Supporting Information

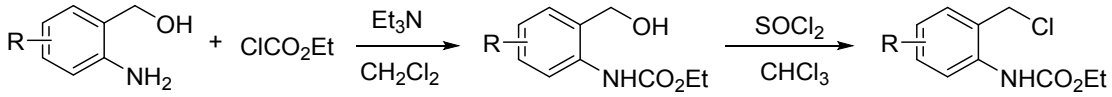
Content

1 General Information

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring, unless otherwise specified. Dichloromethane was purified by passage through a bed of activated alumina. All other reagents and solvents were purchased from Energy Chemical or J&K Chemical Company and used without any further purification. TLC information was recorded on GF 254 plates (Qingdao Haiyang Chemical Co. Ltd., P. R. China) and developed by staining with $KMnO_4$ or ceric ammonium molybdate (CAM). Purification of reaction products were carried out by flash chromatography with silica gel (200-300 mesh, Qingdao Haiyang Chemical Co. Ltd., P. R. China). Melting points were measured with X-4 digital display micro-melting point detector. ^1H NMR spectra were measured on Varian 400 (400 MHz) spectrometers and reported in ppm (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br =broad; integration; coupling constant(s) in Hz), using TMS as an internal standard (TMS at 0.00 ppm) in $CDCl_3$. ^{13}C NMR spectra were recorded on V400 spectrometer and reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm). High-resolution mass spectra were obtained using an Agilent 6230 TOF LC/MS with an (atmospheric pressure photo-ionization (APPI) or electrospray (ESI) source with purine and HP-0921 as an internal calibrants. HR-EI-MS were performed on an

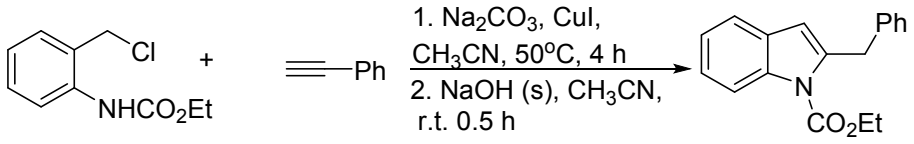
API-Qstar-Pulsar-1 spectrometer. HPLC was Agilent Technologies 1260 infinity II.

2 General procedure for preparation of N-(ortho-chloromethyl)aryl amides



To a solution of 2-amino benzyl (3g, 20.5 mmol) in 35 mL of DCM was added dropwise ethyl chloroformate (3.2g, 22.5 mmol), then Et_3N (22.5mmol) was added dropwise slowly. After addition, the mixture was stirred for 4 h at room temperature. The organic phase was dried and concentrated under reduced pressure to afford the desired *N*-protected 2-aminobenzyl alcohol without purification. *N*-protected 2-aminobenzyl alcohol was dissolved in $CHCl_3$ (20 mL), and $SOCl_2$ (1.2 equiv) was added dropwise at 0 °C. Then, the mixture was stirred at r.t. for 2 h and monitored by TLC. After completion, the reaction was qunenched with aqueous $NaHCO_3$ solution and the mixture was extracted with DCM (3*10 mL). The combined organic phases were washed with brine before being dried (Na_2SO_4) and concentrated in vacuum. Purification by flash column chromatography on silica gel eluting with EtOAc/petroleum ether yielded ethyl [2-(chloromethyl)aryl]-carbamates.

3 General Procedure A for the [4+1]-cycloaddition of *O*-aminobenzyl chloride with alkyne:



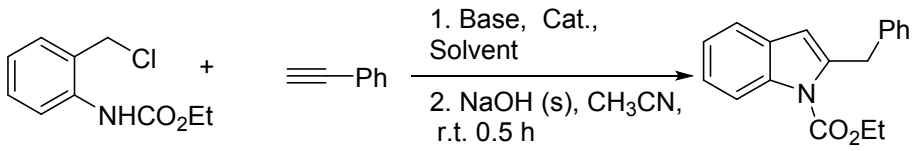
1a **2a** **3a**

To a 10 mL round bottom flask with magnetic stirring bar were added starting materials **1a** (0.1 mmmol, 1.0 eq.), Alkyne (0.12 mmol, 1.2 eq.), Na_2CO_3 (0.12 mmol, 1.2 eq.) and CuI (0.005 mmol). After dry acetonitrile 2 mL was added, and the mixture was stirred at 50°C in an oil bath for 2~4 hours. The reaction was monitored by TLC. After the starting material **1a** was reacted, NaOH solid (0.1 mmol, 1 eq.) was added to the reaction solution, and the reaction was carried out for half an hour. To the residue was

added water (10 mL) and extracted with ethyl acetate (5 mL * 3). The combined organic fractions were dried over Na_2SO_4, and concentrated under vacuum to yield the crude product, which was purified by column chromatography on silica gel (petroleum:ethyl acetate = 50:1 to 30:1) to afford the desired product **3a**.

4 The experimental results

Optimization of reaction conditions (Table 1)

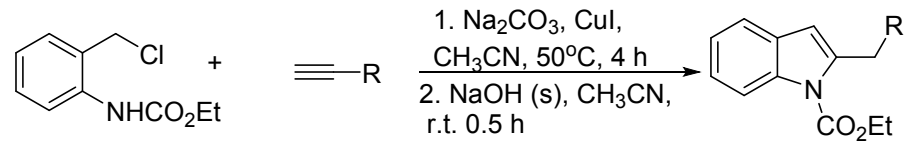


1a **2a** **3a**

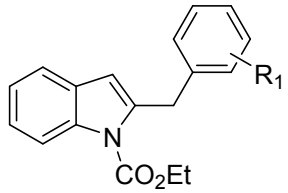
Entry[a]	Cat.	Solvent	Base	T(°C)	T(h)	Yield(b/%)
1	CuI	CH_3CN	Na_2CO_3	r.t.	12	46
2	CuI	CH_3CN	Na_2CO_3	50	2	85
3	CuI	CH_3CN	K_2CO_3	50	2	35
4	CuI	CH_3CN	Cs_2CO_3	50	2	30
5	CuI	CH_3CN	NaOH	50	2	16
6	CuI	CH_3CN	$NaHCO_3$	50	2	84
7	CuI	CH_3CN	NEt_3	50	2	< 10
8	CuI	CH_3CN	Py.	50	2	< 10
9	CuI	CH_3CN	Piperidine	50	2	< 10
10	CuI	CH_3CN	CH_3CO_2Na	50	2	60
11	CuI	DMSO	Na_2CO_3	50	2	trace
12	CuI	THF	Na_2CO_3	50	2	53
13	CuI	$CHCl_3$	Na_2CO_3	50	2	13
14	CuI	Tol.	Na_2CO_3	50	2	32
15	CuI	Dioxane	Na_2CO_3	50	2	34
16	CuI	DMF	Na_2CO_3	50	2	60
17	CuI	CH_2Cl_2	Na_2CO_3	50	2	49
18	CuI	EA	Na_2CO_3	50	2	56
19	CuI	CH_3OH	Na_2CO_3	50	2	trace
20	Ag_2O	CH_3CN	Na_2CO_3	50	2	46
21	$Pd(AcO)_2$	CH_3CN	Na_2CO_3	50	2	trace
22	$CuCO_3$	CH_3CN	Na_2CO_3	50	2	51
23	$Cu(AcO)_2$	CH_3CN	Na_2CO_3	50	2	76
24	$Cu(CF_3SO_3)_2$	CH_3CN	Na_2CO_3	50	2	50
25	Cu_2O	CH_3CN	Na_2CO_3	50	2	74

[a] Reaction conditions: a mixture of **1a** (1.0 mmol), **2a** (1.2 mmol), base (1.2 mmol) and Cat. (0.5mmol%) in solvent (2.0 mL) was stirred at 50°C for a certain period of time. [b] Isolated yield.

Scheme 1. Substrate Scope 1

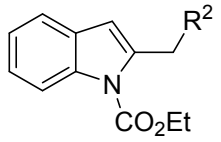


1a **2a-r** **3a-r**

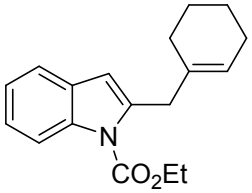


R^1= H, **3a**, 89%
R^1= *o*-Cl, **3b**, 87%
R^1= *o*-F, **3c**, 80%
R^1= *m*-Me, **3d**, 90%
R^1= *m*-Cl, **3e**, 88%
R^1= *m*-Br, **3f**, 88%
R^1= *m*-C≡CH, **3g**, 87%
R^1= *p*-Me, **3h**, 86%

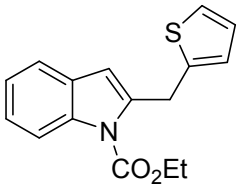
R^1= *p*-Et, **3i**, 88%
R^1= *p*-^{t}Bu, **3j**, 91%
R^1= *p*-OMe, **3k**, 91%
R^1= *p*-F, **3l**, 89%
R^1= *p*-Cl, **3m**, 81%
R^1= *p*-NO_2, **3n**, 90%



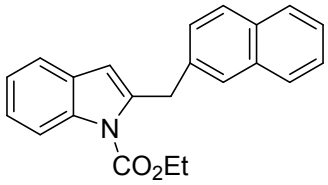
R^2= CO_2Me, **3o**, 92%
R^2= CO_2Et, **3p**, 93%



3q, 86%

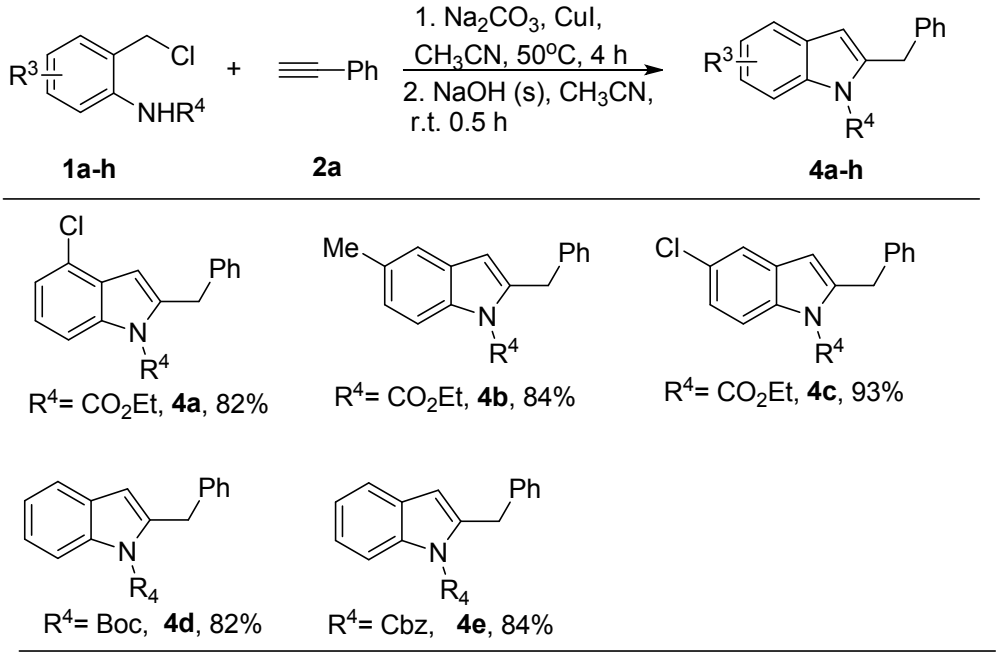


3r, 91%

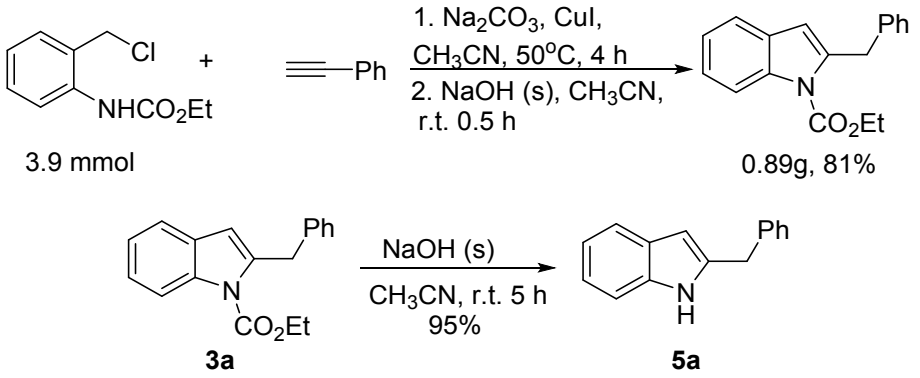


3s, 84%

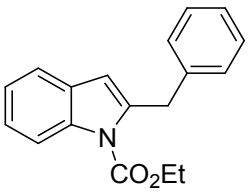
Scheme 2. Substrate Scope 2



Scheme 3. Gram scale experiment and product derivation

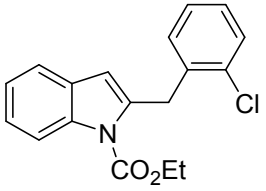


5 Structural characterization



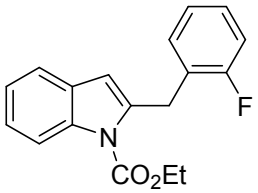
ethyl 2-benzyl-1H-indole-1-carboxylate**(3a)**

Colorless oil, yield 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.3 Hz, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.37 – 7.25(m, 7H), 6.24 (s, 1H), 4.47-4.42 (m, 4H), 1.41 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.91, 140.46, 139.01, 136.81, 129.26, 128.86, 128.47, 126.39, 123.79, 123.00, 120.03, 115.75, 110.00, 63.07, 36.35, 14.27. HR-EI-MS (positive) *m/z* 302.1157 $[M+Na]^+$ (calcd for $C_{18}H_{17}NNaO_2$ 302.1157).



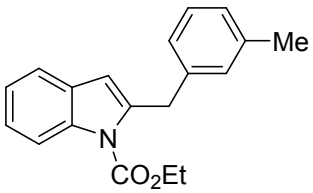
ethyl 2-(2-chlorobenzyl)-1H-indole-1-carboxylate (**3b**)

White solid, m.p.: 59-63 ^{o}C, yield 87%, reaction time 4 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.3 Hz, 1H), 7.47 (t, *J* = 8.3 Hz, 2H), 7.33 – 7.21 (m, 4H), 7.10 (d, *J* = 8.3 Hz, 1H), 6.20 (s, 1H), 4.50 (s, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.83, 138.46, 137.18, 136.94, 134.06, 130.13, 129.45, 129.25, 127.89, 126.95, 123.93, 123.06, 120.06, 115.78, 110.13, 63.12, 34.24, 14.08. HR-EI-MS (positive) *m/z* 336.0766 $[M+Na]^+$ (calcd for $C_{18}H_{16}ClNNaO_2$ 336.0767).



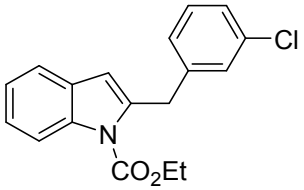
ethyl 2-(2-fluorobenzyl)-1H -indole-1-carboxylate (**3c**)

White oil, yield 80%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.32-7.08 (m, 7H), 6.23 (s, 1H), 4.47-4.42 (m, 4H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.16, 159.71, 151.87, 138.71, 136.86, 130.56, 130.52, 128.19, 124.14, 124.10, 123.88, 123.02, 120.02, 115.74, 109.95, 63.12, 29.73, 29.47, 29.43, 14.15. HR-EI-MS (positive) *m/z* 320.1060 $[M+Na]^+$ (calcd for $C_{18}H_{16}FNNaO_2$ 320.1063).



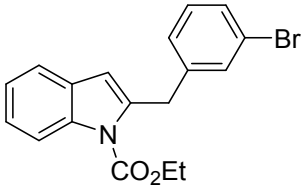
ethyl 2-(3-methylbenzyl)-1H-indole-1-carboxylate(**3d**)

Yellow solid, m.p.: 55-57 ^{o}C, yield 90%, reaction time 4 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.3 Hz, 1H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.33-7.25 (m, 3H), 7.13-7.08 (m, 3H), 6.26 (s, 1H), 4.47 (q, *J* = 7.2 Hz, 2H), 4.40 (s, 2H), 2.39 (s, 3H), 1.44 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.93, 140.65, 138.93, 138.03, 136.89, 129.63, 129.34, 128.35, 127.14, 125.97, 123.75, 122.98, 120.03, 115.76, 109.95, 63.05, 36.27, 21.47, 14.27. HR-EI-MS (positive) *m/z* 316.1315 $[M+Na]^+$ (calcd for $C_{19}H_{19}NNaO_2$ 316.1313).



ethyl 2-(3-chlorobenzyl)-1H-indole-1-carboxylate(**3e**)

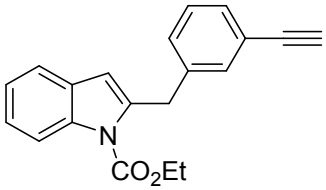
Yellow solid, m.p.: 41-42 ^{o}C, yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.32- 7.23 (m, 5H), 7.13-7.11 (m, 1H), 6.29 (s, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 4.39 (s, 2H), 1.41 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.76, 141.13, 139.29, 136.77, 134.24, 129.65, 129.12, 128.85, 126.97, 126.58, 123.99, 123.08, 120.12, 115.79, 110.29, 63.14, 35.89, 14.25. HR-EI-MS (positive) *m/z* 336.0766 $[M+Na]^+$ (calcd for $C_{18}H_{16}ClNNaO_2$ 336.0767).



ethyl 2-(3-bromobenzyl)-1H-indole-1-carboxylate(**3f**)

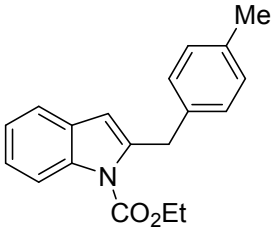
Colorless oil, yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.40-7.39 (m, 2H), 7.29- 7.17 (m, 4H), 6.29 (s, 1H), 4..47-4.36 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 151.76, 141.42, 139.27, 136.77, 131.78, 129.96, 129.51, 129.12, 127.44,

123.99, 123.08, 122.49, 120.12, 115.79, 110.31, 63.14, 35.86, 14.26. HR-EI-MS (positive) *m/z* 380.0260 $[M+Na]^+$ (calcd for $C_{18}H_{16}BrNNaO_2$ 380.0262).



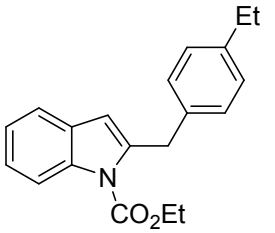
ethyl 2-(3-ethynylbenzyl)-1H-indole-1-carboxylate(**3g**)

Colorless oil, yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.41-7.38 (m, 2H), 7.31-7.22 (m, 4H), 6.26 (s, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 4.38 (s, 2H), 3.07 (s, 1H), 1.40 (t, *J* = 7.2 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 151.79, 139.60, 139.31, 136.79, 132.41, 130.22, 129.43, 129.16, 128.43, 123.92, 123.04, 122.16, 120.08, 115.77, 110.24, 83.69, 63.11, 35.97, 14.25. HR-EI-MS (positive) *m/z* 326.1160 $[M+Na]^+$ (calcd for $C_{20}H_{17}NNaO_2$ 326.1157).



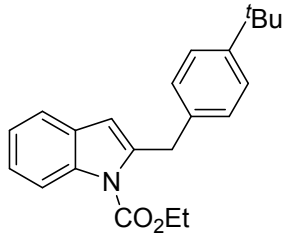
ethyl 2-(4-methylbenzyl)-1H-indole-1-carboxylate(**3h**)

Colorless oil, yield 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.30-7.16 (m, 6H), 6.22 (s, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 4.37 (s, 2H), 2.38 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 151.94, 140.90, 136.84, 135.87, 129.31, 129.14, 128.80, 123.70, 122.94, 119.99, 115.72, 109.82, 63.03, 35.92, 21.10, 14.29. HR-EI-MS (positive) *m/z* 316.1311 $[M+Na]^+$ (calcd for $C_{19}H_{19}NNaO_2$ 316.1313).



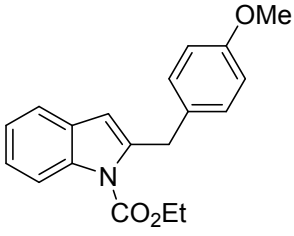
ethyl 2-(4-ethylbenzyl)-1H-indole-1-carboxylate(**3i**)

Colorless oil, yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.31- 7.18 (m, 6H), 6.22 (s, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 4.37 (s, 2H), 2.68 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.94, 142.32, 140.88, 136.82, 136.10, 129.30, 128.83, 127.93, 123.69, 122.93, 119.98, 115.71, 109.82, 63.03, 35.93, 28.51, 15.71, 14.27. HR-EI-MS (positive) *m/z* 330.1473 $[M+Na]^+$ (calcd for $C_{20}H_{21}NNaO_2$ 330.1470).



ethyl 2-(4-(tert-butyl)benzyl)-1H-indole-1-carboxylate(**3j**)

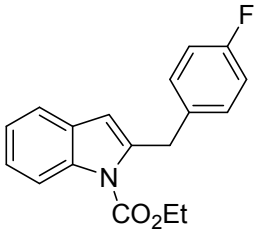
Colorless oil, yield 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 - 8.12 (m, 1H), 7.43-7.15 (m, 6H), 6.21 (brs, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 4.35 (s, 2H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.94, 149.22, 140.81, 136.84, 135.88, 129.31, 128.52, 125.32, 123.67, 122.92, 119.97, 115.69, 109.80, 63.00, 35.80, 34.44, 31.43, 14.21. HR-EI-MS (positive) *m/z* 358.1780 $[M+Na]^+$ (calcd for $C_{22}H_{25}NNaO_2$ 358.1783).



ethyl 2-(4-methoxybenzyl)-1H-indole-1-carboxylate(**3k**)

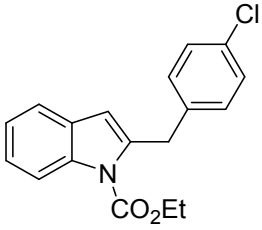
Colorless oil, yield 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.29- 7.17 (m, 4H), 6.91- 6.87

(m, 2H), 6.20 (s, 1H), 4.46 (q, J = 7.1 Hz, 2H), 4.35 (s, 2H), 3.84 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 158.21, 151.93, 141.18, 136.83, 130.98, 129.91, 129.29, 123.69, 122.94, 119.98, 115.70, 113.86, 109.72, 63.04, 55.29, 35.47, 14.31. HR-EI-MS (positive) *m/z* 332.1263 $[M+Na]^+$ (calcd for $C_{19}H_{19}NNaO_3$ 332.1263).



