Catalytic asymmetric synthesis of 3,4'-indole-pyrazole derivatives featuring axially chiral bis-pentatomic heteroaryls

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Supporting Information

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1.General methods and materials

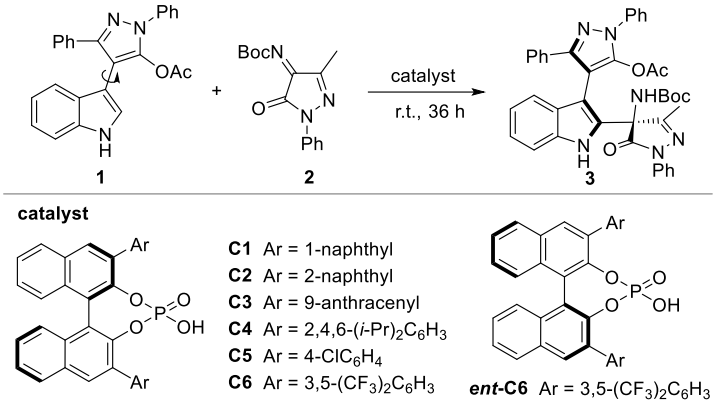
High Performance Liquid Chromatography (HPLC) was analyzed by chiral column in comparison with authentic racemates, using a Daicel Chiralpak AD-H Column (250 x 4.6 mm), Daicel Chiralpak AD-H Column (250 x 4.6 mm) , Daicel Chiralpak IC-H Column (250 x 4.6 mm) or OD-H Column (250 x 4.6 mm). UV detection was performed at 220 nm or 254 nm. Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ on Bruker 400, 600, 700 MHz, or JEOL 600 NMR instrument (at 600 or 700 MHz for ^1H, and at 150, or 175 MHz for ^{13}C). Proton chemical shifts are reported in parts per million (δ scale). The ^1H NMR chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as standard. The ^{13}C NMR chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$: δ = 77.00 ppm). High-resolution mass spectra (HRMS) were obtained using Agilent P/N G1969-90010 or Waters/Acquity UPLC-Synapt G2HDMS. High-resolution mass spectra were reported for the molecular ion $[M+H]^+$ or $[M+Na]^+$. Melting points were recorded on BUCHI Melting Point M-565 instrument. X-ray diffraction experiment was carried out on an Agilent Gemini and the data obtained were deposited at the Cambridge Crystallographic Data Centre. Column chromatography was performed on silica gel (200-300 mesh) using an eluent of ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates; products were visualized using UV light. All reagents and solvents were obtained from commercial sources and used without further purification. Pyrazolon-Derived N-Boc Ketimines[1] were prepared according to the literature procedures. Oil baths were used as the heat source.

Reference

1. U. Kaya, P. Chauhan, S. Mahajan, K. Deckers, A. Valkonen, K. Rissanen and D. Enders, Squaramide-Catalyzed Asymmetric aza-Friedel–Crafts/N,O-Acetalization Domino Reactions Between 2-Naphthols and Pyrazolinone Ketimines, *Angew. Chem., Int. Ed.,* **2017**, *56*, 15358-15362.

2. Optimization of the reaction conditions

Table 1. Optimization of the Reaction Conditions



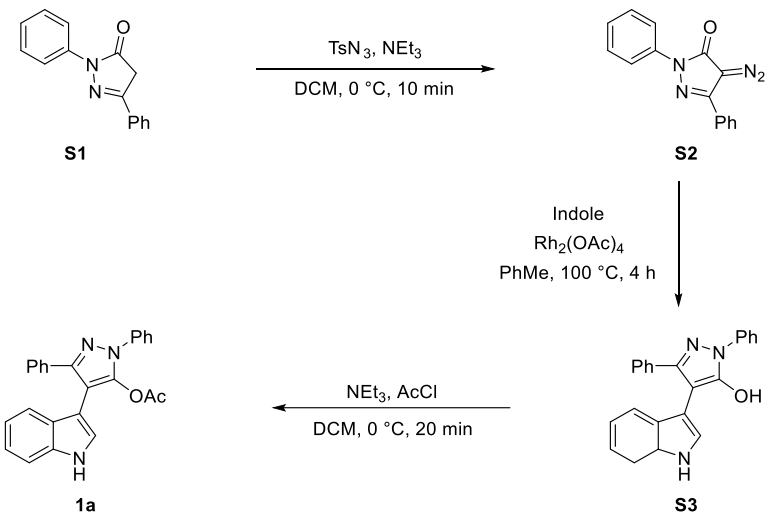
Entry[a]	catalyst	Solvent	T (°C)	Yield (%)[b]	dr[c]	*ee* (%)[d]
1	**C1**	CH_2Cl_2	r.t.	78	>19:1	5
2	**C2**	CH_2Cl_2	r.t.	68	>19:1	53
3	**C3**	CH_2Cl_2	r.t.	49	>19:1	5
4	**C4**	CH_2Cl_2	r.t.	39	>19:1	39
5	**C5**	CH_2Cl_2	r.t.	44	>19:1	45
6	**C6**	CH_2Cl_2	r.t.	75	>19:1	93
7	**C6**	DCE	r.t.	37.4	>19:1	93
8[e]	**C6**	$CHCl_3$	r.t.	93	>19:1	95
9	**C6**	Toluene	r.t.	53	>19:1	69
10	**C6**	CH_3CN	r.t.	55	>19:1	39
11	**C6**	THF	r.t.	N.R.	-	-
12	**C6**	CH_3CN	r.t.	N.R.	-	-
13	**C6**	EtOAc	r.t.	N.R.	-	-
14	**C6**	Ether	r.t.	N.R.	-	-
15	**C6**	DMSO	r.t.	N.R.	-	-
16	**C6**	Dioxane	r.t.	N.R.	-	-
17	**C6**	DMF	r.t.	N.R.	-	-
18[f]	**C6**	$CHCl_3$	r.t.	90	>19:1	91
19[g]	**C6**	$CHCl_3$	r.t.	93	>19:1	93
20[h]	**C6**	CHCl3	r.t.	93	>19:1	95
21[i]	**C6**	$CHCl_3$	0	93	>19:1	97
23[j]	**C6**	$CHCl_3$	-20	78	>19:1	99
24	**(*S*)-C6**	$CHCl_3$	0	88	>19:1	-97

[a]Conditions: **1** (0.1 mmol), **2** (0.12 mmol), and catalyst 20 mol % in solvent (1.0 mL) at r.t. for 36 h. [b]Isolated yield. [c]Determined by NMR. [d]The enantiomeric excess was determined by HPLC. [e]For 9h. [f]10 mol% **C6** was used, for 34h. [g]15 mol % **C6** was used, for 8h. [h]20 mol % **C6** was used, for

12 h. [i]15 mol % **C6** was used, for 12 h. [j]15 mol % **C6** was used, for 36h.

3. Experimental procedures

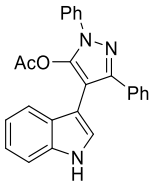
3.1 Preparation of substrates 1



2,5-Diphenyl-2,4-dihydro-3*H*-pyrazol-3-one (**S1**) (10.0 mmol) and 4-methylbenzenesulfonyl azide (12.0 mmol) was dissolved in a 250 ml flask. Et_3N (2 mmol) was added at 0 ℃. After the reaction completed (monitored by TLC), the solvent was removed under reduced and the crude product was directly purified by flash column chromatography (petroleum:EtOAc = 10:1), to afford the **S2** (Orage solid yield 59%).

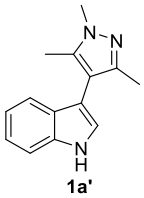
4-Diazo-2,5-diphenyl-2,4-dihydro-3*H*-pyrazol-3-one (**S2**) (2.0 mmol) indole (2.0mmol) and Rhodium(II) acetate dimmer (0.04 mmol) was dissolved in toluence under argon. The mixture was refluxed at 100 ℃ for 4 hours. After the reaction completed (monitored by TLC), filtration of the reaction mixture afforded **S3** (pink solid, 62% yield).

Et_3N (2.4 mmol) was added to a solution of 4-(7,7a-dihydro-1*H*-indol-3-yl)-1,3-diphenyl-1*H*-pyrazol-5-ol (**S3**) (2.0 mmol) in DCM. After 20 min, acetyl chloride (2.0 mmol) was added dropwise. After the reaction completed (monitored by TLC), water was added. The reaction mixture was extracted with DCM (3 times) and the combined organic layers were dried over Na_2SO_4.The solvent was removed under vacuo and the crude product was directly purify by flash column chromatography (petroleum:EtOAc = 10:1), to afford the desired product **1a** (white solid, 73% yield).



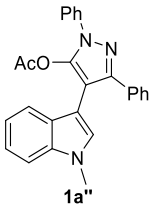
1a

R_f = 0.3 (petroleum/EtOAc = 3:1, v/v); White solid; 73% yield. **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 8.28 (s, 1H), 7.63 – 7.59 (m, 2H), 7.57 – 7.53 (m, 2H), 7.41 – 7.35 (m, 2H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.18 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.15 – 7.10 (m, 3H), 7.09 – 7.05 (m, 1H), 6.97 – 6.94 (m, 1H), 6.87 (d, *J* = 2.5 Hz, 1H), 1.90 (s, 3H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ = 166.5, 166.5, 149.0, 141.5, 137.1, 135.0, 132.4, 128.3, 127.1, 126.8, 126.6, 126.6, 126.5, 125.6, 122.8, 122.0, 121.1, 119.1, 118.8, 118.8, 110.2, 104.8, 102.8, 19.2. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{19}N_3NaO_2^+$ 416.1370; Found 416.1367.



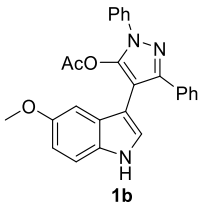
1a'

R_f = 0.3 (petroleum/EtOAc = 1:1, v/v); White solid; 53% yield. **^{1}H NMR (600 MHz, DMSO-*d*$_6$)** δ = 11.16 (s, 1H), 7.38 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.23 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.19 (d, *J* = 1.9 Hz, 1H), 7.08 – 7.04 (m, 1H), 6.97 – 6.93 (m, 1H), 3.67 (s, 3H), 2.09 (s, 3H), 2.01 (s, 3H). **^{13}C NMR (151 MHz, DMSO-*d*$_6$)** δ = 144.8, 136.8, 136.7, 127.4, 124.4, 121.5, 119.7, 119.2, 112.2, 111.8, 107.8, 36.3, 13.0, 10.6. **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{14}H_{15}N_3^+$ 226.1139; Found 226.1146.



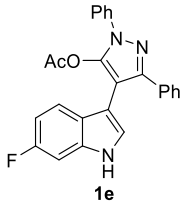
1a''

R_f = 0.3 (petroleum/EtOAc = 10:1, v/v); White solid; 76% yield. **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 7.62 – 7.59 (m, 2H), 7.59 – 7.55 (m, 2H), 7.39 – 7.36 (m, 2H), 7.34 (dt, *J* = 7.7, 0.7 Hz, 1H), 7.27 – 7.24 (m, 1H), 7.23 (dt, *J* = 8.4, 1.4 Hz, 1H), 7.15 – 7.10 (m, 5H), 6.98 – 6.94 (m, 1H), 6.85 (s, 1H), 3.65 (s, 3H), 1.92 (s, 3H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ = 167.6, 150.0, 142.5, 138.3, 137.0, 133.6, 129.3, 129.3, 128.3, 128.3, 128.2, 127.8, 127.8, 127.7, 127.6, 127.6, 127.3, 127.3, 123.1, 121.8, 120.5, 119.5, 109.3, 104.4, 103.9, 32.9, 20.4. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{21}NaN_3O_2^+$ 430.1526; Found 430.1518.



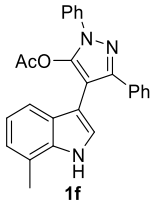
1b

R_f = 0.4 (petroleum/EtOAc = 3:1, v/v); White solid; 86% yield. **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 8.32 (s, 1H), 7.70 (dd, J = 9.0, 1.8 Hz, 2H), 7.67 – 7.63 (m, 2H), 7.52 – 7.47 (m, 2H), 7.40 – 7.36 (m, 1H), 7.26 – 7.21 (m, 3H), 7.19 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 2.4 Hz, 1H), 6.83 (dd, J = 8.4, 2.4 Hz, 1H), 6.75 (d, J = 2.4 Hz, 1H), 3.62 (s, 3H), 2.07 (s, 3H).**^{13}C NMR (151 MHz, $CDCl_3$)** δ = 167.7, 154.3, 150.2, 142.5, 138.2, 133.7, 131.2, 129.4, 128.3, 128.0, 127.8, 127.2, 124.3, 123.2, 113.0, 112.0, 105.8, 104.0, 101.5, 55.7, 20.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{21}N_3NaO_3^+$ 446.1476; Found 446.1477.



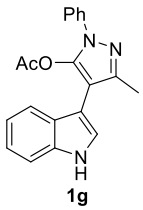
1e

R_f = 0.3 (petroleum/EtOAc = 3:1, v/v); White solid; 77% yield. **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 8.5 (s, 1H), 7.7 – 7.7 (m, 2H), 7.7 – 7.6 (m, 2H), 7.5 – 7.5 (m, 2H), 7.4 – 7.4 (m, 3H), 7.3 – 7.2 (m, 3H), 7.1 (d, J = 2.8 Hz, 1H), 6.9 (t, J = 7.7 Hz, 1H), 2.1 (s, 3H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ = 162.7, 145.3, 137.9, 133.3, 130.1, 128.5, 124.6, 123.5, 123.3, 123.10 (d, J = 46.1 Hz), , 122.8, 119.79 (d, J = 58.4 Hz), 118.4, 116.4, 114.8, 102.7, 100.0, 98.6, 15.6, 15.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{18}FN_3NaO_2^+$ 434.1276; Found 434.1284.



1f

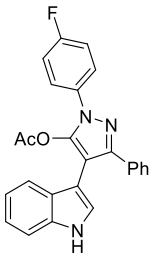
R_f = 0.4 (petroleum/EtOAc = 3:1, v/v); White solid; 83% yield. **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 8.21 (s, 1H), 7.75 – 7.69 (m, 2H), 7.69 – 7.64 (m, 2H), 7.53 – 7.47 (m, 2H), 7.41 – 7.36 (m, 1H), 7.34 (dd, J = 9.8, 2.8 Hz, 1H), 7.27 – 7.20 (m, 3H), 7.04 – 6.99 (m, 3H), 2.48 (s, 3H), 2.03 (s, 3H).**^{13}C NMR (171 MHz, $CDCl_3$)** δ = 167.6, 150.2, 142.6, 138.2, 135.7, 133.6, 129.4, 128.3, 127.9, 127.8, 127.7, 126.4, 123.7, 123.2, 122.9, 120.4, 120.2, 118.1, 106.5, 104.0, 20.4, 16.7. **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{21}N_3O_2^+$ 430.1526; Found 430.1522.



1g

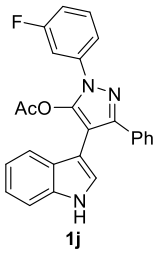
R_f = 0.2 (petroleum/EtOAc = 3:1, v/v); White solid; 43% yield. **^{1}H NMR (600 MHz, DMSO-d_6)** δ = 11.32 (s, 1H), 7.59 – 7.54 (m, 2H), 7.48 (d, J = 7.8 Hz, 2H), 7.46 (d, J = 7.8 Hz, 1H), 7.41 (dt, J = 7.8, 1.2 Hz, 1H), 7.35 – 7.32 (m, 2H), 7.13 – 7.09 (m, 1H), 7.04 – 7.00 (m, 1H), 2.24 (s, 3H), 2.07 (s, 3H). **^{13}C NMR (151 MHz, DMSO-d_6)** δ = 168.2, 147.9, 141.2, 138.4, 136.7, 130.0, 127.5, 126.4, 124.6,

122.2, 121.9, 119.7, 119.6, 112.4, 105.5, 104.5, 20.5, 14.1. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{17}NaN_3O_2^+$ 354.1213; Found 354.1212.



1i

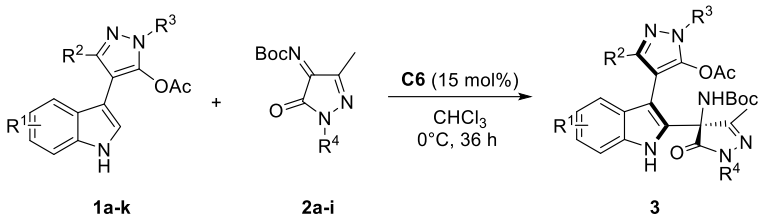
R_f = 0.3 (petroleum/EtOAc = 3:1, v/v); White solid; 77% yield. **^{1}H NMR (600 MHz, CDCl3)** δ = 8.34 (s, 1H), 7.66 – 7.62 (m, 2H), 7.54 (ddd, J = 8.4, 3.0, 1.2 Hz, 1H), 7.51 (dt, J = 9.6, 2.4 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.32 (dt, J = 8.4, 1.2 Hz, 1H), 7.26 – 7.21 (m, 3H), 7.21 – 7.18 (m, 1H), 7.09 – 7.05 (m, 2H), 6.99 (d, J = 2.4 Hz, 1H), 2.06 (s, 3H). **^{13}C NMR (151 MHz, CDCl3)** δ = 167.5, 163.0 (d, J = 247.1 Hz), 150.6, 142.6, 139.6 (d, J = 10.2 Hz), 136.1, 133.3, 130.7 (d, J = 9.2 Hz), 128.4, 128.2, 127.8, 126.7, 124.0, 122.4, 120.2, 120.1, 118.1 (d, J = 3.0 Hz), 114.5, 114.3, 111.4, 110.4, 110.2, 105.7, 104.5, 20.4. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{18}FN_3NaO_2^+$ 412.1276. Found 434.1277.



1j

R_f = 0.3 (petroleum/EtOAc = 3:1, v/v); White solid; 73% yield. **^{1}H NMR (700 MHz, CDCl3)** δ = 8.37 (s, 1H), 7.73 – 7.68 (m, 2H), 7.69 – 7.65 (m, 2H), 7.47 (d, J = 7.7 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.30 – 7.25 (m, 3H), 7.23 – 7.19 (m, 3H), 7.13 – 7.08 (m, 1H), 7.04 (d, J = 2.4 Hz, 1H), 2.05 (d, 3H). **^{13}C NMR (176 MHz, CDCl3)** δ = 162.8, 157.1 (d, J = 247.5 Hz), 145.4, 137.8, 131.3, 129.5 (d, J = 3.1 Hz), 128.6, 123.5, 123.2, 122.9, 121.9, 120.4, 120.4, 119.1, 117.5, 115.3 (d, J = 34.3 Hz), 111.5 (d, J = 22.9 Hz), 106.5, 101.1, 99.0, 15.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{18}FN_3NaO_2^+$ 412.1276; Found 434.1281.

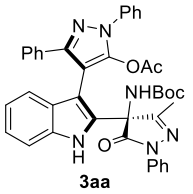
3.2 Synthesis of 3



1a-k **2a-i** **3**

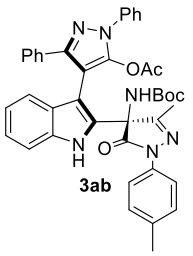
A mixture of **1** (0.1 mmol), **2** (0.12 mmol), **C6** (15 mmol%) and $CHCl_3$ (1.0 mL)

was stirred at 0 °C until the reaction completed (monitored by TLC). The reaction mixture was purified by flash chromatography on silica gel to give compound **3** and further analyzed by NMR, HRMS and HPLC.



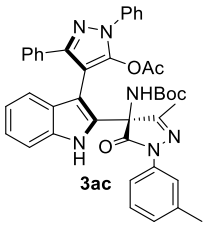
3aa

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 93% yield (63.4 mg, 0.093 mmol); M.P. 153.4 – 154.8 °C; $[\alpha]D^{20}$ = +8.50 (c = 0.25, CH_3OH); HPLC (Daicel chiracel® AD-H, n-Hexane/i-PrOH = 88/12, flow rate: 1.0 mL/min, λ = 254 nm, T = 25°C), t_R = 8.709 min (minor), 37.281 min (minor); 97% ee; **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 10.21 (s, 1H), 8.21 (d, *J* = 7.7 Hz, 2H), 7.74 – 7.66 (m, 4H), 7.50 (t, *J* = 7.7 Hz, 3H), 7.43 – 7.38 (m, 3H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.22 – 7.12 (m, 5H), 7.03 (t, *J* = 7.7 Hz, 1H), 6.79 (s, 1H), 1.80 (s, 3H), 1.27 (s, 3H), 1.16 (s, 9H). **^{13}C NMR (176 MHz, DMSO-d_6)** δ = 169.7, 167.1, 157.9, 154.8, 148.8, 144.3, 139.0, 137.9, 136.6, 133.2, 129.9, 129.3, 128.7, 128.4, 128.2, 128.2, 128.1, 127.3, 127.3, 126.6, 124.6, 122.8, 122.3, 119.9, 119.7, 117.5, 112.5, 102.0, 101.9, 101.9, 80.2, 66.2, 28.4, 19.5, 14.2. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{36}N_6NaO_5^+$ 703.2640; Found 703.2637.



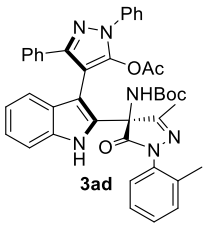
3ab

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 95% yield (66.2 mg, 0.095 mmol); M.P. 149.6 – 151.8 °C. HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 85:15, 1.0 mL/min, at 254nm): t_R = 4.497 min (minor), t_R = 6.786 min (major); 96% ee $[\alpha]_D^{20}$ = −35.7 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 9.92 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 7.2 Hz, 4H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.22 – 7.11 (m, 6H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.48 (s, 1H), 2.34 (s, 3H), 1.77 (s, 3H), 1.31 (s, 3H), 1.24 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 169.0, 165.4, 157.3, 152.5, 148.2, 143.6, 136.9, 135.9, 135.1, 133.4, 132.0, 128.3, 128.2, 127.6, 127.4, 127.0, 126.7, 125.4, 124.7, 122.8, 122.0, 119.8, 119.7, 116.7, 111.0, 104.1, 100.3, 65.3, 62.0, 26.9, 19.9, 18.5, 13.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{41}H_{38}N_6NaO_5^+$ 717.2796; Found 717.2791.



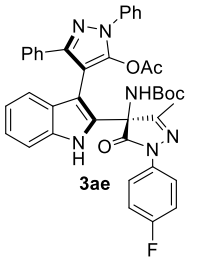
3ac

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 94% yield (65.9 mg, 0.094 mmol); M.P. 154.6 – 155.8 °C. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 7.564 min (minor), t_R = 34.014min (major); 93% ee $[\alpha]_D^{20}$ = −32.2 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 9.90 (s, 1H), 7.97(d, *J* = 12.0 Hz, 2H), 7.69 (t, *J* = 8.4 Hz, 4H), 7.53 – 7.46 (m, 3H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.13 (m, 5H), 7.03 (t, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 7.2 Hz, 1H), 6.49 (s, 1H), 2.39 (s, 3H), 1.78 (s, 3H), 1.28 (d, *J* = 1.4 Hz, 3H), 1.24 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 169.2, 165.4, 157.4, 152.4, 148.2, 143.7, 137.7, 137.5, 136.9, 135.9, 132.0, 128.2, 127.7, 127.6, 127.4, 127.0, 126.7, 125.4, 124.6, 124.5, 122.9, 122.0, 119.8, 119.7, 117.4, 113.9, 111.0, 104.3, 100.3, 65.4, 59.4, 26.9, 20.6, 18.3, 13.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{41}H_{38}N_6NaO_5^+$ 717.2796; Found 717.2987.



3ad

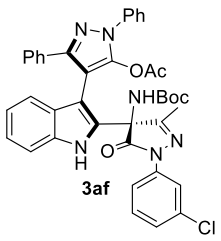
R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 92% yield (64.2 mg, 0.092 mmol); M.P. 153.6 – 154.8 °C. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 220nm): t_R = 14.304 min (major), t_R = 55.674 min (minor); 93% ee $[\alpha]_D^{20}$ = −42.2 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 9.85 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.74 – 7.65 (m, 4H), 7.49 (t, *J* = 7.8 Hz, 3H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.25 – 7.13 (m, 5H), 7.03 (t, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.43 (s, 1H), 2.39 (s, 3H), 1.77 (s, 3H), 1.27 (s, 3H), 1.24 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 170.2, 166.5, 153.3, 149.3, 144.8, 138.8, 138.6, 138.0, 137.0, 133.1, 129.4, 128.8, 128.7, 128.6, 128.1, 127.9, 126.5, 125.8, 125.7, 124.1, 123.2, 121.0, 120.9, 118.5, 115.6, 114.9, 112.1, 105.4, 101.4, 67.5, 60.5, 28.0, 21.8, 19.5, 14.6. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{41}H_{38}N_6NaO_5^+$ 717.2796; Found 717.2795.



3ae

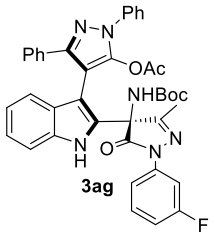
R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 99% yield (68.9 mg, 0.096 mmol); M.P. 146.8 – 150.7°C . HPLC (Daicel Chiralpak IG-, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 13.204 min (minor), t_R = 34.990 min (major); 97% ee $[\alpha]_D^{20}$ = −21.7 (c = 0.25 , CH_3OH). **^{1}H**

NMR (600 MHz, $CDCl_3$) δ = 9.7 (s, 1H), 8.0 (t, J = 9.0, 4.8 Hz, 2H), 7.7 (d, J = 8.4 Hz, 2H), 7.6 (d, J = 7.8 Hz, 2H), 7.5 (t, J = 7.8 Hz, 2H), 7.4 – 7.4 (m, 2H), 7.4 (d, J = 7.8 Hz, 1H), 7.2 – 7.1 (m, 4H), 7.1 – 7.0 (m, 3H), 6.3 (s, 1H), 1.8 (s, 3H), 1.4 (s, 3H), 1.3 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 169.8, 166.2, 159.5 (d, J = 244.5 Hz), 158.4, 153.5, 149.2, 144.5, 137.8, 136.6, 134.6, 132.9, 129.2, 129.2, 128.6, 128.4, 127.9 (d, J = 34.7 Hz), 126.3, 125.5, 123.9, 122.9, 120.8 (d, J = 12.8 Hz), 119.3, 115.4 (d, J = 22.5 Hz), 111.7, 105.1, 101.1, 66.2, 27.9, 19.5, 14.4. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{35}FN_6NaO_5^+$ 721.2546; Found 721.2546.



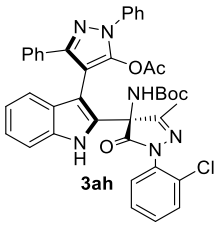
3af

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 93% yield (66.5 mg, 0.093 mmol); M.P. 170.2 – 174.5℃. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 7.230 min (major), t_R = 39.801 min (minor); 93% ee $[\alpha]_D^{20}$ = −38.0 (c = 0.25, CH_3OH). **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 9.74 (s, 1H), 8.07 (t, J = 2.1 Hz, 1H), 7.95 (d, J = 7.4 Hz, 1H), 7.69 – 7.51 (m, 4H), 7.50 – 7.40 (m, 2H), 7.35 (d, J = 8.4 Hz, 1H), 7.33 – 7.29 (m, 1H), 7.27 (d, J = 8.4 Hz, 1H), 7.16 – 7.02 (m, 6H), 6.96 (t, J = 7.7 Hz, 1H), 6.33 (s, 1H), 1.70 (s, 3H), 1.23 (s, 3H), 1.21 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 169.2, 165.2, 157.9, 152.6, 148.2, 143.6, 138.4, 136.8, 135.8, 133.7, 132.0, 129.0, 128.4, 127.7, 127.4, 127.0, 126.8, 125.4, 124.2, 123.7, 123.0, 121.9, 120.0, 119.8, 117.0, 114.5, 110.9, 104.4, 100.1, 81.9, 65.4, 26.9, 18.4, 13.4. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{35}ClN_6NaO_5^+$ 737.2250; Found 737.2250.



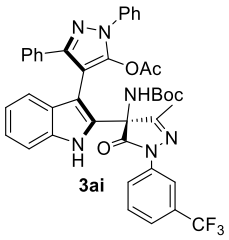
3ag

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 85% yield (59.5 mg, 0.085 mmol); M.P. 170.0 – 172.8 ℃. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 6.164 min (major), t_R = 32.515 min (minor); 96% ee $[\alpha]_D^{20}$ = −25.0 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 9.66 (s, 1H), 8.35 – 8.24 (m, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.70 – 7.64 (m, 4H), 7.54 (t, J = 7.8 Hz, 2H), 7.43 (d, J = 8.2 Hz, 1H), 7.40 (t, J = 7.8 Hz, 1H), 7.34 (d, J = 7.8 Hz, 1H), 7.29 (d, J = 6.6 Hz, 1H), 7.24 – 7.14 (m, 5H), 7.06 – 7.01 (m, 1H), 6.27 (s, 1H), 1.77 (s, 3H), 1.30 (s, 3H), 1.29 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 169.0, 165.2, 161.8 (d, J = 247.2 Hz), 157.3, 152.5, 148.5, 143.6, 138.2 (d, J = 90.6 Hz), 137.5, 135.8, 131.7, 129.5 (d, J = 15.1 Hz), 127.9, 127.5, 127.2, 125.4, 124.7, 123.8, 123.0, 119.8 (d, J = 30.2 Hz), 117.0 (d, J = 3.2 Hz), 116.6, 113.4 (d, J = 21.0 Hz), 110.9, 109.1 (d, J = 25.7 Hz), 103.9, 100.8, 65.3, 26.9, 18.4, 13.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{35}FN_6NaO_5^+$ 721.2546; Found 721.2546.



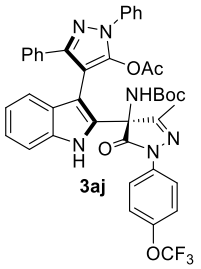
3ah

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 91% yield (64.9 mg, 0.091 mmol); M.P. 127.0 – 129.4 ℃. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 12.423 min (minor), t_R = 19.844 min (major); 97% ee $[\alpha]_D^{20}$ = −35.0 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 10.03 (s, 1H), 8.07 (d, *J* = 7.7 Hz, 2H), 7.67 (d, *J* = 7.0 Hz, 2H), 7.60 (s, 2H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.37 – 7.31 (m, 3H), 7.22 – 7.09 (m, 7H), 7.03 (t, *J* = 7.7 Hz, 1H), 6.60 (s, 1H), 1.77 (s, 3H), 1.29 (s, 3H), 1.26 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 166.8, 159.5, 150.5, 144.2, 137.9, 135.7, 134.8, 132.7, 130.2, 129.5, 129.4, 129.1, 128.7, 128.5, 128.4, 128.1, 128.1, 128.0, 127.7, 127.6, 126.9, 125.4, 124.1, 123.4, 123.3, 120.9, 120.7, 111.3, 105.5, 101.6, 66.3, 65.2, 28.1, 20.2, 20.1, 14.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{35}ClN_6NaO_5^+$ 737.2250; Found 737.2251.



3ai

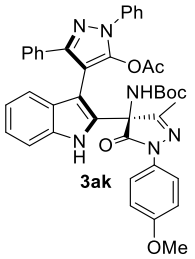
R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 81% yield(60.9 mg, 0.081 mmol); M.P. 127.7 – 129.8 ℃. HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 85:15, 1.0 mL/min, at 254nm): t_R = 4.731 min (minor), t_R = 6.592 min (major); 97% ee $[\alpha]_D^{20}$ = −50.0 (c =0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 10.18 (s, 1H), 8.42 (s, 1H), 8.39 (s, 1H), 7.69 (d, *J* = 7.0 Hz, 2H), 7.68 – 7.62 (m, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.24 – 7.11 (m, 4H), 7.04 (t, *J* = 7.8 Hz, 1H), 1.82 (s, 3H), 1.27 (s, 9H), 1.24 (s, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 171.1, 166.2, 149.4, 144.8, 139.1, 137.9, 133.1, 129.8, 129.5, 128.8, 128.6, 128.2, 128.1, 126.6, 125.0, 124.3, 123.08, 121.36, 121.1, 121.0, 120.5, 114.8, 112.3, 101.4, 66.8, 60.5, 27.9, 19.4, 14.7**. HRMS (ESI-TOF)** m/z: $[M+H]^+$ Calcd for $C_{41}H_{35}F_3N_6O_5^+$ 771.2514; Found 771.2514.



3aj

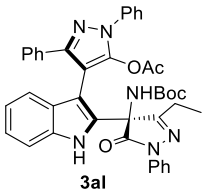
R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 82% yield(62.9 mg, 0.82 mmol); M.P. 152.8 – 154.8℃ . HPLC (Daicel Chiralpak IG, n-hexane/2-propanol = 80:20, 1.0 mL/min, at 254nm): t_R = 7.016 min (minor), t_R = 23.349 min (major); 98% ee $[\alpha]_D^{20}$ = −39.0 (c = 0.25, CH_3OH). **^{1}H NMR**

(600 MHz, $CDCl_3$) δ = 9.85 (s, 1H), 8.13 (d, *J* = 9.2 Hz, 2H), 7.64 (d, *J* = 7.8 Hz, 2H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.40. (t, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.24 – 7.20 (m, 3H), 7.18 (d, *J* = 6.6 Hz, 1H), 7.16 – 7.1. (m, 2H), 7.06 (t, *J* = 7.8 Hz, 1H), 6.58 (s, 1H), 1.75 (s, 3H), 1.32 (s, 3H), 1.22 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 170.1, 166.2, 158.9, 154.0, 149.3, 145.6, 144.6, 137.9, 136.9 (d, *J* = 45.9 Hz), 133.0, 129.3, 128.7, 128.5, 128.0 (d, *J* = 29.0 Hz), 126.4, 125.2, 124.0, 122.9, 121.5, 121.5, 120.9 (d, *J* = 20.8 Hz), 120.5 (d, *J* = 257.0 Hz), 118.8, 111.9, 105.1, 101.2, 66.5, 60.5, 28.0, 19.4, 14.5. **HRMS (ESI-TOF)** m/z: $[M+H]^+$ Calcd for $C_{41}H_{35}F_3N_6O_6^+$787.2463; Found 787.2457.



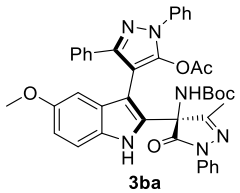
3ak

R_f = 0.60 (petroleum/EtOAc = 3:1, v/v); White solid; 86% yield (61.4 mg, 0.086 mmol); M.P. 139.7 – 140.8℃. HPLC (Daicel Chiralpak OD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 6.908 min (major), t_R = 10.736 min (minor); 96% ee $[\alpha]_D^{20}$ = −57.1 (c = 0.25, CH_3OH). **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 10.36 (s, 1H), 8.10 (d, *J* = 9.0 Hz, 2H), 7.70 (d, *J* = 7.8 Hz, 4H), 7.54 – 7.47 (m, 3H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.23 – 7.09 (m, 4H), 7.03 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 9.6 Hz, 3H), 3.82 (s, 3H), 1.78 (s, 3H), 1.35 (s, 3H), 1.16 (s, 9H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ = 168.9, 165.1, 157.9, 152.5, 148.2, 143.5, 136.7, 136.6, 135.5, 131.9, 131.8, 129.5, 128.4, 127.7, 127.6, 127.1, 126.9, 126.9, 125.3, 124.1, 123.1, 121.9,1 120.1, 119.9, 115.7, 110.6, 104.4, 99.9, 65.2, 54.5, 27.0, 18.6, 13.3. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{41}H_{38}NaN_6O_6^+$ 733.2746; Found 733.2753.



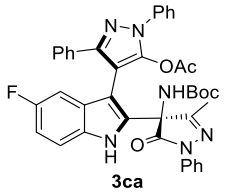
3al

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 95% yield (65.7 mg, 0.095 mmol); M.P. 168.9 – 170.3 ℃. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 6.901 min (major), t_R = 17.438 min (minor); 98% ee. $[\alpha]_D^{20}$ = 18.3 (c = 0.25 , CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 9.97 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 2H), 7.78 – 7.60 (m, 4H), 7.48 (d, *J* = 7.8 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.41 – 7.34 (m, 3H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.23 – 7.09 (m, 5H), 7.02 (t, *J* = 7.8 Hz, 1H), 6.46 (s, 1H), 2.13 (q, *J* = 7.2 Hz, 2H), 1.26 (s, 9H), 1.22 (s, 3H), 0.93 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 170.2, 166.3, 162.0, 148.9, 144.6, 138.6, 137.8, 132.8, 129.1, 128.7, 128.6, 128.3, 127.9, 127.6, 126.2, 125.7, 124.6, 123.8, 122.8, 120.7, 120.6, 117.6, 111.9, 105.0, 101.2, 66.3, 60.3, 27.8, 22.1, 19.1, 8.0. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{41}H_{38}NaN_6O_5^+$ 717.2796; Found.717.2795.



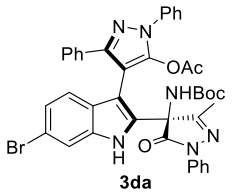
3ba

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 92% yield (65.2 mg, 0.092 mmol); M.P. 149.7 – 151.5 ℃. HPLC (Daicel Chiralpak IG, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 7.016 min (major), t_R = 23.349 min (minor); 97% ee $[\alpha]_D^{20}$ = −7.1 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 10.12 (s, 1H), 8.21 (d, *J* = 8.2 Hz, 2H), 7.70 (t, *J* = 7.0 Hz, 4H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.40 – 7.35 (m, 2H), 7.20 (t, *J* = 7.2 Hz, 2H), 7.16 (d, *J* = 7.2 Hz, 2H), 6.83 (dd, *J* = 9.0, 3.6 Hz, 1H), 6.78 (s, 1H), 6.72 (d, *J* = 2.4 Hz, 1H), 3.64 (s, 3H), 1.77 (s, 3H), 1.30 (s, 3H), 1.15 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 170.9, 166.5, 158.9, 154.9, 149.4, 144.9, 138.7, 138.1, 133.2, 132.4, 129.4, 129.3, 129.0, 128.6, 128.1, 127.8, 126.6, 125.9, 125.0, 123.1, 117.9, 115.2, 113.4, 105.2, 101.6, 101.3, 66.7, 55.8, 27.9, 19.5, 14.6. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ $C_{41}H_{38}NaN_6O_6^+$ 733.2746; Found 733.2750.



3ca

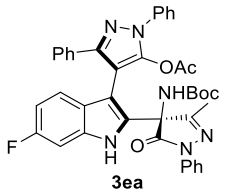
R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 90% yield (62.9 mg, 0.090 mmol); M.P. 172.9 – 174.3 ℃. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 3.539 min (major), t_R = 11.223 min (minor); 96% ee $[\alpha]_D^{20}$ = −33.3 (c = 0.25 , CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 10.19 (s, 1H), 8.09 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 7.0 Hz, 2H), 7.65 (d, *J* = 7.7 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.31 (m, 4H), 7.23 – 7.12 (m, 4H), 6.98 (dd, *J* = 9.1, 2.8 Hz, 1H), 6.89 (s, 1H), 6.50 (s, 1H), 1.78 (s, 3H), 1.29 (s, 3H), 1.26 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 170.9, 166.5, 161.8, 160.2, 149.2, 144.8, 138.5, 138.0, 137.4, 133.0, 129.4, 129.1, 128.6, 128.2, 127.9, 126.4, 125.8, 125.3, 125.1, 123.2, 122.0, 121.9, 117.9, 110.2, 110.1, 105.9, 101.2, 98.9, 98.7, 66.7, 60.5, 27.9, 19.4, 14.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{35}FN_6NaO_5^+$ 721.2546; Found 721.2551.



3da

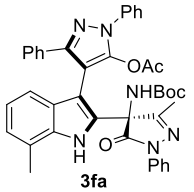
R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 58% yield (43.8 mg, 0.058 mmol); M.P.164-167.3 ℃. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 5.194 min (minor), t_R = 16.300 min (major); 96% ee $[\alpha]_D^{20}$ = −52.9 (c = 0.25, CH_3OH). **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 10.18 (s, 1H), 8.42 (s, 1H), 8.39 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 7.2 Hz, 2H), 7.66 (d, *J* = 6.6 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.43 (t, *J* = 3.6 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.24 – 7.12 (m, 4H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.55 (s, 1H), 1.82 (s, 3H), 1.27 (s, 9H), 1.24 (s, 3H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ = 170.2, 166.4, 158.4, 153.8, 149.2,

144.7, 138.5, 137.9, 136.9, 133.0, 129.3, 128.9, 128.7, 128.5, 128.0, 127.7, 126.4, 125.7, 124.8, 124.0, 123.0, 120.9, 120.8, 117.8, 112.0, 105.3, 101.3, 66.4, 60.4, 27.9, 19.4, 14.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{35}BrNaN_6O_5^+$ 781.1745; Found 781.1739.



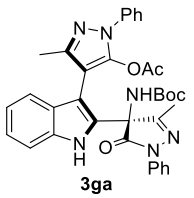
3ea

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 90% yield (62.7 mg, 0.090 mmol); M.P.172.9-174.3 °C. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 11.582 min (minor), t_R = 56.377 min (major); 96% ee $[\alpha]_D^{20}$ = −33.3 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 10.34 (s, 1H), 8.03 (s, 2H), 7.75 – 7.50 (m, 4H), 7.40 (t, J = 7.8 Hz, 2H), 7.35 – 7.21 (m, 3H), 7.20 – 7.00 (m, 6H), 6.69 (s, 1H), 6.52 (s, 1H), 1.71 (s, 3H), 1.21 (s, 3H), 1.18 (s, 9H).1.17 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 169.1, 165.2, 162.0 (d, J = 244.9 Hz), 157.7, 152.6, 148.2, 143.6, 138.8 (d, J = 10.7 Hz), 136.8, 135.7, 131.9, 129.2 (d, J = 9.1 Hz), 128.3, 127.6, 127.4, 127.0, 126.8, 125.4, 124.2, 123.0, 121.9, 119.9 (d, J = 18.2 Hz), 112.1, 110.8, 110.4 (d, J = 21.1 Hz), 104.3 (d, J = 25.0 Hz), 100.1, 65.4, 26.9, 18.4, 13.4. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ $C_{40}H_{35}FN_6\ NaO_5^+$ 721.2546; Found 721.2546.



