Electrophotocatalytic C–H Functionalization of Ethers with High Regioselectivity.

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1. General Information

Commercially available reagents were purchased from Sigma Aldrich, Matrix Chemical, AKSci, Alfa Aesar, Oakwood chemical or TCI, and used as received unless otherwise noted. Silica gel 60 (230-400 mesh) from SiliCycle was used for chromatography, and Merck silica gel plates with a fluorescence F_{254} indicator were used for thin-layer chromatography (TLC) analysis. ^{1}H and ^{13}C NMR spectra were recorded on Mercury-300 (300 MHz), Inova-400 (400 MHz), and Inova-500 (500 MHz) spectrometers. Chemical shifts in ^{1}H NMR spectra are reported in parts per million (ppm) relative to residual chloroform (7.26 ppm) or dimethyl sulfoxide (2.50 ppm) as internal standards. ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet), coupling constant in Hertz (Hz) and number of hydrogen atoms based on integration intensities. ^{13}C NMR chemical shifts are reported in ppm relative to the central peak of $CDCl_3$ (77.16 ppm) CD_3OD (49.00 ppm) or $(CD_3)_2SO$ (39.52 ppm) as internal standards. ^{19}F NMR chemical shifts are reported in ppm relative to the central peak of $C_6H_5CF_3$ (-63.72 ppm) as an internal standard. The mass spectral (MS) data were obtained on a Thermo Fisher Scientific Exactive series DART Mass Spectrometer. Anhydrous acetonitrile, THF, 2-methyltetrahydrofuran and cyclopentyl methyl ether were purchased as Sure/Seal™ bottles from Sigma-Aldrich.

2. General Procedures

Electrode preparation can be found in our pervious report[1].

Materials used for set-up:

Platinum wire (13039-BU from Alfa Aesar, 25 cm). Blue LED strips (Solid Apollo). Holmes Lil' Blizzard 8-inch oscillating table fan (Amazon). June gold 2.0 mm 2B pencil lead refills (Amazon). DC Power supply (Amazon, Dr.Meter 30V/5A). Carbon felt (cut around 7 mm x 7 mm x 7 mm) from C200 Soft Carbon Battery Felt (fuelcellstore, Product Code: 1595010).

The set up was in Fig. S1.

Fig. S1. Experiment set up

Procedure A for compounds 6, 8-30

To an oven-dried 10-mL three-neck flask equipped with a stir bar, a carbon felt anode, and a platinum wire cathode was added TAC **1** (15.2 mg, 0.032 mmol), the heteroarene if solid (0.4 mmol), and $LiClO_4$ (255.3 mg, 2.4 mmol). The cell was sealed using a rubber septum and parafilm then flushed with nitrogen gas for 5 min, followed by the sequential addition via syringe of CH_3CN (2 mL for **6**, **8-12**, 4 mL for **13-28**), the ether (2.0 mL), the heteroarene if liquid (0.4 mmol), trifluoroacetic acid (61 μL, 0.8 mmol) and acetic acid (72 μL, 1.2 mmol). The reaction mixture was then purged with nitrogen gas for an additional 5 min. The solution was then stirred at room temperature under irradiation from two 23W CFL bulbs and electrolysis was initiated at a constant voltage of 1.5 V for 36 h. The reaction mixture was subsequently poured into a saturated sodium bicarbonate solution (ca. 20 mL). The carbon felt anode was washed with EtOAc (3×5 mL) in an ultrasonic bath. The aqueous layer was separated and extracted with EtOAc (3×10 mL), and the combined organic layers and anode extraction were washed with brine and dried over anhydrous Na_2SO_4. Following concentration *in vacuo*, the crude residue was subjected to flash column chromatography on silica gel to yield the desired product.

Procedure B for compounds 31-36

To an oven-dried 10-mL three-neck flask equipped with a stir bar, a carbon felt anode and, a platinum wire cathode was added TAC **1** (15.2 mg, 0.032 mmol), the alkene if solid (0.4 mmol), and $LiClO_4$ (255.3 mg, 2.4 mmol). The cell was sealed using a rubber septum and parafilm then flushed with nitrogen gas for 5 min, followed by the sequential addition via syringe of CH_3CN (2 mL), the ether (2.0 mL), the alkene or alkyne if liquid (0.4 mmol), and acetic acid (229 μL, 4.0 mmol). The reaction mixture was then purged with nitrogen gas for an additional 5 min. The solution was stirred at room temperature under irradiation from two 23W CFL bulbs, and electrolysis was initiated at a constant voltage of 1.5 V for 36 h. The reaction mixture was subsequently poured into a saturated sodium bicarbonate solution (ca. 20 mL). The carbon felt anode was washed with EtOAc (3×5 mL) in an ultrasonic bath. The aqueous layer was separated and extracted with EtOAc (3×10 mL), and the combined organic layers and anode extract were washed with brine and dried over anhydrous Na_2SO_4. Following concentration *in vacuo*, the crude residue was subjected to flash column chromatography on silica gel to yield the desired product.

Procedure C for compounds 37-45

To an oven-dried 10-mL three-neck flask equipped with a stir bar, a carbon felt anode, and a platinum wire cathode was added TAC **1** (15.2 mg, 0.032 mmol), the azole (0.4 mmol), and $LiClO_4$ (255.3 mg, 2.4 mmol). The cell was sealed using a rubber septum and parafilm, then flushed with nitrogen gas for 5 min, followed by the sequential addition via syringe of CH_3CN (2 mL), the ether (2.0 mL), and acetic acid (229 μL, 4.0 mmol). The reaction mixture was then purged with nitrogen gas for an additional 5 min. The solution was stirred at room temperature under irradiation from two 23W CFL bulbs, and electrolysis was initiated at a constant voltage of 2.0 V for 36 h. The reaction mixture was subsequently poured into a saturated sodium bicarbonate solution (ca. 20 mL). The carbon felt anode was washed with EtOAc (3×5 mL) in an ultrasonic bath. The aqueous layer was separated and extracted with EtOAc (3×10 mL), and the combined organic layers and anode extract were washed with brine and dried over anhydrous Na_2SO_4. Following concentration *in vacuo*, the crude residue was subjected to flash column chromatography on silica gel to yield the desired product.

Notes:

1. Even though this reaction has not been found to be sensitive to water, anhydrous lithium perchlorate and anhydrous acetonitrile were used.

2. Ethers were freshly distilled to remove inhibitor and peroxide impurities. Ethers should be pure because peroxide contaminants can react via direct electrolysis.

3. Both acetonitrile and ethers were degassed by the freeze-pump-thaw method.

4. Because the carbon felt can absorb a significant amount of reaction solution, it should be rinsed in an ultrasonic bath for 5 min or more to obtain optimal product yields.

5. In the undivided cell, it is best to keep the anode and cathode relatively close (~0.5 cm) to one another; however, they should not touch.

6. For the cathode, the platinum wire should be immersed in the solution, but not the pencil lead to which it is attached.

7. The carbon felt should be replaced for each reaction.

8. The system was cooled using a fan.

9. High stirring speed is required.

10. After the reaction, care should be taken when removing the septum in case of pressure build up from hydrogen gas generation.

3. Gram Scale Procedures

Electrode preparation can be found in our previous report.[2]

Materials used for set-up:

Platinum foil (42456-FF, 0.05 mm thick from Alfa Aesar, 25 * 25 mm). DC Power supply (Amazon, Dr.Meter 30V/5A). Carbon felt (cut around 20 mm x 10 mm x 7 mm) from C200 Soft Carbon Battery Felt (fuelcellstore, Product Code: 1595010).

The set-up is shown in Fig. S2.

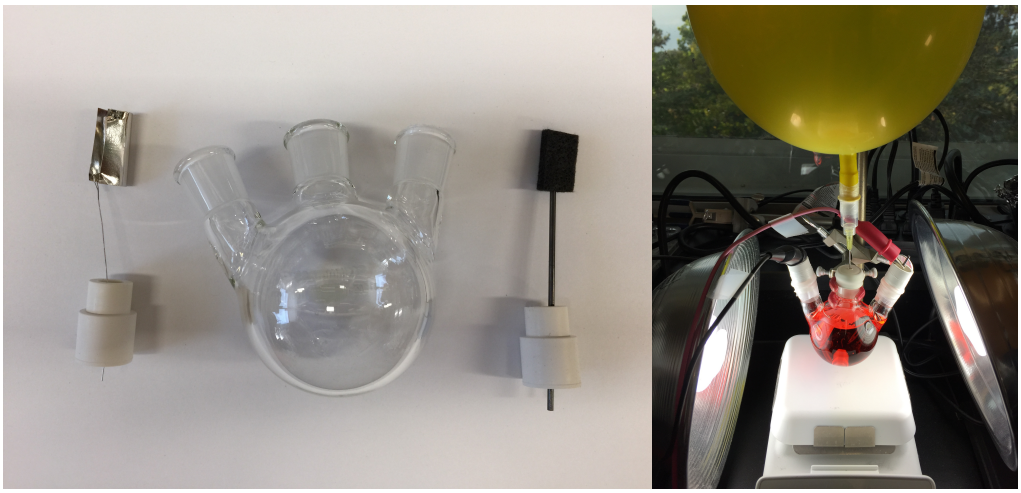


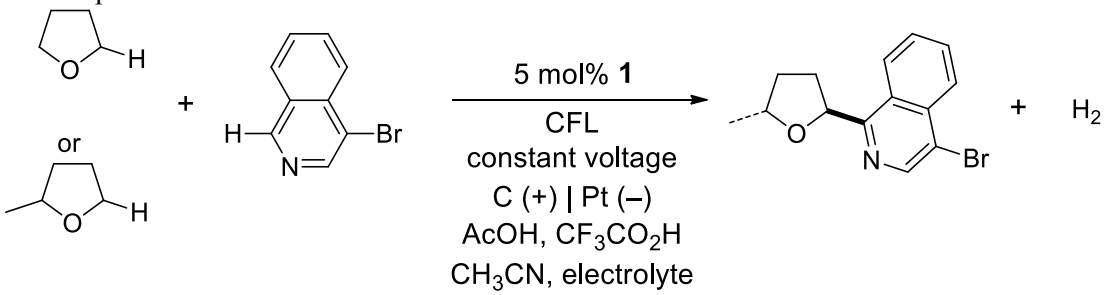
Fig. S2. Large scale experiment set up

Procedure for gram scale reaction

To an oven-dried 100-mL three-neck flask equipped with a stir bar, a carbon felt anode, and a platinum wire cathode was added TAC **1** (303.4 mg, 0.64 mmol), 4-bromoisoquinoline (1.66 g, 8 mmol), and $LiClO_4$ (5.11 g, 48 mmol). The cell was sealed using a rubber septum and parafilm, then flushed with nitrogen gas for 15 min, followed by the sequential addition via syringe of CH_3CN (30 mL), THF (40 mL), trifluoroacetic acid (1.2 mL, 16 mmol) and acetic acid (1.4 mL, 24 mmol). The reaction mixture was then purged with nitrogen gas for an additional 15 min. A nitrogen gas balloon was connected to the flask by a needle. The solution was stirred at room temperature under irradiation from two 23W CFL bulbs, and electrolysis was initiated at a constant voltage of 1.5 V for 72 h. The reaction mixture was subsequently poured into a saturated sodium bicarbonate solution (ca. 400 mL). The carbon felt anode was washed with EtOAc (3×100 mL) in an ultrasonic bath. The aqueous layer was separated and extracted with EtOAc (3×200 mL), and the combined organic layers and anode extract were washed with brine and dried over anhydrous Na_2SO_4. Following concentration *in vacuo*, the crude residue was subjected to flash column chromatography on silica gel to yield 1.6 g of the desired product.

4. Optimization

Table S1. Optimization studies



entry	E_{cell} (V)	electrolyte (equiv)	other	yield (%)[a,b]
1	1.5	$LiClO_4$ (6)	–	42
2	1.5	$LiClO_4$ (6)	no light	<5
3	–	$LiClO_4$ (6)	no current	<5
4	1.5	$LiClO_4$ (6)	no catalyst	<5
5	1.5	$LiClO_4$ (6)	no TFA	8
6	1.5	$LiClO_4$ (6)	DMF solvent	20
7	1.5	$LiPF_6$ (6)	–	15
8	1.5	$TBAPF_6$ (1.5)	–	10
9	1.5	$TBABF_4$ (1.5)	–	7
10	1.5	$LiClO_4$ (6)	–	82 (80)[c,d]
11	3.0	$LiClO_4$ (6)	direct electrolysis	messy
12	1.0	$LiClO_4$ (6)	–	<5[c]
13	1.5	$LiClO_4$ (6)	1.6 g scale	72[c,d]
14[e]	1.5	$LiClO_4$ (6)	–	56 (55) [c,d]
15[e]	1.5	$LiClO_4$ (6)	DCM solvent	<5 [c]
16[e]	1.5	$LiClO_4$ (6)	DMF solvent	8 [c]
17[e]	1.5	$LiPF_6$ (6)	–	30 [c]
18[e]	1.5	$TBABF_4$ (1.5)	–	6 [c]
19[e]	1.5	$TBAClO_4$ (1.5)	–	10 [c]

[a] See procedure parts. Initial reaction conditions: 4-bromoisoquinoline (0.4 mmol, 1.0 equiv), THF (2.0 mL), TAC (0.02 mmol, 0.05 equiv), CH_3CN (4.0 mL), $LiClO_4$ (2.4 mmol, 6.0 equiv), N_2, carbon felt anode, Pt cathode. Reactions performed under constant voltage (CV) conditions with light irradiation for 18 h at rt. [b] Yields were determined by ^1H NMR spectroscopy. [c] TAC (0.032 mmol, 0.08 equiv) ether (2.0 mL) and CH_3CN (2.0 mL) were used in the reaction for 36 h. Others see procedure. [d] Yield of isolated product. [e] 2-MeTHF was used.

5. In situ NMR Analysis

NMR trace	Difference from standard reaction conditions
1	No light
2	No current
3	No catalyst
4	Standard reaction conditions
5	E_{cell} = 3.0 V without catalyst

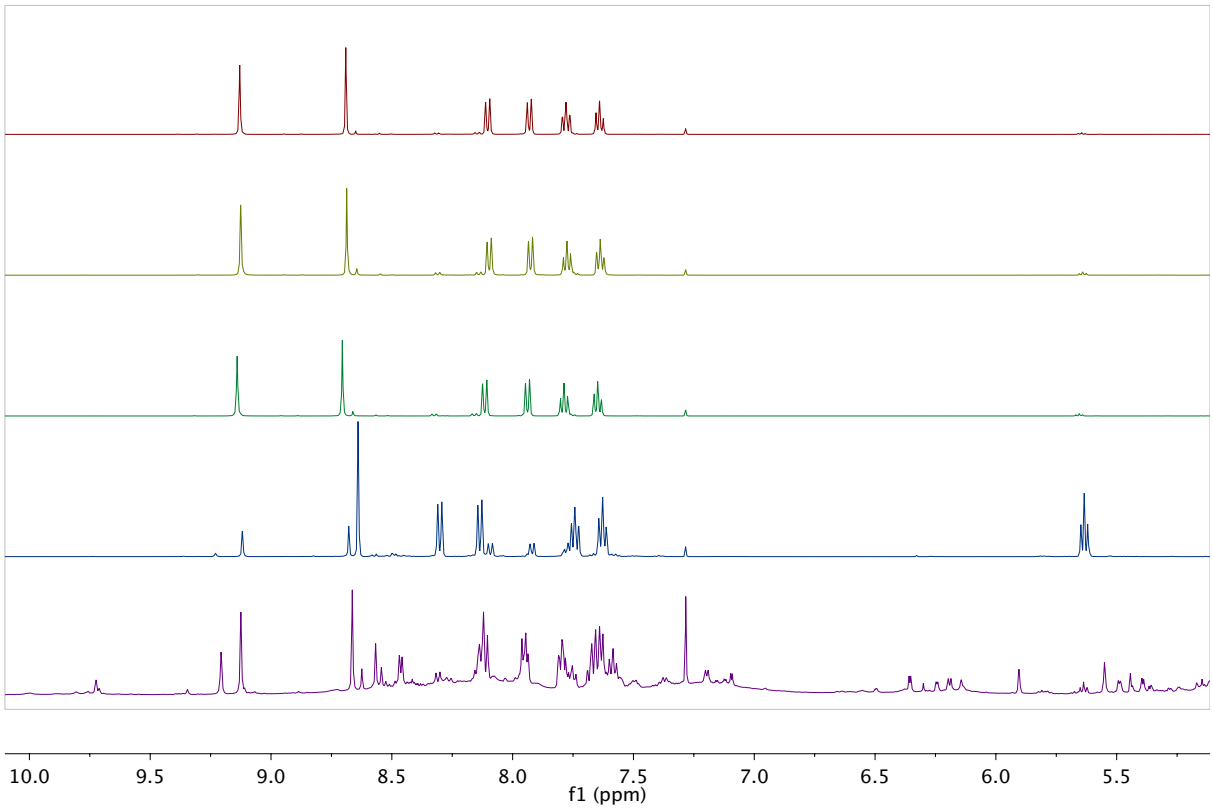


Fig. S3. *In situ* NMR Analysis

6. KIE Experiment

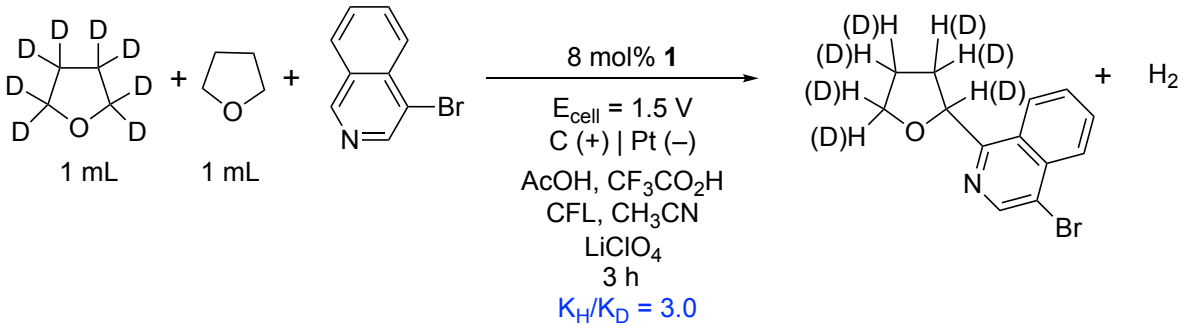
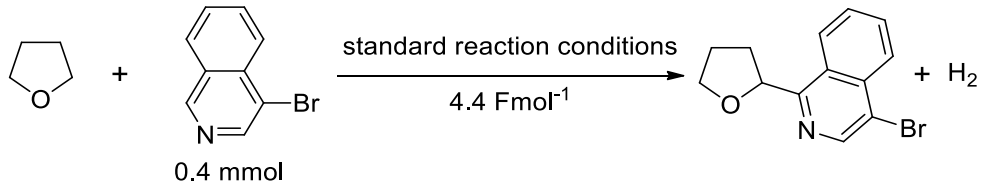


Fig S4. Kinetic isotope effect experiments

7. Current Profile



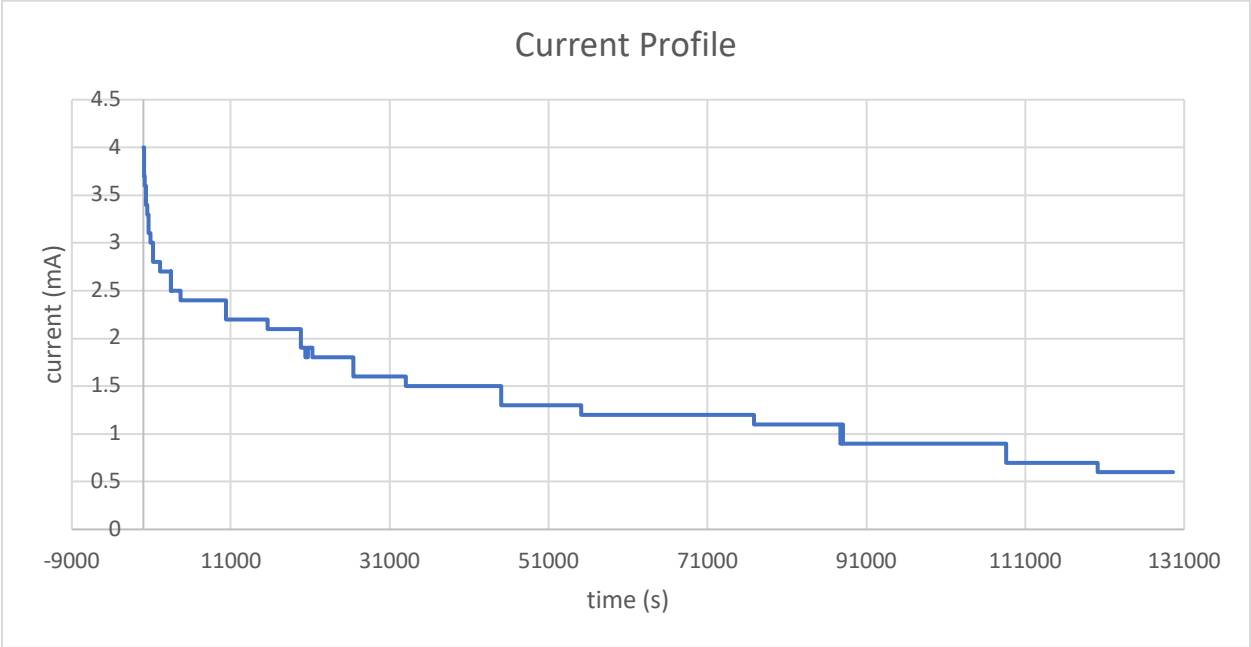
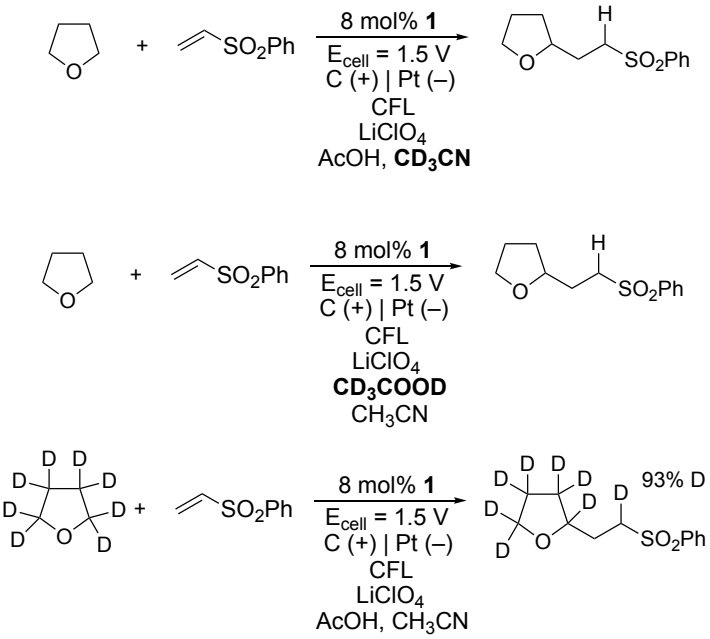


Fig S5. Current Profile

8. Mechanism Studies

Reactions were performed as procedure B with deuterated acetonitrile, deuterated acetic acid or deuterated THF:



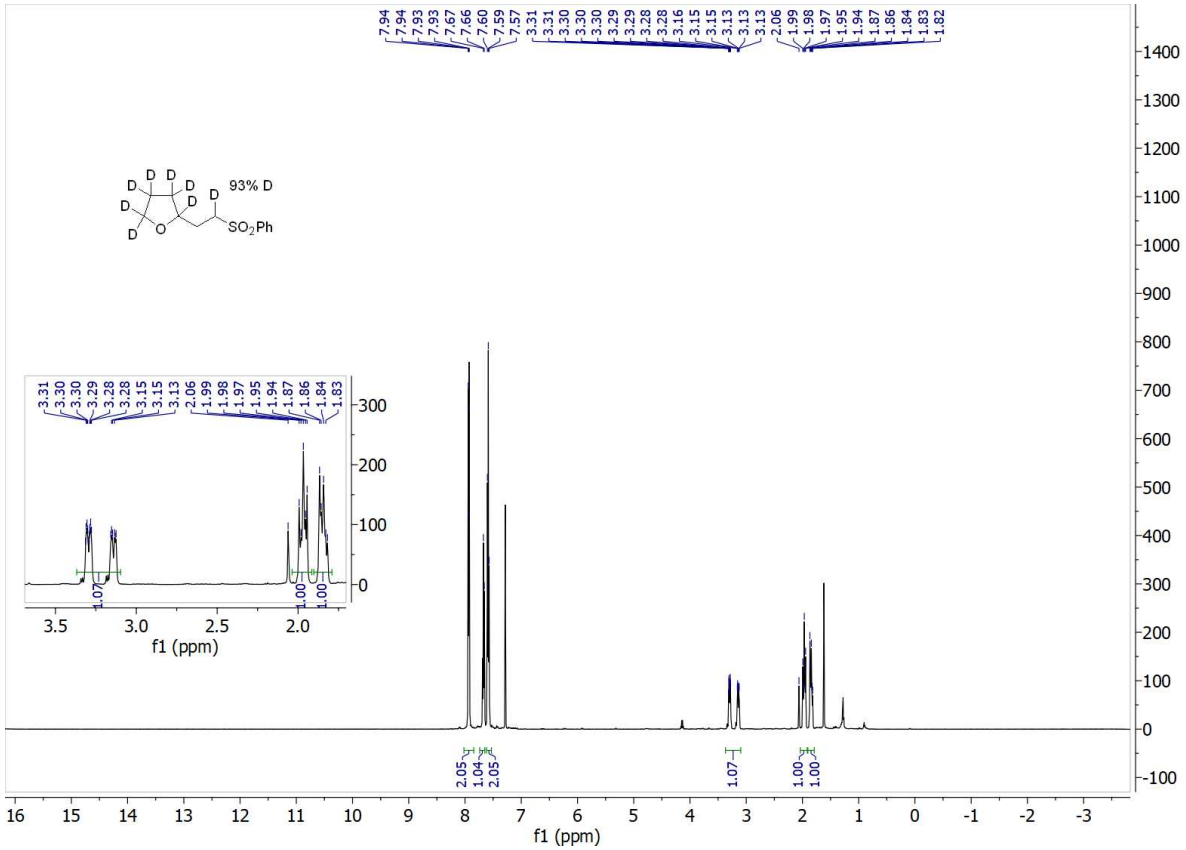
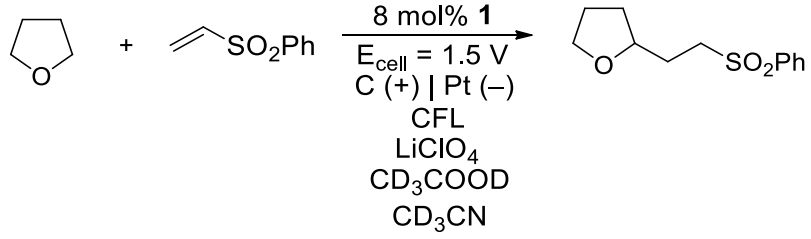
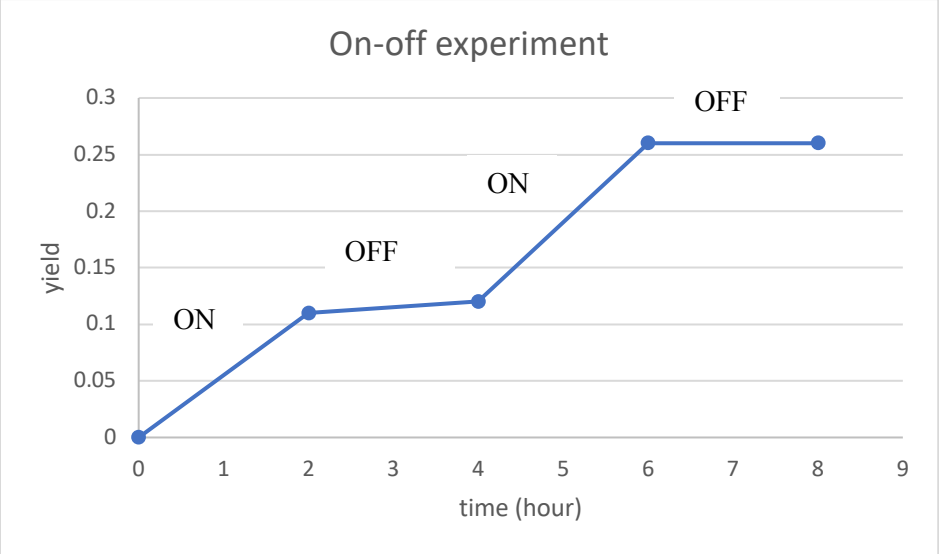


Fig S6. Isotope labeling experiments

On-off experiment procedure: To an oven-dried 10-mL three-neck flask equipped with a stir bar, a carbon felt anode and, a platinum wire cathode was added TAC **1** (15.2 mg, 0.032 mmol), phenyl vinyl sulfone (0.4 mmol, 67.3 mg) and $LiClO_4$ (255.3 mg, 2.4 mmol). The cell was sealed using a rubber septum and parafilm then flushed with nitrogen gas for 5 min, followed by the sequential addition via syringe of CD_3CN (2 mL), the THF (2.0 mL), and CD_3COOD (229 µL, 4.0 mmol). The reaction mixture was then purged with nitrogen gas for an additional 1 min cooled by an ice bath. The mixture was stirred for 5 min and 100 µL reaction aliquot was taken, diluted with $CDCl_3$ followed by adding 1 µL dibromomethane as an internal standard and analyzed by ^1H NMR spectroscopy. The solution was stirred at room temperature under irradiation from two 23W CFL bulbs, and electrolysis was initiated at a constant voltage of 1.5 V for 2 h. Another 100 uL reaction aliquot was taken, diluted with $CDCl_3$ followed by adding 1 µL dibromomethane as an internal standard and analyzed by ^1H NMR spectroscopy. Then light and electricity was switched off and the mixture was stirred in the dark for 2 h. After that, another 100 uL reaction aliquot was taken, diluted with $CDCl_3$ followed by adding 1 µL dibromomethane as an internal standard and analyzed by ^1H NMR spectroscopy. The light and electricity were switched on and the mixture was stirred under light irradiation and electrolysis for 2h. Then another 100 µL reaction aliquot was taken, diluted with $CDCl_3$ followed by adding 1 µL dibromomethane as an internal standard and analyzed by ^1H NMR spectroscopy. Light and electricity was switched off again and the mixture was stirred in the dark for 2 h. After that, another 100 µL reaction aliquot was taken, diluted with $CDCl_3$ followed by adding 1 µL dibromomethane as an internal standard and analyzed by ^1H NMR spectroscopy.

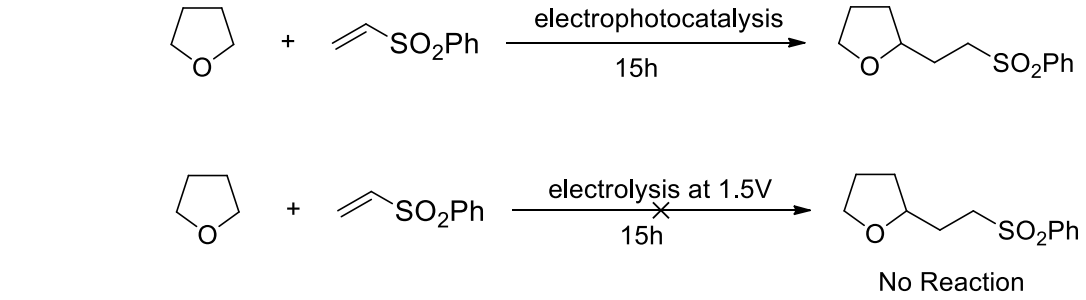




Time (h)	Yield
0	0
2	0.11
4	0.12
6	0.26
8	0.26

Fig S7. On-off experiments

In order to further explore whether the alkene reaction is electrochemical initiated, control reactions were preformed and crude NMR were compared below. No reaction happened in dirctly electrolysis at 1.5V method.



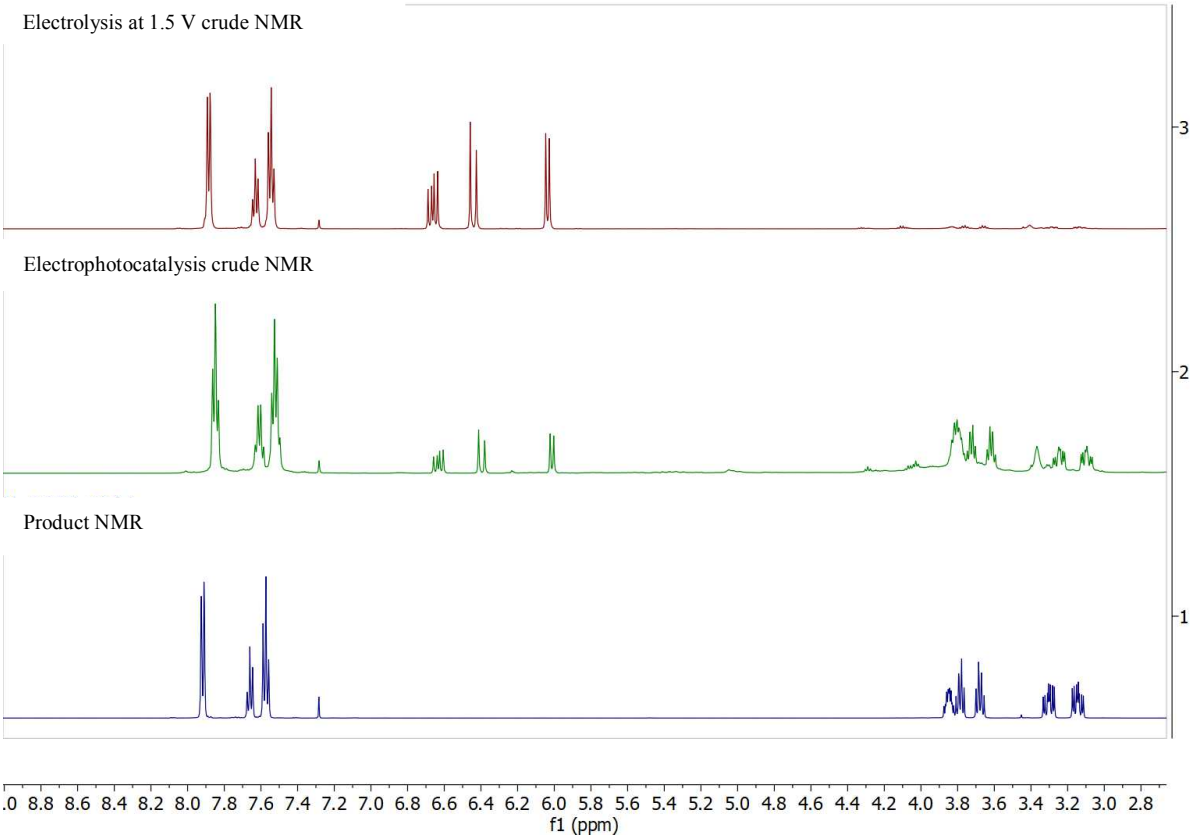
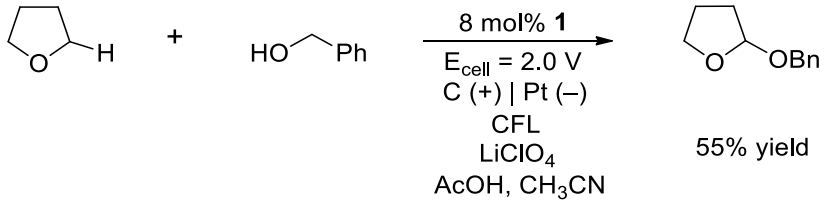


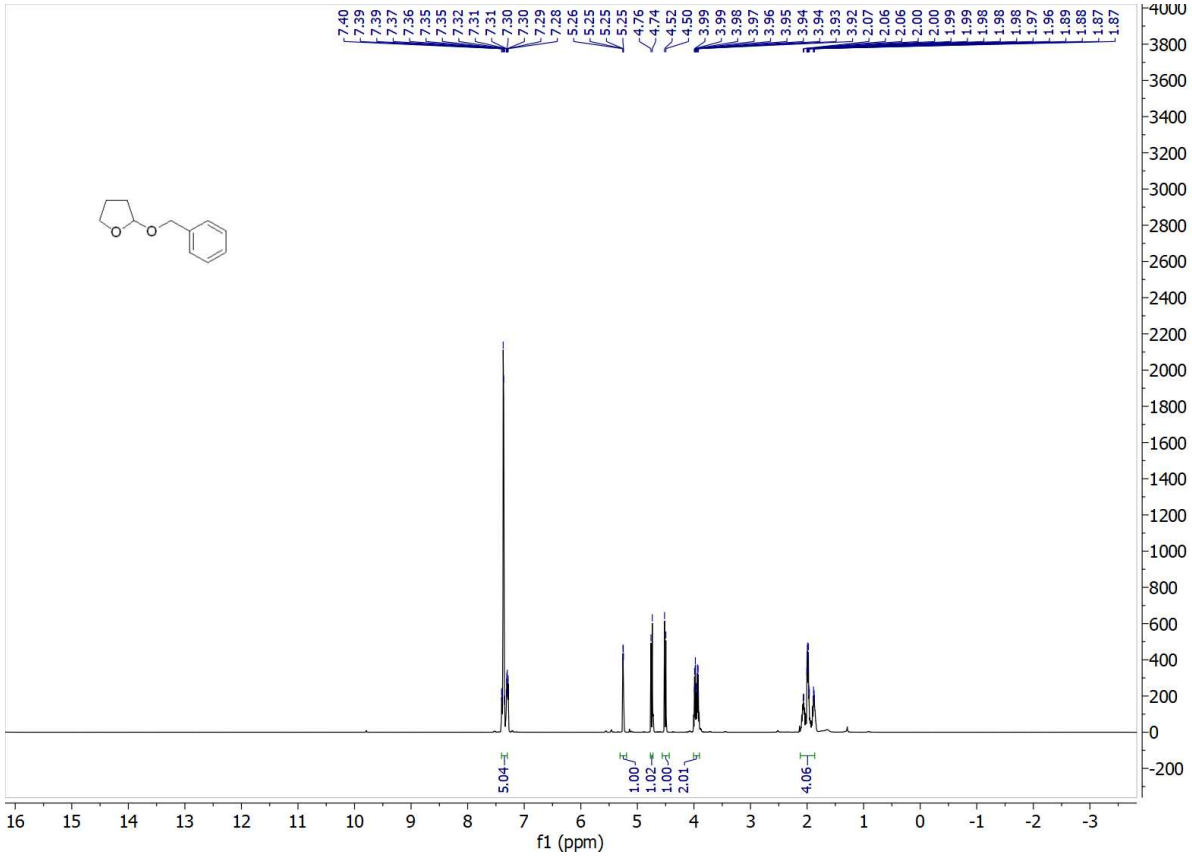
Fig S8. THF and Alkene Reaction at Electrolysis and Electrophotocatalysis

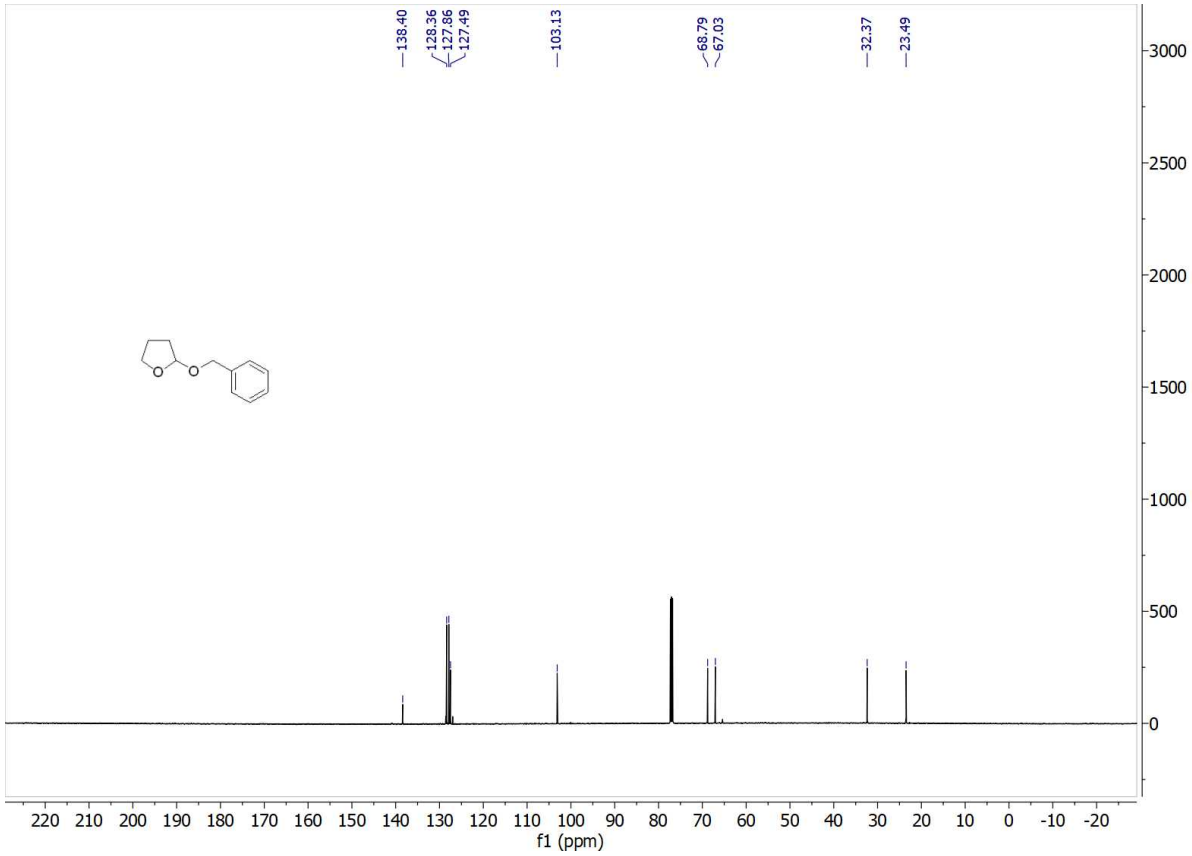
9. Reaction with Alcohol to generate acetal 54.



To an oven-dried 10-mL three-neck flask equipped with a stir bar, a carbon felt anode, and a platinum wire cathode was added TAC **1** (15.2 mg, 0.032 mmol), and $LiClO_4$ (255.3 mg, 2.4 mmol). The cell was sealed using a rubber septum and parafilm, then flushed with nitrogen gas for 5 min, followed by the sequential addition via syringe of CH_3CN (2 mL), the THF (2.0 mL), benzyl alcohol (0.4 mmol, 41.6 μL) and acetic acid (229 μL, 4.0 mmol). The reaction mixture was then purged with nitrogen gas for an additional 5 min. The solution was stirred at room temperature under irradiation from two 23W CFL bulbs, and electrolysis was initiated at a constant voltage of 2.0 V for 24 h. The reaction mixture was subsequently poured into a saturated sodium bicarbonate solution (ca. 20 mL). The carbon felt anode was washed with EtOAc (3×5 mL) in an ultrasonic bath. The aqueous layer was separated and extracted with EtOAc (3×10 mL), and the combined organic layers and anode extract were washed with brine and dried over anhydrous Na_2SO_4. Following concentration *in vacuo*, the crude residue was subjected to flash column chromatography on silica gel to yield the acetal product **54** as a colorless oil in 55% yield (39.2 mg).

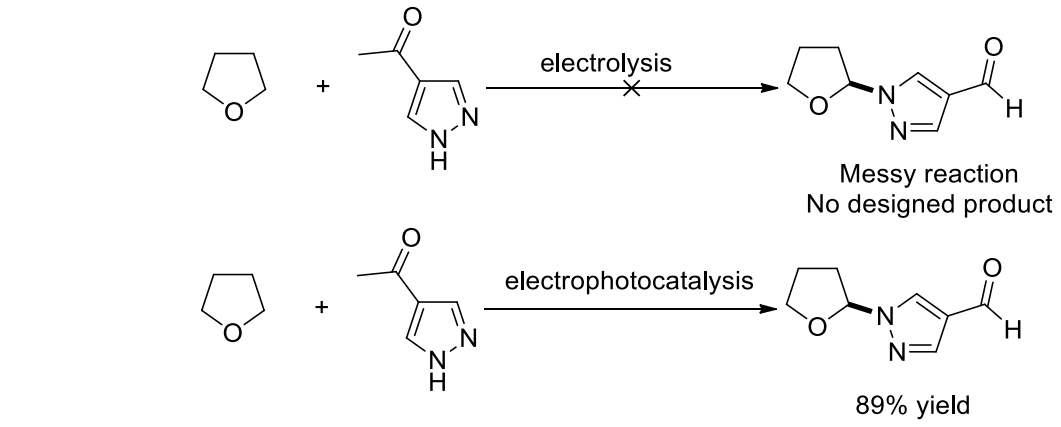
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.30 (m, 5H), 5.25 (dd, *J* = 4.4, 2.0 Hz, 1H), 4.75 (d, *J* = 11.9 Hz, 1H), 4.51 (d, *J* = 11.9 Hz, 1H), 4.01 – 3.90 (m, 2H), 2.12 – 1.86 (m, 4H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.4, 128.4, 127.9, 127.5, 103.1, 68.8, 67.0, 32.4, 23.5. MS (DART) exact mass: calculated for $(M+H)^+$: 179.1067; found: 179.1072.


