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Hypervalent Iodine Mediated Synthesis of Imidazo[1,2-a] pyridine Ethers: Consecutive Methylene Linkage and Insertion of Ethylene Glycol

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1-Experimental Section

All commercially available chemicals and reagents were used without any further purification unless otherwise indicated. ^1H and ^{13}C NMR spectra were recorded at 600, 500, 200 MHz and 150, 125, 50 MHz, respectively. The spectra were recorded in CDCl_3 as solvent. Multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets), etc. and coupling constants (J) were given in Hz. Chemical shifts are reported in ppm relative to TMS as an internal standard. The peaks around delta values of ^1H NMR (7.2), and ^{13}C NMR (77.0) are correspond to deuterated solvent chloroform respectively. Mass spectra were obtained using electron impact (EI) ionization method. Progress of the reactions was monitored by thin layer chromatography (TLC). All products were purified through column chromatography using silica gel 100-200 mesh size using hexane/ethyl acetate as eluent unless otherwise indicated.

General procedure for **3a**

A clean washed boiling tube equipped with a magnetic stir bar was charged with 2-phenylimidazo[1,2-a]pyridine **1a** (0.0485 g, 0.25 mmol), (Diacetoxyiodo)benzene PIDA **2a** (0.1207 g, 0.375 mmol), and ethylene glycol (1mL), the above mixture was stirred for 24h at 100°C temperature. After completion of the reaction, the mixture was poured into 10 mL of NaHCO_3 solution. The product was extracted with ethyl acetate (10 mL \times 3) and dried with anhydrous Na_2SO_4 . Removal of the solvent under reduced pressure, the left out residue was purified through column chromatography using silica gel (80% EtOAc/hexane) to obtain 2-((2-phenylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol **3a** in 74 % yield (0.0495g).

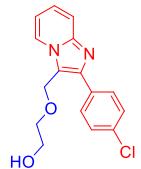
2-Characterization data

2-((2-phenylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (**3a**)

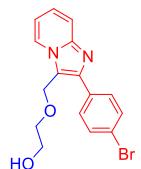
(Eluent: 80% EtOAc/hexane); 74% yield (49.5mg); yellow sticky liquid ^1H NMR (500 MHz, CDCl_3) δ 8.22 (d, J = 6.6 Hz, 1H), 7.76 (d, J = 7.7 Hz, 2H), 7.67 (d, J = 8.9 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.40 (dd, J = 10.5, 4.1 Hz, 1H), 7.24 (d, J = 8.6 Hz, 1H), 6.87 (t, J = 6.7 Hz, 1H), 4.98 (s, 2H), 3.79 (t, J = 5.0 Hz, 2H), 3.66 (t, J = 5.0 Hz, 2H). ^{13}C NMR (150MHz, CDCl_3) δ 145.74, 145.35, 134.06, 128.77, 128.71, 128.14, 125.23, 124.32, 117.61, 116.70, 112.63, 71.30, 62.40, 61.86. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_2[\text{M} + \text{H}]^+$: 269.1285; found: 269.1309. IR (neat): ν = 3407, 2923, 1499, 1076, 1019 cm^{-1} .

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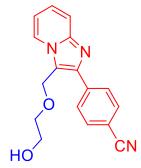
2-((2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3b)

 (Eluent: 70% EtOAc/hexane); 70% yield (52.8 mg); brown solid m.p; 135-137°C. ^1H NMR (200 MHz, CDCl₃) δ 8.18 (d, J = 6.9 Hz, 1H), 7.65 (t, J = 7.9 Hz, 3H), 7.40 (d, J = 8.5 Hz, 2H), 7.27 (t, J = 5.7 Hz, 1H), 6.86 (t, J = 6.8 Hz, 1H), 4.90 (s, 2H), 3.80 (t, J=4.0 Hz 2H), 3.64 (d, J = 4.6 Hz, 2H). ^{13}C NMR (150 MHz, CDCl₃) δ 145.33, 144.52, 134.21, 132.50, 129.91, 128.93, 125.52, 124.26, 117.63, 116.85, 112.86, 71.43, 62.27, 61.91. HRMS(ESI-TOF)m/z: calcd for C₁₆H₁₅N₂O₂Cl[M+H]⁺: 303.0895; found: 303.0919. IR (KBr): ν = 3496, 2931, 1364, 1226, 1092 cm⁻¹.

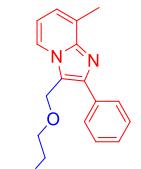
2-((2-(4-bromophenyl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3c)

 (Eluent: 80% EtOAc/hexane); 65% yield (56.2 mg); brown solid m.p; 142-144°C. ^1H NMR (600 MHz, CDCl₃) δ 8.19 (d, J = 6.9 Hz, 1H), 7.67 – 7.62 (m, 3H), 7.60 – 7.57 (m, 2H), 7.29 – 7.25 (m, 1H), 6.89 (t, J = 6.7 Hz, 1H), 4.93 (s, 2H), 3.80 (t, J = 6.0 Hz, 2H), 3.66 (t, J = 6.0 Hz, 2H), ^{13}C NMR (50 MHz, CDCl₃) δ 145.36, 143.83, 132.98, 131.82, 130.16, 125.43, 124.18, 122.40, 120.13, 117.64, 112.79, 71.32, 62.23, 61.88. HRMS(ESI-TOF)m/z: calcd for C₁₆H₁₅N₂O₂Br [M + H]⁺: 349.0390 ; found: 349.0363. IR (KBr): ν = 3401, 2921, 1509, 1101, 753 cm⁻¹.

4-(3-((2-hydroxyethoxy)methyl)imidazo[1,2-a]pyridin-2-yl)benzonitrile (3d)

 (Eluent: 80% EtOAc/hexane); 62% yield (45.4 mg); brown solid m.p; 140-142°C. ^1H NMR(600 MHz, CDCl₃) δ 8.20 (d, J = 6.6 Hz, 1H), 7.88 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 7.9 Hz, 2H), 7.68 (d, J = 9.0 Hz, 1H), 7.33 – 7.29 (m, 1H), 6.93 (t, J = 6.7 Hz, 1H), 4.93 (s, 2H), 3.83 (t, J = 6.0 Hz, 2H), 3.70 (t, J = 6.0 Hz, 2H), ^{13}C NMR (150 MHz, CDCl₃) δ 145.52, 143.48, 138.59, 132.43, 129.04, 126.02, 124.31, 118.95, 117.84, 113.27, 111.52, 105.41, 71.76, 62.11, 61.88. HRMS(ESI-TOF)m/z: calcd for C₁₇H₁₅N₃O₂[M+H]⁺ : 294.1237; found: 294.1219. IR (KBr): ν = 3417, 2927, 2343, 1261, 1104 cm⁻¹.

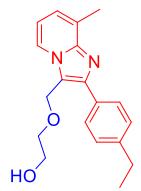
2-((8-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3e)

 (Eluent: 80% EtOAc/hexane); 55% yield (38.7 mg); yellow semi solid; ^1H NMR(200 MHz, CDCl₃) δ 8.02 (d, J = 6.8 Hz, 1H), 7.75 – 7.65 (m, 2H), 7.46 – 7.30 (m, 3H), 7.02 – 6.94 (m, 1H), 6.72 (t, J = 6.8 Hz, 1H), 4.88 (s, 2H), 3.68 (dt, J = 5.3, 2.2 Hz, 2H), 3.55 (dt, J = 3.7, 2.4 Hz, 2H), 2.60 (s, 3H). ^{13}C NMR (150MHz, CDCl₃). δ 145.65, 145.13, 134.21, 128.96, 128.61, 127.99, 127.38, 124.13, 122.17, 117.16, 112.63, 71.28, 62.36,

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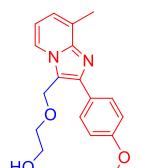
61.61, 17.22. HRMS(ESI-TOF)m/z: calcd for $C_{17}H_{18}N_2O_2[M + Na]^+$: 305.1260; found: 305.1286. IR (neat): ν = 3412, 3050, 1424, 1269, 728 cm^{-1} .

2-((2-(4-ethylphenyl)-8-methylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3f)



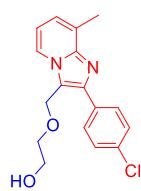
(Eluent: 20% EtOAc/hexane); 71% yield (55.0 mg); sticky liquid; 1H NMR(500 MHz, $CDCl_3$) δ 8.06 (d, J = 6.8 Hz, 1H), 7.66 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.03 (d, J = 6.8 Hz, 1H), 6.77 (t, J = 6.8 Hz, 1H), 4.93 (s, 2H), 3.75 (t, J = 6.0 Hz, 2H), 3.61 (t, J = 6.0 Hz, 2H), 2.71 (q, J =6.0 2H), 2.66 (s, 3H), 1.27 (t, J = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.07, 146.84, 145.54, 132.95, 130.24, 129.56, 128.88, 125.31, 123.37, 118.09, 113.94, 72.41, 63.87, 63.24, 30.11, 18.58, 17.01. HRMS(ESI-TOF)m/z: calcd for $C_{19}H_{22}N_2O_2[M + Na]^+$: 333.1573; found: 333.1585. IR (neat): ν = 3428, 2923, 1461, 1023, 808 cm^{-1} .

2-((2-(4-methoxyphenyl)-8-methylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3g)



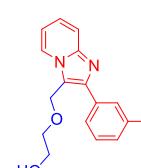
(Eluent: 80% EtOAc/hexane); 65% yield (50.7 mg); brown liquid; 1H NMR(500 MHz, $CDCl_3$) δ 8.00 (d, J = 6.7 Hz, 1H), 7.64 (d, J = 8.7 Hz, 2H), 7.01 – 6.92 (m, 3H), 6.72 (t, J = 6.8 Hz, 1H), 4.88 (s, 2H), 3.80 (s, 3H), 3.80 (t, J = 5.0 Hz, 2H), 3.57 (t, J = 5.0 Hz, 2H), 2.60 (s, 3H). ^{13}C NMR (125MHz, $CDCl_3$) δ 160.98, 147.08, 146.72, 131.46, 128.85, 128.27, 125.25, 123.26, 117.76, 115.51, 113.91, 72.35, 63.91, 63.32, 56.76, 18.58 HRMS(ESI-TOF)m/z: calcd for $C_{18}H_{20}N_2O_3[M + H]^+$: 313.1547; found: 313.1533. IR (neat): ν = 3518, 3006, 1361, 1227, 534 cm^{-1} .

2-((2-(4-chlorophenyl)-8-methylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3h)



(Eluent: 80% EtOAc/hexane); 65% yield (51.3 mg); brown liquid; 1H NMR(200 MHz, $CDCl_3$) δ 8.05 (d, J = 6.8 Hz, 1H), 7.69 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 6.8 Hz, 1H), 6.79 (t, J = 6.8 Hz, 1H), 4.89 (s, 2H), 3.79 – 3.72 (m, 2H), 3.64 – 3.57 (m, 2H), 2.65 (s, 3H). ^{13}C NMR (150MHz, $CDCl_3$) δ 145.38, 142.56, 134.08, 132.80, 130.13, 128.76, 127.64, 123.52, 121.30, 114.56, 112.78, 71.26, 62.36, 61.88, 17.09. HRMS(ESI-TOF)m/z: calcd for $C_{17}H_{17}N_2O_2Cl[M+H]^+$: 317.1051; found: 317.1055. IR (neat): ν = 3400, 2942, 1458, 1039 cm^{-1} .

2-((2-(m-tolyl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3i)

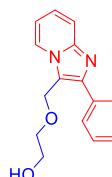


(Eluent: 80% EtOAc/hexane); 61% yield (43.0 mg); yellow solid m.p; 168-170°C 1H NMR(500 MHz, $CDCl_3$) δ 8.10 (d, J = 6.9 Hz, 1H), 7.76 (d, J = 7.2 Hz, 2H), 7.46 (dd, J = 15.5, 7.9 Hz, 3H), 7.39 (t, J = 7.4 Hz, 1H), 6.72 (d, J = 7.0 Hz, 1H), 4.97 (s, 1H).

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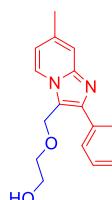
2H), 3.78 (t, J = 5.0 Hz, 2H), 3.64 (t, J = 5.0 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (150MHz, CDCl_3) δ 145.57, 145.20, 138.42, 133.64, 129.51, 129.03, 128.58, 125.81, 125.47, 124.43, 117.28, 116.77, 112.73, 71.36, 63.65, 61.70, 21.55. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_2[\text{M}+\text{H}]^+$: 283.1441; found: 283.1450. IR (KBr): ν = 3426, 2924, 1367, 1099, 802 cm^{-1} .

2-((2-(o-tolyl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3j)



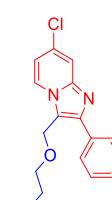
(Eluent: 80% EtOAc/hexane); 60% yield (42.3 mg); yellow semi solid, ^1H NMR(500 MHz, CDCl_3) δ 8.26 (d, J = 6.8 Hz, 1H), 7.66 (d, J = 9.1 Hz, 1H), 7.33 – 7.29 (m, 3H), 7.29 – 7.24 (m, 2H), 6.93 – 6.87 (m, 1H), 4.77 (s, 2H), 3.71 (t, J = 4.4 Hz, 2H), 3.51 (t, J = 4.0 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (150MHz, CDCl_3) δ 145.66, 145.09, 137.71, 132.97, 130.78, 130.49, 128.61, 125.57, 125.44, 124.62, 117.58, 117.34, 112.74, 71.06, 63.69, 62.13, 20.16. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_2[\text{M}+\text{K}]^+$: 321.1000; found: 321.0993. IR (neat): ν = 3414, 2922, 1458, 1101, 754 cm^{-1} .

4-(3-((2-hydroxyethoxy)methyl)-7-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile (3k)



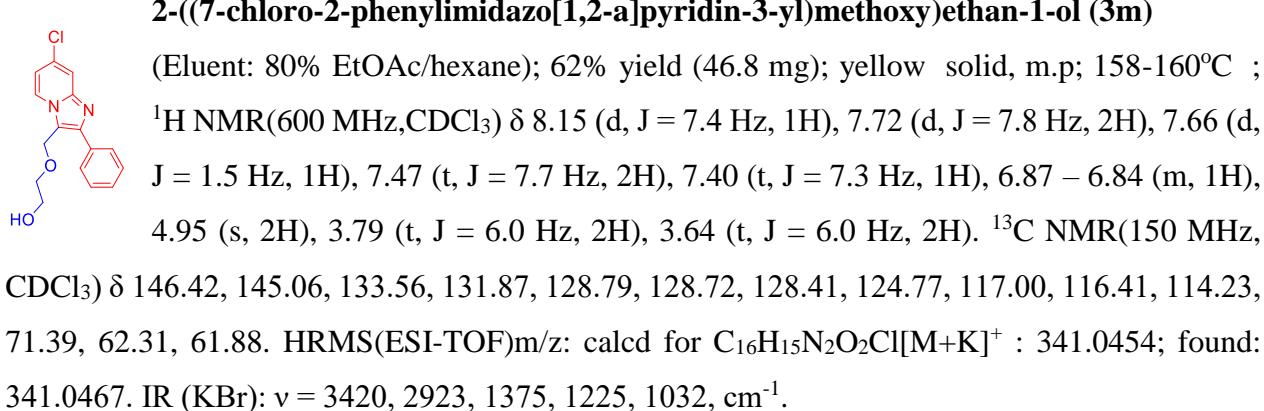
(Eluent: 80% EtOAc/hexane); 66% yield (50.6 mg); brown semi solid; ^1H NMR(600 MHz, CDCl_3) δ 8.00 (d, J = 6.5 Hz, 1H), 7.79 (d, J = 6.9 Hz, 2H), 7.63 (d, J = 7.7 Hz, 2H), 7.36 (s, 1H), 6.69 (d, J = 7.3 Hz, 1H), 4.83 (s, 2H), 3.75 (t, J = 6.0 Hz, 2H), 3.61 (t, J = 6.0 Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (150MHz, CDCl_3) δ 146.36, 146.01, 138.85, 137.12, 132.41, 128.96, 123.43, 119.04, 117.32, 116.18, 115.91, 111.36, 71.57, 62.16, 61.95, 21.50. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_2[\text{M} + \text{H}]^+$: 308.1394; found: 308.1434. IR (neat): ν = 3444, 3056, 2258, 1264, 904 cm^{-1} .

2-((7-chloro-2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3l)

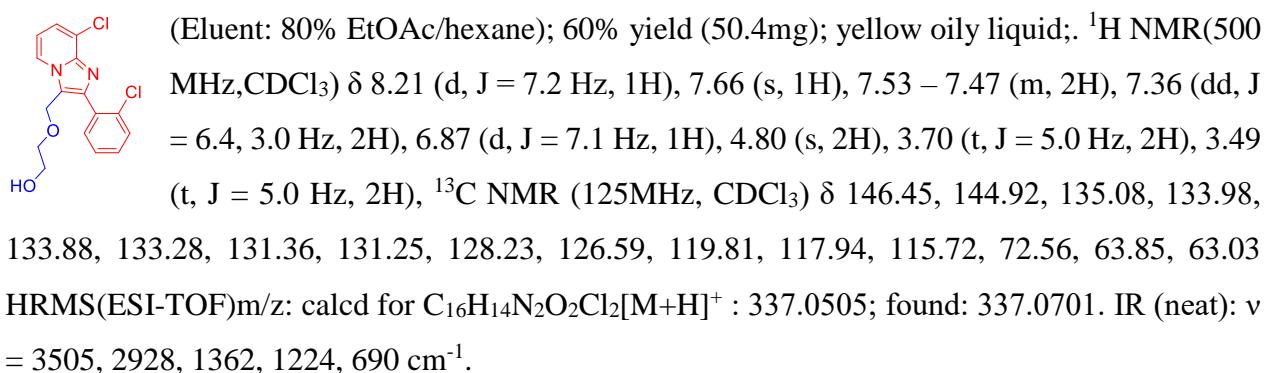


(Eluent: 80% EtOAc/hexane); 62% yield (52.0mg); yellow solid; m.p;155-157°C ^1H NMR(600 MHz, CDCl_3) δ 8.07 (d, J = 7.1 Hz, 1H), 7.60 (dd, J = 10.1, 8.4 Hz, 3H), 7.37 (d, J = 7.4 Hz, 2H), 6.80 (d, J = 7.8 Hz, 1H), 4.86 (d, J = 1.6 Hz, 2H), 3.74 (t, J = 6.0 Hz, 2H), 3.59 (t, J = 6.0 Hz, 2H), ^{13}C NMR (150MHz, CDCl_3) δ 145.32, 143.65, 134.54, 132.02, 129.88, 129.04, 126.92, 122.34, 121.13, 117.94, 117.48, 71.57, 62.20, 61.92. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_2\text{Cl}_2[\text{M}+\text{H}]^+$: 337.0505; found: 337.0533. IR (KBr): ν = 3403, 2926, 1406, 1095, 804 cm^{-1} .

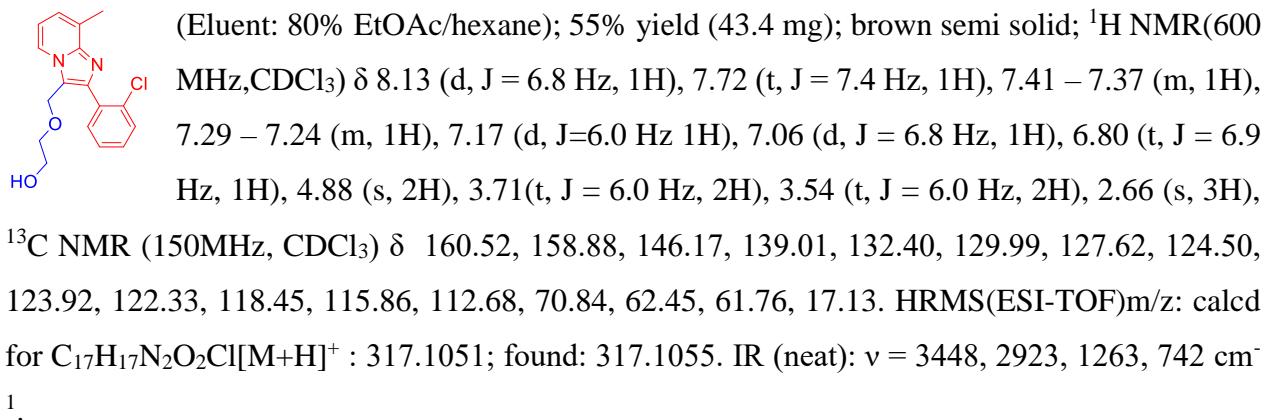
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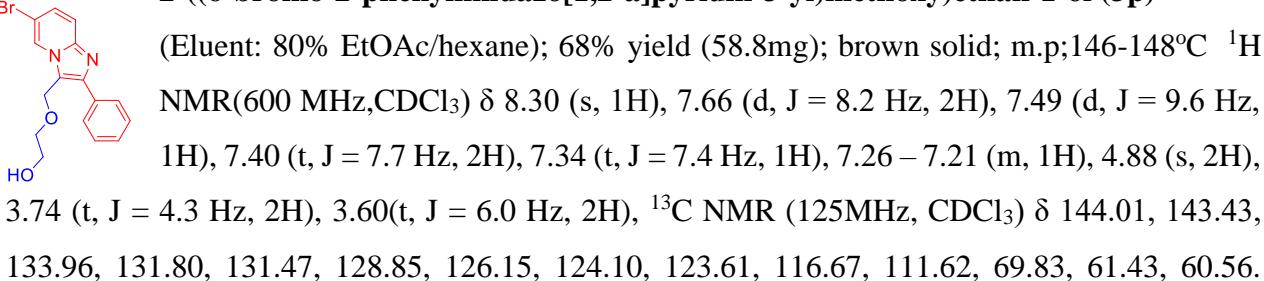
2-((8-chloro-2-(2-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3n)



2-((2-(2-chlorophenyl)-8-methylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3o)



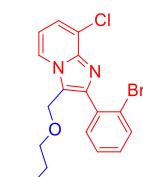
2-((6-bromo-2-phenylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3p)



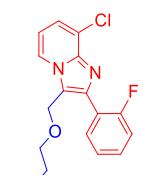
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HRMS(ESI-TOF)m/z: calcd for $C_{16}H_{15}N_2O_2Br[M+Na]^+$:369.0209 ; found: 369.0215. IR (KBr): $\nu = 3441, 2927, 1258, 1093 \text{ cm}^{-1}$.

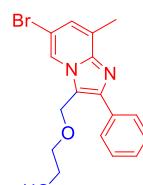
2-((2-(2-bromophenyl)-8-chloroimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3q)

 (Eluent: 80% EtOAc/hexane); 70% yield (66.3 mg); yellow semi solid; ^1H NMR(500 MHz, CDCl_3) δ 8.15 (d, $J = 7.2 \text{ Hz}$, 1H), 7.67 – 7.58 (m, 2H), 7.42 (dd, $J = 13.5, 6.8 \text{ Hz}$, 1H), 7.34 (t, $J = 7.4 \text{ Hz}$, 1H), 7.24 (d, $J = 7.7 \text{ Hz}$, 1H), 6.83 (d, $J = 7.2 \text{ Hz}$, 1H), 4.73 (s, 2H), 3.64 (t, $J = 5.0 \text{ Hz}$, 2H), 3.42 (t, $J = 5.0 \text{ Hz}$, 2H), ^{13}C NMR (125MHz, CDCl_3) δ 146.74, 146.31, 136.06, 134.41, 134.34, 133.87, 131.57, 128.75, 128.26, 126.56, 119.46, 118.05, 115.76, 111.11, 72.45, 63.89, 63.11. HRMS(ESI-TOF)m/z: calcd for $C_{16}H_{14}N_2O_2ClBr[M+Na]^+$: 402.9819; found: 402.9837. IR (neat): $\nu = 3367, 2924, 1258, 1022, 803 \text{ cm}^{-1}$.

2-((8-chloro-2-(2-fluorophenyl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol(3r)

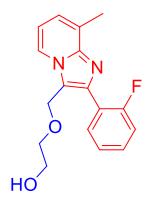
 (Eluent: 80% EtOAc/hexane); 65% yield (52 mg); yellow semi solid; ^1H NMR(500 MHz, CDCl_3) δ 8.22 (d, $J = 7.3 \text{ Hz}$, 1H), 7.67 (dd, $J = 16.5, 1.3 \text{ Hz}$, 2H), 7.40 (td, $J = 7.3, 1.4 \text{ Hz}$, 1H), 7.27 (dd, $J = 8.2, 6.7 \text{ Hz}$, 1H), 7.22 – 7.15 (m, 1H), 6.86 (dd, $J = 7.2, 1.8 \text{ Hz}$, 1H), 4.88 (s, 2H), 3.74 (t, $J = 5.0 \text{ Hz}$, 2H), 3.57 (t, $J = 5.0 \text{ Hz}$, 2H), ^{13}C NMR (125MHz, CDCl_3) δ 161.92, 159.95, 146.82, 141.52, 133.49, 131.77, 131.71, 126.57, 125.99, 122.92, 119.96, 117.80, 117.43, 72.61, 63.77, 63.09. HRMS(ESI-TOF)m/z: calcd for $C_{16}H_{14}N_2O_2Cl F[M + H]^+$: 343.0620; found: 343.0614. IR (neat): $\nu = 3522, 3004, 1367, 1235, 531 \text{ cm}^{-1}$.

2-((6-bromo-8-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3s)

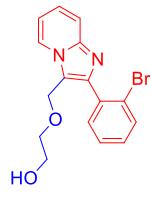
 (Eluent: 80% EtOAc/hexane); 68% yield (61.2 mg); brown semi solid; ^1H NMR(600 MHz, CDCl_3) δ 8.24 (s, 1H), 7.74 (d, $J = 7.9 \text{ Hz}$, 2H), 7.47 (t, $J = 7.5 \text{ Hz}$, 2H), 7.40 (t, $J = 7.4 \text{ Hz}$, 1H), 7.15 (s, 1H), 4.93 (s, 2H), 3.79 (t, $J = 6.0 \text{ Hz}$, 2H), 3.64 (t, $J = 6.0 \text{ Hz}$, 2H), 2.66 (s, 3H), ^{13}C NMR (150MHz, CDCl_3) δ 145.98, 145.92, 144.29, 139.96, 133.87, 128.89, 128.77, 127.35, 122.27, 117.43, 107.28, 71.29, 62.38, 61.91, 17.06. HRMS(ESI-TOF)m/z: calcd for $C_{17}H_{18}N_2O_2Br[M+Na]^+$:361.0546 ; found: 361.2842. IR (neat): $\nu = 3405, 2924, 1254, 1034, 805 \text{ cm}^{-1}$.

2-((2-(2-fluorophenyl)-8-methylimidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3t)

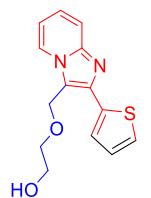
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 (Eluent: 20% EtOAc/hexane); 60% yield (45.0 mg); thick liquid; ^1H NMR(600 MHz, CDCl_3) δ 8.13 (d, J = 6.8 Hz, 1H), 7.56 – 7.53 (m, 1H), 7.49 (dd, J = 5.7, 3.5 Hz, 1H), 7.35 (dd, J = 5.7, 3.5 Hz, 2H), 7.07 (d, J = 6.8 Hz, 1H), 6.81 (t, J = 6.7 Hz, 1H), 4.80 (s, 2H), 3.67 (t, J = 6.0 Hz, 2H), 3.46 (t, J = 6.0 Hz, 2H), 2.65 (s, 3H), ^{13}C NMR (150MHz, CDCl_3) δ 145.84, 142.46, 133.99, 133.40, 132.80, 129.76, 127.76, 126.84, 124.07, 122.49, 118.31, 112.82, 70.88, 62.61, 61.78, 17.25. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{17}\text{H}_{17}\text{N}_2\text{O}_2\text{F}[\text{M}+\text{Na}]^+$:323.1166 ; found: 323.1176. IR (neat): ν = 3461, 2923, 1363, 1092, 801 cm^{-1} .

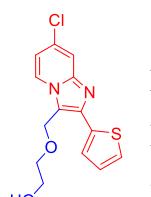
2-((2-(2-bromophenyl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3u)

 (Eluent: 80% EtOAc/hexane); 71% yield (61.4 mg); brown semi solid; ^1H NMR (600 MHz, CDCl_3) δ 8.27 (d, J = 6.7 Hz, 1H), 7.70 – 7.67 (m, 2H), 7.49 (d, J = 7.2 Hz, 1H), 7.40 (d, J = 7.4 Hz, 1H), 7.31 – 7.27 (m, 2H), 6.90 (t, J = 6.5 Hz, 1H), 4.81 (s, 2H), 3.68 (t, J = 6.0 Hz, 2H), 3.48 (t, J = 6.0 Hz, 2H), ^{13}C NMR (50MHz, CDCl_3) δ 145.08, 144.43, 135.03, 132.92, 132.58, 129.97, 127.26, 125.26, 124.79, 123.92, 117.75, 117.69, 112.74, 71.03, 62.52, 61.58, HRMS(ESI-TOF)m/z: calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}_2\text{Br}[\text{M}+\text{Na}]^+$: 369.0209; found: 369.0237. IR (neat): ν = 3407, 2929, 1265, 1102, 741 cm^{-1} .

2-((2-(thiophen-2-yl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3v)

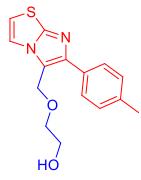
 (Eluent: 20% EtOAc/hexane); 69% yield (47.2 mg); yellow semi solid; ^1H NMR(200 MHz, CDCl_3) δ 8.19 (d, J = 6.9 Hz, 1H), 7.68 (dd, J = 3.0, 1.3 Hz, 1H), 7.61 (s, 1H), 7.55 (dd, J = 5.0, 1.2 Hz, 1H), 7.42 (dd, J = 5.0, 3.0 Hz, 1H), 7.25 (d, J = 1.6 Hz, 1H), 6.86 (t, J = 6.8 Hz, 1H), 5.01 (s, 2H), 3.80 – 3.73 (m, 2H), 3.69 – 3.62 (m, 2H), ^{13}C NMR (150MHz, CDCl_3) δ 145.27, 141.44, 136.90, 127.69, 126.16, 125.37, 124.13, 123.55, 117.48, 116.35, 112.73, 71.14, 62.16, 61.96. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2\text{SO}_2[\text{M}+\text{Na}]^+$:275.0849 ; found:275.0857. IR (neat): ν = 3407, 3055, 1363, 1268, 738 cm^{-1} .

2-((7-chloro-2-(thiophen-2-yl)imidazo[1,2-a]pyridin-3-yl)methoxy)ethan-1-ol (3w)

 (Eluent: 80% EtOAc/hexane); 65% yield (50.0 mg); brown liquid ^1H NMR(200 MHz, CDCl_3) δ 8.11 (d, J = 7.3 Hz, 1H), 7.61 (d, J = 1.9 Hz, 1H), 7.44 (dd, J = 3.6, 1.0 Hz, 1H), 7.39 (dd, J = 5.1, 1.0 Hz, 1H), 7.12 (dd, J = 5.1, 3.6 Hz, 1H), 6.82 (dd, J = 7.3, 2.0 Hz, 1H), 5.04 (s, 2H), 3.77 (dd, J = 5.1, 3.4 Hz, 2H), 3.64 (dd, J = 5.0, 3.3 Hz, 2H). ^{13}C NMR (50MHz, CDCl_3) δ 145.05, 136.11, 134.68, 132.13, 127.82, 126.46, 126.26, 126.01, 124.60, 116.13, 114.29, 71.16, 61.90, 61.80. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{SClO}_2[\text{M}+\text{Na}]^+$:309.0459 ; found:309.0597. IR (neat): ν = 3418, 2924, 1362, 1229, 801 cm^{-1} .

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2-((6-(p-tolyl)imidazo[2,1-b]thiazol-5-yl)methoxy)ethan-1-ol (4a)



(Eluent: 80% EtOAc/hexane); 70% yield (50.4mg); brown semi solid; ^1H NMR(500 MHz, CDCl_3) δ 7.57 (d, $J = 8.0$ Hz, 2H), 7.53 (d, $J = 4.5$ Hz, 1H), 7.26 (d, $J = 3.9$ Hz, 2H), 6.84 (d, $J = 4.4$ Hz, 1H), 4.87 (s, 2H), 3.77 (t, $J = 5.0$ Hz, 2H), 3.62 (t, $J = 5.0$ Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 148.55, 145.59, 136.45, 130.25, 128.30, 126.77, 117.33, 116.94, 111.55, 70.04, 62.08, 60.83, 20.21. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{SO}_2[\text{M} + \text{Na}]^+$:311.0825 ; found: 311.0837. IR (neat): $\nu = 3377, 2927, 1263, 1095, 856\text{ cm}^{-1}$.

2-((6-(4-ethylphenyl)imidazo[2,1-b]thiazol-5-yl)methoxy)ethan-1-ol (4b)



(Eluent: 80% EtOAc/hexane); 71% yield (53.6 mg); brown solid m.p;130-131°C; ^1H NMR(200 MHz, CDCl_3) δ 7.57 (dd, $J = 11.5, 6.3$ Hz, 3H), 7.28 (d, $J = 5.9$ Hz, 2H), 6.85 (d, $J = 4.5$ Hz, 1H), 4.88 (s, 2H), 3.80 (t, $J = 4.0$ Hz, 2H), 3.64 (t, $J = 6.0$ Hz, 2H), 2.70 (q, $J = 7.6$ Hz, 2H), 1.27 (t, $J = 3.4$ Hz, 3H). ^{13}C NMR (150MHz, CDCl_3) δ 149.48, 146.24, 143.80, 131.46, 128.17, 127.91, 118.68, 118.32, 112.45, 71.42, 63.07, 61.62, 28.67, 15.57. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{SO}_2[\text{M} + \text{Na}]^+$:325.0981 ; found: 325.0996. IR (KBr): $\nu = 3529, 3006, 1368, 1231, 535\text{ cm}^{-1}$.

2-((6-(4-chlorophenyl)imidazo[2,1-b]thiazol-5-yl)methoxy)ethan-1-ol (4c)



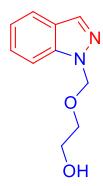
(Eluent: 80% EtOAc/hexane); 62% yield (47.7mg); semi brown solid ^1H NMR(200 MHz, CDCl_3) δ 7.63 (d, $J = 8.6$ Hz, 2H), 7.54 (d, $J = 4.5$ Hz, 1H), 7.44 – 7.38 (m, 2H), 6.88 (d, $J = 4.5$ Hz, 1H), 4.85 (s, 2H), 3.81 (t, $J = 4.0$ Hz, 2H), 3.64 (t, $J = 4.0$ Hz, 2H), ^{13}C NMR (150MHz, CDCl_3) δ 149.77, 145.31, 133.60, 132.68, 129.10, 128.85, 118.98, 118.04, 112.98, 71.40, 63.01, 61.84. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{SClO}_2[\text{M} + \text{H}]^+$: 309.0459; found: 309.2061. IR (neat): $\nu = 3397, 2921, 1470, 1261, 1097, \text{cm}^{-1}$.

2-((6-(4-bromophenyl)imidazo[2,1-b]thiazol-5-yl)methoxy)ethan-1-ol (4d)



(Eluent: 80% EtOAc/hexane); 60% yield (52.6 mg); brown solid m.p;120-122°C; ^1H NMR(200 MHz, CDCl_3) δ 7.54 (d, $J = 5.8$ Hz, 5H), 6.87 (d, $J = 4.5$ Hz, 1H), 4.84 (s, 2H), 3.78 (dd, $J = 5.2, 3.7$ Hz, 2H), 3.64 – 3.58 (m, 2H). ^{13}C NMR (150MHz, CDCl_3) δ 149.89, 145.49, 133.19, 131.85, 129.44, 121.87, 118.93, 117.97, 113.11, 71.29, 63.07, 61.96. HRMS(ESI-TOF)m/z: calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2\text{SBrO}_2[\text{M} + \text{H}]^+$:355.0110; found: 354.9932. IR (KBr): $\nu = 3359, 2927, 1472, 1092, 804\text{ cm}^{-1}$.

