

Supporting information

Enantioselective vinylogous aldol reaction between β,γ -unsaturated amides and isatins

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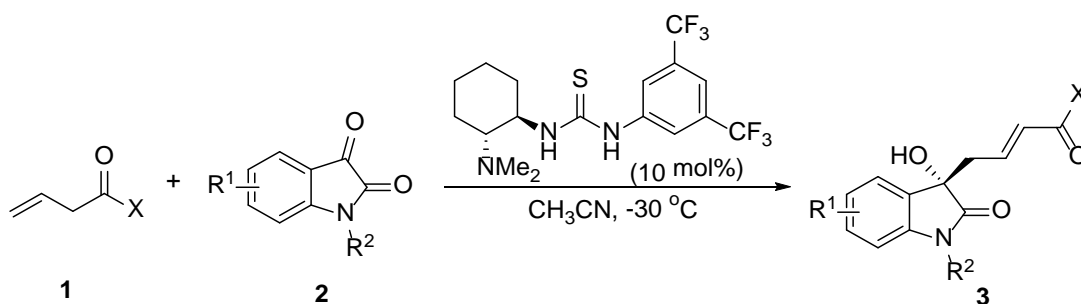
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1. General Information

Melting points were taken on WRS-1B digital melting-point apparatus without correction. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker 400 spectrometer with CDCl_3 or DMSO-d_6 as solvent. The chemical shifts were referenced to tetramethylsilane (0.00 ppm) for ^1H NMR spectra, and the residual solvent peak for ^{13}C NMR (77.00 ppm for CDCl_3 or 39.60 ppm for $\text{d}_6\text{-DMSO}$). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on Nicolet Magna-I 550 spectrometer. High resolution mass spectra (HRMS) were recorded on Micromass GCT and KE 465 LCT Premier/XE with Electron Spray Ionization (ESI-TOF) resource or Electron Impact (EI) resource. Optical rotations were measured on a WZZ-2A digital polarimeter at wavelength of the sodium D-line (589 nm). HPLC analysis was performed on Waters 510 equipment using Daicel Chiralcel OD-H column or Daicel Chiralpak AS-H column. Toluene, THF, and ether were freshly distilled from sodium-benzophenone. Ethyl acetate and CH_2Cl_2 were freshly distilled from CaH_2 . CH_3CN was freshly distilled from P_2O_5 . MeOH was freshly distilled from Magnesium-iodine under N_2 atmosphere. Thin-layer chromatography (TLC) was performed on 10-40 μm silica gel plate. Column chromatography was performed using silica gel (300-400 mesh) eluted with ethyl acetate and CH_2Cl_2 .

Chiral catalysts **C1-C9**¹, allyl amides **1**² and ketimines **2**³ were prepared according to literature procedures.

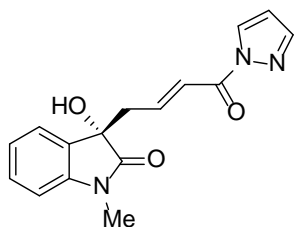
2. General Procedure for the Enantioselective Vinylogous Aldol Reaction



To a solution of β,γ -unsaturated amide **1** (0.3 mmol, 1.5 equiv.) and Takemoto catalyst (0.02 mmol, 10 mol%) in 2 mL CH_3CN was added isatin **2** (0.2 mmol, 1.0 equiv.) at $-30\text{ }^\circ\text{C}$, and the resulting mixture was stirred at this temperature until the reaction was completed (monitored by TLC). The solvent was removed under reduced pressure, and

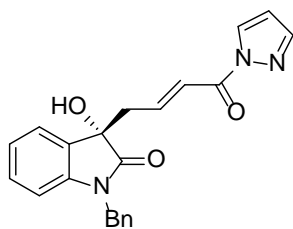
the residue was purified by column chromatography (dichloromethane/ethyl acetate) to afford the desired product **3**.

(*S,E*)-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one
(3aa)



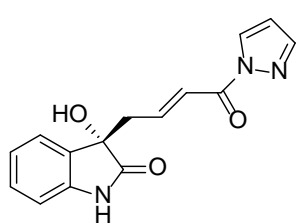
White solid, 51.8 mg, 87% yield, 99% ee; mp: 169.3-170.1 °C; $[\alpha]_D^{20} = -15.8$ (*c* 0.33, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.27 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 0.8 Hz, 1H), 7.40 (dd, *J*₁ = 7.2 Hz, *J*₂ = 0.8 Hz, 1H), 7.35-7.29 (m, 2H), 7.28-7.20 (m, 1H), 7.10 (dt, *J*₁ = 7.6 Hz, *J*₂ = 0.8 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.44 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 4.11 (brs, 1H), 3.19 (s, 3H), 3.09-3.04 (m, 1H), 2.84 (dd, *J*₁ = 14.0 Hz, *J*₂ = 7.6 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.4, 162.5, 144.9, 143.9, 142.9, 130.0, 129.2, 128.6, 124.3, 123.6, 123.4, 109.8, 108.7, 75.6, 41.5, 26.3; IR (KBr, cm⁻¹): ν 3005, 2360, 1712, 1614, 1385, 1353, 1275, 1261, 764, 750; HRMS (ESI) calcd for C₁₆H₁₅N₃NaO₃⁺ ([M+Na]⁺): 320.1006, found: 320.1001; HPLC analysis (Daicel Chiralcel OD-H column, λ = 254 nm, eluent: 90:10 hexane/2-propanol, flow rate: 0.9 mL/min): *t*_R = 52.79 min (major), 74.00 min (minor).

(*S,E*)-1-benzyl-3-hydroxy-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one
(3ab)



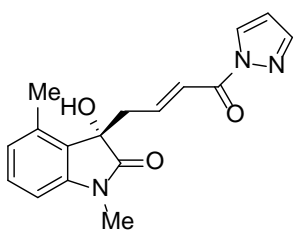
White solid, 66.6 mg, 89% yield, 92% ee; mp 172.1-174.2 °C; $[\alpha]_D^{20} +11.7$ (*c* 0.60, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.27 (d, *J* = 2.8 Hz, 1H), 7.67 (d, *J* = 0.8 Hz, 1H), 7.41 (dd, *J*₁ = 7.6 Hz, *J*₂ = 0.8 Hz, 1H), 7.34 (d, *J* = 15.6 Hz, 1H), 7.23-7.14 (m, 7H), 7.05 (dt, *J*₁ = 7.6 Hz, *J*₂ = 0.4 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.43 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 5.02 (d, *J* = 15.6 Hz, 1H), 4.69 (d, *J* = 15.6 Hz, 1H), 4.00 (brs, 1H), 3.13 (ddd, *J*₁ = 14.0 Hz, *J*₂ = 6.8 Hz, *J*₃ = 1.6 Hz, 1H), 2.96 (dd, *J*₁ = 14.0 Hz, *J*₂ = 8.4 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.3, 162.4, 144.6, 143.9, 142.1, 135.1, 129.9, 129.0, 128.8, 128.6, 127.6, 127.1, 124.3, 123.8, 123.4, 109.9, 109.8, 75.7, 43.9, 41.7; IR (KBr, cm⁻¹): ν 3377, 1717, 1639, 1615, 1463, 1401, 1343, 1276, 971, 945; HRMS (ESI) calcd for C₂₂H₁₉N₃NaO₃⁺ ([M+Na]⁺): 396.1319, found: 396.1316; HPLC analysis (Daicel Chiralcel OD-H column, λ = 254 nm, eluent: 90:10 hexane/2-propanol, flow rate: 0.9 mL/min): *t*_R = 23.21 min (major), 37.11 min (minor).

(*S,E*)-3-hydroxy-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ac)



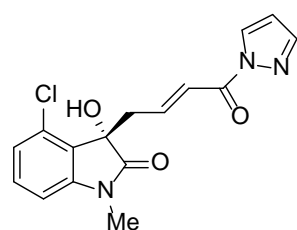
White solid, 48.2 mg, 85% yield, 95% ee; mp 150.7-151.0 °C; $[\alpha]_{\text{D}}^{20} +13.2$ (*c* 0.49, CH₂Cl₂); ¹H NMR (400 MHz, DMSO-*d*₆): δ 10.37 (s, 1H), 8.43 (d, *J* = 2.8 Hz, 1H), 7.89 (d, *J* = 0.8 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.23-7.21 (m, 1H), 7.20-7.19 (m, 1H), 7.15-7.08 (m, 1H), 6.99-6.95 (m, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.62 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 6.29 (s, 1H), 2.92-2.87 (m, 1H), 2.80 (dd, *J*₁ = 14.0 Hz, *J*₂ = 7.6 Hz, 1H); ¹³C{¹H} NMR (100 MHz, DMSO-*d*₆): δ 178.4, 162.2, 146.7, 144.6, 141.5, 131.3, 129.4 129.2, 124.3 122.2, 121.9, 110.7, 109.9, 75.0, 40.8; IR (KBr, cm⁻¹): ν 3006, 1715, 1614, 1470, 1382, 1275, 1261, 1196, 1077, 764; HRMS (ESI) calcd for C₁₅H₁₄N₃O₃⁺ ([M+H]⁺): 284.1030, found: 284.1027; HPLC analysis (Daicel Chiralcel OD-H column, λ = 254 nm, eluent: 90:10 hexane/2-propanol, flow rate: 0.9 mL/min): *t*_R = 17.03 min (major), 26.27 min (minor).

(*S,E*)-3-hydroxy-1,4-dimethyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ad)



White solid, 54.9 mg, 88% yield, 99% ee; mp 184.3-184.5 °C; $[\alpha]_{\text{D}}^{20} +30.9$ (*c* 0.44, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.22 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 0.8 Hz, 1H), 7.29-7.25 (m, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 6.91-6.83 (m, 2H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.42 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 3.80 (s, 1H), 3.17-3.14 (m, 5H), 2.50 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.2, 162.4, 144.5, 143.9, 143.1, 136.0, 129.7, 128.6, 126.1, 125.8, 122.9, 109.8, 106.2, 76.9, 40.5, 26.3, 17.6; IR (KBr, cm⁻¹): ν 3390, 2924, 1712, 1643, 1607, 1385, 1275, 1200, 1077, 765; HRMS (ESI) calcd for C₁₇H₁₇N₃NaO₃⁺ ([M+Na]⁺): 334.1162, found: 334.1166; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): *t*_R = 25.17 min (major), 40.43 min (minor).

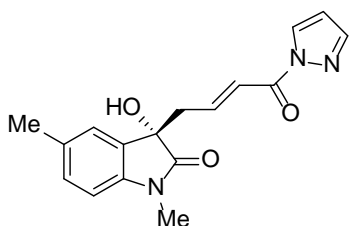
(*S,E*)-4-chloro-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ae)



White solid, 59.9 mg, 90% yield, 91% ee; mp 164.2-164.9 °C; $[\alpha]_{\text{D}}^{20} +11.7$ (*c* 0.46, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.21 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 0.8 Hz, 1H), 7.31-7.23 (m, 2H), 7.04 (dd, *J*₁ = 8.0 Hz, *J*₂ = 0.4 Hz, 1H), 6.88-6.80 (m, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 6.42 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.2 Hz, 1H), 3.97 (s, 1H), 3.42 (ddd, *J*₁ = 13.6 Hz, *J*₂ = 7.6 Hz, *J*₃ = 1.2 Hz, 1H), 3.22 (ddd, *J*₁ = 13.6 Hz, *J*₂ = 7.6 Hz, *J*₃ = 1.2 Hz, 1H), 3.17 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 176.0, 162.4, 144.9, 143.9 143.8, 131.5, 131.2, 128.5, 125.2, 124.4, 123.3, 109.9, 107.2,

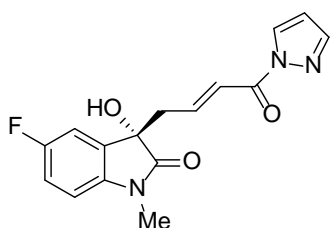
76.7, 39.1, 26.5; IR (KBr, cm^{-1}): ν 3006, 1713, 1643, 1609, 1385, 1276, 1200, 1131, 764, 750; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}^{35}\text{ClN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 354.0616, found: 354.0608; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_{\text{R}} = 24.99$ min (major), 39.72 min (minor).

(*S,E*)-3-hydroxy-1,5-dimethyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3af)



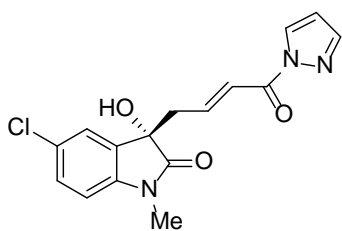
White solid, 55.0 mg, 88% yield, 97% ee; mp 153.6-154.2 °C; $[\alpha]_{\text{D}}^{20} +45.7$ (c 0.46, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ 8.28 (d, $J = 2.8$ Hz, 1H), 7.70 (d, $J = 0.8$ Hz, 1H), 7.32 (d, $J = 15.6$ Hz, 1H), 7.25-7.17 (m, 2H), 7.12 (dd, $J_1 = 8.0$ Hz, $J_2 = 0.8$ Hz, 1H), 6.73 (d, $J = 8.0$ Hz, 1H), 6.44 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.2$ Hz, 1H), 3.62 (brs, 1H), 3.20-3.15 (m, 3H), 3.05 (ddd, $J_1 = 14.0$ Hz, $J_2 = 6.4$ Hz, $J_3 = 1.2$ Hz, 1H), 2.90-2.84 (m, 1H), 2.33 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 177.2, 162.5, 144.9, 143.9, 140.6, 133.0, 130.2, 129.1, 128.6, 125.0, 123.5, 109.8, 108.4, 75.7, 41.6, 26.3, 21.1; IR (KBr, cm^{-1}): ν 3382, 3005, 1712, 1642, 1499, 1385, 1275, 1198, 1096, 764; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{17}\text{N}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 334.1162, found: 334.1160; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_{\text{R}} = 34.88$ min (major), 61.11 min (minor).