7.40 7.39 7.39 7.37 7.36 7.35 7.35 7.32 7.31 7.31 7.30 7.30 7.29 7.28
5.26 5.25 5.25 5.25 4.76 4.74 4.52 4.50
3.99 3.99 3.98 3.97 3.96 3.95 3.94 3.94 3.93 3.92
2.07 2.06 2.06 2.00 2.00 1.99 1.98 1.98 1.98 1.97 1.96 1.89 1.88 1.87 1.87
5.04
1.00
1.02
1.00
2.01
4.06
f1 (ppm)


138.40
128.36
127.86
127.49
103.13
68.79
67.03
32.37
23.49
f1 (ppm)

10. Comparation with Reported Electrolysis Method

THF and 1H-pyrazole-4-carbaldehyde were chose as model reaction substrates to compare the reported electrolysis[3] and the electrophotocatalysis methods. After reaction, crude NMR was obtained and showed below.



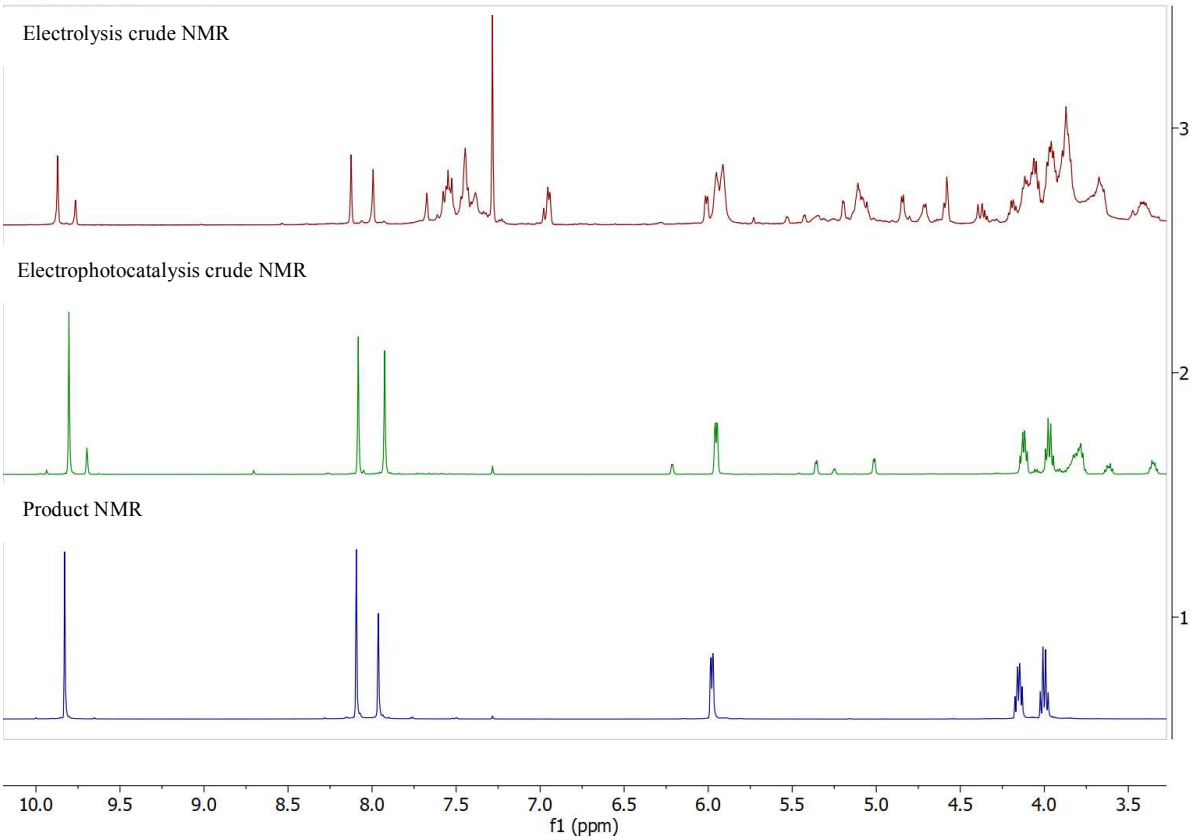
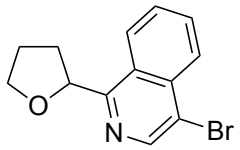


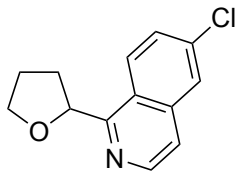
Fig S9. Comparation with Reported Electrolysis Method

11. Characterization



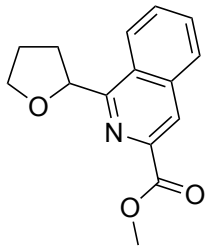
4-Bromo-1-(tetrahydrofuran-2-yl)isoquinoline **(6)**: The title compound was prepared from tetrahydrofuran (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a light yellow oil in 80% yield (89.0 mg).

6: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.66 (s, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.66 – 7.63 (m, 1H), 5.66 (t, *J* = 7.0 Hz, 1H), 4.15 – 4.11 (m, 1H), 4.03 – 3.98 (m, 1H), 2.53 – 2.49 (m, 1H), 2.38 – 2.36 (m, 1H), 2.18 – 2.03 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.2, 143.2, 135.1, 131.1, 128.0, 127.9, 126.6, 125.7, 119.3, 78.8, 69.1, 30.6, 26.1. MS (DART) exact mass: calculated for $(M+H)^+$: 278.0175; found: 278.0187.



6-Chloro-1-(tetrahydrofuran-2-yl)isoquinoline **(8)**: The title compound was prepared from tetrahydrofuran (2.0 mL) and 6-chloroisoquinoline (0.4 mmol, 65.4 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a colorless oil in 81% yield (75.7 mg).

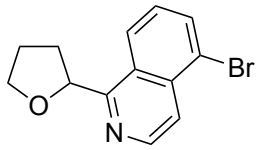
8: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.51 (d, *J* = 5.7 Hz, 1H), 8.34 (d, *J* = 9.0 Hz, 1H), 7.82 (d, *J* = 2.1 Hz, 1H), 7.54 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.50 (d, *J* = 5.7 Hz, 1H), 5.66 (t, *J* = 7.1 Hz, 1H), 4.19 - 4.14 (m, 1H), 4.06 – 4.02 (m, 1H), 2.60 – 2.50 (m, 1H), 2.44 – 2.36 (m, 1H), 2.22 – 2.09 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.8, 142.6, 137.4, 136.1, 128.1, 127.4, 126.0, 124.9, 119.6, 79.3, 69.0, 30.5, 26.1. MS (DART) exact mass: calculated for $(M+H)^+$: 234.0680; found: 234.0688.



Methyl 1-(tetrahydrofuran-2-yl)isoquinoline-3-carboxylate **(9)**: The title compound was prepared from tetrahydrofuran (2.0 mL) and methyl isoquinoline-3-carboxylate (0.4 mmol, 74.9 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography

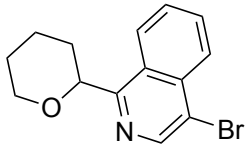
on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a white solid in 72% yield (74.1 mg).

9: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.51 – 8.51 (m, 2H), 7.98 – 7.96 (m, 1H), 7.76 – 7.73 (m, 2H), 5.68 (t, *J* = 7.2 Hz, 1H), 4.22 – 4.14 (m, 1H), 4.07 – 4.04 (m, 4H), 2.76 – 2.67 (m, 1H), 2.47 – 2.39 (m, 1H), 2.27 – 2.11 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.5, 160.0, 140.0, 136.4, 130.5, 129.3, 128.8, 128.2, 126.0, 124.2, 80.5, 69.0, 52.7, 30.2, 26.1. MS (DART) exact mass: calculated for $(M+H)^+$: 258.1125; found: 258.1135.



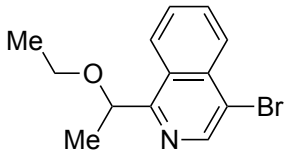
5-Bromo-1-(tetrahydrofuran-2-yl)isoquinoline **(10)**: The title compound was prepared from tetrahydrofuran (2.0 mL) and 5-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a colorless oil in 78% yield (86.8 mg).

10: ^{1}H NMR (500 MHz, Chloroform-*d*) δ ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.60 (d, *J* = 5.9 Hz, 1H), 8.35 (d, *J* = 8.5 Hz, 1H), 8.03 – 7.88 (m, 2H), 7.47 - 7.43 (m, 1H), 5.71 (t, *J* = 7.0 Hz, 1H), 4.18-4.14 (m, 1H), 4.06-4.01 (m, 1H), 2.59-2.54 (m, 1H), 2.42 – 2.38 (m, 1H), 2.19-2.10 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 160.0, 142.9, 135.6, 133.6, 127.8, 127.4, 125.1, 122.3, 119.4, 79.0, 69.1, 30.6, 26.1. MS (DART) exact mass: calculated for $(M+H)^+$: 278.0175; found: 278.0186.



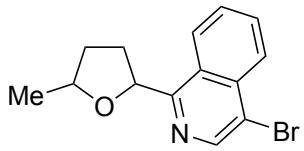
4-Bromo-1-(tetrahydro-2H-pyran-2-yl)isoquinoline **(11)**: The title compound was prepared from tetrahydropyran (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 15% EtOAc/hexanes to yield a white solid in 62% yield (72.5 mg).

11: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 7.81 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.68 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 5.16 (dd, *J* = 10.9, 2.3 Hz, 1H), 4.34 – 4.21 (m, 1H), 3.83 – 3.77 (m, 1H), 2.17 – 1.64 (m, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.3, 143.5, 135.2, 131.1, 127.9, 127.4, 126.7, 125.7, 119.3, 79.0, 69.5, 31.0, 25.9, 23.8. MS (DART) exact mass: calculated for $(M+H)^+$: 292.0332; found: 292.0343.



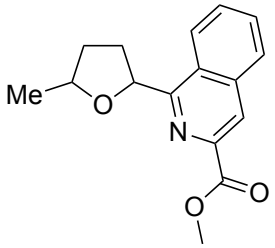
4-Bromo-1-(1-ethoxyethyl)isoquinoline **(12)**: The title compound was prepared from diethyl ether (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 15% EtOAc/hexanes to yield a colorless oil in 52% yield (58.3 mg).

12: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 8.6 Hz, 1H), 8.68 (s, 1H), 8.27 – 8.22 (m, 1H), 7.84 – 7.81 (m, 1H), 7.69 – 7.66 (m, 1H), 5.16 (q, *J* = 6.8 Hz, 1H), 3.57 – 3.50 (m, 1H), 3.45 – 3.38 (m, 1H), 1.71 (d, *J* = 6.7 Hz, 3H), 1.21 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.5, 143.3, 135.3, 131.2, 127.8, 127.4, 126.8, 125.9, 119.3, 79.7, 64.6, 21.6, 15.5. MS (DART) exact mass: calculated for $(M - EtO)^{+}$: 233.9918; found: 233.9922.



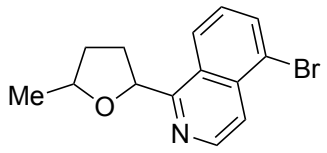
4-Bromo-1-(5-methyltetrahydrofuran-2-yl)isoquinoline **(13):** The title compound was prepared from 2-methyltetrahydrofuran (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a white solid in 55% yield (64.3 mg, diastereoisomers, d.r. = 1 : 1.1).

13: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.41 (dd, *J* = 38.2, 8.5 Hz, 1H), 8.20 (ddd, *J* = 8.5, 2.4, 1.2 Hz, 1H), 7.83 – 7.76 (m, 1H), 7.71 – 7.64 (m, 1H), 5.84 (t, *J* = 7.1 Hz, 0.5H), 5.61 (t, *J* = 7.2 Hz, 0.5H), 4.42 (dt, *J* = 8.0, 6.1 Hz, 0.5H), 4.29 (dt, *J* = 8.0, 6.2 Hz, 0.5H), 2.74 – 2.53 (m, 1H), 2.50 – 2.18 (m, 2H), 1.82 – 1.69 (m, 1H), 1.37 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7, 158.8, 143.2, 143.2, 135.1, 135.1, 131.1, 131.1, 128.2, 128.0, 128.0, 127.9, 126.6, 126.5, 126.1, 125.7, 119.4, 119.2, 79.4, 78.1, 77.0, 76.1, 34.0, 33.2, 31.2, 30.2, 21.4, 21.2. MS (DART) exact mass: calculated for $(M+H)^{+}$: 292.0332; found: 292.0348.



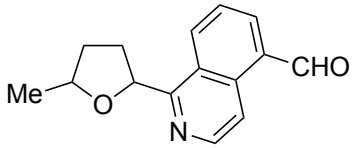
Methyl 1-(5-methyltetrahydrofuran-2-yl)isoquinoline-3-carboxylate **(14):** The title compound was prepared from 2-methyltetrahydrofuran (2.0 mL) and methyl isoquinoline-3-carboxylate (0.4 mmol, 74.9 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a white solid in 41% yield (44.5 mg, diastereoisomers, d.r. = 1 : 1.6) .

14: ^{1}H NMR (599 MHz, Chloroform-*d*) δ 8.58 – 8.47 (m, 2H), 7.97 – 7.89 (m, 1H), 7.78 – 7.63 (m, 2H), 5.80 (t, *J* = 7.2 Hz, 0.37H), 5.61 (t, *J* = 7.4 Hz, 0.63H), 4.50 – 4.39 (m, 0.41H), 4.26 (dt, *J* = 8.2, 6.2 Hz, 0.61H), 4.01 (s, 3H), 2.78 – 2.62 (m, 1H), 2.46 – 2.38 (m, 1H), 2.34 – 2.18 (m, 1H), 1.83 – 1.75 (m, 1H), 1.40 – 1.34 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 160.5, 159.9, 140.0, 136.5, 130.5, 129.3, 129.2, 128.8, 128.8, 128.2, 126.2, 126.0, 124.2, 124.1, 81.2, 79.7, 77.1, 76.1, 52.7, 34.0, 33.0, 31.0, 30.5, 21.5, 21.1. MS (DART) exact mass: calculated for $(M+H)^+$: 272.1281; found: 272.1297.



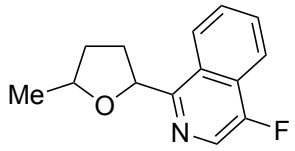
5-Bromo-1-(5-methyltetrahydrofuran-2-yl)isoquinoline **(15):** The title compound was prepared from 2-methyltetrahydrofuran (2.0 mL) and 5-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a white solid in 57% yield (66.6 mg, diastereoisomers, d.r. = 1 : 1.2).

15: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 5.9, 4.0 Hz, 1H), 8.39 (dd, *J* = 40.0, 8.5 Hz, 1H), 8.05 – 7.90 (m, 2H), 7.47 (m, 1H), 5.90 (t, *J* = 7.1 Hz, 0.5H), 5.67 (t, *J* = 7.3 Hz, 0.5H), 4.45 (dt, *J* = 8.1, 6.1 Hz, 0.5H), 4.30 (dt, *J* = 8.0, 6.2 Hz, 0.5H), 2.76 – 2.17 (m, 3H), 1.86 – 1.69 (m, 1H), 1.37 (d, *J* = 7.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6, 159.7, 142.8, 142.8, 135.7, 135.7, 133.7, 133.7, 128.0, 127.6, 127.5, 127.4, 125.4, 125.0, 122.3, 122.2, 119.5, 119.4, 79.7, 78.4, 77.0, 76.2, 34.0, 33.2, 31.7, 30.6, 21.4, 21.1. MS (DART) exact mass: calculated for $(M+H)^+$: 292.0332; found: 292.0350.



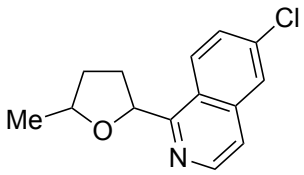
1-(5-Methyltetrahydrofuran-2-yl)isoquinoline-5-carbaldehyde **(16):** The title compound was prepared from 2-methyltetrahydrofuran (2.0 mL) and isoquinoline-5-carbaldehyde (0.4 mmol, 62.9 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 25% EtOAc/hexanes to yield a white solid in 40% yield (38.6 mg, diastereoisomers, d.r. = 1 : 1).

16: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.42 (s, 1H), 9.10 – 8.92 (m, 1H), 8.88 – 8.72 (m, 1H), 8.72 – 8.64 (m, 1H), 8.26 – 8.14 (m, 1H), 7.85 – 7.74 (m, 1H), 5.88 (t, *J* = 7.1 Hz, 0.5H), 5.65 (t, *J* = 7.3 Hz, 0.5H), 4.36 – 4.30 (m, 1H), 2.82 – 2.63 (m, 1H), 2.51 – 2.24 (m, 2H), 1.83 – 1.74 (m, 1H), 1.38 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.6, 192.6, 192.6, 160.4, 159.5, 144.6, 144.5, 139.2, 139.2, 134.3, 134.3, 133.0, 132.6, 130.9, 130.8, 127.1, 126.8, 126.2, 126.1, 117.3, 117.1, 80.1, 78.7, 76.2, 34.0, 33.1, 31.0, 30.0, 21.4, 21.2. MS (DART) exact mass: calculated for $(M+H)^+$: 242.1176; found: 242.1192.



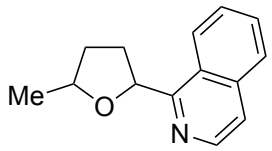
4-Fluoro-1-(5-methyltetrahydrofuran-2-yl)isoquinoline **(17):** The title compound was prepared from 2-methyltetrahydrofuran (2.0 mL) and 4-fluoroisoquinoline (0.4 mmol, 58.9 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a white solid in 61% yield (56.4 mg, diastereoisomers, d.r. = 1 : 1).

17: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 – 8.37 (m, 1H), 8.35 (d, *J* = 1.8 Hz, 1H), 8.17 – 8.03 (m, 1H), 7.84 – 7.60 (m, 2H), 5.82 (t, *J* = 7.1 Hz, 0.5H), 5.59 (t, *J* = 7.3 Hz, 0.5H), 4.50 – 4.19 (m, 1H), 2.77 – 2.53 (m, 1H), 2.49 – 2.15 (m, 2H), 1.84 – 1.67 (m, 1H), 1.38 (d, *J* = 3.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0, 156.0, 154.2 (*J* = 260.8 Hz)., 155.2, 155.1, 130.1, 130.1, 130.1, 130.1, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.1 (*J* = 10.7 Hz), 126.4 (*J* = 17.2 Hz), 125.5 (*J* = 39.1 Hz), 120.1 (*J* = 5.6 Hz), 79.6, 78.2, 76.9, 76.0, 34.0, 33.1, 31.0, 30.1, 21.4, 21.2. ^{19}F NMR (470 MHz, $CDCl_3$) δ -140.8. MS (DART) exact mass: calculated for $(M+H)^+$: 232.1132; found: 232.1145.



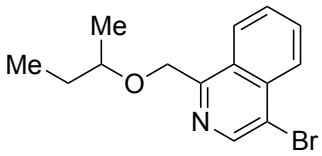
6-Chloro-1-(5-methyltetrahydrofuran-2-yl)isoquinoline **(18):** The title compound was prepared from 2-methyltetrahydrofuran (2.0 mL) and 6-chloroisoquinoline (0.4 mmol, 65.4 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a white solid in 62% yield (61.4 mg, diastereoisomers, d.r. = 1 : 1.1).

18: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (m, 1H), 8.40 (m, 1H), 7.83 (d, *J* = 2.7 Hz, 1H), 7.60 – 7.46 (m, 2H), 5.82 (t, *J* = 7.2 Hz, 0.5H), 5.59 (t, *J* = 7.4 Hz, 0.5H), 4.44 (q, *J* = 6.5 Hz, 0.5H), 4.29 (q, *J* = 6.6 Hz, 0.5H), 2.74 – 2.53 (m, 1H), 2.51 – 2.19 (m, 2H), 1.81 – 1.70 (m, 1H), 1.39 (d, *J* = 3.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.3, 159.4, 142.5, 142.5, 137.5, 137.5, 136.2, 136.1, 131.7, 131.6, 128.1, 128.1, 127.8, 127.4, 126.0, 125.9, 125.2, 124.9, 119.8, 119.6, 80.1, 78.6, 77.0, 76.2, 34.1, 33.1, 31.3, 30.3, 21.4, 21.2. MS (DART) exact mass: calculated for $(M+H)^+$: 248.0837; found: 248.0855.



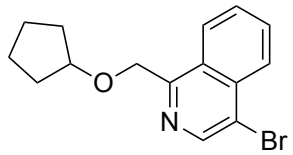
1-(5-Methyltetrahydrofuran-2-yl)isoquinoline **(19):** The title compound was prepared from 2-methyltetrahydrofuran (2.0 mL) and isoquinoline (0.4 mmol, 47.0 μL) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a light yellow oil in 41% yield (35.0 mg, diastereoisomers, d.r. = 1 : 1.0). Characterization data is consistent with reported literature values.[4]

19: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (dd, *J* = 5.7, 1.6 Hz, 1H), 8.42 (dd, *J* = 40.0, 8.5 Hz, 1H), 7.84 (dt, *J* = 8.2, 1.8 Hz, 1H), 7.74 – 7.54 (m, 3H), 5.90 (t, *J* = 7.2 Hz, 0.5H), 5.65 (t, *J* = 7.4 Hz, 1H), 4.58 – 4.24 (m, 1H), 2.75 – 2.55 (m, 1H), 2.51 – 2.21 (m, 2H), 1.84 – 1.71 (m, 1H), 1.40 (dd, *J* = 6.1, 3.1 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 160.1, 159.2, 141.5, 141.5, 136.6, 136.6, 129.8, 129.8, 127.3, 127.2, 127.1, 127.0, 126.9, 125.7, 125.3, 120.6, 120.4, 80.0, 78.4, 76.8, 76.1, 34.1, 33.2, 31.4, 30.4, 21.4, 21.2. MS (DART) exact mass: calculated for $(M+H)^+$: 214.1226; found: 214.1228.



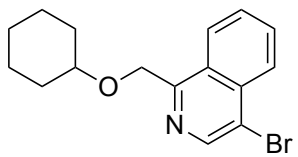
4-Bromo-1-(sec-butoxymethyl)isoquinoline **(20):** The title compound was prepared from sec-butyl methyl ether (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a light yellow oil in 39% yield (45.9 mg).

20: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 7.81 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.69 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 5.18 – 4.91 (m, 2H), 3.54 (q, *J* = 6.1 Hz, 1H), 1.61 – 1.58 (m, 1H), 1.53 – 1.44 (m, 1H), 1.21 (d, *J* = 6.1 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.4, 143.2, 135.2, 131.4, 128.7, 128.2, 126.7, 126.4, 119.9, 77.0, 70.9, 29.2, 19.1, 9.8. MS (DART) exact mass: calculated for $(M+H)^+$: 294.0488; found: 294.0507.



4-Bromo-1-((cyclopentyloxy)methyl)isoquinoline **(21):** The title compound was prepared from cyclopentyl methyl ether (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a white solid in 40% yield (49.0 mg).

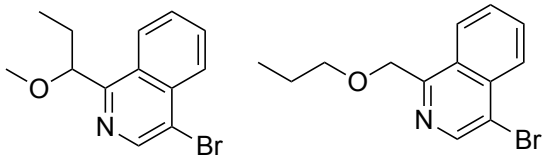
21: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 7.83 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.71 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 5.04 (s, 2H), 4.12 (tt, *J* = 5.6, 2.7 Hz, 1H), 1.83 – 1.56 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.3, 143.2, 135.2, 131.4, 128.7, 128.2, 126.6, 126.5, 119.9, 81.9, 71.5, 32.3, 23.5. MS (DART) exact mass: calculated for $(M+H)^+$: 306.0488; found: 306.0509.



4-Bromo-1-((cyclohexyloxy)methyl)isoquinoline **(22):** The title compound was prepared from methoxycyclohexane (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography

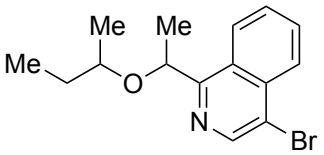
on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a white solid in 51% yield (65.3 mg).

22: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 7.86 – 7.80 (m, 1H), 7.74 – 7.67 (m, 1H), 5.10 (s, 2H), 3.50 – 3.41 (m, 1H), 2.01 – 1.93 (m, 2H), 1.79 – 1.71 (m, 2H), 1.55 (dd, *J* = 9.6, 4.5 Hz, 1H), 1.38 – 1.27 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 143.2, 135.2, 131.4, 128.7, 128.2, 126.6, 126.4, 119.9, 77.8, 70.6, 32.2, 25.7, 24.2. MS (DART) exact mass: calculated for $(M+H)^+$: 320.0645; found: 320.0665.



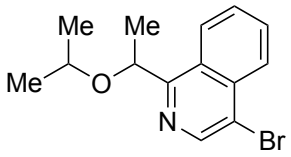
***4-Bromo-1-(1-methoxypropyl)isoquinoline* (23A)** *and* ***4-bromo-1-(propoxymethyl)isoquinoline* (23B):** The title compound was prepared from 1-methoxypropane (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a white solid in 45% yield (50.4 mg) as a mixture of regioisomers.

23: ^{1}H NMR (500 MHz, $CDCl_3$, mixture of **23A and 23B**) δ 8.78 – 8.62 (m, 3H), 8.47 – 8.17 (m, 2H), 7.90 – 7.61 (m, 4H), 5.08 (s, 1H), 4.82 (dd, *J* = 7.7, 6.2 Hz, 1H), 3.54 (t, *J* = 6.7 Hz, 1H), 3.32 (s, 3H), 2.24 – 1.89 (m, 2H), 1.65 (d, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$, mixture of **23A and 23B**) δ 160.3, 157.1, 143.3, 143.2, 135.3, 135.2, 131.4, 131.3, 128.5, 128.3, 127.9, 127.7, 126.8, 126.5, 126.4, 125.8, 120.0, 119.4, 87.0, 73.3, 72.7, 57.2, 29.1, 22.9, 10.7, 10.6. MS (DART) exact mass: calculated for $(M+H)^+$: 280.0332; found: 280.0351.



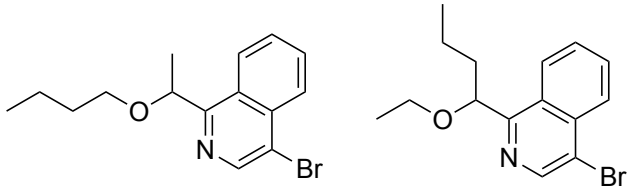
***4-Bromo-1-(1-(sec-butoxy)ethyl)isoquinoline* (24):** The title compound was prepared from sec-butyl ethyl ether (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a colorless oil in 43% yield (53.0 mg).

24: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (dd, *J* = 8.6, 2.0 Hz, 1H), 8.65 (s, 1H), 8.30 – 8.14 (m, 1H), 7.89 – 7.74 (m, 1H), 7.73 – 7.59 (m, 1H), 5.25 – 5.17 (m, 1H), 3.46 – 3.30 (m, 1H), 1.70 (dd, *J* = 6.8, 5.4 Hz, 3H), 1.66 – 1.36 (m, 2H), 1.22 – 0.92 (m, 3H), 0.97 – 0.70 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4, 162.1, 143.1, 135.5, 135.4, 131.2, 131.2, 127.5, 127.5, 127.4, 126.8, 126.7, 126.7, 126.7, 119.3, 119.2, 78.5, 77.8, 75.6, 75.1, 30.0, 28.4, 22.5, 22.2, 20.1, 18.7, 10.0, 9.4. MS (DART) exact mass: calculated for $(M+H)^+$: 308.0645; found: 308.0662.



4-Bromo-1-(1-isopropoxyethyl)isoquinoline **(25):** The title compound was prepared from 2-ethoxypropane (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 25% EtOAc/hexanes to yield a colorless oil in 51% yield (60.0 mg).

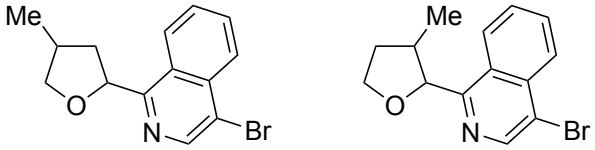
25: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, *J* = 8.6 Hz, 1H), 8.66 (s, 1H), 8.24 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.82 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.67 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 5.26 – 5.22 (m, 1H), 3.60 – 3.55 (m, 1H), 1.69 (d, *J* = 6.7 Hz, 3H), 1.23 (d, *J* = 6.0 Hz, 3H), 1.06 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.2, 143.1, 135.4, 131.2, 127.6, 127.4, 126.7, 126.5, 119.3, 77.7, 69.9, 23.1, 22.4, 21.5. MS (DART) exact mass: calculated for $(M+H)^+$: 294.0488; found: 294.0504.



4-Bromo-1-(1-butoxyethyl)isoquinoline and 4-bromo-1-(1-ethoxybutyl)isoquinoline **(26A and 26B):** The title compound was prepared from 1-ethoxybutane (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a light yellow oil in 56% yield (69.0 mg) as a mixture of regioisomers.

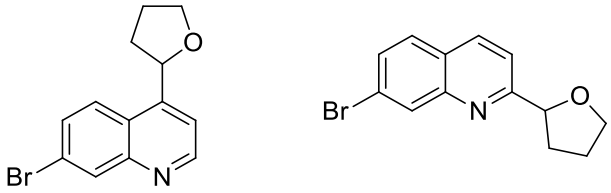
26: ^{1}H NMR (400 MHz, Chloroform-*d* ,mixture of **26A and 26B**) δ 8.83 – 8.54 (m, 2H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.67 – 7.59 (m, 1H), 5.09 (q, *J* = 6.8 Hz, 0.56H), 4.96 – 4.86 (m, 0.44H), 3.45 – 3.27 (m, 2H), 2.15 – 1.80 (m, 1H), 1.67 (dd, *J* = 6.8, 1.1 Hz, 1H), 1.59 – 1.48 (m, 1H), 1.36 – 1.22 (m, 2H), 1.15 (t, *J* = 7.0 Hz, 1H), 0.94 – 0.78 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$, mixture of **26A and**

26B) δ 161.5, 161.3, 143.2, 135.3, 135.3, 131.2, 131.2, 127.8, 127.7, 127.7, 127.4, 126.7, 126.7, 126.1, 126.1, 119.3, 119.3, 84.3, 80.1, 69.1, 64.8, 38.4, 32.0, 21.6, 19.6, 19.3, 15.4, 13.9, 13.9. MS (DART) exact mass: calculated for $(M+H)^+$: 308.0645; found: 308.0663.



4-Bromo-1-(4-methyltetrahydrofuran-2-yl)isoquinoline and 4-bromo-1-(3-methyltetrahydrofuran-2-yl)isoquinoline **(27A and 27B):** The title compound was prepared from 3-methyltetrahydrofuran (2.0 mL) and 4-bromoisoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a light yellow oil in 58% yield (67.8 mg) as a mixture of regioisomers.

27: ^{1}H NMR (500 MHz, $CDCl_3$, mixture of **27A and 27B**) δ 8.71 (d, *J* = 11.2 Hz, 1H), 8.42 – 8.35 (m, 1H), 8.22 (dd, *J* = 8.5, 2.9 Hz, 1H), 7.87 – 7.76 (m, 1H), 7.74 – 7.61 (m, 1H), 5.82 (dd, *J* = 7.8, 5.6 Hz, 0.5H), 5.73 (dd, *J* = 9.3, 6.3 Hz, 0.06H), 5.15 (d, *J* = 7.6 Hz, 0.42H), 4.28 (dd, *J* = 8.2, 6.8 Hz, 0.52H), 4.24 – 4.10 (m, 0.91H), 3.67 (t, *J* = 8.3 Hz, 0.06H), 3.63 – 3.51 (m, 0.51H), 3.16 – 2.86 (m, 0.42H), 2.80 – 2.68 (m, 0.52H), 2.68 – 2.51 (m, 0.66H), 2.43 – 2.25 (m, 0.44H), 2.21 (d, *J* = 12.1 Hz, 0.08H), 2.09 – 1.98 (m, 0.56H), 1.91 – 1.80 (m, 1H), 1.24 – 1.12 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$, mixture of **27A and 27B**) δ 159.4, 158.5, 143.4, 143.2, 135.2, 135.1, 131.1, 128.5, 128.0, 128.0, 127.8, 126.7, 126.6, 125.8, 125.7, 119.5, 119.3, 85.7, 78.4, 76.0, 75.5, 68.3, 39.4, 38.7, 38.6, 34.8, 34.7, 33.6, 17.9, 17.4, 17.0. MS (DART) exact mass: calculated for $(M+H)^+$: 292.0332; found: 292.0348.

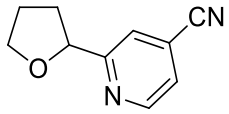


7-bromo-4-(tetrahydrofuran-2-yl)quinoline **(29A) and 7-bromo-2-(tetrahydrofuran-2-yl)quinoline (29B)**: The title compound was prepared from tetrahydrofuran (2.0 mL) and 7-bromoquinoline (0.4 mmol, 83.2 mg) according to general procedure A with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a light yellow oil in 60% yield (66.7 mg) as a mixture of regioisomers.

29A: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.88 (d, *J* = 4.5 Hz, 1H), 8.32 (d, *J* = 2.1 Hz, 1H), 7.80 (d, *J* = 8.9 Hz, 1H), 7.64 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.57 (d, *J* = 4.5 Hz, 1H), 5.56 (t, *J* = 7.2 Hz, 1H), 4.22 (td, *J* = 7.7, 5.8 Hz, 1H), 4.05 (q, *J* = 7.4 Hz, 1H), 2.72 – 2.52 (m, 1H), 2.16 – 1.95 (m, 2H), 1.91 – 1.76 (m, 1H).

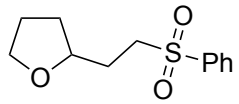
^{13}C NMR (126 MHz, Chloroform-*d*) δ 151.5, 149.8, 148.8, 132.5, 129.9, 124.7, 124.3, 123.1, 116.9, 76.6, 69.1, 34.0, 26.0. MS (DART) exact mass: calculated for $(M+H)^+$: 278.0175; found: 278.0180.

29B: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.27 (d, *J* = 1.9 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.71 – 7.60 (m, 3H), 5.18 (dd, *J* = 7.4, 6.4 Hz, 1H), 4.21 – 4.04 (m, 2H), 2.60 – 2.45 (m, 1H), 2.15 – 2.01 (m, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.8, 148.2, 136.5, 131.5, 129.6, 128.8, 126.0, 123.5, 118.5, 81.9, 69.3, 33.2, 25.9. MS (DART) exact mass: calculated for $(M+H)^+$: 278.0175; found: 278.0181.



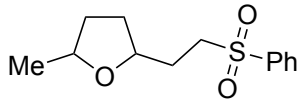
***2-(Tetrahydrofuran-2-yl)isonicotinonitrile* (30)**: The title compound was prepared from tetrahydrofuran (2.0 mL) and 4-pyridinecarbonitrile (0.4 mmol, 41.6 mg) according to general procedure A with an irradiation/electrolysis time of 65 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a yellow oil in 28% yield (19.5 mg).

30: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 4.9 Hz, 1H), 7.74 (s, 1H), 7.41 (d, *J* = 4.9 Hz, 1H), 5.08 (t, *J* = 6.7 Hz, 1H), 4.19 – 4.09 (m, 1H), 4.05 – 4.00 (m, 1H), 2.54 – 2.46 (m, 1H), 2.06 – 1.95 (m, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 165.3, 149.9, 123.4, 121.6, 120.9, 116.8, 80.7, 69.3, 33.1, 25.7. MS (DART) exact mass: calculated for $(M+H)^+$: 175.0866; found: 175.0873.



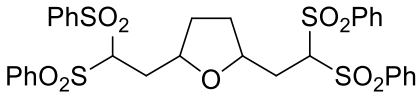
***2-(2-(Phenylsulfonyl)ethyl)tetrahydrofuran* (31):** The title compound was prepared from tetrahydrofuran (2.0 mL) and phenyl vinyl sulfone (0.4 mmol, 67.3 mg) according to general procedure B with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a white solid in 72% yield (69.2 mg).

31: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.82 (m, 2H), 7.72 – 7.62 (m, 1H), 7.62 – 7.50 (m, 2H), 3.91 – 3.82 (m, 1H), 3.82 – 3.74 (m, 1H), 3.72 – 3.61 (m, 1H), 3.30 (ddd, *J* = 14.0, 11.5, 4.8 Hz, 1H), 3.14 (ddd, *J* = 14.1, 11.4, 4.8 Hz, 1H), 2.07 – 1.92 (m, 2H), 1.91 – 1.79 (m, 3H), 1.53 – 1.39 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.2, 133.7, 129.3, 128.0, 77.0, 67.9, 53.6, 31.2, 28.5, 25.6. MS (DART) exact mass: calculated for $(M+H)^+$: 241.0893; found: 241.0909.



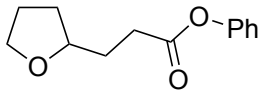
***2-Methyl-5-(2-(phenylsulfonyl)ethyl)tetrahydrofuran* (32):** The title compound was prepared from 2-methyltetrahydrofuran (2.0 mL) and phenyl vinyl sulfone (0.4 mmol, 67.3 mg) according to general procedure B with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a light yellow oil in 60% yield (61.0 mg).

32: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (dt, *J* = 7.2, 1.4 Hz, 2H), 7.72 – 7.64 (m, 1H), 7.62 – 7.54 (m, 2H), 4.10 – 3.65 (m, 2H), 3.35 – 3.10 (m, 2H), 2.08 – 1.81 (m, 4H), 1.76 – 1.52 (m, 2H), 1.24 – 1.08 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.2, 133.7, 129.3, 129.3, 128.1, 128.0, 128.0, 80.8, 75.8, 67.4, 53.5, 52.4, 37.2, 32.9, 32.7, 32.1, 31.1, 29.1, 25.9, 25.7, 21.3, 21.1. MS (DART) exact mass: calculated for $(M+H)^+$: 255.1049; found: 255.1062.



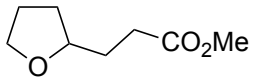
1-(5-Methyltetrahydrofuran-2-yl)isoquinoline **(33):** The title compound was prepared from tetrahydrofuran (2.0 mL) and 1,1-bis(phenylsulfonyl)ethylene (0.4 mmol, 123.4 mg) according to general procedure B with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 60% EtOAc/hexanes to yield a white solid in 65% yield (89.5 mg). Characterization data is consistent with reported literature values.[5]

33: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 15.6, 7.8 Hz, 4H), 7.92 (t, *J* = 8.1 Hz, 4H), 7.86 – 7.62 (m, 4H), 7.62 – 7.41 (m, 8H), 4.95 (dd, *J* = 8.2, 3.0 Hz, 0.83H), 4.79 (t, *J* = 5.3 Hz, 1.17H), 4.34 – 4.19 (m, 0.83H), 4.11 (p, *J* = 6.1 Hz, 1.19H), 2.41 – 2.22 (m, 4H), 2.13 – 1.97 (m, 2H), 1.64 – 1.43 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.2, 137.6, 134.6, 134.6, 134.6, 134.4, 130.0, 129.6, 129.5, 129.3, 129.2, 129.1, 129.1, 129.0, 80.5, 80.4, 76.3, 75.3, 32.2, 31.3, 31.2, 31.0. MS (DART) exact mass: calculated for $(M+H)^+$: 689.1002; found:689.1011.



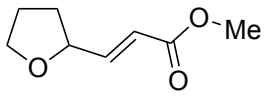
Phenyl 3-(tetrahydrofuran-2-yl)propanoate **(34)**: The title compound was prepared from tetrahydrofuran (2.0 mL) and phenyl acrylate (0.4 mmol, 59.3 mg) according to general procedure B with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a colorless oil. Yield were determined by ^{1}H NMR spectroscopy with dibromomethane as an internal standard. Characterization data is consistent with reported literature values.[6]

34: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 - 7.38 (m, 2H), 7.25 – 7.23 (m, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 3.98 – 3.87 (m, 2H), 3.80 – 3.77 (m, 1H), 2.74 – 2.67 (m, 2H), 2.07 – 1.92 (m, 5H), 1.58 – 1.54 (m, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 172.2, 150.8, 129.4, 125.7, 121.6, 78.1, 67.8, 31.3, 31.3, 30.7, 25.8. MS (DART) exact mass: calculated for $(M - PhO)^+$: 127.0759; found: 127.0761.



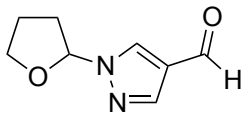
Methyl 3-(tetrahydrofuran-2-yl)propanoate **(35):** The title compound was prepared from tetrahydrofuran (2.0 mL) and methyl acrylate (0.4 mmol, 36.0 μL) according to general procedure B with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a colorless oil. Yield were determined by ^{1}H NMR spectroscopy

with dibromomethane as an internal standard. Characterization data is consistent with reported literature values.[7]



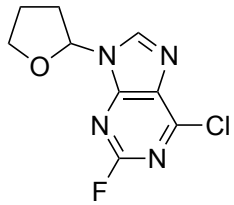
***Methyl 3-(tetrahydrofuran-2-yl)acrylate* (36):** The title compound was prepared from tetrahydrofuran (2.0 mL) and methyl propiolate (0.4 mmol, 35.6 μL) according to general procedure B with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 20% EtOAc/hexanes to yield a colorless oil. Yield were determined by ^{1}H NMR spectroscopy with terephthalonitrile as an internal standard. Characterization data is consistent with reported literature values.[8]

36: ^{1}H NMR (500 MHz, Chloroform-*d*, mixture of ***Z*-36 and *E*-36**) δ 6.94 (dd, *J* = 15.6, 4.8 Hz, 1H), 6.34 (dd, *J* = 11.7, 7.4 Hz, 1H), 6.04 (dd, *J* = 15.6, 1.7 Hz, 1H), 5.80 (dd, *J* = 11.7, 1.6 Hz, 1H), 5.30 (m, 1H), 4.61 – 4.47 (m, 1H), 3.97 – 3.92 (m, 2H), 3.89 – 3.82 (m, 2H), 3.74 (d, *J* = 11.6 Hz, 6H), 2.37 (dd, *J* = 12.6, 6.5 Hz, 1H), 2.20 – 2.10 (m, 1H), 1.97 – 1.90 (m, 4H), 1.76 – 1.67 (m, 1H), 1.58 (dd, *J* = 12.4, 8.2 Hz, 1H).



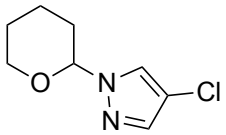
***1-(Tetrahydrofuran-2-yl)-1H-pyrazole-4-carbaldehyde* (37)**: The title compound was prepared from tetrahydrofuran (2.0 ml) and 1H-pyrazole-4-carbaldehyde (0.4 mmol, 38.4 mg) according to general procedure C with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a white solid in 89% yield (59.2 mg).

37: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.83 (s, 1H), 8.09 (s, 1H), 7.96 (s, 1H), 5.98 (dd, *J* = 6.5, 2.1 Hz, 1H), 4.17 – 4.13 (m, 1H), 4.02 – 3.98 (m, 1H), 2.57 – 2.49 (m, 1H), 2.38 – 2.30 (m, 1H), 2.08 – 2.00 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 184.2, 140.9, 131.5, 124.0, 90.8, 69.8, 32.2, 23.8. MS (DART) exact mass: calculated for $(M+H)^+$: 167.0815; found: 167.0825.



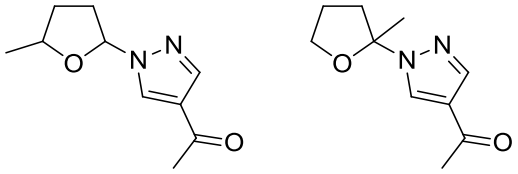
***6-Chloro-2-fluoro-9-(tetrahydrofuran-2-yl)-9H-purine* (38)**: The title compound was prepared from tetrahydrofuran (2.0 ml) and 6-chloro-2-fluoro-9H-purine (0.4 mmol, 69.0 mg) according to general procedure C with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a white solid in 78% yield (75.7 mg).

38: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 6.28 (dd, *J* = 5.9, 3.6 Hz, 1H), 4.31 (ddd, *J* = 8.6, 7.1, 5.8 Hz, 1H), 4.10 (q, *J* = 7.5 Hz, 1H), 2.63 – 2.49 (m, 2H), 2.26 – 2.12 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.01 (*J* = 219.8 Hz), 152.69, 152.55, 144.09 (*J* = 3.3 Hz), 131.06 (*J* = 5.2 Hz), 86.78, 70.12, 32.50, 24.18. ^{19}F NMR (470 MHz, $CDCl_3$) δ -49.4. MS (DART) exact mass: calculated for $(M+H)^+$: 243.0443; found: 243.0460.



