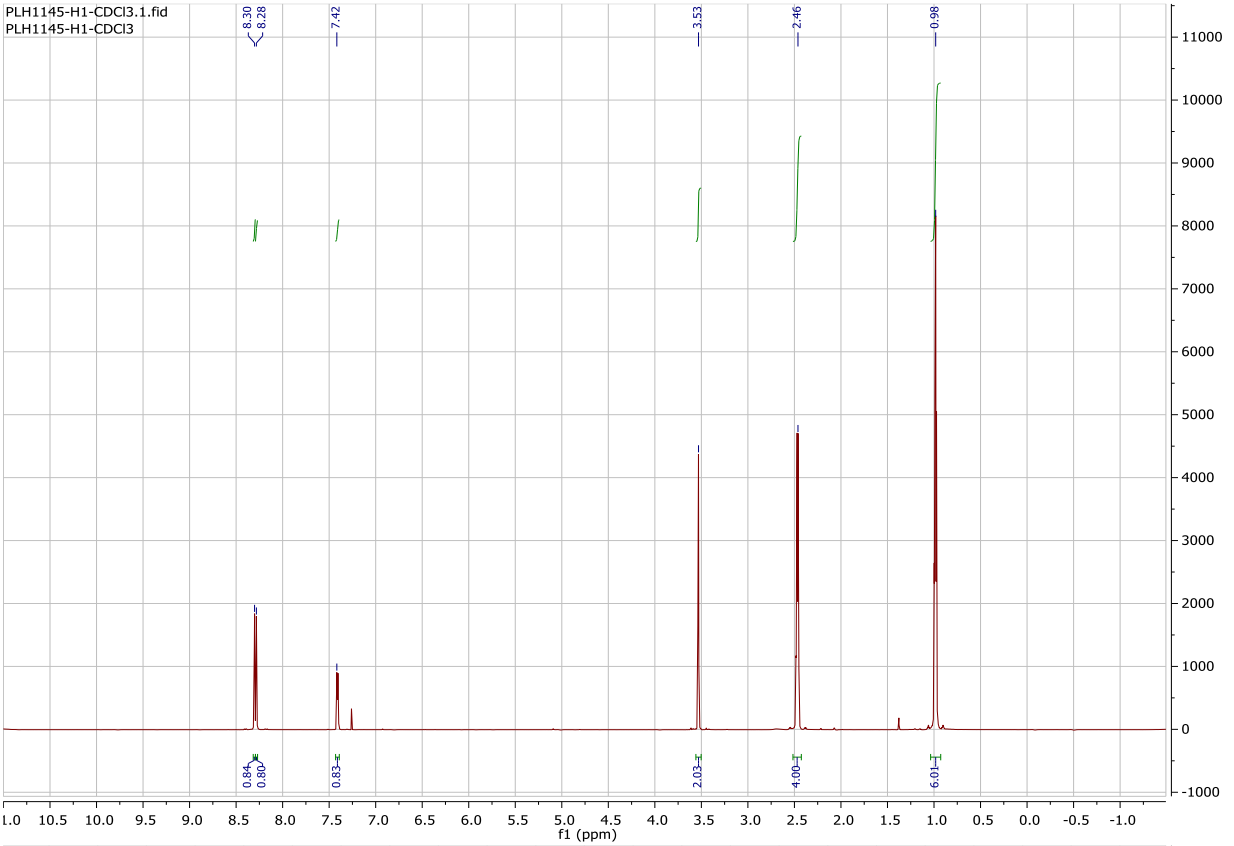
(30)

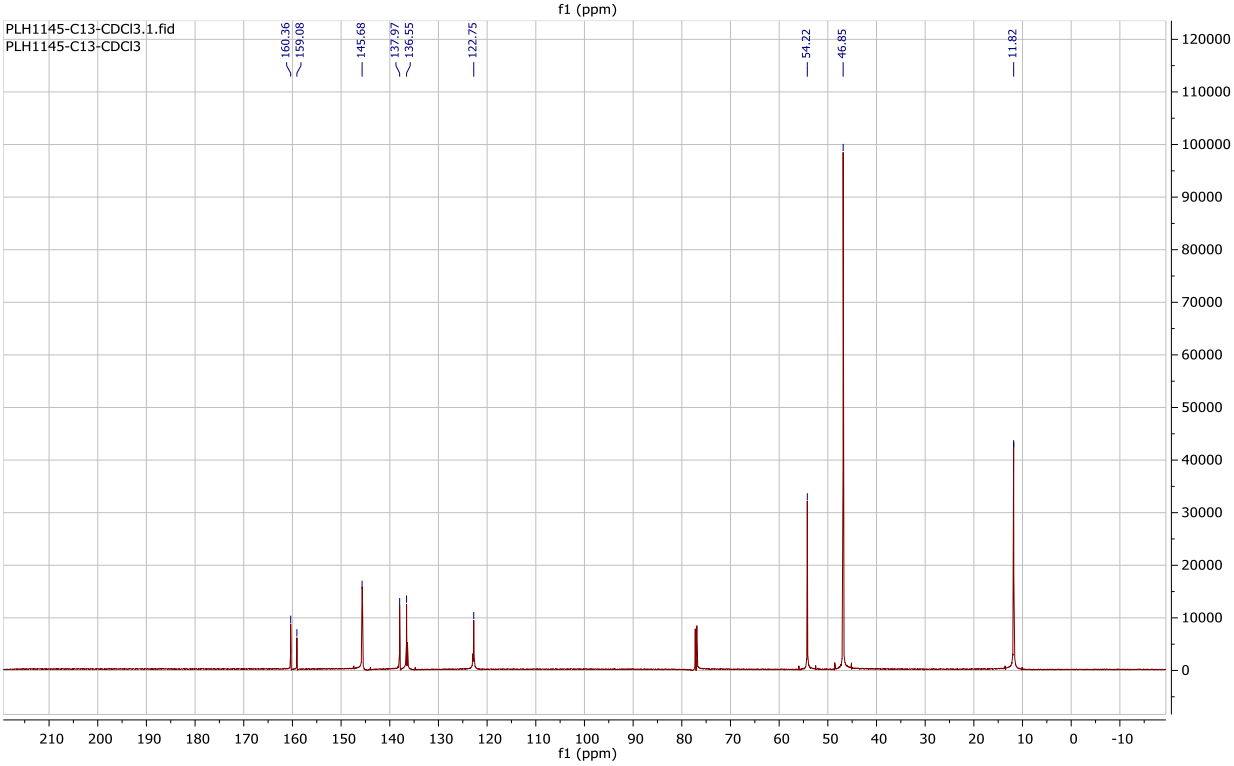

PLH1152pur2-H1-CDCl3.1.fid
PLH1152pur2-H1-CDCl3
7.92
7.84
6.89
3.82
3.46
2.49
1.01
0.59
0.54
0.67
3.17
2.08
4.16
6.00
f1 (ppm)

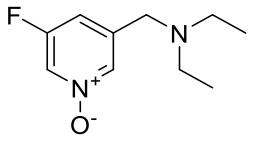

PLH1152-C13-CDCl3.2.fid
PLH1152-C13-CDCl3
157.55
140.13
132.25
125.98
113.30
56.07
54.52
46.96
11.85
f1 (ppm)

(31)

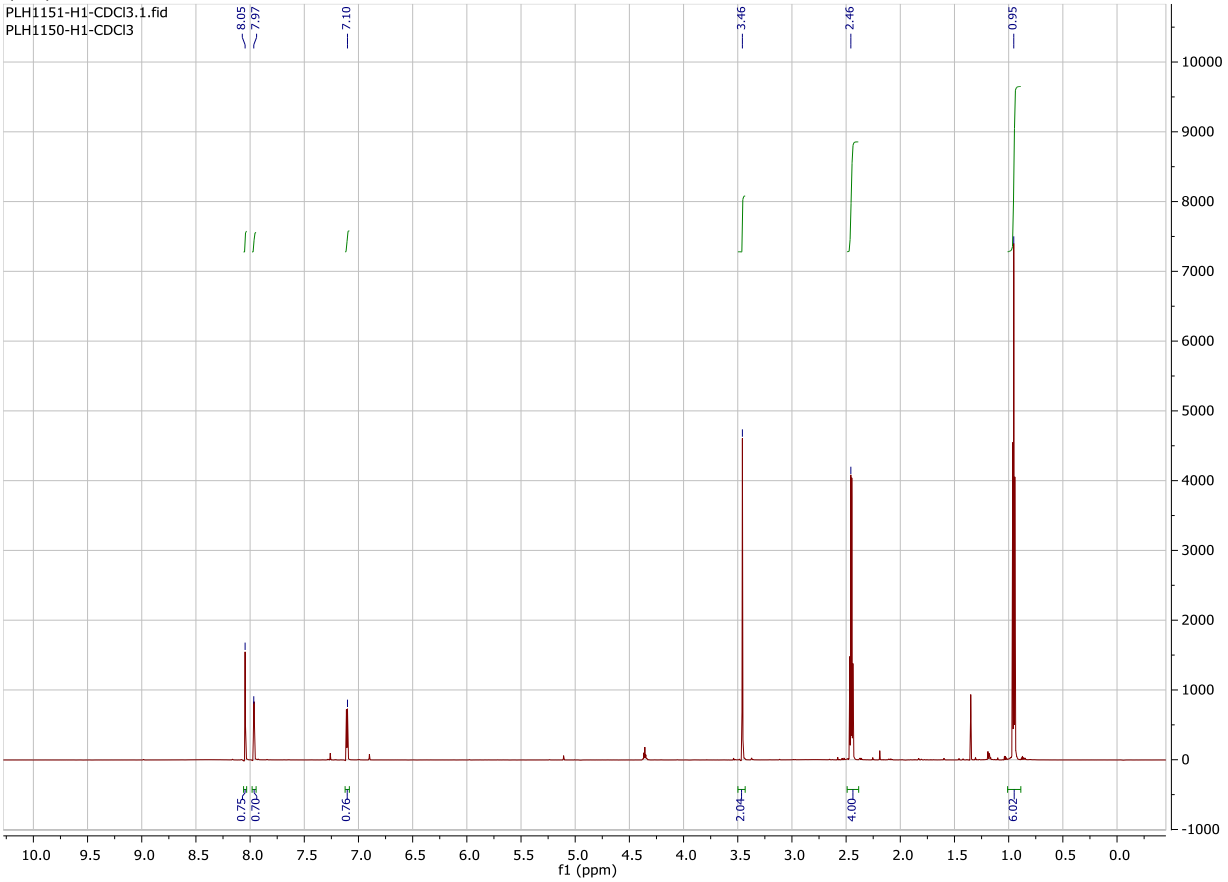

F
N
N

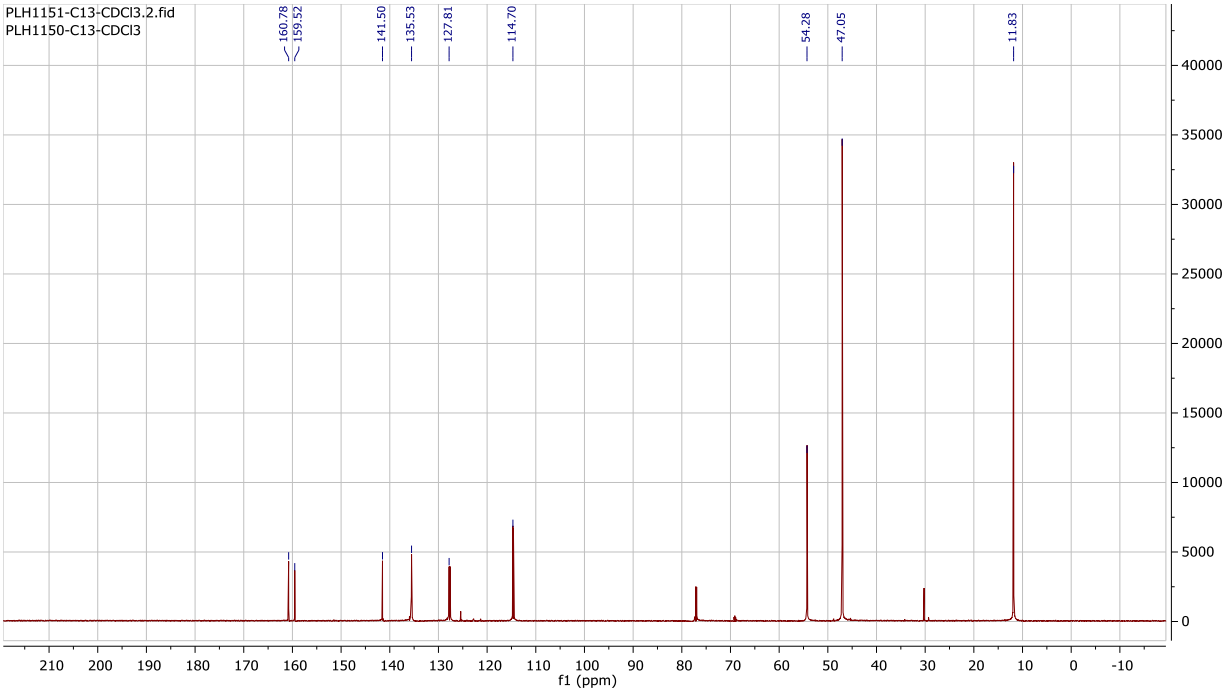

PLH1145-H1-CDCl3.1.fid
PLH1145-H1-CDCl3
8.30
8.28
7.42
3.53
2.46
0.98
0.84
0.80
0.83
2.03
4.00
6.01
f1 (ppm)


PLH1145-C13-CDCl3.1.fid
PLH1145-C13-CDCl3
160.36
159.08
145.68
137.97
136.55
122.75
54.22
46.85
11.82
f1 (ppm)

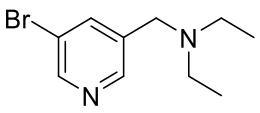

F
N
N+
O-

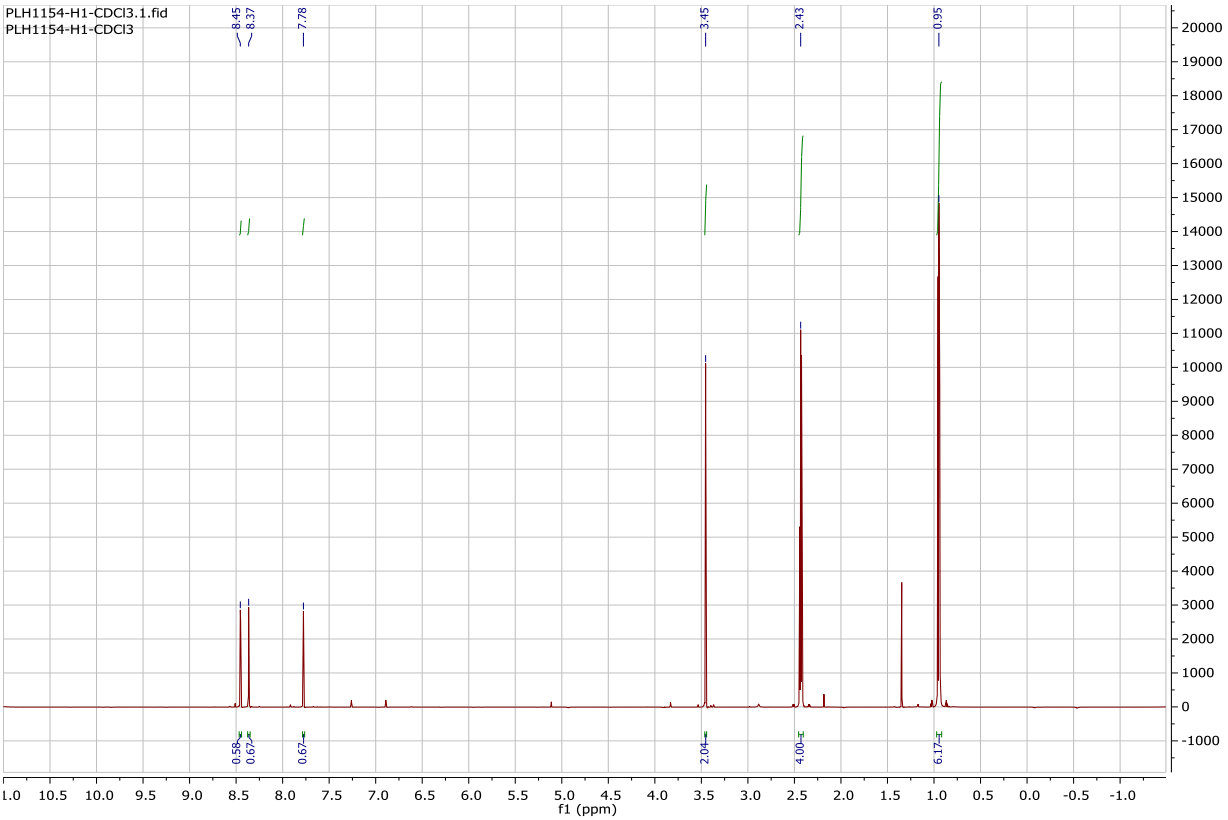
(32)