3fa

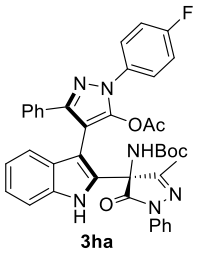
R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 78% yield (54.4 mg, 0.078 mmol);M.P.168.9-170.3 °C. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 8.211 min (minor), t_R = 48.264 min (major); 96% ee $[\alpha]_D^{20}$ = −23.3 (c = , CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ =9.35 (s, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.72 – 7.61 (m, 4H), 7.47 (t, J = 7.8 Hz, 2H), 7.37 (t, J = 7.8 Hz, 1H), 7.30 (t, J = 7.8 Hz, 2H), 7.21 (d, J = 7.8 Hz, 1H), 7.19 – 7.08 (m, 4H), 7.03 (d, J = 7.2 Hz, 1H), 6.97 (t, J = 7.8 Hz, 1H), 6.46 (s, 2H), 2.52 (s, 3H), 1.76 (s, 3H), 1.31 (s, 9H), 1.28 (s, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 168.7, 165.3, 152.3, 148.2, 143.5, 137.5, 136.9, 135.1, 131.9, 128.2, 127.8, 127.45, 127.40, 127.0, 126.7, 125.4, 124.6, 123.7, 123.6, 122.0, 120.2, 119.7, 117.6, 116.8, 104.8, 100.3, 65.2, 59.4, 27.0, 18.4, 15.7, 13.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{41}H_{38}N_6NaO_5^+$ 717.2796; Found 717.2795.



3ga

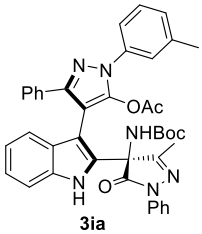
R_f = 0.20 (petroleum/EtOAc = 3:1, v/v); White solid; 87% yield (54.1 mg, 0.087 mmol); M.P.168.9-170.3 °C. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 7.647 min (major), t_R = 38.338 min (minor); -98% ee. $[\alpha]_D^{20}$ = −10.7 (c = 0.25, CH_3OH). **^{1}H NMR**

(700 MHz, $CDCl_3$) δ = 10.16 (s, 1H), 8.06 (s, 2H), 7.60 (d, *J* = 7.7 Hz, 2H), 7.46 (d, *J* = 7.7 Hz, 2H), 7.43 – 7.28 (m, 5H), 7.24 – 7.11 (m, 2H), 7.08 (d, *J* = 7.7 Hz, 1H), 6.42 (s, 1H), 2.19 (s, 3H), 1.85 (s, 3H), 1.30 (s, 9H), 1.26 (s, 3H). **^{13}C NMR (176MHz, $CDCl_3$)** δ = 169.1, 165.5, 157.1, 147.9, 142.5, 137.4, 136.9, 135.6, 128.2, 127.8, 127.3, 126.3, 124.5, 123.7, 122.8, 121.7, 119.6, 119.1, 116.7, 110.9, 103.5, 101.6, 65.4, 26.9, 18.3, 13.1, 12.1. **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{35}H_{34}N_6O_5^+$ 641.2483; Found 641.2491



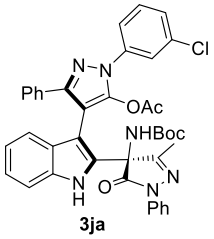
3ha

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 92% yield (64.1 mg, 0.092mmol); M.P.177.0-172.5℃ . HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 6.806 min (minor), t_R = 62.221 min (major); 96% ee $[\alpha]_D^{20}$ = −8.7 (c = 0.25 , CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 9.78 (s, 1H), 7.95 – 7.83 (m, 2H), 7.66 (t, *J* = 7.8 Hz, 4H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.26 – 7.12 (m, 5H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.87 (t, *J* = 8.4 Hz, 1H), 6.41 (s, 1H), 1.77 (s, 3H), 1.32 (s, 3H), 1.28 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 169.1, 165.2, 162.0 (d, *J* = 244.9 Hz), 157.7, 152.6, 148.2, 143.6, 138.8 (d, *J* = 10.7 Hz), 136.8, 135.7, 131.9, 129.2 (d, *J* = 9.2 Hz), 128.3, 127.6, 127.4, 127.0, 126.8, 125.4, 124.2, 123.0, 121.9, 119.9, 119.8, 112.1, 110.8, 110.4 (d, *J* = 21.1 Hz), 104.4, 104.2, 100.1. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ $C_{40}H_{35}FNaN_6O_5^+$ 721.2546; Found.721.2543



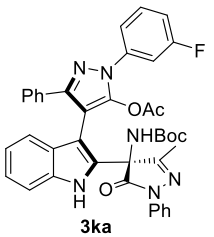
3ia

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 92% yield(63.9 mg, 0.092 mmol), m.p.176.9-177.5 ℃. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 6.164 min (minor), t_R = 32.515 min (major); 95% ee $[\alpha]_D^{20}$ = −58.3 (c = 0.25, CH_3OH). **^{1}H NMR (700 MHz,$CDCL_3$)** δ = 9.95 (s, 1H), 8.14 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 7.0 Hz, 2H), 7.53 (s, 1H), 7.47 (d, *J* = 7.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 3H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.22 – 7.12 (m, 6H), 7.02 (t, *J* = 7.7 Hz, 1H), 6.48 (s, 1H), 2.46 (s, 3H), 1.78 (s, 3H), 1.26 (s, 3H), 1.25 (s, 9H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ = 169.2, 165.3, 157.49, 152.52, 148.1, 143.6, 138.3, 137.6, 136.8, 135.9, 132.0, 128.0, 127.8, 127.6, 127.5, 127.4, 126.9, 125.4, 124.6, 123.8, 122.9, 122.5, 119.8, 119.8, 119.0, 116.7, 111.0, 104.3, 100.2, 65.4, 26.9, 20.4, 18.3, 13.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{41}H_{38}NaN_6O_5^+$ 717.2796; Found 717.2790.



3ja

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 68% yield (49.8 mg, 0.068 mmol); M.P.160.9-163.5℃ . HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 4.671 min (minor), t_R = 30.692 min (major); 97% ee $[\alpha]_D^{20}$ = −15.0 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 10.12 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.22 – 7.16 (m, 5H), 7.14 (t, *J* = 7.8 Hz, 2H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.70 (s, 1H), 1.77 (s, 3H), 1.28 (s, 3H), 1.17 (s, 9H).**^{13}C NMR (151 MHz, $CDCl_3$)** δ = 170.2, 166.3, 158.6, 153.7, 149.7, 144.7, 138.9, 138.5, 137.0, 134.9, 132.7, 130.4, 129.1, 128.5, 128.2, 127.6, 126.4, 125.6, 124.9, 124.0, 122.7, 120.9, 120.8, 120.7, 117.5, 112.1, 104.9, 101.9, 66.5, 53.5, 27.9, 19.4, 14.5. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ $C_{40}H_{35}ClNaN_6O_5^+$ 737.2250; Found 737.2250.



3ka

R_f = 0.40 (petroleum/EtOAc = 3:1, v/v); White solid; 70% yield (47.6 mg, 0.070 mmol); M.P.175.9-177.5℃. HPLC (Daicel Chiralpak AD-H, n-hexane/2-propanol = 88:12, 1.0 mL/min, at 254nm): t_R = 5.104 min (minor), t_R = 41.556 min (major); 91% ee $[\alpha]_D^{20}$ = −16.6 (c = 0.25, CH_3OH). **^{1}H NMR (600 MHz, $CDCl_3$)** δ = 10.12 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 2H), 7.71 – 7.61 (m, 4H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.23 – 7.11 (m, 7H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.70 (s, 1H), 1.77 (s, 3H), 1.28 (s, 3H), 1.17 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ = 170.7, 166.4, 162.0 (d, *J* = 248.1 Hz), 158.8, 149.5, 144.8, 138.6, 137.2, 134.1 (d, *J* = 3.0 Hz), 133.0, 129.0, 128.7 (d, *J* = 23.6 Hz), 128.2, 126.5, 125.7, 125.2 (d, *J* = 8.8 Hz), 125.1, 124.1, 120.9 (d, *J* = 26.6 Hz), 117.8, 116.9 (d, *J* = 23.0 Hz), 112.3, 105.4, 101.4, 66.6, 53.5, 27.9, 19.4, 14.7. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{35}FN_6NaO_5^+$ 721.2546; Found 721.2549.

4. Investigation of configurational stability

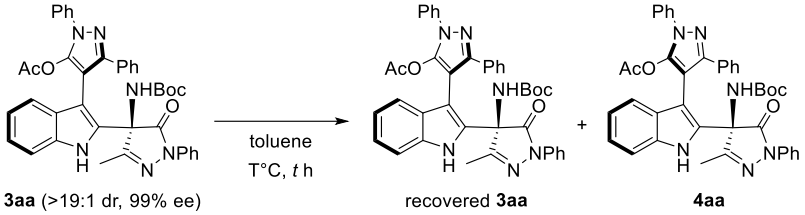
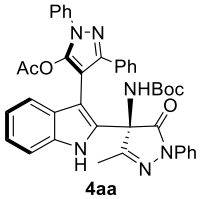


Table3. Investigation of Configurational Stability

Entry	T (°C)	*t* (h)	Yield (%) [a]	**3aa**:**4a** [b]	*ee* [c]
1	80	3	94	>19:1	99
2	80	6	91	15:1	99
3	80	12	86	12:1	99
4	100	3	96	15:1	99
5	100	6	91	12:1	99
6	100	12	85	5:1	99

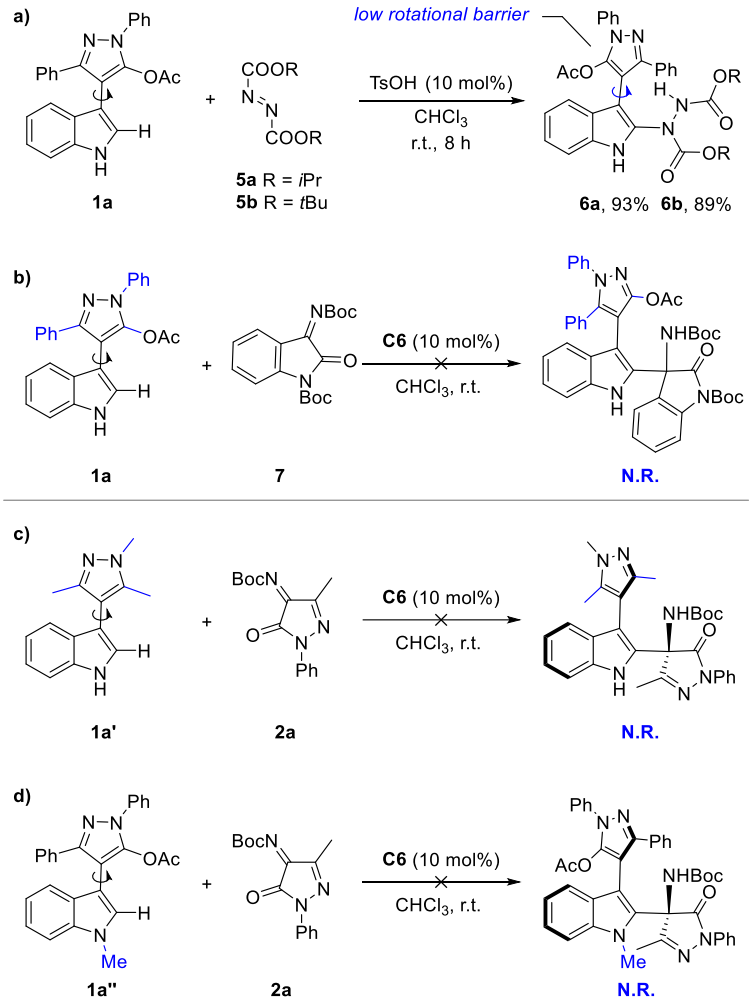
[a]Isolated yield. [b]Determined by crude NMR. [c] The enantiomeric excess was determined by HPLC.

The compound **3aa** (67.7 mg, 0.099 mmol) in toluene (1 mL) was stirred at 80°C or 100°C for 3 h, 6 h and 12 h, purified by flash chromatography on silica gel (petroleum/EtOAc = 5:1, v/v) to give recovered **3aa** and **4aa** then further analyzed by NMR, HRMS and HPLC.

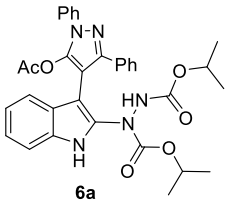


R_f = 0.30 (petroleum/EtOAc = 5:1, v/v); White solid; **^{1}H NMR (700 MHz, $CDCl_3$)** δ = 9.27 (s, 1H), 7.59 – 7.52 (m, 4H), 7.48 – 7.44 (m, 2H), 7.43 – 7.36 (m, 5H), 7.26 – 7.20 (m, 3H), 7.11 – 7.05 (m, 2H), 6.98 – 6.90 (m, 2H), 6.85 (s, 1H), 6.05 (s, 1H), 1.94 (s, 3H), 1.91 (s, 3H), 1.28 (s, 9H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ = 169.1, 165.6, 156.8, 152.4, 150.1, 142.6, 136.9, 136.6, 135.1, 131.6, 128.2, 127.4, 127.3, 127.1, 126.9, 126.8, 125.3, 124.7, 123.8, 123.0, 122.1, 119.7, 119.5, 117.5, 110.5, 104.4, 100.1, 89.4, 65.2, 26.9, 19.1, 13.1. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{40}H_{37}N_6NaO_5^+$ 703.2640; Found 703.2633.

5. Control experiments

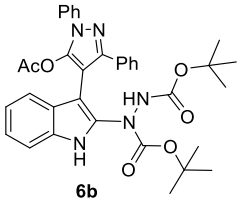


To further probe the stability of the chiral axis in the new 3,4'-indole-pyrazole system, we conducted the reaction of HOMO-raised **1a** with azodicarboxylates **5a** and **5b**. Products **6a** and **6b** were obtained in high yields by using *p*-toluenesulfonic acid (TsOH) as the catalyst. In sharp contrast with **3aa**, **5a** and **5b** have conformationally flexible axis between the bis-pentatomic heteroaryls, no diastereomeric isomers or enantiomers could be identified. This phenomenon indicates that the bulky quaternary carbon introduced to the C2-position of the indole is important for improving the rotation barrier. When imine **7** derived from isatin was used, no product was obtained under the standard conditions. When **1a'** was used to replace **1a**, no product was observed under the standard conditions. When *N*-protected substrate **1a''** was used to replace **1a**, no product was observed under the standard conditions.



6a

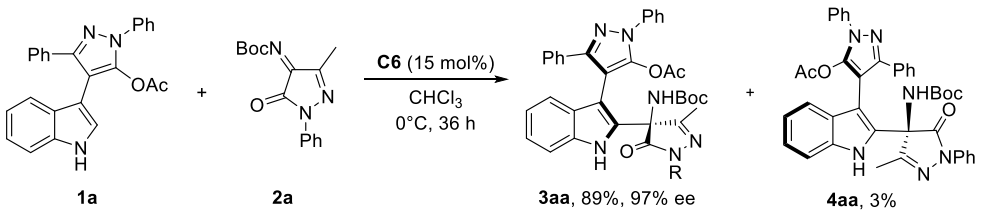
^{1}H NMR (600 MHz, DMSO-d_6) δ = 11.02 (s, 1H), 9.64 (s, 1H), 7.71 (d, J = 7.8 Hz, 2H), 7.56 – 7.50 (m, 4H), 7.40 – 7.33 (m, 2H), 7.16 – 7.11 (m, 3H), 7.01 (t, J = 7.8 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.75 (t, J = 7.2 Hz, 1H), 4.81 (s, 1H), 4.77 (s, 1H), 2.01 (s, 3H), 1.13 (d, J = 13.4 Hz, 12H). **^{13}C NMR (151 MHz, DMSO-D_6)** δ = 167.636, 154.533, 149.536, 143.701, 138.607, 134.011, 133.806, 129.872, 128.471, 128.158, 127.766, 127.044, 126.681, 122.551, 122.199, 119.652, 119.572, 112.282, 102.311, 79.697, 70.719, 69.157, 22.277, 22.131, 20.429. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{33}N_6NaO_6^+$ 618.2324; Found 618.2319.



6b

^{1}H NMR (600 MHz, DMSO-d_6) δ = 10.99 (s, 1H), 9.24 (s, 1H), 7.75 (d, J = 7.8 Hz, 2H), 7.58 – 7.54 (m, 4H), 7.43 – 7.39 (m, 2H), 7.19 – 7.15 (m, 3H), 7.05 – 7.01 (m, 1H), 6.89 (d, J = 7.8 Hz, 1H), 6.79 (d, J = 7.8 Hz, 1H), 2.04 (s, 3H), 1.46 – 1.40 (m, 9H), 1.34 (s, 9H). **^{13}C NMR (151 MHz, DMSO-d_6)** δ = 167.660, 149.635, 143.783, 138.648, 134.701, 134.089, 133.762, 129.854, 128.457, 128.122, 127.712, 127.081, 122.510, 121.993, 119.470, 102.359, 80.306, 79.696, 76.572, 28.547, 28.315, 20.437. **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{37}N_6NaO_6^+$ 646.2637; Found 646.2642.

6. 1 mmol Scale synthesis of compound 3aa

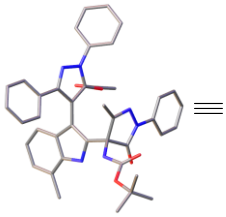


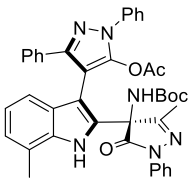
1a **2a** **3aa**, 89%, 97% ee **4aa**, 3%

A mixture of **1a** (1 mmol, 393.4 mg), **2a** (1.2 mmol 344.8 mg), **C6** (0.15 mmol 115.9 mg), and $CHCl_3$ (10 mL) was stirred at 0 ℃ for 36 h. The reaction mixture was concentrated and then the residue was purified by flash chromatography on silica gel (petroleum/EtOAc = 10:1, v/v) to give main compound **3aa** in 89% yield (604.3 mg, 0.890 mmol) and **4aa** in 3% yield (19.6 mg, 0.029 mmol).

7. Crystal data for compound 3fa

To a 10 mL tube containing **3fa** (30.0 mg) was added a 2:1:1 mixture of ethyl acetate, dichloromethane, and petroleum ether (3 mL). A clear solution was obtained through ultrasound treatment and was kept at room temperature for 7 days to get crystals of **3fa**, which were characterized by single crystal X-ray diffraction. The data were collected by an Agilent Gemini. CCDC 2128813 (**3fa**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.





3fa (CCDC 2128813)

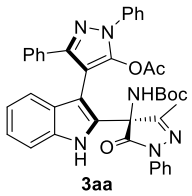
(Ellipsoid contour probability 50%)

Identification code	20210519210101942	
Chemical formula	$C_{41}H_{38}N_6O_5$	
Formula weight	694.77 g/mol	
Temperature	293(2) K	
Wavelength	1.54178 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 13.4858(7) Å	
	b = 13.5152(8) Å	α = 90°
	c = 20.4464(11) Å	β = 90°
Volume	3726.6(4) $Å^3$	γ = 90°
Z	4	
Density (calculated)	1.238 g/cm^3	
Absorption coefficient	0.673 mm^{-1}	
F(000)	1464	
Theta range for data collection	3.92 to 68.40°	
Index ranges	-16<=h<=11, -15<=k<=16, -21<=l<=24	
Reflections collected	72588	
Independent reflections	6774 [R(int) = 0.0794]	
Coverage of independent reflections	99.6%	
Absorption correction	Multi-Scan	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2016/6 (Sheldrick, 2016)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	6774 / 0 / 483	
Goodness-of-fit on F^2	1.062	
Final R indices	4682 data; I>2σ(I)	
	all data	R1 = 0.0563,

		wR2 = 0.1287
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0883P)^2+0.0385P]$ where $P=(F_o^2+2F_c^2)/3$	R1 = 0.0863, wR2 = 0.1573
Absolute structure parameter	0.02(12)	
Largest diff. peak and hole	0.169 and -0.291 eÅ^{-3}	
R.M.S. deviation from mean	0.055 eÅ^{-3}	

8. HPLC chromatograms

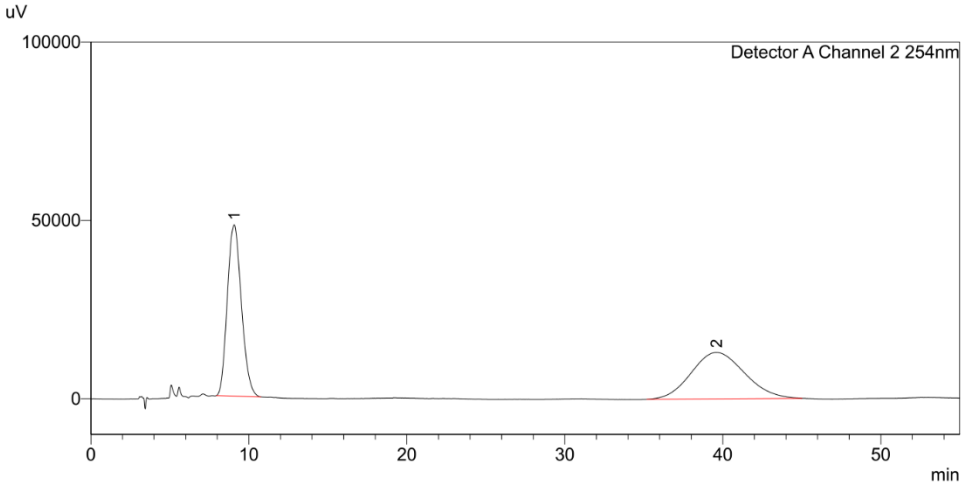
Peak Analysis Report



3aa

Detector A Channel 2 254nm

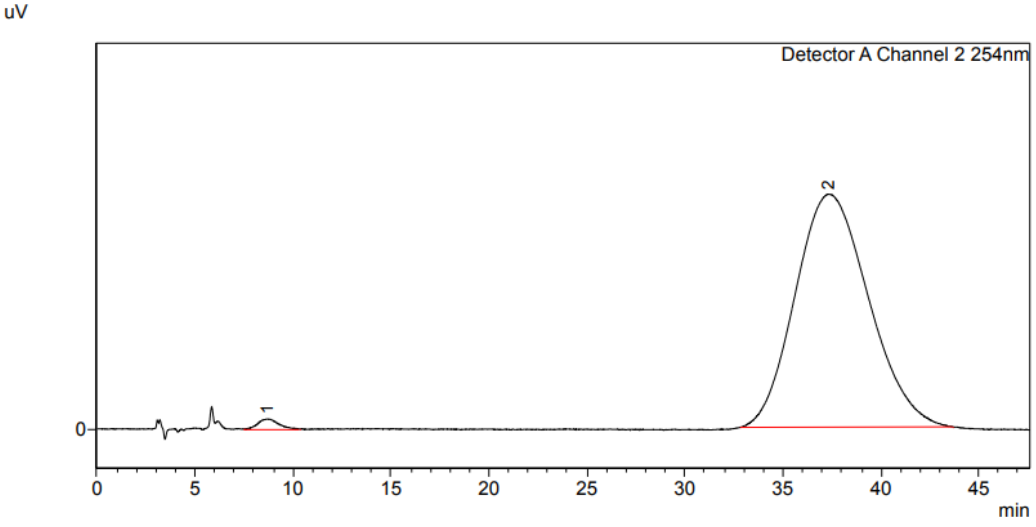
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	9.067	48022	2978526	49.402
2	39.596	13016	3050598	50.598
Total		61038	6029124	100.000



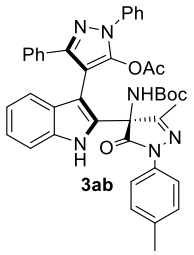
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	8.681	819	63732	1.329
2	37.327	18147	4730906	98.671
Total		18966	4794637	100.000

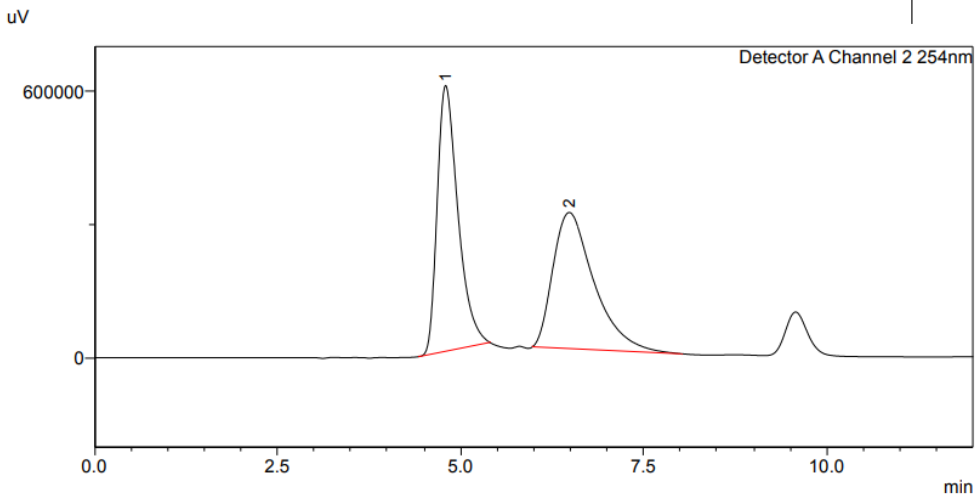


Peak Analysis Report



Detector A Channel 2 254nm

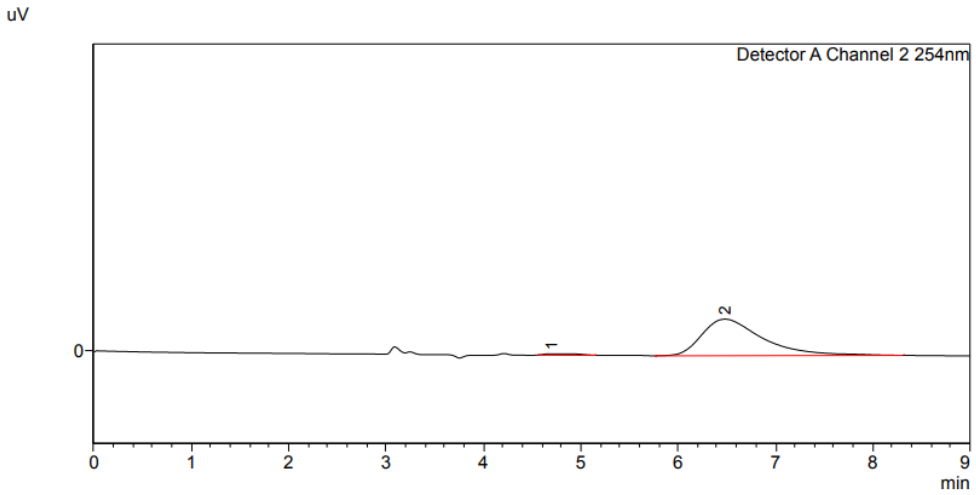
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	4.797	598943	11813857	49.637
2	6.486	306824	11986446	50.363
Total		905766	23800303	100.000



Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	4.703	428	10765	2.041
2	6.483	11922	516806	97.959
Total		12350	527571	100.000



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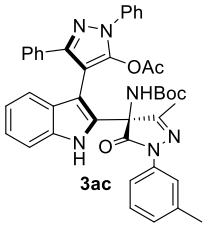
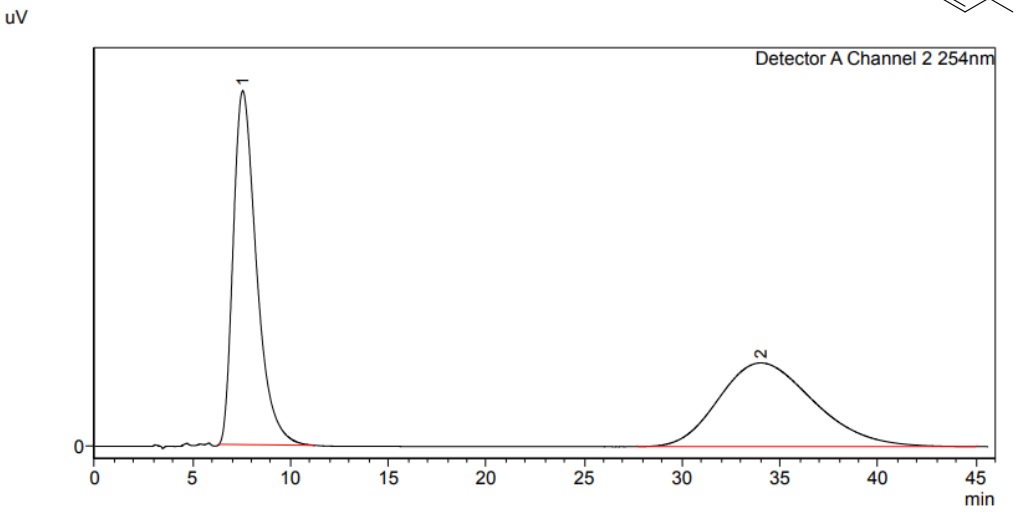


Detector A Channel 2 254nm

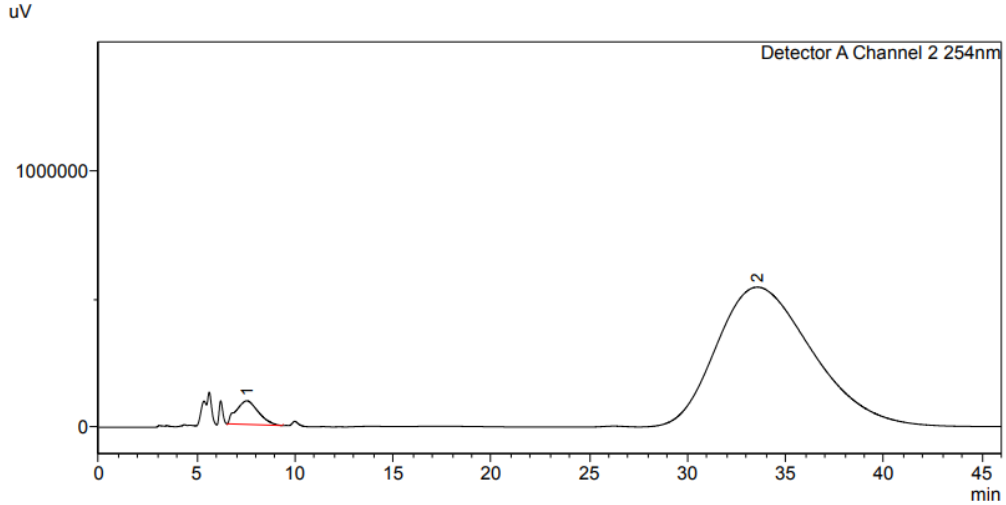
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.564	311018	25657033	50.727
2	34.014	73613	24922025	49.273
Total		384631	50579058	100.000



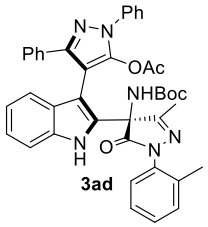
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.559	92688	7264492	3.739
2	33.562	545475	187002955	96.261
Total		638163	194267447	100.000



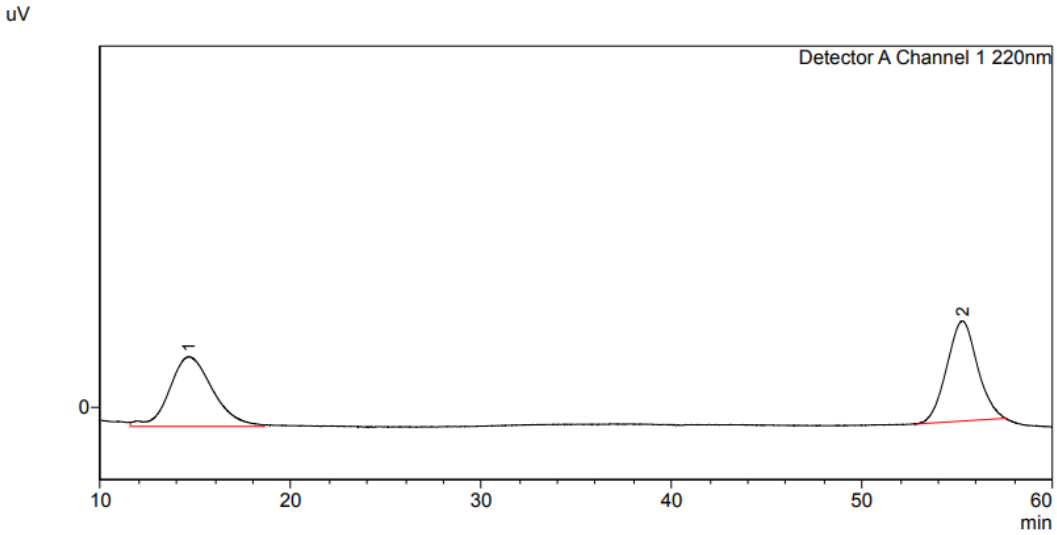
Peak Analysis Report



3ad

Detector A Channel 1 220nm

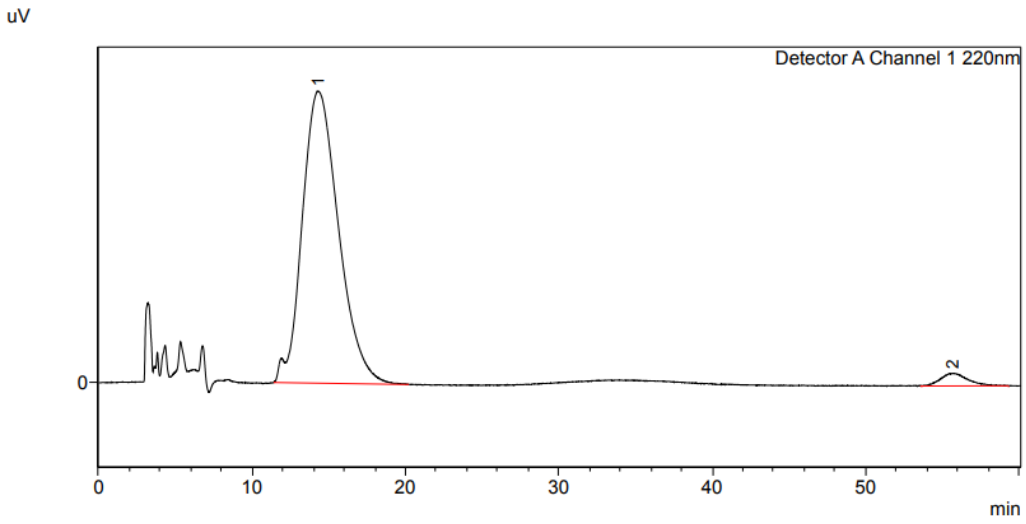
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	14.627	9669	1526312	49.472
2	55.284	13891	1558885	50.528
Total		23560	3085197	100.000



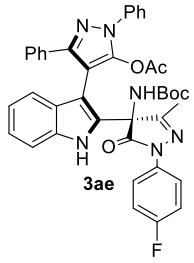
Peak Analysis Report

Detector A Channel 1 220nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	14.304	69743	11492348	96.890
2	55.674	2992	368838	3.110
Total		72735	11861186	100.000

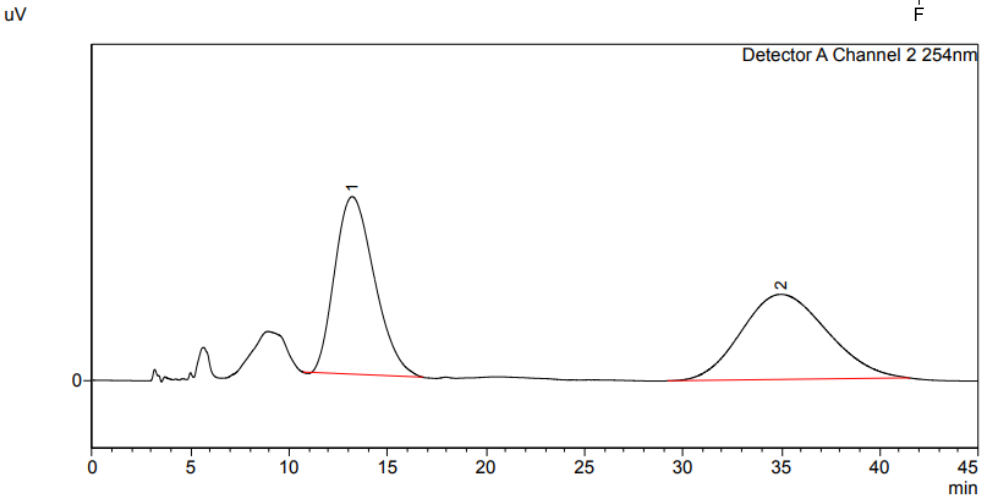


Peak Analysis Report



Detector A Channel 2 254nm

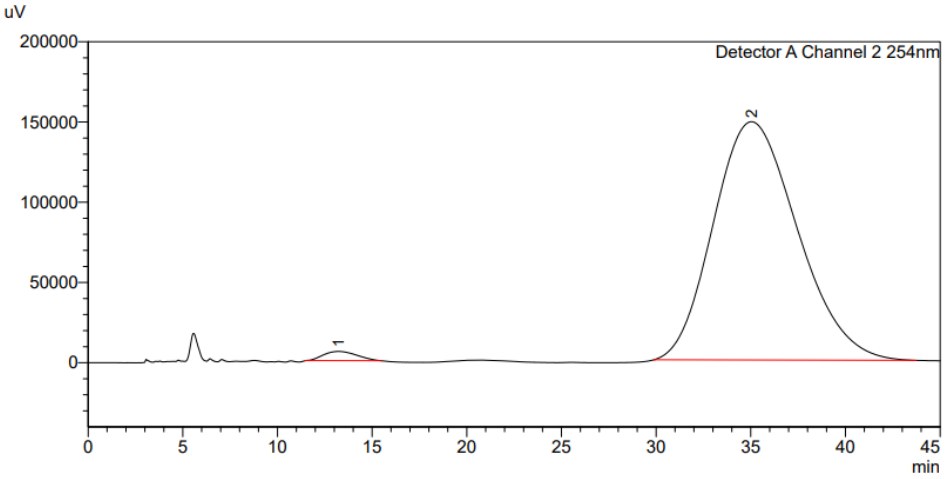
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	13.204	79445	11128876	49.071
2	34.990	38088	11550203	50.929
Total		117533	22679079	100.000



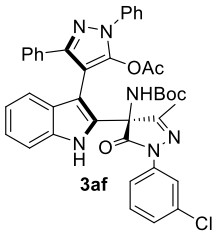
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	13.235	5746	705914	1.515
2	35.055	148458	45897276	98.485
Total		154204	46603189	100.000

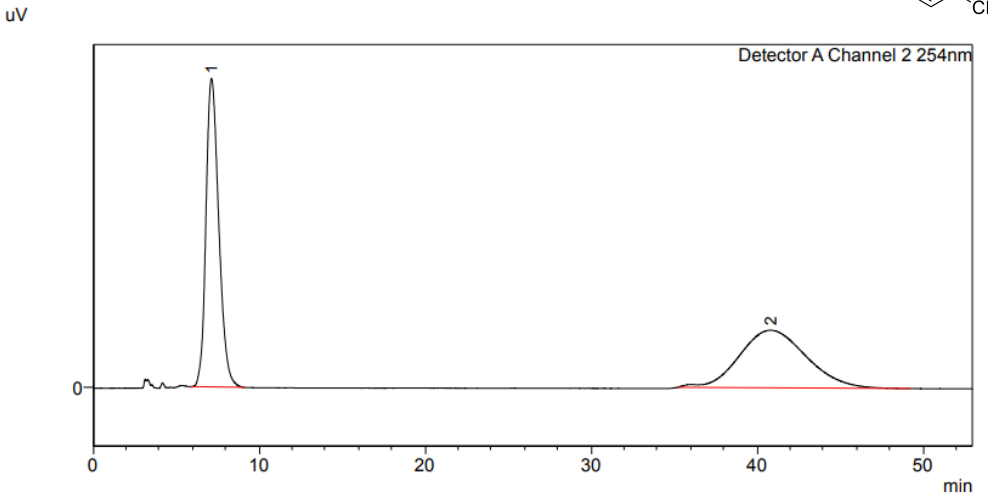


Peak Analysis Report



Detector A Channel 2 254nm

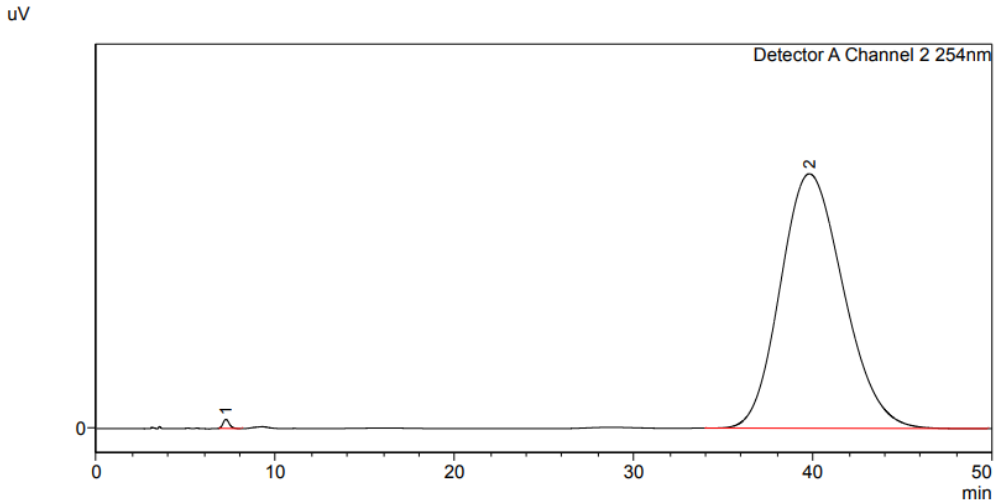
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.153	53938	2886969	50.616
2	40.826	10069	2816729	49.384
Total		64007	5703698	100.000



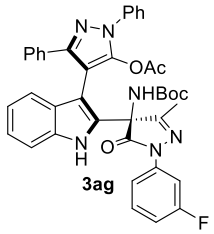
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.230	11919	286764	0.352
2	39.801	331444	81099669	99.648
Total		343363	81386433	100.000