(*S,E*)-5-fluoro-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ag)



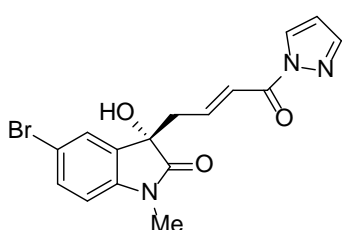
White solid, 61.3 mg, 97% yield, 88% ee; mp 168.5-168.9 °C; $[\alpha]_{\text{D}}^{20} -10.6$ (c 0.51, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ 8.27 (d, $J = 2.8$ Hz, 1H), 7.68 (d, $J = 0.8$ Hz, 1H), 7.32-7.28 (m, 1H), 7.25-7.17 (m, 2H), 7.08-7.00 (m, 2H), 6.44 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.6$ Hz, 1H), 4.54 (brs, 1H), 3.39 (dd, $J_1 = 10.8$ Hz, $J_2 = 2.4$ Hz, 3H), 3.08-3.03 (m, 1H), 2.86 (dd, $J_1 = 14.0$ Hz, $J_2 = 8.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 177.1, 162.4, 147.8 (d, $J = 243.3$ Hz), 144.4, 144.0, 132.1 (d, $J = 2.5$ Hz), 129.3 (d, $J = 8.4$ Hz), 128.7, 124.1, 123.7, 120.1, 117.9 (d, $J = 19.1$ Hz), 109.9, 75.6, 41.5, 28.8; IR (KBr, cm^{-1}): ν 3390, 3005, 1713, 1643, 1417, 1385, 1354, 1275, 1261, 765; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}\text{FN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 338.0911, found: 338.0921; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_{\text{R}} = 24.75$ min (major), 51.62 min (minor).

(*S,E*)-5-chloro-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ah)



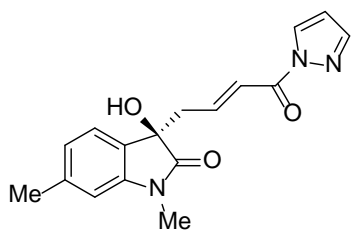
White solid, 62.0 mg, 93% yield, 85% ee; mp: 112.5-113.4 °C; $[\alpha]_D^{20} = +67.4$ (*c* 0.57, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.27 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 0.4 Hz, 1H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.34-7.29 (m, 2H), 7.19-7.12 (m, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.44 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.2 Hz, 1H), 4.57 (brs, 1H), 3.17 (s, 3H), 3.04 (ddd, *J*₁ = 14.4 Hz, *J*₂ = 7.2 Hz, *J*₃ = 1.2 Hz, 1H), 2.88 (dd, *J*₁ = 14.4 Hz, *J*₂ = 8.0 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.0, 162.4, 144.0, 144.0, 141.4, 130.9, 129.9, 128.8, 128.7, 124.8, 123.9, 109.9, 109.7, 75.7, 41.3, 26.4; IR (KBr, cm⁻¹): ν 3390, 1713, 1385, 1354, 1275, 1261, 765, 747; HRMS (ESI) calcd for C₁₆H₁₅³⁵ClN₃O₃⁺ ([M+H]⁺): 332.0797, found: 332.0794; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): *t*_R = 22.99 min (major), 45.88 min (minor).

(*S,E*)-5-bromo-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ai)



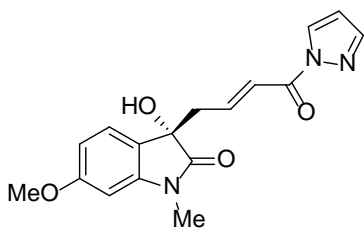
White solid, 62.6 mg, 83% yield, 85% ee; mp 151.2-152.2 °C; $[\alpha]_D^{20} +32.8$ (*c* 0.52, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.28 (d, *J* = 2.8 Hz, 1H), 7.71 (d, *J* = 0.8 Hz, 1H), 7.53 (d, *J* = 1.6 Hz, 1H), 7.46 (dd, *J*₁ = 8.4 Hz, *J*₂ = 2.0 Hz, 1H), 7.33 (d, *J* = 15.6 Hz, 1H), 7.19-7.12 (m, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.45 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.2 Hz, 1H), 3.86 (brs, 1H), 3.17 (s, 3H), 3.03 (ddd, *J*₁ = 14.0 Hz, *J*₂ = 6.8 Hz, *J*₃ = 1.2 Hz, 1H), 2.89 (ddd, *J*₁ = 14.0 Hz, *J*₂ = 8.0 Hz, *J*₃ = 0.8 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 176.7, 162.4, 144.0, 143.9, 142.0, 132.9, 131.1, 128.7, 127.5, 124.1, 116.1, 110.2, 110.0, 75.6, 41.4, 26.4; IR (KBr, cm⁻¹): ν 3390, 1713, 1643, 1609, 1385, 1354, 1201, 1098, 932, 810; HRMS (ESI) calcd for C₁₆H₁₅⁷⁹BrN₃O₃⁺ ([M+H]⁺): 376.0291, found: 376.0290; HPLC analysis (Daicel Chiralcel OD-H column, λ = 254 nm, eluent: 90:10 hexane/2-propanol, flow rate: 0.9 mL/min): *t*_R = 36.12 min (major), 32.48 min (minor).

(*S,E*)-3-hydroxy-1,6-dimethyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3aj)



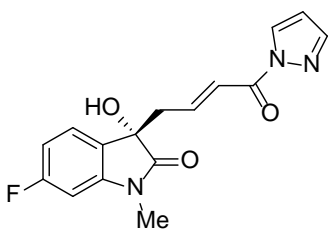
White solid, 51.3 mg, 82% yield, 98% ee; mp 190.1-190.5 °C; $[\alpha]_{\text{D}}^{20}$ -10.2 (*c* 0.42, CH₂Cl₂); ¹H NMR (400 MHz, DMSO-d₆): δ 8.43 (d, *J* = 2.8 Hz, 1H), 7.90 (d, *J* = 0.8 Hz, 1H), 7.21-7.09 (m, 3H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.63 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 6.27 (s, 1H), 3.37 (s, 1H), 3.08 (s, 3H), 2.89 (dd, *J*₁ = 14.4 Hz, *J*₂ = 5.6 Hz, 1H), 2.78 (dd, *J*₁ = 14.8 Hz, *J*₂ = 6.4 Hz, 1H), 2.32 (s, 3H); ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 176.8, 162.2, 147.0, 144.6, 143.1, 139.2, 129.2, 127.8, 123.7, 122.9, 122.1, 110.7, 109.5, 74.6, 40.8, 25.9, 21.5; IR (KBr, cm⁻¹): ν 3390, 2926, 1712, 1642, 1605, 1385, 1354, 1198, 1077; HRMS (ESI) calcd for C₁₇H₁₇N₃NaO₃⁺ ([M+Na]⁺): 334.1162, found: 334.1156; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): *t*_R = 25.35 min (major), 42.36 min (minor).

(*S,E*)-3-hydroxy-6-methoxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ak)



White solid, 57.3 mg, 88% yield, 97% ee; mp 165.7-167.4 °C; $[\alpha]_{\text{D}}^{20}$ -15.6 (*c* 0.36, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.28 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 0.8 Hz, 1H), 7.33-7.20 (m, 3H), 6.56 (dd, *J*₁ = 8.0 Hz, *J*₂ = 2.4 Hz, 1H), 6.44 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 6.40 (d, *J* = 2.0 Hz, 1H), 3.81 (s, 4H), 3.15 (s, 3H), 3.07-3.02 (m, 1H), 2.82 (dd, *J*₁ = 14.0 Hz, *J*₂ = 7.6 Hz, 1H); ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 177.1, 162.2, 160.8, 147.1, 144.6, 144.4, 129.1, 124.7, 122.5, 122.0, 110.7, 106.7, 96.4, 74.3, 55.5, 40.8, 26.0; IR (KBr, cm⁻¹): ν 3391, 1713, 1626, 1417, 1384, 1354, 1275, 1261, 1091; HRMS (ESI) calcd for C₁₇H₁₇N₃NaO₄⁺ ([M+Na]⁺): 350.1111, found: 350.1113; HPLC analysis (Daicel Chiralcel OD-H column, λ = 254 nm, eluent: 90:10 hexane/2-propanol, flow rate: 0.9 mL/min): *t*_R = 34.51 min (major), 40.09 min (minor).

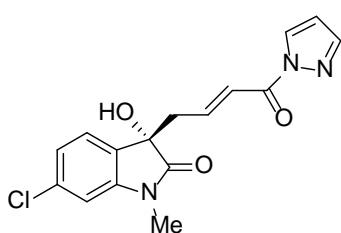
(*S,E*)-6-fluoro-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3al)



White solid, 61.3 mg, 97% yield, 96% ee; mp 182.9-183.7 °C; $[\alpha]_{\text{D}}^{20}$ -12.7 (*c* 0.47, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.29 (d, *J* = 2.8 Hz, 1H), 7.71 (d, *J* = 0.8 Hz, 1H), 7.36-7.30 (m, 2H), 7.25-7.18 (m, 1H), 6.80- 6.75 (m, 1H), 6.59 (dd, *J*₁ = 8.8 Hz, *J*₂ = 2.4 Hz, 1H), 6.45 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz,

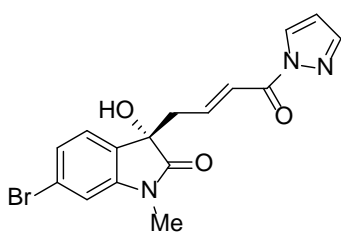
1H), 3.47 (brs, 1H), 3.18 (s, 3H), 3.04 (ddd, $J_1 = 14.0$ Hz, $J_2 = 6.4$ Hz, $J_3 = 1.2$ Hz, 1H), 2.86-2.81 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 177.4, 164.1(d, $J = 246.3$ Hz), 162.5, 144.8, 144.3, 144.0, 128.7, 125.7 (d, $J = 9.8$ Hz), 124.5 (d, $J = 3.1$ Hz), 123.9, 110.0, 109.4 (d, $J = 22.4$ Hz), 97.9, 75.2, 41.5, 26.5; IR (KBr, cm^{-1}): ν 3396, 1713, 1614, 1505, 1384, 1354, 1197, 1133, 1076; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}\text{FN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 338.0911, found: 338.0907; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_{\text{R}} = 19.57$ min (major), 30.82 min (minor).

(*S,E*)-6-chloro-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3am)



White solid, 61.8 mg, 93% yield, 93% ee; mp 138.0-139.5 °C; $[\alpha]_{\text{D}}^{20} -59.7$ (c 0.38, CH_2Cl_2); ^1H NMR (400 MHz, DMSO-d_6): δ 8.44 (d, $J = 2.8$ Hz, 1H), 7.90 (d, $J = 0.8$ Hz, 1H), 7.31 (d, $J = 8.0$ Hz, 1H), 7.22-7.12 (m, 3H), 7.10 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.6$ Hz, 1H), 6.63 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.6$ Hz, 1H), 6.44 (s, 1H), 3.11 (s, 3H), 2.91 (dd, $J_1 = 14.0$ Hz, $J_2 = 5.6$ Hz, 1H), 2.81 (dd, $J_1 = 14.0$ Hz, $J_2 = 6.4$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO-d_6): δ 176.6, 162.1, 146.4, 144.6, 144.6, 134.0, 129.5, 129.1, 125.3, 122.4, 122.1, 110.7, 109.3, 74.3, 40.4, 26.2; IR (KBr, cm^{-1}): ν 3372, 3005, 1713, 1643, 1463, 1385, 1275, 1260, 1199, 1115, 764; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}^{35}\text{ClN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 354.0616, found: 354.0618; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_{\text{R}} = 29.34$ min (major), 42.58 min (minor).

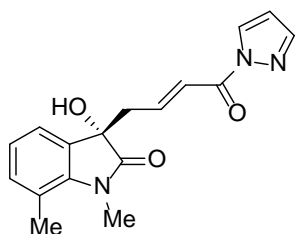
(*S,E*)-6-bromo-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3an)



White solid, 61.9 mg, 82% yield, 90% ee; mp 178.5-179.4 °C; $[\alpha]_{\text{D}}^{20} -25.8$ (c 0.51, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ 8.27 (d, $J = 2.8$ Hz, 1H), 7.69 (d, $J = 0.8$ Hz, 1H), 7.31 (d, $J = 15.6$ Hz, 1H), 7.26-7.18 (m, 3H), 6.98 (d, $J = 1.2$ Hz, 1H), 6.44 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.2$ Hz, 1H), 4.19 (brs, 1H), 3.15 (s, 3H), 3.04 (ddd, $J_1 = 14.0$ Hz, $J_2 = 6.8$ Hz, $J_3 = 0.8$ Hz, 1H), 2.81 (dd, $J_1 = 14.0$ Hz, $J_2 = 7.6$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 177.2, 162.4, 144.3, 144.2, 144.0, 128.7, 128.1, 126.1, 125.6, 123.8, 123.6, 112.2, 110.0, 75.3, 41.3, 26.4; IR (KBr, cm^{-1}): ν 3390, 1712, 1607, 1417, 1385, 1354, 1275, 1261, 764, 750; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}^{79}\text{BrN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 398.0111, found: 398.0110; HPLC analysis (Daicel Chiralcel OD-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/2-propanol, flow rate:

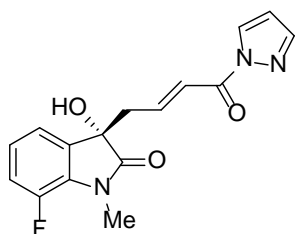
0.9 mL/min): $t_R = 31.35$ min (major), 34.43 min (minor).