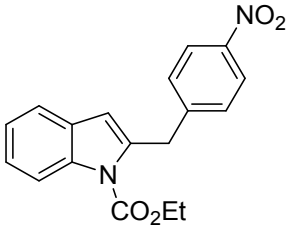
ethyl 2-(4-fluorobenzyl)-1H-indole-1-carboxylate(**3l**)

Colorless oil, yield 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.3 Hz, 1H), 7.50 (d, J = 8.3 Hz, 1H), 7.33- 7.21 (m, 4H), 7.08-7.03 (m, 2H), 6.26 (s, 1H), 4.48 (q, J = 7.2 Hz, 2H), 4.40 (s, 2H), 1.44 (t, J = 7.2 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 162.84, 160.41, 151.85, 140.34, 136.83, 134.71, 134.68, 130.33, 130.25, 129.23, 123.91, 123.07, 120.09, 115.80, 115.34, 115.13, 109.99, 63.11, 35.50, 14.29. HR-EI-MS (positive) *m/z* 320.1063 $[M+Na]^+$ (calcd for $C_{18}H_{16}FNNaO_2$ 320.1063).



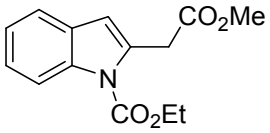
ethyl 2-(4-chlorobenzyl)-1H-indole-1-carboxylate(**3m**)

Colorless oil, yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.2 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H), 7.31- 7.16 (m, 6H), 6.25 (s, 1H), 4.44 (q, J = 7.2 Hz, 2H), 4.37 (s, 2H), 1.42 (t, J = 7.2 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 151.79, 139.79, 137.53, 136.75, 132.14, 130.14, 129.14, 128.55, 123.94, 123.06, 120.08, 115.76, 110.11, 63.12, 35.62, 14.28. HR-EI-MS (positive) *m/z* 336.0765 $[M+Na]^+$ (calcd for $C_{18}H_{16}ClNNaO_2$ 336.0767).



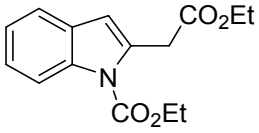
ethyl 2-(4-nitrobenzyl)-1H-indole-1-carboxylate(**3n**)

Colorless oil, yield 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20-8.12 (m, 3H), 7.51-7.28 (m, 5H), 6.38 (brs, 1H), 4.52 (s, 2H), 4.43 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 151.64, 147.02, 146.68, 138.07, 136.63, 129.40, 128.99, 124.30, 123.68, 123.27, 120.27, 115.88, 110.73, 63.27, 36.02, 14.28. HR-EI-MS (positive) *m/z* 347.1008 $[M+Na]^+$ (calcd for $C_{18}H_{16}N_2NaO_4$ 347.1008).



ethyl 2-(2-methoxy-2-oxoethyl)-1H-indole-1-carboxylate (**3o**)

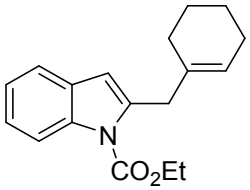
Colorless oil, yield 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.2 Hz, 1H), 7.54-7.25 (m, 3H), 6.53 (brs, 1H), 4.50 (q, J = 7.2 Hz, 2H), 4.05 (s, 2H), 3.75 (s, 3H), 1.49 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.82, 151.83, 136.51, 133.13, 129.01, 128.97, 124.30, 123.10, 120.38, 115.80, 111.11, 63.33, 52.14, 36.20, 29.72, 14.27. HR-EI-MS (positive) *m/z* 284.0898 $[M+Na]^+$ (calcd for $C_{14}H_{15}NNaO_4$ 284.0899).



ethyl 2-(2-ethoxy-2-oxoethyl)-1H-indole-1-carboxylate(**3p**)

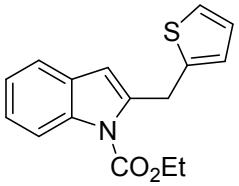
Colorless oil, yield 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.3 Hz, 1H), 7.52-7.28 (m, 3H), 6.53 (brs, 1H), 4.50 (q, J = 7.2 Hz, 2H), 4.22

(q, J = 7.2 Hz, 2H), 4.05 (s, 2H), 1.49 (t, J = 7.2 Hz, 3H), 1.29 (t, J = 7.2 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.32, 151.80, 136.56, 133.33, 129.02, 124.22, 123.05, 120.34, 115.79, 110.99, 63.27, 60.96, 36.41, 14.27, 14.23.HR-EI-MS (positive) *m/z* 298.1055 $[M+Na]^+$ (calcd for $C_{15}H_{17}NNaO_4$ 298.1055).



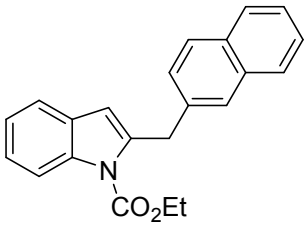
ethyl 2-(cyclohex-1-en-1-ylmethyl)-1H-indole-1-carboxylate(**3q**)

Colorless oil, yield 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.1 Hz, 1H), 7.50 (d, J = 8.1Hz, 1H), 7.30-7.22 (m, 2H), 6.40 (s, 1H), 5.40 (s, 1H), 4.50 (q, J = 7.1 Hz, 2H), 3.67 (s, 2H), 2.08-2.00 (m, 4H), 1.71- 1.62 (m, 4H), 1.50 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.97, 140.01, 136.84, 135.31, 129.40, 123.44, 123.10, 122.82, 119.82, 115.58, 108.96, 62.93, 37.96, 28.78, 25.31, 23.08, 22.45, 14.39. HR-EI-MS (positive) *m/z* 306.1468 $[M+Na]^+$ (calcd for $C_{18}H_{21}NNaO_2$ 306.1470).



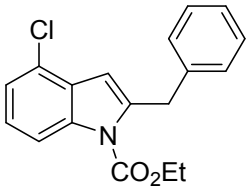
ethyl 2-(thiophen-2-ylmethyl)-1H-indole-1-carboxylate(**3r**)

Colorless oil, yield 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.3 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.30-7.20 (m, 3H), 6.98- 6.89 (m, 2H), 6.40 (s, 1H), 4.61 (s, 2H), 4.49 (q, J = 7.2 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.86, 141.58, 139.80, 129.13, 126.81, 125.64, 123.97, 123.94, 123.04, 120.19, 115.75, 109.62, 63.19, 30.56, 14.30. HR-EI-MS (positive) *m/z* 308.0723 $[M+Na]^+$ (calcd for $C_{16}H_{15}NNaO_2S$ 308.0721).



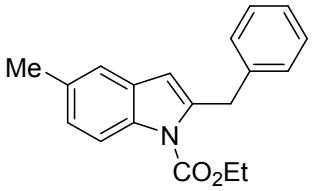
ethyl 2-(naphthalen-2-ylmethyl)-1H-indole-1-carboxylate (**3s**)

Colorless oil, yield 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25-8.22 (m, 1H), 7.91- 7.83 (m, 4H), 7.71 (s, 1H), 7.62-7.28 (m, 5H), 6.31 (s, 1H), 4.61 (s, 2H), 4.46 (dd, J = 7.1, 0.9 Hz, 2H), 1.42 (td, J = 7.1, 0.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.94, 140.43, 136.60, 133.68, 132.33, 129.35, 128.05, 127.84, 127.72, 127.69, 127.63, 127.17, 126.06, 125.53, 123.88, 123.07, 120.12, 115.84, 110.23, 63.12, 36.53, 14.32. HR-EI-MS (positive) *m/z* 352.1313 $[M+Na]^+$ (calcd for $C_{22}H_{19}NNaO_2$ 352.1313).



ethyl 2-benzyl-4-chloro-1H-indole-1-carboxylate(**4a**)

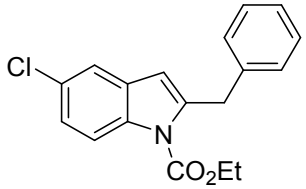
Colorless oil, yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.8 Hz, 1H), 7.38-7.19 (m, 7H), 6.39 (s, 1H), 4.44- 4.42 (m, 4H), 1.39 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.56, 141.18, 138.53, 137.53, 128.76, 128.54, 127.97, 126.51, 125.26, 124.39, 122.76, 114.26, 107.88, 63.39, 36.29, 14.18. HR-EI-MS (positive) *m/z* 336.0765 $[M+Na]^+$ (calcd for $C_{18}H_{16}ClNNaO_2$ 336.0767).



ethyl 2-benzyl-5-methyl-1H-indole-1-carboxylate(**4b**)

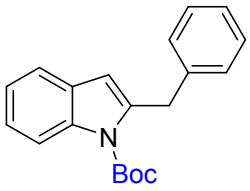
Colorless oil, yield 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J =

8.5 Hz, 1H), 7.36-7.23 (m, 6H), 7.11 (d, *J* = 8.5 Hz, 1H), 6.17 (s, 1H), 4.44-4.39 (m, 4H), 2.45 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.88, 140.41, 139.12, 135.02, 132.42, 129.45, 128.80, 128.40, 126.30, 125.06, 119.98, 115.39, 109.79, 62.91, 36.31, 21.24, 14.24. HR-EI-MS (positive) *m/z* 316.1312 $[M+Na]^+$ (calcd for $C_{19}H_{19}NNaO_2$ 316.1313).



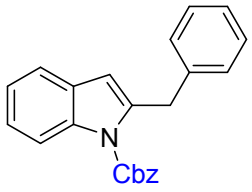
ethyl 2-benzyl-5-chloro-1H-indole-1-carboxylate(**4c**)

Colorless oil, yield 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.9 Hz, 1H), 7.42- 7.22 (m, 7H), 6.15 (s, 1H), 4.46- 4.38 (m, 4H), 1.39 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 151.56, 141.96, 138.56, 135.20, 130.44, 128.81, 128.54, 128.52, 126.51, 123.82, 119.54, 116.74, 109.20, 63.31, 36.32, 14.21. HR-EI-MS (positive) *m/z* 336.0767 $[M+Na]^+$ (calcd for $C_{18}H_{16}ClNNaO_2$ 336.0767).



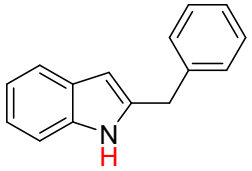
tert-butyl 2-benzyl-1H-indole-1-carboxylate(**4d**)

Colorless oil, yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.3 Hz, 1H), 7.49-7.23 (m, 8H), 6.20 (s, 1H), 4.44 (s, 2H), 1.64 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ 150.55, 140.51, 139.22, 136.96, 132.56, 129.16, 128.97, 128.50, 128.44, 126.37, 123.57, 122.70, 119.97, 115.60, 109.39, 83.89, 36.37, 28.14. HR-EI-MS (positive) *m/z* 330.1471 $[M+Na]^+$ (calcd for $C_{20}H_{21}NNaO_2$ 330.1470).



benzyl 2-benzyl-1H-indole-1-carboxylate (**4e**)

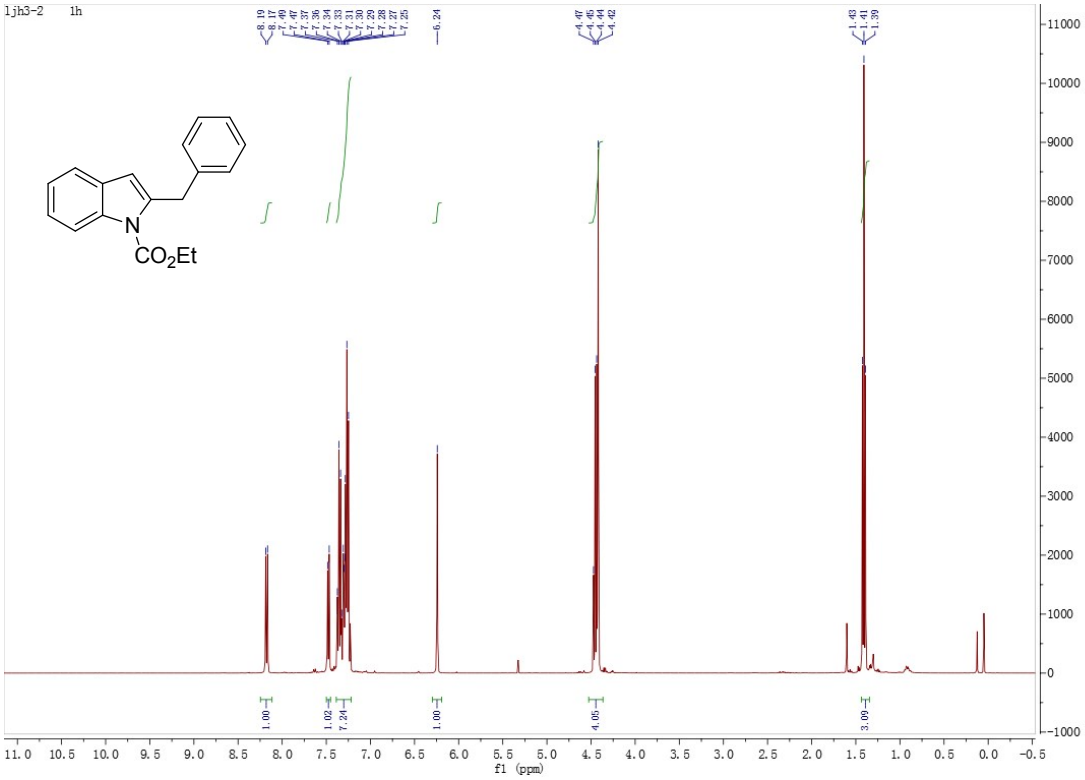
Colorless oil, yield 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.1 Hz, 1H), 7.50-7.42 (m, 7H), 7.37-7.21 (m, 6H), 6.27 (s, 1H), 5.42 (s, 2H), 4.42 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.79, 140.51, 138.90, 136.88, 135.03, 129.33, 128.91, 128.79, 128.72, 128.64, 128.59, 128.48, 128.37, 126.39, 123.92, 123.12, 115.83, 110.26, 68.71, 36.35. HR-EI-MS (positive) *m/z* 364.1313 $[M+Na]^+$ (calcd for $C_{23}H_{19}NNaO_2$ 364.1313).



2-benzyl-1H-indole (**5a**)

Colorless oil, yield 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.40-7.11 (m, 8H), 6.38 (s, 1H), 4.17 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.57, 137.83, 136.31, 128.88, 128.77, 128.72, 126.78, 121.35, 120.04, 119.76, 110.52, 101.14, 34.75. HR-EI-MS (positive) *m/z* 230.0945 $[M+Na]^+$ (calcd for $C_{15}H_{13}NNa$ 230.0946).

6 Original spectrogram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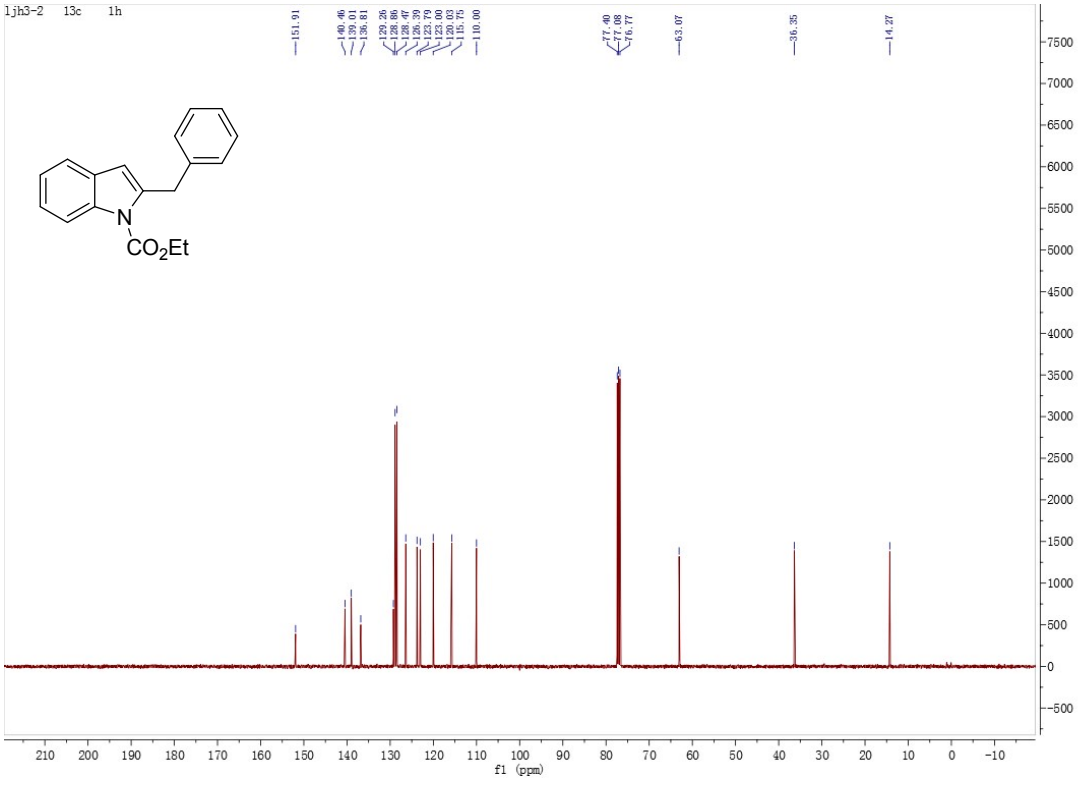
8.17
7.49
7.47
7.37
7.36
7.34
7.33
7.31
7.30
7.29
7.28
7.27
7.25
6.24
4.47
4.45
4.44
4.42
1.43
1.41
1.39
N
CO2Et
1.00
1.02
7.24
1.00
4.05
3.09
f1 (ppm)


