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Enantioselective Intramolecular Pictet-Spengler Type Annulation of Indole-Linked 3-Methyleneisoindolin-1-Ones

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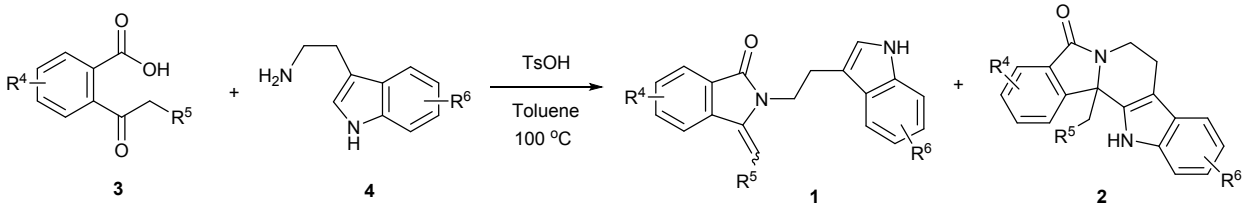
1. General remarks

Chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. Chiral phophoric acids **CPA1-CPA12**, compounds **3a**, **3e**, **3h**, **4a**-**4e**, **4g**, **4j** and **5** were purchased from commercial suppliers. Solvents were dried and purified according to the standard procedures before use. Reactions were monitored by TLC. Racemic products were obtained from corresponding substrates catalyzed by TsOH at 100 ^{o}C. Flash column chromatography was performed on silica gels (200-300 mesh). ^{1}H NMR and ^{13}C NMR (300 and 75 MHz, respectively) spectra were recorded on a Bruker 300 MHz NMR spectrometer in $CDCl_3$ or DMSO-d_6.^{1}H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$, δ 7.26 ppm, DMSO-d_6 at 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, td = triplet of doublets, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$, δ 77.0 ppm, DMSO-d_6 at 39.51 ppm). HRMS data were obtained on a Bruker Daltonics Inc mass instrument (ESI). All enantiomeric ratios have been controlled by co-injections of the pure sample with the racemates. Chiralpak AD-H column, IC-H column and OD-H column were purchased from Daicel Chemical Industries (Hong Kong, China). Optical rotations were measured on a Perkin-Elmer 241 Polarimeter. Melting points were recorded on a Buchi Melting Point B-545.

2. Procedures and characterizations data of compounds

2.1 Synthesis of indol-linked 3-methyleneisoindolin-1-ones 1[1] and racemic isoindolinone fused tetrahydro β-carbolines 2.



3

3a: R^4 = H, R^5 = H
3b: R^4 = 3-F, R^5 = H
3c: R^4 = 4-F, R^5 = H
3d: R^4 = 5-F, R^5 = H
3e: R^4 = 5Cl, R^5 = H
3f: R^4 = 5Br, R^5 = H
3g: R^4 = 5Me, R^5 = H
3h: R^4 = H, R^5 = Ph

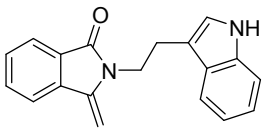
4

4a: R^6 = H
4b: R^6 = 4-F
4c: R^6 = 5-Br
4d: R^6 = 5-OMe
4e: R^6 = 5-OBn
4f: R^6 = 5-Et
4g: R^6 = 5-*i*-Pr
4h: R^6 = 6-Br
4i: R^6 = 7-Me
4j: R^6 = 4,6-diMe
4k: R^6 = 5,7-diMe

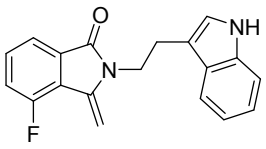
1

2

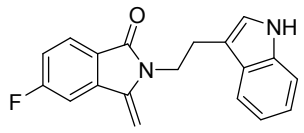
2-Acetylbenzoic acid derivative **3** (**3b**, **3c**, **3d**, **3f** and **3g** were prepared according to literature procedures[2,3]) (1.0 equiv.), tryptamine derivative **4** (**4f**, **4i** and **4k** were prepared according to a literature procedure[4]) (1.5 equiv. and TsOH (10 mol%) were dissolved in toluene in a round-bottomed flaskequipped with a magnetic stirring bar . The reaction mixture was stirred under 100 ℃ until the reaction was completed as determined by TLC. The solvent was removed in vacuo, and the residue was subjected to column chromatography on a silica gel (petroleum ether : ethyl acetate = 10:1 to petroleum ether : DCM : ethyl acetate = 1:2:1) to afford the products**1a-1r** and racemic products **2a-2r**.



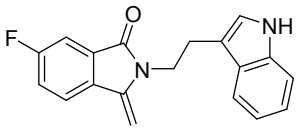
2-(2-(1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1a): white solid, 48% yield. m.p: 151.8-157.2 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.86 (d, J = 7.4 Hz, 1H), 7.79-7.64 (m, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.3 Hz, 1H), 7.38 (d, J = 7.8 Hz, 1H), 7.30-7.10 (m, 2H), 7.06 (s, 1H), 5.22 (d, J = 2.0 Hz, 1H), 4.92 (d, J = 1.9 Hz, 1H), 4.11 (t, J = 7.8 Hz,2H), 3.17 (t, J = 7.8 Hz,2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.09, 141.69, 136.30, 136.24, 131.78, 129.38, 127.32, 122.92, 122.12, 121.93, 119.80, 119.31, 118.51, 112.48, 111.26, 88.83, 40.11, 24.18.HRMS (ESI) Calcd for $C_{19}H_{16}N_2OH^+$ $[M+H]^+$289.1335; Found: 289.1332.



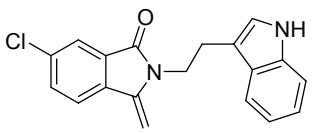
(2-(1H-indol-3-yl)ethyl)-4-fluoro-3-methyleneisoindolin-1-one (1b): yellow solid, 27% yield. m.p: 144.2-146.8 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.68 (dd, J = 13.7, 7.6 Hz, 2H), 7.46 (td, J = 7.8, 4.5 Hz, 1H), 7.37 (d, J = 7.7 Hz, 1H), 7.32-7.21 (m, 2H), 7.19-7.12 (m, 1H), 7.07 (d, J = 2.2 Hz, 1H), 5.48 (d, J = 2.0 Hz, 1H), 5.10 (d, J = 1.8 Hz, 1H), 4.24-3.93 (m, 2H), 3.16 (t, J = 7.8 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 166.02, 157.7 (d, J= 254.3 Hz), 138.52(d, J=3.6 Hz), 136.26,132.44, 130.84 (d, J= 7.0 Hz), 127.31, 122.10, 122.03, 119.42, 119.12, 119.08, 119.06(d, J= 20.0 Hz), 118.50, 112.42, 111.25, 94.61 (d, J = 7.5 Hz), 40.03, 24.11. HRMS (ESI) Calcd for $C_{19}H_{15}FN_2OH^+$ $[M+H]^+$307.1241; Found: 307.1239.



2-(2-(1H-indol-3-yl)ethyl)-5-fluoro-3-methyleneisoindolin-1-one (1c): yellow solid, 32% yield. m.p: 131.2-134.7 ℃.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.81 (dd, J = 8.3, 4.9 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.43-7.29 (m, 2H), 7.26-7.11 (m, 3H), 7.07 (d, J = 2.0 Hz, 1H), 5.16 (d, J = 2.5 Hz, 1H), 4.91 (d, J = 2.5 Hz, 1H), 4.08 (t, J= 7.8 Hz, 2H), 3.15 (t, J= 7.8 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 166.13, 165. 46 (d, J = 249.8 Hz), 141.00 (d, J = 3.1 Hz), 136.25, 127.35, 125.50, 125.48, 125.10 (d, J = 9.8 Hz), 122.07, 119.44, 118.52, 117.25, 116.94, 112.55, 111.24, 107.13(d, J = 24.0 Hz), 89.72, 40.31, 24.14.HRMS (ESI) Calcd for $C_{19}H_{15}FN_2OH^+$ $[M+H]^+$307.1241; Found: 307.1242.

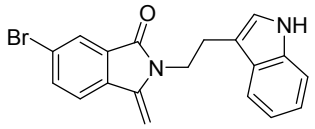


2-(2-(1H-indol-3-yl)ethyl)-6-fluoro-3-methyleneisoindolin-1-one (1d): yellow solid, 28% yield. m.p: 150.1-152.4 ℃.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.74-7.59 (m, 2H), 7.50 (dd, J = 7.4, 2.1 Hz, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.33-7.10 (m, 3H), 7.07 (d, J = 1.1 Hz, 1H), 5.15 (d, J = 2.2 Hz, 1H), 4.89 (d, J = 2.2 Hz, 1H), 4.09 (t, J = 7.8 Hz, 2H), 3.15 (t, J= 7.8 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 165.86, 163.65 (d, J = 248.3 Hz), 140.97, 136.24, 131.47 (d, J = 9.0 Hz), 127.34, 122.08, 121.72, 121.61, 119.53, 119.45, 119.21, 118.52, 112.55, 111.23, 109.80 (d, J = 23.8 Hz), 88.98, 40.36, 24.19.HRMS (ESI) Calcd for $C_{19}H_{15}FN_2OH^+$ $[M+H]^+$307.1241; Found: 307.1233.

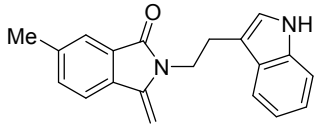


2-(2-(1H-indol-3-yl)ethyl)-6-chloro-3-methyleneisoindolin-1-one (1e): white solid, 36% yield. m.p: 155.7-157.9 ℃. ^{1}H NMR (300 MHz, $CDCl_3$)

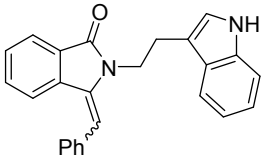
δ 8.12 (s, 1H), 7.80 (d, J = 1.6 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.53 (dd, J = 8.2, 1.8 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.30-7.09 (m, 2H), 7.06 (d, J = 2.0 Hz, 1H), 5.17 (d, J = 2.5 Hz, 1H), 4.90 (d, J = 2.5 Hz, 1H), 4.08 (t, J = 7.8Hz, 2H), 3.14 (t, J = 7.8Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 165.73, 140.98, 136.24, 135.62, 134.53, 131.96, 130.97, 127.33, 123.17, 122.10, 122.06, 121.14, 119.47, 118.51, 112.53, 111.23, 89.58, 40.33, 24.15.HRMS (ESI) Calcd for $C_{19}H_{15}ClN_2OH^+$ $[M+H]^+$323.0946 (^{35}Cl), 325.0916 (^{37}Cl); Found: 323.0939 (^{35}Cl), 325.0925 (^{37}Cl).



(2-(1H-indol-3-yl)ethyl)-6-bromo-3-methyleneisoindolin-1-one (1f): yellow solid, 16% yield. m.p: 164.4-166.2 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.96 (s, 1H), 7.68 (dd, J = 8.0, 1.4 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.37 (d, J = 8.1 Hz, 1H), 7.30-7.09 (m, 1H), 7.06 (s, 1H), 5.18 (d, J = 2.4 Hz, 1H), 4.91 (d, J = 2.4 Hz, 1H), 4.07 (t, J = 7.8 Hz, 1H), 3.14 (t, J = 7.8 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$) δ 165.61, 140.99, 136.22, 134.93, 134.74, 131.12, 127.30, 126.14, 123.49, 122.05, 121.37, 119.43, 118.47, 112.43, 111.24, 89.74, 40.30, 24.12.HRMS (ESI) Calcd for $C_{19}H_{15}BrN_2OH^+$ $[M+H]^+$367.0441 (^{79}Br), 369.0420 (^{81}Br); Found:367.0435 (^{79}Br), 369.0417 (^{81}Br).

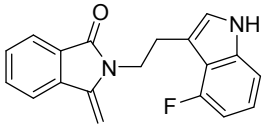


(2-(1H-indol-3-yl)ethyl)-6-methyl-3-methyleneisoindolin-1-one (1g): white solid, 44% yield. m.p: 202.4-205.4 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.71 (d, J = 7.7 Hz, 1H), 7.64 (s, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.37 (dd, J = 7.7, 4.1 Hz, 2H), 7.31-7.10 (m, 2H), 7.07 (d, J = 2.1 Hz, 1H), 5.14 (d, J = 2.2 Hz, 1H), 4.84 (d, J = 2.2 Hz, 1H), 4.19-3.95 (m, 2H), 3.27-3.02 (m, 2H), 2.47 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.23, 141.83, 139.80, 136.27, 133.91, 132.78, 129.67, 127.41, 123.22, 122.06, 122.02, 119.64, 119.41, 118.62, 112.77, 111.20, 87.99, 40.11, 24.22, 21.55.HRMS (ESI) Calcd for $C_{20}H_{18}N_2OH^+$ $[M+H]^+$303.1492; Found: 303.1495.

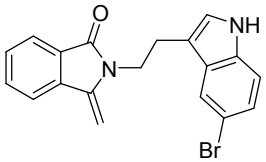


2-(2-(1H-indol-3-yl)ethyl)-3-benzylideneisoindolin-1-one (1h): white solid, 54% yield. m.p: 183.7-184.4 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.91 (d, J = 7.5 Hz, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.63 (td, J = 7.5, 1.0 Hz, 1H), 7.52 (t, J = 7.1 Hz, 1H), 7.47-7.32 (m, 5H), 7.30-7.23 (m, 1H), 7.21 (d, J = 7.9 Hz, 1H), 7.13 (t, J = 7.1 Hz, 1H), 7.04-6.96 (m, 1H), 6.98 (s, 1H), 6.48 (d, J = 2.1 Hz, 1H), 4.11-3.94 (m, 2H),

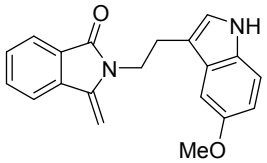
2.84-2.57 (m, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 168.81, 138.46, 135.91, 134.96, 134.63, 131.88, 129.70, 128.94, 128.43, 128.30, 127.52, 127.15, 123.12, 121.86, 121.69, 119.28, 119.08, 118.79, 112.20, 110.83, 106.59, 42.23, 24.14.HRMS (ESI) Calcd for $C_{25}H_{20}N_2OH^+$ $[M+H]^+$365.1648; Found: 365.1643.



2-(2-(4-fluoro-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1i): yellow solid, 37% yield. m.p: 146.5-148.3 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.84 (d, J = 7.5 Hz, 1H), 7.77-7.43 (m, 4H), 7.35 (d, J = 7.5 Hz, 1H), 7.14 (s, 1H), 7.01 (t, J = 7.9 Hz, 1H), 5.19 (s, 1H), 4.86 (s, 1H), 4.08 (t, J = 7.6 Hz, 2H), 3.13 (t, J = 7.6 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.05, 141.72, 136.31, 134.91, 131.83, 129.44, 129.33, 128.61, 124.40, 123.02, 122.66, 120.61, 119.82, 117.89, 114.01, 104.80, 88.64, 39.97, 24.30.HRMS (ESI) Calcd for $C_{19}H_{15}FN_2OH^+$ $[M+H]^+$307.1241; Found: 307.1244.

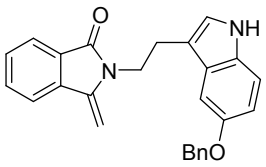


2-(2-(5-bromo-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1j): white solid, 17% yield. m.p:173.0-174.3 ℃. ^{1}H NMR (300 MHz, DMSO-d6) δ 11.03 (s, 1H), 7.96 (d, J = 7.6 Hz, 1H), 7.73-7.65 (m, 3H), 7.56 (t, J = 7.4 Hz, 1H), 7.31-7.24 (m, 2H), 7.15 (dd, J = 8.7, 1.7 Hz, 1H), 5.46 (d, J = 2.0 Hz, 1H), 5.08 (d, J = 2.2 Hz, 1H), 3.99 (t, J = 7.5 Hz, 2H), 2.99 (t, J = 7.3 Hz, 2H).^{13}C NMR (75 MHz, DMSO-d6) δ 165.91, 140.81,136.03, 134.84, 132.18, 129.64, 129.10, 128.60, 124.75, 123.39, 122.38, 120.56, 120.46, 113.39, 111.06, 110.93, 90.27, 23.51.HRMS (ESI) Calcd for $C_{19}H_{15}BrN_2OH^+$ $[M+H]^+$367.0441 (^{79}Br), 369.0420 (^{81}Br); Found: 367.0430 (^{79}Br), 369.0412 (^{81}Br).

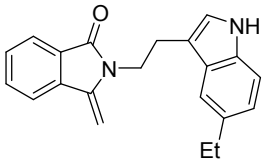


2-(2-(5-methoxy-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1k): white solid, 48% yield. m.p: 158.9-163.3 ℃.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.84 (d, J = 7.3 Hz, 1H), 7.68 (d, J = 7.5 Hz, 1H), 7.57 (td, J = 7.4, 1.1 Hz, 1H), 7.49 (td, J = 7.4, 1.0 Hz, 1H), 7.29-7.19 (m, 1H), 7.12 (d, J = 2.2 Hz, 1H), 7.04 (d, J = 2.0 Hz, 1H), 6.85 (dd, J = 8.8, 2.4 Hz, 1H), 5.18 (d, J = 2.2 Hz, 1H), 4.87 (d, J = 2.2 Hz, 1H), 4.09 (t, J =7.8 Hz, 2H), 3.83 (s, 3H), 3.12 (t, J =7.7 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.11,

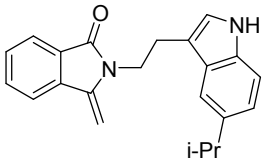
153.94, 141.76, 136.33, 131.79, 131.39, 129.40, 127.78, 122.94, 122.82, 119.80, 112.40, 112.20, 111.95, 100.34, 88.73, 55.79, 40.08, 24.23.HRMS (ESI) Calcd for $C_{20}H_{18}N_2O_2H^+$ $[M+H]^+$319.1441; Found: 319.1438.



2-(2-(5-(benzyloxy)-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1l): white solid, 56% yield. m.p: 160.3-162.4 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.82 (d, J = 7.3 Hz, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.55 (td, J = 7.4, 1.0 Hz, 1H), 7.51-7.43 (m, 3H), 7.40-7.35 (m, 2H), 7.34-7.27 (m, 1H), 7.22 (d, J = 9.0 Hz, 1H), 7.17 (d, J = 2.2 Hz, 1H), 7.01 (d, J = 2.0 Hz, 1H), 6.91 (dd, J = 8.8, 2.3 Hz, 1H), 5.14 (d, J = 2.3 Hz, 1H), 5.04 (s, 2H), 4.80 (d, J = 2.3 Hz, 1H), 4.04 (t, J = 7.7 Hz, 2H), 3.08 (t, J = 7.7 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.08, 153.14, 141.74, 137.62, 136.34, 131.80, 131.54, 129.41, 128.44, 127.78, 127.72, 127.66, 122.97, 122.90, 119.81, 112.94, 112.52, 111.93, 102.02, 88.76, 70.86, 40.12, 24.22.HRMS (ESI) Calcd for $C_{26}H_{22}N_2O_2H^+$ $[M+H]^+$395.1754; Found: 395.1749.

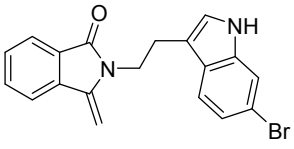


2-(2-(5-ethyl-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1m): white solid, 21% yield. m.p: 263.8-265.3 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.84 (d, J = 7.3 Hz, 1H), 7.68 (d, J = 7.5 Hz, 1H), 7.57 (t, J = 7.3 Hz, 1H), 7.53-7.43 (m, 2H), 7.27 (d, J = 8.5 Hz, 2H), 7.09-6.99 (m, 2H), 5.20 (d, J = 2.2 Hz, 1H), 4.89 (d, J = 2.2 Hz, 1H), 4.08 (t, J = 7.8 Hz, 2H), 3.13 (t, J = 7.8 Hz, 2H), 2.74 (dd, J = 15.2, 7.7 Hz, 2H), 1.27 (t, J = 7.5 Hz,3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.12, 141.80, 136.36, 135.40, 134.72, 131.78, 129.40, 127.59, 122.99, 122.60, 122.17, 119.80, 116.98, 112.42, 110.97, 88.77, 40.22, 29.02, 24.20, 16.48.HRMS (ESI) Calcd for $C_{21}H_{20}N_2OH^+$ $[M+H]^+$316.1576; Found: 316.1573.

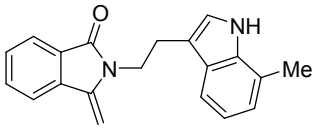


2-(2-(5-isopropyl-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1n): white solid, 32% yield. m.p: 121.4-124.7 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.85 (d, J = 7.4 Hz, 1H), 7.69 (d, J = 7.5 Hz, 1H), 7.58 (td, J = 7.4, 1.1 Hz, 1H), 7.53-7.48 (m, 2H), 7.29 (d, J = 8.4 Hz, 1H), 7.09 (dd, J = 8.4, 1.4 Hz, 1H), 7.05 (d, J = 2.1 Hz, 1H), 5.21 (d, J = 2.3 Hz, 1H), 4.91 (d, J = 2.2 Hz, 1H), 4.13-4.08(m, 2H), 3.18-3.13 (m, 2H), 3.00 (dq, J = 13.7, 6.8 Hz, 1H), 1.30 (d, J = 6.9 Hz, 6H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.11,

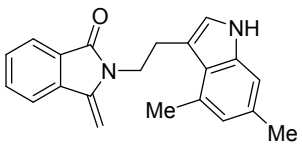
141.79, 140.07, 136.35, 134.78, 131.77, 129.39, 127.45, 122.97, 122.17, 121.17, 119.79, 115.36, 112.49, 110.99, 88.74, 40.24, 34.19, 24.63, 24.17.HRMS (ESI) Calcd for $C_{22}H_{22}N_2OH^+$ $[M+H]^+$331.1805; Found: 331.1799.



2-(2-(6-bromo-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1o): white solid, 23% yield. m.p: 149.5-152.6 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.82 (d, J = 7.4 Hz, 1H), 7.68 (d, J = 7.5 Hz, 1H), 7.62-7.44 (m, 4H), 7.20 (dd, J = 8.4, 1.5 Hz, 1H), 7.04 (d, J = 2.1 Hz, 1H), 5.18 (d, J = 2.3 Hz, 1H), 4.84 (d, J = 2.3 Hz, 1H), 4.06 (t, J = 7.6 Hz, 2H), 3.11 (t, J = 7.6 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.12, 141.76, 137.02, 136.32, 131.88, 129.48, 129.33, 126.37, 123.02, 122.73, 122.66, 119.85, 115.62, 114.14, 112.99, 88.72, 40.01, 24.05.HRMS (ESI) Calcd for $C_{20}H_{18}N_2OH^+$ $[M+H]^+$303.1492; Found: 303.1495.HRMS (ESI) Calcd for $C_{19}H_{15}BrN_2OH^+$ $[M+H]^+$367.0441(^{79}Br), 369.0420 (^{81}Br); Found:367.0438 (^{79}Br), 369.0419 (^{81}Br).

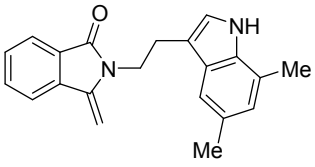


2-(2-(7-methyl-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1p): white solid, 26% yield. m.p: 154.7-157.4 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.70 (d, J = 7.4 Hz, 1H), 7.61-7.48 (m, 3H), 7.19-6.91 (m, 3H), 5.22 (s, 1H), 4.92 (s, 1H), 4.10 (t, J = 7.8 Hz, 2H), 3.15 (t, J = 7.7 Hz, 2H), 2.49 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.08, 141.75, 136.35, 135.83, 131.79, 129.41, 126.90, 122.99, 122.57, 121.81, 120.42, 119.82, 119.66, 116.31, 113.14, 88.79, 40.14, 24.33, 16.56.HRMS (ESI) Calcd for $C_{20}H_{18}N_2OH^+$ $[M+H]^+$303.1492; Found: 303.1486.



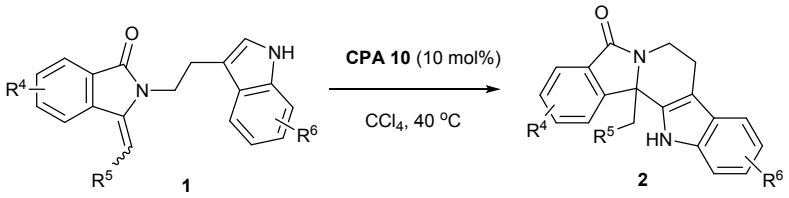
2-(2-(4,6-dimethyl-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1q): white solid, 23% yield. m.p: 143.7-145.9 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.86 (d, J = 7.3 Hz, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.59 (td, J = 7.5, 1.2 Hz, 1H), 7.55-7.46 (m, 1H), 7.33 (s, 1H), 7.05 (d, J = 2.1 Hz, 1H), 6.86 (s, 1H), 5.22 (d, J = 2.3 Hz, 1H), 4.93 (d, J = 2.2 Hz, 1H), 4.12-4.07(m, 2H), 3.13 (t, J = 7.8 Hz, 2H), 2.45 (s, 3H), 2.44 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.06, 141.74, 136.36, 134.16, 131.76, 129.44,

129.37, 128.85, 127.16, 124.30, 122.95, 121.94, 120.07, 119.80, 115.86, 112.61, 88.80, 40.21, 24.33, 21.42, 16.49.HRMS (ESI) Calcd for $C_{21}H_{20}N_2OH^+$ $[M+H]^+$317.1648; Found: 317.1642.



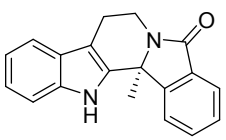
2-(2-(5,7-dimethyl-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1r): white solid, 25% yield. m.p: 131.8-134.9 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.85 (d, J = 7.3 Hz, 1H), 7.69 (d, J = 7.5 Hz, 1H), 7.58 (td, J = 7.4, 1.1 Hz, 1H), 7.55-7.45 (m, 1H), 7.08-6.87 (m, 2H), 6.73 (s, 1H), 5.18 (d, J = 2.3 Hz, 1H), 4.85 (d, J = 2.3 Hz, 1H), 4.10-4.05 (m, 2H), 3.38-3.17 (t, J = 7.9 Hz, 2H), 2.77 (s, 3H), 2.41 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 167.07, 141.82, 137.17, 136.37, 131.87, 131.79, 130.22, 129.41, 123.63, 123.08, 123.00, 121.53, 119.81, 113.36, 108.99, 88.70, 41.30, 26.0, 21.39, 20.22.HRMS (ESI) Calcd for $C_{21}H_{20}N_2OH^+$ $[M+H]^+$317.1648; Found: 317.1642.

2.2 Enantioselective intramolecular Pictet-Spengler type annulation of isoindole-1-ones 1.



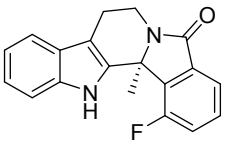
1 2

To a solution of**1** (0.1 mmol)in dry CCl_4 (1.5 mL) was added**CPA10** (10 mol%).The mixture was stirred at 40℃until the reaction was completed as determined by TLC. The solvent was removed in vacuo, and the residue was purified by column chromatography on a silica gel (petroleum : ethyl acetate = 10: 1 to petroleum : DCM : ethyl acetate = 1:2:1) to afford the product **2**.

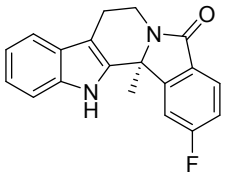


13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2a): white solid, m.p: 313.3-315.2 ℃, 92% yield, 96% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:30/70, 1.0 mL/min, t_{minor} = 4.121 min, t_{major} = 7.134 min). $[\alpha]_D^{20}$ = -164.5 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.37 (s, 1H), 8.32 (d, J = 7.8 Hz, 1H), 7.72 (t, J = 6.0 Hz, 2H), 7.52 (t, J = 7.3 Hz, 1H), 7.38 (dd, J = 7.6, 2.8 Hz, 2H), 7.09 (t, J = 7.3 Hz, 1H), 6.97 (t, J = 7.4 Hz, 1H), 4.52 (dd, J = 13.2, 5.0 Hz, 1H), 3.43-3.38

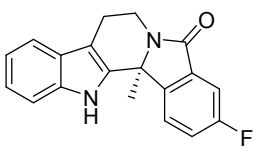
(m, 1H), 2.93-2.57 (m, 2H), 1.85 (s, 3H).^{13}C NMR (75 MHz, DMSO-d6) δ 167.25, 149.36, 136.19, 135.20, 132.28, 130.27, 128.66, 126.00, 123.22, 122.80, 121.65, 118.93, 118.37, 111.25, 106.38, 62.05, 35.47, 25.91, 21.49.HRMS (ESI) Calcd for $C_{19}H_{16}N_2OH^+$ $[M+H]^+$289.1335; Found: 289.1322.



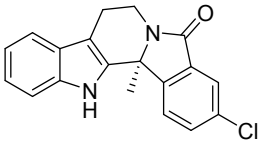
1-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2b): yellow solid, m.p: 321.9-323.4 ℃, 52 % yield, 91% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:20/80, 1.0 mL/min, t_{minor}= 7.352 min, t_{major} = 13.171 min). $[\alpha]_D^{20}$ = -142.5 (c 1.0, ethanol).^{1}H NMR (300 MHz, DMSO-d_6) δ 10.61 (s, 1H), 7.68-7.52 (m, 3H), 7.47 (d, J = 8.0 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.09 (t, J = 7.6 Hz, 1H), 6.98 (t, J = 7.4 Hz, 1H), 4.52 (dd, J = 13.2, 5.2 Hz, 1H), 3.45 (dd, J = 12.2, 5.4 Hz, 1H), 2.93-2.60 (m, 2H), 1.93 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 165.88, 156.88 (d, J = 248.3 Hz), 136.58, 134.32 (d, J = 16.72 Hz), 133.90, 133.65 (d, J = 4.0 Hz), 131.58 (d, J = 3.8 Hz), 125.93, 121.82, 119.74 ((d, J = 3.8 Hz), 119.40 (d, J = 20.2 Hz), 119.07, 118.26, 112.12, 107.28, 61.41, 35.56, 24.51, 21.46.HRMS (ESI) Calcd for $C_{19}H_{15}FN_2OH^+$ $[M+H]^+$307.1241; Found: 307.1234.



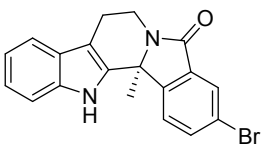
2-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2c): yellow solid, m.p: 323.6-324.9 ℃, 86% yield, 95% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:10/90, 1.0 mL/min, t_{minor} =15.982 min, t_{major} = 34.650 min). $[\alpha]_D^{20}$ = -142.9 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.35 (s, 1H), 8.22 (dd, J = 9.0, 2.2 Hz, 1H), 7.77 (dd, J = 8.3, 5.1 Hz, 1H), 7.45-7.27 (m, 3H), 7.10 (t, J = 7.6 Hz, 1H), 6.98 (t, J = 7.5 Hz, 1H), 4.50 (dd, J = 13.5, 5.3 Hz, 1H), 3.43 (dd, J = 11.7, 4.5 Hz, 1H), 2.94-2.59 (m, 2H), 1.85 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 166.19, 164.83 (d, J = 247.5 Hz), 151.78 (d, J = 9.8 Hz), 136.17, 134.45, 126.64, 125.92 , 125.70 (d, J = 9.8 Hz), 121.77, 118.98, 118.41, 116.31 (d, J = 23.3 Hz), 111.26, 110.25 (d, J = 24.7 Hz), 106.66, 61.85, 35.57, 25.77, 21.37.HRMS (ESI) Calcd for $C_{19}H_{15}FN_2OH^+$ $[M+H]^+$307.1241; Found: 307.1230.



3-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2d): yellow solid, m.p: 341.9-343.3 ℃, 94% yield, 94% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:20/80, 1.0 mL/min, t_{minor}= 5.451 min, t_{major} = 12.187 min). $[\alpha]_D^{20}$ = -137.9 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d6) δ 11.38 (s, 1H), 8.36 (dd, *J* = 8.4, 4.5 Hz, 1H), 7.60 (td, *J* = 9.0, 2.3 Hz, 1H), 7.51 (dd, *J* = 7.8, 2.3 Hz, 1H), 7.38 (dd, *J* = 7.9, 2.9 Hz, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 4.51 (dd, *J* = 13.1, 5.2 Hz, 1H), 3.45 (d, *J* = 4.8 Hz, 1H), 2.73 (dtd, *J* = 20.8, 15.5, 5.1 Hz, 2H), 1.84 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 166.09 (d, *J* = 3.2 Hz), 162.47 (d, *J* = 243.8 Hz), 145.24, 136.22, 134.95, 132.53 (d, *J* = 8.6 Hz), 125.98, 124.94 (d, *J* = 8.5 Hz), 121.76, 119.68 (d, *J* = 23.4 Hz), 119.00, 118.44, 111.27, 109.77 (d, *J* = 23.4 Hz), 106.41, 61.97, 35.67, 25.89, 21.5. HRMS (ESI) Calcd for $C_{19}H_{15}FN_2OH^+$ $[M+H]^+$307.1241; Found: 307.1229.

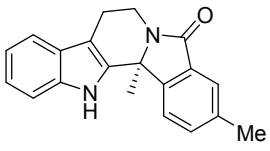


3-chloro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2e): yellow solid, m.p: 335.9-338.4 ℃, 94% yield, 88% ee, HPLC condition: Chiralpak AD-H ethanol/n-hexane:30/70, 1.0 mL/min, t_{minor}= 3.671 min, t_{major} = 4.296 min). $[\alpha]_D^{20}$ = -166.9 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.37 (s, 1H), 8.35 (d, *J* = 8.2 Hz, 1H), 7.81 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.73 (d, *J* = 1.9 Hz, 1H), 7.38 (dd, *J* = 7.8, 5.2 Hz, 2H), 7.10 (t, *J* = 7.1 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 4.51 (dd, *J* = 13.5, 5.1 Hz, 1H), 3.43 (dd, *J* = 11.6, 5.0 Hz, 1H), 2.91-2.60 (m, 2H), 1.84 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 165.75, 147.84, 136.21, 134.57, 133.64, 132.30, 132.22, 125.94, 124.72, 122.94, 121.75, 118.97, 118.40, 111.25, 106.53, 62.05, 35.62, 25.72, 21.44.HRMS (ESI) Calcd for $C_{19}H_{15}ClN_2OH^+$ $[M+H]^+$323.0946 (^{35}Cl), 325.0916 (^{37}Cl); Found:323.0936 (^{35}Cl), 325.0920 (^{37}Cl).

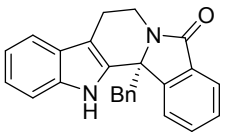


3-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2f): white solid, m.p: 343.1-345.0 ℃, 97% yield, 89% ee, HPLC condition: Chiralpak AD-H ethanol/n-hexane:30/70, 1.0 mL/min, t_{minor} =3.735 min, t_{major} = 4.327 min). $[\alpha]_D^{20}$ = -150.0 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.39 (s, 1H), 8.29 (d, *J* = 8.2 Hz, 1H), 7.94 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.86 (d, *J* = 1.7 Hz, 1H), 7.38 (dd, *J* = 7.3, 5.8 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 4.50 (dd, *J* = 13.2, 5.2 Hz, 1H),

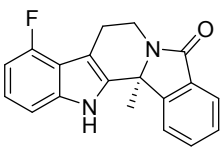
3.46-3.44 (m, 1H), 2.88-2.58 (m, 2H), 1.84 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 165.69, 148.28, 136.22, 135.06, 134.53, 132.57, 129.55, 125.93, 125.09, 121.95, 121.80, 119.02, 118.45, 111.29, 106.58, 62.13, 35.66, 25.69, 21.49.HRMS (ESI) Calcd for $C_{19}H_{15}BrN_2OH^+$ $[M+H]^+$367.0441 (^{79}Br), 369.0420 (^{81}Br); Found: 367.04328 (^{79}Br), 369.0411 (^{81}Br).



3,13b-dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2g): white solid, m.p: 259.7-263.6 ℃, 76% yield, 84% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:30/70, 1.0 mL/min, t_{minor} =5.958 min, t_{major} = 14.497 min). $[\alpha]_D^{20}$ = -111.4 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6)δ 11.31 (s, 1H), 8.18 (d, J = 8.3 Hz, 1H), 7.52 (d, J = 3.8 Hz, 2H), 7.37 (dd, J = 7.7, 2.6 Hz, 2H), 7.08 (t, J = 7.6 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1H), 4.51 (dd, J = 13.4, 5.4 Hz, 1H), 3.41-3.37 (m, 1H), 2.94-2.55 (m, 2H), 2.38 (s, 3H), 1.82 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 167.29, 146.73, 138.27, 136.16, 135.41, 132.98, 130.44, 125.99, 123.21, 122.49, 121.54, 118.84, 118.29, 111.18, 106.15, 61.76, 54.91, 35.41, 25.95, 21.45, 20.77.HRMS (ESI) Calcd for $C_{20}H_{18}N_2OH^+$ $[M+H]^+$303.1492; Found: 303.1492.

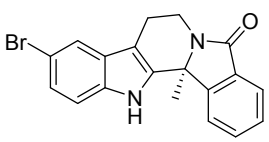


13b-benzyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2h): white solid, m.p: 241.3-243.7 ℃, 53% yield, 22% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:20/80, 1.0 mL/min, t_{minor} =6.090 min, t_{major} = 13.146 min). $[\alpha]_D^{20}$ = -56.3 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.53 (s, 1H), 8.46 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.4 Hz, 1H), 7.57-7.28 (m, 4H), 7.13 (t, J = 7.5 Hz, 1H), 7.09-6.93 (m, 4H), 6.82 (bs, 2H), 4.54 (dd, J = 13.1, 5.2 Hz, 1H), 3.80-3.55 (m, 2H), 3.46-3.40 (m, 1H), 2.97-2.57 (m, 2H).^{13}C NMR (75 MHz, DMSO-d_6) δ167.62, 146.91, 136.27, 134.96, 134.51, 131.72, 131.07, 129.78, 128.45, 127.53, 126.50, 126.01, 123.36, 122.82, 121.72, 118.96, 118.39, 111.32, 107.03, 65.55, 42.99, 35.65, 21.50.HRMS (ESI) Calcd for $C_{25}H_{20}N_2OH^+$ $[M+H]^+$365.1648; Found: 365.1643.

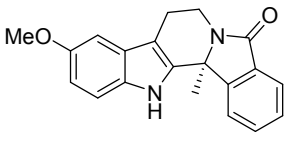


9-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2i): white solid, m.p: 153.3-156.1 ℃, 81% yield, 70% ee, HPLC

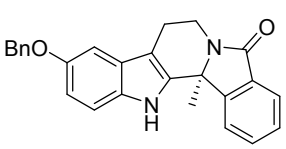
condition: Chiralpak AD-H isopropyl alcohol/n-hexane:10/90, 1.0 mL/min, t_{minor} = 16.450 min, t_{major} = 19.763 min). $[\alpha]_D^{20}$ = -117.5 (c 1.0, ethanol).^{1}H NMR (300 MHz, DMSO-d_6)δ 11.67 (s, 1H), 8.30 (d, J = 7.9 Hz, 1H), 7.72 (t, J = 6.3 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.21 (d, J = 8.2 Hz, 1H), 7.03 (td, J = 8.0, 5.4 Hz, 1H), 6.71 (dd, J = 11.0, 7.8 Hz, 1H), 4.50 (dd, J = 13.3, 5.1 Hz, 1H), 3.46-3.40 (m, 1H), 3.03-2.70 (m, 2H), 1.85 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 167.18, 156.33 (d, J = 243.7 Hz), 149.06, 138.82 (d, J = 11.9 Hz), 135.46, 132.37, 130.25 , 128.79, 123.28, 122.78, 122.16 (d, J = 7.7 Hz), 107.89 (d, J = 3.0 Hz), 104.31, 104.01, 104.77, 61.87, 35.39, 25.88, 22.81.HRMS (ESI) Calcd for $C_{19}H_{15}FN_2OH^+$ $[M+H]^+$307.1241; Found: 307.1234.



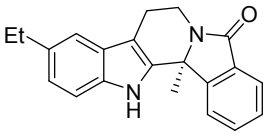
10-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2j): yellow solid, m.p: 161.4-163.5 ℃, 86% yield, 85% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:10/90, 1.0 mL/min, t_{minor} = 19.434 min, t_{major} = 47.258 min). $[\alpha]_D^{20}$ = -34.5 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.58 (s, 1H), 8.29 (d, J = 8.0 Hz, 1H), 7.72 (dt, J = 4.0, 3.1 Hz, 2H), 7.59 (d, J = 1.7 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.34 (d, J = 8.6 Hz, 1H), 7.20 (dd, J = 8.6, 1.9 Hz, 1H), 4.51 (dd, J = 13.3, 5.3 Hz, 1H), 3.41 (dd, J = 11.8, 4.7 Hz, 1H), 2.99-2.57 (m, 2H), 1.84 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 167.12, 148.99, 136.80, 134.88, 132.30, 130.22, 128.72, 127.85, 124.04, 123.22, 122.72, 120.74, 113.21, 111.40, 106.35, 61.90, 35.28, 25.83, 21.29.HRMS (ESI) Calcd for $C_{19}H_{15}BrN_2OH^+$ $[M+H]^+$367.0441 (^{79}Br), 369.0420 (^{81}Br); Found:367.0438 (^{79}Br), 369.0414 (^{81}Br).



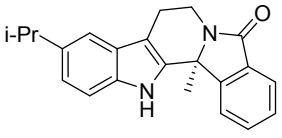
10-methoxy-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2k): white solid, m.p: 130.3-131.9 ℃, 96% yield, 91% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:30/70, 1.0 mL/min, t_{minor}= 4.332 min, t_{major} = 5.804 min). $[\alpha]_D^{20}$ = -50.0 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.19 (s, 1H), 8.29 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 6.9 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.26 (d, J = 8.7 Hz, 1H), 6.89 (d, J = 2.0 Hz, 1H), 6.73 (dd, J = 8.8, 2.3 Hz, 1H), 4.51 (dd, J = 13.2, 5.2 Hz, 1H), 3.72 (s, 3H), 3.44-3.40 (m, 1H), 2.89-2.56 (m, 2H), 1.83 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6)δ 167.22, 153.38, 149.40, 135.81, 132.25, 131.22, 130.26, 128.63, 126.35, 123.20, 122.79, 111.94, 111.58, 106.22, 100.32, 62.08, 55.39, 35.49, 25.98, 21.57.HRMS (ESI) Calcd for $C_{20}H_{18}N_2O_2H^+$ $[M+H]^+$319.1441; Found: 319.1436.



10-(benzyloxy)-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2l): white solid, m.p: 110.4-113.7 ℃, 98% yield, 93% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:10/90, 1.0 mL/min, t_{minor} =10.615 min, t_{major} = 12.738 min). $[\alpha]_D^{20}$ = -41.0 (c 1.0, ethanol). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.14 (d, J = 14.8 Hz, 1H), 8.01 (d, J = 5.9 Hz, 1H), 7.88 (d, J = 7.4 Hz, 1H), 7.57 (t, J = 7.0 Hz, 1H), 7.45 (t, J = 5.2 Hz, 3H), 7.43-7.29 (m, 3H), 7.26 (t, J = 4.3 Hz, 2H), 7.01 (d, J = 2.0 Hz, 1H), 6.90 (dd, J = 8.8, 2.3 Hz, 1H), 4.83 (dd, J = 13.4, 5.6 Hz, 1H), 3.45 (td, J = 13.1, 5.0 Hz, 1H), 2.96 (ddd, J = 17.1, 11.4, 6.0 Hz, 1H), 2.81 (dd, J = 15.5, 4.6 Hz, 1H), 1.92 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 168.40, 153.37, 148.94, 137.49, 135.58, 132.18, 131.71, 130.88, 128.65, 128.45, 127.73, 127.49, 126.94, 124.17, 121.64, 113.09, 111.90, 107.72, 102.40, 70.95, 62.46, 35.75, 26.23, 21.87.HRMS (ESI) Calcd for $C_{26}H_{22}N_2O_2H^+$ $[M+H]^+$395.1754; Found: 395.1748.