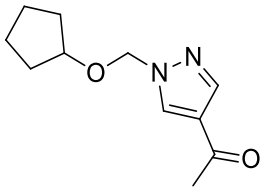
4-Chloro-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazole **(39)**: The title compound was prepared from tetrahydro-2H-pyran (2.0 ml) and 4-chloro-1H-pyrazole (0.4 mmol, 41.0 mg) according to general procedure C with a reaction time of 48 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 30% EtOAc/hexanes to yield a light yellow oil in 73% yield (54.5 mg).

39: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.59 (s, 1H), 7.46 (s, 1H), 5.31 (dd, *J* = 7.5, 4.5 Hz, 1H), 4.06 – 3.99 (m, 1H), 3.72 – 3.64 (m, 1H), 2.08 – 1.98 (m, 3H), 1.73 – 1.58 (m, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 137.9, 125.7, 110.7, 88.0, 67.7, 30.3, 24.9, 22.1. MS (DART) exact mass: calculated for $(M+H)^+$: 187.0633; found: 187.0642.



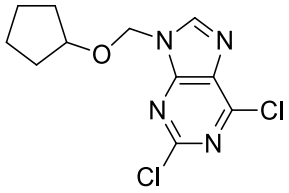
1-(1-(5-methyltetrahydrofuran-2-yl)-1H-pyrazol-4-yl)ethanone **(40A) and** ***1-(1-(1-methyltetrahydrofuran-2-yl)-1H-pyrazol-4-yl)ethanone*** **(40B)**: The title compound was prepared from 2-methyltetrahydrofuran (2.0 ml) and 1-(1H-pyrazol-4-yl)ethanone (0.4 mmol, 44.0 mg) according to general procedure C with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a light yellow oil in 80% yield (62.1 mg, as a mixture of regioisomers and diastereoisomers (d.r. = 1 : 1.5).

40: ^{1}H NMR (500 MHz, Chloroform-*d*, mixture of **40A and 40B**) δ 8.19 – 7.99 (m, 1.3H), 7.91 7.90 (m, 1.3H), 5.99 (dd, *J* = 6.6, 3.4 Hz, 0.61H), 5.92 – 5.88 (m, 1H), 4.50 – 4.22 (m, 1H), 4.14 – 3.98 (m, 0.56H), 2.93 – 2.81 (m, 0.27H), 2.60 – 2.32 (m, 5.85H), 2.27 – 1.96 (m, 1.6H), 1.84 – 1.52 (m, 2.2H), 1.33 (m, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 192.1, 140.7, 140.4, 130.4, 130.2, 129.2, 124.0, 90.7, 90.7, 78.8, 77.2, 69.5, 37.7, 33.3, 31.8, 31.5, 31.3, 27.9, 27.8, 27.0, 24.3, 21.1, 20.8. MS (DART) exact mass: calculated for $(M+H)^+$: 195.1128; found: 195.1133.



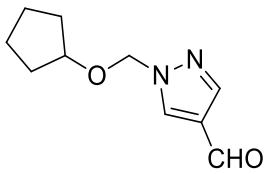
1-(1-((cyclopentyloxy)methyl)-1H-pyrazol-4-yl)ethanone **(41)**: The title compound was prepared from cyclopentyl methyl ether (2.0 ml) and 1-(1H-pyrazol-4-yl)ethanone (0.4 mmol, 44.0 mg) according to general procedure C with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a colorless oil in 55% yield (45.8 mg).

41: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.08 (s, 1H), 7.95 (s, 1H), 5.46 (s, 2H), 4.07 (dt, *J* = 5.6, 2.3 Hz, 1H), 2.47 (s, 3H), 1.80 – 1.65 (m, 4H), 1.65 – 1.48 (m, 4H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 192.1, 140.5, 131.9, 125.2, 80.8, 79.7, 32.2, 28.0, 23.4. MS (DART) exact mass: calculated for $(M+H)^+$: 209.1285; found: 209.1289.



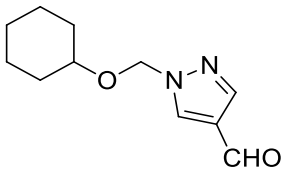
2,6-dichloro-9-((cyclopentyloxy)methyl)-9H-purine **(42)**: The title compound was prepared from cyclopentyl methyl ether (2.0 ml) and 2,6-dichloropurine (0.4 mmol, 75.6 mg) according to general procedure C with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 60% EtOAc/hexanes to yield a colorless oil in 52% yield (59.7 mg).

42: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.28 (s, 1H), 5.65 (s, 2H), 4.15 – 3.91 (m, 1H), 1.77 – 1.50 (m, 8H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 153.5, 153.3, 152.0, 145.7, 130.6, 81.5, 72.0, 32.4, 23.4. MS (DART) exact mass: calculated for $(M+H)^+$: 287.0461; found: 287.0466.



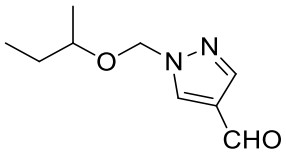
1-((cyclopentyloxy)methyl)-1H-pyrazole-4-carbaldehyde **(43)**: The title compound was prepared from cyclopentyl methyl ether (2.0 ml) and 1H-pyrazole-4-carbaldehyde (0.4 mmol, 38.4 mg) according to general procedure C with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a colorless oil in 49% yield (38.1 mg).

43: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.93 (s, 1H), 8.13 (s, 1H), 8.02 (s, 1H), 5.50 (s, 2H), 4.09 (dt, *J* = 5.9, 2.5 Hz, 1H), 1.97 – 1.36 (m, 8H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 184.1, 184.1, 140.6, 132.9, 125.3, 81.0, 79.8, 32.2, 23.4. MS (DART) exact mass: calculated for $(M+H)^+$: 195.1128; found: 195.1132.



1-((cyclohexyloxy)methyl)-1H-pyrazole-4-carbaldehyde **(44)**: The title compound was prepared from methoxycyclohexane (2.0 ml) and 1H-pyrazole-4-carbaldehyde (0.4 mmol, 38.4 mg) according to general procedure C with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a light yellow oil in 46% yield (38.3 mg).

44: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.93 (s, 1H), 8.15 (s, 1H), 8.01 (s, 1H), 5.55 (s, 2H), 3.51 (dt, *J* = 9.1, 5.2 Hz, 1H), 1.85 – 1.67 (m, 5H), 1.38 – 1.17 (m, 7H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 184.1, 184.1, 140.5, 132.8, 125.3, 79.0, 77.1, 32.0, 25.4, 23.8. MS (DART) exact mass: calculated for $(M+H)^+$: 209.1285; found: 209.1290.



1-(sec-butoxymethyl)-1H-pyrazole-4-carbaldehyde **(45)**: The title compound was prepared from sec-butyl methyl ether (2.0 ml) and 1H-pyrazole-4-carbaldehyde (0.4 mmol, 38.4 mg) according to general procedure C with a reaction time of 36 hours. The crude residue was purified by column chromatography on silica gel with an eluent of hexanes to 50% EtOAc/hexanes to yield a light yellow oil in 51% yield (37.2 mg).

45: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.93 (s, 1H), 8.14 (s, 1H), 8.01 (s, 1H), 5.53 (s, 2H), 3.60 (q, *J* = 6.1 Hz, 1H), 1.65 – 1.37 (m, 2H), 1.13 (d, *J* = 6.1 Hz, 3H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 184.1, 140.5, 132.9, 125.3, 79.4, 76.6, 29.1, 19.2, 9.5. MS (DART) exact mass: calculated for $(M+H)^+$: 183.1128; found: 183.1132.

12. References

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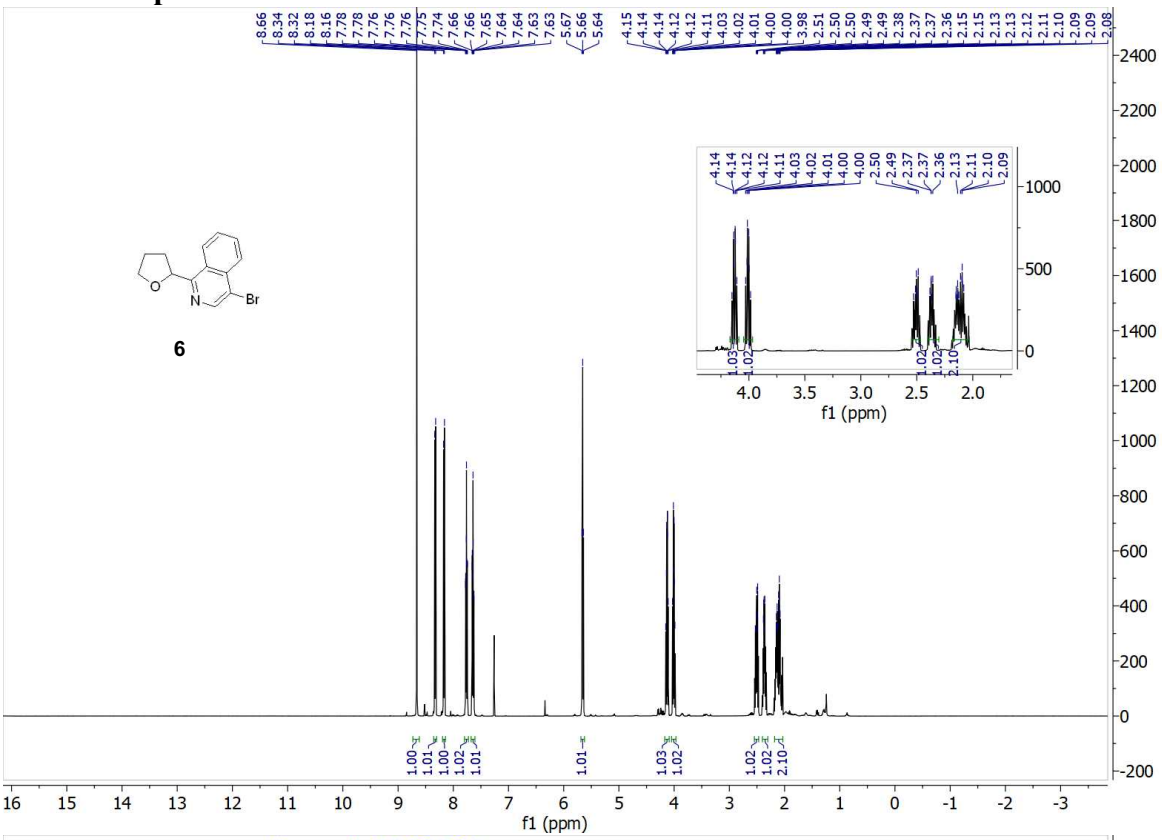
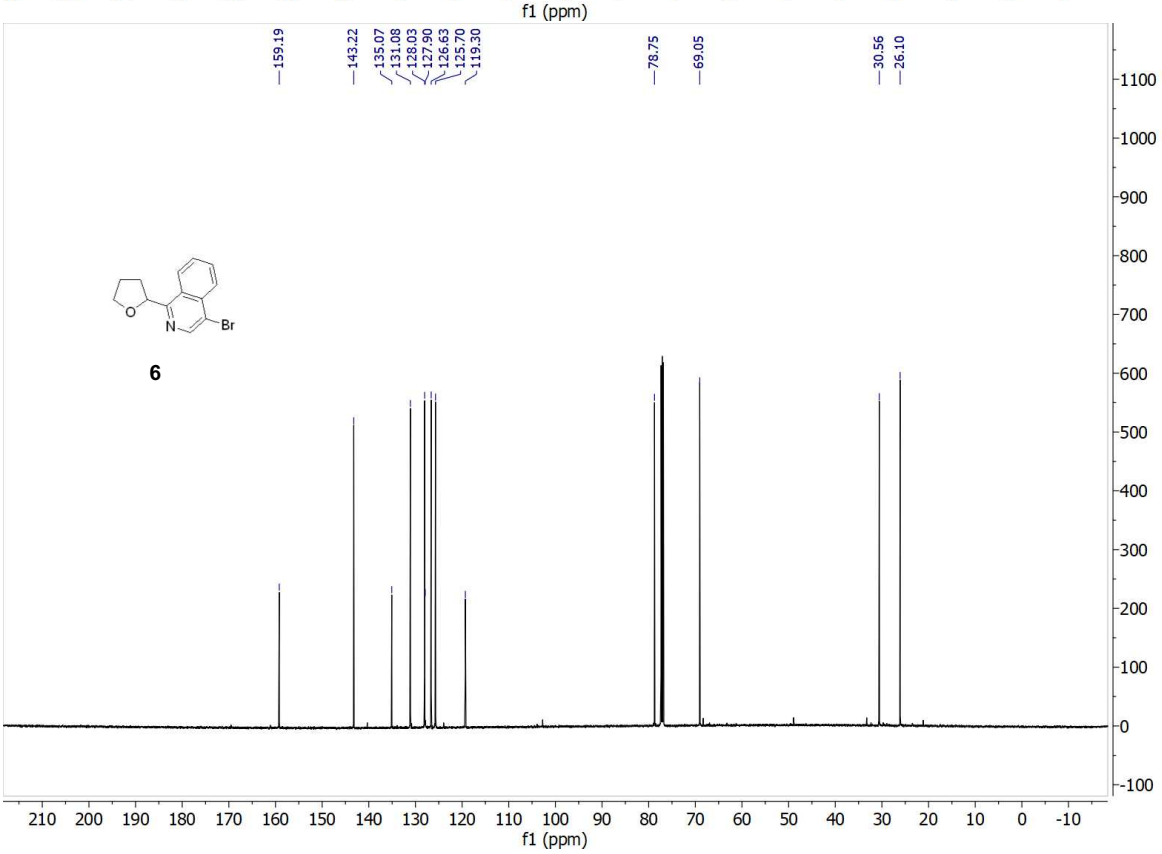
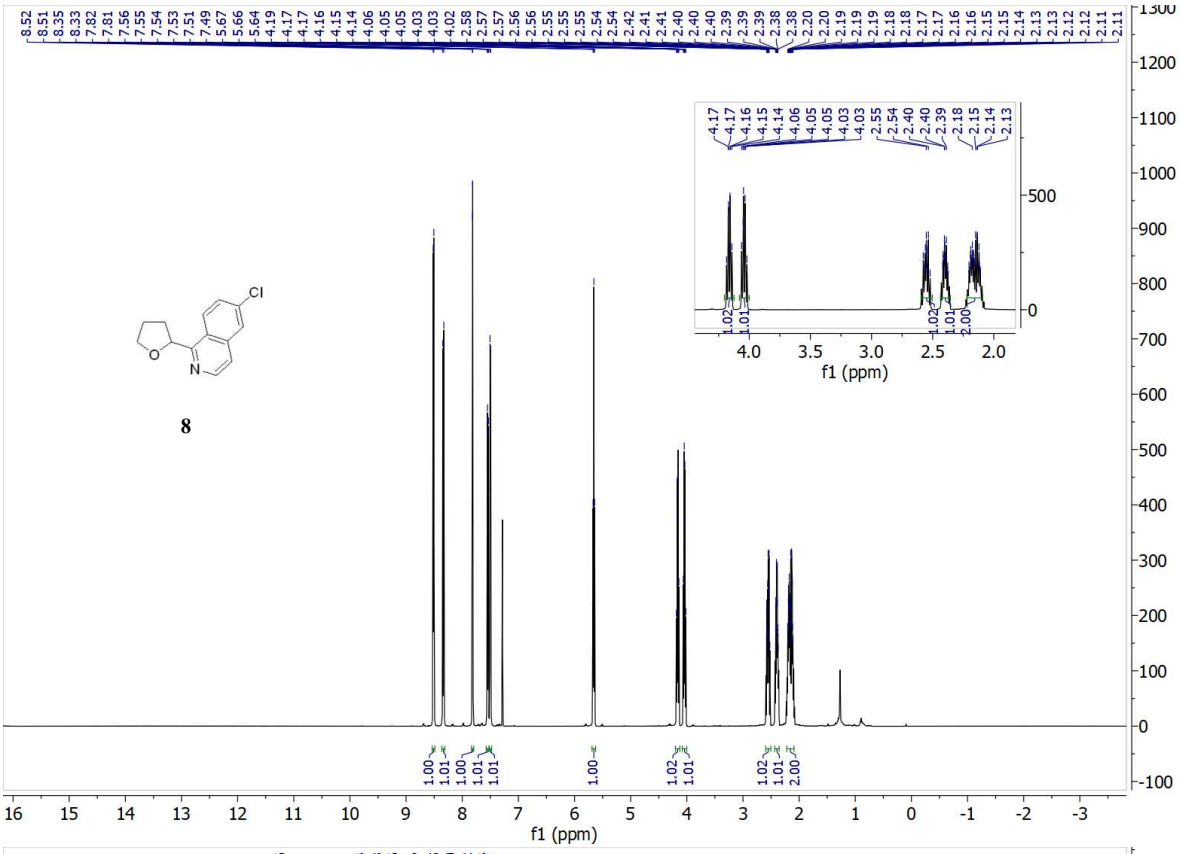
13. NMR Spectral Data



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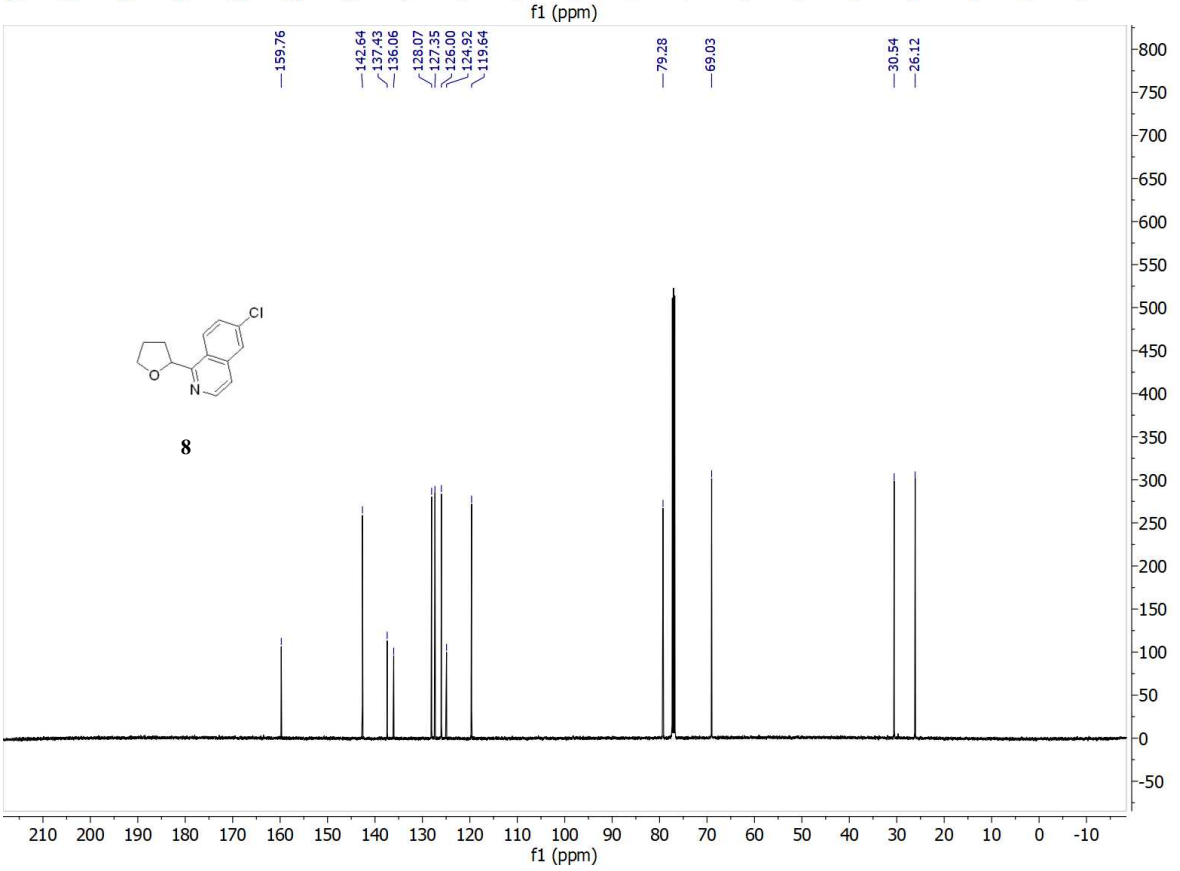
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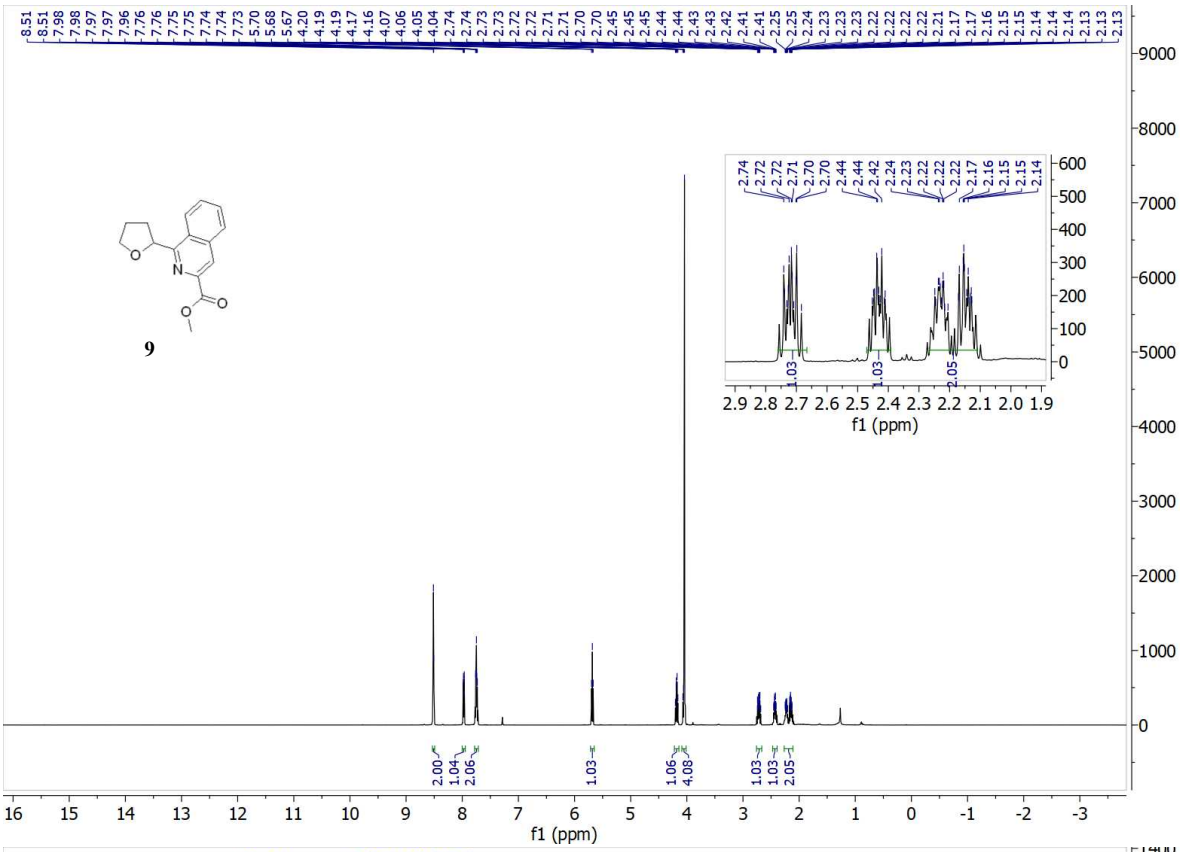
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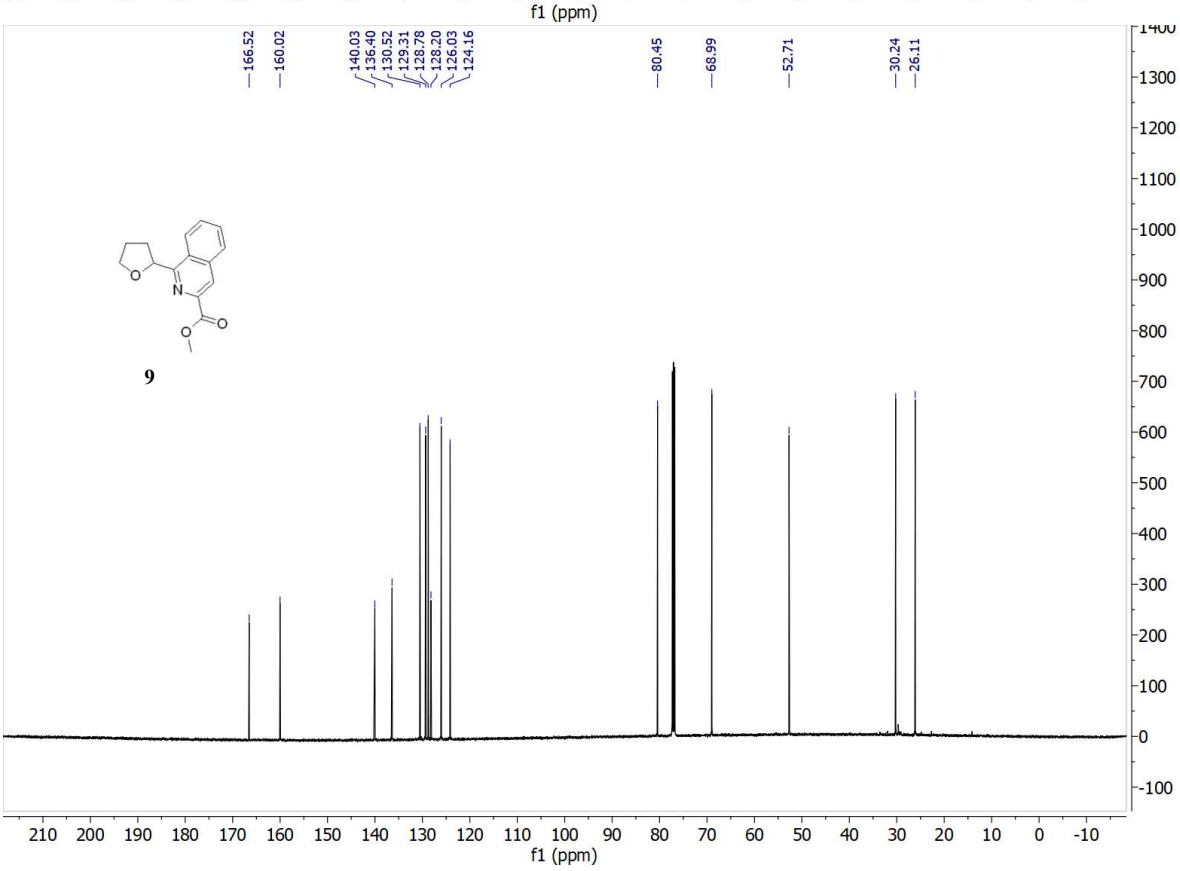
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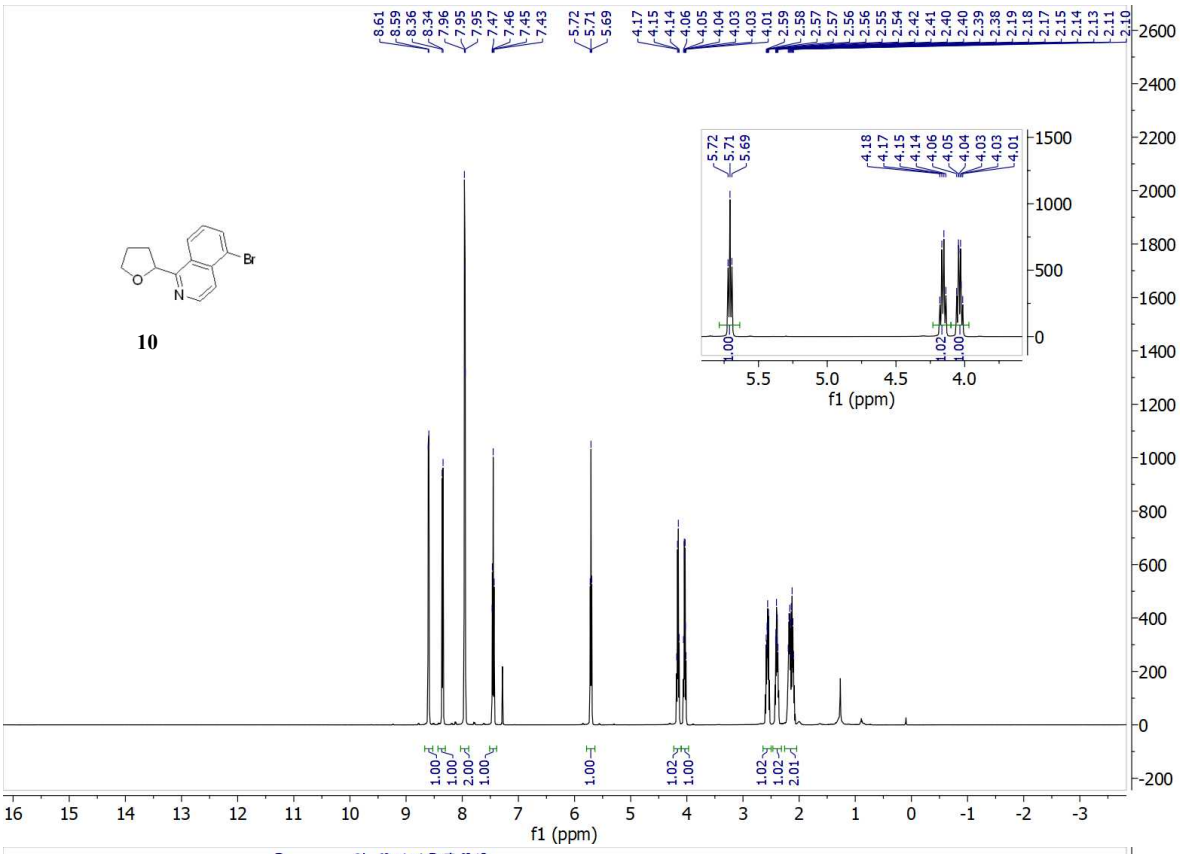
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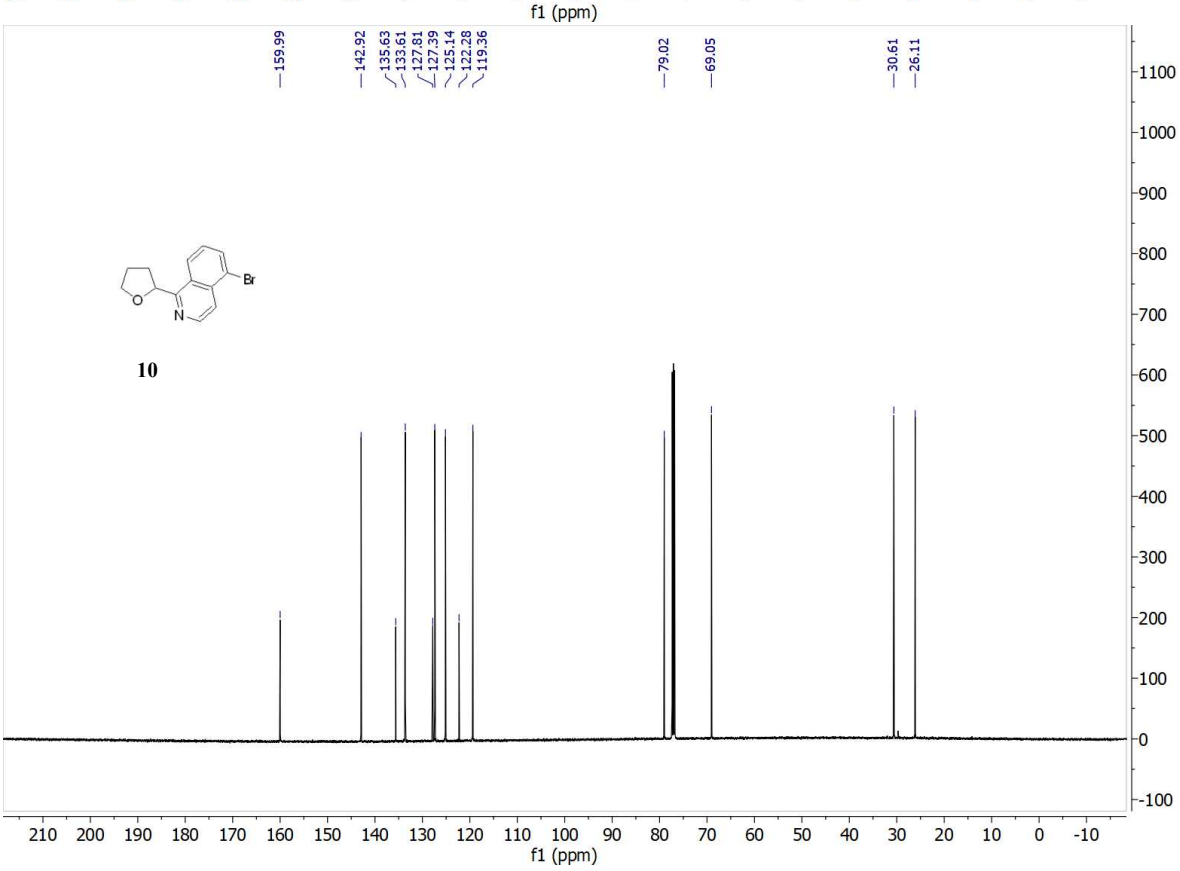
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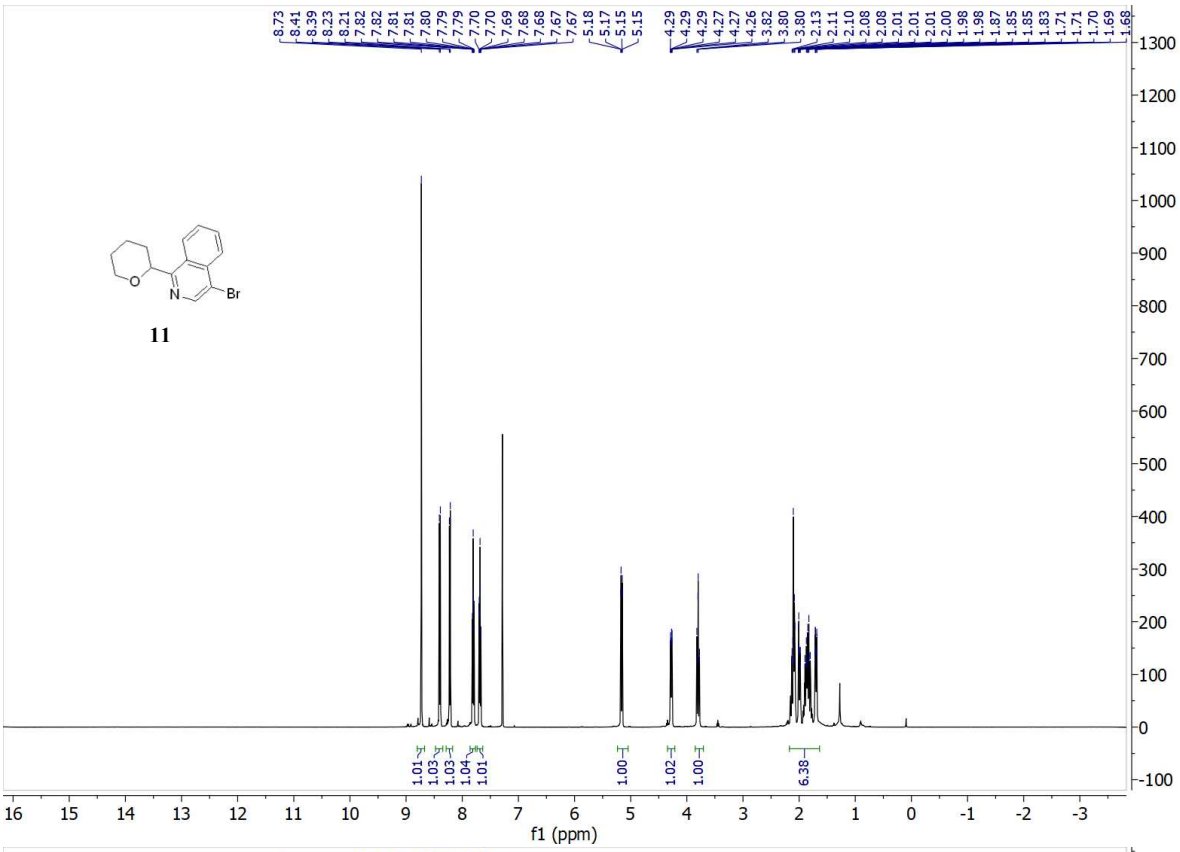
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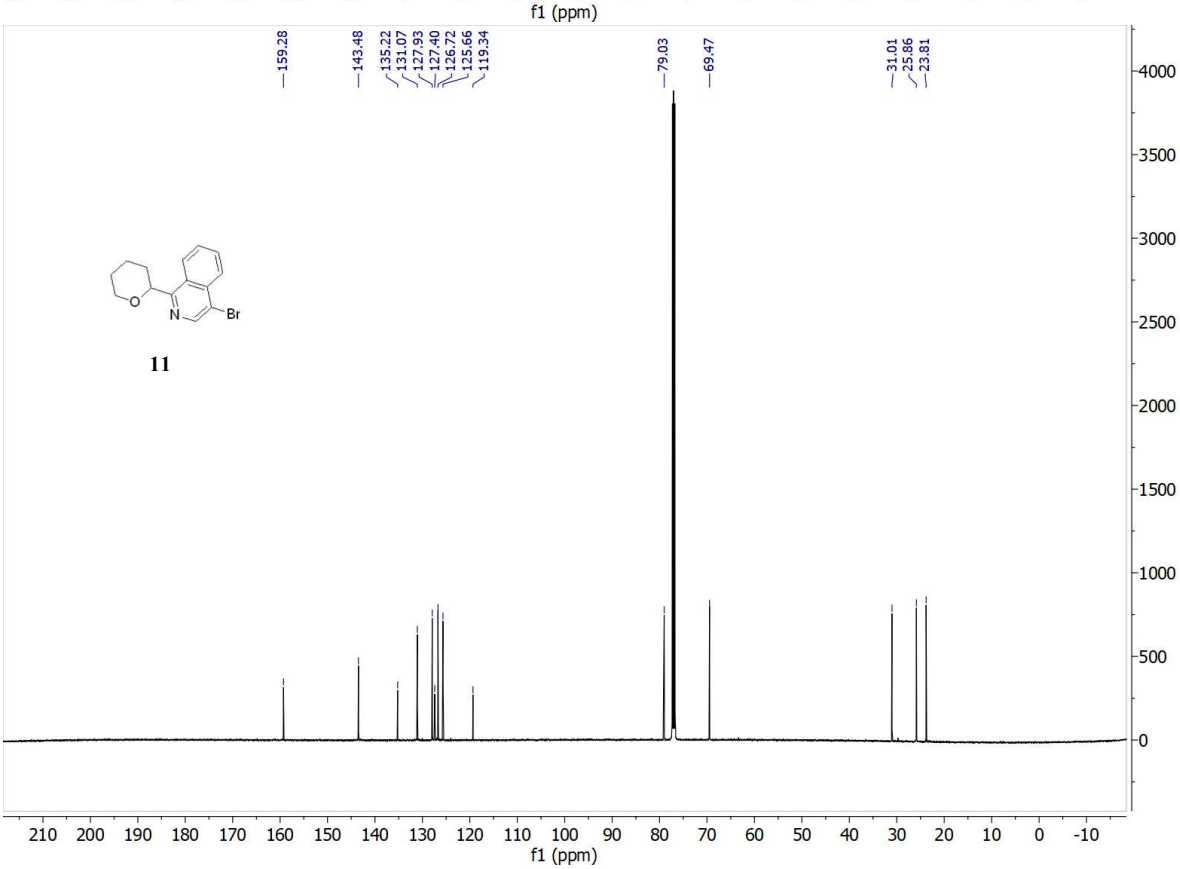
Br

11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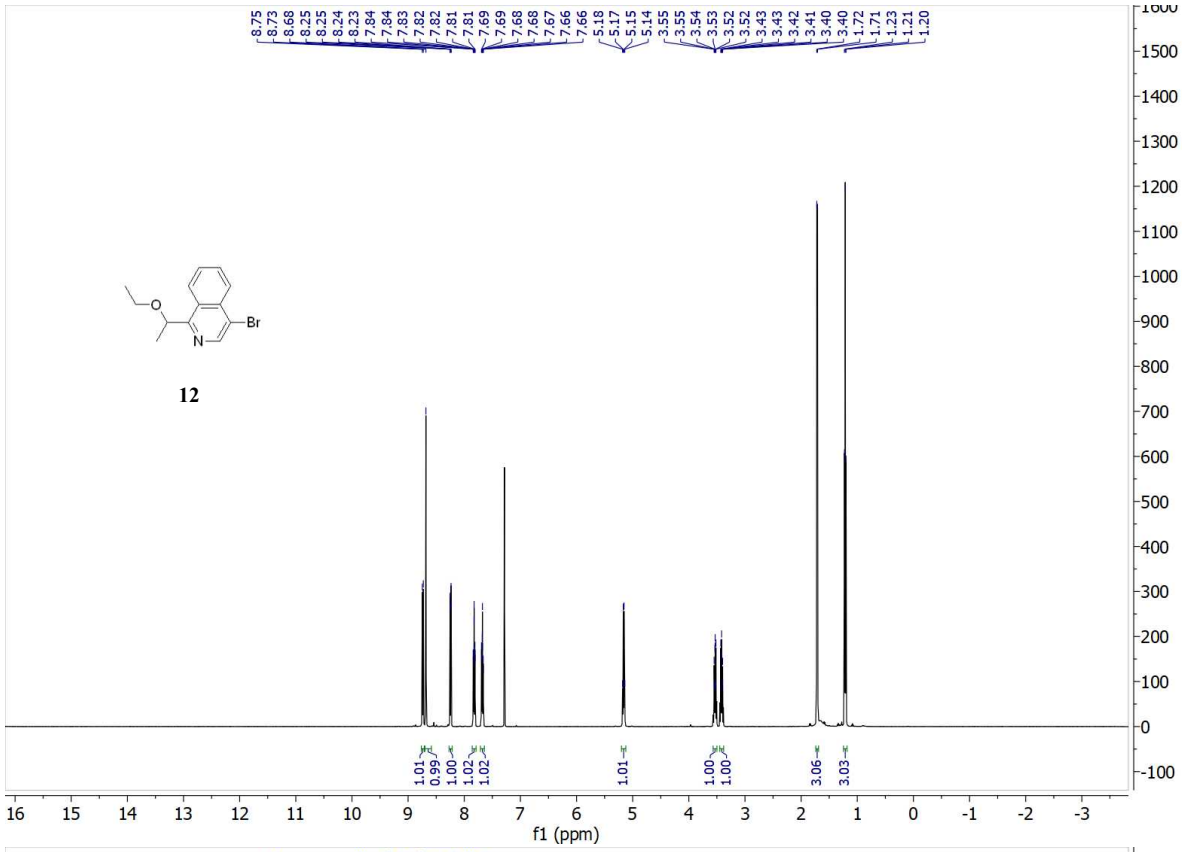
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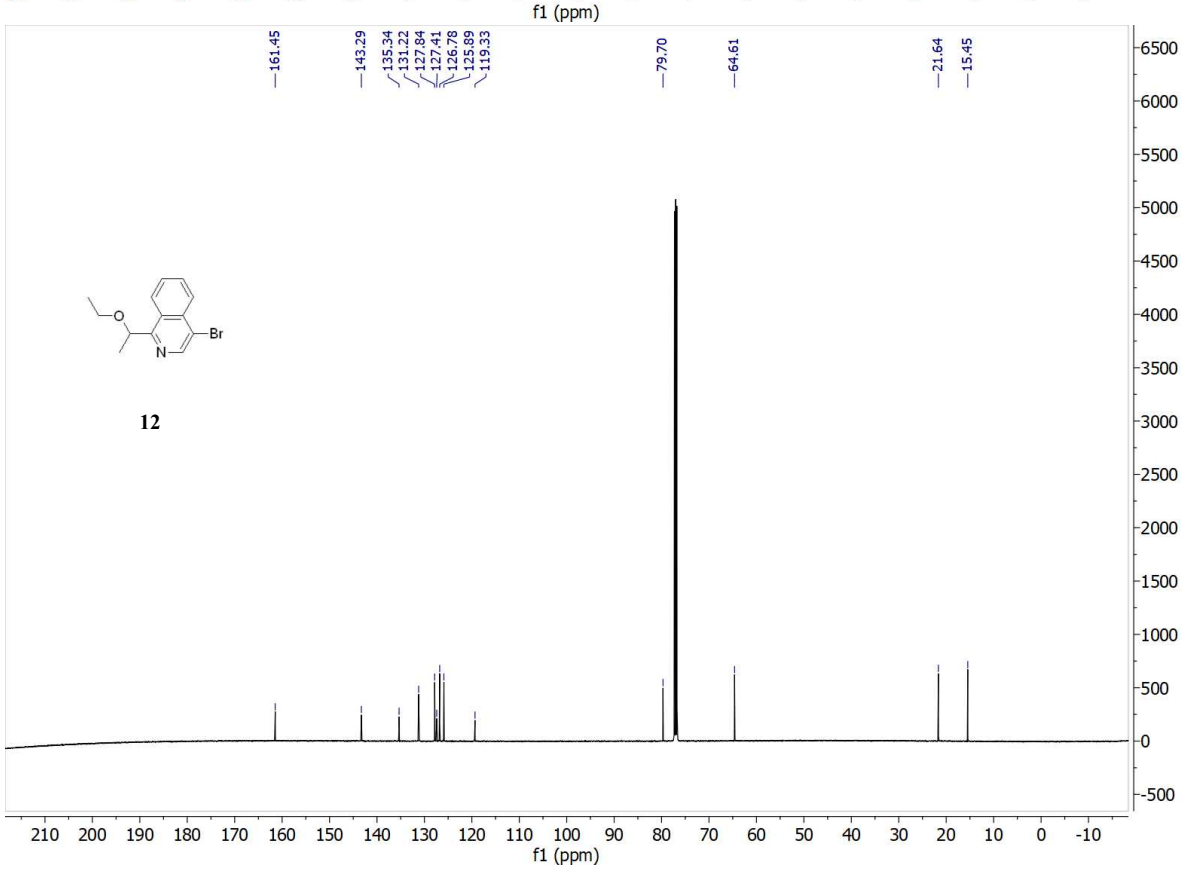
3.03
f1 (ppm)

