Supporting Information

Rhodium(III)-Catalyzed C−H Allylation of Indoles with Allyl Alcohols via *β*-Hydroxide Elimination

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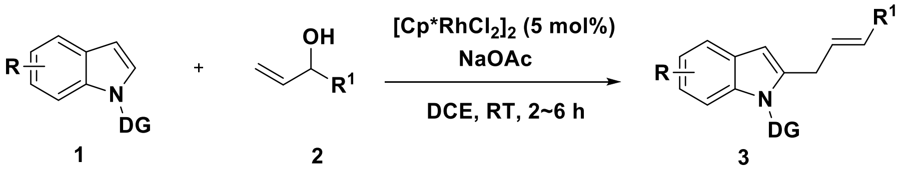
(A) General Information

The reagents (chemicals) were purchased from commercial sources and used without further purification. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15-0.2 mm thickness). All products were characterized by their NMR and MS spectra. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane (TMS). Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd) and broad (br). High-resolution mass spectra (HRMS) were measured on Micromass Ultra Q-TOF spectrometer. All *N*-carbamoylindoles **1** were prepared by following the procedure as described in the literature.[1] Allyl alcohols **2a**,[2] **2b**,[2] **2c**,[3] **2d**,[2] **2e**,[2] **2f**,[2] **2g**,[4] **2h**,[5] **2i**,[6] and **2j**[7] were prepared by following the procedure as described in the literature. **2k**, **2l**, **2n**, **2o**, and **2p** are commercial materials.

(B) General Procedures

General Procedure for C-H activation:



To a dry tube was equipped with *N*-ethoxy-indole-1-carboxamides **1** (0.2 mmol, 1 equiv), allylic alcohols **2** (0.3 mmol, 1.5 equiv), [Cp*RhCl$_2$]$_2$ (0.01 mmol, 0.05 equiv), NaOAc (0.12 mmol, 0.6 equiv) and 2 mL 1,2-dichloroethane. The resulting mixture was stirred at room temperature for 2~6 h under Ar atmosphere. Then, the solution was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na$_2$SO$_4$, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 6/1 ~ 4/1, v/v) to give desired products **3**.

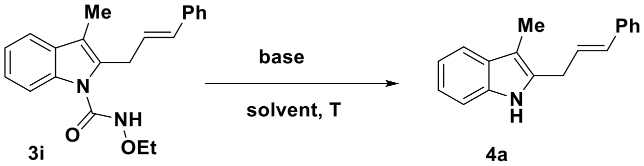
(C) The Gram-scale Preparation of 3i

With Cp*Rh^{III} catalyst: To a dry round bottom flask was equipped with *N*-ethoxy-indole-1-carboxamides **1i** (1.0 g, 4.58 mmol, 1 equiv), allylic alcohols **2a** (922 mg, 6.87 mmol, 1.5 equiv), $[Cp^*RhCl_2]_2$ (85.0 mg, 0.13 mmol, 0.03 equiv), NaOAc (225.5 mg, 2.75 mmol, 0.6 equiv) and 40 mL 1,2-dichloroethane. The resulting mixture was stirred at room temperature for 6 h under Ar atmosphere. Then, the solution was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 6/1 ~ 4/1, v/v) to give the desired product **3i** (1.13 g, 74% yield).

With Ru^{II} catalyst: To a dry round bottom flask was equipped with *N*-ethoxy-indole-1-carboxamides **1i** (1.0 g, 4.58 mmol, 1 equiv), allylic alcohols **2a** (922 mg, 6.87 mmol, 1.5 equiv), $[\{RuCl_2(p\text{-cymene})\}_2]$ (140.3 mg, 0.23 mmol, 0.05 equiv), NaOAc (375.9 mg, 4.58 mmol, 1 equiv) and 40 mL 1,2-dichloroethane. The resulting mixture was stirred at 45 °C for 6 h under Ar atmosphere. Then, the solution was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 6/1 ~ 4/1, v/v) to give the desired product **3i** (597.0 mg, 39% yield).

Removal of the Directing Group:

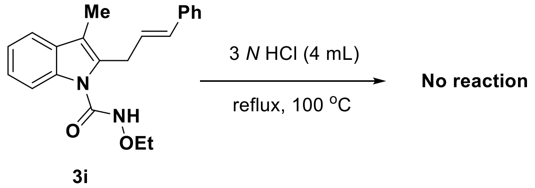
The optimization of reaction conditions for removal of the directing group[a]



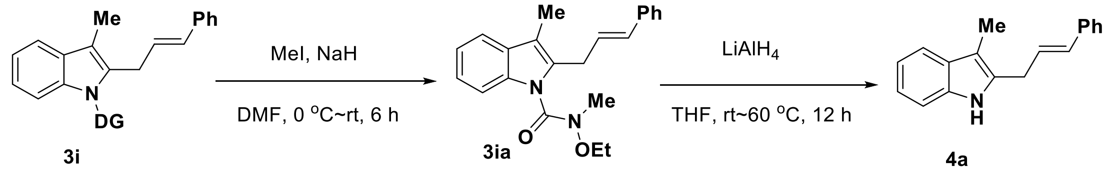
entry	solvent	base	T (°C)	**4a** Yield (%)
1	THF/H_2O = 3/1 (v/v)	LiOH (4.0 equiv)	60	NR
2	THF/H_2O = 3/1 (v/v)	NaOH (4.0 equiv)	60	NR
3	THF/H_2O = 3/1 (v/v)	KOH (4.0 equiv)	60	NR
4	THF/H_2O = 3/1 (v/v)	KOH (4.0 equiv)	80	NR
5	THF/H_2O = 3/1 (v/v)	KOH (4.0 equiv)	100	NR
6	THF	*t*-BuOK (2.0 equiv)	rt	0
7	THF	*t*-BuONa (2.0 equiv)	rt	NR
8	EtOH	KOH (4.0 equiv)	100	NR
9	*n*-propanol/H_2O = 1/2 (v/v)	KOH (4.0 equiv)	100	NR

[a] Reaction conditions: **3a** (0.2 mmol, 1 equiv), base, in 4 mL solvent, Ar atmosphere.

Condition 10



Condition 11

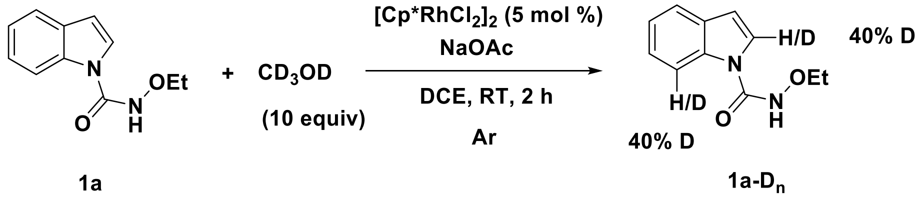


a) To a solution of **3i** (0.52 g, 1.55 mmol, 1 equiv) in dry DMF (20 mL) was added NaH (74.6 mg, 60%, dispersion in mineral oil, 1.2 equiv) portionwise at 0 °C. The resulting mixture was stirred for 30 mins at room temperature, and then MeI (441.0 mg, 2 equiv) was added into the solution. The reaction was stirred for 6 hours at room temperature. Then, the reaction was quenched with saturated NH_4Cl solution. The solution was diluted with EtOAc and washed by brine. The combined organic layers were dried with Na_2SO_4, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 15/1 ~ 10/1, v/v) to give the desired product **3ia** (498.0 mg, 92% yield). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.53 – 7.46 (m, 1H), 7.38 – 7.34 (m, 1H), 7.31 – 7.26 (m, 3H), 7.26 – 7.16 (m, 4H), 6.44 (d, *J* = 15.8 Hz, 1H), 6.25 (dt, *J* = 15.8, 6.5 Hz, 1H), 3.96 – 3.70 (m, 4H), 3.19 (s, 3H), 2.29 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR (126 MHz, CDCl$_3$)** δ 153.89, 137.30, 135.42, 134.10, 131.54, 130.00, 128.64, 127.36, 127.08, 126.18, 123.02, 121.31, 118.72, 113.24, 111.95, 69.69, 37.64, 28.55, 13.70, 8.81 ppm. **HRMS (ESI) m/z:** calculated for $C_{22}H_{25}N_2O_2^+$ $[M + H]^+$: 349.1916, found: 349.1909.

b) To a solution of **3ia** (50.0 mg, 0.14 mmol, 1 equiv) in anhydrous THF (5 mL) was added $LiAlH_4$ (27.2 mg, 5 equiv) portionwise at room temperature. The resulting mixture was stirred for 30 mins, and then the reaction was heated to 60 °C for 12 hours under Ar atmosphere. The reaction was quenched with saturated NH_4Cl solution. The solution was diluted with EtOAc and washed by brine. The combined organic layers were dried with Na_2SO_4, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 15/1 ~ 10/1, v/v) to give the product **4a** (21.0 mg, 59% yield). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.75 (s, 1H), 7.55 – 7.48 (m, 1H), 7.38 – 7.33 (m, 2H), 7.33 – 7.27 (m, 2H), 7.27 – 7.19 (m, 2H), 7.17 – 7.06 (m, 2H), 6.51 (d, *J* = 15.8 Hz, 1H), 6.33 (dt, *J* = 15.8, 6.6 Hz, 1H), 3.65 (dd, *J* = 6.6, 1.2 Hz, 2H), 2.28 (s, 3H) ppm. **^{13}C NMR (126 MHz, CDCl$_3$)** δ 137.12, 135.49, 132.21, 132.07, 129.54, 128.76, 127.60, 126.68, 126.32, 121.42, 119.24, 118.40, 110.45, 107.69, 29.94, 8.61 ppm. **HRMS (ESI) m/z:** calculated for $C_{18}H_{18}N^+$ $[M + H]^+$: 248.1439, found: 248.1430.

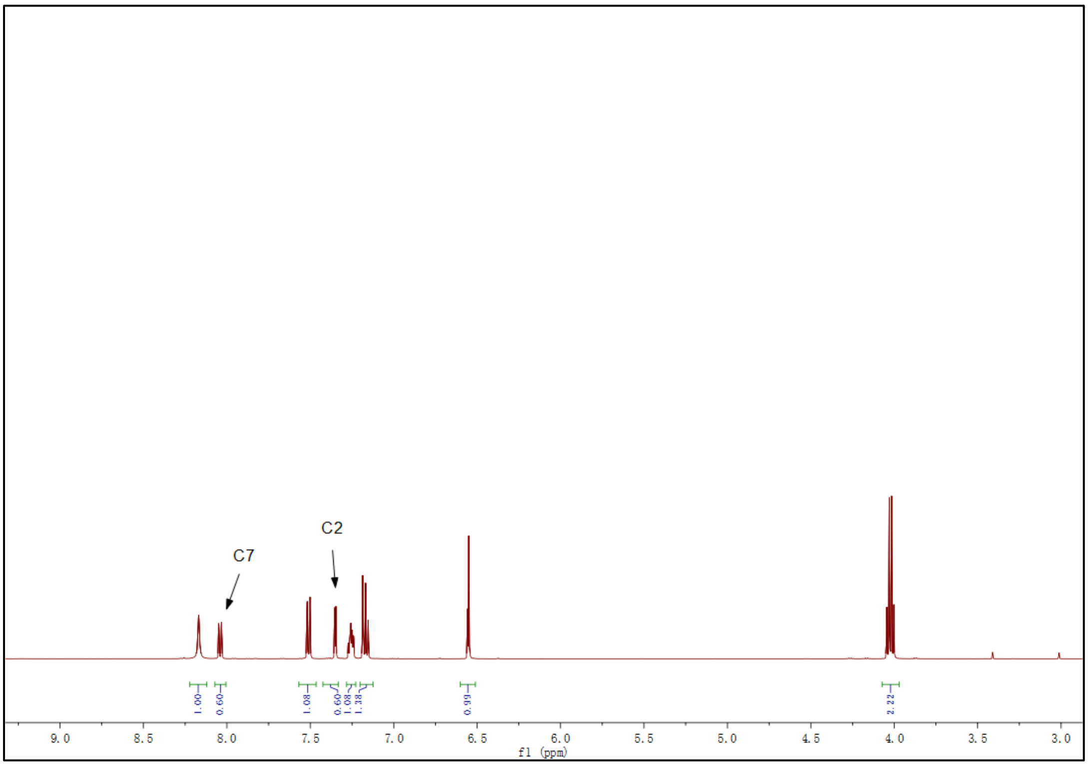
(D) MECHANISTIC EXPERIMENTS

Deuterium Incorporation Experiment A:

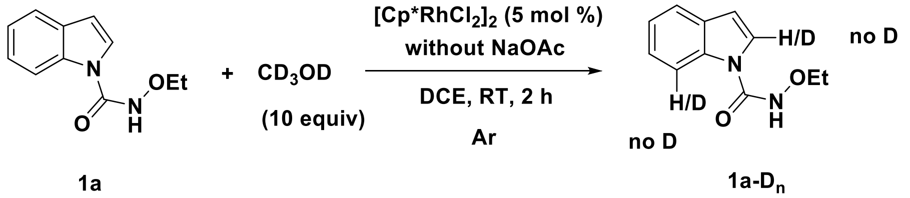


To a dry tube was equipped with *N*-ethoxy-1H-indole-1-carboxamide (**1a**, 0.2 mmol), 5 mol% $[Cp^*RhCl_2]_2$, and NaOAc (0.12 mmol, 0.6 equiv), followed by adding DCE (2 mL) and CD_3OD (2 mmol, 10 equiv). The mixture was stirred at room temperature for 2 h under Ar atmosphere. The resulting mixture was directly concentrated and purified by column chromatography on silica gel to give the product. *Found H/D exchange occurred at the C2-position of the indole (40% D) and the C7-position of the indole (40% D)*.

^{1}H NMR of the product **1a-D$_n$** of the reaction

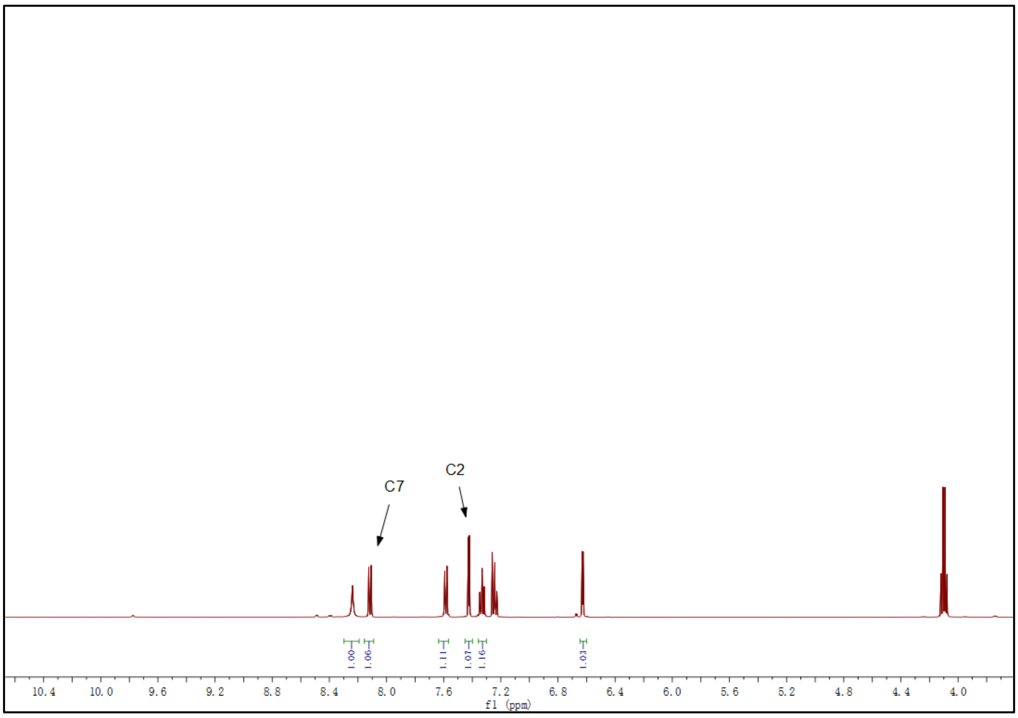


Deuterium Incorporation Experiment B:

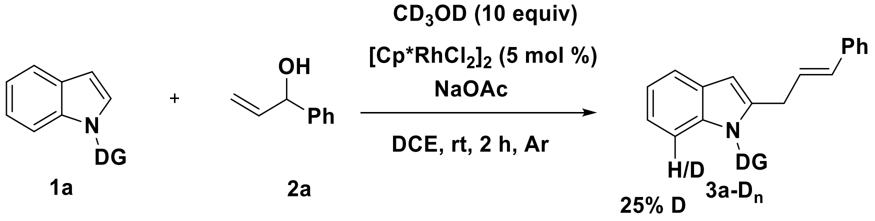


To a reaction tube was added *N*-ethoxy-1H-indole-1-carboxamide (**1a**, 0.2 mmol), 5 mol% $[Cp^*RhCl_2]_2$, and dry DCE (2 mL). Then, CD_3OD (2 mmol, 10 equiv) was added and the mixture was stirred at room temperature for 2 h under Ar atmosphere. The resulting mixture was directly concentrated and purified by column chromatography on silica gel to give the crude product. *No obvious H/D exchange was detected at the C2-position and the C7-position of the indole.*

^{1}H NMR of the product **1a-D_n** of this reaction.

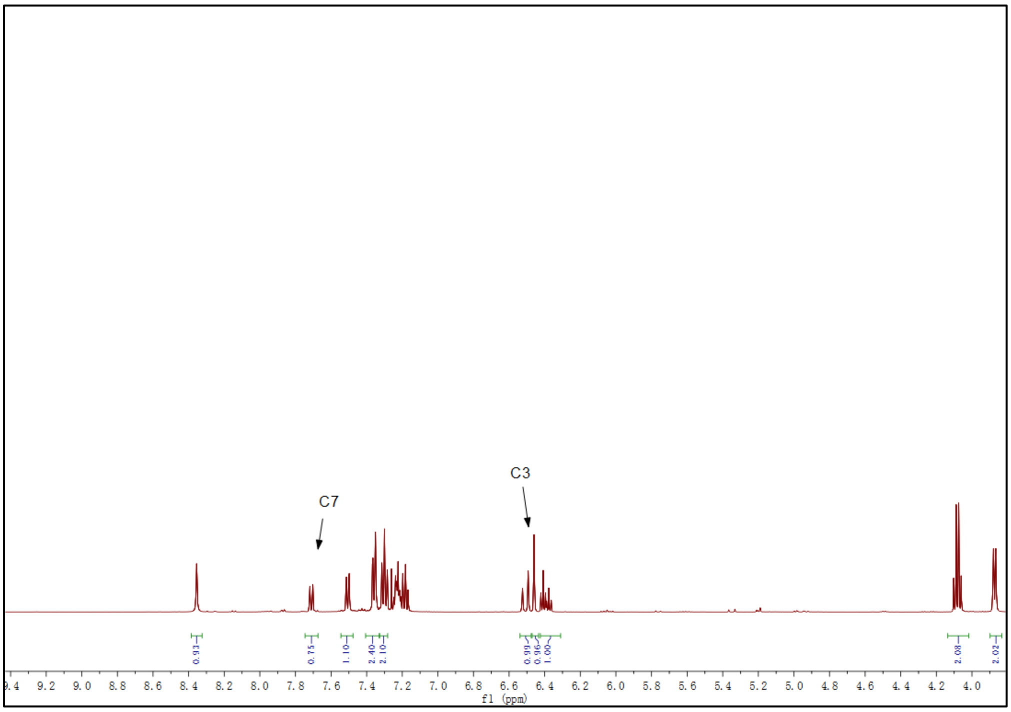


Deuterium Incorporation Experiment C:

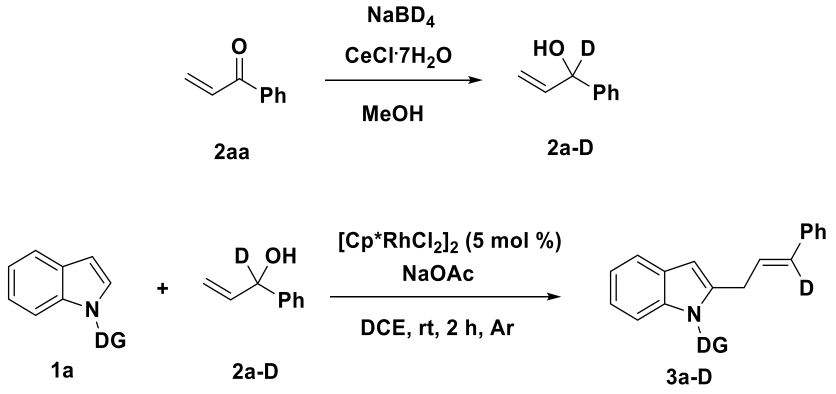


To a dry tube was equipped with *N*-ethoxy-1H-indole-1-carboxamide (**1a**, 0.2 mmol), **2a** (0.3 mmol, 1.5 equiv), 5 mol% $[Cp^*RhCl_2]_2$ and NaOAc (0.12 mmol, 0.6 equiv), followed by adding DCE (2 mL) and CD_3OD (2 mmol, 10 equiv). The reaction tube was stirred at room temperature for 2 h under Ar atmosphere. The resulting mixture was directly concentrated and purified by column chromatography on silica gel to give the crude product. *Found H/D exchange occurred at the C7-position of the indole (25% D)*.