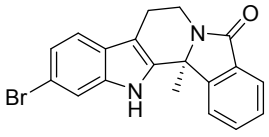


10-ethyl-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2m): white solid, m.p: 272.8-274.3 ℃, 93% yield, 85% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:20/80, 1.0 mL/min, t_{minor} =7.131 min, t_{major} = 8.256 min). $[\alpha]_D^{20}$ = -74.8 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.24 (s, 1H), 8.30 (d, J = 7.6 Hz, 1H), 7.71 (t, J = 7.3 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 8.2 Hz, 1H), 7.18 (s, 1H), 6.94 (d, J = 8.2 Hz, 1H), 4.52 (dd, J = 13.3, 5.0 Hz, 1H), 3.36 (dd, J = 13.0, 4.7 Hz, 1H), 2.83-2.67 (m, 2H), 2.66-2.58 (m, 2H), 1.84 (s, 3H), 1.16 (t, J = 7.5 Hz, 3H).^{13}C NMR (75 MHz, DMSO-d_6)δ167.28, 149.45, 135.27, 134.74, 134.35, 132.27, 130.29, 128.64, 126.20, 123.22, 122.82, 122.14, 116.80, 111.07, 106.07, 62.11, 35.53, 28.51, 25.94, 21.54, 16.78.HRMS (ESI) Calcd for $C_{21}H_{20}N_2OH^+$ $[M+H]^+$317.1648; Found: 317.1641.

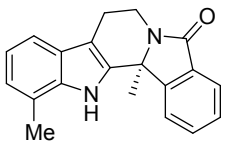


10-isopropyl-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2n): white solid, m.p: 280.8-284.3 ℃, 95% yield, 85% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:20/80, 1.0 mL/min, t_{minor} = 6.576 min, t_{major} = 7.426 min). $[\alpha]_D^{20}$ = -50.9 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.20 (s, 1H), 8.31 (d, J = 7.6 Hz, 1H), 7.71 (t, J = 7.3 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.29 (d, J = 8.3 Hz, 1H), 7.21 (s, 1H), 6.99 (d, J = 7.1 Hz, 1H), 4.52 (dd, J = 13.2, 5.1 Hz, 1H),

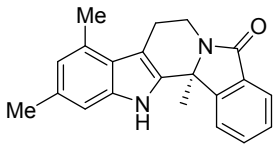
3.43-3.41 (m, 1H), 2.91 (dt, *J* = 13.5, 6.8 Hz, 1H), 2.84-2.60 (m, 2H), 1.84 (s, 3H), 1.20 (d, *J* = 6.9 Hz, 6H).^{13}C NMR (75 MHz, DMSO-d_6) δ 167.18, 149.40, 139.08, 135.24, 134.78, 132.16, 130.24, 128.53, 126.02, 123.13, 122.74, 120.60, 115.10, 110.98, 106.13, 62.02, 35.47, 33.58 , 25.88, 24.62, 21.47.HRMS (ESI) Calcd for $C_{22}H_{22}N_2OH^+$ $[M+H]^+$331.1805; Found: 331.1795.



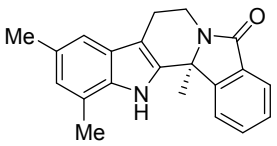
11-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2o): white solid, m.p: 144.9-148.3 ℃, 97% yield, 85% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:10/90, 1.0 mL/min, t_{minor} =15.417 min, t_{major} = 18.012 min). $[\alpha]_D^{20}$ = -155.0 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.58 (s, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 7.75-7.70(m, 2H), 7.63-7.45 (m, 2H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.10 (dd, *J* = 8.4, 1.7 Hz, 1H), 4.51 (dd, *J* = 13.2, 5.4 Hz, 1H), 3.37 (dd, *J* = 13.2, 4.9 Hz, 1H), 2.92-2.55 (m, 2H), 1.84 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6)δ 167.24, 149.05, 137.06, 136.23, 132.39, 130.27, 128.80, 125.10, 123.31, 122.78, 121.89, 120.21, 114.24, 113.81, 106.85, 61.97, 35.35, 25.83, 21.37.HRMS (ESI) Calcd for $C_{19}H_{15}BrN_2OH^+$ $[M+H]^+$367.0441(^{79}Br), 369.0420 (^{81}Br); Found: 367.0433 (^{79}Br), 369.0417 (^{81}Br).



12,13b-dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2p): white solid, m.p: 164.6-168.3 ℃, 94% yield, 88% ee, HPLC condition: Chiralpak OD-H isopropyl alcohol/n-hexane:20/80, 1.0 mL/min, t_{minor} =8.009 min, t_{major} = 9.449 min). $[\alpha]_D^{20}$ = -187.0 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6)δ 10.92 (s, 1H), 8.50 (d, *J* = 7.7 Hz, 1H), 7.73 (t, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.34-7.10 (m, 1H), 6.88 (d, *J* = 4.5 Hz, 2H), 4.51 (dd, *J* = 13.3, 5.0 Hz, 1H), 3.35-3.32 (m, 1H), 2.79-2.65 (m, 2H), 2.51 (s, 3H), 1.89 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 167.35, 149.65, 135.69, 135.06, 132.27, 130.23, 128.57, 125.74, 123.20, 123.12, 122.37, 120.54, 119.21, 115.91, 107.10, 62.34, 35.57, 25.81, 21.69, 17.18.HRMS (ESI) Calcd for $C_{20}H_{18}N_2OH^+$ $[M+H]^+$303.1492; Found: 303.1483.

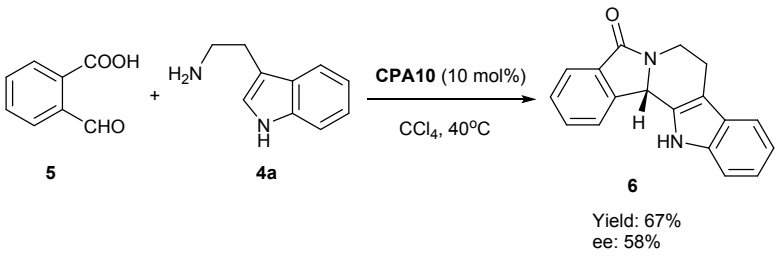


9,11,13b-trimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2q): white solid, m.p: 270.6-271.6 ℃, 92% yield, 82% ee, HPLC condition: Chiralpak IC-H isopropyl alcohol/n-hexane:30/70, 1.0 mL/min, t_{minor} =7.610 min, t_{major} = 9.223 min). $[\alpha]_D^{20}$ = -146.2 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ10.79 (s, 1H), 8.48 (d, J = 7.9 Hz, 1H), 7.79-7.63 (m, 2H), 7.51 (t, J = 7.3 Hz, 1H), 6.98 (s, 1H), 6.71 (s, 1H), 4.51 (dd, J = 13.2, 4.8 Hz, 1H), 3.34 (dd, J = 13.0, 4.9 Hz, 1H), 2.81-2.55 (m, 2H), 2.47 (s, 3H), 2.29 (s, 3H), 1.87 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ 167.36, 149.71, 135.06, 134.10, 132.24, 130.24, 128.54, 127.63, 126.01, 124.06, 123.19, 123.12, 120.18, 115.51, 106.61, 62.36, 35.59, 25.84, 21.70, 21.14, 17.10.HRMS (ESI) Calcd for $C_{21}H_{20}N_2OH^+$ $[M+H]^+$317.1648; Found: 317.1641.

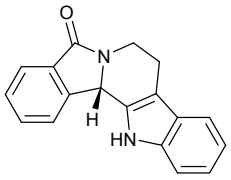


10,12,13b-trimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2r): white solid, m.p: 118.3-120.1 ℃, 94% yield, 93% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:20/80, 1.0 mL/min, t_{minor} =7.812 min, t_{major} = 8.491 min). $[\alpha]_D^{20}$ = -110.3 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.13 (s, 1H), 8.30 (d, J = 7.7 Hz, 1H), 7.70 (t, J = 7.5 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 6.96 (s, 1H), 6.51 (s, 1H), 5.76 (s, 1H), 4.47 (dd, J = 13.3, 5.4 Hz, 1H), 3.35 (dd, J = 12.8, 4.5 Hz, 1H), 3.16-2.76 (m, 2H), 2.45 (s, 3H), 2.30 (s, 3H), 1.83 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6)δ 167.32, 149.62, 136.70, 133.89, 132.25, 130.55, 130.31, 129.50, 128.63, 123.21, 123.03, 122.89, 121.90, 108.94, 106.66, 61.95, 35.66, 25.87, 23.80, 21.38, 19.44.HRMS (ESI) Calcd for $C_{21}H_{20}N_2OH^+$ $[M+H]^+$317.1648; Found: 317.1651.

2.3 Enantioselective intramolecular Pictet-Spengler type annulation of 2-formylbenzoic acid5 with tryptamine 4a.

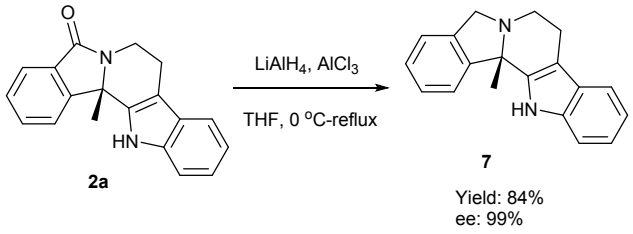


To a solution of **5** (0.1 mmol), **4a** (0.15 mmol) in anhydrous CCl_4 (1.5 mL) was added**CPA10** (10 mol%). The mixture was stirredat 40℃ until the reaction was completed as determined by TLC. The solvent was removed in vacuo, and the residue was purified by column chromatography on a silica gel (petroleum ether : ethyl acetate = 10 : 1 to petroleum ether : ethyl acetate = 2: 1) to afford the product **6**.



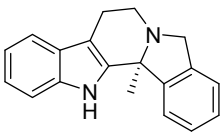
7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(6): white solid, m.p: 289.3-293.6 ℃, 68% yield, 57% ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:10/90, 1.0 mL/min, t_{minor} =28.190 min, t_{major} = 49.703 min). $[\alpha]_D^{20}$ = +71.7 (c 1.0, ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ11.36 (s, 1H), 8.31 (d, J = 7.4 Hz, 1H), 7.73 (dd, J = 15.8, 7.7 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.41 (d, J = 8.4 Hz, 2H), 7.10 (t, J = 7.5 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.04 (s, 1H), 4.60 (dd, J = 13.1, 5.4 Hz, 1H), 3.34 (dd, J = 12.9, 4.7 Hz, 1H), 2.90-2.61 (m, 2H), 2.50 (s, 1H).^{13}C NMR (75 MHz, DMSO-d_6) δ 167.20, 143.67, 136.48 , 131.90, 131.72, 130.91, 128.64, 126.18, 123.80, 123.16, 121.56, 118.89, 118.17, 111.30, 107.19, 56.67, 37.73, 21.42.HRMS (ESI) Calcd for $C_{18}H_{15}N_2OH^+$ $[M+H]^+$275.1179; Found: 275.1177.

2.4 Reduction of 2a[5]



To a suspension of $LiAlH_4$ (0.4 mmol) and $AlCl_3$ (0.4 mmol) in anhydrous THF was added to a solution of **2a** (0.1 mmol) in THF dropwise at 0 °C. After the addition, the mixture was heated to reflux for 4 h. After the reaction wascooled,dichloromethane (50 m L) was added to dilute the

reaction mixture, and water was added dropwise at 0 °C to quench the reaction. Then the solid which precipitated out was removed by filtration, and the organic phase obtained was dried with Na_2SO_4 and concentrated. The residue was purified to give **7**. [5]



13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indole(7): white solid, m.p: 184.3-185.8 ℃, 84% yield, >99 % ee, HPLC condition: Chiralpak AD-H isopropyl alcohol/n-hexane:30/70, 1.0 mL/min, t_{minor} =4.950 min, t_{major} = 6.116 min). $[\alpha]_D^{20}$ = -163.4 (c 1.0, ethanol).^{1}H NMR (300 MHz, $CDCl_3$)δ 7.71 (s, 1H), 7.55-7.42 (m, 2H), 7.29 (dd, *J* = 13.5, 7.8 Hz, 3H), 7.23-7.19 (m, 2H), 7.16-7.06 (m, 2H), 4.21 (q, *J* = 12.7 Hz, 2H), 3.65-3.35 (m, 2H), 3.16 (ddd, *J* = 17.2, 11.2, 6.2 Hz, 1H), 2.64 (dd, *J* = 16.1, 4.3 Hz, 1H), 1.87 (s, 3H).

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3. B. Lu, M. Zhao, G. Ding, X. Xie, L. Jiang, V. Ratovelomanana-Vidal and Z. Zhang, *ChemCatChem*. 2017, **9**, 3989-3996.
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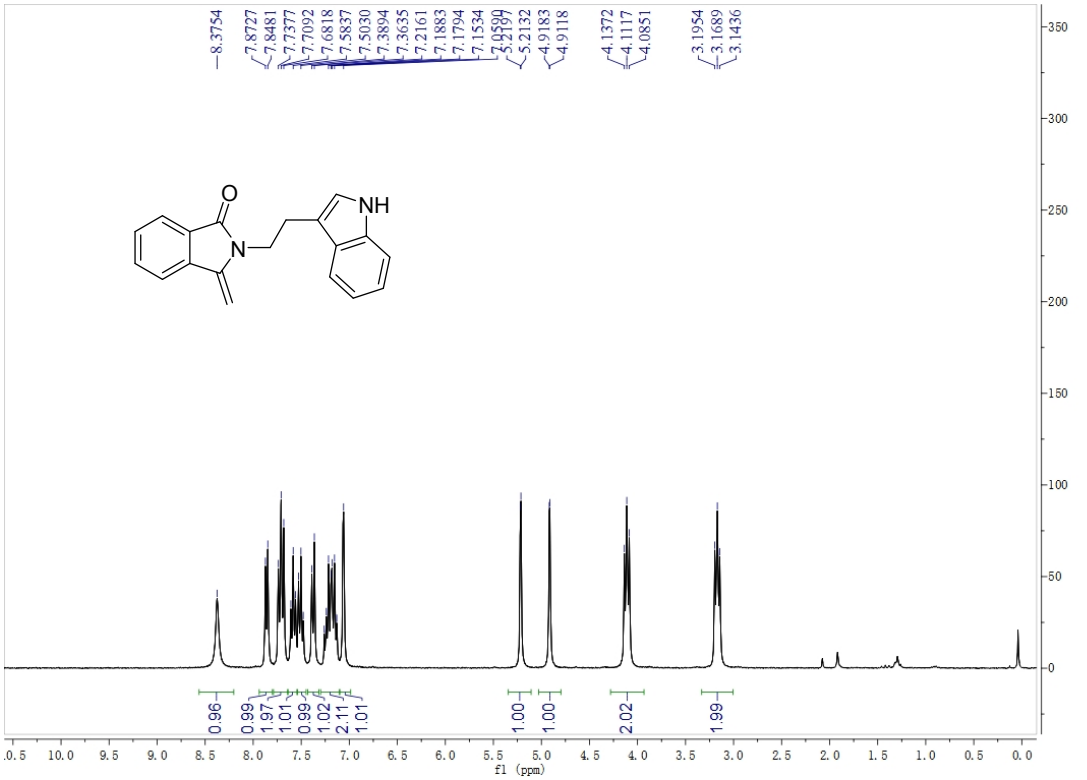
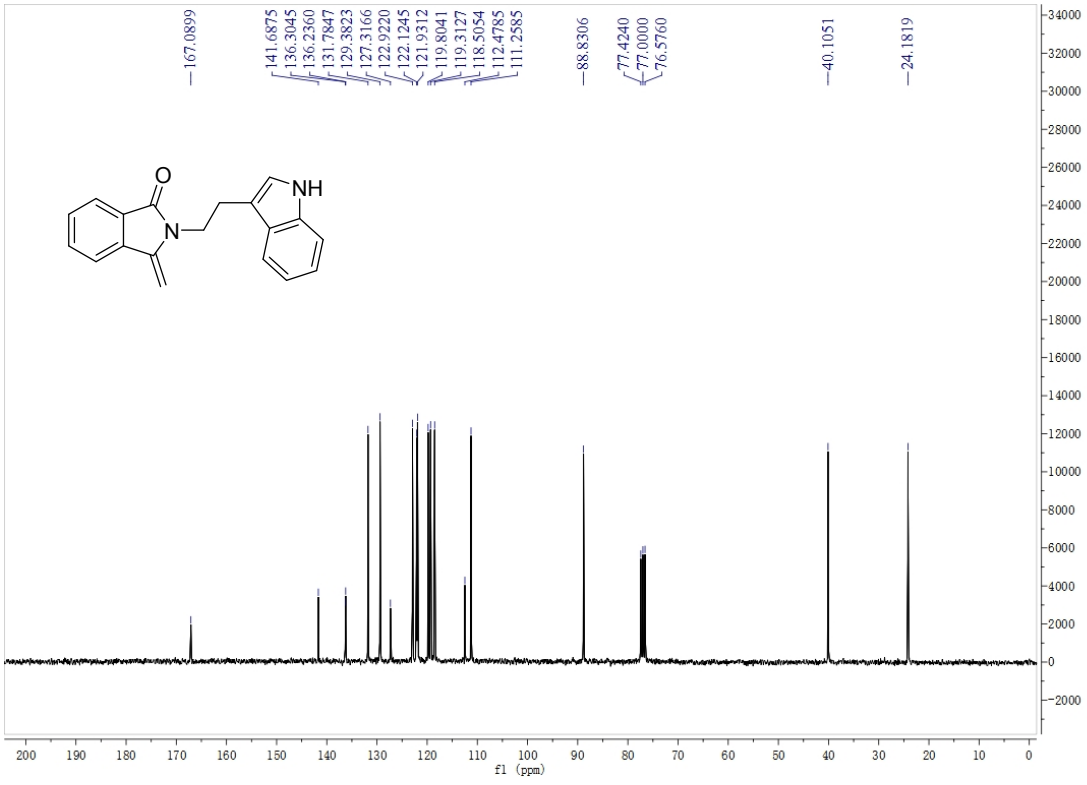
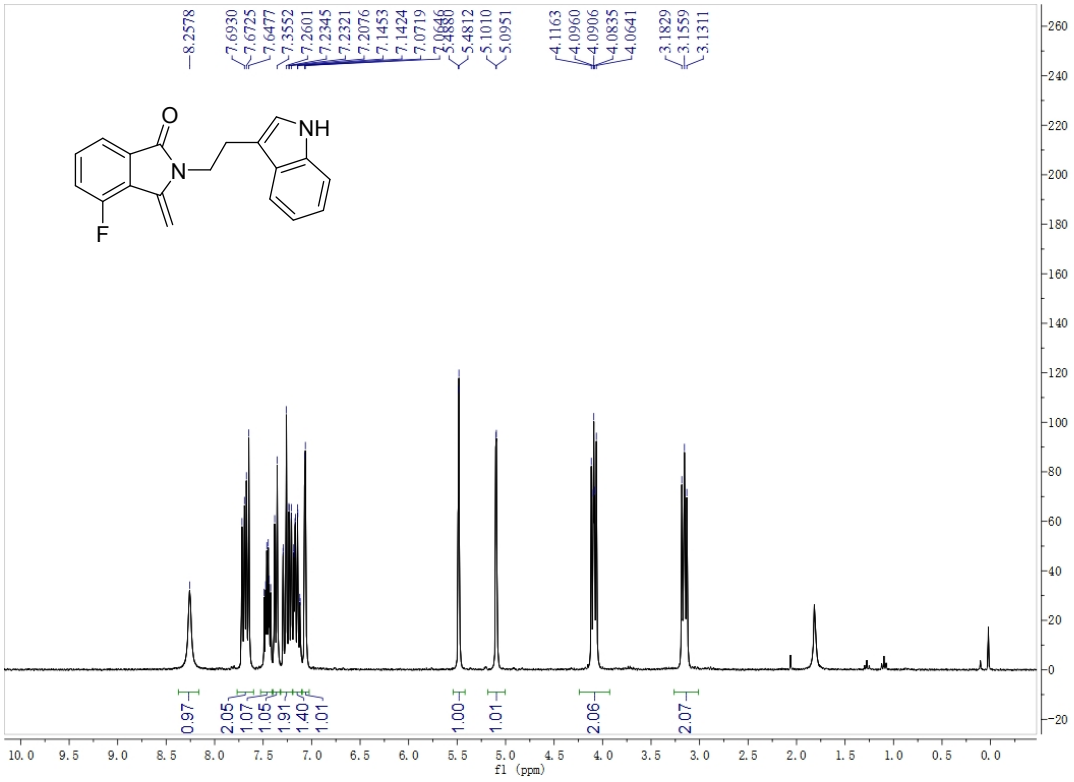
3. ^{1}H NMR and ^{13}C NMR spectra

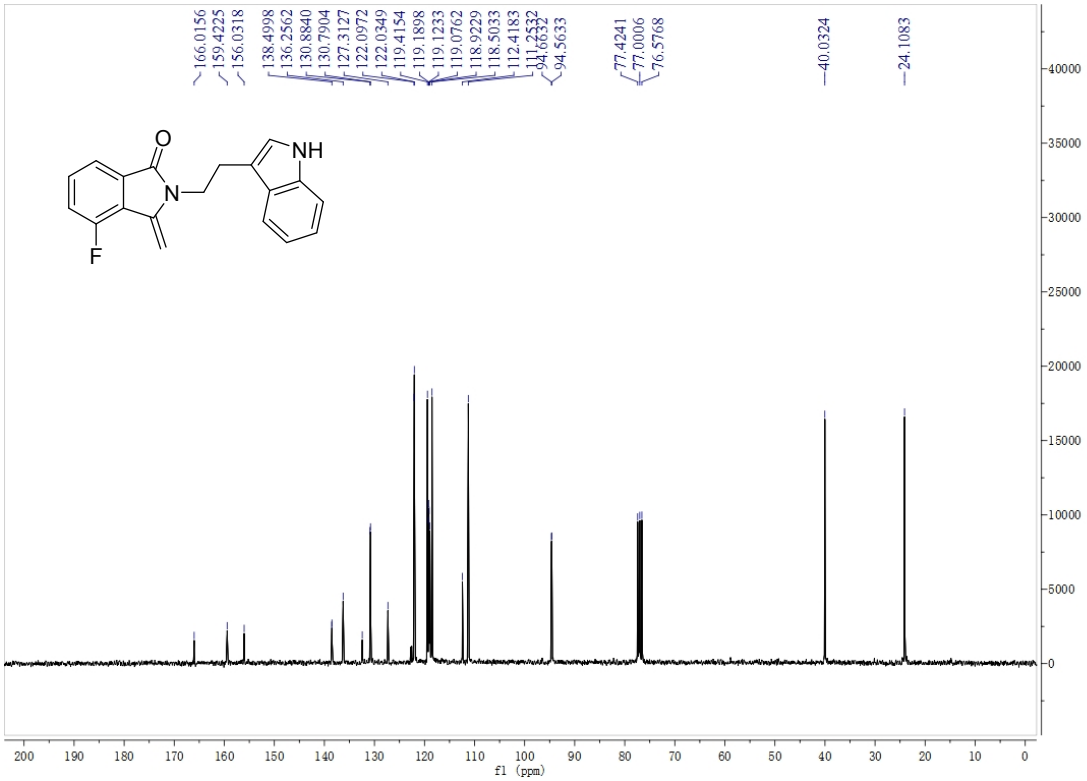
2-(2-(1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1a)



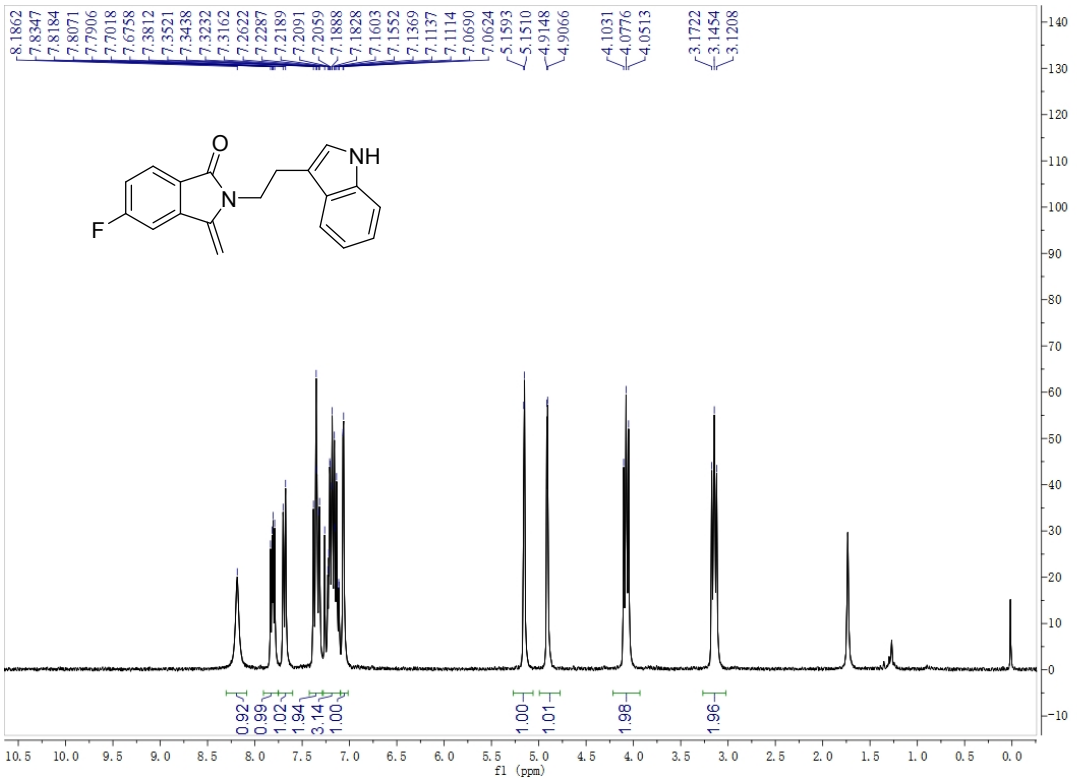


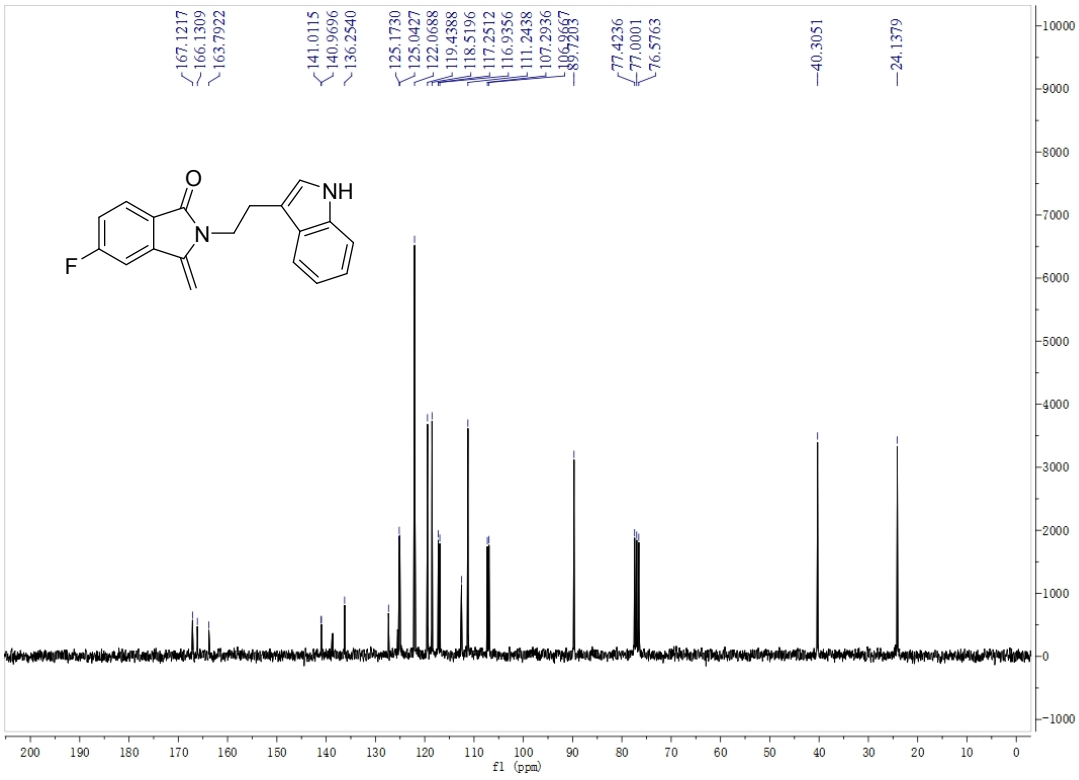
(2-(1H-indol-3-yl)ethyl)-4-fluoro-3-methyleneisoindolin-1-one (1b)



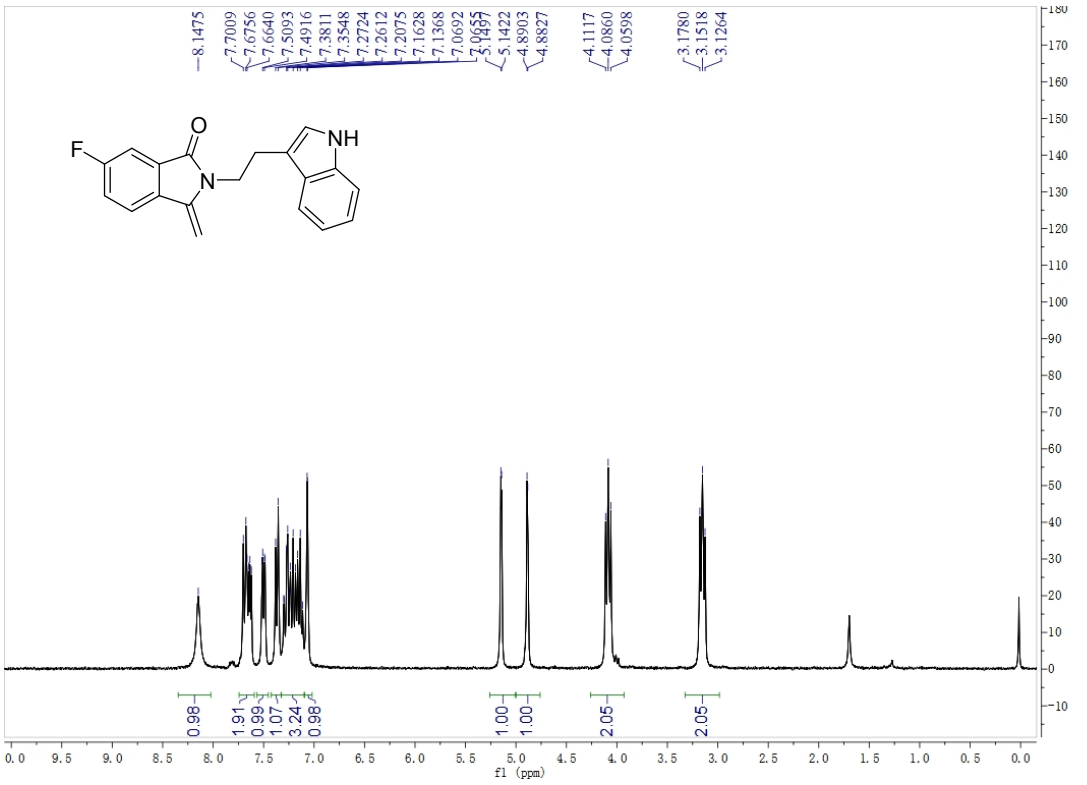


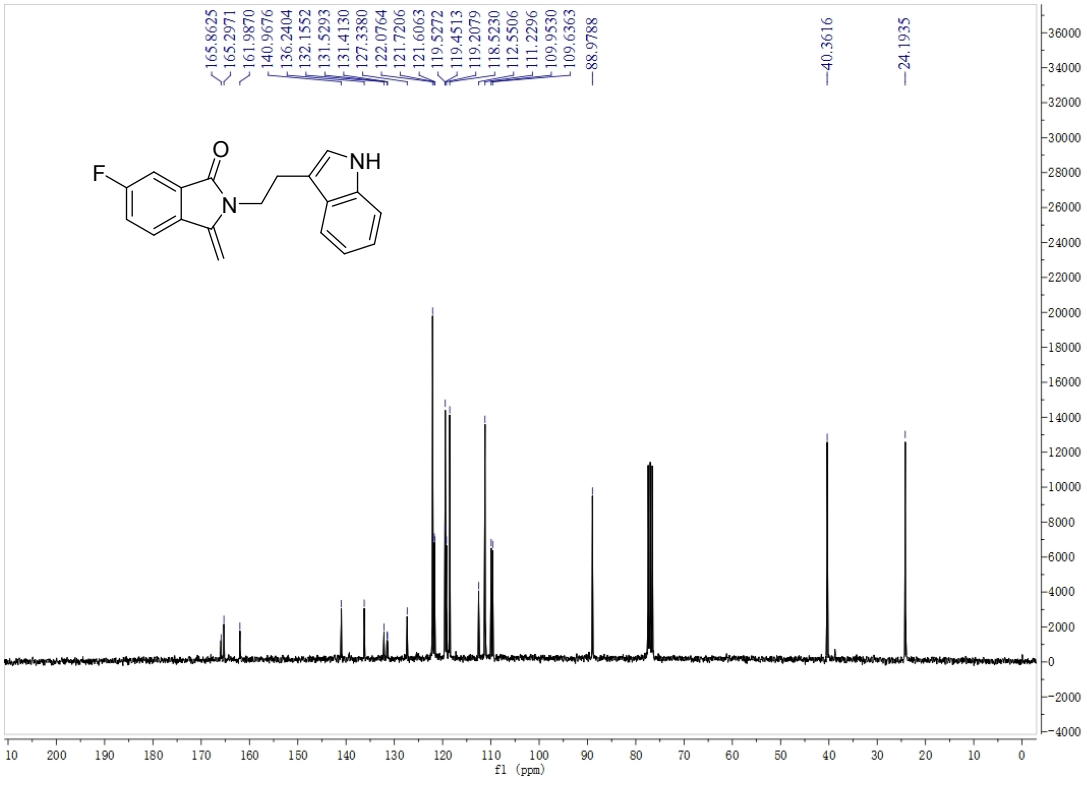
2-(2-(1H-indol-3-yl)ethyl)-5-fluoro-3-methyleneisoindolin-1-one (1c)



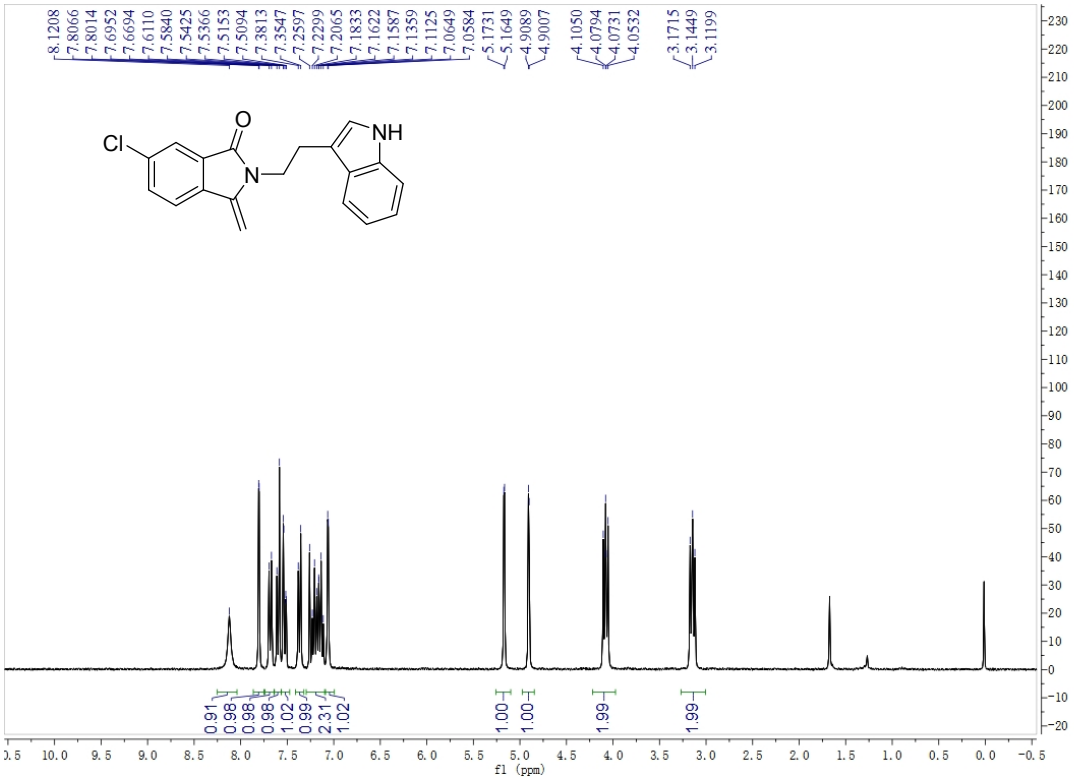


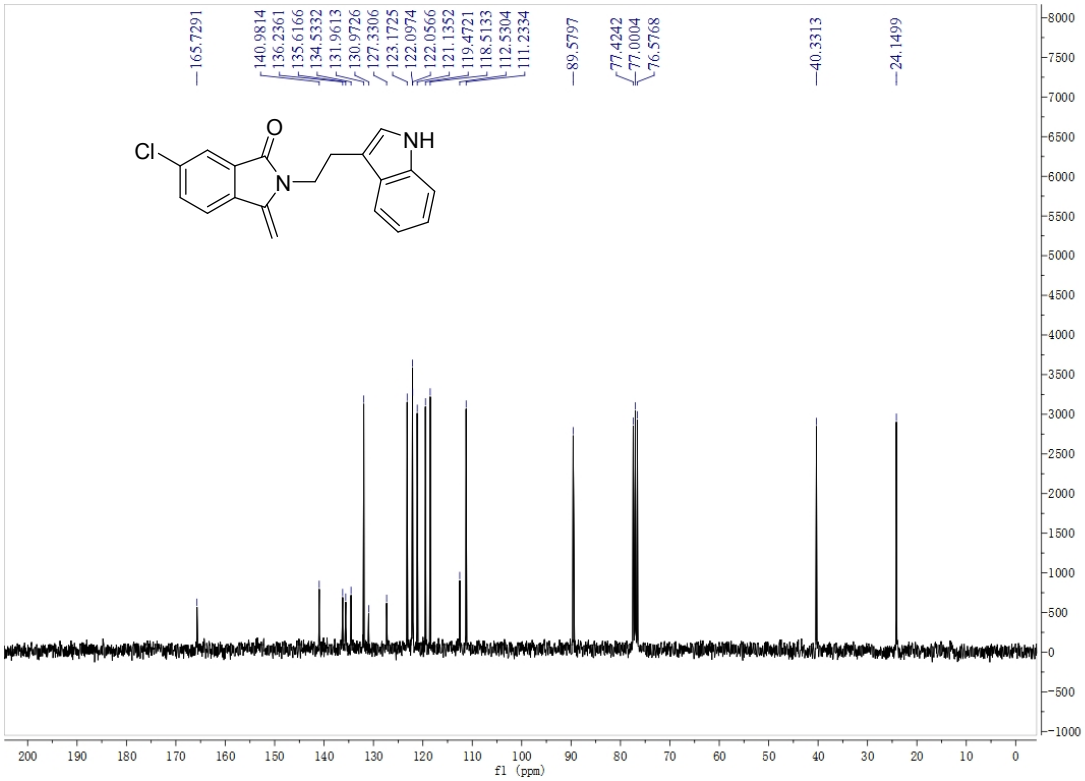
2-(2-(1H-indol-3-yl)ethyl)-6-fluoro-3-methyleneisoindolin-1-one (1d)





2-(2-(1H-indol-3-yl)ethyl)-6-chloro-3-methyleneisoindolin-1-one (1e)





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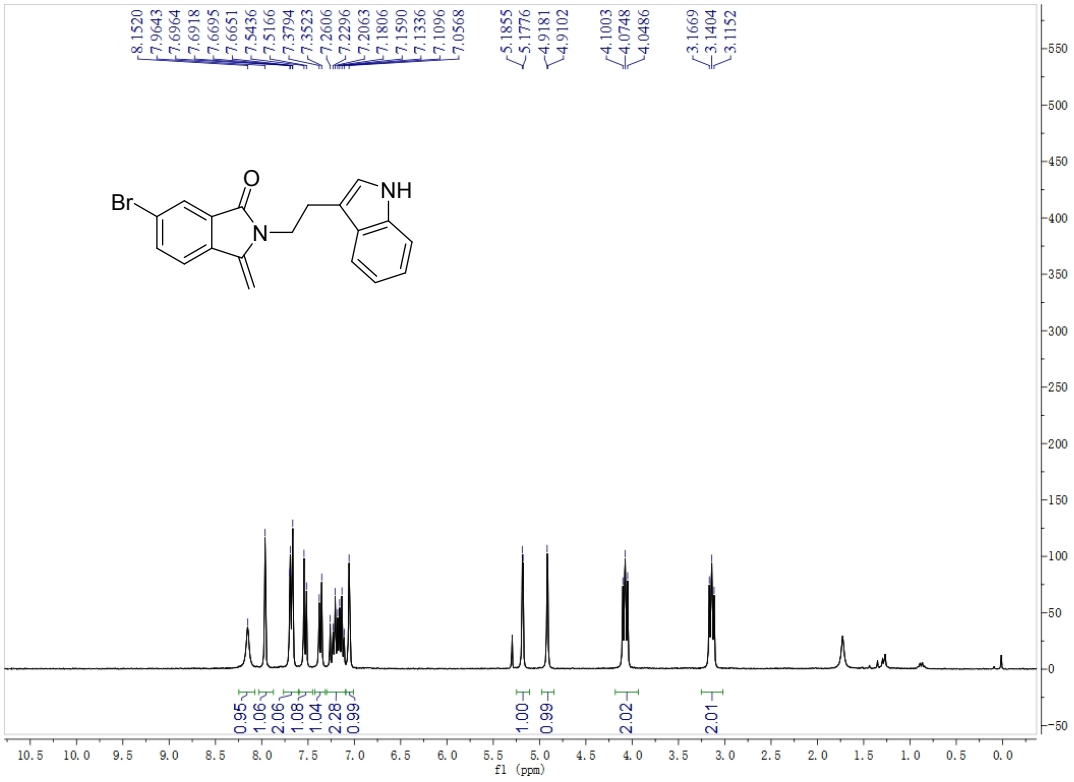

