Supporting Information

MOF confinement enables selective synthesis of novel oxazoles from indole and formaldehyde

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1. Experimental

1.1 Methods

Unless specially indicated, all chemical reagents were purchased from commercial sources and were used as received without further purification. Transmission electron microscopy (TEM) and EDS elemental mapping were carried out on JEM-F200 at 200 kV. Fourier transform infrared spectroscopy (FT-IR) spectra were recorded on a Thermo Fisher Scientific Nicolet iS50 FT-IR spectrophotometer. Inductively coupled plasma-optical emission spectroscopy (ICP-OES) data for the content of W was carried out on an ICPE9000 emission spectrometer. N_2 sorption curves were obtained by Micromeritics ASAP 2420-4MP Plus automated sorption analyzer under 77 K. The powder X-ray diffraction (PXRD) patterns were collected by Cu-Kα radiation (λ = 1.5406 Å) at a Rigaku UltimaIv X-ray diffractometer. ^{1}H NMR spectra were performed on a Bruker Advance NEO 600 MHz.

1.2 Materials preparation

Synthesis of PTA@UiO-66

The UiO-66 sample was synthesized using $ZrCl_4$ and terephthalic acid (H_2BDC) as reactants according to the reported method with minor modifications[1]. Typically, 25 mL of dimethylformamide (DMF) solution of $ZrCl_4$ (330 mg) and 10 mL of DMF solution of H_2BDC (228 mg), and three different quantities of PTA (1.0, 2.0, and 3.0 g) were mixed in a 50 mL glass vial. Then, 6 mL of acetic acid was added, sealed, and allowed to react at 120 °C for 24 hours. The product was isolated by centrifugation and rinsed with DMF and MeOH. Finally, PTA@UiO-66 was dried at 80 °C under a vacuum overnight. The loaded PTA was 3.1%, 12.1%, 24.3%, respectively, calculated based on the ICP-OES measurement W content.

Synthesis of POM@UiO-66

Typically, $ZrCl_4$ (1120 mg) and H_2BDC (840 mg) in 220 mL of dimethylformamide (DMF) solution were mixed with 1.0 g of different kinds of POM (Silicotungstic acid, STA and Phosphomolybdic acid, PMA) in a 500 mL glass bottle. Then, 21 mL of acetic acid was added, sealed, and allowed to react at 120 °C for 24 hours. The product was isolated by centrifugation and rinsed with DMF and MeOH. Finally, the obtained STA@UiO-66 and PMA@UiO-66 were dried in vacuum at 80 ℃ overnight. The loaded STA and PMA were 11.6% and 13.4%, respectively, calculated from the W/Mo content measured by ICP-OES.

Synthesis of PTA@MIL-101

PTA@MIL-101 was synthesized according to the literature with some modifications[2]. In a typical procedure, 533 mg $CrCl_3 \cdot 6H_2O$ (2.0 mmol), 333 mg H_2BDC (2.0 mmol) and 2.0 g PTA were dispersed in 12 mL H_2O. After vigorous stirring at room temperature for 3 min, the mixed solution was transferred into a Teflon-lined stainless-steel autoclave and heated at 210 ℃ for 24 h. As mentioned previously, a significant amount of nonreacted terephthalic acid is present both outside and within the pores of PTA@MIL-101. After filtration, the collected MIL-101 was washed twice with DMF. Then a solvothermal treatment was sequentially performed using ethanol (95 % EtOH with 5 % water) at 80 ℃ for 24 h. The solid was finally dried overnight at 150 ℃ under air atmosphere.

Synthesis of MIL-101-SO_3H

The MIL-101-SO_3H sample was synthesized using CrO_3 and Monosodium 2-sulfoterephthalic (H2BDC-SO3Na) acid as reactants[3]. Typically, 25 mL of deionized water solution of CrO_3 (665 mg) and H2BDC-SO3Na (1685 mg) and concentrated aqueous hydrochloric acid (0.5 mL, 12 N)were mixed in a 50 mL glass vial. Then, sealed and allowed to react at 180 °C for 6 days. The product was isolated by centrifugation and rinsed with DMF and MeOH. Finally, MIL-101-SO_3H was dried at 120 °C under a vacuum overnight.

2. Catalytic experiments

Confined reaction process of indole with formaldehyde

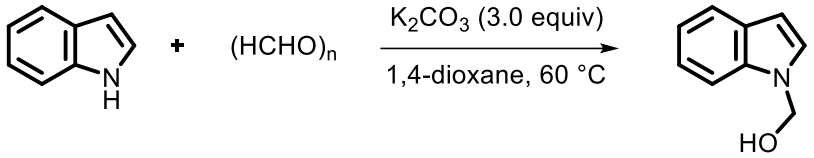
MOF catalyst (50 mg) or related homogeneous catalyst (10 mg), 100 μL of formaldehyde solution (~ 37%), indole or its derivative (0.30 mmol) were added to a 25 mL Schlenk tube equipped with a magnetic stirring bar. The mixture was sonicated for 10 minutes to promote uniform dispersion/dissolution of the catalyst. The mixture was stirred at 50 ℃ for 2 hours. After the reaction, the solid was isolated by centrifugation, washed several times with methanol, and dried in vacuum for later use. The product was isolated by preparative thin layer chromatography using a mixture of ethyl acetate and petroleum ether as the eluent.

The reaction process of (1*H*-indol-1-yl)methanol and formaldehyde to generate 1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol

PTA@UiO-66 catalyst (50 mg), 100 μL formaldehyde solution (~37%), and pre-synthesized (1*H*-indol-1-yl)methanol (0.20 mmol) were added to a 25 mL Schlenk tube equipped with a magnetic

stirring bar. The mixture was sonicated for 10 minutes to promote uniform dispersion/dissolution of the catalyst. The mixture was reacted at 50 ℃ for 2 hours. After the reaction, the solid was separated by centrifugation, washed several times with methanol, and dried in vacuum for later use. The product was isolated by preparative thin layer chromatography using a mixture of ethyl acetate and petroleum ether as the eluent.

General procedure for the synthesis of the reaction intermediate IM2.



This step was performed based on a literature procedure with some modifications[4]. A mixture of indole (1.0 mmol, 1.0 equiv), paraformaldehyde (2.0 mmol, 2.0 equiv), and K_2CO_3 (3.0 mmol, 3.0 equiv) in 1,4-dioxane (50 mL) was heated to 60 °C for 8 hours. Upon completion, the reaction mixture was quenched with brine (30 mL) and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. Purification of the crude product afforded **IM2** in approximately 90% yield.

3. References

[1] G.C. Shearer, J.G. Vitillo, S. Bordiga, S. Svelle, U. Olsbye, K.P. Lillerud, Functionalizing the Defects: Postsynthetic Ligand Exchange in the Metal Organic Framework UiO-66, Chem. Mater., 28 (2016) 7190–7193.

[2] Q. Deng, G. Nie, L. Pan, J.-J. Zou, X. Zhang, L. Wang, Highly selective self-condensation of cyclic ketones using MOF-encapsulating phosphotungstic acid for renewable high-density fuel, Green Chem., 17 (2015) 4473–4481.

[3] G. Akiyama, R. Matsuda, H. Sato, M. Takata, S. Kitagawa, Cellulose Hydrolysis by a New Porous Coordination Polymer Decorated with Sulfonic Acid Functional Groups, Adv. Mater., 23 (2011) 3294–3297.

[4] Xiao-Yu Zhou and Xia Chen, K_2CO_3-Promoted Highly Selective N-Hydroxymethylation of Indoles Under Metal- and Lewis Acid-Free Conditions. Letters in Organic Chemistry, 2021, 18, 160. DOI: 10.2174/1570178617999200728214752.

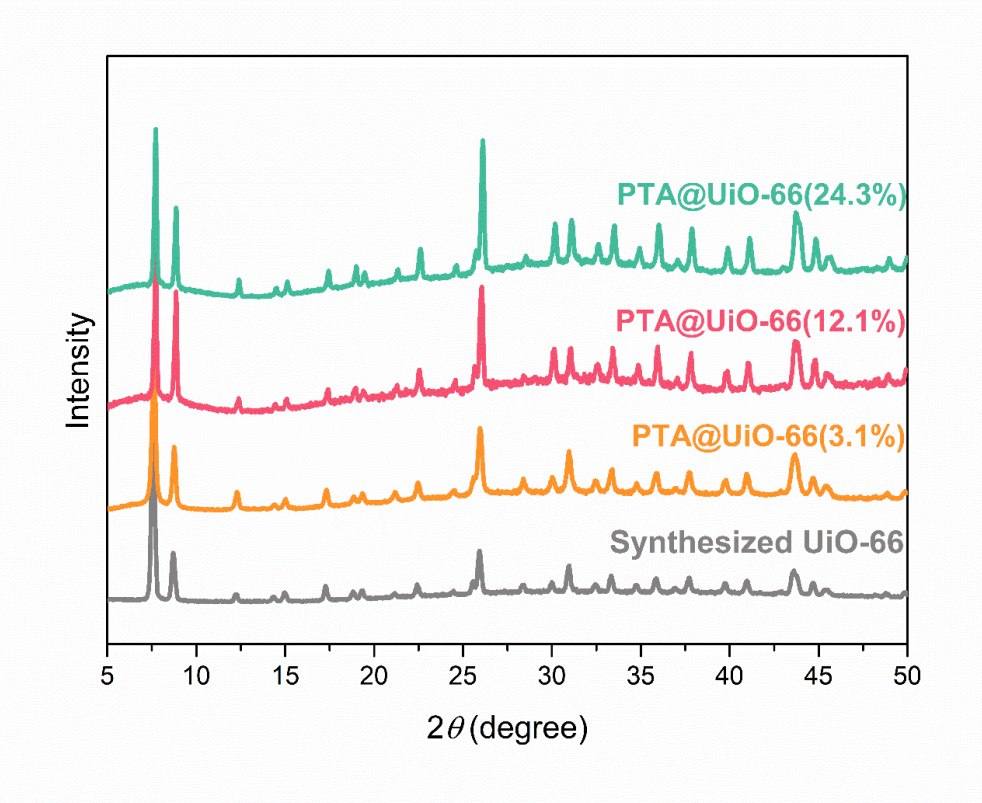


Fig. S1. PXRD patterns of catalysts.

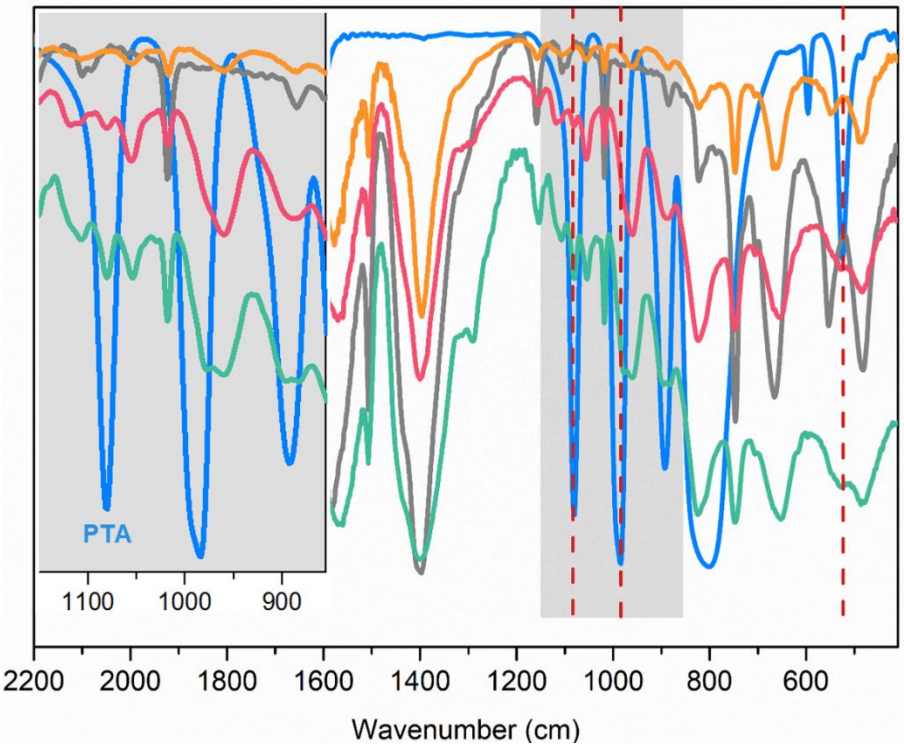


Figure S2. FT-IR spectraof catalysts. Green, PTA@UiO-66(34.3%); Prink, PTA@UiO-66(12.1%); Orange, PTA@UiO-66(3.1%); Gray, UiO-66; Blue, PTA.

