

Supporting Information

Direct enantio- and diastereoselective Mannich reactions of isatin-derived ketimines with oxo-indanecarboxylates catalyzed by chiral thiourea derived from hydroquinidine

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1. General Information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purification. All solvents were obtained from commercial sources and were purified according to standard procedures. For thin-layer chromatography (TLC), silica gel plates (HSGF 254) were used and compounds were visualized by irradiation with UV light. Purification of reaction products was carried out by flash column chromatography using silica gel (200-300 mesh). ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury-300BB (300 MHz), a Bruker NMR Spectrometer (400 MHz), or a Bruker NMR Spectrometer (500 MHz). All chemical shifts (δ) were given in ppm. Chemical shifts (δ ppm) are relative to the resonance of the deuterated solvent as the internal standard (CDCl_3 , δ 7.26 ppm for proton NMR, δ 77.16 ppm for carbon NMR). Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in Hertz (Hz). Mass spectra were recorded on the Bruker Agilent 1290 MicroTOF Q II. Melting points were measured on a melting point apparatus and were uncorrected. The ee values determination was carried out using chiral HPLC (Waters) with Chiracel IA-3 column, Chiracel IC-3 column. Optical rotations were measured on a Shanghai ShenGuang SGW-2 Polarimeter at $\lambda = 589$ nm. Optical rotations are reported as follows: $[\alpha]_{\text{D}}^{25}$ (c=g/100 mL, solvent)

2. Starting materials

All ketimines were prepared using reported procedures from corresponding isatins.¹ The chiral urea **3a**² and thioureas **3b**², **3c**³, **3d**⁴ and **3e**⁵ were prepared according to the procedure had been reported. All oxo-indanecarboxylates were prepared using reported procedures from corresponding Indanones⁶.

3. General procedure for racemic mixtures of Mannich reaction

Without protection of inert gases, oxo-indanecarboxylates (0.15 mmol, 1.5 equiv) and ketimines (0.1 mmol, 1 equiv) were dissolved in toluene (1 mL), the mixture was stirred at room temperature, DBU (3 μL , 0.2 equiv) was added in one portion, the resulting suspension was stirred at room temperature. Until complete disappearance of the starting materials detected by TLC, directly concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA=5:1).

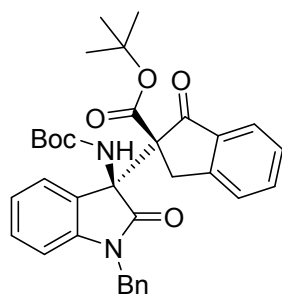
4. General procedure for enantio- and diastereoselective Mannich reaction

Method A: Without protection of inert gases, oxo-indanecarboxylates (0.15 mmol, 1.5 equiv) and cat **3e** (10 mol %) were dissolved in MTBE (1 mL), the mixture was stirred at -50 °C, ketimines (0.1 mmol, 1 equiv) was added in one portion, the resulting suspension was stirred at -50 °C. Until complete disappearance of the starting materials detected by TLC, directly concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA=5:1).

Method B: Without protection of inert gases, oxo-indanecarboxylates (0.15 mmol, 1.5 equiv) and cat **3e** (10 mol %) were dissolved in MTBE (1 mL), the mixture was stirred at -40 °C, ketimines (0.1 mmol, 1 equiv) was added in one portion, the resulting suspension was stirred at -40 °C. Until complete disappearance of the starting materials detected by TLC, directly concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA=5:1).

Method C: Without protection of inert gases, oxo-indanecarboxylates (0.15 mmol, 1.5 equiv) and cat **3e** (5 mol %) were dissolved in CHCl₃ (1 mL), the mixture was stirred at -50 °C, ketimines (0.1 mmol, 1 equiv) was added in one portion, the resulting suspension was stirred at -50 °C. Until complete disappearance of the starting materials detected by TLC, directly concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA=5:1).

tert-butyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4aa**)



Method A, white solid, 56.8 mg, 99% yield, mp = 76-77 °C, $[\alpha]_D^{25} = 81.2$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 95%, dr = 87:13 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 19.144$ min, $t_{\text{minor}} = 7.516$ min), Minor-($t_{\text{major}} = 13.205$ min, $t_{\text{minor}} = 7.023$ min)].

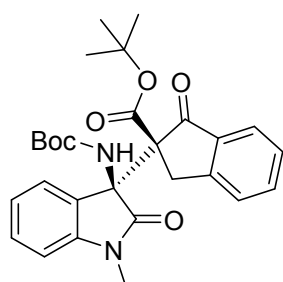
Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.93 – 7.65 (m, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.51 – 7.30 (m, 4H), 7.26 – 7.11 (m, 6H), 7.08 – 6.90 (m, 1H), 6.80 (s, 1H), 5.17 – 4.83 (m, 1H), 4.54 (br, 1H), 3.41 (d, *J* = 18.2 Hz, 1H), 2.63 (br, 1H), 1.46 (s,

9H), 1.35 – 1.25 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 173.67, 153.85, 151.43, 143.87, 136.13, 135.73, 135.18, 129.55, 129.37, 128.75, 128.18, 127.99, 127.75, 127.68, 126.13, 125.85, 124.75, 124.42, 122.98, 109.19, 84.15, 79.87, 44.55, 32.03, 31.55, 30.31, 29.80, 29.42, 28.31, 27.89.

HRMS (ESI): calculated for $\text{C}_{34}\text{H}_{37}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 569.2646, found 569.2646.

tert-butyl (S)-2-((S)-3-((*tert*-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ba**)



Method A, white solid, 49.0 mg, 99% yield, mp = 81-82 °C, $[\alpha]_{\text{D}}^{25} = 49.2$ ($c = 0.5$, CHCl_3). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 90%, dr = 83:17 [Chiralpak IC-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 37.667$ min, $t_{\text{minor}} = 43.351$ min),

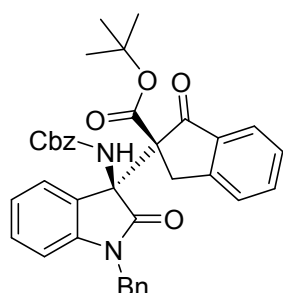
Minor-($t_{\text{major}} = 11.549$ min, $t_{\text{minor}} = 27.223$ min)].

Data for the major isomer: ^1H NMR (400 MHz, CDCl_3) δ 7.82 – 7.65 (m, 1H), 7.60 – 7.50 (m, 1H), 7.51 – 7.36 (m, 1H), 7.37 – 7.27 (m, 3H), 7.24 – 7.13 (m, 1H), 6.97 (s, 1H), 6.80 (d, $J = 7.8$ Hz, 1H), 3.45 (d, $J = 18.1$ Hz, 1H), 3.13 (s, 3H), 3.00 – 2.46 (m, 1H), 1.44 (s, 9H), 1.26 (br, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ 173.74, 153.84, 151.40, 144.59, 135.68, 135.37, 129.66, 129.50, 127.97, 127.77, 126.10, 125.75, 124.69, 124.39, 122.81, 108.33, 84.17, 79.88, 77.36, 29.79, 28.25, 27.89, 27.84, 26.55.

HRMS (ESI): calculated for $\text{C}_{28}\text{H}_{33}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 493.2332, found 493.2332.

tert-butyl (S)-2-((S)-1-benzyl-3-(((benzyloxy)carbonyl)amino)-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ca**)



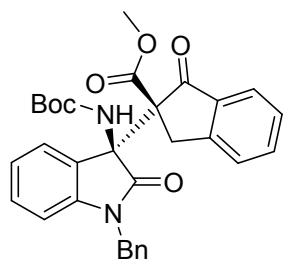
Method A, white solid, 55.1 mg, 92% yield, mp = 84-85 °C, $[\alpha]_{\text{D}}^{25} = 94.8$ ($c = 0.5$, CHCl_3). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 95%, dr = 79:21 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254

nm, 1 mL/min, Major-($t_{\text{major}} = 15.395$ min, $t_{\text{minor}} = 11.545$ min), Minor-($t_{\text{major}} = 14.564$ min, $t_{\text{minor}} = 10.994$ min)].

Data for the major isomer: ^1H NMR (400 MHz, CDCl_3) δ 7.96 – 7.79 (m, 1H), 7.78 – 7.56 (m, 3H), 7.45 – 7.26 (m, 11H), 7.25 – 7.07 (m, 3H), 6.77 – 6.50 (m, 1H), 5.12 – 4.90 (m, 3H), 4.52 (br, 1H), 3.47 (d, $J = 18.3$ Hz, 1H), 2.63 (br, 1H), 1.44 (s, 9H).
 ^{13}C NMR (101 MHz, CDCl_3) δ 172.69, 154.45, 151.25, 142.91, 135.94, 135.44, 135.36, 132.56, 128.80, 128.50, 128.45, 128.15, 128.08, 127.92, 127.83, 127.46, 126.08, 125.75, 124.83, 124.49, 115.92, 115.65, 110.72, 110.64, 84.65, 67.12, 44.61, 31.54, 30.16, 29.72, 27.75.

HRMS (ESI): calculated for $\text{C}_{37}\text{H}_{35}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 603.2490, found 603.2490.

methyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ab**)



Method C, white solid, 52.2 mg, 99% yield, mp = 85-86 °C, $[\alpha]_{\text{D}}^{25} = 96.8$ ($c = 0.5$, CHCl_3). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 99%, dr = 91:9 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 21.016$ min, $t_{\text{minor}} = 7.595$ min),

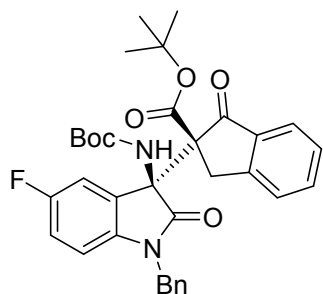
Minor-($t_{\text{major}} = 31.231$ min, $t_{\text{minor}} = 14.313$ min)].

Data for the major isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.87 – 7.64 (m, 1H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.51 – 7.26 (m, 5H), 7.26 – 6.89 (m, 6H), 6.80 (d, $J = 6.8$ Hz, 1H), 5.16 – 4.78 (m, 1H), 4.62 (br, 1H), 3.78 (s, 3H), 3.46 (d, $J = 18.3$ Hz, 1H), 2.86 (br, 1H), 1.27 (br, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 173.55, 153.87, 151.13, 143.77, 135.98, 135.88, 135.57, 135.36, 129.60, 129.40, 128.69, 128.09, 127.83, 127.64, 126.02, 125.86, 124.81, 124.55, 122.96, 109.17, 80.04, 77.28, 53.40, 44.51, 29.67, 28.18.

HRMS (ESI): calculated for $\text{C}_{31}\text{H}_{31}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 527.2177, found 527.2177.

tert-butyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-5-fluoro-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4da**)



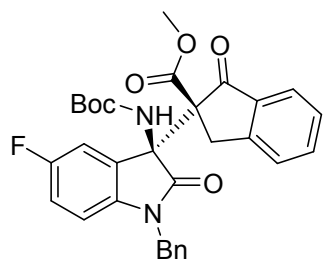
Method A, white solid, 58.5 mg, 99% yield, mp = 86-87 °C, $[\alpha]_D^{25} = 80$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 94%, dr = 82:18 [Chiralpak IC-3, hexane/i-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 21.949$ min, $t_{\text{minor}} = 39.401$ min), Minor-($t_{\text{major}} = 6.370$ min, $t_{\text{minor}} = 18.779$ min)].

Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.94 – 7.64 (m, 1H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.51 – 7.26 (m, 5H), 7.25 – 7.10 (m, 4H), 7.03 – 6.84 (m, 1H), 6.70 (s, 1H), 5.05 – 4.85 (m, 1H), 4.55 (br, 1H), 3.40 (d, *J* = 18.1 Hz, 1H), 2.68 (br, 1H), 1.44 (s, 9H), 1.35 – 1.26 (m, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 173.56, 160.36, 158.42, 153.91, 151.30, 139.86, 135.82, 135.67, 135.33, 135.01, 128.82, 128.12, 127.92, 127.80, 126.14, 125.87, 124.84, 124.56, 115.77 (d, *J* = 23.5 Hz), 109.66, 84.33, 80.16, 44.70, 32.03, 31.55, 30.31, 29.80, 29.46, 28.33, 27.85.

HRMS (ESI): calculated for C₃₄H₃₆FN₂O₆ [M+H]⁺: 587.2552, found 587.2552.

methyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-5-fluoro-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4db**)



Method C, white solid, 54.3 mg, 99% yield, mp = 70-71 °C, $[\alpha]_D^{25} = 96$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 99%, dr = 88:12 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 17.092$ min, $t_{\text{minor}} = 6.967$ min), Minor-($t_{\text{major}} = 19.957$ min, $t_{\text{minor}} = 16.404$ min)].

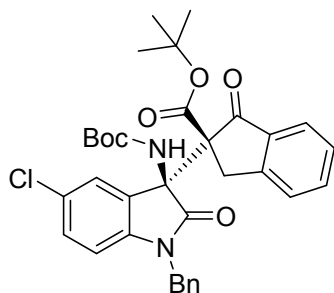
Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.91 – 7.71 (m, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.55 – 7.26 (m, 5H), 7.24 – 6.79 (m, 5H), 6.70 (s, 1H), 5.41 – 4.75 (m, 1H), 4.61 (br, 1H), 3.76 (s, 3H), 3.44 (d, *J* = 18.3 Hz, 1H), 2.87 (br, 1H), 1.39 – 1.27 (m, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 173.43, 160.26, 158.34, 153.91, 151.00, 139.80, 136.06, 135.67, 135.49, 128.75, 128.23, 127.98, 127.86, 127.75, 126.05, 125.89, 124.91,

124.70, 115.83 (d, $J = 23.5$ Hz), 109.66 (d, $J = 8.0$ Hz), 80.30, 53.45, 44.65, 31.94, 31.45, 30.21, 29.71, 29.35, 28.20.

HRMS (ESI): calculated for $C_{31}H_{30}FN_2O_6$ $[M+H]^+$: 545.2082, found 545.2081.

tert-butyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-5-chloro-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ea**)



Method A, white solid, 60.3 mg, 99% yield, mp = 78-79 °C, $[\alpha]_D^{25} = 112.4$ ($c = 0.5$, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 94%, dr = 84:16 [Chiralpak IC-3, hexane/*i*-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{major} = 19.563$ min, $t_{minor} = 36.908$ min), Minor-($t_{major} = 6.042$ min, $t_{minor} =$

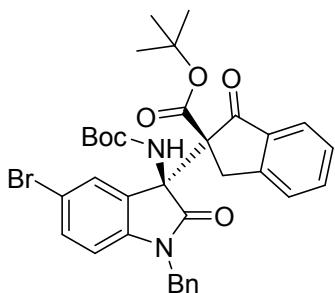
12.775 min)].

Data for the major isomer: 1H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.66 (m, 1H), 7.60 (t, $J = 7.3$ Hz, 1H), 7.58 – 7.29 (m, 5H), 7.28 – 6.95 (m, 5H), 6.73 (s, 1H), 5.08 – 4.89 (m, 1H), 4.57 (br, 1H), 3.45 (d, $J = 18.1$ Hz, 1H), 2.68 (br, 1H), 1.47 (s, 9H), 1.38 – 1.28 (m, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.34, 153.94, 151.32, 142.43, 135.91, 135.67, 135.62, 135.36, 129.43, 129.32, 128.84, 128.80, 128.13, 127.84, 126.12, 125.86, 125.34, 124.84, 124.55, 110.15, 84.46, 80.22, 44.67, 32.03, 31.55, 30.31, 29.80, 29.46, 28.35, 27.85.

HRMS (ESI): calculated for $C_{34}H_{36}ClN_2O_6$ $[M+H]^+$: 603.2256, found 603.2257.

tert-butyl (S)-2-((S)-1-benzyl-5-bromo-3-((*tert*-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4fa**)



Method A, white solid, 64.7 mg, 99% yield, mp = 83-84 °C, $[\alpha]_D^{25} = 72$ ($c = 0.5$, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 93%, dr = 85:15 [Chiralpak IC-3, hexane/*i*-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{major} = 19.834$ min, t_{minor}

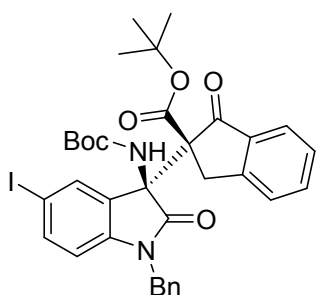
= 38.317 min), Minor-($t_{\text{major}} = 6.072$ min, $t_{\text{minor}} = 11.749$ min)].

Data for the major isomer: ^1H NMR (300 MHz, CDCl_3) δ 7.80 (br, 1H), 7.67 – 7.47 (m, 2H), 7.46 – 7.26 (m, 4H), 7.26 – 7.01 (m, 5H), 6.65 (d, $J = 7.4$ Hz, 1H), 5.03 – 4.84 (m, 1H), 4.55 (br, 1H), 3.43 (d, $J = 18.2$ Hz, 1H), 2.67 (br, 1H), 1.44 (s, 9H), 1.35 – 1.23 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 173.25, 153.92, 151.32, 142.90, 135.65, 135.61, 135.39, 132.33, 132.21, 128.85, 128.81, 128.14, 127.95, 127.86, 127.03, 126.12, 125.87, 124.86, 124.54, 110.67, 84.51, 80.27, 53.55, 44.66, 31.70, 31.56, 30.31, 29.81, 28.36, 27.86.

HRMS (ESI): calculated for $\text{C}_{34}\text{H}_{36}\text{BrN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 647.1751, found 647.1751.

tert-butyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-5-iodo-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ga**)



Method A, white solid, 69.5 mg, 99% yield, mp = 80-81 °C, $[\alpha]_{\text{D}}^{25} = 60.8$ ($c = 0.5$, CHCl_3). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 94%, dr = 84:16 [Chiralpak IC-3, hexane/*i*-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 22.199$ min, $t_{\text{minor}} = 43.875$

min), Minor-($t_{\text{major}} = 6.304$ min, $t_{\text{minor}} = 11.251$ min)].

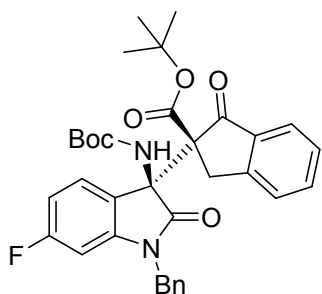
Data for the major isomer: ^1H NMR (300 MHz, CDCl_3) δ 7.94 – 7.64 (m, 2H), 7.63 – 7.46 (m, 2H), 7.45 – 7.26 (m, 4H), 7.26 – 6.99 (m, 4H), 6.56 (d, $J = 7.6$ Hz, 1H), 5.07 – 4.84 (m, 1H), 4.54 (br, 1H), 3.44 (d, $J = 18.4$ Hz, 1H), 2.64 (br, 1H), 1.45 (s, 9H), 1.35 – 1.23 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 172.92, 153.81, 151.28, 143.46, 138.16, 138.05, 135.53, 135.48, 135.30, 133.38, 128.75, 128.70, 128.03, 127.76, 126.00, 125.76, 124.75, 124.49, 124.40, 111.19, 84.45, 80.15, 44.50, 31.94, 31.46, 30.22, 29.71, 29.37, 28.27, 27.78.

HRMS (ESI): calculated for $\text{C}_{34}\text{H}_{36}\text{IN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 695.1613, found 695.1614.

tert-butyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-6-fluoro-2-oxoindolin-

3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ha**)



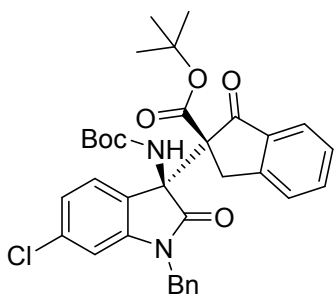
Method A, white solid, 58.5 mg, 99% yield, mp = 73-74 °C, $[\alpha]_D^{25} = 103.2$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 93%, dr = 82:18 [Chiralpak IC-3, hexane/i-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 25.210$ min, $t_{\text{minor}} = 36.502$ min), Minor-($t_{\text{major}} = 6.492$ min, $t_{\text{minor}} = 22.753$ min)].

Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.90 – 7.64 (m, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.53 – 7.26 (m, 6H), 7.25 – 6.88 (m, 3H), 6.82 – 6.28 (m, 2H), 5.13 – 4.74 (m, 1H), 4.52 (br, 1H), 3.41 (d, *J* = 18.1 Hz, 1H), 2.67 (br, 1H), 1.43 (s, 9H), 1.35 – 1.25 (m, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 173.92, 164.62, 162.66, 153.90, 151.29, 145.51, 135.88, 135.74, 135.60, 135.31, 128.88, 128.11, 127.89, 126.19, 125.87, 124.81, 124.47, 123.48, 109.00, 98.06 (d, *J* = 22.1 Hz), 84.25, 80.12, 44.76, 31.55, 30.31, 29.81, 29.47, 28.33, 27.86.

HRMS (ESI): calculated for C₃₄H₃₆FN₂O₆ [M+H]⁺: 587.2552, found 587.2551.

tert-butyl (*S*)-2-((*S*)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-6-chloro-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ia**)



Method A, white solid, 60.2 mg, 99% yield, mp = 73-74 °C, $[\alpha]_D^{25} = 72.8$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 92%, dr = 84:16 [Chiralpak IA-3, hexane/i-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 14.721$ min, $t_{\text{minor}} = 6.531$ min), Minor-($t_{\text{major}} = 9.719$ min, $t_{\text{minor}} = 6.249$ min)].

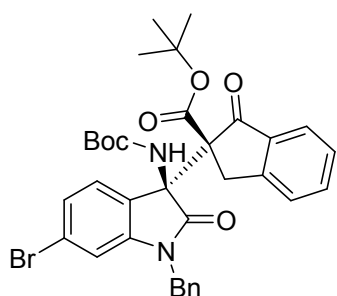
Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.89 – 7.64 (m, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.51 – 7.27 (m, 6H), 7.25 – 7.11 (m, 3H), 7.07 – 6.87 (m, 1H), 6.77 (s, 1H), 5.07 – 4.76 (m, 1H), 4.51 (br, 1H), 3.40 (d, *J* = 18.0 Hz, 1H), 2.65 (br, 1H), 1.43 (s, 9H), 1.34 – 1.25 (m, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 173.82, 153.90, 151.28, 145.15, 135.67, 135.58, 135.34,

135.31, 135.09, 128.89, 128.13, 128.09, 127.90, 126.25, 125.88, 124.84, 124.47, 122.89, 122.73, 109.88, 84.27, 80.21, 44.71, 32.01, 31.54, 30.31, 29.81, 29.47, 28.34, 27.86.

HRMS (ESI): calculated for $C_{34}H_{36}ClN_2O_6$ $[M+H]^+$: 603.2256, found 603.2256.

tert-butyl (S)-2-((S)-1-benzyl-6-bromo-3-((*tert*-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ja**)



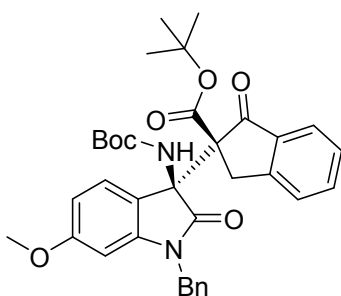
Method A, white solid, 64.6 mg, 99% yield, mp = 87-88 °C, $[a]_D^{25} = 91.6$ ($c = 0.5$, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 92%, dr = 84:16 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{major} = 13.748$ min, $t_{minor} = 6.516$ min), Minor-($t_{major} = 9.411$ min, $t_{minor} = 6.168$ min)].

Data for the major isomer: 1H NMR (300 MHz, $CDCl_3$) δ 7.87 – 7.63 (m, 1H), 7.63 – 7.54 (m, 1H), 7.53 – 7.26 (m, 5H), 7.26 – 7.01 (m, 4H), 6.91 (s, 1H), 5.10 – 4.82 (m, 1H), 4.53 (br, 1H), 3.39 (d, $J = 18.1$ Hz, 1H), 2.66 (br, 1H), 1.42 (s, 9H), 1.35 – 1.24 (m, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.56, 153.86, 151.19, 145.17, 135.86, 135.56, 135.47, 135.24, 128.80, 128.04, 127.99, 127.80, 126.17, 125.79, 125.59, 124.74, 124.39, 123.21, 123.01, 112.50, 84.18, 80.11, 44.60, 31.94, 31.46, 30.22, 29.71, 29.37, 28.24, 27.76.

HRMS (ESI): calculated for $C_{34}H_{36}BrN_2O_6$ $[M+H]^+$: 647.1751, found 647.1750.

tert-butyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-6-methoxy-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ka**)



Method A, white solid, 59.7 mg, 99% yield, mp = 93-94 °C, $[a]_D^{25} = 72.6$ ($c = 0.5$, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 96%, dr = 85:15 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{major} = 19.538$ min,

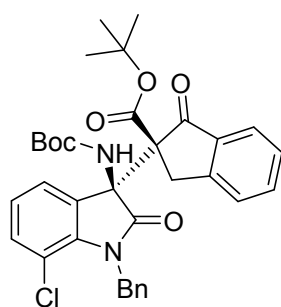
$t_{\text{minor}} = 8.048 \text{ min}$), Minor-($t_{\text{major}} = 11.777 \text{ min}$, $t_{\text{minor}} = 8.634 \text{ min}$)).

Data for the major isomer: ^1H NMR (300 MHz, CDCl_3) δ 7.87 – 7.67 (m, 1H), 7.65 – 7.54 (m, 1H), 7.53 – 7.28 (m, 4H), 7.28 – 7.08 (m, 5H), 6.56 – 6.19 (m, 2H), 5.12 – 4.89 (m, 1H), 4.55 (br, 1H), 3.76 (s, 3H), 3.43 (d, $J = 18.2 \text{ Hz}$, 1H), 2.67 (br, 1H), 1.47 (s, 9H), 1.36 – 1.26 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 173.92, 160.90, 153.92, 151.44, 145.18, 136.09, 135.81, 135.72, 135.14, 128.77, 128.17, 127.96, 127.70, 126.22, 125.84, 125.46, 124.74, 124.39, 106.47, 97.32, 84.03, 79.78, 77.36, 55.38, 44.56, 32.03, 31.55, 30.30, 29.80, 28.36, 27.89.

HRMS (ESI): calculated for $\text{C}_{35}\text{H}_{39}\text{N}_2\text{O}_7$ $[\text{M}+\text{H}]^+$: 599.2752, found 599.2751.

tert-butyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-7-chloro-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4la**)



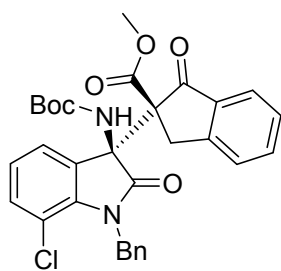
Method A, white solid, 60.3 mg, 99% yield, mp = 82–83 °C, $[\alpha]_{\text{D}}^{25} = 42$ ($c = 0.5$, CHCl_3). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 90%, dr = 88:12 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 12.425 \text{ min}$, $t_{\text{minor}} = 5.730 \text{ min}$), Minor-($t_{\text{major}} = 8.634 \text{ min}$, $t_{\text{minor}} = 5.444 \text{ min}$)].

Data for the major isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.84 – 7.64 (m, 1H), 7.52 (t, $J = 7.3 \text{ Hz}$, 1H), 7.48 – 7.26 (m, 4H), 7.25 – 7.03 (m, 6H), 6.94 (s, 1H), 5.48 – 5.02 (m, 2H), 3.45 (d, $J = 18.2 \text{ Hz}$, 1H), 2.69 (br, 1H), 1.45 (s, 9H), 1.37 – 1.24 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 174.60, 166.23, 161.44, 153.62, 151.11, 140.01, 137.52, 135.36, 135.22, 132.19, 128.31, 127.93, 127.75, 127.51, 126.99, 125.81, 124.65, 123.68, 123.06, 115.45, 84.30, 80.11, 45.66, 31.95, 31.44, 30.19, 29.71, 28.23, 28.04, 27.78.

HRMS (ESI): calculated for $\text{C}_{34}\text{H}_{36}\text{ClN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 603.2256, found 603.2254.

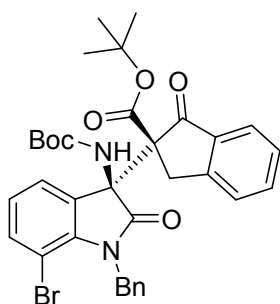
methyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-7-chloro-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4lb**)



Method C, white solid, 55.9 mg, 99% yield, mp = 68-69 °C, $[\alpha]_D^{25} = 44.4$ ($c = 0.5$, CHCl_3). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 97%, dr = 87:13 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 14.927$ min, $t_{\text{minor}} = 6.778$ min), Minor-($t_{\text{major}} = 20.596$ min, $t_{\text{minor}} = 8.938$ min)].

Data for the major isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.91 – 7.67 (m, 1H), 7.57 (t, $J = 7.4$ Hz, 1H), 7.48 – 7.30 (m, 3H), 7.28 – 7.03 (m, 7H), 6.95 (s, 1H), 5.50 – 5.04 (m, 2H), 3.80 (s, 3H), 3.53 (d, $J = 18.5$ Hz, 1H), 2.90 (br, 1H), 1.39 – 1.24 (m, 9H). ^{13}C NMR (126 MHz, CDCl_3) δ 174.59, 153.89, 150.96, 140.00, 137.46, 136.03, 135.48, 135.30, 132.33, 128.34, 128.12, 127.92, 127.53, 127.06, 126.59, 125.90, 124.81, 123.73, 122.85, 115.52, 80.37, 77.28, 53.51, 45.71, 31.53, 30.30, 30.16, 29.71, 28.19. HRMS (ESI): calculated for $\text{C}_{31}\text{H}_{30}\text{ClN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 561.1787, found 561.1786.

tert-butyl (*S*)-2-((*S*)-1-benzyl-7-bromo-3-((*tert*-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ma**)

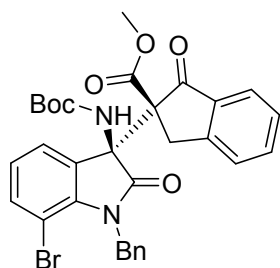


Method A, white solid, 64.6mg, 99% yield, mp = 63-64 °C, $[\alpha]_D^{25} = 27.2$ ($c = 0.5$, CHCl_3). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 85%, dr = 88:12 [Chiralpak IA-3, hexane/i-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 14.540$ min, $t_{\text{minor}} = 6.781$ min), Minor-($t_{\text{major}} = 9.718$ min, $t_{\text{minor}} = 6.098$ min)].

Data for the major isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.83 – 7.65 (m, 1H), 7.61 – 7.27 (m, 6H), 7.25 – 7.12 (m, 5H), 6.88 (s, 1H), 5.52 – 5.26 (m, 1H), 5.15 (br, 1H), 3.47 (d, $J = 18.0$ Hz, 1H), 2.71 (br, 1H), 1.45 (s, 9H), 1.36 – 1.24 (m, 9H). ^{13}C NMR (126 MHz, CDCl_3) δ 174.90, 153.89, 151.17, 141.53, 137.56, 135.66, 135.45, 135.32, 134.72, 128.44, 128.36, 128.02, 127.78, 127.40, 126.97, 125.87, 124.74, 124.09, 123.83, 102.65, 84.40, 80.29, 45.48, 32.05, 31.55, 30.31, 29.80, 29.47, 28.32, 27.87.

HRMS (ESI): calculated for $\text{C}_{34}\text{H}_{36}\text{BrN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 647.1751, found 647.1751.

methyl (S)-2-((S)-1-benzyl-7-bromo-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4mb**)



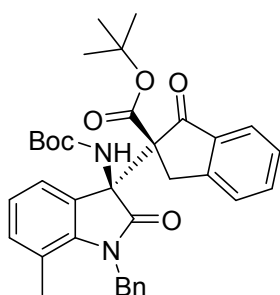
Method C, white solid, 60.3 mg, 99% yield, mp = 72-73 °C, $[\alpha]_D^{25} = 75.6$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 97%, dr = 87:13 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 15.771$ min, $t_{\text{minor}} = 6.949$ min), Minor-($t_{\text{major}} = 20.316$ min, $t_{\text{minor}} = 8.828$ min)].

Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.82 – 7.68 (m, 1H), 7.66 – 7.28 (m, 6H), 7.25 – 7.04 (m, 5H), 6.86 (s, 1H), 5.52 – 5.26 (m, 1H), 5.17 (br, 1H), 3.78 (s, 3H), 3.52 (d, *J* = 18.3 Hz, 1H), 2.95 (br, 1H), 1.40 – 1.26 (m, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 174.82, 153.91, 150.93, 141.44, 137.39, 135.70, 135.49, 135.28, 128.29, 128.11, 127.86, 127.35, 126.94, 126.58, 126.08, 125.87, 124.81, 124.73, 124.10, 102.63, 80.39, 77.27, 53.52, 45.44, 31.53, 30.30, 30.16, 29.71, 28.20.

HRMS (ESI): calculated for C₃₁H₃₀BrN₂O₆ [M+H]⁺: 605.1282, found 605.1281.

tert-butyl (S)-2-((S)-1-benzyl-3-((tert-butoxycarbonyl)amino)-7-methyl-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4na**)



Method B, white solid, 57.1 mg, 98% yield, mp = 90-91 °C, $[\alpha]_D^{25} = 46$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 87%, dr = 87:13 [Chiralpak IA-3, hexane/i-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 22.895$ min, $t_{\text{minor}} = 7.433$ min), Minor-($t_{\text{major}} = 12.990$ min, $t_{\text{minor}} = 6.186$ min)].

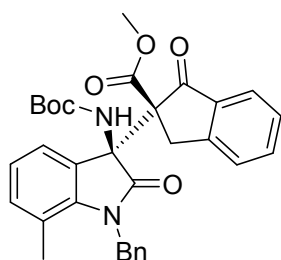
Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.89 – 7.67 (m, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.51 – 7.27 (m, 4H), 7.25 – 7.07 (m, 5H), 7.03 – 6.57 (m, 2H), 5.38 – 4.76 (m, 2H), 3.54 (d, *J* = 18.2 Hz, 1H), 2.77 (br, 1H), 2.30 (s, 3H), 1.49 (s, 9H), 1.40 – 1.26 (m, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 175.07, 153.81, 151.28, 142.12, 137.92, 135.62, 135.11,

133.61, 128.68, 128.56, 127.89, 127.65, 126.97, 126.58, 126.06, 125.68, 124.67, 124.57, 122.78, 119.67, 84.13, 79.74, 46.17, 30.35, 30.21, 30.16, 29.71, 28.27, 28.04, 27.82, 19.26.

HRMS (ESI): calculated for $C_{35}H_{39}N_2O_6$ $[M+H]^+$: 583.2803, found 583.2804.

methyl (S)-2-((S)-1-benzyl-3-((tert-butoxycarbonyl)amino)-7-methyl-2-oxoindolin-3-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4nb**)



Method C, white solid, 53.8 mg, 99% yield, mp = 78-79 °C, $[\alpha]_D^{25} = 105.6$ ($c = 0.5$, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 97%, dr = 90:10 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{major} = 22.910$ min, $t_{minor} = 7.143$ min),

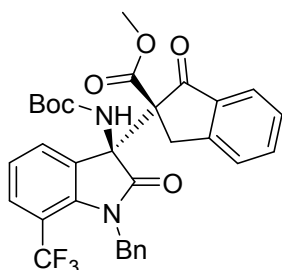
Minor-($t_{major} = 36.438$ min, $t_{minor} = 9.346$ min)].

Data for the major isomer: 1H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.70 (m, 1H), 7.59 (t, $J = 7.2$ Hz, 1H), 7.54 – 7.29 (m, 4H), 7.28 – 7.12 (m, 5H), 7.00 (d, $J = 5.6$ Hz, 1H), 6.90 (s, 1H), 5.31 – 4.92 (m, 2H), 3.83 (s, 3H), 3.61 (d, $J = 18.3$ Hz, 1H), 3.11 (br, 1H), 2.33 (s, 3H), 1.39 – 1.29 (m, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 175.13, 153.94, 151.08, 142.15, 137.84, 135.88, 135.56, 135.49, 135.36, 133.75, 128.69, 128.59, 128.06, 127.02, 126.58, 125.76, 124.81, 122.88, 121.91, 119.77, 80.02, 77.26, 53.44, 46.22, 31.50, 30.16, 29.71, 29.37, 28.23, 19.26.

HRMS (ESI): calculated for $C_{32}H_{33}N_2O_6$ $[M+H]^+$: 541.2333, found 541.2333.

methyl (S)-2-((S)-1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxo-7-(trifluoromethyl)indolin-3-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4ob**)



Method C, white solid, 59.1 mg, 99% yield, mp = 68-69 °C, $[\alpha]_D^{25} = 64.4$ ($c = 0.5$, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 96%, dr = 92:8 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{major} = 9.390$ min, $t_{minor} = 5.829$ min),

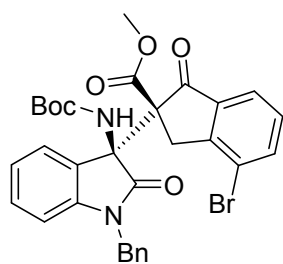
Minor-($t_{\text{major}} = 12.184\text{min}$, $t_{\text{minor}} = 6.544\text{min}$).

Data for the major isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.83 – 7.67 (m, 1H), 7.66 – 7.47 (m, 3H), 7.45 – 7.28 (m, 3H), 7.24 – 6.99 (m, 6H), 5.24 – 4.85 (m, 2H), 3.78 (s, 3H), 3.57 (d, $J = 18.3$ Hz, 1H), 3.05 (br, 1H), 1.38 – 1.25 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 175.81, 153.86, 150.79, 142.37, 136.23, 135.63, 135.49, 135.29, 128.25, 128.02, 127.86, 127.81, 126.65, 126.43, 126.07, 125.94, 124.92, 124.73, 124.44, 122.33, 112.91 (d, $J = 32.7$ Hz), 80.58, 77.26, 53.55, 47.37, 31.52, 30.29, 30.16, 29.71, 28.16.