^{1}H NMR of the product **$3a\text{-}D_n$**



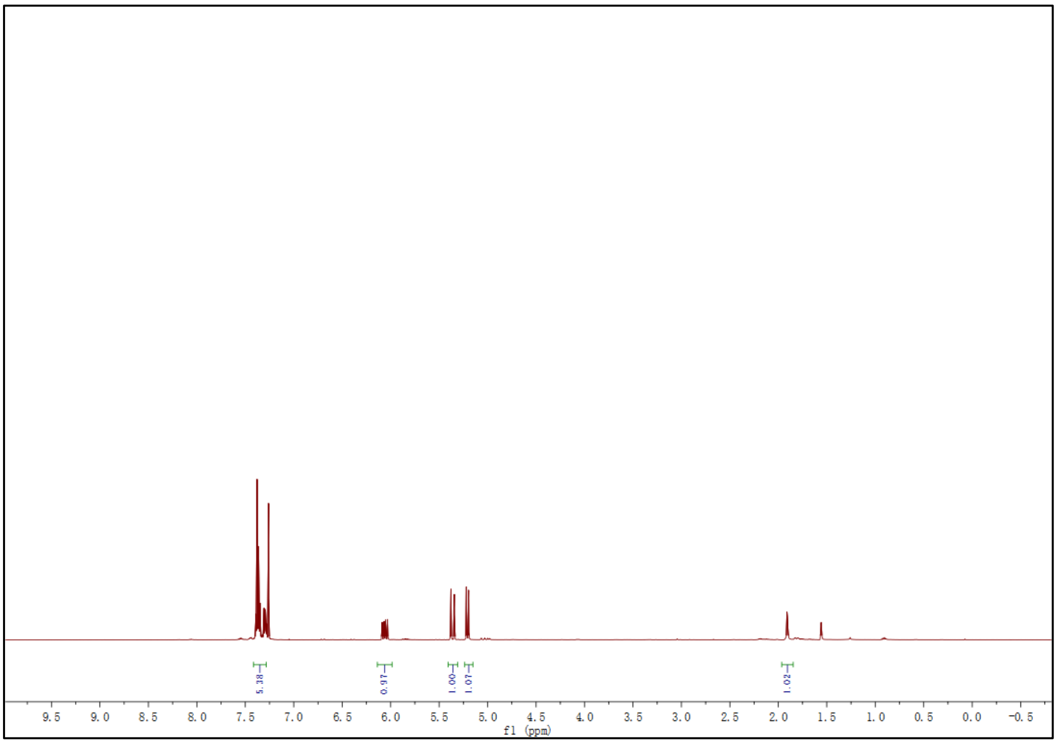
Deuterium Incorporation Experiment D:



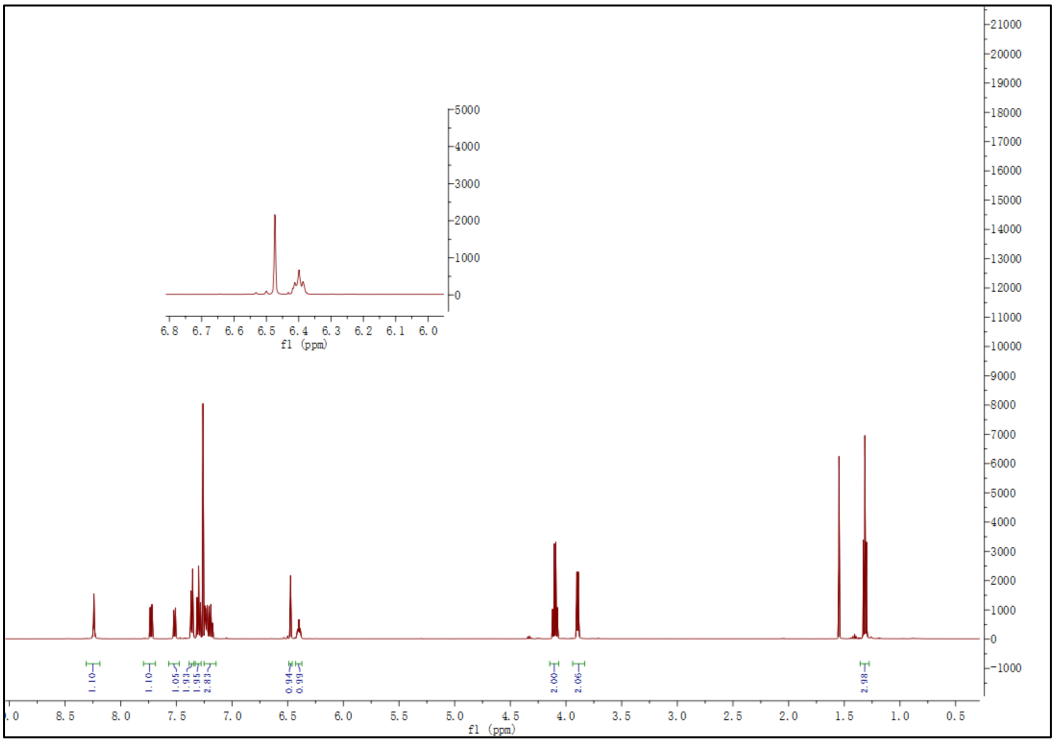
Synthesis of compound **2a-D**.[8] To a solution of **2aa** (150.0 mg, 1.13 mmol, 1 equiv) in methanol was added $CeCl\cdot 7H_2O$ (1.13 mmol, 1 equiv). The resulting mixture was cooled to 0 °C and then $NaBD_4$ (42.9 mg, 1 equiv) was added portionwise. The mixture was stirred for 1 h and then saturated NH_4Cl aqueous solution was added. The resulting mixture was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na_2SO_4, concentrated and purified by column chromatography on silica gel to give the product **2a-D** (92.0 mg, 60% yield). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.42 – 7.28 (m, 5H), 6.14 – 5.99 (m, 1H), 5.36 (dd, J = 17.1, 1.4 Hz, 1H), 5.21 (dd, J = 10.3, 1.4 Hz, 1H), 1.91 (s, 1H).

To a dry tube was equipped with *N*-ethoxy-1H-indole-1-carboxamide (**1a**, 41.0 mg, 0.2 mmol), **2a-D** (0.3 mmol, 1.5 equiv), 5 mol % $[Cp^*RhCl_2]_2$ and NaOAc (0.12 mmol, 0.6 equiv), followed by adding DCE (2 mL) and CD_3OD (2 mmol, 10 equiv). The reaction tube was stirred at room temperature for 2 h under Ar atmosphere. The resulting mixture was directly concentrated and purified by column chromatography on silica gel to give the corresponding product **3a-D** (48.0 mg, 75% yield). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.24 (br, 1H), 7.73 (dd, J = 8.2, 0.6 Hz, 1H), 7.52 (d, J = 7.5 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.32 – 7.27 (m, 2H), 7.25 – 7.17 (m, 3H), 6.47 (d, J = 0.7 Hz, 1H), 6.40 (t, J = 6.3 Hz, 1H), 4.10 (q, J = 7.0 Hz, 2H), 3.90 (d, J = 6.6 Hz, 2H), 1.32 (t, J = 7.0 Hz, 3H) ppm.

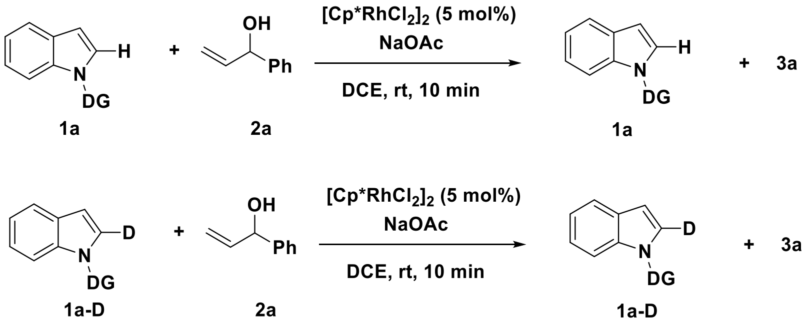
^{1}H NMR of **2a-D**



^{1}H NMR of the product **3a-D**



Determination of the Kinetic Isotope Effect (KIE):

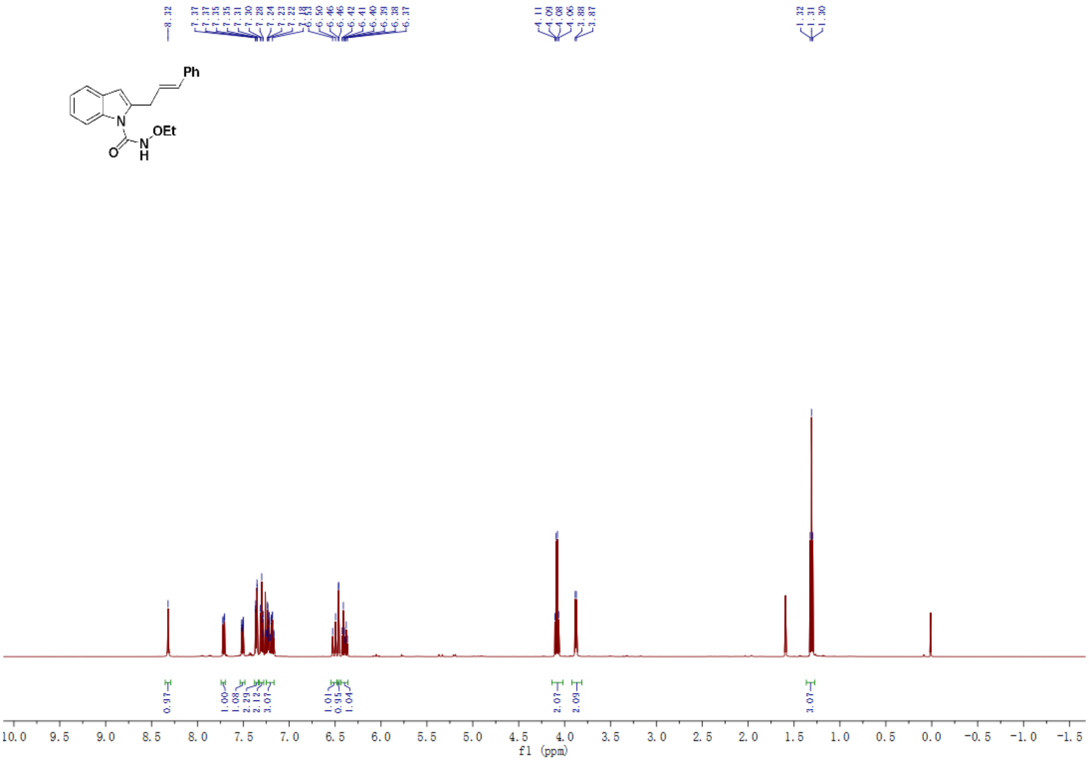


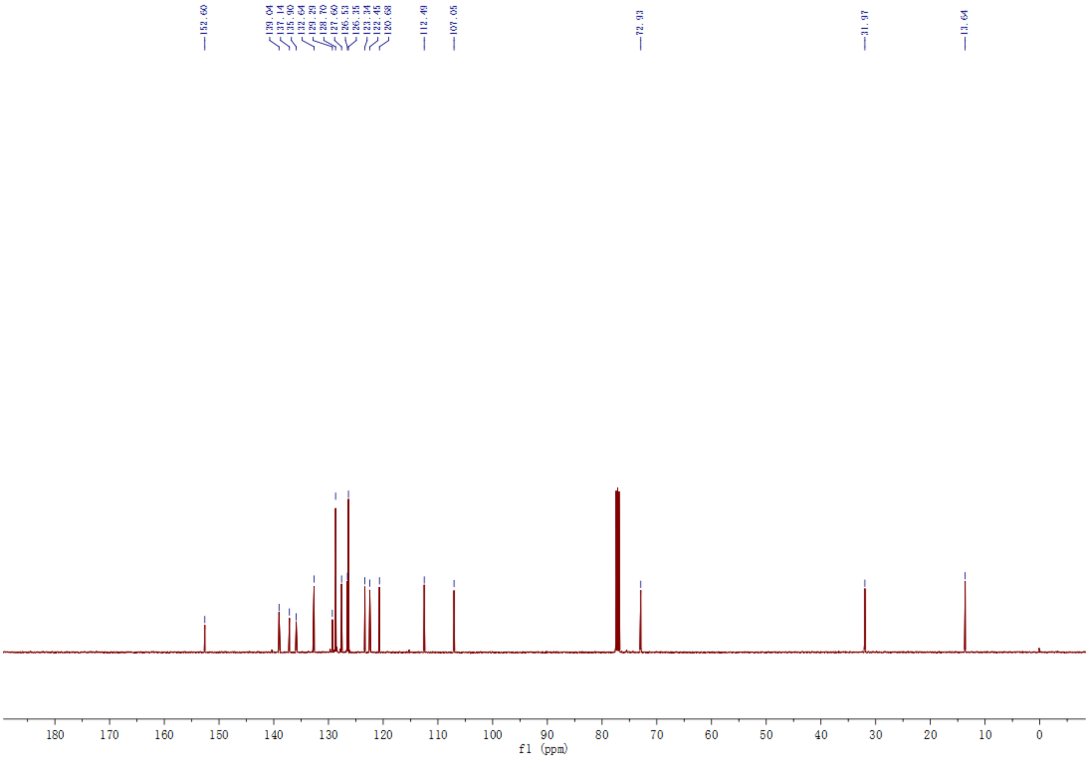
1a (21.0 mg, 0.1 mmol) was allowed to react with **2a** (21.0 mg, 0.15 mmol) in dry DCE (2 mL) in the presence of NaOAc (0.6 equiv) and 5 mol % [Cp*RhCl$_2$]$_2$. The mixture was stirred at room temperature under Ar atmosphere. The reaction was stopped after 10 min, and the crude mixture was purified using column chromatography on silica gel to give the corresponding product **3a** (18.0 mg, 28% yield).

1a-D (21.0 mg, 0.1 mmol, 95% D) was allowed to react with **2a** (21.0 mg, 0.15 mmol) in dry DCE (2 mL) in the presence of NaOAc (0.6 equiv) and 5 mol % [Cp*RhCl$_2$]$_2$. The mixture was stirred at room temperature under Ar atmosphere. The reaction was stopped after 10 min, and the crude mixture was purified using column chromatography on silica gel to give the corresponding product **3a** (22.5 mg, 35% yield). *A kinetic isotopic effect of these two reactions was thus determined to be* $k_H/k_D = 0.76$.

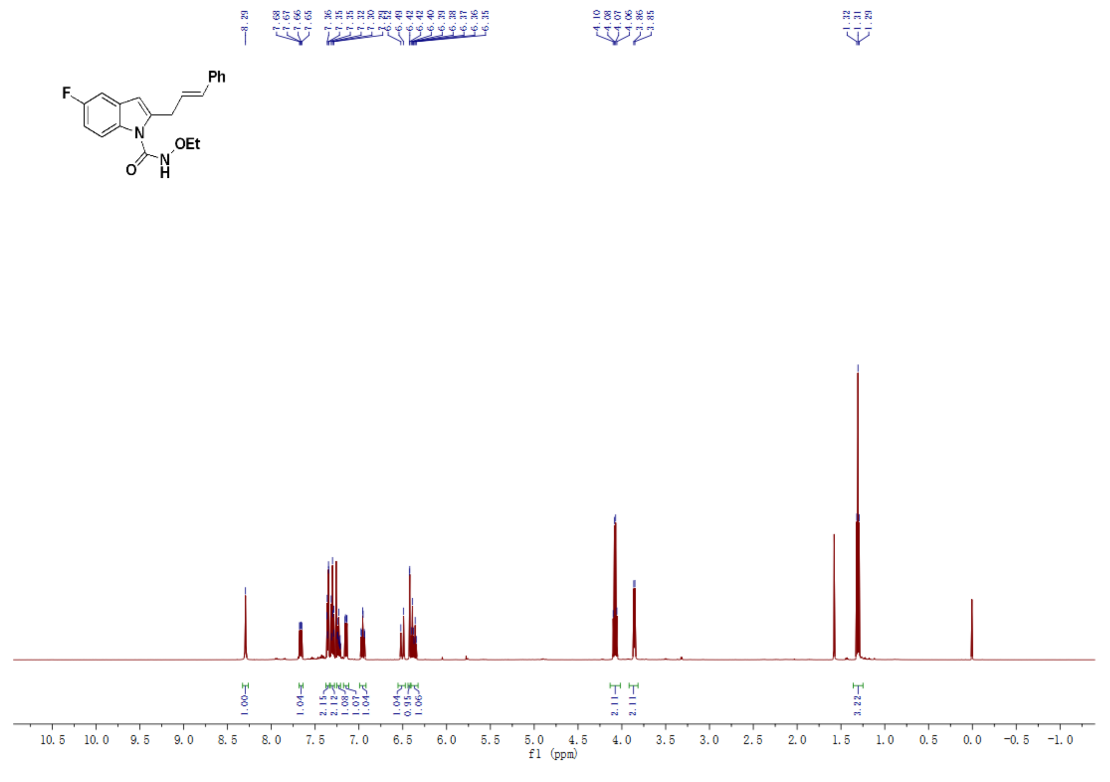
(E) Copies of NMR Spectra for the Products.

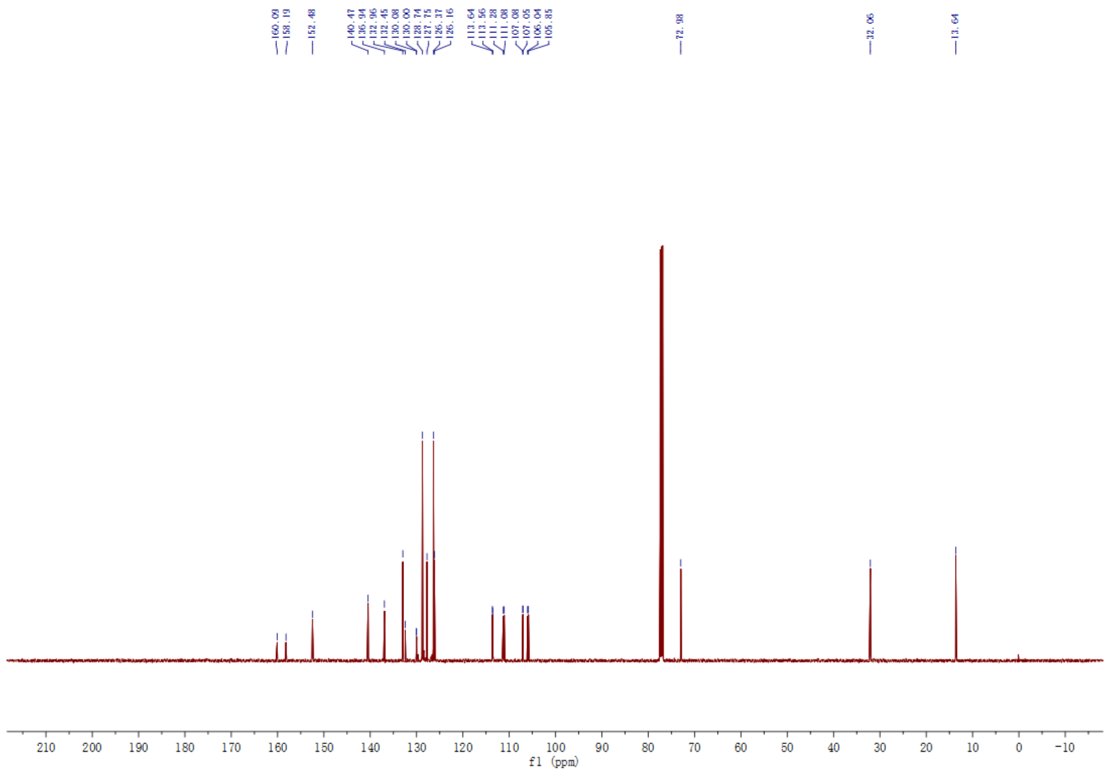
2-cinnamyl-N-ethoxy-1H-indole-1-carboxamide (3a)

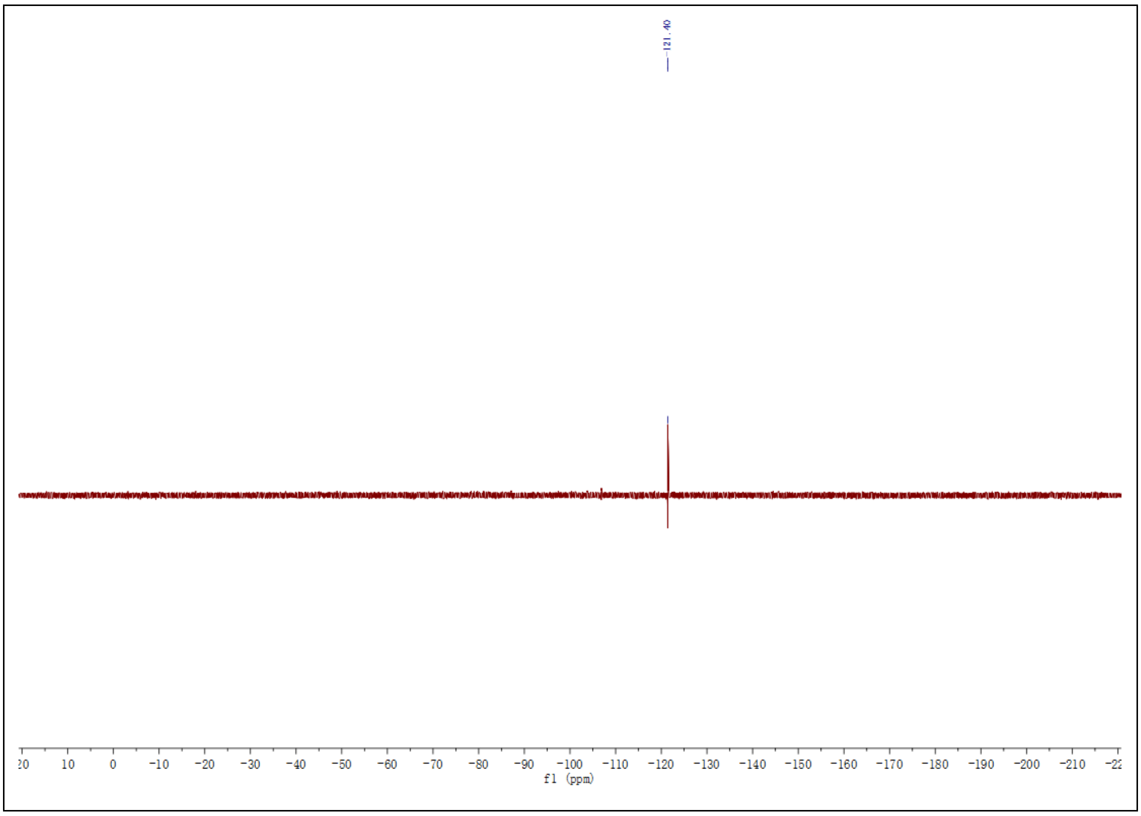




2-cinnamyl-N-ethoxy-5-fluoro-1H-indole-1-carboxamide (3b)



