Electronic supplementary information

Removable Directing Group Assisted Rh(III)-catalyzed Direct C-H Bond Activation/Annulation Cascade to Highly Fused Isoquinolines

Yilang Cheng,[a,b,c] Xu Han,[a,b] Junyou Li,[a,b] Yu Zhou*[a,b] and Hong Liu*[a,b,c]

[a]State Key Laboratory of Drug Research and CAS Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Shanghai, 201203, China;

[b]University of Chinese Academy of Sciences, No. 19A Yuquan Road, Beijing 100049, China

[c]School of Life Science and Technology, ShanghaiTech University, 100 Haike Road, Shanghai 201210, China.

*E-mail: zhouyu@simm.ac.cn (Yu Zhou); E-mail: hliu@simm.ac.cn (Hong Liu)

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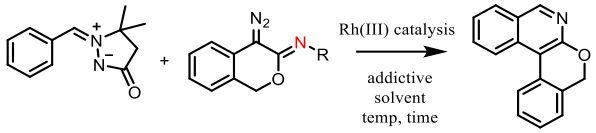
I. General Information

Commercially available reagents were purchased from commercial sources (J&K, Sigma-Aldrich, Adamas-beta, Energy, Bidepharm, Accela, etc.), and used without further purification. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15–0.2 mm thickness), visualized by irradiation with UV light (254 nm). Column chromatography was performed using silica gel FCP 300-400. Nuclear magnetic resonance spectra were recorded on a Brucker AMX-500MHz instrument (TMS as IS). Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Low and high resolution mass were measured by the ESI method with a Tsou-ESI mass spectrometer. All the starting arylacrylamides are known compounds, and were synthesized according to known procedures[1].

II. Optimization of the reaction conditions

Table S1. The additional optimization of the reaction conditions[a]



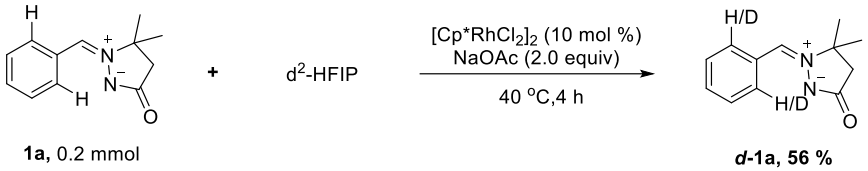
1a **2a** **3aa**

Entry	Catalyst (mol %)	Additive (mol %)	Solvent (mL)	Temp (℃)	Yield of **3aa** (%)[b]	Time(h)
1	$[Cp^*RhCl_2]_2$ (10)	NaOAc	DCE	100	36	12
2	$[Cp^*RhCl_2]_2$ (10)	AgOAc	DCE	100	28	12
3	$[Cp^*RhCl_2]_2$ (10)	CsOAc	DCE	100	29	12
4	$[Cp^*RhCl_2]_2$ (10)	$Cu(OAc)_2$	DCE	100	Trace	12
5	$[Cp^*RhCl_2]_2$ (10)	KOAc	DCE	100	30	12
6	$[Cp^*RhCl_2]_2$ (10)	K_2CO_3	DCE	100	33	12
7	$[Cp^*RhCl_2]_2$ (10)	AgOTf	DCE	100	Trace	12
8	$[Cp^*RhCl_2]_2$ (10)	$AgNO_3$	DCE	100	Trace	12
9	$[Cp^*RhCl_2]_2$ (10)	$Zn(OAc)_2$	DCE	100	Nd	12
10	$[Cp^*RhCl_2]_2$ (10)	$Cu(OTf)_2$	DCE	100	28	12
11	$[Cp^*RhCl_2]_2$ (10)	PivOH	DCE	100	Trace	12
12	$[Cp^*RhCl_2]_2$ (10)	-	DCE	100	Trace	12
13[c]	$[Cp^*RhCl_2]_2$ (10)	$Cu(OAc)_2$	HFIP	40	59	4
14[c]	$[Cp^*RhCl_2]_2$ (10)	HOAc	HFIP	40	45	4
15	$[Cp^*RhCl_2]_2$ (10)	NaOAc	MeOH	40	trace	12
16	$[Cp^*RhCl_2]_2$ (10)	NaOAc	EtOH	40	trace	12

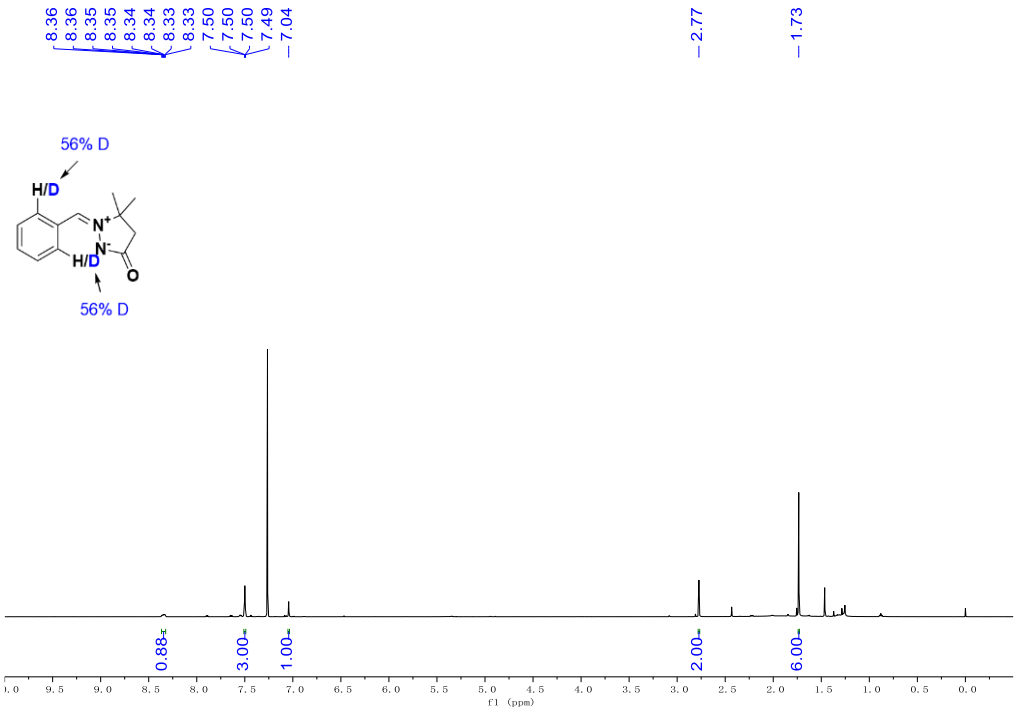
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), $[Cp^*RhCl_2]_2$ (10 mol %), $AgSbF_6$ (20 mol %), additive (2.0 equiv) in solvent (2.0 mL) under air for 12 h. [b]Determined by ^{1}H-NMR spectroscopy using dibromomethane as an internal standard. [c]no $AgSbF_6$.

III. Mechanistic investigations

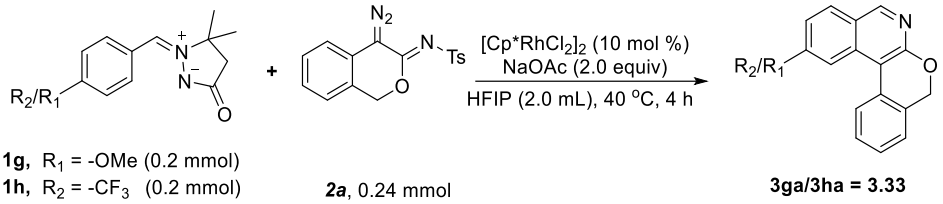
1) H/D Exchange Experiment.



A mixture of **1a** (40.5 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (12.4 mg, 0.02 mmol, 10 mol %), NaOAc (32.5 mg, 0.4 mmol, 2 equiv), and d^2-HFIP was added into a pressure tube. The resulting mixture was stirred at 40 °C for 4 h. Afterward, the mixture was diluted with CH_2Cl_2 and filtered through a pad of Celite, which was washed with CH_2Cl_2 for three times. The combined organic layer was collected and concentrated in vacuo to yield the crude product which was further purified by flash chromatography eluting with DCM/MeOH = 50:1 to afford the deuterium product as a colorless oil. H/D exchange occurred at the C2-position of azomethine imine (56% D).



2) Competition Experiment.

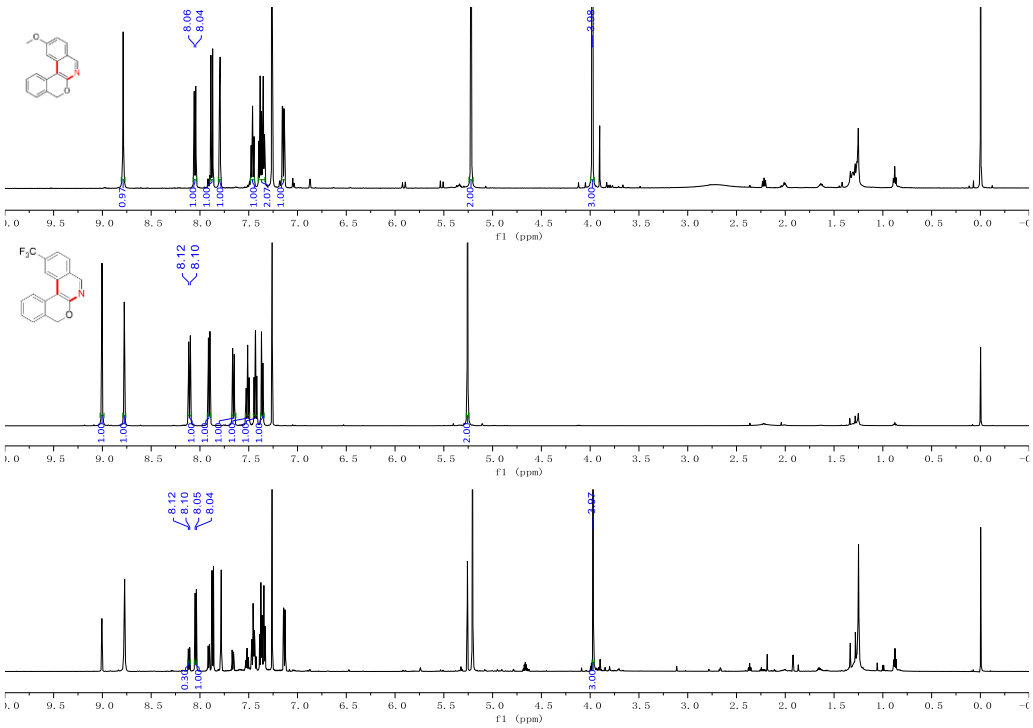


1g, R_1 = -OMe (0.2 mmol)
1h, R_2 = $-CF_3$ (0.2 mmol)

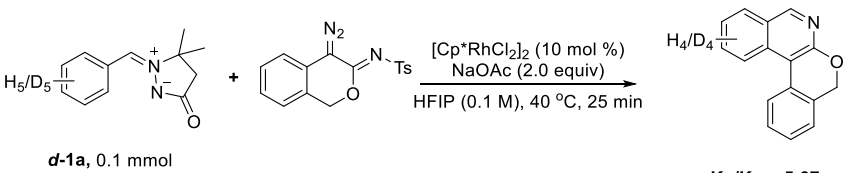
2a, 0.24 mmol

3ga/3ha = 3.33

To a mixture of **1g** (46.5 mg, 0.2 mmol, 1.0 equiv), **1h** (54.1 mg, 0.2 mmol, 1.0 equiv), $[Cp^*RhCl_2]_2$ (12.4 mg, 0.02 mmol, 10 mol %), and NaOAc (32.8 mg, 0.4 mmol, 2 equiv) was added **2a** (78.6 mg, 0.24 mmol, 1.2 equiv) and HFIP (2.0 mL, 0.1 M). The resulting mixture was stirred at 40 °C for 4 h. After the reaction was completed, EA was added and the mixture was filtered through a pad of Celite which was subsequently washed with EA. The combined organic layer was concentrated under vacuum and purified by flash chromatography to yield the mixture of **3ga** and **3ha**. The ratio of products was calculated according to ^{1}H NMR spectra.



3) KIE Experiment.



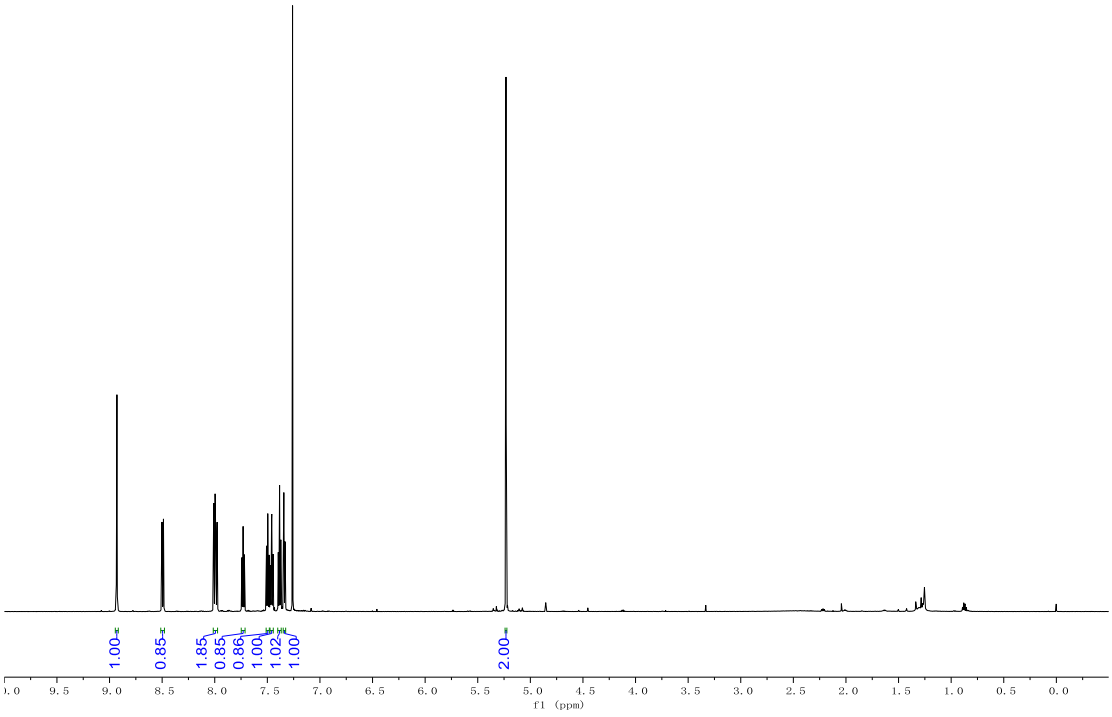
***d*-1a**, 0.1 mmol
1a, 0.1 mmol

2a, 0.24 mmol

K_H/K_D = 5.67

Compounds **1a** (20.3 mg, 0.1 mmol, 1.0 equiv) and ***d*^{5}-1a** (20.8 mg, 0.1 mmol, 1.0 equiv) were successively added to a mixture of $[Cp^*RhCl_2]_2$ (12.4 mg, 0.02 mmol, 10 mol%), NaOAc

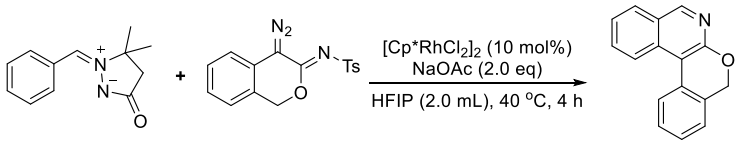
(32.9 mg, 0.4 mmol, 2 equiv), and **2a** (78.9 mg, 0.24 mmol, 1.2 equiv) in HFIP (2.0 mL, 0.1M). The resulting mixture was stirred at 40 °C for 25 min. Then the reaction was stopped and filtered through a pad of Celite which was subsequently washed with EA (10 mL ×3) and the combined organic layer was concentrated under reduced pressure. The mixture of **3aa** and d^4-**3aa** was isolated by flash chromatography eluting with Hexane/EA from 20:1 to 10:1. The KIE value was determined using ^{1}H NMR.



k_H/k_D = 0.85/(1-0.85) = 5.67

IV. General Synthetic Procedures and Characterization Data

(a) General procedure for the synthesis of products 3aa



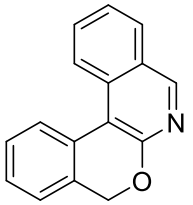
1a, 0.2mmol **2a**, 0.24mmol **3aa**

A pressure tube was charged with azomethine imine **1a** (0.2 mmol), **2a** (0.24 mmol), [Cp*RhCl$_2$]$_2$ (12.3 mg, 0.02 mmol), NaOAc (32.8 mg, 0.4 mmol) and HFIP (2

mL). The reaction mixture was stirred at 40 ℃ for 4 h. After the reaction was completed, EA was added and the mixture was filtered through a pad of Celite which was subsequently washed with EA. The combined organic layer was concentrated under under reduced pressure and the residue was purified by silica gel chromatography using PE/EA (10:1) to afford the desired product **3aa**.

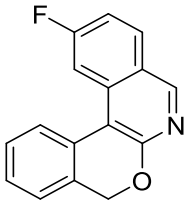
(b) Characterization of compounds

5H-isochromeno[3,4-c]isoquinoline(3aa).



It was obtained as a white solid (75% yield); mp 110.1-111.7 ºC; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.92 (s, 1H), 8.48 (d, *J* = 8.6 Hz, 1H), 7.98 (t, *J* = 8.7 Hz, 2H), 7.72 (ddd, *J* = 8.5, 6.8, 1.3 Hz, 1H), 7.49 (ddd, *J* = 8.0, 6.9, 0.9 Hz, 1H), 7.45 (td, *J* = 7.7, 1.4 Hz, 1H), 7.37 (td, *J* = 7.4, 1.1 Hz, 1H), 7.34 – 7.31 (m, 1H), 5.22 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.1, 151.6, 134.3, 133.0, 131.3, 129.8, 128.8, 128.3, 127.8, 126.9, 126.4, 125.4, 124.8, 123.7, 109.5, 69.5; LRMS (ESI): m/z 252.1 [M + H]$^{+}$; HRMS (ESI): calcd for $C_{16}H_{12}NO^{+}$ [M + H]$^{+}$, 234.0913; found, 234.0910.

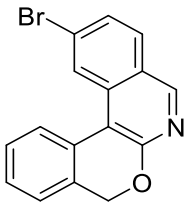
11-fluoro-5H-isochromeno[3,4-c]isoquinoline(3ba).



It was obtained as a yellow solid (75% yield); mp 131.4-133.9 ºC; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.88 (s, 1H), 8.08 (dd, *J* = 11.3, 2.4 Hz, 1H), 7.98 (dd, *J* = 9.0, 5.9 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 1H), 7.47 (td, *J* = 7.6, 1.4 Hz, 1H), 7.39 (td, *J* = 7.4, 1.1 Hz, 1H), 7.33 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.28 – 7.23 (m, 2H), 5.22 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.6 (d, *J* = 252.2 Hz), 159.8, 151.4, 135.8 (d, *J* = 10.9 Hz), 132.8, 131.8 (d, *J* = 10.4 Hz), 129.5, 128.5, 128.0, 125.7, 125.5, 124.1, 115.4 (d, *J* =

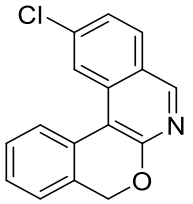
25.7 Hz), 109.2 (d, *J* = 5.6 Hz), 107.8 (d, *J* = 23.3 Hz), 69.5. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -105.5; LRMS (ESI): m/z 252.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_{10}FNO^+$ $[M + H]^+$, 252.0819; found, 252.0821.

11-bromo-5H-isochromeno[3,4-c]isoquinoline(3ca).



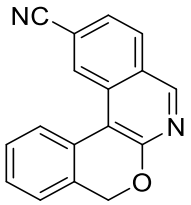
It was obtained as a white solid (82% yield); mp 157.6-158.7 ºC; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.88 (d, *J* = 0.8 Hz, 1H), 8.66 – 8.62 (m, 1H), 7.93 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.56 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.49 (td, *J* = 7.6, 1.4 Hz, 1H), 7.40 (td, *J* = 7.4, 1.1 Hz, 1H), 7.36 – 7.30 (m, 1H), 5.22 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.9, 151.7, 135.3, 133.0, 130.3, 129.4, 128.8, 128.5, 128.3, 126.9, 126.2, 126.2, 125.6, 125.3, 108.8, 69.7; LRMS (ESI): m/z 312.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_{10}BrNO^+$ $[M + H]^+$, 312.0019; found, 312.0010.

11-chloro-5H-isochromeno[3,4-c]isoquinoline(3da).



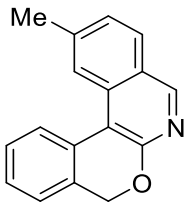
It was obtained as a white solid (78% yield); mp 157.7-159.0 ºC; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.88 (d, *J* = 0.8 Hz, 1H), 8.44 (d, *J* = 1.9 Hz, 1H), 7.91 (t, *J* = 8.3 Hz, 2H), 7.48 (td, *J* = 7.6, 1.4 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.35 – 7.30 (m, 1H), 5.22 (s, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.2, 150.8, 137.7, 134.5, 132.4, 129.9, 128.8, 128.2, 127.7, 125.6, 125.5, 125.0, 124.5, 122.4, 69.1; LRMS (ESI): m/z 268.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_{10}ClNO^+$ $[M + H]^+$, 268.0518; found, 268.0524.

5H-isochromeno[3,4-c]isoquinoline-11-carbonitrile(3ea).



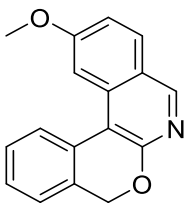
It was obtained as a yellow solid (56% yield); mp 223.7-225.6 ºC; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.00 (s, 1H), 8.84 (d, *J* = 1.3 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.63 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.53 (td, *J* = 7.6, 1.3 Hz, 1H), 7.45 (td, *J* = 7.5, 1.1 Hz, 1H), 7.37 (dd, *J* = 7.5, 1.3 Hz, 1H), 5.27 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 160.2, 151.8, 133.2, 133.1, 130.2, 130.1, 129.0, 128.9, 128.7, 127.27, 126.5, 125.9, 125.4, 118.8, 114.9, 109.9, 69.8; LRMS (ESI): m/z 259.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{10}N_2O^+$ $[M + H]^+$, 259.0866; found, 259.0867.

11-methyl-5H-isochromeno[3,4-c]isoquinoline(3fa).



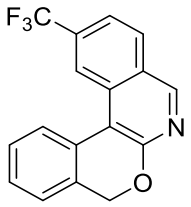
It was obtained as a white solid (81% yield); mp 110.1-112.3 ºC; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.84 (d, *J* = 0.8 Hz, 1H), 8.25 (s, 1H), 8.00 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.46 (td, *J* = 7.6, 1.5 Hz, 1H), 7.37 (td, *J* = 7.4, 1.1 Hz, 1H), 7.32 (ddd, *J* = 8.2, 3.8, 1.4 Hz, 2H), 5.20 (s, 2H), 2.57 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 151.3, 141.9, 134.7, 133.1, 130.1, 128.7, 128.4, 127.7, 127.2, 126.4, 125.4, 125.4, 122.8, 109.0, 77.4, 77.2, 76.9, 69.6, 22.7; LRMS (ESI): m/z 248.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{13}NO^+$ $[M + H]^+$, 248.1070; found, 248.1067.

11-methoxy-5H-isochromeno[3,4-c]isoquinoline(3ga).



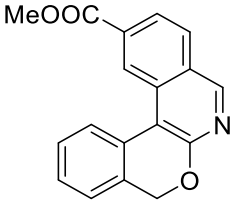
It was obtained as a white solid (69% yield); mp 150.0-151.9 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.79 (s, 1H), 8.05 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.88 (d, *J* = 9.0 Hz, 1H), 7.80 (d, *J* = 2.3 Hz, 1H), 7.46 (td, *J* = 7.5, 1.5 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.14 (dd, *J* = 9.0, 2.3 Hz, 1H), 5.22 (s, 2H), 3.98 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.0, 158.7, 149.7, 136.0, 132.4, 130.2, 129.5, 127.9, 127.2, 125.1, 124.8, 122.0, 117.3, 108.5, 101.9, 69.1, 55.1; LRMS (ESI): m/z 264.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{13}NO_2^+$ $[M + H]^+$, 264.1019; found, 264.1015.

11-(trifluoromethyl)-5H-isochromeno[3,4-c]isoquinoline(3ha).



It was obtained as a white solid (80% yield); mp 142.2-144.6 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.00 (s, 1H), 8.78 (s, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.66 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.51 (td, *J* = 7.6, 1.4 Hz, 1H), 7.43 (td, *J* = 7.5, 1.1 Hz, 1H), 7.36 (dd, *J* = 7.5, 1.3 Hz, 1H), 5.26 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.4, 151.1, 132.8, 132.6, 132.6– 131.8 (q, *J* = 32.2 Hz)), 129.5, 128.6, 128.4, 128.0, 127.0, 126.7– 120.2 (q, *J* = 273.4 Hz), 125.8, 125.2, 121.1 (q, *J* = 4.6 Hz), 120.2 – 119.9 (q, *J* = 2.9 Hz), 109.9, 69.2; ^{19}F NMR (471 MHz, Chloroform-*d*) δ -62.9; LRMS (ESI): m/z 302.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{10}F_3NO^+$ $[M + H]^+$, 302.0787; found, 302.0782.

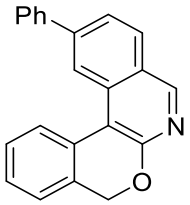
Methyl-5H-isochromeno[3,4-c]isoquinoline-11-carboxylate(3ia).



It was obtained as a yellow solid (74% yield); mp 165.5-167.2 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.20 (d, *J* = 1.2 Hz, 1H), 8.97 (d, *J* = 0.9 Hz, 1H), 8.04 (dd, *J* = 8.6, 1.4 Hz, 1H), 8.01 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.96 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.50 (td, *J* =

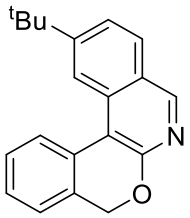
7.6, 1.4 Hz, 1H), 7.41 (td, *J* = 7.5, 1.1 Hz, 1H), 7.34 (ddd, *J* = 7.5, 1.5, 0.7 Hz, 1H), 5.24 (s, 2H), 4.00 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.7, 159.6, 151.5 133.5, 133.0, 132.2, 129.3, 129.0, 128.8, 128.3, 128.1, 126.7, 126.6, 125.5, 124.2, 110.5, 69.6, 52.7; LRMS (ESI): m/z 292.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{13}NO_3^+$ $[M + H]^+$, 292.0968; found, 292.0962.

11-phenyl-5H-isochromeno[3,4-c]isoquinoline(3ja).



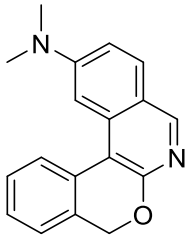
It was obtained as a yellow oil (85% yield); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.96 (s, 1H), 8.68 (d, *J* = 1.5 Hz, 1H), 8.08 – 8.03 (m, 2H), 7.78 – 7.71 (m, 3H), 7.56 – 7.52 (m, 2H), 7.51 – 7.44 (m, 2H), 7.41 (td, *J* = 7.4, 1.2 Hz, 1H), 7.36 (dd, *J* = 7.4, 1.4 Hz, 1H), 5.26 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.6, 151.4, 144.0, 140.6, 134.6, 133.0, 129.9, 129.3, 129.1, 128.5, 128.2, 127.81 127.7, 126.3, 125.9, 125.5, 124.7, 121.6, 109.6, 69.5; LRMS (ESI): m/z 310.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{22}H_{15}NO^+$ $[M + H]^+$, 310.1233; found, 310.1226.

11-(tert-butyl)-5H-isochromeno[3,4-c]isoquinoline(3ka).



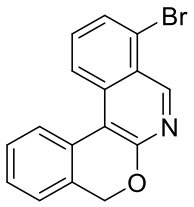
It was obtained as a colorless oil (88% yield); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.89 (s, 1H), 8.48 (d, *J* = 1.7 Hz, 1H), 8.03 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.94 (d, *J* = 8.7 Hz, 1H), 7.60 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.50 (td, *J* = 7.5, 1.6 Hz, 1H), 7.42 – 7.35 (m, 2H), 5.24 (s, 2H), 1.47 (s, 9H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.4, 154.5, 151.1, 134.5, 133.2, 130.3, 128.4, 127.7, 126.2, 125.5, 125.4, 123.9, 118.9, 109.6, 69.6, 35.7, 31.2; LRMS (ESI): m/z 277.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{20}H_{19}NO^+$ $[M + H]^+$, 277.1335; found, 277.1331.

N,N-dimethyl-5H-isochromeno[3,4-c]isoquinolin-11-amine(3la).



It was obtained as a yellow solid (67% yield); mp 141.2-143.1 ^{o}C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.67 (s, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.50 (d, *J* = 2.4 Hz, 1H), 7.45 (td, *J* = 7.5, 1.9 Hz, 1H), 7.39 – 7.33 (m, 2H), 7.12 (dd, *J* = 9.2, 2.4 Hz, 1H), 5.22 (s, 2H), 3.20 (s, 6H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 152.6, 148.8, 132.5, 130.5, 130.4, 128.2, 127.3, 125.4, 124.7, 119.9, 114.5, 100.8, 69.6, 40.4; LRMS (ESI): m/z 290.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{20}H_{19}NO^+$ $[M + H]^+$, 209.1539; found, 290.1534.

