Supporting Information

Modulating confinement space in metal-organic frameworks enables highly selective indole C3-formylation

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Contents

1. Materials and General 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 an FEI Tecnai G2 F30 TMP TEM at 200 kV. Fourier transform infrared spectroscopy (FT-IR) spectra were recorded on a Bruker INVENIO-R FT-IR spectrophotometer. Inductively coupled plasma-optical emission spectroscopy (ICP-OES) data for the content of Cu was carried out on an iCAP7200plus ICP 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 SmartLab-SE X-ray diffractometer. ^{1}H NMR spectra were performed on a Bruker Advance III 400 MHz. The DFT calculation support provided by the Scientific Compass platform.

2. Catalyst Preparation and catalytic reaction processes

Synthesis of MIL-100

MIL-100(Cr) was prepared according to a literature procedure.[1] Benzene-1,3,5-tricarboxylic acid (H_3BTC, 1.05 g, 5.0 mmol), a hydrofluorohydric solution (1.0 mL, 40%), and 24 mL of deionized water were added to chromium(VI) oxide (CrO_3, 0.5 g, 5.0 mmol) and stirred for a few minutes at room temperature. The mixture was then sealed in a Teflon-lined stainless-steel autoclave (50 mL) and heated at 220 ℃ for 4 days, followed by slow cooling to room temperature at a rate of 13 ℃ h^{-1}. The solid product was recovered by filtration, washed three times with ample water and methanol, and dried at 70 ℃ under an air atmosphere. MIL-100(Al) was prepared according to a literature procedure.[2] $Al(NO_3)_3 \cdot 9H_2O$ (230 mg, 0.61 mmol), $btcMe_3$ (104 mg, 0.41 mmol), HNO_3 (0.77 mL, 0.77 mmol), 5 mL of deionized water were added and stirred for a few minutes at room temperature. The mixture was then sealed in a Teflon-lined stainless-steel autoclave (20 mL) and heated at 210 ℃ for 4 hours.

The resulting yellowish powdered sample was collected by filtration, washed with purified water, and dried at room temperature. MIL-100(Fe) was prepared according to a literature procedure.[3] $Fe(NO_3)_3 \cdot 9H_2O$ (2.2 g, 5.0 mmol), H_3BTC (0.735 g, 3.5 mmol), and 25 mL of deionized water were added and stirred for a few minutes at room temperature. The mixture was then sealed in a Teflon-lined stainless-steel autoclave (50 mL) and heated at 160 ℃ for 12 hours. The resulting brown powdered sample was collected by filtration, washed with purified water, and dried at room temperature.

Synthesis of PTA⊂MIL-100

The one-pot synthesis of phosphotungstic acid (PTA) encapsulated in MIL-100(Cr) was performed by adding three different quantities of PTA (1.0, 2.0, and 3.0 g) to the synthesis mentioned above solution. Then, syntheses were performed as explained above to generate $PTA_{1.0}$⊂MIL-100, $PTA_{2.0}$⊂MIL-100, and $PTA_{3.0}$⊂MIL-100, respectively. Wash the solid products by filtering them with sufficient hot water and methanol to thoroughly remove the free PTA and dry them at 120 °C in a vacuum.

Synthesis of PTA⊂UiO-66

Typically, 25 mL of dimethylformamide (DMF) solution of $ZrCl_4$ (165 mg) and 5 mL of DMF solution of H_2BDC (114 mg), and 1.0 g PTA were mixed in a 50 mL glass vial. Then, 3 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 24.47%, calculated based on the ICP-OES measurement W content.

Synthesis of MIL-101-SO_3H

The MIL-101-SO_3H sample was synthesized using CrO_3 and Monosodium 2-sulfoterephthalic (H_2BDC-SO_3Na) acid as reactants.[4] Typically, 25 mL of deionized water solution of CrO_3 (665 mg) and H_2BDC-SO_3Na (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.

Indole C-3 formylation reaction process

Add MOF catalyst (60 mg) or related homogeneous catalyst (0.01 mmol), 2.0 mL untreated $CH(OMe)_3$ to a 25 mL Schlenk tube equipped with a magnetic stirring bar, indole, or its derivatives (0.20 mmol). The mixture was sonicated for 10 min to promote uniform catalyst dispersion/dissolution. The mixture was stirred at 60 °C for 12 hours. After the reaction, the solid was separated by centrifugation, washed several times with methanol, and dried in a vacuum for later use. The product was isolated by preparative thin-layer chromatography using a mixture of ethyl acetate and petroleum ether as eluent.

Indole C-3 formylation reaction process under anhydrous conditions

Into a 25 mL Schlenk tube equipped with a magnetic stirring bar, add MOF catalyst ($PTA_{2.0}$⊂MIL-100, 60 mg) dried under vacuum at 150 ℃, 2.0 mL anhydrous treated $CH(OMe)_3$, dried indole (0.20 mmol). The mixture was sealed and sonicated for 10 minutes to ensure the catalyst was evenly dispersed. The mixture was stirred at 50 °C for 12 hours. After the reaction, the solid catalyst was centrifuged and washed several times with methanol. The product was isolated by preparative thin-layer chromatography using a mixture of ethyl acetate and petroleum ether as eluent.

Reaction process of indole-3-carbaldehyde with indole

Add MOF catalyst (60 mg) or homogeneous catalyst (0.01 mmol), 2.0 mL $CH(OMe)_3$, indole (0.20 mmol), indole-3-carbaldehyde (0.20 mmol). The mixture was sonicated for 10 min to disperse/dissolve the catalyst homogeneously. The mixture was reacted at 60 °C for 5 hours. After the reaction, the heterogeneous catalyst is centrifuged, washed several times with methanol, and dried in a vacuum for later use; the homogeneous catalyst can be directly used for product separation. The product was isolated by preparative thin-layer chromatography using a mixture of ethyl acetate and petroleum ether as eluent.

Indole C3-formylation reaction intermediate capture process

Add $PTA_{2.0}$⊂MIL-100-Cr catalyst (60 mg), 2.0 mL untreated $CH(OMe)_3$ to a 25 mL Schlenk tube equipped with a magnetic stirring bar, indole (0.20 mmol). The mixture was sonicated for 10 min to promote uniform catalyst dispersion/dissolution. The

mixture was stirred, reacted at 60 °C for 1 hour, and cooled rapidly with liquid nitrogen. Subsequently, the solid catalyst is separated by centrifugation, a small amount of the supernatant liquid is extracted, and the insoluble matter is filtered with a filter membrane. The chemical composition of the filtrate was analyzed using high-resolution mass spectrometry.

References

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Table S1. Composition and physicochemical properties of PTA⊂MIL-100-Cr

PTA added (g)	Cr (wt%)	W (wt%)	PTA (wt%)	S_{BET} (m^2/g)	V_{total} (cm^3/g)
0	13.56	0	0	1514	0.98
1	11.56	18.31	23.90	863	0.37
2	9.63	23.17	30.23	673	0.29
3	9.38	23.61	30.81	651	0.30

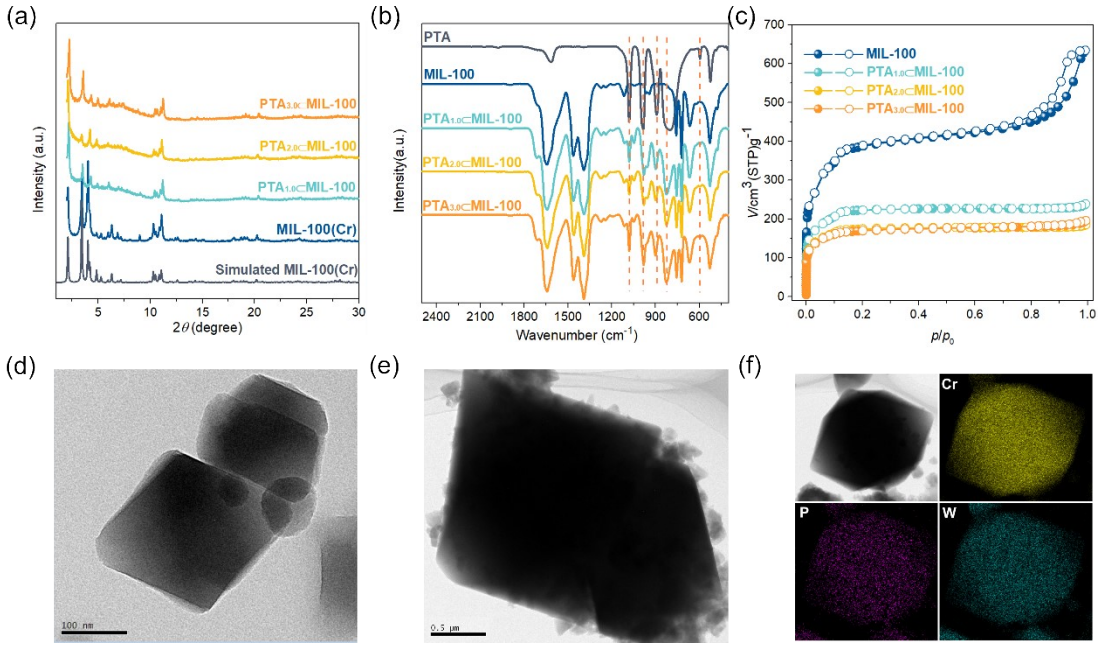


Fig. S1 Catalyst performance characterization, (a) PXRD patterns of catalysts, (b) FT-IR spectra of catalysts, (c) N_2 adsorption (filled) and desorption (open) isotherm profiles of catalysts, (d) TEM of MIL-100-Cr, (e) TEM and (f) EDS-Mapping of $PTA_{2.0}$⊂MIL-100-Cr.

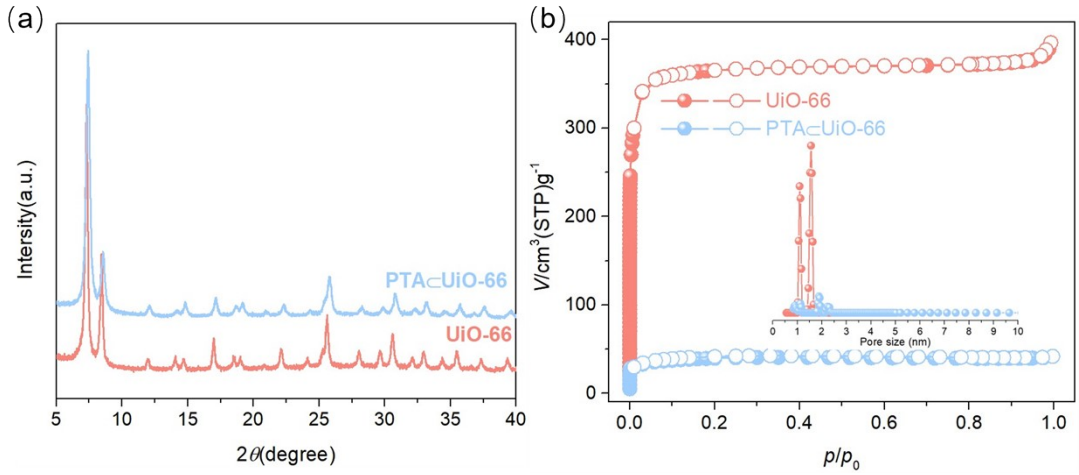


Fig. S2 PXRD (a) and BET (b) of PTA⊂UiO-66.

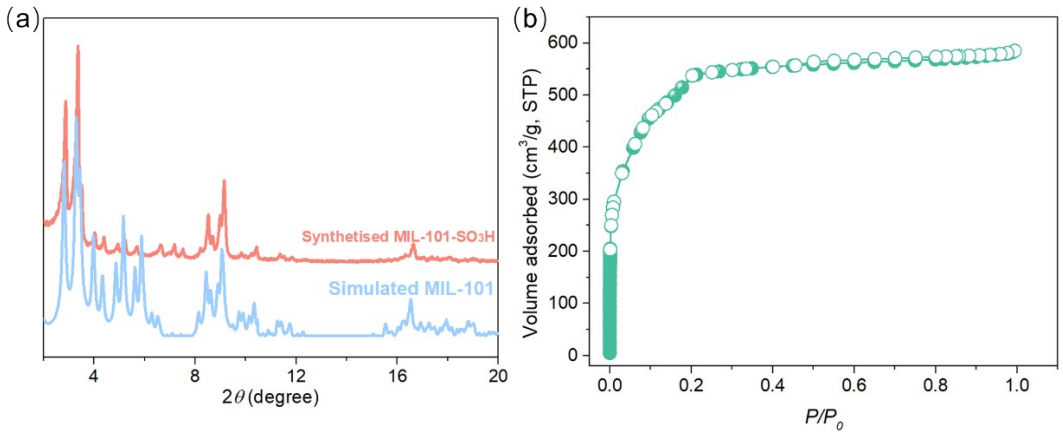


Fig. S3 PXRD (a) and BET (b) of MIL-101-SO_3H.