(*S,E*)-3-hydroxy-1,7-dimethyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ao)



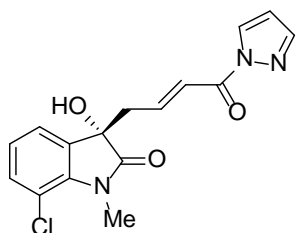
White solid, 50.3 mg, 81% yield, 96% ee; mp 137.6-137.6 °C; $[\alpha]_D^{20} -13.7$ (c 0.48, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ 8.26 (d, $J = 2.8$ Hz, 1H), 7.67 (d, $J = 0.4$ Hz, 1H), 7.31-7.27 (m, 1H), 7.25-7.18 (m, 2H), 7.04 (d, $J = 7.6$ Hz, 1H), 6.96 (t, $J = 7.6$ Hz, 1H), 6.42 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.6$ Hz, 1H), 4.16 (brs, 1H), 3.43 (s, 3H), 3.05-3.00 (m, 1H), 2.86 (dd, $J_1 = 14.0$ Hz, $J_2 = 8.0$ Hz, 1H), 2.52 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 178.0, 162.5, 144.9, 143.8, 140.5, 133.6, 129.9, 128.6, 123.3, 123.2, 122.1, 120.3, 109.8, 74.9, 41.8, 29.7, 18.9; IR (KBr, cm^{-1}): ν 3390, 1712, 1385, 1353, 1274, 1261, 1197, 1077; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{17}\text{N}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 334.1162, found: 334.1166; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_R = 33.76$ min (major), 54.40 min (minor).

(*S,E*)-7-fluoro-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ap)



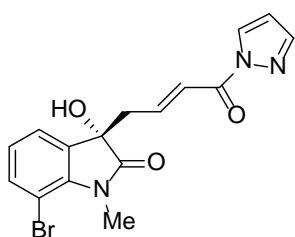
White solid, 58.6 mg, 93% yield, 89% ee; mp 154.2-154.3 °C; $[\alpha]_D^{20} +17.1$ (c 0.42, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ 8.27 (d, $J = 2.8$ Hz, 1H), 7.69 (d, $J = 0.8$ Hz, 1H), 7.31 (d, $J = 15.6$ Hz, 1H), 7.23-7.12 (m, 2H), 7.02 (dt, $J_1 = 8.8$ Hz, $J_2 = 2.4$ Hz, 1H), 6.77 (dd, $J_1 = 8.4$ Hz, $J_2 = 4.0$ Hz, 1H), 6.44 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.6$ Hz, 1H), 4.44 (brs, 1H), 3.17 (s, 3H), 3.05 (ddd, $J_1 = 14.4$ Hz, $J_2 = 6.8$ Hz, $J_3 = 1.2$ Hz, 1H), 2.89-2.84 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 177.2, 162.4, 159.5 (d, $J = 240.9$ Hz), 144.2, 144.0, 138.7 (d, $J = 1.9$ Hz), 130.9 (d, $J = 7.9$ Hz), 128.7, 123.9, 116.1 (d, $J = 23.5$ Hz), 112.5 (d, $J = 24.9$ Hz), 109.9, 109.4, 75.8, 41.4, 26.4; IR (KBr, cm^{-1}): ν 3382, 1712, 1643, 1623, 1495, 1385, 1354, 1275, 1198, 1105; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{14}\text{FN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 338.0911, found: 338.0903; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_R = 26.50$ min (major), 42.25 min (minor).

(*S,E*)-7-chloro-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3aq)



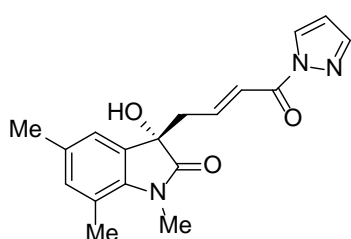
White solid, 56.4 mg, 85% yield, 84% ee; mp 116.3-118.1 °C; $[\alpha]_{\text{D}}^{20} +45.3$ (*c* 0.23, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.27 (d, *J* = 2.8 Hz, 1H), 7.68 (s, 1H), 7.32-7.18 (m, 4H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.44 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 4.64 (brs, 1H), 3.54 (s, 3H), 3.04 (dd, *J*₁ = 14.0 Hz, *J*₂ = 6.0 Hz, 1H), 2.83 (dd, *J*₁ = 14.0 Hz, *J*₂ = 8.0 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.8, 162.4, 144.3, 143.9, 138.7, 132.1, 132.1, 128.7, 124.2, 123.8, 122.8, 116.1, 110.0, 75.1, 41.5, 29.7; IR (KBr, cm⁻¹): ν 3391, 1713, 1611, 1495, 1385, 1354, 1275, 1201, 1070, 932; HRMS (ESI) calcd for C₁₆H₁₄³⁵ClN₃NaO₃⁺ ([M+Na]⁺): 354.0616, found: 354.0620; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): *t*_R = 22.00 min (major), 29.08 min (minor).

(*S,E*)-7-bromo-3-hydroxy-1-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ar)



White solid, 61.5 mg, 82% yield, 85% ee; mp 130.1-130.5 °C; $[\alpha]_{\text{D}}^{20} -12.7$ (*c* 0.33, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.28 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 0.8 Hz, 1H), 7.43 (dd, *J*₁ = 8.4 Hz, *J*₂ = 1.2 Hz, 1H), 7.33 (dd, *J*₁ = 7.2 Hz, *J*₂ = 0.8 Hz, 1H), 7.28 (d, *J* = 6.4 Hz, 1H), 7.26-7.18 (m, 1H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.44 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 4.22 (brs, 1H), 3.57 (s, 3H), 3.05-3.00 (m, 1H), 2.83 (dd, *J*₁ = 14.4 Hz, *J*₂ = 8.0 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.9, 162.4, 144.2, 144.30, 140.2, 135.5, 132.4, 128.7, 124.6, 123.9, 123.4, 109.9, 102.9, 75.0, 41.6, 30.0; IR (KBr, cm⁻¹): ν 3363, 3005, 1713, 1643, 1458, 1385, 1275, 1261, 1199, 1099, 764; HRMS (ESI) calcd for C₁₆H₁₄⁷⁹BrN₃NaO₃⁺ ([M+Na]⁺): 398.0111, found: 398.0105; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): *t*_R = 22.32 min (major), 29.24 min (minor).

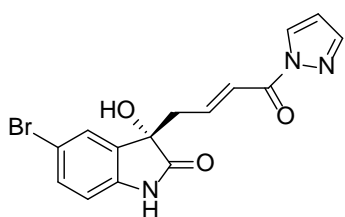
(*S,E*)-3-hydroxy-1,5,7-trimethyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3as)



White solid, 53.6 mg, 82% yield, 97% ee; mp 169.7-170.7 °C; $[\alpha]_{\text{D}}^{20} +34.7$ (*c* 0.50, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.27 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 0.8 Hz, 1H), 7.30 (d, *J* = 15.6 Hz, 1H), 7.21-7.14 (m, 1H), 7.05 (s, 1H), 6.85 (s, 1H), 6.43 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 3.96 (brs, 1H), 3.41 (s, 3H), 3.00 (ddd, *J*₁ = 14.4 Hz, *J*₂ = 6.8 Hz, *J*₃ = 1.2 Hz, 1H), 2.91-2.85

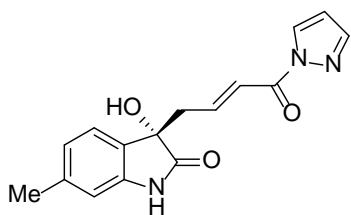
(m, 1H), 2.48 (s, 3H), 2.26 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 177.8, 162.5, 145.2, 143.8, 138.1, 134.1, 132.8, 130.0, 128.6, 123.3, 122.7, 120.0, 109.8, 75.0, 41.8, 29.6, 20.7, 18.7; IR (KBr, cm^{-1}): ν 3312, 2922, 1713, 1690, 1640, 1385, 1275, 1261, 764; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{20}\text{N}_3\text{O}_3^+$ ($[\text{M}+\text{H}]^+$): 326.1499, found: 326.1501; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_{\text{R}} = 115.27$ min (major), 107.91 min (minor).

(*S,E*)-5-bromo-3-hydroxy-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3at)



White solid, 57.8 mg, 80% yield, 82% ee; mp 157.3-157.9 °C; $[\alpha]_{\text{D}}^{20} +7.3$ (c 0.49, CH_2Cl_2); ^1H NMR (400 MHz, DMSO-d_6): δ 10.51 (s, 1H), 8.44 (d, $J = 2.8$ Hz, 1H), 7.91 (d, $J = 1.2$ Hz, 1H), 7.45 (d, $J = 2.0$ Hz, 1H), 7.40 (dd, $J_1 = 8.4$ Hz, $J_2 = 2.0$ Hz, 1H), 7.22 (d, $J = 15.6$ Hz, 1H), 7.10-7.02 (m, 1H), 6.79 (d, $J = 8.4$ Hz, 1H), 6.64 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.6$ Hz, 1H), 6.41 (s, 1H), 2.92 (ddd, $J_1 = 14.4$ Hz, $J_2 = 6.8$ Hz, $J_3 = 1.2$ Hz, 1H), 2.84 (dd, $J_1 = 14.4$ Hz, $J_2 = 7.6$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO-d_6): δ 177.8, 162.2, 146.4, 144.6, 140.8, 133.8, 132.1, 129.1, 127.2, 122.4, 113.5, 111.9, 110.7, 75.0, 40.4; IR (KBr, cm^{-1}): ν 3282, 2359, 1714, 1642, 1385, 1355, 1275, 1261, 1197, 764; HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{12}^{79}\text{BrN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 383.9954, found: 383.9952; HPLC analysis (Daicel Chiralcel OD-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/2-propanol, flow rate: 0.9 mL/min): $t_{\text{R}} = 24.44$ min (major), 27.72 min (minor).

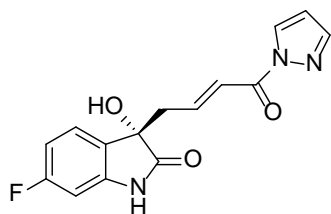
(*S,E*)-3-hydroxy-6-methyl-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3au)



White solid, 47.5 mg, 80% yield, 96% ee; mp 166.6-167.2 °C; $[\alpha]_{\text{D}}^{20} +19.4$ (c 0.41, CH_2Cl_2); ^1H NMR (400 MHz, DMSO-d_6): δ 10.32 (s, 1H), 8.43 (d, $J = 2.8$ Hz, 1H), 7.90 (d, $J = 0.8$ Hz, 1H), 7.22-7.16 (m, 2H), 7.12-7.07 (m, 1H), 6.63 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.6$ Hz, 1H), 6.52 (dd, $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz, 1H), 6.37 (d, $J = 2.0$ Hz, 1H), 6.16 (s, 1H), 3.72 (s, 3H), 2.88 (dd, $J_1 = 14.4$ Hz, $J_2 = 6.4$ Hz, 1H), 2.76 (dd, $J_1 = 14.0$ Hz, $J_2 = 8.0$ Hz, 1H), $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO-d_6): δ 178.8, 162.2, 160.5, 147.2, 144.6, 142.8, 129.2, 125.2, 123.2, 122.1, 110.7, 106.5, 96.8, 74.7, 55.3, 40.9; IR (KBr, cm^{-1}): ν 3381, 2923, 1712, 1642, 1499, 1385, 1198, 1095, 933; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{15}\text{N}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 320.1006, found: 320.1011; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_{\text{R}} = 97.87$ min (major), 139.61 min (minor).

(*S,E*)-6-fluoro-3-hydroxy-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one

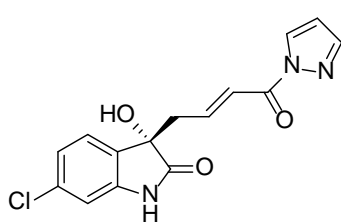
(3av)



White solid, 58.9 mg, 98% yield, 84% ee; mp 176.5-176.6 °C; $[\alpha]_D^{20} +23.6$ (*c* 0.37, CH₂Cl₂); ¹H NMR (400 MHz, DMSO-d₆): δ 10.54 (s, 1H), 8.43 (d, *J* = 2.8 Hz, 1H), 7.9 (s, 1H), 7.29 (dd, *J*₁ = 8.0 Hz, *J*₂ = 5.6 Hz, 1H), 7.2 (d, *J* = 15.6 Hz, 1H), 7.13-7.06 (m, 1H), 6.80-6.75 (m, 1H), 6.66-6.63 (m, 2H), 6.34 (s, 1H), 2.90 (dd, *J*₁ = 14.4 Hz, *J*₂ = 6.4 Hz, 1H), 2.80 (dd, *J*₁ = 14.0 Hz, *J*₂ = 8.0 Hz, 1H); ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 178.6, 162.9 (d, *J* = 241.5 Hz), 162.2, 146.7, 144.7, 143.3 (d, *J* = 12.4 Hz), 129.2, 127.3 (d, *J* = 2.6 Hz), 125.9 (d, *J* = 10.0 Hz), 122.3, 110.8, 108.0 (d, *J* = 22.3 Hz), 98.3, 74.6, 40.6; IR (KBr, cm⁻¹): ν 3281, 1721, 1626, 1386, 1275, 1141, 930, 764; HRMS (ESI) calcd for C₁₅H₁₂FN₃NaO₃⁺ ([M+Na]⁺): 324.0755, found: 324.0758; Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): *t*_R = 105.75 min (major), 74.61 min (minor).