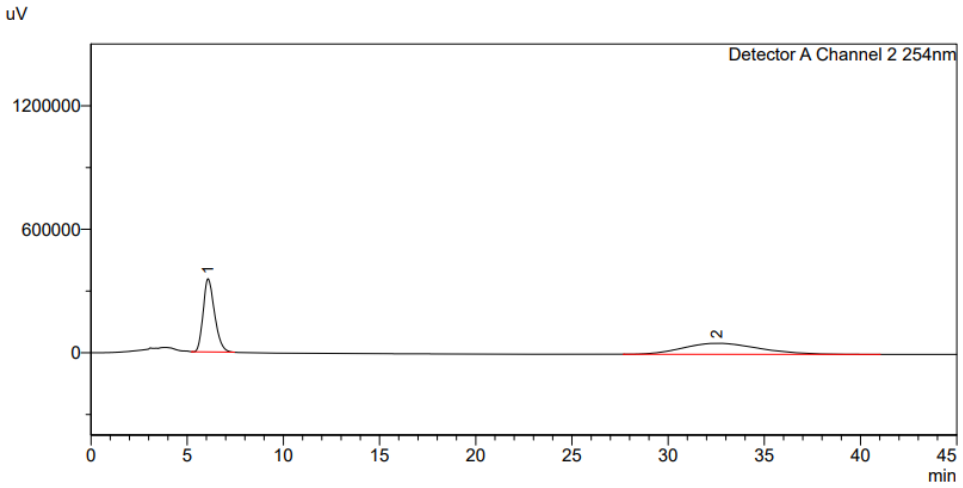


Peak Analysis Report



Detector A Channel 2 254nm

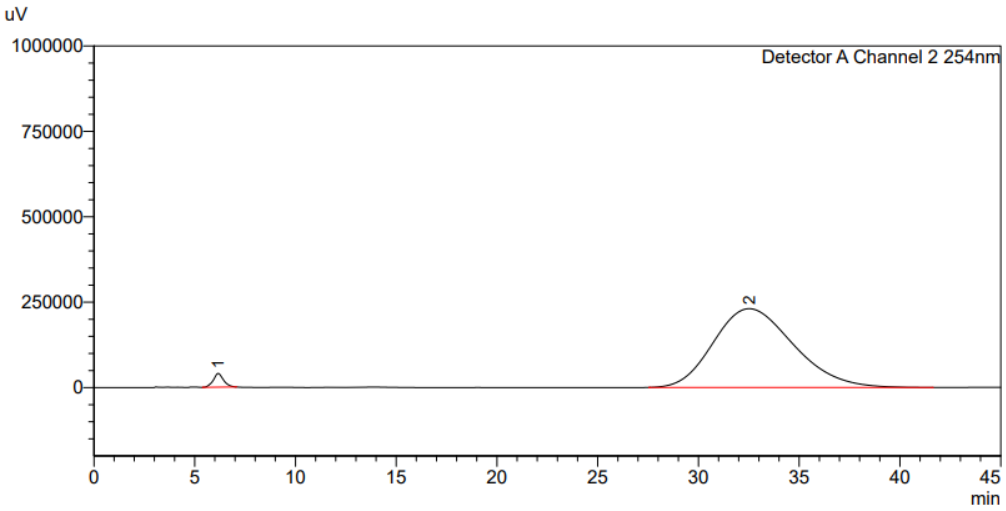
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.086	355413	14659042	49.753
2	32.529	53695	14804882	50.247
Total		409109	29463924	100.000



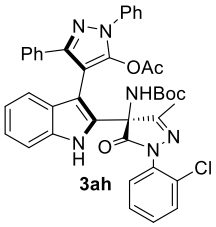
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.164	40257	1423369	2.181
2	32.515	230548	63835051	97.819
Total		270805	65258420	100.000



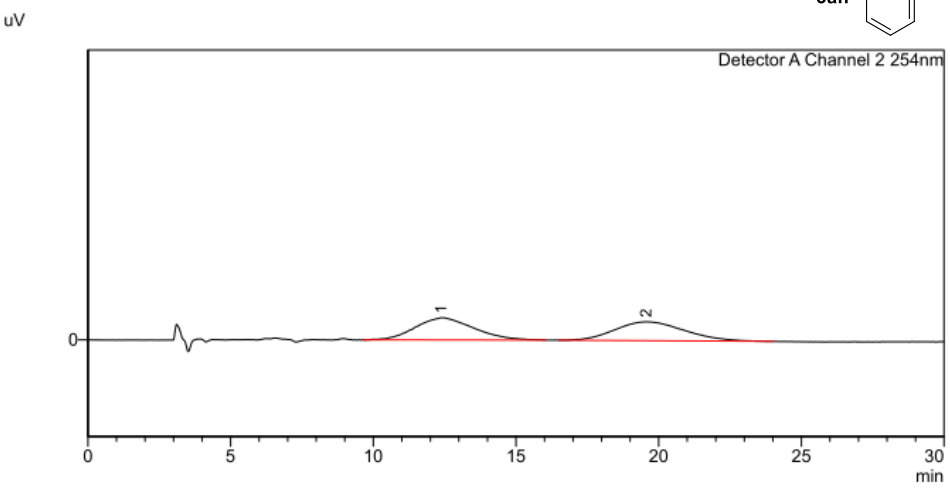
Peak Analysis Report



3ah

Detector A Channel 2 254nm

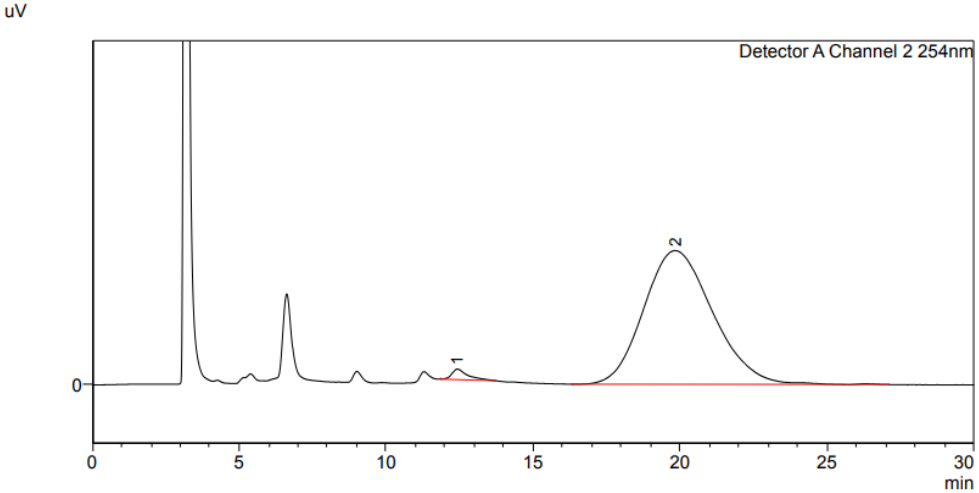
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	12.363	2298	324216	49.405
2	19.560	1953	332026	50.595
Total		4251	656242	100.000



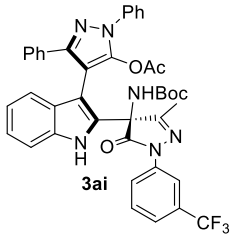
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	12.423	1849	70034	1.801
2	19.844	23333	3818466	98.199
Total		25182	3888501	100.000

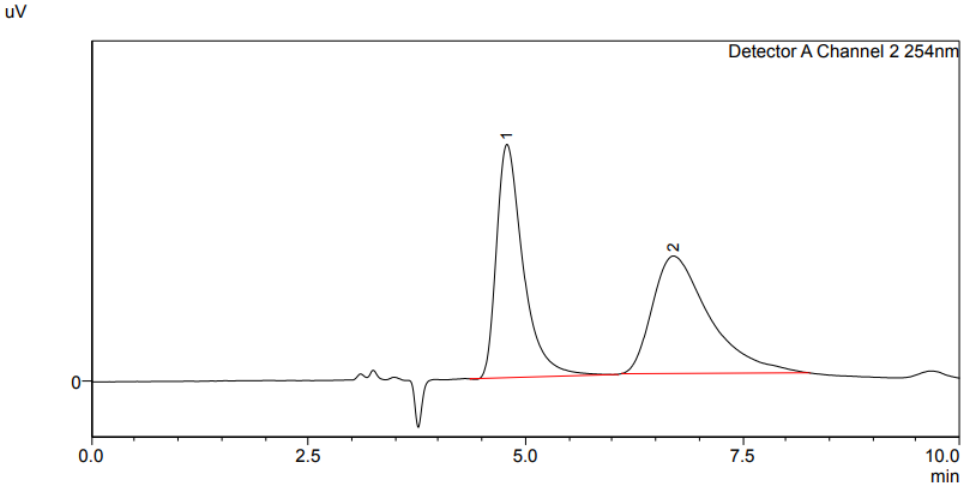


Peak Analysis Report



Detector A Channel 2 254nm

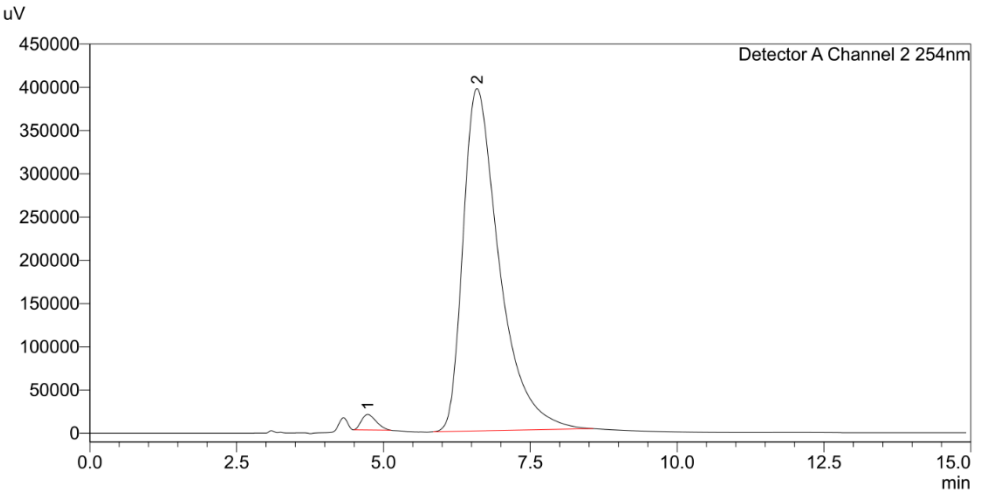
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	4.787	34285	733096	48.238
2	6.704	17238	786655	51.762
Total		51523	1519751	100.000



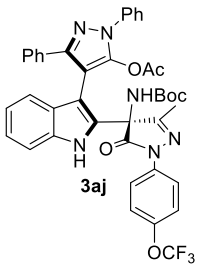
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	4.731	17899	314311	1.812
2	6.592	395875	17034637	98.188
Total		413773	17348948	100.000



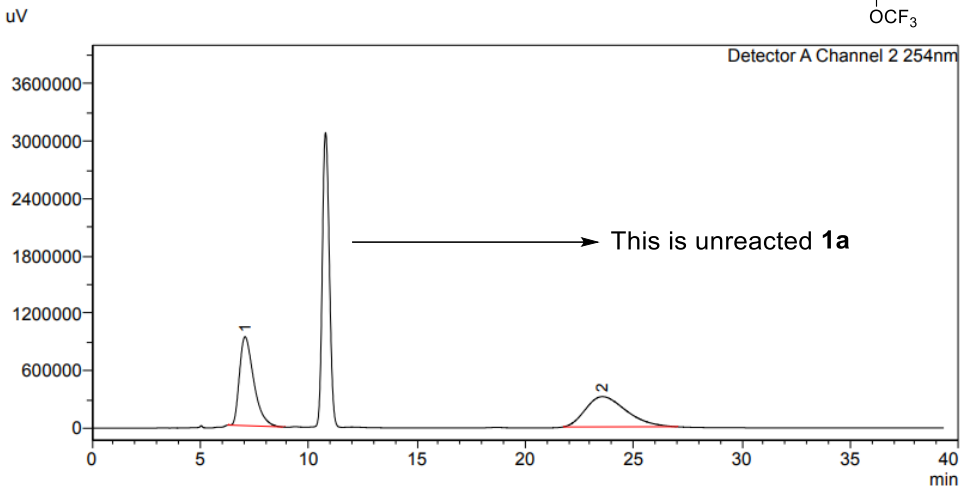
Peak Analysis Report



3aj

Detector A Channel 2 254nm

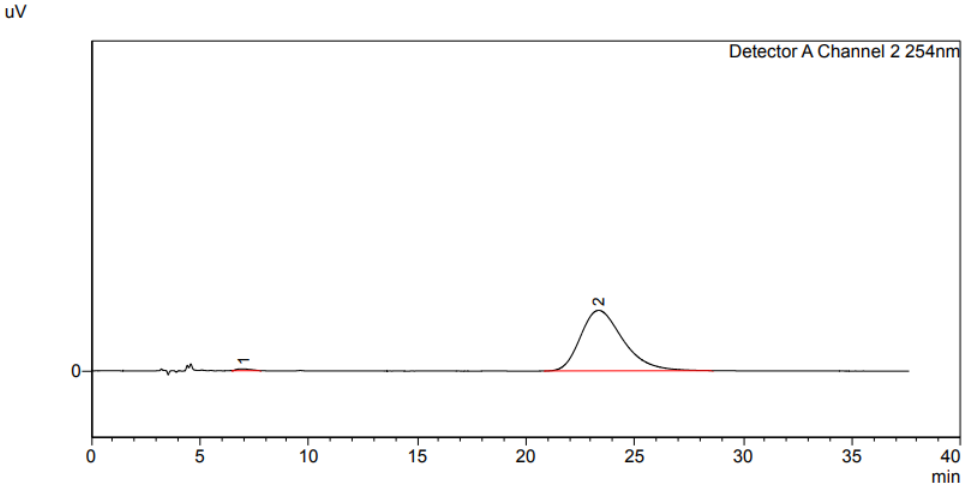
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.074	932064	42733536	50.828
2	23.566	316301	41341671	49.172
Total		1248365	84075207	100.000



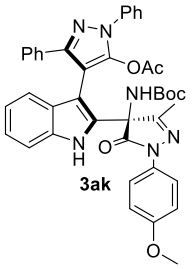
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.016	1002	42587	0.845
2	23.349	36780	4997311	99.155
Total		37782	5039898	100.000

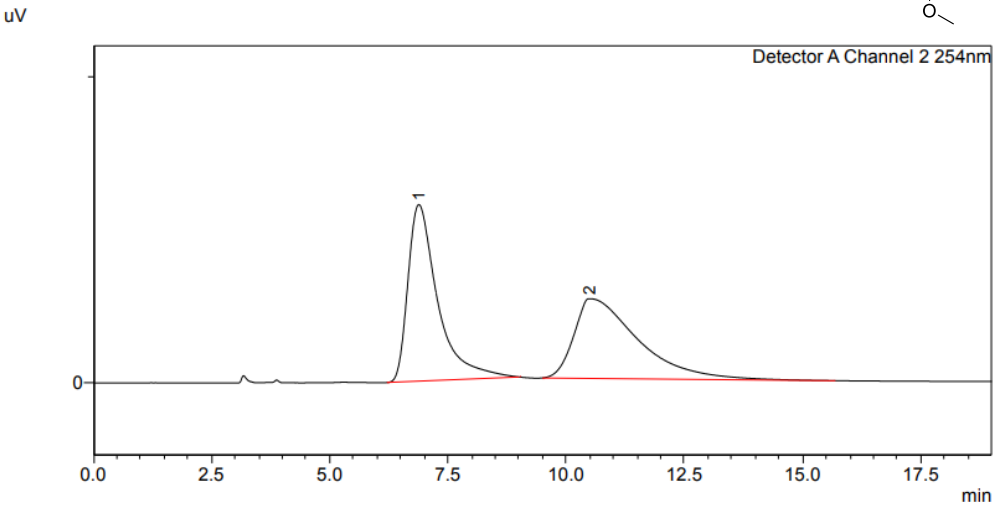


Peak Analysis Report



Detector A Channel 2 254nm

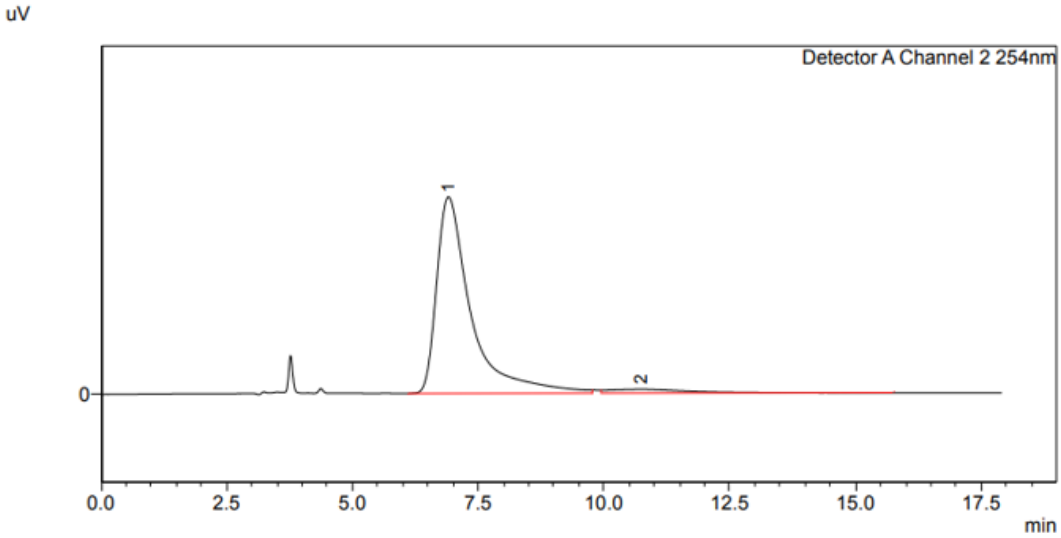
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.886	173333	7593544	50.900
2	10.500	78076	7324948	49.100
Total		251409	14918492	100.000



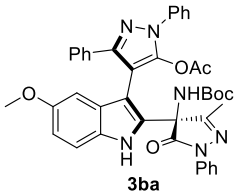
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.908	112999	5368004	95.866
2	10.736	2194	231481	4.134
Total		115192	5599485	100.000



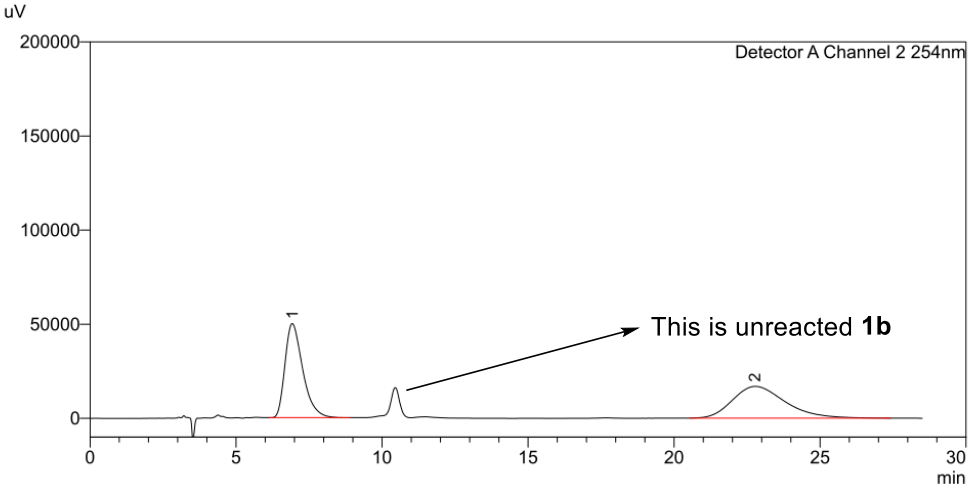
Peak Analysis Report



3ba

Detector A Channel 2 254nm

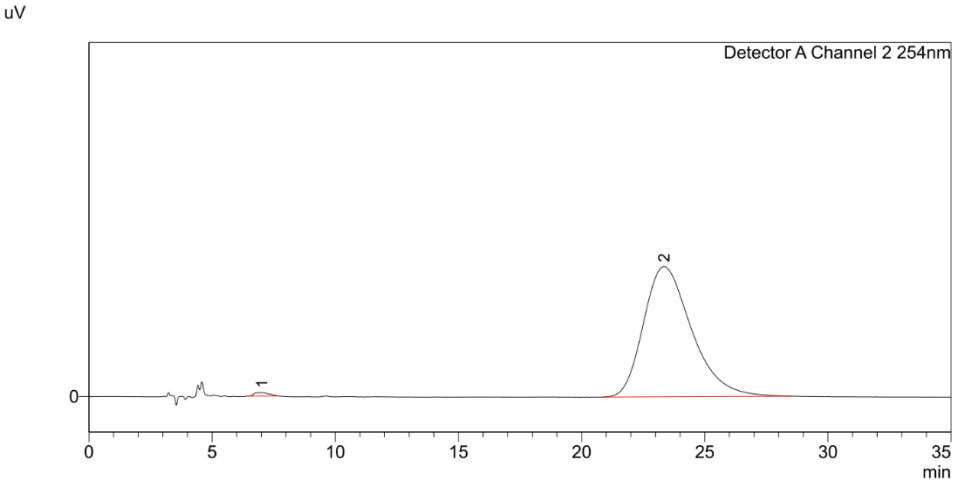
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.923	50009	2110645	49.929
2	22.765	16838	2116631	50.071
Total		66847	4227276	100.000



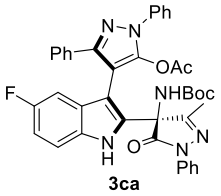
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.016	1002	42587	0.845
2	23.349	36780	4997311	99.155
Total		37782	5039898	100.000



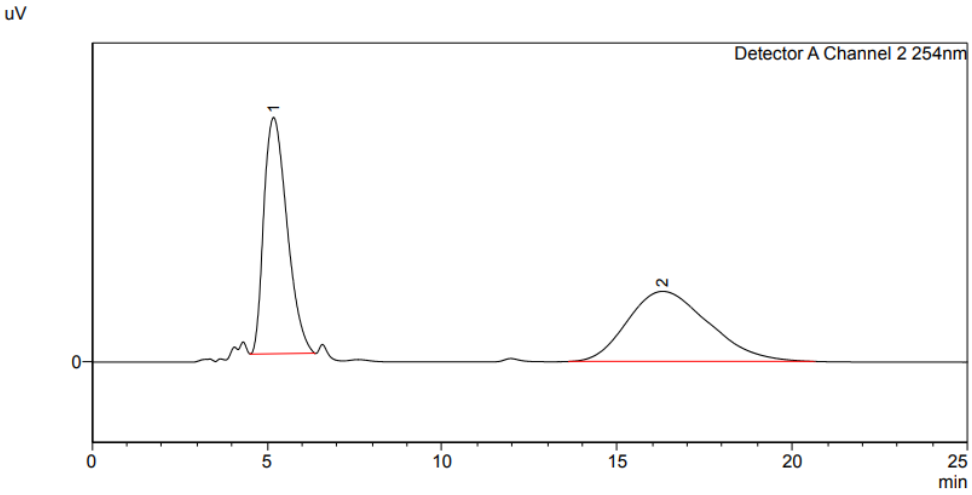
Peak Analysis Report



3ca

Detector A Channel 2 254nm

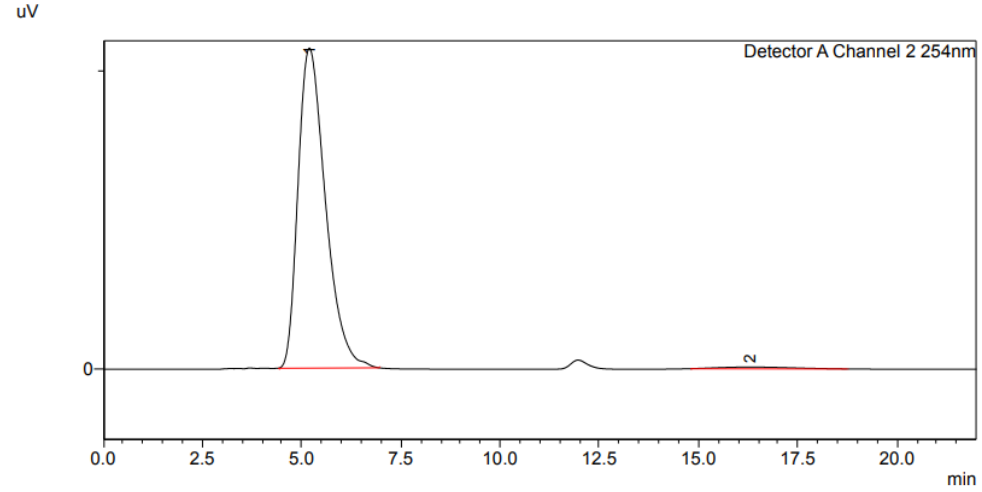
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	5.193	118797	5475010	49.075
2	16.289	35228	5681512	50.925
Total		154025	11156522	100.000



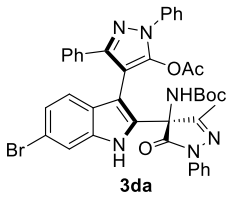
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	5.194	322260	15479352	98.596
2	16.300	1713	220454	1.404
Total		323974	15699806	100.000



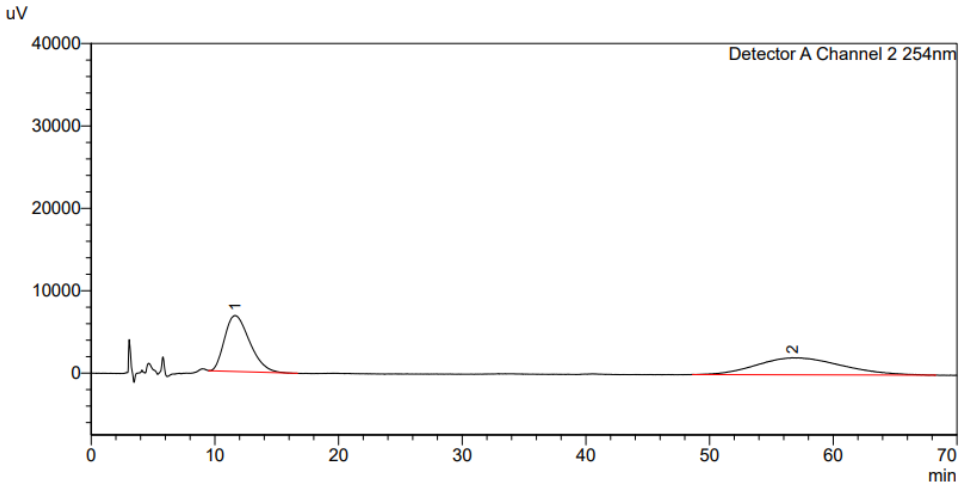
Peak Analysis Report



3da

Detector A Channel 2 254nm

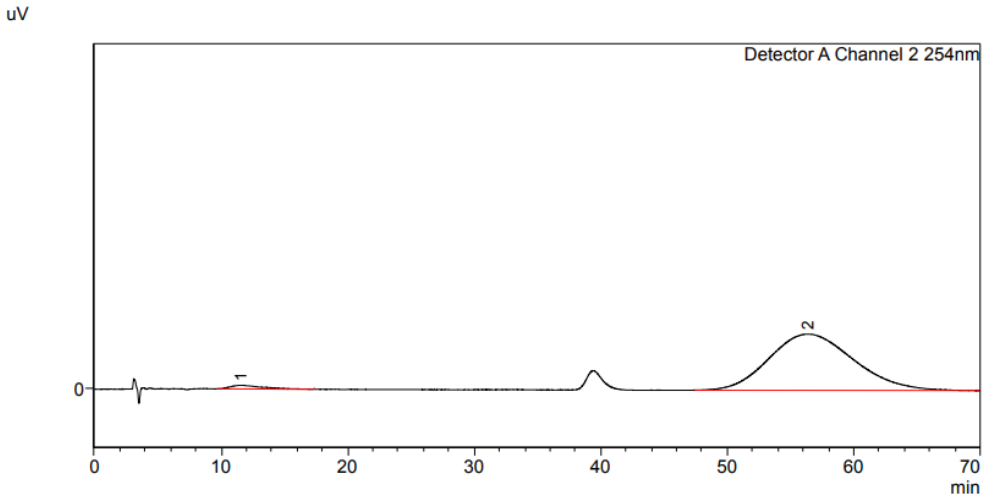
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	11.632	6787	956267	49.333
2	56.686	2062	982116	50.667
Total		8850	1938383	100.000



Peak Analysis Report

Detector A Channel 2 254nm

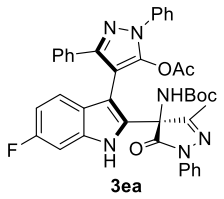
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	11.582	640	113040	2.429
2	56.377	9781	4540822	97.571
Total		10420	4653862	100.000



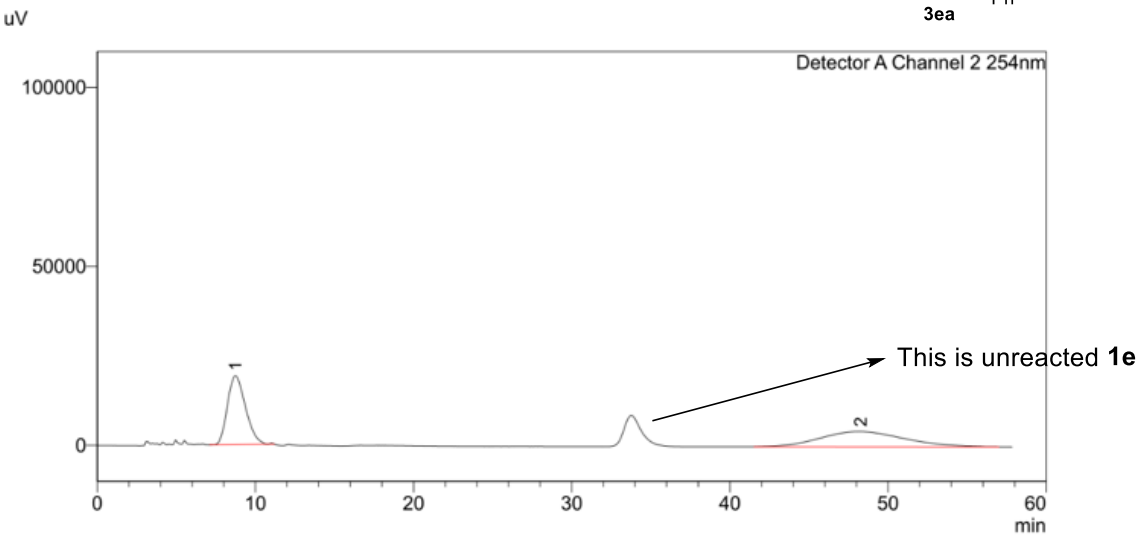
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	8.735	19216	1524305	49.794
2	48.264	4199	1536890	50.206
Total		23415	3061195	100.000



3ea

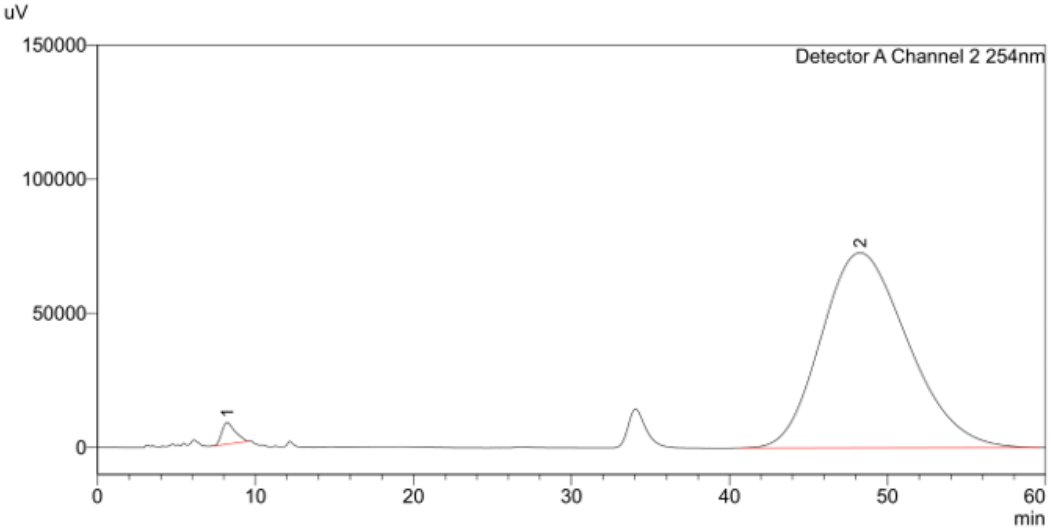


This is unreacted **1e**

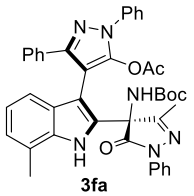
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	8.211	8036	468284	1.658
2	48.264	72747	27771234	98.342
Total		80783	28239518	100.000



Peak Analysis Report

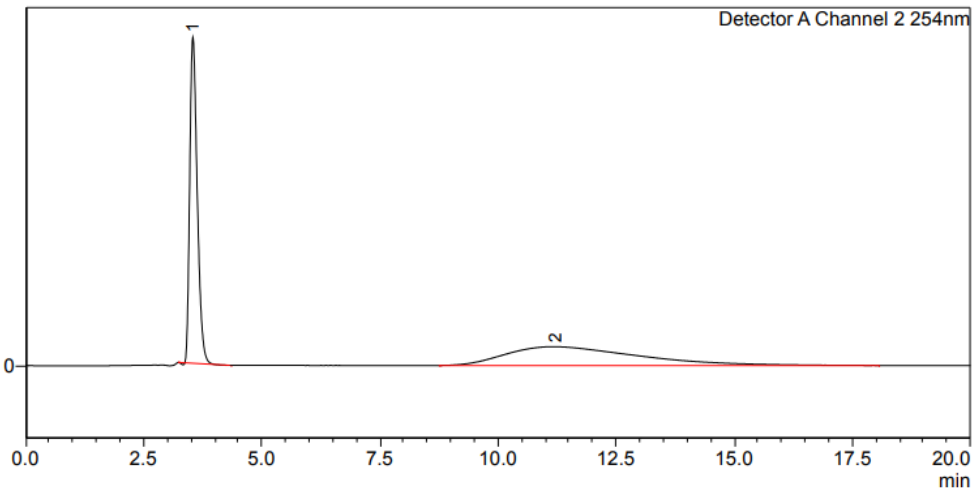


3fa

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	3.544	182493	2007529	49.628
2	11.217	10509	2037587	50.372
Total		193002	4045115	100.000

uV

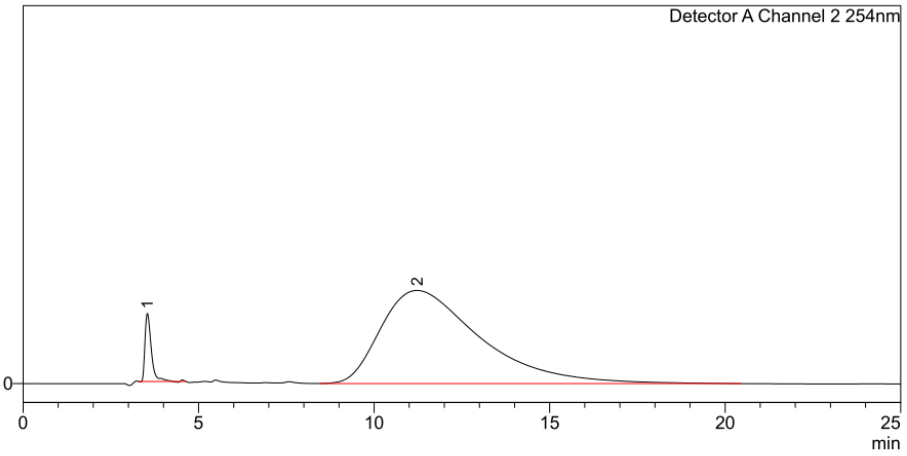


Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	3.539	36078	456387	4.481
2	11.223	49303	9727447	95.519
Total		85381	10183834	100.000

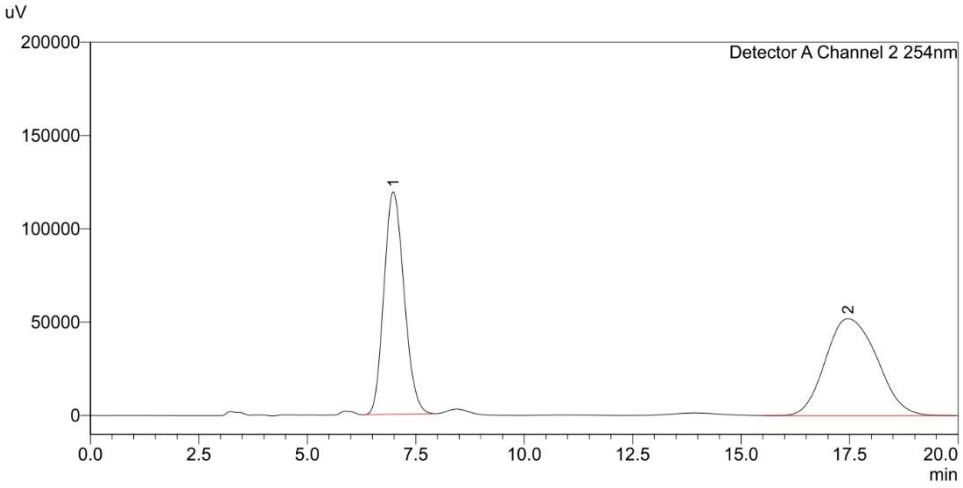
uV

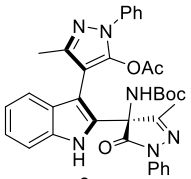


Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.982	119143	3844295	47.188
2	17.462	51983	4302449	52.812
Total		171126	8146744	100.000



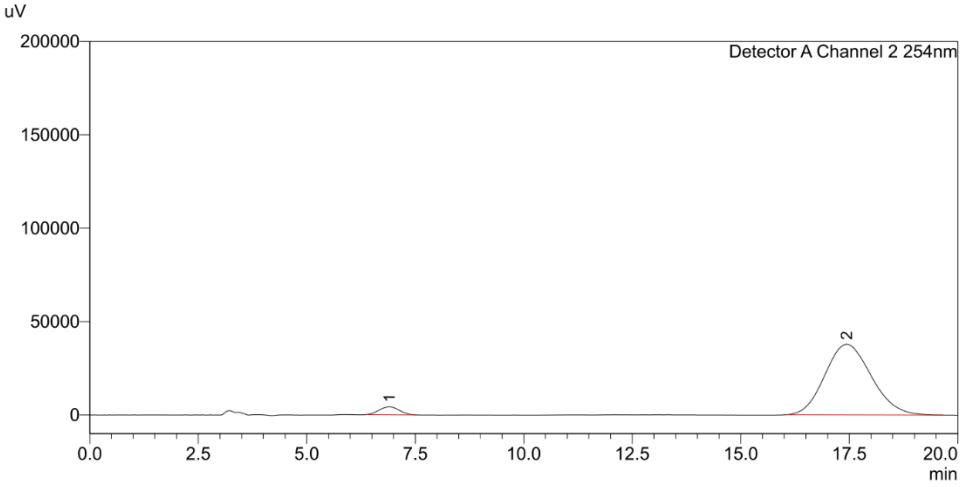


3ga

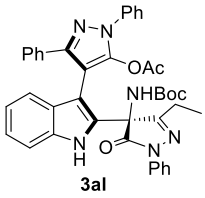
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.901	4173	135160	4.580
2	17.438	37778	2815803	95.420
Total		41951	2950964	100.000



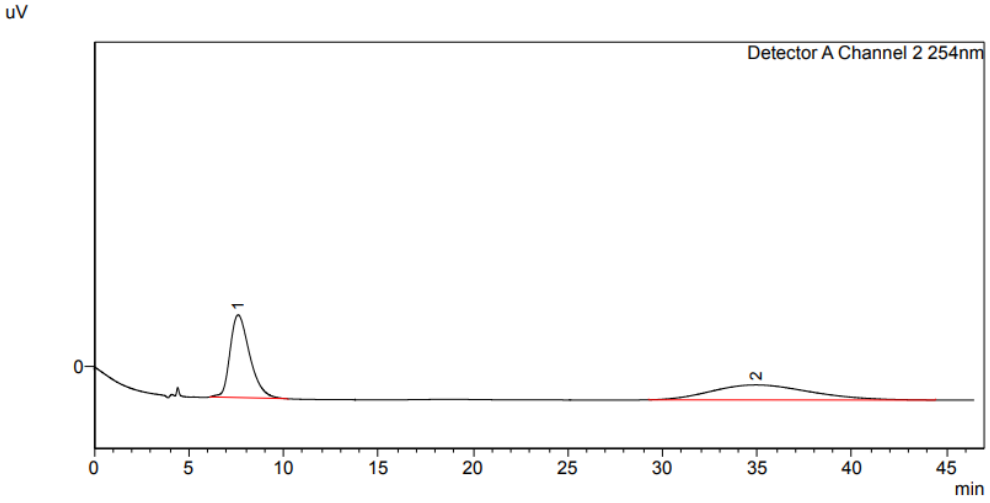
Peak Analysis Report



3al

Detector A Channel 2 254nm

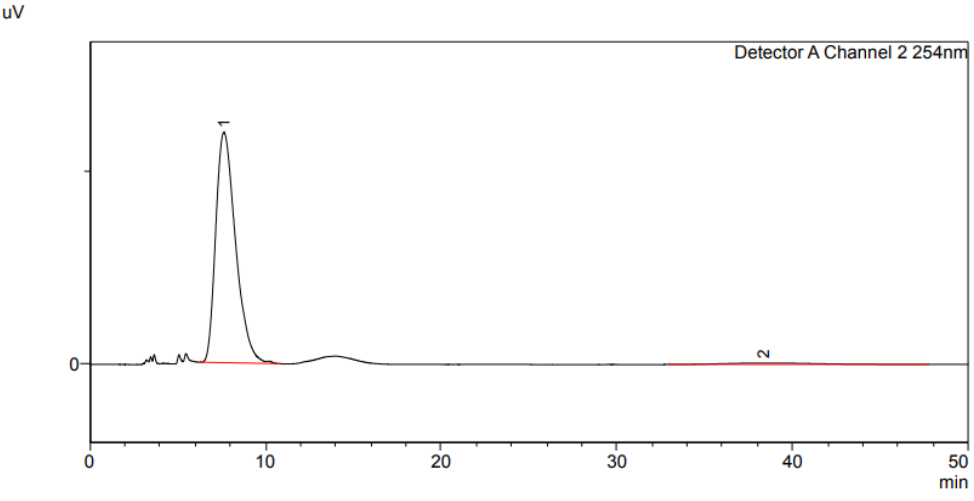
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.609	51090	3687167	52.362
2	34.952	9246	3354558	47.638
Total		60336	7041725	100.000



