Direct C*α*-Heteroarylation of Structurally Diverse Ethers *via* a Mild *N*-Hydroxy Succinimide Mediated Cross-Dehydrogenative Coupling Reaction

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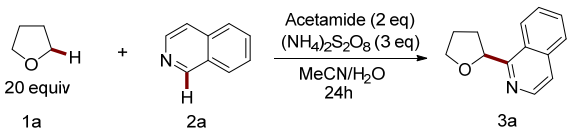
The screening of reaction conditions

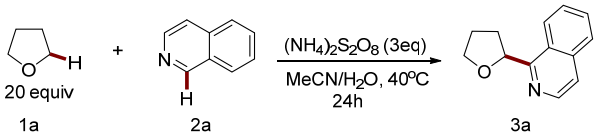
Table S1 The screening of reaction temperature [a]



Entry	Tem (°C)	Yield [b]
1	25	14%
2	30	46%
3	35	65%
4	40	77%
5	45	74%

[a] Conditions employed **1a** (10 mmol), **2a** (0.5 mmol), $(NH_4)_2S_2O_8$ (1.5 mmol), acetamide (1.0 mmol), 24 h, and a solvent mixture (1.5 mL, MeCN:H_2O = 1:1), unless otherwise noted; [b] Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

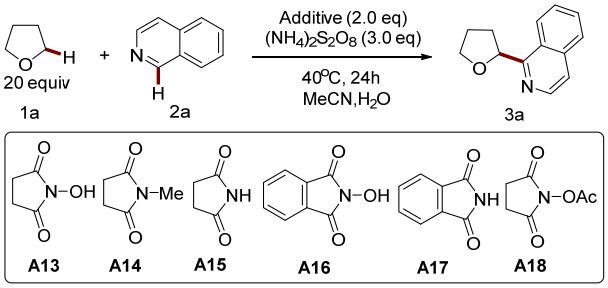
Table S2 The screening of the amount of acetamide [a]



Entry	Acetamide (equiv)	Yield [b]
1	8	78%
2	5	80%
3	2	77%
4	1	68%
5	0.5	58%

[a] Conditions employed **1a** (10 mmol), **2a** (0.5 mmol), $(NH_4)_2S_2O_8$ (1.5 mmol), 40 °C, 24 h, and a solvent mixture (1.5 mL, MeCN:H_2O = 1:1), unless otherwise noted; [b] Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

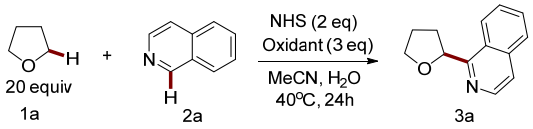
Table S3 Further validation of the promotion effect of NHS in the reaction [a]



Entry	Additive	Yield [b]
12	A13	88%
13	A14	62%
14	A15	71%
15	A16	70%
16	A17	65%
17	A18	48%

[a] Conditions employed **1a** (10.0 mmol), **2a** (0.5 mmol), $(NH_4)_2S_2O_8$ (1.5 mmol), additive (1.0 mmol), 40 °C, 24 h, and a solvent mixture (1.5 mL, MeCN:H_2O = 1:1), unless otherwise noted; [b] Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

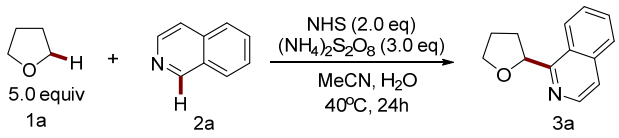
Table S4 The screening of the oxidant with NHS as the additive [a]



Entry	Oxidant	Yield(%) [b]
1	$(NH_4)_2S_2O_8$	88%
2	BPO	n.d [c]
3	TBHP	n.d [c]
4	$Na_2S_2O_8$	53%
5	$K_2S_2O_8$	45%

[a] Conditions employed **1a** (10.0 mmol), **2a** (0.5 mmol), oxidant (1.5 mmol), NHS (1.0 mmol), 40 °C, 24 h, and a solvent mixture (1.5 mL, MeCN:H_2O = 1:1), unless otherwise noted; [b] Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard; [c] not detected.

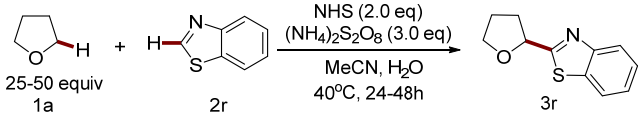
Table S5 Further reaction condition optimization with 5 equivalent of THF as coupling partner [a]



Entry	Additive	Yield(%) [b]
1	-	60%
2	TBAB (30 mol%) [c]	63%
3	$Sc(OTf)_3$ (10 mol%)	60%
4	TFA (1 equiv) [c]	60%
5	-	30% [d]

[a] Conditions employed **1a** (2.5 mmol), **2a** (0.5 mmol), $(NH_4)_2S_2O_8$ (1.5 mmol), NHS (1.0 mmol), 40 °C, 24 h, and a solvent mixture (1.5 mL, MeCN:H_2O = 1:1), unless otherwise noted; [b] Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard; [c] TBAB: tetrabutylammonium bromide, TFA: trifluoroacetic acid; [d] quinuclidin-3-ol (**A11**) was used instead.

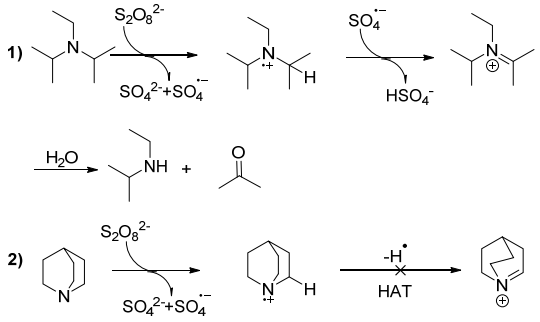
Table S6 Further reaction condition optimization with benzothiazole as coupling partner [a]



Entry	THF (equiv)	Time (h)	Yield [b]
1	20	24	56%
2	20	48	57%
3	50	24	60%
4	20	24	52% [c]

[a] Conditions employed **1a** (10-25 mmol), **2a** (0.5 mmol), $(NH_4)_2S_2O_8$ (1.5 mmol), NHS (1.0 mmol), 40 °C, 24-48 h, and a solvent mixture (1.5 mL, MeCN:H_2O = 1:1), unless otherwise noted; [b] Isolated yield was reported; [c] quinuclidin-3-ol (**A11**) was used instead.

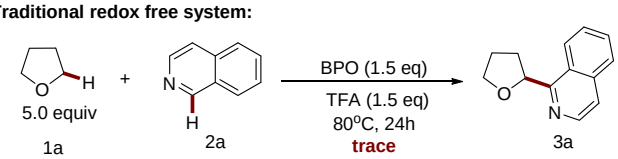
The proposed quenching mechanism of amine additives



Scheme S1 Proposed quenching mechanism of DIEA in the reaction

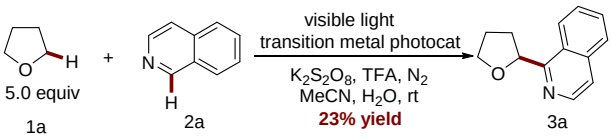
The comparison of Cα-heteroarylation methodologies of ether

Traditional redox free system:



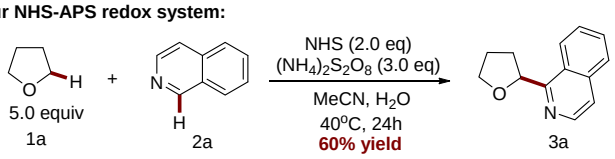
Eur. J. Org. Chem. **2015**, 4973-4981

Visible light driven photoredox system:



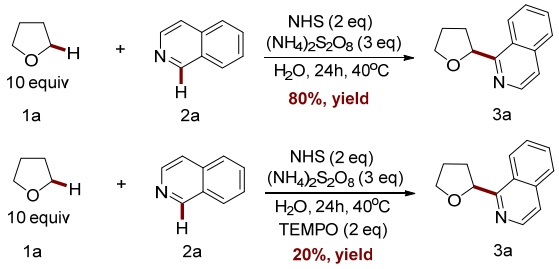
Angew. Chem. Int. Ed. **2015**, 54, 1565-1569

Our NHS-APS redox system:



Scheme S2 The experimental result with three different reaction systems

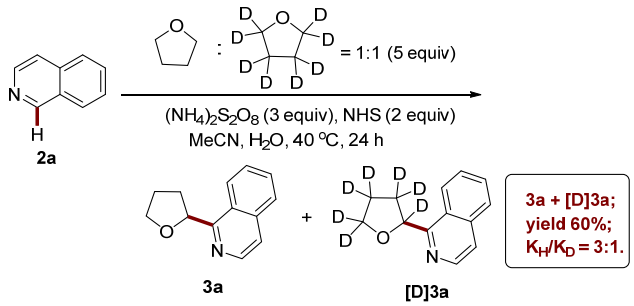
The radical quenching experiment



Scheme S3 The experiment to validate radical based mechanism

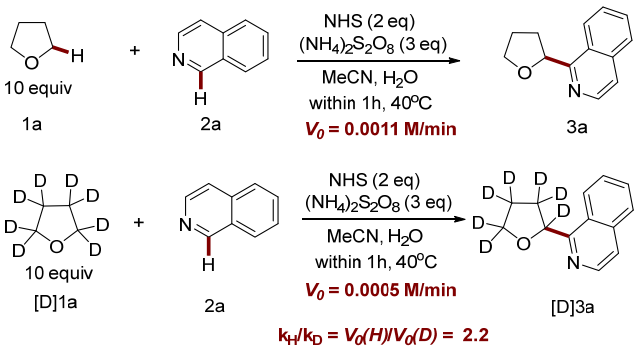
Kinetic Isotope Effect Experiments (KIE)[1]

The KIE value determined from an intermolecular competition reaction



Scheme S4 Intermolecular competition KIE experiment

The KIE value determined from two parallel reactions



Scheme S5 KIE experiment employing two parallel reactions

Table S7 The initial rate determination of two parallel reactions employing THF and d^8-THF as coupling partner [a]

Ether	Time(min)	NMR Yield (%) [b]	[Product](M)	V_0
THF	10	5	0.01	0.0011M/min
	20	12	0.026	
	30	16	0.035	
	40	22	0.047	
	50	27	0.057	
	60	31	0.067	

Ether	Time(min)	NMR Yield (%)	[Product](M)	V_0
d^8-THF	10	2	0.004	0.0005M/min
	20	5	0.01	
	30	7	0.013	
	40	9	0.02	
	50	11	0.024	
	60	12	0.026	

[a] To a solution of THF(or THF-d_8) (5.00 mmol, 10.0 equiv.), isoquinoline (0.50 mmol, 1.0 equiv.) in 1.5 mL of CH_3CN/H_2O (1: 1) was added $(NH_4)_2S_2O_8$ (1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (1.00 mmol, 2.0 equiv.), the reaction mixture was heated at 40 °C; [b] Analyzed by

NMR spectroscopy for the formation of product with CH_2Br_2 as an internal standard.

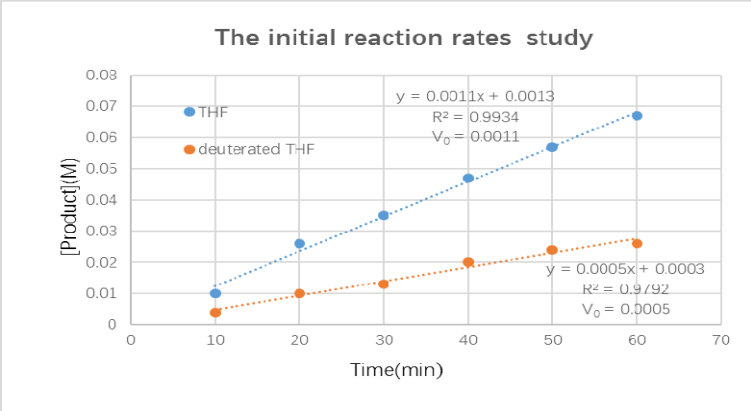
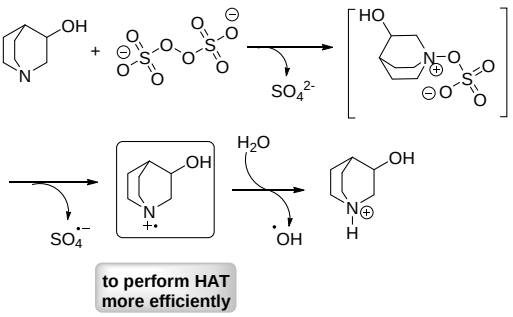


Fig. S1 The initial rate determination of two parallel reactions

The study of the redox reaction of quinuclidine structure with APS

Notes: The ^{1}H NMR spectra of quinuclidine and quinuclidin-3-ol in deuterated water were monitored after treating with APS. These two additives were totally protonated to produce the corresponding sulfate complexes even at 20 °C (Figure S2). It should be noted that the protonic acid, such as HSO_4^-, H_2SO_4, could not be generated via a heat-induced decomposition of APS or $Na_2S_2O_8$ in water at 40°C or 20°C.[2] Furthermore, the EPR data of the solution of APS in water was collected with 5,5-dimethyl-1-pyrroline N-oxide (DMPO) as free-radical spin-trapping agent. In the presence of quinuclidine, the signal of hydroxyl radical was detected,[3] while no distinct signal was observed without additive (Fig. S3). Based on these findings, we concluded that quinuclidine additives might function via the redox reaction with APS to generate the active radical species, such as sulfate radical, nitrogen based radical cation, and hydroxyl radical. The mechanism of the redox reaction of quinuclidine structure with persulfate was proposed accordingly (Scheme S6).[2]



Scheme S6 The proposed redox reaction mechanism of quinuclidin-3-ol with APS

The ^{1}H NMR study of the redox reactions of quinuclidine structure with APS

General procedure: To a solution of quinuclidine or quinuclidin-3-ol (0.4 mmol, 1.0 equiv.) in D_2O (0.6 mL), was added $(NH_4)_2S_2O_8$ (0.6 mmol, 1.5 equiv.). The resulting

solution was stirred at 40 °C or 20 °C for 24 h, the ^{1}H NMR data of the reaction mixture was then collected accordingly.

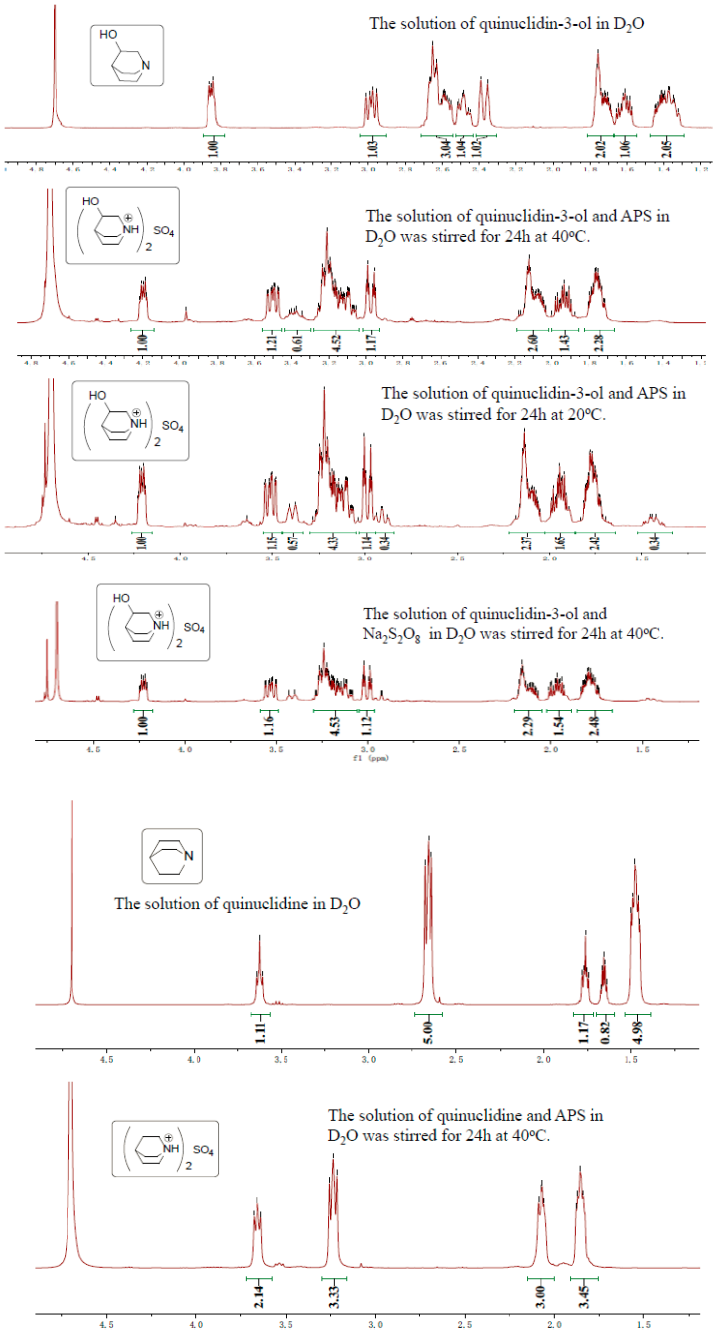


Fig. S2 The ^{1}H NMR spectra of the reaction solution of quinuclidin-3-ol or quinuclidine with APS

Electroparamagnetic resonance (EPR) study of the redox reactions of quinuclidine structure with APS

General procedure: the samples were prepared immediately before the acquisition, after tuning the ESR instrument parameters. The preparation is described as follows:

A solution of quinuclidine additives (0.05 mmol, 1 equiv.), DMPO (0.05 mmol, 1 equiv.) in H_2O (1.0 mL) was added to APS (0.05 mmol, 1 equiv.) in ESR tubes.

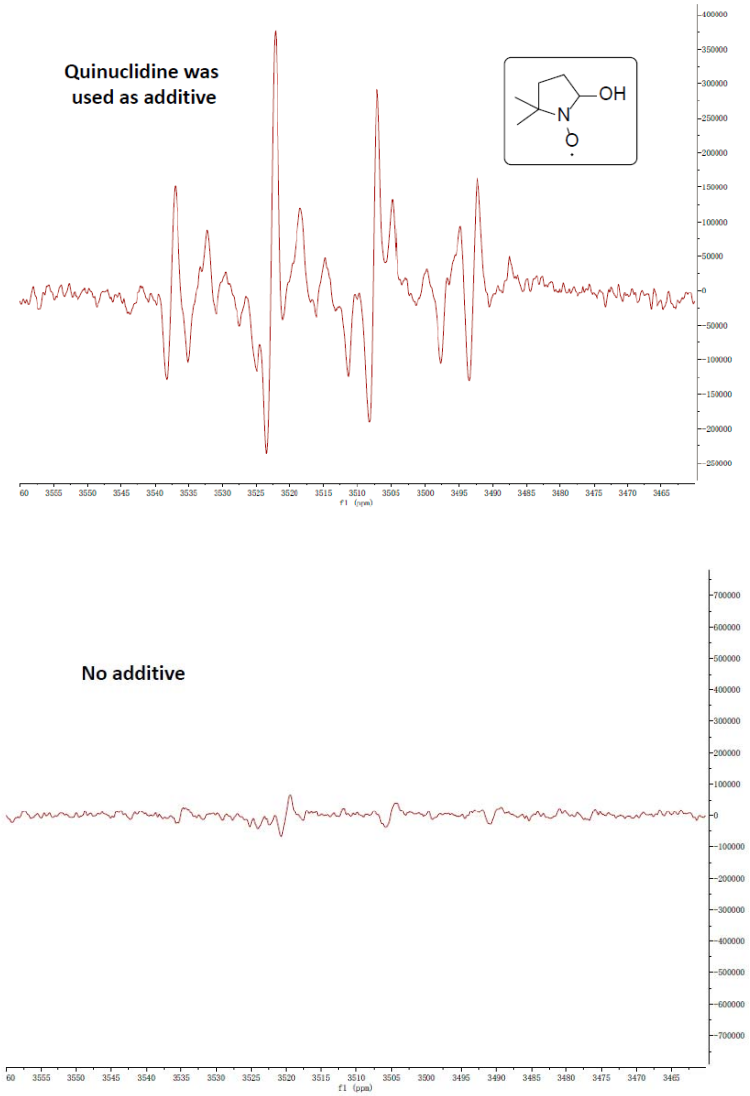
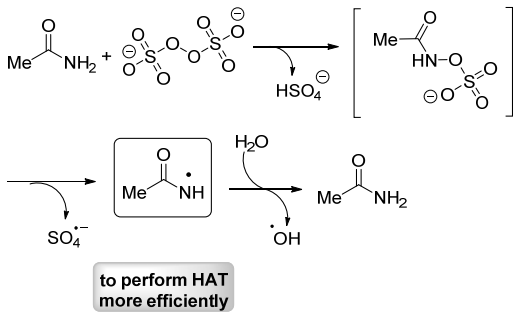


Fig. S3 The EPR spectra of the solution of APS in water

The study of the redox reaction of amide additives with APS

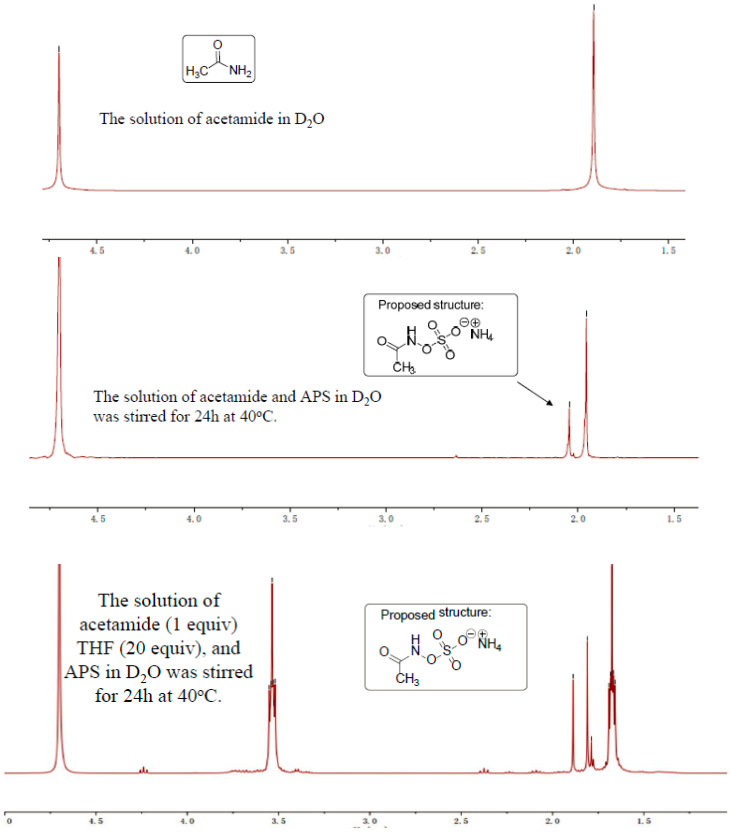
Notes: The ^{1}H NMR spectra of amide additives in deuterated water were monitored after treating with APS. Acetamide and NHS, as the additives to efficiently promote the reaction, displayed remarkable new ^{1}H NMR signals, while no distinct new ^{1}H NMR signals was detected for less efficient methanesulfonamide (Fig. S4). Moreover, in the presence of acetamide and NHS, the hydroxyl radical signal was also detected in the EPR experiment of the solution of APS in water with 5,5-dimethyl-1-pyrroline N-oxide (DMPO) as free-radical spin-trapping agent (Fig. S5). At last, APS mediated dimerization via a nitrogen-nitrogen bond, a typical reaction of nitrogen-concerted radial,[4] was observed by MS for *N*-phenylacetamide (Scheme S8 and Figure S6). Therefore, we envisioned that the redox intermediate with nitrogen-oxygen bond might be developed initially in this process, thereafter provides active radical species

to further mediate HAT process. The mechanism of the redox reaction was proposed (Scheme S7).



Scheme S7 Proposed redox reaction mechanism of acetamide with APS

General procedure: To a solution of amide additives (0.4 mmol, 1.0 equiv.) in D_2O (0.6 mL), was added $(NH_4)_2S_2O_8$ (0.6 mmol, 1.5 equiv.). The resulting solution was stirred at 40 °C or 20 °C for 24 h, the ^1H NMR data of the reaction mixture was then collected accordingly.



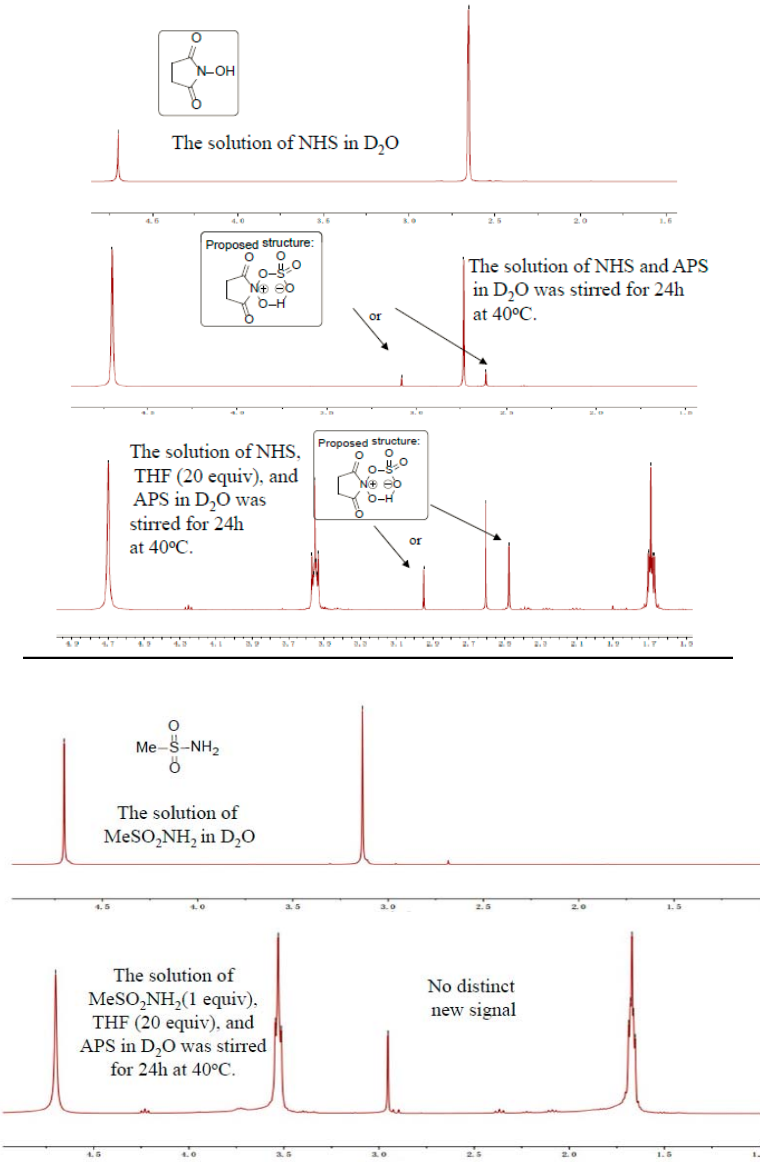


Fig. S4 The ^{1}H NMR spectra of the reaction solution of acetamide or NHS with APS

Electroparamagnetic resonance (EPR) study of the redox reactions of amide additive with APS

General procedure: the samples were prepared immediately before the acquisition, after tuning the ESR instrument parameters. The preparation is described as follows:

A solution of amide additive (0.05 mmol, 1 equiv.), DMPO (0.05 mmol, 1 equiv.) in H_2O (1.0 mL) was added to APS (0.05 mmol, 1 equiv.) in ESR tubes.

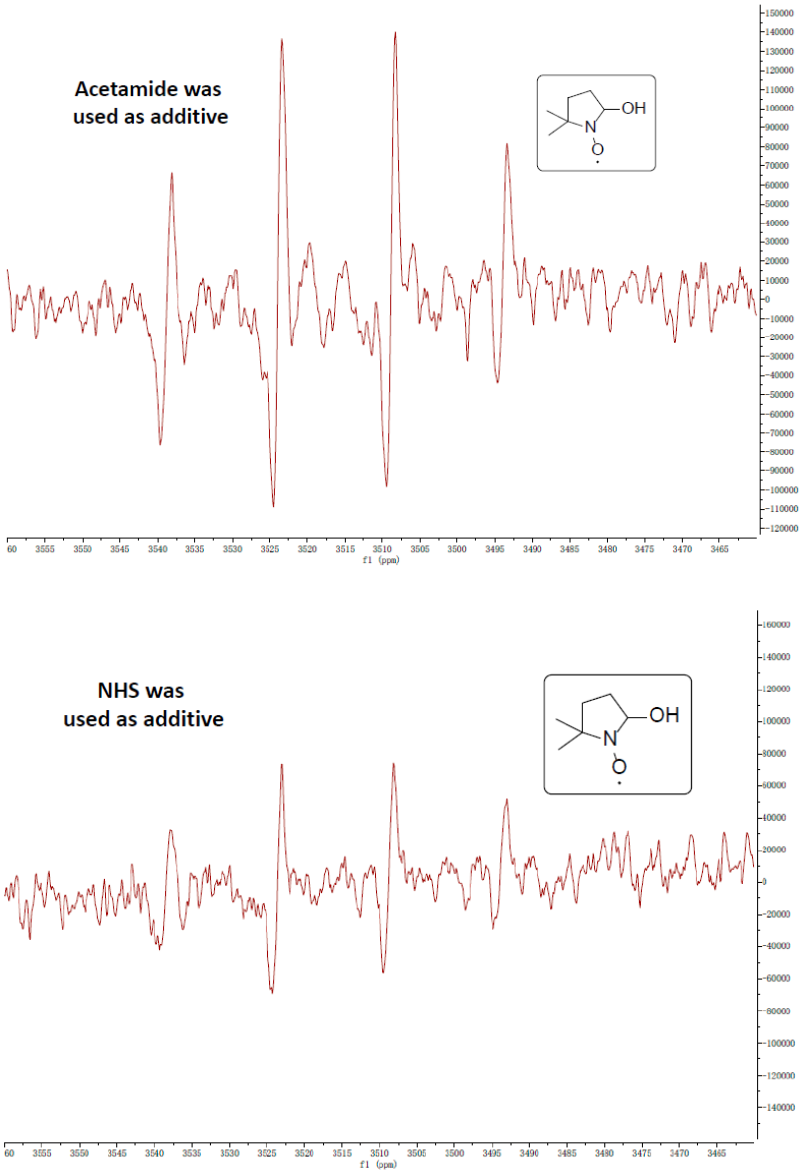
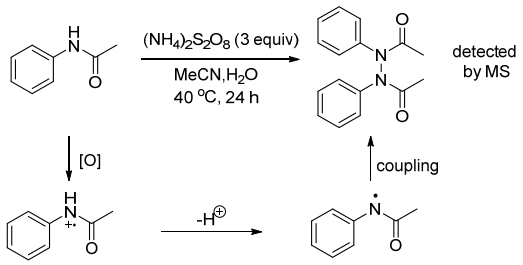


Fig. S5 The EPR spectra of the solution of APS in water with NHS and acetamide as additives

The MS study of the redox reaction of amide with APS



Scheme S8 APS mediated redox dimerization of N-phenylacetamide

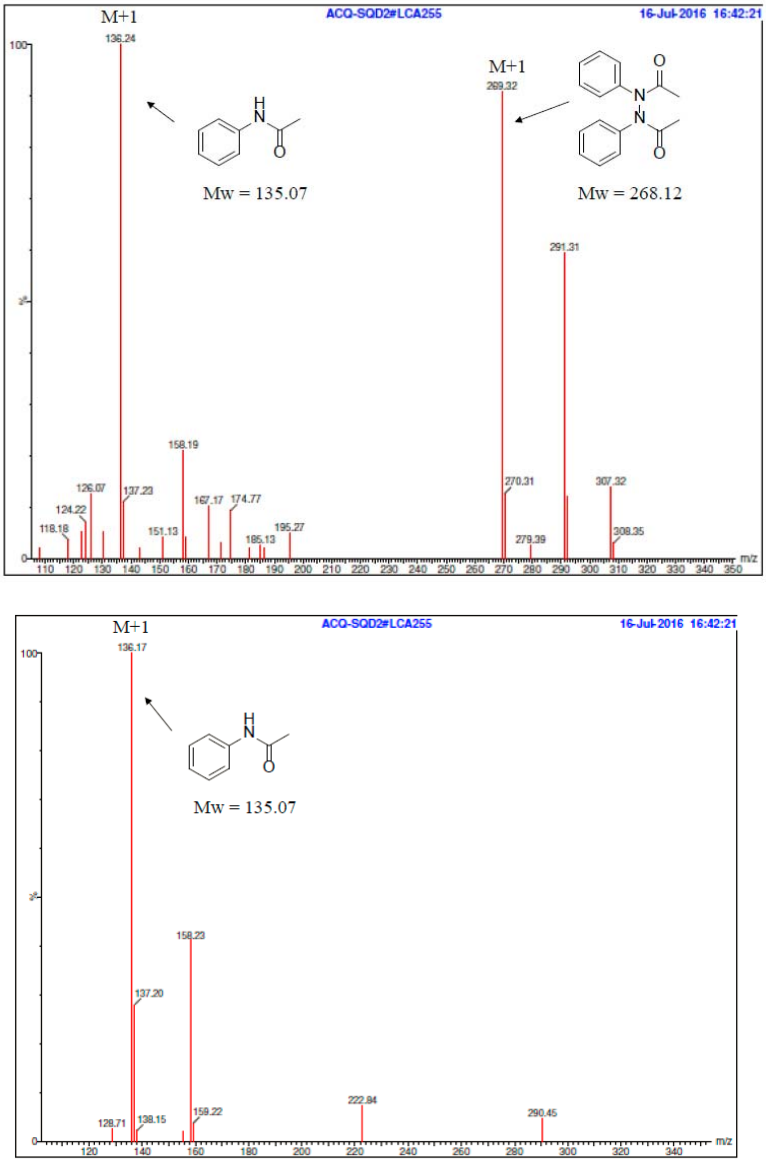
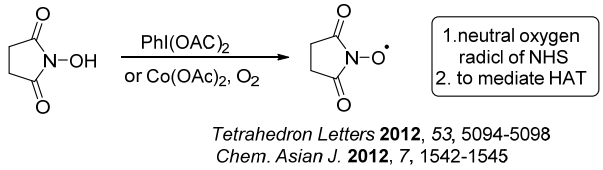


Fig. S6 MS data of N-phenylacetamide and crude product

The validation of neutral oxygen radical of NHS



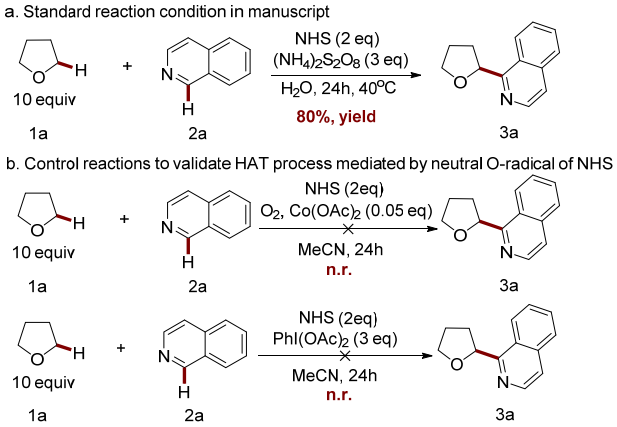
Tetrahedron Letters **2012**, *53*, 5094-5098
Chem. Asian J. **2012**, *7*, 1542-1545

Scheme S9 The reported approach to generate neutral oxygen radical of NHS

Notes: NHS is able to produce neutral oxygen radical after treated with $PhI(OAc)_2$ or $Co(OAc)_2/O_2$ to mediate HAT process according to Yamamoto's work.[5] Therefore, the

control reactions (Scheme S10), as well as EPR experiment of NHS after treating with APS and $PhI(OAc)_2$ immediately, were performed to investigate if neutral oxygen radical was involved in our NHS/APS reaction system. The experiment result suggests that this radical might not be generated in our reaction system.

The control reactions to validate neutral oxygen radical of NHS

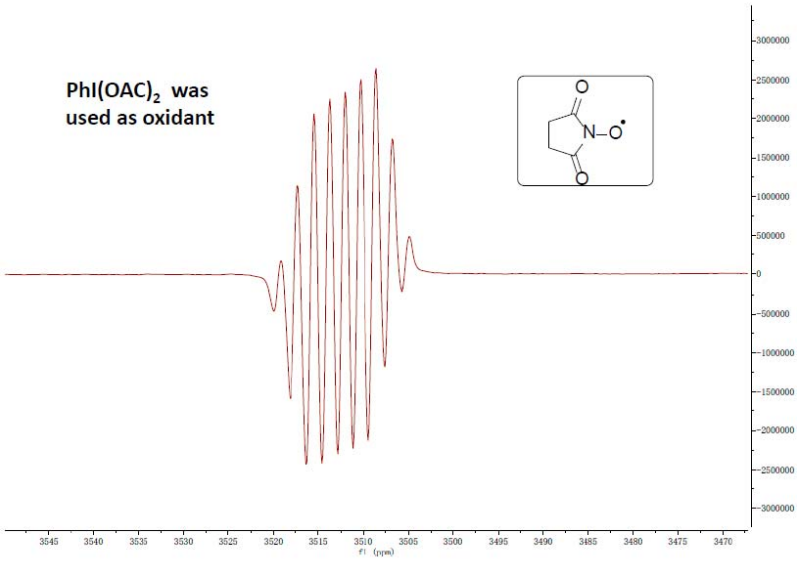


Scheme S10 Control reactions to generate neutral oxygen radical of NHS

Electroparamagnetic resonance (EPR) study

General procedure: the samples were prepared immediately before the acquisition, after tuning the ESR instrument parameters. The preparation is described as follows:

A solution of NHS (0.05 mmol, 1 equiv.) in CH_2Cl_2 (1.0 mL) was added to oxidant (0.05 mmol, 1 equiv.) in ESR tubes.[5]



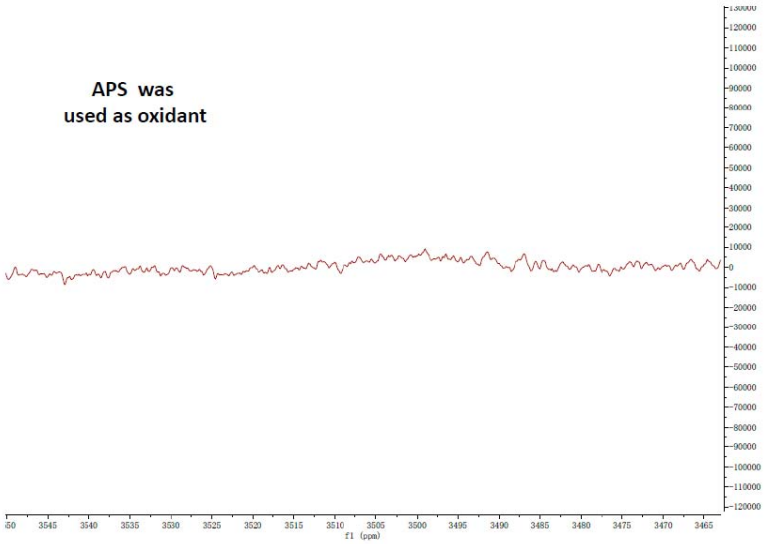
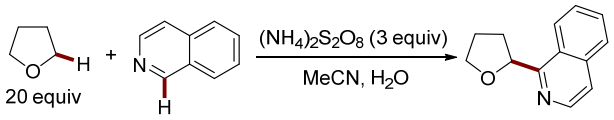


Fig. S7 The EPR spectra of the solution of NHS in water

The preliminary kinetic study of the reaction

Notes: The reaction kinetic was preliminary studied by collecting the time curve of the reaction with NHS or quinuclidin-3-ol as the additive. With NHS or quinuclidin-3-ol as additive at 40 ºC, the yield kept increasing during 24 h, and eventually 88% or 82% of yield were achieved. However, in the absence of these two additives, the highest yield (13%) was reached at 3 h, thereafter remained unchanged. Raising the temperature to 70 ºC (APS is easy to decompose at this temperature) resulted in moderate yield (less than 2 h, 63% yield).