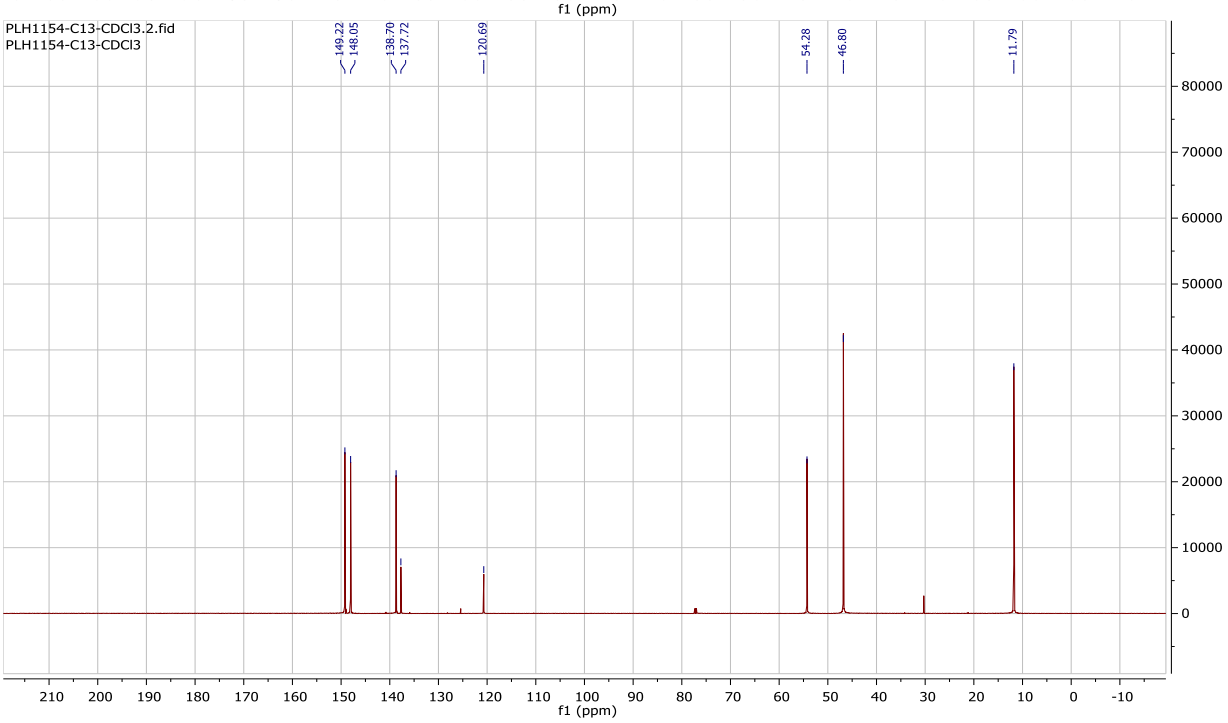

PLH1151-H1-CDCl3.1.fid
PLH1150-H1-CDCl3
8.05
7.97
7.10
3.46
2.46
0.95
0.75
0.70
0.76
2.04
4.00
6.02
f1 (ppm)

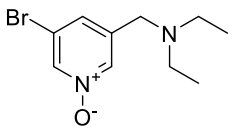

PLH1151-C13-CDCl3.2.fid
PLH1150-C13-CDCl3
160.78
159.52
141.50
135.53
127.81
114.70
54.28
47.05
11.83
f1 (ppm)

(33)

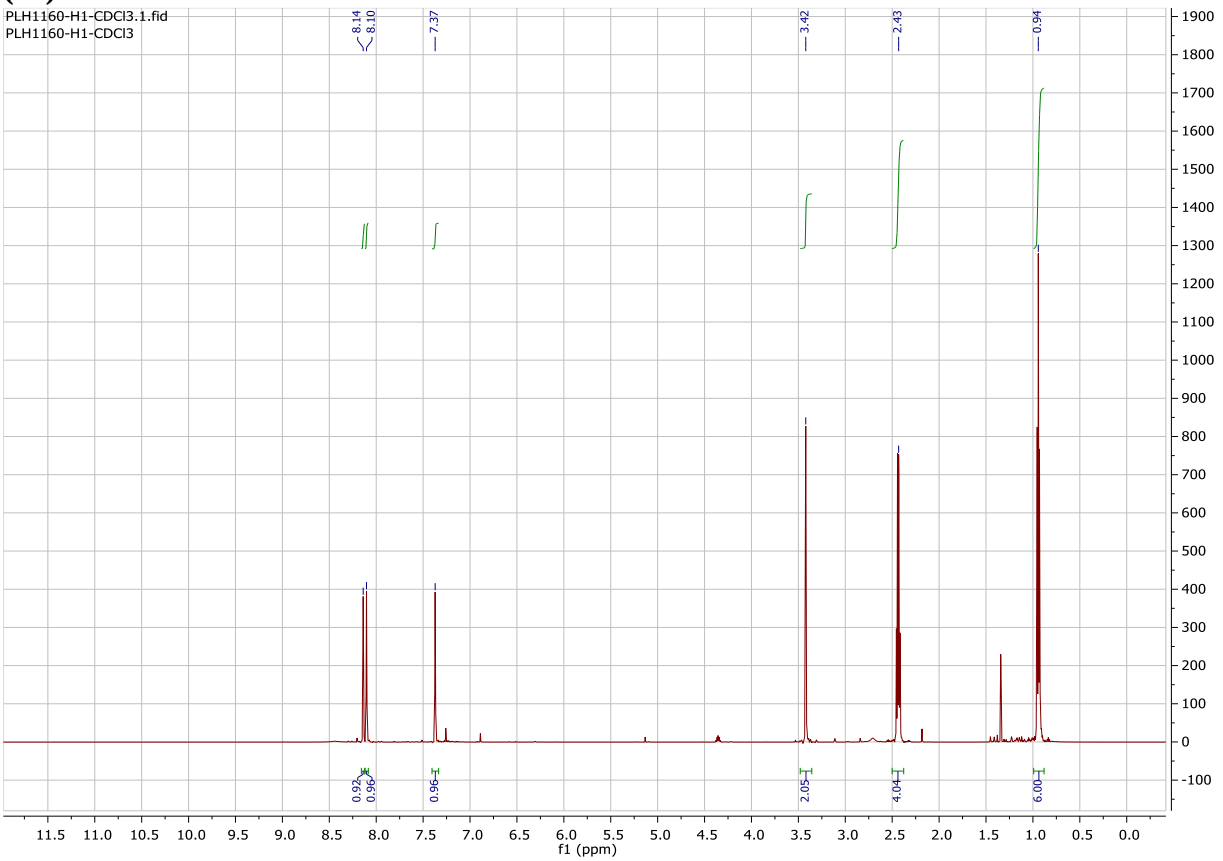

Br
N
N

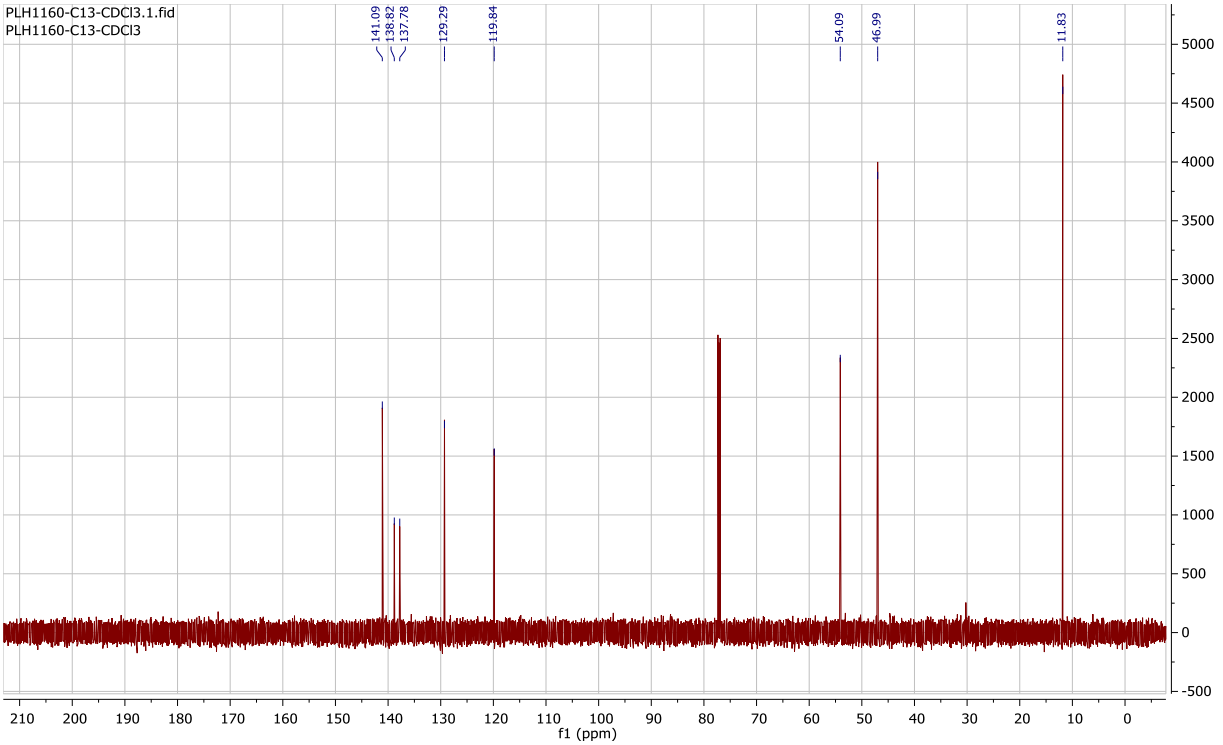

PLH1154-H1-CDCl3.1.fid
PLH1154-H1-CDCl3
8.45
8.37
7.78
3.45
2.43
0.95
0.58
0.67
0.67
2.04
4.00
6.17
f1 (ppm)


PLH1154-C13-CDCl3.2.fid
PLH1154-C13-CDCl3
149.22
148.05
138.70
137.72
120.69
54.28
46.80
11.79
f1 (ppm)

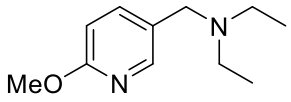

Br
N
N+
O-

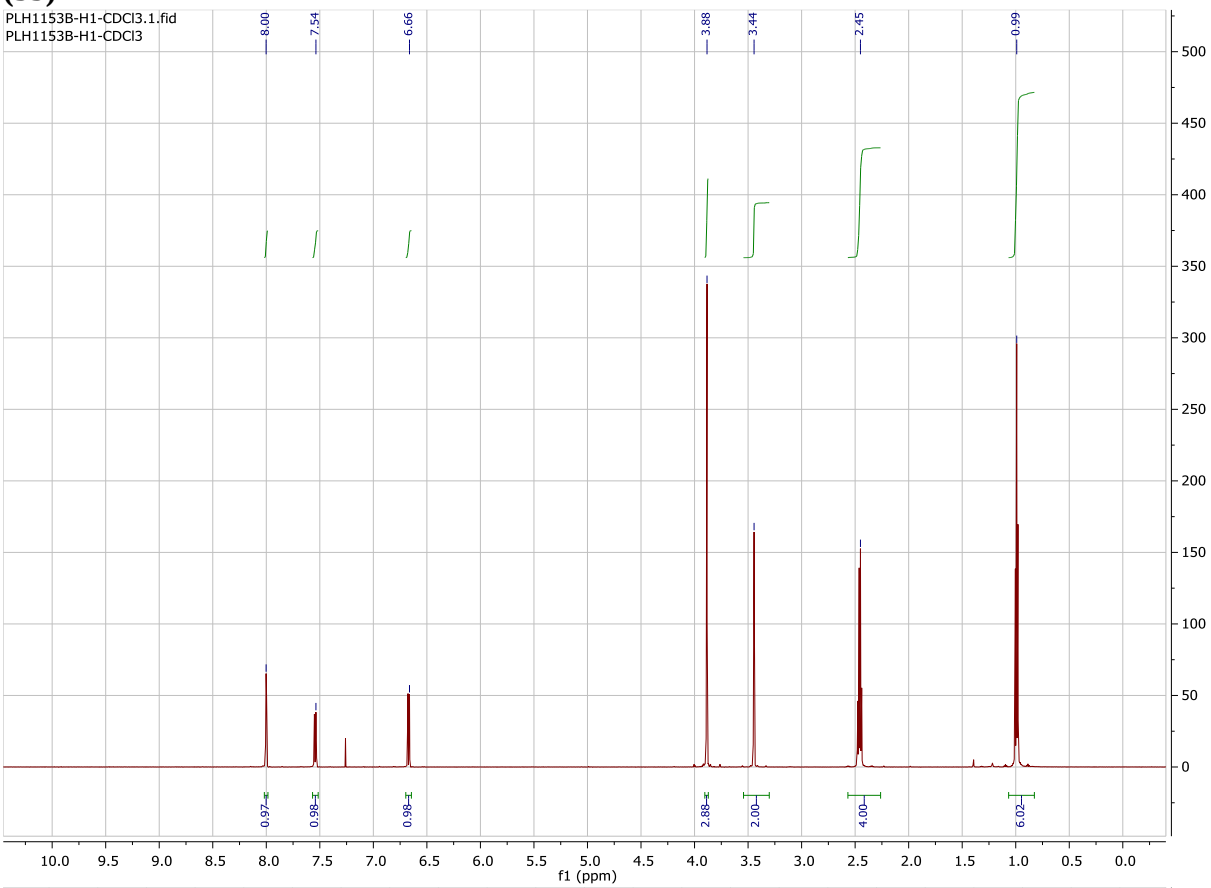
(34)

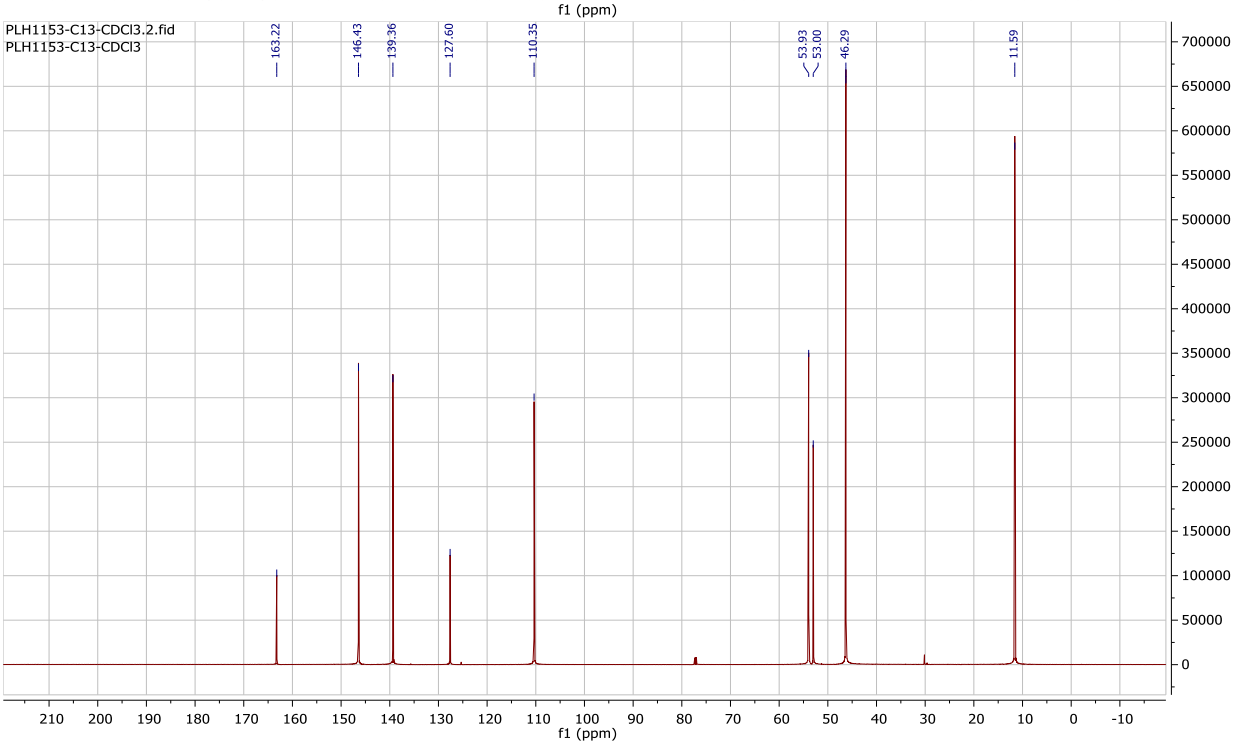

PLH1160-H1-CDCl3.1.fid
PLH1160-H1-CDCl3
8.14
8.10
7.37
3.42
2.43
0.94
0.92
0.96
0.96
2.05
4.04
6.00
f1 (ppm)

