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The Regioselective Iodination of Quinolines, Pyridones, Pyridines and Uracil

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Supporting Information

Table of Content

1. General considerations

1.a. Reagent Information: All solvents were bought from Merck/Aldrich in sure-seal bottle and were used as received. For column chromatography, silica gel (60–120 mesh or 100–200 mesh) obtained from SRL Co.. A gradient elution using pet ether and ethyl acetate was performed, based on Merck aluminum TLC sheets (silica gel 60F254).

1.b. Analytical Information: All isolated compounds were characterized by ^{1}H, ^{13}C NMR spectroscopy, gas chromatography mass spectra (GC-MS) and HRMS (ESI). Nuclear Magnetic Resonance spectra were recorded on a Bruker 400 MHz or 500 MHz instrument. Unless mentioned, all ^{1}H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform-d (7.26 ppm) in the deuterated solvent and all ^{13}C NMR spectra were reported in ppm relative to chloroform-d ($CDCl_3$) (77.23 ppm). All GC analyses were performed on an Agilent 7890A GC system with an FID detector using a J & W DB-1 column (10 m, 0.1 mm I.D.) using *n*-decane as the internal standard. GCMS analysis was done by Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector). High-resolution mass spectra (HRMS) were recorded on a micro-mass ESI TOF (time of flight) mass spectrometer.

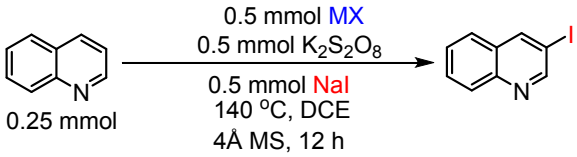
1.c. Description of Reaction Tube:

Fig.1. Pictorial description of reaction tube for oxidative *α*-trifluoromethylation: Fisherbrand Disposable Borosilicate Glass Tubes (16*125mm) with Threaded End (Fisher Scientific Order No. 1495935A) [left]; Kimble Black Phenolic Screw Thread Closures with Open Tops (Fisher Scientific Order No. 033407E) [right]; Thermo Scientific National PTFE/Silicone Septa for Sample Screw Thread Caps (Fisher Scientific Order No. 03394A) [right].

2. Experimental Section

2.a. Optimization of Reaction Condition

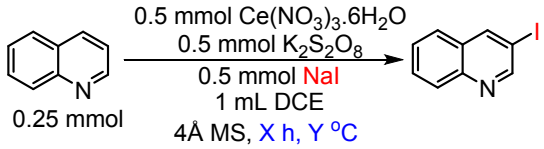
Table S1: Variation of Metal Sources - As found from the control experiment use of metal is obvious to achieve the desire product. We started screening different metal salts.



Entry	Metal Sources	GC Yield (%)
1	$Bi(NO_3)_3.5H_2O$	30
1	$Ni(NO_3)_2$	35
2	CuBr	5
3	**$Ce(NO_3)_3.6H_2O$**	**40**
4	$CoCl_2.6H_2O$	1
5	$NiSO_4$	-
6	$SnCl_2.2H_2O$	-
7	$MnSO_4.H_2O$	-
8[a]	$Ni(NO_3)_2$	37
9[b]	$Pd(Oac)_2$	6

[a] 1 mmol NH_4I ; [b] 20 mol%

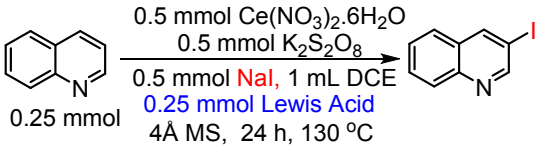
Table S2: Variation of Temperature and Time - From metal salt screening it has been found that $Ce(NO_3)_3.6H_2O$ is the best metal salt for the conversion. Later on we optimized the temperature and time simultaneously along with the $Ce(NO_3)_3.6H_2O$ as the metal salt. The optimized data is tabulated below.



Entry	Temperature	Time	GC Yield (%)
1	110 °C	16 h	2
2	120 °C	16 h	6
3	130 °C	12 h	48
4	130 °C	16 h	50
5	**130 °C**	**24 h**	**55**
6	140 °C	24 h	56

Following the result further optimization was carried out at 130 °C for 24 hour.

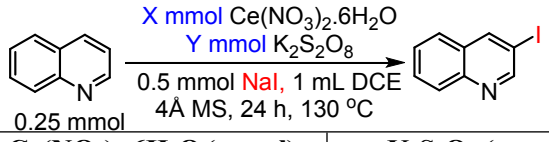
Table S3: Variation of Lewis Acids - a series of Lewis acids was then varied and tried to figure out whether Lewis acid has any effect on the reaction. The optimized results are shown in the following table.



Entry	Lewis Acids	GC Yield (%)
1	-	55
2	**TFA**	**62**
3	$AlMe_3$	54
4	PTSA	35
5	$BF_3.OEt_2$	13
6	$FeCl_3.6H_2O$	20
7	$B(O^iPr)_3$	1
8[a]	-	5

[a] I_2 in place of NaI

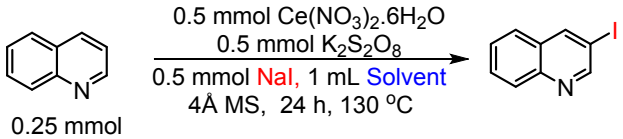
Table S4: Variation of Amount of $Ce(NO_3)_2.6H_2O$ & $K_2S_2O_8$. So, TFA, $AlMe_3$ or PTSA can enhance the reaction. Further screening was made on the equivalent ration of metal salt and amount of oxidizing agent, i.e. $K_2S_2O_8$. Optimization data tabulated below.



Entry	$Ce(NO_3)_2.6H_2O$ (mmol)	$K_2S_2O_8$ (mmol)	GC Yield (%)
1	0.25	-	9
2	0.50	-	22
3	0.75	-	26
4	1.00	-	28
5	0.25	0.50	26
6	**0.50**	**0.50**	**62**
7	0.75	0.50	61
8	1.00	0.50	55
9	1.00	1.00	36

From the above result it is clear that 0.50 mmol $Ce(NO_3)_3.6H_2O$ and 0.50 mmol $K_2S_2O_8$ is proper ratio to get a good conversion for 0.25 mmol of substrate.

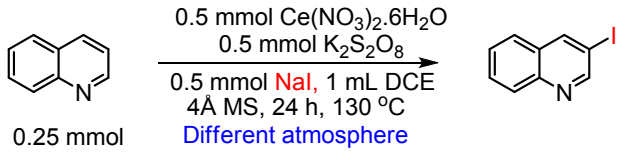
Table S5: Variation of Solvents - we then tried to find the best solvent required for the maximum conversion. A series of solvent has been used for the solvent screening. The optimized condition is shown below.



Entry	Solvent	GC Yield (%)
1	Cyclohexane	2
2	Toluene	0
3	DMF	0
4	Decalin	0
5	Trifluorotoluene	-
6	**DCE**	**62**

So, DCE is the best solvent for the reaction.

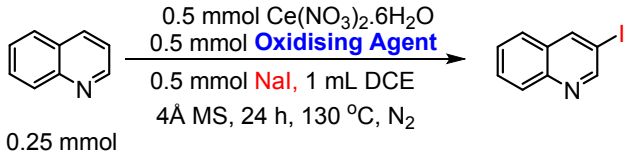
Table S5: Reaction atmosphere variation - After that we put the reaction in N_2, O_2 and air. The optimization data is shown below.



Entry	Atmosphere	GC Yield (%)
1	**N_2**	**75**
2	O_2	74
3	Air	65

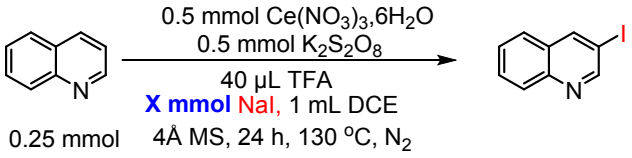
So, maintaining N_2 atmosphere enhances the reaction. So further studies have been carried out in N_2 atm.

Table S6: Variation of different oxidising source - Different oxidizing agent was then screened to know the best oxidizing agent for the iodination. The optimized data is given below.



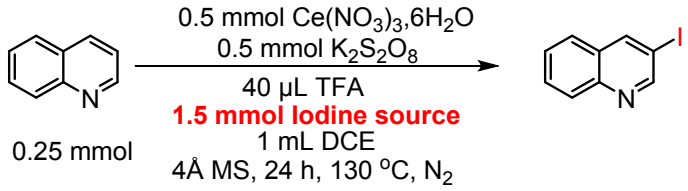
Entry	Oxidising agent	GC Yield(%)
1	**$K_2S_2O_8$**	**75**
2	$(NH_4)_2S_2O_8$	34
3	TEMPO	4
4	Para benzoquinone	0

Table S7: Variation of NaI amount - Amount of Sodium iodide is varied to achieve the improve reaction condition.



Entry	Amount of $Ce(NO_3)_3$ (mmol)	Amount of $K_2S_2O_8$ (mmol)	Amount of NaI (mmol)	GC Yield (%)
1	0.5	0.5	0.25	40
2	0.5	0.5	0.5	75
3	**0.5**	**0.5**	**0.75**	**86**
4	0.5	0.5	1.0	82

Table S8: Variation of iodine source- Different iodine sources has been varied and it is found that sodium iodide is most effective iodinating reagent for this transformation.

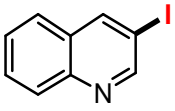


Entry	Iodine Source	GC Yield(%)
1	**NaI**	**85**
2	KI	68
3	NIS	20
4	Molecular iodine	40
5	TBAI	0

2.b. <u>General Procedure</u> for Iodination of Quinolines, Pyridones, Pyridines and Uracil

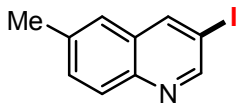
In a clean, oven–dried screw cap reaction tube, with previously placed magnetic stir–bar heterocycle (0.5 mmol) (for solid compounds); NaI (3.0 equiv, 1.5 mmol, 224.8 mg); Cerus nitrate hexahydrate ($Ce(NO_3)_3.6H_2O$) (2.0 equiv, 1.0 mmol 434 mg); Potassium perdisulphate ($K_2S_2O_8$) (2.0 equiv, 1.0 mmol 270 mg); molecular shieves 4 Å (150 mg) and Trifluoroacetic acid (80 µL) were taken. The reaction tube was tightly sealed and allowed for vacuum by high vacuum pump and nitrogen gas was passed using Schlenk line. Thus making the reaction tube completely N_2 atmosphere, solvent DCE (2 mL) was added by syringe (for liquid starting material substrate was added by micro syringe). The tube was placed in a preheated oil bath at 130 ˚C. The reaction mixture was vigorously stirred for 24h. Upon completion of the reaction the reaction mixture was cooled to room temperature, and dried, then the residue was diluted with ethyl acetate (3x10 mL) and transferred to separating funnel. Ethyl acetate (10 mL) and water (15 mL) were added to the filtrate. The combined organic extract was dried over Na_2SO_4 and solvent evaporated on a rotary evaporator. The mixture was purified by column chromatography over silica gel (60-120/100-200 mesh size) and petroleum ether/ethyl acetate.

2.c. Characterization Data

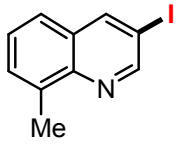


3-iodoquinoline (Table 2, Entry 2a): Iodinated product was obtained following the general procedure on a 0.5 mmol (64.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (99:1 v/v). Pale white solid compound obtained. Yield 78% (99 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.03 (d, *J* = 2.1 Hz, 1H), 8.54 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.06 (dq, *J* = 8.5, 1.0 Hz, 1H), 7.76 – 7.68 (m, 2H), 7.56 (ddd, *J* = 8.2, 6.8, 1.2 Hz,

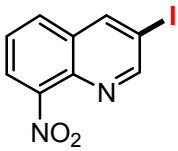
1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 90.0, 127.0, 127.6, 129.7, 130.2, 137.3, 143.9, 146.5, 155.8. Calculated mass 255.9623 (Molecular formula - C_9H_7IN), Observed mass 255.9625.[1,2]



3-iodo-6-methylquinoline (Table 2, Entry 2b): Iodinated product was obtained following the general procedure on a 0.5 mmol (71.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (95:5 v/v). White crystalline solid compound. Yield 62% (83 mg). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.94 (s, 1H), 8.47 – 8.42 (m, 1H), 7.97 (t, *J* = 6.2 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.47 – 7.41 (m, 1H), 2.53 (d, *J* = 2.6 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 21.9, 89.7, 125.8, 128.9, 130.2, 132.9, 138.0, 143.8, 144.5, 154.5. Calculated mass 269.9780 (Molecular formula – $C_{10}H_9IN$), Observed mass 269.9791.[1,2]

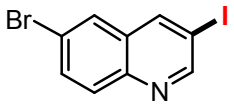


3-iodo-8-methylquinoline (Table 2, Entry 2c): Iodinated product was obtained following the general procedure on a 0.5 mmol (71.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (97:3 v/v). Brownish solid compound. Yield 45% (61 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.38 (dd, *J* = 8.5, 1.7 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.48 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.30 (dq, *J* = 7.5, 1.0 Hz, 1H), 2.78 (d, *J* = 1.0 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 18.3, 95.6, 100.2, 122.7, 130.1, 130.9, 137.7, 138.7, 140.8, 150.1. Calculated mass 269.9780 (Molecular formula – $C_{10}H_9IN$), Observed mass 269.9773.[1]

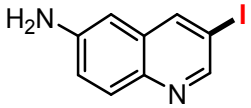


3-iodo-8-nitroquinoline(Table 2, Entry 2d): Iodinated product was obtained following the general procedure on a 0.5 mmol (87 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200

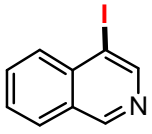
mesh). Eluent: pet ether: ethyl acetate (95:5 v/v). Yellow Solid . Yield 80% (120 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.17 (d, *J* = 2.1 Hz, 1H), 8.65 (d, *J* = 2.1 Hz, 1H), 8.06 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.93 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.64 (dd, *J* = 8.3, 7.5 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 92.3, 124.4, 126.6, 130.6, 131.2, 137.9, 143.9, 148.5, 158.1. Calculated mass 300.9474 (Molecular formula - $C_9H_6IN_2O_2$), Observed mass 300.9454.[2]



6-bromo-3-iodoquinoline (Table 2, Entry 2e): iodinated product was obtained following the general procedure on a 0.5 mmol (104 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (98:2 v/v). White Solid . Yield 65% (108 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.06 – 9.00 (d, *J* = 2.1 Hz, 1H), 8.47 – 8.41 (dd, *J* = 2.2, 0.8 Hz, 1H), 7.96 – 7.90 (d, *J* = 9.0 Hz, 1H), 7.89 – 7.84 (d, *J* = 2.1 Hz, 1H), 7.82 – 7.74 (dd, *J* = 9.0, 2.2 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 91.15, 121.61, 128.96, 130.97, 131.38, 133.77, 142.87, 145.04, 156.16. Calculated mass 333.8723 (Molecular formula – C_9H_6BrIN), Observed mass 333.8725.[1,2]

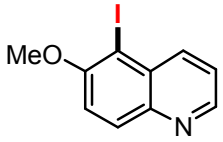


5-iodoquinolin-6-amine (Table 2, Entry 2f): Iodinated product was obtained following the general procedure on a 0.5 mmol (72 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (96:4 v/v) Brownish solid compound. Yield 55% (74 mg). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.61 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.22 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 1H), 7.37 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.22 (d, *J* = 8.9 Hz, 1H), 4.58 (s, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 81.1, 120.3, 123.0, 131.0, 131.5, 138.2, 143.9, 146.2, 147.1. Calculated mass 270.9732 (Molecular formula – $C_9H_8IN_2$), Observed mass 269.9748.[2]

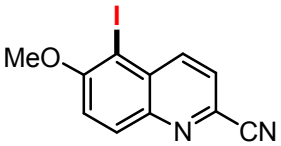


4-iodoisoquinoline (Table 2, Entry 2g): iodinated product was obtained following the general procedure on a 0.5 mmol (64.5 mg) scale reaction. The reaction was continued for 24

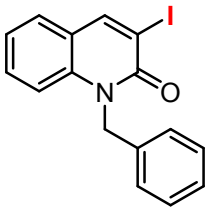
h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (95:5 v/v). White Solid . Yield 72% (92 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.22 (s, 1H), 8.93 (s, 1H), 8.06 – 8.02 (m, 1H), 7.96 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.86 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.72 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.55, 148.84, 137.88, 133.27, 131.06, 129.45, 129.16, 128.89, 97.20.[1,2]



5-iodo-6-methoxyquinoline (Table 2, Entry 2h): iodinated product was obtained following the general procedure on a 0.5 mmol (79.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (90:10 v/v). Yellowish Solid . Yield 60% (85 mg). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.04 – 8.98 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.90 – 8.85 (m, 1H), 8.51 – 8.46 (m, 1H), 7.80 – 7.73 (dd, *J* = 8.7, 4.7 Hz, 1H), 7.63 – 7.58 (d, *J* = 9.3 Hz, 1H), 4.14 – 4.09 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 57.72, 86.45, 118.73, 123.01, 126.65, 132.13, 138.38, 144.45, 145.51, 158.85. Melting point: 113 °C.

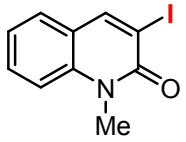


5-iodo-6-methoxyquinoline-2-carbonitrile (Table 2, Entry 2i): iodinated product was obtained following the general procedure on a 0.5 mmol (92 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). White Solid . Yield 70% (109 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 – 8.52 (dd, *J* = 8.8, 0.8 Hz, 1H), 8.19 – 8.13 (dd, *J* = 9.4, 0.8 Hz, 1H), 7.71 – 7.66 (d, *J* = 8.7 Hz, 1H), 7.56 – 7.52 (d, *J* = 9.3 Hz, 1H), 4.21 – 3.92 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 57.54, 85.76, 117.44, 118.30, 125.14, 132.04, 132.22, 132.42, 140.91, 144.71, 159.10. Calculated mass 310.9681 (Molecular formula – $C_{11}H_8IN_2O$), Observed mass 310.9673. Melting point: above 200 °C.

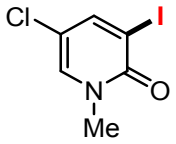


1-benzyl-3-iodoquinolin-2(1H)-one (Table 3, Entry 5a): iodinated product was obtained following the general procedure on a 0.5 mmol (117.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (90:10 v/v). Pale white Solid. Yield 65% (117 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 2.0 Hz, 1H), 7.68 – 7.60

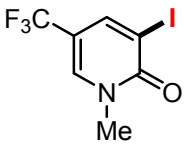
(m, 2H), 7.34 – 7.21 (m, 3H), 7.21 – 7.16 (m, 2H), 7.00 (d, *J* = 8.9 Hz, 1H), 6.80 (d, *J* = 9.5 Hz, 1H), 5.51 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.23, 139.19, 139.15, 138.42, 137.27, 136.05, 129.09, 127.65, 126.69, 123.14, 122.92, 117.22, 85.32, 46.13. Melting point: 163 °C.



3-iodo-1-methylquinolin-2(1H)-one (Table 3, Entry 5b): iodinated product was obtained following the general procedure on a 0.5 mmol (79.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Pale white Solid. Yield 68% (97 mg). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.88 – 7.86 (d, *J* = 2.0 Hz, 1H), 7.83 – 7.79 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.59 – 7.55 (d, *J* = 9.5 Hz, 1H), 7.15 – 7.09 (d, *J* = 8.9 Hz, 1H), 6.74 – 6.70 (d, *J* = 9.5 Hz, 1H), 3.80 – 3.60 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 29.74, 85.27, 116.37, 122.87, 137.21, 137.96, 139.21, 139.70, 162.19. Calculated mass 285.9723 (Molecular formula – $C_{10}H_9INO$), Observed mass 285.9723. Melting point: 133 °C.

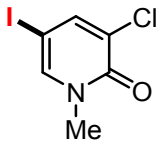


5-chloro-3-iodo-1-methylpyridin-2(1H)-one (Table 3, Entry 5c): iodinated product was obtained following the general procedure on a 0.25 mmol (35.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v) yellowish -white crystalline solid compound. Yield 88% (59 mg) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 2.4 Hz, 1H), 7.73 (dq, *J* = 2.5, 1.2 Hz, 1H), 3.64 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 40.0, 93.0, 110.7, 138.3, 144.1, 159.9.

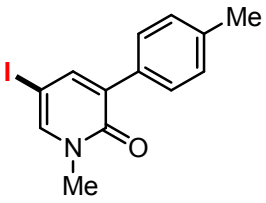


3-iodo-1-methyl-5-(trifluoromethyl)pyridin-2(1H)-one (Table 3, Entry 5d): Iodinated product was obtained following the general procedure on a 0.5 mmol (88.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate

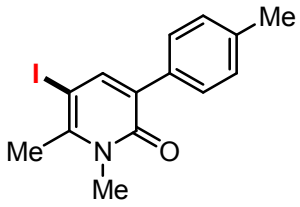
(85:15 v/v) White crystalline solid. Yield 80% (121 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 2.5 Hz, 1H), 7.75 (dq, *J* = 2.5, 1.2 Hz, 1H), 3.62 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 40.0, 92.8, 110.7 (q, *J*= 35.6 Hz), 122.37 (q, *J*= 271.3 Hz), 138.4, 144.1, 159.8. Calculated mass 303.9446 (Molecular formula – $C_7H_6INOF_3$), Observed mass 303.9463.



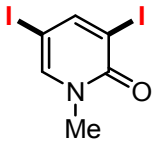
3-chloro-5-iodo-1-methylpyridin-2(1H)-one (Table 3, Entry 5e): iodinated product was obtained following the general procedure on a 0.25 mmol (71.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (80:20 v/v) sluggish White solid compound. Yield 69% (93 mg). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 2.2 Hz, 1H), 7.48 (d, *J* = 2.4 Hz, 1H), 3.55 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 38.6, 61.7, 127.4, 142.0, 144.5, 158.1. Calculated mass 269.9183 (Molecular formula – C_6H_6INOCl), Observed mass 269.9170.



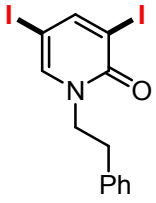
5-iodo-1-methyl-3-p-tolylpyridin-2(1H)-one (Table 3, Entry 5f): iodinated product was obtained following the general procedure on a 0.25 mmol (50 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (93:17 v/v). Pale white Solid . Yield 60% (49 mg). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.68 – 8.55 (d, *J* = 3.1 Hz, 1H), 8.28 – 8.14 (d, *J* = 3.0 Hz, 1H), 7.67 – 7.49 (m, 2H), 7.35 – 7.14 (d, *J* = 7.9 Hz, 2H), 3.75 – 3.63 (s, 3H), 2.43 – 2.33 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 21.48, 39.57, 128.57, 129.31, 130.05, 130.58, 130.65, 131.91, 138.37, 139.21, 161.48.



5-iodo-1,6-dimethyl-3-p-tolylpyridin-2(1H)-one (Table 3, Entry 5g): iodinated product was obtained following the general procedure on a 0.25 mmol (53 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Pale white Solid . Yield 55% (47 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 – 8.14 (s, 1H), 7.60 – 7.56 (m, 2H), 7.26 – 7.21 (d, *J* = 8.0 Hz, 2H), 3.82 – 3.60 (s, 3H), 2.99 – 2.75 (s, 3H), 2.50 – 2.26 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 18.54, 21.49, 33.13, 100.19, 127.99, 128.61, 129.31, 131.80, 132.26, 138.84, 148.02, 161.66. Melting point: 130 °C.