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-10
-20
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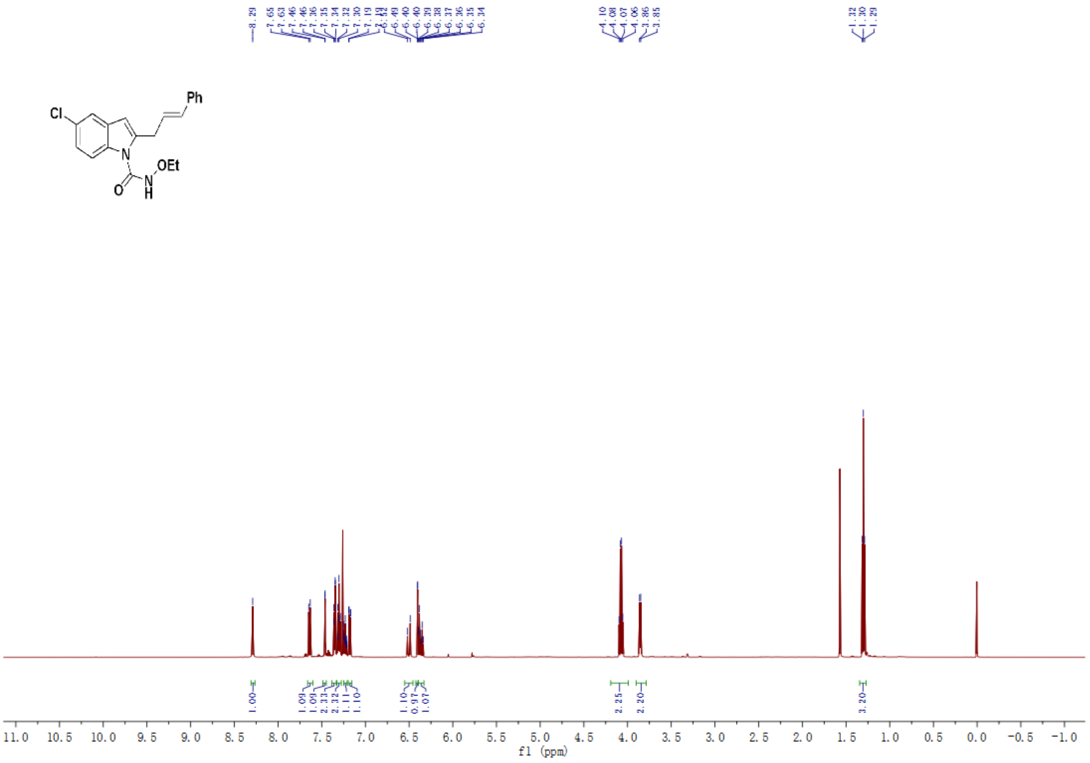
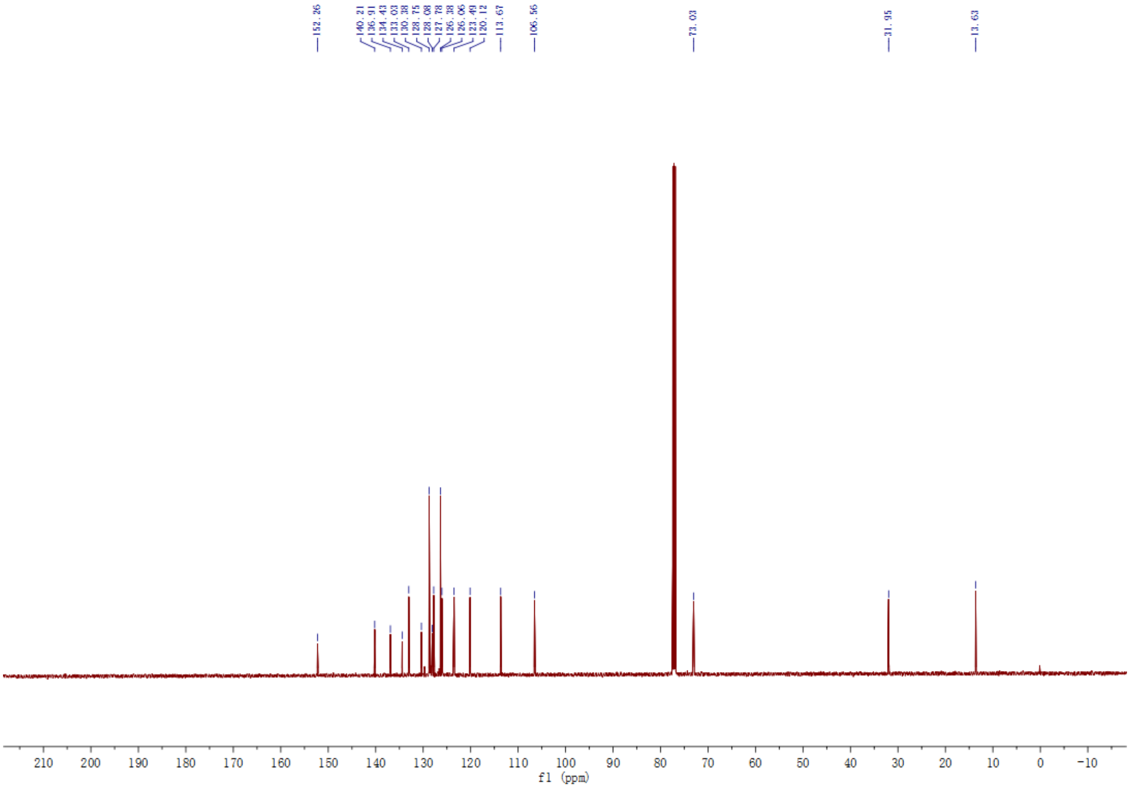
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

5-chloro-2-cinnamyl-N-ethoxy-1H-indole-1-carboxamide (3c)





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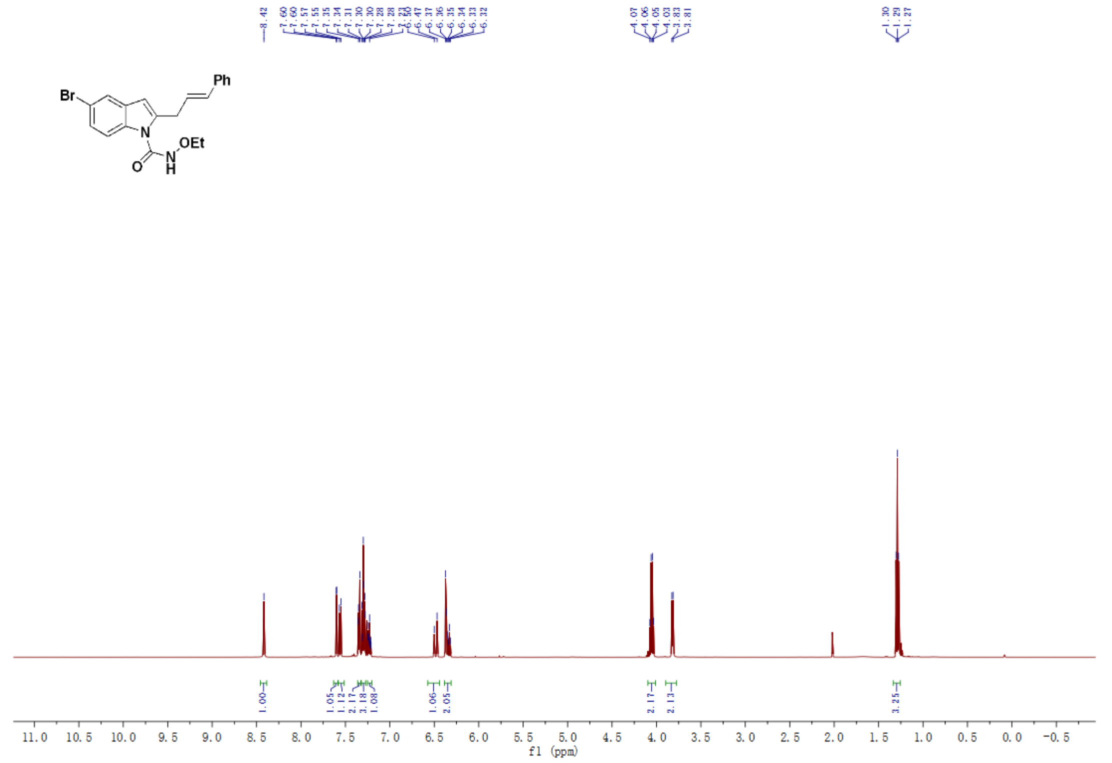

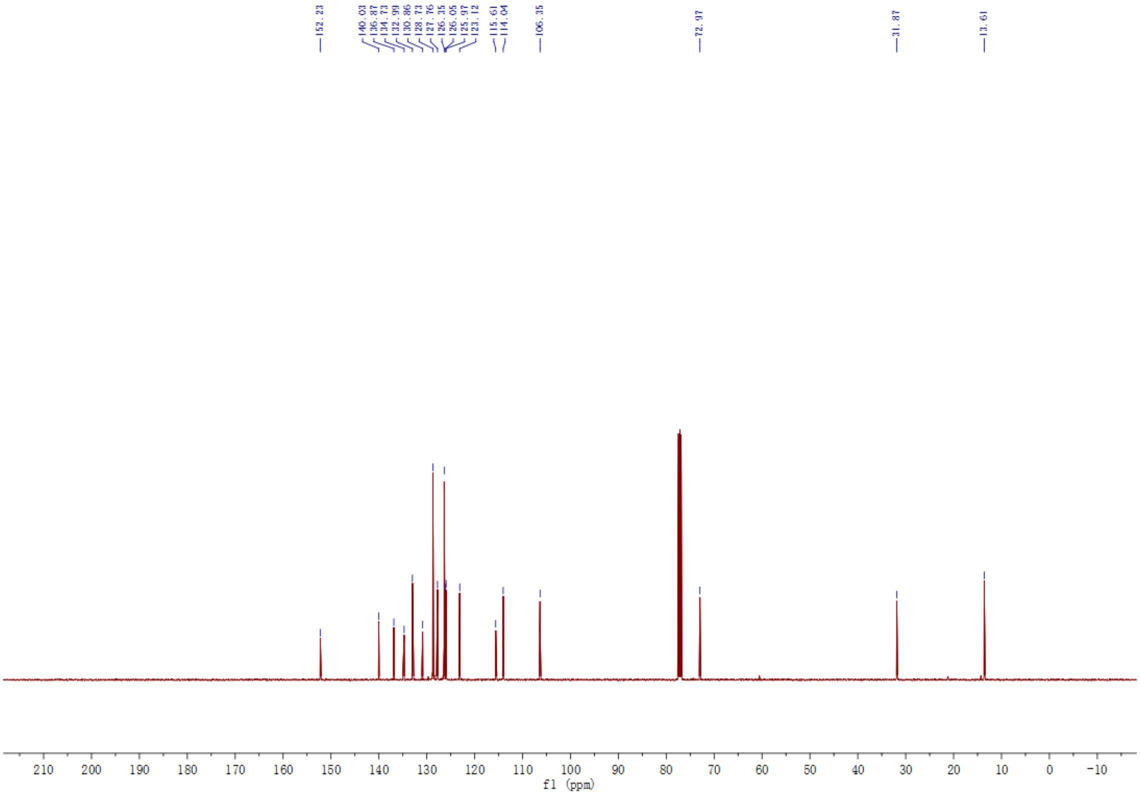

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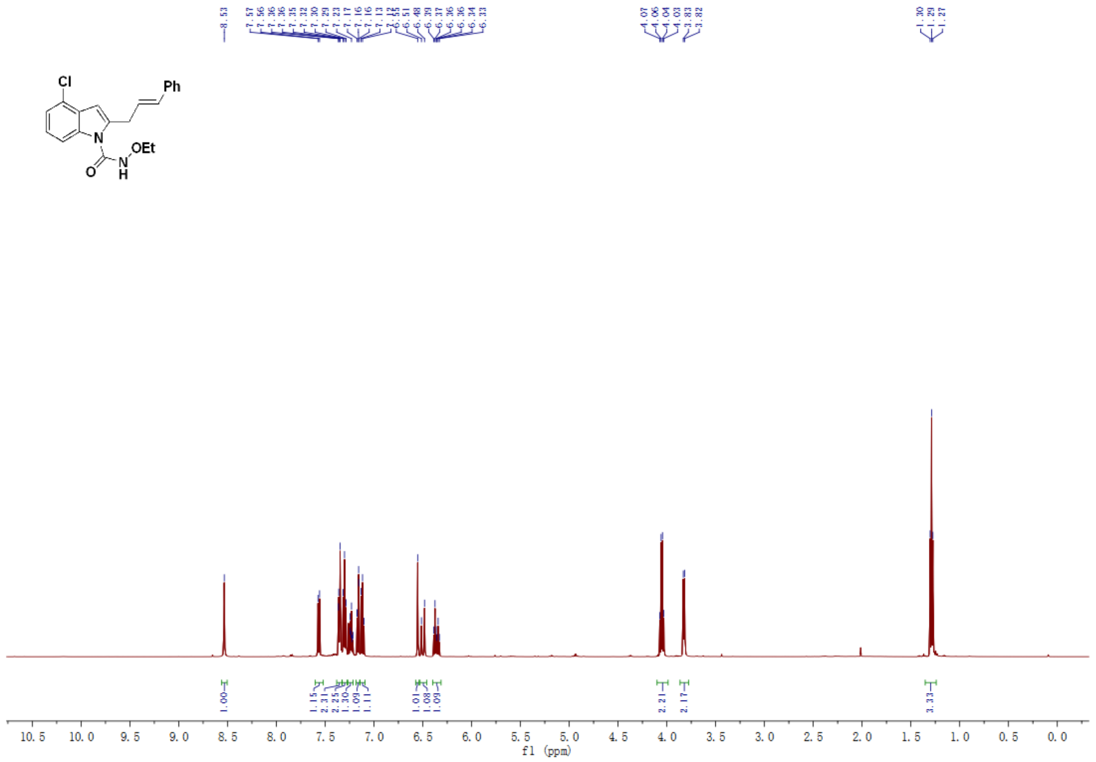
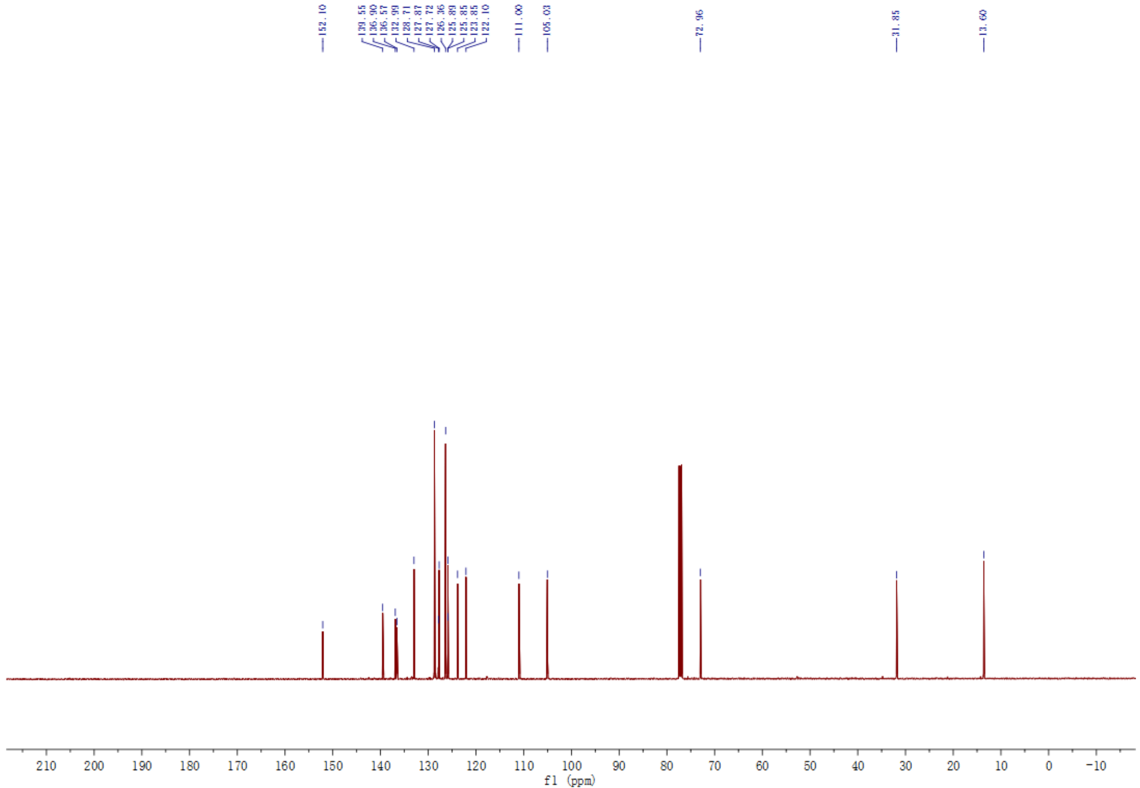
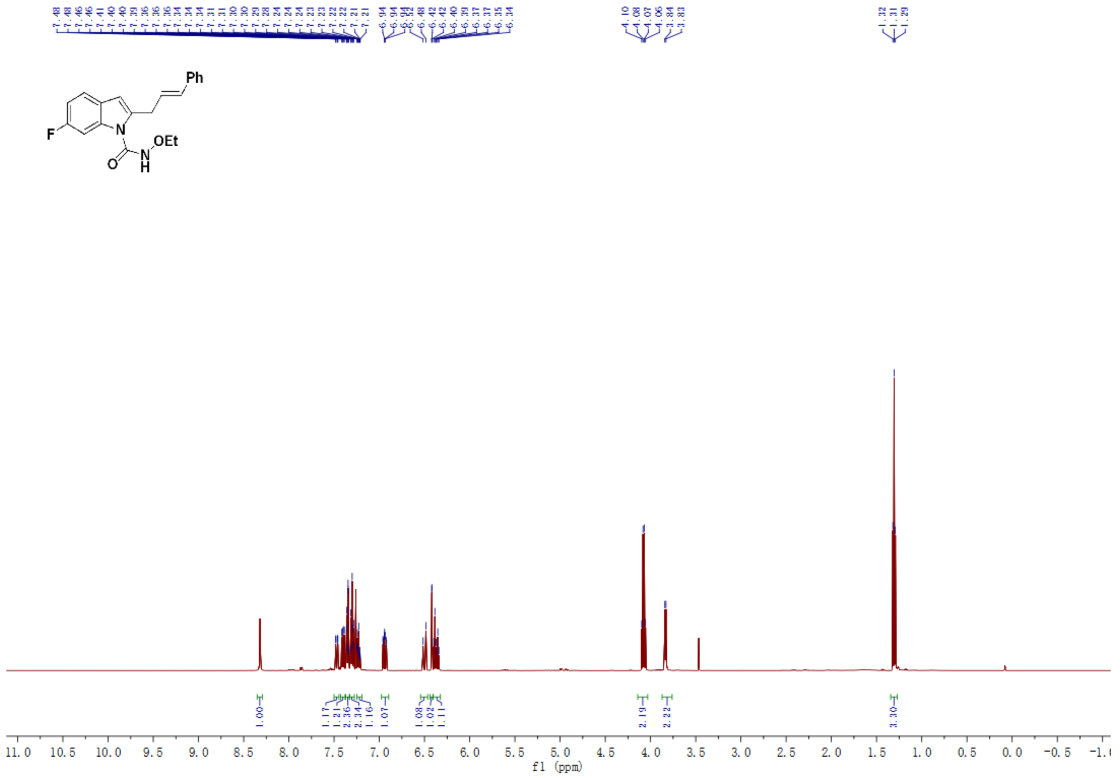
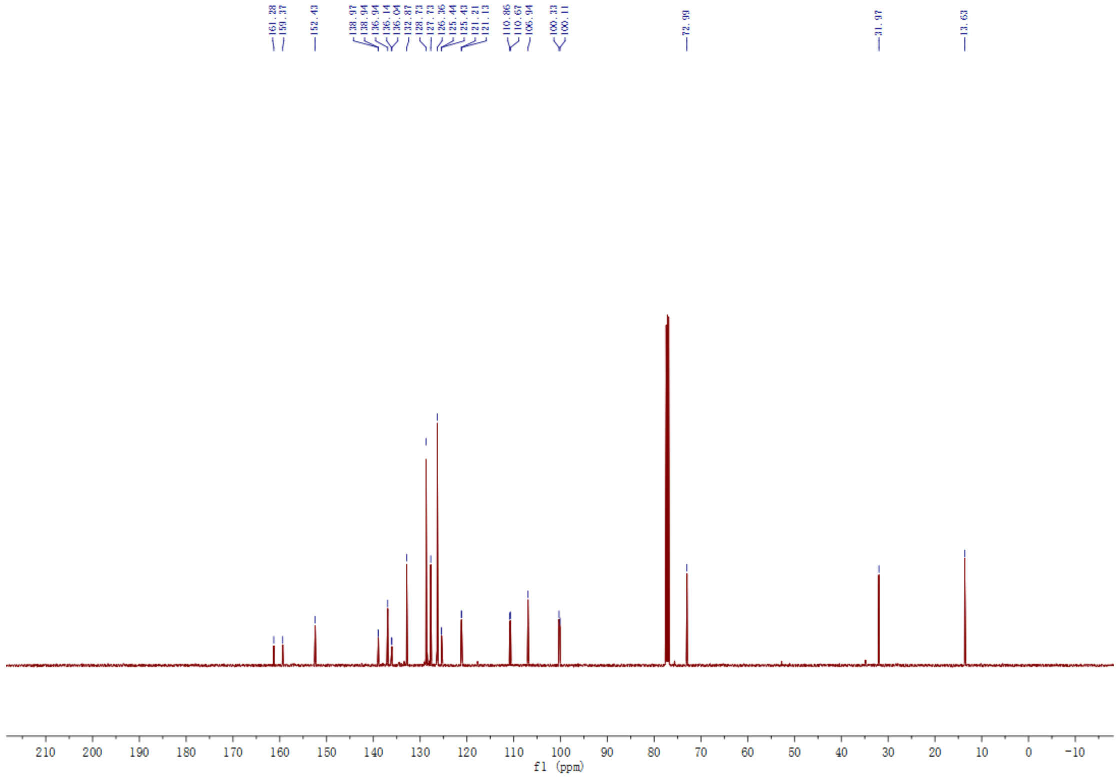
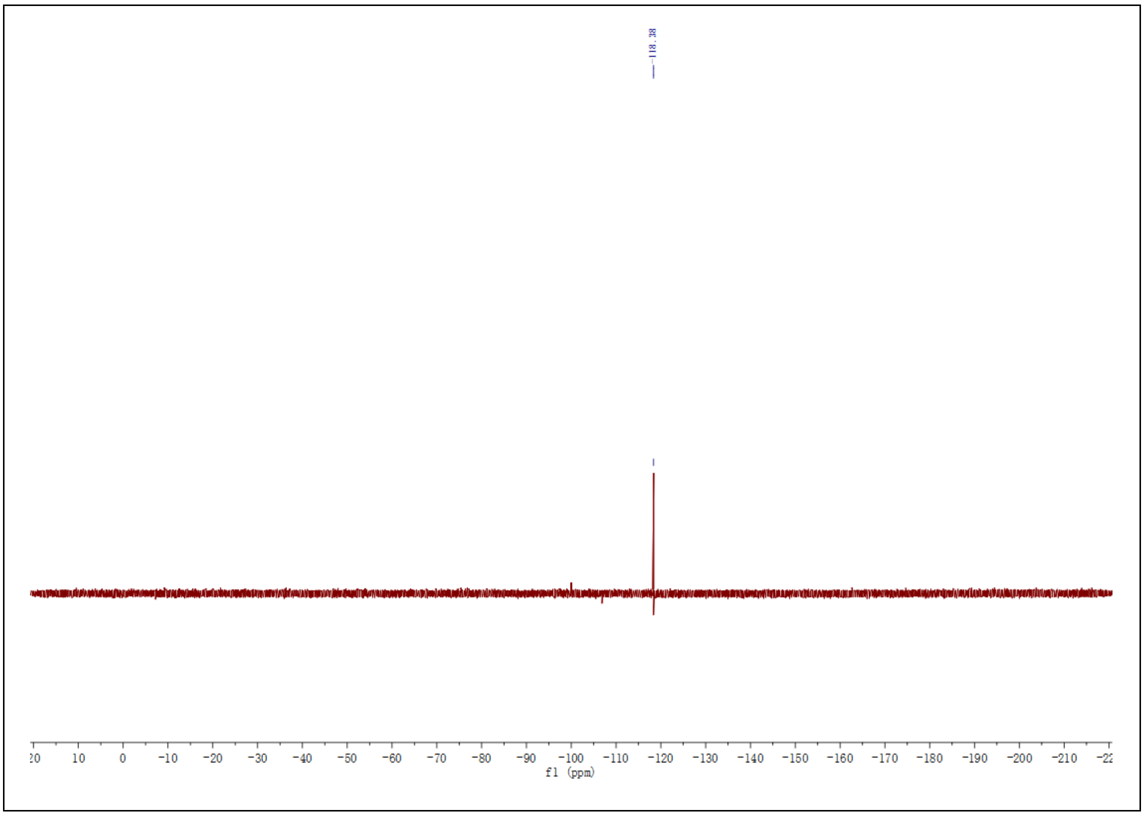




