

# Enantioselective [3 + 2] Annulation Between Tryptanthrin-derived Ketimines and 2-Naphthols: Access to Polycyclic Indolo[2,1-*b*]quinazoline Derivatives

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## Supporting Information

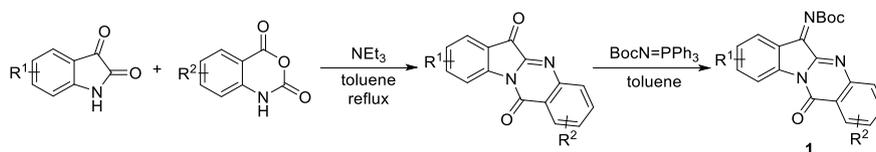
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## 1. General Methods

Chemical reagents were purchased from commercial sources and were used as received unless mentioned otherwise. Reactions were monitored by thin-layer chromatography (TLC).  $^1\text{H}$  NMR (400 MHz) and  $^{13}\text{C}$  NMR (101 MHz) spectra were recorded in  $\text{DMSO-}d_6$  and  $\text{CDCl}_3$ .  $^1\text{H}$  NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS), with the solvent resonance employed as the internal standard ( $\text{DMSO-}d_6$  at 2.50 ppm and  $\text{CDCl}_3$  at 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration.  $^{13}\text{C}$  NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ( $\text{DMSO-}d_6$  at 39.52 ppm and  $\text{CDCl}_3$  at 77.16 ppm). The enantiomeric excesses were determined by chiral HPLC analysis. HPLC analysis was performed on Agilent 1260 II. Chiral AD-H and IC columns were manufactured by Daicel Chemical Industries. HRMS was recorded on the Agilent 6545 LC/Q-TOF mass spectrometer. Optical rotations were measured with a Rudolph Autopol-III polarimeter. Melting points were recorded on a OptiMelt MPA 1000.

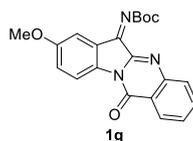
## 2. General procedure for the synthesis of tryptanthrine-derived ketimines **1**<sup>1</sup>



The tryptanthrine and substituted tryptantrines were prepared according to the following procedures. To a flame-dried flask was added substituted isatin (20 mmol), substituted isatoic anhydride (22 mmol, 1.1 equiv), toluene (25 mL), and triethyl amine (100 mmol, 5 equiv). The mixture was refluxed for 12 h. After completion (monitored by TLC), the mixture was cooled to room temperature and filtered. The filter cake was washed with EtOH (15 mL $\times$ 2) and dried to give the substituted tryptanthrine, which was used for the next step without further purification.

To a flame-dried flask was added the substituted tryptanthrine (5 mmol), BocN=PPh<sub>3</sub> (10 mmol), and toluene (20 mL). The resulting mixture was refluxed to completion (monitored by TLC). After cooling to room temperature, the solvent was removed under vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether /ethylacetate/ dichloromethane = 15:1:1–10:1:1) to give ketimine **1**.

### *tert*-Butyl (*Z*)-(8-methoxy-12-oxoindolo[2,1-*b*]quinazolin-6(12*H*)-ylidene)carbamate (**1g**)



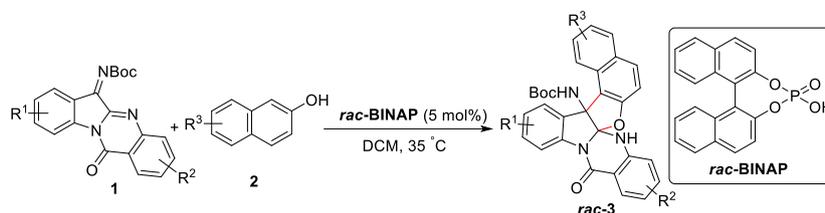
The product was purified by flash column chromatography (petroleum ether : ethyl acetate : dichloromethane = 10:1:1 as the eluent). Yellow solid; 65% yield.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.47 – 8.34 (m, 2H), 7.78 (s, 2H), 7.64 – 7.56 (m, 1H), 7.39 (s, 1H), 7.18 (d,  $J$  = 8.5 Hz, 1H), 3.86 (s, 3H), 1.72 (s, 9H).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  160.1, 158.7, 158.1, 153.5, 146.8, 142.6, 137.4, 134.7, 129.6, 127.4, 124.4, 123.3, 122.4, 118.7, 107.6, 84.0, 56.0, 28.4.

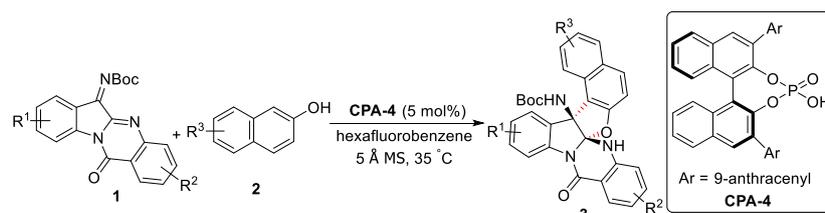
HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd. for  $\text{C}_{21}\text{H}_{19}\text{N}_3\text{O}_4\text{Na}$  400.1268, found 400.1274.

### 3. General procedure for the synthesis of racemic compounds 3



In an oven-dried tube, *rac*-BINAP (0.005 mmol), ketimines 1 (0.1 mmol), and DCM (2.0 ml) were added. To this suspension, 2-naphthol 2 (0.12 mmol) was then added. The resulting reaction mixture was stirred at 35 °C until the reaction was complete (monitored by TLC). The reaction mixture was concentrated under vacuum, and the residue was purified by flash chromatography on silica gel (petroleum ether : ethylacetate = 8:1–6:1) to give the racemic product 3.

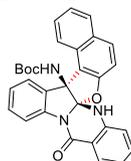
### 4. General procedure for the synthesis of compounds 3



In an oven-dried tube, CPA-4 (0.005 mmol), ketimines 1 (0.1 mmol), dry 5 Å MS (50 mg), and hexafluorobenzene (4.0 ml) were added. To this suspension, 2-naphthol 2 (0.12 mmol) was then added. The resulting reaction mixture was stirred at 35 °C until the reaction was complete (monitored by TLC). The reaction mixture was concentrated under vacuum, and the residue was purified by flash chromatography on silica gel (petroleum ether : ethylacetate = 8:1–6:1) to give the product 3.

*tert*-Butyl

**((4*S*,15*aR*)-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2''':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3a)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 49.0 mg, 99% yield; mp 138.2–140.1 °C; >20:1 dr, 97% ee;  $[\alpha]_{\text{D}}^{20} = +299.44$  ( $c$  2.0,  $\text{CH}_2\text{Cl}_2$ ).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_{\text{R}} = 13.0$  min (minor), 8.9 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 8.65 (d, *J* = 7.6 Hz, 2H), 8.38 (d, *J* = 8.1 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.87 – 7.68 (m, 3H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.41 (dt, *J* = 23.4, 7.6 Hz, 2H), 7.30 – 6.66 (m, 5H), 1.47 – 0.57 (m, 9H).

**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)** δ 159.0, 155.0, 154.6, 143.1, 141.0, 134.5, 132.2, 130.8, 129.8, 129.4, 129.1, 127.7, 127.6, 125.0, 123.6, 122.1, 119.9, 117.7, 116.3, 115.8, 114.1, 113.2, 112.0, 79.3, 72.5, 27.6.

**HRMS (ESI-TOF)** *m/z* [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>26</sub>N<sub>3</sub>O<sub>4</sub> 492.1918, found 492.1926.

*tert*-Butyl

**((4*cS*,15*aR*)-12-methyl-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3b)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 49.9 mg, 99% yield; mp 131.2–132.9 °C; >20:1 dr, 99% ee; [α]<sub>D</sub><sup>20</sup> = + 180.76 (*c* 0.7, CH<sub>2</sub>Cl<sub>2</sub>).

**The ee was determined by HPLC** (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min, λ = 254 nm) *t*<sub>R</sub> = 16.2 min (minor), 8.4 min (major).

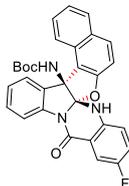
**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 8.42 (dd, *J* = 117.9, 7.5 Hz, 3H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 6.7 Hz, 2H), 7.71 (t, *J* = 6.5 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 2H), 7.06 (td, *J* = 18.2, 17.5, 7.8 Hz, 4H), 2.34 (s, 3H), 1.28 – 0.61 (m, 9H).

**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)** δ 159.0, 154.9, 154.5, 141.2, 140.9, 135.5, 130.7, 129.7, 129.4, 129.0, 128.8, 127.7, 127.1, 124.9, 123.5, 122.2, 117.6, 116.1, 115.7, 115.6, 113.9, 113.5, 113.3, 112.0, 79.2, 72.4, 27.5, 20.2.

**HRMS (ESI-TOF)** *m/z* [M + H]<sup>+</sup> calcd. for C<sub>31</sub>H<sub>28</sub>N<sub>3</sub>O<sub>4</sub> 506.2074, found 506.2080.

*tert*-Butyl

**((4*cS*,15*aR*)-12-fluoro-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3c)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 50.3 mg, 99% yield; mp 147.2–148.9 °C; >20:1 dr, 99% ee; [α]<sub>D</sub><sup>20</sup> = + 286.00 (*c* 1.1, CH<sub>2</sub>Cl<sub>2</sub>).

**The ee was determined by HPLC** (Chiralpak IB, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min, λ = 254 nm) *t*<sub>R</sub> = 11.6 min (minor), 7.9 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 8.91 – 8.53 (m, 2H), 8.28 (d, *J* = 8.1 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.78 – 7.66 (m, 3H), 7.52 – 7.41 (m, 2H), 7.40 – 7.33 (m, 1H),

7.29 – 6.73 (m, 4H), 1.38 – 0.81 (m, 9H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 158.0, 156.0 (d, *J* = 237.6 Hz, 1C), 154.5, 140.5, 139.8, 130.9, 129.8, 129.4, 129.0 (d, *J* = 7.8 Hz, 1C), 127.7, 125.3, 123.5, 122.3 (d, *J* = 23.7 Hz, 1C), 117.8, 117.5, 116.2, 114.7, 114.6, 113.1, 112.6 (d, *J* = 23.9 Hz, 1C), 112.0, 79.3, 72.5, 27.6.

HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>24</sub>FN<sub>3</sub>O<sub>4</sub>Na 532.1643, found 532.1653.

*tert*-Butyl

((4*cS*,15*aR*)-12-chloro-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3d)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 50.9 mg, 97% yield; mp 154.9–156.0 °C; >20:1 dr, 98% ee; [α]<sub>D</sub><sup>20</sup> = +257.33 (*c* 1.6, CH<sub>2</sub>Cl<sub>2</sub>).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min, λ = 254 nm) *t*<sub>R</sub> = 7.6 min (minor), 6.6 min (major).

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.16 – 8.67 (m, 1H), 8.66 – 8.53 (m, 1H), 8.29 (d, *J* = 8.1 Hz, 1H), 8.01 – 7.89 (m, 2H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.79 – 7.66 (m, 2H), 7.64 – 7.54 (m, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 1H), 7.18 – 6.69 (m, 3H), 1.36 – 0.78 (m, 9H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 157.7, 154.8, 154.4, 141.9, 140.5, 134.3, 130.8, 129.8, 129.4, 129.3, 129.0, 127.7, 126.4, 125.4, 125.3, 123.7, 123.6, 122.3, 117.9, 117.4, 116.3, 115.1, 112.7, 111.9, 79.3, 72.5, 27.5.

HRMS (ESI-TOF) *m/z* [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>ClN<sub>3</sub>O<sub>4</sub> 526.1528, found 526.1532.

*tert*-Butyl

((4*cS*,15*aR*)-12-bromo-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3e)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 56.6 mg, 99% yield; mp 159.2–160.4 °C; >20:1 dr, 99% ee; [α]<sub>D</sub><sup>20</sup> = +175.73 (*c* 1.5, CH<sub>2</sub>Cl<sub>2</sub>).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min, λ = 254 nm) *t*<sub>R</sub> = 7.7 min (minor), 6.6 min (major).

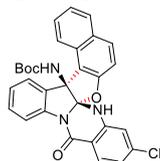
<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.85 (s, 1H), 8.58 (d, *J* = 7.7 Hz, 1H), 8.27 (d, *J* = 8.1 Hz, 1H), 8.08 (d, *J* = 2.4 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 8.8 Hz, 1H), 7.71 (dd, *J* = 16.9, 8.3 Hz, 3H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 7.26 – 6.78 (m, 4H), 1.31 – 0.74 (m, 9H).

<sup>13</sup>C NMR (101 MHz, DMSO) δ 157.7, 154.8, 154.4, 142.3, 140.5, 137.0, 131.0, 129.8, 129.6, 129.41, 129.37, 129.0, 127.7, 125.4, 123.6, 122.2, 118.3, 117.4, 116.3, 115.6, 112.7, 111.9, 111.0, 79.3, 72.5, 27.5.

HRMS (ESI-TOF) *m/z* [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>BrN<sub>3</sub>O<sub>4</sub> 570.1023, found 570.1023.

*tert*-Butyl

((4*cS*,15*aR*)-13-chloro-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3f)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 51.5 mg, 98% yield; mp 156.7–157.9 °C; >20:1 dr, 92% ee; [α]<sub>D</sub><sup>20</sup> = +294.25 (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>).

The ee was determined by HPLC (Chiralpak IB, ethanol/*n*-hexane 20/80, flow rate = 1.0 mL/min, λ = 254 nm) *t*<sub>R</sub> = 7.7 min (minor), 5.9 min (major).

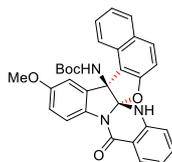
<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.25 – 8.65 (m, 1H), 8.64 – 8.48 (m, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.77 – 7.60 (m, 2H), 7.49 – 7.40 (m, 1H), 7.40 – 7.32 (m, 1H), 7.27 (s, 1H), 7.19 – 6.75 (m, 4H), 1.47 – 0.71 (m, 9H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 158.2, 154.7, 154.4, 144.3, 140.5, 139.1, 130.9, 129.8, 129.5, 129.4, 129.0, 127.7, 125.3, 123.6, 122.4, 120.1, 117.4, 117.3, 116.2, 115.2, 112.8, 112.7, 111.9, 79.3, 72.5, 27.6.

HRMS (ESI-TOF) *m/z* [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>ClN<sub>3</sub>O<sub>4</sub> 526.1528, found 526.1531.

*tert*-Butyl

((4*cS*,15*aR*)-6-methoxy-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3g)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 50.5 mg, 97% yield; mp 138.2–140.1 °C; >20:1 dr, 99% ee; [α]<sub>D</sub><sup>20</sup> = +262.37 (*c* 0.6, CH<sub>2</sub>Cl<sub>2</sub>).

The ee was determined by HPLC (Chiralpak IB, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min, λ = 254 nm) *t*<sub>R</sub> = 14.3 min (minor), 11.7 min (major).

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.00 – 8.28 (m, 2H), 8.20 (d, *J* = 7.8 Hz, 1H), 8.06 – 7.86 (m, 2H), 7.86 – 7.64 (m, 2H), 7.60 – 7.34 (m, 2H), 7.34 – 6.38 (m, 6H), 3.65 (s, 3H), 1.45 – 0.56 (m, 9H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 158.4, 156.7, 155.0, 154.5, 142.9, 134.3, 130.9, 129.7, 129.4, 129.1, 129.0, 127.7, 127.4, 123.6, 122.0, 119.8, 117.4, 117.0, 115.7, 114.1, 113.6, 113.4, 111.9, 109.9, 79.3, 72.4, 55.5, 27.6.

HRMS (ESI-TOF)  $m/z$   $[M + Na]^+$  calcd. for  $C_{31}H_{27}N_3O_5Na$  544.1843, found 544.1852.

*tert*-Butyl

**((4*cS*,15*aR*)-6-methyl-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3h)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 49.4 mg, 98% yield; mp 144.3–145.1 °C; >20:1 dr, 99% ee;  $[\alpha]_D^{20} = +307.74$  ( $c$  1.1,  $CH_2Cl_2$ ).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 17.6$  min (minor), 9.4 min (major).

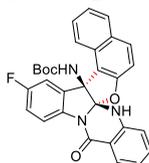
$^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  8.93 – 8.26 (m, 2H), 8.18 (d,  $J = 8.2$  Hz, 1H), 8.00 (d,  $J = 7.8$  Hz, 1H), 7.93 (d,  $J = 8.2$  Hz, 1H), 7.81 (d,  $J = 8.8$  Hz, 1H), 7.73 (t,  $J = 7.4$  Hz, 1H), 7.52 (t,  $J = 7.1$  Hz, 2H), 7.43 (t,  $J = 7.5$  Hz, 1H), 7.29 – 6.50 (m, 5H), 2.20 (s, 3H), 1.45 – 0.76 (d,  $J = 23.5$  Hz, 9H).

$^{13}C$  NMR (101 MHz,  $DMSO-d_6$ )  $\delta$  158.7, 155.0, 154.5, 143.0, 138.7, 134.4, 134.2, 130.7, 129.7, 129.3, 129.1, 127.7, 127.4, 123.9, 123.5, 122.0, 119.8, 117.6, 116.0, 115.8, 115.7, 114.1, 113.3, 111.9, 79.3, 72.4, 27.6, 20.8.

HRMS (ESI-TOF)  $m/z$   $[M + H]^+$  calcd. for  $C_{31}H_{28}N_3O_4$  506.2074, found 522.2079.

*tert*-Butyl

**((4*cS*,15*aR*)-6-fluoro-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3i)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 50.3 mg, 99% yield; mp 142.4–144.1 °C; >20:1 dr, 97% ee;  $[\alpha]_D^{20} = +284.75$  ( $c$  1.6,  $CH_2Cl_2$ ).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 16.9$  min (minor), 7.0 min (major).

$^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  8.90 – 8.45 (m, 2H), 8.34 – 8.25 (m, 1H), 8.01 (d,  $J = 7.8$  Hz, 1H), 7.94 (d,  $J = 8.2$  Hz, 1H), 7.84 (d,  $J = 8.8$  Hz, 1H), 7.77 – 7.69 (m, 1H), 7.59 – 7.49 (m, 2H), 7.48 – 7.40 (m, 1H), 7.27 – 7.18 (m, 1H), 7.18 – 6.66 (m, 4H), 1.44 – 0.72 (m, 9H).

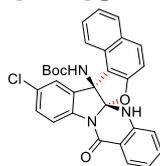
$^{13}C$  NMR (101 MHz,  $DMSO-d_6$ )  $\delta$  159.1 (d,  $J = 242.4$  Hz, 1C), 158.7, 154.8, 154.7, 143.0, 137.3, 134.6, 131.2, 129.8, 129.4, 128.9, 128.0, 127.5, 123.7, 122.2, 119.9, 117.4 (d,  $J = 8.1$  Hz, 1C), 116.8, 115.7, 113.8, 113.3, 112.0, 110.6, 79.5, 72.3, 27.5.

HRMS (ESI-TOF)  $m/z$   $[M + H]^+$  calcd. for  $C_{30}H_{25}FN_3O_4$  510.1824, found 510.1835.

*tert*-Butyl

**((4*cS*,15*aR*)-6-chloro-10-oxo-10,15-dihydro-4*cH*-**

**naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-b]quinazolin-4c-yl)carbamate (3j)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 51.5 mg, 98% yield; mp 142.4–144.1 °C; >20:1 dr, 99% ee;  $[\alpha]_D^{20} = +255.31$  (c 2.6, CH<sub>2</sub>Cl<sub>2</sub>).

**The ee was determined by HPLC** (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 13.6$  min (minor), 6.9 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  8.89 – 8.44 (m, 2H), 8.30 (d,  $J = 8.7$  Hz, 1H), 8.02 (d,  $J = 7.8$  Hz, 1H), 7.95 (d,  $J = 8.2$  Hz, 1H), 7.84 (d,  $J = 8.8$  Hz, 1H), 7.79 – 7.65 (m, 2H), 7.59 – 7.50 (m, 1H), 7.49 – 7.40 (m, 2H), 7.21 – 6.93 (m, 4H), 1.45 – 0.73 (m, 9H).

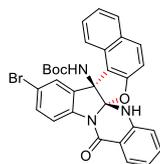
**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  158.9, 154.9, 154.7, 143.2, 139.8, 134.8, 131.3, 129.8, 129.5, 129.2, 128.9, 128.5, 128.0, 127.6, 123.8, 123.1, 122.2, 120.0, 117.6, 116.7, 115.8, 113.7, 113.1, 112.0, 79.6, 72.3, 27.6.

**HRMS (ESI-TOF)**  $m/z$  [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>ClN<sub>3</sub>O<sub>4</sub> 526.1528, found 526.1534.

*tert*-Butyl

**((4cS,15aR)-6-bromo-10-oxo-10,15-dihydro-4cH-**

**naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-b]quinazolin-4c-yl)carbamate (3k)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 56.3 mg, 99% yield; mp 133.9–134.9 °C; >20:1 dr, 97% ee;  $[\alpha]_D^{20} = +170.88$  (c 1.9, CH<sub>2</sub>Cl<sub>2</sub>).

**The ee was determined by HPLC** (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 14.9$  min (minor), 6.8 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  8.96 – 8.42 (m, 2H), 8.24 (d,  $J = 8.6$  Hz, 1H), 8.01 (d,  $J = 7.8$  Hz, 1H), 7.95 (d,  $J = 8.2$  Hz, 1H), 7.90 – 7.79 (m, 2H), 7.78 – 7.70 (m, 1H), 7.62 – 7.51 (m, 2H), 7.50 – 7.41 (m, 1H), 7.23 – 6.75 (m, 4H), 1.45 – 0.77 (m, 9H).

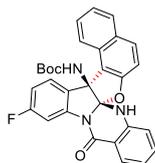
**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  158.9, 154.9, 154.7, 143.1, 140.2, 134.8, 132.1, 131.2, 129.8, 129.5, 128.9, 128.0, 127.6, 126.0, 123.7, 122.1, 112.0, 118.0, 116.7, 116.3, 115.8, 113.7, 113.0, 112.0, 79.5, 72.2, 27.6.

**HRMS (ESI-TOF)**  $m/z$  [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>BrN<sub>3</sub>O<sub>4</sub> 570.1023, found 570.1029.

*tert*-Butyl

**((4cS,15aR)-7-fluoro-10-oxo-10,15-dihydro-4cH-**

**naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-b]quinazolin-4c-yl)carbamate (3l)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 49.8 mg, 98% yield; mp 213.6–215.3 °C; >20:1 dr, 97% ee;  $[\alpha]_D^{20} = +267.22$  ( $c$  1.7,  $\text{CH}_2\text{Cl}_2$ ).

The ee was determined by HPLC (Chiralpak IB, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 10.8$  min (minor), 8.6 min (major).

**$^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )**  $\delta$  8.89 – 8.43 (m, 2H), 8.07 – 7.98 (m, 2H), 7.94 (d,  $J = 8.2$  Hz, 1H), 7.83 (d,  $J = 8.8$  Hz, 1H), 7.78 – 7.65 (m, 2H), 7.59 – 7.51 (m, 1H), 7.48 – 7.40 (m, 1H), 7.19 – 6.74 (m, 5H), 1.46 – 0.72 (m, 9H).

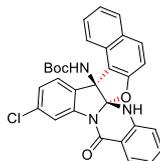
**$^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )**  $\delta$  162.4 (d,  $J = 244.4$  Hz, 1C), 159.1, 154.9, 154.5, 143.2, 142.1, 134.9, 131.0, 129.8, 129.4, 128.9, 127.8, 127.6, 124.8, 123.7, 122.1, 120.0, 117.4, 115.9, 113.6, 113.5, 112.0, 111.7 (d,  $J = 22.2$  Hz, 1C), 103.7 (d,  $J = 29.3$  Hz, 1C), 79.4, 72.0, 27.6.

**HRMS (ESI-TOF)**  $m/z$   $[\text{M} + \text{H}]^+$  calcd. for  $\text{C}_{30}\text{H}_{25}\text{FN}_3\text{O}_4$  510.1824, found 510.1826.

*tert*-Butyl

**((4*cS*,15*aR*)-7-chloro-10-oxo-10,15-dihydro-4*cH*-**

**naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3m)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 51.4 mg, 98% yield; mp 138.9–140.6 °C; >20:1 dr, 98% ee;  $[\alpha]_D^{20} = +320.83$  ( $c$  0.6,  $\text{CH}_2\text{Cl}_2$ ).

The ee was determined by HPLC (Chiralpak IB, ethanol/*n*-hexane 5/95, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 17.6$  min (minor), 11.3 min (major).

**$^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )**  $\delta$  8.95 – 8.45 (m, 2H), 8.33 – 8.27 (m, 1H), 8.01 (d,  $J = 7.8$  Hz, 1H), 7.95 (d,  $J = 8.2$  Hz, 1H), 7.85 (d,  $J = 8.8$  Hz, 1H), 7.79 – 7.66 (m, 2H), 7.60 – 7.52 (m, 1H), 7.49 – 7.41 (m, 1H), 7.25 – 7.18 (m, 1H), 7.17 – 6.67 (m, 4H), 1.43 – 0.73 (m, 9H).

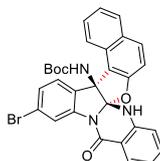
**$^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )**  $\delta$  159.1, 154.9, 154.6, 143.2, 142.0, 134.9, 133.5, 131.2, 129.8, 129.4, 128.9, 127.9, 127.6, 124.9, 123.7, 122.2, 120.0, 117.0, 115.9, 113.5, 113.2, 112.0, 79.5, 72.1, 27.5.

**HRMS (ESI-TOF)**  $m/z$   $[\text{M} + \text{H}]^+$  calcd. for  $\text{C}_{30}\text{H}_{25}\text{ClN}_3\text{O}_4$  526.1528, found 526.1537.

*tert*-Butyl

**((4*cS*,15*aR*)-7-bromo-10-oxo-10,15-dihydro-4*cH*-**

**naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3n)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 53.0 mg, 93% yield; mp 151.8–153.2 °C; >20:1 dr, 98% ee;  $[\alpha]_{\text{D}}^{20} = +212.37$  ( $c$  0.7,  $\text{CH}_2\text{Cl}_2$ ).

The ee was determined by HPLC (Chiralpak IB, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_{\text{R}} = 11.5$  min (minor), 8.2 min (major).

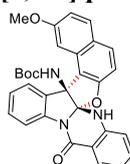
$^1\text{H NMR}$  (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.99 – 8.19 (m, 3H), 8.01 (d,  $J = 7.7$  Hz, 1H), 7.95 (d,  $J = 8.2$  Hz, 1H), 7.85 (d,  $J = 8.8$  Hz, 1H), 7.80 – 7.62 (m, 2H), 7.56 (t,  $J = 7.5$  Hz, 1H), 7.45 (t,  $J = 7.5$  Hz, 1H), 7.33 (d,  $J = 8.1$  Hz, 1H), 7.27 – 7.77 (m, 4H), 1.41 – 0.61 (m, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  159.1, 154.9, 154.6, 143.2, 142.1, 134.9, 131.1, 129.8, 129.4, 128.9, 127.9, 127.8, 127.6, 125.1, 123.7, 122.1, 121.8, 120.0, 118.7, 116.9, 115.8, 113.5, 113.1, 112.0, 79.5, 72.2, 27.5.

HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{Na}]^+$  calcd. for  $\text{C}_{30}\text{H}_{24}\text{BrN}_3\text{O}_4\text{Na}$  594.0827, found 594.0842.

*tert*-Butyl

((4*cS*,15*aR*)-3-methoxy-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3o)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 51.0 mg, 98% yield; mp 208.0–209.8 °C; >20:1 dr, 98% ee;  $[\alpha]_{\text{D}}^{20} = +294.75$  ( $c$  1.8,  $\text{CH}_2\text{Cl}_2$ ).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_{\text{R}} = 13.6$  min (minor), 9.6 min (major).

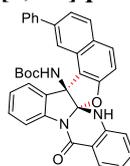
$^1\text{H NMR}$  (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.98 – 8.12 (m, 2H), 8.01 (d,  $J = 7.7$  Hz, 1H), 7.90 – 7.82 (m, 2H), 7.77 (d,  $J = 7.5$  Hz, 1H), 7.71 (d,  $J = 8.7$  Hz, 1H), 7.53 (t,  $J = 7.5$  Hz, 1H), 7.38 (t,  $J = 7.7$  Hz, 1H), 7.20 – 7.09 (m, 3H), 7.06 (t,  $J = 7.5$  Hz, 1H), 6.99 – 6.35 (m, 2H), 4.03 (s, 3H), 1.43 – 0.79 (m, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  159.0, 158.4, 155.1, 143.0, 140.6, 134.5, 131.6, 131.0, 130.4, 129.5, 127.5, 125.2, 125.1, 123.8, 119.9, 116.7, 116.1, 116.0, 115.9, 115.4, 114.1, 113.1, 109.3, 101.2, 79.3, 72.3, 55.3, 27.6.

HRMS (ESI-TOF)  $m/z$   $[\text{M} + \text{H}]^+$  calcd. for  $\text{C}_{31}\text{H}_{28}\text{N}_3\text{O}_5$  522.2023, found 522.2037.

*tert*-Butyl

((4*cS*,15*aR*)-10-oxo-3-phenyl-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3p)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 56.3 mg, 99% yield; mp 175.8–177.6 °C; >20:1 dr, 99% ee;  $[\alpha]_{\text{D}}^{20} = +324.4$  ( $c$

2.1, CH<sub>2</sub>Cl<sub>2</sub>).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 12.3$  min (minor), 8.7 min (major).

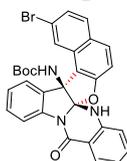
<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.77 (s, 1H), 8.59 – 8.26 (m, 2H), 8.03 (d,  $J = 8.6$  Hz, 2H), 7.92 (d,  $J = 7.5$  Hz, 2H), 7.83 (d,  $J = 8.8$  Hz, 1H), 7.78 – 7.74 (m, 1H), 7.69 (d,  $J = 7.4$  Hz, 1H), 7.61 (t,  $J = 7.7$  Hz, 2H), 7.57 – 7.52 (m, 1H), 7.50 – 7.45 (m, 1H), 7.38 (t,  $J = 7.7$  Hz, 1H), 7.25 – 6.78 (m, 5H), 1.28 – 0.96 (m, 9H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  159.0, 155.3, 155.0, 143.0, 140.7, 140.3, 139.0, 134.6, 130.4, 130.1, 129.5, 129.3, 129.04, 128.95, 128.0, 127.5, 127.2, 125.3, 124.0, 122.9, 120.0, 119.2, 117.8, 116.2, 116.0, 114.1, 113.4, 112.1, 79.5, 72.4, 27.6.

HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd. for C<sub>36</sub>H<sub>30</sub>N<sub>3</sub>O<sub>4</sub> 568.2231, found 568.2232.

*tert*-Butyl

((4*cS*,15*aR*)-3-bromo-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3q)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 56.5 mg, 99% yield; mp 205.9–207.2 °C; >20:1 dr, 95% ee;  $[\alpha]_D^{20} = +290.13$  (*c* 0.4, CH<sub>2</sub>Cl<sub>2</sub>).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 9.2$  min (minor), 7.7 min (major).

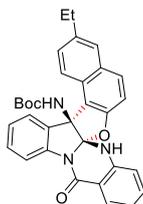
<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  9.02 – 8.36 (m, 2H), 8.29 (d,  $J = 8.1$  Hz, 1H), 8.00 (d,  $J = 7.8$  Hz, 1H), 7.90 (d,  $J = 8.8$  Hz, 1H), 7.84 (d,  $J = 8.8$  Hz, 1H), 7.68 – 7.47 (m, 3H), 7.42 – 7.33 (m, 1H), 7.23 – 6.76 (m, 5H), 1.29 – 0.69 (m, 9H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  158.9, 155.4, 155.1, 143.0, 140.7, 134.6, 131.6, 130.8, 130.3, 129.6, 128.1, 127.4, 126.5, 125.3, 123.8, 121.4, 120.0, 117.0, 116.3, 116.0, 113.9, 113.6, 112.7, 79.5, 72.1, 27.6.

HRMS (ESI-TOF)  $m/z$  [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>BrN<sub>3</sub>O<sub>4</sub> 570.1023, found 570.1029.

*tert*-Butyl

((4*cS*,15*aR*)-2-ethyl-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3r)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 51.4 mg, 99% yield; mp 128.4–130.2 °C; >20:1 dr, 98% ee;  $[\alpha]_D^{20} = +306.75$  (*c* 0.7, CH<sub>2</sub>Cl<sub>2</sub>).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 12.7$  min (minor), 8.6 min (major).

$^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ )  $\delta$  9.02 – 8.36 (m, 2H), 8.29 (d,  $J = 8.1$  Hz, 1H), 8.01 (d,  $J = 7.6$  Hz, 1H), 7.73 (d,  $J = 9.4$  Hz, 3H), 7.62 (d,  $J = 8.5$  Hz, 1H), 7.53 (t,  $J = 7.2$  Hz, 1H), 7.35 (t,  $J = 7.7$  Hz, 1H), 7.27 – 6.44 (m, 5H), 2.77 (q,  $J = 7.5$  Hz, 2H), 1.34 – 0.59 (m, 12H).

$^{13}\text{C NMR}$  (101 MHz, DMSO- $d_6$ )  $\delta$  158.9, 155.0, 154.0, 143.1, 140.9, 138.7, 134.5, 130.2, 130.0, 129.2, 128.8, 127.5, 127.36, 127.35, 127.0, 125.0, 123.5, 122.3, 119.8, 117.5, 116.2, 115.7, 114.0, 112.9, 111.8, 79.3, 72.5, 28.1, 27.5, 15.5.

HRMS (ESI-TOF)  $m/z$   $[M + H]^+$  calcd. for  $\text{C}_{32}\text{H}_{30}\text{N}_3\text{O}_4$  520.2231, found 520.2233.

*tert*-Butyl

((4*cS*,15*aR*)-2-bromo-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3s)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 56.3 mg, 99% yield; mp 170.4–171.9 °C; >20:1 dr, 95% ee;  $[\alpha]_D^{20} = +143.43$  ( $c$  0.7,  $\text{CH}_2\text{Cl}_2$ ).

The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 11.7$  min (minor), 8.3 min (major).

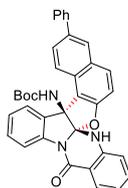
$^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ )  $\delta$  8.85 – 8.41 (m, 2H), 8.29 (d,  $J = 8.1$  Hz, 1H), 8.22 (s, 1H), 8.01 (d,  $J = 7.8$  Hz, 1H), 7.90 – 7.77 (m, 2H), 7.74 – 7.64 (m, 1H), 7.58 – 7.50 (m, 1H), 7.41 – 7.31 (m, 1H), 7.29 – 6.95 (m, 5H), 1.40 – 0.61 (m, 9H).

$^{13}\text{C NMR}$  (101 MHz, DMSO- $d_6$ )  $\delta$  158.9, 154.9, 143.0, 140.8, 134.6, 131.0, 131.0, 130.5, 130.0, 129.3, 127.6, 127.5, 125.1, 124.4, 123.5, 119.9, 118.0, 116.3, 116.2, 115.8, 113.9, 113.5, 113.4, 113.2, 79.3, 72.2, 27.5.

HRMS (ESI-TOF)  $m/z$   $[M + H]^+$  calcd. for  $\text{C}_{30}\text{H}_{25}\text{BrN}_3\text{O}_4$  570.1023, found 570.1029.

*tert*-Butyl

((4*cS*,15*aR*)-10-oxo-2-phenyl-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-4*c*-yl)carbamate (3t)



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 55.5 mg, 98% yield; mp 170.6–172.1 °C; >20:1 dr, 98% ee;  $[\alpha]_D^{20} = +296.6$  ( $c$  1.9,  $\text{CH}_2\text{Cl}_2$ ).

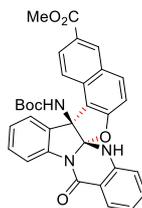
The ee was determined by HPLC (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 14.4$  min (minor), 10.0 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.23 – 8.48 (m, 2H), 8.33 (d, *J* = 8.1 Hz, 1H), 8.29 – 8.25 (m, 1H), 8.13 – 8.07 (m, 1H), 8.07 – 8.00 (m, 1H), 7.90 (d, *J* = 8.9 Hz, 1H), 7.83 (d, *J* = 7.3 Hz, 2H), 7.80 – 7.73 (m, 1H), 7.58 – 7.49 (m, 3H), 7.43 – 7.33 (m, 2H), 7.28 – 6.79 (m, 5H), 1.28 – 0.74 (m, 9H).

**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)** δ 159.0, 155.1, 154.8, 143.1, 140.9, 139.8, 135.1, 134.6, 132.0, 131.3, 130.2, 129.3, 129.1, 128.2, 127.6, 127.5, 126.7, 126.5, 125.1, 123.6, 123.0, 119.9, 117.7, 116.3, 115.8, 114.1, 113.3, 112.4, 79.4, 72.4, 27.6.

**HRMS (ESI-TOF)** *m/z* [M + H]<sup>+</sup> calcd. for C<sub>36</sub>H<sub>30</sub>N<sub>3</sub>O<sub>4</sub> 568.2231, found 568.2233.

**methyl** **((3*cS*,15*aR*)-4*c*-((*tert*-butoxycarbonyl)amino)-10-oxo-10,15-dihydro-4*cH*-naphtho[1'',2'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazoline-2-carboxylate (3u)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 54.2 mg, 99% yield; mp 215.0–216.8 °C; >20:1 dr, 97% ee; [α]<sub>D</sub><sup>20</sup> = +186.00 (*c* 0.8, CH<sub>2</sub>Cl<sub>2</sub>).

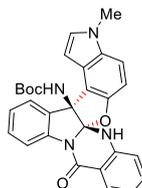
**The ee was determined by HPLC** (Chiralpak IC, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min, λ = 254 nm) *t<sub>R</sub>* = 24.8 min (minor), 18.3 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 8.99 – 8.48 (m, 3H), 8.29 (d, *J* = 8.1 Hz, 1H), 8.21 (d, *J* = 8.8 Hz, 1H), 8.06 (d, *J* = 8.9 Hz, 1H), 8.01 (d, *J* = 7.7 Hz, 1H), 7.80 – 7.64 (m, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.42 – 7.31 (m, 1H), 7.19 (d, *J* = 8.8 Hz, 1H), 7.17 – 7.11 (m, 2H), 7.11 – 6.83 (m, 2H), 3.92 (s, 3H), 1.44 – 0.67 (m, 9H).

**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)** δ 166.3, 158.9, 156.6, 154.9, 142.9, 140.8, 134.6, 132.7, 132.0, 131.4, 129.4, 128.8, 127.5, 126.6, 125.2, 124.4, 123.3, 120.0, 118.1, 116.2, 116.0, 115.8, 113.9, 113.7, 113.1, 79.4, 72.1, 52.2, 27.5.

**HRMS (ESI-TOF)** *m/z* [M + H]<sup>+</sup> calcd. for C<sub>32</sub>H<sub>28</sub>N<sub>3</sub>O<sub>6</sub> 550.1973, found 520.1986.

***tert*-Butyl** **((3*cS*,14*aR*)-1-methyl-9-oxo-9,14-dihydroindolo[4'',5'':4',5']furo[2',3':2,3]indolo[2,1-*b*]quinazolin-3*c*(1*H*)-yl)carbamate (3w)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–6:1 as the eluent).

Light yellow solid; 46.4 mg, 94% yield; mp 158.3–160.9 °C; >20:1 dr, 54% ee; [α]<sub>D</sub><sup>20</sup> = –124.2 (*c* 1.6, CH<sub>2</sub>Cl<sub>2</sub>).

**The ee was determined by HPLC** (Chiralpak AD-H, isopropanol/*n*-hexane 30/70, flow rate = 1.0

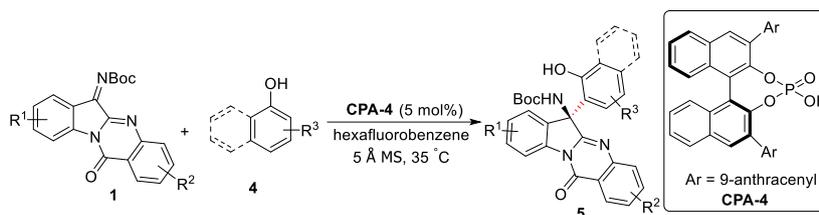
mL/min,  $\lambda = 254$  nm)  $t_R = 29.0$  min (minor), 22.7 min (major).

**$^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )**  $\delta$  8.86 (s, 1H), 8.52 (dd,  $J = 8.4, 1.1$  Hz, 1H), 8.28 (dd,  $J = 8.1, 1.5$  Hz, 2H), 7.93 – 7.79 (m, 1H), 7.72 (d,  $J = 8.1$  Hz, 1H), 7.64 – 7.50 (m, 3H), 7.44 (t,  $J = 7.4$  Hz, 1H), 7.15 (d,  $J = 8.8$  Hz, 2H), 6.86 (s, 1H), 6.64 (dd,  $J = 8.7, 2.3$  Hz, 1H), 3.58 (s, 3H), 1.45 – 0.64 (m, 9H).