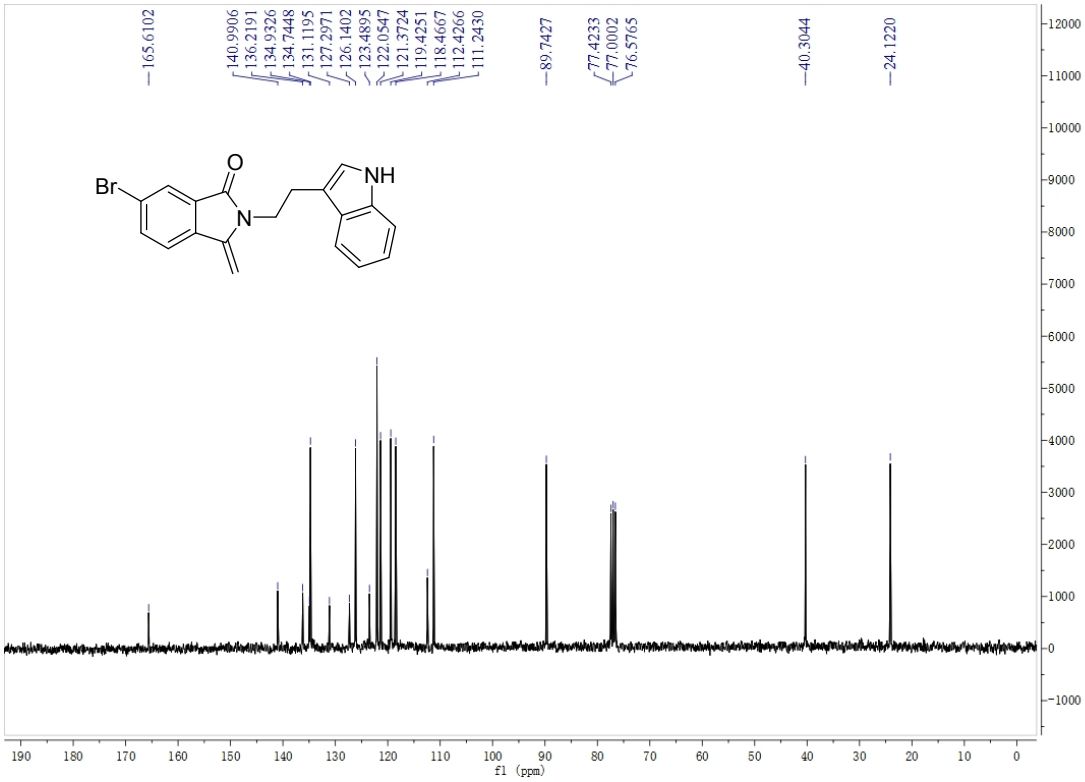

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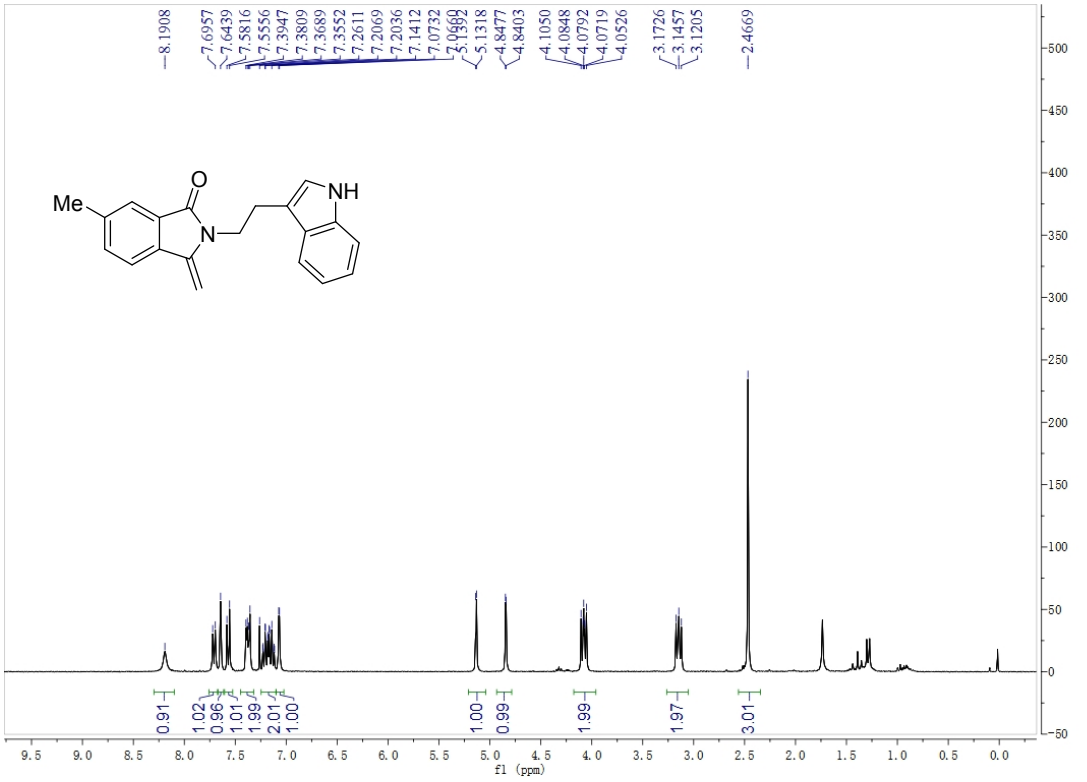

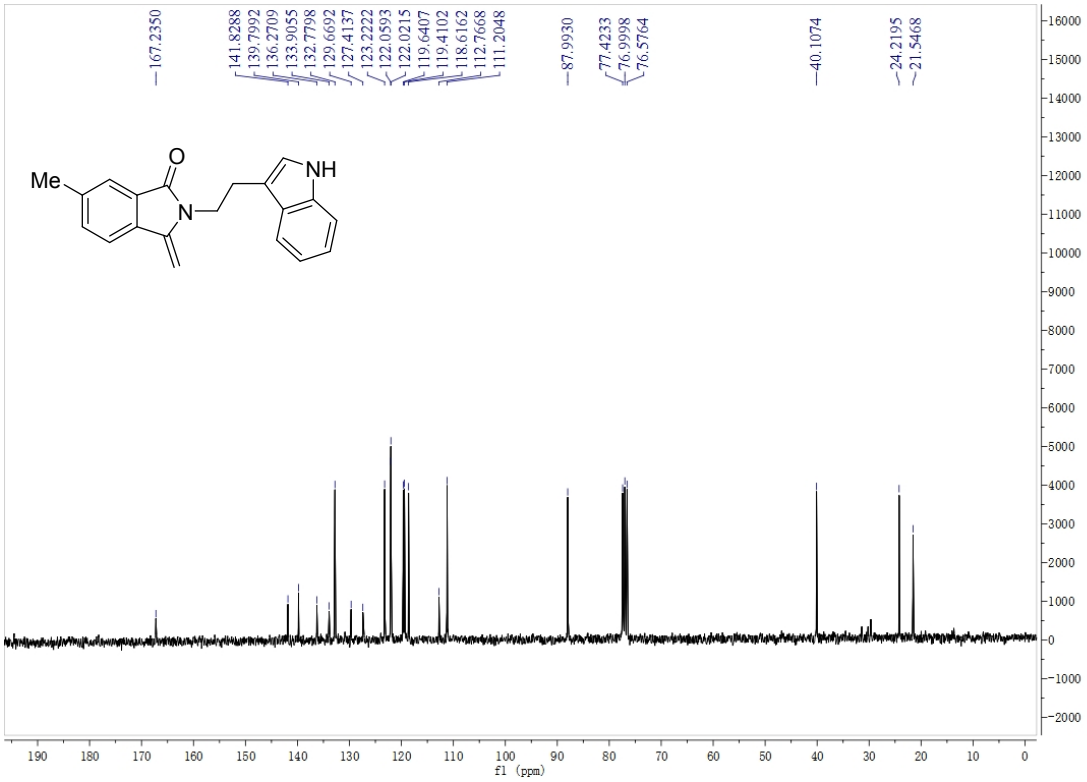

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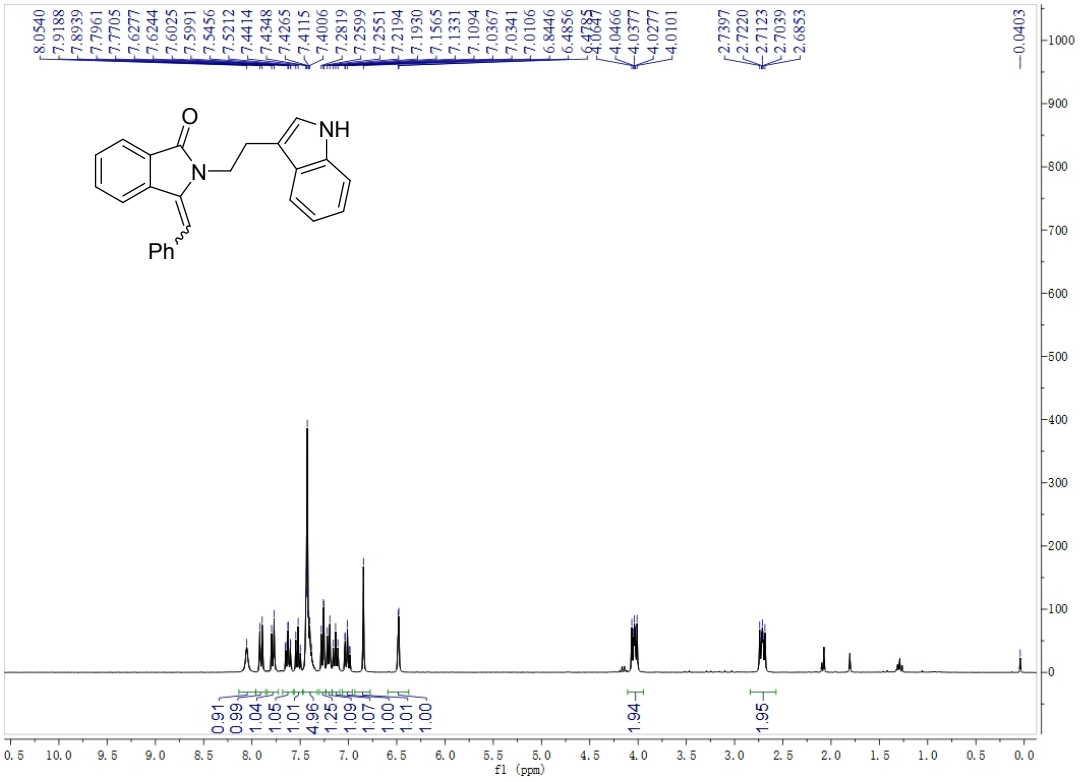

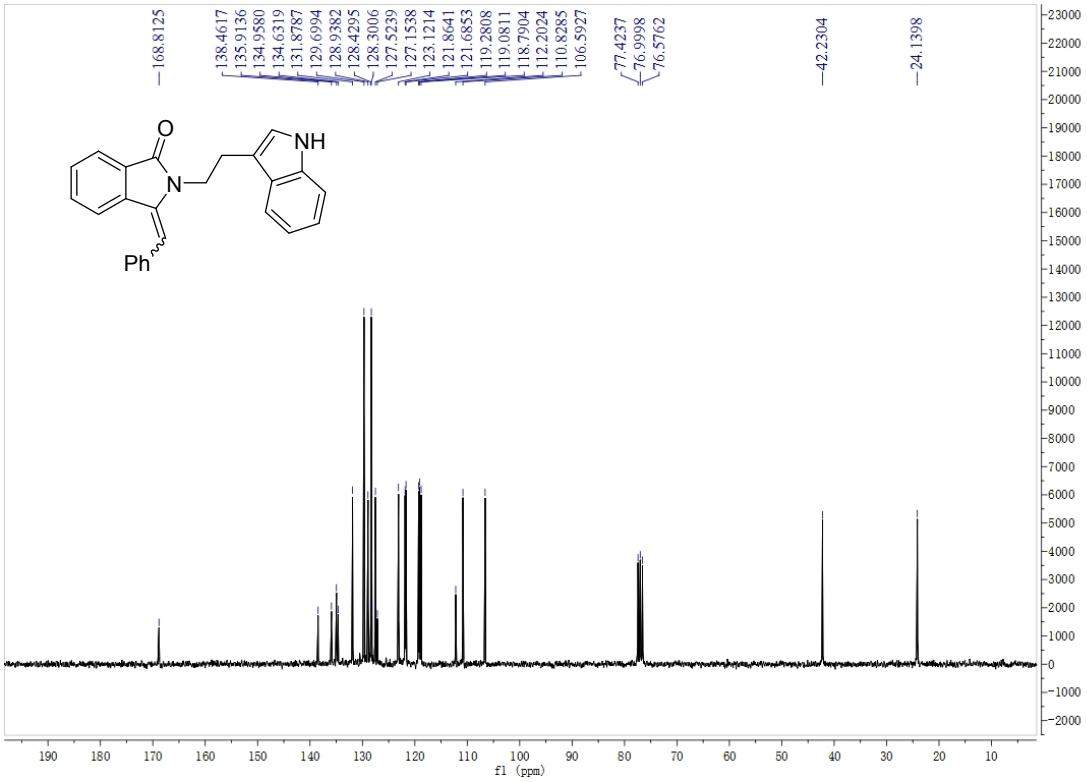

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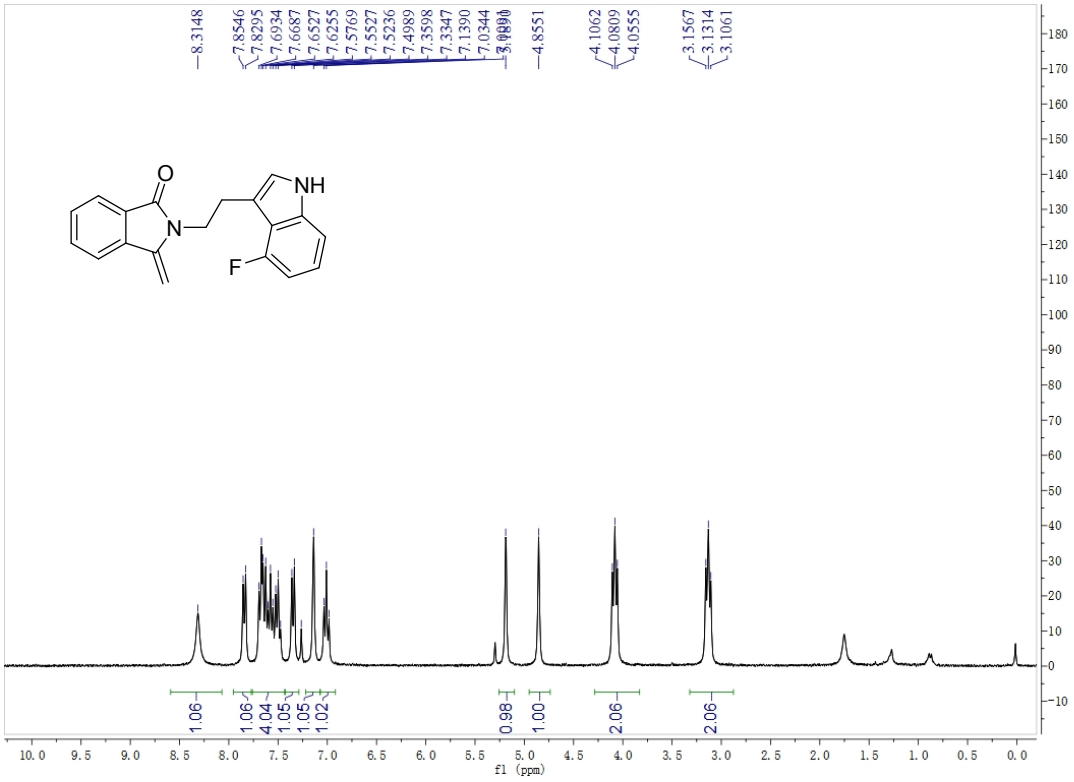

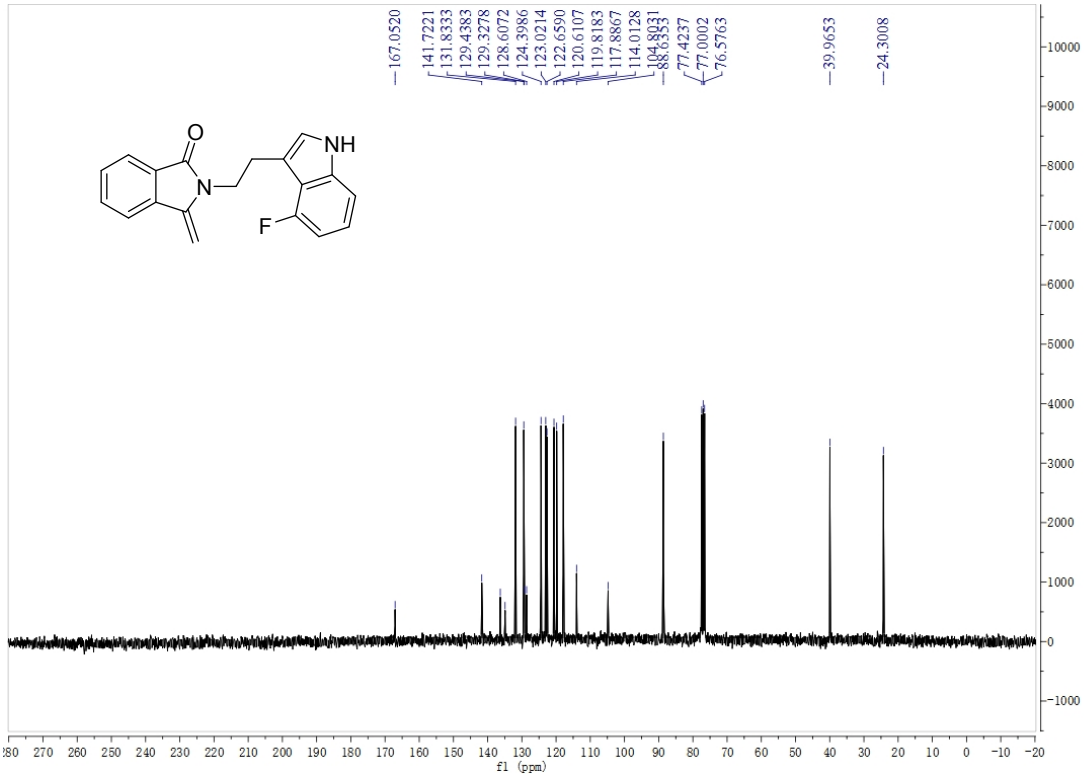

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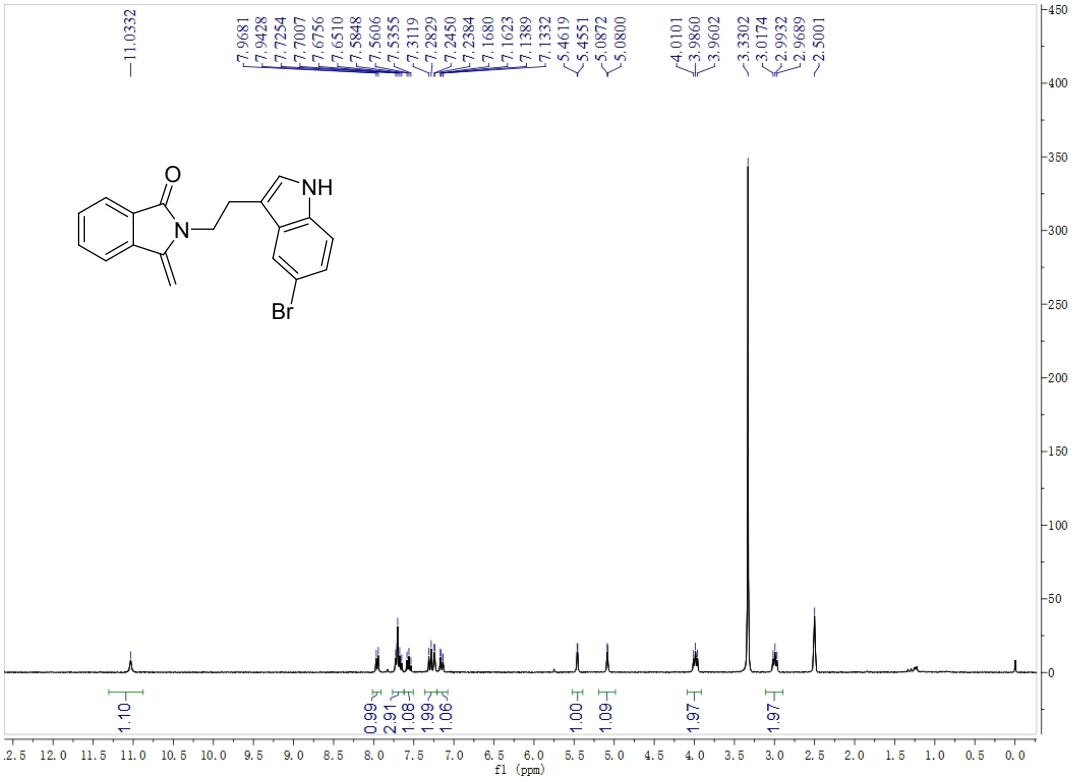
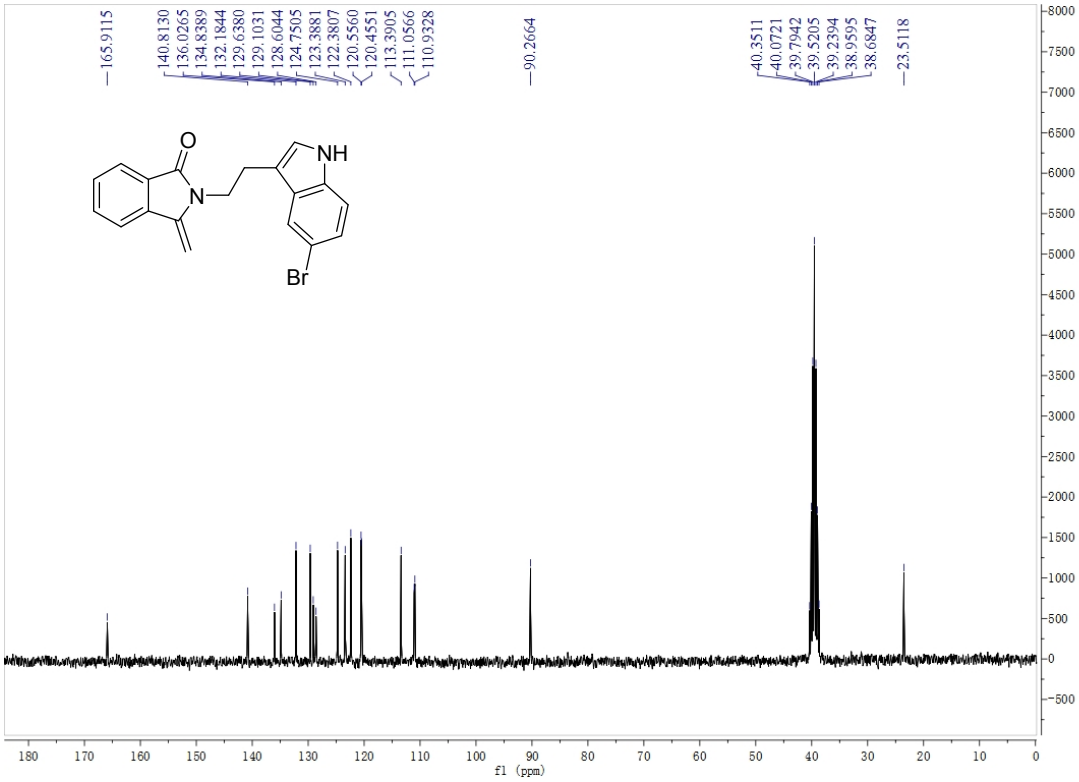
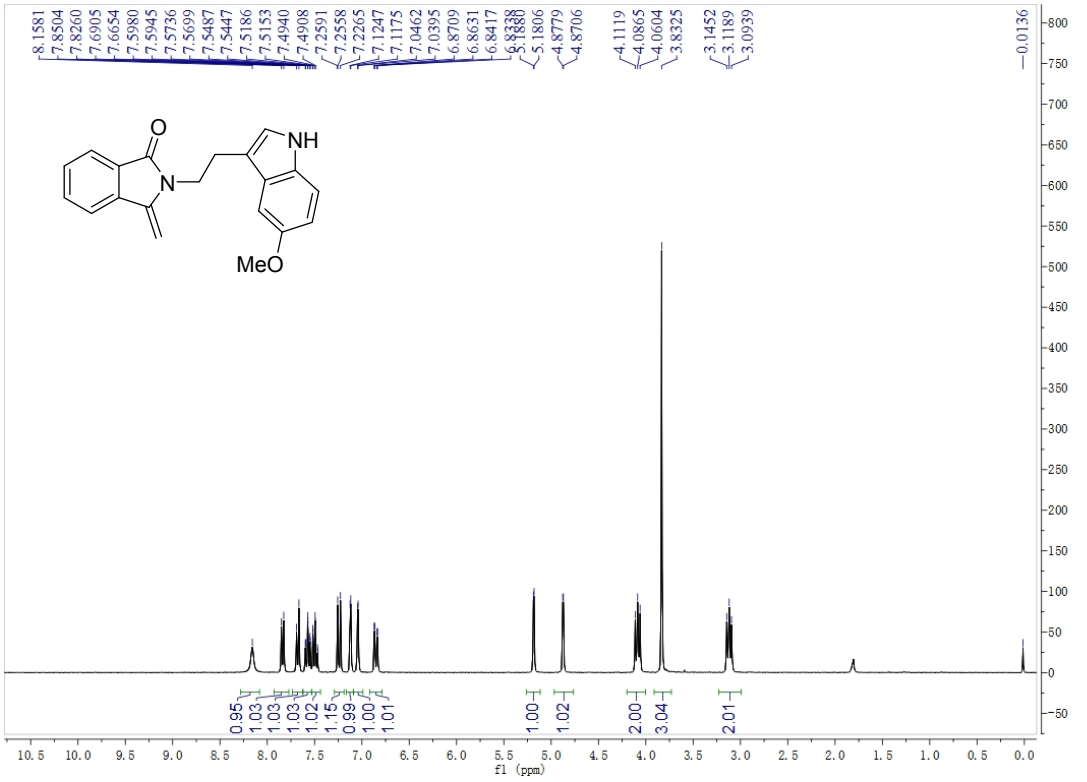
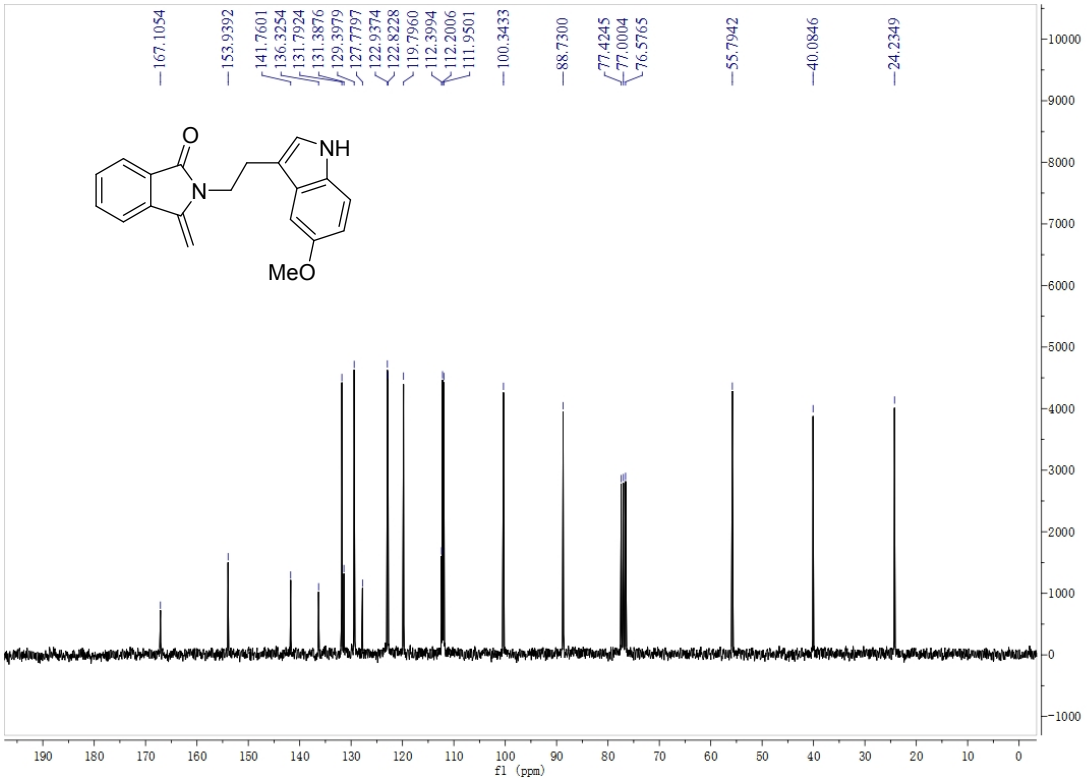




2-(2-(5-methoxy-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1k)





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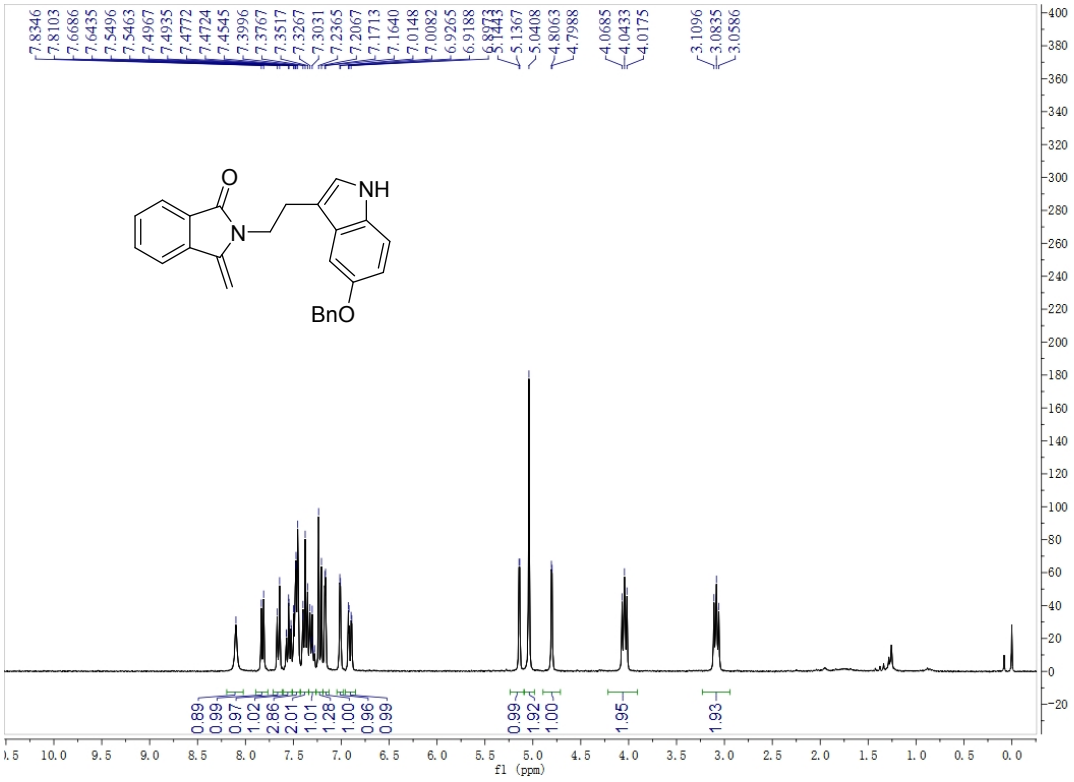

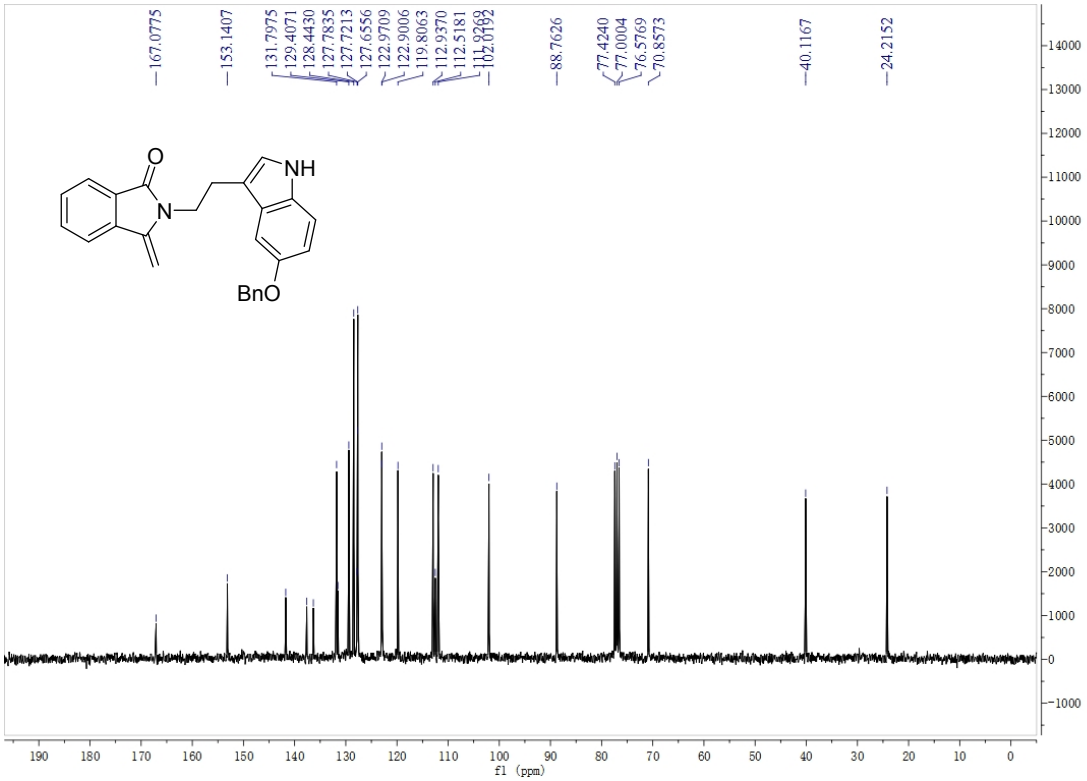

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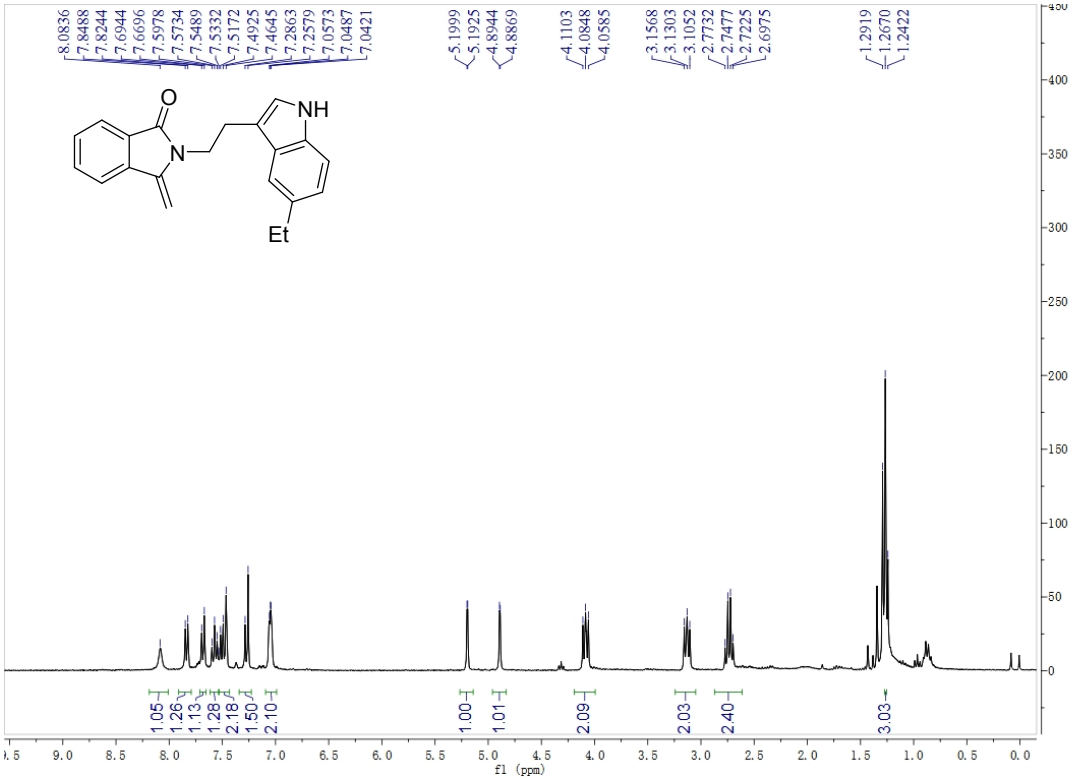
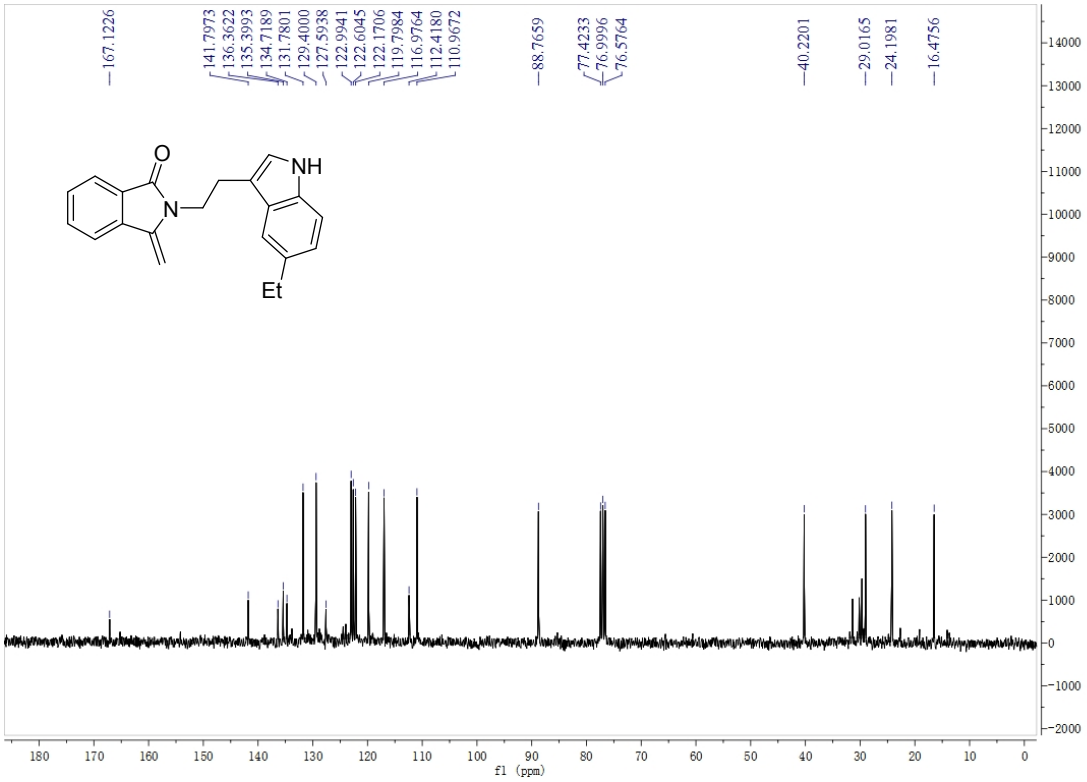
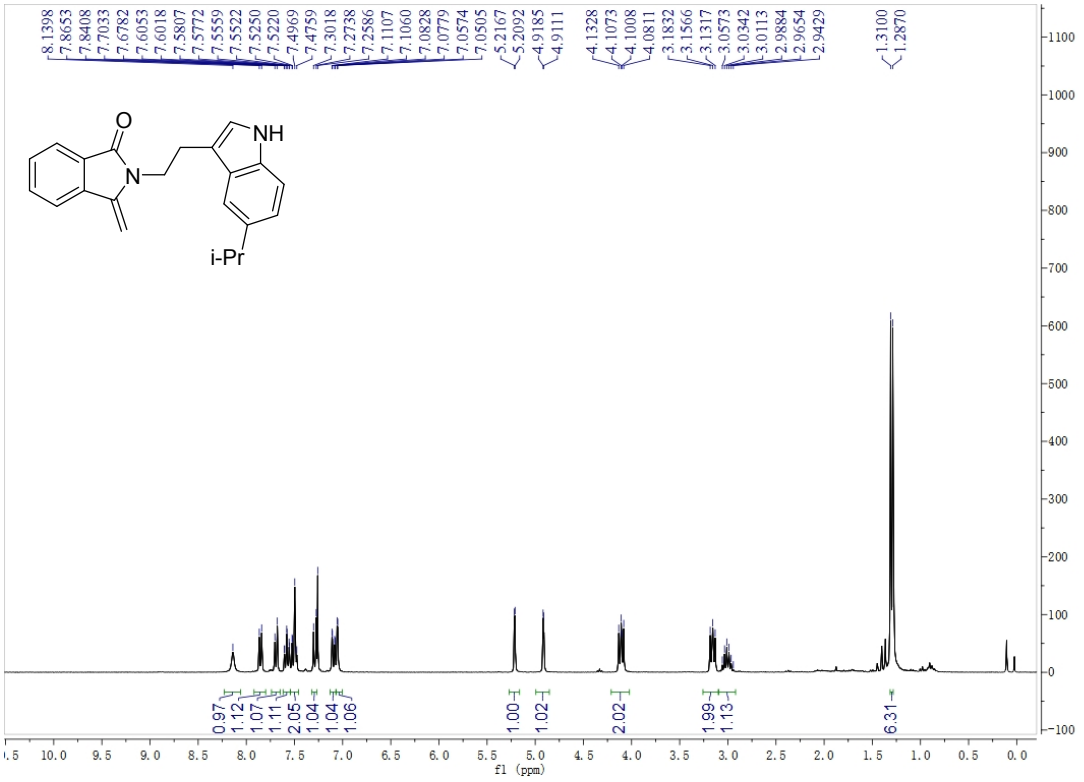
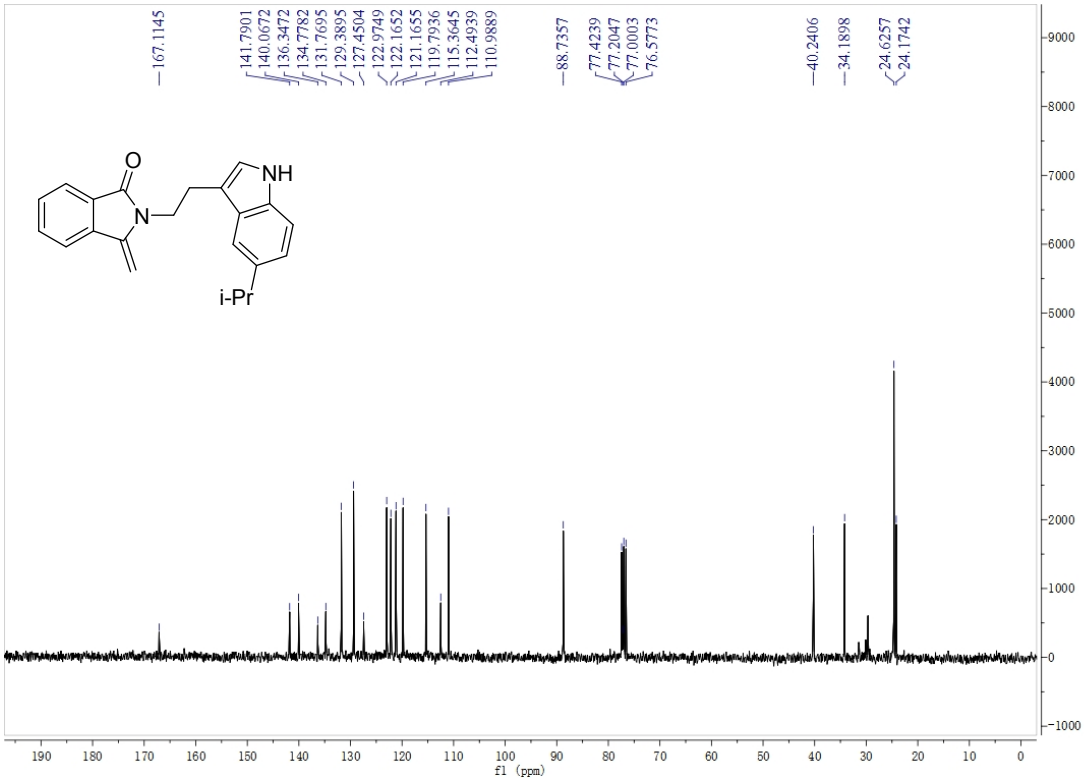




2-(2-(5-isopropyl-1H-indol-3-yl)ethyl)-3-methyleneisoindolin-1-one (1n)