(*S,E*)-6-chloro-3-hydroxy-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one

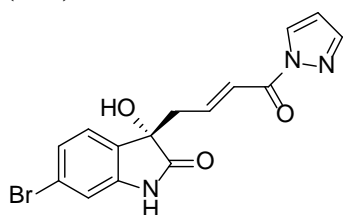
(3aw)



White solid, 57.4 mg, 90% yield, 90% ee; mp 181.7-182.9 °C; $[\alpha]_D^{20} +13.3$ (*c* 0.45, CH₂Cl₂); ¹H NMR (400 MHz, DMSO-d₆): δ 10.53 (s, 1H), 8.43 (d, *J* = 2.8 Hz, 1H), 7.90 (d, *J* = 0.8 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 15.6 Hz, 1H), 7.14-7.06 (m, 1H), 7.03 (dd, *J*₁ = 8.0 Hz, *J*₂ = 2.0 Hz, 1H), 6.84 (d, *J* = 2.0 Hz, 1H), 6.63 (dd, *J*₁ = 2.8 Hz, *J*₂ = 1.6 Hz, 1H), 6.38 (s, 1H), 2.93-2.87 (m, 1H), 2.80 (dd, *J*₁ = 14.4 Hz, *J*₂ = 8.0 Hz, 1H); ¹³C{¹H} NMR (100 MHz, DMSO-d₆): δ 178.3, 162.2, 146.5, 144.6, 143.0, 133.6, 130.2, 129.1, 125.8, 122.4, 121.6, 110.7, 110.0, 74.6, 40.5; IR (KBr, cm⁻¹): ν 3006, 1715, 1385, 1275, 1261, 1197, 1133, 1076, 764, 750; HRMS (ESI) calcd for C₁₅H₁₂³⁵ClN₃NaO₃⁺ ([M+Na]⁺): 340.0459, found: 340.0451; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): *t*_R = 23.19 min (major), 35.14 min (minor).

(*S,E*)-6-bromo-3-hydroxy-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one

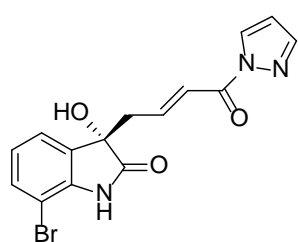
(3ax)



White solid, 55.2 mg, 76% yield, 90% ee; mp 186.6-186.8 °C; $[\alpha]_D^{20} -22.6$ (*c* 0.52, CH₂Cl₂); ¹H NMR (400 MHz, DMSO-d₆): δ 10.51 (s, 1H), 8.44 (d, *J* = 2.4 Hz, 1H), 7.90 (d, *J* = 0.8 Hz, 1H), 7.23-7.16 (m, 3H), 7.13-7.06 (m, 1H),

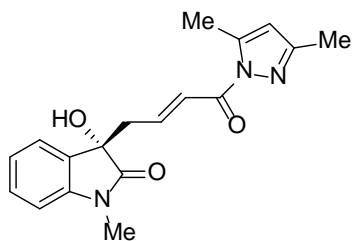
6.97 (d, $J = 1.6$ Hz, 1H), 6.64 (dd, $J_1 = 2.8$ Hz, $J_2 = 1.6$ Hz, 1H), 6.37 (s, 1H), 2.89 (dd, $J_1 = 14.8$ Hz, $J_2 = 6.8$ Hz, 1H), 2.79 (dd, $J_1 = 14.4$ Hz, $J_2 = 8.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6): δ 178.1, 162.1, 146.4, 144.6, 143.2, 130.6, 129.1, 126.1, 124.5, 122.4, 121.9, 112.7, 110.7, 74.7, 40.4; IR (KBr, cm^{-1}): ν 3313, 1715, 1612, 1385, 1354, 1275, 1261, 1198, 1077, 764; HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{12}^{79}\text{BrN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 383.9954, found: 383.9959; HPLC analysis (Daicel Chiralcel OD-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/2-propanol, flow rate: 0.9 mL/min): $t_{\text{R}} = 25.55$ min (major), 41.26 min (minor).

(*S,E*)-7-bromo-3-hydroxy-3-(4-oxo-4-(1*H*-pyrazol-1-yl)but-2-en-1-yl)indolin-2-one (3ay)



White solid, 53.4 mg, 74% yield, 79% ee; mp 131.7-131.9 °C; $[\alpha]_{\text{D}}^{20} +37.1$ (c 0.53, CH_2Cl_2); ^1H NMR (400 MHz, DMSO- d_6): δ 10.69 (s, 1H), 8.44 (d, $J = 2.4$ Hz, 1H), 7.90 (d, $J = 0.8$ Hz, 1H), 7.42 (dd, $J_1 = 8.0$ Hz, $J_2 = 0.8$ Hz, 1H), 7.28 (d, $J = 7.2$ Hz, 1H), 7.22 (d, $J = 15.6$ Hz, 1H), 7.16-7.09 (m, 1H), 6.95 (t, $J = 8.0$ Hz, 1H), 6.64 (dd, $J_1 = 2.4$ Hz, $J_2 = 1.2$ Hz, 1H), 6.44 (s, 1H), 2.93-2.88 (m, 1H), 2.82 (dd, $J_1 = 14.4$ Hz, $J_2 = 7.6$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6): δ 178.2, 162.2, 146.5, 144.6, 140.9, 133.3, 132.2, 129.2, 123.7, 123.4, 122.4, 110.7, 102.3, 75.7, 40.6; IR (KBr, cm^{-1}): ν 3285, 1721, 1626, 1502, 1461, 1386, 1275, 1200, 1141, 765; HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{12}^{79}\text{BrN}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 383.9954, found: 383.9956; HPLC analysis (Daicel Chiralcel OD-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/2-propanol, flow rate: 0.9 mL/min): $t_{\text{R}} = 19.26$ min (major), 31.11 min (minor).

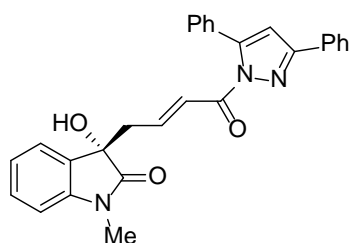
(*S,E*)-3-(4-(3,5-dimethyl-1*H*-pyrazol-1-yl)-4-oxobut-2-en-1-yl)-3-hydroxy-1-methylindolin-2-one (3ba)



White solid, 60.3 mg, 93% yield, 81% ee; mp 175.6-177.3 °C; $[\alpha]_{\text{D}}^{20} +12.1$ (c 0.42, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ 7.40 (d, $J = 7.2$ Hz, 1H), 7.34-7.30 (m, 2H), 7.12-7.04 (m, 2H), 6.83 (dd, $J_1 = 7.6$ Hz, $J_2 = 4.0$ Hz, 1H), 5.95 (s, 1H), 4.17 (brs, 1H), 3.18 (d, $J = 7.2$ Hz, 3H), 3.04 (ddd, $J_1 = 14.0$ Hz, $J_2 = 6.8$ Hz, $J_3 = 1.2$ Hz, 1H), 2.81 (dd, $J_1 = 14.0$ Hz, $J_2 = 8.0$ Hz, 1H), 2.52 (s, 3H), 2.21 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 177.2, 164.4, 151.9, 144.3, 143.0, 142.5, 129.9, 129.1, 125.5, 124.3, 123.3, 111.4, 108.6, 75.6, 41.4, 26.3, 14.5, 13.7; IR (KBr, cm^{-1}): ν 3391, 2924, 1712, 1643, 1614, 1468, 1385, 1354, 1275, 1197, 1078; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{19}\text{N}_3\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 348.1319, found: 348.1322; HPLC

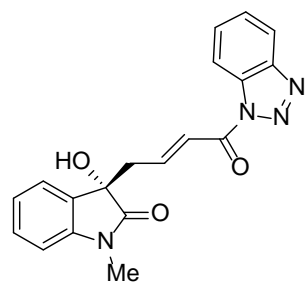
analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_R = 38.77$ min (major), 33.95 min (minor).

(*S,E*)-3-(4-(3,5-diphenyl-1*H*-pyrazol-1-yl)-4-oxobut-2-en-1-yl)-3-hydroxy-1-methylindolin-2-one (3ca)



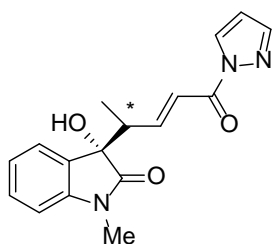
White solid, 79.2 mg, 88% yield, 92% ee; mp 187.3-187.5 °C; $[\alpha]_D^{20} +7.9$ (*c* 0.60, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 7.90-7.88 (m, 2H), 7.53 (d, *J* = 15.6 Hz, 1H), 7.47-7.38 (m, 9H), 7.32 (dt, *J*₁ = 8.0 Hz, *J*₂ = 0.8 Hz, 1H), 7.10-6.99 (m, 2H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.72 (s, 1H), 3.28 (s, 1H), 3.17 (s, 3H), 3.08 (ddd, *J*₁ = 14.0 Hz, *J*₂ = 6.8 Hz, *J*₃ = 1.2 Hz, 1H), 2.88 (ddd, *J*₁ = 14.0 Hz, *J*₂ = 8.4 Hz, *J*₃ = 0.4 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.1, 163.5, 153.4, 147.5, 143.3, 143.0, 131.6, 131.2, 130.0, 129.2, 128.9, 128.7, 127.8, 126.3, 125.5, 124.3, 123.3, 110.1, 108.7, 75.6, 41.5, 26.3; IR (KBr, cm⁻¹): ν 3331, 2351, 1701, 1621, 1381, 1351, 1091, 1071, 930, 779; HRMS (ESI) calcd for C₂₈H₂₃N₃NaO₃⁺ ([M+Na]⁺): 472.1632, found: 472.1637; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_R = 59.25$ min (major), 32.11 min (minor).

(*S,E*)-3-(4-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)-4-oxobut-2-en-1-yl)-3-hydroxy-1-methylindolin-2-one (3da)



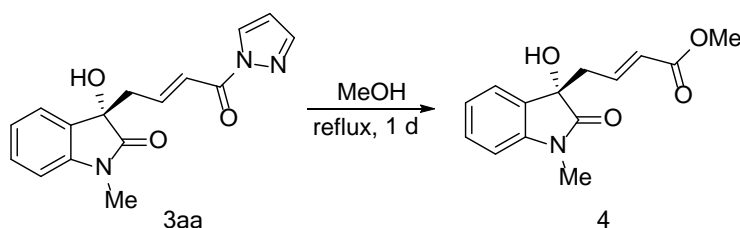
White solid, 63.9 mg, 92% yield, 88% ee; mp 173.5-175.1 °C; $[\alpha]_D^{20} +41.8$ (*c* 0.42, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.30 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.66-7.62 (m, 1H), 7.56-7.40 (m, 4H), 7.34 (dt, *J*₁ = 8.0 Hz, *J*₂ = 0.8 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 3.70 (s, 1H), 3.22 (s, 3H), 3.14 (ddd, *J*₁ = 14.0 Hz, *J*₂ = 6.8 Hz, *J*₃ = 0.8 Hz, 1H), 2.94 (dd, *J*₁ = 14.0 Hz, *J*₂ = 7.6 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.2, 162.9, 146.1, 142.9, 131.3, 130.3, 130.1, 129.0, 126.2, 124.2, 124.0, 123.4, 120.1, 114.6, 108.8, 75.6, 41.6, 26.4; IR (KBr, cm⁻¹): ν 3382, 3005, 1705, 1639, 1615, 1471, 1377, 1353, 1275, 1261; HRMS (ESI) calcd for C₁₉H₁₆N₄NaO₃⁺ ([M+Na]⁺): 371.1115, found: 371.1117; HPLC analysis (Daicel Chiralpak AS-H column, $\lambda = 254$ nm, eluent: 90:10 hexane/EtOH, flow rate: 0.7 mL/min): $t_R = 49.99$ min (major), 56.11 min (minor).