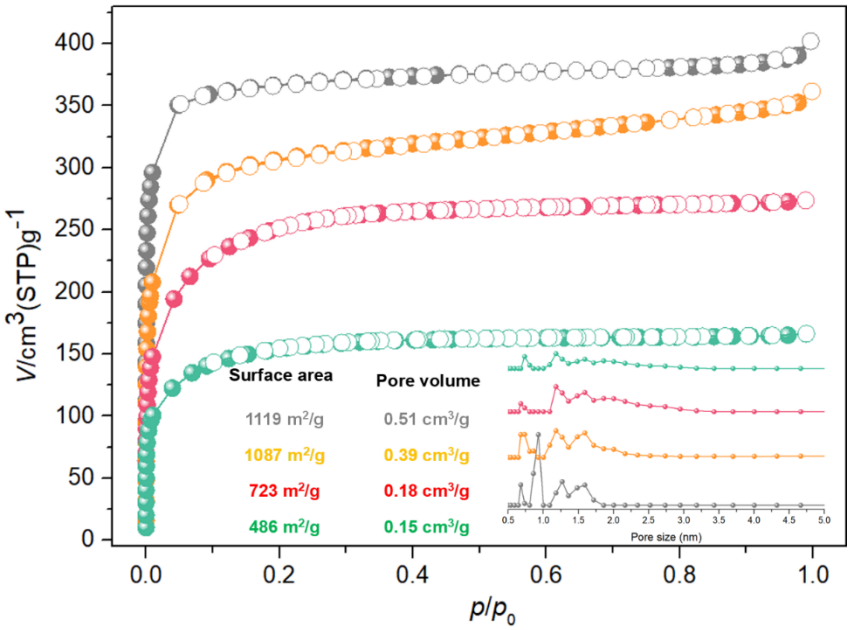


Fig. S3. N_2 adsorption (filled) and desorption (open) isotherm profiles of catalysts. Green, PTA@UiO-66(34.3%); Prink, PTA@UiO-66(12.1%); Orange, PTA@UiO-66(3.1%); Gray, UiO-66.

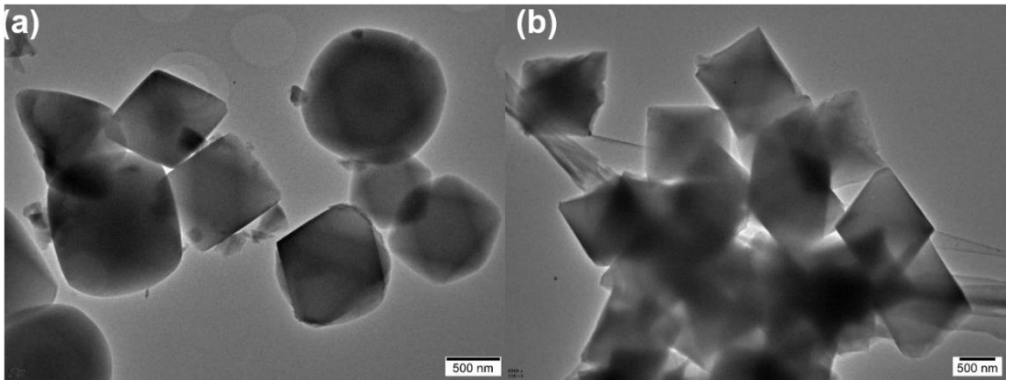


Fig. S4. (a) TEM of UiO-66, (b) and PTA@UiO-66.

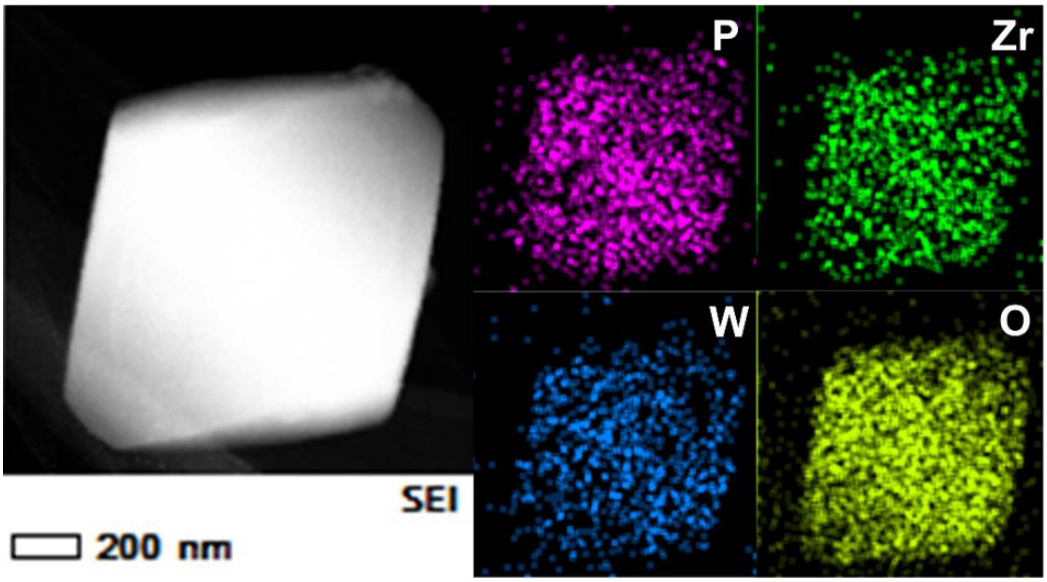


Fig. S5. EDS-Mapping of PTA@UiO-66.

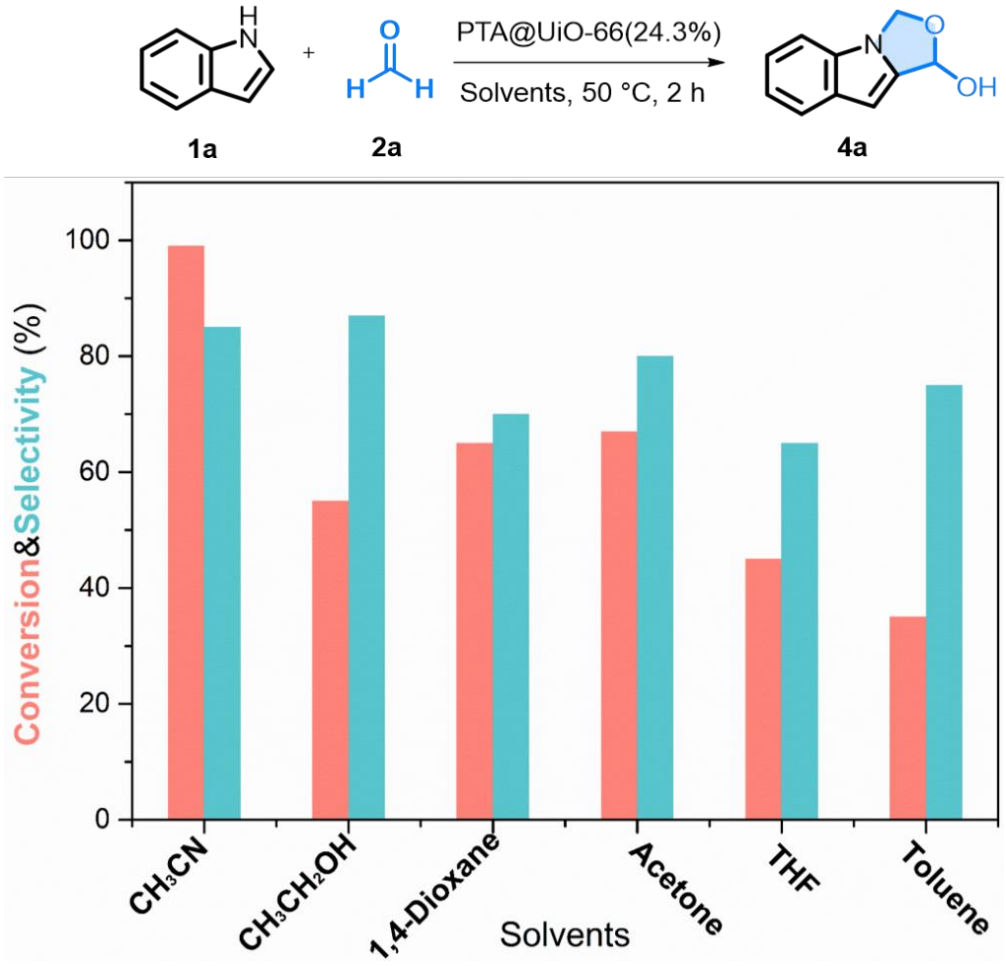


Fig. S6. Solvent optimization process.

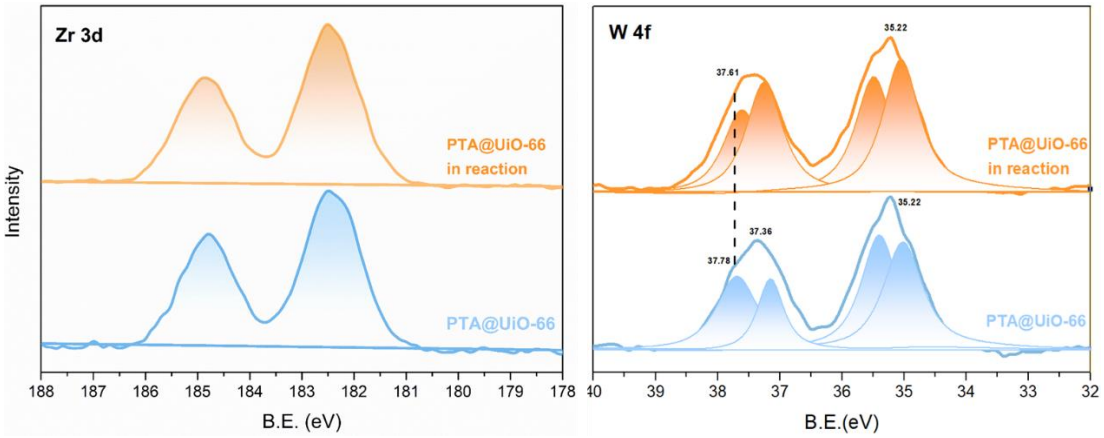


Fig. S7. Comparison of XPS spectra of Zr 3d (left) and W 4f (right) in PTA@UiO-66 with rapid termination reaction and without catalytic reaction.

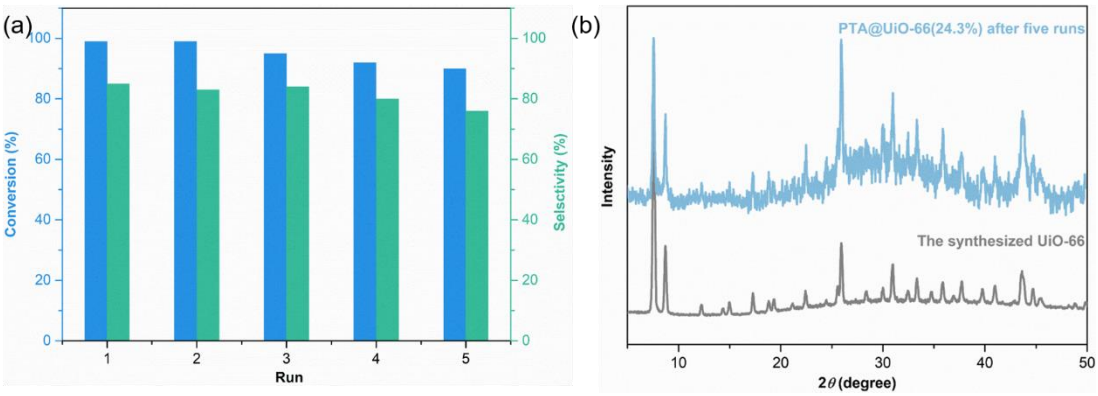


Fig. S8. Reuse of PTA@UiO-66(24.3%) in reaction (a); PXRD pattern of PTA@UiO-66(24.3%) recovered after five runs (b).