12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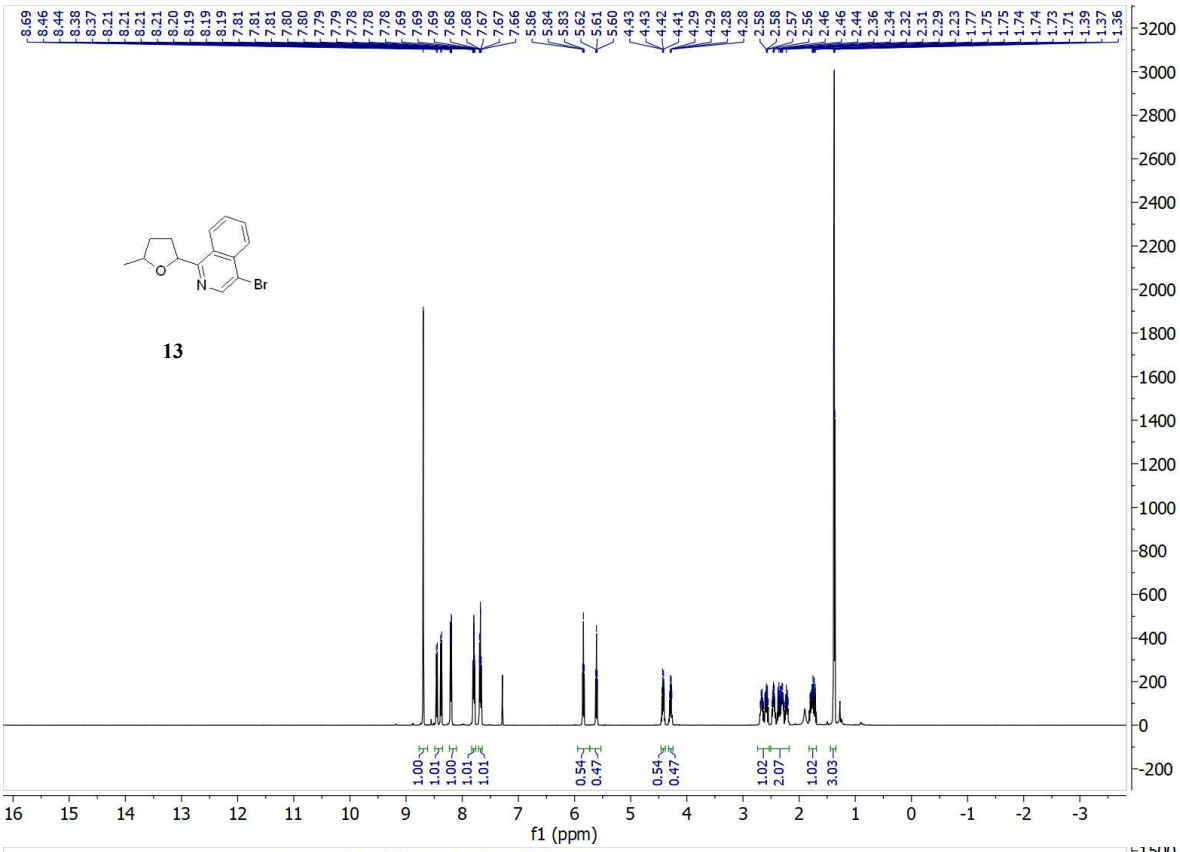
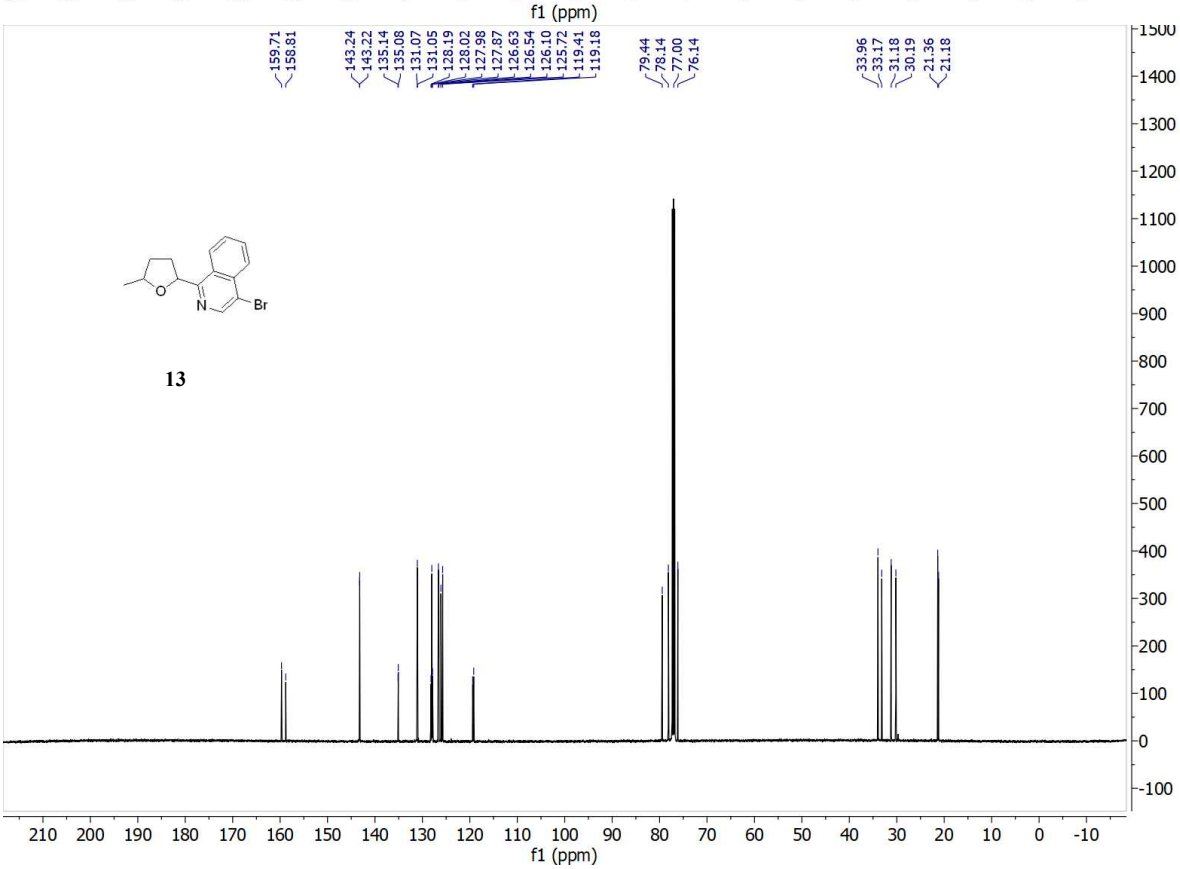
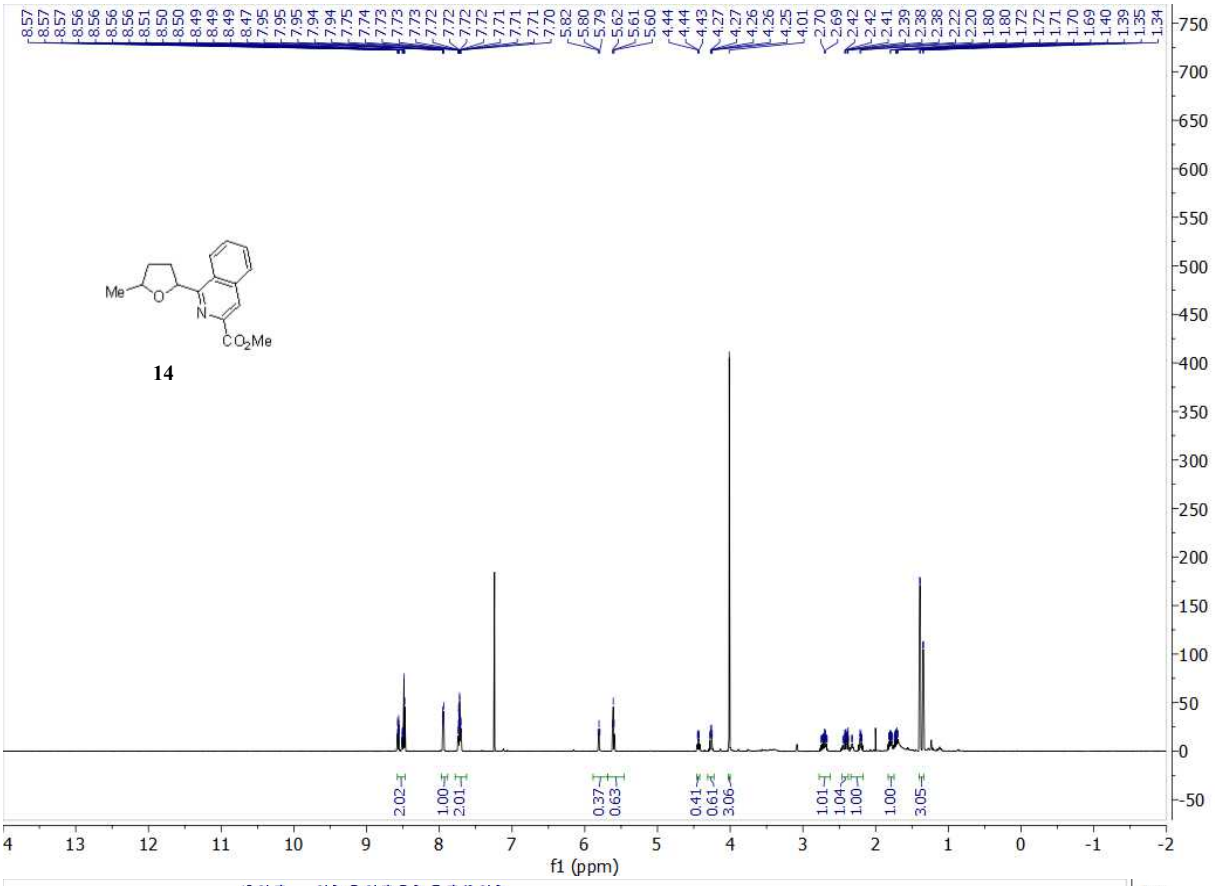
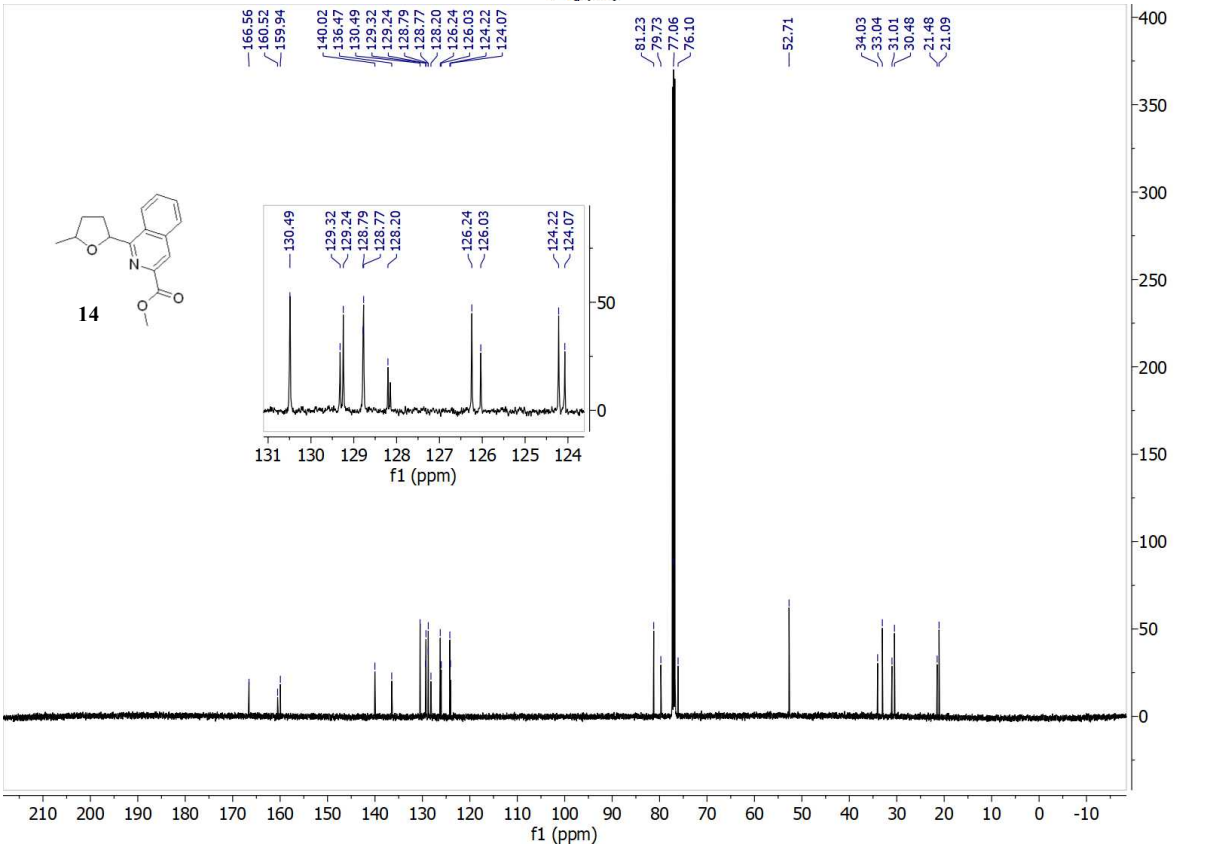
143.29
135.34
131.22
127.84
127.41
126.78
125.89
119.33
79.70
64.61
21.64
15.45
O
N
Br
f1 (ppm)

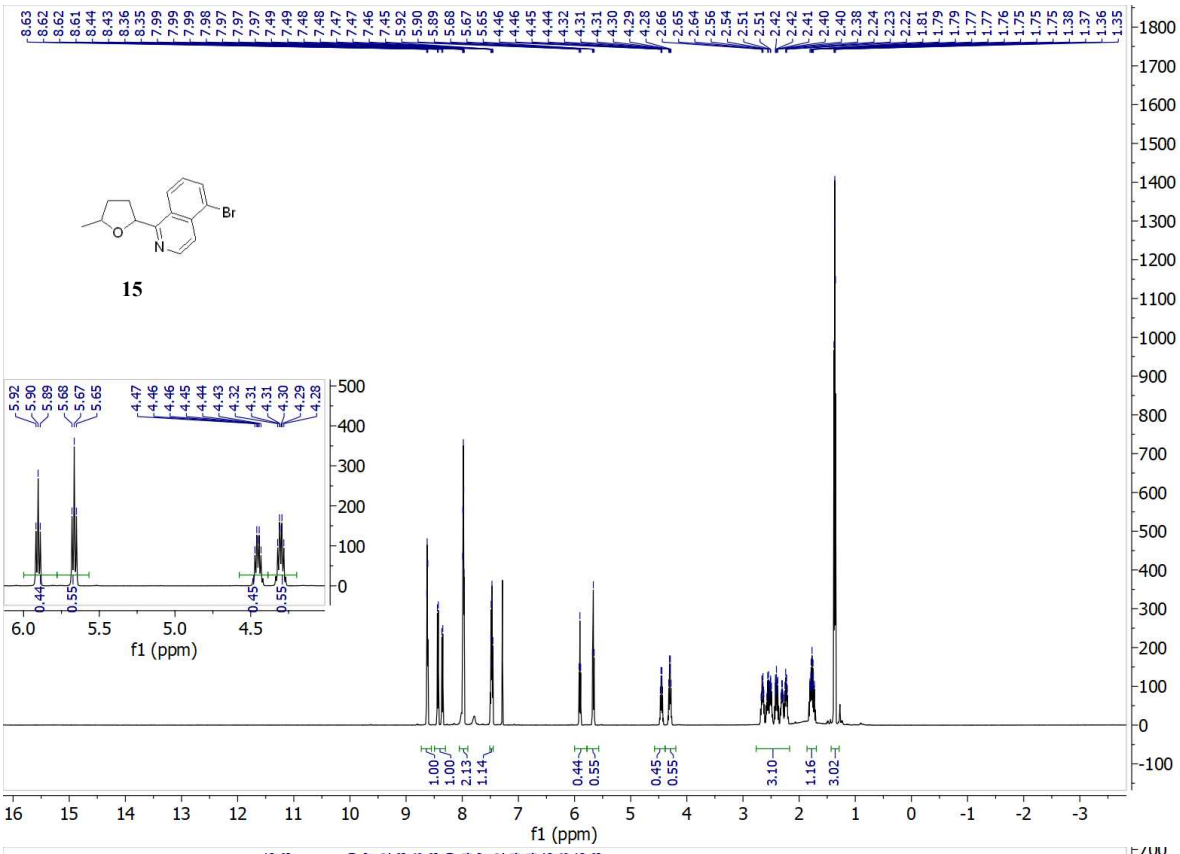
12

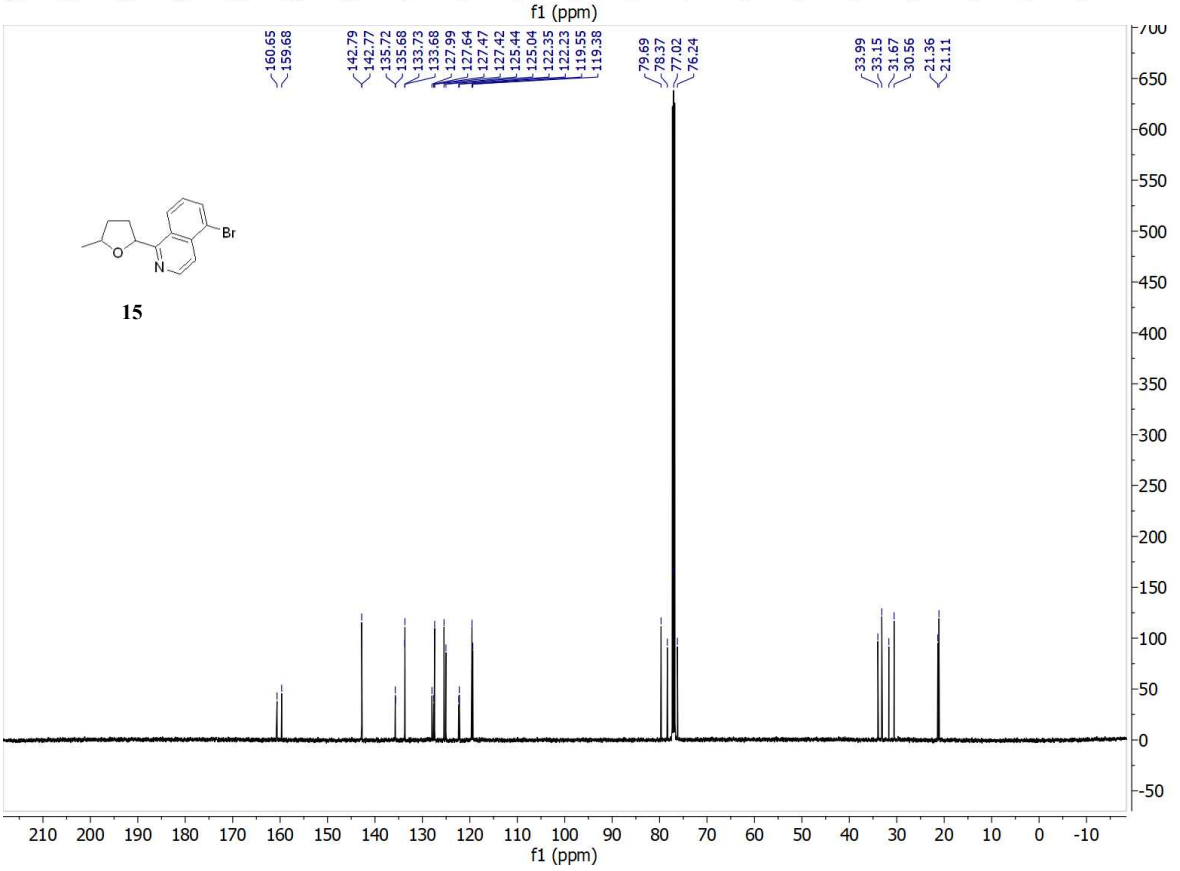

8.69 8.46 8.44 8.38 8.37 8.21 8.21 8.21 8.21 8.20 8.19 8.19 8.19 7.81 7.81 7.81 7.80 7.80 7.79 7.79 7.78 7.78 7.78 7.78 7.69 7.69 7.69 7.68 7.68 7.67 7.67 7.67 7.66 5.86 5.84 5.83 5.62 5.61 5.60 4.43 4.43 4.42 4.41 4.29 4.29 4.28 4.28 2.58 2.58 2.57 2.56 2.46 2.46 2.44 2.36 2.34 2.32 2.31 2.29 2.23 1.77 1.75 1.75 1.74 1.74 1.73 1.71 1.39 1.37 1.36
O
N
Br
13
1.00 1.01 1.00 1.01 1.01 0.54 0.47 0.54 0.47 1.02 2.07 1.02 3.03
f1 (ppm)

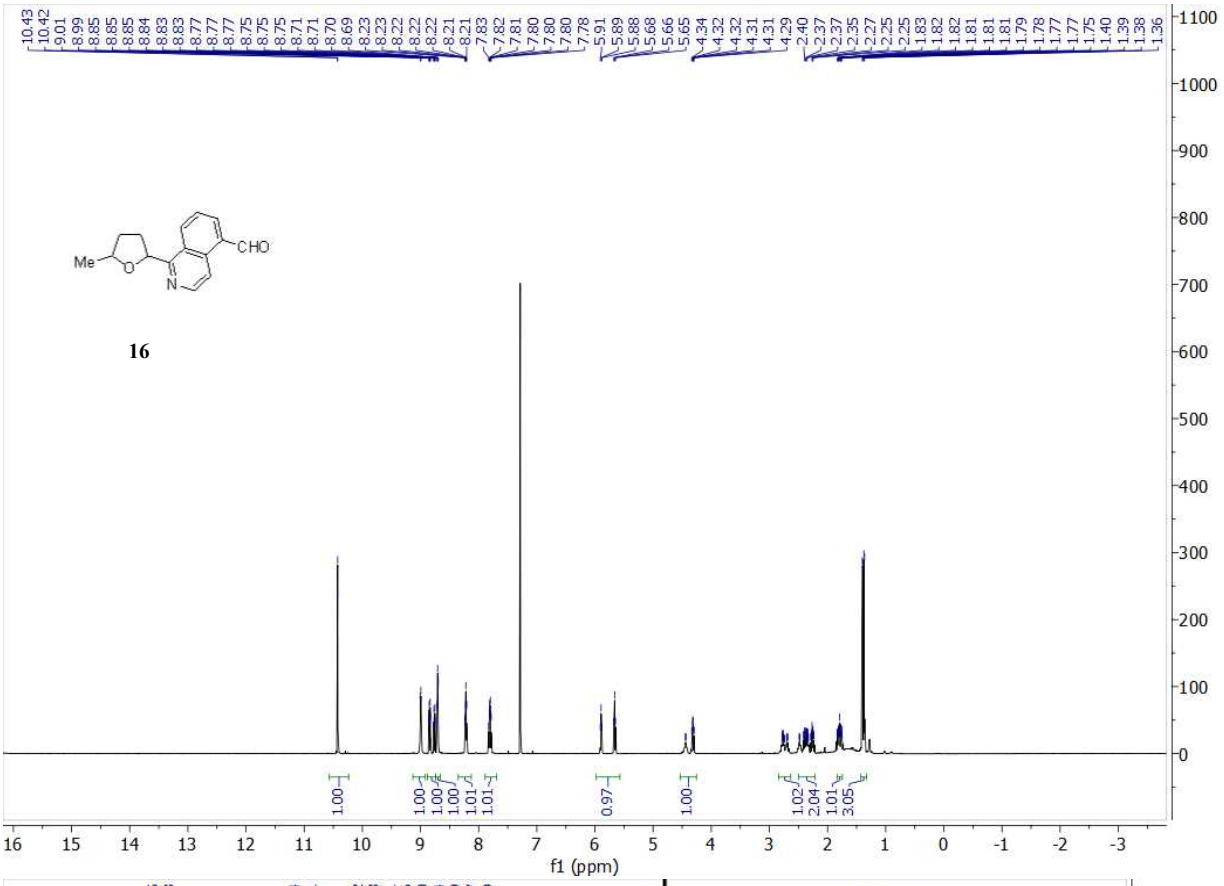

159.71 158.81 143.24 143.22 135.14 135.08 131.07 131.05 128.19 128.02 127.98 127.87 126.63 126.54 126.10 125.72 119.41 119.18 79.44 78.14 77.00 76.14 33.96 33.17 31.18 30.19 21.36 21.18
O
N
Br
13
f1 (ppm)


Me
O
N
CO2Me
14
f1 (ppm)


14
f1 (ppm)


Br
O
N
15
f1 (ppm)


Br
O
N
15
f1 (ppm)



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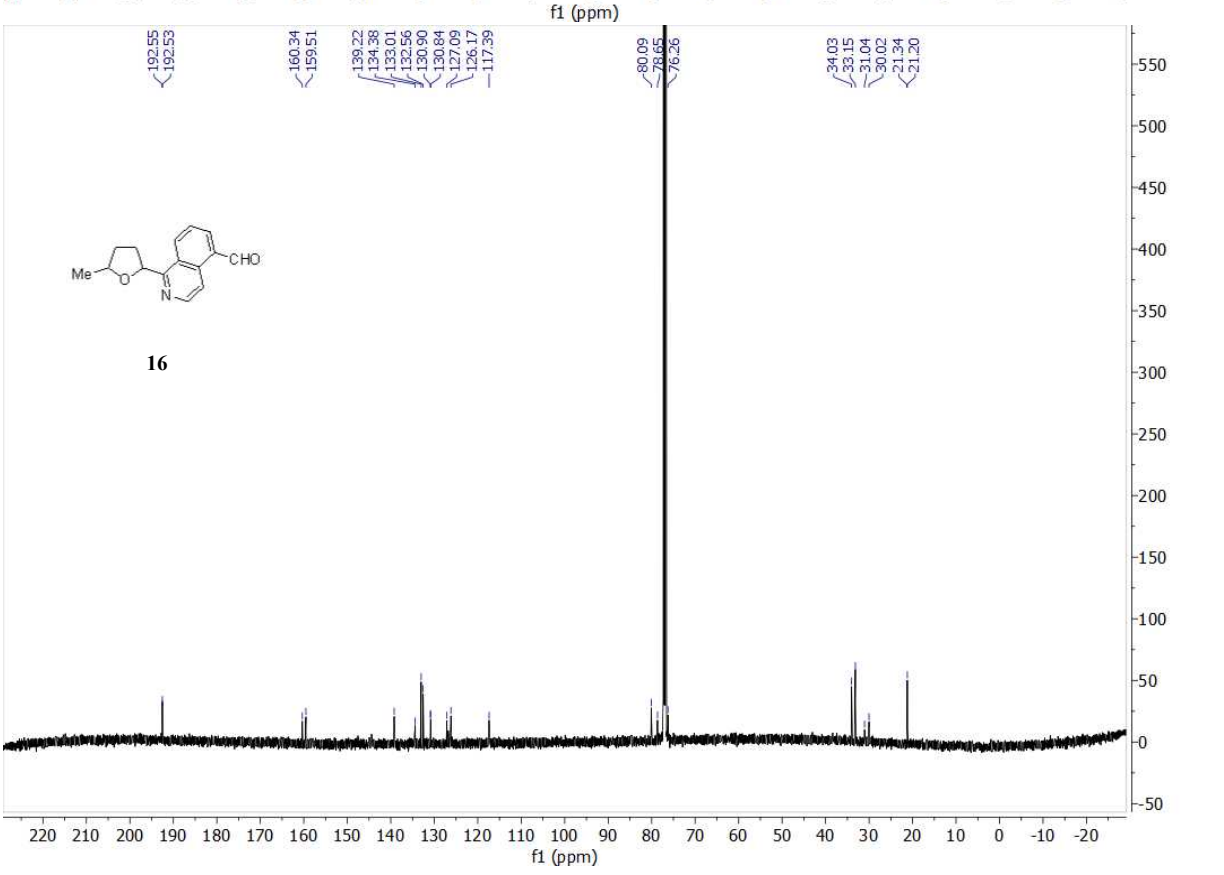

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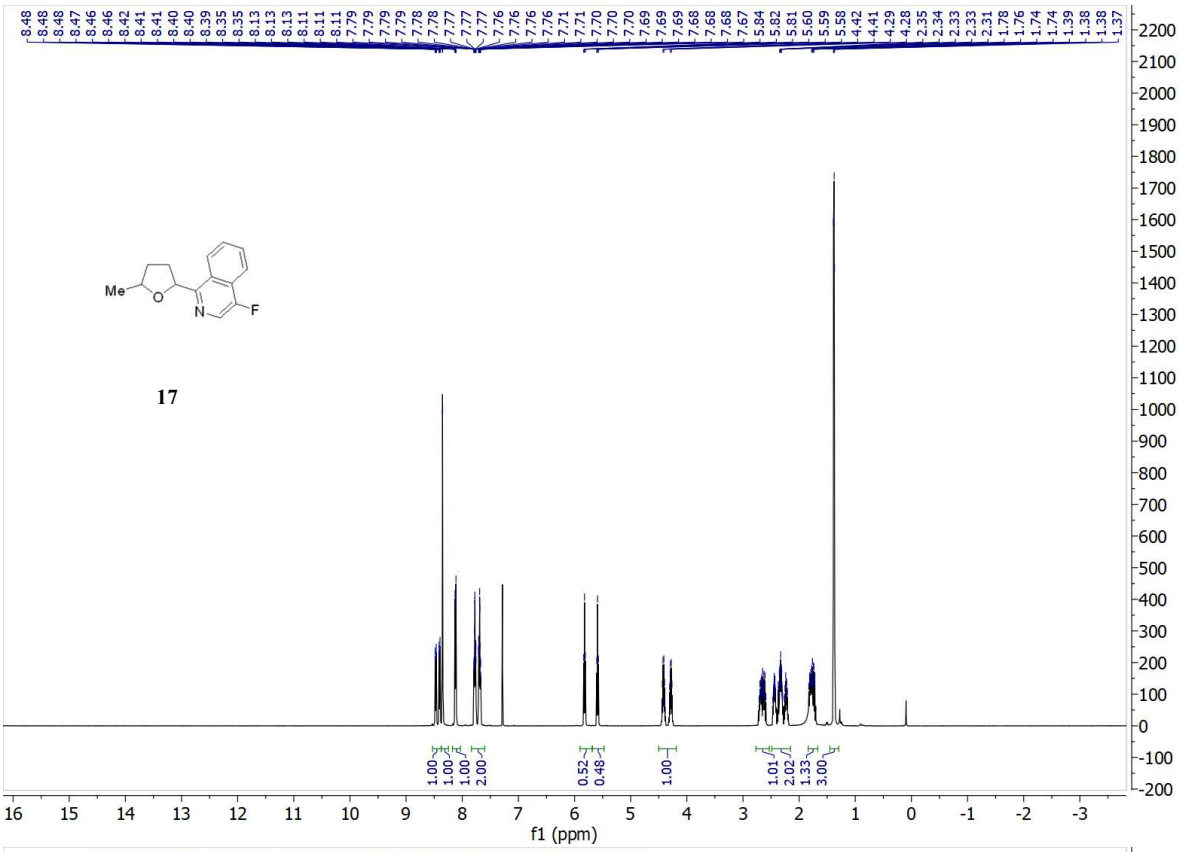
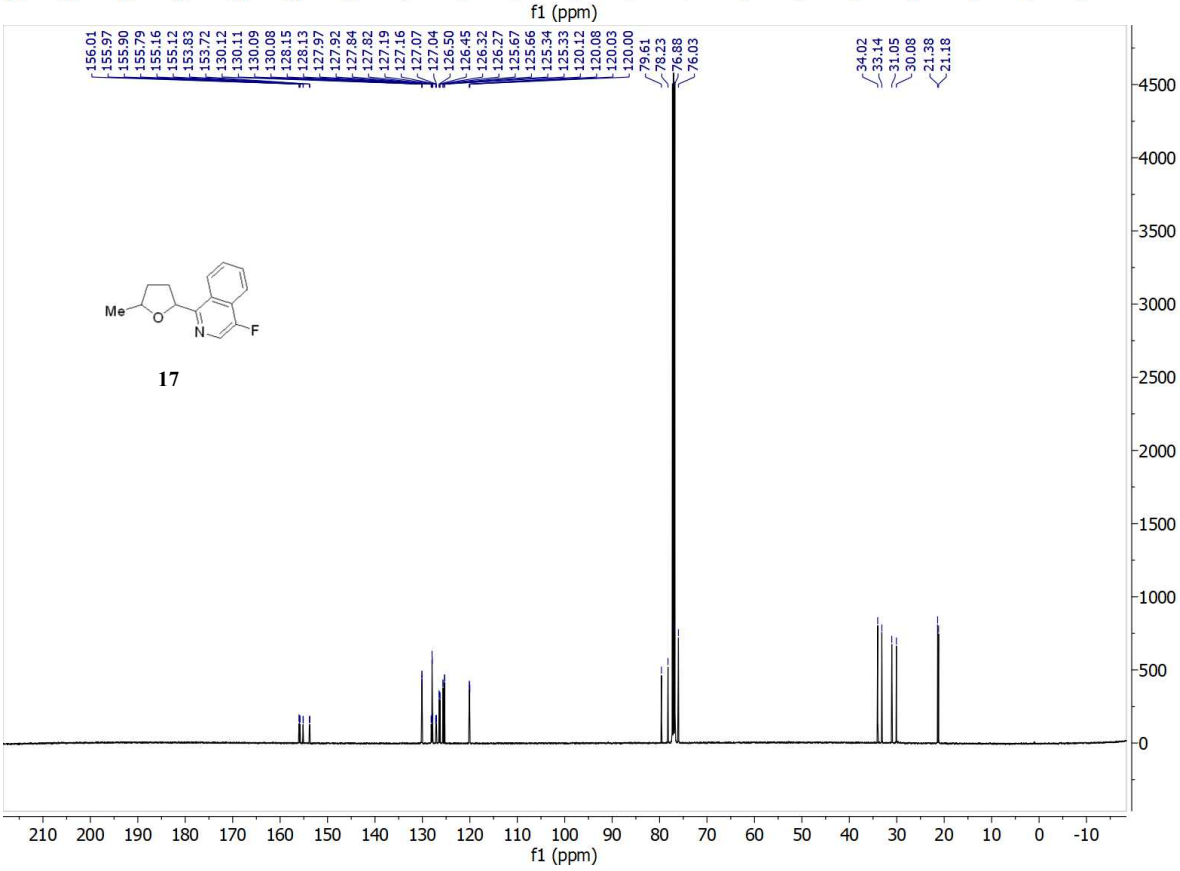
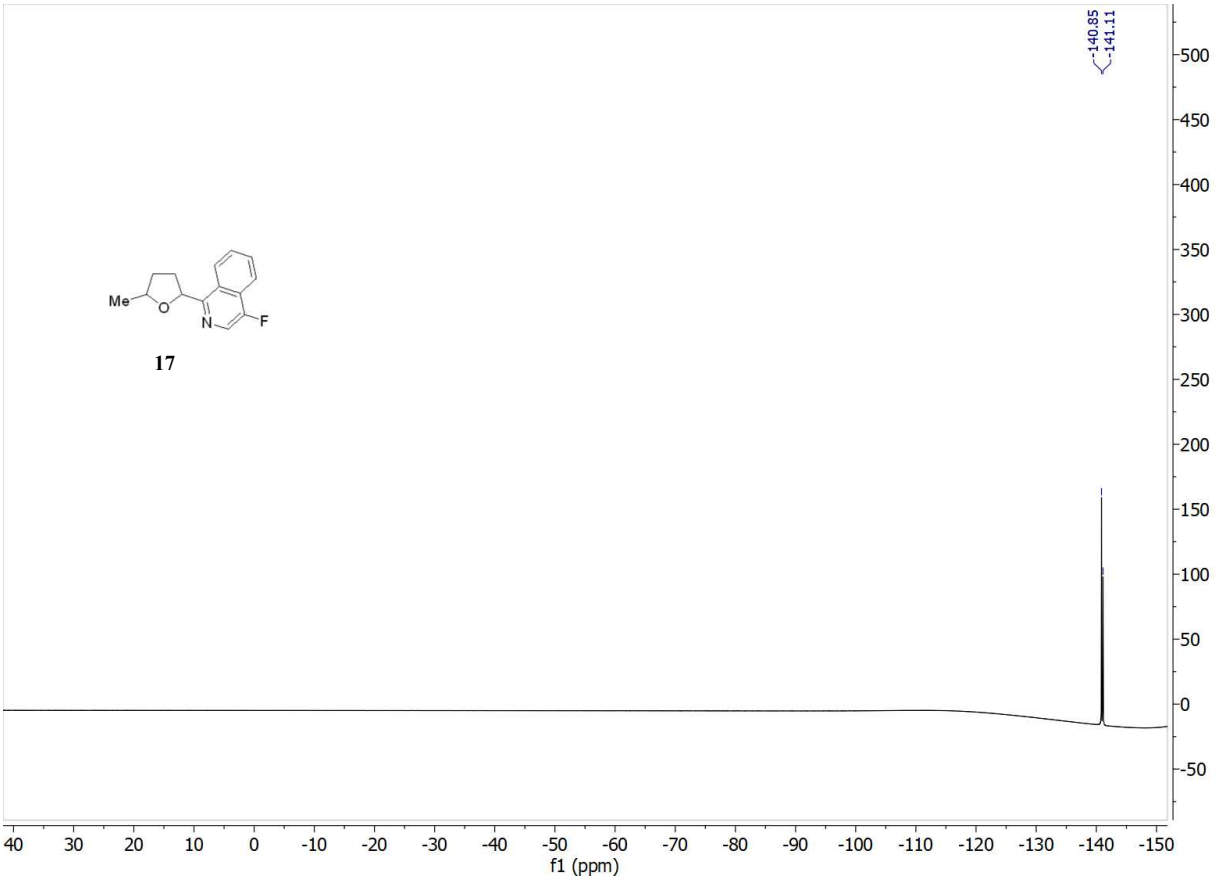
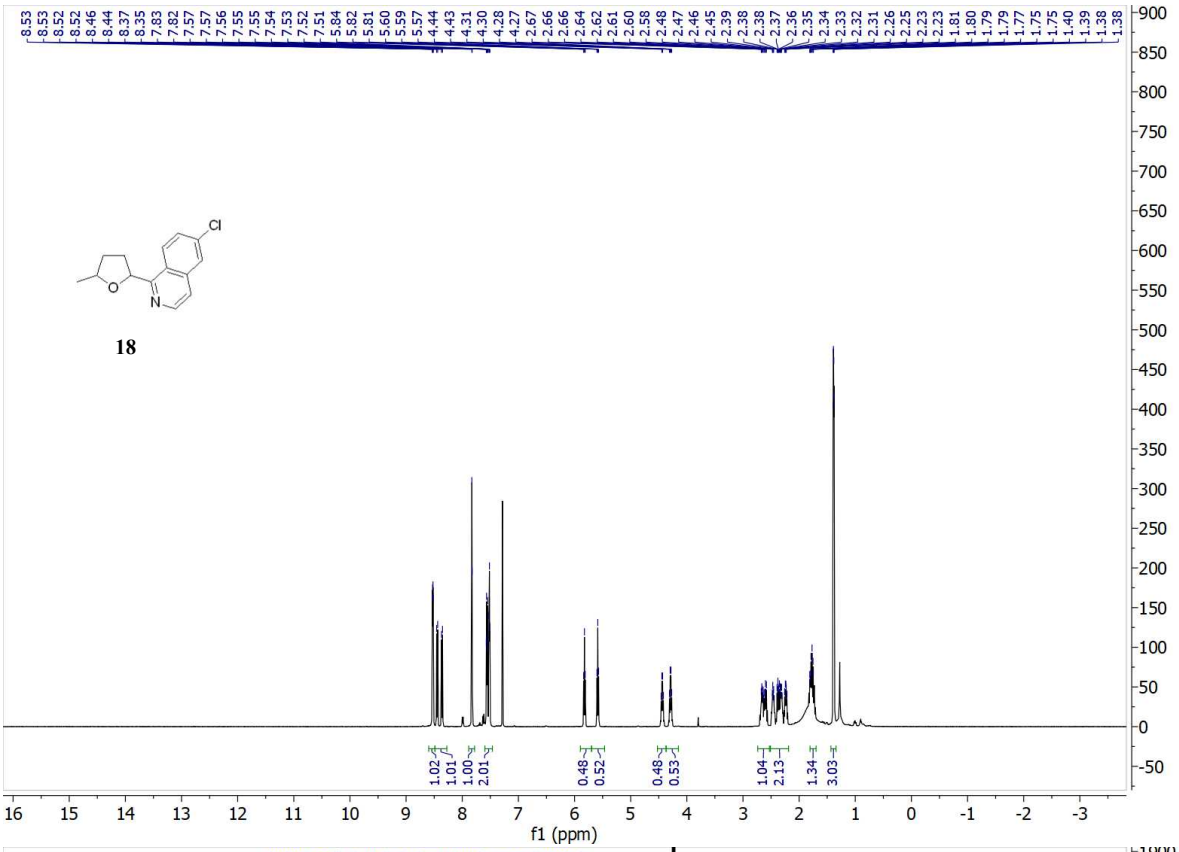
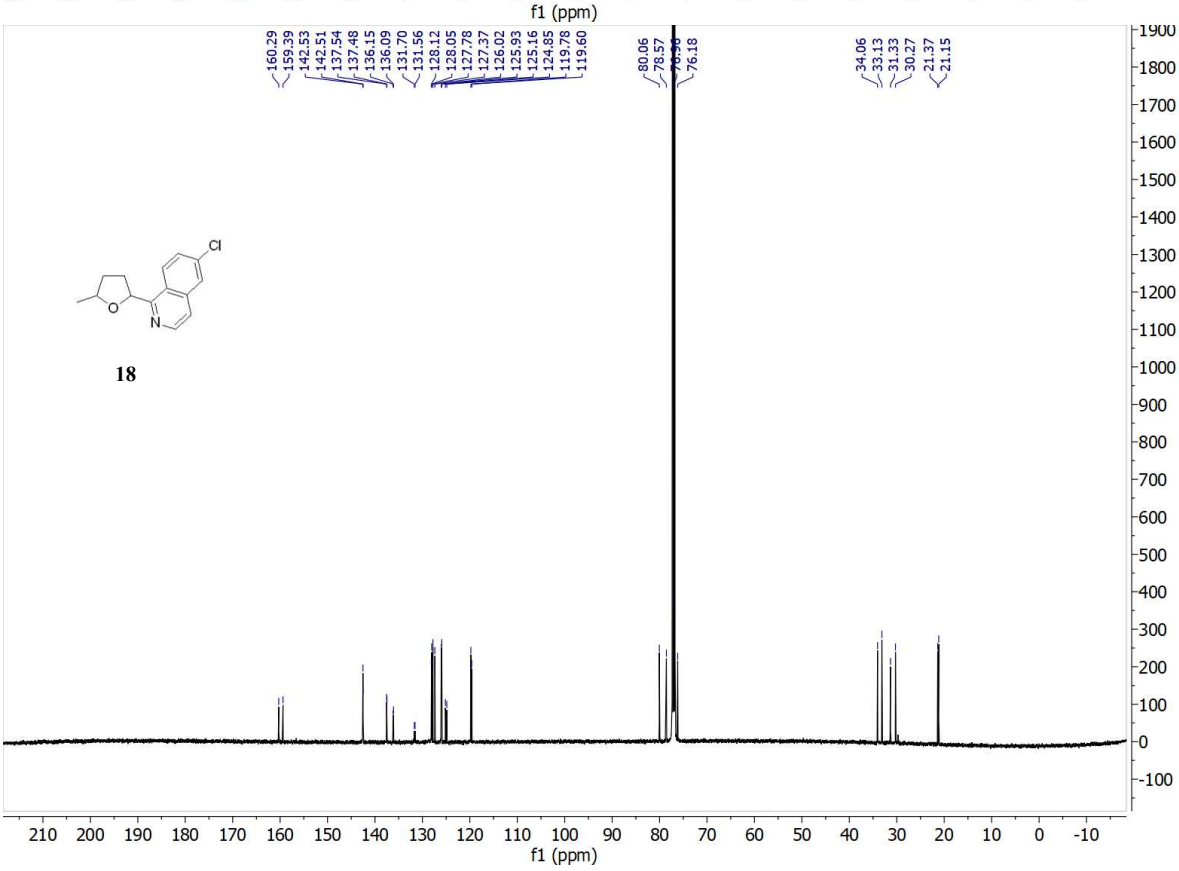