HRMS (ESI): calculated for $\text{C}_{32}\text{H}_{30}\text{F}_3\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 595.2050, found 595.2050.

methyl (S)-2-((S)-1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-4-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylat (**4ac**)



Method C, white solid, 60.2 mg, 99% yield, mp = 76-77 °C, $[\alpha]_{\text{D}}^{25} = 72.8$ ($c = 0.5$, CHCl_3). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 99%, dr = 80:20 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 37.978$ min, $t_{\text{minor}} = 6.595$ min),

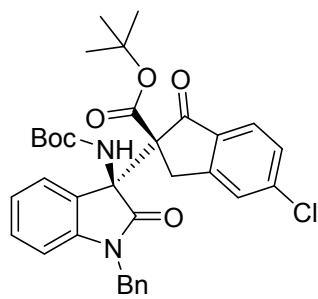
Minor-($t_{\text{major}} = 32.189$ min, $t_{\text{minor}} = 11.685$ min)].

Data for the major isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.81 – 7.62 (m, 2H), 7.52 – 7.29 (m, 7H), 7.25 – 6.88 (m, 3H), 6.75 (d, $J = 7.7$ Hz, 1H), 5.09 – 4.92 (m, 1H), 4.72 (br, 1H), 3.83 (s, 3H), 3.49 (d, $J = 18.8$ Hz, 1H), 2.95 (br, 1H), 1.37 – 1.27 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 173.72, 153.82, 150.63, 144.01, 138.55, 138.16, 137.53, 135.65, 129.93, 129.83, 129.53, 128.89, 128.79, 127.59, 127.55, 123.59, 123.32, 123.06, 121.19, 109.61, 80.17, 77.27, 53.58, 44.82, 31.53, 30.16, 29.71, 29.37, 28.19.

HRMS (ESI): calculated for $\text{C}_{31}\text{H}_{30}\text{BrN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 605.1282, found 605.1282.

tert-butyl (S)-2-((S)-1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-5-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4ad**)



Method A, white solid, 60.1mg, 99% yield, mp = 63-64 °C, $[\alpha]_{\text{D}}^{25} = 27.2$ ($c = 0.5$, CHCl_3). Enantiomeric excess and

diastereomer ratio were established by HPLC analysis, ee = 95%, dr = 82:18

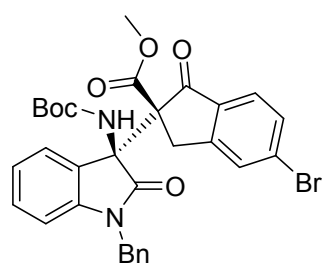
[Chiralpak IA-3, hexane/i-PrOH = 90:10, 254 nm, 1 mL/min, Major-(t_{major} = 15.348 min, t_{minor} = 7.163 min), Minor-(t_{major} = 12.411 min, t_{minor} = 6.337 min)].

Data for the major isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.80 – 7.56 (m, 1H), 7.53 – 7.27 (m, 6H), 7.25 – 6.56 (m, 6H), 5.15 – 4.76 (m, 1H), 4.52 (br, 1H), 3.34 (d, J = 18.4 Hz, 1H), 2.36 (br, 1H), 1.46 (s, 9H), 1.34 – 1.24 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 173.37, 153.81, 152.76, 143.81, 141.62, 136.08, 134.18, 129.70, 129.57, 128.84, 128.82, 128.69, 128.39, 127.90, 126.40, 126.18, 125.77, 125.53, 123.16, 109.16, 84.46, 79.98, 44.55, 32.05, 31.56, 30.32, 29.82, 29.48, 28.32, 27.91.

HRMS (ESI): calculated for $\text{C}_{34}\text{H}_{36}\text{ClN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 603.2256, found 603.2256.

methyl (*S*)-2-((*S*)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-5-bromo-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4ae**)



Method C, white solid, 60.1 mg, 99% yield, mp = 76–77 °C,

$[\alpha]_{\text{D}}^{25} = 72.8$ (c = 0.5, CHCl_3). Enantiomeric excess and

diastereomer ratio were established by HPLC analysis, ee =

99%, dr = 82:18 [Chiralpak AD-H, hexane/i-PrOH

=80:20, 254 nm, 1 mL/min, Major-(t_{major} = 42.464 min, t_{minor}

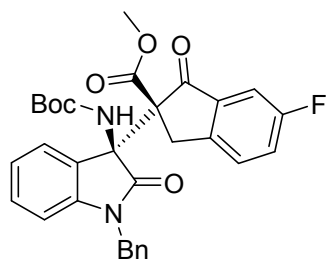
= 9.950 min), Minor-(t_{major} = 24.555min, t_{minor} = 14.650min)].

Data for the major isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.77 – 7.48 (m, 2H), 7.47 – 7.28 (m, 6H), 7.24 – 6.68 (m, 5H), 4.97 (d, J = 14.8 Hz, 1H), 4.57 (br, 1H), 3.78 (s, 3H), 3.38 (d, J = 18.6 Hz, 1H), 2.67 (br, 1H), 1.35 – 1.22 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 173.37, 153.87, 152.65, 143.79, 136.01, 134.48, 131.84, 131.67, 130.85, 129.84, 129.69, 129.44, 129.34, 128.86, 128.39, 127.96, 125.95, 125.75, 123.22, 109.22, 80.25, 77.37, 53.60, 44.58, 31.59, 30.26, 29.81, 29.47, 28.28.

HRMS (ESI): calculated for $\text{C}_{31}\text{H}_{30}\text{BrN}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 605.1282, found 605.1283.

methyl (*S*)-2-((*S*)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-6-fluoro-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4af**)



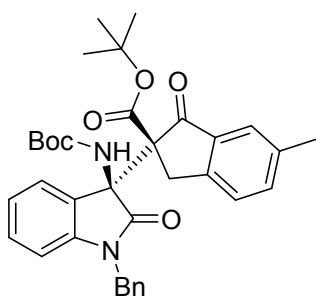
Method C, white solid, 54.1 mg, 99% yield, mp = 79-80 °C, $[\alpha]_D^{25} = 104$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 99%, dr > 99:1 [Chiralpak AD-H, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 15.858$ min, $t_{\text{minor}} = 6.935$ min), Minor-($t_{\text{major}} = 18.188$ min, $t_{\text{minor}} = 28.792$ min)].

Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.57 – 7.26 (m, 6H), 7.26 – 6.90 (m, 6H), 6.82 (d, $J = 6.8$ Hz, 1H), 4.96 (d, $J = 15.0$ Hz, 1H), 4.63 (br, 1H), 3.79 (s, 3H), 3.41 (d, $J = 18.2$ Hz, 1H), 2.83 (br, 1H), 1.34 – 1.22 (m, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 173.45, 163.52, 161.54, 153.79, 146.50, 143.77, 137.28 (d, $J = 7.7$ Hz), 135.93, 129.72, 128.71, 128.10, 127.69, 127.24 (d, $J = 8.0$ Hz), 124.34, 123.20, 123.01, 110.63, 110.45, 109.22, 80.16, 77.26, 53.51, 44.51, 31.92, 31.48, 30.17, 29.71, 29.34, 28.16.

HRMS (ESI): calculated for C₃₁H₃₀FN₂O₆ [M+H]⁺: 545.2082, found 545.2081.

tert-butyl (S)-2-((S)-1-benzyl-3-((*tert*-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-6-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4ag**)



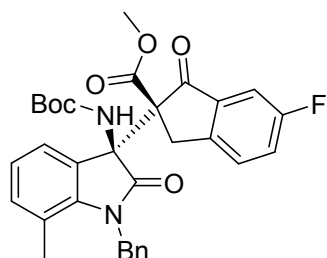
Method A, white solid, 58.1 mg, 99% yield, mp = 63-64 °C, $[\alpha]_D^{25} = 82.8$ (c = 0.5, CHCl₃). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 94%, dr = 82:18 [Chiralpak IA-3, hexane/i-PrOH = 90:10, 254 nm, 1 mL/min, Major-($t_{\text{major}} = 14.357$ min, $t_{\text{minor}} = 7.536$ min), Minor-($t_{\text{major}} = 11.478$ min, $t_{\text{minor}} = 6.696$ min)].

Data for the major isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.77 – 7.55 (m, 1H), 7.53 – 7.27 (m, 5H), 7.25 – 6.94 (m, 6H), 6.78 (s, 1H), 5.18 – 4.77 (m, 1H), 4.53 (br, 1H), 3.36 (d, $J = 18.0$ Hz, 1H), 2.64 (br, 1H), 2.39 (s, 3H), 1.46 (s, 9H), 1.36 – 1.19 (m, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 173.59, 153.71, 148.79, 143.80, 137.88, 136.43, 136.05, 135.89, 135.79, 129.41, 129.23, 128.65, 128.07, 127.58, 125.71, 125.44, 124.58, 124.19, 122.88, 109.10, 83.95, 79.72, 44.46, 30.33, 29.71, 29.52, 28.38, 28.22, 27.83, 27.80, 21.13.

HRMS (ESI): calculated for $C_{35}H_{39}N_2O_6$ $[M+H]^+$: 583.2803, found 583.2803.

methyl (S)-2-((S)-1-benzyl-3-((tert-butoxycarbonyl)amino)-7-methyl-2-oxoindolin-3-yl)-6-fluoro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4nf**)



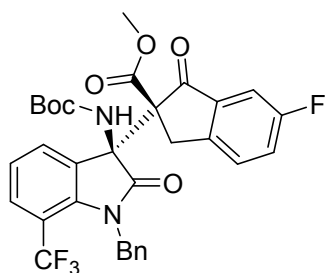
Method C, white solid, 60.4 mg, 99% yield, mp = 68-69 °C, $[\alpha]_D^{25} = 48.4$ (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 94%, dr = 80:20 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{major} = 20.758$ min, $t_{minor} = 6.621$ min), Minor-($t_{major} = 32.967$ min, $t_{minor} = 10.797$ min)].

Data for the major isomer: 1H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.26 (m, 4H), 7.26 – 7.10 (m, 6H), 6.99 (d, $J = 6.1$ Hz, 1H), 6.89 (s, 1H), 5.24 – 4.87 (m, 2H), 3.82 (s, 3H), 3.54 (d, $J = 18.1$ Hz, 1H), 3.04 (br, 1H), 2.31 (s, 3H), 1.39 – 1.27 (m, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.96, 163.50, 161.52, 153.86, 146.45, 142.13, 137.76, 137.27 (d, $J = 7.3$ Hz), 133.88, 133.67, 128.68, 128.60, 127.57, 127.14 (d, $J = 8.2$ Hz), 126.58, 126.45, 123.21, 123.02, 119.85, 110.55 (d, $J = 22.3$ Hz), 80.13, 77.25, 53.55, 46.21, 31.52, 30.16, 29.71, 29.35, 28.22, 19.24.

HRMS (ESI): calculated for $C_{32}H_{32}FN_2O_6$ $[M+H]^+$: 559.2239, found 559.2239.

methyl (S)-2-((S)-1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxo-7-(trifluoromethyl)indolin-3-yl)-6-fluoro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**4of**)



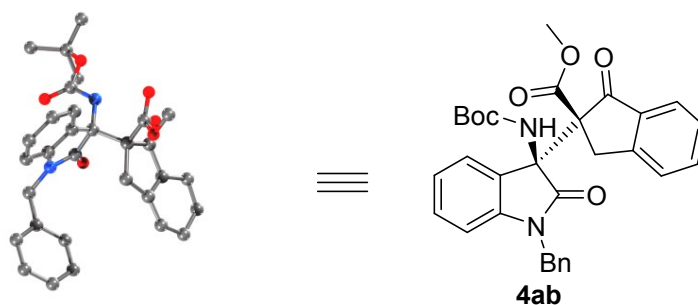
Method C, white solid, 65.3 mg, 99% yield, mp = 84-85 °C, $[\alpha]_D^{25} = 64.8$ (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 91%, dr = 83:17 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major-($t_{major} = 9.876$ min, $t_{minor} = 5.504$ min), Minor-($t_{major} = 10.716$ min, $t_{minor} = 6.713$ min)].

Data for the major isomer: 1H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.45 (m, 2H), 7.44 – 7.27 (m, 3H), 7.26 – 6.83 (m, 7H), 5.27 – 4.80 (m, 2H), 3.79 (s, 3H), 3.52 (d, $J = 18.0$ Hz, 1H), 2.97 (br, 1H), 1.37 – 1.25 (m, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 175.66, 163.56, 161.58, 153.88, 146.18, 142.39, 137.01 (d, $J = 8.0$ Hz), 136.15, 128.05, 127.99, 127.94, 127.38 (d, $J = 7.9$ Hz), 126.75, 126.51, 123.49, 123.30, 122.41, 122.25, 113.10, 112.84, 110.63 (d, $J = 22.5$ Hz), 80.69, 53.66, 47.34, 31.94, 31.52, 30.16, 29.73, 29.71, 28.14.

HRMS (ESI): calculated for $\text{C}_{32}\text{H}_{29}\text{F}_4\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$: 613.1956, found 613.1956.

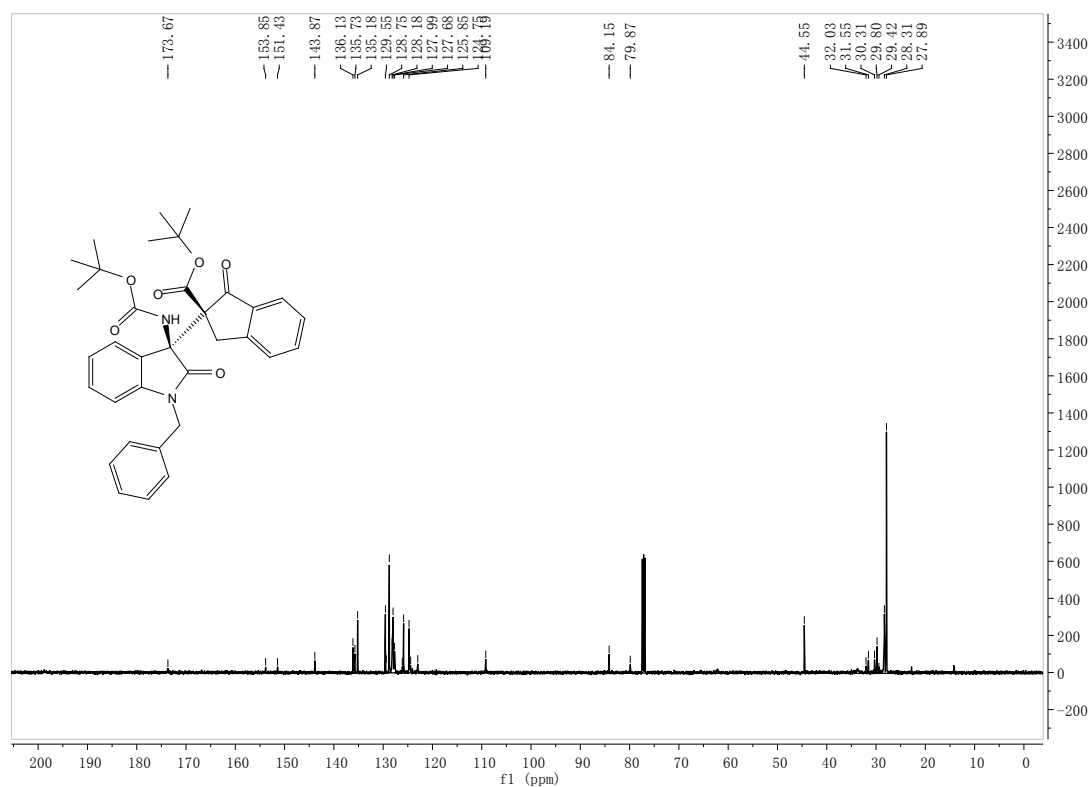
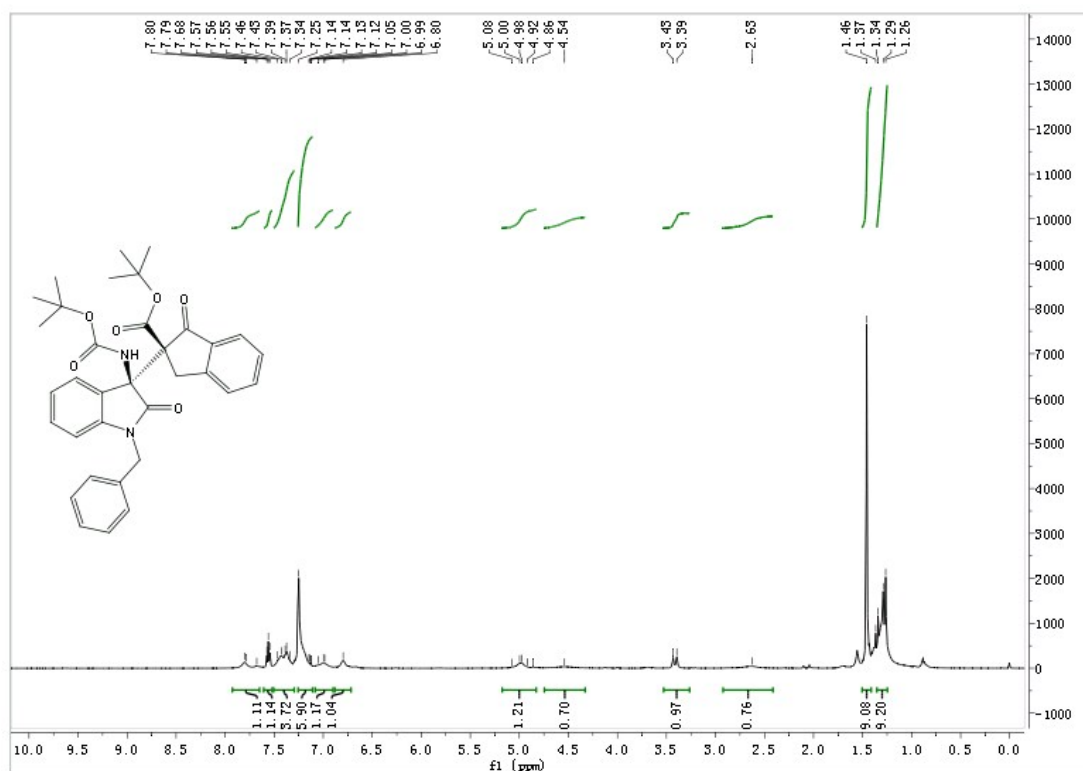
6. The X-ray data for **4ab**.

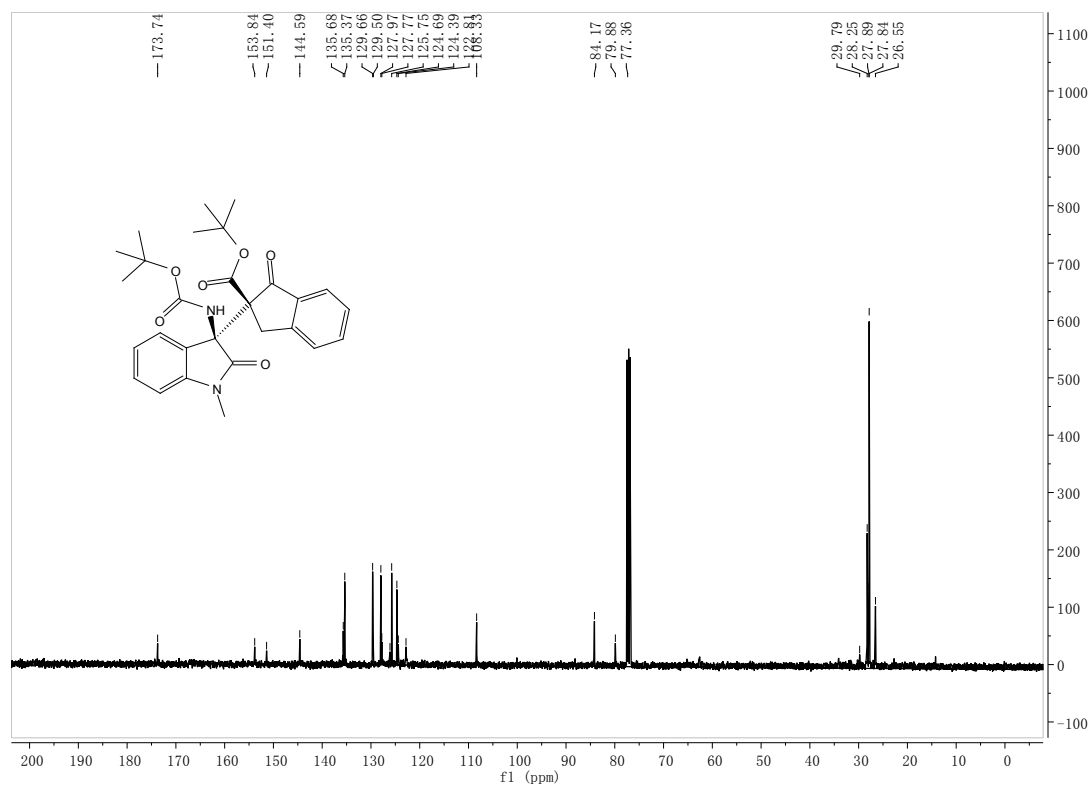
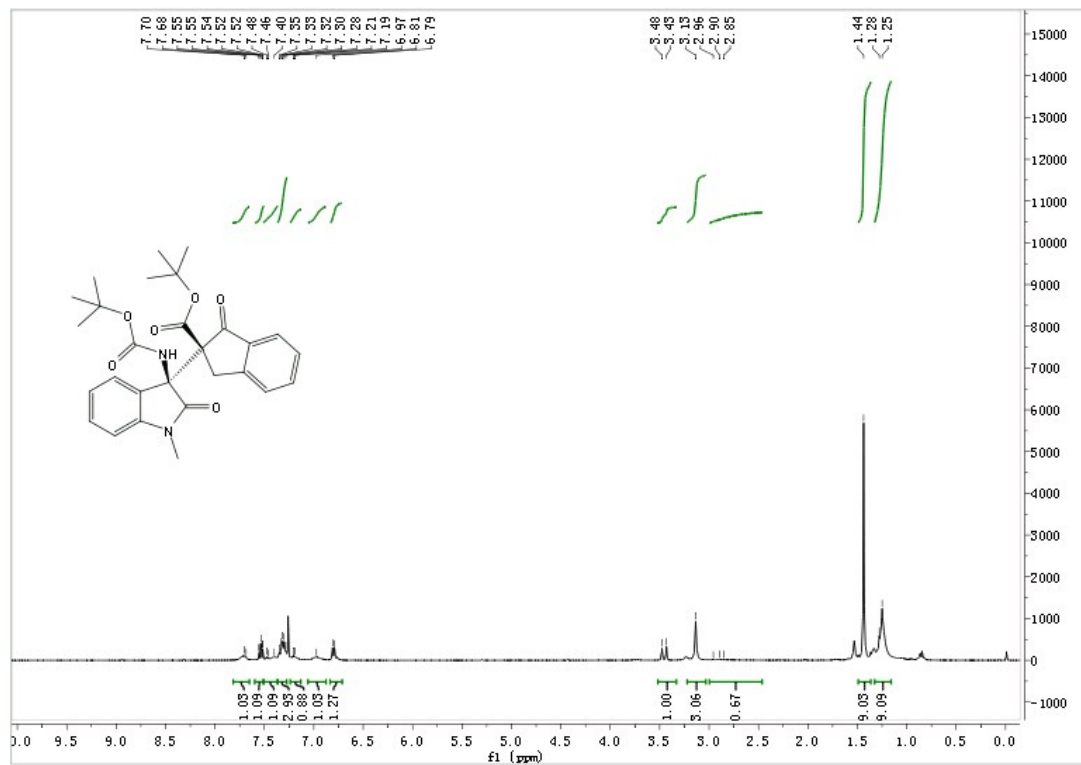


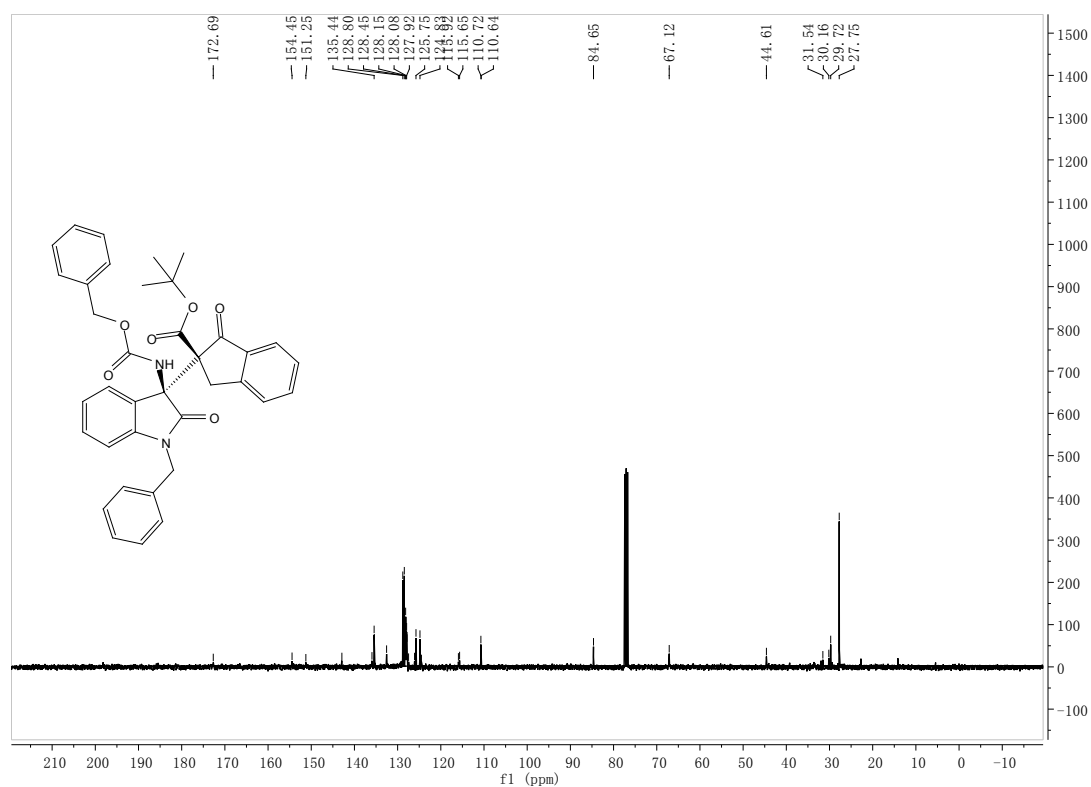
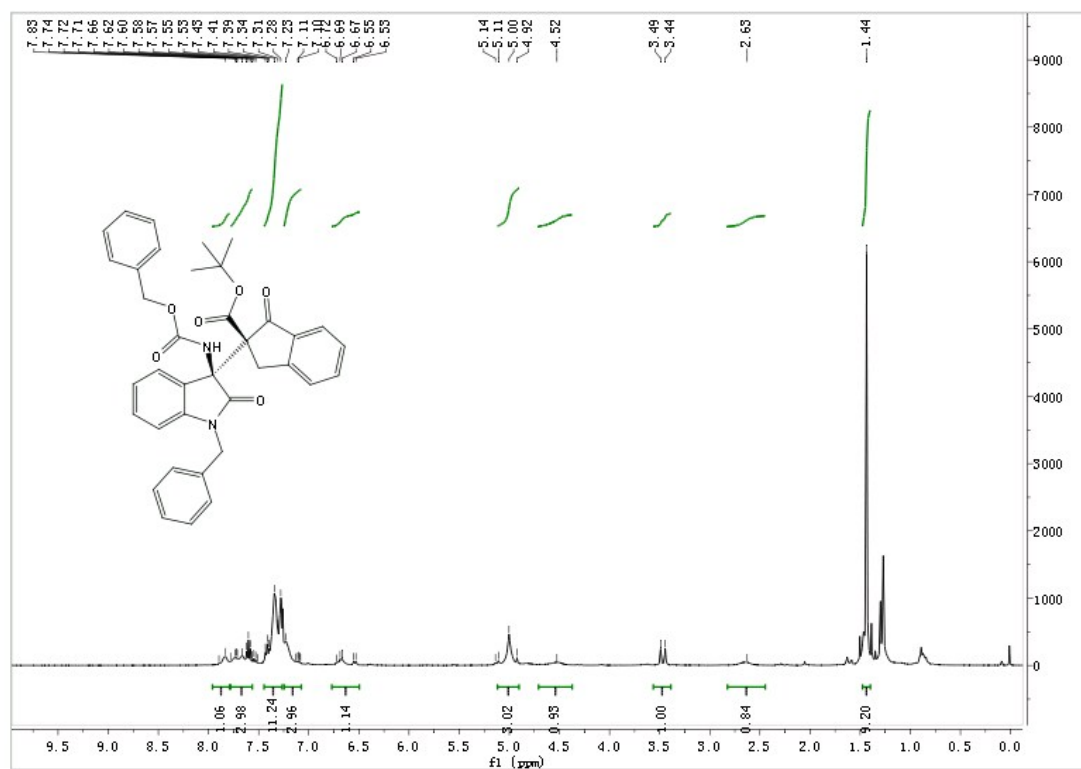
The product **4ab** was recrystallized from PE and EA.

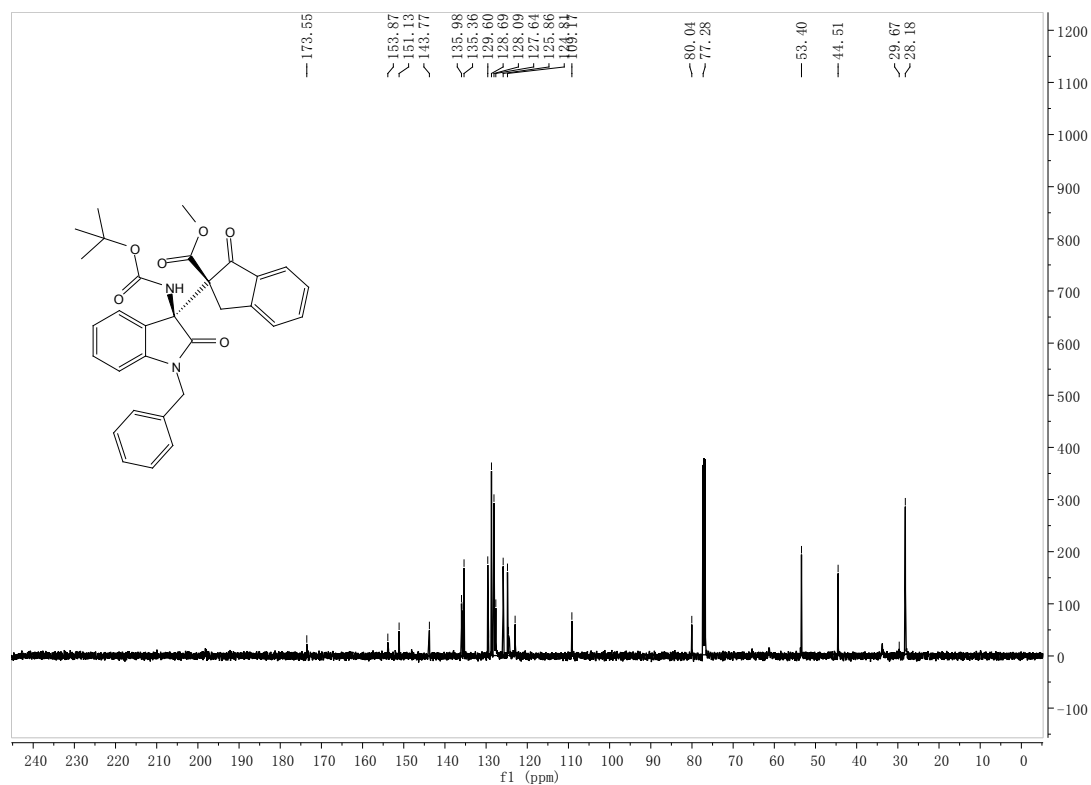
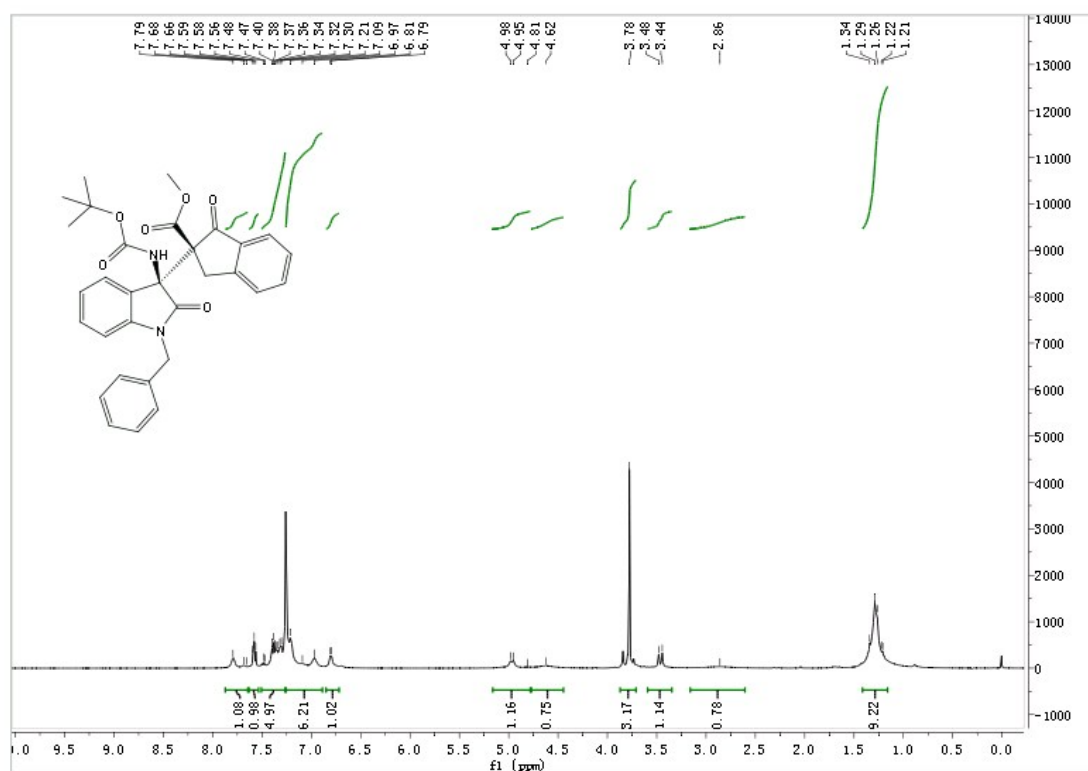
CCDC- 1853680 (**4ab**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic DataCentre via [www.ccdc.cam.ac.uk/ data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

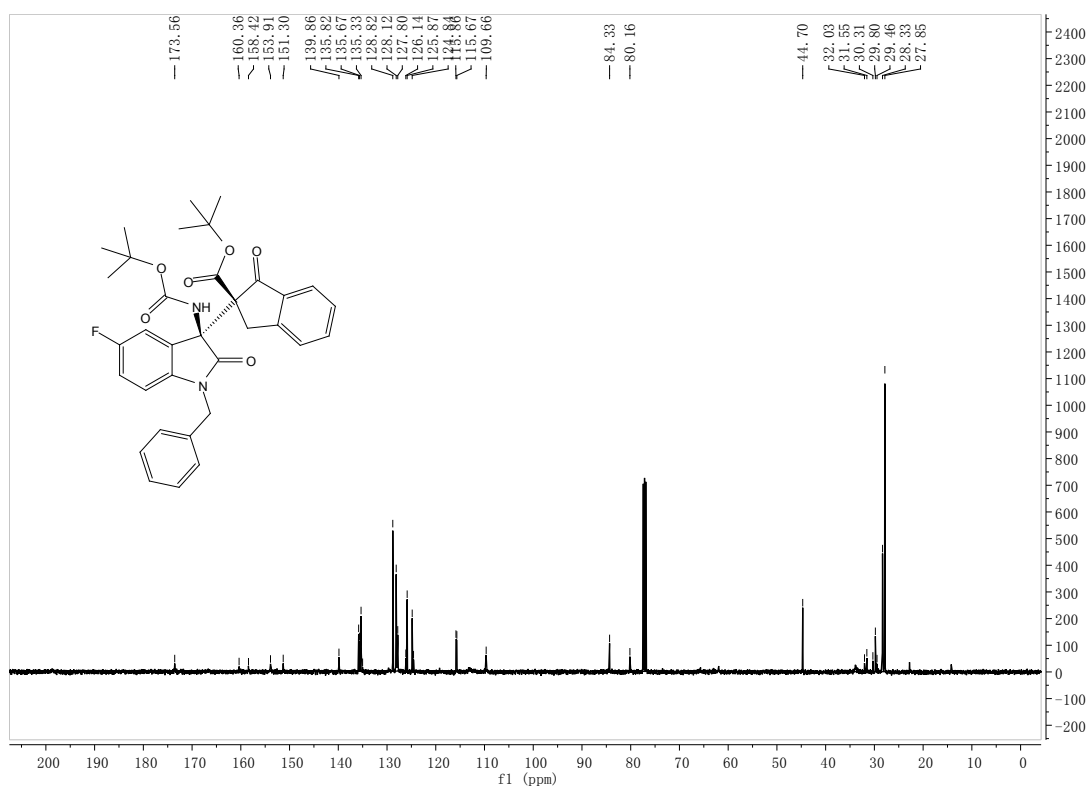
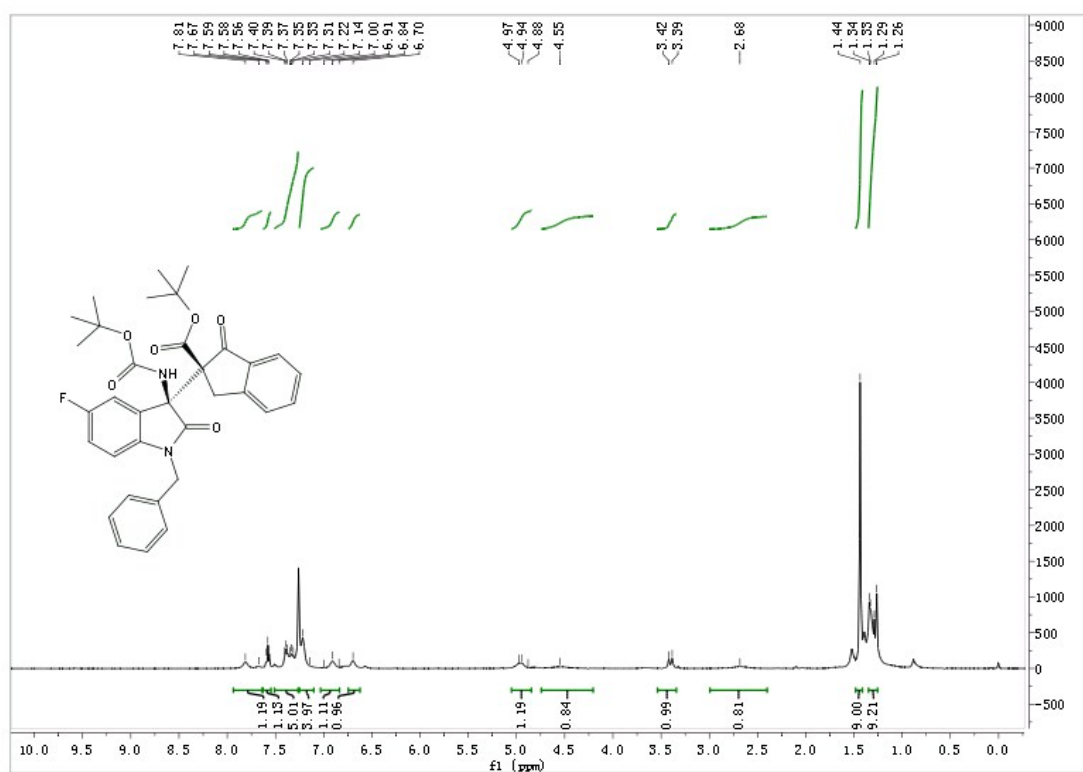
7. NMR spectra of addition products