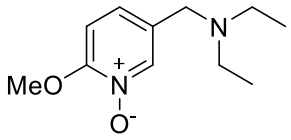

PLH1160-C13-CDCl3.1.fid
PLH1160-C13-CDCl3
141.09
138.82
137.78
129.29
119.84
54.09
46.99
11.83
f1 (ppm)

(35)

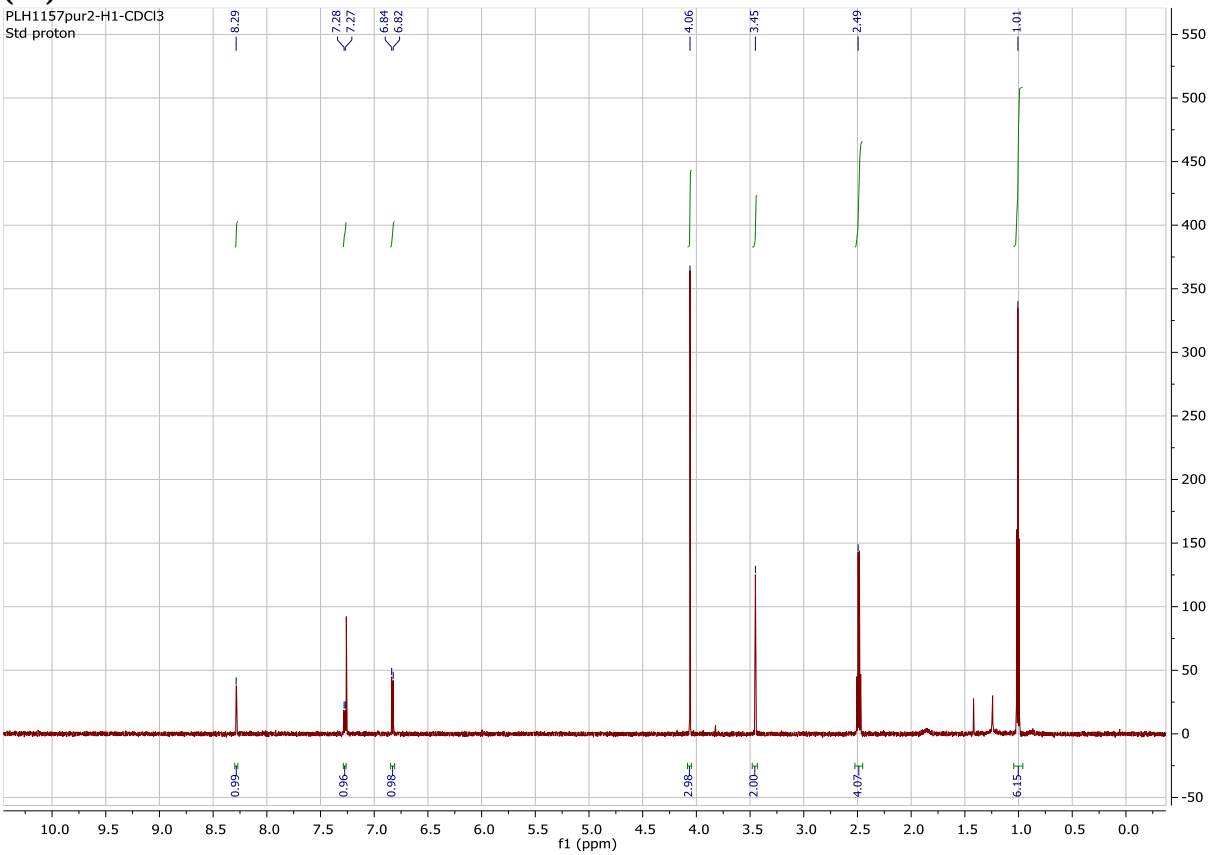

MeO
N
N

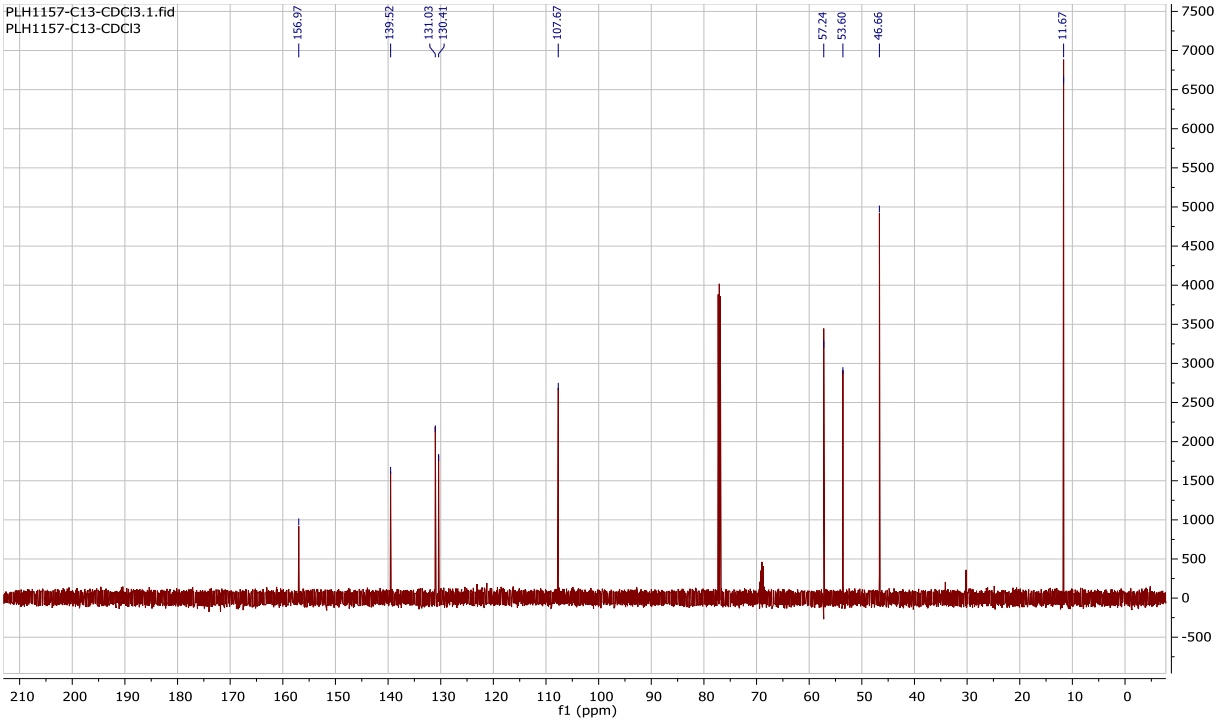

PLH1153B-H1-CDCl3.1.fid
PLH1153B-H1-CDCl3
8.00
7.54
6.66
3.88
3.44
2.45
0.99
0.97
0.98
0.98
2.88
2.00
4.00
6.02
f1 (ppm)


PLH1153-C13-CDCl3.2.fid
PLH1153-C13-CDCl3
163.22
146.43
139.36
127.60
110.35
53.93
53.00
46.29
11.59
f1 (ppm)

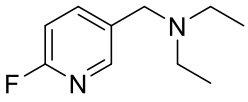

MeO
N
+
N
O-

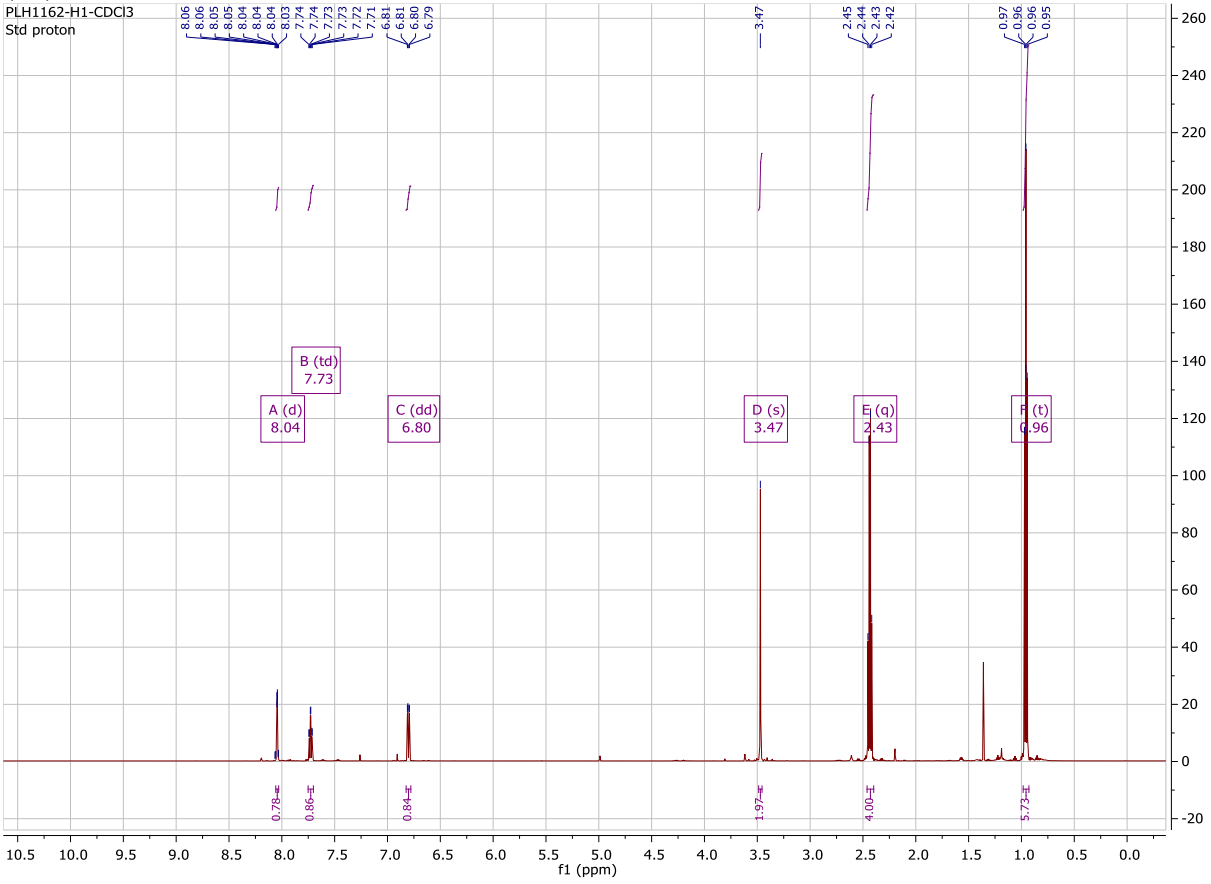
(36)

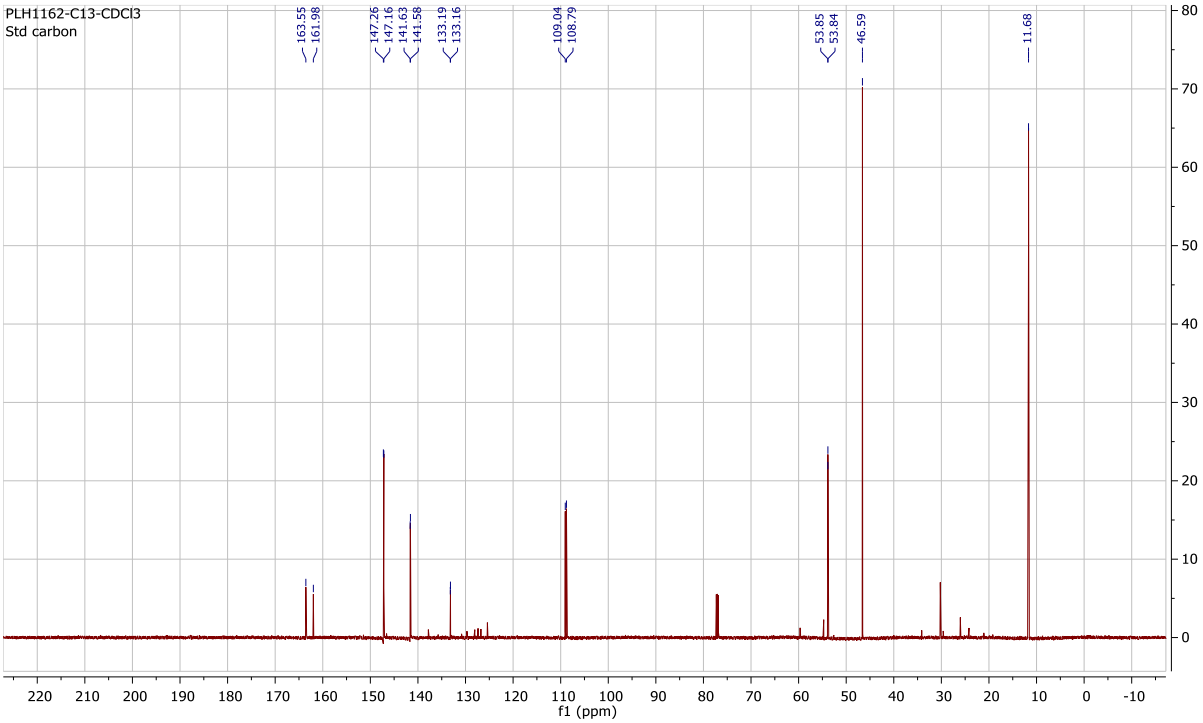

PLH1157pur2-H1-CDCl3
Std proton
8.29
7.28
7.27
6.84
6.82
4.06
3.45
2.49
1.01
0.99
0.96
0.98
2.98
2.00
4.07
6.15
f1 (ppm)