Peak Analysis Report

Detector A Channel 2 254nm

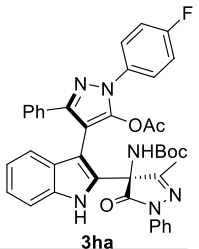
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.647	357793	28104871	97.177
2	38.338	2170	816337	2.823
Total		359963	28921209	100.000



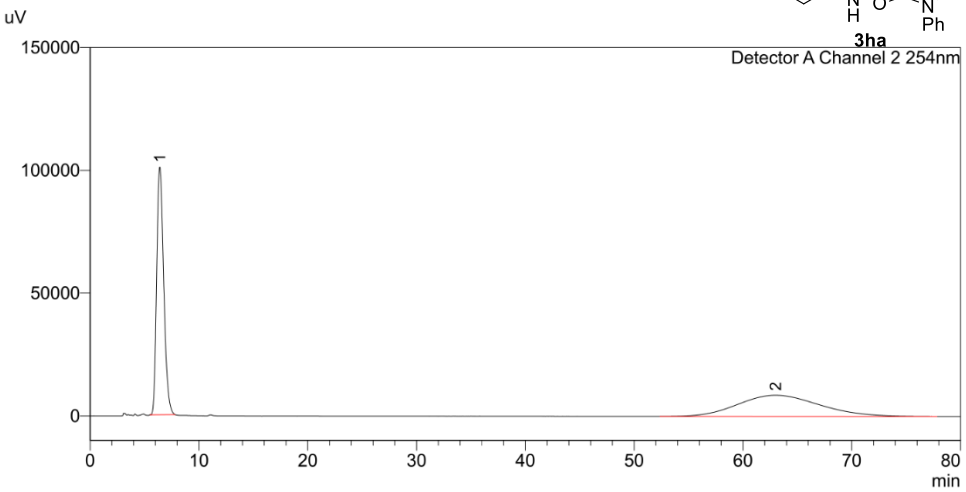
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.398	100920	4536468	50.145
2	63.000	8616	4510145	49.855
Total		109536	9046614	100.000



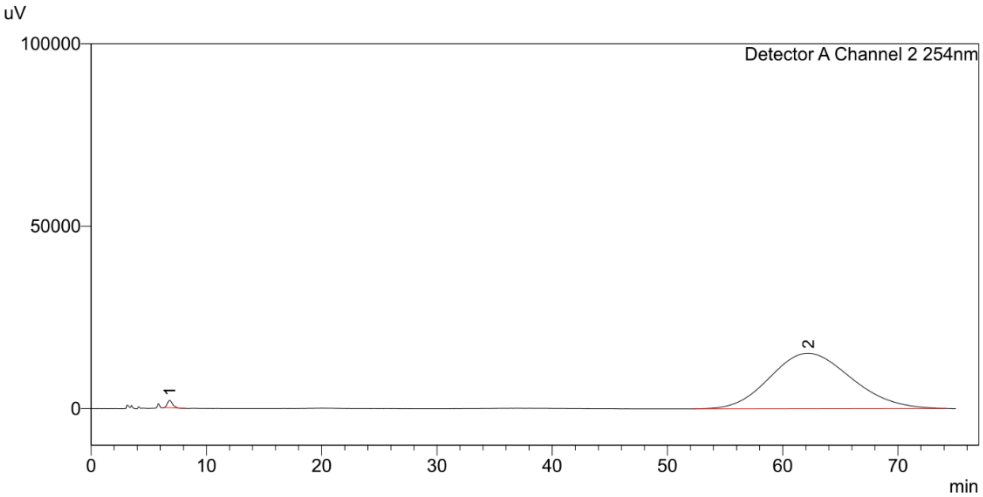
3ha



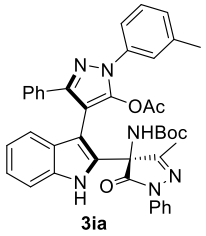
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.806	2023	64474	0.857
2	62.221	15199	7462702	99.143
Total		17222	7527176	100.000



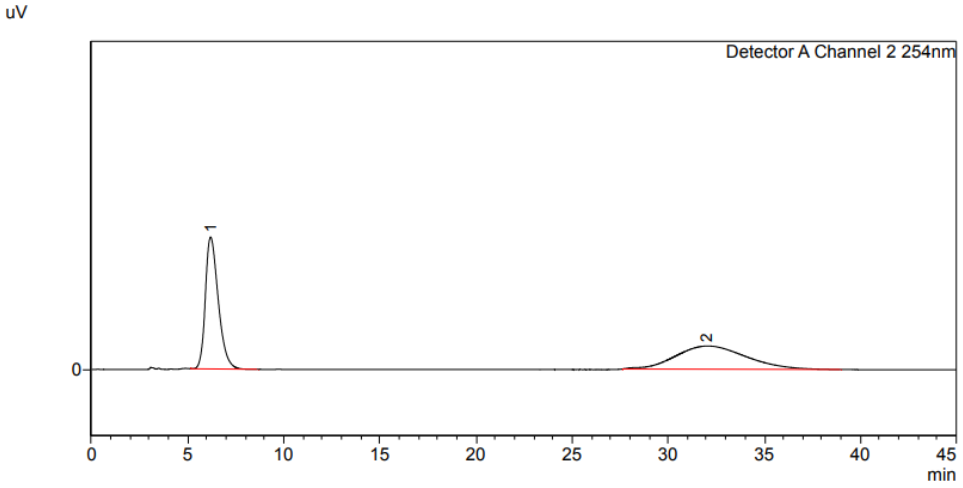
Peak Analysis Report



3ia

Detector A Channel 2 254nm

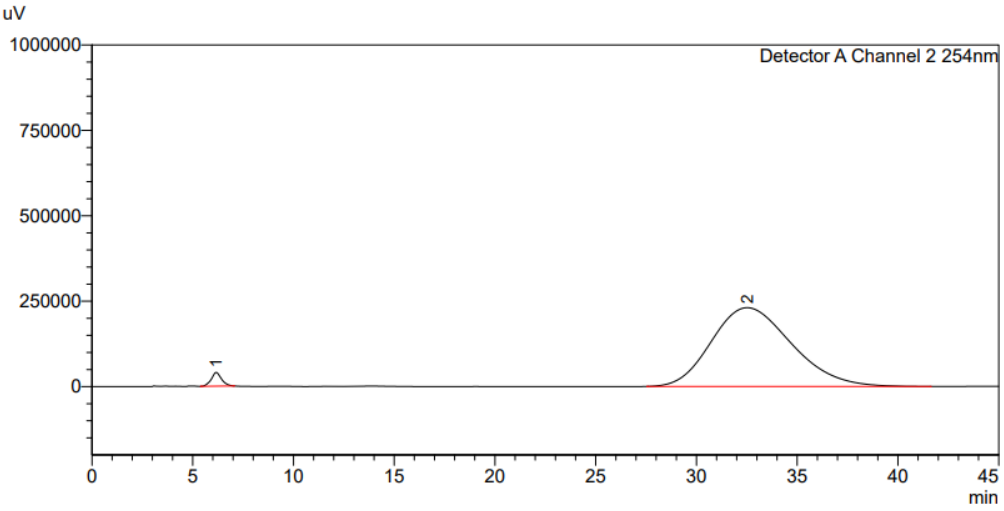
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.194	60376	2816365	50.911
2	32.016	10616	2715527	49.089
Total		70993	5531892	100.000



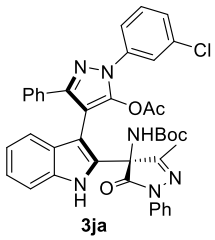
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.164	40257	1423369	2.181
2	32.515	230548	63835051	97.819
Total		270805	65258420	100.000



Peak Analysis Report

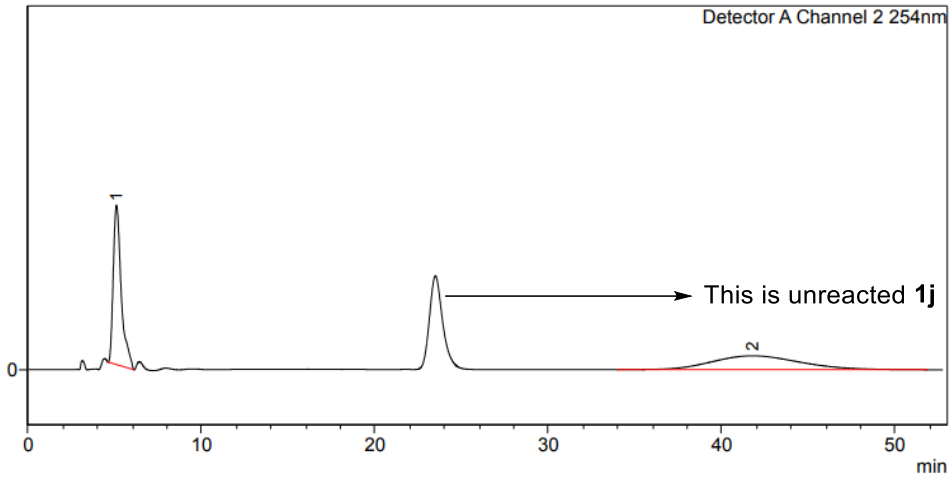


3ja

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	5.088	87660	2812551	50.995
2	41.759	7633	2702791	49.005
Total		95293	5515342	100.000

uV

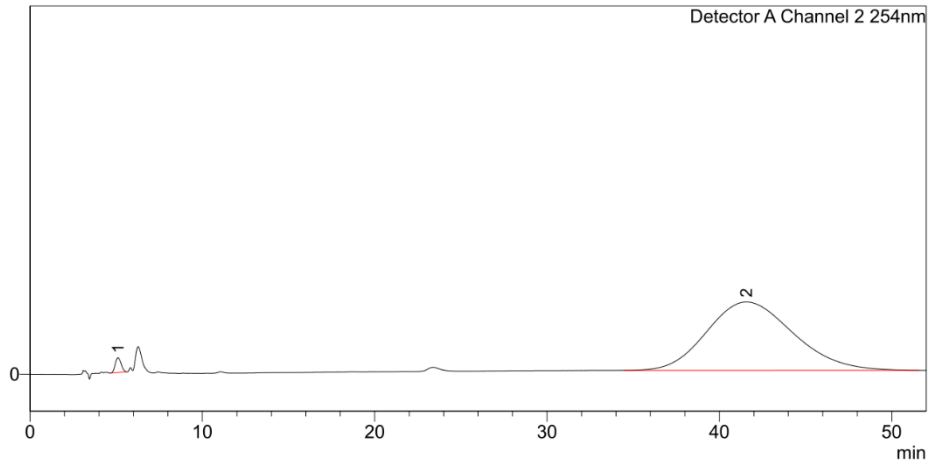


Peak Analysis Report

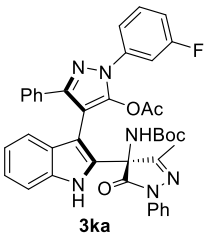
Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	5.104	3997	95397	1.451
2	41.556	18567	6481348	98.549
Total		22564	6576744	100.000

uV



Peak Analysis Report

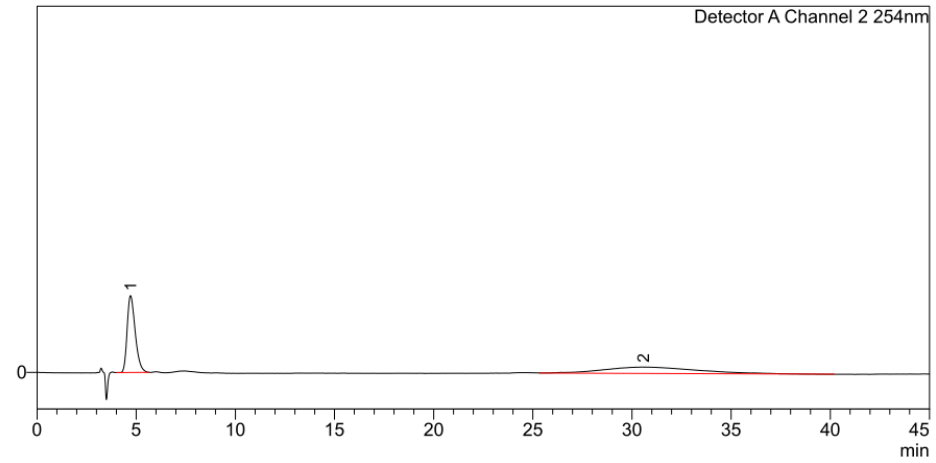


3ka

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	4.712	20985	592294	51.047
2	30.579	1725	567989	48.953
Total		22710	1160283	100.000

uV

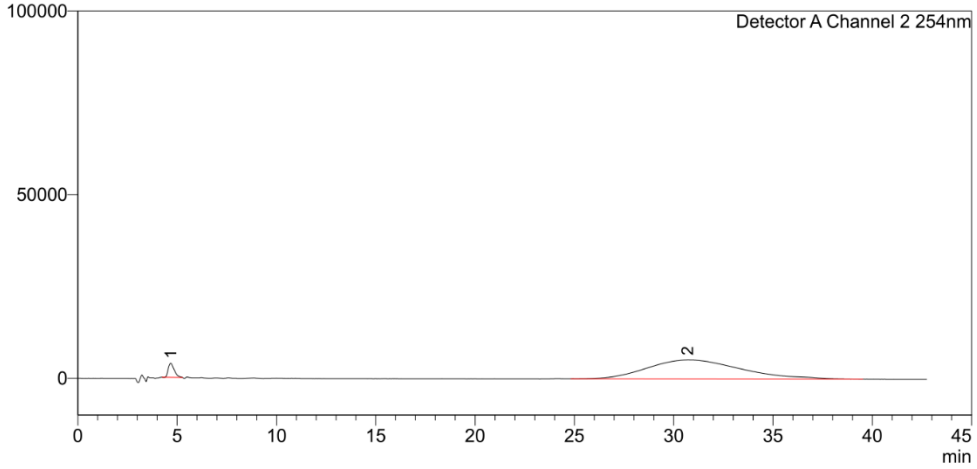


Peak Analysis Report

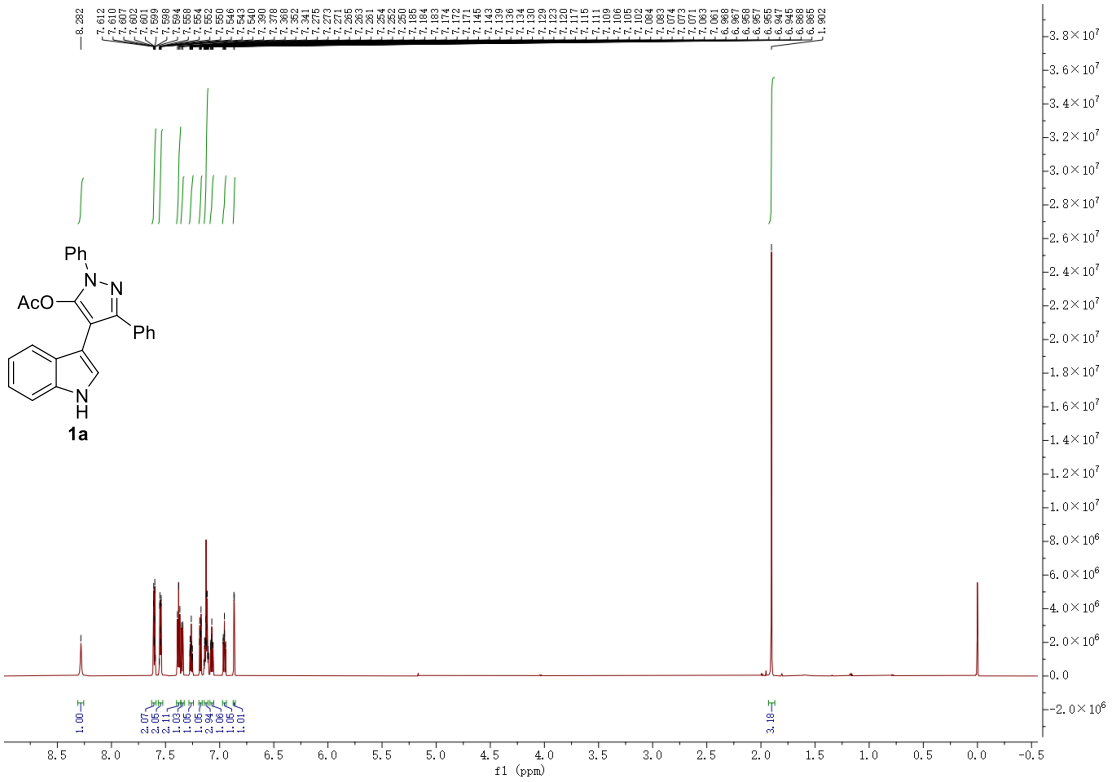
Detector A Channel 2 254nm

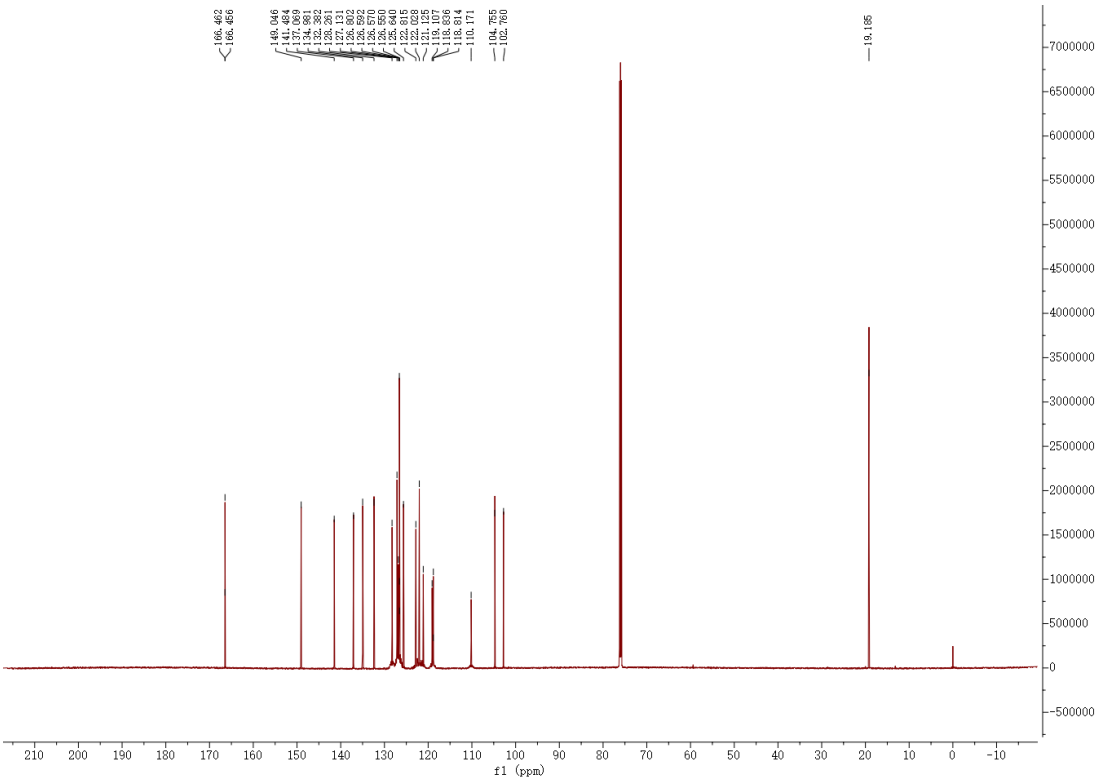
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	4.671	3823	79975	4.494
2	30.692	5179	1699481	95.506
Total		9002	1779456	100.000

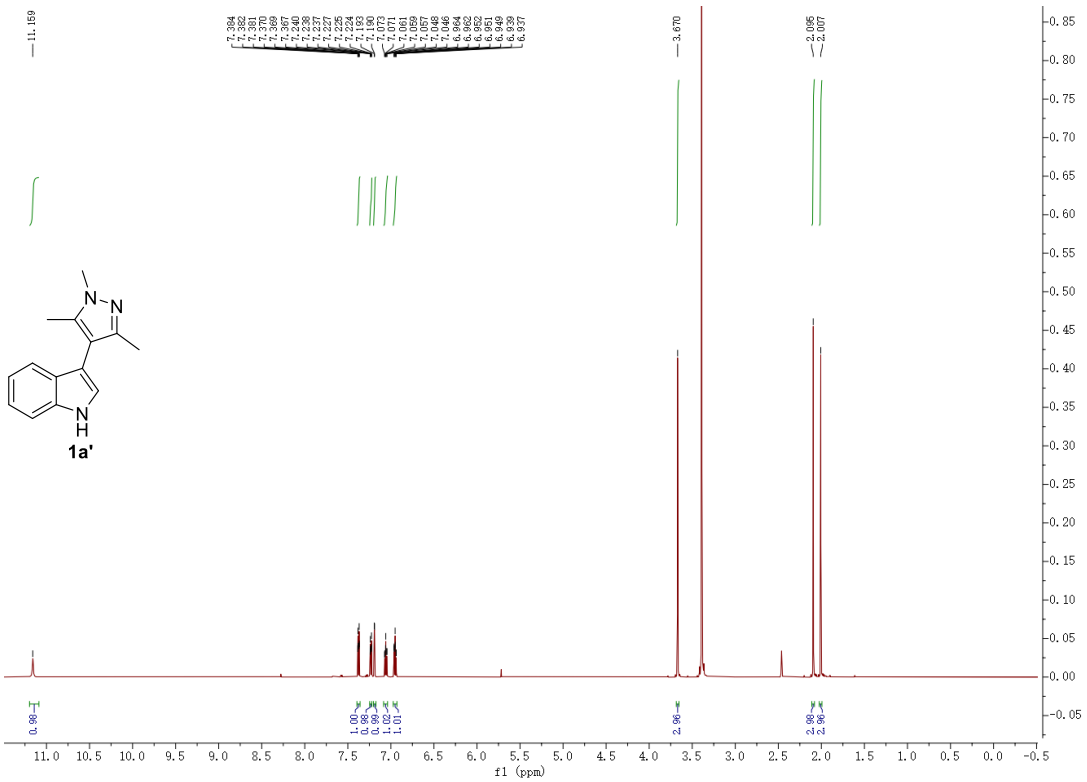
uV



9. NMR Spectra






11.159
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6.951
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3.670
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2.007
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1.02
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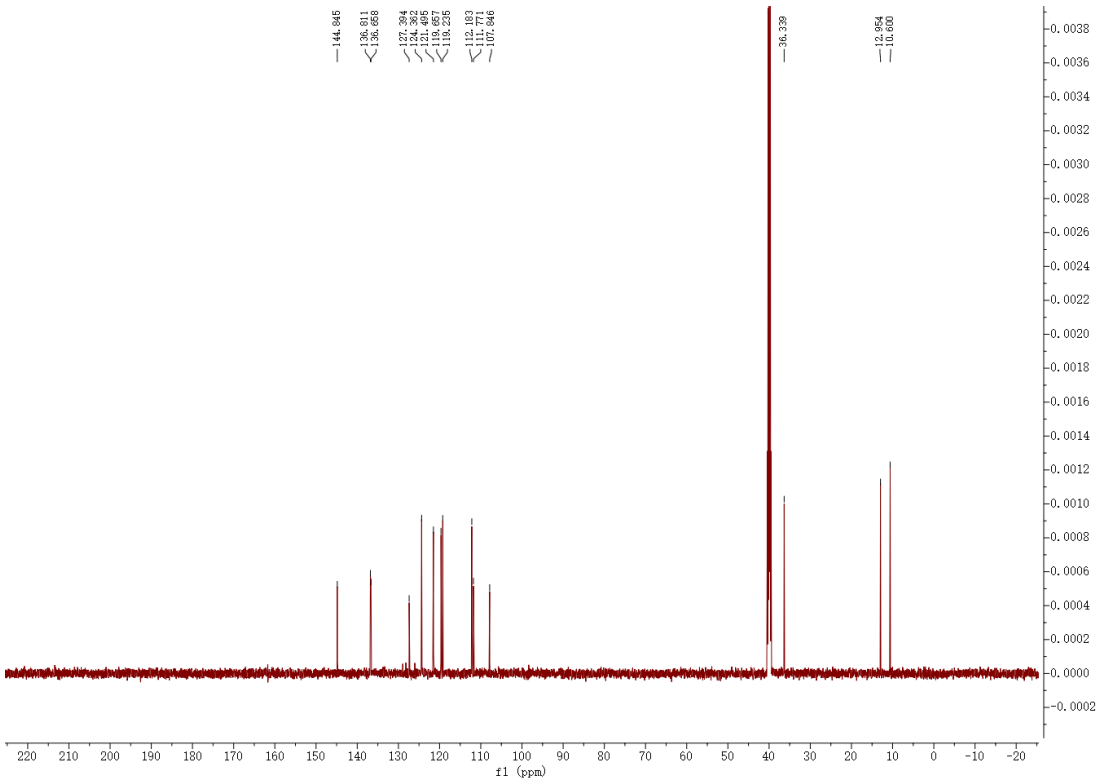
2.98
2.96
1a'
f1 (ppm)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136.658
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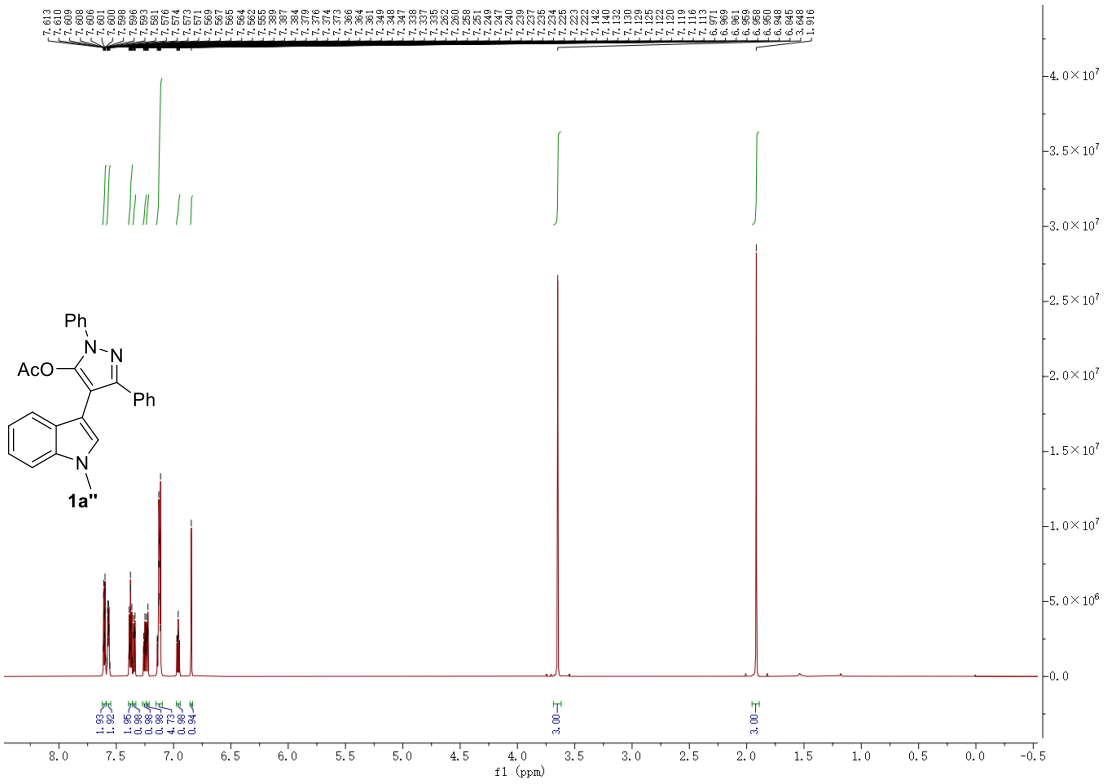
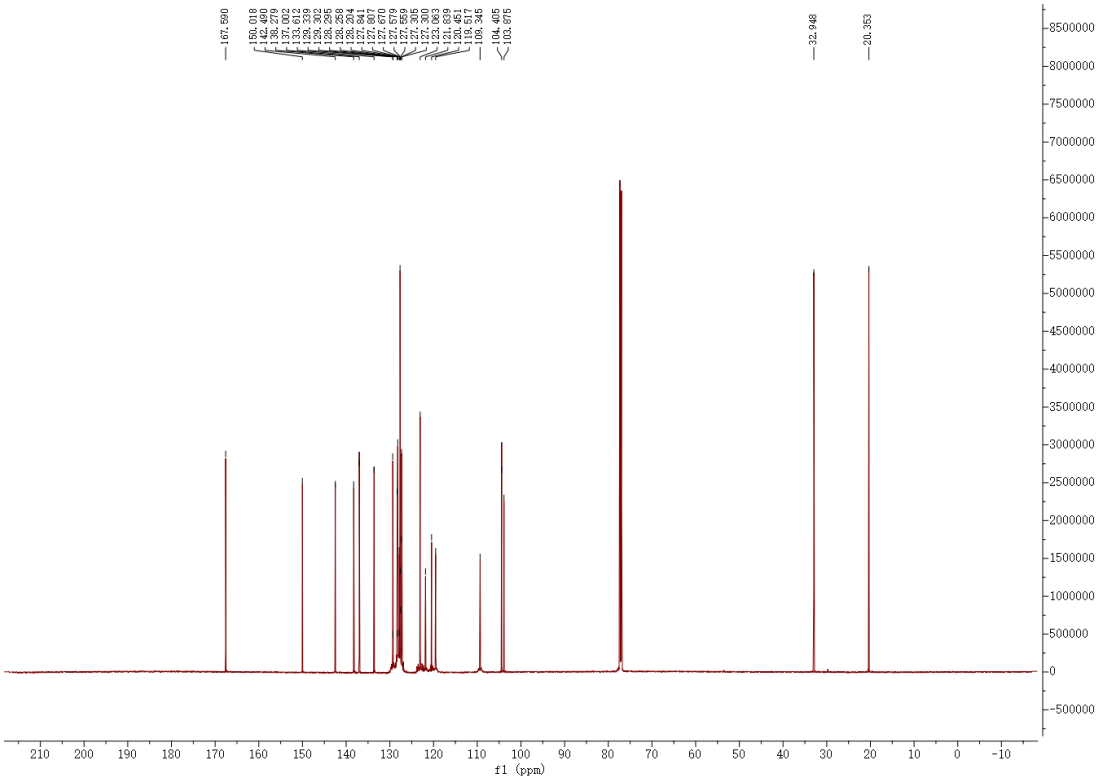
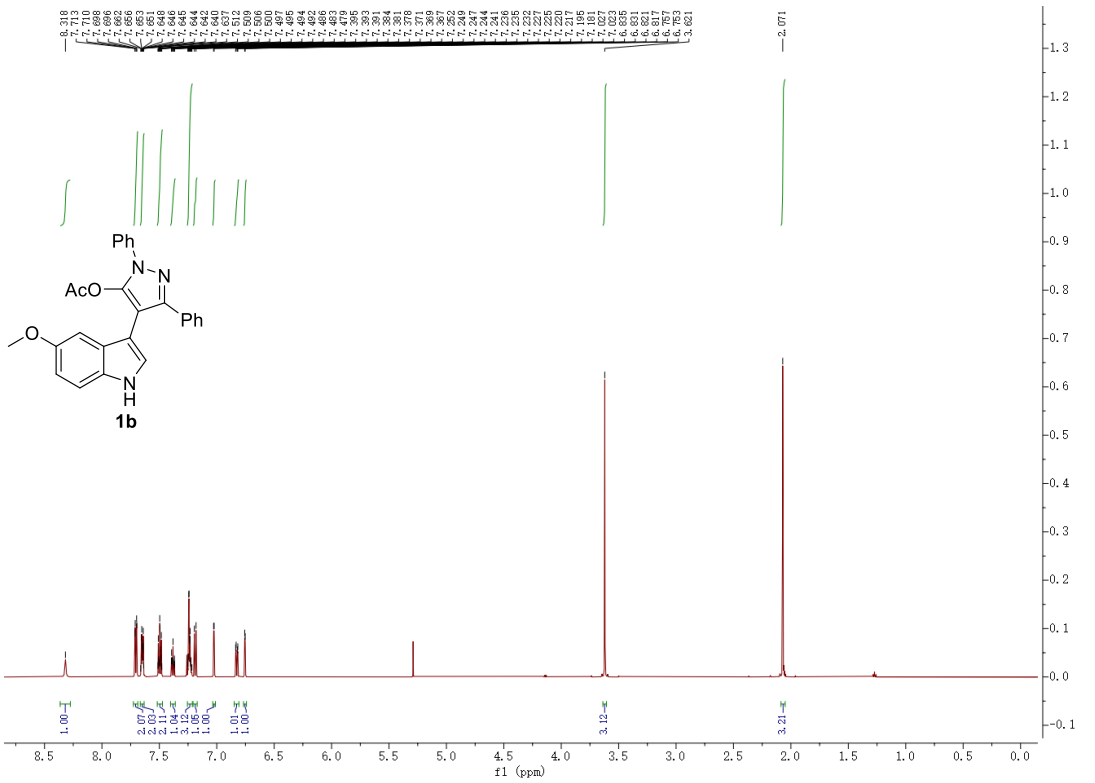
119.657
119.235
112.183
111.771
107.946
36.339
12.954
10.600
f1 (ppm)


Ph
N
N
AcO
Ph
N
1a''
f1 (ppm)


f1 (ppm)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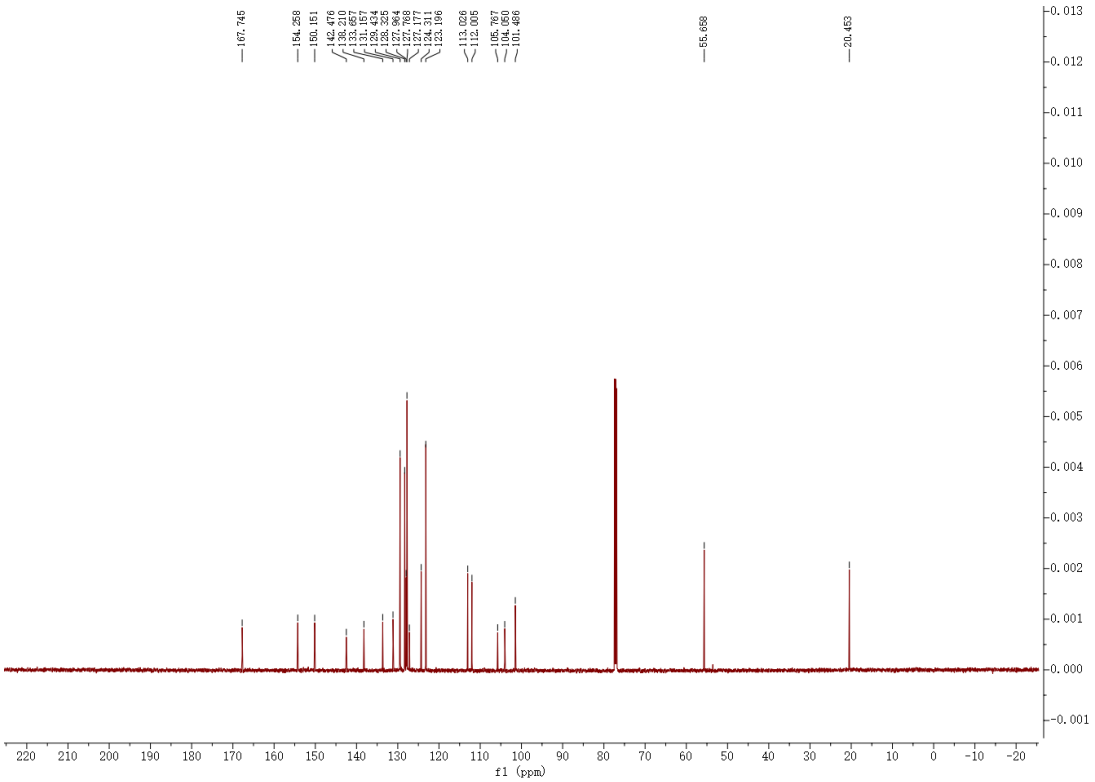
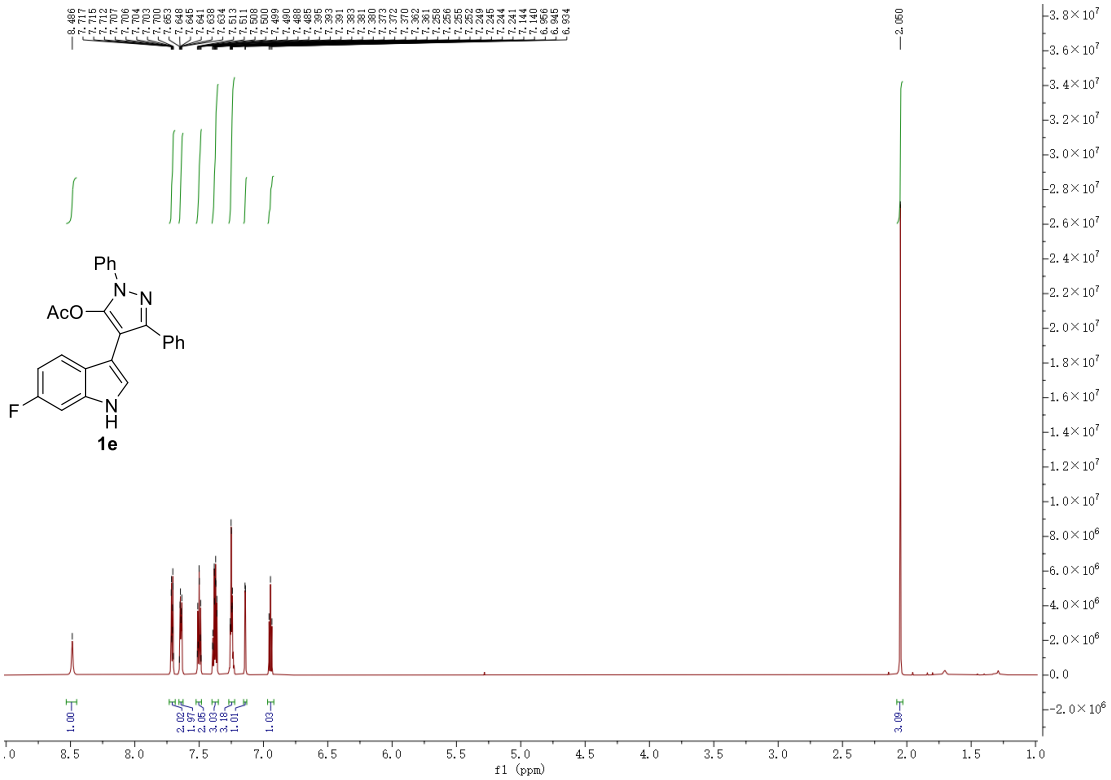
AcO
Ph
O
N
H
1b
f1 (ppm)