Table S8 The preliminary kinetic study of NHS and quinuclidin-3-ol promoted CDC reaction [a]



1a 2a 3a

Entry	Time (h)	Yield (%) [b,c]	Yield (%) [b, d]	Yield (%) [b,e]	Yield (%) [b, f]
1	2	40%	36%	4%	63%
2	4	50%	44%	8%	63%
3	8	65%	61%	11%	64%
4	16	81%	76%	12%	60%
5	20	84%	79%	12%	53%
6	24	88%	82%	14%	50%

[a] Conditions employed **1a** (10.0 mmol), **2a** (0.5 mmol), $(NH_4)_2S_2O_8$ (1.5 mmol), 24 h, and a solvent mixture (1.5 mL, MeCN:H_2O = 1:1), unless otherwise noted; [b] Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard; [c] performed with NHS (1.0 mmol) at 40 ºC; [d] performed with Quinuclidin-3-ol (1.0 mmol) at 40 ºC; [e] performed at 40 ºC without additive; [f] performed at 70ºC without additive.

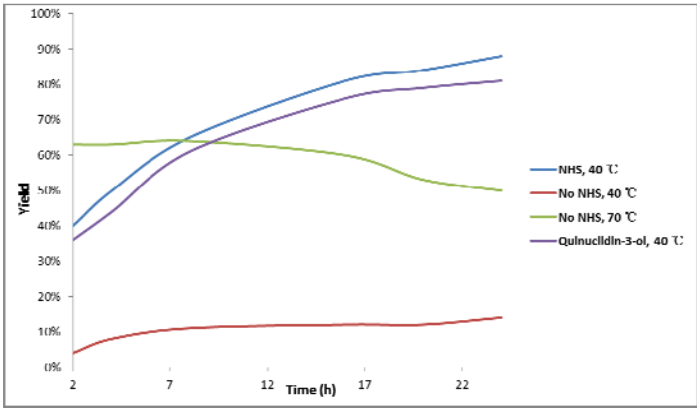


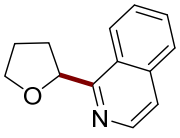
Fig. S8 The preliminary kinetic study of NHS and quinuclidin-3-ol promoted CDC reaction

Experiment Procedures and Product Characterization

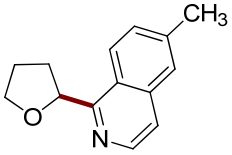
Commercial reagents and solvents were used as received, unless otherwise stated. Organic solution was concentrated under reduced pressure on a Büchi rotary evaporator using an isopropyl alcohol-dry ice bath. Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel plates (Qingdao Haiyang Chemical China), and the compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine. Flash chromatography was performed on silica gel 200–300 mesh (purchased from Qingdao Haiyang Chemical China) with commercial solvents (purchased from Adamas-beta®). The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 400 Spectrometer (400 and 100 MHz for ^{1}H and ^{13}C NMR, respectively) and are internally referenced to residual solvent signals (note: $CDCl_3$ referenced at 7.26 and 77.00 ppm in ^{1}H and ^{13}C NMR, respectively; d^6-DMSO referenced at 2.50 and 39.52 ppm in ^{1}H and ^{13}C NMR, respectively). Multiplicities were given as s (singlet), d (doublet), t (triplet), dd (double of doublet), and m (multiplets). Coupling constants were reported in Hertz (Hz). Data for ^{13}C NMR are reported in terms of chemical shift. High-resolution mass spectrometry (HRMS) was recorded on Waters LCT Premier XE spectrometer.

General procedure for Cα-heteroarylation of ether

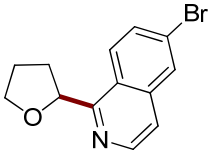
To a 10 mL sealed tube equipped with a magnetic stir bar was charged a heteroarene (0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (1.00 mmol, 2.0 equiv.), 1.5 mL H_2O, and 1.5 mL solvent mixture (MeCN:H_2O = 1:1). After stirring at 40 °C for the indicated time, the reaction mixture was diluted with 2.5 mL of aqueous NaOH (1 M), and extracted with EtOAc (20 mL × 3). The combined organic extracts were washed with brine (20 mL × 2), dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.



1-(Tetrahydrofuran-2-yl)isoquinoline (±3a): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (80 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.46 (d, *J* = 5.7 Hz, 1H), 8.29 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.65 - 7.58 (m, 1H), 7.58 - 7.50 (m, 2H), 5.68 (t, *J* = 7.1 Hz, 1H), 4.15 (dd, *J* = 14.4, 7.4 Hz, 1H), 4.03 - 3.97 (m, 1H), 2.52 - 2.43 (m, 1H), 2.42 - 2.31 (m, 1H), 2.19 - 2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.42, 141.38, 136.32, 129.63, 127.12, 126.92, 126.40, 125.08, 120.33, 78.92, 68.80, 30.59, 25.96; HRMS (ESI) Calcd. for $C_{13}H_{14}NO$ [$(M+H)^+$] 200.1075, found 200.1081.

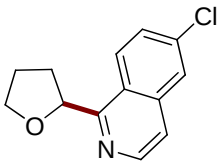


6-Methyl-1-(tetrahydrofuran-2-yl)isoquinoline (±3b): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 6-methylisoquinoline (72 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (94 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.43 (d, *J* = 5.7 Hz, 1H), 8.19 (d, *J* = 8.7 Hz, 1H), 7.56 (s, 1H), 7.45 (d, *J* = 5.7 Hz, 1H), 7.40 (dd, *J* = 8.7, 1.6 Hz, 1H), 5.67 (t, *J* = 7.1 Hz, 1H), 4.17 (dd, *J* = 14.4, 7.5 Hz, 1H), 4.04 - 3.98 (m, 1H), 2.50 (s, 3H), 2.49 - 2.33 (m, 2H), 2.22 - 2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.19, 141.58, 139.92, 136.75, 129.20, 126.09, 124.90, 119.91, 78.99, 68.84, 30.70, 26.05, 21.73; HRMS (ESI) Calcd. for $C_{14}H_{16}NO$ [$(M+H)^+$] 214.1232, found 214.1239.

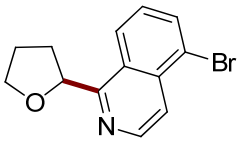


6-Bromo-1-(tetrahydrofuran-2-yl)isoquinoline (±3c): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 6-bromoisoquinoline (104 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (118 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.45 (d, *J* = 5.7 Hz, 1H), 8.18 (d, *J* = 9.0 Hz, 1H), 7.91 (d, *J* = 1.7 Hz, 1H), 7.60 (dd, *J* = 9.0, 1.9 Hz, 1H), 7.41 (d, *J* = 5.7 Hz,

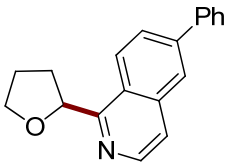
1H), 5.58 (t, *J* = 7.1 Hz, 1H), 4.10 (dd, *J* = 14.6, 7.3 Hz, 1H), 3.98 (dd, *J* = 14.2, 7.8 Hz, 1H), 2.61 - 2.42 (m, 1H), 2.37 - 2.29 (m, 1H), 2.22 - 1.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.72, 142.46, 137.56, 130.43, 129.20, 127.15, 124.94, 124.47, 119.33, 79.08, 68.88, 30.41, 25.98; HRMS (ESI) Calcd. for $C_{13}H_{13}BrNO$ [$(M+H)^+$] 278.0181, found 278.0167.



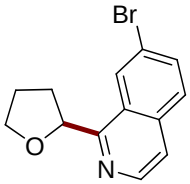
6-Chloro-1-(tetrahydrofuran-2-yl)isoquinoline (±3d): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 6-chloroisoquinoline (82 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (105 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.46 (d, *J* = 5.7 Hz, 1H), 8.28 (d, *J* = 9.0 Hz, 1H), 7.76 (d, *J* = 1.7 Hz, 1H), 7.49 (dd, *J* = 9.0, 1.9 Hz, 1H), 7.44 (d, *J* = 5.7 Hz, 1H), 5.61 (t, *J* = 7.1 Hz, 1H), 4.12 (dd, *J* = 14.6, 7.3 Hz, 1H), 4.00 (dd, *J* = 14.2, 7.8 Hz, 1H), 2.59 - 2.43 (m, 1H), 2.39 - 2.31 (m, 1H), 2.19 - 2.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.62, 142.51, 137.29, 135.91, 127.92, 127.23, 125.86, 124.79, 119.50, 79.16, 68.89, 30.41, 26.00; HRMS (ESI) Calcd. for $C_{13}H_{13}ClNO$ [$(M+H)^+$] 234.0686, found 234.0690.



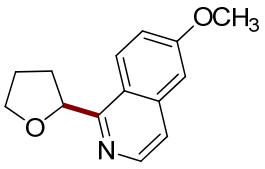
5-Bromo-1-(tetrahydrofuran-2-yl)isoquinoline (±3e): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 5-bromoisoquinoline (104 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (125 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.56 (d, *J* = 5.9 Hz, 1H), 8.30 (d, *J* = 8.5 Hz, 1H), 7.92 (s, 1H), 7.91 - 7.88 (m, 1H), 7.40 (dd, *J* = 8.4, 7.6 Hz, 1H), 5.67 (t, *J* = 7.0 Hz, 1H), 4.12 (dd, *J* = 14.3, 7.5 Hz, 1H), 4.03 - 3.97 (m, 1H), 2.61 - 2.44 (m, 1H), 2.44 - 2.30 (m, 1H), 2.21 - 2.01 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 159.75, 142.66), 135.35, 133.38, 127.55, 127.16, 124.91, 122.03, 119.11, 78.77, 68.82, 30.40, 25.90; HRMS (ESI) Calcd. for $C_{13}H_{13}BrNO$ [$(M+H)^+$] 278.0181, found 278.0186.



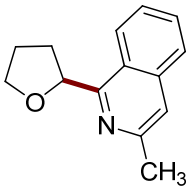
6-Phenyl-1-(tetrahydrofuran-2-yl)isoquinoline (±3f): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 6-phenylisoquinoline (103 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (20% ethyl acetate/petroleum ether) to provide the title compound as a white solid (131 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.51 (d, *J* = 5.7 Hz, 1H), 8.39 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 1.5 Hz, 1H), 7.83 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.73 - 7.66 (m, 2H), 7.59 (d, *J* = 5.7 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 5.72 (t, *J* = 7.1 Hz, 1H), 4.20 (dd, *J* = 14.5, 7.4 Hz, 1H), 4.07 - 4.02 (m, 1H), 2.59 - 2.50 (m, 1H), 2.47 - 2.34 (m, 1H), 2.24 - 2.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.38, 142.20, 141.85, 139.89, 136.76, 128.85, 127.97, 127.33, 126.65, 125.75, 125.50, 124.73, 120.57, 79.03, 68.84, 30.59, 26.02; HRMS (ESI) Calcd. for $C_{19}H_{18}NO$ $[(M+H)^+]$ 276.1388, found 276.1383.



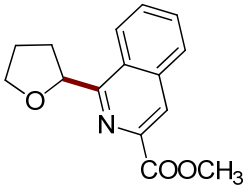
7-Bromo-1-(tetrahydrofuran-2-yl)isoquinoline (±3g): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 7-bromoisoquinoline (104 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (118 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.49 (dd, *J* = 10.2, 3.2 Hz, 2H), 7.71 - 7.63 (m, 2H), 7.49 (d, *J* = 5.6 Hz, 1H), 5.57 (t, *J* = 7.1 Hz, 1H), 4.12 (dd, *J* = 14.5, 7.5 Hz, 1H), 4.03 - 3.98 (m, 1H), 2.57 - 2.48 (m, 1H), 2.43 - 2.30 (m, 1H), 2.21 - 2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.61, 141.81, 134.83, 133.20, 128.80, 127.82, 127.52, 120.85, 120.09, 79.03, 68.89, 30.35, 26.00; HRMS (ESI) Calcd. for $C_{13}H_{13}BrNO$ $[(M+H)^+]$ 278.0181, found 278.0187.



6-Methoxy-1-(tetrahydrofuran-2-yl)isoquinoline (±3h): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 6-methoxyisoquinoline (80 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (83 mg, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.40 (d, *J* = 5.7 Hz, 1H), 8.23 (d, *J* = 9.3 Hz, 1H), 7.45 (d, *J* = 5.7 Hz, 1H), 7.20 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.04 (d, *J* = 2.3 Hz, 1H), 5.62 (t, *J* = 7.2 Hz, 1H), 4.16 (dd, *J* = 14.5, 7.4 Hz, 1H), 4.00 (dd, *J* = 14.1, 7.8 Hz, 1H), 3.91 (s, 3H), 2.53 - 2.42 (m, 1H), 2.40 - 2.32 (m, 1H), 2.20 - 2.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.23, 158.94, 142.13, 138.59, 127.03, 122.21, 119.80, 104.70, 79.16, 68.87, 55.32, 30.75, 26.07; HRMS (ESI) Calcd. for $C_{14}H_{16}NO_2$ $[(M+H)^+]$ 230.1181, found 230.1202.

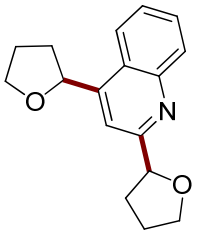


3-methyl-1-(tetrahydrofuran-2-yl)isoquinoline (±3i): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 3-methylisoquinoline (72 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (83 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.30 (d, *J* = 8.3 Hz, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.38 (s, 1H), 5.65 (t, *J* = 7.1 Hz, 1H), 4.20 (dd, *J* = 14.3, 7.3 Hz, 1H), 4.02 (dd, *J* = 14.2, 7.5 Hz, 1H), 2.67 (s, 3H), 2.58 - 2.50 (m, 1H), 2.40 - 2.32 (m, 1H), 2.21 - 2.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.72, 150.03, 137.28, 129.51, 126.59, 125.88, 125.17, 124.59, 118.32, 79.67, 68.86, 30.59, 25.98, 24.28; HRMS (ESI) Calcd. for $C_{14}H_{16}NO$ $[(M+H)^+]$ 214.1232, found 214.1237.

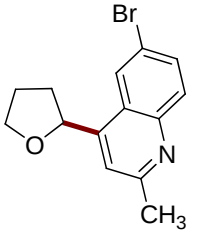


Methyl 1-(tetrahydrofuran-2-yl)isoquinoline-3-carboxylate (±3j): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), methyl isoquinoline-3-carboxylate (94 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5

mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (20% ethyl acetate/petroleum ether) to provide the title compound as a white solid (104 mg, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.53 - 8.44 (m, 2H), 7.94 (dd, *J* = 6.6, 2.7 Hz, 1H), 7.77 - 7.64 (m, 2H), 5.65 (t, *J* = 7.2 Hz, 1H), 4.16 (dd, *J* = 14.7, 7.5 Hz, 1H), 4.07 - 3.94 (m, 4H), 2.73 - 2.64 (m, 1H), 2.50 - 2.33 (m, 1H), 2.28 - 2.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.50, 160.01, 140.02, 136.38, 130.51, 129.31, 128.77, 128.17), 126.00, 124.14, 80.40, 68.98, 52.69, 30.26, 26.10; HRMS (ESI) Calcd. for $C_{15}H_{16}NO_3$ [$(M+H)^+$] 258.1130, found 258.1125.

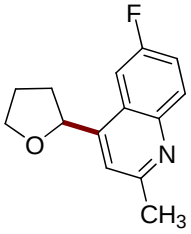


2,4-bis(tetrahydrofuran-2-yl)quinoline (±3k): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), quinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 72 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title mixture as a colourless oil (102mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.07 (dd, *J* = 8.1, 6.0 Hz, 1H), 7.87 (t, *J* = 8.4 Hz, 1H), 7.76 - 7.62 (m, 2H), 7.49 (dd, *J* = 8.2, 7.0 Hz, 1H), 5.57 (dd, *J* = 17.0, 7.2 Hz, 1H), 5.22 - 5.07 (m, 1H), 4.29 - 4.10 (m, 2H), 4.08 - 3.95 (m, 2H), 2.66 - 2.53 (m, 1H), 2.51 - 2.43 (m, 1H), 2.15 - 1.93 (m, 5H), 1.92 - 1.76 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.56, 163.10, 150.01, 149.74, 147.54, 147.38, 129.81, 129.68, 128.89, 128.95, 125.80, 124.74, 124,70, 123.12, 123,02, 113.72, 113.00, 82.21, 81.95, 77.11, 76.90, 69.26, 69.09, 68.92, 68.83, 33.82, 33.72, 33.49, 32.99, 25.90, 25.87. HRMS (ESI) Calcd. for $C_{17}H_{20}NO_2$ [$(M+H)^+$] 270.1489, found 270.1491.

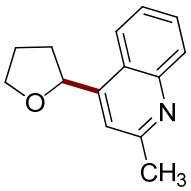


6-Bromo-2-methyl-4-(tetrahydrofuran-2-yl)quinoline (±3l): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 6-bromo-2-methylquinoline (111 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash

chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (127 mg, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.93 (d, *J* = 2.1 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.67 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.41 (s, 1H), 5.41 (t, *J* = 7.2 Hz, 1H), 4.17 (dd, *J* = 13.5, 7.7 Hz, 1H), 3.99 (dd, *J* = 15.3, 7.1 Hz, 1H), 2.67 (s, 3H), 2.61 - 2.50 (m, 1H), 2.11 - 1.90 (m, 2H), 1.81 - 1.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.47, 148.31, 146.36, 132.17, 130.98, 125.34, 125.02, 119.28, 117.92, 68.85, 33.72, 25.87, 25.40; HRMS (ESI) Calcd. for $C_{14}H_{15}BrNO$ [$(M+H)^+$] 292.0337, found 292.0401.

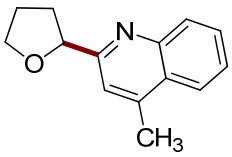


6-Fluoro-2-methyl-4-(tetrahydrofuran-2-yl)quinoline (±3m): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 6-fluoro-2-methylquinoline (81 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (102 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.99 (dd, *J* = 9.1, 5.6 Hz, 1H), 7.43 - 7.34 (m, 3H), 5.38 (t, *J* = 7.2 Hz, 1H), 4.23 - 4.11 (m, 1H), 3.98 (dd, *J* = 15.4, 7.1 Hz, 1H), 2.68 (s, 3H), 2.57 - 2.49 (m, 1H), 2.09 - 1.89 (m, 2H), 1.81 - 1.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.82, 158.37, 159.23, 158.20, 148,62, 149.56, 144.85, 131.60, 131.51, 124.34, 124.25, 118.83, 118.58, 117.84, 106.85, 106.63, 68.84, 33.46, 25.81, 25.21; HRMS (ESI) Calcd. for $C_{14}H_{15}FNO$ [$(M+H)^+$] 232.1138, found 232.1143.

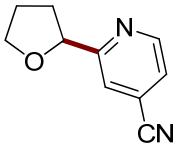


2-Methyl-4-(tetrahydrofuran-2-yl)quinoline (±3n): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 2-methylquinoline (72 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (85 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.03 (dd, *J* = 8.4, 0.5 Hz, 1H), 7.81 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.64 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.47 - 7.43 (m, 1H), 7.42 (d, *J* = 0.7 Hz, 1H), 5.54 (t, *J* = 7.1 Hz, 1H), 4.25 - 4.14 (m, 1H), 4.07 - 3.94 (m, 1H), 2.72

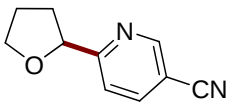
(s, 3H), 2.63 - 2.51 (m, 1H), 2.09 - 1.91 (m, 2H), 1.87 - 1.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.08, 149.42, 147.78, 129.23, 128.99, 125.51, 123.84, 123.00, 117.21, 76.75, 68.98, 63.48, 33.88, 25.97; HRMS (ESI) Calcd. for $C_{14}H_{16}NO$ [$(M+H)^+$] 214.1232, found 214.1245.



4-Methyl-2-(tetrahydrofuran-2-yl)quinoline (±3o): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 4-methylquinoline (72 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (83 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.05 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.72 -7.64 (m, 1H), 7.54 - 7.48 (m, 1H), 7.44 (s, 1H), 5.13 (t, J = 6.9 Hz, 1H), 4.23 - 4.14 (m, 1H), 4.06 - 4.01 (m, 1H), 2.70 (s, 3H), 2.56 - 2.44 (m, 1H), 2.13 - 1.93 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 163.04, 147.27, 144.90, 129.48, 129.08, 127.40, 125.76, 123.64, 118.54, 82.03, 69.21, 33.28, 25.93, 18.85; HRMS (ESI) Calcd. for $C_{14}H_{16}NO$ [$(M+H)^+$] 214.1232, found 214.1240.

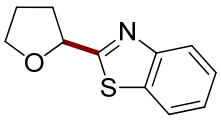


2-(Tetrahydrofuran-2-yl) isonicotinonitrile (±3p): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), isonicotinonitrile (52 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (49 mg, 56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.71 (dd, J = 5.0, 0.7 Hz, 1H), 7.74 - 7.69 (m, 1H), 7.38 (dd, J = 4.8, 1.3 Hz, 1H), 5.08 - 5.02 (m, 1H), 4.15 - 4.07 (m, 1H), 4.04 - 3.96 (m, 1H), 2.51 - 2.41 (m, 1H), 2.05 - 1.89 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.23, 149.91, 123.37, 121.59, 120.88, 116.72, 80.63 , 69.28, 33.03, 25.65; HRMS (ESI) Calcd. for $C_{10}H_{11}N_2O$ [$(M+H)^+$] 175.0871, found 175.0880.

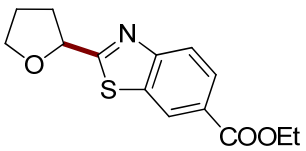


6-(Tetrahydrofuran-2-yl)nicotinonitrile (±3q): According to the general procedure,

tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), nicotinonitrile (52 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (54 mg, 62% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.79 (d, *J* = 1.4 Hz, 1H), 7.93 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 5.04 (dd, *J* = 7.4, 5.9 Hz, 1H), 4.07 (ddd, *J* = 6.3, 5.6, 2.4 Hz, 1H), 4.02 - 3.94 (m, 1H), 2.50 - 2.39 (m, 1H), 2.06 - 1.87 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 167.76, 151.73, 139.73, 119.67, 116.76, 107.98, 80.79, 69.25, 32.97, 25.62; HRMS (ESI) Calcd. for $C_{10}H_{11}N_2O$ [$(M+H)^+$] 175.0871, found 175.0880.

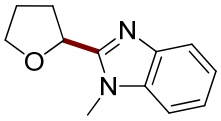


2-(Tetrahydrofuran-2-yl)benzo[d]thiazole (±3r): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), benzo[d]thiazole (68 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (5% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (57 mg, 56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.97 (d, *J* = 8.2 Hz, 1H), 7.88 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.46 (ddd, *J* = 8.3, 7.3, 1.3 Hz, 1H), 7.38 - 7.34 (m, 1H), 5.35 (dd, *J* = 7.8, 5.4 Hz, 1H), 4.19 - 4.13 (m, 1H), 4.03 - 3.98 (m, 1H), 2.57 - 2.48 (m, 1H), 2.32 - 2.22 (m, 1H), 2.09 - 1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 176.43, 153.68, 134.74, 125.95, 124.79, 122.79, 121.80, 78.77, 69.49, 33.41, 25.72; HRMS (ESI) Calcd. for $C_{11}H_{12}NOS$ [$(M+H)^+$] 206.0640, found 206.0645.

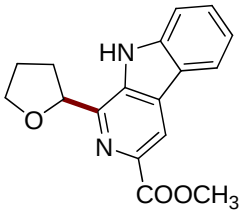


Ethyl 2-(tetrahydrofuran-2-yl)benzo[d]thiazole-6-carboxylate (±3s): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), ethyl benzo[d]thiazole-6-carboxylate (104 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (67 mg, 48% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.60 (d, *J* = 1.3 Hz, 1H), 8.14 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.98 (d, *J* = 8.6 Hz, 1H), 5.35 (dd, *J* = 7.9, 5.4 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.22 - 4.11 (m, 1H), 4.01 (dd, *J* = 15.3, 7.1 Hz, 1H), 2.58 - 2.49 (m, 1H), 2.31 - 2.23 (m, 1H), 2.09 - 1.96 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H);

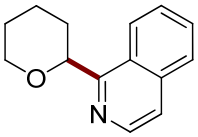
^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 180.25, 166.17, 156.57, 134.60, 127.13, 126.91, 123.93, 122.40, 78.75), 69.54, 61.21, 33.33, 25.68, 14.32; HRMS (ESI) Calcd. for $C_{14}H_{16}NO_3S$ [$(M+H)^+$] 278.0851, found 278.0847.



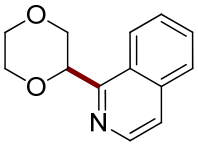
1-Methyl-2-(tetrahydrofuran-2-yl)-1H-benzo[d]imidazole (±3u): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), 1-methyl-1H-benzo[d]imidazole (66 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (50% ethyl acetate/petroleum ether) to provide the title compound as a white solid (46 mg, 45% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76 (dd, *J* = 6.7, 1.8 Hz, 1H), 7.36 - 7.18 (m, 3H), 5.19 (t, *J* = 6.9 Hz, 1H), 3.93 (t, *J* = 6.8 Hz, 2H), 3.84 (s, 3H), 2.86 - 2.71 (m, 1H), 2.42 - 2.28 (m, 1H), 2.24 - 2.14 (m, 1H), 2.12 - 1.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 153.49, 141.79, 136.35, 122.62, 121.90, 119.69, 109.09, 73.48, 68.63, 30.13, 29.26, 25.96; HRMS (ESI) Calcd. for $C_{12}H_{15}N_2O$ [$(M+H)^+$] 203.1184, found 203.1189.



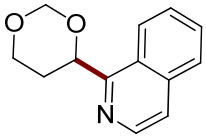
Methyl 1-(tetrahydrofuran-2-yl)-9H-pyrido[3,4-b]indole-3-carboxylate (±3w): According to the general procedure, tetrahydrofuran (360 mg, 5.00 mmol, 10.0 equiv.), methyl 9H-pyrido[3,4-b]indole-3-carboxylate [6] (113 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% methanol/ dichloromethane) to provide the title compound as a white solid (135 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.70 (s, 1H), 8.78 (s, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 7.63 - 7.50 (m, 2H), 7.33 - 7.29 (m, 1H), 5.51 (t, *J* = 7.1 Hz, 1H), 4.16 (dd, *J* = 14.0, 7.8 Hz, 1H), 4.10 - 3.99 (m, 4H), 2.66 - 2.58 (m, 1H), 2.43 - 2.34 (m, 1H), 2.12 - 1.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.70, 145.37, 140.31, 136.61, 134.97, 129.39, 128.71, 121.64, 121.31, 120.51, 116.79, 111.90, 82.78, 69.02, 52.55, 32.20, 25.43; HRMS (ESI) Calcd. for $C_{17}H_{17}N_2O_3$ [$(M+H)^+$] 297.1239, found 297.1243.



1-(Tetrahydro-2H-pyran-2-yl)isoquinoline (±4a): According to the general procedure, tetrahydro-2H-pyran (430 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of MeCN/H_2O (1: 1) were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (91 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.41 (dd, *J* = 5.6, 0.9 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.52 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.49 - 7.40 (m, 2H), 5.07 (d, *J* = 11.1 Hz, 1H), 4.15 (d, *J* = 12.7 Hz, 1H), 3.67 (t, *J* = 11.6 Hz, 1H), 2.09 - 1.84 (m, 3H), 1.81 - 1.63 (m, 2H), 1.54 (d, *J* = 12.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.47, 141.51, 136.42, 129.56, 127.15, 126.79, 125.83, 125.03, 120.33, 79.08, 69.20, 30.88, 25.70, 23.79; HRMS (ESI) Calcd. for $C_{14}H_{16}NO$ [$(M+H)^+$] 214.1232, found 214.1227.

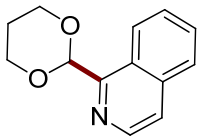


1-(1,4-Dioxan-2-yl)isoquinoline (±4b): According to the general procedure, 1,4-dioxane (440 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 12 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a white solid (97 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.48 (d, *J* = 5.7 Hz, 1H), 8.26 (d, *J* = 8.6 Hz, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.63 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.60 - 7.53 (m, 2H), 5.42 (dd, *J* = 9.6, 3.0 Hz, 1H), 4.14 (dd, *J* = 11.9, 3.0 Hz, 1H), 4.11 - 3.98 (m, 3H), 3.90 - 3.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 155.79, 141.61, 136.26, 129.84, 127.27, 126.30, 124.51, 120.88, 75.65, 70.08, 67.38, 66.32; HRMS (ESI) Calcd. for $C_{13}H_{14}NO_2$ [$(M+H)^+$] 216.1025, found 216.0968.

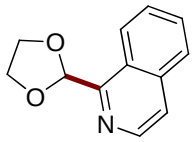


1-(1,3-Dioxan-4-yl)isoquinoline(±4c major isomer): According to the general procedure, 1,3-dioxane (440 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy

succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of MeCN/H_2O (1: 1) were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (20% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (49 mg, 46% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.50 (d, *J* = 5.7 Hz, 1H), 8.47 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.68 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.65 – 7.57 (m, 2H), 5.47 (dd, *J* = 11.1, 2.6 Hz, 1H), 5.30 (d, *J* = 6.3 Hz, 1H), 5.06 (d, *J* = 6.3 Hz, 1H), 4.34 (dd, *J* = 11.4, 4.7 Hz, 1H), 4.06 - 3.99 (m, 1H), 2.78 - 2.60 (m, 1H), 1.91 - 1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.57, 141.52, 136.77, 129.94, 127.39, 127.21, 126.22, 125.36, 121.11, 94.21, 78.71, 66.94, 30.48; HRMS (ESI) m/z calculated for $C_{13}H_{14}NO_2$ [$(M+H)^+$] 216.1025, found 216.1032.

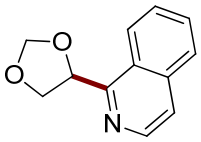


1-(1,3-dioxan-2-yl) isoquinoline (±4c minor isomer): According to the general procedure, 1,3-dioxane (440 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of MeCN/H_2O (1: 1) were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (20% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (30 mg, 28% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.69 (d, *J* = 8.6 Hz, 1H), 8.49 (d, *J* = 5.7 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.71 - 7.56 (m, 3H), 6.11 (s, 1H), 4.39 (dd, *J* = 11.3, 4.5 Hz, 2H), 4.17 - 4.10 (m, 2H), 2.53 - 2.41 (m, 1H), 1.60 - 1.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 154.88, 141.20, 137.04, 130.03, 127.19, 126.95, 126.38, 125.88, 122.00, 104.30, 67.86, 25.96; HRMS (ESI) Calcd. for $C_{13}H_{14}NO_2$ [$(M+H)^+$] 216.1025, found 216.1032.

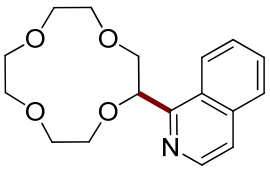


1-(1,3-Dioxolan-2-yl)isoquinoline (±4d major isomer): According to the general procedure, 1,3-dioxolane (370 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (83 mg, 82% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.53 (d, *J* = 5.6 Hz, 1H), 8.39 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.75 - 7.53 (m, 3H), 6.46 (s, 1H), 4.41 - 4.28 (m, 2H), 4.25 - 4.12 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 154.57, 141.45, 136.68,

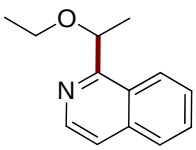
129.99, 127.29, 127.16, 126.28, 125.14, 121.88, 103.46, 65.45; HRMS (ESI) Calcd. for $C_{12}H_{12}NO_2$ [$(M+H)^+$] 202.0868, found 202.0859.



1-(1,3-dioxolan-4-yl) isoquinoline (±4d minor isomer): According to the general procedure, 1,3-dioxolane (370 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (10 mg, 10% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.50 (d, *J* = 5.7 Hz, 1H), 8.36 (d, *J* = 8.6 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.75 - 7.68 (m, 1H), 7.65 (dd, *J* = 11.2, 3.9 Hz, 2H), 5.80 (t, *J* = 6.7 Hz, 1H), 5.29 (s, 1H), 5.20 (s, 1H), 4.57 (dd, *J* = 8.1, 6.5 Hz, 1H), 4.42 (dd, *J* = 8.0, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 156.29, 141.44, 136.59, 130.12 (s), 127.52, 127.42, 126.85, 124.93, 121.21, 96.00, 76.15, 68.43; HRMS (ESI) Calcd. for $C_{12}H_{12}NO_2$ [$(M+H)^+$] 202.0868, found 202.0859.

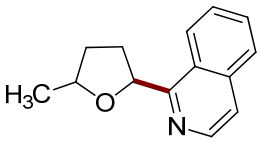


1-(1,4,7,10-Tetraoxacyclododecan-2-yl)isoquinoline (±4e): According to the general procedure, 1,4,7,10-tetraoxacyclododecane (440 µL, 2.50 mmol, 5.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% methanol/ dichloromethane) to provide the title compound as a colourless oil (114 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.55 (d, *J* = 8.6 Hz, 1H), 8.48 (d, *J* = 5.7 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.68 - 7.62 (m, 1H), 7.61 - 7.53 (m, 2H), 5.64 (dd, *J* = 9.5, 2.4 Hz, 1H), 4.14 - 4.08 (m, 1H), 3.95 - 3.67 (m, 12H), 3.55 - 3.47 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.34, 141.30, 136.24, 129.56, 127.04, 126.84, 126.33, 125.03, 120.24, 78.85, 68.71, 67.69, 53.29, 30.48, 25.90, 25.36, 18.91; HRMS (ESI) Calcd. for $C_{17}H_{22}NO_4$ [$(M+H)^+$] 304.1549, found 304.1540.

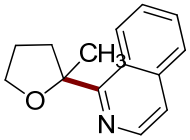


1-(1-Ethoxyethyl)isoquinoline (±4f): According to the general procedure, diethyl

ether (370 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.) $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of MeCN/H_2O (1: 1) were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (65 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.69 (d, *J* = 8.6 Hz, 1H), 8.46 (d, *J* = 5.7 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.9 Hz, 2H), 5.17 (q, *J* = 6.7 Hz, 1H), 3.53 - 3.47 (m, 1H), 3.43 - 3.36 (m, 1H), 1.70 (d, *J* = 6.8 Hz, 3H), 1.19 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 161.79, 141.52, 136.81, 129.87, 127.39, 126.85, 126.05, 125.57, 120.50, 80.09, 64.47, 21.63, 15.45; HRMS (ESI) Calcd. for $C_{13}H_{16}NO$ [$(M+H)^+$] 202.1232, found 202.1239.

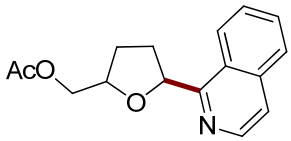


1-(5-Methyltetrahydrofuran-2-yl) isoquinoline (±4g major isomer): According to the general procedure, 2-methyltetrahydrofuran (430 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of MeCN/H_2O (1: 1) were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (59mg, 55% yield; diastereoisomers, d.r. 1.7: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.48 (d, *J* = 5.7 Hz, 1H), 8.41(8.33) (d, *J* = 8.4 Hz, 1H); 7.79 (d, *J* = 8.0 Hz, 1H), 7.64 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.61 - 7.52 (m, 2H), 5.61(5.86) (t, *J* = 7.3 Hz, 1H), 4.30 - 4.22(4.49 - 4.40) (m, 1H), 2.67 - 2.51 (m, 1H), 2.48 - 2.33 (m, 1H), 2.32 - 2.17 (m, 1H), 1.81 - 1.67 (m, 1H), 1.38(1.37) (d, J = 6.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.02 (159.06), 141.49, 136.52 (136.43), 129.70 (129.68), 127.20 (127.13), 126.99 (126.95), 126.47, 125.58 (125.20), 120.53 (120.31), 79.88 (78.37), 76.73 (75.96), 33.99 (33.10), 31.36 (30.29), 21.32 (21.06). HRMS (ESI) m/z calculated for $C_{14}H_{16}NO$ [$(M+H)^+$] 214.1232, found 214.1237.