ljh3-2 13c 1h
151.91
140.46
139.01
136.81
129.26
128.86
128.47
126.39
123.79
123.00
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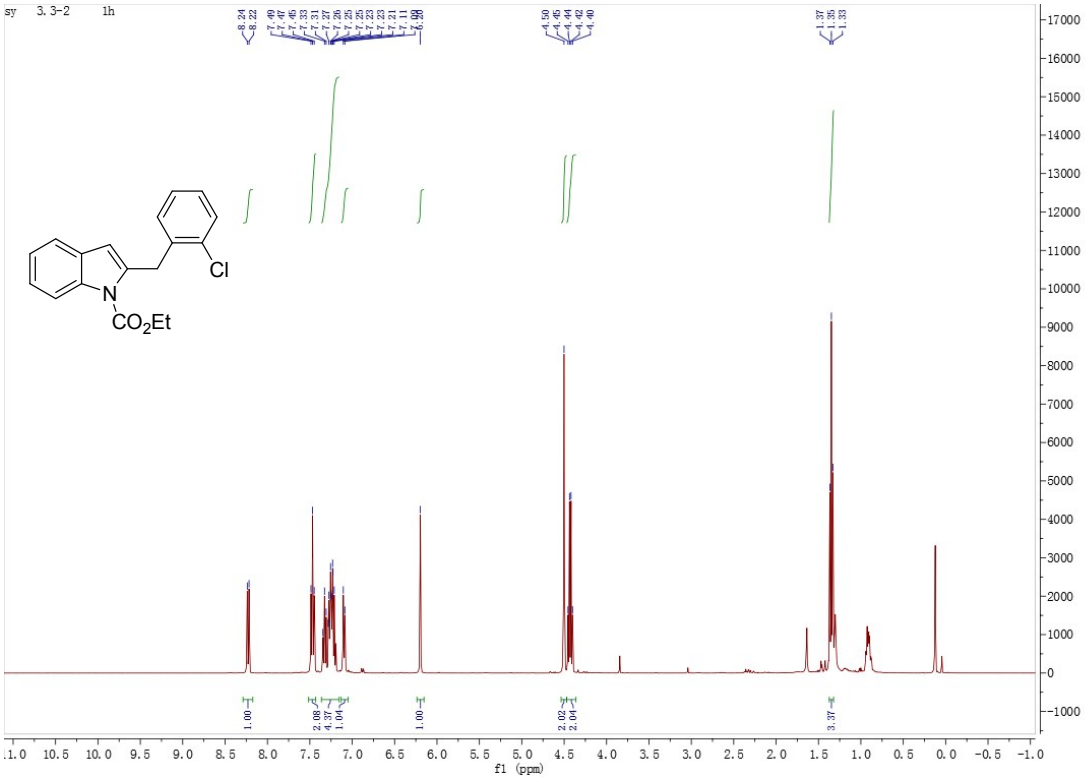
115.75
110.00
77.40
77.08
76.77
63.07
36.35
14.27
N
CO2Et
f1 (ppm)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N
CO2Et
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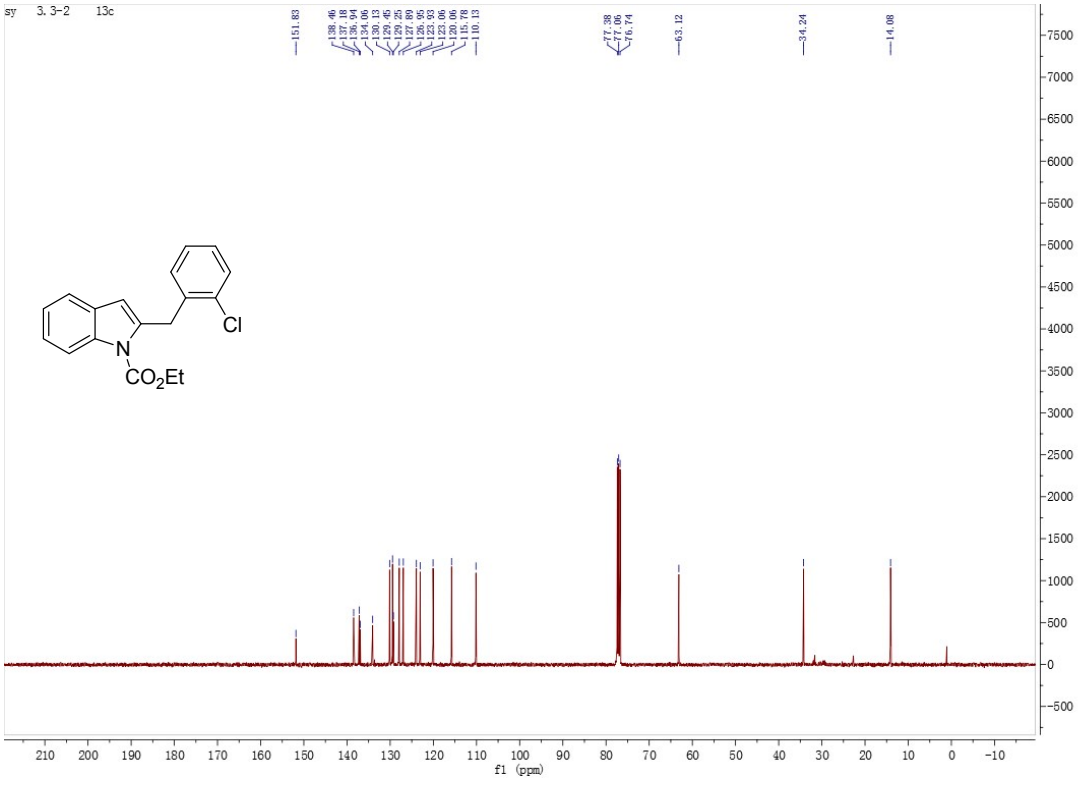
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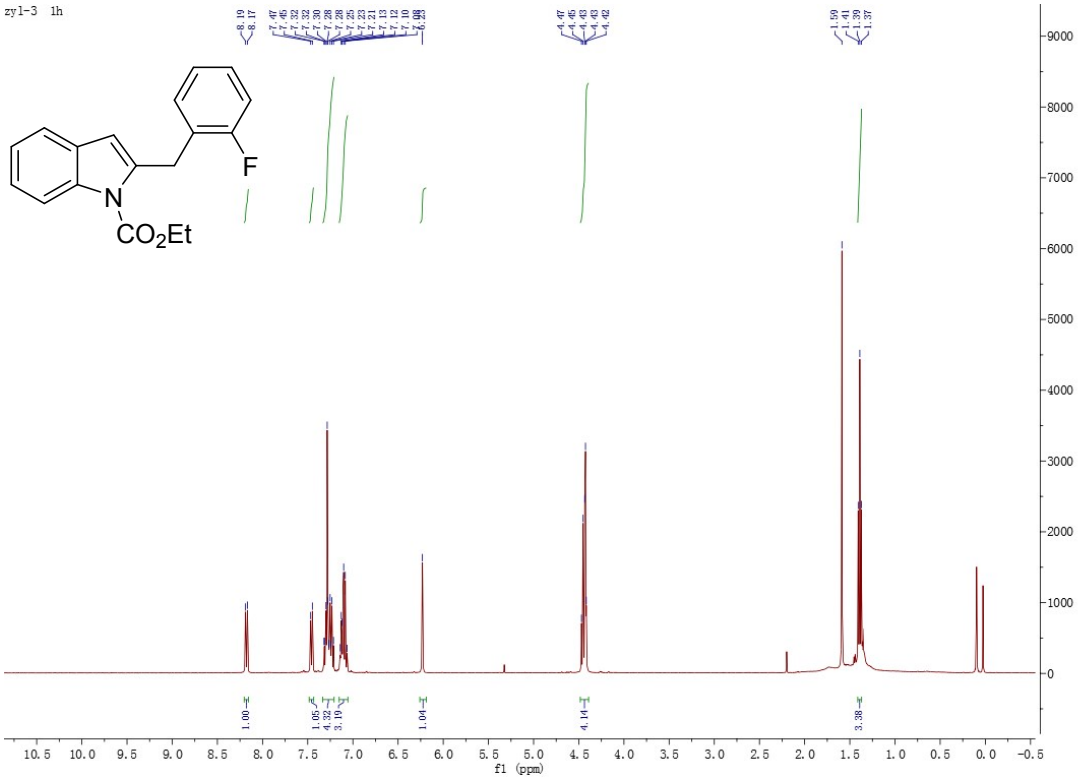
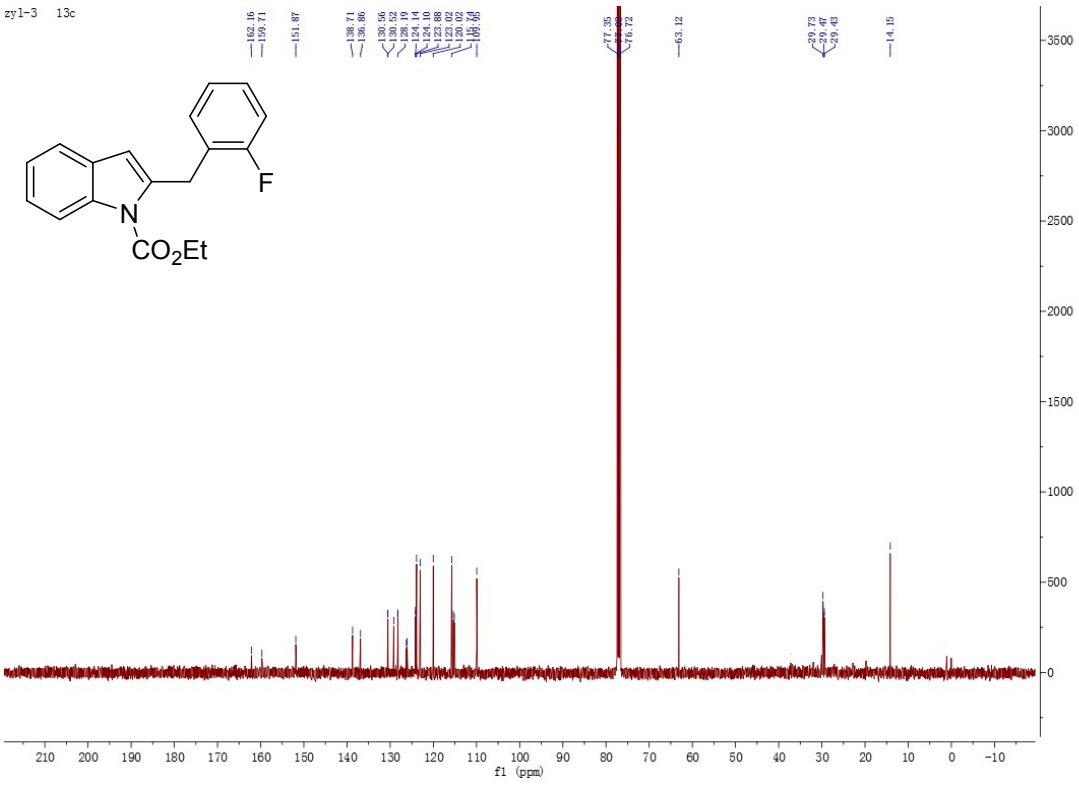
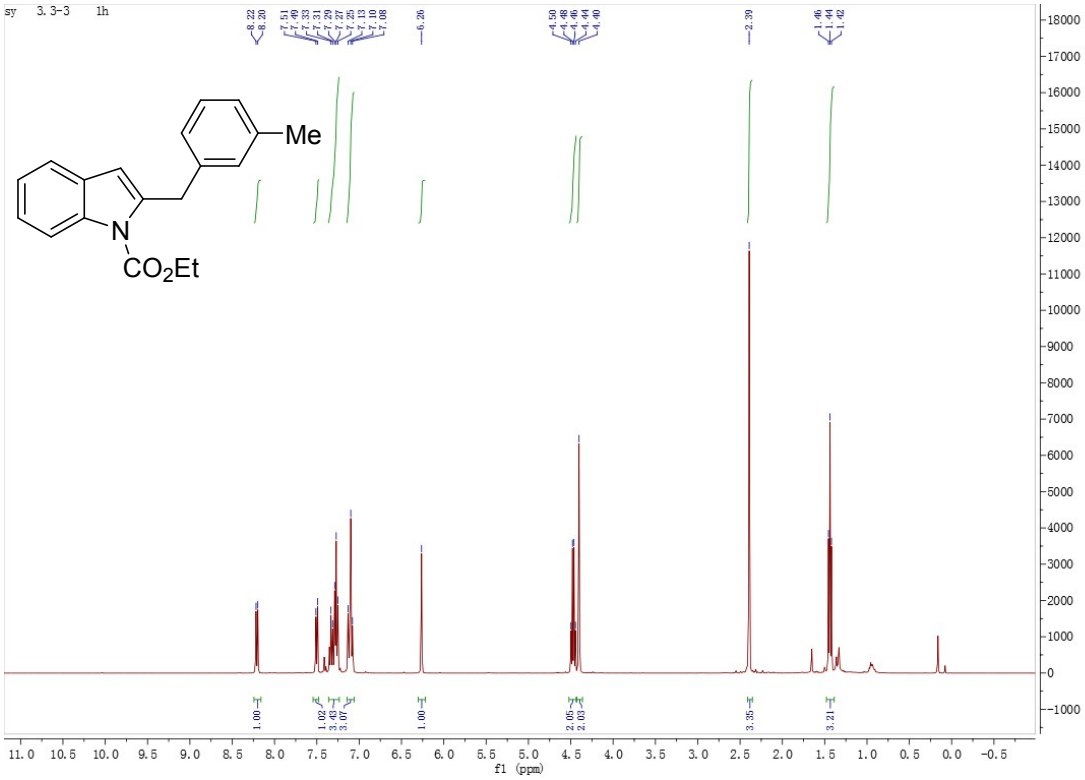
N
CO2Et
f1 (ppm)


zyl-3 1h
F
N
CO2Et
f1 (ppm)


zyl-3 13c
F
N
CO2Et
f1 (ppm)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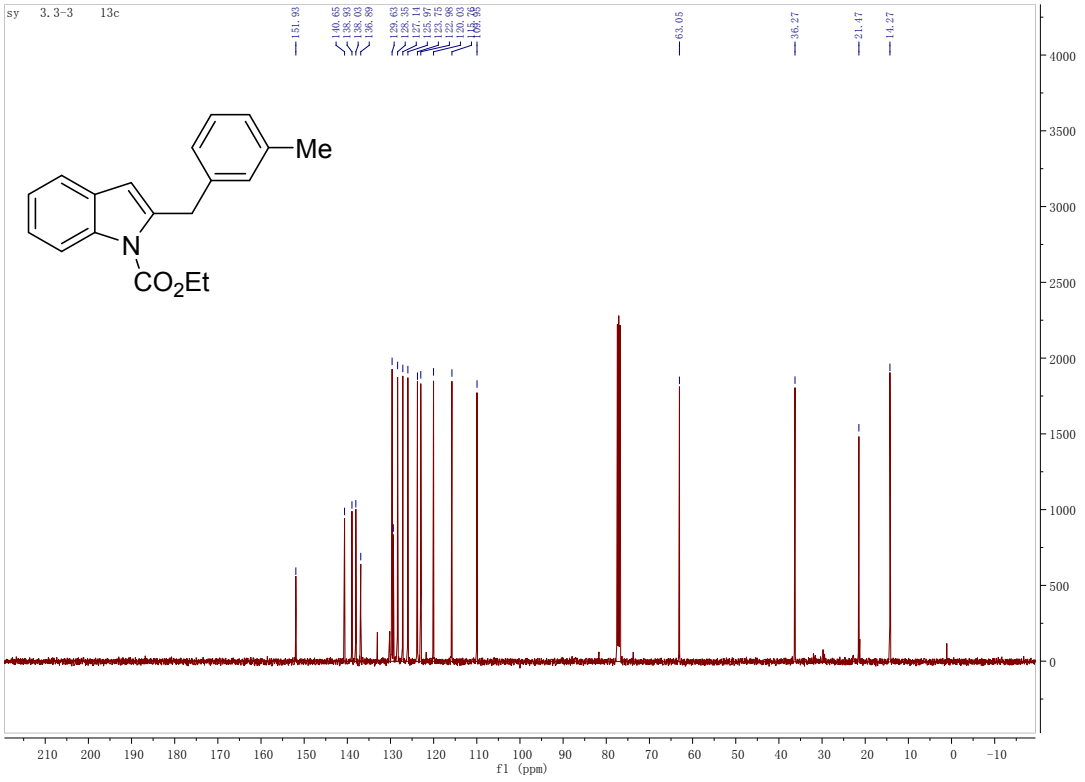
Me
N
CO2Et
f1 (ppm)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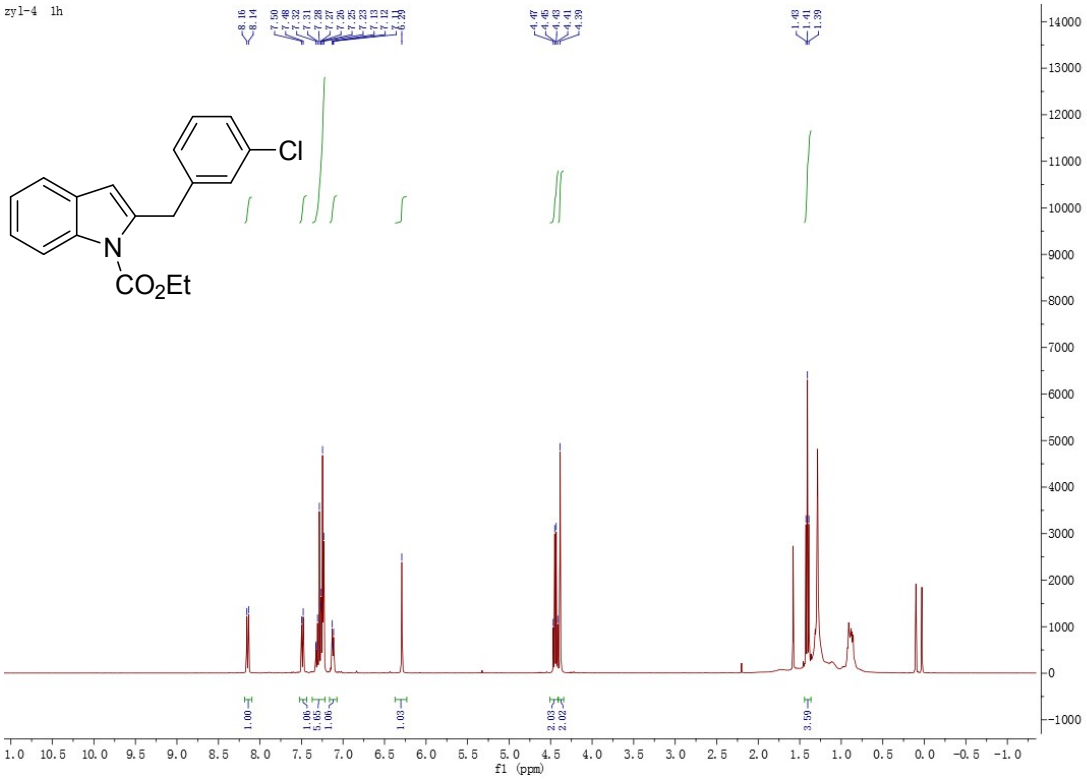
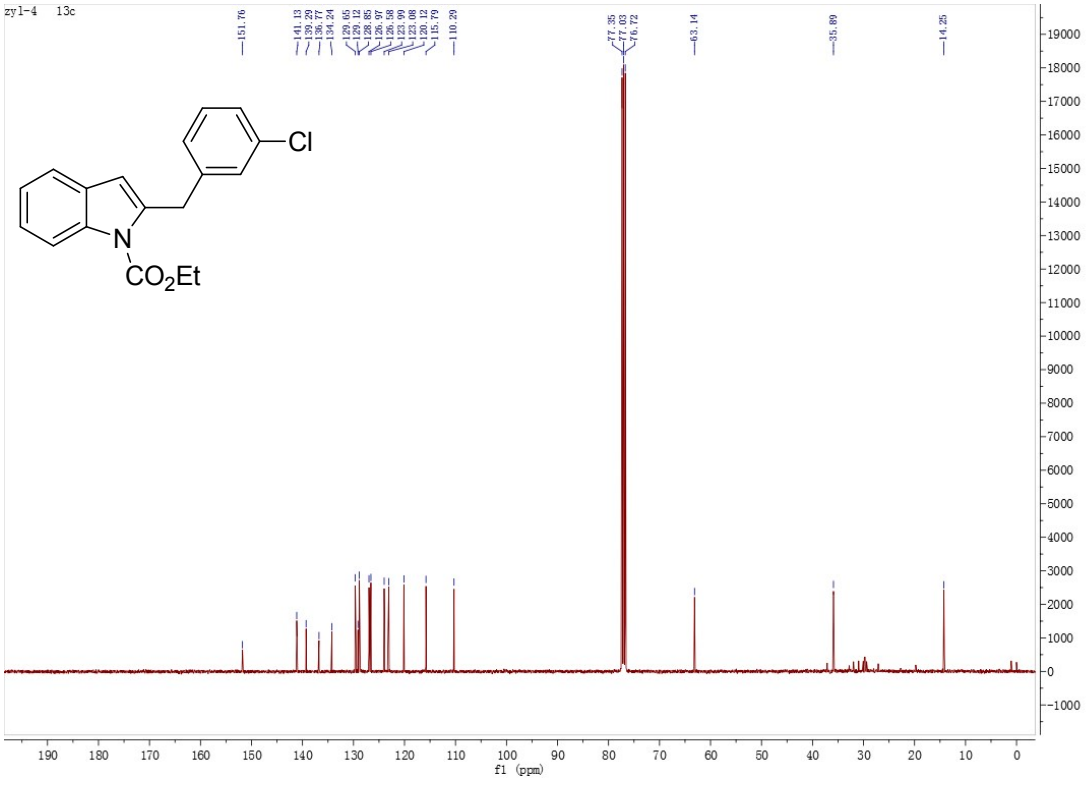
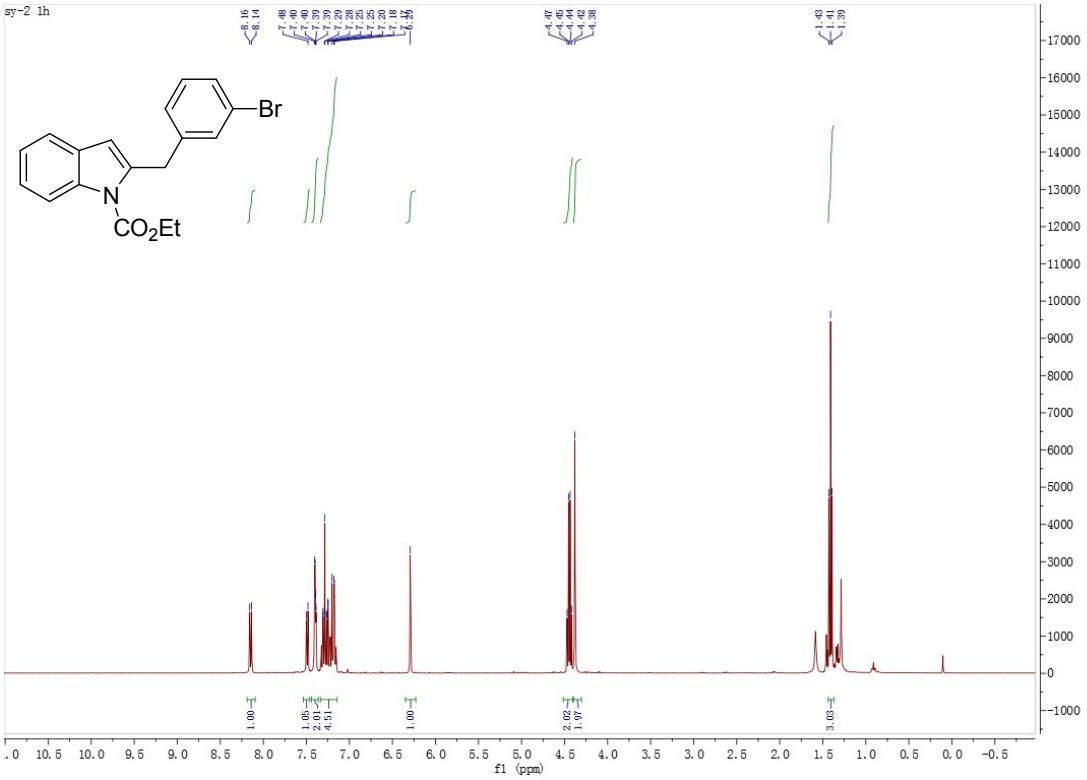
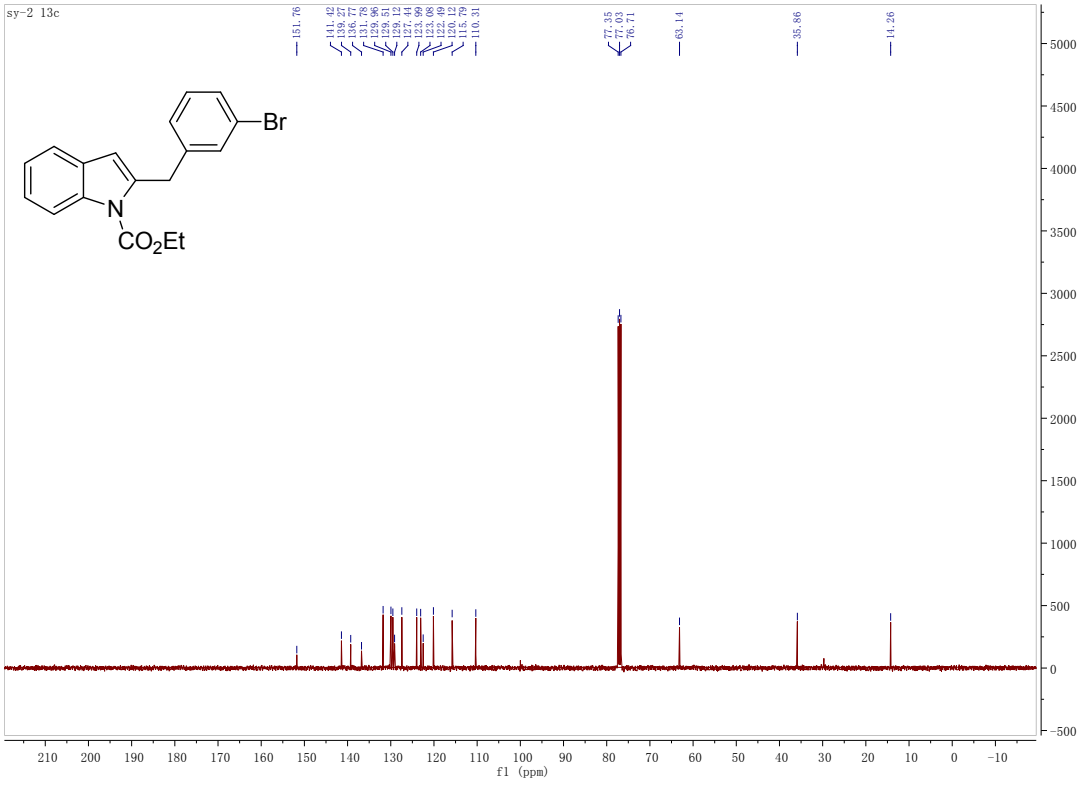
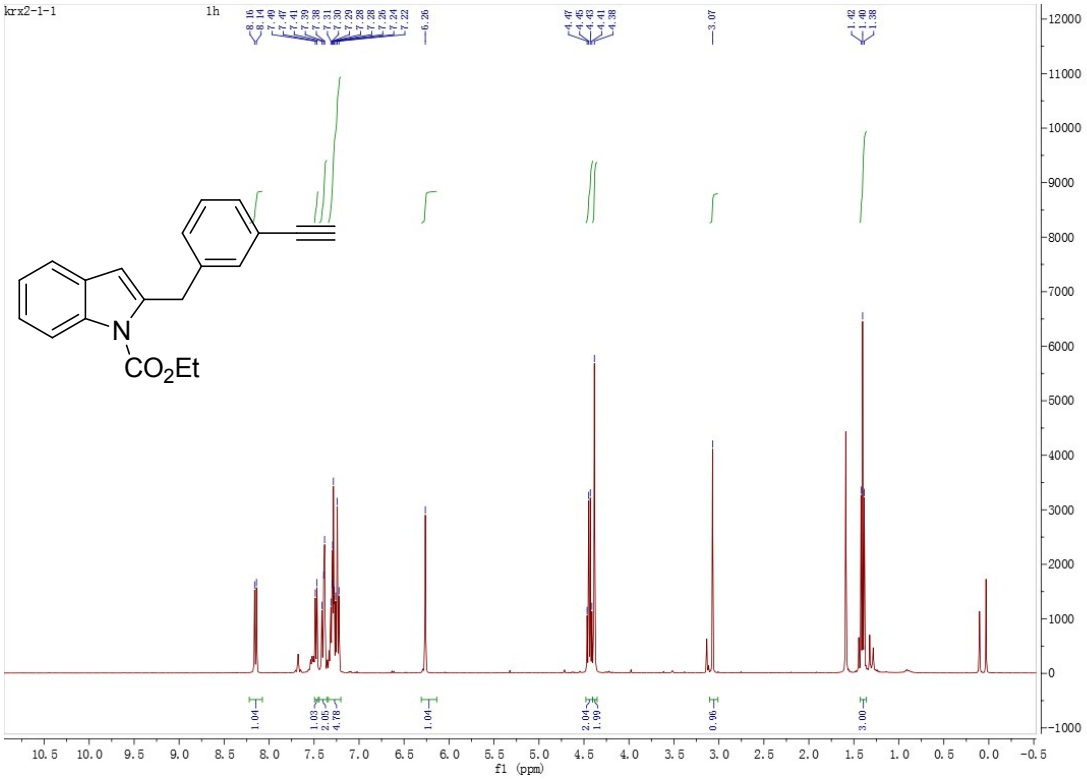
Me
N
CO2Et
f1 (ppm)