2-((1H-indazol-1-yl)methoxy)ethan-1-ol (5a)



(Eluent: 50% EtOAc/hexane); 70% yield (33.6 mg); yellow thick liquid ^1H NMR(500 MHz, CDCl_3) δ 8.04 (s, 1H), 7.76 (d, $J = 8.1$ Hz, 1H), 7.58 (d, $J = 8.4$ Hz, 1H), 7.45 (dd, $J = 11.3, 4.0$ Hz, 1H), 7.22 (t, $J = 7.5$ Hz, 1H), 5.83 (s, 2H), 3.67 (t, $J = 6.0$ Hz, 2H), 3.62 (t, $J = 6.0$ Hz, 2H), ^{13}C NMR (50 MHz, CDCl_3) δ 139.80, 138.26, 134.62, 127.12, 124.80, 121.54, 121.25, 109.36, 78.19, 77.68, 77.05, 76.41, 70.41, 61.69, HRMS(ESI-TOF)m/z: calcd for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_2[\text{M} + \text{H}]^+$: 193.0972 ; found: 193.0978. IR (neat): $\nu = 3431, 2926, 1260, 812, 514 \text{ cm}^{-1}$.

bis(imidazo[1,2-a]pyridin-3-yl)methane (12)¹

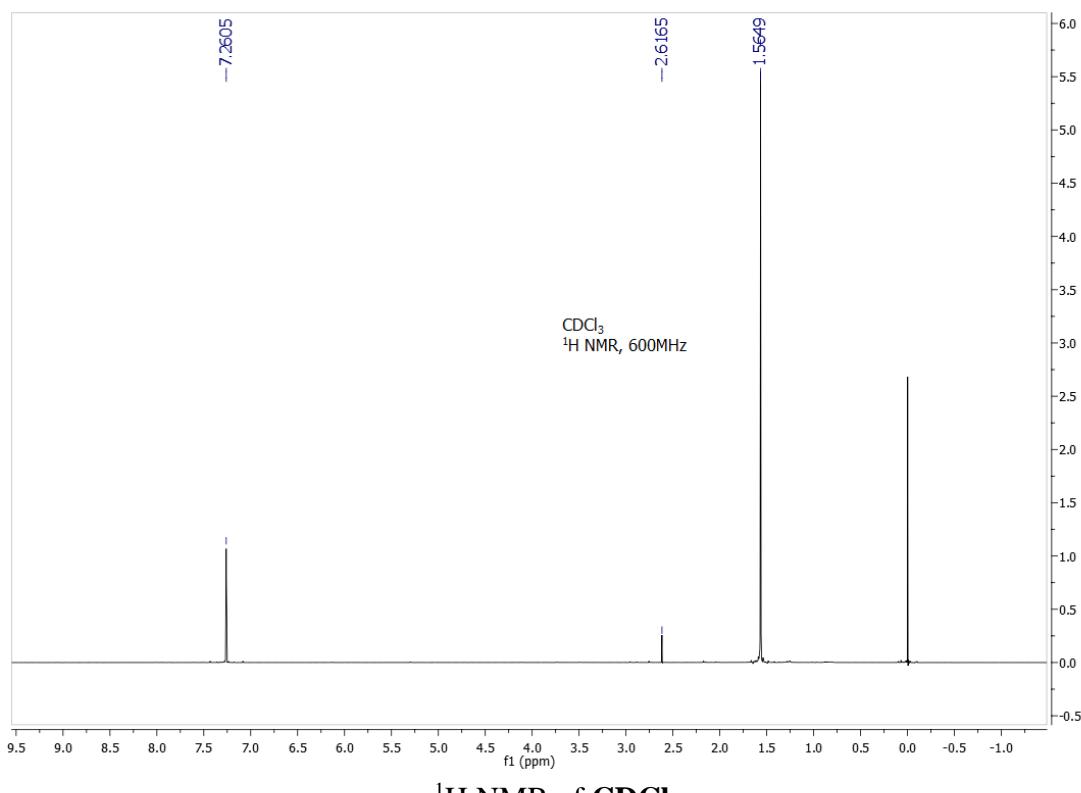


Eluent: 60% EtOAc/hexane); 65% yield (40.3 mg); yellow thick liquid ^1H NMR (600 MHz, CDCl_3) δ 8.23 (d, $J = 6.8$ Hz, 1H), 8.15 (d, $J = 5.0$ Hz, 1H), 7.65 – 7.62 (m, 2H), 7.45 (d, $J = 8.1$ Hz, 1H), 7.26 (s, 1H), 7.23 – 7.20 (m, 1H), 6.82 (t, $J = 6.7$ Hz, 1H), 6.68 – 6.65 (m, 1H), 6.49 (d, $J = 8.3$ Hz, 1H), 4.90 (s, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 146.16, 132.50, 124.21, 123.31, 118.22, 118.04, 112.64, 20.10. IR (neat): $\nu = 2923, 1454, 1264, 1093, 802 \text{ cm}^{-1}$.

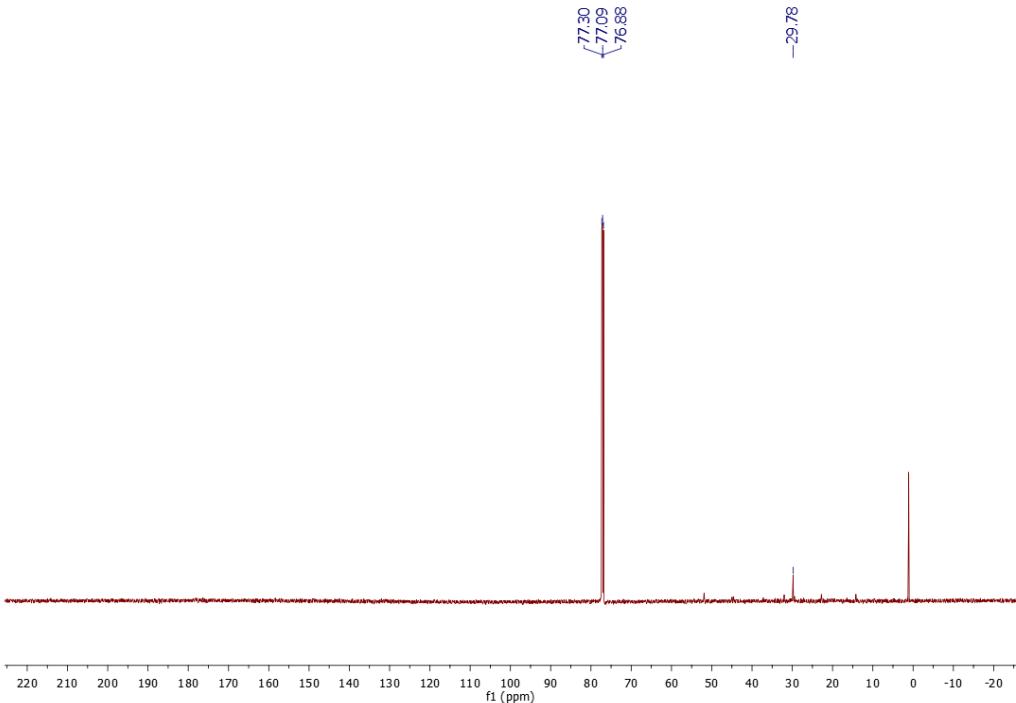
3-References

- (1) P. Liu, Z. Shen, Y. Yuan and P. Sun, Synthesis of Symmetrical Methylene-Bridged Imidazoheterocycles Using DMSO as Methylene Source under Metal-Free Conditions, *Org. Biomol. Chem.*, 2016, **14**, 6523.

4. Copies of ^1H and ^{13}C NMR of spectra

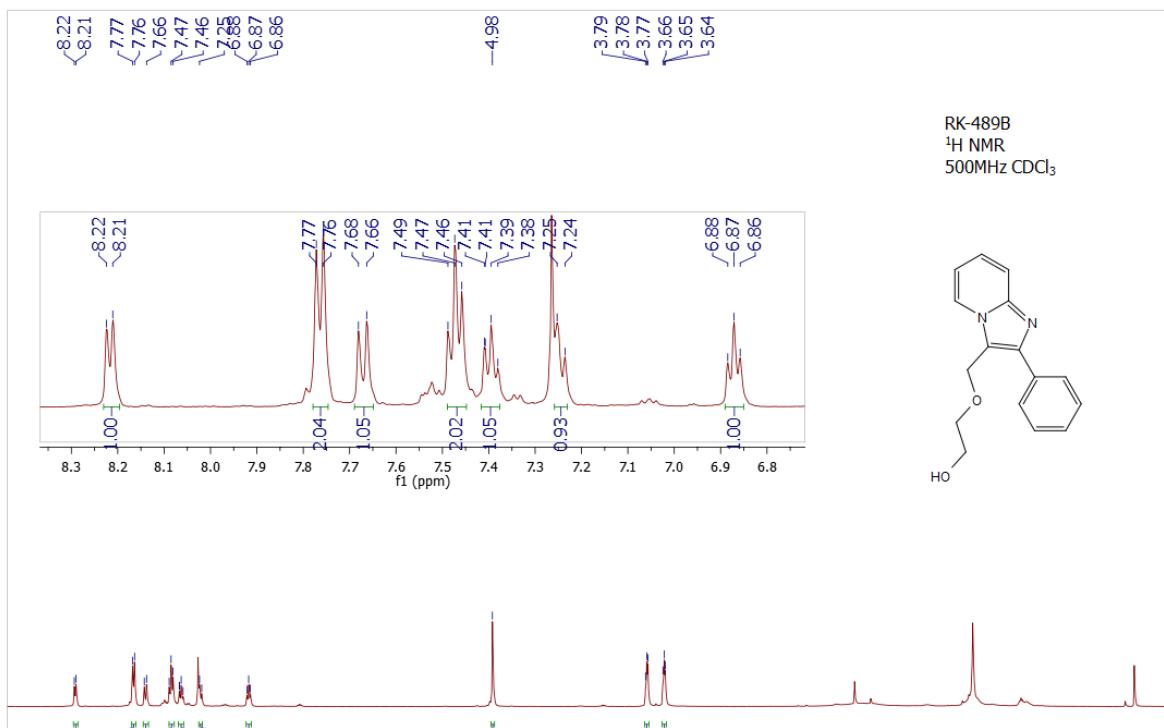


^1H NMR of CDCl_3

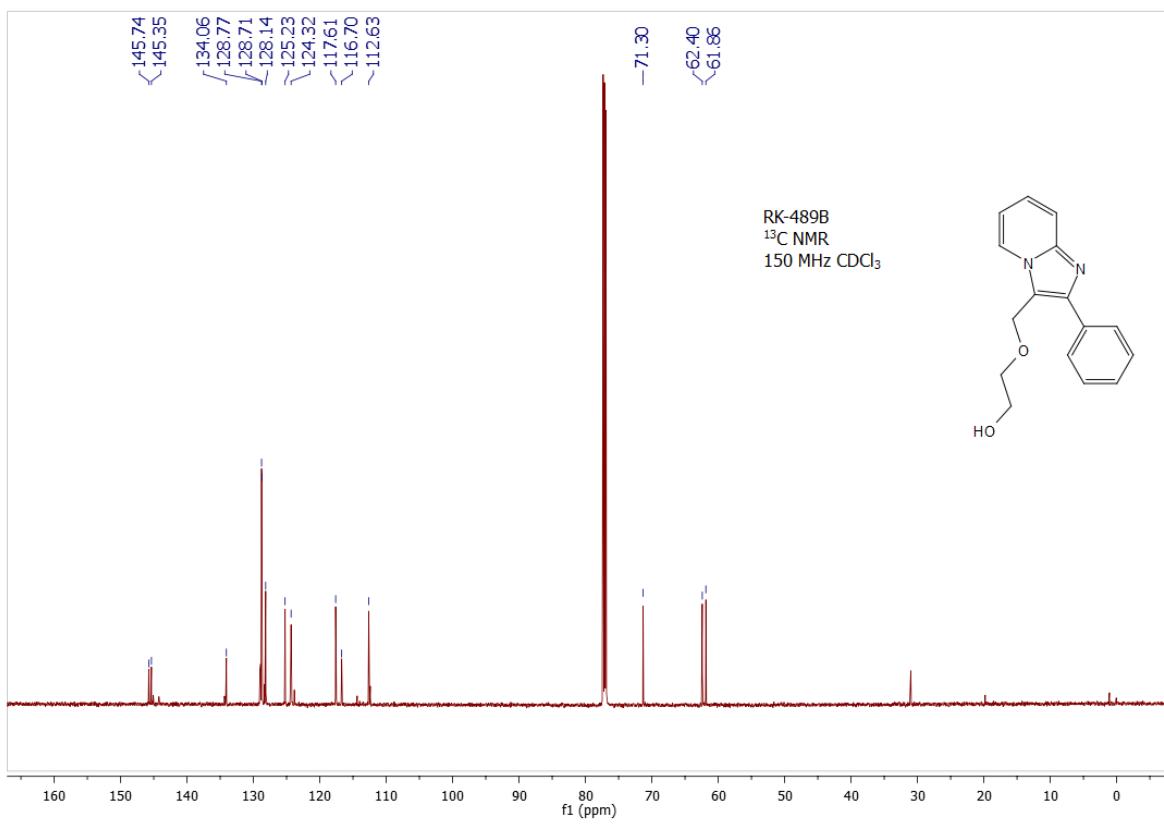


^{13}C NMR of CDCl_3

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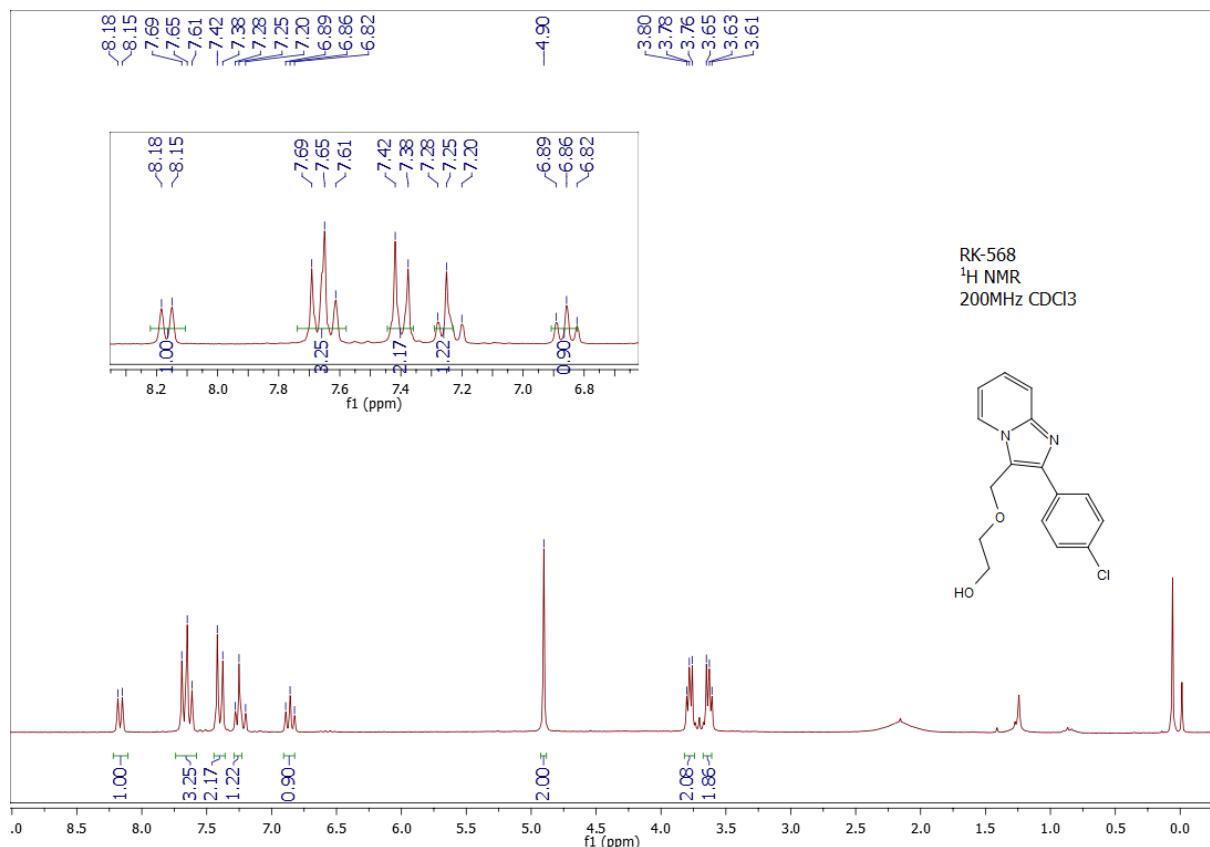


¹H NMR 3a

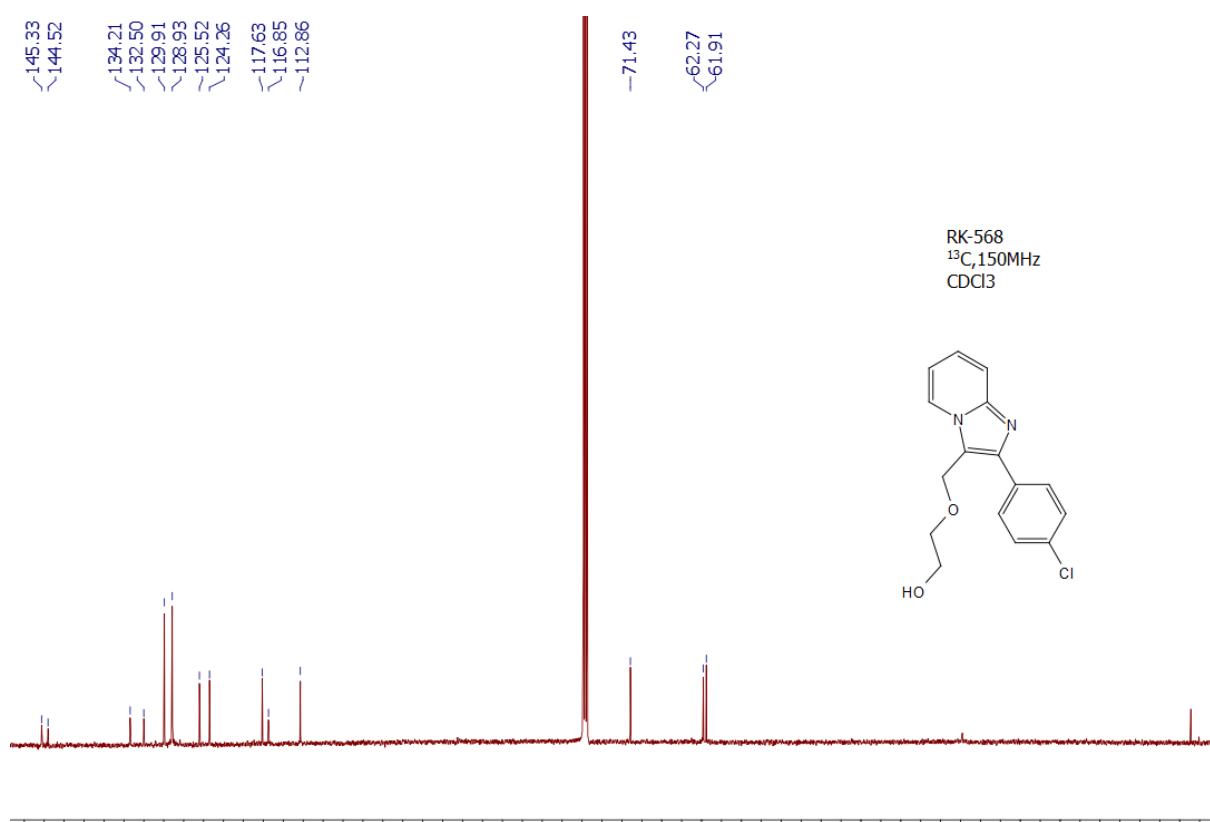


¹³C NMR 3a

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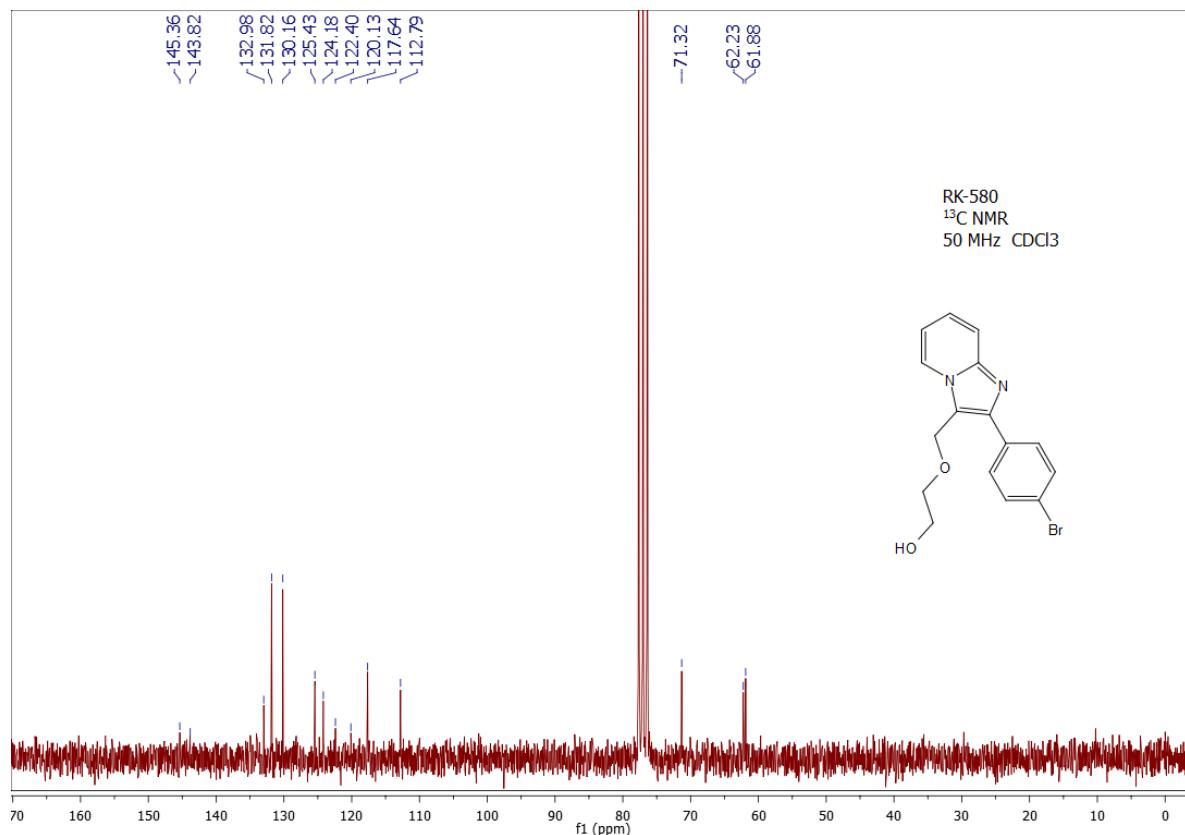
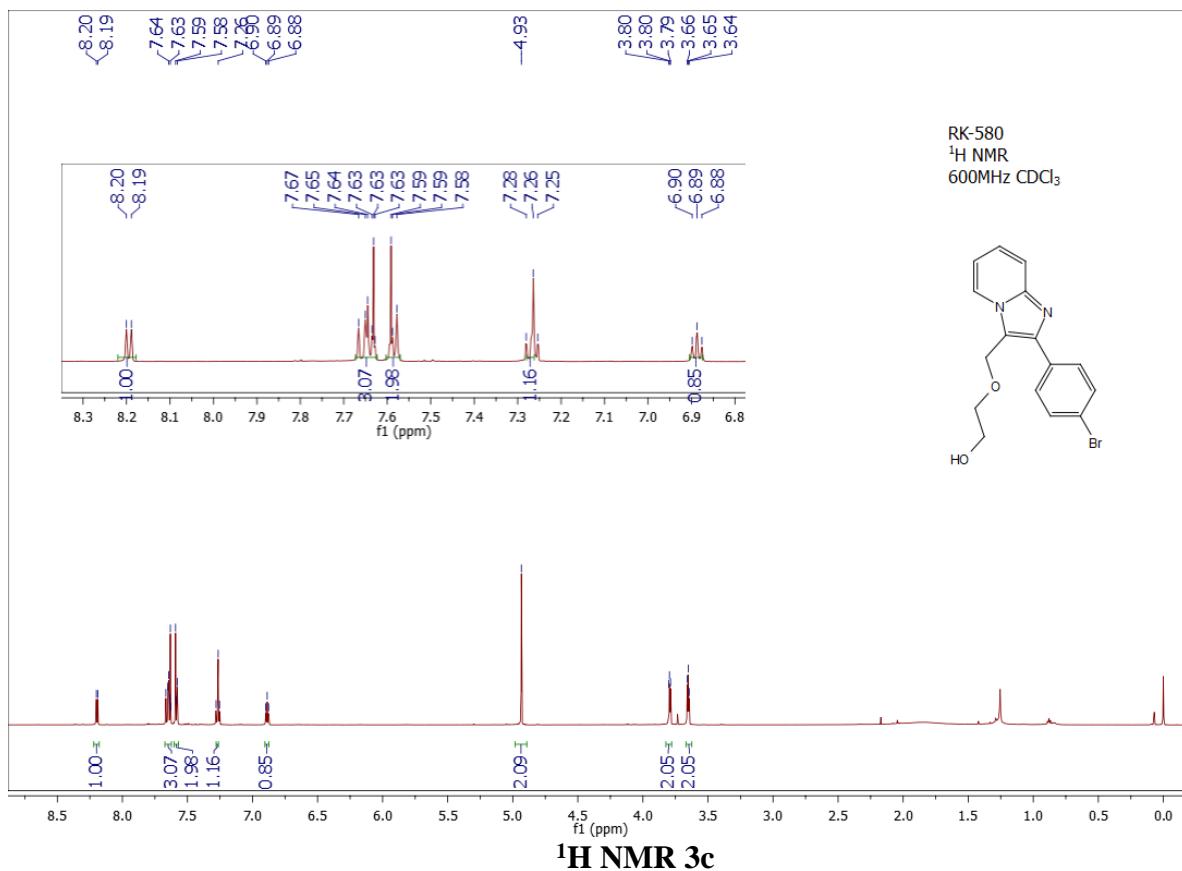


¹H NMR 3b

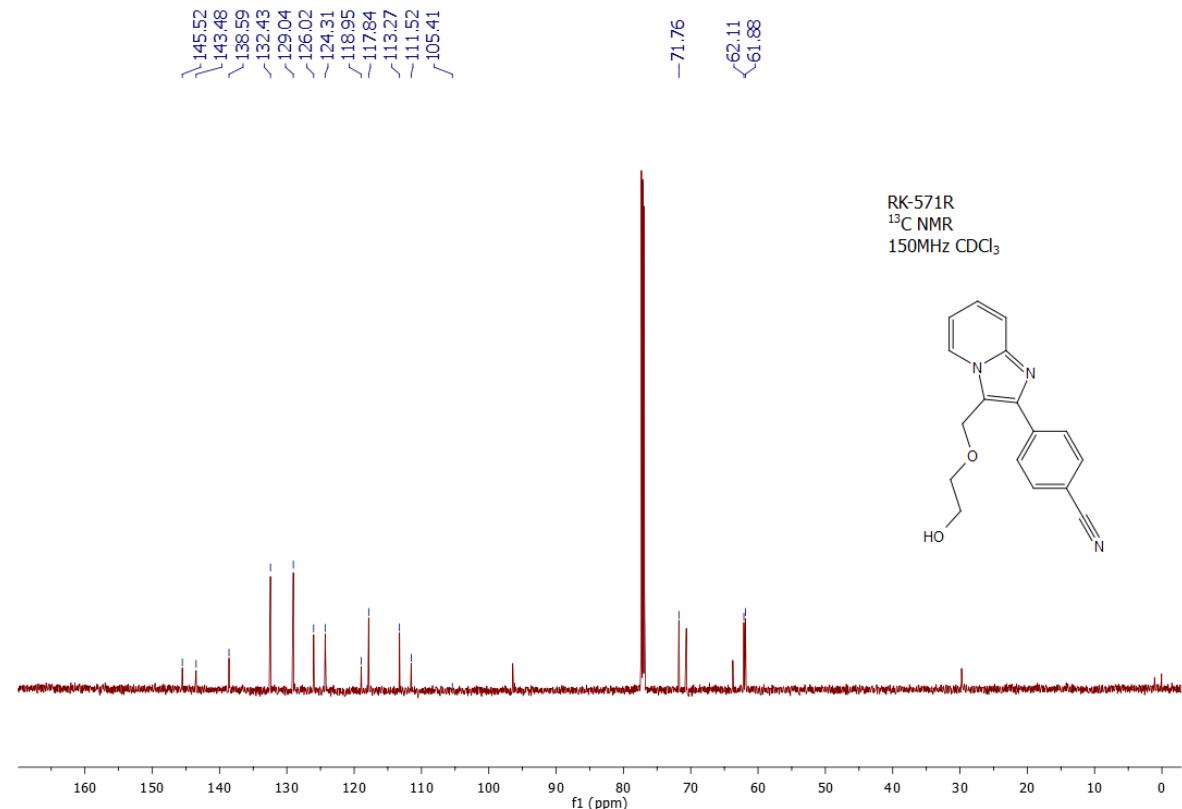
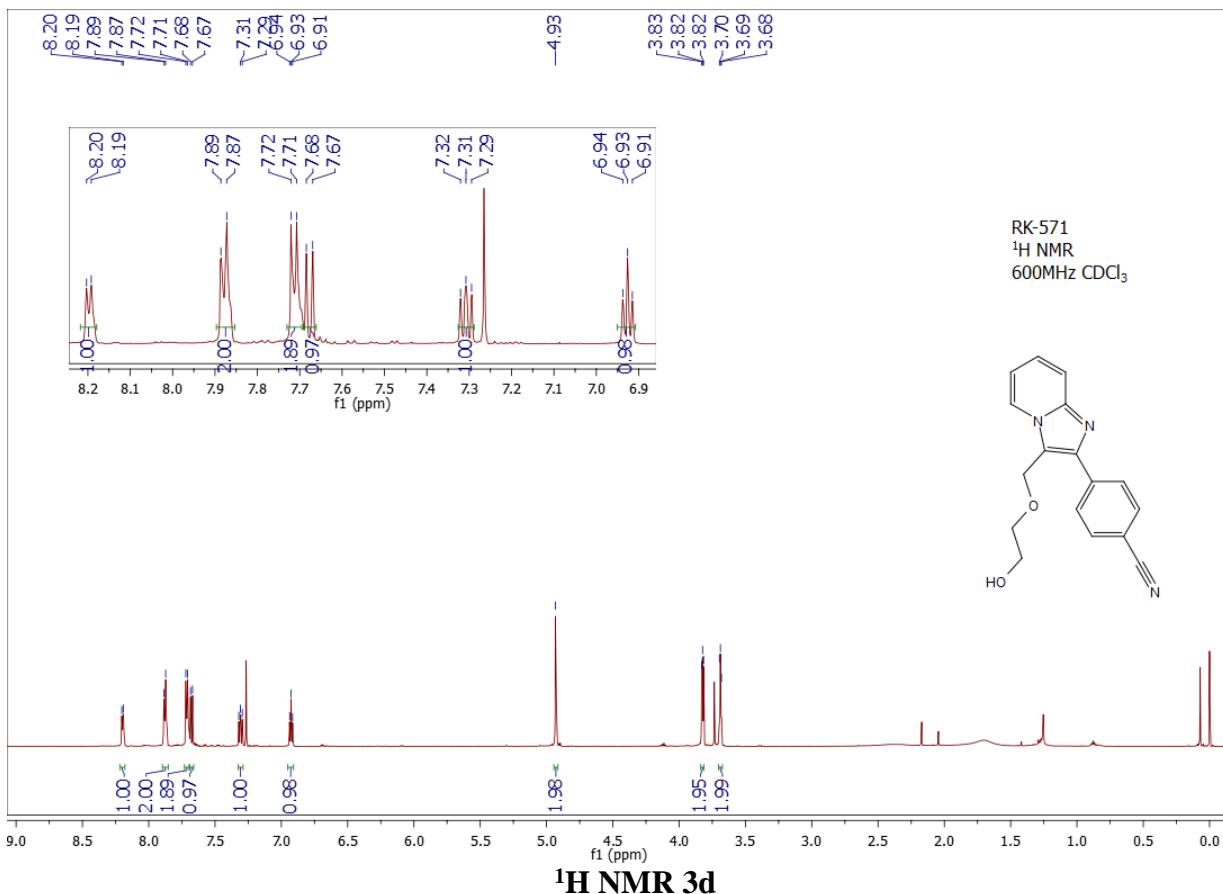