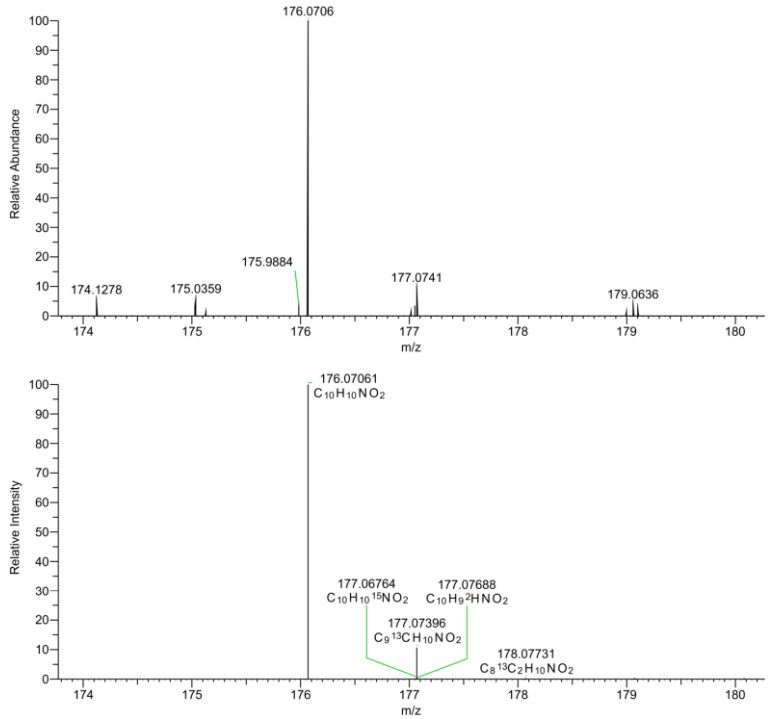
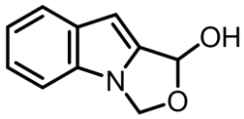
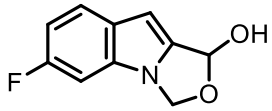


Fig. S9 High-resolution mass spectrometry of product (**4a, [**M+H]) (top), molecular mass simulation of (**4a, [**M+H]) (bottom).

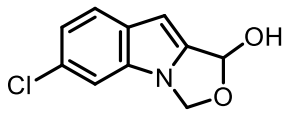
1. NMR data of products



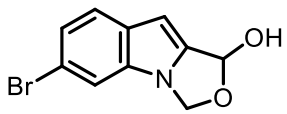
1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol (**4a**)**:** Yellow solid, 85%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.10 (s, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 6.93 (t, *J* = 7.4 Hz, 1H), 6.26 (t, *J* = 7.2 Hz, 1H), 5.36 (d, *J* = 7.2 Hz, 2H), 4.04 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 136.39, 128.62, 126.46, 121.62, 119.35, 119.31, 114.63, 110.64, 68.85. HRMS: calcd for $[M + H]^+$, m/z = 176.0706, found m/z = 176.0705.



6-Fluoro-1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol (4b): Yellow solid, 65%; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.52 (dd, *J* = 8.7, 5.5 Hz, 1H), 7.32 (dd, *J* = 10.5, 2.4 Hz, 1H), 7.20 (s, 1H), 6.85 (ddd, *J* = 9.7, 8.6, 2.4 Hz, 1H), 6.36 (t, *J* = 7.3 Hz, 1H), 5.40 (d, *J* = 7.3 Hz, 2H), 4.09 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 160.28, 158.73, 136.43, 127.04 (d, *J* = 3.6 Hz), 125.31, 120.36 (d, *J* = 10.1 Hz), 114.73, 107.77, 107.61, 97.25, 97.08, 68.99. HRMS: calcd for $[M + H]^+$, m/z = 194.0617, found m/z = 194.0612.

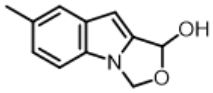


6-Chloro-1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol (**4c**)**:** Yellow solid, 71%; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.60 (d, *J* = 1.9 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.23 (s, 1H), 7.01 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.40 (s, 1H), 5.43 (s, 2H), 4.09 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 136.71, 127.58, 127.27, 126.63, 120.68, 119.61, 114.64, 110.70, 68.96. HRMS: calcd for $[M + H]^+$, m/z = 210.0321, found m/z = 210.0317.

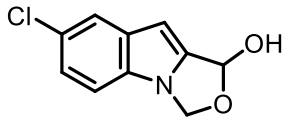


6-Bromo-1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol (**4d**)**:** Yellow solid, 74%; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.74 (d, *J* = 1.8 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.22 (s, 1H), 7.13 (dd, *J* = 8.4, 1.8

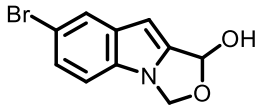
Hz, 1H), 6.40 (t, *J* = 7.3 Hz, 1H), 5.43 (d, *J* = 7.3 Hz, 2H), 4.09 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 137.14, 130.12, 127.50 (d, *J* = 2.6 Hz), 122.17, 121.07, 114.67 (d, *J* = 7.1 Hz), 113.61, 68.96. HRMS: calcd for $[M + H]^+$, m/z = 253.9816, found m/z = 253.9811.



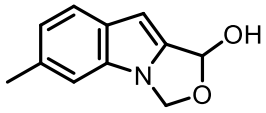
6-Methyl-1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol (**4e**): Yellow solid, 87%; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.37 (d, *J* = 8.3 Hz, 1H), 7.34 (s, 1H), 7.06 (s, 1H), 6.95 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.27 (t, *J* = 7.1 Hz, 1H), 5.39 (d, *J* = 7.1 Hz, 2H), 4.04 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 134.84, 128.83, 127.76, 126.52, 123.19, 118.93, 114.12, 110.36, 68.84, 21.70. HRMS: calcd for $[M + H]^+$, m/z = 190.0868, found m/z = 190.0862.



7-Chloro-1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol (**4f**)**:** Yellow solid, 73%; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.59 (d, *J* = 2.1 Hz, 1H), 7.53 (d, *J* = 8.7 Hz, 1H), 7.29 (s, 1H), 7.14 (dd, *J* = 8.6, 2.1 Hz, 1H), 6.42 (t, *J* = 7.2 Hz, 1H), 5.45 (d, *J* = 7.1 Hz, 2H), 4.09 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 134.85, 129.62, 128.23, 124.13, 121.59, 118.58, 114.16, 112.36, 69.07. HRMS: calcd for $[M + H]^+$, m/z = 210.0321, found m/z = 210.0316.

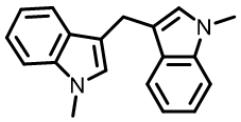


7-Bromo-1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol (**4g**)**:** Yellow solid, 75%; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.74 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 8.8 Hz, 1H), 7.25 (s, 2H), 6.44 (t, *J* = 7.2 Hz, 1H), 5.45 (d, *J* = 7.3 Hz, 2H), 4.09 (s, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 135.10, 130.31, 128.06, 124.16, 121.62, 114.11, 112.84, 112.16, 69.07. HRMS: calcd for $[M + H]^+$, m/z = 253.9816, found m/z = 253.9813.

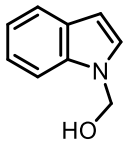


7-Methyl-1*H*,3*H*-oxazolo[3,4-*a*]indol-1-ol (**4h**)**:** Yellow solid, 78%; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.39 – 7.33 (m, 2H), 7.06 (s, 1H), 6.95 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.26 (t, *J* = 7.2 Hz, 1H), 5.39 (d, *J* = 7.2 Hz, 2H), 4.04 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 134.83,

128.81, 127.74, 126.51, 123.17, 118.93, 114.10, 110.35, 68.84, 21.70. HRMS: calcd for $[M + H]^+$, m/z = 190.0868, found m/z = 190.0865.