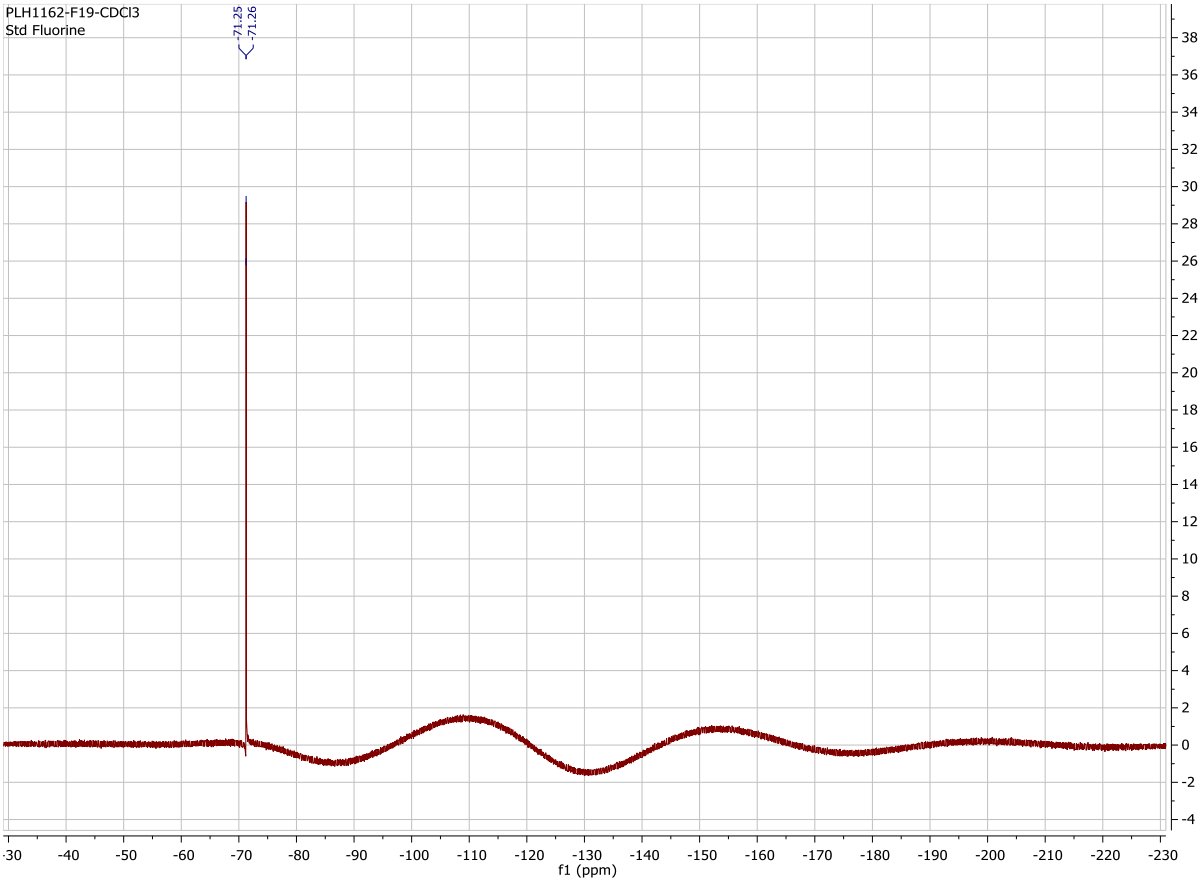

PLH1157-C13-CDCl3.1.fid
PLH1157-C13-CDCl3
156.97
139.52
131.03
130.41
107.67
57.24
53.60
46.66
11.67
f1 (ppm)

(37)

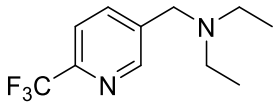

F
N
N

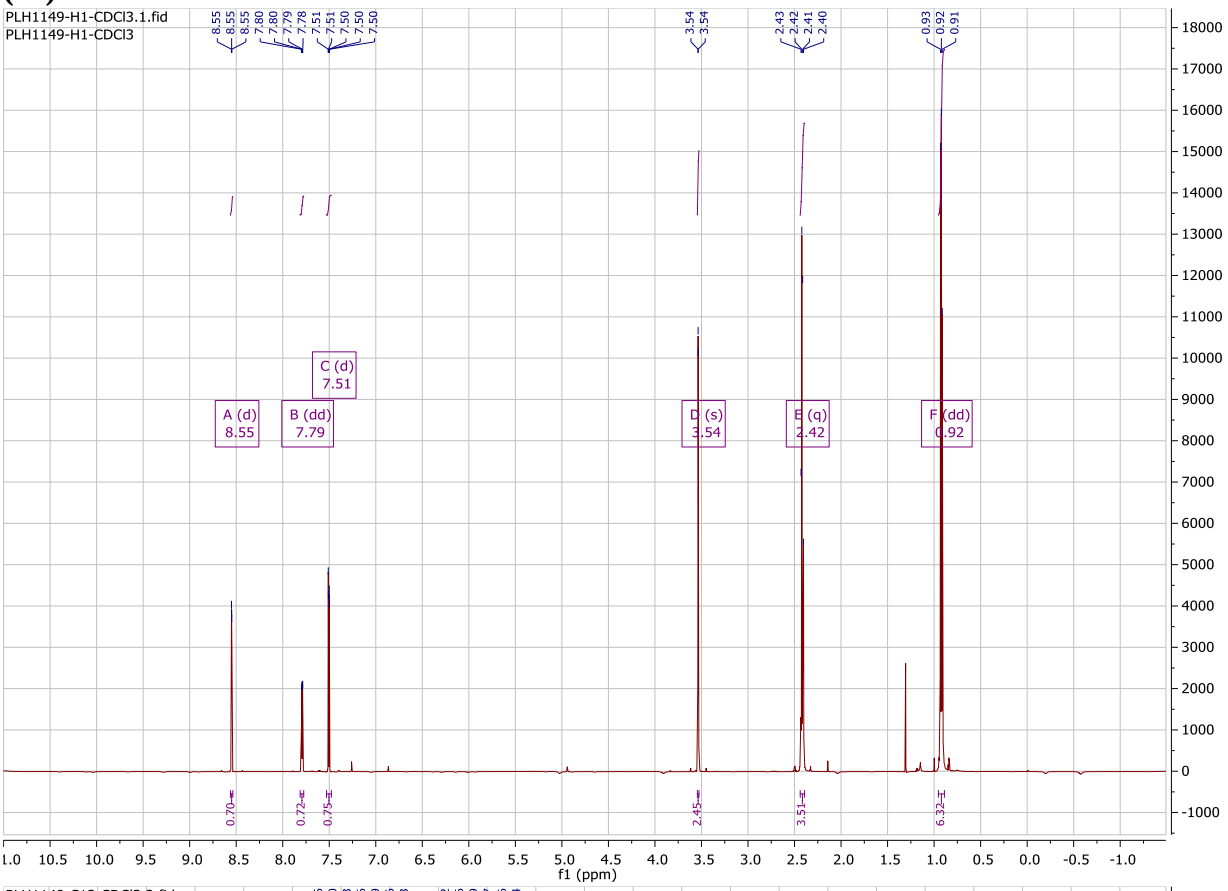

PLH1162-H1-CDCl3
Std proton
8.06 8.06 8.05 8.05 8.04 8.04 8.04 8.03
7.74 7.74 7.73 7.73 7.72 7.71
6.81 6.81 6.80 6.79
3.47
2.45 2.44 2.43 2.42
0.97 0.96 0.96 0.95
B (td) 7.73
A (d) 8.04
C (dd) 6.80
D (s) 3.47
E (q) 2.43
F (t) 0.96
0.78 0.86 0.84 1.97 4.00 5.73
f1 (ppm)

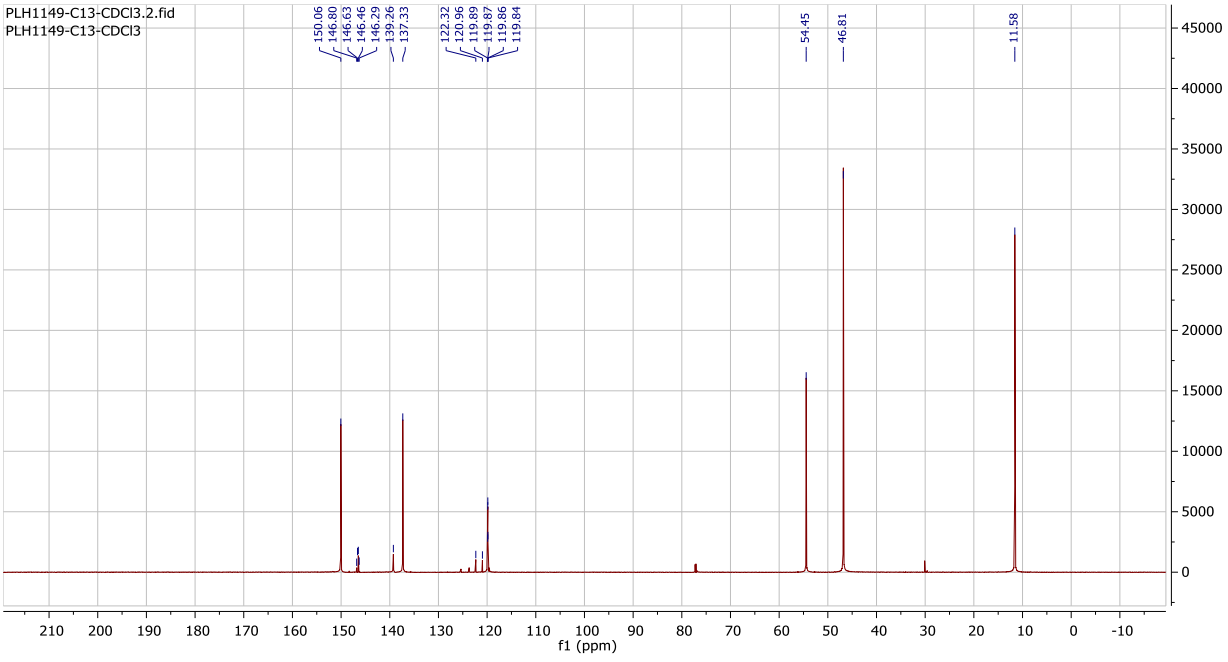

PLH1162-C13-CDCl3
Std carbon
163.55
161.98
147.26
147.16
141.63
141.58
133.19
133.16
109.04
108.79
53.85
53.84
46.59
11.68
f1 (ppm)


PLH1162-F19-CDCl3
Std Fluorine
-71.25
-71.26
f1 (ppm)

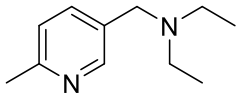
(39)

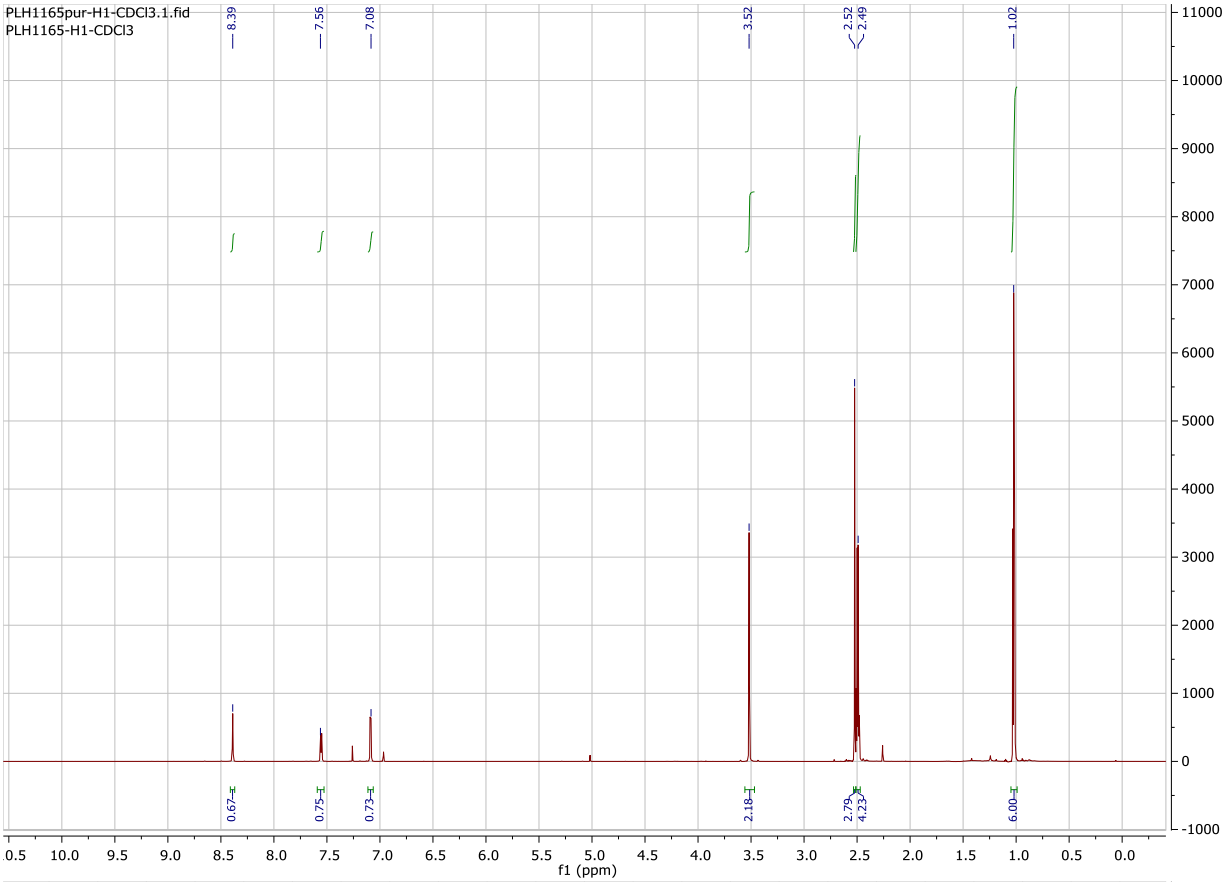

N
F3C
N

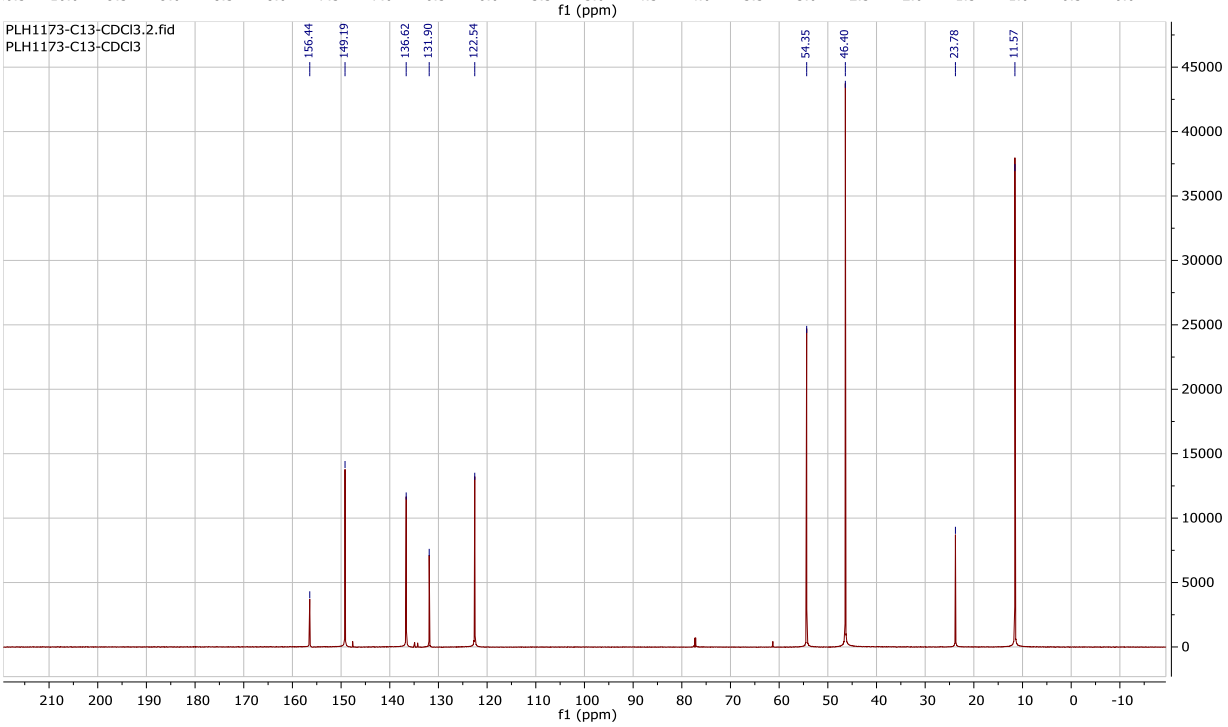

PLH1149-H1-CDCl3.1.fid
PLH1149-H1-CDCl3
A (d) 8.55
B (dd) 7.79
C (d) 7.51
D (s) 3.54
E (q) 2.42
F (dd) 0.92
f1 (ppm)

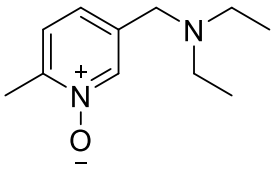

PLH1149-C13-CDCl3.2.fid
PLH1149-C13-CDCl3
f1 (ppm)

(41)