(3*S*)-3-hydroxy-1-methyl-3-((*E*)-5-oxo-5-(1*H*-pyrazol-1-yl)pent-3-en-2-yl)indolin-2-one (3ga)



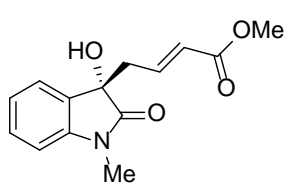
White solid, 52.9 mg, 85% yield, 98% ee, 96:4 dr; mp 146.1-147.3 °C; 96:4 dr, 98% ee; $[\alpha]_{\text{D}}^{20}$ -46.0 (*c* 0.30, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.26 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 0.8 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.36-7.30 (m, 2H), 7.16-7.09 (m, 2H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.43 (dd, *J*₁ = 1.6 Hz, *J*₂ = 2.8 Hz, 1H), 3.19-3.11 (m, 4H), 1.21 (d, *J* = 6.8 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.0, 162.6, 150.7, 143.9, 134.5, 130.0, 128.6, 128.4, 124.3, 123.1, 121.6, 109.8, 108.5, 78.2, 45.4, 26.1, 13.3; HRMS (EI) calcd for C₁₄H₁₅NO₄⁺ ([M]⁺): 311.1264, found: 311.1267; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 87.5:12.5 hexane/EtOH, flow rate: 0.9 mL/min): *t*_R = 31.83 min (major), 70.96 min (minor).

3. Esterification of Product 3aa



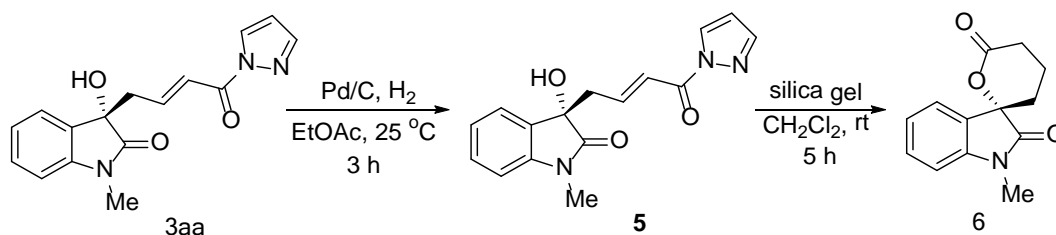
Compound **3aa** (99% ee, 0.2 mmol) and methanol (5 mL) were added to a reaction tube, and the solution was stirred under reflux for 1 day (monitored by TLC). The solvent was concentrated, and the residue was purified by column chromatography on silica gel (5:1 CH₂Cl₂/EtOAc) to provide product **4**.

methyl (*S,E*)-4-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)but-2-enoate (4)



Liquid, 89.7 mg, 99% yield, 99% ee; $[\alpha]_{\text{D}}^{20}$ -30.2 (*c* 0.31, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 7.37-7.28 (m, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.88-6.80 (m, 2H), 5.84 (d, *J* = 15.6 Hz, 1H), 4.06 (brs, 1H), 3.68 (s, 3H), 3.15 (s, 3H), 2.91 (ddd, *J*₁ = 14.0 Hz, *J*₂ = 6.8 Hz, *J*₃ = 1.6 Hz, 1H), 2.68 (dd, *J*₁ = 14.0 Hz, *J*₂ = 8.4 Hz, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 177.3, 166.3, 142.8, 141.2, 129.8, 129.2, 125.2, 124.1, 123.2, 108.6, 75.5, 51.5, 40.8, 26.2; IR (KBr, cm⁻¹): ν 3370, 3058, 2950, 1701, 1612, 1468, 1276, 1090, 980, 756; HRMS (EI) calcd for C₁₄H₁₅NO₄⁺ ([M]⁺): 261.0996, found: 261.1004; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 85:5 hexane/EtOH, flow rate: 0.9 mL/min): *t*_R = 32.38 min (major), 39.73 min (minor).

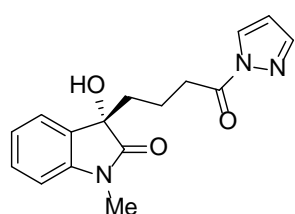
4. Transformation of Product 3aa to Spirolactone 6



Compound **3aa** (99% ee, 0.2 mmol) was dissolved in 2 mL EtOAc, and 20 mol% Pd catalyst (10% w/w Pd/C, 42.6 mg) was added at room temperature. The mixture was stirred under an atmosphere of hydrogen for 3 hours (monitored by TLC). After the reaction was completed, the resulting mixture was filtered through a celite pad, and washed with CH₂Cl₂. The filtrate was concentrated, and provided product **5** with quantitative yield and excellent enantioselectivity (99% ee).

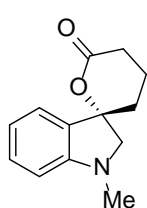
Next, compound **5** (0.2 mmol), silica gel (4.0 g) and CH₂Cl₂ (30 mL) were added to a round bottom flask with a magnetic stir bar. The mixture was stirred at room temperature for 5 hours (monitored by TLC). After the reaction was completed, the resulting mixture was filtered through a silica pad, and washed with CH₂Cl₂. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel (10:1 CH₂Cl₂/EtOAc) to provide spiro lactone **6**.

(S)-3-hydroxy-1-methyl-3-(4-oxo-4-(1H-pyrazol-1-yl)butyl)indolin-2-one (**5**)



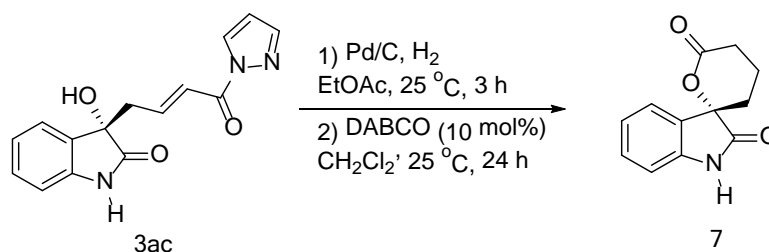
Liquid, 59.9 mg, quantitative yield, 99% ee; $[\alpha]_D^{20}$ -30.8 (*c* 0.41, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 8.10 (d, *J* = 2.8 Hz, 1H), 7.56 (s, 1H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.31 (t, *J* = 0.8 Hz, 1H), 3.93 (brs, 1H), 3.09 (s, 3H), 3.00 (t, *J* = 7.6 Hz, 1H), 2.06-1.91 (m, 2H), 1.62-1.51 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 178.2, 171.4, 143.8, 143.2, 129.9, 129.5, 128.1, 123.9, 123.1, 109.4, 108.4, 76.2, 37.4, 33.6, 26.1, 18.0; IR (KBr, cm⁻¹): ν 3384, 3137, 3058, 2947, 1701, 1617, 1384, 1201, 1089, 922; HRMS (EI) for calcd for C₁₆H₁₇N₃O₃⁺ ([M]⁺): 299.1264, found: 299.1268; HPLC analysis (Daicel Chiralpak AS-H column, λ = 254 nm, eluent: 87.5:12.5 hexane/EtOH, flow rate: 0.9 mL/min): *t*_R = 35.75 min (major), 44.19 min (minor).

(S)-1-methyl-4',5'-dihydrospiro[indoline-3,2'-pyran]-6'(3'H)-one (6)



White solid, 46.1 mg, 77% yield, 99% ee; mp 158.8-162.9 °C; $[\alpha]_D^{20}$ -98.9 (*c* 0.21, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ 7.39-7.34 (m, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 3.18 (s, 3H), 2.94-2.86 (m, 1H), 2.71-2.56 (m, 2H), 2.21-2.13 (m, 1H), 2.08-2.02 (m, 1H), 1.98-1.91 (m, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 173.8, 169.9, 142.9, 130.6, 128.0, 123.8, 123.3, 108.6, 81.6, 29.4, 29.3, 26.3, 15.5; IR (KBr, cm⁻¹): ν 2960, 2920, 1720, 1612, 1377, 1322, 1245, 1038, 994, 760; HRMS (EI) calcd for C₁₃H₁₃NO₃⁺ ([M]⁺): 231.0890, found: 231.0898; HPLC analysis (Daicel Chiralcel OD-H column, λ = 254 nm, eluent: 80:20 hexane/EtOH, flow rate: 0.9 mL/min): *t*_R = 27.41 min (major), 35.61 min (minor).

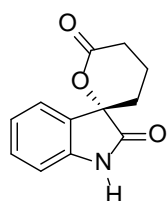
5. Transformation of Product 3ac to Spirolactone 7



Compound **3ac** (95% ee, 0.5 mmol) was dissolved in 5 mL EtOAc, and 20 mol% Pd catalyst (10% w/w Pd/C, 106.4 mg, 0.10 mmol) was added at room temperature. The mixture was stirred under an atmosphere of hydrogen for 3 hours (monitored by TLC). After the reaction was completed, the resulting mixture was filtered through a celite pad, and washed with CH₂Cl₂. After removing the solvent under reduced pressure, the crude reduction product was used directly.

Then, DABCO (5.6 mg, 0.05 mmol) was added to a solution of the crude product in CH₂Cl₂ (5.0 mL), and the mixture stirred at 25 °C for 24 hours (monitored by TLC). After removing the solvent under reduced pressure, the residue was purified by column chromatography (5:1 CH₂Cl₂/EtOAc) to get spiro lactone **7**.

(S)-4',5'-dihydrospiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (7)



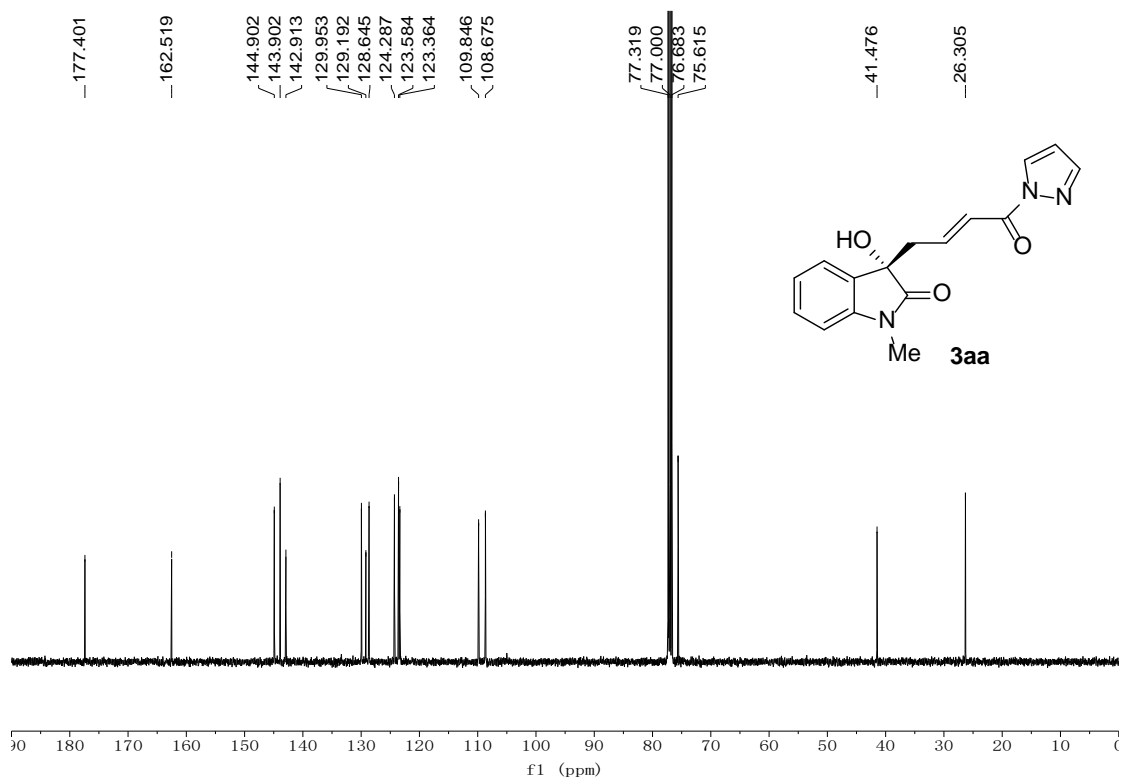
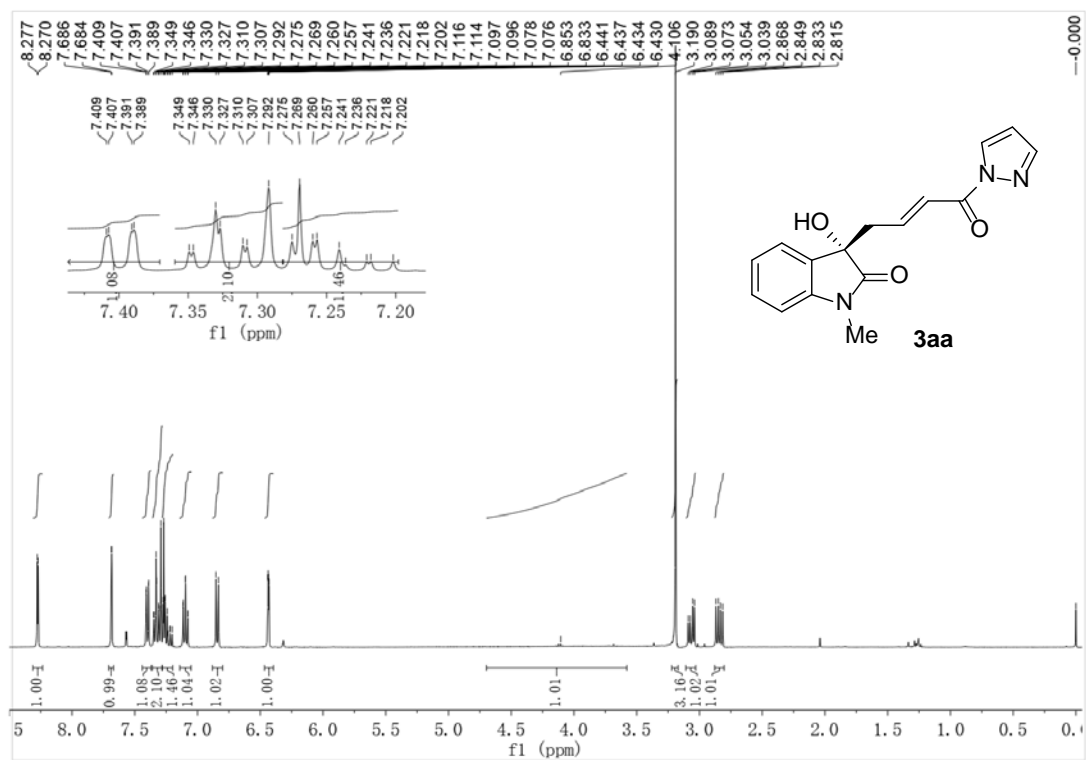
Colorless oil, 94.1 mg, 87% yield, 97% ee; $[\alpha]_D^{25}$ -85.1 (*c* 1.34, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 8.82 (s, H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.30-7.26 (m, 1H), 7.09-7.05 (m, 1H), 6.92-6.89 (m, 1H), 2.94-2.87 (m, 1H), 2.73-2.65 (m, 1H), 2.63-2.52 (m, 1H), 2.20-2.05 (m, 2H), 2.01-1.92 (m, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 176.1, 170.2, 140.1, 130.6, 128.5, 124.2, 123.3, 110.7, 82.1, 29.6, 29.4, 15.5; HPLC analysis (Daicel Chiralpak AS-