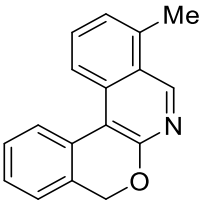
9-bromo-5H-isochromeno[3,4-c]isoquinoline(3ma).



It was obtained as a white solid (83% yield); mp 157.6-158.7 ^{o}C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.29 (d, *J* = 0.9 Hz, 1H), 8.41 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.88 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.69 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.49 (dd, *J* = 8.6, 7.4 Hz, 1H), 7.43 (td, *J* = 7.6, 1.5 Hz, 1H), 7.38 (td, *J* = 7.4, 1.2 Hz, 1H), 7.32 (ddd, *J* = 7.4, 1.6, 0.8 Hz, 1H), 5.21 (s, 2H).

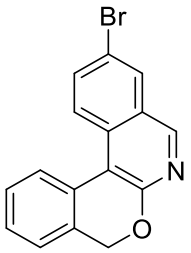
; ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.6, 151.3, 135.8, 133.1, 131.3, 129.3, 129.0, 128.4, 128.1, 126.7, 125.5, 124.9, 123.6, 123.6, 109.2, 69.6; LRMS (ESI): m/z 312.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_{10}BrNO^+$ $[M + H]^+$, 312.0019; found, 312.0014.

9-methyl-5H-isochromeno[3,4-c]isoquinoline(3na).



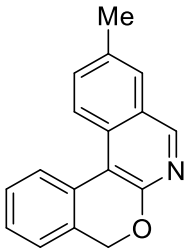
It was obtained as a white solid (72% yield); mp 167.2-168.8 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.15 (s, 1H), 8.36 (d, *J* = 8.7 Hz, 1H), 7.99 (d, *J* = 7.7 Hz, 1H), 7.61 (dd, *J* = 8.7, 7.0 Hz, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.39 (td, *J* = 7.4, 1.1 Hz, 1H), 7.35 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.29 (d, *J* = 6.3 Hz, 1H), 5.24 (s, 2H), 2.82 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 158.9, 148.4, 136.5, 134.7, 133.1, 131.1, 123.0, 128.3, 127.7, 126.77, 125.9, 125.8, 125.4, 122.1, 109.7, 69.5, 19.0; LRMS (ESI): m/z 248.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{13}NO^+$ $[M + H]^+$, 248.1070; found, 248.1063.

10-bromo-5H-isochromeno[3,4-c]isoquinoline(3oa).



It was obtained as a white solid (85% yield); mp 123.8-124.8 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.83 (d, *J* = 0.8 Hz, 1H), 8.34 (d, *J* = 9.1 Hz, 1H), 8.10 (d, *J* = 2.1 Hz, 1H), 7.89 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.75 (dd, *J* = 9.1, 2.1 Hz, 1H), 7.45 (td, *J* = 7.6, 1.5 Hz, 1H), 7.39 (td, *J* = 7.5, 1.2 Hz, 1H), 7.33 (dd, *J* = 7.5, 1.4 Hz, 1H), 5.22 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.4, 150.6, 134.6, 133.1, 132.8, 130.7, 129.4, 128.6, 128.3, 128.0, 126.4, 125.7, 125.6, 118.3, 109.8, 69.6; LRMS (ESI): m/z 312.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_{10}BrNO^+$ $[M + H]^+$, 312.0019; found, 312.0020.

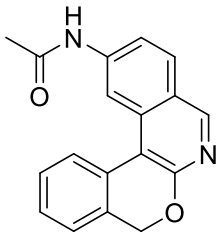
10-methyl-5H-isochromeno[3,4-c]isoquinoline(3pa).



It was obtained as a white solid (88% yield); mp 169.8-171.1 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.83 (s, 1H), 8.37 (d, *J* = 8.7 Hz, 1H), 7.97 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.54 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.43 (td, *J* = 7.6, 1.5 Hz, 1H), 7.36

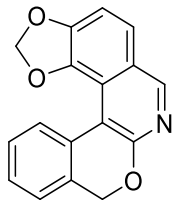
(td, *J* = 7.4, 1.2 Hz, 1H), 7.31 (dd, *J* = 7.5, 1.4 Hz, 1H), 5.20 (s, 2H), 2.52 (d, *J* = 1.0 Hz, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 158.6, 150.9, 134.5, 133.6, 133.0, 132.5, 129.9, 128.3, 127.7, 127.5, 127.2, 126.3, 125.3, 123.5, 109.4, 69.5, 21.3; LRMS (ESI): m/z 248.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{13}NO^+$ $[M + H]^+$, 248.1070; found, 248.1064.

N-(5H-isochromeno[3,4-c]isoquinolin-11-yl)acetamide(3qa).



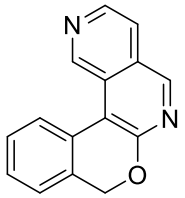
It was obtained as a yellow solid (70% yield); mp 116.7-118.1 ºC; ^{1}H NMR (500 MHz, Methanol-d_4) δ 8.97 (d, *J* = 2.1 Hz, 1H), 8.72 (s, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 1H), 7.53 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.41 – 7.38 (m, 2H), 5.17 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (126 MHz, Methanol-d_4) δ 172.2, 160.4, 151.4, 143.1, 136.4, 134.1, 130.9, 130.6, 129.5, 129.0, 127.0, 126.3, 125.1, 112.0, 112.7, 110.6, 70.4, 24.2; LRMS (ESI): m/z 291.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{14}N_2O_2^+$ $[M + H]^+$, 291.1128; found, 291.1131.

9H-[1,3]dioxolo[4,5-f]isochromeno[3,4-c]isoquinoline(3ra).



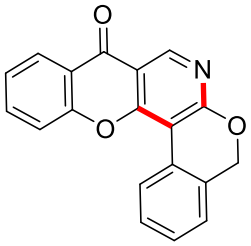
It was obtained as a yellow solid (74% yield); mp 64.3-65.0 ºC; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.87 (s, 1H), 7.65 (d, *J* = 8.6 Hz, 1H), 7.64 – 7.60 (m, 1H), 7.42 (td, *J* = 7.6, 1.5 Hz, 1H), 7.35 (td, *J* = 7.4, 1.2 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.23 (d, *J* = 8.6 Hz, 1H), 6.19 (s, 2H), 5.24 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.9, 152.6, 148.8, 139.4, 131.1, 129.4, 128.4, 127.7, 127.4, 125.2, 124.4, 124.3, 120.3, 110.0, 105.2, 101.5, 69.8; LRMS (ESI): m/z 278.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{11}NO_3^+$ $[M + H]^+$, 278.0812; found, 278.0809.

8H-isochromeno[3,4-c][2,6]naphthyridine(3sa).



It was obtained as a yellow solid (56% yield); mp 145.7-147.6 ºC;^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.96 (s, 1H), 9.01 (s, 1H), 8.62 (d, *J* = 5.7 Hz, 1H), 7.99 (d, *J* = 7.7 Hz, 1H), 7.82 (d, *J* = 5.6 Hz, 1H), 7.52 (td, *J* = 7.6, 1.3 Hz, 1H), 7.49 – 7.43 (m, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 5.30 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.8, 150.8, 148.8, 141.6, 133.0, 128.9, 128.9, 128.6, 128.3, 128.3, 127.2, 125.7, 120.1, 109.5, 69.7; LRMS (ESI): m/z 235.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{15}H_{10}N_2O^+$ $[M + H]^+$, 235.0866; found, 235.0869.

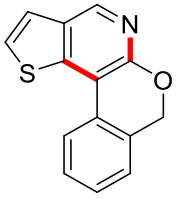
5H,9H-chromeno[2,3-d]isochromeno[3,4-b]pyridin-9-one(3ta)



3ta

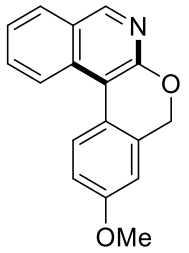
It was obtained as a white solid (85% yield); mp 172.2-175.4 ºC; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.16 (s, 1H), 8.48 (dd, *J* = 8.0, 1.3 Hz, 1H), 8.35 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.83 – 7.76 (m, 1H), 7.62 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.51 (td, *J* = 7.7, 1.4 Hz, 1H), 7.47 (ddd, *J* = 8.2, 7.2, 1.0 Hz, 1H), 7.44 (td, *J* = 7.5, 1.2 Hz, 1H), 7.29 – 7.27 (m, 1H), 5.40 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 175.64, 165.77, 159.43, 155.77, 149.15, 135.45, 130.69, 129.10, 128.88, 126.83, 126.80, 126.33, 125.30, 124.96, 122.30, 117.96, 114.83, 104.64, 69.71. LRMS (ESI): m/z 302.0 $[M + H]^+$; HRMS (ESI): calcd for $C_{19}H_{11}NO_3^+$ $[M + H]^+$, 302.0812; found, 302.0817.

7H-isochromeno[3,4-b]thieno[2,3-d]pyridine(3ua)



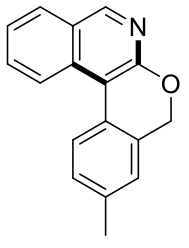
It was obtained as a yellow solid (65% yield); mp 107.4-109.2 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.71 (s, 1H), 8.12 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.49 (td, *J* = 7.7, 1.3 Hz, 1H), 7.42 (d, *J* = 0.9 Hz, 2H), 7.38 (td, *J* = 7.5, 1.1 Hz, 1H), 7.27 – 7.24 (m, 1H), 5.32 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.56, 146.08, 144.47, 135.59, 133.42, 130.37, 129.97, 129.96, 127.24, 126.30, 125.60, 123.96, 112.75, 70.43. LRMS (ESI): m/z 240.0 $[M + H]^+$; HRMS (ESI): calcd for $C_{14}H_9NOS^+$ $[M + H]^+$, 230.0478; found, 230.0477.

3-methoxy-5H-isochromeno[3,4-c]isoquinoline(3ab).



It was obtained as a yellow oil (84% yield); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.86 (d, *J* = 0.8 Hz, 1H), 8.43 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.95 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.69 (ddd, *J* = 8.5, 6.8, 1.4 Hz, 1H), 7.46 (ddd, *J* = 8.0, 6.8, 1.0 Hz, 1H), 6.98 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.86 (d, *J* = 2.7 Hz, 1H), 5.18 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.4, 158.4, 150.5 134.8, 134.0, 130.9, 128.7, 127.7, 126.9, 124.7, 123.7, 122.5, 113.7, 111.0, 109.5, 69.5, 55.5; LRMS (ESI): m/z 264.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{13}NO_2^+$ $[M + H]^+$, 264.1019; found, 264.1016.

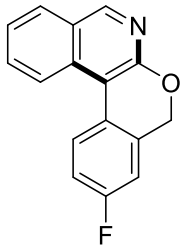
3-methyl-5H-isochromeno[3,4-c]isoquinoline(3ac).



It was obtained as a white solid (81% yield); mp 88.3-90.1 °C;^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.47 (d, *J* = 8.6 Hz, 1H), 7.97 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.71 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.48 (ddd, *J* = 8.0, 6.8, 1.1 Hz, 1H), 7.28 – 7.24 (d, 1H), 7.16 – 7.13 (m, 1H), 5.19 (s, 2H), 2.43 (s, 3H); ^{13}C

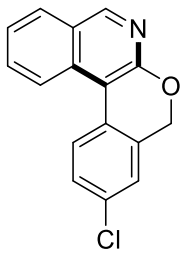
NMR (126 MHz, Chloroform-*d*) δ 151.0, 138.0, 134.2, 133.1, 131.1, 129.0, 128.8, 127.0, 126.8, 126.3, 126.1, 124.7, 123.8, 109.6, 69.5, 21.2; LRMS (ESI): m/z 248.2 [M + H]$^+$; HRMS (ESI): calcd for $C_{17}H_{13}NO^+$ [M + H]$^+$, 248.1070; found, 248.1074.

3-fluoro-5H-isochromeno[3,4-c]isoquinoline(3ad).



It was obtained as a white solid (72% yield); mp 105.4-107.2 ºC;^{1}H NMR (500 MHz, Methanol-d_4) δ 8.81 (s, 1H), 8.37 – 8.30 (m, 1H), 8.00 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.93 – 7.85 (m, 1H), 7.73 (ddd, *J* = 8.5, 6.8, 1.4 Hz, 1H), 7.49 (ddd, *J* = 7.9, 6.7, 0.9 Hz, 1H), 7.14 (t, *J* = 8.3 Hz, 2H), 5.12 (s, 2H); ^{13}C NMR (126 MHz, Methanol-d_4) δ 162.34 (d, *J* = 247.9 Hz), 158.14, 150.80, 135.53 (d, *J* = 7.6 Hz), 133.9, 131.7, 128.7, 127.9 (d, *J* = 8.2 Hz), 126.8, 125.4 (d, *J* = 3.3 Hz), 125.0, 123.1, 114.8 (d, *J* = 22.0 Hz), 112.3 (d, *J* = 22.9 Hz), 108.9, 68.4 (d, *J* = 2.1 Hz); ^{19}F NMR (471 MHz, Methanol-d_4) δ -115.1 (q, *J* = 8.1 Hz); LRMS (ESI): m/z 252.1 [M + H]$^+$; HRMS (ESI): calcd for $C_{16}H_{10}FNO^+$ [M + H]$^+$, 252.0819; found, 252.0814.

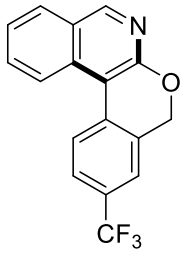
3-chloro-5H-isochromeno[3,4-c]isoquinoline(3ae).



It was obtained as a white solid (72% yield); mp 170.2-171.6 ºC;^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.95 (s, 1H), 8.43 (d, *J* = 8.6 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.97 (d, *J* = 2.0 Hz, 1H), 7.78 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.52 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 7.35 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 5.19 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 152.6, 134.4, 134.2, 132.0, 131.7, 131.2, 129.1, 127.8,

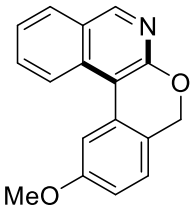
126.9, 126.7, 126.3, 125.2, 123.4, 69.1; LRMS (ESI): m/z 264.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{11}NO_3^+$ $[M + H]^+$, 252.0819; found, 252.0817. LRMS (ESI): m/z 268.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_{10}ClNO_3^+$ $[M + H]^+$, 268.0524; found, 268.0531.

3-(trifluoromethyl)-5H-isochromeno[3,4-c]isoquinoline(3af).



It was obtained as a yellow solid (78% yield); mp 142.2-144.6 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.97 (s, 1H), 8.41 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.2 Hz, 1H), 8.03 – 7.98 (m, 1H), 7.76 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.69 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.59 – 7.57 (m, 1H), 7.52 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 1H), 5.25 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.6, 153.1, 134.2, 133.41 133.3, 131.9, 129.6 (q, *J* = 32.9 Hz), 129.0, 127.2 – 120.7 (q, *J* = 272.8 Hz), 126.9, 126.4, 125.4 – 125.2 (m), 125.2, 123.2, 122.3 (q, *J* = 3.8 Hz), 108.3, 69.0; ^{19}F NMR (471 MHz, Chloroform-*d*) δ -62.5; LRMS (ESI): m/z 282.8 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{10}F_3NO^+$ $[M + H]^+$, 302.0787; found, 302.0791.

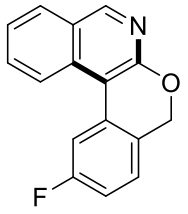
2-methoxy-5H-isochromeno[3,4-c]isoquinoline(3ag).



It was obtained as a yellow oil (79% yield); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.92 (s, 1H), 8.49 (d, *J* = 8.6 Hz, 1H), 7.98 – 7.95 (d, 1H), 7.71 (ddd, *J* = 8.5, 6.8, 1.3 Hz, 1H), 7.53 (d, *J* = 2.5 Hz, 1H), 7.48 (ddd, *J* = 7.9, 6.8, 1.0 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 6.90 (dd, *J* = 8.3, 2.5 Hz, 1H), 5.16 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.8, 159.4, 151.9, 134.4, 131.4, 131.1, 128.9, 126.9, 126.4, 125.5,

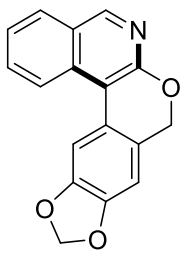
124.9, 123.7, 113.0, 112.5, 109.4, 69.3, 55.7; LRMS (ESI): m/z 264.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{13}NO_2^+$ $[M + H]^+$, 264.1019; found, 264.1018.

2-fluoro-5H-isochromeno[3,4-c]isoquinoline(3ah).



It was obtained as a yellow solid (88% yield); mp 167.2-168.8 ºC;^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.98 (d, *J* = 2.1 Hz, 1H), 7.80 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.52 (ddd, *J* = 11.3, 7.8, 1.2 Hz, 1H), 7.48 – 7.39 (m, 3H), 7.36 (td, *J* = 7.4, 1.2 Hz, 1H), 7.29 (dd, *J* = 7.5, 1.5 Hz, 1H), 5.25 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 158.8 (d, *J* = 234.6 Hz), 155.9, 151.6, 130.8, 129.5, 128.3 (d, *J* = 4.8 Hz), 127.9 (d, *J* = 14.5 Hz), 127.5 (d, *J* = 2.2 Hz), 127.3, 124.6 (d, *J* = 7.9 Hz), 124.3 (d, *J* = 3.9 Hz), 124.0, 123.4 (d, *J* = 14.6 Hz), 115.9 (d, *J* = 22.0 Hz), 106.3, 69.4; ^{19}F NMR (471 MHz, Chloroform-*d*) δ -62.5; LRMS (ESI): m/z 264.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{13}H_{10}FNO^+$ $[M + H]^+$, 252.0819; found, 252.0817.

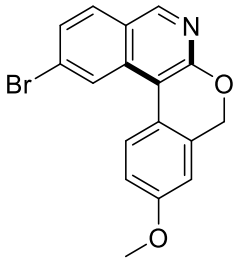
8H-[1,3]dioxolo[4',5':6,7]isochromeno[3,4-c]isoquinoline(3ai).



It was obtained as a yellow solid (78% yield); mp 166.6-168.5 ºC;^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.88 (s, 1H), 8.39 (d, *J* = 8.6 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.71 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.50 – 7.44 (m, 2H), 6.81 (s, 1H), 6.04 (s, 2H), 5.11 (s, 2H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 158.6, 150.9, 148.0, 147.4, 134.0, 131.2, 128.9, 127.2, 127.0, 124.9, 123.9, 123.6, 109.8, 107.1, 106.4, 101.6, 69.5; LRMS (ESI):

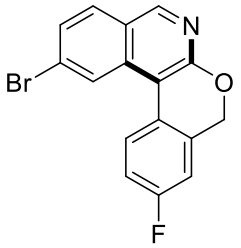
m/z 264.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{11}NO_3^+$ $[M + H]^+$, 252.0819; found, 252.0817. LRMS (ESI): m/z 278.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{11}NO_3^+$ $[M + H]^+$, 278.0810; found, 278.0812.

11-bromo-3-methoxy-5H-isochromeno[3,4-c]isoquinoline(3aj).



It was obtained as a white solid (93% yield); mp 166.8-168.2 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.83 (s, 1H), 8.59 (d, *J* = 1.7 Hz, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.55 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.03 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.87 (d, *J* = 2.6 Hz, 1H), 5.19 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.7, 150.1, 134.9, 134.7, 130.2, 128.3, 127.5, 126.5, 126.2, 125.2, 121.8, 113.9, 111.3, 108.9, 69.6, 55.5; LRMS (ESI): m/z 342.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{17}H_{12}BrNO_2^+$ $[M + H]^+$, 342.0124; found, 342.0127.

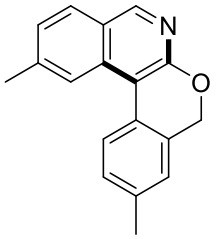
11-bromo-3-fluoro-5H-isochromeno[3,4-c]isoquinoline(3ak).



It was obtained as a white solid (77% yield); mp 197.5-200.5 °C;^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.88 (s, 1H), 8.55 (d, *J* = 1.7 Hz, 1H), 7.90 (dd, *J* = 8.6, 5.1 Hz, 1H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.58 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.20 (td, *J* = 8.5, 2.7 Hz, 1H), 7.06 (dd, *J* = 8.2, 2.7 Hz, 1H), 5.19 (s, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.4 (d, *J* = 249.9 Hz), 159.3 , 151.4 , 135.2 (d, *J* = 7.3 Hz), 135.0 , 130.3 , 128.6 , 127.8 (d, *J* = 8.1 Hz), 126.9 , 125.9 , 125.4 (d, *J* = 3.4 Hz), 125.2 , 115.6 (d, *J* = 21.7 Hz), 112.9 (d, *J* = 22.6 Hz), 108.0 , 69.0 (d, *J* = 2.1 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ -

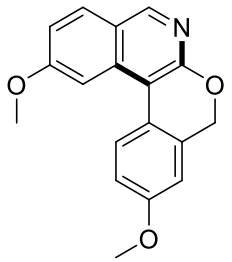
112.5 (t, *J* = 7.0 Hz); LRMS (ESI): m/z 330.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{16}H_9BrFNO_2^+$ $[M + H]^+$, 329.9924; found, 329.9931.

3,11-dimethyl-5H-isochromeno[3,4-c]isoquinoline(3al).



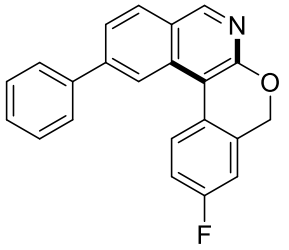
It was obtained as a withe solid (81% yield); mp 107.5-108.8 ºC;^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.82 (s, 1H), 8.24 (s, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.31 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.29 – 7.26 (m, 1H), 7.15 – 7.13 (m, 1H), 5.17 (s, 2H), 2.57 (d, *J* = 1.0 Hz, 3H), 2.43 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 159.0, 150.7, 141.6, 137.7, 134.5, 133.1, 129.0, 128.5, 127.2, 127.0, 126.2, 126.0, 125.3, 122.7, 109.0, 69.5, 22.6, 21.2; LRMS (ESI): m/z 262.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{15}NO^+$ $[M + H]^+$, 262.1226; found, 262.1225.

3,11-dimethoxy-5H-isochromeno[3,4-c]isoquinoline(3am).



It was obtained as a yellow oil (85% yield); ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 7.97 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.74 (d, *J* = 2.3 Hz, 1H), 7.12 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.00 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.88 (d, *J* = 2.7 Hz, 1H), 5.18 (s, 2H), 3.97 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.0, 159.2, 158.7, 149.4, 136.0, 134.7, 130.5, 126.6, 122.7, 117., 113.7, 111.2, 108.8, 102.3, 69.5, 55.5; LRMS (ESI): m/z 294.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{18}H_{15}NO_3^+$ $[M + H]^+$, 294.1125; found, 294.1125.

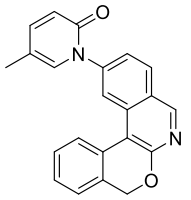
3-fluoro-11-phenyl-5H-isochromeno[3,4-c]isoquinoline(3an).



It was obtained as a withe solid (63% yield); mp 182.9- 184.0 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.93 (s, 1H), 8.56 (d, *J* = 1.5 Hz, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 8.00 (dd, *J* = 8.6, 5.2 Hz, 1H), 7.74 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.72 – 7.69 (m, 2H), 7.55 – 7.50 (m, 2H), 7.47 – 7.43 (m, 1H), 7.17 (td, *J* = 8.6, 2.7 Hz, 1H), 7.07 (dd, *J* = 8.2, 2.6 Hz, 1H), 5.20 (s, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.2 (d, *J* = 249.5 Hz), 159.0, 151.18, 144.2, 140.5, 135.3 (d, *J* = 7.3 Hz), 134.4, 129.3, 129.1, 128.3, 127.9 (d, *J* = 8.2 Hz), 127.6, 126.0 (d, *J* = 3.3 Hz), 125.9, 124.9, 121.4, 115.4 (d, *J* = 21.5 Hz), 112.8 (d, *J* = 22.5 Hz), 109.0, 69.0; ^{19}F NMR (471 MHz, Chloroform-*d*) δ -113.1 (q, *J* = 8.0 Hz); LRMS (ESI): m/z 328.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{22}H_{14}FNO^+$ $[M + H]^+$, 328.1132; found, 328.1134.

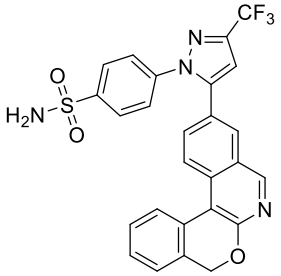
Procedure for the Diversification of Clinical Drugs: Product **4b** was prepared starting from substrate **4a**. Substrate **4a** (0.2 mmol, 1 equiv), 5,5-dimethylpyrazolidin-3-one (0.24mmol, 1.2 equiv), **2a** (0.24mmol, 1.2equiv), [Cp*RhCl2]2 (0.02 mmol, 0.1 equiv), and NaOAc (0.4 mmol, 2 equiv) were mixed in a Schlenk tube and to this mixture was added HFIP (2.0 mL). The resulting mixture was stirred at 40°C for 12 h. Upon completion of the reaction, the mixture was filtered through a pad of Celite and washed with EA (10 mL × 3). The combined organic layer was concentrated under reduced pressure and the crude residue was purified by silica gel chromatography (PE:EA=1:1) to give the desired product 4b.

1-(5H-isochromeno[3,4-c]isoquinolin-11-yl)-5-methylpyridin-2(1H)-one(4b).



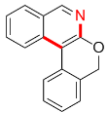
It was obtained as a withe solid (33% yield); mp 111.2-113.2 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.97 (s, 1H), 8.46 (s, 1H), 8.08 (d, *J* = 8.7 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.51 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.47 (t, *J* = 7.1 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.35 – 7.30 (m, 3H), 7.18 (s, 1H), 6.68 (d, *J* = 9.4 Hz, 1H), 5.24 (s, 2H), 2.13 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 161.8, 159.8, 151.5, 143.6, 143.2, 134.7, 134.7, 133.0, 130.2, 129.4, 128.9, 128.3, 126.5, 126.0, 125.6, 123.9, 121.8, 121.5, 115.8, 69.7, 17.3; LRMS (ESI): m/z 341.2 $[M + H]^+$; HRMS (ESI): calcd for $C_{22}H_{17}N_2O_2^+$ $[M + H]^+$, 341.1285; found, 341.1280.

4-(5-(5H-isochromeno[3,4-c]isoquinolin-10-yl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide(5b)

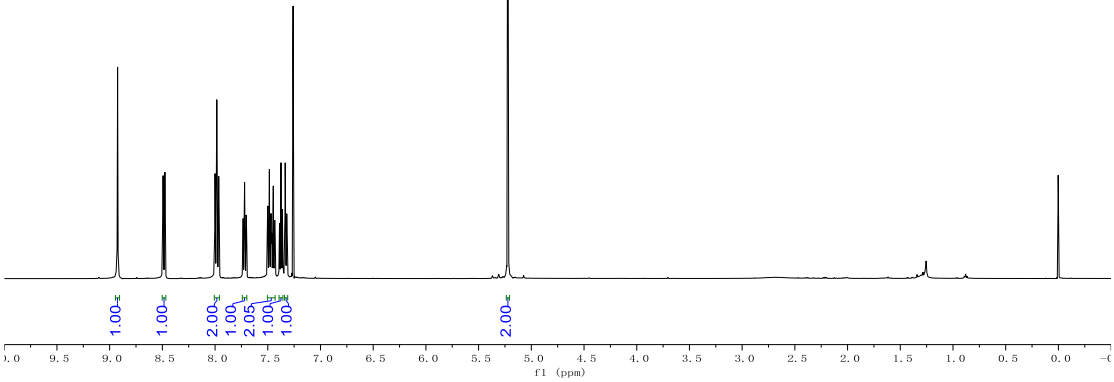


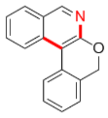
It was obtained as a yellow solid (46% yield); mp 263.0-265.8 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.05 (d, *J* = 0.7 Hz, 1H), 8.26 (d, *J* = 1.4 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.97 – 7.93 (m, 2H), 7.73 – 7.67 (m, 2H), 7.55 – 7.48 (m, 4H), 7.43 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.39 (td, *J* = 7.4, 1.1 Hz, 1H), 7.32 (td, *J* = 7.6, 1.5 Hz, 1H), 7.17 (d, *J* = 7.7 Hz, 1H), 5.18 (s, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.44, 151.76, 144.71, 144.36, 141.05, 132.89, 132.77, 131.04, 129.69, 128.75, 128.49, 128.13, 127.12, 126.33, 125.81, 125.64, 125.61, 125.17, 124.34, 108.90, 107.60, 68.62; ^{19}F NMR (471 MHz, DMSO-d_6) δ -60.79; LRMS (ESI): m/z 523.1 $[M + H]^+$; HRMS (ESI): calcd for $C_{26}H_{17}F_3N_4O_3S^+$ $[M + H]^+$, 523.1046; found, 523.1051.