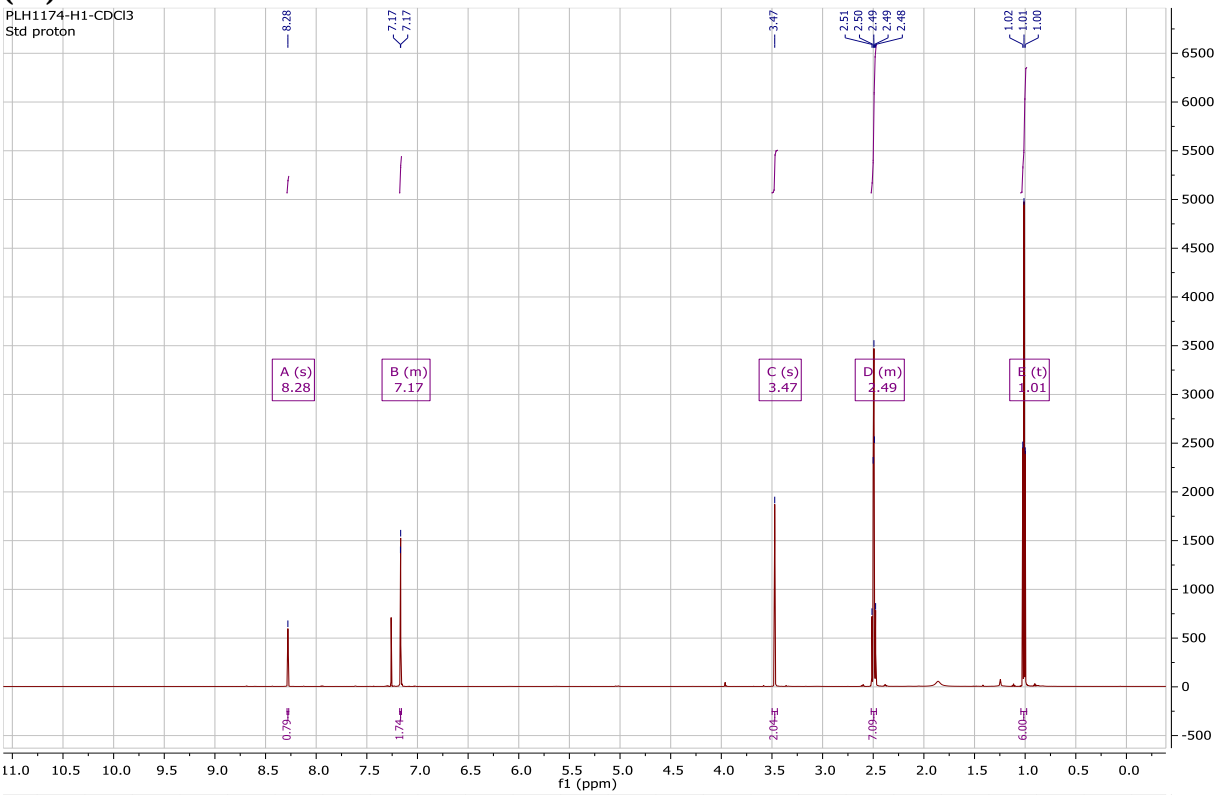

N
N

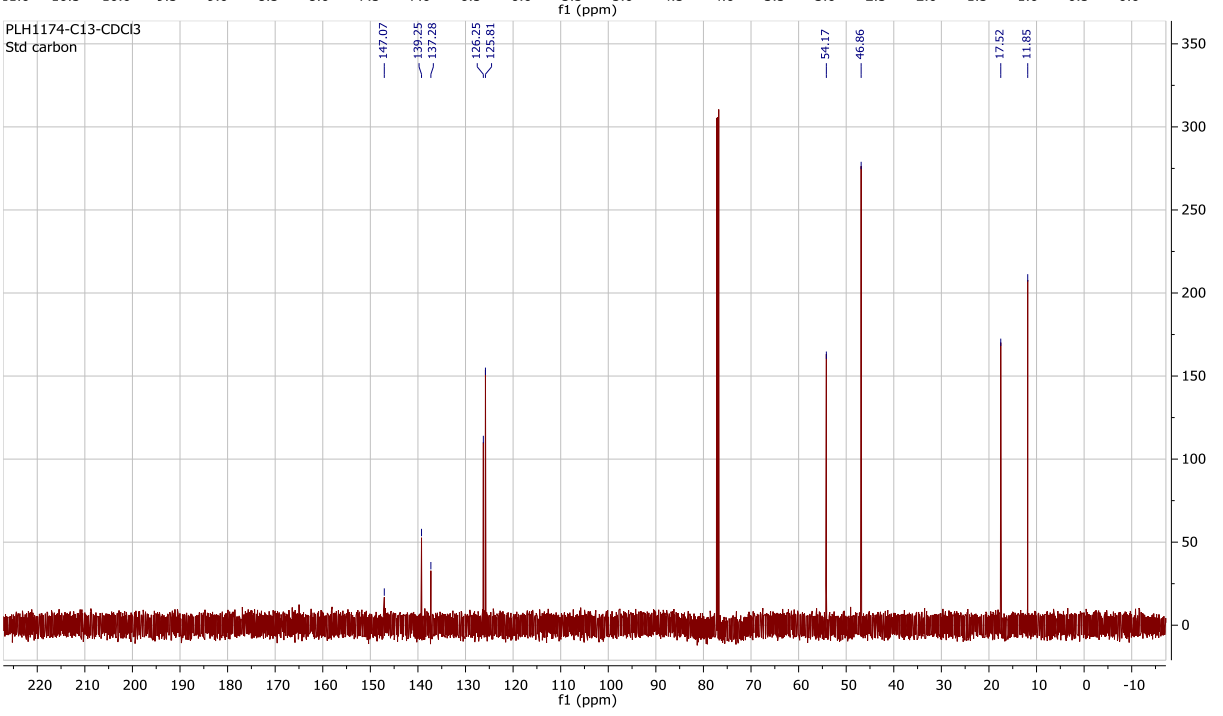

PLH1165pur-H1-CDCl3.1.fid
PLH1165-H1-CDCl3
8.39
7.56
7.08
3.52
2.52
2.49
1.02
0.67
0.75
0.73
2.18
2.79
4.23
6.00
f1 (ppm)


PLH1173-C13-CDCl3.2.fid
PLH1173-C13-CDCl3
156.44
149.19
136.62
131.90
122.54
54.35
46.40
23.78
11.57
f1 (ppm)

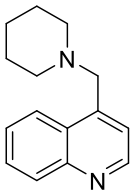


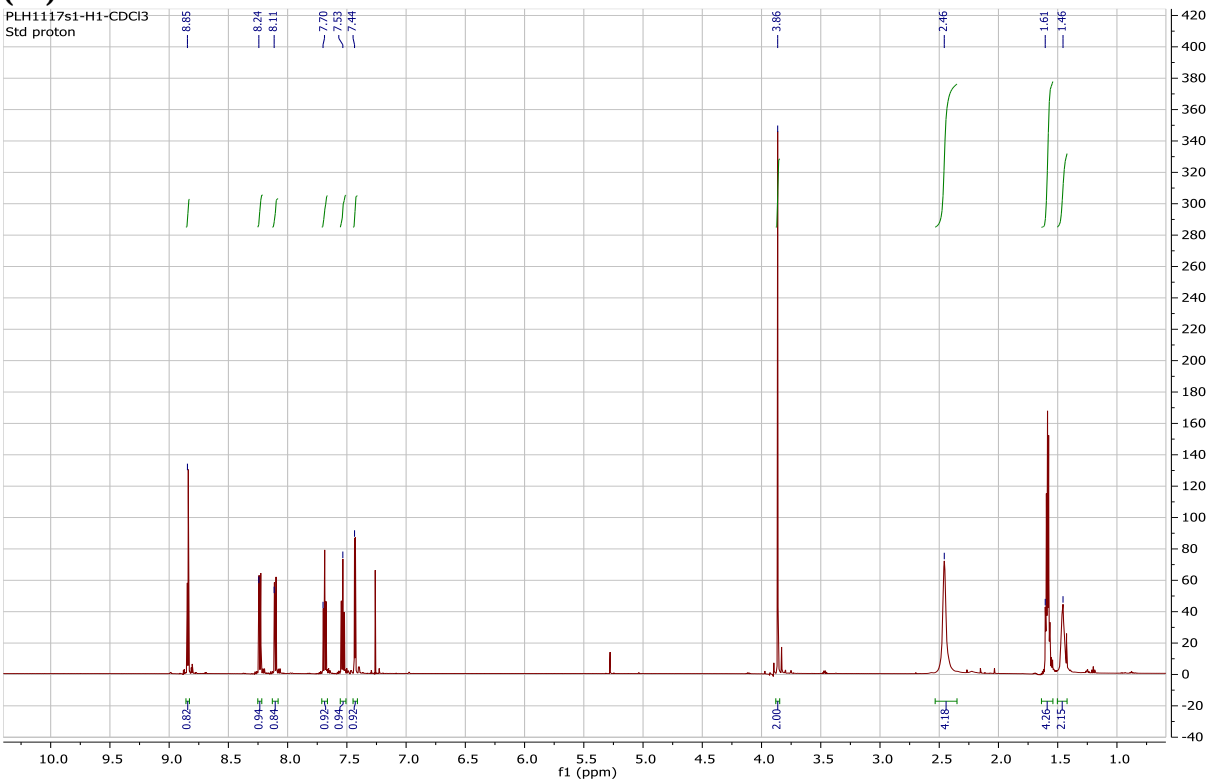
(42)

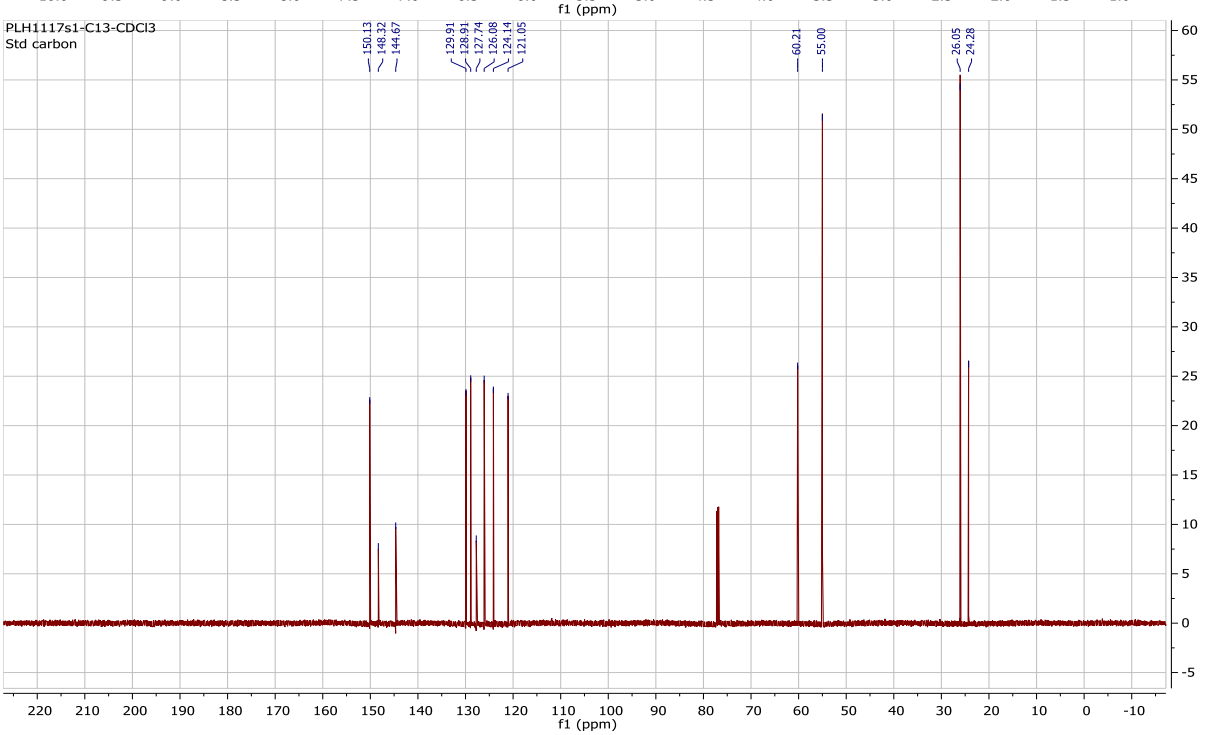

PLH1174-H1-CDCl3
Std proton
A (s)
8.28
B (m)
7.17
C (s)
3.47
D (m)
2.49
E (t)
1.01
f1 (ppm)

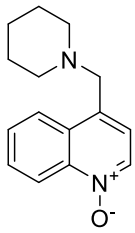

PLH1174-C13-CDCl3
Std carbon
f1 (ppm)

(43)

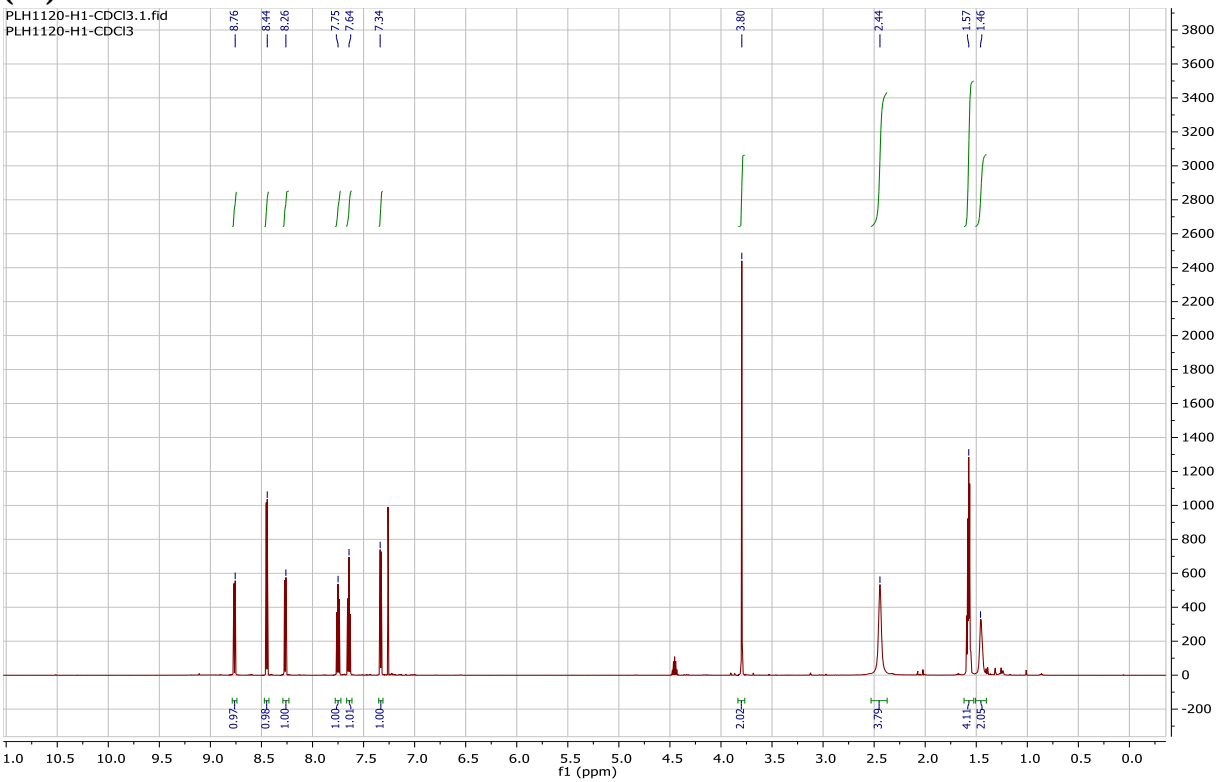


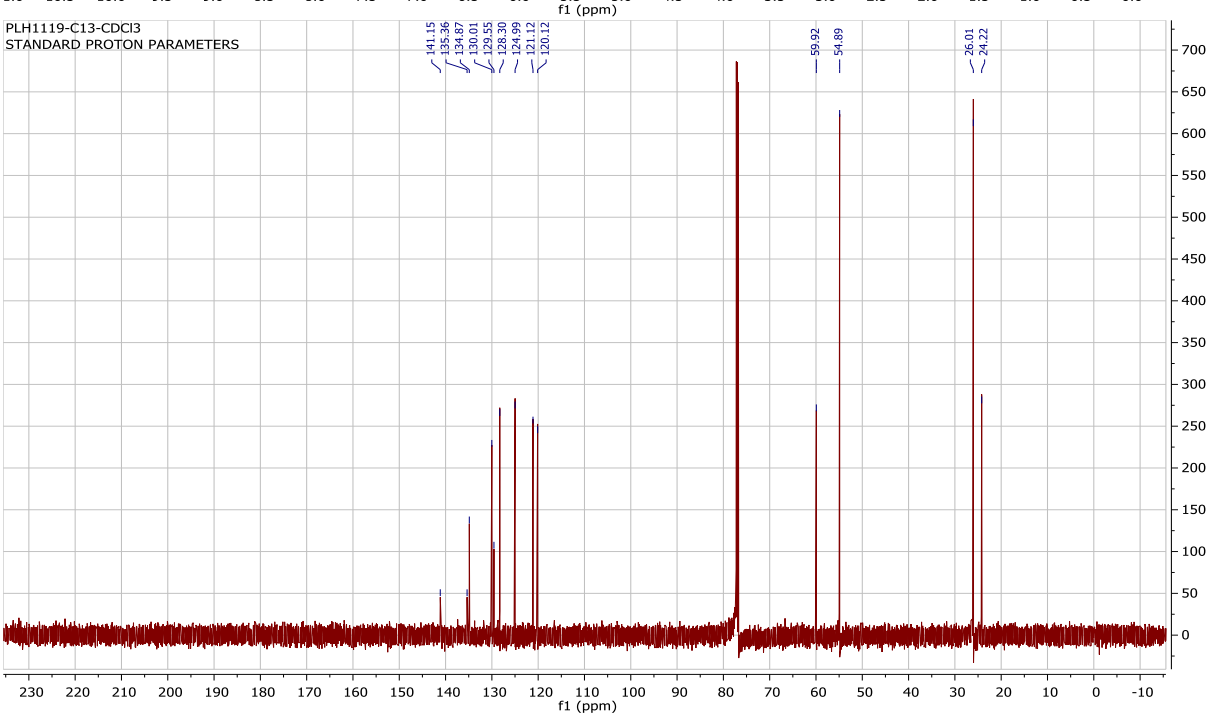

PLH1117s1-H1-CDCl3
Std proton
8.85
8.24
8.11
7.70
7.53
7.44
3.86
2.46
1.61
1.46
0.82
0.94
0.84
0.92
0.94
0.92
2.00
4.18
4.26
2.15
f1 (ppm)