¹³C NMR 3b

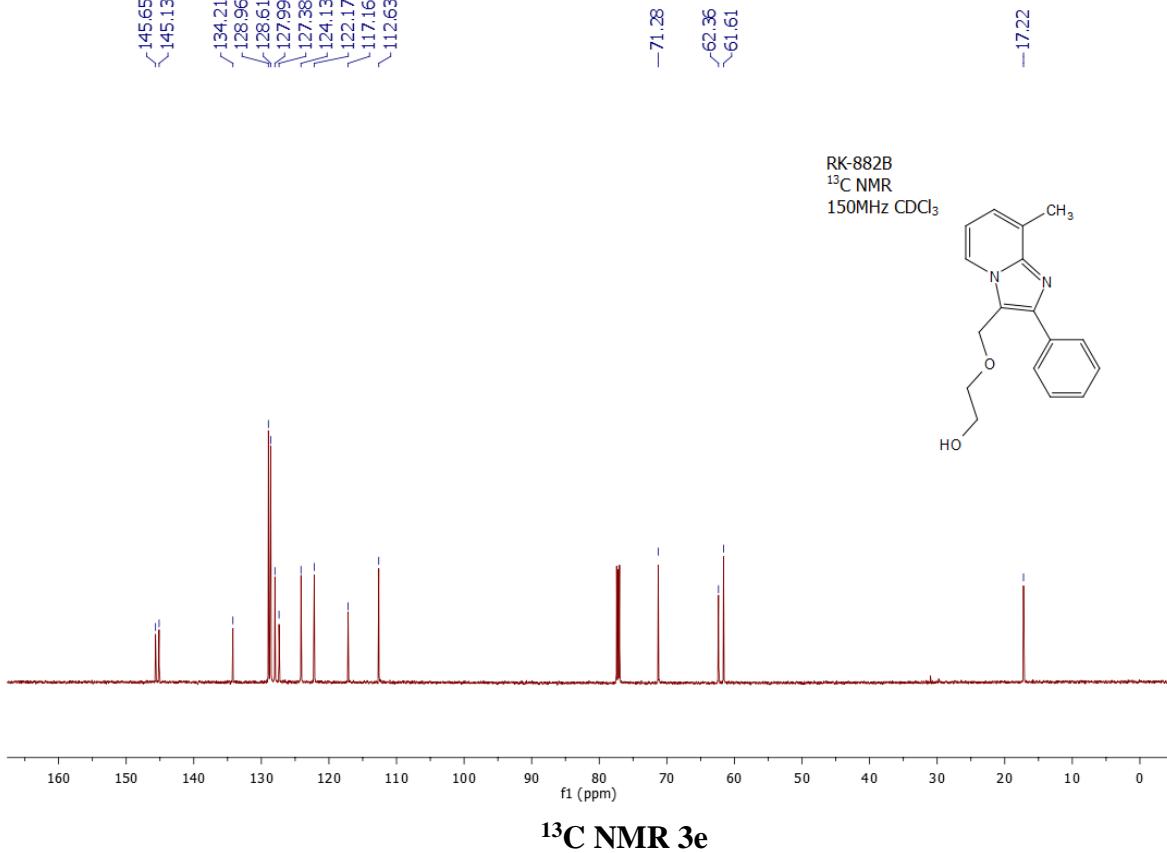
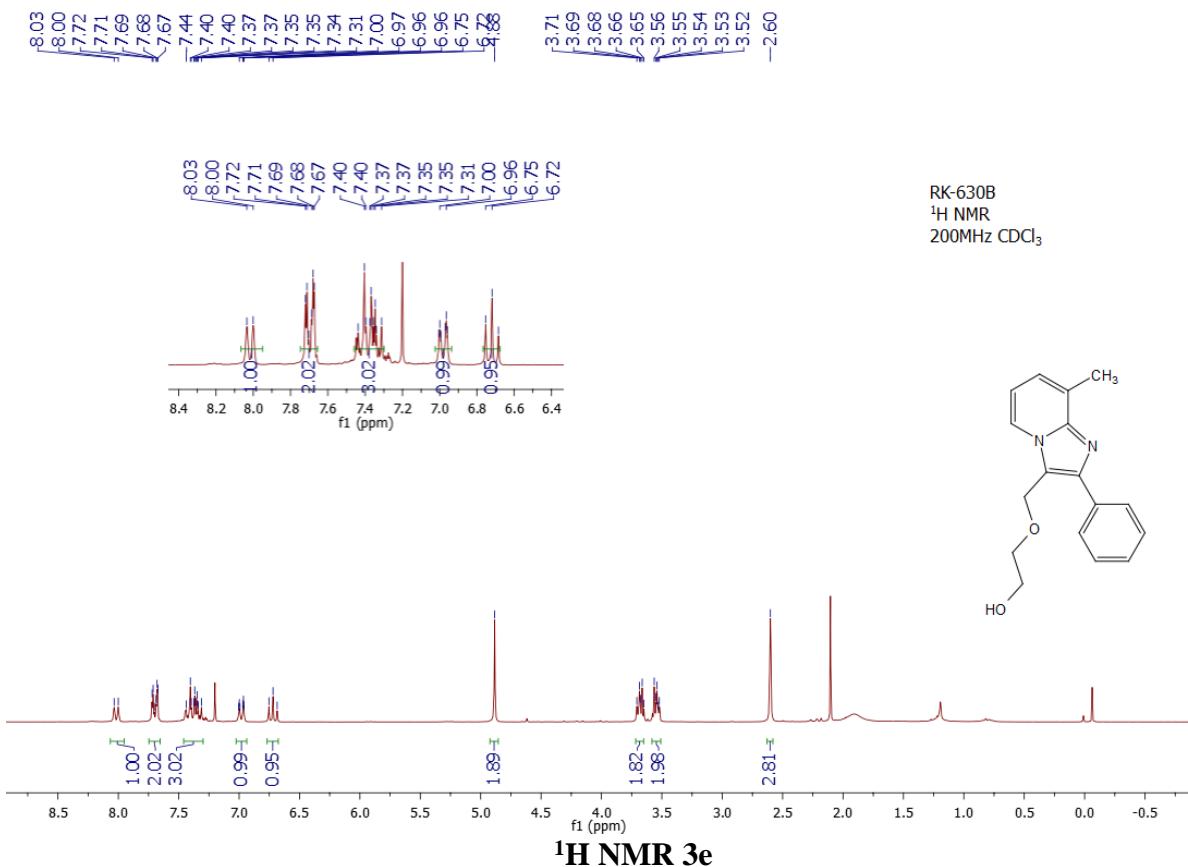
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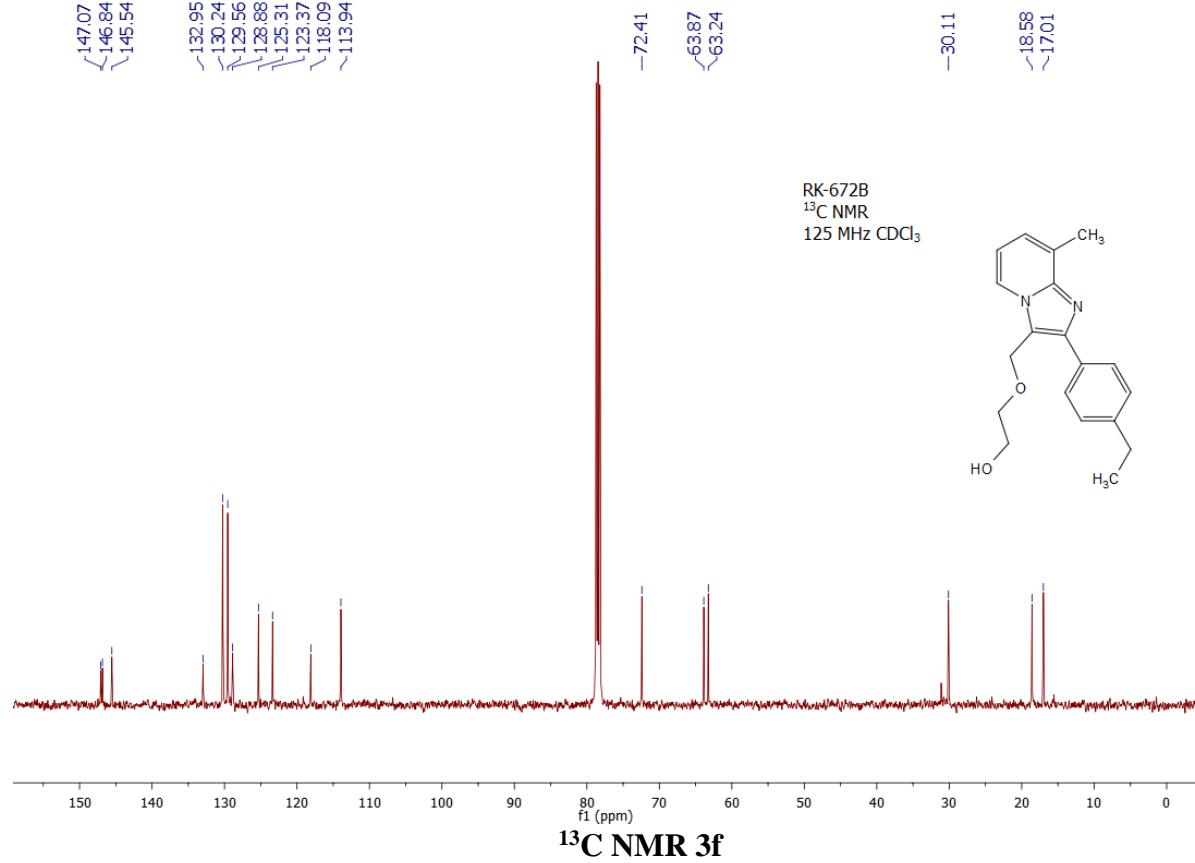
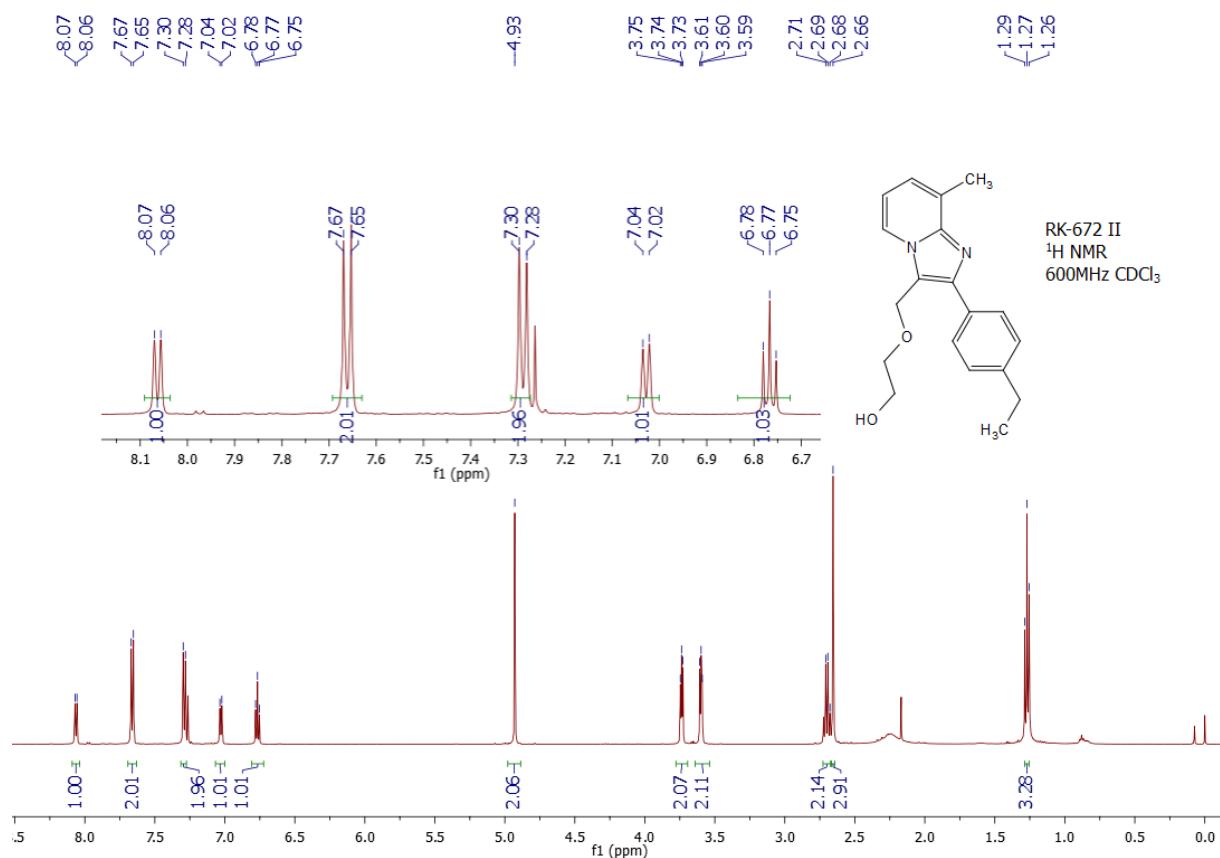
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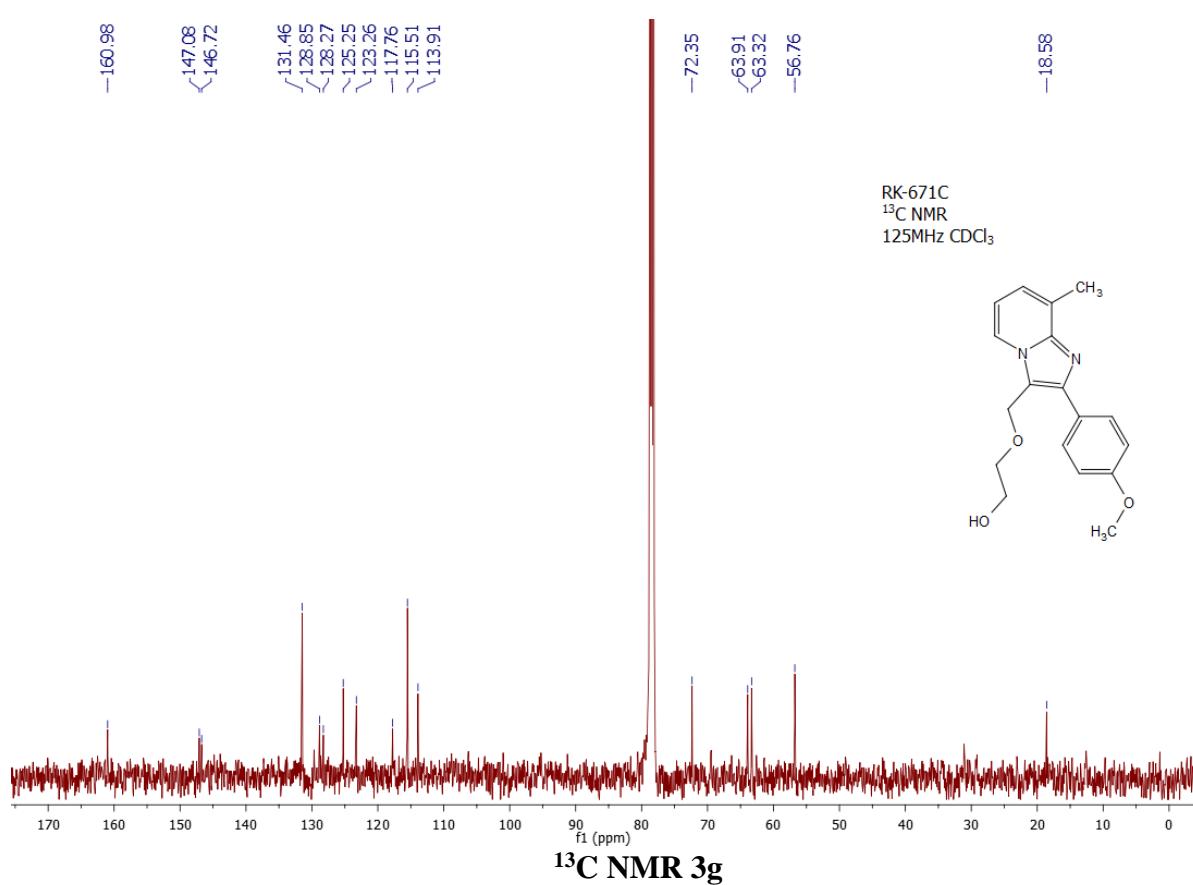
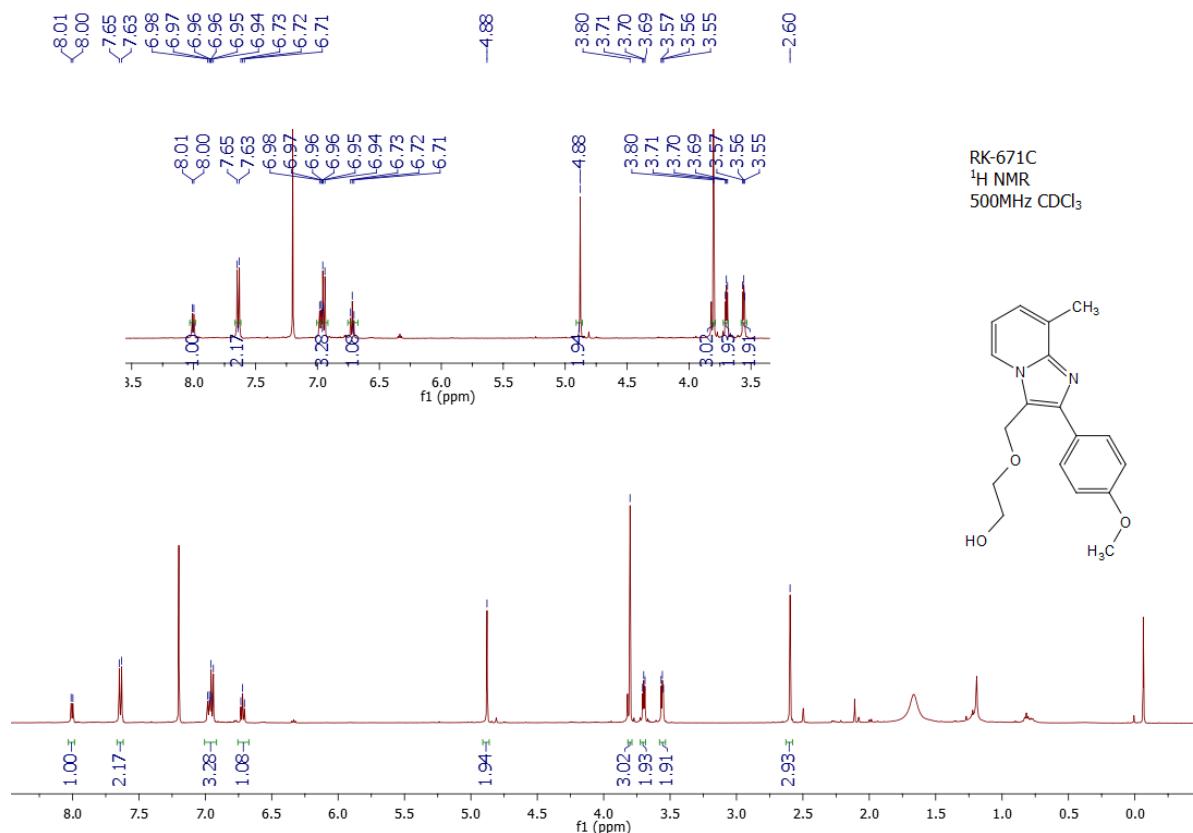


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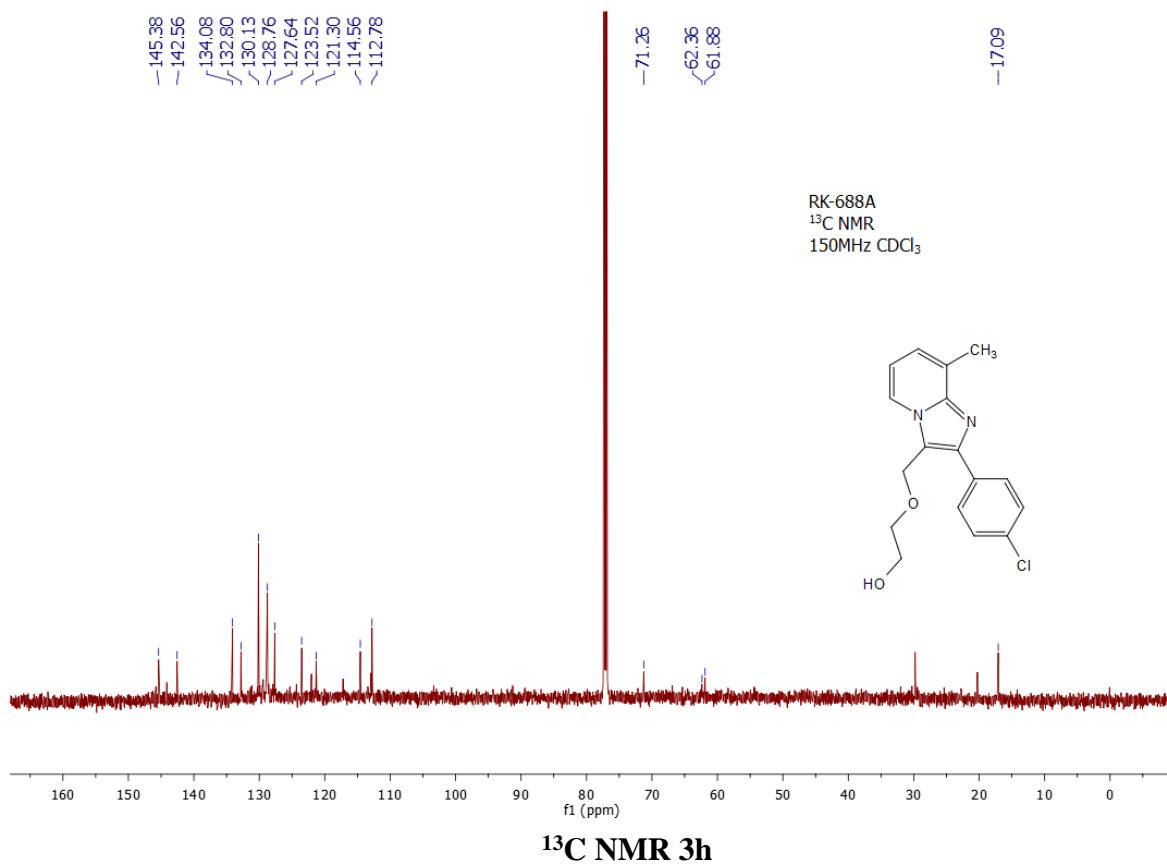
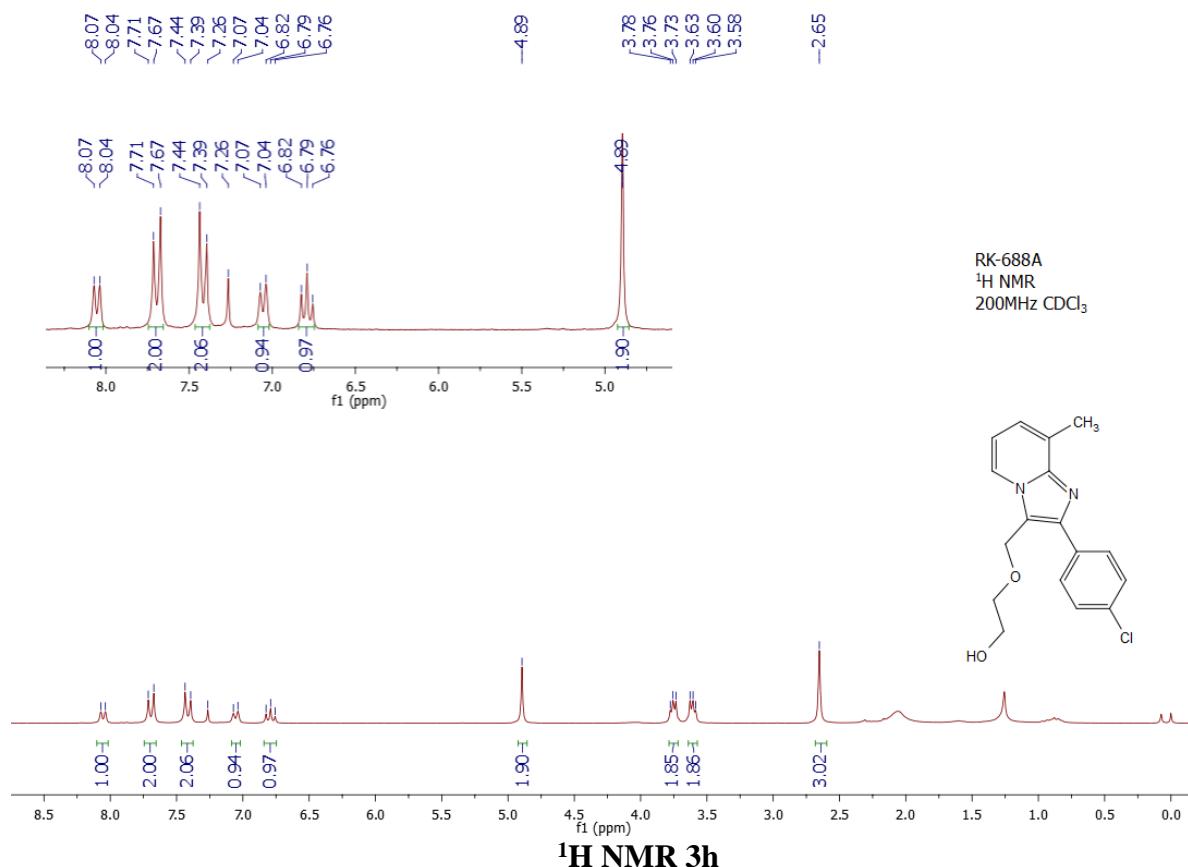


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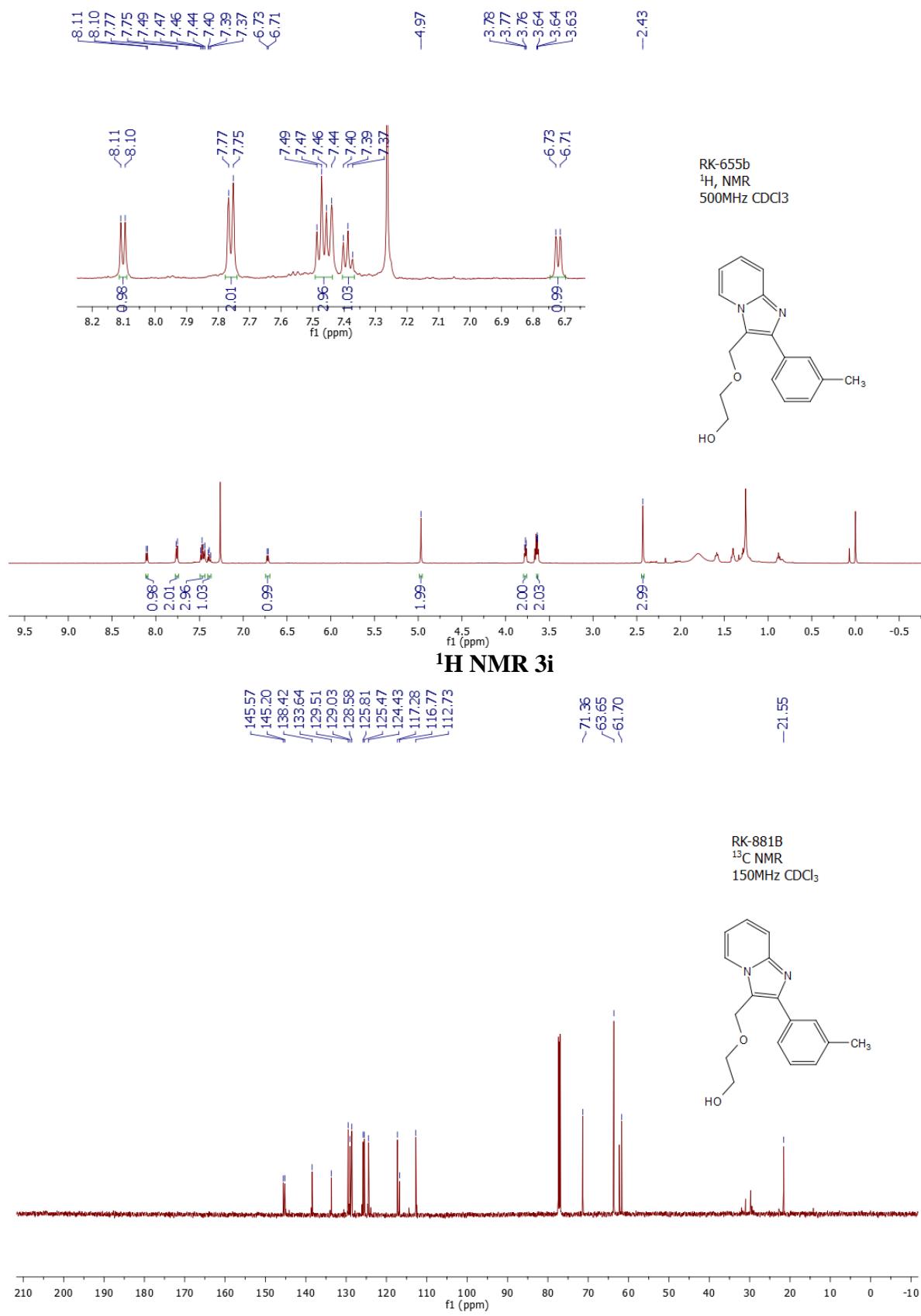