Me
O
N
F
17
f1 (ppm)

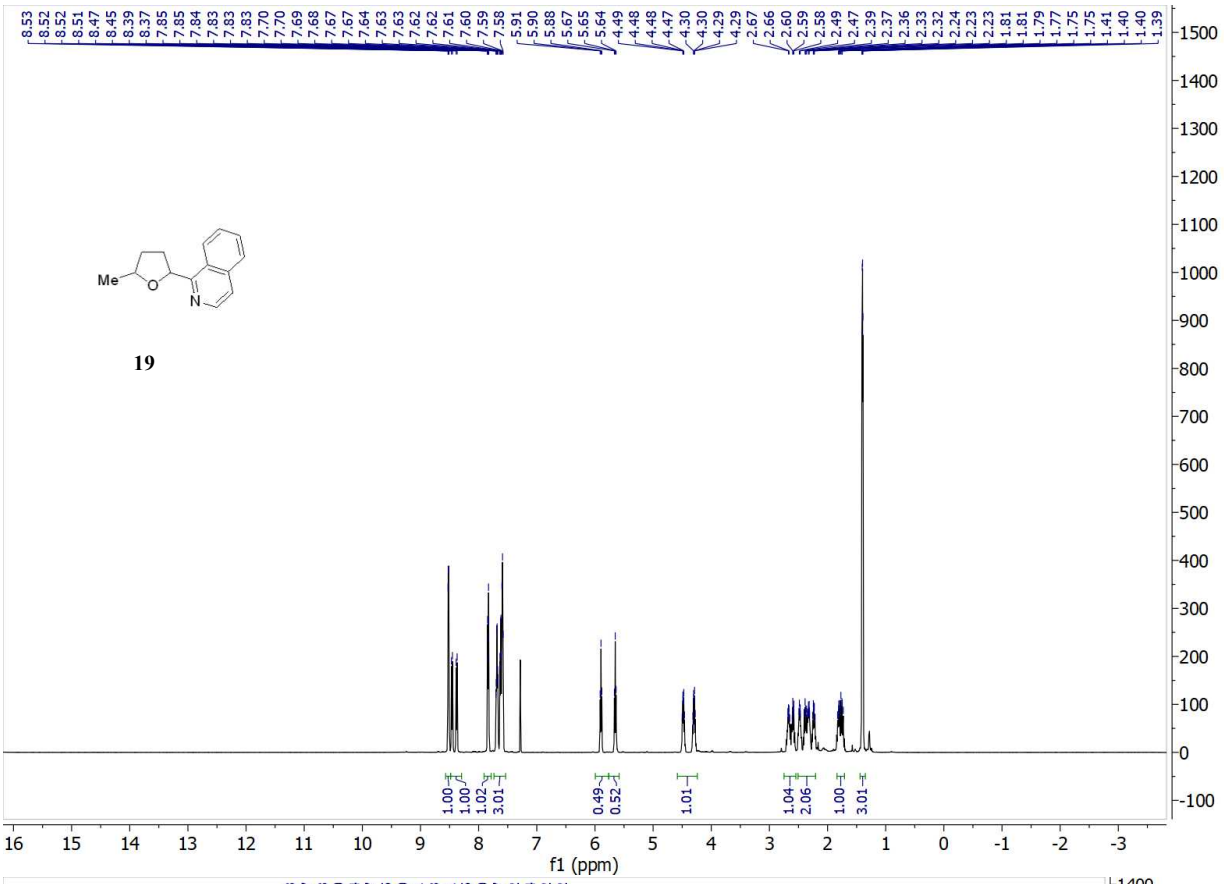

Me
O
N
F
17
f1 (ppm)

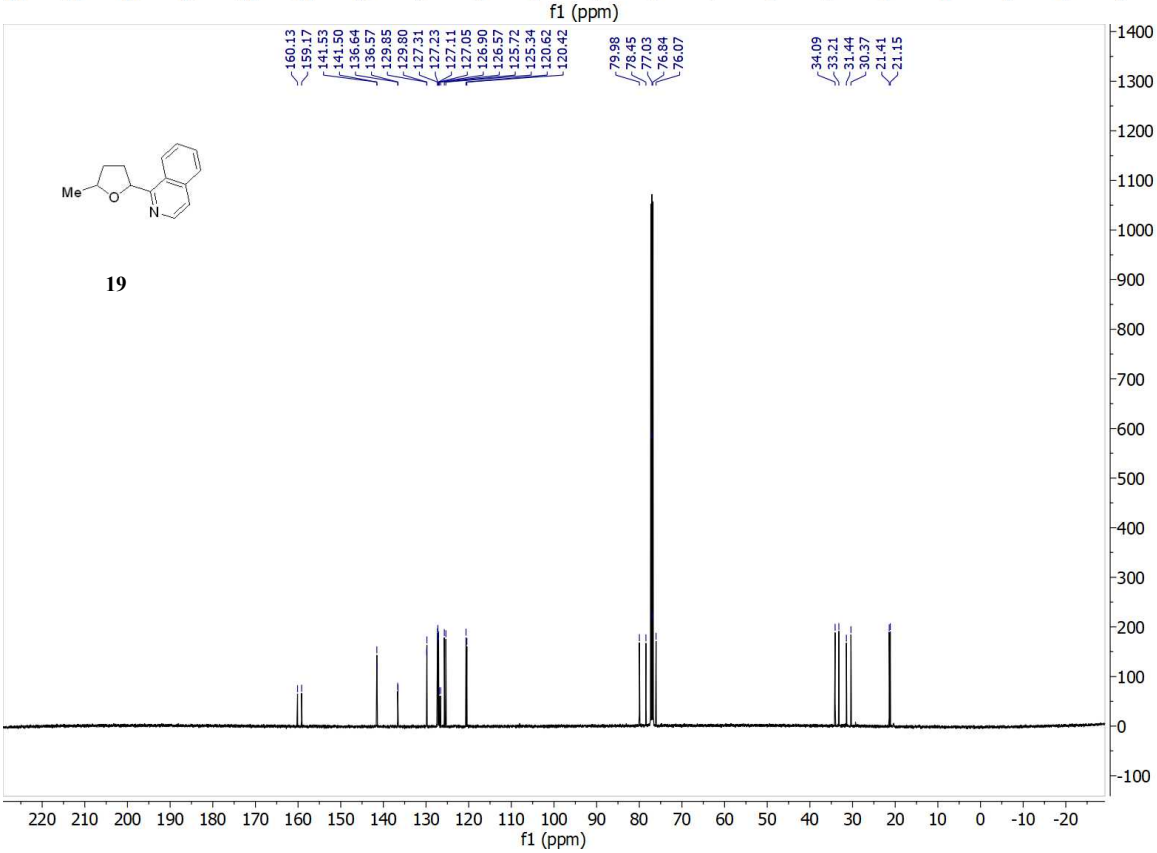

-140.85
-141.11
Me
O
N
F
500
450
400
350
300
250
200
150
100
50
0
-50
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150
f1 (ppm)

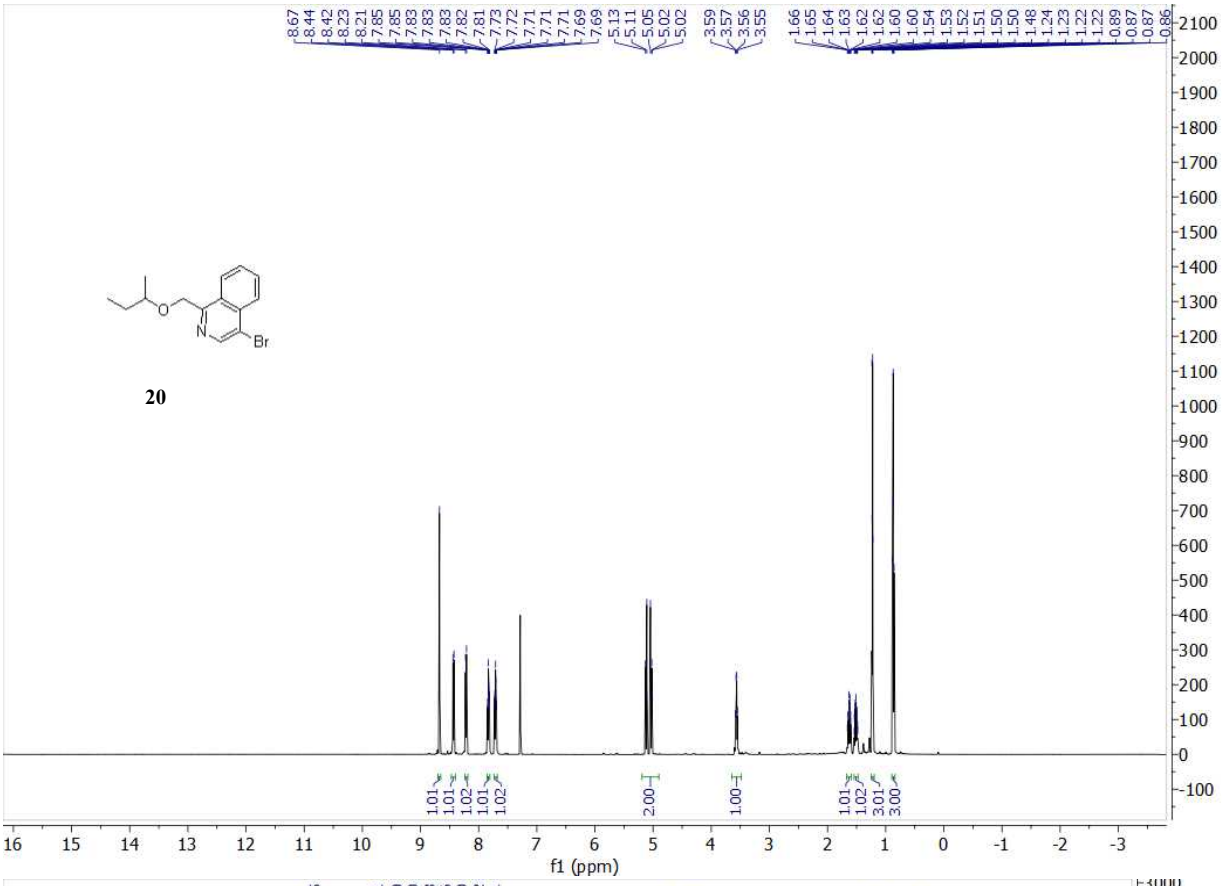
17


Cl
O
N
18
f1 (ppm)


Cl
O
N
18
f1 (ppm)


Me
O
N
19
f1 (ppm)


Me
O
N
19
f1 (ppm)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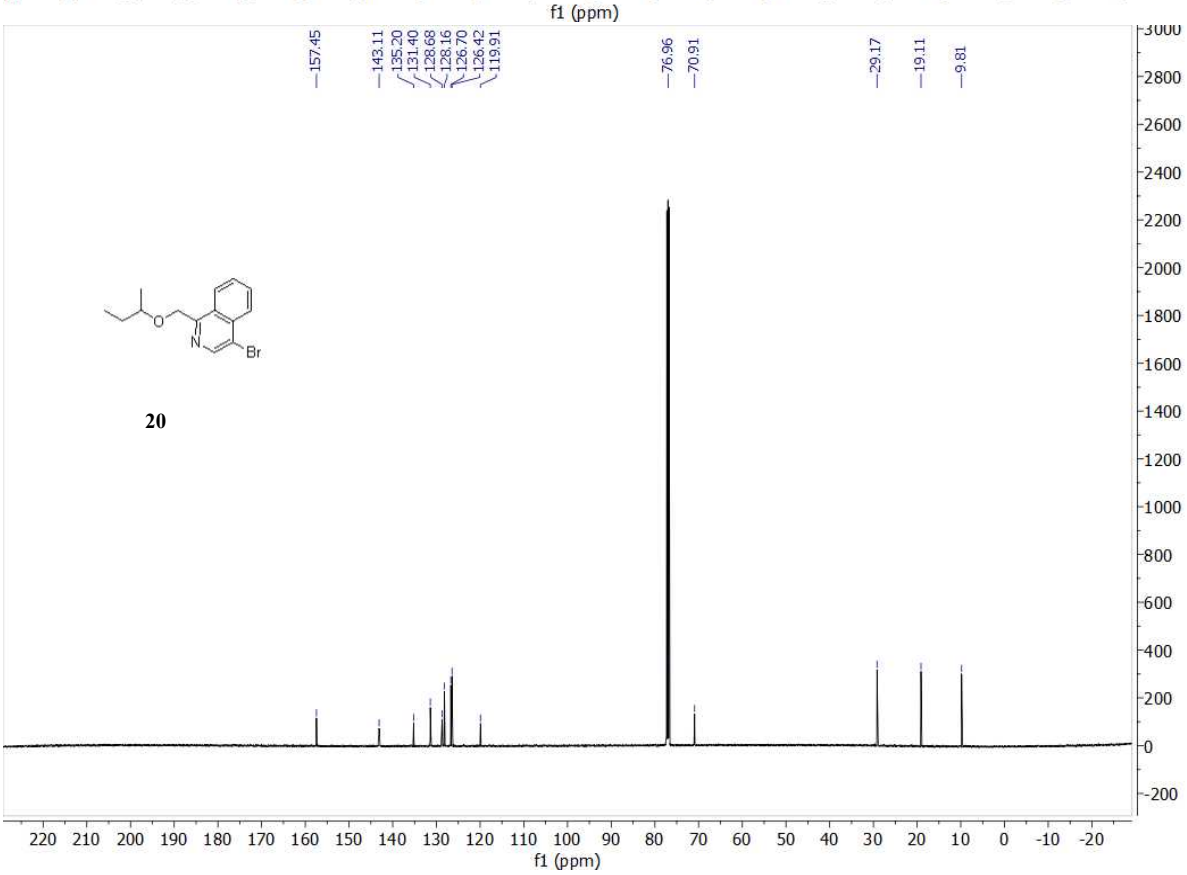
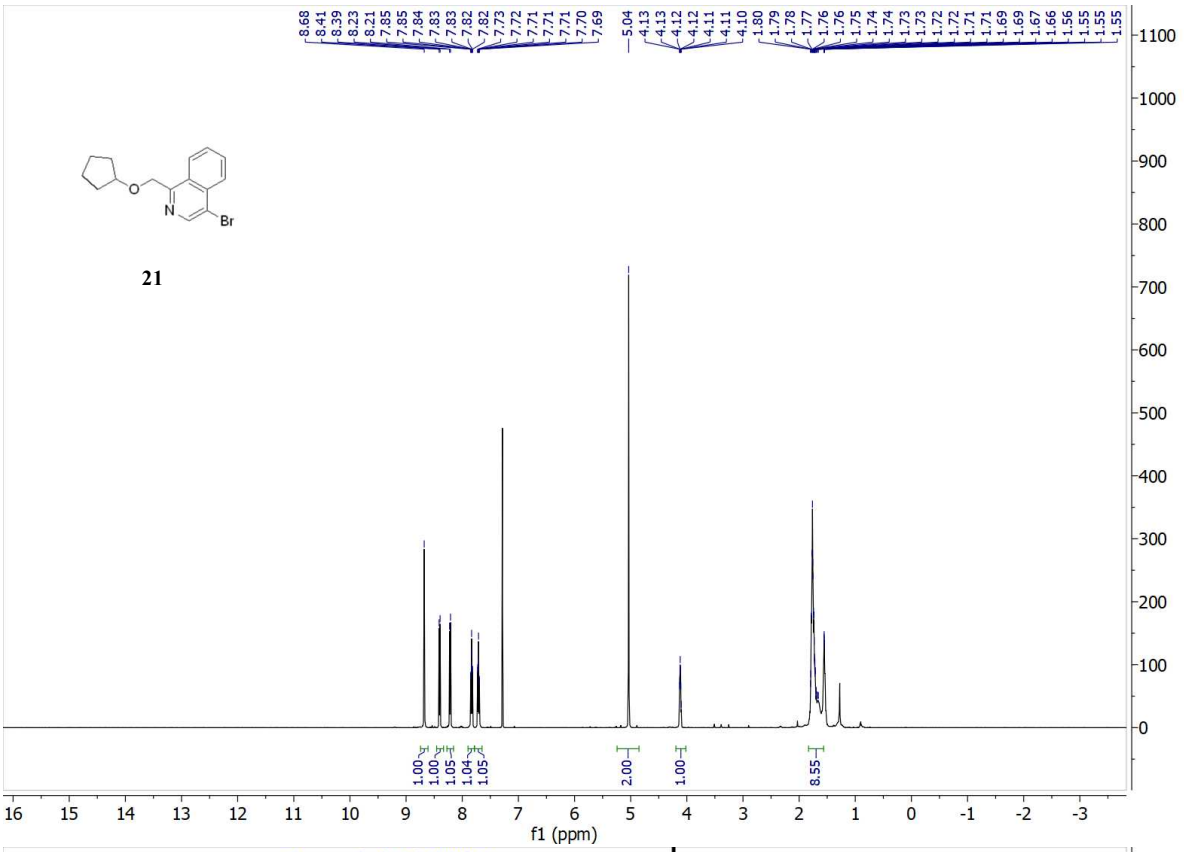
8.44
8.42
8.23
8.21
7.85
7.85
7.83
7.83
7.83
7.82
7.81
7.73
7.72
7.71
7.71
7.71
7.71
7.69
7.69
5.13
5.11
5.05
5.02
5.02
3.59
3.57
3.56
3.55
1.66
1.65
1.64
1.63
1.62
1.62
1.60
1.60
1.54
1.53
1.52
1.51
1.50
1.50
1.48
1.24
1.23
1.22
1.22
0.89
0.87
0.87
0.86
1.01
1.01
1.02
1.01
1.02
2.00
1.00
1.01
1.02
3.01
3.00
f1 (ppm)

20


157.45
143.11
135.20
131.40
128.68
128.16
126.70
126.42
119.91
76.96
70.91
29.17
19.11
9.81
f1 (ppm)

20


8.68
8.41
8.39
8.23
8.21
7.85
7.85
7.84
7.83
7.83
7.82
7.82
7.73
7.72
7.71
7.71
7.71
7.70
7.69
5.04
4.13
4.13
4.12
4.12
4.11
4.11
4.10
1.80
1.79
1.78
1.77
1.76
1.76
1.75
1.74
1.74
1.73
1.73
1.72
1.72
1.71
1.71
1.69
1.69
1.67
1.66
1.56
1.55
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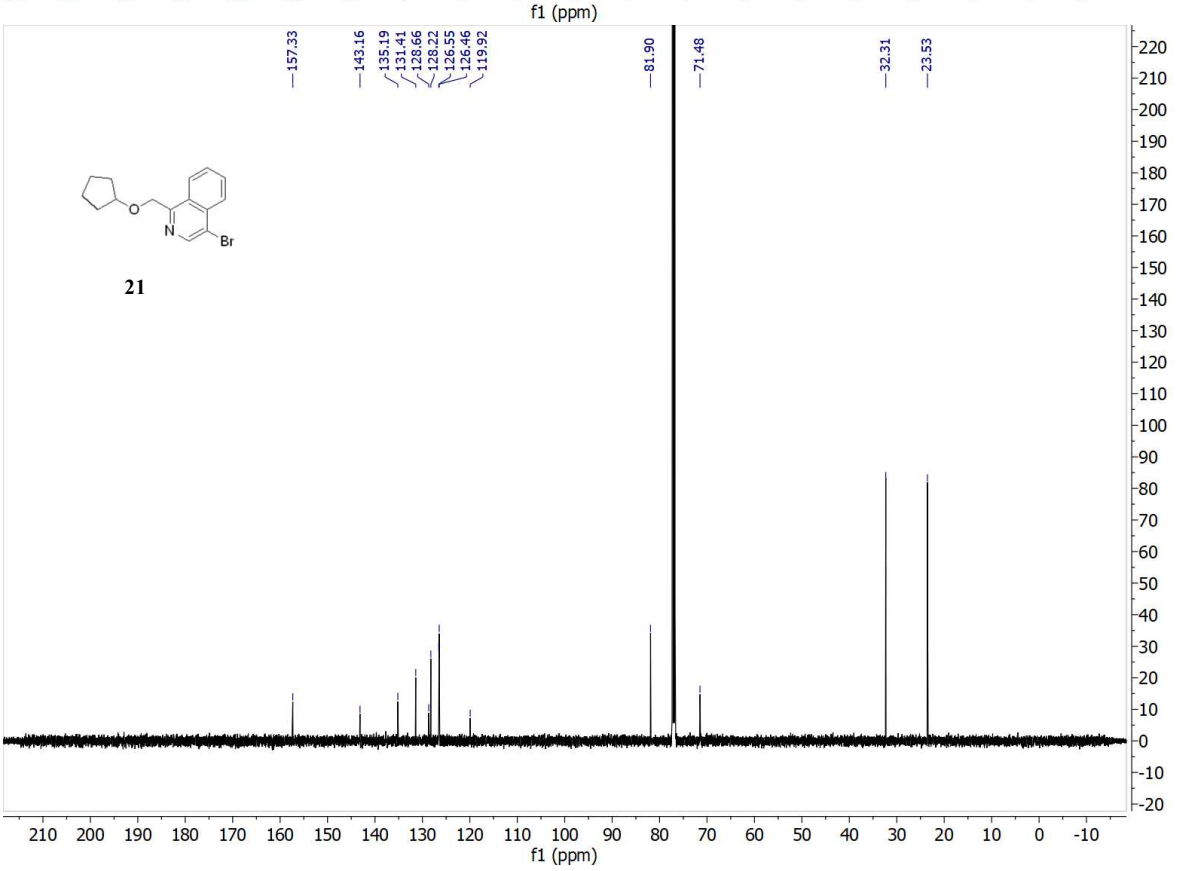
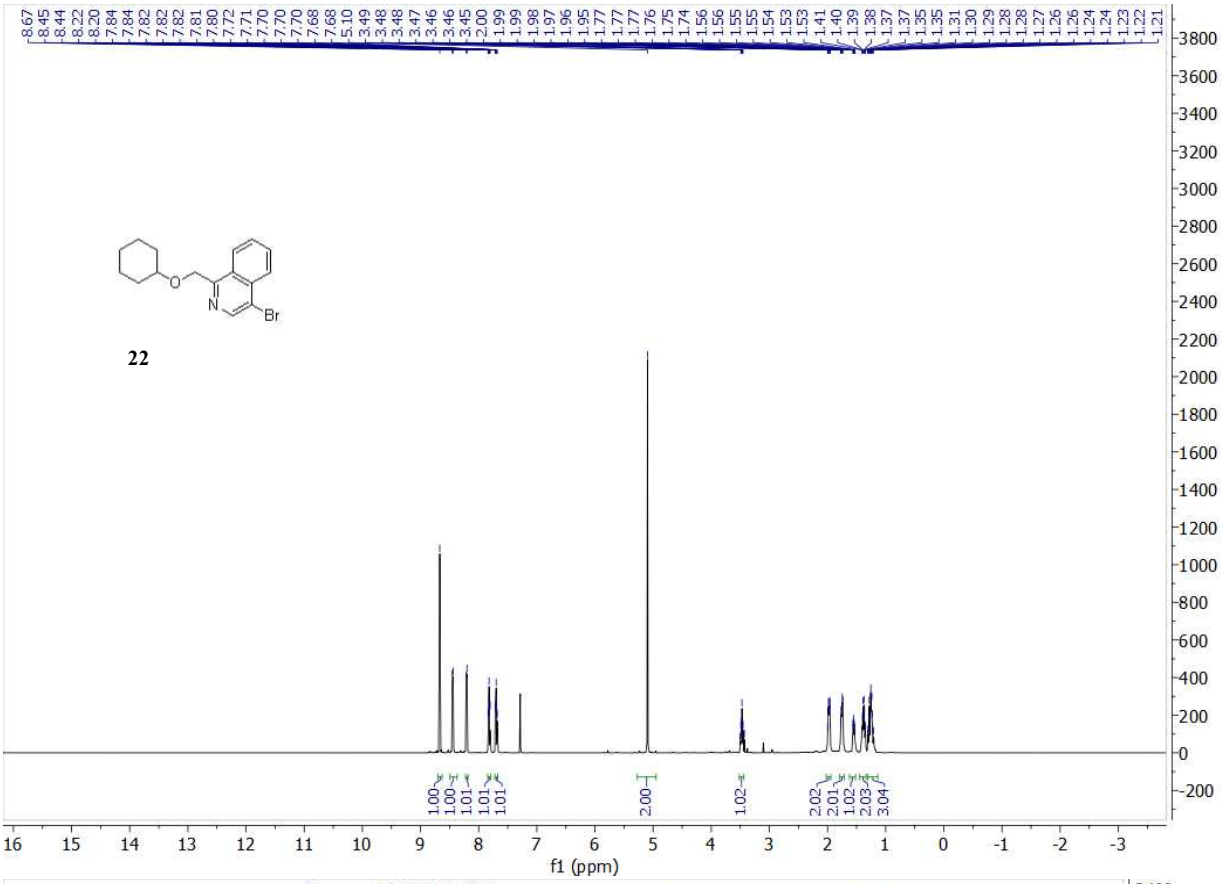
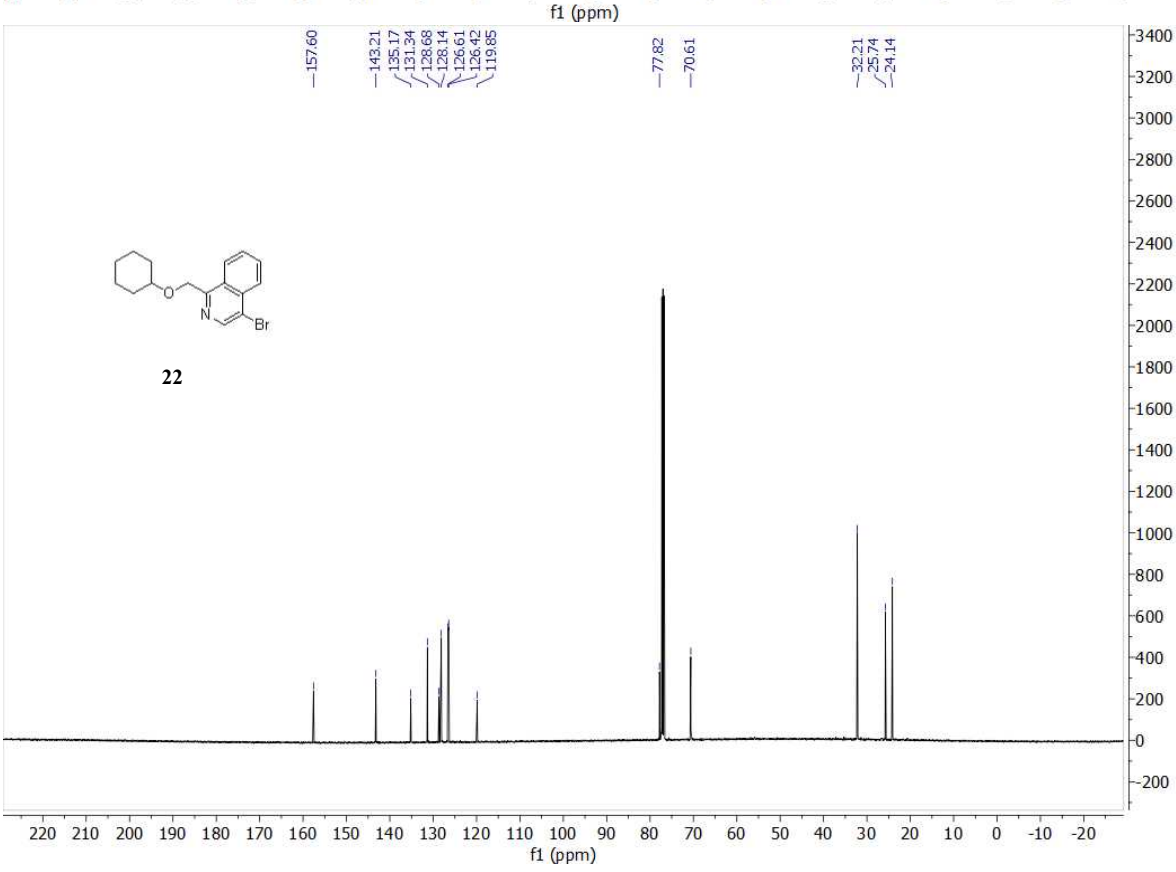
1.05
2.00
1.00
8.55
f1 (ppm)

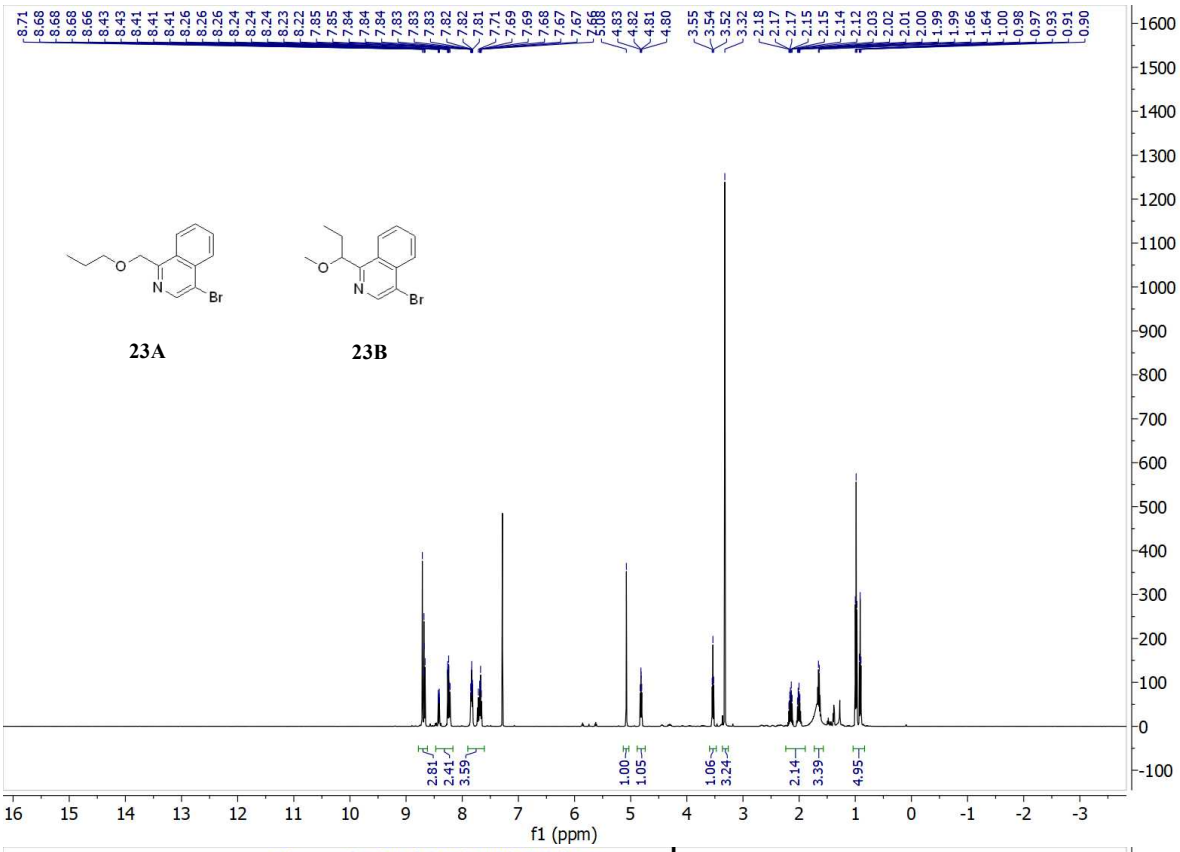
21

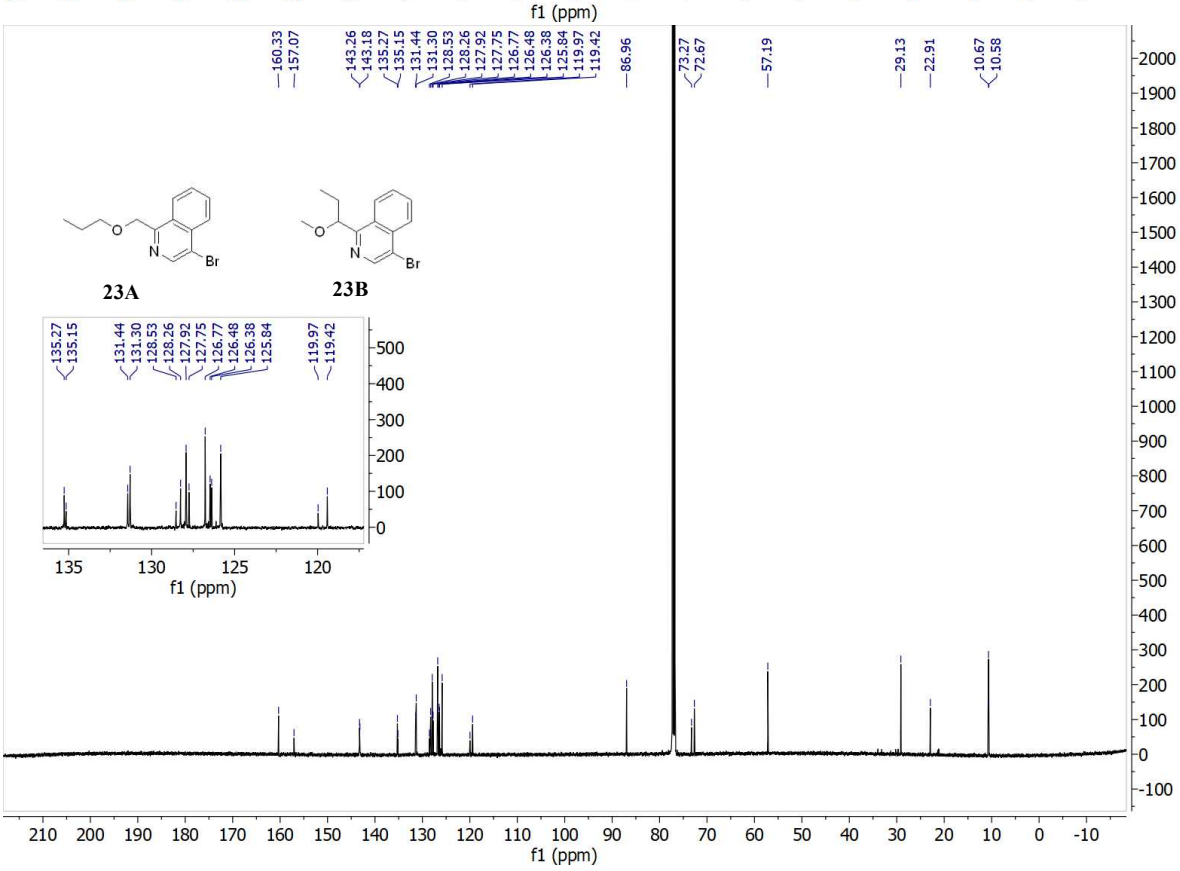

157.33
143.16
135.19
131.41
128.66
128.22
126.55
126.46
119.92
81.90
71.48
32.31
23.53
f1 (ppm)

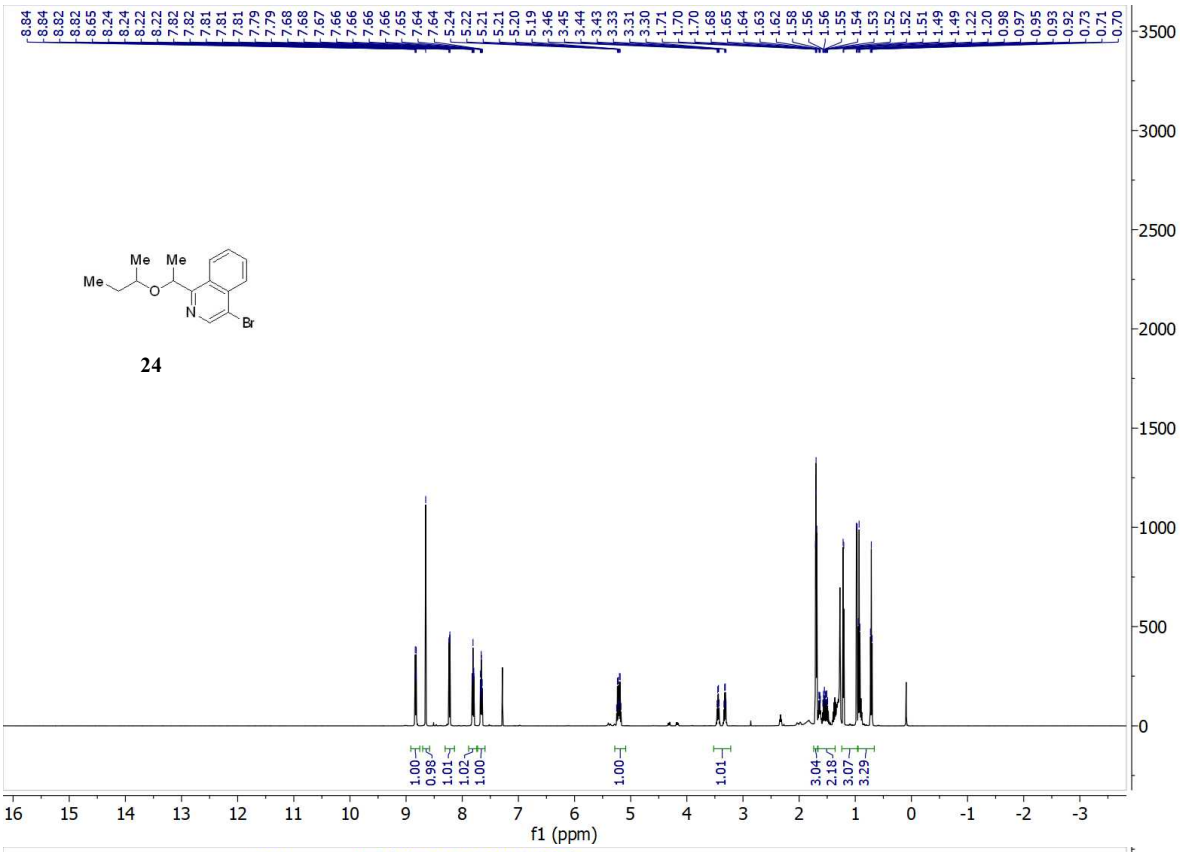
21


8.67 8.45 8.44 8.22 8.20 7.84 7.84 7.82 7.82 7.82 7.81 7.80 7.72 7.71 7.70 7.70 7.70 7.68 7.68 5.10 3.49 3.48 3.48 3.47 3.46 3.46 3.45 2.00 1.99 1.99 1.98 1.97 1.96 1.95 1.77 1.77 1.77 1.76 1.75 1.74 1.56 1.56 1.55 1.55 1.54 1.53 1.53 1.41 1.40 1.39 1.38 1.37 1.37 1.35 1.35 1.31 1.30 1.29 1.28 1.28 1.27 1.26 1.24 1.24 1.23 1.22 1.21
O
N
Br
22
1.00 1.00 1.01 1.01 1.01 2.00 1.02 2.02 2.01 1.02 2.03 3.04
f1 (ppm)

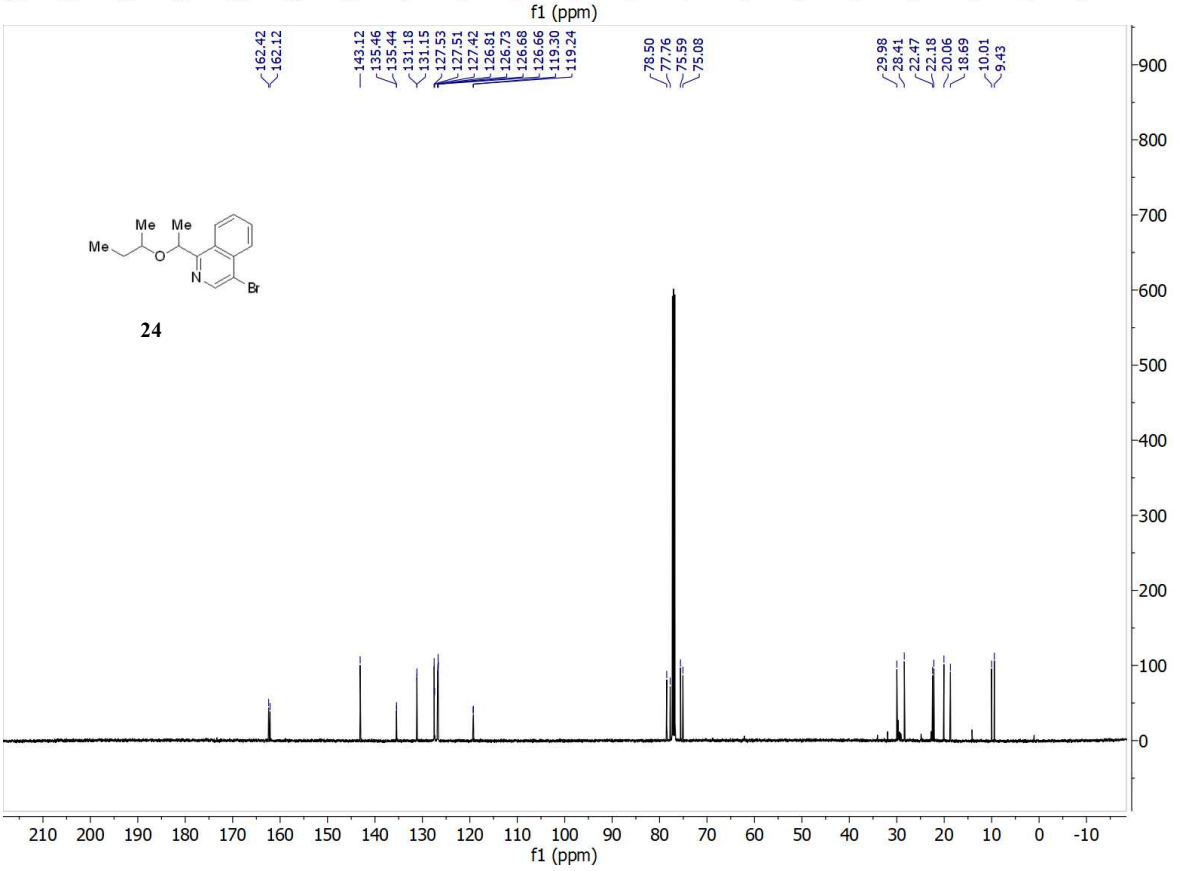

157.60 143.21 135.17 131.34 128.68 128.14 126.61 126.42 119.85 77.82 70.61 32.21 25.74 24.14
O
N
Br
22
f1 (ppm)


23A
23B
f1 (ppm)

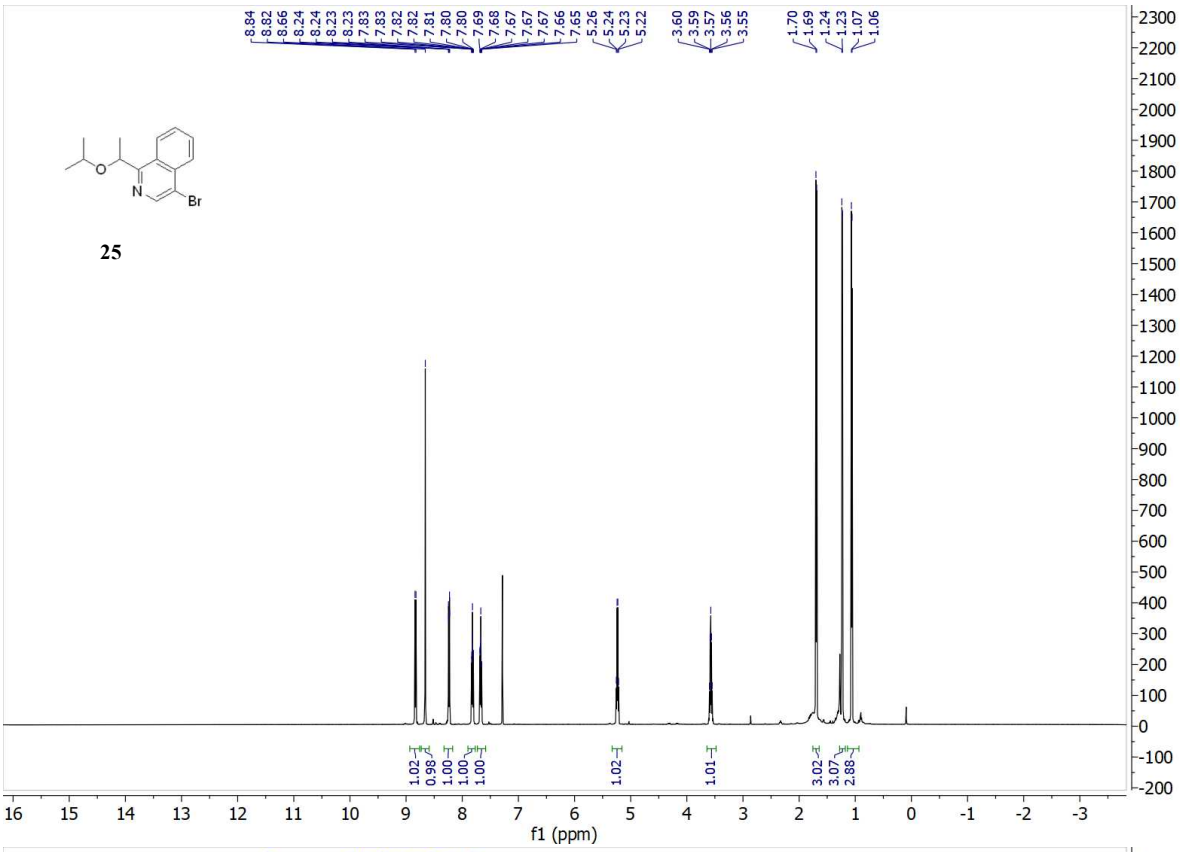

23A
23B
f1 (ppm)
f1 (ppm)