V. Charts of compounds



3aa





3aa


8.88
8.10
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7.48
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7.25
7.25
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7.25
7.23
7.23
5.22


N
F
O

3ba

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1.00
1.02
1.00
1.00
1.02
1.00
1.00
2.00
f1 (ppm)


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163.59
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131.71
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128.02
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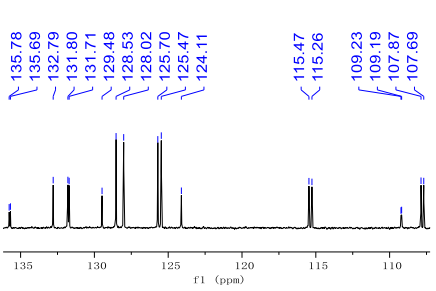
109.23
109.19
107.87
107.69


69.54


N
F
O

3ba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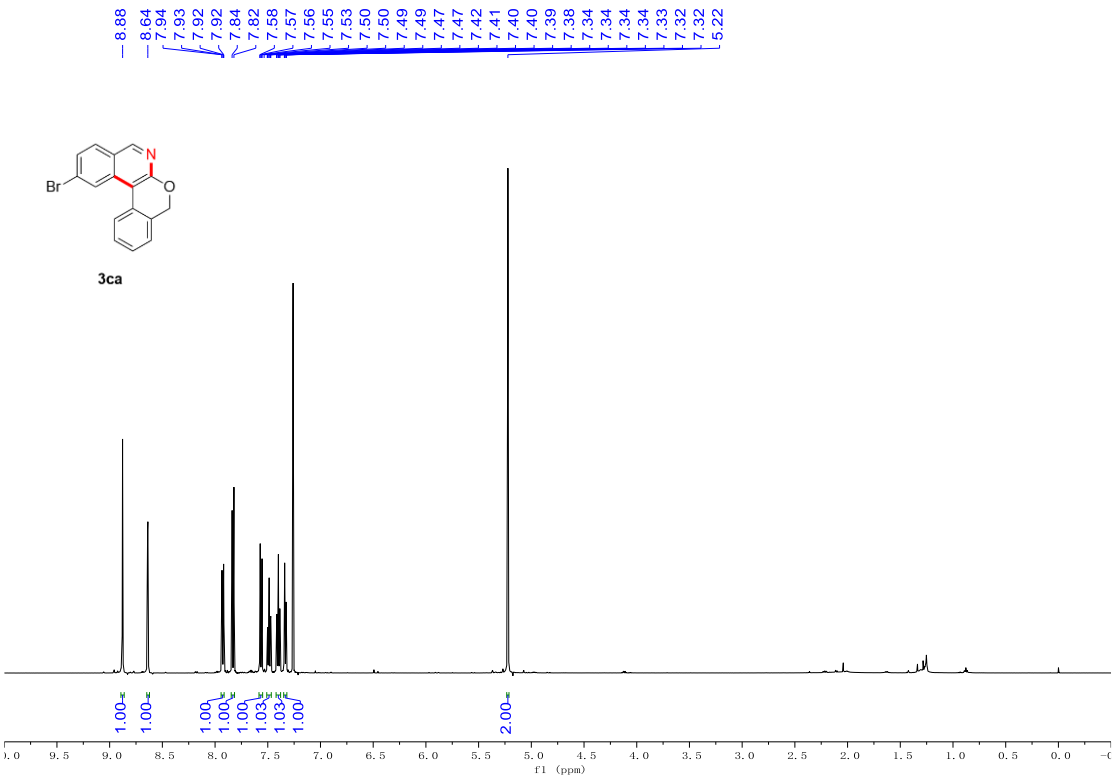
109.19
107.87
107.69
f1 (ppm)

f1 (ppm)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7.38
7.34
7.34
7.34
7.34
7.33
7.32
7.32
5.22
Br
N
O
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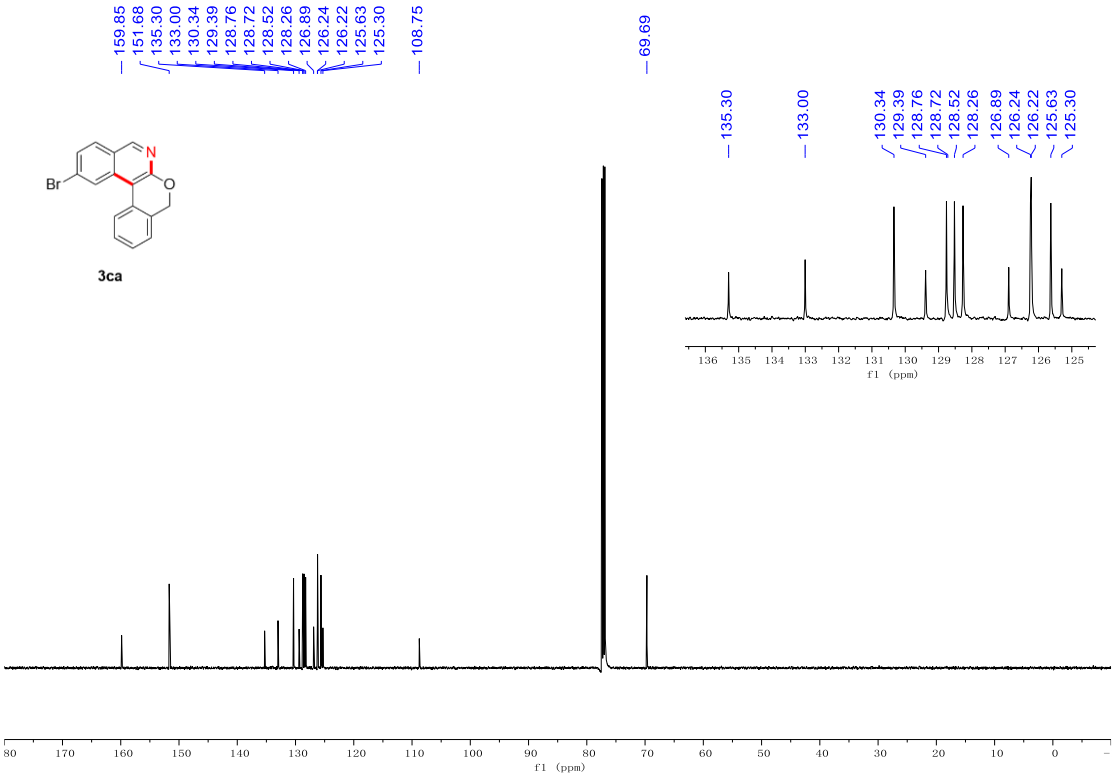
1.00
1.00
1.03
1.03
1.00
2.00
f1 (ppm)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128.26
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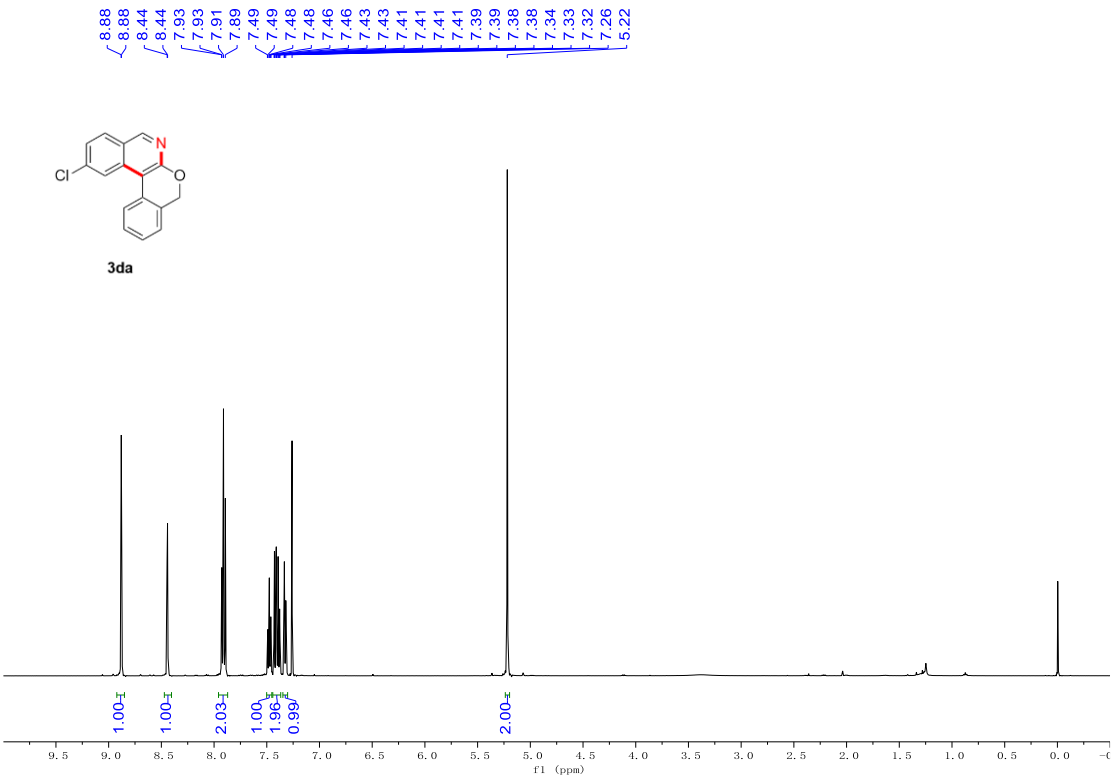
125.63
125.30
108.75
69.69
Br
N
O
3ca
135.30
133.00
130.34
129.39
128.76
128.72
128.52
128.26
126.89
126.24
126.22
125.63
125.30
f1 (ppm)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8.88
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7.91
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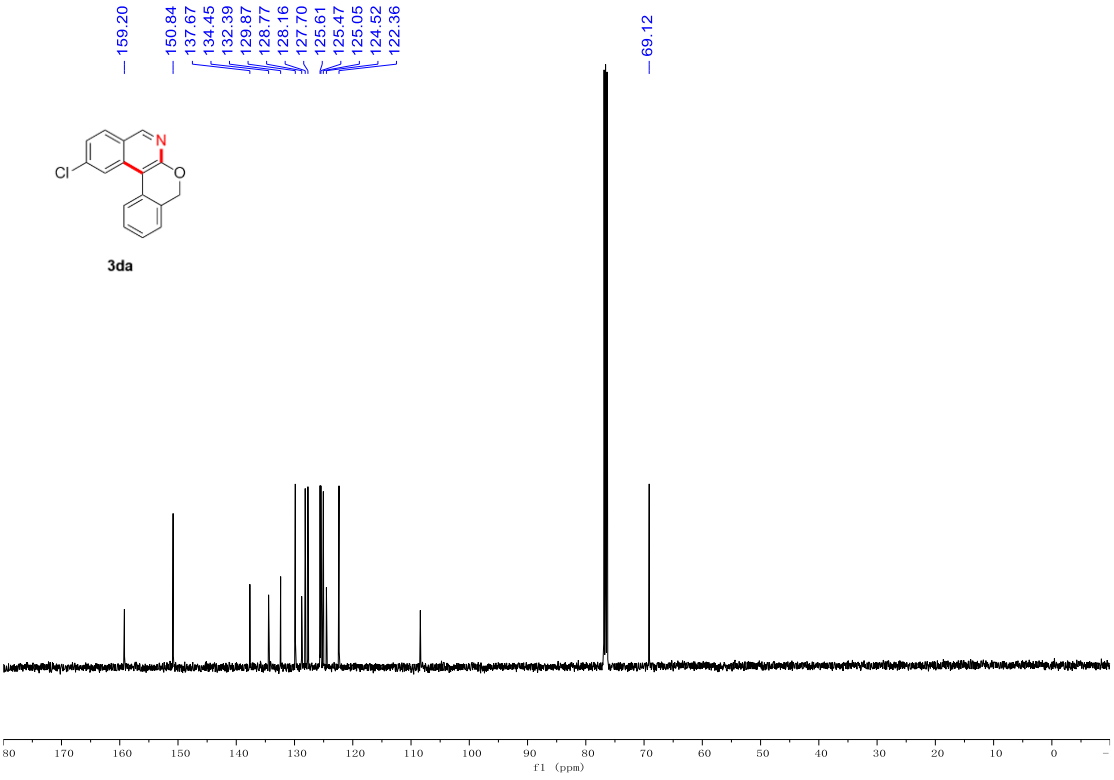
7.49
7.48
7.48
7.46
7.46
7.43
7.43
7.41
7.41
7.41
7.41
7.39
7.39
7.38
7.38
7.34
7.33
7.32
7.26
5.22
Cl
N
O
3da
1.00
1.00
2.03
1.00
1.96
0.99
2.00
f1 (ppm)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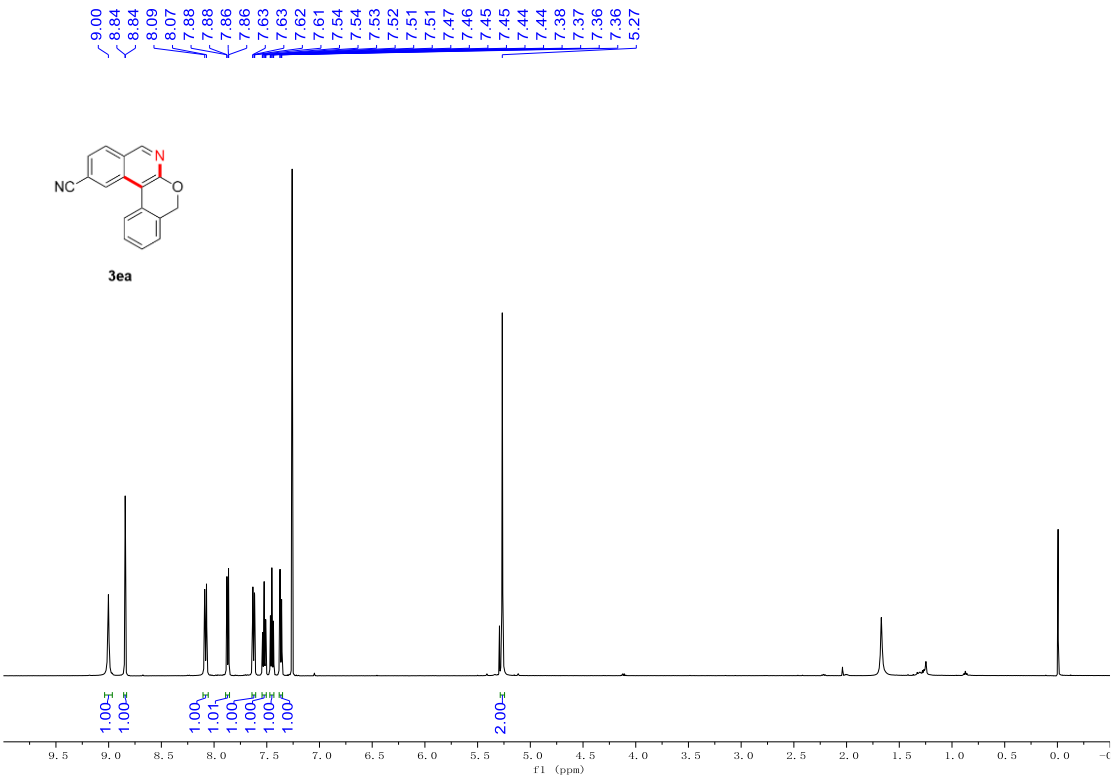
134.45
132.39
129.87
128.77
128.16
127.70
125.61
125.47
125.05
124.52
122.36
69.12
Cl
N
O
3da
f1 (ppm)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8.84
8.09
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7.88
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7.86
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7.63
7.62
7.61
7.54
7.54
7.53
7.52
7.51
7.51
7.47
7.46
7.45
7.45
7.44
7.44
7.38
7.37
7.36
7.36
5.27
NC
N
O
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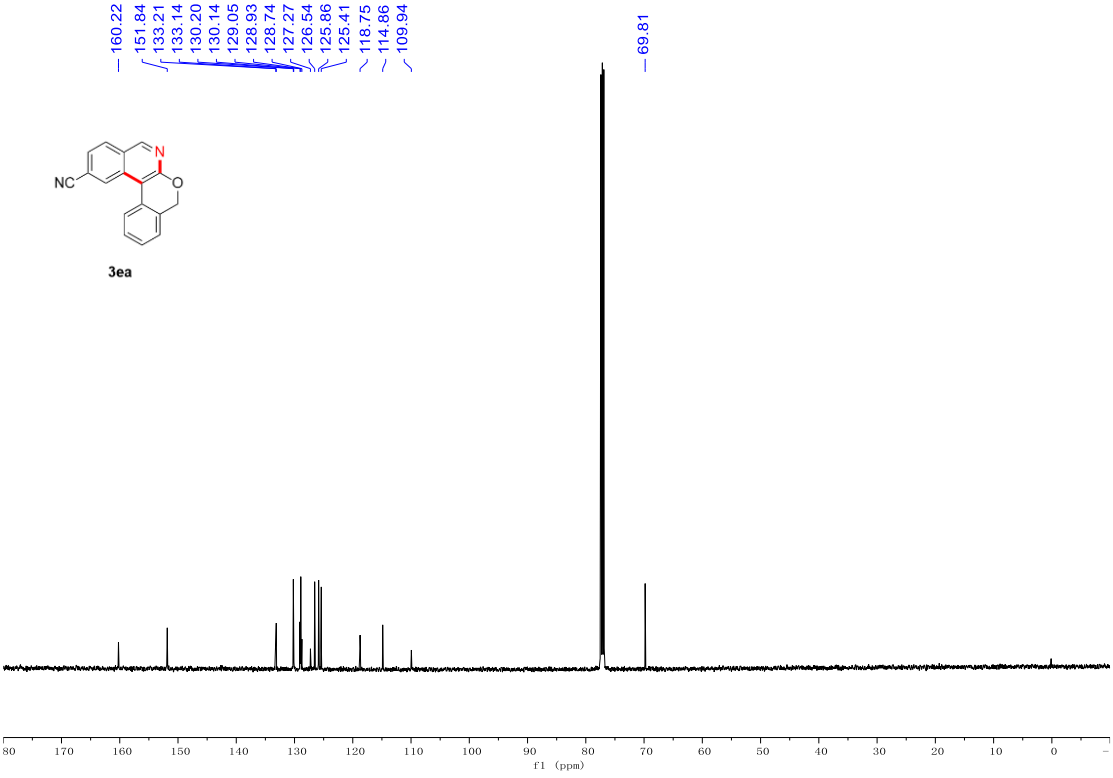
1.00
1.00
1.01
1.00
1.00
1.00
2.00
f1 (ppm)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128.93
128.74
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125.41
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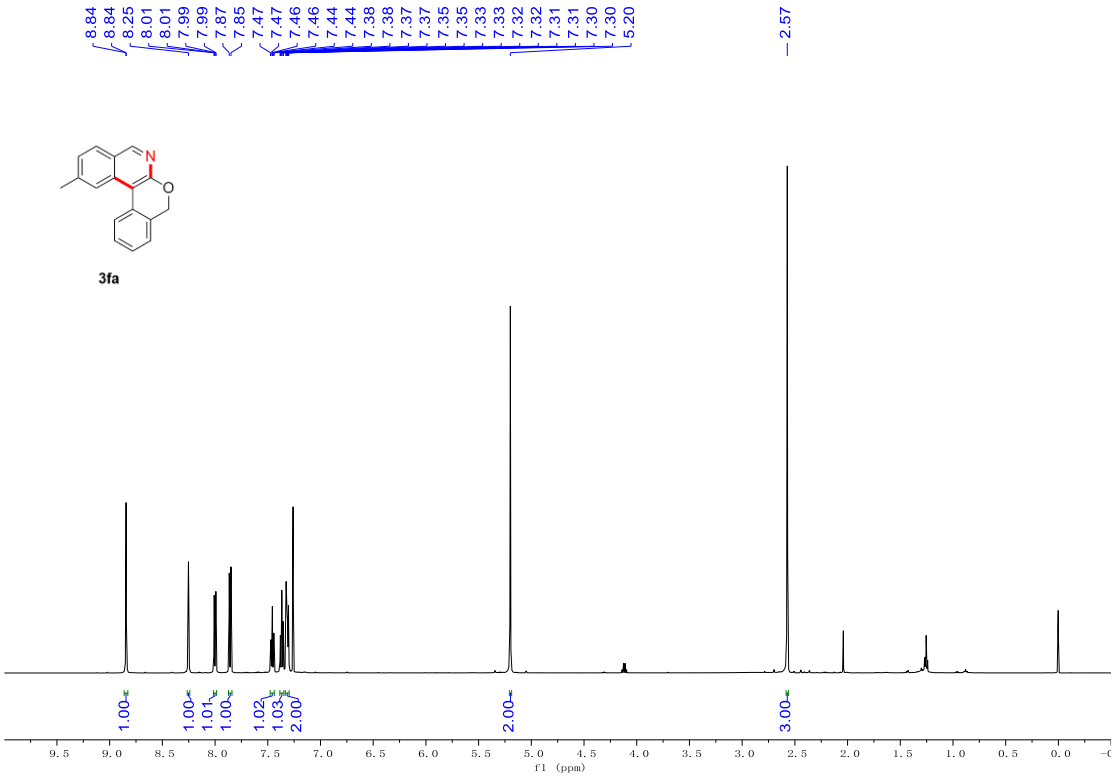
114.86
109.94
69.81
NC
N
O
3ea
f1 (ppm)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8.84
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7.99
7.87
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7.47
7.47
7.46
7.46
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7.44
7.38
7.38
7.37
7.37
7.35
7.35
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
5.20
2.57
N
O
3fa
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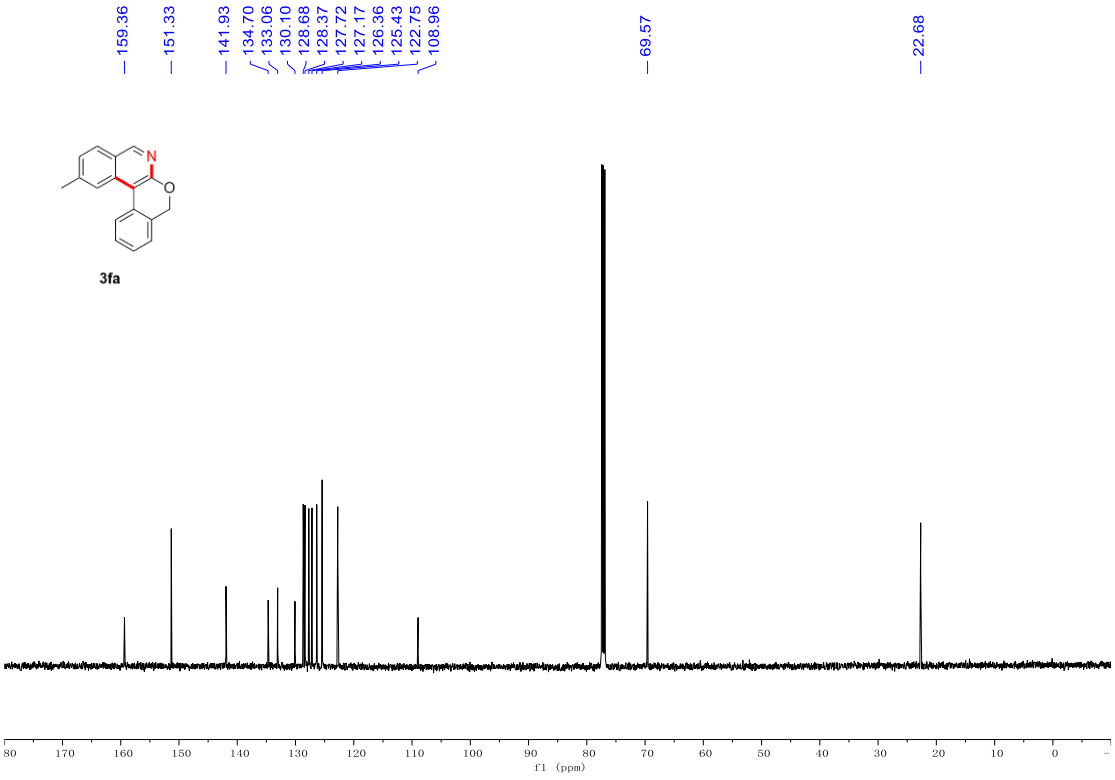
1.00
1.01
1.00
1.02
1.03
2.00
2.00
3.00
f1 (ppm)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133.06
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128.37
127.72
127.17
126.36
125.43
122.75
108.96
69.57
22.68
N
O
3fa
f1 (ppm)


8.79
8.06
8.06
8.04
8.04
7.89
7.87
7.80
7.79
7.48
7.48
7.46
7.46
7.45
7.44
7.40
7.40
7.38
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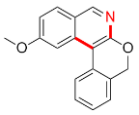
7.16
7.15
7.14
7.13
5.22
3.98



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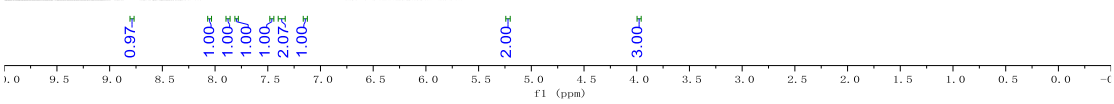
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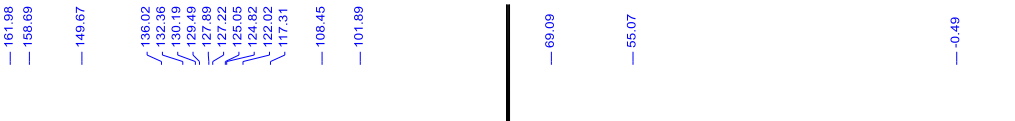
1.00
1.00
1.00
2.07
1.00
2.00
3.00
f1 (ppm)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158.69
149.67
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130.19
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127.22
125.05
124.82
122.02
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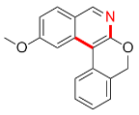
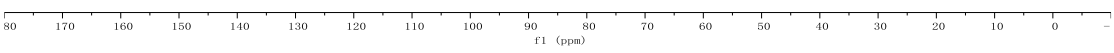
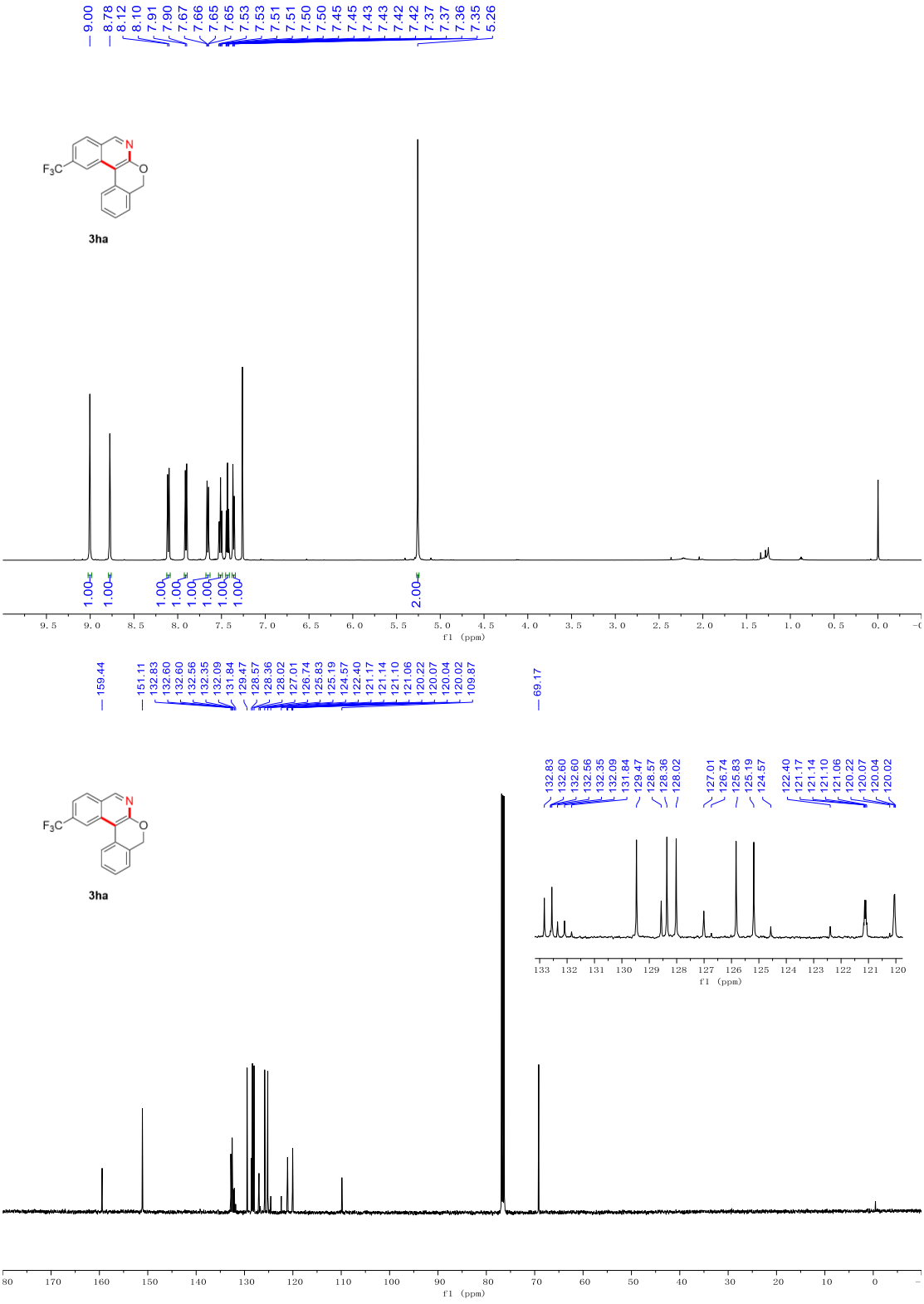
108.45
101.89
69.09
55.07
-0.49