2-cinnamyl-N-ethoxy-6-fluoro-1H-indole-1-carboxamide (3f)



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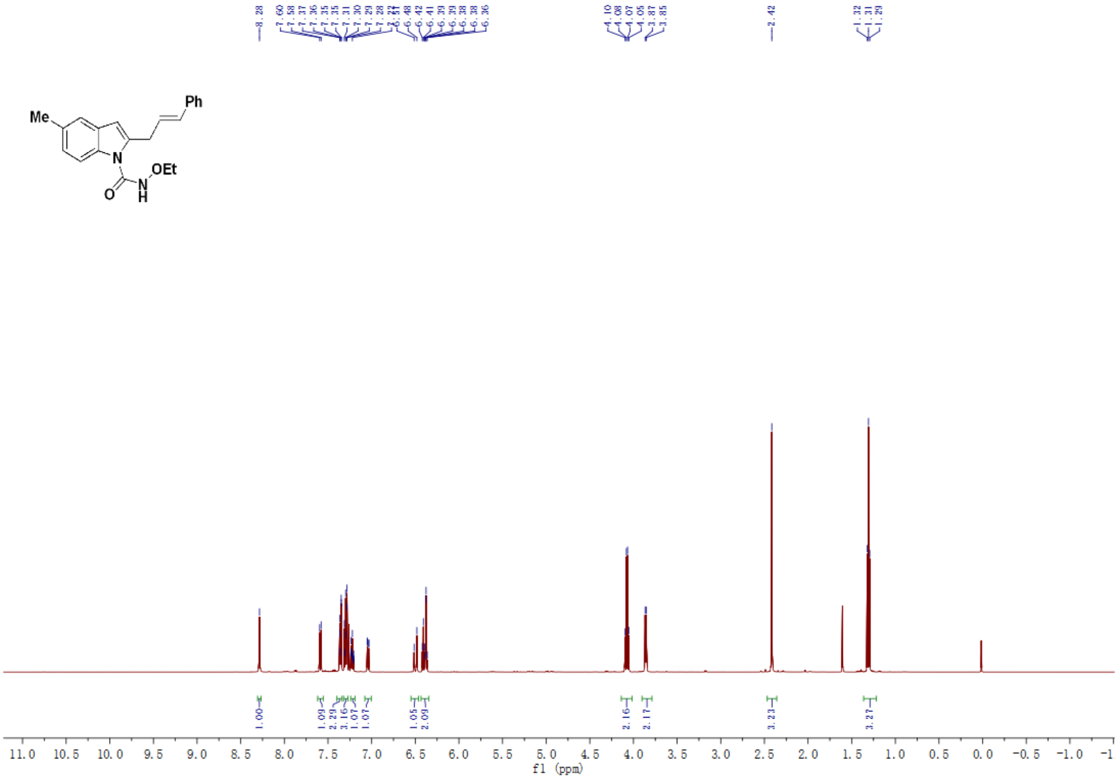
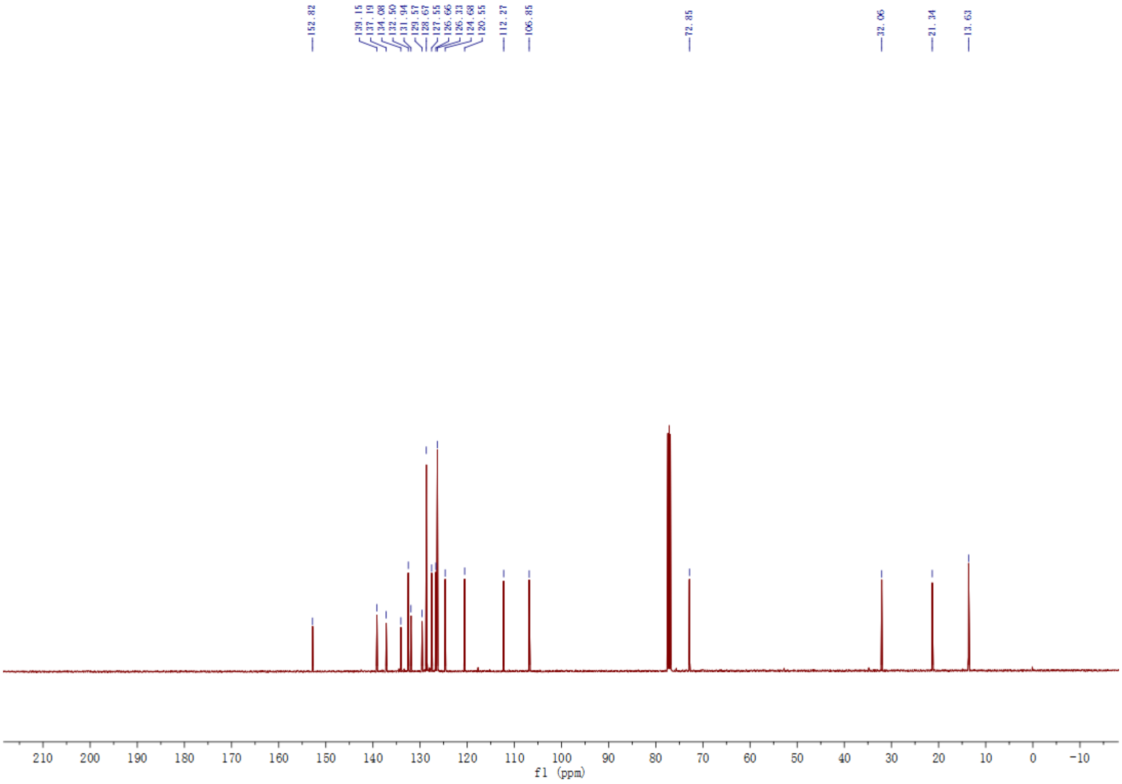
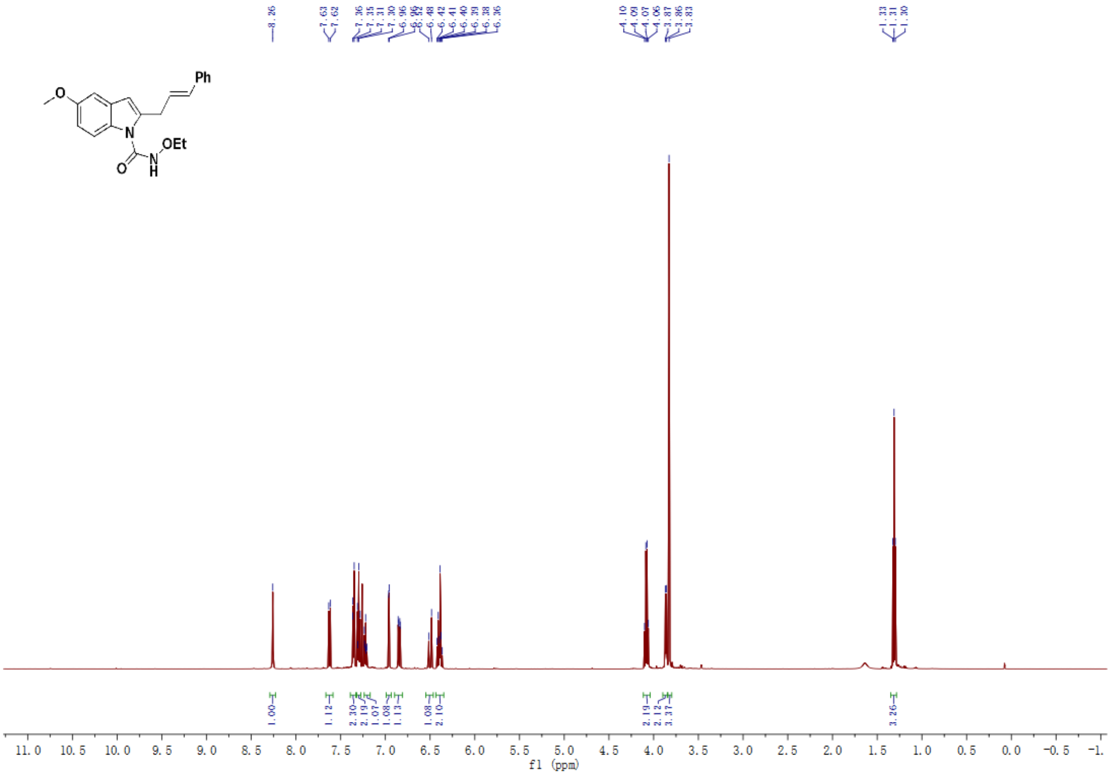
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-22
f1 (ppm)

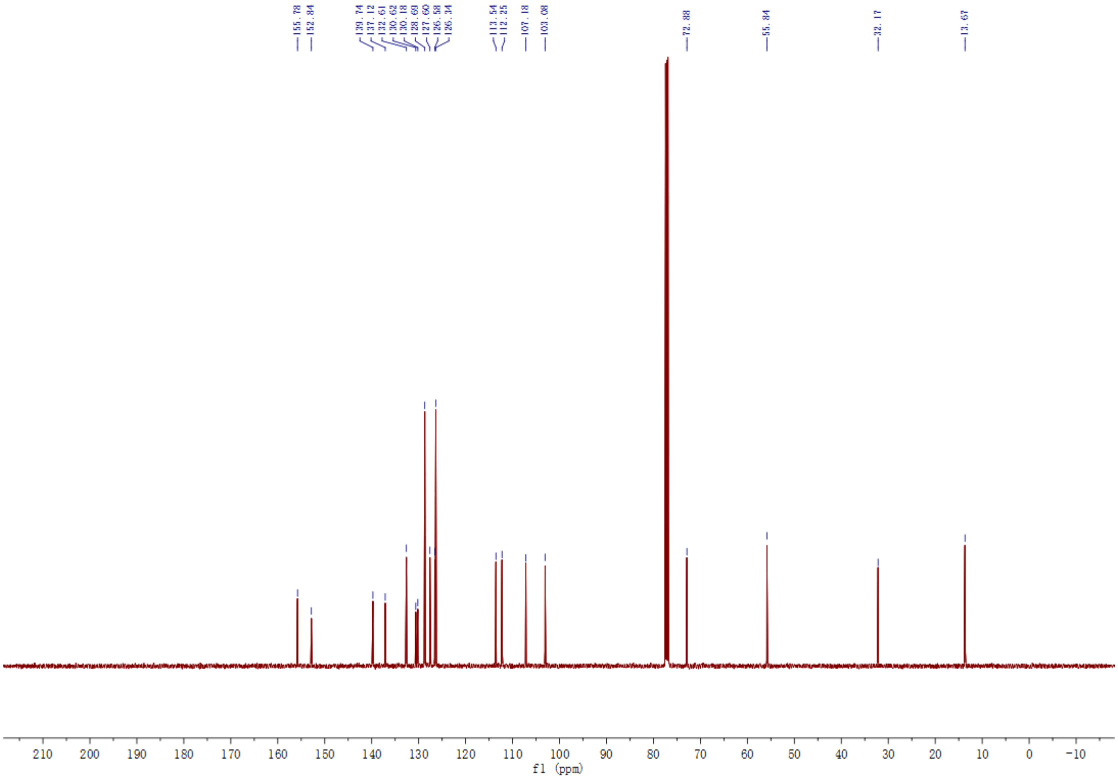
2-cinnamyl-N-ethoxy-5-methyl-1H-indole-1-carboxamide (3g)





2-cinnamyl-N-ethoxy-5-methoxy-1H-indole-1-carboxamide (3h)





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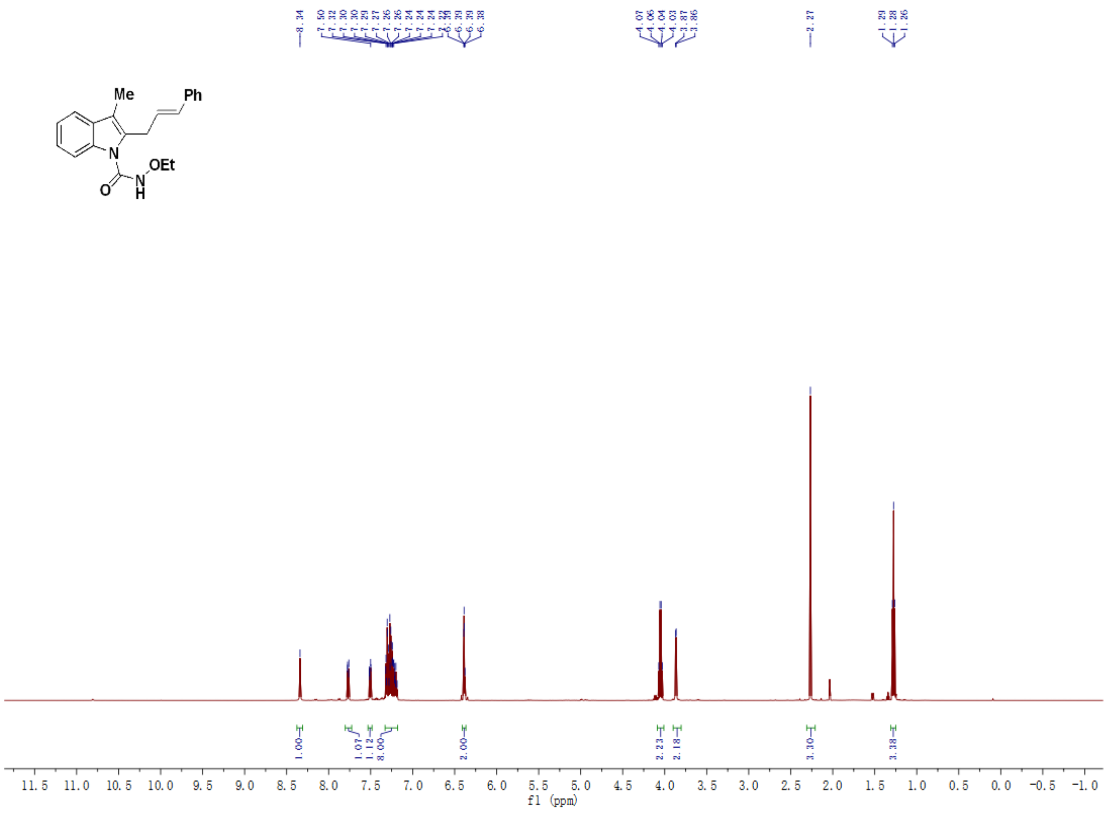
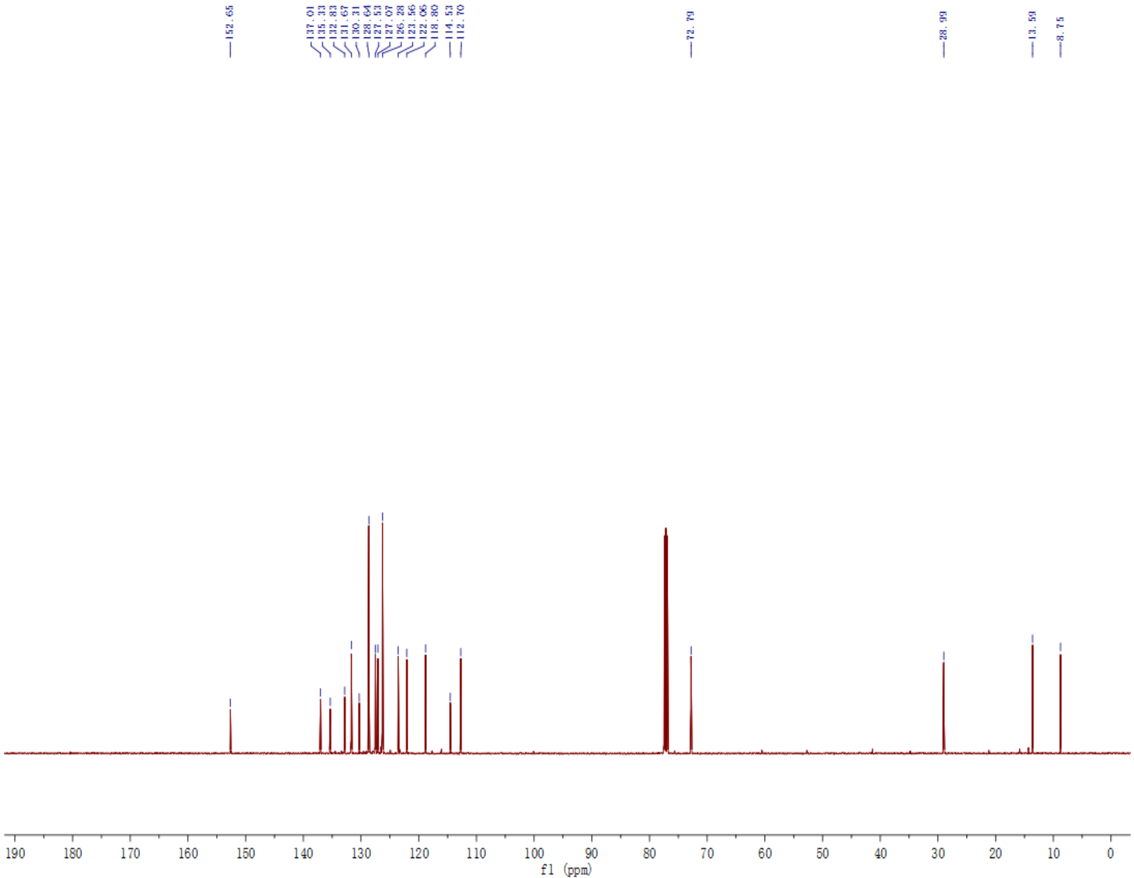
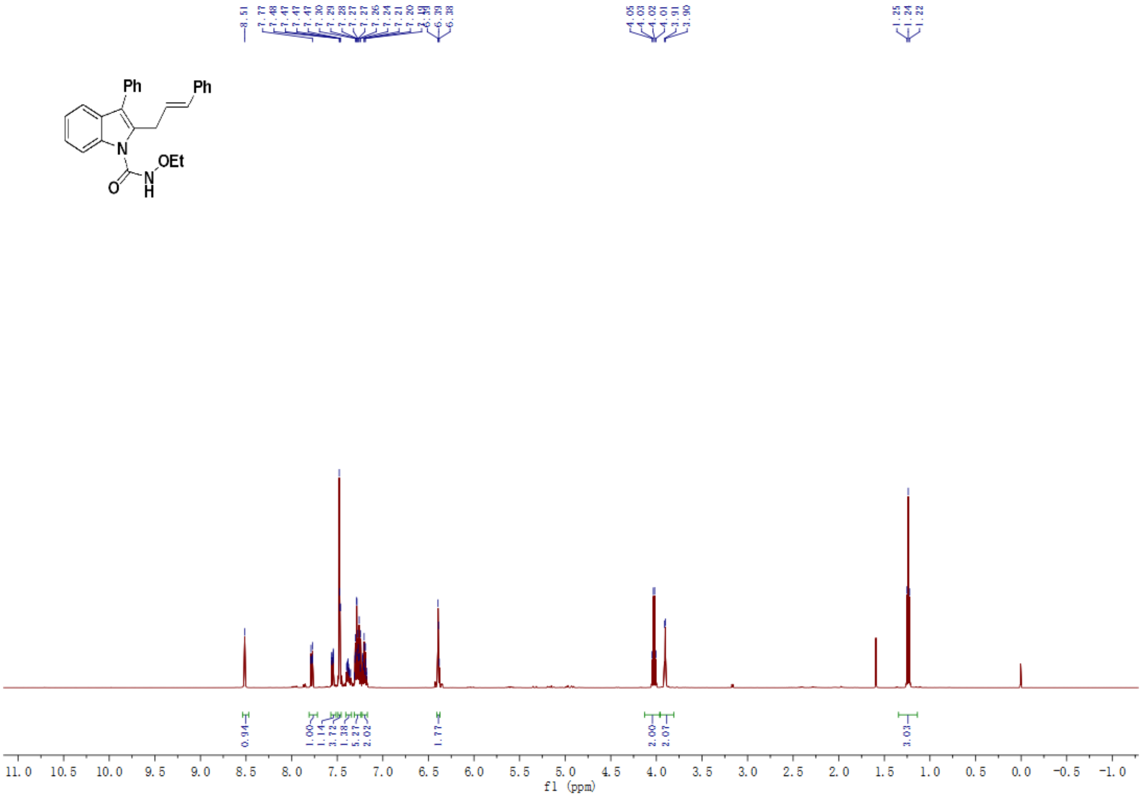
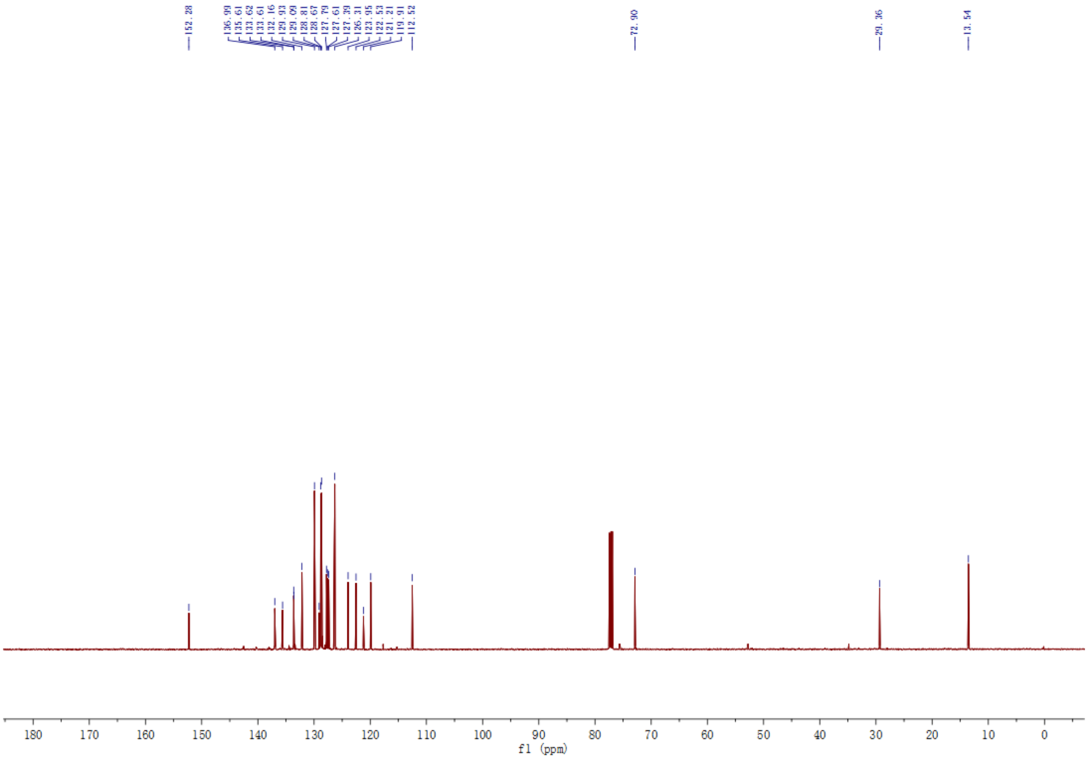