f1 (ppm)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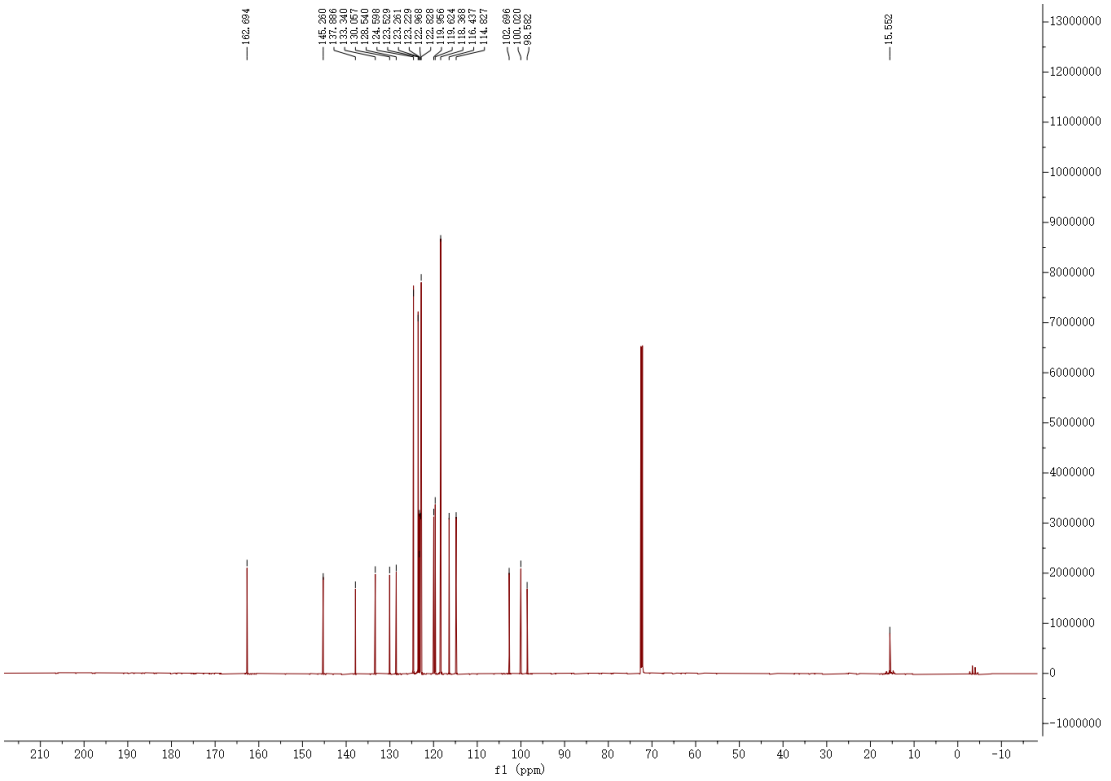
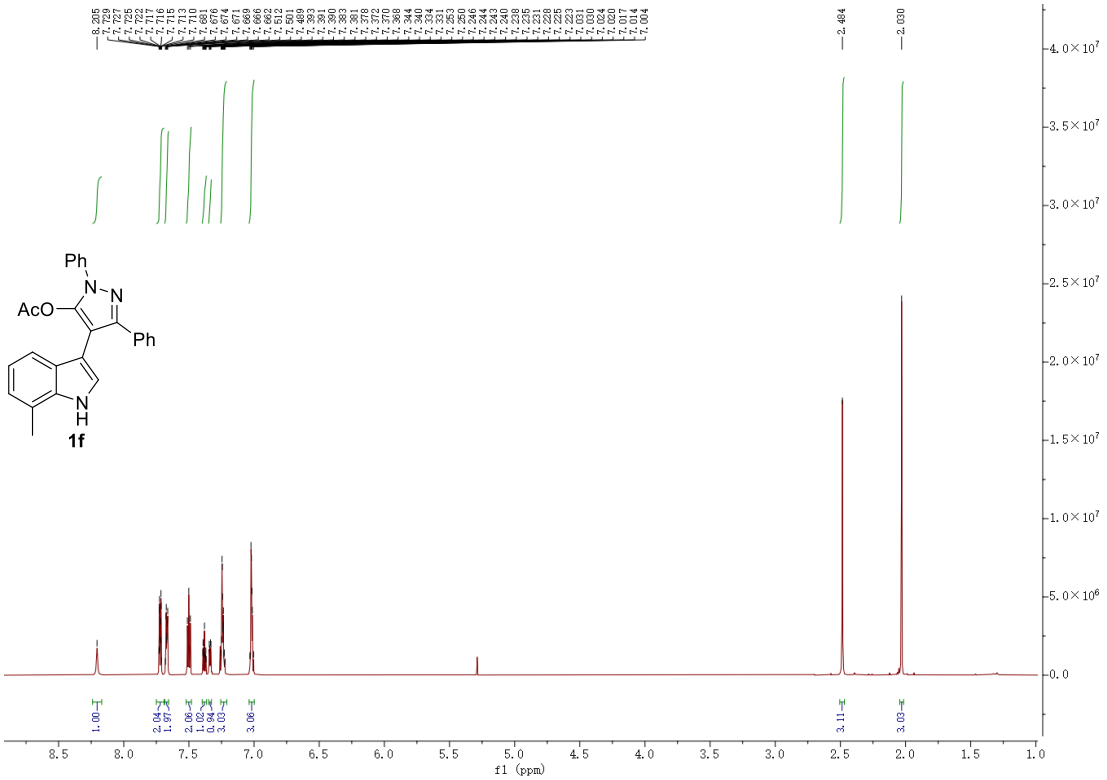
N
AcO
Ph
F
N
H
1e
f1 (ppm)


f1 (ppm)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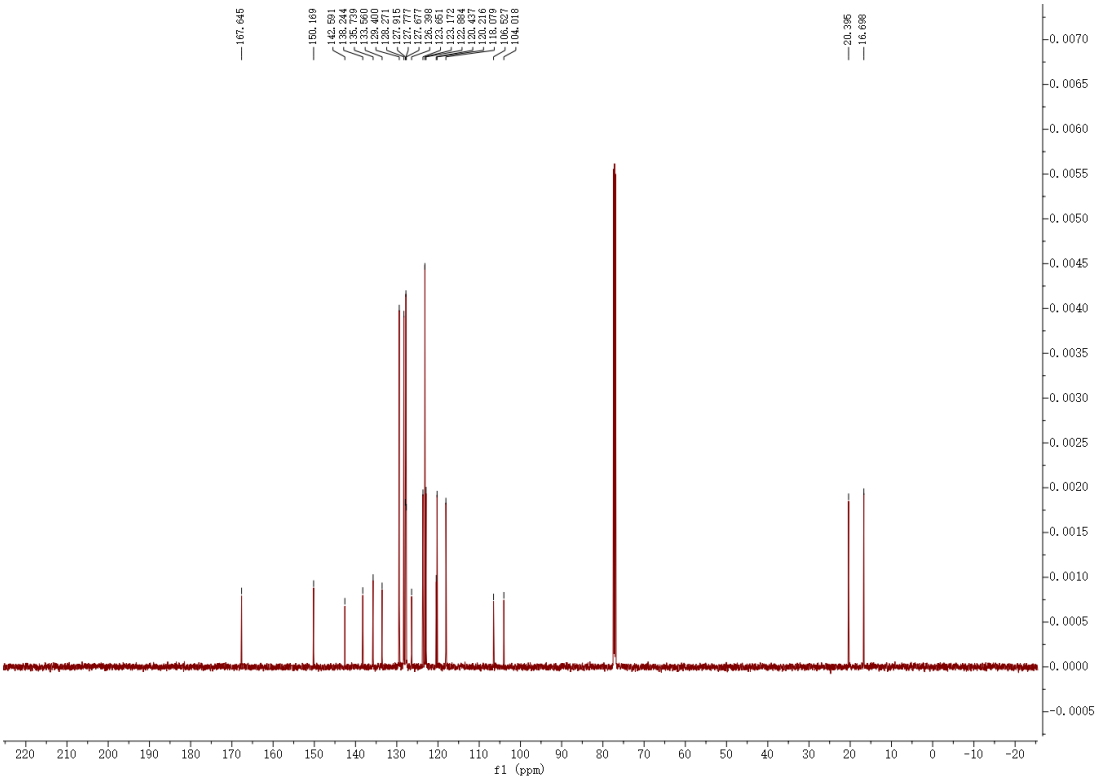
N
N
AcO
Ph
N
H
1f
f1 (ppm)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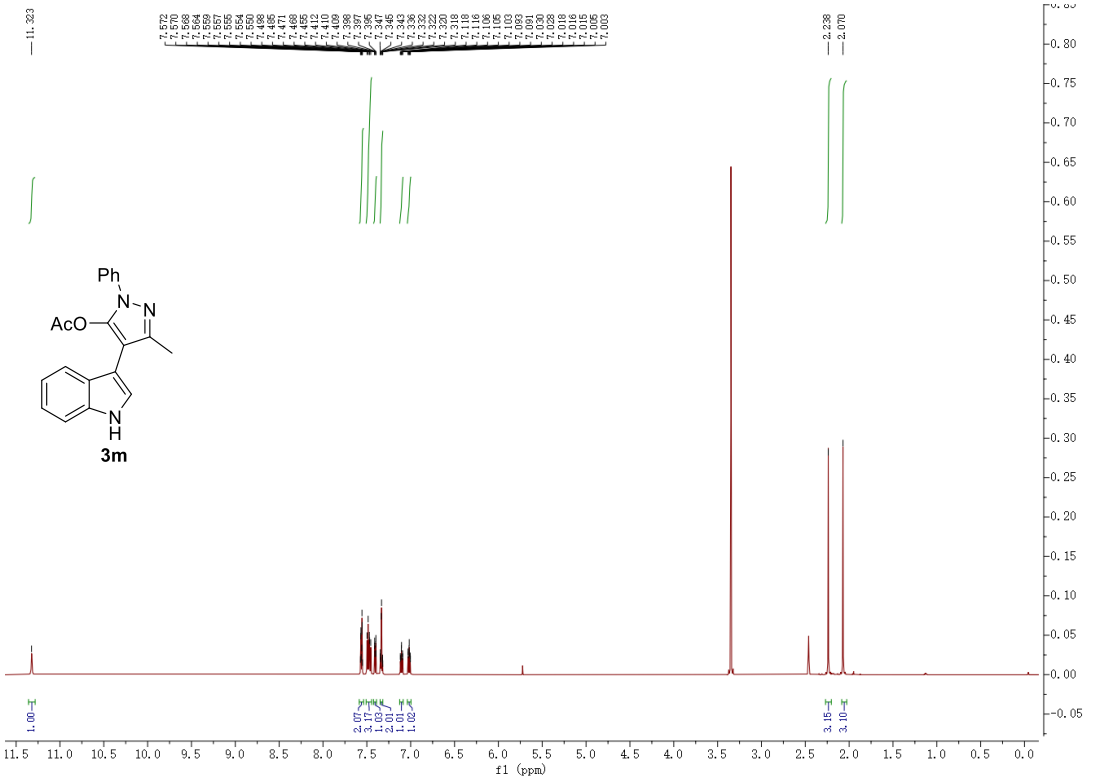
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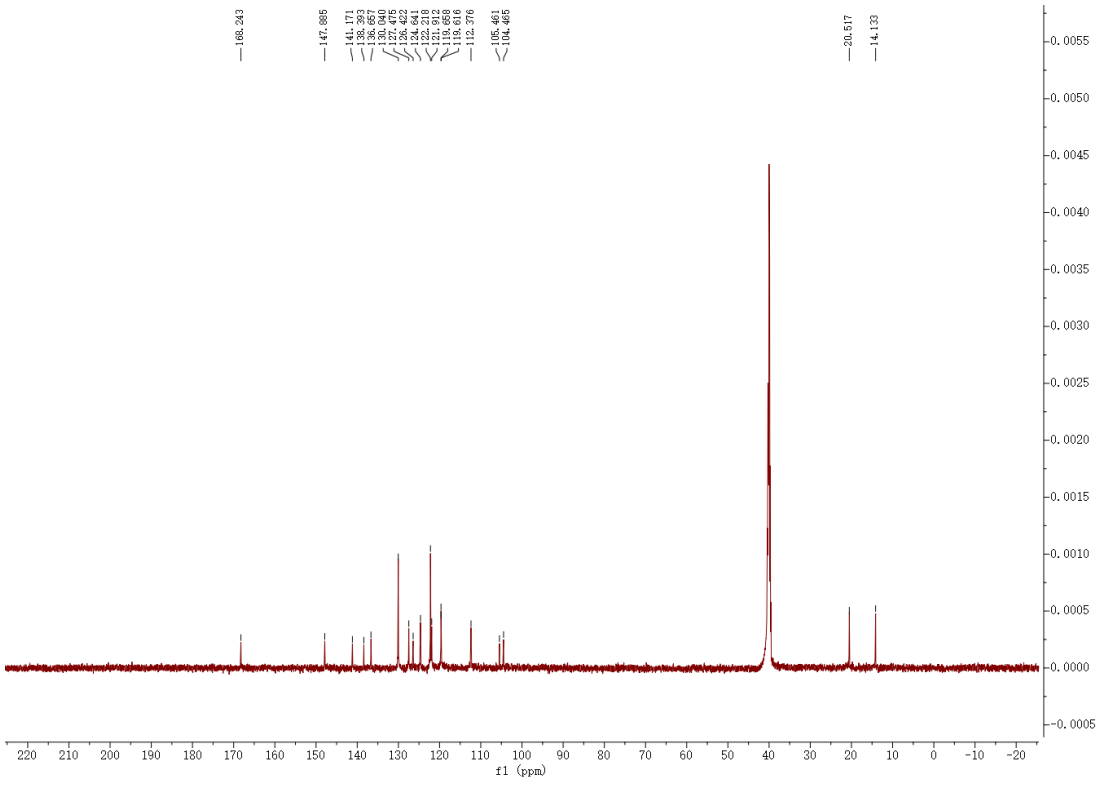
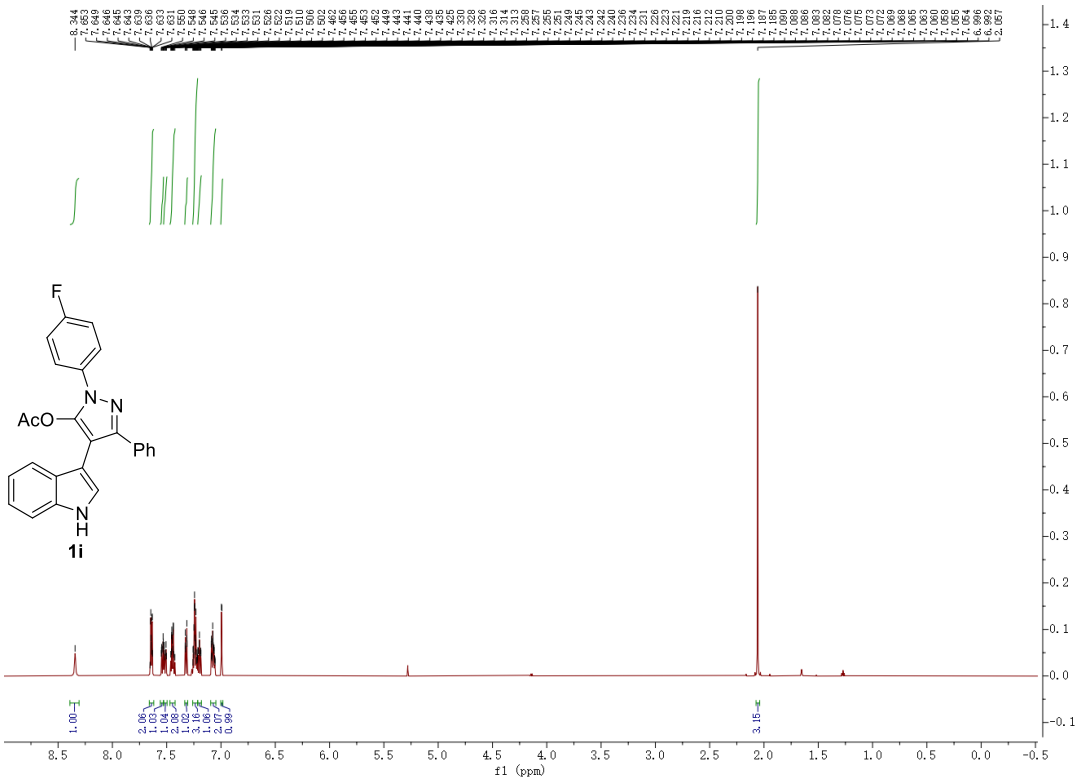
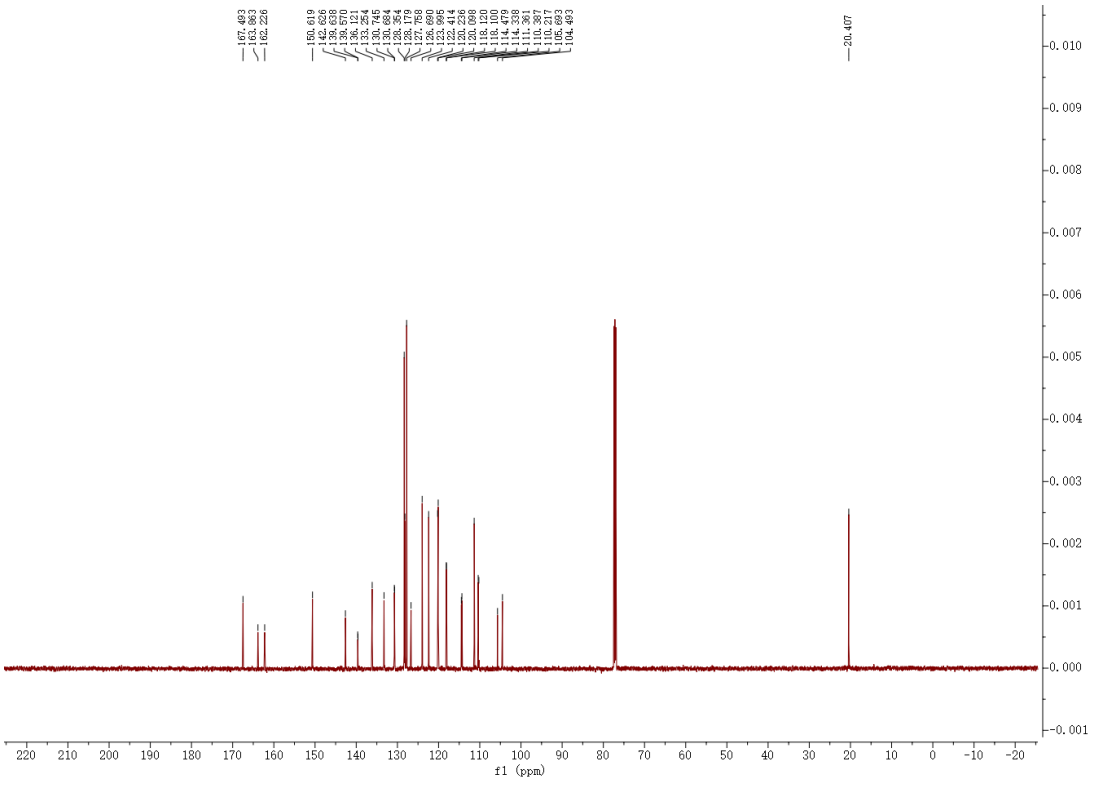
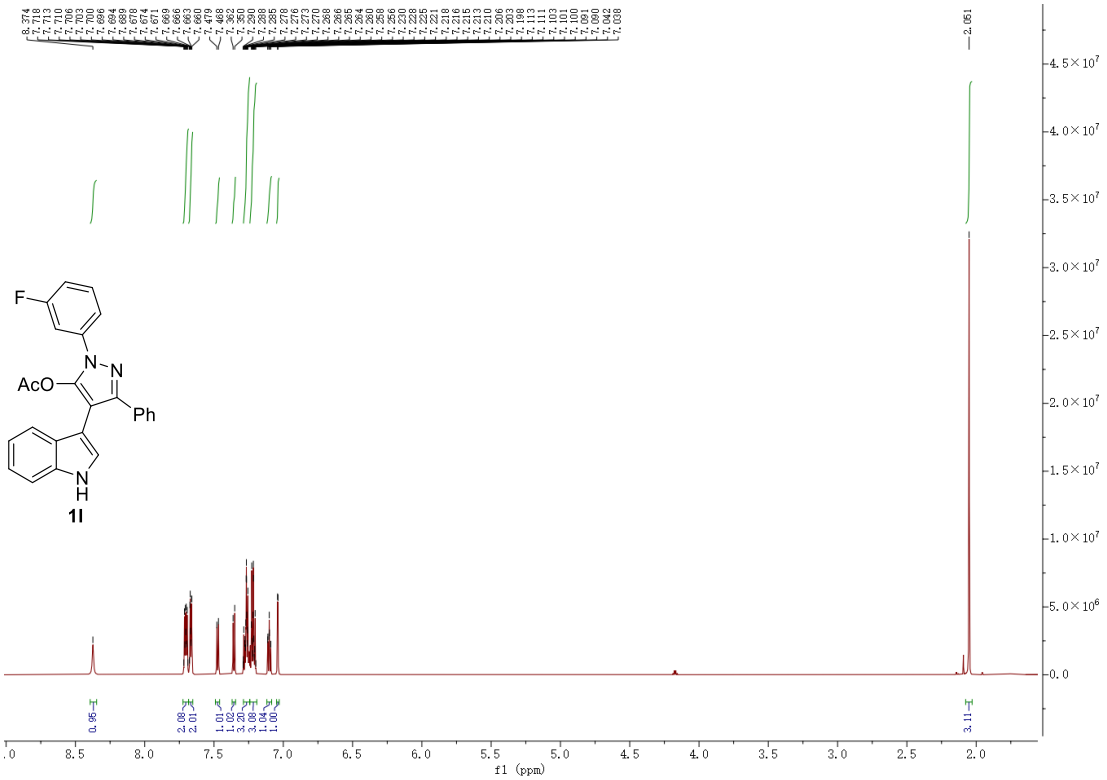
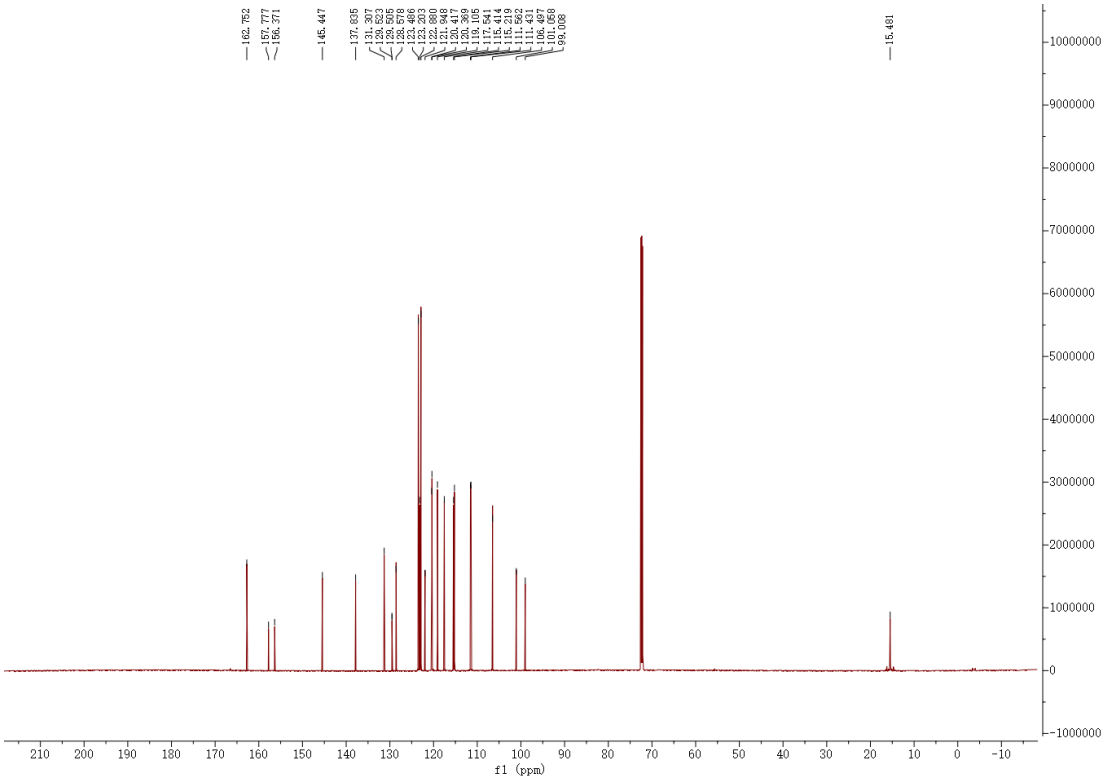
7.570
7.568
7.564
7.559
7.557
7.555
7.554
7.550
7.488
7.485
7.471
7.469
7.455
7.412
7.410
7.409
7.398
7.397
7.345
7.343
7.336
7.332
7.322
7.320
7.318
7.118
7.116
7.106
7.105
7.103
7.093
7.091
7.030
7.028
7.018
7.016
7.015
7.005
1.003
2.238
2.070
Ph
N
N
AcO
N
H
3m
1.00
2.07
3.13
1.07
2.01
1.01
1.02
3.15
3.10
f1 (ppm)

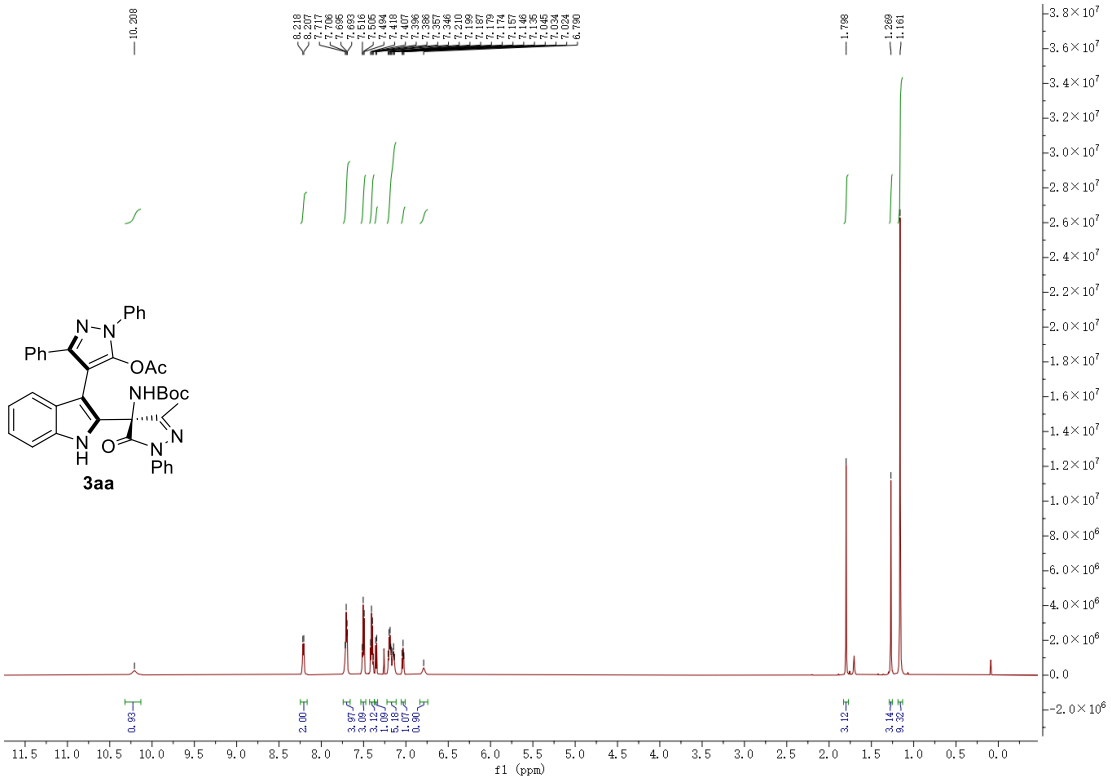

168.243
147.885
141.171
138.393
136.657
130.040
127.445
126.422
124.641
122.218
121.932
119.658
119.616
112.376
105.461
104.465
20.517
14.133
f1 (ppm)


F
N
N
AcO
Ph
N
H
1i
f1 (ppm)


f1 (ppm)


F
N
N
AcO
Ph
N
H
1l
f1 (ppm)


f1 (ppm)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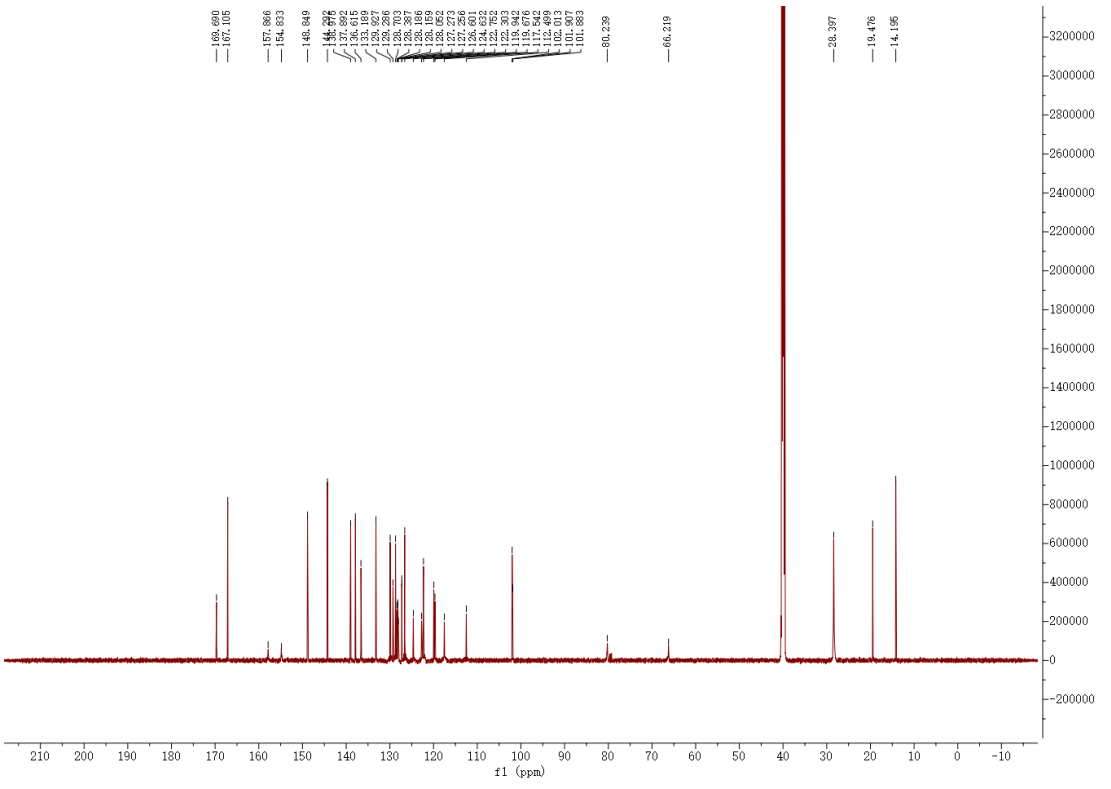
8.218
8.207
7.717
7.706
7.695
7.693
7.516
7.505
7.494
7.418
7.407
7.396
7.388
7.357
7.346
7.210
7.199
7.187
7.179
7.174
7.167
7.146
7.135
7.045
7.034
7.024
6.790
1.798
1.269
1.161
Ph
N
N
Ph
OAc
NHBoc
N
H
O
N
Ph
3aa
0.93
2.00
3.07
3.09
3.12
1.09
5.18
1.07
0.90
3.12
3.14
9.32
f1 (ppm)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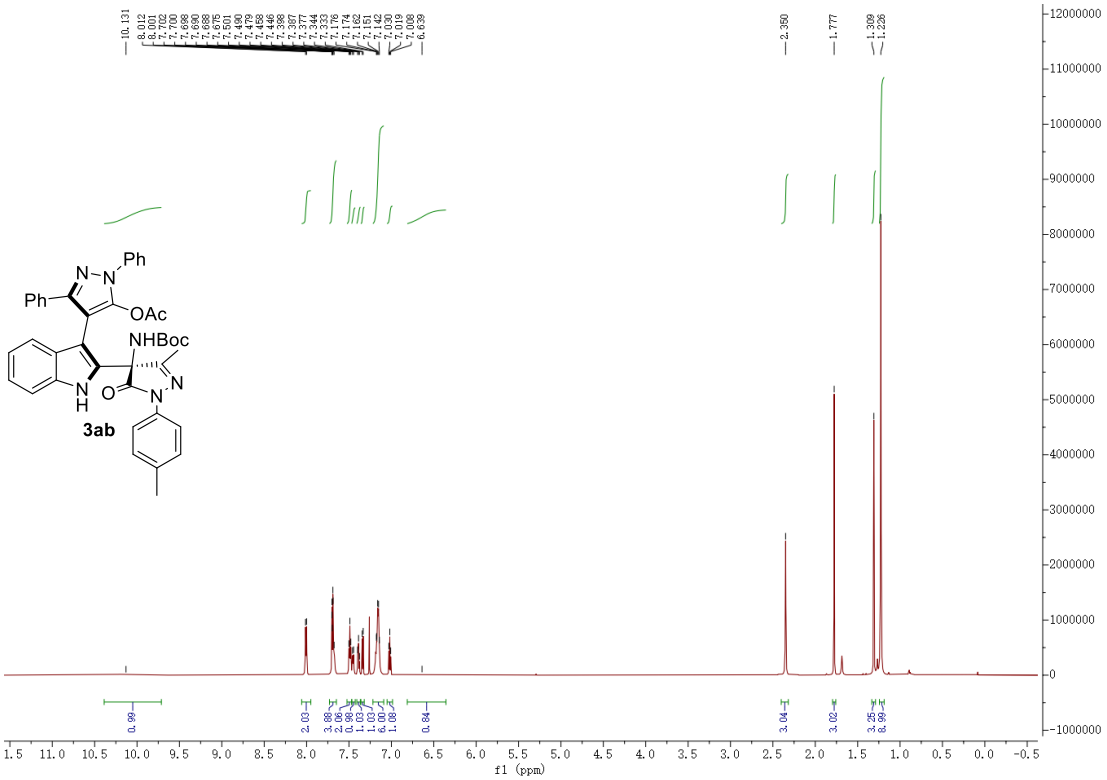
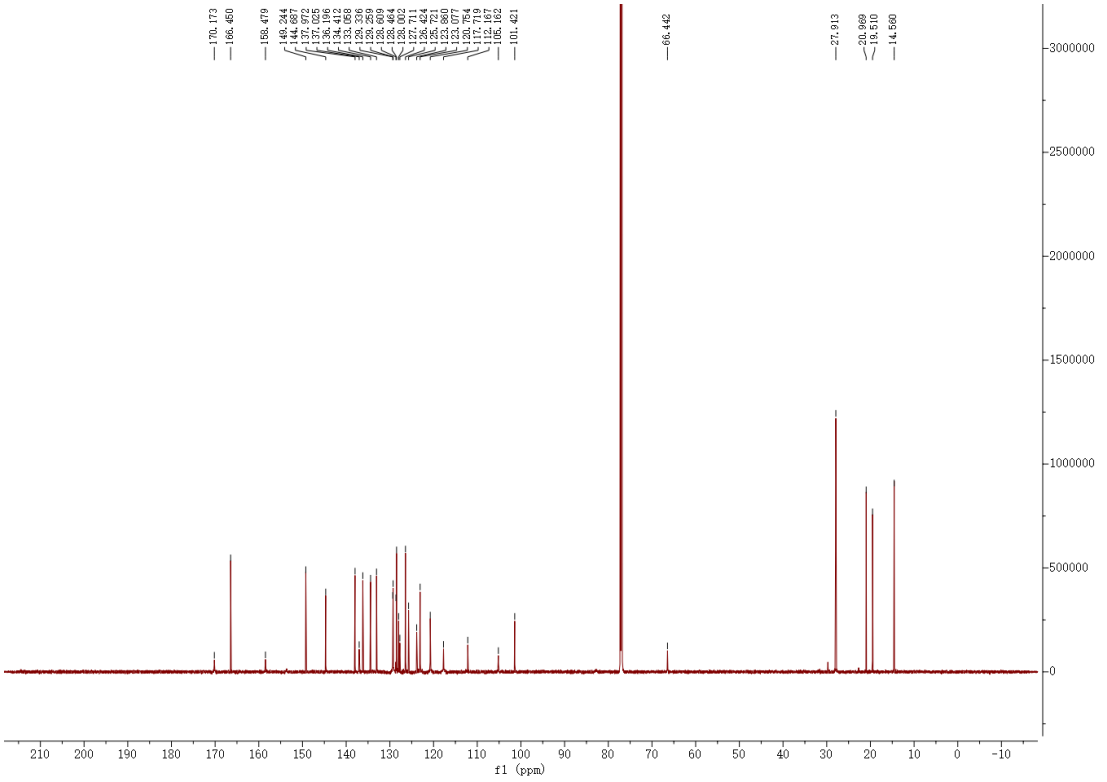
157.866
154.833
148.849
80.239
66.219
28.397
19.476
14.195
f1 (ppm)


10.131
8.012
8.001
7.702
7.700
7.698
7.688
7.675
7.501
7.490
7.479
7.468
7.446
7.398
7.387
7.377
7.344
7.333
7.176
7.174
7.162
7.151
7.144
7.030
7.019
7.008
6.639
2.360
1.777
1.309
1.228
Ph
N
N
Ph
OAc
NHBoc
N
H
O
N
3ab
0.99
2.03
3.88
2.98
1.03
1.03
6.00
1.08
0.84
3.04
3.02
3.25
3.99
f1 (ppm)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144.697
137.972
137.025
136.196
134.447
133.058
129.336
129.259
129.060
128.464
128.002
127.711
126.424
126.272
123.880
123.077
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112.167
105.162
101.421
66.442
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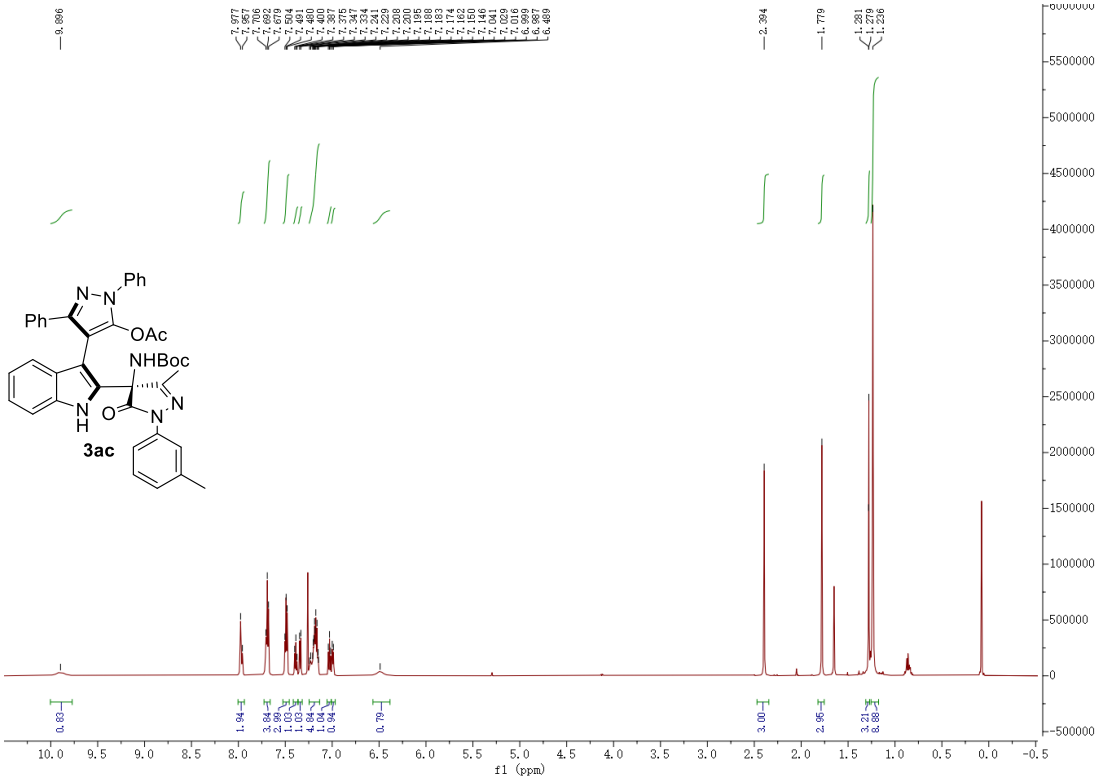
20.969
19.510
14.560
f1 (ppm)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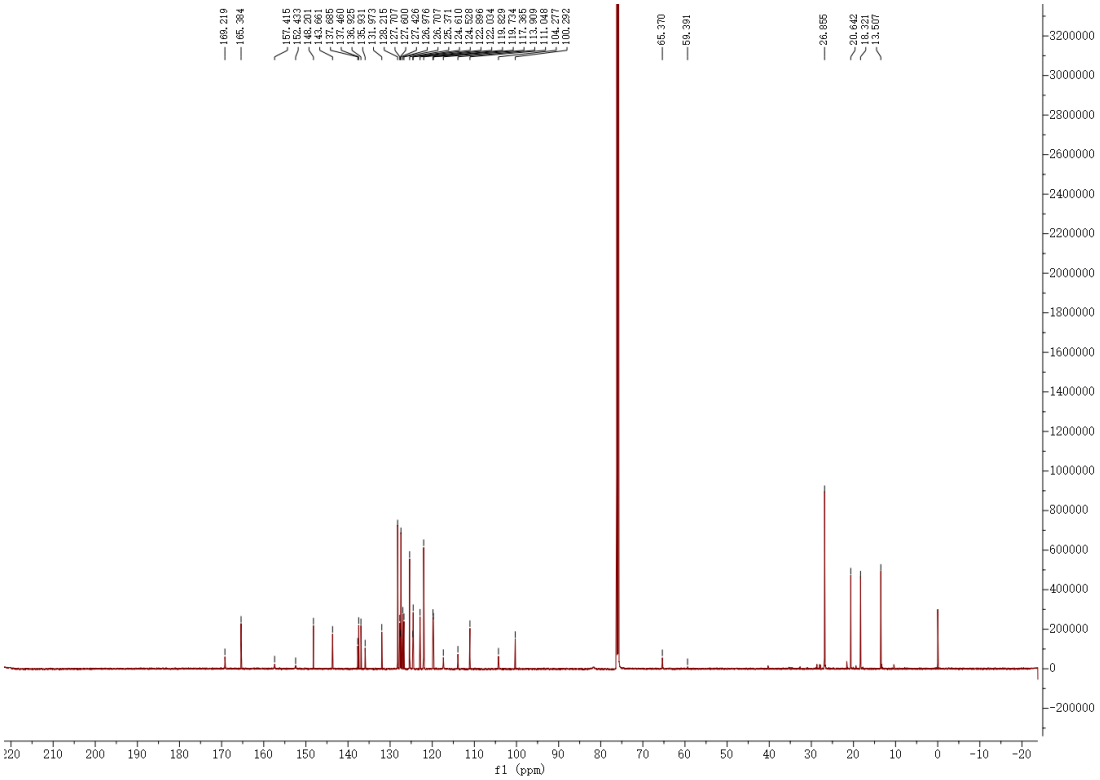
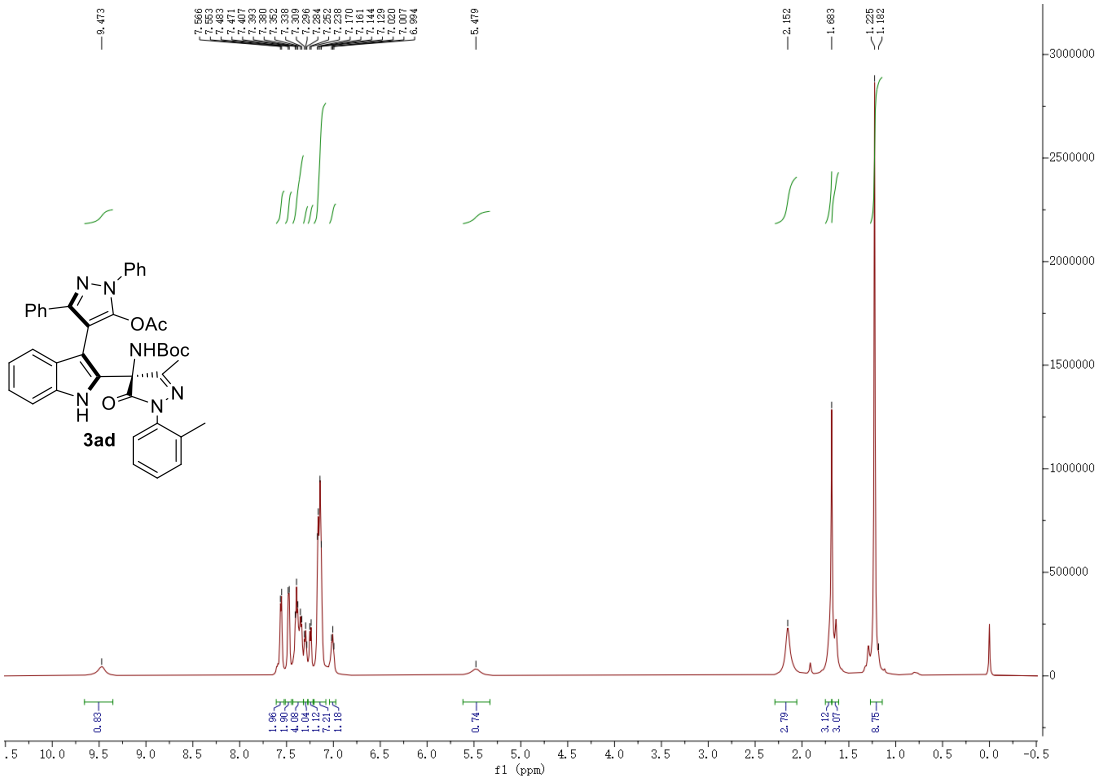
Ph
OAc
NHBoc
N
H
O
3ac
f1 (ppm)