PLH1117s1-C13-CDCl3
Std carbon
150.13
148.32
144.67
129.91
128.91
127.74
126.08
124.14
121.05
60.21
55.00
26.05
24.28
f1 (ppm)

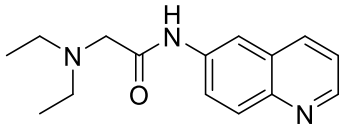


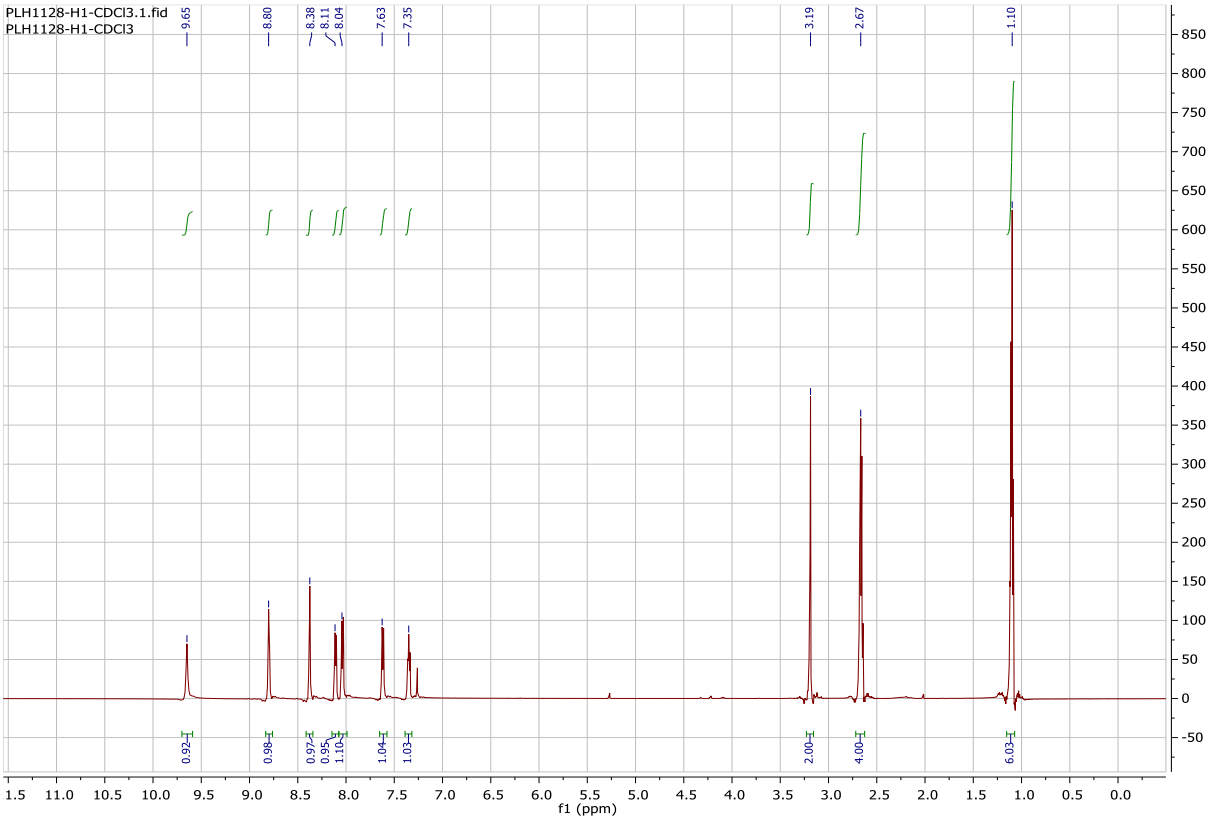
(44)

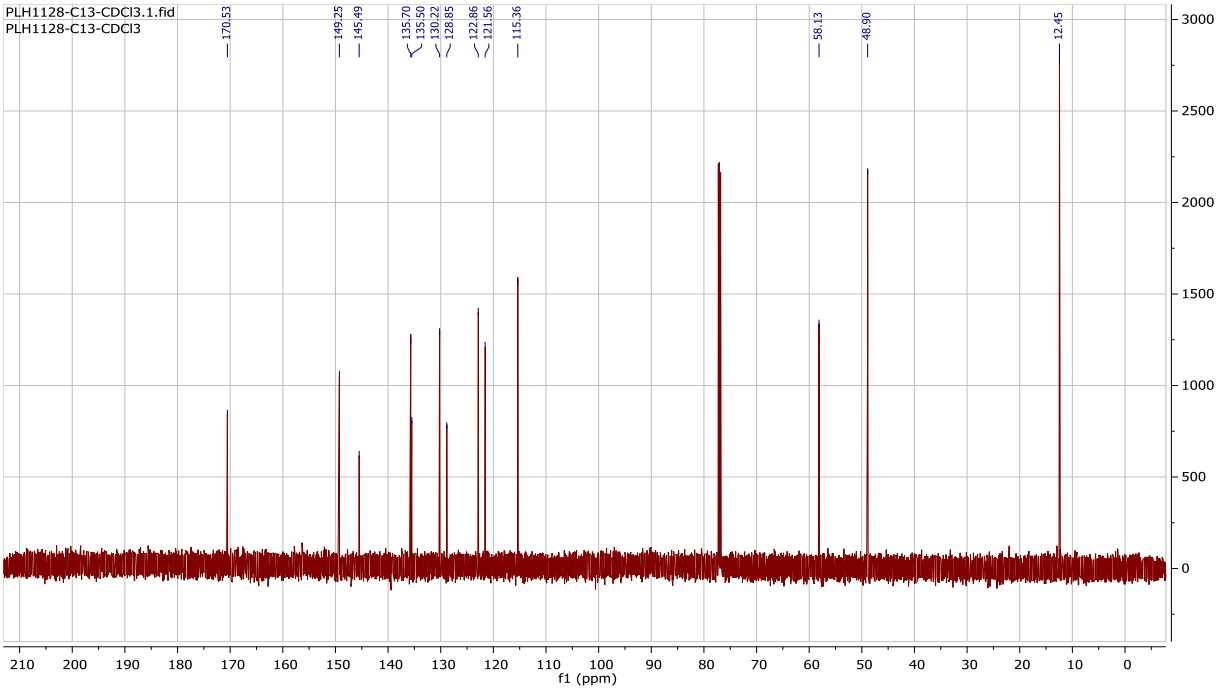

PLH1120-H1-CDCl3.1.fid
PLH1120-H1-CDCl3
8.76
8.44
8.26
7.75
7.64
7.34
3.80
2.44
1.57
1.46
0.97
0.98
1.00
1.00
1.01
1.00
2.02
3.79
4.11
2.05
f1 (ppm)

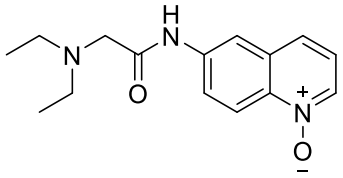

PLH1119-C13-CDCl3
STANDARD PROTON PARAMETERS
141.15
135.36
134.87
130.01
129.55
128.30
124.99
121.12
120.12
59.92
54.89
26.01
24.22
f1 (ppm)

(45)

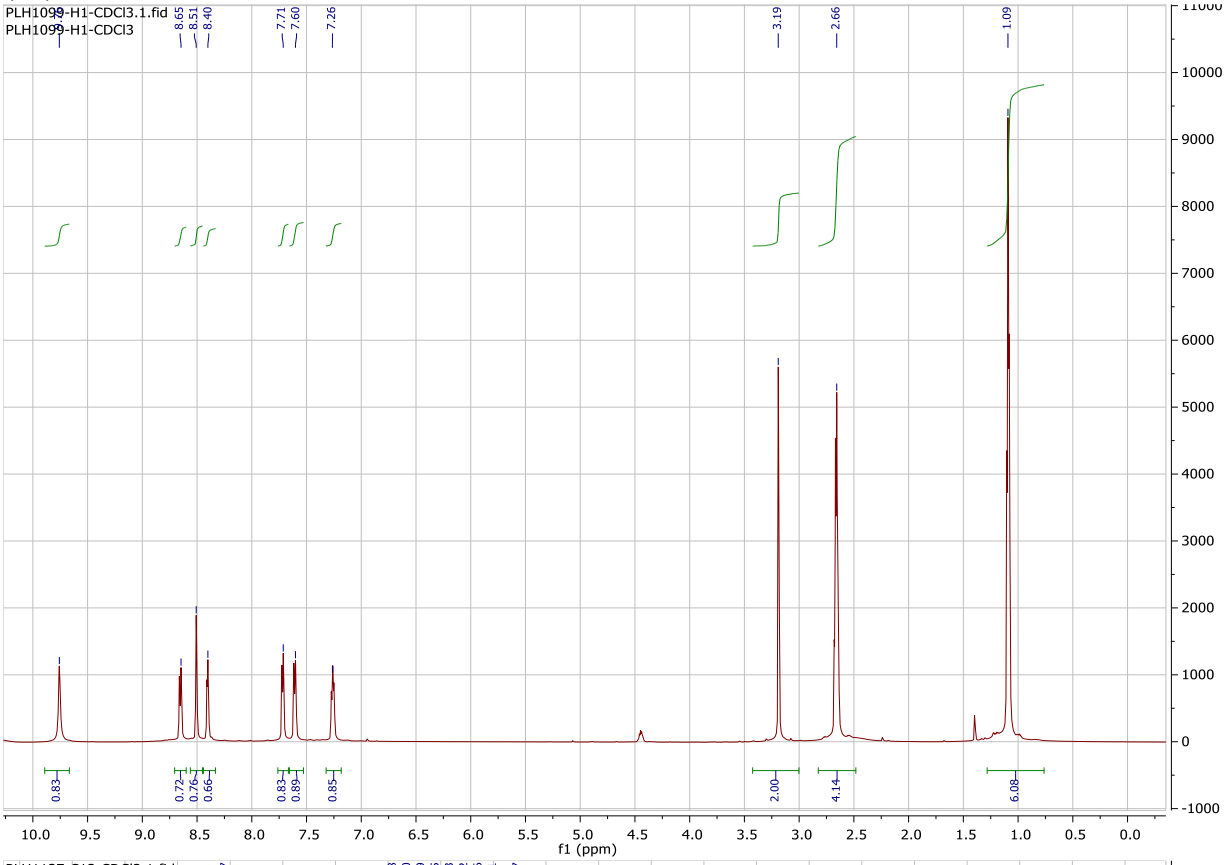


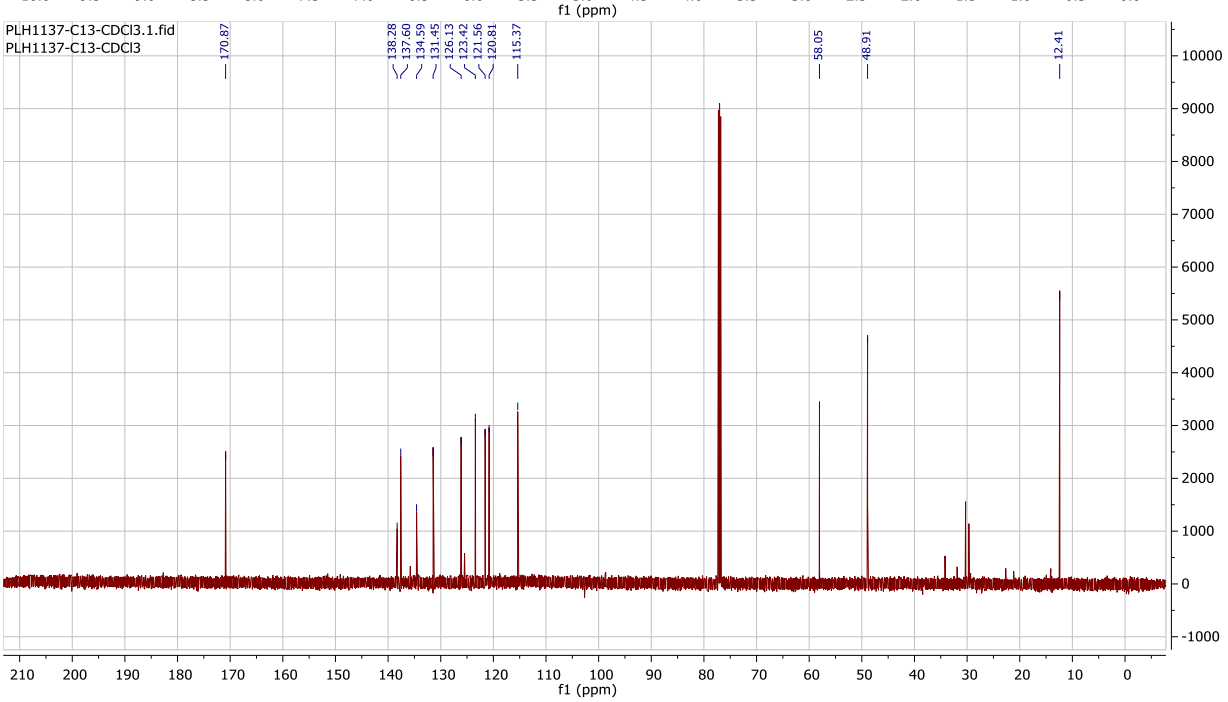

PLH1128-H1-CDCl3.1.fid
PLH1128-H1-CDCl3
9.65
8.80
8.38
8.11
8.04
7.63
7.35
3.19
2.67
1.10
0.92
0.98
0.97
0.95
1.10
1.04
1.03
2.00
4.00
6.03
f1 (ppm)


PLH1128-C13-CDCl3.1.fid
PLH1128-C13-CDCl3
170.53
149.25
145.49
135.70
135.50
130.22
128.85
122.86
121.56
115.36
58.13
48.90
12.45
f1 (ppm)