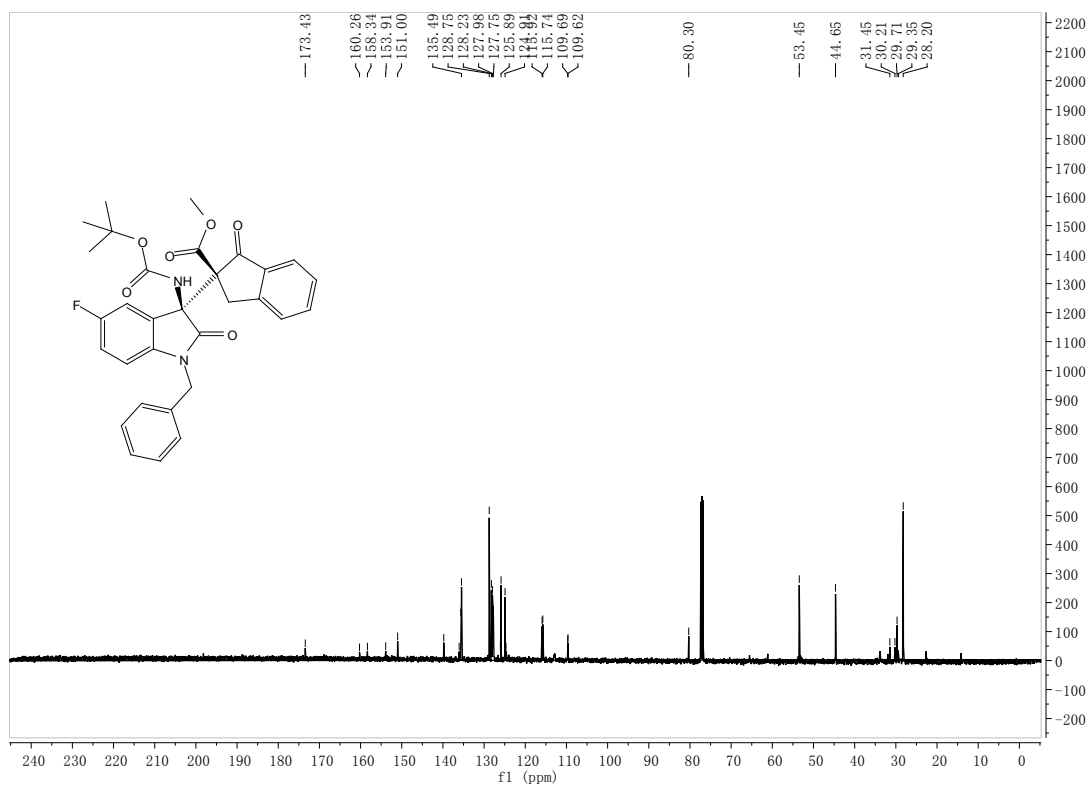
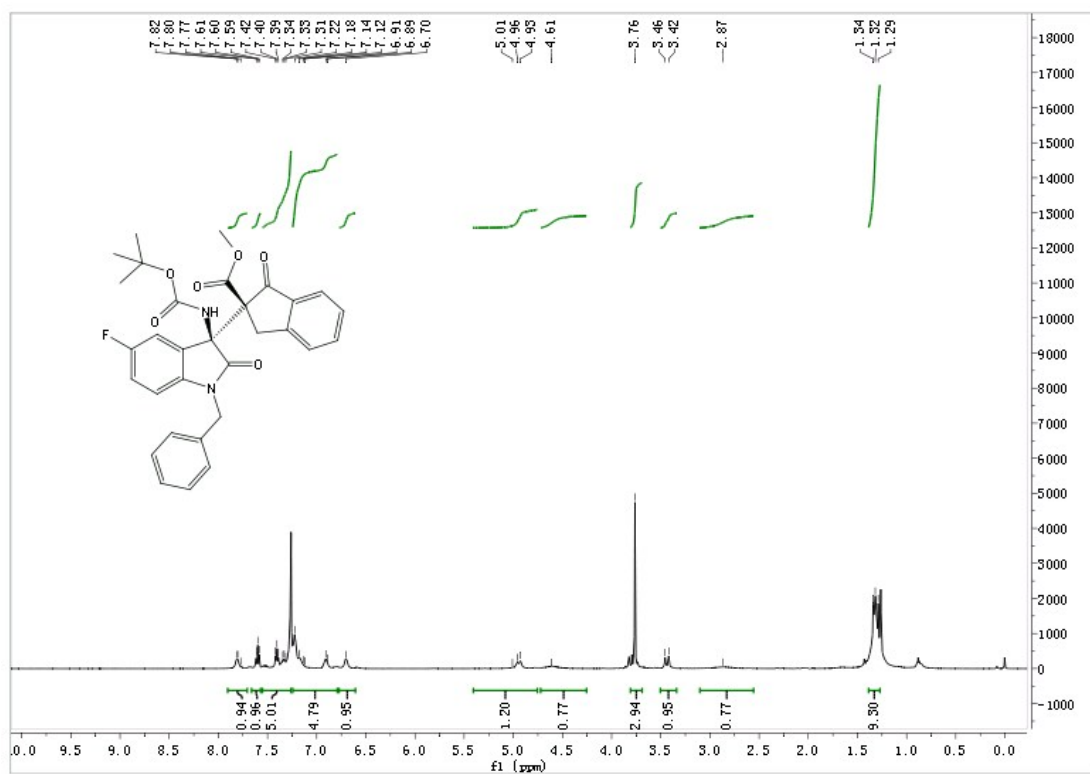


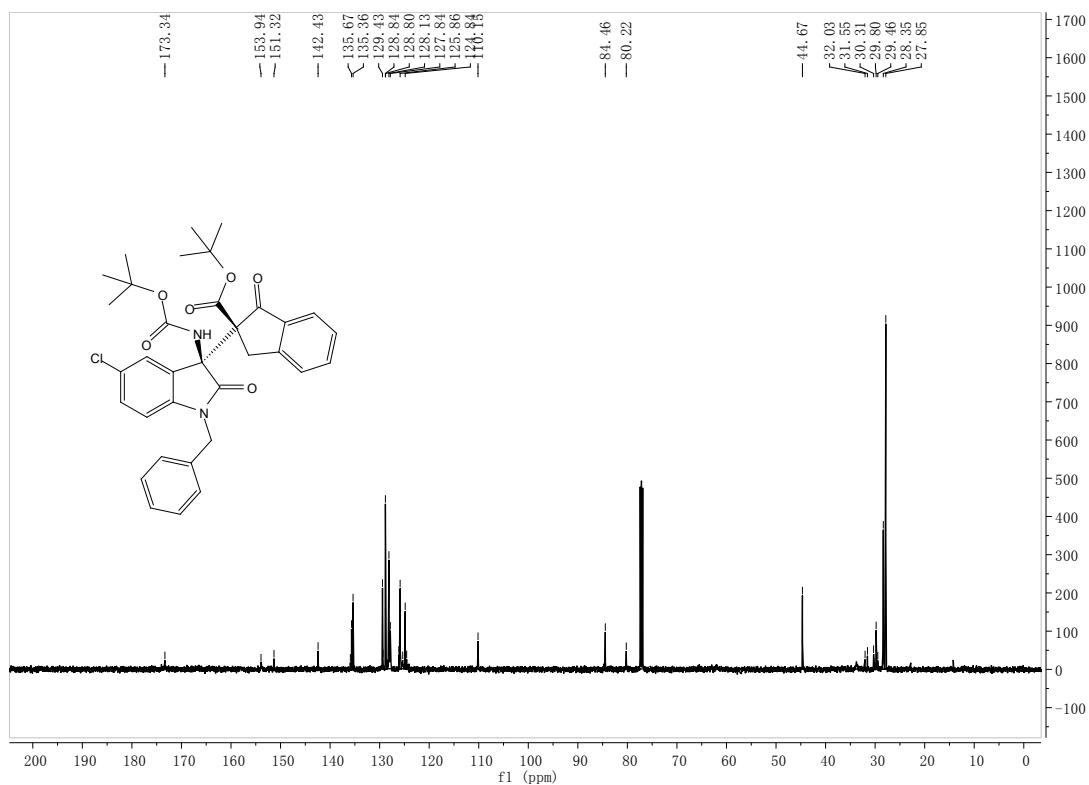
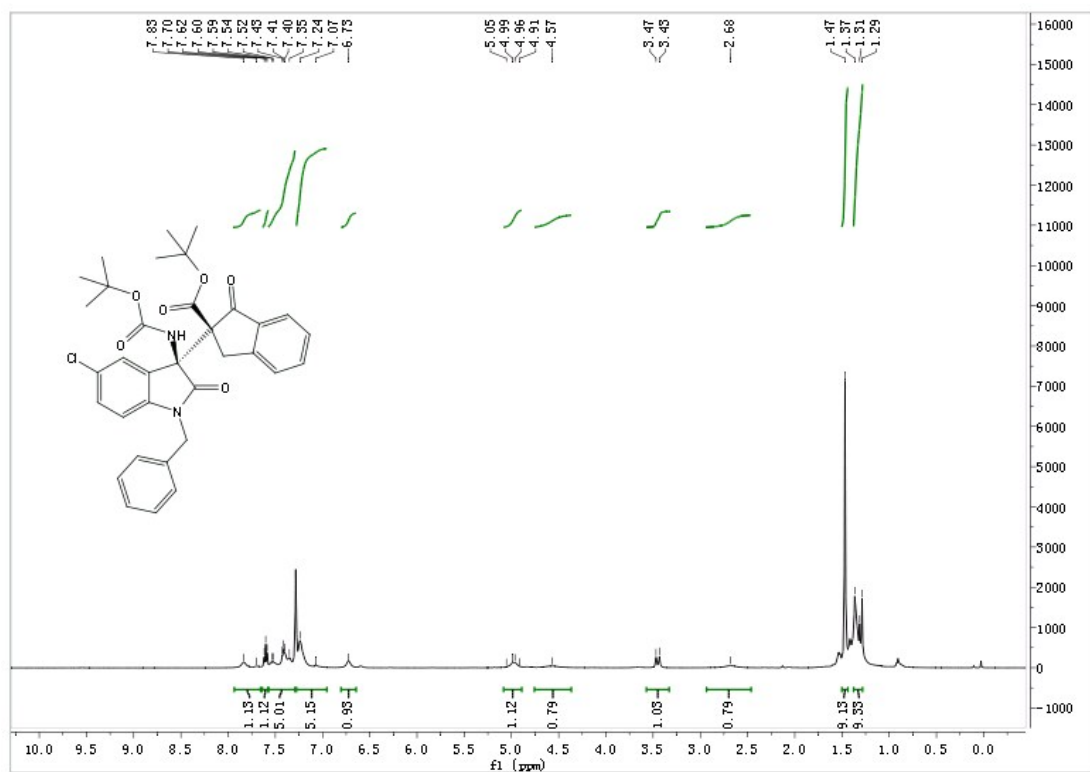


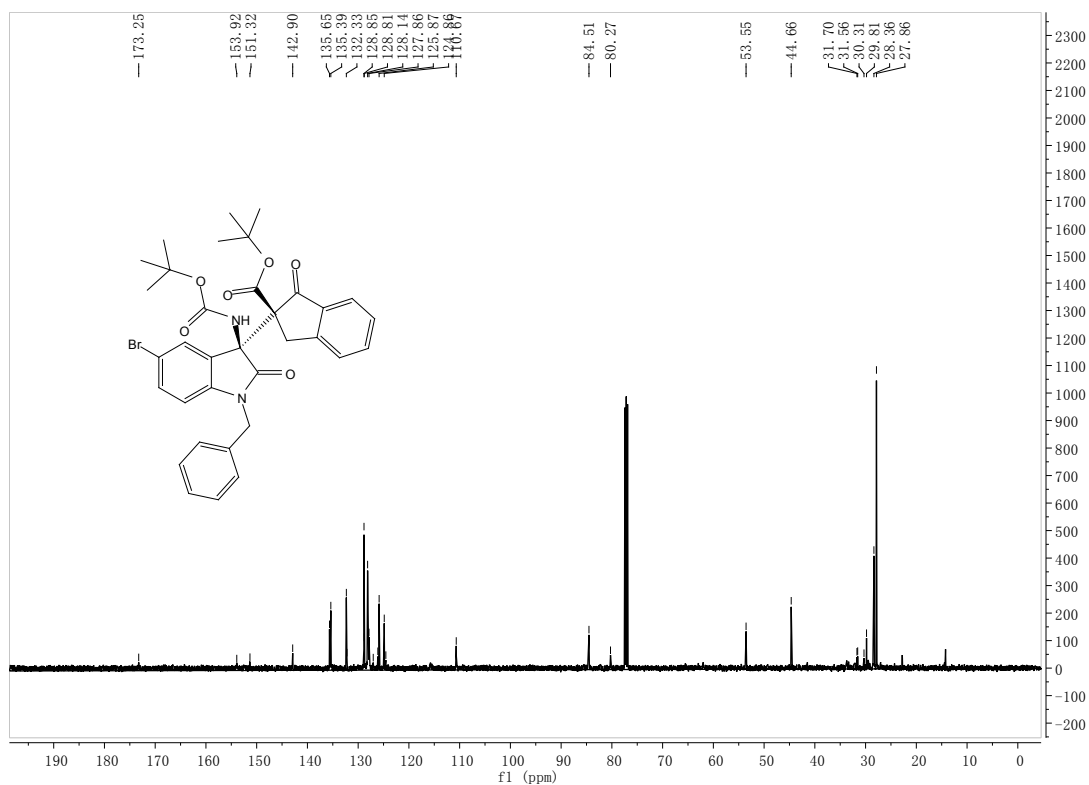
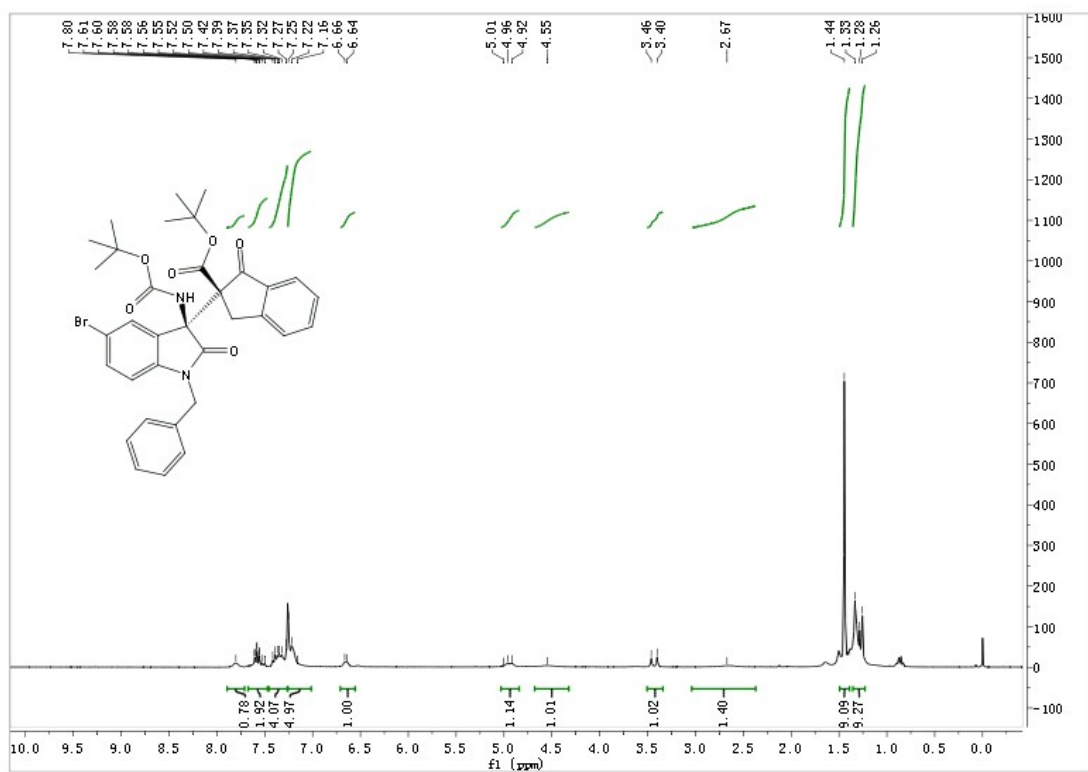


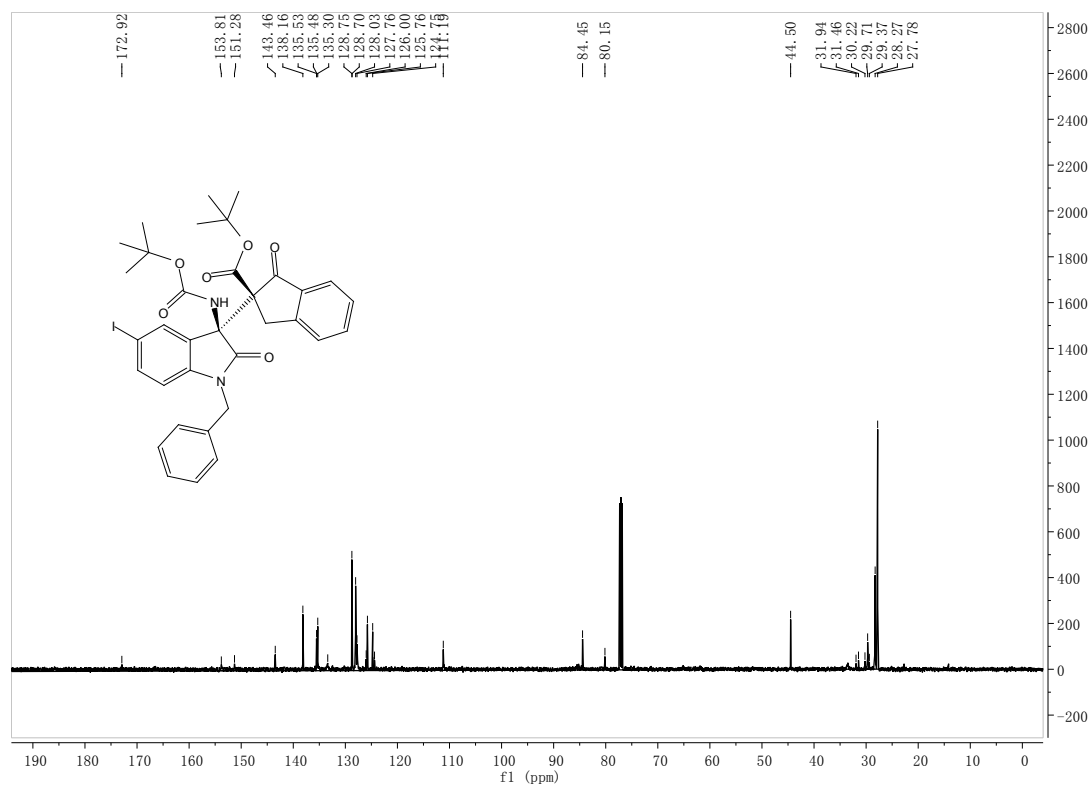
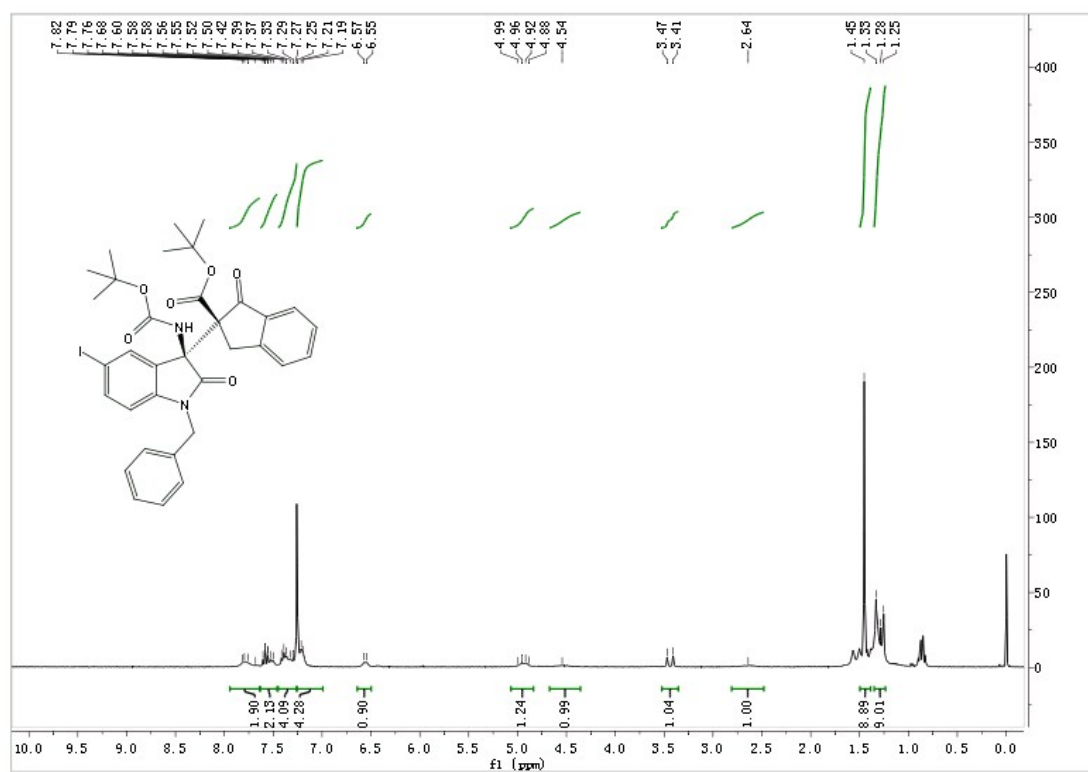


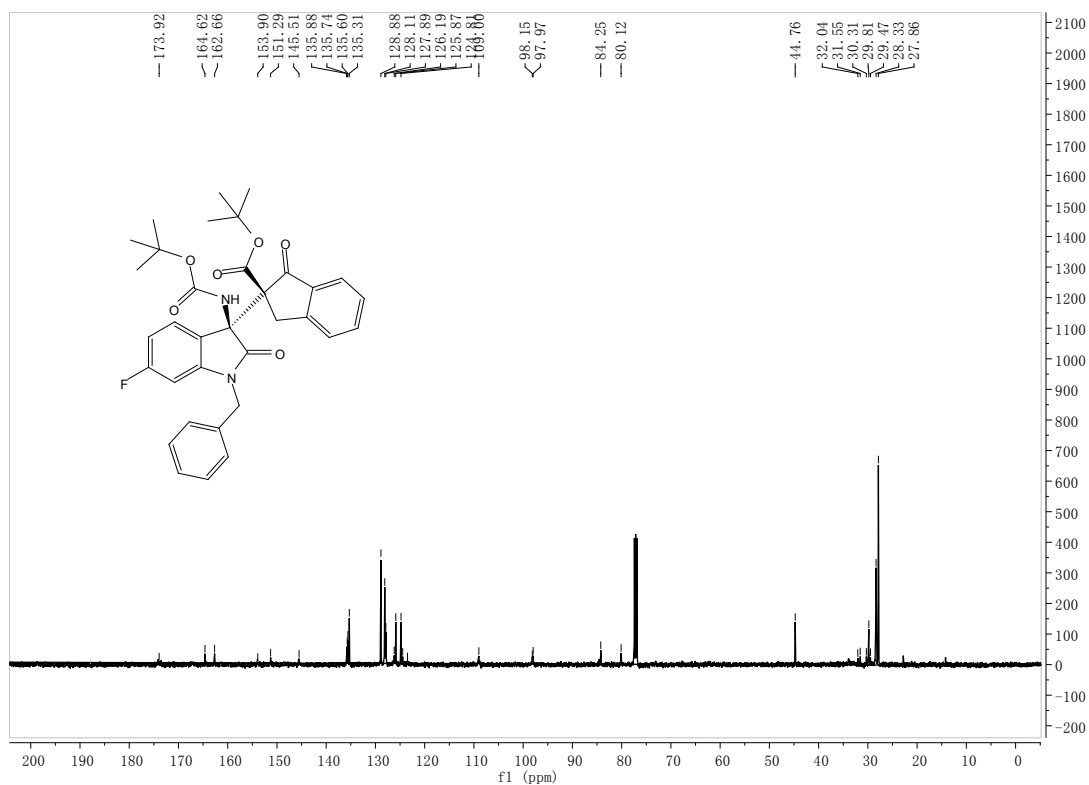
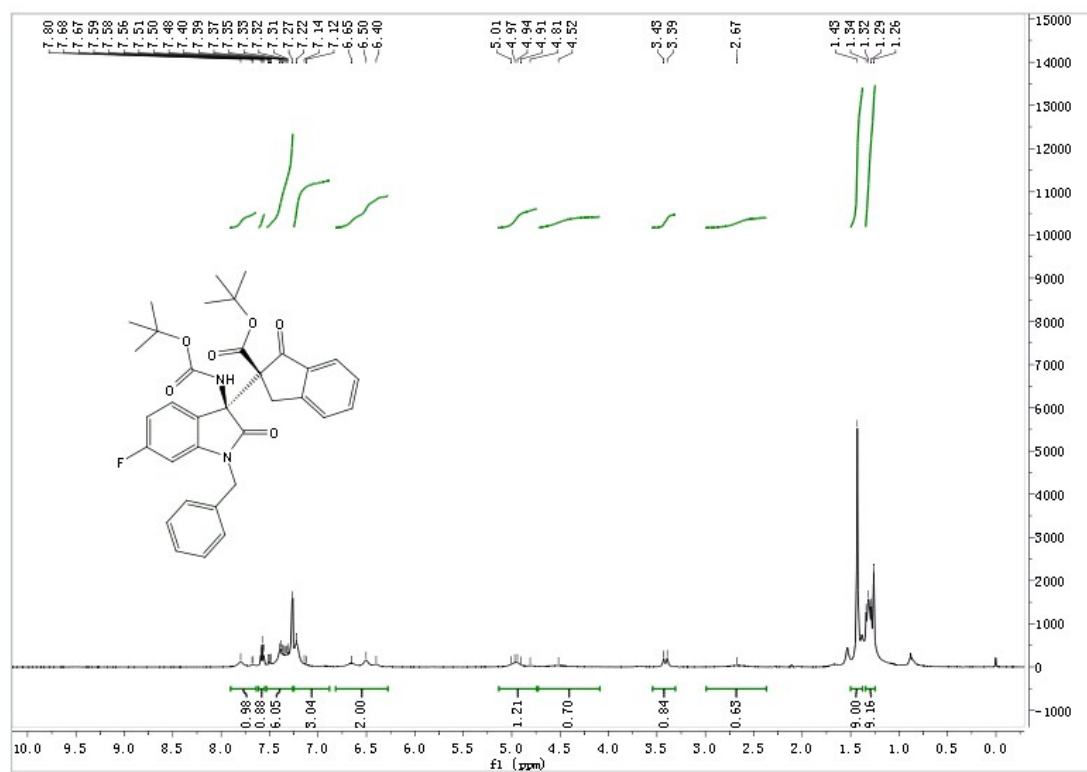


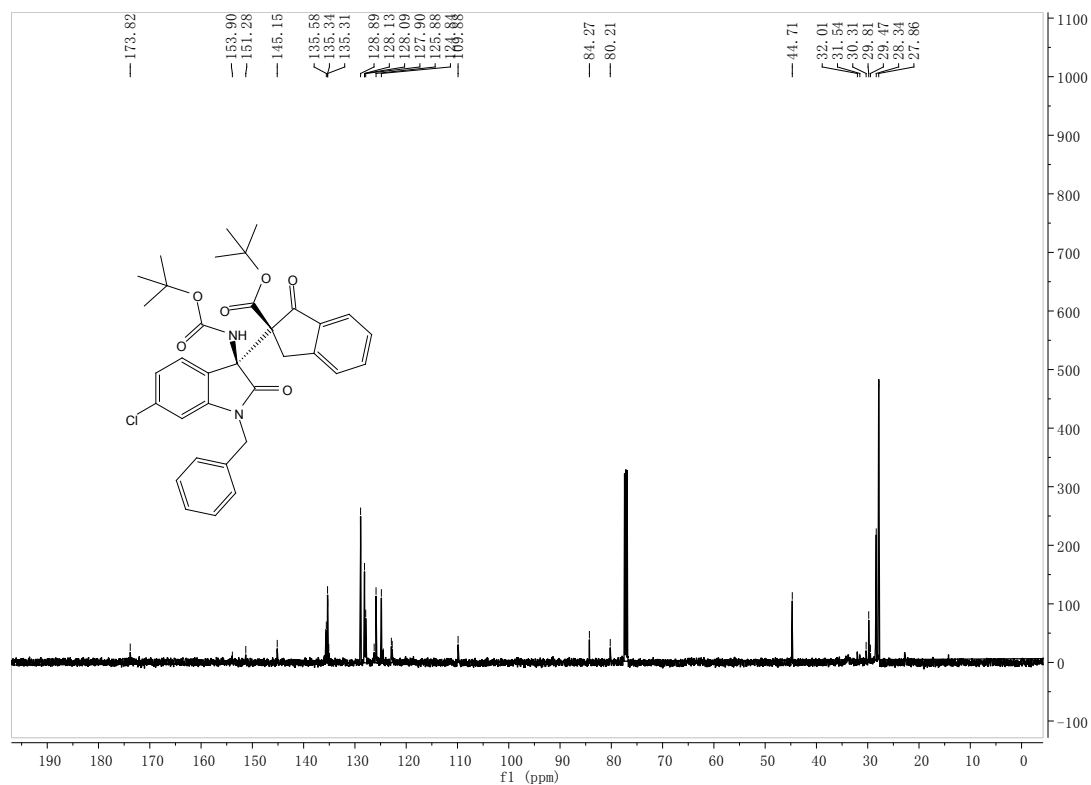
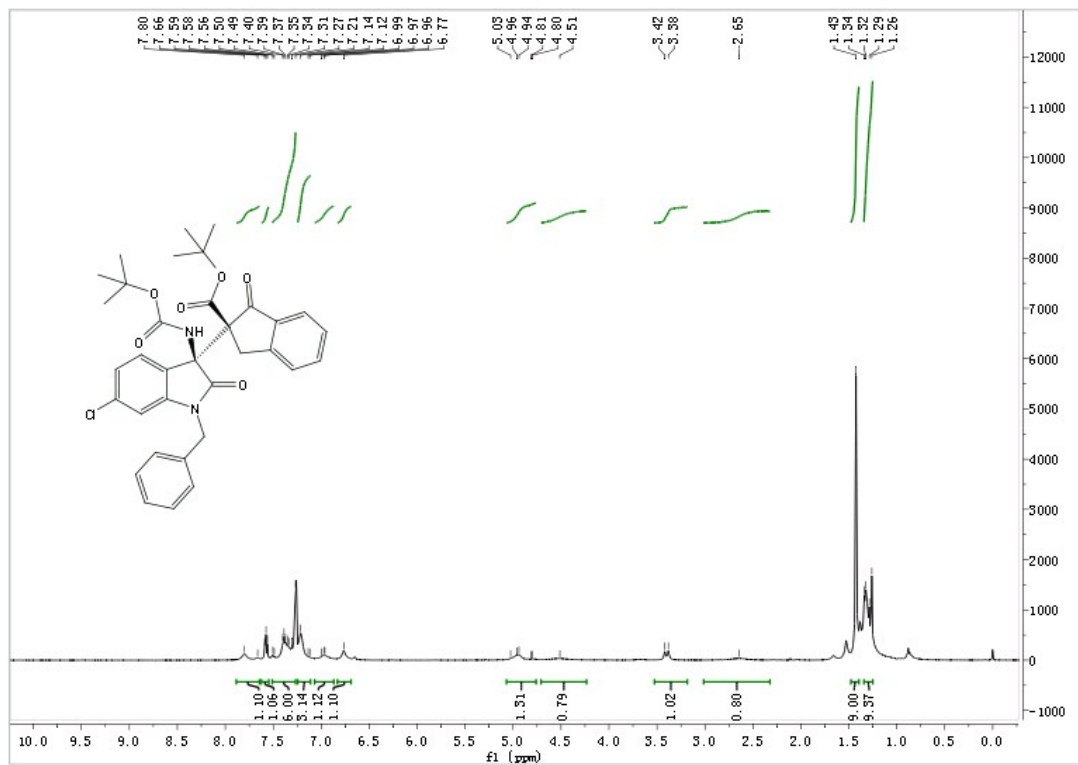


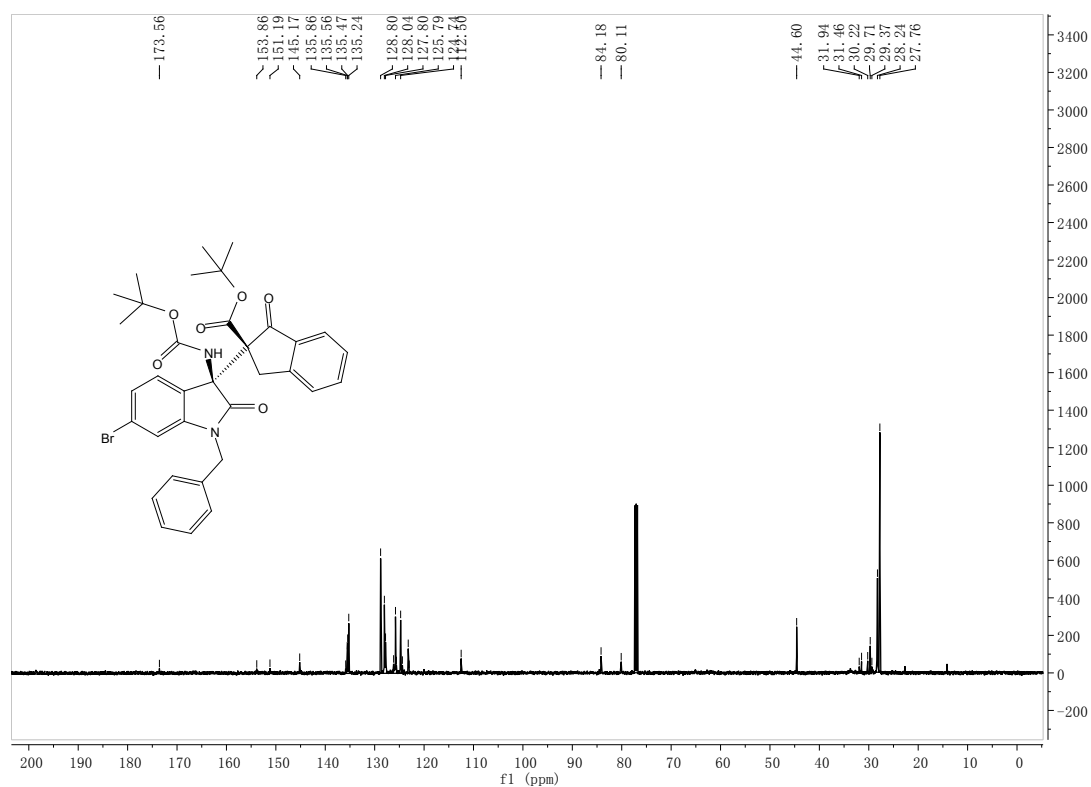
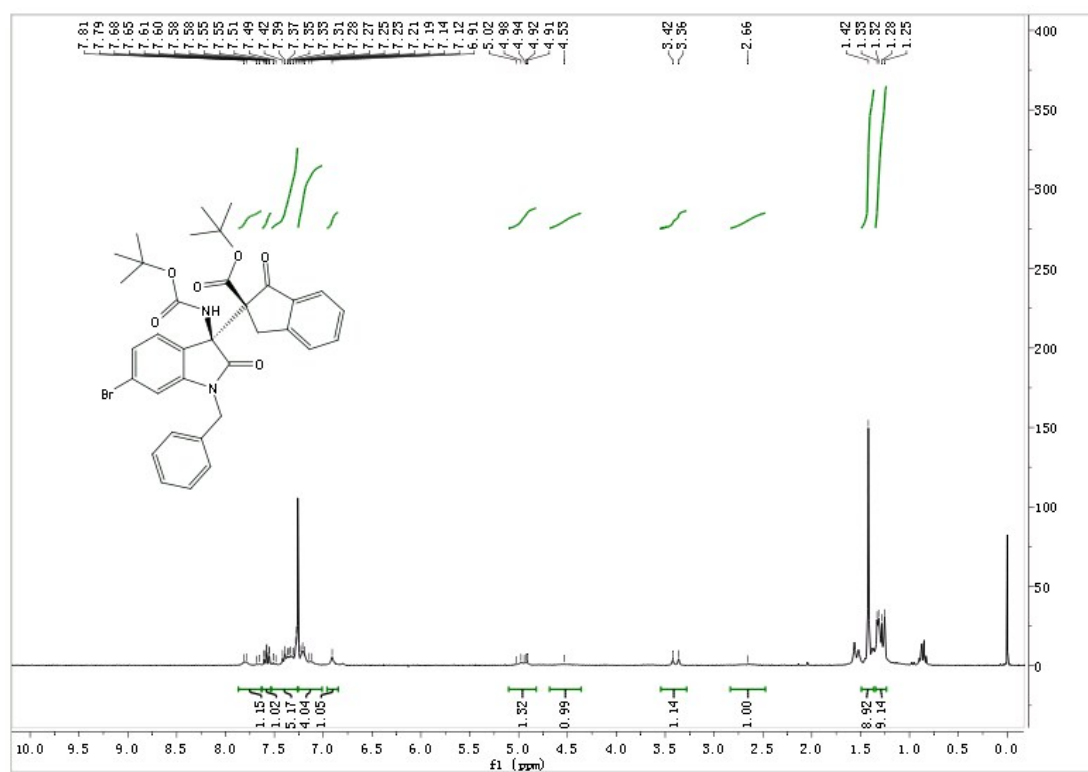