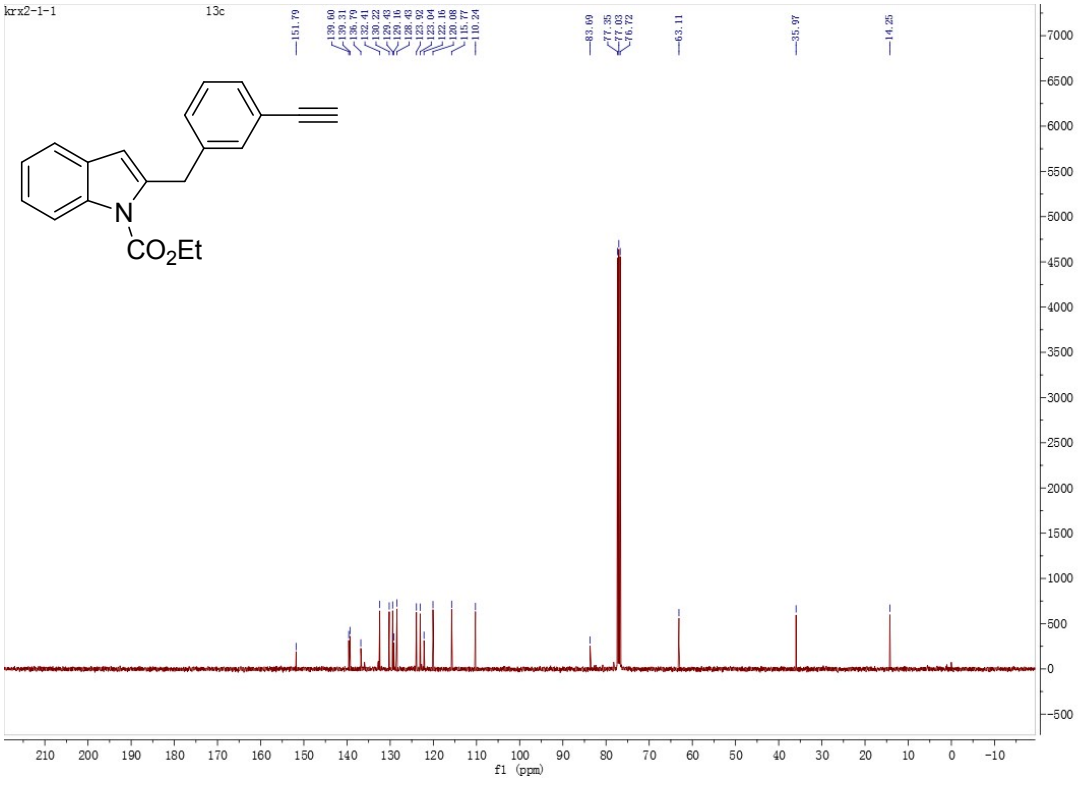

zyl-4 1h
Cl
N
CO2Et
f1 (ppm)

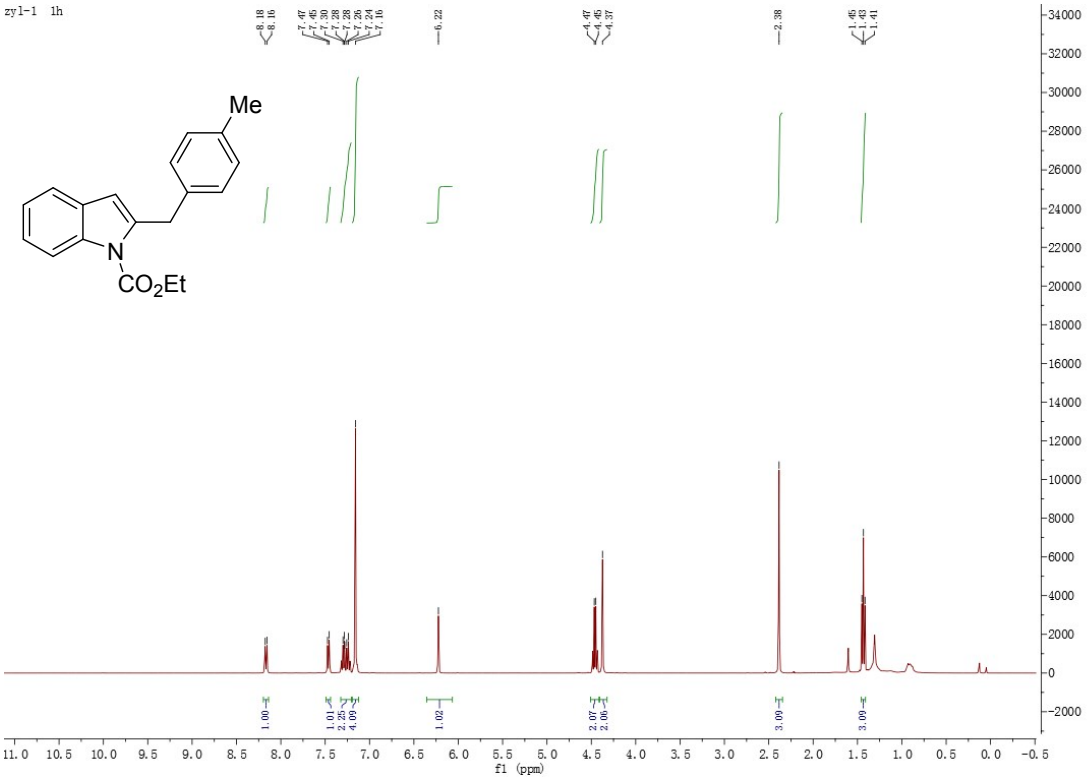

zyl-4 13c
Cl
N
CO2Et
f1 (ppm)

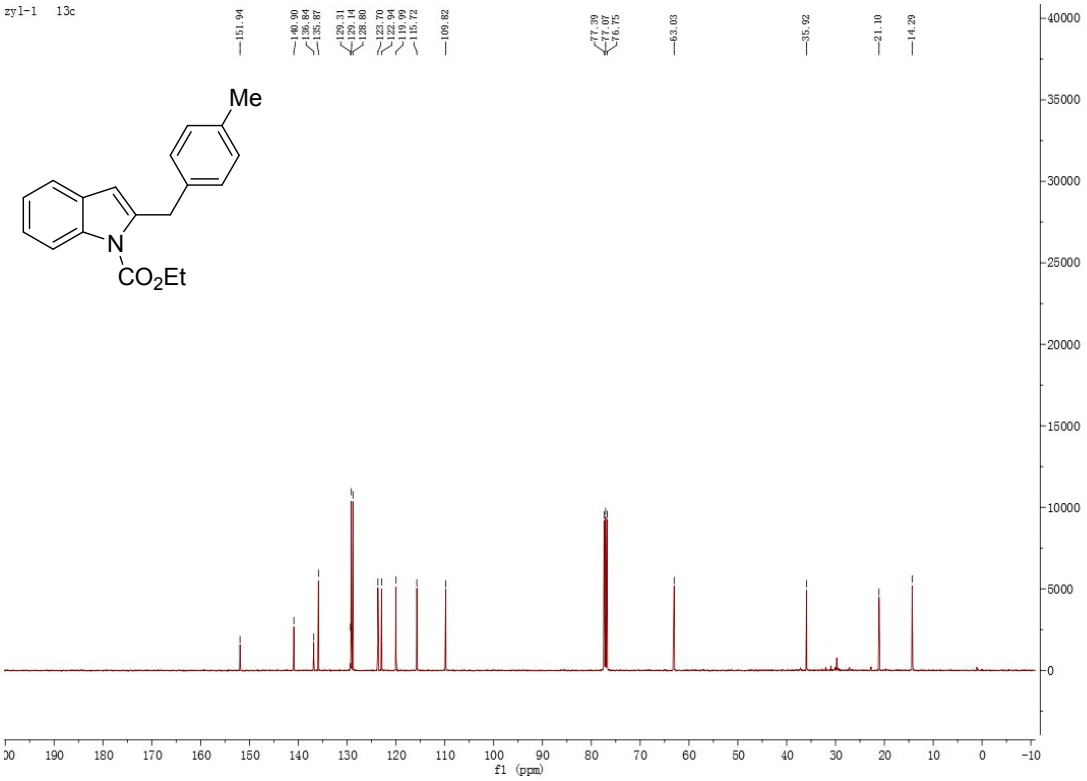

sy-2 1h
Br
N
CO2Et
f1 (ppm)

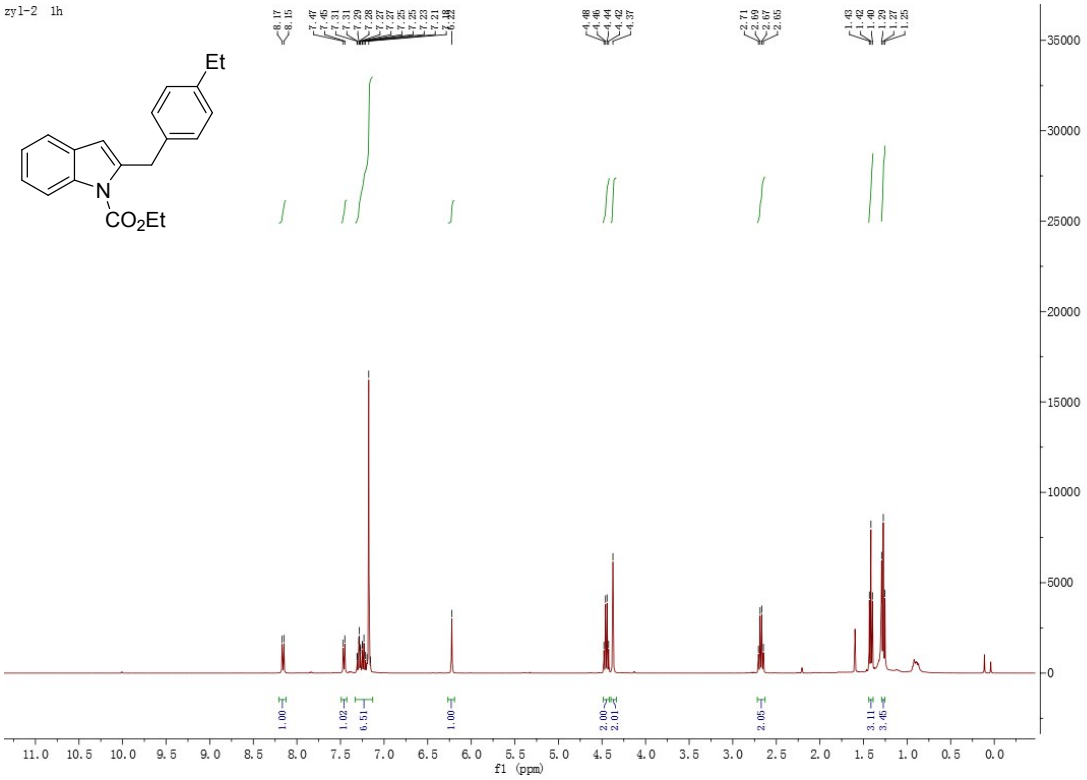

sy-2 13c
Br
N
CO2Et
f1 (ppm)

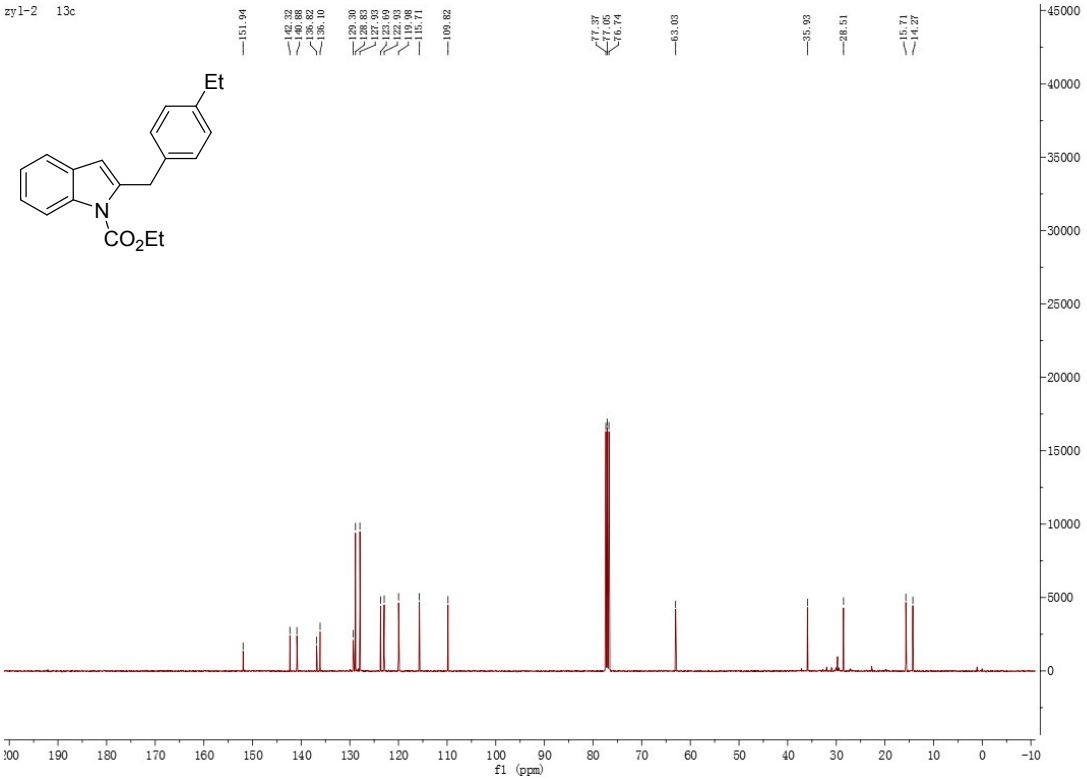

krx2-1-1
1h
N
CO2Et
f1 (ppm)

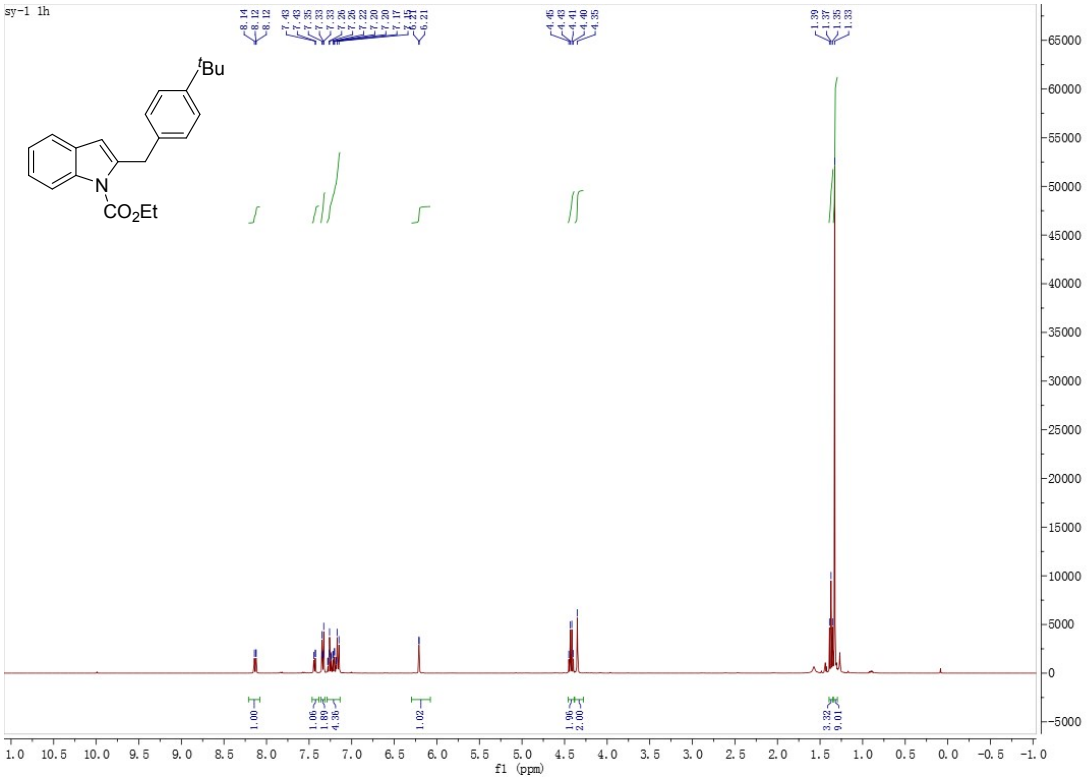

krx2-1-1
13c
N
CO2Et
f1 (ppm)

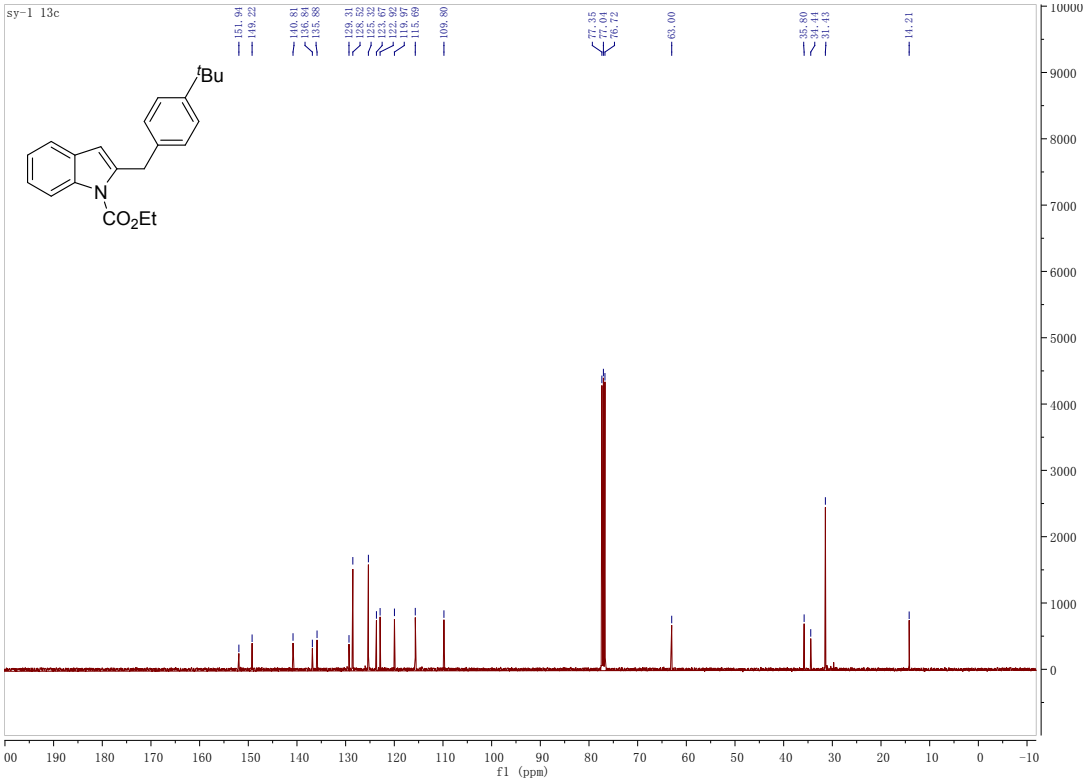

zyl-1 1h
Me
N
CO2Et
f1 (ppm)