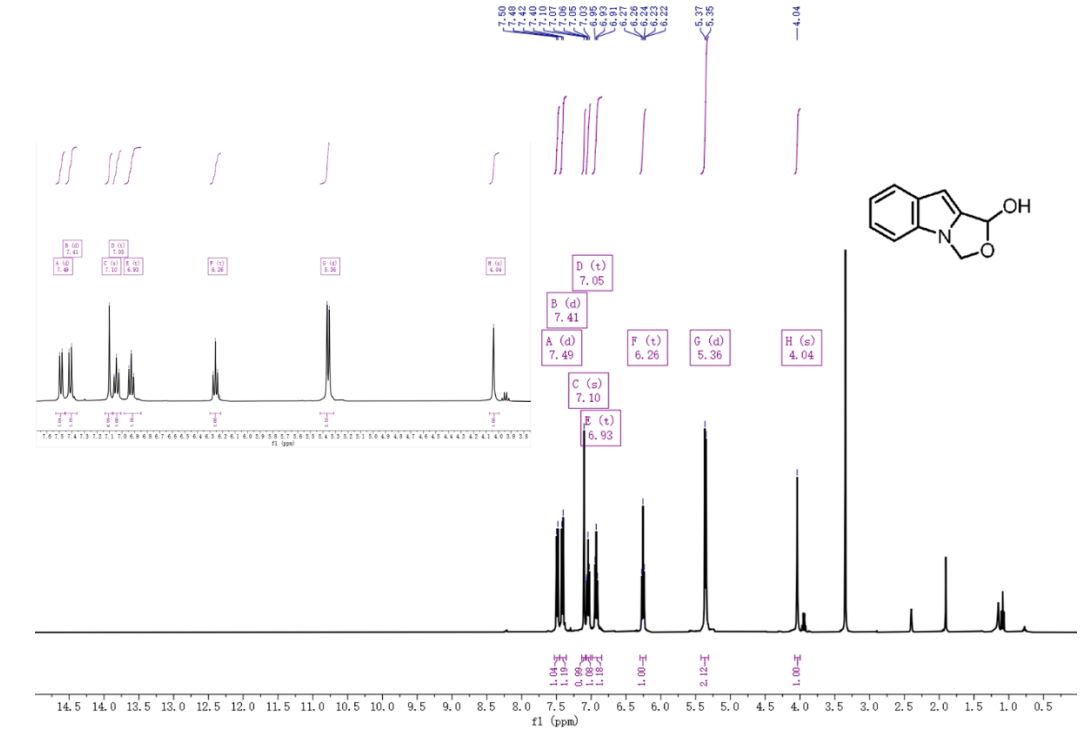


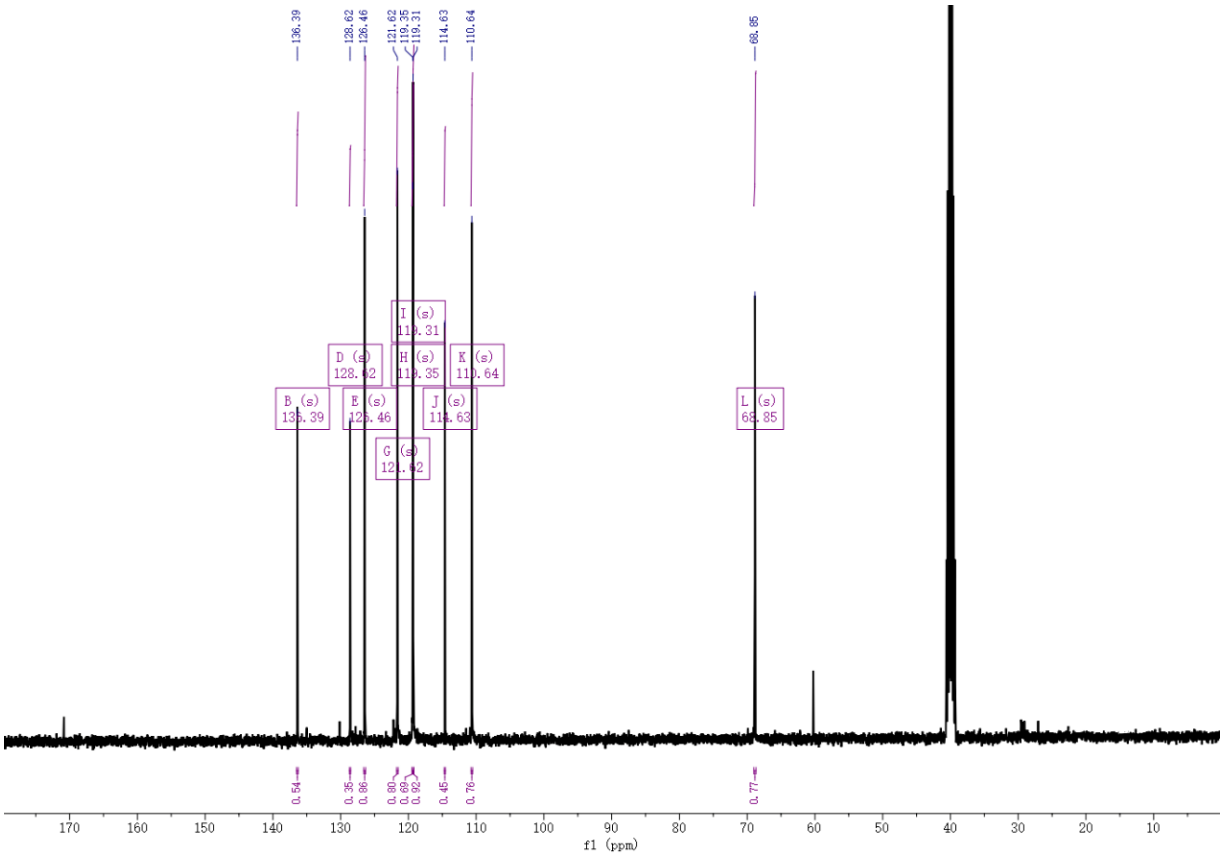
Bis(1-methyl-1*H*-indol-3-yl)methane (**5a**)**:** Yellow solid, ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 7.9 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 2H), 7.00 (t, *J* = 7.5 Hz, 2H), 6.69 (s, 2H), 4.13 (s, 2H), 3.59 (s, 6H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 132.49, 123.26, 122.29, 116.73, 114.62, 113.90, 109.65, 104.41, 27.87, 16.25. HRMS: calcd for $[M + H]^+$, m/z = 275.1548, found m/z = 275.1542.

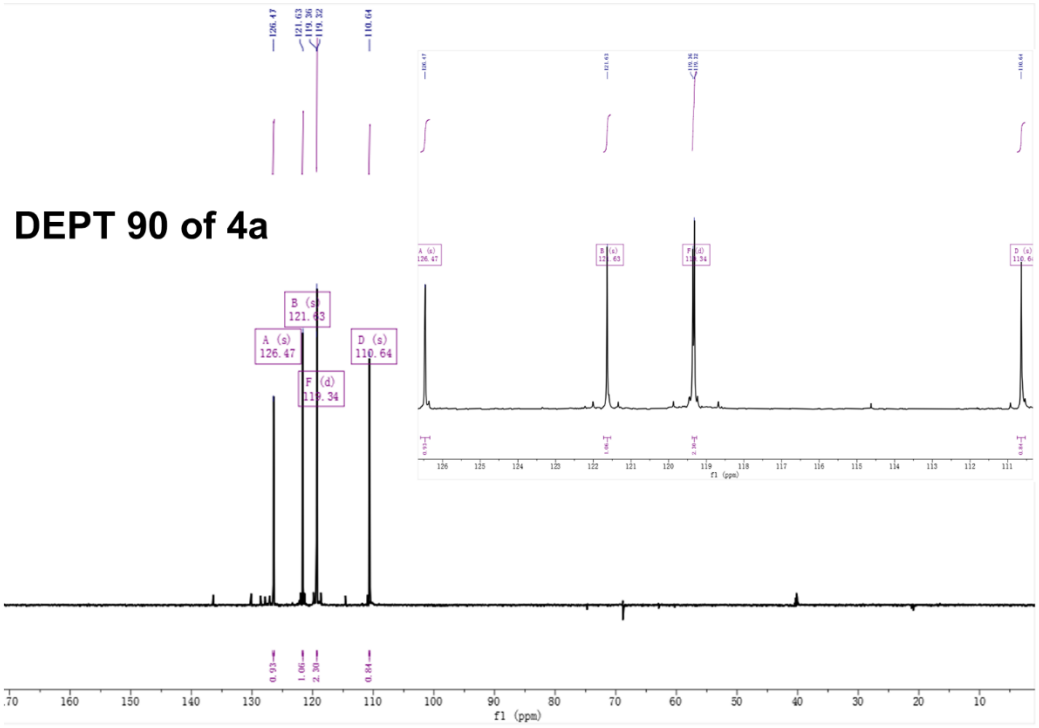


(1*H*-indol-1-yl)methanol (**3a**)**:**^{1}H NMR (600 MHz, DMSO-d_6) δ 7.55 (d, *J* = 7.8 Hz, 2H), 7.39 (d, *J* = 3.2 Hz, 1H), 7.14 (t, *J* = 8.2 Hz, 1H), 7.04 (t, *J* = 7.9 Hz, 1H), 6.43 (d, *J* = 4.0 Hz, 1H), 5.51 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 135.92, 129.05, 128.89, 121.60, 120.79, 119.87, 110.78, 101.59, 69.05.