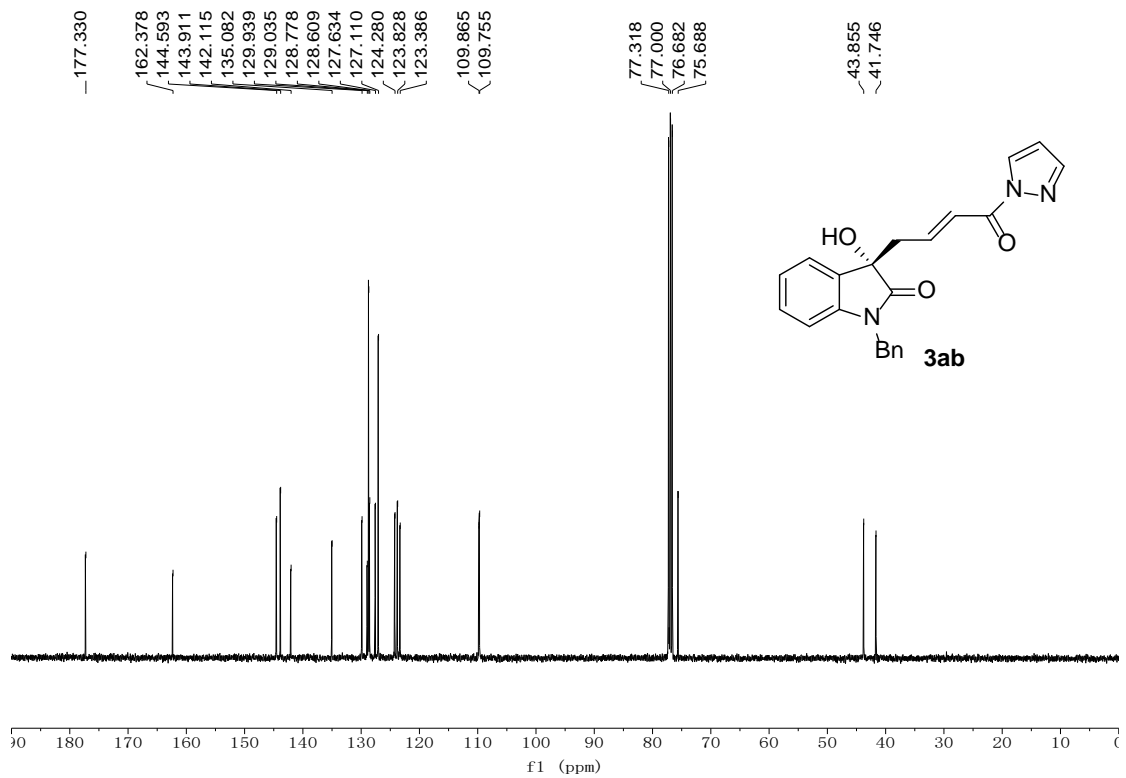
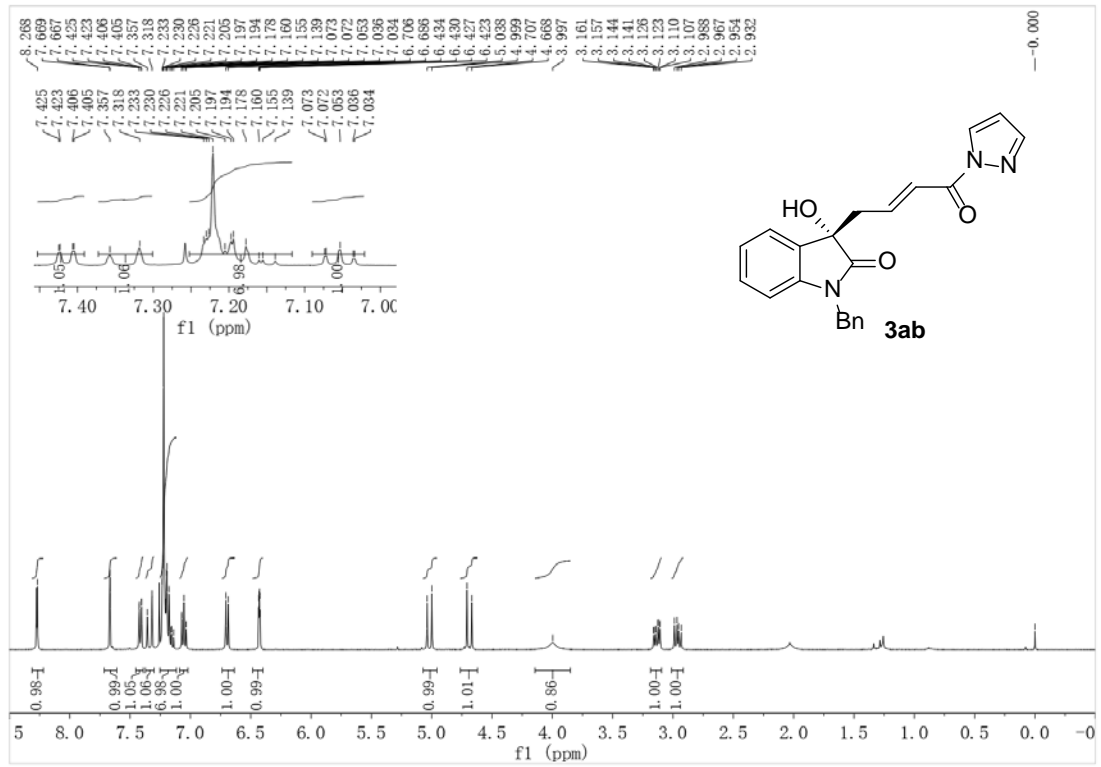
H column, $\lambda = 254$ nm, eluent: 70:30 hexane/2-propanol, flow rate: 0.9 mL/min): $t_R = 25.92$ min (major), 23.85 min (minor).

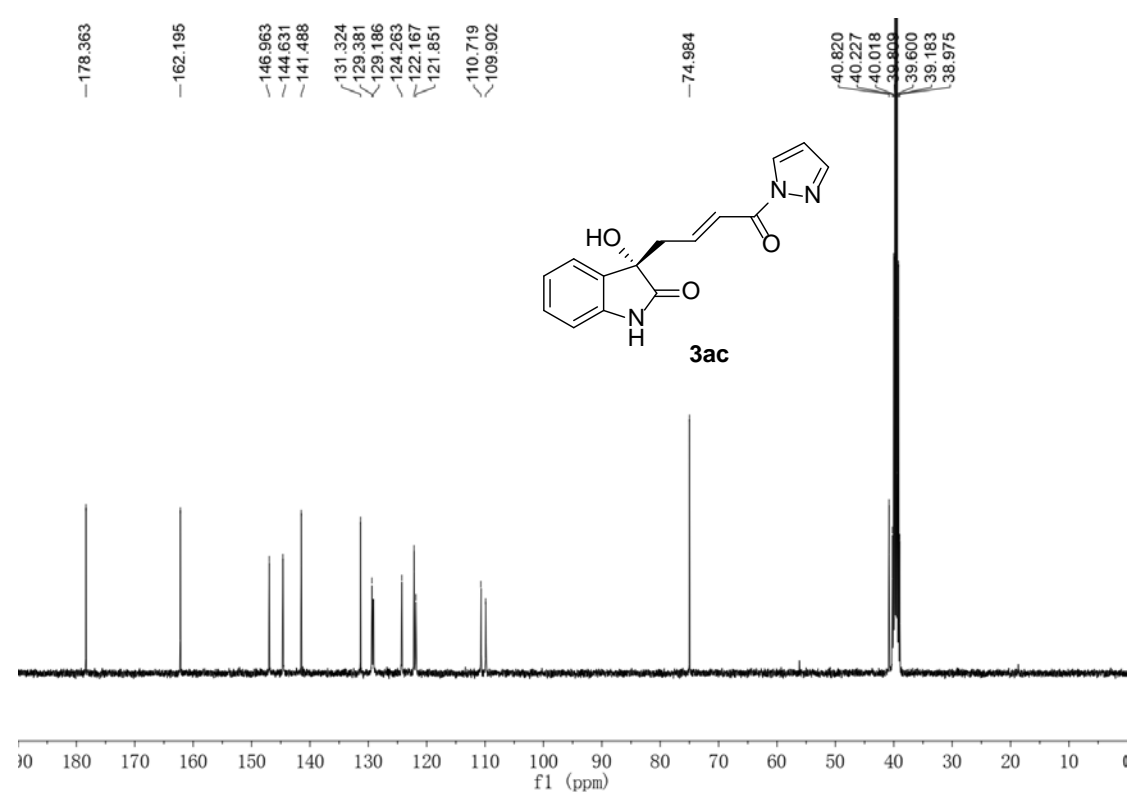
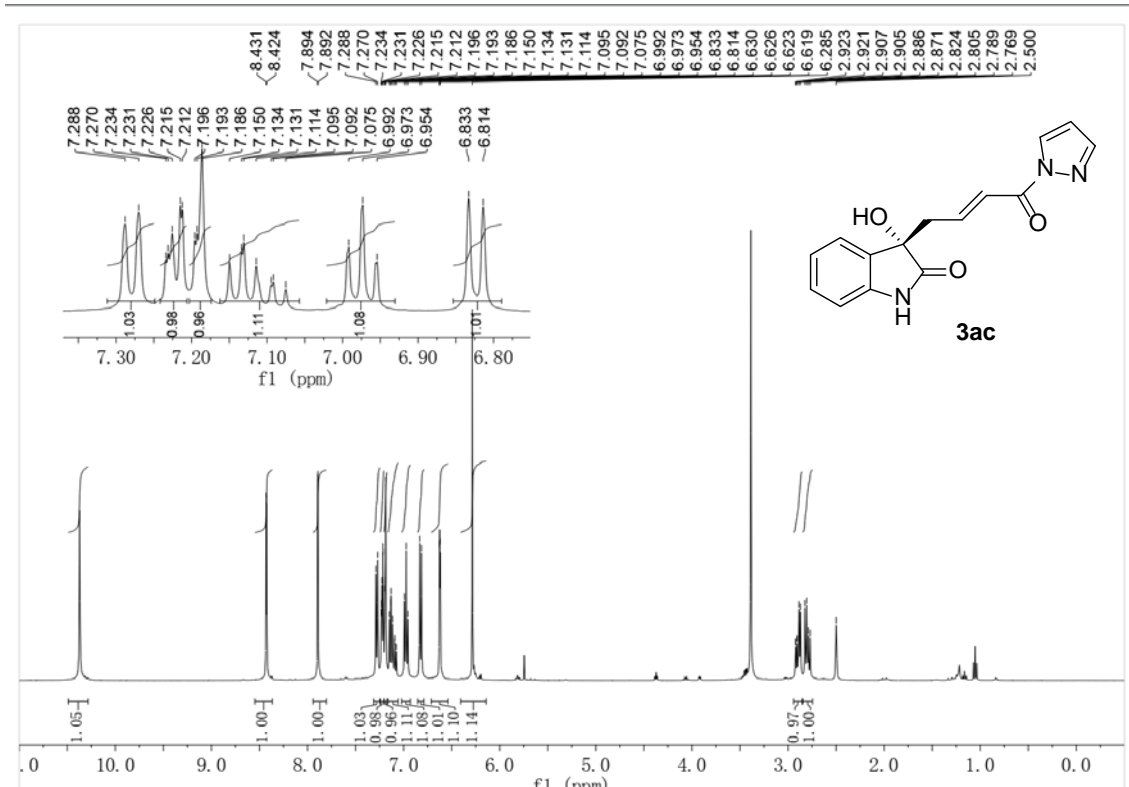
6. References