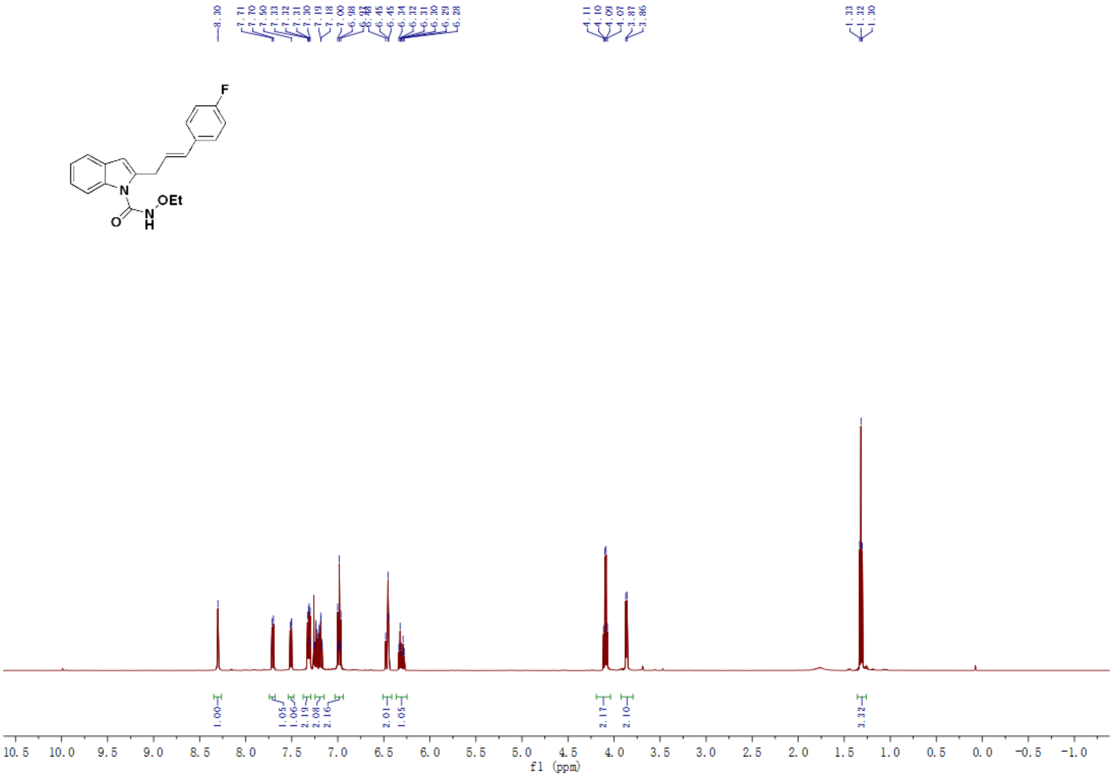


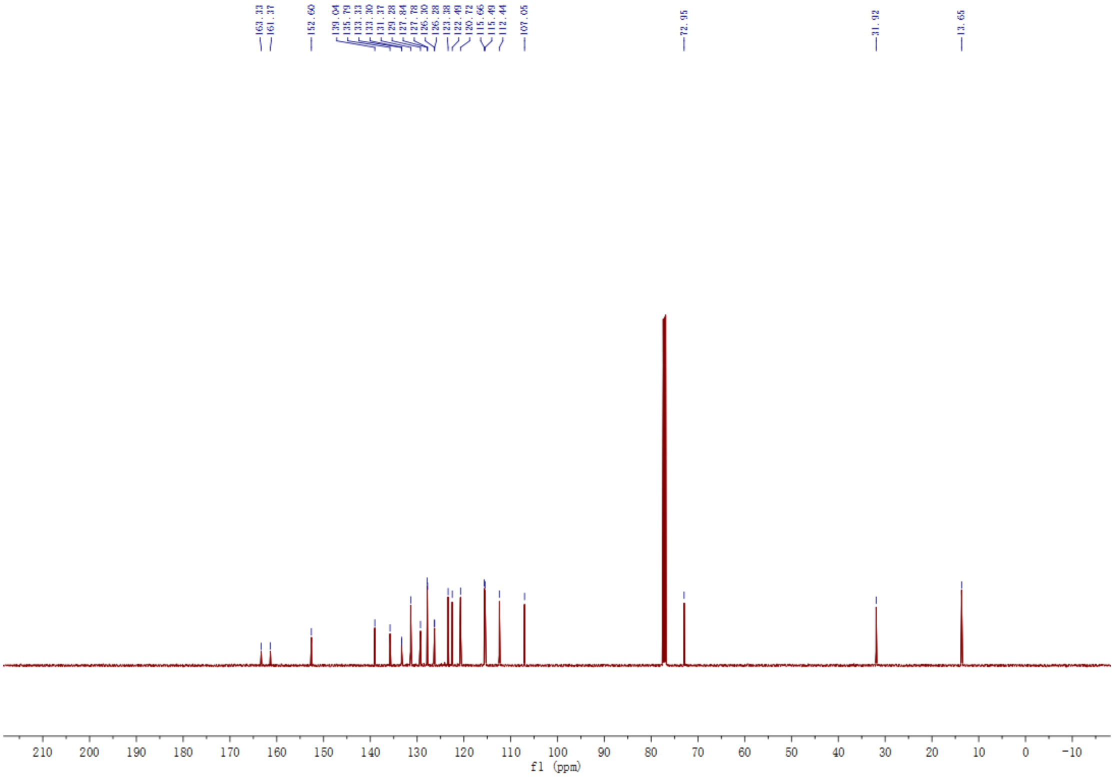
2-cinnamyl-N-ethoxy-3-phenyl-1H-indole-1-carboxamide (3j)

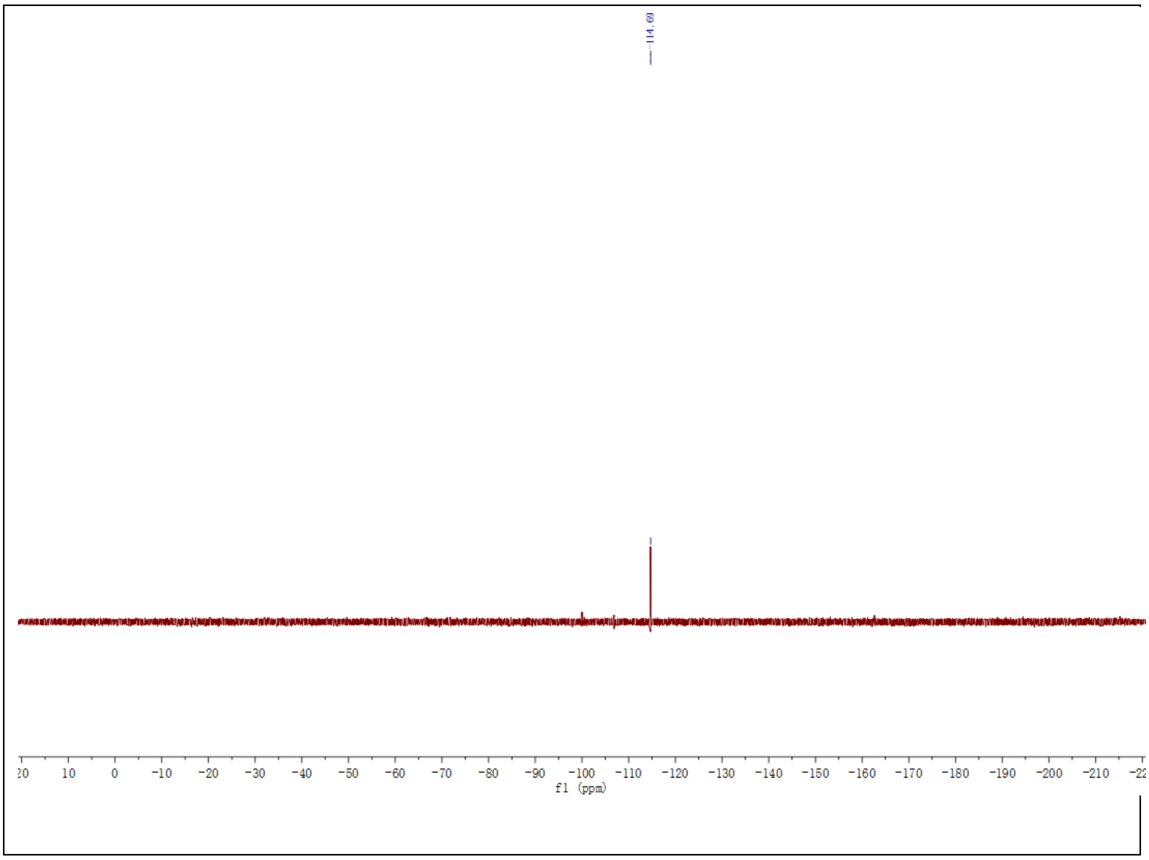




(E)-N-ethoxy-2-(3-(4-fluorophenyl)allyl)-1H-indole-1-carboxamide (3k)



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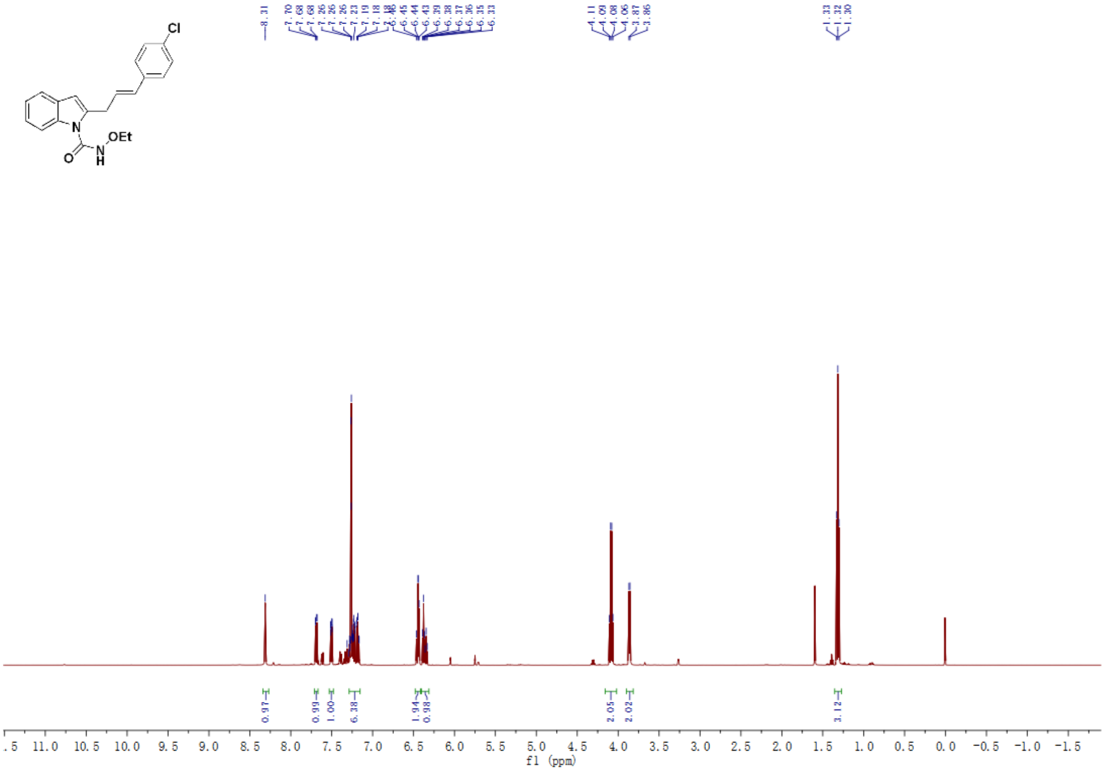
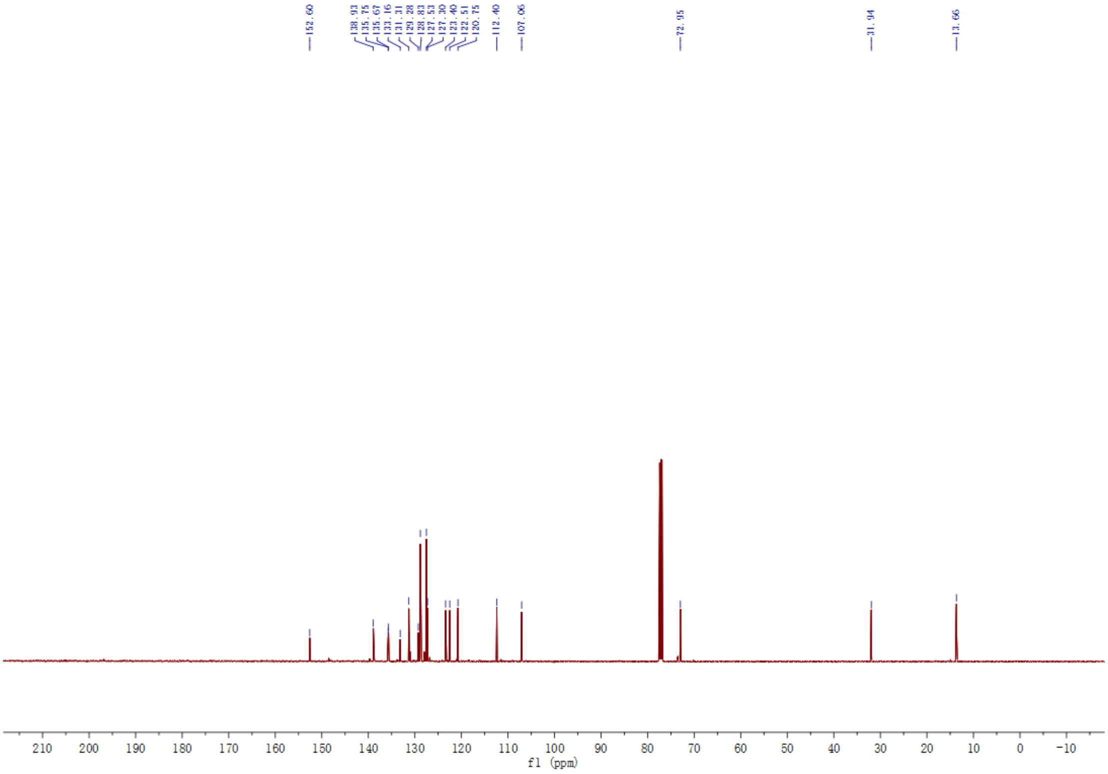
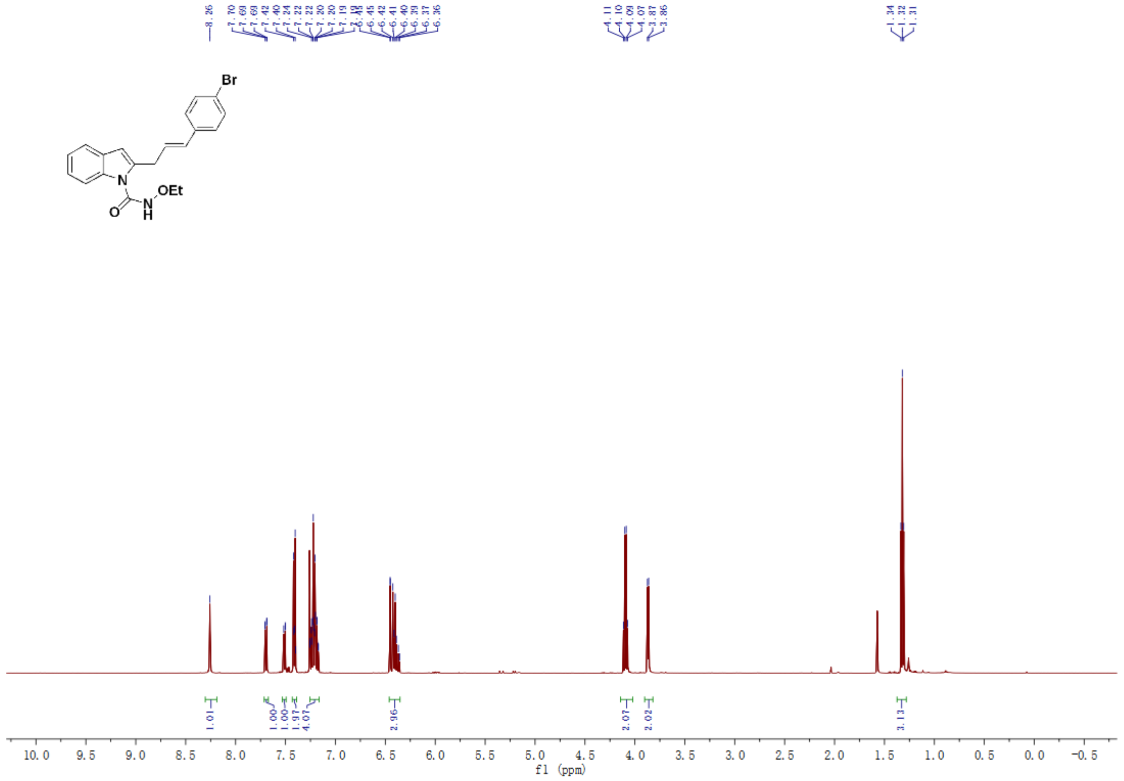
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-22
f1 (ppm)