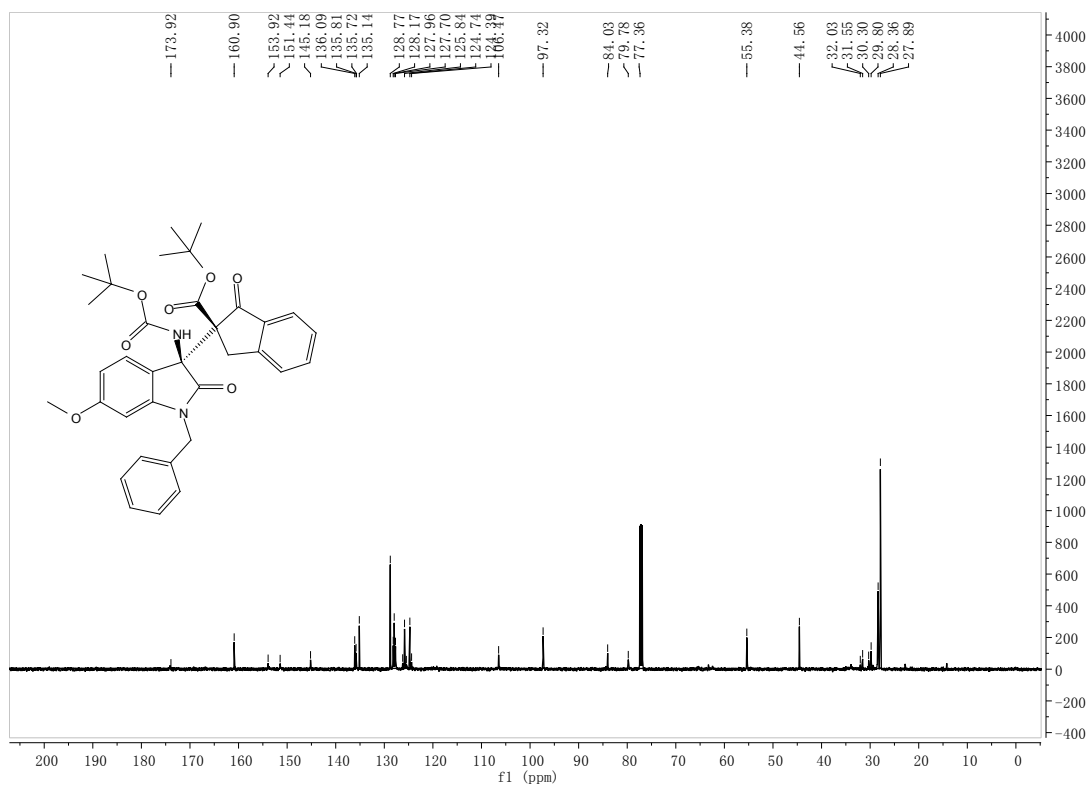
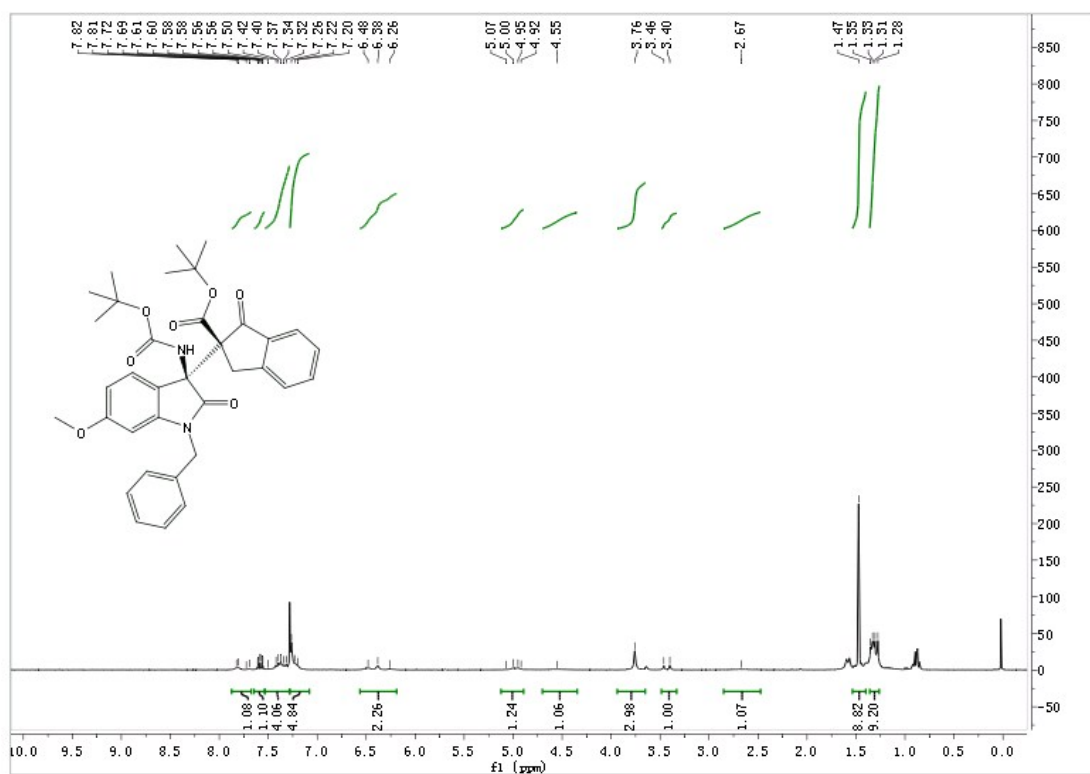


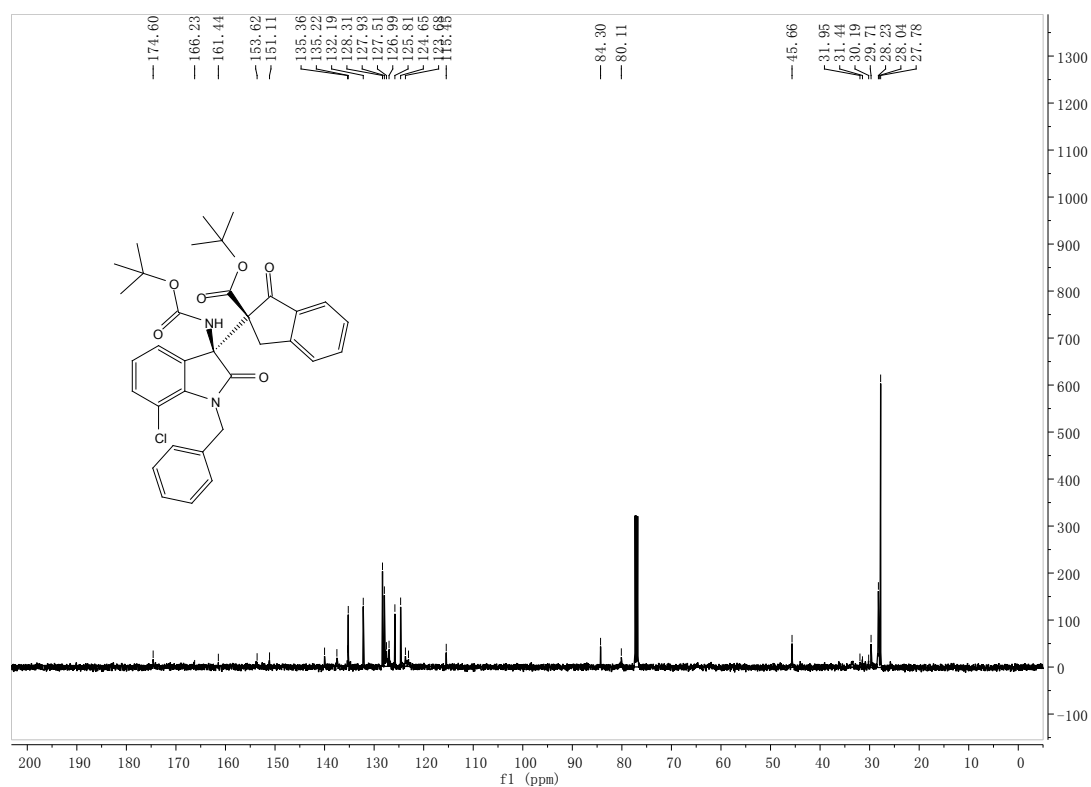
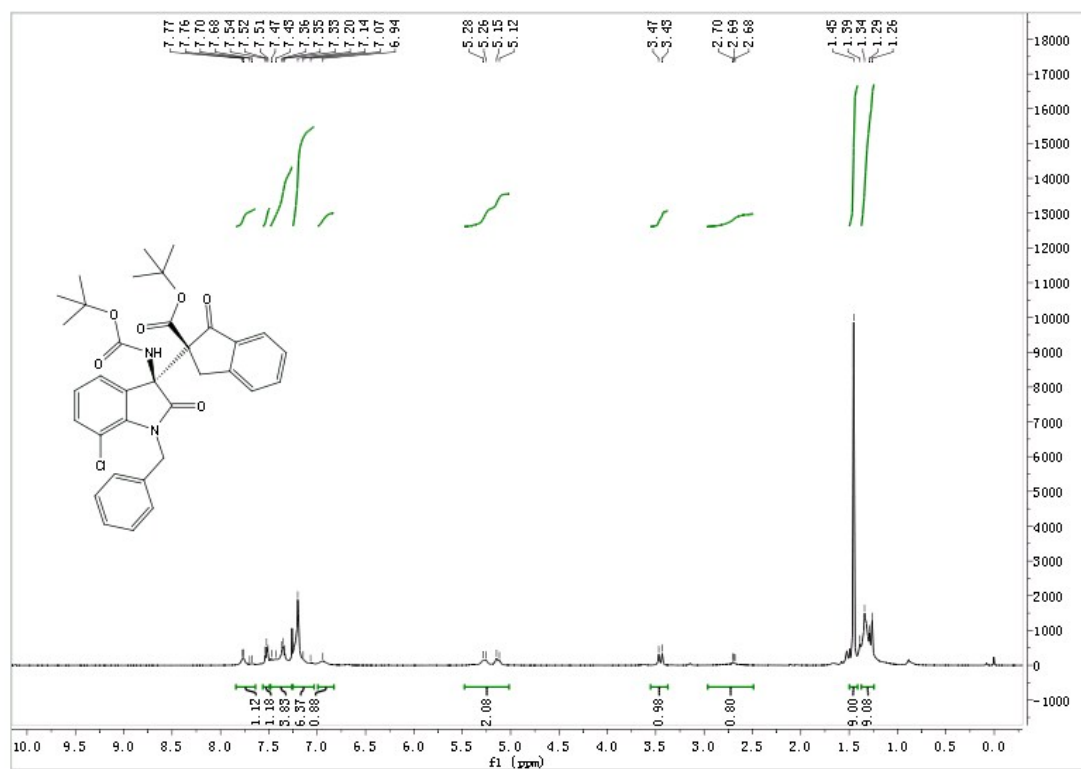


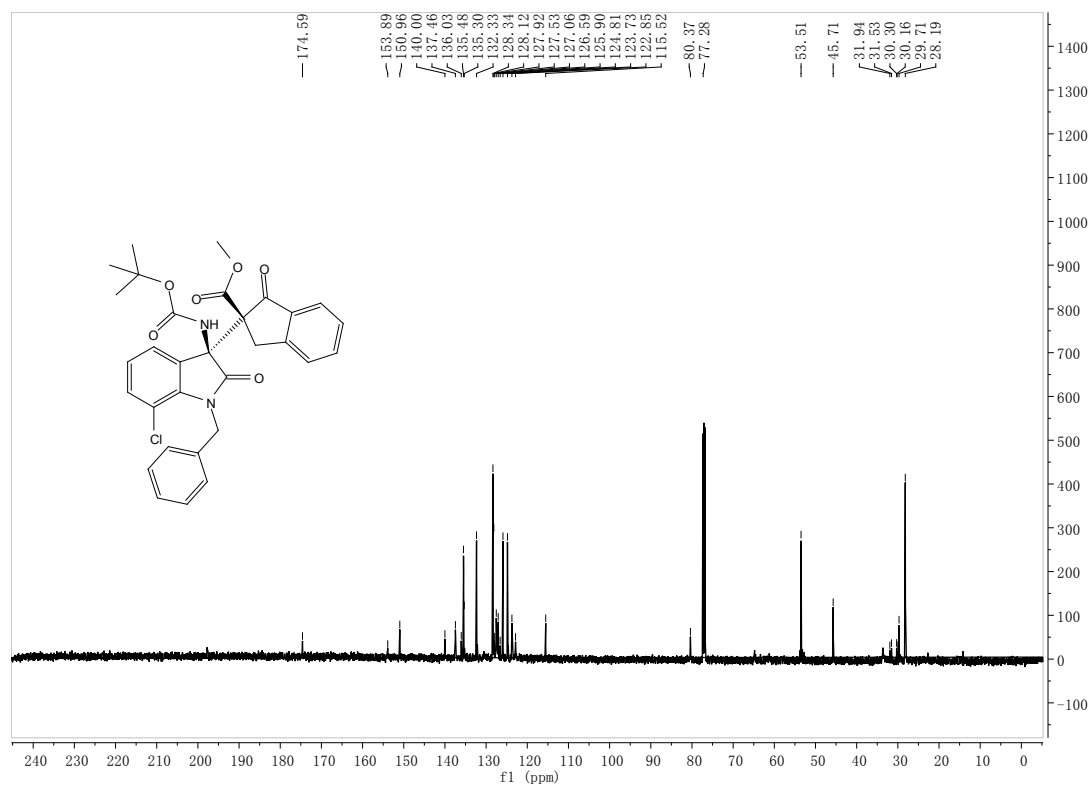
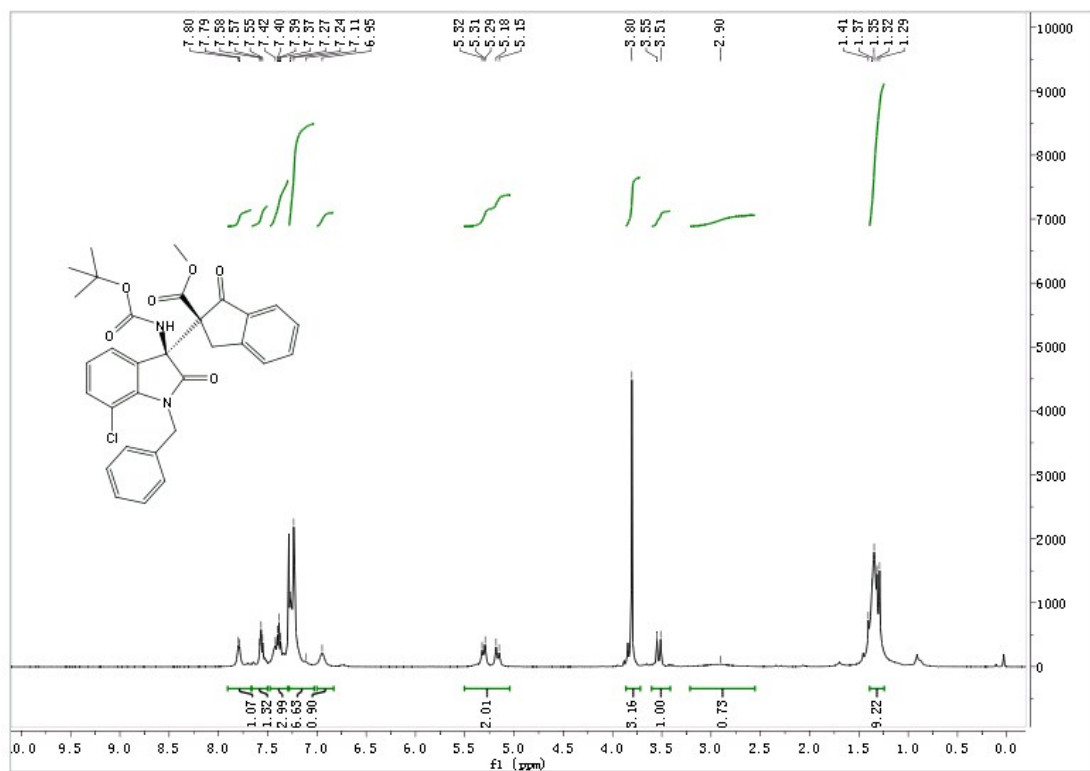


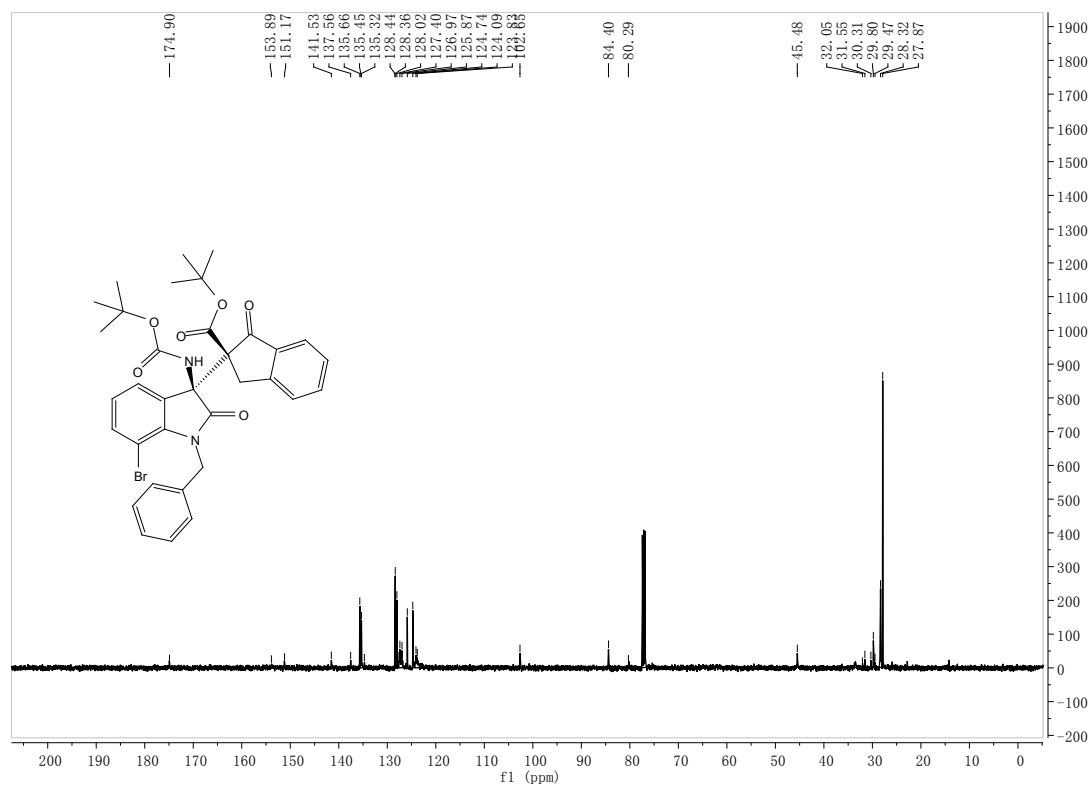
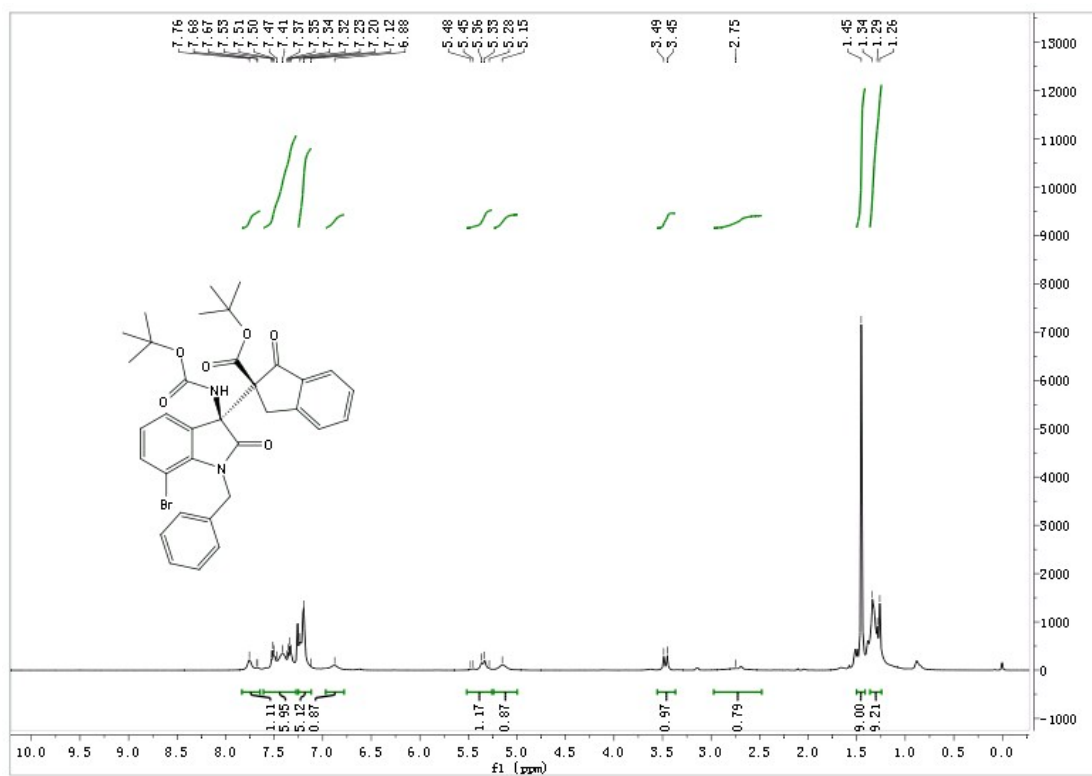


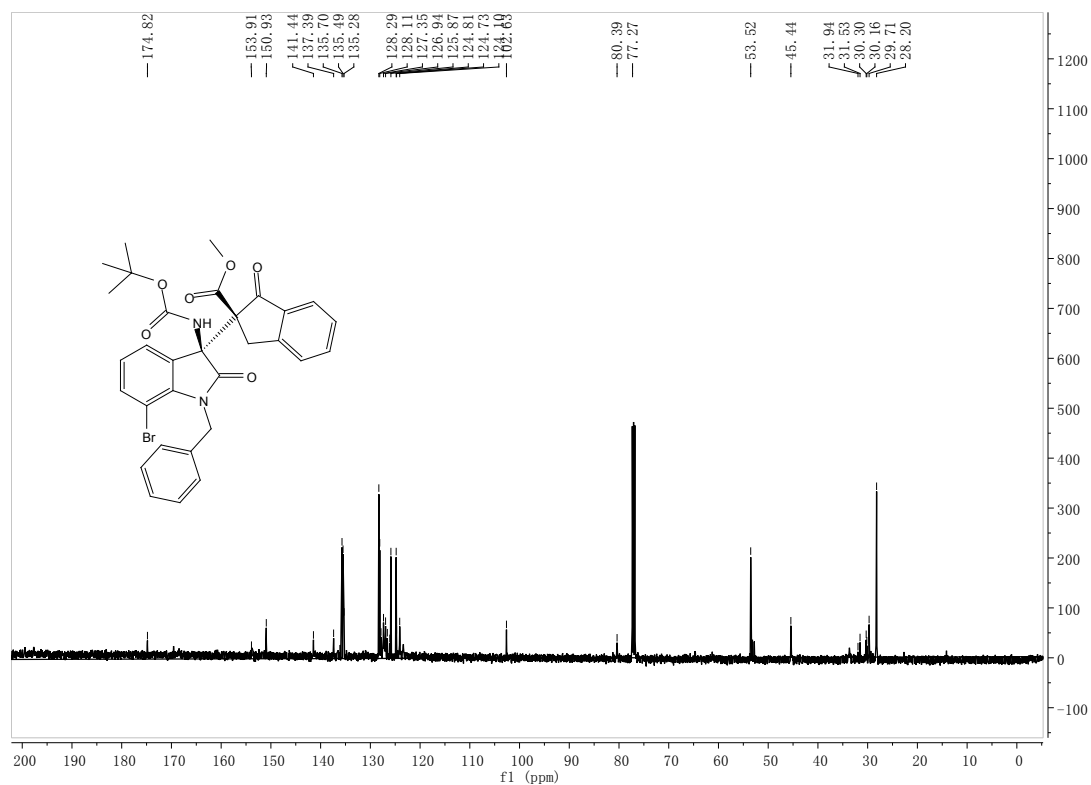
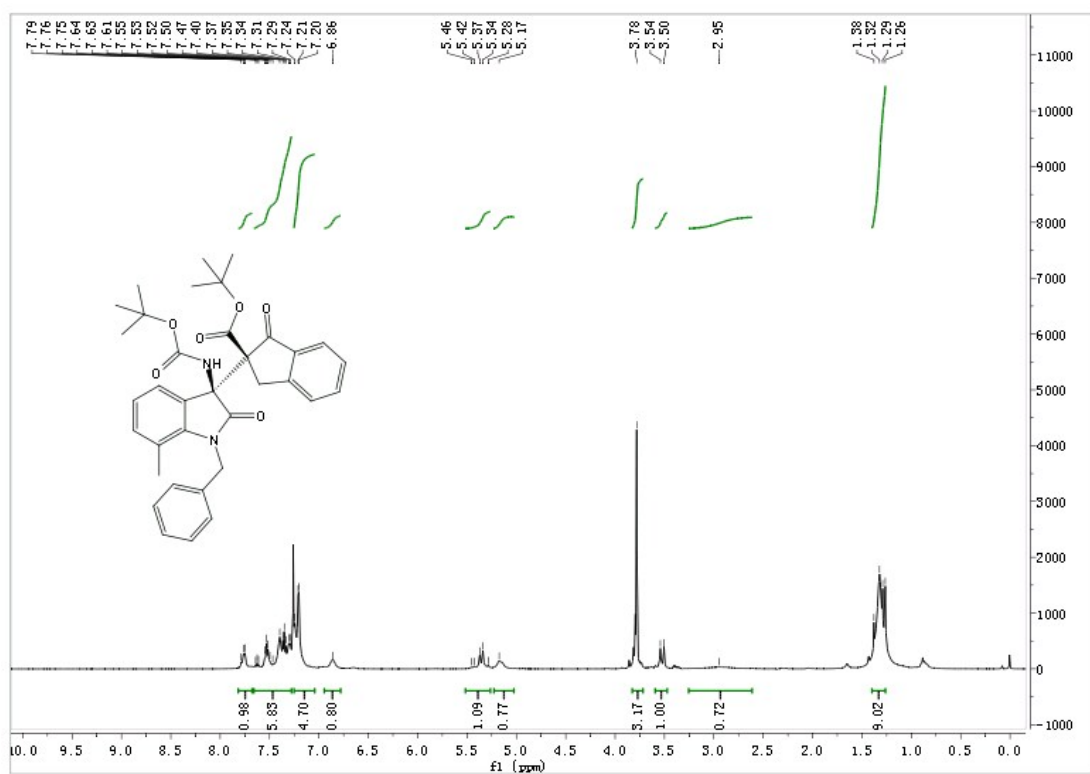


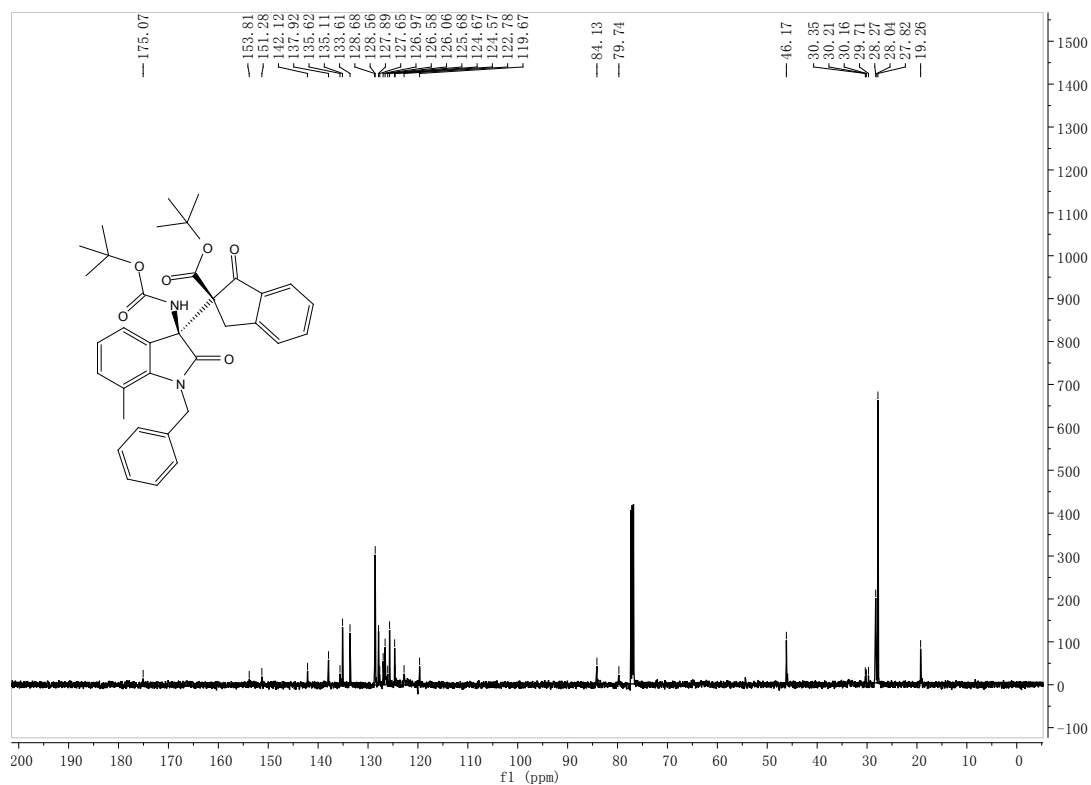
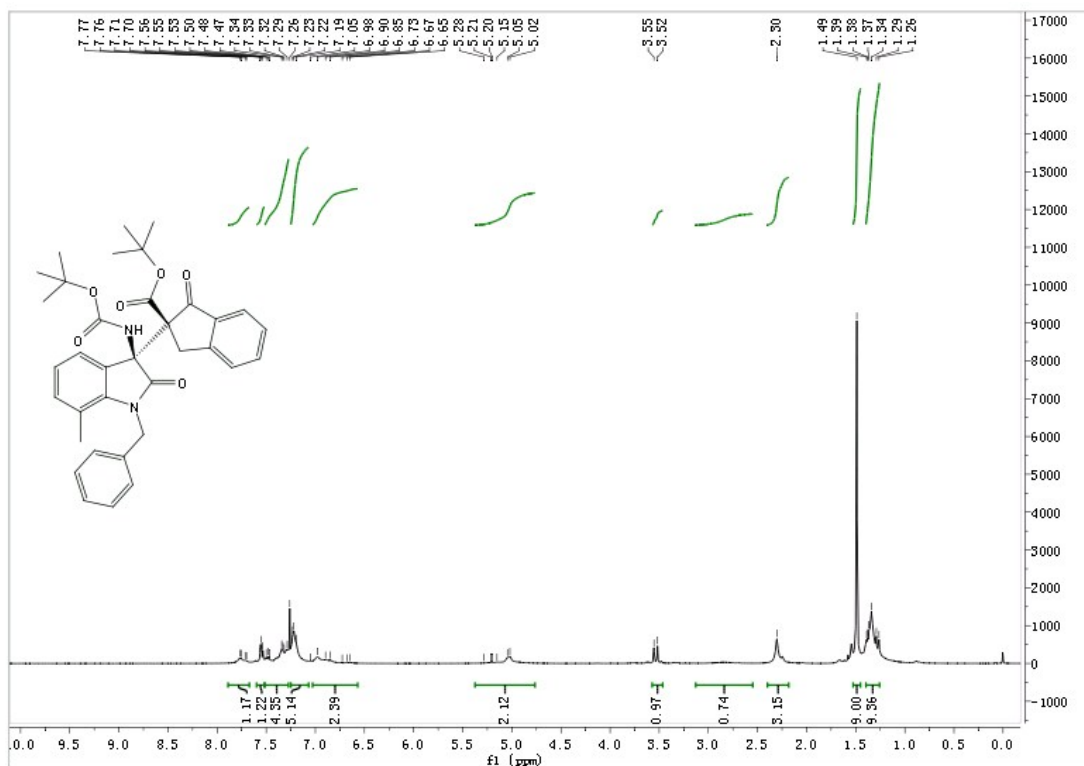


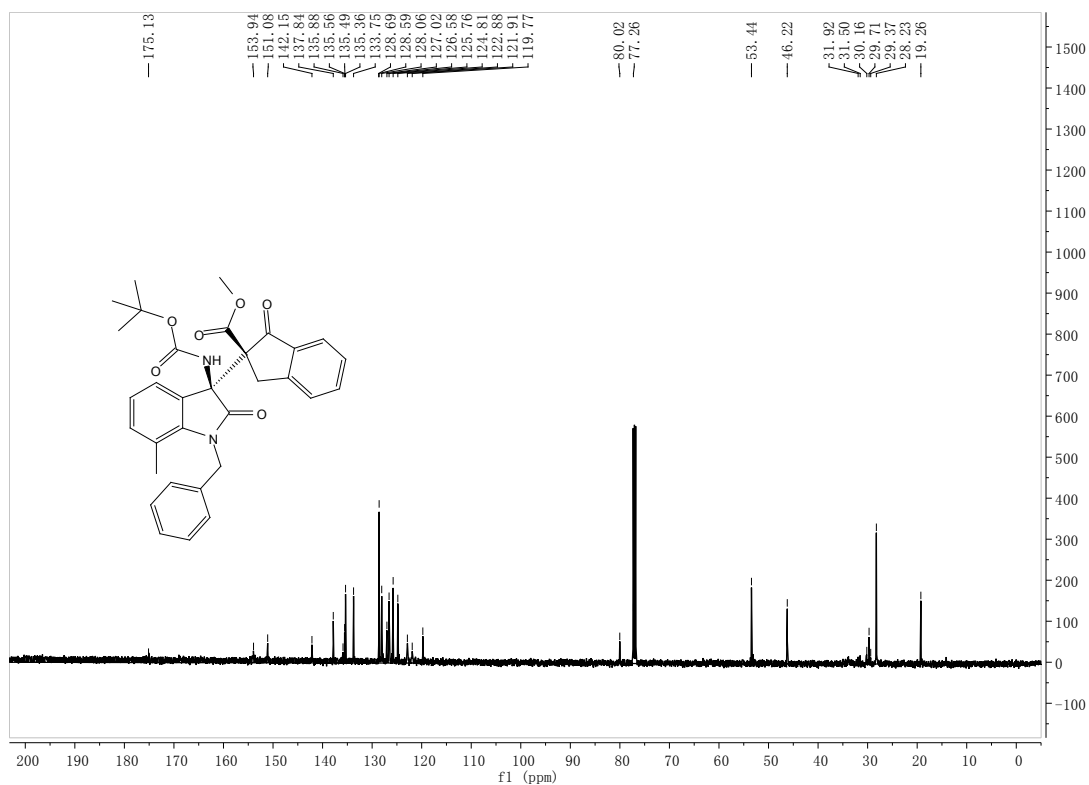
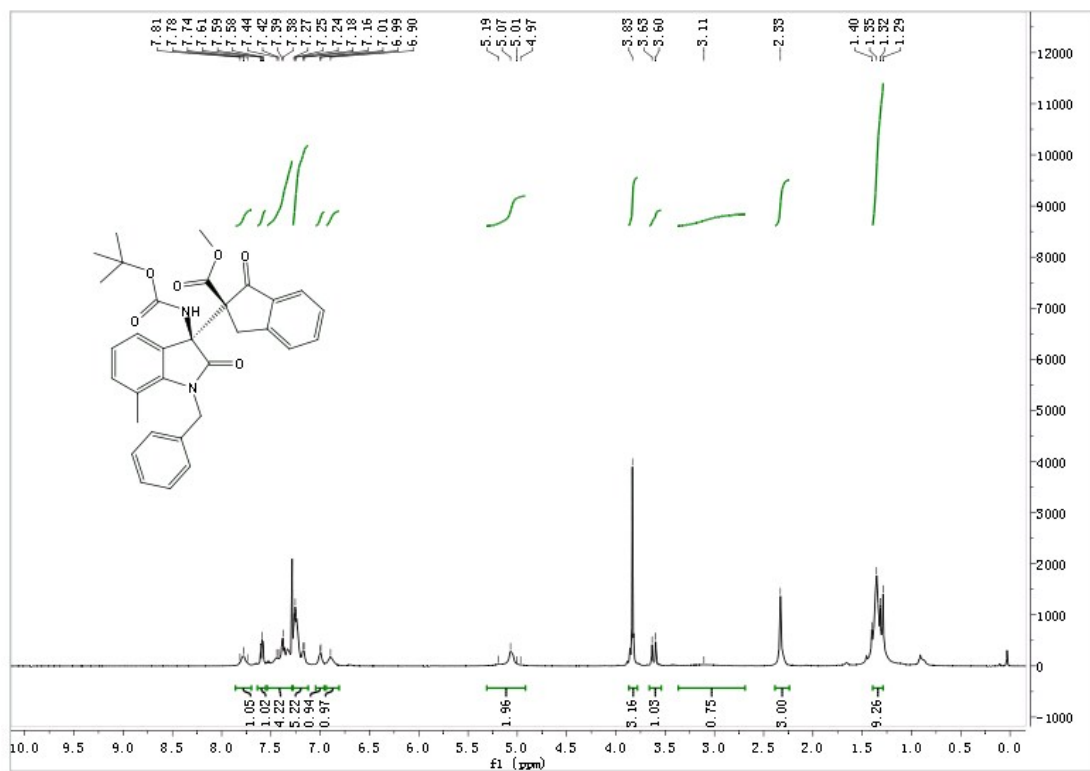