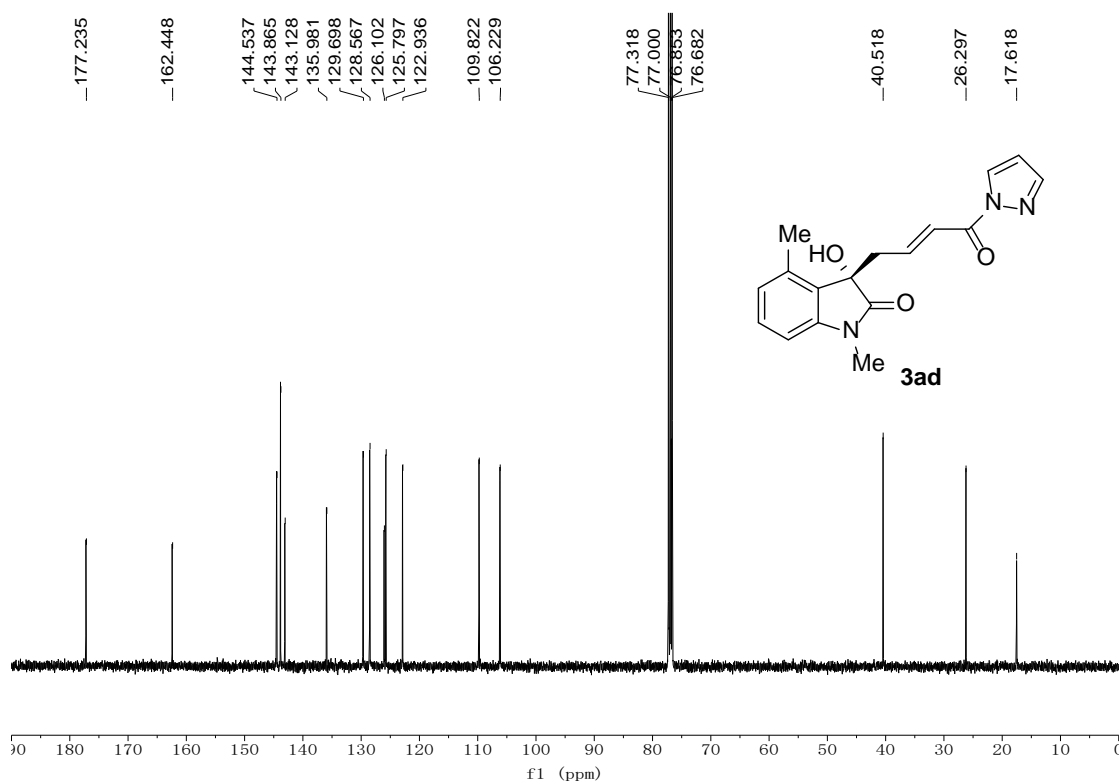
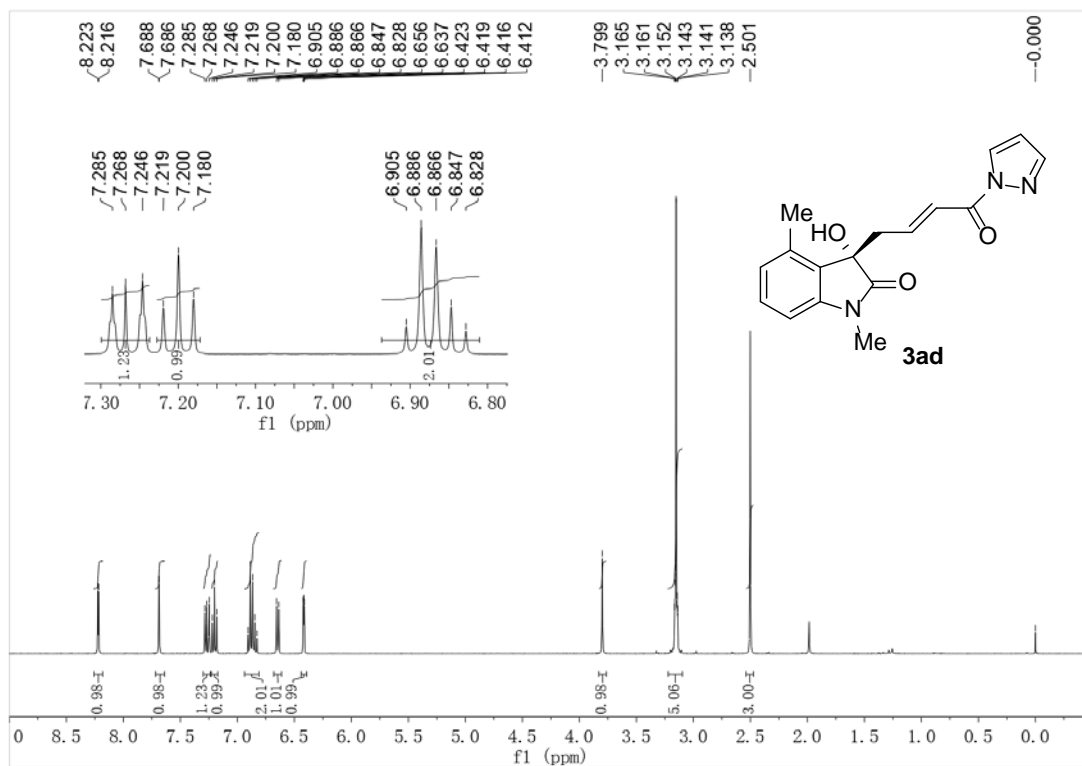
1. (a) Okino, T.; Hoashi, Y.; Furukawa, T.; Xu, X.; Takemoto, Y. Enantio- and Diastereoselective Michael Reaction of 1,3-Dicarbonyl Compounds to Nitroolefins Catalyzed by a Bifunctional Thiourea. *J. Am. Chem. Soc.* **2005**, *127*, 119-125. (b) Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. Highly Enantioselective Conjugate Addition of Nitromethane to Chalcones Using Bifunctional Cinchona Organocatalysts. *Org. Lett.* **2005**, *7*, 1967-1969. (c) McCooey, S. H.; Connon, S. J. Readily Accessible 9-Epi-amino Cinchona Alkaloid Derivatives Promote Efficient, Highly Enantioselective Additions of Aldehydes and Ketones to Nitroolefins. *Org. Lett.* **2007**, *9*, 599-602. (d) Yang, W.; Du, D.-M. Highly Enantioselective Michael Addition of Nitroalkanes to Chalcones Using Chiral Squaramides as Hydrogen Bonding Organocatalysts. *Org. Lett.* **2010**, *12*, 5450-5453.
2. (a) Zhang, H.-J.; Shi, C.-Y.; Zhong, F.; Yin, L. Direct Asymmetric Vinylogous and Bisvinylogous Mannich-Type Reaction Catalyzed by a Copper(I) Complex. *J. Am. Chem. Soc.* **2017**, *139*, 2196-2199. (b) Sun, X.; Zhou, L.; Wang, C.-J.; Zhang, X. Rh-Catalyzed Highly Enantioselective Synthesis of 3-Arylbutanoic Acids. *Angew. Chem. Int. Ed.* **2007**, *46*, 2623-2626.
3. Yan, W.-J.; Wang, D.; Feng, J.-C.; Li, P.; Zhao, D.-P.; Wang, R. Synthesis of N-Alkoxy carbonyl Ketimines Derived from Isatins and Their Application in Enantioselective Synthesis of 3-Aminooxindoles. *Org. Lett.* **2012**, *14*, 2512-2515.

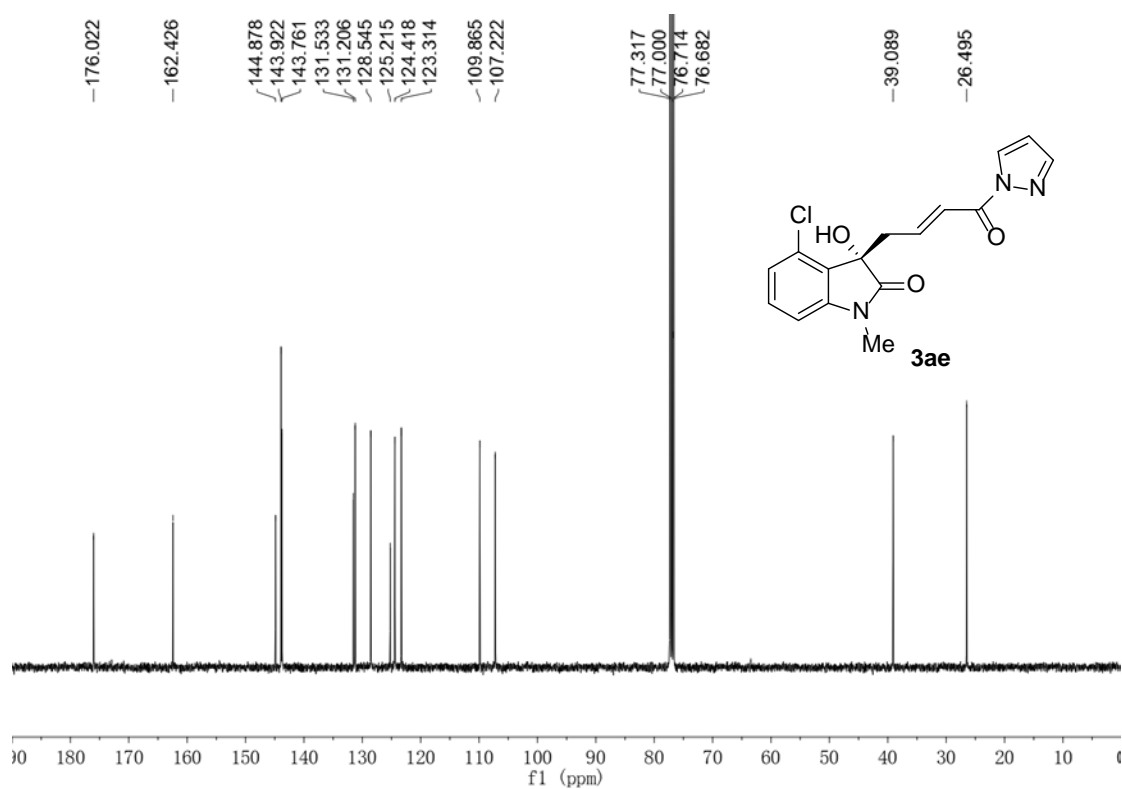
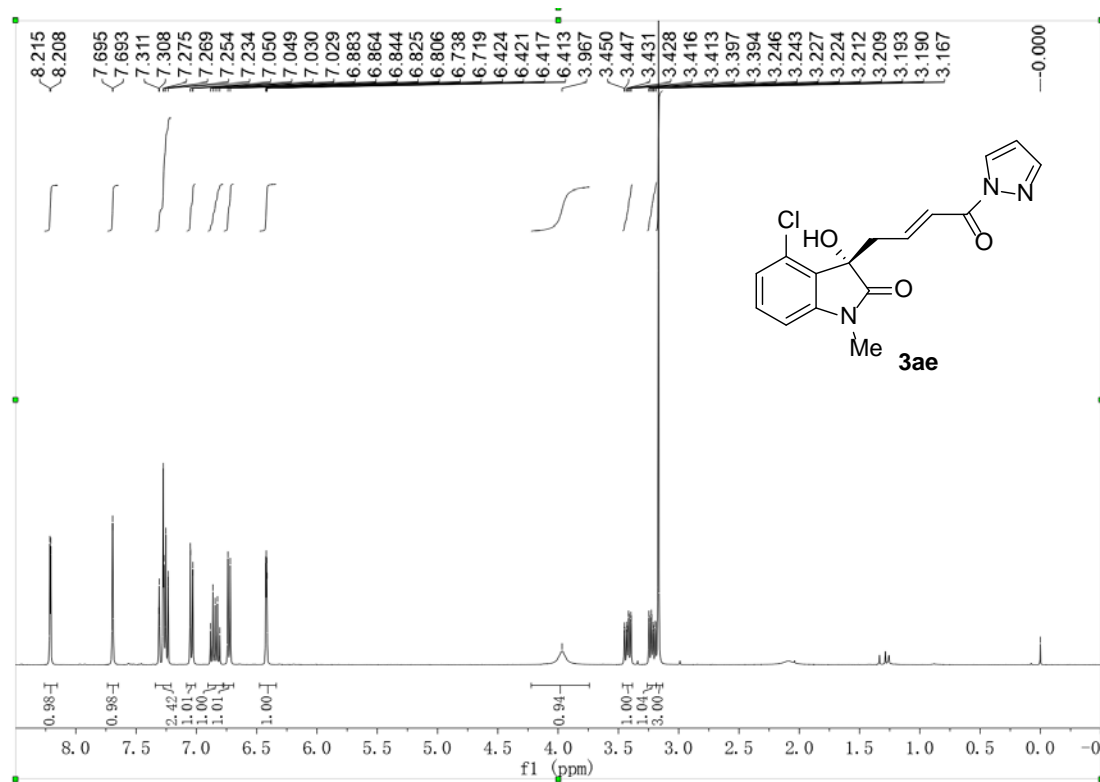
7. Copies of NMR Spectra of the Products 3-7