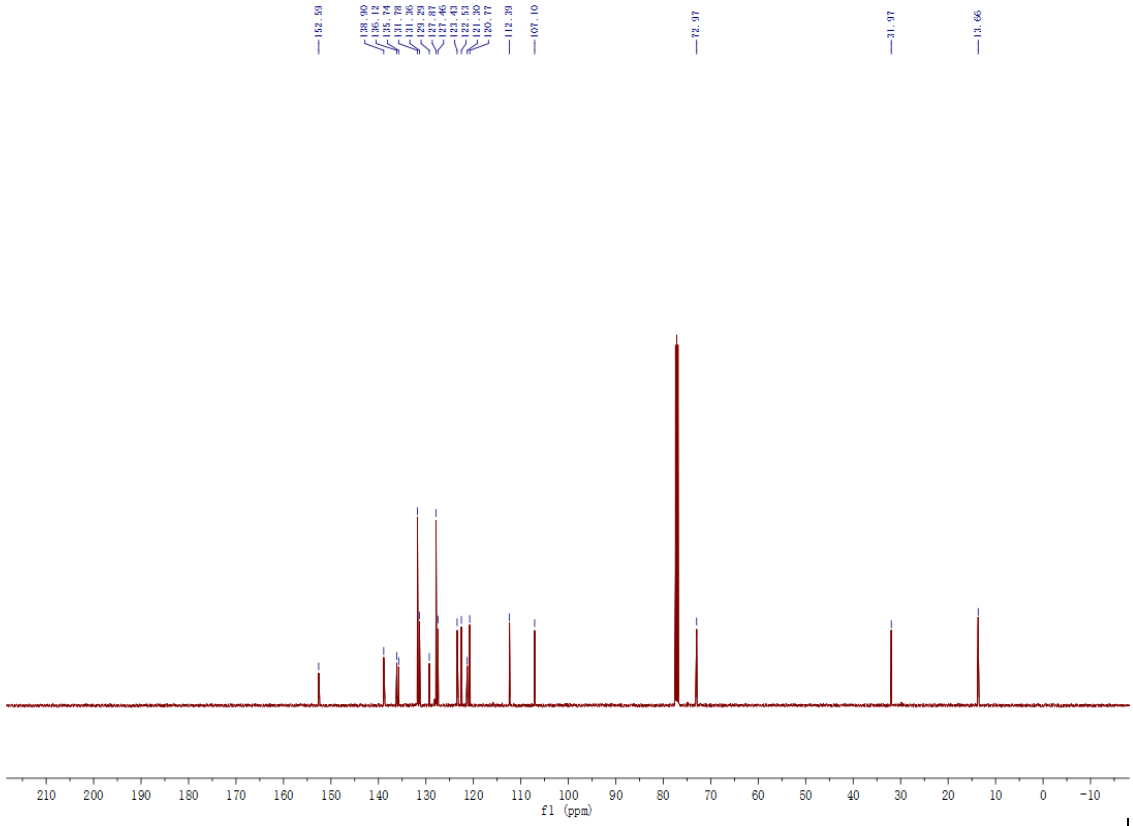
(E)-2-(3-(4-chlorophenyl)allyl)-N-ethoxy-1H-indole-1-carboxamide (3l)



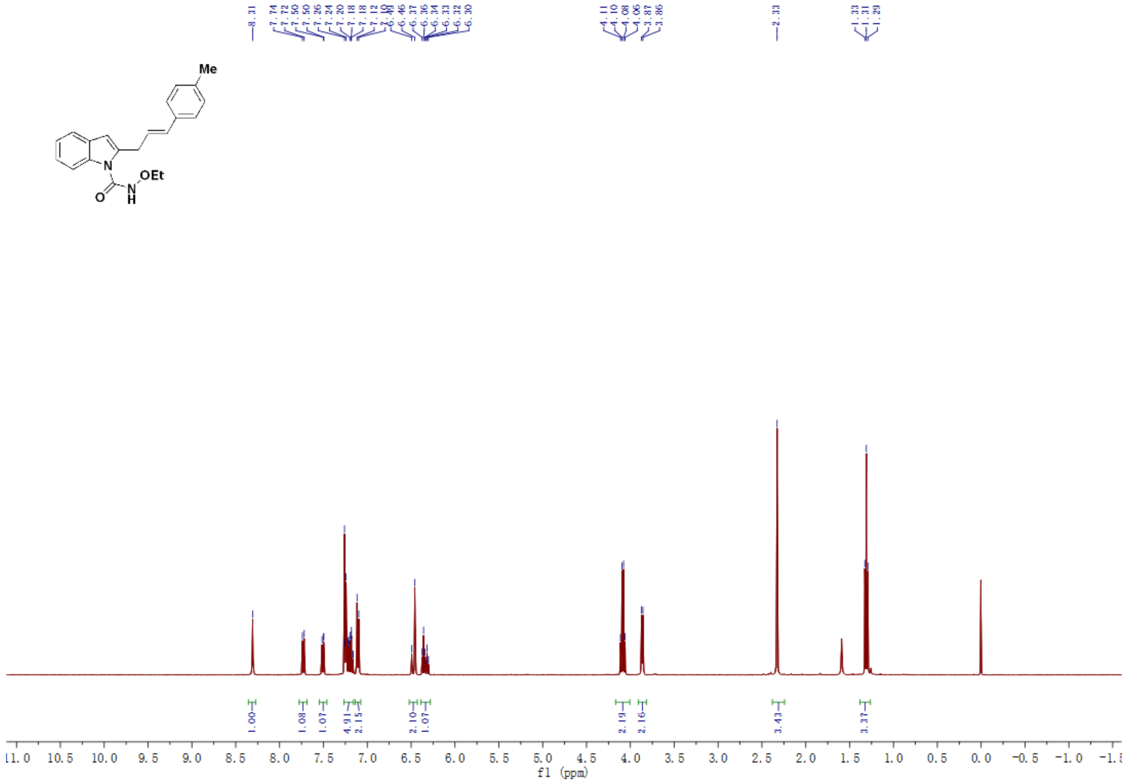


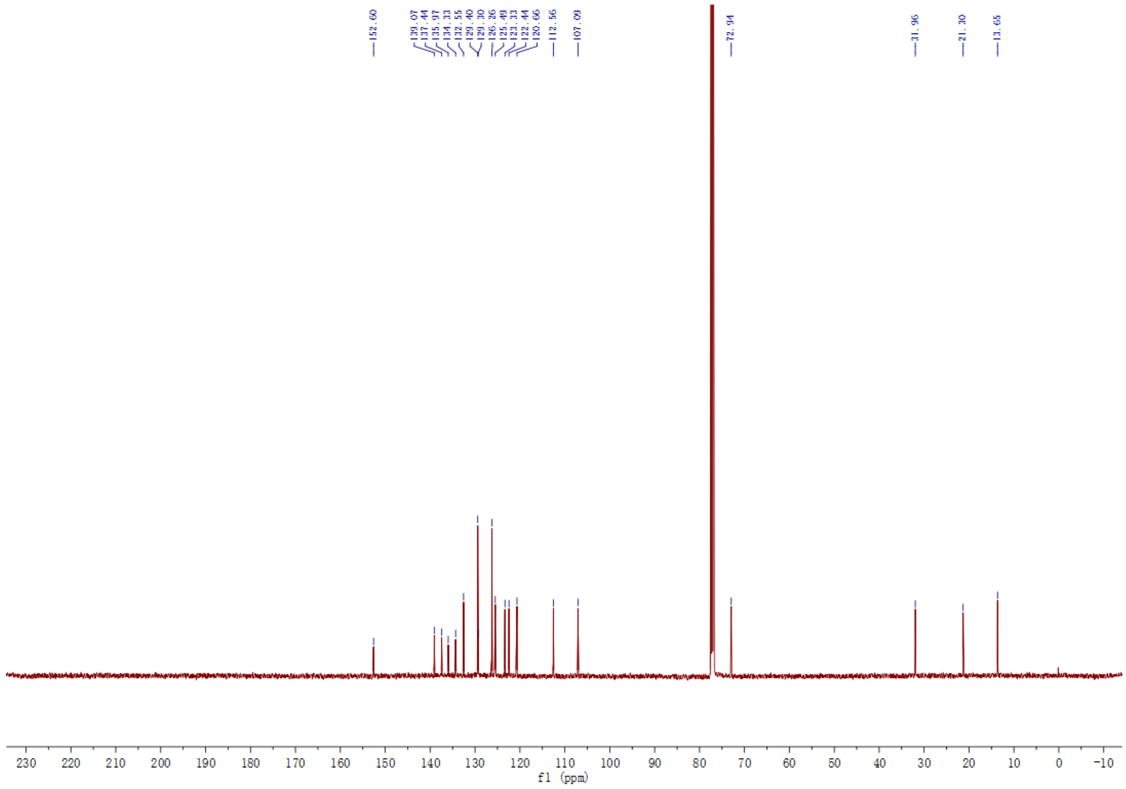
(E)-2-(3-(4-bromophenyl)allyl)-N-ethoxy-1H-indole-1-carboxamide (3m)



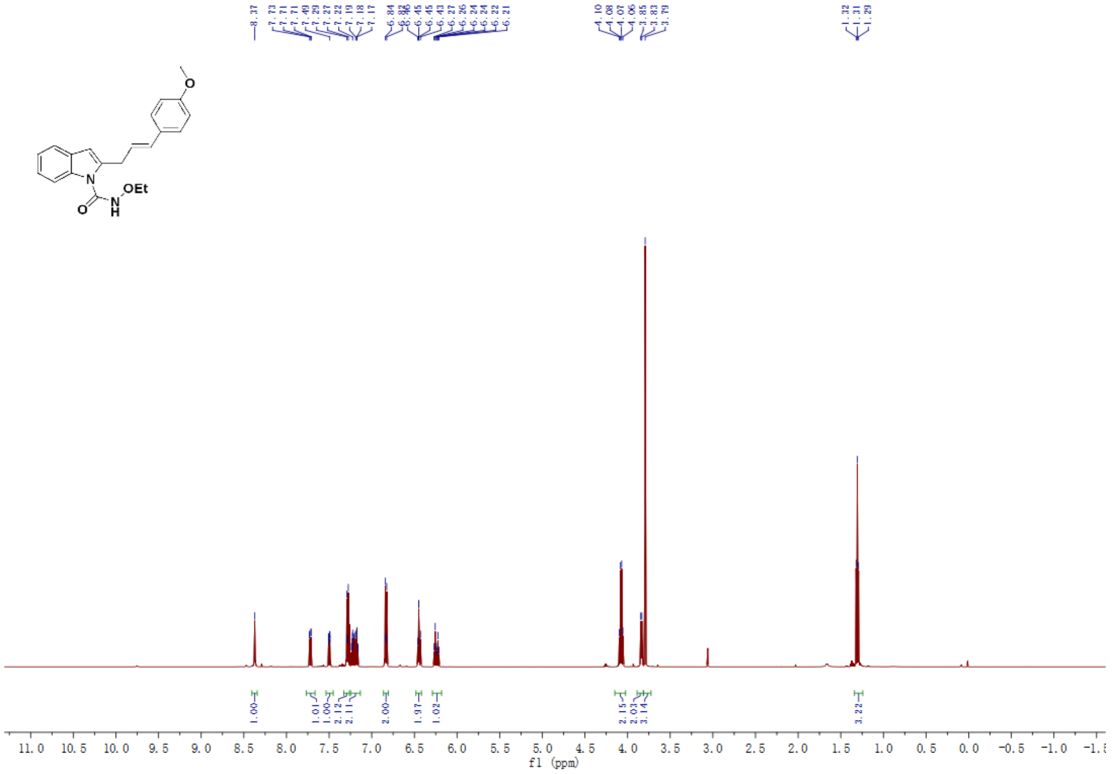


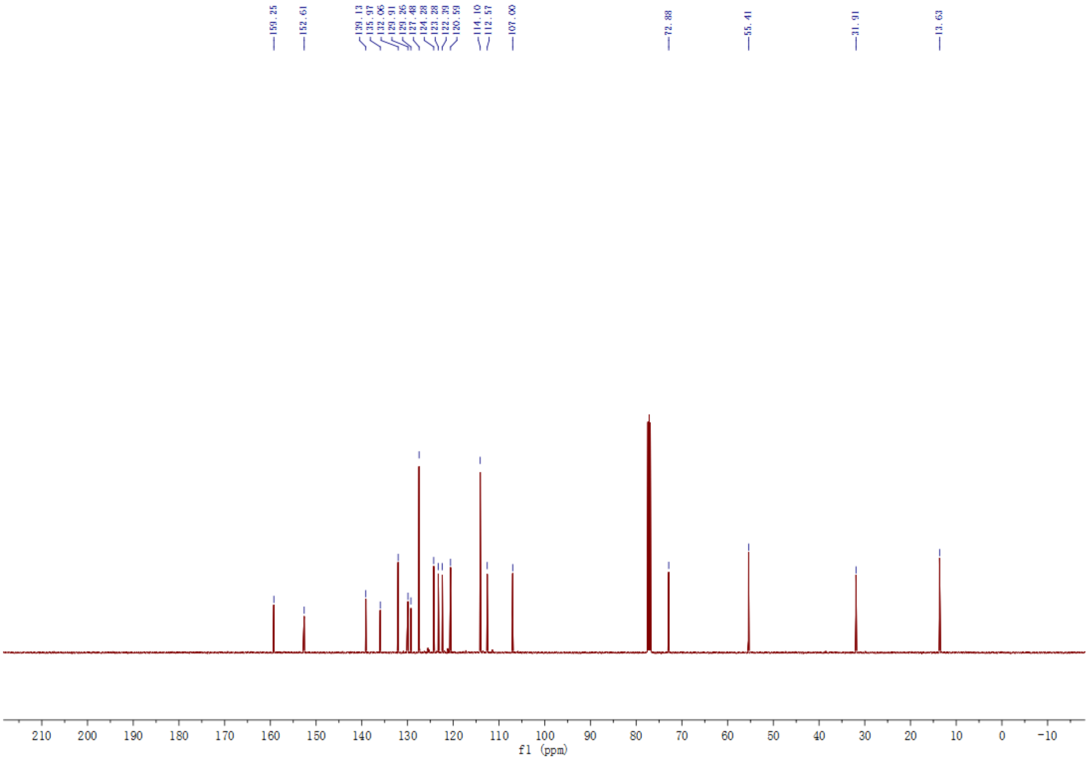
(E)-N-ethoxy-2-(3-(p-tolyl)allyl)-1H-indole-1-carboxamide (3n)



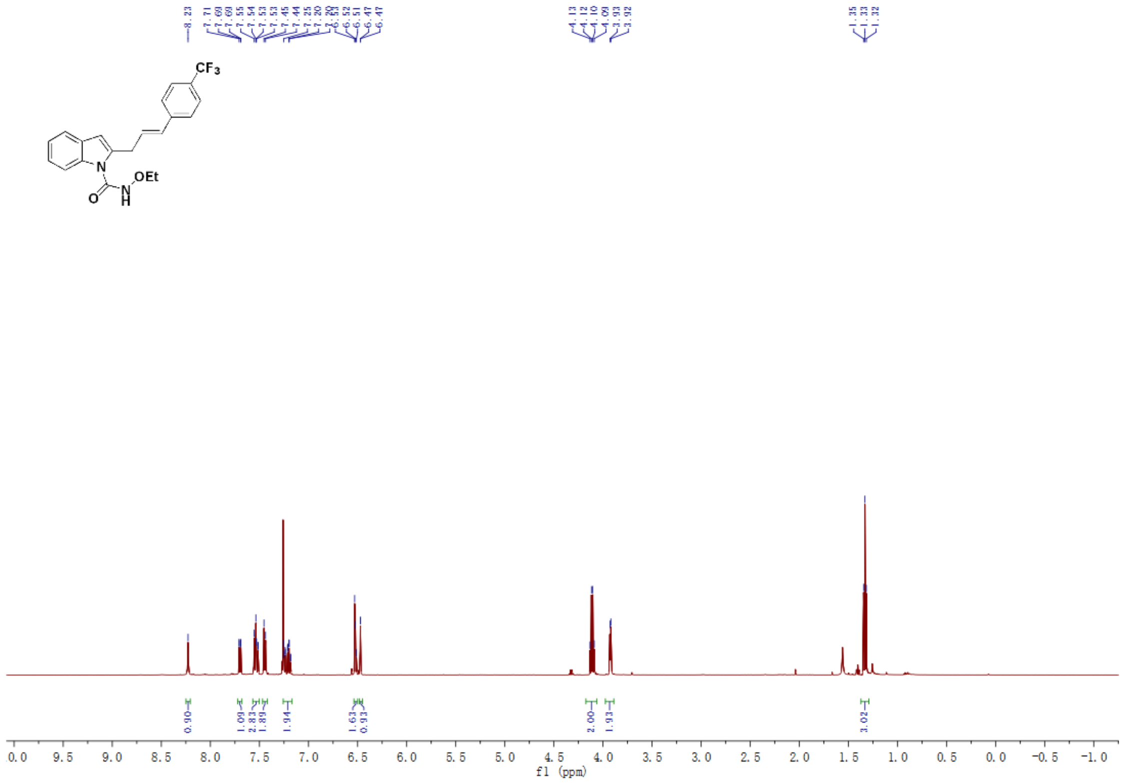


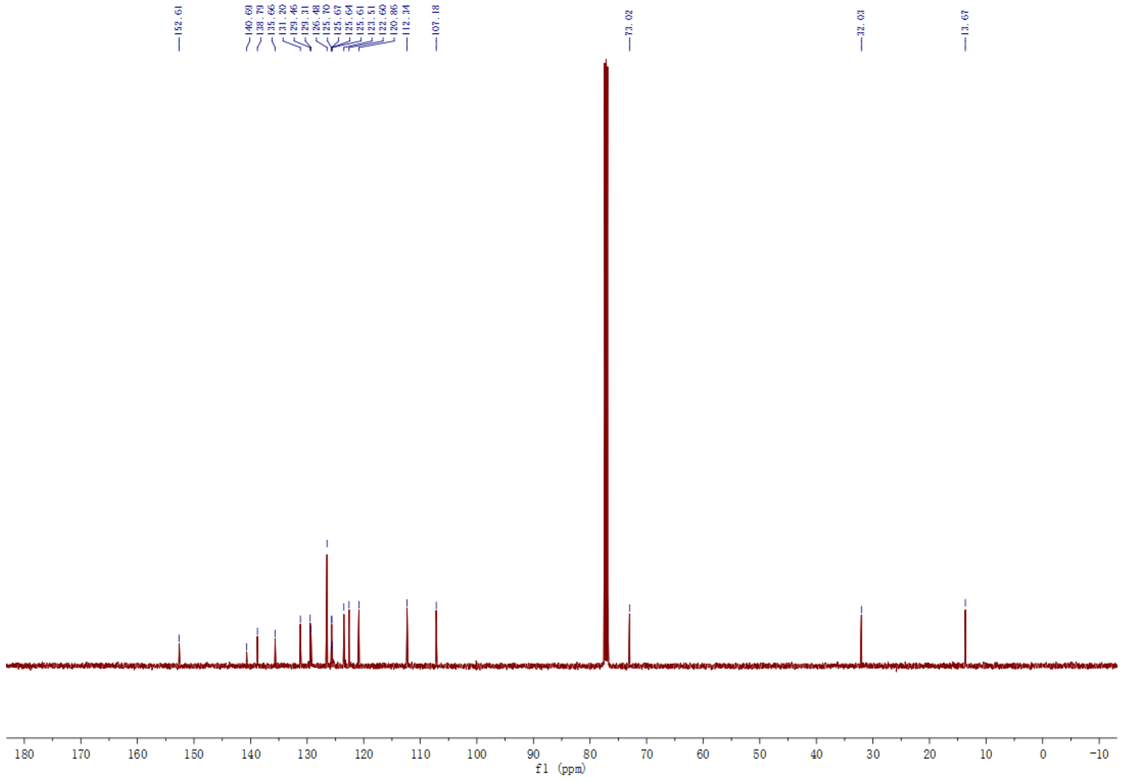
(E)-N-ethoxy-2-(3-(4-methoxyphenyl)allyl)-1H-indole-1-carboxamide (3o)

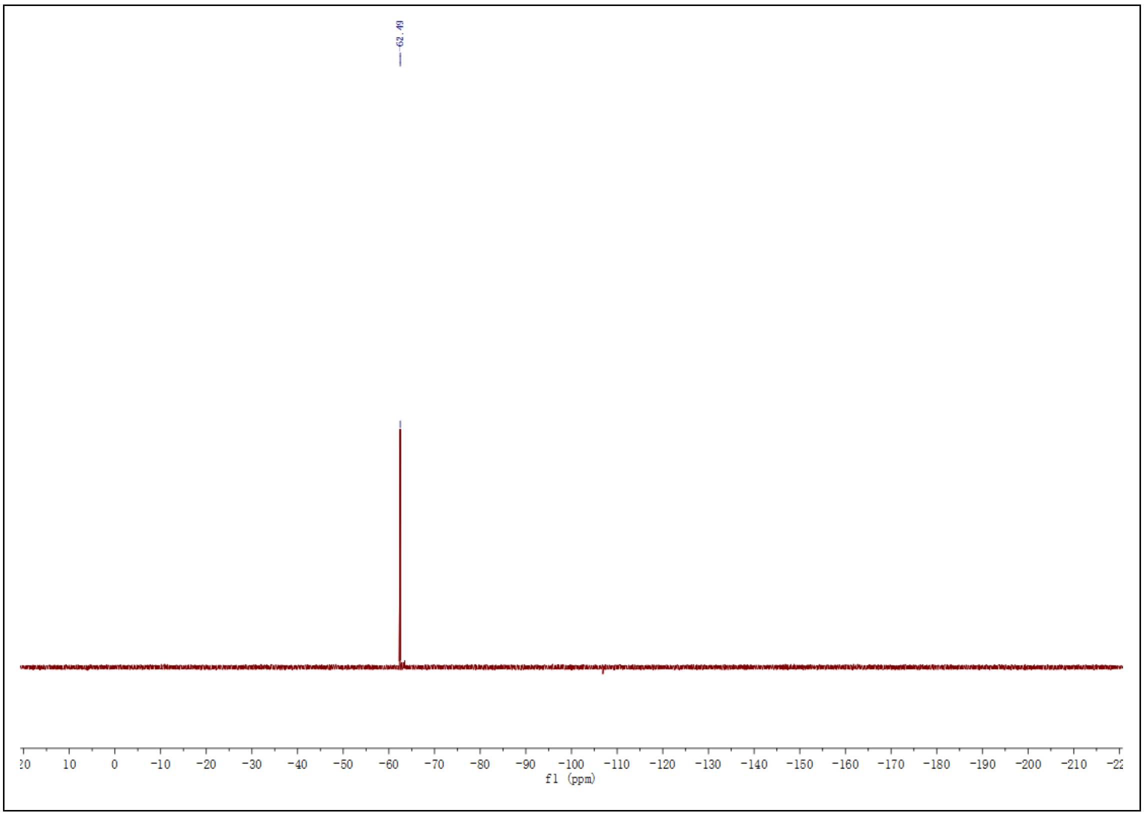




(E)-N-ethoxy-2-(3-(4-(trifluoromethyl)phenyl)allyl)-1H-indole-1-carboxamide (3p)