**$^{13}\text{C}$  NMR (101 MHz, DMSO- $d_6$ )**  $\delta$  160.8, 159.3, 150.7, 147.1, 138.8, 134.8, 132.1, 129.2, 128.7, 127.5, 127.1, 126.8, 126.4, 125.6, 123.7, 120.8, 116.0, 111.9, 110.4, 110.2, 105.6, 78.8, 63.3, 32.5, 27.6.

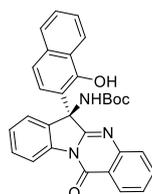
**HRMS (ESI-TOF)**  $m/z$   $[\text{M} + \text{H}]^+$  calcd. for  $\text{C}_{29}\text{H}_{27}\text{N}_4\text{O}_4$  495.2027, found 495.2029.

## 5. General procedure for the synthesis of compounds 5



In an oven-dried tube, CPA-4 (0.005 mmol), ketimines **1** (0.1 mmol), dry 5 Å MS (50 mg), and hexafluorobenzene (4.0 ml) were added. To this suspension, 1-naphthol or substituted phenol **4** (0.12 mmol) was then added. The resulting reaction mixture was stirred at 35 °C until the reaction was complete (monitored by TLC). The reaction mixture was concentrated under vacuum, and the residue was purified by flash chromatography on silica gel (petroleum ether : ethylacetate = 8:1–3:1) to give the product **5**.

***tert*-Butyl (S)-(6-(1-hydroxynaphthalen-2-yl)-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)carbamate (5a)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–3:1 as the eluent).

White solid; 48.6 mg, 99% yield; mp 137.5–139.6 °C; 65% ee;  $[\alpha]_D^{20} = -248.44$  ( $c$  2.0,  $\text{CH}_2\text{Cl}_2$ ).

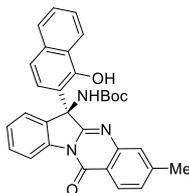
**The ee was determined by HPLC** (Chiralpak AD-H, isopropanol/*n*-hexane 15/85, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 12.6$  min (minor), 13.6 min (major).

**$^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )**  $\delta$  10.64 (s, 1H), 8.50 (d,  $J = 8.0$  Hz, 2H), 8.33 (dd,  $J = 8.0, 1.5$  Hz, 1H), 8.16 (d,  $J = 8.3$  Hz, 1H), 7.92 – 7.84 (m, 1H), 7.81 (d,  $J = 7.4$  Hz, 1H), 7.74 (d,  $J = 8.0$  Hz, 1H), 7.62 (t,  $J = 7.5$  Hz, 1H), 7.54 (t,  $J = 7.7$  Hz, 1H), 7.52 – 7.27 (m, 6H), 1.05 (s, 9H).

**$^{13}\text{C}$  NMR (101 MHz, DMSO- $d_6$ )**  $\delta$  162.89, 159.00, 154.37, 151.38, 146.14, 139.53, 134.99, 134.04, 133.63, 129.21, 127.39, 127.30, 126.91, 126.78, 126.74, 126.57, 125.87, 125.23, 125.06, 124.48, 122.40, 121.21, 119.13, 118.64, 115.99, 79.12, 65.98, 27.66.

**HRMS (ESI-TOF)**  $m/z$   $[\text{M} + \text{H}]^+$  calcd. for  $\text{C}_{30}\text{H}_{26}\text{N}_3\text{O}_4$  492.1918, found 492.1924.

***tert*-Butyl (S)-(6-(1-hydroxynaphthalen-2-yl)-3-methyl-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)carbamate (5b)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–3:1 as the eluent).

White solid; 49.5 mg, 98% yield; mp 153.5–155.3 °C; 72% ee;  $[\alpha]_D^{20} = -230.07$  (*c* 2.2, CH<sub>2</sub>Cl<sub>2</sub>).

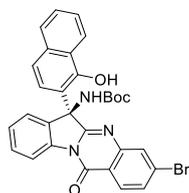
**The ee was determined by HPLC** (Chiralpak AD-H, isopropanol/*n*-hexane 15/85, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 20.7$  min (minor), 11.9 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  10.87 (s, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 8.47 (s, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 8.10 (s, 1H), 7.78 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.69–7.60 (m, 2H), 7.59–7.39 (m, 5H), 7.36 (d, *J* = 8.9 Hz, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 2.46 (s, 3H), 1.04 (s, 9H).

**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  162.1, 158.9, 154.3, 151.7, 143.9, 139.6, 137.3, 136.2, 134.1, 133.4, 129.3, 127.3, 126.8, 126.7, 126.6, 126.0, 125.3, 125.1, 124.7, 122.5, 121.0, 119.1, 118.3, 116.1, 79.1, 66.0, 27.6, 20.8.

**HRMS (ESI-TOF)**  $m/z$  [M + H]<sup>+</sup> calcd. for C<sub>31</sub>H<sub>28</sub>N<sub>3</sub>O<sub>4</sub> 506.2074, found 506.2081.

***tert*-Butyl (S)-(3-bromo-6-(1-hydroxynaphthalen-2-yl)-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)carbamate (5c)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–3:1 as the eluent).

White solid; 56.4 mg, 99% yield; mp 139.3–141.1 °C; 73% ee;  $[\alpha]_D^{20} = -268.36$  (*c* 1.9, CH<sub>2</sub>Cl<sub>2</sub>).

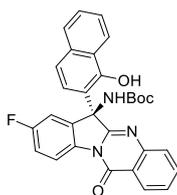
**The ee was determined by HPLC** (Chiralpak AD-H, isopropanol/*n*-hexane 15/85, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 19.2$  min (minor), 11.1 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  10.33 (s, 1H), 8.59–8.44 (m, 2H), 8.41 (d, *J* = 2.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 8.00 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.68 (d, *J* = 8.7 Hz, 1H), 7.58–7.31 (m, 7H), 1.06 (s, 9H).

**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  163.5, 157.9, 154.4, 150.8, 145.5, 139.3, 137.7, 134.0, 133.9, 129.4, 129.2, 128.6, 127.4, 127.0, 126.8, 125.7, 125.3, 125.0, 124.3, 122.9, 122.3, 119.8, 119.4, 119.2, 116.0, 79.2, 65.8, 27.7.

**HRMS (ESI-TOF)**  $m/z$  [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>Br 572.1008, found 572.1016.

***tert*-Butyl (S)-(8-fluoro-6-(1-hydroxynaphthalen-2-yl)-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)carbamate (5d)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–3:1 as the eluent).

White solid; 50.3 mg, 99% yield; mp 124.4–126.9 °C; 71% ee;  $[\alpha]_{\text{D}}^{20} = -318.97$  (*c* 1.8, CH<sub>2</sub>Cl<sub>2</sub>).

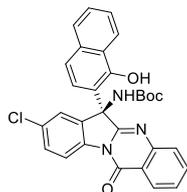
**The ee was determined by HPLC** (Chiralpak AD-H, isopropanol/*n*-hexane 15/85, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_{\text{R}} = 9.3$  min (minor), 12.7 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  10.30 (s, 1H), 8.63–8.40 (m, 2H), 8.34 (d, *J* = 7.9 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.85 (dd, *J* = 12.7, 8.0 Hz, 2H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.66–7.53 (m, 2H), 7.51–7.26 (m, 5H), 1.10 (s, 9H).

**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  162.6, 160.5 (d, *J* = 244.4 Hz, 1C), 158.9, 154.5, 150.7, 146.5, 136.5 (d, *J* = 8.1 Hz, 1C), 136.0 (d, *J* = 2.0 Hz, 1C), 134.9, 134.1, 127.43, 127.38, 127.1, 126.8, 126.5, 125.6, 125.3, 125.0, 122.3, 121.2, 119.5, 119.2, 117.4 (d, *J* = 8.1 Hz, 1C), 115.6 (d, *J* = 23.2 Hz, 1C), 111.6 (d, *J* = 25.3 Hz, 1C), 79.4, 65.6, 27.7.

**HRMS (ESI-TOF)**  $m/z$  [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>F 510.1824, found 510.1830.

***tert*-Butyl (S)-(8-chloro-6-(1-hydroxynaphthalen-2-yl)-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)carbamate (5e)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–3:1 as the eluent).

White solid; 51.0 mg, 97% yield; mp 122.8–124.7 °C; 70% ee;  $[\alpha]_{\text{D}}^{20} = -267.6$  (*c* 2.0, CH<sub>2</sub>Cl<sub>2</sub>).

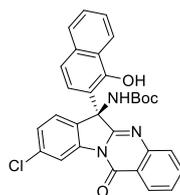
**The ee was determined by HPLC** (Chiralpak AD-H, isopropanol/*n*-hexane 15/85, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_{\text{R}} = 9.9$  min (minor), 13.2 min (major).

**<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  10.17 (s, 1H), 8.50 (d, *J* = 8.6 Hz, 2H), 8.35 (dd, *J* = 8.0, 1.5 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.93–7.78 (m, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.66–7.54 (m, 3H), 7.53–7.44 (m, 3H), 7.41 (t, *J* = 7.6 Hz, 1H), 1.11 (s, 9H).

**<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  162.2, 159.0, 154.6, 150.4, 146.6, 138.5, 136.4, 135.0, 134.0, 130.6, 129.0, 127.5, 127.4, 127.2, 126.8, 126.6, 125.5, 125.3, 124.9, 123.9, 122.2, 121.1, 119.61, 119.57, 117.3, 79.4, 65.3, 27.7.

**HRMS (ESI-TOF)**  $m/z$  [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>Cl 526.1528, found 526.1537.

***tert*-Butyl (S)-(9-chloro-6-(1-hydroxynaphthalen-2-yl)-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)carbamate (5f)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–3:1 as the eluent).

White solid; 52.1 mg, 99% yield; mp 142.8–145.1 °C; 64% ee;  $[\alpha]_D^{20} = -286.8$  (*c* 1.9, CH<sub>2</sub>Cl<sub>2</sub>).

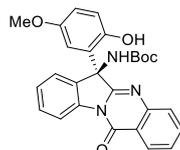
The ee was determined by HPLC (Chiralpak AD-H, isopropanol/*n*-hexane 15/85, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 8.1$  min (minor), 12.9 min (major).

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  10.21 (s, 1H), 8.53 (s, 1H), 8.49 (d, *J* = 1.8 Hz, 1H), 8.34 (dd, *J* = 7.9, 1.6 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.94 – 7.78 (m, 2H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.67 – 7.54 (m, 2H), 7.52 – 7.35 (m, 5H), 1.11 (s, 9H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  162.5, 159.1, 154.6, 150.5, 146.5, 140.6, 135.2, 134.0, 133.1, 132.9, 127.5, 127.4, 127.2, 126.7, 126.6, 126.5, 125.6, 125.56, 125.3, 124.9, 122.2, 121.0, 119.5, 119.4, 115.7, 79.4, 65.2, 27.8.

HRMS (ESI-TOF) *m/z* [M + H]<sup>+</sup> calcd. for C<sub>30</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>Cl 526.1528, found 526.1536.

**tert-Butyl (S)-(6-(2-hydroxy-5-methoxyphenyl)-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)carbamate (5g)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–3:1 as the eluent).

White solid; 46.2 mg, 98% yield; mp 124.1–126.0 °C; 63% ee;  $[\alpha]_D^{20} = -79.3$  (*c* 0.68, CH<sub>2</sub>Cl<sub>2</sub>).

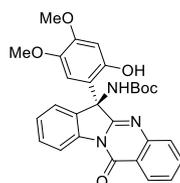
The ee was determined by HPLC (Chiralpak IB, ethanol/*n*-hexane 10/90, flow rate = 0.8 mL/min,  $\lambda = 254$  nm)  $t_R = 9.3$  min (minor), 13.6 min (major).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  10.86 (s, 1H), 8.63 (d, *J* = 8.0 Hz, 1H), 8.38 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.85 – 7.68 (m, 2H), 7.64 – 7.40 (m, 4H), 7.04 (d, *J* = 8.8 Hz, 1H), 6.80 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.29 (d, *J* = 3.0 Hz, 1H), 6.12 (s, 1H), 3.57 (s, 3H), 1.13 (s, 9H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  162.8, 159.3, 153.9, 153.3, 150.6, 145.4, 139.9, 134.9, 130.5, 127.7, 127.4, 127.0, 126.8, 125.4, 124.3, 122.0, 117.6, 115.9, 115.2, 81.1, 67.2, 55.8, 28.0.

HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd. for C<sub>27</sub>H<sub>25</sub>N<sub>3</sub>O<sub>5</sub>Na 494.1686, found 494.1688.

**tert-Butyl (S)-(6-(2-hydroxy-4,5-dimethoxyphenyl)-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)carbamate (5h)**



The product was purified by flash column chromatography (petroleum ether : ethyl acetate = 8:1–

3:1 as the eluent).

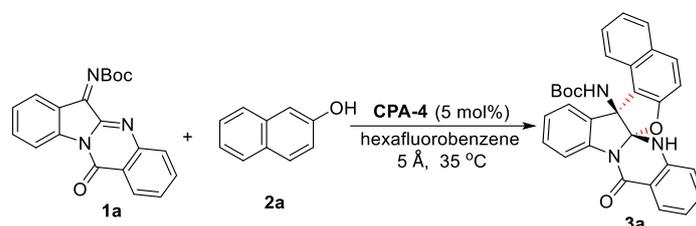
White solid; 49.6 mg, 99% yield; mp 197.7–199.6 °C; 68% ee;  $[\alpha]_{\text{D}}^{20} = -99.8$  ( $c$  1.5,  $\text{CH}_2\text{Cl}_2$ ).

The ee was determined by HPLC (Chiralpak AD-H, isopropanol/*n*-hexane 15/85, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_{\text{R}} = 28.8$  min (minor), 14.9 min (major).

$^1\text{H NMR}$  (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.24 (s, 1H), 8.42 (d,  $J = 7.7$  Hz, 1H), 8.33 (dd,  $J = 7.9, 1.5$  Hz, 1H), 8.26 (s, 1H), 7.90 – 7.77 (m, 1H), 7.68 (d,  $J = 7.8$  Hz, 1H), 7.59 (t,  $J = 7.5$  Hz, 1H), 7.48 – 7.34 (m, 2H), 7.27 (t,  $J = 7.5$  Hz, 1H), 7.23 (s, 1H), 6.20 (s, 1H), 3.78 (s, 3H), 3.61 (s, 3H), 1.04 (s, 9H).  
 $^{13}\text{C NMR}$  (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  162.8, 159.2, 154.5, 149.3, 148.2, 147.1, 141.3, 139.7, 134.6, 134.4, 128.4, 127.2, 126.9, 126.4, 126.3, 123.4, 121.2, 115.9, 115.6, 112.4, 101.2, 79.0, 64.6, 56.5, 55.3, 27.7.

HRMS (ESI-TOF)  $m/z$   $[M + H]^+$  calcd. for  $\text{C}_{28}\text{H}_{28}\text{N}_3\text{O}_6$  502.1973, found 502.1975.

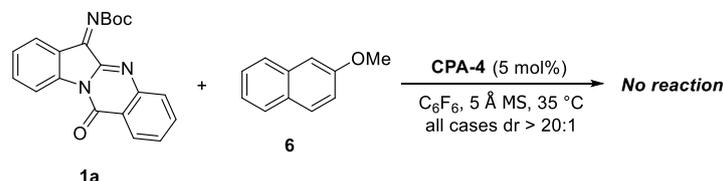
## 6. Gram-scale experiment



In a 150 mL dry round bottom flask equipped with a magnetic stirring bar, the ketimine **1a** (2.5 mmol, 1.0 equiv) were added to a solution of 2-naphthol **2a** (3.0 mmol, 1.2 equiv) and CPA-4 (5 mol %) in hexafluorobenzene (100 mL) at 35 °C. And then, the mixture was stirred at the same temperature for 23 h. After completion of the reaction (monitored by TLC), the hexafluorobenzene was removed under vacuum and the residues were isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 8:1–6:1) to give the product **3a** as a light yellow solid, 1.22 g, 99% yield, >20:1 dr and 98% ee.

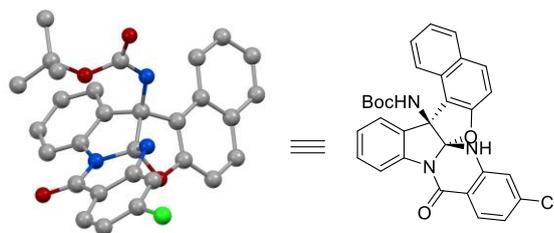
## 7. Control experiment

In an oven-dried tube, CPA-4 (0.005 mmol), ketimines **1** (0.1 mmol), dry 5 Å MS (50 mg), and hexafluorobenzene (4.0 ml) were added. To this suspension, 2-methoxynaphthalene **6** (0.12 mmol) was then added. The resulting reaction mixture was stirred at 35 °C for 24 h. TLC analysis showed no reaction taking place.



## 8. X-ray Crystal Structure of Compounds 3f and 5a

Single crystals of compound **3f** were prepared from the DMSO. For the X-ray analysis of compounds **3f**, a suitable crystal was selected for structure determination on a Xcalibur, Eos, Gemini diffractometer. Each crystal was kept at 293(2) K during data collection. Using Olex2<sup>2</sup>, the structure was solved with the ShelXS<sup>3</sup> structure solution program using Direct Methods and refined with the ShelXL<sup>3</sup> refinement package using Least Squares minimisation.



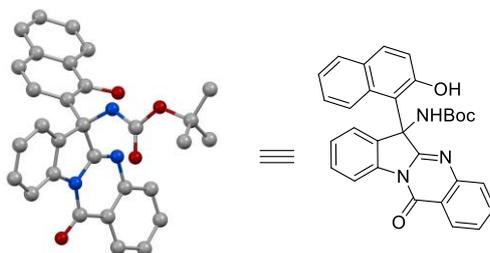
ORTEP of **3f** (at 50% level)

Crystal data and structure refinement (after solvents removal) for **3f** (CCDC-2312826)

Identification code	<b>3f</b> •DMSO
Empirical formula	C <sub>32</sub> H <sub>30</sub> ClN <sub>3</sub> O <sub>5</sub> S
Formula weight	604.10
Temperature/K	293(2)
Crystal system	monoclinic
Space group	P2 <sub>1</sub>
a/Å	9.0863(5)
b/Å	16.8287(11)
c/Å	9.8355(6)
α/°	90
β/°	91.730(5)
γ/°	90
Volume/Å <sup>3</sup>	1503.27(16)
Z	2
ρ <sub>calc</sub> /cm <sup>3</sup>	1.335
μ/mm <sup>-1</sup>	2.148
F(000)	632.0
Crystal size/mm <sup>3</sup>	0.2 × 0.15 × 0.1
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/°	8.996 to 143.38
Index ranges	-11 ≤ h ≤ 8, -17 ≤ k ≤ 20, -11 ≤ l ≤ 11
Reflections collected	10152
Independent reflections	4993 [R <sub>int</sub> = 0.0299, R <sub>sigma</sub> = 0.0430]
Data/restraints/parameters	4993/26/407
Goodness-of-fit on F <sup>2</sup>	1.042
Final R indexes [I >= 2σ (I)]	R <sub>1</sub> = 0.0499, wR <sub>2</sub> = 0.1190
Final R indexes [all data]	R <sub>1</sub> = 0.0606, wR <sub>2</sub> = 0.1306
Largest diff. peak/hole / e Å <sup>-3</sup>	0.35/-0.34
Flack parameter	-0.026(19)

Single crystals of compound *rac*-**5a** were prepared from the mixture solvent of ethyl acetate and hexane. For the X-ray analysis of compounds *rac*-**5a**, a suitable crystal was selected for structure determination on a Xcalibur, Eos, Gemini diffractometer. Each crystal was kept at 293(2) K during data collection. Using Olex2<sup>2</sup>, the structure was solved with the ShelXS<sup>3</sup> structure solution program

using Direct Methods and refined with the ShelXL<sup>3</sup> refinement package using Least Squares minimisation.



ORTEP of *rac*-**5a** (at 50% level)

Crystal data and structure refinement (after solvents removal) for *rac*-**5a** (CCDC-2312827)

Identification code	<i>rac</i> - <b>5a</b>
Empirical formula	C <sub>30</sub> H <sub>25</sub> N <sub>3</sub> O <sub>4</sub>
Formula weight	491.53
Temperature/K	193.0
Crystal system	monoclinic
Space group	P2 <sub>1</sub> /n
a/Å	7.7314(12)
b/Å	20.881(3)
c/Å	15.894(3)
α/°	90
β/°	101.278(9)
γ/°	90
Volume/Å <sup>3</sup>	2516.4(7)
Z	4
ρ <sub>calc</sub> /g/cm <sup>3</sup>	1.297
μ/mm <sup>-1</sup>	0.454
F(000)	1032.0
Crystal size/mm <sup>3</sup>	0.03 × 0.02 × 0.02
Radiation	GaKα (λ = 1.34139)
2θ range for data collection/°	10.8 to 111.182
Index ranges	-9 ≤ h ≤ 9, -25 ≤ k ≤ 25, -19 ≤ l ≤ 19
Reflections collected	15091
Independent reflections	4819 [R <sub>int</sub> = 0.1088, R <sub>sigma</sub> = 0.1147]
Data/restraints/parameters	4819/0/338
Goodness-of-fit on F <sup>2</sup>	0.958
Final R indexes [I ≥ 2σ (I)]	R <sub>1</sub> = 0.0740, wR <sub>2</sub> = 0.1687
Final R indexes [all data]	R <sub>1</sub> = 0.1521, wR <sub>2</sub> = 0.2145
Largest diff. peak/hole / e Å <sup>-3</sup>	0.36/-0.37

## 9. General experimental procedures for in vitro cytotoxicity assay

The human leukemia cells K562 were purchased from Chinese Academy of Sciences, Kunming Cell Bank. All the cells were cultured in RPMI-1640 medium (GIBICO, USA), supplemented with 10% fetal bovine serum (Hyclone, USA) and Penicillin-Streptomycin (respectively 100 U/mL) in 5% CO<sub>2</sub> at 37 °C. The cytotoxicity assay was performed according to the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) method in 96-well microplates. Briefly, 5000 cells were seeded into each well of 96-well cell culture plates and allowed to grow for 24 h before the drug is added. K562 tumor cell line was exposed to compounds (**3c**, **3d**, **3e**, **3i**, **3j**, **3l**, **3m**, **3s**, *rac*-**3i**, and *rac*-**3j**) at the concentrations of 1, 2, 4, 8 and 20 μmol·L<sup>-1</sup> in triplicates for 48 h, comparable to cisplatin (Aladdin, China). Then the MTT reagent was added to reaction with the cancer cells for 4 hours. At least, measure the OD value at 490 wavelengths. The average 50% inhibitory concentration (IC<sub>50</sub>) of all the compounds is calculated by IBM SPSS Statistics (version 19). Each concentration was analyzed in triplicate at least, and the whole experiment was repeated three times.

**Table S1. Cell Inhibitory Assay of target products in K562 Cells**

compound	IC <sub>50</sub> (μM) <sup>a</sup>
<b>3c</b>	27.22
<b>3d</b>	47.6775
<b>3e</b>	55.5635
<b>3i</b>	21.4195
<b>3j</b>	21.326
<b>3l</b>	31.31
<b>3m</b>	27.449
<b>3s</b>	27.456
<i>rac</i> - <b>3i</b>	26.5132
<i>rac</i> - <b>3j</b>	25.7016
<b>cisplatin</b> <sup>b</sup>	23.734

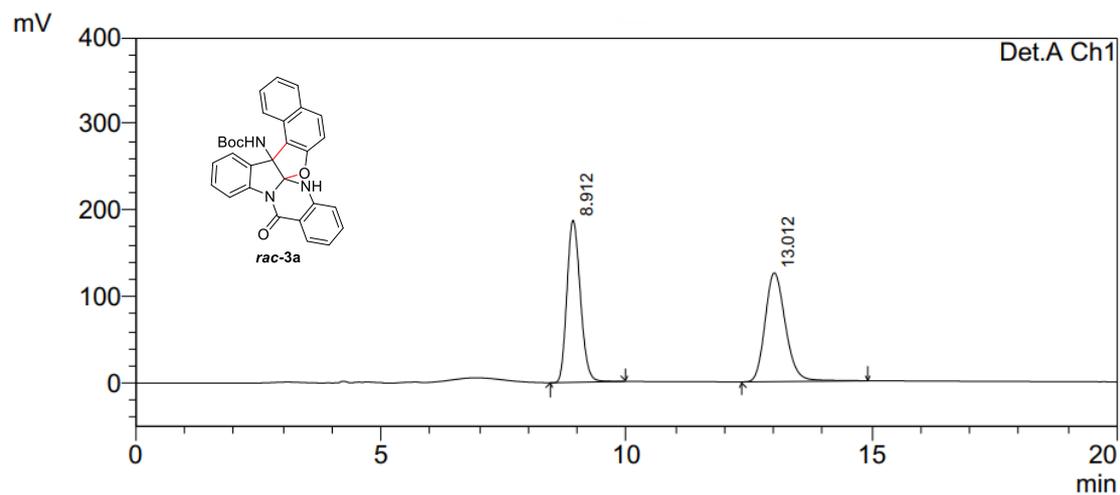
<sup>a</sup>IC<sub>50</sub> is the concentration of a compound that affords a 50% reduction in cell growth (after 48 h of incubation), expressed as the mean of triplicate experiments. <sup>b</sup>Commercially available broad-spectrum anticancer drug cisplatin as a positive control.

## 10. References

1. Gahtory, D.; Chouhan, M.; Sharma, R.; Nair, V. A. *Org. Lett.* **2013**, *15*, 3942–3945
2. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J, Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339-341.
3. Sheldrick, G. M. *Acta Cryst.* **2008**, A64, 112-122.
4. Sheldrick, G. M. *Acta Cryst.* **2015**, C71, 3-8.

## 11. HPLC spectra of compounds 3 and 5

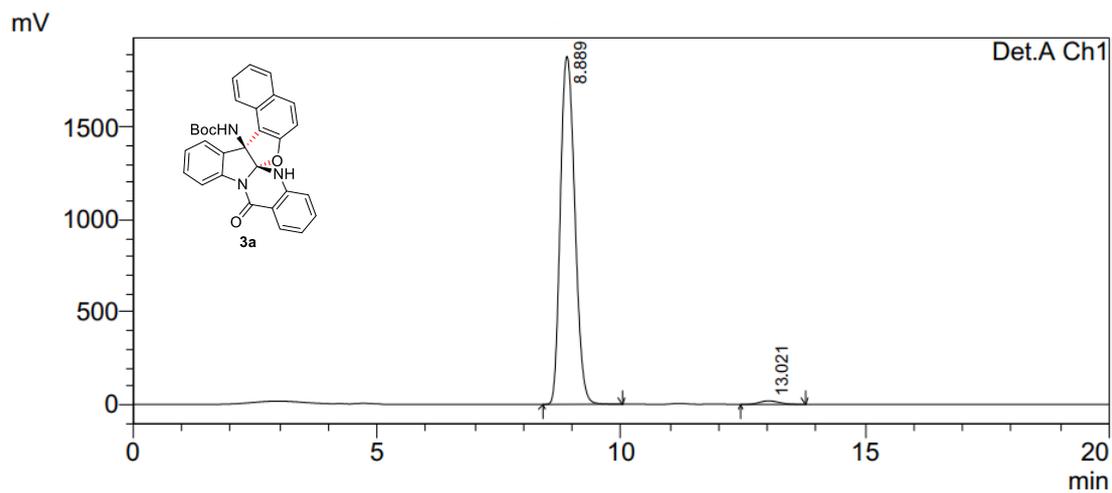
HPLC spectra of **3a**



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	8.912	3568794	187432	49.543
2	13.012	3634693	125759	50.457
Total		7203487		100.000

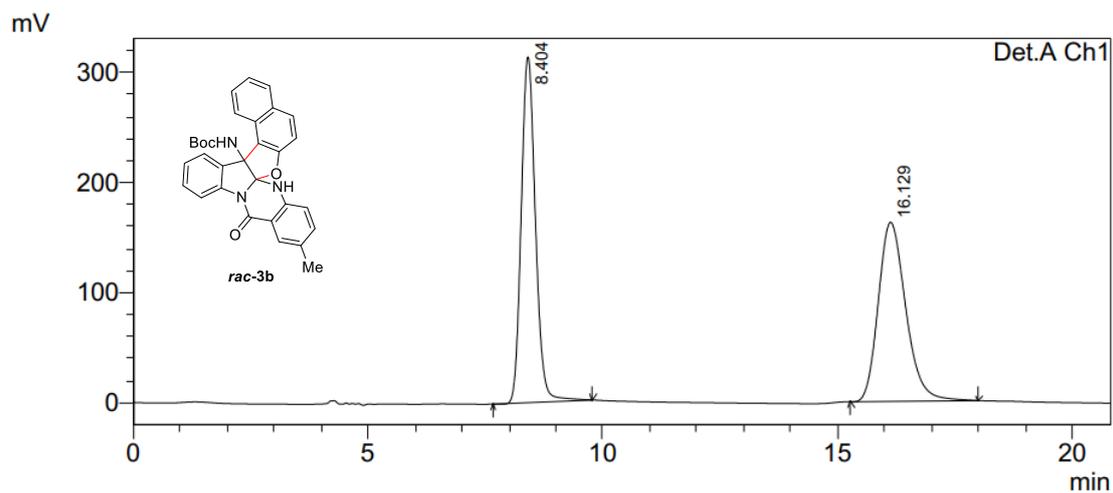


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	8.889	38850562	1885442	98.619
2	13.021	543957	19260	1.381
Total		39394519		100.000

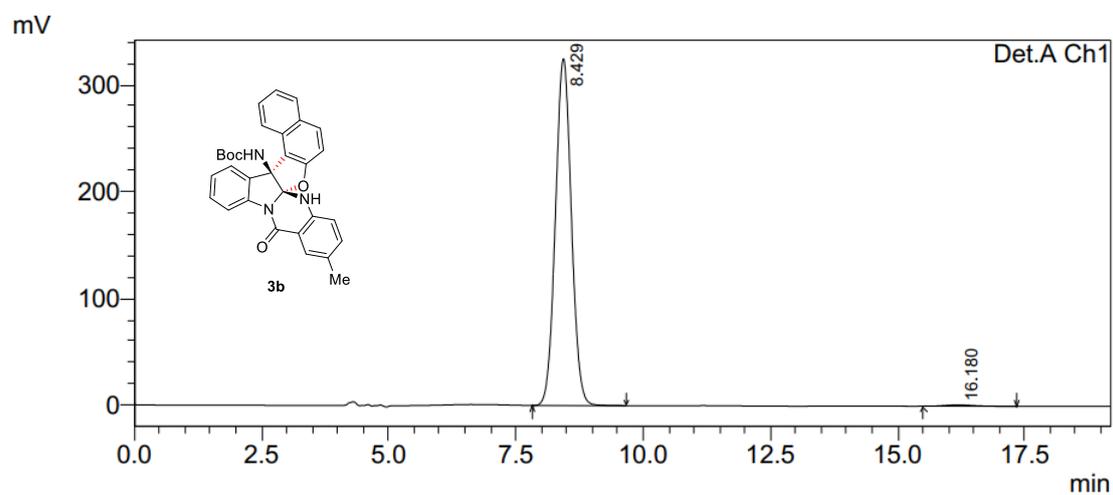
### HPLC spectra of **3b**



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	8.404	6607530	314262	49.902
2	16.129	6633535	162895	50.098
Total		13241065		100.000

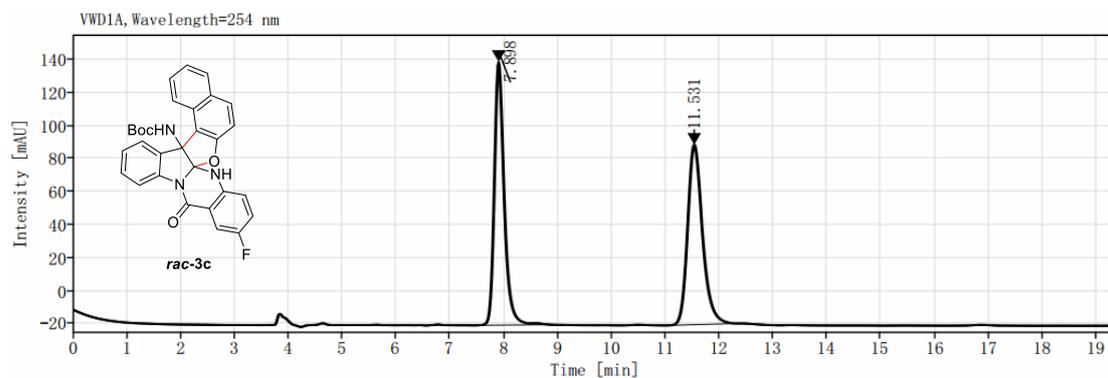


PeakTable

Detector A Ch1 254nm

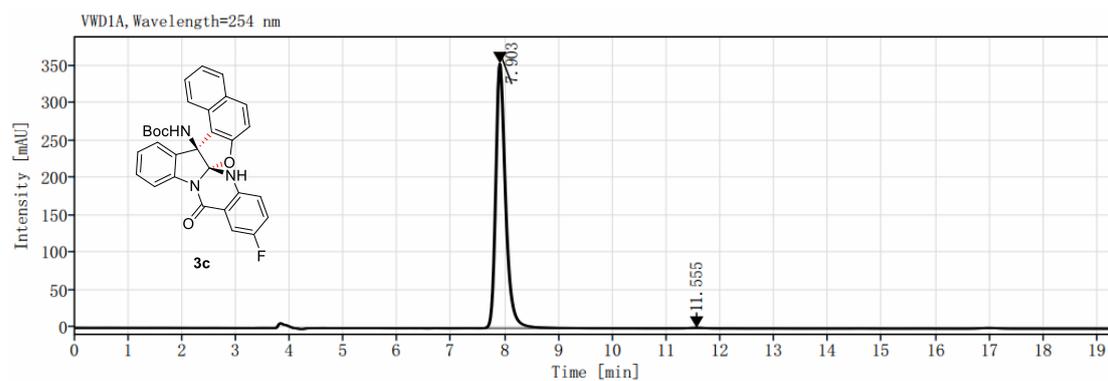
Peak#	Ret. Time	Area	Height	Area %
1	8.429	7100134	324987	99.313
2	16.180	49139	1242	0.687
Total		7149273		100.000

## HPLC spectra of 3c



Signal: VWD1A, Wavelength=254 nm

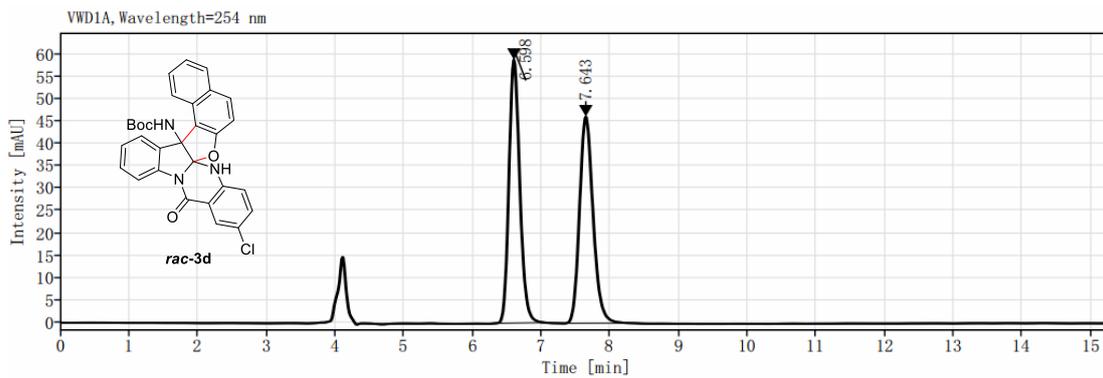
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
7.898	1.45	159.52	59.40	2035.316	49.40
11.531	1.30	109.03	40.60	2084.391	50.60
				Total	100.00



Signal: VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
7.903	2.24	353.66	99.79	4526.588	99.65
11.555	1.46	0.76	0.21	15.944	0.35
				Total	100.00

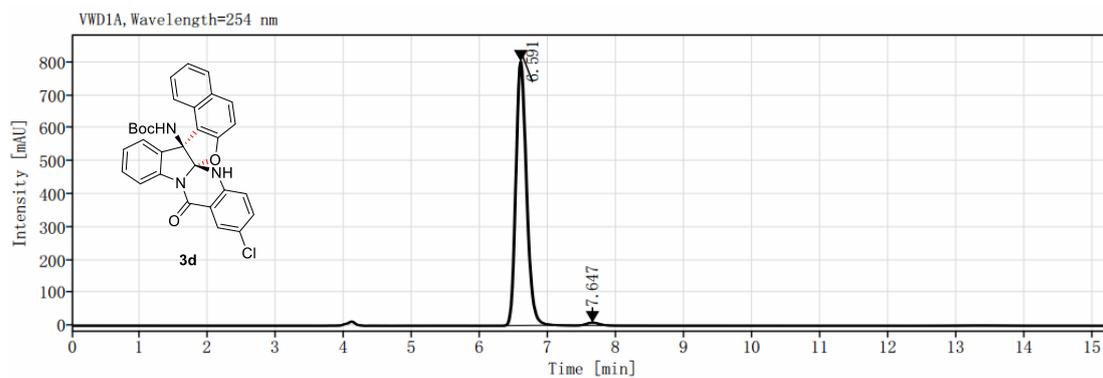
## HPLC spectra of 3d



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
6.598	0.74	58.97	56.01	649.141	50.50
7.643	0.99	46.32	43.99	636.166	49.50
Total					100.00

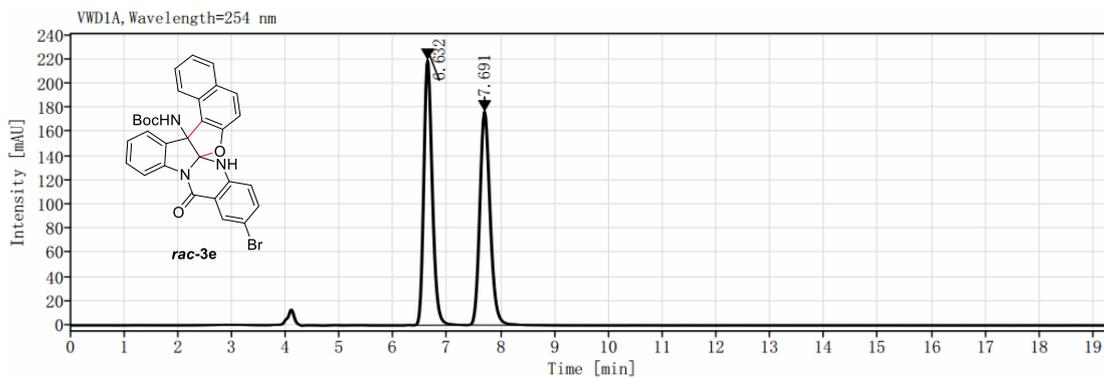


Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
6.591	0.85	803.32	98.91	8773.056	98.76
7.647	0.46	8.85	1.09	110.589	1.24
Total					100.00

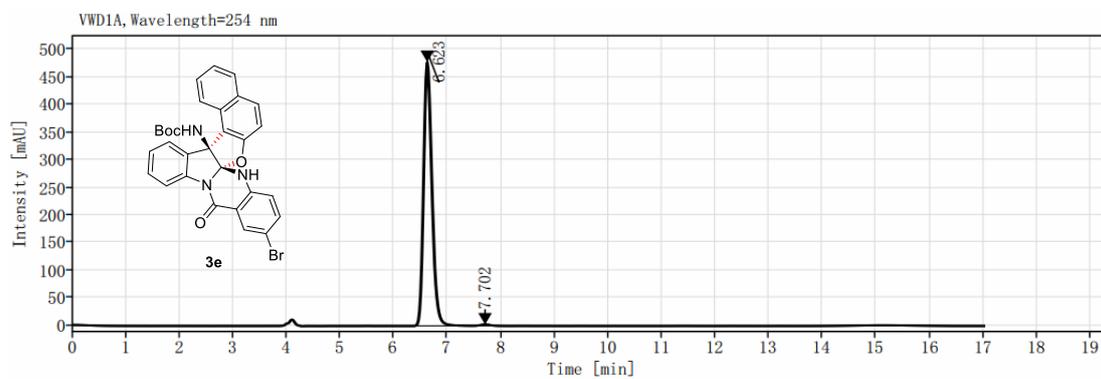
### HPLC spectra of 3e



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
6.632	0.99	219.69	55.41	2390.946	50.46
7.691	1.88	176.80	44.59	2347.398	49.54
				Total	100.00