2. NMR spectra of some products



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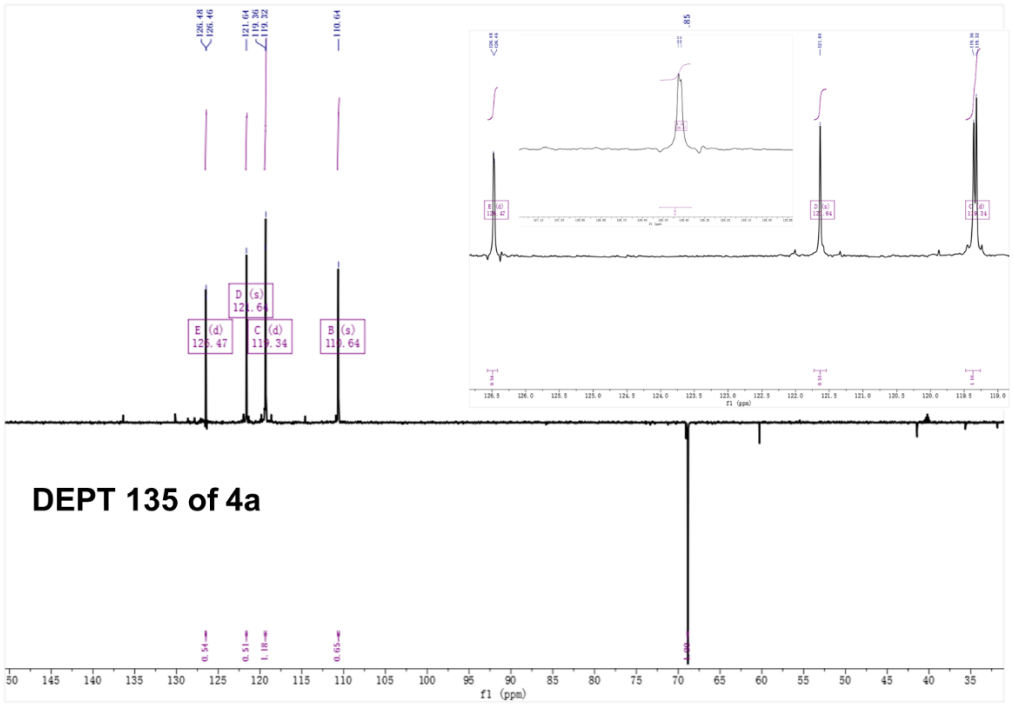
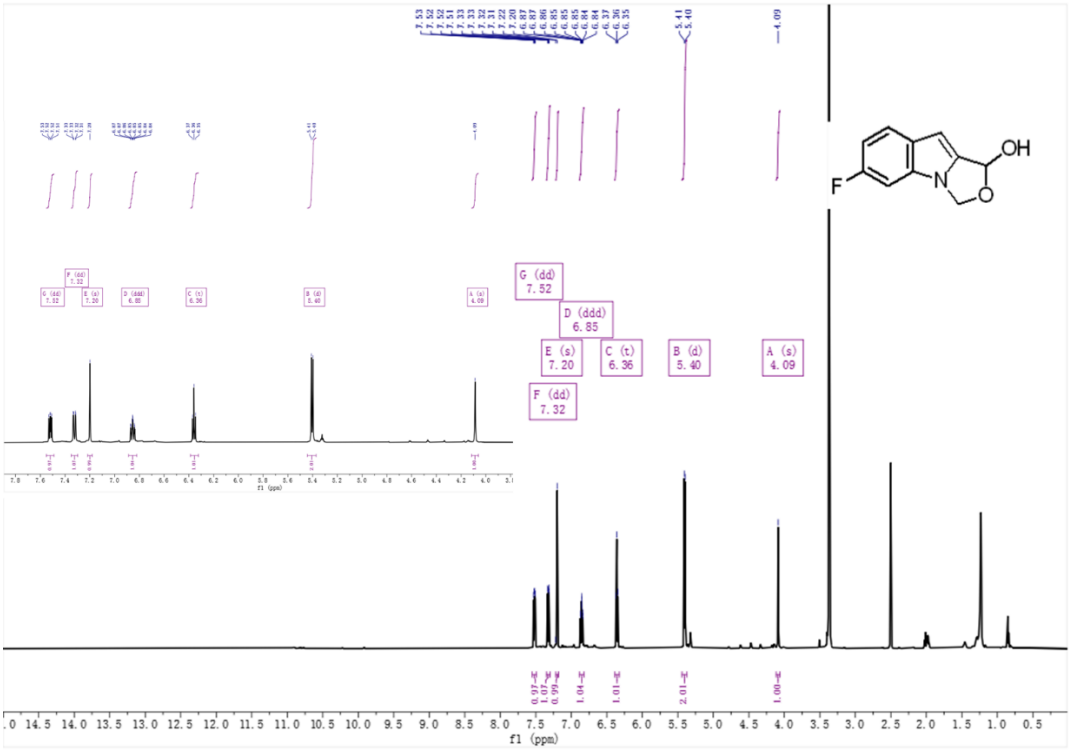
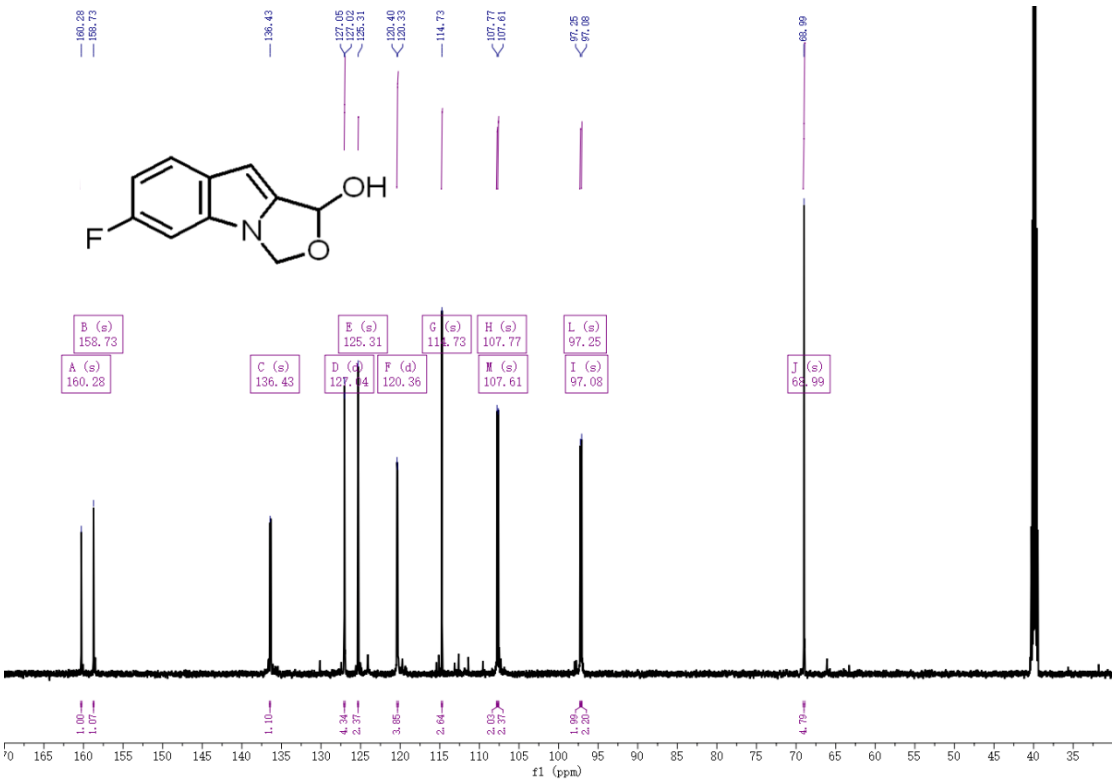
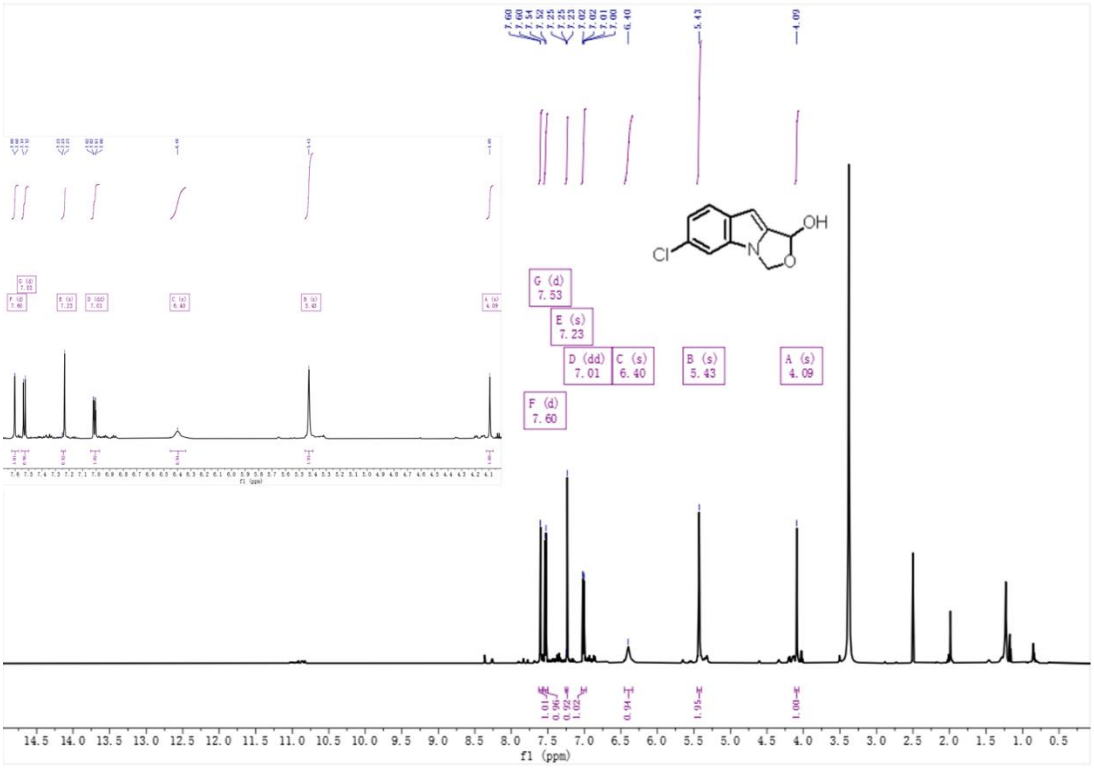
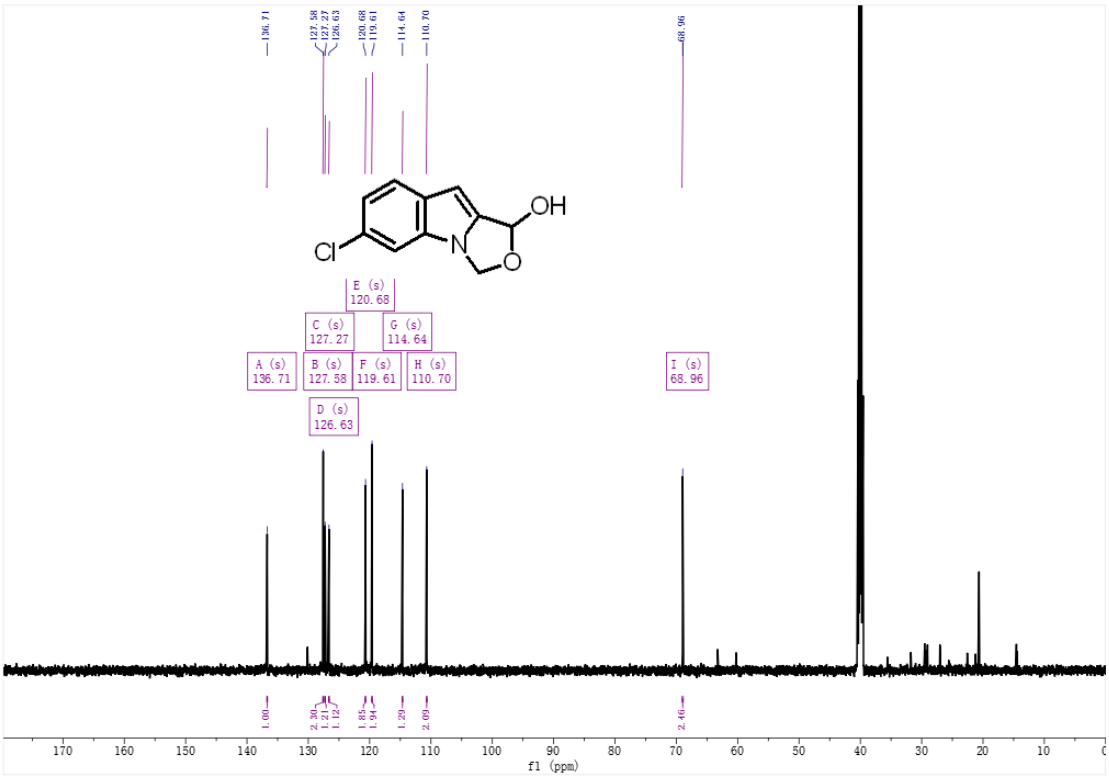
f1 (ppm)

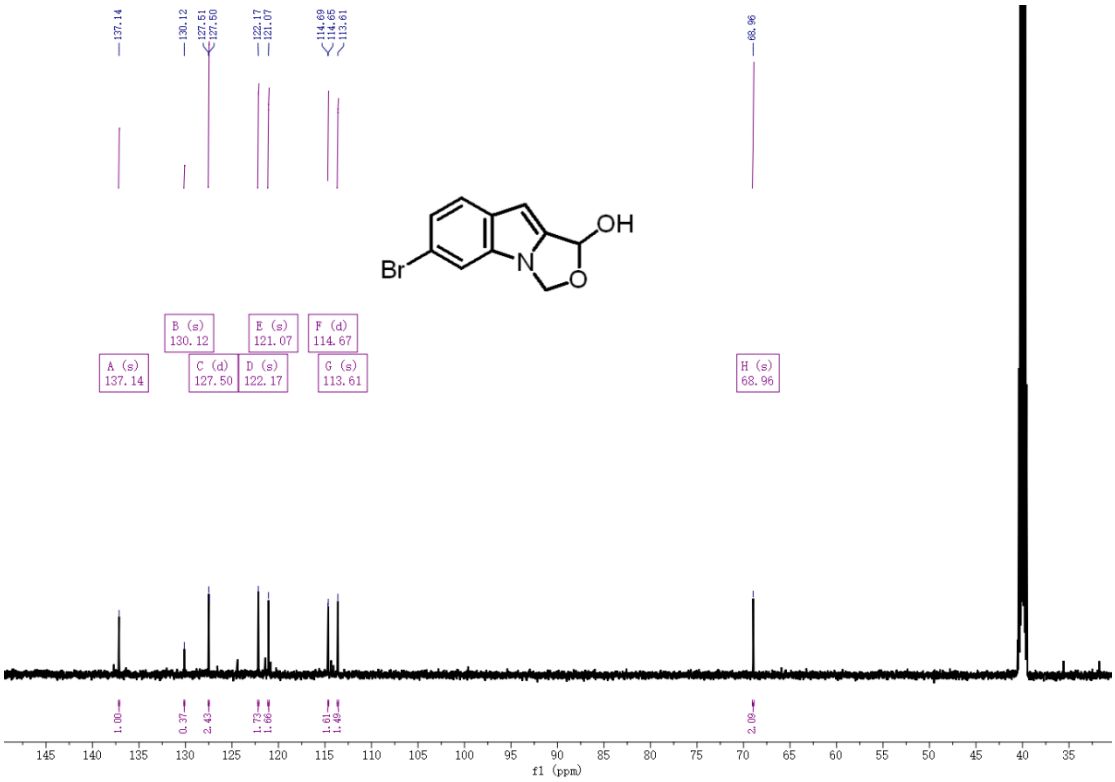

DEPT 135 of 4a
D (s)
121.64
E (d)
126.47
C (d)
119.34
B (s)
110.64
f1 (ppm)

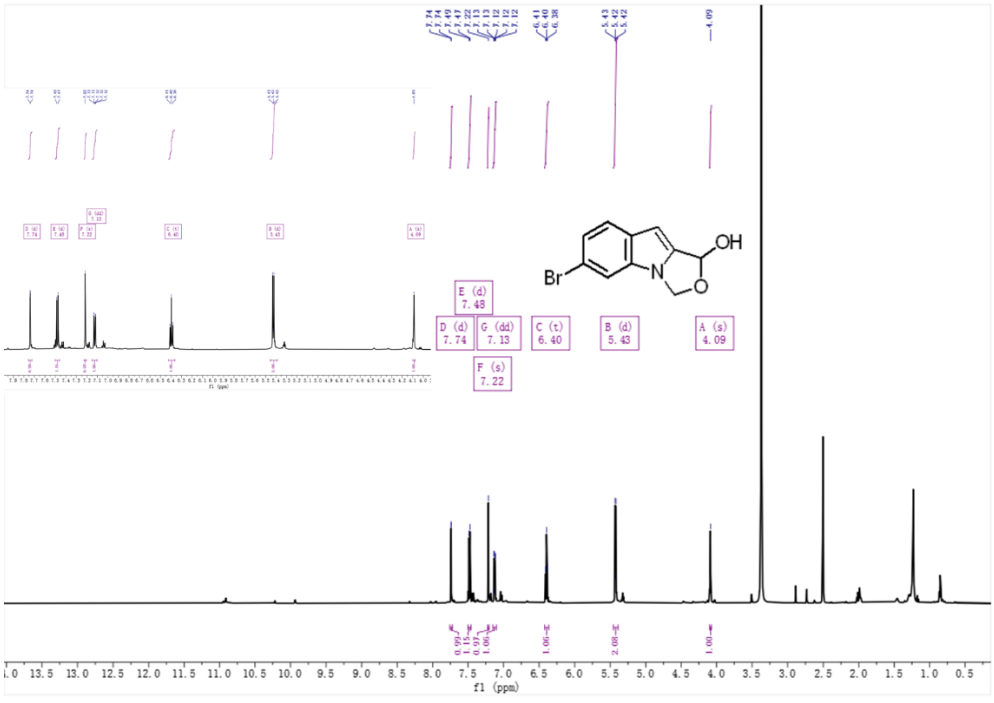

OH
F
N
O
G (dd)
7.52
D (ddd)
6.85
E (s)
7.20
C (t)
6.36
B (d)
5.40
A (s)
4.09
F (dd)
7.32
f1 (ppm)