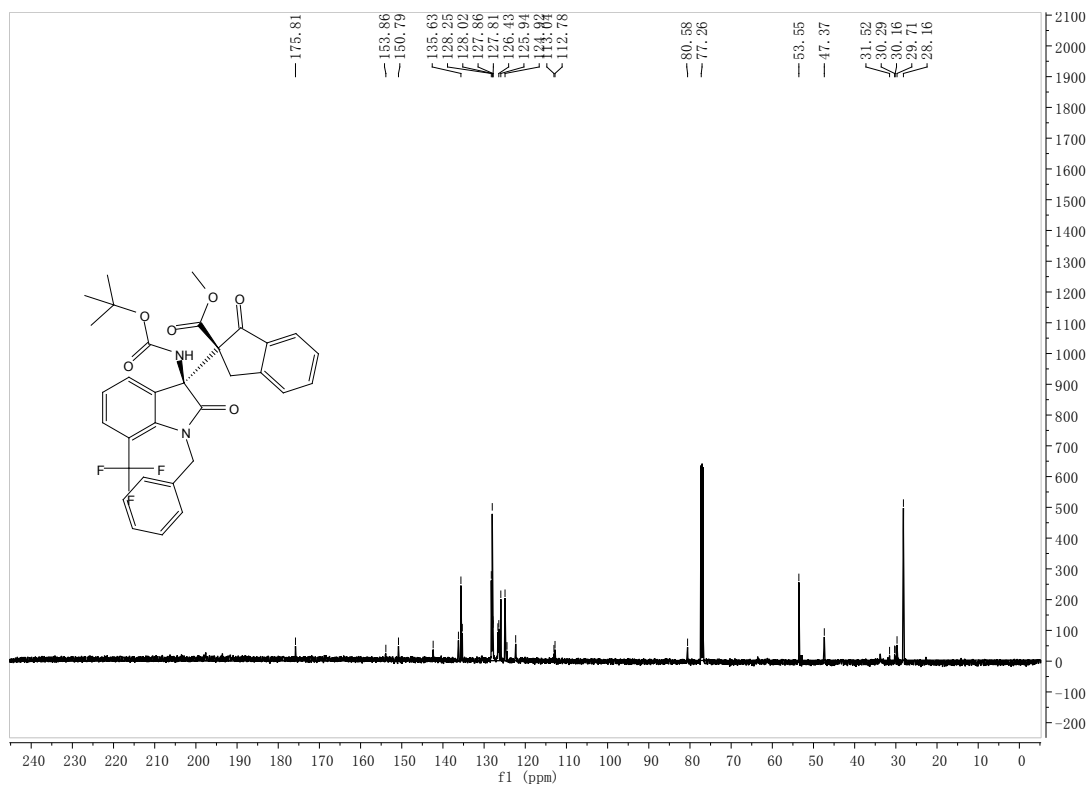
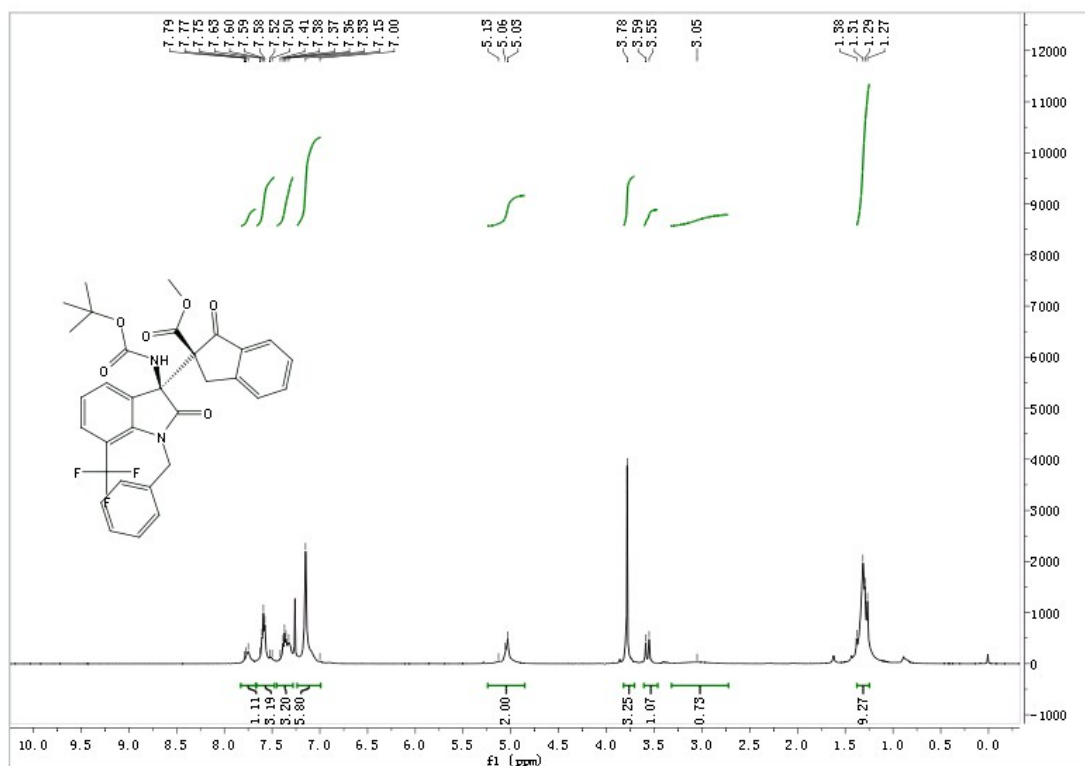


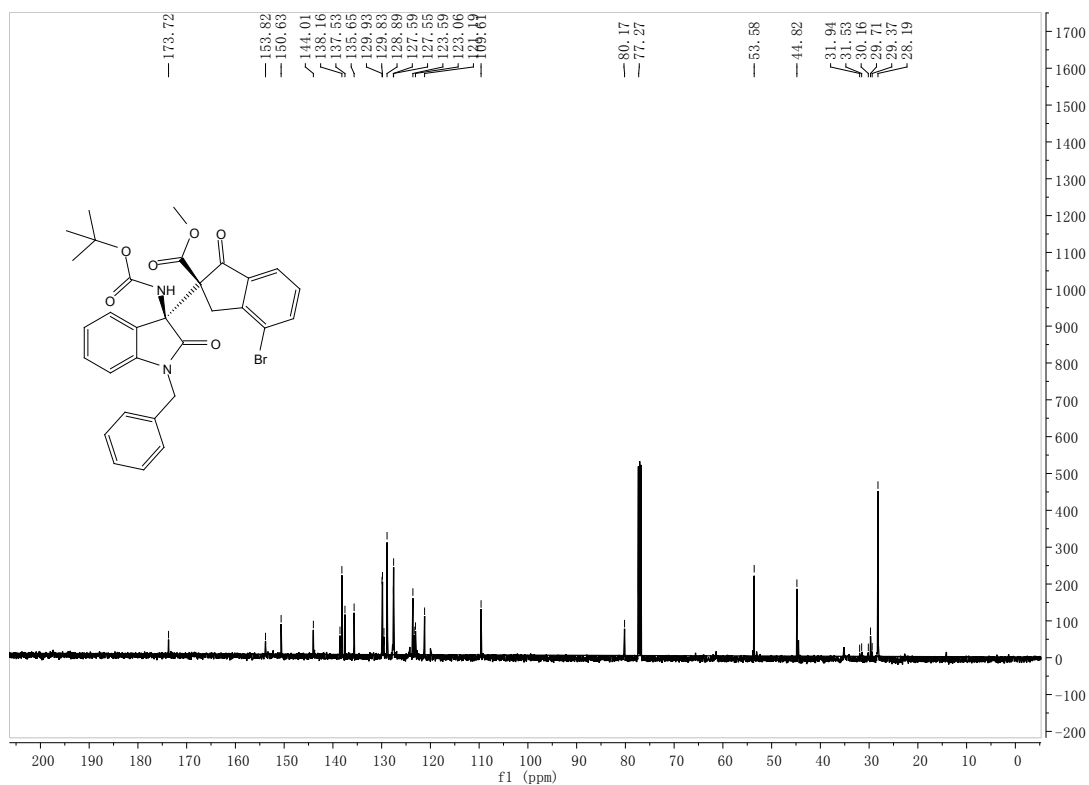
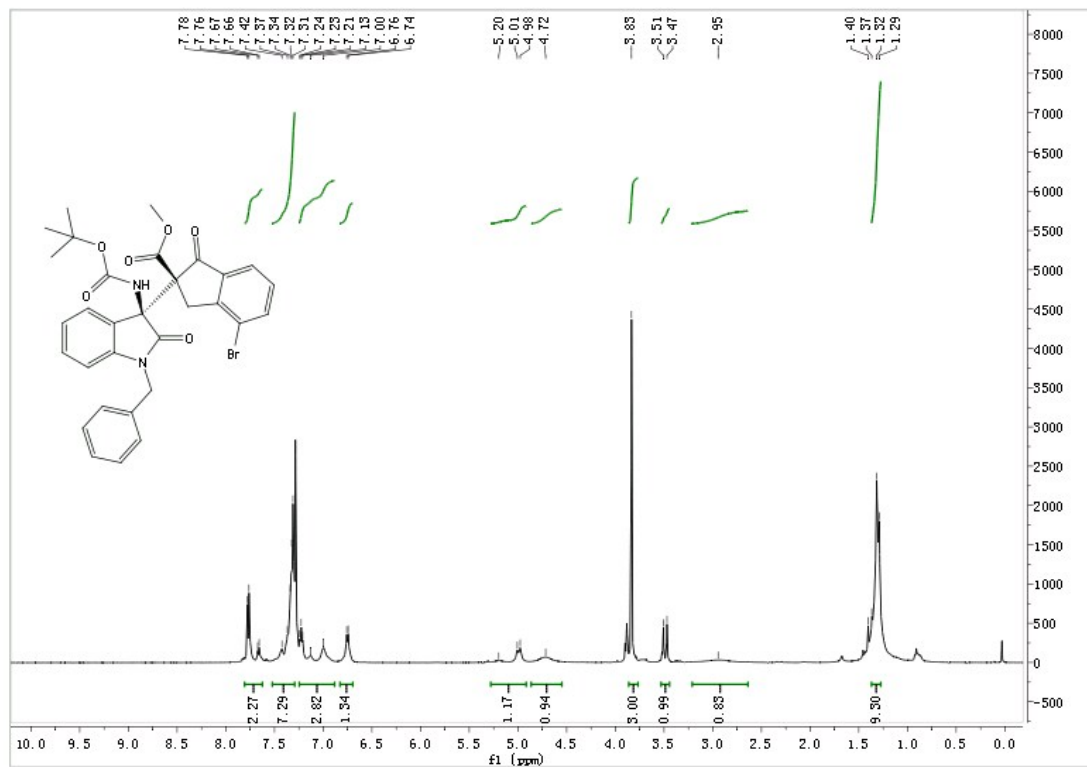


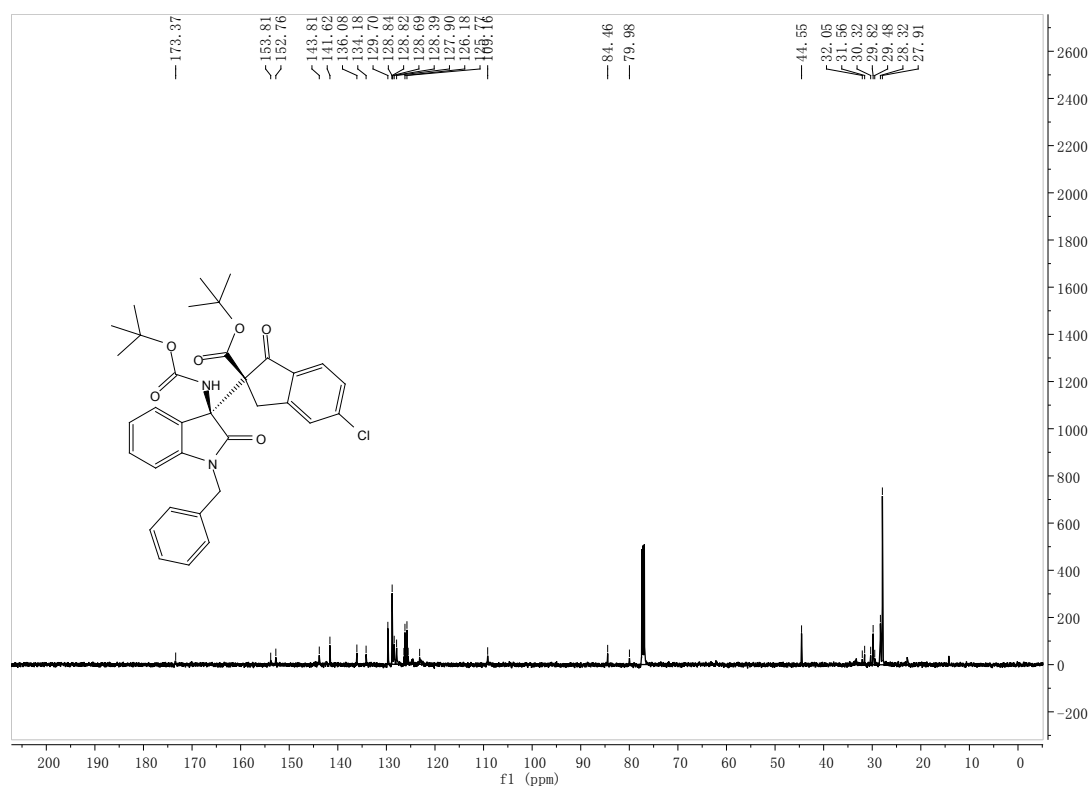
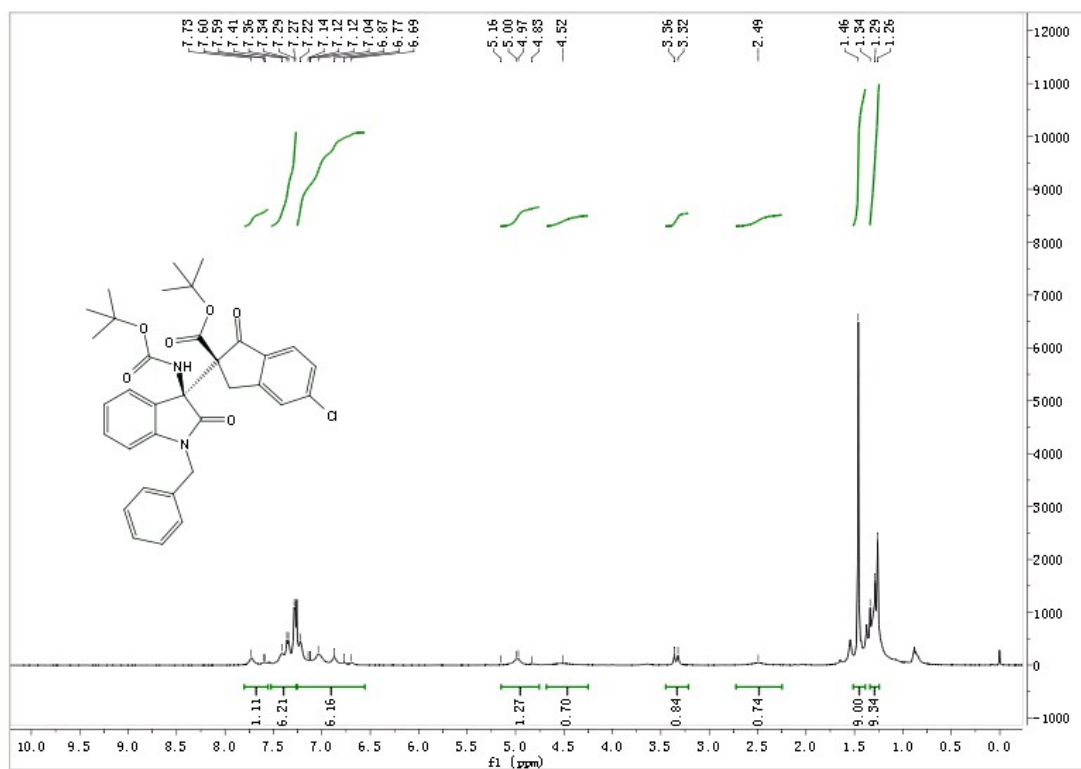


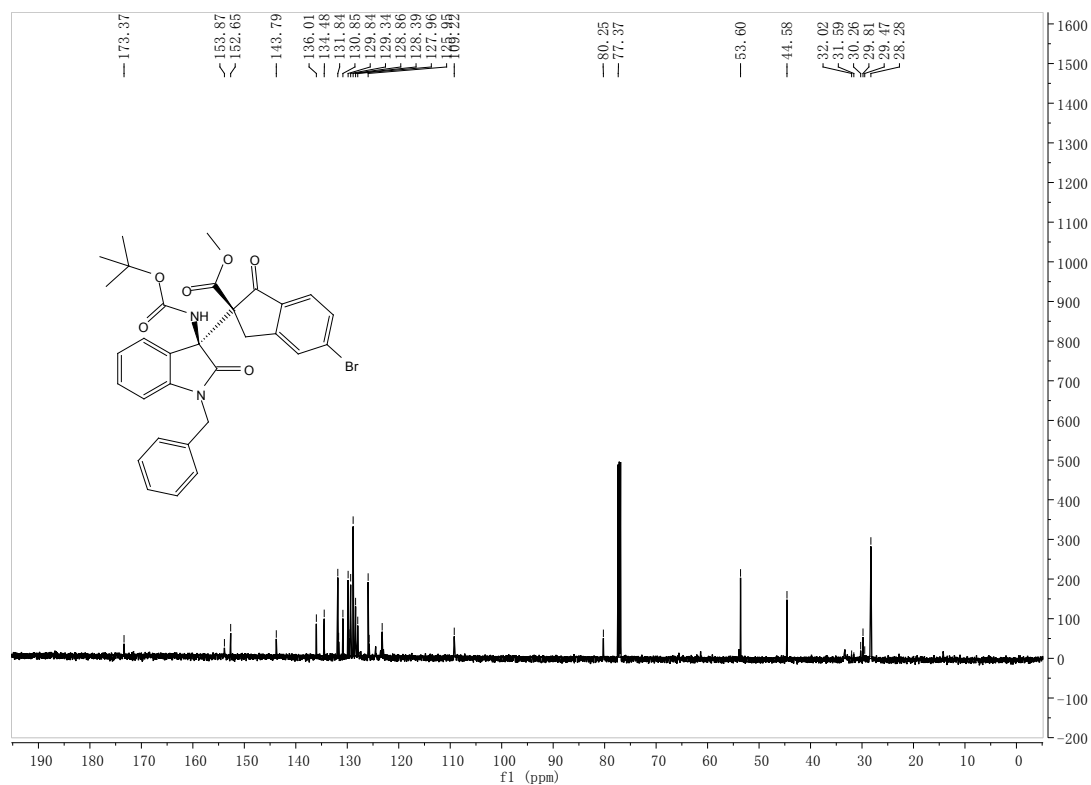
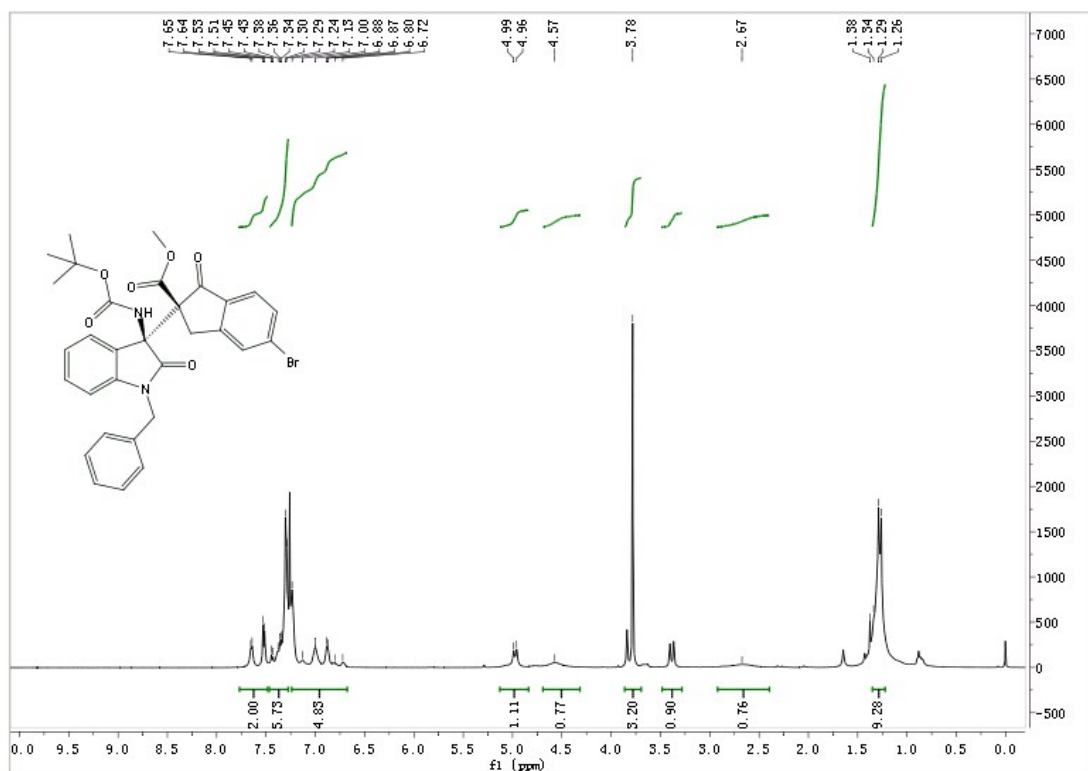


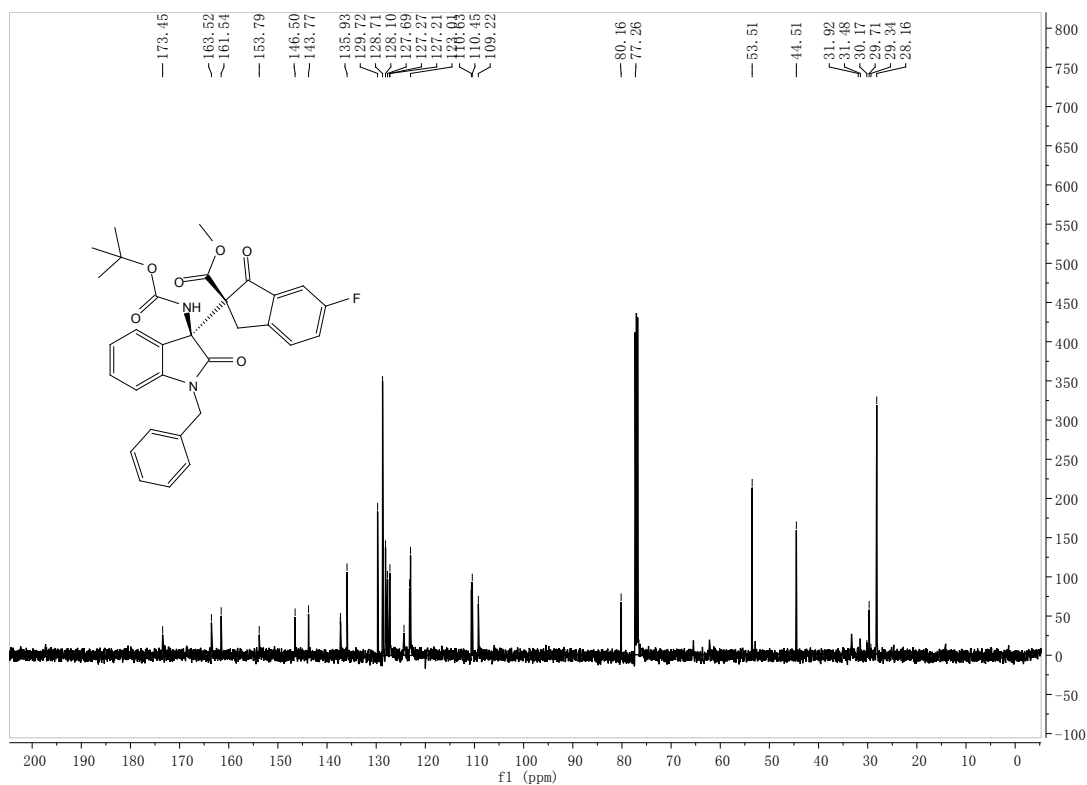
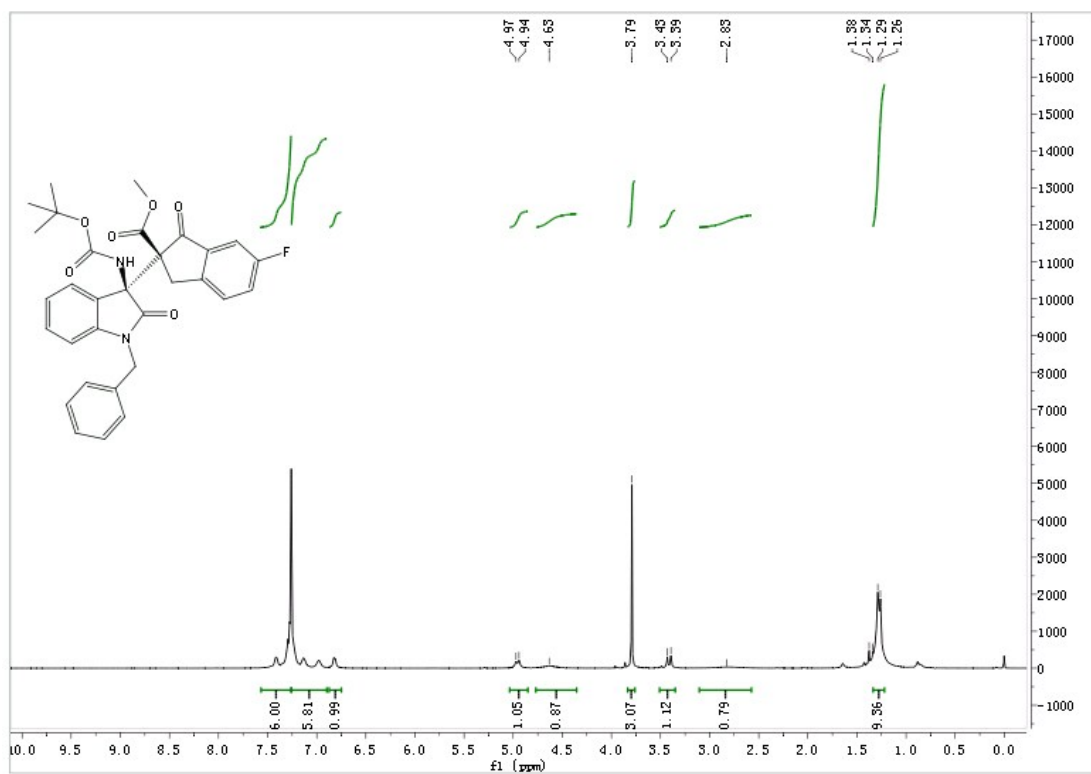


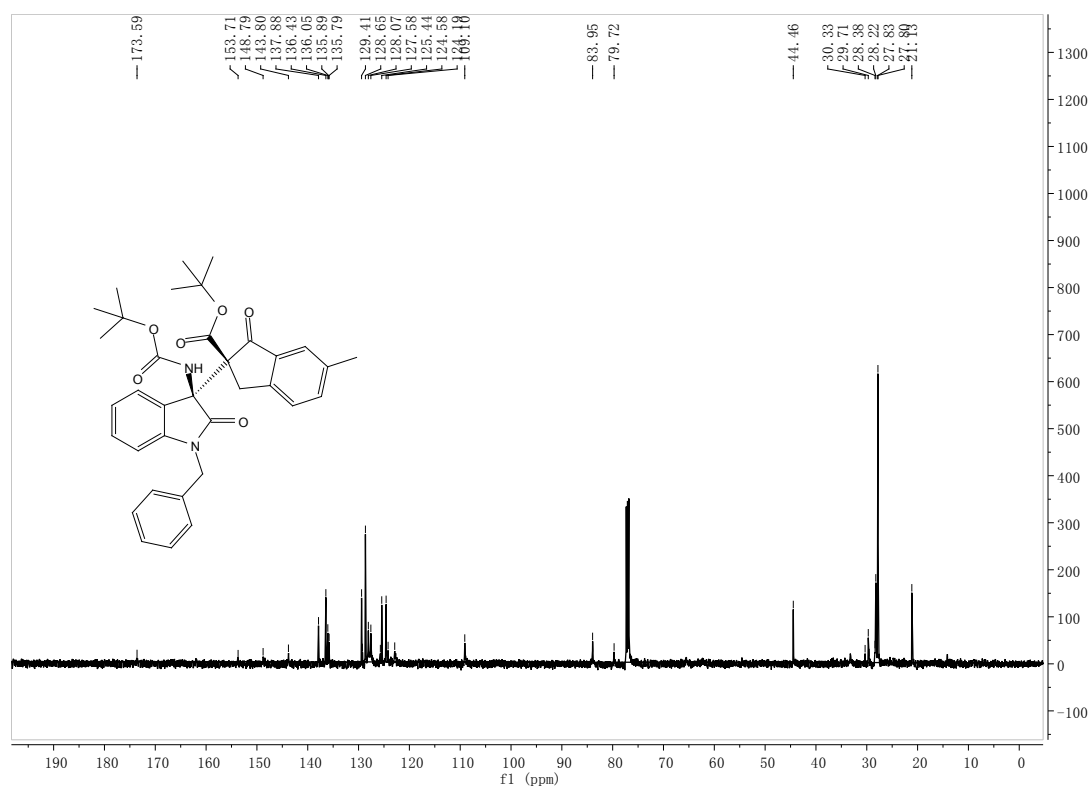
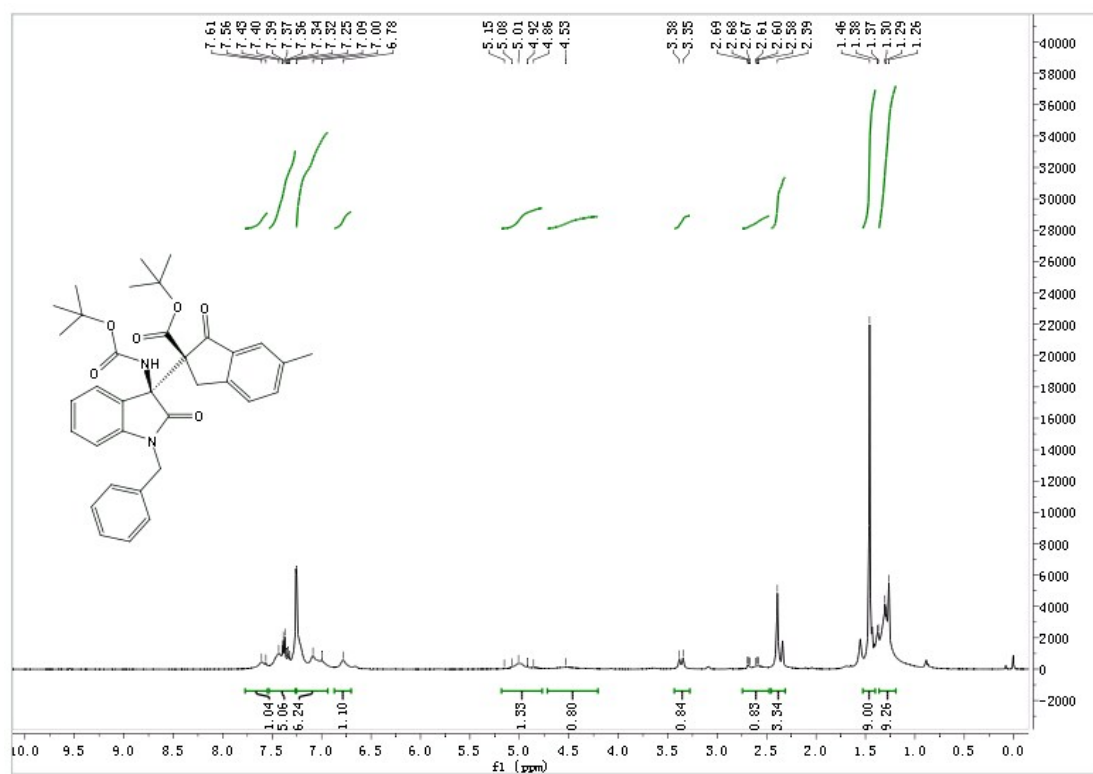


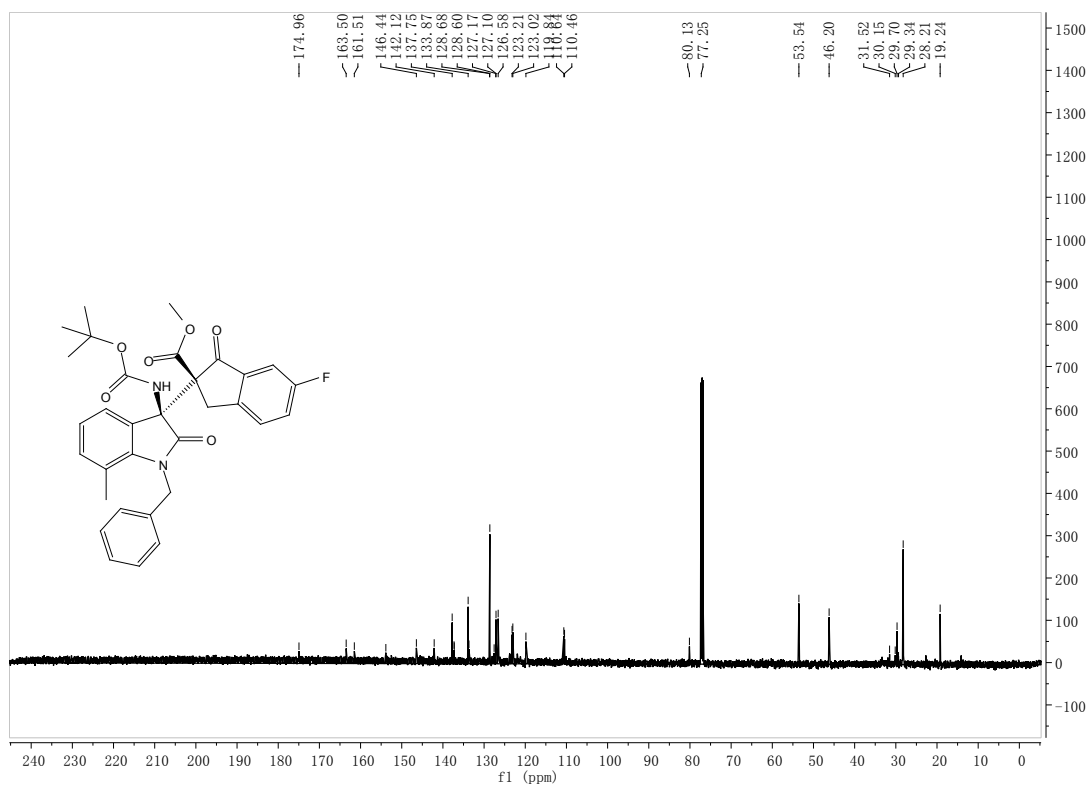
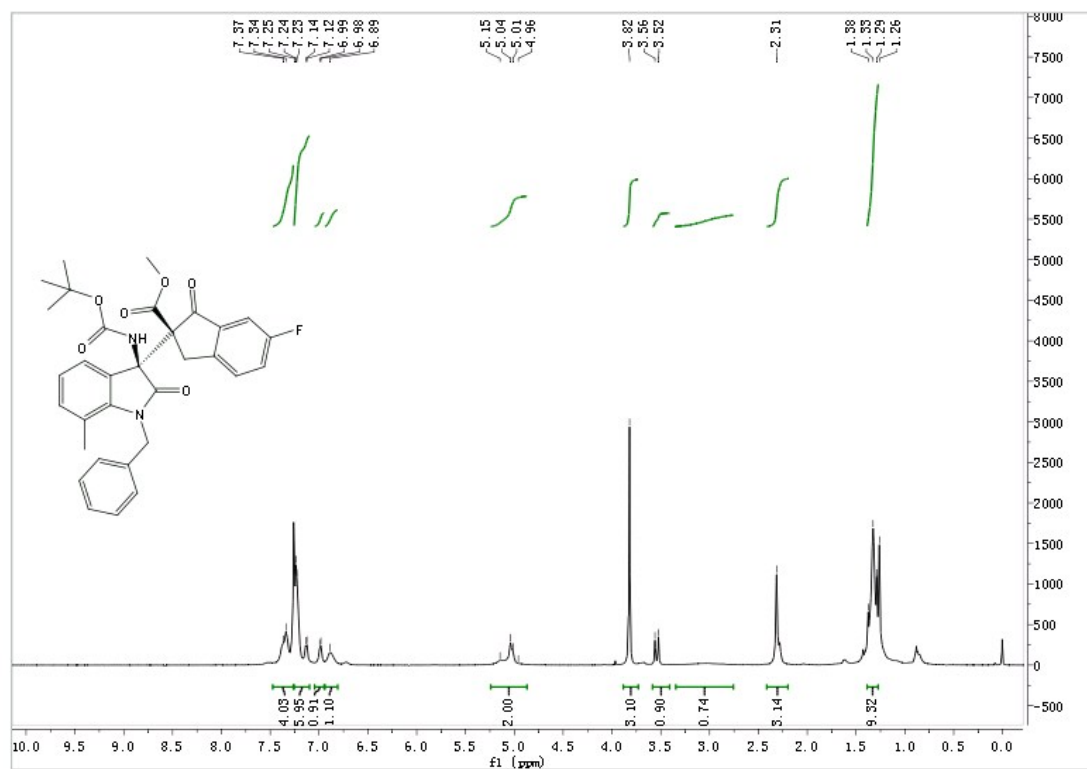