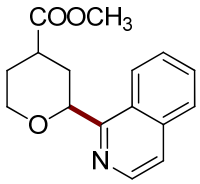


1-(2-methyltetrahydrofuran -2-yl)isoquinoline (±4g minor isomer): According to the general procedure, 2-methyltetrahydrofuran (430 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of MeCN/H_2O (1: 1) were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash

chromatography (10% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (29mg, 27% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.01 (d, *J* = 8.6 Hz, 1H), 8.42 (d, *J* = 5.6 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.65 - 7.58 (m, 1H), 7.56 - 7.50 (m, 2H), 4.14 - 3.98 (m, 1H), 3.82 - 3.68 (m, 1H), 3.32 - 3.17 (m, 1H), 2.11 - 1.97 (m, 2H), 1.93 - 1.81 (m, 1H), 1.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 163.68, 140.44, 137.25, 129.32, 128.00, 127.26, 126.27, 126.10, 120.33, 88.28, 67.71, 37.56, 28.29, 25.03; HRMS (ESI) Calcd. for $C_{14}H_{16}NO$ [$(M+H)^+$] 214.1232, found 214.1237.

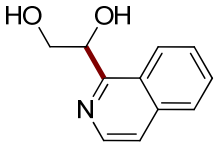


(5-(Isoquinolin-1-yl)tetrahydrofuran-2-yl)methyl acetate (±4h): According to the general procedure, (tetrahydrofuran-2-yl)methyl acetate (720 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (20% ethyl acetate/petroleum ether) to provide the title compound (diastereoisomers, d.r. 2.2: 1) as a colourless oil (95 mg, 70% yield); major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.47(8.45) (d, *J* = 5.7 Hz, 1H), 8.30(8.39) (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.69 - 7.64 (m, 1H), 7.63 - 7.55 (m, 2H), 5.87(5.74) (t, *J* = 6.9 Hz, 1H), 4.62 - 4.57(4.44 - 4.38) (m, 1H), 4.30 - 4.20(4.18 - 4.14) (m, 2H), 2.58 - 2.51(2.69 - 2.60) (m, 1H), 2.49 - 2.37 (m, 1H), 2.35 - 2.16 (m, 1H), 2.11(2.00) (s, 3H), 1.95 - 1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.16(171.02.9), 159.03(158.64), 141.46(141.37), 136.54(136.47), 129.87(129.81), 127.29(127.21), 127.17(127.04), 126.75(126.45), 125.50(125.08), 120.75(120.64), 80.32(79.10), 77.96(77.20), 66.53(66.53), 30.94(29.91), 28.26(28.09), 20.97(20.84);. HRMS (ESI) Calcd. for $C_{16}H_{18}NO_3$ [$(M+H)^+$] 272.1287, found 272.1289.

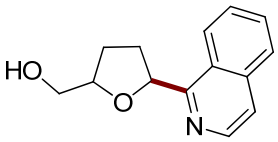


Methyl 2-(isoquinolin-1-yl)tetrahydro-2H-pyran-4-carboxylate (±4i): According to the general procedure, methyl tetrahydro-2H-pyran-4-carboxylate (720 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (20% ethyl acetate/petroleum ether) to provide the title compound as a colourless oil (84 mg, 62% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.54 (d, *J* =

5.7 Hz, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.70 - 7.65 (m, 1H), 7.63 (ddd, *J* = 8.2, 7.0, 1.4 Hz, 1H), 7.58 (d, *J* = 5.7 Hz, 1H), 5.57 (dd, *J* = 10.1, 2.6 Hz, 1H), 4.09 - 4.04 (m, 1H), 3.91 - 3.84 (m, 1H), 3.84 (s, 3H), 3.18 - 3.13 (m, 1H), 2.47 - 2.42 (m, 1H), 2.35 - 2.24 (m, 1H), 2.15 - 2.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 175.35, 158.96, 141.70, 136.36, 129.81, 127.27, 127.24, 125.97, 124.86, 120.50, 73.93, 65.42, 51.90, 37.07, 31.56, 27.28; HRMS (ESI) Calcd. for $C_{16}H_{18}NO_3$ [$(M+H)^+$] 272.1287, found 272.1282.

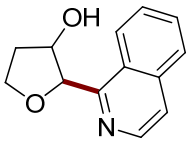


1-(Isoquinolin-1-yl)ethane-1,2-diol (±4j): According to the general procedure, 2,2-dimethyl-1,3-dioxolane (510 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of MeCN/H_2O (1: 1) were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (ethyl acetate) to provide the title compound as a colourless oil (70mg, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.45 (d, *J* = 5.7 Hz, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.73 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.69 - 7.59 (m, 2H), 5.55 (dd, *J* = 6.3, 3.2 Hz, 1H), 4.10 (dd, *J* = 11.5, 3.2 Hz, 1H), 3.76 (dd, *J* = 11.5, 6.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.69, 140.33, 136.47, 130.54, 127.74, 127.56, 125.33, 124.01, 121.10, 70.51, 67.60; HRMS (ESI) Calcd. for $C_{11}H_{12}NO_2$ [$(M+H)^+$] 190.0868, found 190.0879.

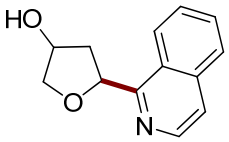


(5-(Isoquinolin-1-yl)tetrahydrofuran-2-yl)methanol (±4k): According to the general procedure, (tetrahydrofuran-2-yl)methanol (510 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (ethyl acetate) to provide the title compound (diastereoisomers, d.r. 2: 1) as a colourless oil (84 mg, 73% yield). Major: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.43 (d, *J* = 5.8 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.76 - 7.68 (m, 1H), 7.67 - 7.57 (m, 2H), 6.02 (dd, *J* = 8.5, 2.8 Hz, 1H), 4.50 - 4,45 (m, 1H), 4.24 (dd, *J* = 11.9, 2.4 Hz, 1H), 3.68 (m, 1H), 2.74 - 2.59 (m, 1H), 2.34 - 2.18 (m, 2H), 2.04 - 1.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 162.17, 140.50, 136.30, 130.36, 127.63, 127.49, 125.15, 123.76, 120.59, 82.10, 76.45, 63.70, 34.32, 25.31. Minor: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.49 (d, *J* = 5.7 Hz, 1H), 8.28 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H),

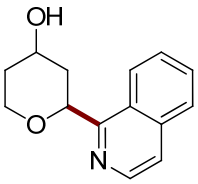
7.72 - 7.64 (m, 1H), 7.60 - 7.57 (m, 2H), 5.85 (t, *J* = 7.1 Hz, 1H), 4.53 - 4.47 (m, 1H), 3.83 (dd, *J* = 11.6, 3.3 Hz, 1H), 3.70 - 3.66 (m, 1H), 2.57 - 2.43 (m, 2H), 2.26 - 2.18 (m, 2H), 2.01 - 1.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.44, 141.47, 136.50, 129.91, 127.38, 127.17, 126.28, 124.97, 120.61, 80.32, 79.19, 65.02, 31.77, 27.70. HRMS (ESI) Calcd. for $C_{14}H_{16}NO_2$ [$(M+H)^+$] 230.1181, found 230.1185.



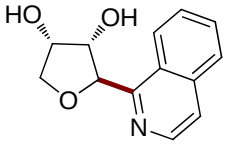
2-(Isoquinolin-1-yl)tetrahydrofuran -3-ol (±4l major isomer): According to the general procedure, tetrahydrofuran-2-ol (440 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (ethyl acetate) to provide the title mixture as a colourless oil (50 mg, 47% yield; diastereoisomers, d.r. 4.9: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.45(8.39) (d, *J* = 5.6 Hz, 1H), 8.39 - 8.35 (m, 1H), 7.84 - 7.80 (m, 1H), 7.74 - 7.66 (m, 1H), 7.66 - 7.57 (m, 2H), 6.95 (br, 1H), 6.11(5.27) (dd, *J* = 8.8, 1.6 Hz, 1H), 4.57 - 4.55(4.95 - 4.93) (m, 1H), 4.42 - 3.97 (m, 2H), 2.68 - 2.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.06(157.72), 140.71(139.73), 136.69(136.44), 130.51(130.43), 127.75 (127.67), 127.27 (127.10), 126.62 (125.80), 124.60, 121.26 (120.99), 78.67 (78.35), 75.21 (73.28), 72.32 (67.58), 38.95 (34.97). HRMS (ESI) Calcd. for $C_{13}H_{14}NO_2$ [$(M+H)^+$] 216.1025, found 216.1031.



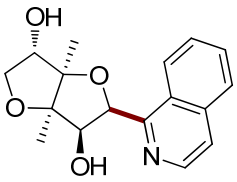
5-(Isoquinolin -1-yl) tetrahydrofuran-2-ol (±4l minor isomer): According to the general procedure, tetrahydrofuran-2-ol (440 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (ethyl acetate) to provide the title mixture as a colourless oil (25 mg, 23% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.45 (t, *J* = 7.5 Hz, 2H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.60 (dd, *J* = 13.9, 6.8 Hz, 2H), 5.43 (d, *J* = 4.4 Hz, 1H), 4.96 - 4.92 (m, 1H), 4.32 - 4.16 (m, 2H), 2.47 - 2.38 (m, 1H), 2.14 - 2.09 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.45, 141.40, 136.50, 130.00, 127.35, 127.26, 126.90, 125.19, 120.85, 77.40, 76.18, 72.80, 40.15. HRMS (ESI) Calcd. for $C_{13}H_{14}NO_2$ [$(M+H)^+$] 216.1025, found 216.1031.



2-(Isoquinolin-1-yl)tetrahydro-2H-pyran-4-ol (±4m): According to the general procedure, tetrahydro-2H-pyran-4-ol (510 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (ethyl acetate) to provide the title compound as a colourless oil (80 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.51 (d, *J* = 5.7 Hz, 1H), 8.34 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.69 - 7.63 (m, 1H), 7.63 - 7.55 (m, 2H), 5.76 (dd, *J* = 11.2, 2.3 Hz, 1H), 4.54 - 4.45 (m, 1H), 4.30 - 4.21 (m, 1H), 4.04 - 4.00 (m, 1H), 2.44 - 2.37 (m, 1H), 2.15 - 2.00 (m, 2H), 1.78 - 1.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.15, 141.64, 136.51, 129.85, 127.32, 127.15, 126.16, 125.05, 120.63, 72.21, 64.15, 63.34, 37.84, 32.92; HRMS (ESI) Calcd. for $C_{14}H_{16}NO_2$ $[(M+H)^+]$ 230.1181, found 230.1187.



(*3S,4S*)-2-(Isoquinolin-1-yl)tetrahydrofuran-3,4-diol (±4n): According to the general procedure, 1,4-anhydroerythritol (520 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (ethyl acetate) to provide the title compound as a colourless oil (87 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.46 (d, *J* = 5.8 Hz, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.79 - 7.73 (m, 1H), 7.72 - 7.66 (m, 2H), 5.81 (d, *J* = 6.2 Hz, 1H), 4.84 (dd, *J* = 6.1, 5.2 Hz, 1H), 4.46 - 4.43 (m, 1H), 4.20 - 4.18 (m, 1H), 4.15 - 4.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.63, 139.60, 136.87, 131.07, 128.24, 127.84, 127.46, 125.12, 121.74, 75.60, 74.45, 73.63, 72.39; HRMS (ESI) Calcd. for $C_{13}H_{14}NO_3$ $[(M+H)^+]$ 232.0974, found 232.0970.



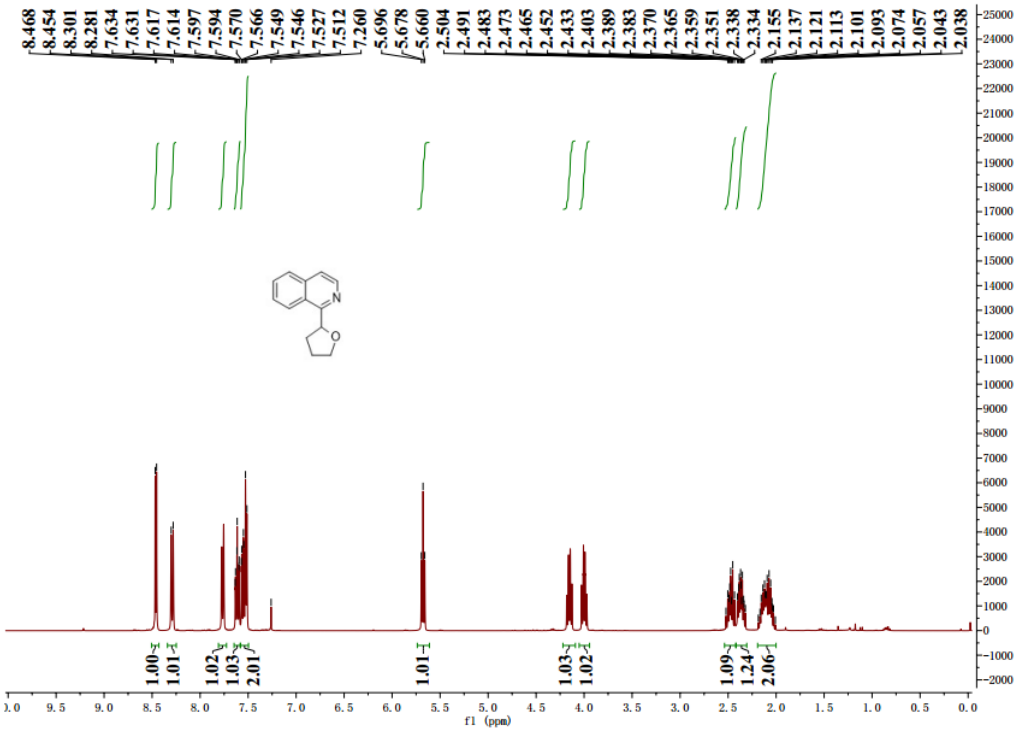
(*3R,3aR,6S,6aR*)-2-(Isoquinolin-1-yl)-3a,6a-dimethylhexahydrofuro[3,2-b]furan-

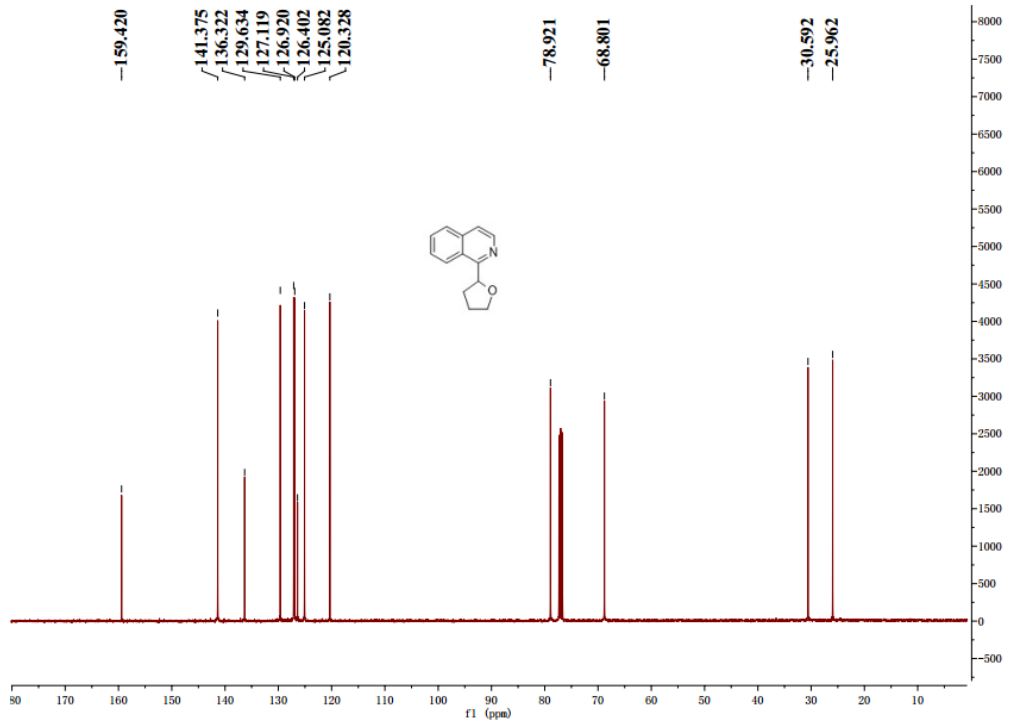
3,6-diol (±4o): According to the general procedure, isosorbide (870 mg, 5.00 mmol, 10.0 equiv.), isoquinoline (65 mg, 0.50 mmol, 1.0 equiv.), $(NH_4)_2S_2O_8$ (342 mg, 1.50 mmol, 3.0 equiv.), N-Hydroxy succinimide (115 mg, 1.00 mmol, 2.0 equiv.) and 1.5 mL of H_2O were used. After 24 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (ethyl acetate) to provide the title compound as a colourless oil (98 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.47 (d, *J* = 5.7 Hz, 1H), 8.31 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.73 - 7.67 (m, 1H), 7.65 - 7.59 (m, 2H), 5.51 (d, *J* = 6.2 Hz, 1H), 4.96 - 4.88 (m, 1H), 4.82 (dd, *J* = 11.4, 5.4 Hz, 2H), 4.57 (d, *J* = 3.2 Hz, 1H), 4.20 (dd, *J* = 10.1, 3.5 Hz, 1H), 4.11 (d, *J* = 10.1 Hz, 1H), 2.90 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 156.77, 141.33, 136.54, 130.25, 127.54, 127.33, 126.85, 125.10, 121.18, 88.13, 83.47, 82.29, 76.85, 75.87; HRMS (ESI) Calcd. for $C_{17}H_{20}NO_4$ [$(M+H)^+$] 302.1392, found 302.1387.

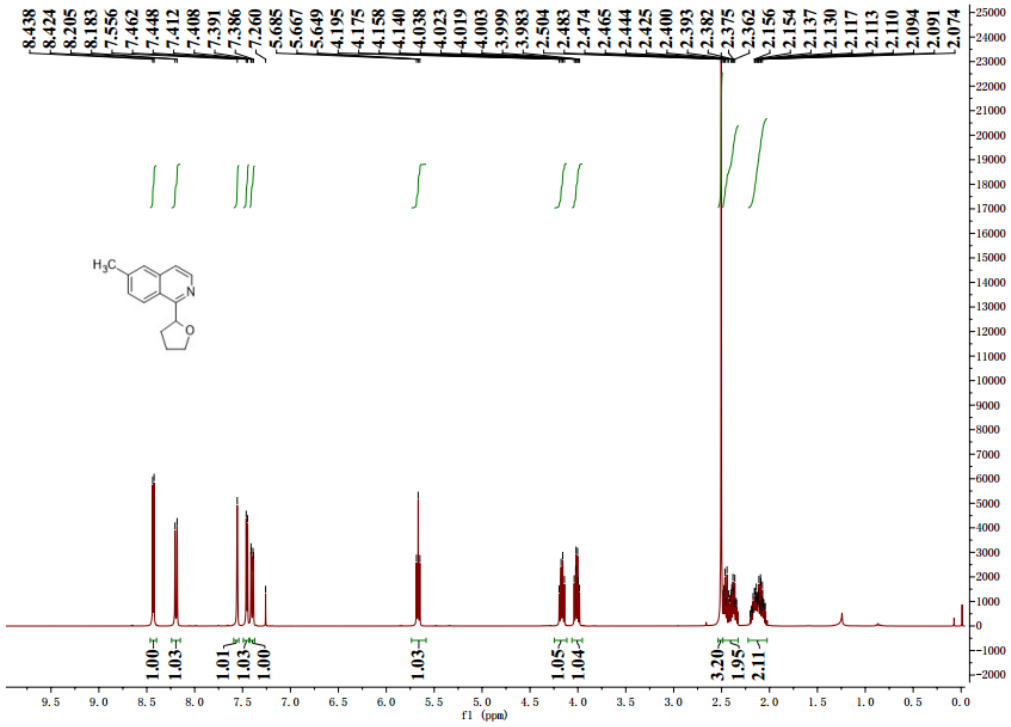
References

1. E. M. Simmons, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 3066-3072.
2. (a) X.-D. Feng, X.-Q. Guo, K.-Y. Qiu, *Polymer Bull.* **1987**, *18*, 19-26. (b) D. Hunkeler, A. E. Hamielec, *Macromol.* **1991**, *24*, 2160-2171. (c) X.-D. Feng, K.-Y. Qiu, *Chin. Polym. Bull.* **2005**, *4*, 23-34.
3. I. Mangion, Y.-Z. Liu, M. Reibarkh, R. T. Williamson, C. J. Welch, *J. Org. Chem.* **2016**, *81*, 6937−6944.
4. (a) T. Gieshoff, D. Schollmeyer, S. R. Waldvogel, *Angew. Chem. Int. Ed.* **2016**, *55*, 9437-9440; (b) M. V. D. Almeida, D. H. R. Barton, I. Bytheway, J. A. Ferreira, M. B. Hall, W. Liu, D. K. Taylor, L. Thomson, *J. Am. Chem. Soc.* **1995**, *117*, 4870-4874.
5. H.-Y. Yao, Y. Tang, K. Yamamoto, *Tetrahedron Lett.* **2012**, *53*, 5094-5098.
6. R. Ikeda, T. Kimura, T. Tsutsumi, S. Tamura, N. Sakai, T. Konakahara, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3506-3515.