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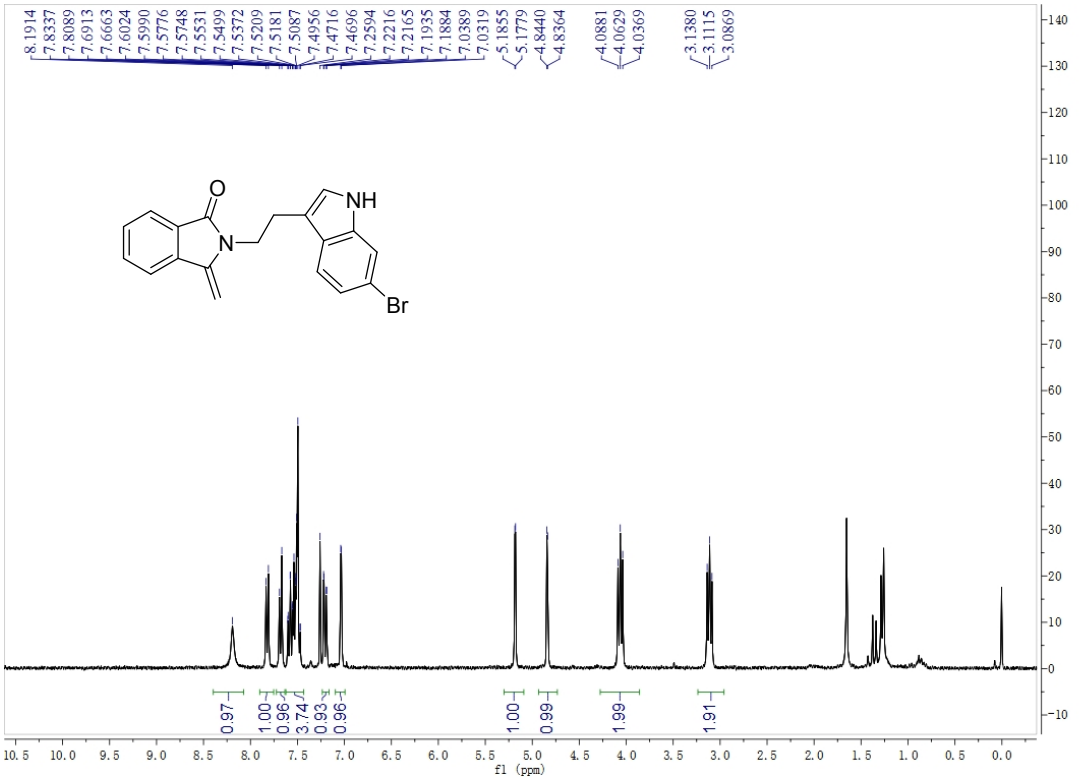

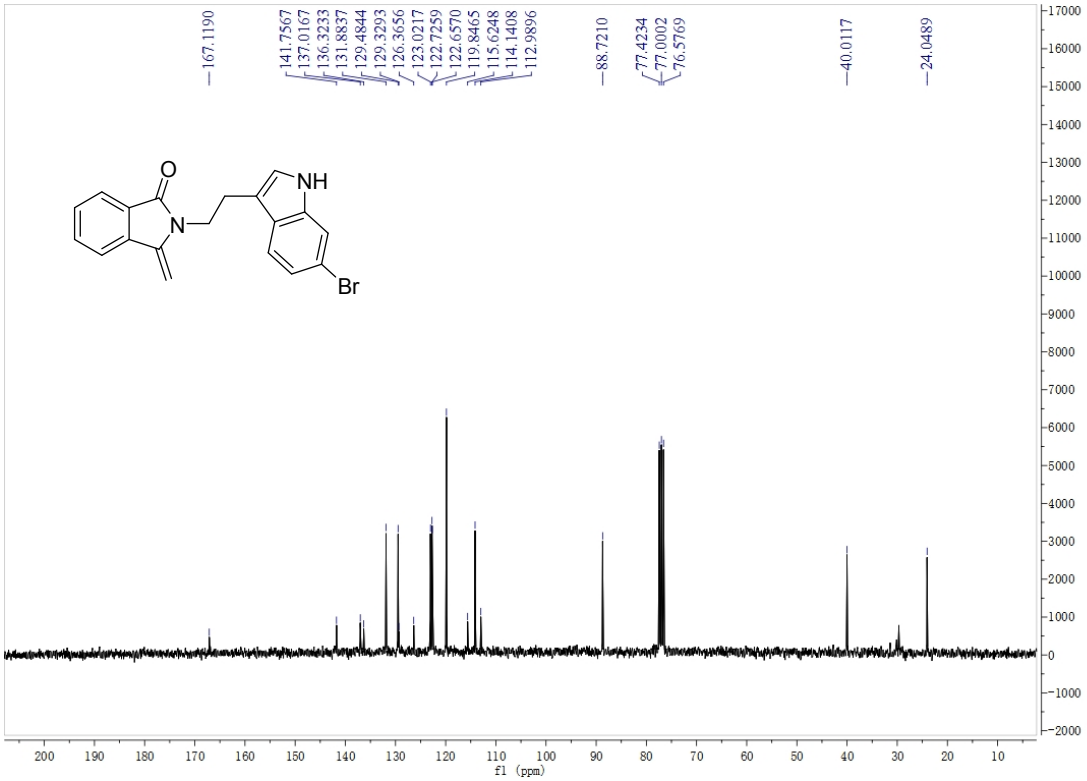

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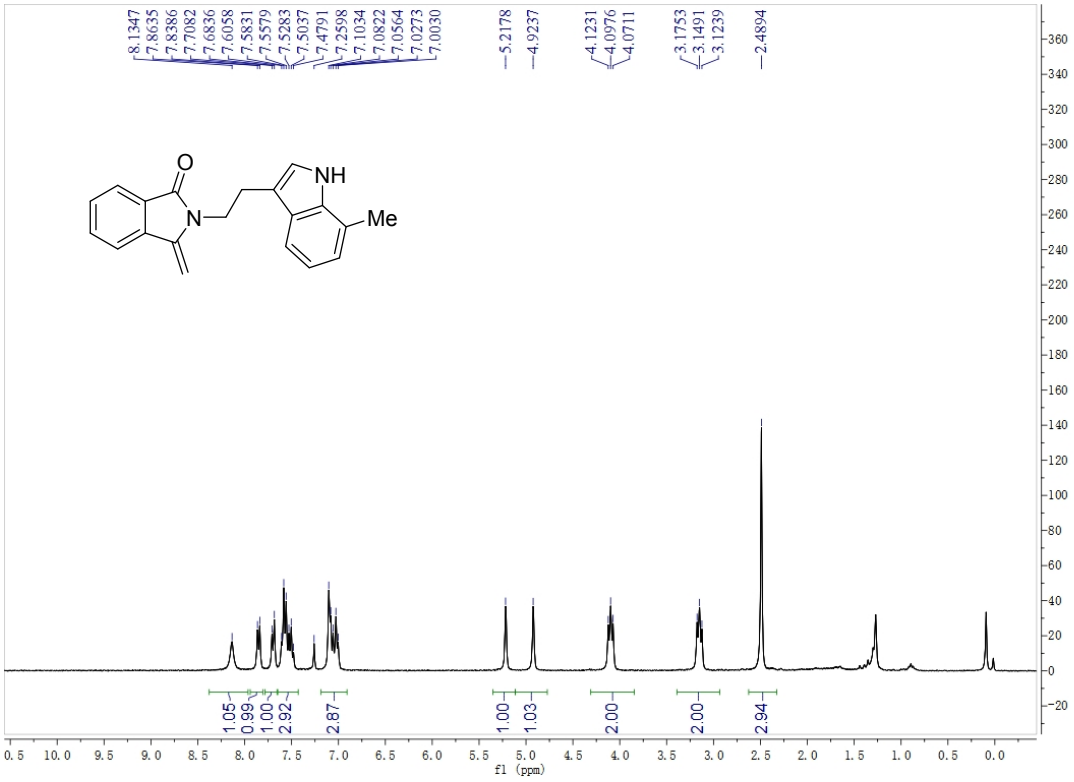

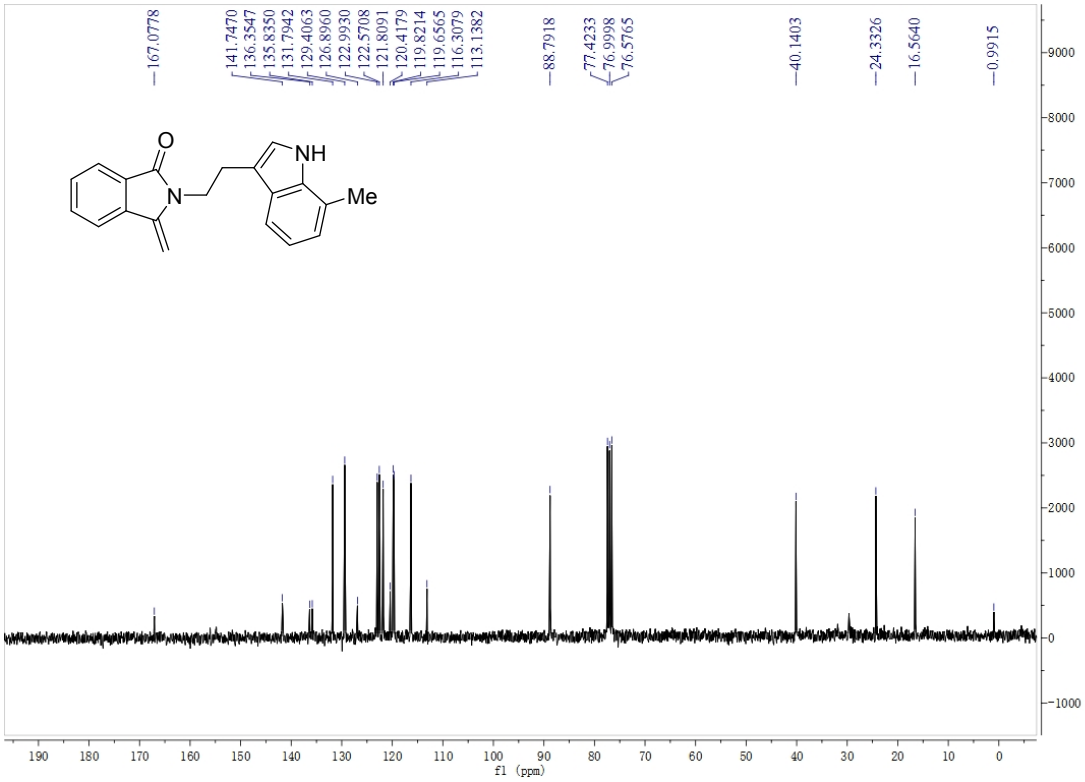

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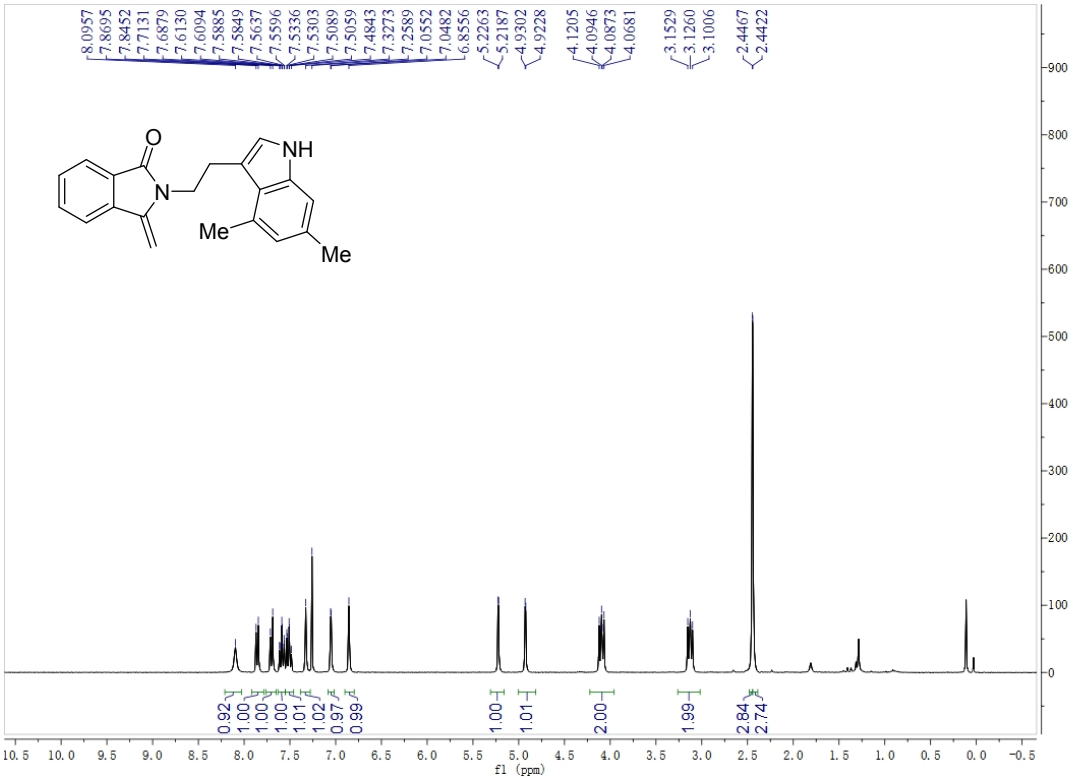

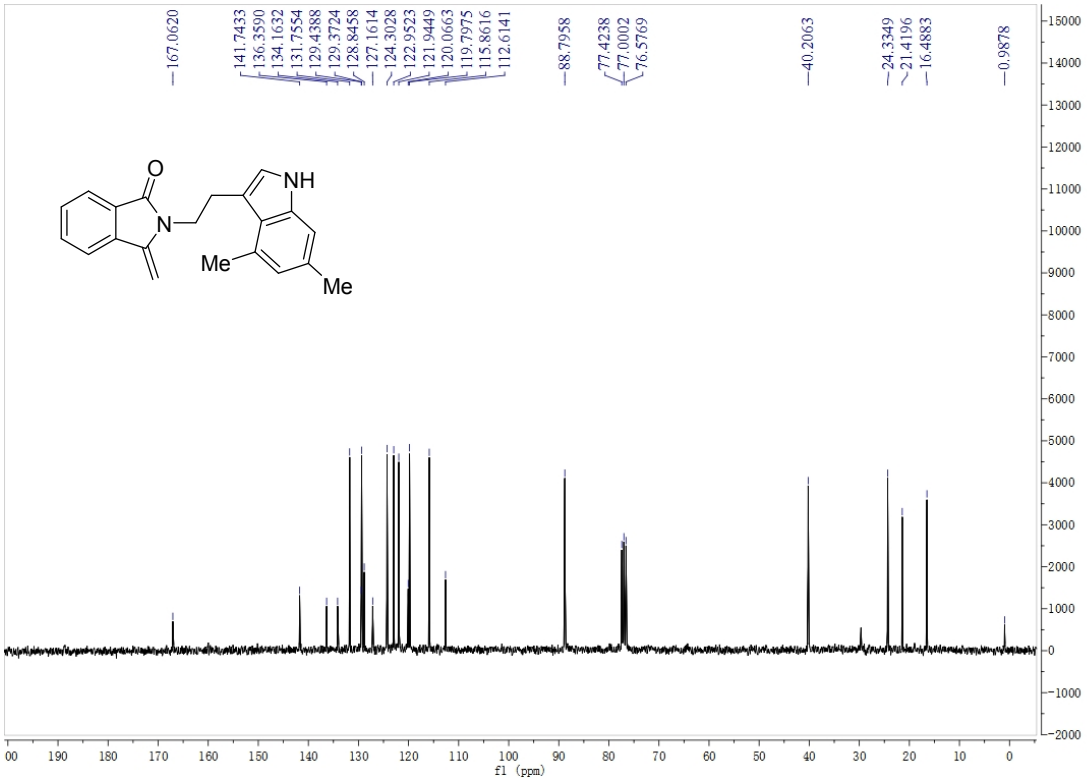

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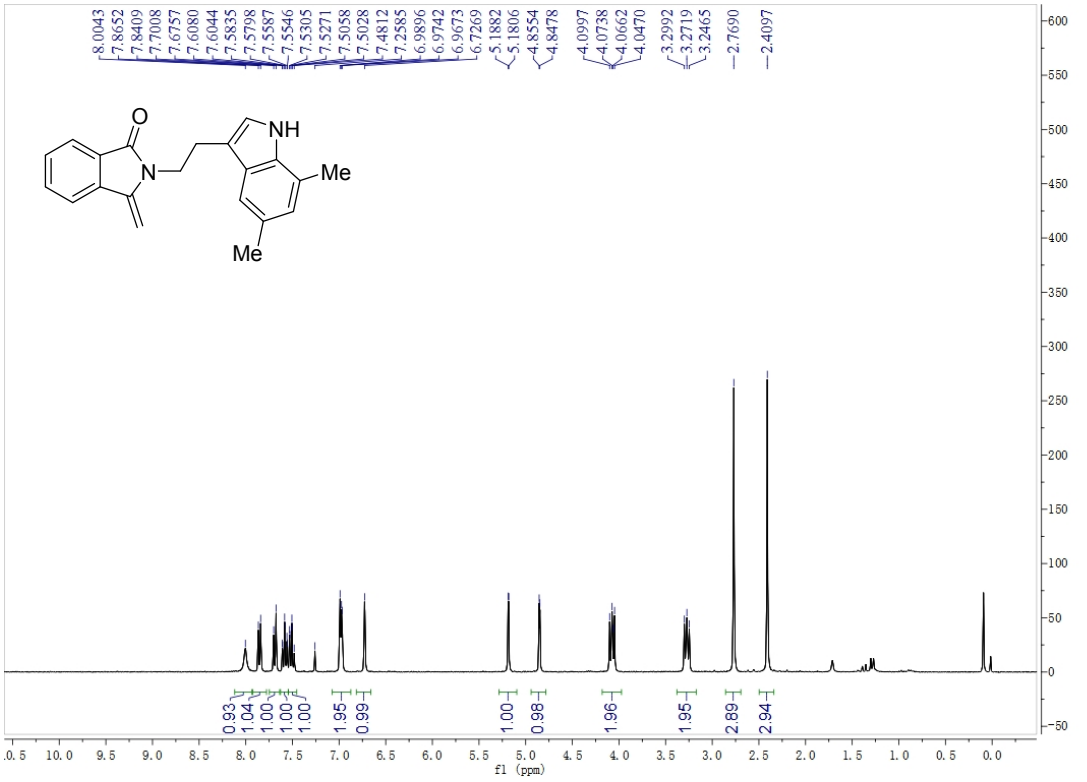
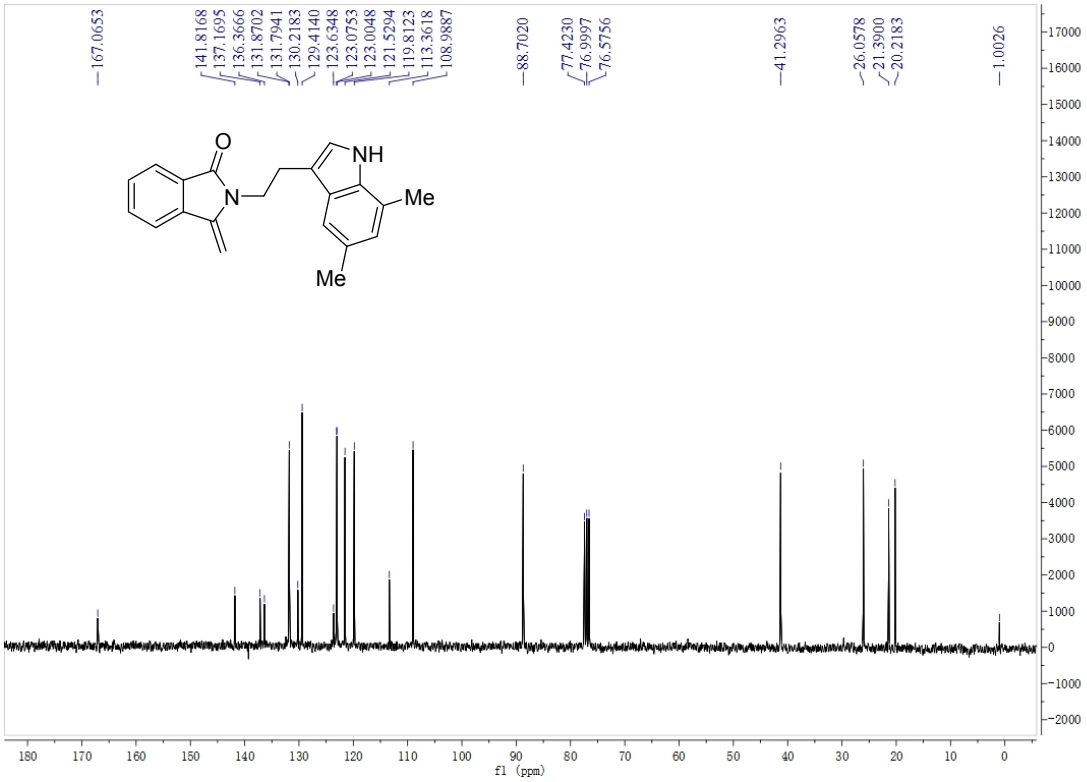
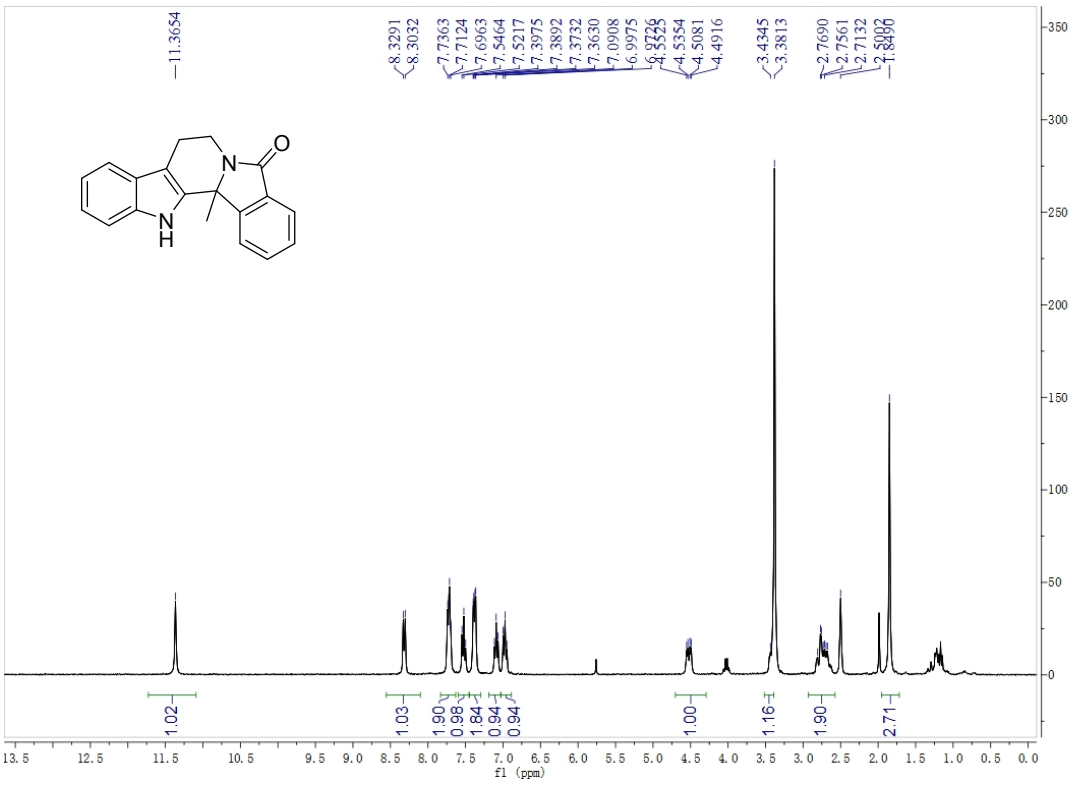
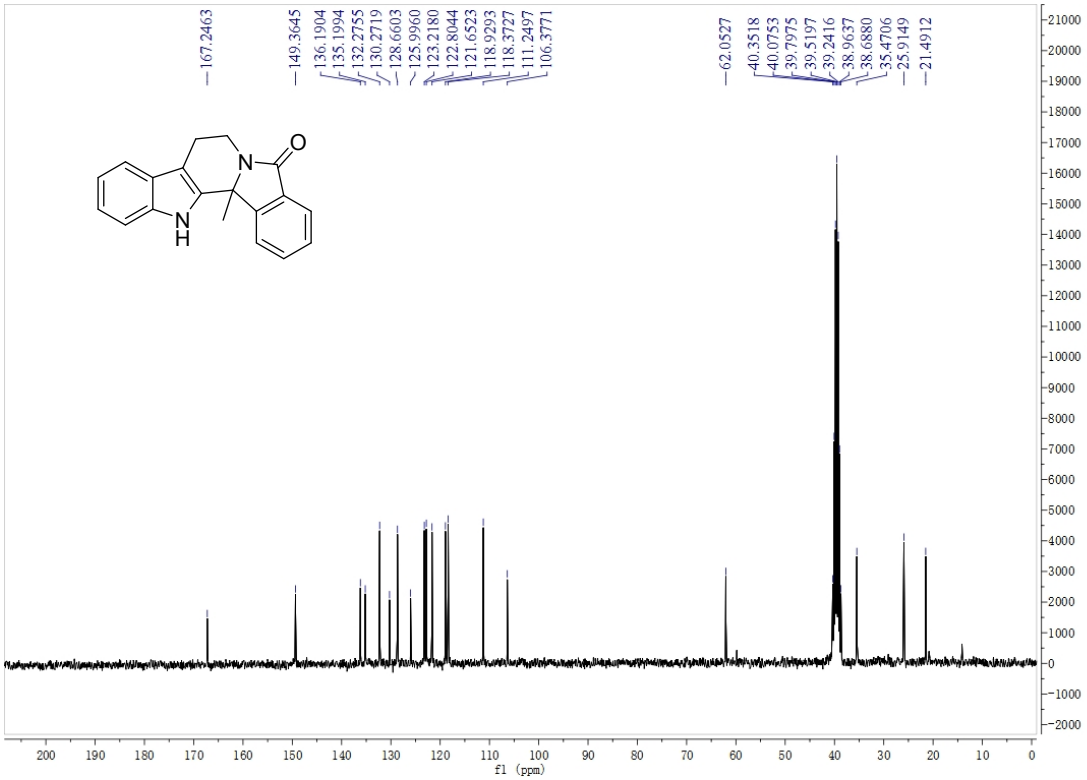


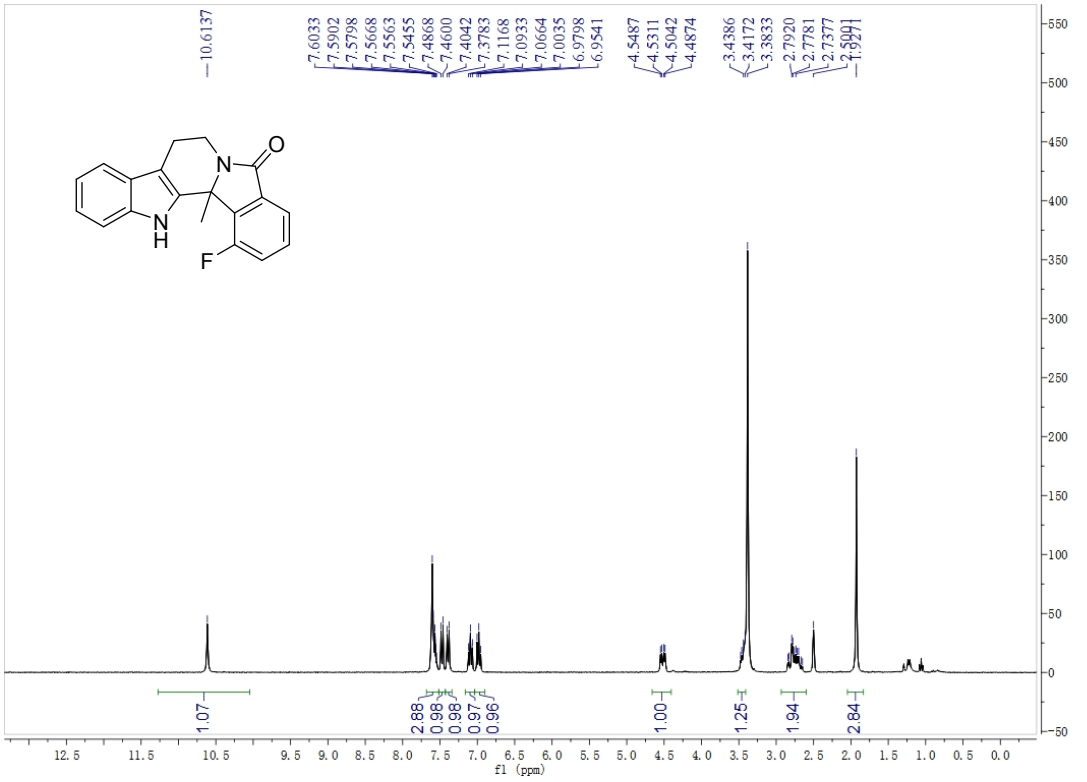


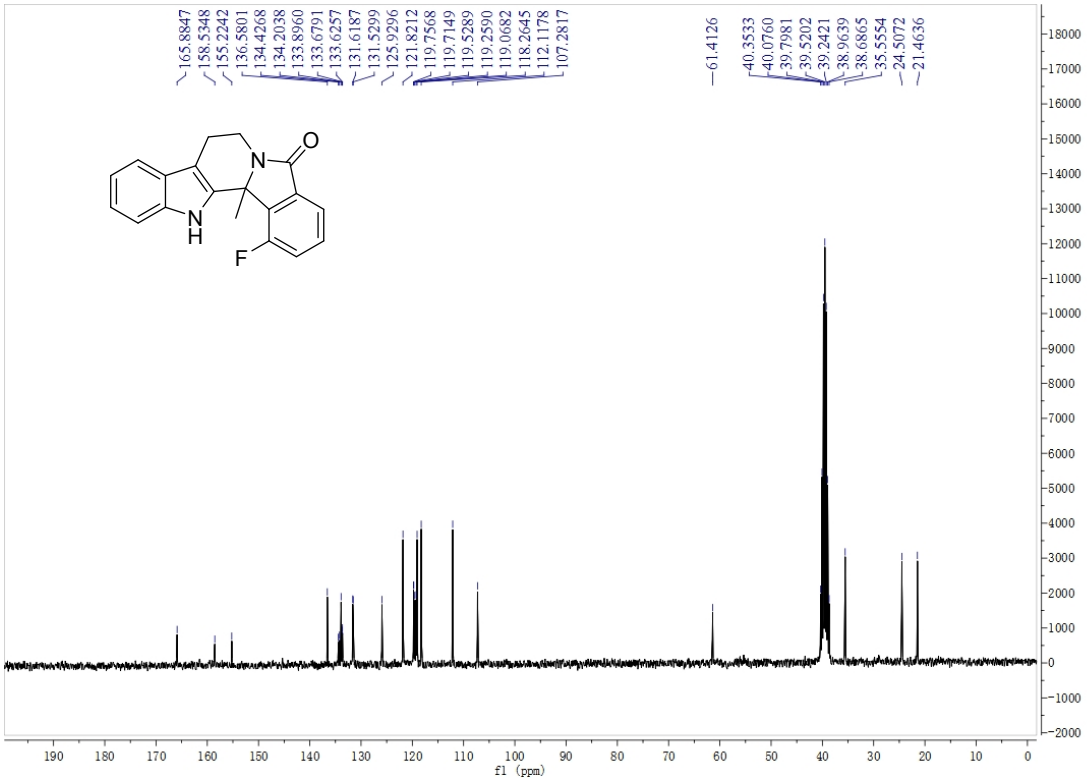
13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2a)



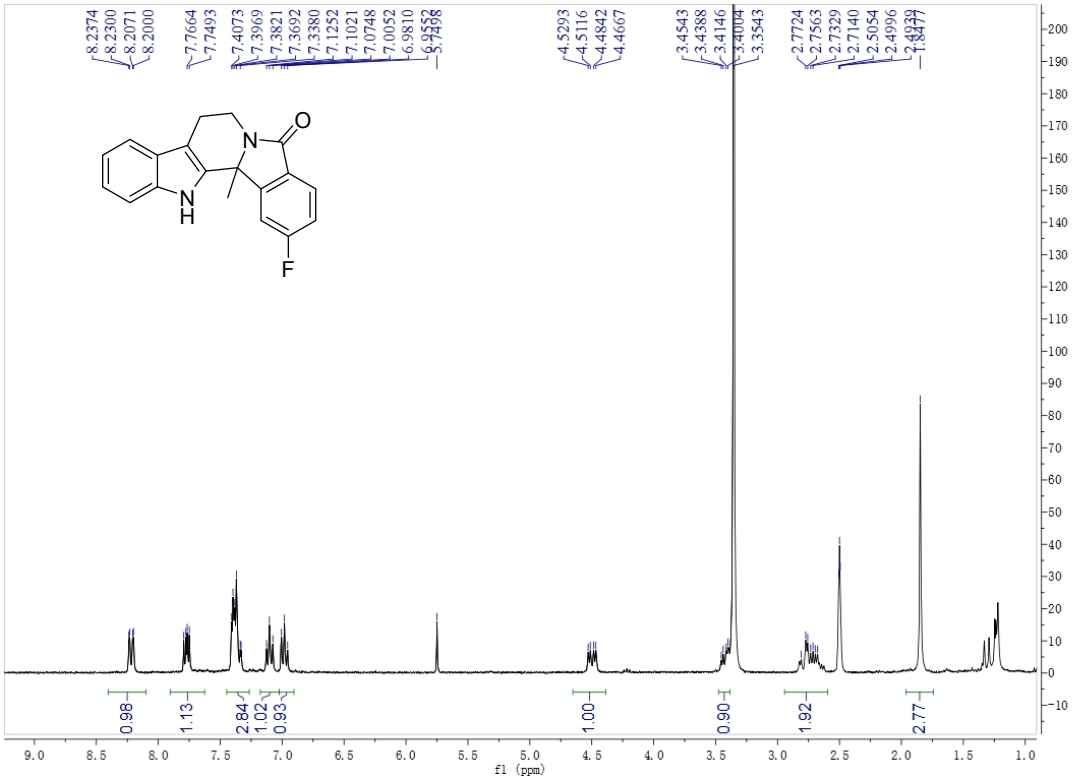


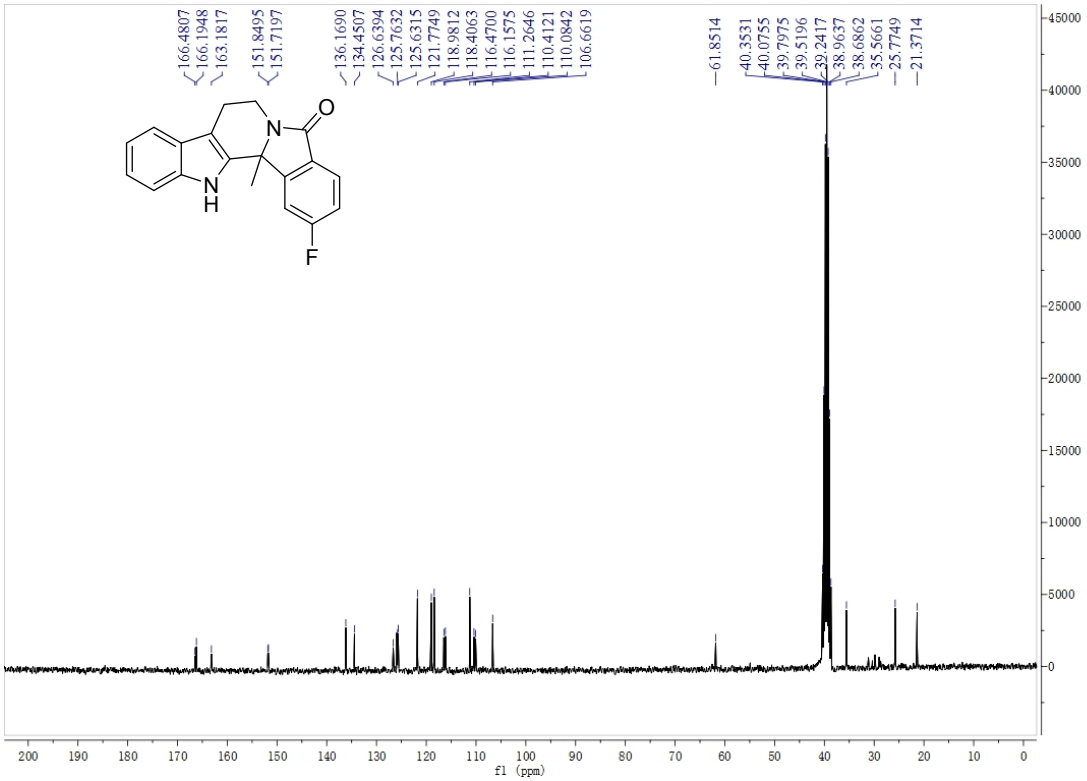
1-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2b)



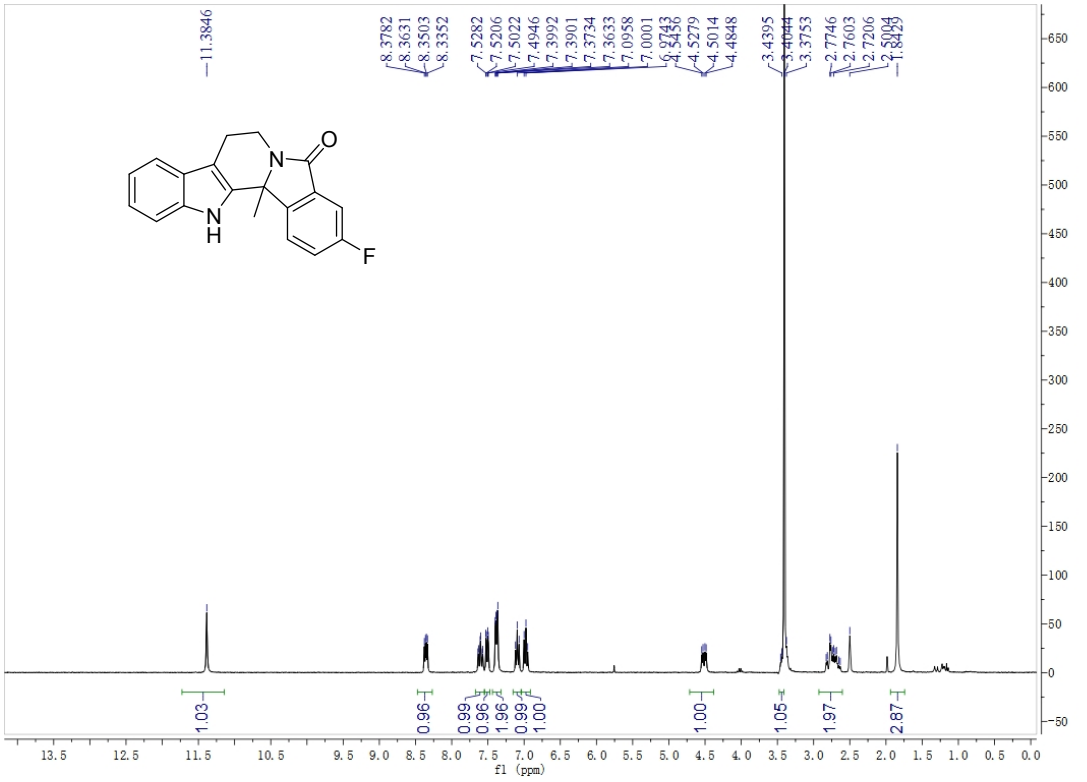


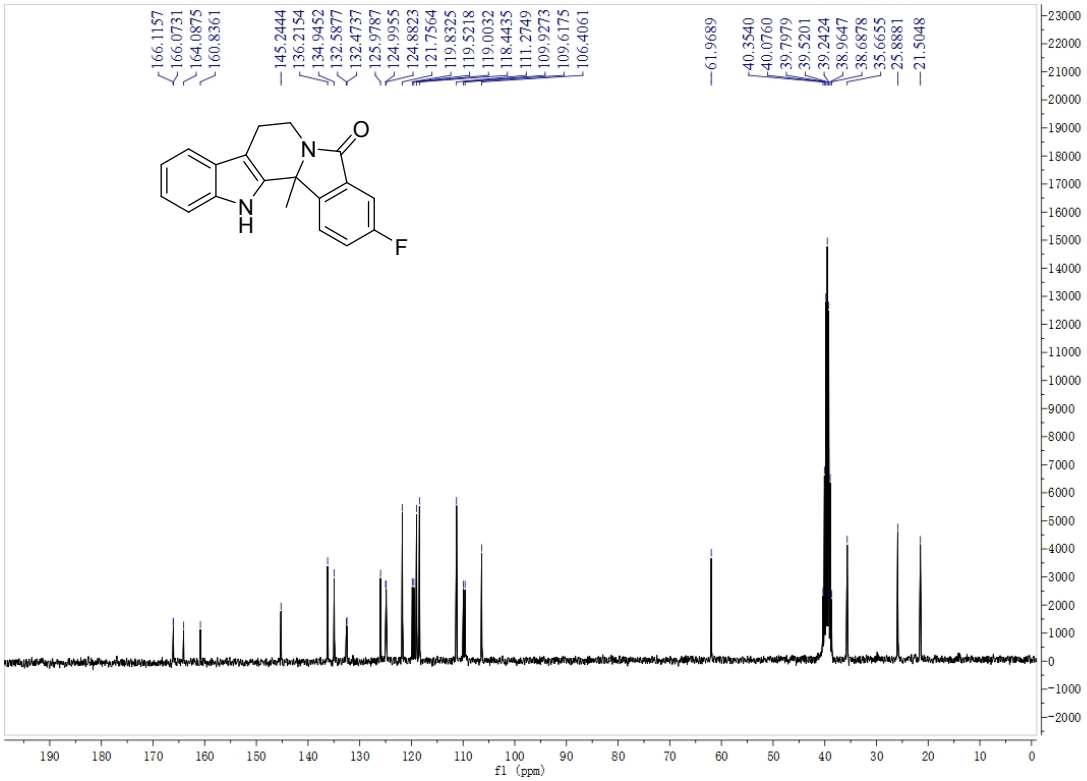
2-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2c)