3ga


f1 (ppm)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7.90
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7.53
7.51
7.51
7.50
7.50
7.45
7.45
7.43
7.43
7.42
7.42
7.37
7.37
7.36
7.35
5.26
F3C
N
O
3ha
1.00
1.00
1.00
1.00
1.00
1.00
1.00
2.00
f1 (ppm)
159.44
151.11
132.83
132.60
132.60
132.56
132.35
132.09
131.84
129.47
128.57
128.36
128.02
127.01
126.74
125.83
125.19
124.57
122.40
121.17
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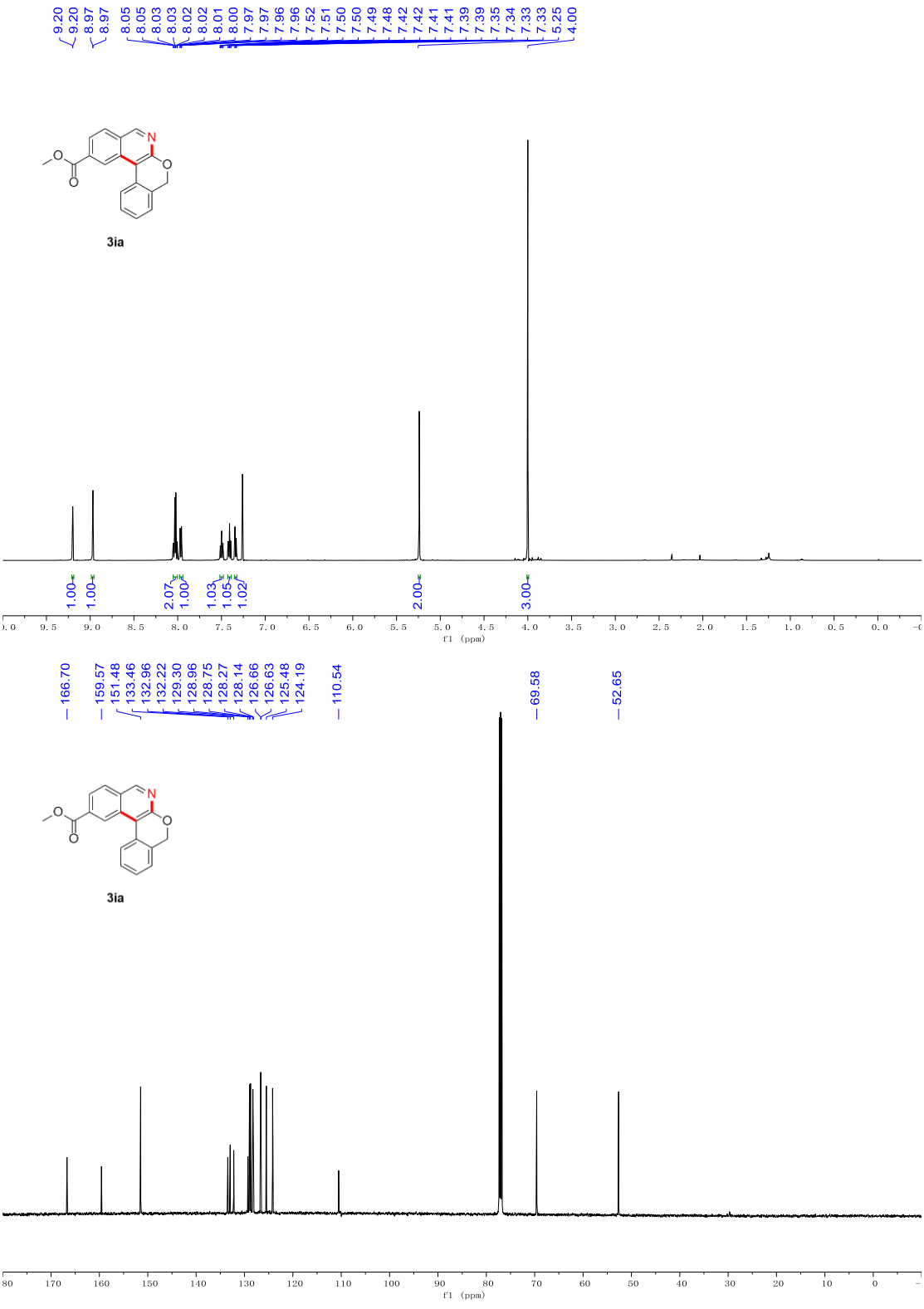
121.10
121.06
120.22
120.07
120.04
120.02
109.87
69.17
f1 (ppm)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8.05
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8.03
8.02
8.02
8.01
8.00
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7.97
7.96
7.96
7.52
7.51
7.50
7.50
7.49
7.48
7.42
7.42
7.41
7.41
7.39
7.39
7.35
7.34
7.33
7.33
5.25
4.00
3ia
1.00
1.00
2.07
1.00
1.03
1.05
1.02
2.00
3.00
f1 (ppm)
166.70
159.57
151.48
133.46
132.96
132.22
129.30
128.96
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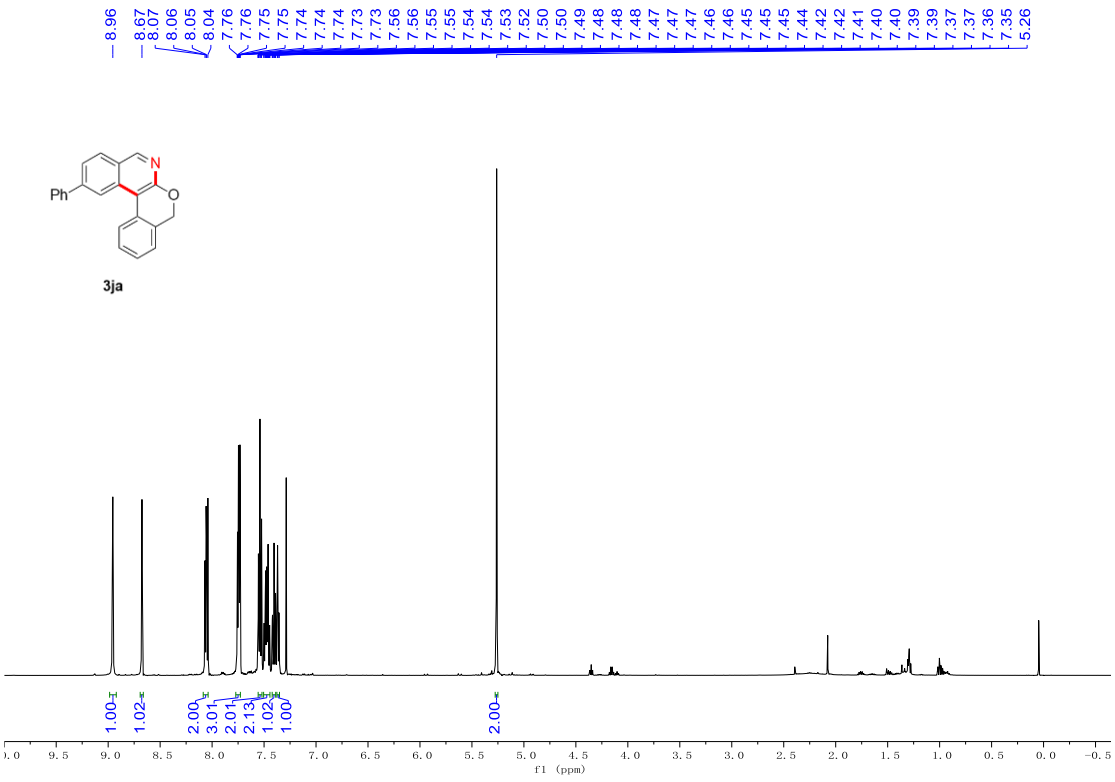
f1 (ppm)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7.74
7.73
7.73
7.56
7.56
7.55
7.55
7.54
7.54
7.53
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7.50
7.49
7.48
7.48
7.48
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7.47
7.47
7.46
7.46
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7.45
7.45
7.44
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7.42
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7.40
7.39
7.39
7.37
7.37
7.36
7.35
5.26
Ph
N
O
3ja
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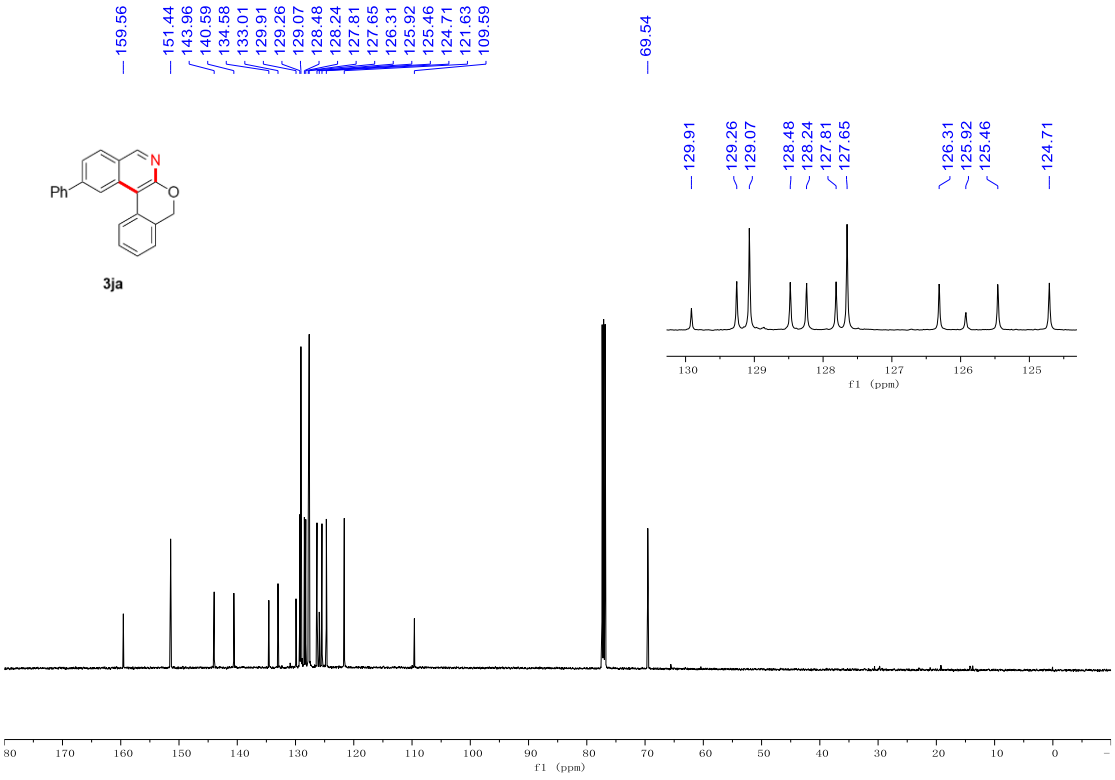
1.02
2.00
3.01
2.01
2.13
1.02
1.00
2.00
f1 (ppm)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129.26
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128.48
128.24
127.81
127.65
126.31
125.92
125.46
124.71
121.63
109.59
69.54
129.91
129.26
129.07
128.48
128.24
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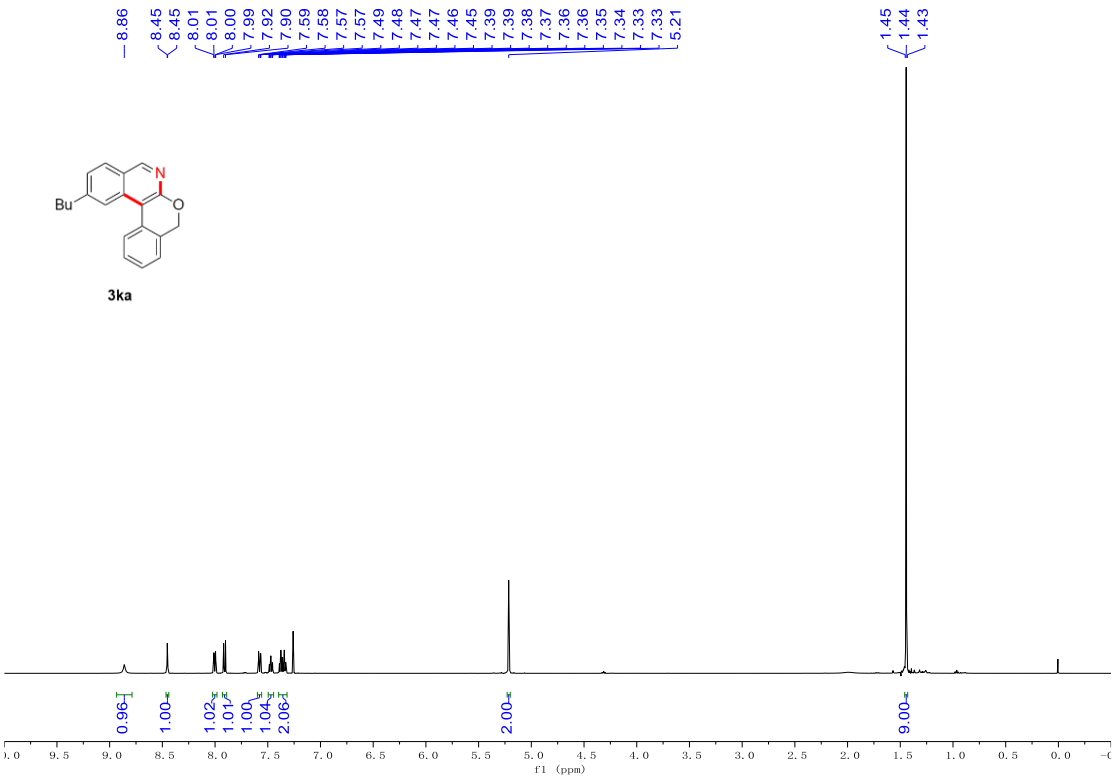
127.65
126.31
125.92
125.46
124.71
Ph
N
O
3ja
f1 (ppm)
f1 (ppm)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7.92
7.90
7.59
7.58
7.57
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7.49
7.48
7.47
7.47
7.46
7.45
7.39
7.39
7.38
7.37
7.36
7.36
7.35
7.34
7.33
7.33
5.21
1.45
1.44
1.43
Bu
N
O
3ka
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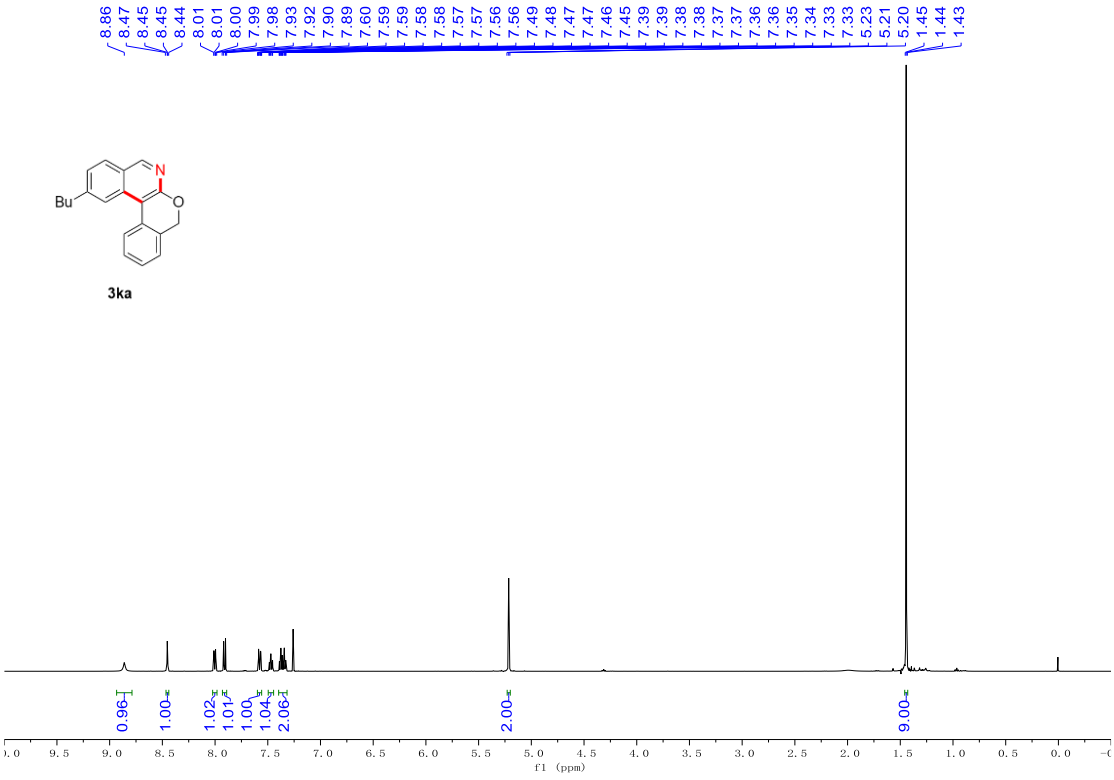
1.00
1.02
1.01
1.00
1.04
2.06
2.00
9.00
f1 (ppm)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8.45
8.45
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8.01
8.00
7.99
7.98
7.93
7.92
7.90
7.89
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7.59
7.59
7.58
7.58
7.57
7.57
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7.56
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7.48
7.47
7.47
7.46
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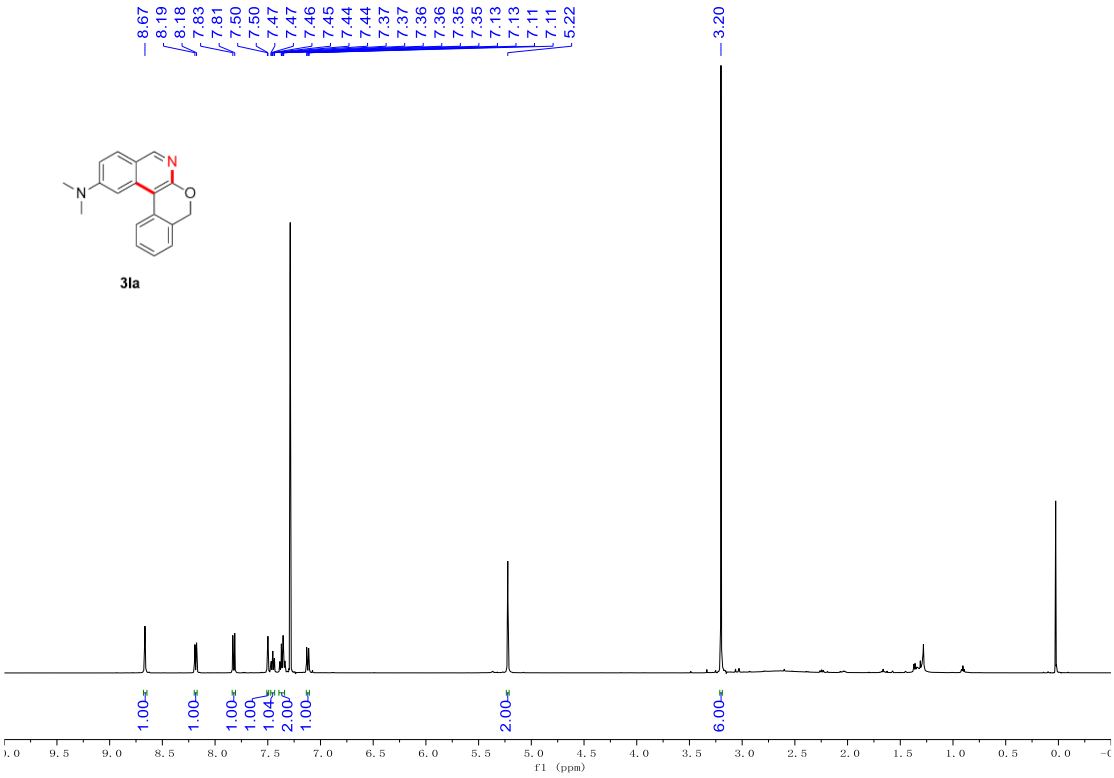
7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.34
7.33
7.33
5.23
5.21
5.20
1.45
1.44
1.43
Bu
N
O
3ka
0.96
1.00
1.02
1.01
1.00
1.04
2.06
2.00
9.00
f1 (ppm)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7.47
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7.46
7.45
7.44
7.44
7.37
7.37
7.36
7.36
7.35
7.35
7.13
7.13
7.11
7.11
5.22
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N
O
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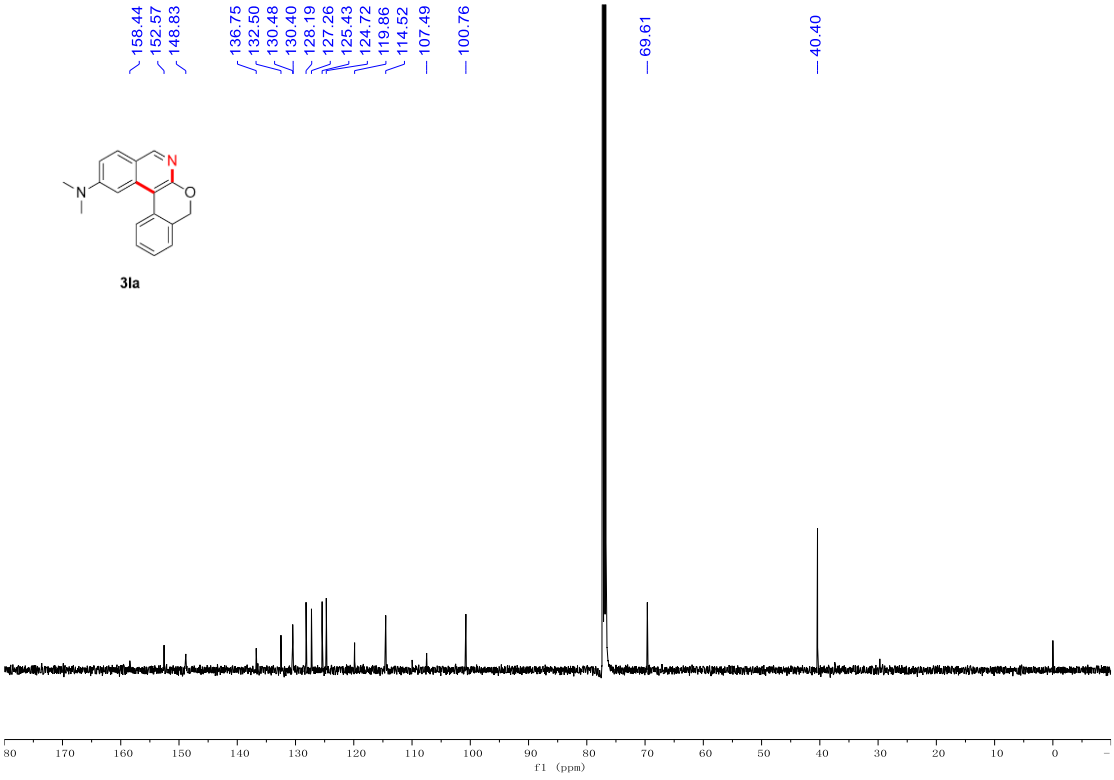
1.00
1.00
1.00
2.00
1.00
2.00
6.00
f1 (ppm)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130.48
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128.19
127.26
125.43
124.72
119.86
114.52
107.49
100.76
69.61
40.40
N
O
3la
f1 (ppm)


9.29
9.29
8.42
8.41
8.41
8.40
8.40
8.39
7.89
7.89
7.87
7.87
7.70
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7.31
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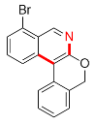
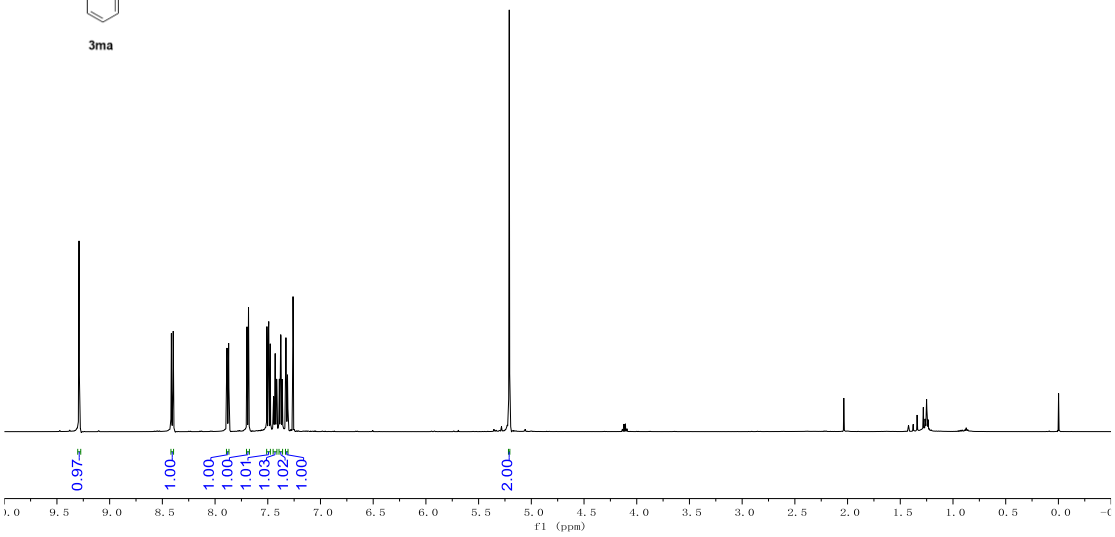
7.31
7.31
5.21


Br
N
O

3ma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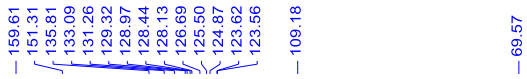
1.01
1.03
1.02
1.00
2.00
f1 (ppm)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133.09
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128.44
128.13
126.69
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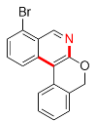
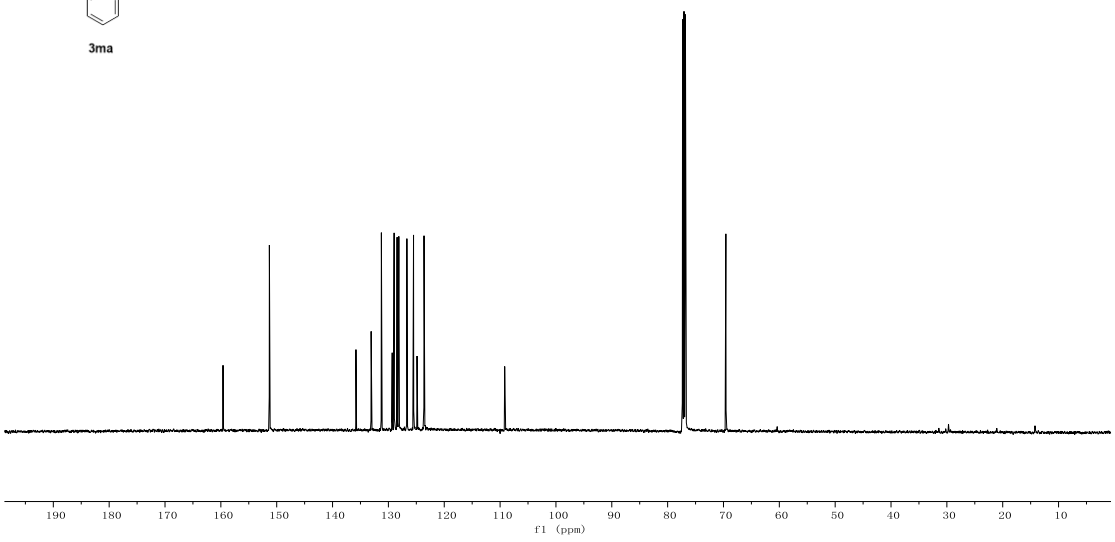
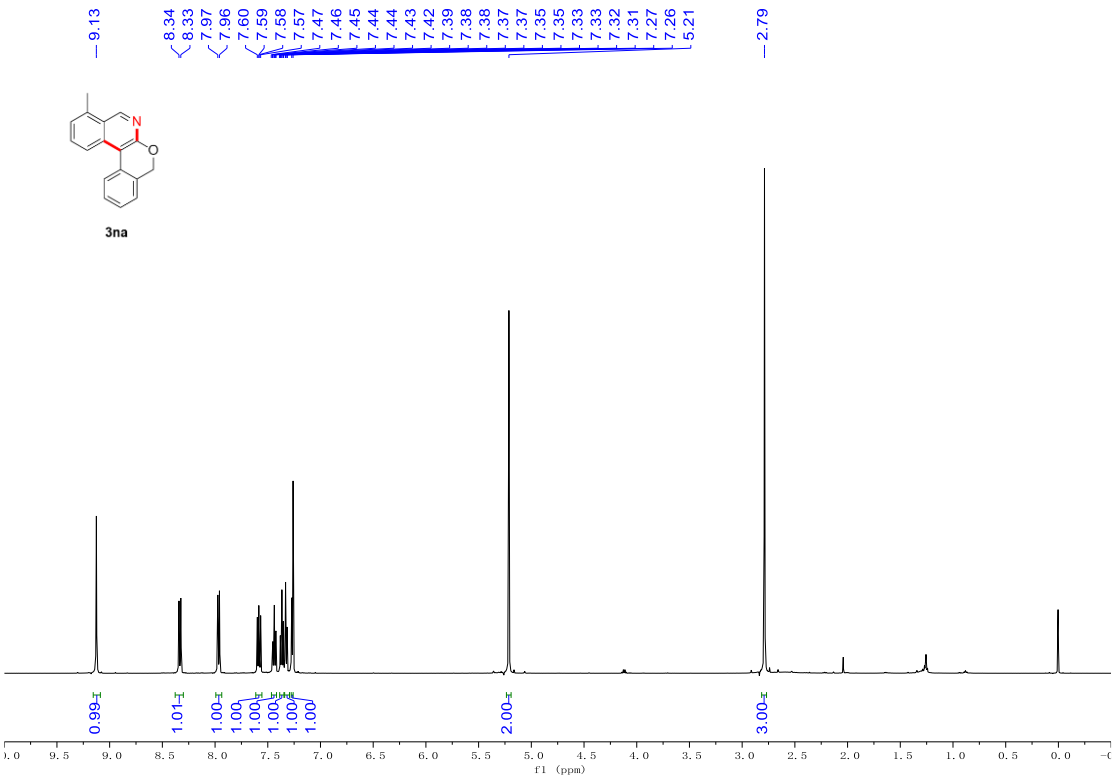
124.87
123.62
123.56
109.18
69.57