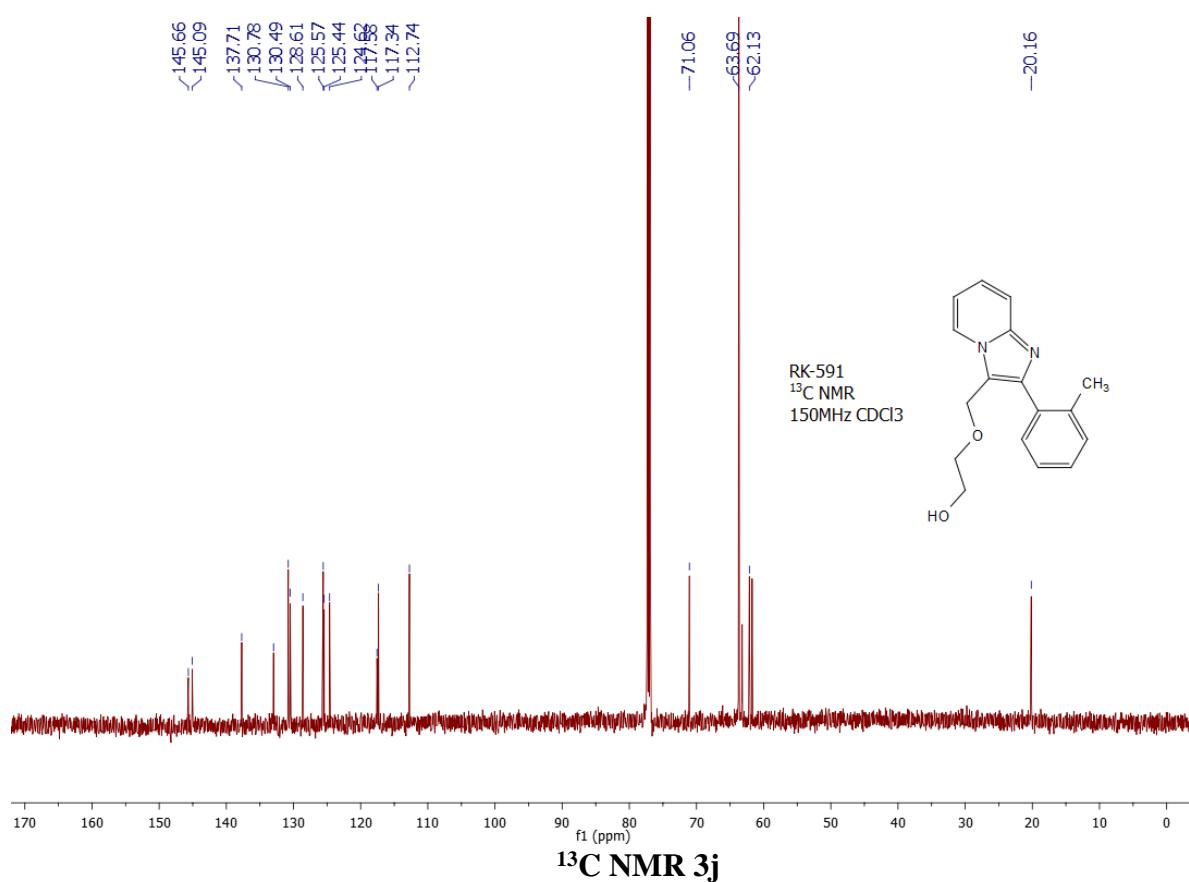
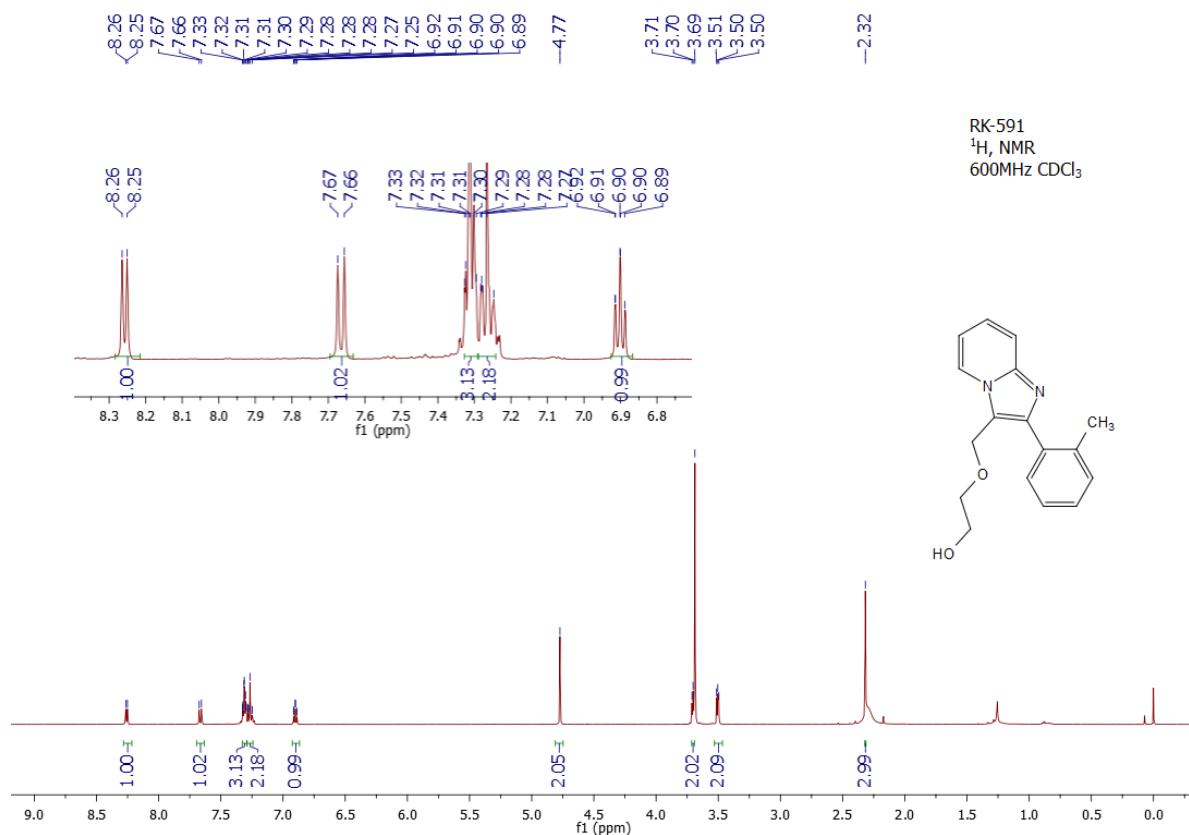
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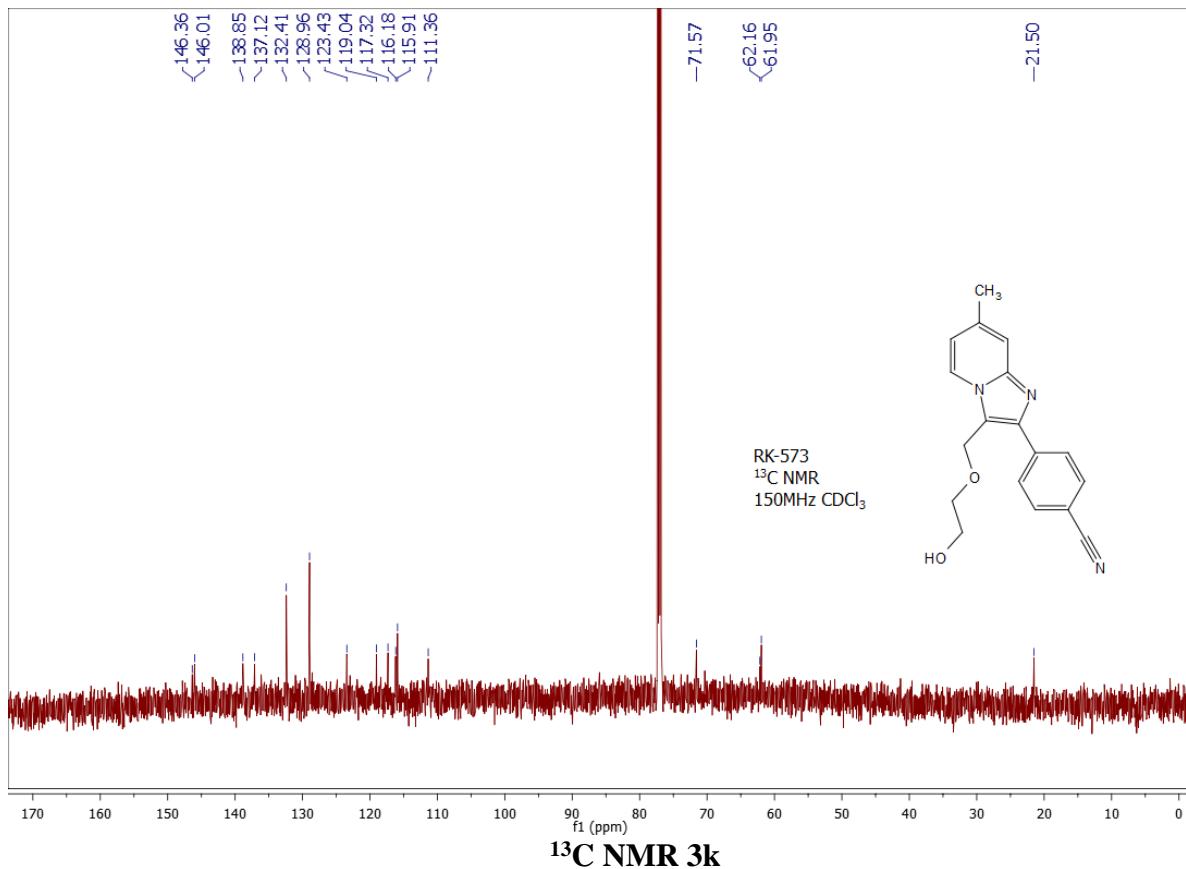
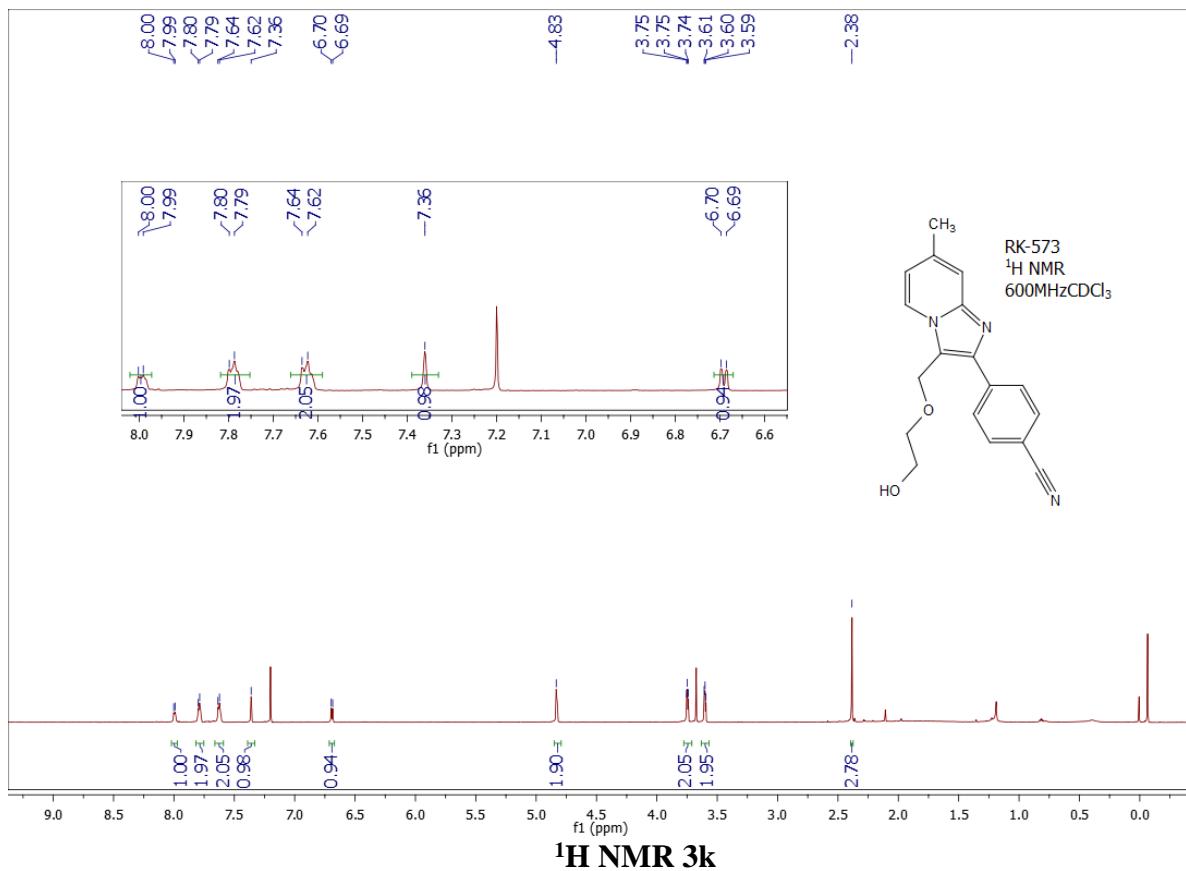
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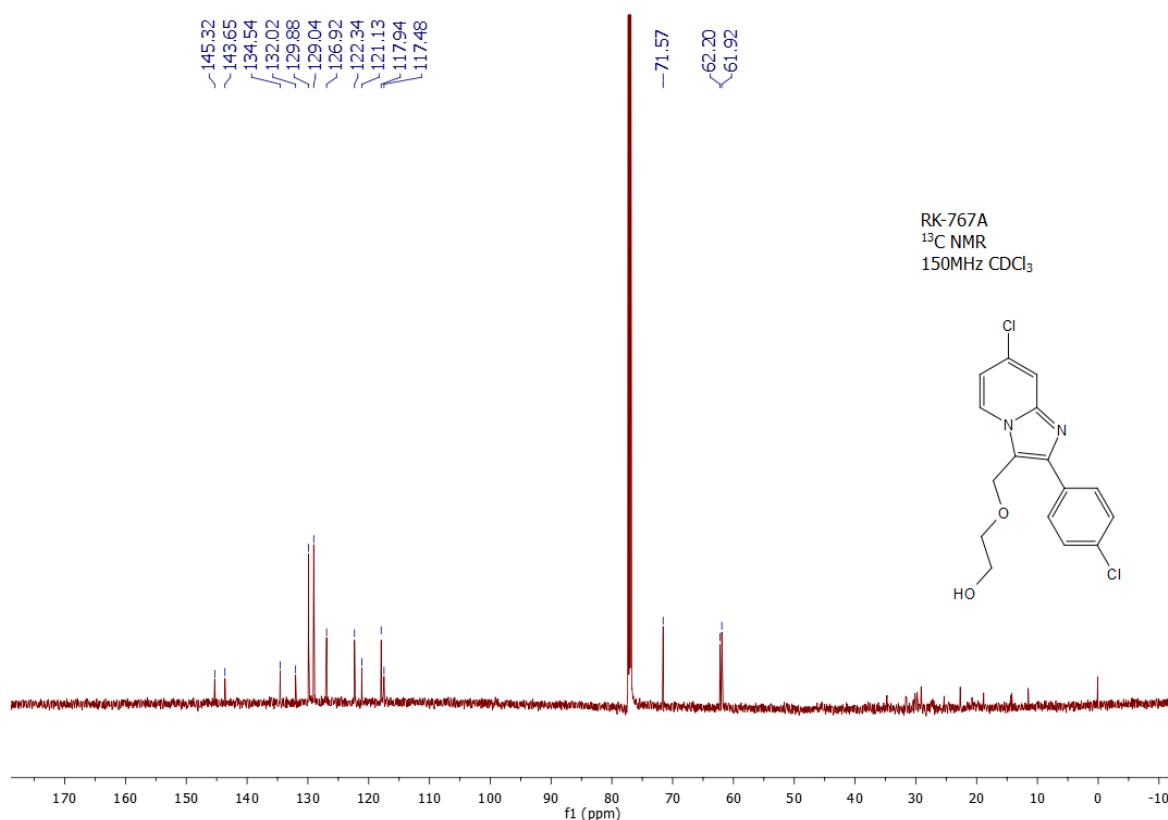
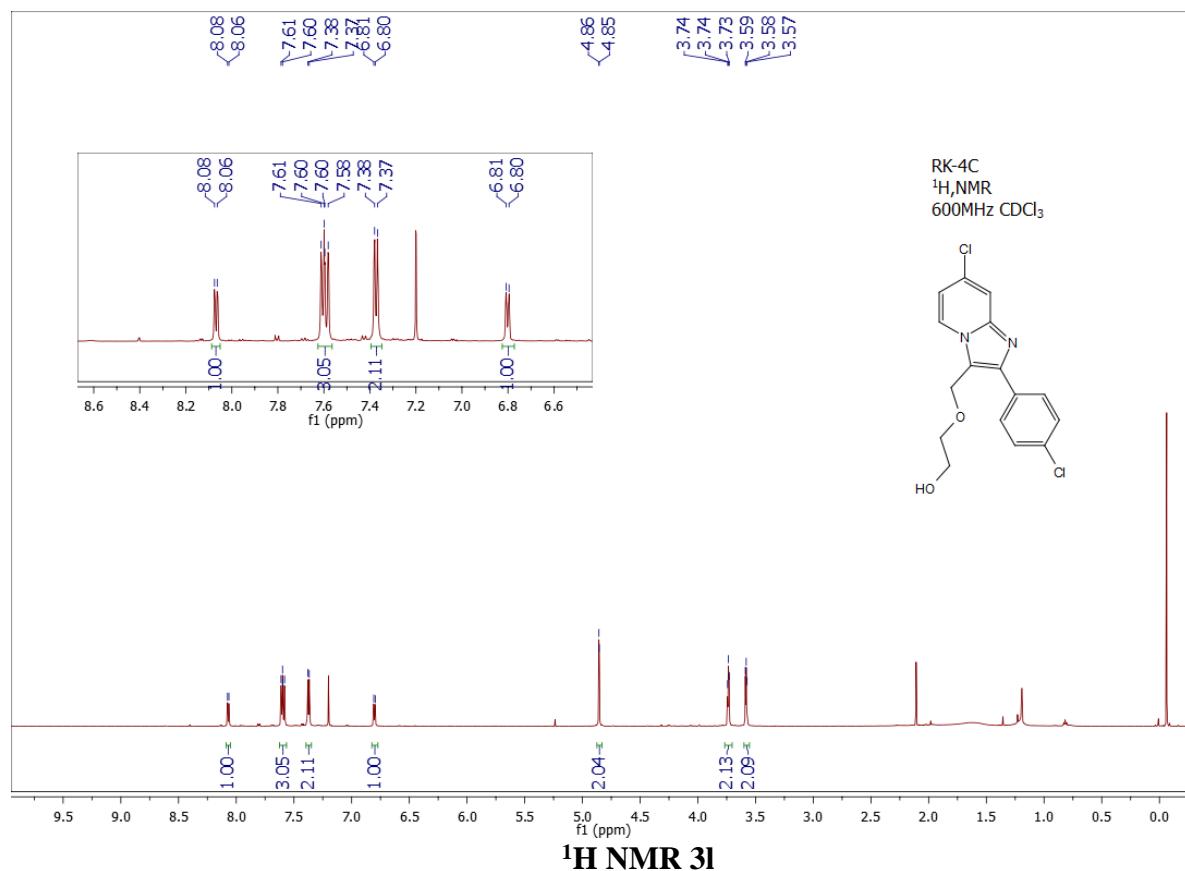
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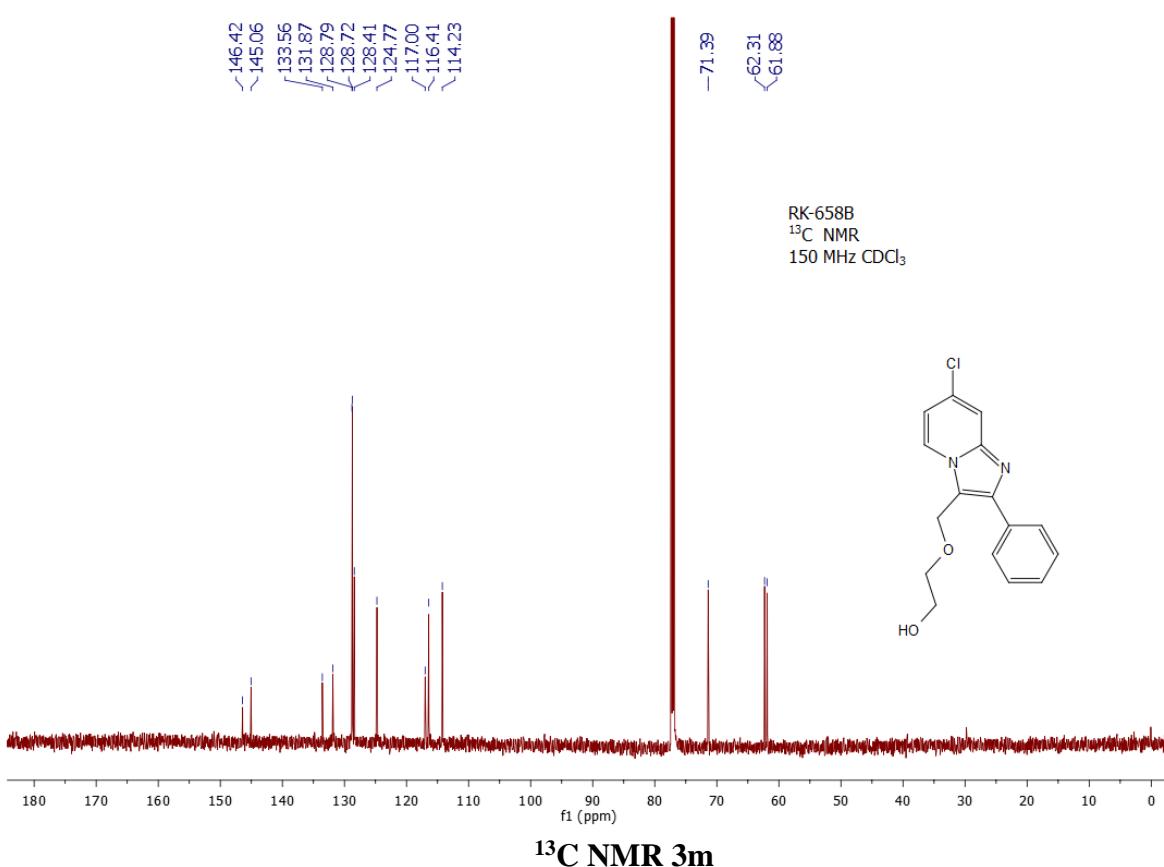
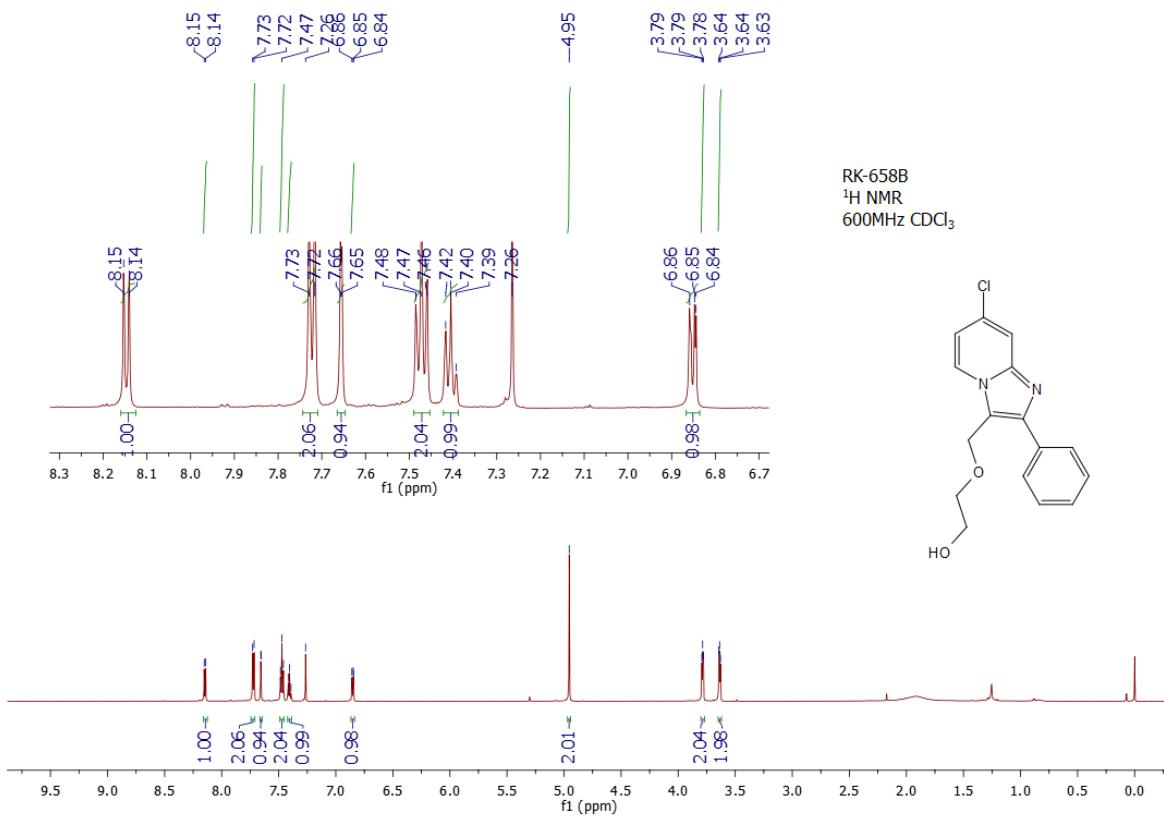
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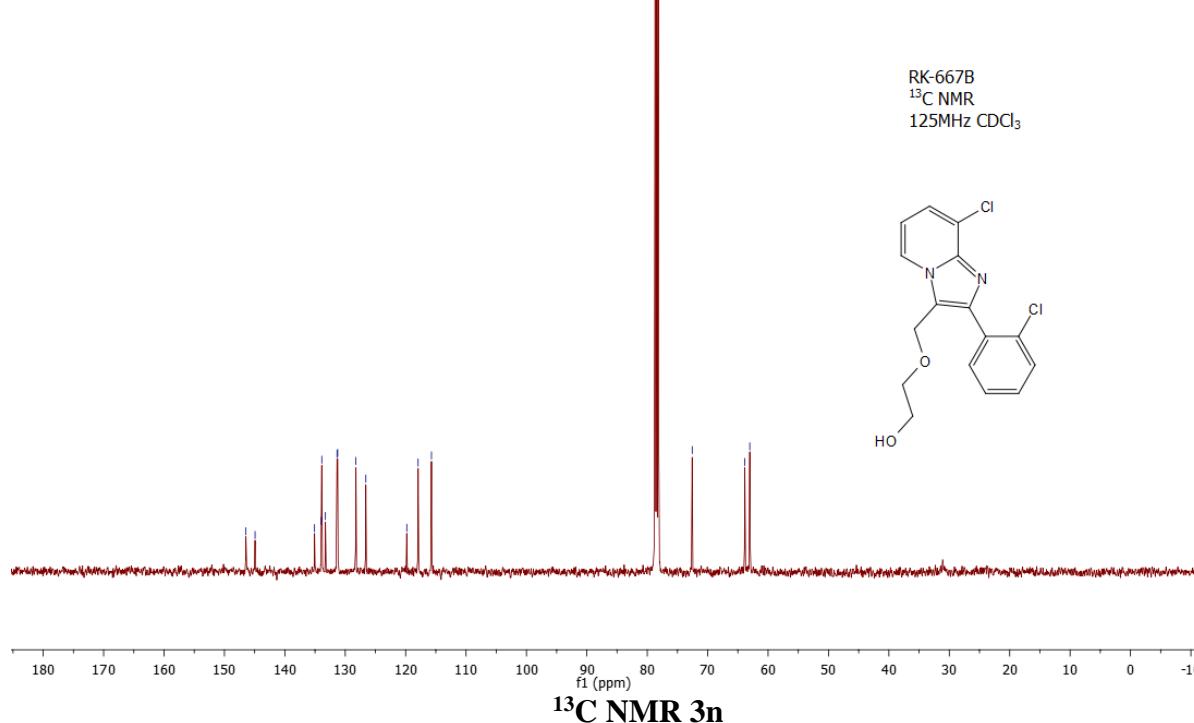
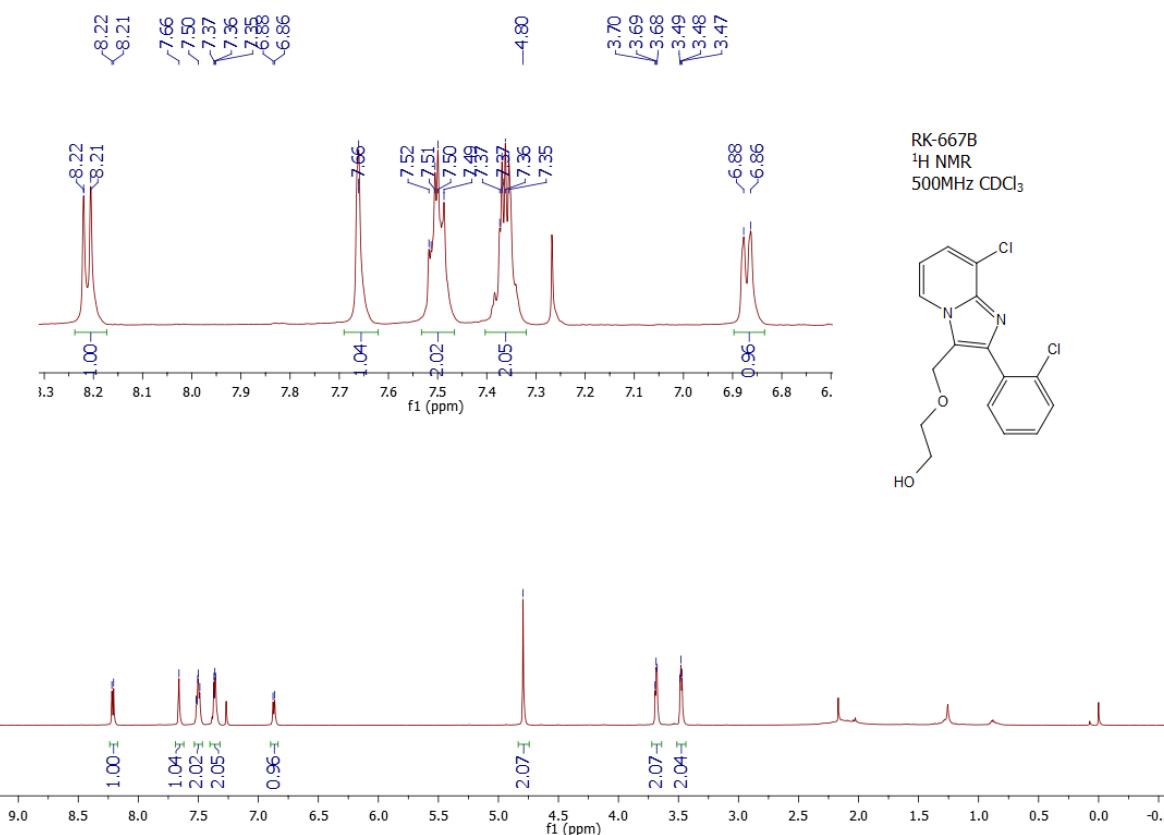
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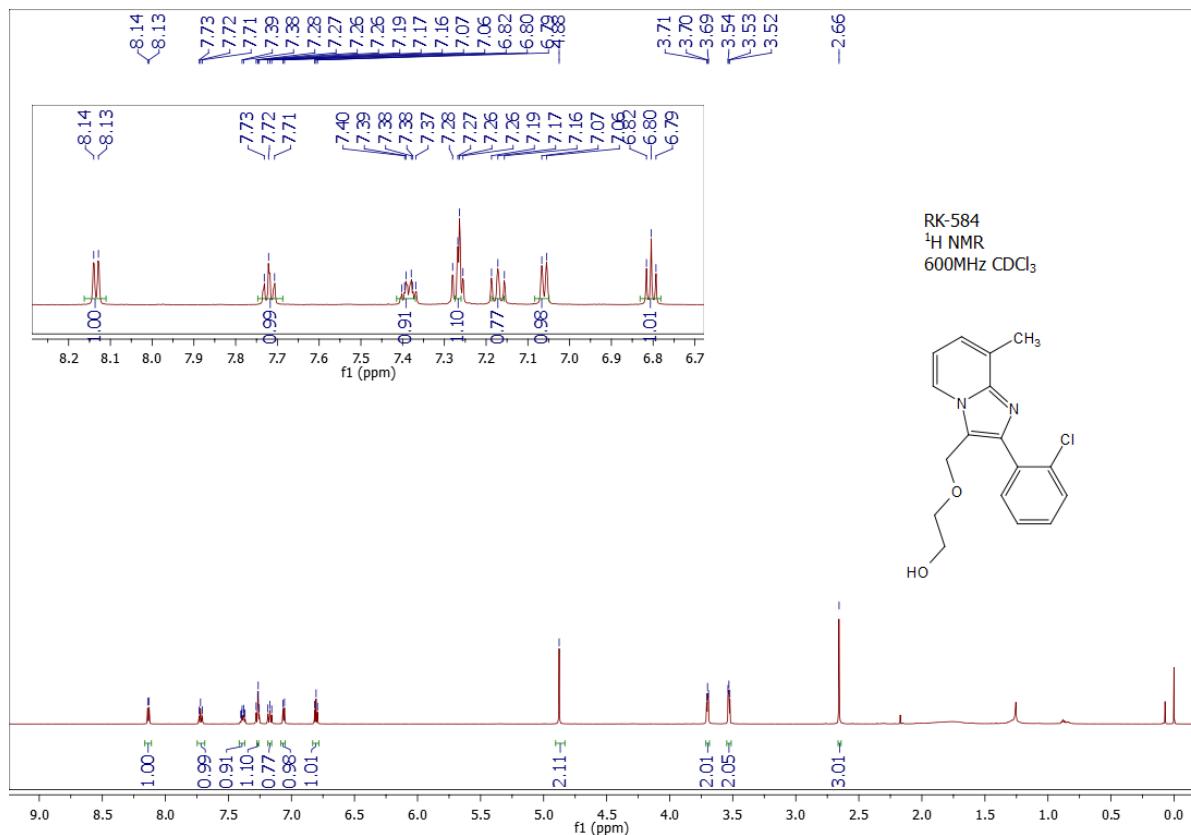
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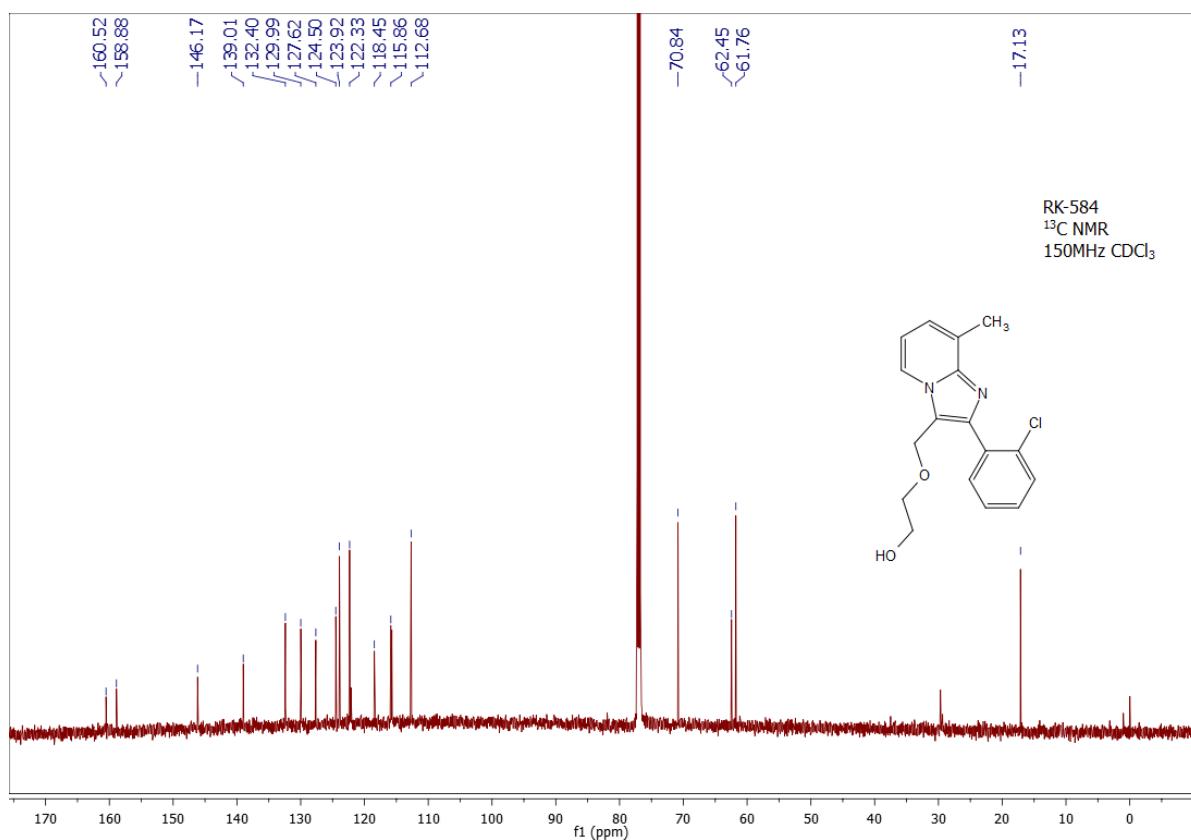
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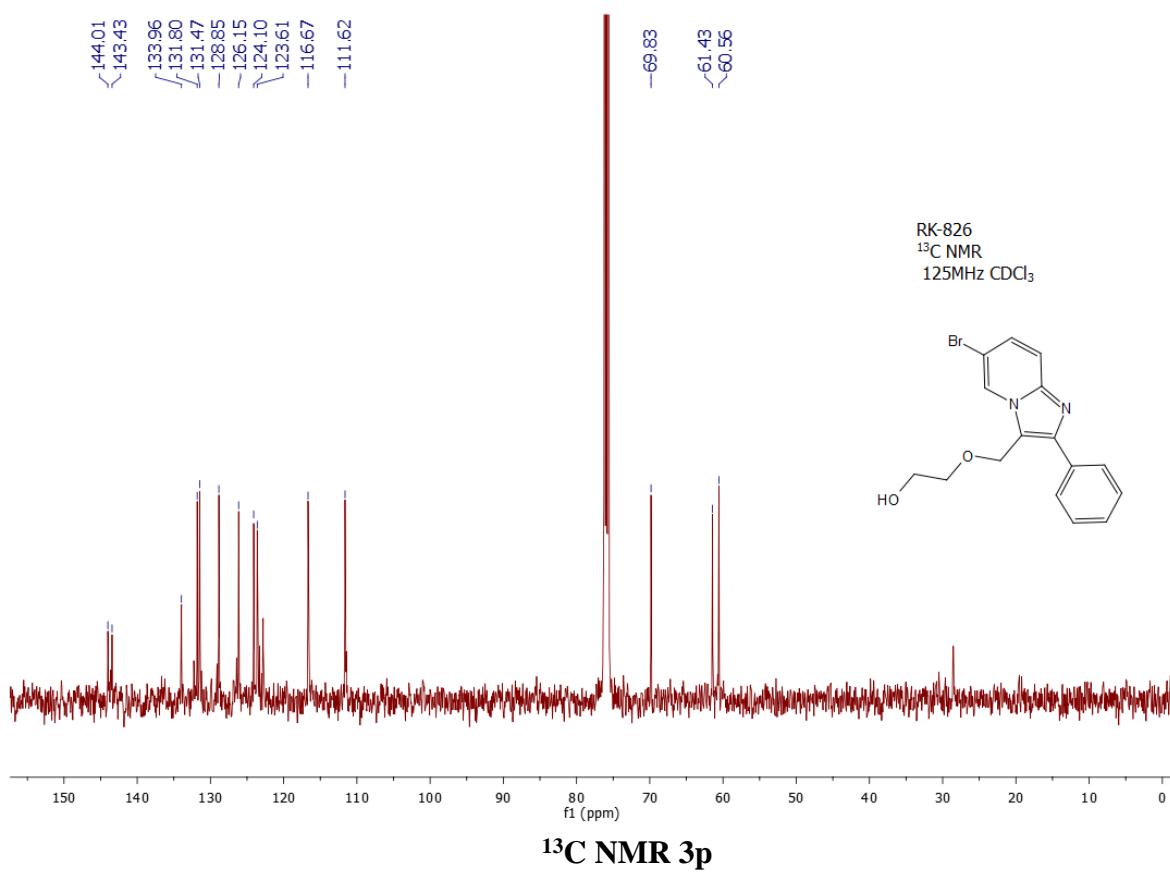
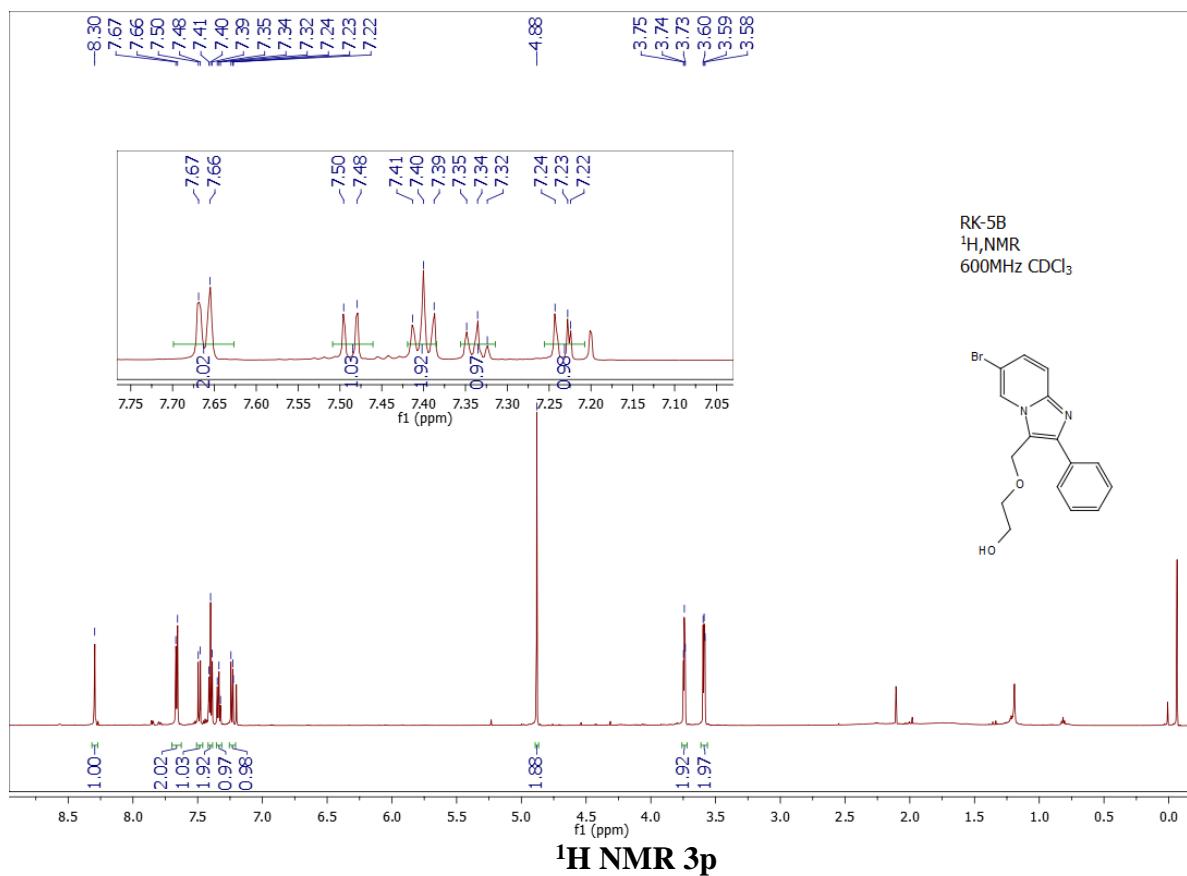