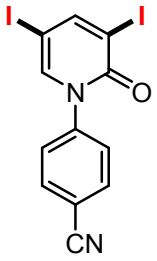


3,5-diiodo-1-methylpyridin-2(1H)-one (Table 3, Entry 5h): Iodinated product was obtained following the general procedure on a scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (88:12 v/v) Black solid compound. Yield 66% (118 mg). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 2.3 Hz, 1H), 7.52 (d, *J* = 2.4 Hz, 1H), 3.57 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 39.4, 63.7, 94.3, 143.8, 154.9, 159.2. Calculated mass 361.8539 (Molecular formula – $C_6H_6I_2NO$), Observed mass 361.8539.

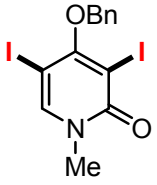


3,5-diiodo-1-phenethylpyridin-2(1H)-one (Table 3, Entry 5i): iodinated product was obtained following the general procedure on a 0.5 mmol (99.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (95:5 v/v). Brownish solid . Yield 50% (112 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 – 8.03 (d, *J* = 2.3 Hz, 1H), 7.33 – 7.24 (m, 3H), 7.16 – 7.14 (d, *J* = 1.7 Hz, 1H), 7.14 – 7.10 (dd, *J* = 4.0, 1.7 Hz, 2H), 4.15 – 4.09 (m, 2H), 3.05 – 2.99 (t, *J* = 7.3 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 35.12, 54.05, 63.46, 94.51, 127.26, 129.02, 129.11, 137.37, 143.41, 154.83,

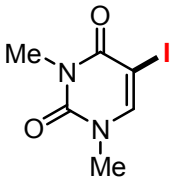
158.56. Calculated mass 473.8822 (Molecular formula – $C_{13}H_{11}I_2NNaO$), Observed mass 473.8822.



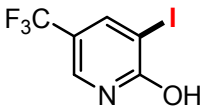
4-(3,5-diiodo-2-oxopyridin-1(2H)-yl)benzonitrile (Table 3, Entry 5j): iodinated product was obtained following the general procedure on a 0.5 mmol (98 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (98:2 v/v). Yellow Solid . Yield 42% (93 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 – 8.16 (d, *J* = 2.3 Hz, 1H), 7.84 – 7.77 (m, 2H), 7.58 – 7.48 (m, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 29.90, 65.31, 95.64, 113.41, 117.80, 127.56, 133.57, 141.87, 143.67, 155.71. Calculated mass 470.8462 (Molecular formula – $C_{12}H_6I_2N_2NaO$), Observed mass 473.8822. Melting point: above 200 °C.



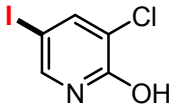
4-(benzyloxy)-3,5-diiodo-1-methylpyridin-2(1H)-one (Table 3, Entry 5k): iodinated product was obtained following the general procedure on a 0.5 mmol (107.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (80:20 v/v). Yellow Solid . Yield 68% (158 mg). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 – 7.66 (s, 1H), 7.65 – 7.60 (m, 2H), 7.46 – 7.36 (m, 3H), 5.09 – 5.03 (s, 2H), 3.62 – 3.58 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 38.82, 64.88, 74.64, 86.55, 128.74, 128.95, 128.96, 135.41, 144.13, 161.63, 167.00. Calculated mass 489.8771 (Molecular formula – $C_{13}H_{11}I_2NNaO_2$), Observed mass 489.8774. Melting point: 150 °C.



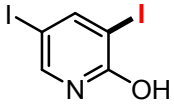
5-iodo-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (Table 3, Entry 5l): iodinated product was obtained following the general procedure on a 0.5 mmol (70 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (80:20 v/v) Brownish solid compound. Yield 72% (97 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (s, 1H), 3.42 (s, *J* = 3.0 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 29.7, 37.4, 67.3, 147.6, 160.6. Calculated mass 266.9631 (Molecular formula – $C_6H_8IN_2O_2$), Observed mass 266.9644. Melting point: above 200 °C.



3-iodo-5-(trifluoromethyl)pyridin-2-ol (Table 3, Entry 5m): iodinated product was obtained following the general procedure on a 0.5 mmol (81.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (80:20 v/v) White solid compound. Yield 72% (104 mg). ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.31 – 8.18 (m, 1H), 7.93 – 7.81 (m, 1H). ^{13}C NMR (101 MHz, Methanol-d_4) δ 162.37, 146.97, 136.58, 124.15 (q, *J*= 270.54Hz), 112.54 (q, *J*= 35.2 Hz), 93.52. Calculated mass 289.9290 (Molecular formula – C_6H_4INO), Observed mass 289.9288. Melting point: 182 °C.

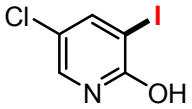


3-chloro-5-iodopyridin-2-ol (Table 3, Entry 5n): iodinated product was obtained following the general procedure on a 0.5 mmol (64.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Pale white Solid . Yield 75% (96 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 – 8.55 (d, *J* = 2.8 Hz, 1H), 8.47 – 8.41 (d, *J* = 2.8 Hz, 1H). ^{13}C NMR (126 MHz, Methanol-d_4) δ 126.60, 132.35, 133.95, 136.71, 160.84. Calculated mass 255.8940 (Molecular formula – C_5H_3ClINO), Observed mass 255.8955. Melting point: 200 °C.



3,5-diiodopyridin-2-ol (Table 3, Entry 5o): iodinated product was obtained following the general procedure on a 0.5 mmol (110 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Yellow Solid . Yield 38% (66 mg). ^{1}H

NMR (400 MHz, Chloroform-*d*) δ 8.79 – 8.70 (dd, *J* = 3.0, 1.2 Hz, 1H), 8.56 – 8.46 (dd, *J* = 2.8, 1.2 Hz, 1H). ^{13}C NMR (126 MHz, Methanol-d_4) δ 91.54, 133.15, 138.28, 144.53, 162.19. Calculated mass 347.837 (Molecular formula – $C_5H_3I_2NO$), Observed mass 347.833. Melting point: above 200 °C.



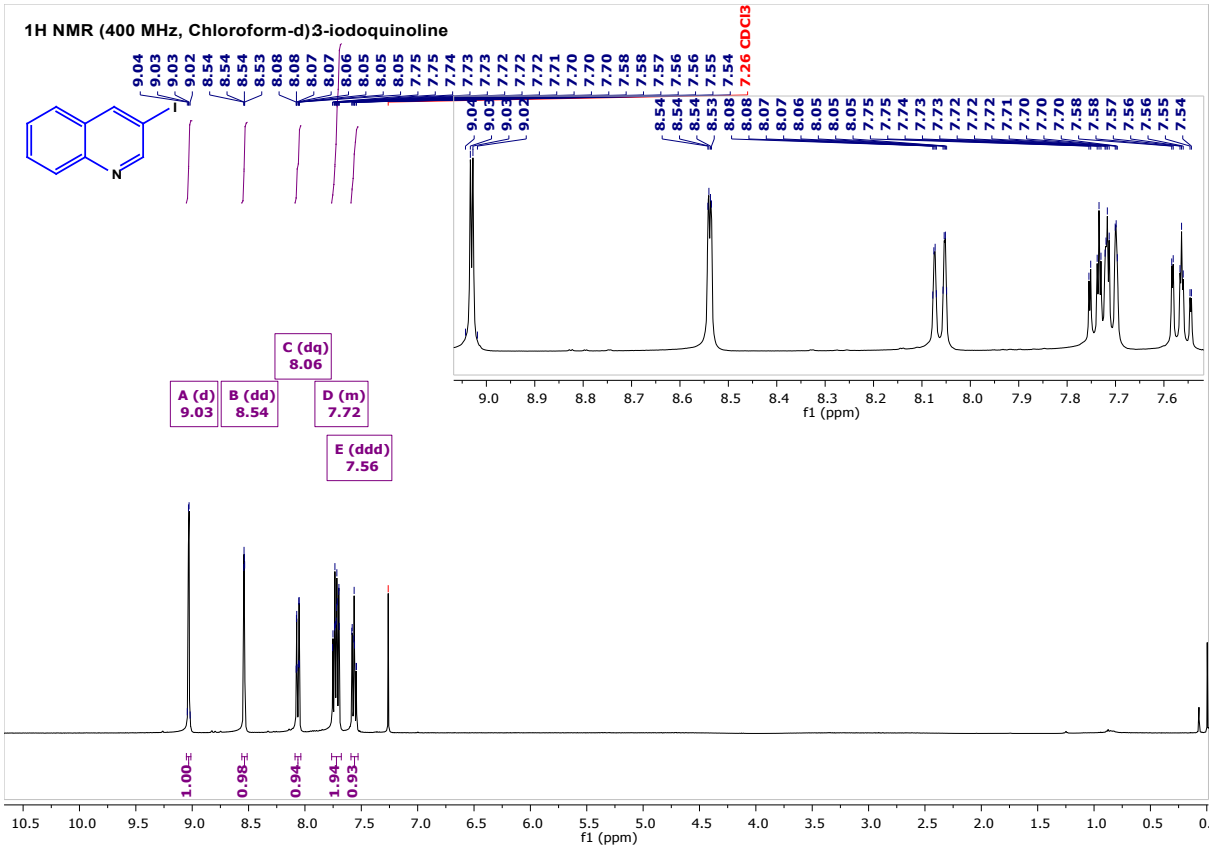
5-chloro-3-iodopyridin-2-ol (Table 3, Entry 5p): iodinated product was obtained following the general procedure on a 0.5 mmol (64.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (83:17 v/v). Yellow Solid . Yield 36% (46 mg). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.23 (s, 1H), 8.52 (d, *J* = 2.9 Hz, 1H), 8.16 (d, *J* = 2.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 153.28, 141.93, 139.45, 137.87, 109.00. Calculated mass 255.8940 (Molecular formula – C_5H_3ClINO), Observed mass 255.8924. Melting point: above 200 °C.

Reference:

1. K. Sun, Y. Lv, J. Wang, J. Sun, L. Liu, M. Jia, X. Liu, Z. Li and X. Wang, *Org. Lett.,* 2015, **17**, 4408-4411

2. K. K. Sharma, D. I. Patel and R. Jain *Chem. Commun.***,** 2015, **51**, 15129-15132.

Table 2, Entry 2a


1H NMR (400 MHz, Chloroform-d)3-iodoquinoline
9.04 9.03 9.03 9.02 8.54 8.54 8.54 8.53 8.08 8.07 8.07 8.06 8.05 8.05 8.05 7.75 7.75 7.74 7.73 7.73 7.72 7.72 7.71 7.70 7.70 7.70 7.58 7.58 7.57 7.56 7.56 7.55 7.54 7.26 CDCl3
I
N
C (dq) 8.06
A (d) 9.03
B (dd) 8.54
D (m) 7.72
E (ddd) 7.56
1.00 0.98 0.94 1.94 0.93
f1 (ppm)

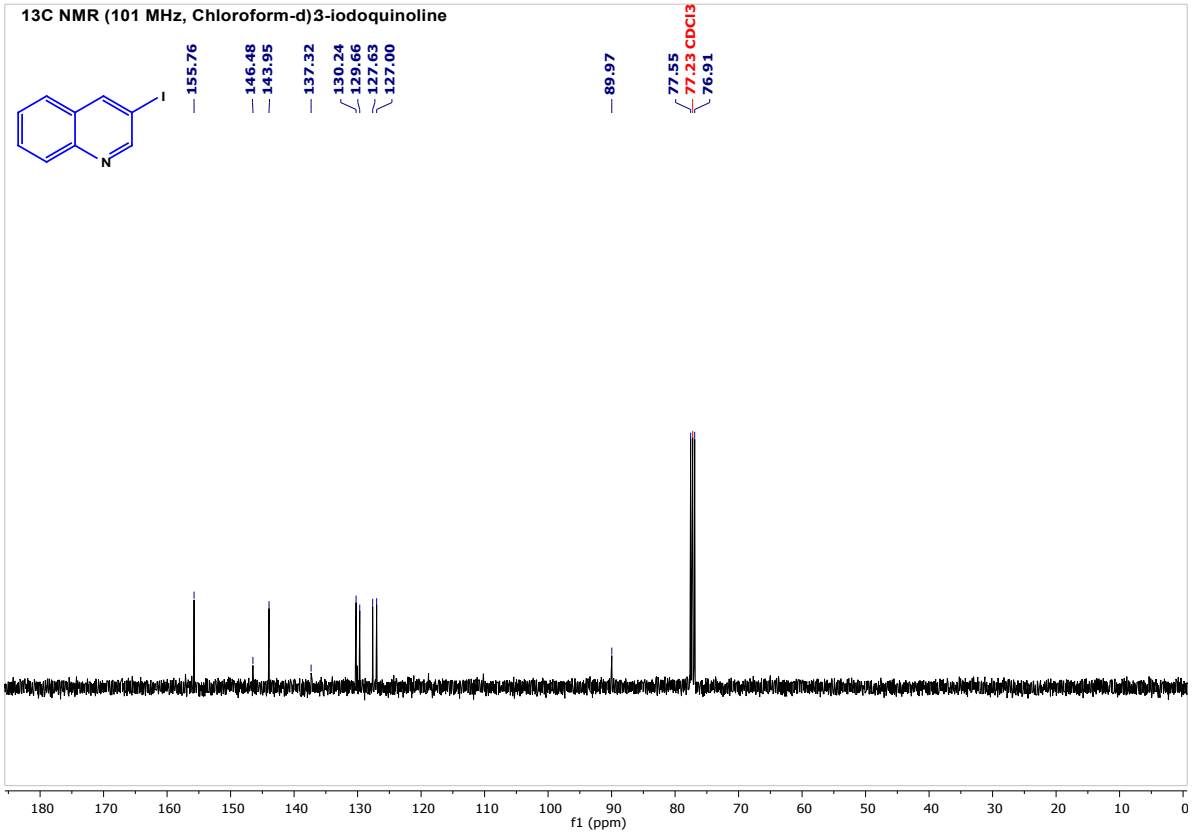
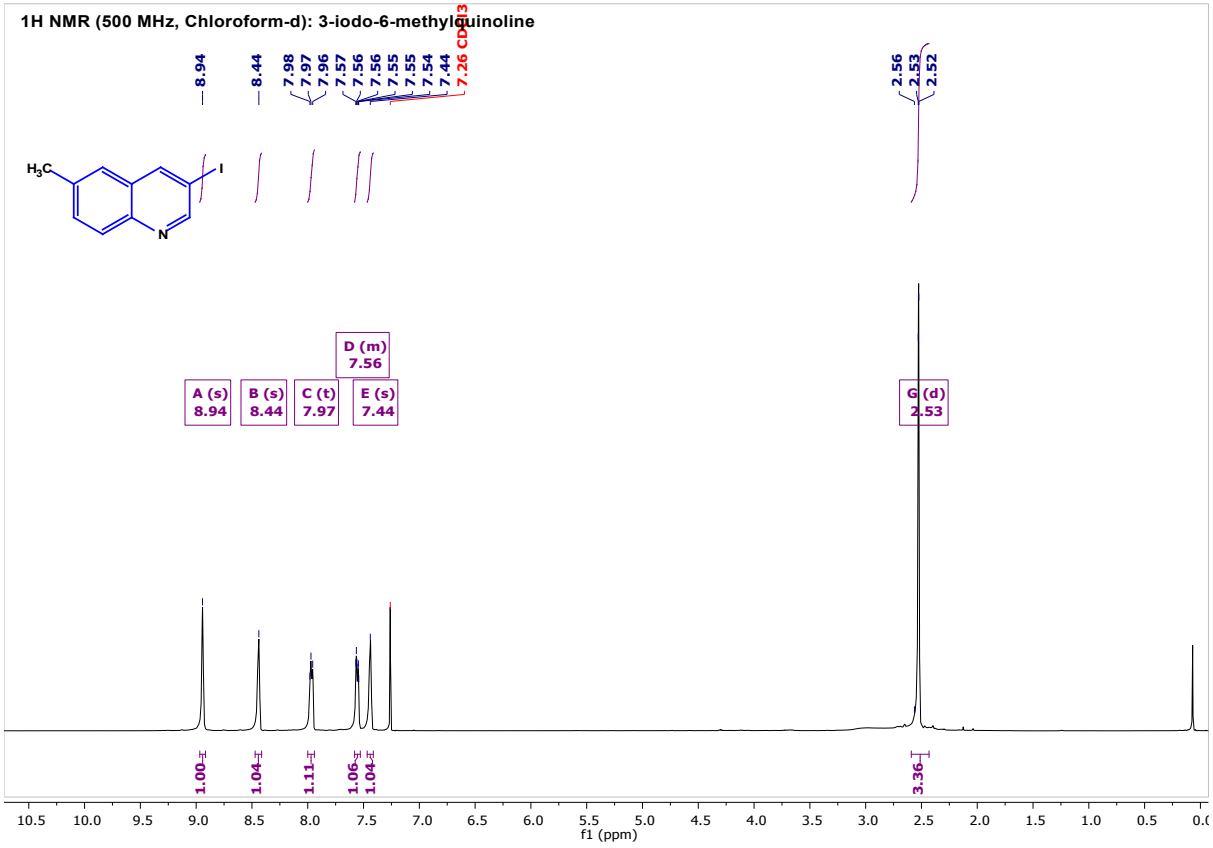

13C NMR (101 MHz, Chloroform-d)3-iodoquinoline
155.76 146.48 143.95 137.32 130.24 129.66 127.63 127.00 89.97 77.55 77.23 CDCl3 76.91
I
N
f1 (ppm)

Table 2, Entry 2b



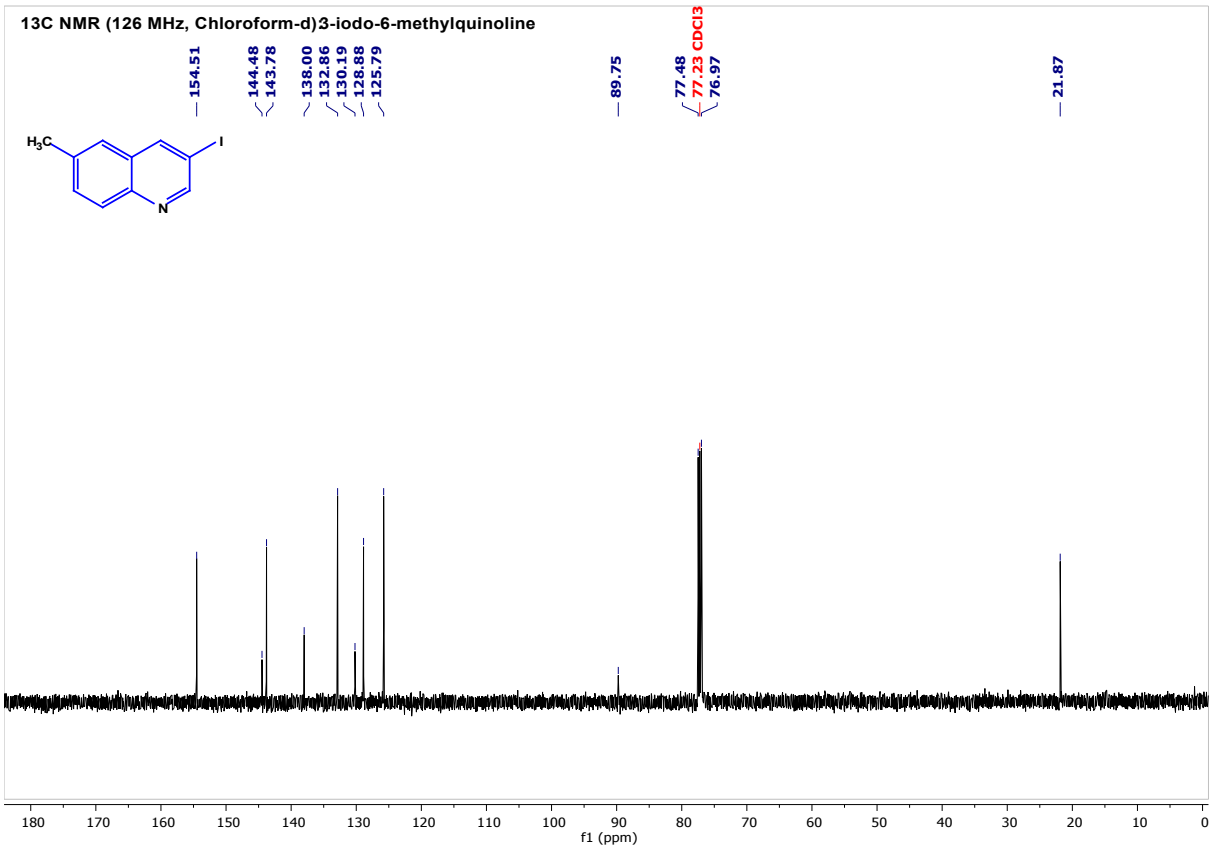
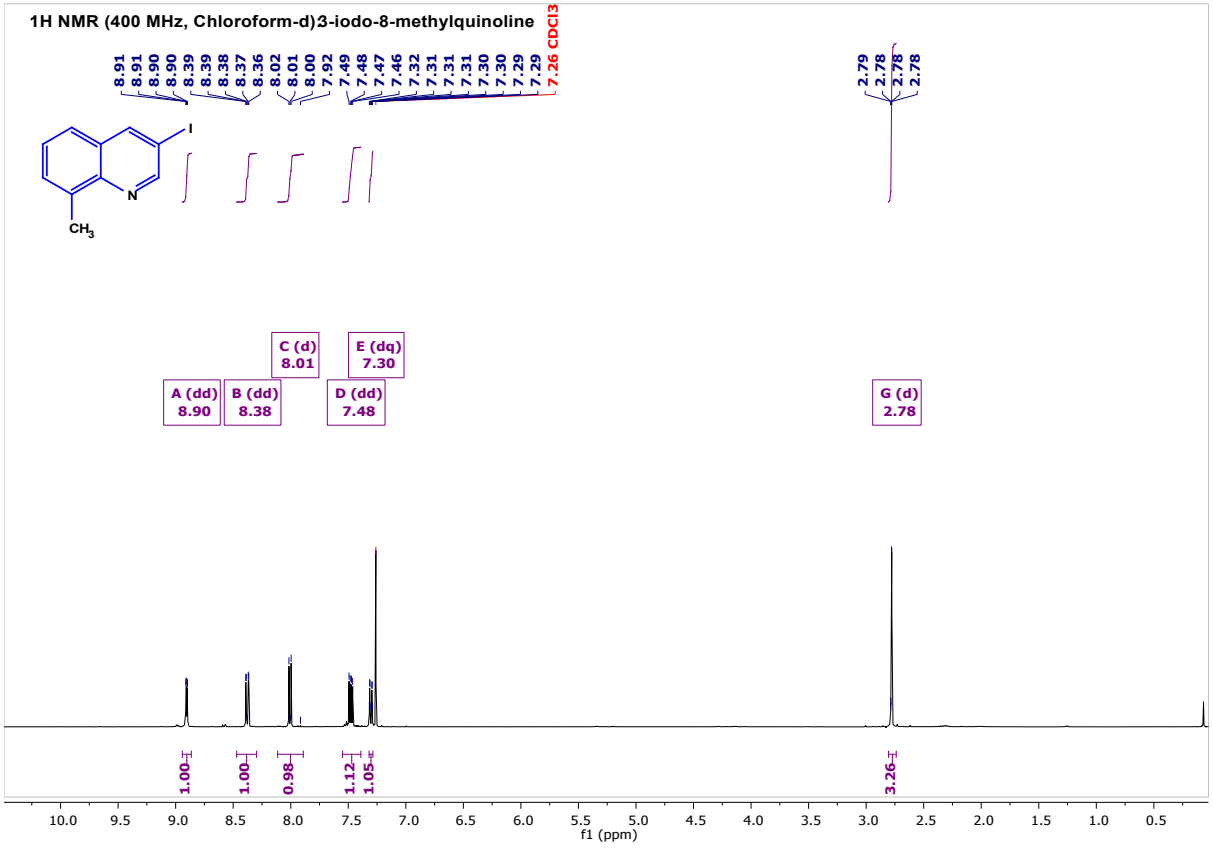