24



24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7.83
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7.82
7.82
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7.80
7.80
7.69
7.68
7.67
7.67
7.67
7.67
7.66
7.65
5.26
5.24
5.23
5.22
3.60
3.59
3.57
3.56
3.55
1.70
1.69
1.24
1.23
1.07
1.06
O
N
Br
25
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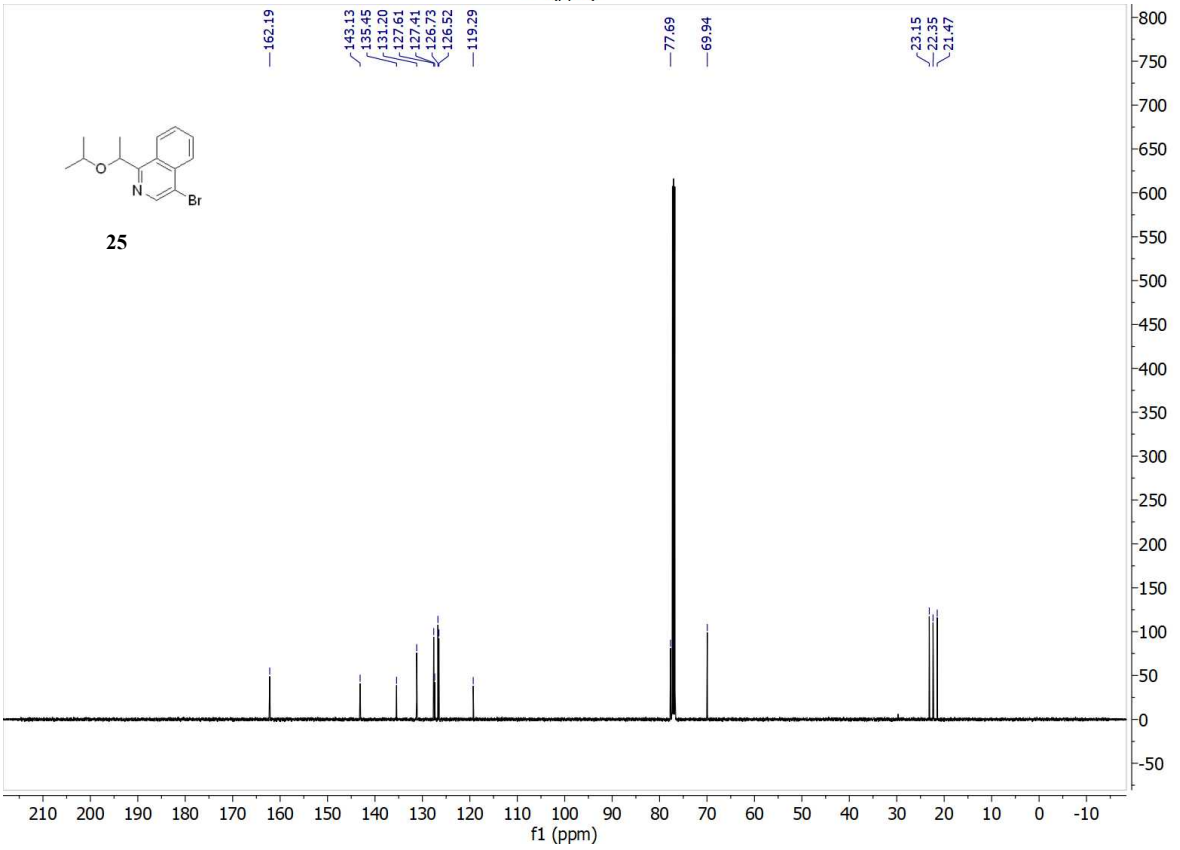
1.00
1.00
1.00
1.02
1.01
3.02
3.07
2.88
f1 (ppm)


162.19
143.13
135.45
131.20
127.61
127.41
126.73
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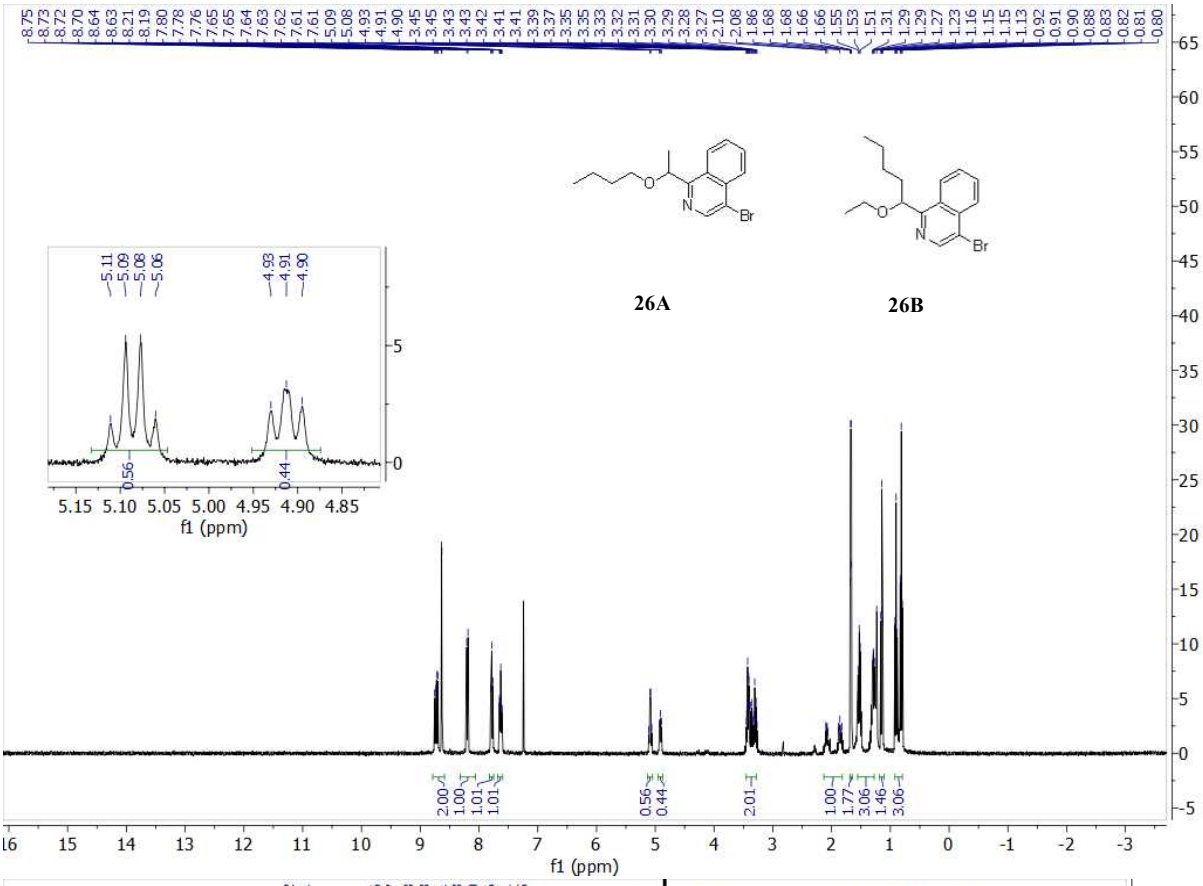
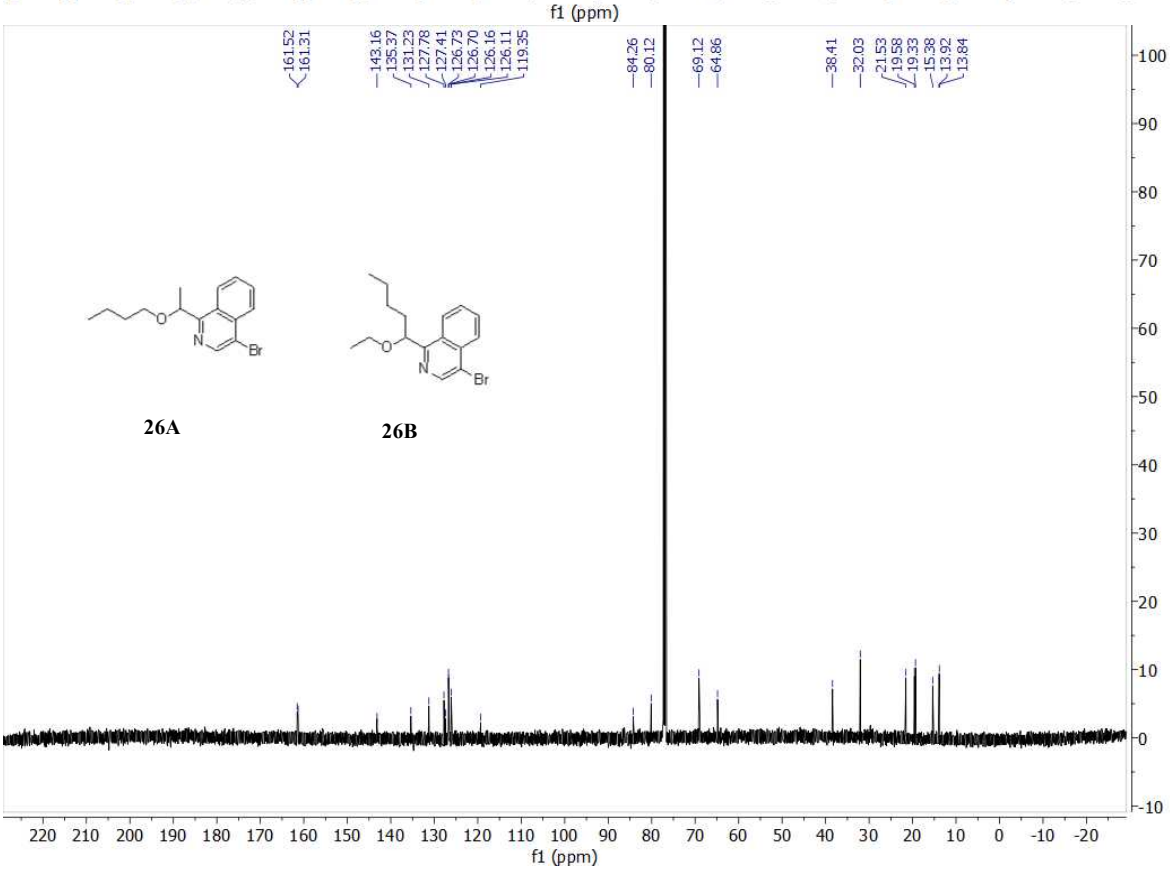
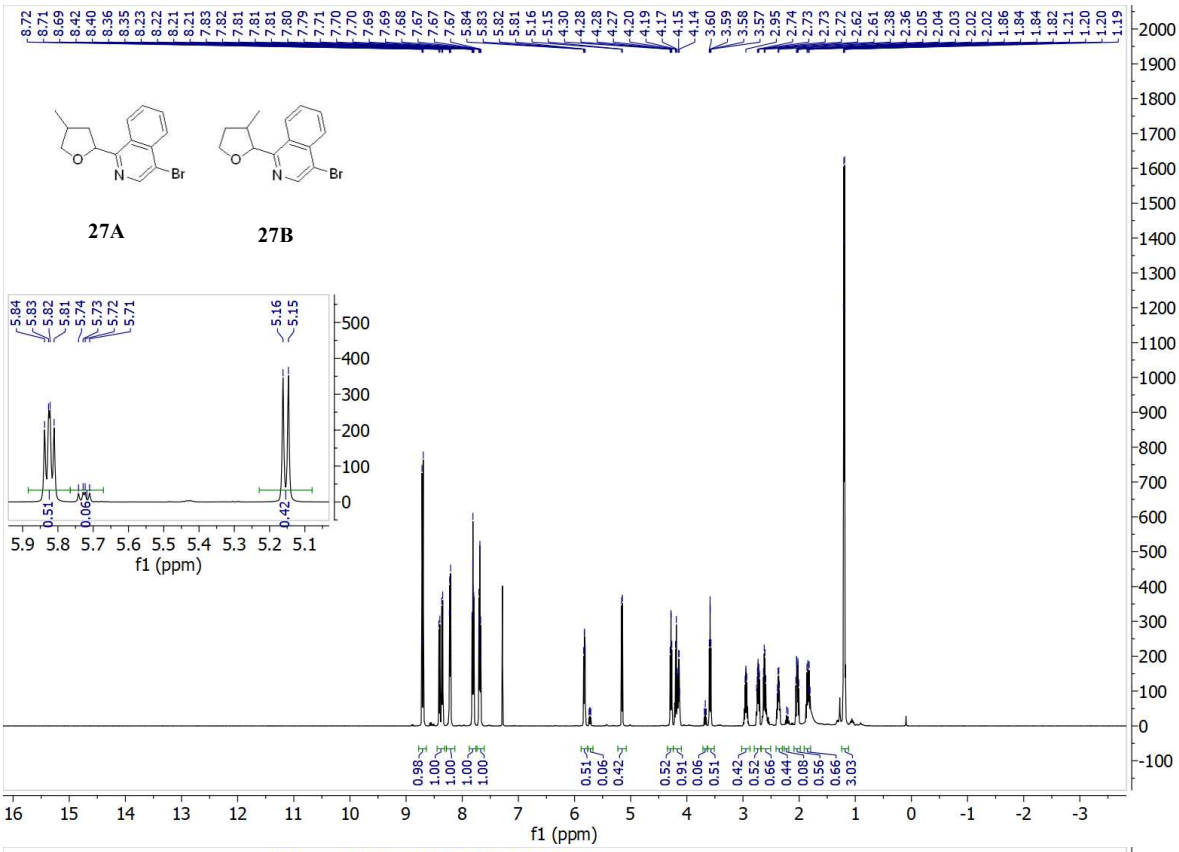
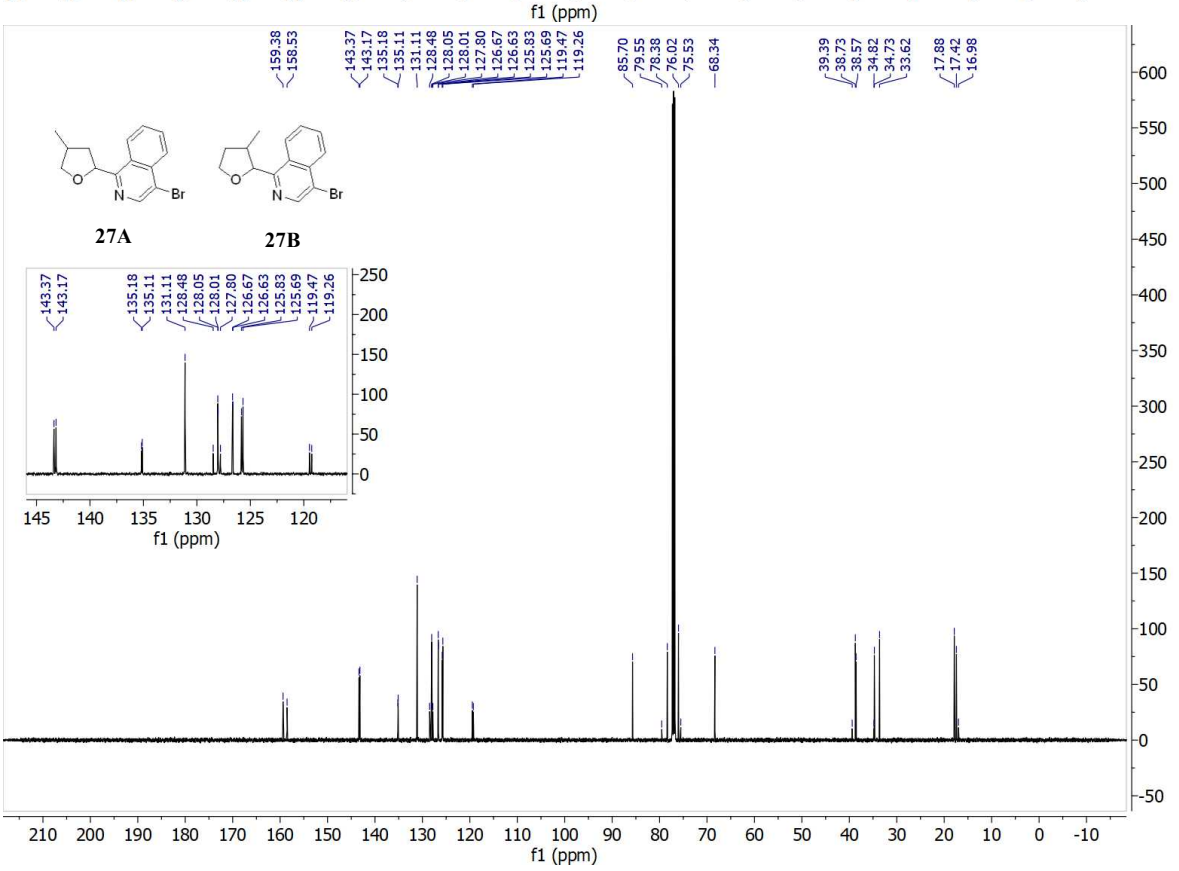
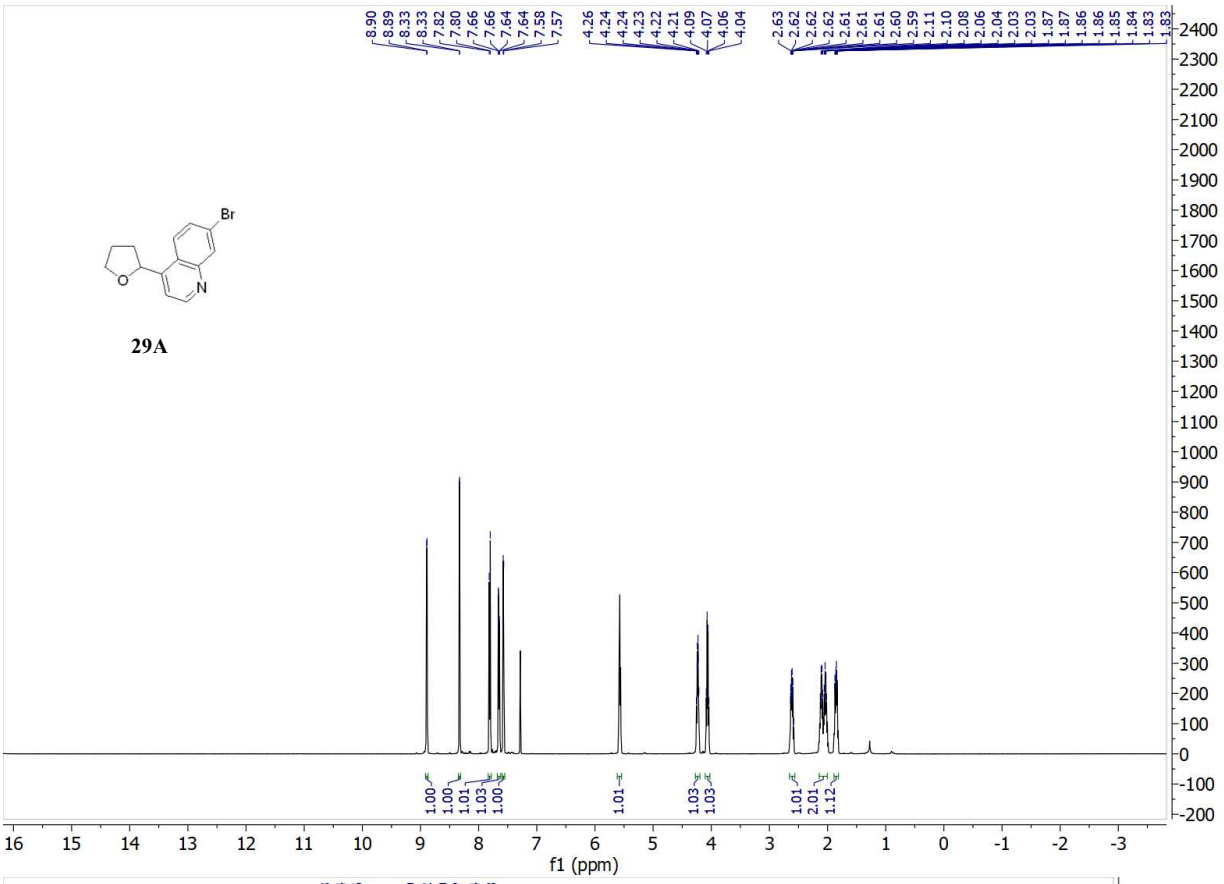
119.29
77.69
69.94
23.15
22.35
21.47
O
N
Br
25
f1 (ppm)


26A
26B
f1 (ppm)


26A
26B
f1 (ppm)


27A
27B
f1 (ppm)


27A
27B
f1 (ppm)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7.82
7.80
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7.66
7.64
7.64
7.58
7.57
4.26
4.24
4.24
4.23
4.22
4.21
4.09
4.07
4.06
4.04
2.63
2.62
2.62
2.62
2.61
2.61
2.61
2.60
2.59
2.11
2.10
2.08
2.06
2.04
2.03
2.03
1.87
1.87
1.86
1.86
1.85
1.84
1.83
1.83
Br
O
N
29A
1.00
1.00
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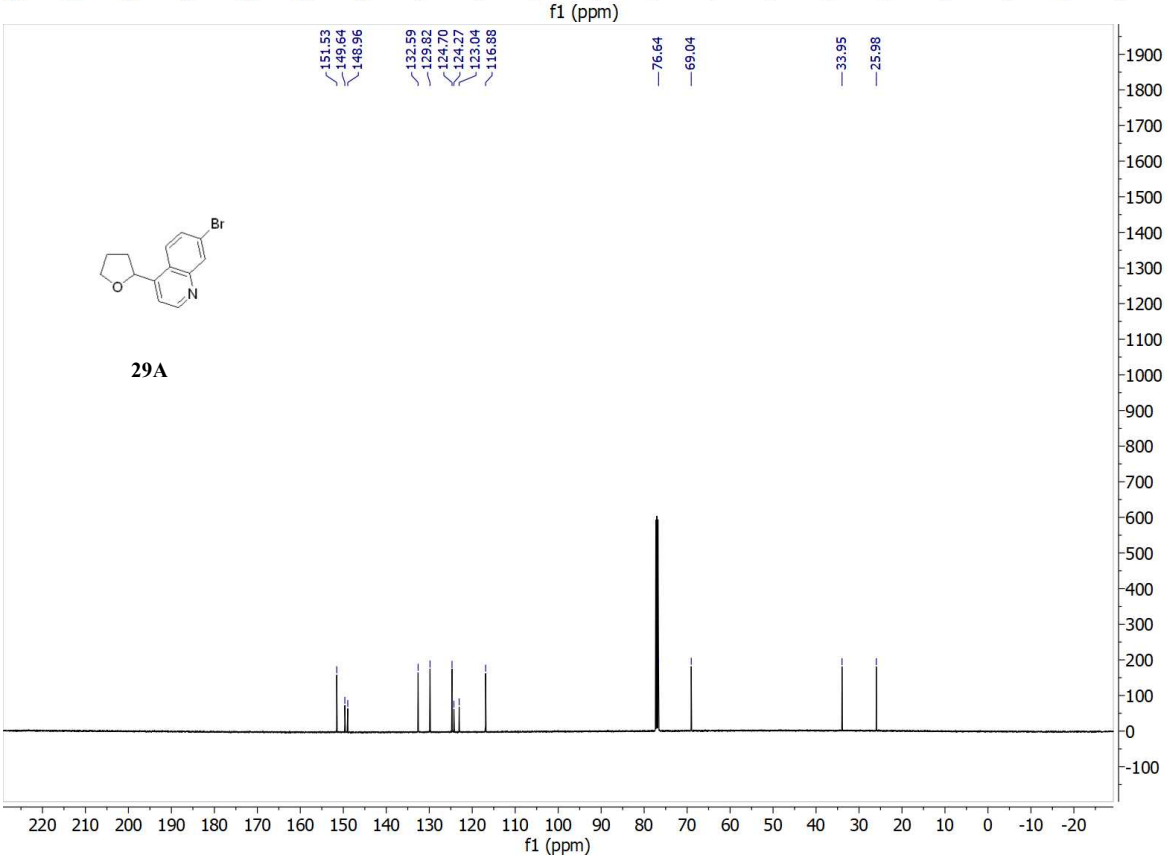
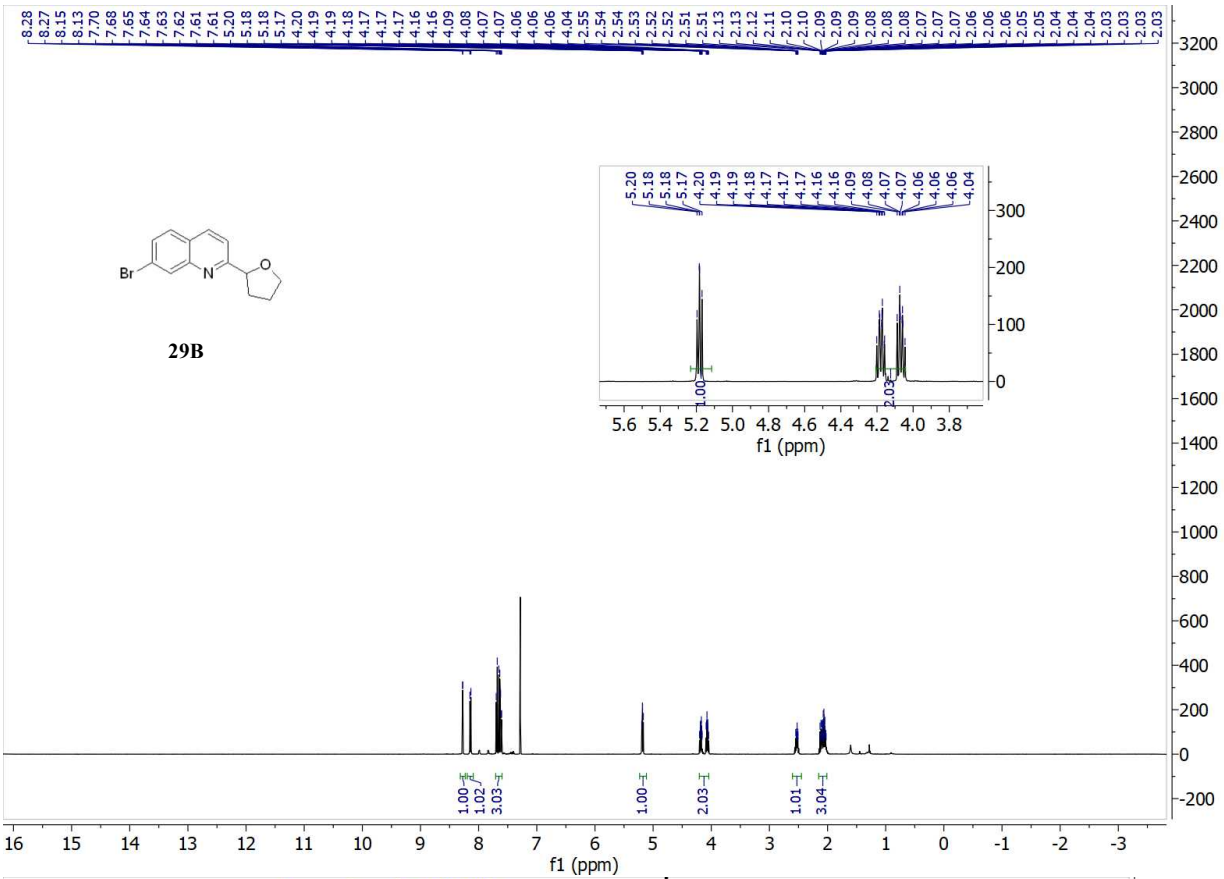
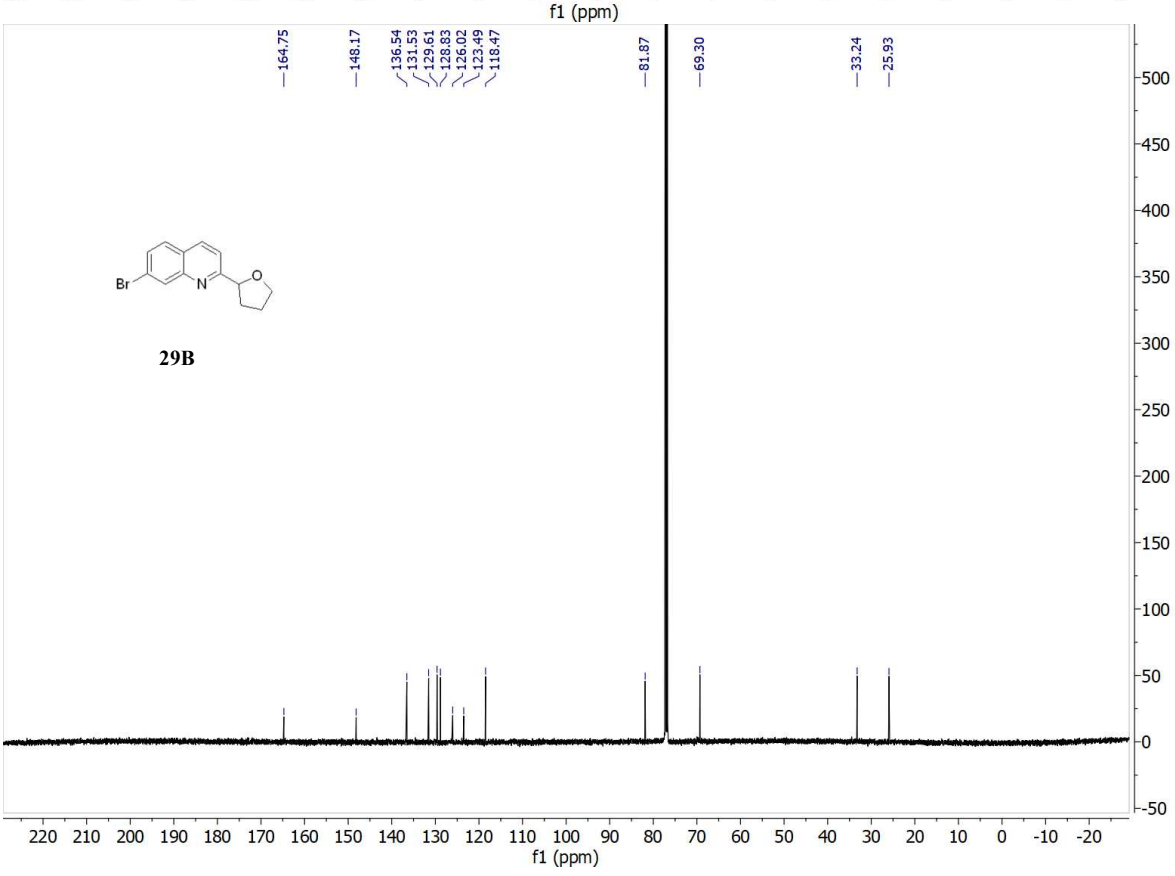
1.03
1.00
1.01
1.03
1.03
1.01
2.01
1.12
f1 (ppm)


151.53
149.64
148.96
132.59
129.82
124.70
124.27
123.04
116.88
76.64
69.04
33.95
25.98
Br
O
N
29A
f1 (ppm)


Br
N
O
29B
f1 (ppm)


164.75
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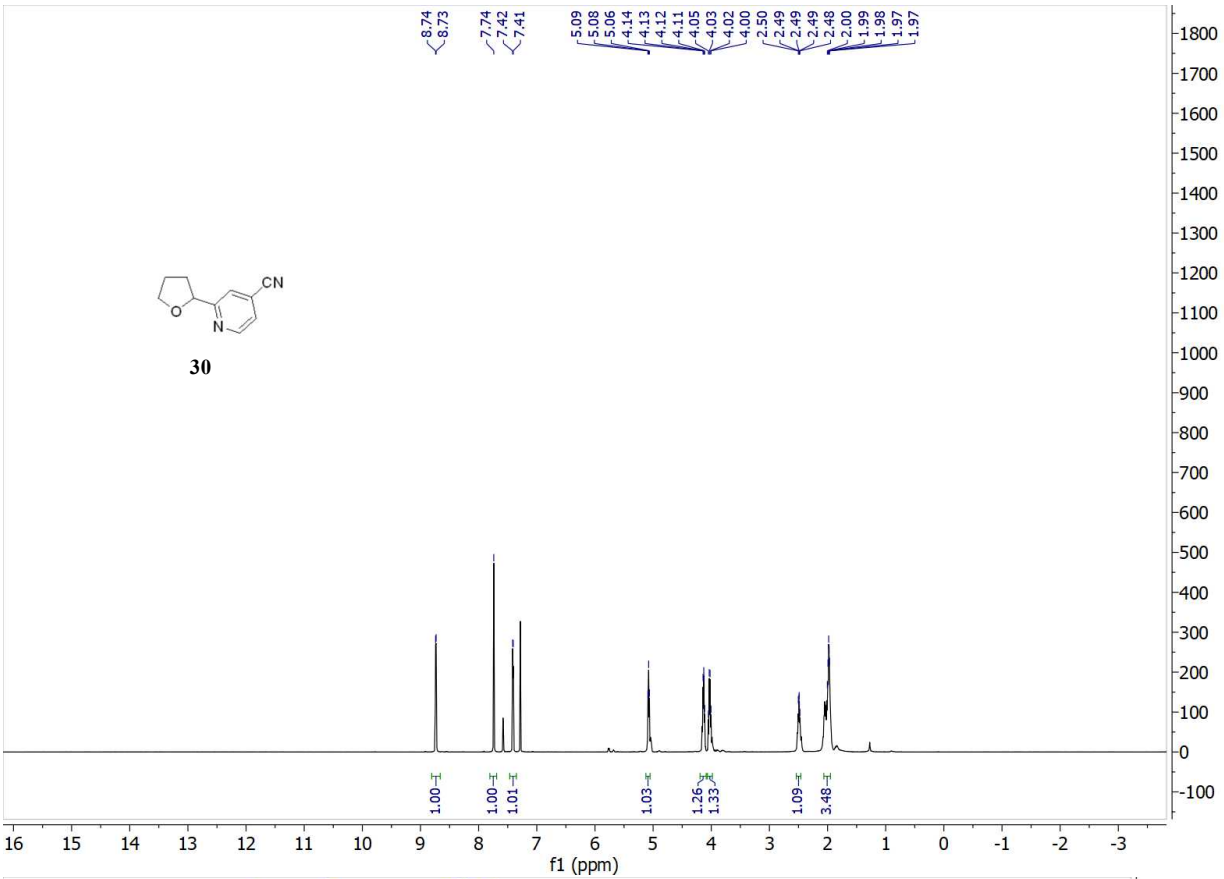
136.54
131.53
129.61
128.83
126.02
123.49
118.47
81.87
69.30
33.24
25.93
Br
N
O
29B
f1 (ppm)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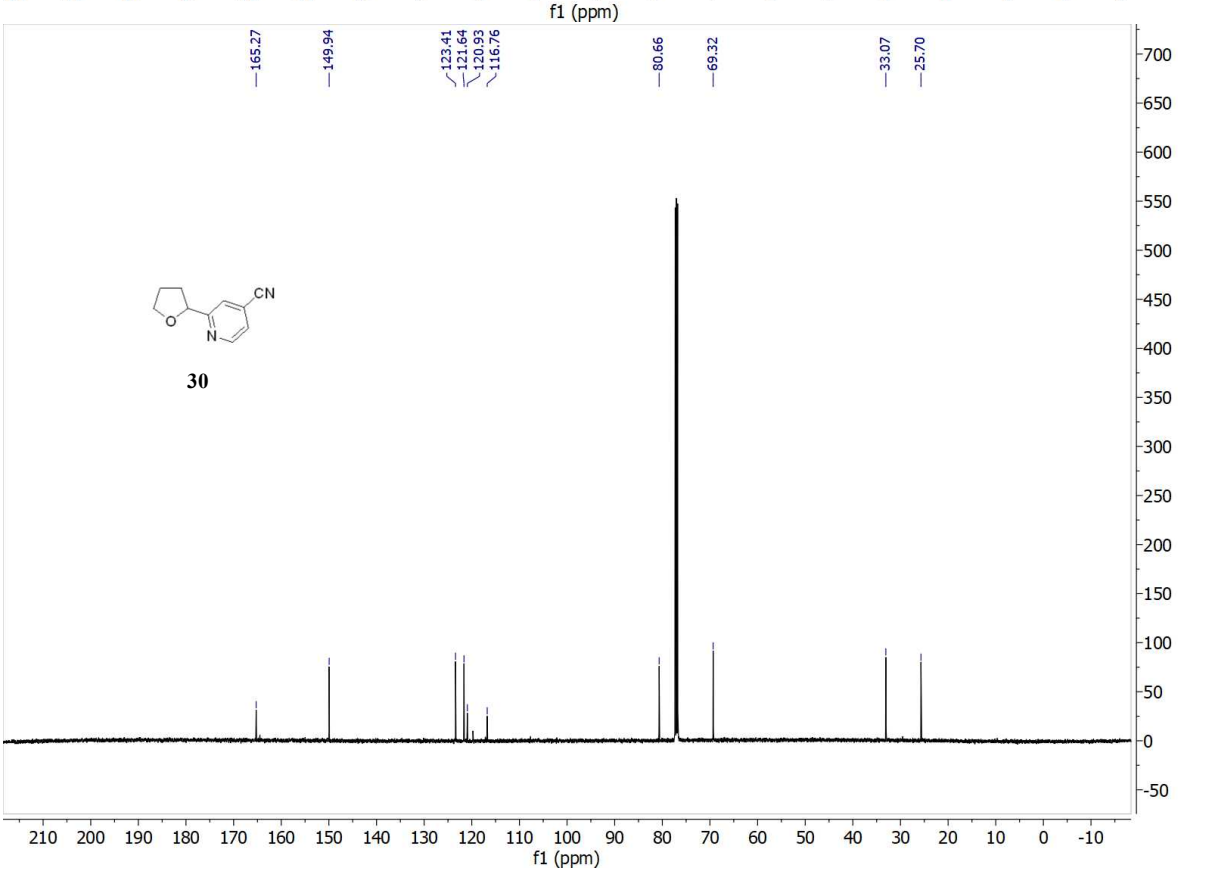
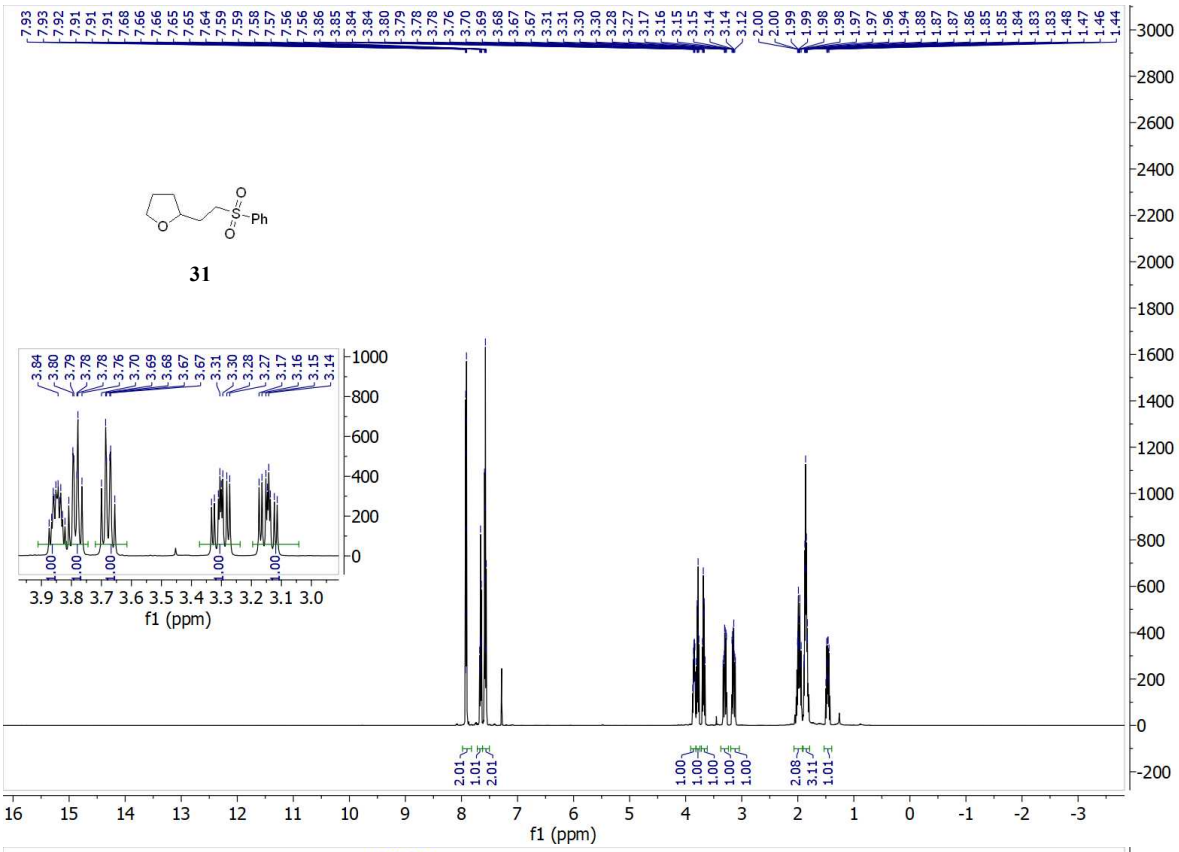
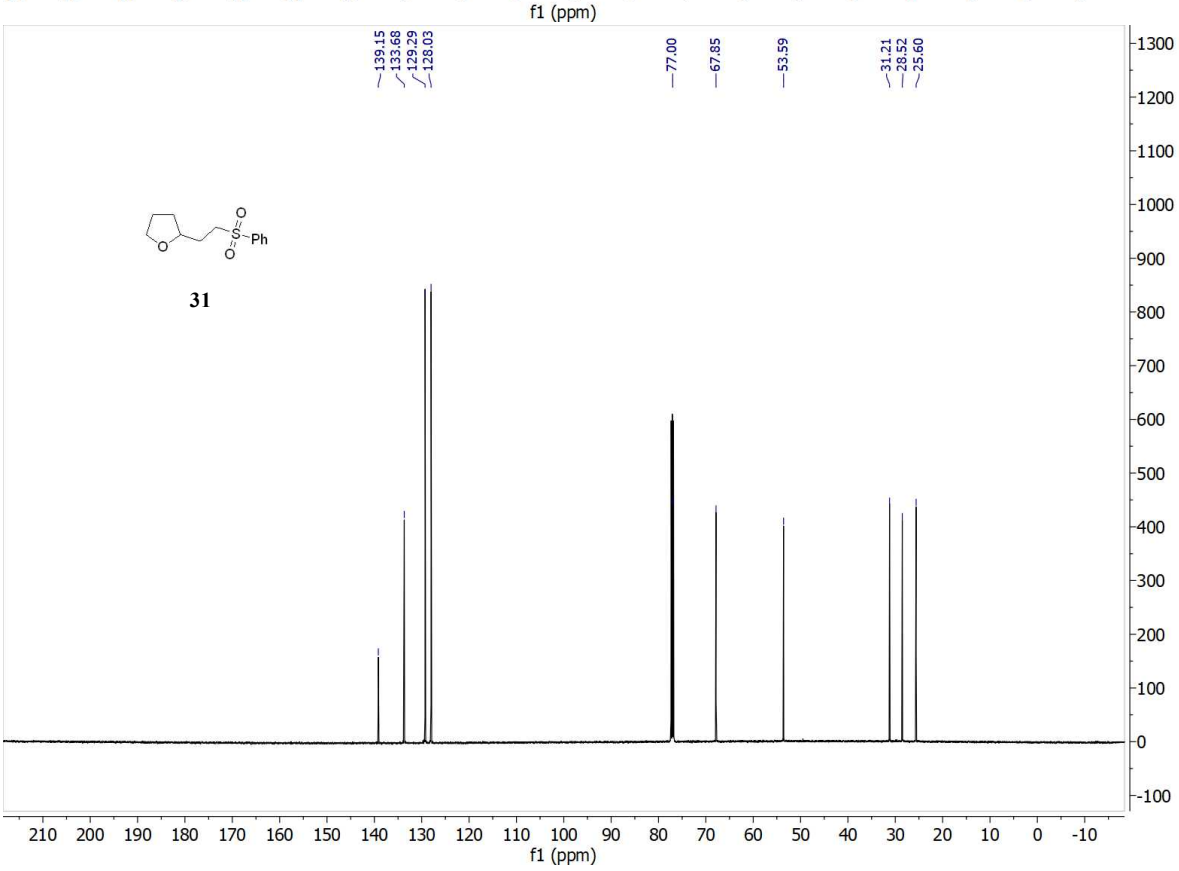
7.74
7.42
7.41
5.09
5.08
5.06
4.14
4.13
4.12
4.11
4.05
4.03
4.02
4.00
2.50
2.49
2.49
2.49
2.48
2.00
1.99
1.98
1.97
1.97
CN
O
N
1.00
1.00
1.01
1.03
1.26
1.33
1.09
3.48
f1 (ppm)