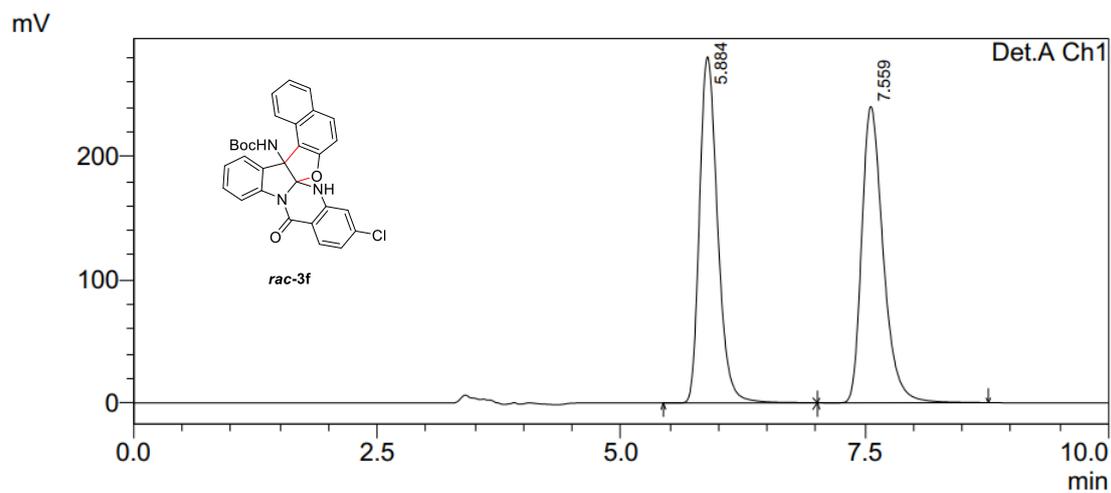


Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
6.623	1.13	477.72	99.51	5180.232	99.42
7.702	0.62	2.37	0.49	30.326	0.58
				Total	100.00

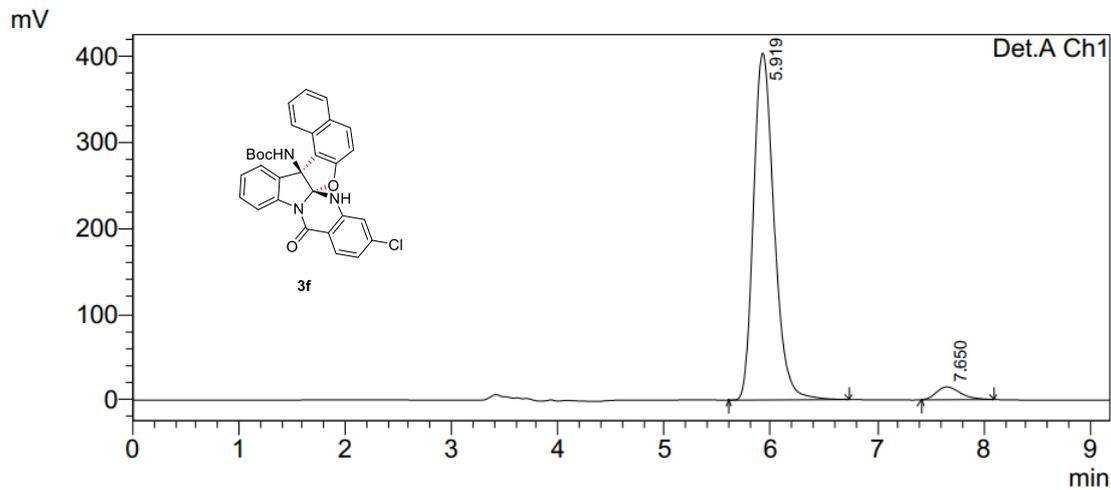
### HPLC spectra of 3f



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	5.884	3624580	280760	49.582
2	7.559	3685727	240274	50.418
Total		7310307		100.000

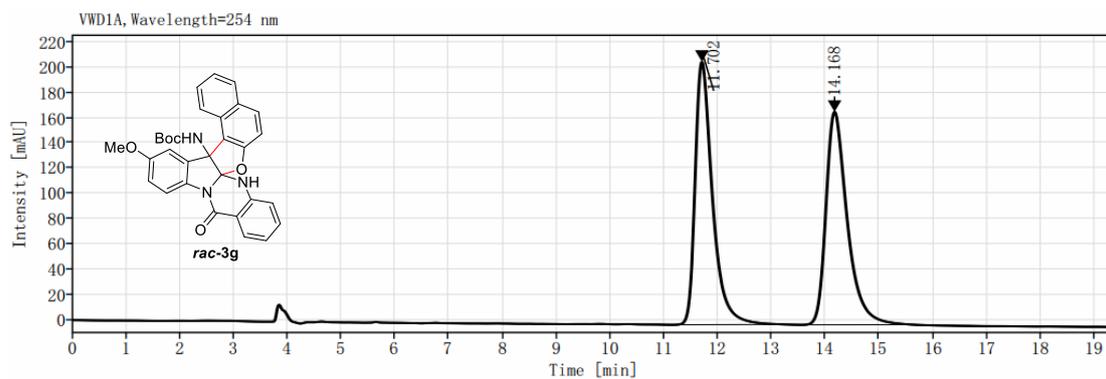


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	5.919	5421911	403673	95.828
2	7.650	236025	14952	4.172
Total		5657935		100.000

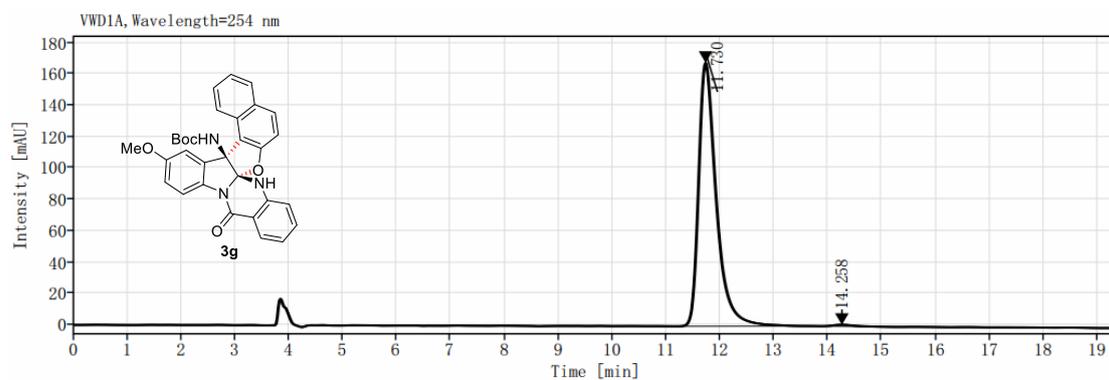
## HPLC spectra of **3g**



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
11.702	2.10	208.31	55.25	4665.516	50.06
14.168	2.08	168.70	44.75	4654.047	49.94
Total					100.00

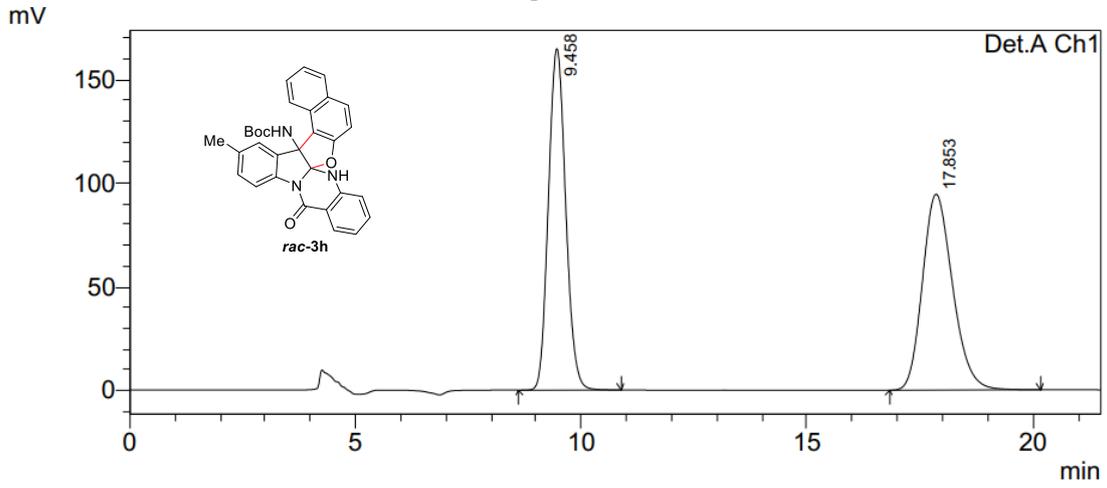


Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
11.730	2.54	168.33	99.42	3816.228	99.33
14.258	1.08	0.98	0.58	25.803	0.67
Total					100.00

HPLC spectra of **3h**

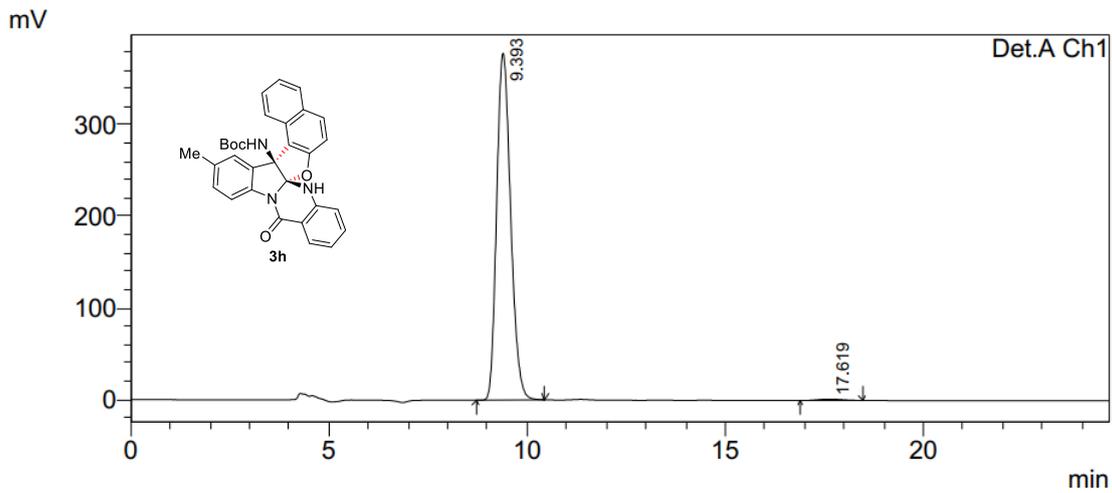


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	9.458	4394406	165082	49.972
2	17.853	4399341	94745	50.028
Total		8793747		100.000



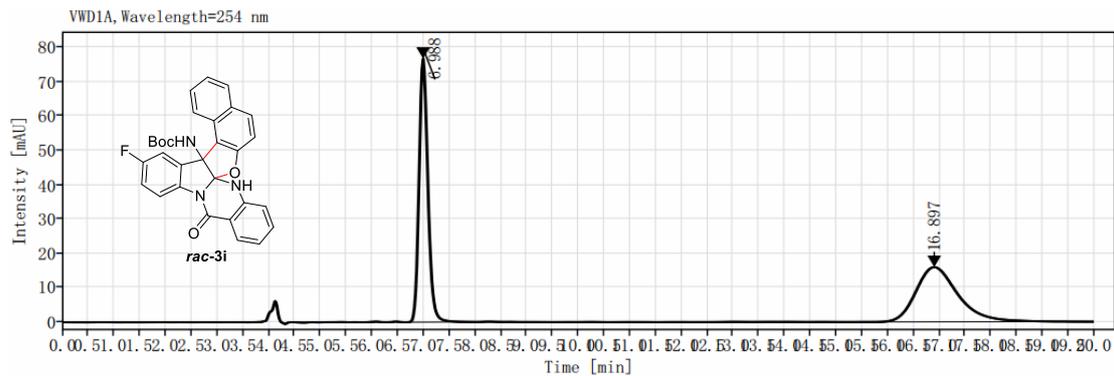
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	9.393	9292055	378594	99.347
2	17.619	61072	1442	0.653
Total		9353127		100.000

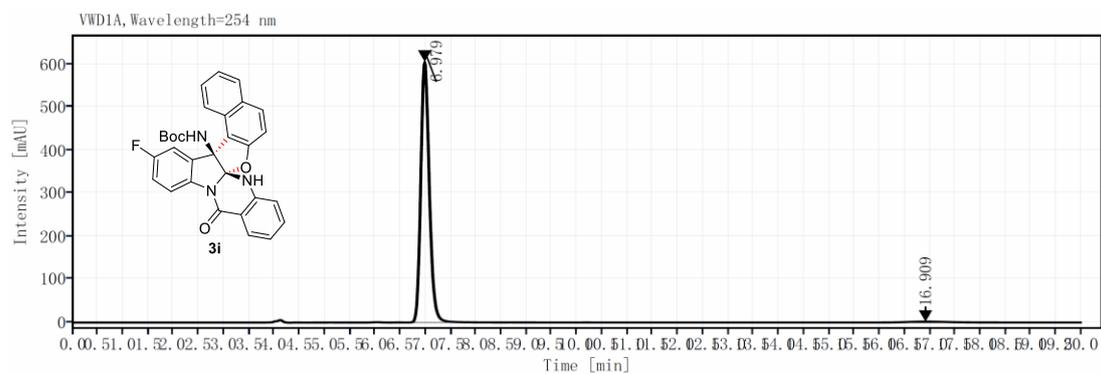
## HPLC spectra of **3i**



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
6.988	1.37	76.76	82.80	918.153	50.32
16.897	4.12	15.95	17.20	906.329	49.68
				Total	100.00

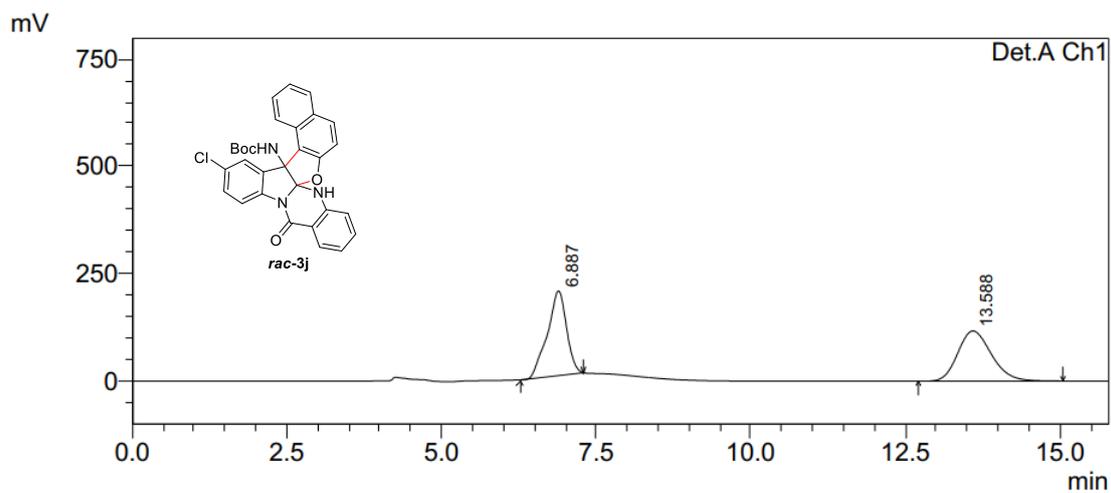


Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
6.979	1.88	605.47	99.67	7130.448	98.54
16.909	2.20	2.00	0.33	105.825	1.46
				Total	100.00

### HPLC spectra of 3j

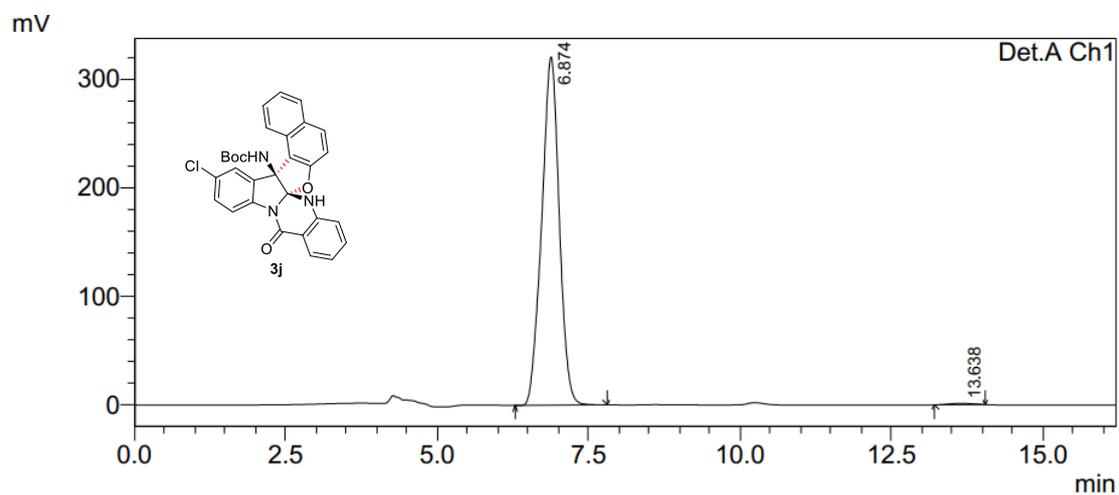


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	6.887	4256549	197091	49.091
2	13.588	4414180	116790	50.909
Total		8670729		100.000



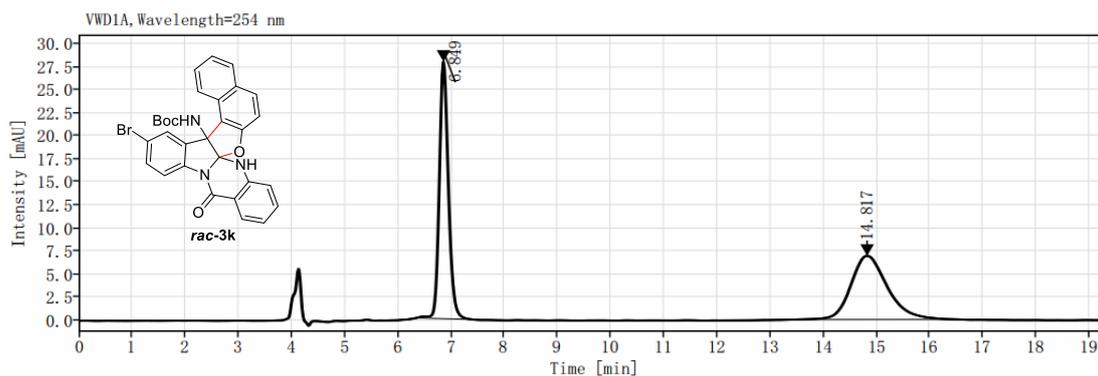
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

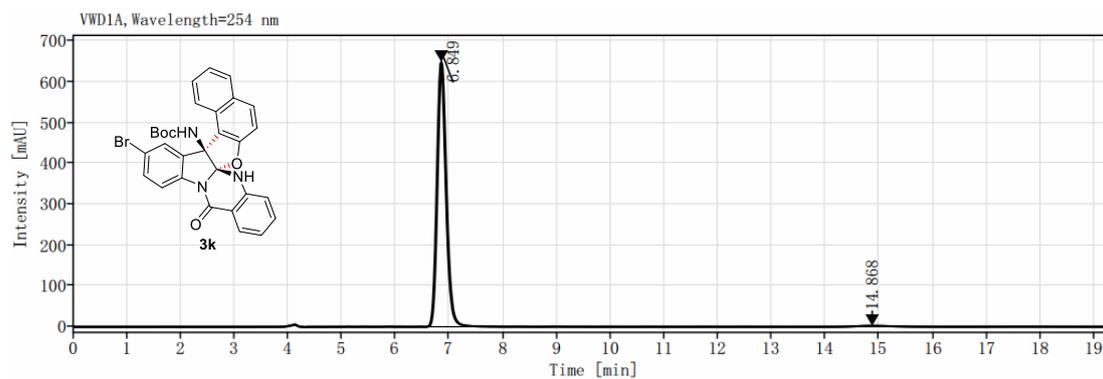
Peak#	Ret. Time	Area	Height	Area %
1	6.874	6445210	320000	99.461
2	13.638	34927	1242	0.539
Total		6480137		100.000

### HPLC spectra of 3k



Signal: VWD1A, Wavelength=254 nm

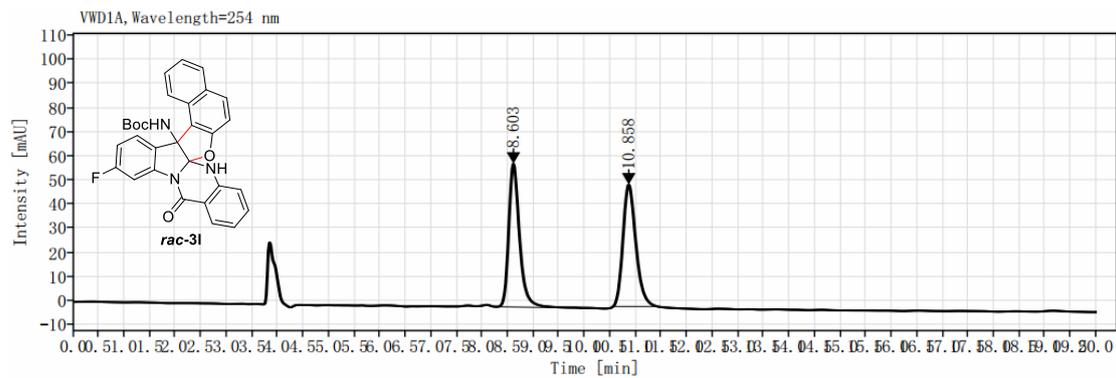
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
6.849	1.05	27.86	80.13	331.311	50.18
14.817	3.07	6.91	19.87	328.961	49.82
Total					100.00



Signal: VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
6.849	1.35	650.06	99.62	7541.904	98.51
14.868	2.70	2.46	0.38	113.842	1.49
Total					100.00

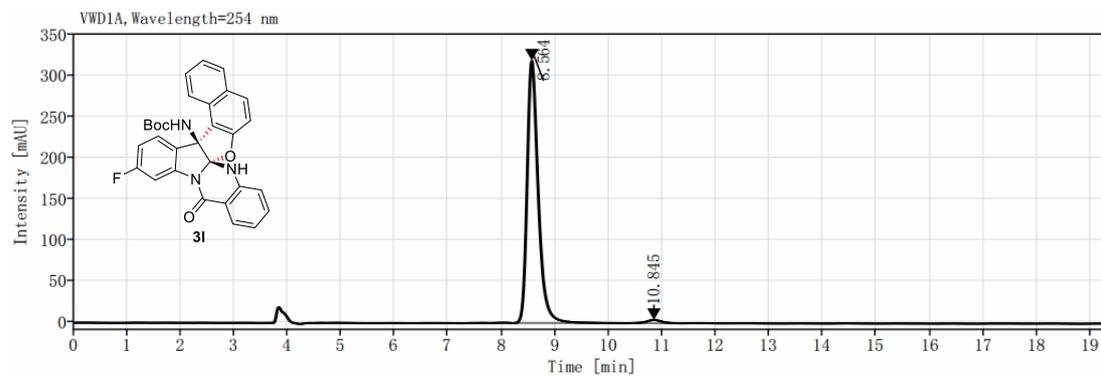
## HPLC spectra of 31



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.603	1.94	59.41	54.04	875.192	49.69
10.858	0.87	50.53	45.96	885.975	50.31
				Total	100.00

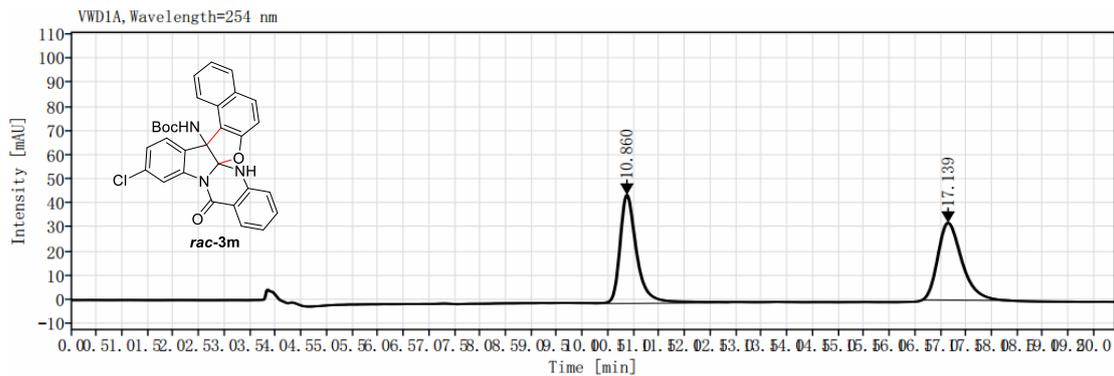


Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.564	1.97	319.76	98.74	4584.438	98.31
10.845	0.98	4.10	1.26	78.673	1.69
				Total	100.00

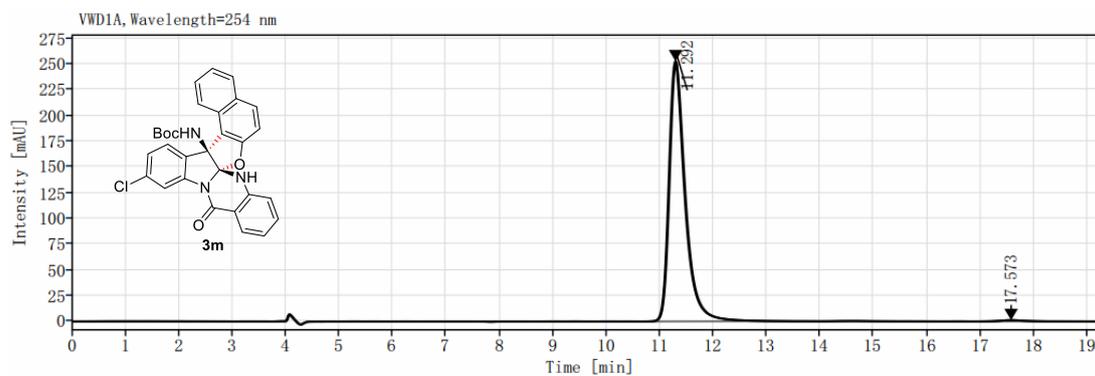
### HPLC spectra of 3m



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
10.860	2.66	45.00	58.40	1039.896	49.74
17.139	1.71	32.06	41.60	1050.678	50.26
				Total	100.00

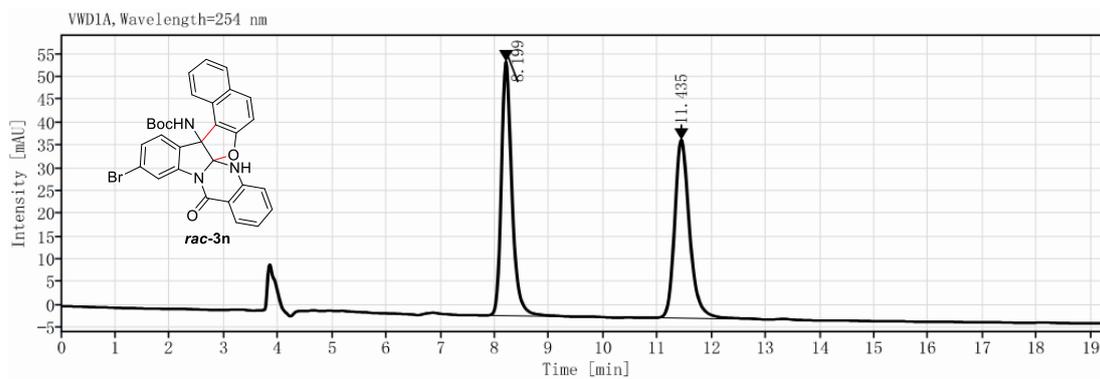


Signal:

VWD1A, Wavelength=254 nm

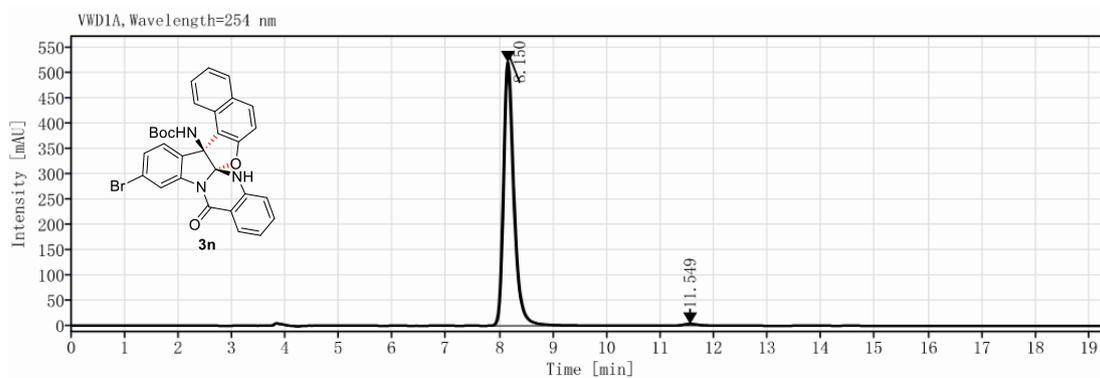
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
11.292	2.96	252.85	99.51	5287.111	99.23
17.573	1.70	1.25	0.49	41.294	0.77
				Total	100.00

## HPLC spectra of 3n



Signal: VWD1A, Wavelength=254 nm

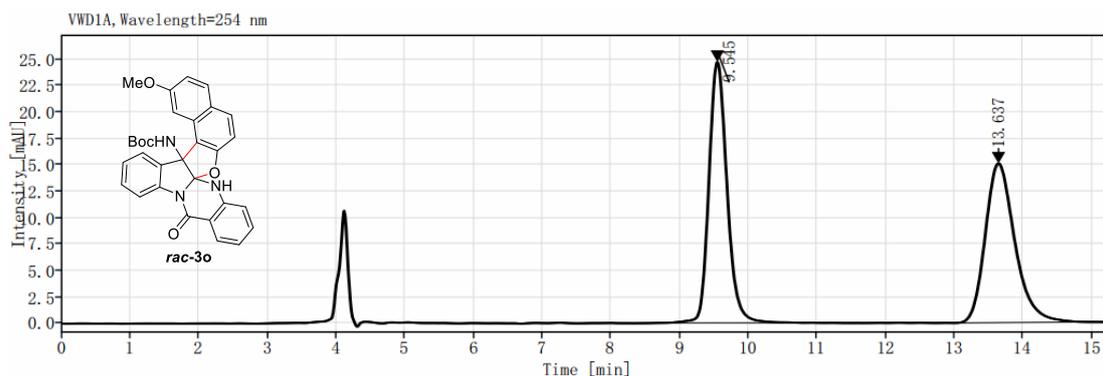
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.199	1.67	55.70	58.75	757.974	50.04
11.435	2.09	39.10	41.25	756.784	49.96
Total					100.00



Signal: VWD1A, Wavelength=254 nm

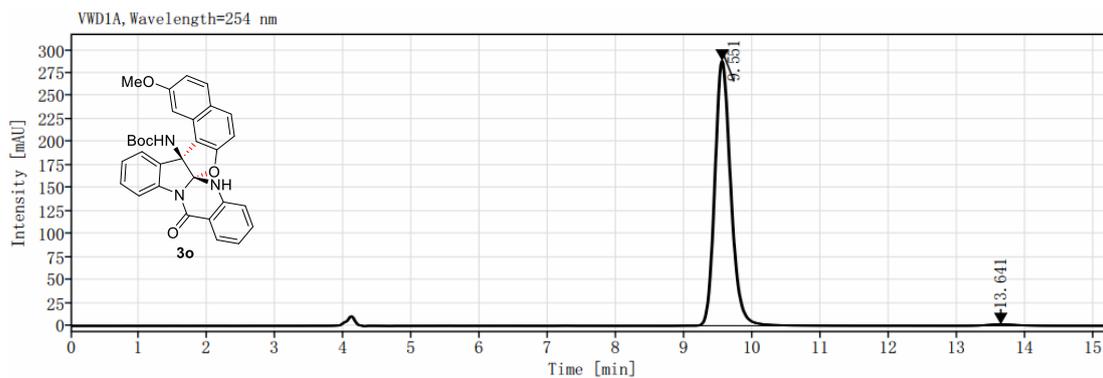
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.150	2.88	521.83	99.32	7032.768	99.01
11.549	1.21	3.57	0.68	70.567	0.99
Total					100.00

### HPLC spectra of **3o**



Signal: VWD1A, Wavelength=254 nm

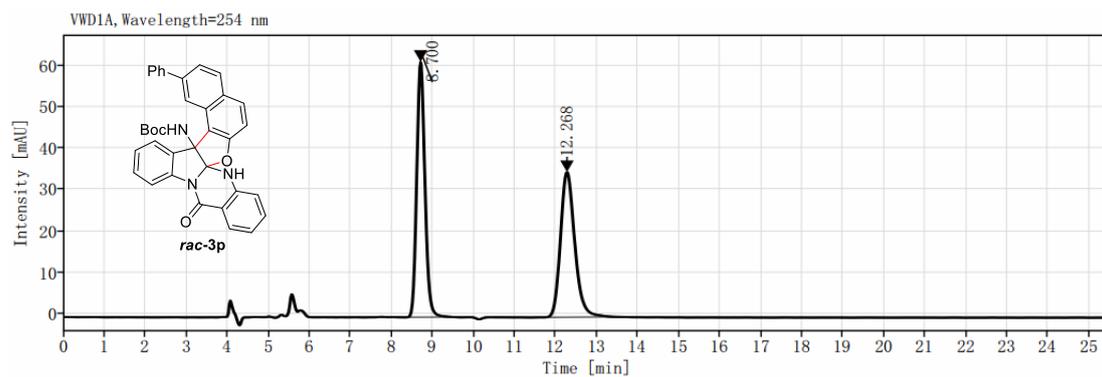
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.545	2.07	24.70	62.10	452.713	50.11
13.637	1.97	15.07	37.90	450.780	49.89
				Total	100.00



Signal: VWD1A, Wavelength=254 nm

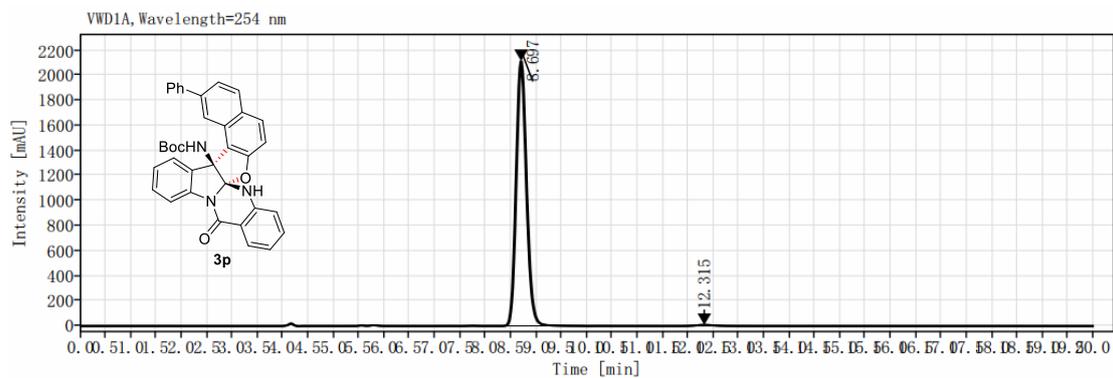
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.551	2.35	288.31	99.45	4696.758	99.03
13.641	1.47	1.59	0.55	46.111	0.97
				Total	100.00

### HPLC spectra of 3p



Signal: VWD1A, Wavelength=254 nm

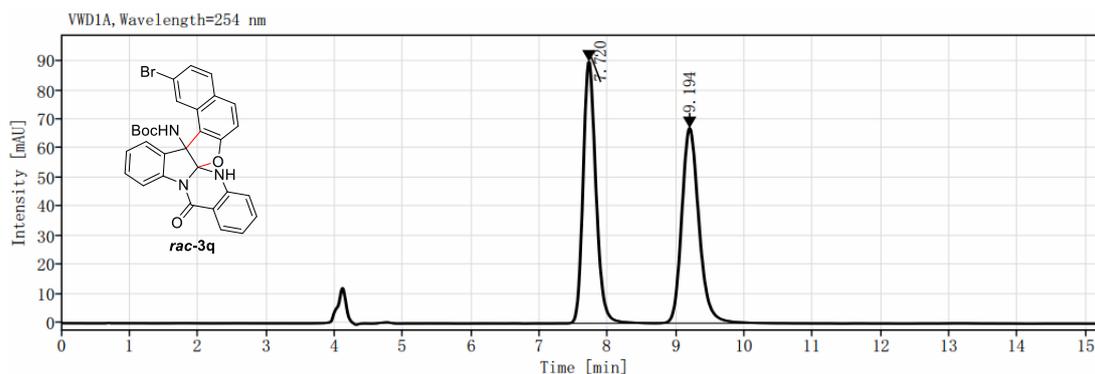
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.700	1.34	62.05	63.76	860.062	50.28
12.268	1.74	35.27	36.24	850.611	49.72
Total					100.00



Signal: VWD1A, Wavelength=254 nm

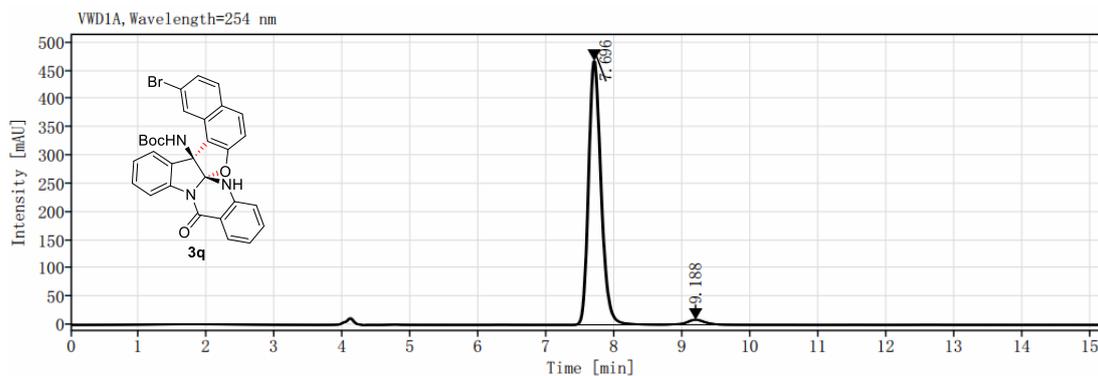
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.697	1.48	2116.07	99.61	29898.653	99.35
12.315	1.00	8.20	0.39	194.613	0.65
Total					100.00

### HPLC spectra of 3q



Signal: VWD1A, Wavelength=254 nm

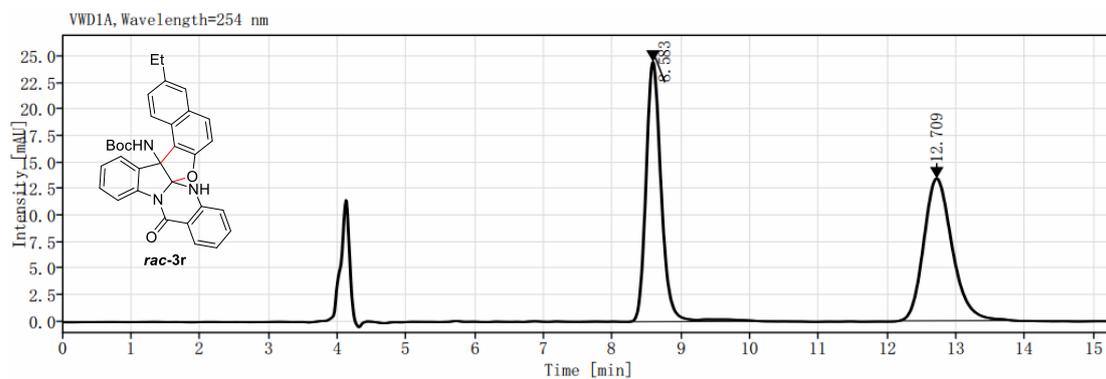
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
7.720	1.31	89.98	57.29	1173.515	49.92
9.194	1.84	67.09	42.71	1177.170	50.08
Total					100.00



Signal: VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
7.696	1.32	467.57	98.13	5970.789	97.28
9.188	1.29	8.92	1.87	166.979	2.72
Total					100.00

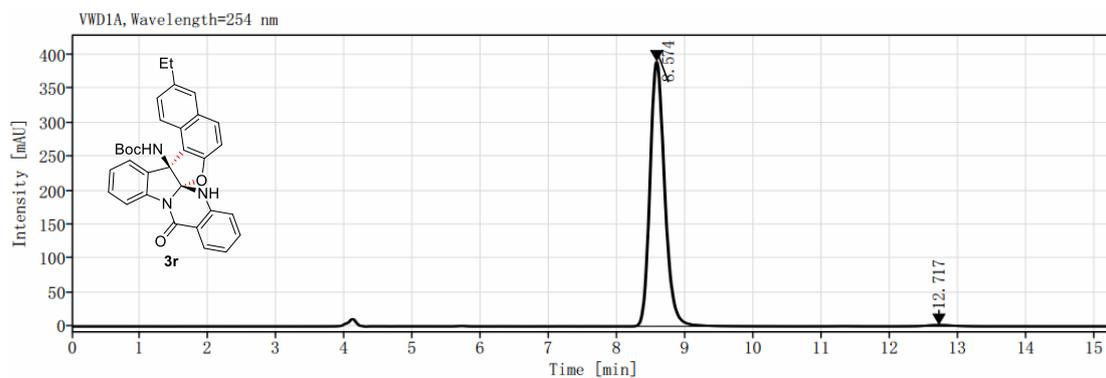
## HPLC spectra of 3r



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.583	1.96	24.51	64.63	379.270	49.61
12.709	1.65	13.41	35.37	385.158	50.39
				Total	100.00