Table 2, Entry 2c



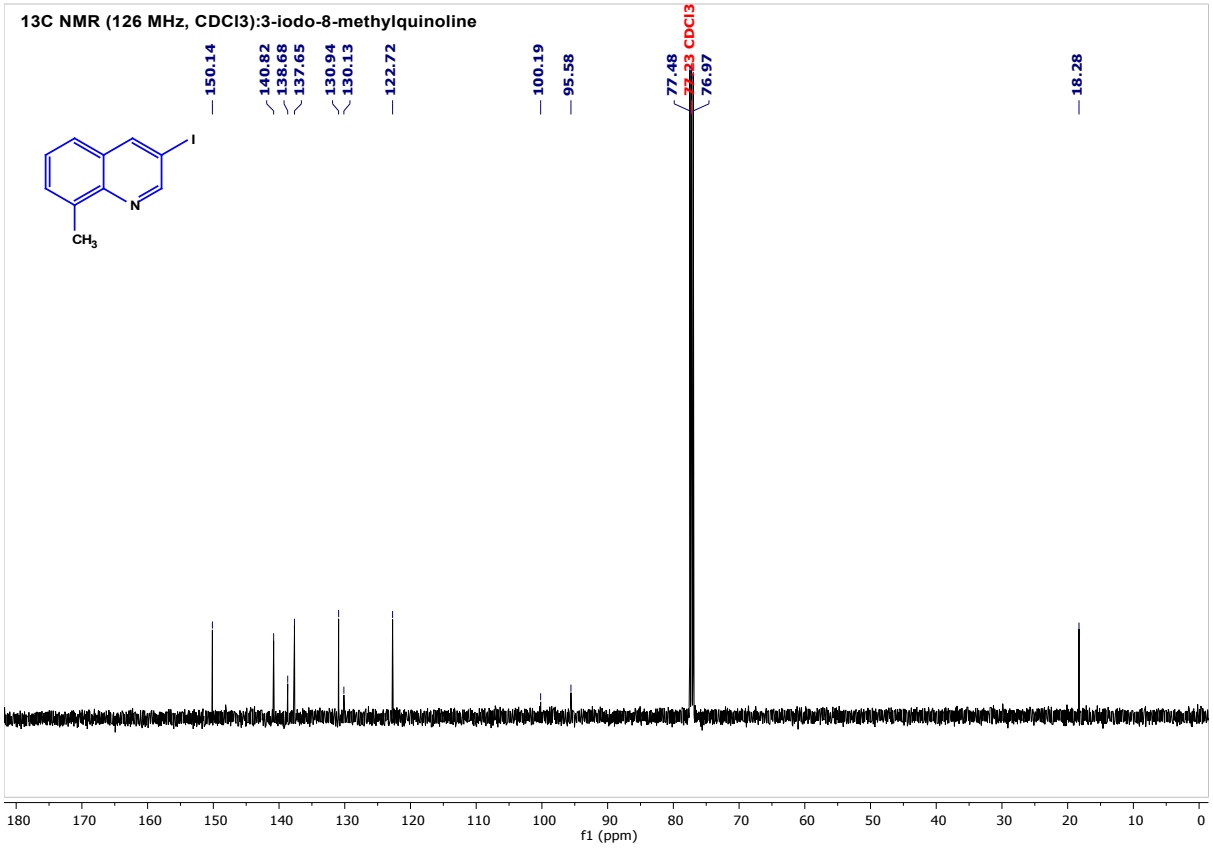
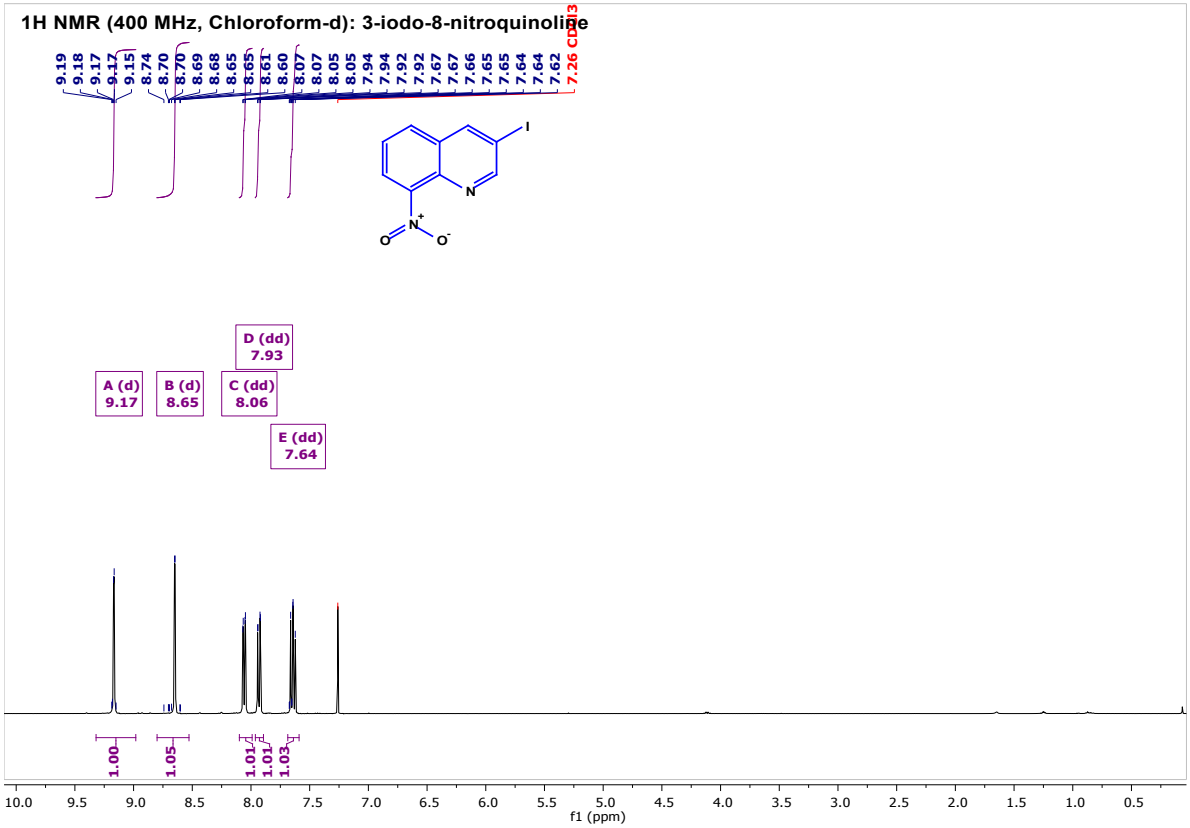


Table 2, Entry 2d



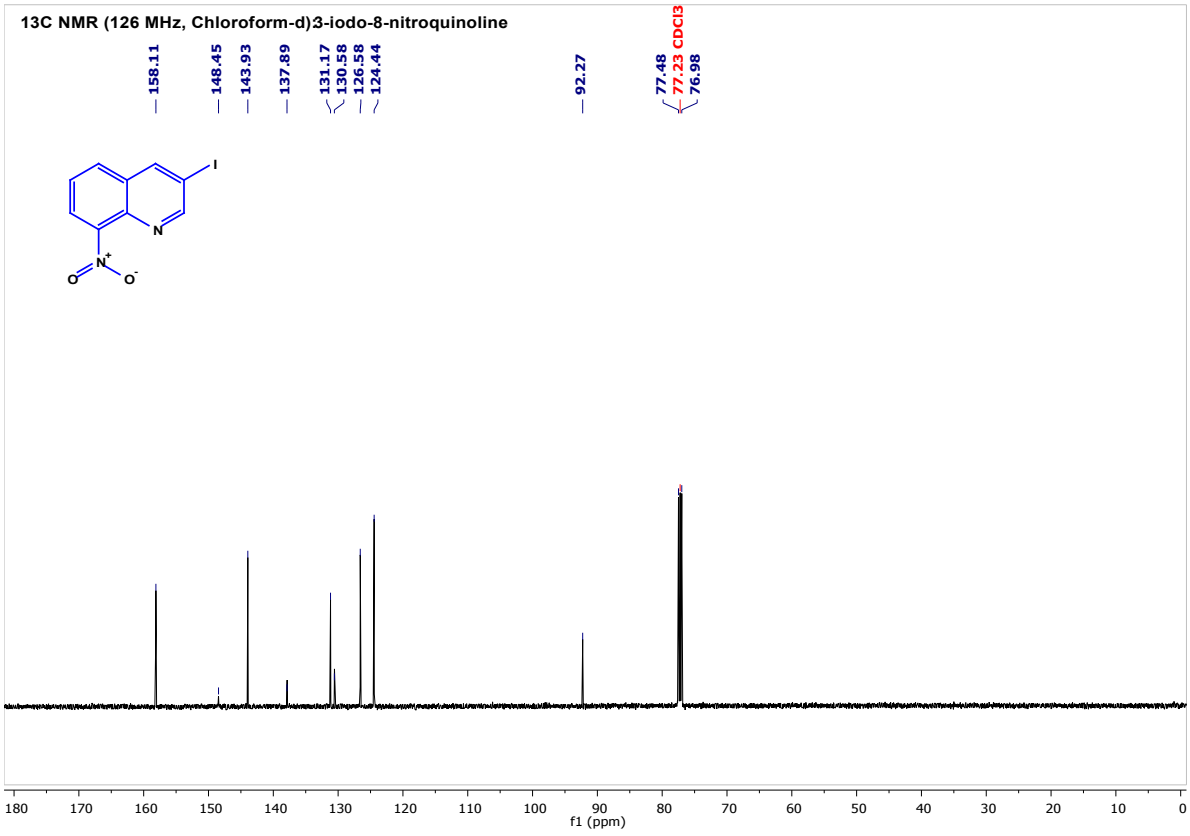
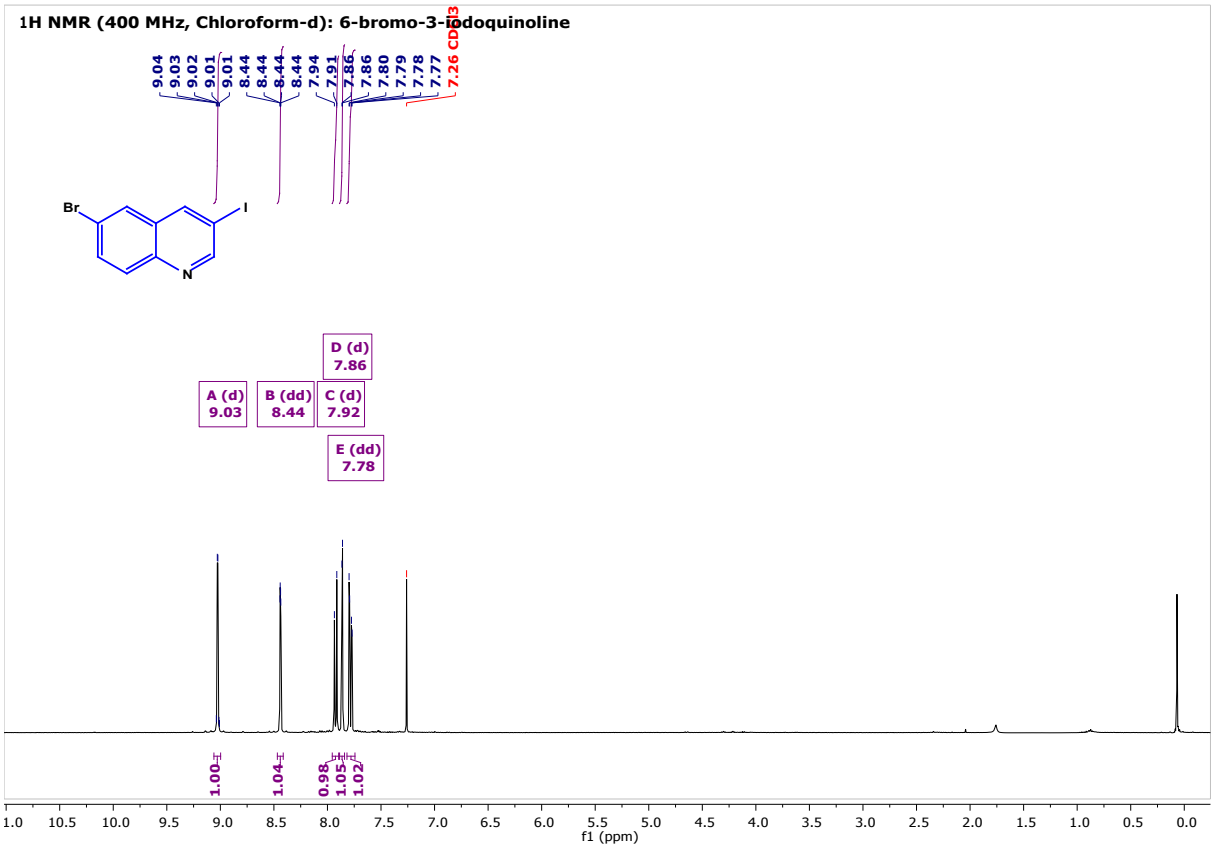


Table 2, Entry 2e



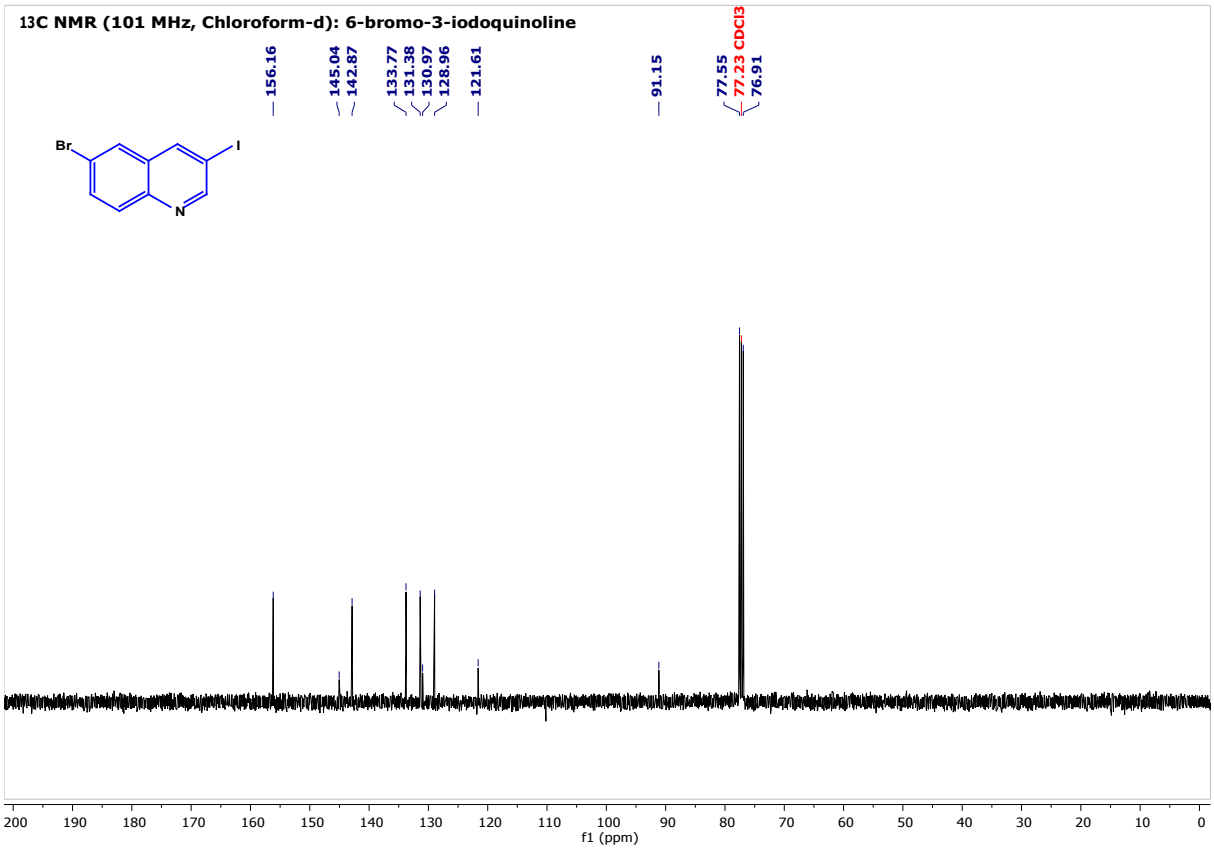
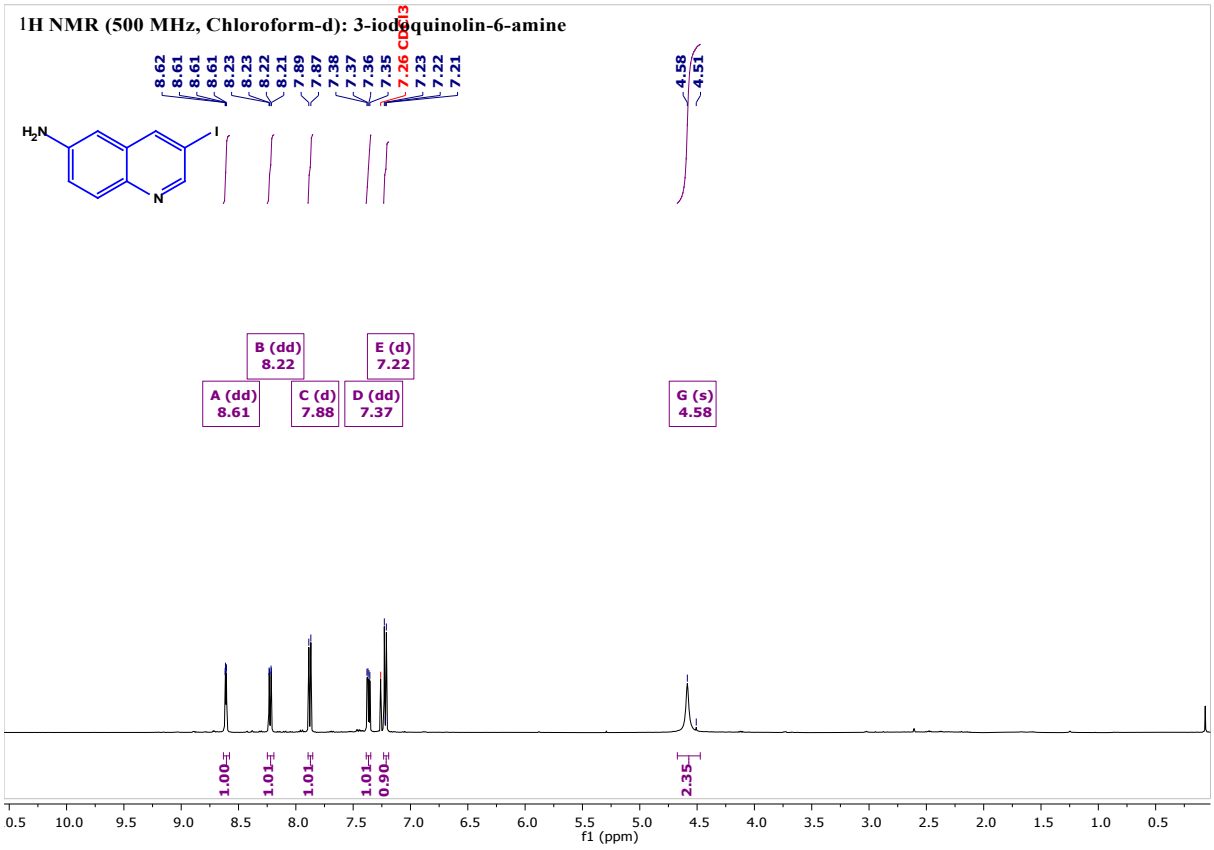
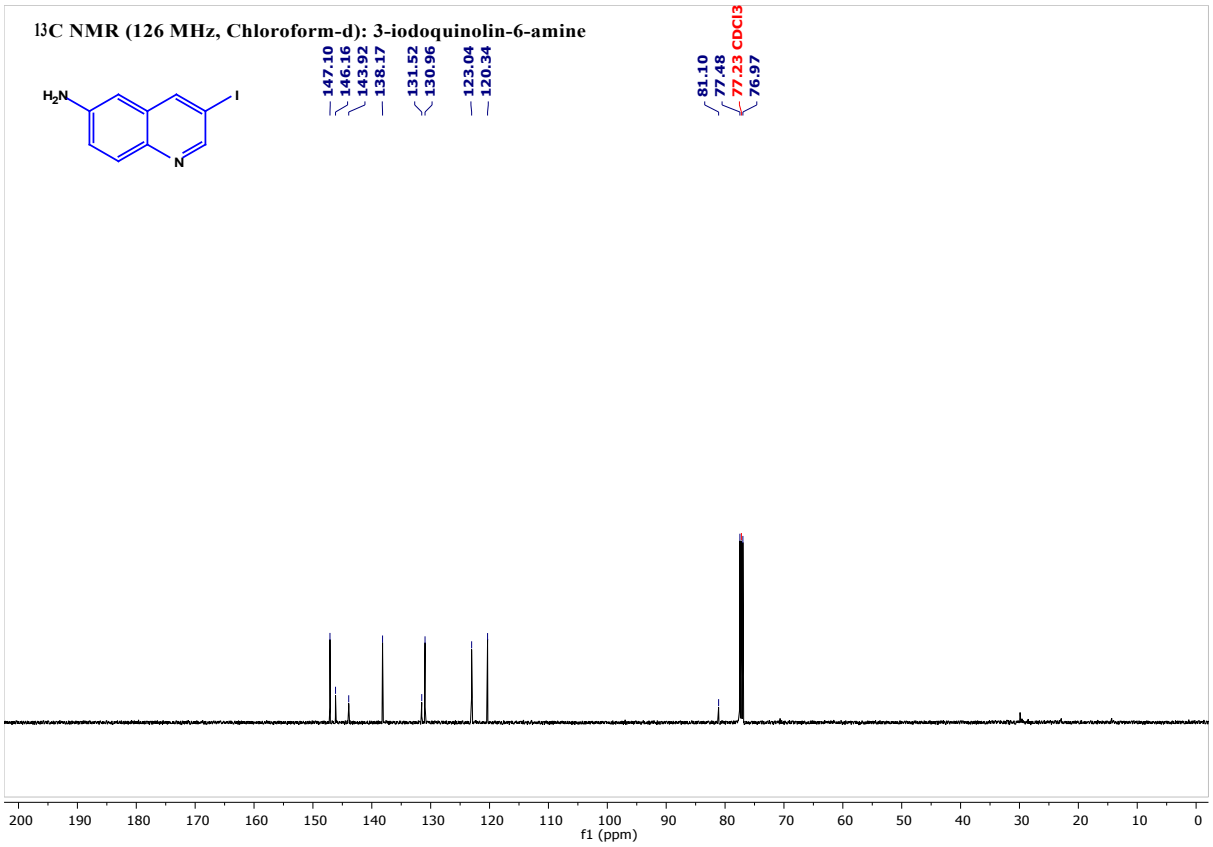