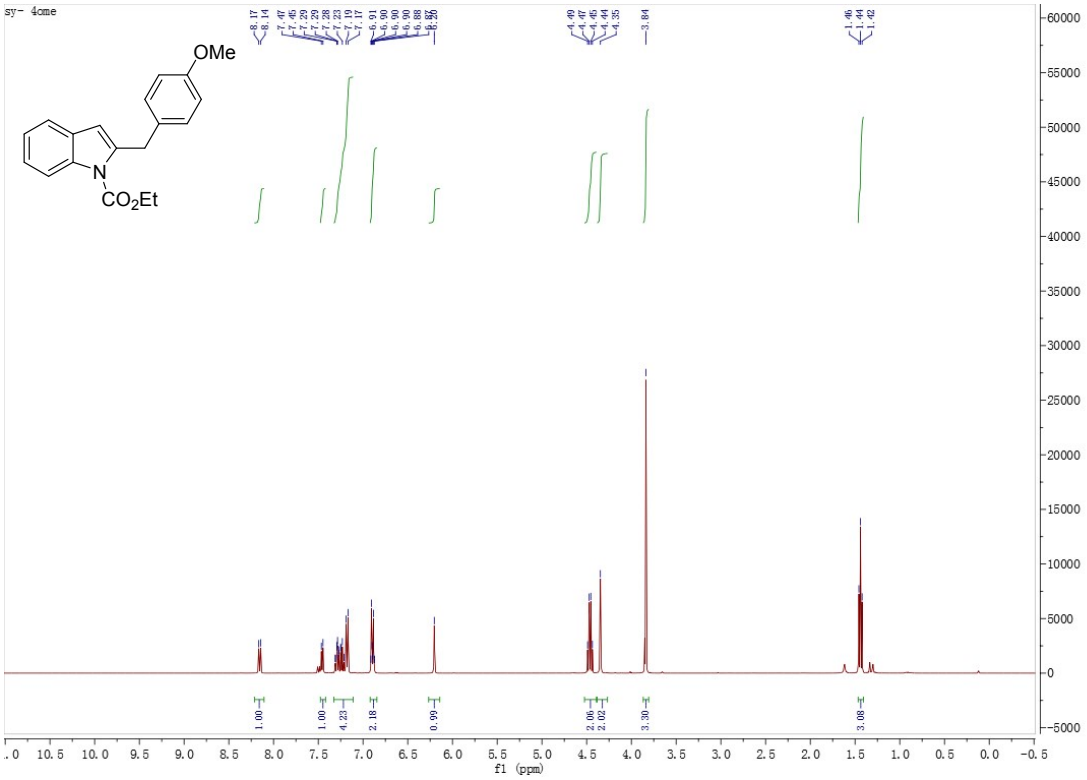

zyl-1 13c
Me
N
CO2Et
f1 (ppm)

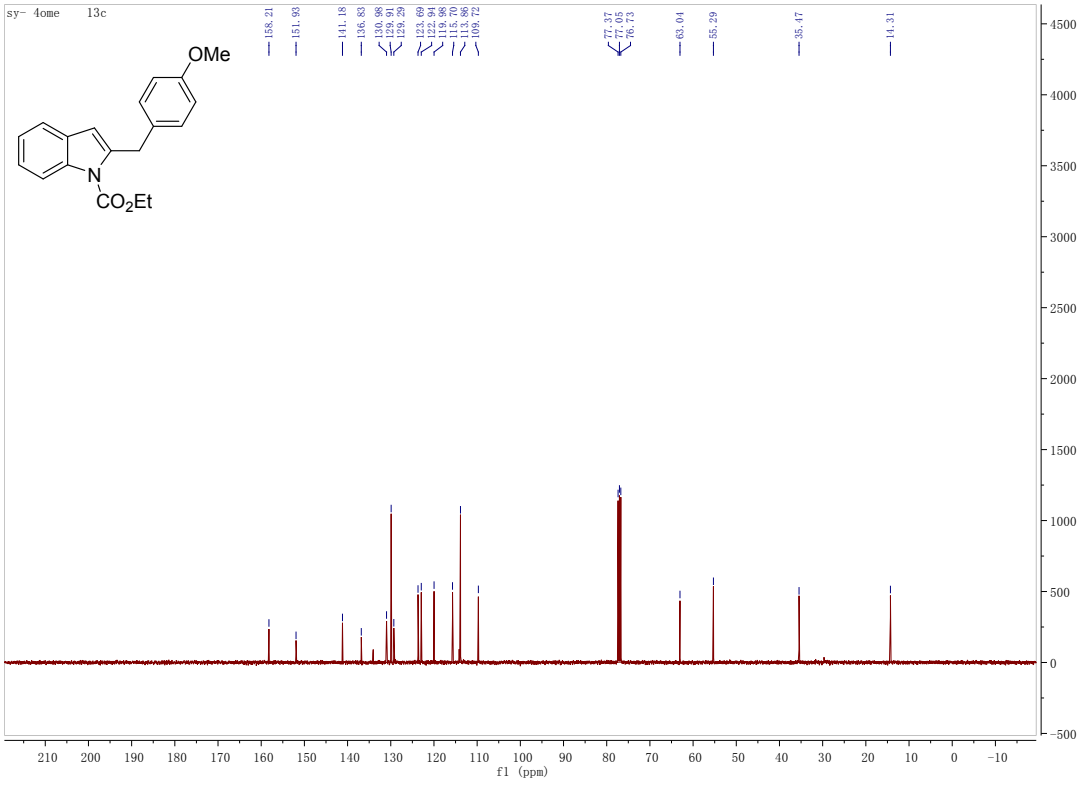

zy1-2 1h
Et
N
CO2Et
f1 (ppm)

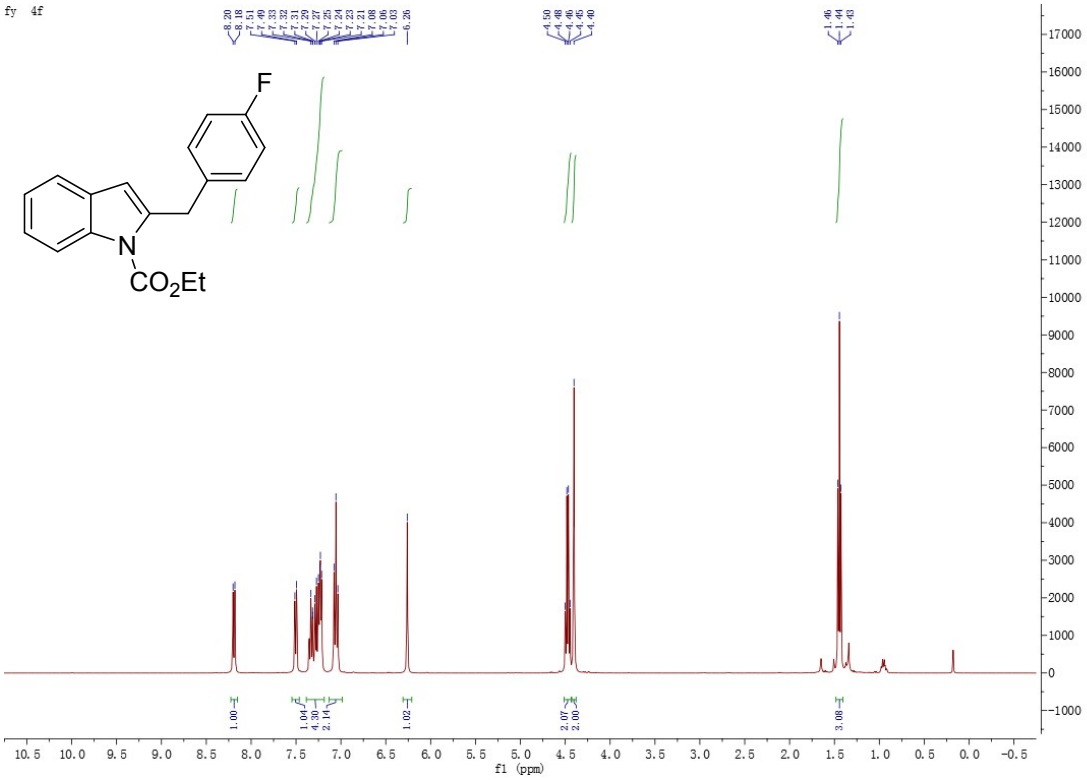

zy1-2 13c
Et
N
CO2Et
f1 (ppm)

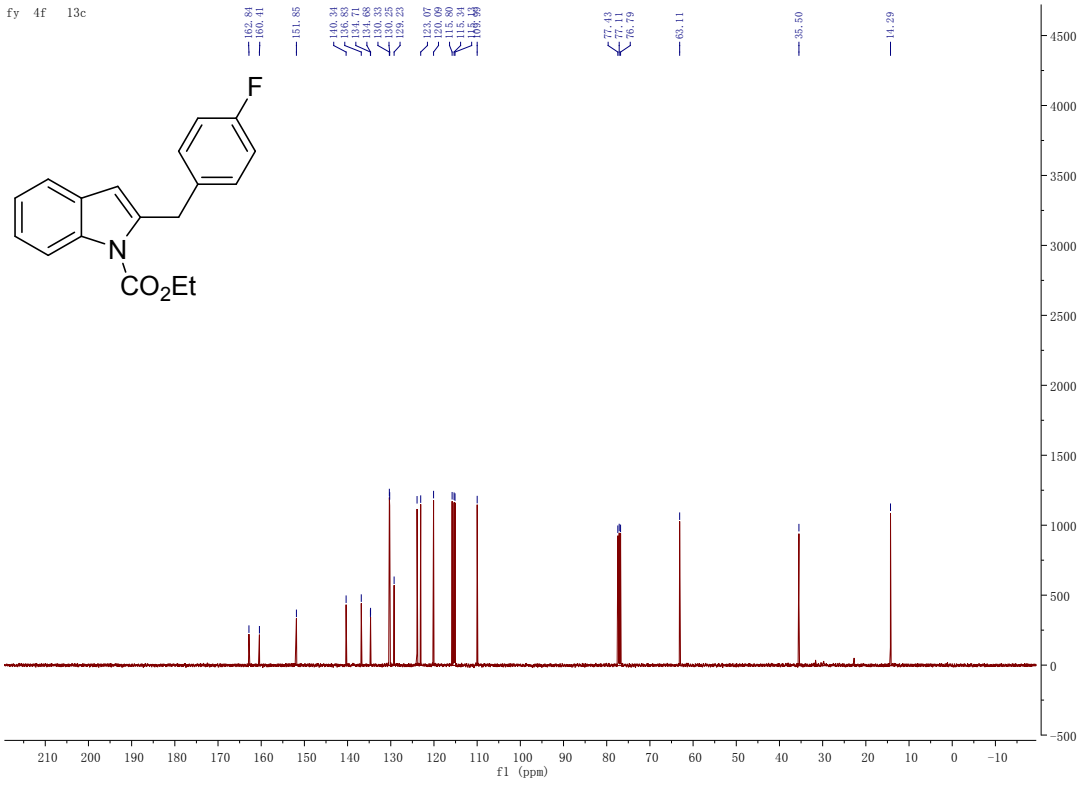

sy-1 1h
tBu
N
CO2Et
f1 (ppm)

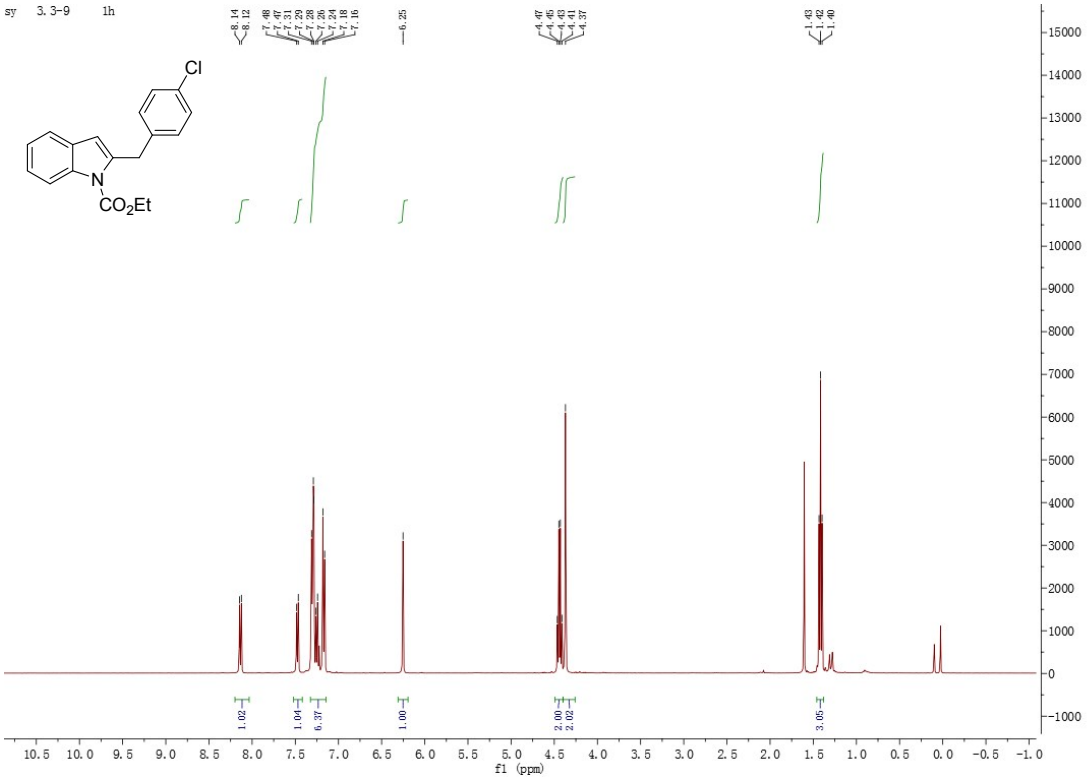

sy-1 13c
tBu
N
CO2Et
f1 (ppm)

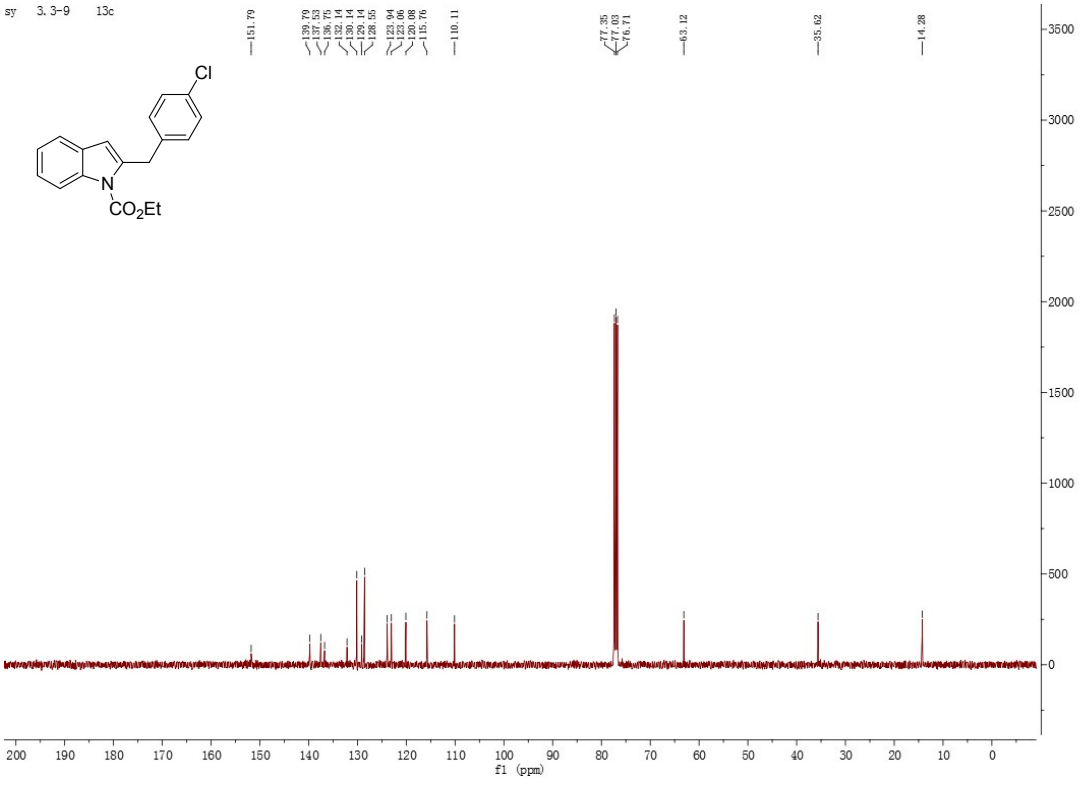

sy- 4ome
OMe
N
CO2Et
8.17
8.14
7.47
7.45
7.29
7.28
7.23
7.19
7.17
6.91
6.90
6.90
6.89
6.88
6.87
6.85
4.49
4.47
4.45
4.44
4.35
3.84
1.46
1.44
1.42
1.00
1.00
4.23
2.18
0.99
2.00
2.02
3.30
3.08
f1 (ppm)

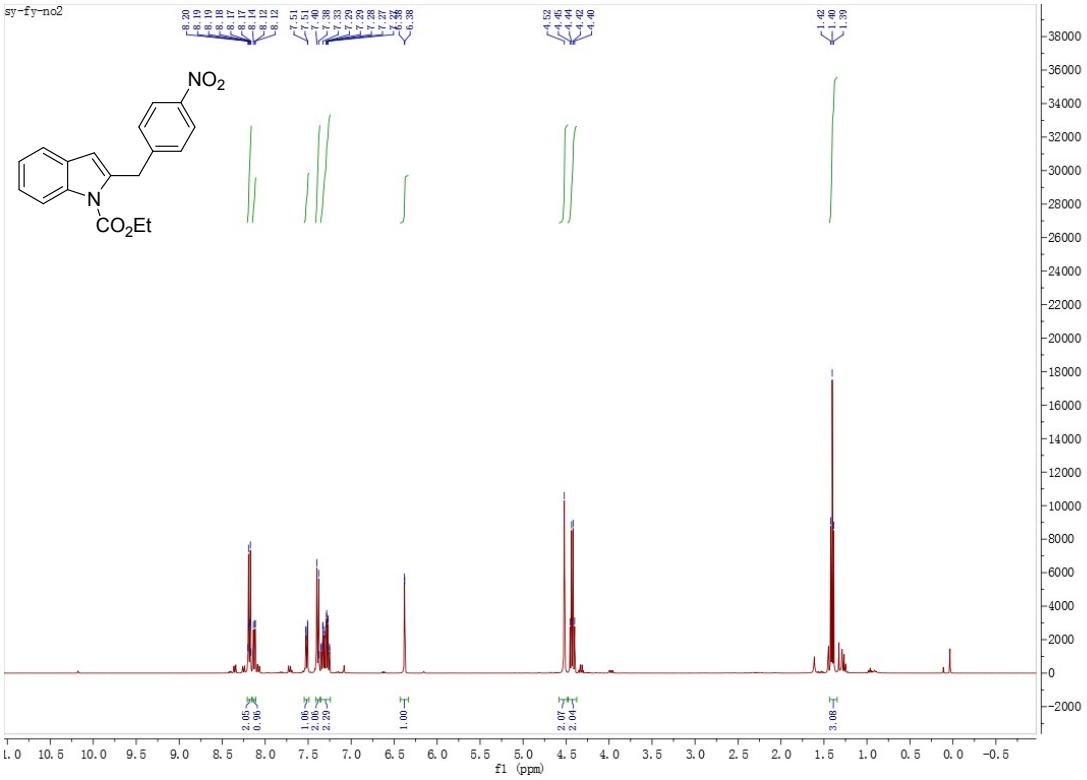

sy- 4ome 13c
OMe
N
CO2Et
158.21
151.93
141.18
136.83
130.98
129.91
129.29
123.69
122.94
119.98
115.70
113.98
109.72
77.37
77.05
76.73
63.04
55.29
35.47
14.31
f1 (ppm)

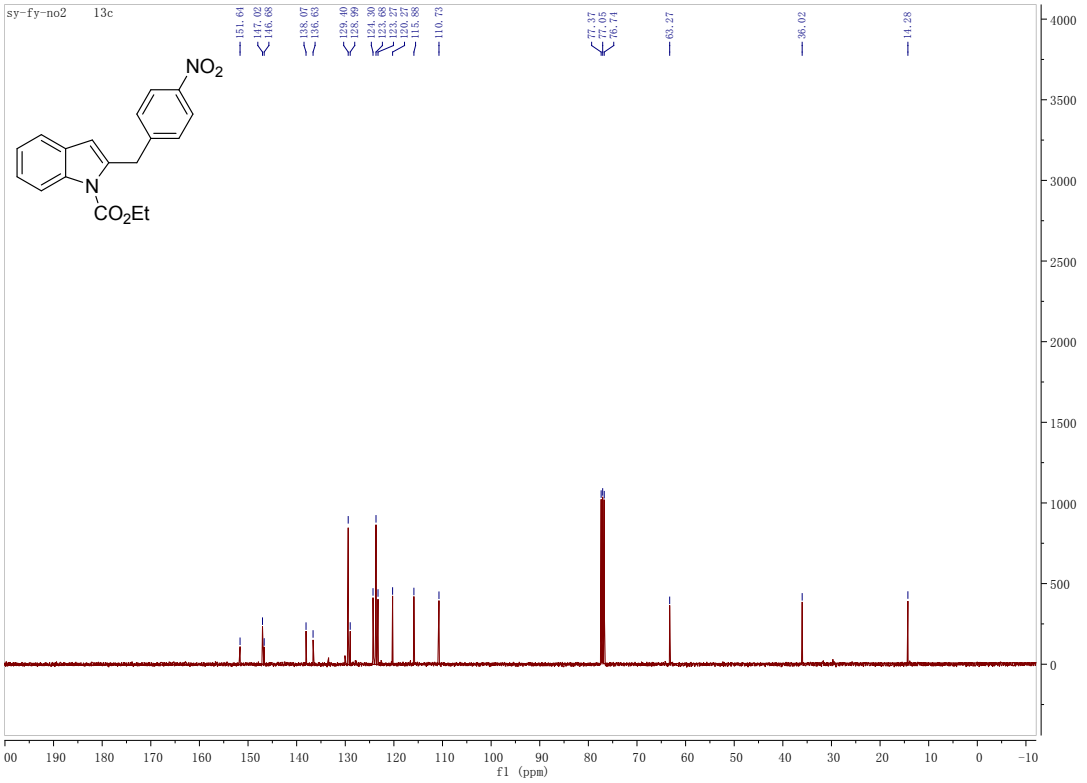

fy 4f
F
N
CO2Et
f1 (ppm)