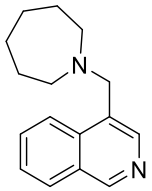


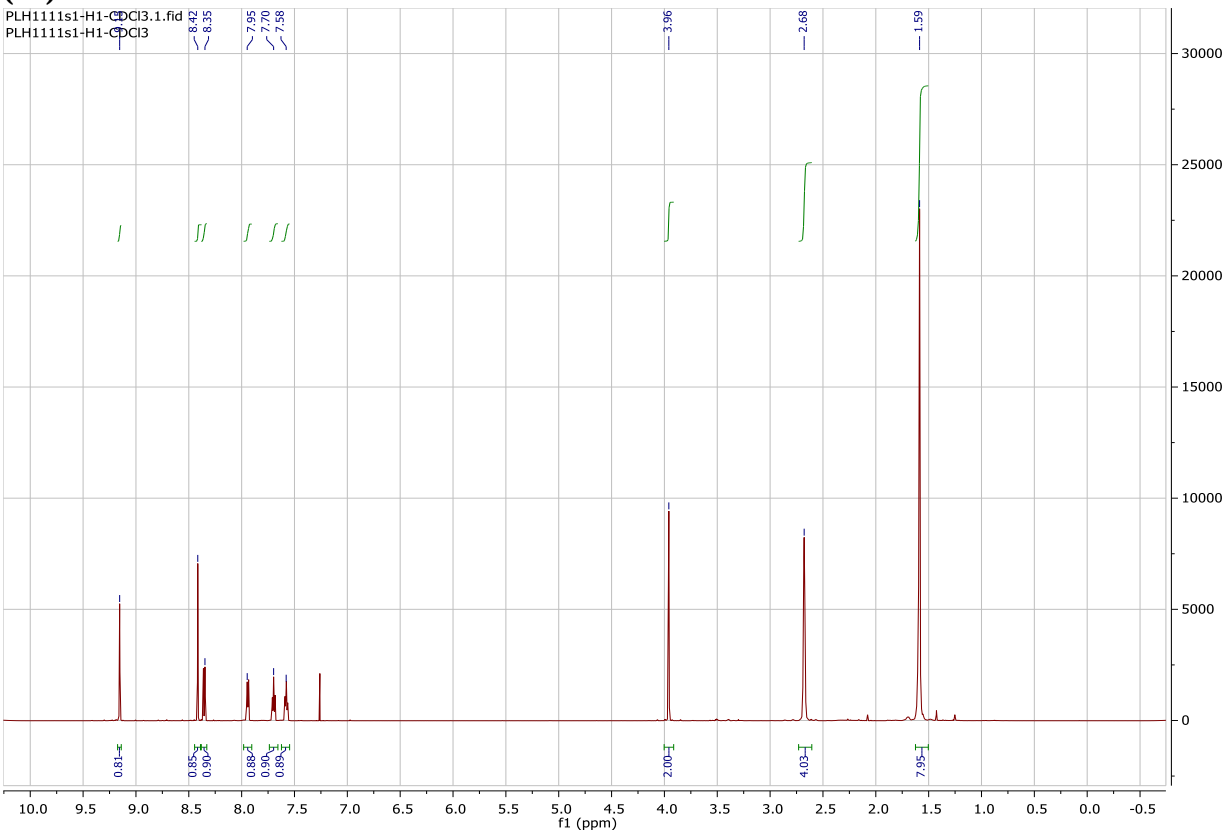
(46)

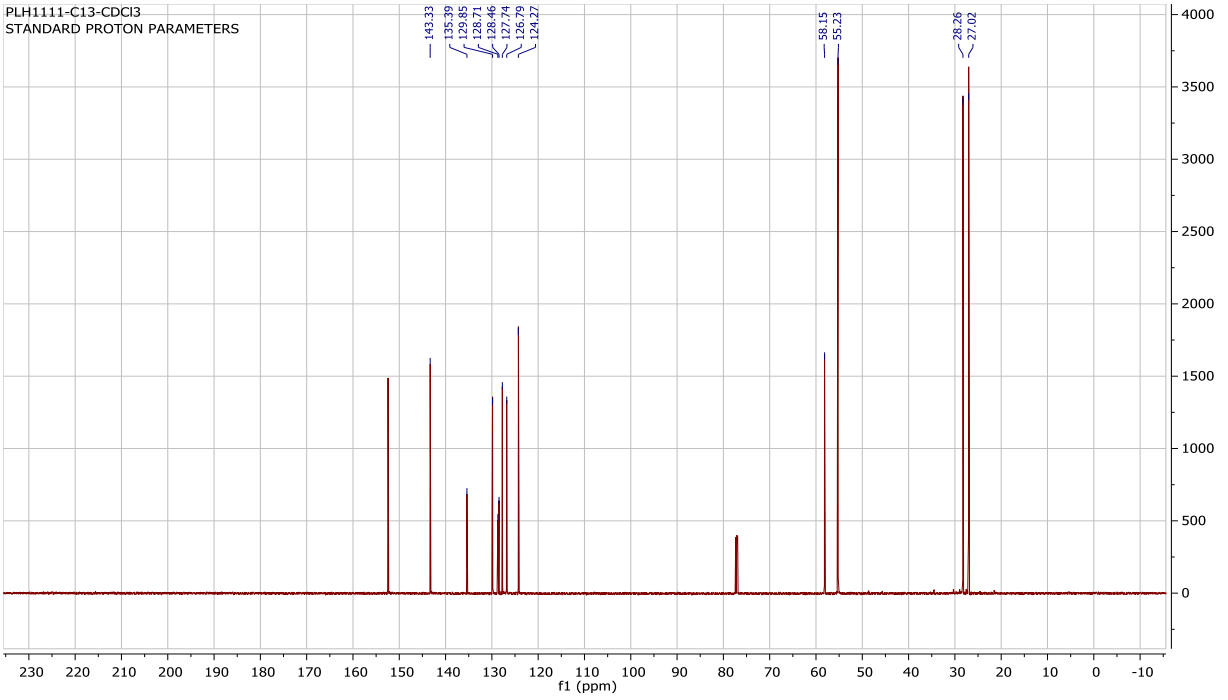

PLH1099-H1-CDCl3.1.fid
PLH1099-H1-CDCl3
8.65
8.51
8.40
7.71
7.60
7.26
3.19
2.66
1.09
0.83
0.72
0.76
0.66
0.83
0.89
0.85
2.00
4.14
6.08
f1 (ppm)

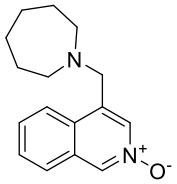

PLH1137-C13-CDCl3.1.fid
PLH1137-C13-CDCl3
170.87
138.28
137.60
134.59
131.45
126.13
123.42
121.56
120.81
115.37
58.05
48.91
12.41
f1 (ppm)

(47)

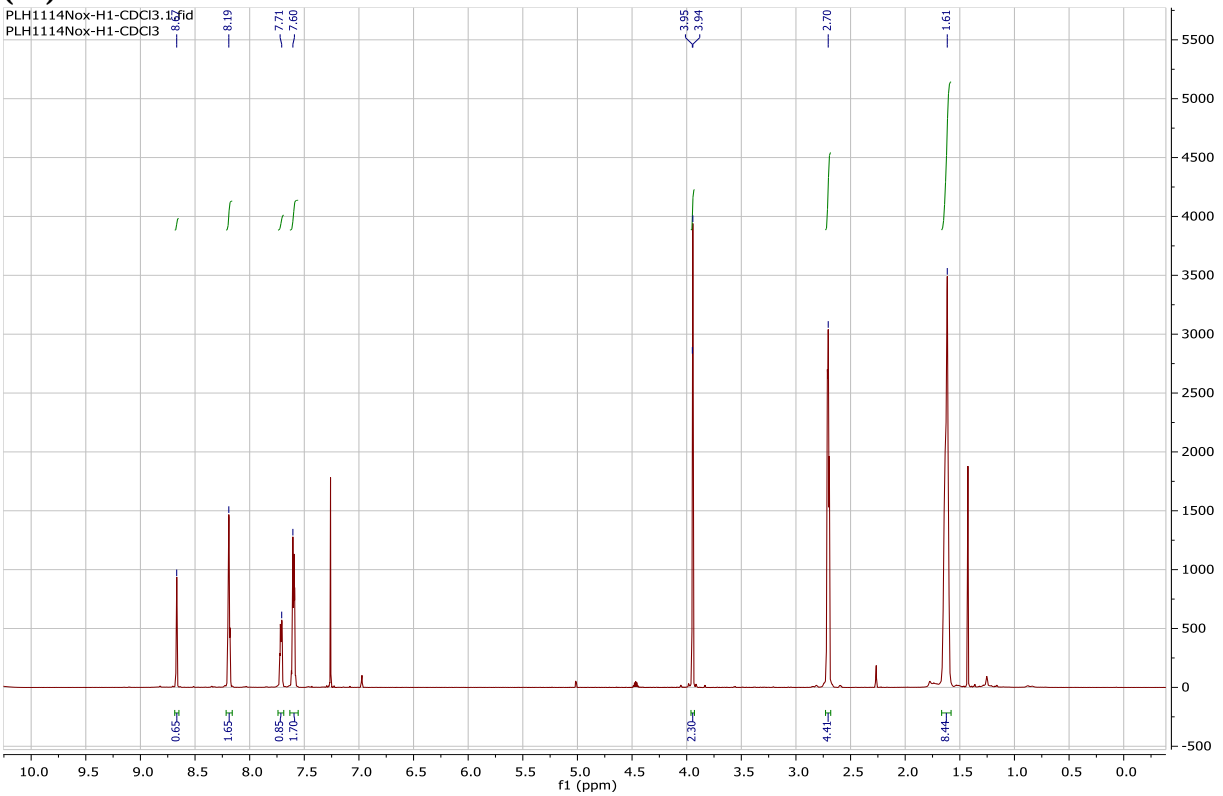


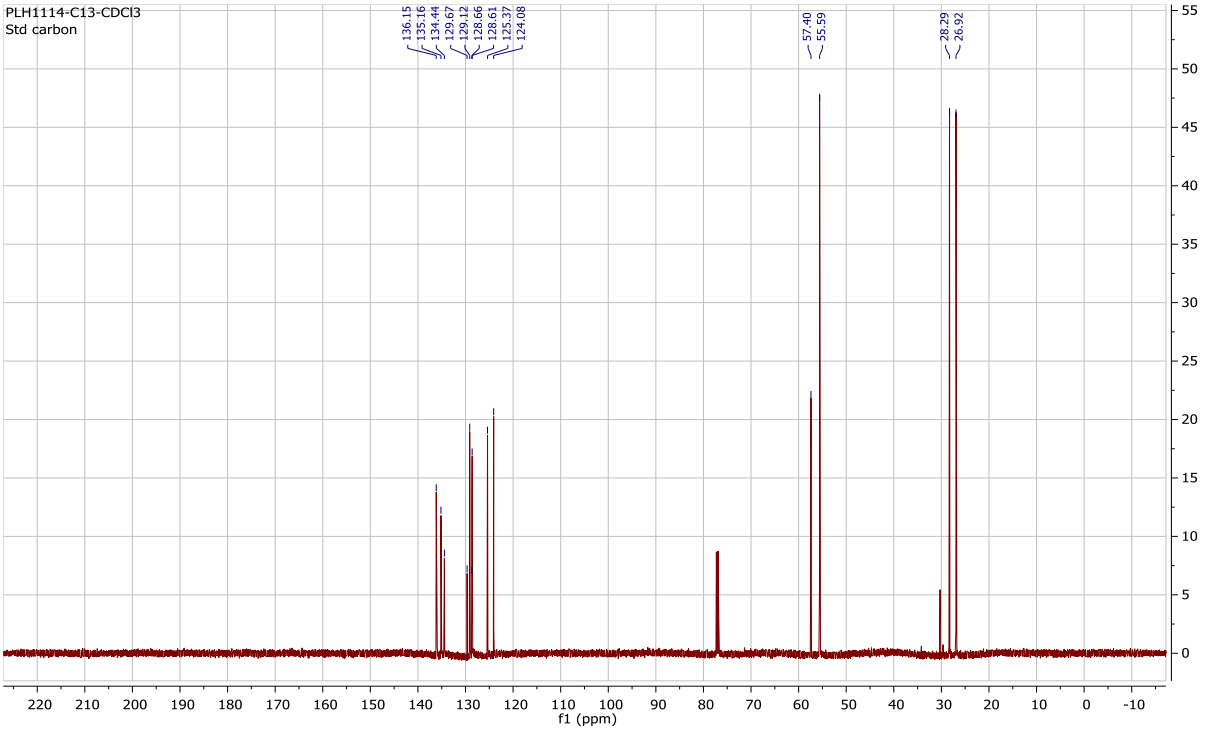

PLH1111s1-H1-CDCl3.1.fid
PLH1111s1-H1-CDCl3
8.42
8.35
7.95
7.70
7.58
3.96
2.68
1.59
0.81
0.85
0.90
0.88
0.90
0.89
2.00
4.03
7.95
f1 (ppm)

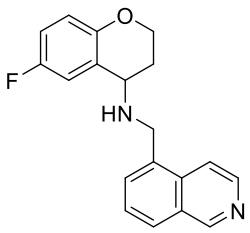

PLH1111-C13-CDCl3
STANDARD PROTON PARAMETERS
143.33
135.39
129.85
128.71
128.46
127.74
126.79
124.27
58.15
55.23
28.26
27.02
f1 (ppm)



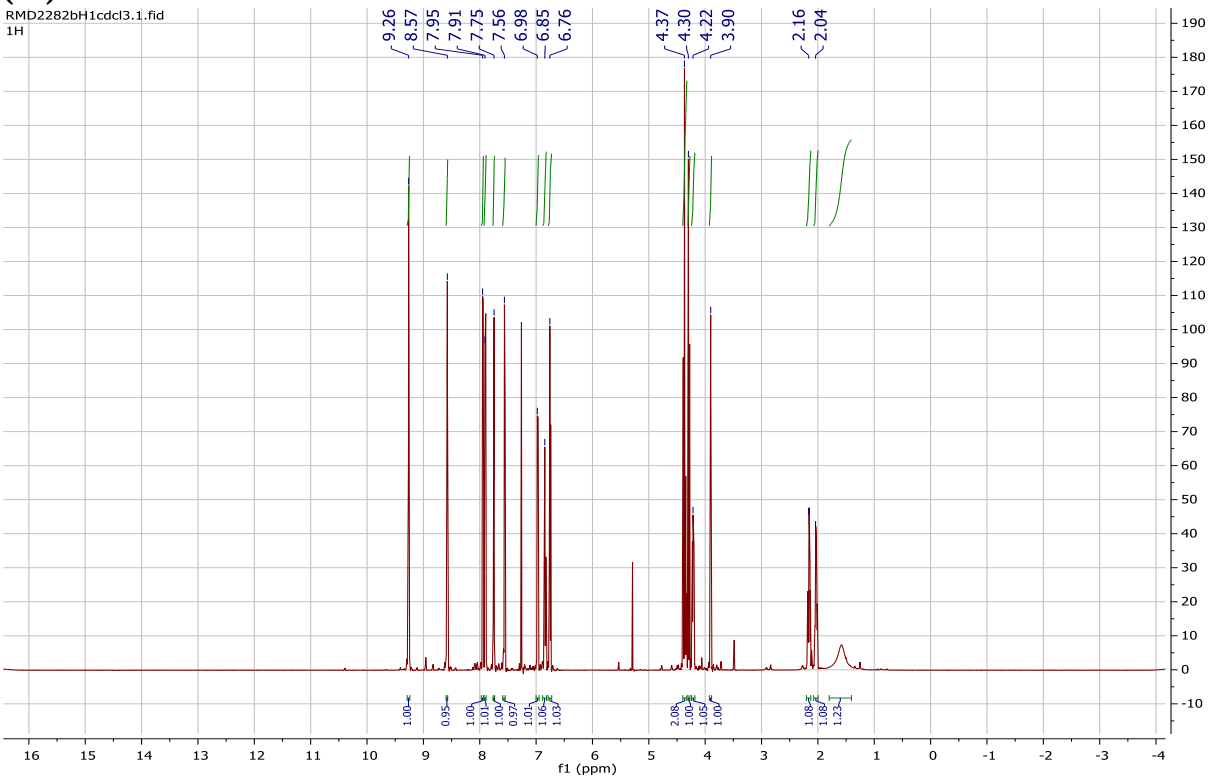
(48)