Table 2, Entry 2f





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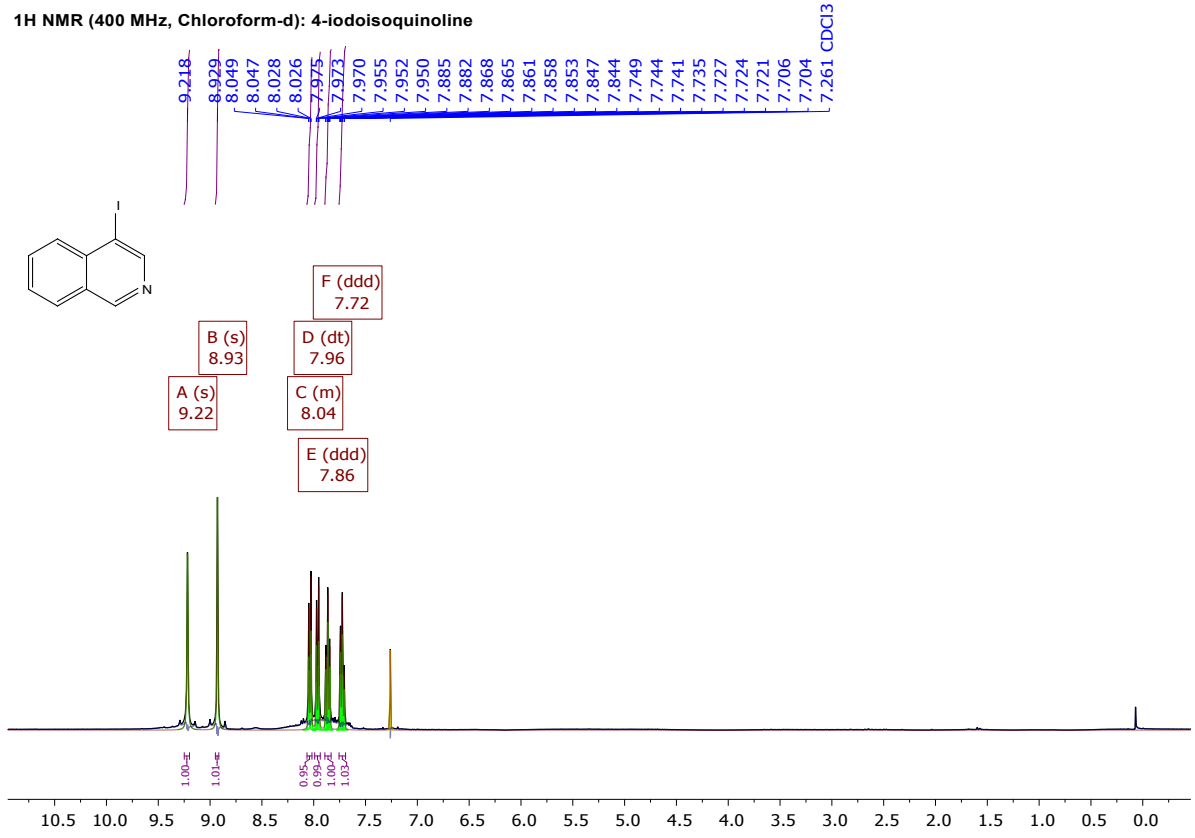

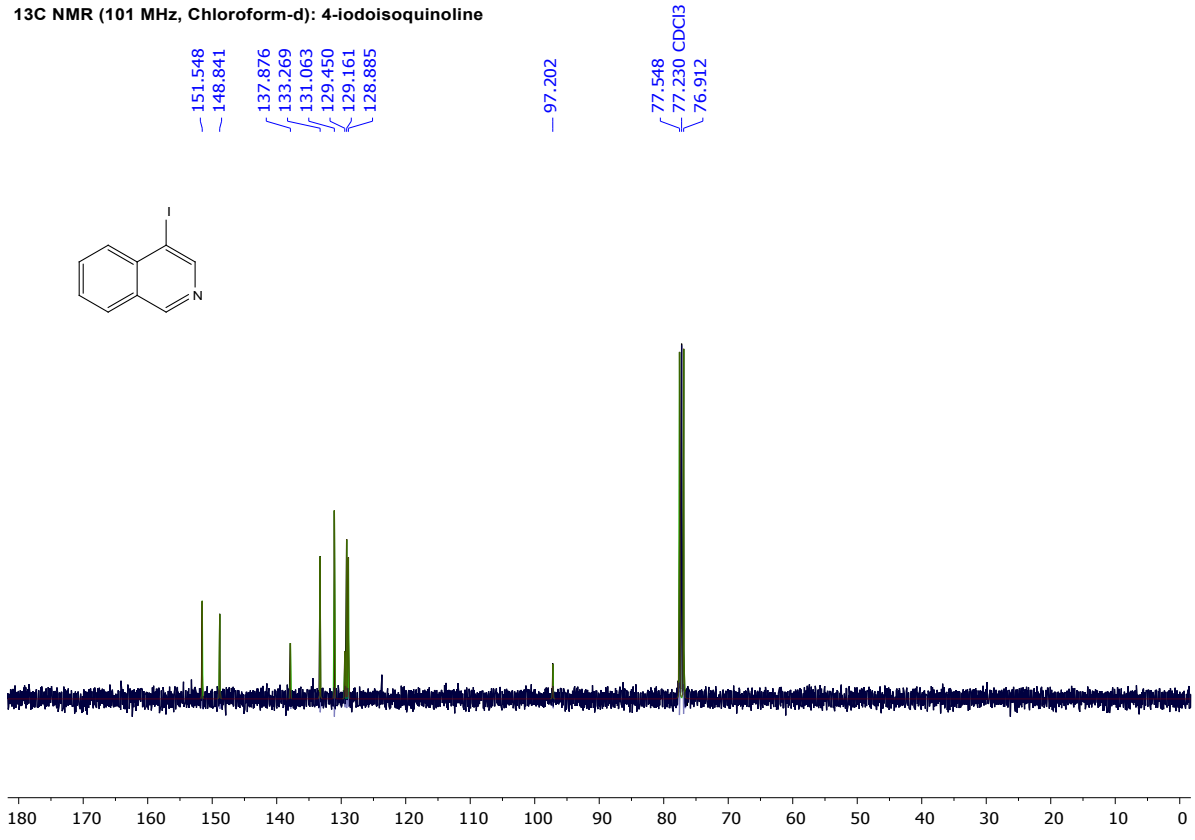

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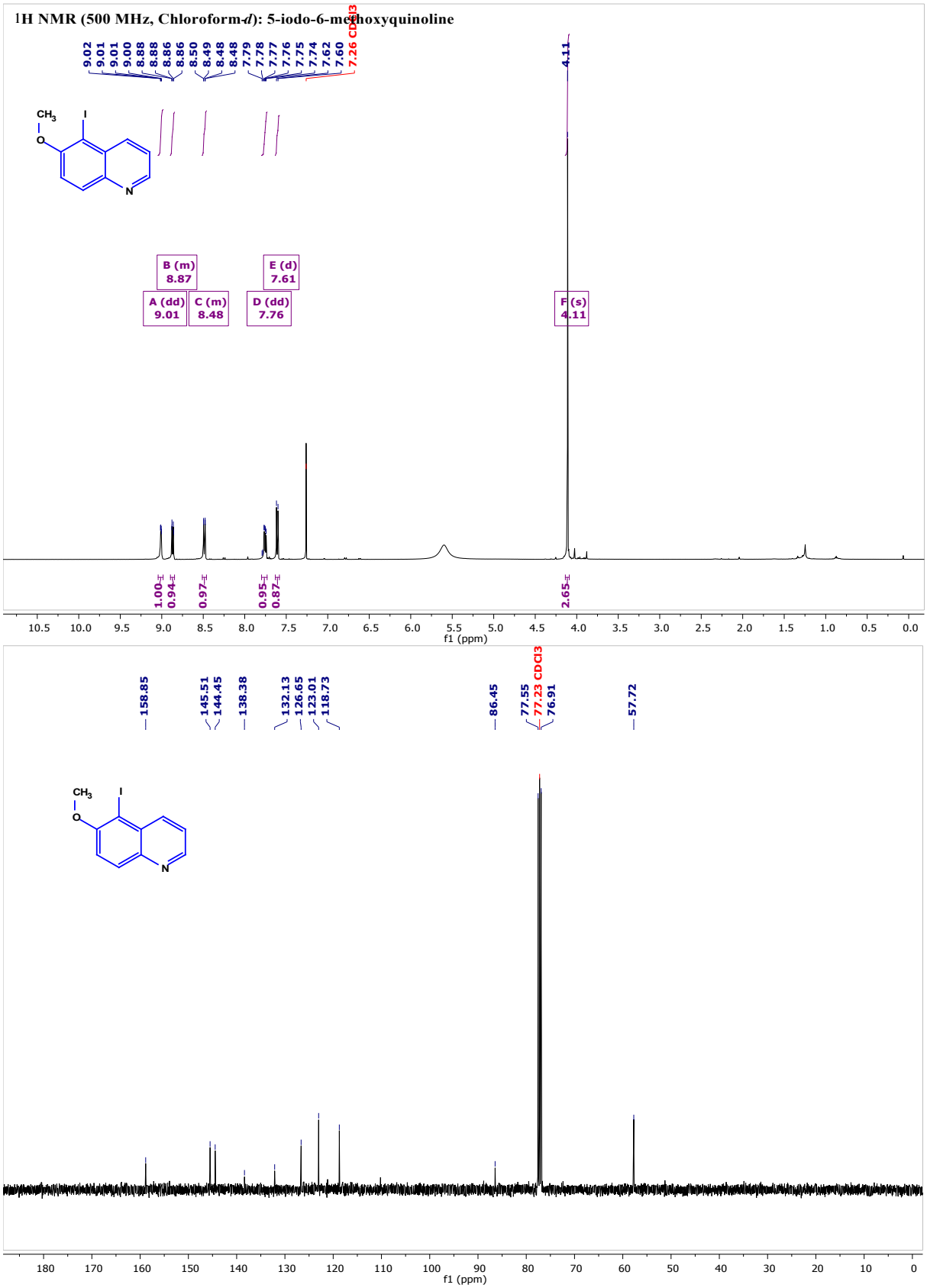

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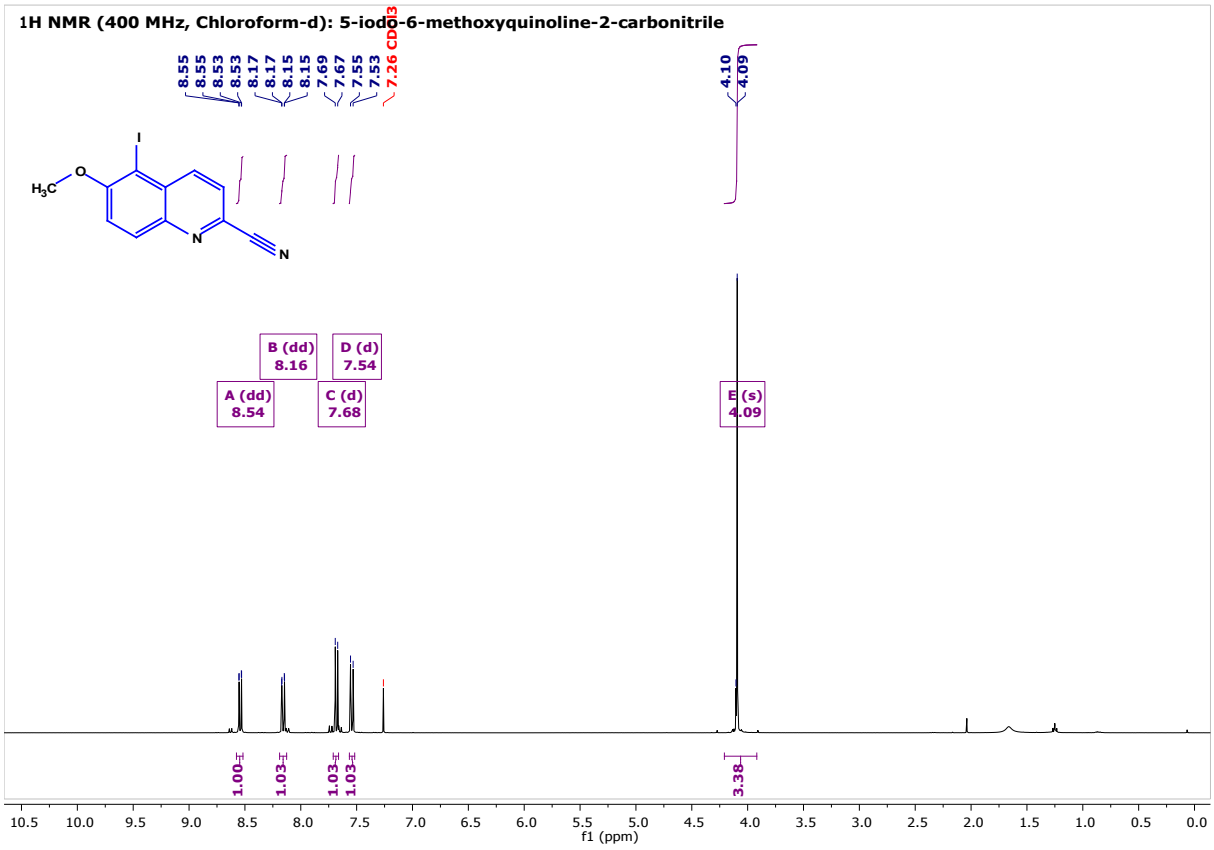

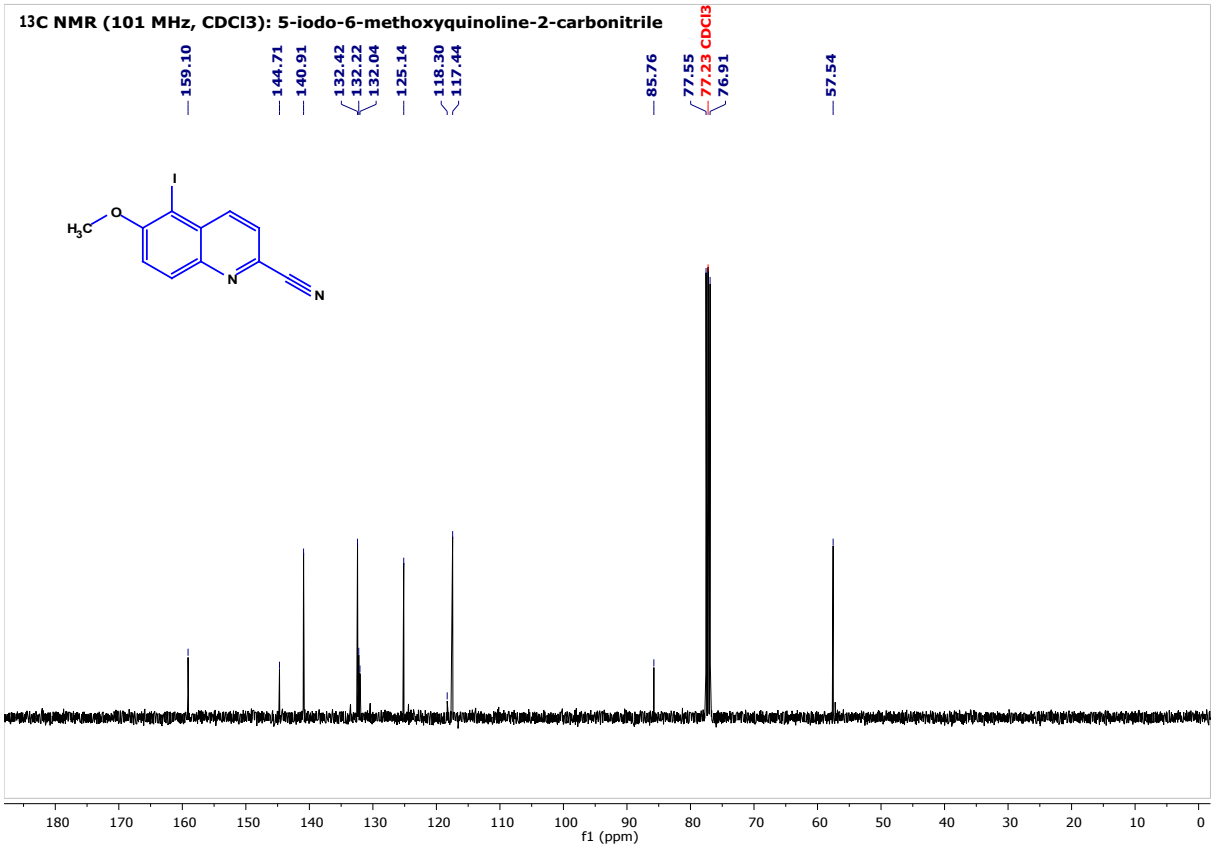

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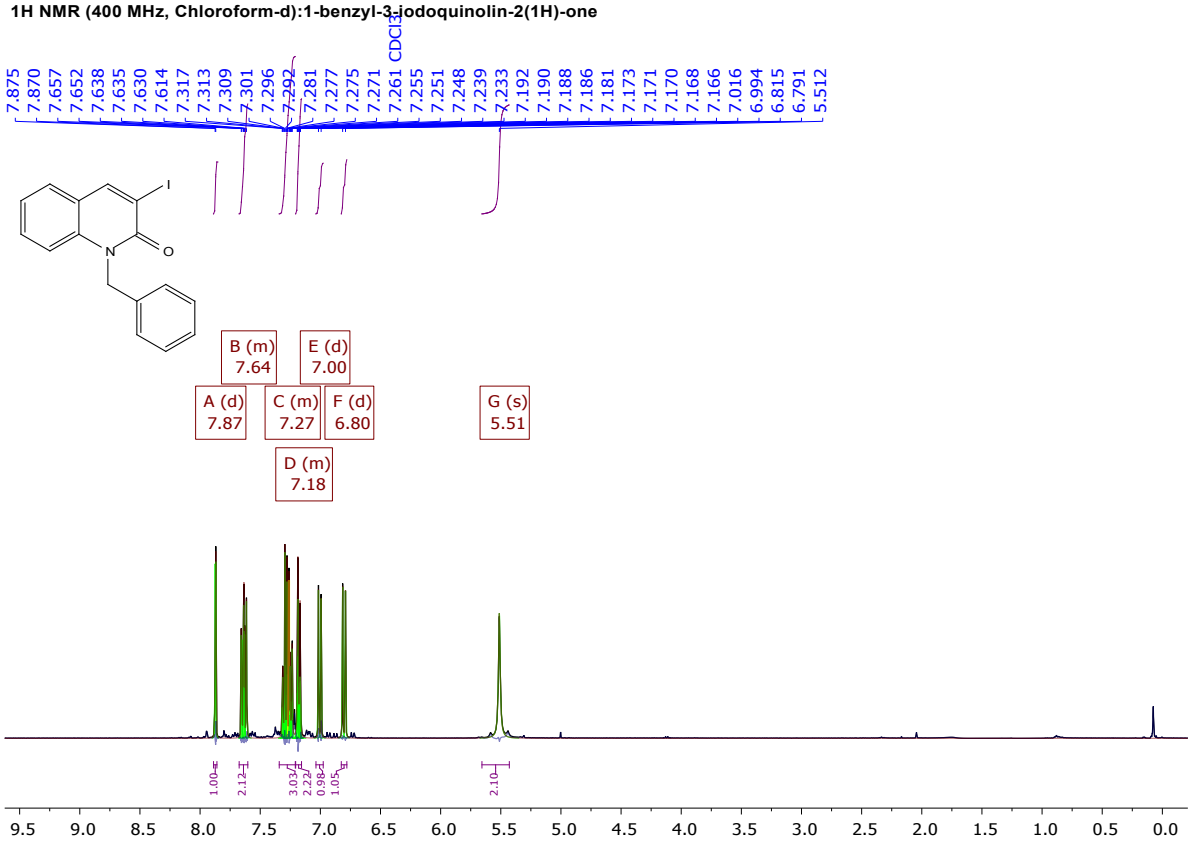