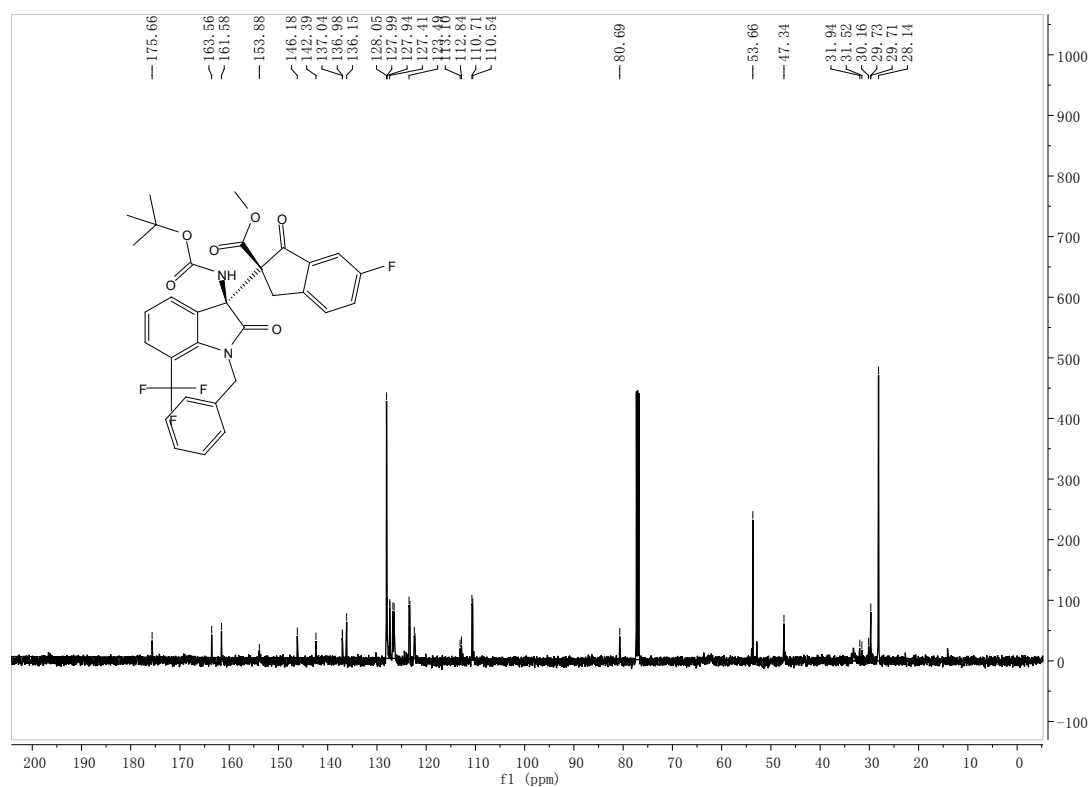
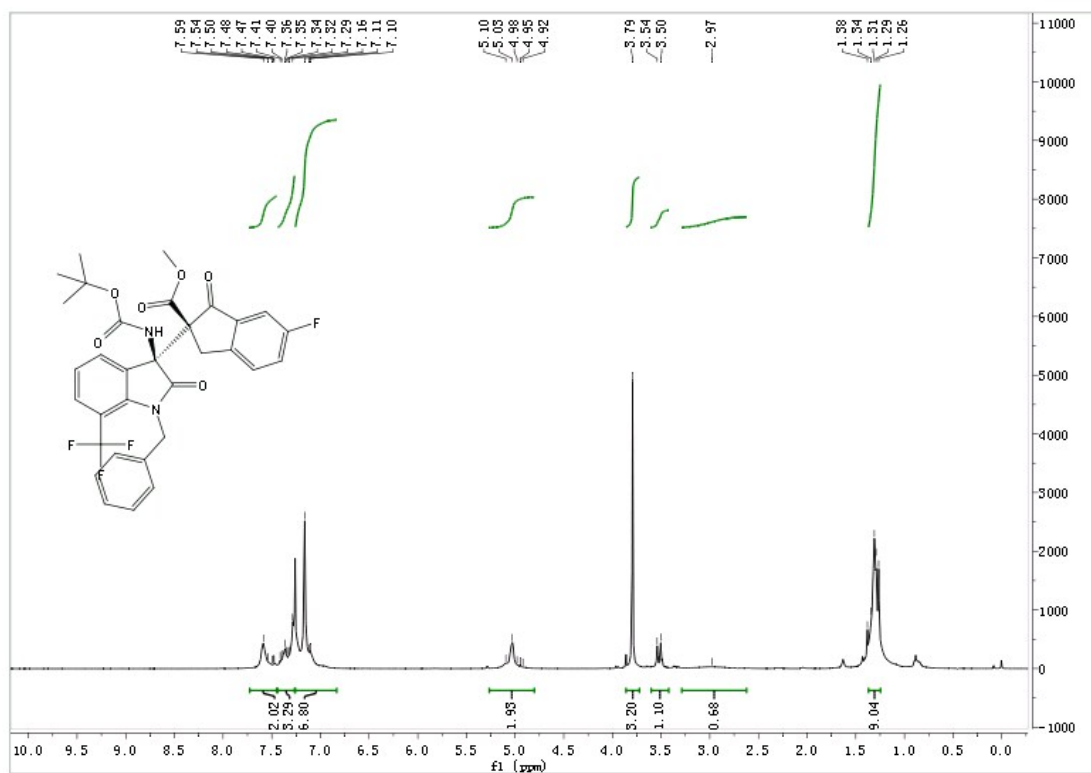




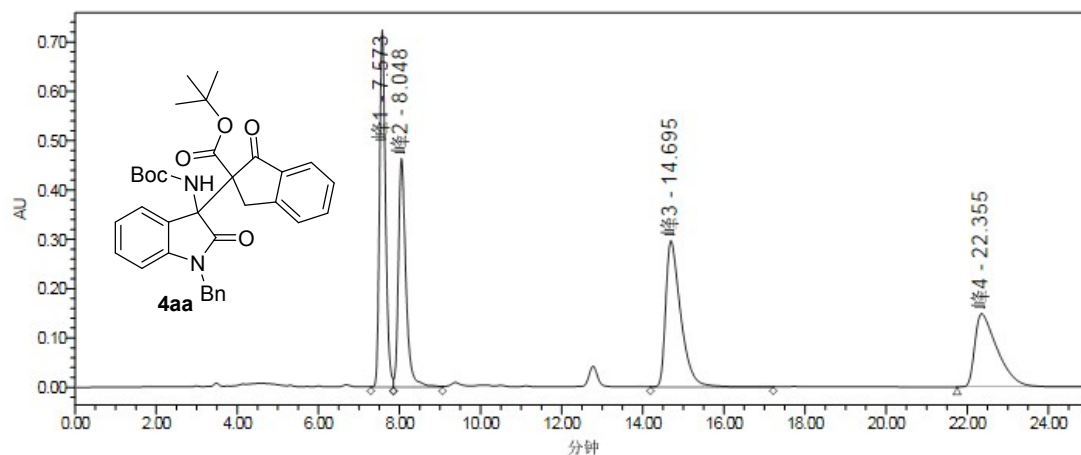








8. HPLC traces of all compounds



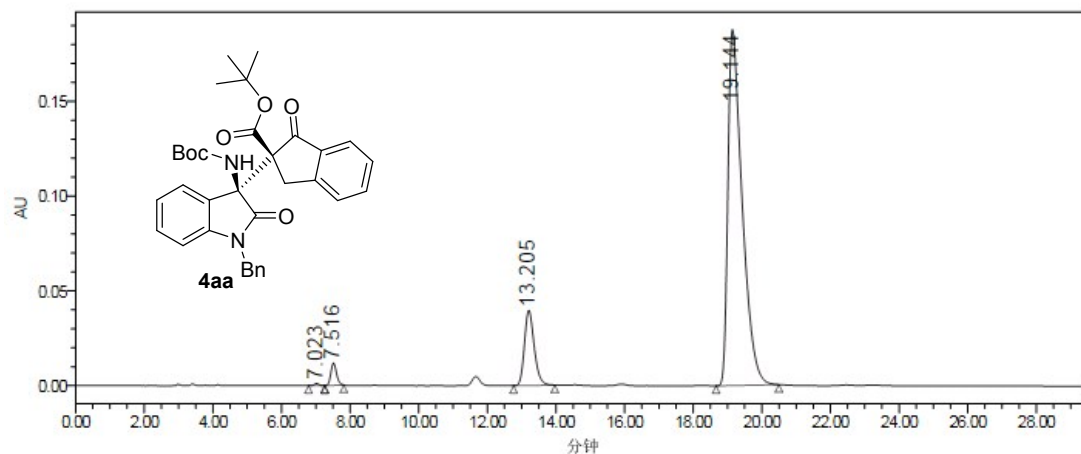
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	7.573	7459985	27.80	722767
2	W2489 ChA 254nm	峰2	8.048	5983316	22.29	462865
3	W2489 ChA 254nm	峰3	14.695	7641509	28.47	296057
4	W2489 ChA 254nm	峰4	22.355	5752760	21.44	148294

remark: 峰→Peak↵

分钟→time (min)↵

峰→mAU↵



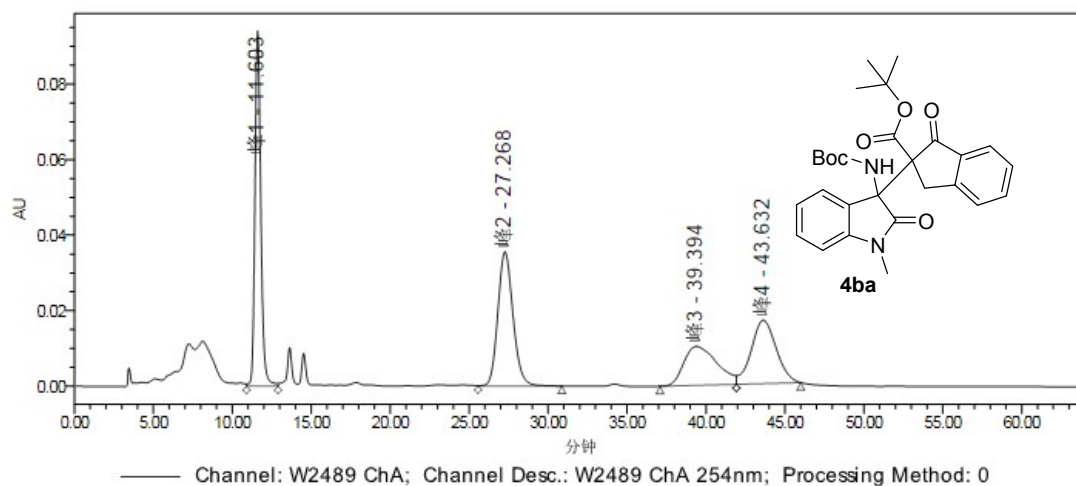
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	7.023	11503	0.18	1164
2	W2489 ChA 254nm	7.516	134750	2.13	11783
3	W2489 ChA 254nm	13.205	783242	12.39	39541
4	W2489 ChA 254nm	19.144	5390458	85.29	187640

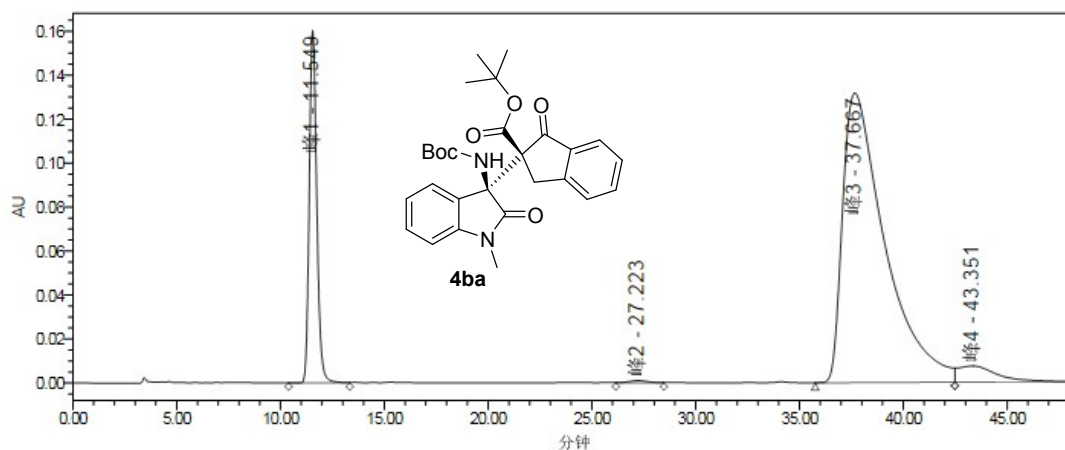
remark: 峰→Peak↵

分钟→time (min)↵

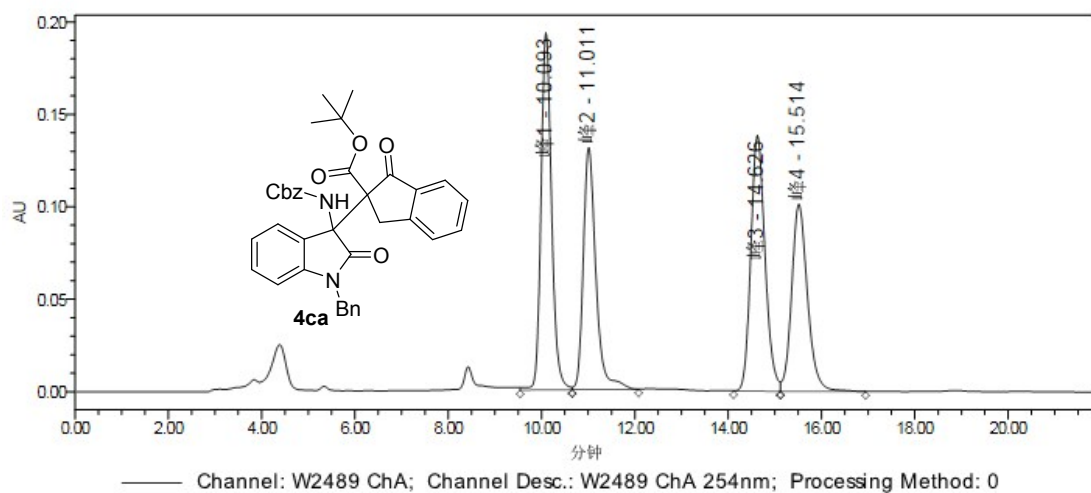
峰→mAU↵



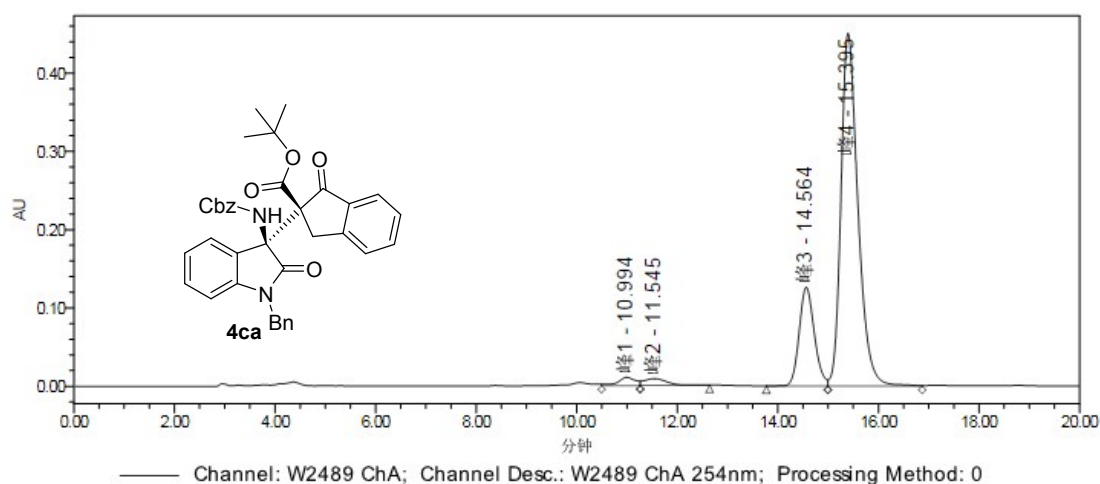
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	11.603	2431907	29.86	94010
2	W2489 ChA 254nm	峰2	27.268	2370904	29.11	35497
3	W2489 ChA 254nm	峰3	39.394	1502253	18.44	10326
4	W2489 ChA 254nm	峰4	43.632	1840594	22.60	16752



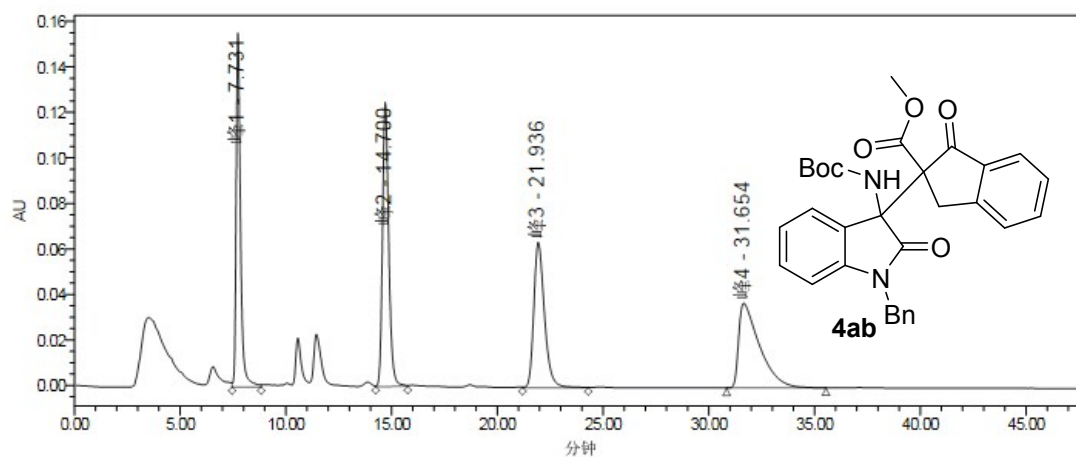
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	11.549	4014336	17.00	160075
2	W2489 ChA 254nm	峰2	27.223	66310	0.28	984
3	W2489 ChA 254nm	峰3	37.667	18580674	78.68	131640
4	W2489 ChA 254nm	峰4	43.351	954083	4.04	7301



	Channel Description	Peak Name	RT (min)	Area (面积*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	10.093	3019734	28.02	192904
2	W2489 ChA 254nm	峰2	11.011	2445907	22.70	130679
3	W2489 ChA 254nm	峰3	14.626	2923611	27.13	138132
4	W2489 ChA 254nm	峰4	15.514	2387348	22.15	101018

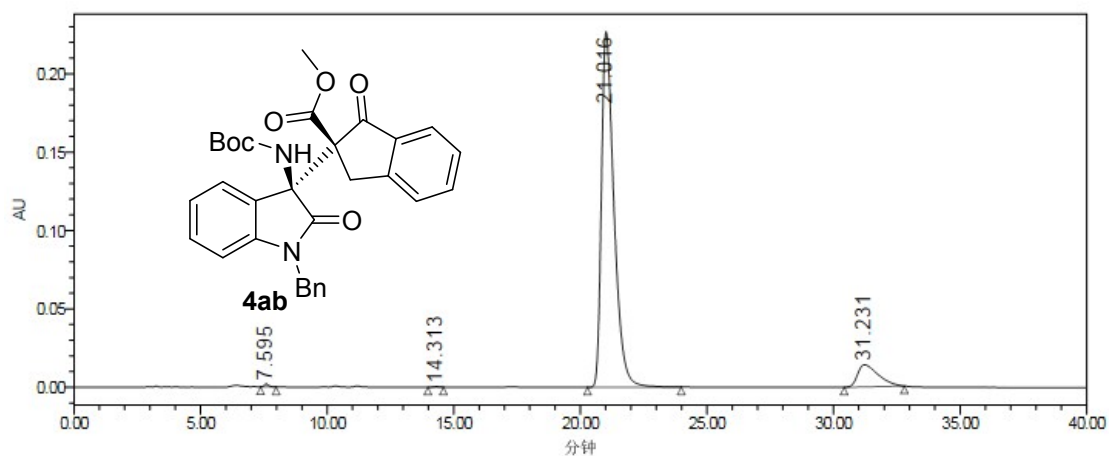


	Channel Description	Peak Name	RT (min)	Area (面积*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	10.994	249657	1.82	10330
2	W2489 ChA 254nm	峰2	11.545	265742	1.94	8683
3	W2489 ChA 254nm	峰3	14.564	2641343	19.28	126126
4	W2489 ChA 254nm	峰4	15.395	10542064	76.96	450515



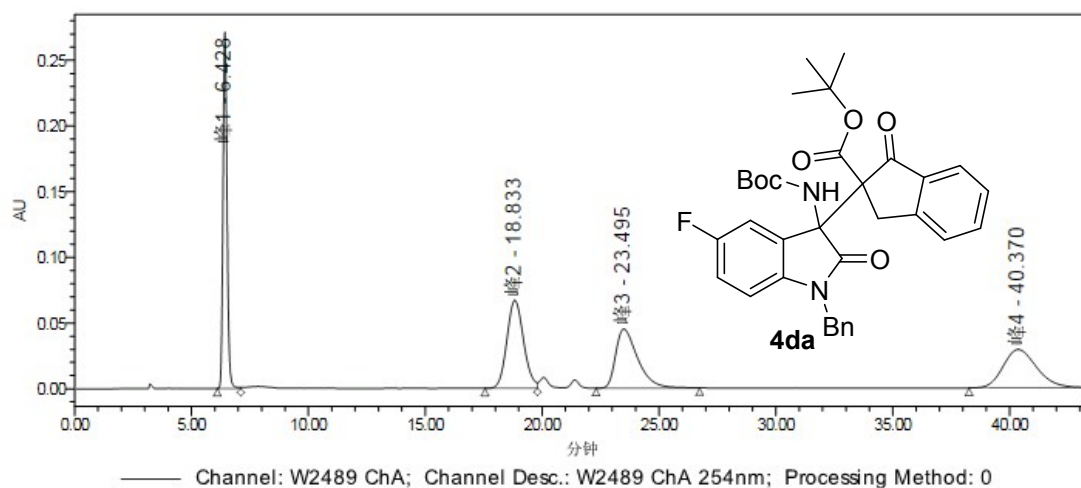
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	7.731	2217122	23.21	155380
2	W2489 ChA 254nm	峰2	14.700	2549509	26.69	124696
3	W2489 ChA 254nm	峰3	21.936	2233423	23.38	63704
4	W2489 ChA 254nm	峰4	31.654	2553628	26.73	37161

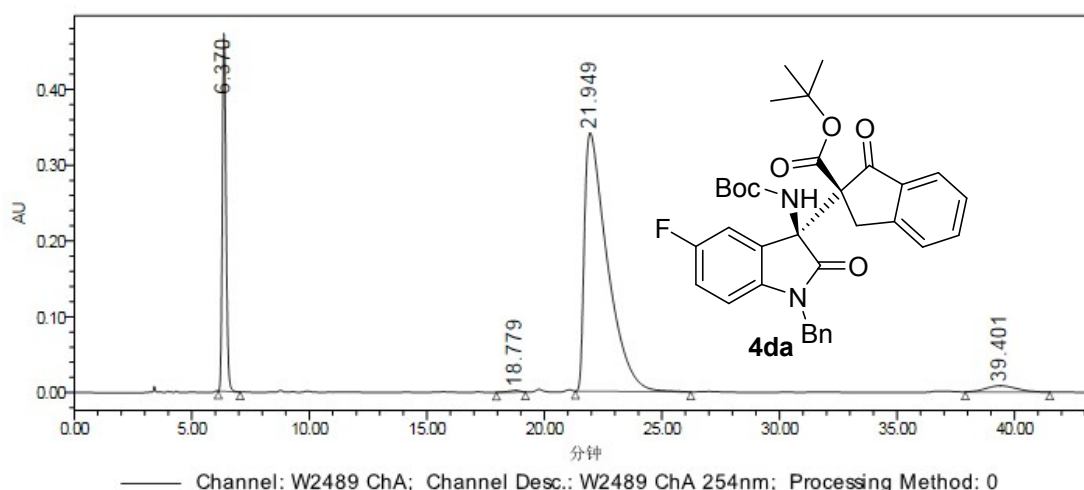
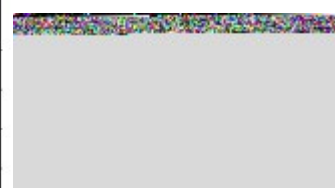


Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	7.595	24611	0.28	1842
2	W2489 ChA 254nm	14.313	6782	0.08	393
3	W2489 ChA 254nm	21.016	7796509	90.27	226738
4	W2489 ChA 254nm	31.231	808534	9.36	14161

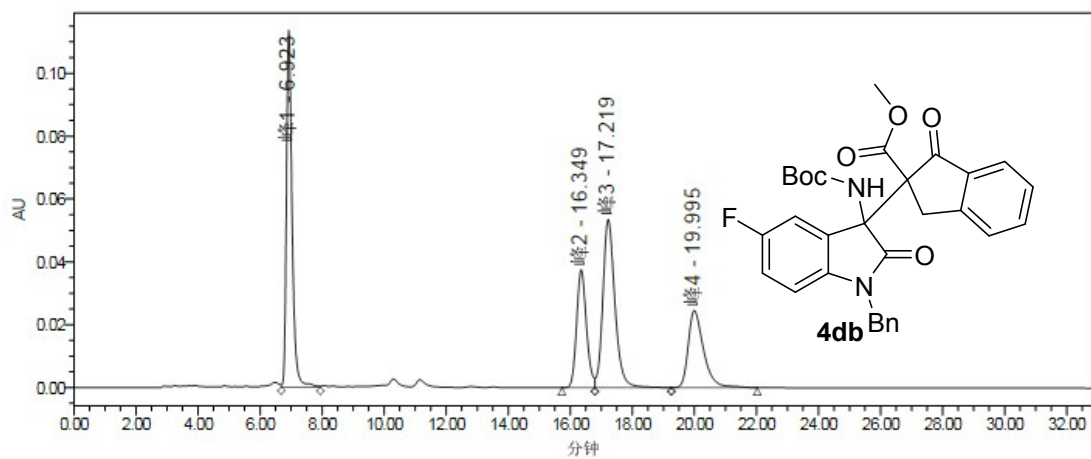


	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.428	3262471	26.27	271144
2	W2489 ChA 254nm	峰2	18.833	3317276	26.71	66958
3	W2489 ChA 254nm	峰3	23.495	2931430	23.61	44948
4	W2489 ChA 254nm	峰4	40.370	2906237	23.40	29130



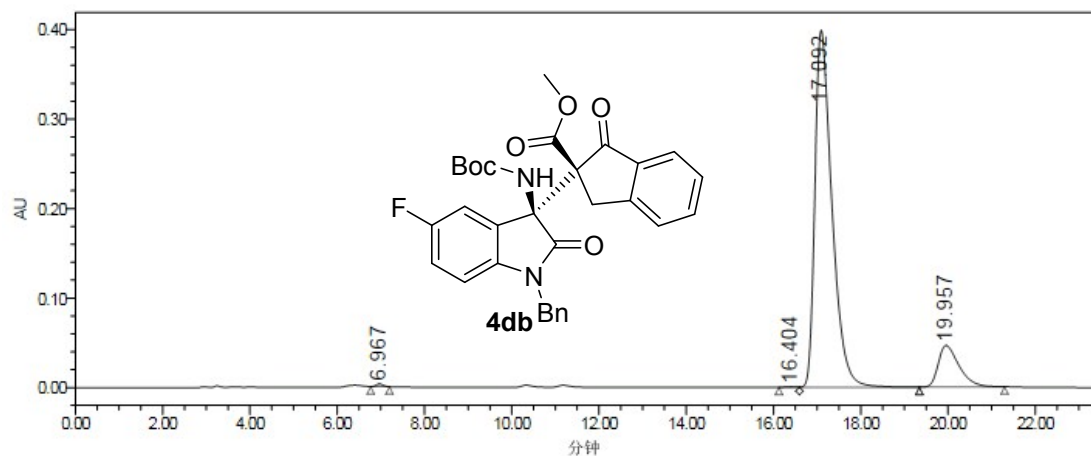
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.370	5158532	17.74	471776
2	W2489 ChA 254nm	18.779	76591	0.26	2320
3	W2489 ChA 254nm	21.949	23109072	79.45	340820
4	W2489 ChA 254nm	39.401	741643	2.55	8183





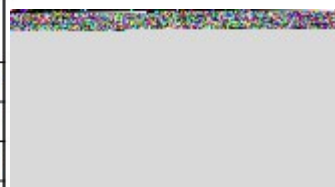
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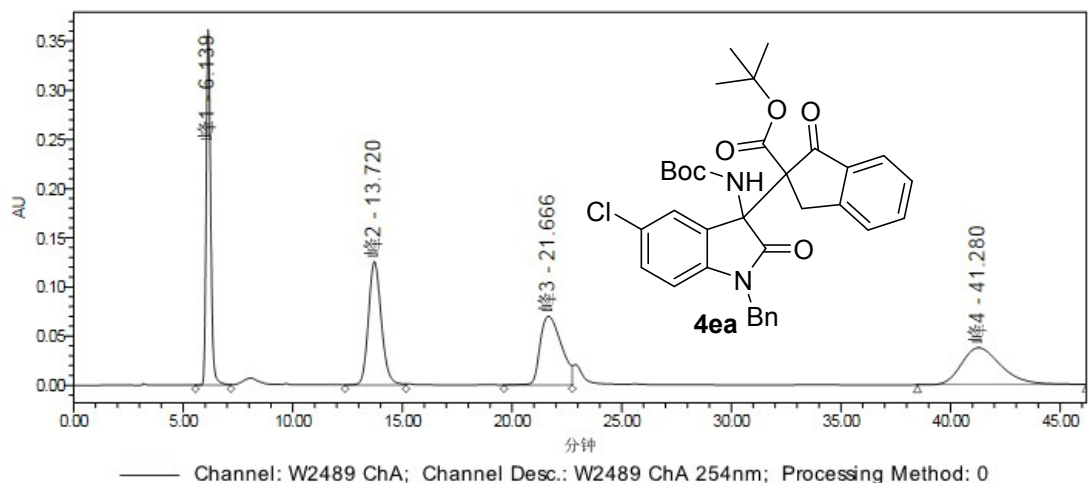
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.923	1439106	31.62	113363
2	W2489 ChA 254nm	峰2	16.349	822157	18.07	37457
3	W2489 ChA 254nm	峰3	17.219	1445972	31.78	53542
4	W2489 ChA 254nm	峰4	19.995	843352	18.53	24526



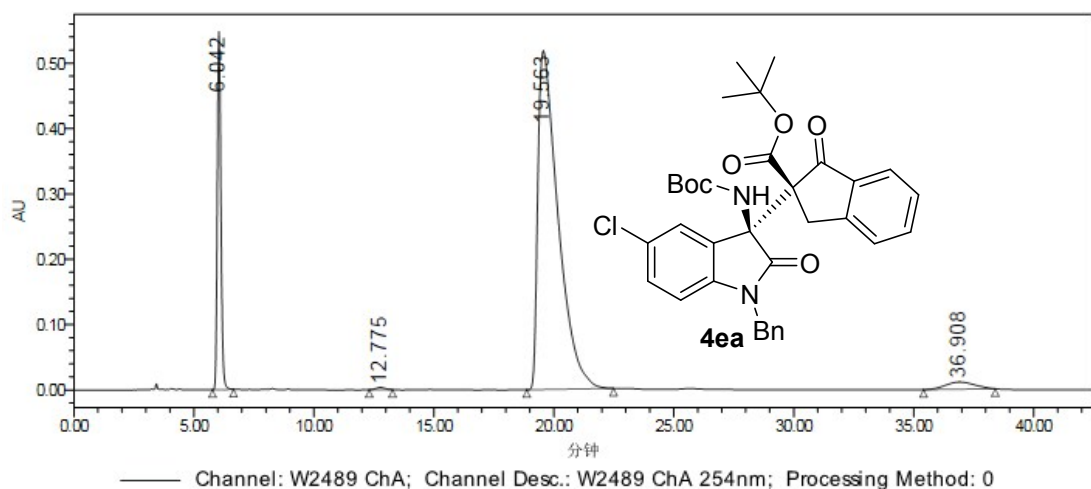
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.967	34356	0.28	3042
2	W2489 ChA 254nm	16.404	9923	0.08	579
3	W2489 ChA 254nm	17.092	10832902	87.28	398963
4	W2489 ChA 254nm	19.957	1533897	12.36	46464

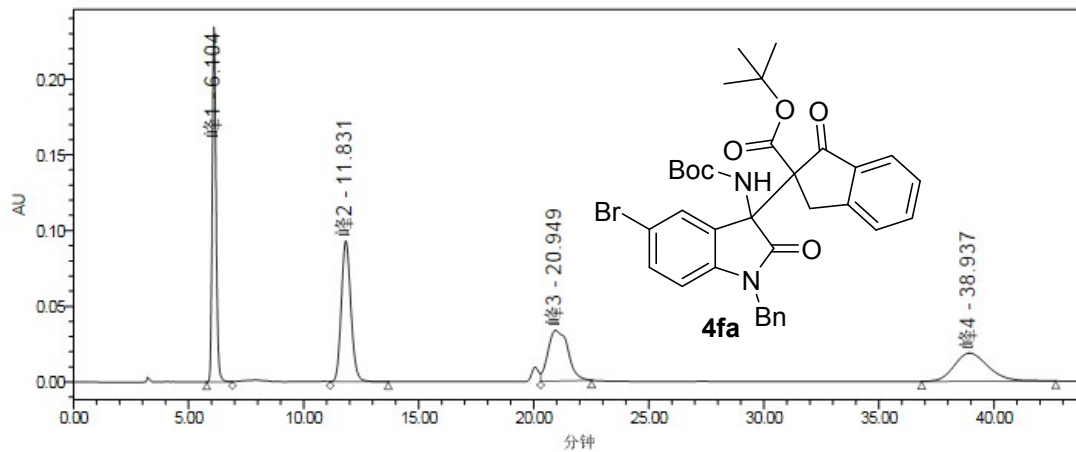




	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.139	5134849	26.02	361197
2	W2489 ChA 254nm	峰2	13.720	5141442	26.05	125355
3	W2489 ChA 254nm	峰3	21.666	4697733	23.81	69762
4	W2489 ChA 254nm	峰4	41.280	4759227	24.12	37641

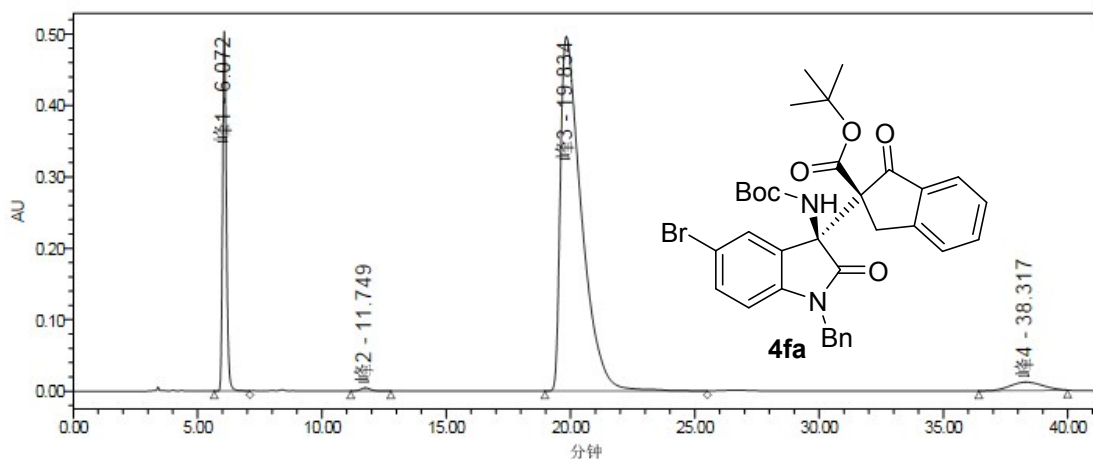


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.042	5686644	15.34	547141
2	W2489 ChA 254nm	12.775	93360	0.25	3322
3	W2489 ChA 254nm	19.563	30366112	81.89	518325
4	W2489 ChA 254nm	36.908	933641	2.52	10964