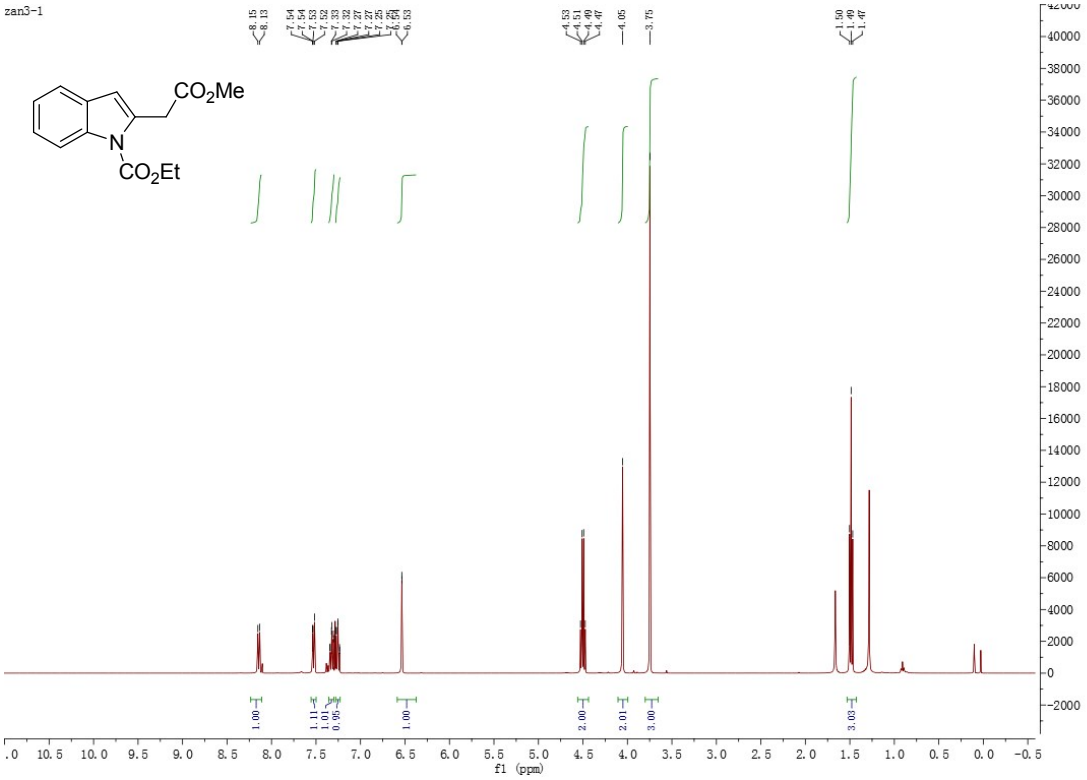

fy 4f 13c
F
N
CO2Et
f1 (ppm)

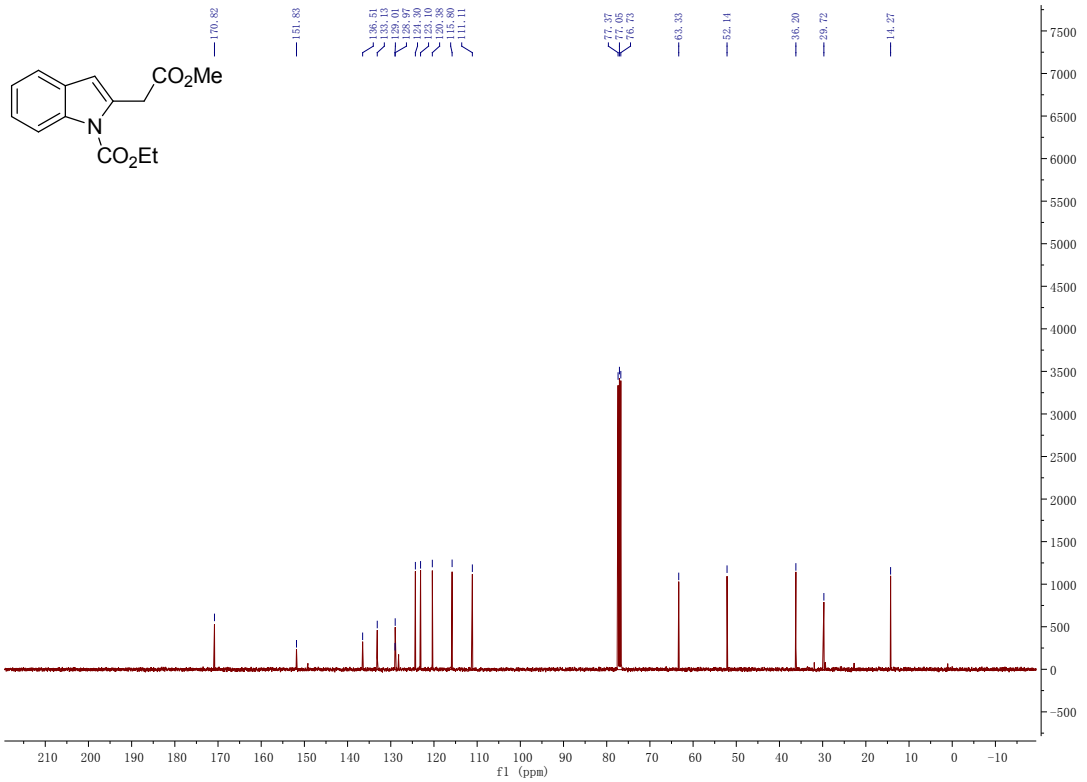

sy 3.3-9 1h
Cl
N
CO2Et
8.14
8.12
7.48
7.47
7.31
7.29
7.28
7.26
7.24
7.18
7.16
6.25
4.47
4.46
4.43
4.41
4.37
1.43
1.42
1.40
1.02
1.04
6.37
1.00
2.00
2.02
3.05
f1 (ppm)

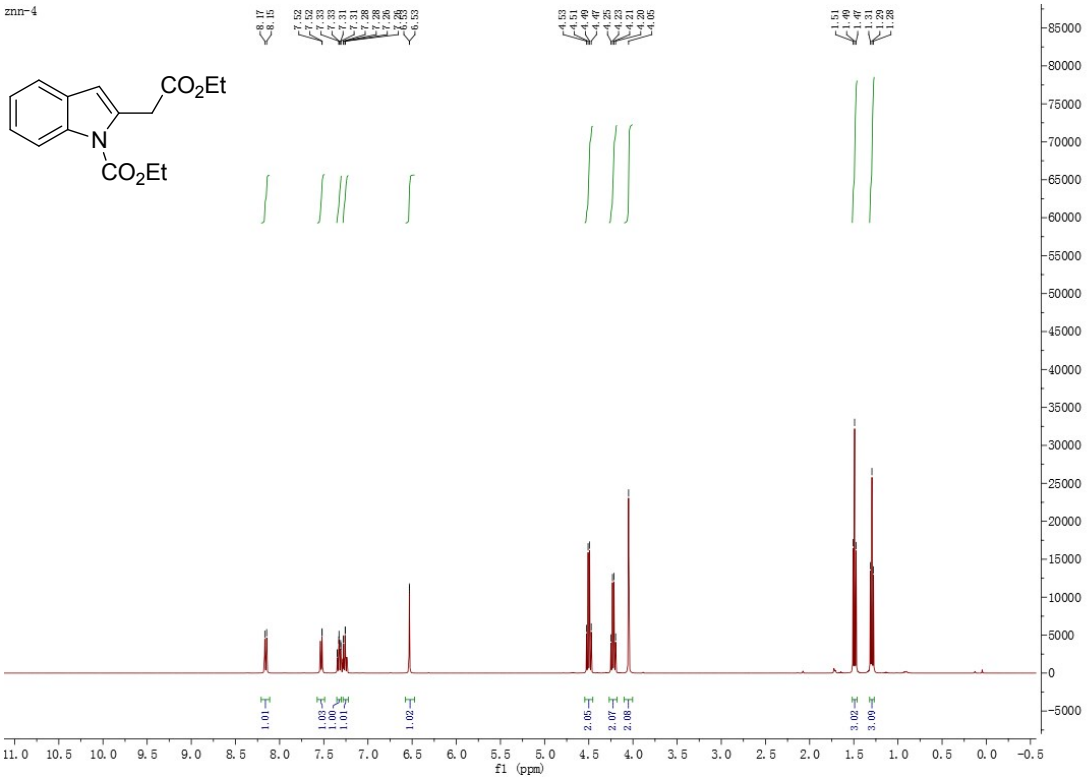

sy 3.3-9 13c
Cl
N
CO2Et
151.79
139.79
137.53
136.75
132.14
130.14
129.14
128.55
123.94
123.06
120.08
115.76
110.11
77.35
77.03
76.71
63.12
35.62
14.28
f1 (ppm)

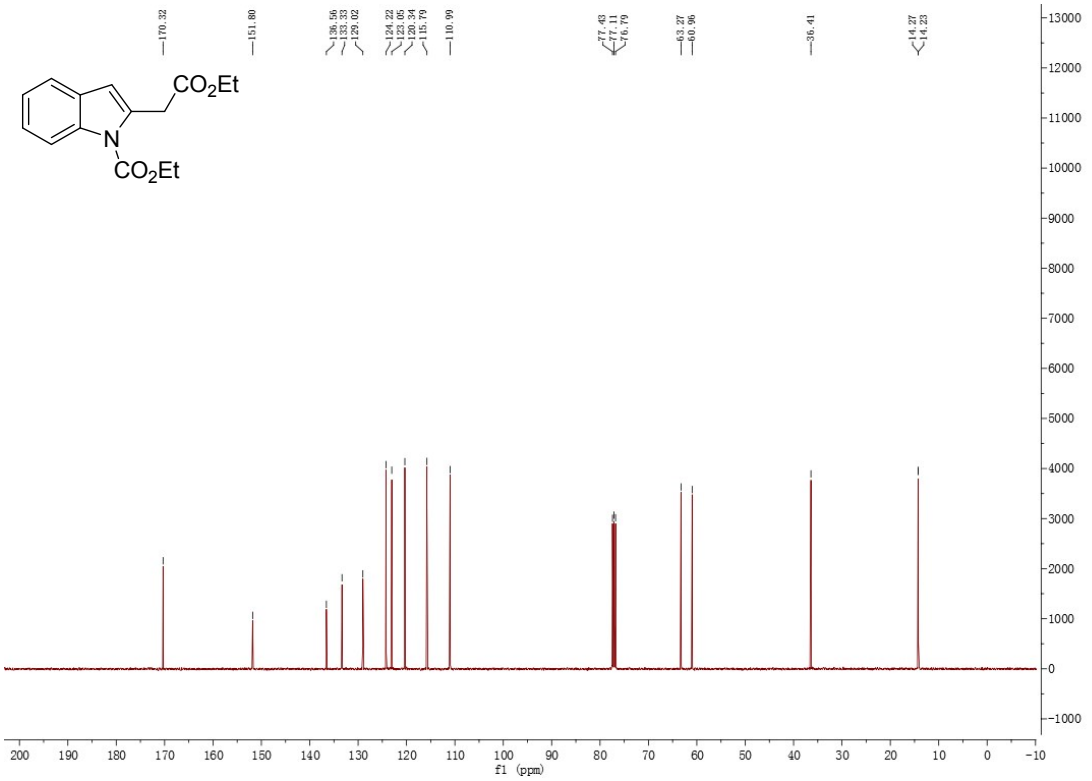

sy-fy-no2
NO2
N
CO2Et
f1 (ppm)

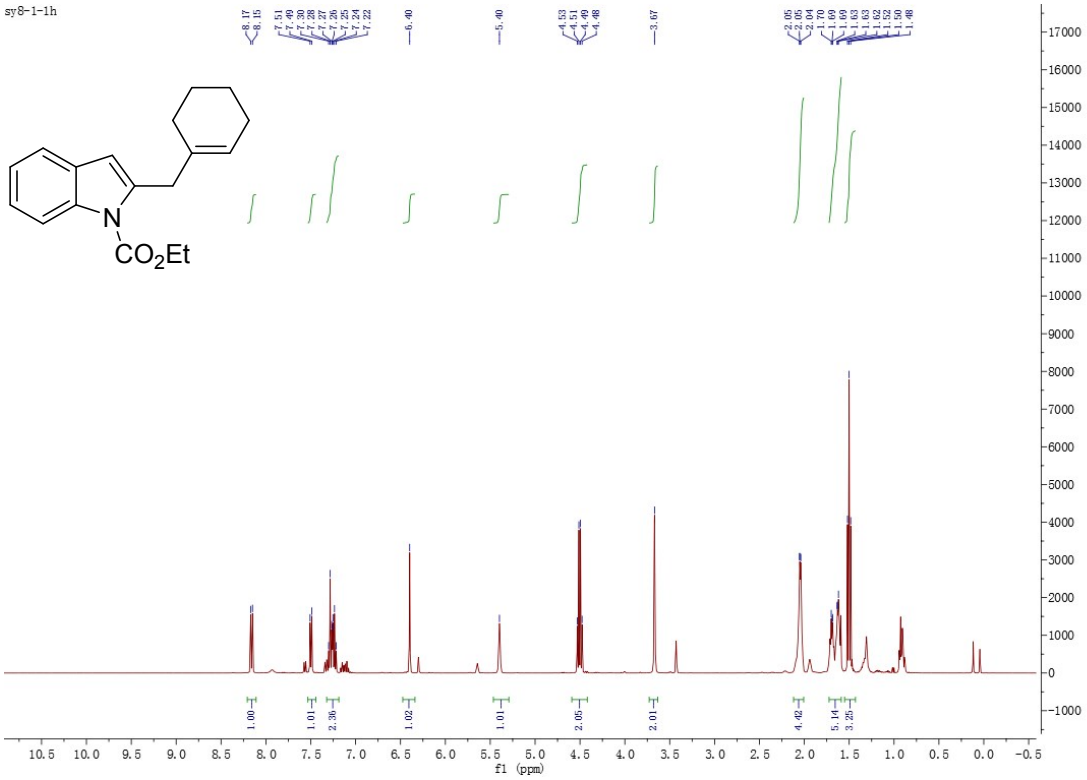

sy-fy-no2 13c
NO2
N
CO2Et
f1 (ppm)

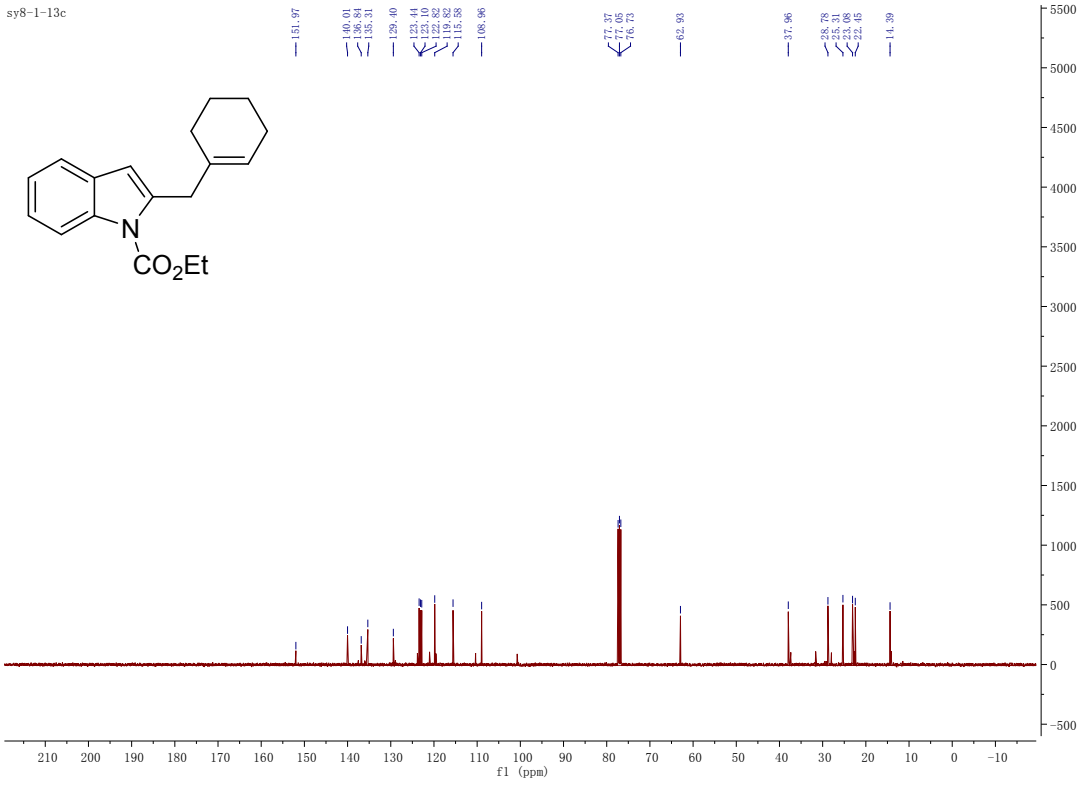

zan3-1
CO2Me
N
CO2Et
f1 (ppm)

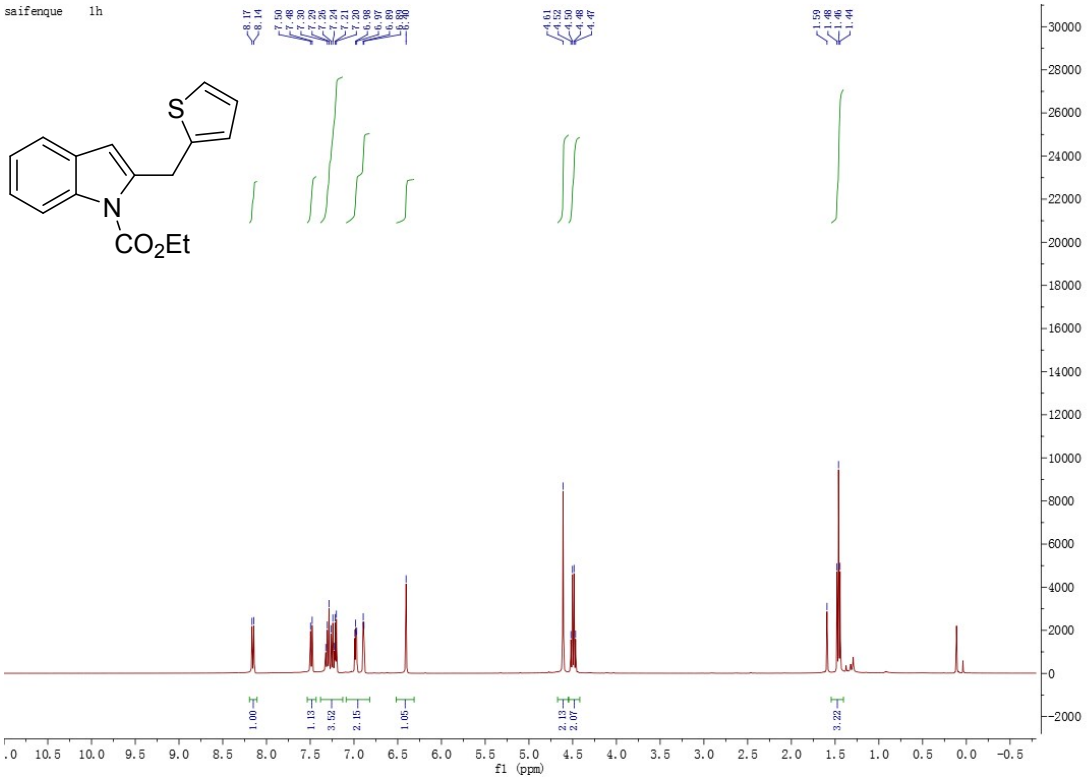

CO2Me
N
CO2Et
f1 (ppm)

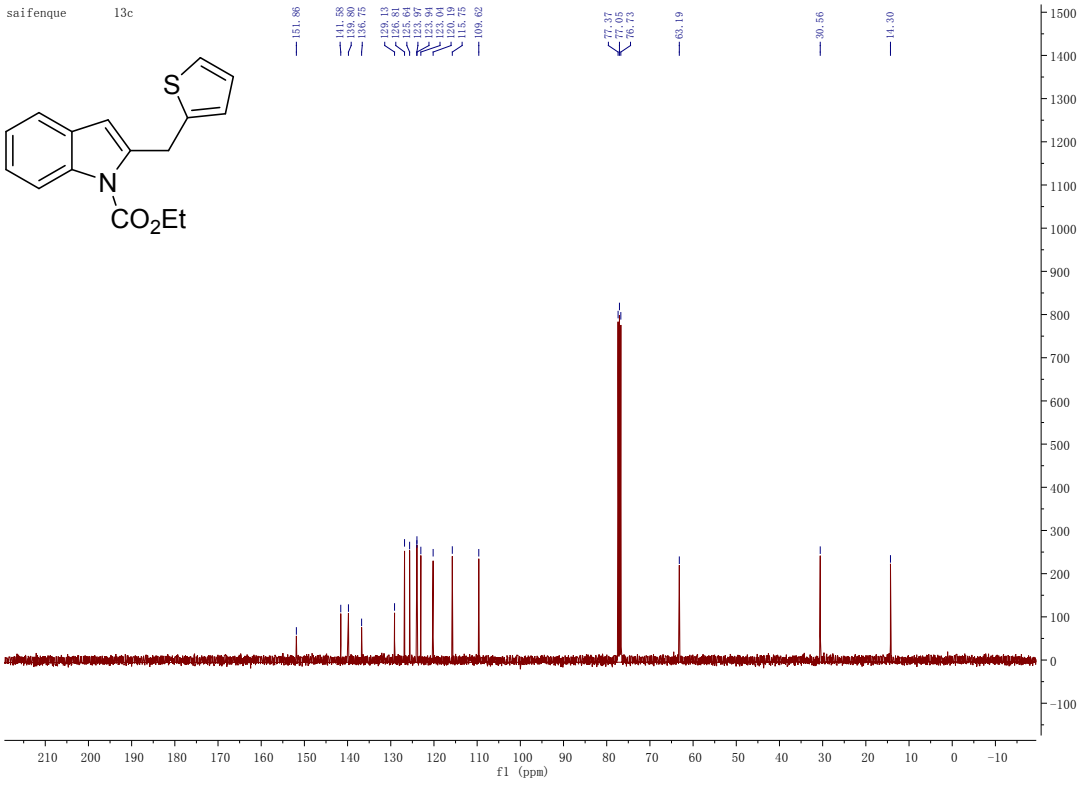

znn-4
CO2Et
N
CO2Et
f1 (ppm)