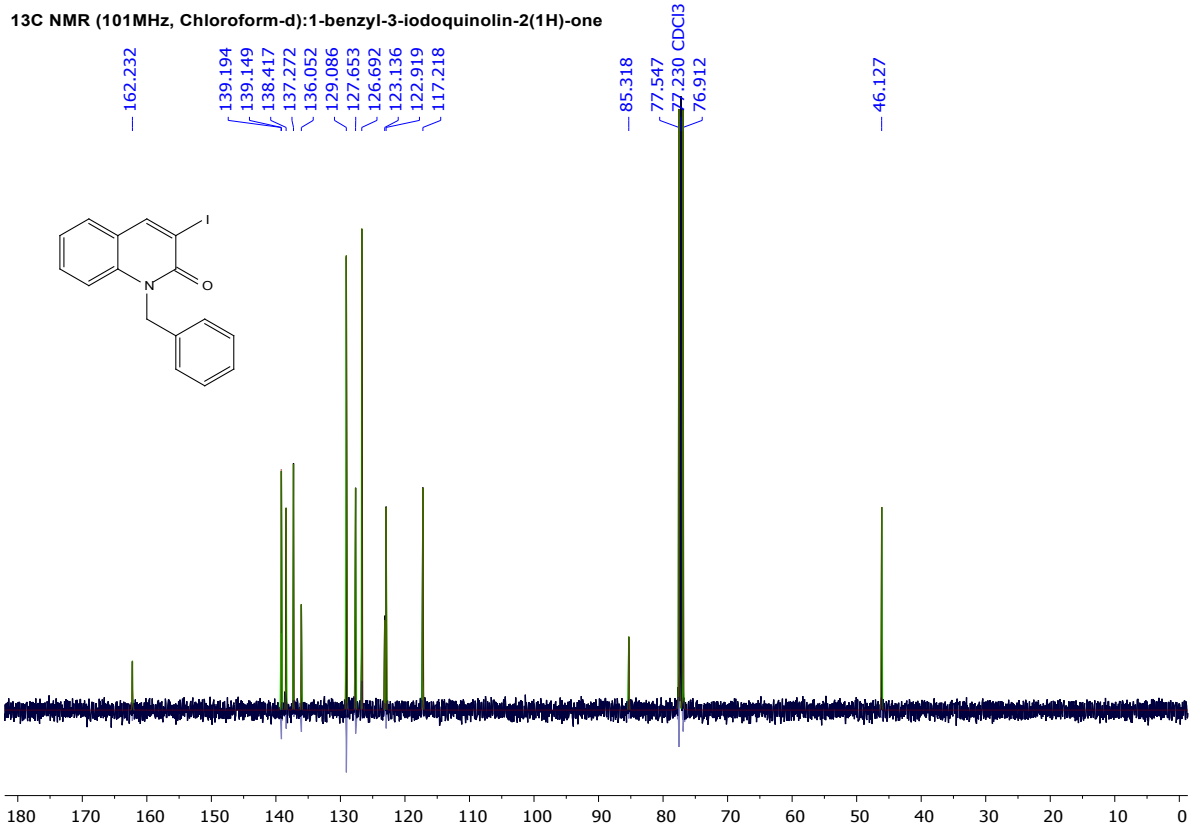

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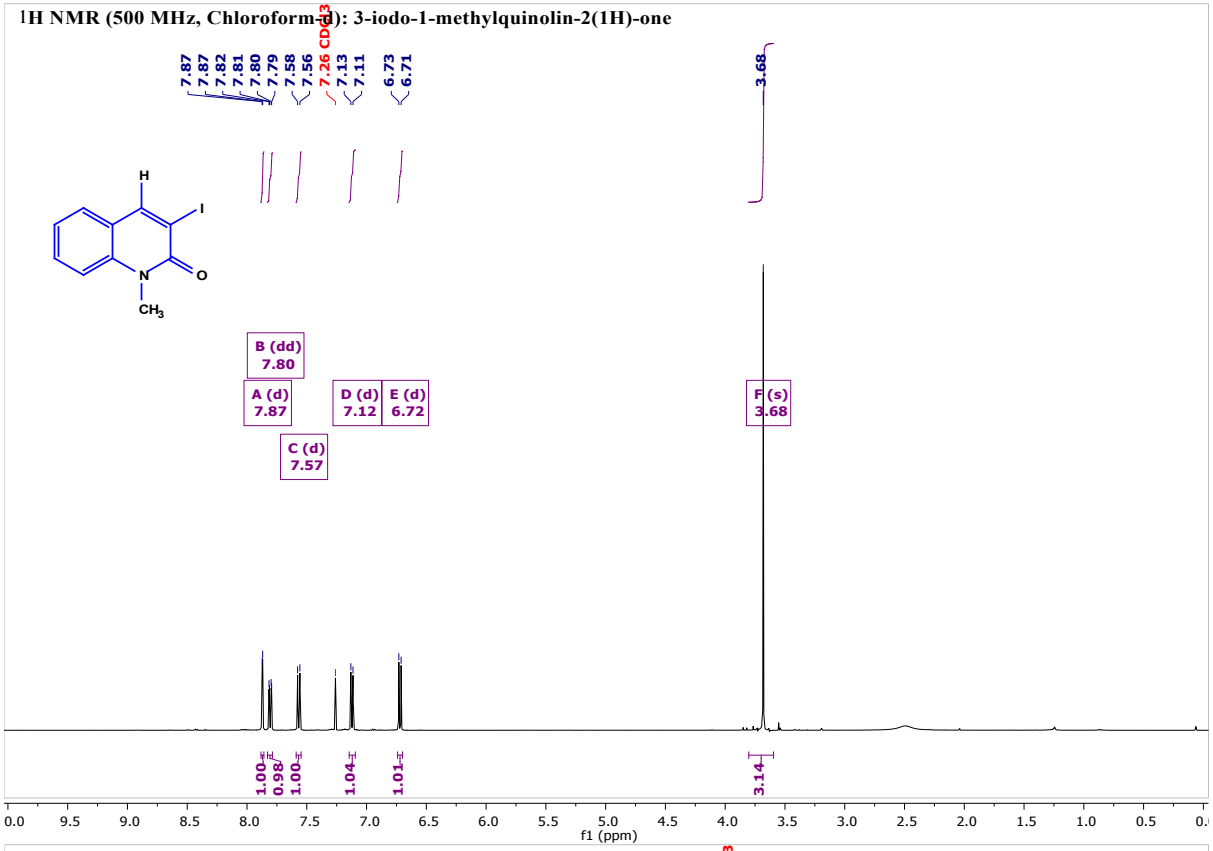

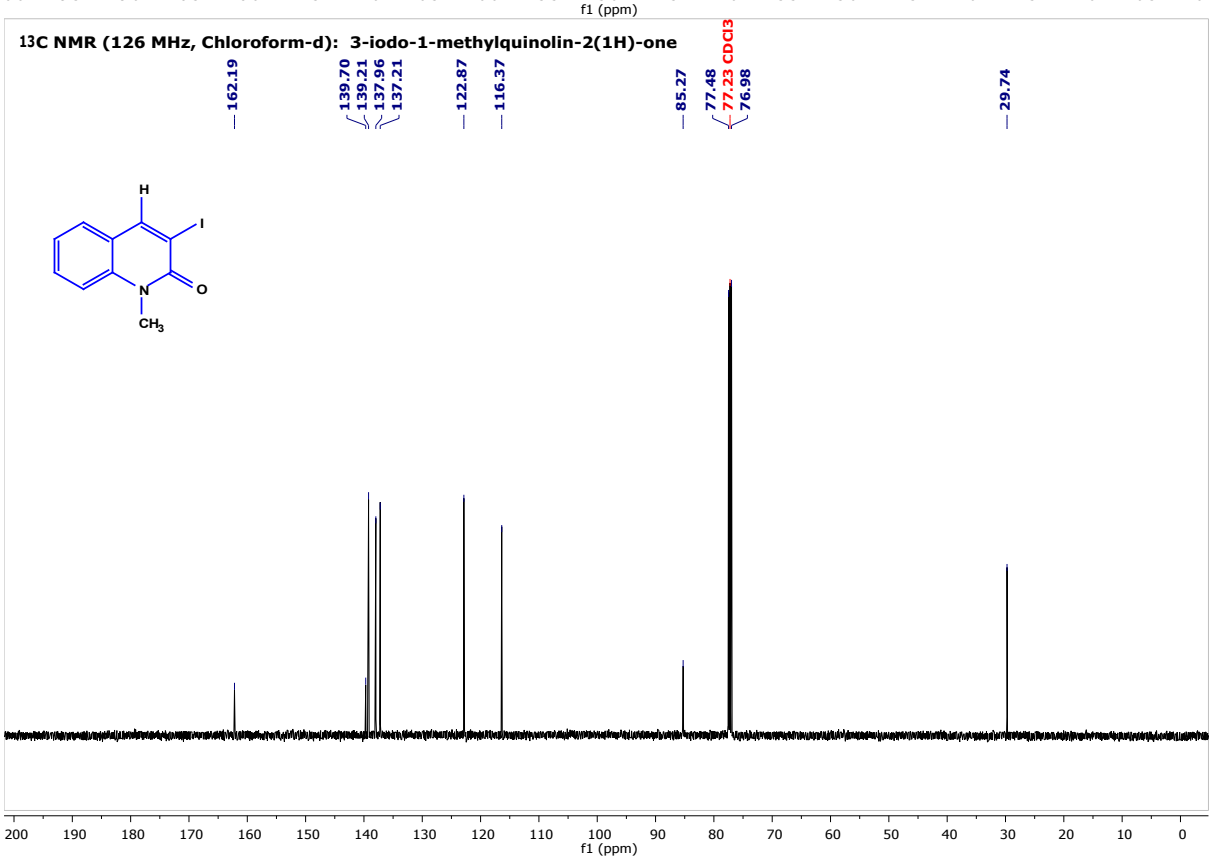

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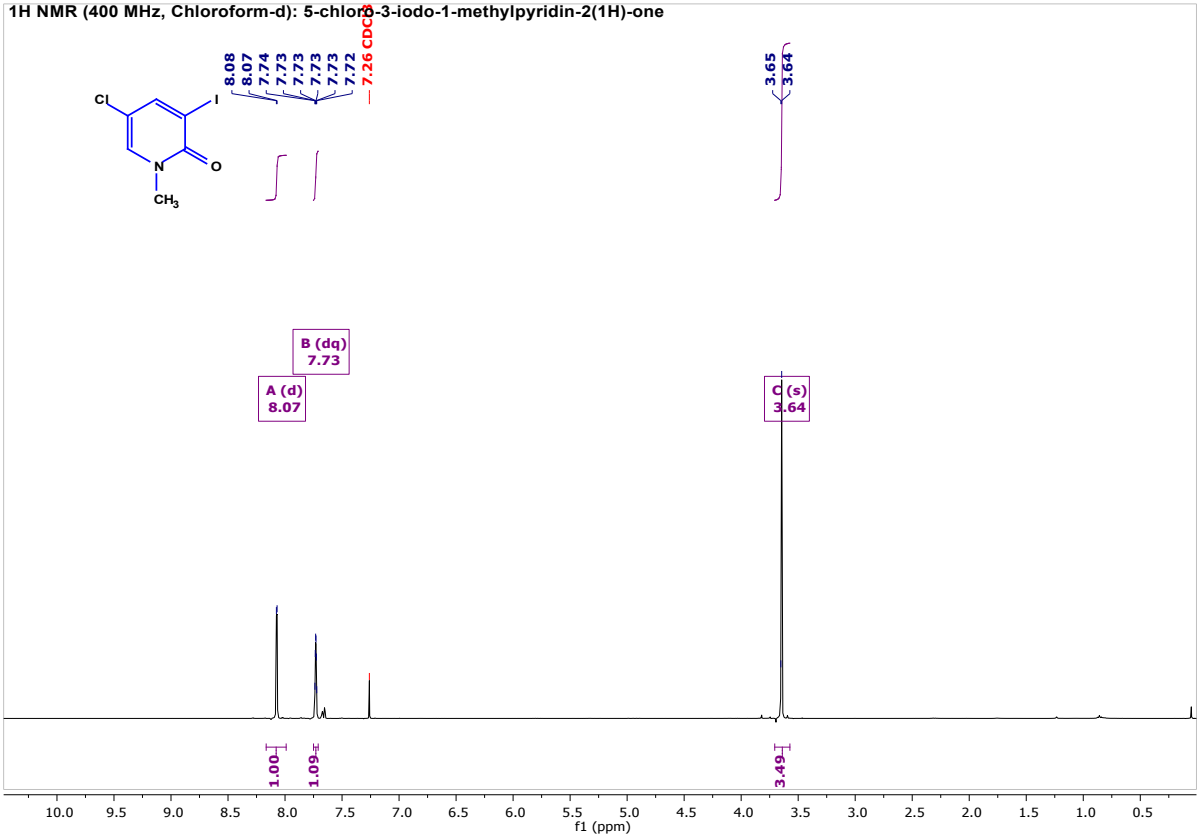

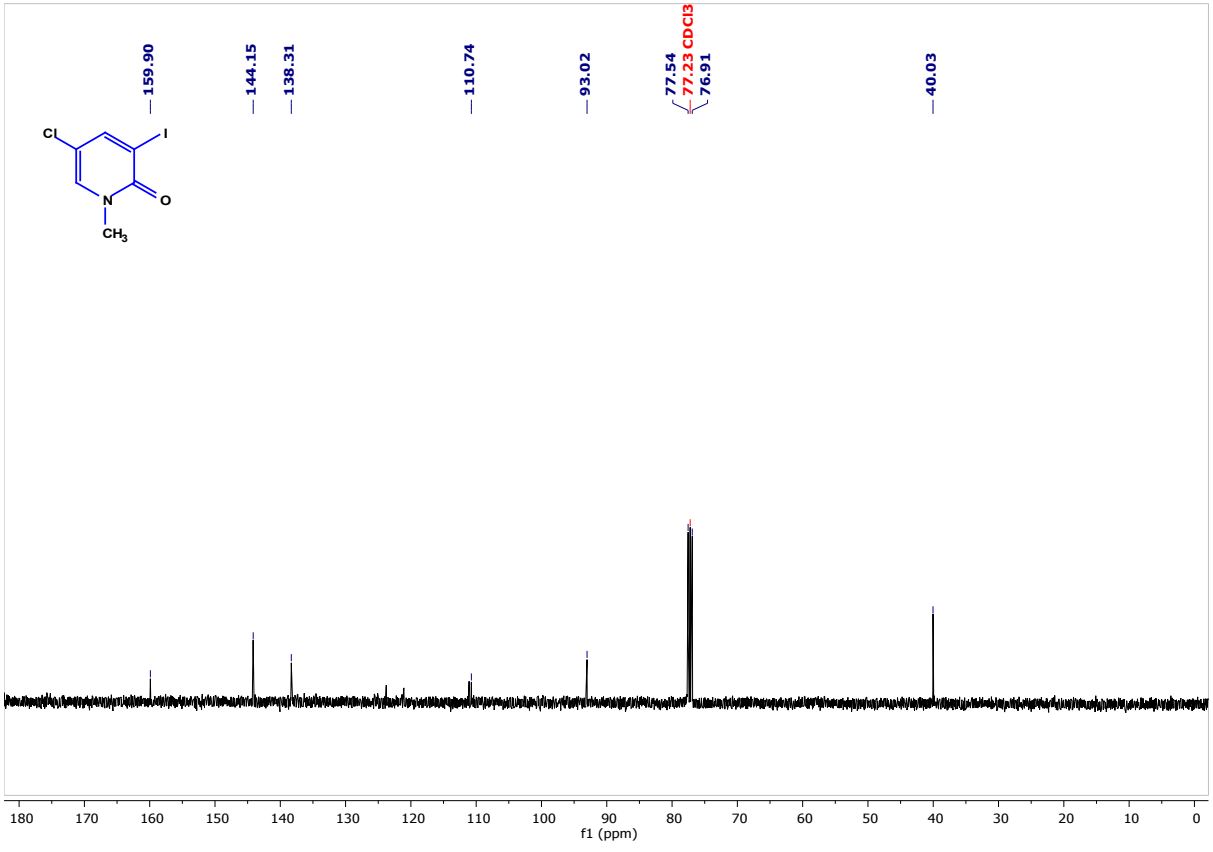

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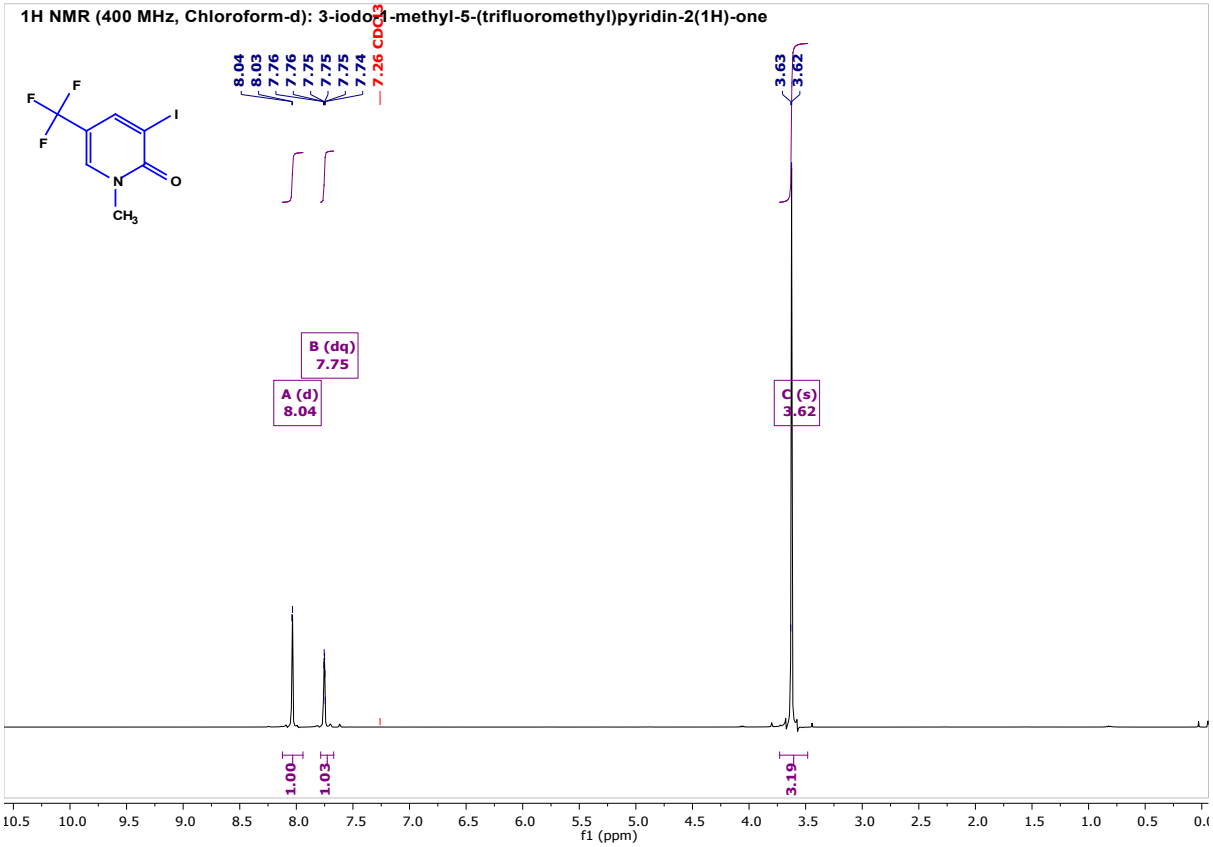

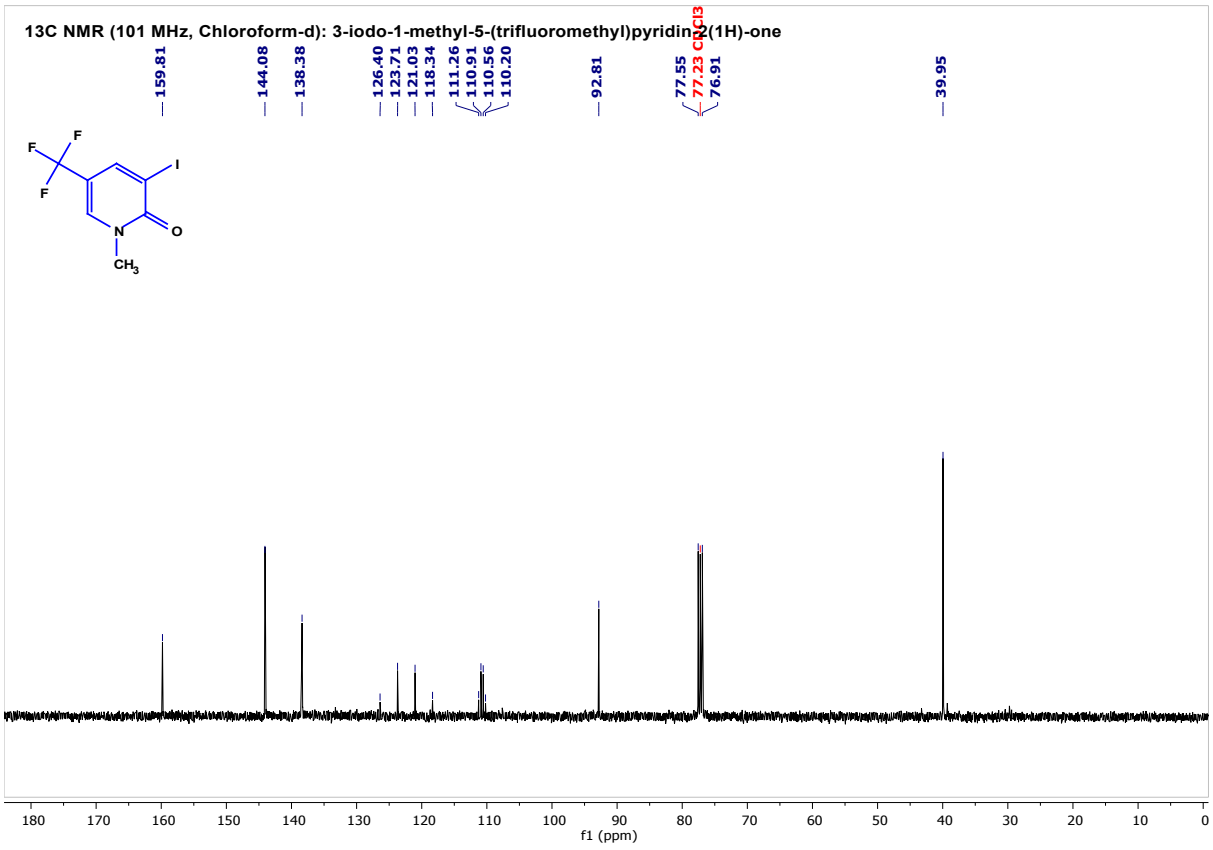

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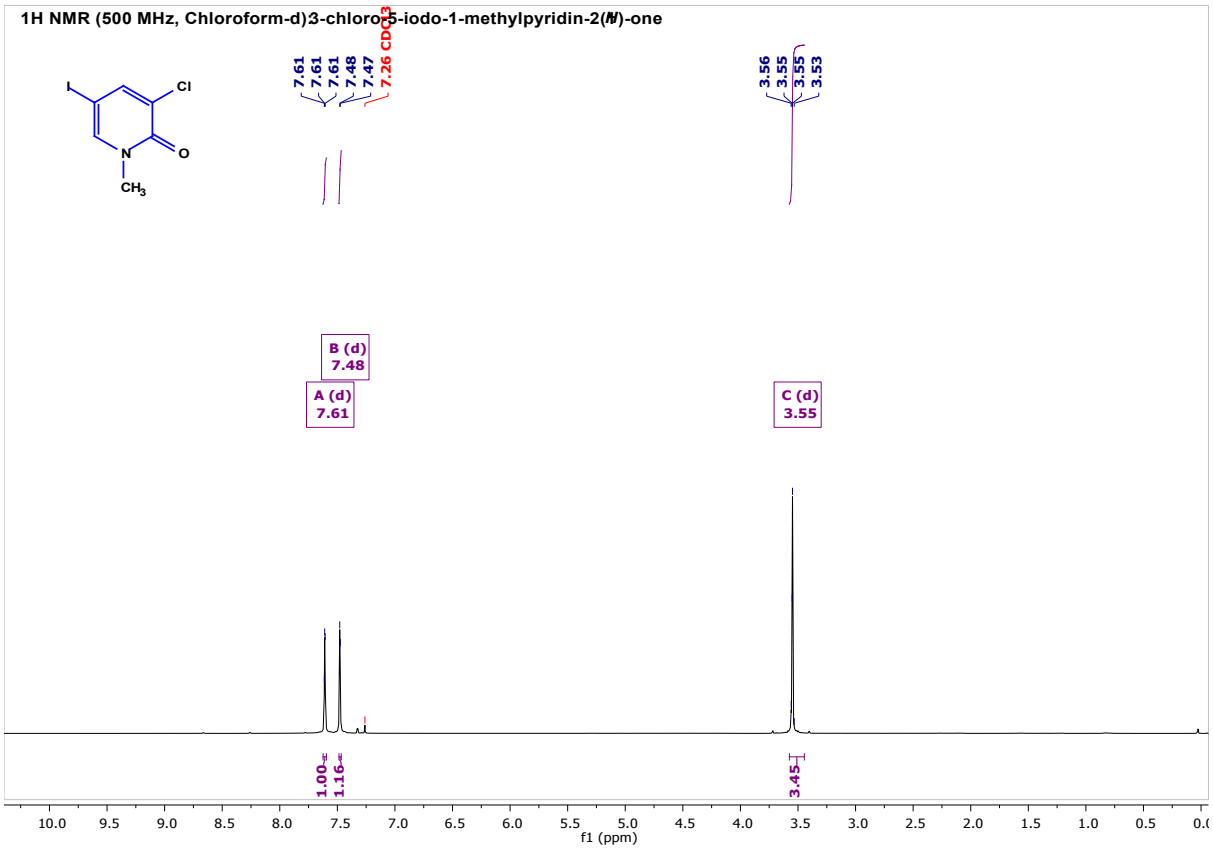