f1 (ppm)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7.471
7.407
7.393
7.380
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7.338
7.309
7.296
7.284
7.252
7.238
7.170
7.161
7.144
7.129
7.107
7.007
6.994
5.479
2.152
1.883
1.225
1.182
Ph
Ph
N
N
OAc
NHBoc
N
O
N
H
N
3ad
0.83
1.96
1.90
1.48
1.04
1.12
7.21
1.18
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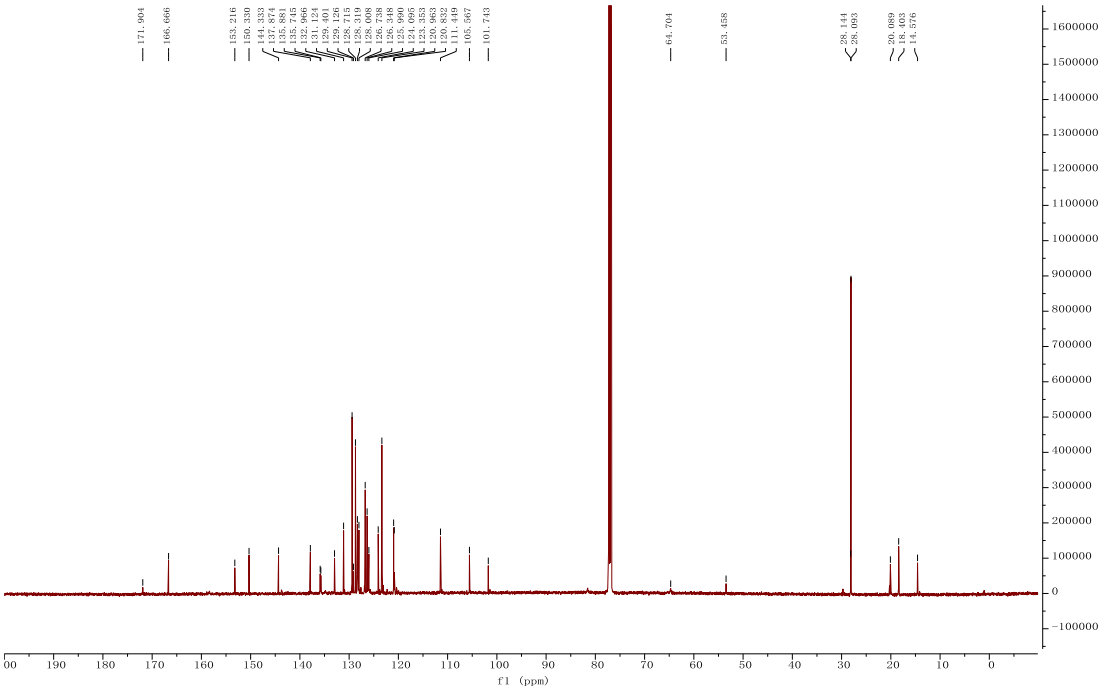
2.79
3.12
3.07
8.76
f1 (ppm)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150.330
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131.124
129.401
129.126
128.775
128.319
128.008
126.738
125.344
125.040
124.095
123.353
120.983
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101.743
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28.144
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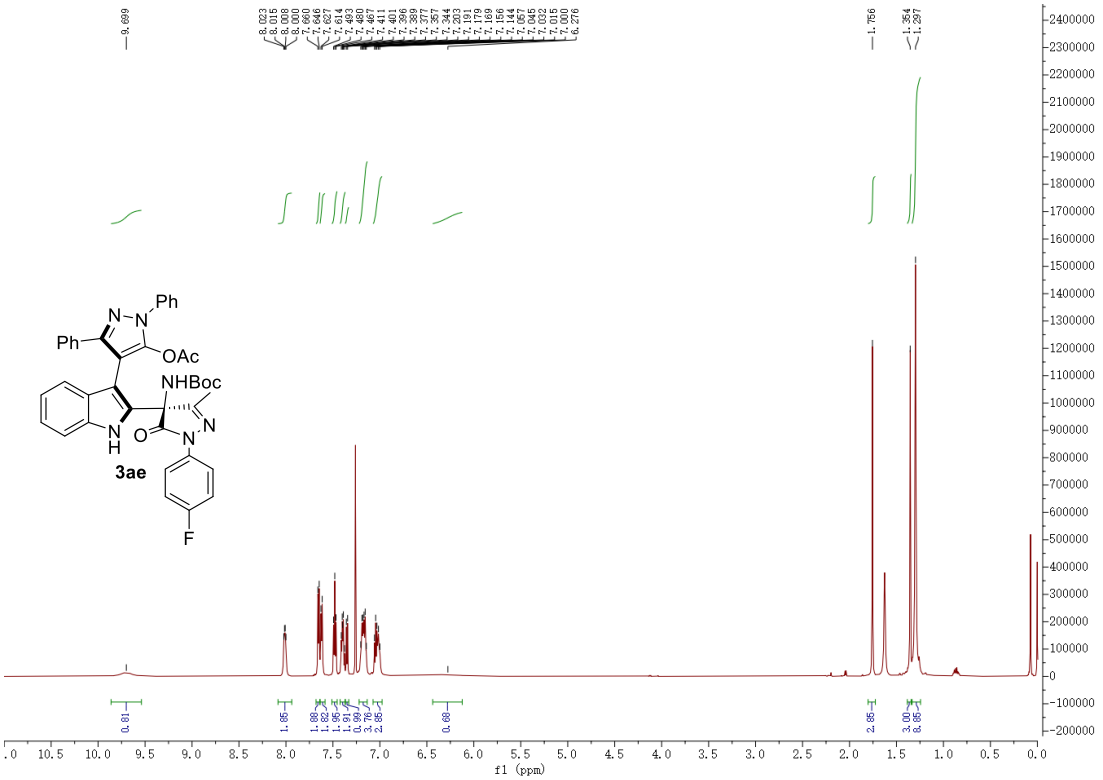
20.089
18.403
14.576
f1 (ppm)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8.000
7.660
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7.627
7.464
7.453
7.480
7.467
7.411
7.401
7.396
7.389
7.377
7.357
7.344
7.233
7.191
7.178
7.169
7.156
7.144
7.087
7.046
7.032
7.015
7.000
6.976
1.756
1.364
1.297
Ph
N
N
Ph
OAc
NHBoc
N
H
O
N
N
3ae
F
0.81
1.05
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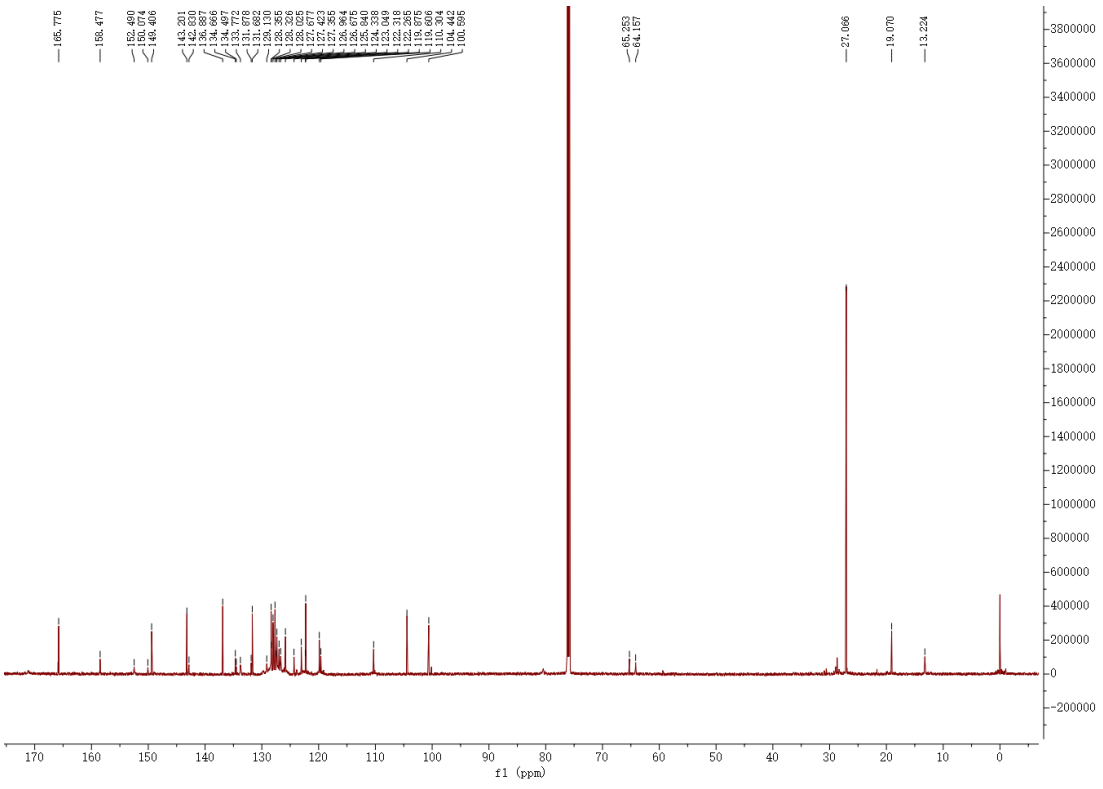
1.82
1.95
1.91
0.99
3.76
2.85
0.68
2.05
3.00
8.85
f1 (ppm)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142.830
136.887
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133.772
131.678
131.682
129.170
128.355
128.326
128.025
127.677
127.423
127.355
126.964
126.675
126.640
124.338
123.049
122.318
122.295
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104.442
100.695
65.253
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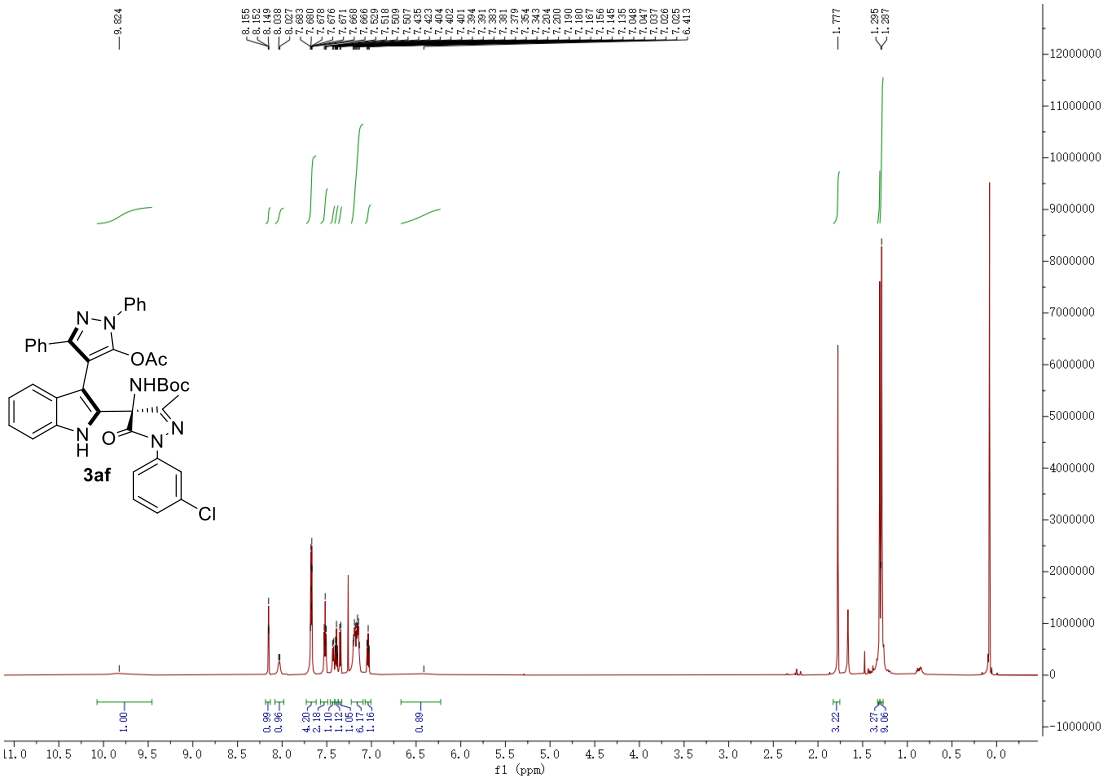
19.070
13.224
f1 (ppm)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7.671
7.668
7.666
7.529
7.518
7.509
7.507
7.435
7.423
7.404
7.402
7.401
7.394
7.391
7.383
7.381
7.379
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7.343
7.264
7.200
7.190
7.180
7.167
7.156
7.145
7.135
7.048
7.047
7.037
7.026
7.025
6.413
1.777
1.295
1.287
Ph
N
N
Ph
OAc
NHBoc
N
O
N
H
3af
Cl
1.00
0.99
0.96
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1.07
1.05
6.17
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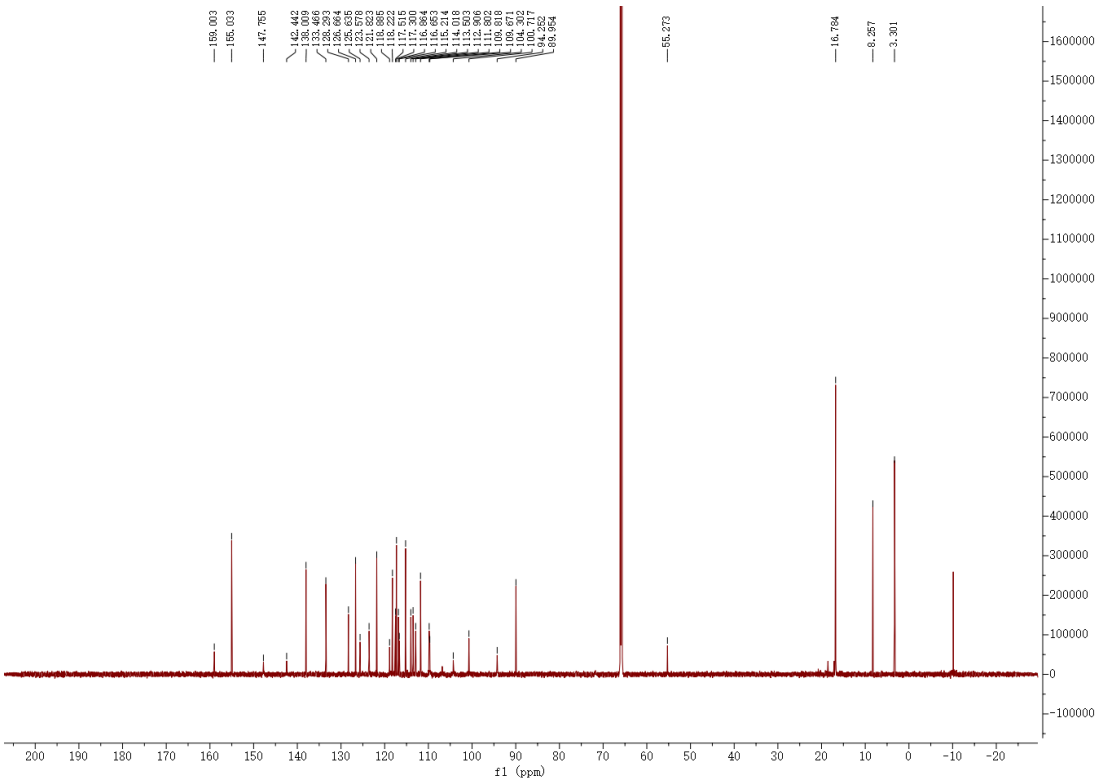
9.86
f1 (ppm)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155.033
147.765
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133.466
128.293
126.464
125.636
123.578
121.823
118.885
118.225
117.615
117.300
116.864
116.465
115.214
114.018
113.503
112.966
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109.818
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104.702
104.217
94.252
89.954
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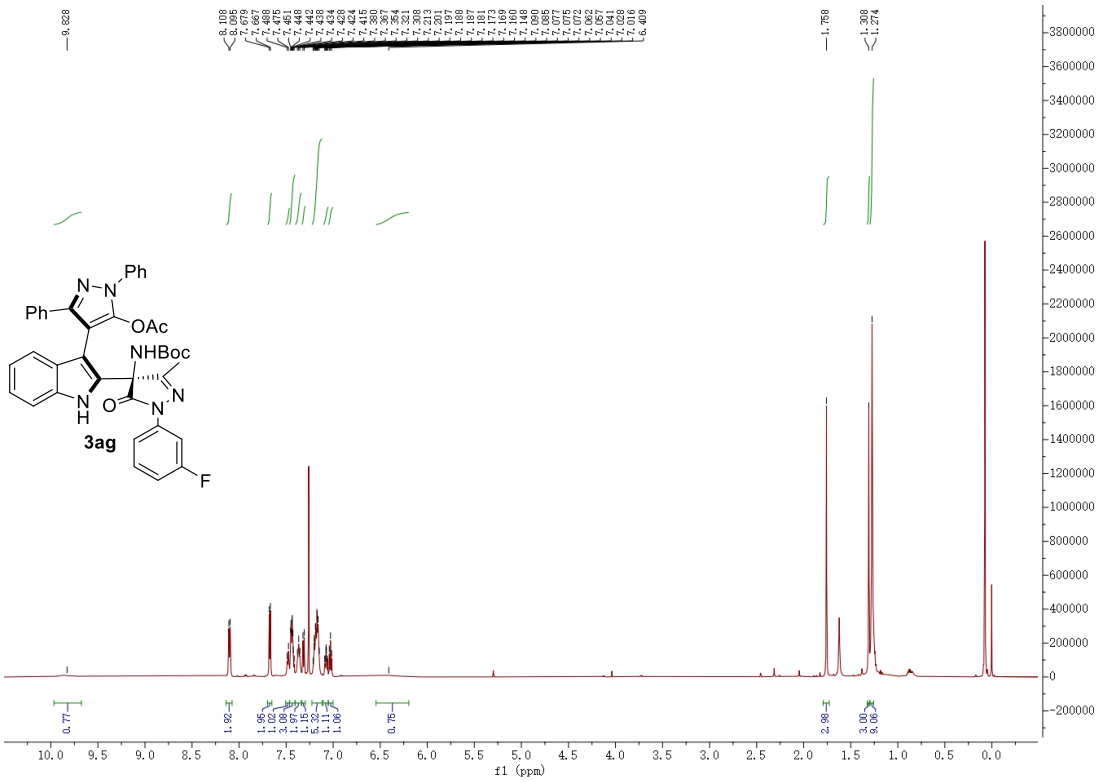
16.784
8.257
3.301
f1 (ppm)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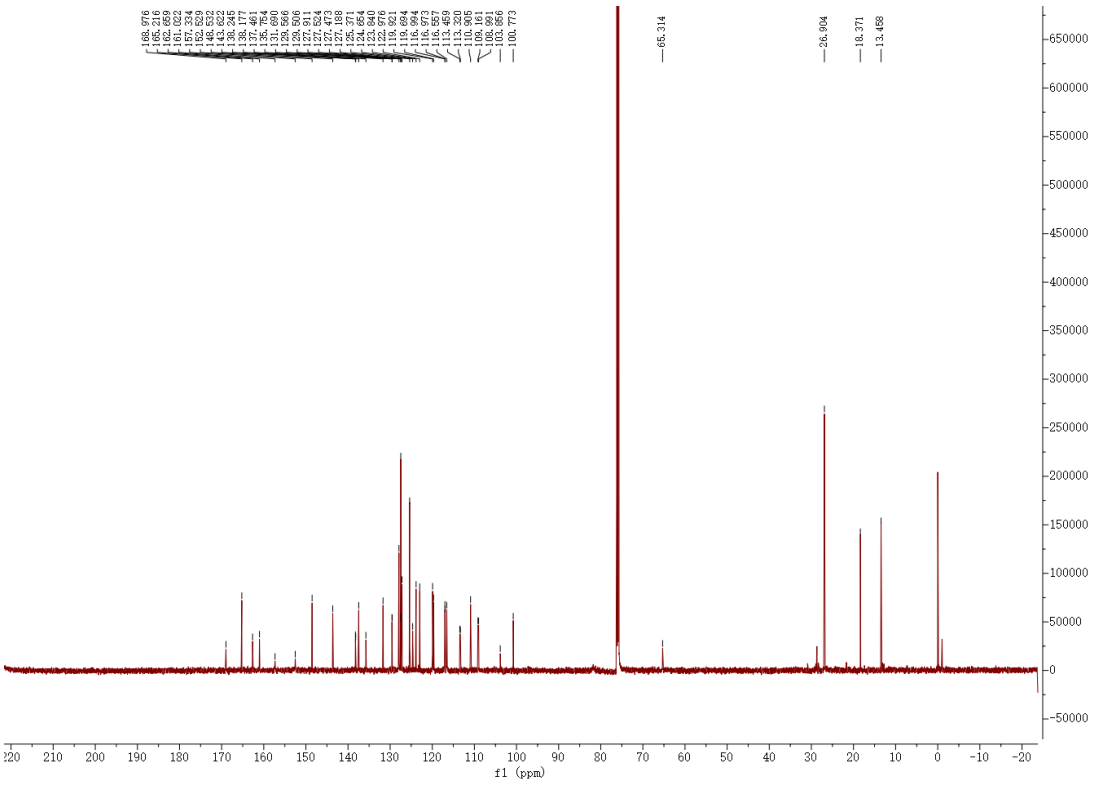
f1 (ppm)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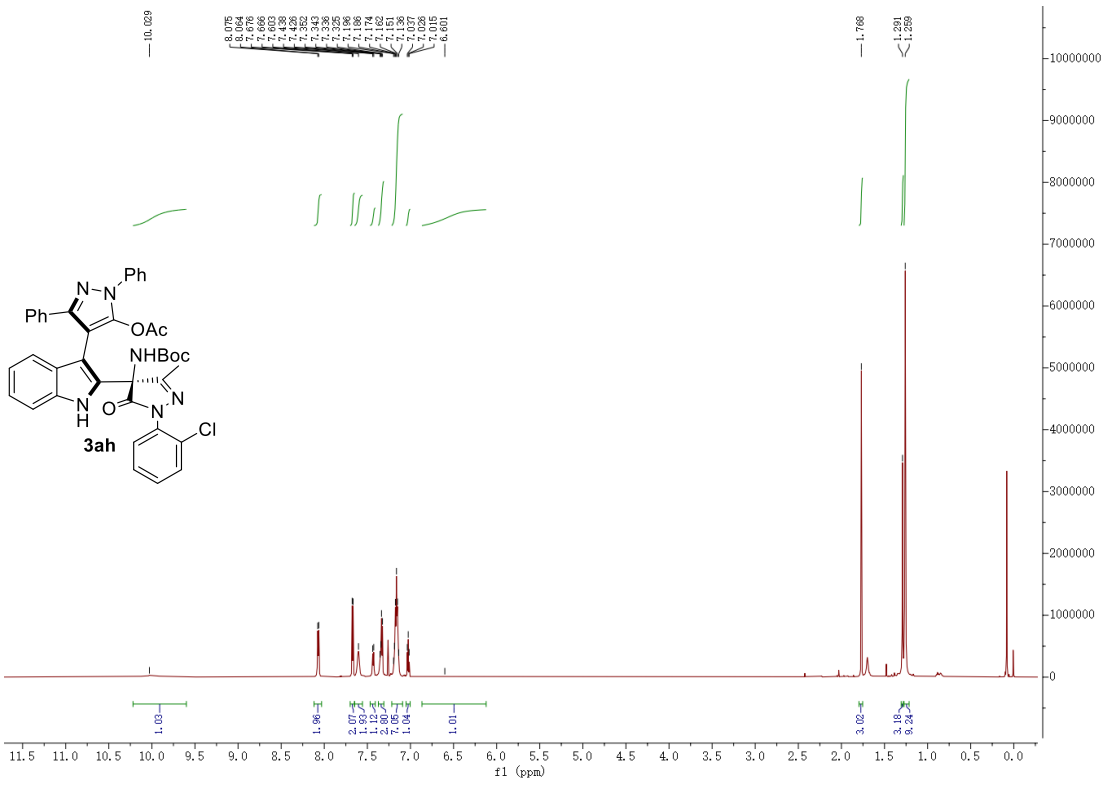
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7.335
7.205
7.196
7.186
7.174
7.162
7.151
7.136
7.037
7.026
7.015
6.601
1.768
1.291
1.289
Ph
N
N
Ph
OAc
NHBoc
N
O
N
H
N
Cl
3ah
1.03
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1.12
2.80
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1.01
3.02
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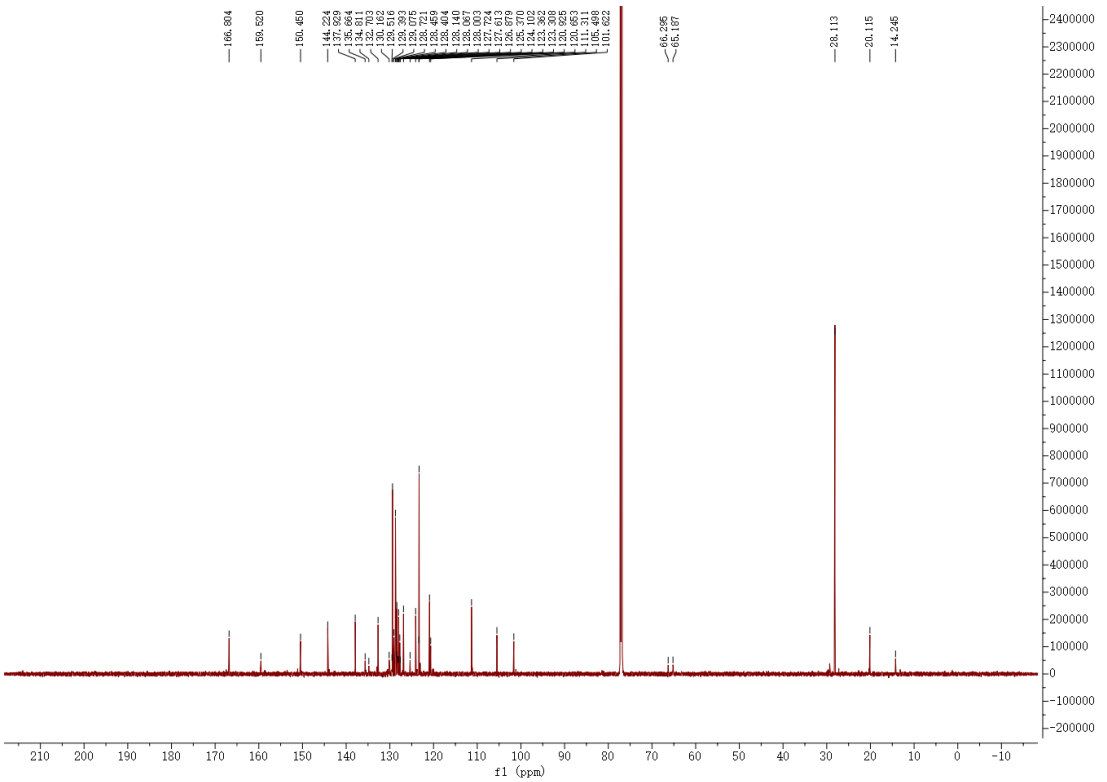
9.24
f1 (ppm)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150.450
144.224
137.928
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132.703
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128.791
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128.404
128.140
128.067
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127.724
127.613
126.979
125.370
124.102
123.362
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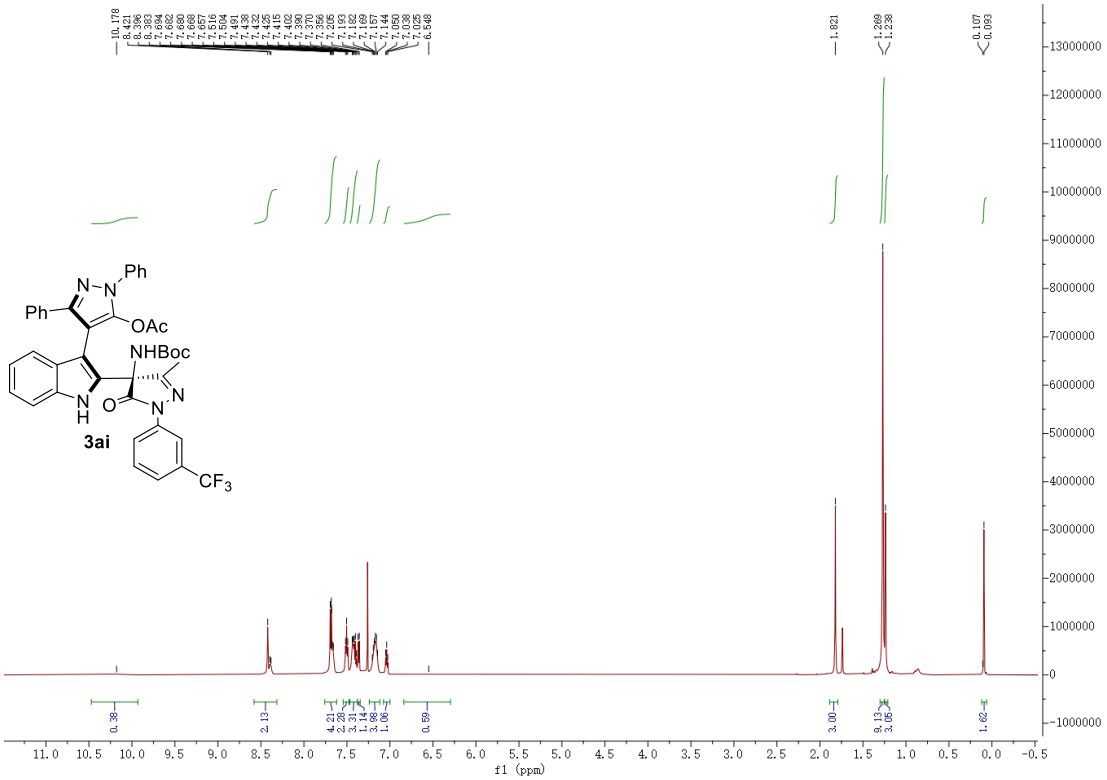
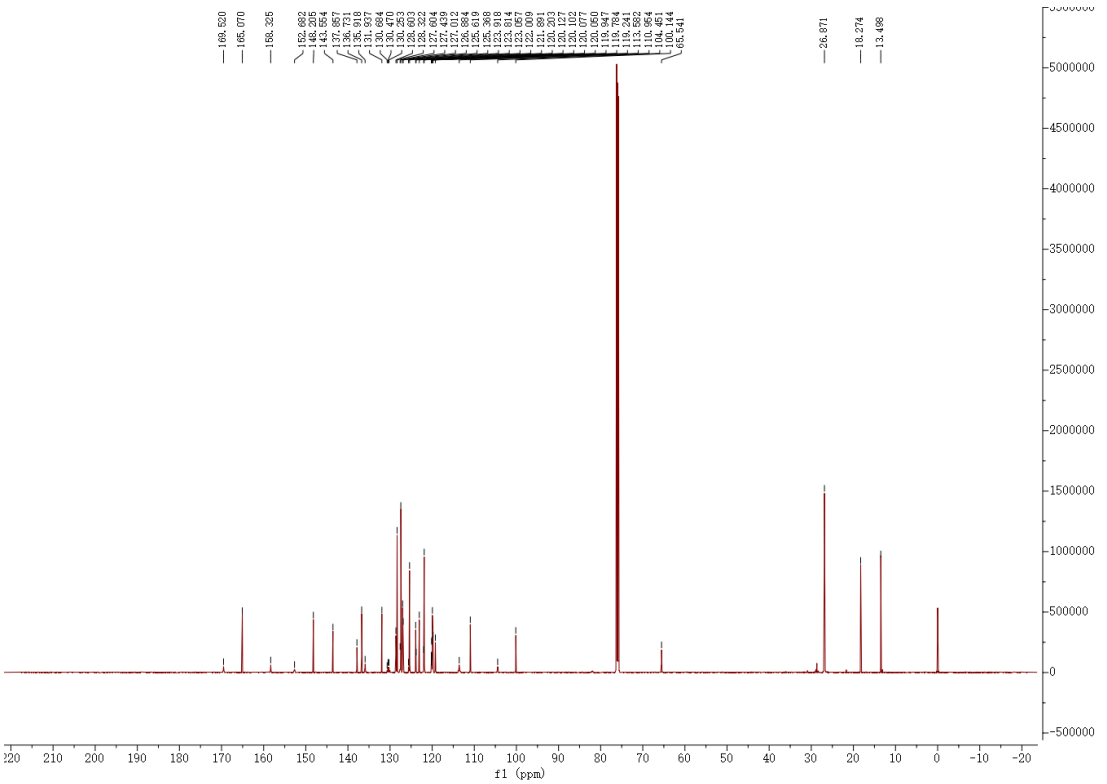
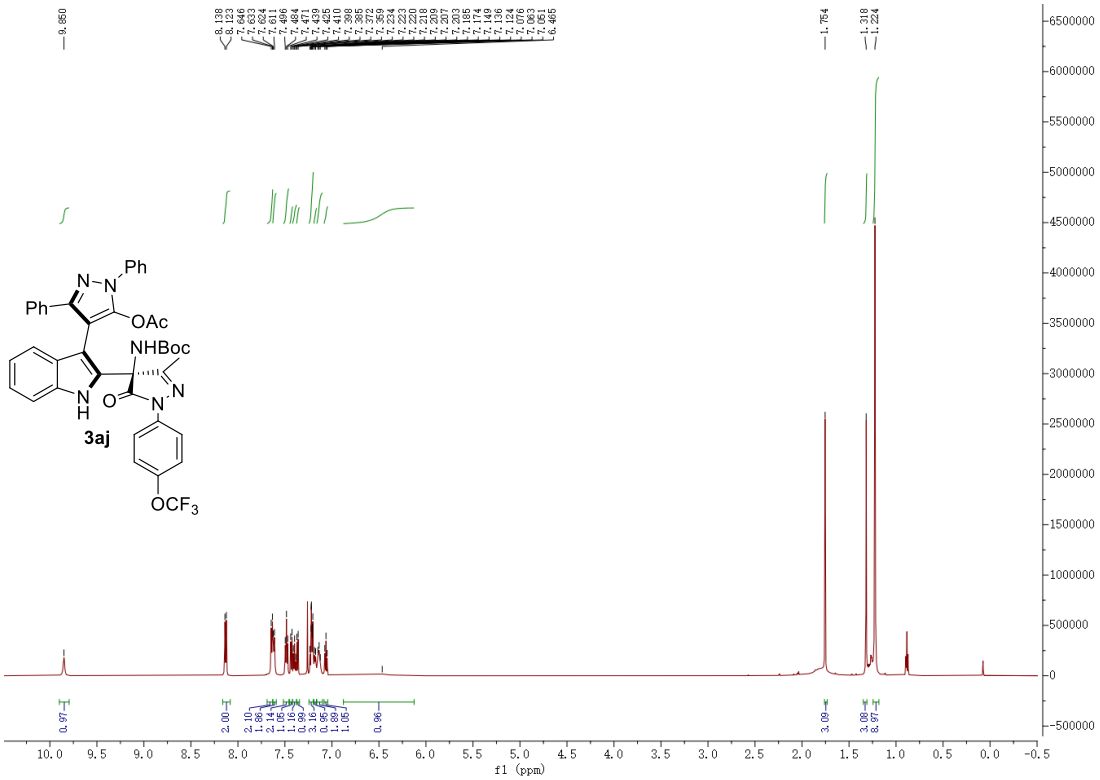
65.167
28.113
20.115
14.245
f1 (ppm)


Ph
N
N
Ph
OAc
NHBoc
N
O
N
H
3ai
CF3
f1 (ppm)


f1 (ppm)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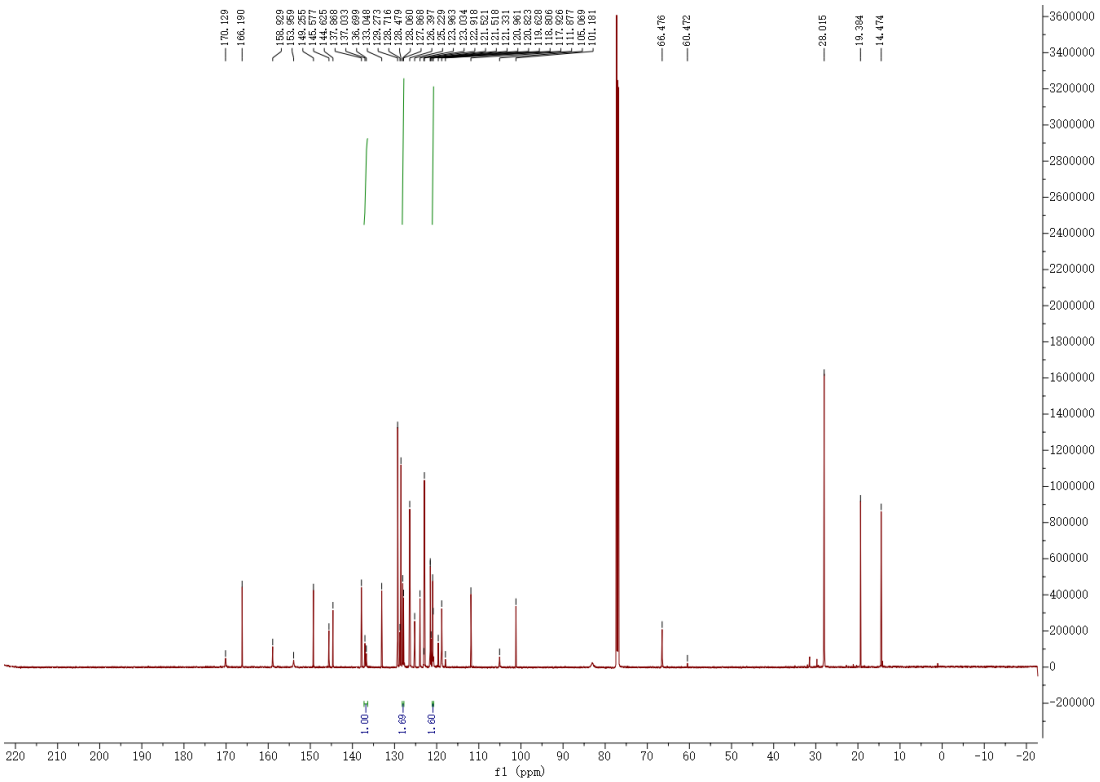