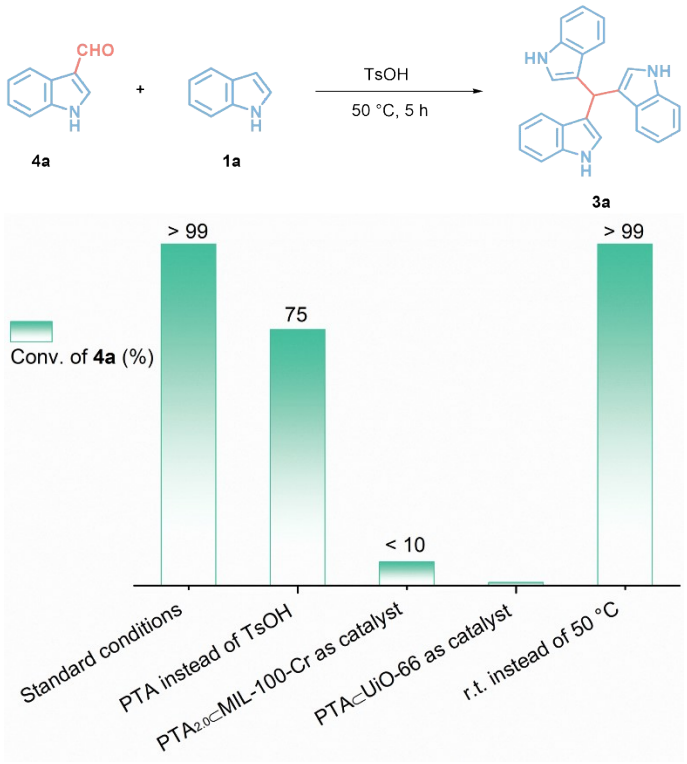


Fig. S4 The reaction of **4a** and indole over different Brønsted acid catalysts.

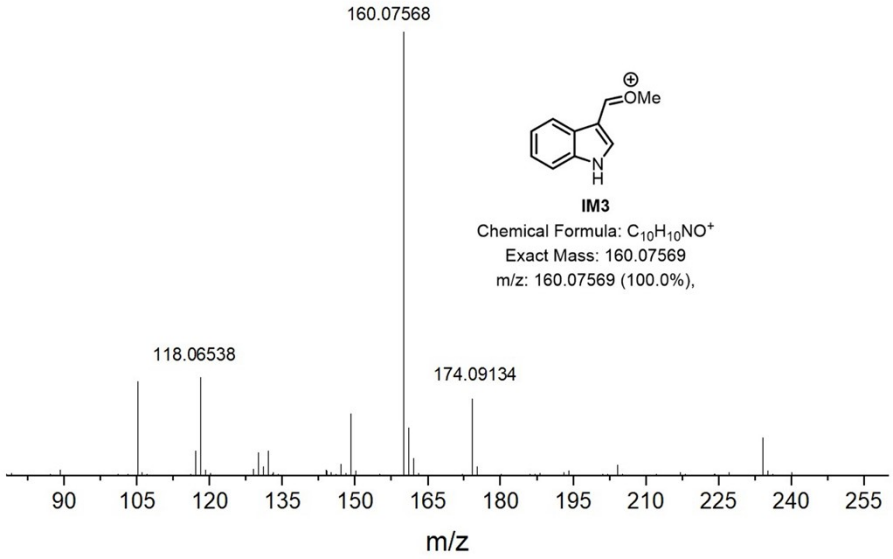
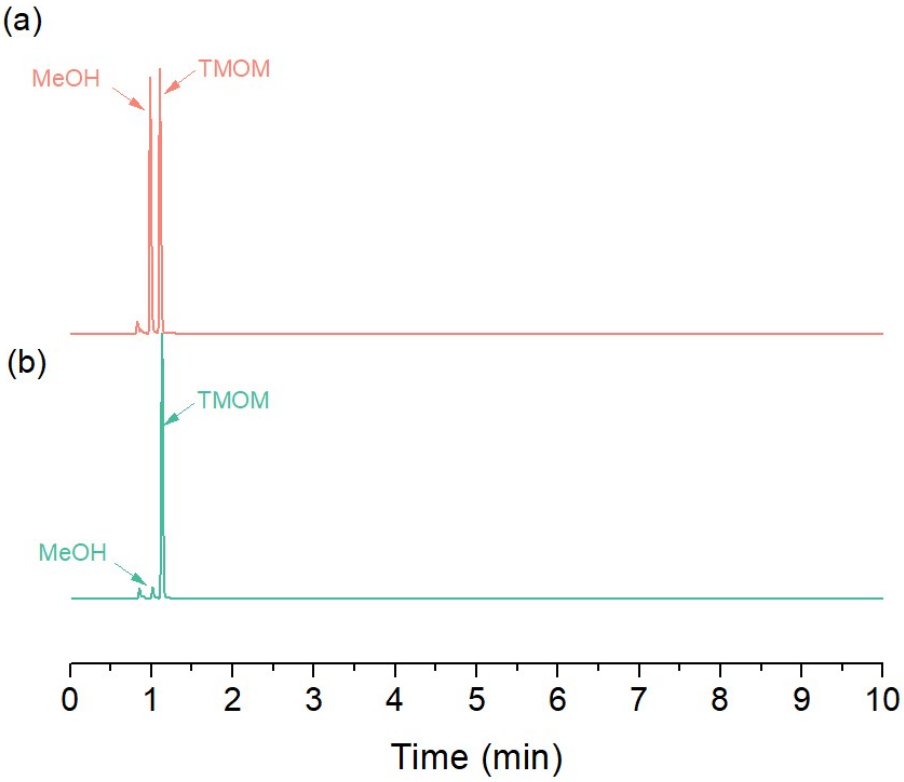


Fig. S5 High-resolution mass spectrometry data. The analysis showed that the reaction process successfully captured the critical intermediate **IM3** (m/z: cal. 160.07569; found, 160.07568).



Gas chromatography(GC). (a) GC spectrum using trimethoxymethane(TMOM) and methanol as solvents; (b) GC spectrum of the reaction solution using $PTA_{2.0}$⊂MIL-100-Cr as the catalyst.

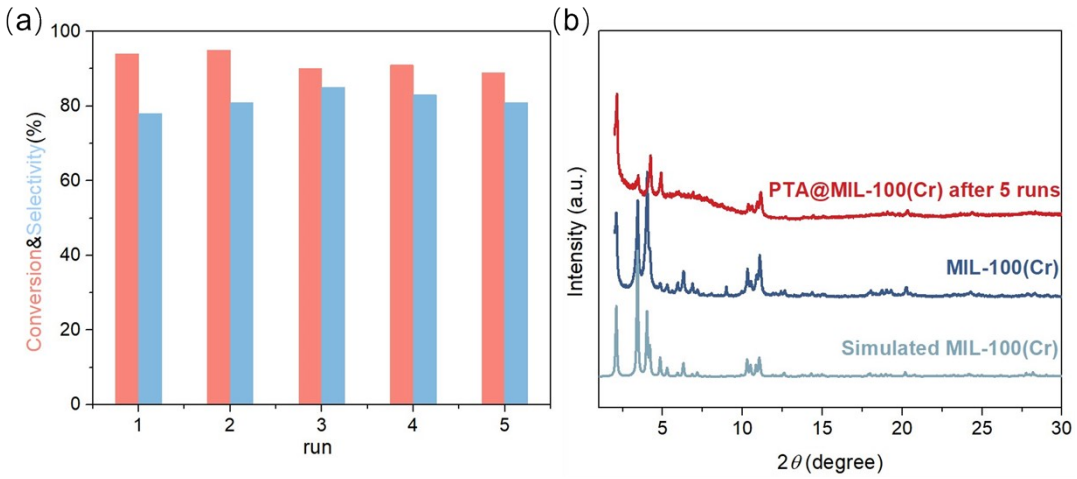
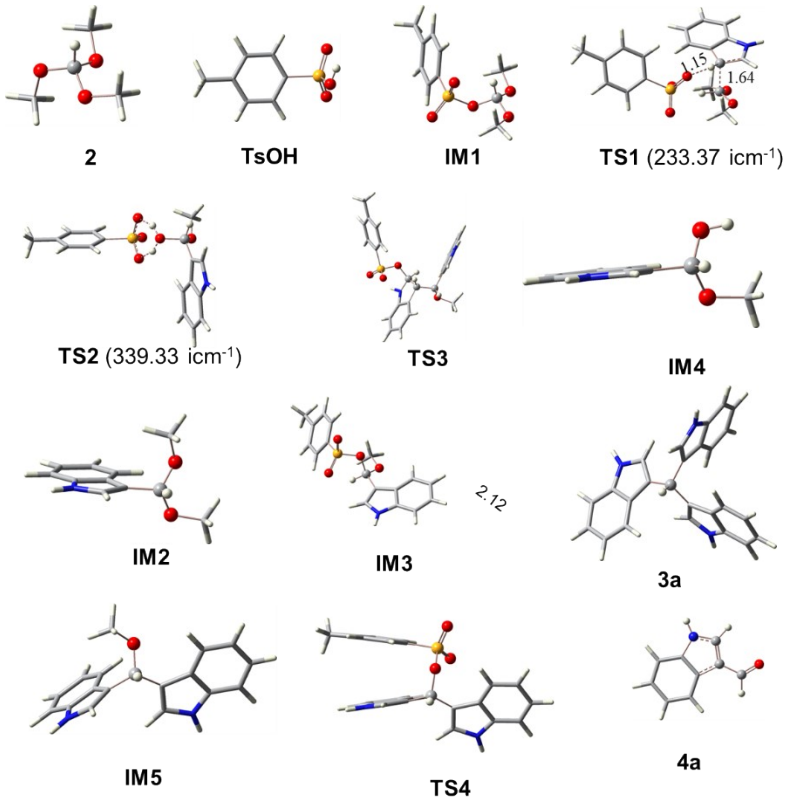


Fig. S6 Reuse of $PTA_{2.0}$⊂MIL-100-Cr in indole C-3 formylation reaction (a); PXRD pattern of $PTA_{2.0}$⊂MIL-100-Cr recovered after five runs (b).

3. Computational study

All calculations have been performed using the DFT method implemented in the commercial Gaussian 16 program package. Molecular geometries of the model complexes were optimized at the PBE0(D3BJ)/6-31G(d) level. As soon as the convergences of optimizations were obtained, the frequency calculations at the same group were performed to identify all the stationary points as minima or transition states. And the intrinsic reaction coordinate (IRC) analyses have confirmed that all fixed issues were smoothly connected. All optimized geometries mentioned were built by GaussView 6.0.



Cartesian coordinates of the stationary points

2				**TsOH**			
C	-0.906	-0.42	-0.054	S	-0.374	-0.316	-1.812
H	-0.549	-1.428	-0.054	O	1.0049	-0.316	-1.812
O	-0.429	0.2546	-1.221	O	-1.094	0.8693	-1.812
O	-0.429	0.2546	1.1137	O	-0.794	-0.947	-0.335
O	-2.336	-0.419	-0.054	H	-1.337	-0.401	0.2312
C	-0.906	1.6029	-1.222	C	-0.994	-1.426	-2.863

H	-0.539	2.111	-0.355
H	-0.558	2.1034	-2.102
H	-1.976	1.6033	-1.21
C	-2.813	-1.765	-0.142
H	-2.463	-2.323	0.7007
H	-3.883	-1.764	-0.148
H	-2.451	-2.213	-1.043
C	-0.845	-0.46	2.2806
H	-0.251	-0.154	3.1164
H	-1.876	-0.249	2.4793
H	-0.721	-1.51	2.1191

IM1

C	1.2599	1.91	0.0625
H	1.06	1.6705	1.1192
O	0.5017	2.9232	-0.422
O	2.5415	2.2263	-0.19
C	3.5021	1.348	0.3876
H	3.2831	1.1745	1.4488
H	3.5446	0.3895	-0.142
H	4.4608	1.8593	0.2932
C	-0.876	2.816	-0.131
H	-1.047	2.6257	0.9378
H	-1.32	3.7756	-0.4
H	-1.347	2.0183	-0.716
S	0.5133	-0.689	0.0507
O	0.9054	0.6698	-0.703
O	0.9818	-0.639	1.4286
O	0.9392	-1.758	-0.842
C	-1.252	-0.654	0.0551
C	-1.94	-0.84	-1.142
C	-3.324	-0.755	-1.137
C	-4.031	-0.496	0.0445
C	-3.312	-0.323	1.2293
C	-1.923	-0.399	1.245
H	-1.395	-1.049	-2.057
H	-3.871	-0.896	-2.066
H	-3.846	-0.128	2.1554
C	-0.255	-2.562	-3.227
C	-0.77	-3.5	-4.114
C	-2.047	-3.325	-4.663
C	-2.793	-2.192	-4.31
C	-2.271	-1.26	-3.422
H	0.7564	-2.702	-2.803
H	-0.173	-4.383	-4.387
H	-3.795	-2.041	-4.74
H	-2.862	-0.365	-3.153
C	-2.606	-4.332	-5.593
H	-3.345	-3.867	-6.292
H	-1.797	-4.811	-6.198
H	-3.129	-5.133	-5.011

TS1

C	-2.045	0.4562	0.9637
H	-1.265	0.786	1.6537
O	-3.183	1.1899	0.9735
C	-3.184	2.318	1.8384
H	-3.338	1.9937	2.8748
H	-2.25	2.8827	1.759
H	-4.017	2.9496	1.5257
C	-0.767	2.4096	-0.347
C	-1.741	3.1631	-1.023
C	-1.846	4.5434	-0.904
C	-0.912	5.1665	-0.083
C	0.0814	4.4332	0.586
C	0.1642	3.0505	0.4691
C	-1.035	0.9985	-0.613
C	-2.063	1.0117	-1.585
H	-2.611	5.1125	-1.424
H	-0.95	6.245	0.0373
H	0.7978	4.9613	1.2082
H	0.9109	2.4572	0.9916
H	-0.255	0.2212	-0.611
H	-2.529	0.1703	-2.08
N	-2.507	2.2579	-1.763
H	-3.291	2.5113	-2.347