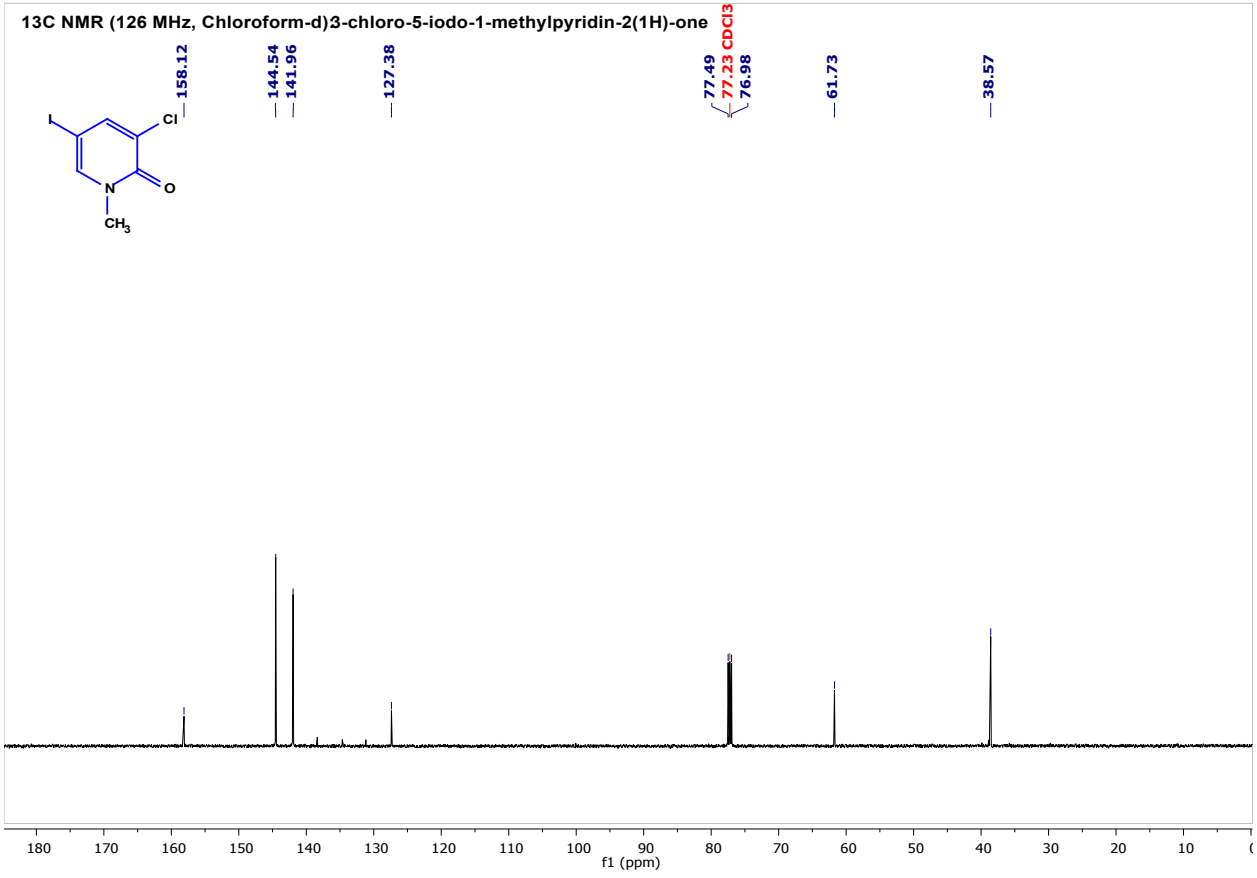

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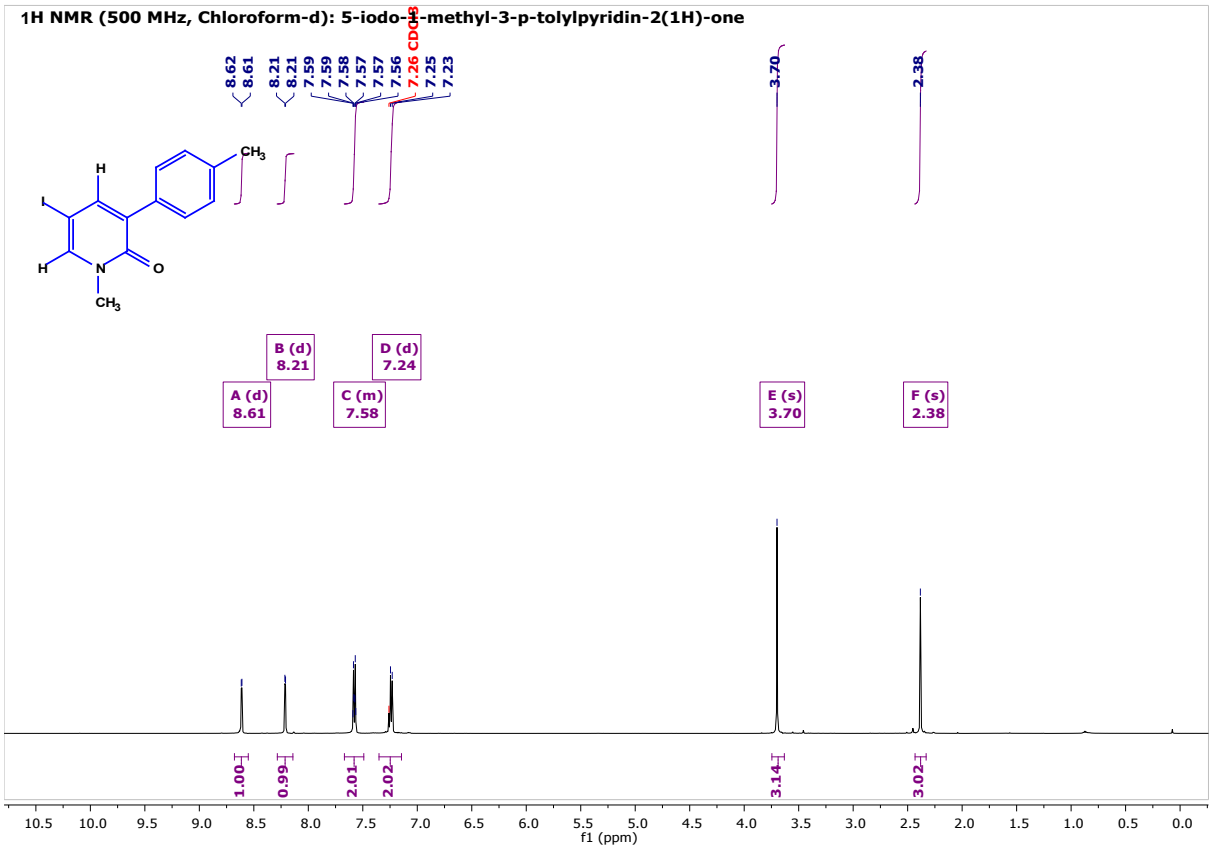

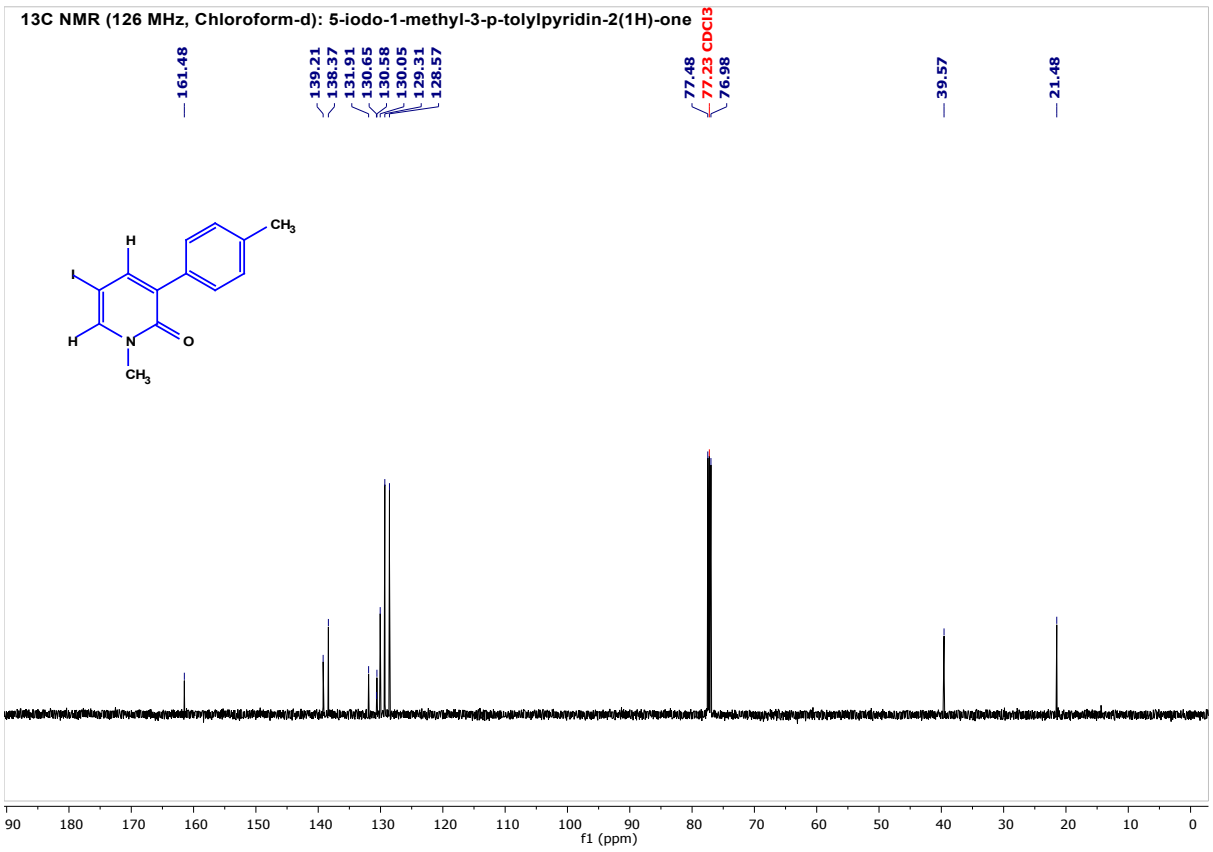

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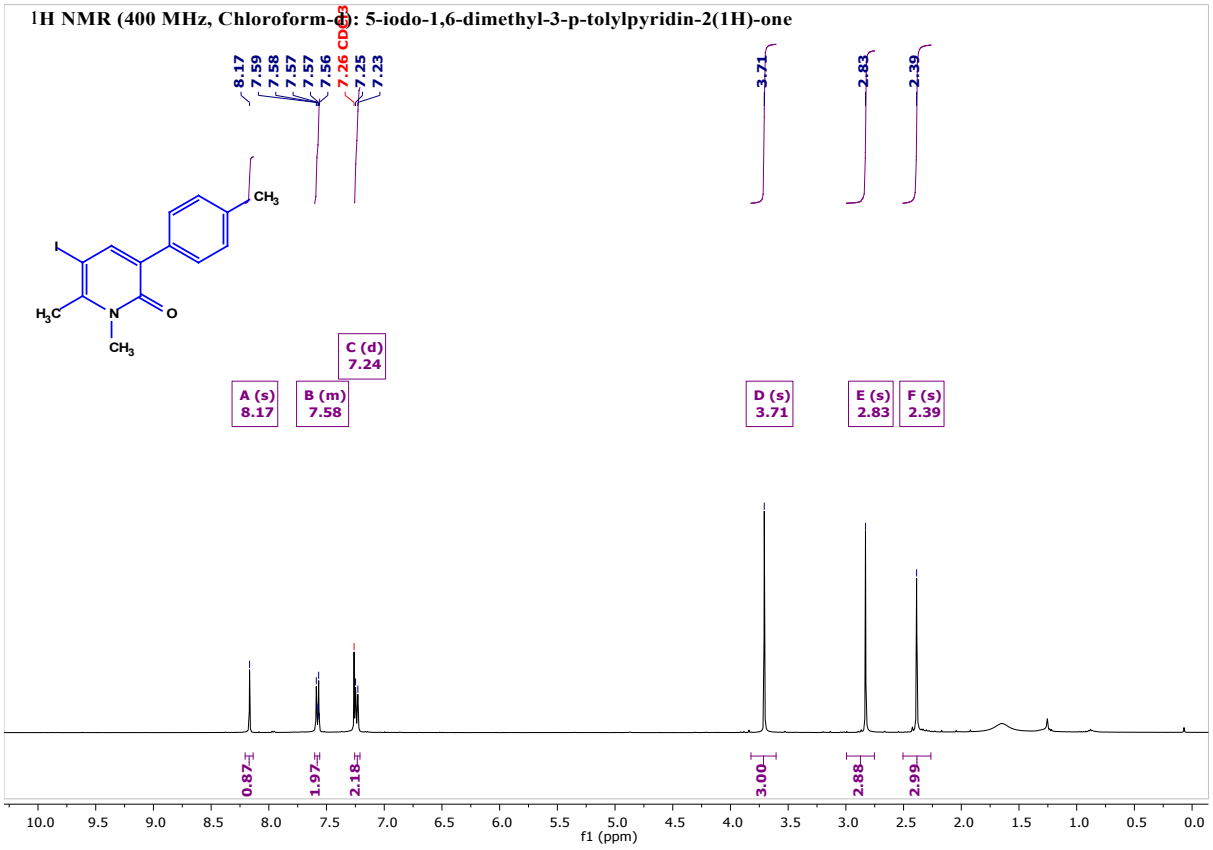

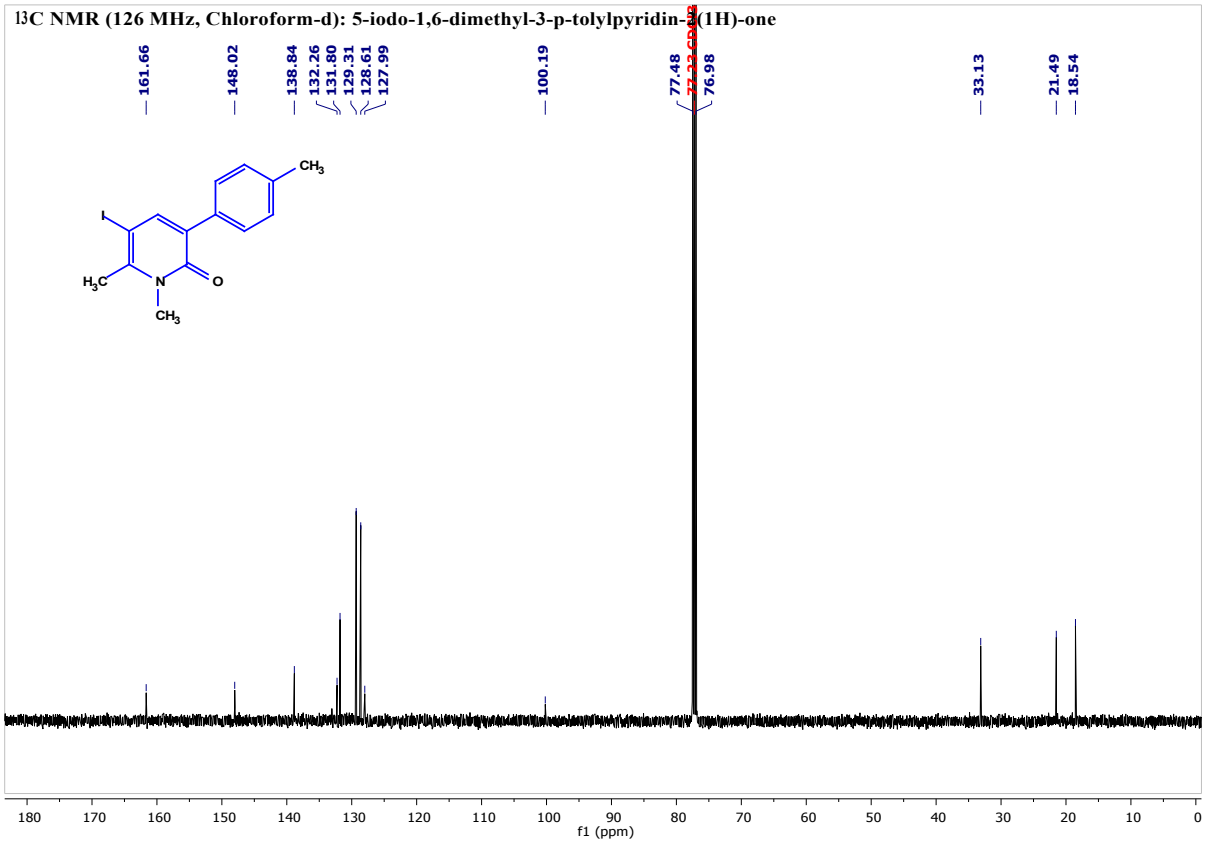

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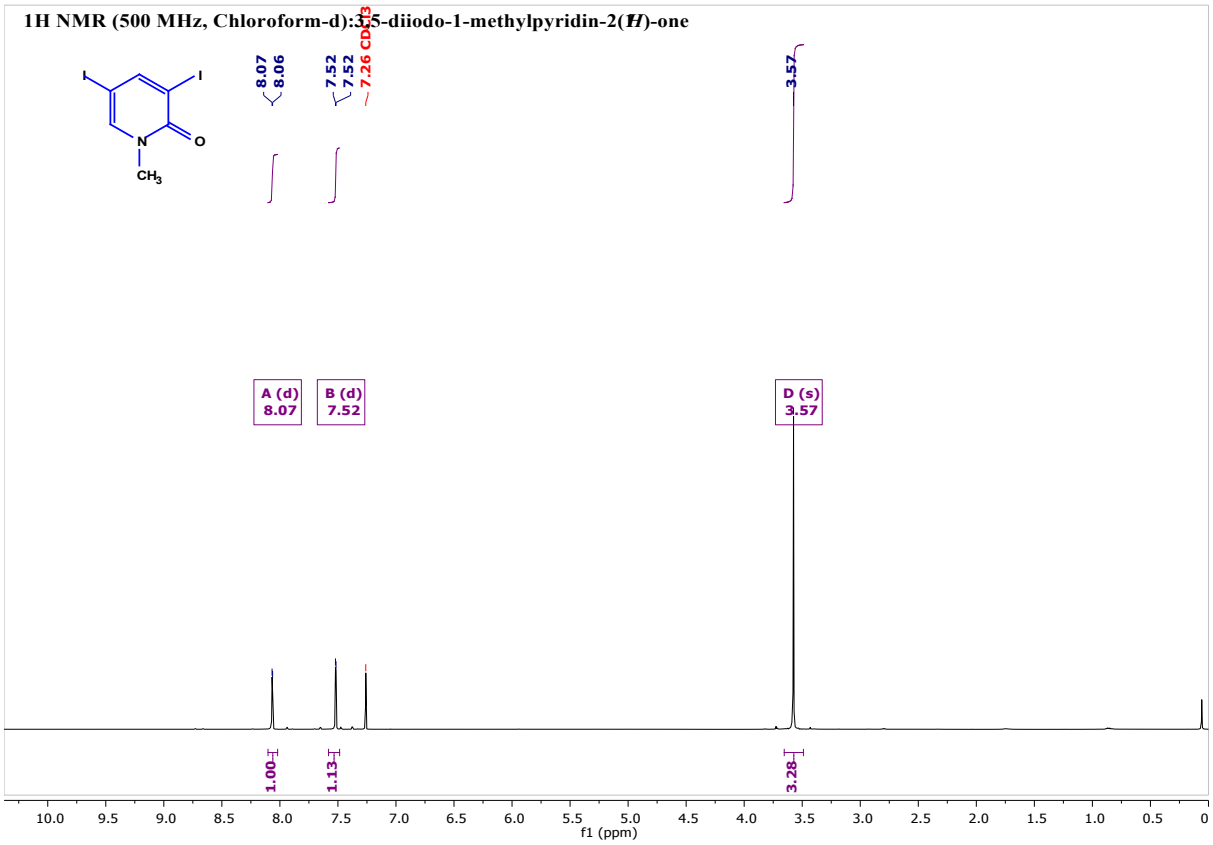