Spectral Data for the Products



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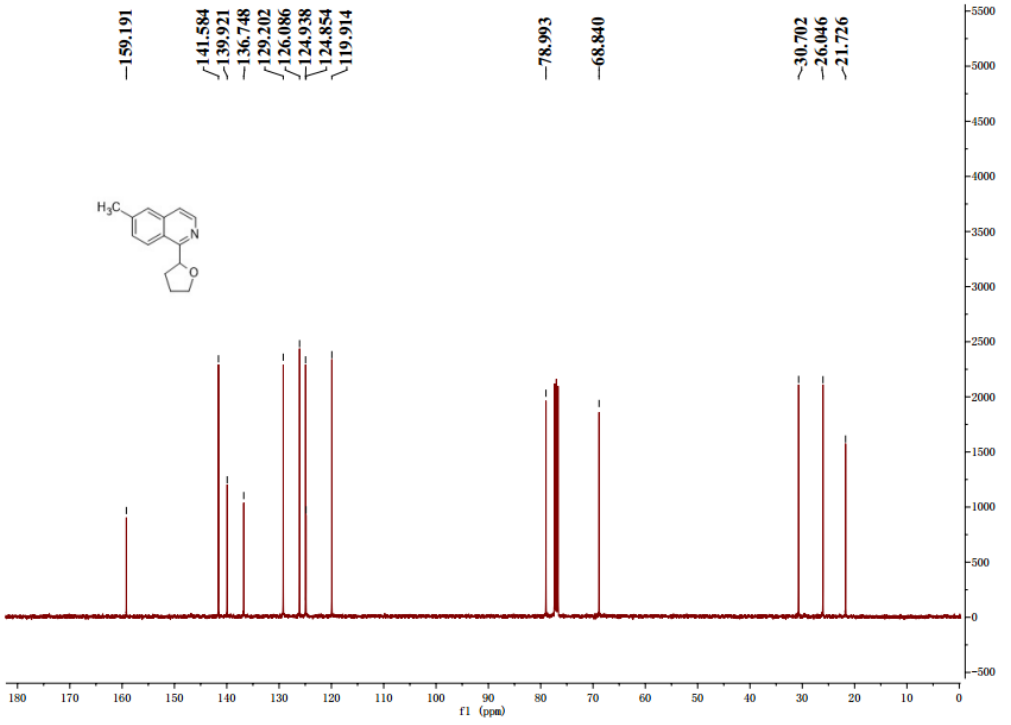
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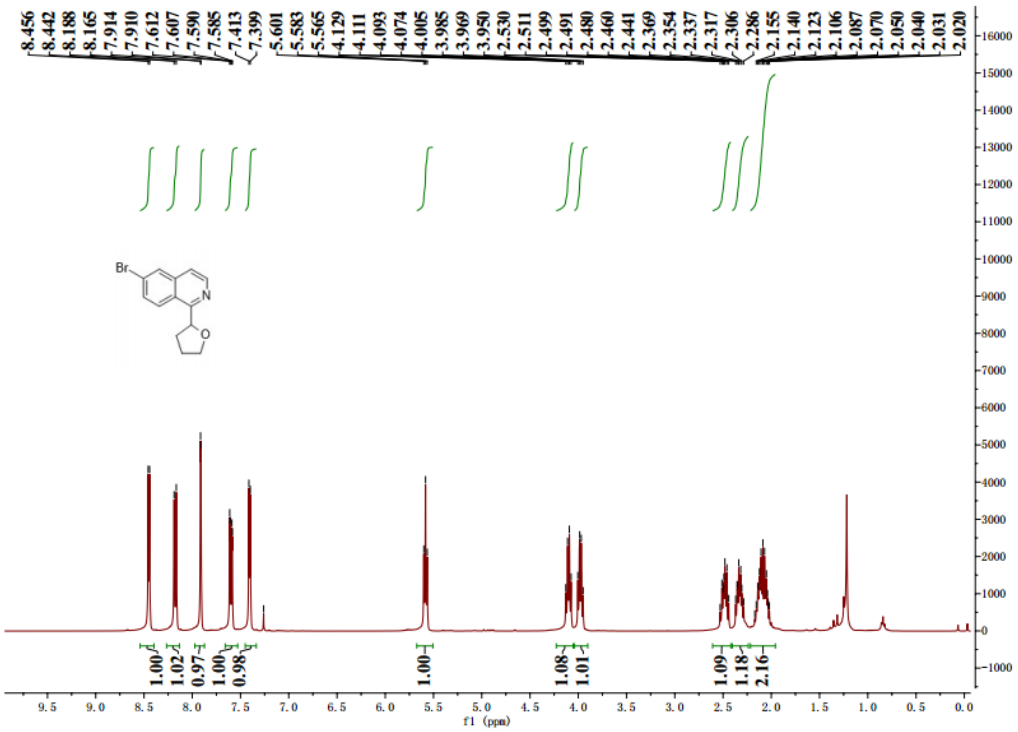
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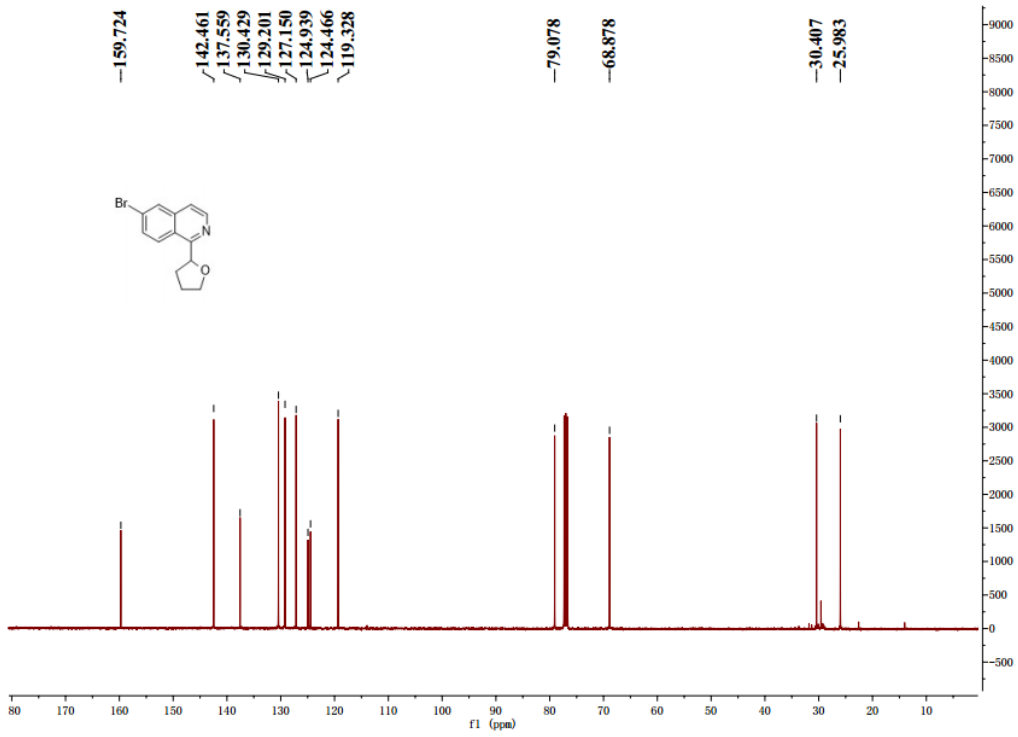
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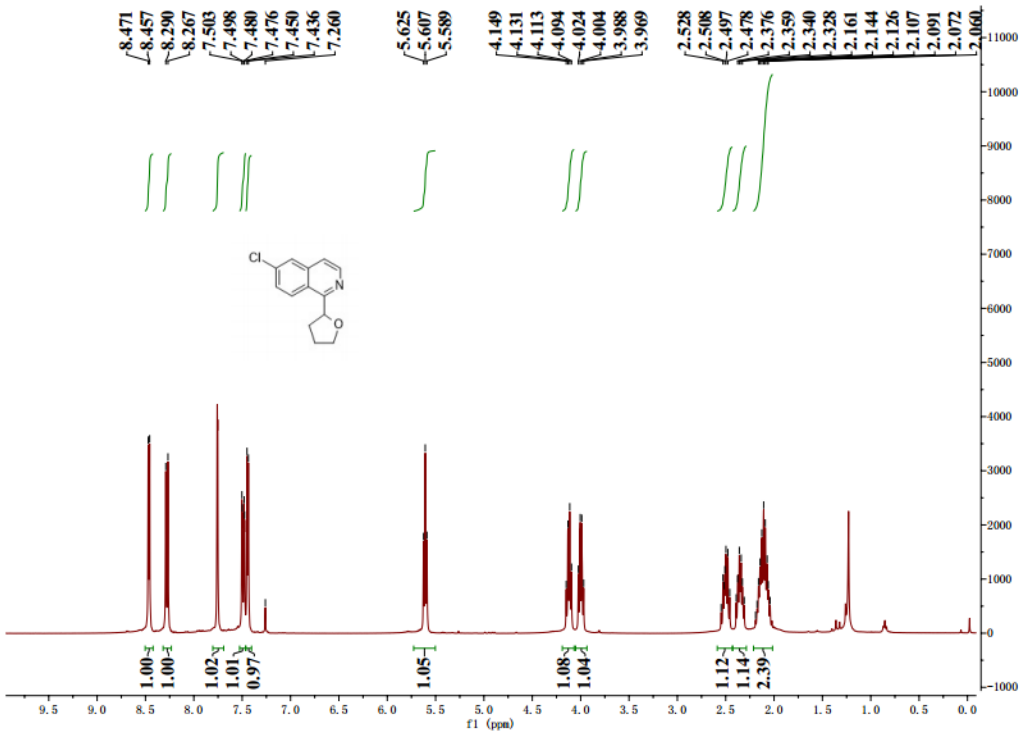
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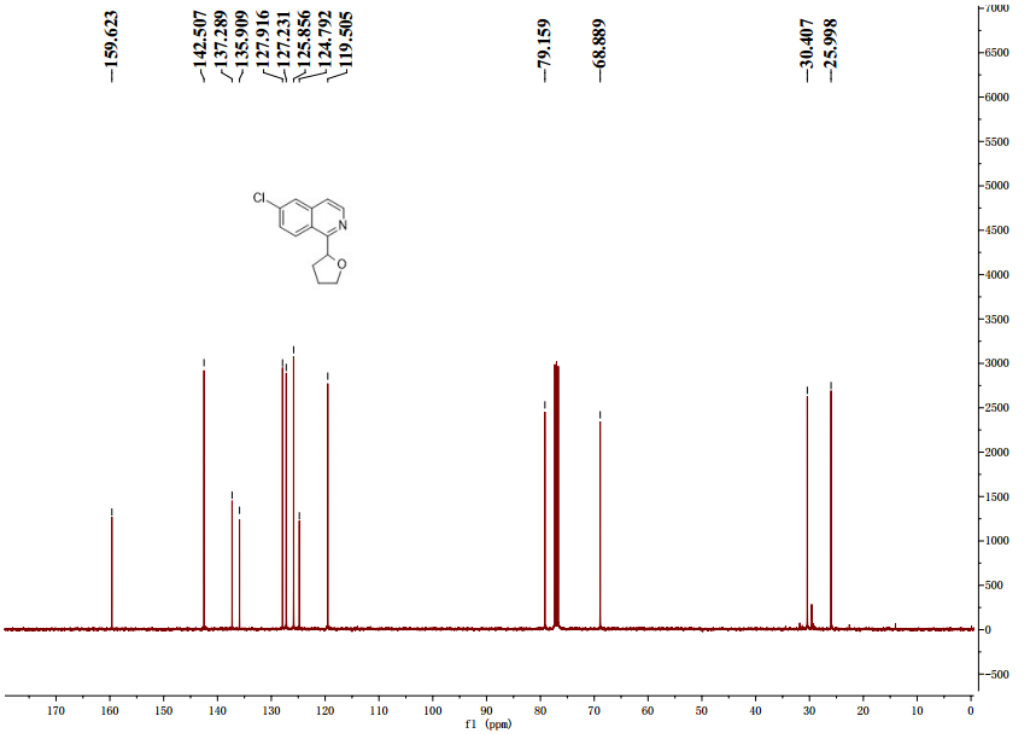
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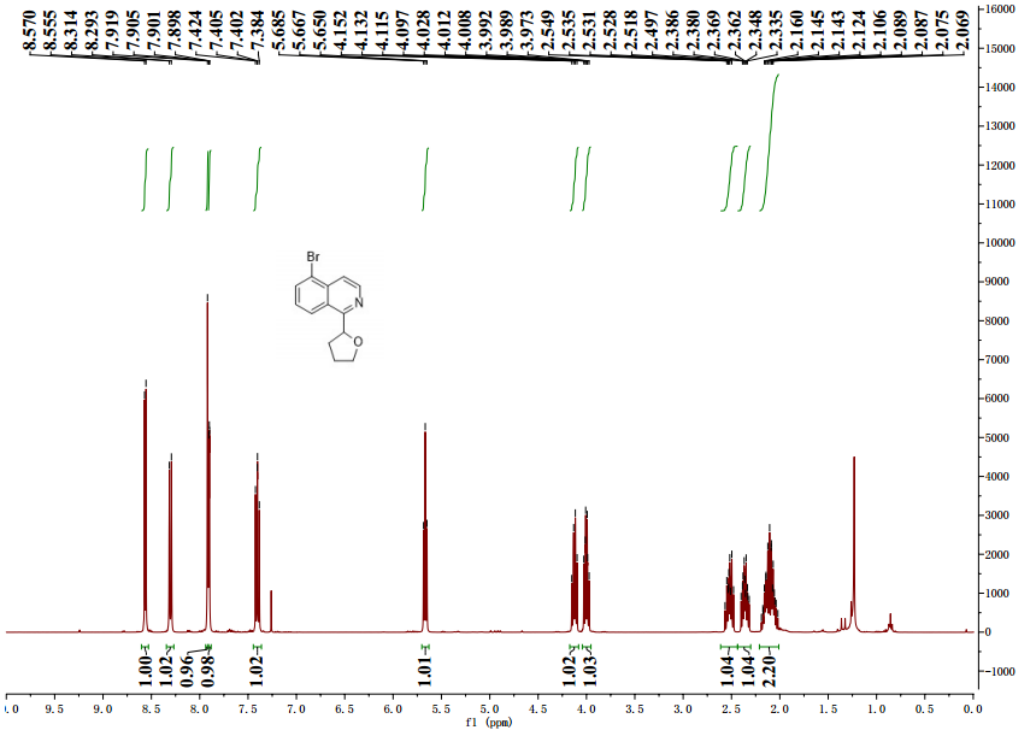
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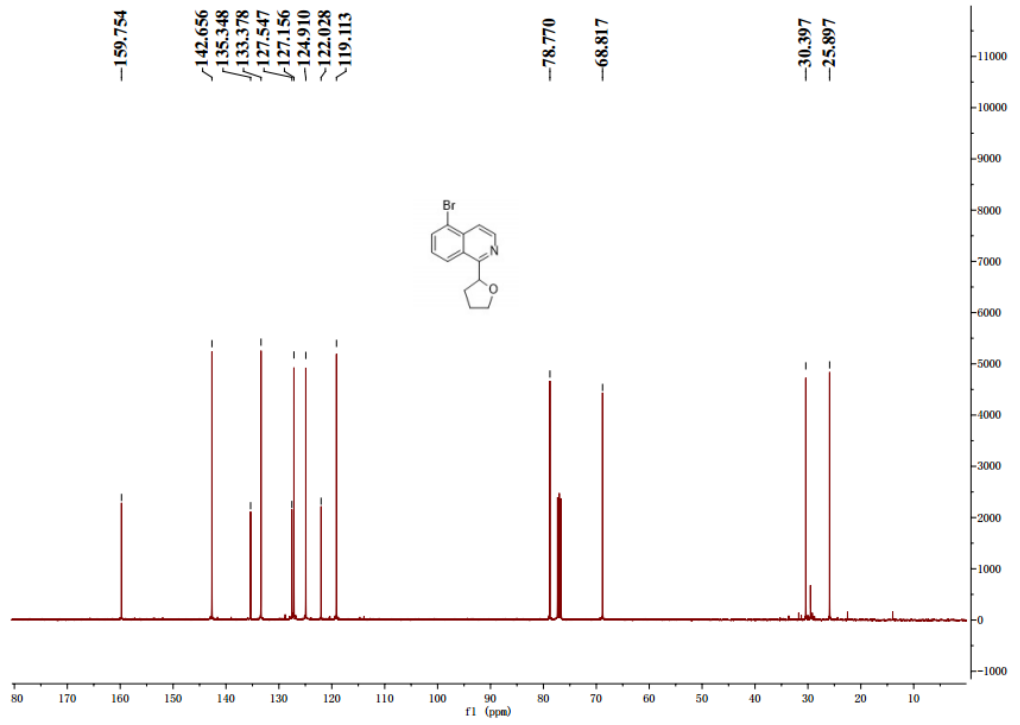
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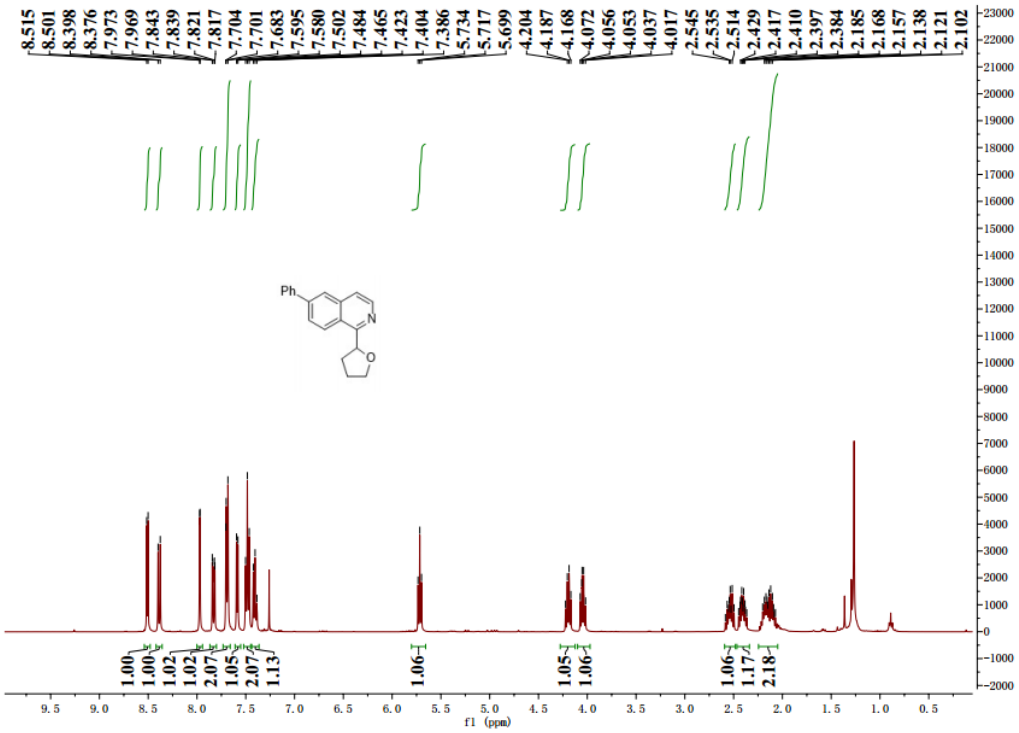
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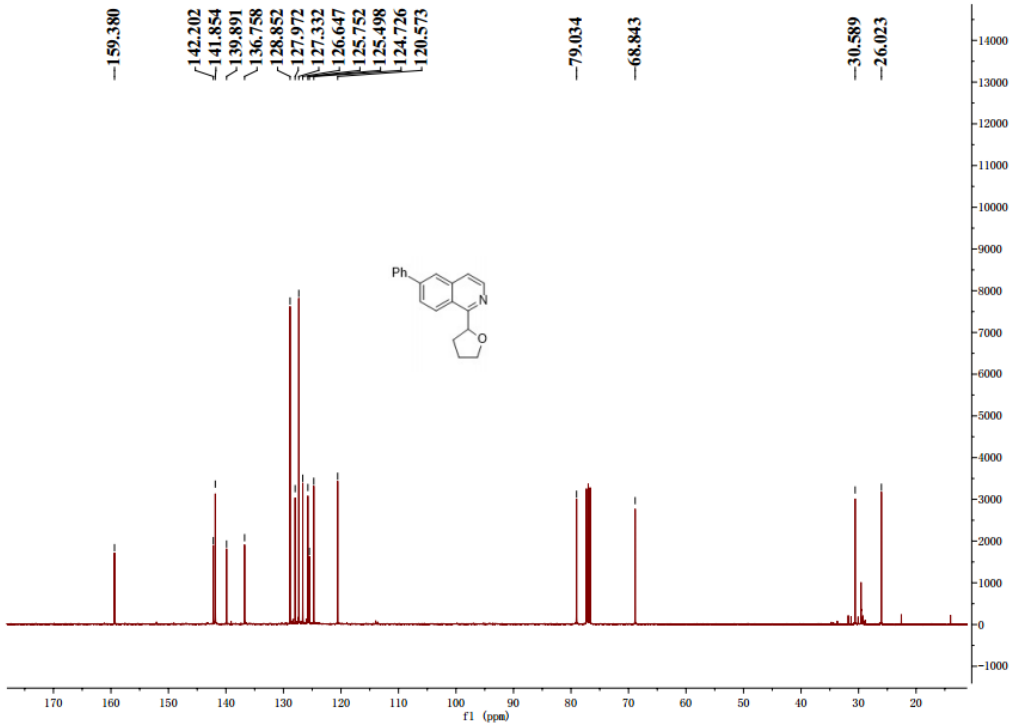
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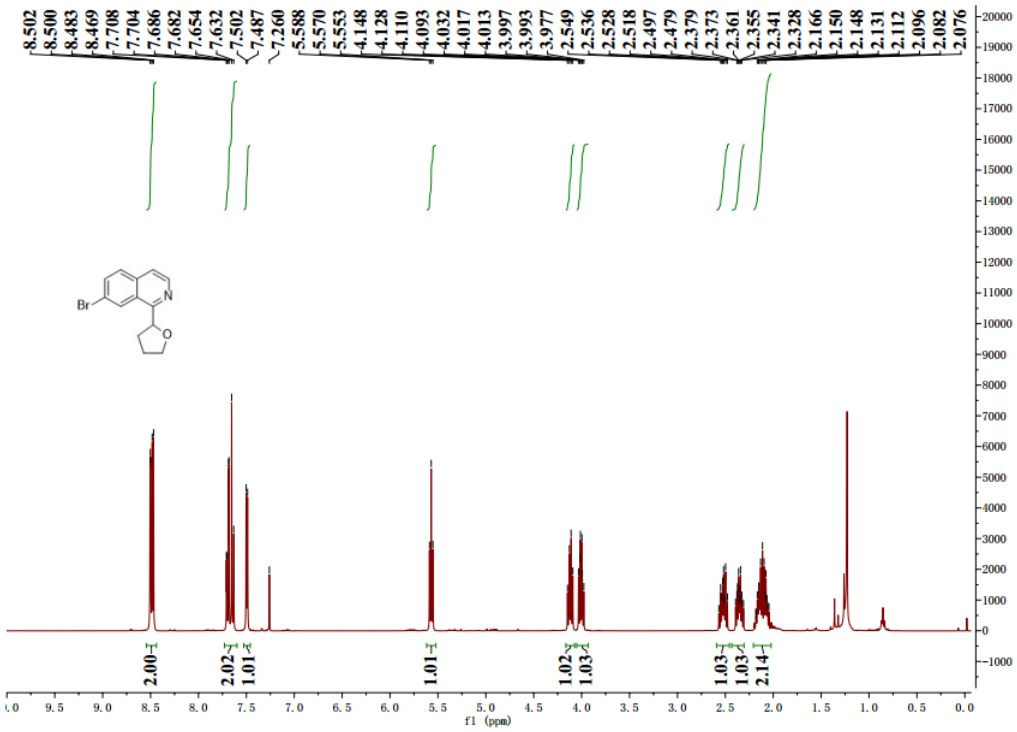
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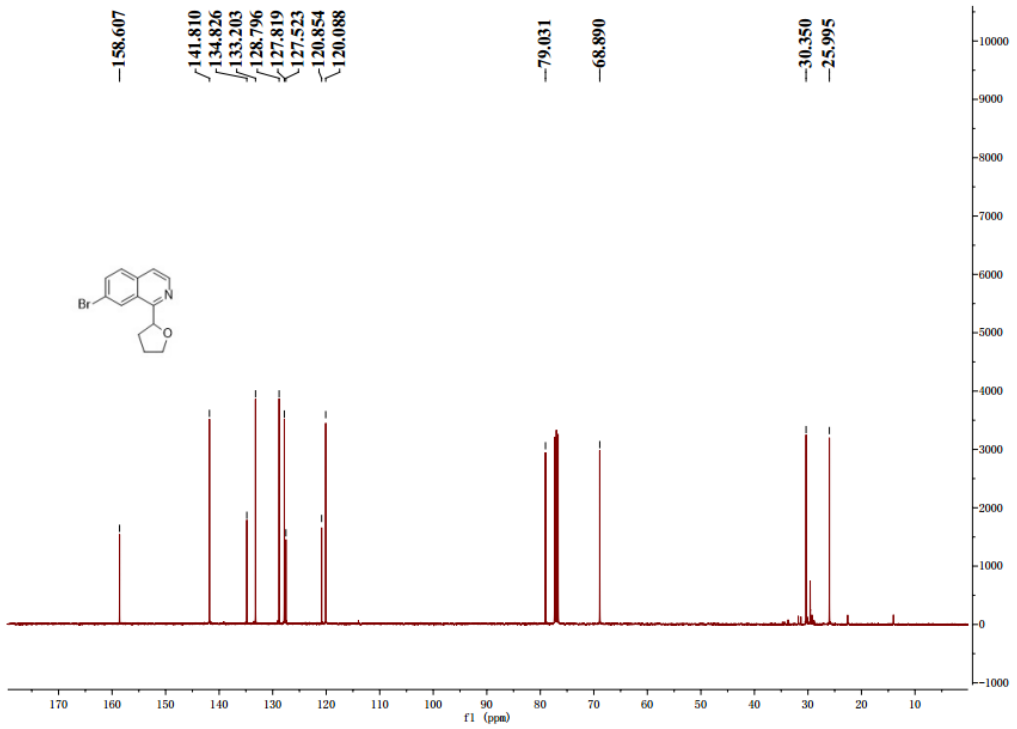
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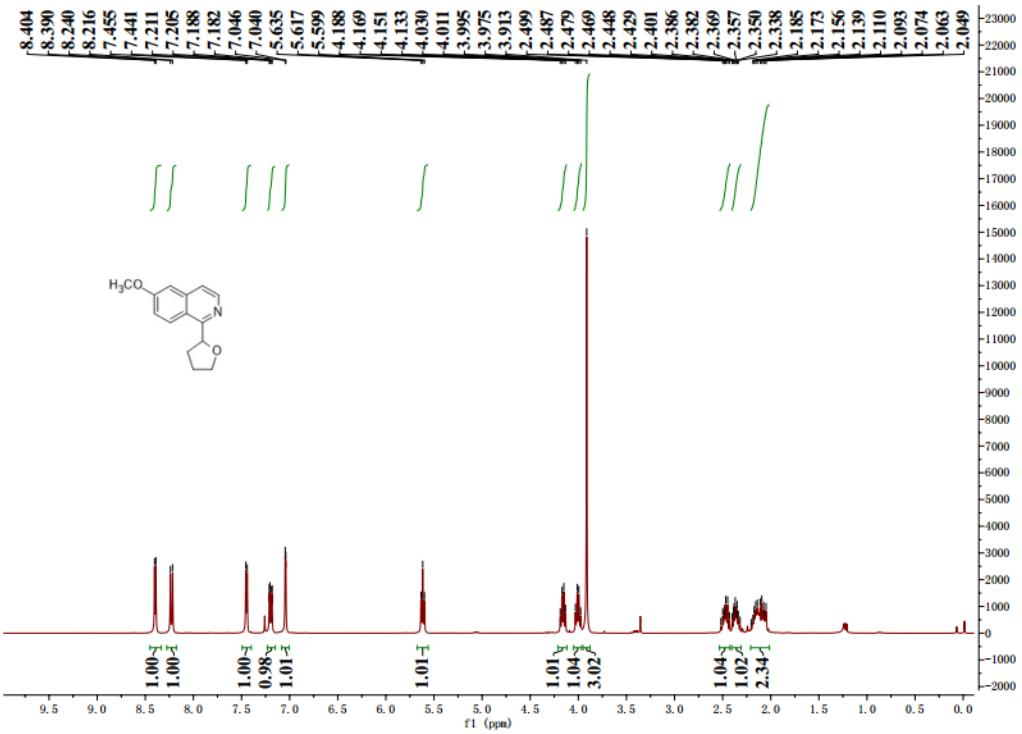
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5.635
5.617
5.599
4.188
4.169
4.151
4.133
4.030
4.011
3.995
3.975
3.913
2.499
2.487
2.479
2.469
2.448
2.429
2.401
2.386
2.382
2.369
2.357
2.350
2.338
2.185
2.173
2.156
2.139
2.110
2.093
2.074
2.063
2.049
H3CO
N
O
1.00
1.00
1.00
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1.01
1.01
1.01
1.04
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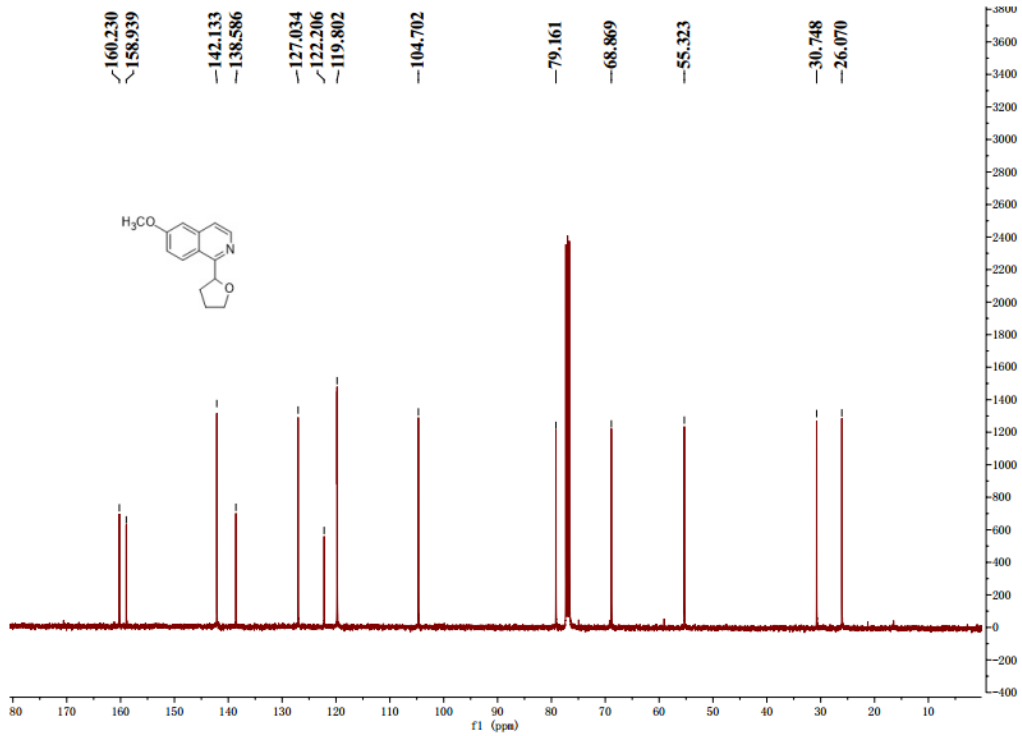
1.04
1.02
2.34
f1 (ppm)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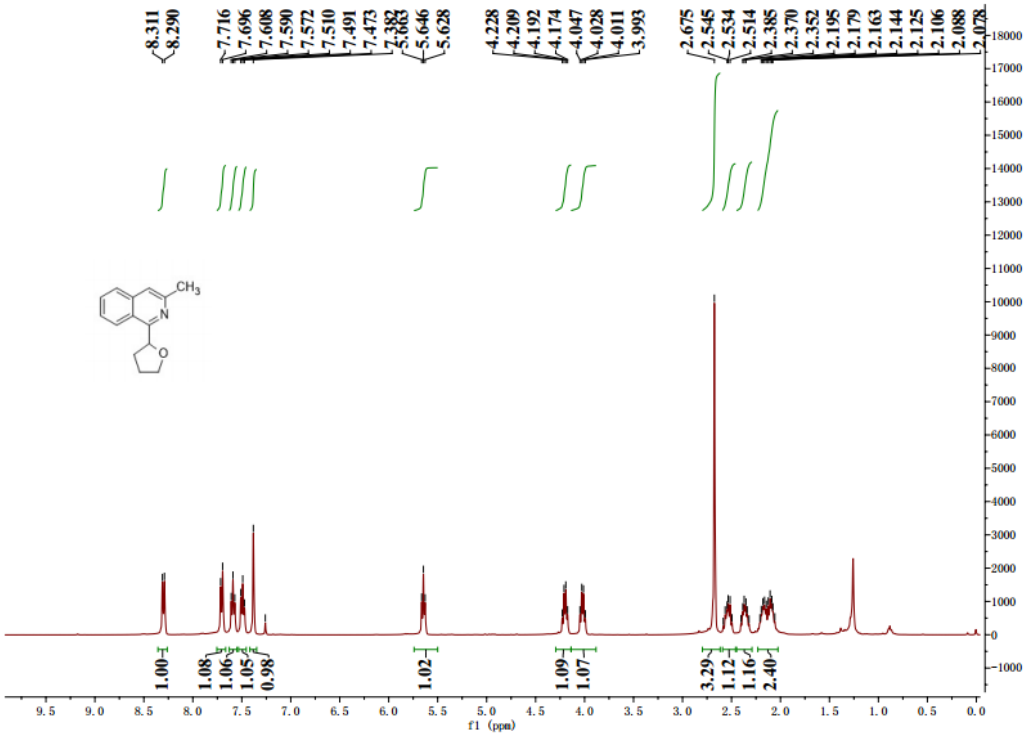
H3CO
N
O
f1 (ppm)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4.209
4.192
4.174
4.047
4.028
4.011
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2.534
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2.385
2.370
2.352
2.195
2.179
2.163
2.144
2.125
2.106
2.088
2.078
CH3
N
O
1.00
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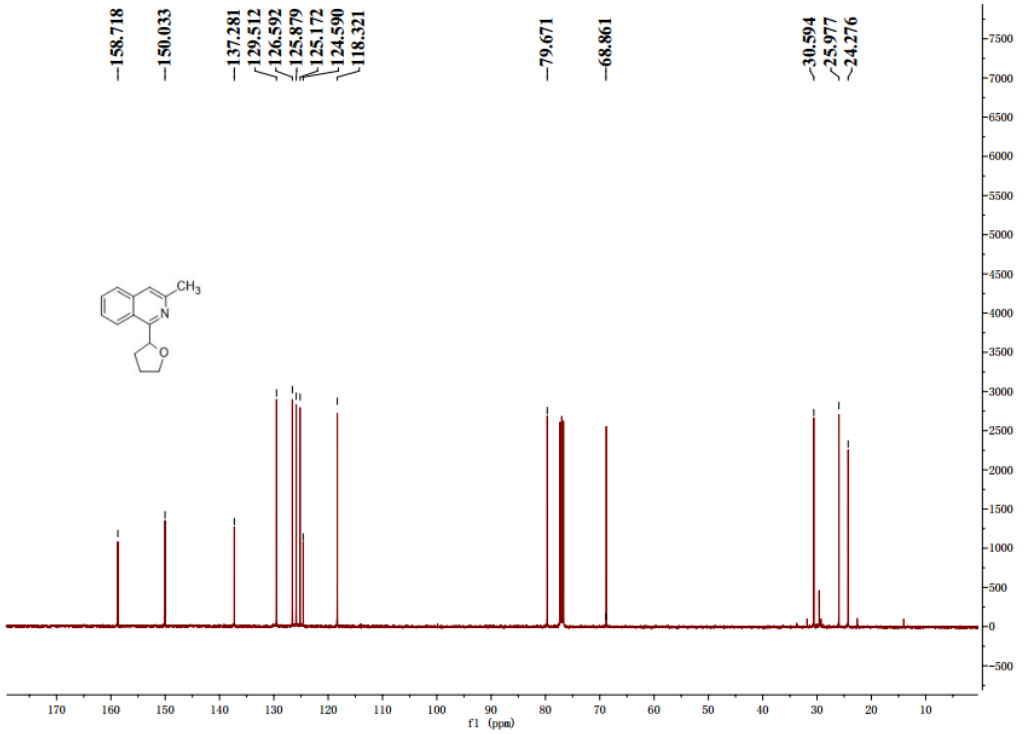
f1 (ppm)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CH3
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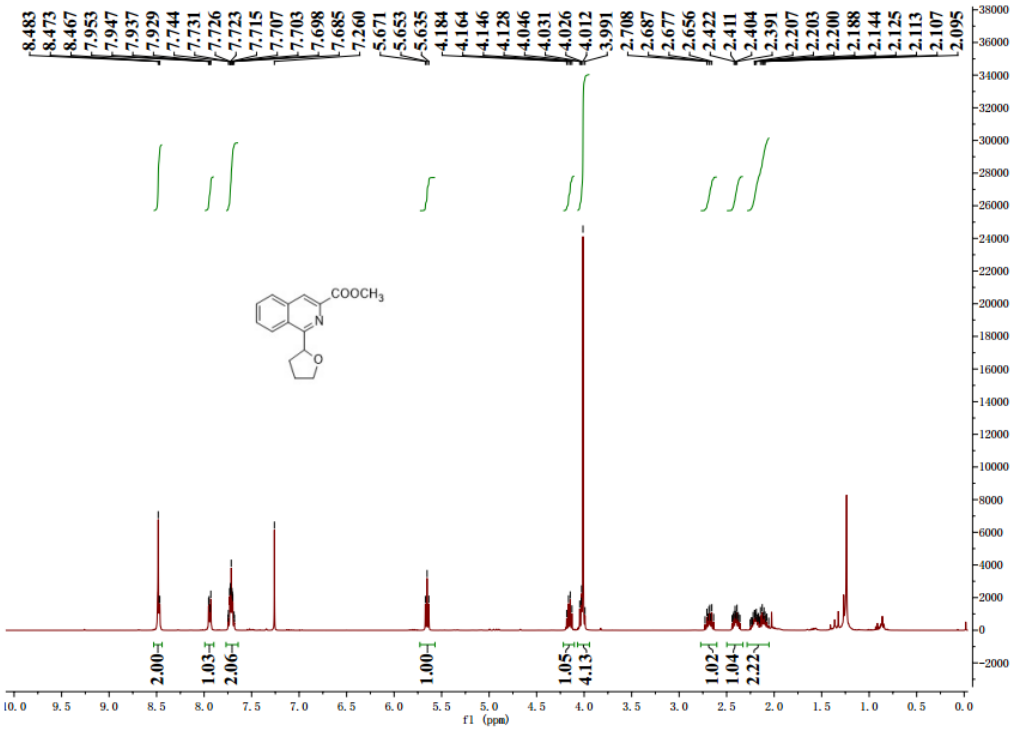
O
f1 (ppm)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7.715
7.707
7.703
7.698
7.685
7.260
5.671
5.653
5.635
4.184
4.164
4.146
4.128
4.046
4.031
4.026
4.012
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2.677
2.656
2.422
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2.404
2.391
2.207
2.203
2.200
2.188
2.144
2.125
2.113
2.107
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2.06
1.00
1.05
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1.02
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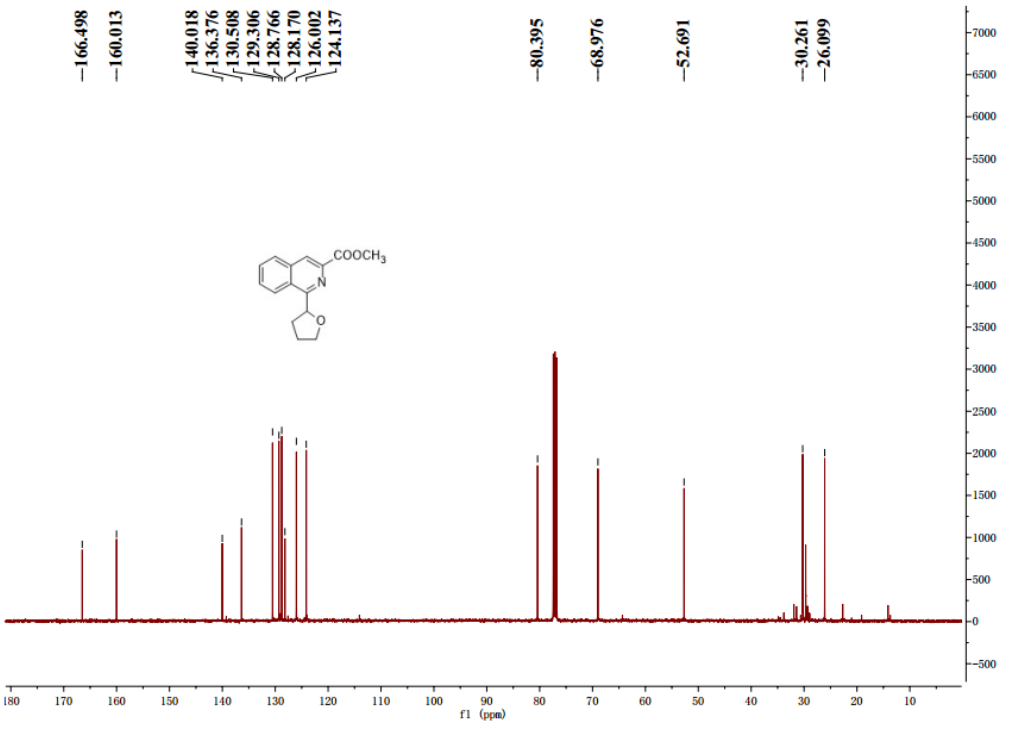
2.22
f1 (ppm)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80.395
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30.261
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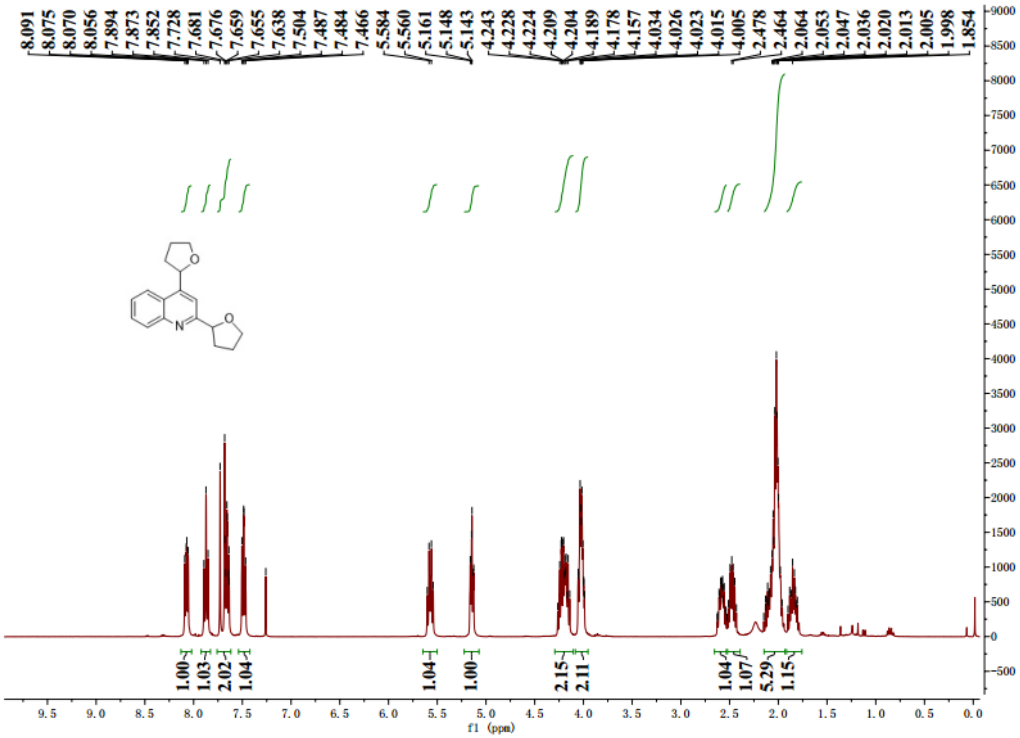
COOCH3
f1 (ppm)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7.728
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7.676
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7.638
7.504
7.487
7.484
7.466
5.584
5.560
5.161
5.148
5.143
4.243
4.228
4.224
4.209
4.204
4.189
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4.034
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4.023
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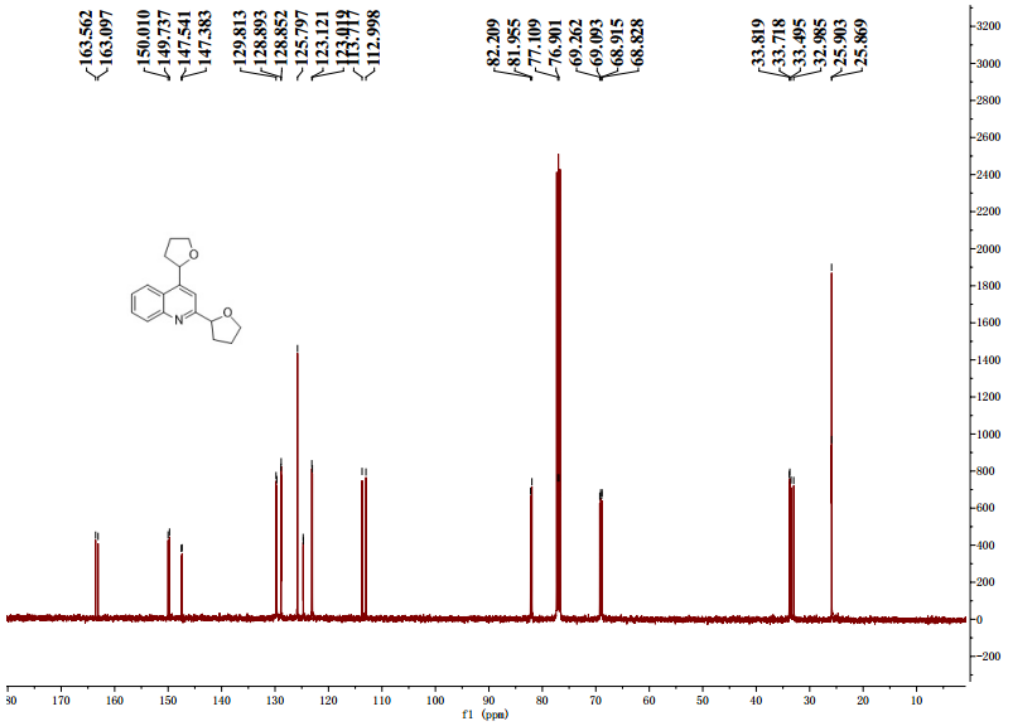
f1 (ppm)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112.998
82.209
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77.109
76.901
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68.915
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32.985
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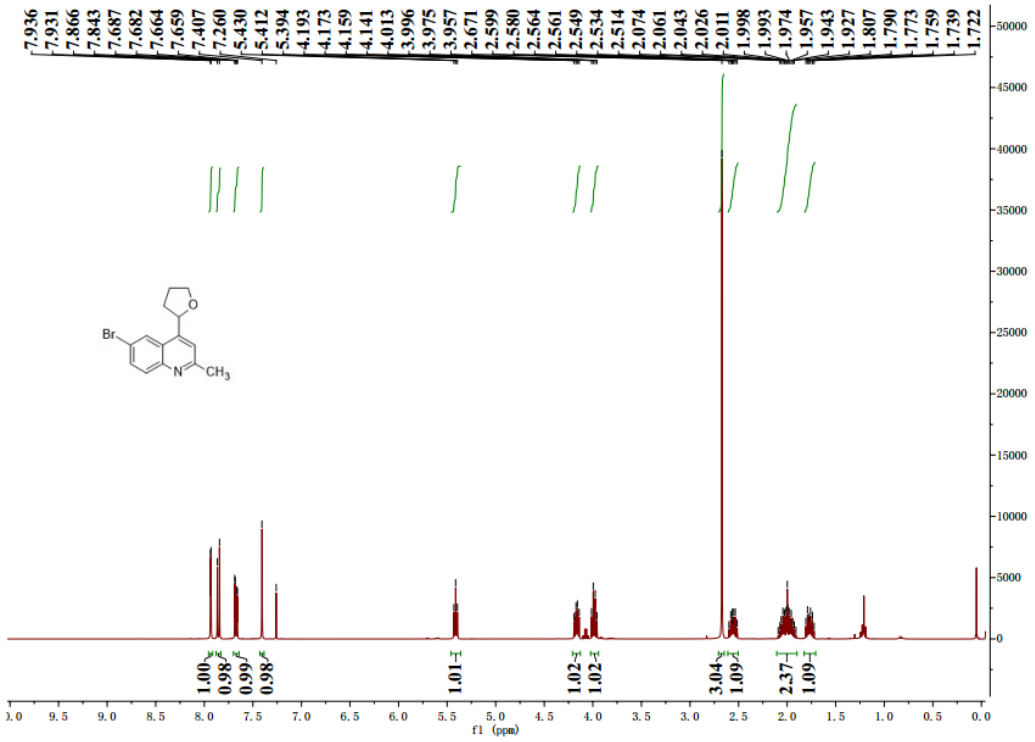
25.869
f1 (ppm)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7.407
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5.412
5.394
4.193
4.173
4.159
4.141
4.013
3.996
3.975
3.957
2.671
2.599
2.580
2.564
2.561
2.549
2.534
2.514
2.074
2.061
2.043
2.026
2.011
1.998
1.993
1.974
1.957
1.943
1.927
1.807
1.790
1.773
1.759
1.739
1.722
Br
N
CH3
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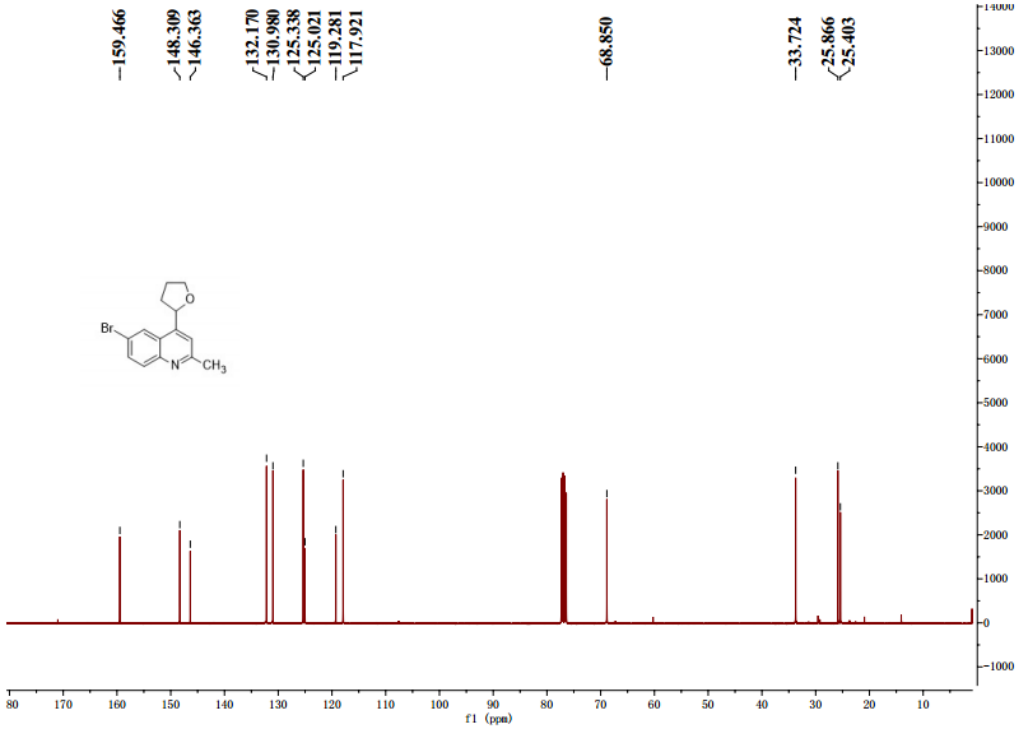
0.99
0.98
1.01
1.02
1.02
3.04
1.09
2.37
1.09
f1 (ppm)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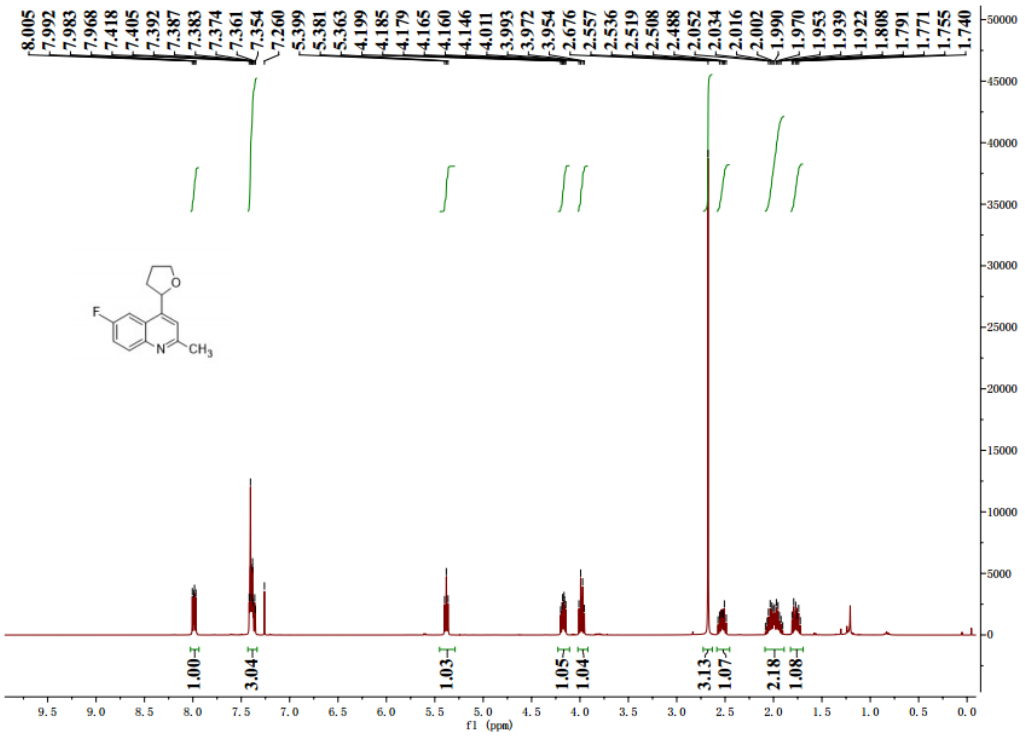
Br
N
CH3
f1 (ppm)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7.361
7.354
7.260
5.399
5.381
5.363
4.199
4.185
4.179
4.165
4.160
4.146
4.011
3.993
3.972
3.954
2.676
2.557
2.536
2.519
2.508
2.488
2.052
2.034
2.016
2.002
1.990
1.970
1.953
1.939
1.922
1.808
1.791
1.771
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1.05
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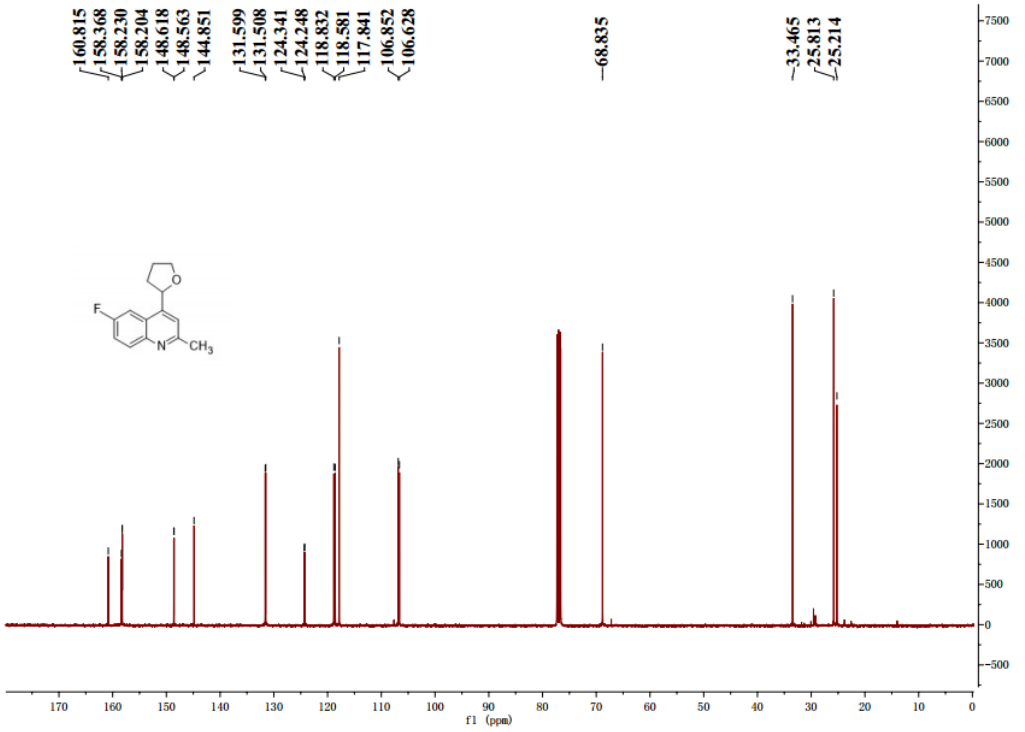
3.13
1.07
2.18
1.08
f1 (ppm)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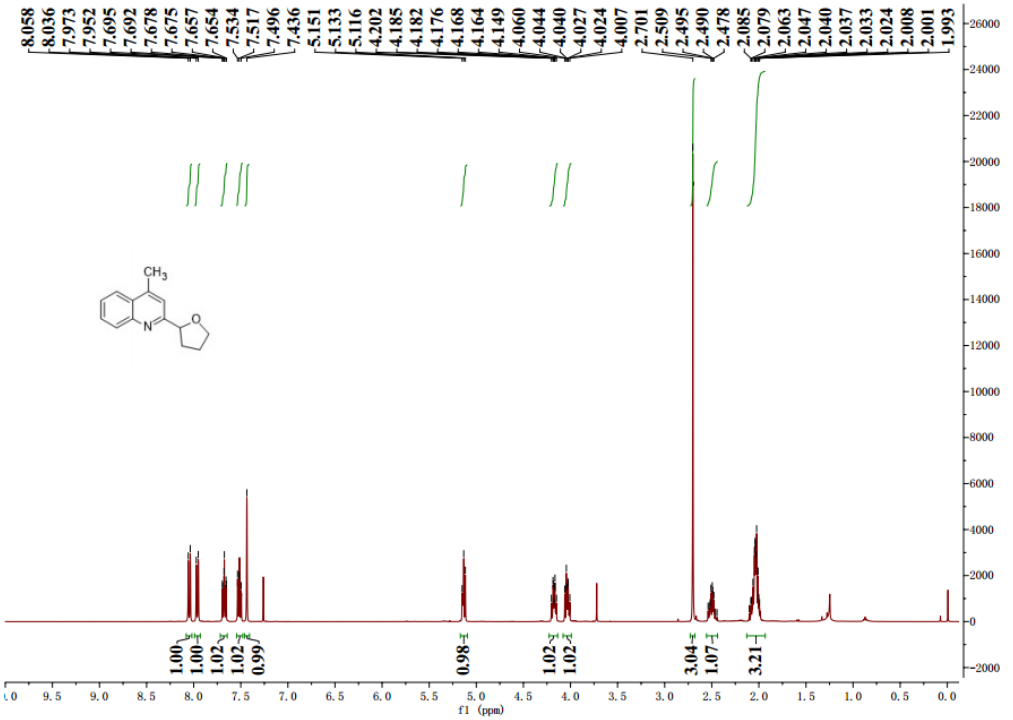
33.465
25.813
25.214
f1 (ppm)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7.695
7.692
7.678
7.675
7.657
7.654
7.534
7.517
7.496
7.436
5.151
5.133
5.116
4.202
4.185
4.182
4.176
4.168
4.164
4.149
4.060
4.044
4.040
4.027
4.024
4.007
2.701
2.509
2.495
2.490
2.478
2.085
2.079
2.063
2.047
2.040
2.037
2.033
2.024
2.008
2.001
1.993
CH3
N
O
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1.00
1.02
1.02
0.99
0.98
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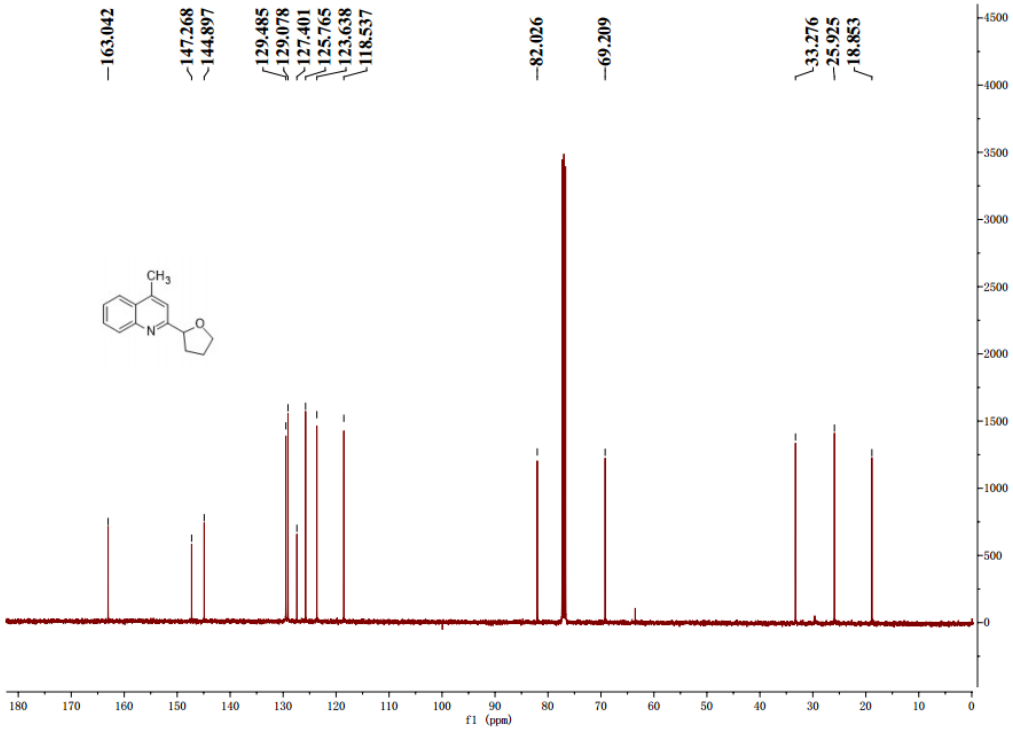
1.02
3.04
1.07
3.21
f1 (ppm)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144.897
129.485
129.078
127.401
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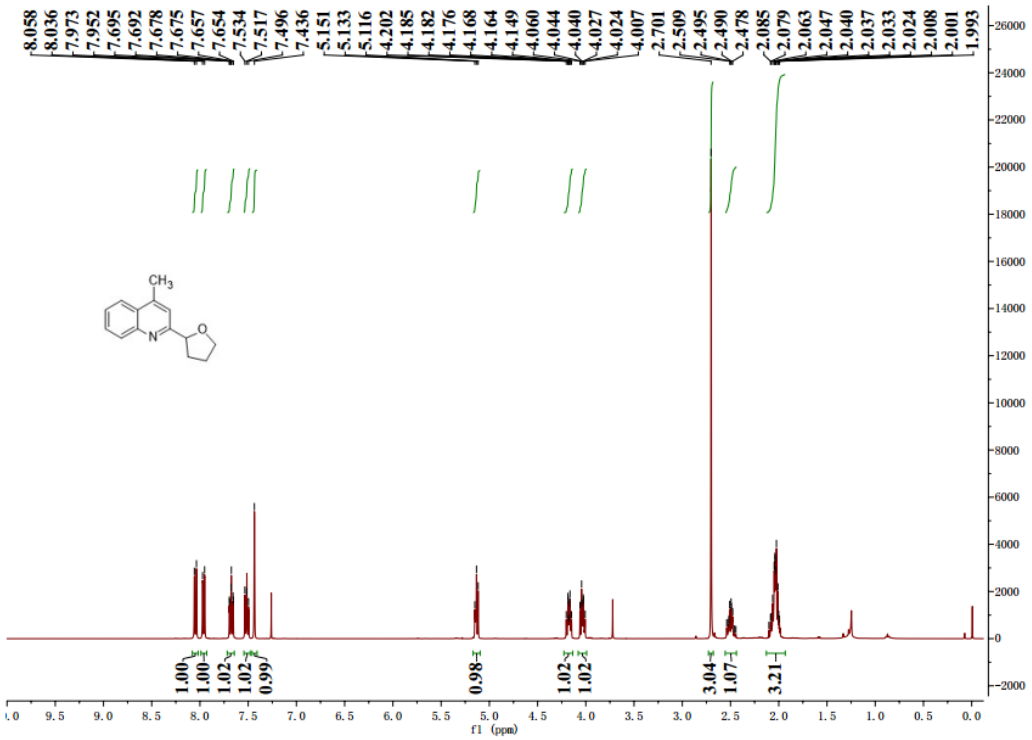
123.638
118.537
82.026
69.209
33.276
25.925
18.853
CH3
N
O
f1 (ppm)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8.036
7.973
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5.151
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5.116
4.202
4.185
4.182
4.176
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4.164
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4.044
4.040