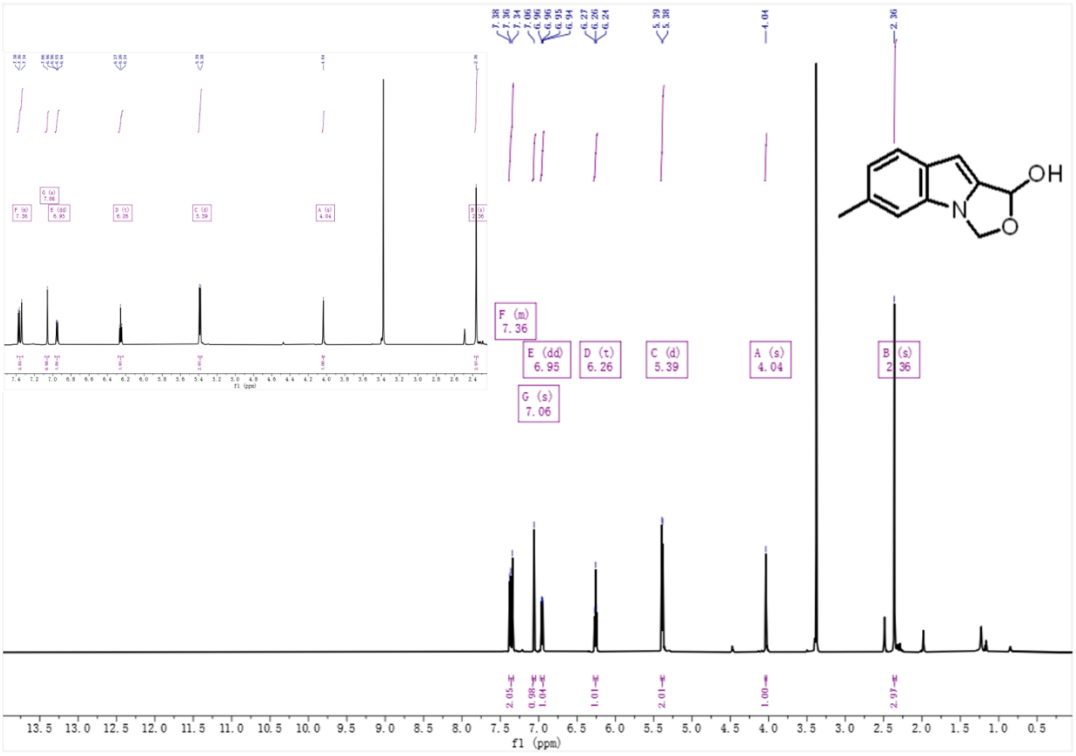

OH
F
N
O
B (s)
158.73
A (s)
160.28
C (s)
136.43
E (s)
125.31
D (d)
127.04
F (d)
120.36
G (s)
114.73
H (s)
107.77
M (s)
107.61
L (s)
97.25
I (s)
97.08
J (s)
68.99
f1 (ppm)

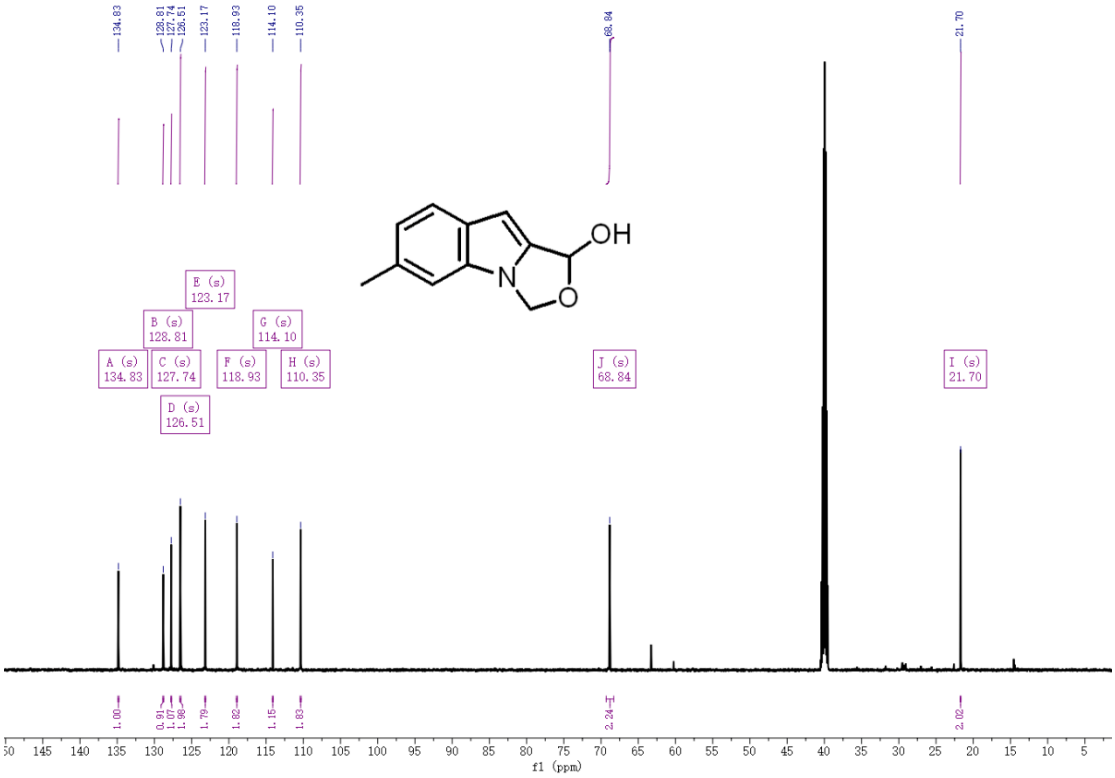

OH
Cl
N
O
G (d)
7.53
E (s)
7.23
D (dd)
7.01
C (s)
6.40
B (s)
5.43
A (s)
4.09
F (d)
7.60
f1 (ppm)

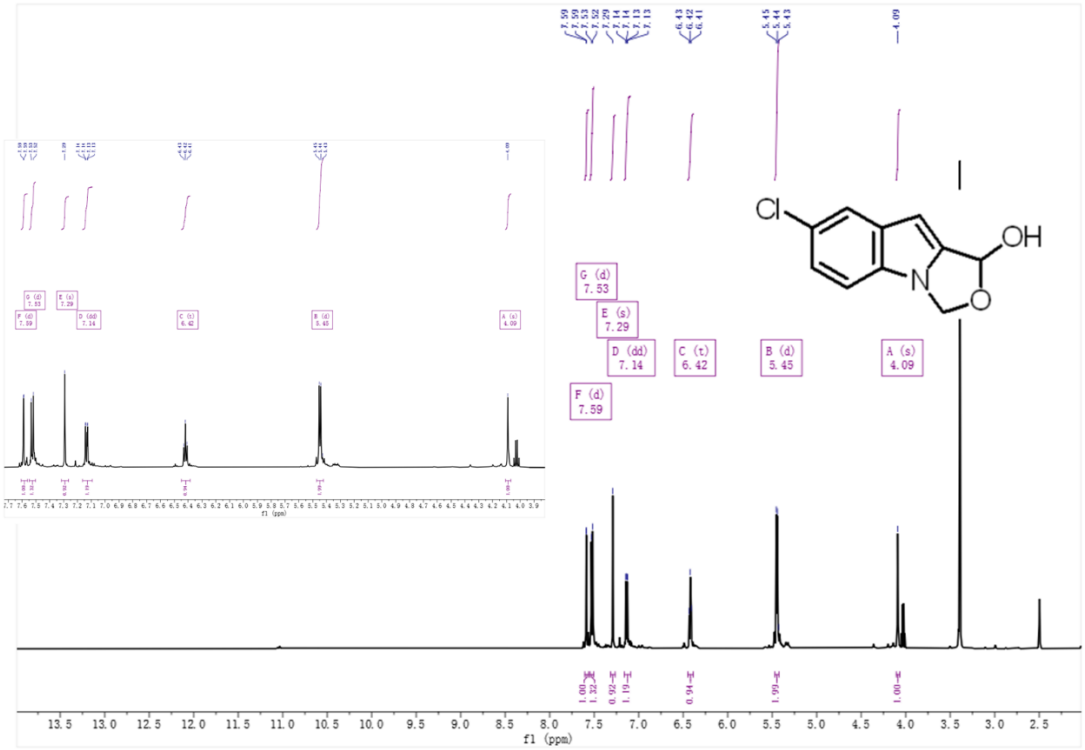

OH
Cl
N
O
E (s)
120.68
C (s)
127.27
G (s)
114.64
A (s)
136.71
B (s)
127.58
F (s)
119.61
H (s)
110.70
D (s)
126.63
I (s)
68.96
f1 (ppm)

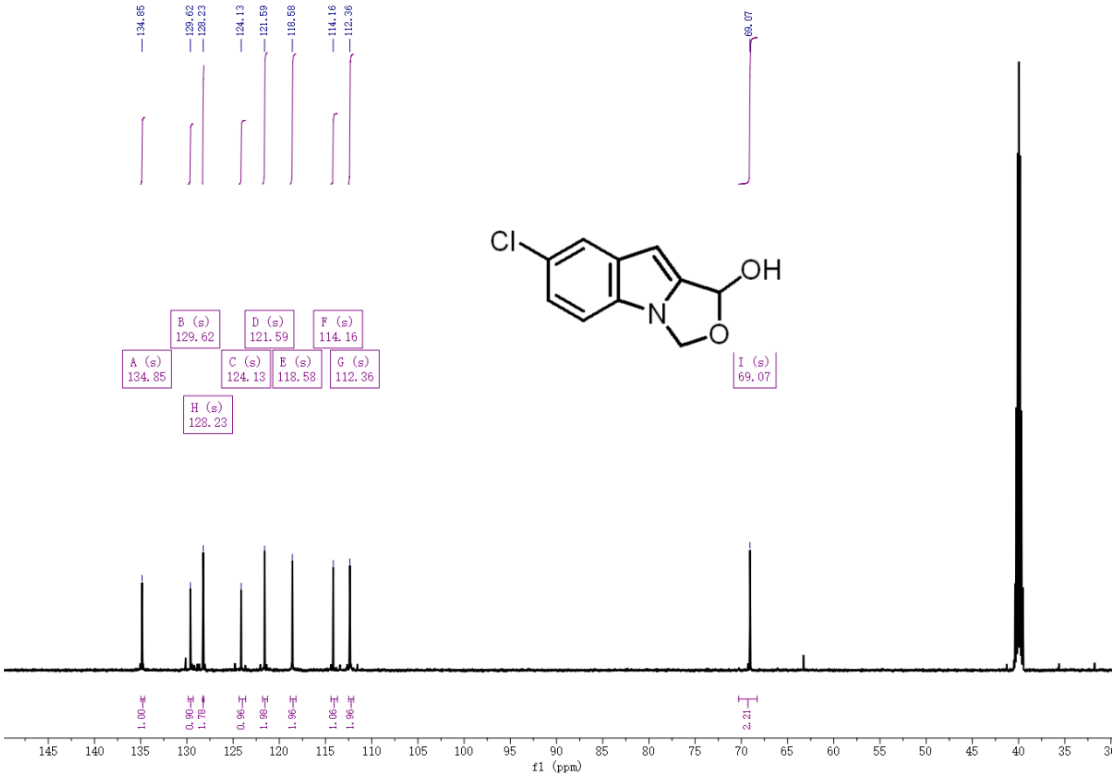

137.14
130.12
127.51
127.50
122.17
121.07
114.69
114.65
113.61
68.96
OH
Br
N
O
B (s) 130.12
E (s) 121.07
F (d) 114.67
A (s) 137.14
C (d) 127.50
D (s) 122.17
G (s) 113.61
H (s) 68.96
1.00
0.37
2.43
1.73
1.66
1.61
1.40
2.09
f1 (ppm)