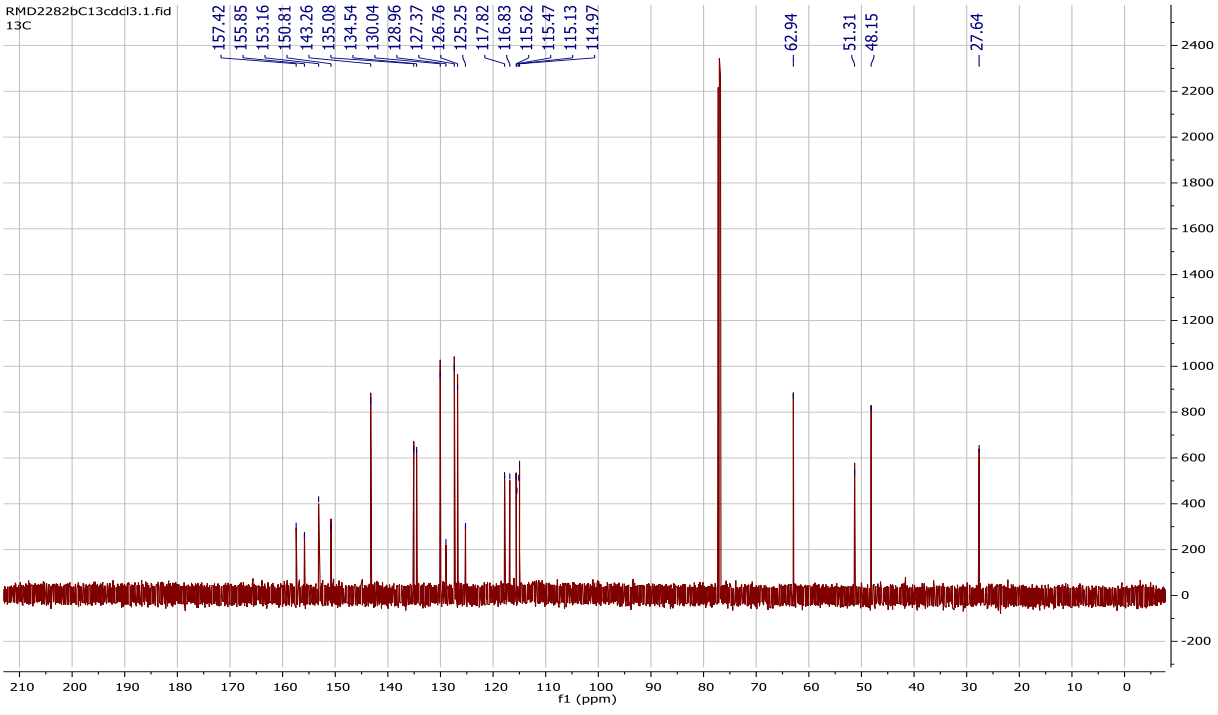

PLH1114Nox-H1-CDCl3.1.fid
PLH1114Nox-H1-CDCl3
8.19
7.71
7.60
3.95
3.94
2.70
1.61
0.65
1.65
0.85
1.70
2.30
4.41
8.44
f1 (ppm)

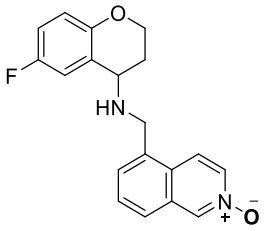

PLH1114-C13-CDCl3
Std carbon
136.15
135.16
134.44
129.67
129.12
128.66
128.61
125.37
124.08
57.40
55.59
28.29
26.92
f1 (ppm)


O
F
HN
N

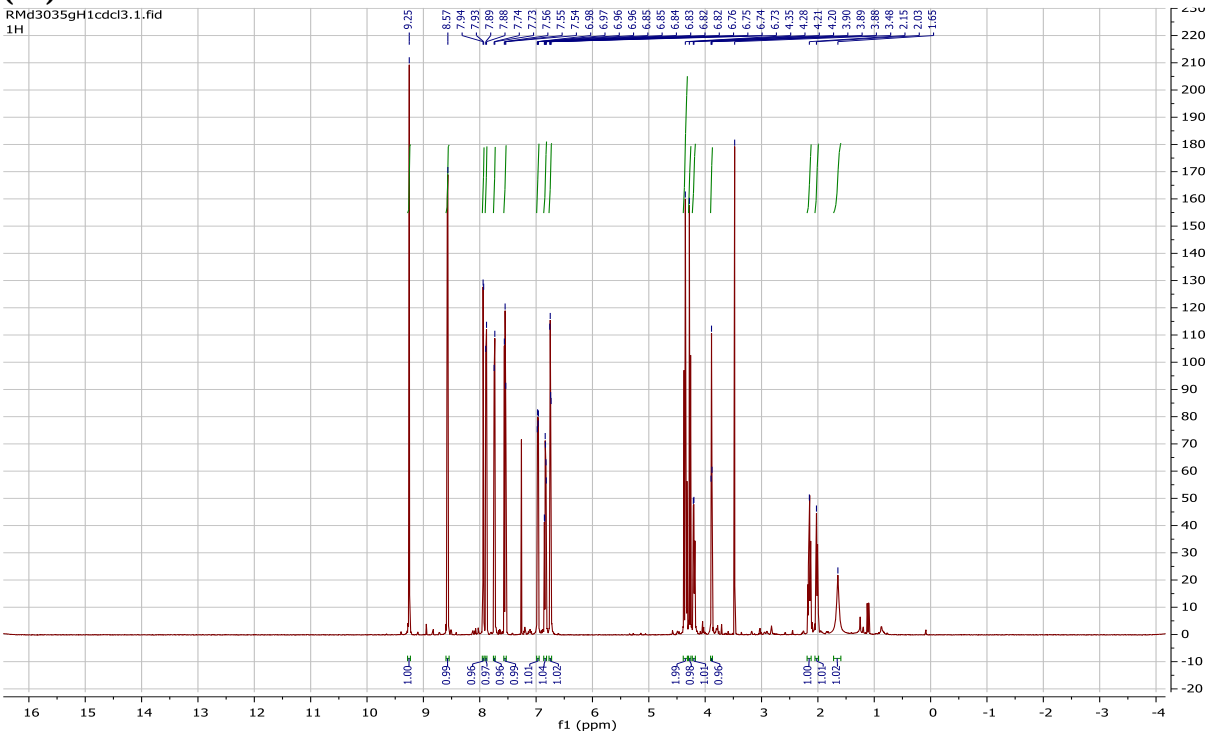
(49)

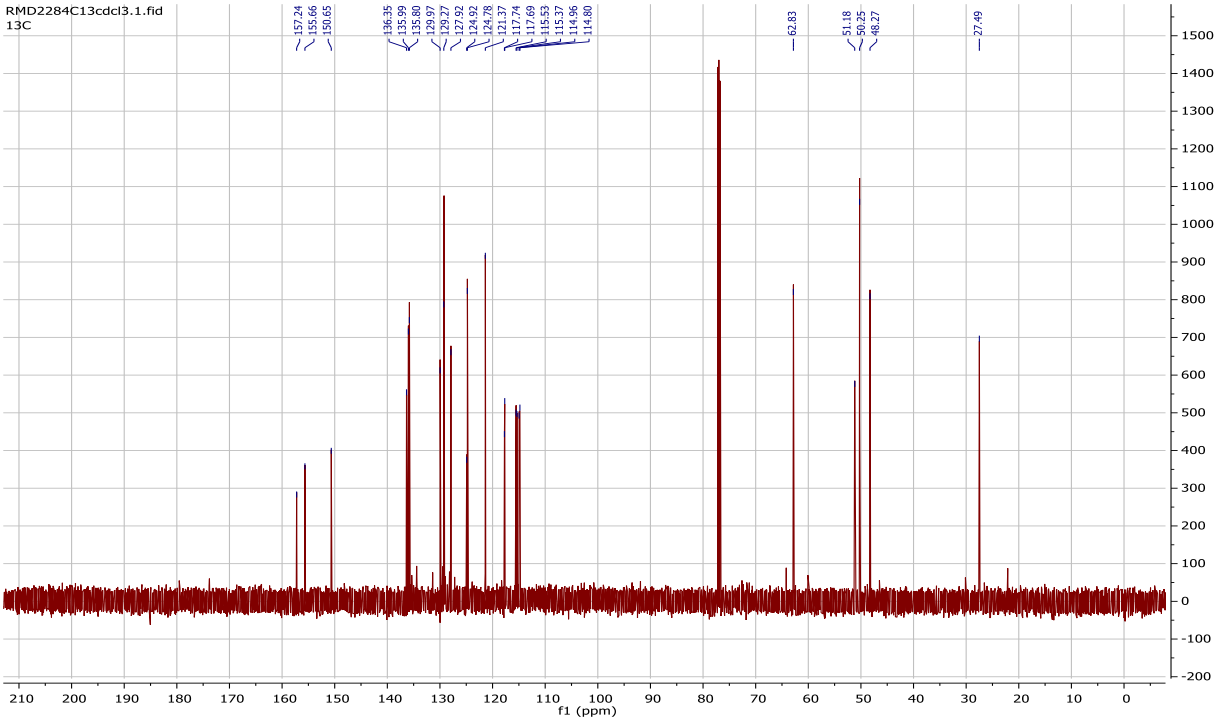

RMD2282bH1cdcl3.1.fid
1H
9.26
8.57
7.95
7.91
7.75
7.56
6.98
6.85
6.76
4.37
4.30
4.22
3.90
2.16
2.04
f1 (ppm)

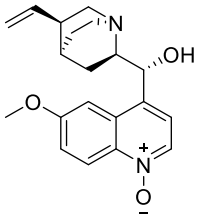

RMD2282bC13cdcl3.1.fid
13C
157.42
155.85
153.16
150.81
143.26
135.08
134.54
130.04
128.96
127.37
126.76
125.25
117.82
116.83
115.62
115.47
115.13
114.97
62.94
51.31
48.15
27.64
f1 (ppm)


O
F
HN
N
O

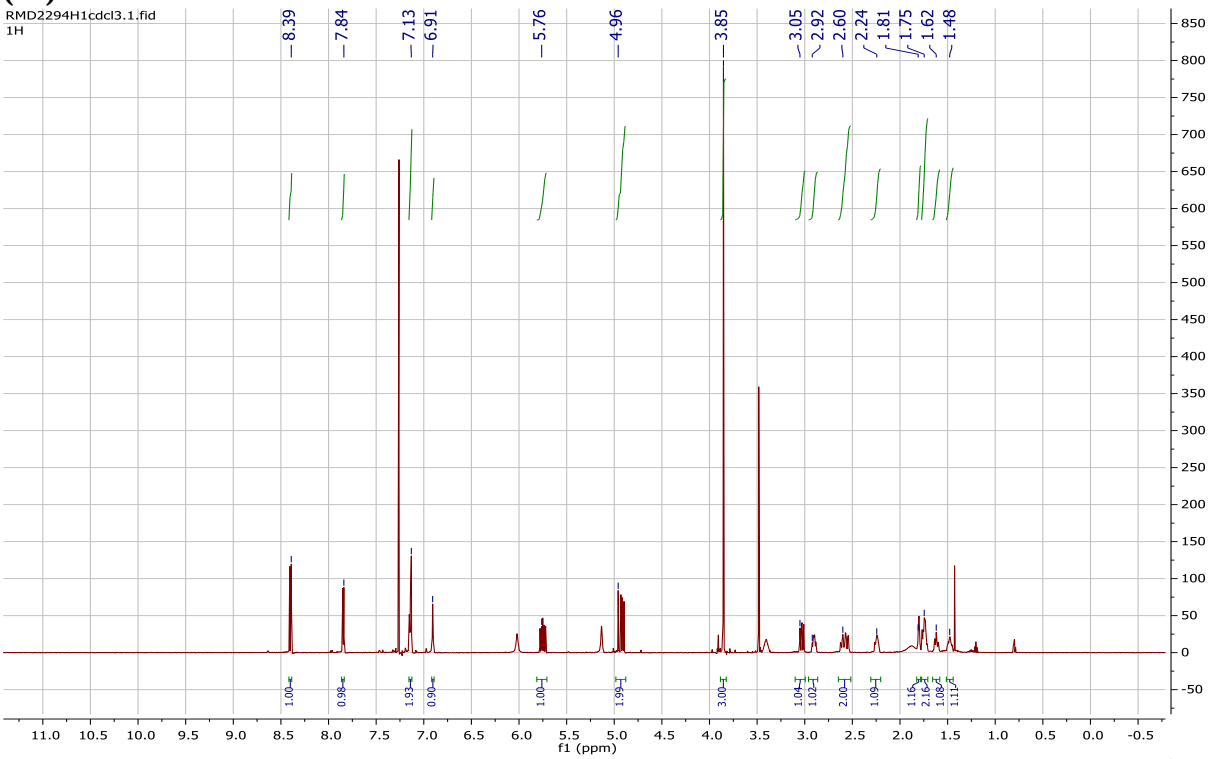
(50)

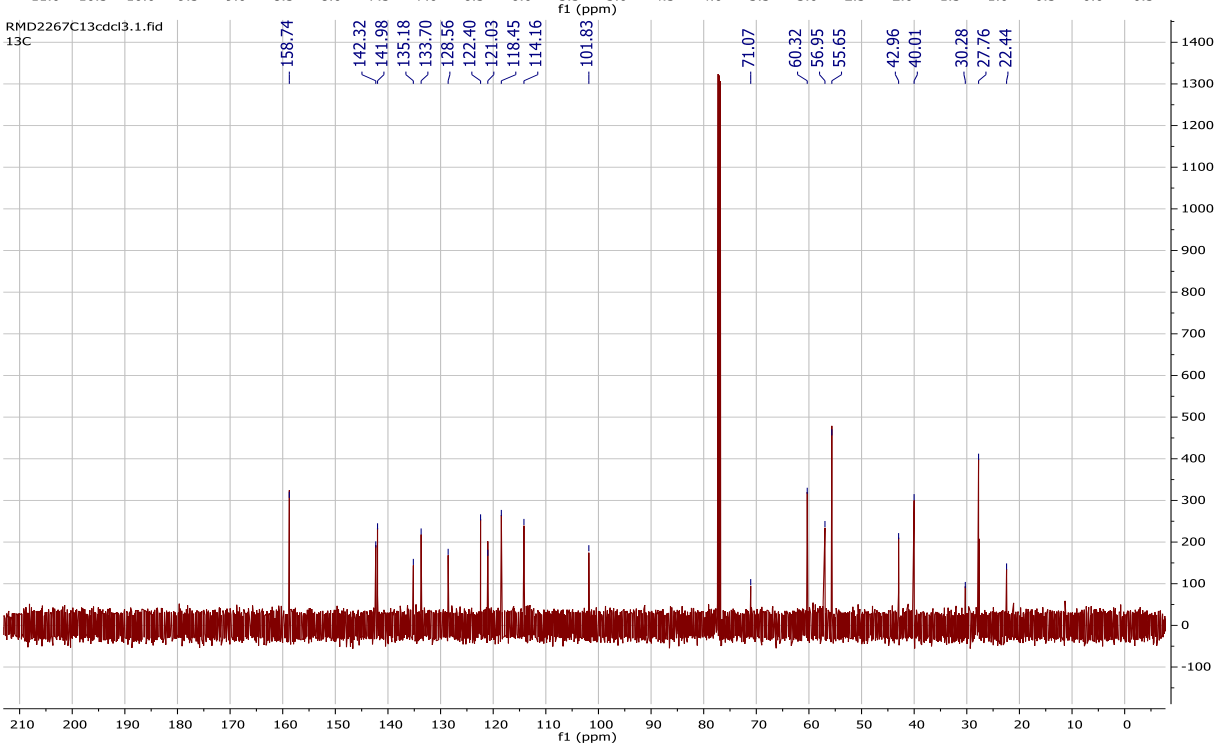

RMd3035gH1cdcl3.1.fid
1H
f1 (ppm)


RMD2284C13cdcl3.1.fid
13C
f1 (ppm)


N
OH
O
N
+
O
-

(52)


RMD2294H1cdcl3.1.fid
1H
8.39
7.84
7.13
6.91
5.76
4.96
3.85
3.05
2.92
2.60
2.24
1.81
1.75
1.62
1.48
f1 (ppm)


RMD2267C13cdcl3.1.fid
13C
158.74
142.32
141.98
135.18
133.70
128.56
122.40
121.03
118.45
114.16
101.83
71.07
60.32
56.95
55.65
42.96
40.01
30.28
27.76
22.44
f1 (ppm)