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4.024
4.007
2.701
2.509
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2.079
2.063
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2.037
2.033
2.024
2.008
2.001
1.993
CH3
N
O
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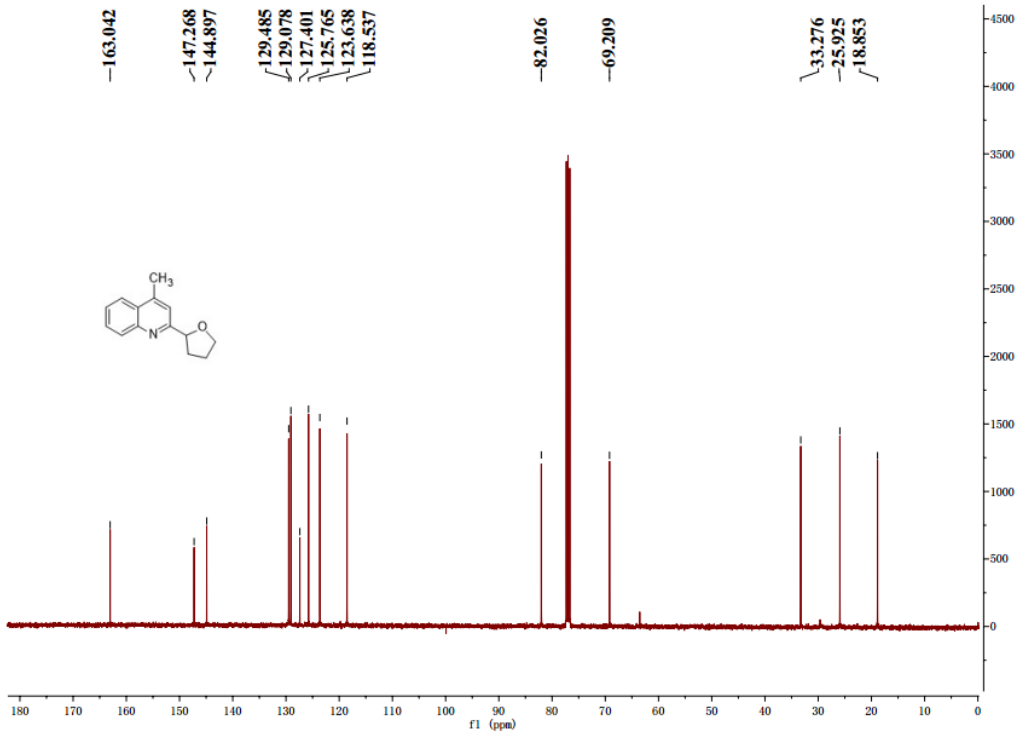
1.00
1.02
1.02
0.99
0.98
1.02
1.02
3.04
1.07
3.21
f1 (ppm)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144.897
129.485
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125.765
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82.026
69.209
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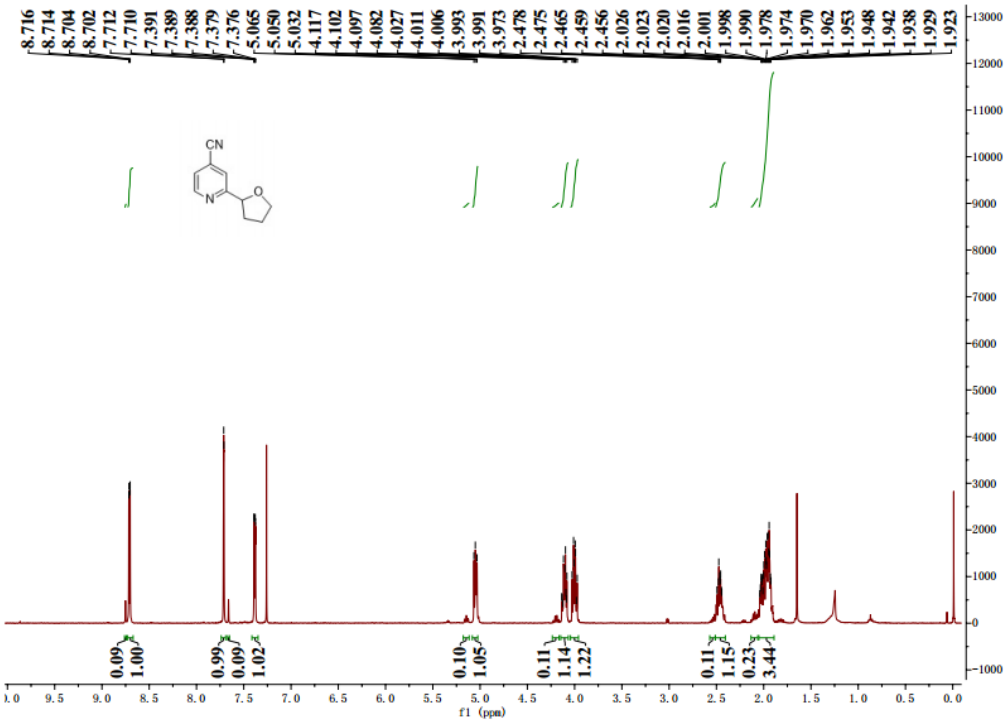
25.925
18.853
CH3
N
O
f1 (ppm)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5.032
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4.102
4.097
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1.938
1.929
1.923
CN
N
O
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0.99
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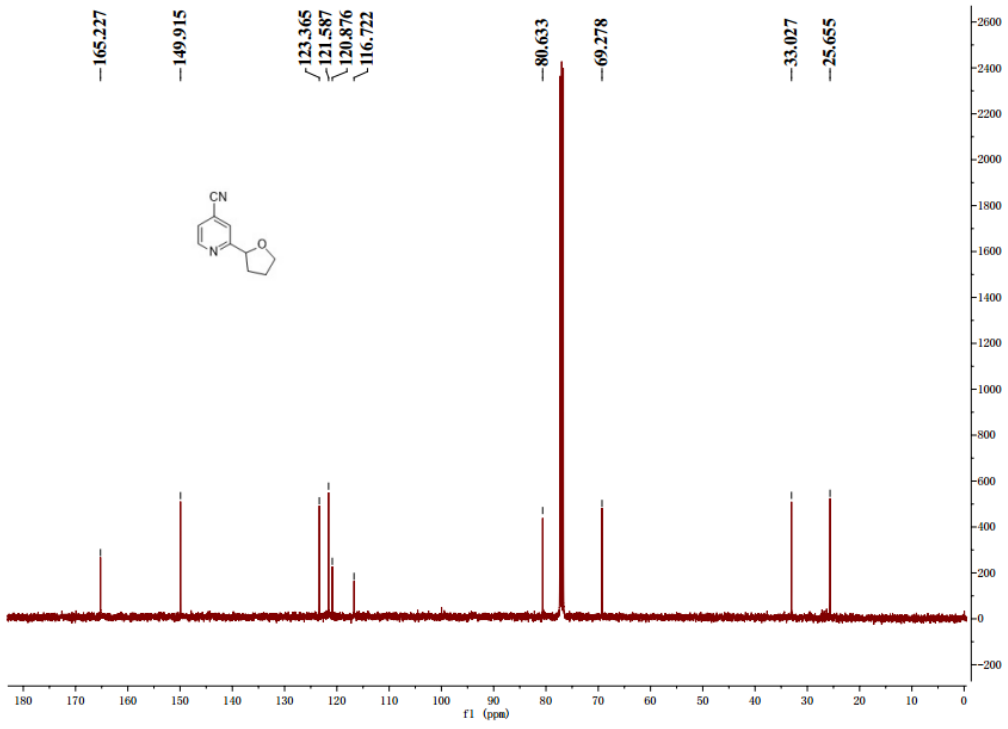
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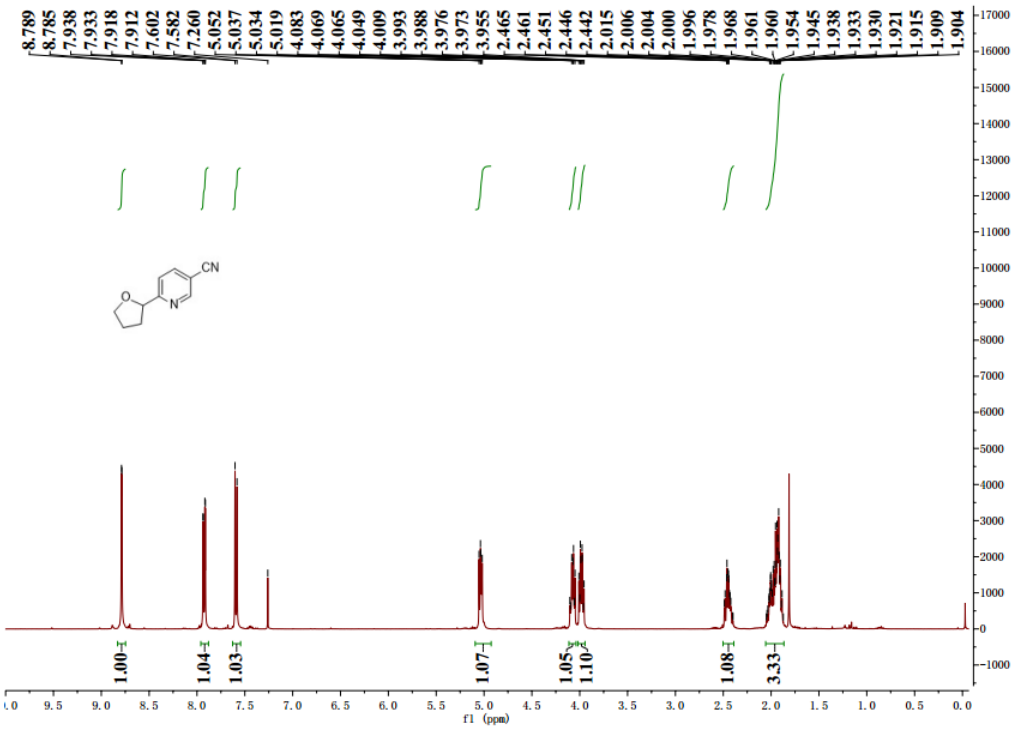
O
f1 (ppm)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4.069
4.065
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4.009
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3.988
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3.955
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1.915
1.909
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1.03
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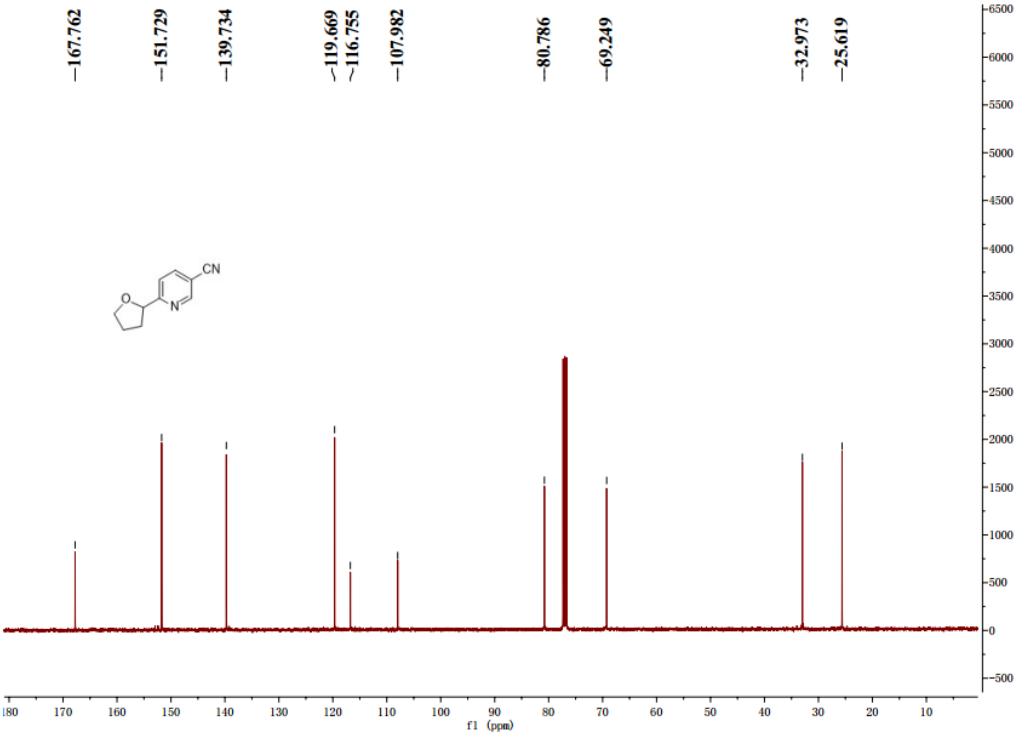
f1 (ppm)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O
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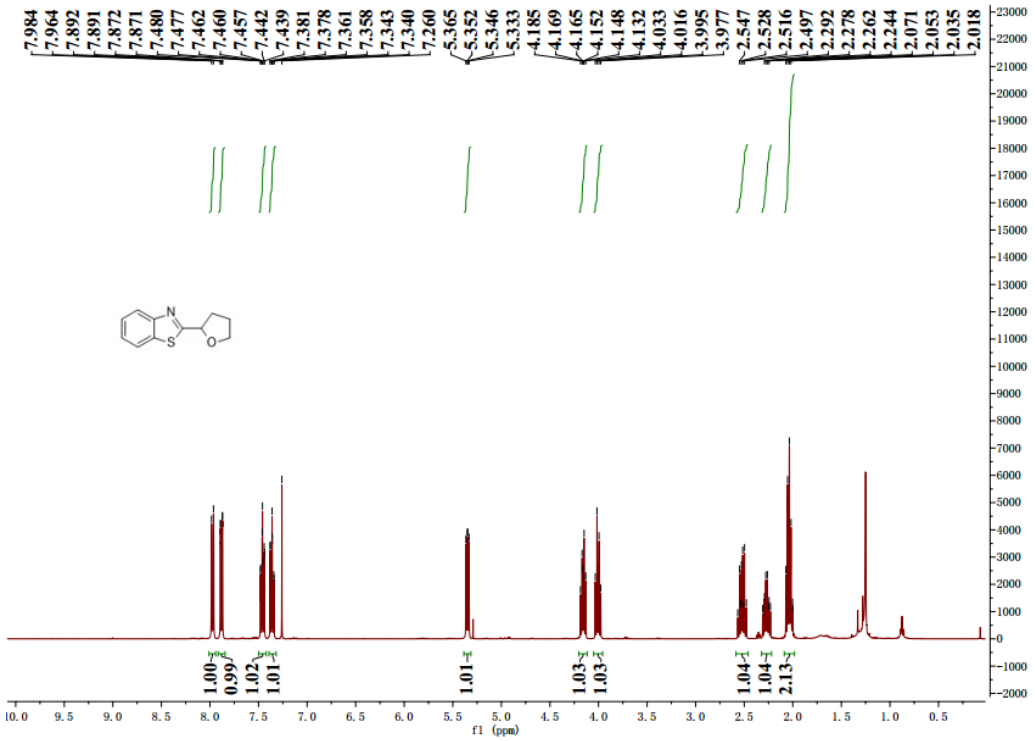
f1 (ppm)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2.262
2.244
2.071
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1.01
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1.04
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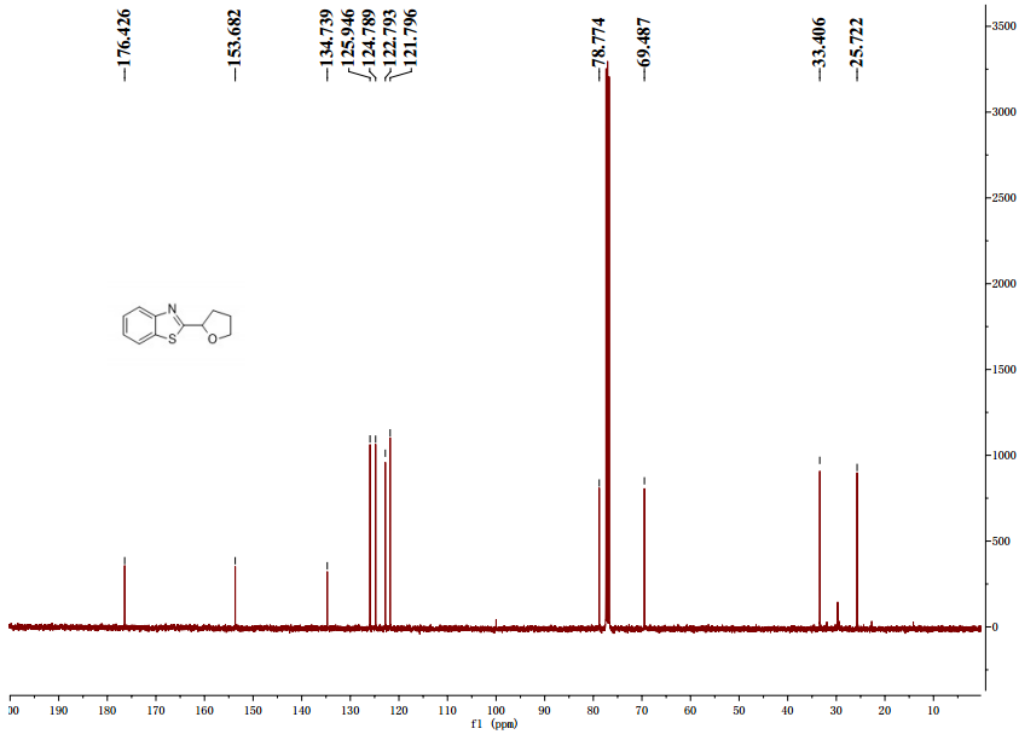
f1 (ppm)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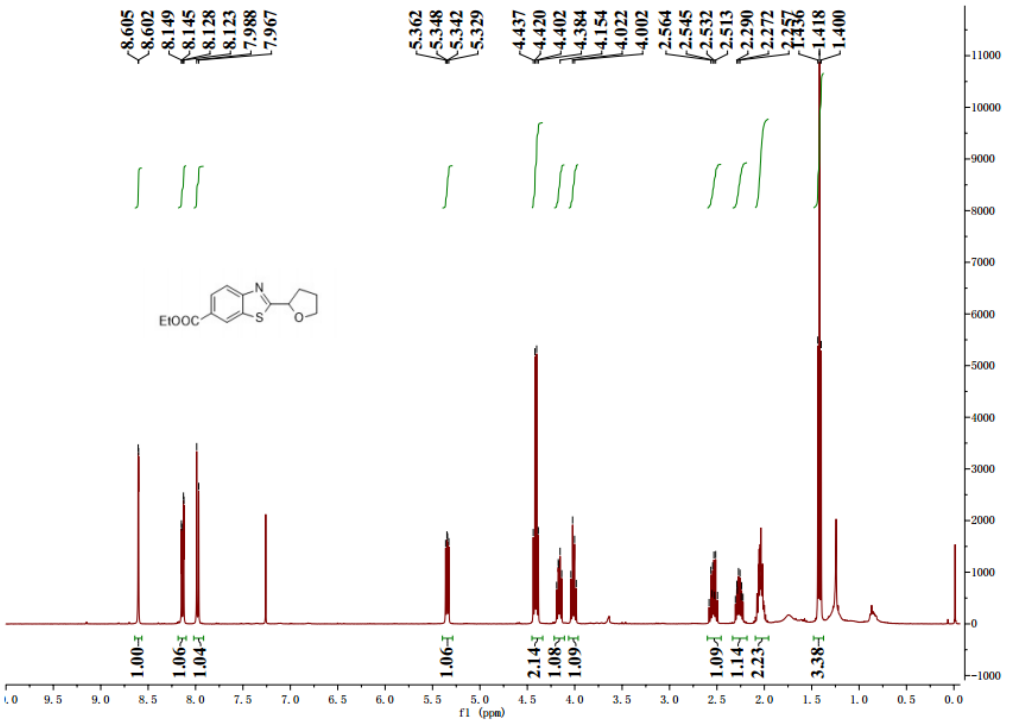
f1 (ppm)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4.402
4.384
4.154
4.022
4.002
2.564
2.545
2.532
2.513
2.290
2.272
2.257
1.436
1.418
1.400
EtOOC
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1.08
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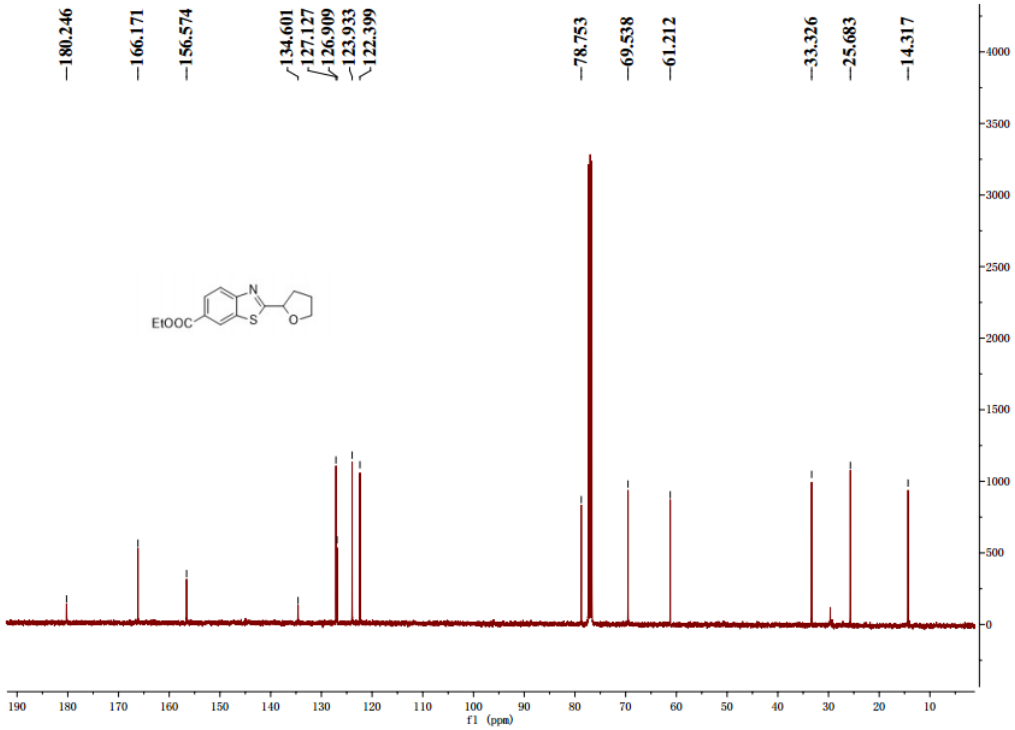
1.09
1.14
2.23
3.38
f1 (ppm)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61.212
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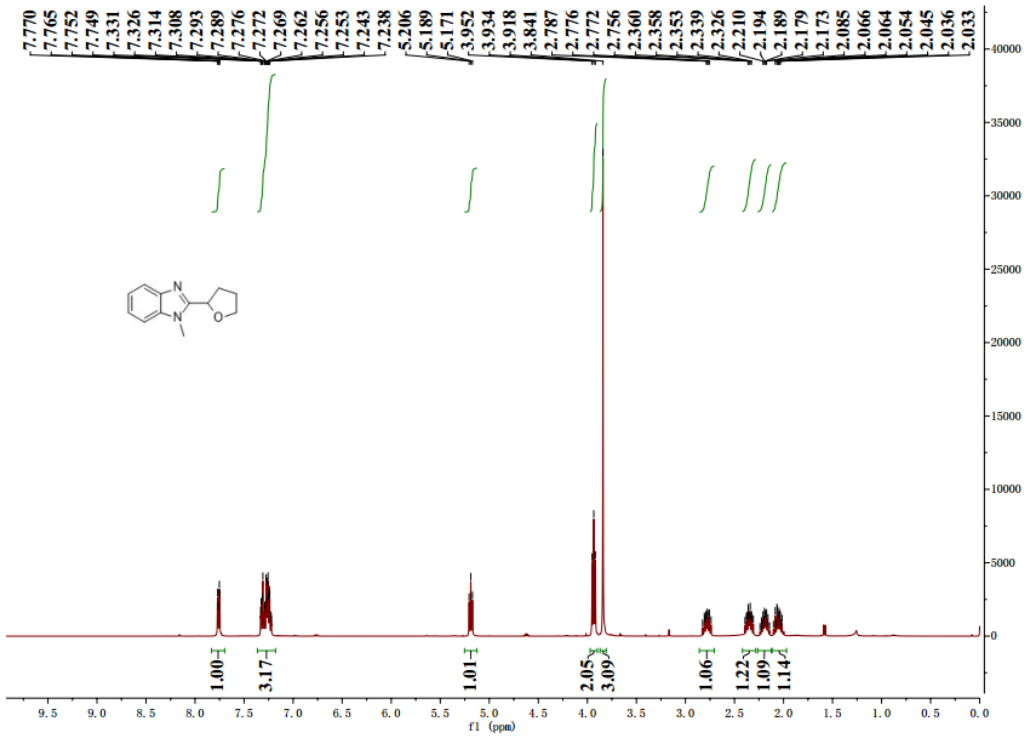
25.683
14.317
EtOOC
f1 (ppm)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7.256
7.253
7.243
7.238
5.206
5.189
5.171
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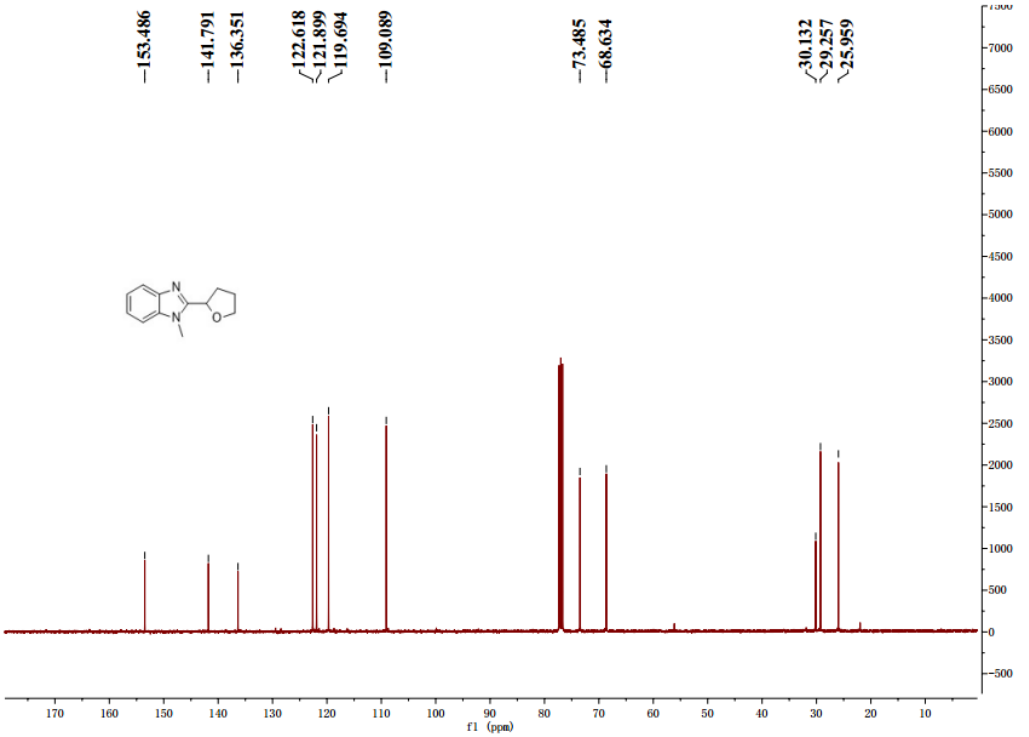
f1 (ppm)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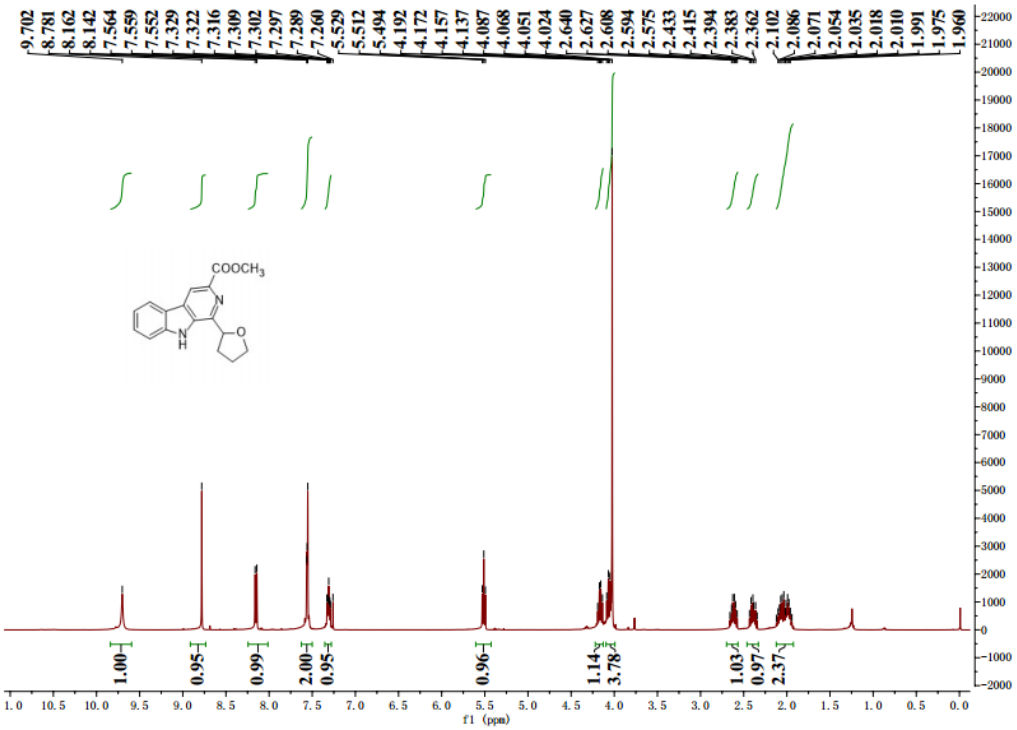
29.257
25.959
f1 (ppm)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7.552
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7.322
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7.309
7.302
7.297
7.289
7.260
5.529
5.512
5.494
4.192
4.172
4.157
4.137
4.087
4.068
4.051
4.024
2.640
2.627
2.608
2.594
2.575
2.433
2.415
2.394
2.383
2.362
2.102
2.086
2.071
2.054
2.035
2.018
2.010
1.991
1.975
1.960
COOCH3
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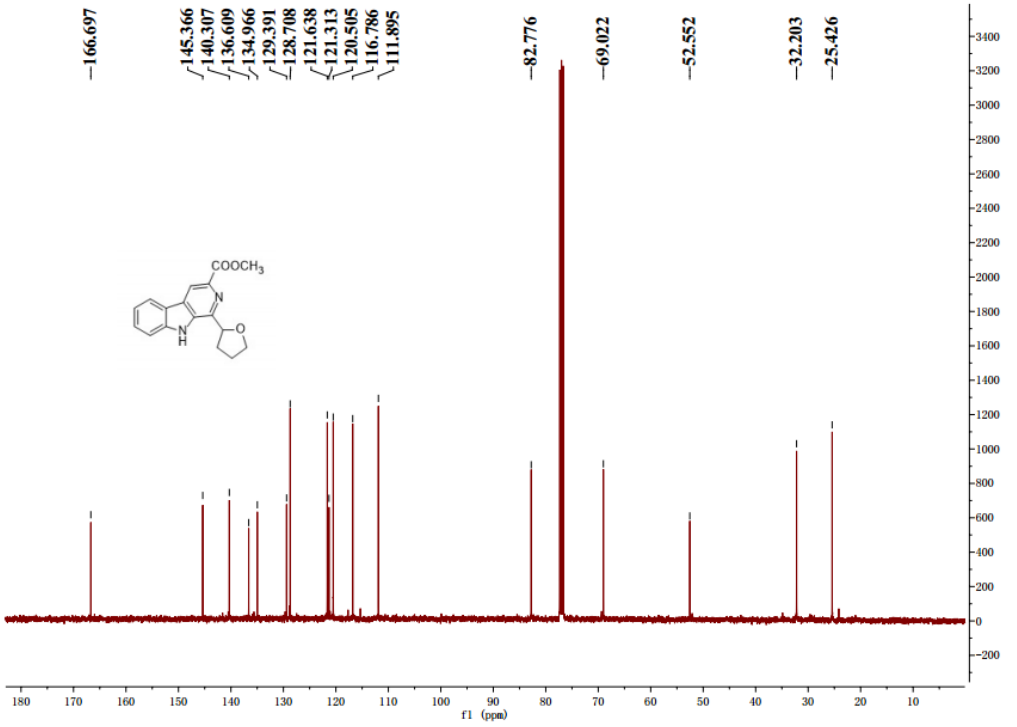
2.00
0.95
0.96
1.14
3.78
1.03
0.97
2.37
f1 (ppm)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121.638
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111.895
82.776
69.022
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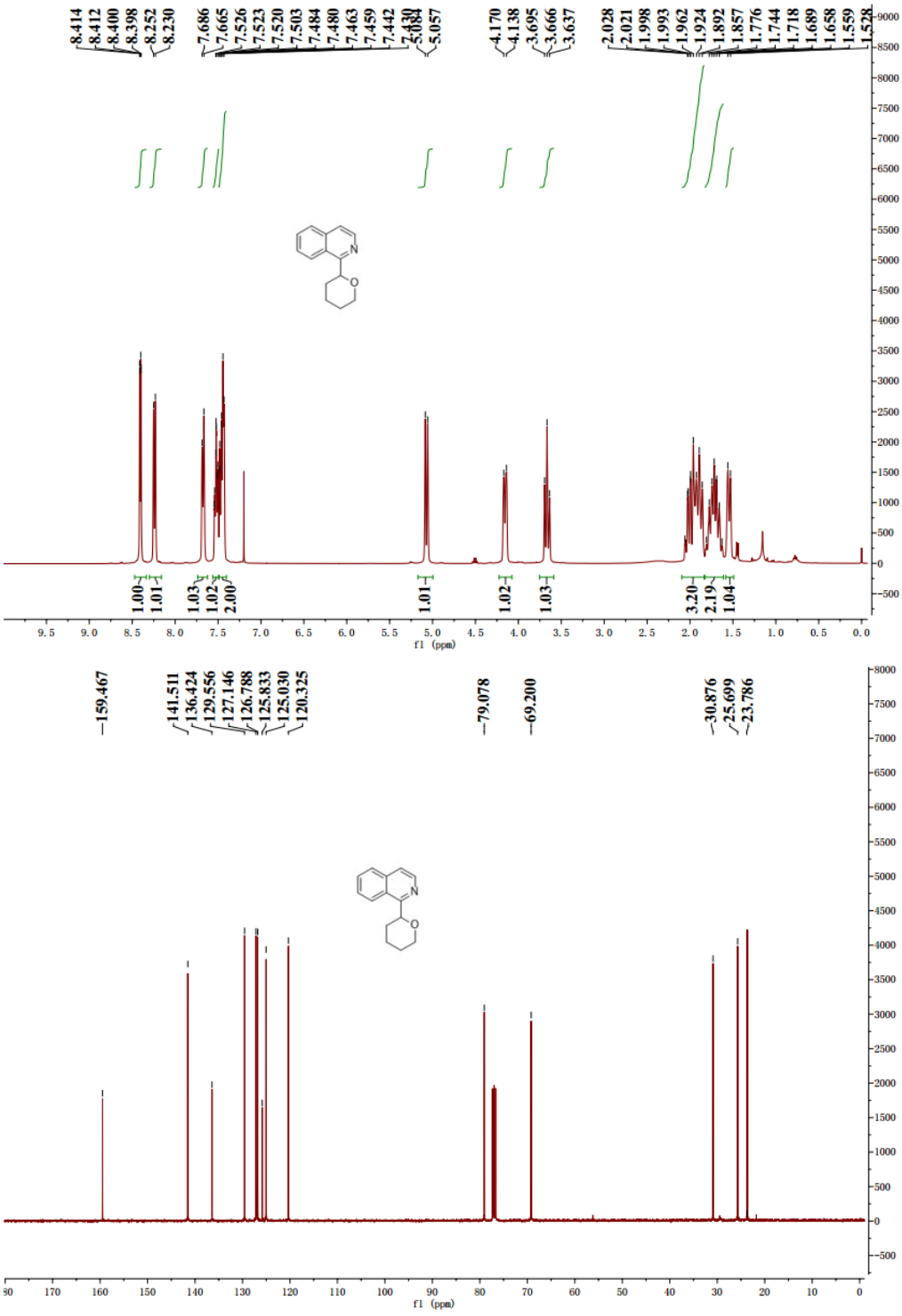
32.203
25.426
COOCH3
f1 (ppm)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7.523
7.520
7.503
7.484
7.480
7.463
7.459
7.442
7.430
5.084
5.057
4.170
4.138
3.695
3.666
3.637
2.028
2.021
1.998
1.993
1.962
1.924
1.892
1.857
1.776
1.744
1.718
1.689
1.658
1.559
1.528
1.00
1.01
1.03
1.02
2.00
1.01
1.02
1.03
3.20
2.19
1.04
f1 (ppm)
159.467
141.511
136.424
129.556
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125.833
125.030
120.325
79.078
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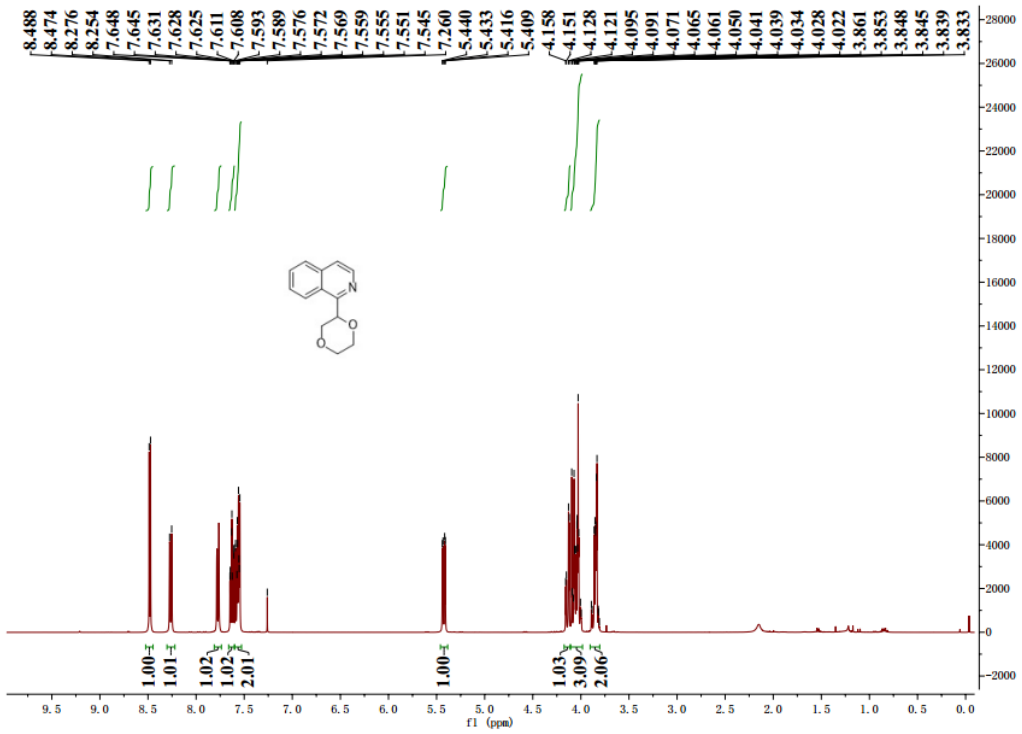
30.876
25.699
23.786
f1 (ppm)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7.628
7.625
7.611
7.608
7.593
7.589
7.576
7.572
7.569
7.559
7.555
7.551
7.545
7.260
5.440
5.433
5.416
5.409
4.158
4.151
4.128
4.121
4.095
4.091
4.071
4.065
4.061
4.050
4.041
4.039
4.034
4.028
4.022
3.861
3.853
3.848
3.845
3.839
3.833
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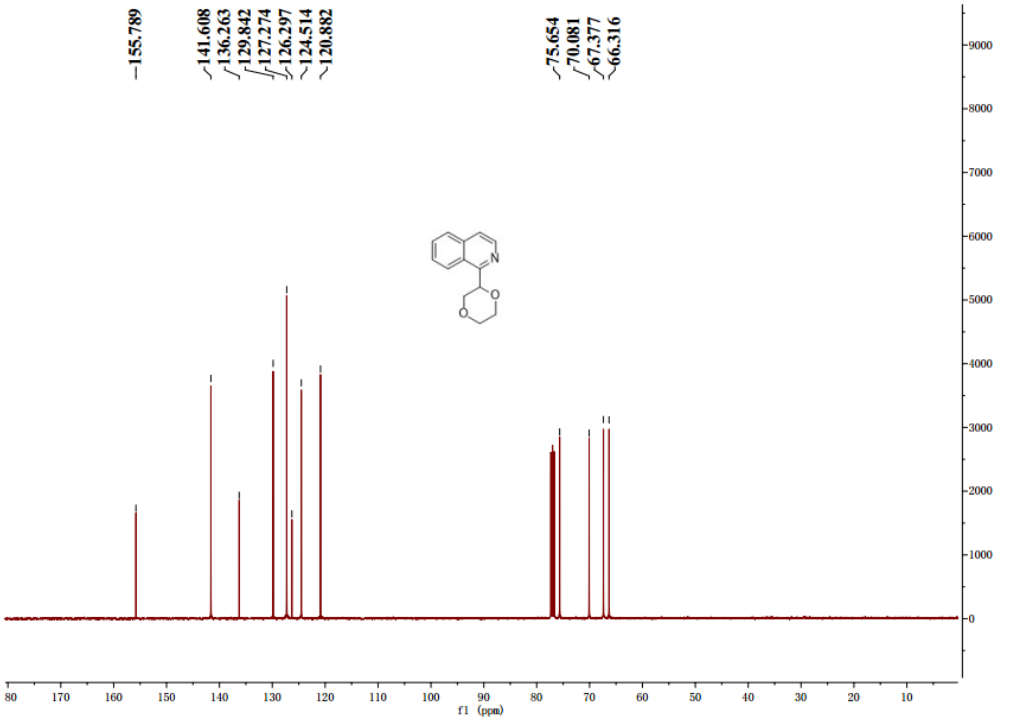
1.01
1.02
1.02
2.01
1.00
1.03
3.09
2.06
f1 (ppm)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120.882
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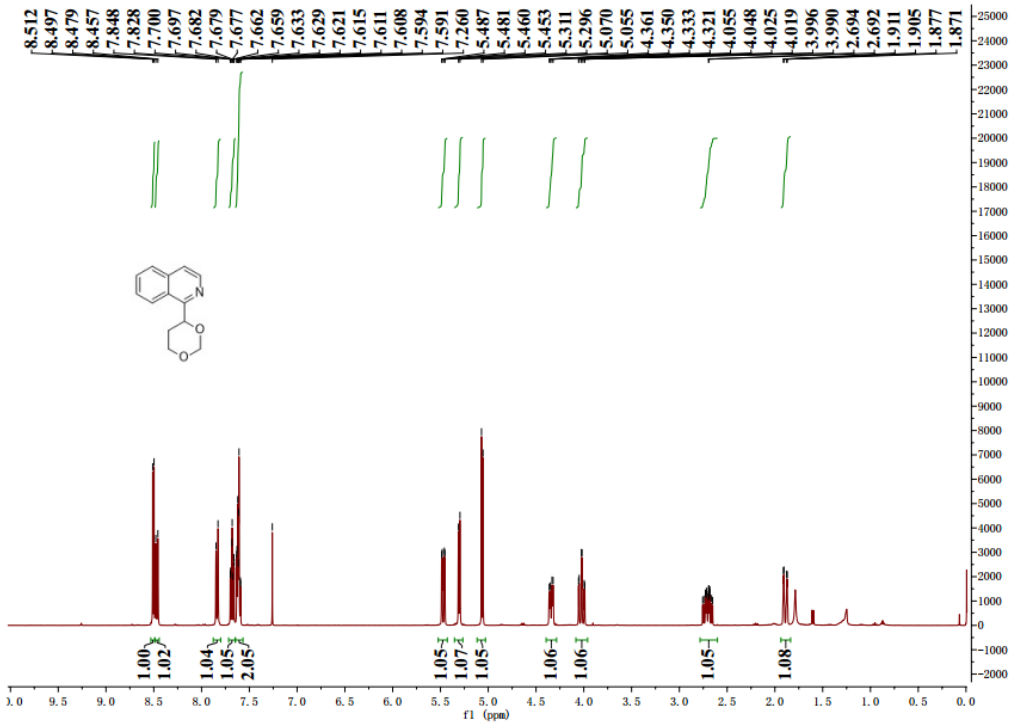
67.377
66.316
f1 (ppm)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8.479
8.457
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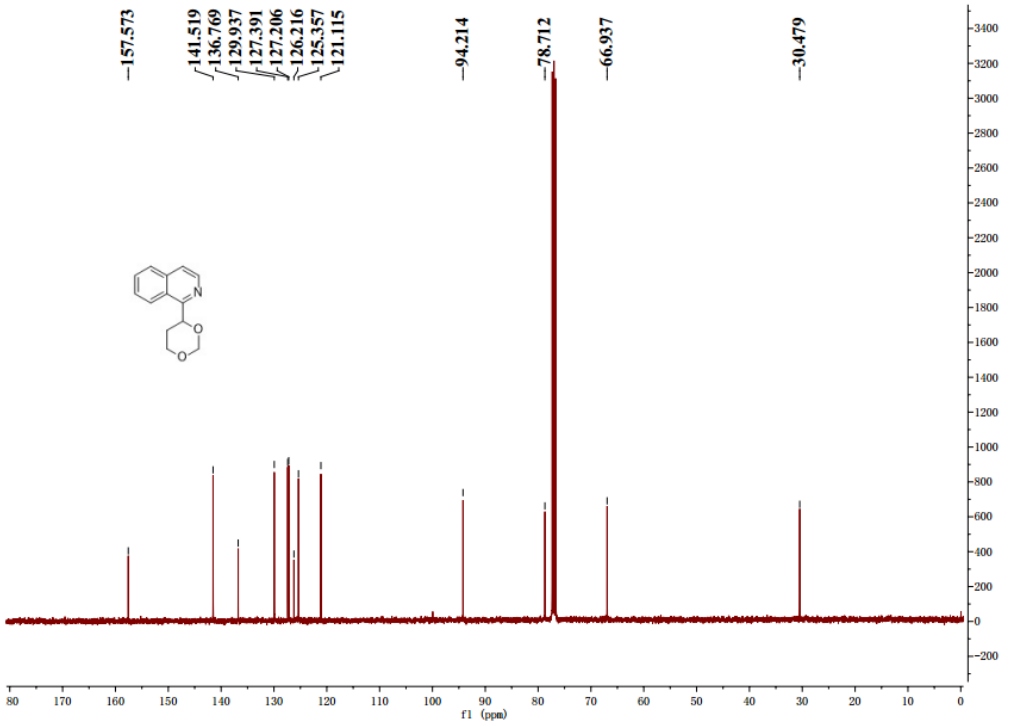
7.828
7.700
7.697
7.682
7.679
7.677
7.662
7.659
7.633
7.629
7.621
7.615
7.611
7.608
7.594
7.591
7.260
5.487
5.481
5.460
5.453
5.311
5.296
5.070
5.055
4.361
4.350
4.333
4.321
4.055
4.048
4.025
4.019
3.996
3.990
2.694
2.692
1.911
1.905
1.877
1.871
1.00
1.02
1.04
1.05
2.05
1.05
1.07
1.05
1.06
1.06
1.05
1.08
f1 (ppm)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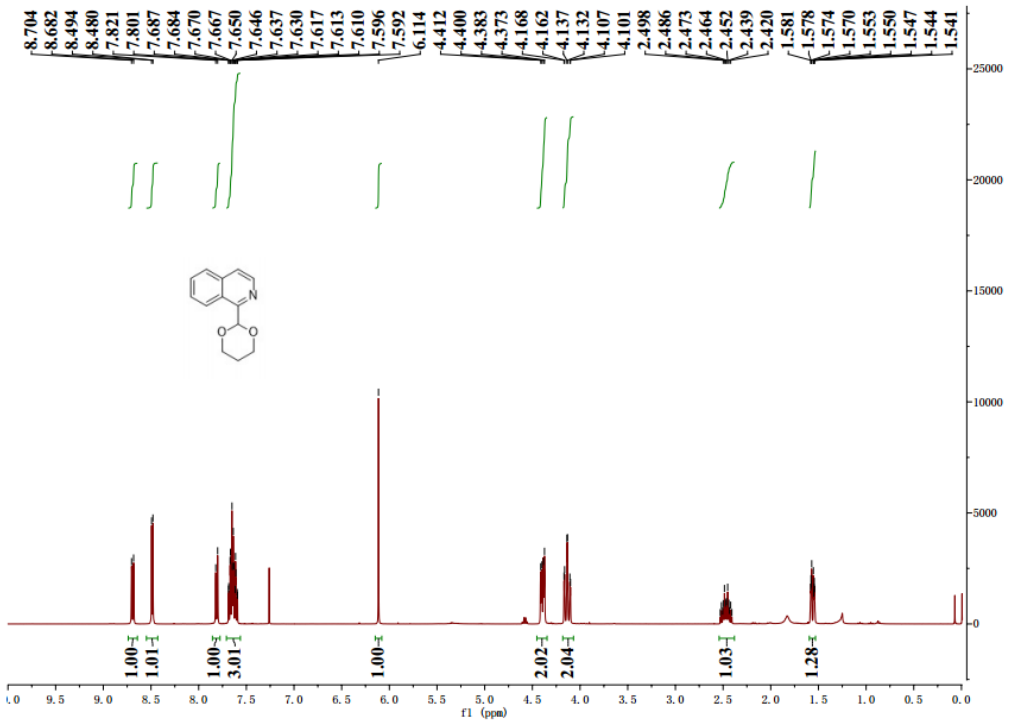
141.519
136.769
129.937
127.391
127.206
126.216
125.357
121.115
94.214
78.712
66.937
30.479
f1 (ppm)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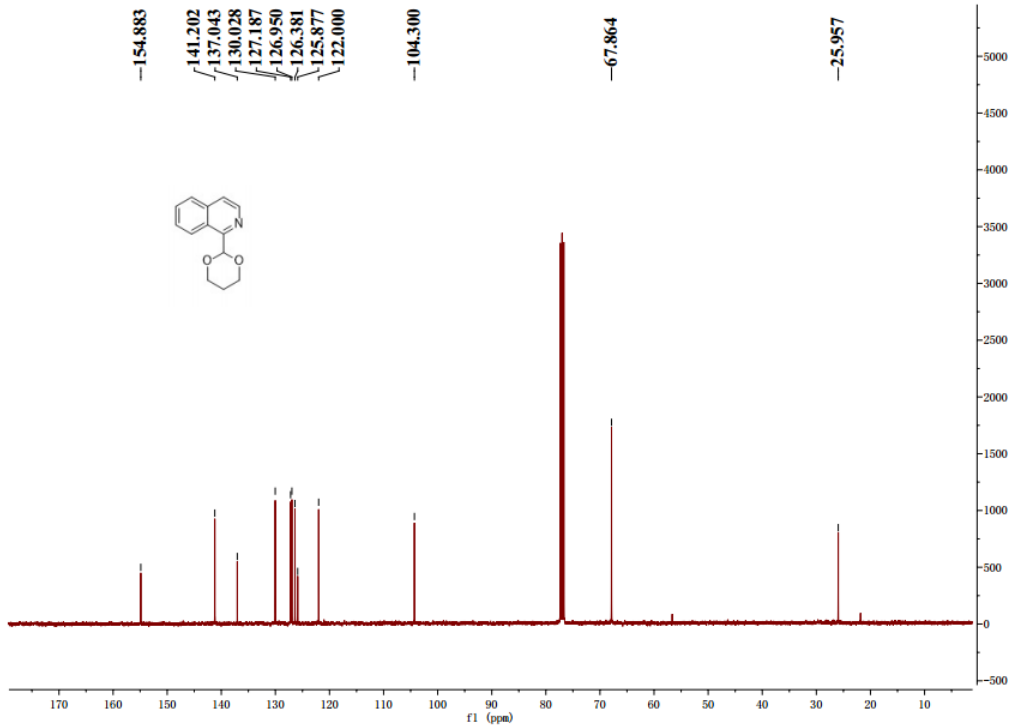
8.682
8.494
8.480
7.821
7.801
7.687
7.684
7.670
7.667
7.650
7.646
7.637
7.630
7.617
7.613
7.610
7.596
7.592
6.114
4.412
4.400
4.383
4.373
4.168
4.162
4.137
4.132
4.107
4.101
2.498
2.486
2.473
2.464
2.452
2.439
2.420
1.581
1.578
1.574
1.570
1.553
1.550
1.547
1.544
1.541
1.00
1.01
1.00
3.01
1.00
2.02
2.04
1.03
1.28
f1 (ppm)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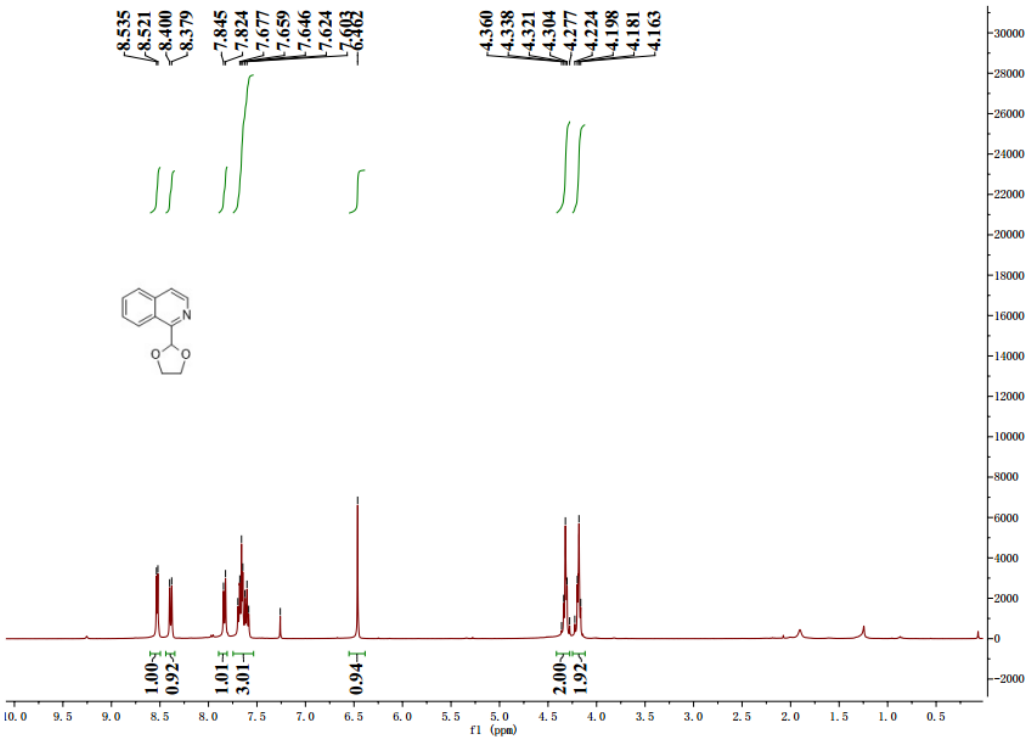
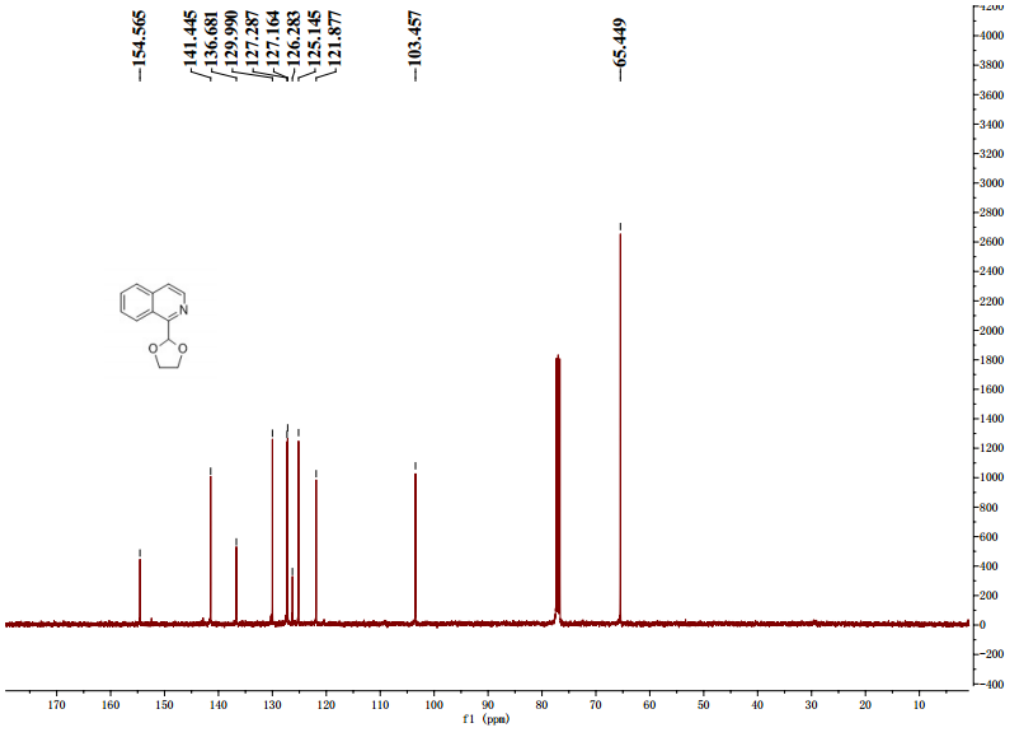
126.381
125.877
122.000
104.300
67.864
25.957
f1 (ppm)