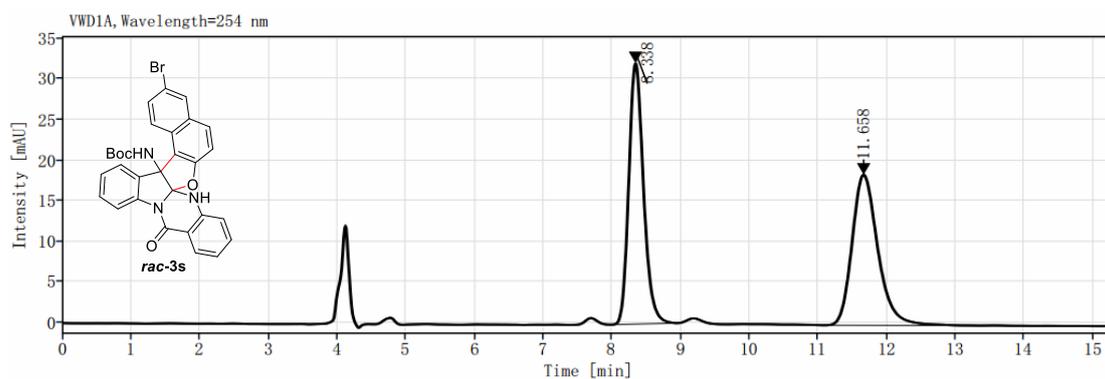


Signal:

VWD1A, Wavelength=254 nm

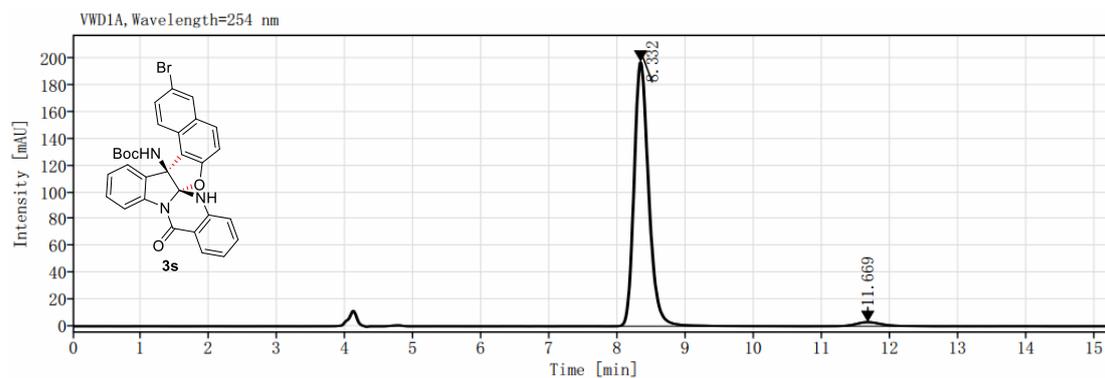
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.574	2.10	390.16	99.53	5869.822	99.12
12.717	1.44	1.84	0.47	52.275	0.88
				Total	100.00

### HPLC spectra of 3s



Signal: VWD1A, Wavelength=254 nm

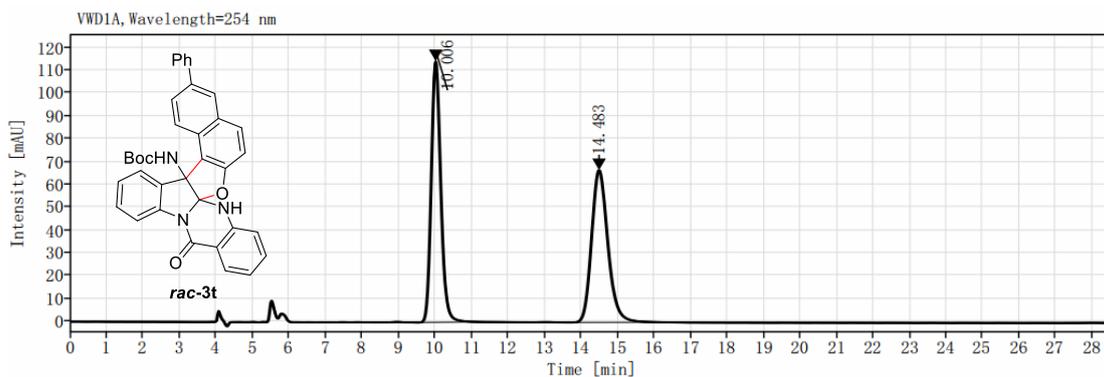
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.338	0.95	32.15	63.41	478.337	49.65
11.658	2.28	18.55	36.59	485.102	50.35
Total					100.00



Signal: VWD1A, Wavelength=254 nm

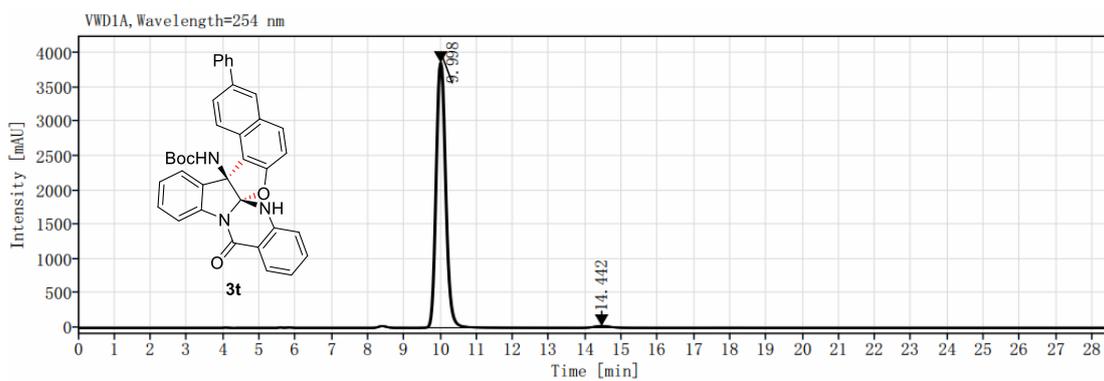
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.332	2.19	197.93	98.49	2955.499	97.33
11.669	1.67	3.04	1.51	81.077	2.67
Total					100.00

### HPLC spectra of 3t



Signal: VWD1A, Wavelength=254 nm

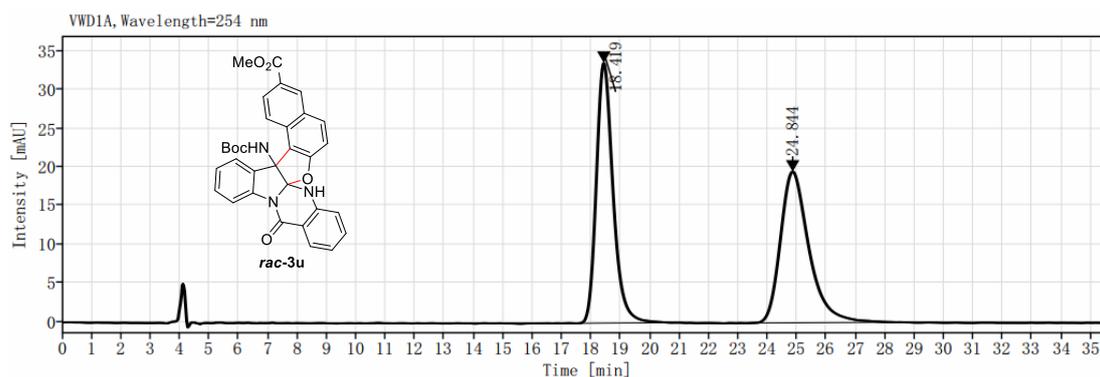
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
10.006	1.92	114.40	63.16	2080.408	50.10
14.483	2.65	66.71	36.84	2072.333	49.90
				Total	100.00



Signal: VWD1A, Wavelength=254 nm

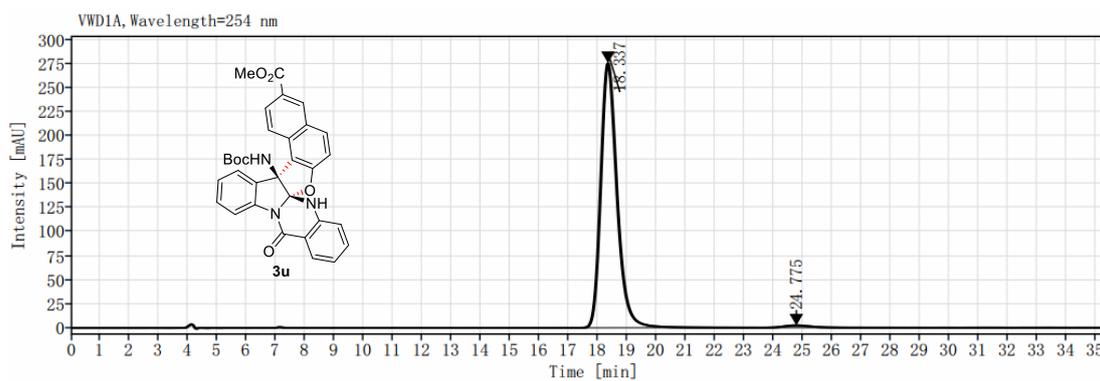
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.998	2.31	3854.47	99.36	70680.182	99.06
14.442	1.00	24.78	0.64	673.022	0.94
				Total	100.00

## HPLC spectra of 3u



Signal: VWD1A, Wavelength=254 nm

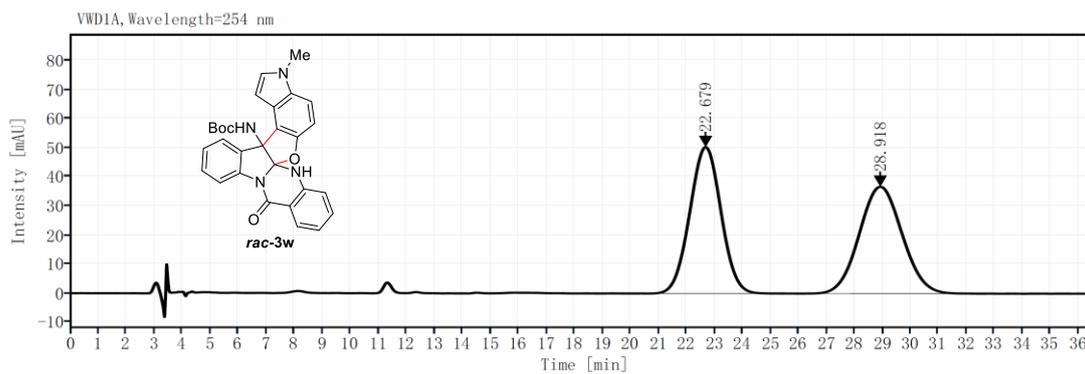
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
18.419	3.23	33.60	63.24	1327.682	50.16
24.844	5.10	19.53	36.76	1319.102	49.84
				Total	100.00



Signal: VWD1A, Wavelength=254 nm

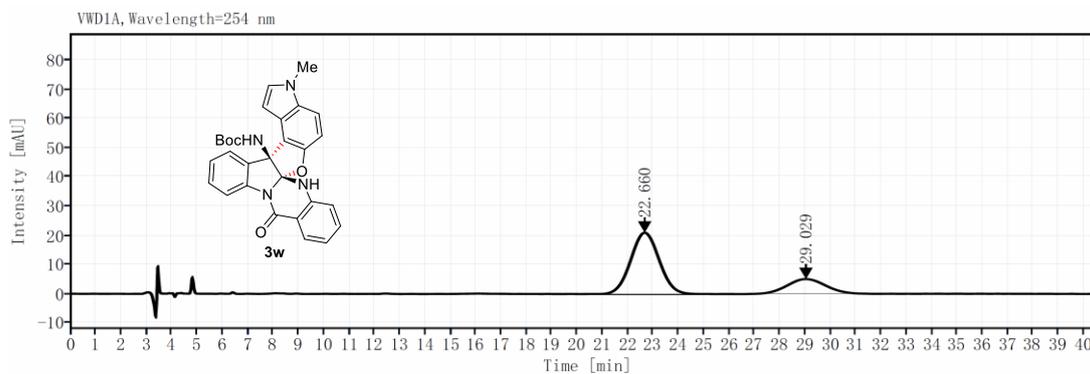
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
18.337	4.78	276.38	99.14	10678.175	98.57
24.775	3.01	2.39	0.86	155.390	1.43
				Total	100.00

## HPLC spectra of 3w



Signal: VWD1A, Wavelength=254 nm

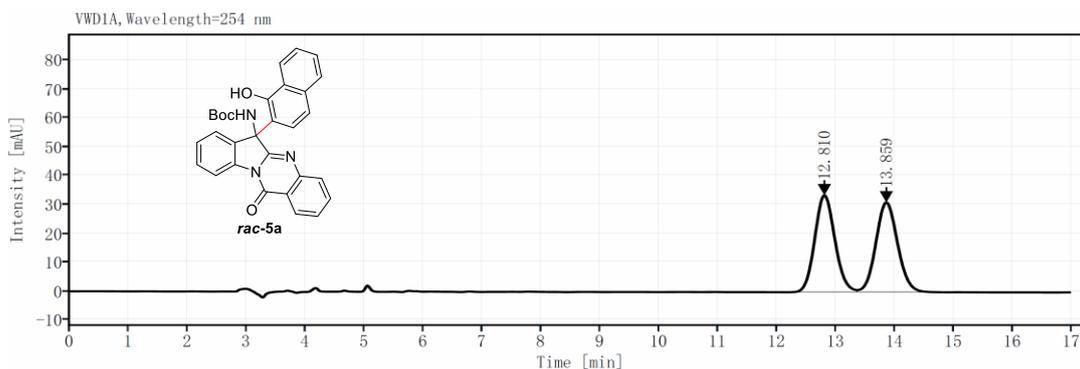
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
22.679	5.71	50.40	57.80	3915.375	49.95
28.918	8.69	36.79	42.20	3923.964	50.05
Total					100.00



Signal: VWD1A, Wavelength=254 nm

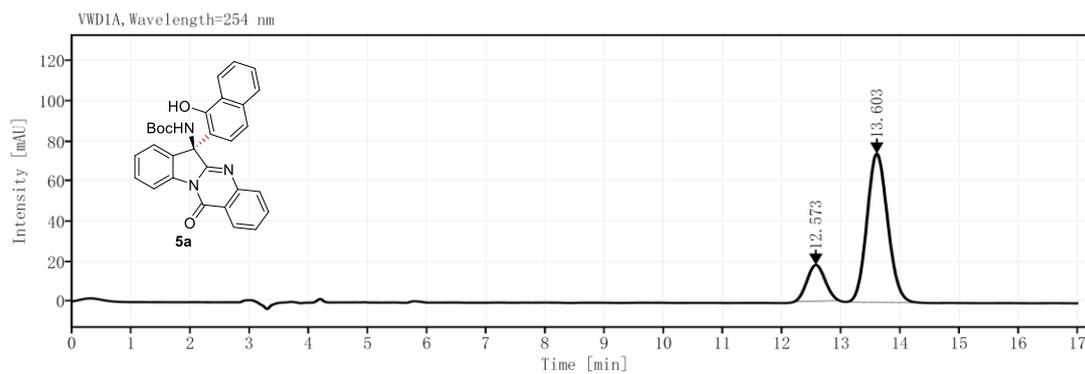
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
22.660	5.83	21.16	81.06	1689.366	76.77
29.029	3.90	4.94	18.94	511.100	23.23
Total					100.00

## HPLC spectra of 5a



Signal: VWD1A, Wavelength=254 nm

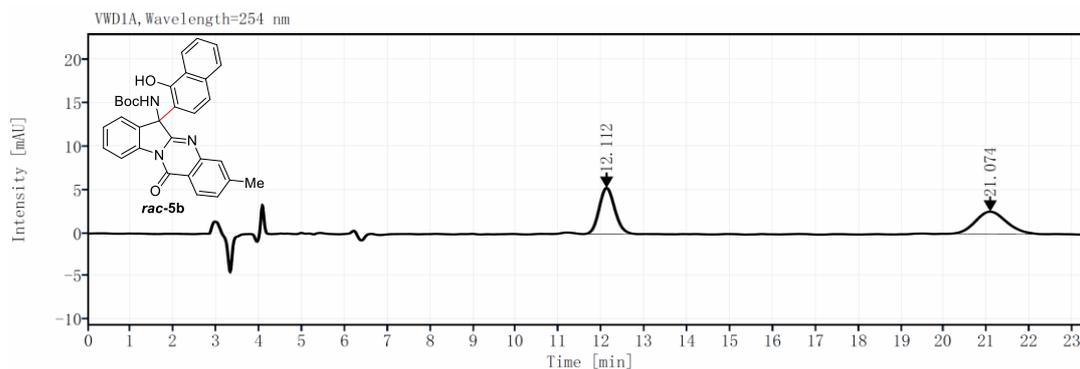
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
12.810	1.19	33.59	51.91	798.553	50.05
13.859	1.42	31.12	48.09	797.076	49.95
Total					100.00



Signal: VWD1A, Wavelength=254 nm

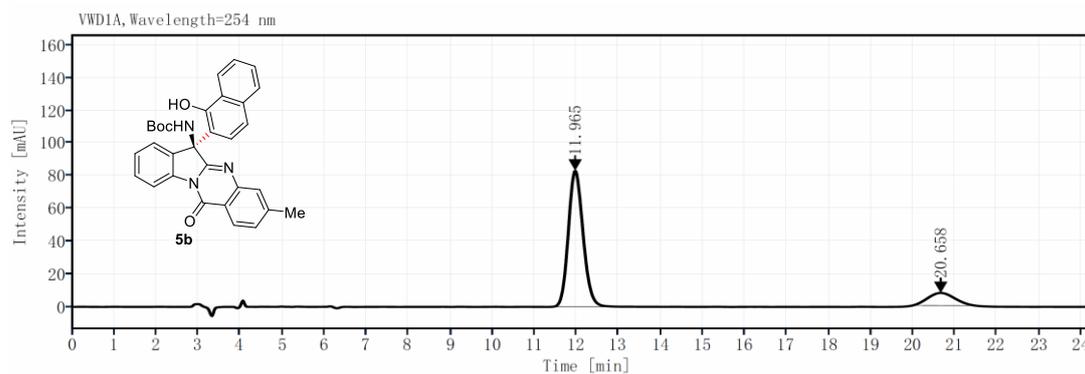
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
12.573	0.77	18.07	19.61	384.224	17.54
13.603	1.44	74.08	80.39	1806.879	82.46
Total					100.00

## HPLC spectra of 5b



Signal: VWD1A, Wavelength=254 nm

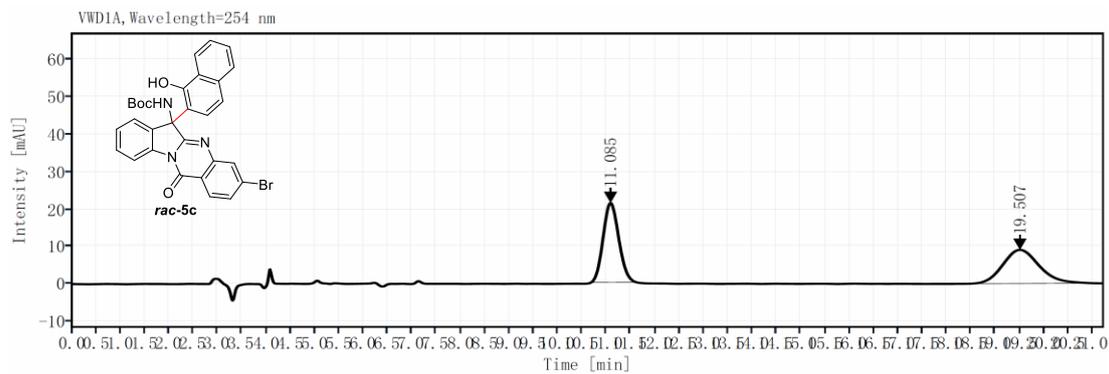
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
12.112	1.38	5.34	67.40	135.181	50.72
21.074	2.34	2.58	32.60	131.341	49.28
				Total	100.00



Signal: VWD1A, Wavelength=254 nm

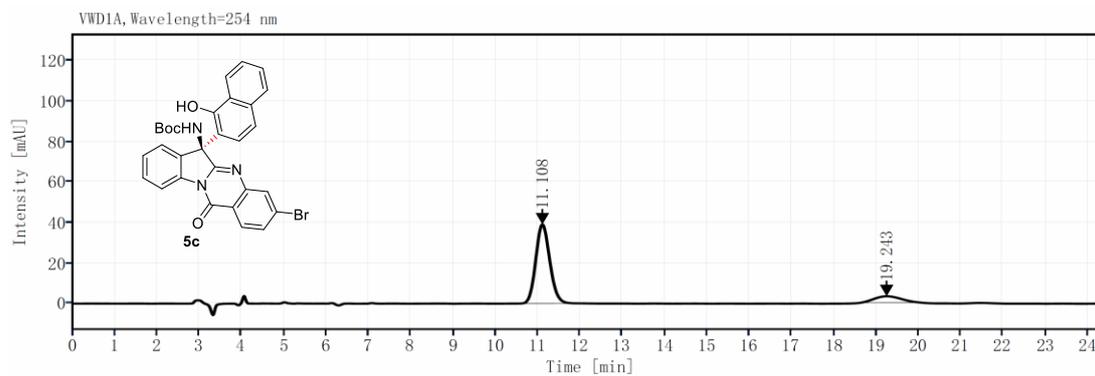
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
11.965	2.98	83.24	91.64	2028.346	85.84
20.658	1.47	7.59	8.36	334.613	14.16
				Total	100.00

## HPLC spectra of 5c



Signal: VWD1A, Wavelength=254 nm

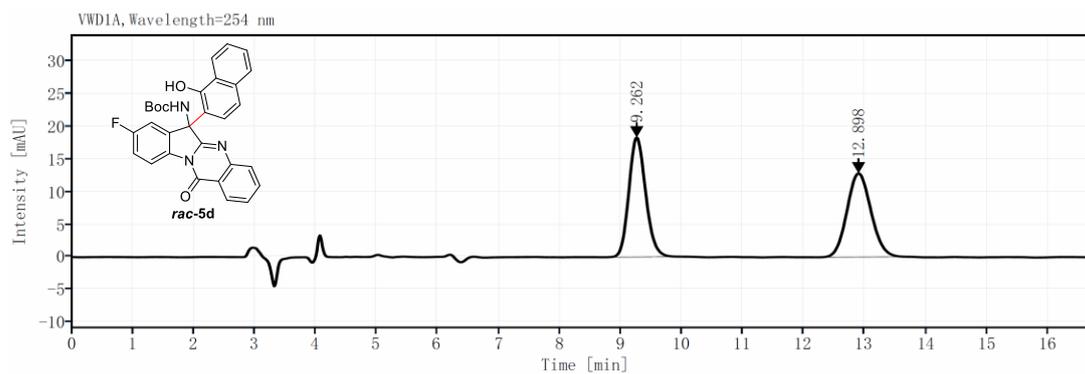
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
11.085	0.93	21.21	70.20	474.952	50.20
19.507	2.73	9.00	29.80	471.131	49.80
				Total	100.00



Signal: VWD1A, Wavelength=254 nm

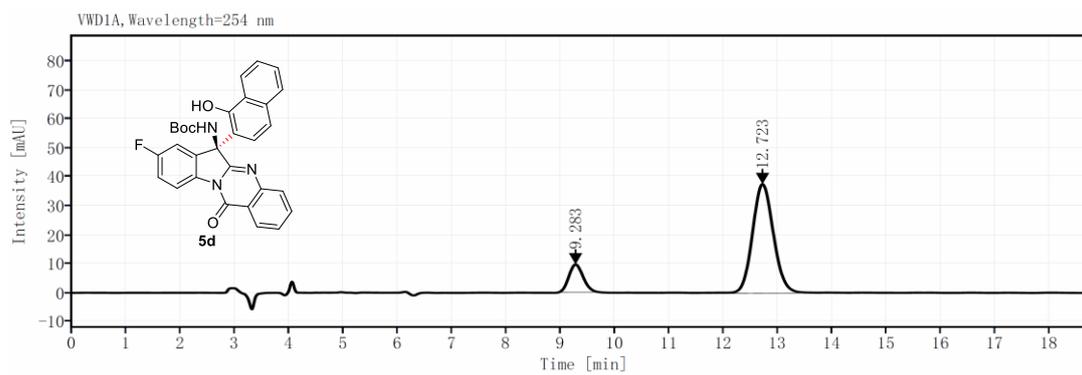
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
11.108	2.21	39.16	92.42	909.574	86.40
19.243	1.44	3.21	7.58	143.168	13.60
				Total	100.00

## HPLC spectra of 5d



Signal: VWD1A, Wavelength=254 nm

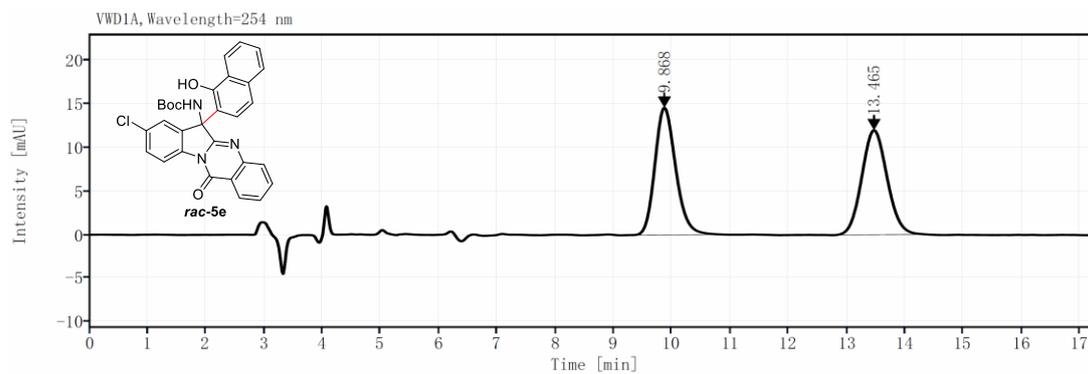
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.262	1.31	18.33	58.81	351.849	50.06
12.898	1.58	12.83	41.19	351.058	49.94
				Total	100.00



Signal: VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.283	0.72	9.57	20.21	173.306	14.49
12.723	2.44	37.76	79.79	1022.686	85.51
				Total	100.00

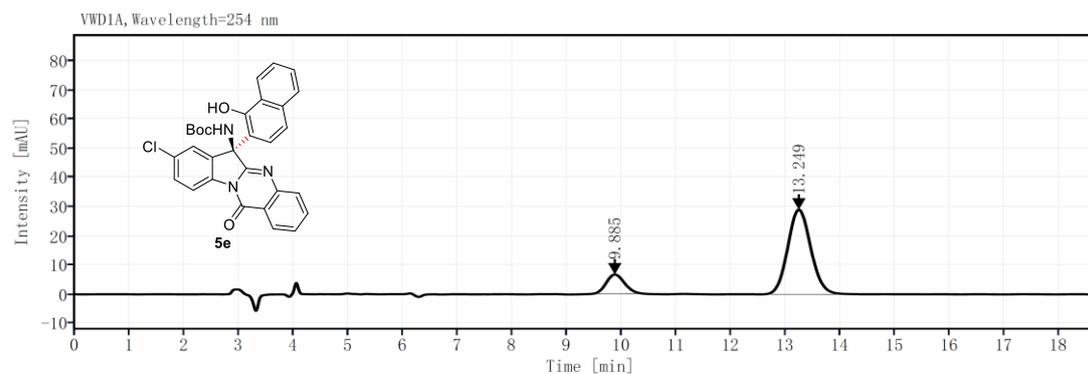
## HPLC spectra of 5e



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.868	1.68	14.61	54.91	363.933	50.08
13.465	1.74	12.00	45.09	362.706	49.92
				Total	100.00

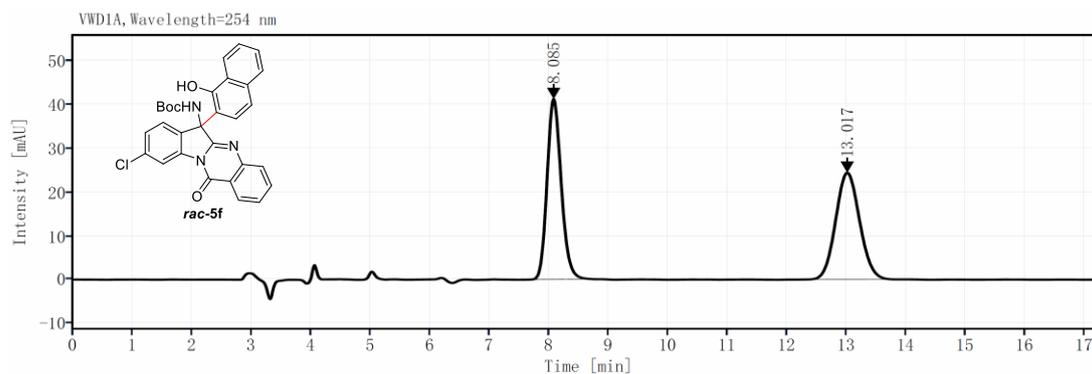


Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.885	0.90	6.55	18.40	150.639	15.01
13.249	2.08	29.06	81.60	853.164	84.99
				Total	100.00

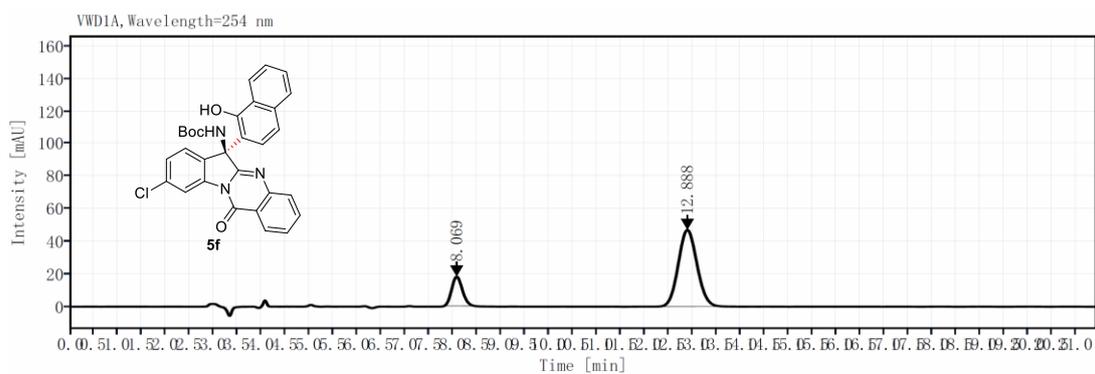
## HPLC spectra of 5f



Signal:

VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.085	1.22	41.26	62.81	683.193	49.95
13.017	1.77	24.43	37.19	684.593	50.05
Total					100.00

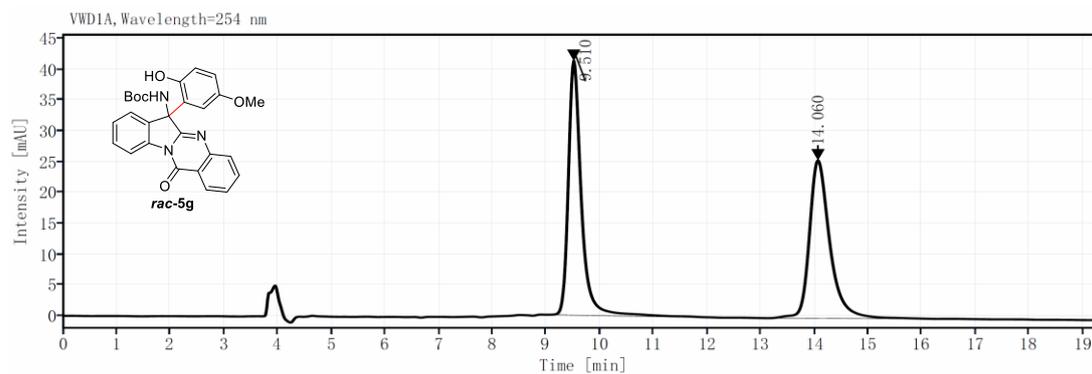


Signal:

VWD1A, Wavelength=254 nm

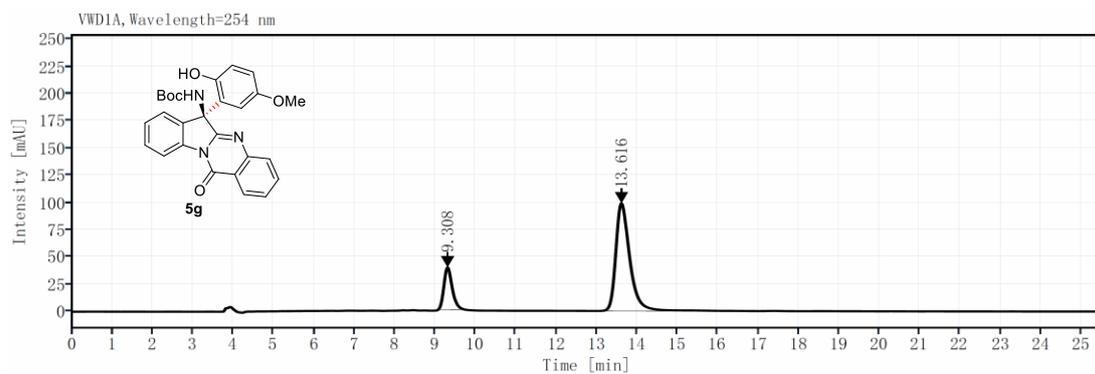
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
8.069	0.62	17.96	27.61	277.282	17.78
12.888	2.03	47.09	72.39	1282.423	82.22
Total					100.00

## HPLC spectra of **5g**



Signal: VWD1A, Wavelength=254 nm

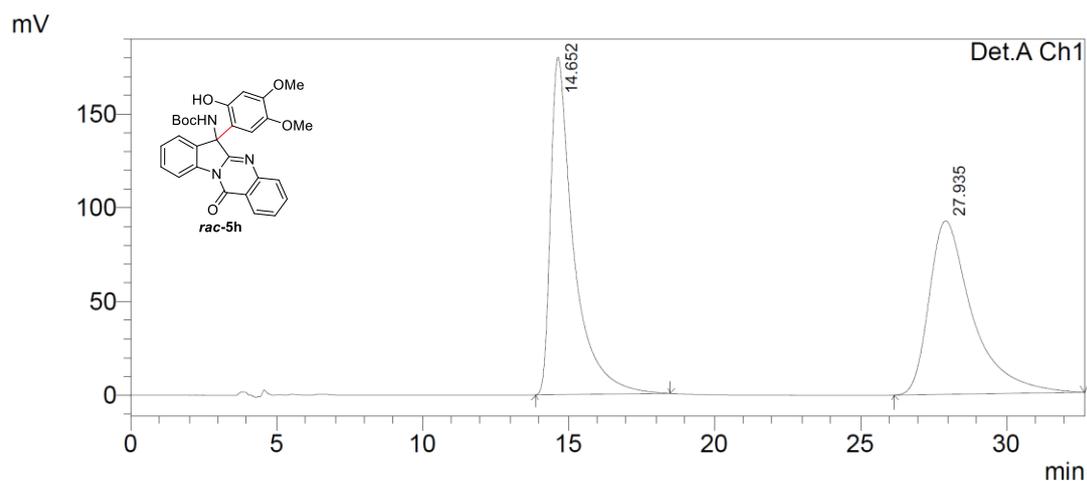
Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.510	3.25	41.35	61.68	702.223	50.67
14.060	3.18	25.69	38.32	683.727	49.33
				Total	100.00



Signal: VWD1A, Wavelength=254 nm

Retention Time [min]	Peak Width [min]	Peak Height [mAU]	Peak Height %	Peak Area [mAU*s]	Peak Area %
9.308	0.64	38.65	28.11	548.806	18.60
13.616	4.04	98.87	71.89	2401.315	81.40
				Total	100.00

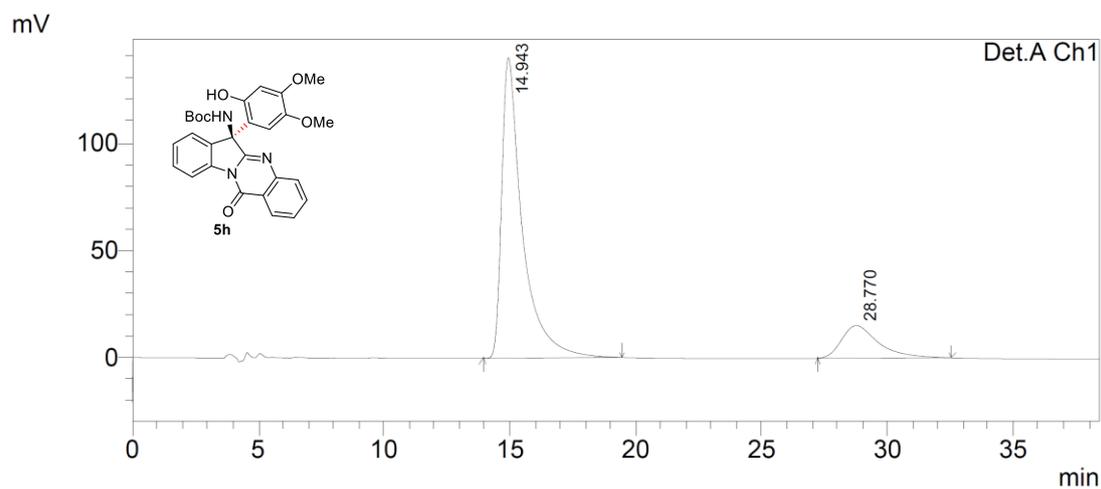
### HPLC spectra of 5h



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %
1	14.652	9871392	180039	50.793
2	27.935	9563053	92566	49.207
Total		19434446		100.000



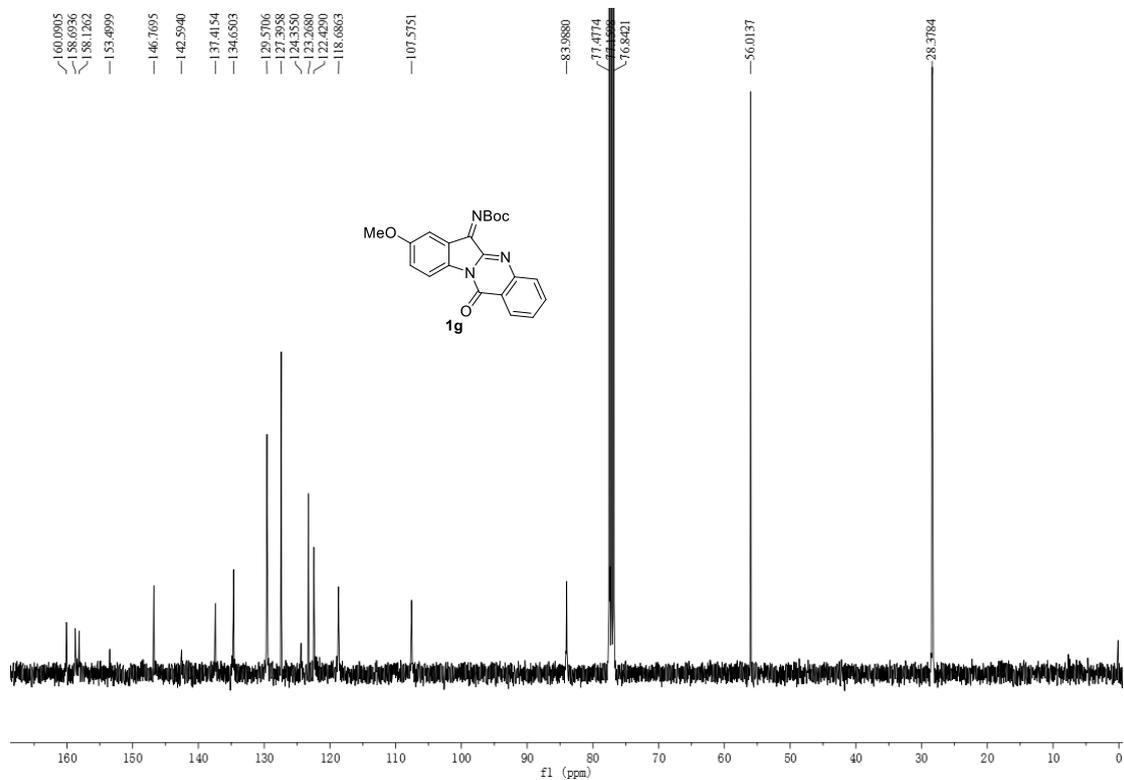
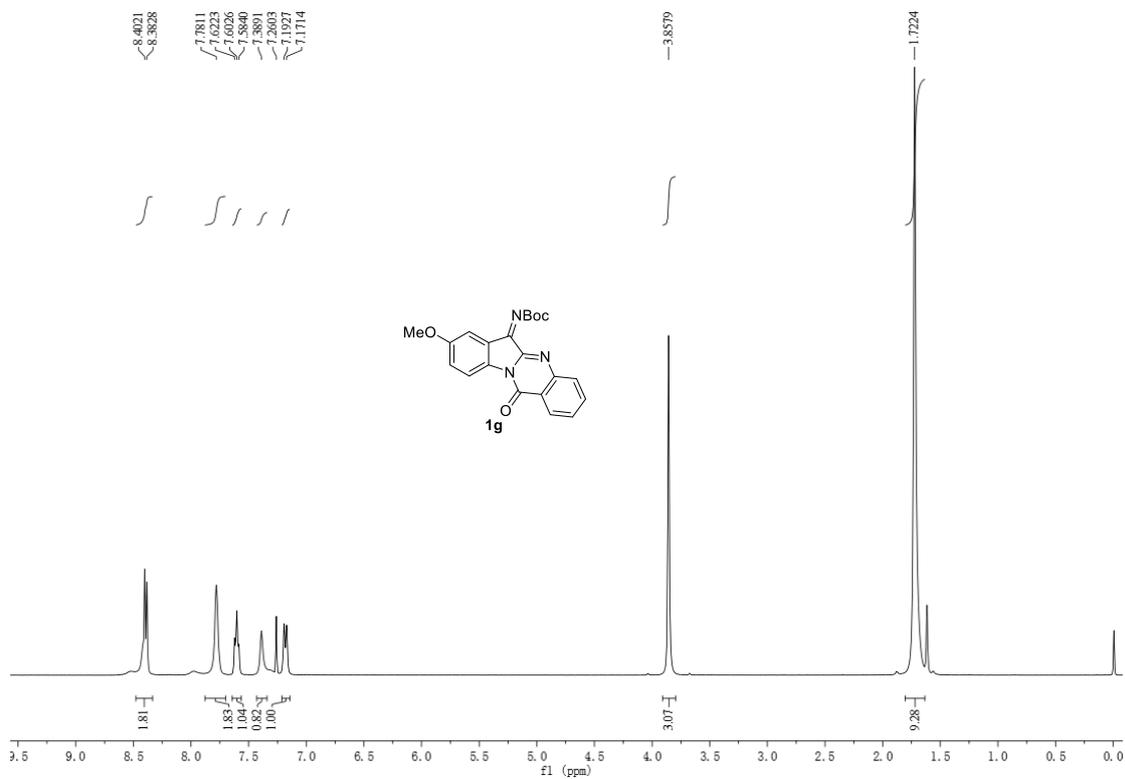
PeakTable