Br
N
O

3ma


f1 (ppm)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7.58
7.57
7.47
7.46
7.45
7.44
7.44
7.43
7.42
7.39
7.38
7.38
7.37
7.37
7.35
7.35
7.33
7.33
7.32
7.31
7.27
7.26
5.21
2.79
N
O
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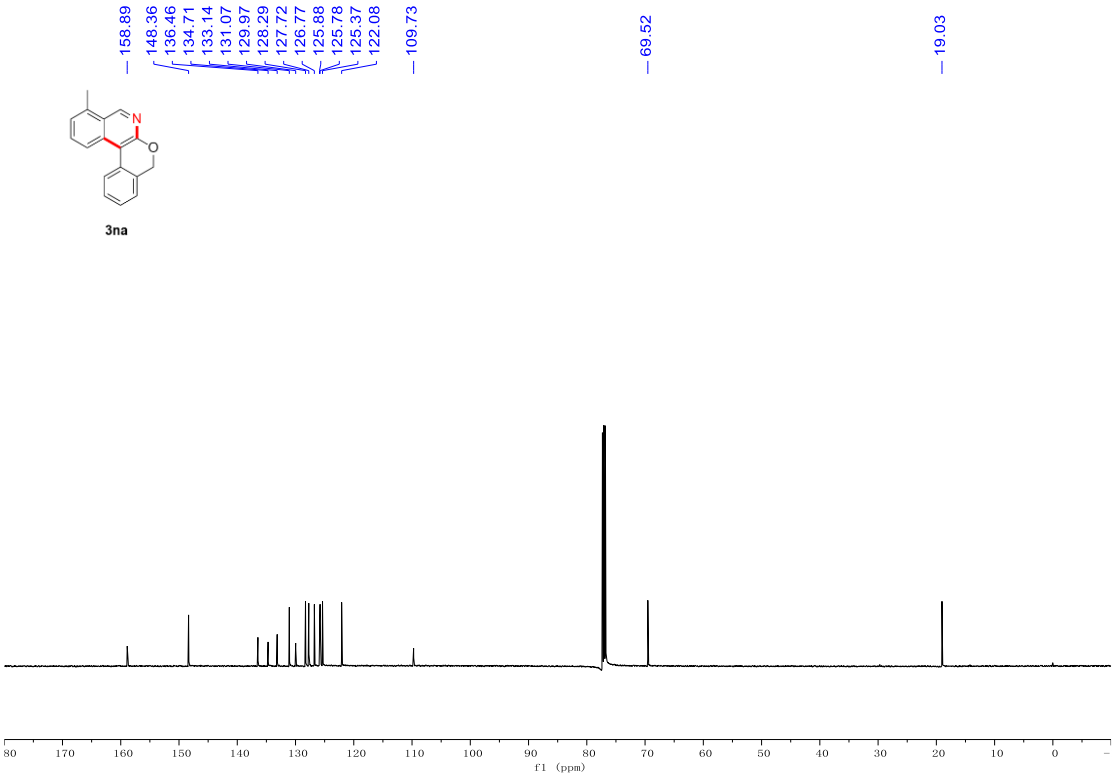
1.00
1.00
1.00
1.00
1.00
1.00
2.00
3.00
f1 (ppm)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128.29
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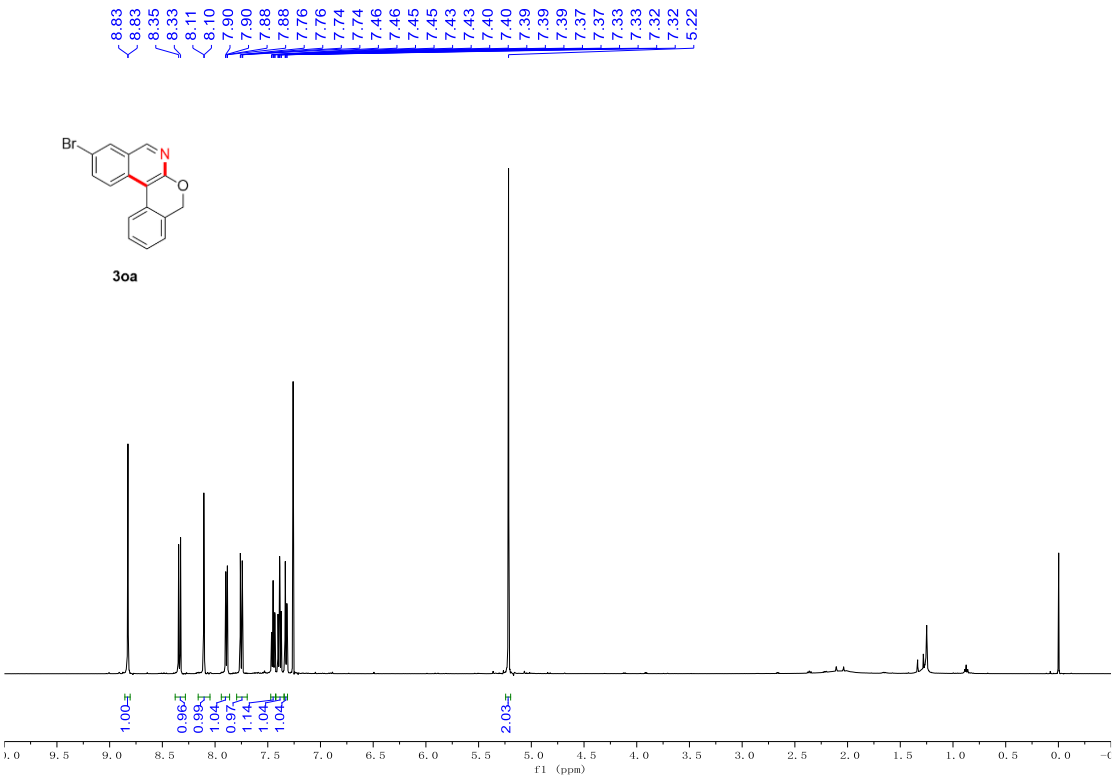
125.37
122.08
109.73
69.52
19.03
N
O
3na
f1 (ppm)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7.88
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7.39
7.39
7.39
7.37
7.37
7.33
7.33
7.32
7.32
5.22
Br
N
O
3oa
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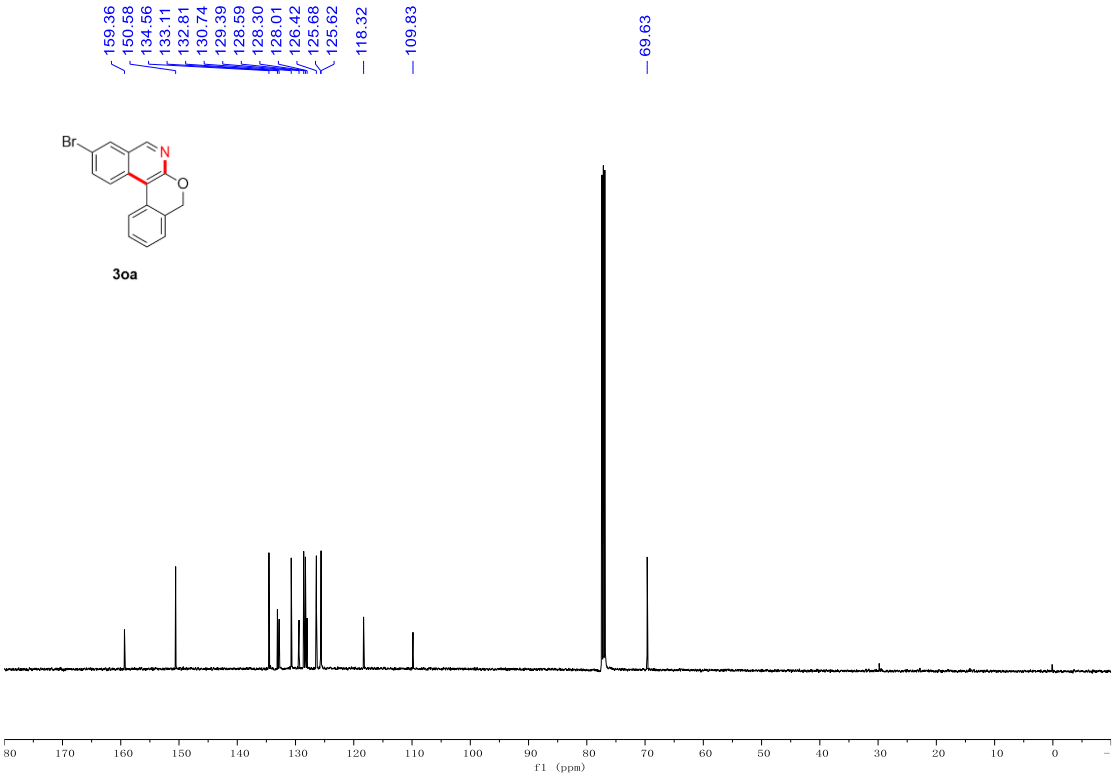
0.96
0.99
1.04
0.97
1.14
1.04
1.04
2.03
f1 (ppm)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118.32
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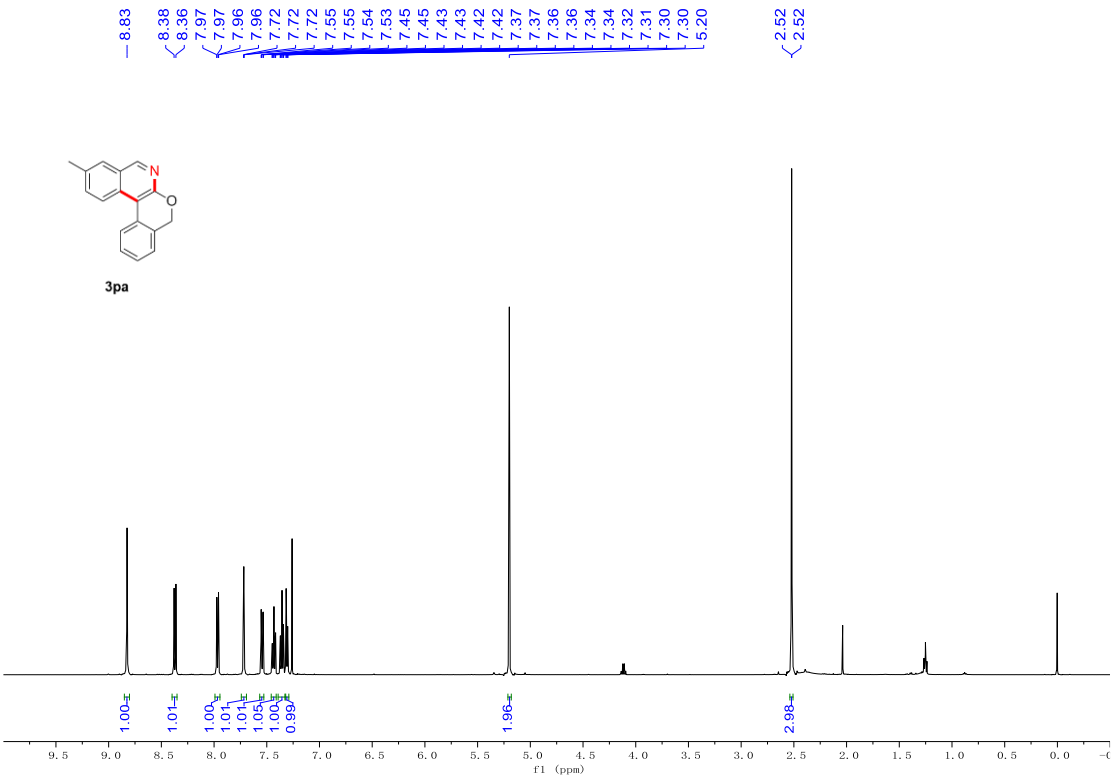
69.63
Br
N
O
3oa
f1 (ppm)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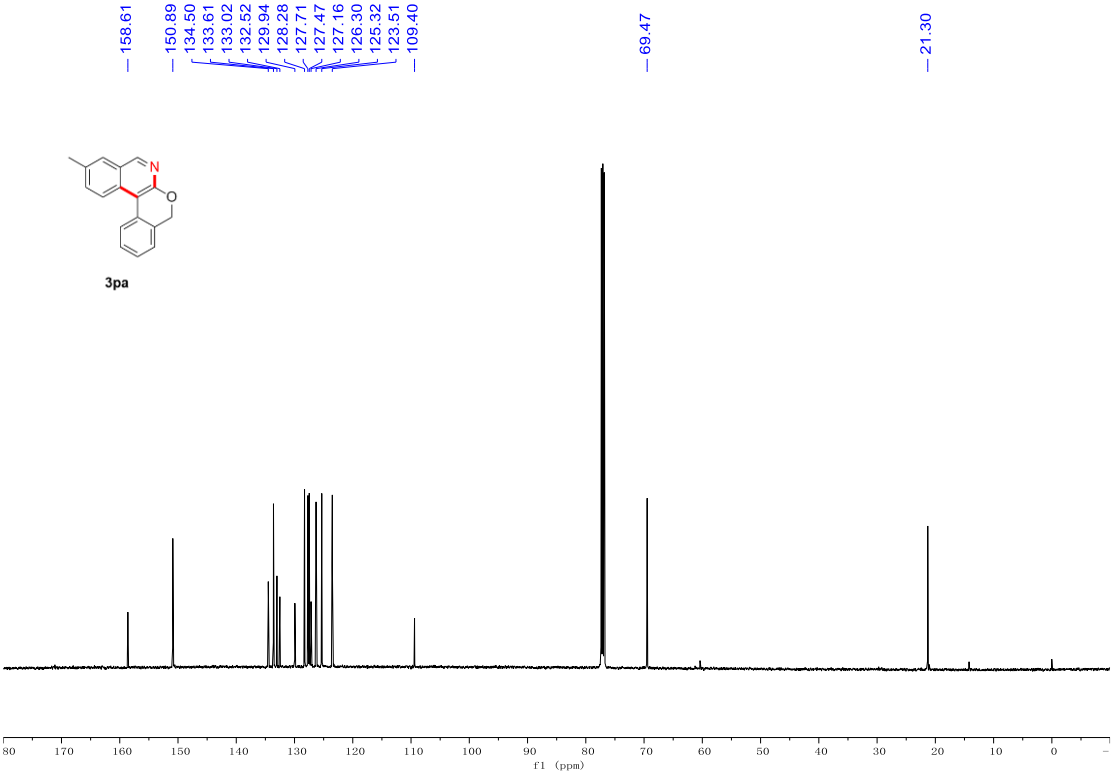
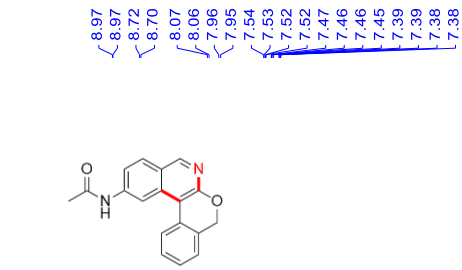
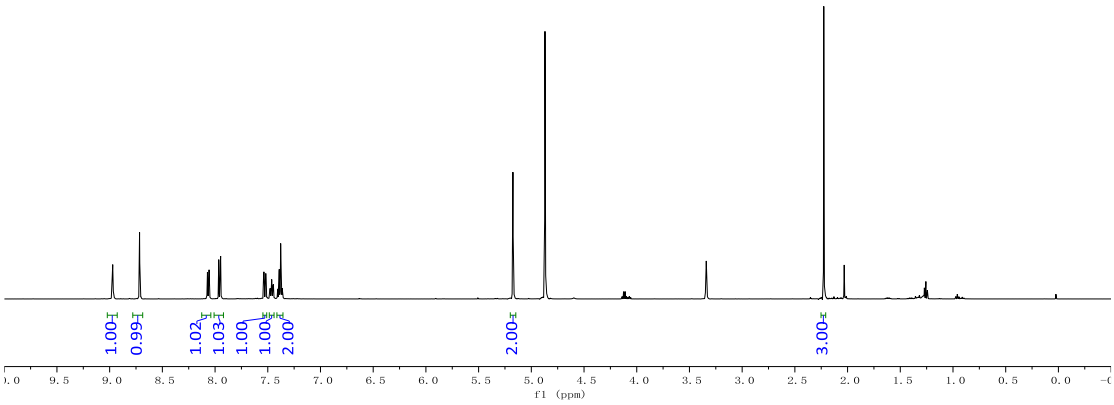
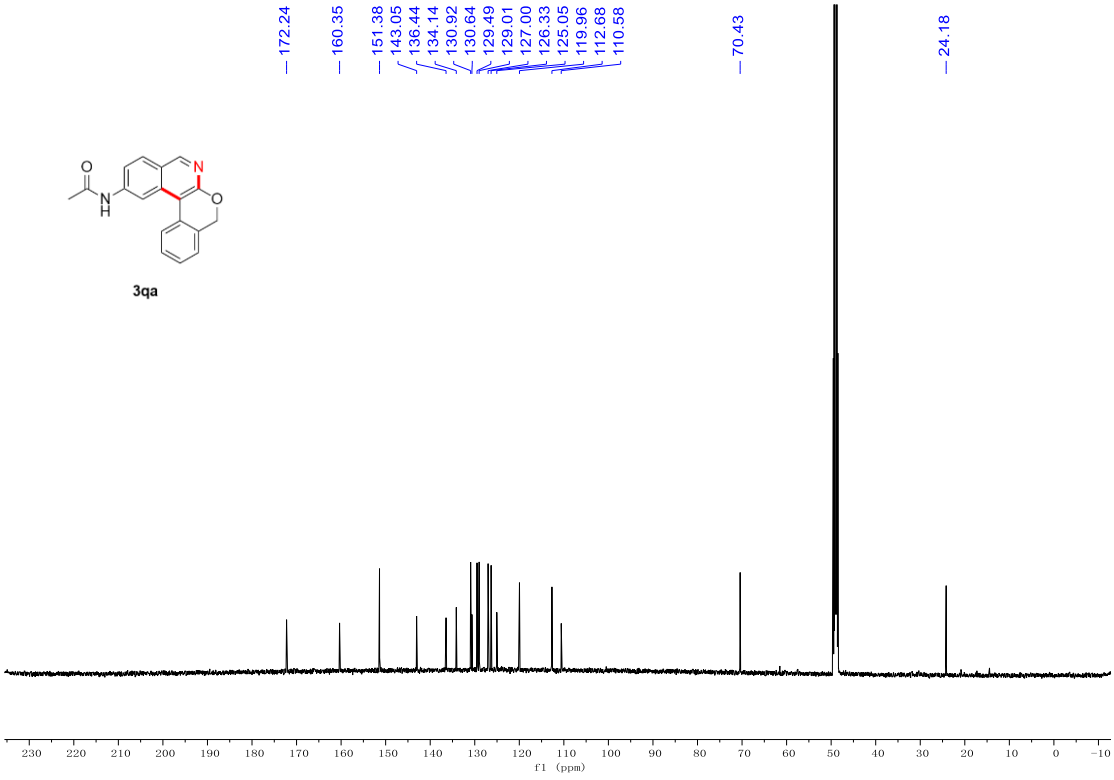
7.36
7.34
7.34
7.32
7.31
7.30
7.30
5.20
2.52
2.52
3pa
1.00
1.01
1.00
1.01
1.01
1.05
1.00
0.99
1.96
2.98
f1 (ppm)


158.61
150.89
134.50
133.61
133.02
132.52
129.94
128.28
127.71
127.47
127.16
126.30
125.32
123.51
109.40
69.47
21.30
3pa
f1 (ppm)


8.97
8.97
8.72
8.70
8.07
8.06
7.96
7.95
7.54
7.53
7.52
7.52
7.47
7.46
7.46
7.45
7.39
7.39
7.38
7.38
5.17
2.23

3qa


1.00
0.99
1.02
1.03
1.00
1.00
2.00
2.00
3.00
f1 (ppm)


172.24
160.35
151.38
143.05
136.44
134.14
130.92
130.64
129.49
129.01
127.00
126.33
125.05
119.96
112.68
110.58
70.43
24.18
f1 (ppm)

3qa


8.87
7.65
7.64
7.63
7.63
7.63
7.61
7.61
7.61
7.43
7.43
7.42
7.42
7.40
7.40
7.36
7.36
7.35
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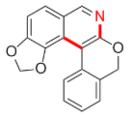
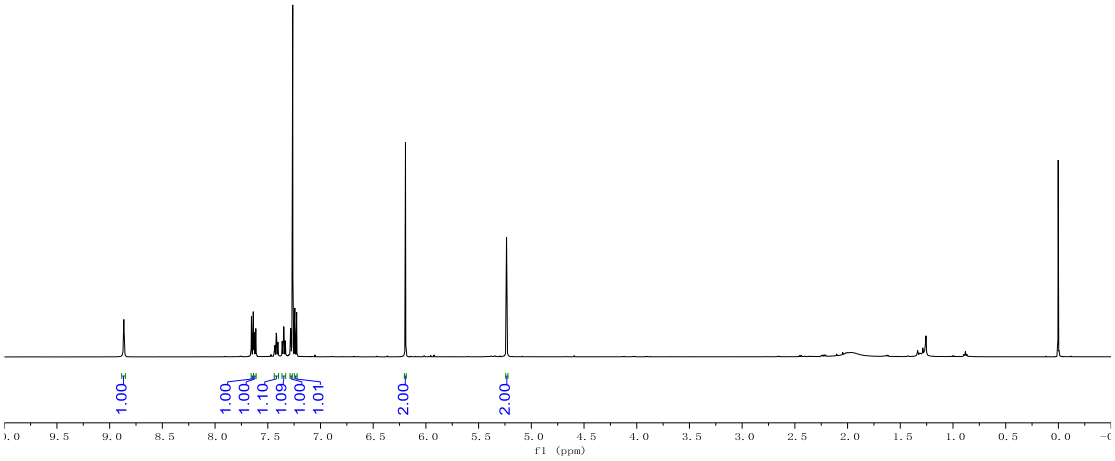
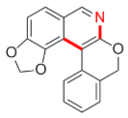
7.27
7.27
7.24
7.23
6.19
5.24


N
O
O
O

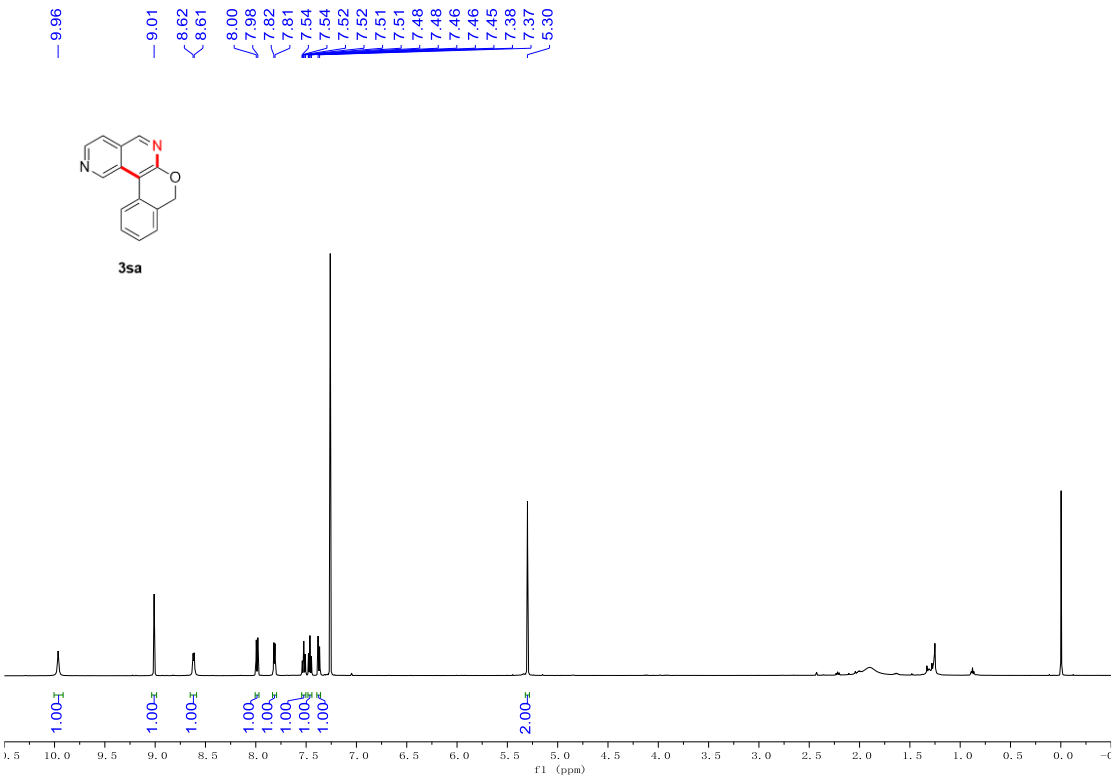
3ra

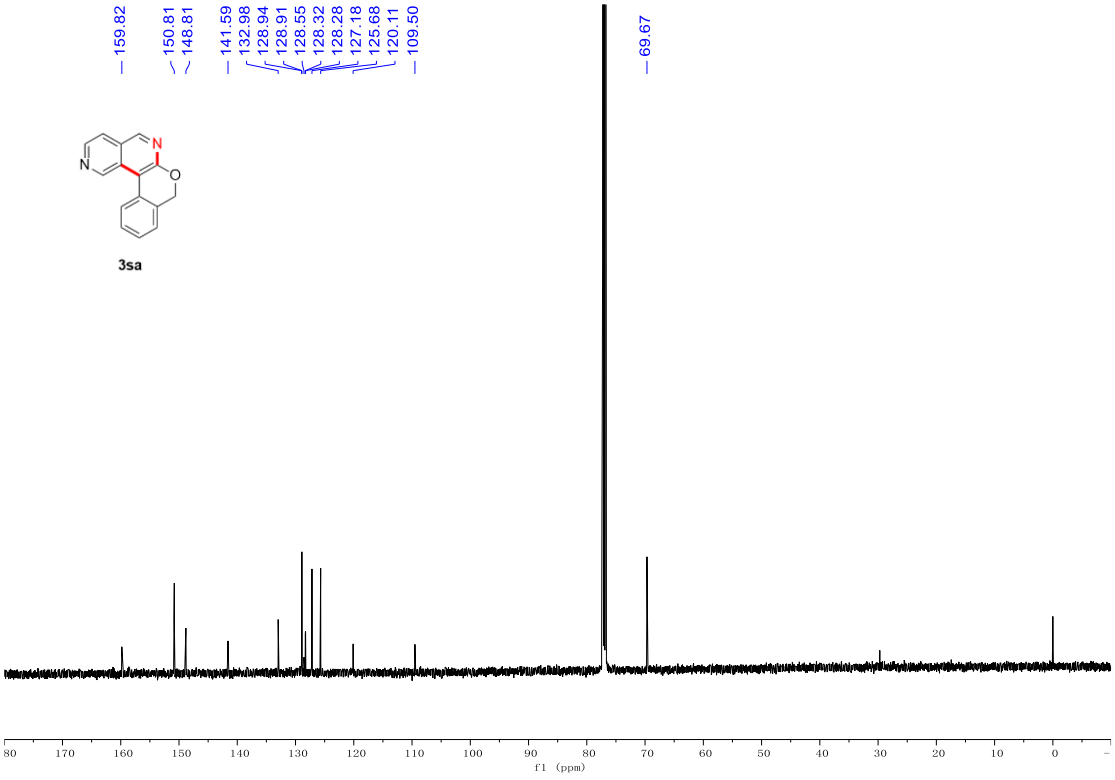

1.00
1.00
1.00
1.10
1.09
1.00
1.01
2.00
2.00
f1 (ppm)