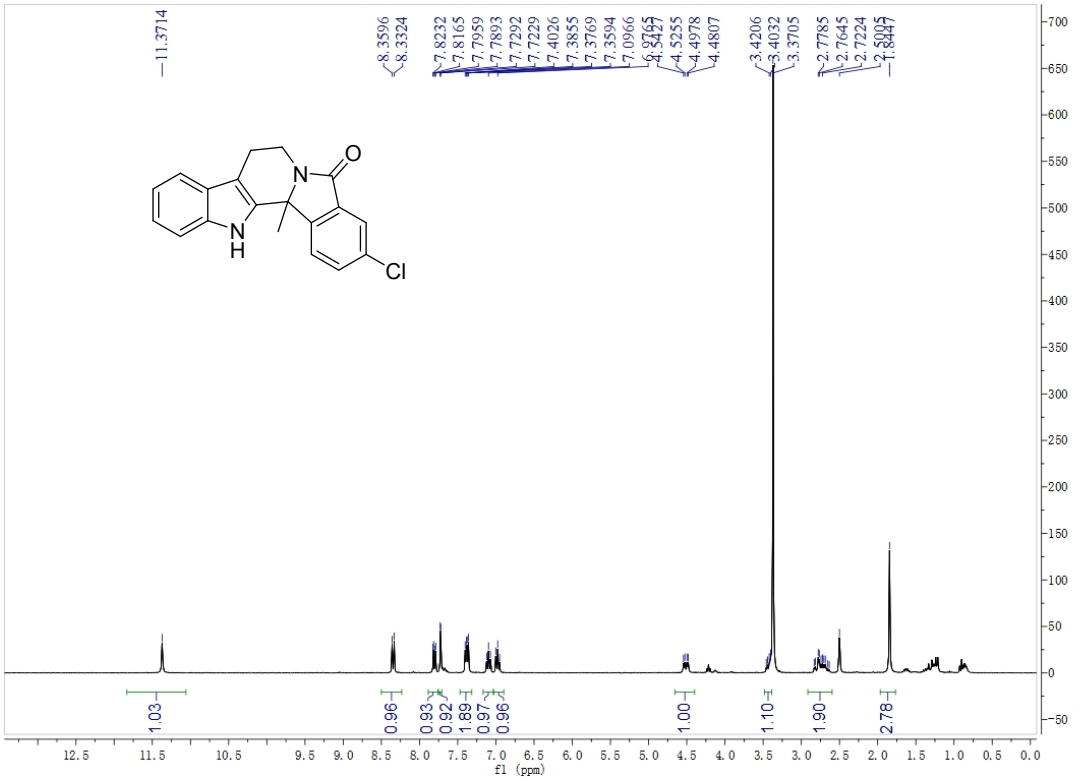


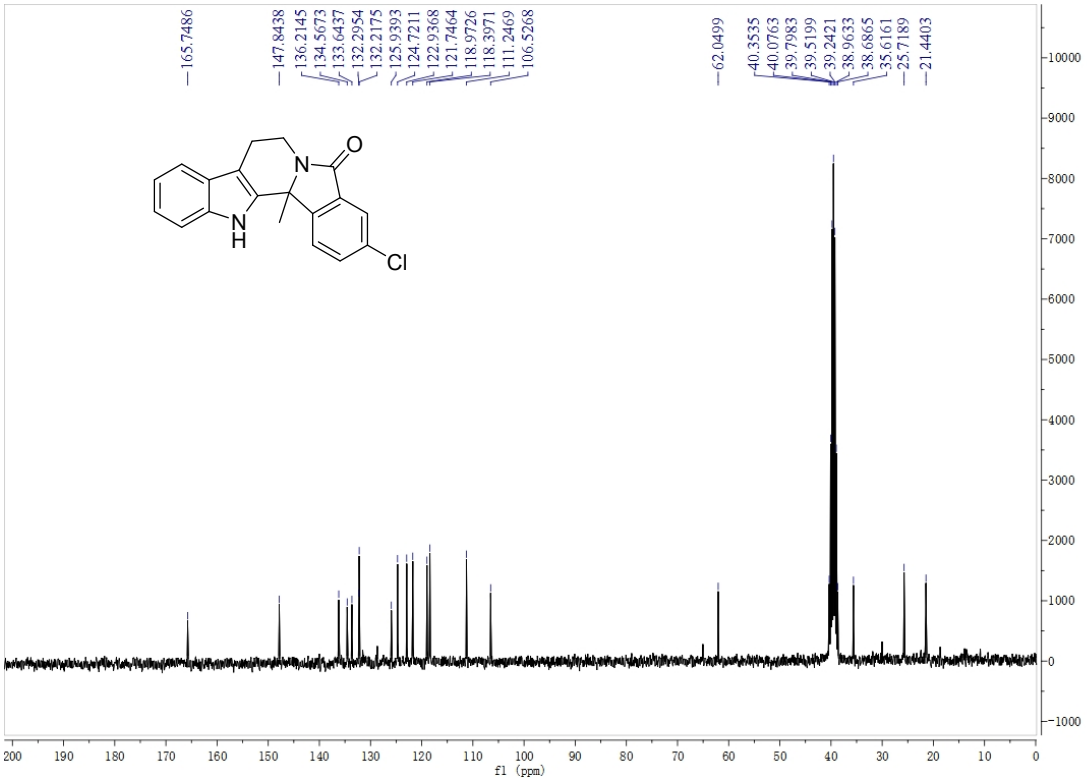
3-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2d)



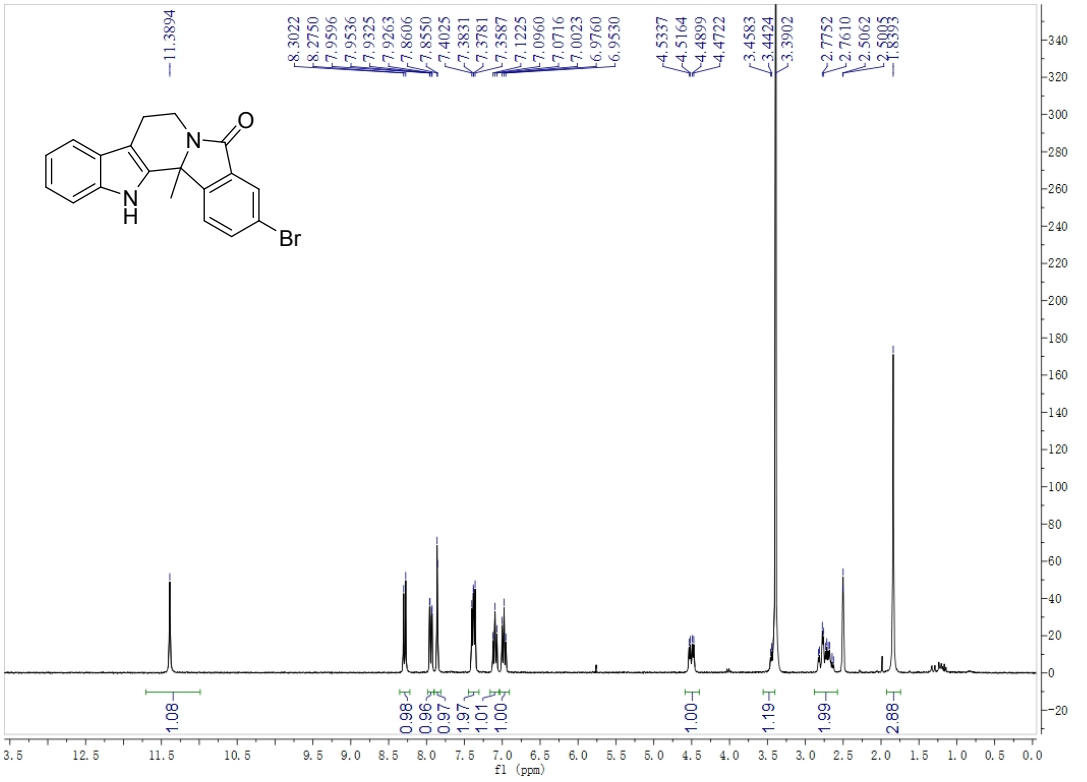


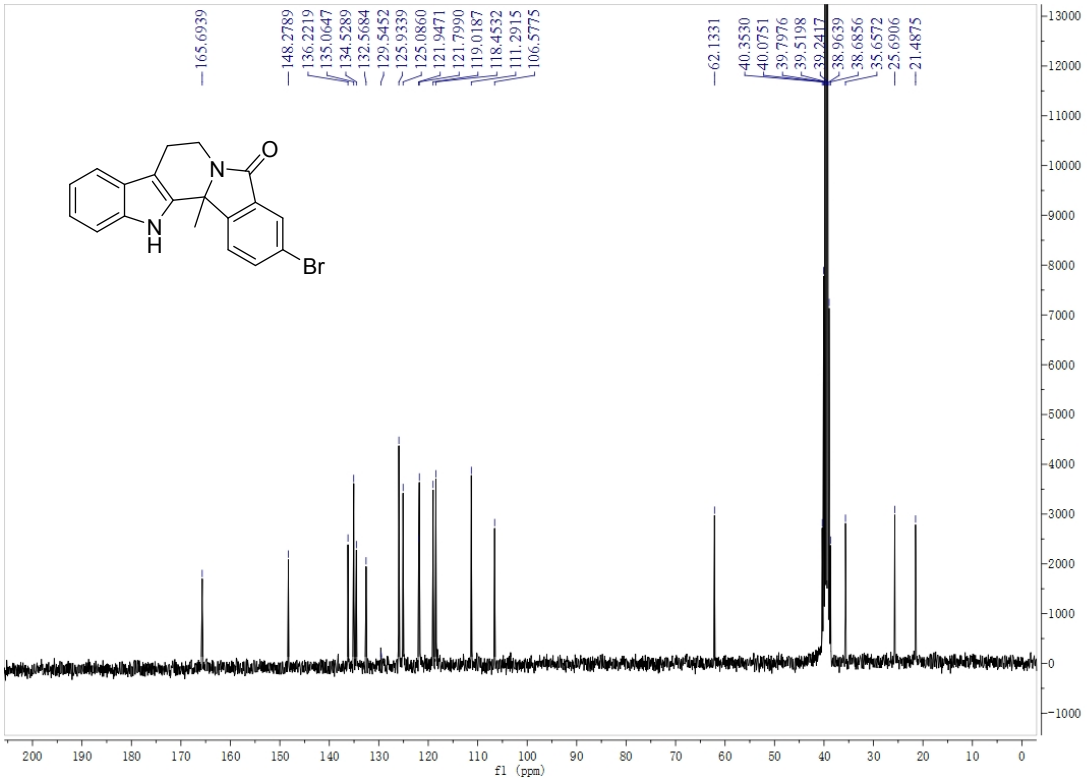
3-chloro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2e)



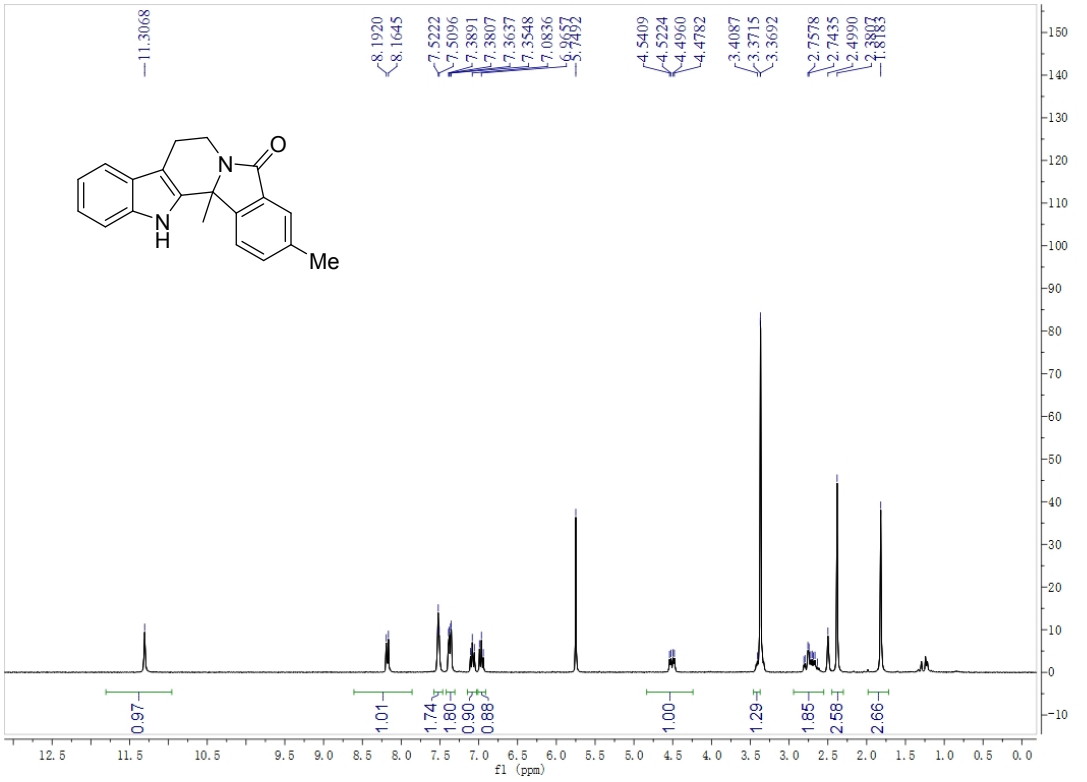


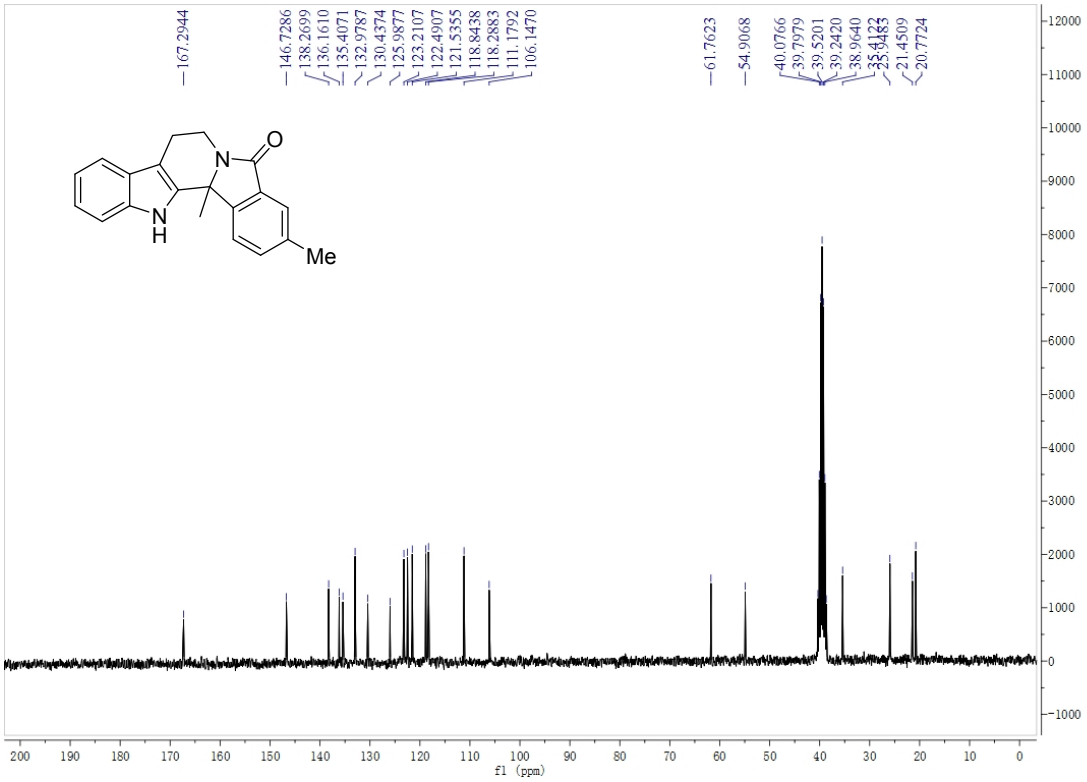
3-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2f)



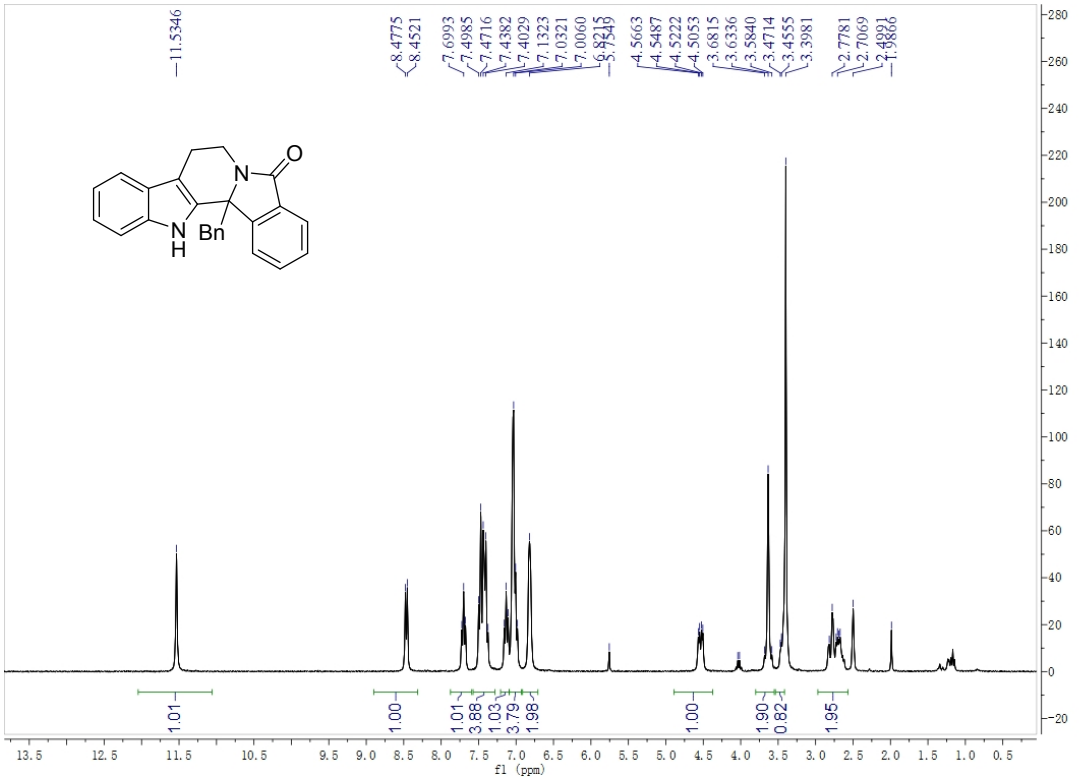


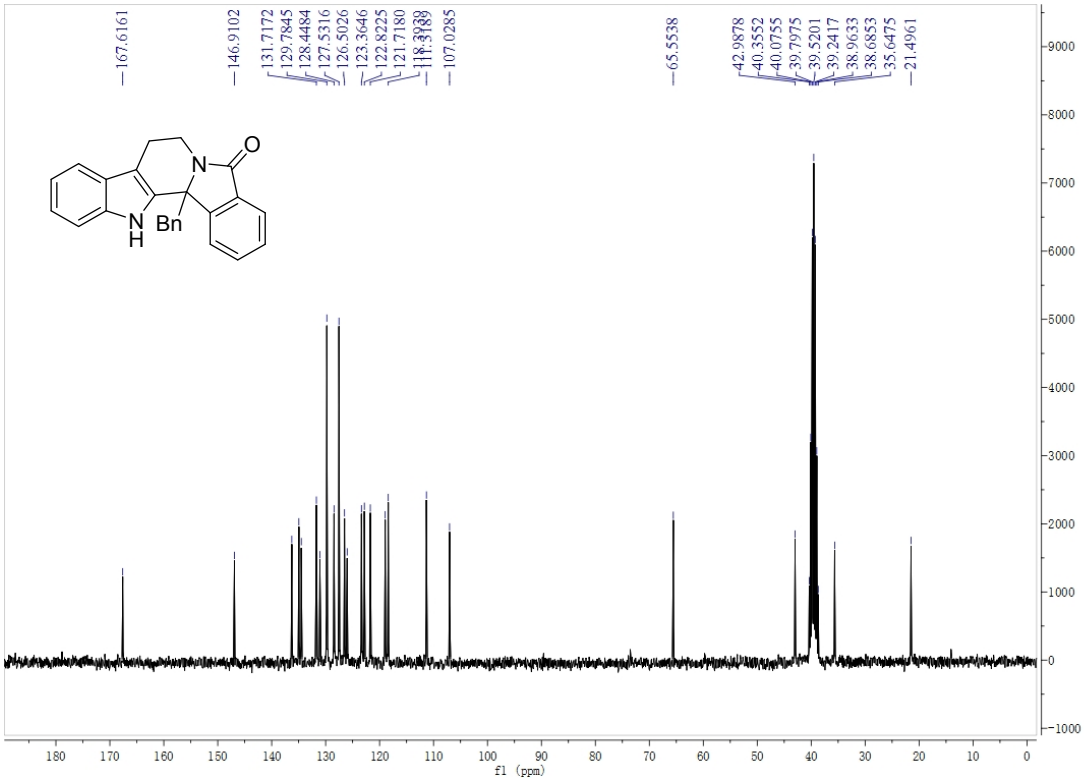
3,13b-dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2g)



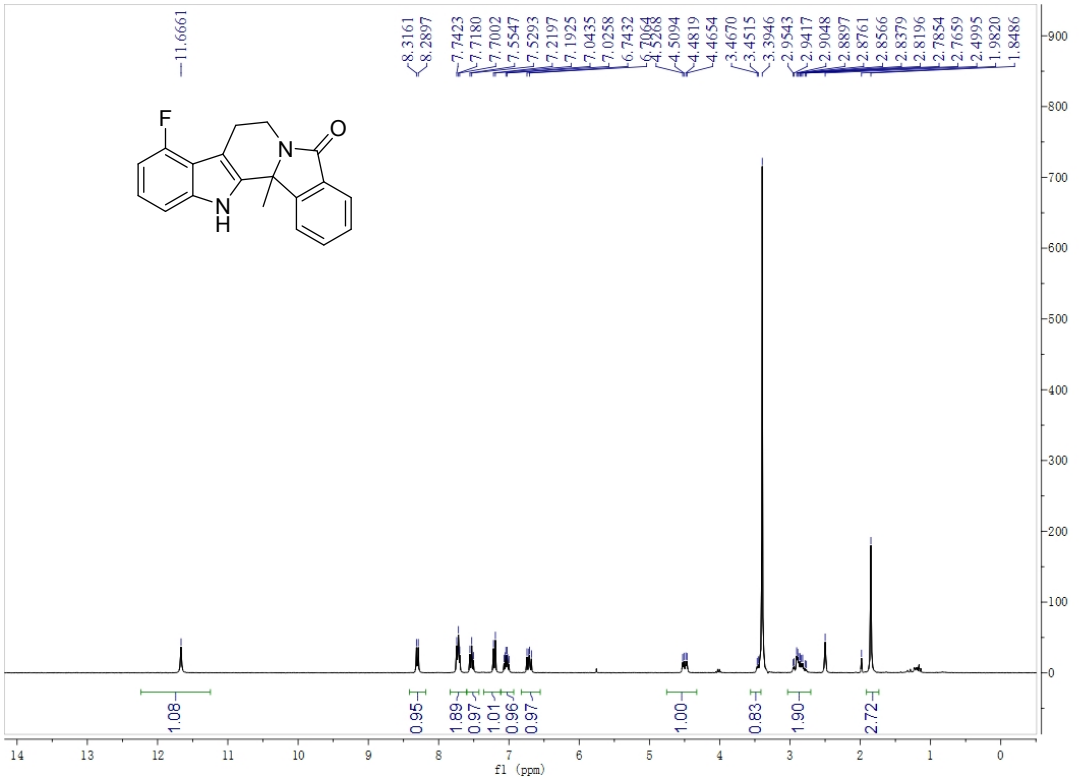


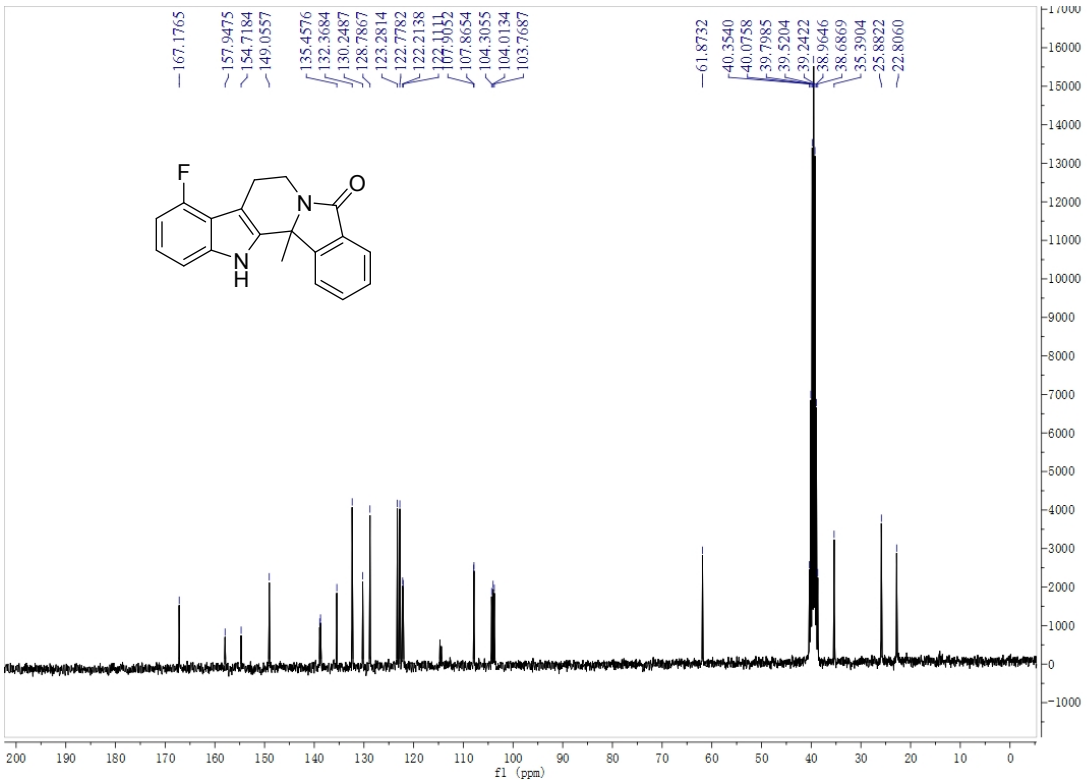
13b-benzyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2h)



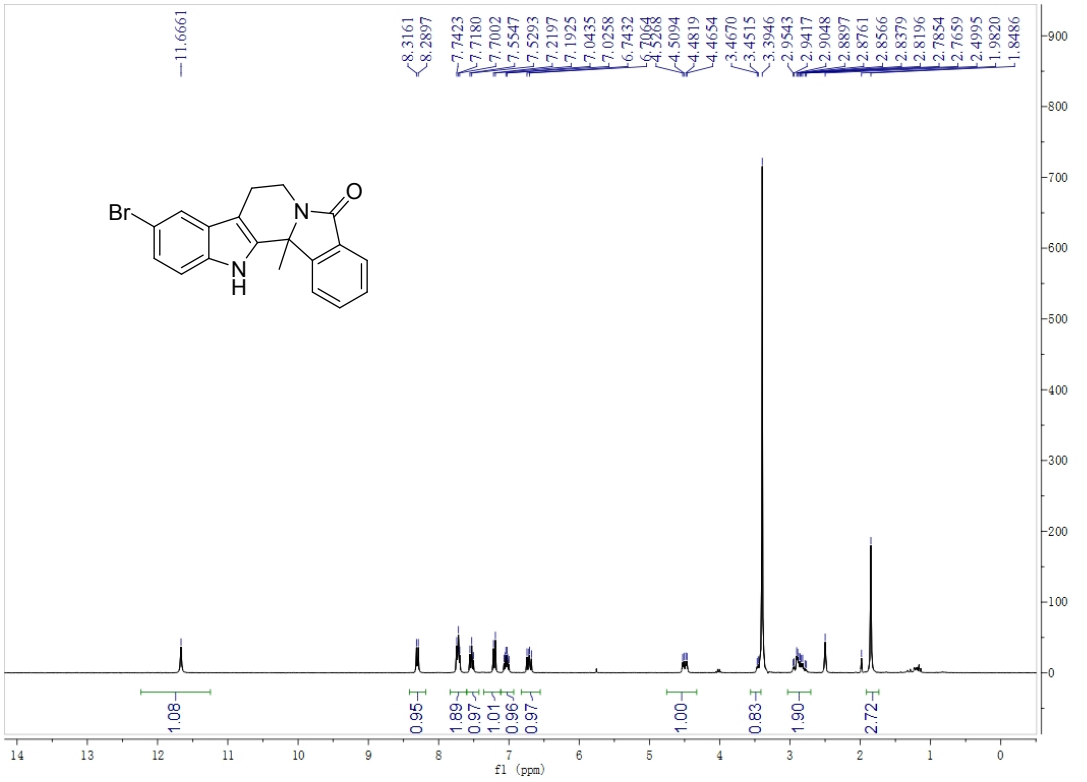


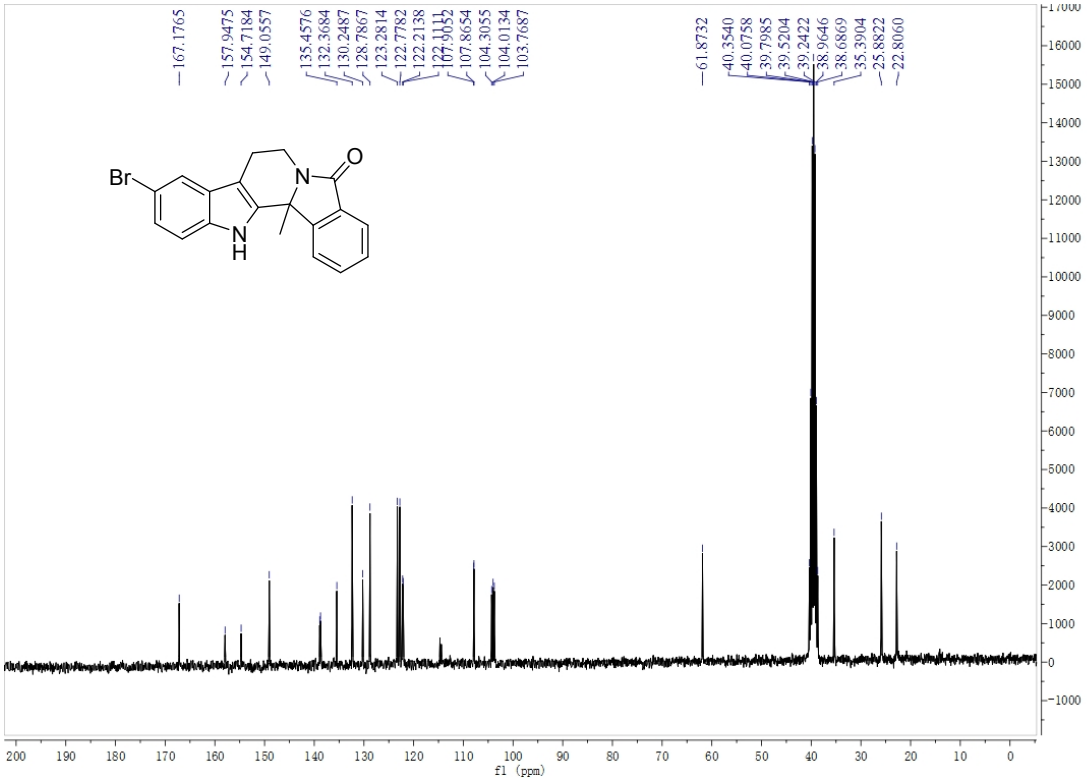
9-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2i)



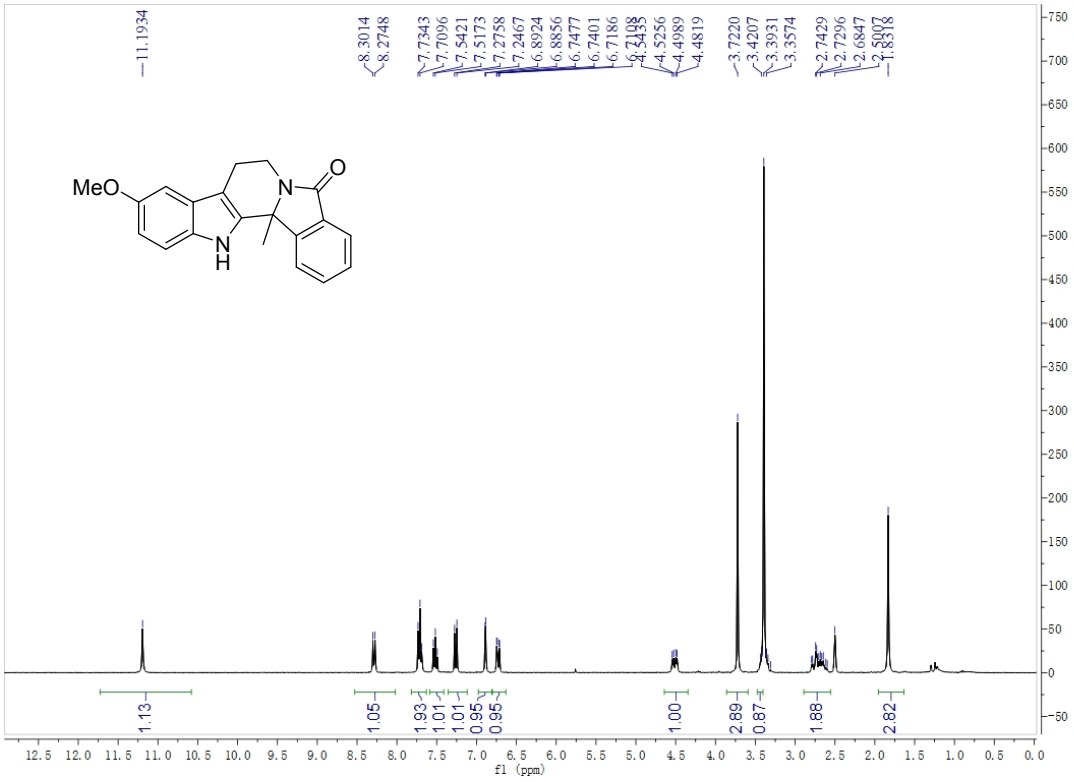


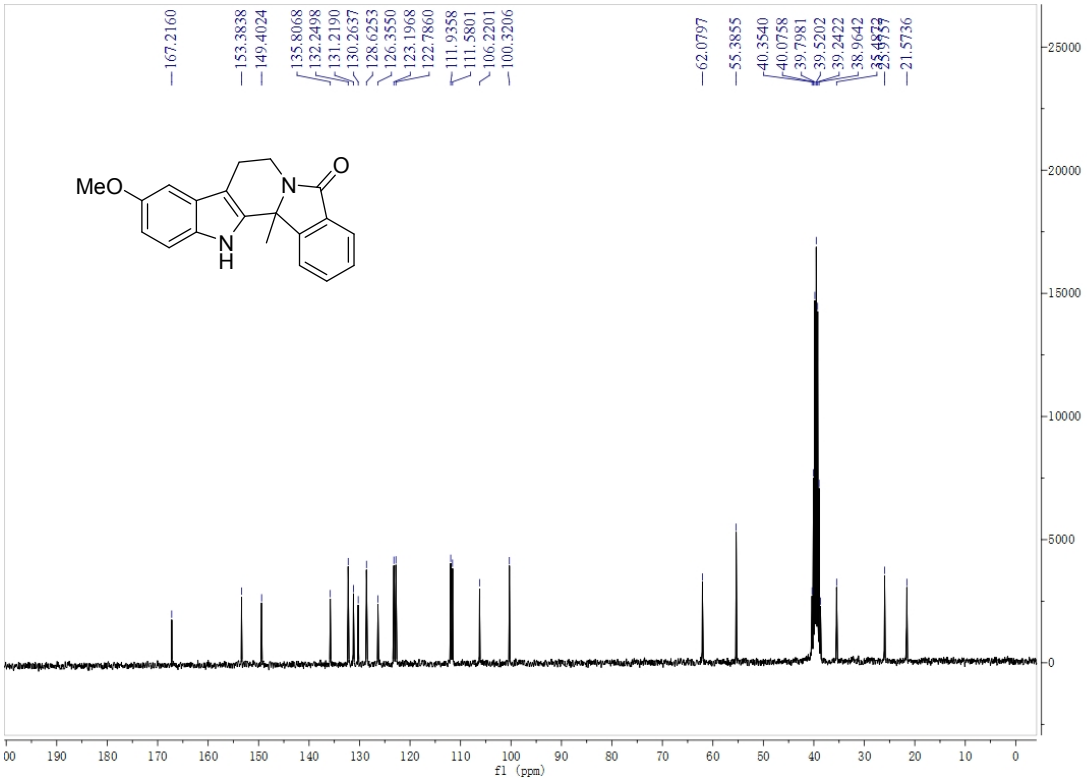
10-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2j)



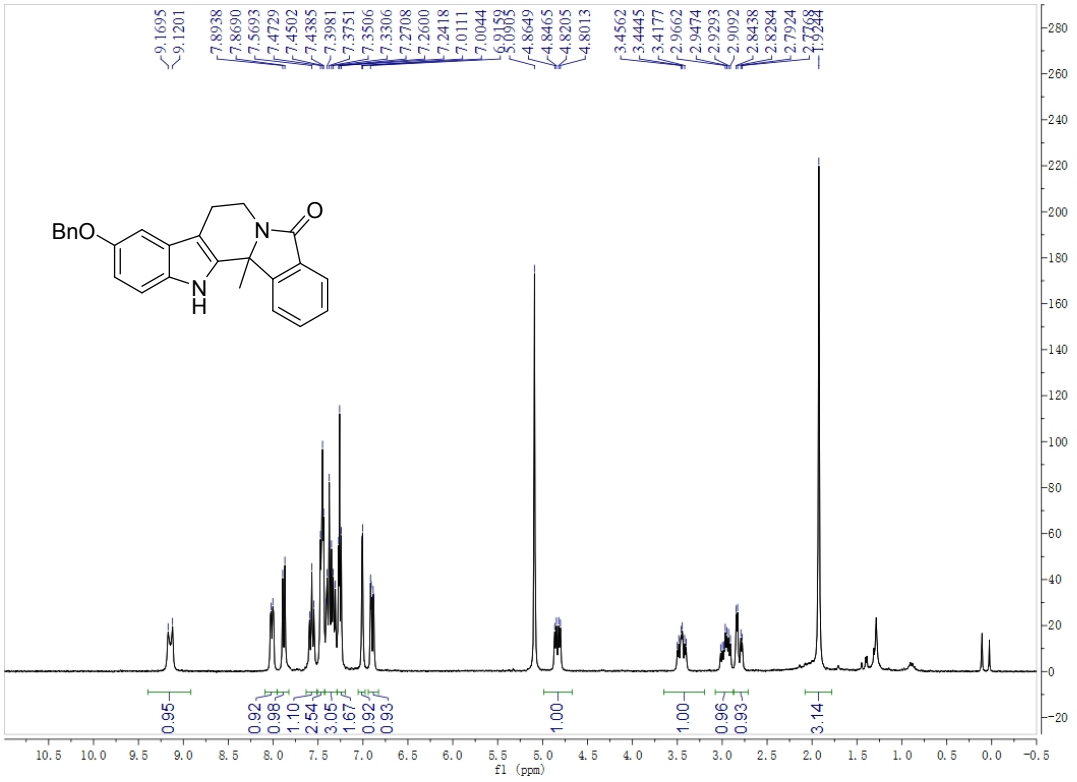


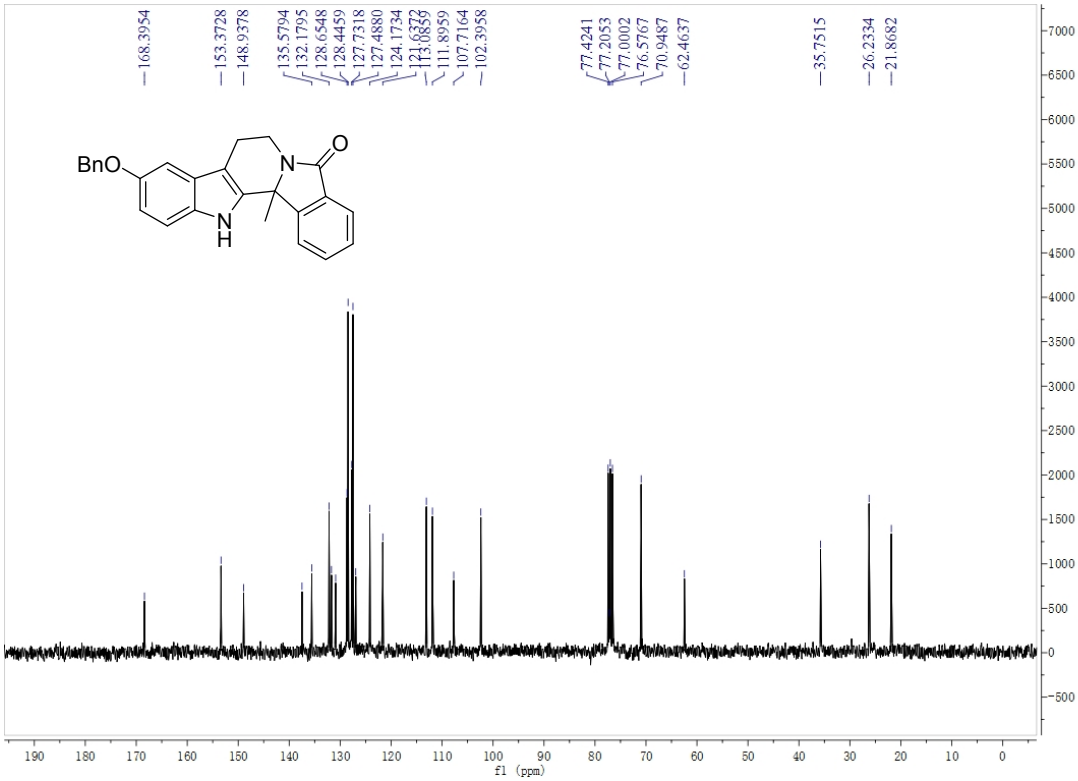
10-methoxy-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2k)



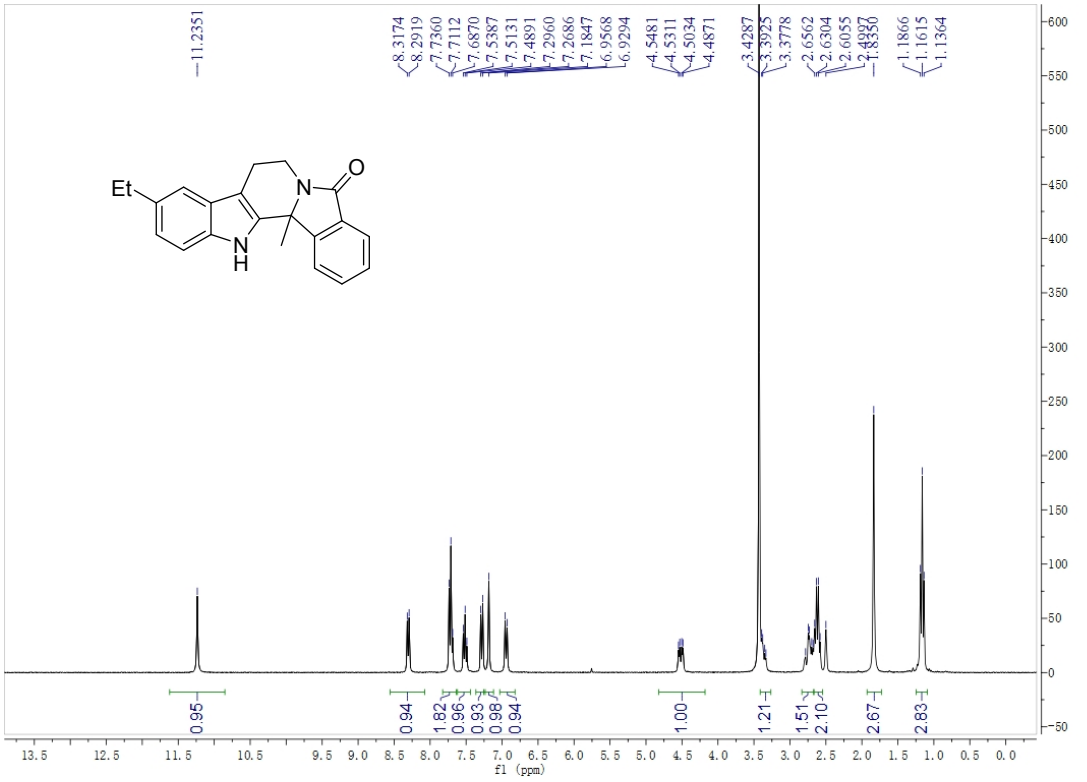


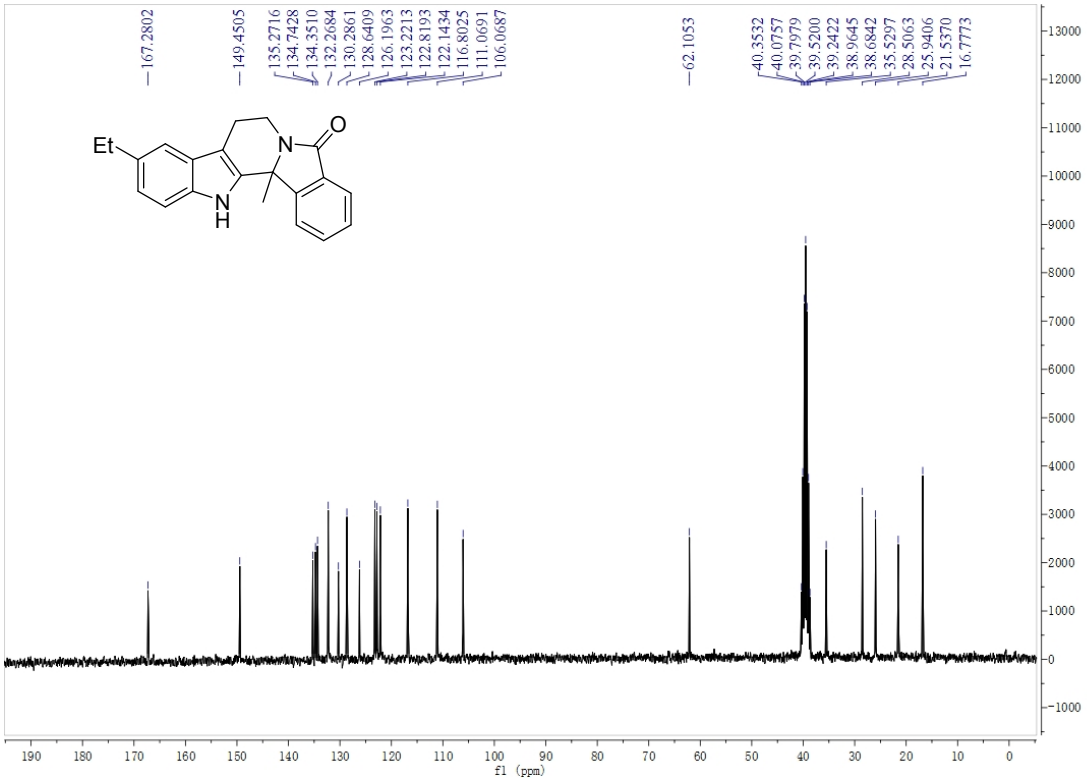
10-(benzyloxy)-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2l)