¹H NMR **3o**

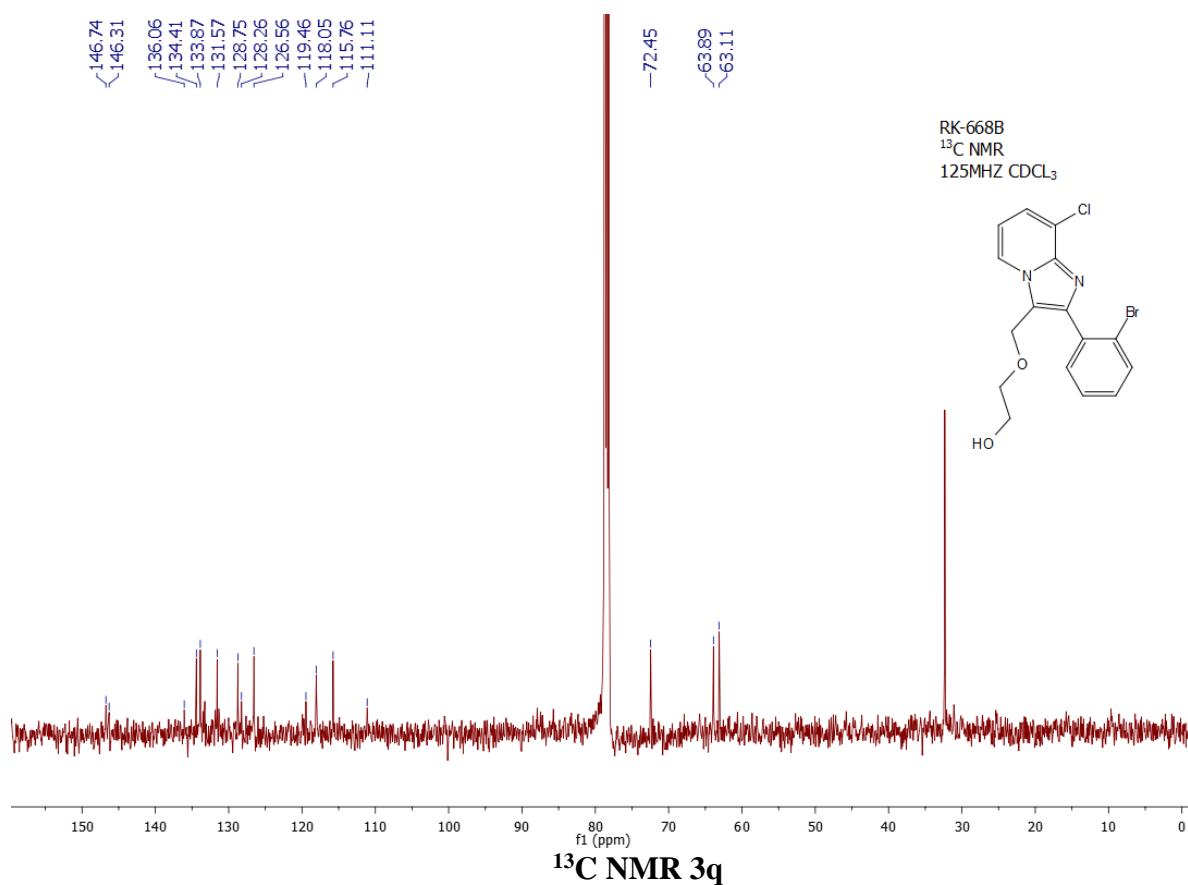
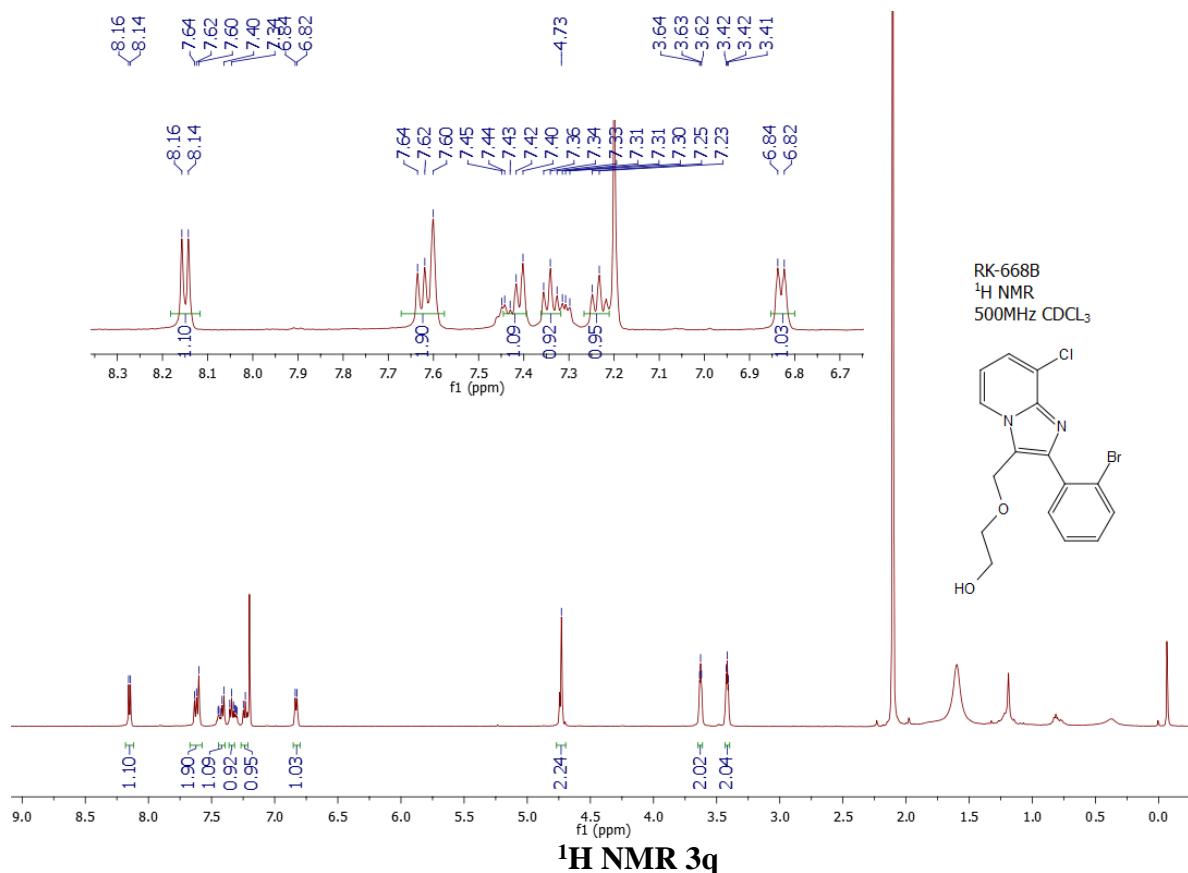


¹³C NMR **3o**

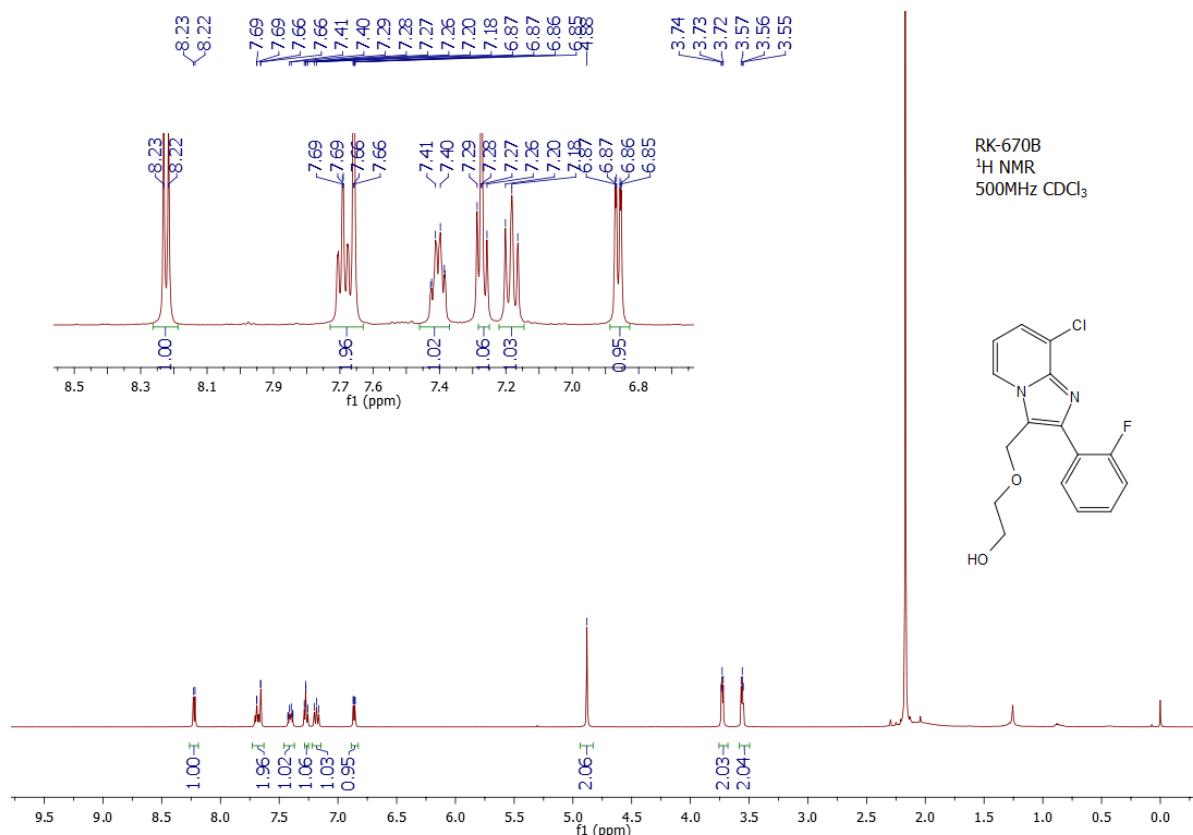
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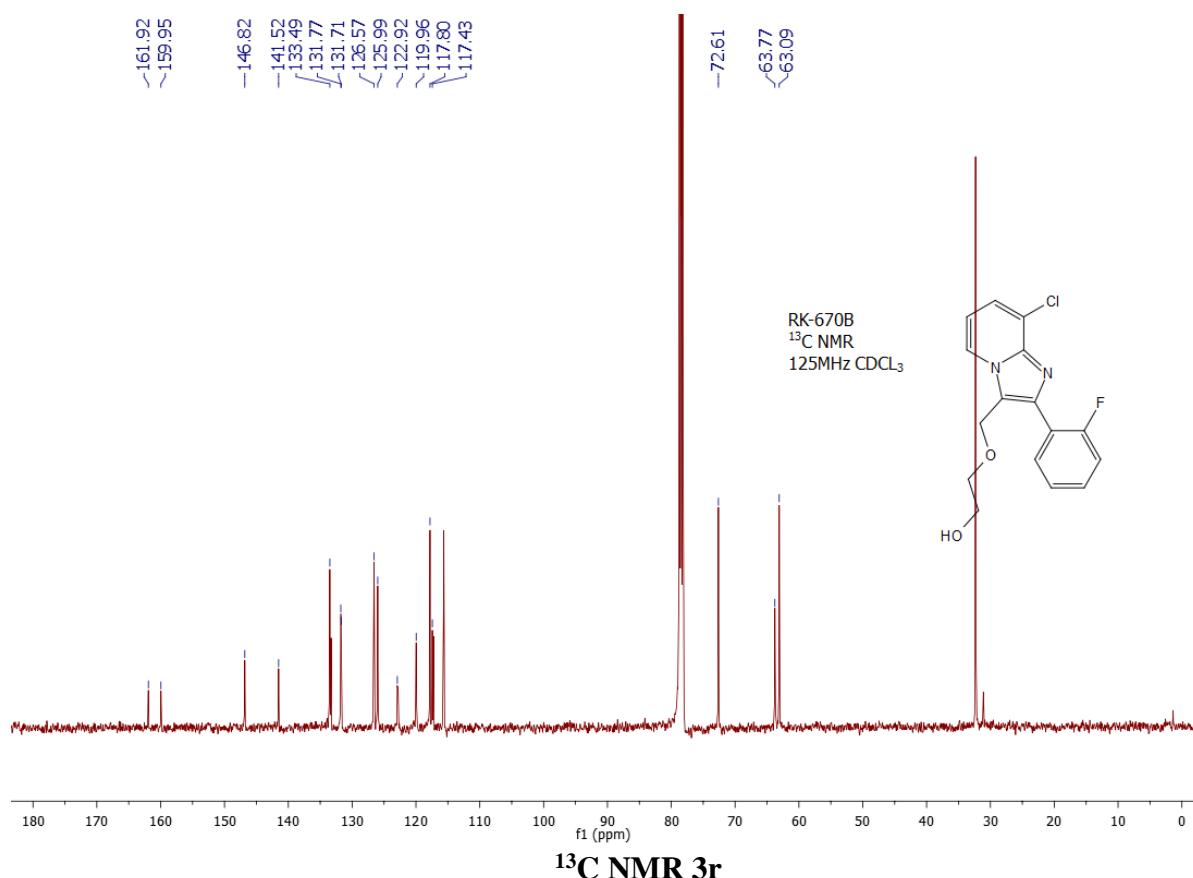
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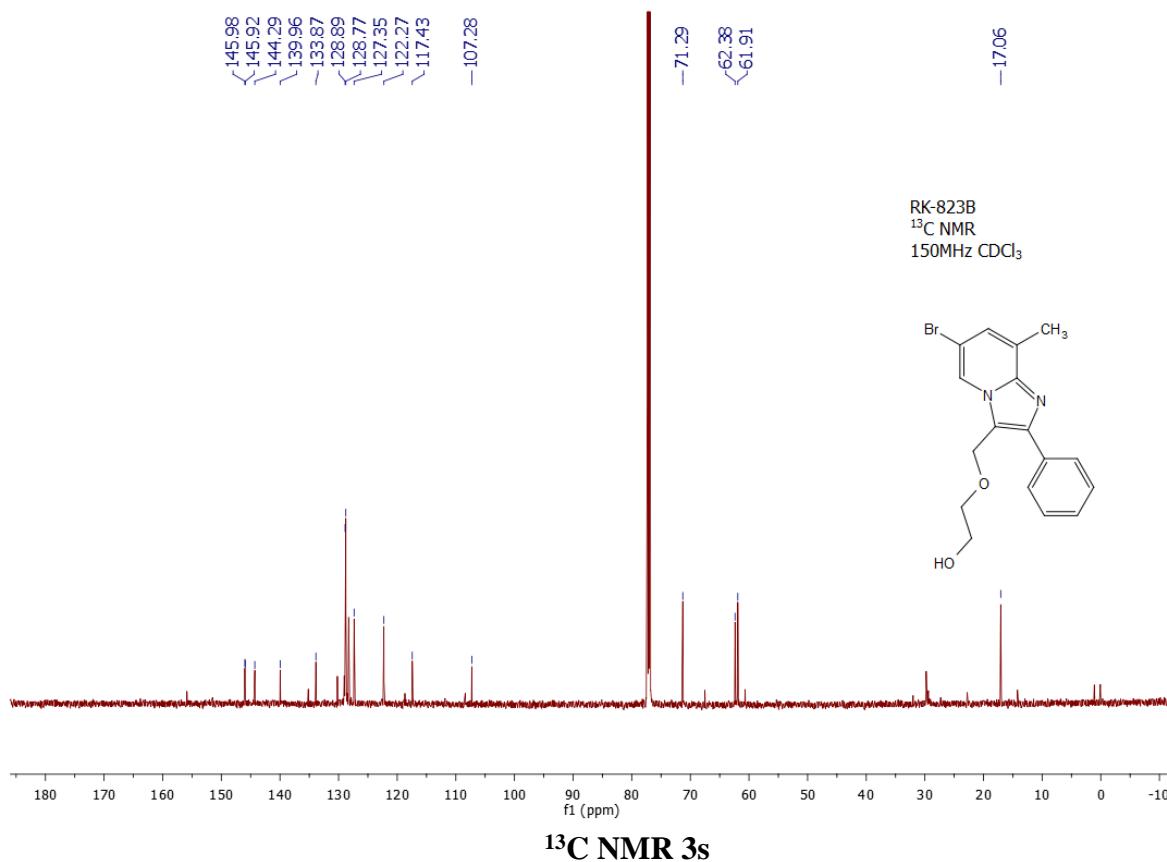
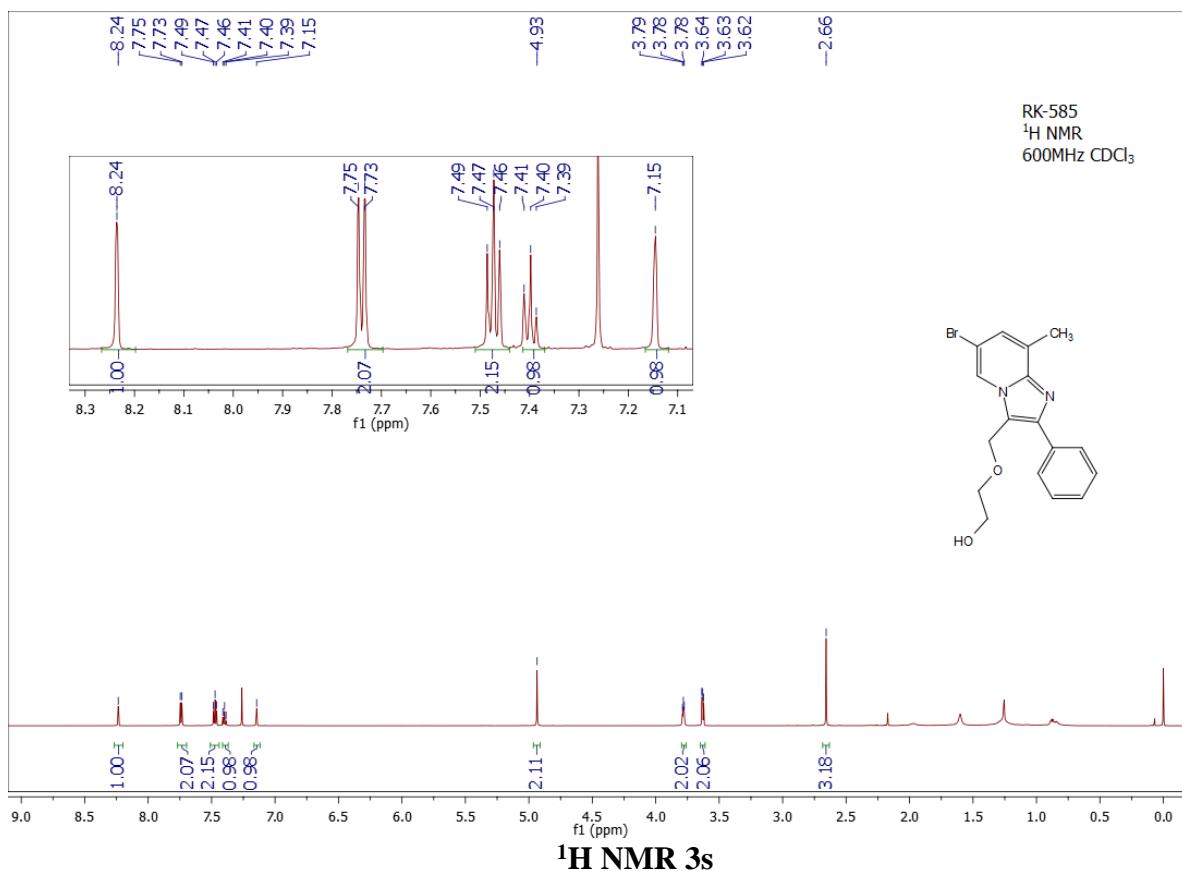
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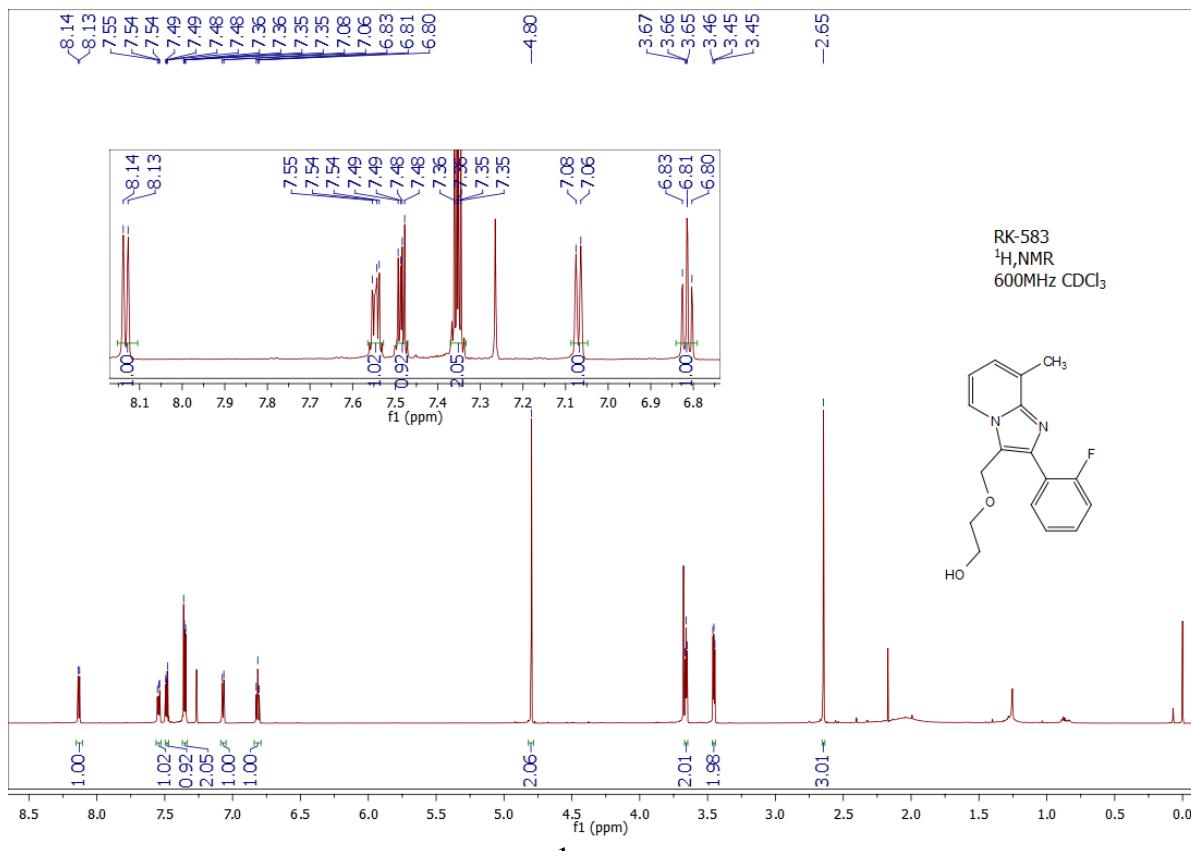
¹H NMR 3r



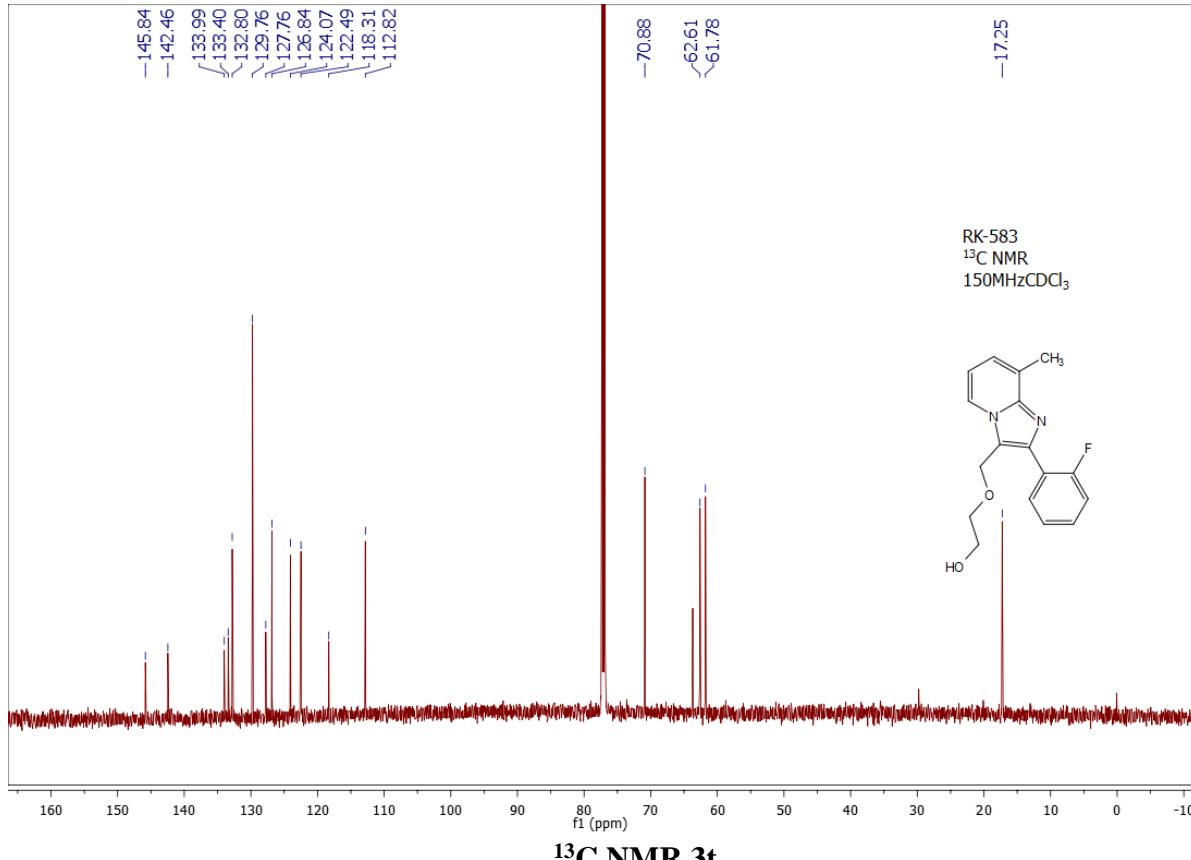
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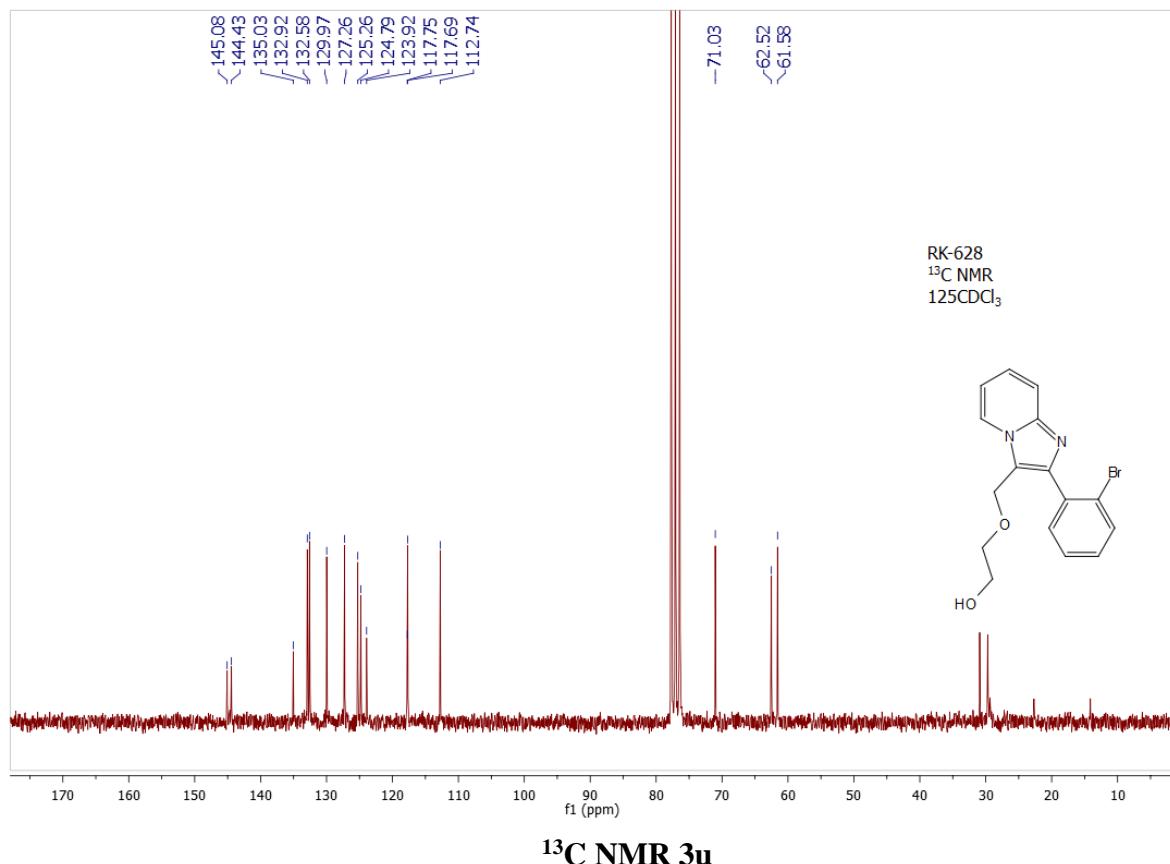
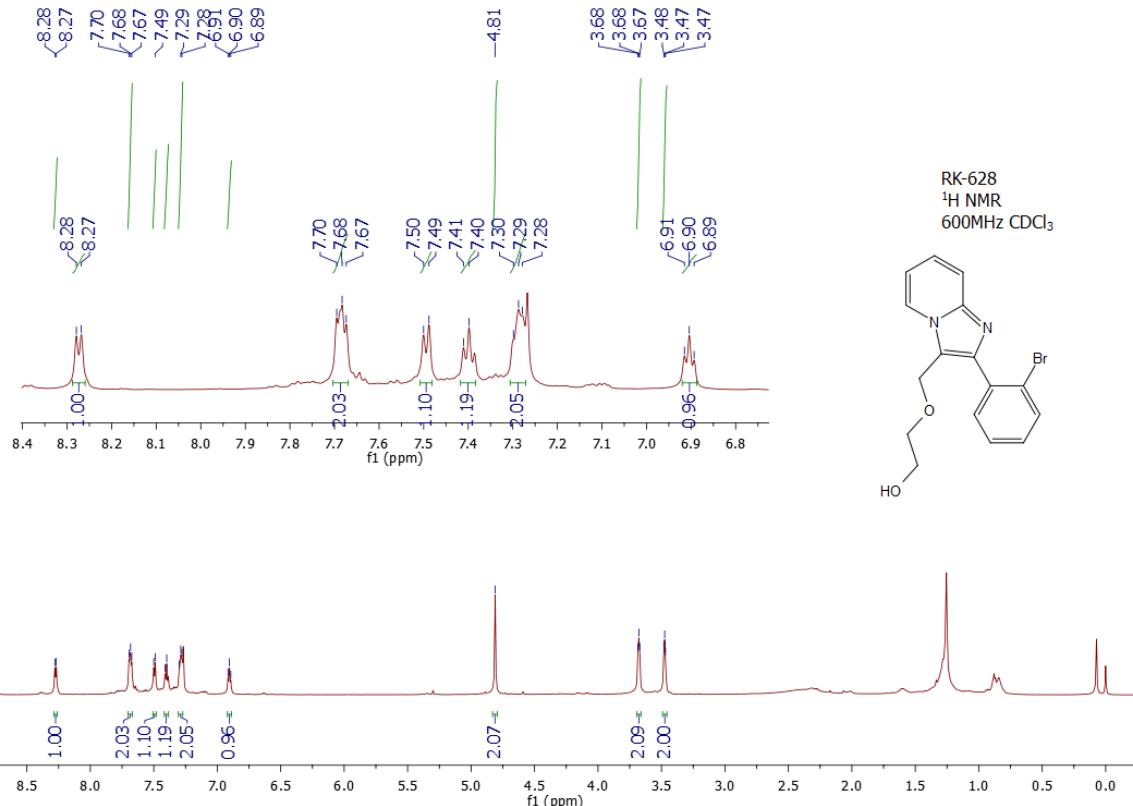