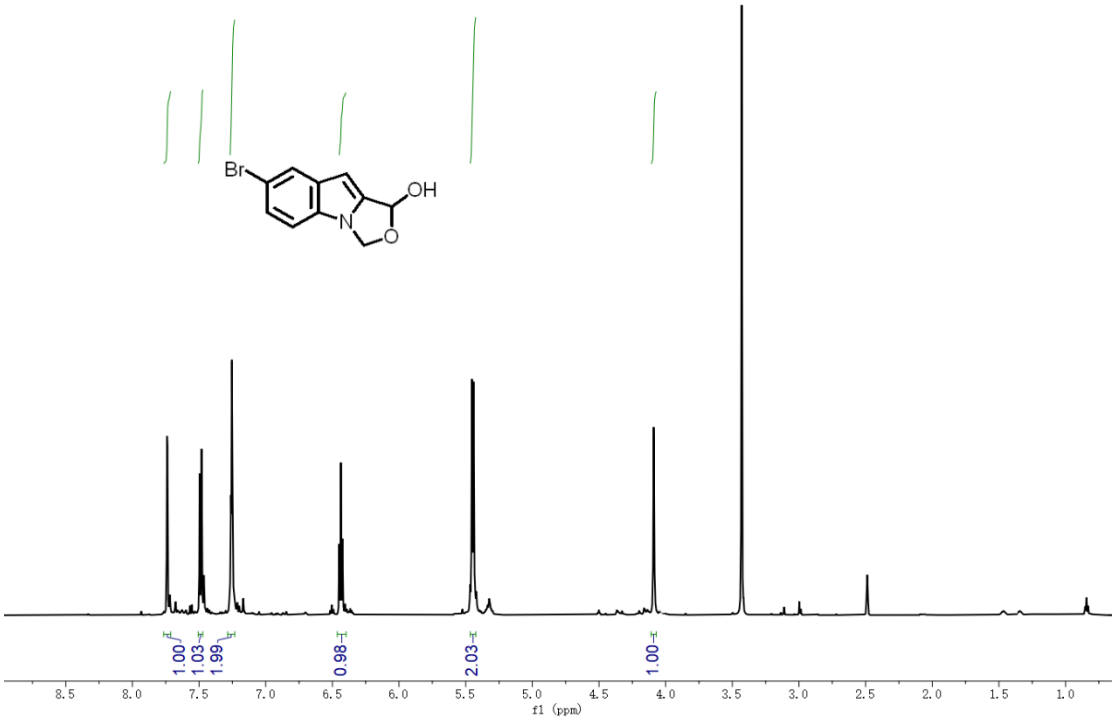

OH
Br
N
O
E (d) 7.48
D (d) 7.74
G (dd) 7.13
C (t) 6.40
B (d) 5.43
A (s) 4.09
F (s) 7.22
f1 (ppm)

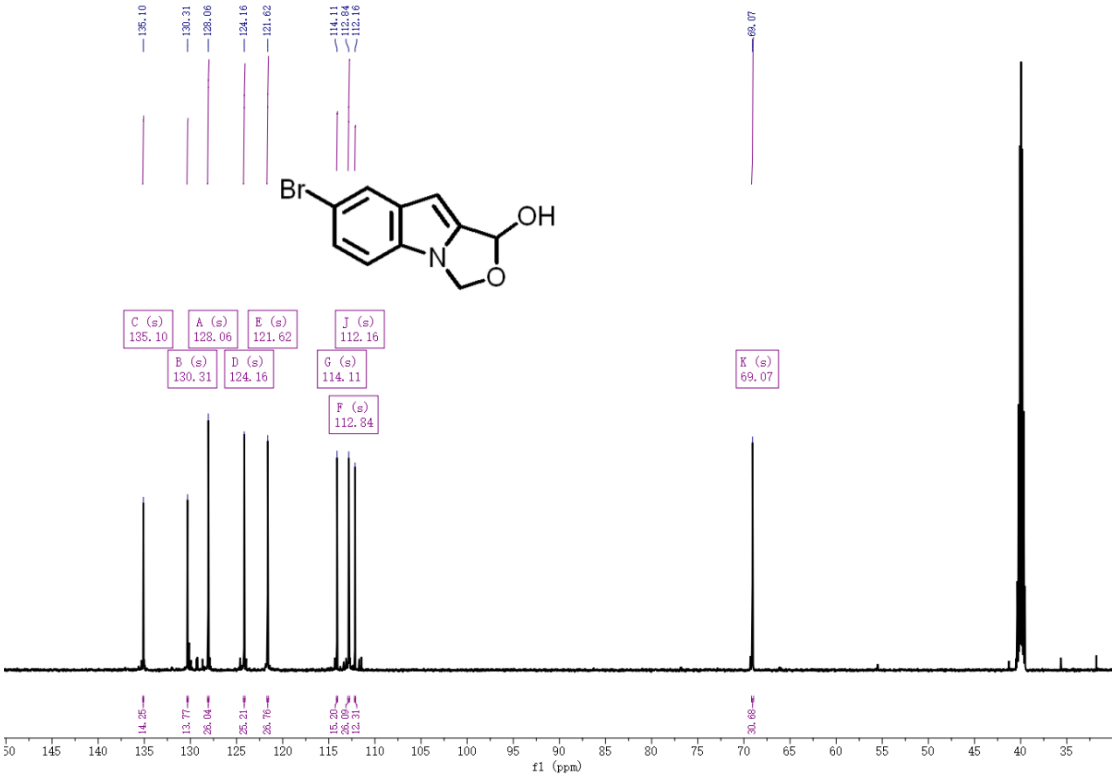

OH
N
O
F (m)
7.36
E (dd)
6.95
D (t)
6.26
C (d)
5.39
A (s)
4.04
B (s)
2.36
G (s)
7.06
f1 (ppm)

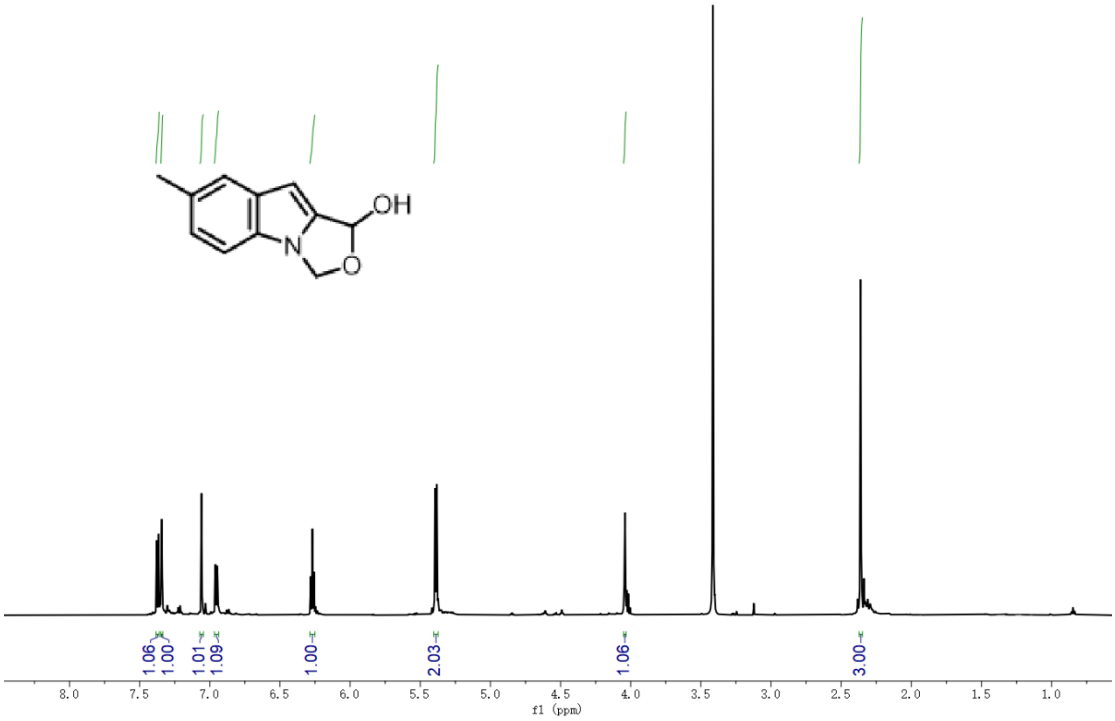

OH
N
O
E (s)
123.17
B (s)
128.81
G (s)
114.10
A (s)
134.83
C (s)
127.74
F (s)
118.93
H (s)
110.35
D (s)
126.51
J (s)
68.84
I (s)
21.70
f1 (ppm)

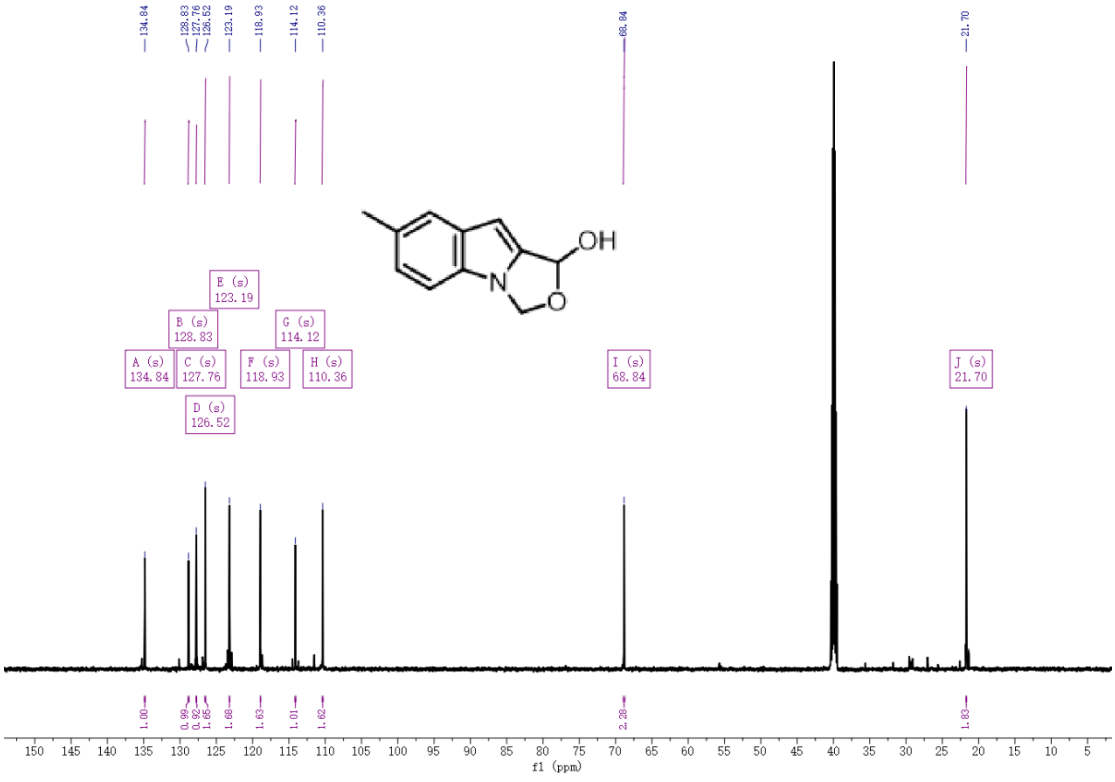

Cl
OH
N
O
G (d)
7.53
E (s)
7.29
D (dd)
7.14
C (t)
6.42
B (d)
5.45
A (s)
4.09
F (d)
7.59
f1 (ppm)