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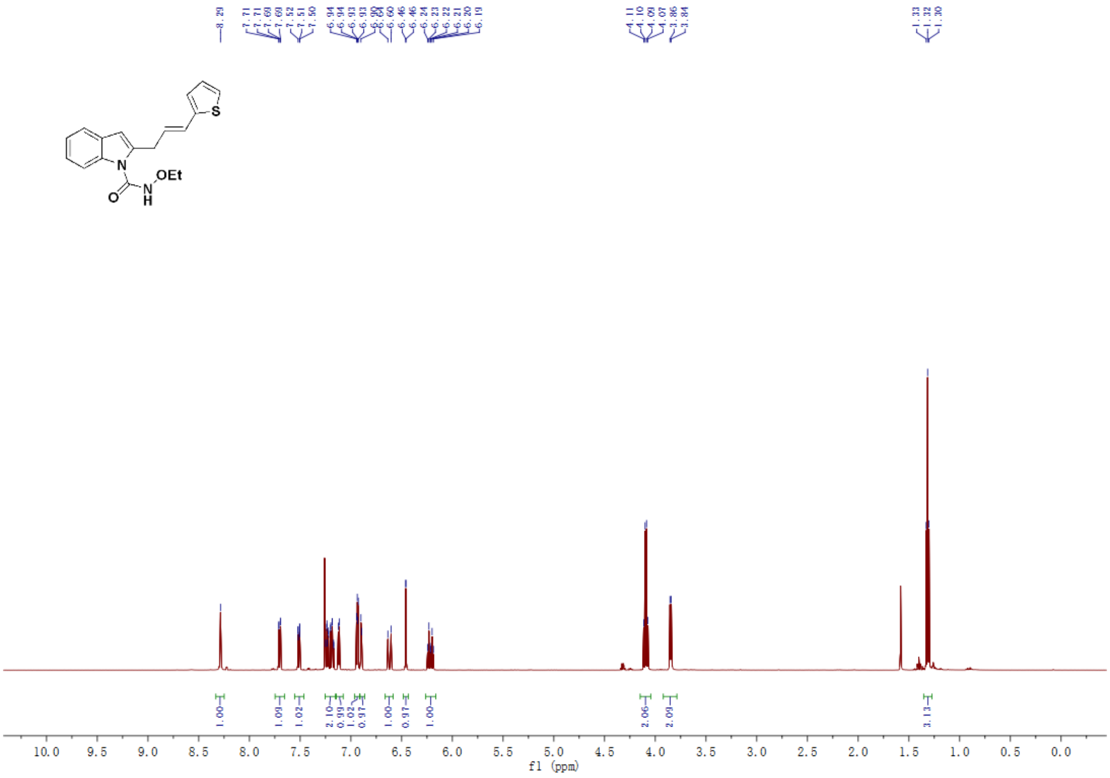
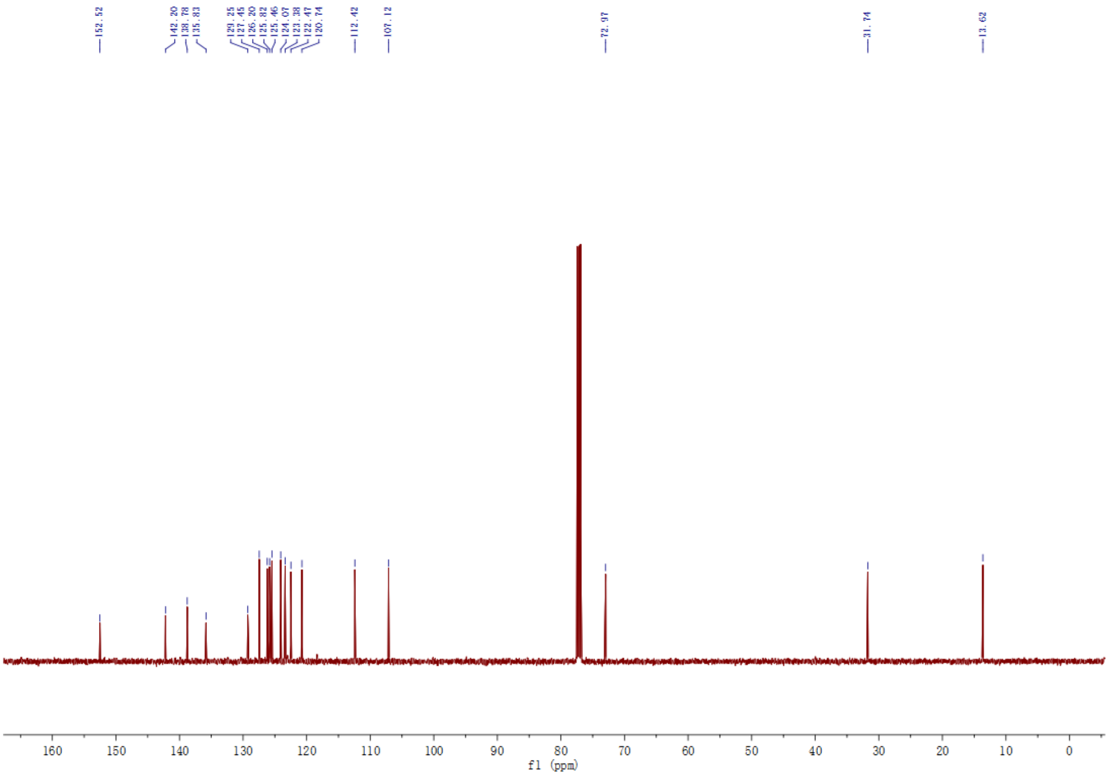
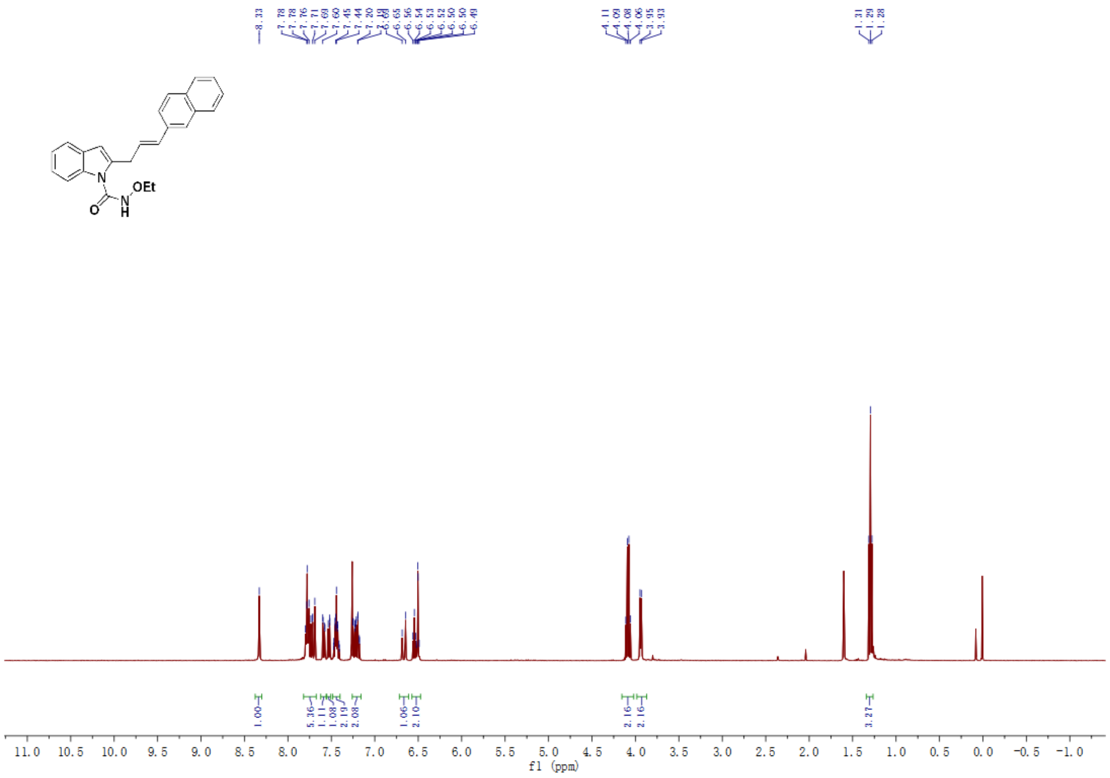
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-22
f1 (ppm)

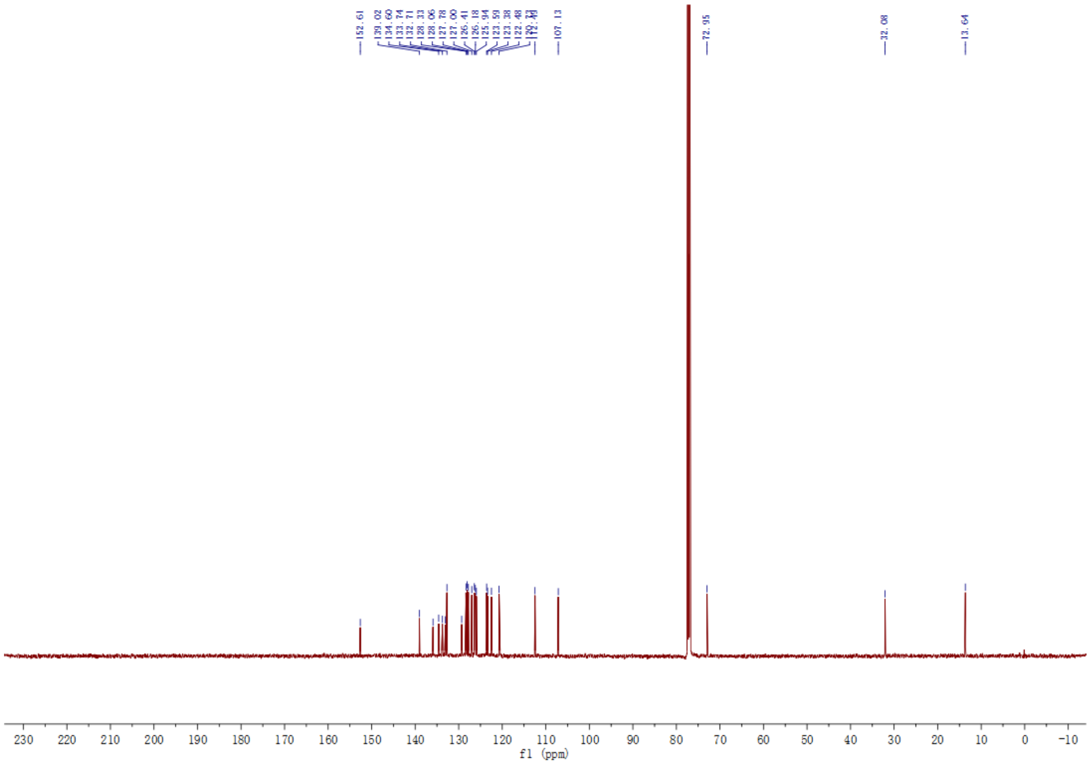
(E)-N-ethoxy-2-(3-(thiophen-2-yl)allyl)-1H-indole-1-carboxamide (3q)



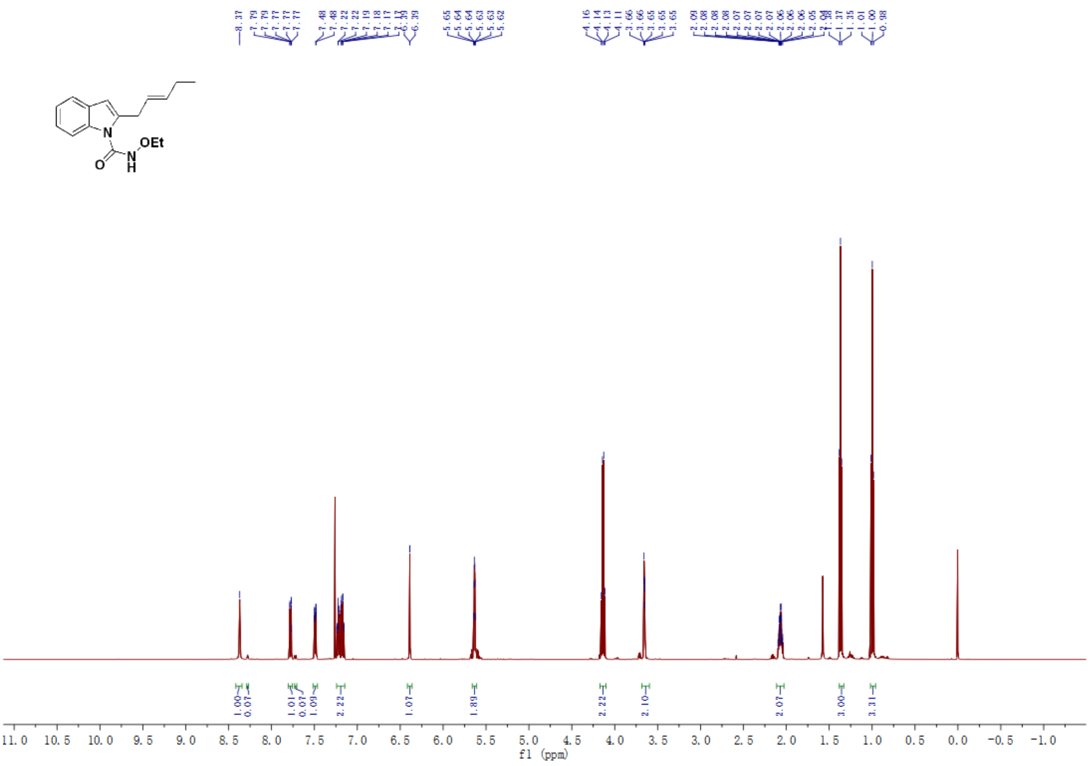


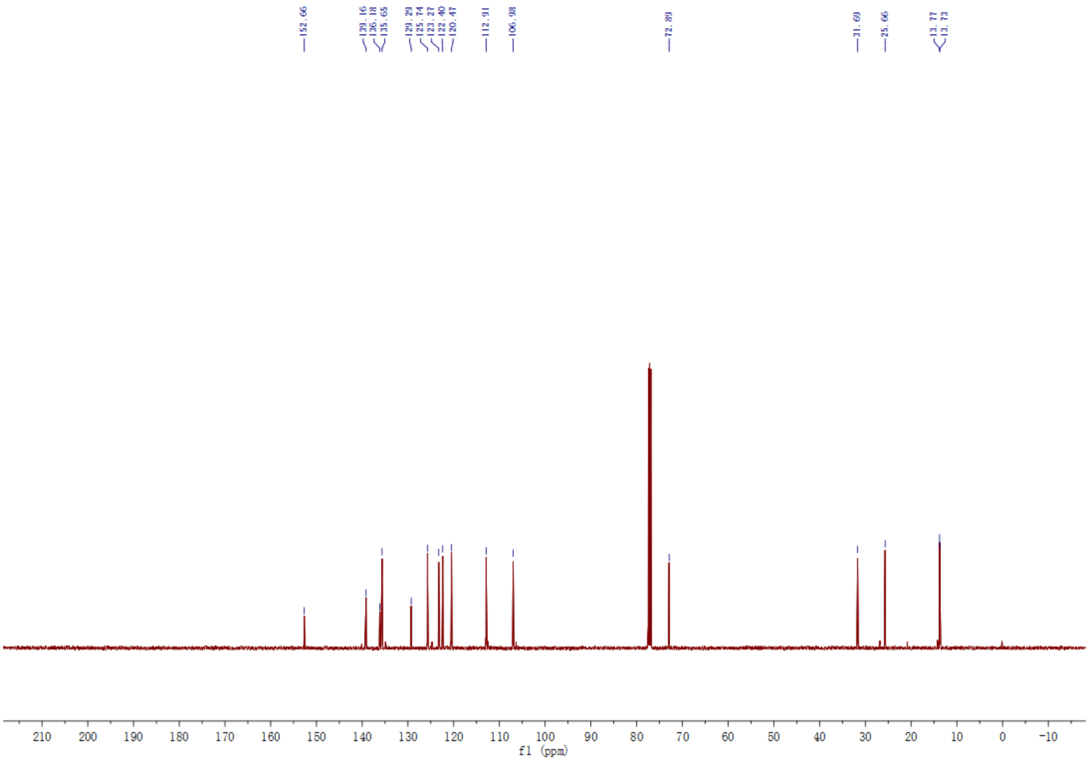
(E)-N-ethoxy-2-(3-(naphthalen-2-yl)allyl)-1H-indole-1-carboxamide (3r)



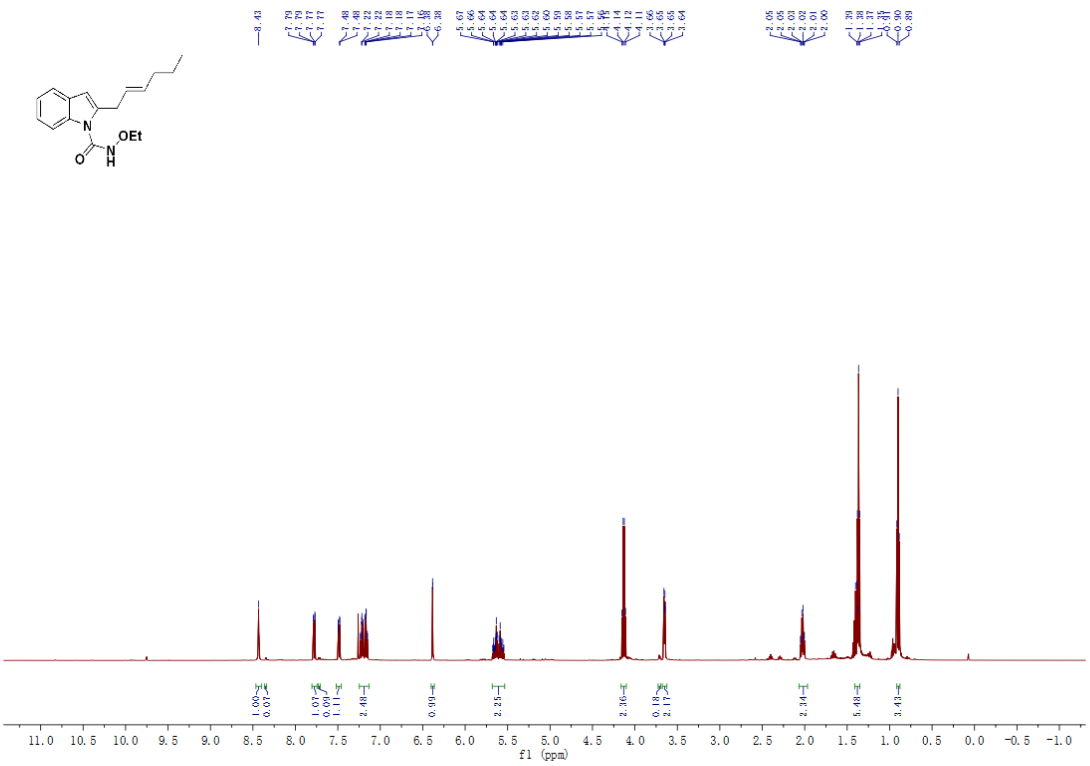


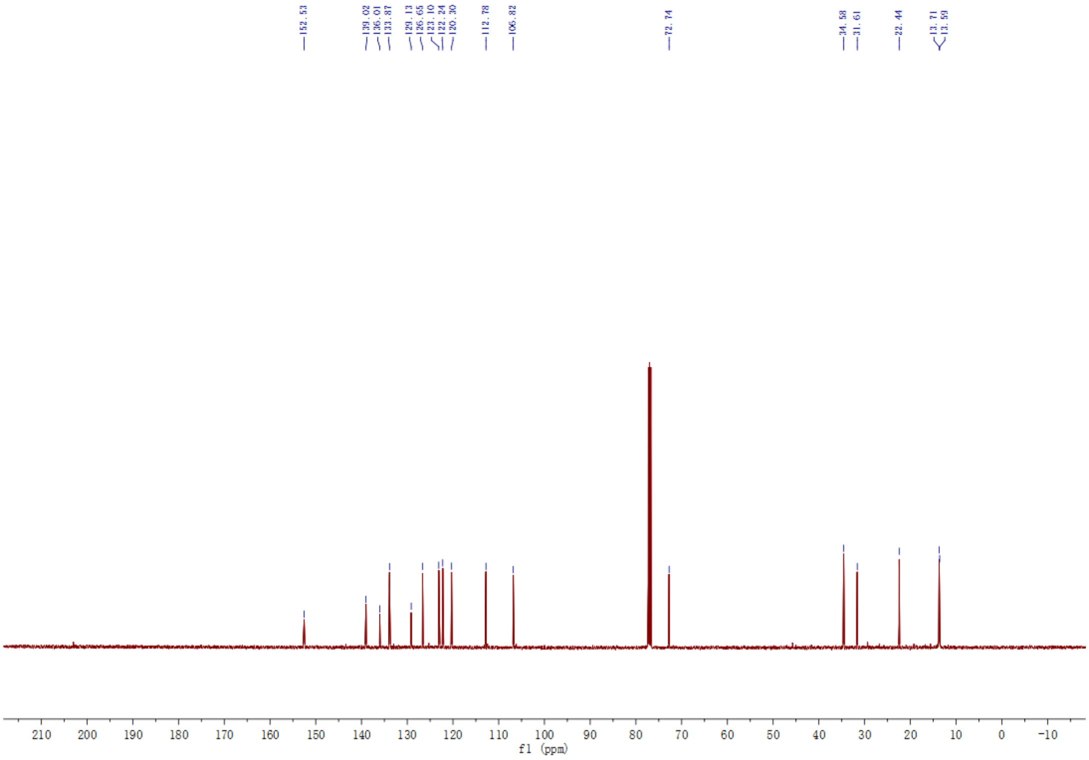
(E)-N-ethoxy-2-(pent-2-en-1-yl)-1H-indole-1-carboxamide (3s)