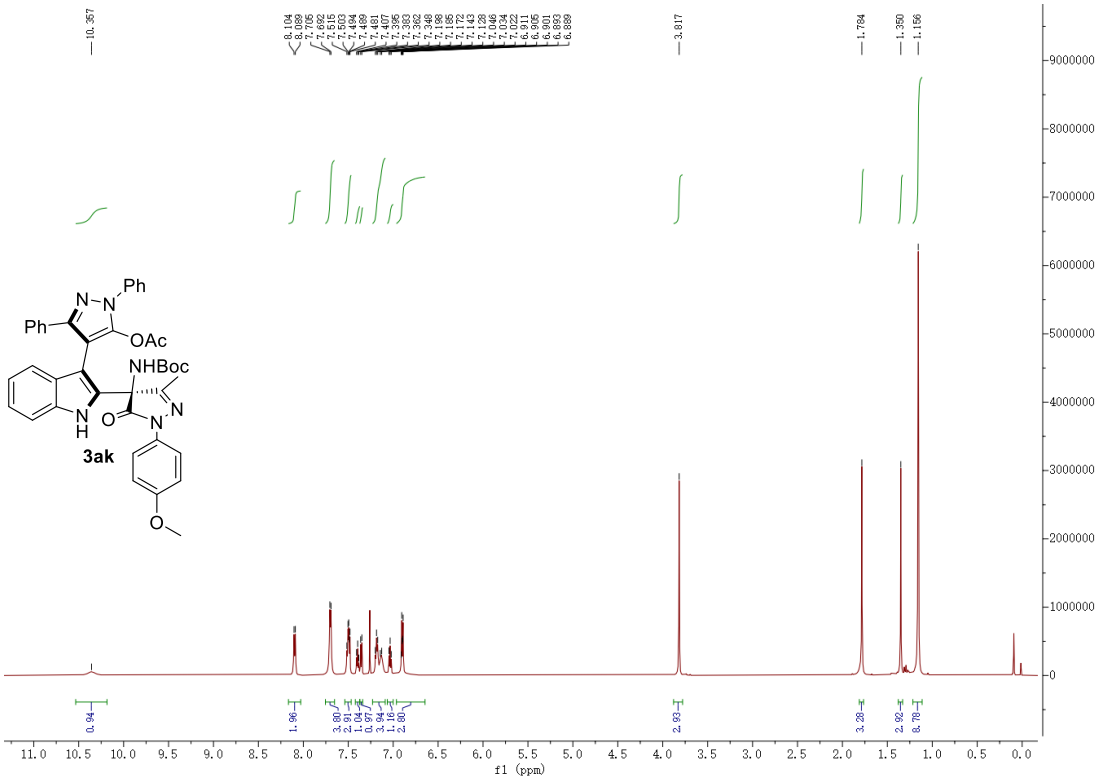
10.367
8.104
8.089
8.070
7.705
7.692
7.515
7.503
7.494
7.489
7.481
7.407
7.385
7.363
7.362
7.348
7.188
7.185
7.172
7.143
7.128
7.046
7.034
7.022
6.911
6.905
6.901
6.893
6.889
3.817
1.784
1.350
1.156
Ph
N
N
Ph
OAc
NHBoc
N
H
O
N
N
3ak
O
0.94
1.96
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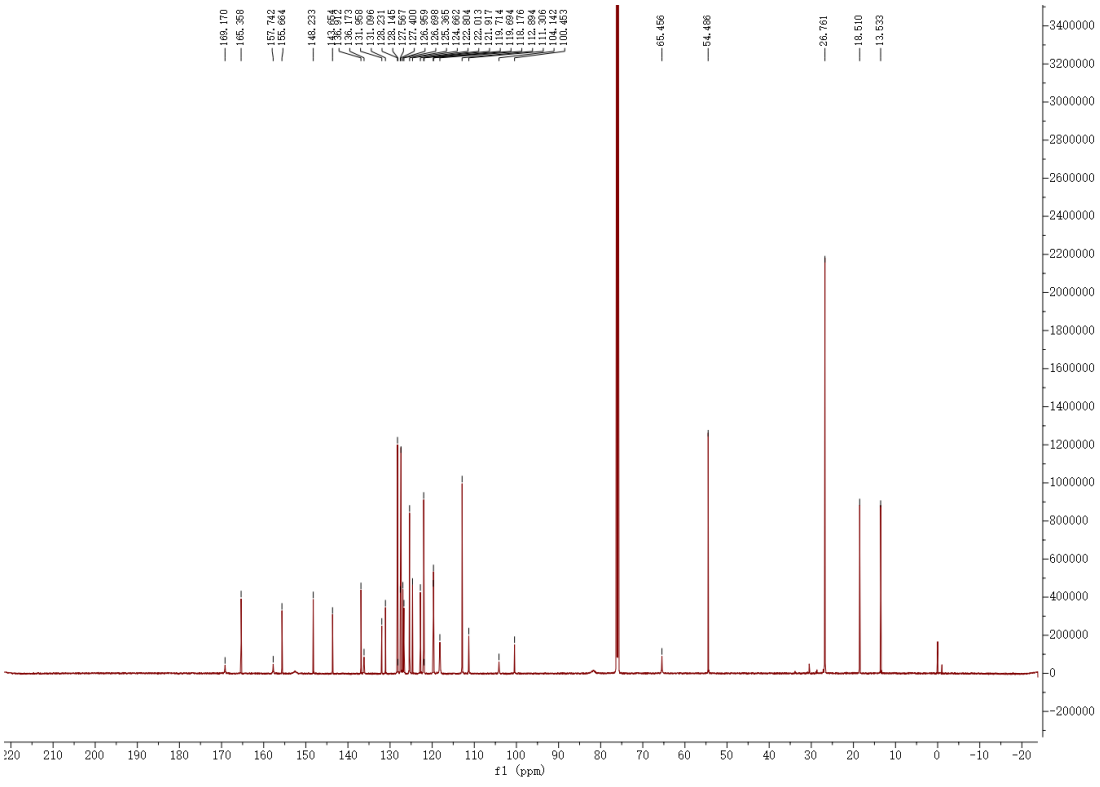
3.14
1.16
2.80
2.83
3.28
2.82
8.78
f1 (ppm)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136.173
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128.145
127.567
127.400
126.859
126.669
125.985
124.662
122.804
122.013
121.917
119.714
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111.306
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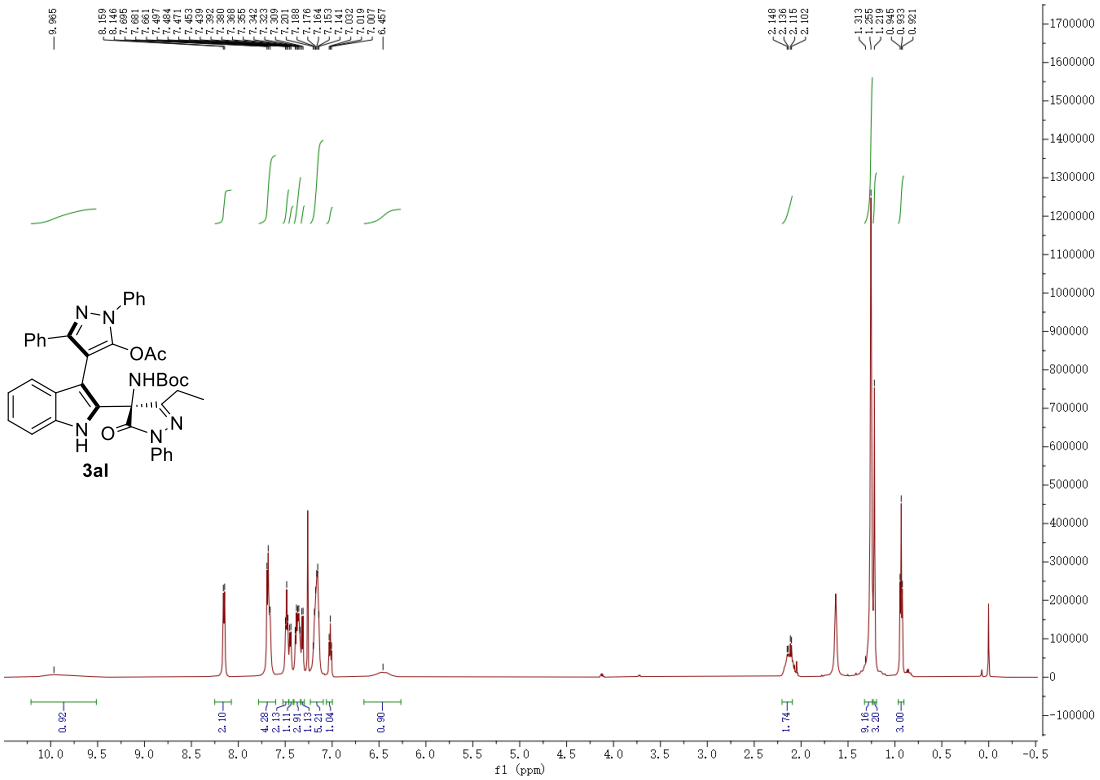
54.486
26.761
18.510
13.533
f1 (ppm)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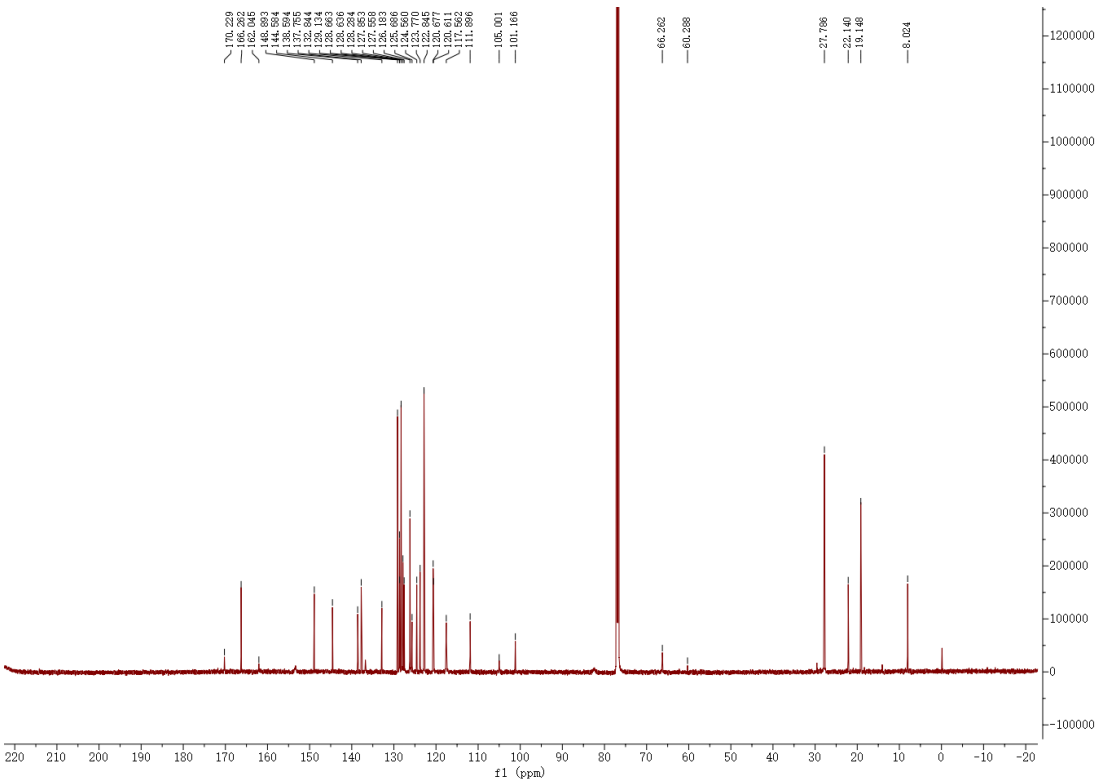
f1 (ppm)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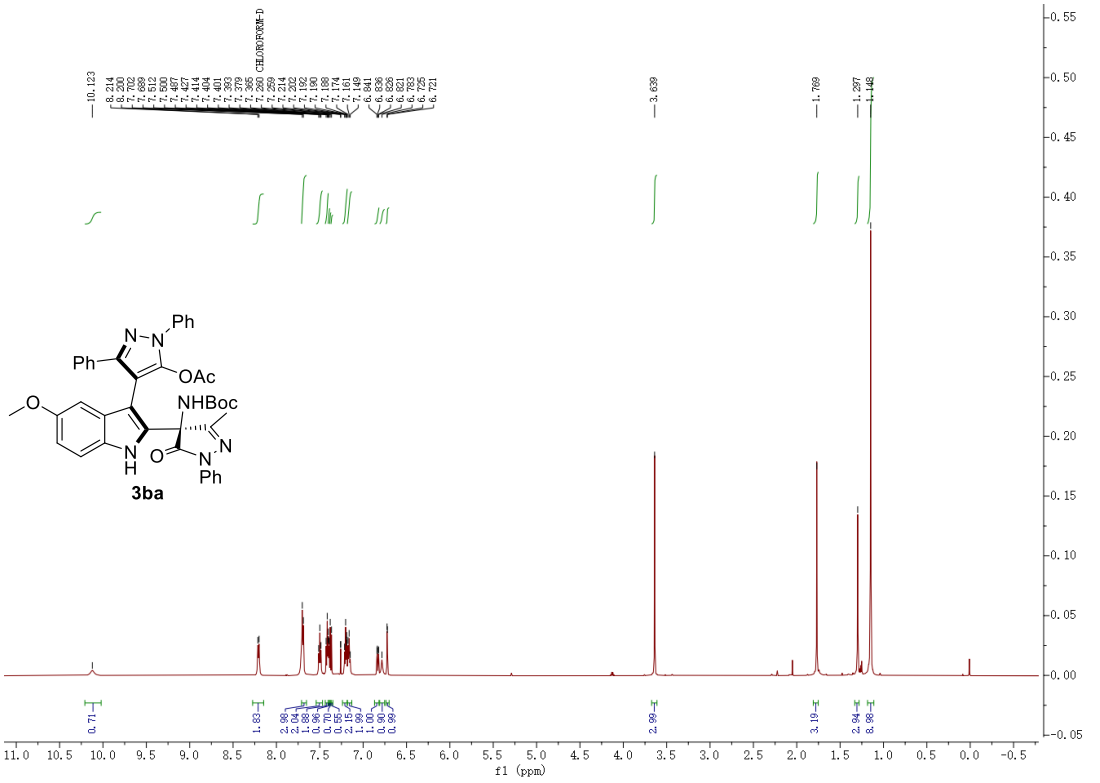
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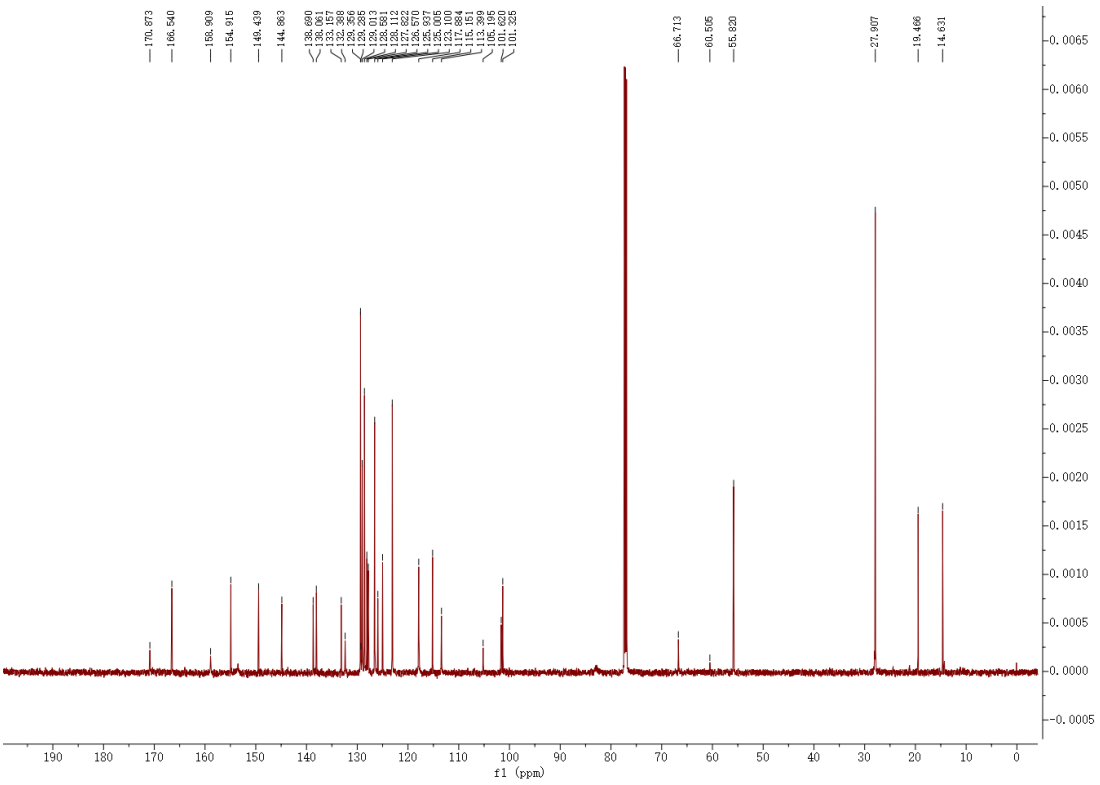

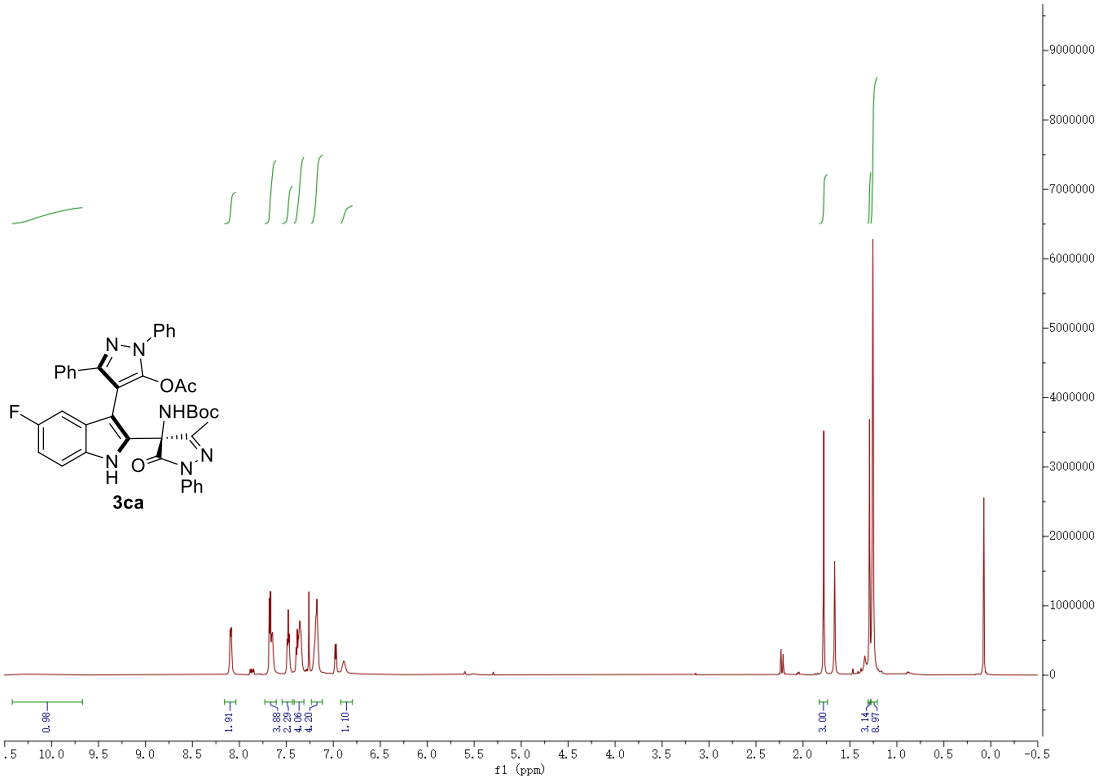
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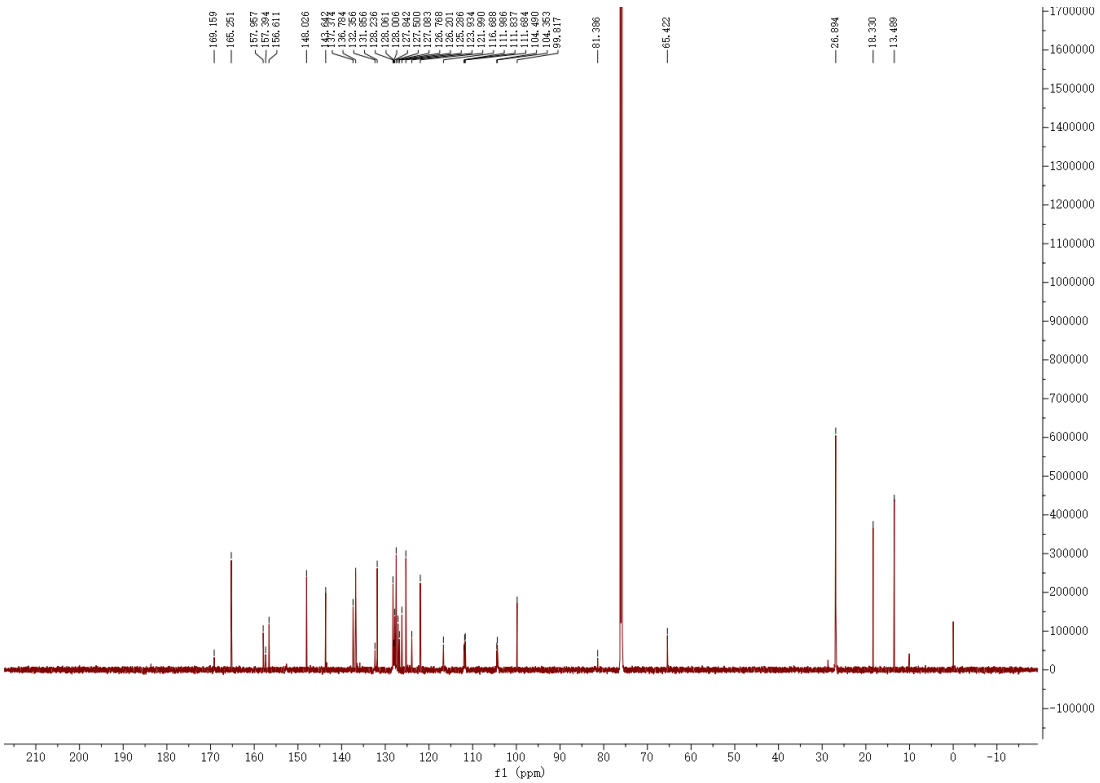
N
Ph
OAc
F
NHBoc
N
H
O
N
N
Ph
3ca
f1 (ppm)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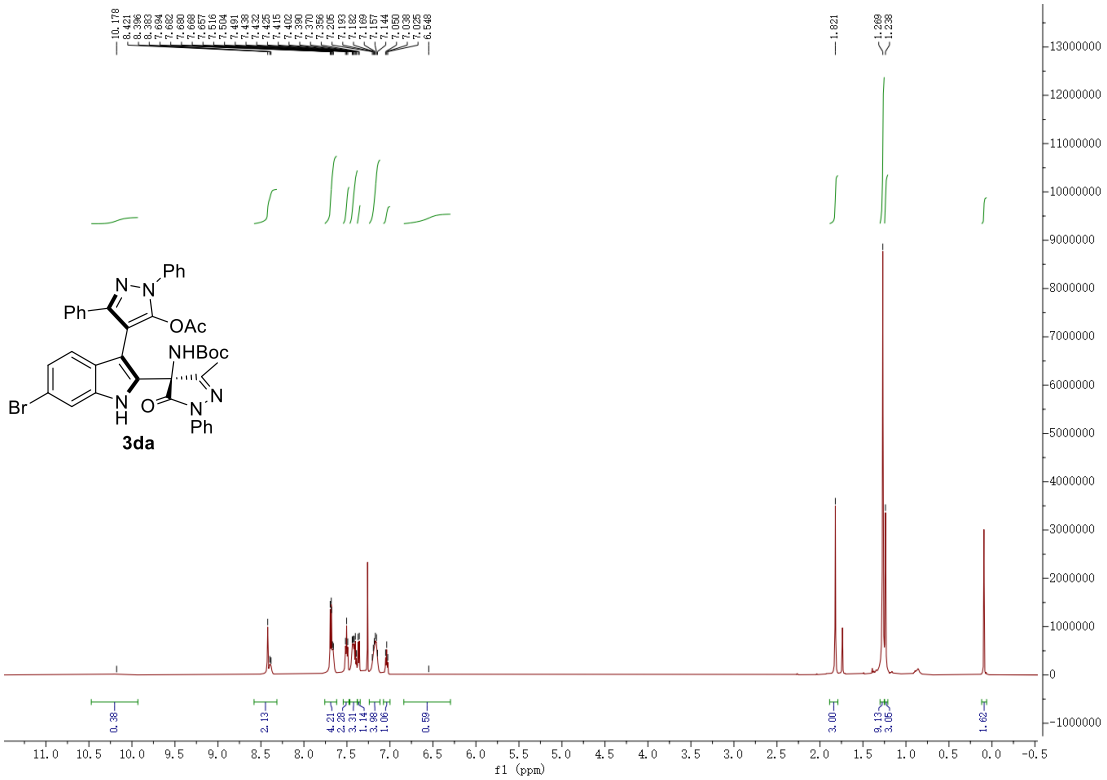
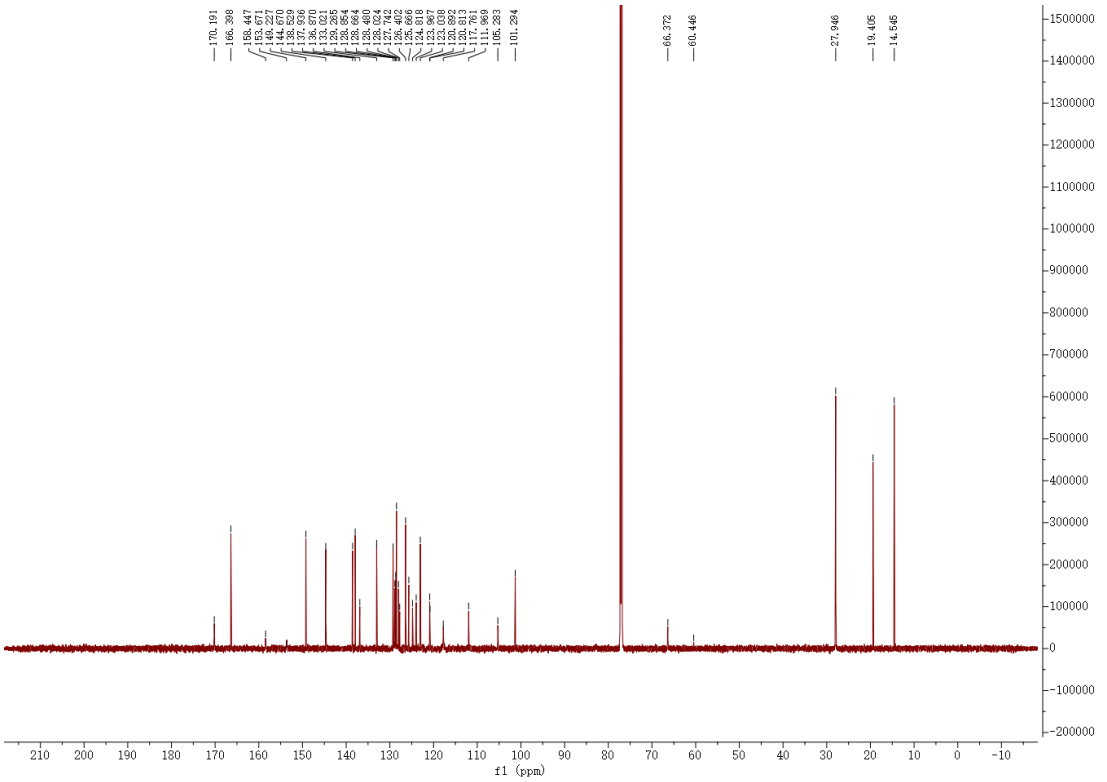
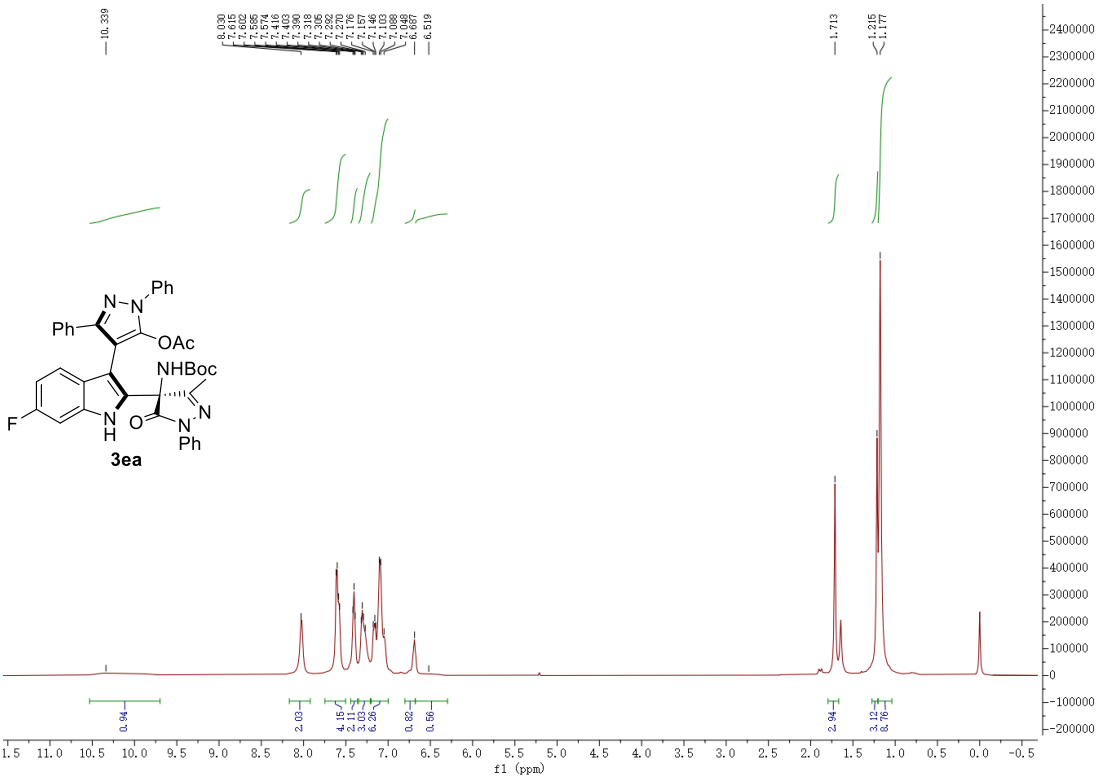
157.394
156.611
148.026
81.386
65.422
26.894
18.330
13.499
f1 (ppm)


Ph
N
N
Ph
OAc
NHBoc
Br
N
H
O
N
N
Ph
3da
f1 (ppm)


f1 (ppm)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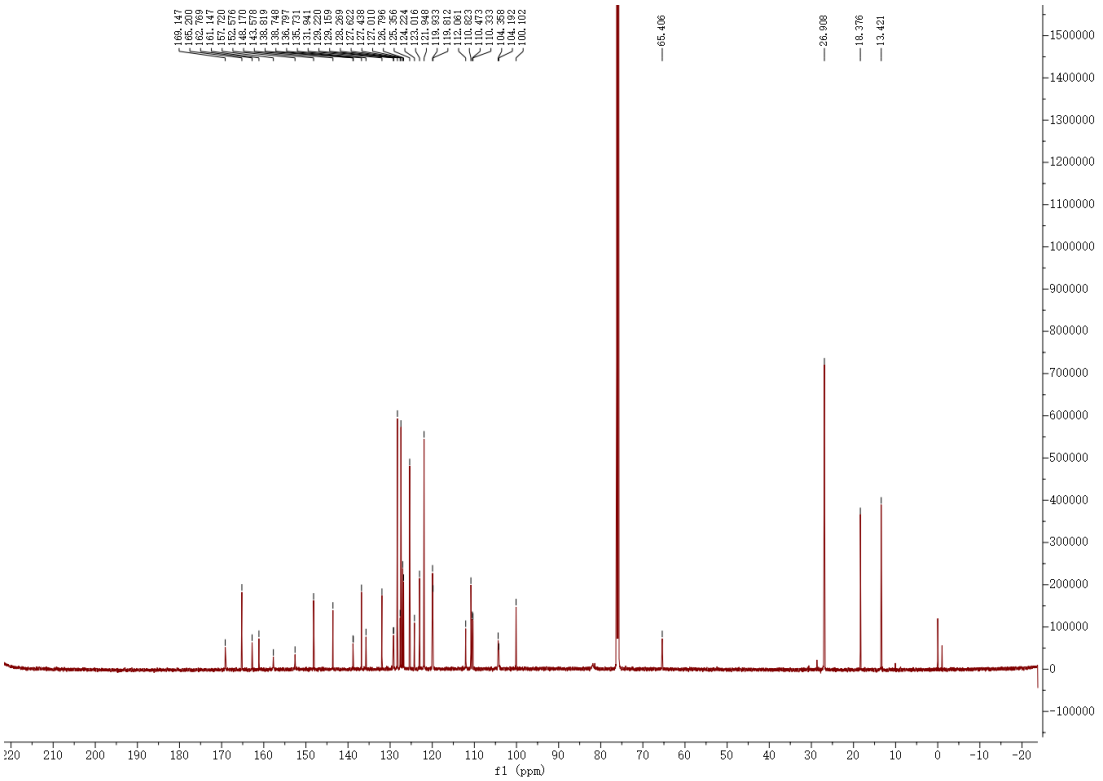
7.615
7.602
7.595
7.574
7.416
7.403
7.390
7.318
7.305
7.292
7.270
7.176
7.157
7.146
7.103
7.088
7.068
6.697
6.519
1.713
1.215
1.177
Ph
N
N
Ph
OAc
NHBoc
F
N
H
O
N
N
Ph
3ea
0.94
2.03
4.15
2.11
3.03
6.26
0.82
0.56
2.94
3.12
8.76
f1 (ppm)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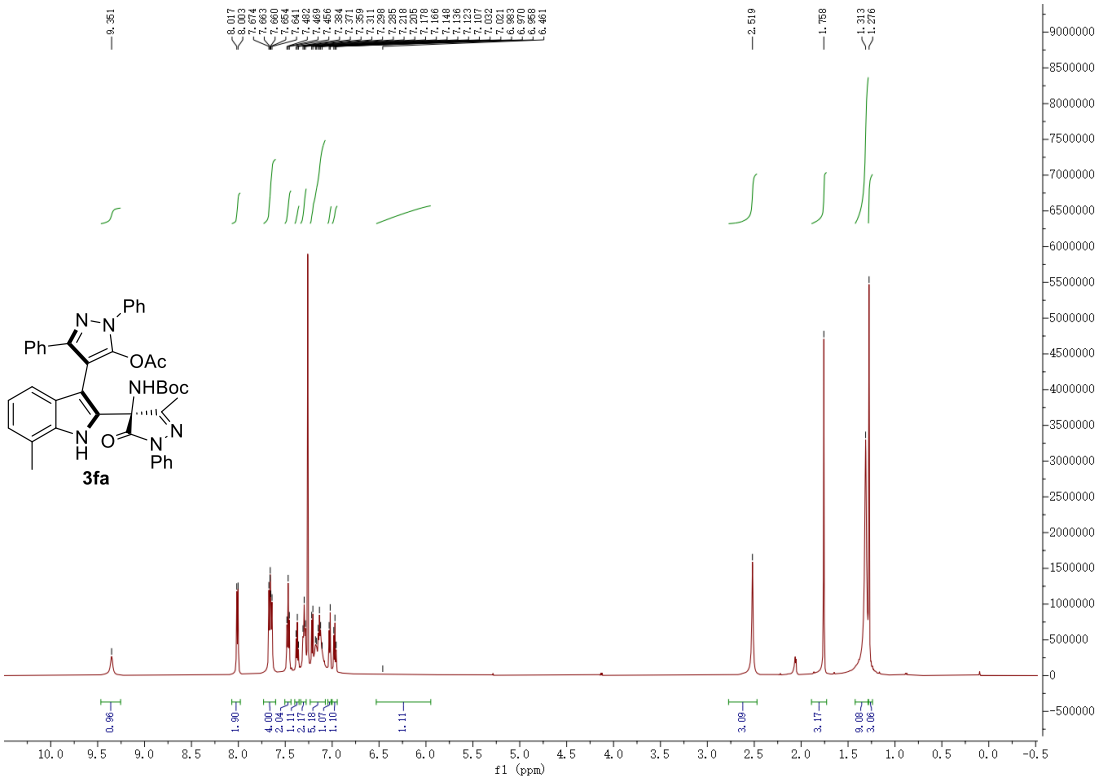
162.769
161.147
157.720
152.576
148.170
143.578
138.819
138.748
136.797
135.771
131.941
129.220
129.159
128.289
127.662
127.438
127.010
126.796
125.765
124.224
123.016
121.948
119.932
119.812
112.061
110.823
110.473
110.333
104.358
104.192
100.102
65.406
26.908
18.376
13.421
f1 (ppm)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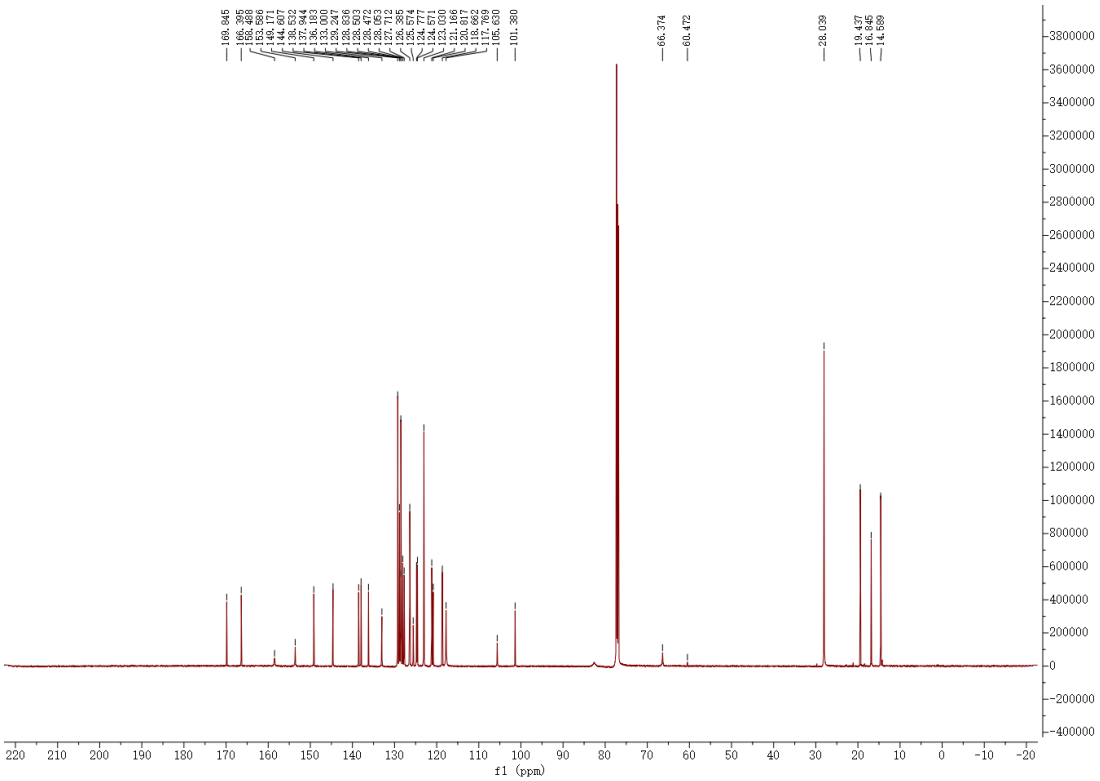
8.017
8.003
7.674
7.663
7.660
7.654
7.644
7.482
7.469
7.456
7.394
7.371
7.359
7.311
7.298
7.255
7.218
7.205
7.178
7.166
7.149
7.136
7.123
7.107
7.022
7.021
6.883
6.870
6.858
6.461
2.519
1.768
1.313
1.276
Ph
N
N
Ph
OAc
NHBoc
N
H
O
N
N
Ph
3fa
0.96
1.90
4.00
2.04
1.11
1.11
2.17
5.18
1.07
1.10
1.11
3.09
3.17
9.08
3.06
f1 (ppm)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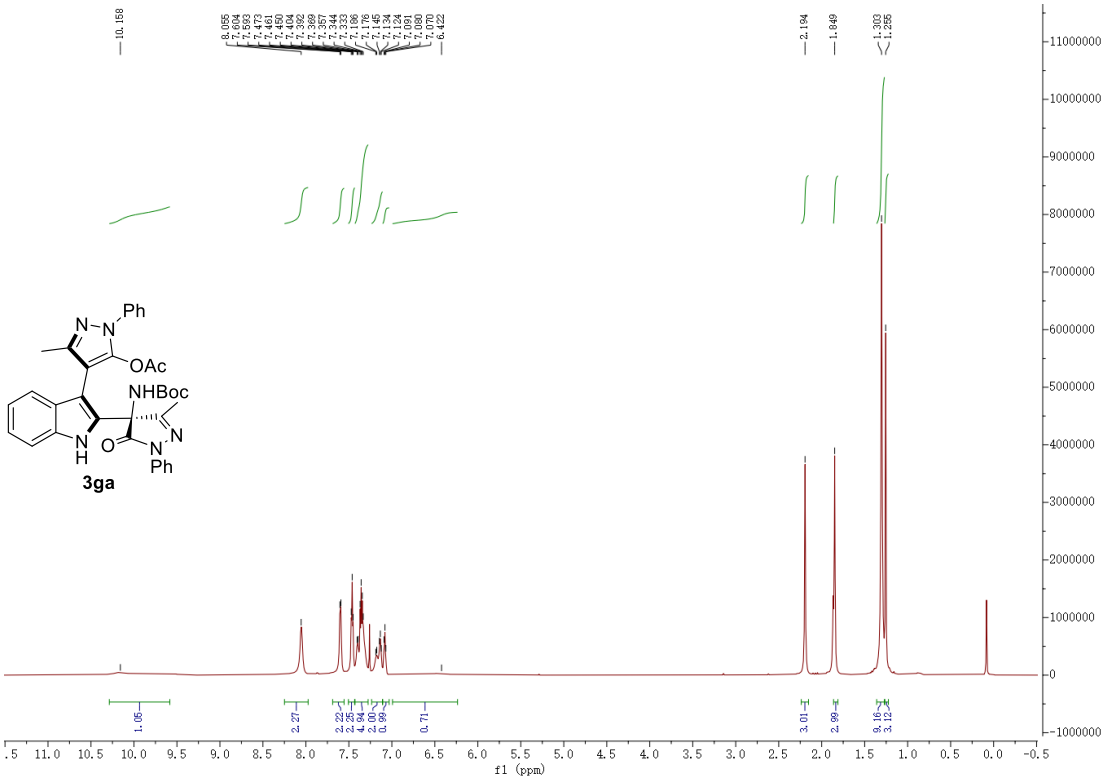
169.395
168.888
153.866
144.171
144.007
138.532
137.944
136.183
135.000
129.247
128.836
128.803
128.472
128.455
127.712
126.385
125.574
125.277
124.871
123.030
121.166
120.837
118.862
117.769
105.630
101.380
66.374
60.472
28.039
19.437
15.845
14.589
f1 (ppm)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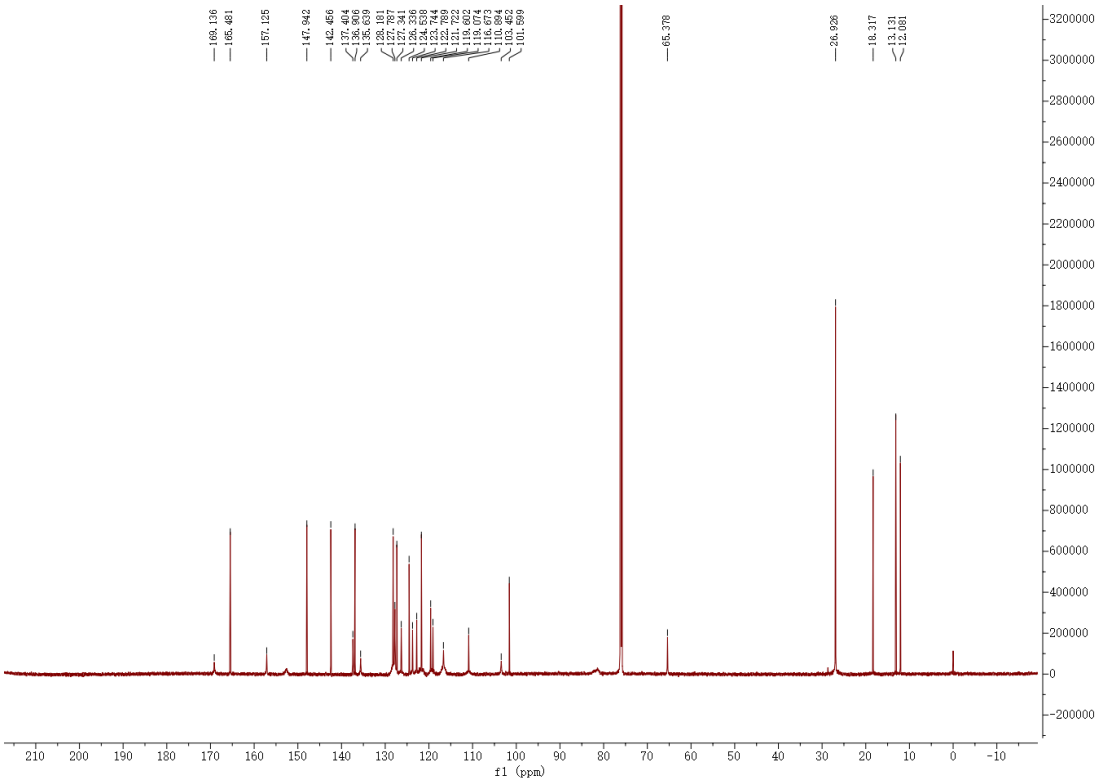
7.473
7.461
7.450
7.404
7.382
7.369
7.357
7.344
7.333
7.186
7.175
7.145
7.134
7.124
7.091
7.080
7.070
6.422
2.194
1.849
1.303
1.295
Ph
N
N
OAc
NHBoc
N
H
O
N
N
Ph
3ga
1.05
2.27
2.22
2.25
4.84
2.00
0.99
0.71
3.01
2.99
9.16
3.12
f1 (ppm)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142.456
137.404
136.806
135.659
129.191
128.787
127.341
126.238
124.598
123.744
122.789
121.722
119.802
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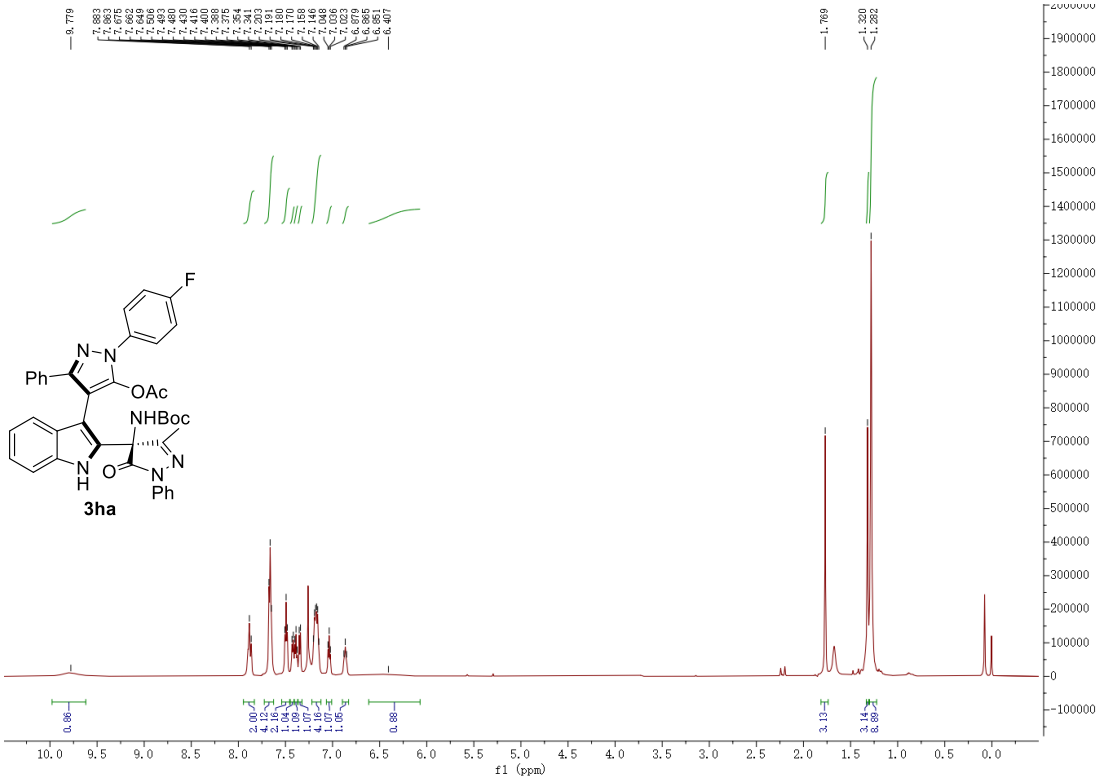
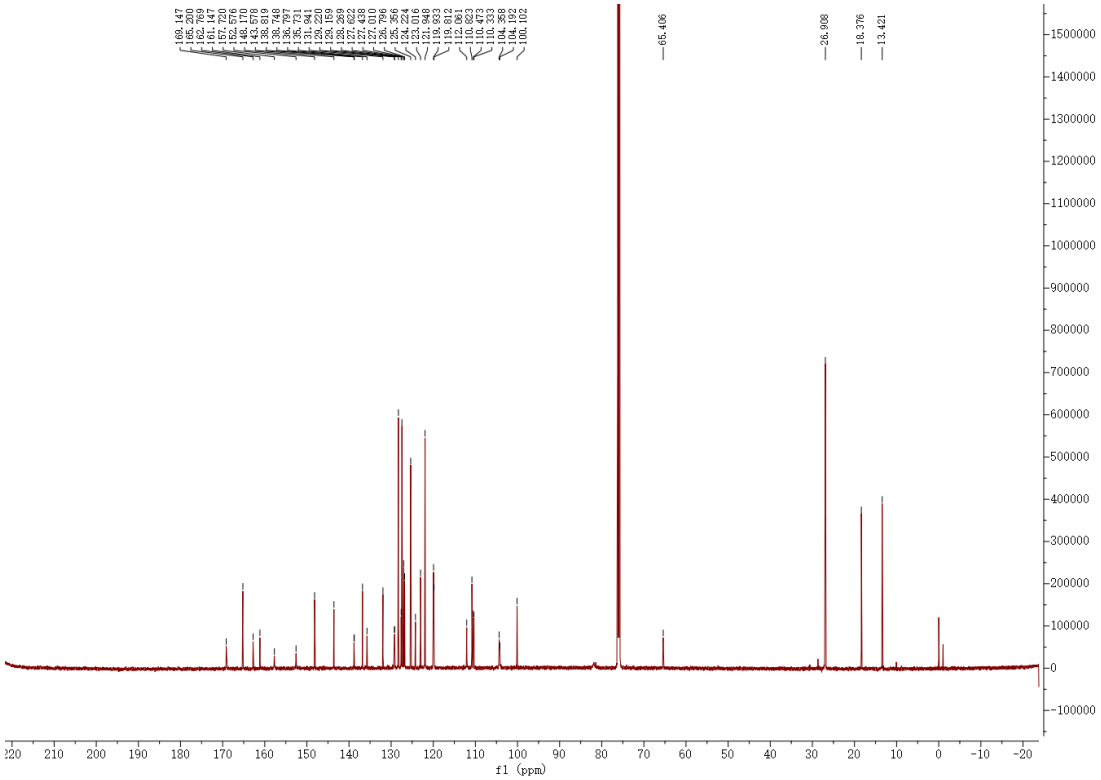
110.894
103.452
101.899
65.378
26.926
18.317
13.131
12.081
f1 (ppm)