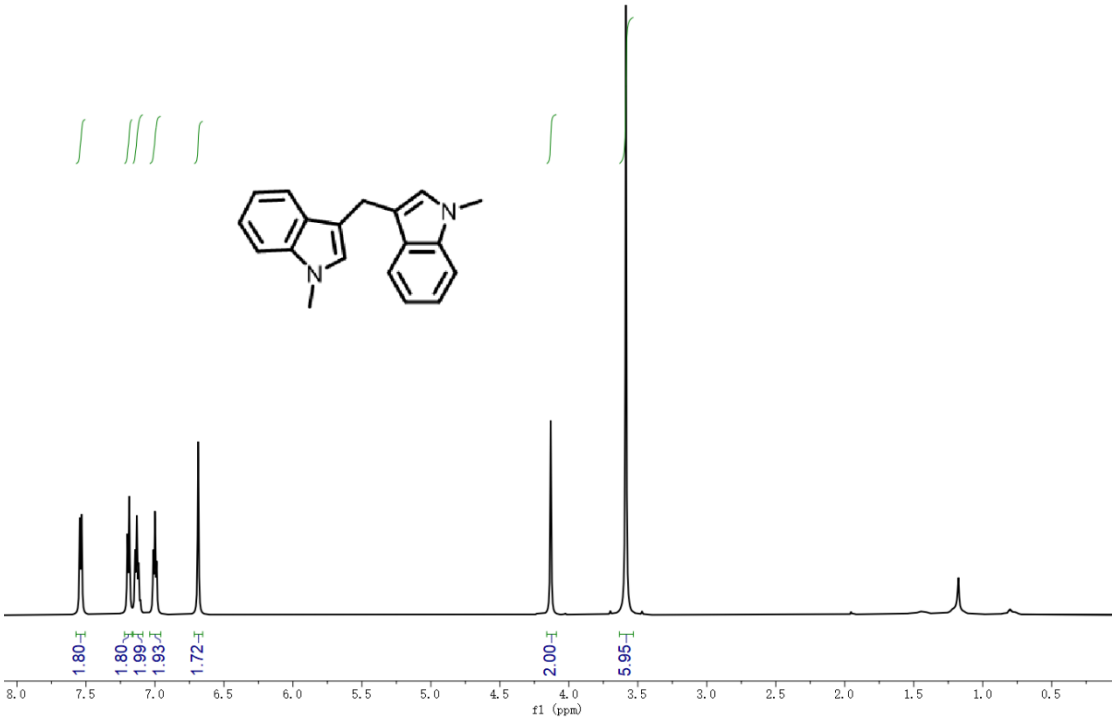

Cl
OH
N
O
A (s)
134.85
B (s)
129.62
C (s)
124.13
D (s)
121.59
E (s)
118.58
F (s)
114.16
G (s)
112.36
H (s)
128.23
I (s)
69.07
f1 (ppm)

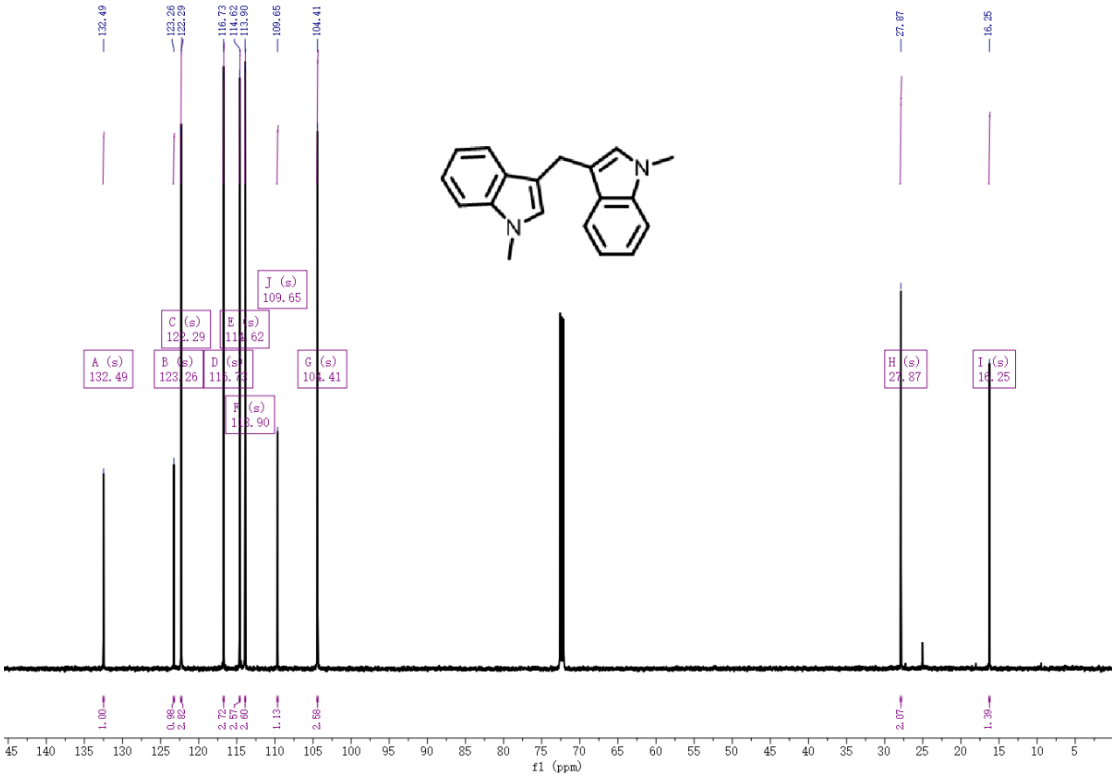

Br
OH
N
O
1.00
1.03
1.99
0.98
2.03
1.00
f1 (ppm)

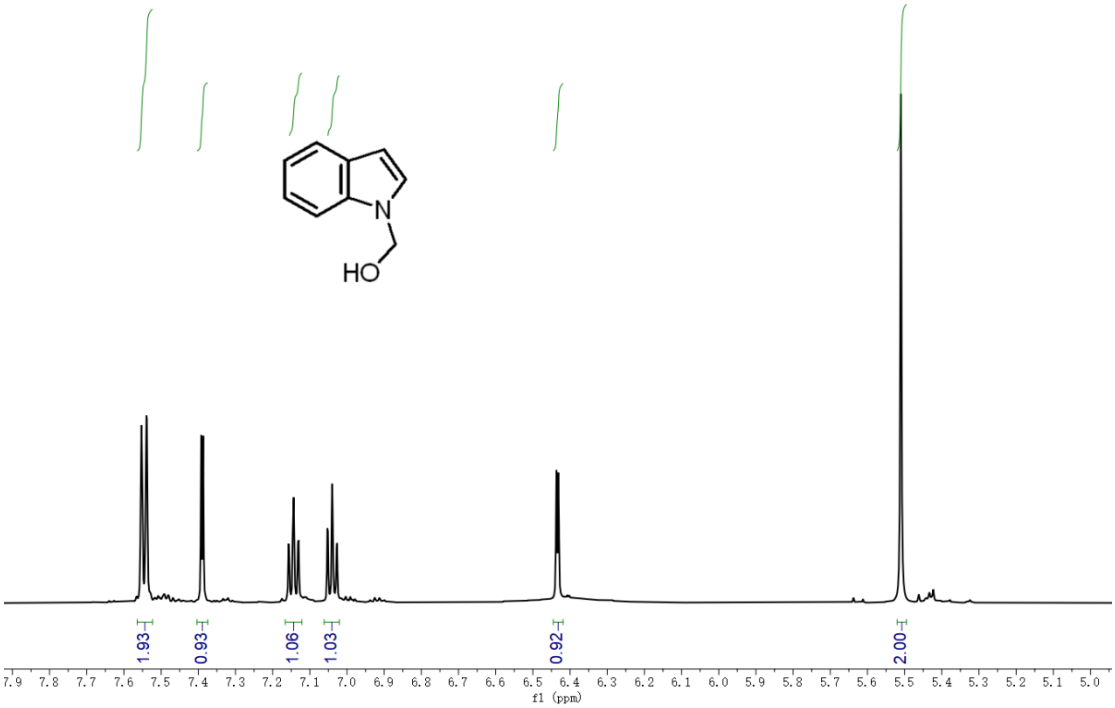

135.10
130.31
128.06
124.16
121.62
114.11
112.84
112.16
69.07
Br
OH
N
O
C (s) 135.10
A (s) 128.06
E (s) 121.62
J (s) 112.16
B (s) 130.31
D (s) 124.16
G (s) 114.11
F (s) 112.84
K (s) 69.07
f1 (ppm)

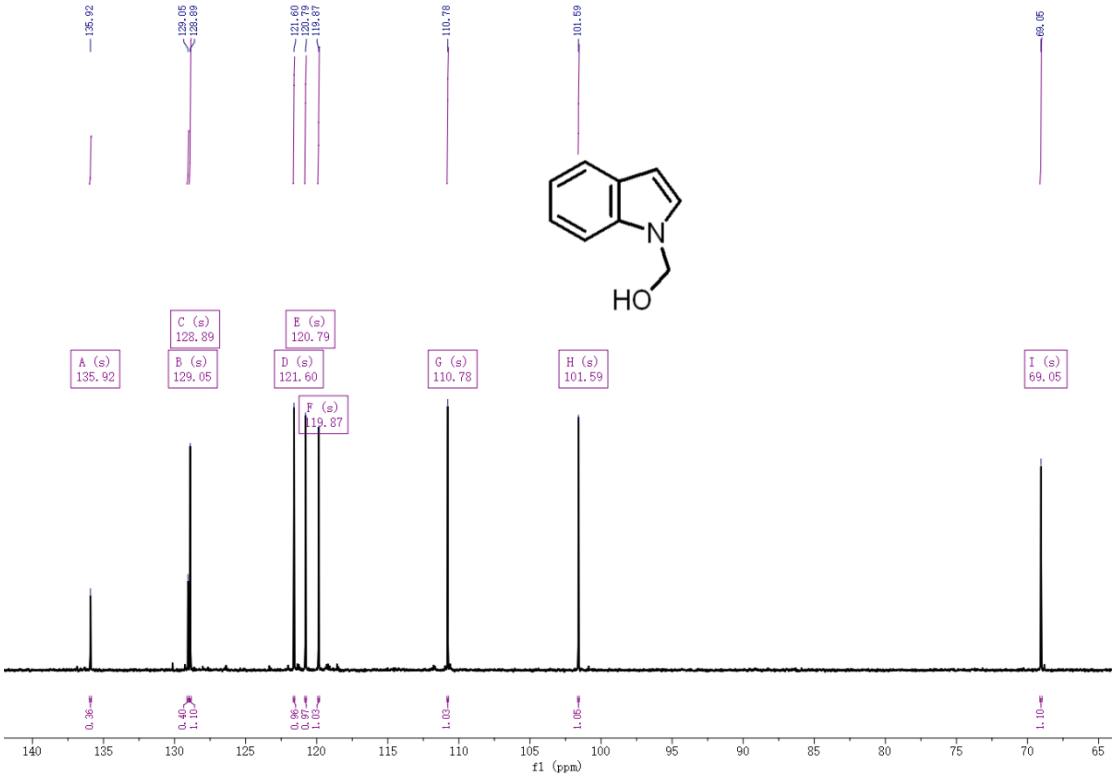

OH
N
O
1.06
1.00
1.01
1.09
1.00
2.03
1.06
3.00
f1 (ppm)


134.84
128.83
127.76
126.52
123.19
118.93
114.12
110.36
68.84
21.70
OH
N
O
E (s)
123.19
B (s)
128.83
G (s)
114.12
A (s)
134.84
C (s)
127.76
F (s)
118.93
H (s)
110.36
D (s)
126.52
I (s)
68.84
J (s)
21.70
f1 (ppm)


1.80
1.80
1.99
1.93
1.72
2.00
5.95
f1 (ppm)


132.49
123.26
122.29
116.73
114.62
113.90
109.65
104.41
27.87
16.25
A (s) 132.49
B (s) 123.26
C (s) 122.29
D (s) 116.73
E (s) 114.62
F (s) 113.90
G (s) 104.41
H (s) 27.87
I (s) 16.25
J (s) 109.65
1.00
0.98
2.82
2.72
2.57
2.60
1.13
2.58
2.07
1.39
f1 (ppm)


HO
1.93
0.93
1.06
1.03
0.92
2.00
f1 (ppm)


135.92
129.05
128.89
121.60
120.79
119.87
110.78
101.59
69.05
HO
A (s) 135.92
C (s) 128.89
B (s) 129.05
E (s) 120.79
D (s) 121.60
F (s) 119.87
G (s) 110.78
H (s) 101.59
I (s) 69.05
f1 (ppm)