H	-1.36	-0.271	2.1638
C	-5.531	-0.434	0.0354
H	-5.96	-1.443	0.0045
H	-5.918	0.062	0.9297
H	-5.902	0.1028	-0.843

IM2

C	-1.855	1.7851	-0.617
H	-0.997	2.1602	-1.202
O	-3.044	2.1496	-1.262
O	-1.81	2.2936	0.6868
C	-0.596	2.9168	1.0419
H	0.2412	2.3536	0.6063
H	-0.528	3.9453	0.659
H	-0.521	2.9263	2.1317
C	-3.593	3.3939	-0.88
H	-4.543	3.4854	-1.41
H	-3.763	3.4398	0.1986
H	-2.945	4.2347	-1.172
C	-2.725	-0.309	0.0961
C	-2.177	-0.927	1.2201
C	-2.97	-1.611	2.1293
C	-4.351	-1.602	1.9262
C	-4.911	-0.955	0.8269
C	-4.096	-0.308	-0.103
C	-1.608	0.3037	-0.699
C	-0.366	-0.246	-0.006
H	-2.527	-2.137	2.9697
H	-4.995	-2.125	2.6279
H	-5.989	-0.96	0.6875
H	-4.52	0.1872	-0.971
H	0.4332	0.4678	0.1986
N	-0.76	-0.826	1.233
H	-0.414	-0.397	2.0811

IM3

C	3.8694	0.3407	0.1379
C	4.1004	1.7334	0.2131
S	1.8	-0.929	0.658
O	1.7945	-2.17	1.4648
O	1.4071	0.2904	1.419
O	1.0297	-1.058	-0.61
C	3.5015	-0.698	0.1768
C	4.26	-1.817	-0.162
C	5.57	-1.657	-0.585
C	6.1476	-0.386	-0.677
C	5.373	0.722	-0.327
C	4.0551	0.5734	0.0983
H	3.8175	-2.805	-0.071
H	6.1617	-2.533	-0.844
H	5.8103	1.7169	-0.383
H	3.4558	1.4316	0.385
C	7.5696	-0.232	-1.138
H	7.7006	-0.612	-2.16
H	7.881	0.8177	-1.129
H	8.2597	-0.793	-0.496
O	-2.188	-0.964	0.88
C	-1.709	-1.564	2.0868
H	-2.326	-1.258	2.9059
H	-1.743	-2.629	1.9932
H	-0.701	-1.253	2.2641

TS2

C	0.3821	-0.931	0.9613
C	-0.513	0.0424	0.2339
C	-2.071	0.2286	2.0853
C	-0.989	-0.381	2.9621
C	-0.274	-1.498	2.2072
H	-0.249	0.3421	-0.777
H	-0.993	-2.267	1.9056
H	-2.507	1.1204	2.5353
H	-2.879	-0.482	1.878
H	-1.461	-0.759	3.8726
H	-0.269	0.3931	3.2552
H	0.5015	-1.961	2.8241
H	0.6586	-1.707	0.2511
N	-1.541	0.6216	0.7553

C	5.3598	2.295	0.0221	C	-2.204	1.7111	0.0599
C	6.4051	1.4257	-0.255	C	-2.307	2.9298	0.731
C	6.1969	0.0393	-0.336	C	-2.64	1.5521	-1.25
C	4.9403	-0.514	-0.142	C	-2.881	4.0148	0.0789
C	2.4644	0.1553	0.3971	H	-1.921	3.0408	1.7402
C	1.9104	1.4082	0.6015	C	-3.21	2.6537	-1.886
H	5.5193	3.3678	0.0843	H	-2.542	0.5838	-1.734
H	7.4024	1.826	-0.411	C	-3.339	3.8745	-1.23
H	7.0391	-0.61	-0.556	H	-2.962	4.9677	0.5913
H	4.783	-1.585	-0.205	H	-3.564	2.5447	-2.906
H	0.8723	1.6485	0.813	H	-3.791	4.7203	-1.738
N	2.8864	2.3387	0.4954	C	3.9615	1.9051	-0.408
H	2.7457	3.3299	0.6103	C	2.6743	1.6062	0.3916
C	1.6664	-1.024	0.4332	C	3.5462	-0.786	0.2562
H	0.6577	-0.934	0.831	C	4.3433	-0.476	-1.04
O	2.2585	-2.187	0.5925	C	4.1185	0.9415	-1.576
C	1.4346	-3.249	1.1033	H	3.2152	0.9708	-2.196
H	1.6802	-3.385	2.1596	H	4.84	1.8304	0.2443
H	0.3749	-3.004	0.9865	H	4.0778	-1.205	-1.813
H	1.6873	-4.152	0.5461	H	5.4077	-0.623	-0.82
S	-1.653	-0.137	0.124	H	4.9529	1.2391	-2.218
O	-1.084	0.7556	1.1574	H	3.9192	2.9447	-0.749
O	-1.497	-1.577	0.4439	N	2.3742	0.1398	0.2741
O	-1.13	0.1977	-1.246	C	3.0482	-2.233	0.1669
C	-3.397	0.1806	0.0318	H	2.5647	-2.552	1.0962
C	-3.862	1.2889	-0.671	H	2.3555	-2.374	-0.668
C	-5.224	1.5573	-0.694	H	3.9129	-2.885	0.0046
C	-6.134	0.7327	-0.025	C	4.4332	-0.695	1.5108
C	-5.643	-0.373	0.6712	H	3.8179	-0.774	2.4122
C	-4.281	-0.656	0.7026	H	5.1437	-1.528	1.5102
H	-3.158	1.9207	-1.203	H	5.0161	0.2275	1.5597
H	-5.59	2.4211	-1.244	C	1.5103	2.3718	-0.251
H	-6.337	-1.026	1.1948	H	0.5914	2.2618	0.3332
H	-3.895	-1.521	1.2317	H	1.7396	3.4418	-0.281
C	-7.609	1.017	-0.082	H	1.3217	2.0288	-1.274
H	-8.045	0.6493	-1.02	C	2.8251	2.1131	1.8336
H	-8.142	0.5312	0.7406	H	3.1038	3.1722	1.8007
H	-7.811	2.092	-0.031	H	1.885	2.0233	2.3822

IM4			
C	0.3915	-0.104	0
C	1.5421	0.7053	-6E-05
C	2.8323	0.1953	-7E-05
C	2.9488	-1.19	-2E-05
C	1.8174	-2.017	5E-05
C	0.5302	-1.49	7E-05
C	-0.742	0.8075	0
C	-0.208	2.1187	5E-05
H	3.7071	0.8378	-1E-04
H	3.9368	-1.639	-1E-05
H	1.9505	-3.094	8E-05
H	-0.338	-2.14	9E-05
H	-0.723	3.0704	4E-05
N	1.1145	2.0393	3E-05
H	1.7357	2.839	7E-05
C	-2.097	0.5655	2E-05
H	-2.718	1.3363	-0.461
TS4			
C	2.2189	0.0238	0.0762
C	3.4473	0.465	-0.476
C	4.5874	-0.337	-0.499
C	4.4844	-1.607	0.0471
C	3.283	-2.061	0.6186
C	2.1532	-1.259	0.6486
C	1.2836	1.1069	-0.081
C	1.9673	2.1351	-0.687
H	5.5219	0.0171	-0.924
H	5.3535	-2.257	0.0475
H	3.2503	-3.051	1.0639
H	1.2463	-1.593	1.1446
H	1.6245	3.1226	-0.967
N	3.2538	1.75	-0.929
H	3.9647	2.3348	-1.34
C	-0.164	1.0874	0.2624
H	-0.548	2.1181	0.3487
O	-0.459	0.3479	1.4176
H	3.5968	1.5787	2.3891
O	1.541	-0.205	1.3842
C	-1.761	-2.342	-0.925
H	-1.507	-3.276	-0.442
C	-0.835	-1.816	-1.859
O	-0.884	-0.805	-2.558
O	0.3194	-2.587	-1.872
C	1.3781	-2.056	-2.648
H	2.1502	-2.828	-2.675
H	1.0468	-1.812	-3.659
H	1.7827	-1.148	-2.179
C	-2.97	-1.716	-0.541
O	-3.461	-0.646	-0.893
O	-3.604	-2.449	0.4588
C	-4.942	-2.065	0.7112
H	-5.264	-2.634	1.5843
H	-5.03	-0.991	0.9001
H	-5.583	-2.305	-0.144
IM5			
C	2.1866	0.071	-0.283
C	3.3132	0.6262	-0.94
C	4.4273	-0.137	-1.287
C	4.4029	-1.484	-0.963
C	3.306	-2.055	-0.294
C	2.2032	-1.293	0.0581
C	1.2478	1.1461	-0.095
C	1.8334	2.2777	-0.613
H	5.2837	0.3048	-1.788
H	5.2548	-2.107	-1.216
H	3.3372	-3.108	-0.03
H	1.3857	-1.727	0.6273
H	1.4585	3.2919	-0.656
N	3.0601	1.9665	-1.123
H	3.7004	2.628	-1.534
C	-0.125	1.0382	0.4683
H	-0.481	2.0302	0.7949
O	-0.235	0.1026	1.5078

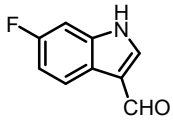
C	0.0367	0.9444	2.6033	C	0.451	0.4926	2.6842
H	1.1308	1.0109	2.5899	H	1.529	0.5821	2.5067
H	-0.387	1.9486	2.7394	H	0.0635	1.449	3.0611
H	-0.282	0.3048	3.4273	H	0.2642	-0.287	3.4236
C	-2.495	0.3216	-0.538	C	-2.561	0.3779	-0.068
C	-2.848	-1.026	-0.453	C	-2.909	-0.97	-0.166
C	-4.119	-1.48	-0.147	C	-4.117	-1.496	0.2572
C	-5.078	-0.496	0.0858	C	-5.016	-0.587	0.8102
C	-4.753	0.8611	0.0072	C	-4.697	0.7689	0.9199
C	-3.46	1.2861	-0.304	C	-3.468	1.2674	0.4836
C	-1.03	0.4076	-0.859	C	-1.167	0.5477	-0.601
C	-0.656	-1.022	-0.988	C	-0.832	-0.829	-1.037
H	-4.364	-2.536	-0.088	H	-4.358	-2.551	0.1679
H	-6.093	-0.791	0.3303	H	-5.981	-0.94	1.1594
H	-5.525	1.6011	0.1918	H	-5.422	1.4498	1.3535
H	-3.226	2.3448	-0.36	H	-3.236	2.3241	0.5775
H	0.3251	-1.428	-1.207	H	-1.099	1.2395	-1.45
N	-1.683	-1.777	-0.743	H	0.097	-1.172	-1.48
H	-1.653	-2.792	-0.741	N	-1.813	-1.636	-0.766

4a				**3a**			
C	-0.331	-0.07	0	C	-2.338	5.462	0.3189
C	-1.512	0.707	0	C	-3.347	6.3079	-0.205
C	-2.787	0.1473	0	C	-4.208	7.0355	0.6181
C	-2.868	-1.238	0	C	-4.044	6.8999	1.9876
C	-1.71	-2.033	0	C	-3.052	6.0604	2.5274
C	-0.445	-1.464	0	C	-2.199	5.3389	1.7087
C	0.7859	0.8597	0	C	-1.651	4.8788	-0.802
C	0.2237	2.1254	0	C	-2.256	5.3699	-1.927
H	-3.681	0.765	1E-05	H	-4.978	7.6813	0.2043
H	-3.844	-1.714	0	H	-4.698	7.4514	2.6578
H	-1.811	-3.114	0	H	-2.959	5.977	3.6066
H	0.4484	-2.079	0	H	-1.438	4.6825	2.1176
H	0.7366	3.0774	0	H	-2.036	5.1733	-2.968
N	-1.128	2.0397	1E-05	N	-3.267	6.2338	-1.576
H	-1.762	2.8227	-7E-05	H	-3.868	6.7176	-2.221
C	2.1815	0.7321	1E-05	C	-0.498	3.9242	-0.736
O	2.6672	1.437	-0.922	H	-0.357	3.666	-1.803

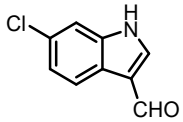
H	2.446	-0.293	-0.157	C	1.9924	4.7089	-0.91
				C	2.7297	5.7958	-0.376
				C	4.0786	5.9979	-0.67
				C	4.6896	5.0875	-1.518
				C	3.9781	3.9997	-2.055
				C	2.6406	3.7997	-1.757
				C	0.6522	4.8197	-0.4
				C	0.6283	5.9298	0.4007
				H	4.6305	6.8353	-0.251
				H	5.7394	5.2146	-1.768
				H	4.4927	3.3014	-2.71
				H	2.0984	2.9453	-2.149
				H	-0.192	6.3458	0.9679
				N	1.8693	6.5194	0.4144
				H	2.1146	7.338	0.9449
				C	-0.556	1.7448	-0.746
				C	0.7608	1.4086	-0.338
				C	1.5329	0.4615	-1.013
				C	0.9659	-0.156	-2.116
				C	-0.338	0.1609	-2.539
				C	-1.1	1.1009	-1.867
				C	-1.033	2.7389	0.1688
				C	-0.03	2.9669	1.0696
				H	2.5402	0.2161	-0.686
				H	1.5393	-0.898	-2.664
				H	-0.75	-0.343	-3.409
				H	-2.107	1.3389	-2.201
				H	0.0082	3.6416	1.9137
				N	1.0487	2.1692	0.7682
				H	1.9155	2.1482	1.2785

4. NMR data of products

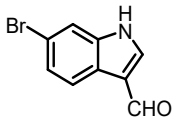
Almost all products are commercially available:



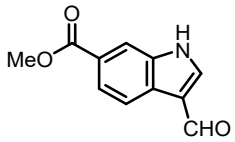
6-Fluoro-1*H*-indole-3-carbaldehyde (**4b**)**:** 63%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (s, 1H), 9.92 (s, 1H), 8.31 (s, 1H), 8.07 (dd, J = 8.7Hz, 1H), 7.32 (dd, J = 8.7 Hz, 1H), 7.13 – 7.05 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.48, 158.82, 139.64, 137.69, 122.34, 121.25, 118.50, 110.81, 99.14.