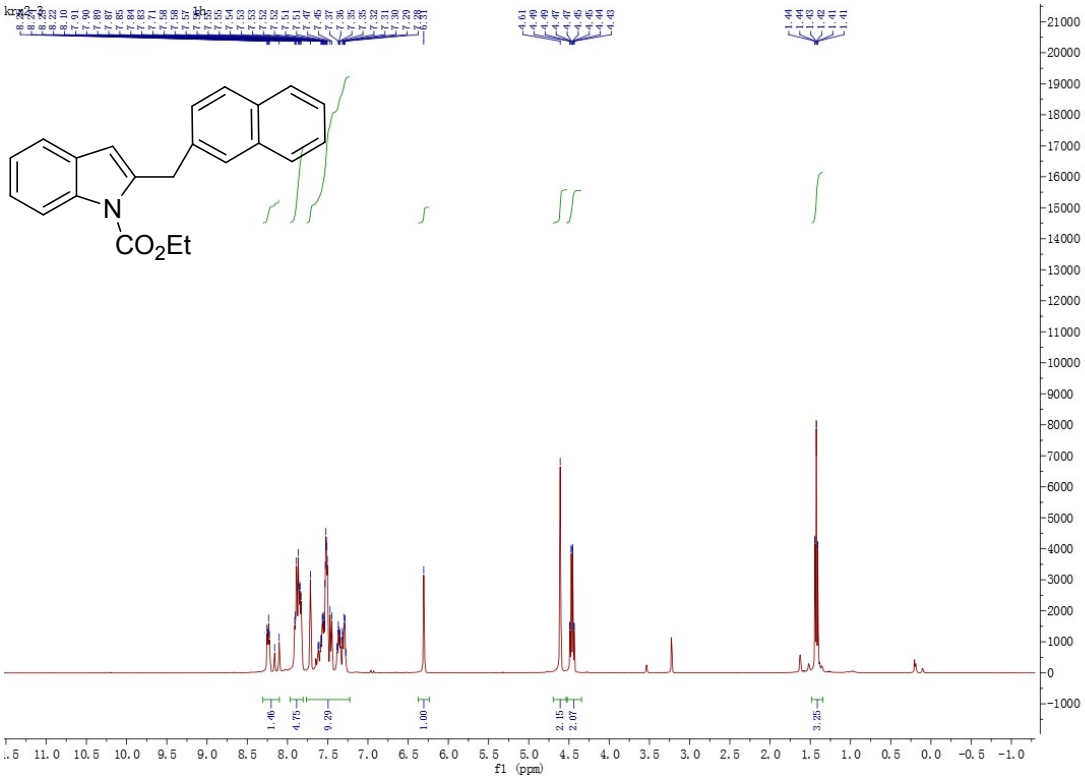

CO2Et
N
CO2Et
f1 (ppm)

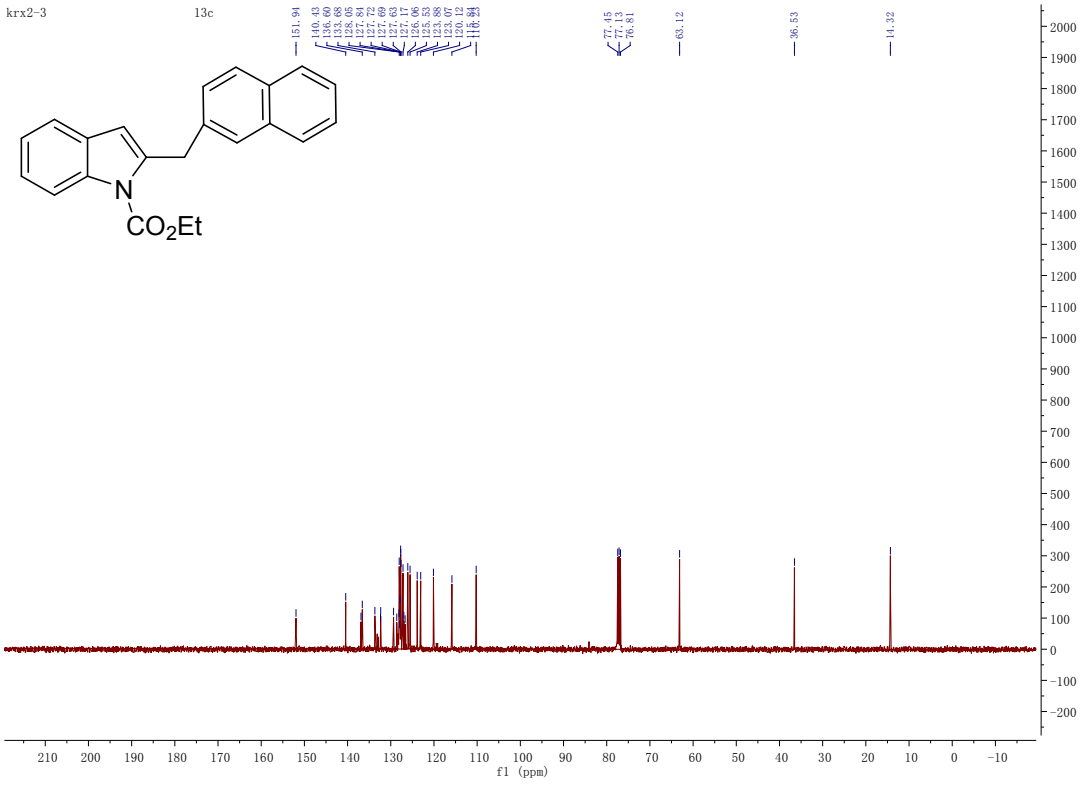

sy8-1-1h
8.17
8.15
7.51
7.49
7.30
7.28
7.27
7.26
7.25
7.24
7.22
6.40
5.40
4.53
4.51
4.49
4.48
3.67
2.05
2.04
1.70
1.69
1.65
1.63
1.62
1.52
1.50
1.48
1.00
1.01
2.38
1.02
1.01
2.05
2.01
4.42
5.14
3.26
f1 (ppm)

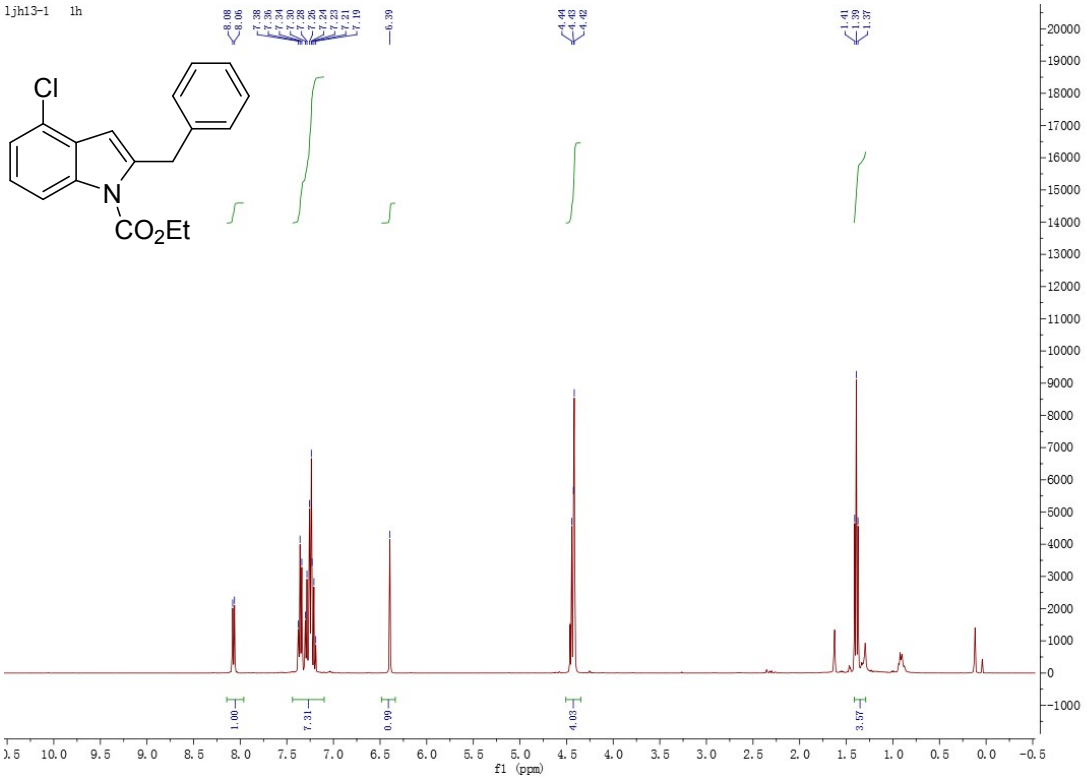

sy8-1-13c
151.97
140.01
136.84
135.31
129.40
123.44
123.10
121.82
119.82
115.58
108.96
77.37
77.05
76.73
62.93
37.96
28.78
25.31
23.08
22.45
14.39
f1 (ppm)

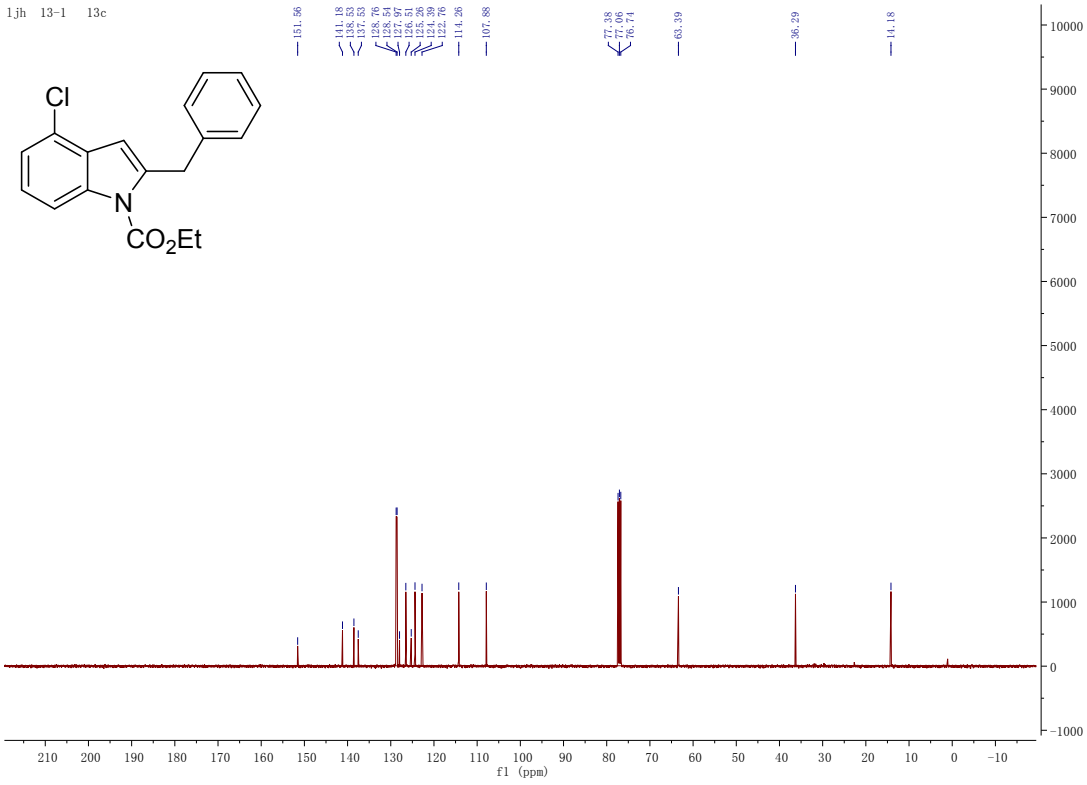

saifenque 1h
S
N
CO2Et
f1 (ppm)

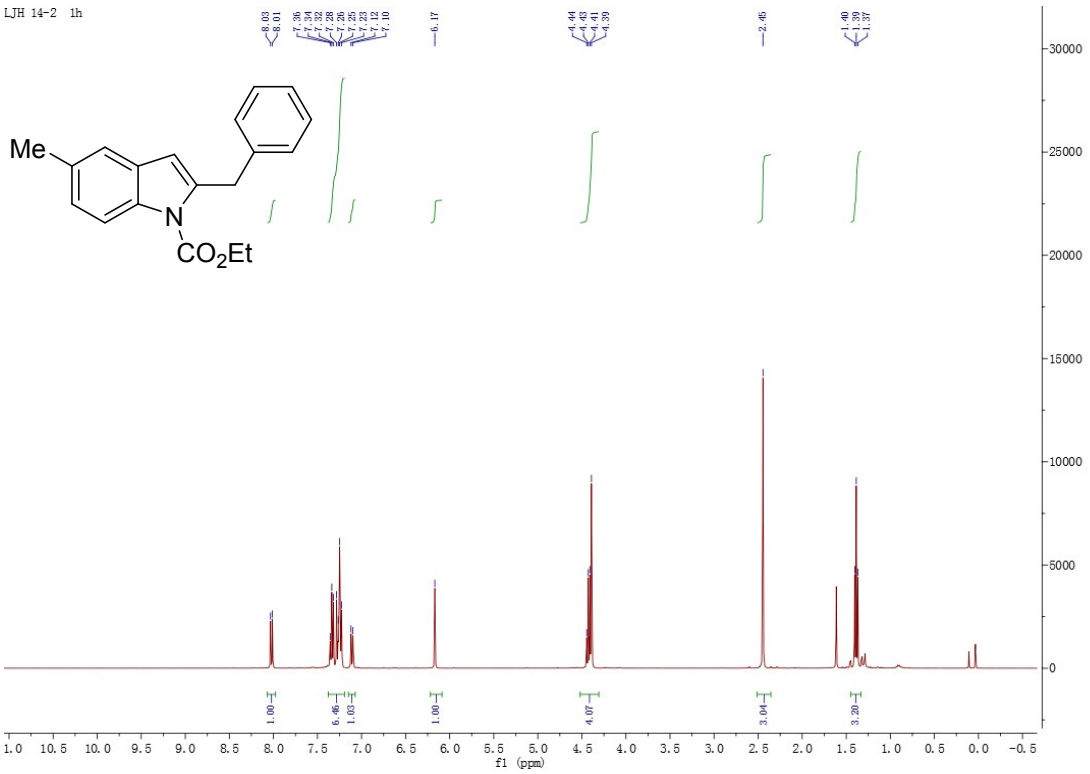

saifenque 13c
S
N
CO2Et
f1 (ppm)

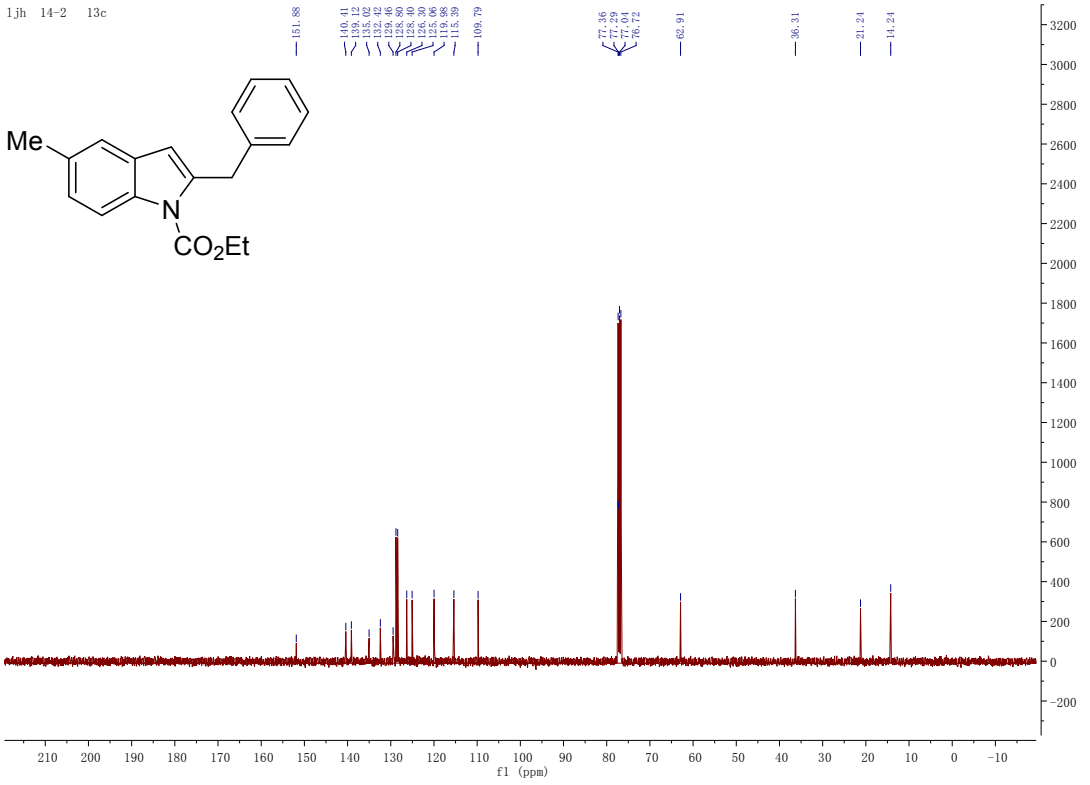

N
CO2Et
1.40
4.75
9.29
1.00
2.15
2.07
3.25
f1 (ppm)

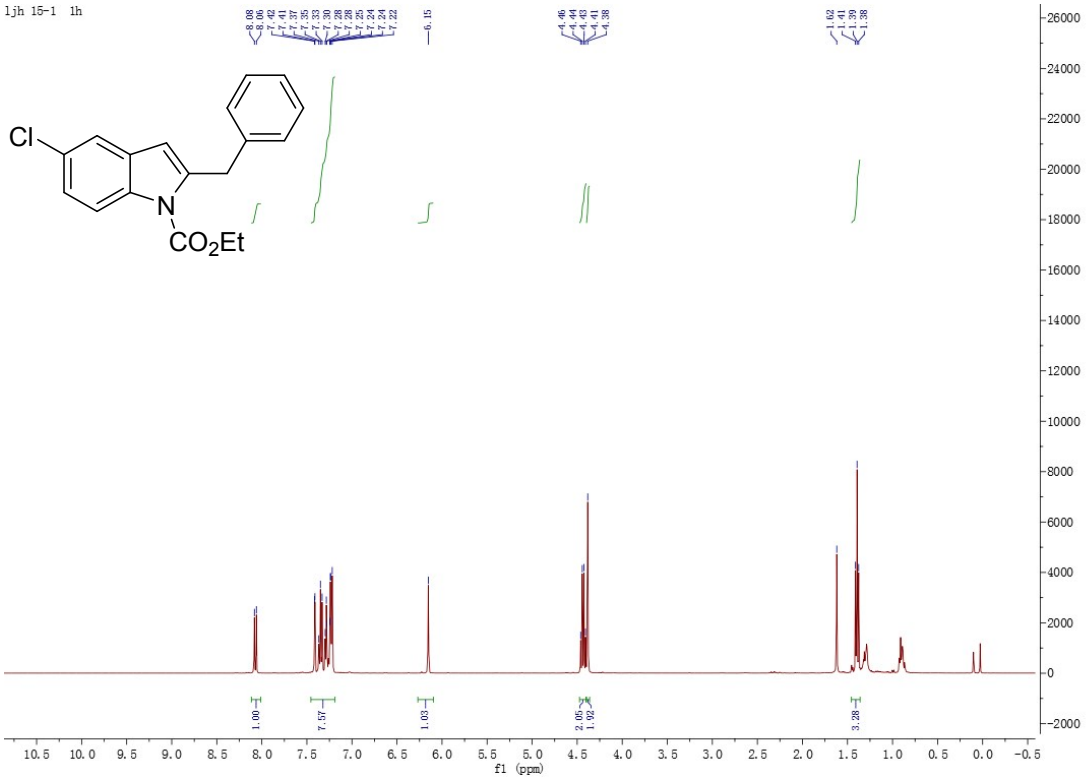

krx2-3
13c
N
CO2Et
151.94
140.43
136.60
133.68
128.05
127.84
127.72
127.69
127.63
127.17
126.06
125.53
123.98
123.15
120.12
77.45
77.13
76.81
63.12
36.53
14.32
f1 (ppm)

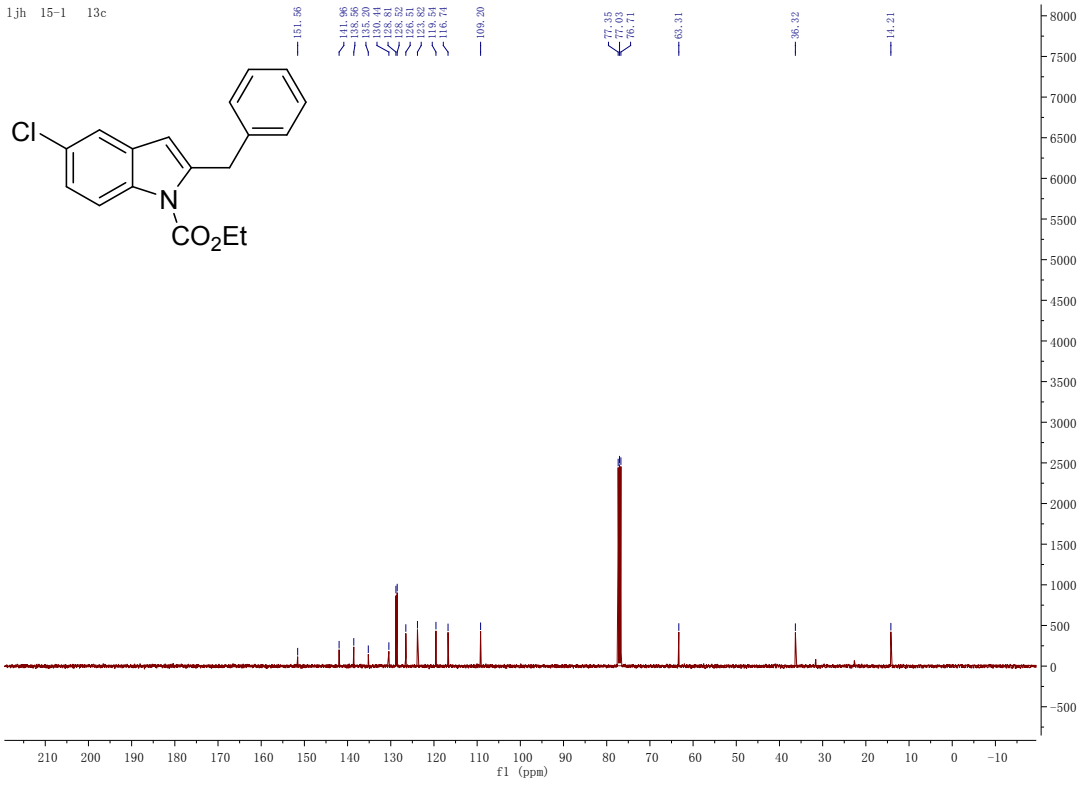

ljh13-1 1h
Cl
N
CO2Et
f1 (ppm)