¹H NMR 3t

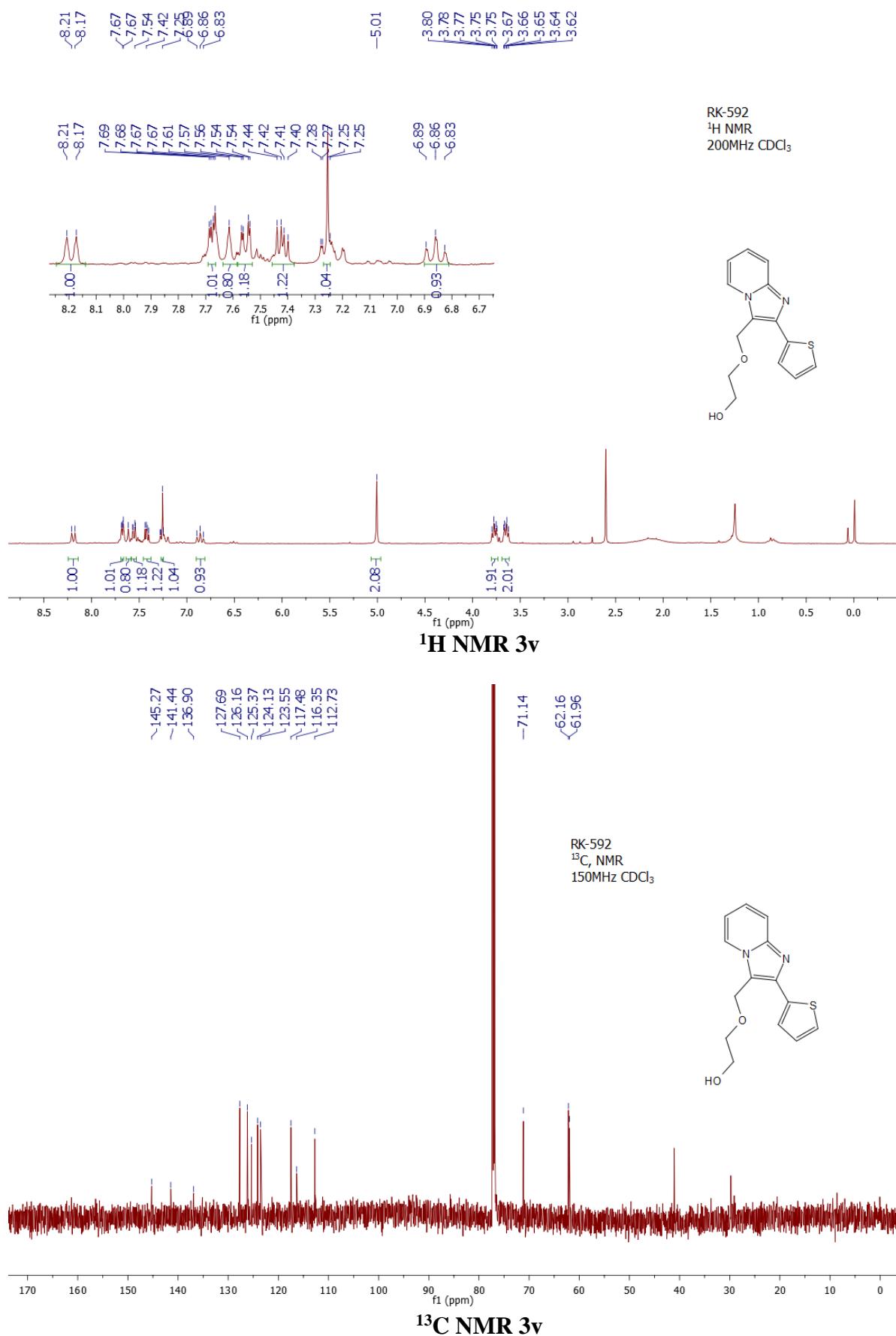


¹³C NMR 3t

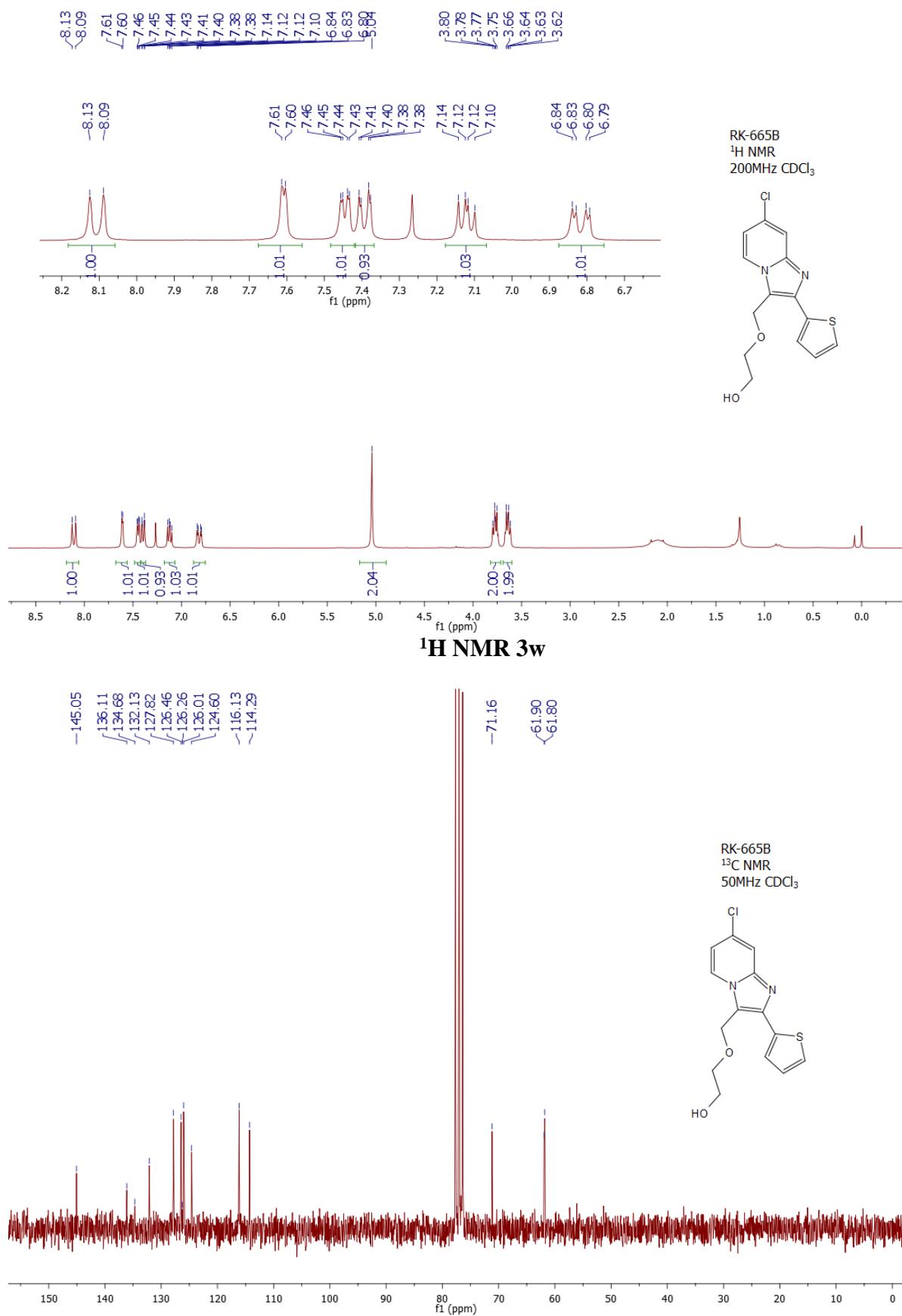
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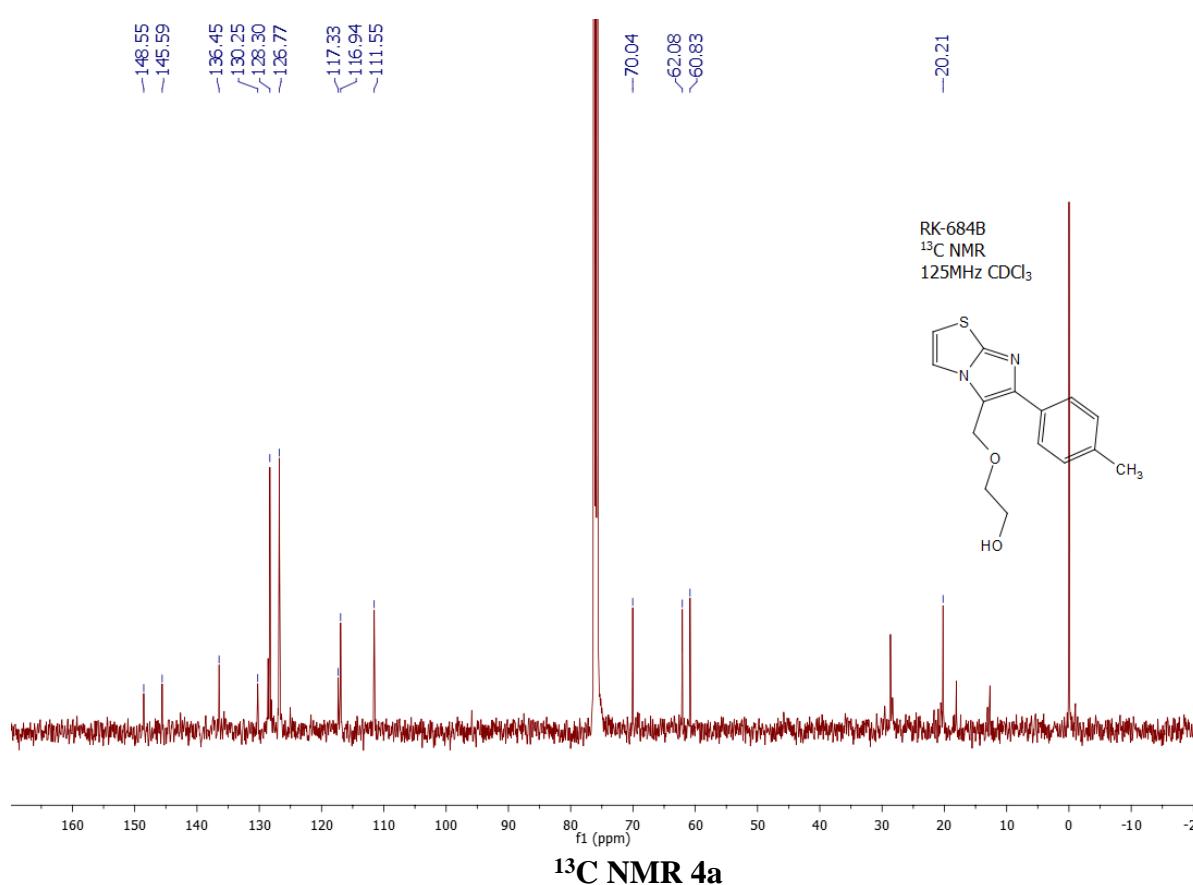
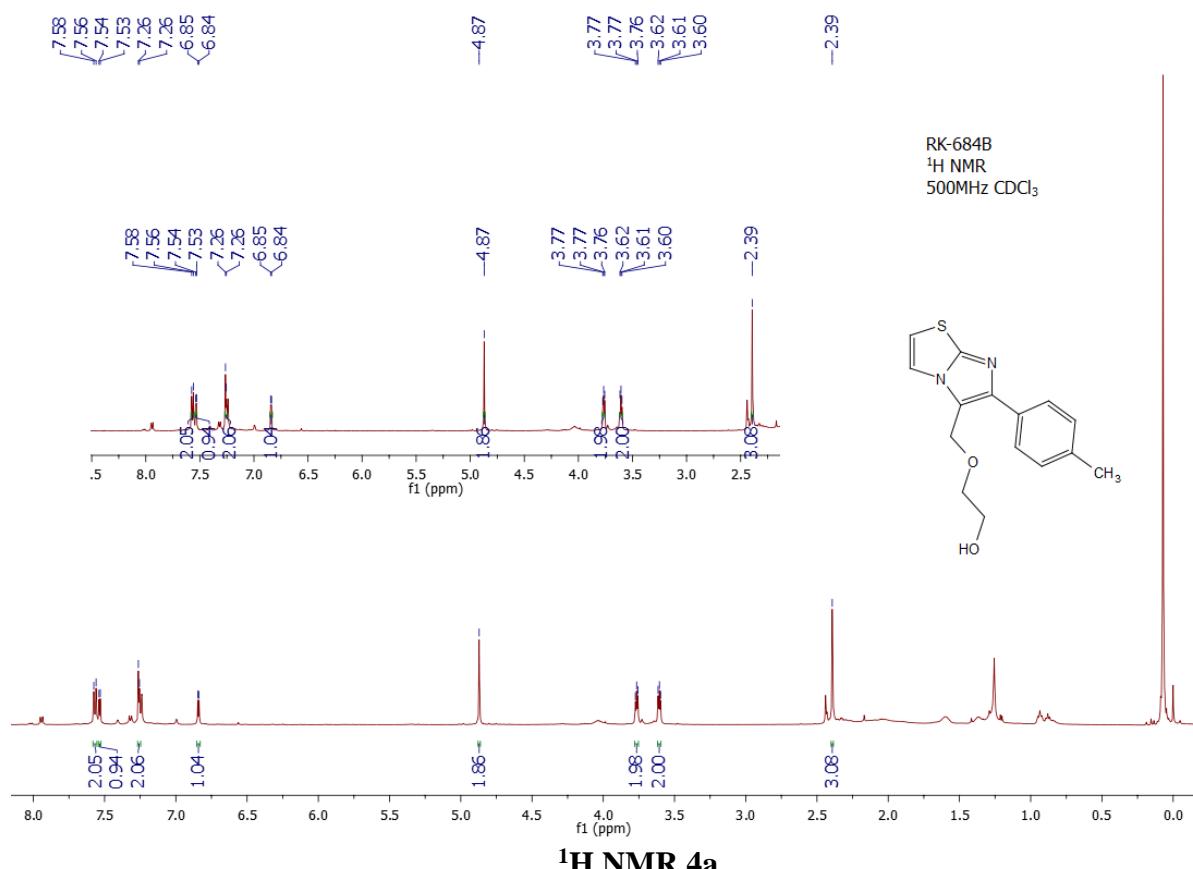


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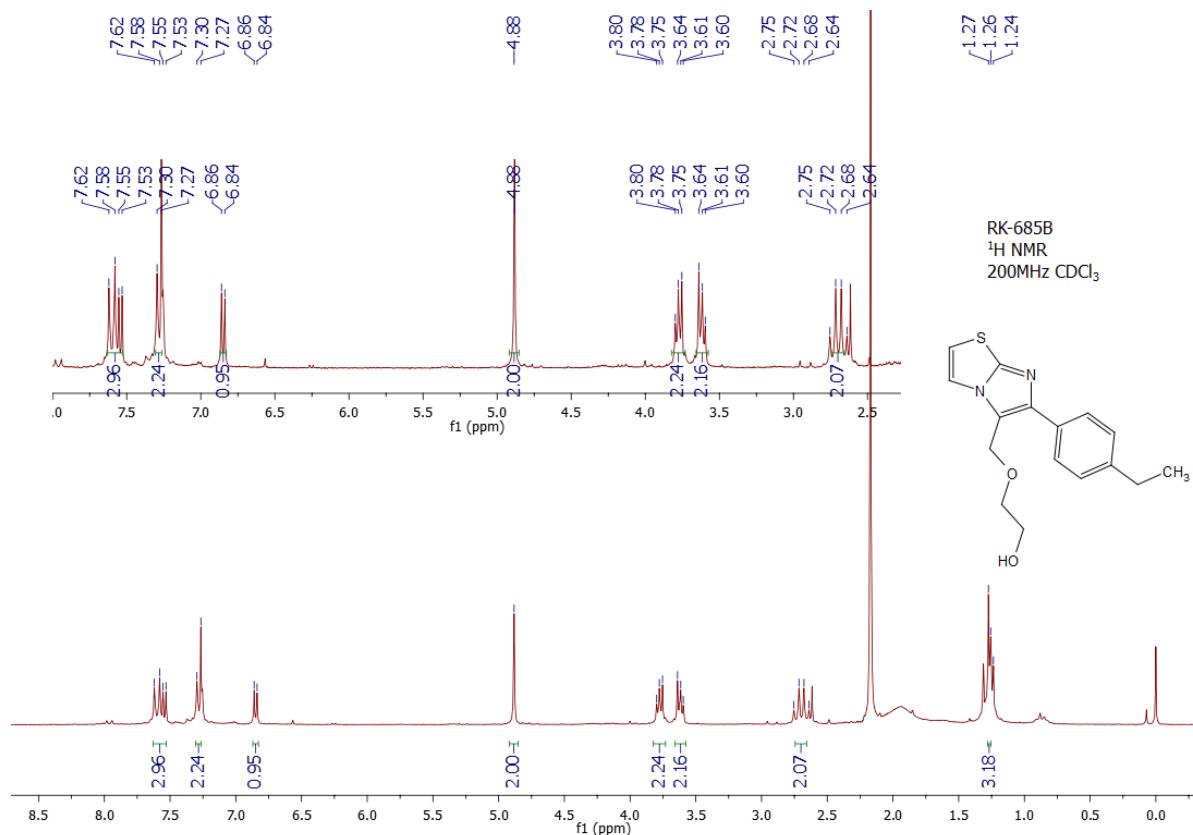


^{13}C NMR **3w**

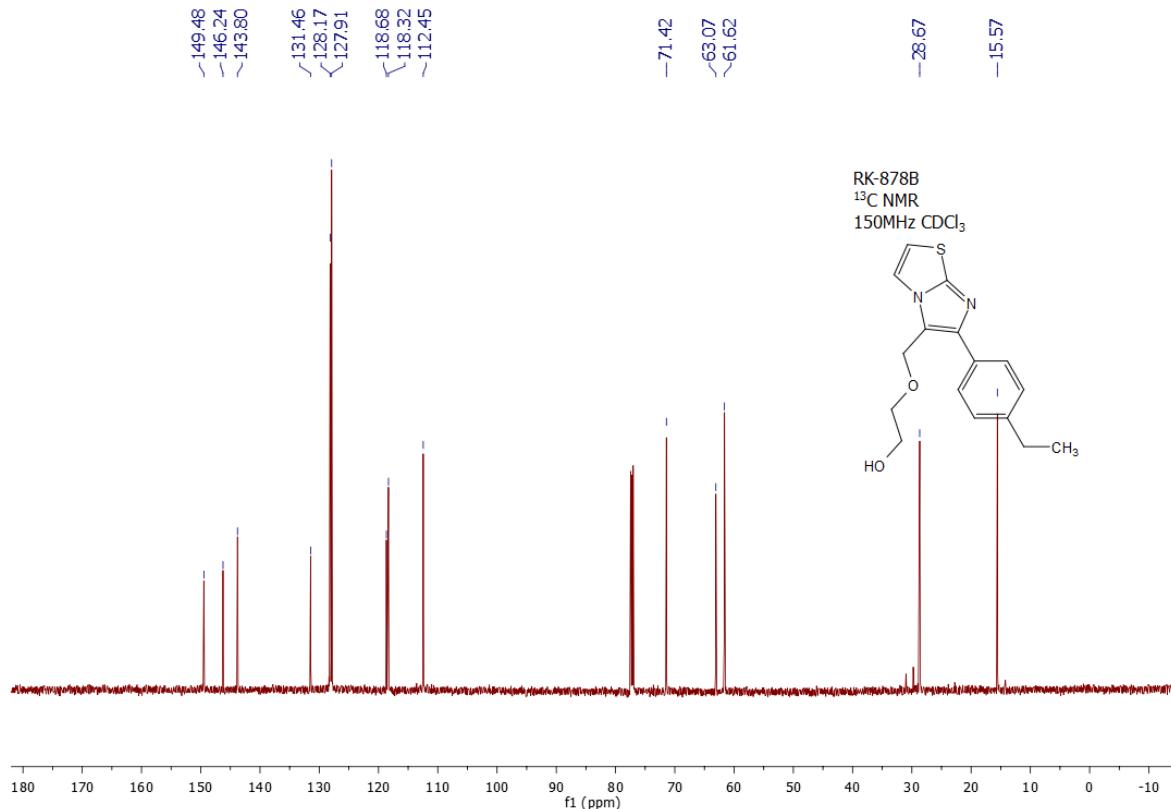
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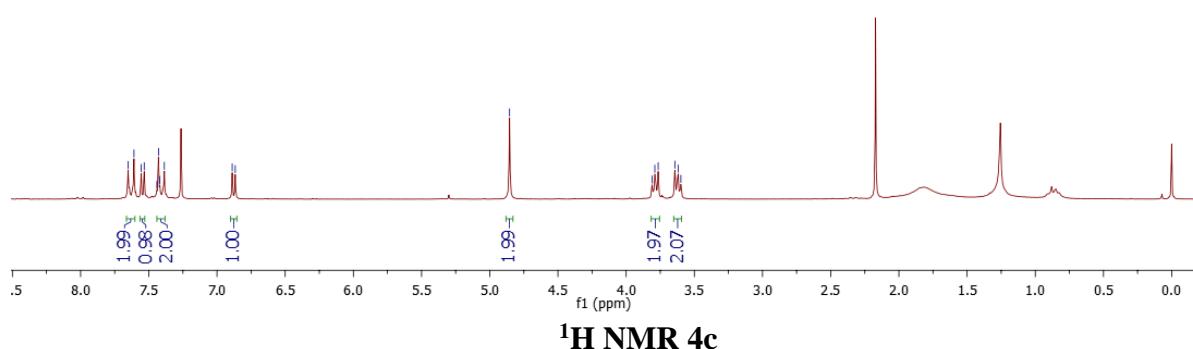
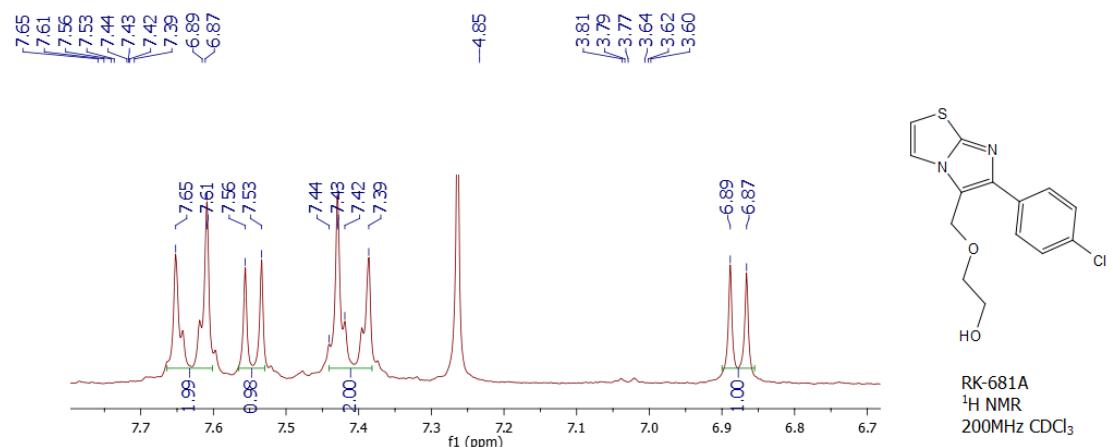


¹H NMR 4b



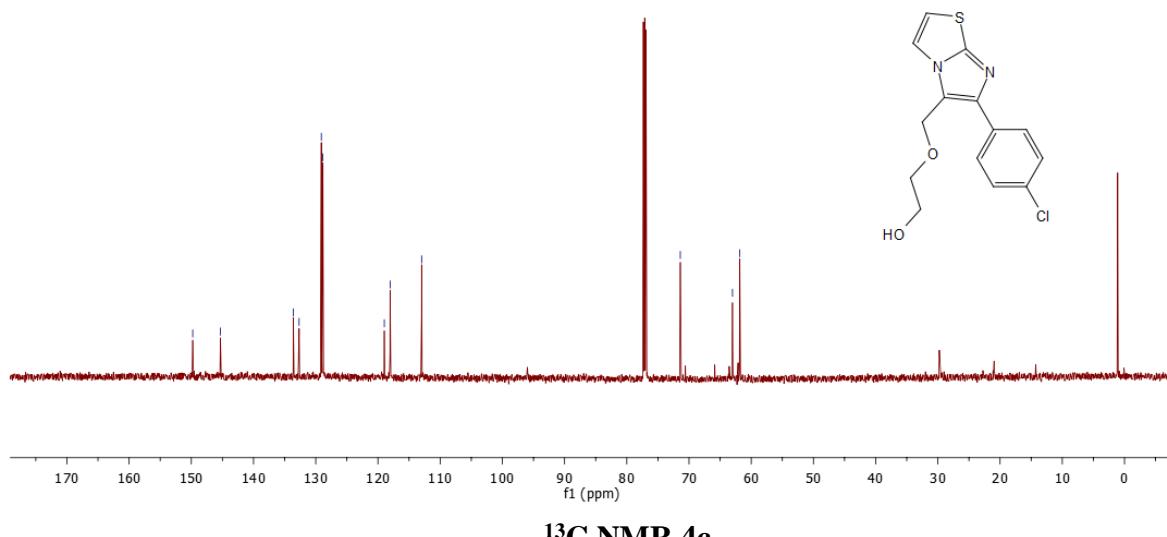
¹³C NMR 4b

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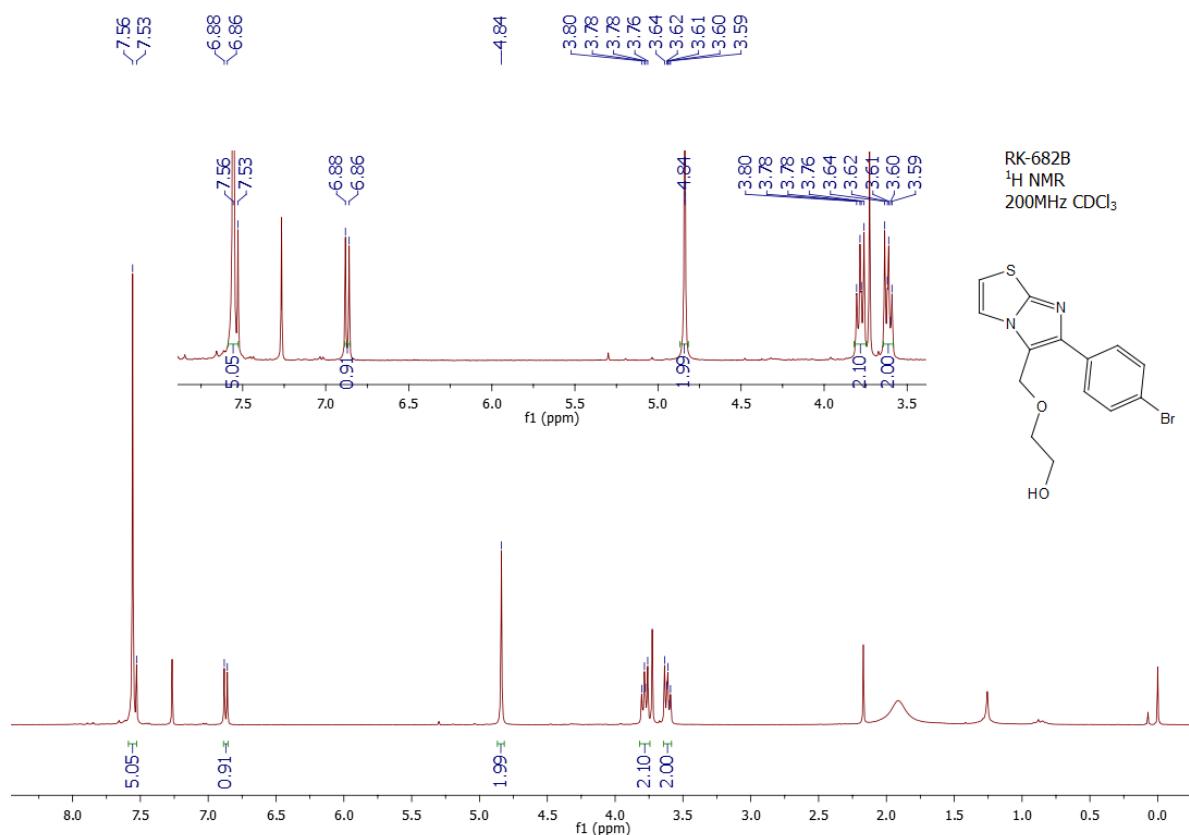


-149.77
-145.31
-133.60
-132.68
-129.10
-128.85
-118.98
-118.04
-112.98
-71.40
-63.01
-61.84

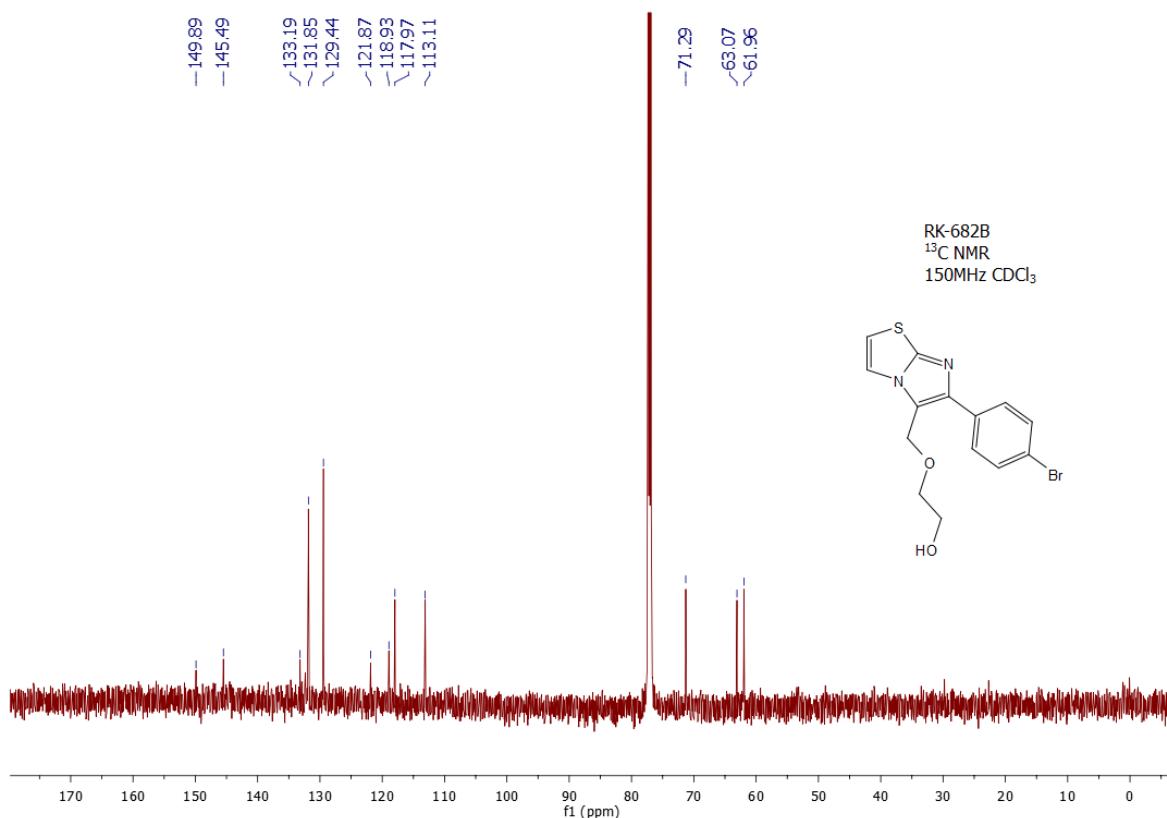
RK-879B
¹³C NMR
150MHz CDCl₃



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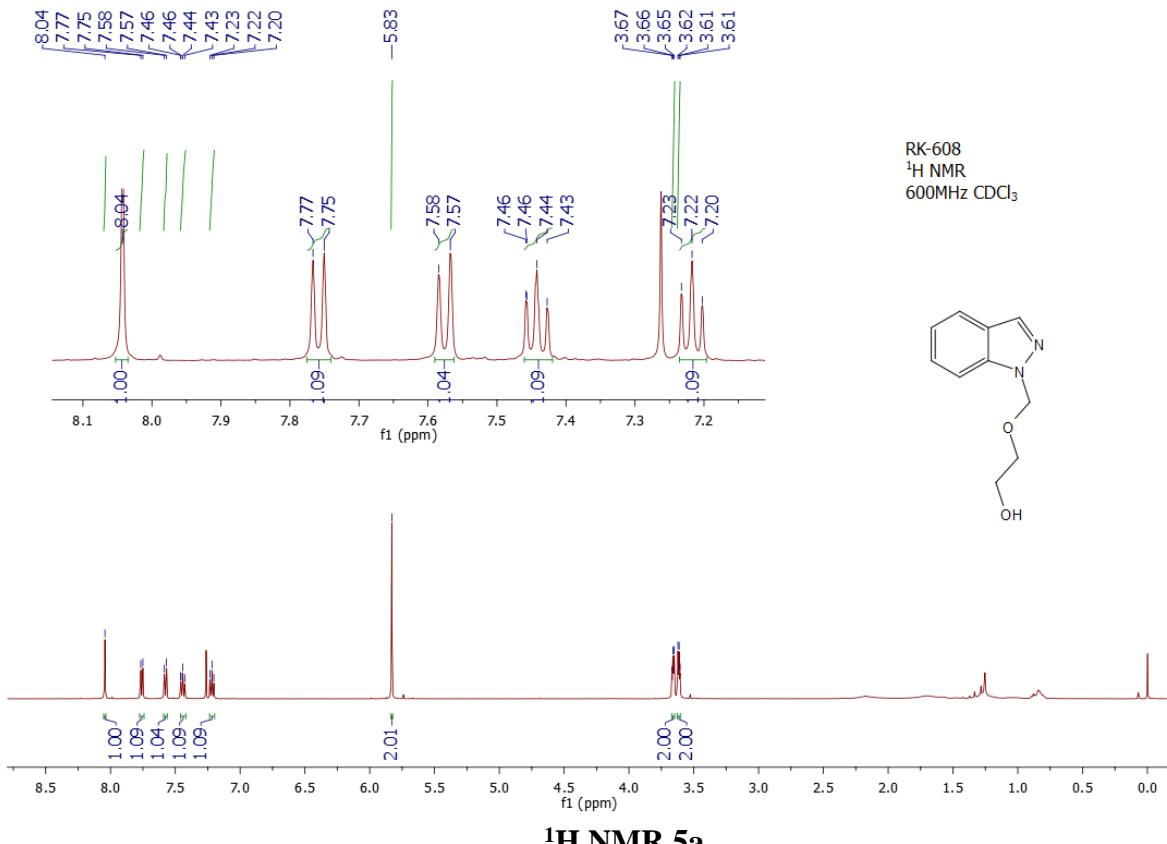


¹H NMR 4d

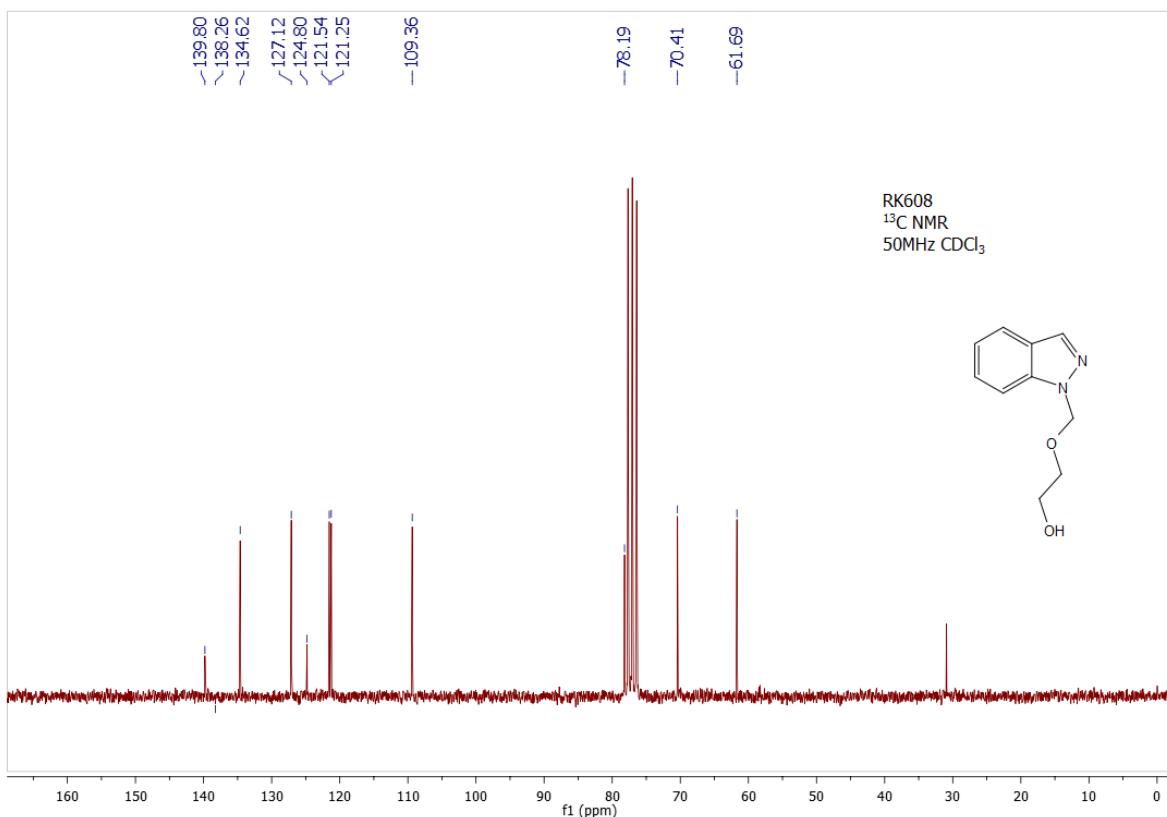


¹³C NMR 4d

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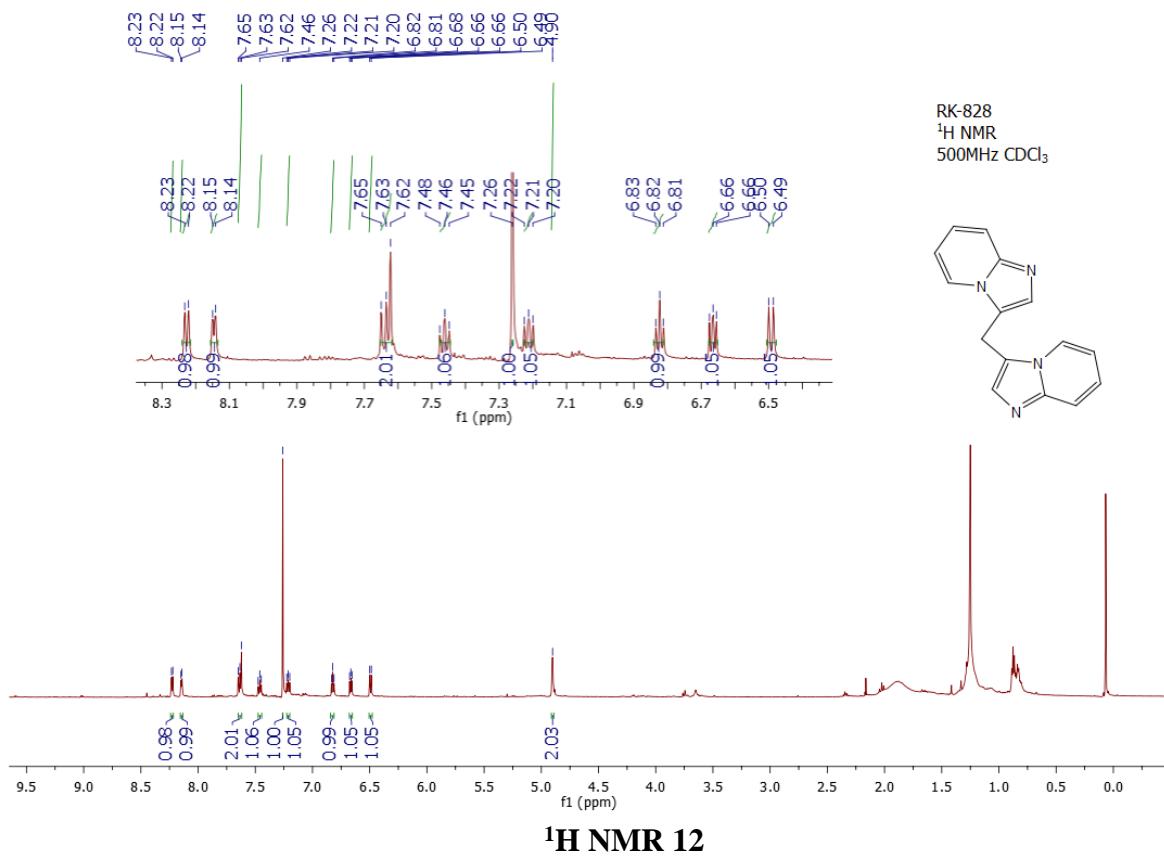


¹H NMR 5a



¹³C NMR 5a

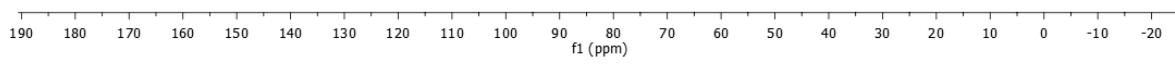
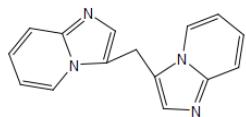
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-146.16
-132.50
-124.21
-123.31
-118.22
-118.04
-112.64