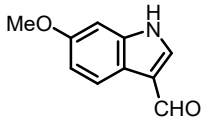
6-Chloro-1*H*-indole-3-carbaldehyde (4c): 61%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.23 (s, 1H), 9.93 (s, 1H), 8.34 (s, 1H), 8.07 (d, J = 1.9 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.25 (dd, J = 8.4, 1.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.58, 139.75, 137.97, 128.37, 123.33, 122.91, 122.55, 118.43, 112.69.



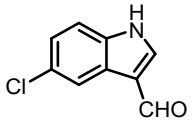
6-Bromo-1*H*-indole-3-carbaldehyde (**4d**)**:** 55%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.23 (s, 1H), 9.93 (s, 1H), 8.33 (s, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 1.8 Hz, 1H), 7.37 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.54, 139.38, 138.30, 128.37, 125.35, 122.91, 122.53, 116.38, 115.55.



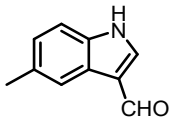
Methyl 3-formyl-1*H*-indole-6-carboxylate (**4e**)**:** 51%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.46 (s, 1H), 9.99 (s, 1H), 8.52 (d, J = 2.9 Hz, 1H), 8.23 – 8.10 (m, 2H), 7.84 (d, J = 8.3 Hz, 1H), 2.51 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.72, 167.10, 141.40, 136.92, 128.22, 124.99, 123.23, 121.14, 118.50, 114.63, 52.53.



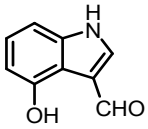
6-Methoxy-1*H*-indole-3-carbaldehyde (**4f**)**:** 73%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 9.86 (s, 1H), 8.16 (s, 1H), 7.93 (d, J = 8.6 Hz, 1H), 6.99 (d, J = 2.3 Hz, 1H), 6.86 (dd, J = 8.7, 2.3 Hz, 1H), 3.79 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.20, 157.23, 138.49, 138.18, 121.89, 118.75, 118.47, 112.28, 95.95, 55.72.



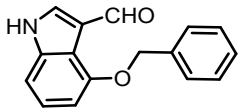
5-Chloro-1*H*-indole-3-carbaldehyde (**4g**)**:** 42%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.31 (s, 1H), 9.94 (s, 1H), 8.38 (s, 1H), 8.07 (s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.60, 139.90, 135.96, 127.26, 125.75, 123.96, 120.35, 118.03, 114.60.



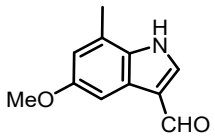
5-Methyl-1*H*-indole-3-carbaldehyde (**4h**)**:** 81%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 9.89 (s, 1H), 8.22 (d, J = 3.1 Hz, 1H), 7.90 (s, 1H), 7.08 (d, J = 8.0 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.30, 138.86, 135.82, 131.51, 125.36, 124.86, 121.04, 118.29, 112.49, 21.77.



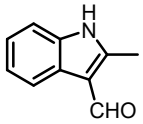
4-Hydroxy-1*H*-indole-3-carbaldehyde (**4i**)**:** 86%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.38 (s, 1H), 10.55 (s, 1H), 9.64 (s, 1H), 8.37 (d, J = 3.0 Hz, 1H), 7.12 (t, J = 7.9 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.54 (d, J = 7.7 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.63, 151.64, 140.11, 139.44, 126.35, 118.99, 114.37, 107.21, 104.11.



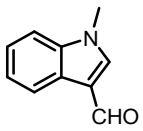
4-(Benzyloxy)-1*H*-indole-3-carbaldehyde (**4j**)**:** 78%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.26 (s, 1H), 10.32 (s, 1H), 8.07 (d, J = 3.1 Hz, 1H), 7.54 (d, J = 6.8 Hz, 2H), 7.43 (m, 2H), 7.35 (d, J = 8.3 Hz, 1H), 7.18 – 7.10 (m, 2H), 6.88 (d, J = 6.8 Hz, 1H), 5.29 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.66, 153.16, 138.55, 137.72, 130.34, 128.98, 128.33, 128.07, 123.97, 121.46, 118.56, 116.05, 114.97, 106.53, 104.07, 69.95.



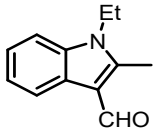
5-Methoxy-7-methyl-1*H*-indole-3-carbaldehyde (**4k**)**:** 58%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 9.90 (s, 1H), 8.22 (d, J = 3.3 Hz, 1H), 7.42 (d, J = 2.5 Hz, 1H), 6.76 – 6.65 (m, 1H), 3.77 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.32, 156.21, 138.48, 131.93, 125.03, 123.29, 118.88, 114.27, 100.43, 55.67, 17.10.



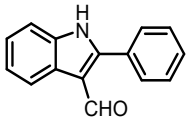
2-Methyl-1*H*-indole-3-carbaldehyde (4l): 81%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.99 (s, 1H), 10.06 (s, 1H), 8.04 (d, J = 6.6 Hz, 1H), 7.42 – 7.36 (m, 1H), 7.27 – 7.11 (m, 2H), 2.69 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.69, 148.96, 135.79, 126.03, 123.06, 122.31, 120.41, 114.09, 111.82, 12.13.



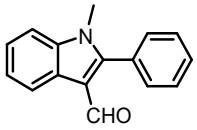
1-Methyl-1*H*-indole-3-carbaldehyde (4m): 77%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 8.29 (s, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.31 (m, 2H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.83, 141.97, 128.94, 125.98, 124.98, 123.96, 121.37, 117.9, 111.41, 33.81.



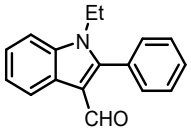
1-Ethyl-2-methyl-1*H*-indole-3-carbaldehyde (4n): 83%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1H), 8.10 (d, J = 7.3 Hz, 1H), 7.57 (d, J = 7.9 Hz, 1H), 7.23 (m, 2H), 4.26 (q, J = 7.2 Hz, 2H), 2.73 (s, 3H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.71, 148.91, 136.20, 125.65, 123.19, 122.70, 120.60, 113.97, 110.63, 38.12, 15.01, 10.23.



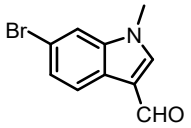
2-Phenyl-1*H*-indole-3-carbaldehyde (4o): 87%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.42 (s, 1H), 9.97 (s, 1H), 8.24 – 8.19 (m, 1H), 7.81 – 7.77 (m, 2H), 7.64 – 7.57 (m, 3H), 7.52 (d, J = 7.8 Hz, 1H), 7.28 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.99, 149.56, 136.38, 130.36, 130.31, 130.24, 129.45, 126.23, 124.19, 122.92, 121.53, 113.94, 112.49.



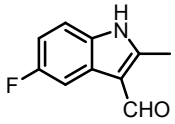
1-Methyl-2-phenyl-1*H*-indole-3-carbaldehyde (4p): 90%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.62 (s, 1H), 8.23 (d, J = 7.7 Hz, 1H), 7.71 – 7.61 (m, 7H), 7.36 (m, 2H), 3.70 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.66, 151.70, 137.58, 131.47, 130.36, 129.14, 128.56, 125.00, 124.24, 123.43, 121.33, 114.90, 111.49, 31.54.



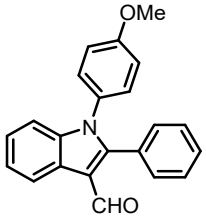
1-Ethyl-2-phenyl-1*H*-indole-3-carbaldehyde (**4q**)**:** 89%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.55 (s, 1H), 8.24 (d, J = 7.7 Hz, 1H), 7.67 (m, 6H), 7.35 (dd, J = 7.8, 6.9 Hz, 2H), 4.16 (q, J = 7.1 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.57, 151.41, 136.31, 131.16, 130.38, 129.20, 128.76, 128.07, 125.22, 124.27, 123.37, 121.51, 115.37, 111.59, 15.34.



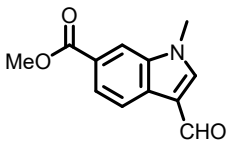
6-Bromo-1-methyl-1*H*-indole-3-carbaldehyde (**4s**)**:** 80%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 8.34 (s, 1H), 8.23 (d, J = 2.0 Hz, 1H), 7.60 (d, J = 8.7 Hz, 1H), 7.48 (dd, J = 8.2, 1.9 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.04, 142.75, 136.96, 126.71, 126.51, 123.44, 116.64, 115.79, 113.71, 34.04.



5-Fluoro-2-methyl-1*H*-indole-3-carbaldehyde (**4t**)**:** 75%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 10.03 (s, 1H), 7.72 (dd, J = 8.0, 4.6 Hz, 1H), 7.39 (dd, J = 8.0, 4.6 Hz, 1H), 7.02 (m, 1H), 2.68 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.78, 160.28, 157.95, 150.36, 132.37, 114.21, 113.07, 110.97, 105.65, 12.05.