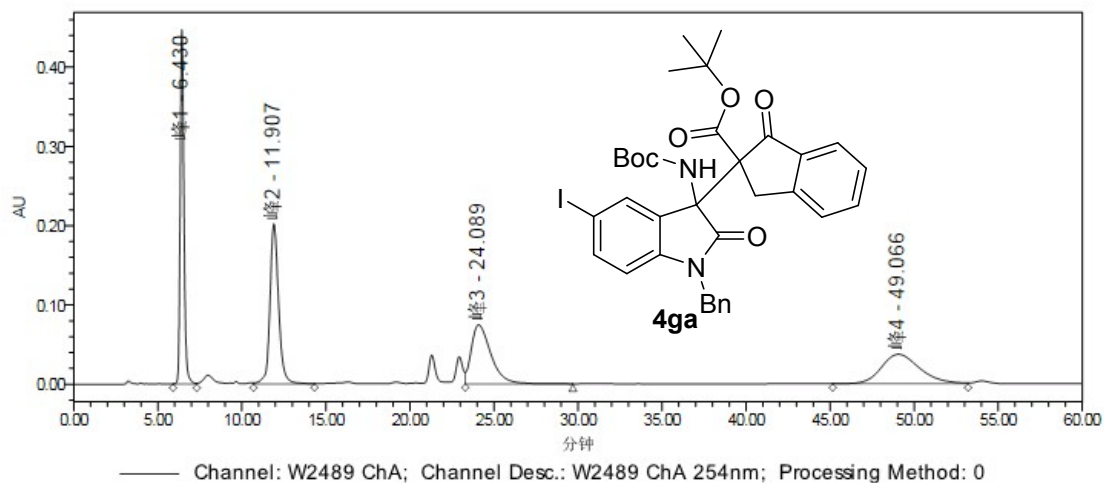
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.104	2698501	28.90	234162
2	W2489 ChA 254nm	峰2	11.831	2695137	28.87	93053
3	W2489 ChA 254nm	峰3	20.949	2029447	21.74	33412
4	W2489 ChA 254nm	峰4	38.937	1913150	20.49	18621

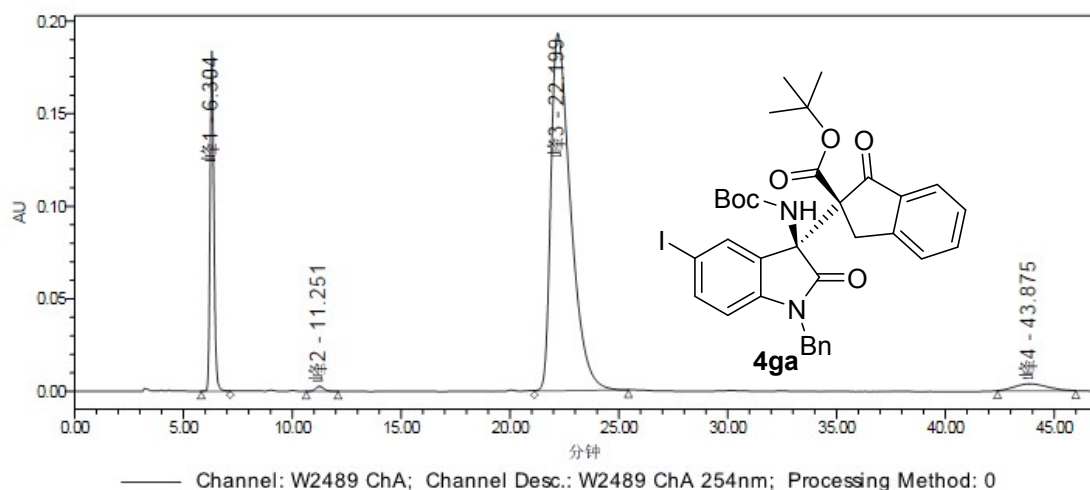


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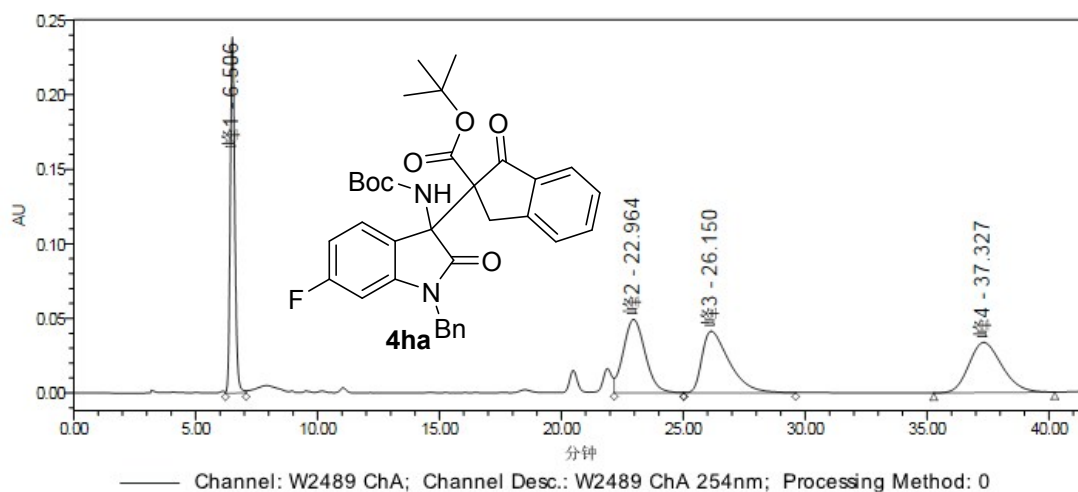
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.072	5337623	14.92	503796
2	W2489 ChA 254nm	峰2	11.749	120140	0.34	4353
3	W2489 ChA 254nm	峰3	19.834	29249989	81.74	496575
4	W2489 ChA 254nm	峰4	38.317	1074376	3.00	11736



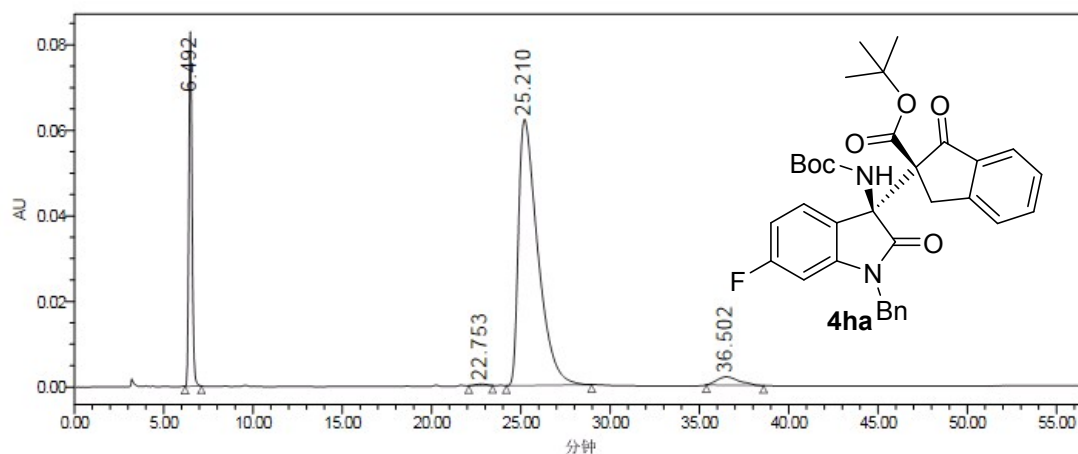
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.430	6908963	26.35	446533
2	W2489 ChA 254nm	峰2	11.907	7252585	27.66	201730
3	W2489 ChA 254nm	峰3	24.089	6055260	23.09	74355
4	W2489 ChA 254nm	峰4	49.066	6004864	22.90	37260



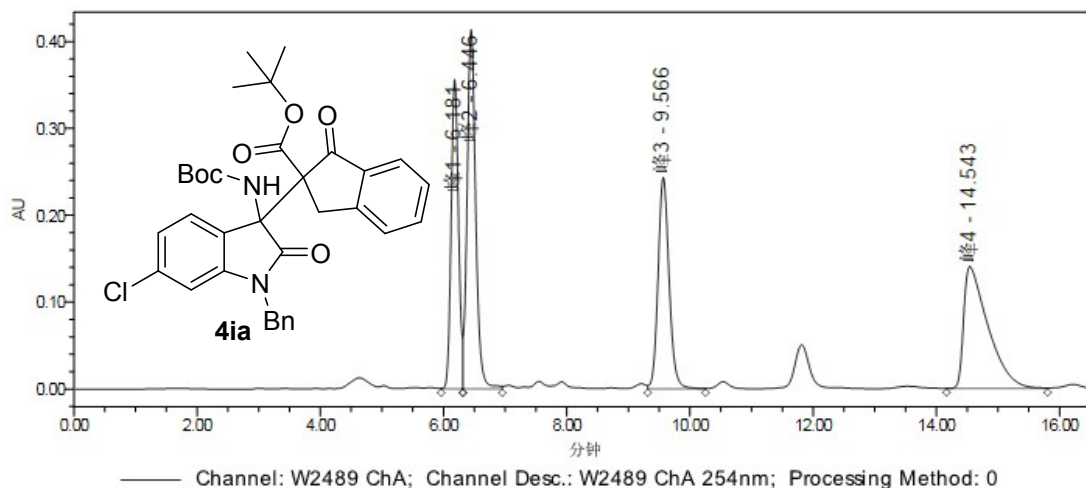
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.304	2260571	15.21	183687
2	W2489 ChA 254nm	峰2	11.251	72933	0.49	2680
3	W2489 ChA 254nm	峰3	22.199	12139017	81.69	192966
4	W2489 ChA 254nm	峰4	43.875	386570	2.60	3692



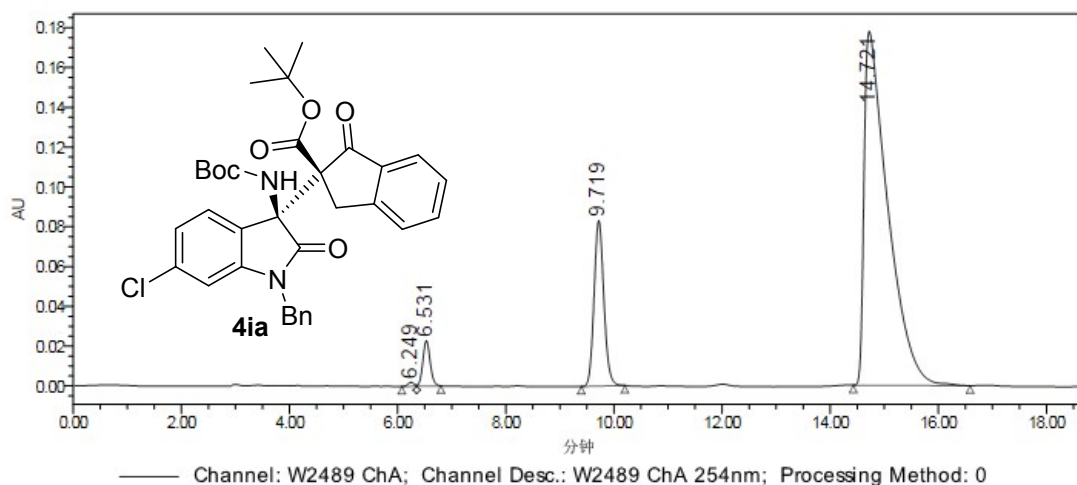
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.506	3088056	24.63	238456
2	W2489 ChA 254nm	峰2	22.964	3066960	24.46	49137
3	W2489 ChA 254nm	峰3	26.150	3212199	25.62	41275
4	W2489 ChA 254nm	峰4	37.327	3171784	25.30	33634



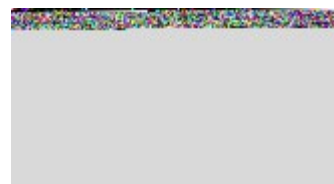
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1	W2489 ChA 254nm	6.492	1041845	17.65	82893
2	W2489 ChA 254nm	22.753	15877	0.27	345
3	W2489 ChA 254nm	25.210	4675840	79.20	62220
4	W2489 ChA 254nm	36.502	170618	2.89	1936

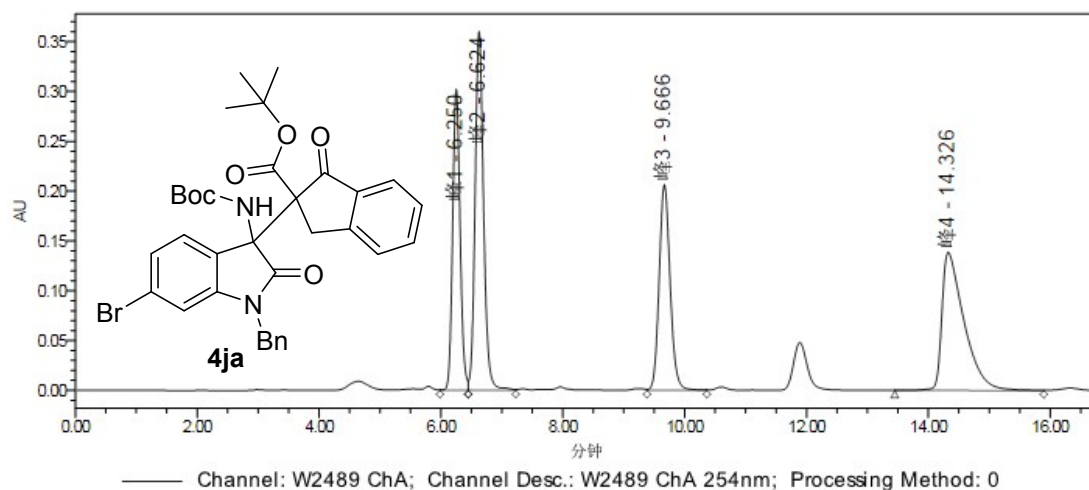


	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.181	2935440	21.24	355750
2	W2489 ChA 254nm	峰2	6.446	3989438	28.87	413118
3	W2489 ChA 254nm	峰3	9.566	3018542	21.84	243201
4	W2489 ChA 254nm	峰4	14.543	3874996	28.04	140475

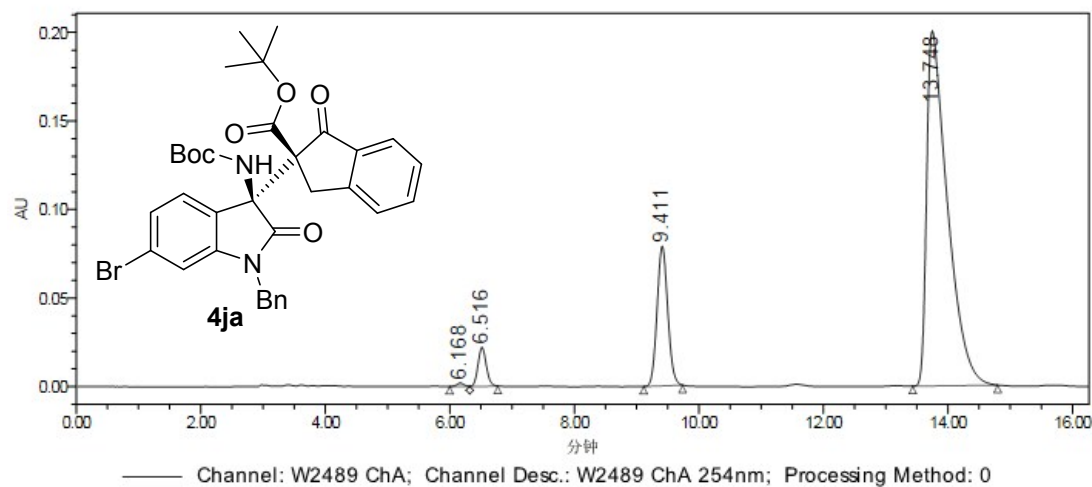


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.249	16007	0.24	2033
2	W2489 ChA 254nm	6.531	214909	3.22	22861
3	W2489 ChA 254nm	9.719	1046275	15.67	83197
4	W2489 ChA 254nm	14.721	5398389	80.87	177618

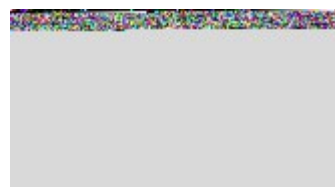


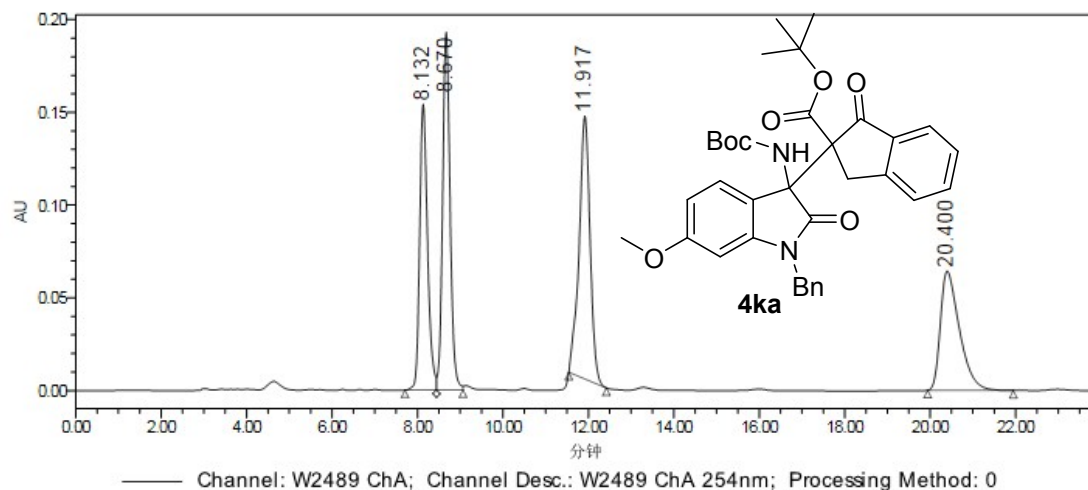


	Channel Description	Peak Name	RT (min)	Area (碘*sec)	% Area	Height (碘)
1	W2489 ChA 254nm	峰1	6.250	2567275	21.19	302049
2	W2489 ChA 254nm	峰2	6.624	3490246	28.80	359961
3	W2489 ChA 254nm	峰3	9.666	2579112	21.28	206308
4	W2489 ChA 254nm	峰4	14.326	3481139	28.73	138462

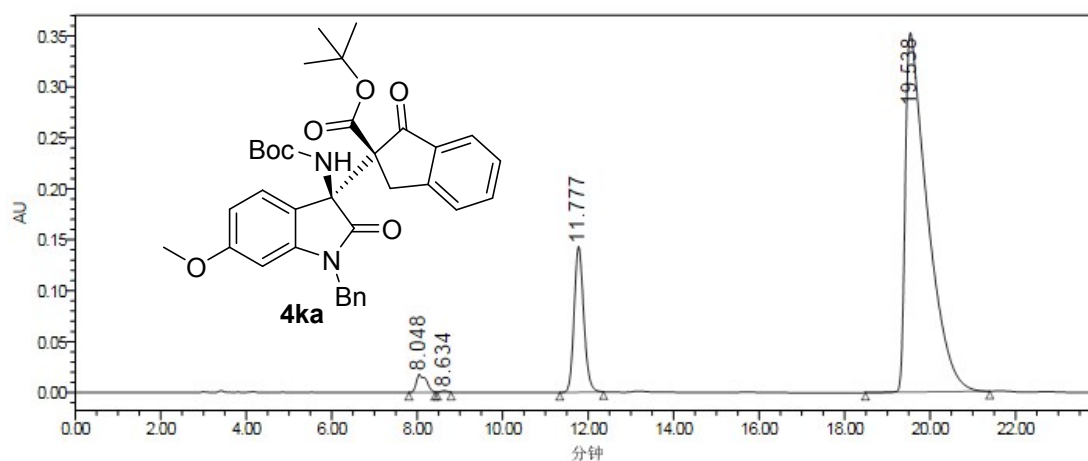
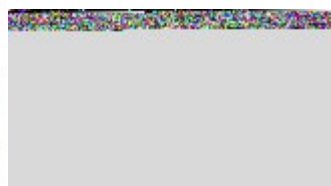


	Channel Description	RT (min)	Area (碘*sec)	% Area	Height (碘)
1	W2489 ChA 254nm	6.168	15210	0.26	1882
2	W2489 ChA 254nm	6.516	202973	3.50	21848
3	W2489 ChA 254nm	9.411	937519	16.16	78806
4	W2489 ChA 254nm	13.748	4644596	80.08	200346



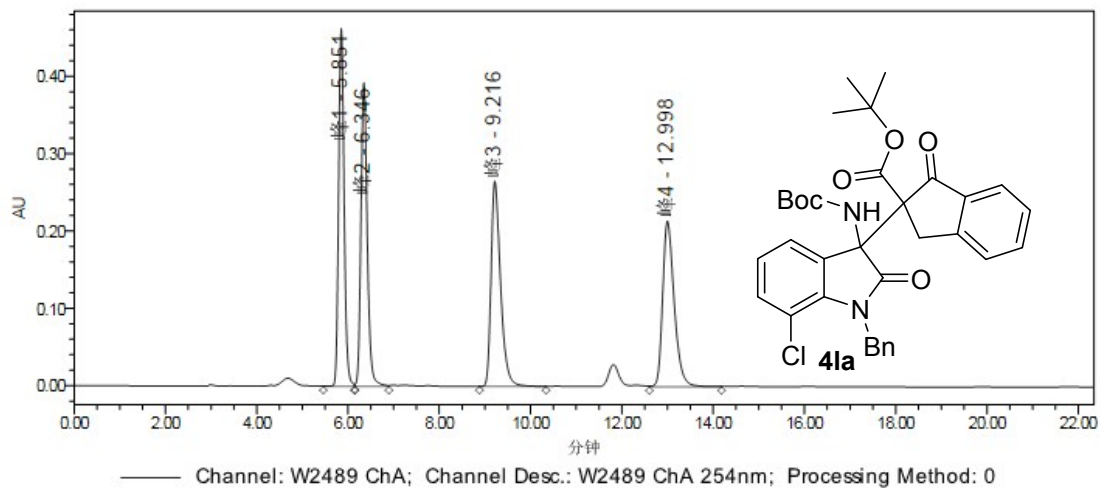


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	8.132	1972256	22.36	153888
2	W2489 ChA 254nm	8.670	2337128	26.50	192496
3	W2489 ChA 254nm	11.917	2525014	28.63	141570
4	W2489 ChA 254nm	20.400	1985940	22.52	64275

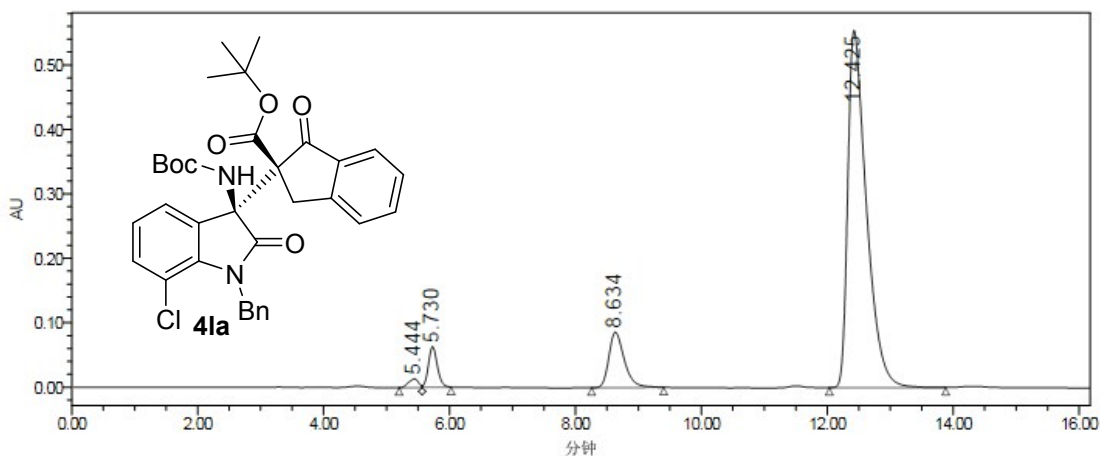


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	8.048	289760	1.91	17580
2	W2489 ChA 254nm	8.634	16518	0.11	1538
3	W2489 ChA 254nm	11.777	2244345	14.77	142690
4	W2489 ChA 254nm	19.538	12647506	83.22	352164



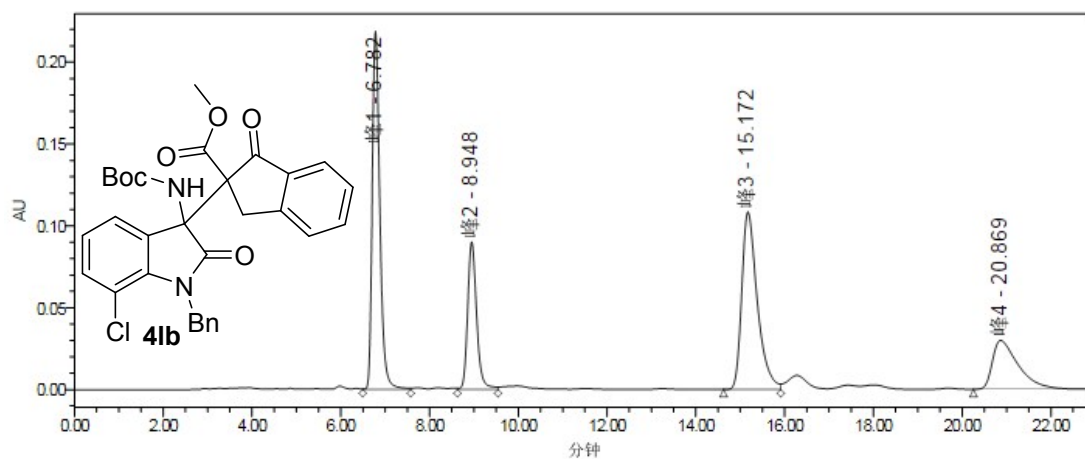


	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	5.851	3862652	25.35	462060
2	W2489 ChA 254nm	峰2	6.346	3768808	24.73	391845
3	W2489 ChA 254nm	峰3	9.216	3842778	25.22	265112
4	W2489 ChA 254nm	峰4	12.998	3763786	24.70	213826



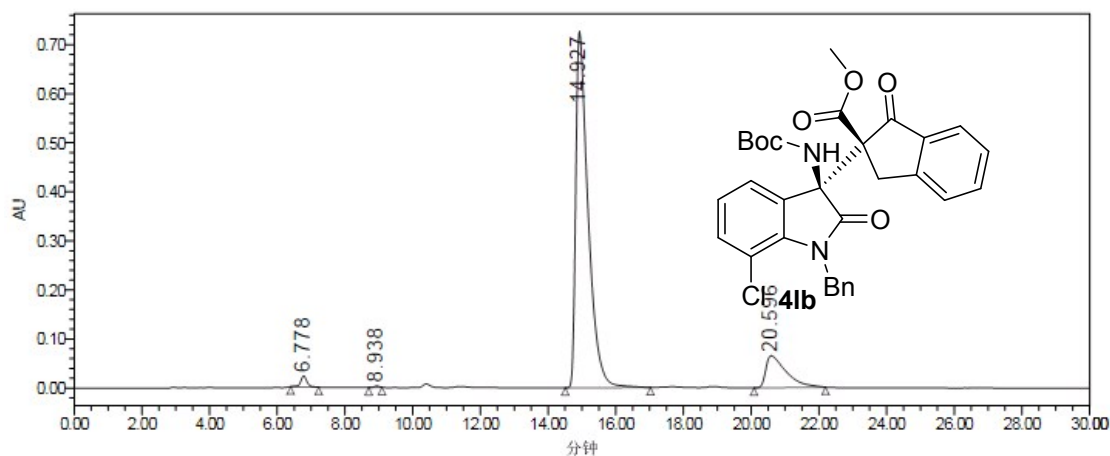
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	5.444	147358	1.08	13533
2	W2489 ChA 254nm	5.730	625285	4.58	63069
3	W2489 ChA 254nm	8.634	1469255	10.77	86098
4	W2489 ChA 254nm	12.425	11398725	83.56	554087





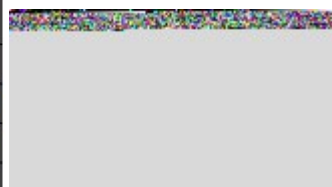
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

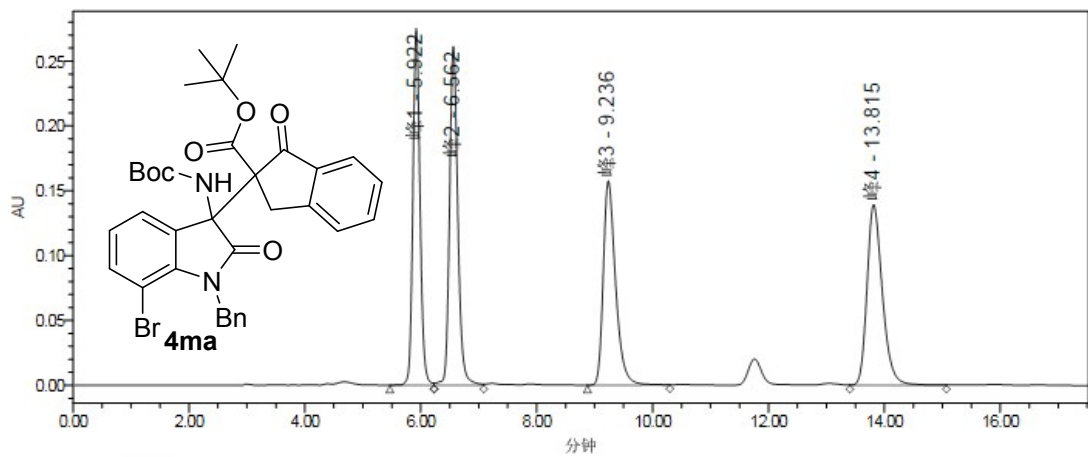
	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	6.782	2609714	33.75	218571
2	W2489 ChA 254nm	峰2	8.948	1262712	16.33	90053
3	W2489 ChA 254nm	峰3	15.172	2639812	34.14	108402
4	W2489 ChA 254nm	峰4	20.869	1220345	15.78	29934



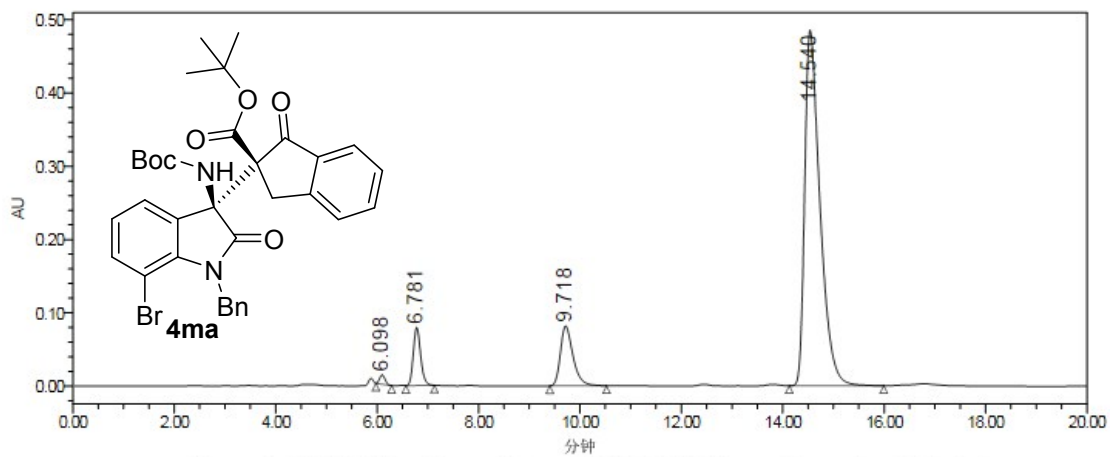
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	6.778	287578	1.35	22474
2	W2489 ChA 254nm	8.938	28784	0.13	2578
3	W2489 ChA 254nm	14.927	18327157	85.78	726079
4	W2489 ChA 254nm	20.596	2720745	12.74	65232

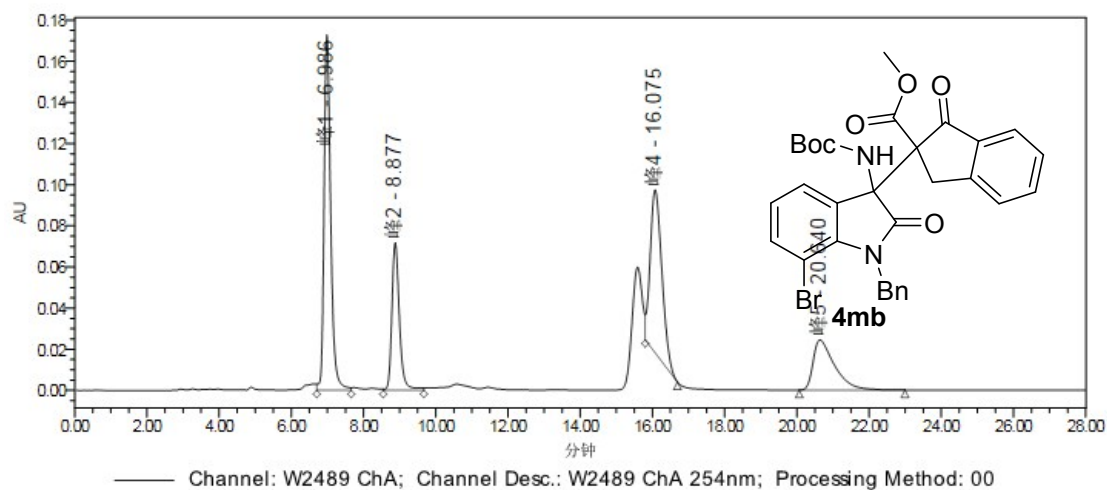




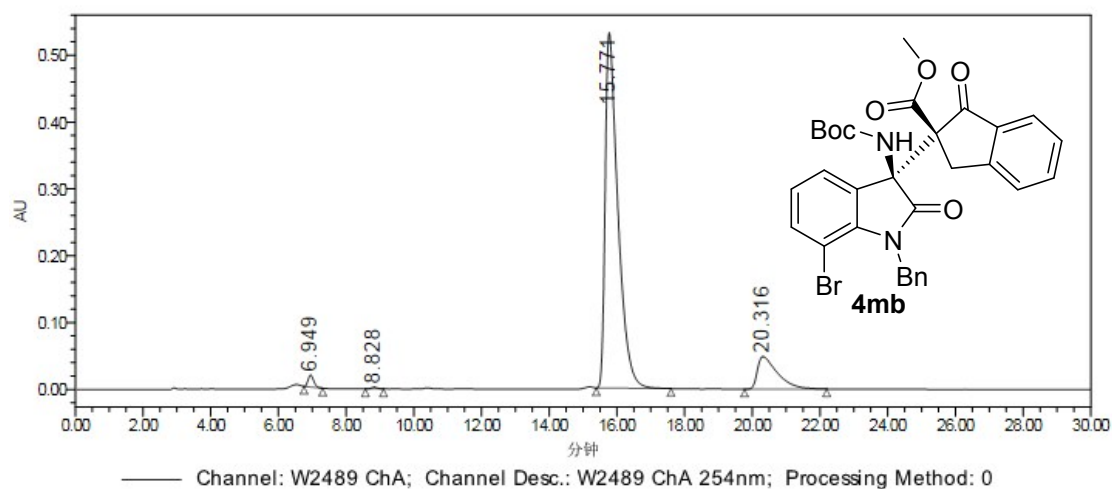
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	5.922	2346540	23.86	274734
2	W2489 ChA 254nm	峰2	6.562	2592228	26.36	261224
3	W2489 ChA 254nm	峰3	9.236	2322183	23.61	157390
4	W2489 ChA 254nm	峰4	13.815	2574514	26.18	139278



	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.098	96033	0.77	12587
2	W2489 ChA 254nm	6.781	797944	6.41	79095
3	W2489 ChA 254nm	9.718	1408832	11.31	81663
4	W2489 ChA 254nm	14.540	10152395	81.51	484853

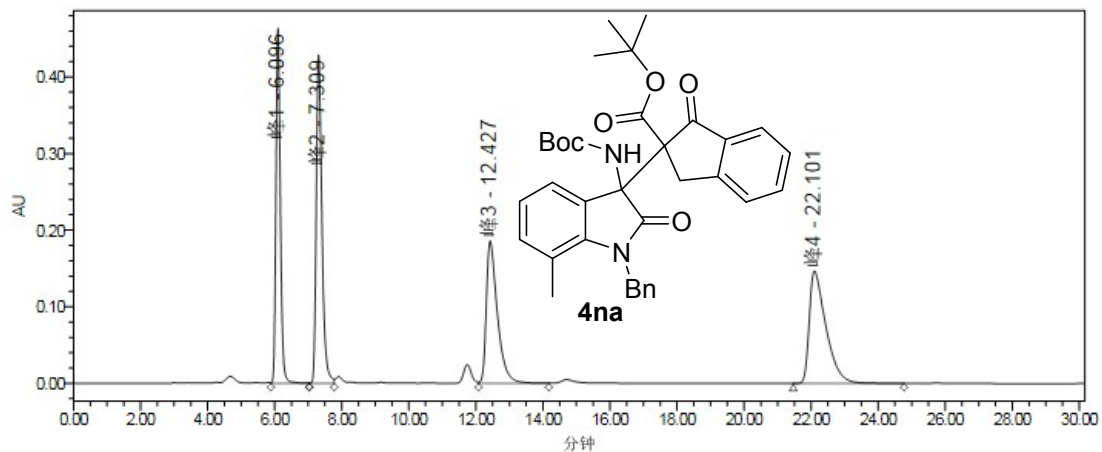


	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.986	2197211	36.49	172576
2	W2489 ChA 254nm	峰2	8.877	1038309	17.24	71679
3	W2489 ChA 254nm	峰4	16.075	1780648	29.57	79167
4	W2489 ChA 254nm	峰5	20.640	1005083	16.69	24388