8.535
8.521
8.400
8.379
7.845
7.824
7.677
7.659
7.646
7.624
7.603
6.482
4.360
4.338
4.321
4.304
4.277
4.224
4.198
4.181
4.163
1.00
0.92
1.01
3.01
0.94
2.00
1.92
f1 (ppm)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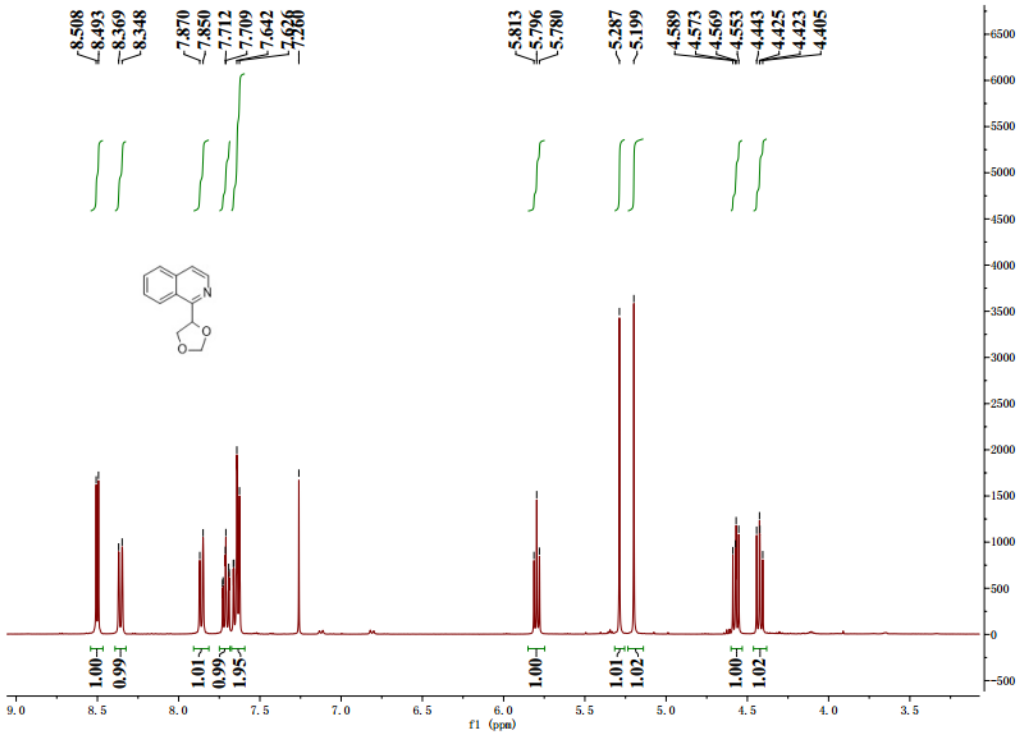
127.164
126.283
125.145
121.877
103.457
65.449
f1 (ppm)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8.369
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7.712
7.709
7.642
5.813
5.796
5.780
5.287
5.199
4.589
4.573
4.569
4.553
4.443
4.425
4.423
4.405
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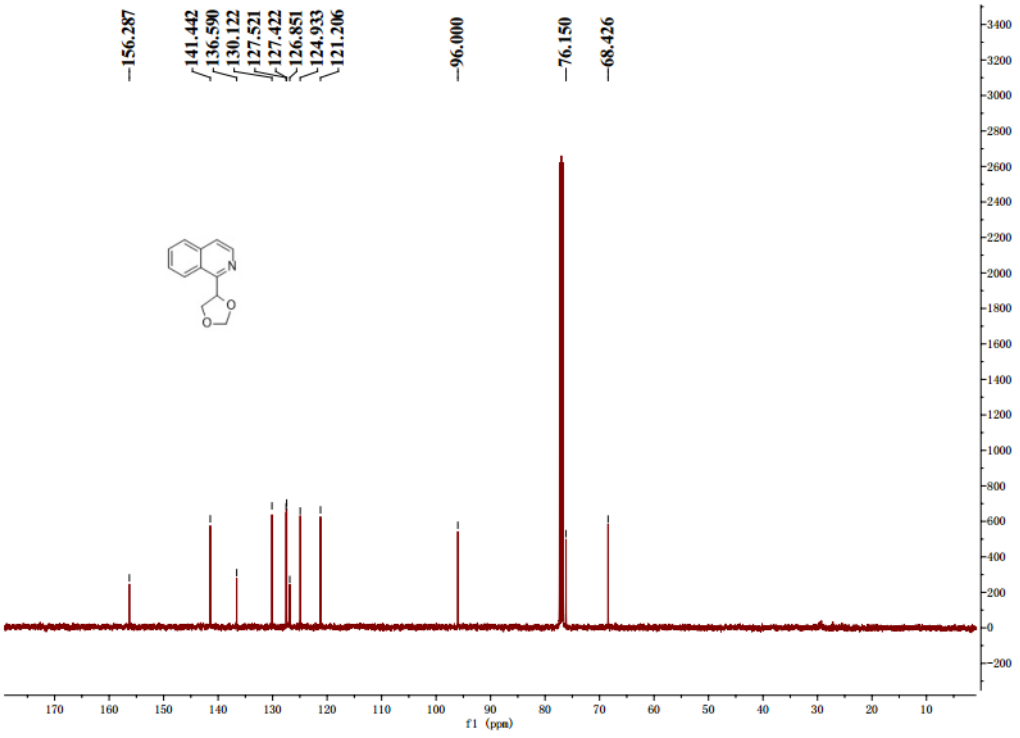
0.99
1.01
0.99
1.95
1.00
1.01
1.02
1.00
1.02
f1 (ppm)


156.287
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130.122
127.521
127.422
126.851
124.933
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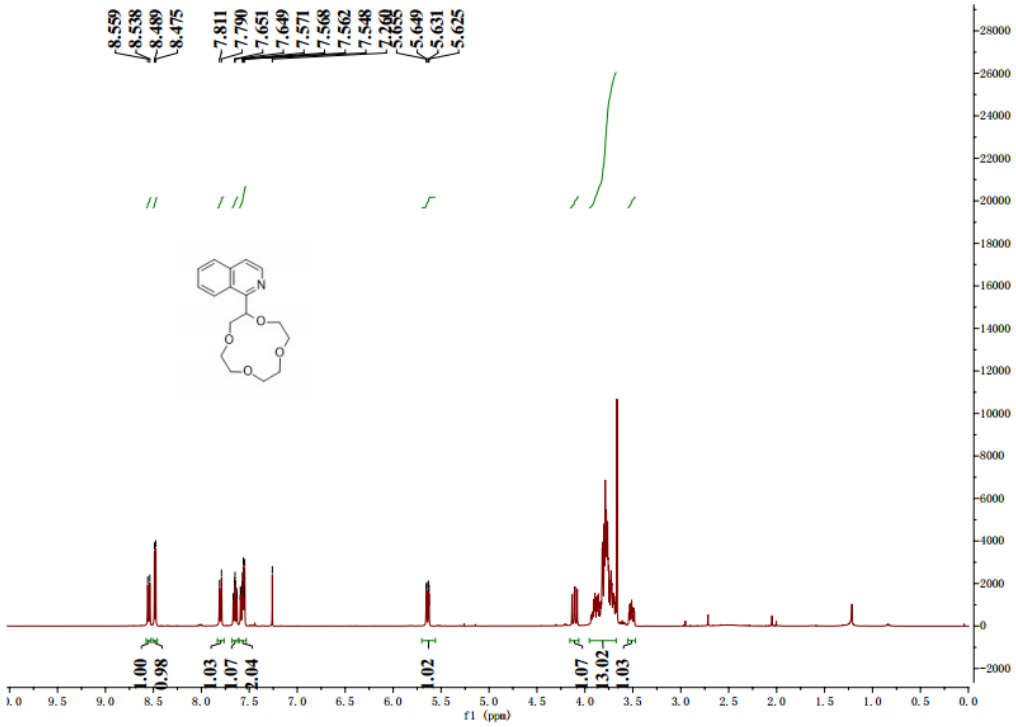
96.000
76.150
68.426
f1 (ppm)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7.649
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7.568
7.562
7.548
5.649
5.631
5.625
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0.98
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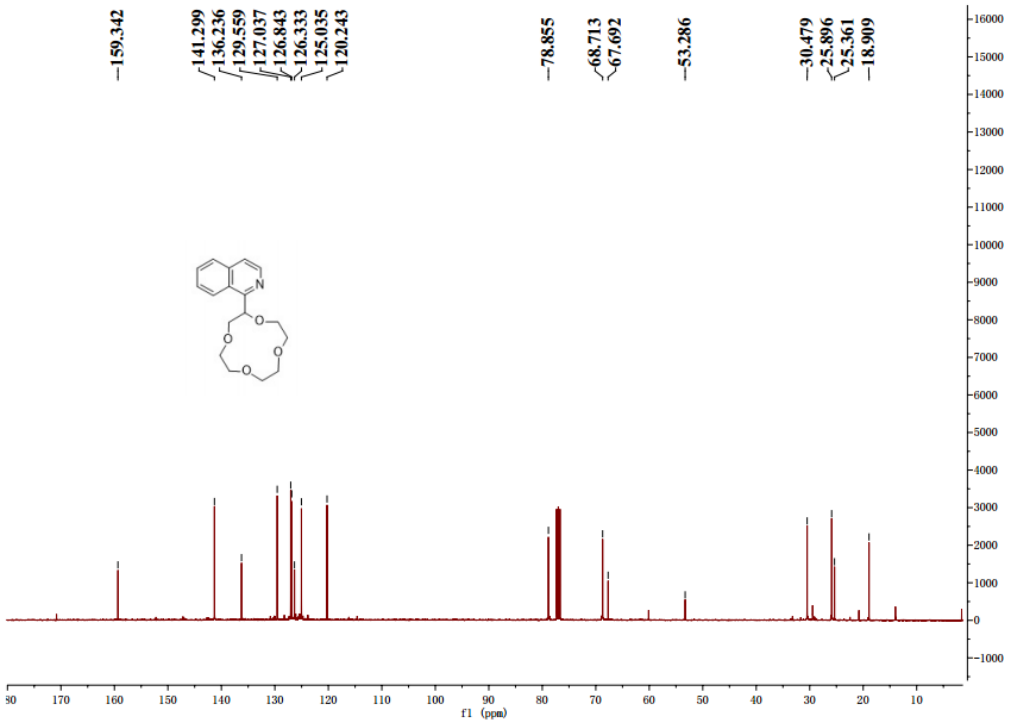
1.07
2.04
1.02
1.07
3.02
1.03
f1 (ppm)