Detector A Ch1 254nm

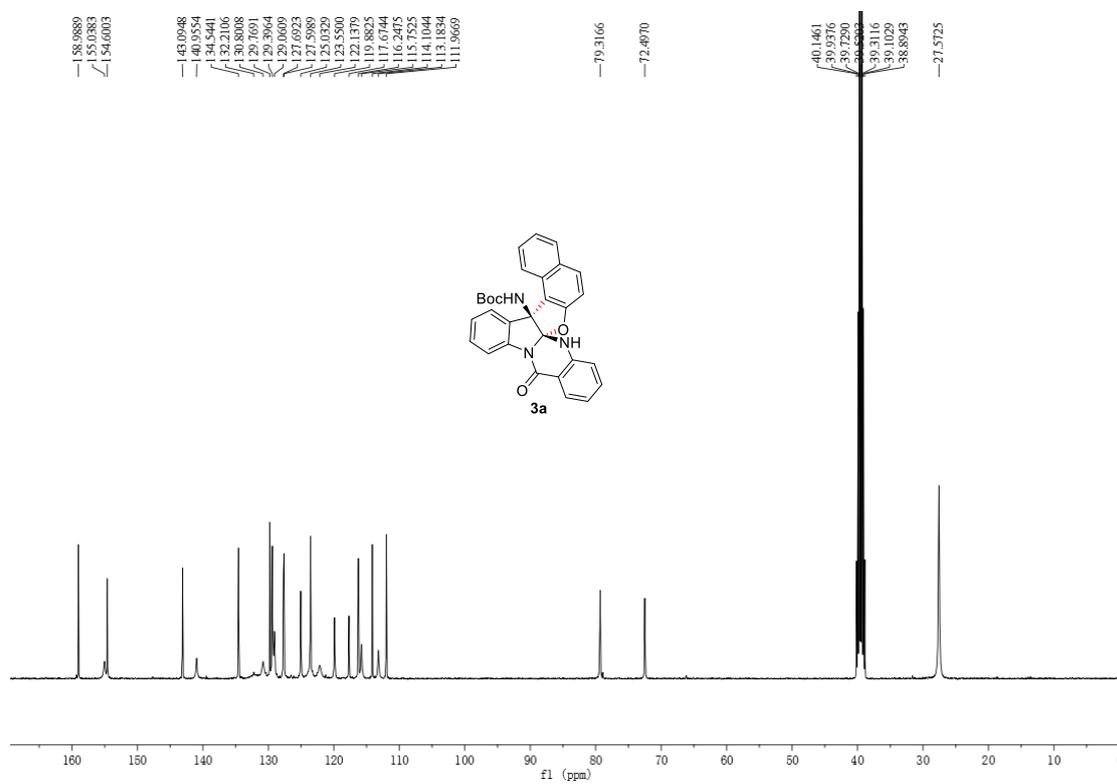
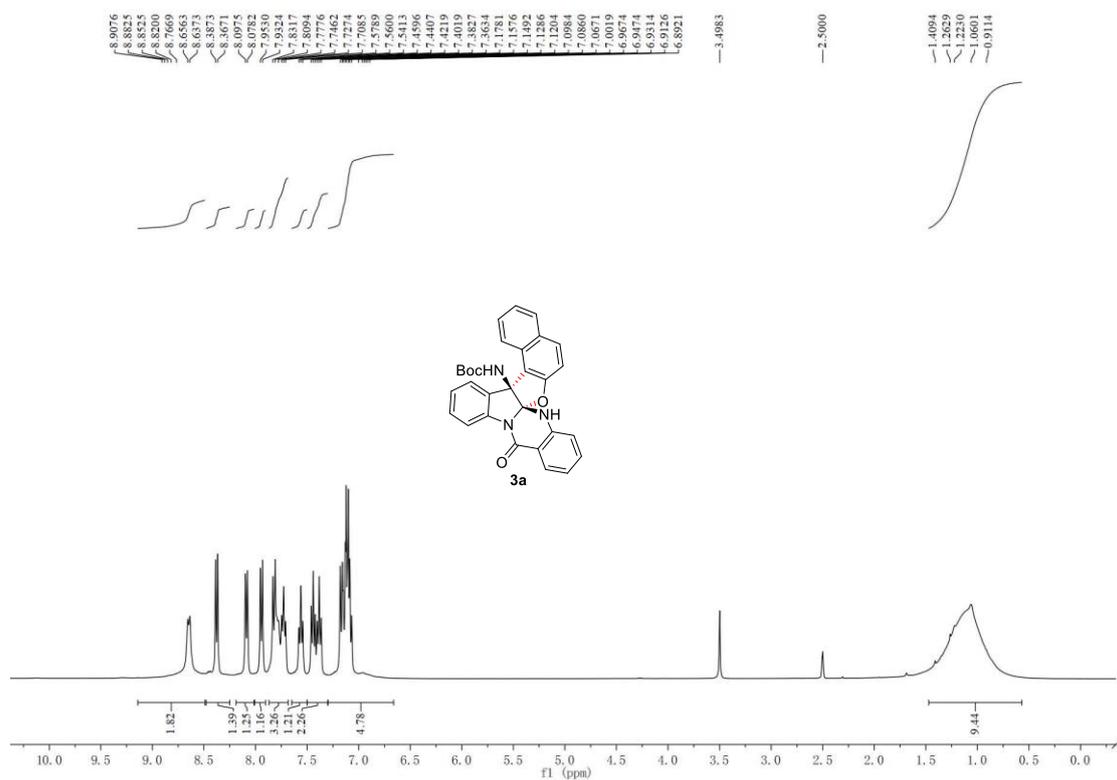
Peak#	Ret. Time	Area	Height	Area %
1	14.943	7970303	139895	83.686
2	28.770	1553704	15205	16.314
Total		9524008		100.000

## 12. $^1\text{H}$ and $^{13}\text{C}$ NMR spectra of compounds 1, 3 and 5

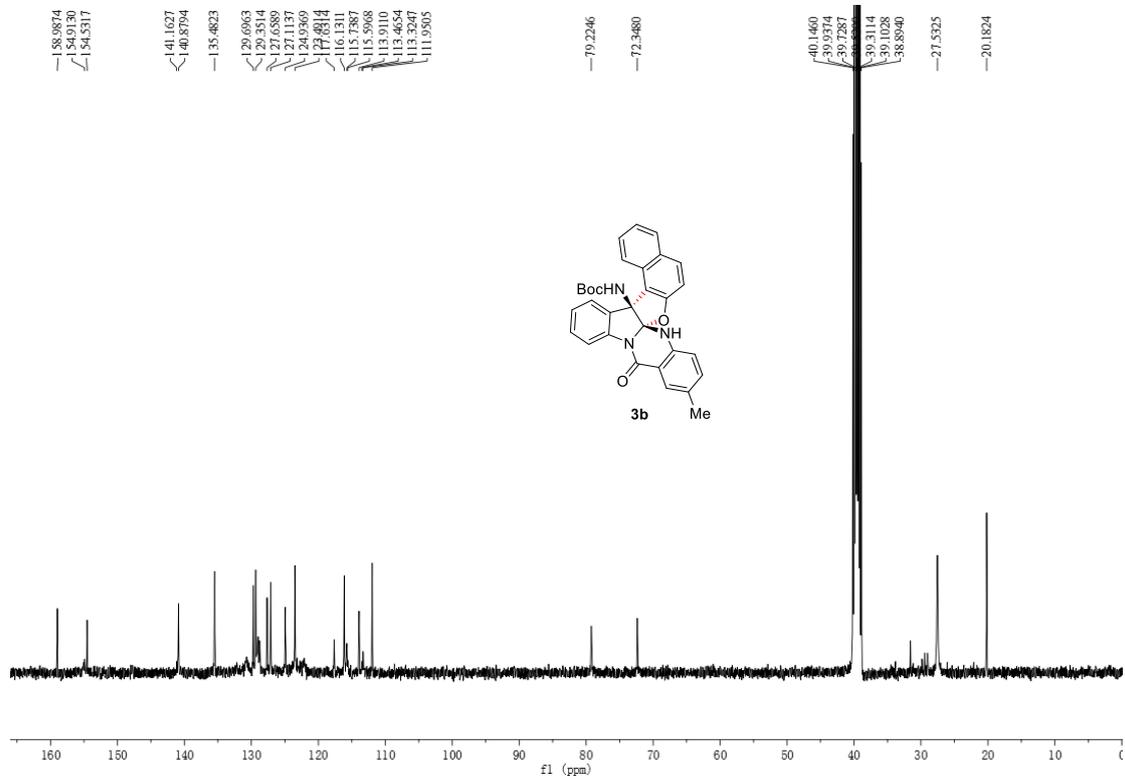
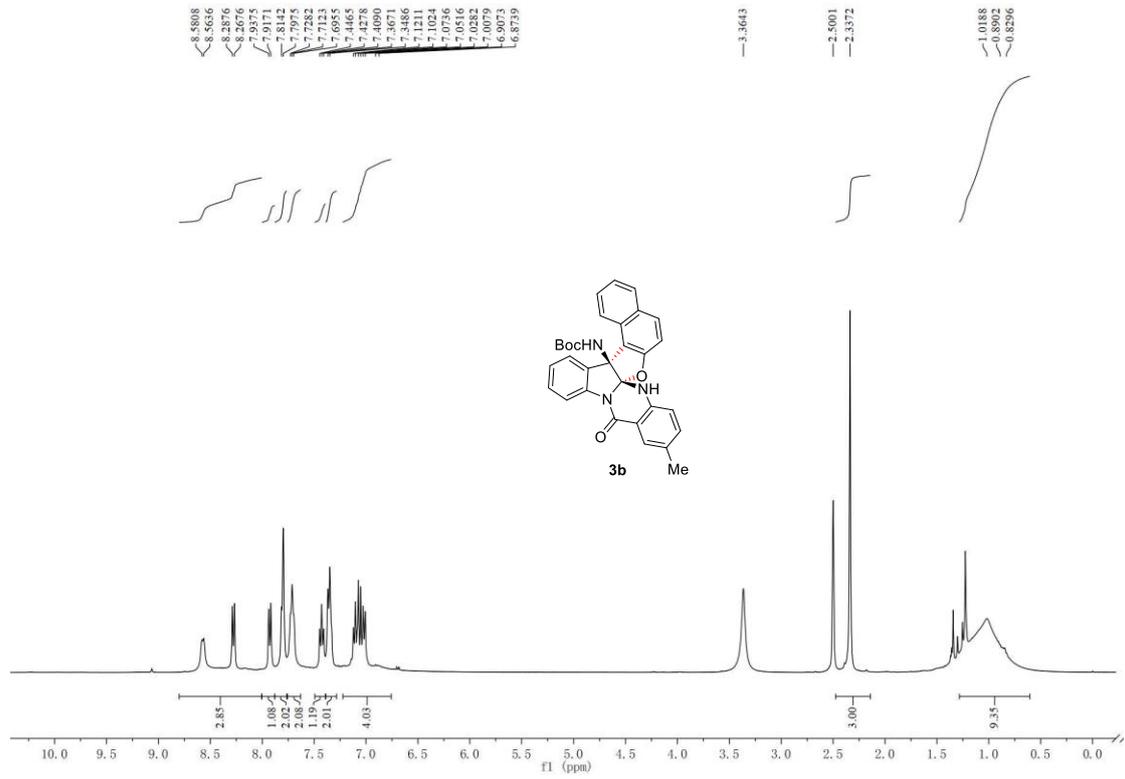
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **1g**



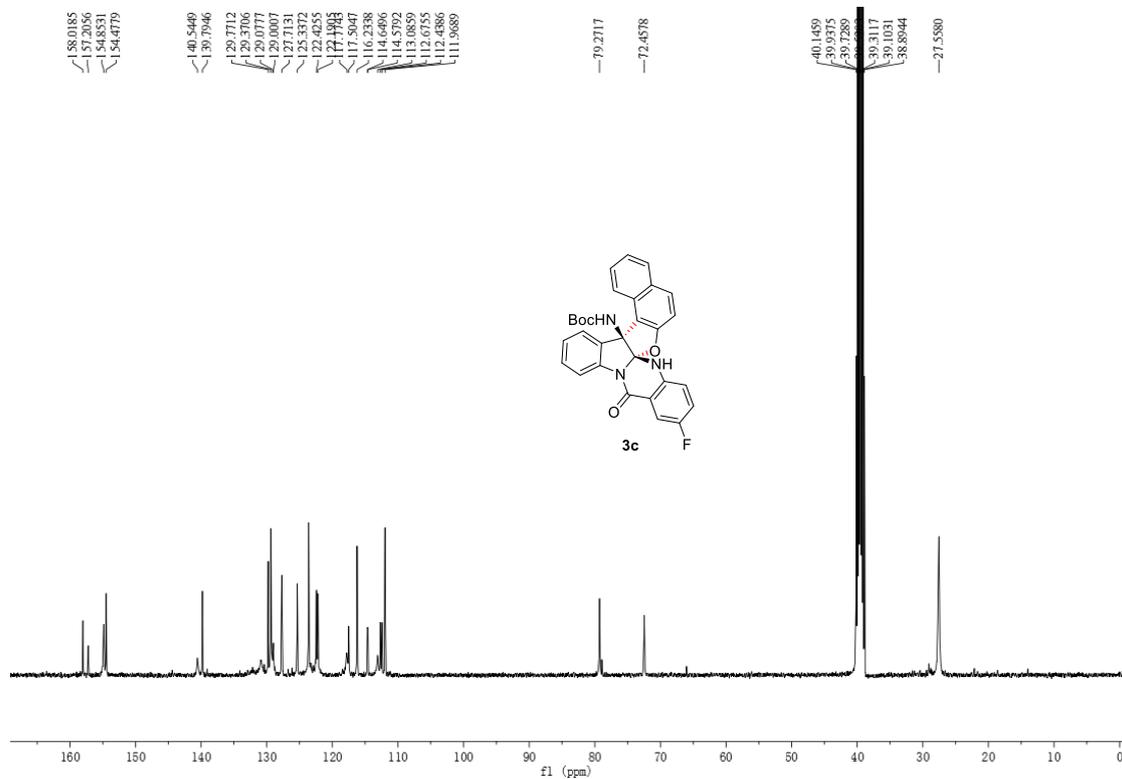
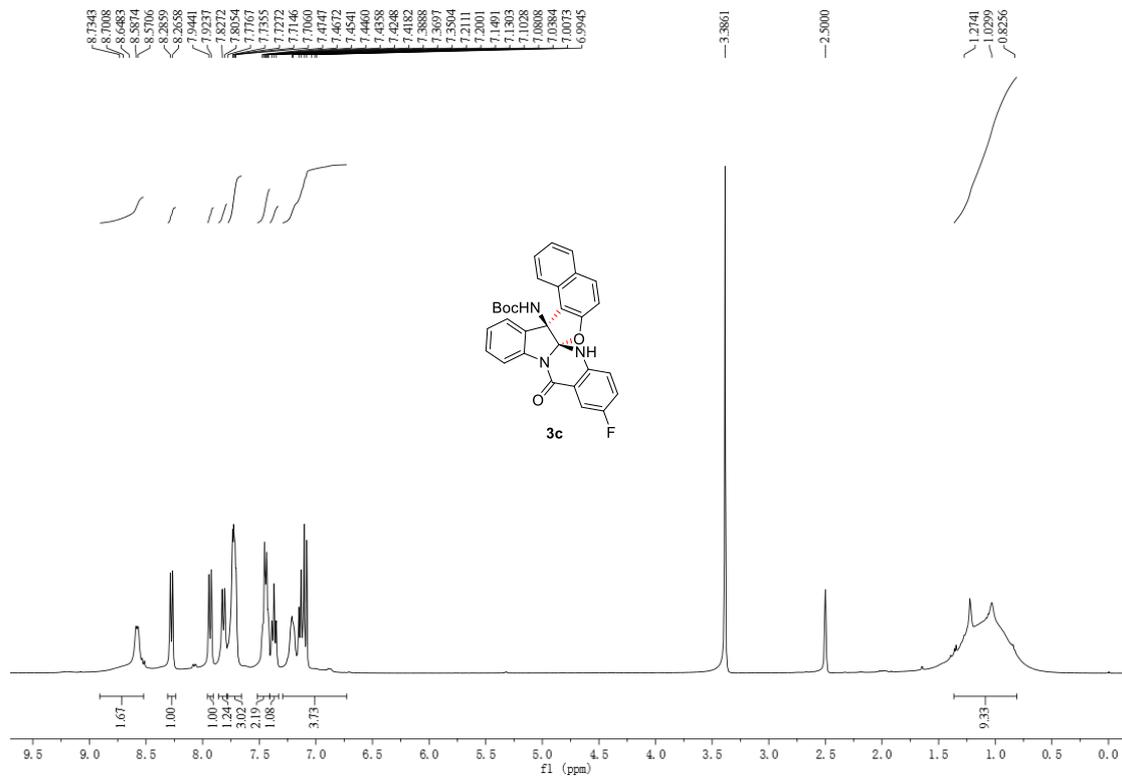
# $^1\text{H}$ NMR and $^{13}\text{C}$ NMR of **3a**



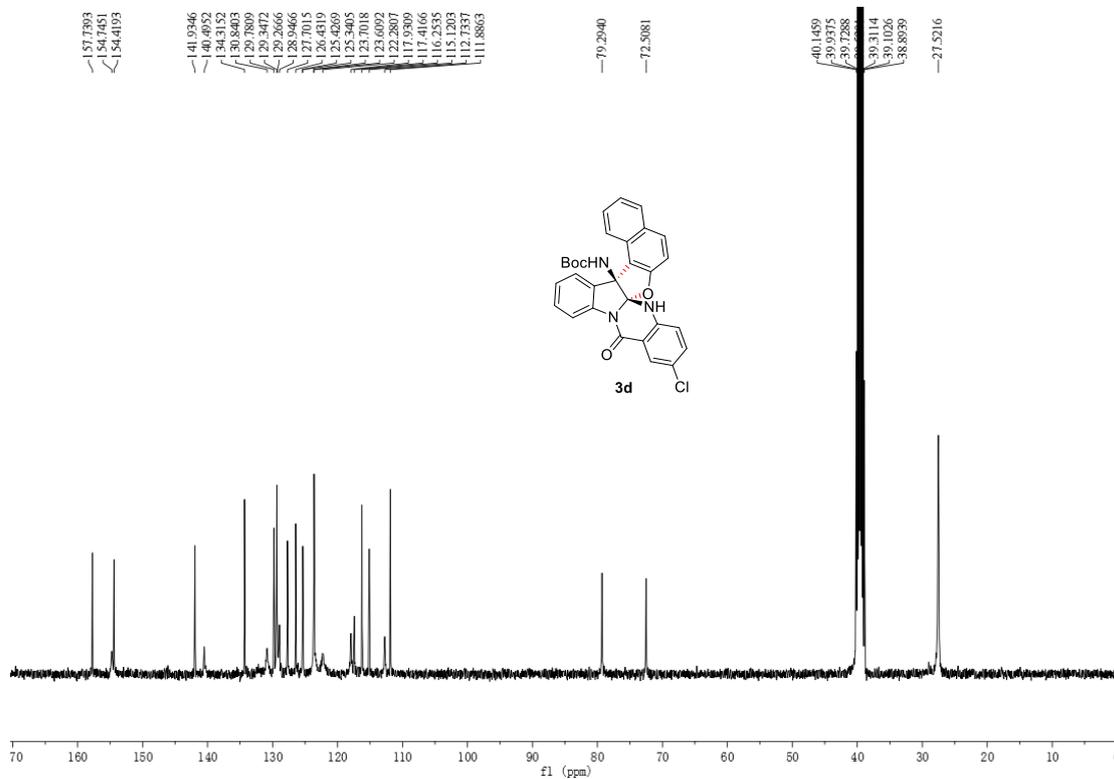
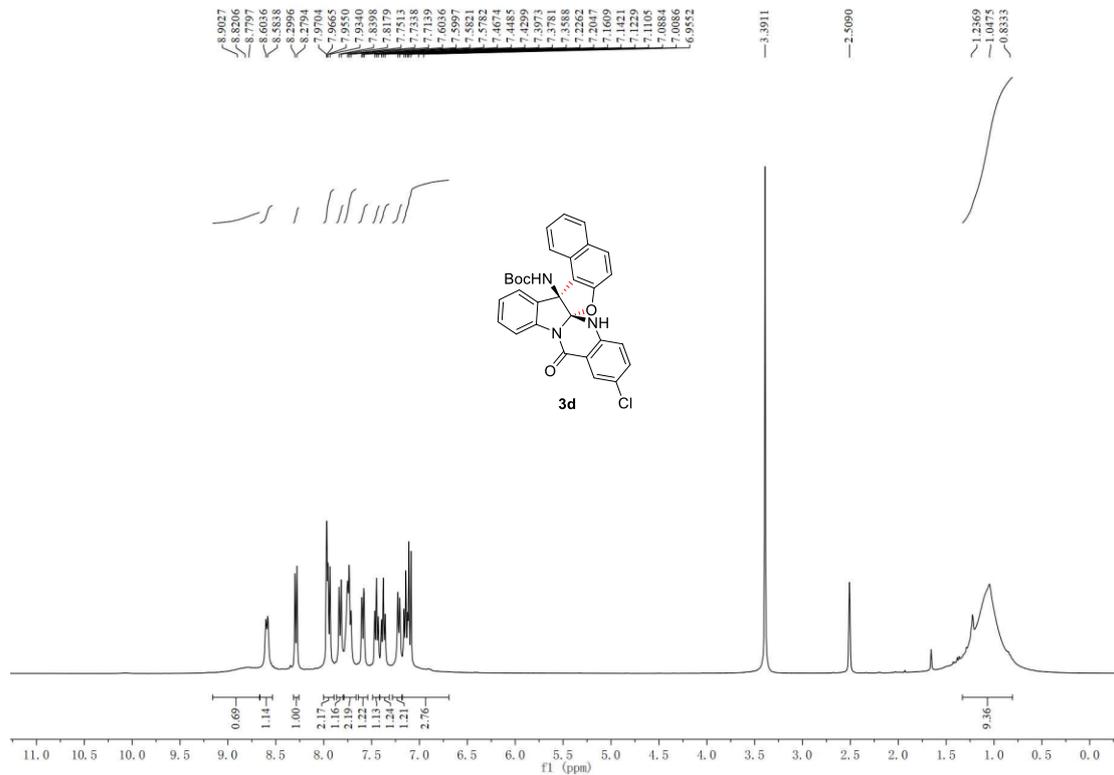
<sup>1</sup>H NMR and <sup>13</sup>C NMR of **3b**



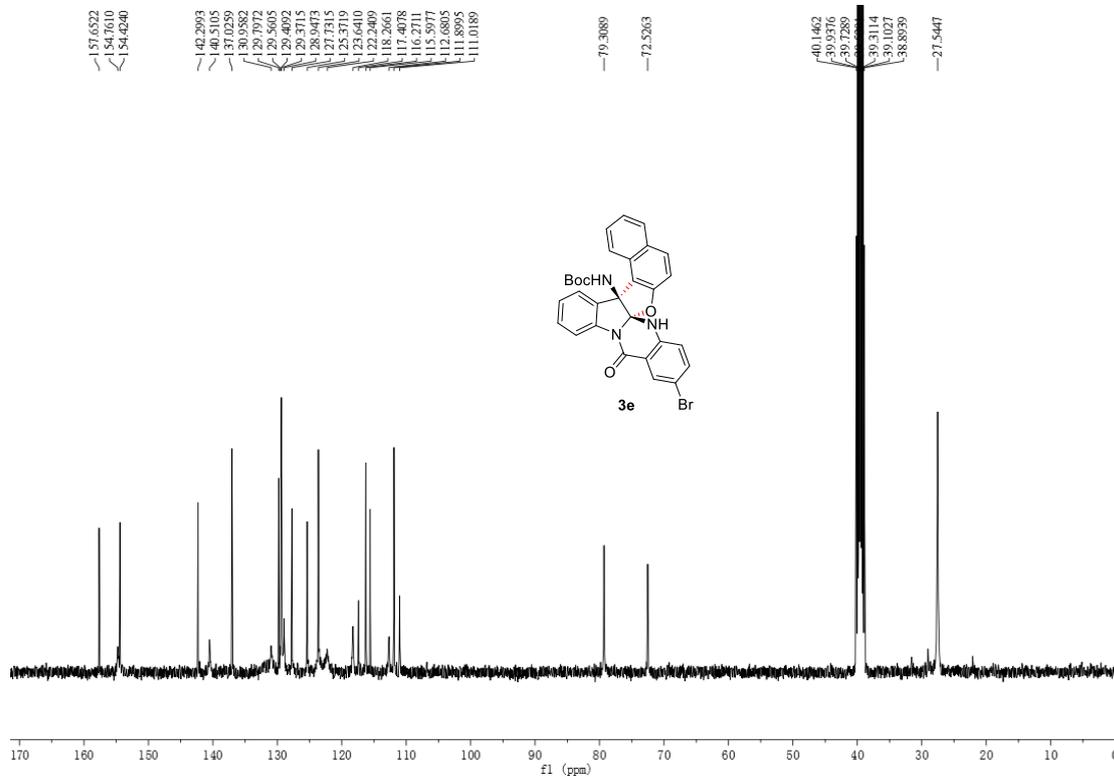
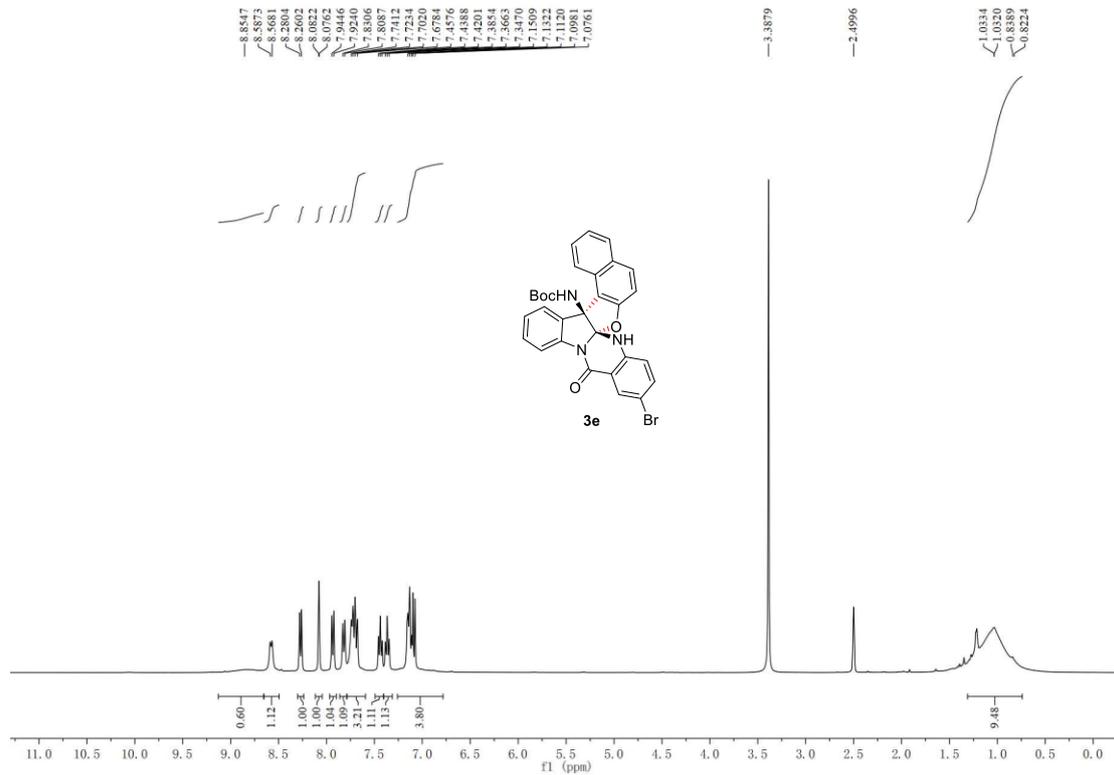
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **3c**



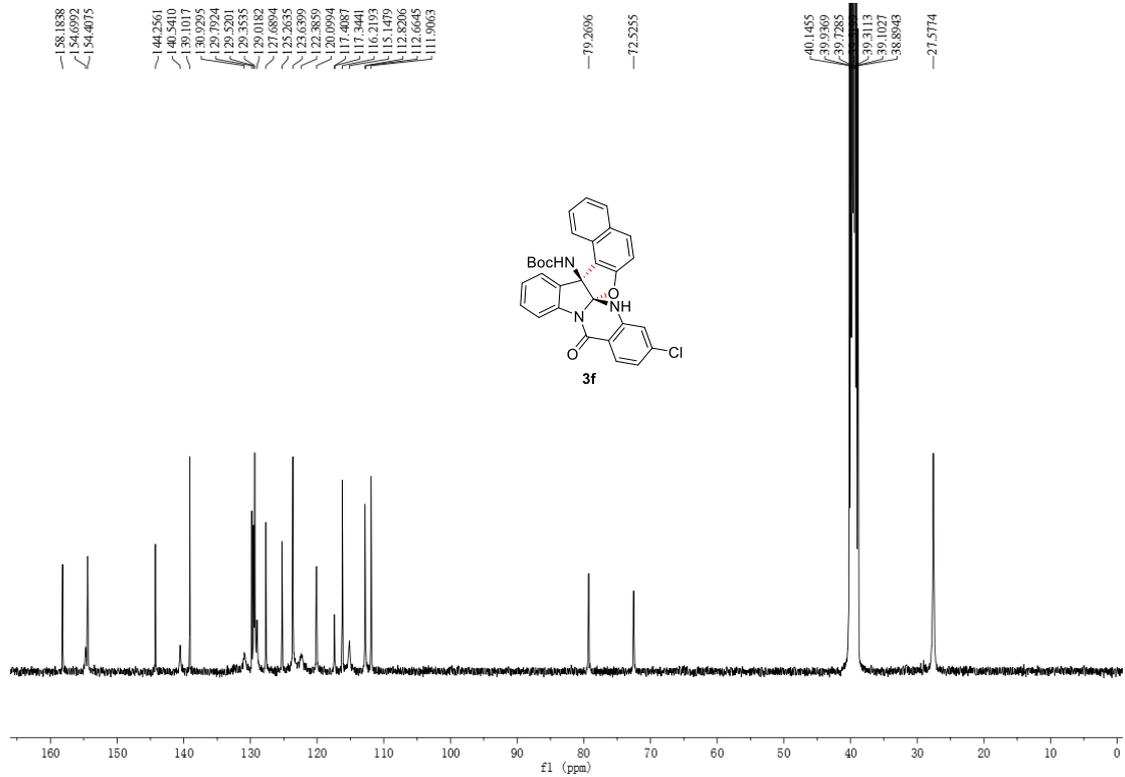
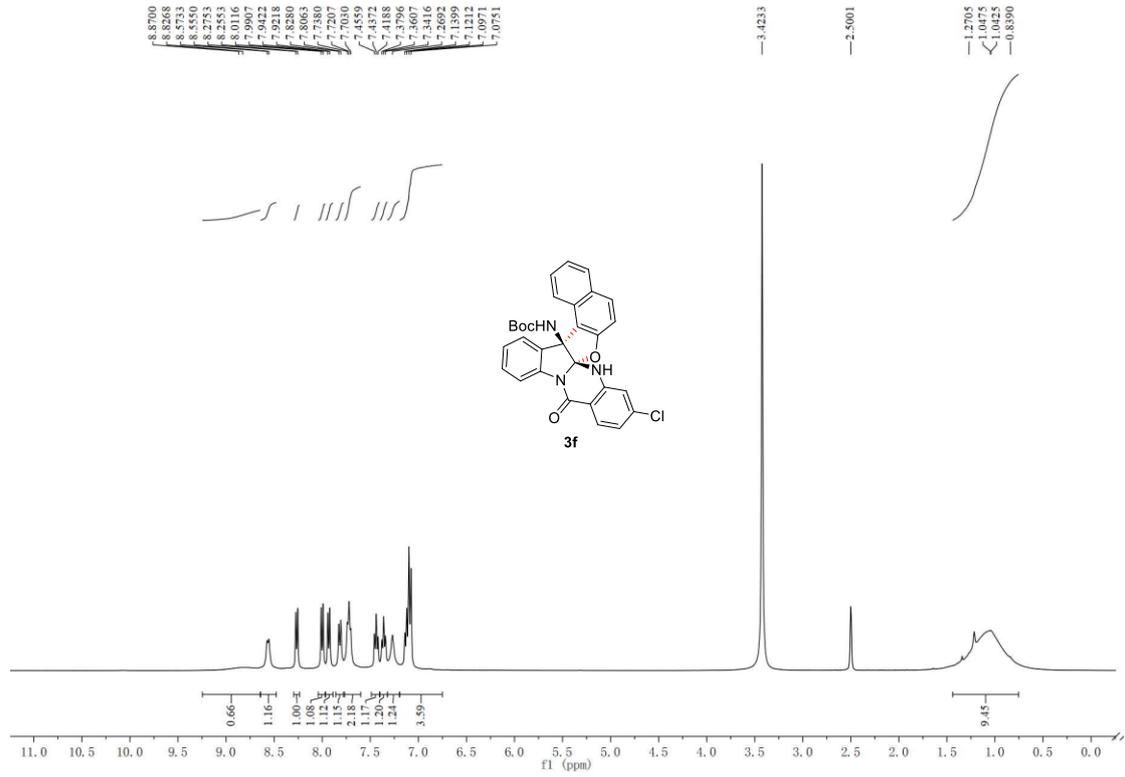
# $^1\text{H}$ NMR and $^{13}\text{C}$ NMR of **3d**



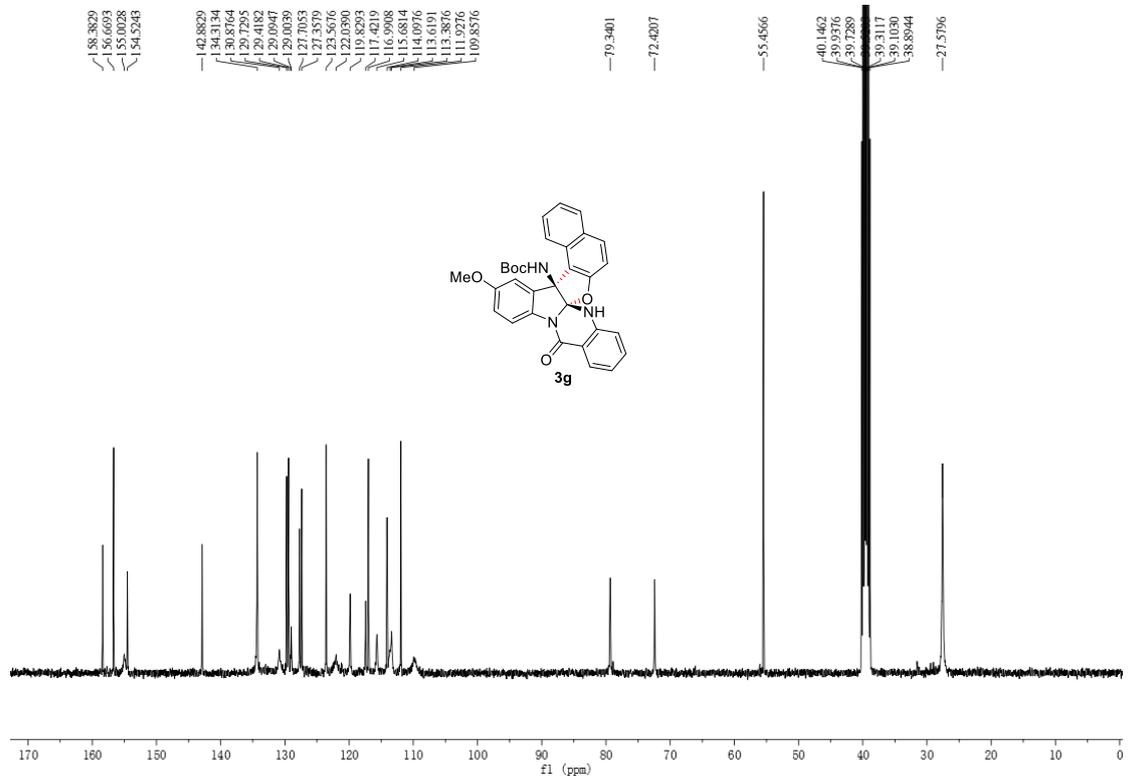
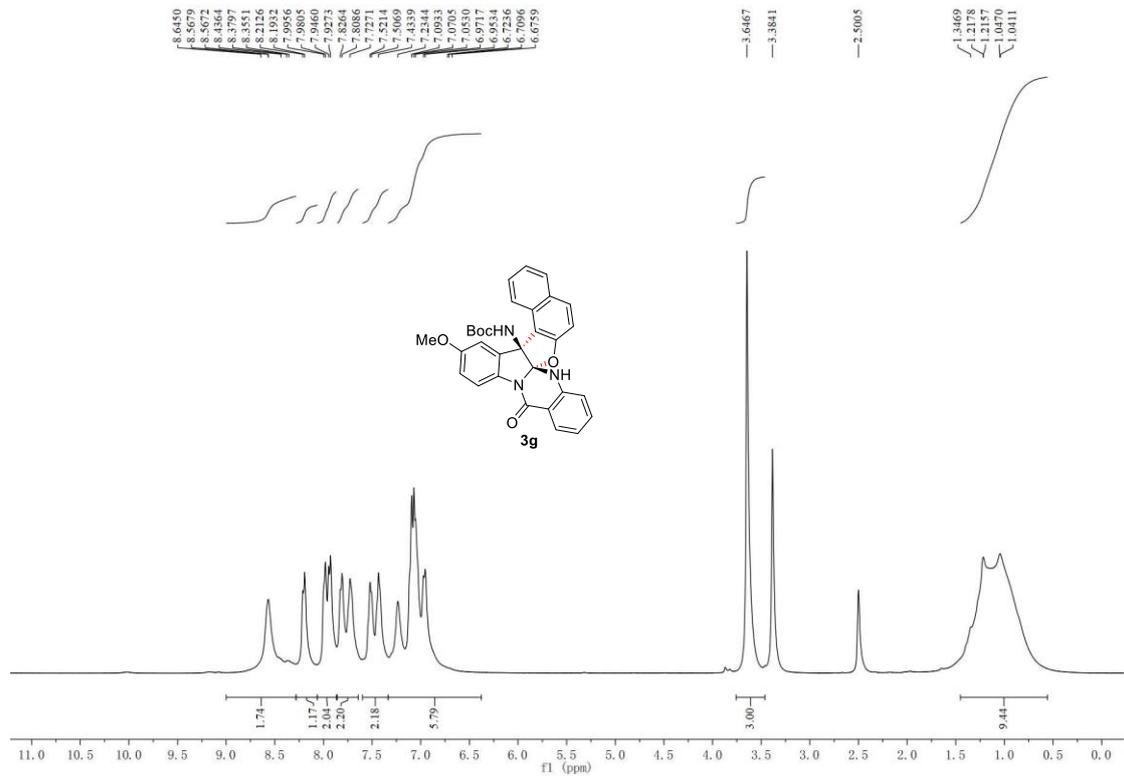
# <sup>1</sup>H NMR and <sup>13</sup>C NMR of 3e