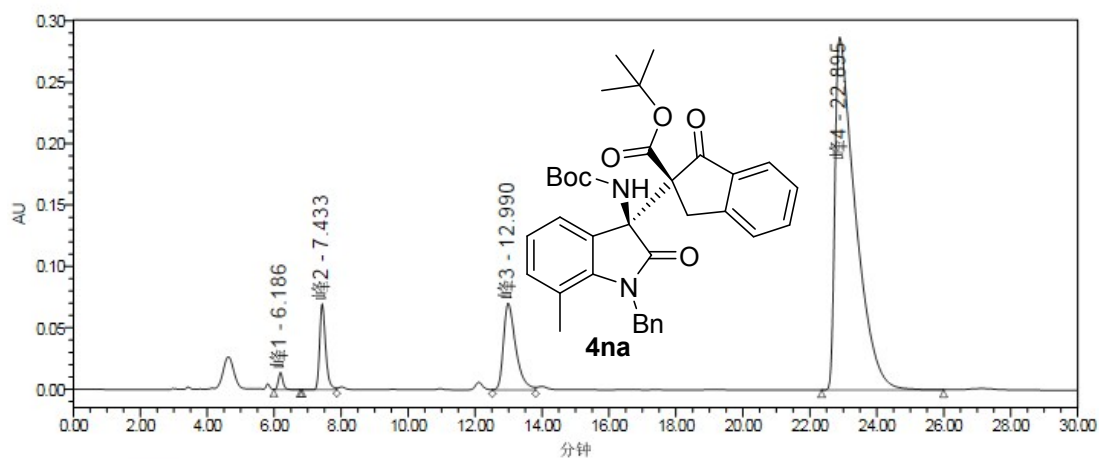


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.949	207032	1.28	17802
2	W2489 ChA 254nm	8.828	33114	0.21	2516
3	W2489 ChA 254nm	15.771	13862353	86.02	531582
4	W2489 ChA 254nm	20.316	2013012	12.49	48835



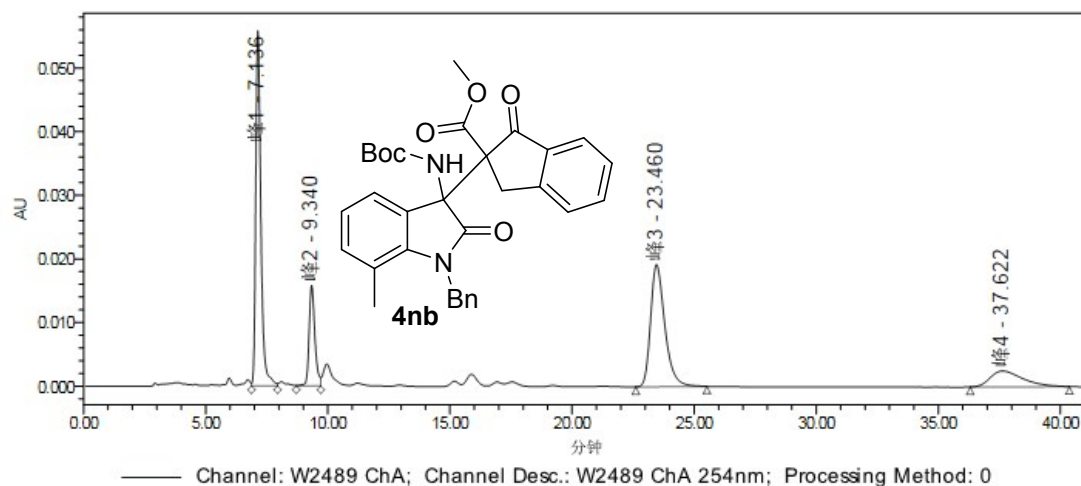


	Channel Description	Peak Name	RT (min)	Area (磺*sec)	% Area	Height (磺)
1	W2489 ChA 254nm	峰1	6.096	4261670	22.86	463344
2	W2489 ChA 254nm	峰2	7.309	5035021	27.01	428705
3	W2489 ChA 254nm	峰3	12.427	4271734	22.91	185720
4	W2489 ChA 254nm	峰4	22.101	5076163	27.23	146684

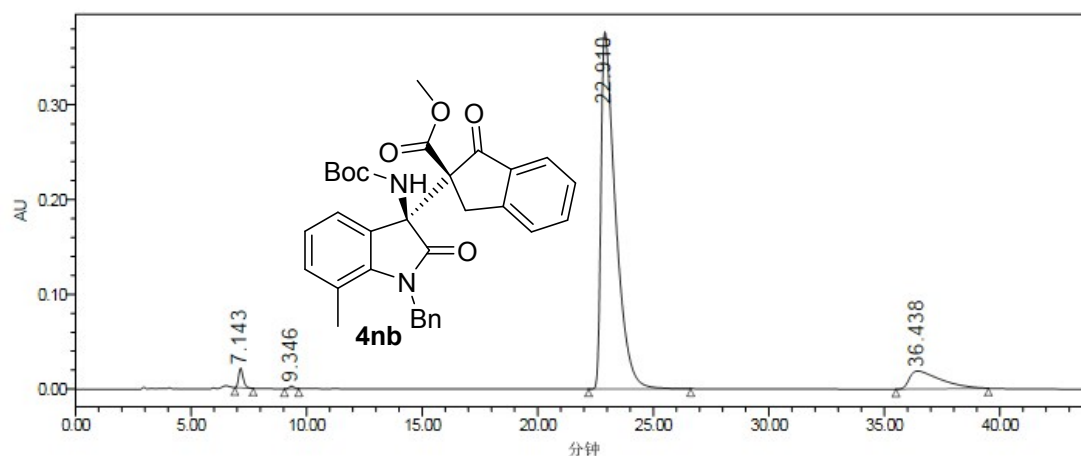


	Channel Description	Peak Name	RT (min)	Area (磺*sec)	% Area	Height (磺)
1	W2489 ChA 254nm	峰1	6.186	128324	0.86	13590
2	W2489 ChA 254nm	峰2	7.433	867844	5.79	69707
3	W2489 ChA 254nm	峰3	12.990	1799160	12.01	70322
4	W2489 ChA 254nm	峰4	22.895	12185540	81.34	286921

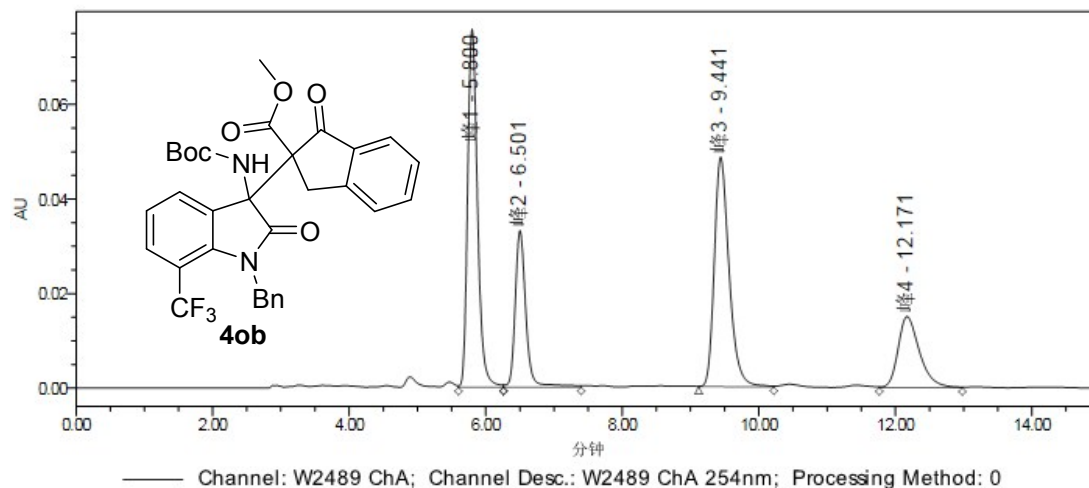




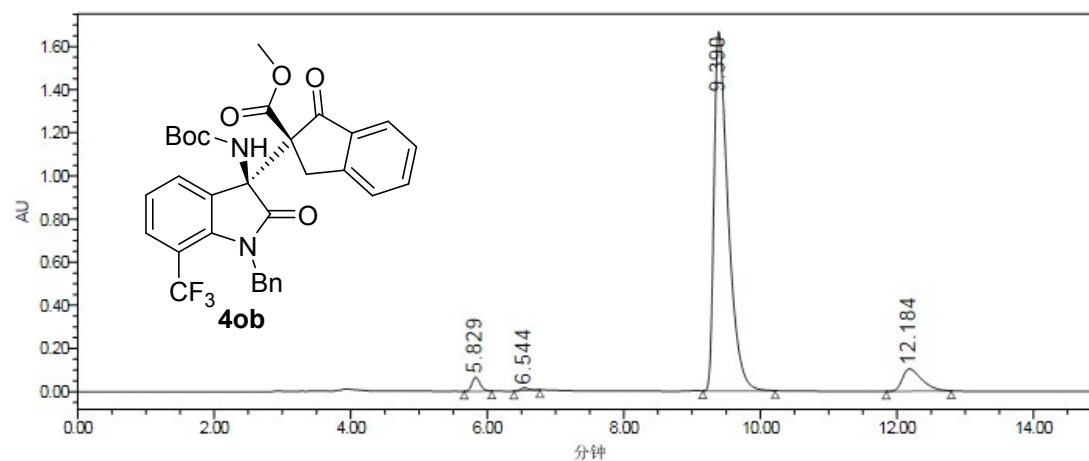
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	7.136	816871	39.14	55792
2	W2489 ChA 254nm	峰2	9.340	259677	12.44	15779
3	W2489 ChA 254nm	峰3	23.460	778101	37.28	19175
4	W2489 ChA 254nm	峰4	37.622	232537	11.14	2505



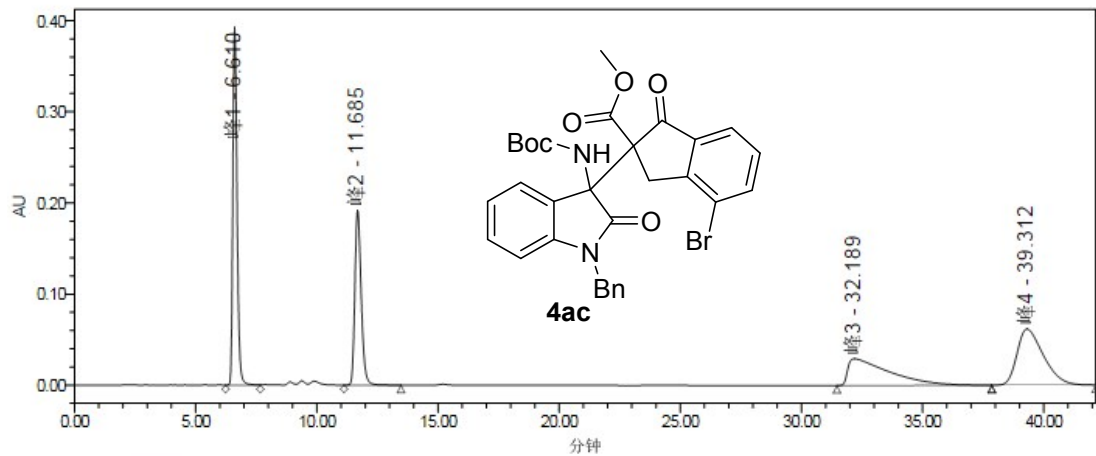
	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	7.143	288021	1.56	20577
2	W2489 ChA 254nm	9.346	41111	0.22	2770
3	W2489 ChA 254nm	22.910	16423144	88.70	376519
4	W2489 ChA 254nm	36.438	1762865	9.52	18893



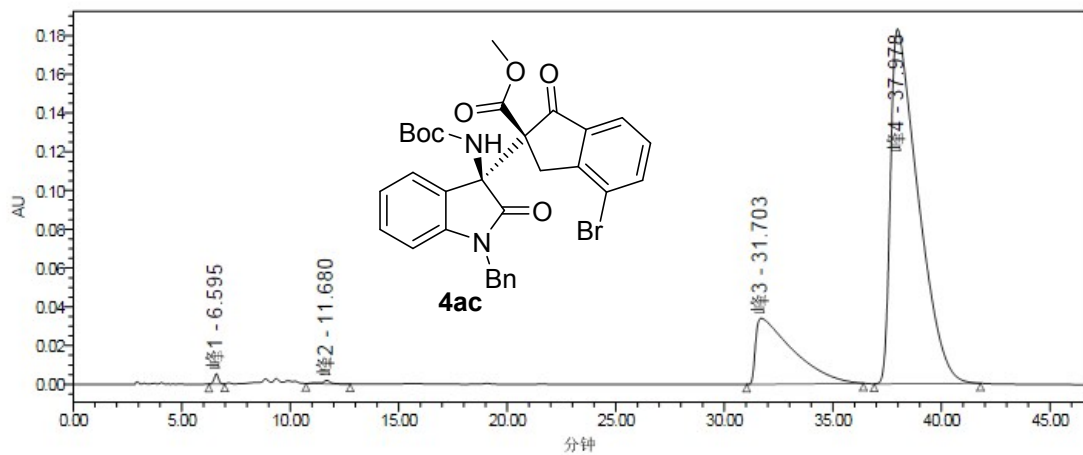
	Channel Description	Peak Name	RT (min)	Area (磺*sec)	% Area	Height (磺)
1	W2489 ChA 254nm	峰1	5.800	759902	34.84	75714
2	W2489 ChA 254nm	峰2	6.501	361755	16.59	33110
3	W2489 ChA 254nm	峰3	9.441	729557	33.45	48493
4	W2489 ChA 254nm	峰4	12.171	329647	15.12	15060



	Channel Description	RT (min)	Area (磺*sec)	% Area	Height (磺)
1	W2489 ChA 254nm	5.829	536309	2.03	64056
2	W2489 ChA 254nm	6.544	114904	0.43	12386
3	W2489 ChA 254nm	9.390	23749273	89.75	1664633
4	W2489 ChA 254nm	12.184	2059693	7.78	103266

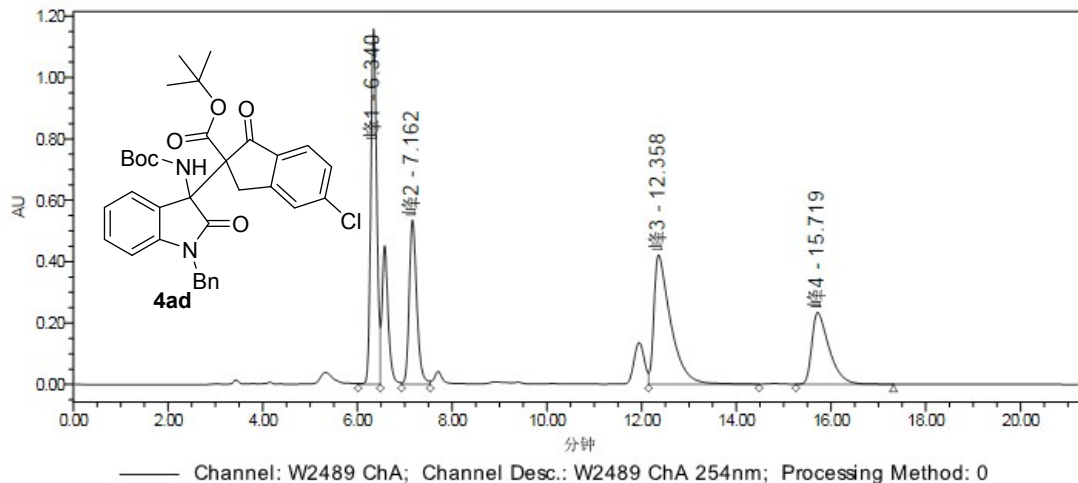


	Channel Description	Peak Name	RT (min)	Area (碘*sec)	% Area	Height (碘)
1	W2489 ChA 254nm	峰1	6.610	4791354	29.11	392663
2	W2489 ChA 254nm	峰2	11.685	3499667	21.27	191816
3	W2489 ChA 254nm	峰3	32.189	3473126	21.10	29237
4	W2489 ChA 254nm	峰4	39.312	4692574	28.51	61751

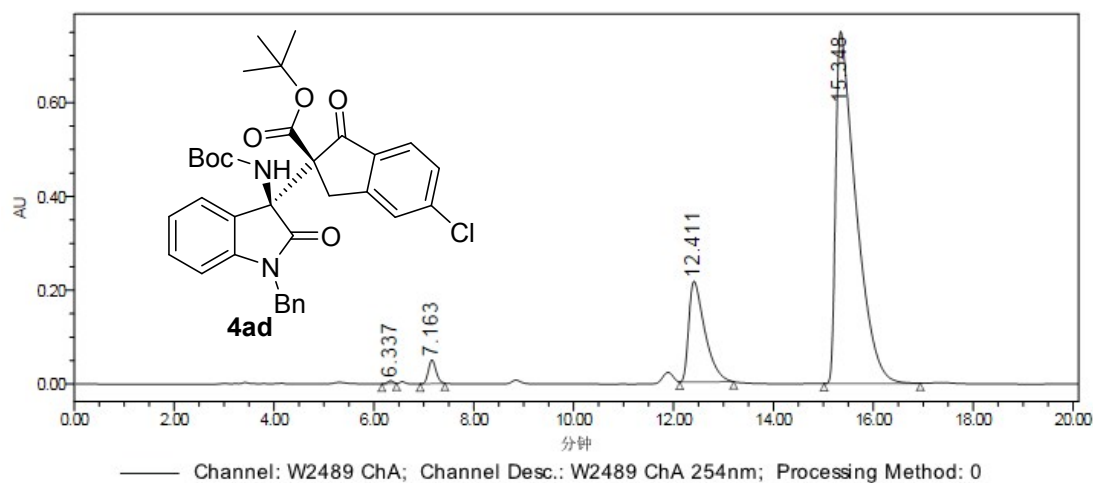


	Channel Description	Peak Name	RT (min)	Area (碘*sec)	% Area	Height (碘)
1	W2489 ChA 254nm	峰1	6.595	75009	0.37	5327
2	W2489 ChA 254nm	峰2	11.680	49651	0.24	1758
3	W2489 ChA 254nm	峰3	31.703	4063488	19.94	34060
4	W2489 ChA 254nm	峰4	37.978	16187281	79.45	182925



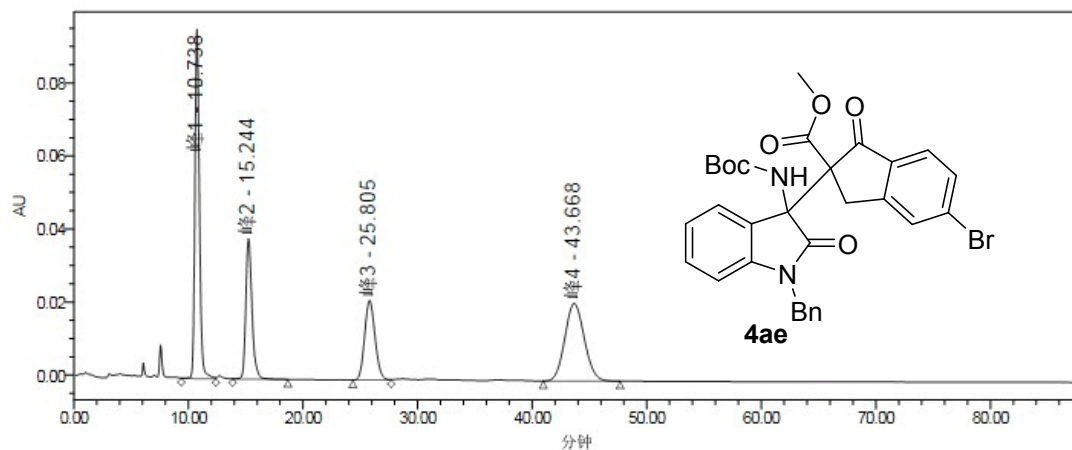


	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.340	10073563	31.13	1157026
2	W2489 ChA 254nm	峰2	7.162	5964540	18.43	534581
3	W2489 ChA 254nm	峰3	12.358	10390915	32.11	421229
4	W2489 ChA 254nm	峰4	15.719	5928595	18.32	233186

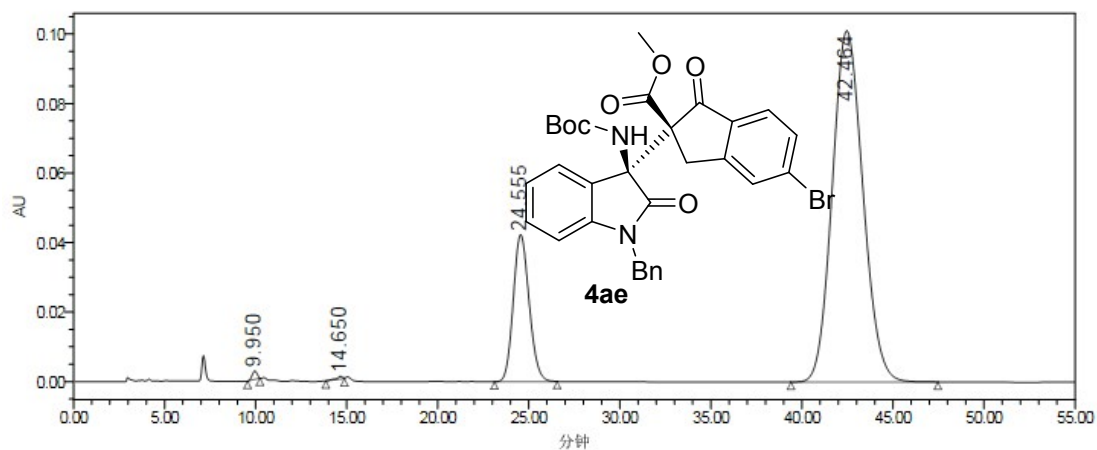


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.337	45164	0.17	5772
2	W2489 ChA 254nm	7.163	540326	2.04	50389
3	W2489 ChA 254nm	12.411	4804394	18.11	214491
4	W2489 ChA 254nm	15.348	21141541	79.68	750580



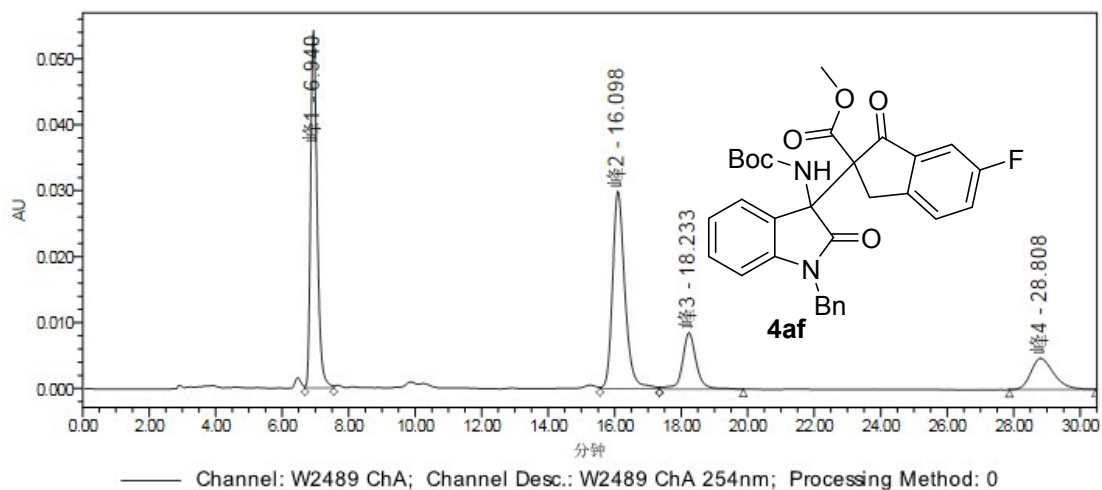


	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	10.738	2613391	32.84	95613
2	W2489 ChA 254nm	峰2	15.244	1454273	18.27	38398
3	W2489 ChA 254nm	峰3	25.805	1376826	17.30	21753
4	W2489 ChA 254nm	峰4	43.668	2514647	31.59	21243

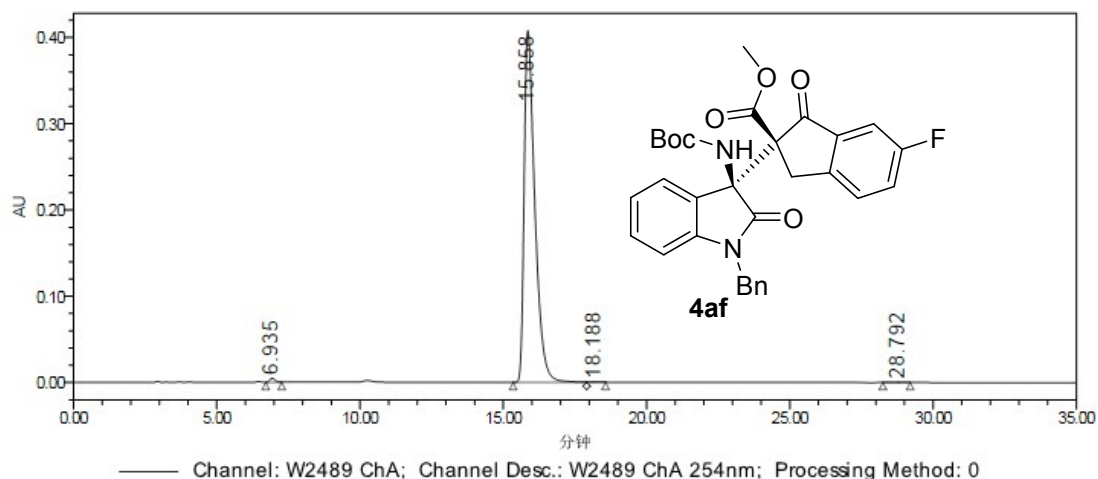


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	9.950	45577	0.31	2367
2	W2489 ChA 254nm	14.650	18027	0.12	784
3	W2489 ChA 254nm	24.555	2565641	17.73	42311
4	W2489 ChA 254nm	42.464	11839910	81.83	101065



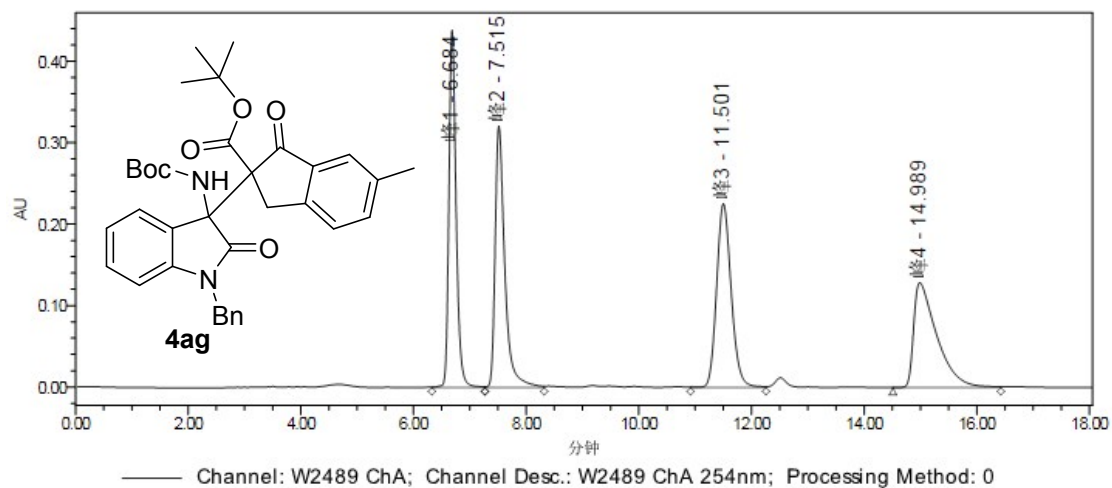


	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.940	736390	37.25	54160
2	W2489 ChA 254nm	峰2	16.098	771691	39.03	29893
3	W2489 ChA 254nm	峰3	18.233	243100	12.30	8521
4	W2489 ChA 254nm	峰4	28.808	225913	11.43	4732

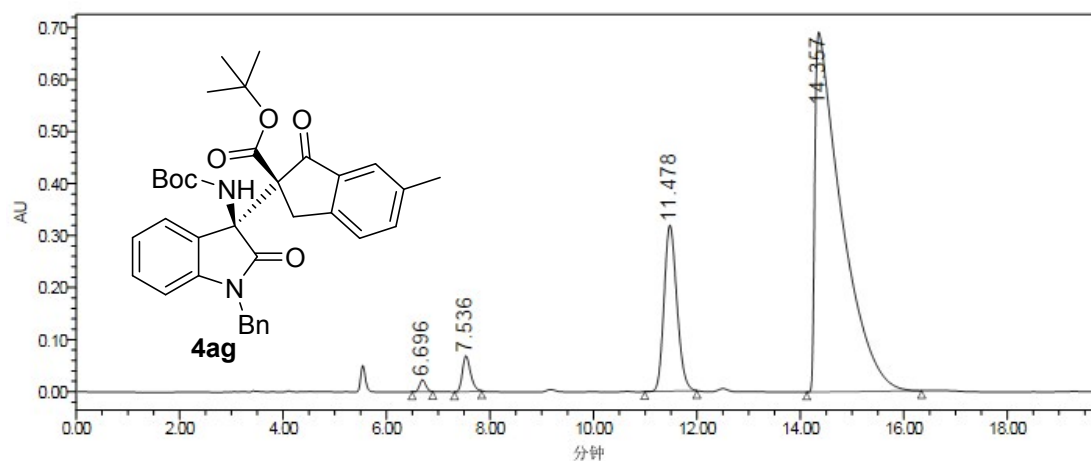


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.935	63153	0.59	4695
2	W2489 ChA 254nm	15.858	10589644	99.26	407522
3	W2489 ChA 254nm	18.188	10065	0.09	388
4	W2489 ChA 254nm	28.792	5808	0.05	182



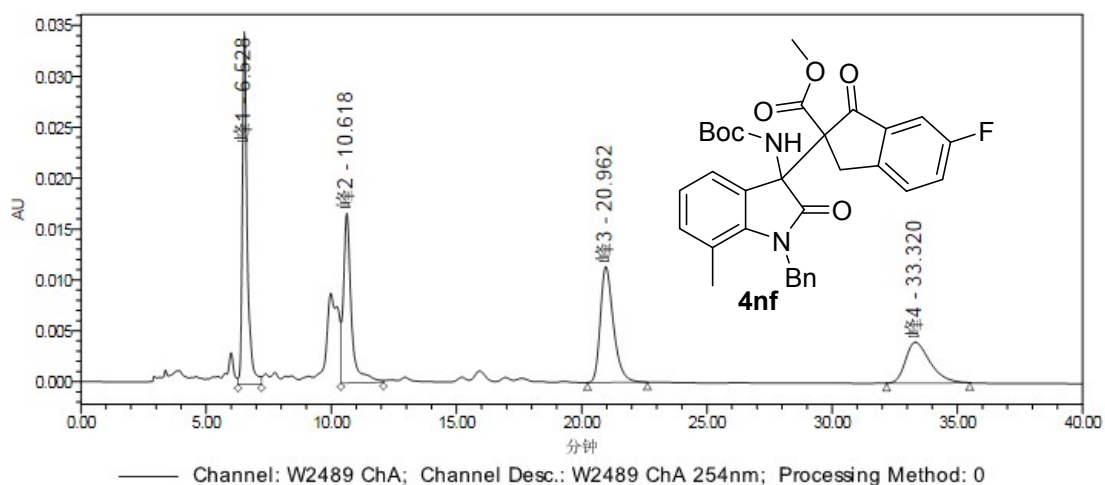


	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.684	3908848	25.22	438442
2	W2489 ChA 254nm	峰2	7.515	3840089	24.77	321222
3	W2489 ChA 254nm	峰3	11.501	4073612	26.28	225660
4	W2489 ChA 254nm	峰4	14.989	3678884	23.73	128905

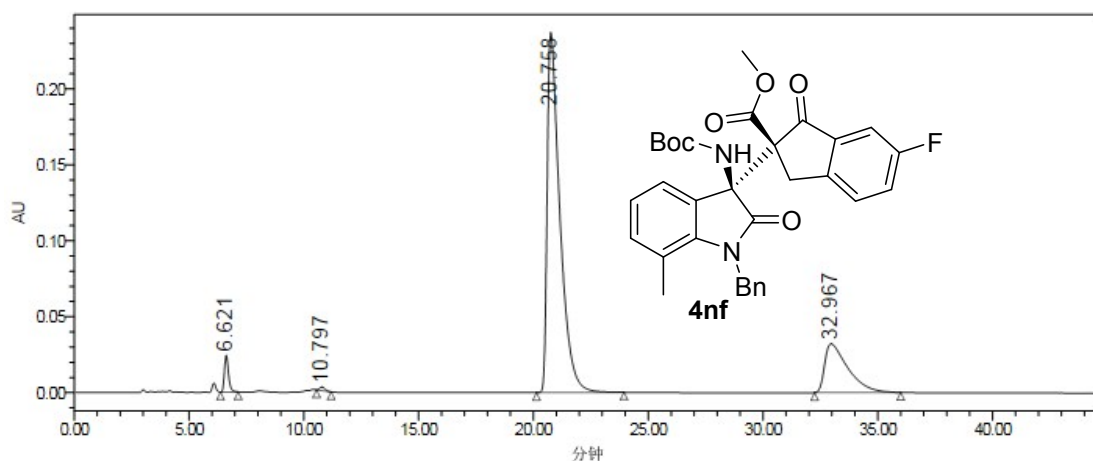


	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.696	191337	0.61	22714
2	W2489 ChA 254nm	7.536	750368	2.41	68089
3	W2489 ChA 254nm	11.478	5504150	17.67	319121
4	W2489 ChA 254nm	14.357	24712243	79.31	691612

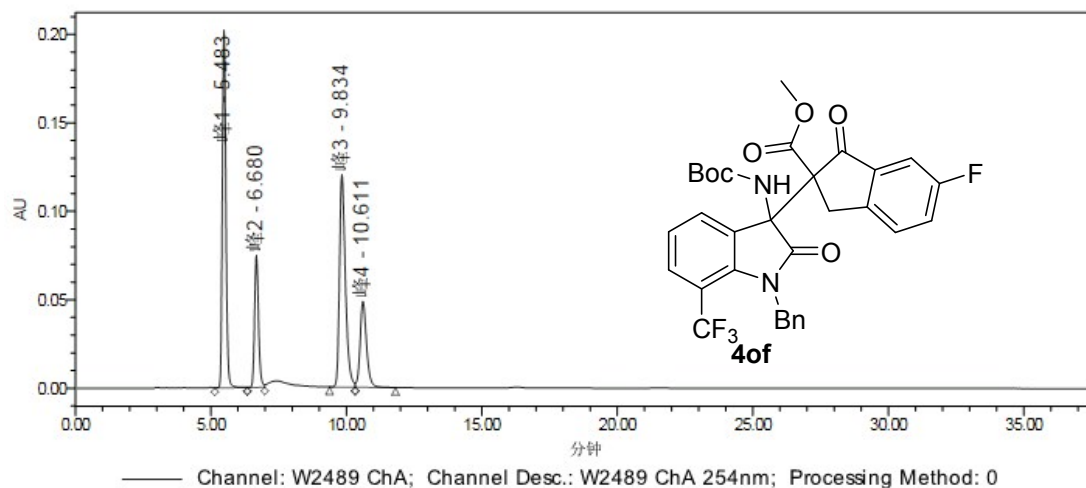




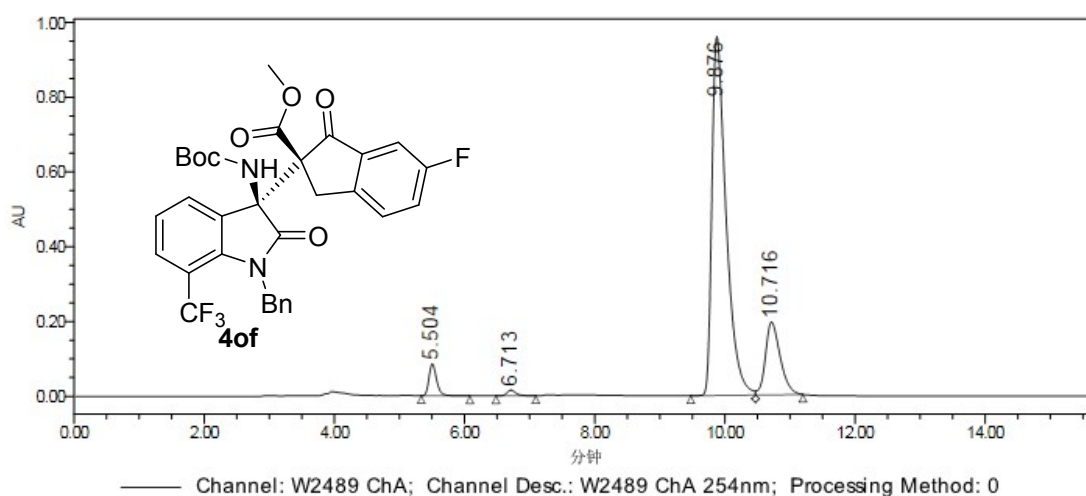
	Channel Description	Peak Name	RT (min)	Area (面积*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	6.528	467964	30.70	34606
2	W2489 ChA 254nm	峰2	10.618	368145	24.15	16653
3	W2489 ChA 254nm	峰3	20.962	415533	27.26	11374
4	W2489 ChA 254nm	峰4	33.320	272588	17.88	4020



	Channel Description	RT (min)	Area (面积*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	6.621	301725	2.58	24201
2	W2489 ChA 254nm	10.797	38627	0.33	2500
3	W2489 ChA 254nm	20.758	9105879	77.78	237088
4	W2489 ChA 254nm	32.967	2260539	19.31	32148



	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1	5.483	1841011	35.16	202016
2	W2489 ChA 254nm	峰2	6.680	762267	14.56	74409
3	W2489 ChA 254nm	峰3	9.834	1827614	34.91	119922
4	W2489 ChA 254nm	峰4	10.611	804765	15.37	48486



	Channel Description	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	5.504	693371	3.76	85333
2	W2489 ChA 254nm	6.713	146517	0.80	15401
3	W2489 ChA 254nm	9.876	14514733	78.81	959004
4	W2489 ChA 254nm	10.716	3063585	16.63	194566

9. Reference

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- 2 del Pozo, S.; Vera, S.; Oiarbide, M.; Palomo, C. *Journal of the American Chemical Society* **2017**, *139*, 15308.

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