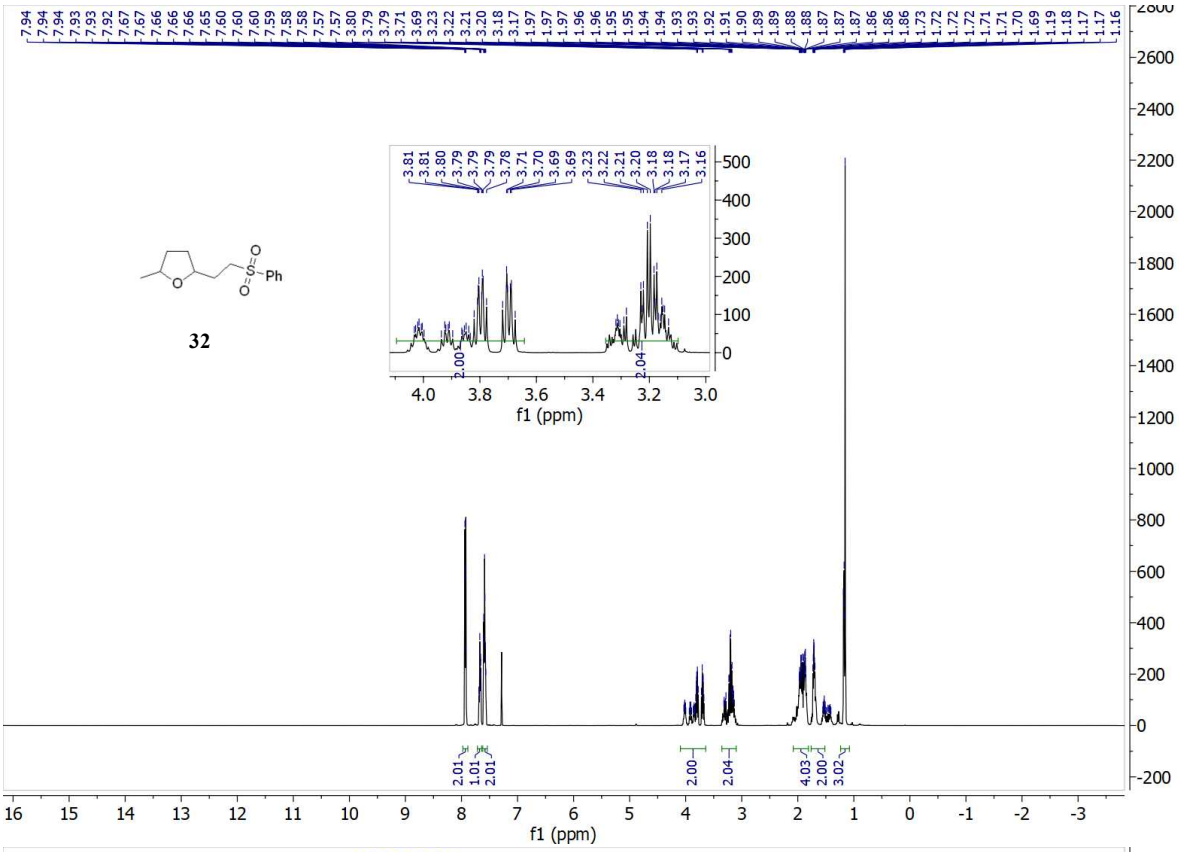
30

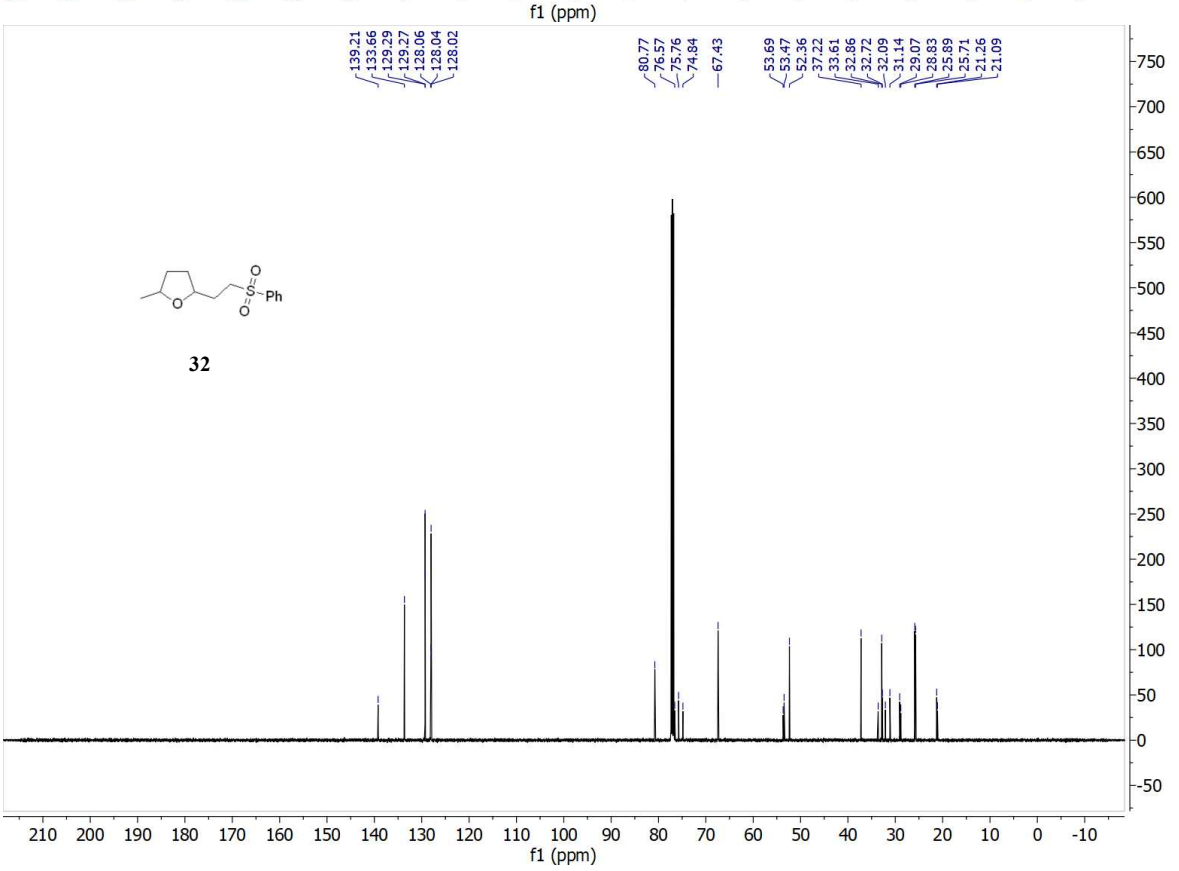

165.27
149.94
123.41
121.64
120.93
116.76
80.66
69.32
33.07
25.70
CN
O
N
f1 (ppm)

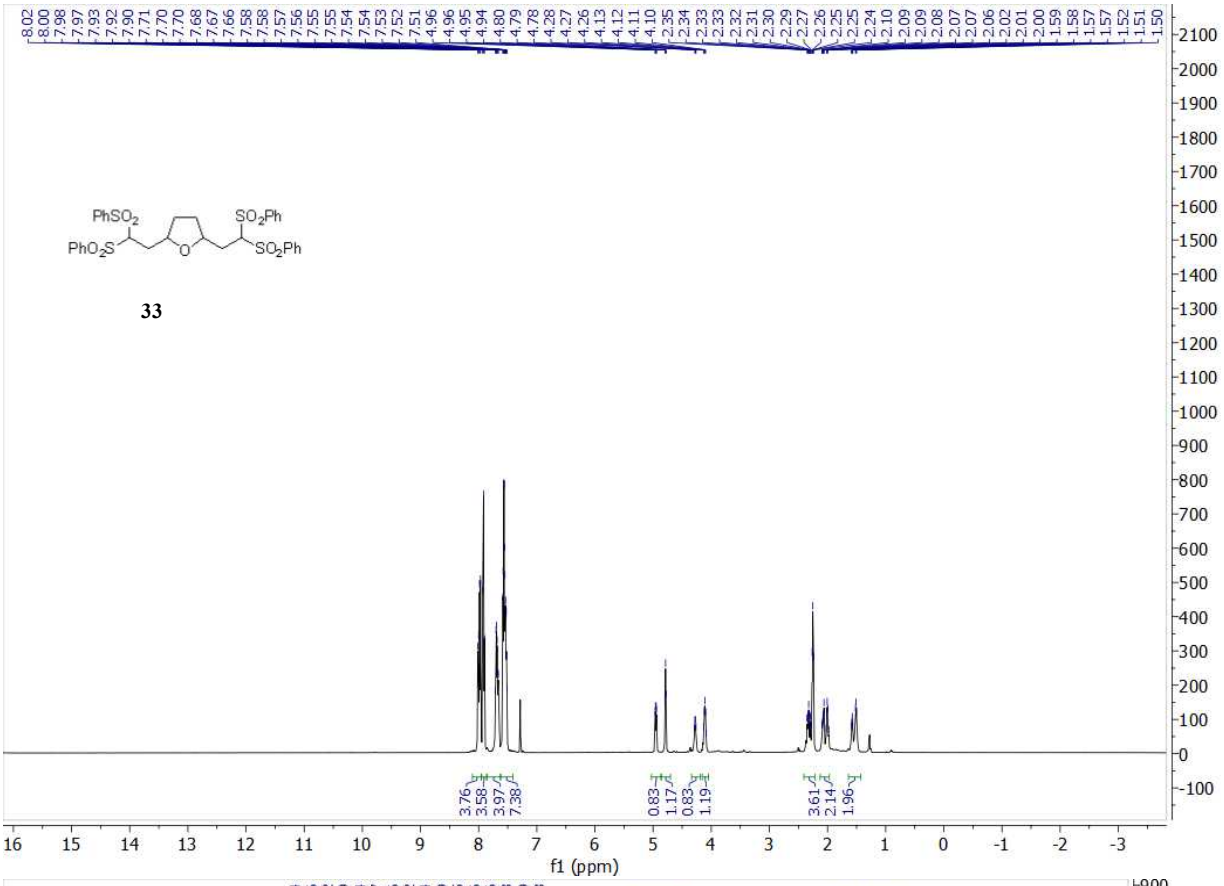
30


Ph
31
f1 (ppm)

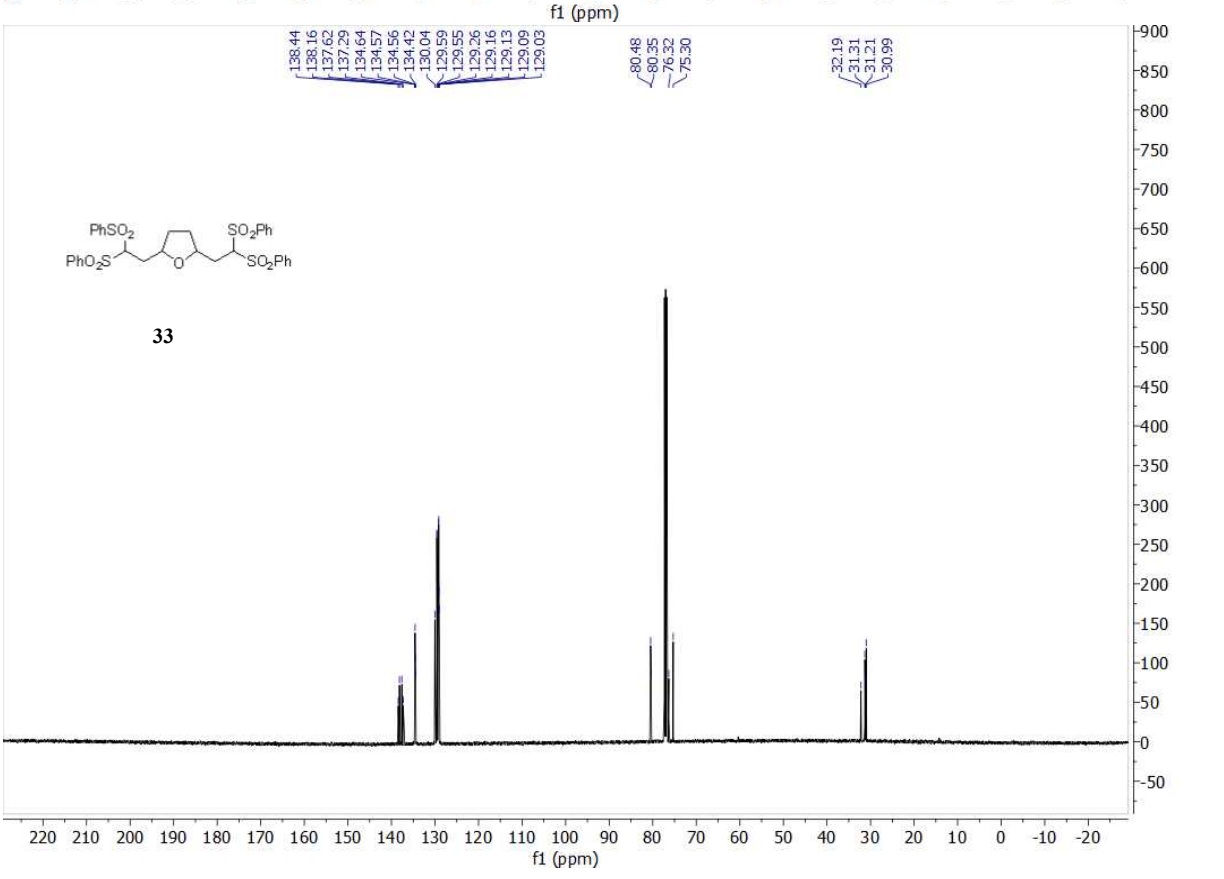

Ph
31
f1 (ppm)


32
f1 (ppm)


32
f1 (ppm)


PhSO2
SO2Ph
PhO2S
SO2Ph
O

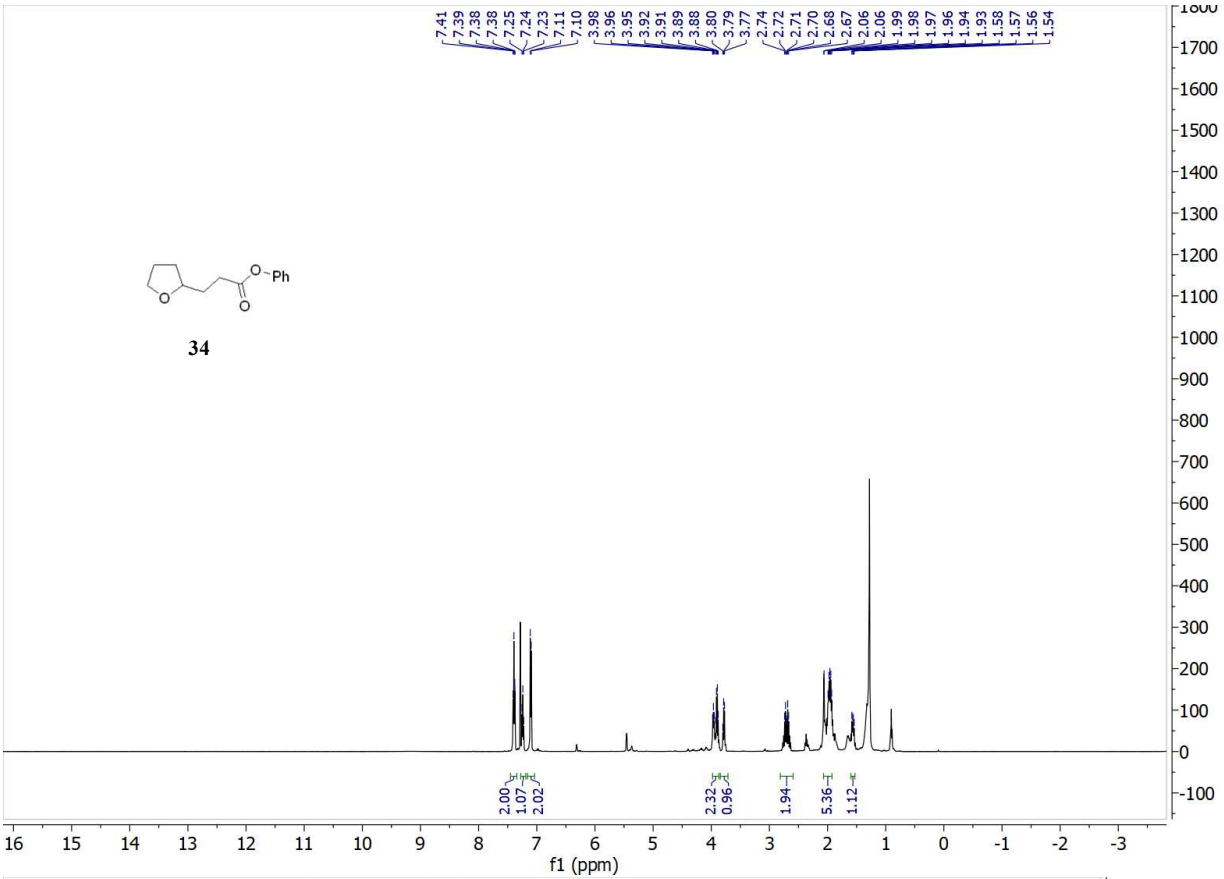
33


f1 (ppm)

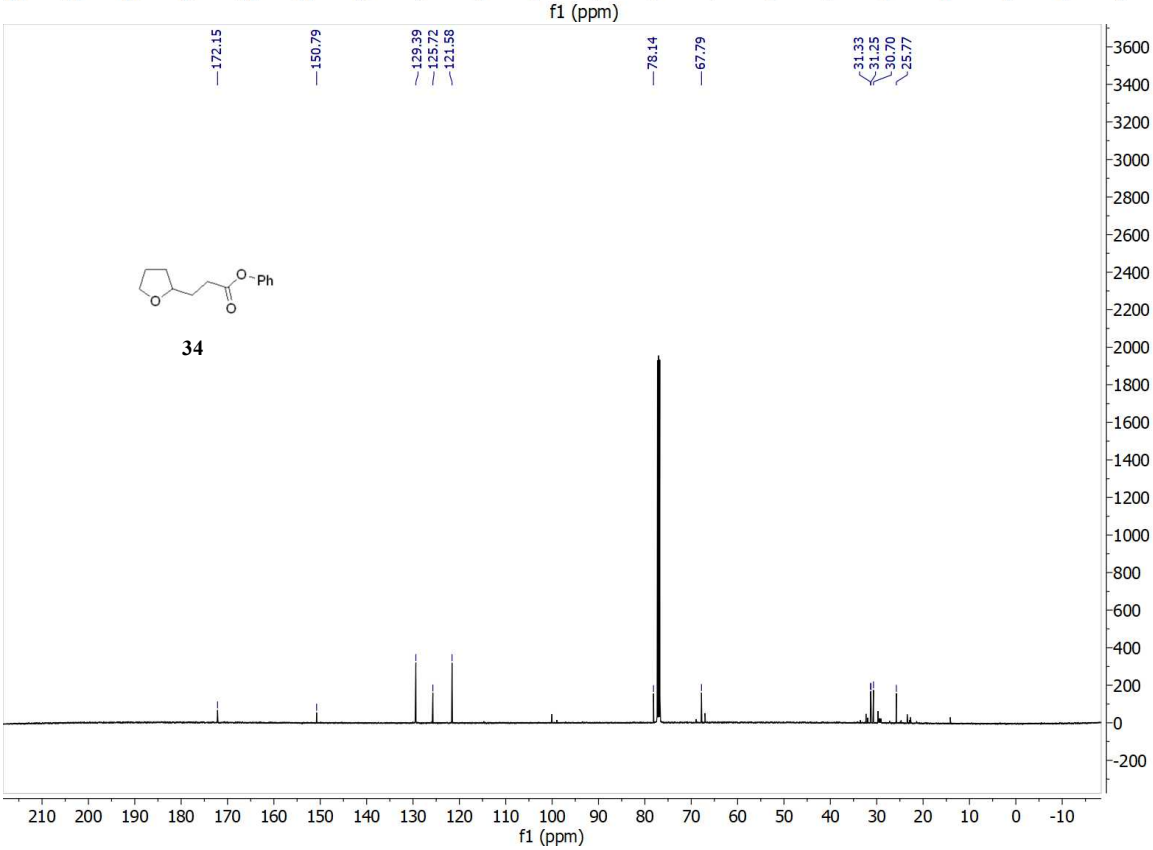
PhSO2
SO2Ph
PhO2S
SO2Ph
O

33

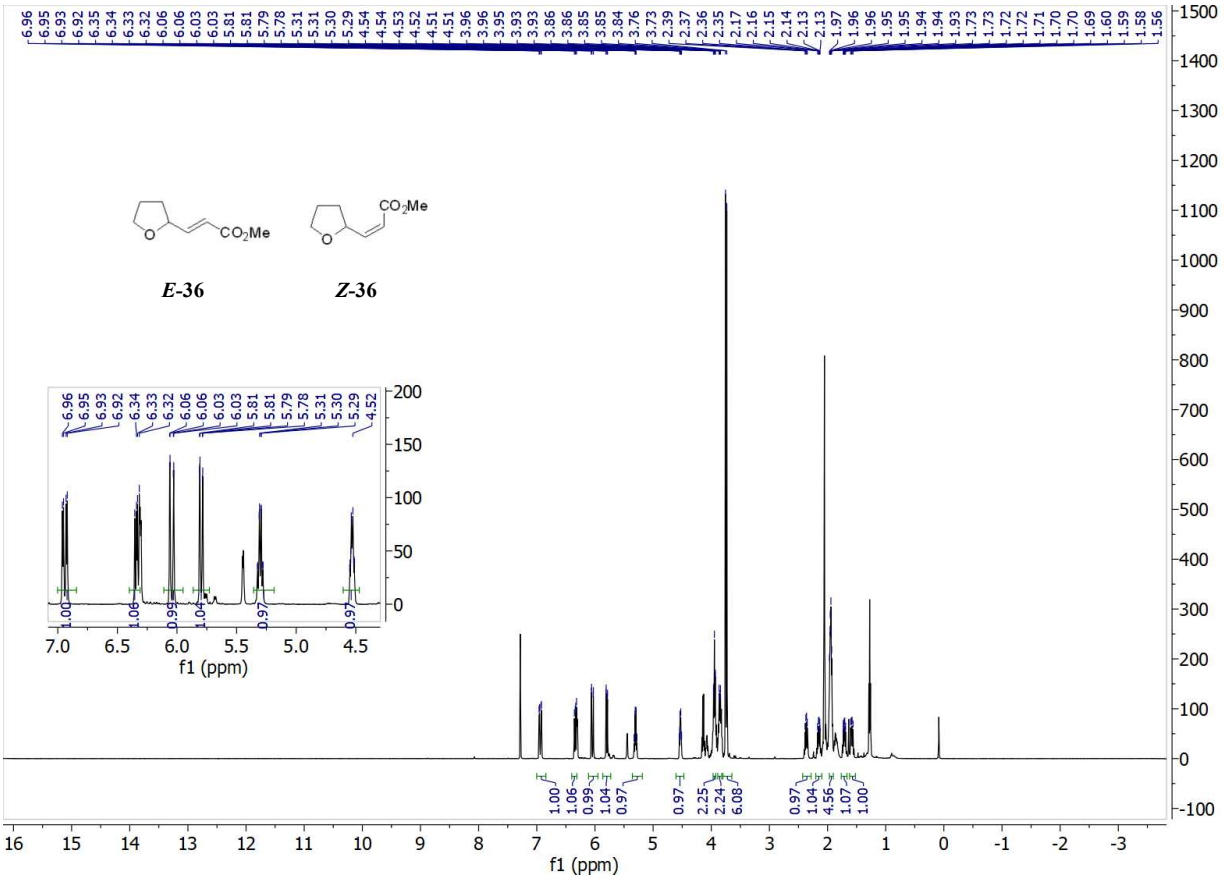
f1 (ppm)

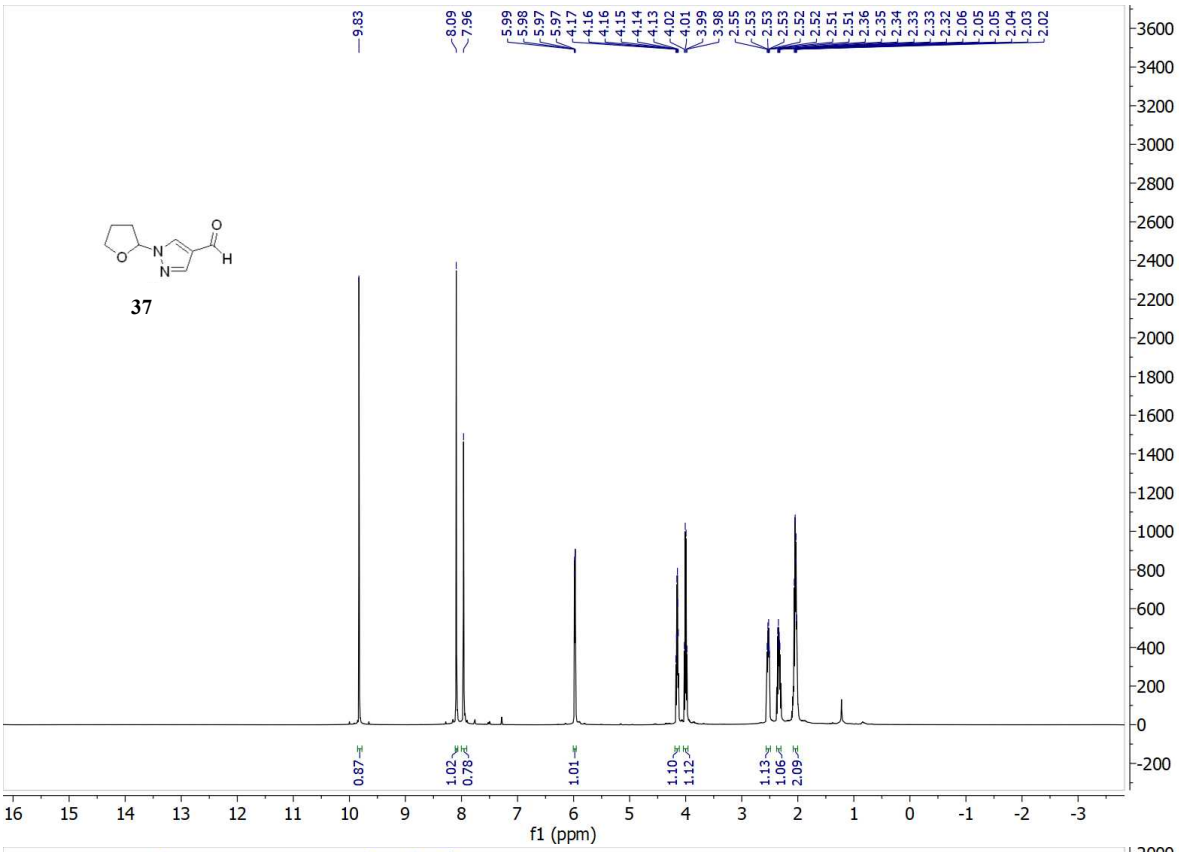

7.41
7.39
7.38
7.38
7.25
7.24
7.23
7.11
7.10
3.98
3.96
3.95
3.92
3.91
3.89
3.88
3.80
3.79
3.77
2.74
2.72
2.71
2.70
2.68
2.67
2.06
2.06
1.99
1.98
1.97
1.96
1.94
1.93
1.58
1.57
1.56
1.54
Ph
O
O
2.00
1.07
2.02
2.32
0.96
1.94
5.36
1.12
f1 (ppm)

34

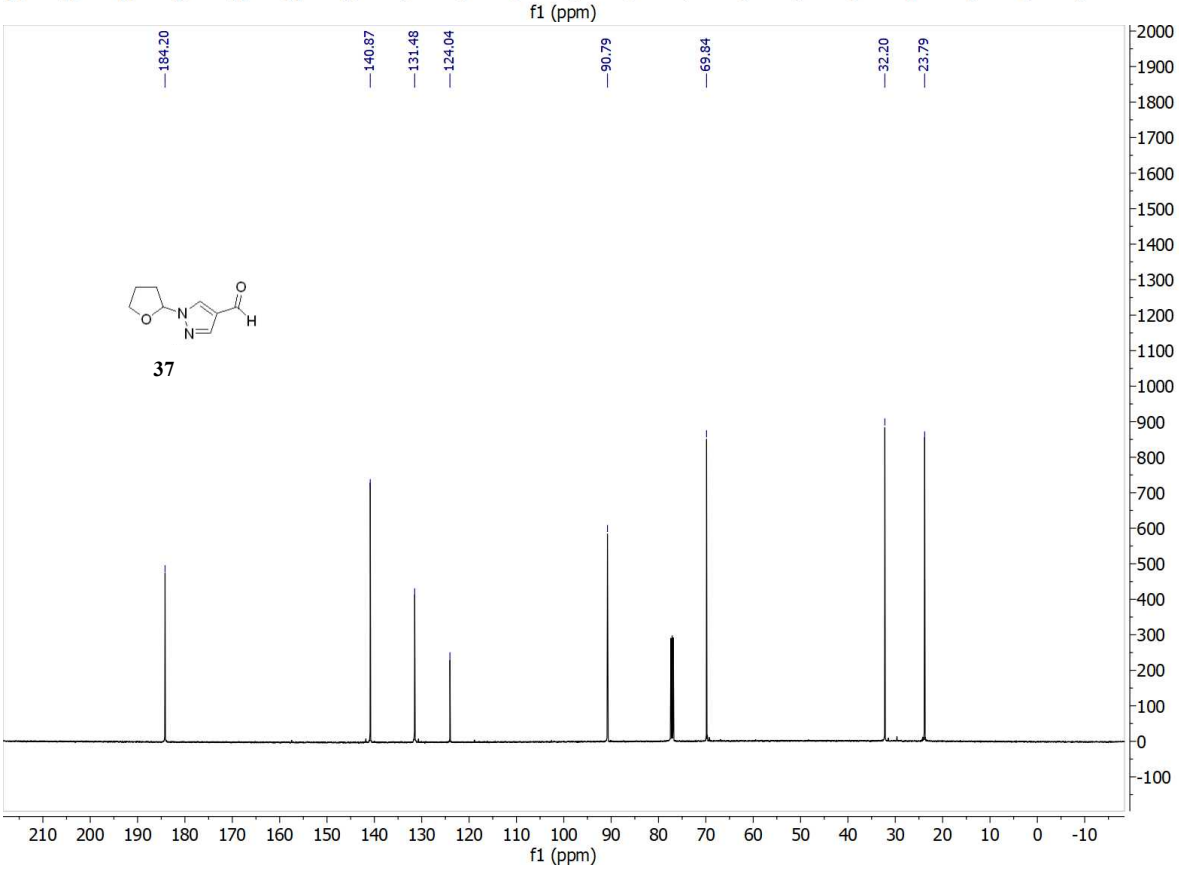

172.15
150.79
129.39
125.72
121.58
78.14
67.79
31.33
31.25
30.70
25.77
Ph
O
O
f1 (ppm)

34

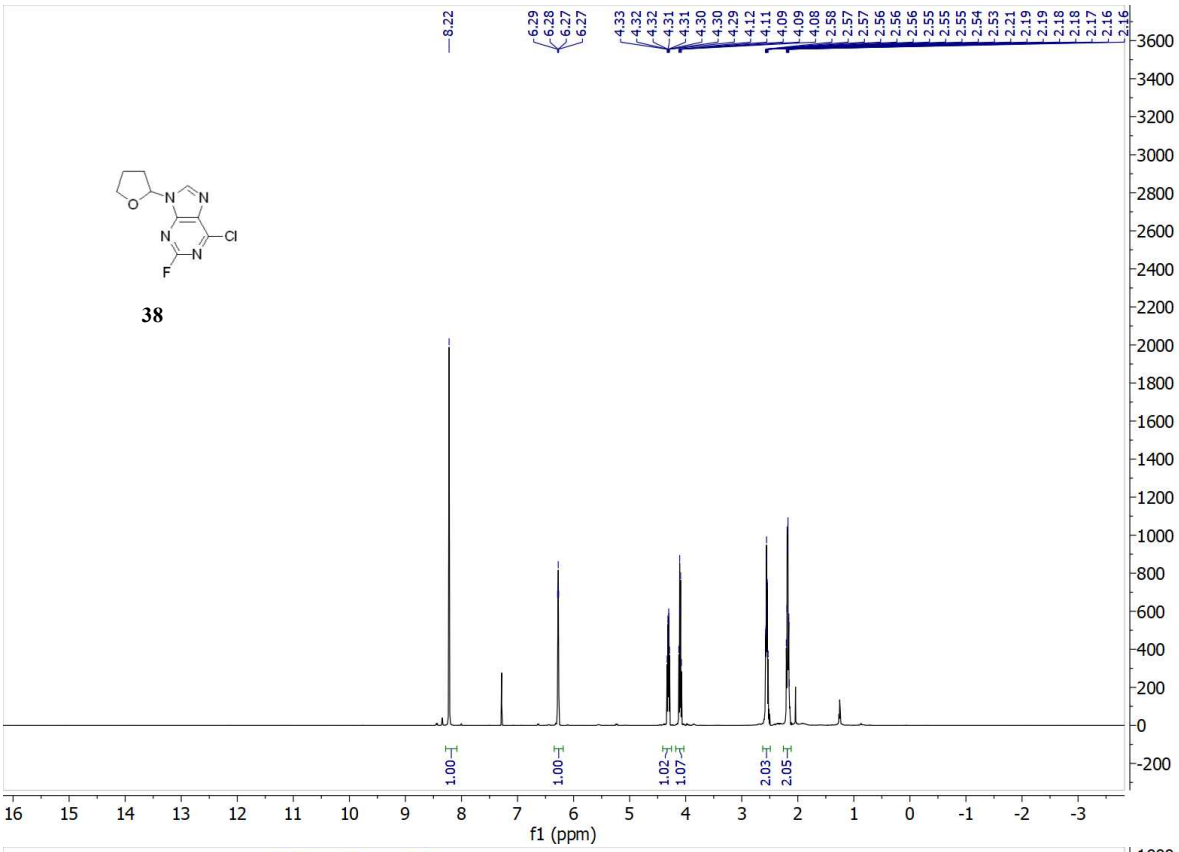

CO2Me
CO2Me
E-36
Z-36
f1 (ppm)
f1 (ppm)


9.83
8.09
7.96
0.87
1.02
0.78
1.01
1.10
1.12
1.13
1.06
2.09
f1 (ppm)

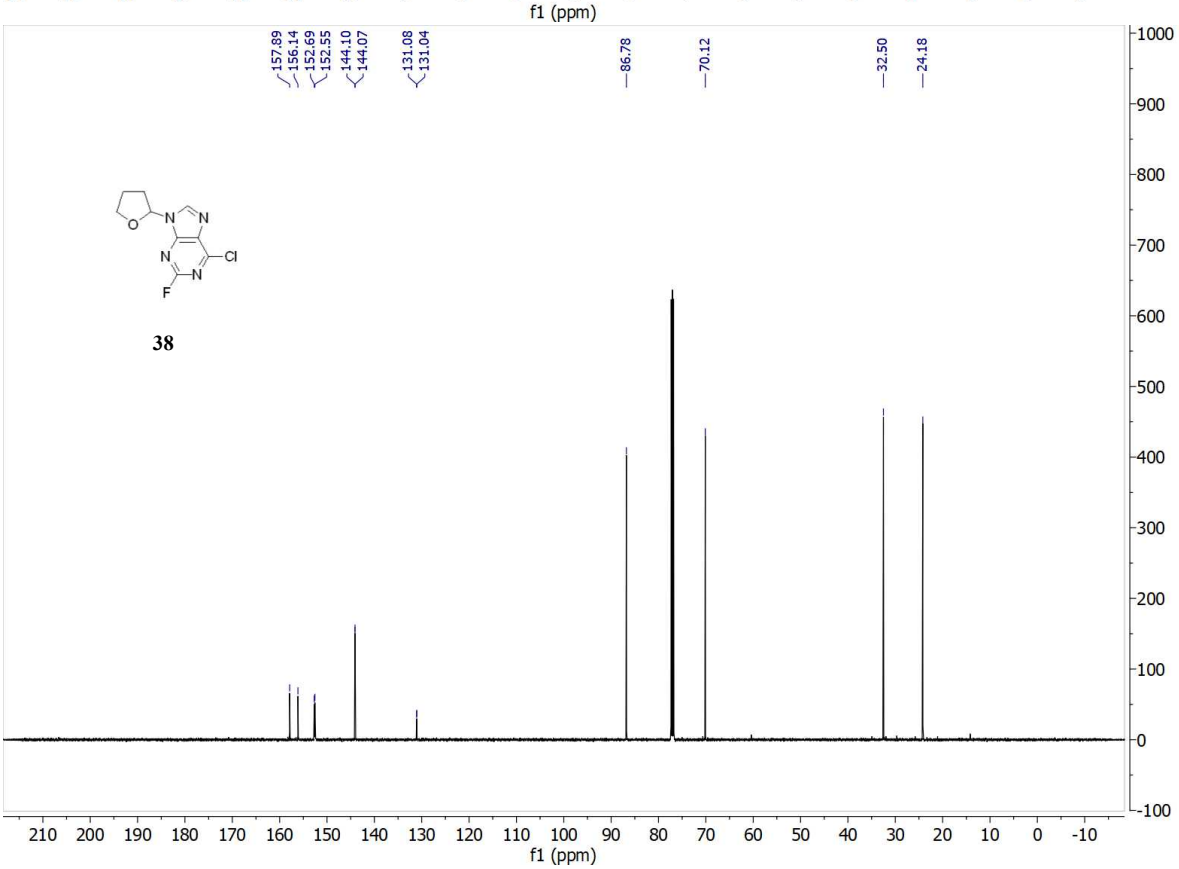
37


184.20
140.87
131.48
124.04
90.79
69.84
32.20
23.79
f1 (ppm)

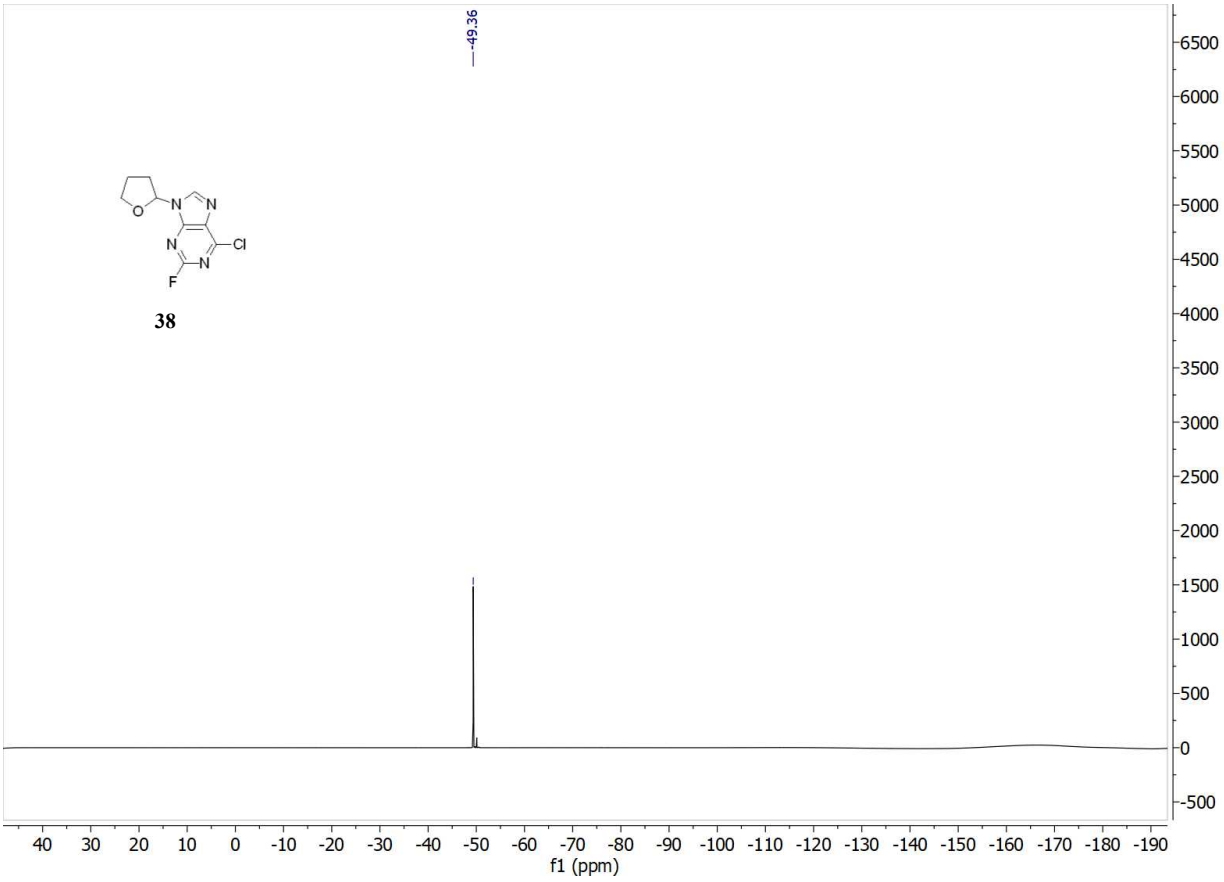
37


8.22
6.29
6.28
6.27
6.27
4.33
4.32
4.32
4.31
4.31
4.30
4.30
4.29
4.12
4.11
4.09
4.09
4.08
2.58
2.57
2.57
2.56
2.56
2.56
2.55
2.55
2.55
2.54
2.53
2.21
2.19
2.19
2.18
2.18
2.17
2.16
2.16
1.00
1.00
1.02
1.07
2.03
2.05
f1 (ppm)