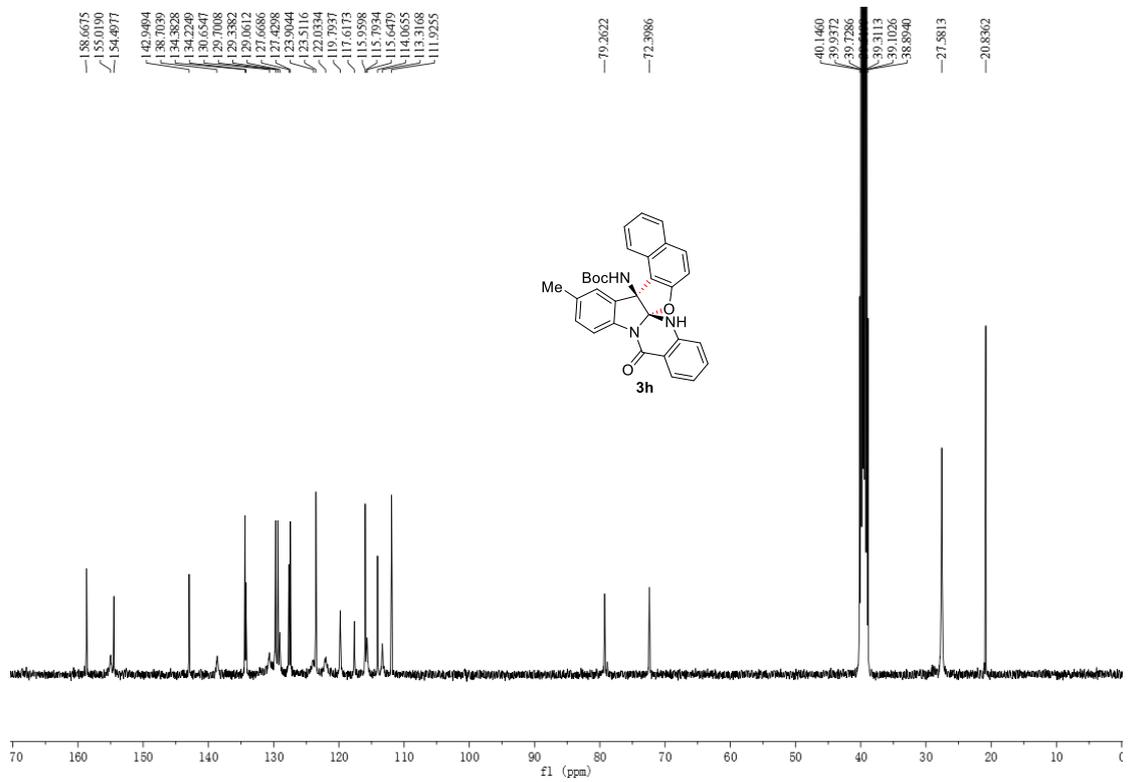
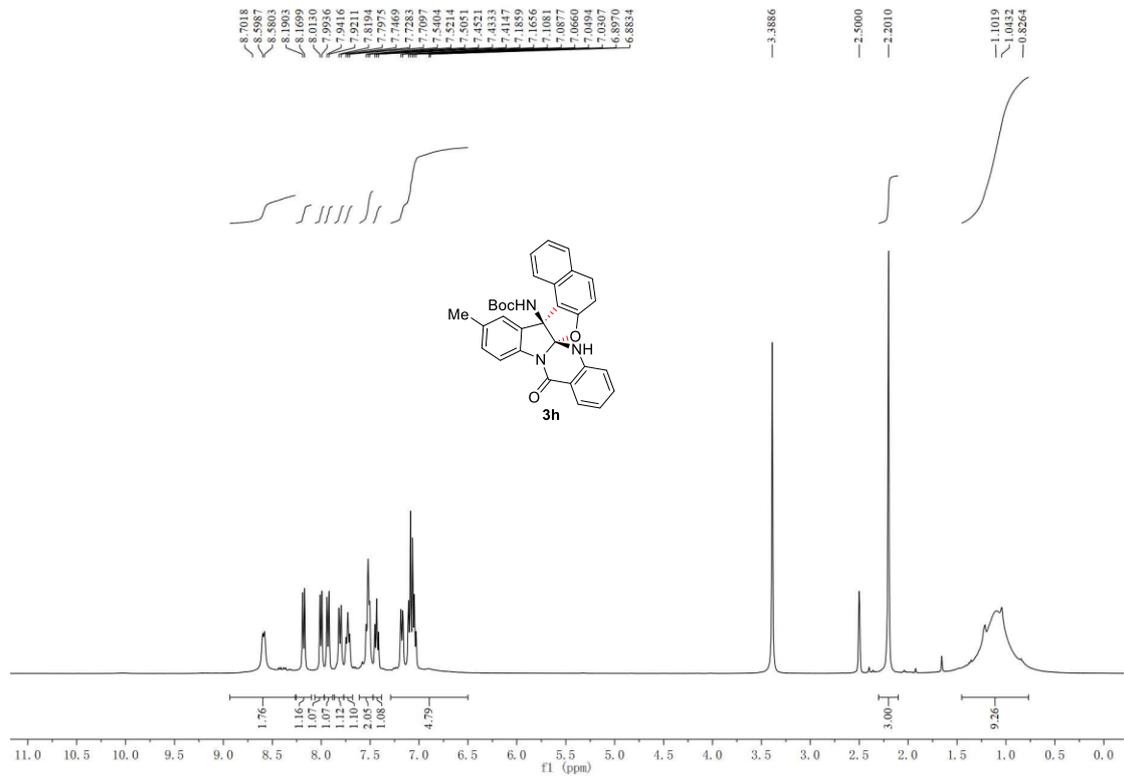
<sup>1</sup>H NMR and <sup>13</sup>C NMR of **3f**



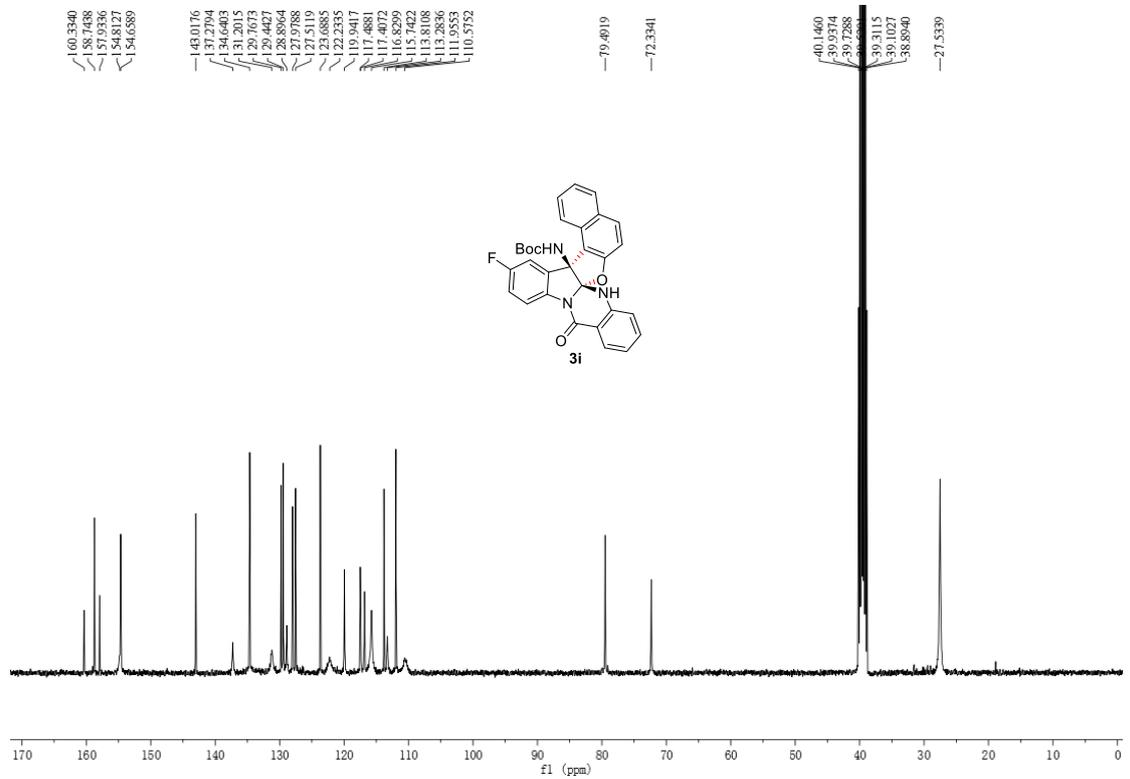
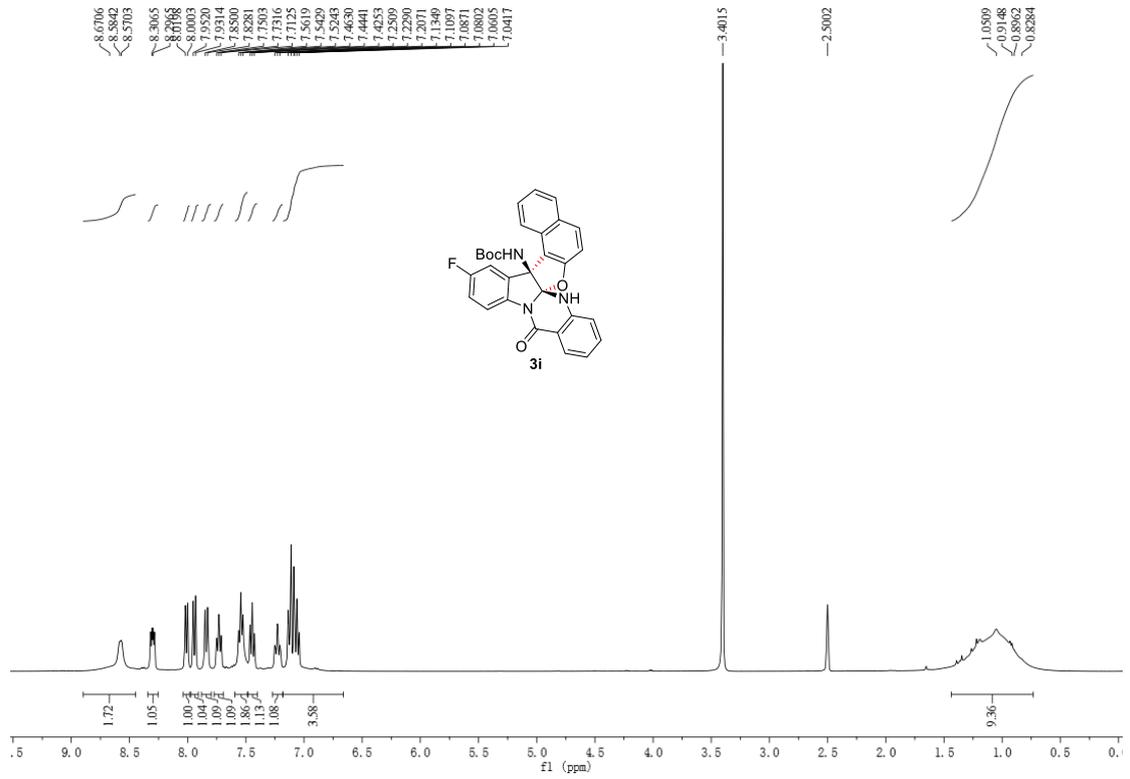
# $^1\text{H}$ NMR and $^{13}\text{C}$ NMR of **3g**



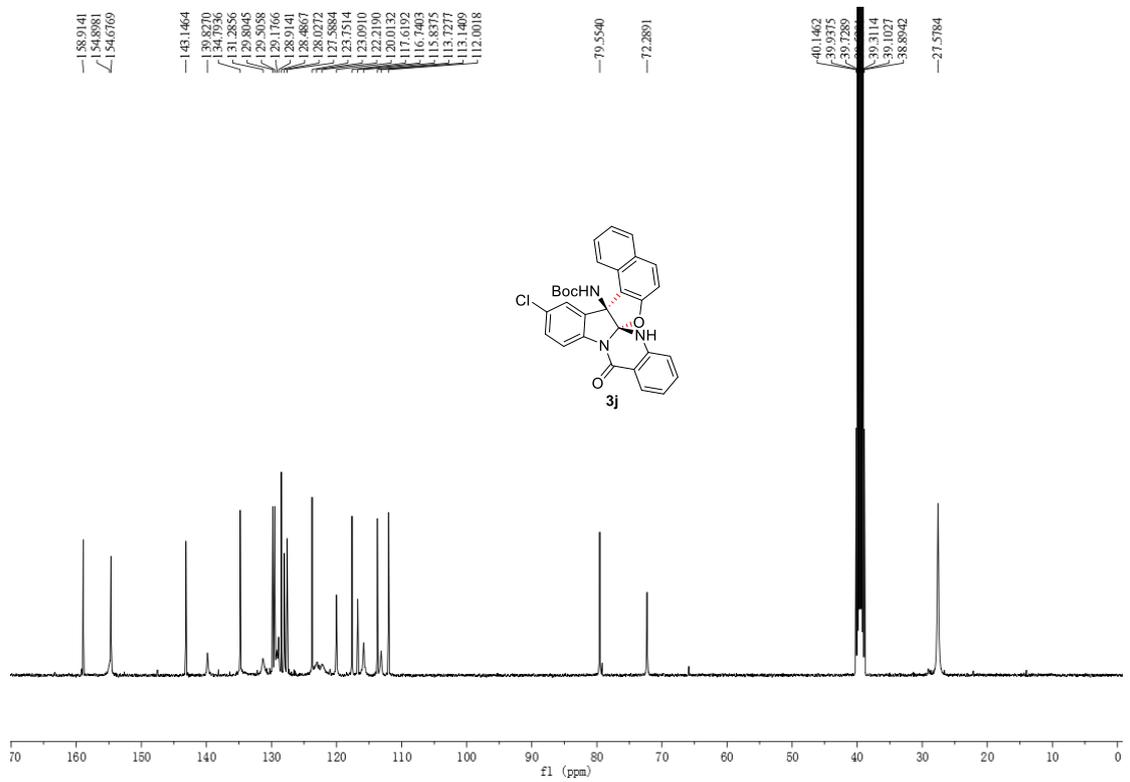
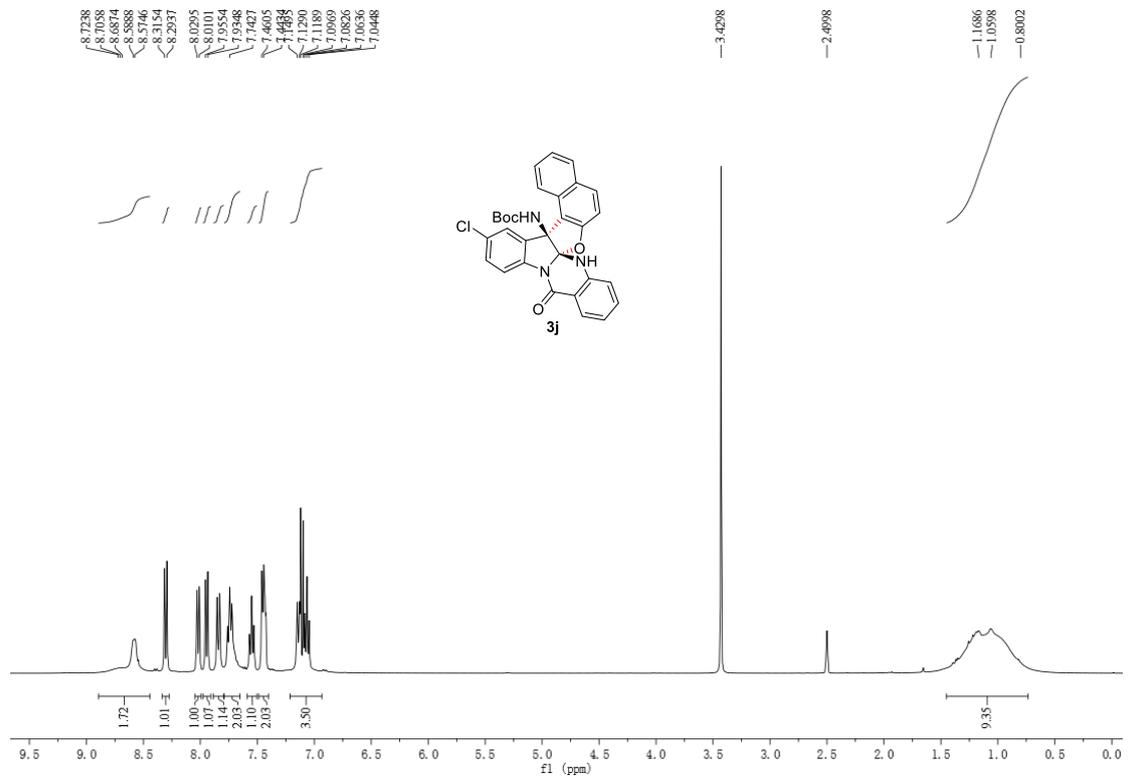
# $^1\text{H}$ NMR and $^{13}\text{C}$ NMR of **3h**



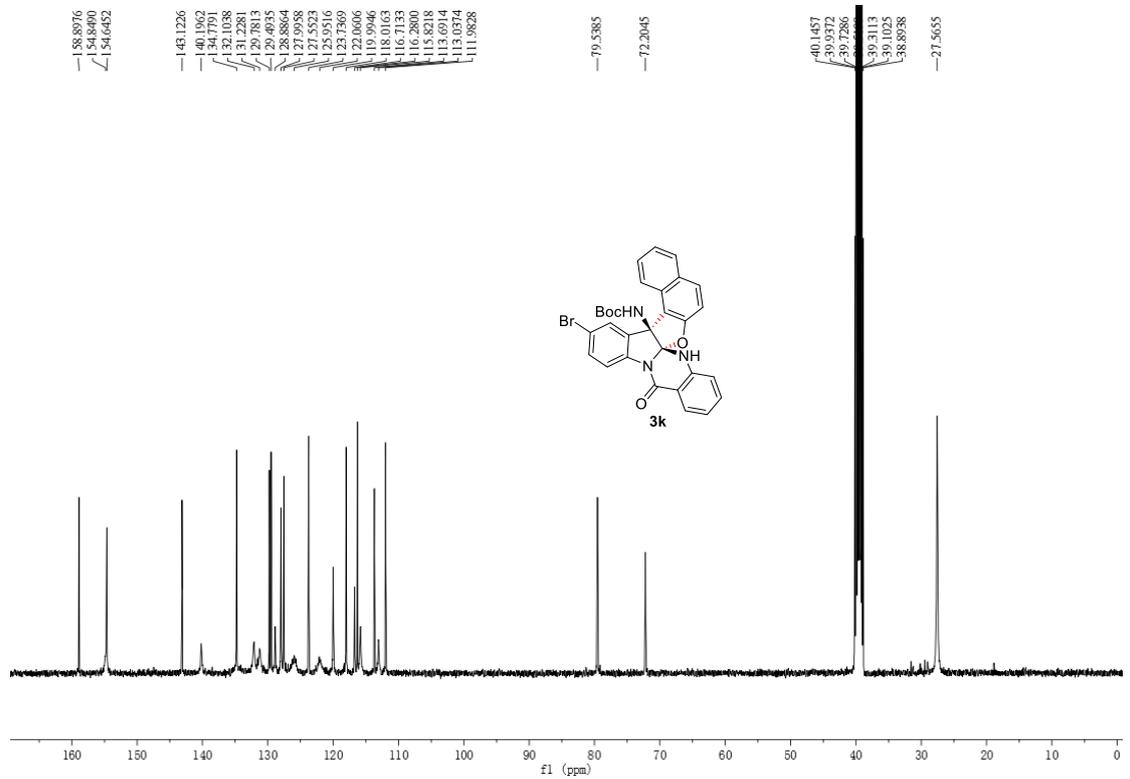
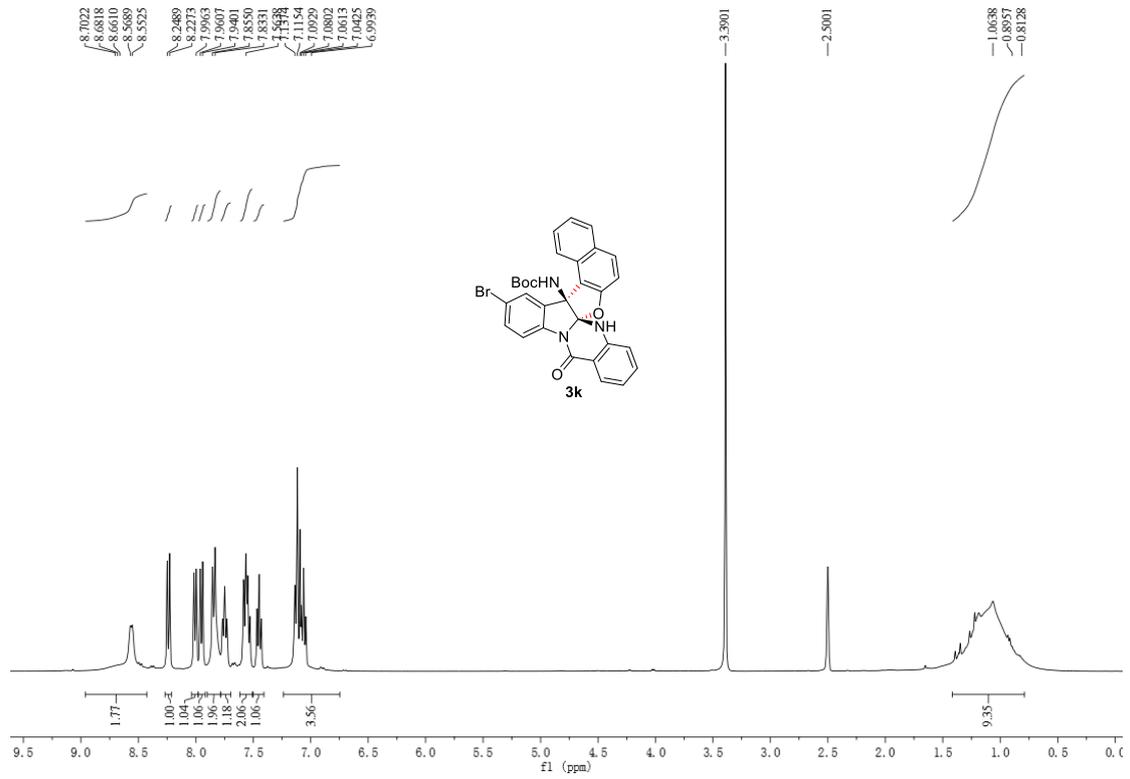
# $^1\text{H}$ NMR and $^{13}\text{C}$ NMR of **3i**



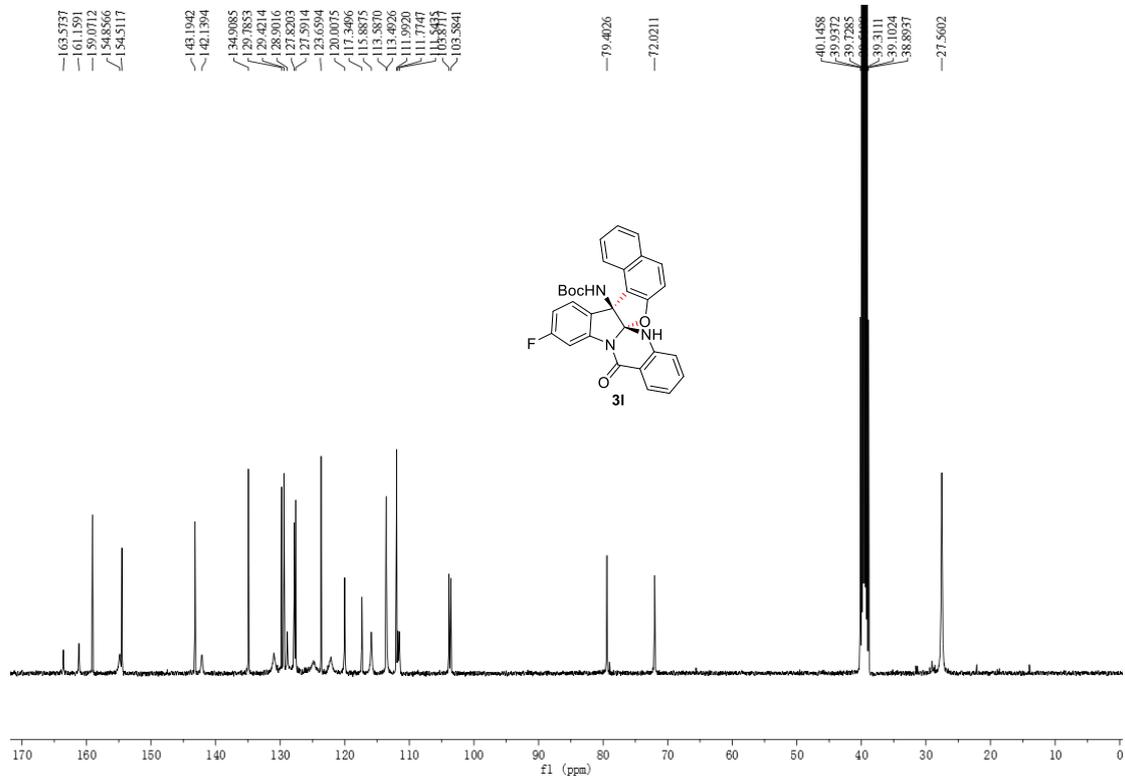
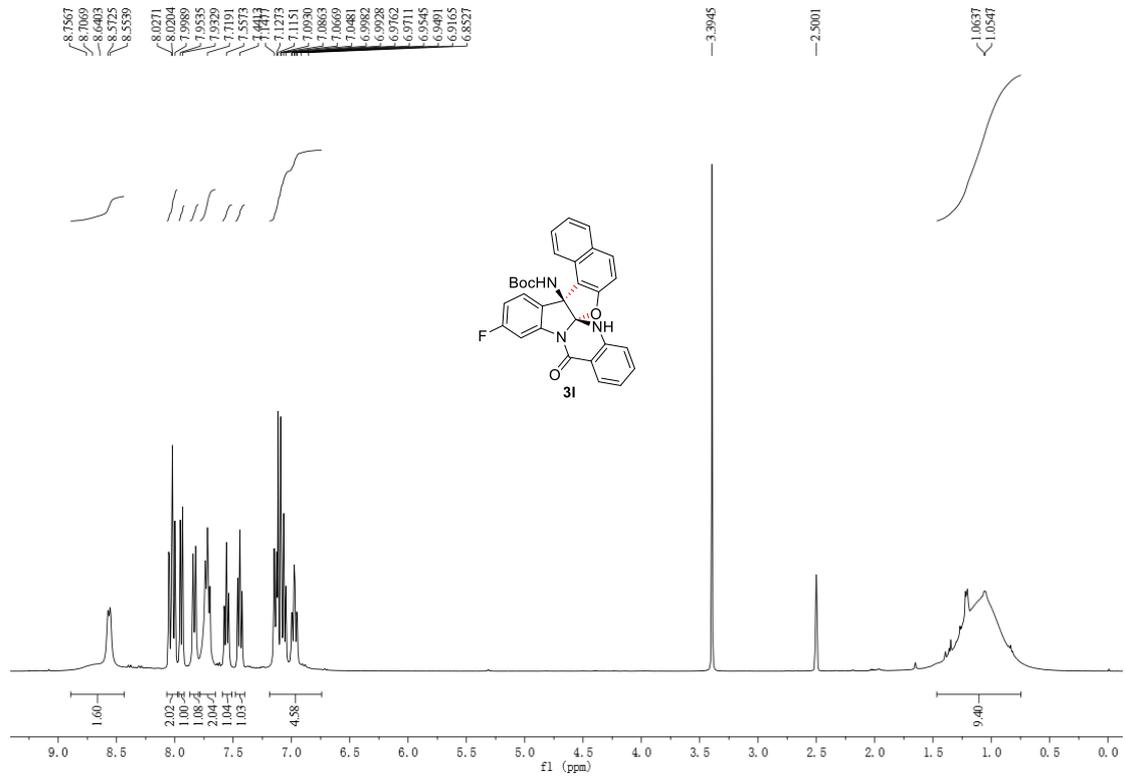
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **3j**



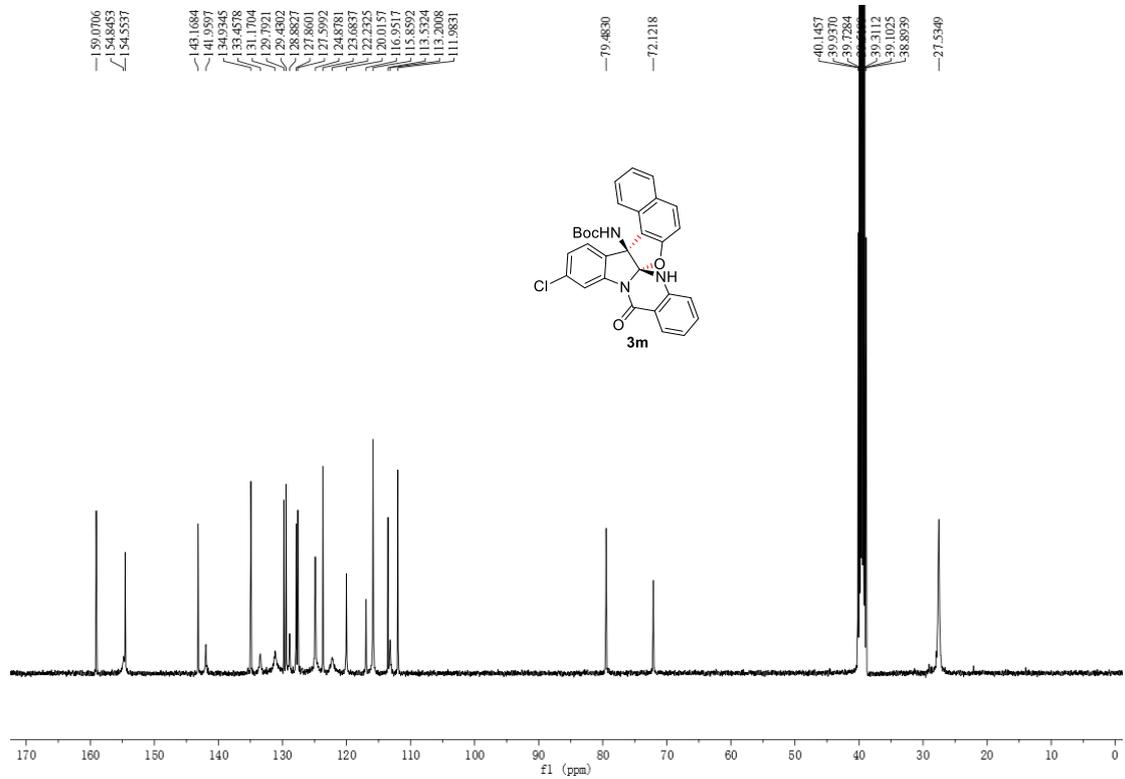
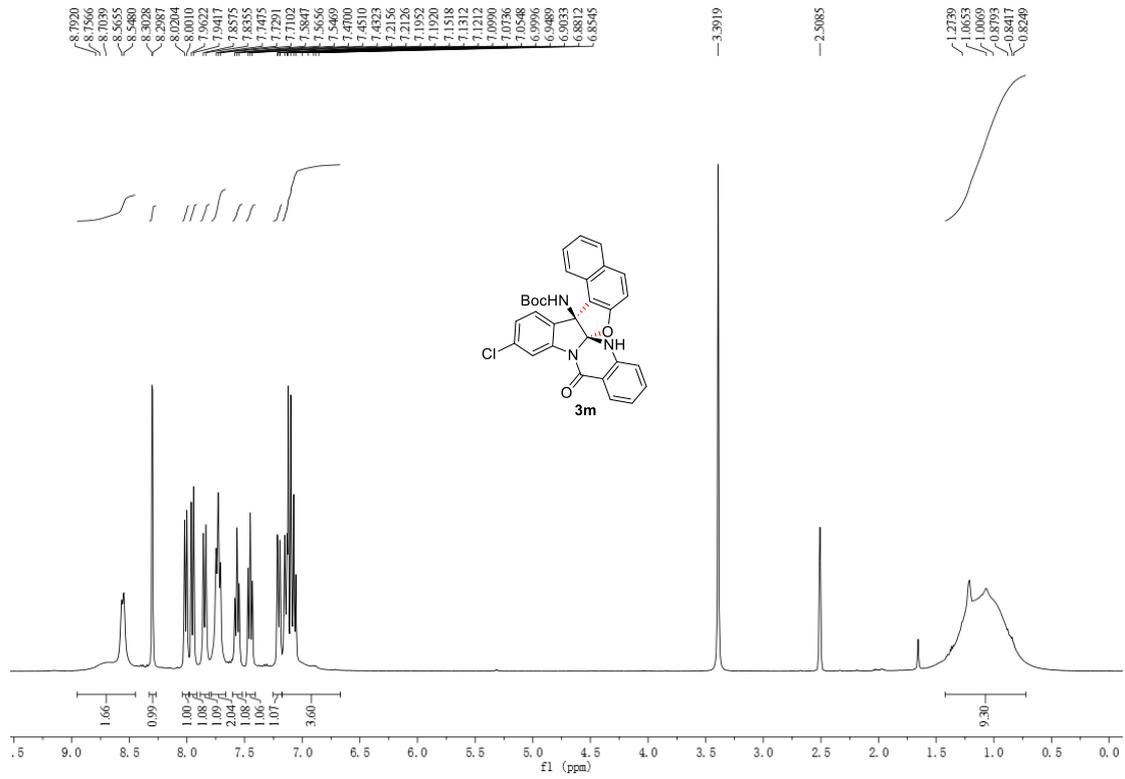
# <sup>1</sup>H NMR and <sup>13</sup>C NMR of 3k



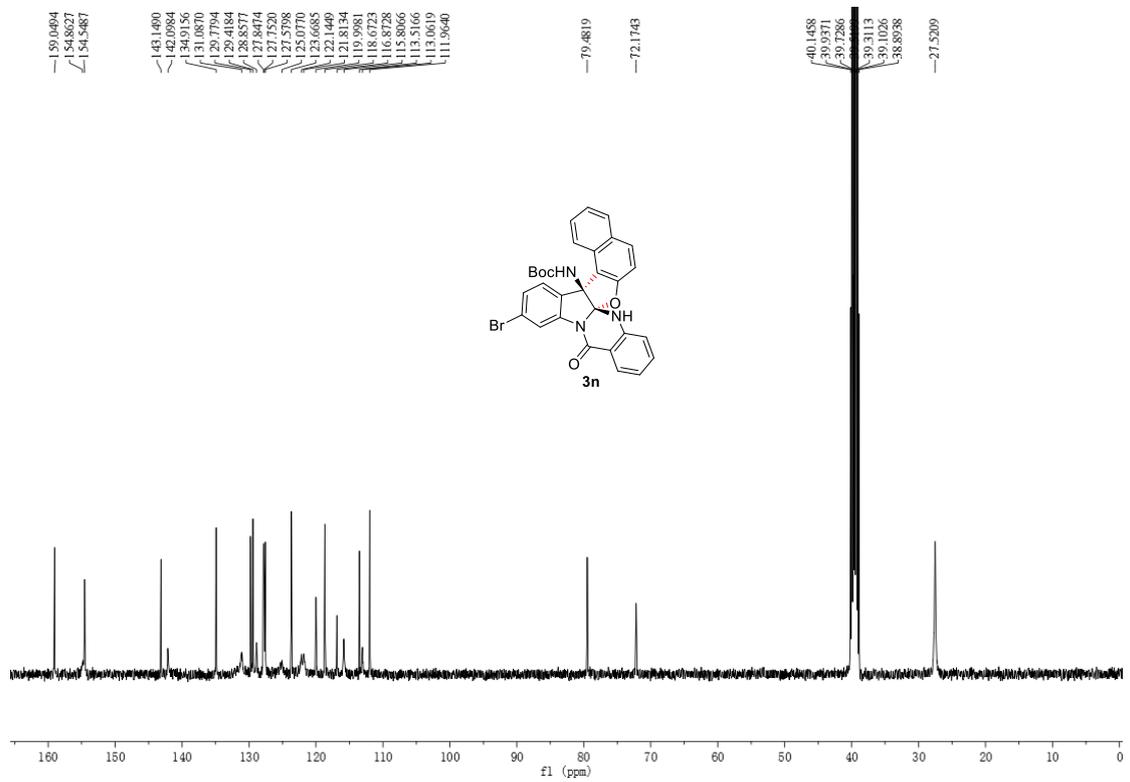
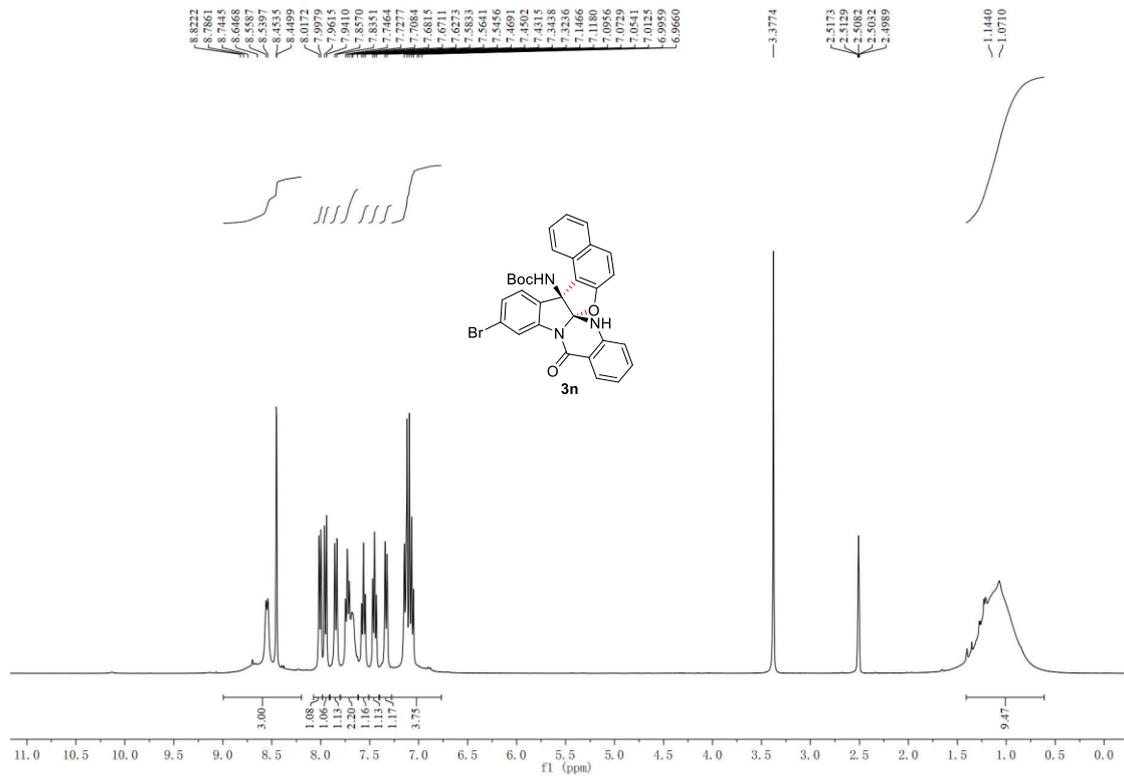
<sup>1</sup>H NMR and <sup>13</sup>C NMR of **31**