159.342
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127.037
126.843
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125.035
120.243
78.855
68.713
67.692
53.286
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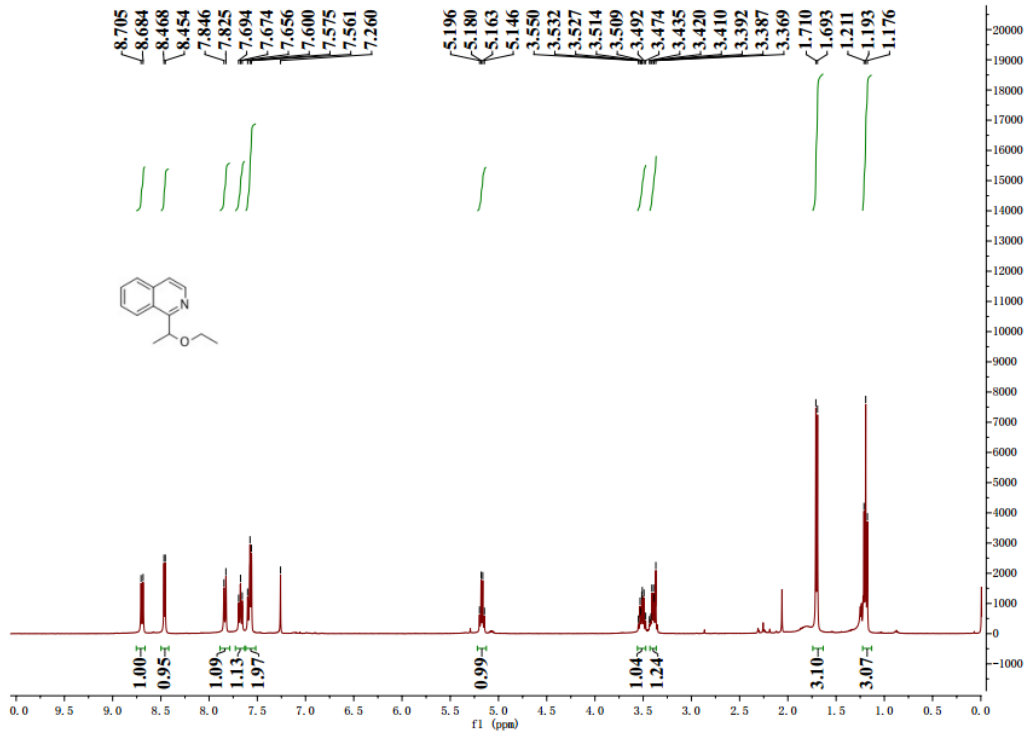
25.896
25.361
18.909
f1 (ppm)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7.674
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7.600
7.575
7.561
7.260
5.196
5.180
5.163
5.146
3.550
3.532
3.527
3.514
3.509
3.492
3.474
3.435
3.420
3.410
3.392
3.387
3.369
1.710
1.693
1.211
1.193
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1.97
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1.24
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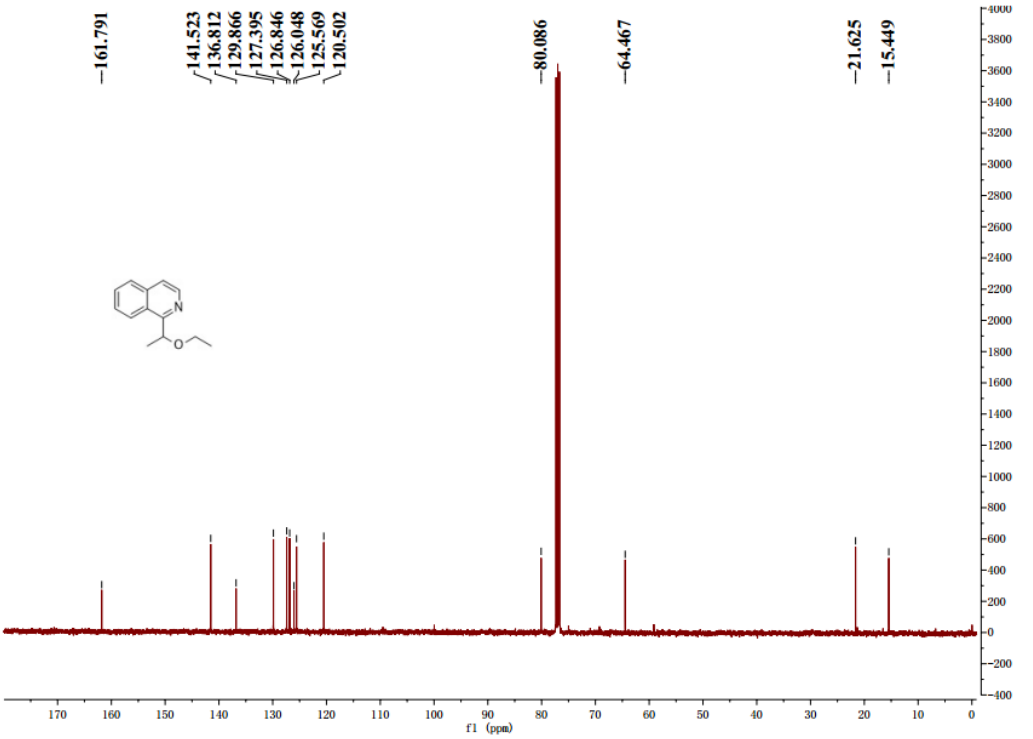
3.07
f1 (ppm)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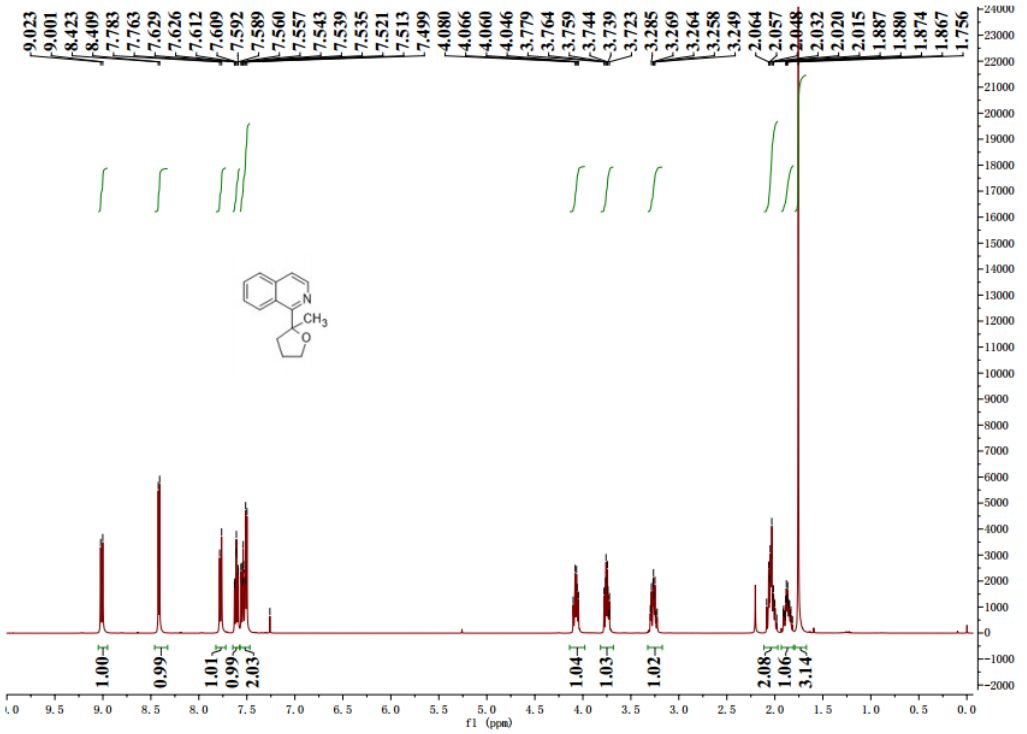
f1 (ppm)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7.560
7.557
7.543
7.539
7.535
7.521
7.513
7.499
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4.066
4.060
4.046
3.779
3.764
3.759
3.744
3.739
3.723
3.285
3.269
3.264
3.258
3.249
2.064
2.057
2.048
2.032
2.020
2.015
1.887
1.880
1.874
1.867
1.756
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0.99
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1.04
1.03
1.02
2.08
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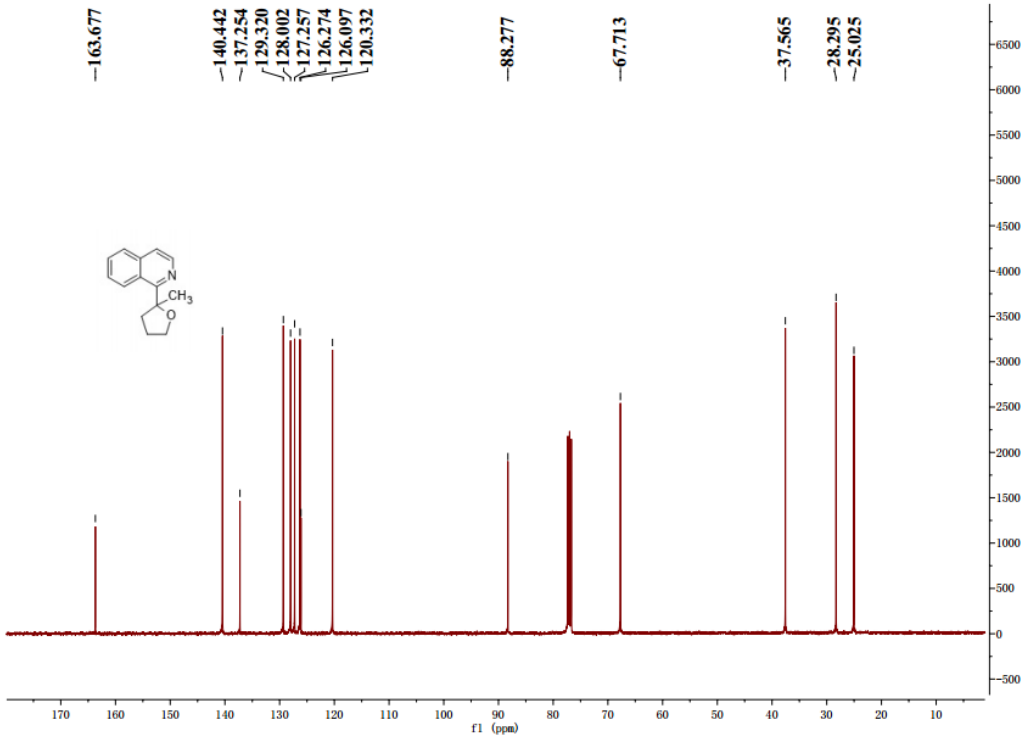
f1 (ppm)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126.097
120.332
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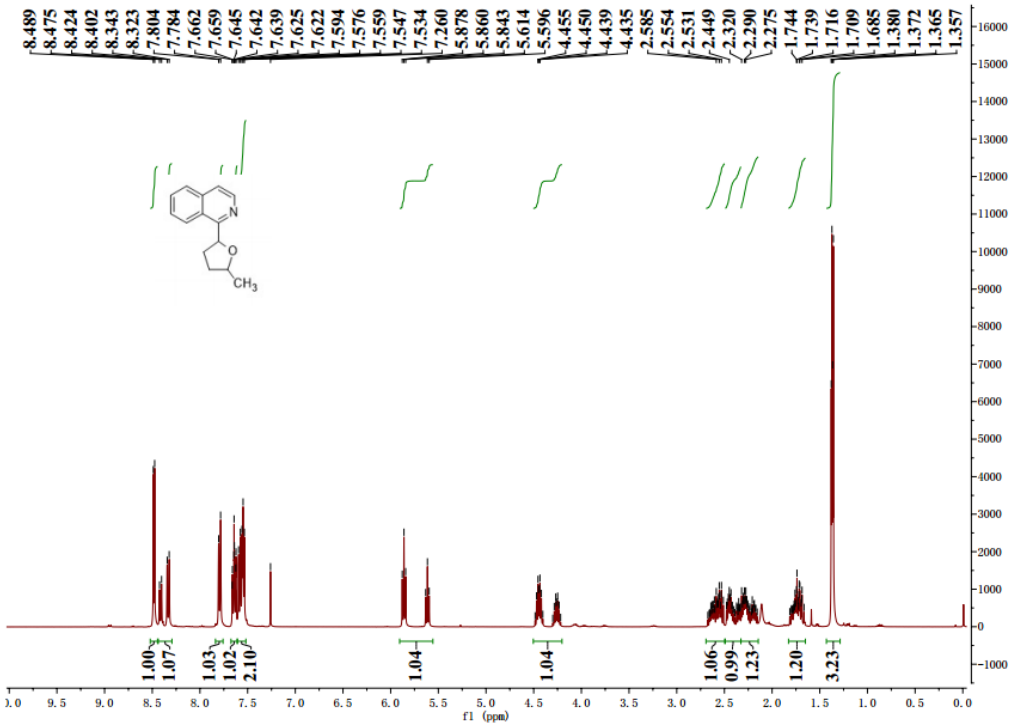
37.565
28.295
25.025
f1 (ppm)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7.639
7.625
7.622
7.594
7.576
7.559
7.547
7.534
7.260
5.878
5.860
5.843
5.614
5.596
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4.450
4.439
4.435
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2.554
2.531
2.449
2.320
2.290
2.275
1.744
1.739
1.716
1.709
1.685
1.380
1.372
1.365
1.357
N
O
CH3
1.00
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1.03
1.02
2.10
1.04
1.04
1.06
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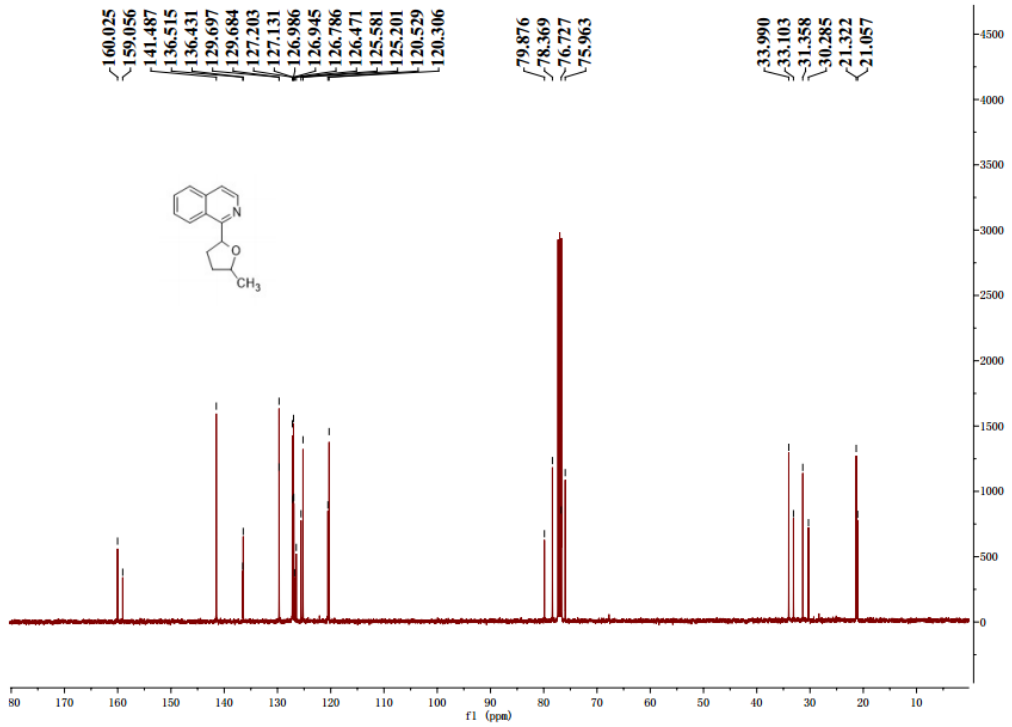
1.20
3.23
f1 (ppm)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126.471
125.581
125.201
120.529
120.306
79.876
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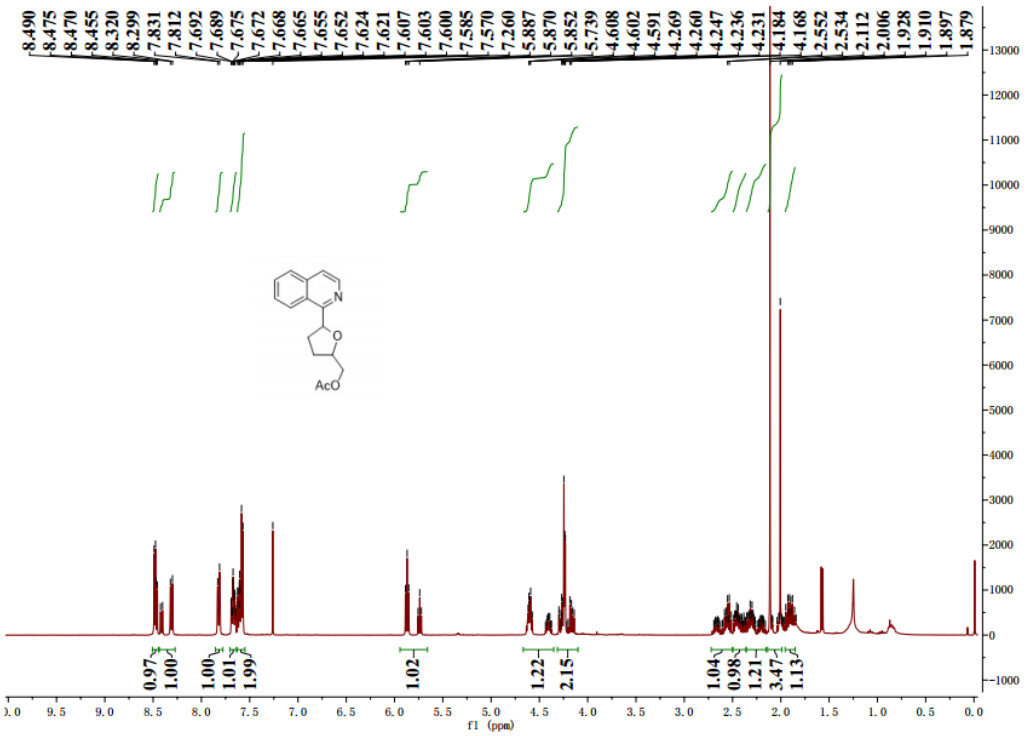
75.963
33.990
33.103
31.358
30.285
21.322
21.057
N
O
CH3
f1 (ppm)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7.665
7.655
7.652
7.624
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7.607
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7.600
7.585
7.570
7.260
5.887
5.870
5.852
5.739
4.608
4.602
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2.006
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1.910
1.897
1.879
0.97
1.00
1.00
1.01
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1.02
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2.15
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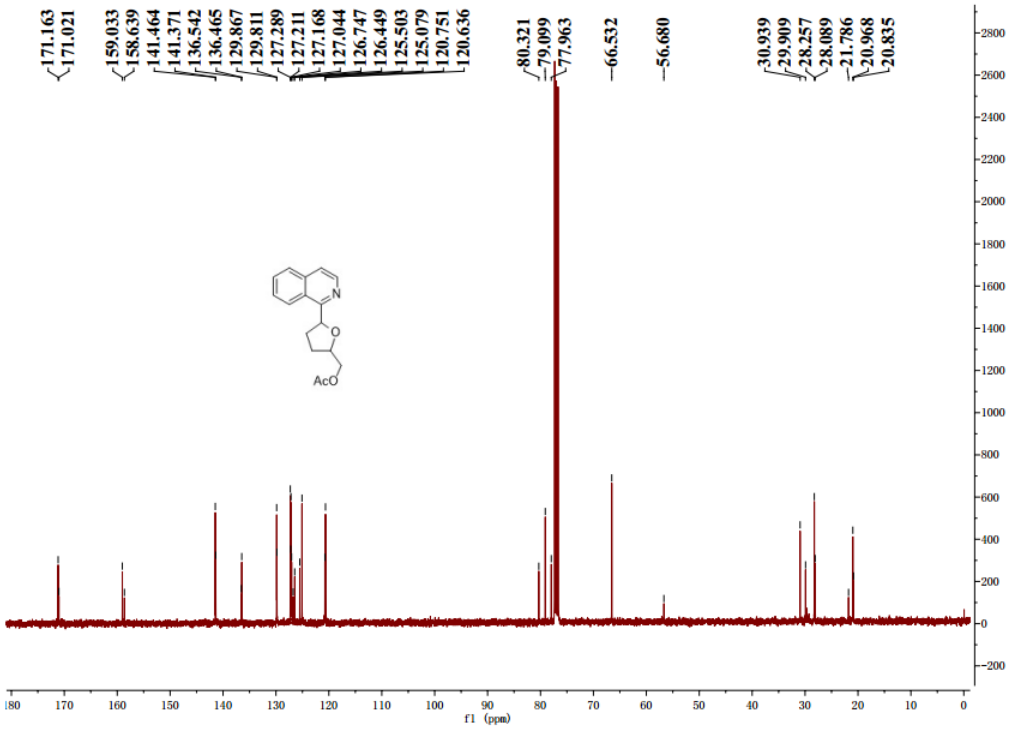
1.13
f1 (ppm)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136.465
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127.211
127.168
127.044
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125.079
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120.636
80.321
79.099
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66.532
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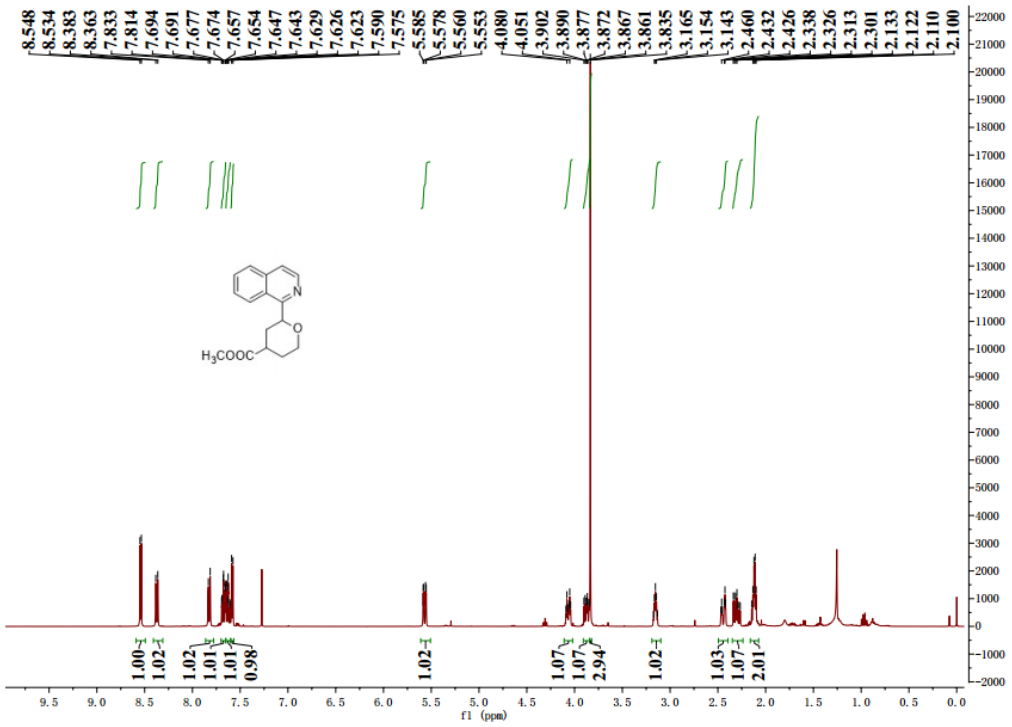
30.939
29.909
28.257
28.089
21.786
20.968
20.835
f1 (ppm)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7.643
7.629
7.626
7.623
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5.578
5.560
5.553
4.080
4.051
3.902
3.890
3.877
3.872
3.867
3.861
3.835
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3.154
3.143
2.460
2.432
2.426
2.338
2.326
2.313
2.301
2.133
2.122
2.110
2.100
N
O
H3COOC
1.00
1.02
1.02
1.01
1.01
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1.02
1.07
1.07
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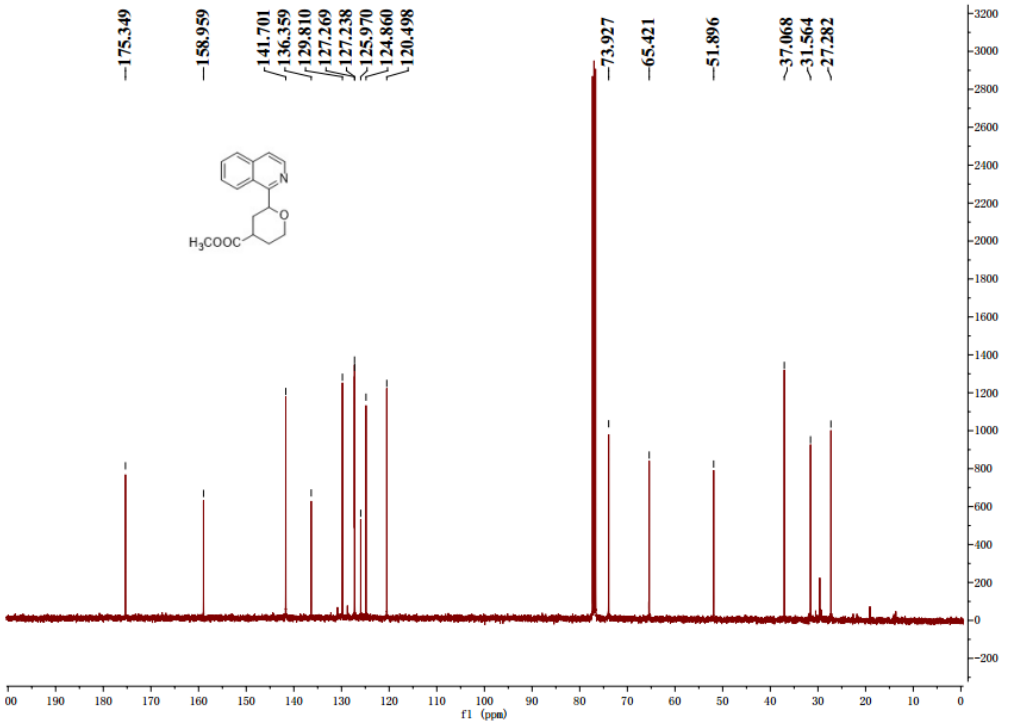
1.03
1.07
2.01
f1 (ppm)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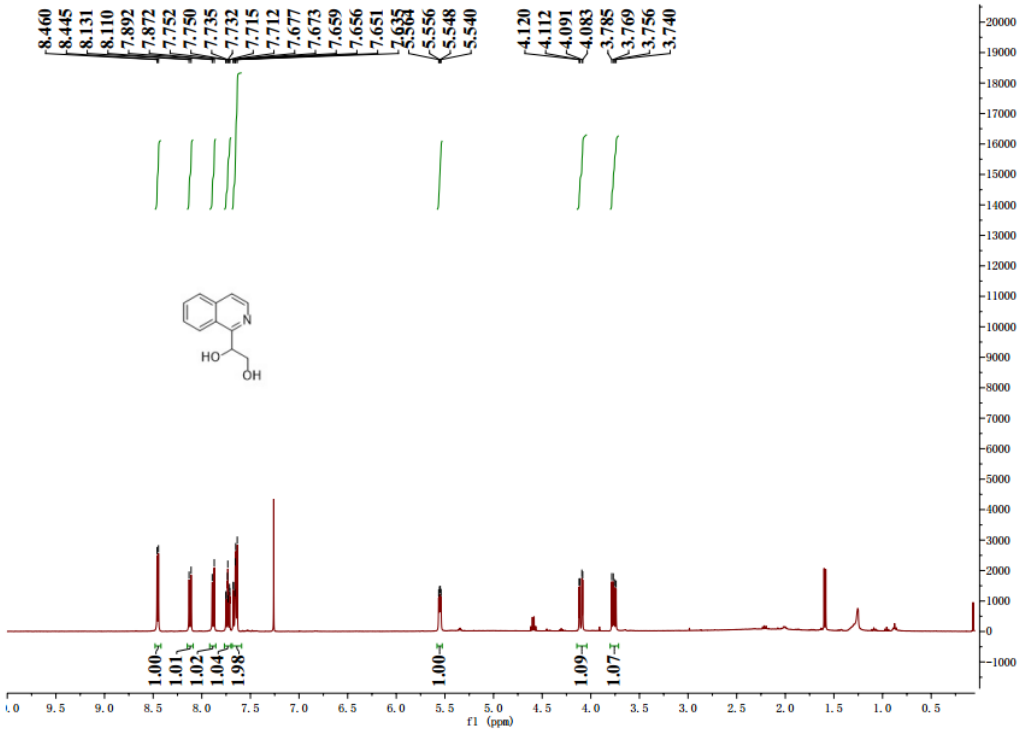
51.896
37.068
31.564
27.282
N
O
H3COOC
f1 (ppm)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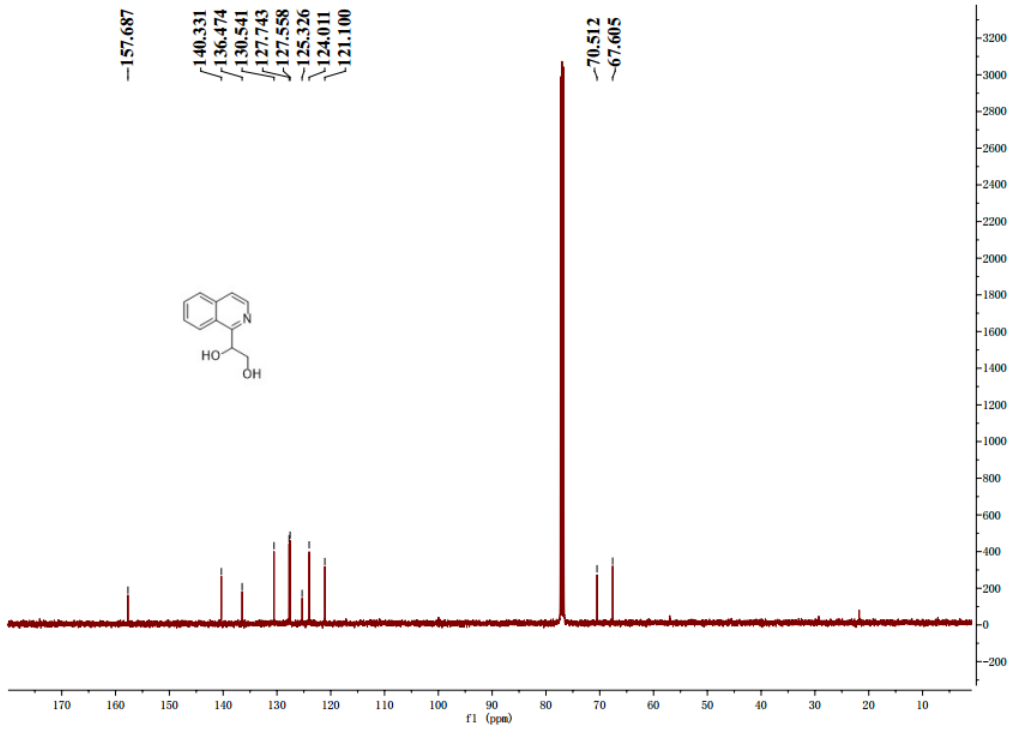
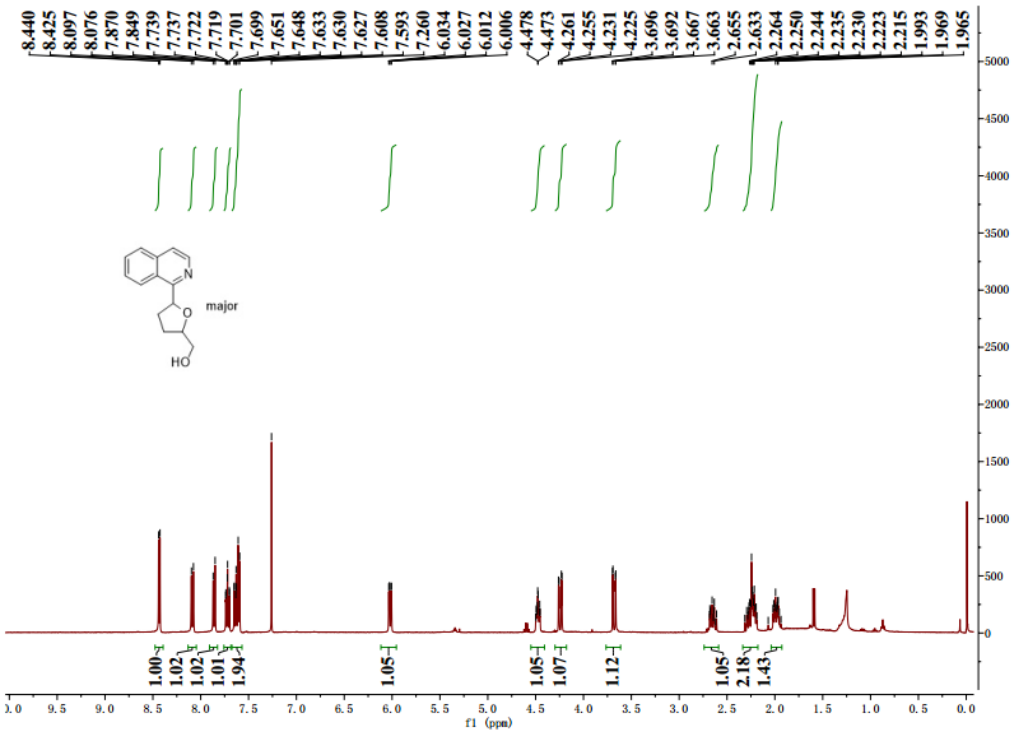
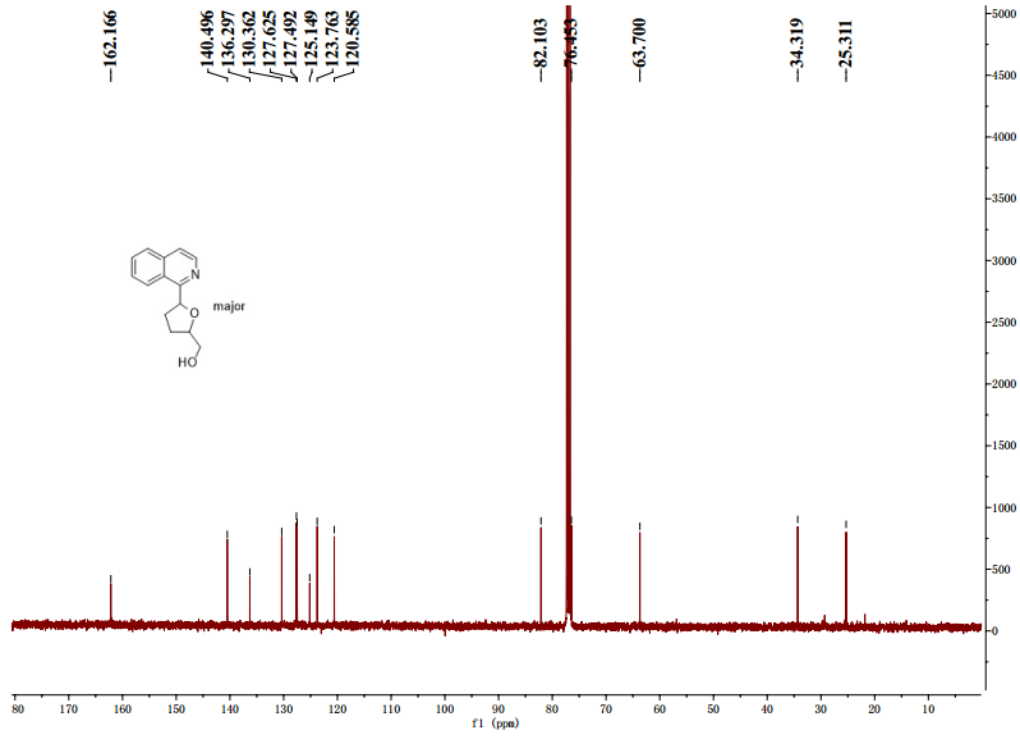
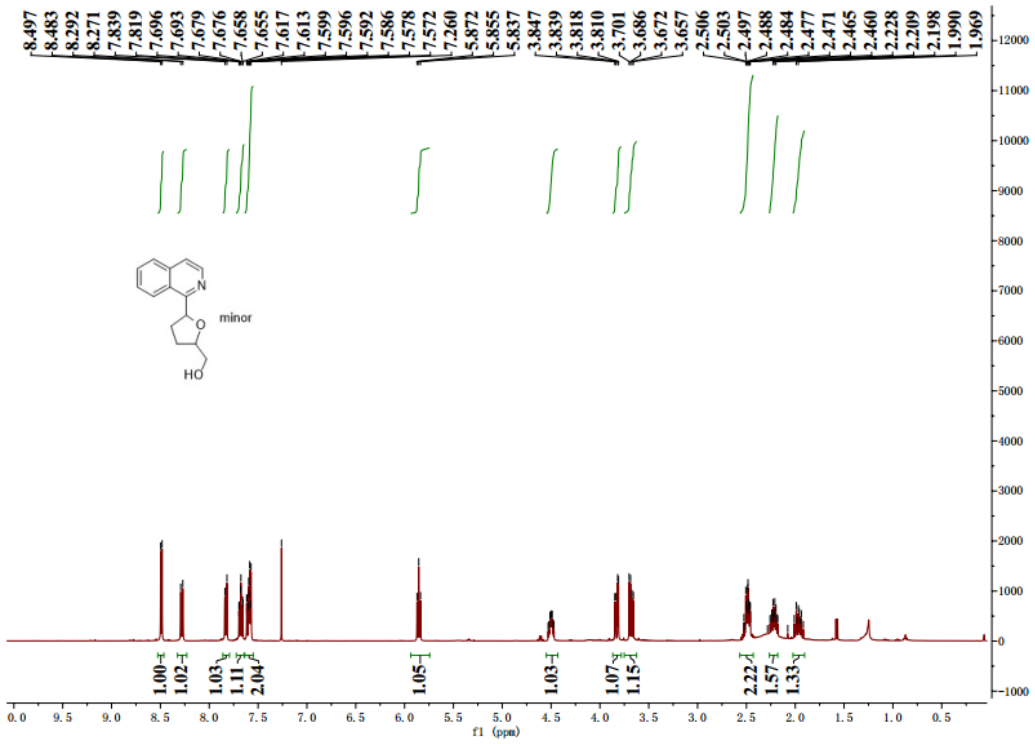
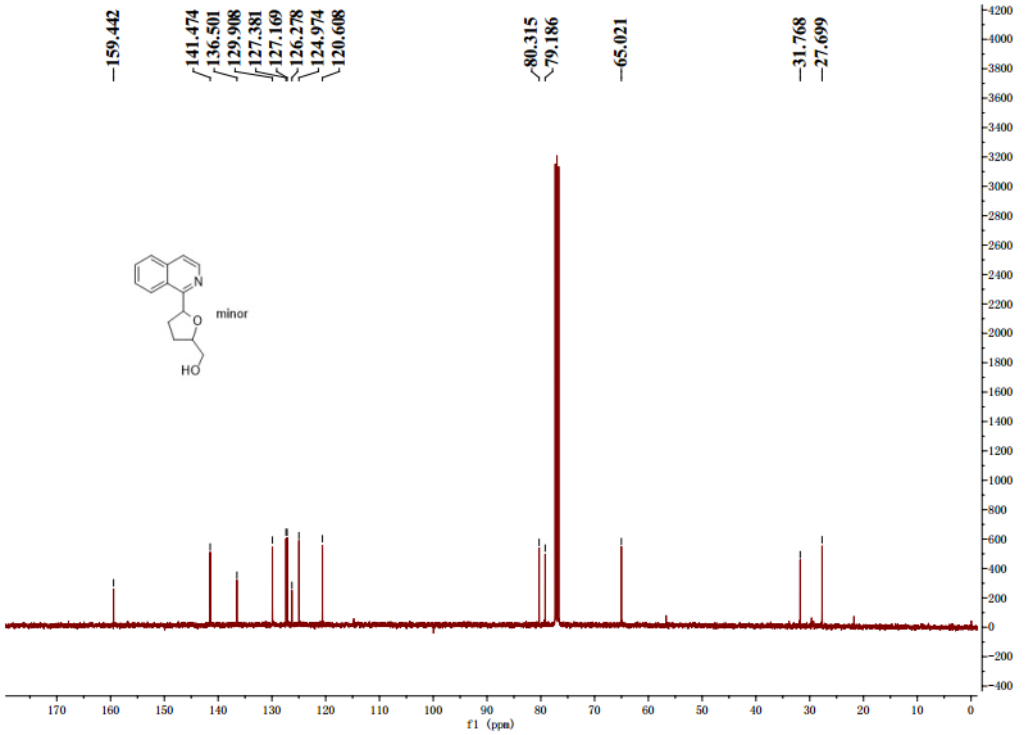
7.677
7.673
7.659
7.656
7.651
7.635
5.564
5.556
5.548
5.540
4.120
4.112
4.091
4.083
3.785
3.769
3.756
3.740
HO
OH
1.00
1.01
1.02
1.04
1.98
1.00
1.09
1.07
f1 (ppm)