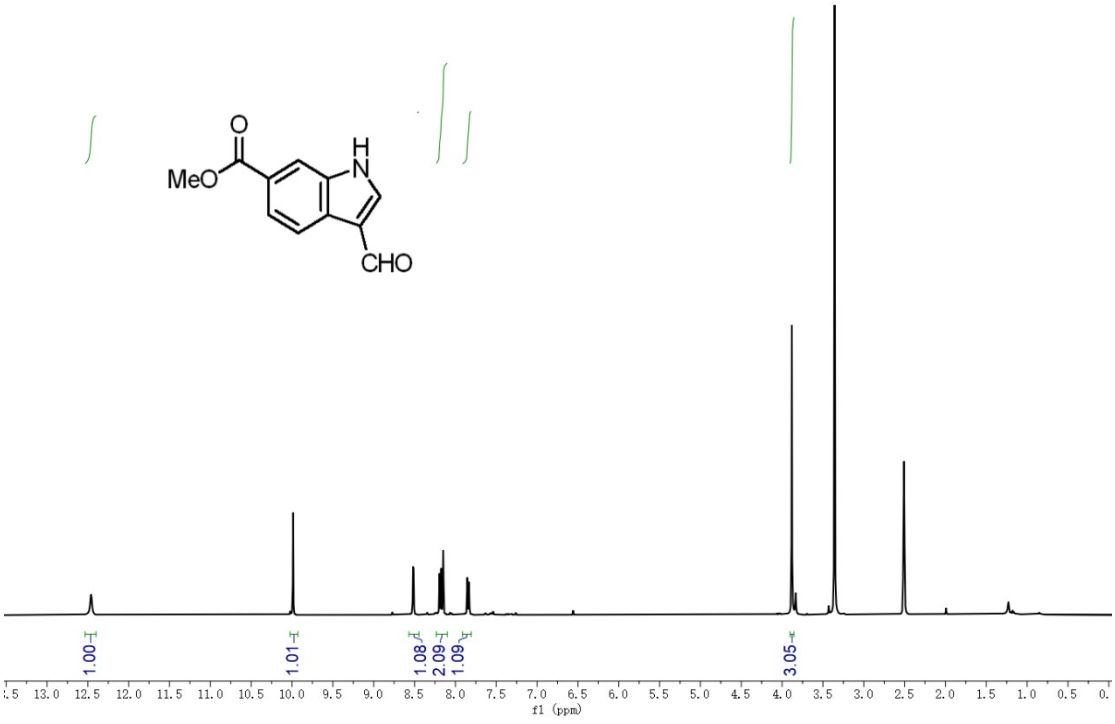


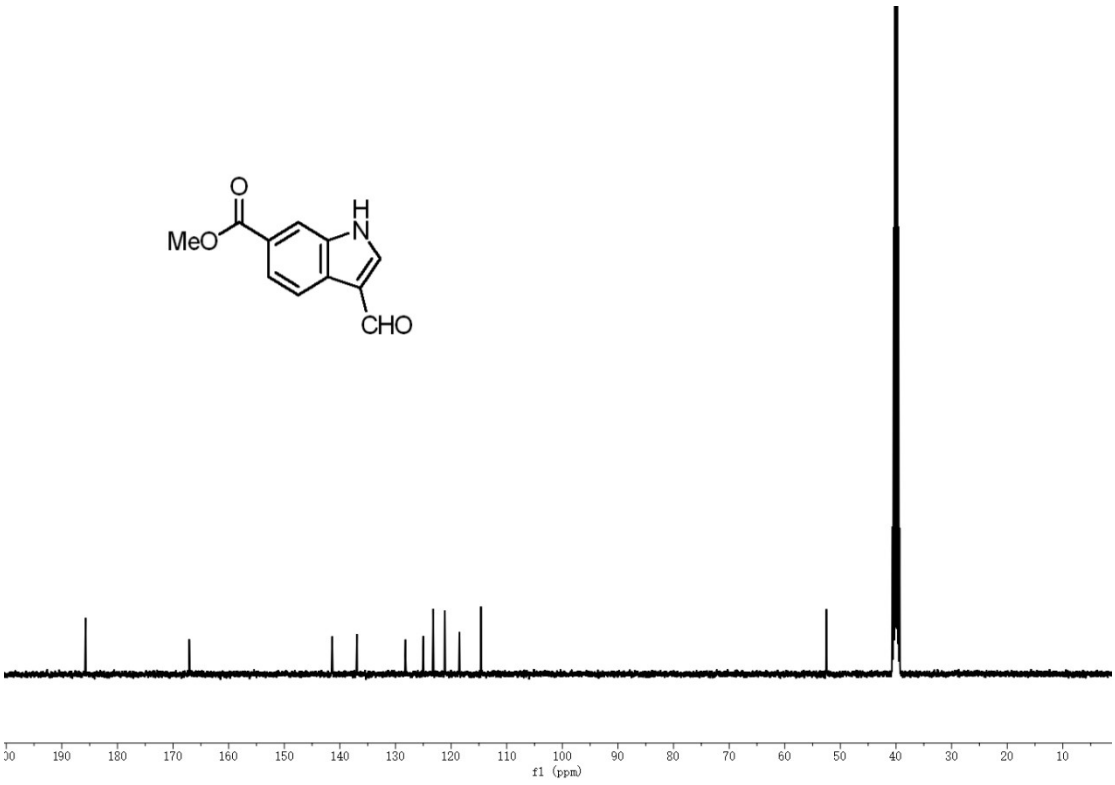
1-(4-Methoxyphenyl)-2-phenyl-1*H*-indole-3-carbaldehyde (**4r**)**:** 79%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 8.35 – 8.26 (m, 1H), 7.48 – 7.28 (m, 9H), 7.13 (d, J = 7.8 Hz, 1H), 7.04 – 6.99 (m, 2H), 3.78 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.42, 159.48, 151.56, 138.70, 131.66, 129.98, 129.89, 128.83, 128.73, 128.71, 124.94, 124.81, 123.78, 121.55, 115.63, 115.14, 111.58, 55.85.

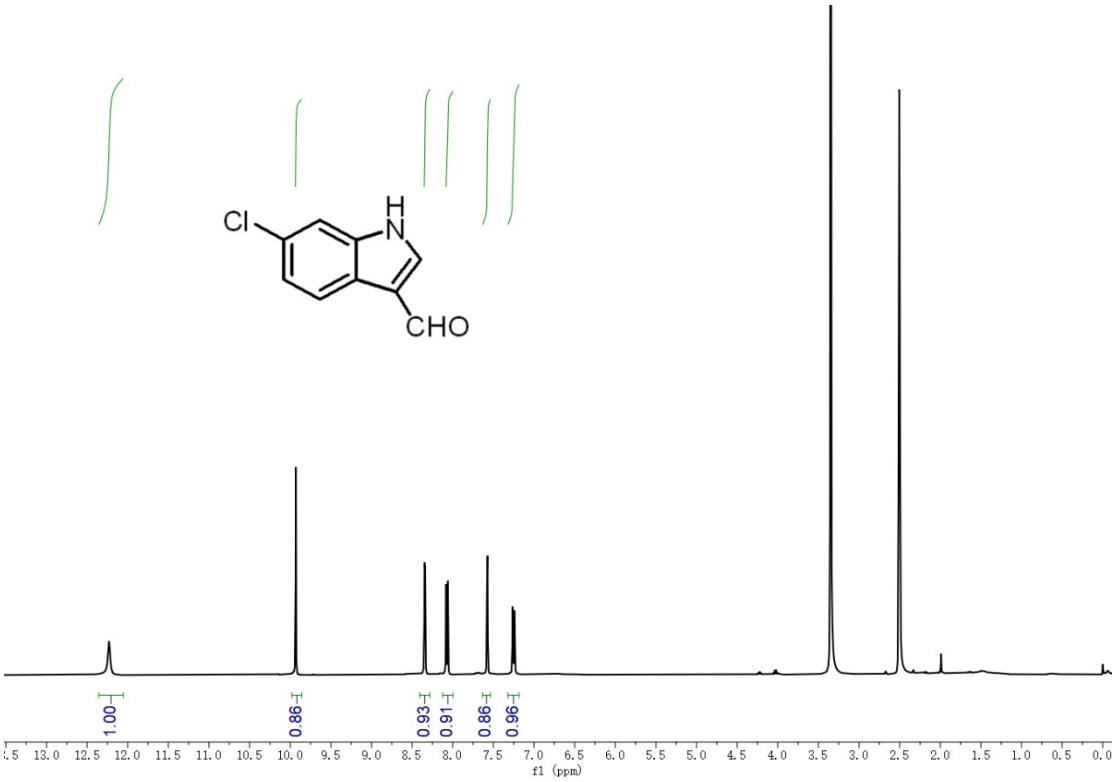


1-(4-Methoxyphenyl)-2-phenyl-1*H*-indole-3-carbaldehyde (**4-4s**)**:** 71%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.96 (s, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 1.4 Hz, 1H), 7.94 (dd, J = 8.4, 1.5 Hz, 1H), 7.76 (s, 1H), 3.89 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.27, 167.47, 141.01, 137.42, 128.89, 125.83, 123.93, 121.70, 118.05, 112.17, 52.24, 33.95.