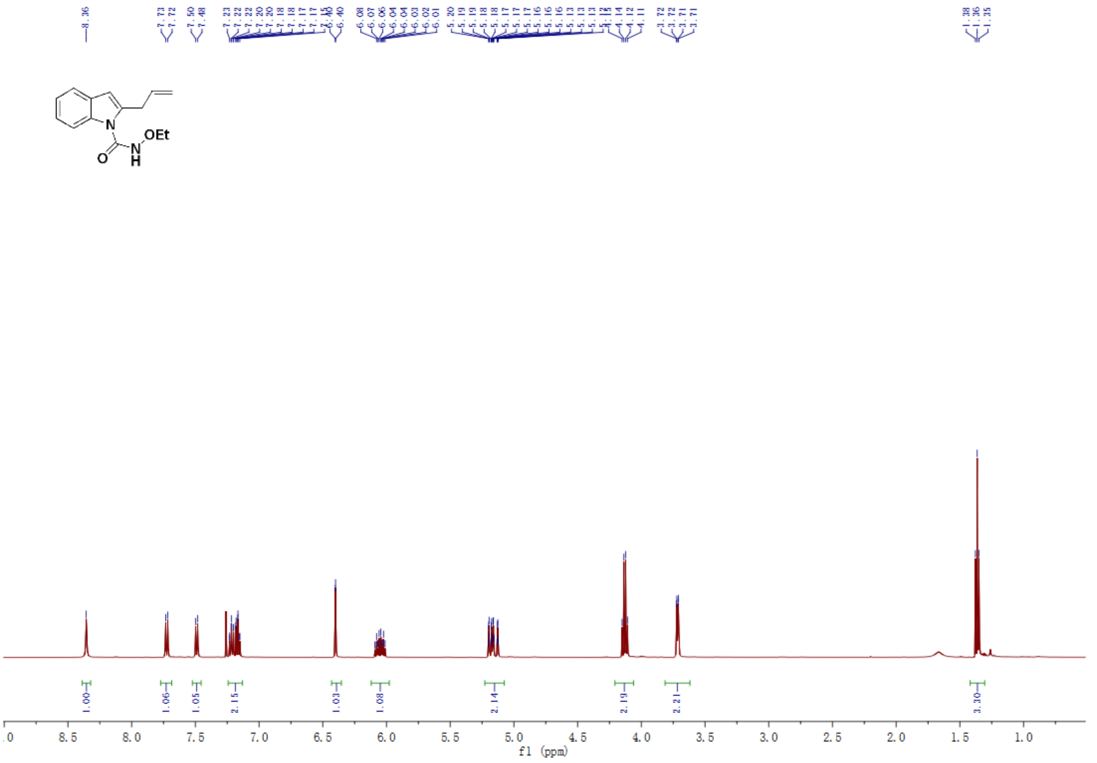


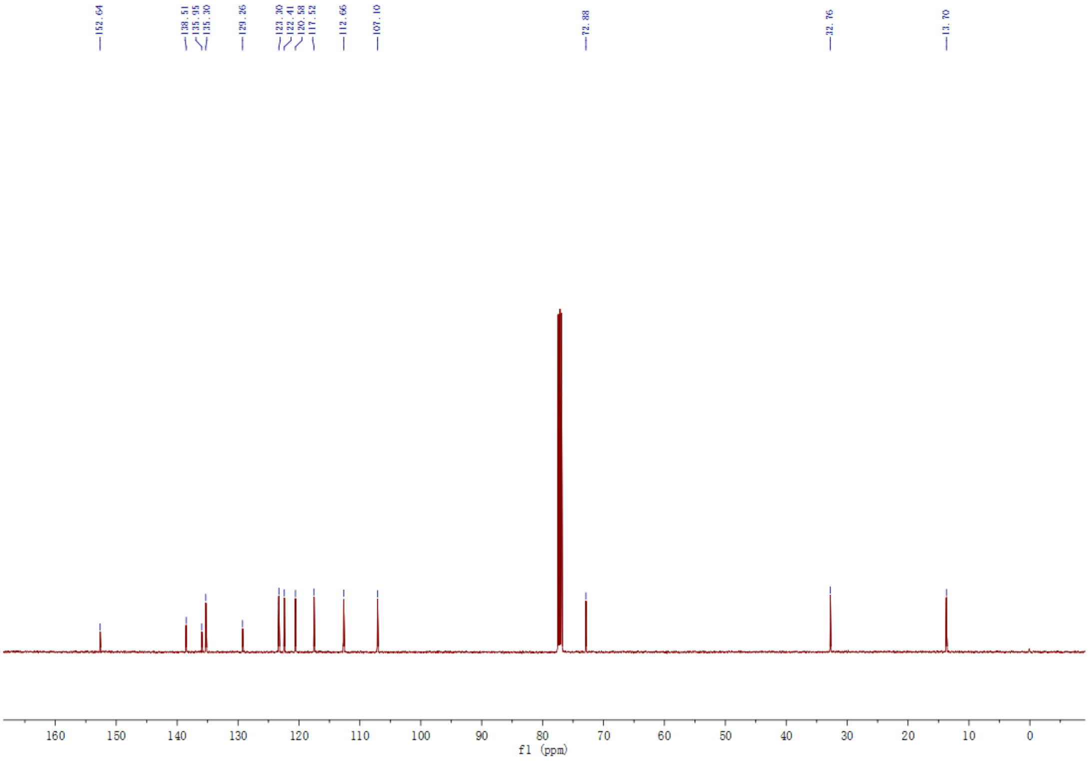
(E)-N-ethoxy-2-(hex-2-en-1-yl)-1H-indole-1-carboxamide (3t)



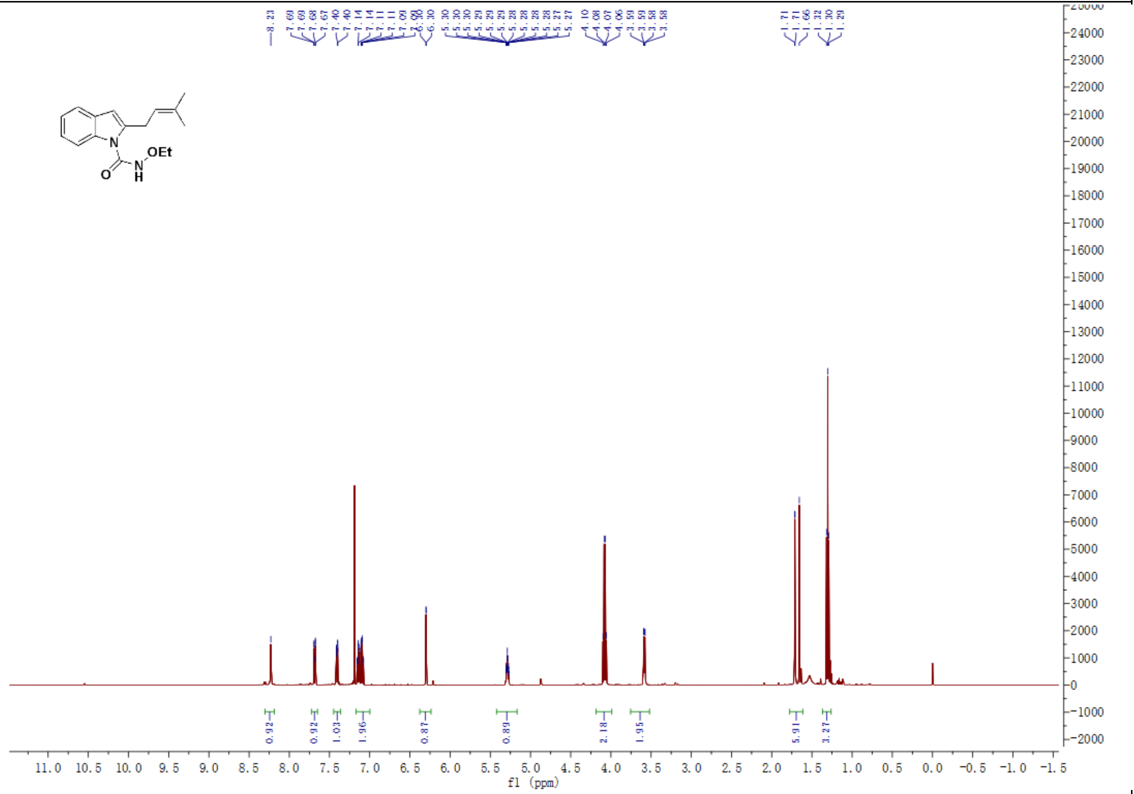


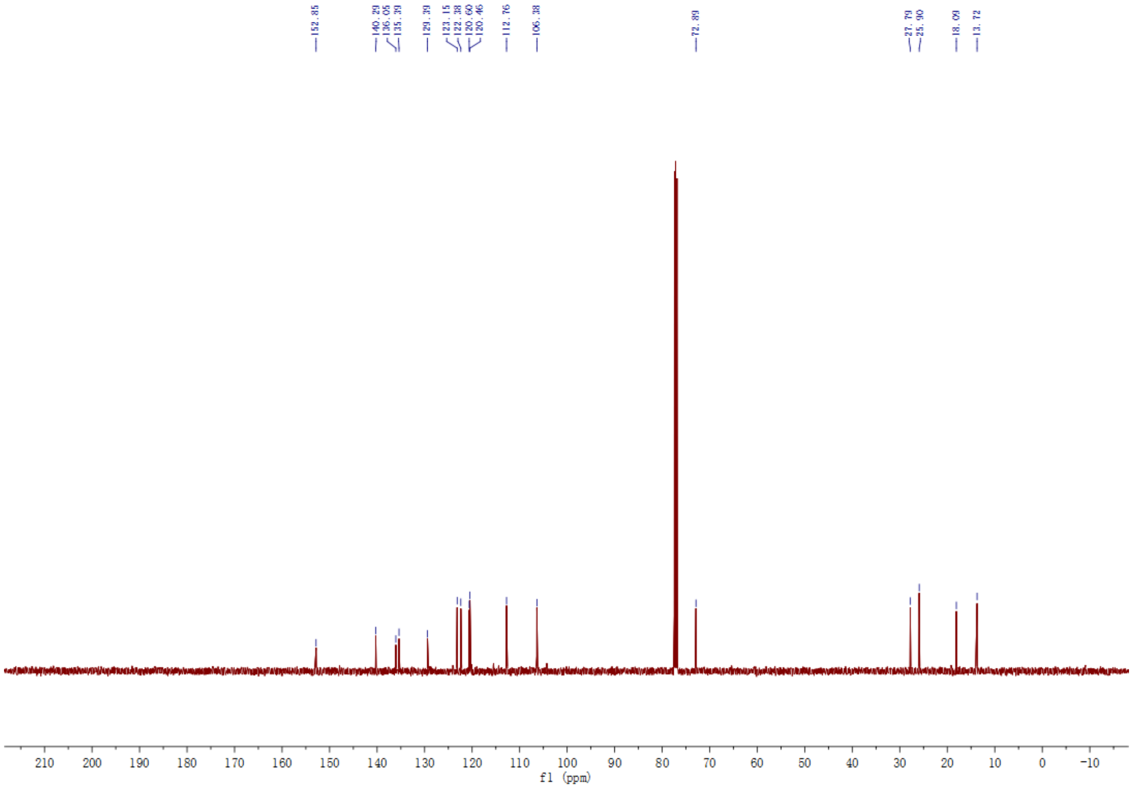
2-allyl-N-ethoxy-1H-indole-1-carboxamide (3u)



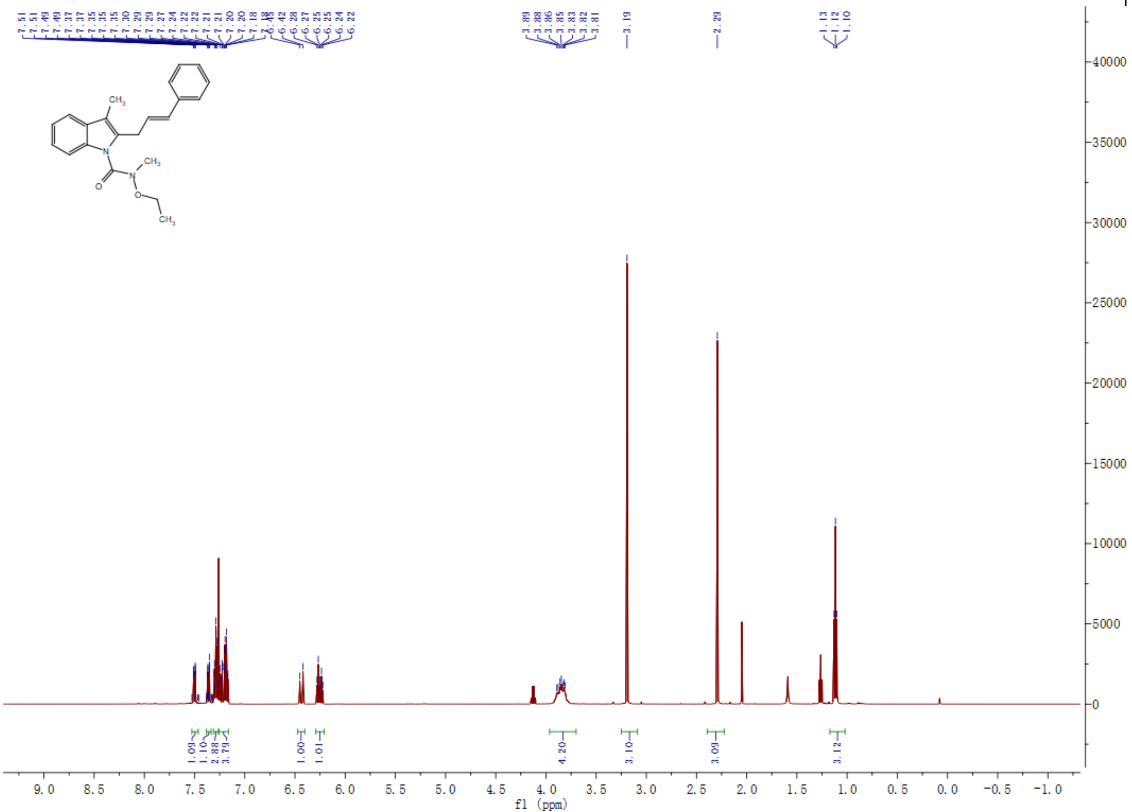


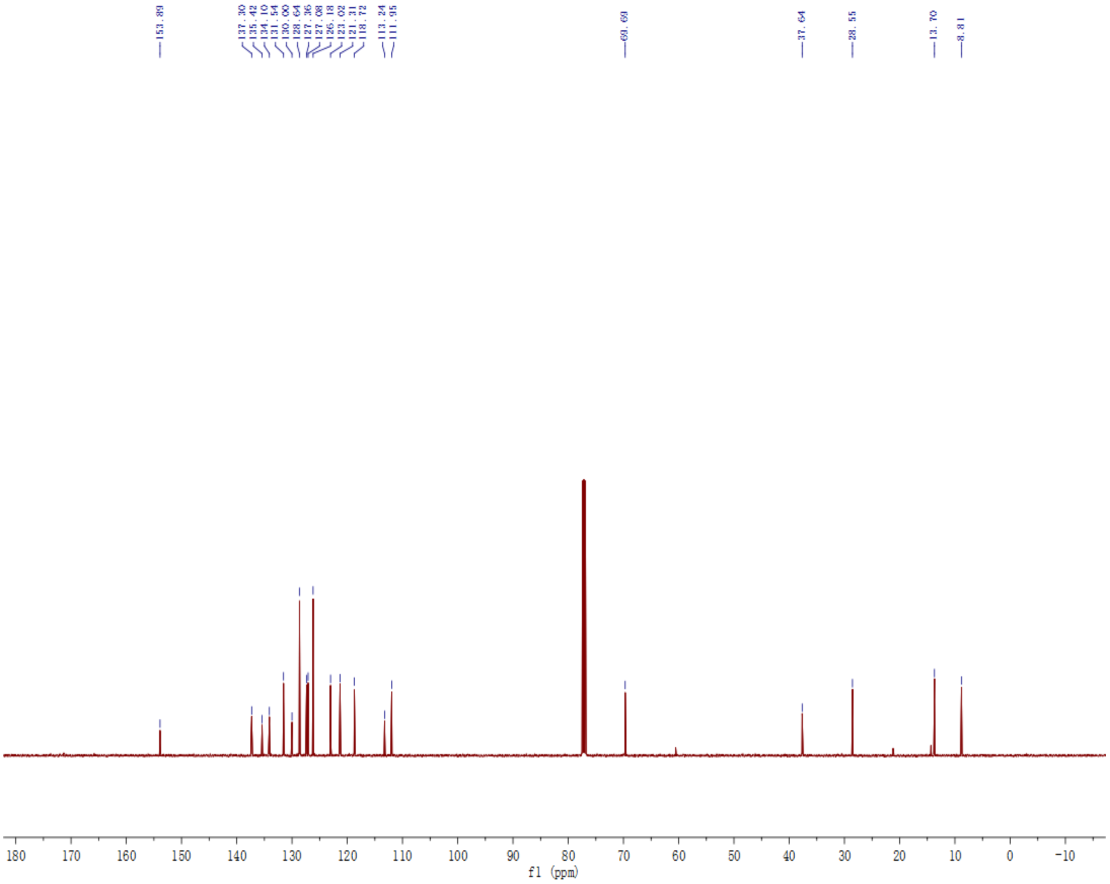
N-ethoxy-2-(3-methylbut-2-en-1-yl)-1H-indole-1-carboxamide (3v)



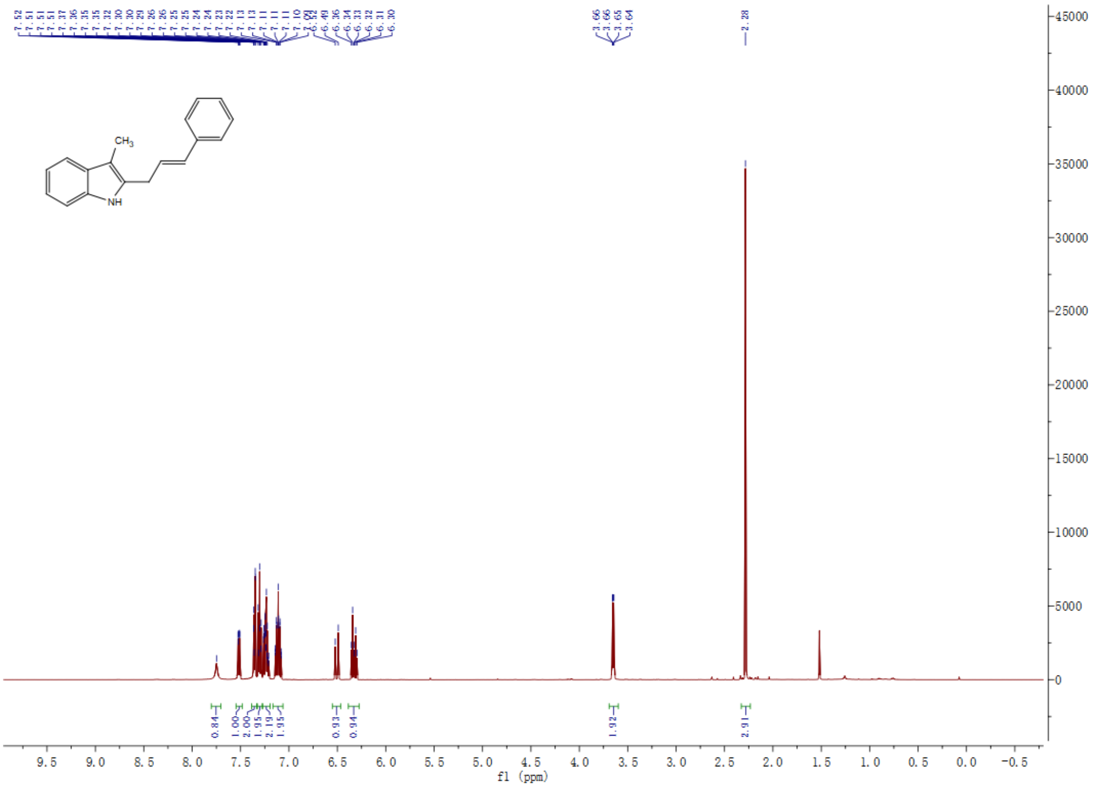


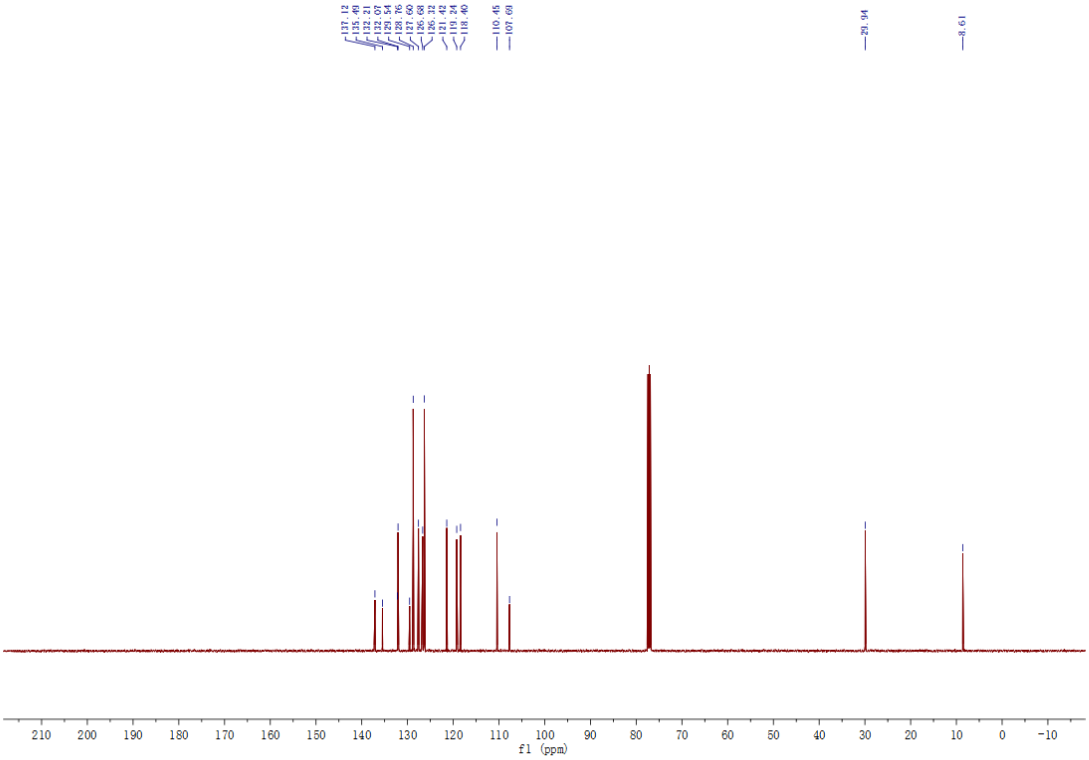
2-cinnamyl-N-ethoxy-N,3-dimethyl-1H-indole-1-carboxamide (3ia)





2-cinnamyl-3-methyl-1H-indole (4a)





(F) Supplementary References.

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