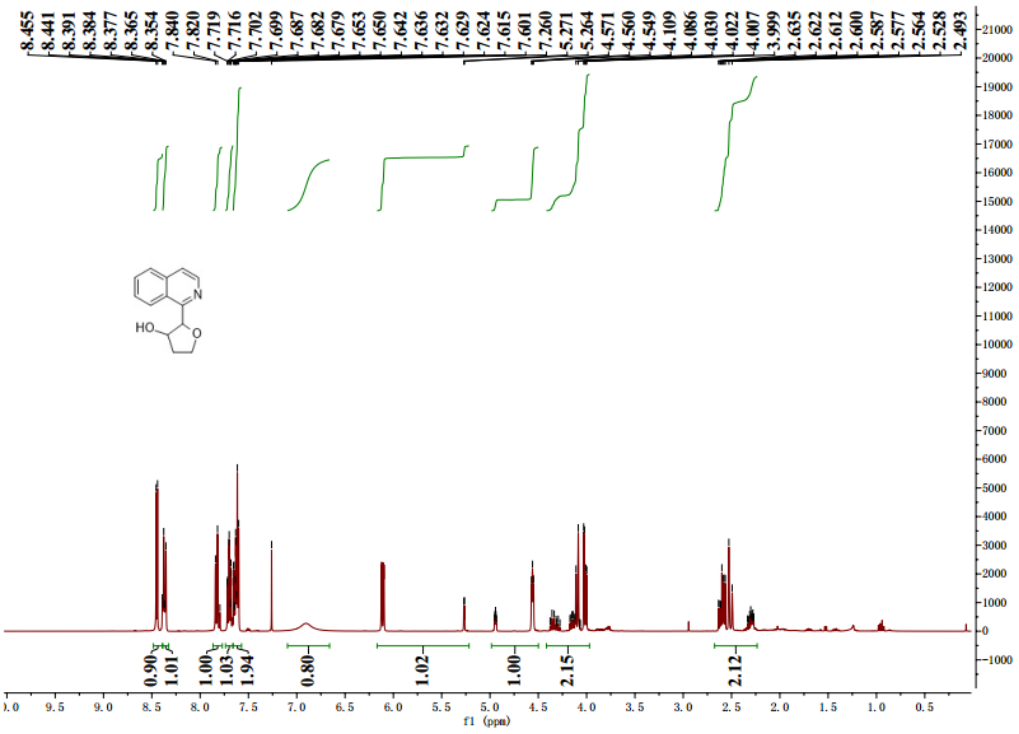

157.687
140.331
136.474
130.541
127.743
127.558
125.326
124.011
121.100
70.512
67.605
HO
OH
f1 (ppm)

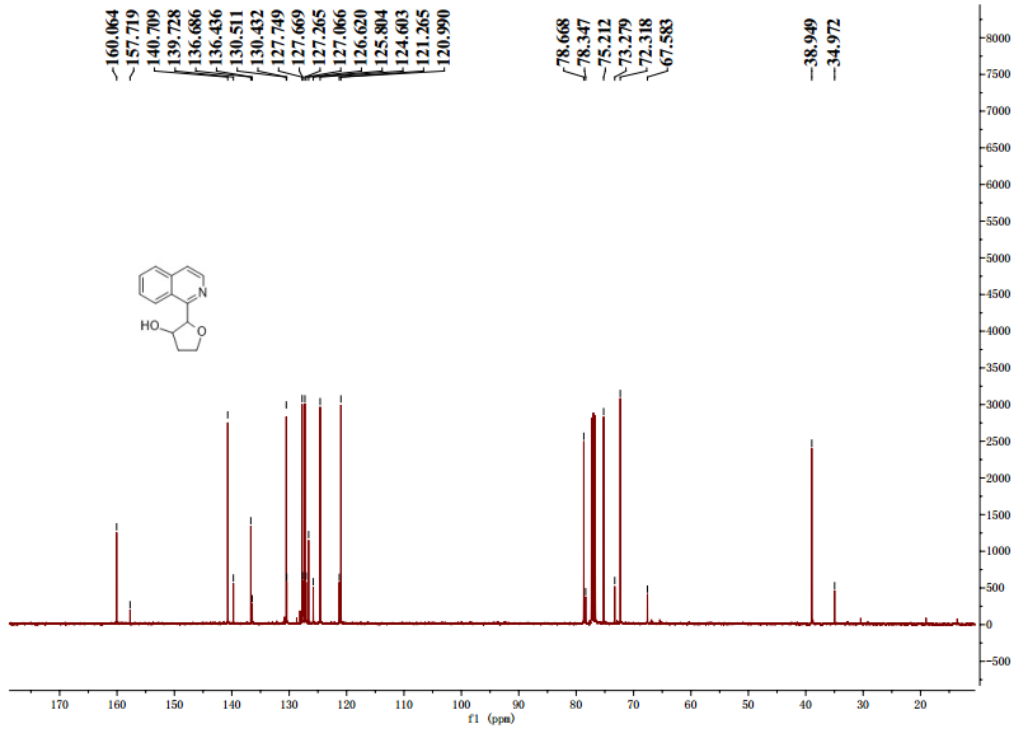

8.440
8.425
8.097
8.076
7.870
7.849
7.739
7.737
7.722
7.719
7.701
7.699
7.651
7.648
7.633
7.630
7.627
7.608
7.593
7.260
6.034
6.027
6.012
6.006
4.478
4.473
4.261
4.255
4.231
4.225
3.696
3.692
3.667
3.663
2.655
2.633
2.264
2.250
2.244
2.235
2.230
2.223
2.215
1.993
1.969
1.965
major
HO
1.00
1.02
1.02
1.01
1.94
1.05
1.05
1.07
1.12
1.05
2.18
1.43
f1 (ppm)

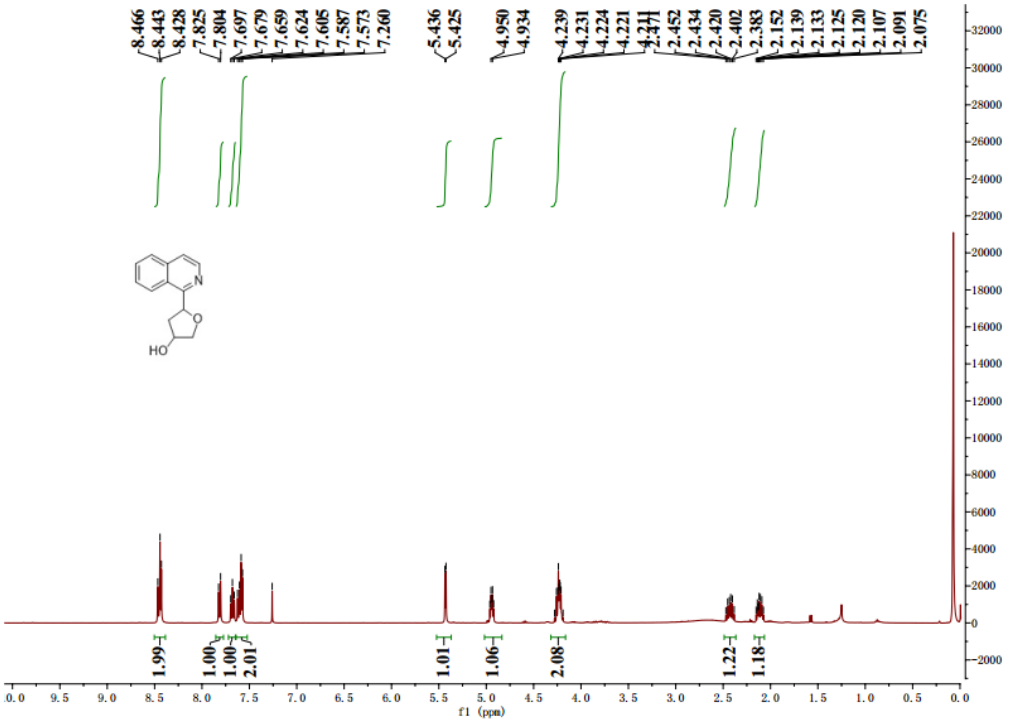

162.166
140.496
136.297
130.362
127.625
127.492
125.149
123.763
120.585
82.103
76.433
63.700
34.319
25.311
major
HO
f1 (ppm)

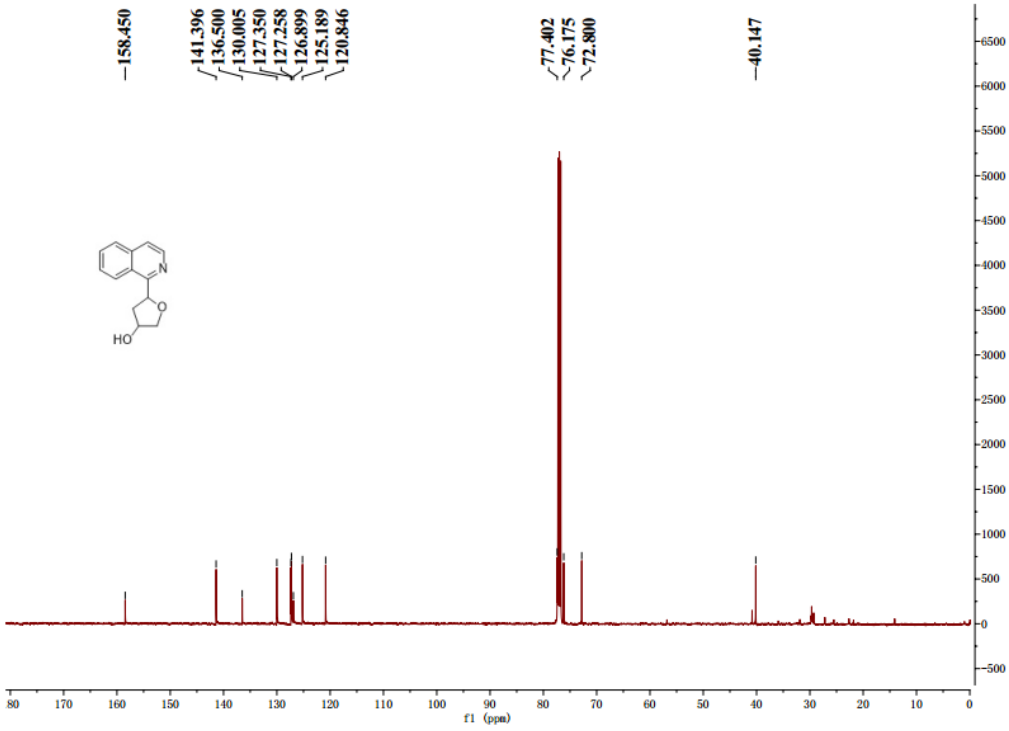

8.497
8.483
8.292
8.271
7.839
7.819
7.696
7.693
7.679
7.676
7.658
7.655
7.617
7.613
7.599
7.596
7.592
7.586
7.578
7.572
7.260
5.872
5.855
5.837
3.847
3.839
3.818
3.810
3.701
3.686
3.672
3.657
2.506
2.503
2.497
2.488
2.484
2.477
2.471
2.465
2.460
2.228
2.209
2.198
1.990
1.969
minor
HO
1.00
1.02
1.03
1.11
2.04
1.05
1.03
1.07
1.15
2.22
1.57
1.33
f1 (ppm)

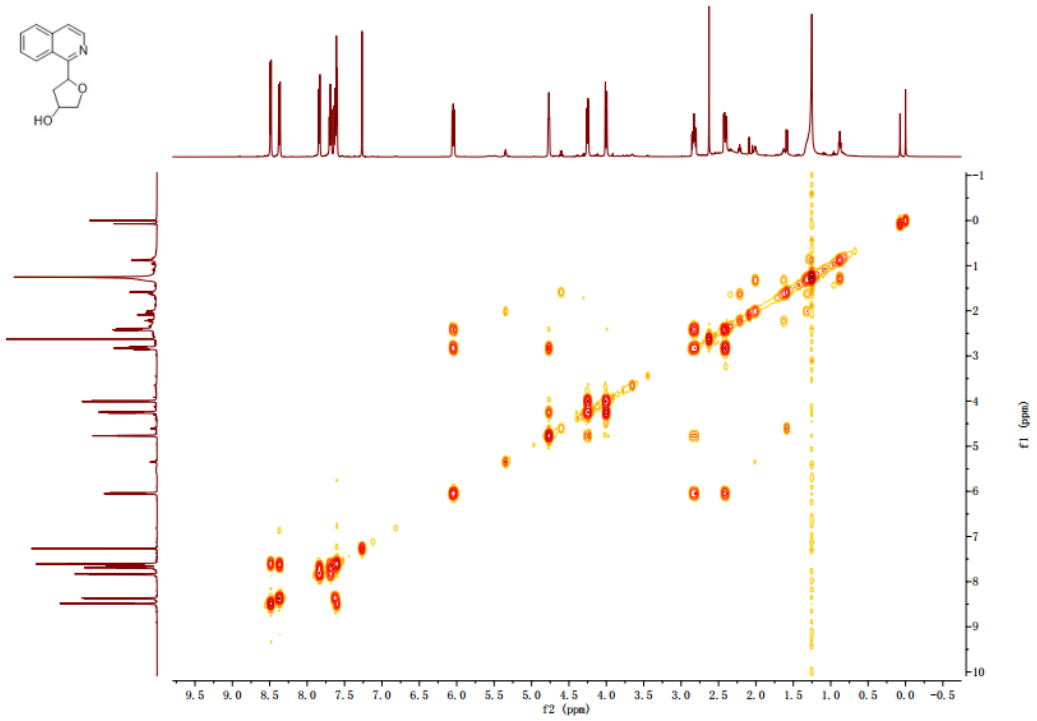

159.442
141.474
136.501
129.908
127.381
127.169
126.278
124.974
120.608
80.315
79.186
65.021
31.768
27.699
minor
HO
f1 (ppm)

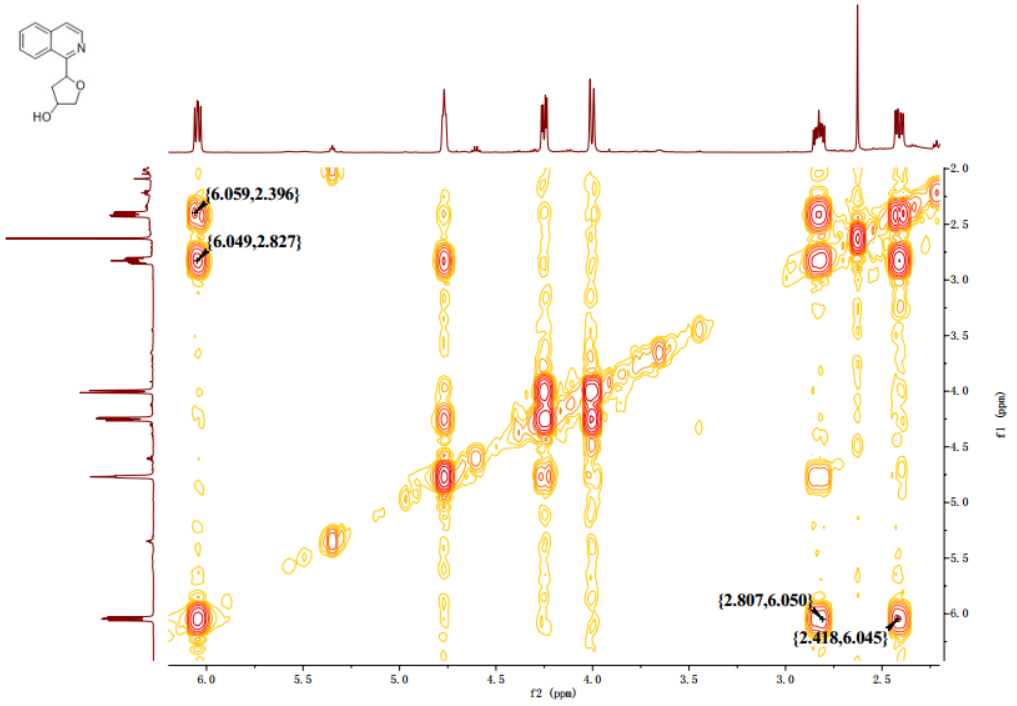

8.455
8.441
8.391
8.384
8.377
8.365
8.354
7.840
7.820
7.719
7.716
7.702
7.699
7.687
7.682
7.679
7.653
7.650
7.642
7.636
7.632
7.629
7.624
7.615
7.601
7.260
5.271
5.264
4.571
4.560
4.549
4.109
4.086
4.030
4.022
4.007
3.999
2.635
2.622
2.612
2.600
2.587
2.577
2.564
2.528
2.493
HO
N
O
0.90
1.01
1.00
1.03
1.94
0.80
1.02
1.00
2.15
2.12
f1 (ppm)

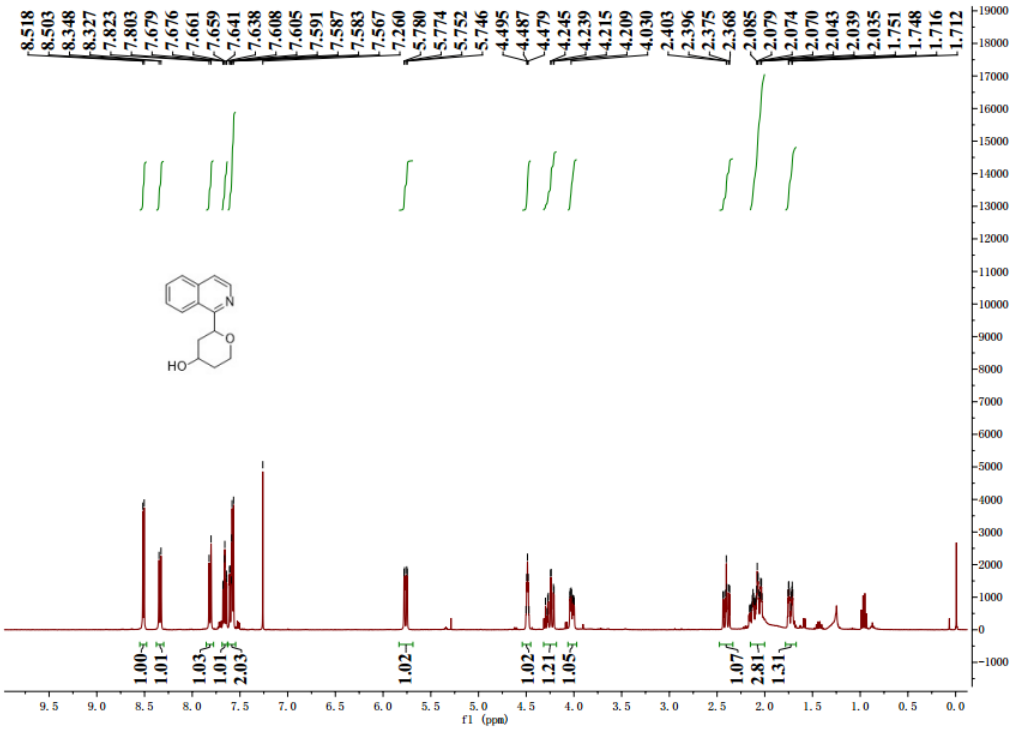

160.064
157.719
140.709
139.728
136.686
136.436
130.511
130.432
127.749
127.669
127.265
127.066
126.620
125.804
124.603
121.265
120.990
78.668
78.347
75.212
73.279
72.318
67.583
38.949
34.972
HO
N
O
f1 (ppm)

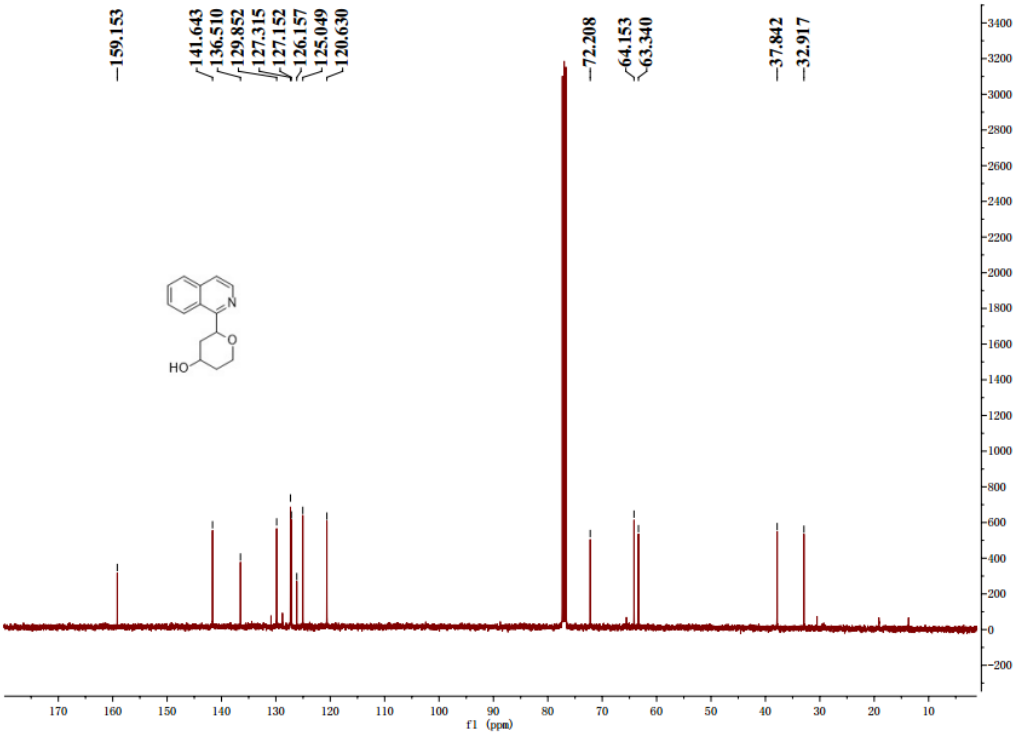

8.466
8.443
8.428
7.825
7.804
7.697
7.679
7.659
7.624
7.605
7.587
7.573
7.260
5.436
5.425
4.950
4.934
4.239
4.231
4.224
4.221
4.211
2.452
2.434
2.420
2.402
2.383
2.152
2.139
2.133
2.125
2.120
2.107
2.091
2.075
HO
1.99
1.00
1.00
2.01
1.01
1.06
2.08
1.22
1.18
f1 (ppm)

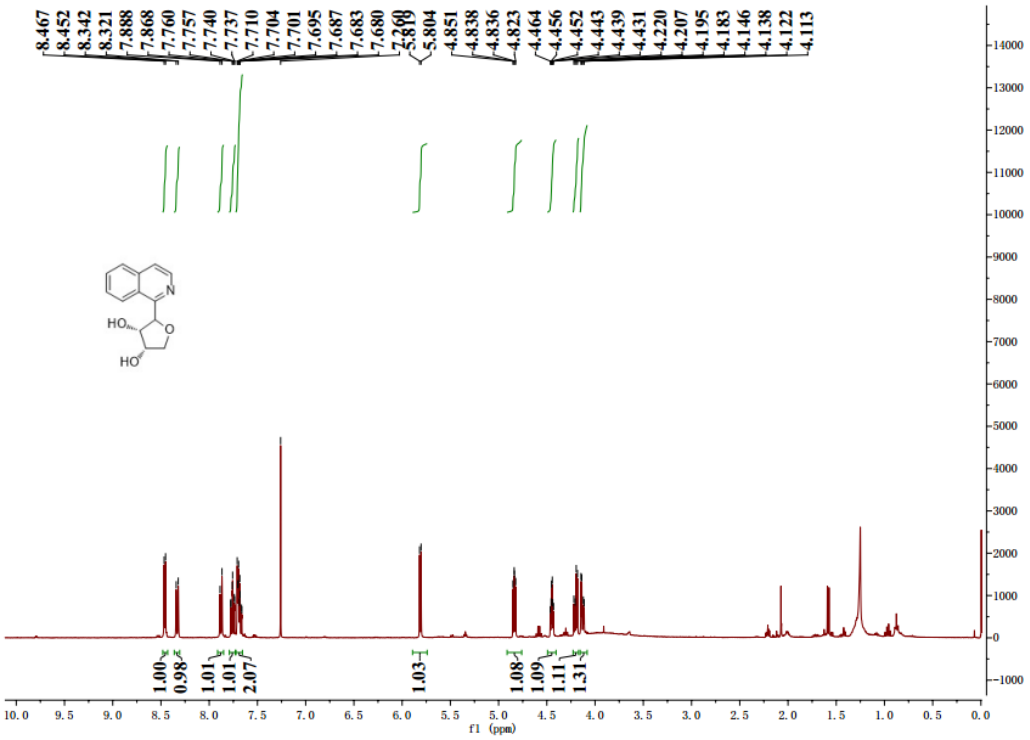

158.450
141.396
136.500
130.005
127.350
127.258
126.899
125.189
120.846
77.402
76.175
72.800
40.147
HO
f1 (ppm)

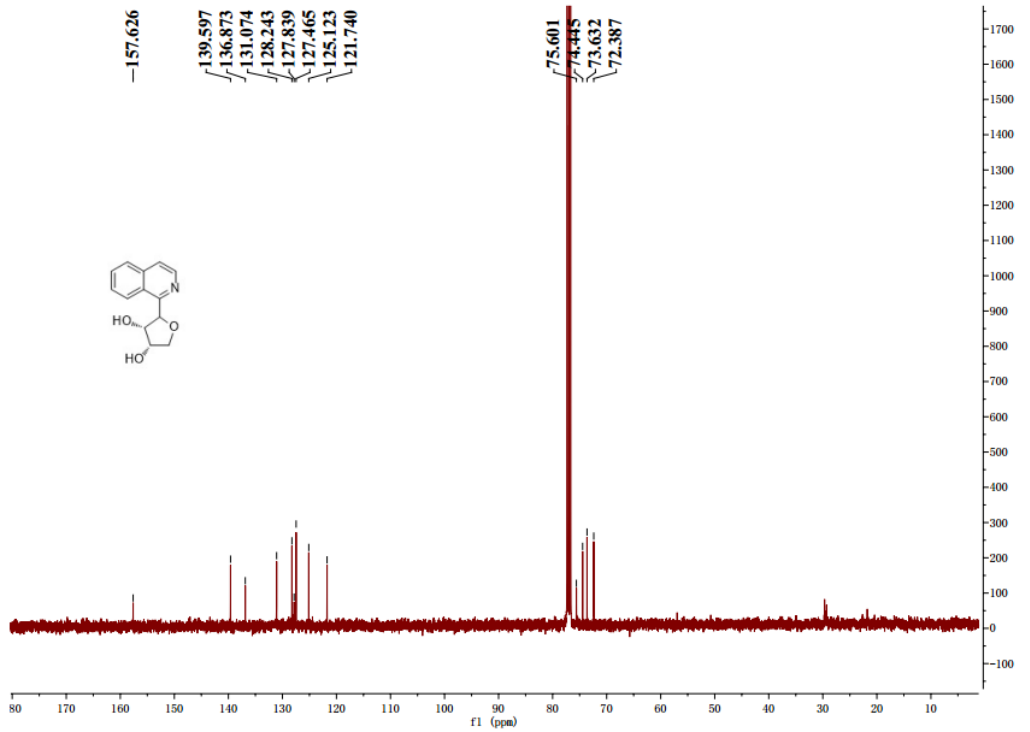

HO
f2 (ppm)
f1 (ppm)

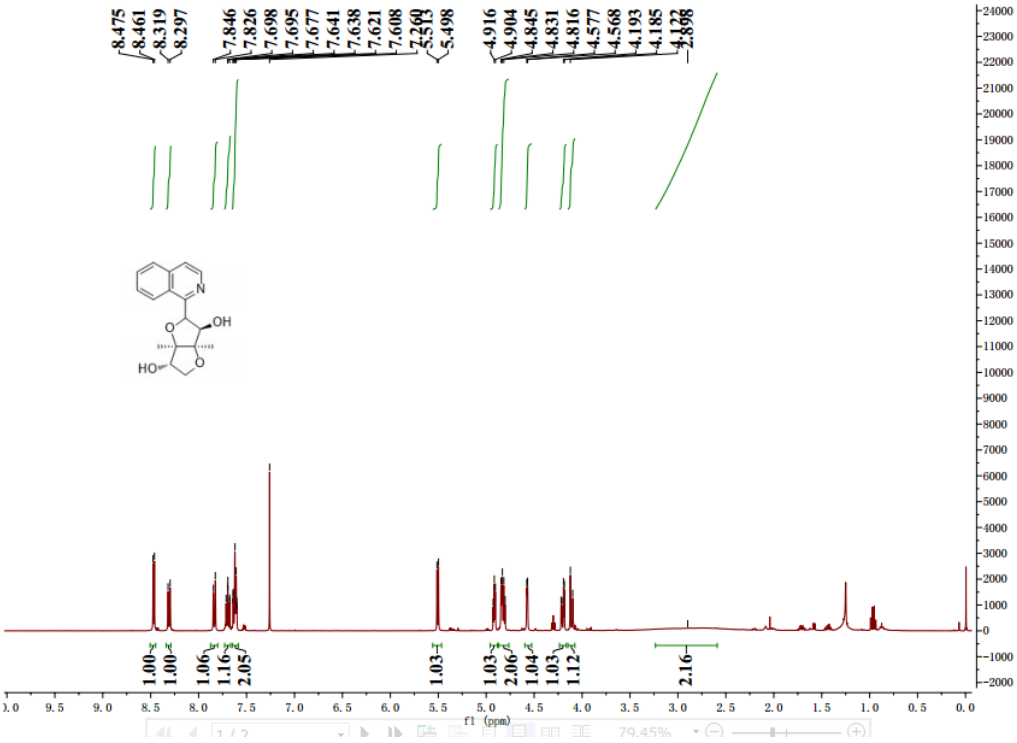

HO
{6.059,2.396}
{6.049,2.827}
{2.807,6.050}
{2.418,6.045}
f2 (ppm)
f1 (ppm)


8.518
8.503
8.348
8.327
7.823
7.803
7.679
7.676
7.661
7.659
7.641
7.638
7.608
7.605
7.591
7.587
7.583
7.567
7.260
5.780
5.774
5.752
5.746
4.495
4.487
4.479
4.245
4.239
4.215
4.209
4.030
2.403
2.396
2.375
2.368
2.085
2.079
2.074
2.070
2.043
2.039
2.035
1.751
1.748
1.716
1.712
HO
1.00
1.01
1.03
1.01
2.03
1.02
1.02
1.21
1.05
1.07
2.81
1.31
f1 (ppm)


159.153
141.643
136.510
129.852
127.315
127.152
126.157
125.049
120.630
72.208
64.153
63.340
37.842
32.917
HO
f1 (ppm)


8.467
8.452
8.342
8.321
7.888
7.868
7.760
7.757
7.740
7.737
7.710
7.704
7.701
7.695
7.687
7.683
7.680
5.804
4.851
4.838
4.836
4.823
4.464
4.456
4.452
4.443
4.439
4.431
4.220
4.207
4.195
4.183
4.146
4.138
4.122
4.113
1.00
0.98
1.01
1.01
2.07
1.03
1.08
1.09
1.11
1.31
f1 (ppm)


157.626
139.597
136.873
131.074
128.243
127.839
127.465
125.123
121.740
75.601
74.445
73.632
72.387
f1 (ppm)


8.475
8.461
8.319
8.297
7.846
7.826
7.698
7.695
7.677
7.641
7.638
7.621
7.608
5.498
4.916
4.904
4.845
4.831
4.816
4.577
4.568
4.193
4.185
1.00
1.00
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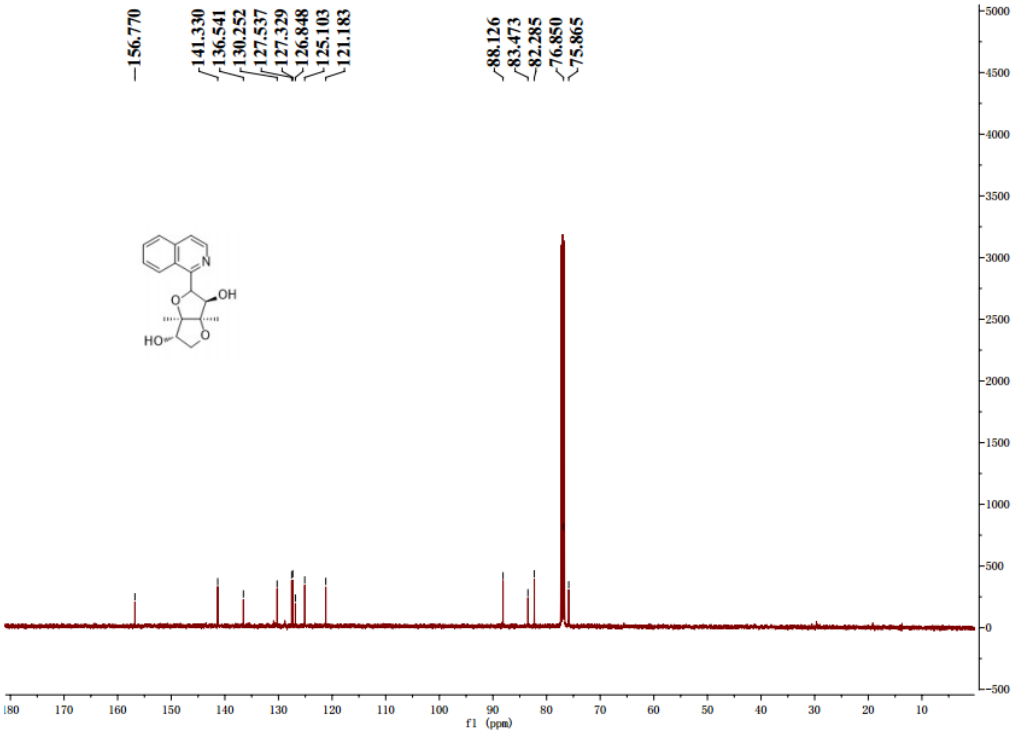
2.06
1.04
1.03
1.12
2.16
f1 (ppm)


156.770
141.330
136.541
130.252
127.537
127.329
126.848
125.103
121.183
88.126
83.473
82.285
76.850
75.865
f1 (ppm)