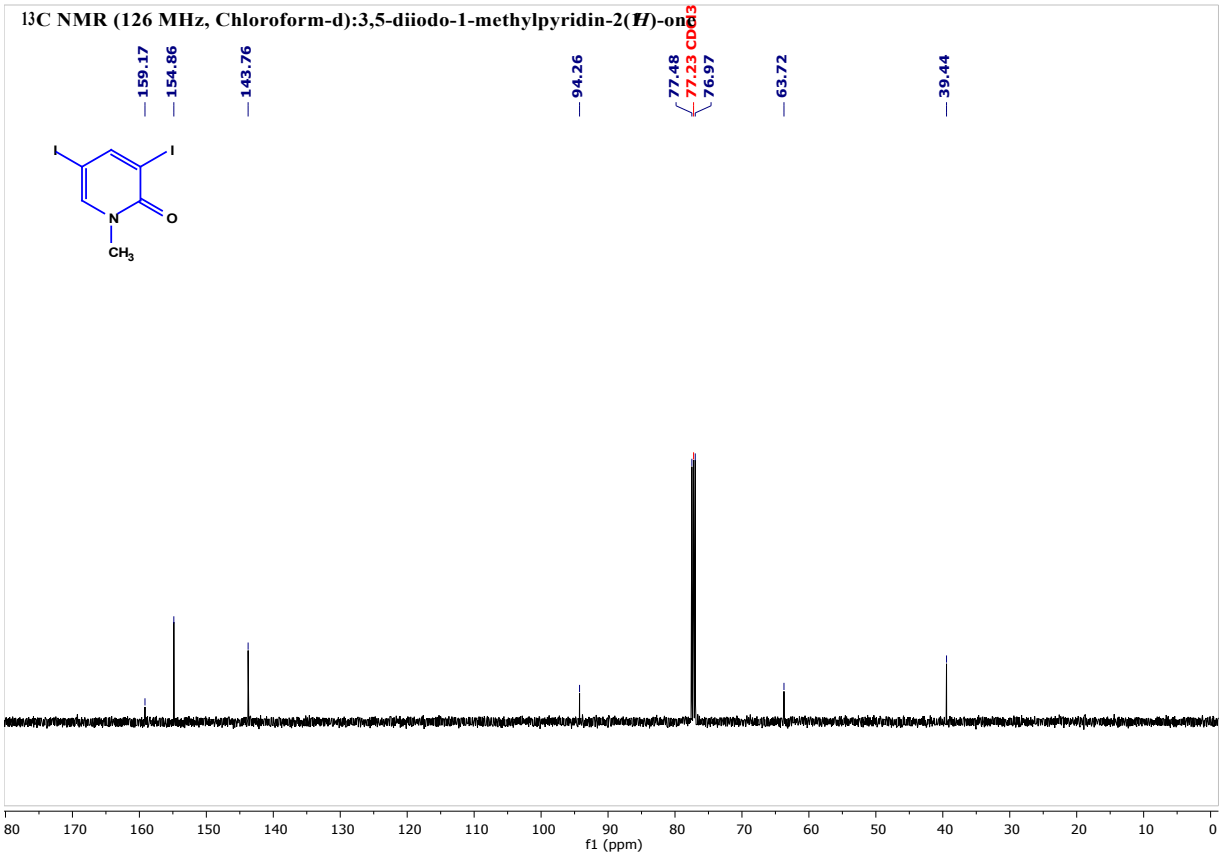

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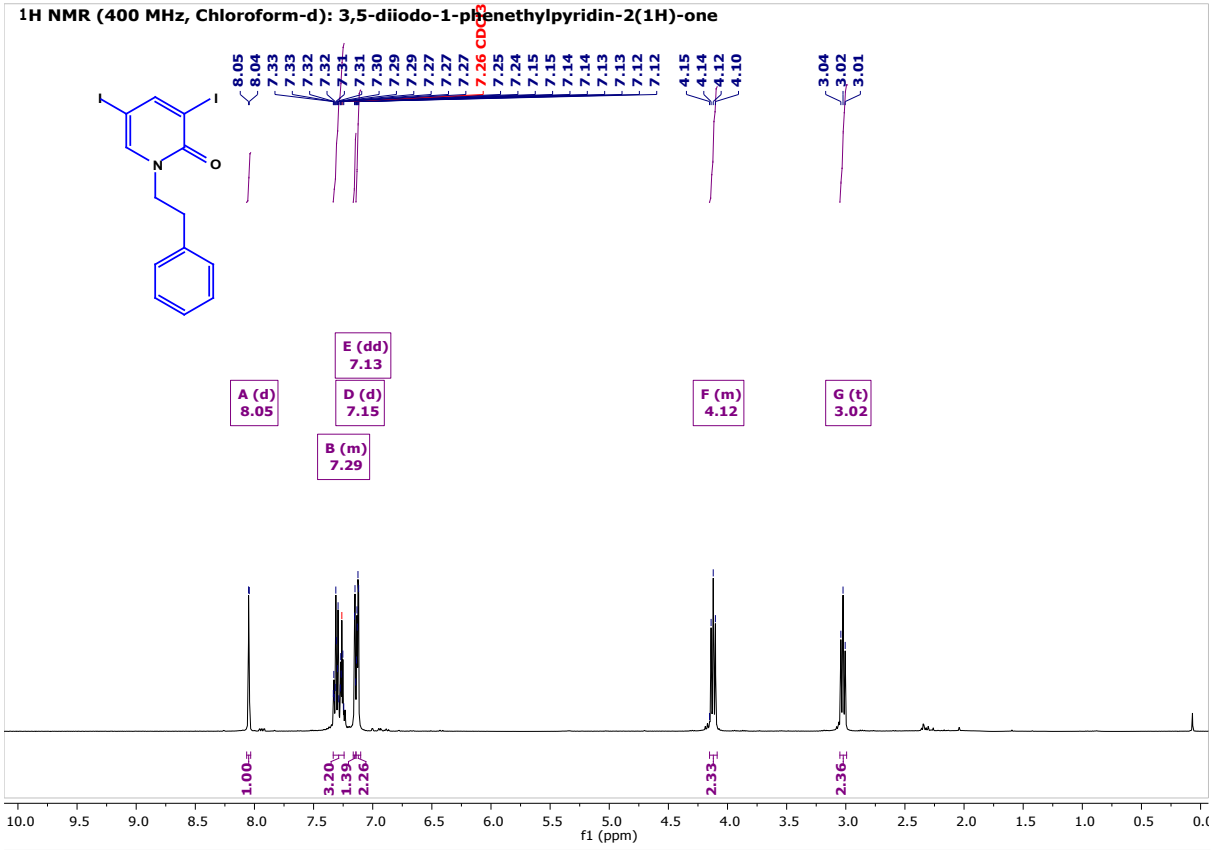

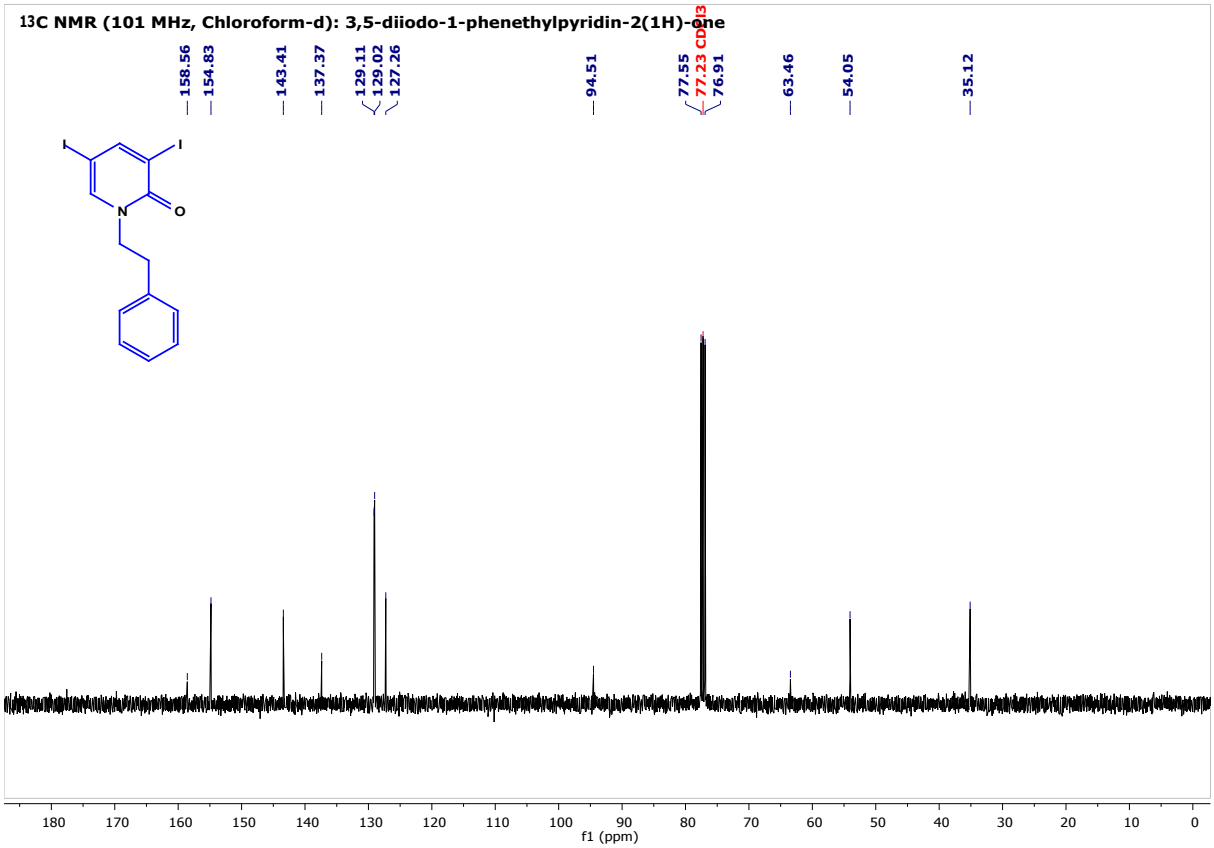

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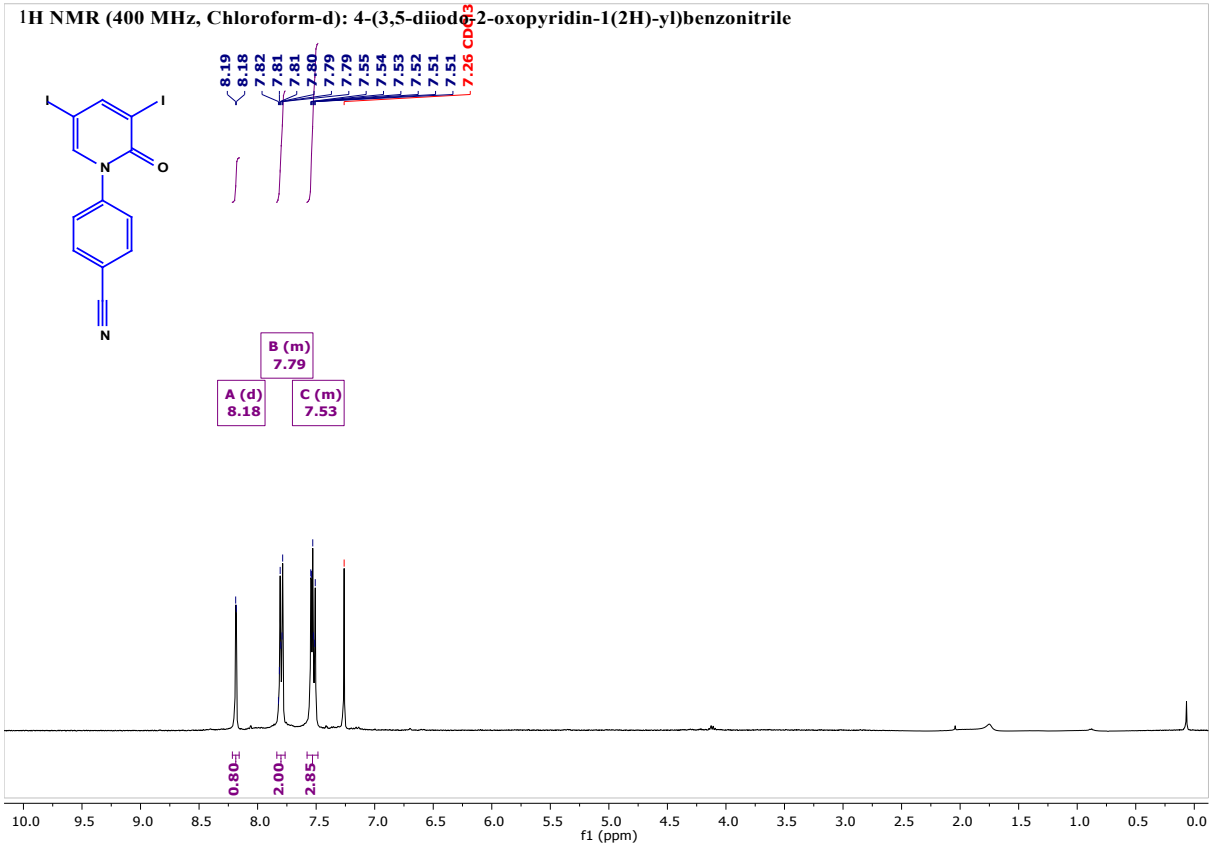

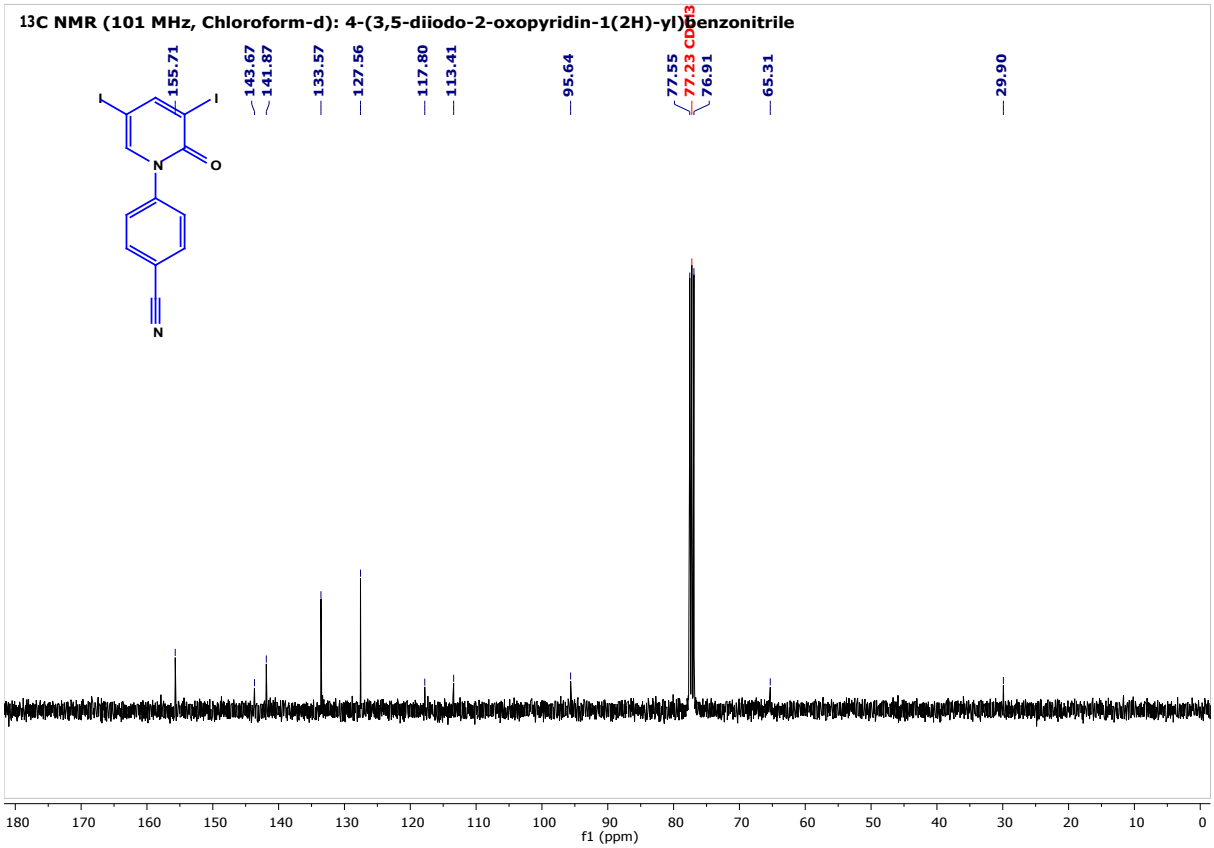

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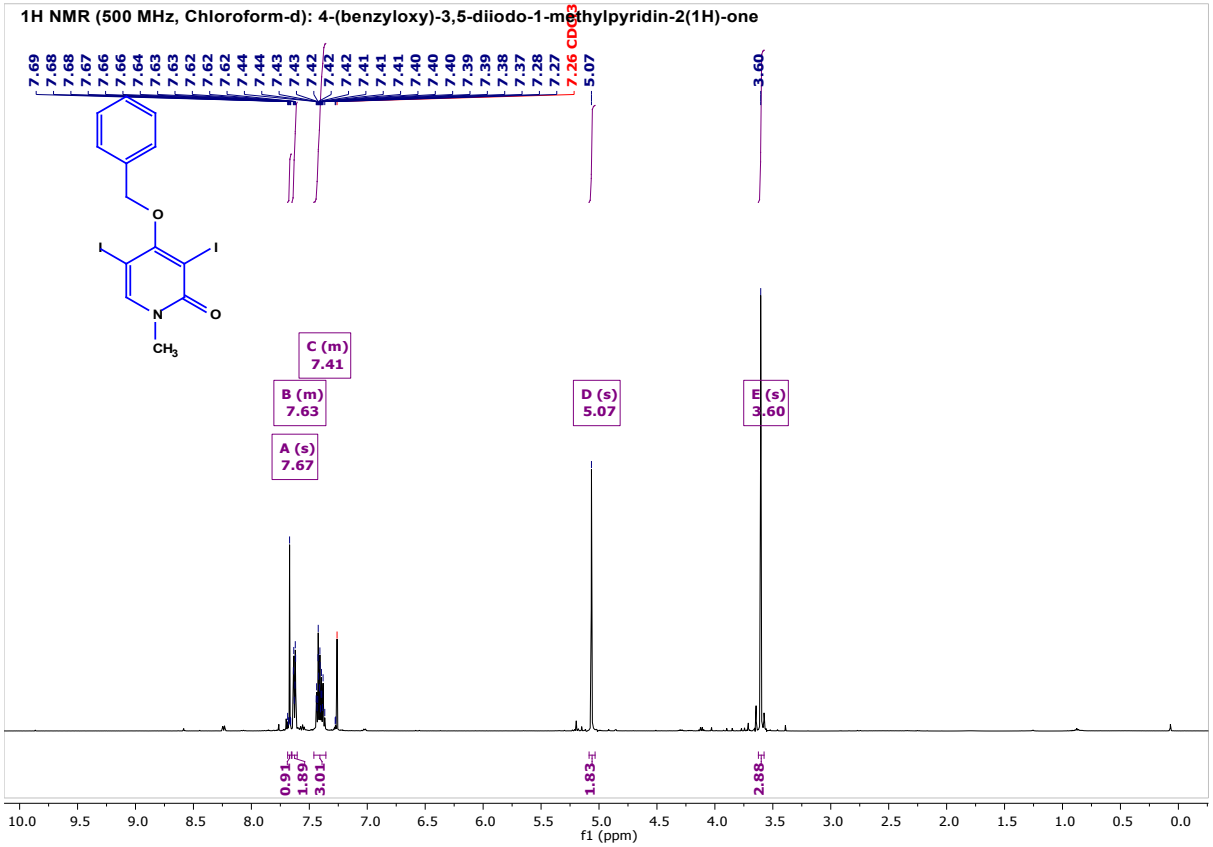

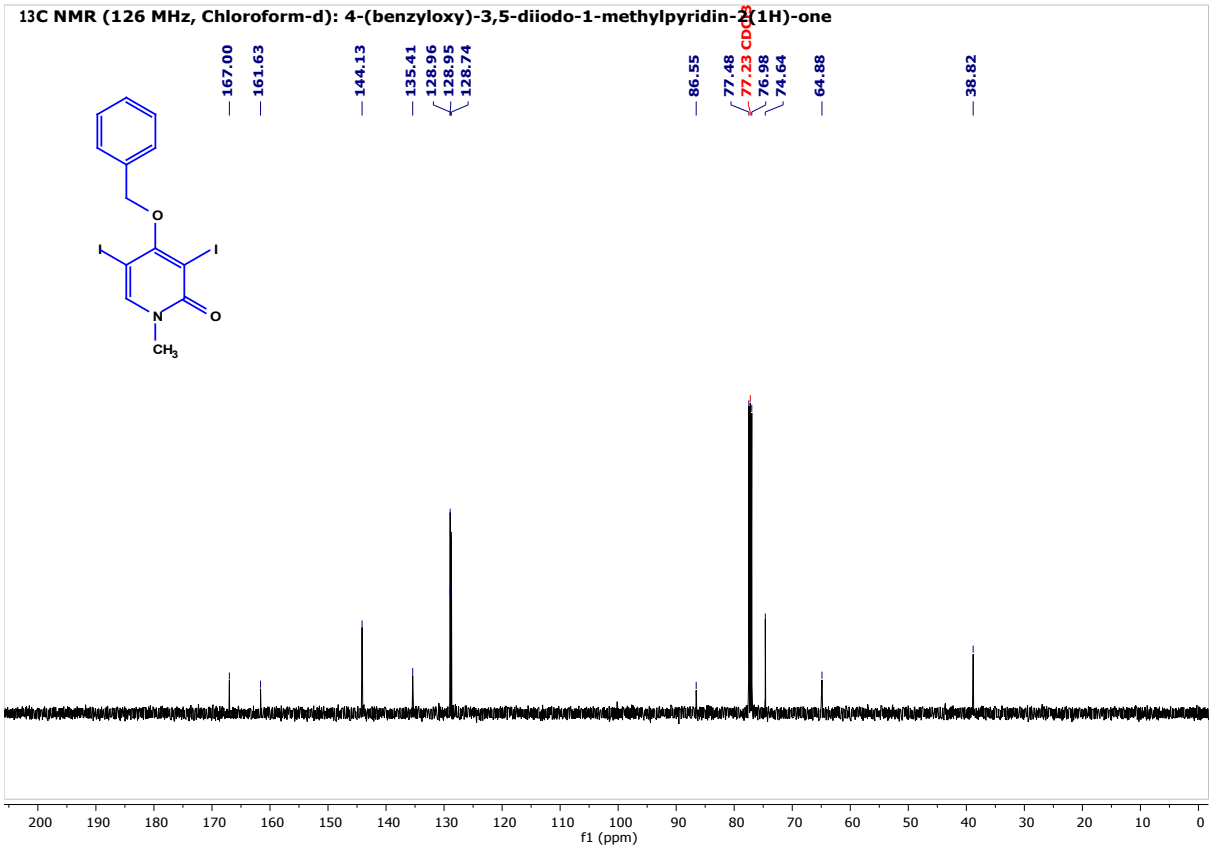

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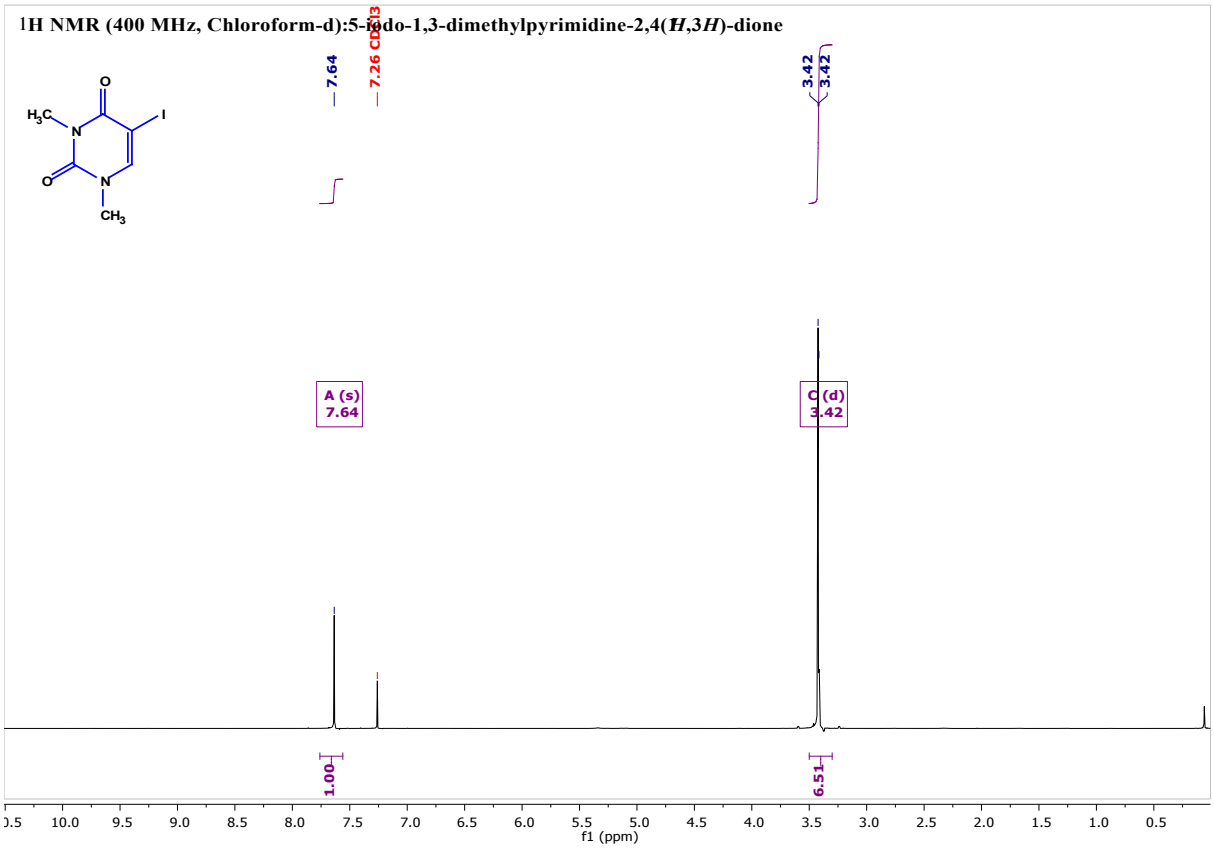