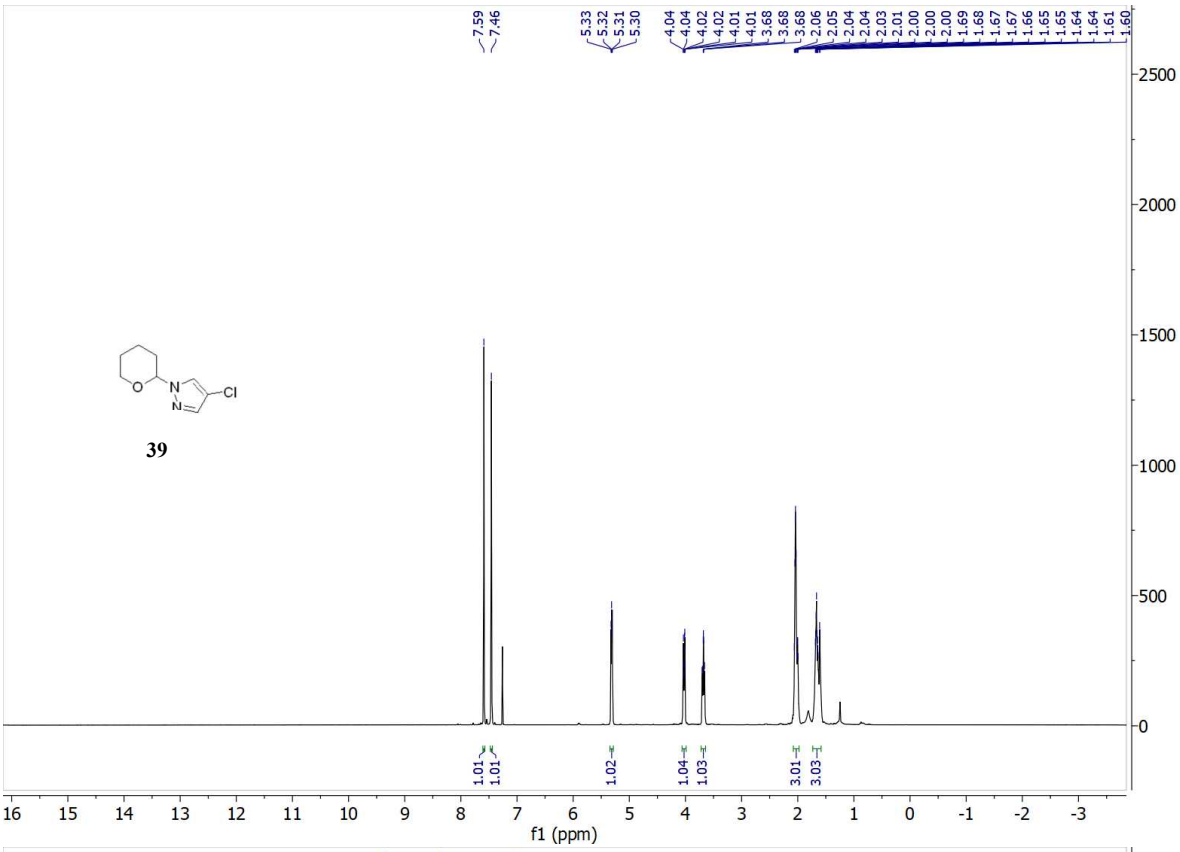
38

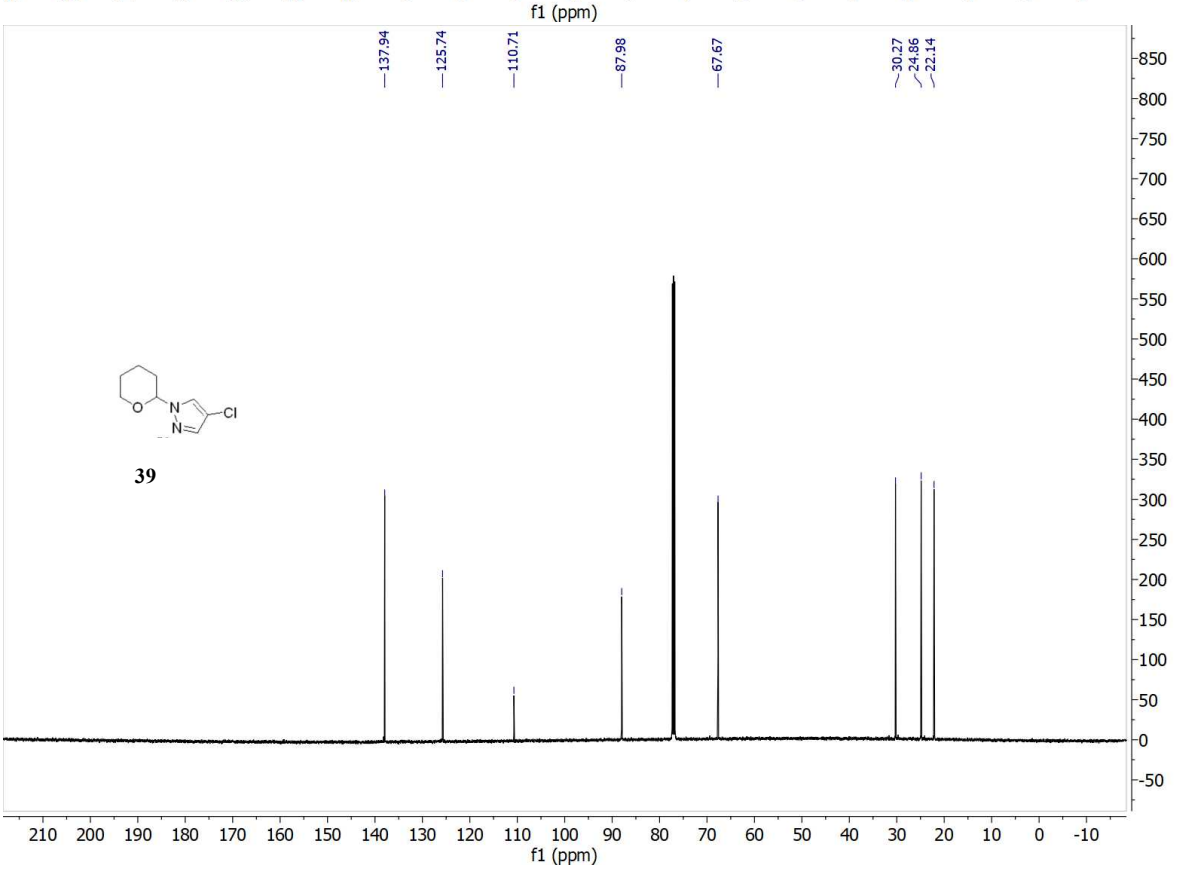

157.89
156.14
152.69
152.55
144.10
144.07
131.08
131.04
86.78
70.12
32.50
24.18
f1 (ppm)

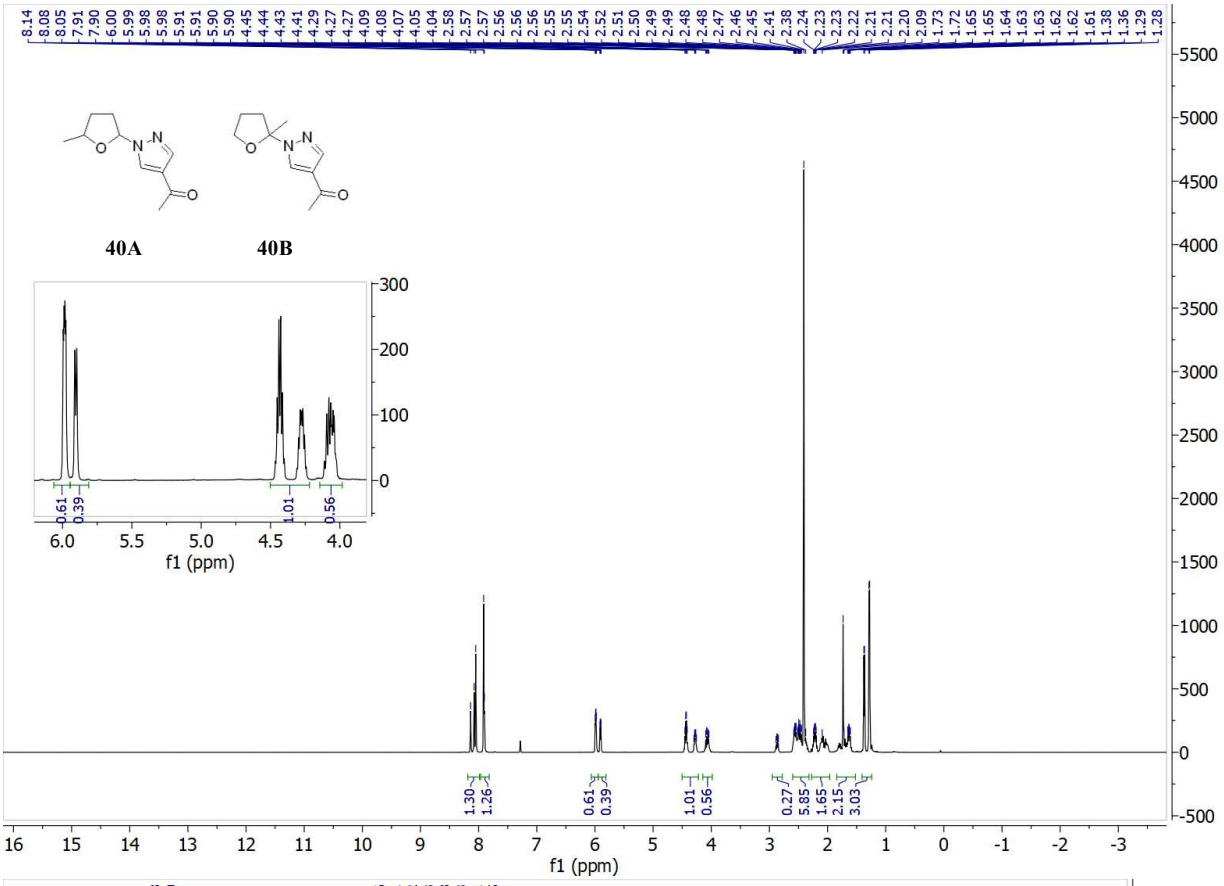
38

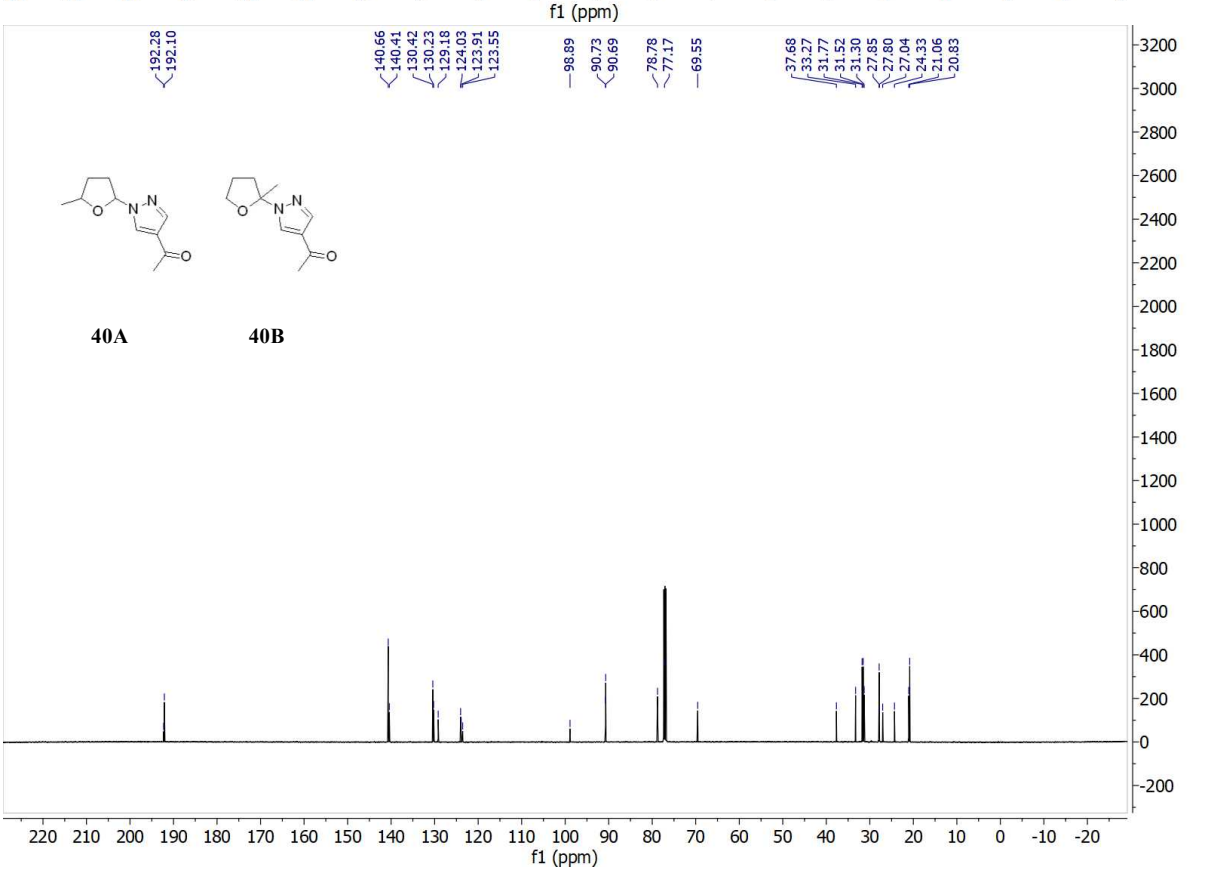

-49.36
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)
O
N
N
N
N
Cl
F

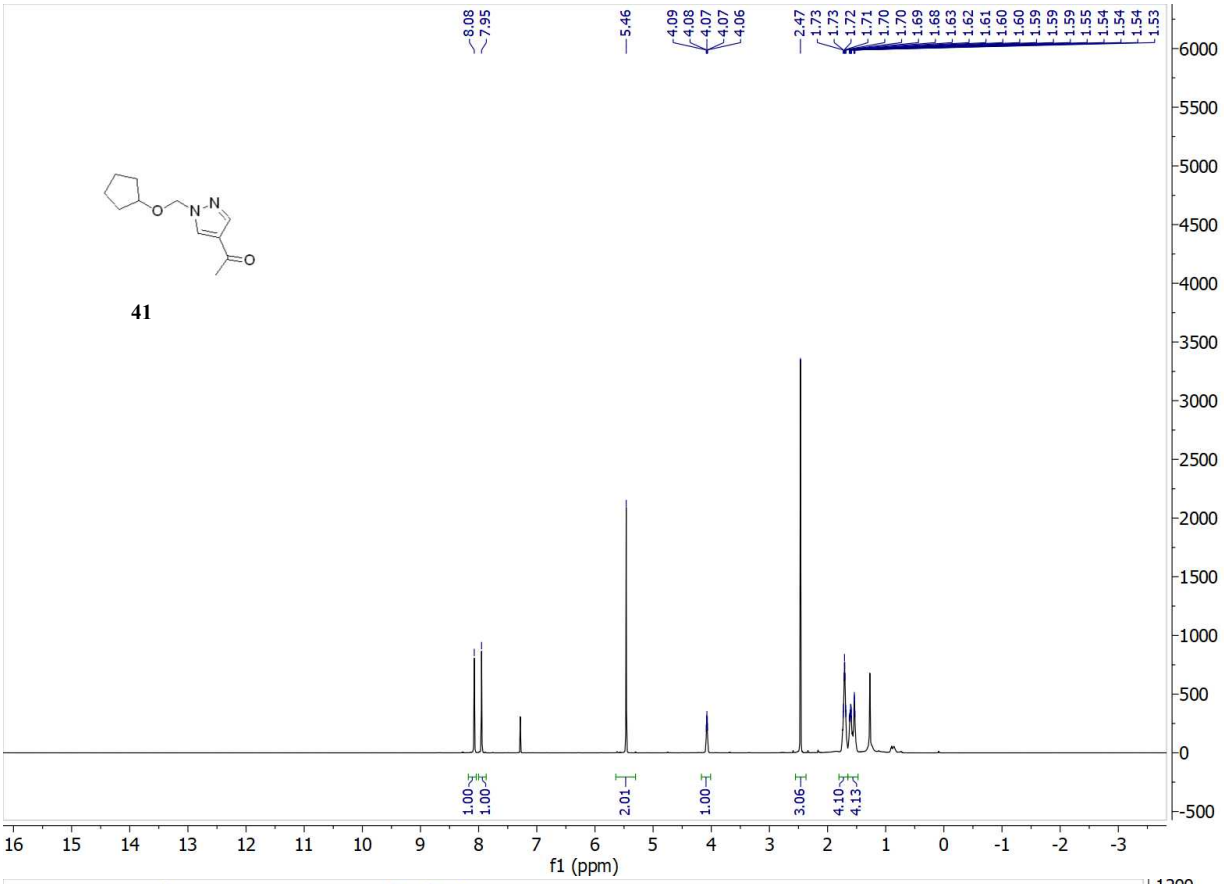
38


7.59
7.46
5.33
5.32
5.31
5.30
4.04
4.04
4.02
4.02
4.01
4.01
3.68
3.68
3.68
2.06
2.05
2.04
2.04
2.03
2.01
2.00
2.00
2.00
1.69
1.68
1.67
1.67
1.66
1.65
1.65
1.64
1.64
1.61
1.60
1.01
1.01
1.02
1.04
1.03
3.01
3.03
Cl
39
f1 (ppm)

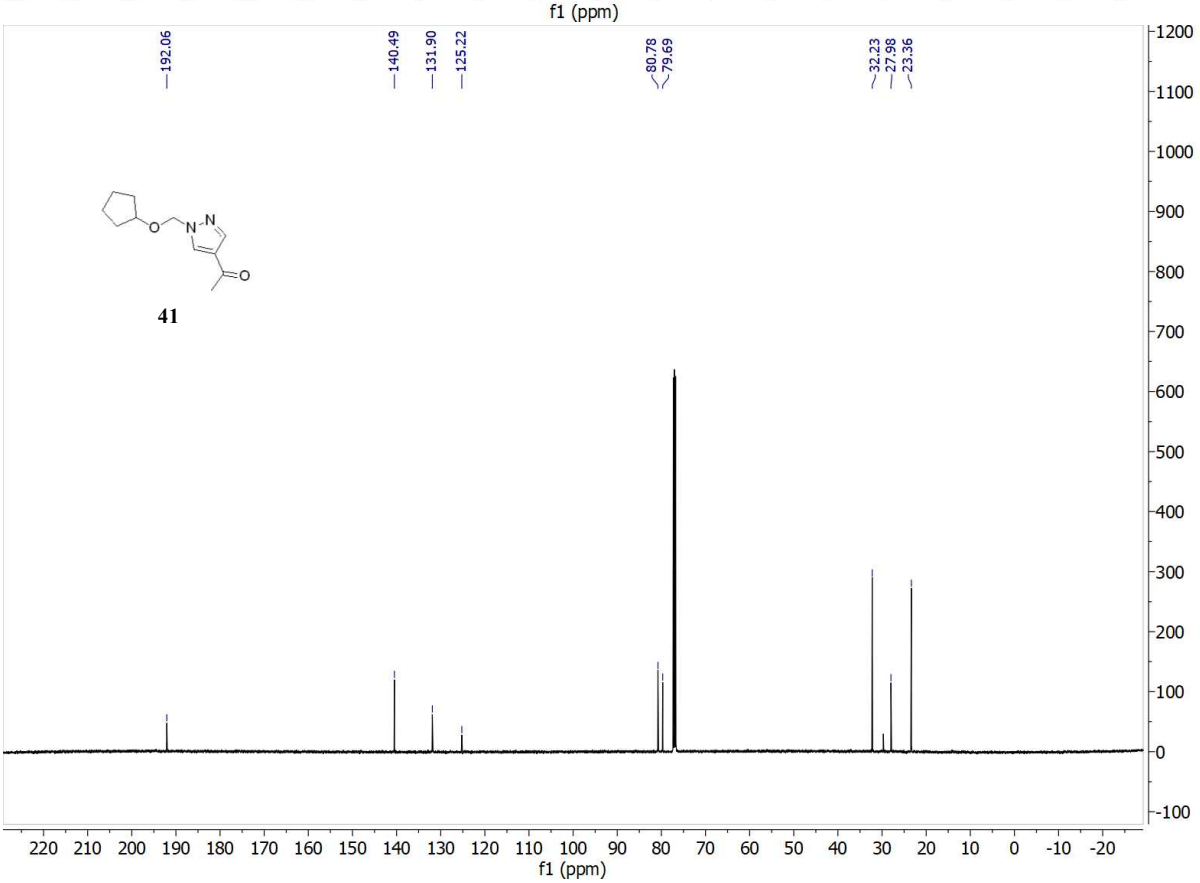

137.94
125.74
110.71
87.98
67.67
30.27
24.86
22.14
Cl
39
f1 (ppm)


40A
40B
f1 (ppm)

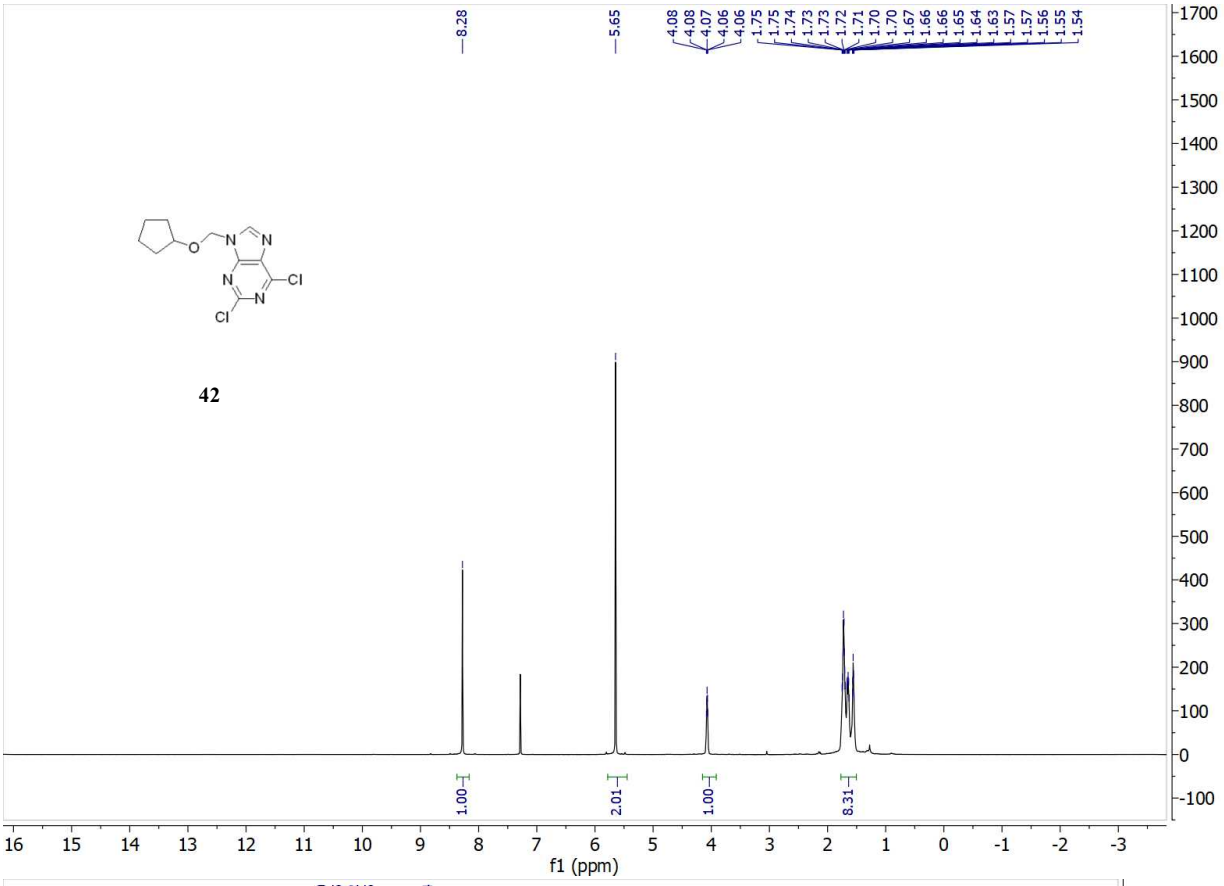

40A
40B
f1 (ppm)


8.08
7.95
5.46
4.09
4.08
4.07
4.07
4.06
2.47
1.73
1.73
1.72
1.71
1.70
1.70
1.69
1.68
1.63
1.62
1.61
1.60
1.60
1.59
1.59
1.59
1.55
1.54
1.54
1.54
1.53
1.00
1.00
2.01
1.00
3.06
4.10
4.13
f1 (ppm)

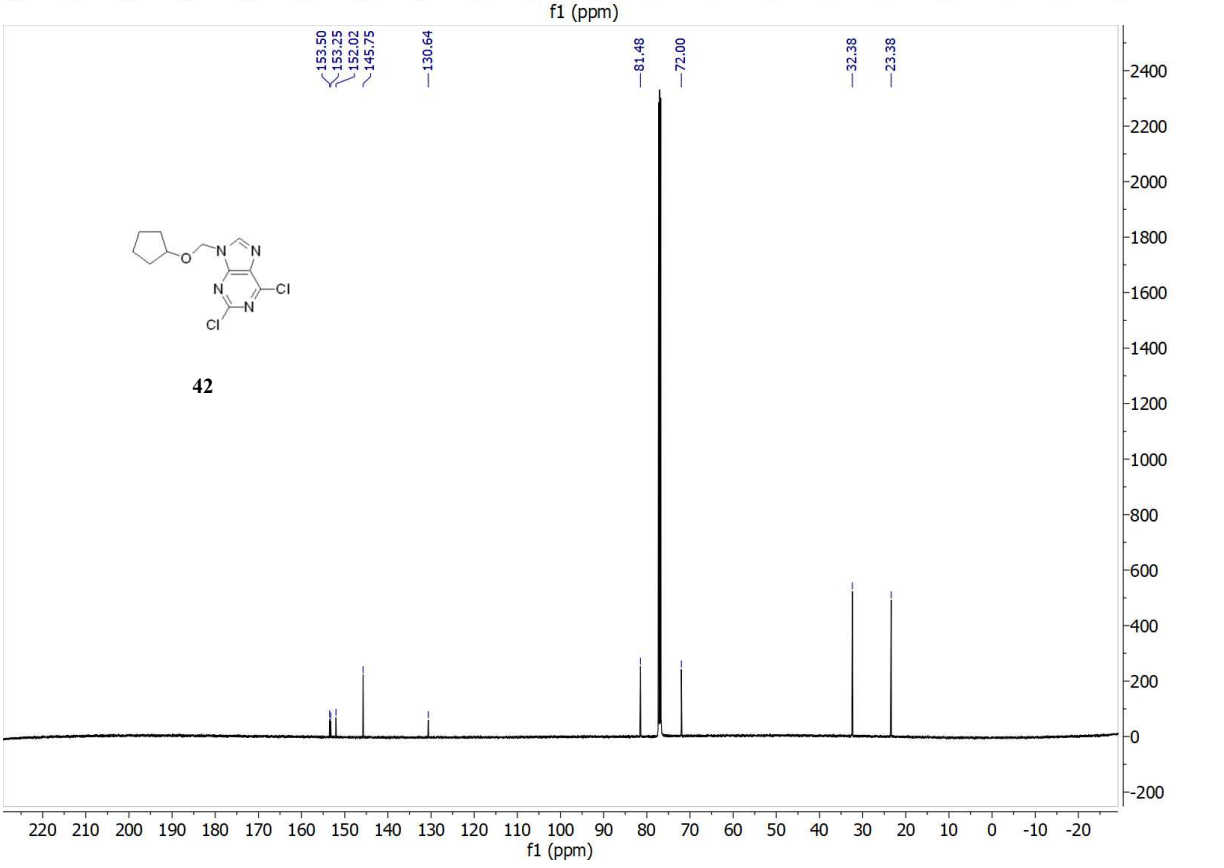
41


192.06
140.49
131.90
125.22
80.78
79.69
32.23
27.98
23.36
f1 (ppm)

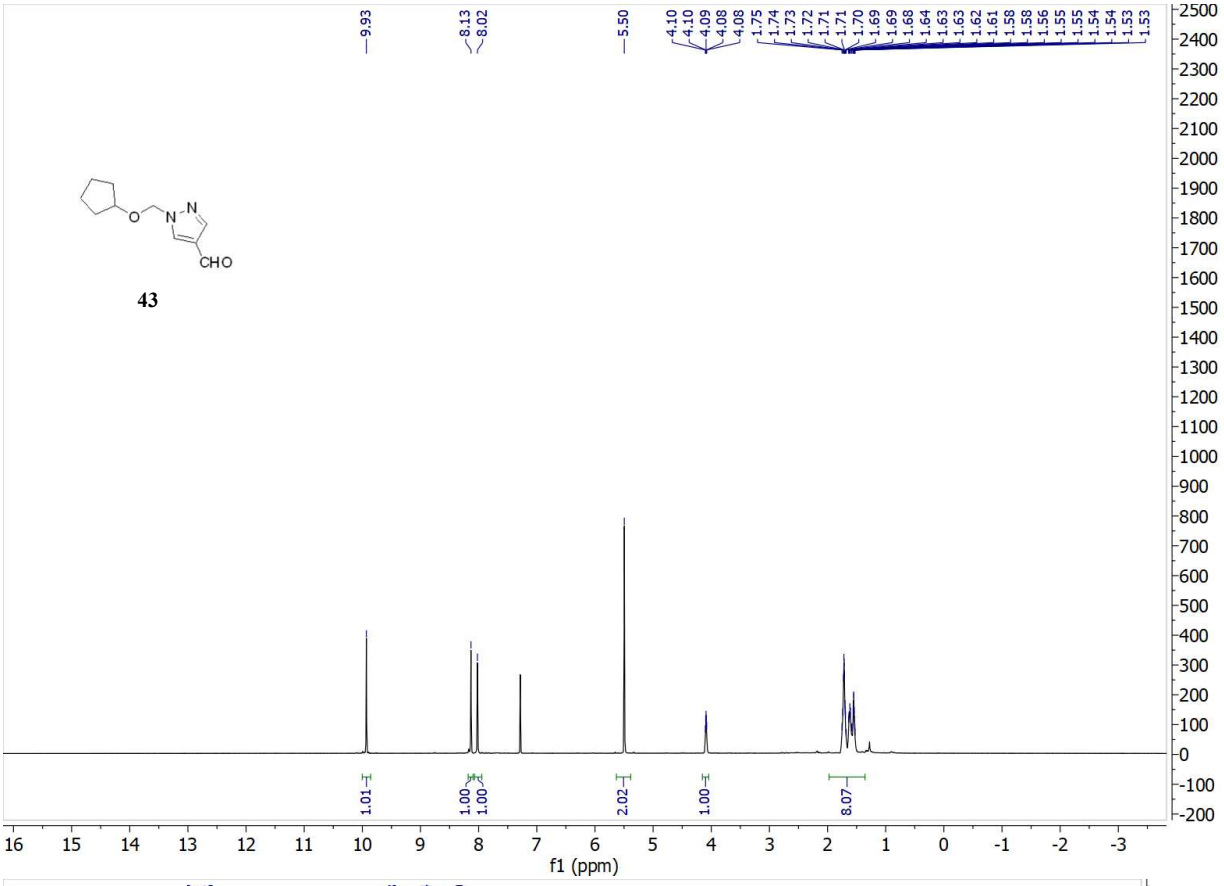
41


8.28
5.65
4.08
4.08
4.07
4.06
4.06
1.75
1.75
1.74
1.73
1.73
1.72
1.71
1.70
1.70
1.67
1.66
1.66
1.65
1.64
1.63
1.57
1.57
1.56
1.55
1.54
1.00
2.01
1.00
8.31
f1 (ppm)

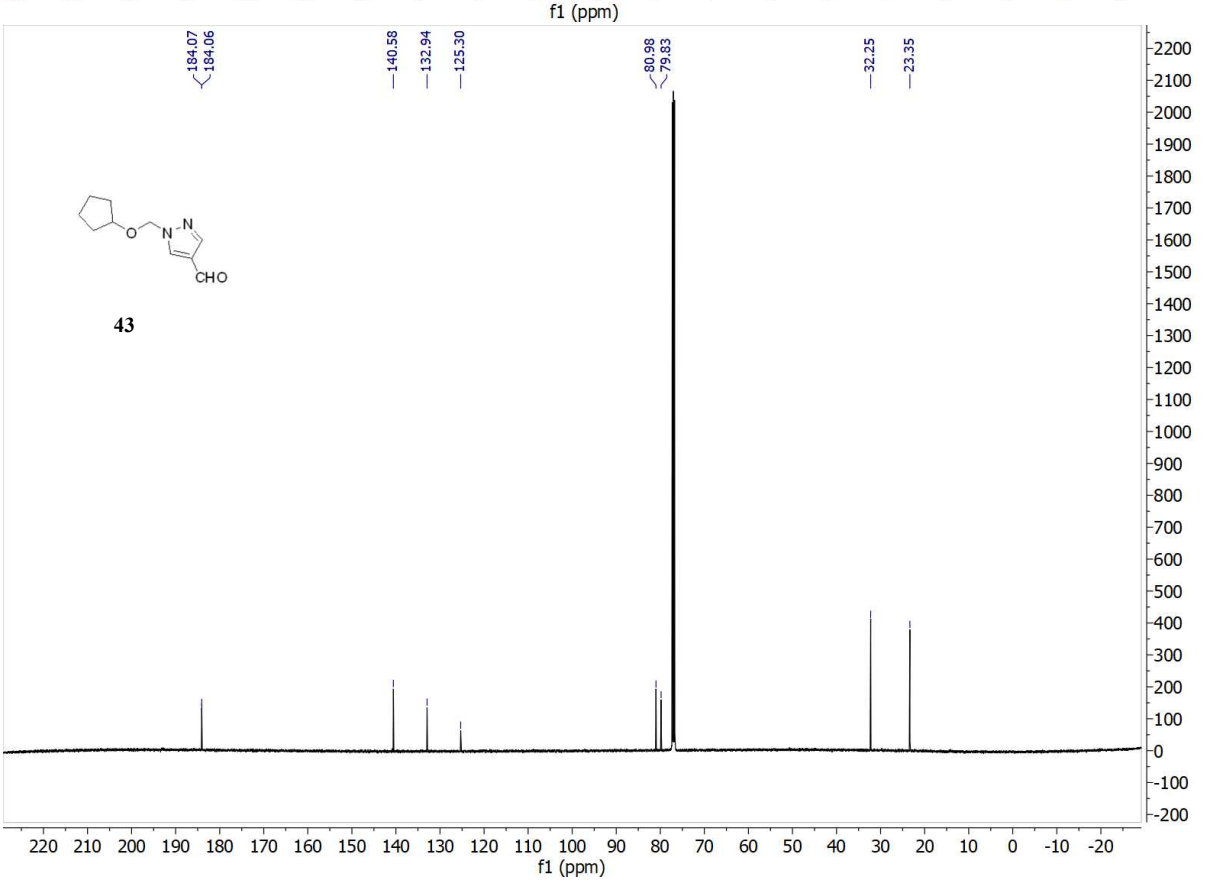
42


153.50
153.25
152.02
145.75
130.64
81.48
72.00
32.38
23.38
f1 (ppm)

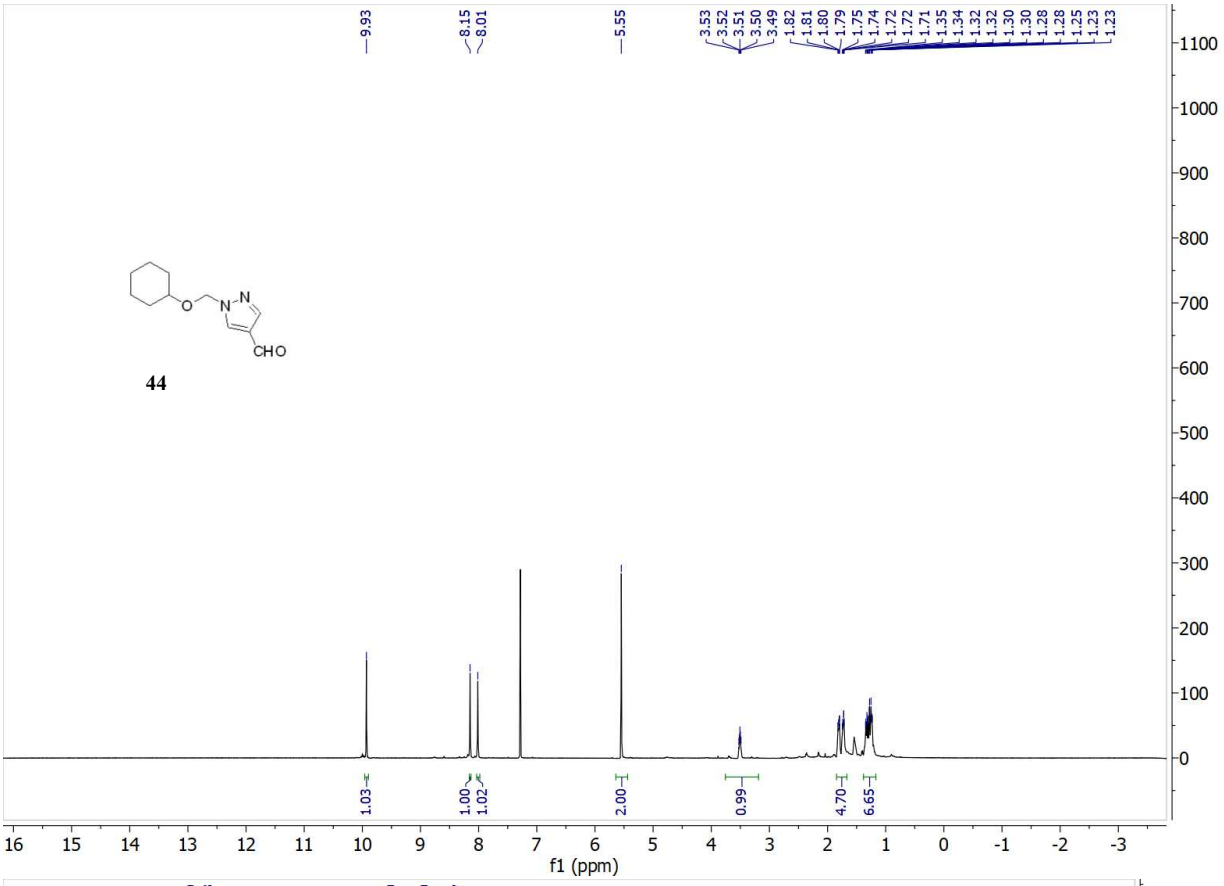
42


9.93
8.13
8.02
5.50
4.10
4.10
4.09
4.08
4.08
1.75
1.74
1.73
1.72
1.71
1.71
1.71
1.70
1.69
1.69
1.68
1.64
1.63
1.63
1.62
1.61
1.58
1.58
1.56
1.55
1.55
1.54
1.54
1.53
1.53
O
N
N
CHO
1.01
1.00
1.00
2.02
1.00
8.07
f1 (ppm)

43


184.07
184.06
140.58
132.94
125.30
80.98
79.83
32.25
23.35
O
N
N
CHO
f1 (ppm)

43


9.93
8.15
8.01
5.55
3.53
3.52
3.51
3.50
3.49
1.82
1.81
1.80
1.79
1.75
1.74
1.72
1.72
1.71
1.35
1.34
1.32
1.32
1.30
1.30
1.28
1.28
1.25
1.23
1.23
1.03
1.00
1.02
2.00
0.99
4.70
6.65
f1 (ppm)

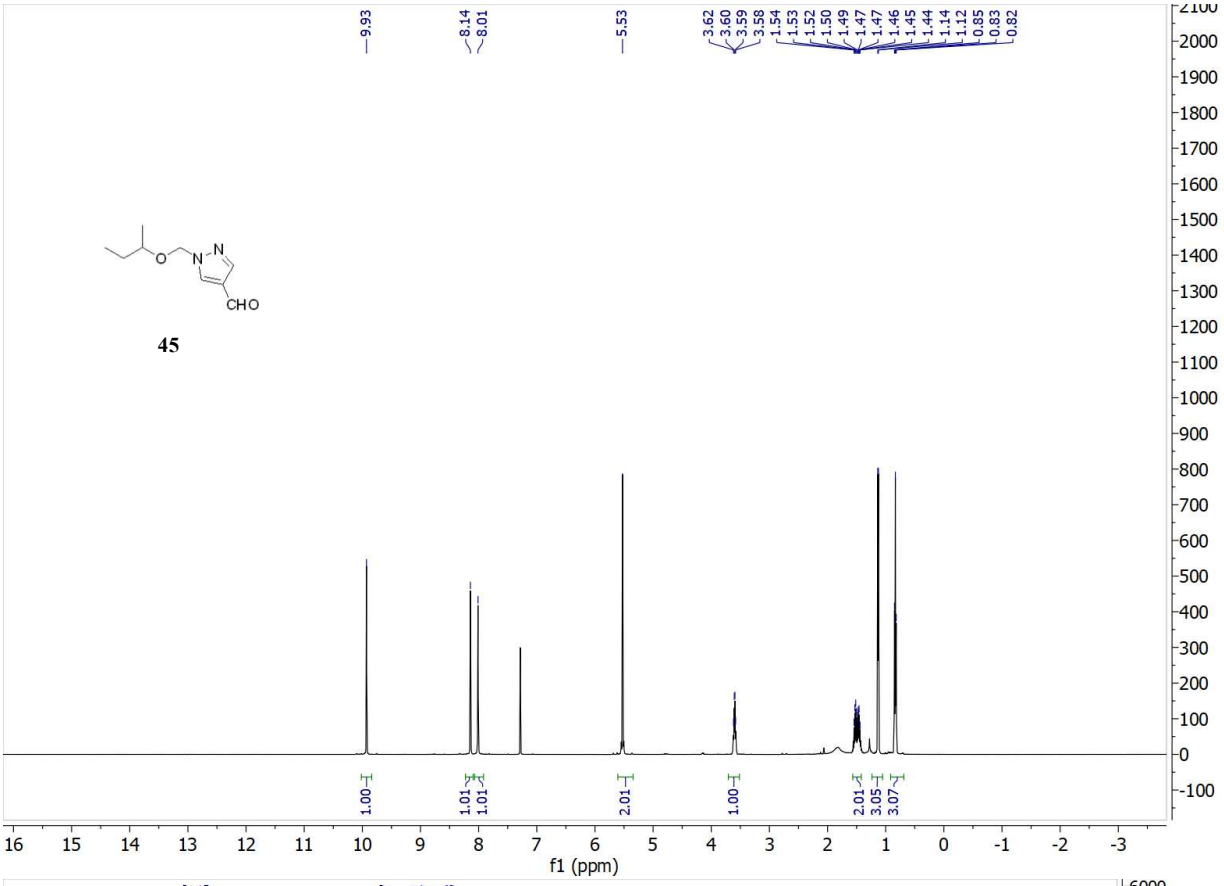

O
N
N
CHO

44

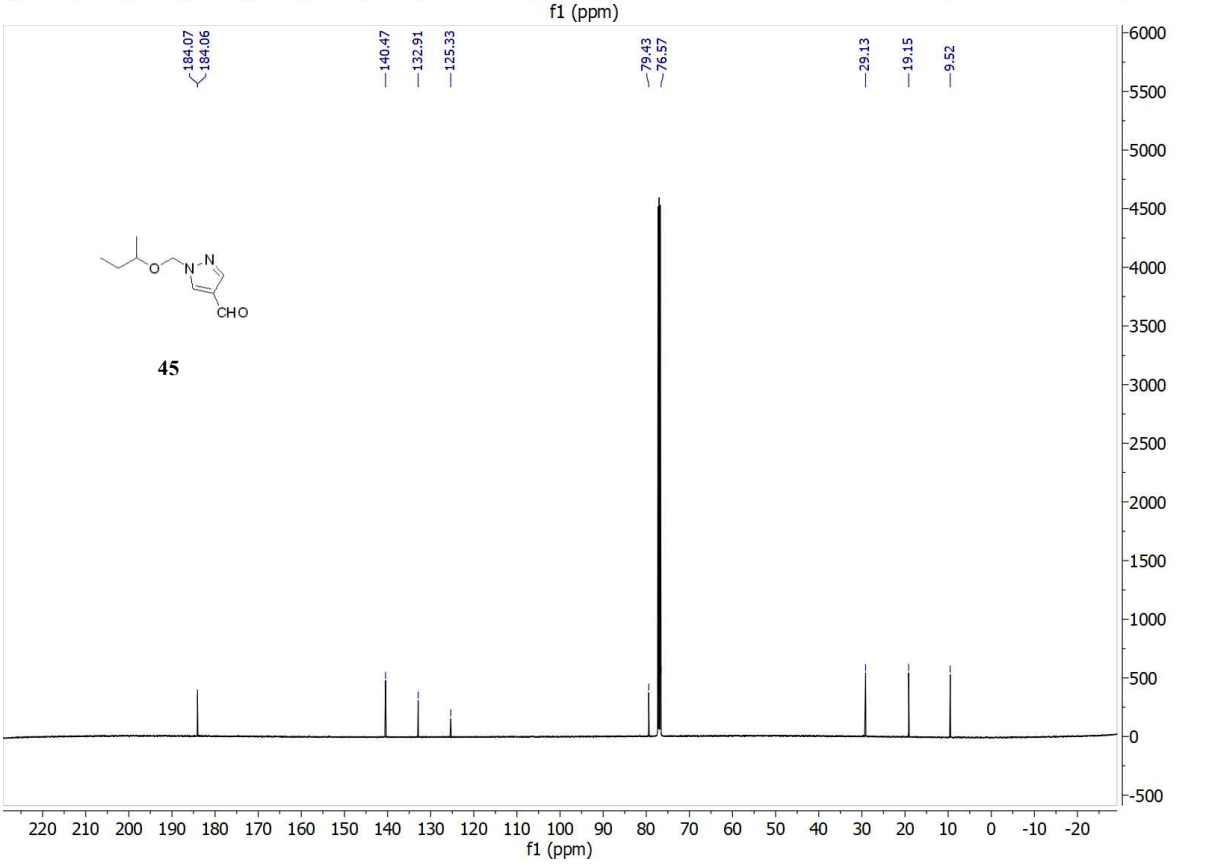
184.09
184.08
140.50
132.80
125.27
78.95
77.12
32.00
25.43
23.81
f1 (ppm)

O
N
N
CHO

44


9.93
8.14
8.01
5.53
3.62
3.60
3.59
3.58
1.54
1.53
1.52
1.50
1.49
1.47
1.47
1.46
1.45
1.44
1.14
1.12
0.85
0.83
0.82
1.00
1.01
1.01
2.01
1.00
2.01
3.05
3.07
CHO
f1 (ppm)

45


184.07
184.06
140.47
132.91
125.33
79.43
76.57
29.13
19.15
9.52
CHO
f1 (ppm)

45