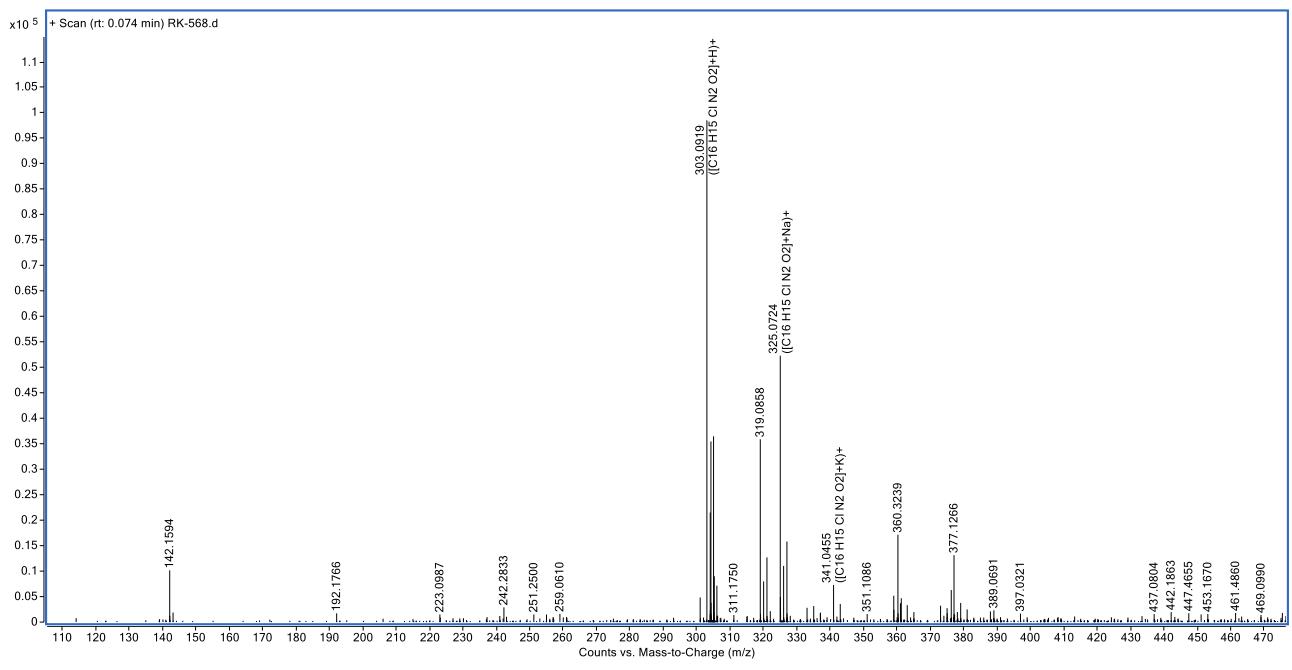
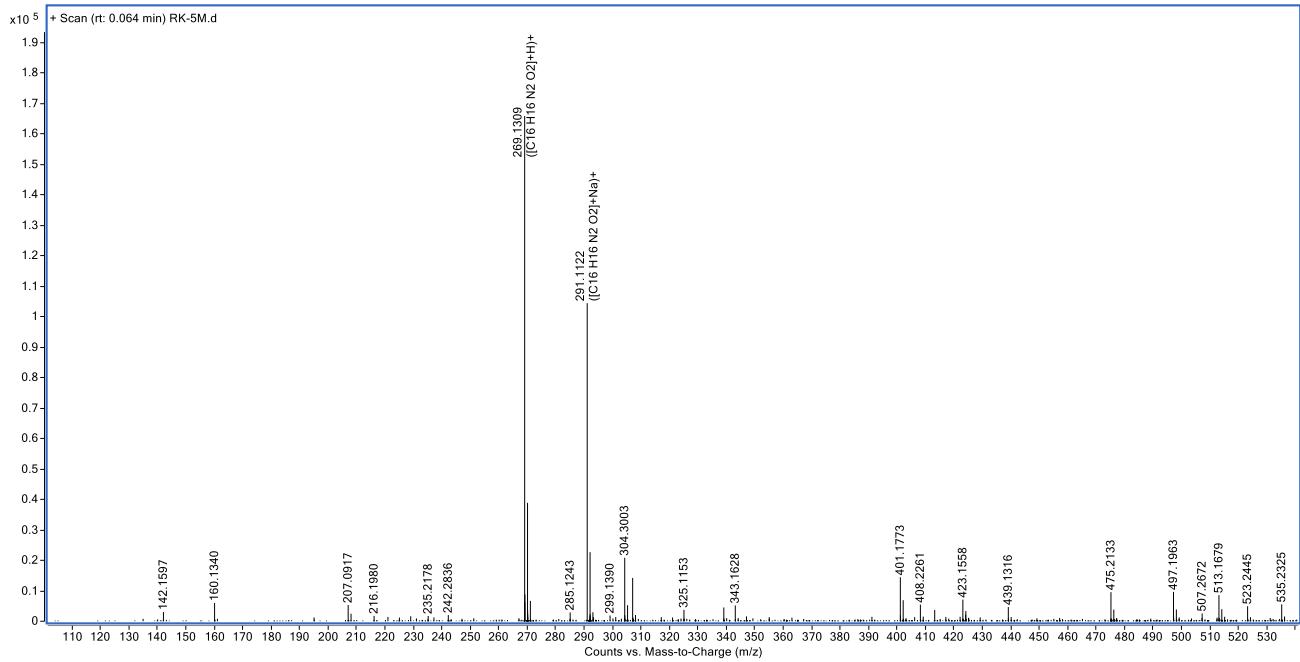
-20.10

RK-880B
¹³C NMR
150MHz CDCl₃

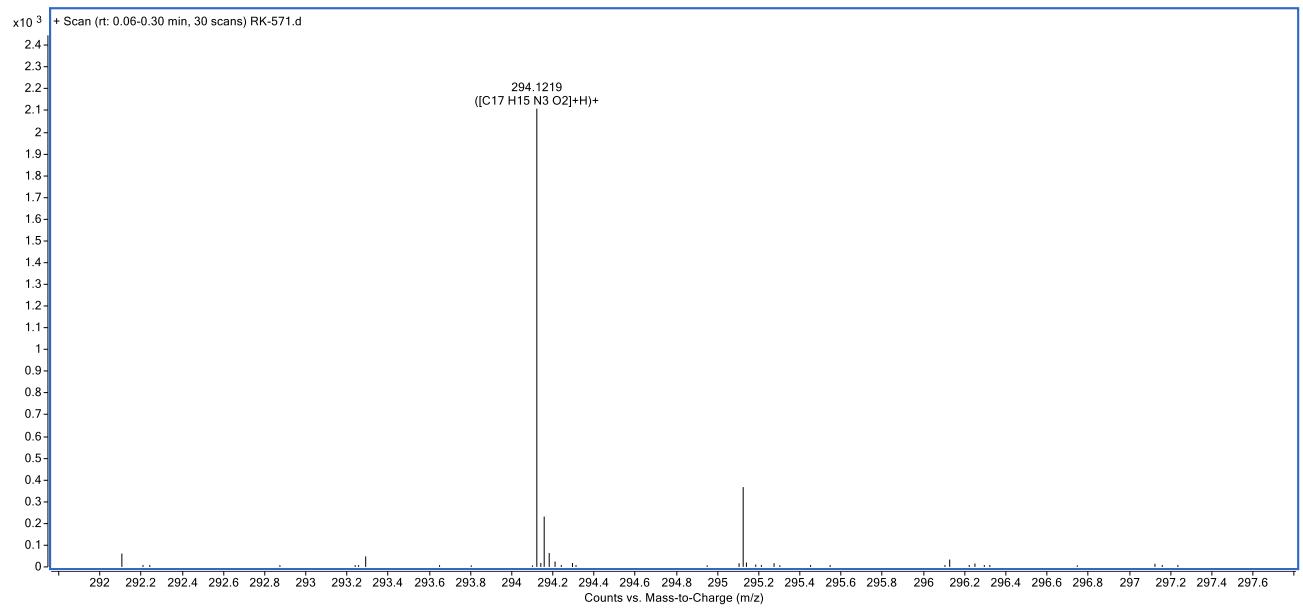
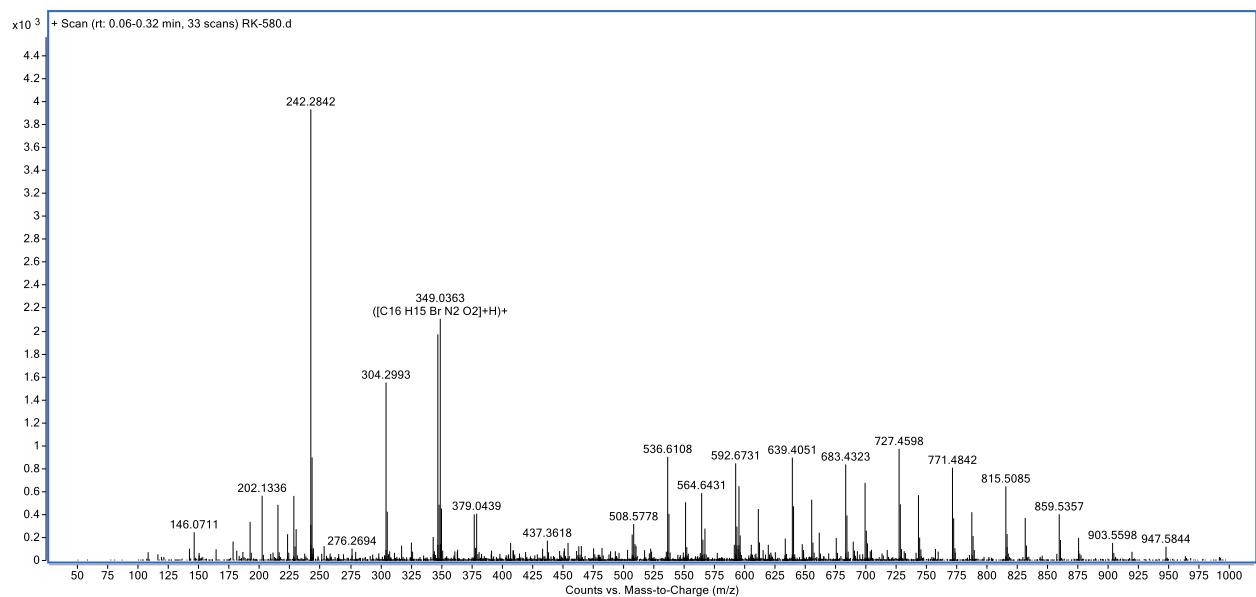


¹³C NMR 12

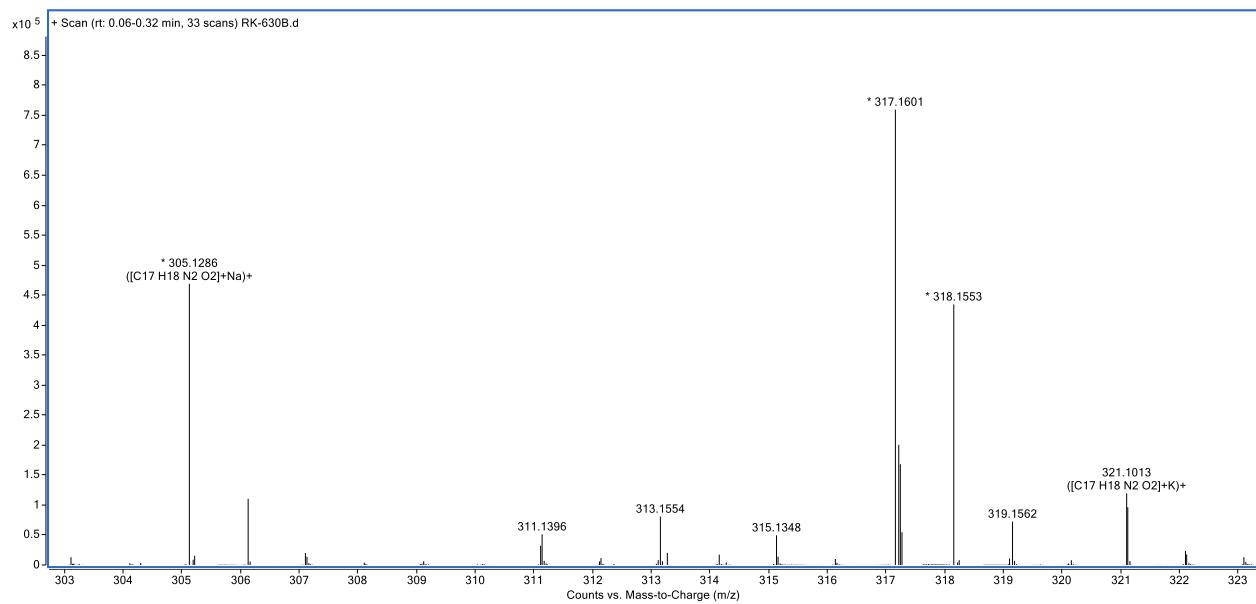
5. HRMS Spectra Copy



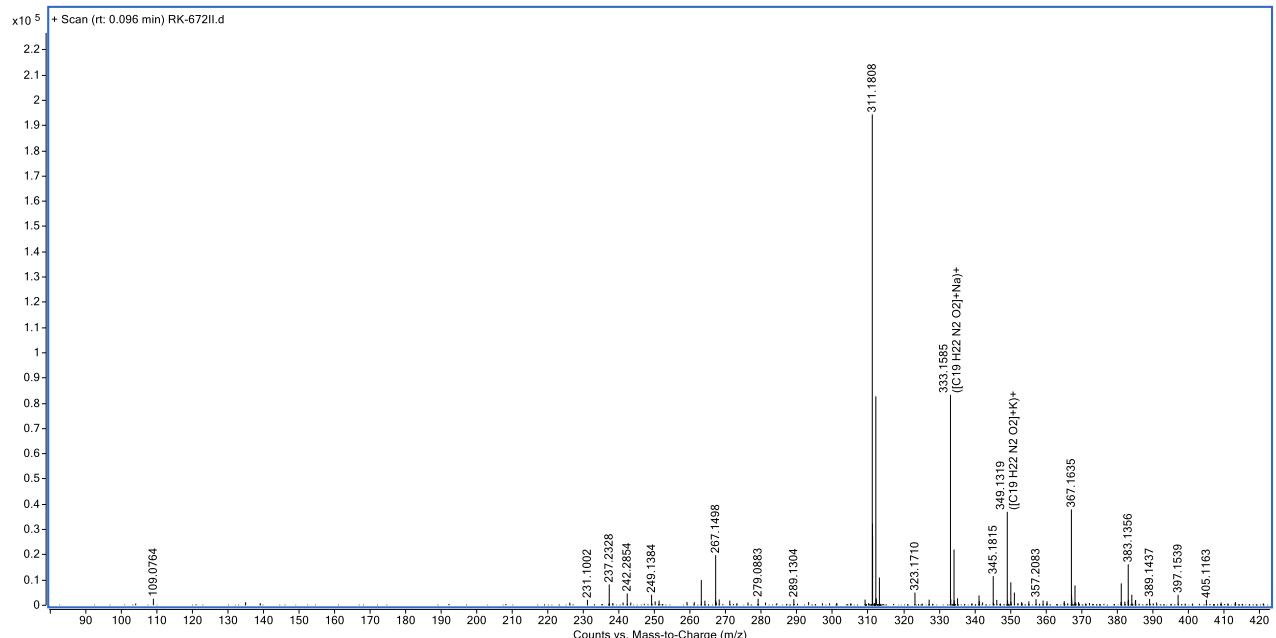
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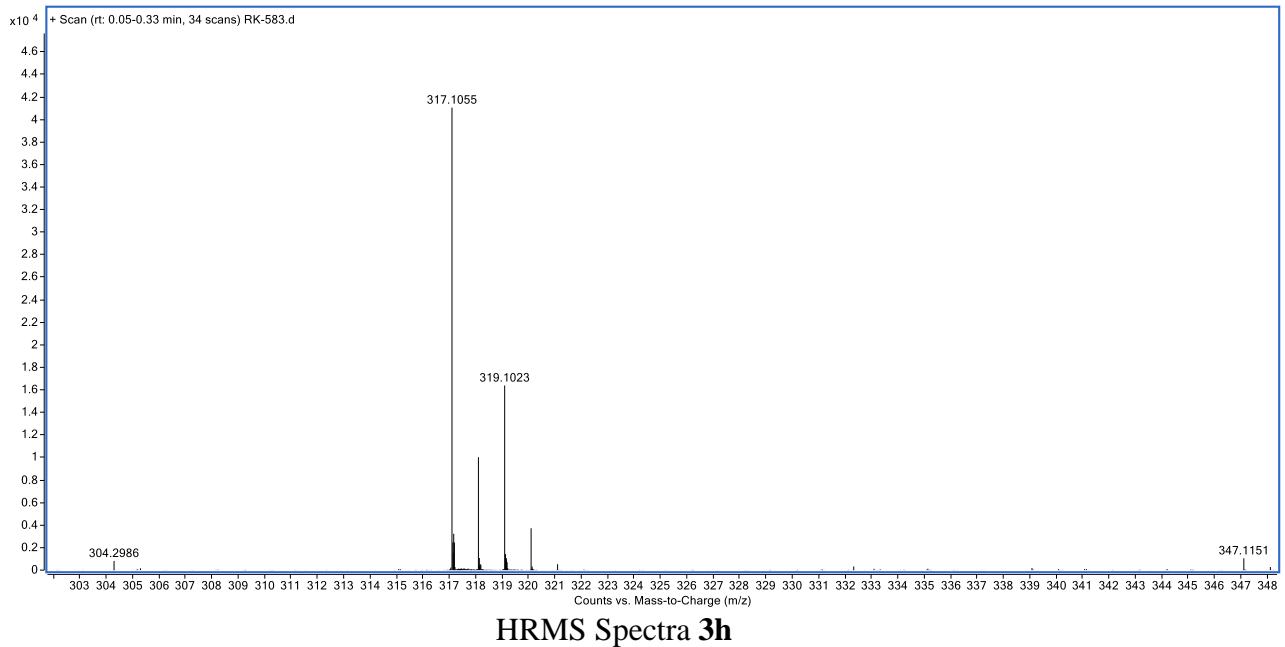
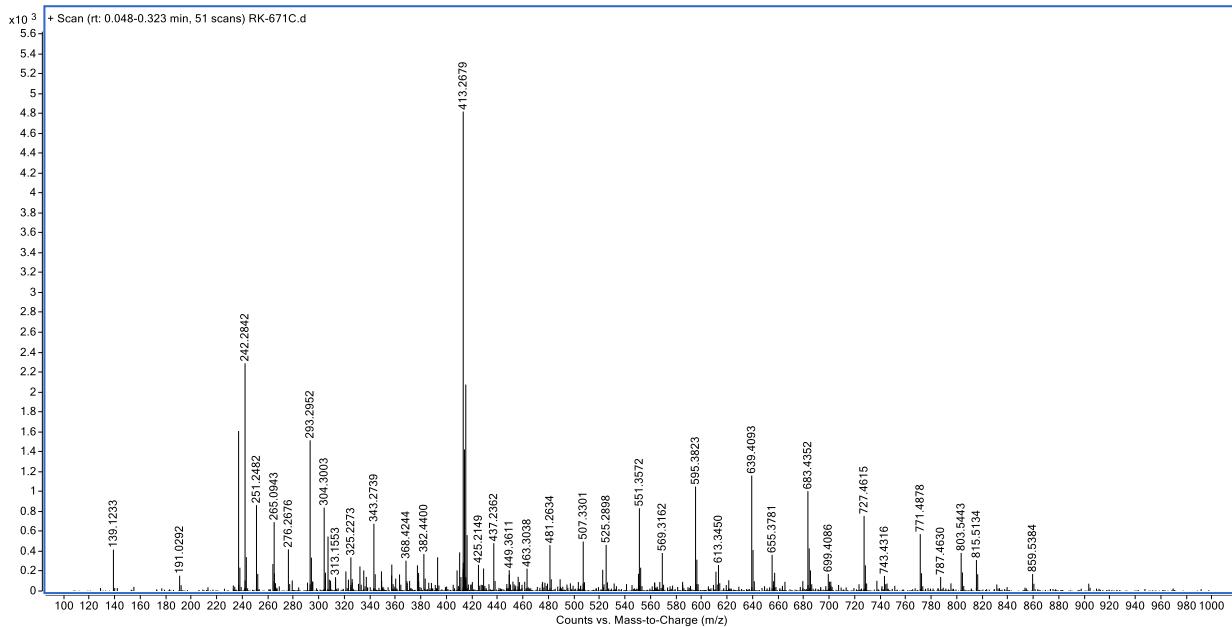
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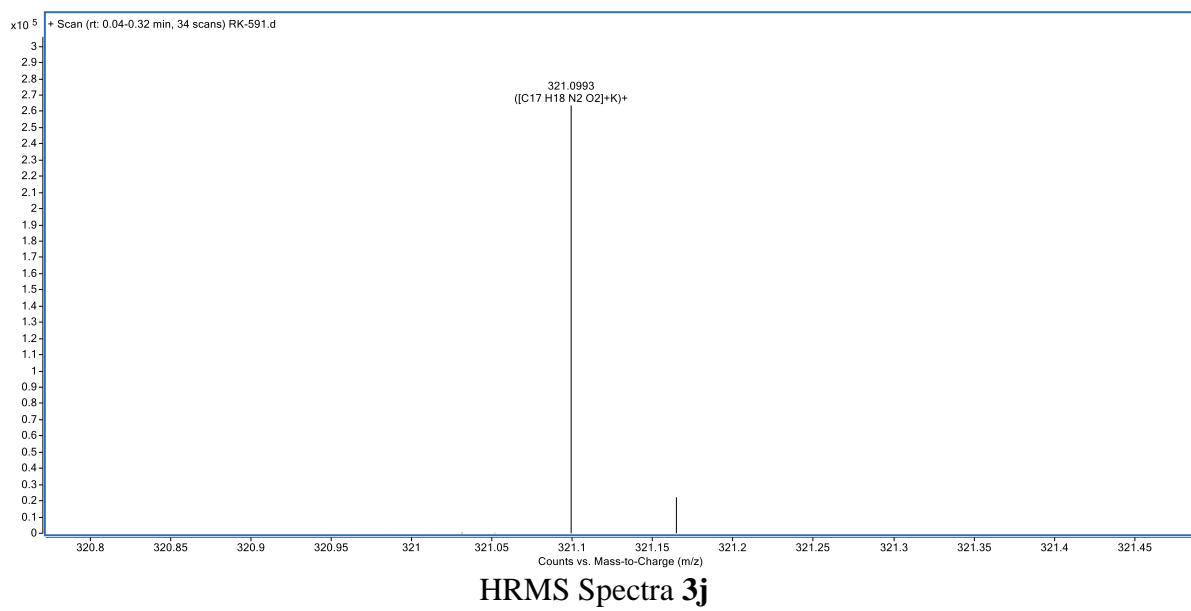
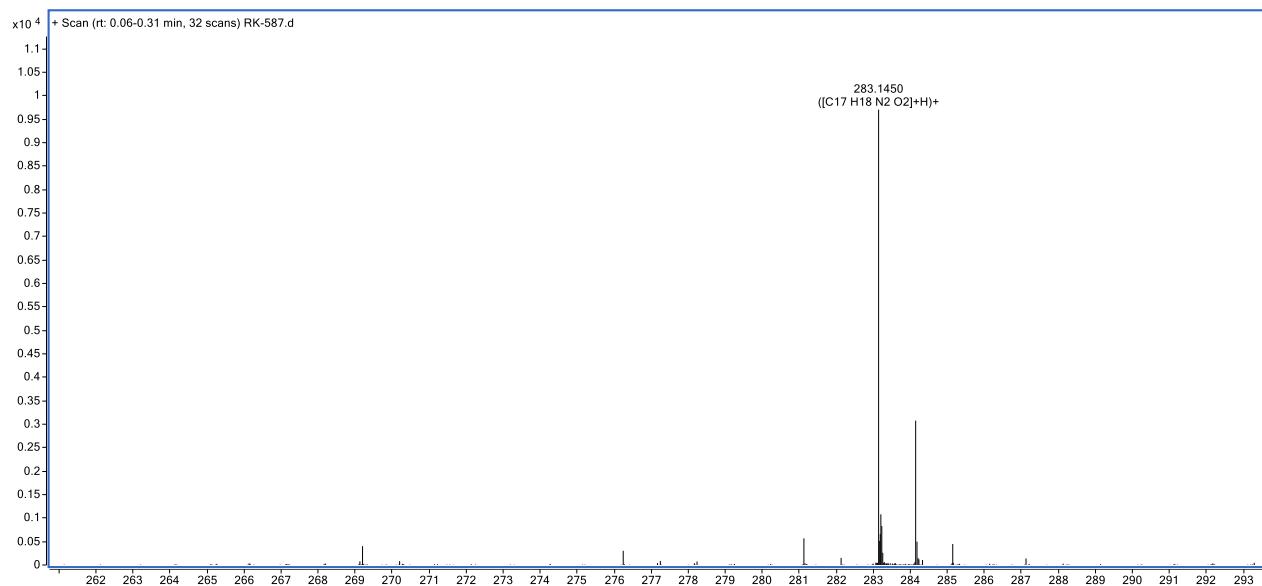
HRMS Spectra 3e