5. NMR spectra of some products



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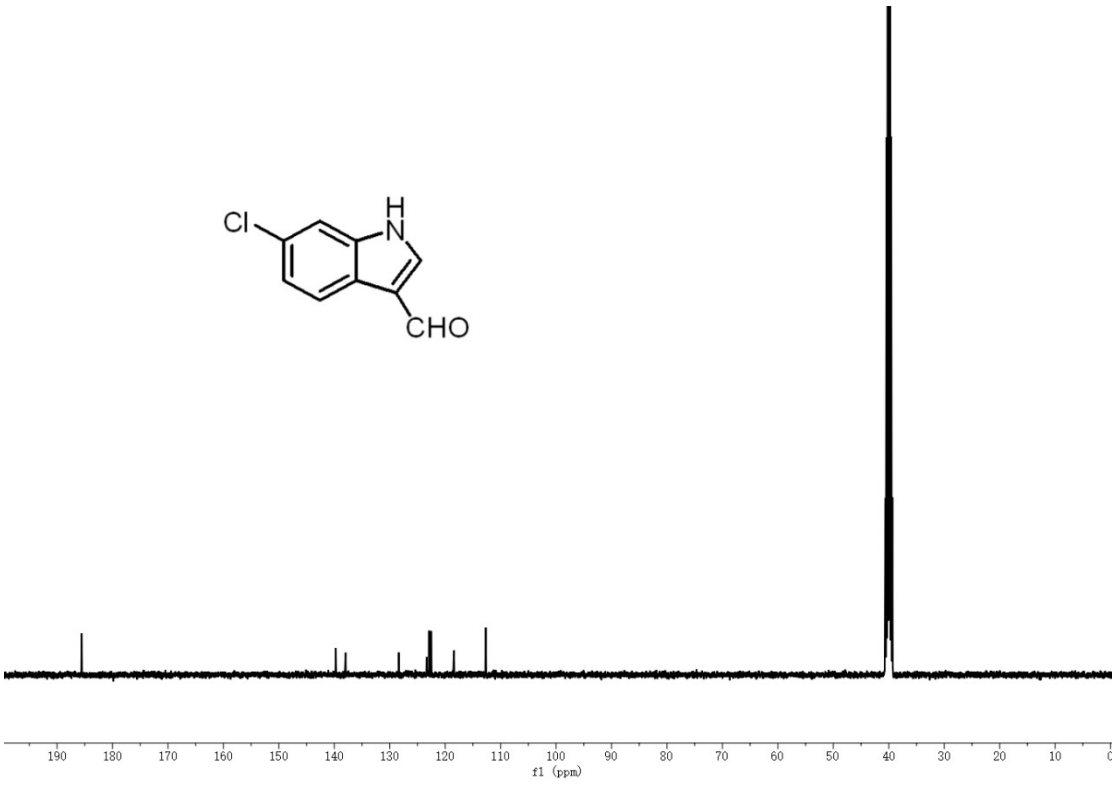
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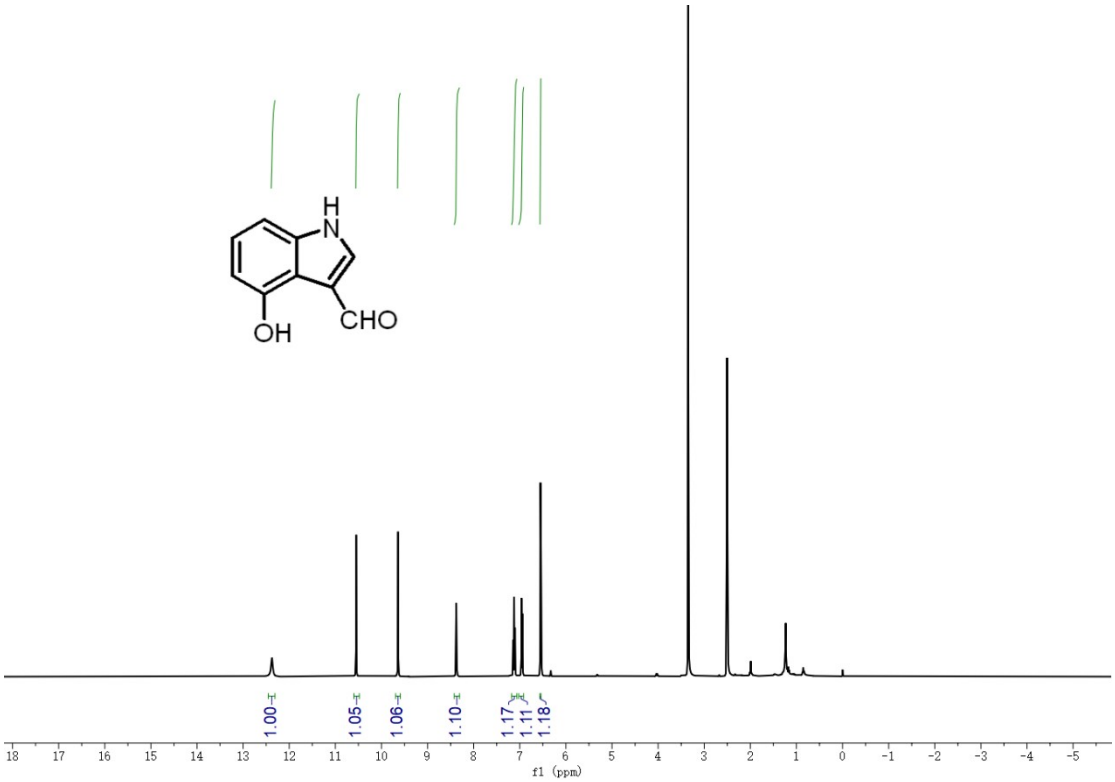
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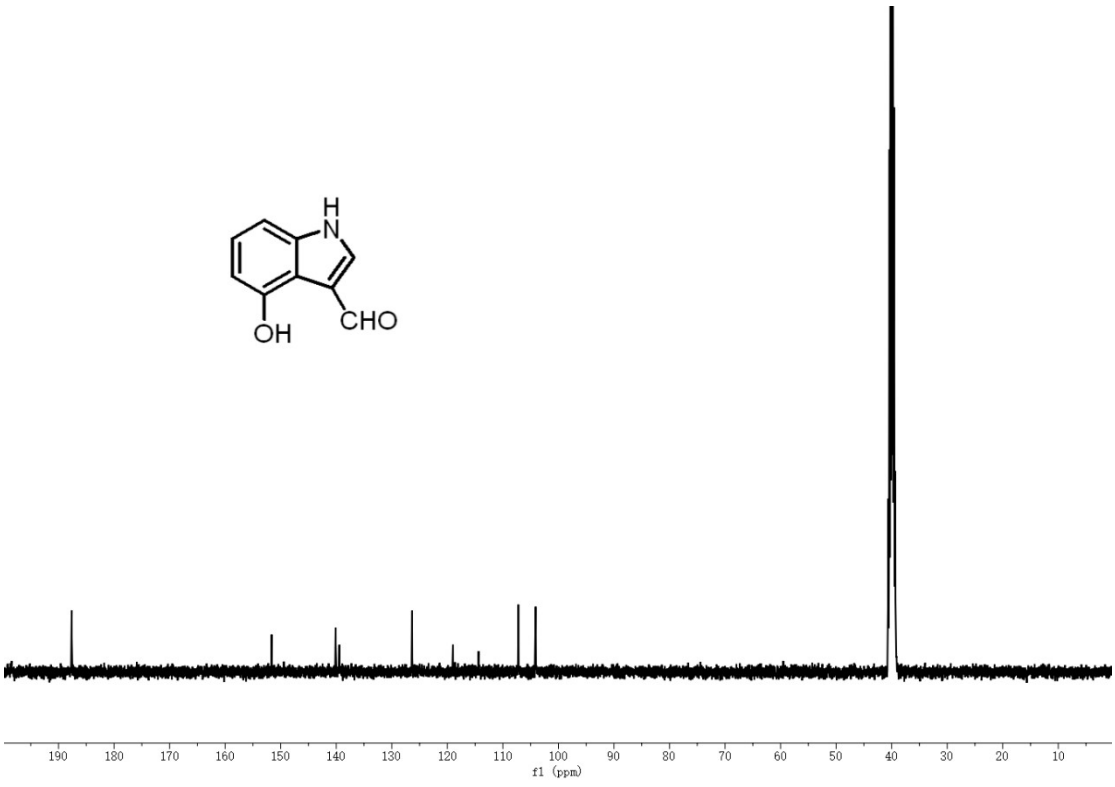
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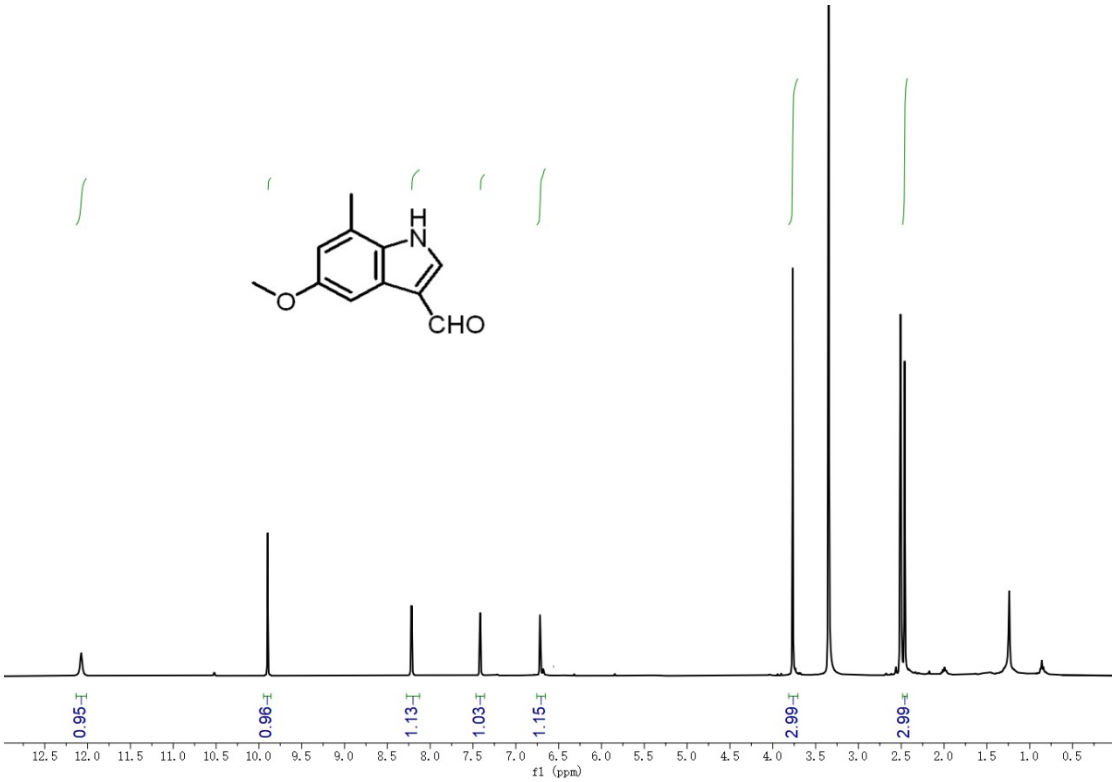
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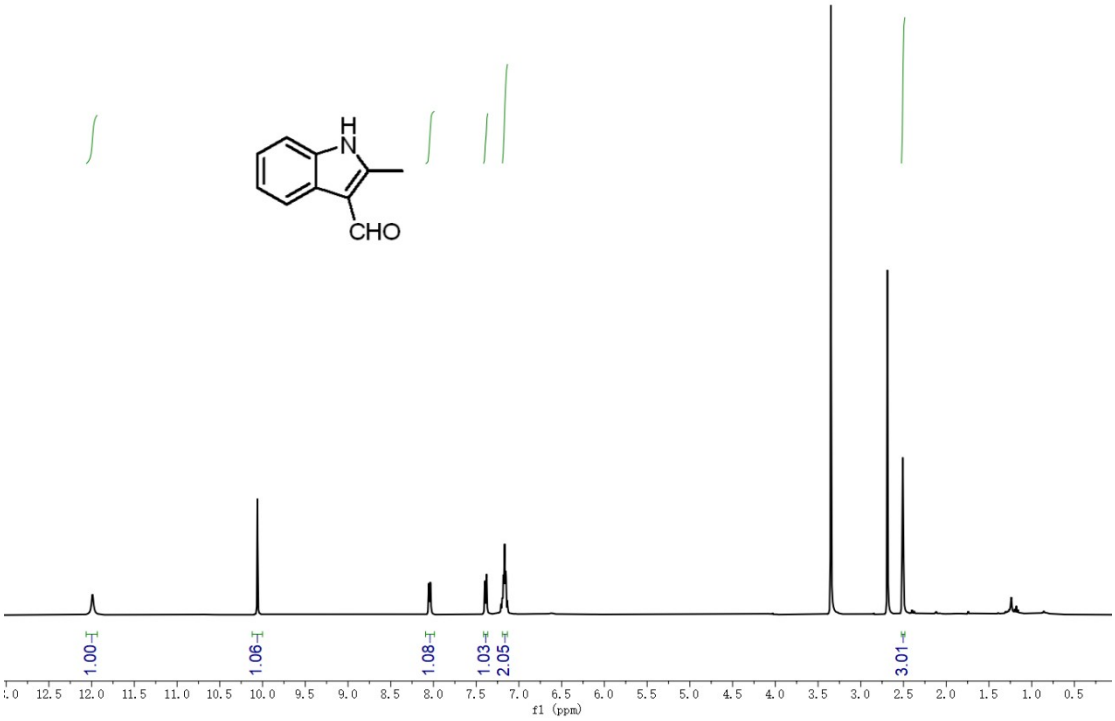
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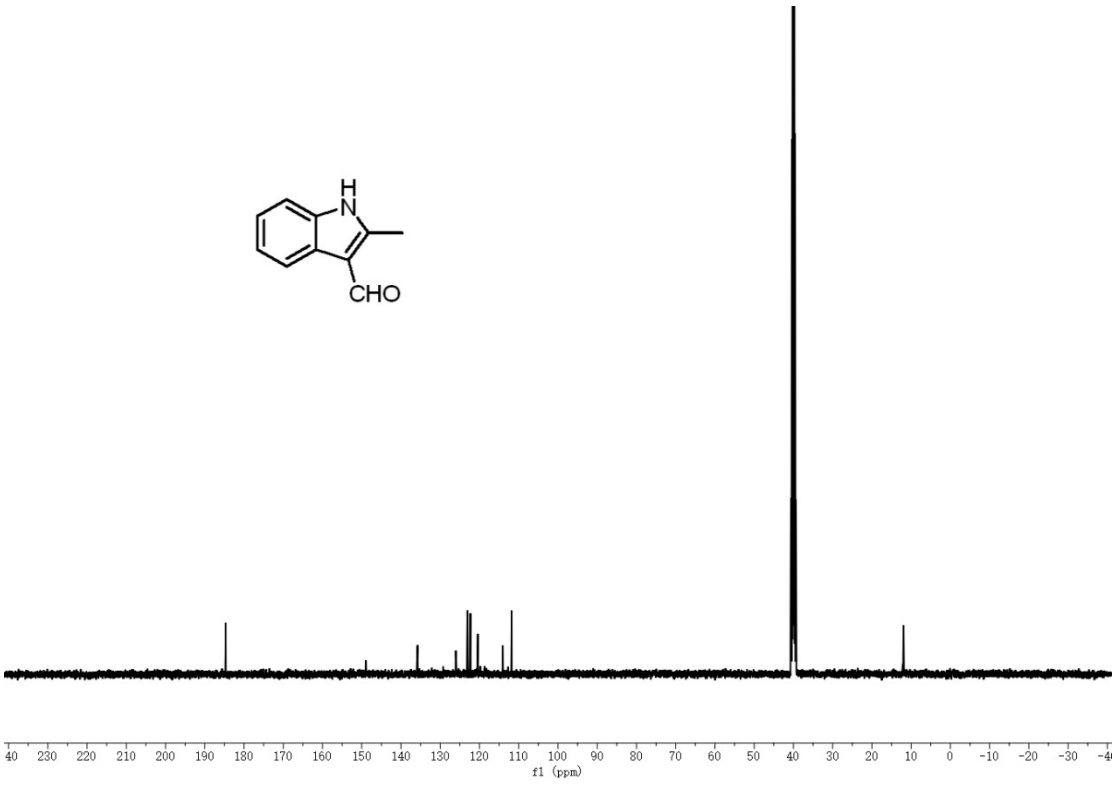