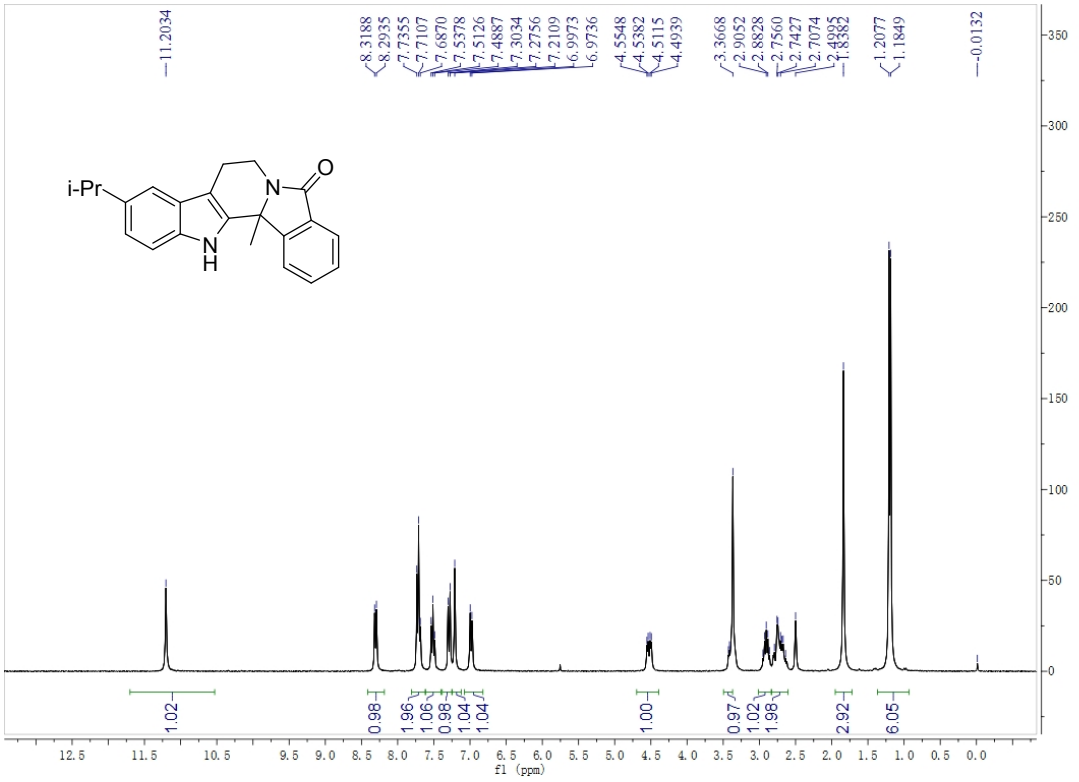


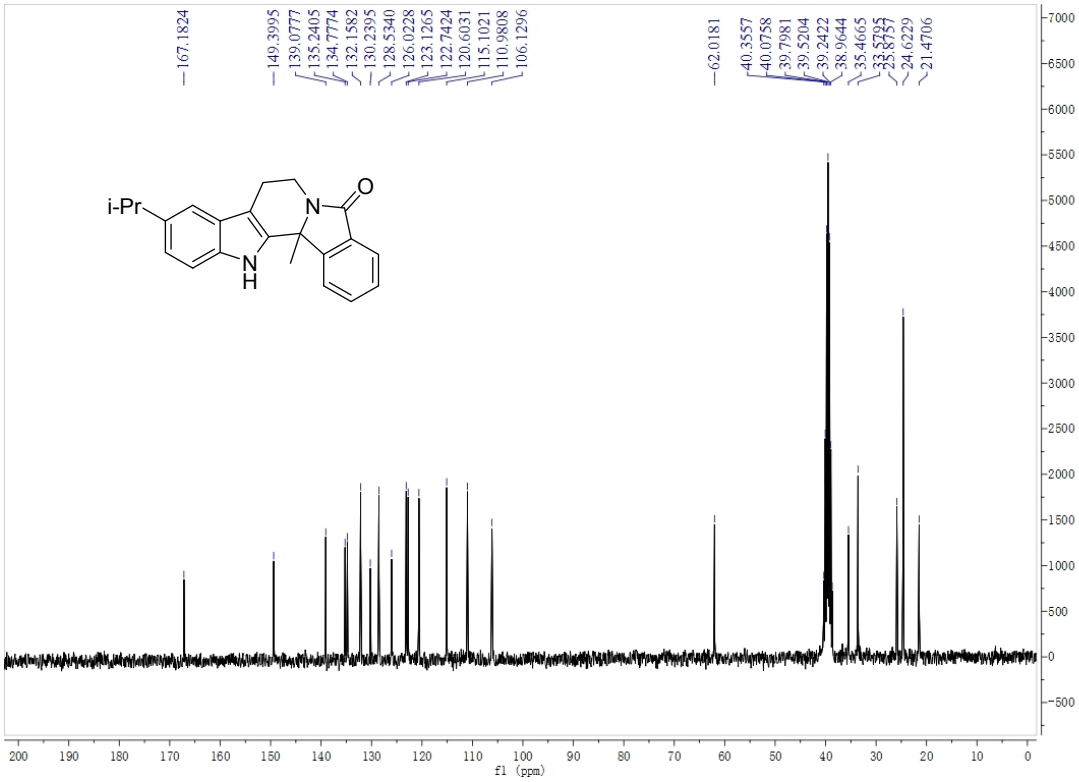
10-ethyl-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2m)



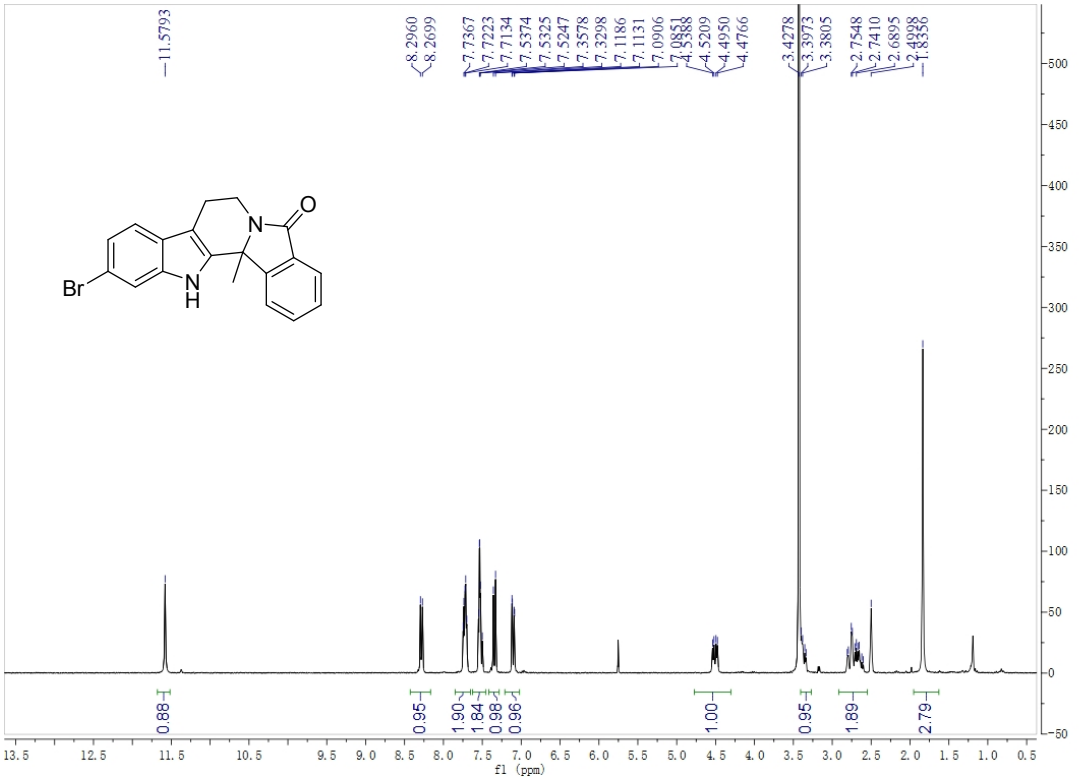


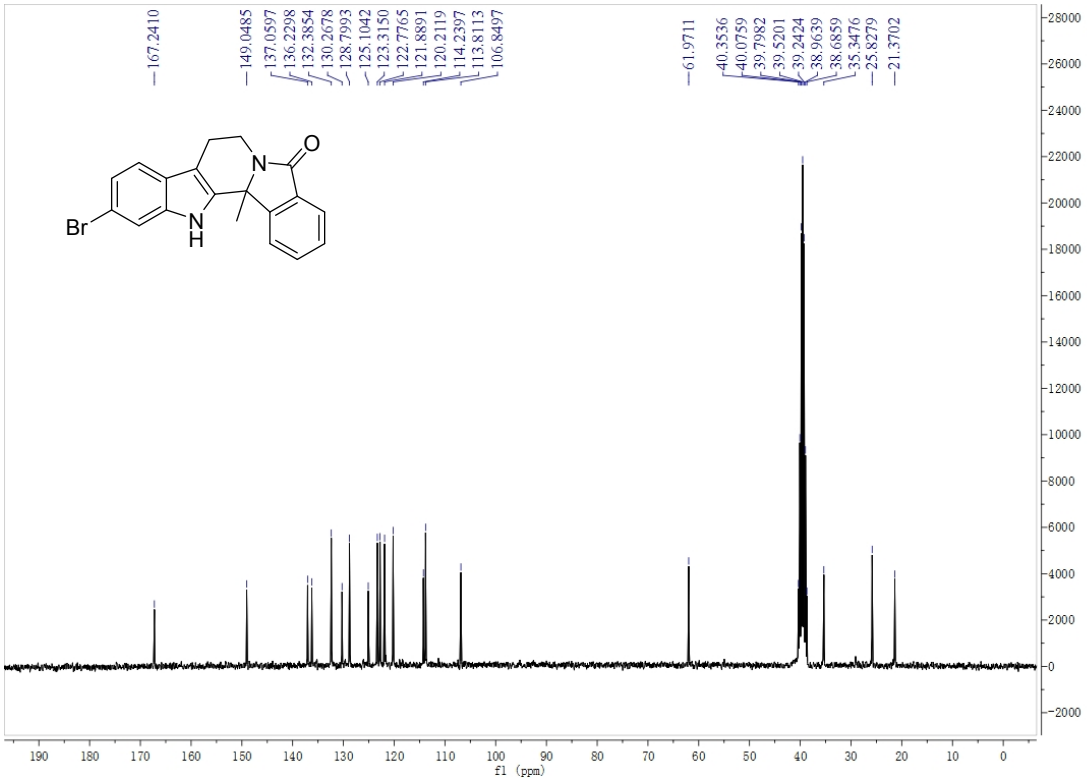
10-isopropyl-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2n)



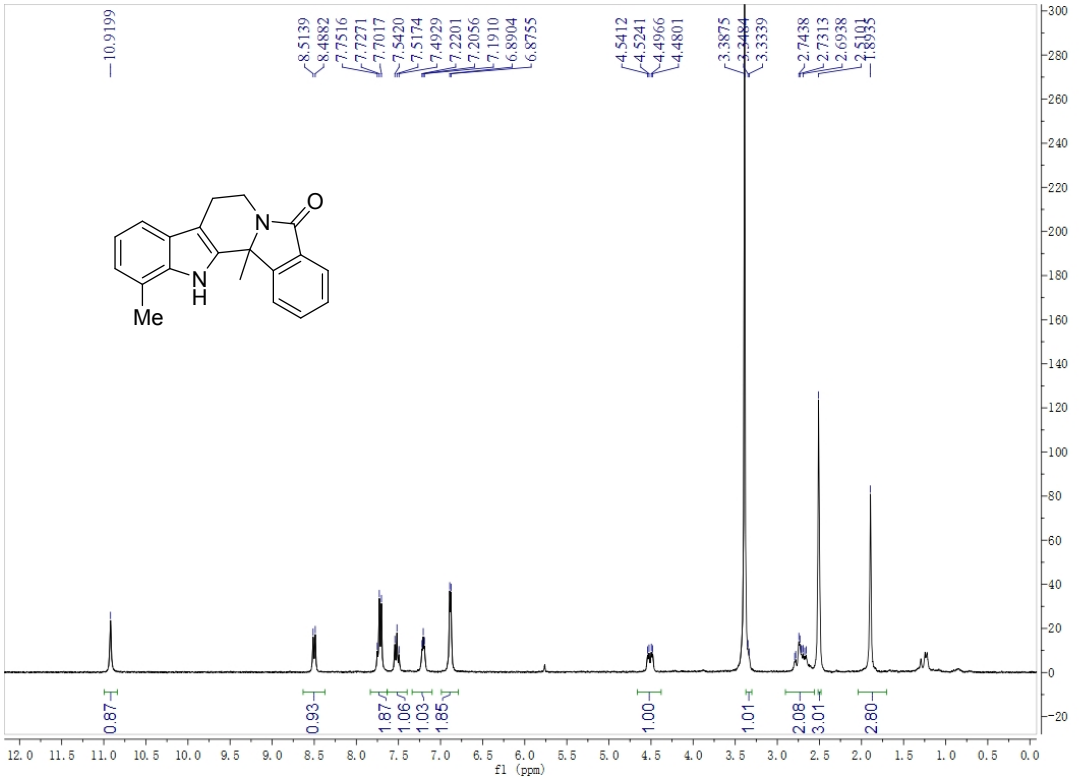


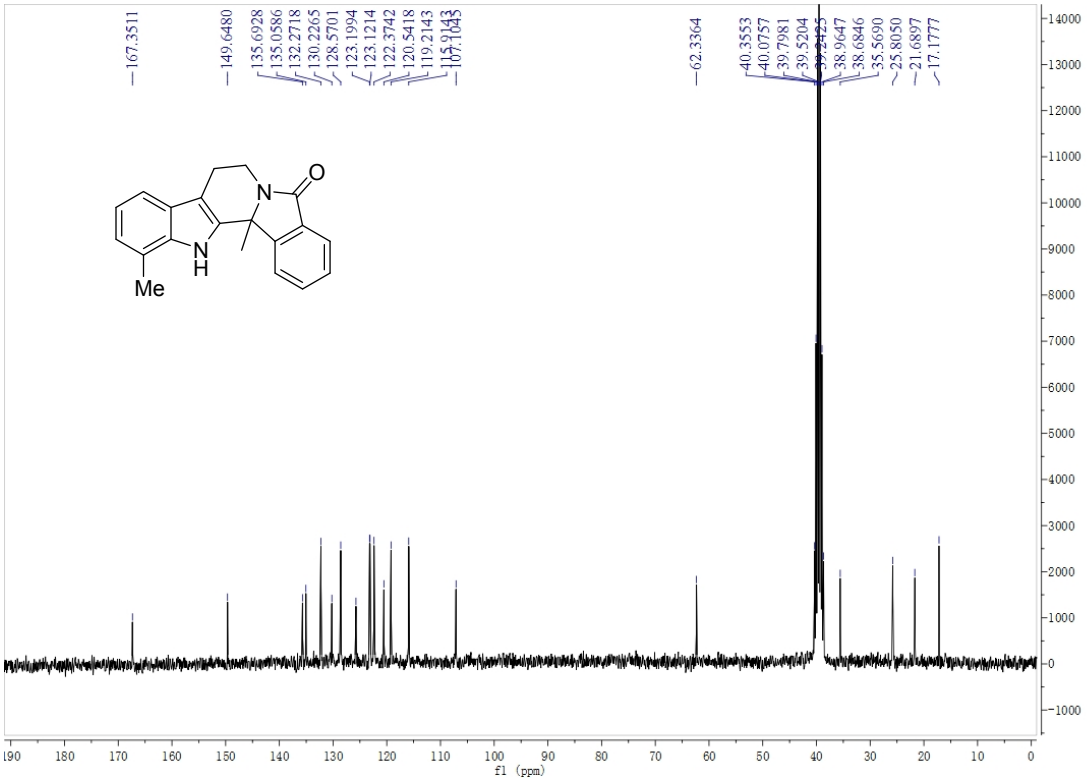
11-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2o)



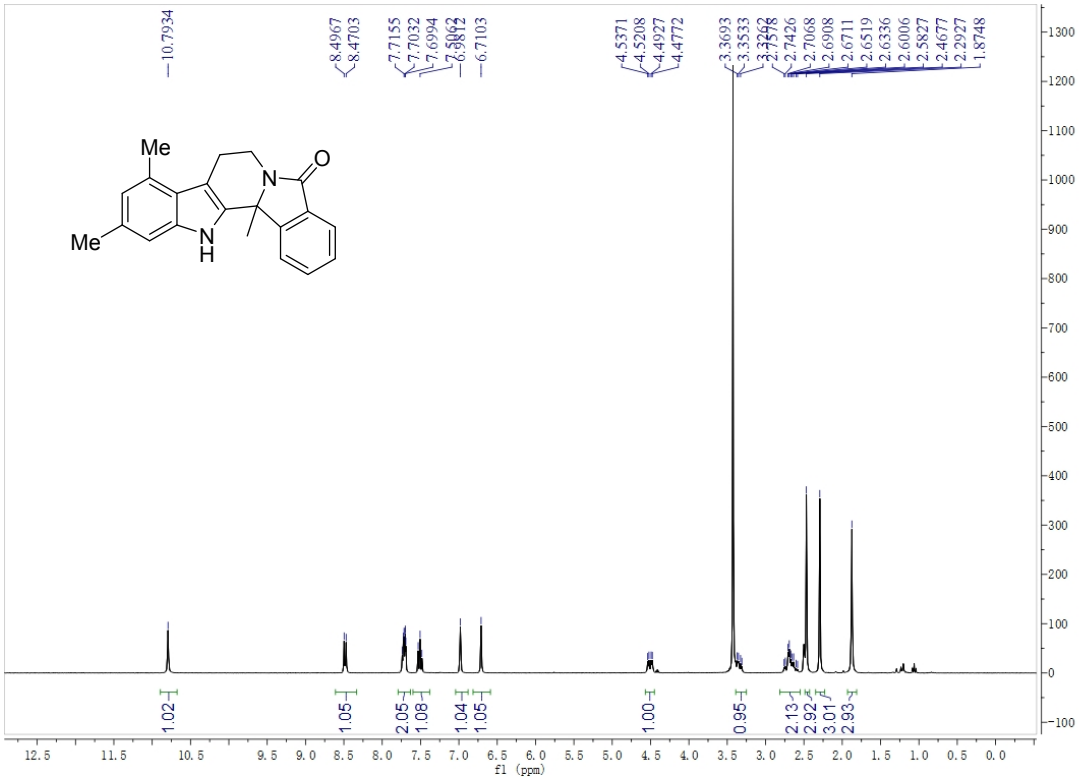


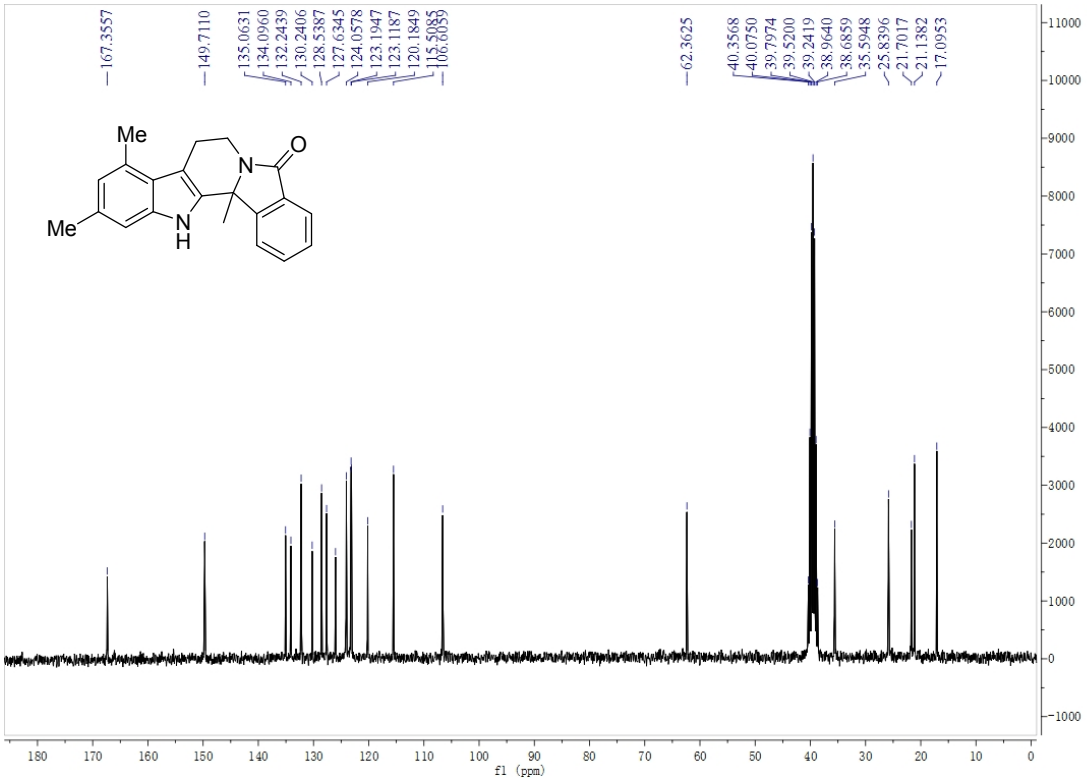
12,13b-dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2p)



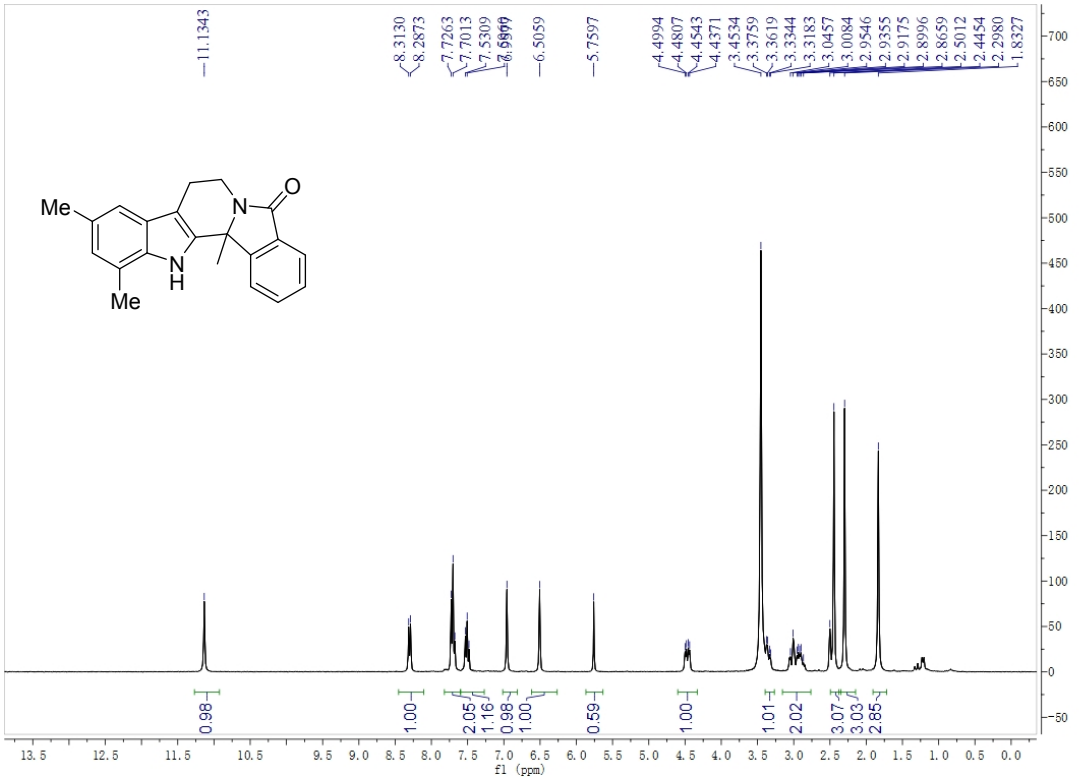


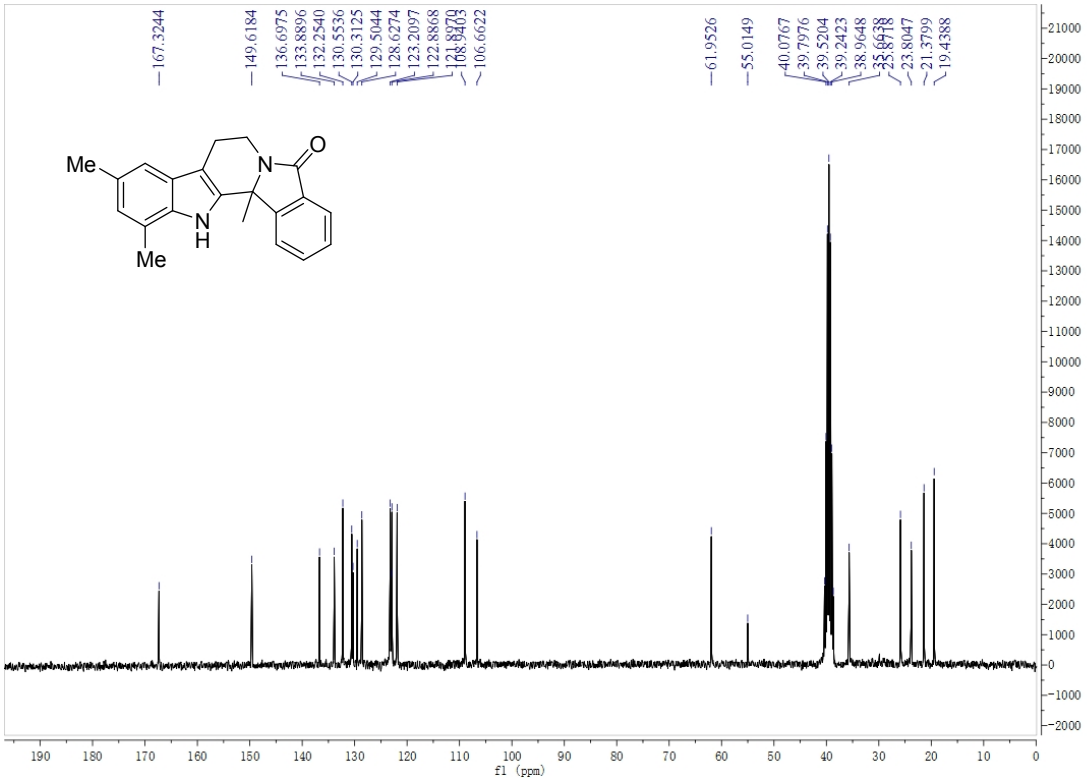
9,11,13b-trimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2q)



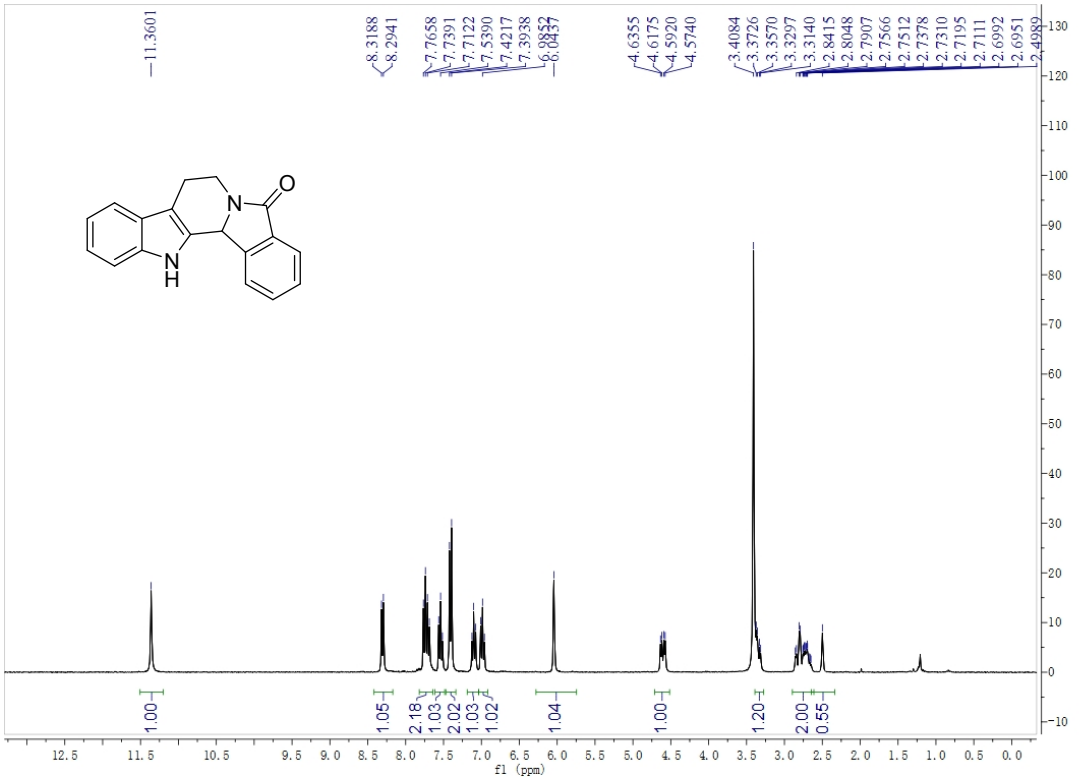


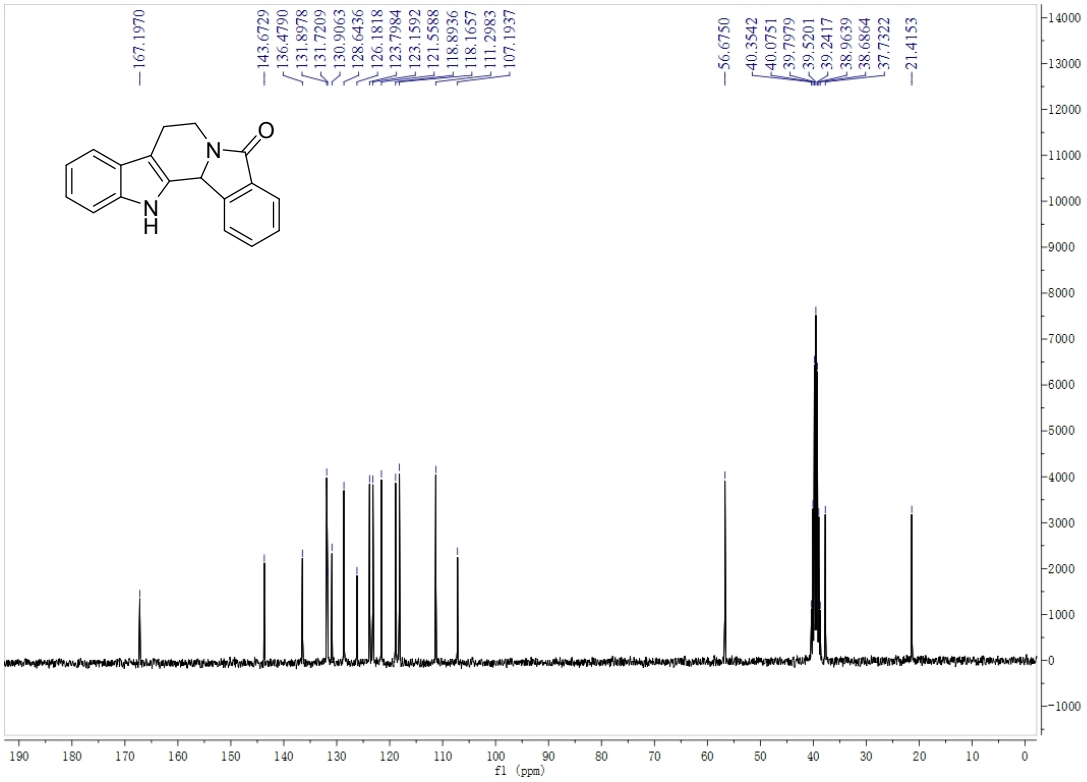
10,12,13b-trimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2r)



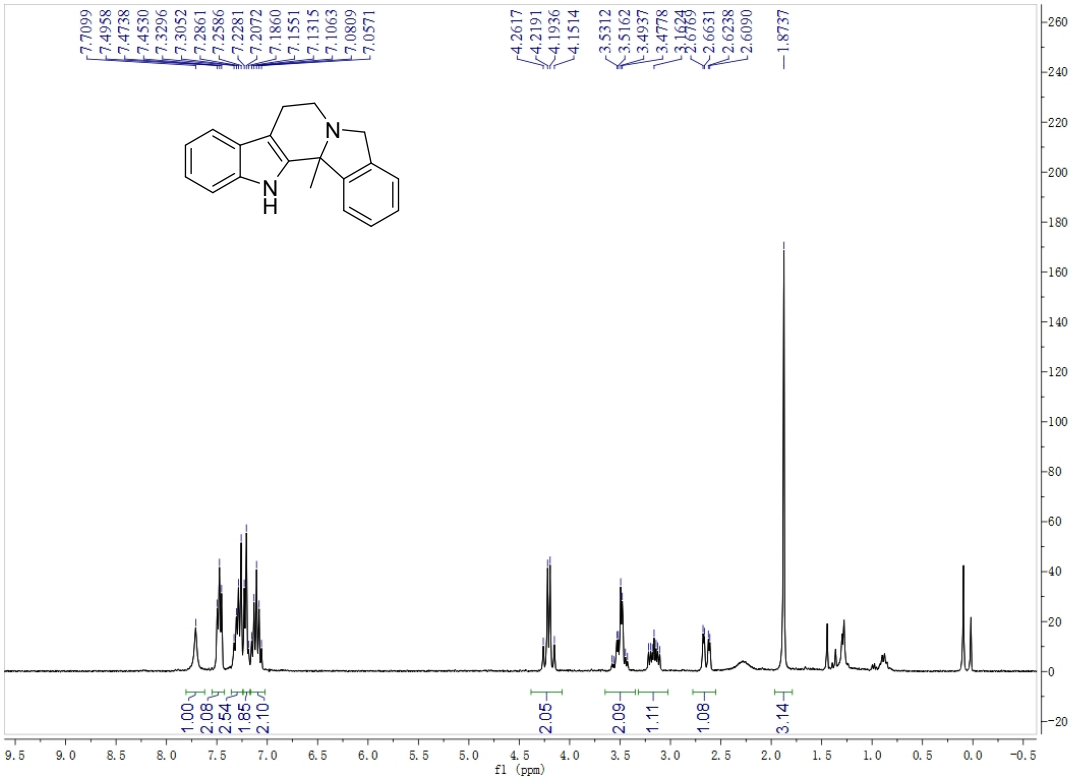


7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (6)



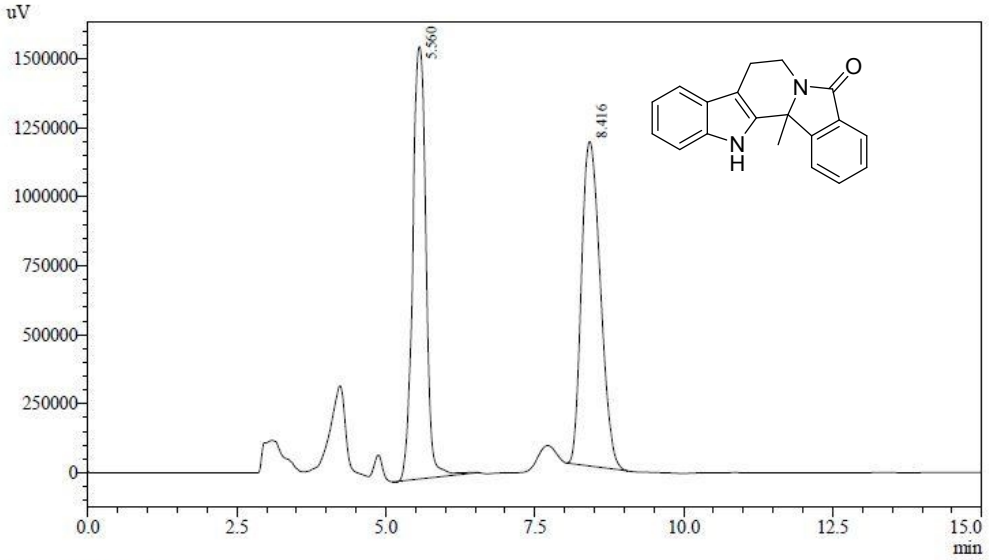


13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indole (7)



4. HPLC Charts of Products

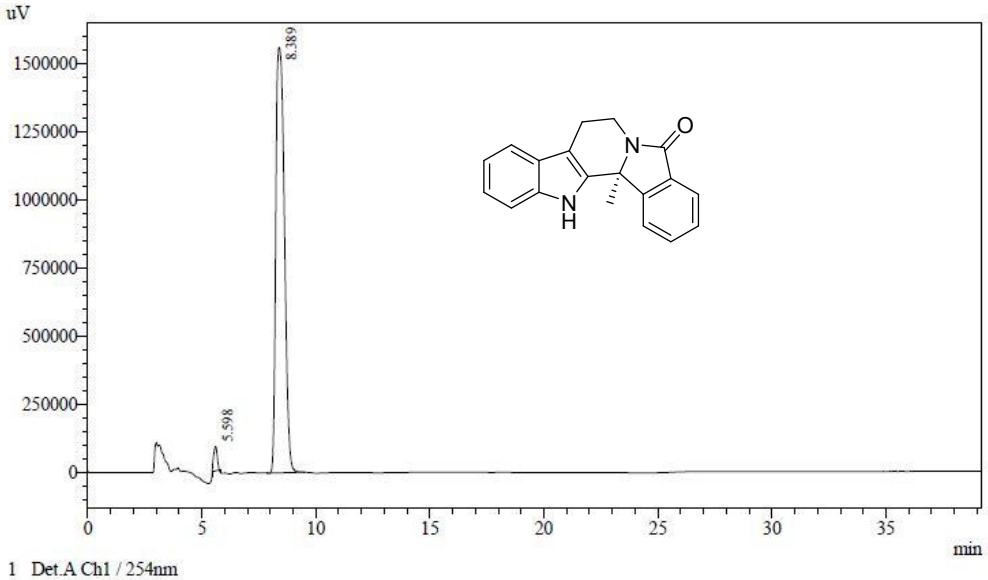
13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2a)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.560	24177498	1567495	48.196	57.129
2	8.416	25987262	1176264	51.804	42.871
Total		50164760	2743759	100.000	100.000

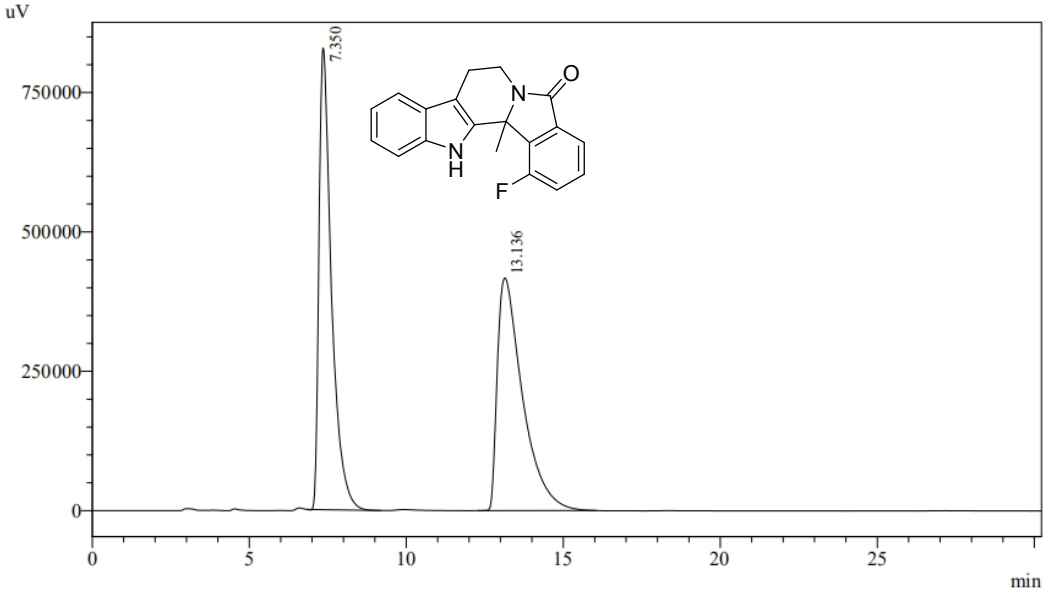


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.598	938910	90502	2.250	5.478
2	8.389	40799515	1561669	97.750	94.522
Total		41738425	1652171	100.000	100.000

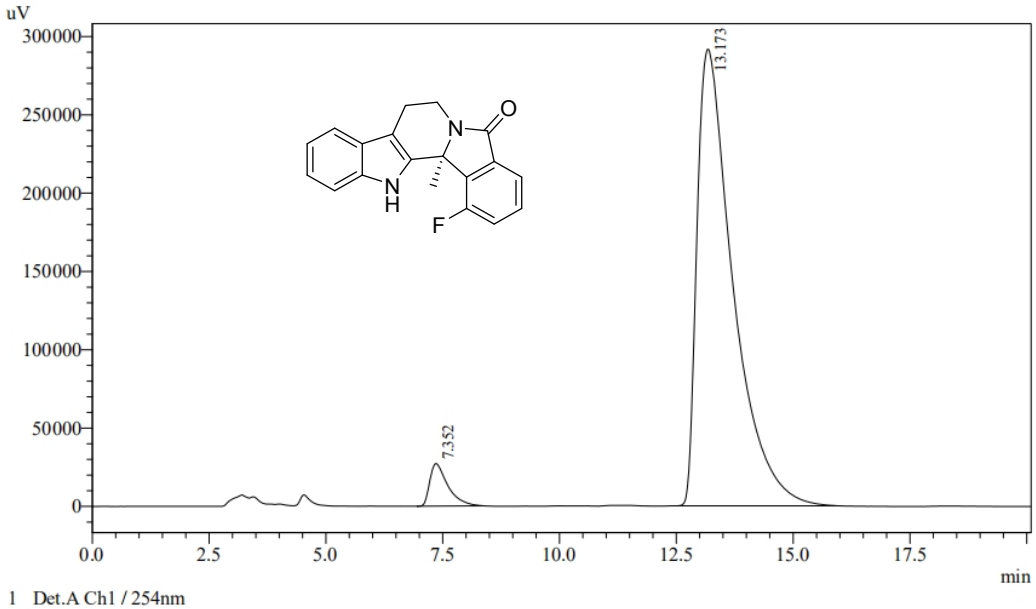
1-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2b)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.350	22916024	827928	49.627	66.489
2	13.136	23260381	417289	50.373	33.511
Total		46176405	1245217	100.000	100.000