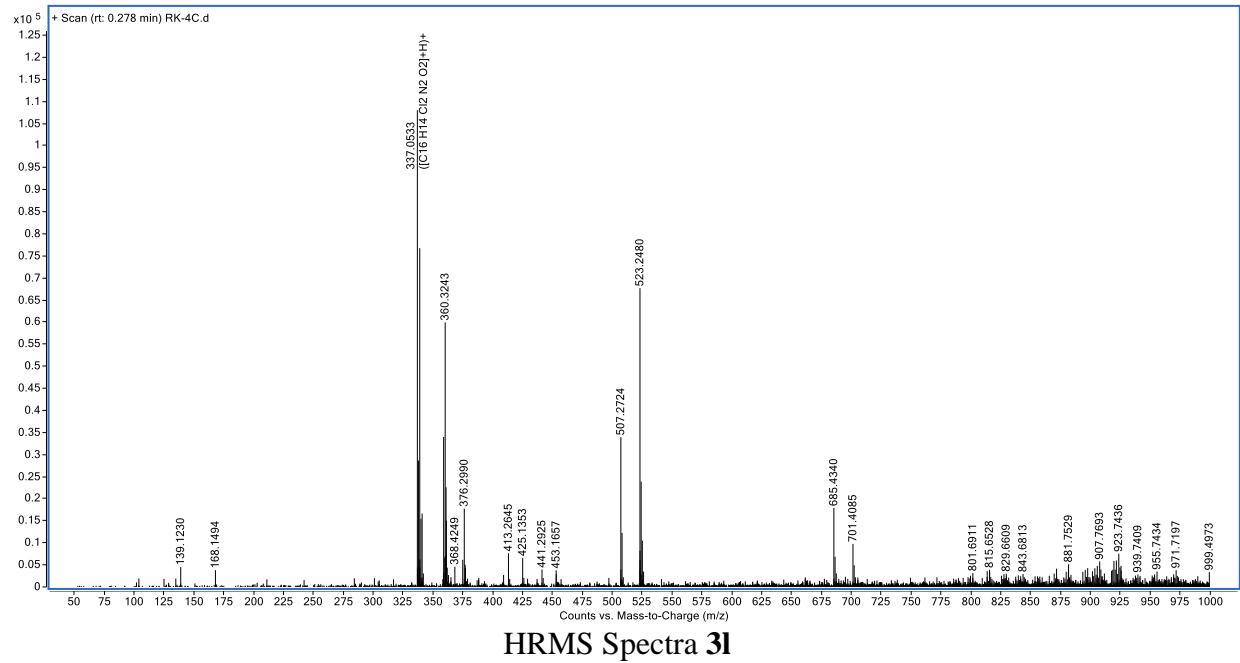
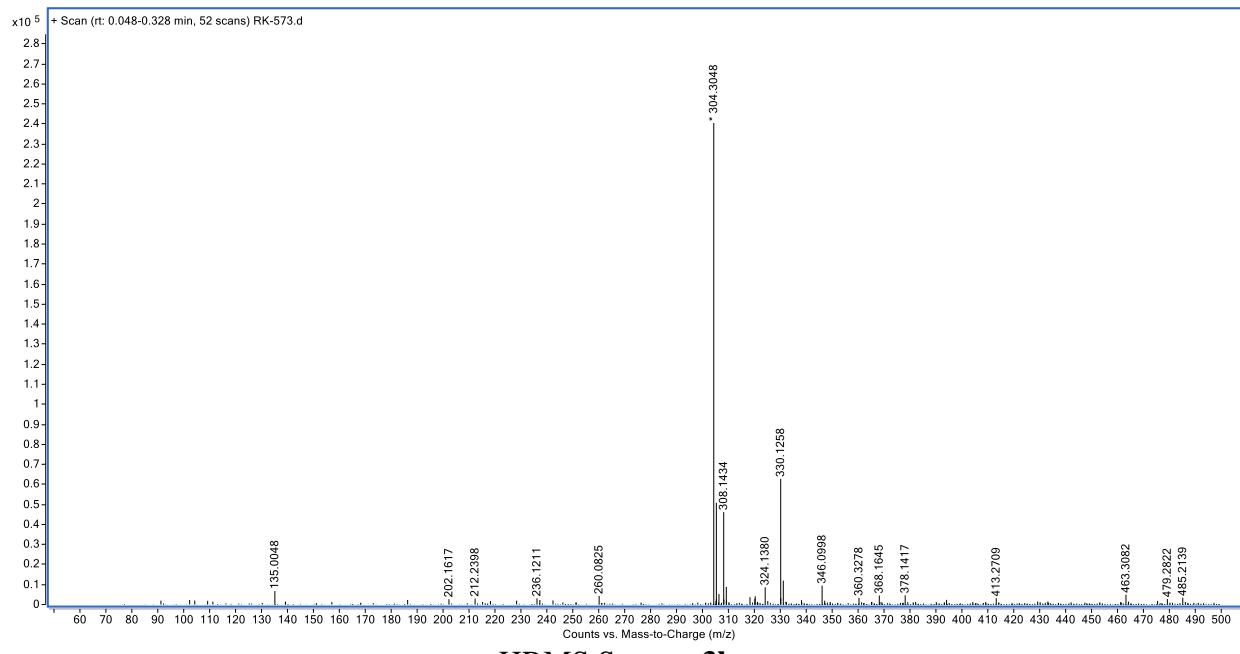
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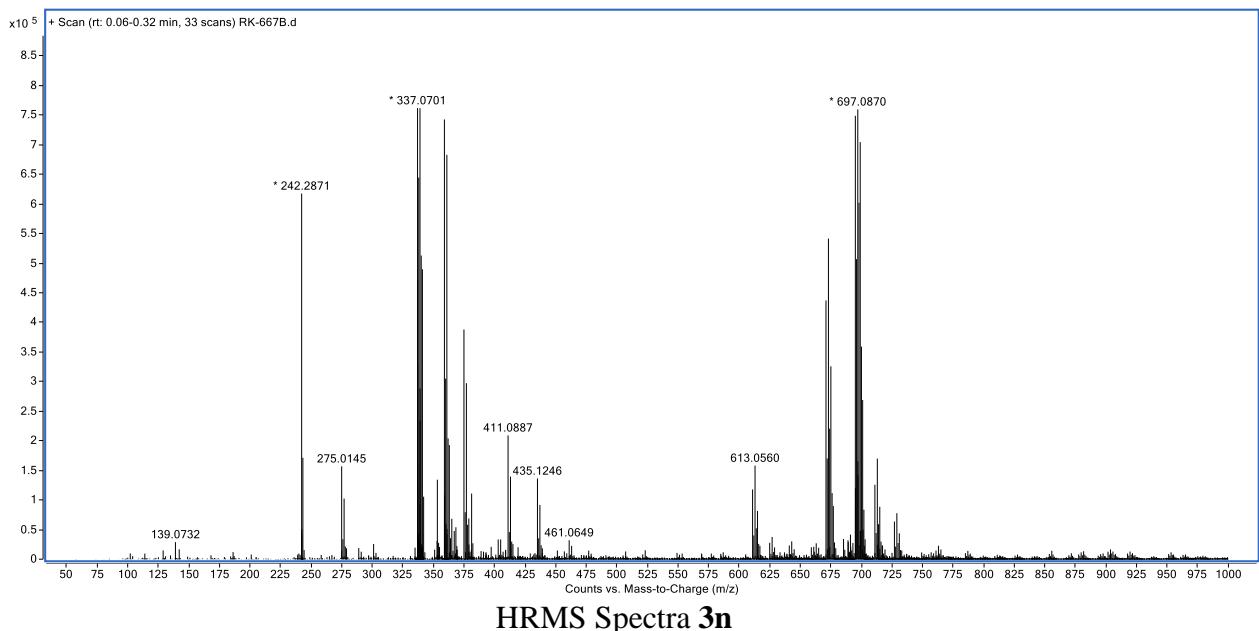
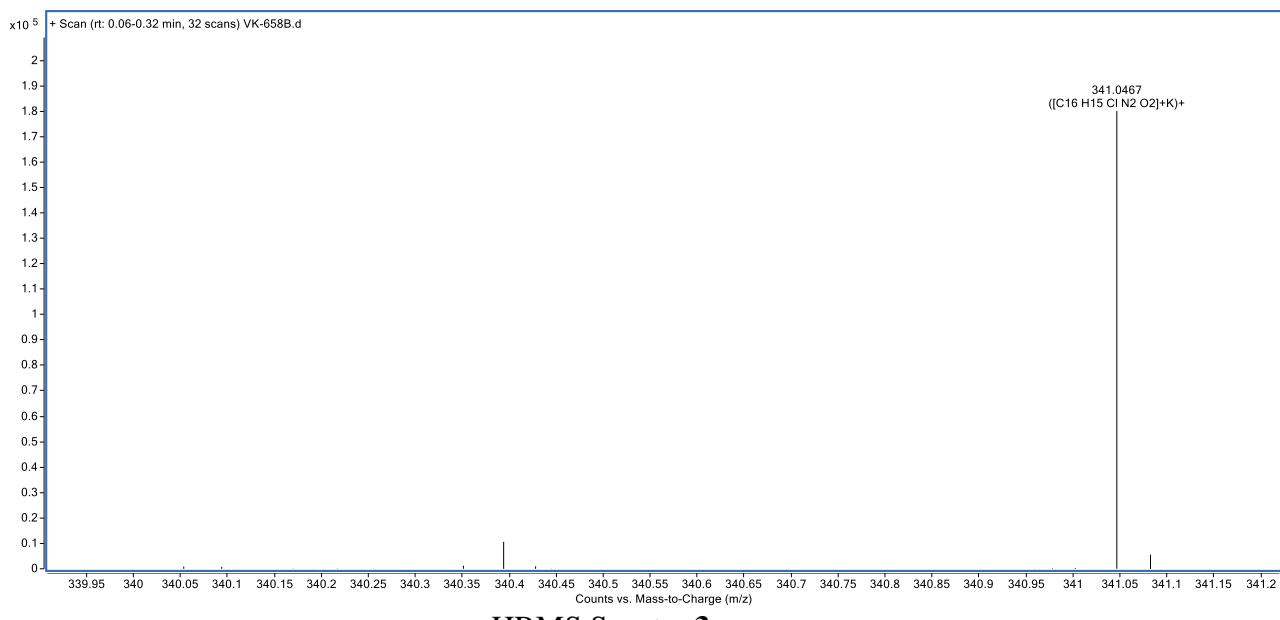
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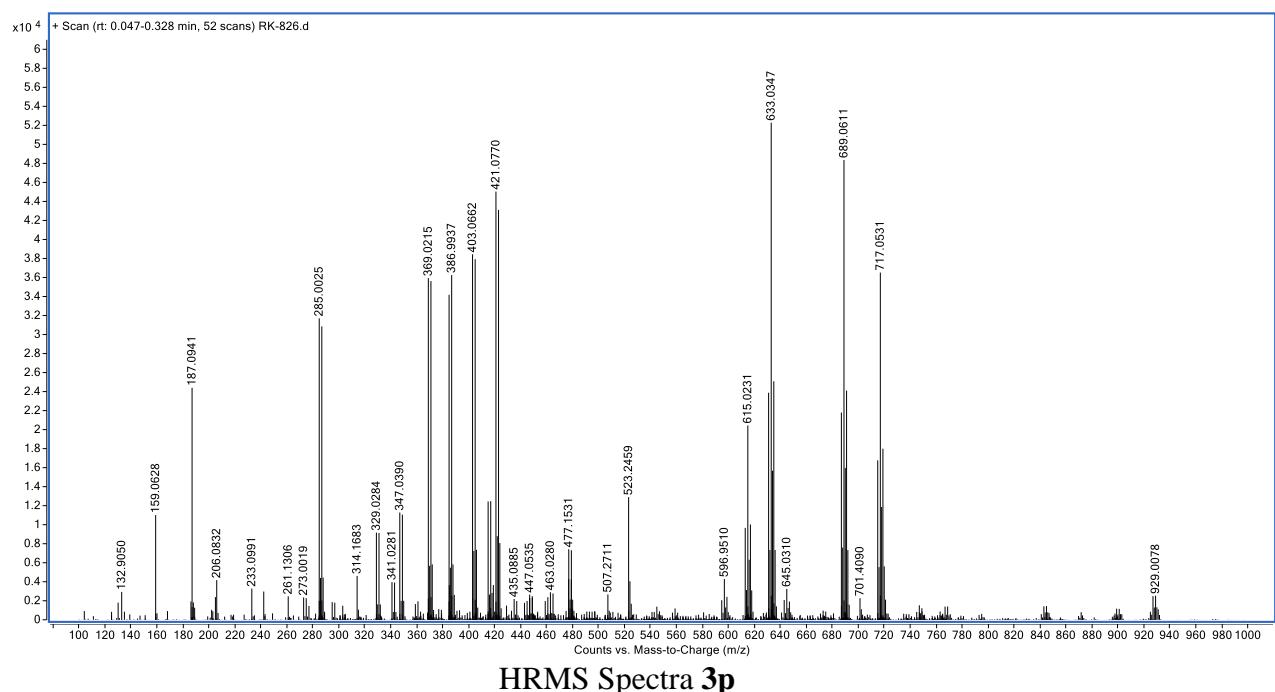
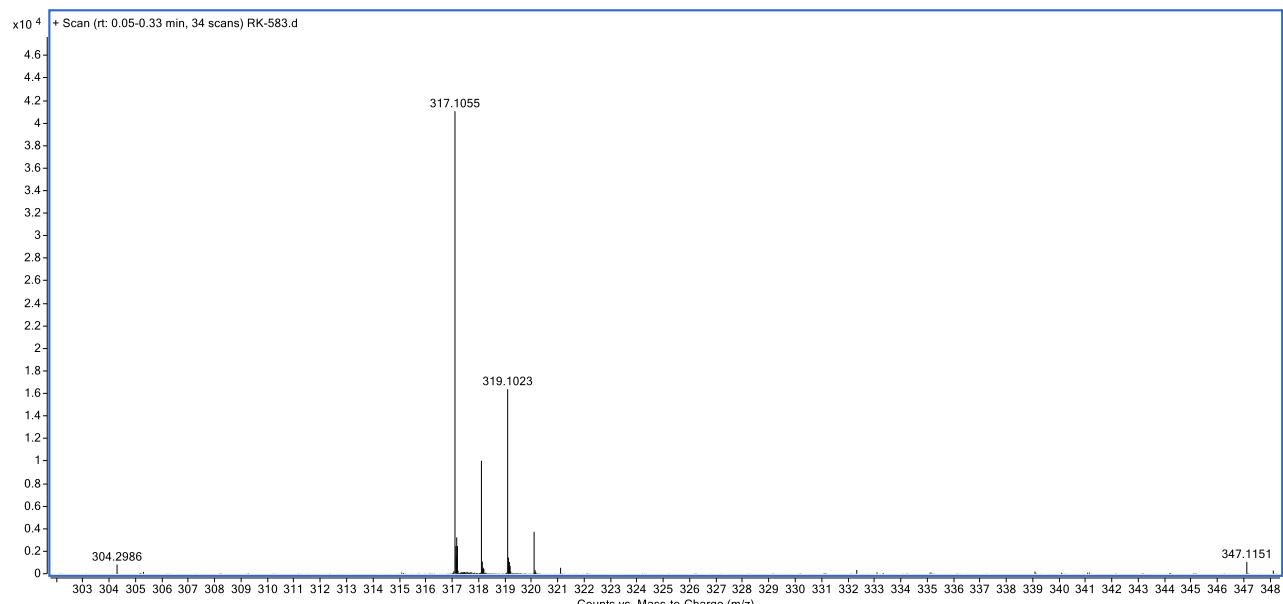
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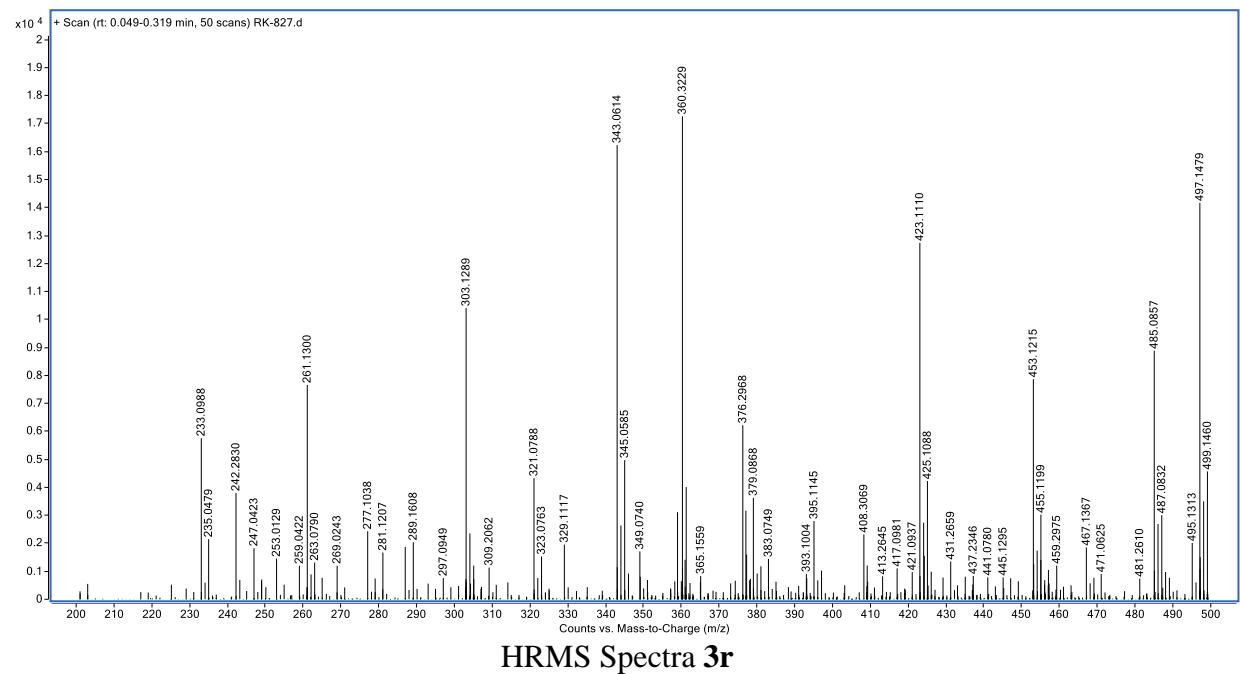
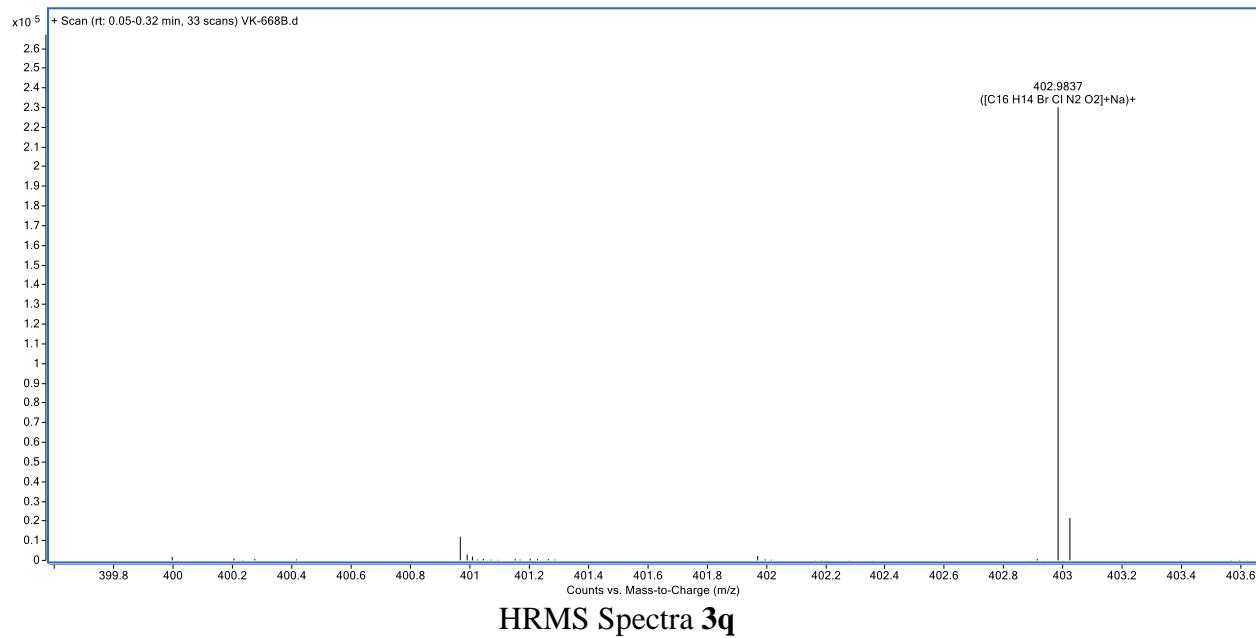
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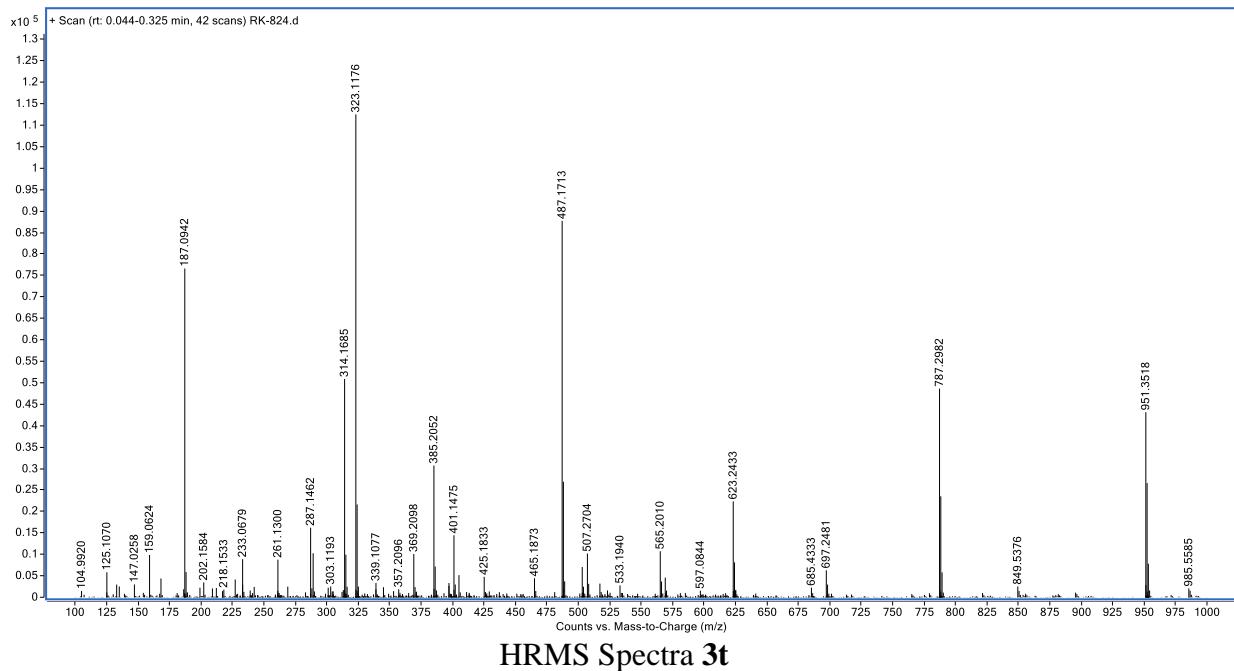
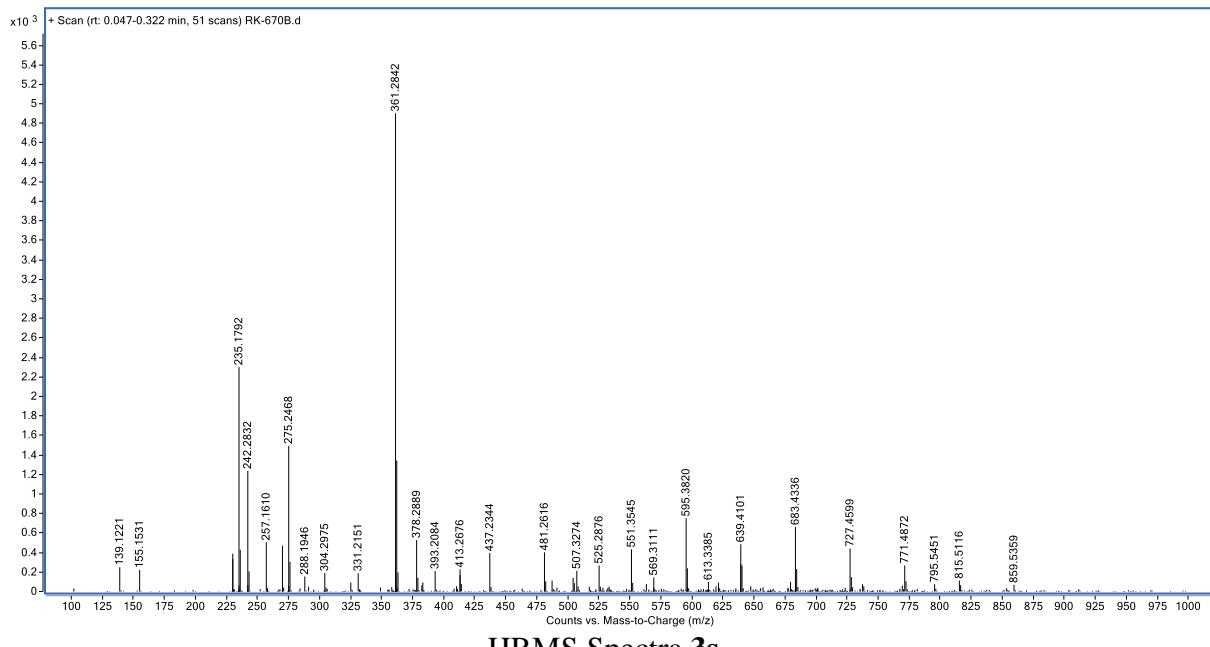
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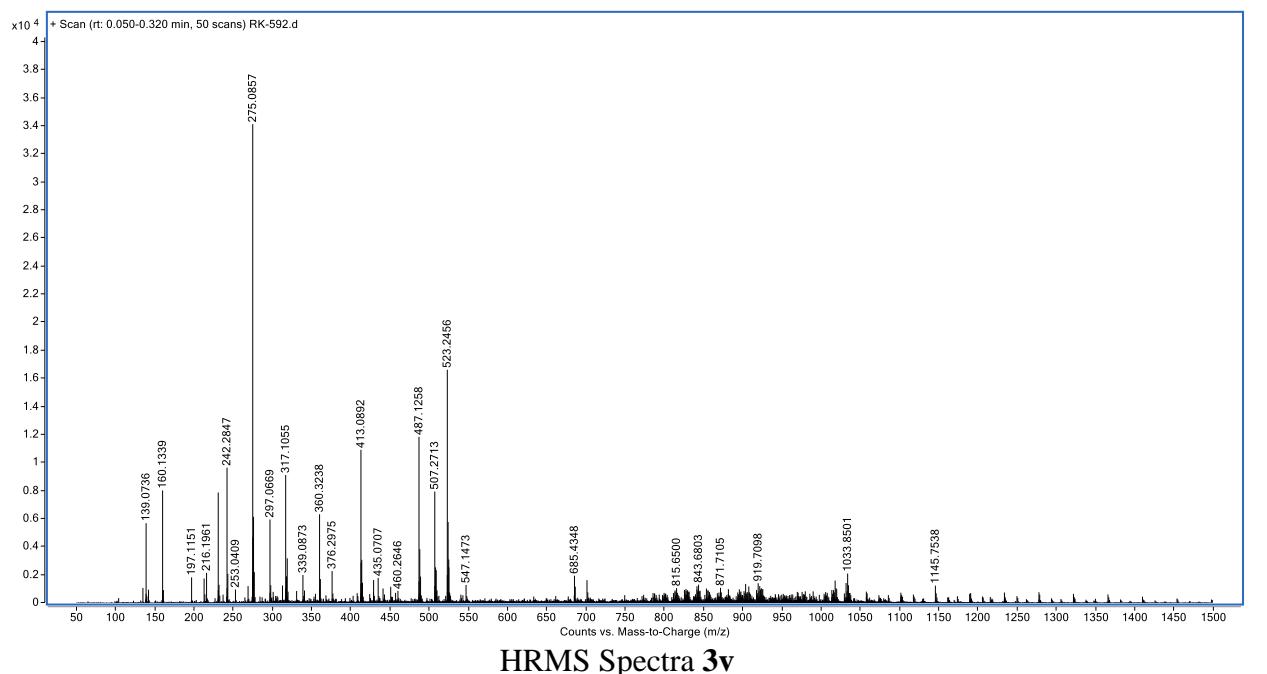
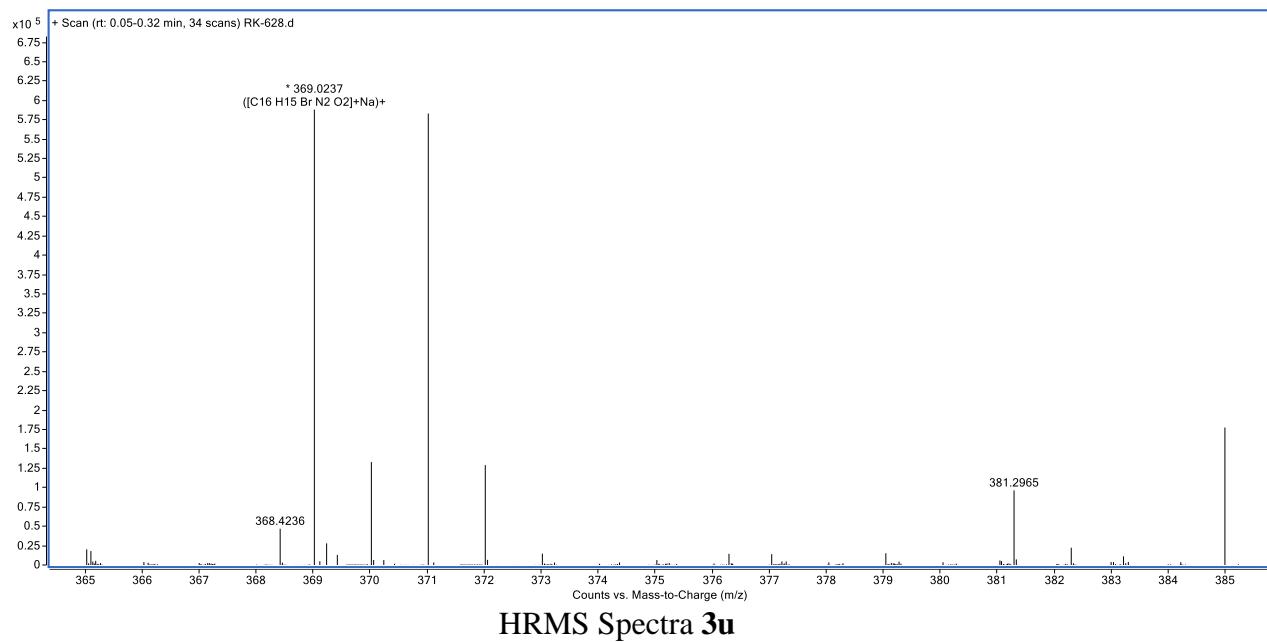
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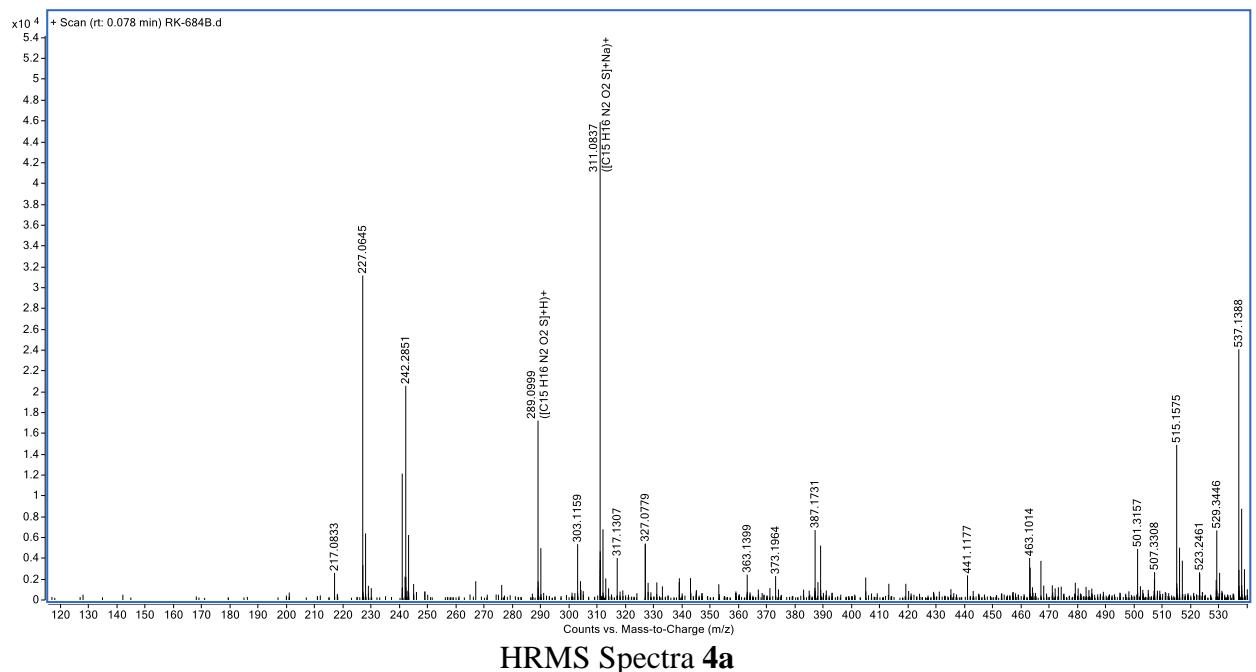
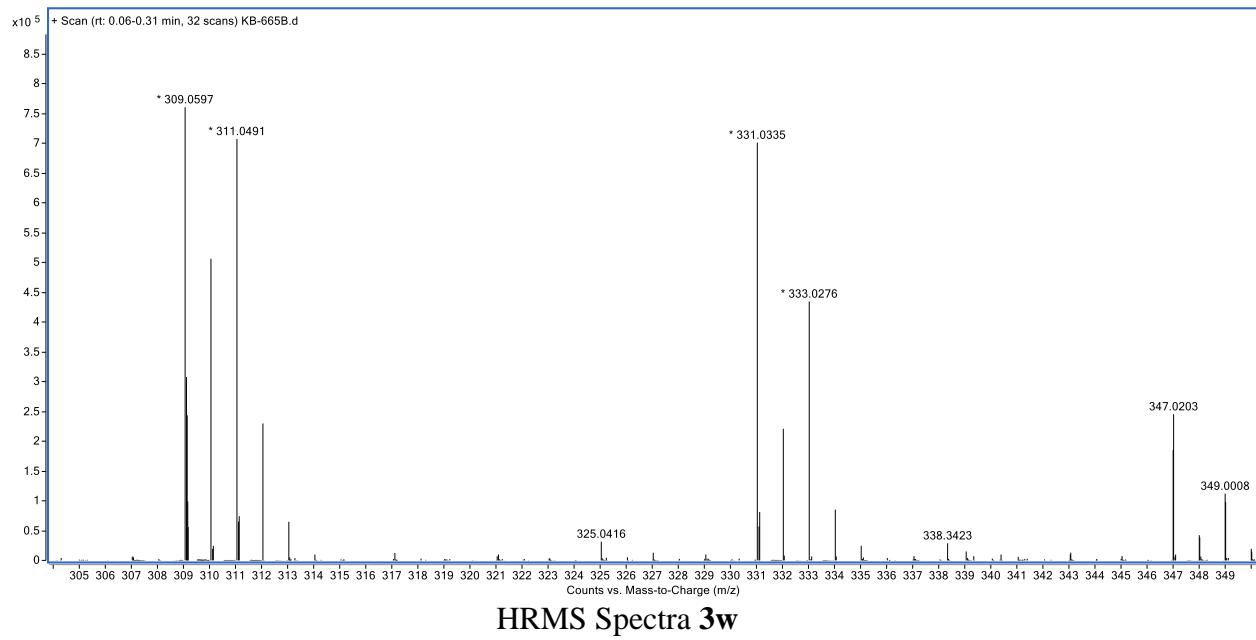
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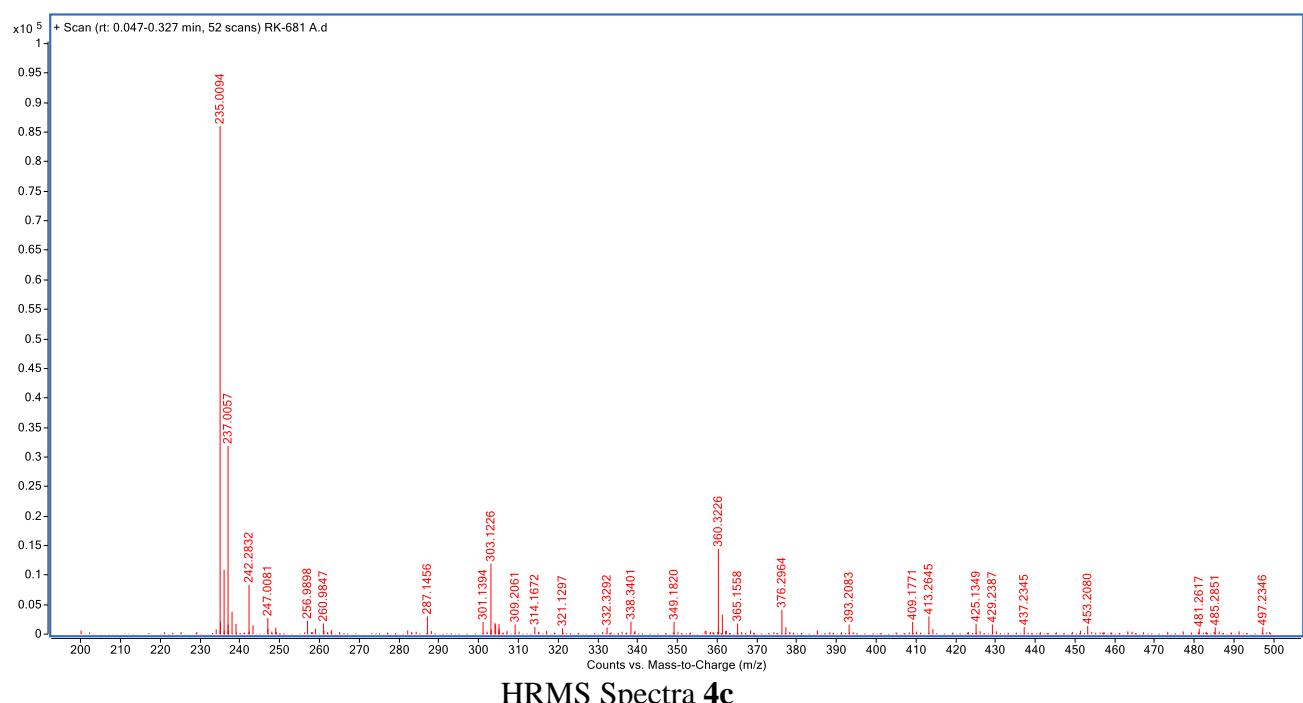
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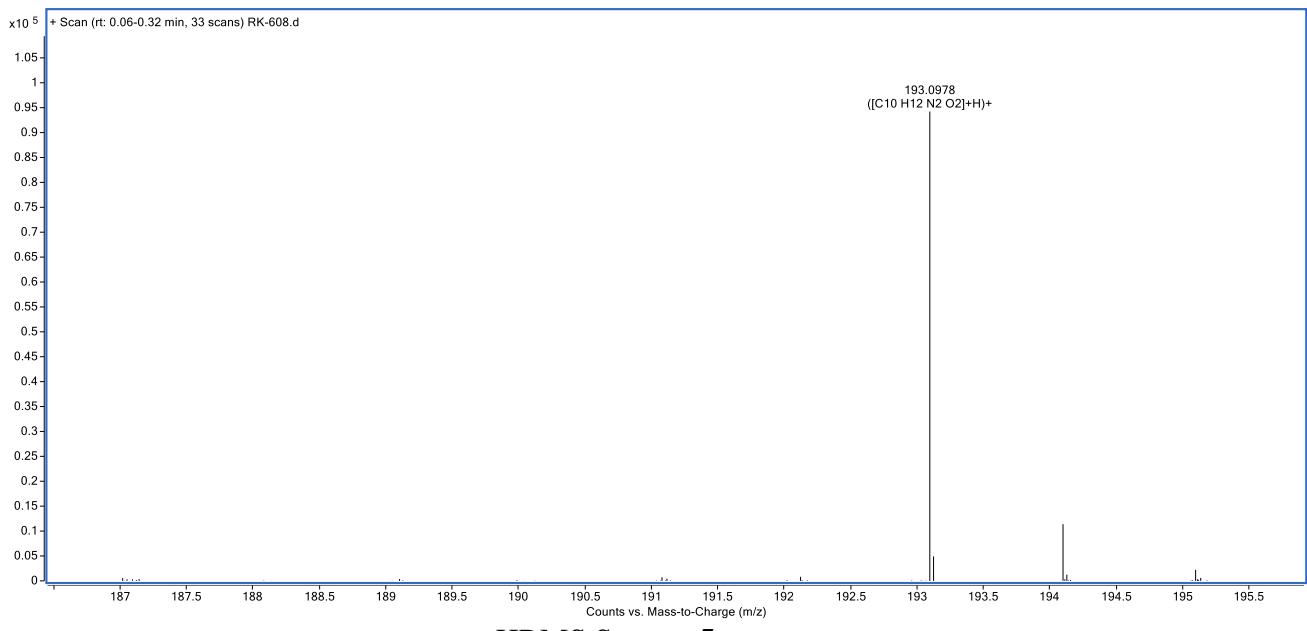
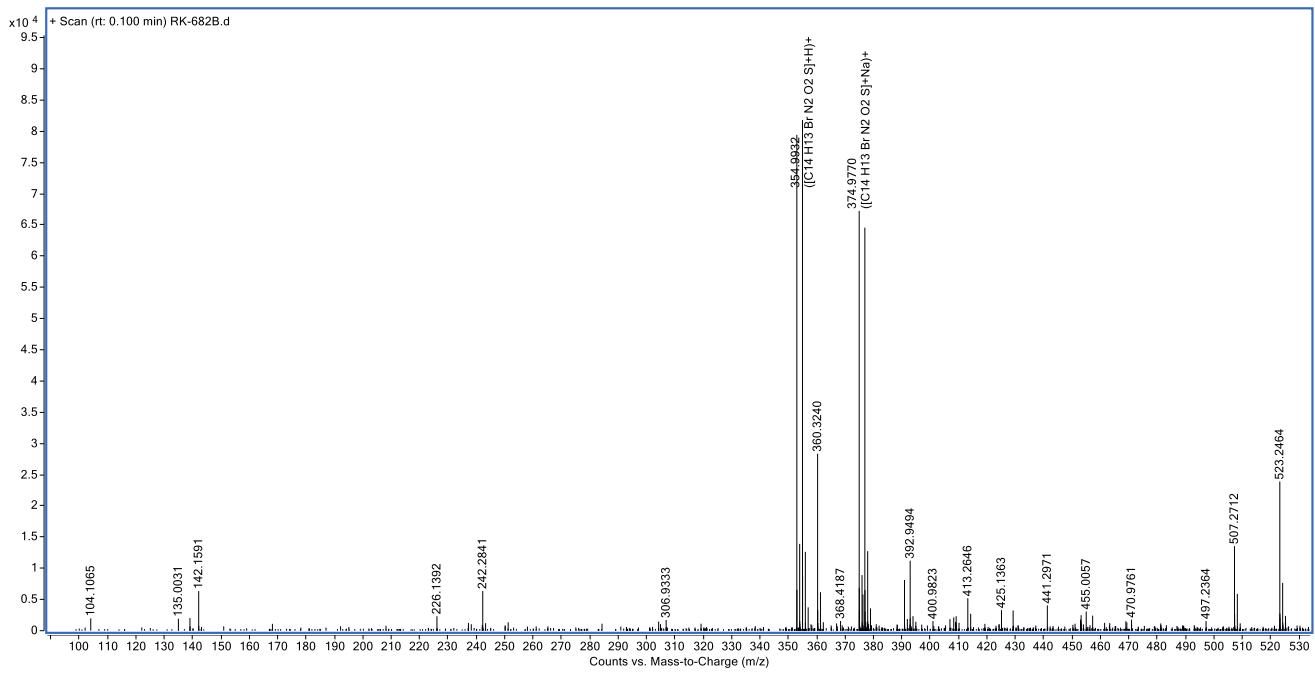


HRMS Spectra 4b

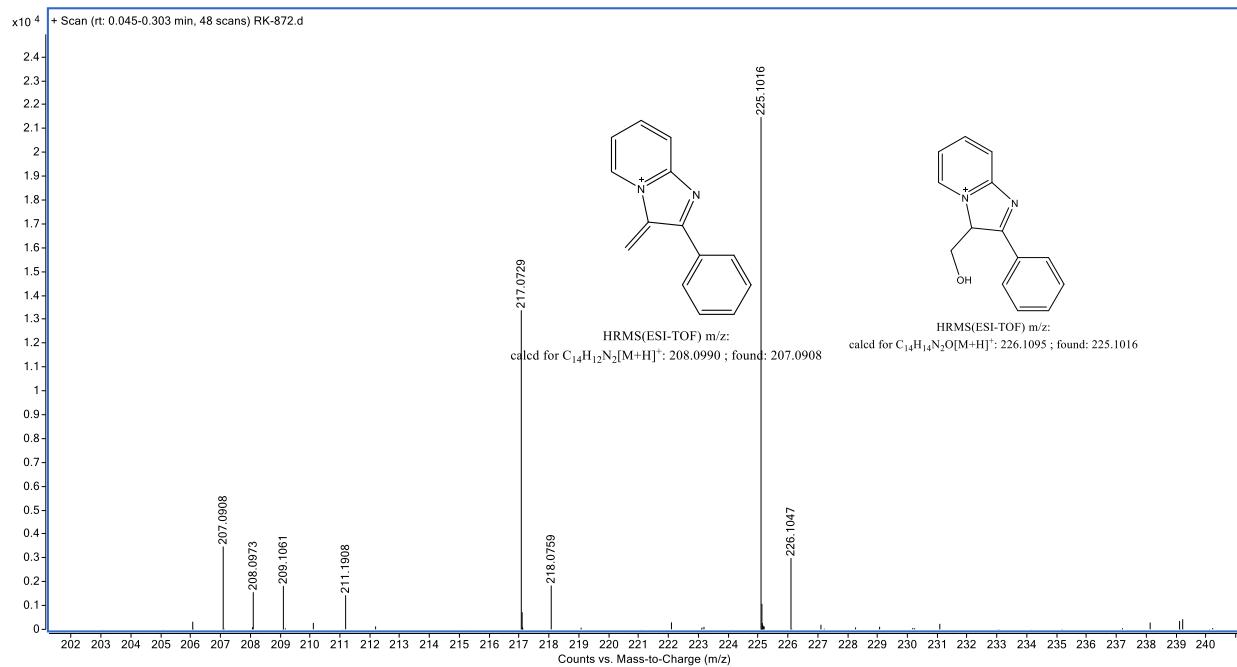


HRMS Spectra 4c

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[Type text]



HRMS Spectra intermediate **A** and **B**