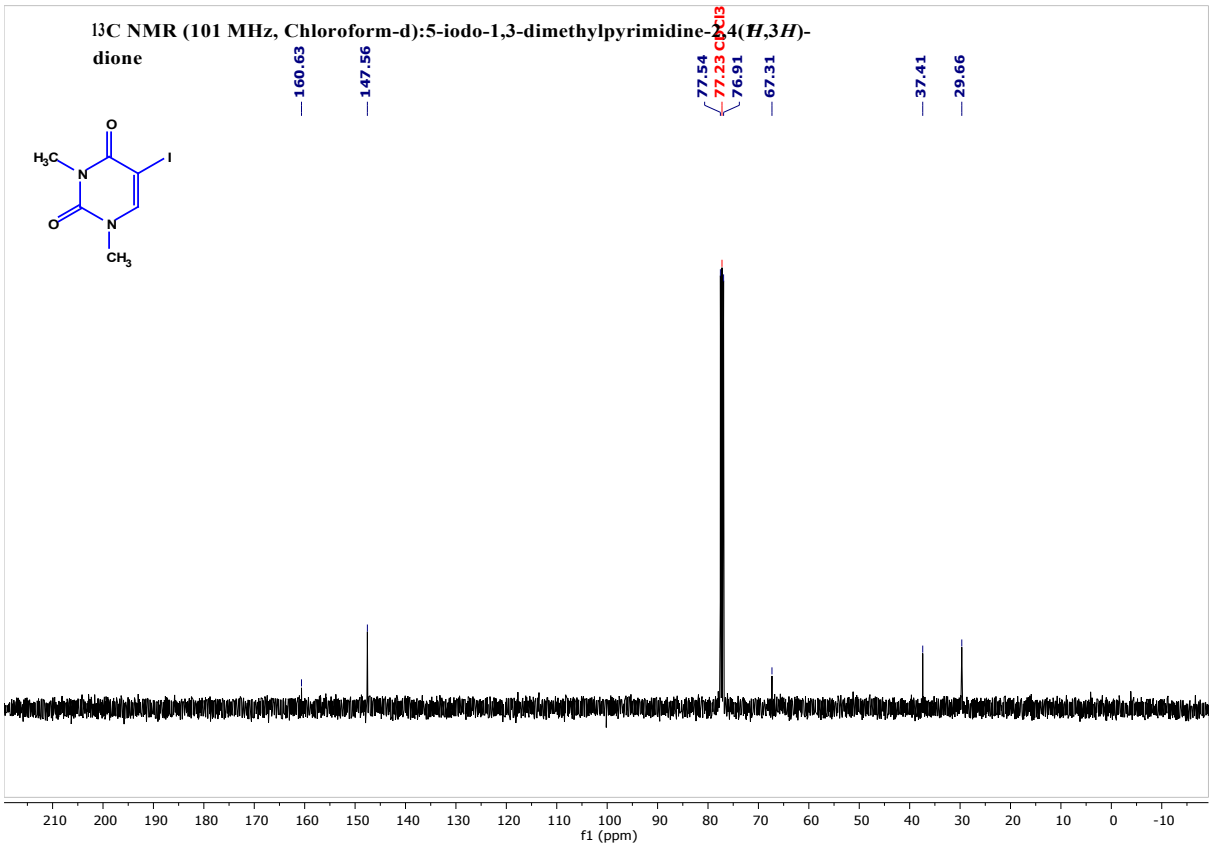

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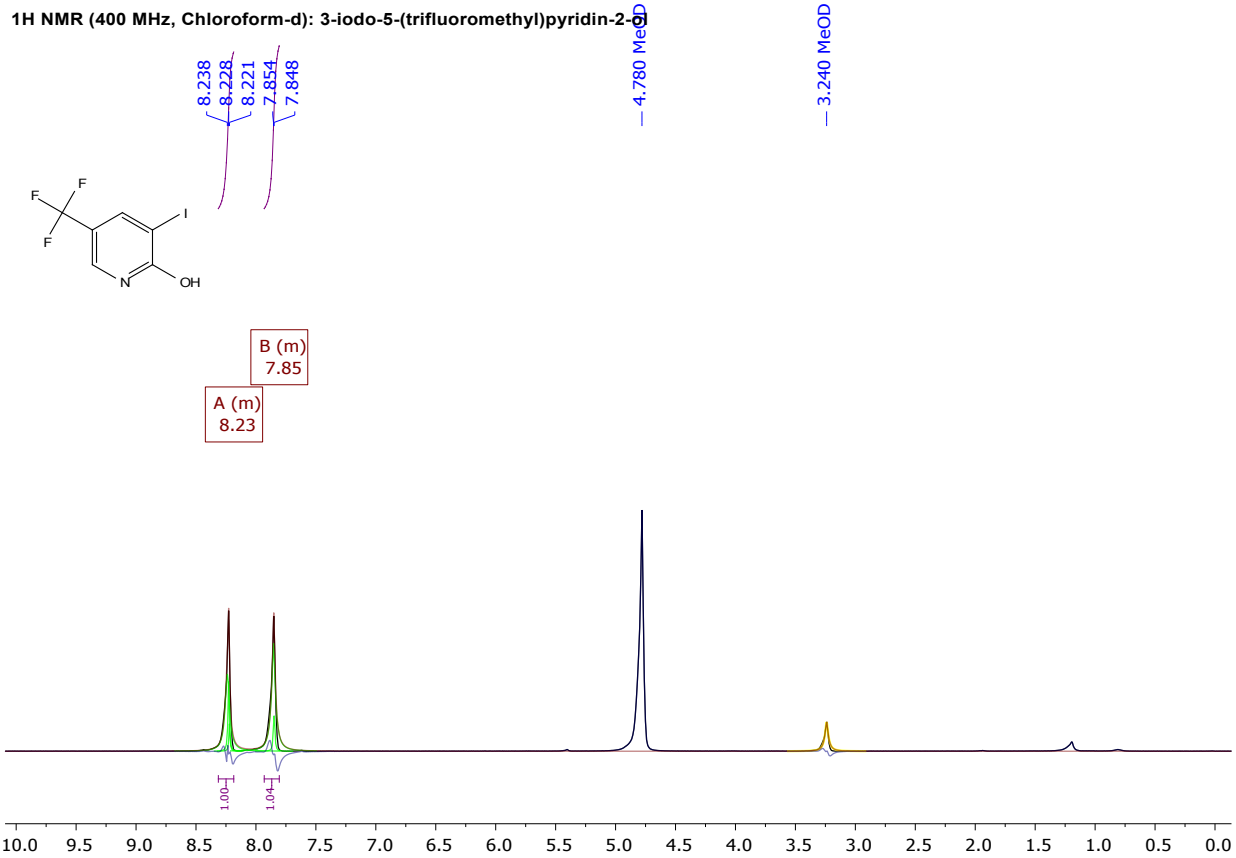

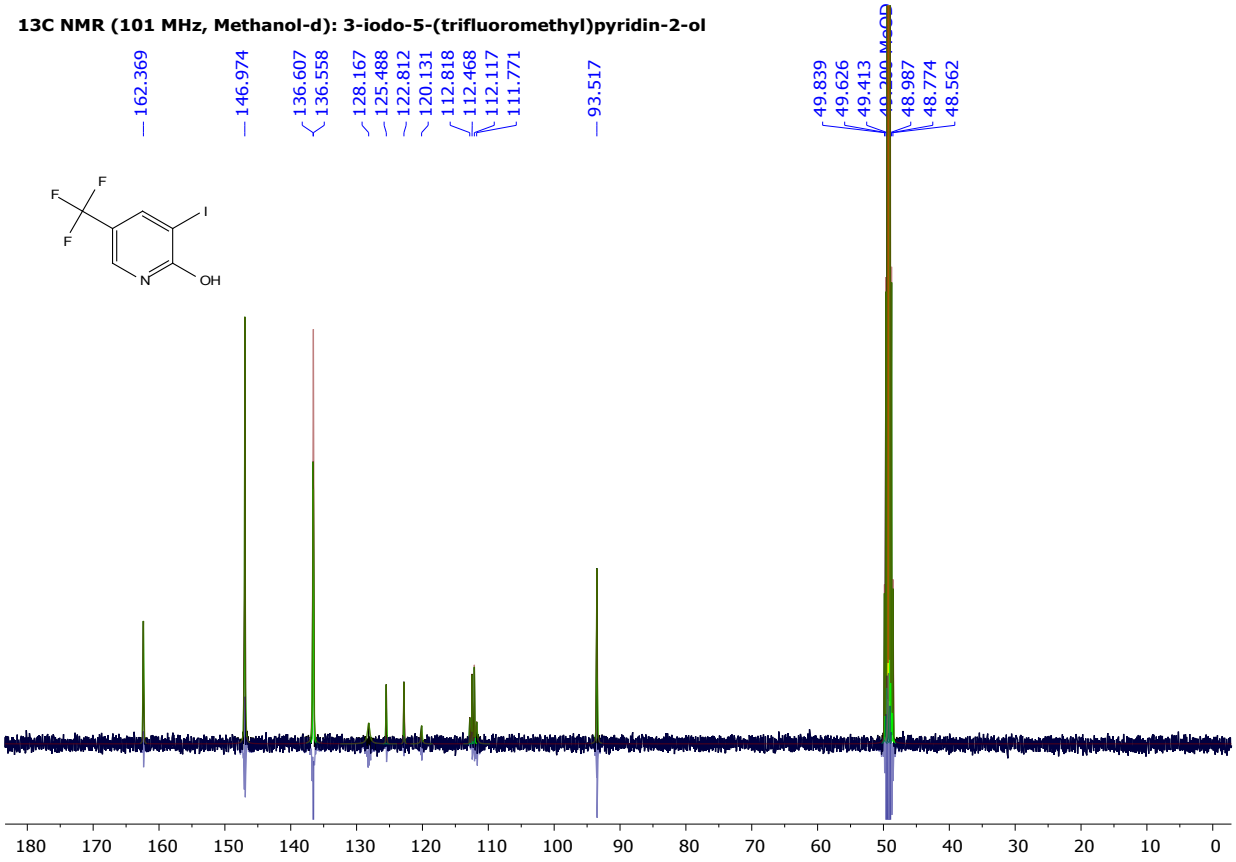

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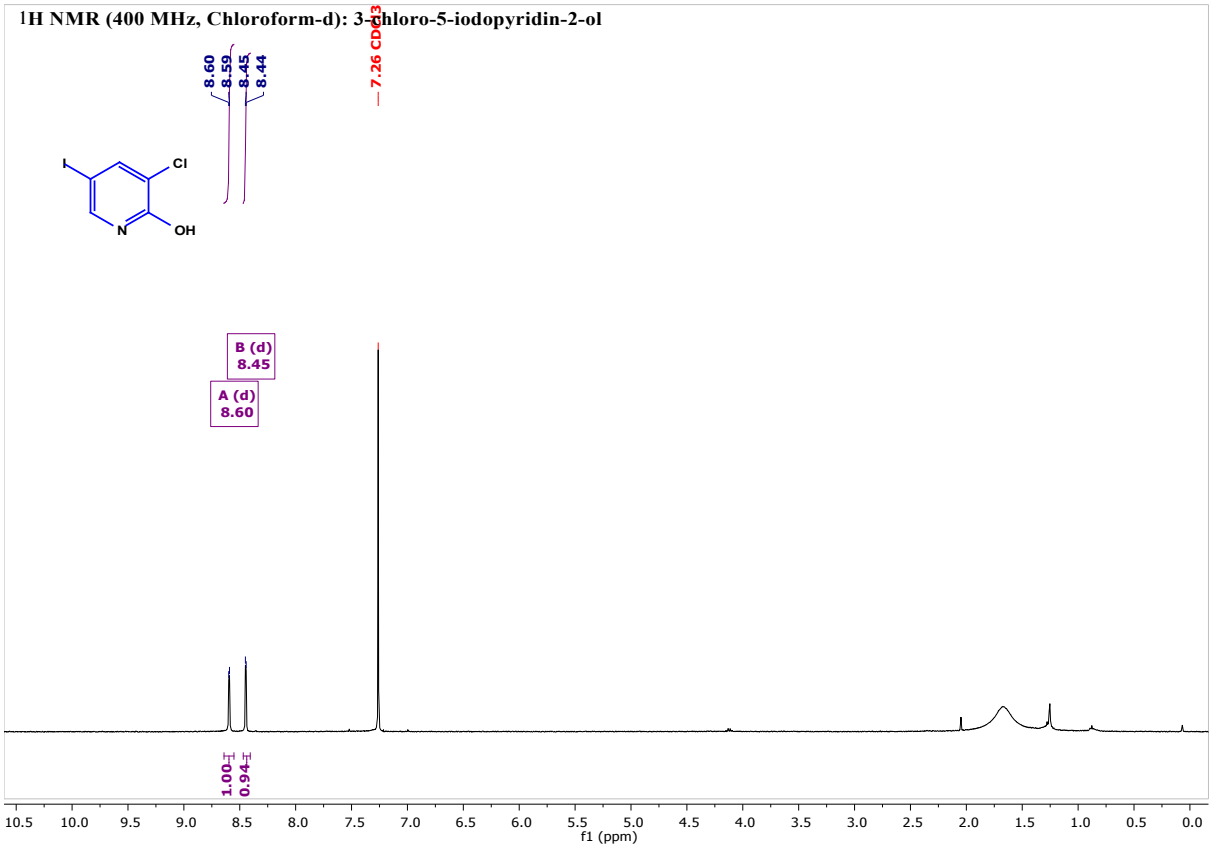

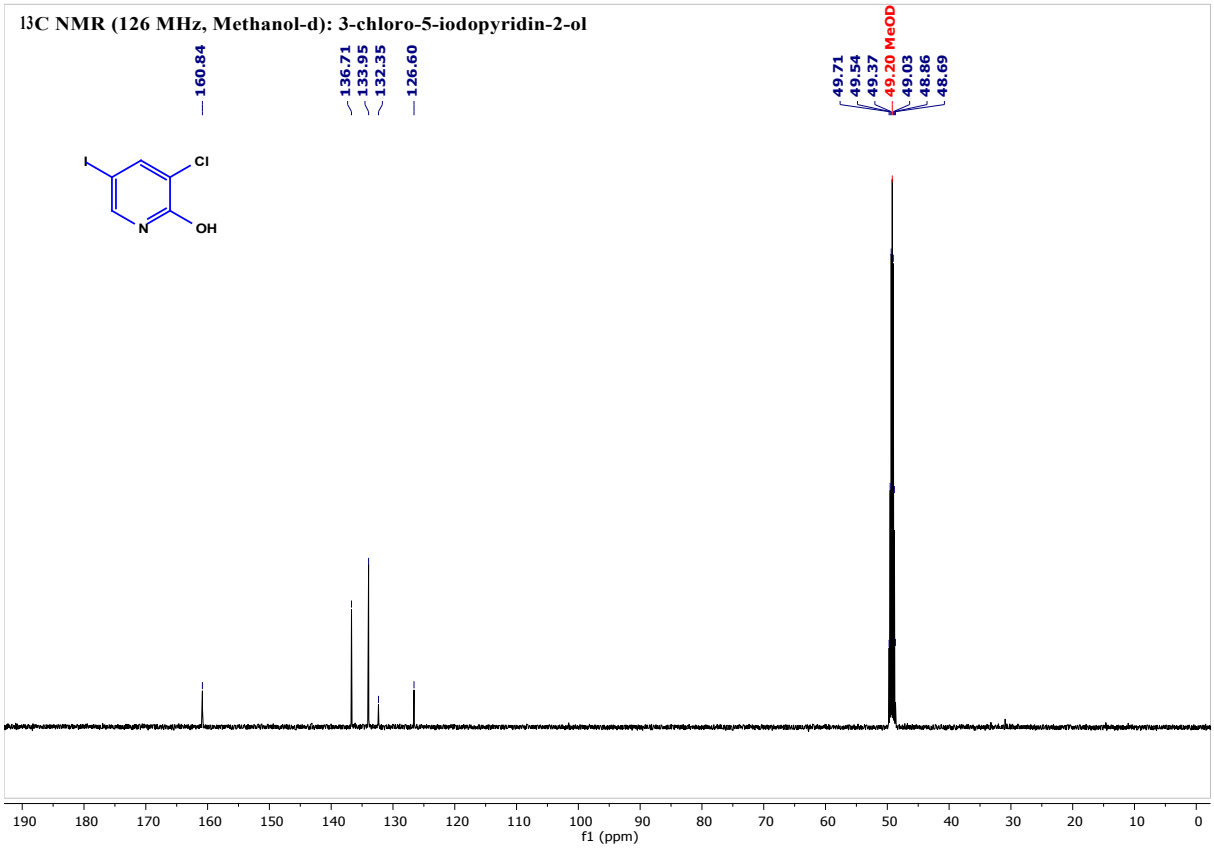

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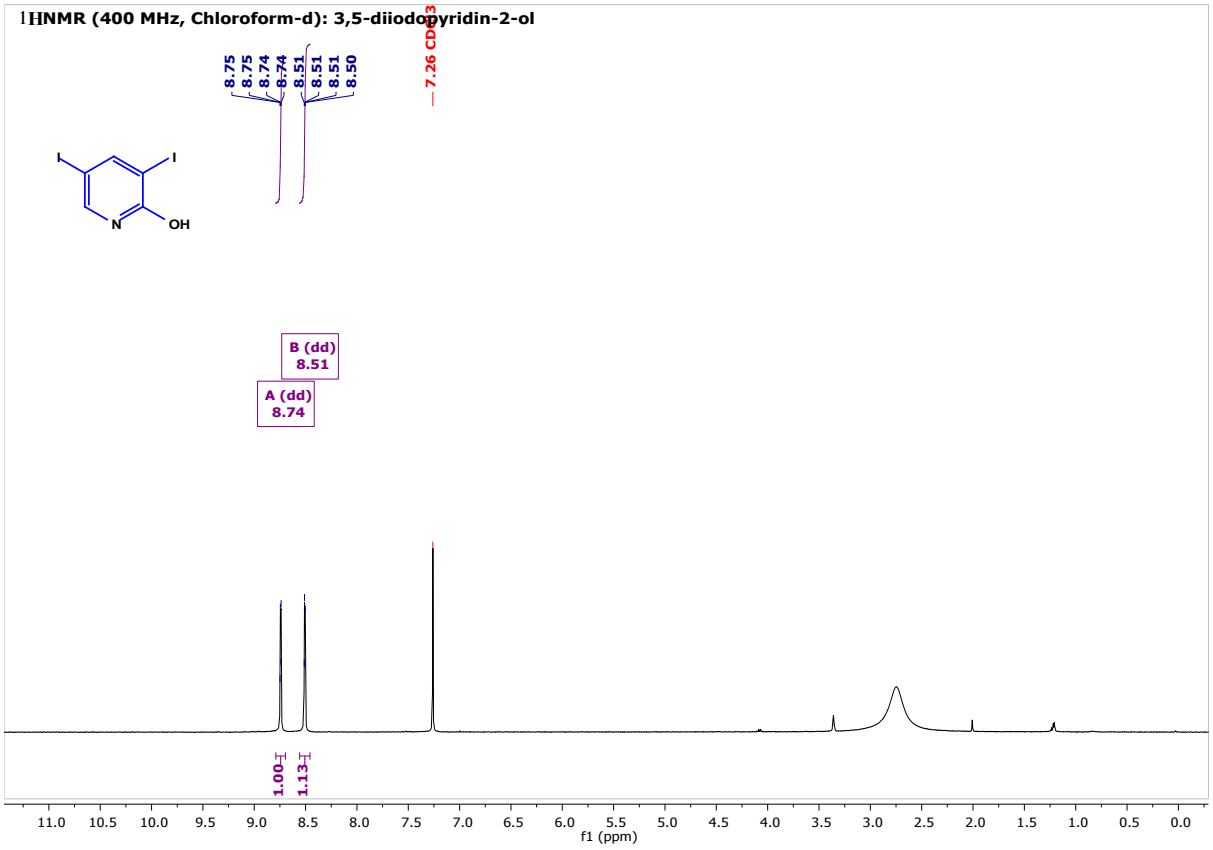

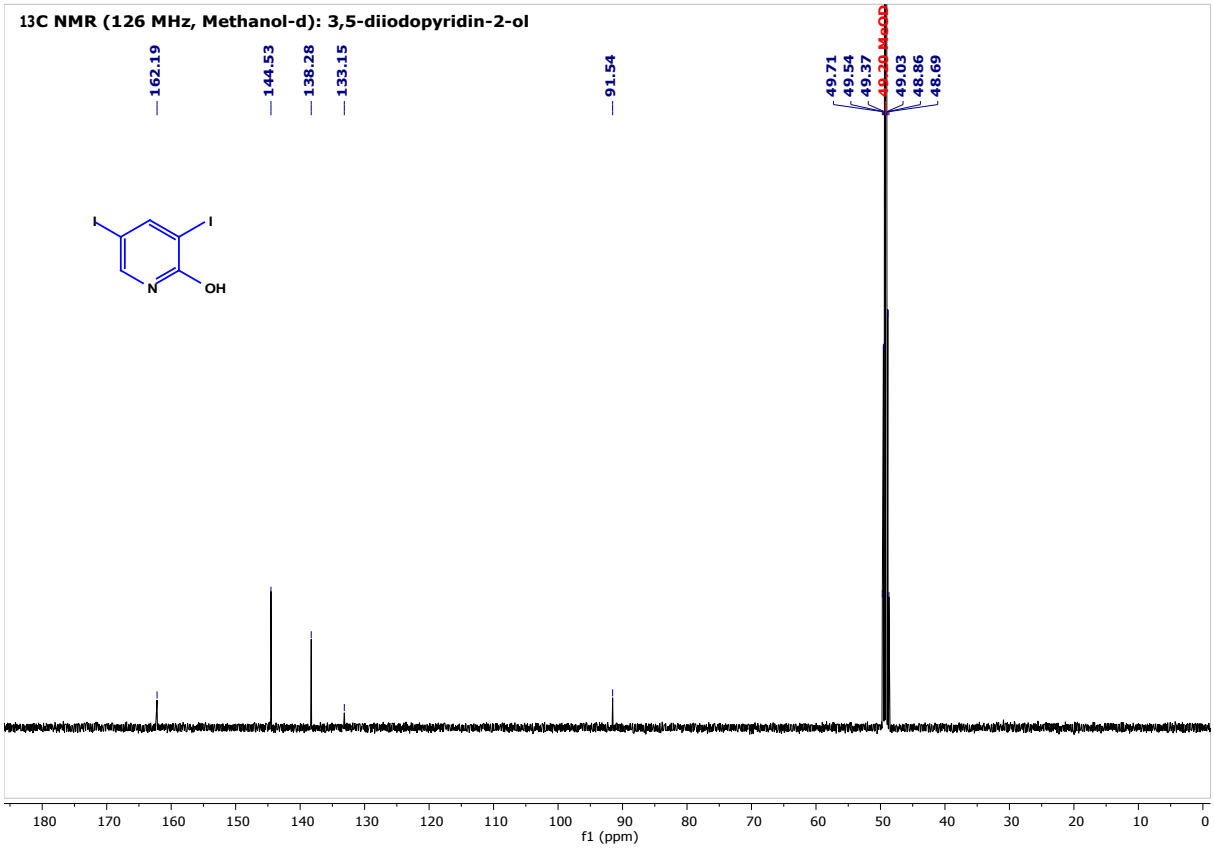

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