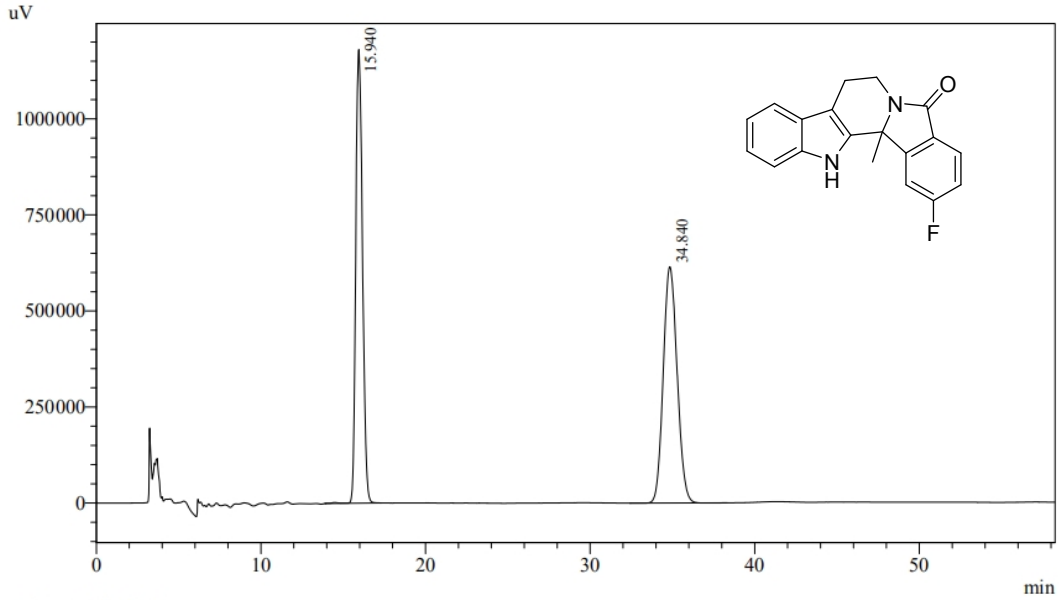


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.352	729044	27168	4.468	8.523
2	13.173	15589479	291594	95.532	91.477
Total		16318523	318762	100.000	100.000

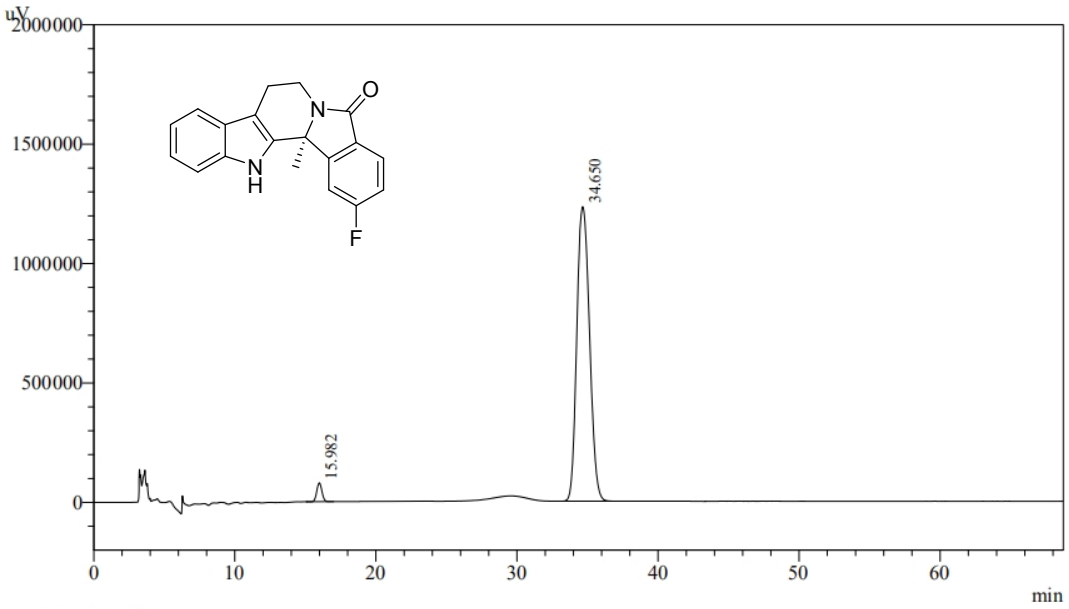
2-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2c)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.940	33633687	1180575	48.311	65.754
2	34.840	35985361	614858	51.689	34.246
Total		69619048	1795433	100.000	100.000

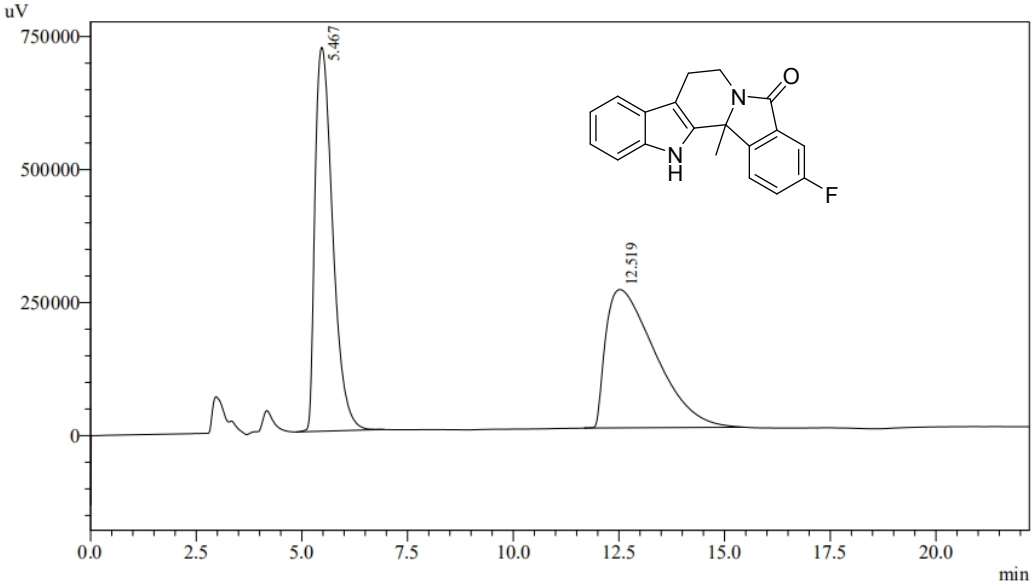


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.982	1988969	78609	2.507	5.991
2	34.650	77362903	1233428	97.493	94.009
Total		79351873	1312038	100.000	100.000

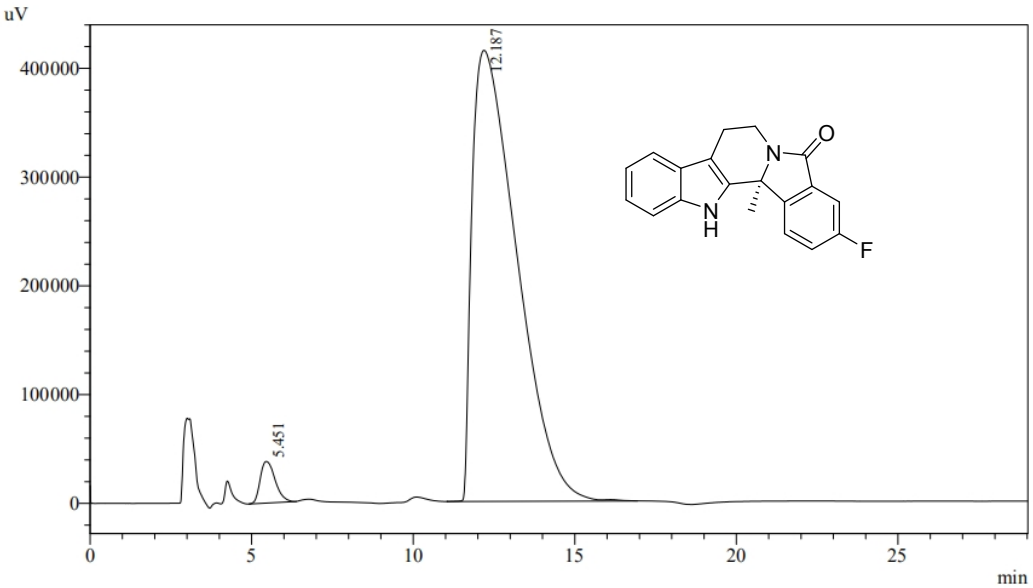
3-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2d)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.467	21045868	721507	49.850	73.510
2	12.519	21172479	259997	50.150	26.490
Total		42218346	981504	100.000	100.000

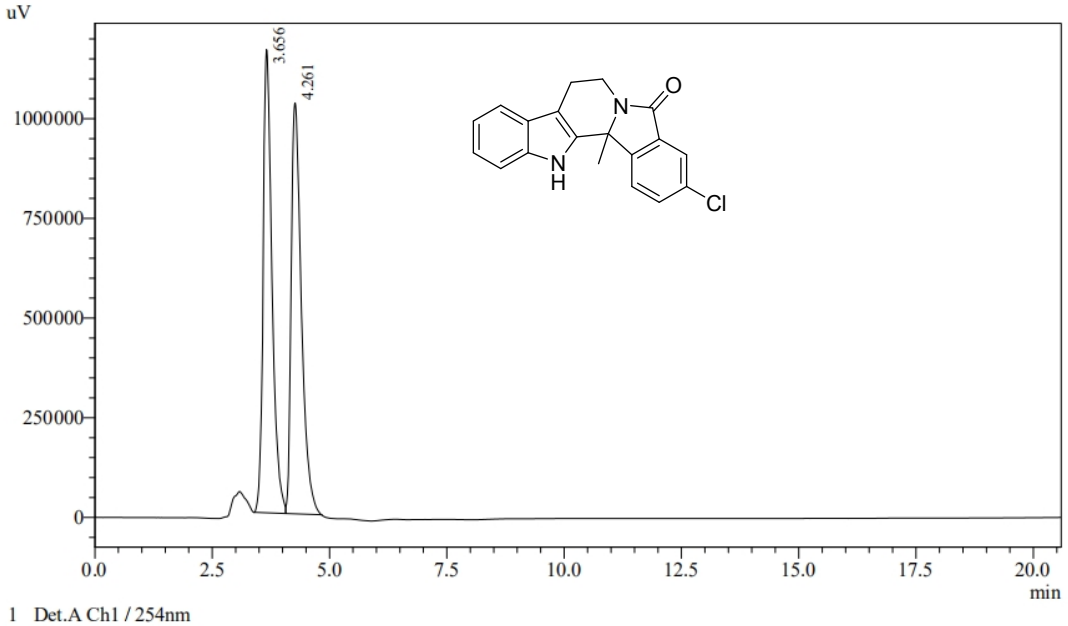


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.451	1234517	38285	2.992	8.450
2	12.187	40032593	414774	97.008	91.550
Total		41267110	453059	100.000	100.000

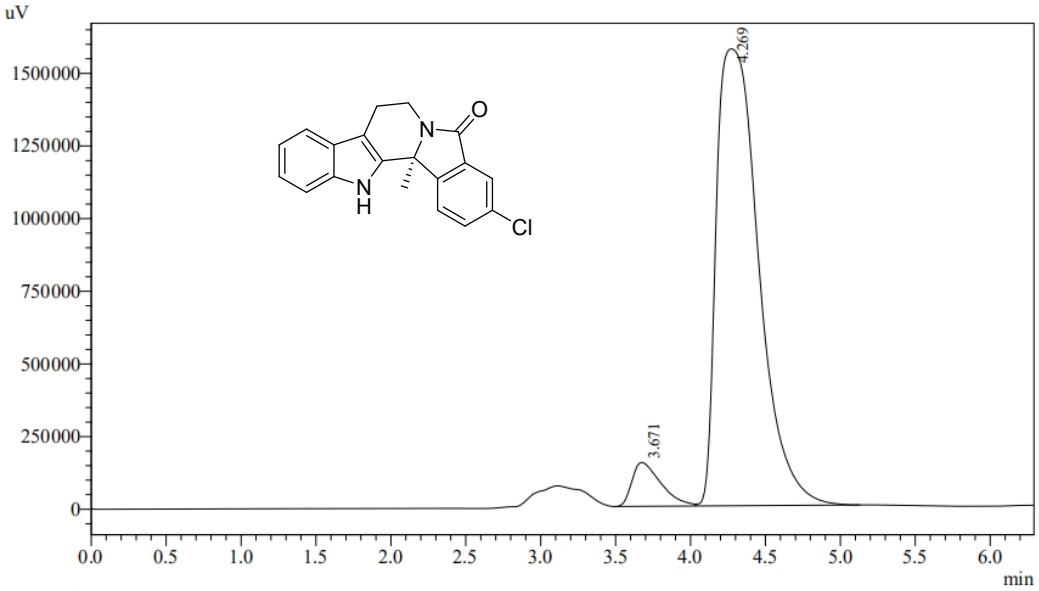
3-chloro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2e)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	3.656	15262614	1161467	49.602	52.994
2	4.261	15507835	1030210	50.398	47.006
Total		30770449	2191678	100.000	100.000

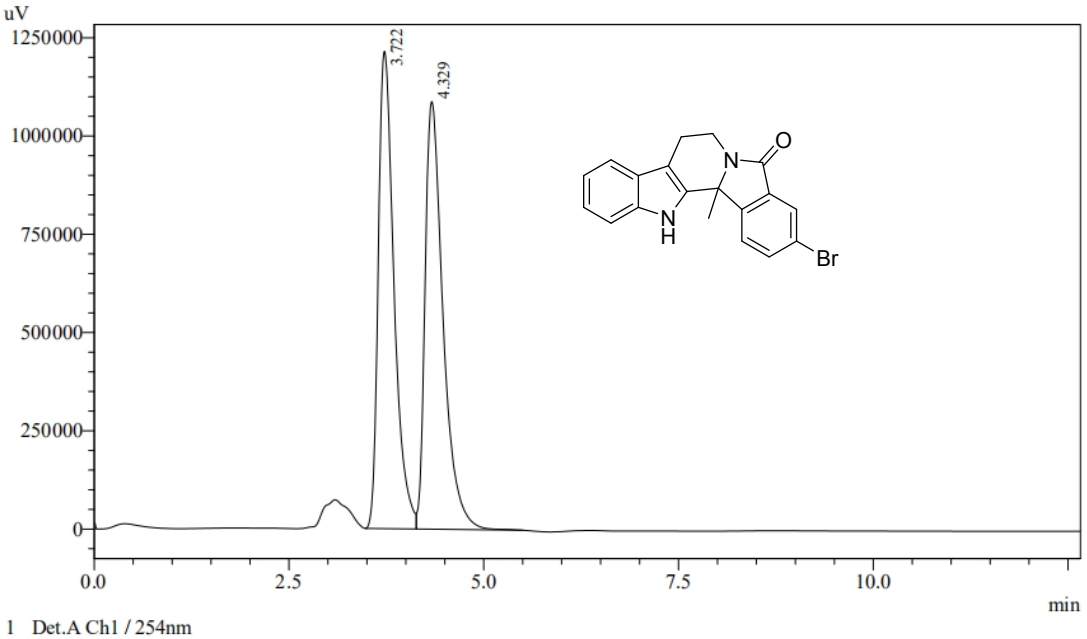


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	3.671	2029183	151822	6.156	8.806
2	4.269	30935971	1572304	93.844	91.194
Total		32965154	1724126	100.000	100.000

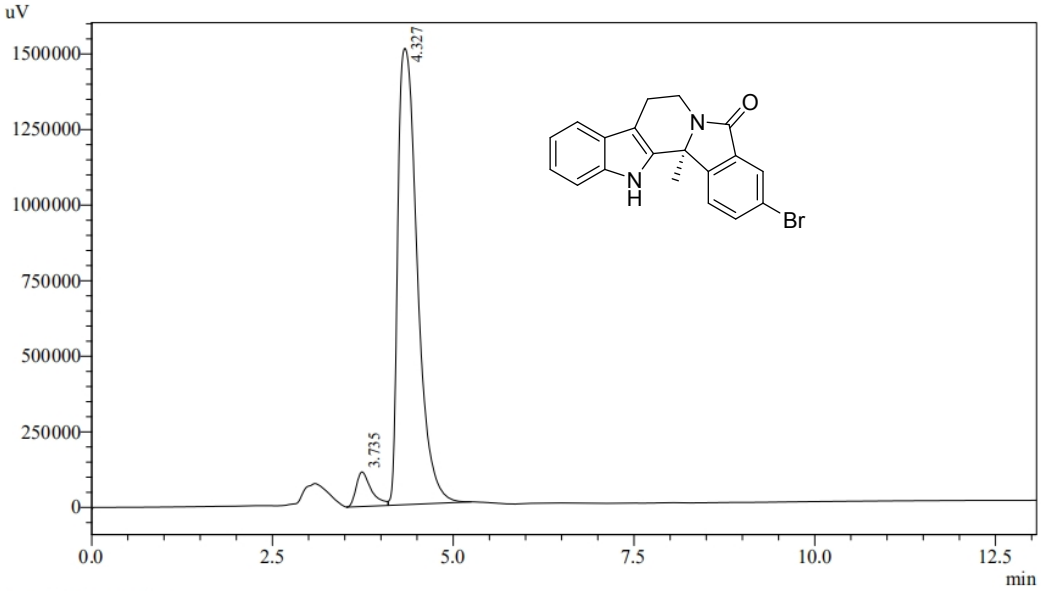
3-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2f)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	3.722	17037373	1214233	49.346	52.737
2	4.329	17488900	1088205	50.654	47.263
Total		34526273	2302438	100.000	100.000

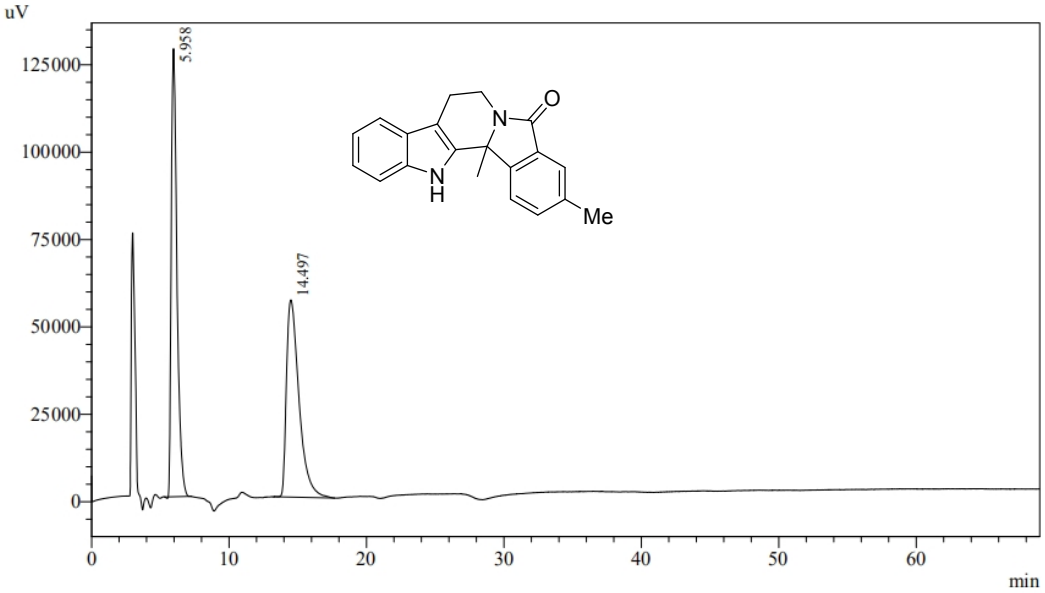


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	3.735	1661870	114350	5.555	7.041
2	4.327	28257338	1509772	94.445	92.959
Total		29919208	1624123	100.000	100.000

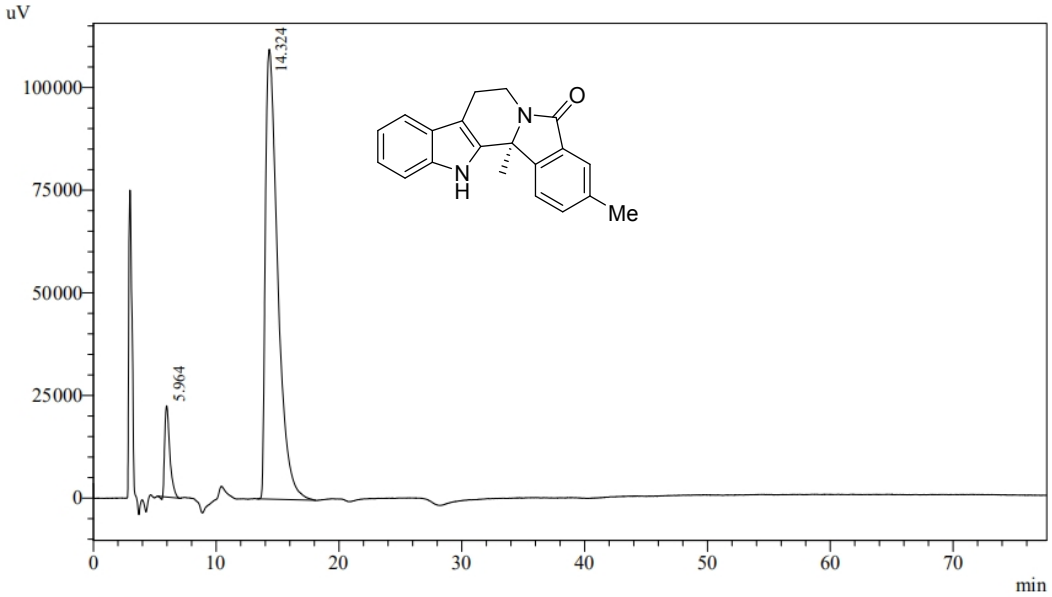
3,13b-dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2g)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.958	3714553	128161	50.940	69.438
2	14.497	3577487	56408	49.060	30.562
Total		7292040	184569	100.000	100.000

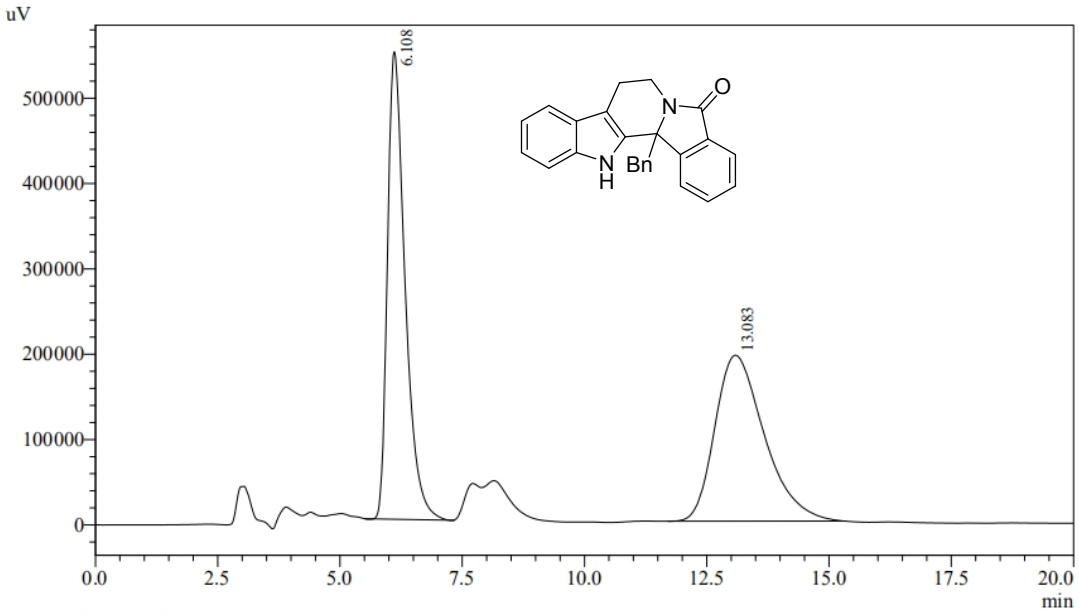


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.964	635134	22213	7.673	16.858
2	14.324	7641933	109551	92.327	83.142
Total		8277067	131764	100.000	100.000

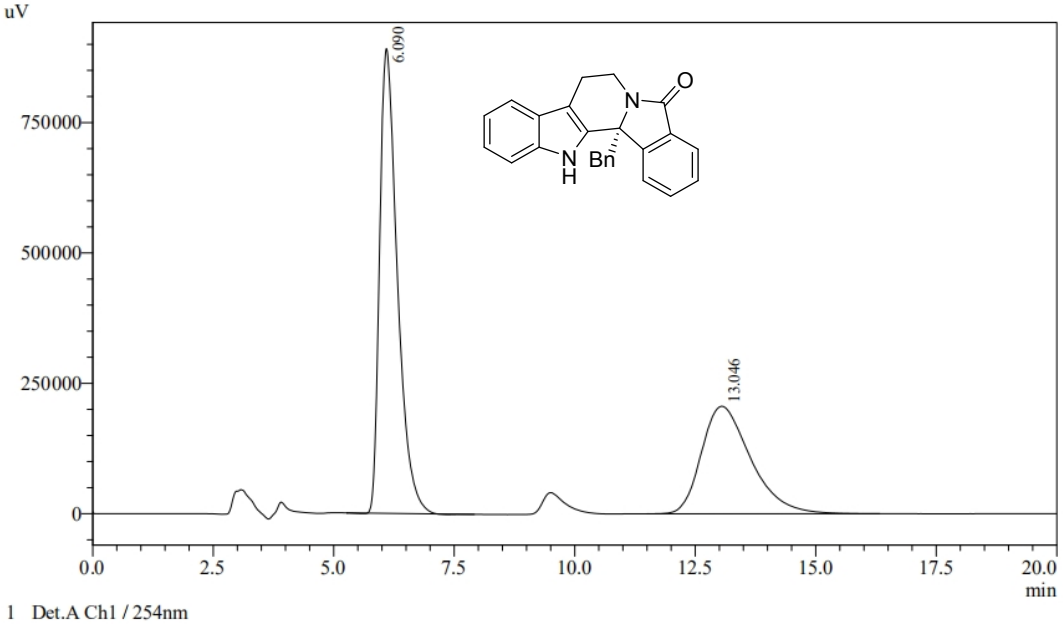
13b-benzyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2h)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.108	13739640	547690	50.096	73.804
2	13.083	13686950	194398	49.904	26.196
Total		27426590	742087	100.000	100.000

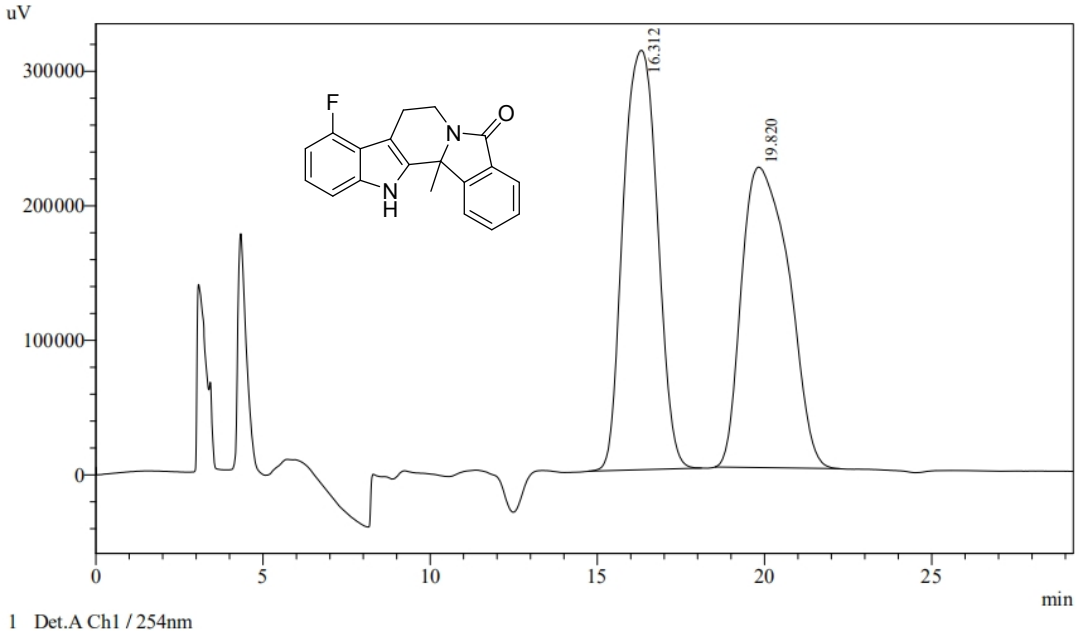


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.090	22837167	890935	60.924	81.214
2	13.046	14647497	206083	39.076	18.786
Total		37484664	1097018	100.000	100.000

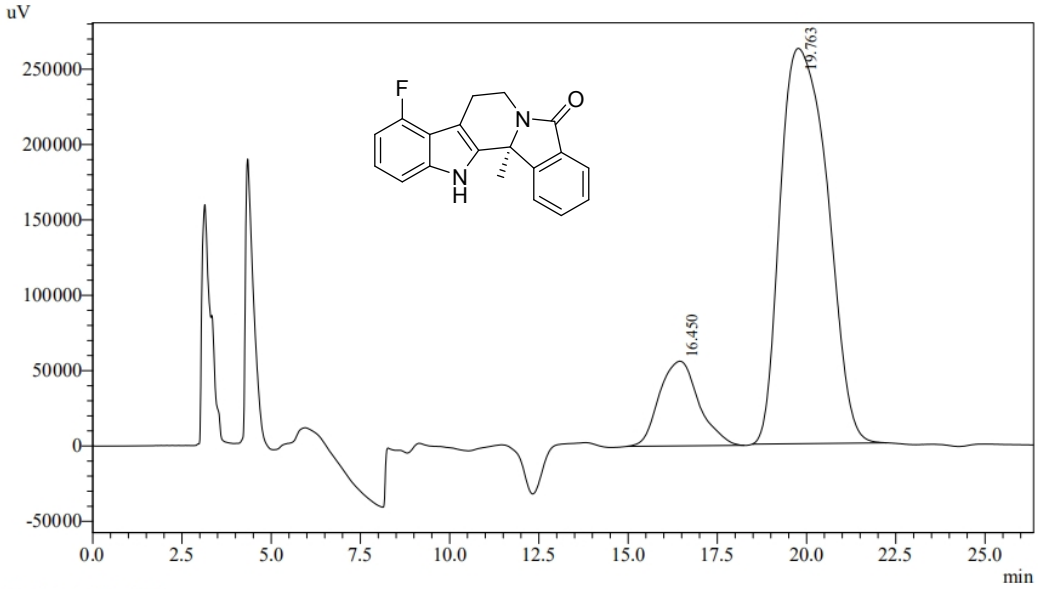
9-fluoro-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2i)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.312	22279461	311806	50.320	58.266
2	19.820	21995757	223339	49.680	41.734
Total		44275218	535145	100.000	100.000

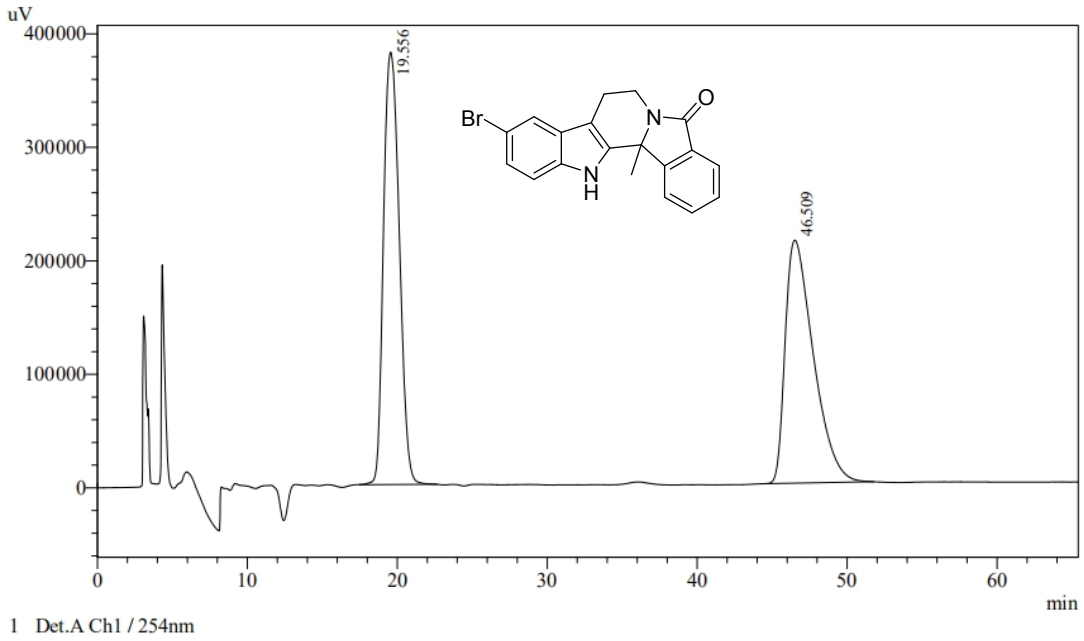


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.450	4323618	56199	15.136	17.647
2	19.763	24242273	262265	84.864	82.353
Total		28565891	318465	100.000	100.000

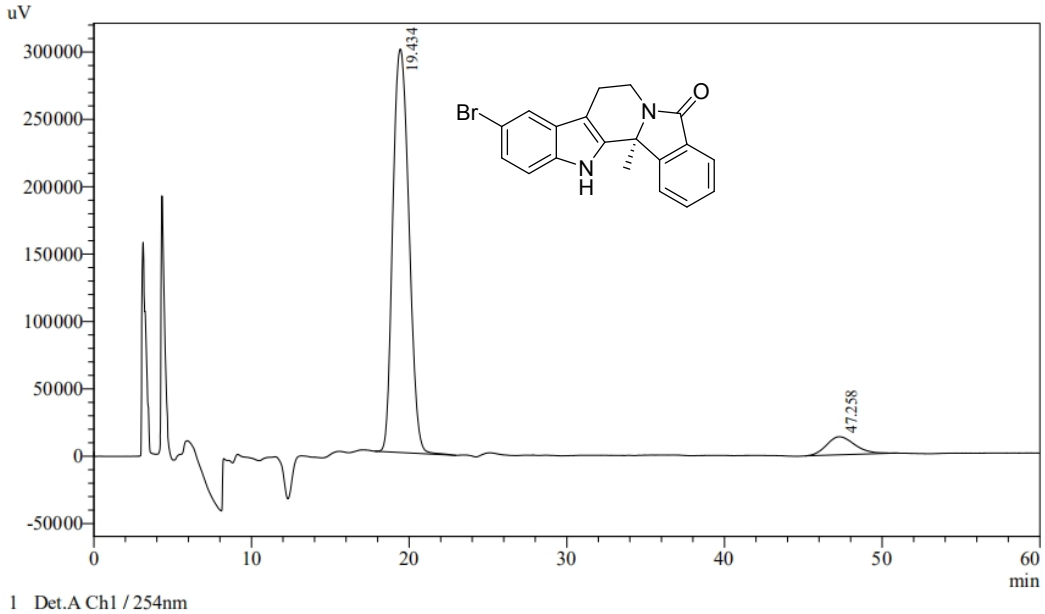
10-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2j)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.556	27880669	381065	49.923	64.019
2	46.509	27966263	214175	50.077	35.981
Total		55846931	595240	100.000	100.000

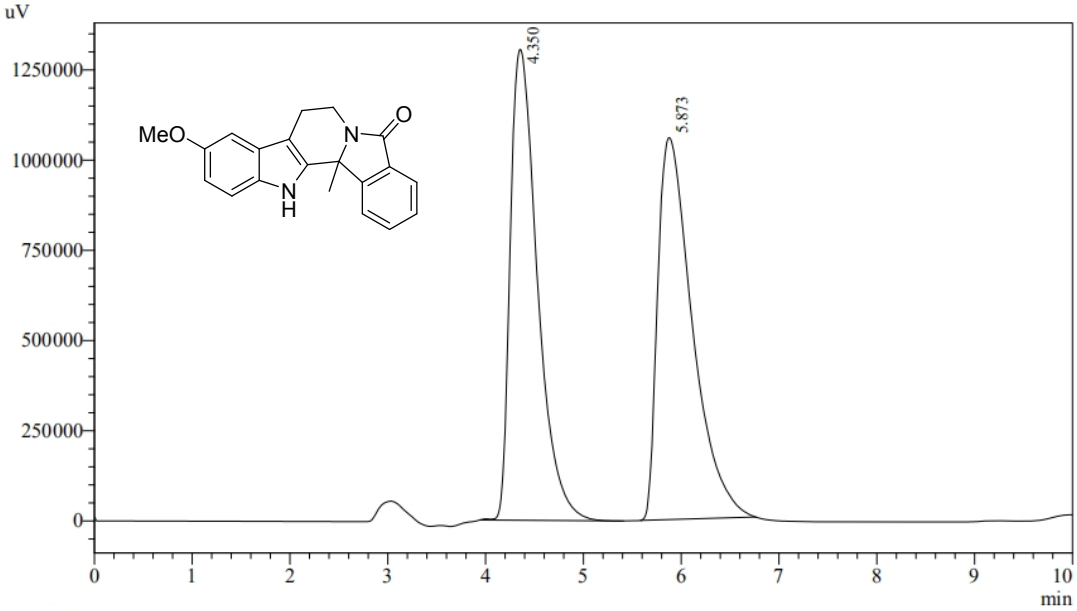


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.434	21266836	299474	92.660	95.707
2	47.258	1684549	13433	7.340	4.293
Total		22951384	312907	100.000	100.000

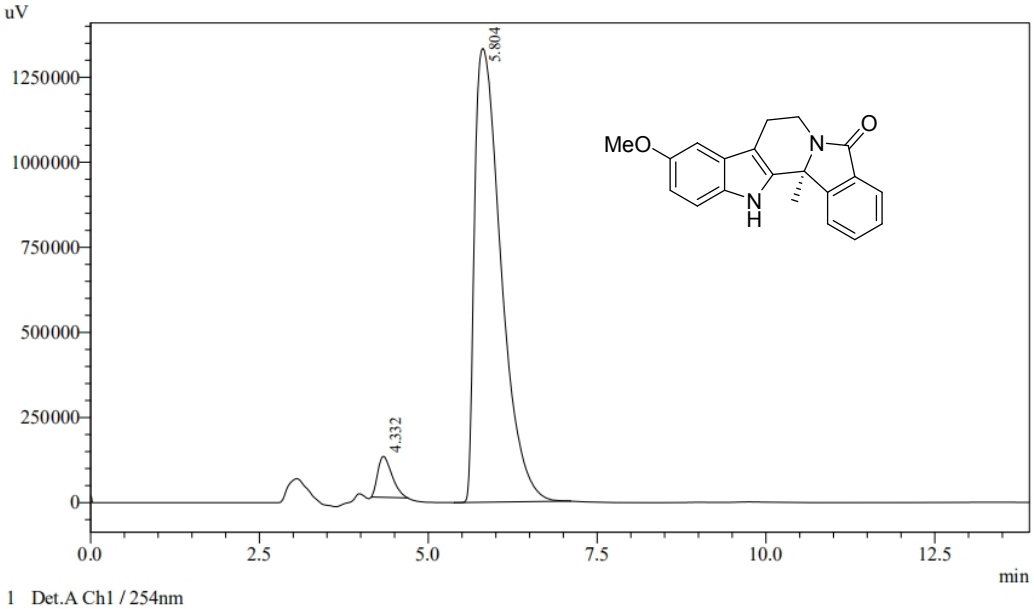
10-methoxy-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2k)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.350	25218273	1304677	49.219	55.206
2	5.873	26018815	1058607	50.781	44.794
Total		51237089	2363285	100.000	100.000

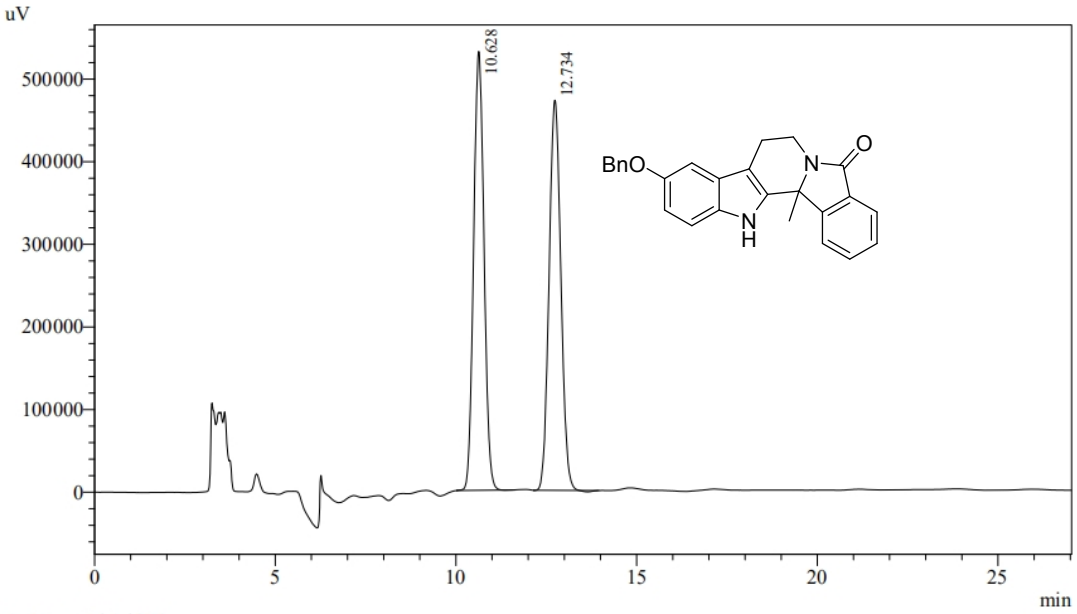


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.332	1768864	120356	4.633	8.278
2	5.804	36410165	1333524	95.367	91.722
Total		38179028	1453880	100.000	100.000

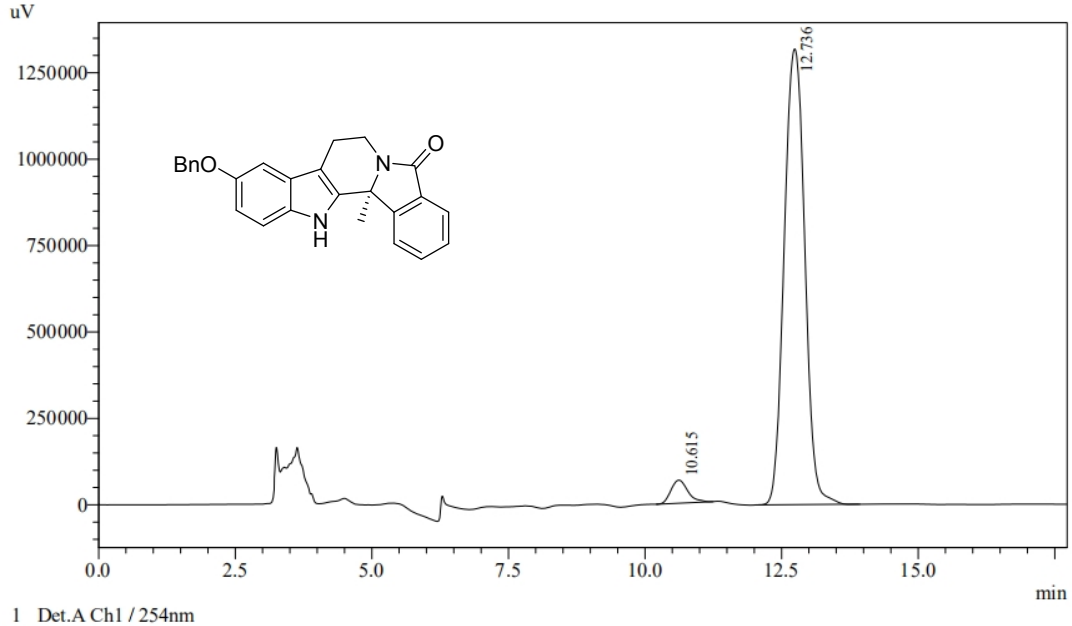
10-(benzyloxy)-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2l)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.628	10645033	531059	49.906	52.936
2	12.734	10685110	472146	50.094	47.064
Total		21330143	1003205	100.000	100.000