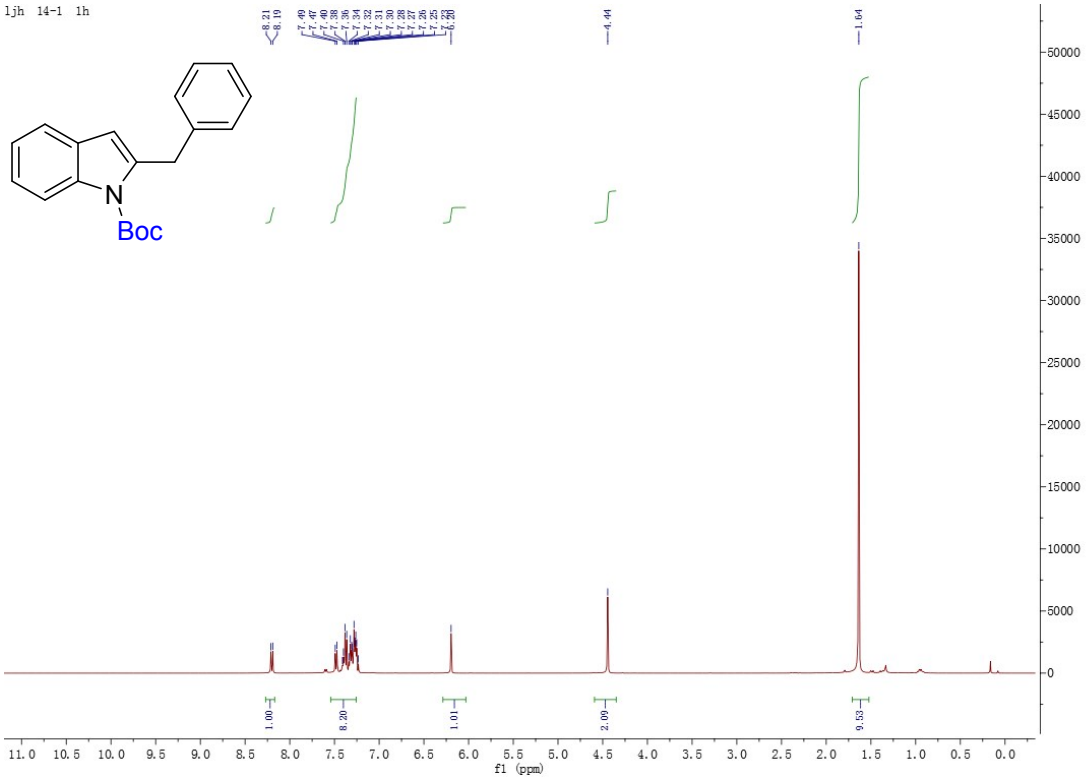

ljh 13-1 13c
Cl
N
CO2Et
f1 (ppm)

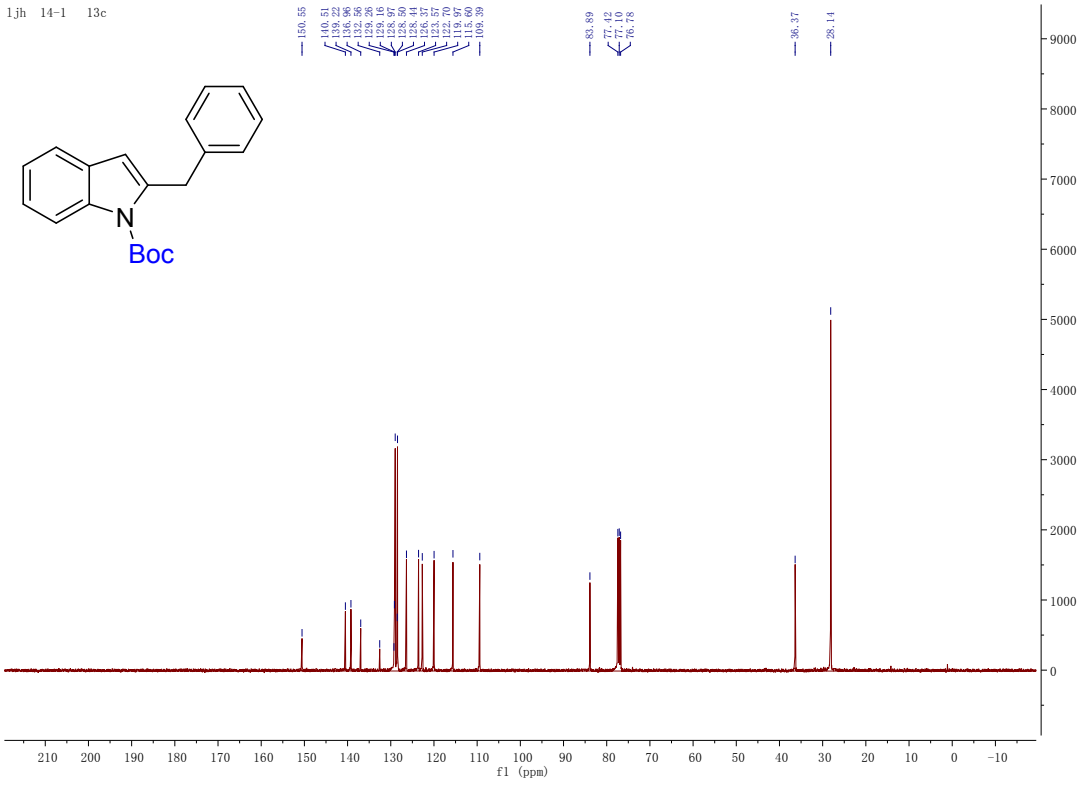

LJH 14-2 1h
Me
N
CO2Et
f1 (ppm)

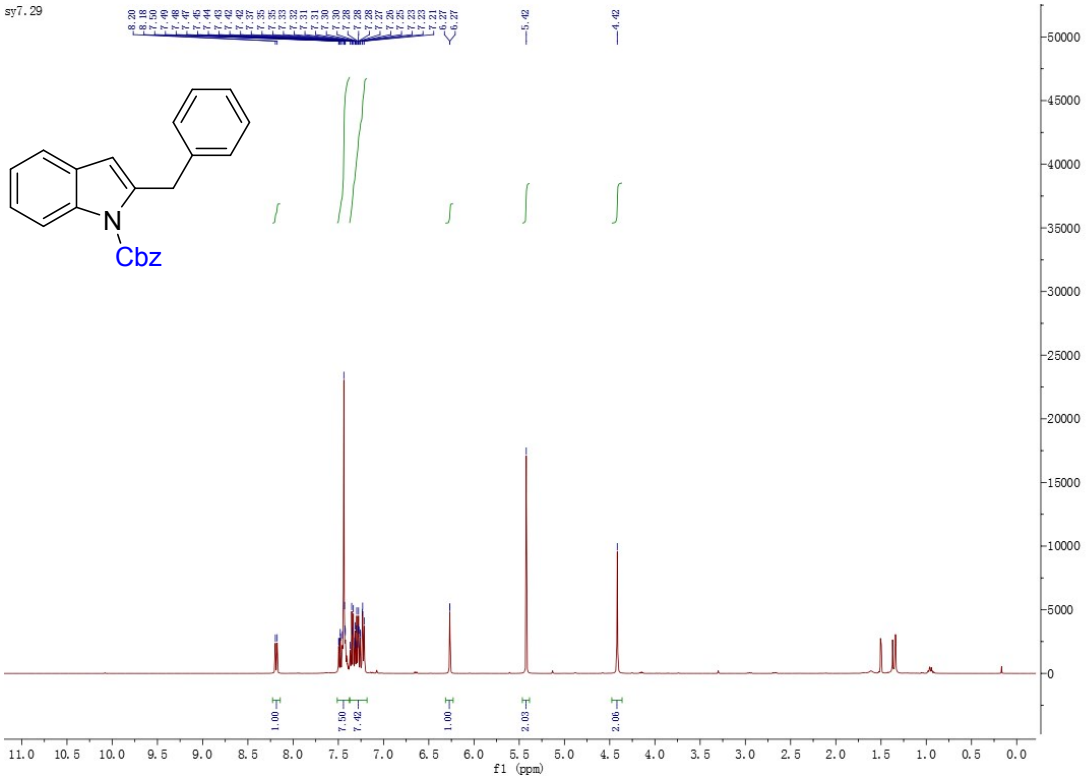

1jh 14-2 13c
Me
N
CO2Et
f1 (ppm)

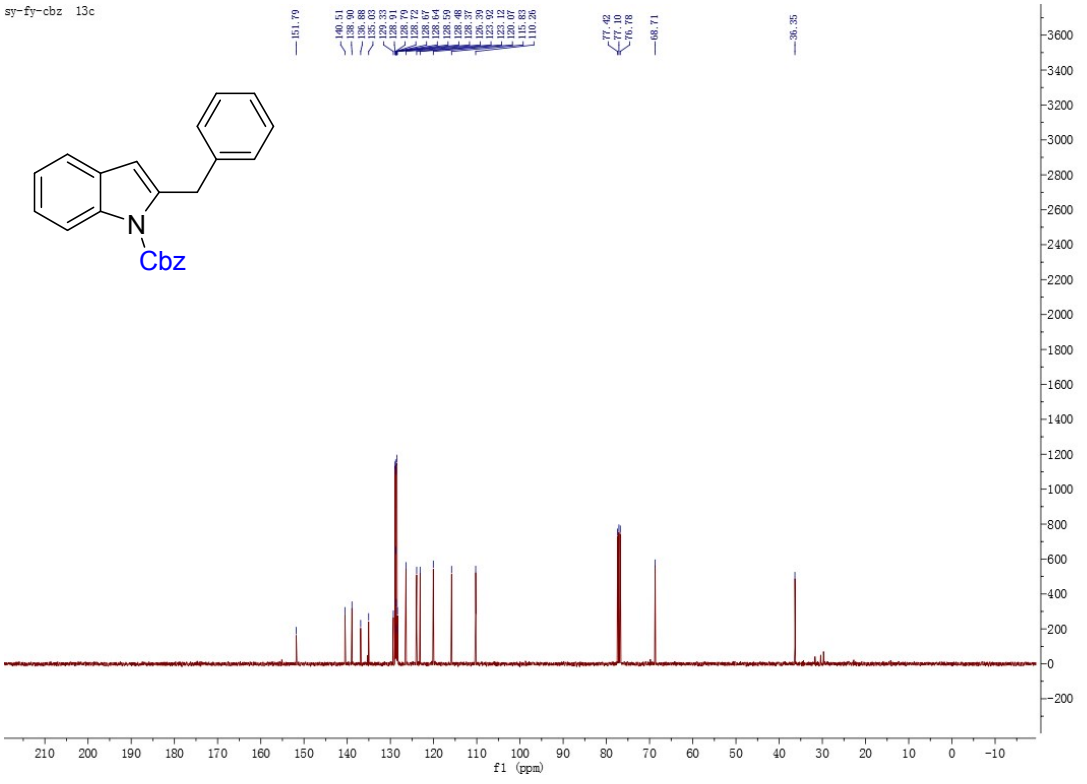

ljh 15-1 1h
Cl
N
CO2Et
f1 (ppm)

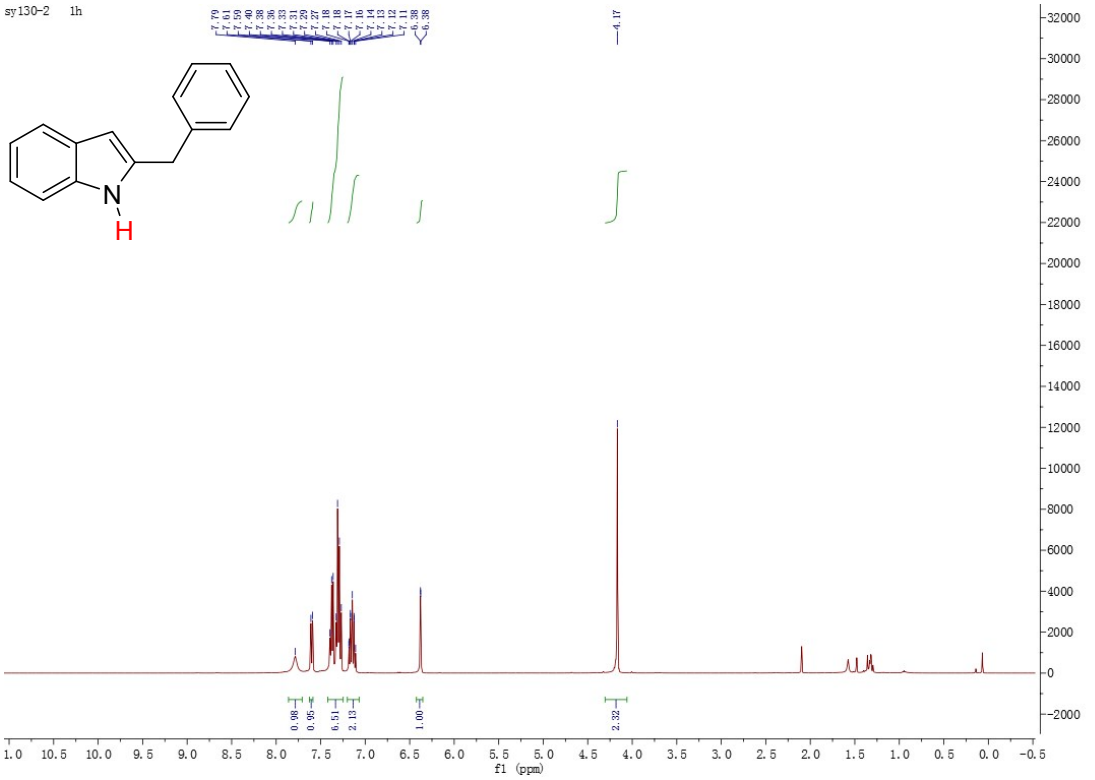

ljh 15-1 13c
Cl
N
CO2Et
f1 (ppm)

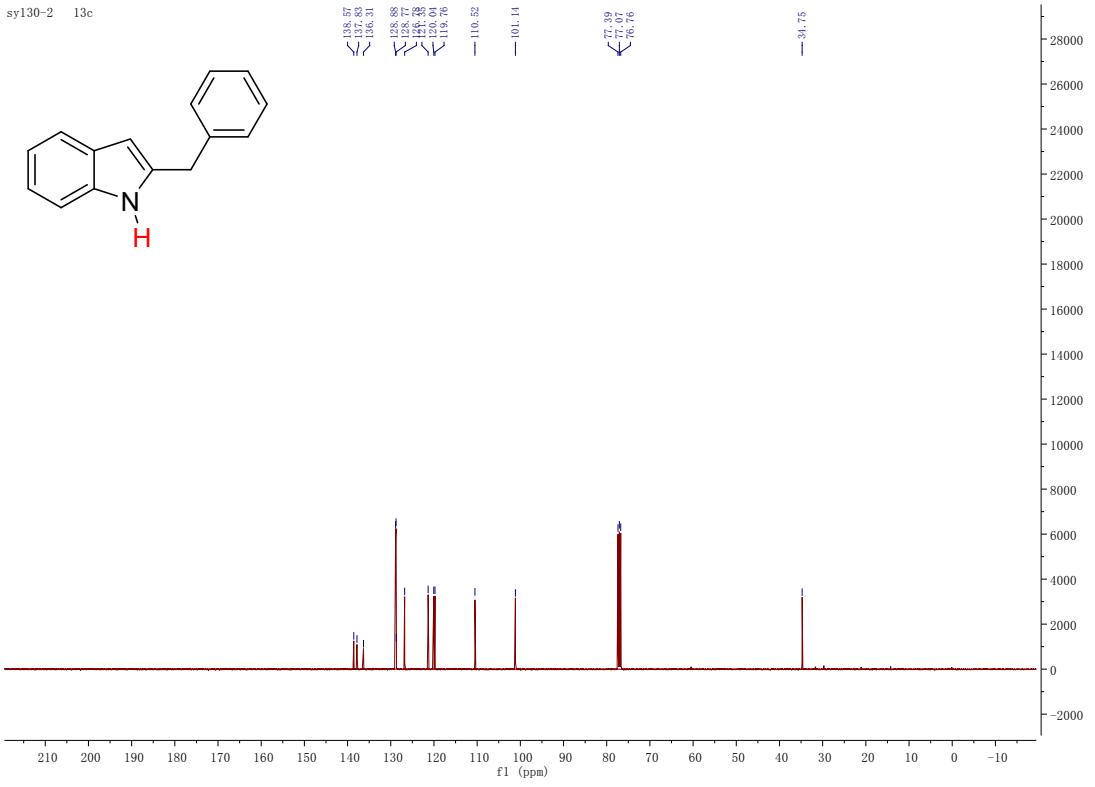

ljh 14-1 1h
Boc
f1 (ppm)


ljh 14-1 13c
Boc
f1 (ppm)

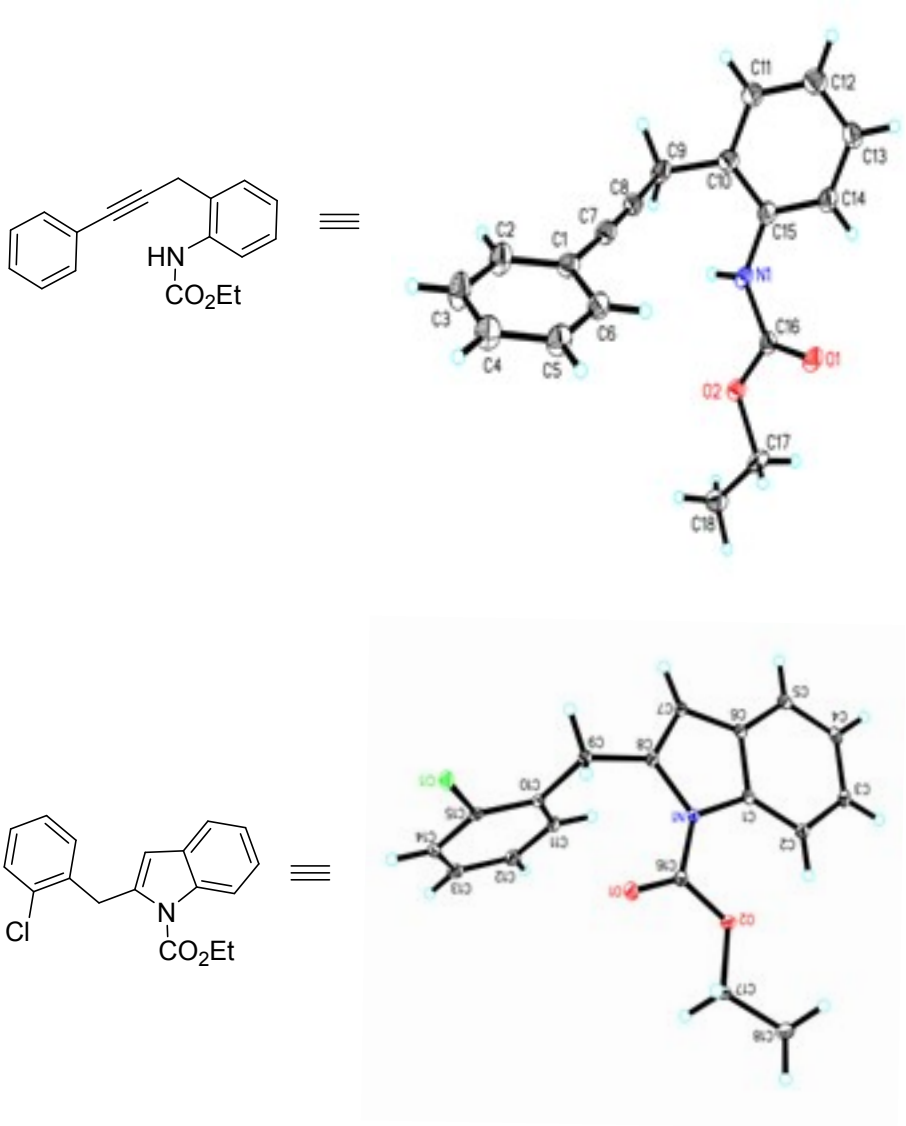

sy7.29
N
Cbz
f1 (ppm)


sy-fy-cbz 13c
N
Cbz
f1 (ppm)

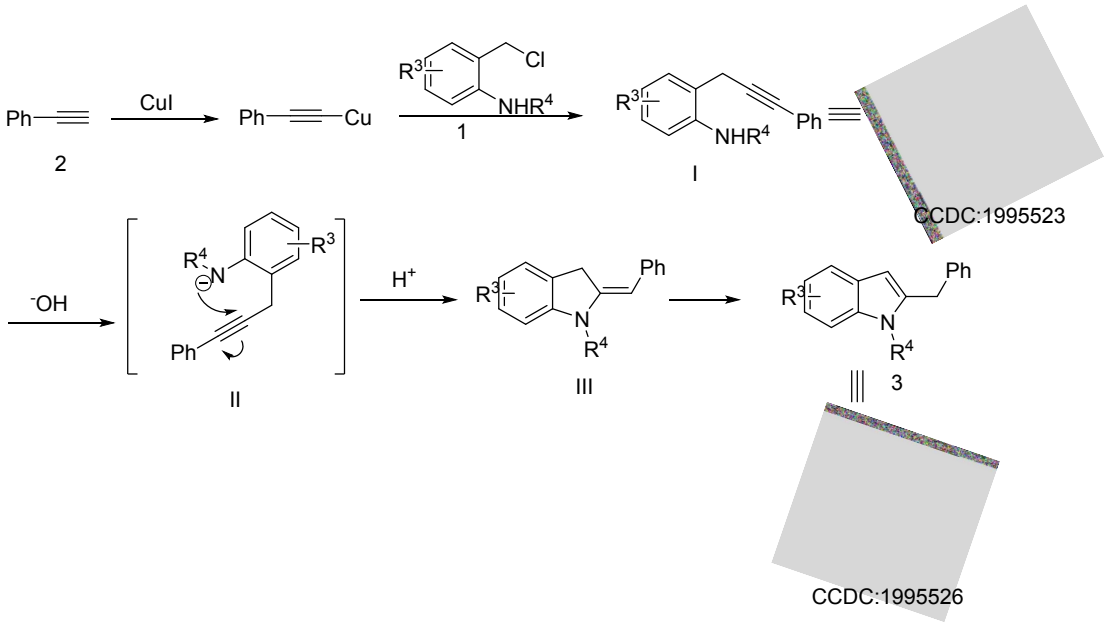




7 X-Ray crystal data of 3a and the intermediate 2a



8 A Plausible Reaction Mechanism


Ph
2
CuI
Ph
Cu
R3
Cl
NHR4
1
R3
NHR4
Ph
I
CCDC:1995523
-OH
R4
N
R3
Ph
II
H+
R3
Ph
N
R4
III
R3
Ph
N
R4
3
CCDC:1995526