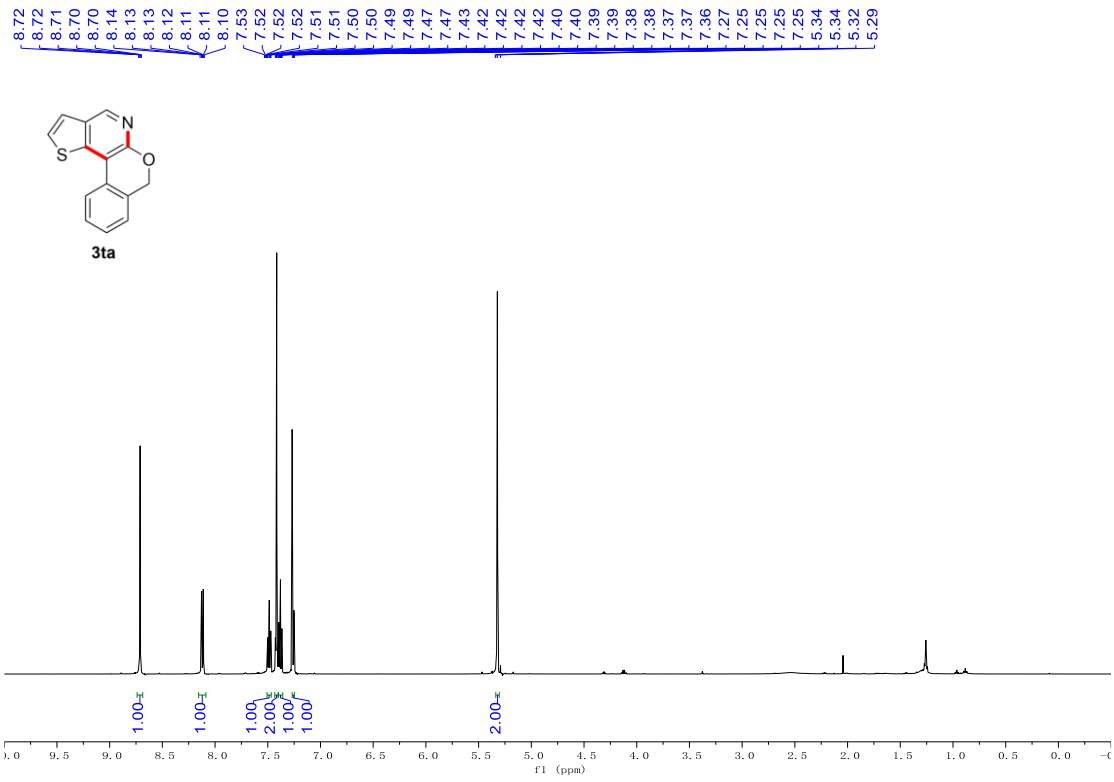

N
O
O
O

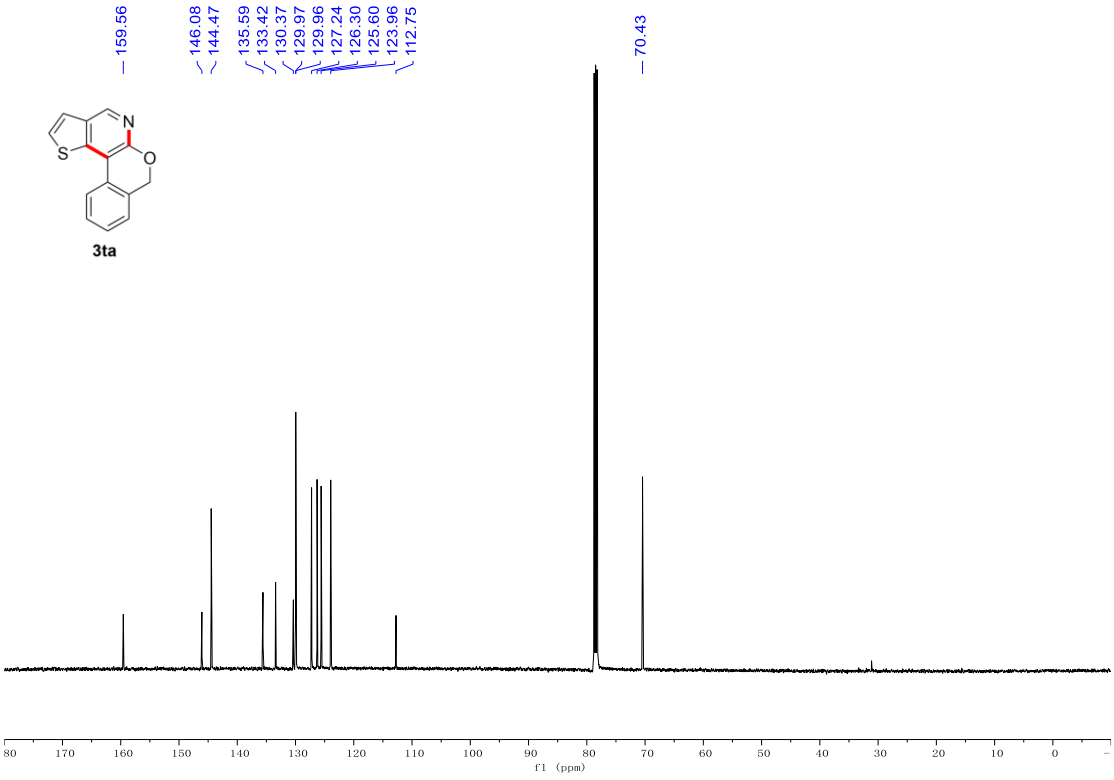
3ra

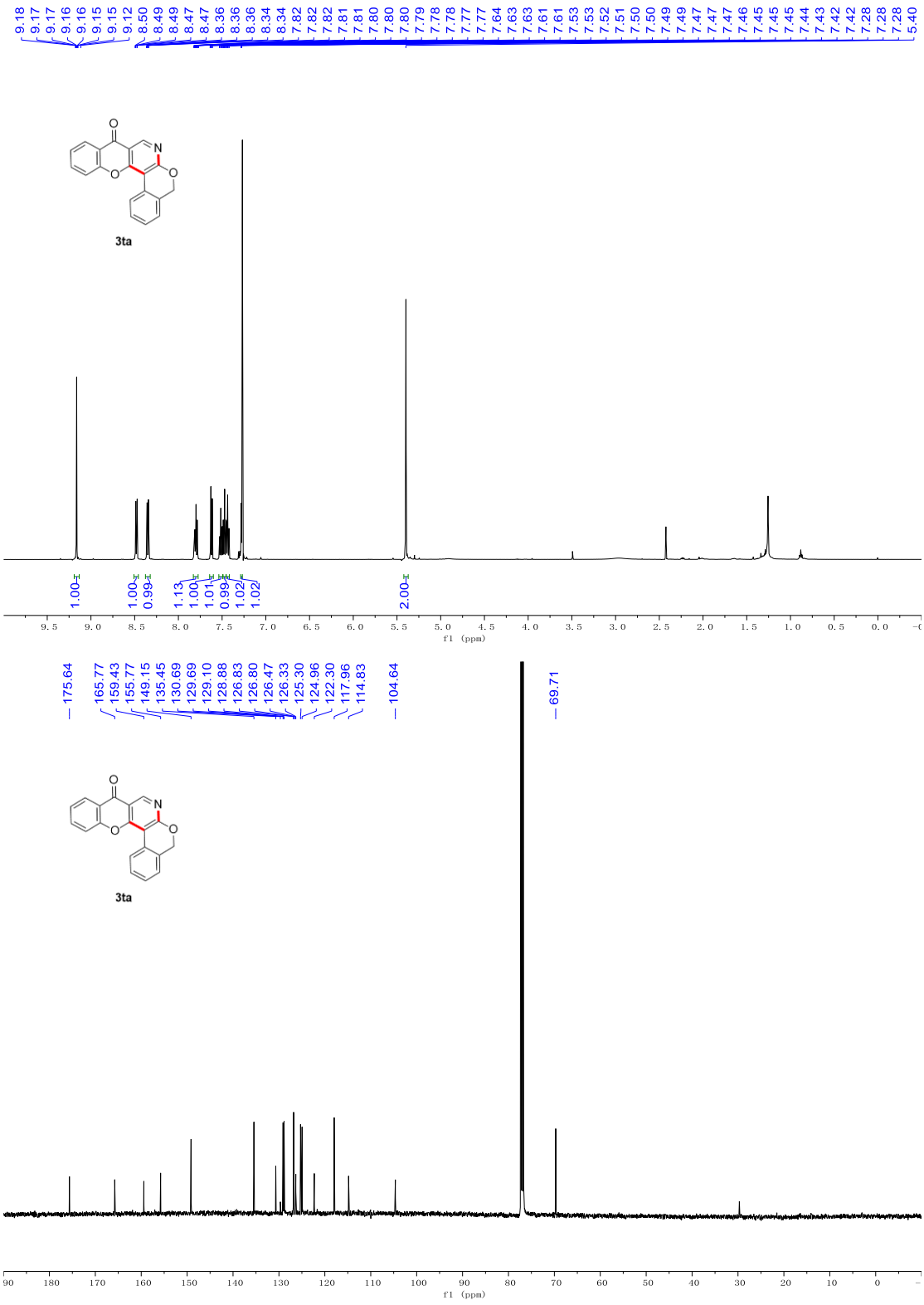
159.90
152.62
148.76
139.42
131.14
129.43
128.42
127.66
127.37
125.17
124.41
124.28
120.26
109.97
105.21
101.46
69.84
f1 (ppm)

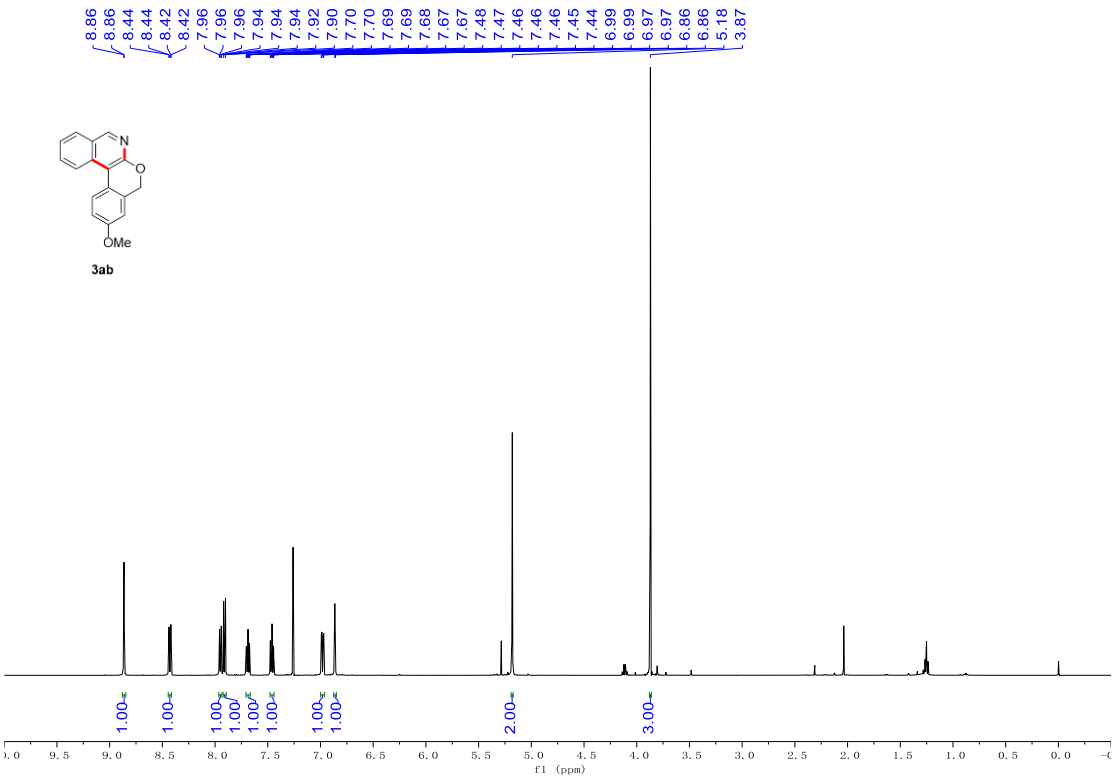

9.96
9.01
8.62
8.61
8.00
7.98
7.82
7.81
7.54
7.54
7.52
7.52
7.51
7.51
7.48
7.48
7.46
7.46
7.45
7.38
7.37
5.30
3sa
1.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
2.00
f1 (ppm)

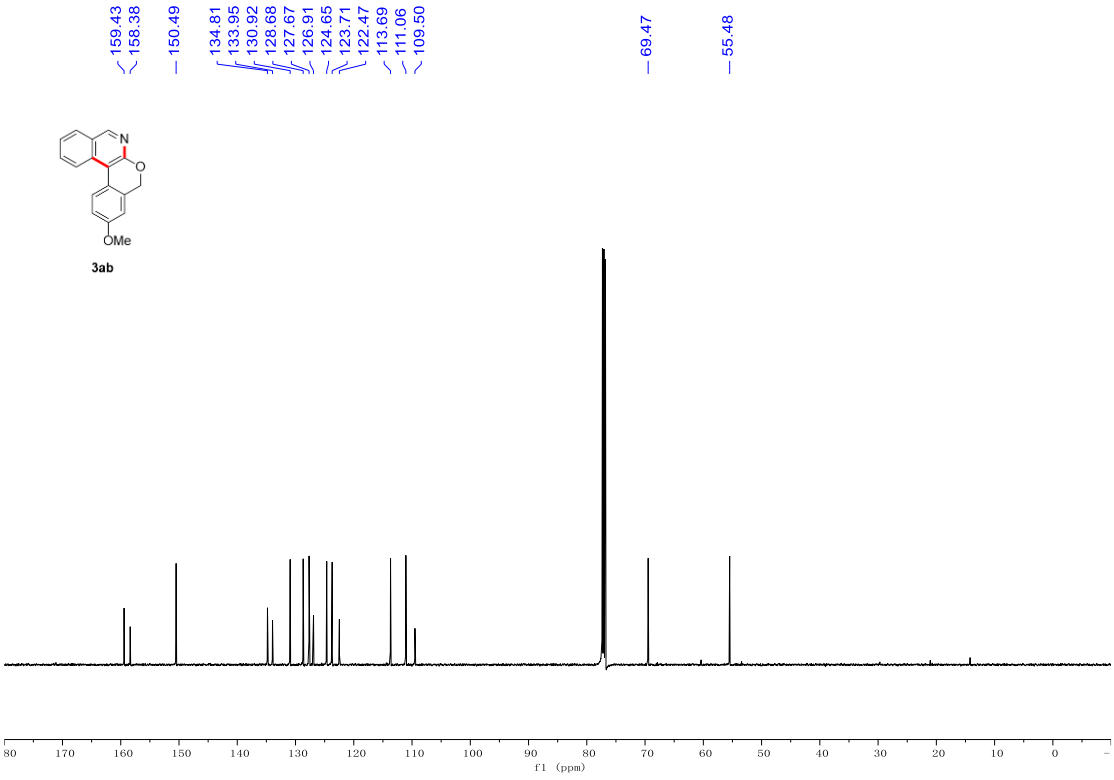

159.82
150.81
148.81
141.59
132.98
128.94
128.91
128.55
128.32
128.28
127.18
125.68
120.11
109.50
69.67
3sa
f1 (ppm)


8.72
8.72
8.71
8.70
8.70
8.14
8.13
8.13
8.12
8.11
8.11
8.10
7.53
7.52
7.52
7.52
7.51
7.51
7.50
7.50
7.49
7.49
7.47
7.47
7.43
7.42
7.42
7.42
7.42
7.40
7.40
7.39
7.39
7.38
7.38
7.37
7.37
7.36
7.27
7.25
7.25
7.25
5.34
5.34
5.32
5.29
N
S
O
3ta
1.00
1.00
1.00
2.00
1.00
1.00
2.00
f1 (ppm)


159.56
146.08
144.47
135.59
133.42
130.37
129.97
129.96
127.24
126.30
125.60
123.96
112.75
70.43
N
S
O
3ta
f1 (ppm)


9.18 9.17 9.17 9.16 9.16 9.15 9.15 9.12 8.50 8.49 8.49 8.47 8.47 8.36 8.36 8.36 8.34 8.34 7.82 7.82 7.82 7.81 7.81 7.80 7.80 7.80 7.79 7.78 7.78 7.77 7.77 7.64 7.63 7.63 7.61 7.61 7.53 7.53 7.52 7.51 7.50 7.50 7.49 7.49 7.47 7.47 7.47 7.46 7.45 7.45 7.45 7.44 7.43 7.42 7.42 7.28 7.28 7.28 5.40
3ta
1.00 1.00 0.99 1.13 1.00 1.01 0.99 1.02 1.02 2.00
f1 (ppm)
175.64 165.77 159.43 155.77 149.15 135.45 130.69 129.69 129.10 128.88 126.83 126.80 126.47 126.33 125.30 124.96 122.30 117.96 114.83 104.64 69.71
3ta
f1 (ppm)


8.86
8.86
8.44
8.44
8.42
8.42
7.96
7.96
7.96
7.94
7.94
7.94
7.92
7.90
7.70
7.70
7.69
7.69
7.68
7.67
7.67
7.48
7.47
7.46
7.46
7.46
7.45
7.44
6.99
6.99
6.97
6.97
6.86
6.86
5.18
3.87
N
O
OMe
3ab
1.00
1.00
1.00
1.00
1.00
1.00
1.00
2.00
3.00
f1 (ppm)


159.43
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130.92
128.68
127.67
126.91
124.65
123.71
122.47
113.69
111.06
109.50
69.47
55.48
N
O
OMe
3ab
f1 (ppm)


8.90
8.48
8.46
7.98
7.98
7.97
7.96
7.96
7.96
7.89
7.88
7.73
7.73
7.72
7.71
7.71
7.70
7.70
7.50
7.49
7.48
7.48
7.48
7.47
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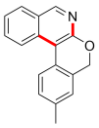
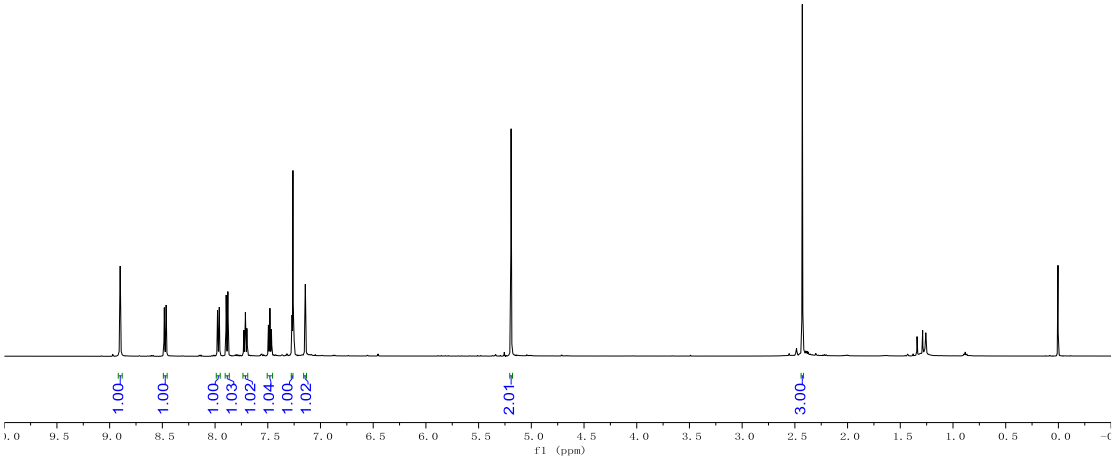
7.25
7.15
7.14
7.14
5.19
2.43


N
O

3ac


1.00
1.00
1.00
1.03
1.02
1.04
1.00
1.02
2.01
3.00
f1 (ppm)


8.81
8.35
8.33
8.33
8.01
8.01
8.01
8.00
8.00
7.99
7.91
7.90
7.90
7.90
7.90
7.89
7.89
7.74
7.74
7.73
7.73
7.72
7.71
7.71
7.51
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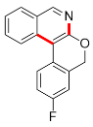
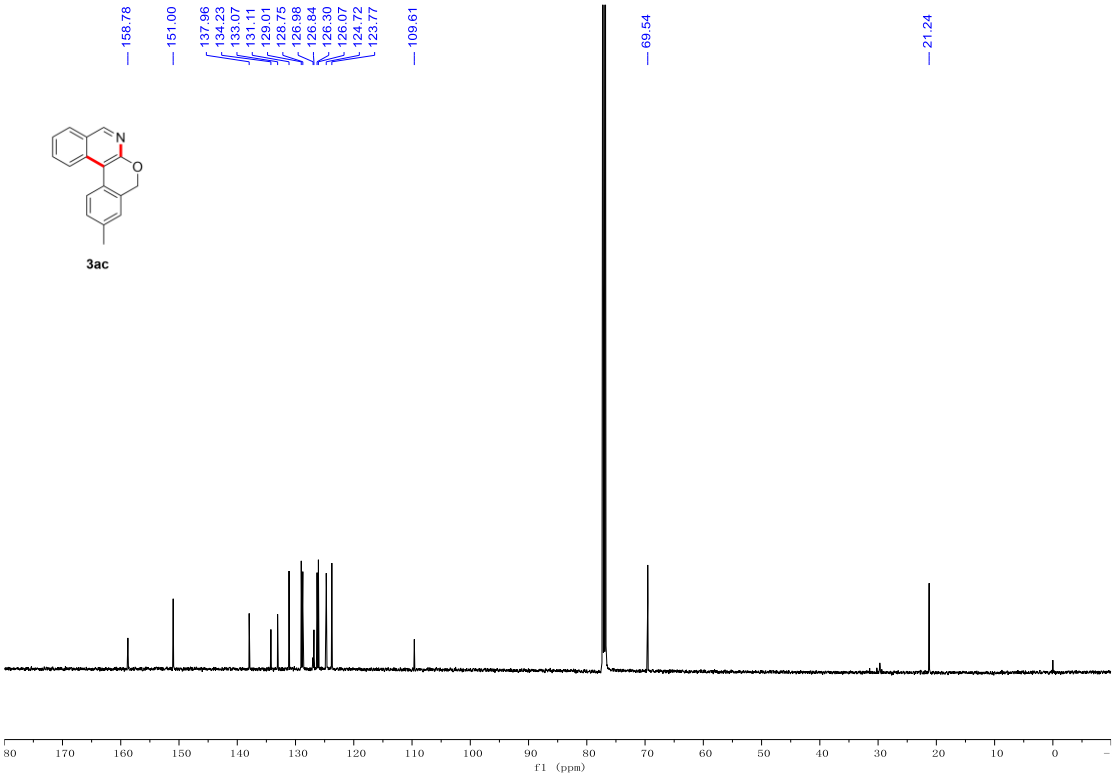
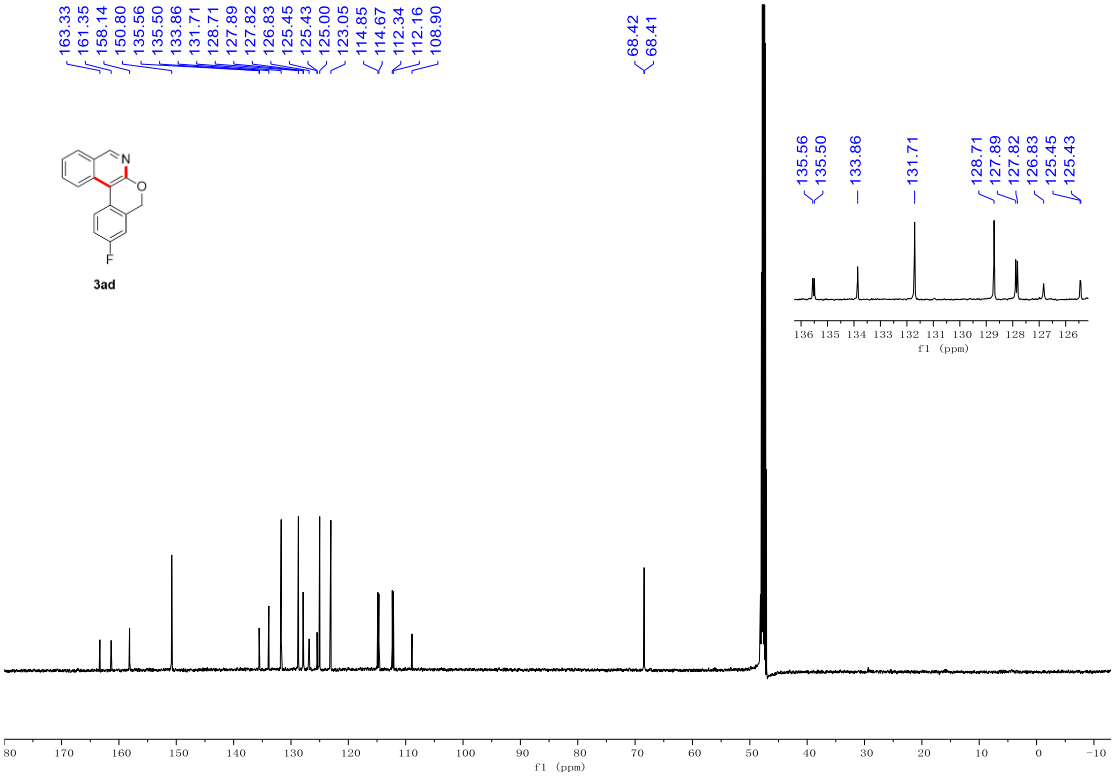
7.16
7.16
7.15
7.14
7.13
5.12


N
O
F

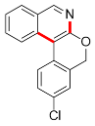
3ad

0.97
1.00
1.00
1.00
1.00
1.00
2.00
2.00
f1 (ppm)

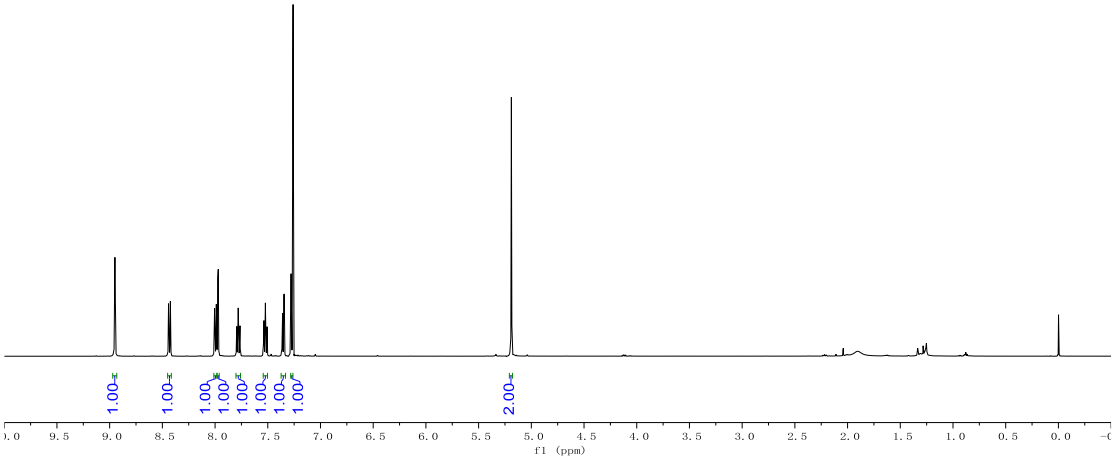

158.78
151.00
137.96
134.23
133.07
131.11
129.01
128.75
126.98
126.84
126.30
126.07
124.72
123.77
109.61
69.54
21.24
3ac
f1 (ppm)

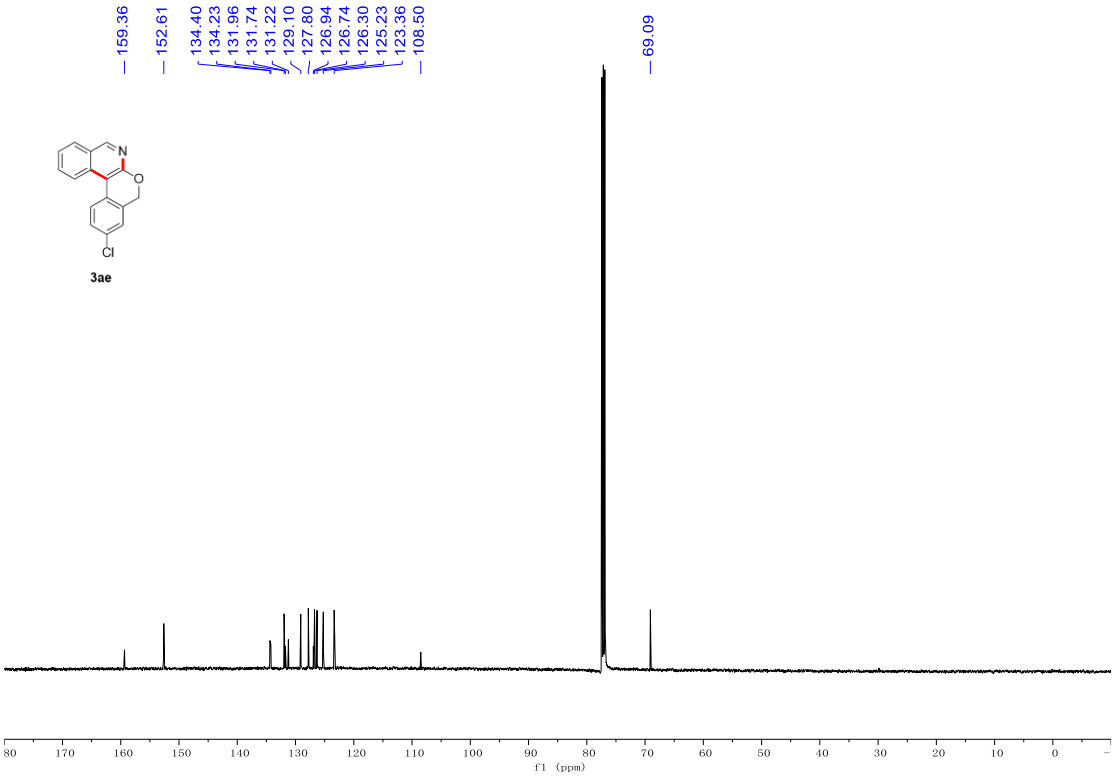

163.33
161.35
158.14
150.80
135.56
135.50
133.86
131.71
128.71
127.89
127.82
126.83
125.45
125.43
125.00
123.05
114.85
114.67
112.34
112.16
108.90
68.42
68.41
3ad
135.56
135.50
133.86
131.71
128.71
127.89
127.82
126.83
125.45
125.43
f1 (ppm)