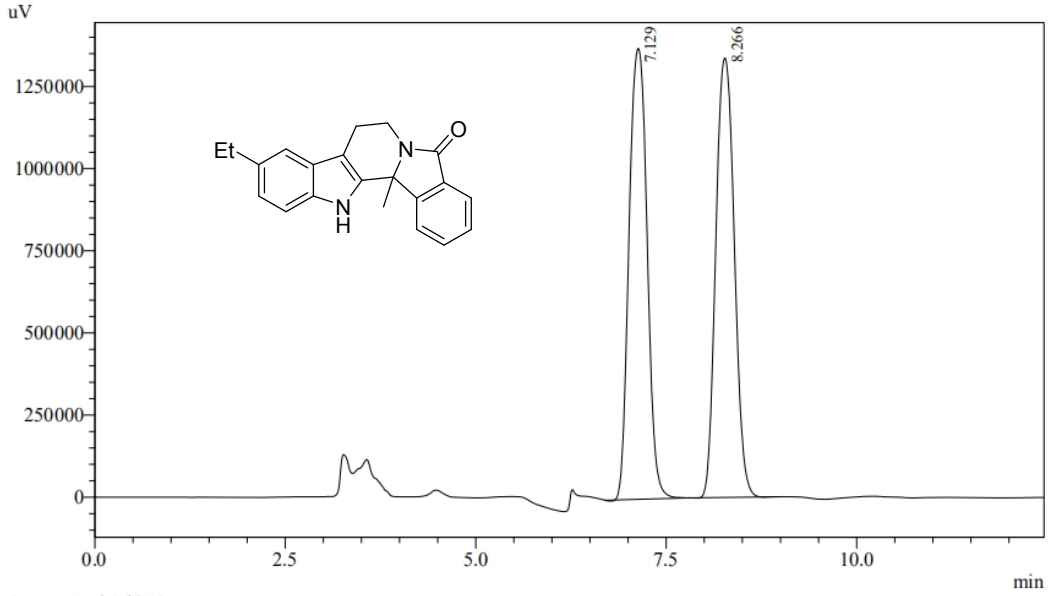


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.615	1424633	66512	3.960	4.803
2	12.736	34549242	1318399	96.040	95.197
Total		35973875	1384911	100.000	100.000

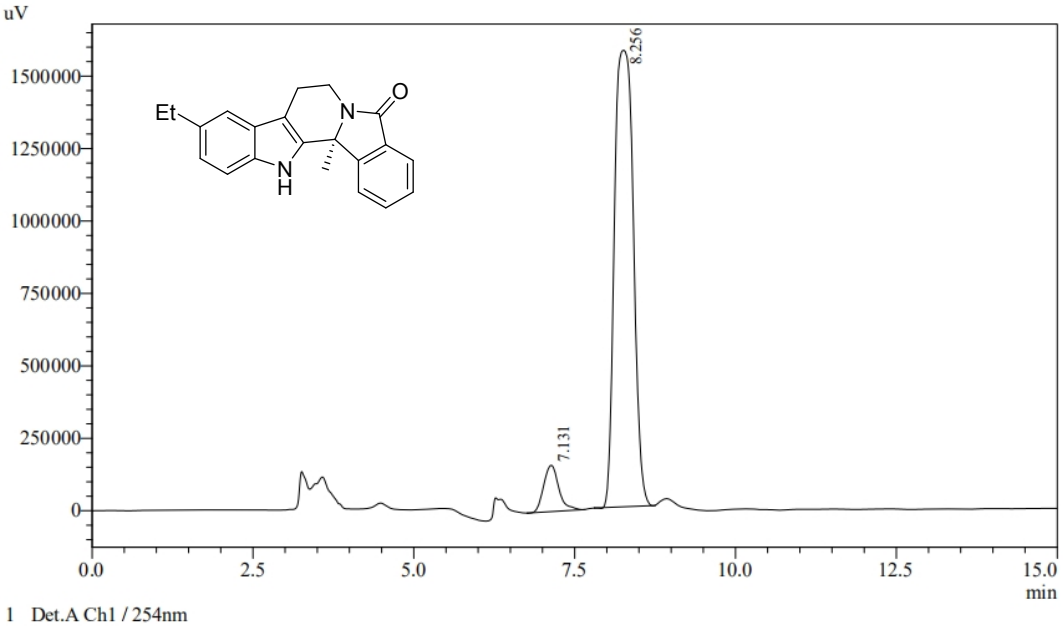
10-ethyl-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2m)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.129	22615825	1372387	50.015	50.641
2	8.266	22602084	1337632	49.985	49.359
Total		45217908	2710018	100.000	100.000

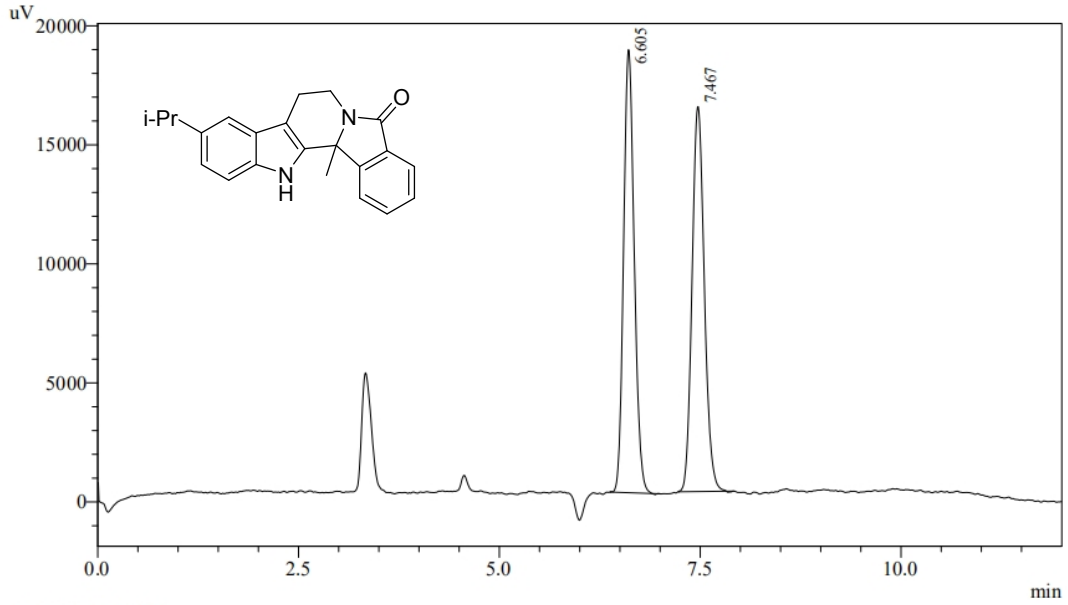


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.131	2613615	159935	7.515	9.216
2	8.256	32164733	1575407	92.485	90.784
Total		34778348	1735342	100.000	100.000

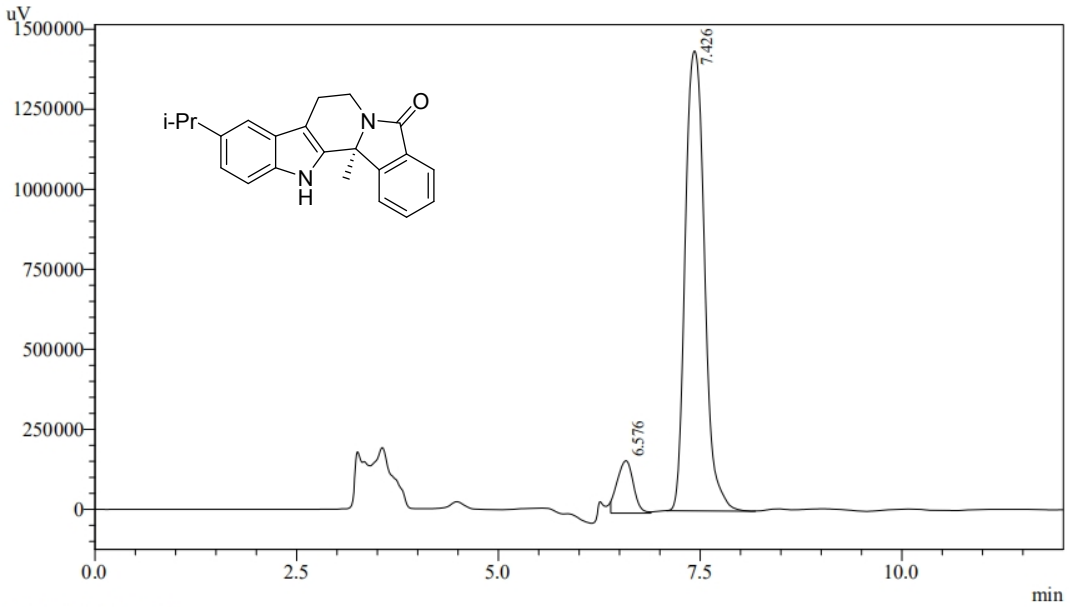
10-isopropyl-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2n)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.605	170840	18604	49.931	53.502
2	7.467	171314	16168	50.069	46.498
Total		342154	34772	100.000	100.000

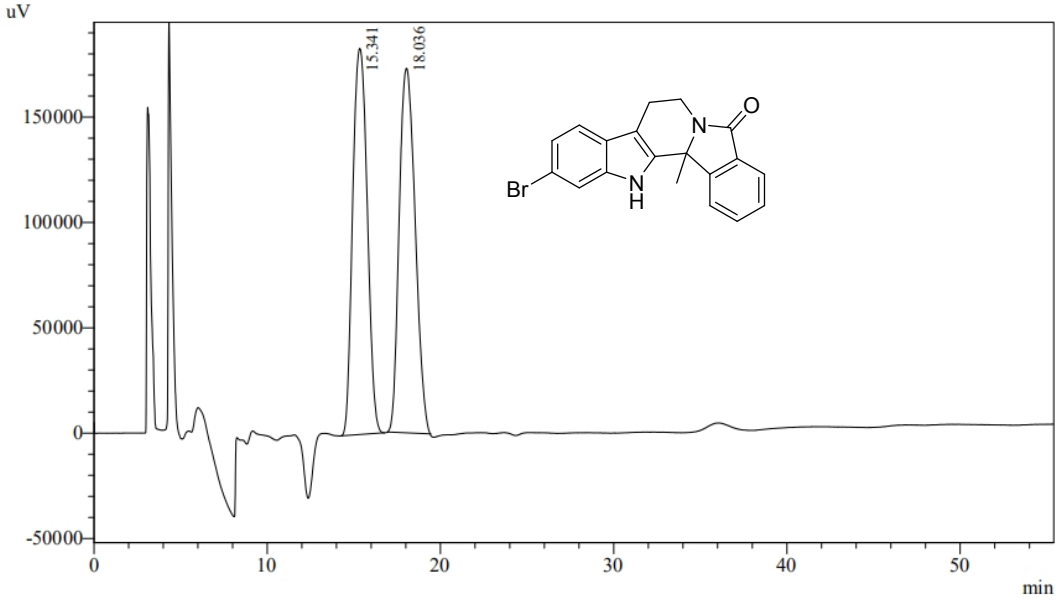


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.576	2285349	163474	8.759	10.216
2	7.426	23806602	1436742	91.241	89.784
Total		26091951	1600217	100.000	100.000

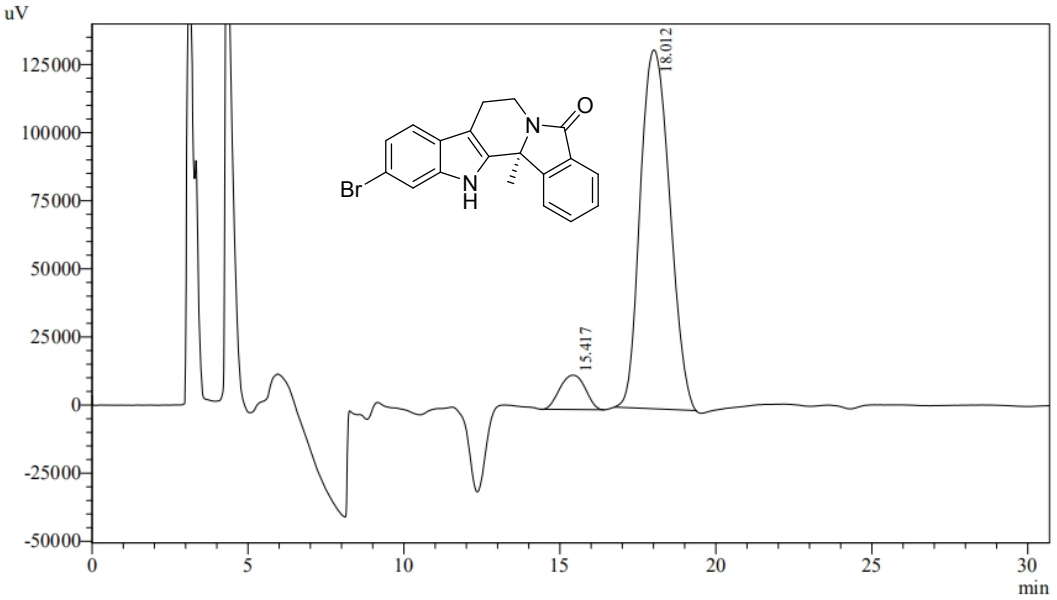
11-bromo-13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2o)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.341	10706847	183230	49.085	51.438
2	18.036	11106020	172984	50.915	48.562
Total		21812867	356215	100.000	100.000

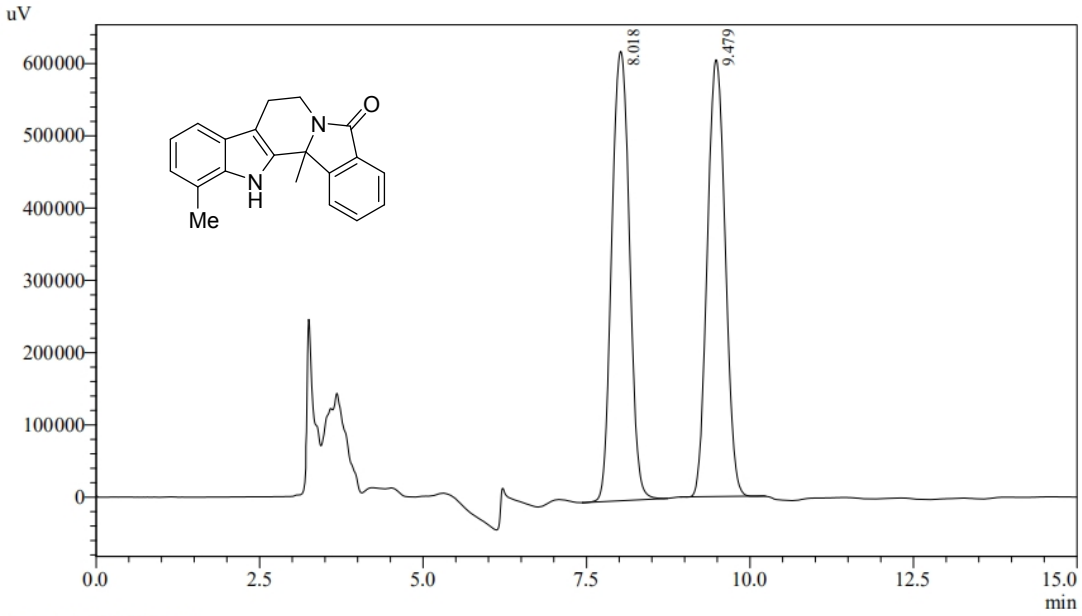


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.417	717237	12614	7.639	8.742
2	18.012	8671598	131682	92.361	91.258
Total		9388835	144296	100.000	100.000

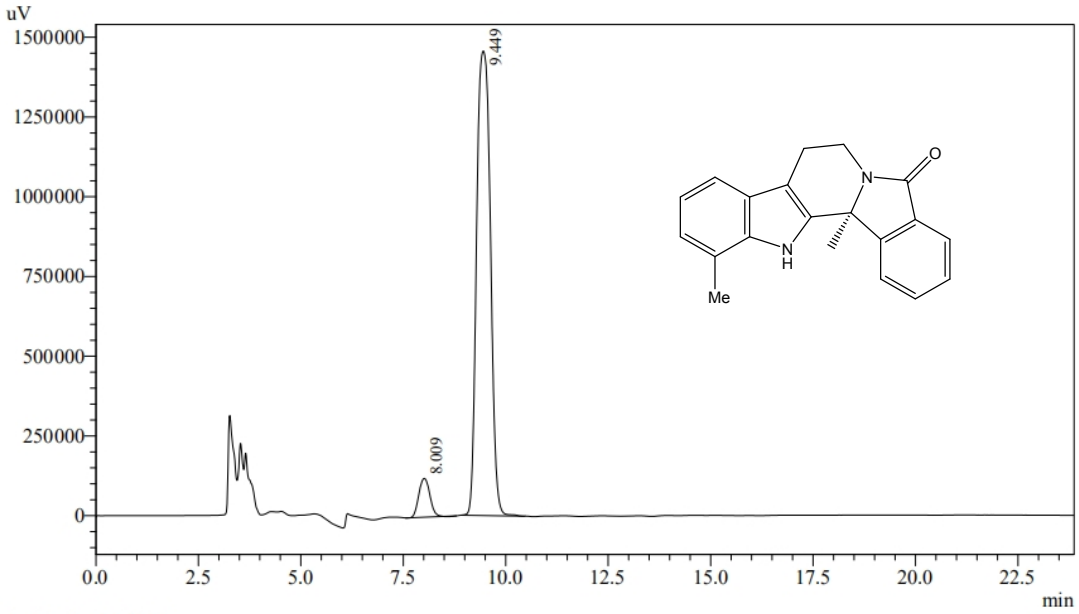
12,13b-dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2p)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.018	11748519	621879	50.424	50.705
2	9.479	11551141	604597	49.576	49.295
Total		23299661	1226476	100.000	100.000

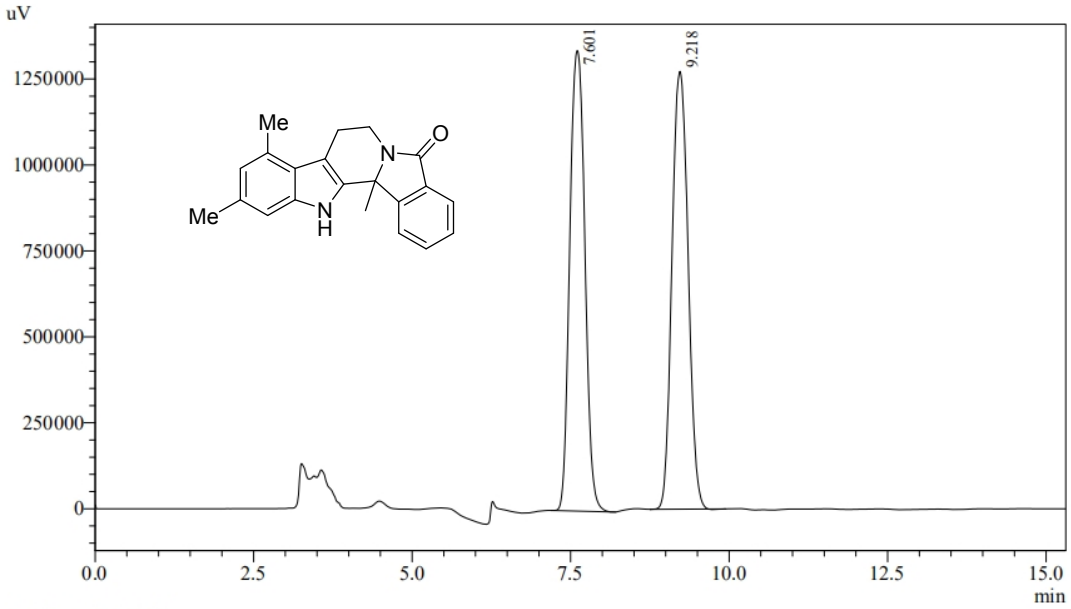


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.009	2294659	121658	6.315	7.711
2	9.449	34041465	1456141	93.685	92.289
Total		36336123	1577799	100.000	100.000

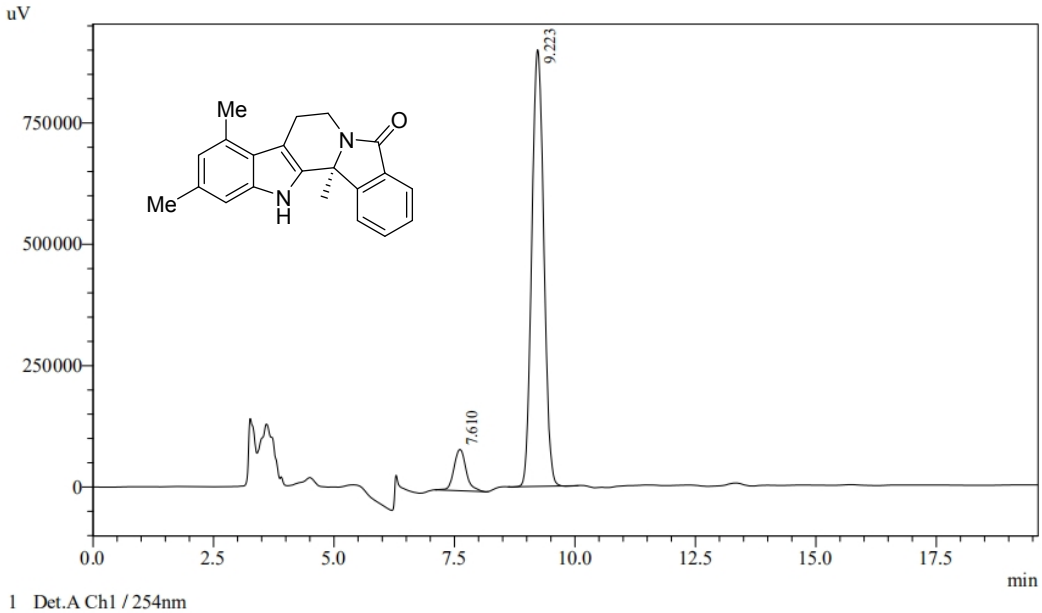
9,11,13b-trimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2q)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.601	22243772	1339164	49.688	51.263
2	9.218	22523172	1273200	50.312	48.737
Total		44766944	2612364	100.000	100.000

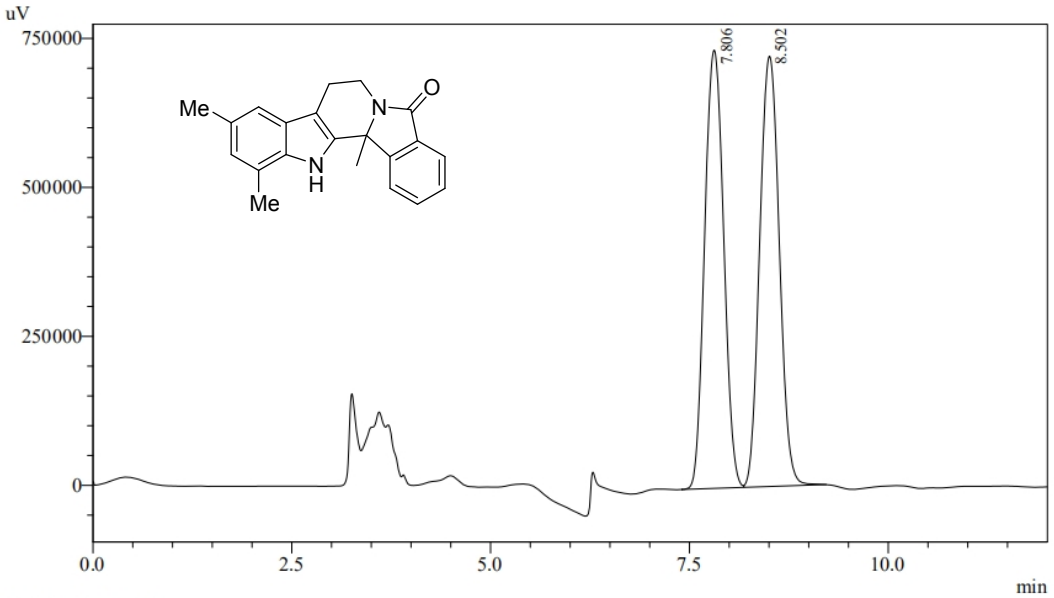


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

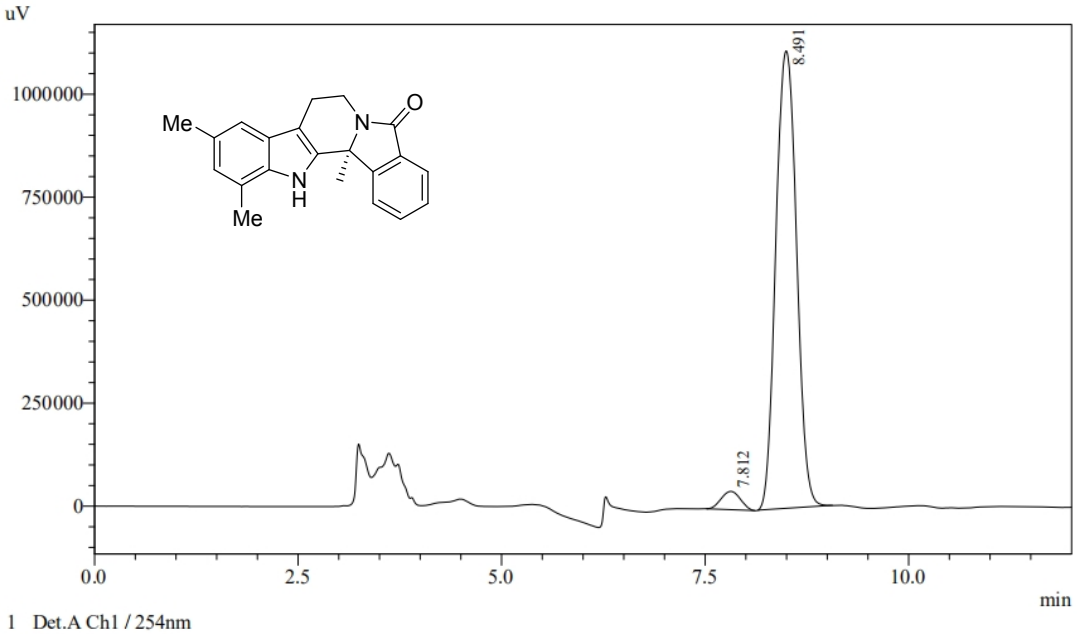
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.610	1487422	84949	8.699	8.630
2	9.223	15611351	899447	91.301	91.370
Total		17098773	984396	100.000	100.000

10,12,13b-trimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one(2r)



Detector A Ch1 254nm

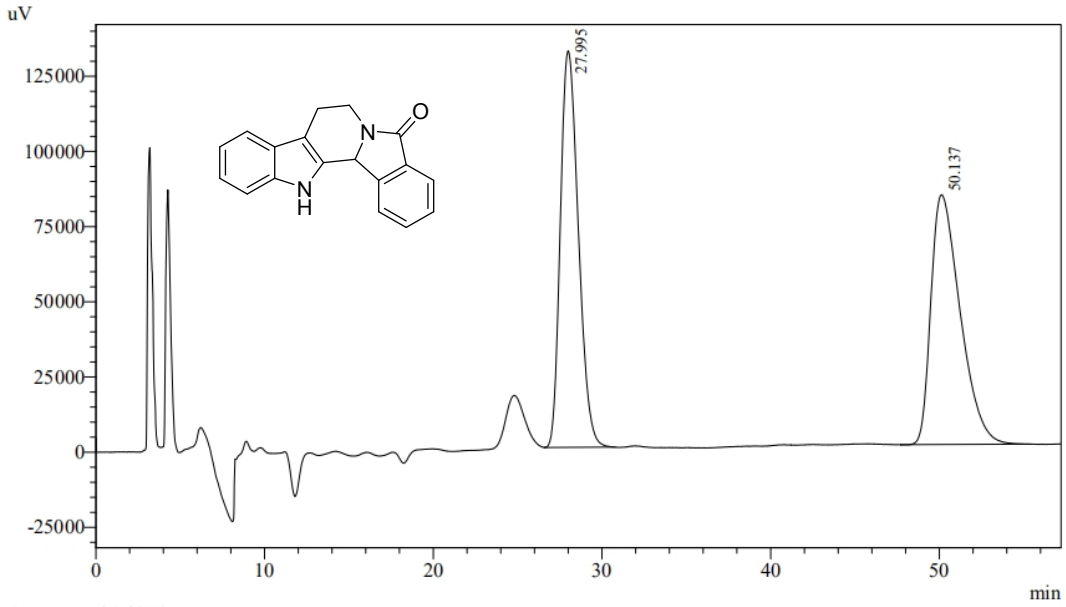
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.806	12244370	735404	49.795	50.450
2	8.502	12345428	722284	50.205	49.550
Total		24589798	1457688	100.000	100.000



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.812	728531	44425	3.570	3.848
2	8.491	19675728	1110086	96.430	96.152
Total		20404260	1154511	100.000	100.000

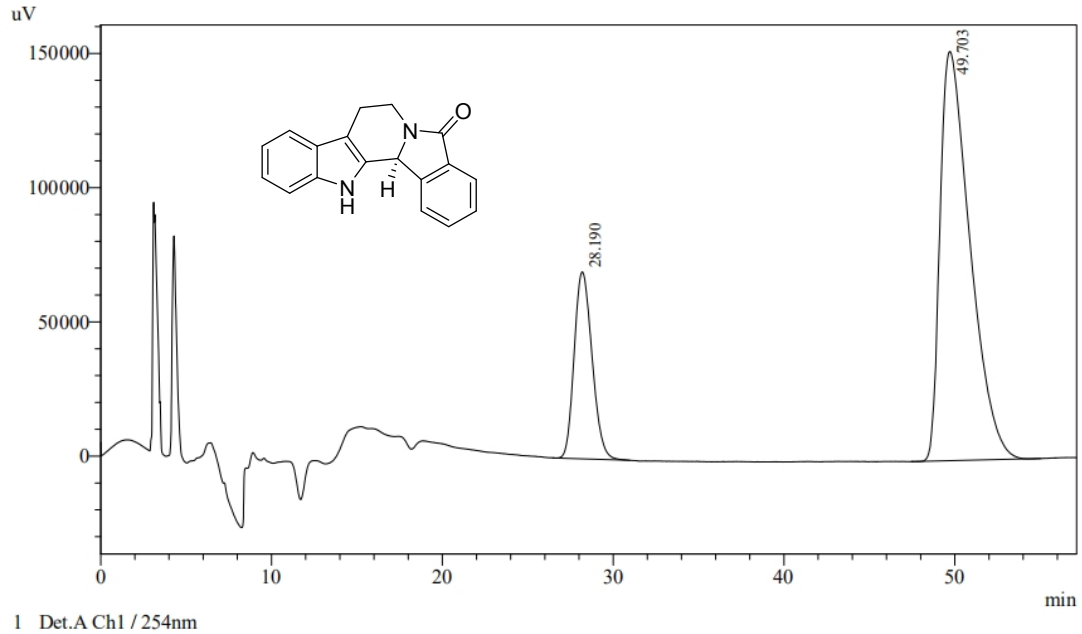
7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (6)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.995	9784198	131854	49.429	61.352
2	50.137	10010387	83059	50.571	38.648
Total		19794586	214913	100.000	100.000

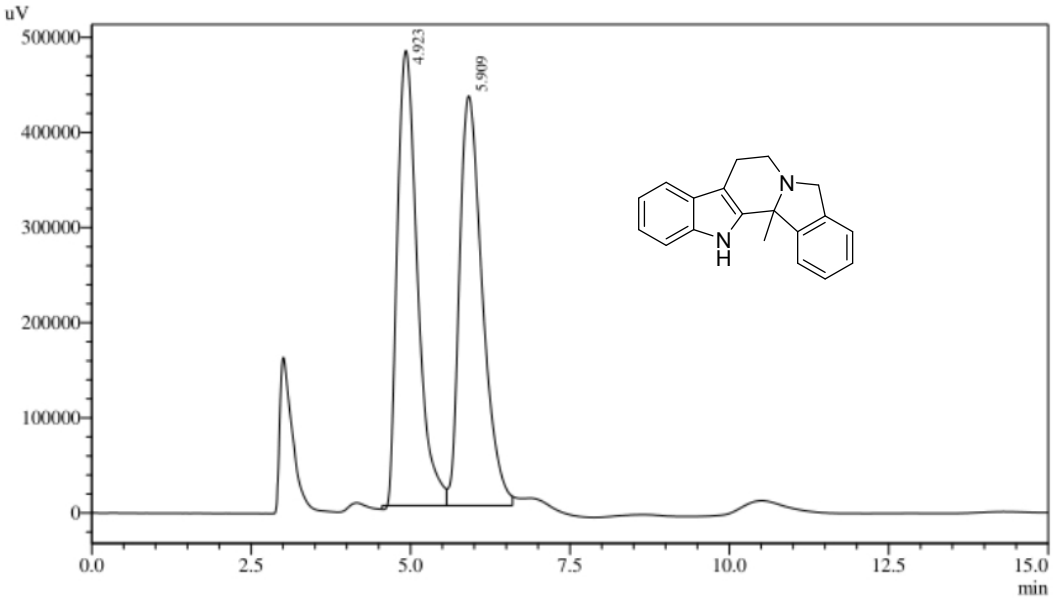


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.190	5068841	69651	21.419	31.363
2	49.703	18595972	152431	78.581	68.637
Total		23664814	222082	100.000	100.000

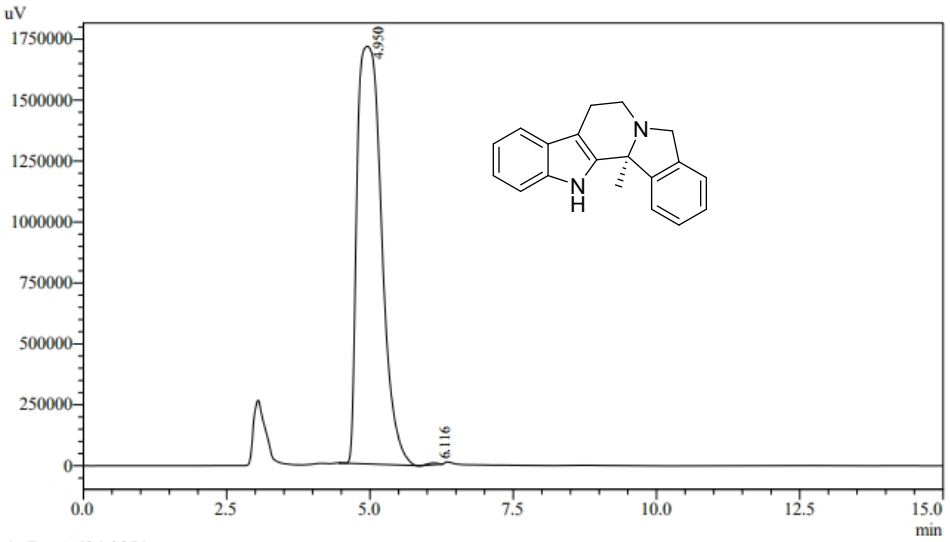
13b-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indole (7)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.923	10520261	478533	49.409	52.630
2	5.909	10771987	430710	50.591	47.370
Total		21292248	909243	100.000	100.000

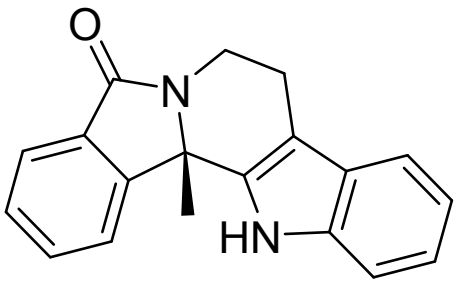


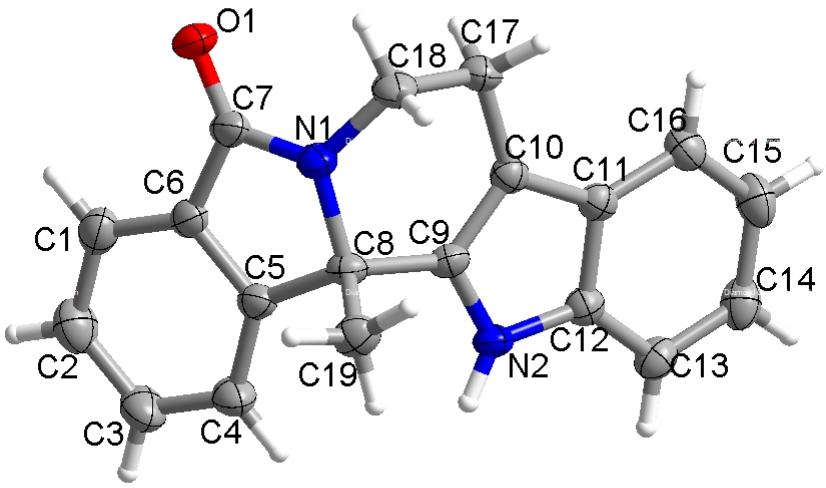
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.950	50931568	1712635	99.816	99.580
2	6.116	94042	7217	0.184	0.420
Total		51025610	1719852	100.000	100.000

5. X-ray crystal structure of (*S*)-2a





Flack parameter: 0.2 (3)

Table 1 Crystal data and structure refinement for 20200658.

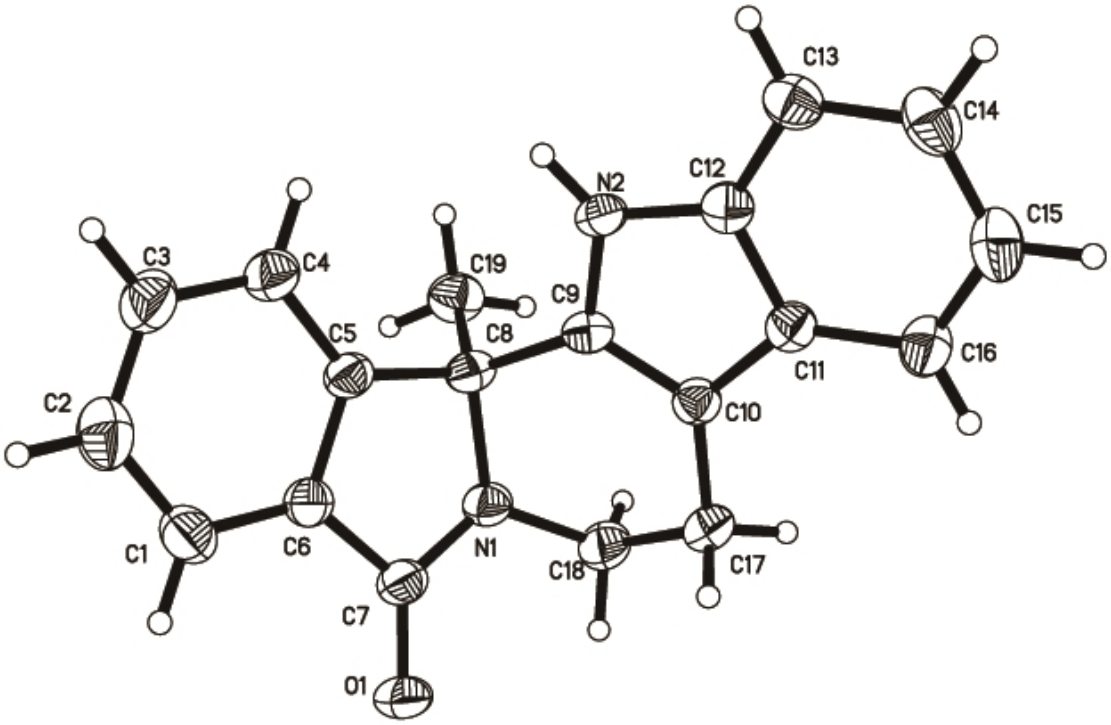
Identification code	20200658
Empirical formula	C19H16N2O
Formula weight	288.34
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	P212121
a/Å	7.4363(4)

b/Å	14.1125(9)
c/Å	14.2240(9)
α /°	90
β /°	90
γ /°	90
Volume/Å3	1492.72(15)
Z	4
ρ calcg/cm3	1.283
μ /mm-1	0.635
F(000)	608.0
Crystal size/mm3	0.16 × 0.1 × 0.08
Radiation	CuK α (λ = 1.54184)
2Θ range for data collection/°	8.826 to 142.17
Index ranges	-6 ≤ h ≤ 8, -16 ≤ k ≤ 17, -17 ≤ l ≤ 16
Reflections collected	6222
Independent reflections	2815 [Rint = 0.0346, Rsigma = 0.0481]
Data/restraints/parameters	2815/0/188
Goodness-of-fit on F2	1.021
Final R indexes [I>=2 σ (I)]	R1 = 0.0496, wR2 = 0.1201
Final R indexes [all data]	R1 = 0.0607, wR2 = 0.1301
Largest diff. peak/hole / e Å-3	0.15/-0.20
Flack parameter	0.2(3)

Table 2 Fractional Atomic Coordinates (×104) and Equivalent Isotropic Displacement Parameters (Å2×103) for 20200658. Ueq is defined as 1/3 of of the trace of the orthogonalised UIJ tensor.

Atom	x	y	z	U(eq)
O1	10810(3)	3329(3)	2013(2)	74.5(9)
N1	8076(4)	4059(2)	2228(2)	49.2(7)

N2	3731(4)	3433(2)	3337(2)	45.7(6)
C3	5286(3)	1490.1(18)	803(2)	72.7(12)
C2	7074(4)	1227.8(15)	688(2)	74.2(12)
C1	8436(3)	1800.8(18)	1040.5(19)	64.2(10)
C6	8011(2)	2636.0(16)	1508.2(16)	48.2(8)
C5	6222(3)	2898.3(14)	1623.0(15)	46.3(7)
C4	4860(2)	2325.3(18)	1270.2(19)	60.0(9)
C7	9168(5)	3348(3)	1931(2)	54.0(9)
C8	6129(4)	3839(2)	2126(2)	44.4(7)
C9	5395(4)	3794(2)	3114(2)	42.6(7)
C10	6255(4)	4098(2)	3899(2)	43.4(7)
C11	5071(5)	3921(2)	4672(2)	44.7(7)
C12	3510(5)	3500(2)	4293(2)	45.4(7)
C13	2070(5)	3207(3)	4856(3)	53.0(8)
C14	2228(6)	3341(3)	5811(3)	61.3(10)
C15	3751(6)	3759(3)	6201(3)	65.7(10)
C16	5182(6)	4054(3)	5645(3)	57.3(9)
C17	8117(5)	4497(3)	3896(3)	54.2(9)
C18	8648(5)	4777(3)	2902(3)	59.8(9)
C19	5149(6)	4582(3)	1540(3)	59.5(9)


C13
C14
N2
C12
C15
C3
C4
C19
C9
C5
C8
C11
C16
C2
C10
C1
C6
N1
C18
C17
C7
O1