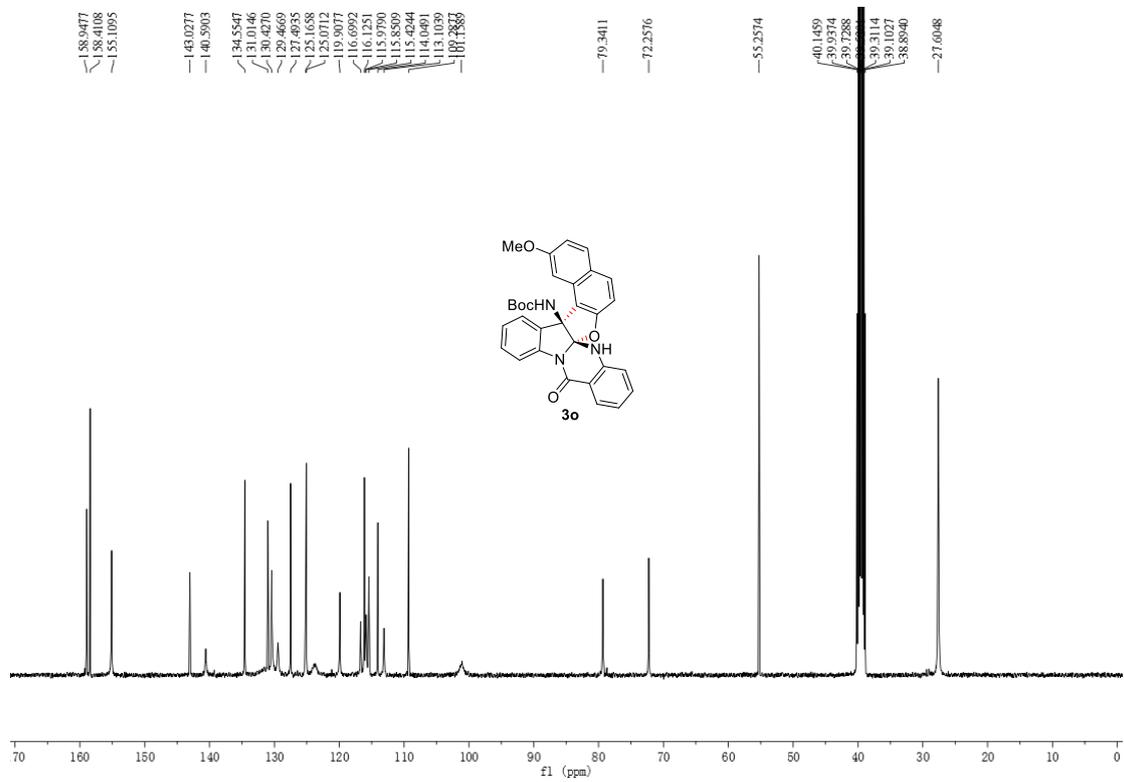
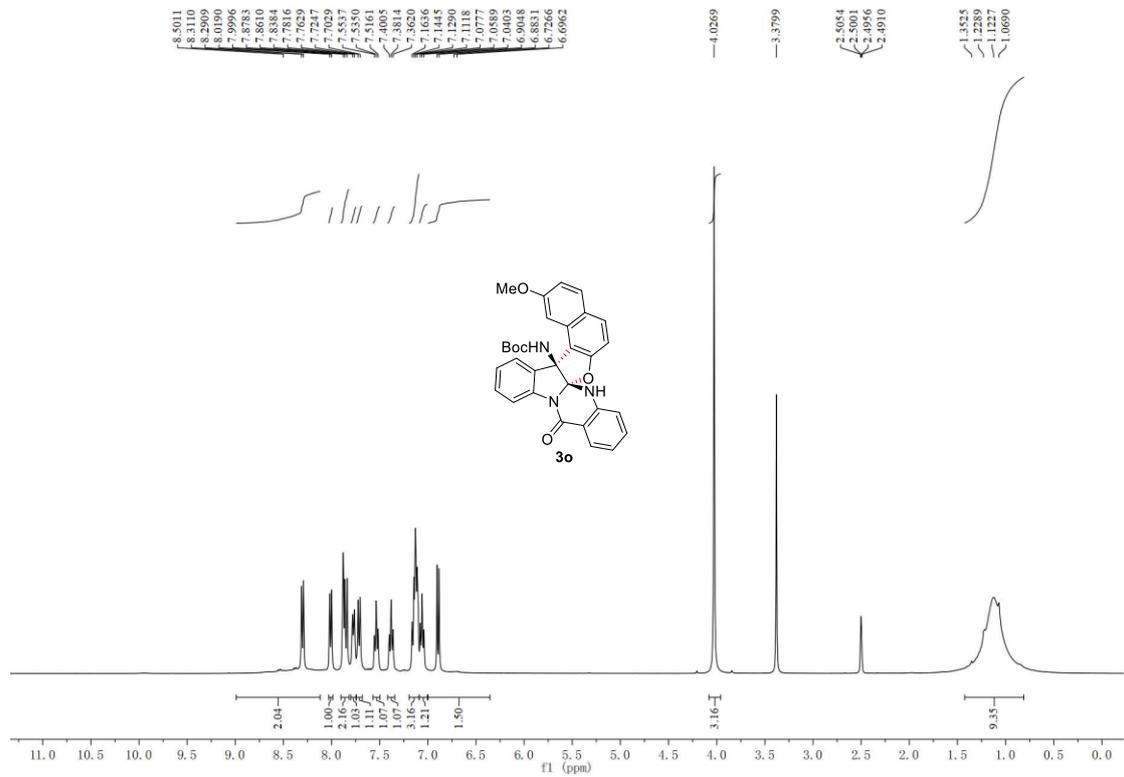
<sup>1</sup>H NMR and <sup>13</sup>C NMR of **3m**



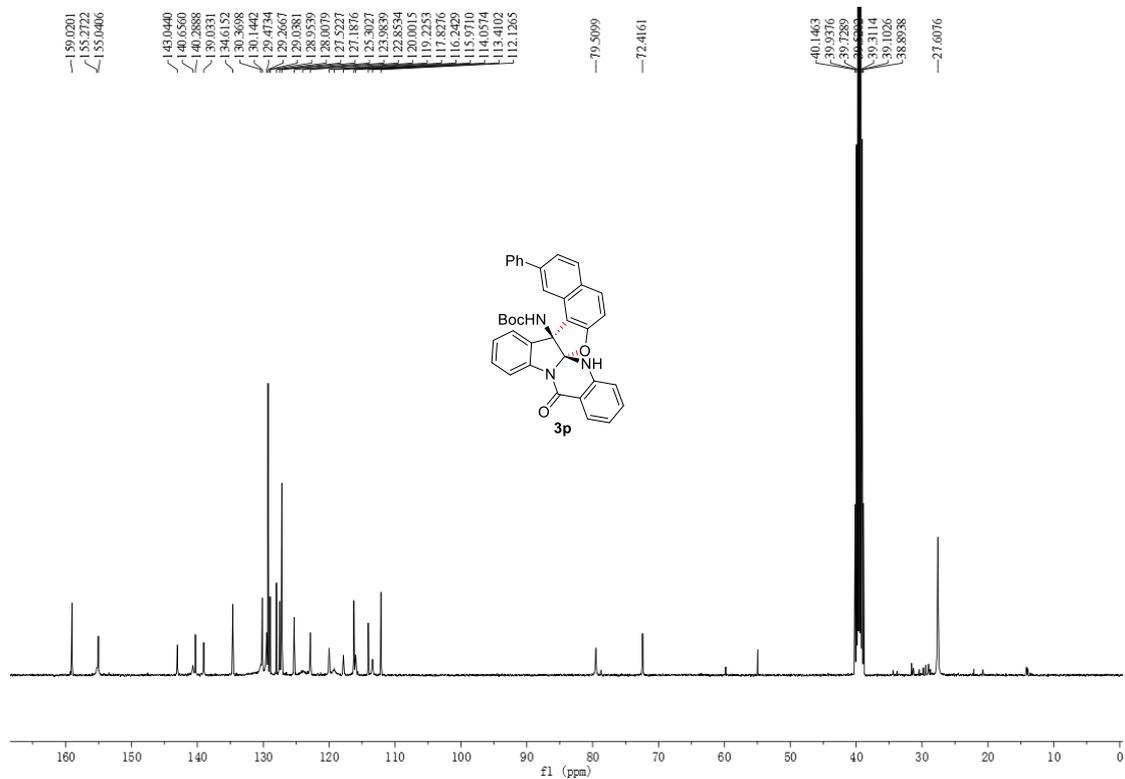
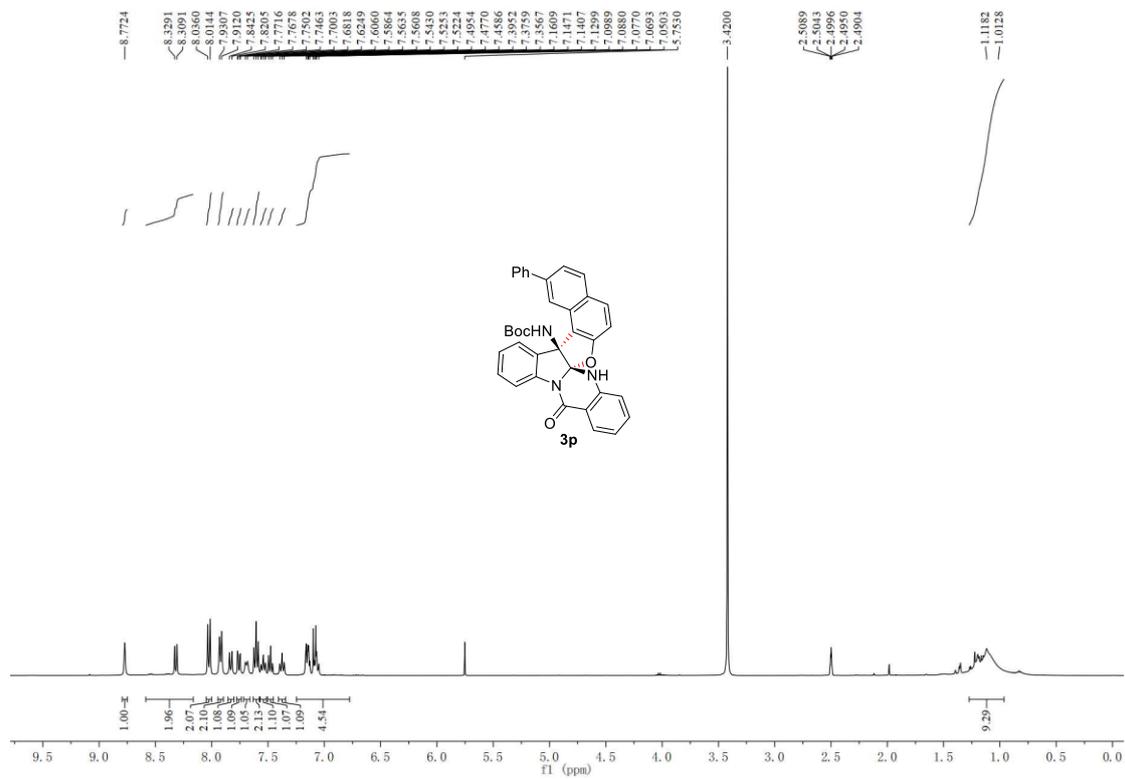
# $^1\text{H}$ NMR and $^{13}\text{C}$ NMR of **3n**



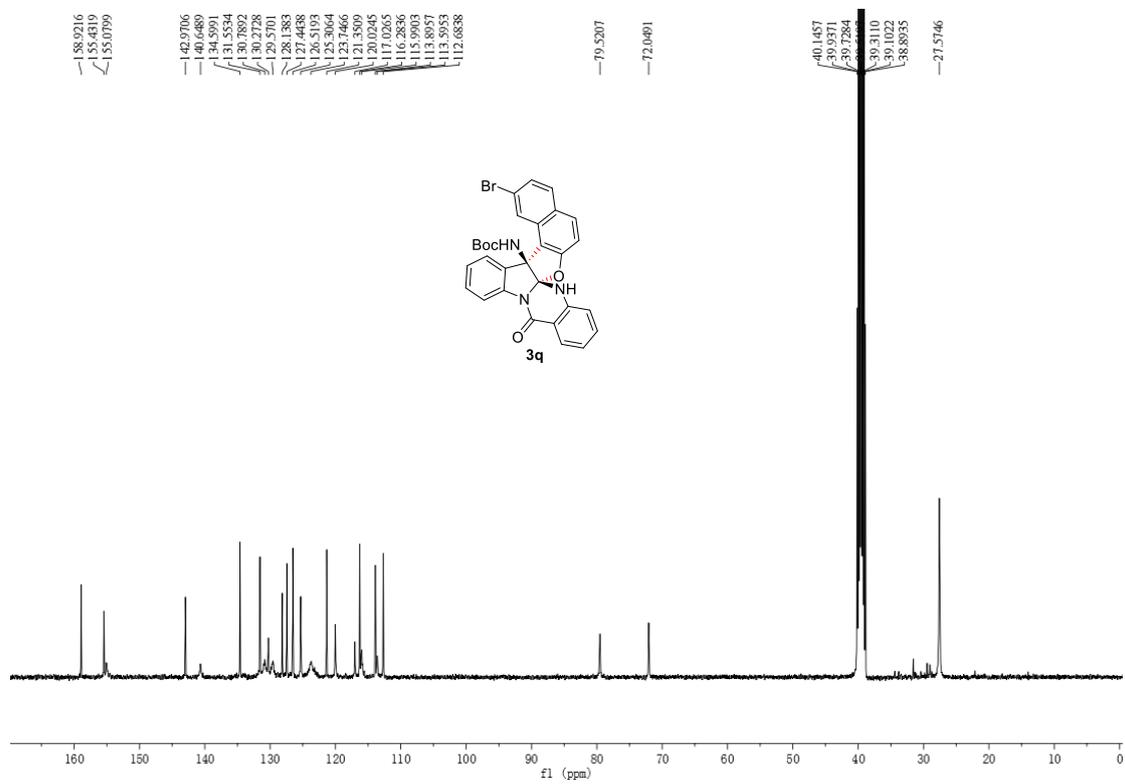
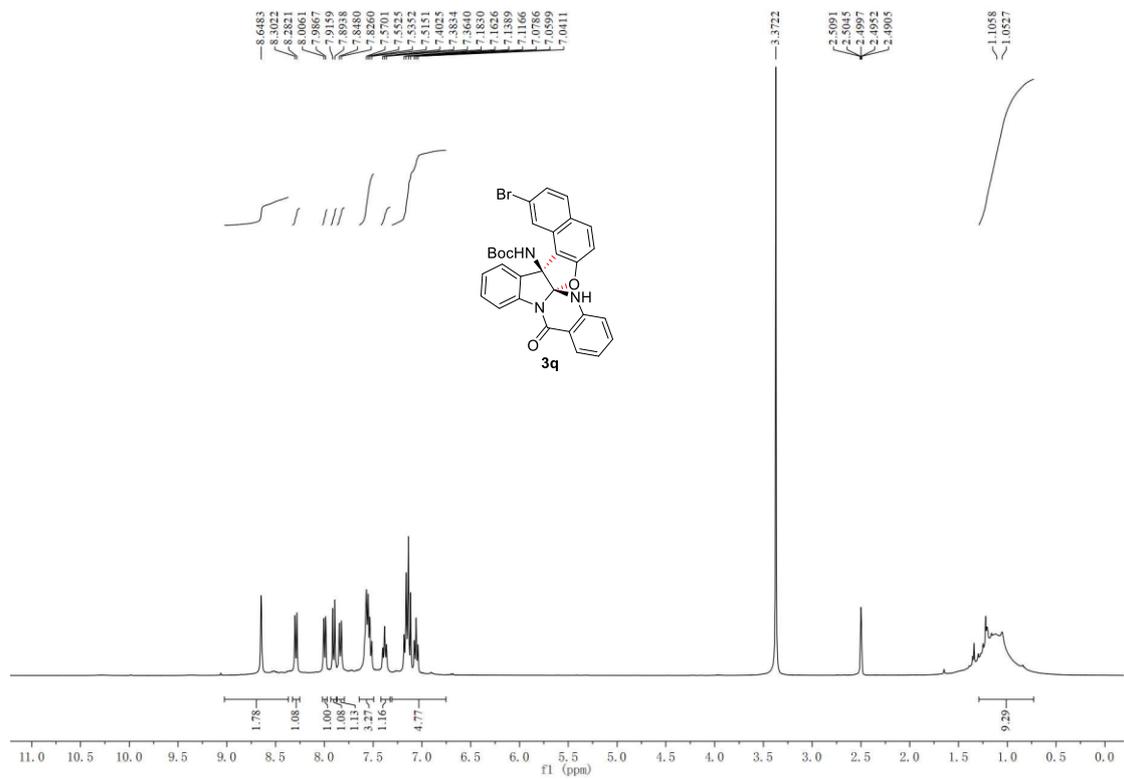
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **3o**



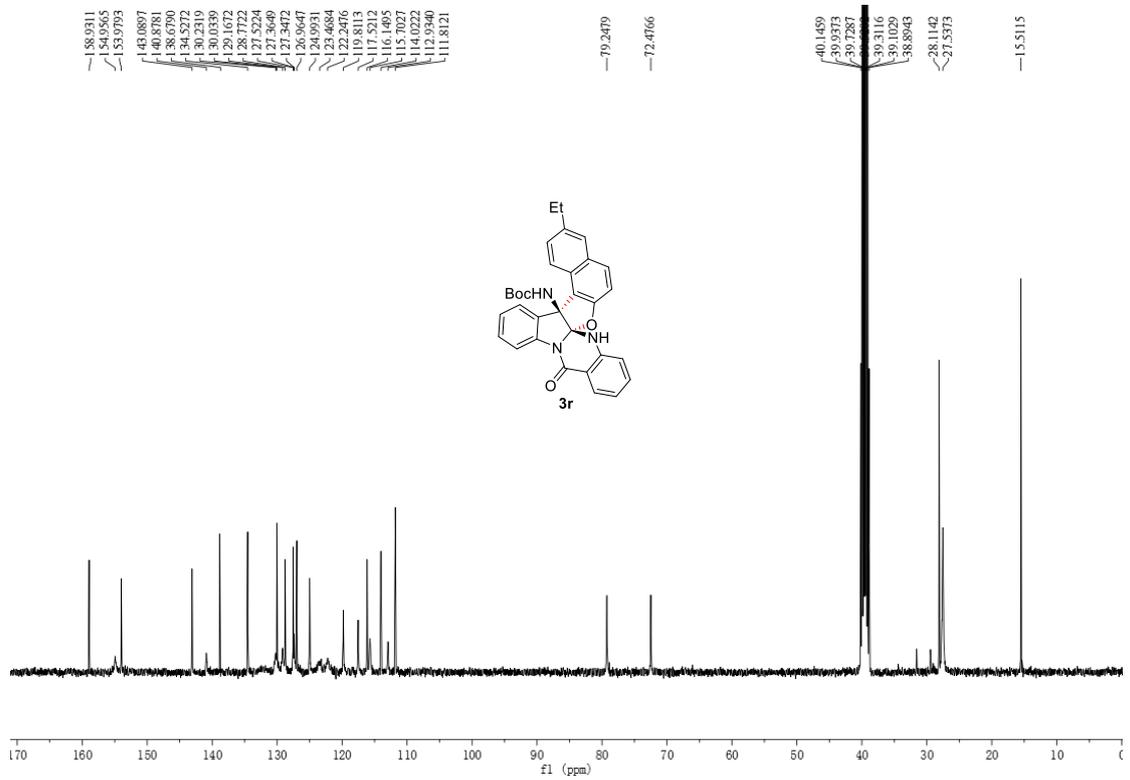
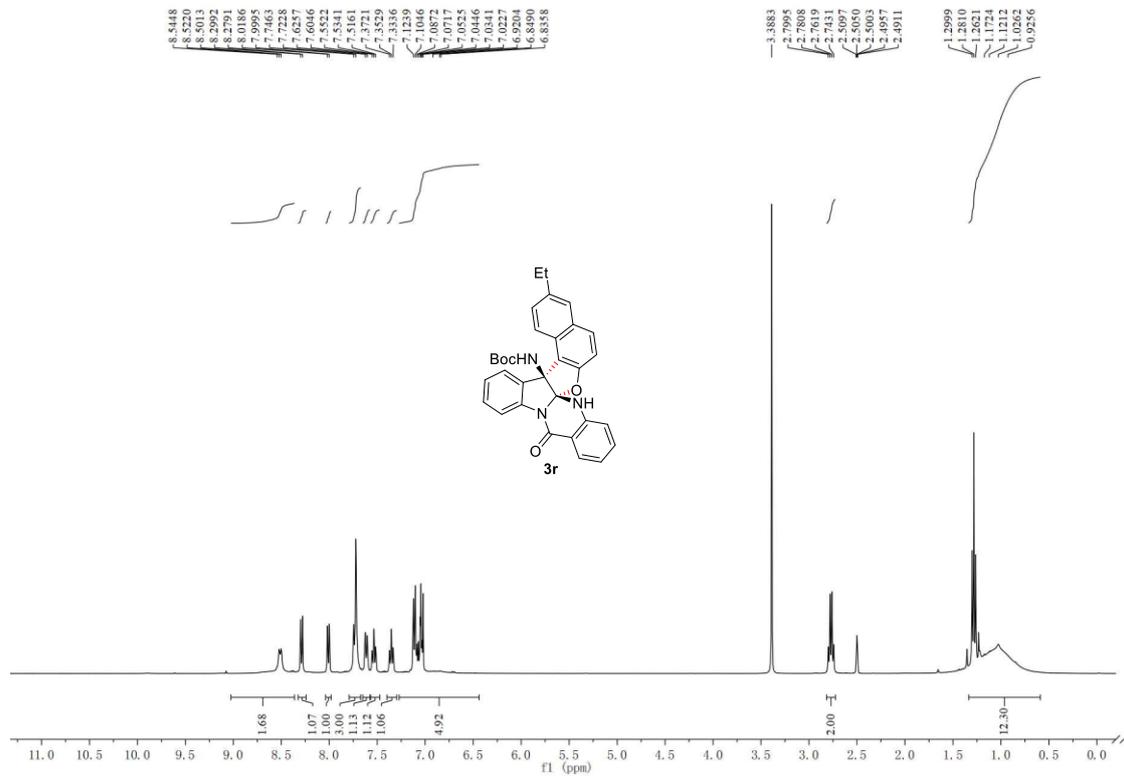
# $^1\text{H}$ NMR and $^{13}\text{C}$ NMR of **3p**



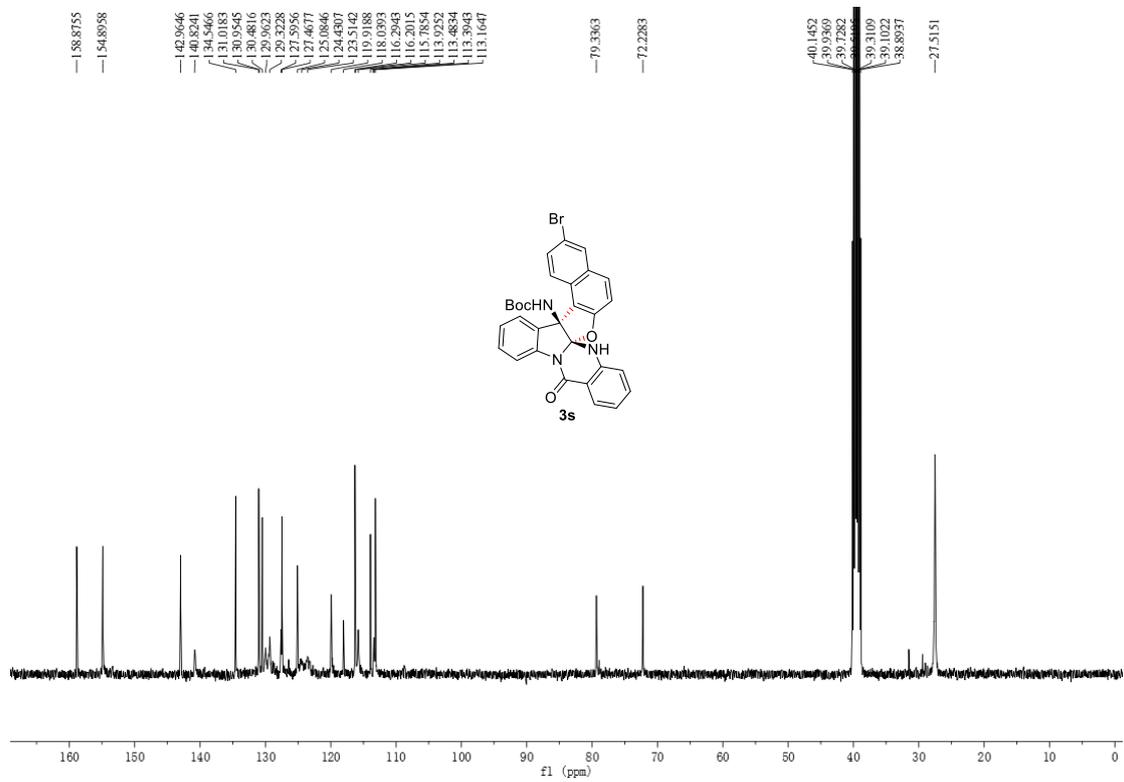
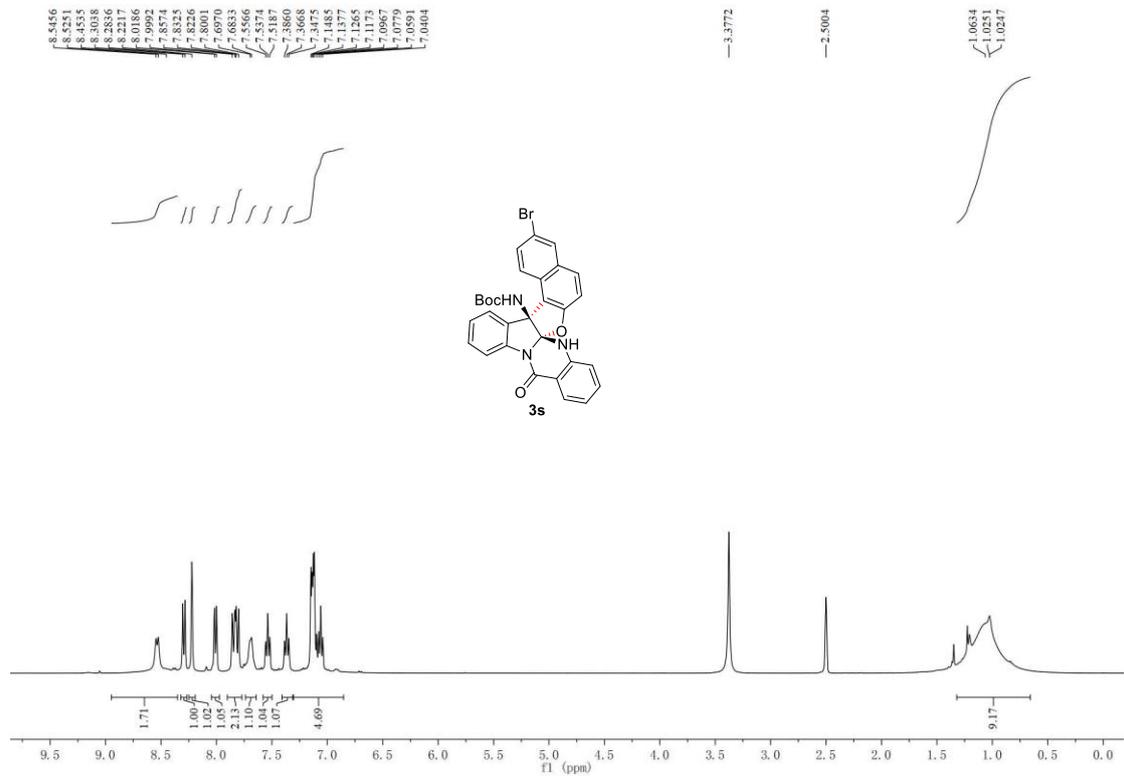
<sup>1</sup>H NMR and <sup>13</sup>C NMR of **3q**



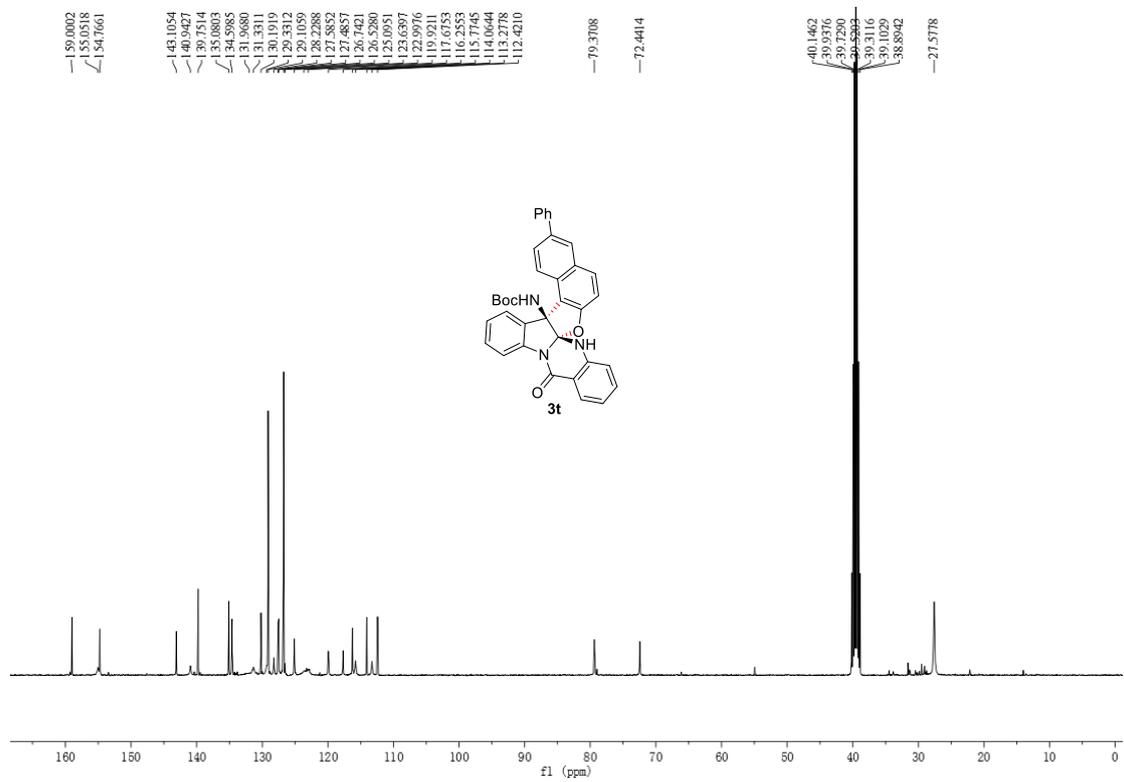
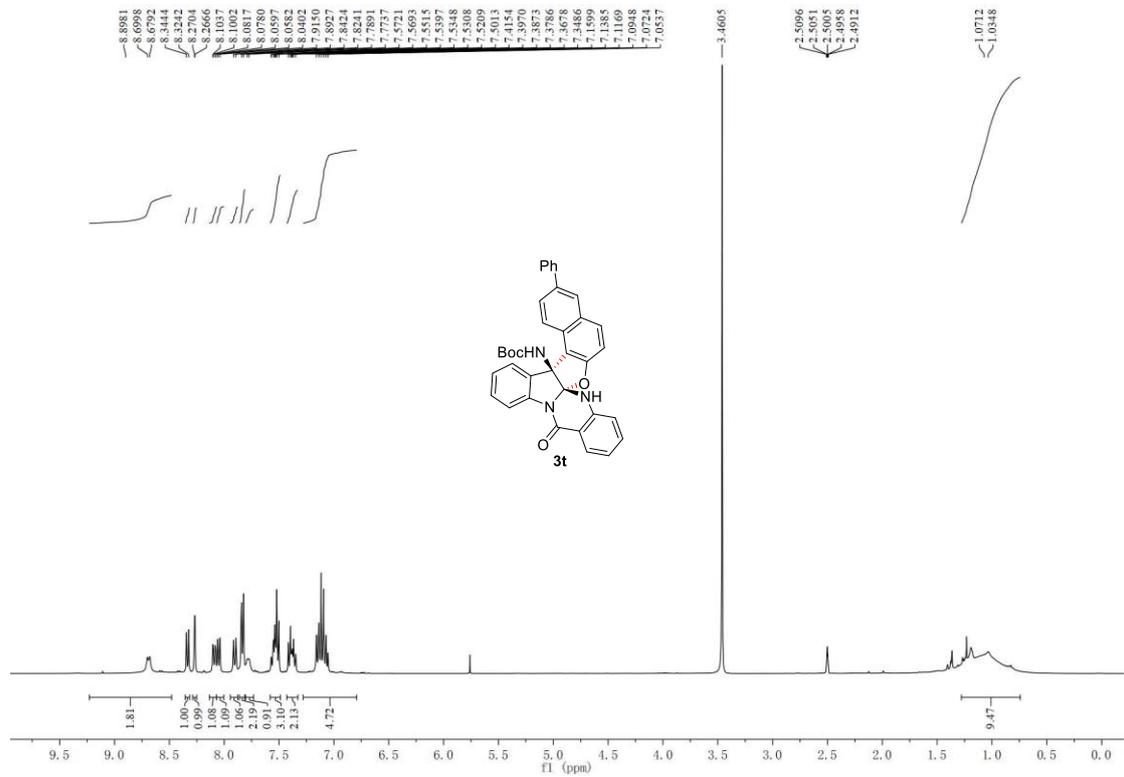
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **3r**



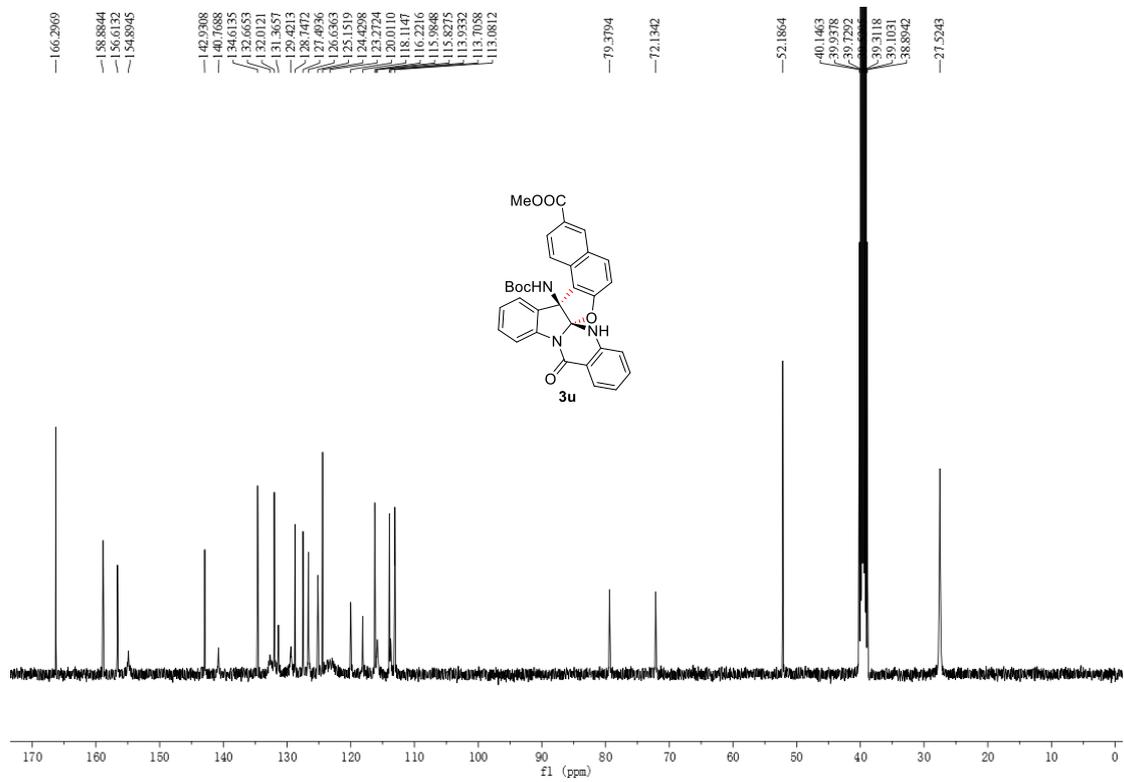
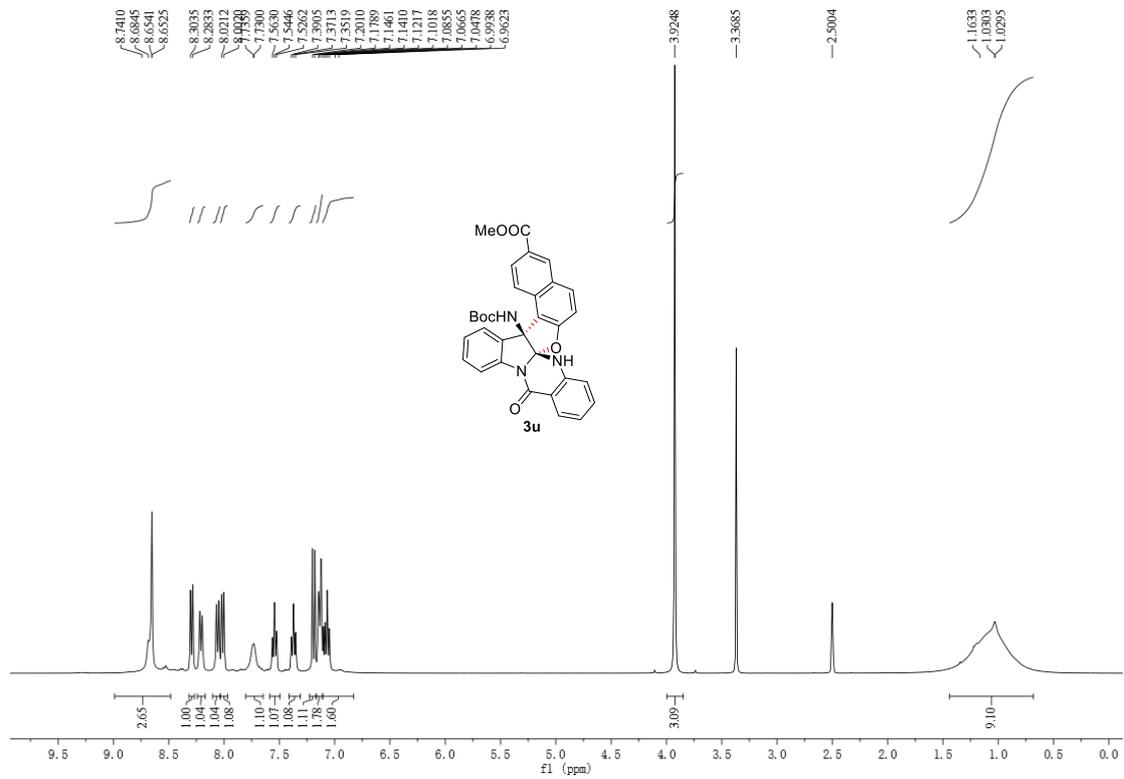
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **3s**



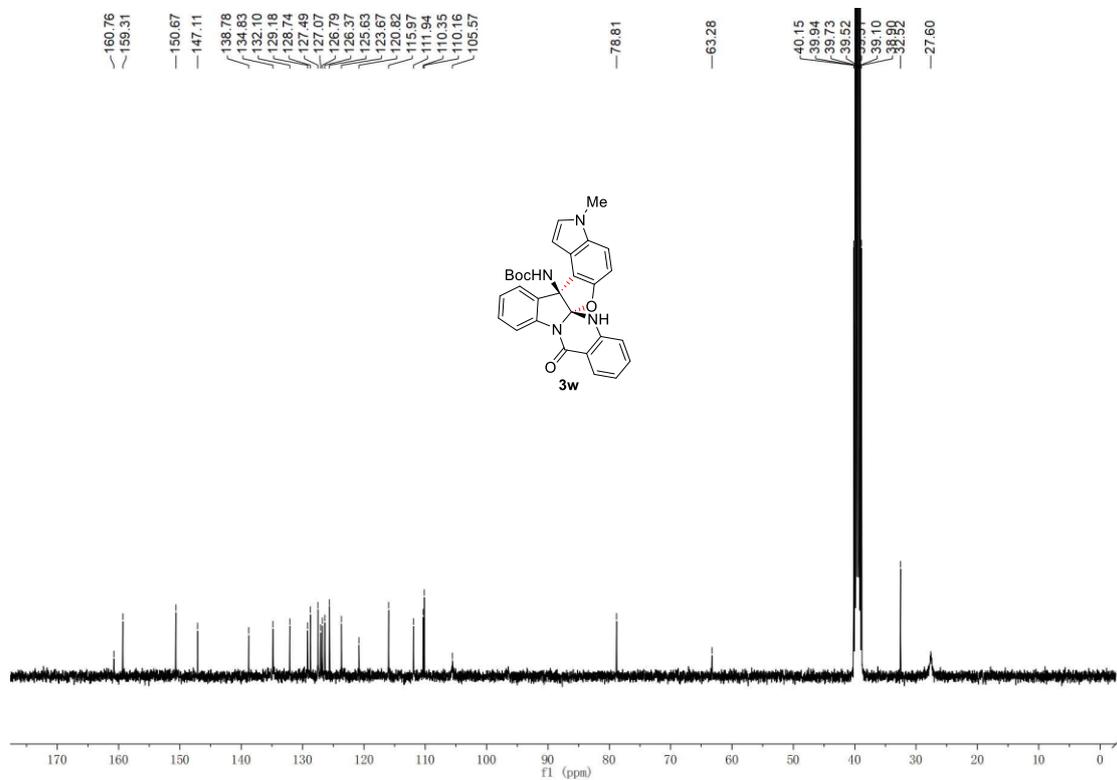
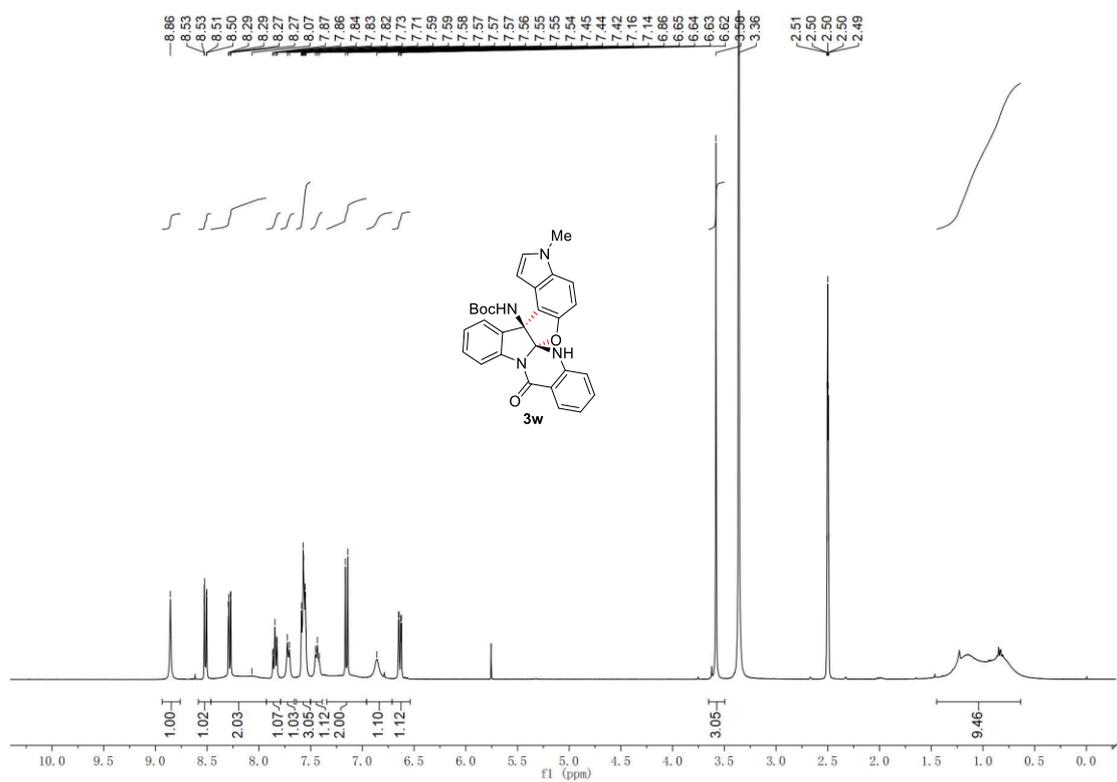
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **3t**