8.95
8.44
8.42
8.00
7.99
7.97
7.97
7.80
7.79
7.78
7.78
7.78
7.77
7.76
7.54
7.54
7.53
7.52
7.52
7.51
7.51
7.36
7.36
7.35
7.34
7.28
7.27
7.26
5.19


N
O
Cl

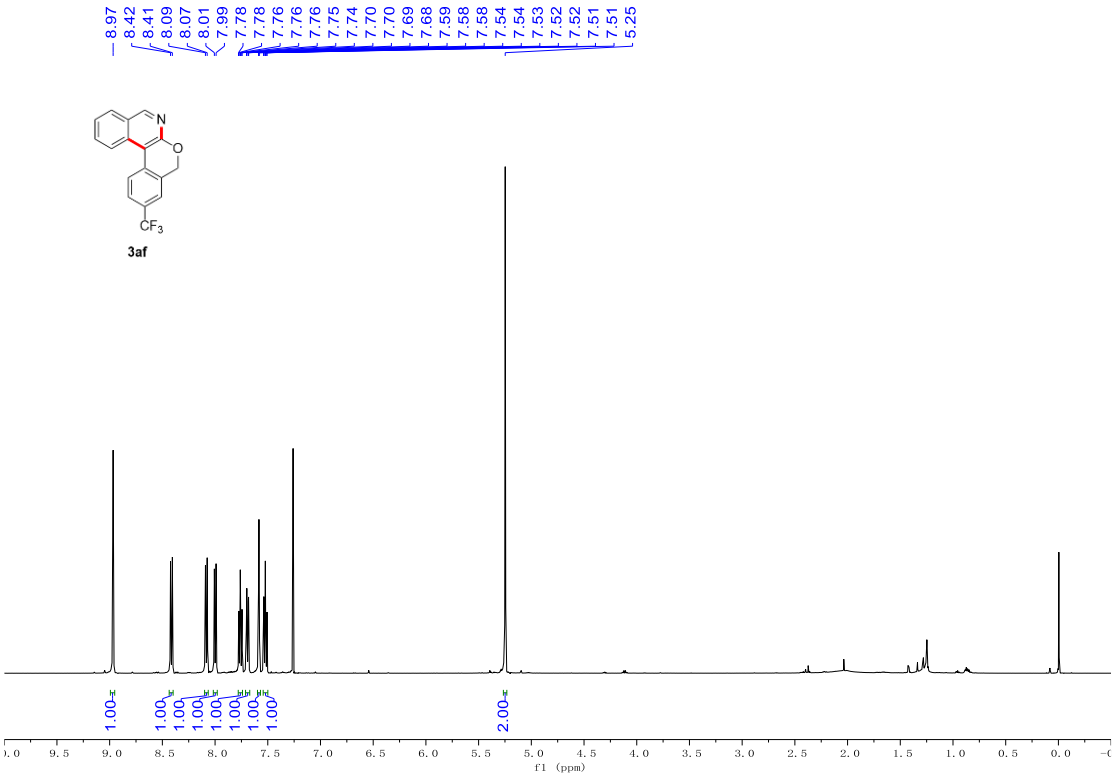
3ae


1.00
1.00
1.00
1.00
1.00
1.00
1.00
2.00
f1 (ppm)


159.36
152.61
134.40
134.23
131.96
131.74
131.22
129.10
127.80
126.94
126.74
126.30
125.23
123.36
108.50
69.09
f1 (ppm)

N
O
Cl

3ae


8.97
8.42
8.41
8.09
8.07
8.01
7.99
7.78
7.78
7.76
7.76
7.76
7.75
7.74
7.70
7.70
7.69
7.68
7.59
7.58
7.58
7.54
7.54
7.53
7.52
7.52
7.51
7.51
5.25
N
O
CF3
3af
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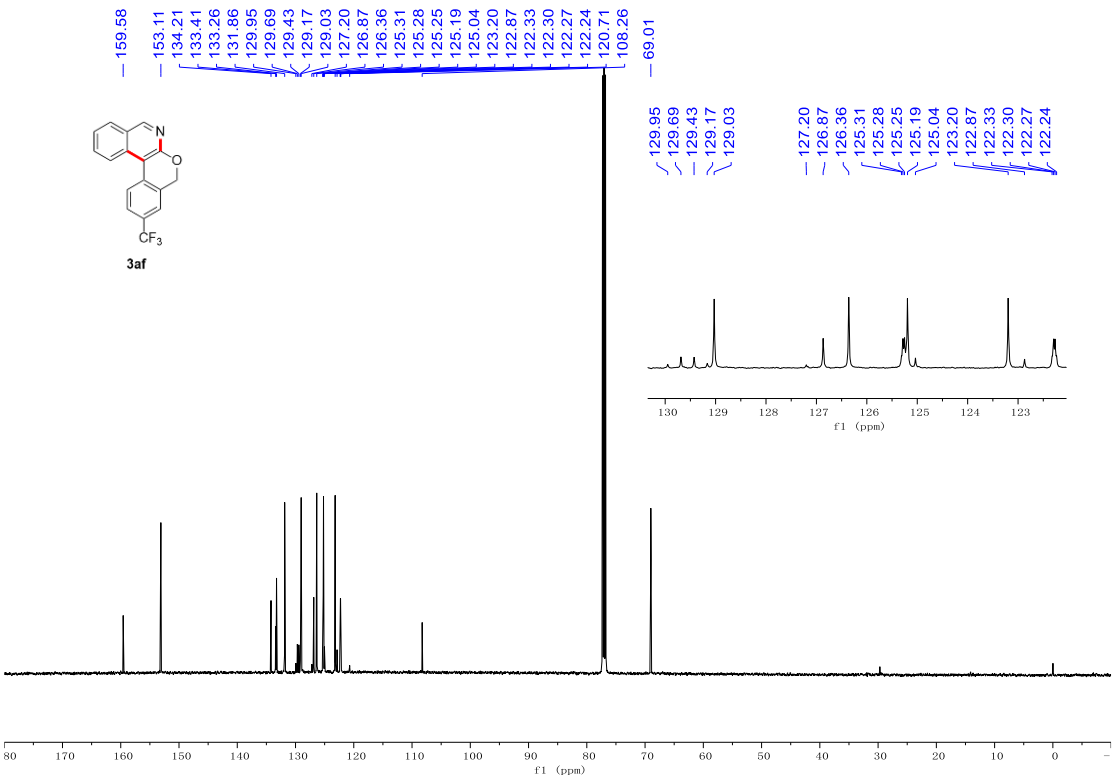
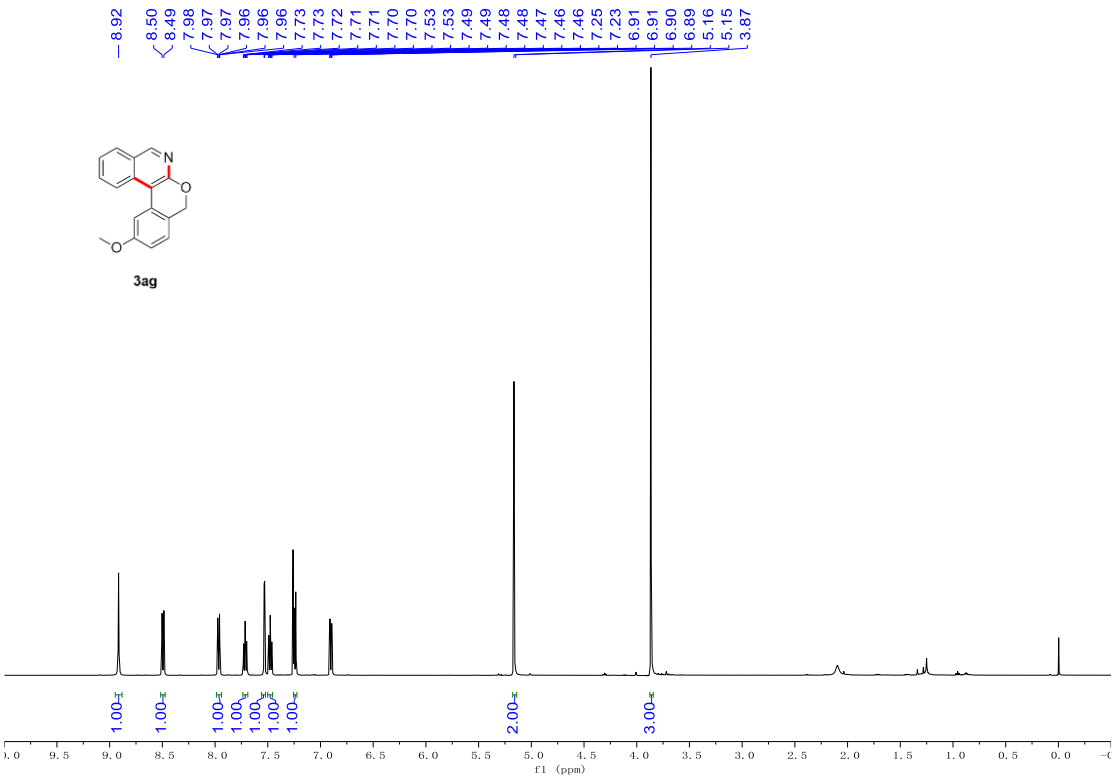
1.00
1.00
1.00
1.00
1.00
1.00
1.00
2.00
f1 (ppm)


159.58
153.11
134.21
133.41
133.26
131.86
129.95
129.69
129.43
129.17
129.03
127.20
126.87
126.36
125.31
125.28
125.25
125.19
125.04
123.20
122.87
122.33
122.30
122.27
122.24
120.71
108.26
69.01
N
O
CF3
3af
f1 (ppm)
f1 (ppm)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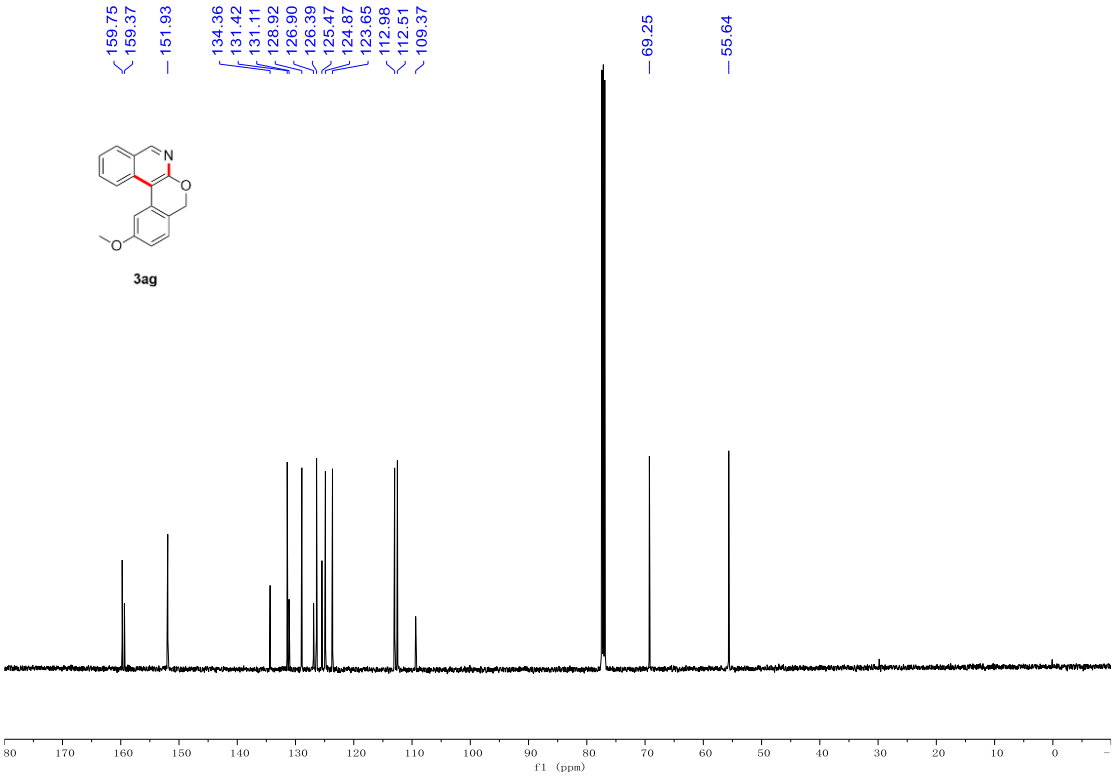
7.97
7.96
7.96
7.96
7.73
7.73
7.72
7.71
7.71
7.70
7.70
7.53
7.53
7.49
7.49
7.48
7.48
7.47
7.46
7.46
7.25
7.23
6.91
6.91
6.90
6.89
5.16
5.15
3.87
N
O
O
3ag
1.00
1.00
1.00
1.00
1.00
1.00
2.00
3.00
f1 (ppm)


159.75
159.37
151.93
134.36
131.42
131.11
128.92
126.90
126.39
125.47
124.87
123.65
112.98
112.51
109.37
69.25
55.64
N
O
O
3ag
f1 (ppm)


8.98
8.98
7.81
7.81
7.79
7.79
7.54
7.54
7.52
7.52
7.52
7.52
7.50
7.50
7.48
7.48
7.47
7.47
7.46
7.46
7.45
7.44
7.44
7.43
7.43
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7.42
7.42
7.41
7.40
7.40
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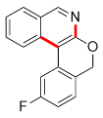
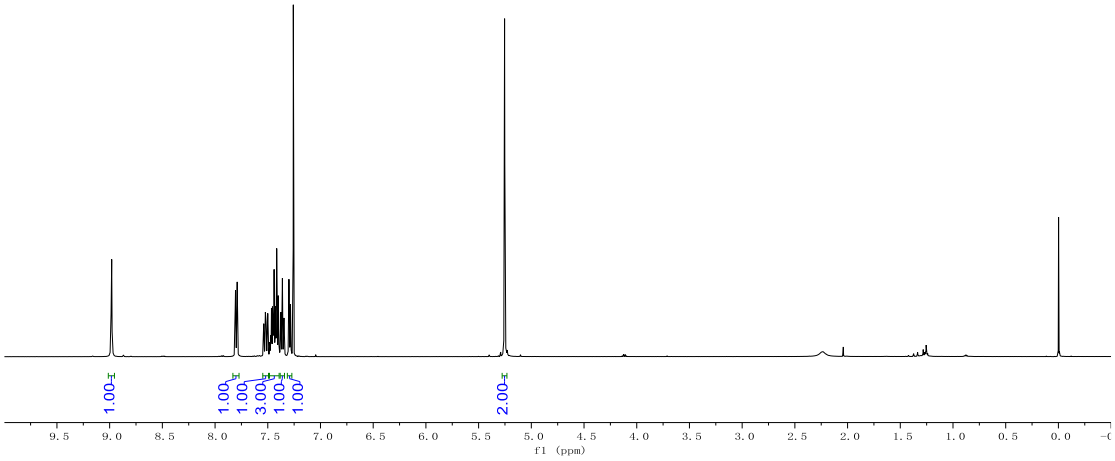
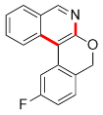
7.28
5.25


N
O
F

3ah

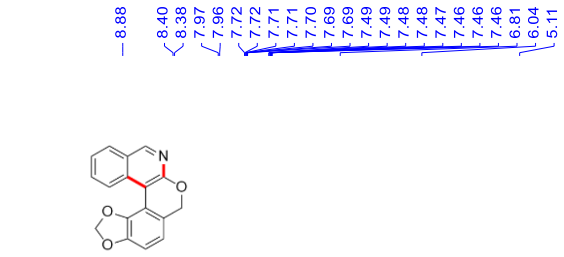

1.00
1.00
1.00
3.00
1.00
1.00
2.00
f1 (ppm)


159.76
157.89
155.87
151.55
130.76
129.45
128.27
128.23
127.97
127.86
127.46
127.45
127.26
124.60
124.53
124.34
124.31
123.99
123.50
123.39
115.98
115.81
106.34

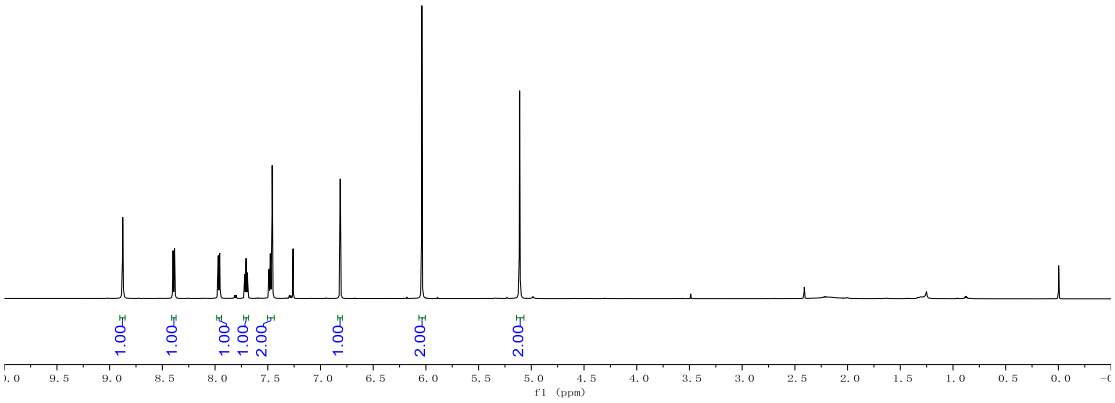

N
O
F

3ah

69.41
128.27
128.23
127.97
127.86
127.46
127.45
127.26
124.60
124.53
124.34
124.31
123.99
123.50
123.39
f1 (ppm)
f1 (ppm)


8.88
8.40
8.38
7.97
7.96
7.72
7.72
7.71
7.71
7.70
7.69
7.69
7.49
7.49
7.48
7.48
7.47
7.46
7.46
7.46
6.81
6.04
5.11

3ai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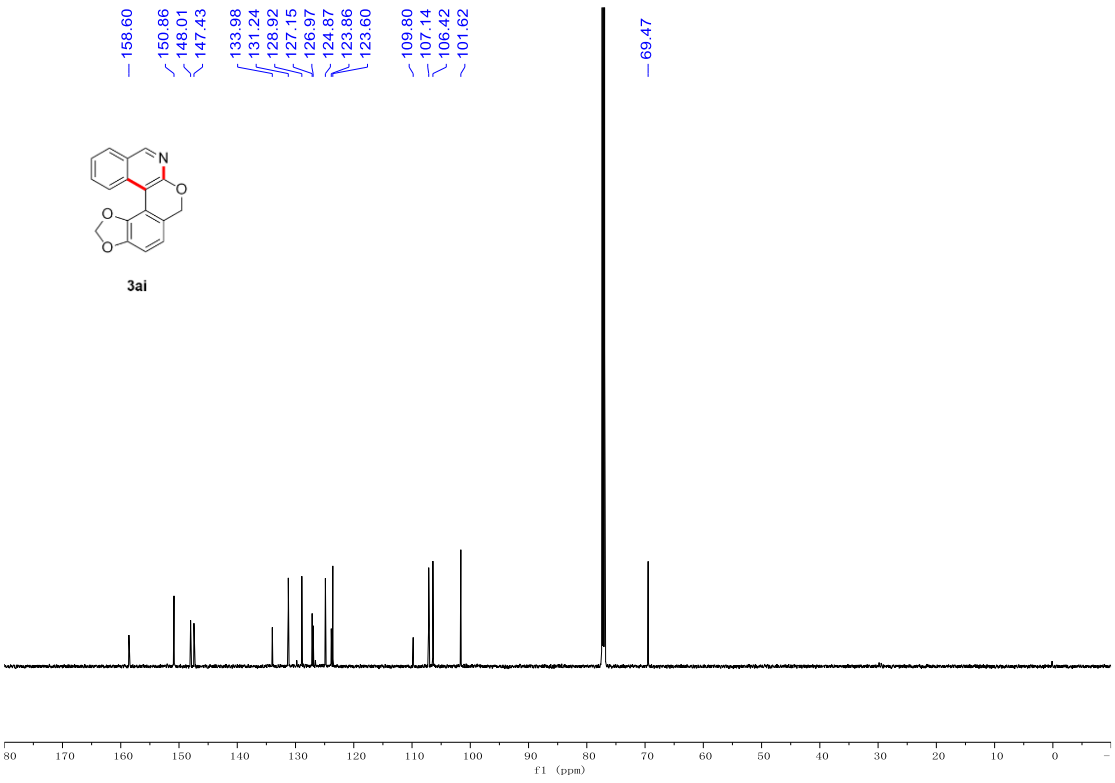
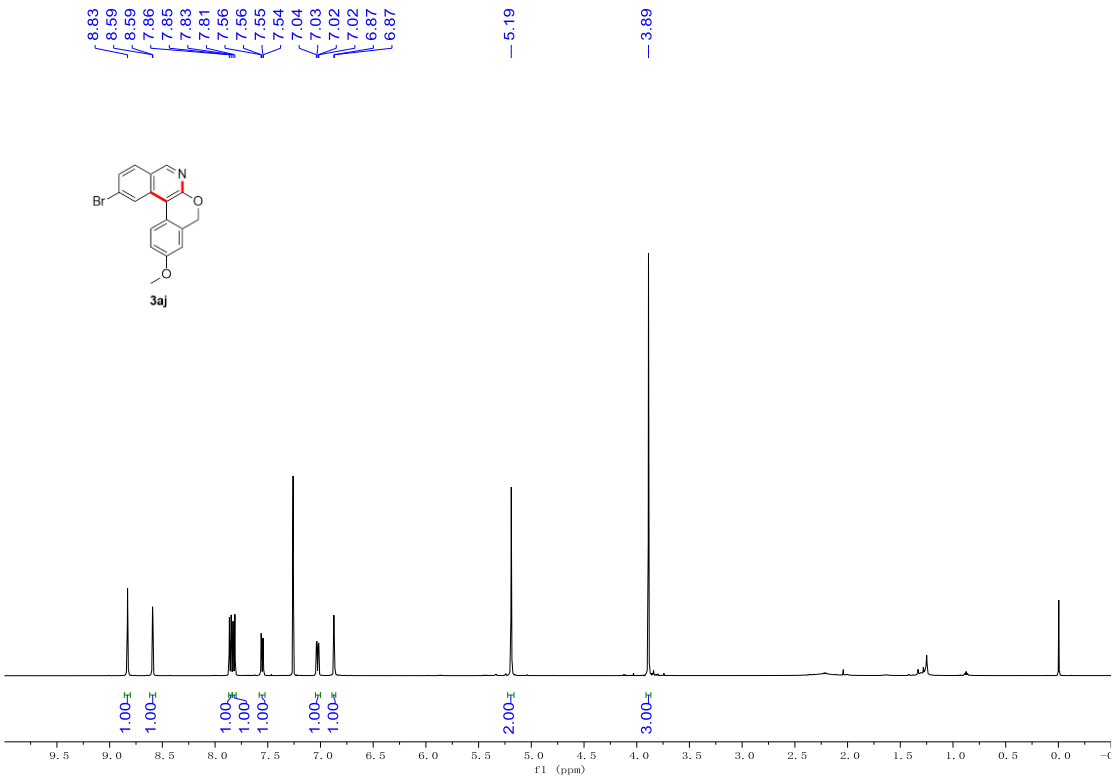
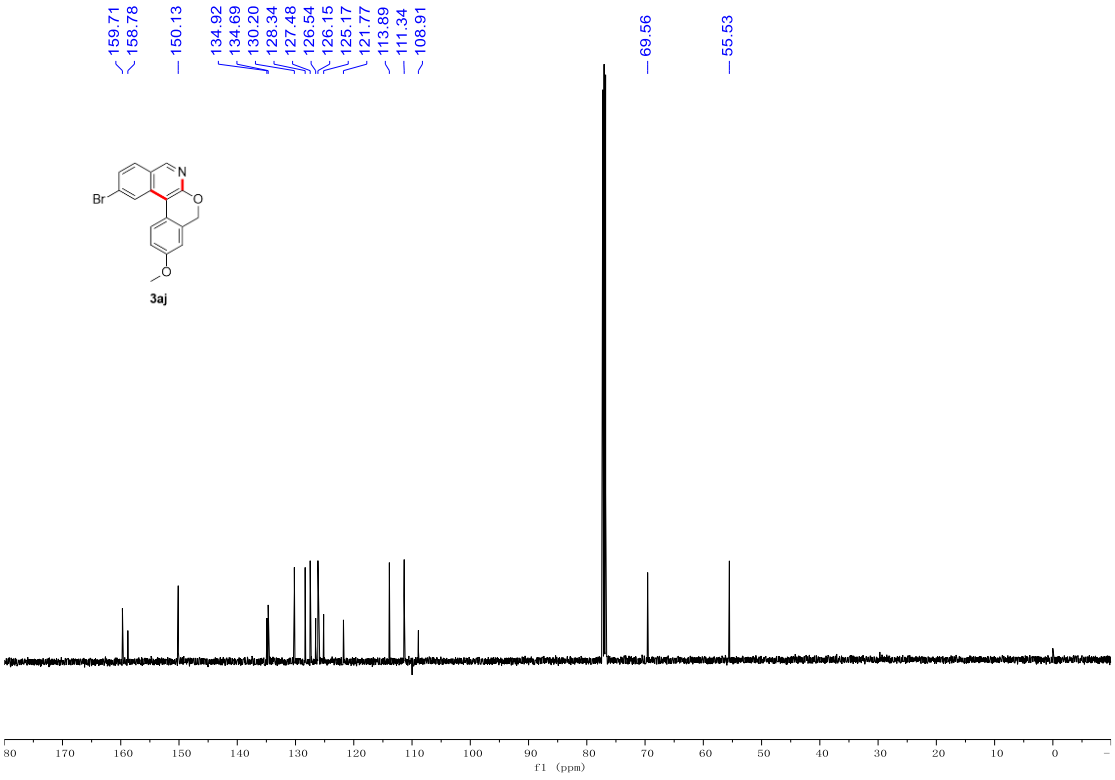
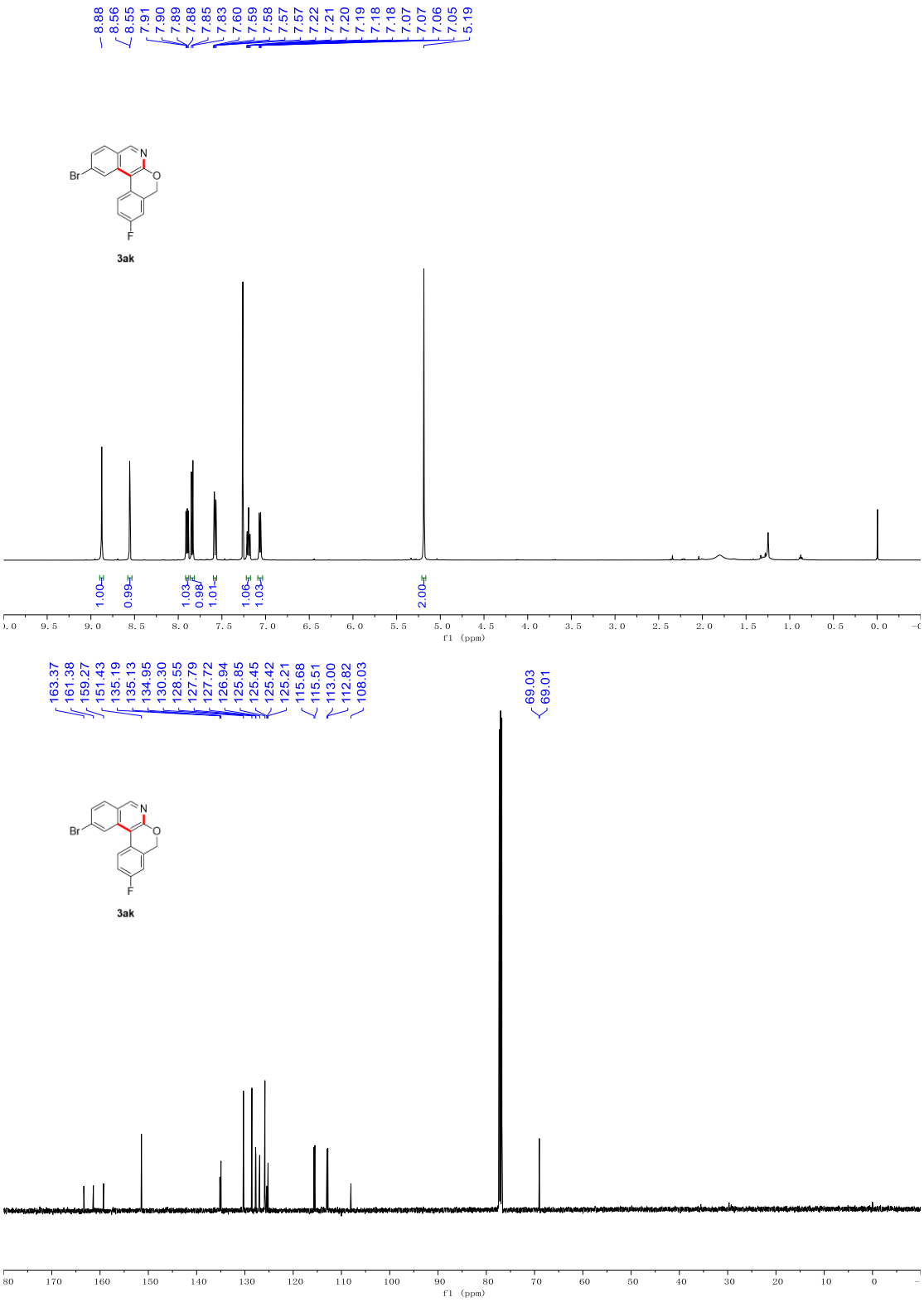
1.00
1.00
1.00
2.00
1.00
2.00
2.00
f1 (ppm)