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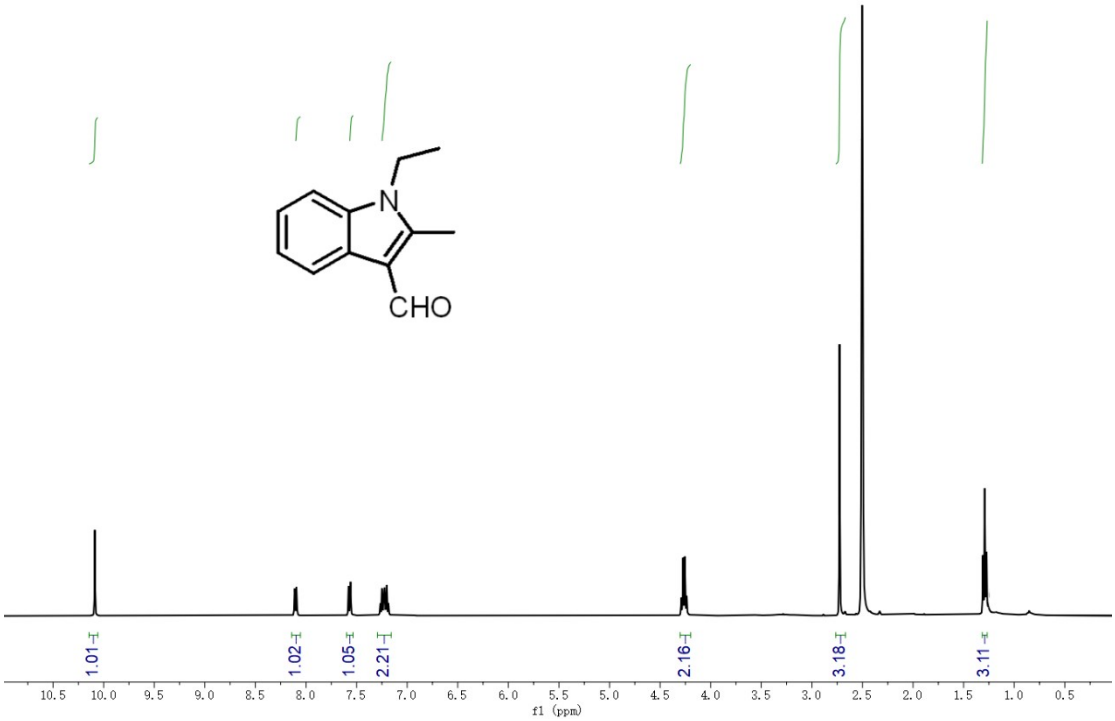
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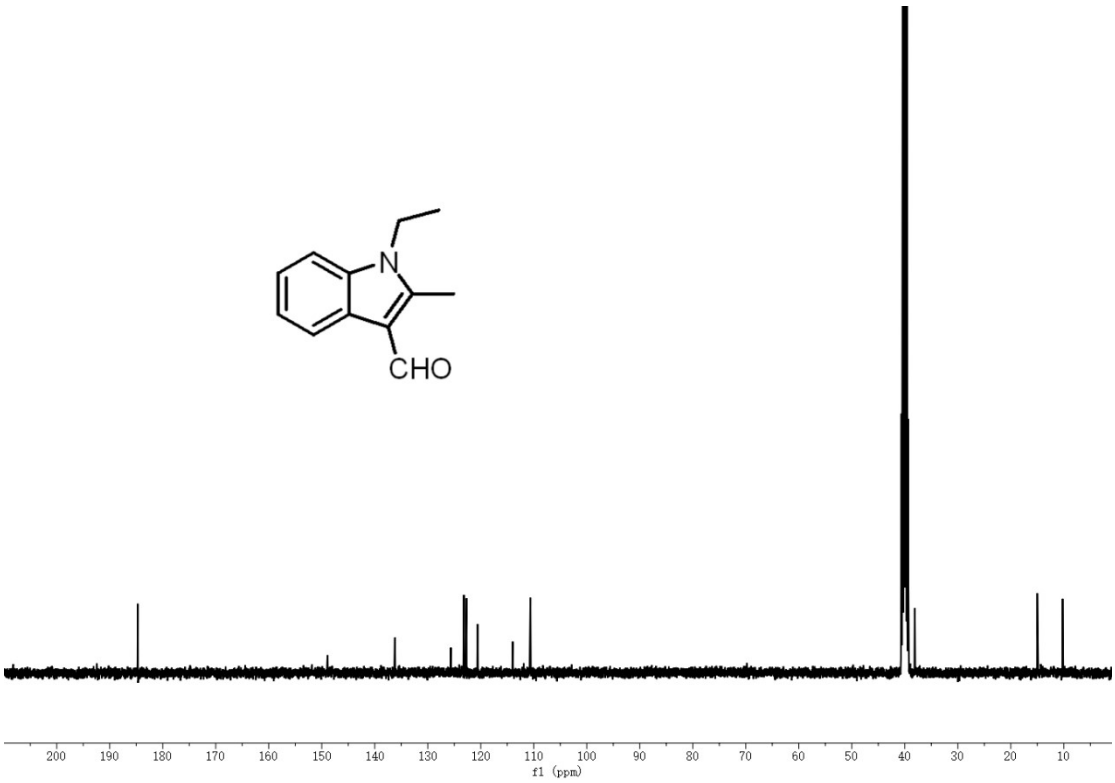
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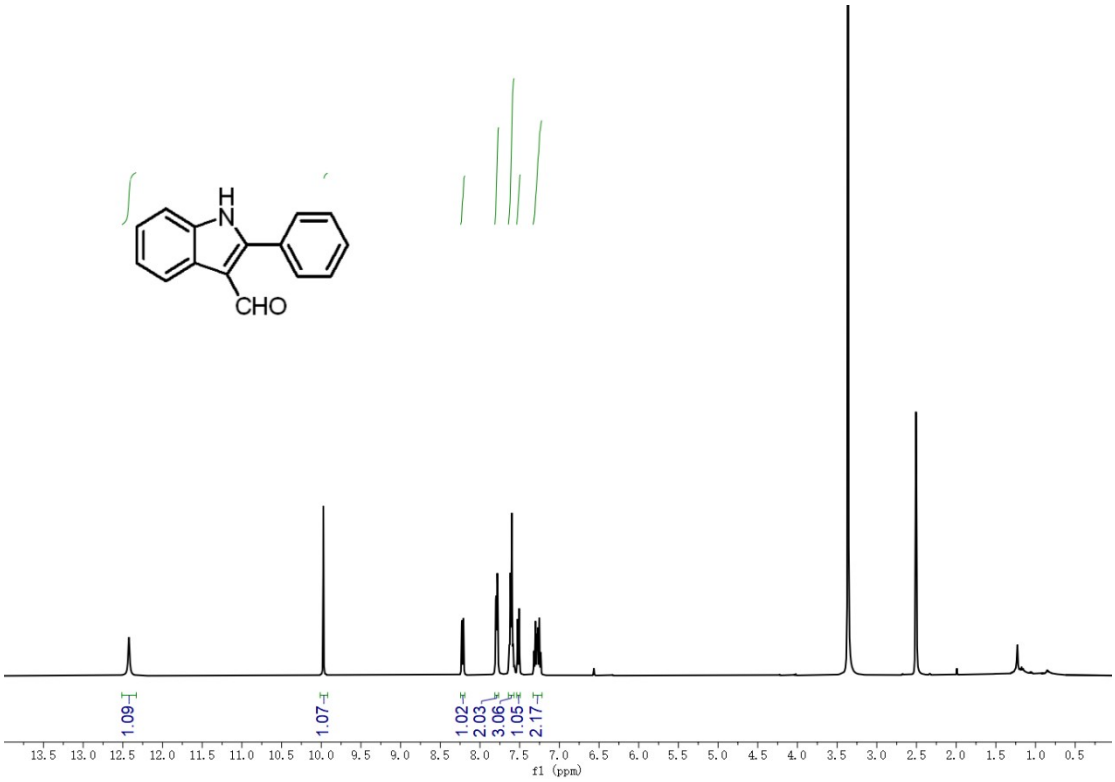
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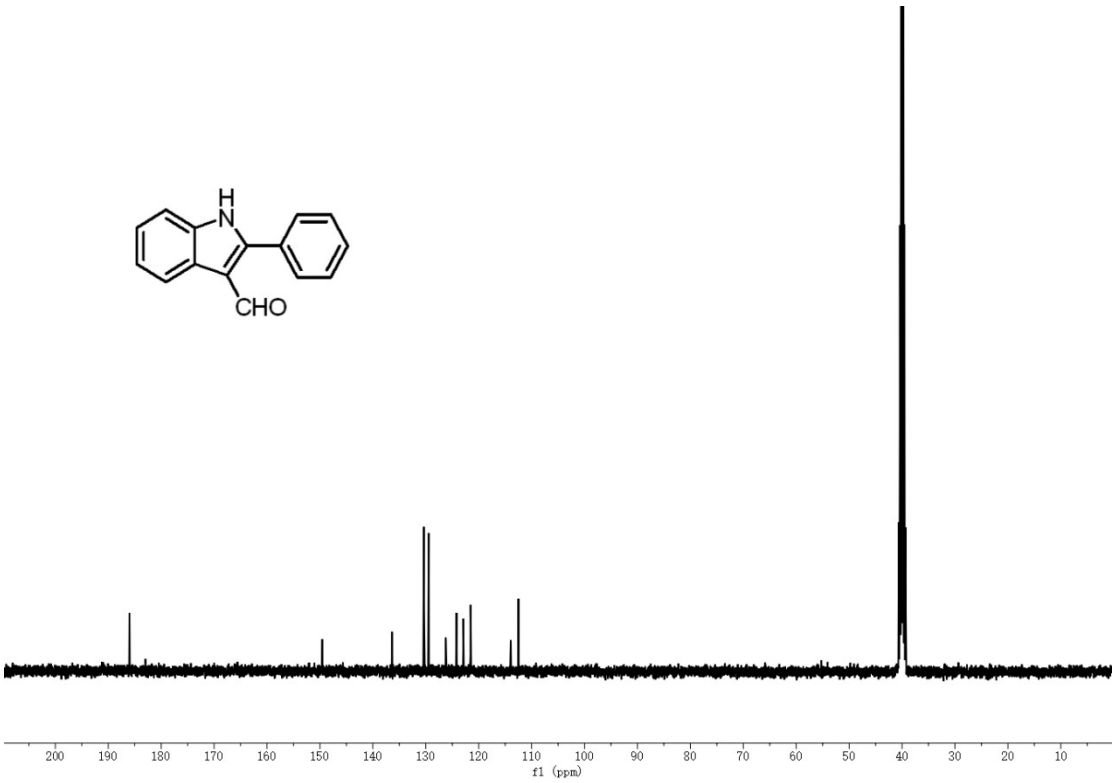
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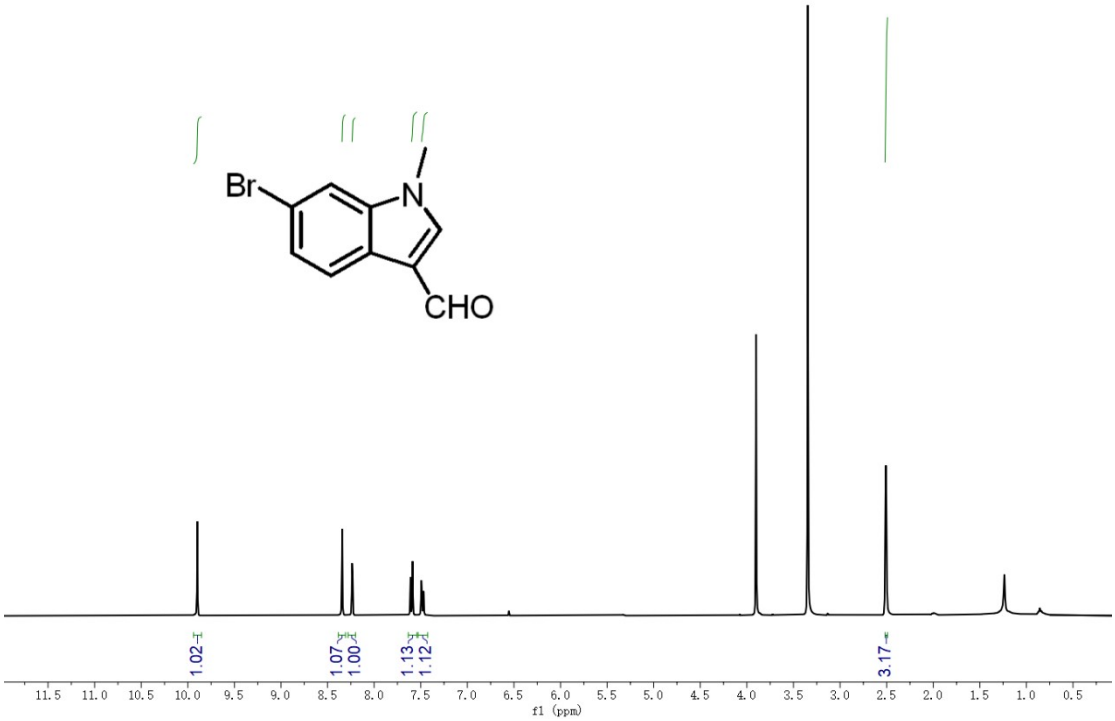
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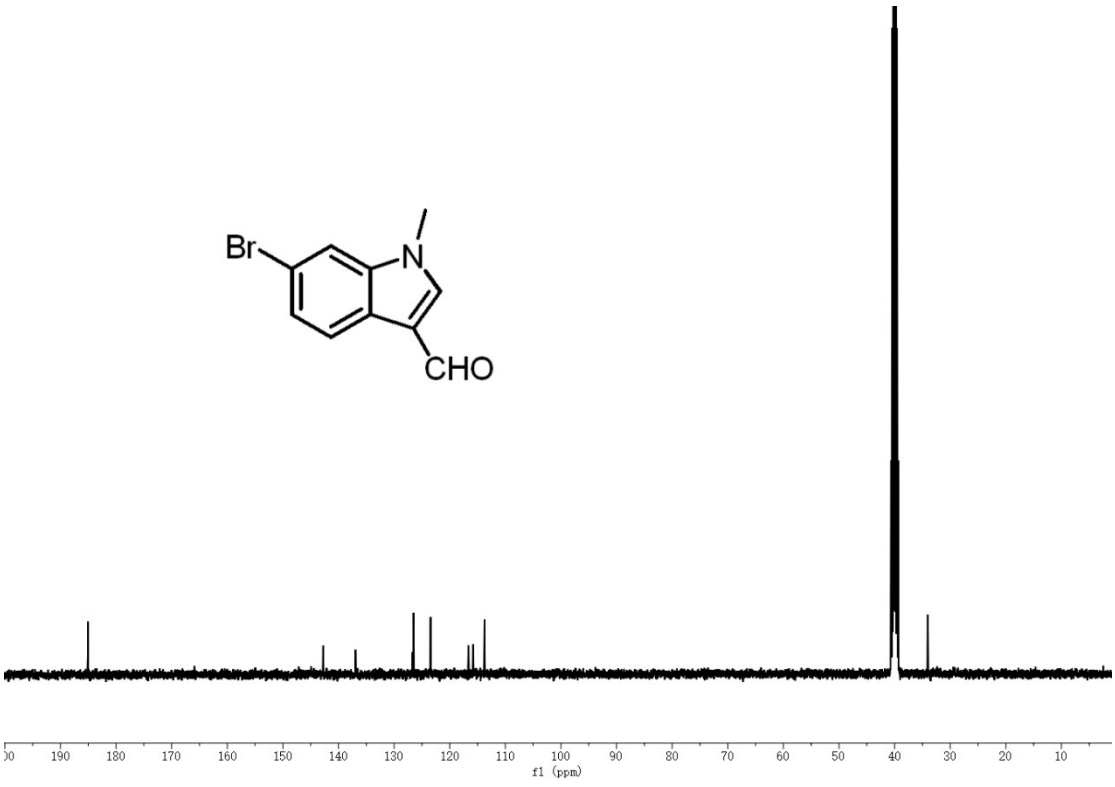