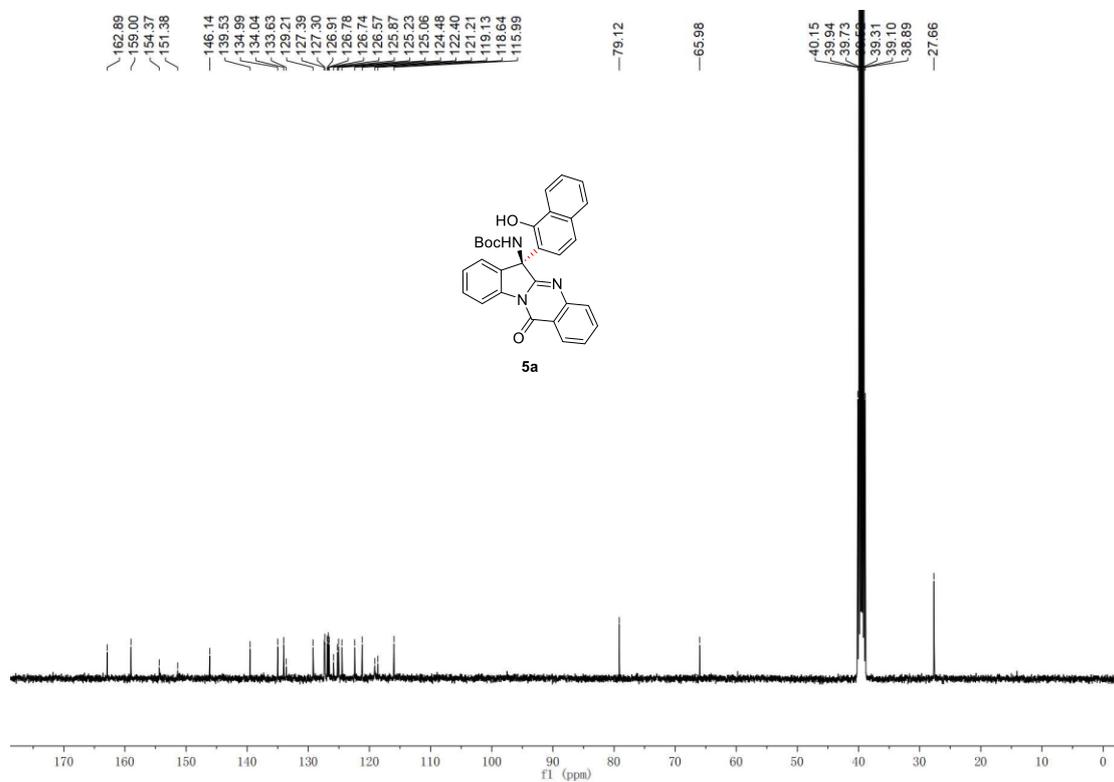
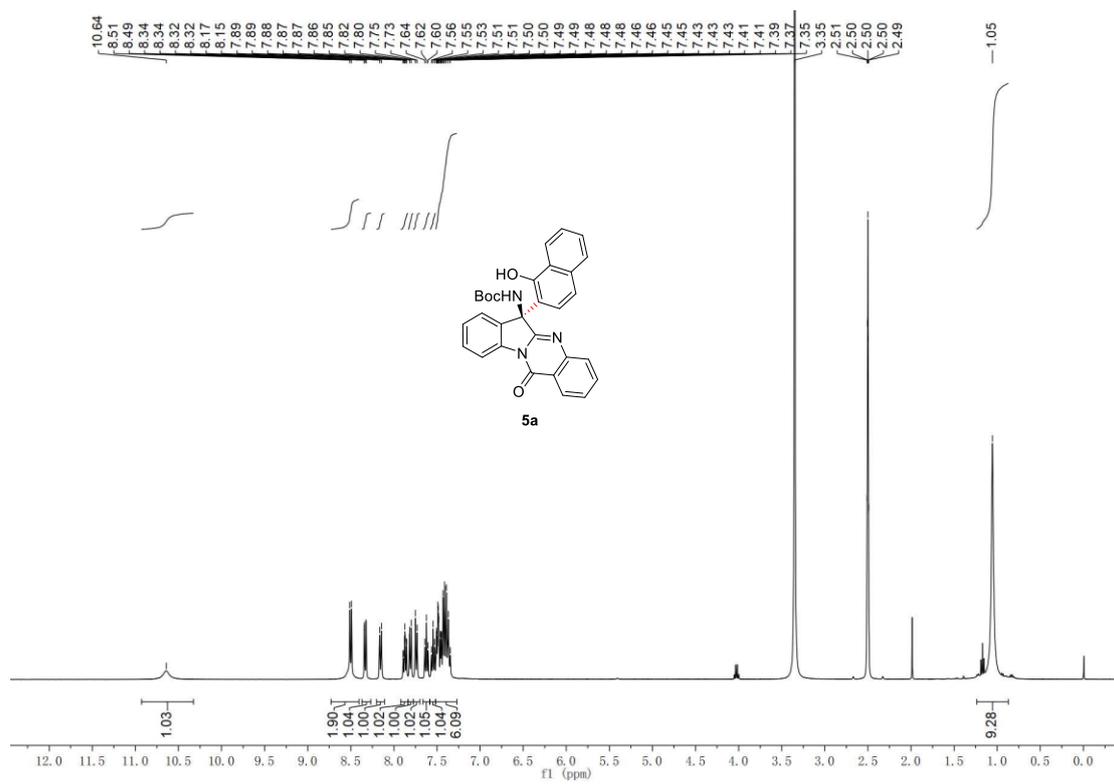
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **3u**



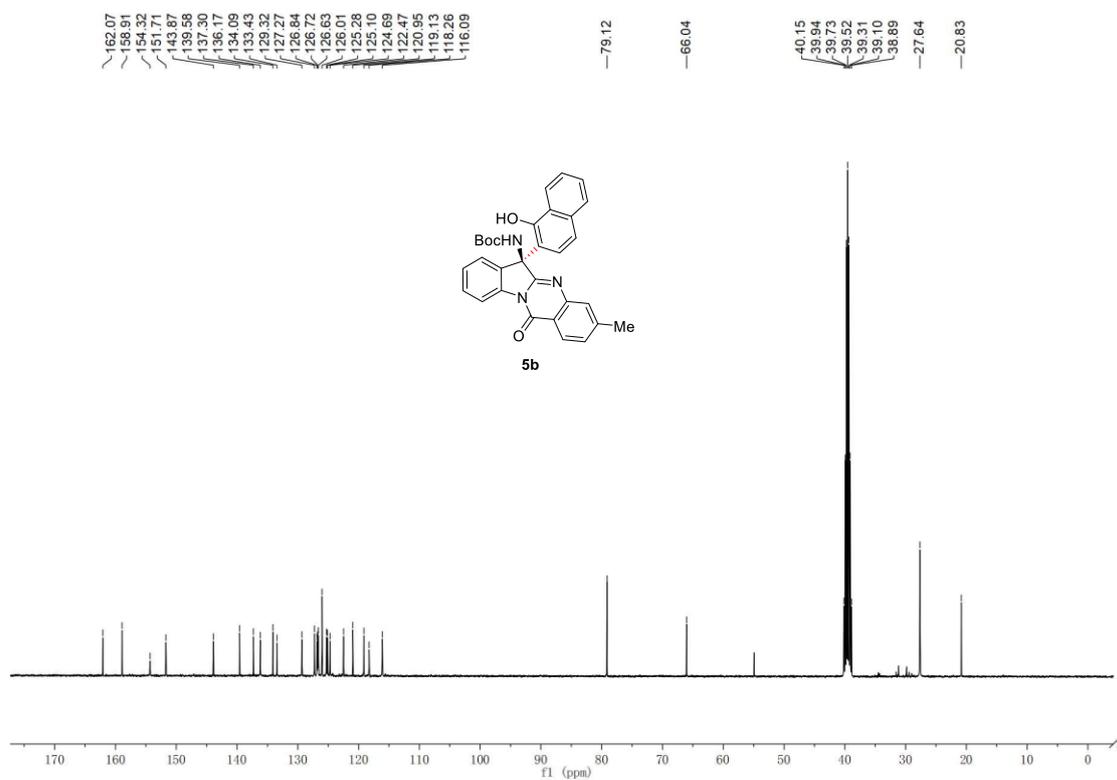
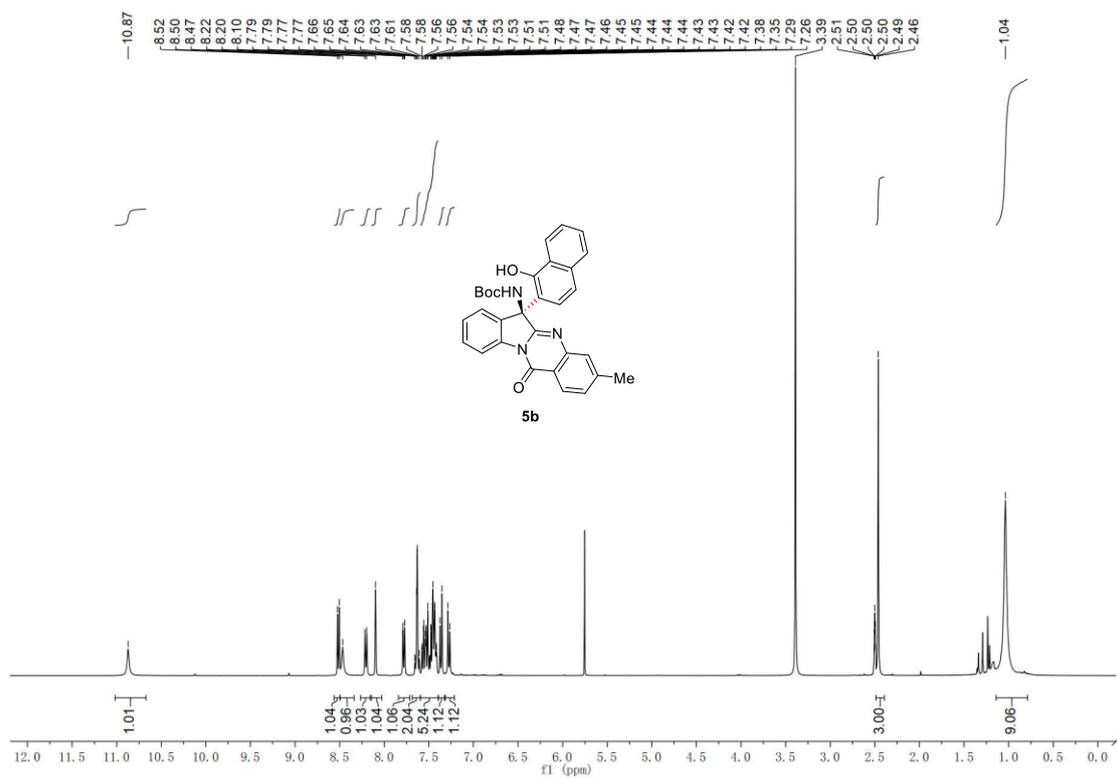
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **3w**



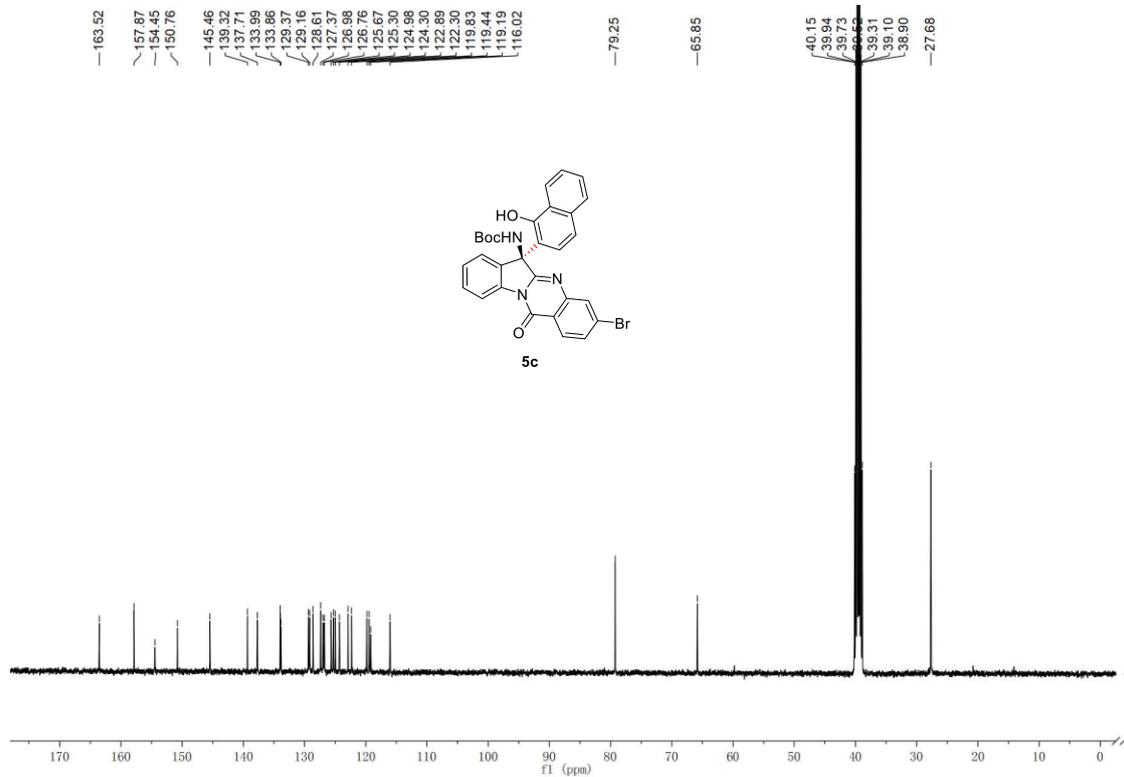
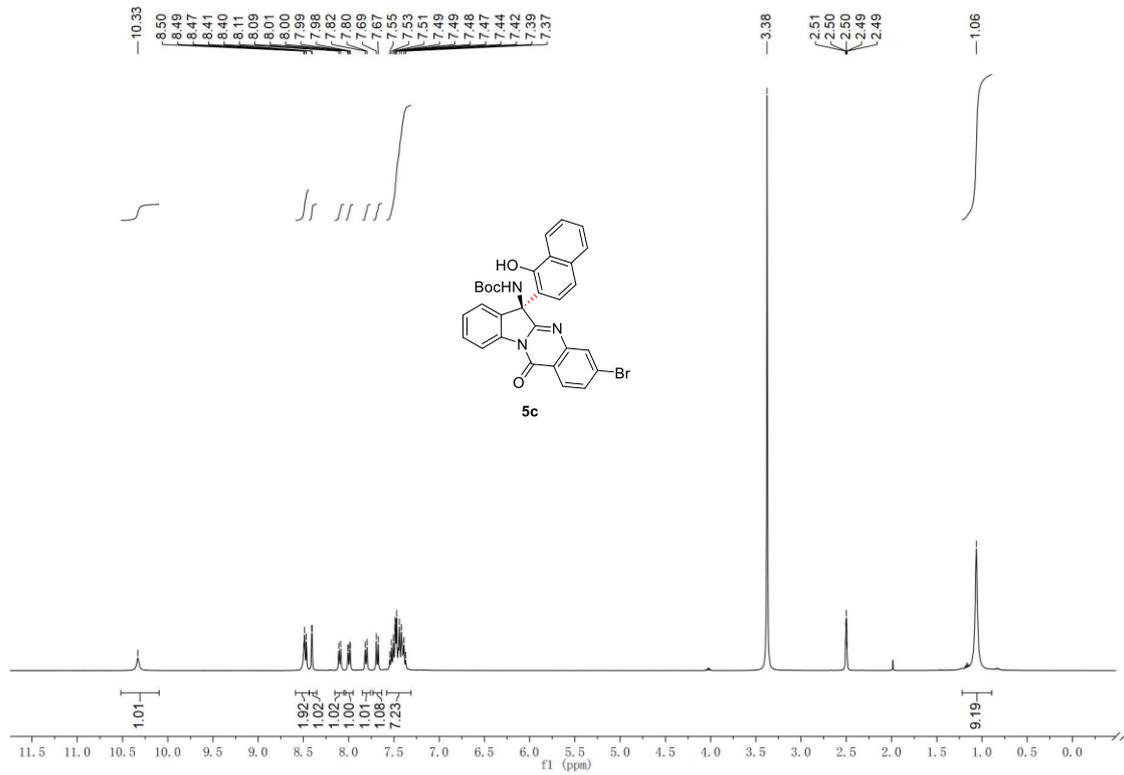
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **5a**



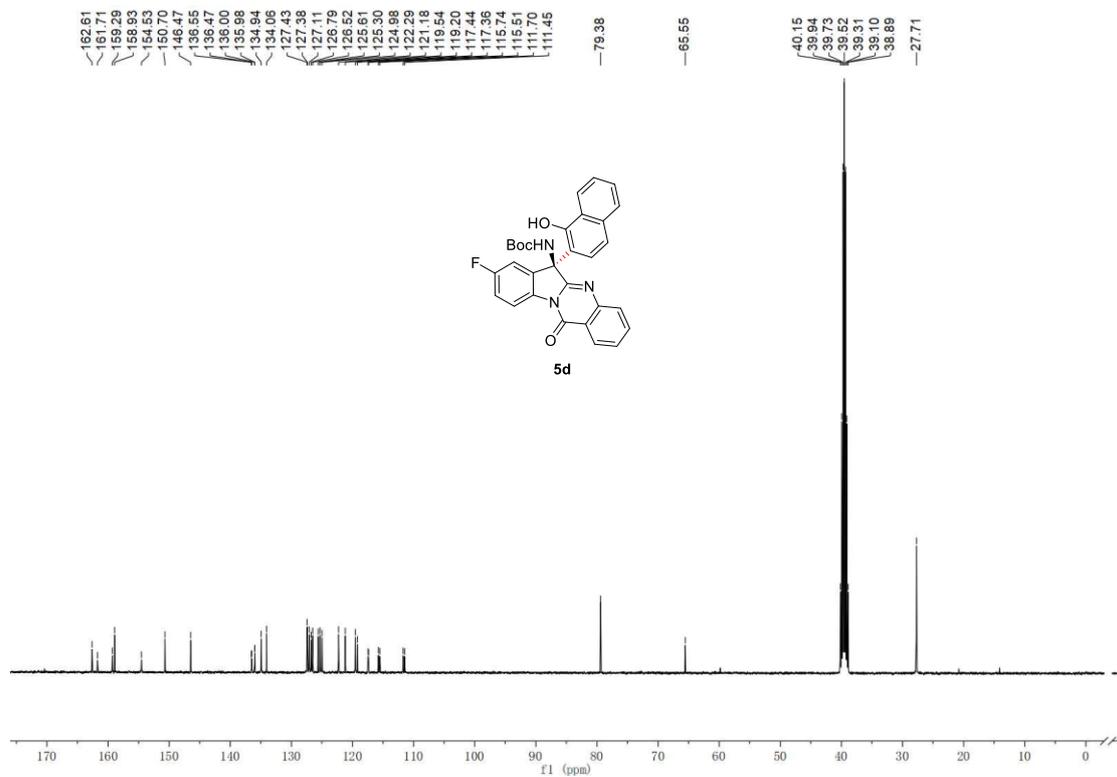
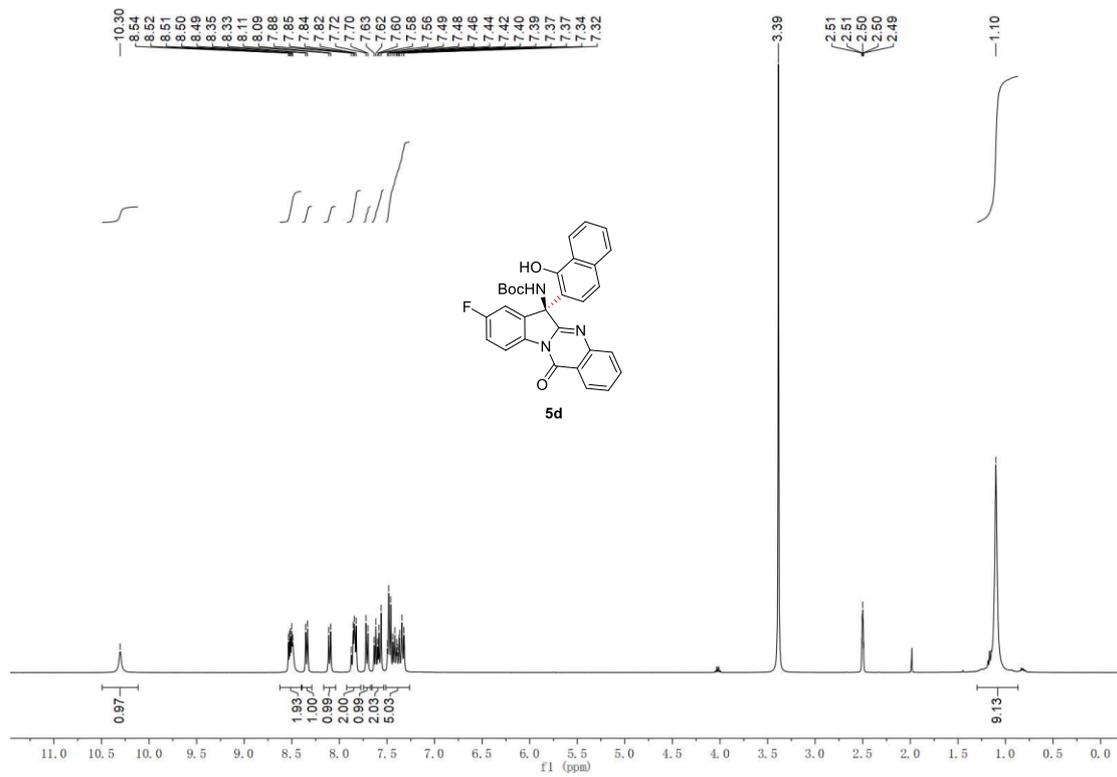
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **5b**



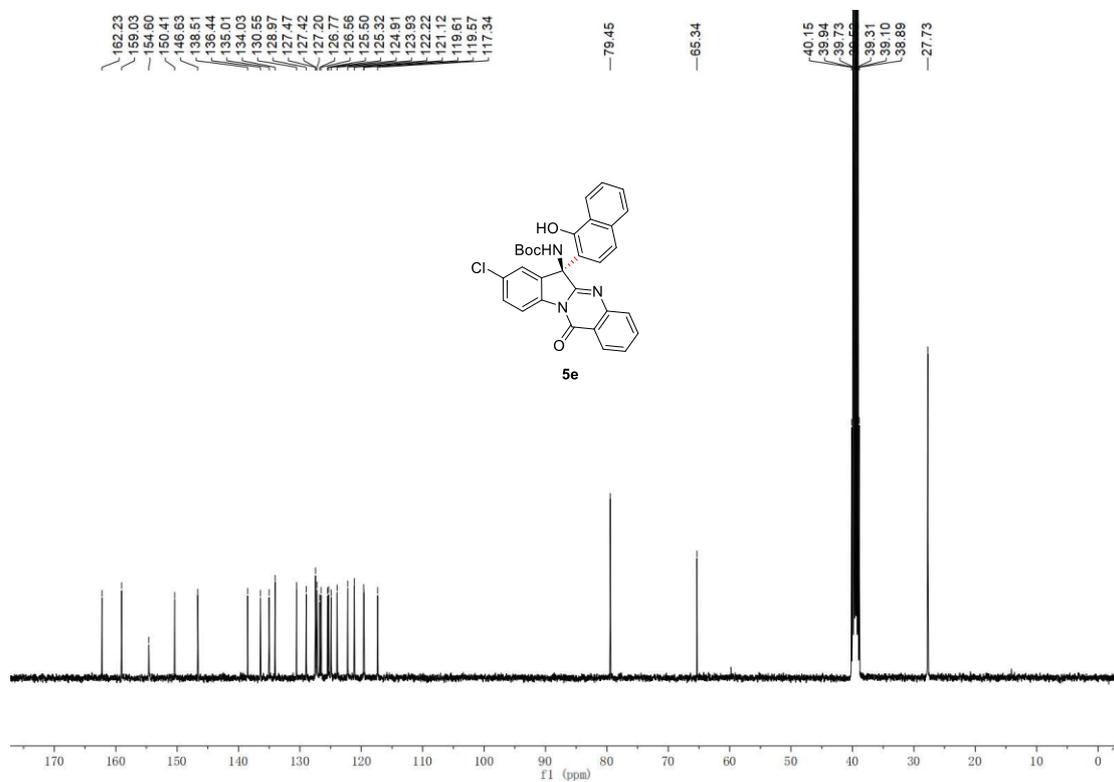
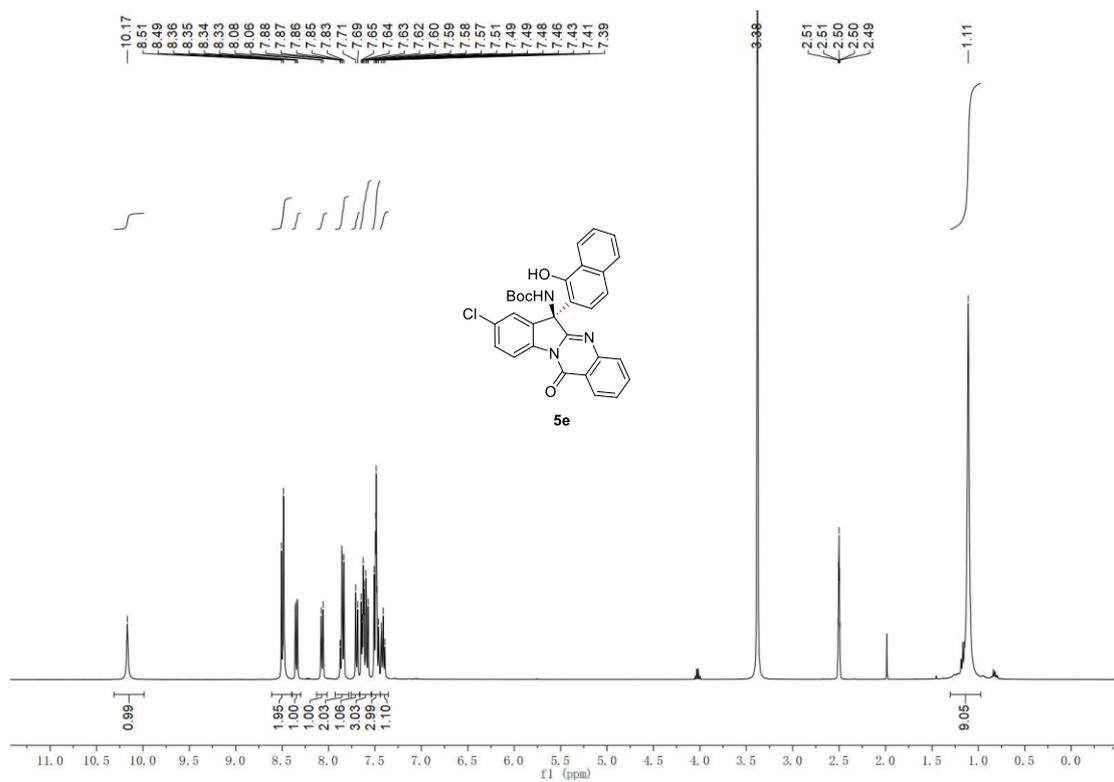
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **5c**



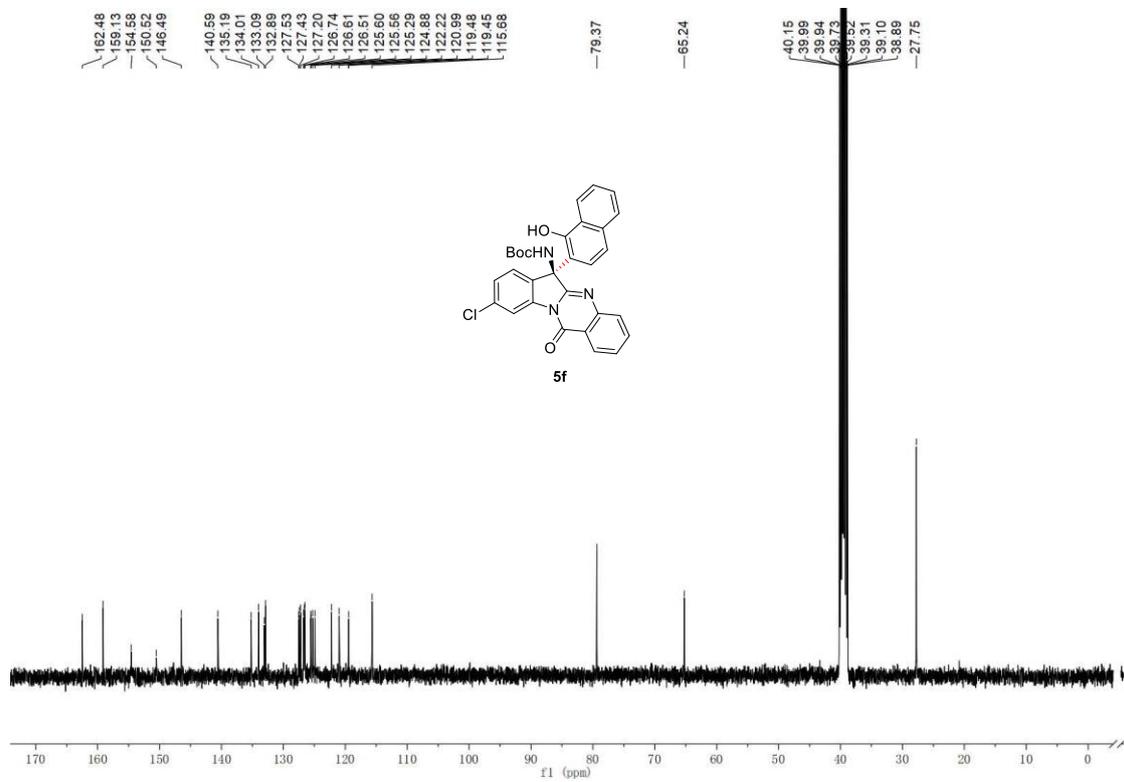
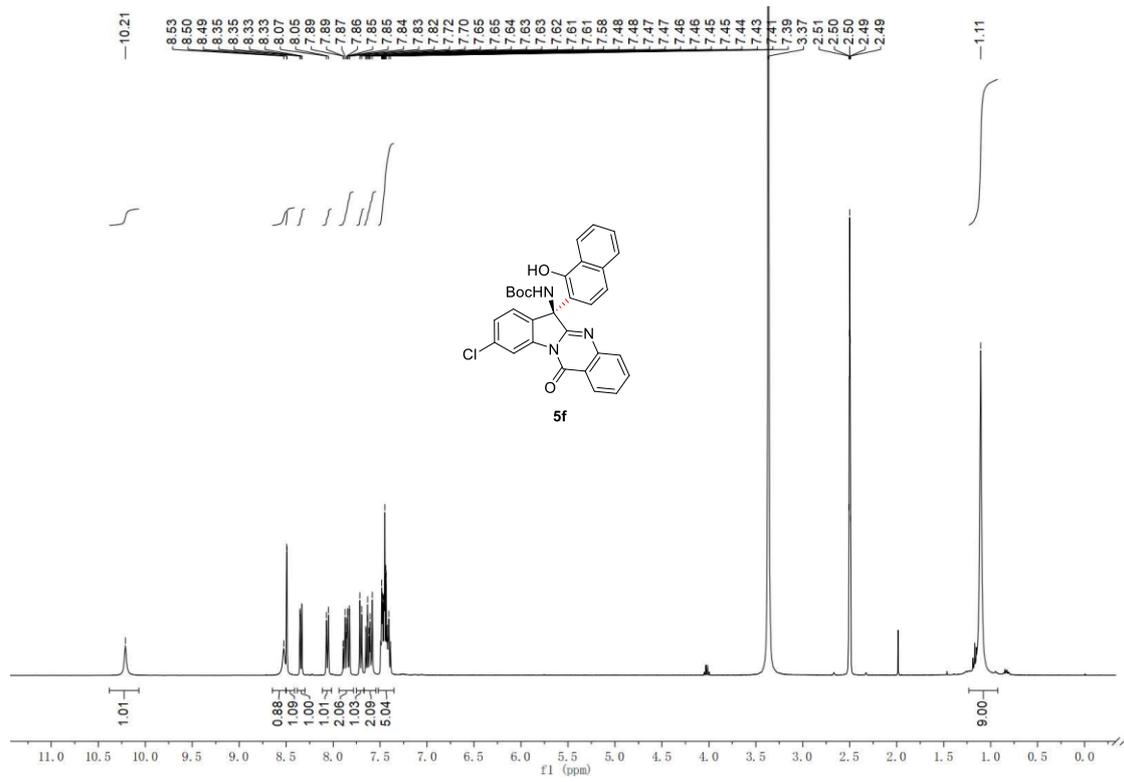
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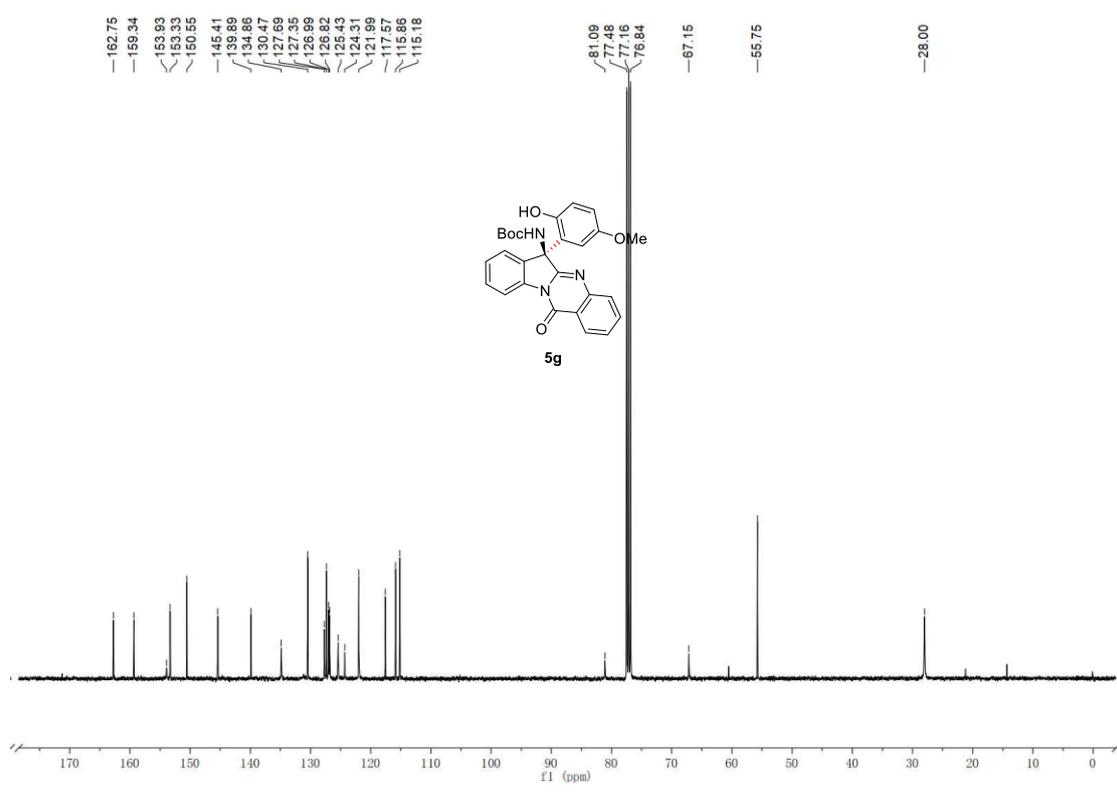
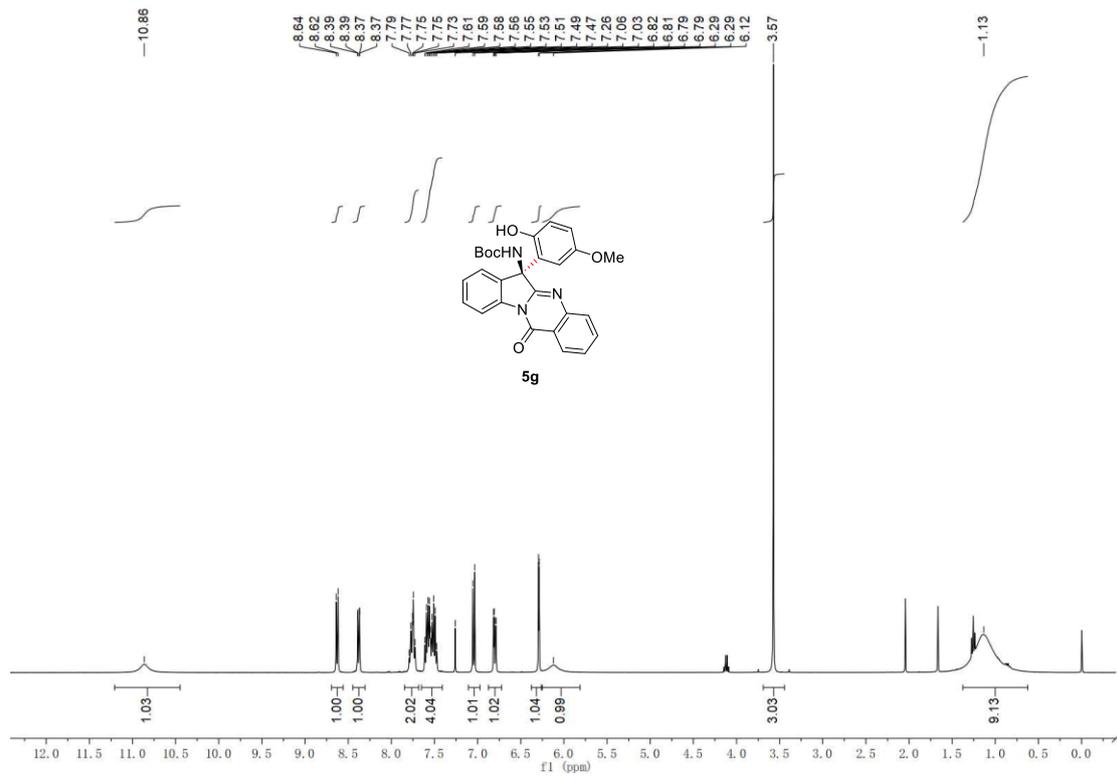
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **5e**



$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **5f**



$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **5g**



$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR of **5h**