F
N
N
Ph
OAc
NHBoc
N
O
N
Ph
N
H
3ha
f1 (ppm)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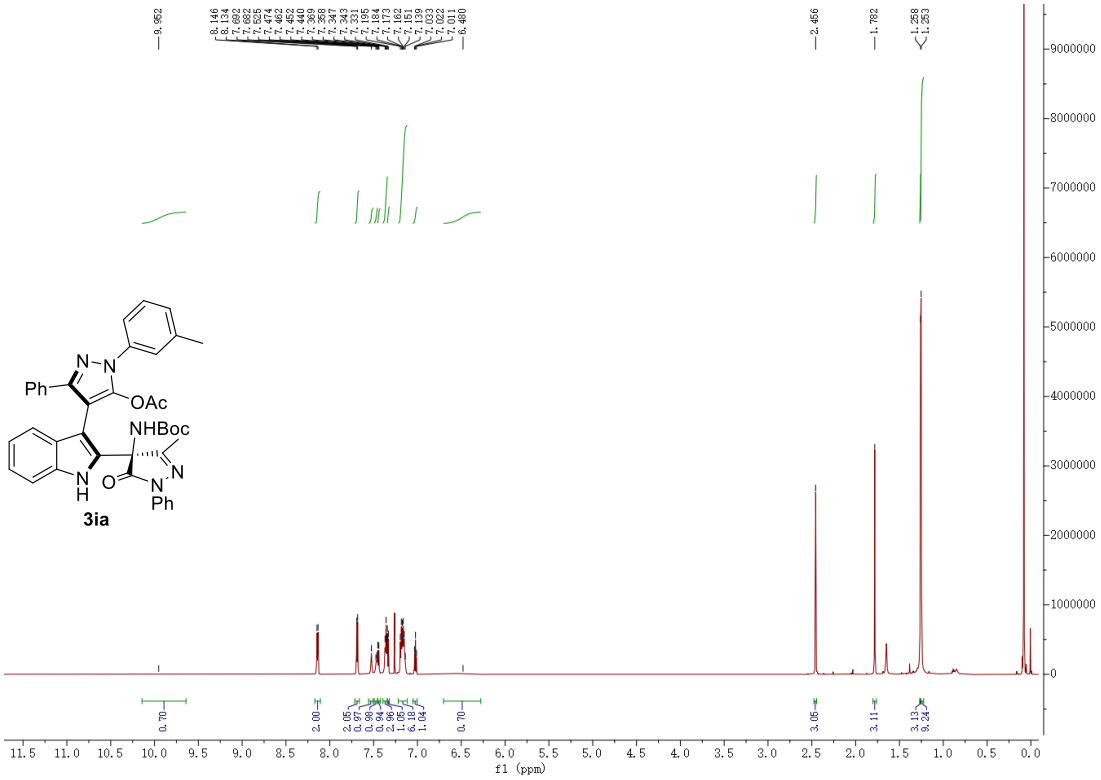
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7.625
7.474
7.464
7.462
7.440
7.398
7.389
7.347
7.343
7.331
7.195
7.184
7.173
7.162
7.151
7.139
7.033
7.022
7.011
6.980
2.456
1.782
1.558
1.533
Ph
OAc
NHBoc
N
H
O
N
N
Ph
3ia
0.70
2.00
2.05
0.97
0.88
0.84
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1.05
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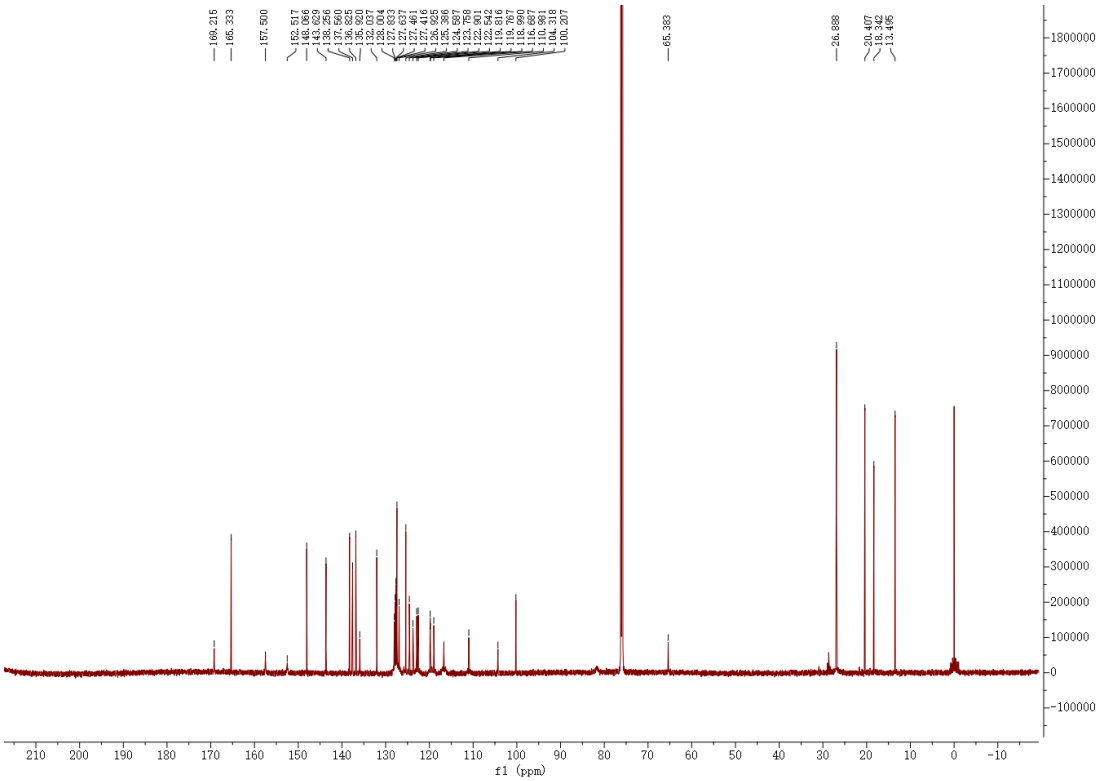
1.04
0.70
3.05
3.11
3.13
9.24
f1 (ppm)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137.560
136.825
136.520
132.037
130.164
129.033
127.637
127.461
127.416
126.595
125.386
124.587
122.768
122.601
122.542
119.816
119.767
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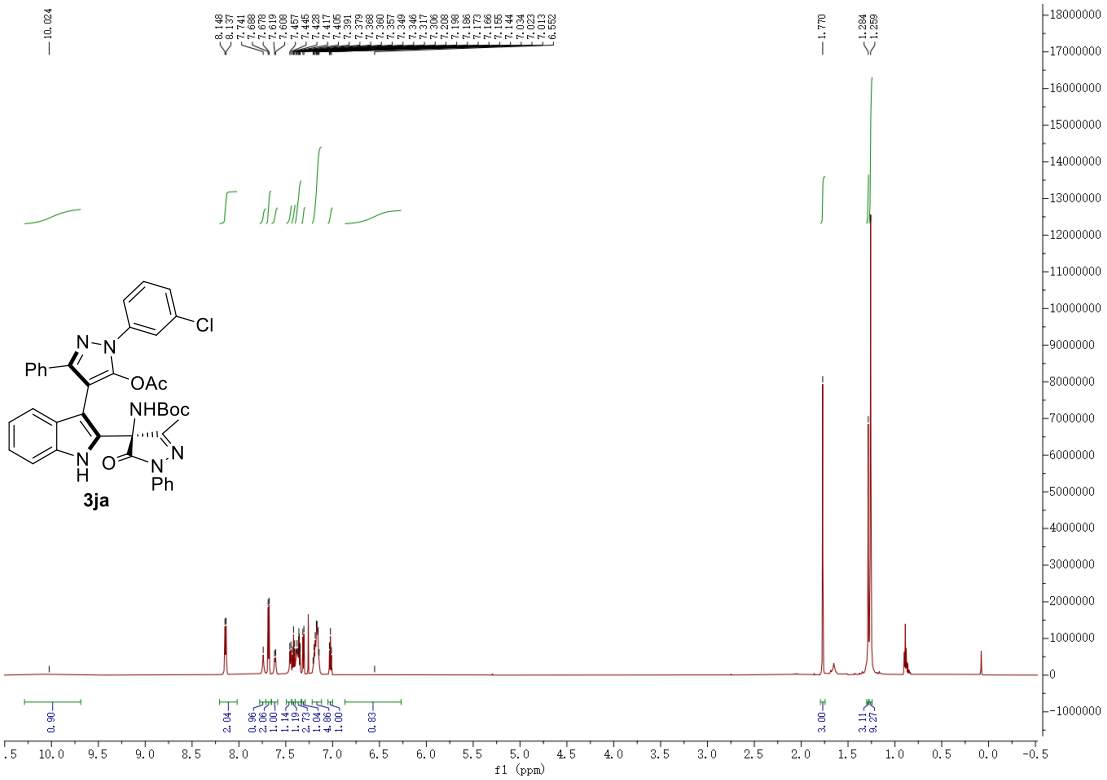
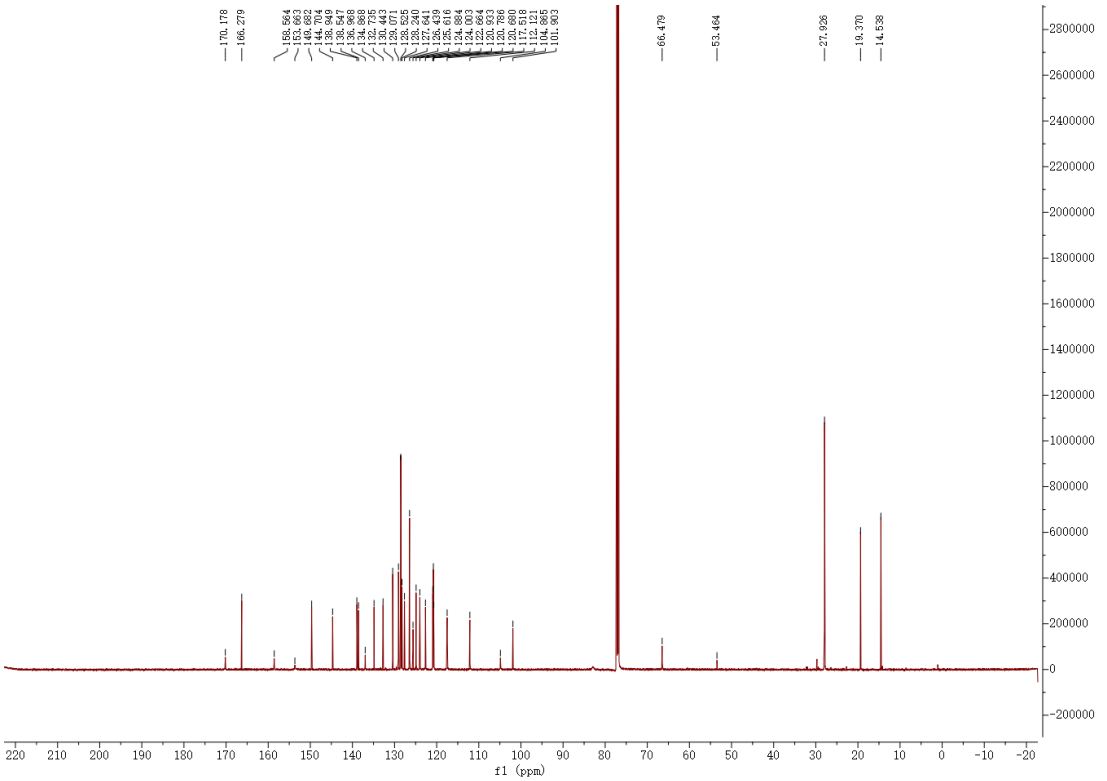
110.981
104.318
100.207
65.383
26.888
20.407
18.342
13.496
f1 (ppm)


Cl
Ph
OAc
NHBoc
N
H
O
Ph
3ja
f1 (ppm)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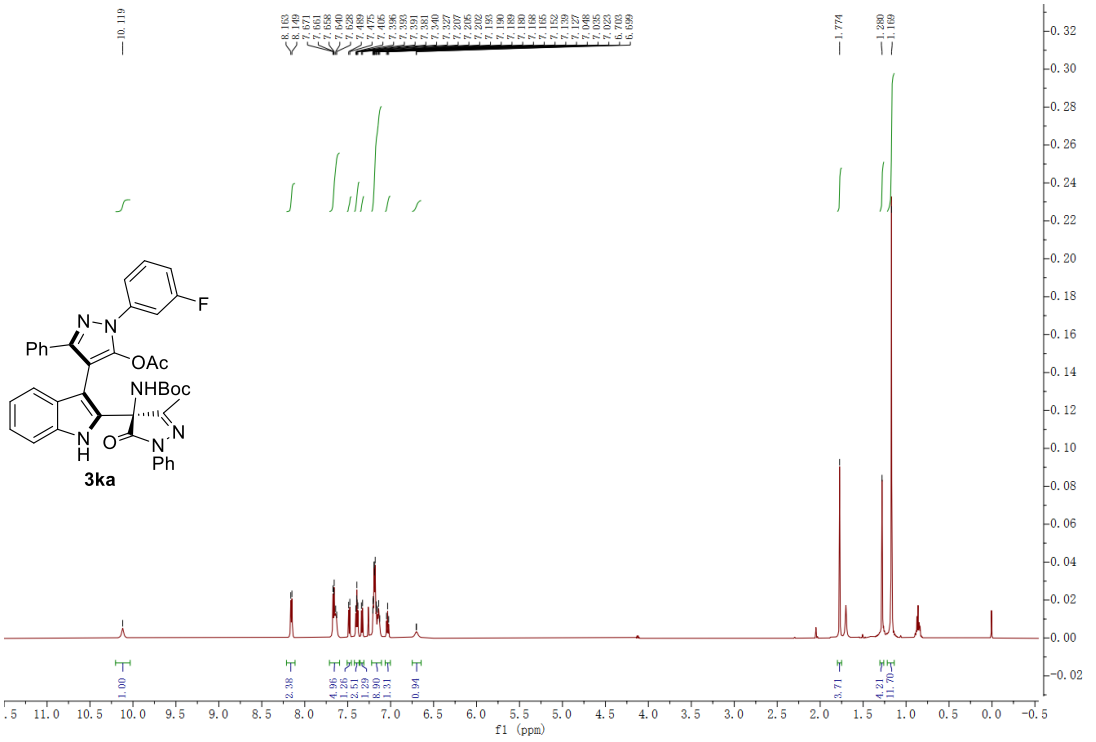
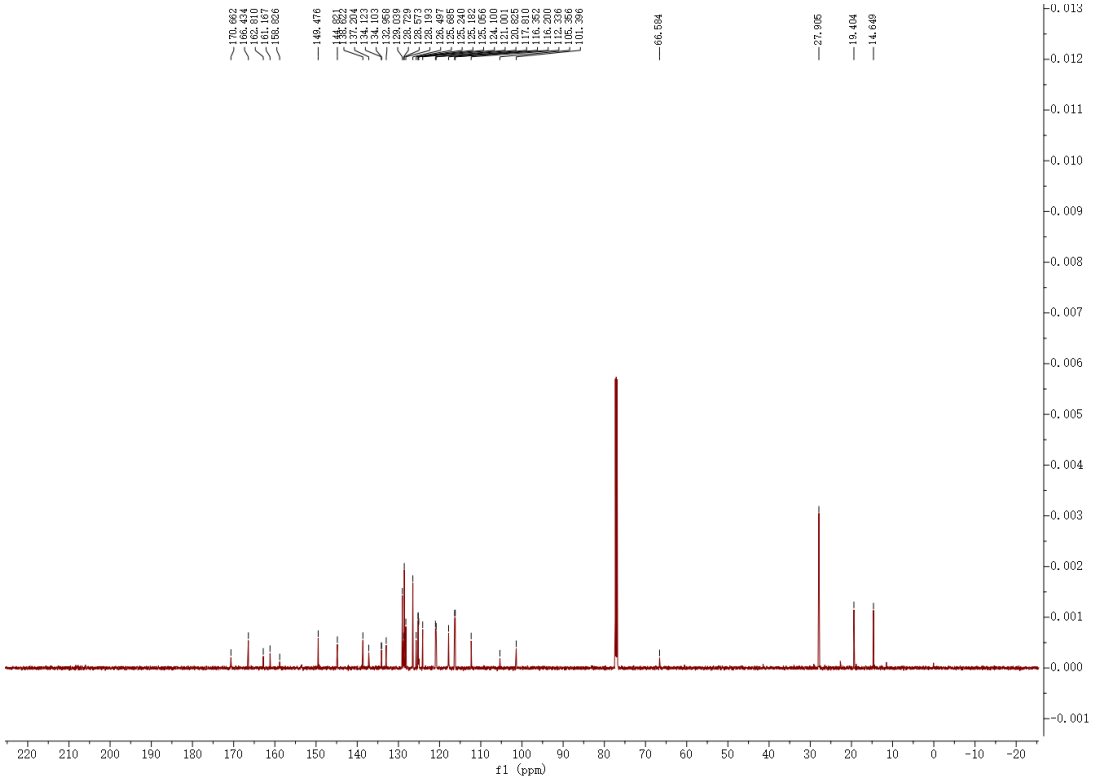
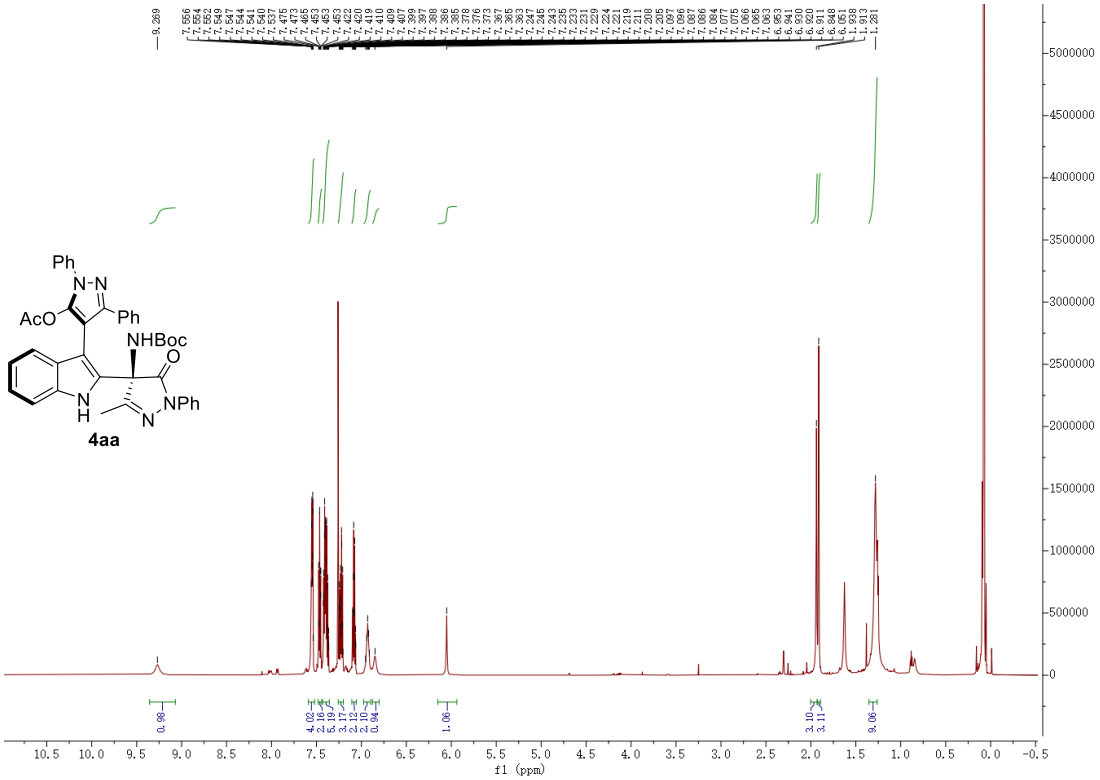

F
Ph
OAc
NHBoc
O
N
Ph
H
3ka
f1 (ppm)


f1 (ppm)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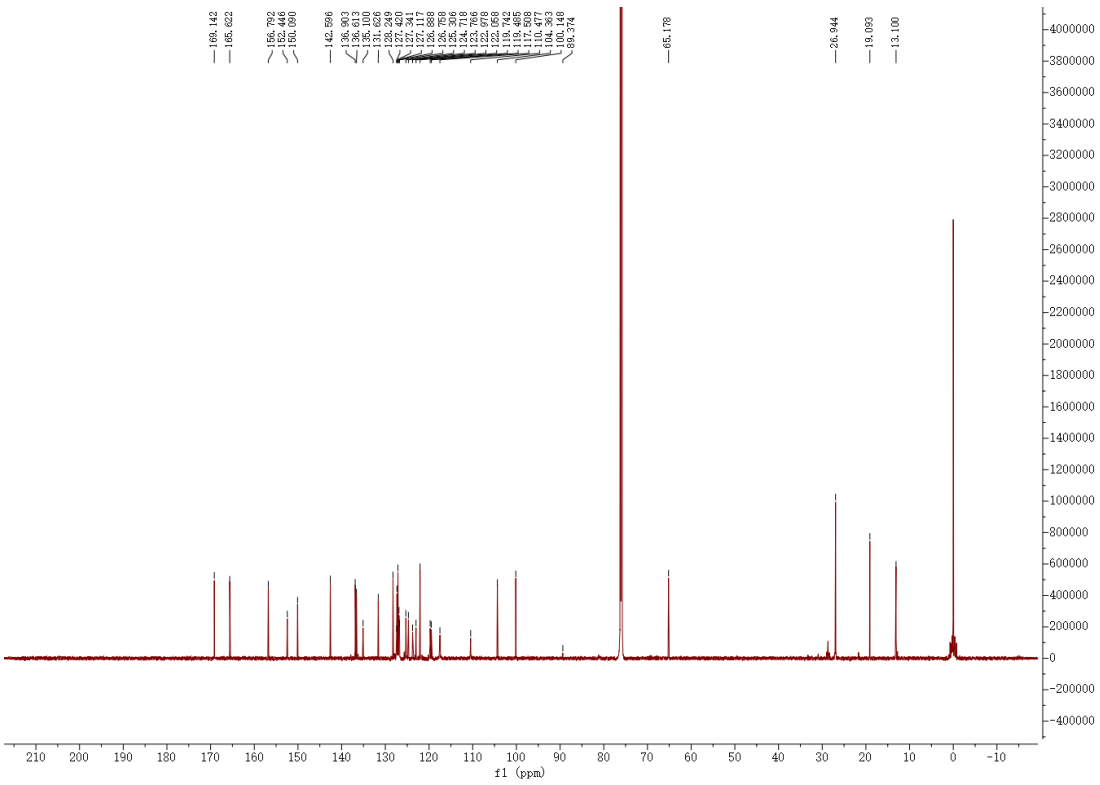
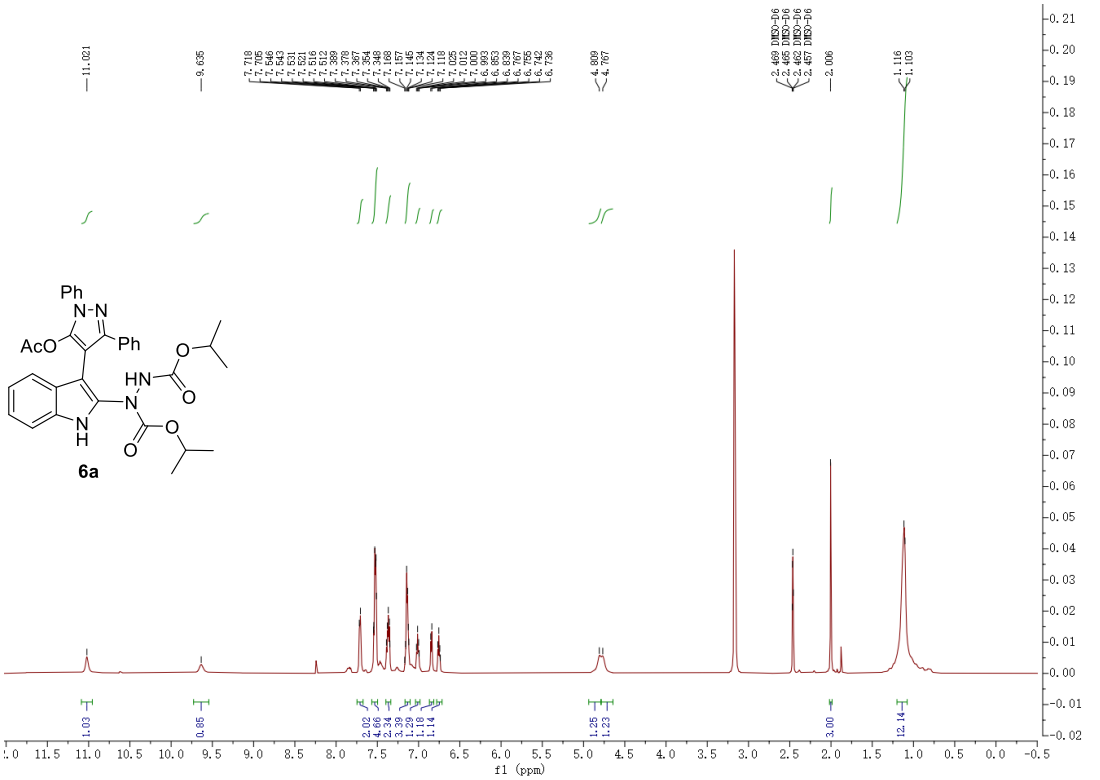
AcO
Ph
NHBoc
O
N
H
NPh
N
4aa
f1 (ppm)


f1 (ppm)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7.621
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7.612
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7.378
7.367
7.364
7.348
7.188
7.157
7.145
7.134
7.124
7.118
7.025
7.013
7.000
6.993
6.653
6.639
6.627
6.755
6.742
6.738
4.809
4.767
2.469
2.465
2.462
2.457
2.006
1.116
1.103
Ph
N-N
AcO
Ph
HN
O
N
O
N
H
O
O
6a
1.03
0.85
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3.39
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1.18
1.14
1.25
1.23
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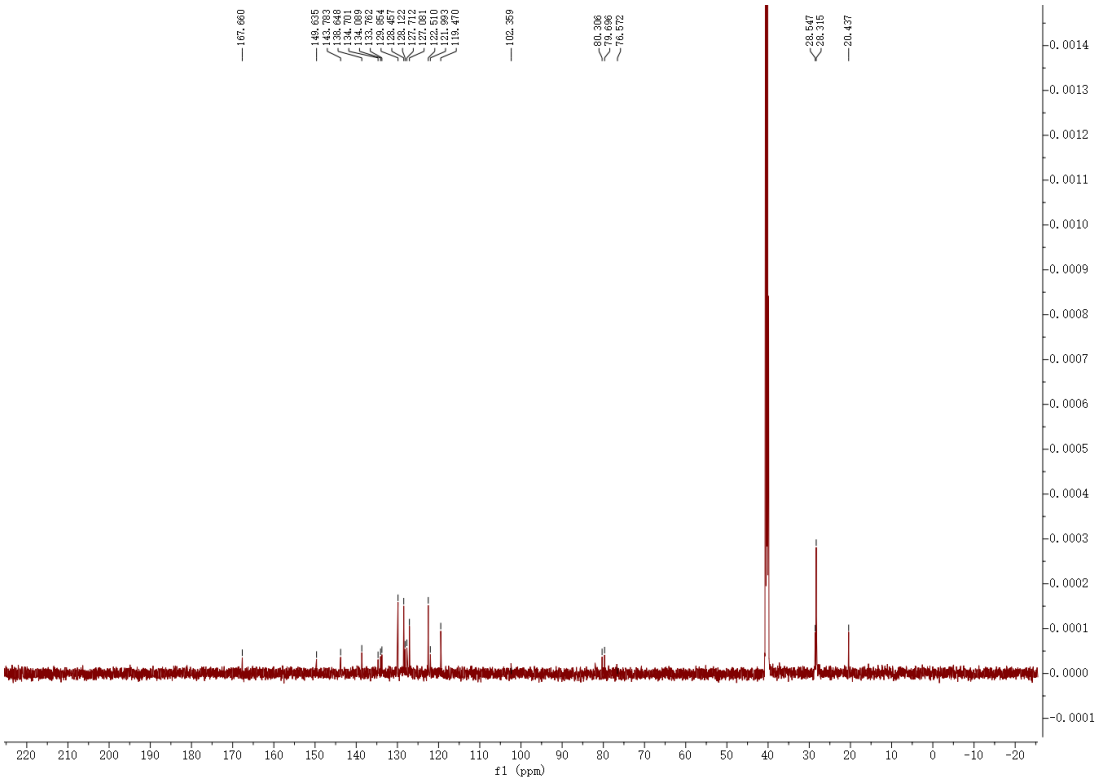
12.14
f1 (ppm)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128.122
127.712
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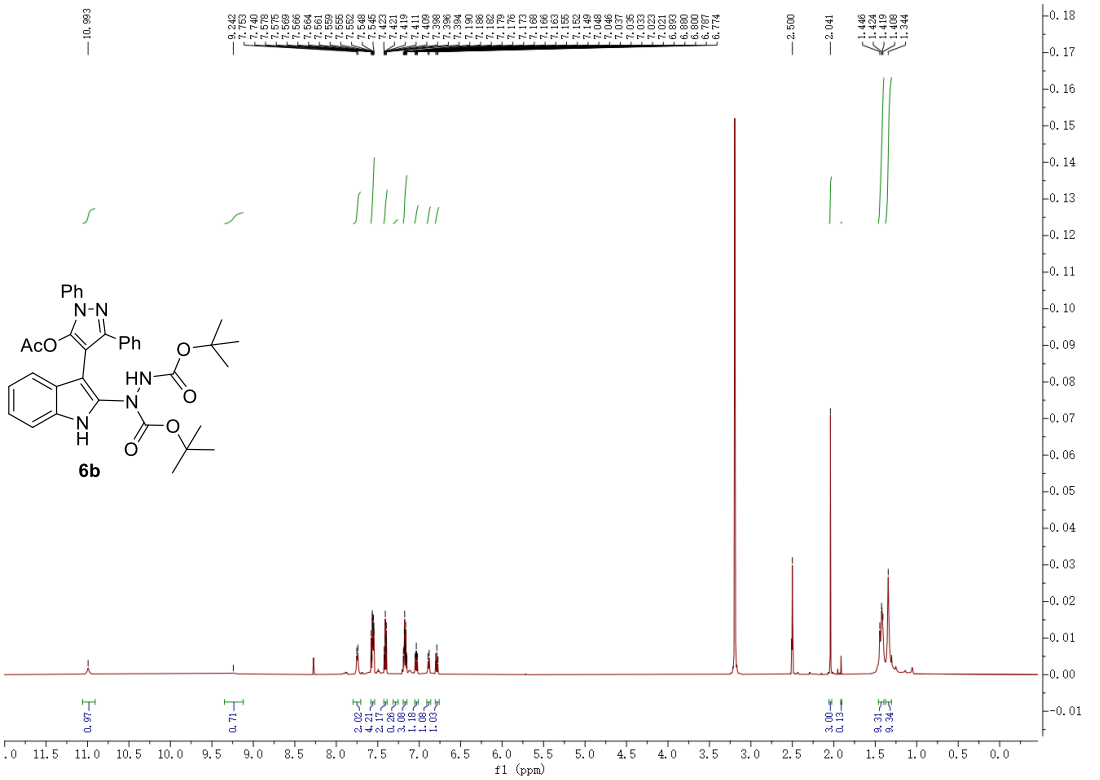
79.696
76.572
28.547
28.315
20.437
f1 (ppm)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7.548
7.545
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7.419
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7.409
7.398
7.394
7.190
7.188
7.182
7.179
7.176
7.173
7.168
7.166
7.163
7.155
7.153
7.149
7.048
7.046
7.037
7.035
7.033
7.023
7.021
6.885
6.880
6.800
6.787
6.774
2.500
2.041
1.446
1.424
1.419
1.408
1.344
Ph
N-N
AcO
Ph
O
HN
O
N
N
H
O
O
6b
0.97
0.71
2.02
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1.09
1.05
3.00
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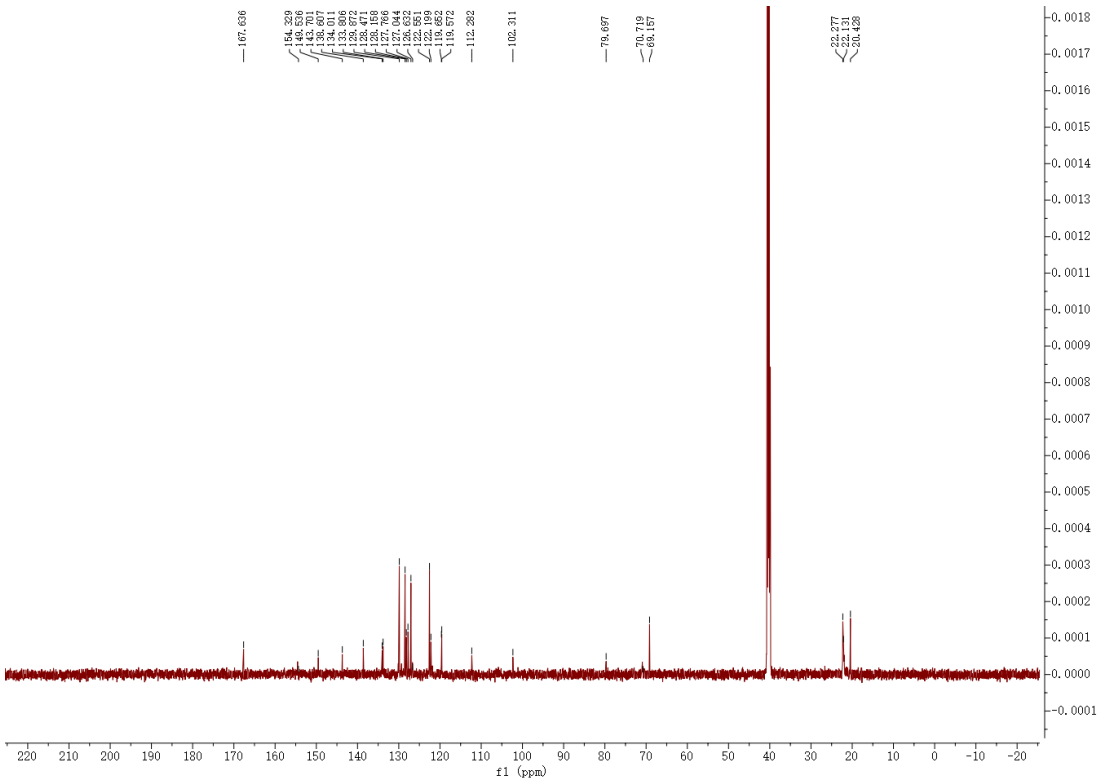
f1 (ppm)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154.329
149.536
143.701
138.607
134.011
133.806
128.972
128.647
128.158
127.766
127.044
126.652
122.551
122.199
119.652
119.572
112.282
102.311
79.697
70.719
69.157
22.277
22.131
20.428
f1 (ppm)