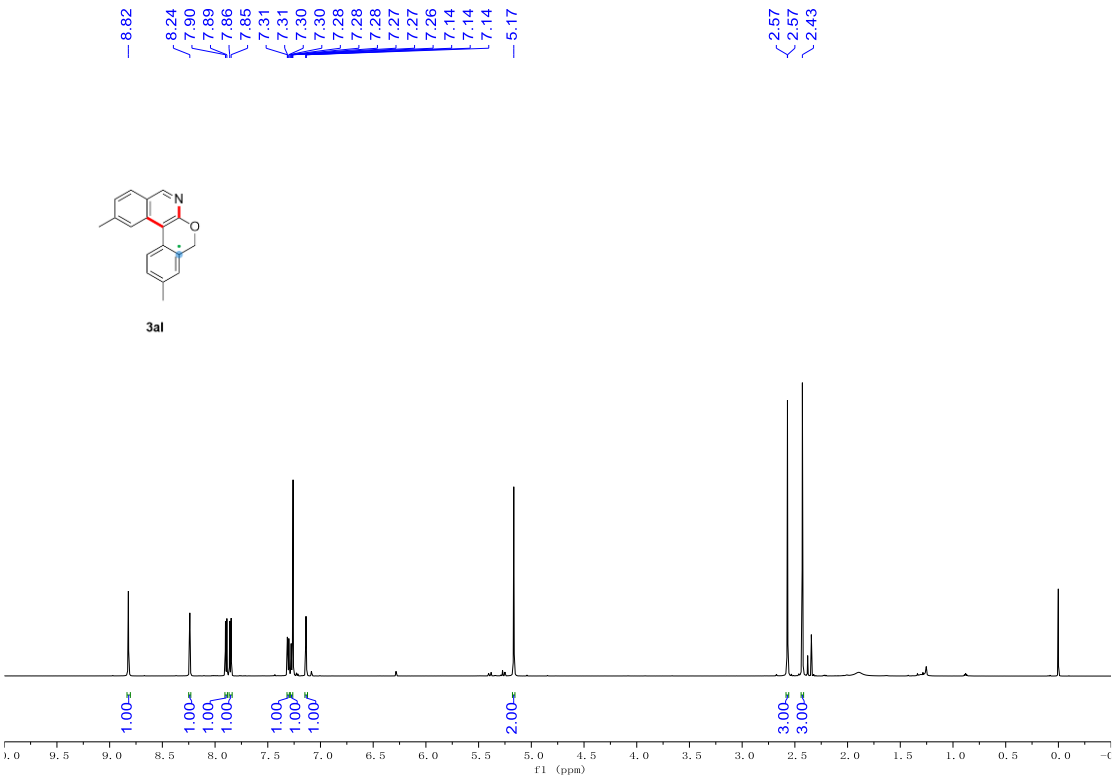

158.60
150.86
148.01
147.43
133.98
131.24
128.92
127.15
126.97
124.87
123.86
123.60
109.80
107.14
106.42
101.62
69.47
f1 (ppm)

3ai


8.83
8.59
8.59
7.86
7.85
7.83
7.81
7.56
7.56
7.55
7.54
7.04
7.03
7.02
7.02
6.87
6.87
5.19
3.89
Br
N
O
O
3aj
1.00
1.00
1.00
1.00
1.00
1.00
2.00
3.00
f1 (ppm)


159.71
158.78
150.13
134.92
134.69
130.20
128.34
127.48
126.54
126.15
125.17
121.77
113.89
111.34
108.91
69.56
55.53
Br
N
O
O
3aj
f1 (ppm)


8.88
8.56
8.55
7.91
7.90
7.89
7.88
7.85
7.83
7.60
7.59
7.58
7.57
7.57
7.22
7.21
7.20
7.19
7.18
7.18
7.07
7.07
7.06
7.05
5.19
Br
N
O
F
3ak
1.00
0.99
1.03
0.98
1.01
1.06
1.03
2.00
f1 (ppm)
163.37
161.38
159.27
151.43
135.19
135.13
134.95
130.30
128.55
127.79
127.72
126.94
125.85
125.45
125.42
125.21
115.68
115.51
113.00
112.82
108.03
69.03
69.01
Br
N
O
F
3ak
f1 (ppm)


8.82
8.24
7.90
7.89
7.86
7.85
7.31
7.31
7.30
7.30
7.28
7.28
7.28
7.27
7.27
7.26
7.14
7.14
7.14
5.17
2.57
2.57
2.43
3al
1.00
1.00
1.00
1.00
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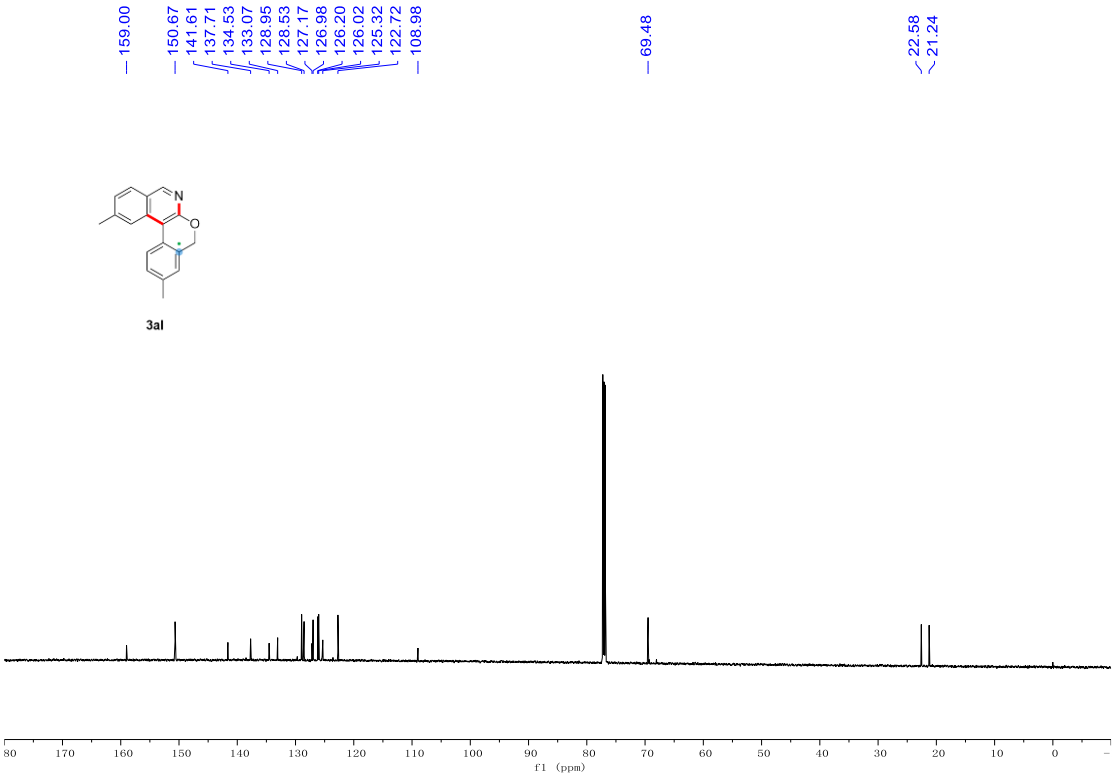
1.00
2.00
3.00
3.00
f1 (ppm)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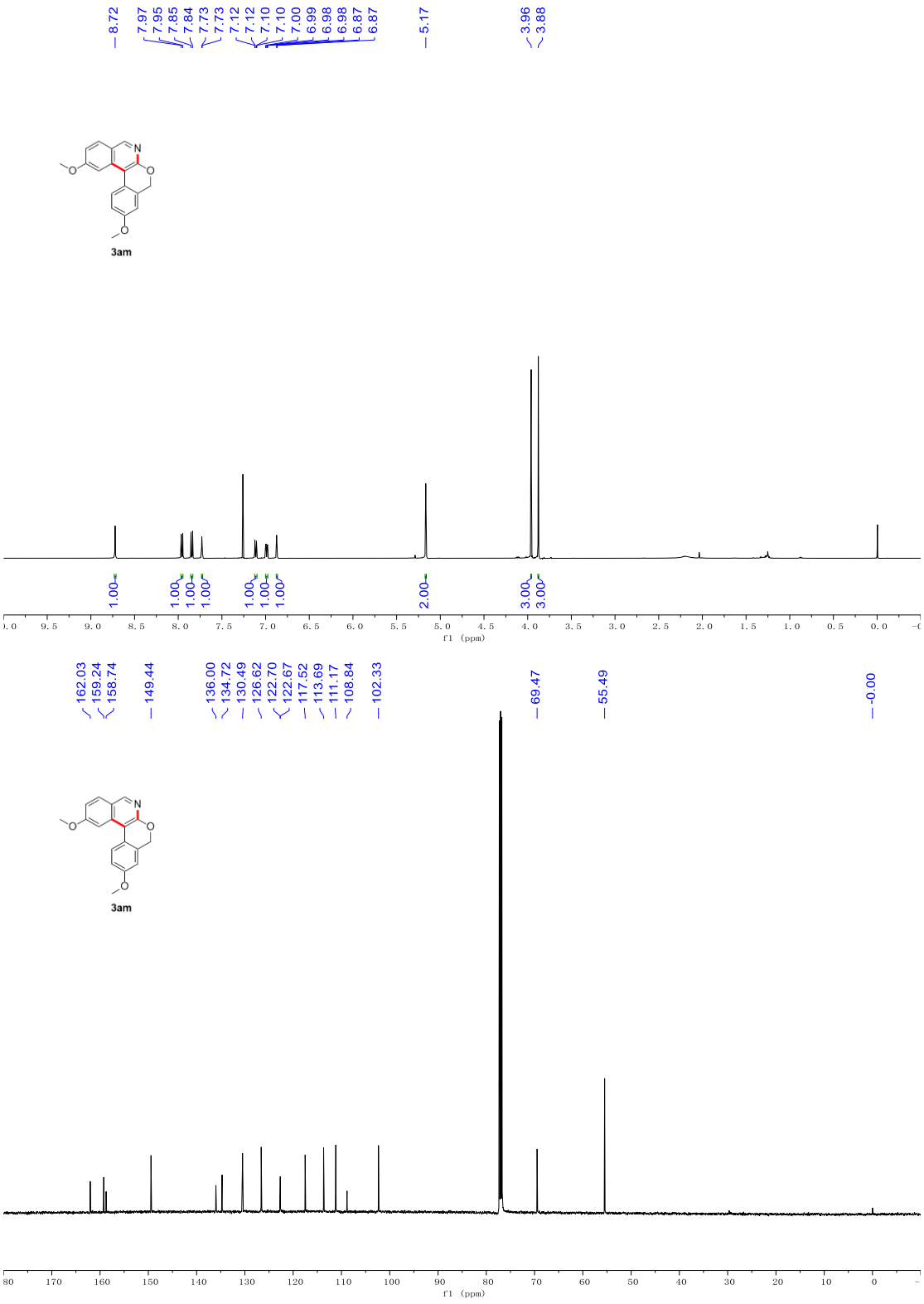
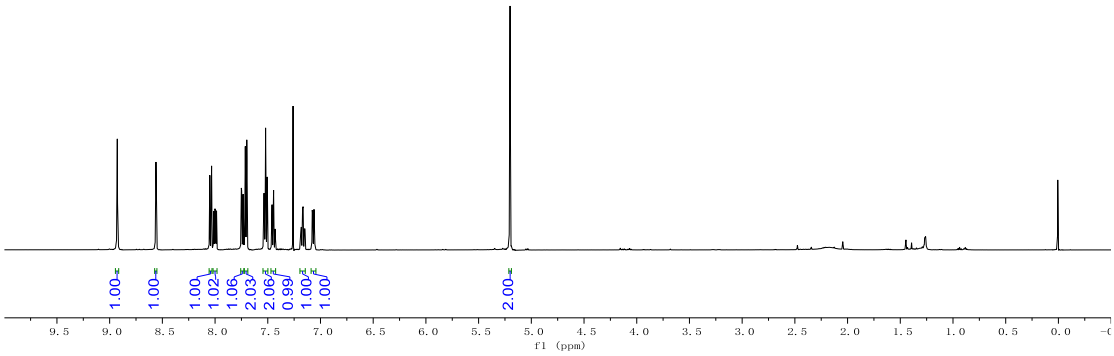
141.61
137.71
134.53
133.07
128.95
128.53
127.17
126.98
126.20
126.02
125.32
122.72
108.98
69.48
22.58
21.24
3al
f1 (ppm)


8.72
7.97
7.95
7.85
7.84
7.73
7.73
7.12
7.12
7.10
7.10
7.00
6.99
6.98
6.98
6.87
6.87
5.17
3.96
3.88
3am
1.00
1.00
1.00
1.00
1.00
1.00
2.00
3.00
3.00
f1 (ppm)
162.03
159.24
158.74
149.44
136.00
134.72
130.49
126.62
122.70
122.67
117.52
113.69
111.17
108.84
102.33
69.47
55.49
-0.00
3am
f1 (ppm)


8.93
8.56
8.56
8.05
8.03
8.01
8.00
8.00
7.99
7.75
7.75
7.73
7.73
7.72
7.71
7.70
7.70
7.54
7.54
7.54
7.52
7.52
7.52
7.51
7.51
7.46
7.46
7.46
7.45
7.45
7.44
7.44
7.43
7.43
7.43
7.19
7.18
7.17
7.16
7.15
7.15
7.08
7.07
7.06
7.06
5.20


Ph
N
O
F

3an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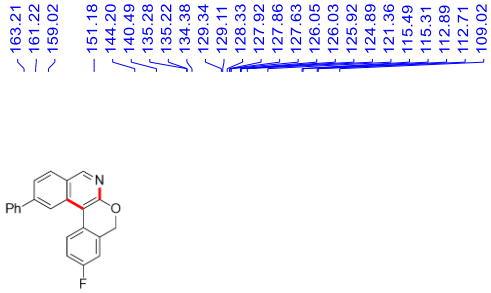
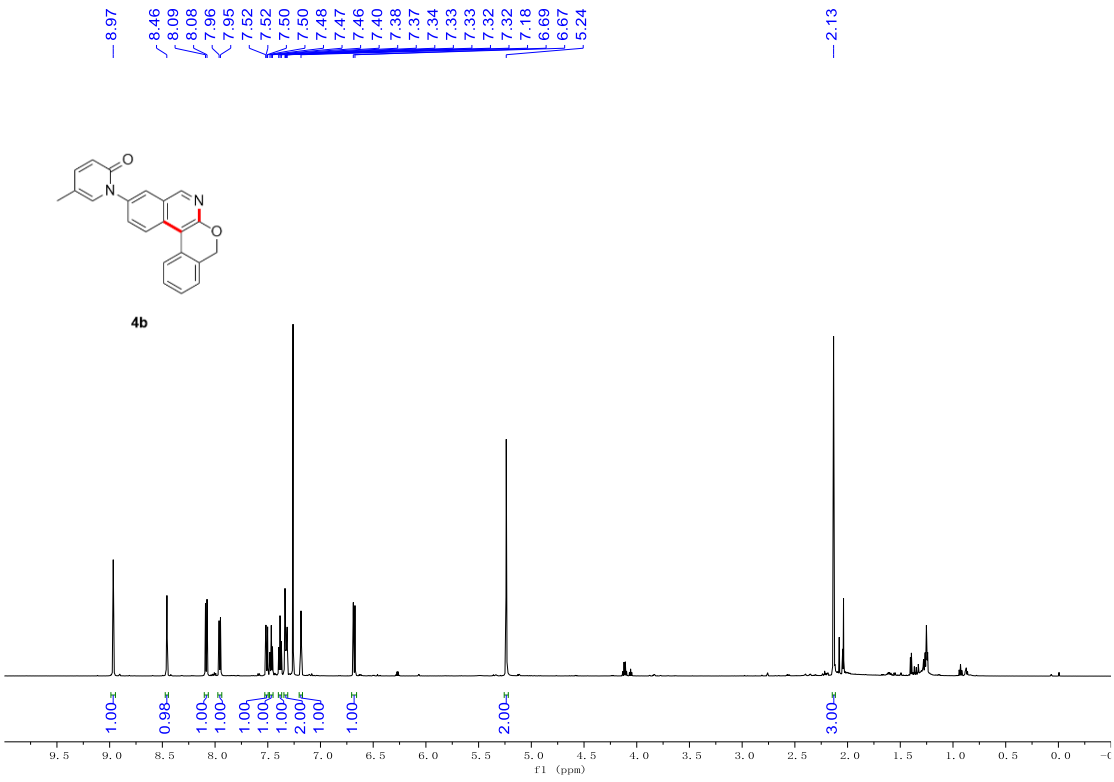
1.00
1.02
1.06
2.03
2.06
0.99
1.00
1.00
2.00
f1 (ppm)


Ph
N
O
F

3an

163.21
161.22
159.02
151.18
144.20
140.49
135.28
135.22
134.38
129.34
129.11
128.33
127.92
127.86
127.63
126.05
126.03
125.92
124.89
121.36
115.49
115.31
112.89
112.71
109.02
69.01
f1 (ppm)

135.28
135.22
134.38
129.34
129.11
128.33
127.92
127.86
127.63
126.05
126.03
125.92
124.89
121.36
115.49
115.31
112.89
112.71
f1 (ppm)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8.09
8.08
7.96
7.95
7.52
7.52
7.50
7.50
7.48
7.47
7.46
7.40
7.38
7.37
7.34
7.33
7.33
7.32
7.32
7.18
6.69
6.67
5.24
2.13
4b
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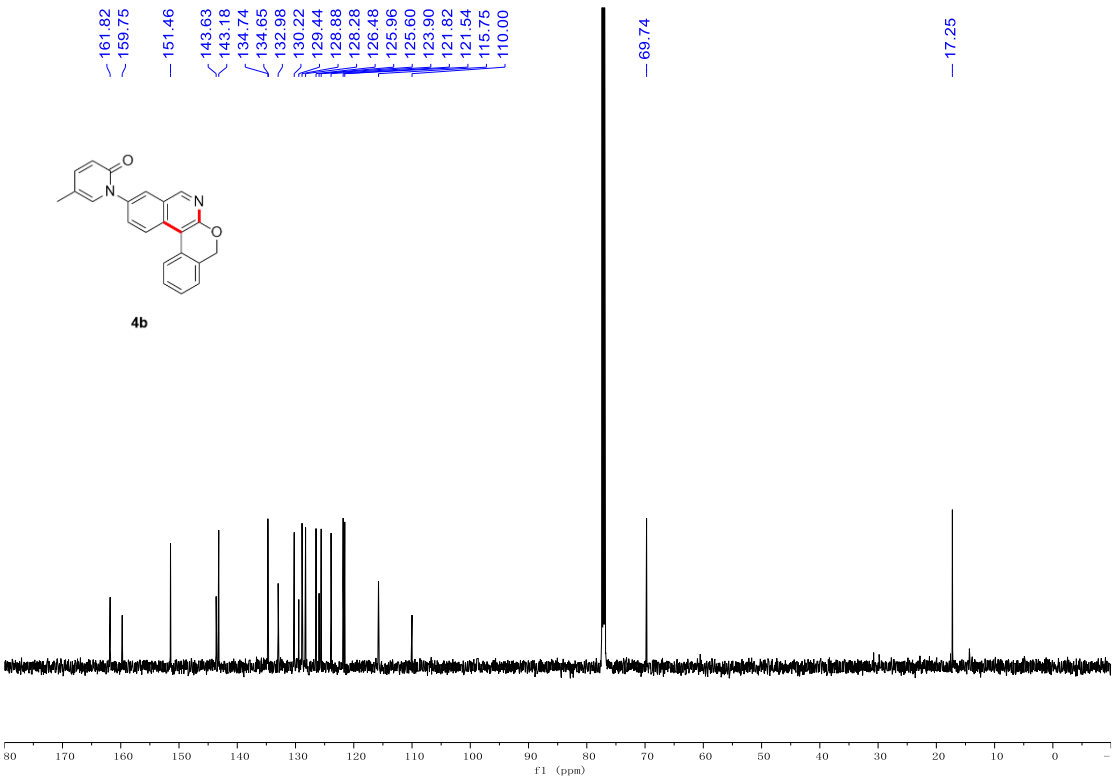
0.98
1.00
1.00
1.00
1.00
2.00
1.00
1.00
2.00
3.00
f1 (ppm)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143.18
134.74
134.65
132.98
130.22
129.44
128.88
128.28
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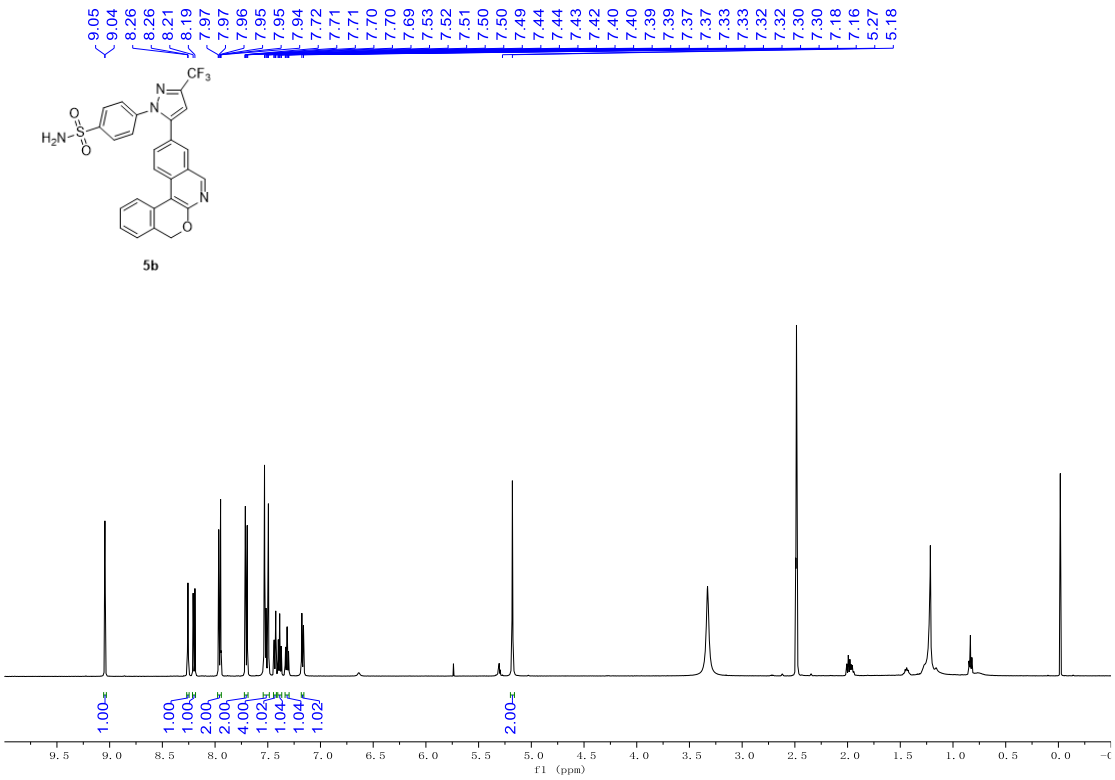
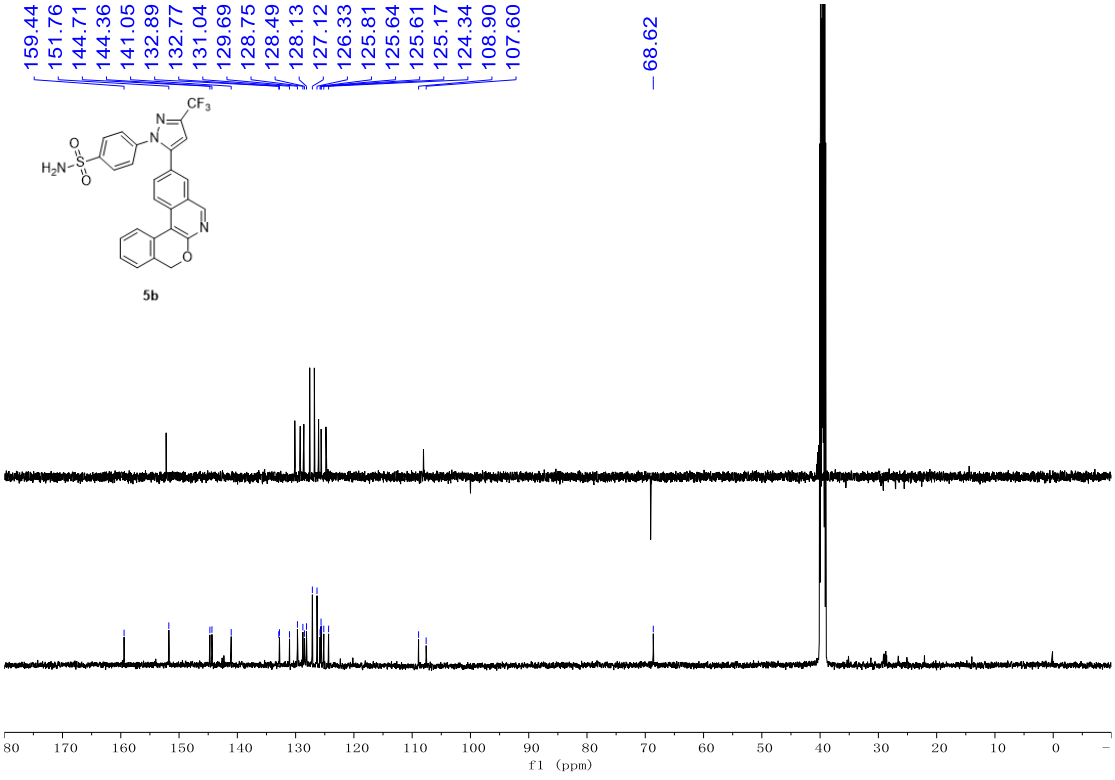
125.96
125.60
123.90
121.82
121.54
115.75
110.00
69.74
17.25
4b
f1 (ppm)


9.05
9.04
8.26
8.26
8.21
8.19
7.97
7.97
7.96
7.95
7.95
7.94
7.72
7.71
7.71
7.70
7.70
7.69
7.53
7.52
7.51
7.50
7.50
7.49
7.44
7.44
7.43
7.42
7.40
7.40
7.39
7.39
7.37
7.37
7.33
7.33
7.32
7.32
7.30
7.30
7.18
7.16
5.27
5.18
CF3
N
N
O
S
O
H2N
N
O
5b
1.00
1.00
1.00
2.00
2.00
4.00
1.02
1.04
1.04
1.02
2.00
f1 (ppm)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144.36
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132.89
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131.04
129.69
128.75
128.49
128.13
127.12
126.33
125.81
125.64
125.61
125.17
124.34
108.90
107.60
68.62
CF3
N
N
O
S
O
H2N
N
O
5b
f1 (ppm)

VI. Reference

1. (a)A. Ren, P. Lu and Y. Wang, Convenient preparation of 4-diazoisochroman-3-imines and 3-subsituted 3,5-dihydroisochromeno[3,4-d][1,2,3]triazoles, *Chem. Commun.*, 2017, **53**, 3769-3772; (b)M. Zhang, F. Wu, H. Wang, J. Wu and W. Chen, Copper-Catalyzed Sequential Azomethine Imine-Alkyne Cycloaddition and Umpolung Thiolation Reactions, *Adv. Synth. Catal.*, 2017, **359**, 2768-2772.