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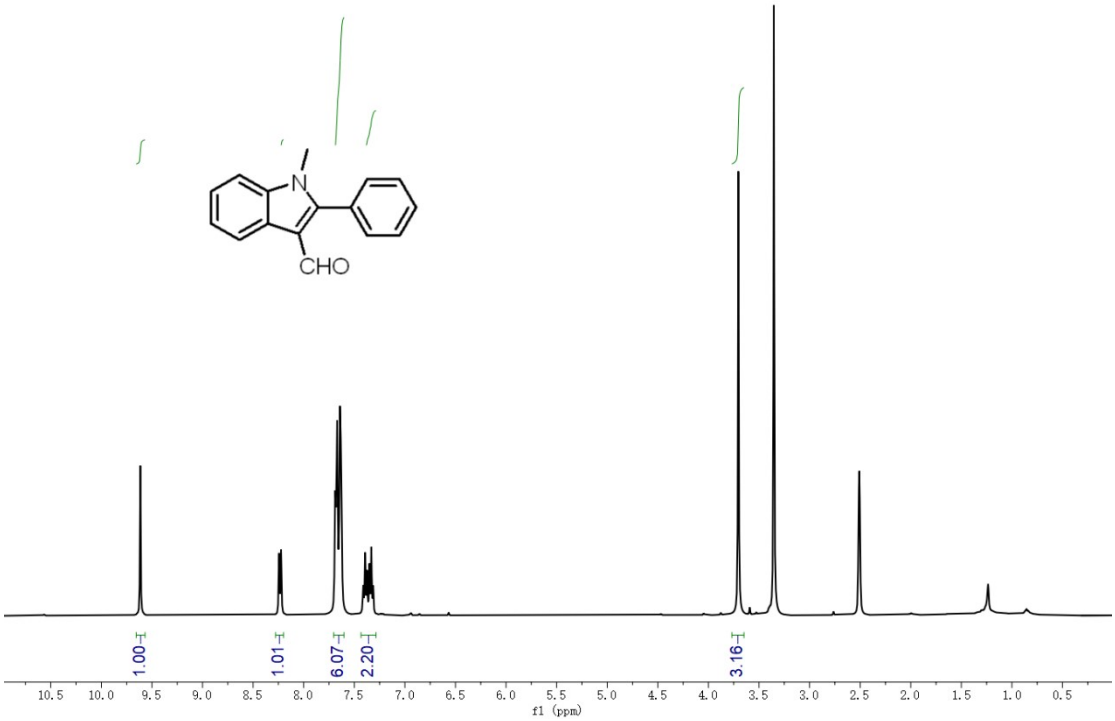
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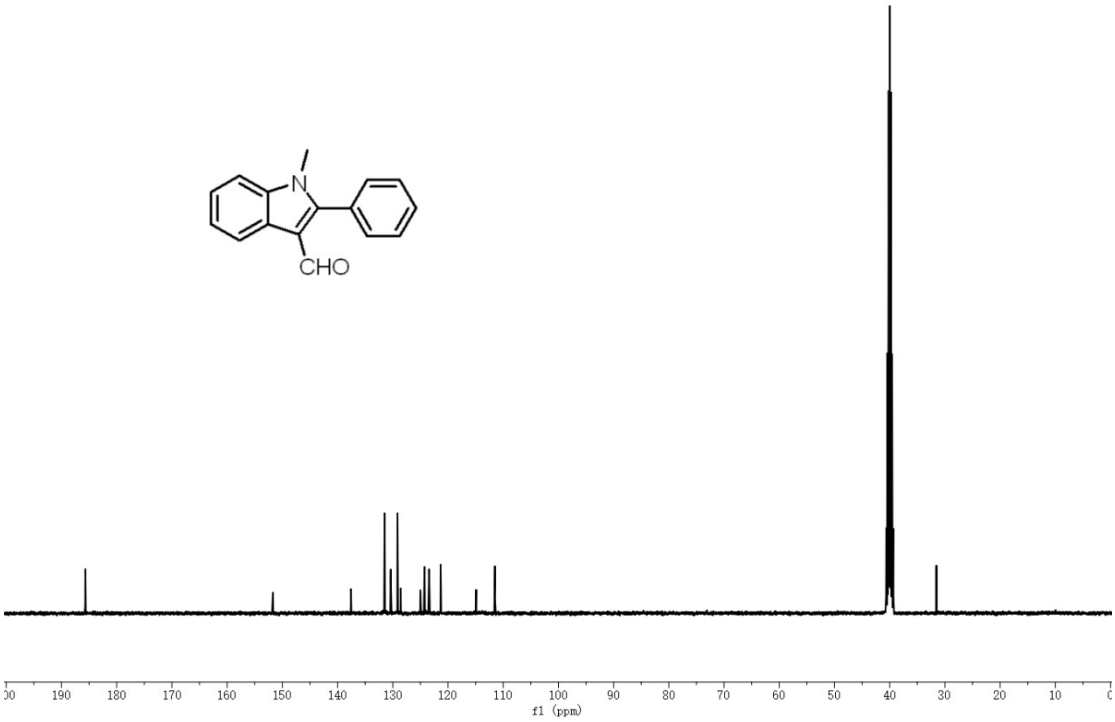
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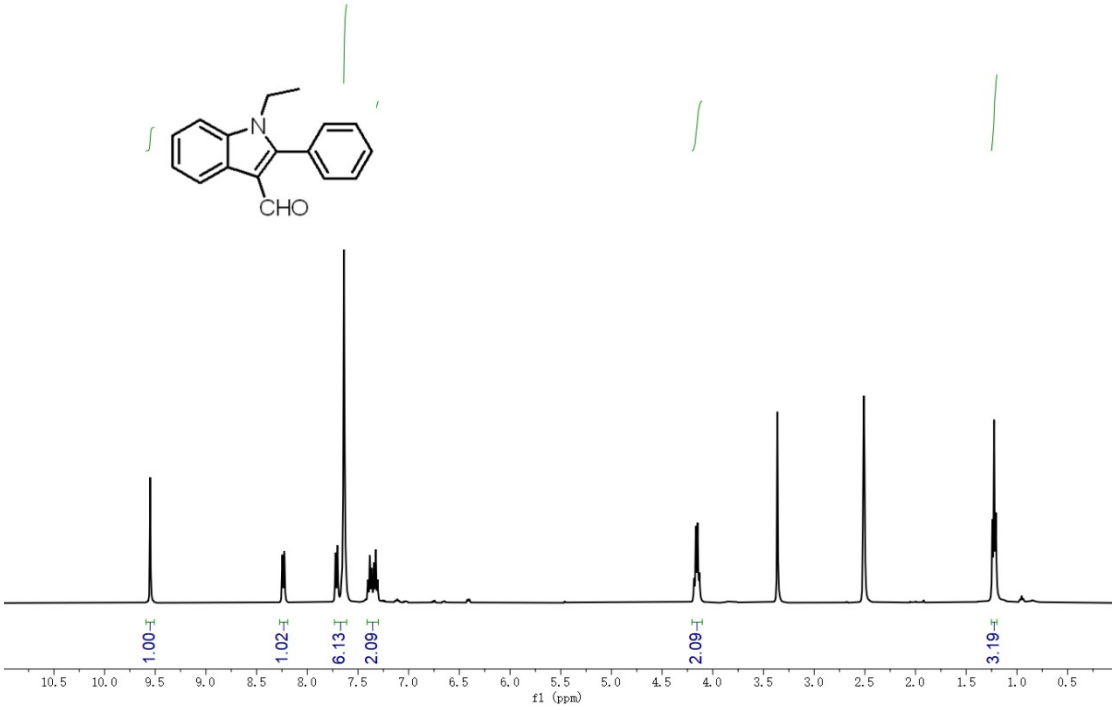
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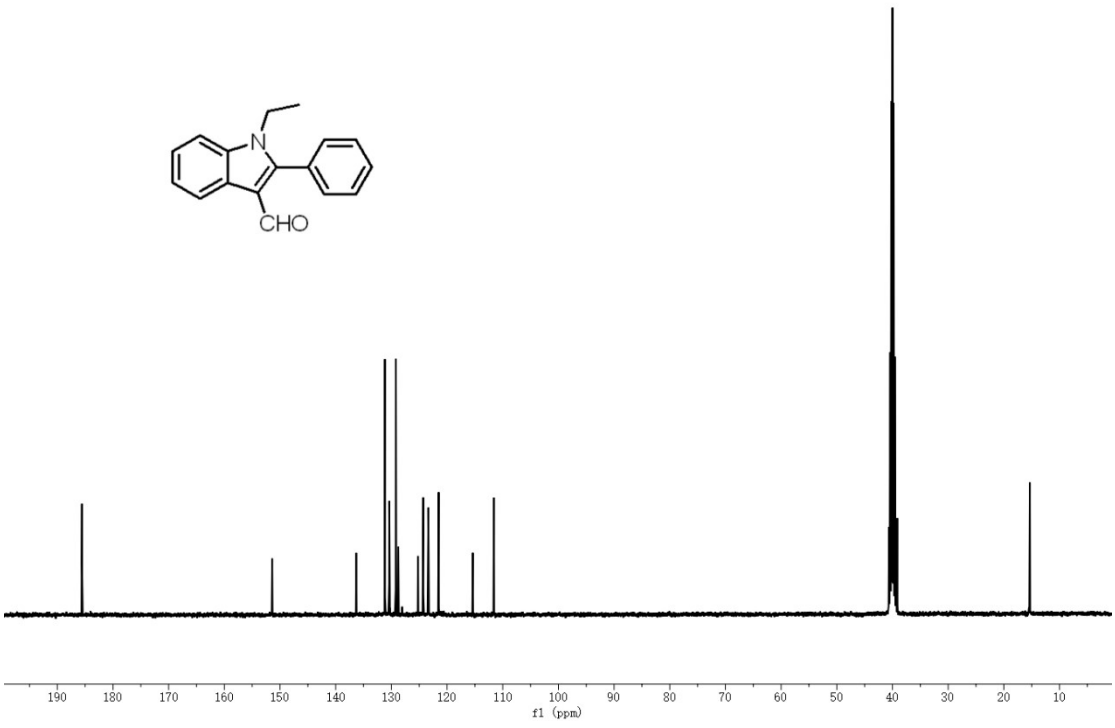
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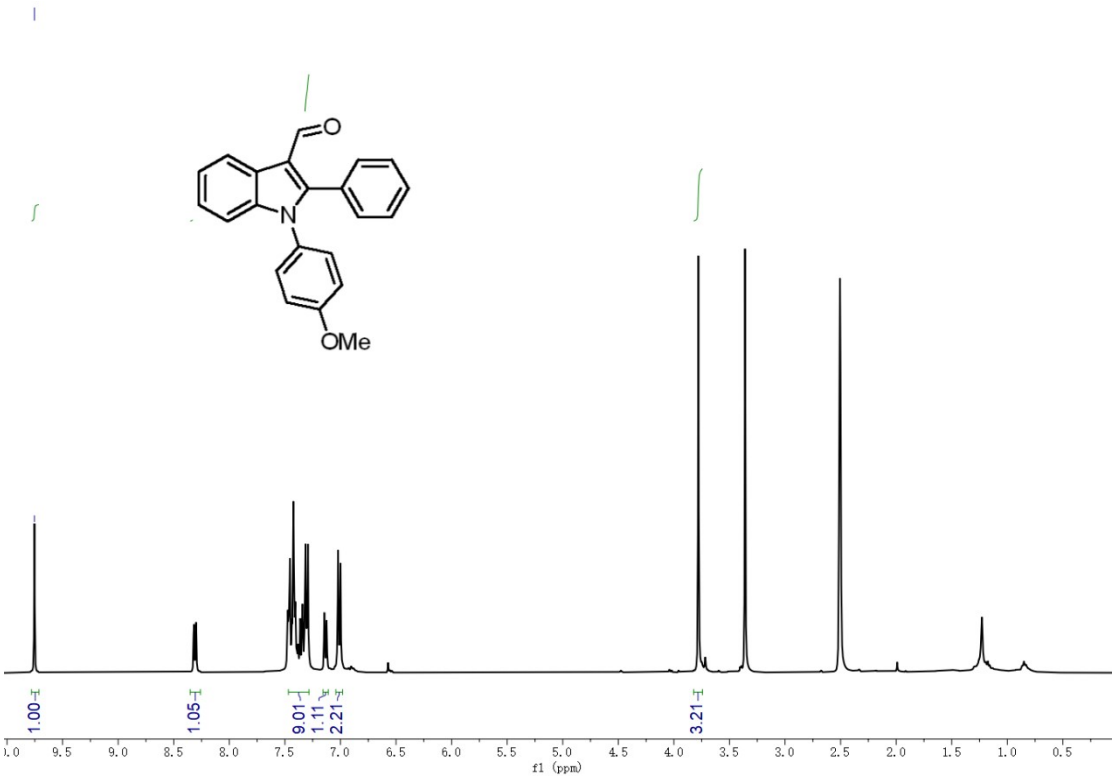
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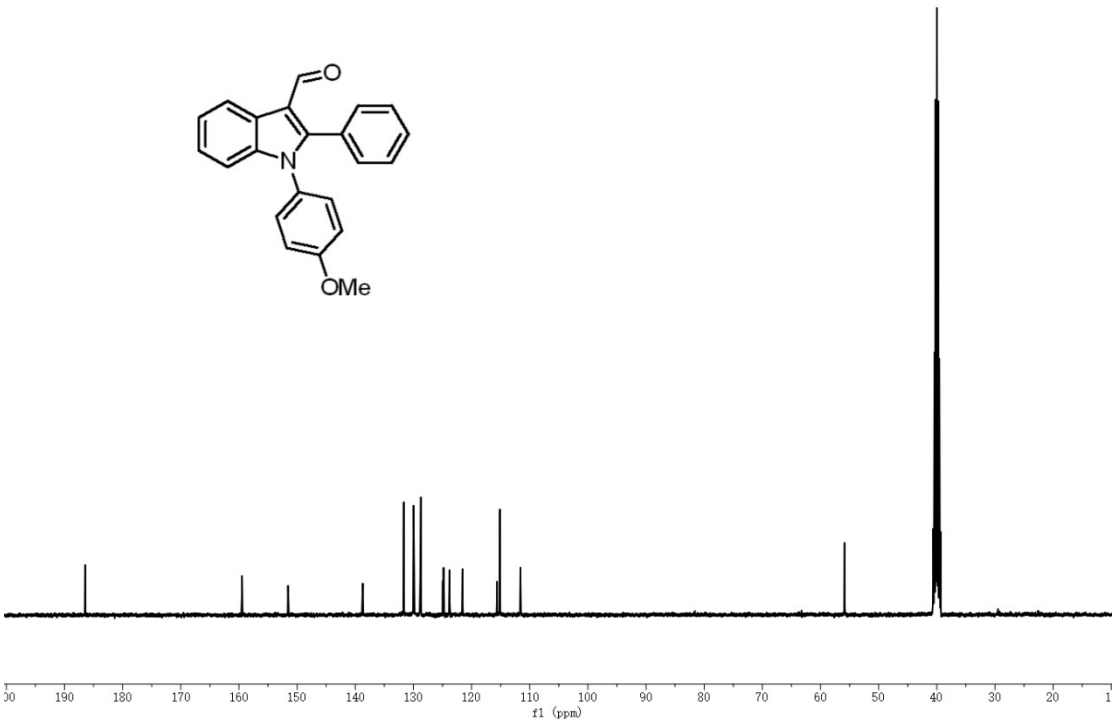
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