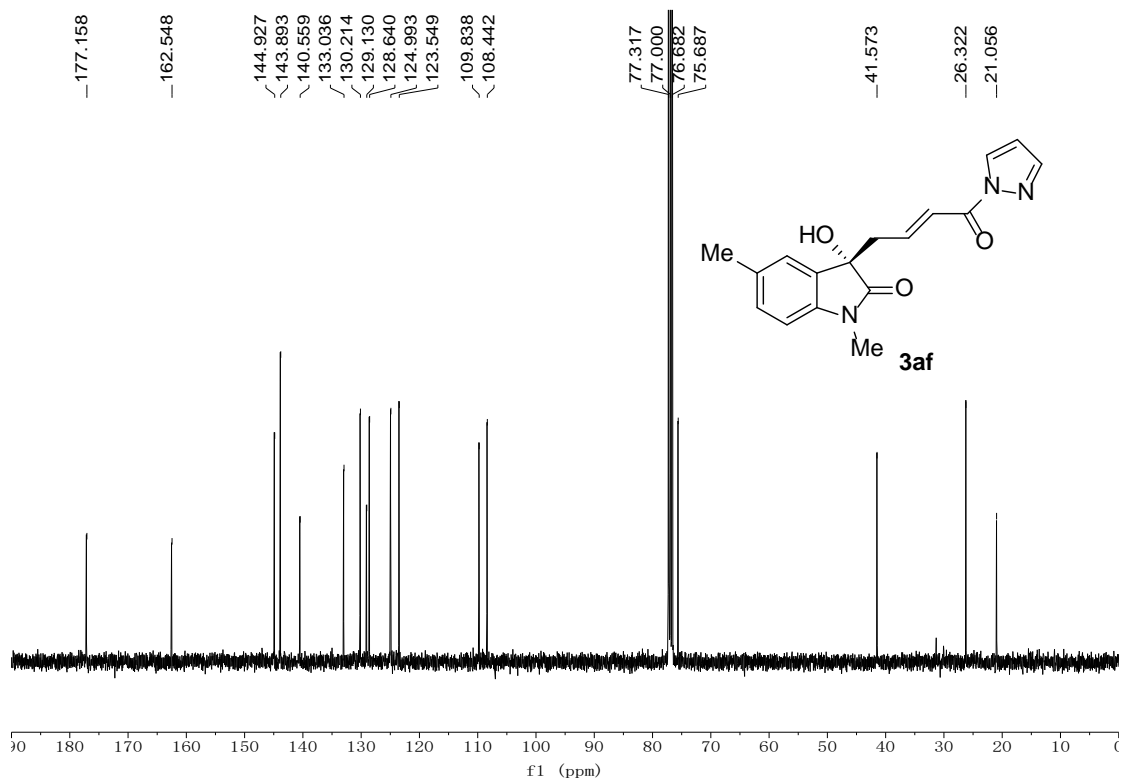
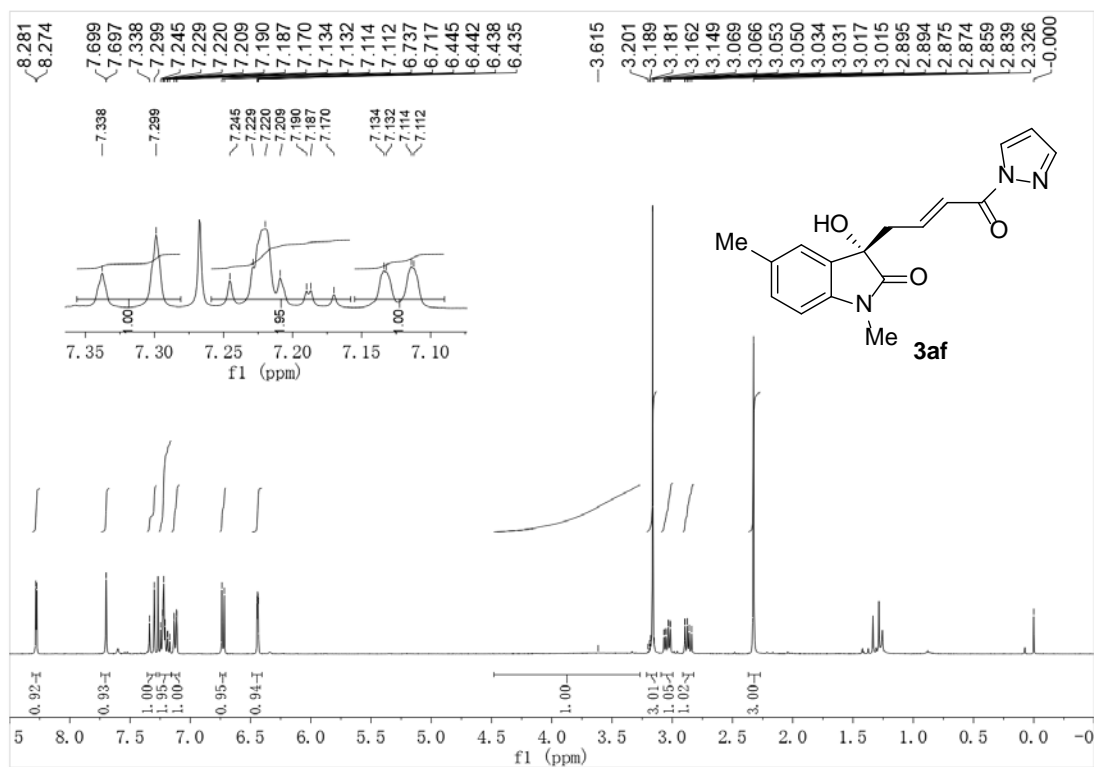


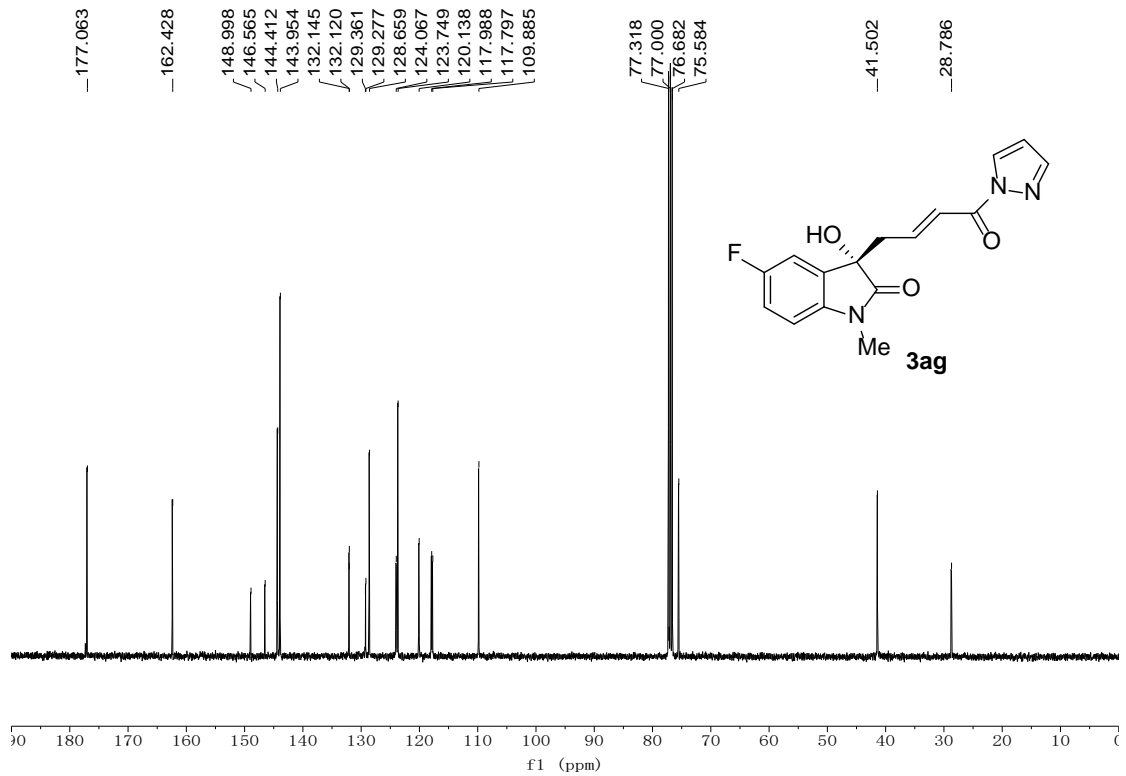
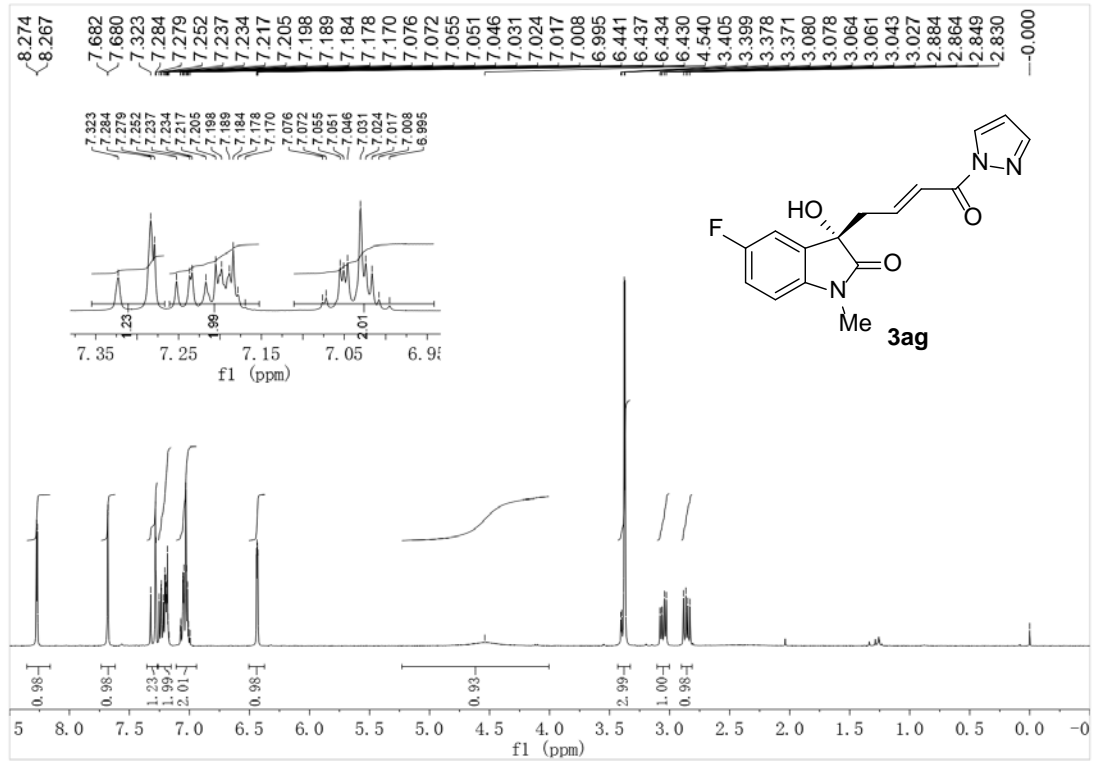


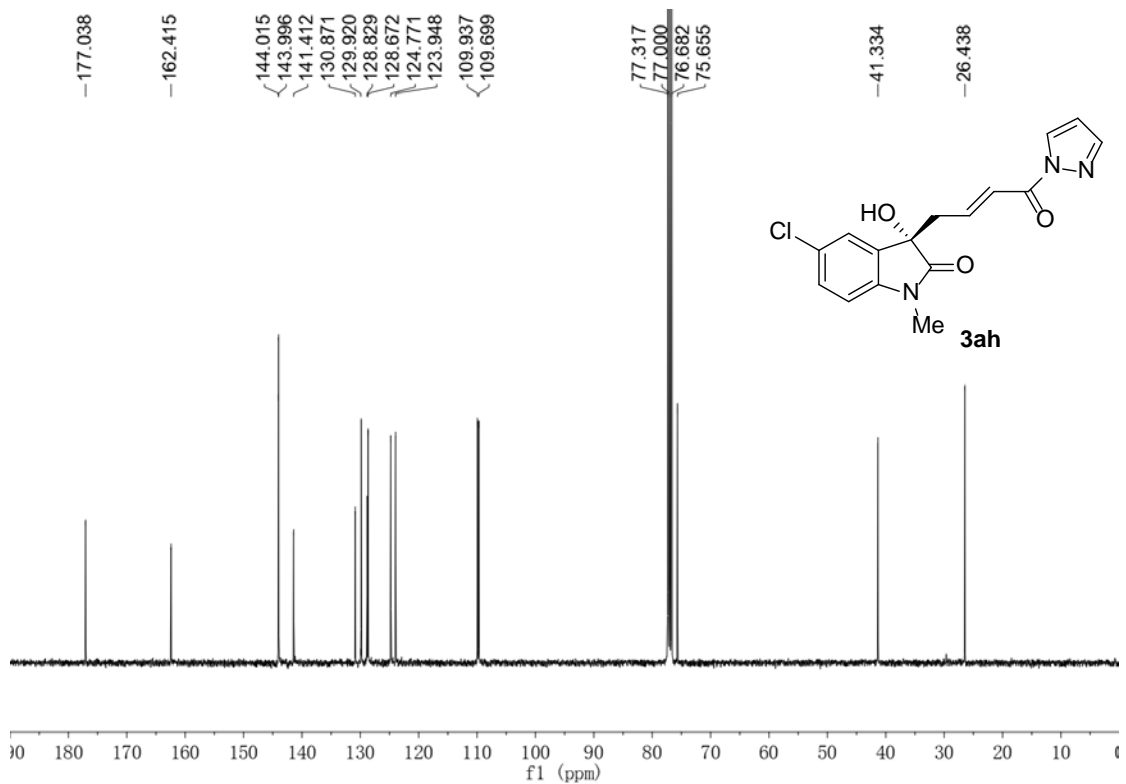
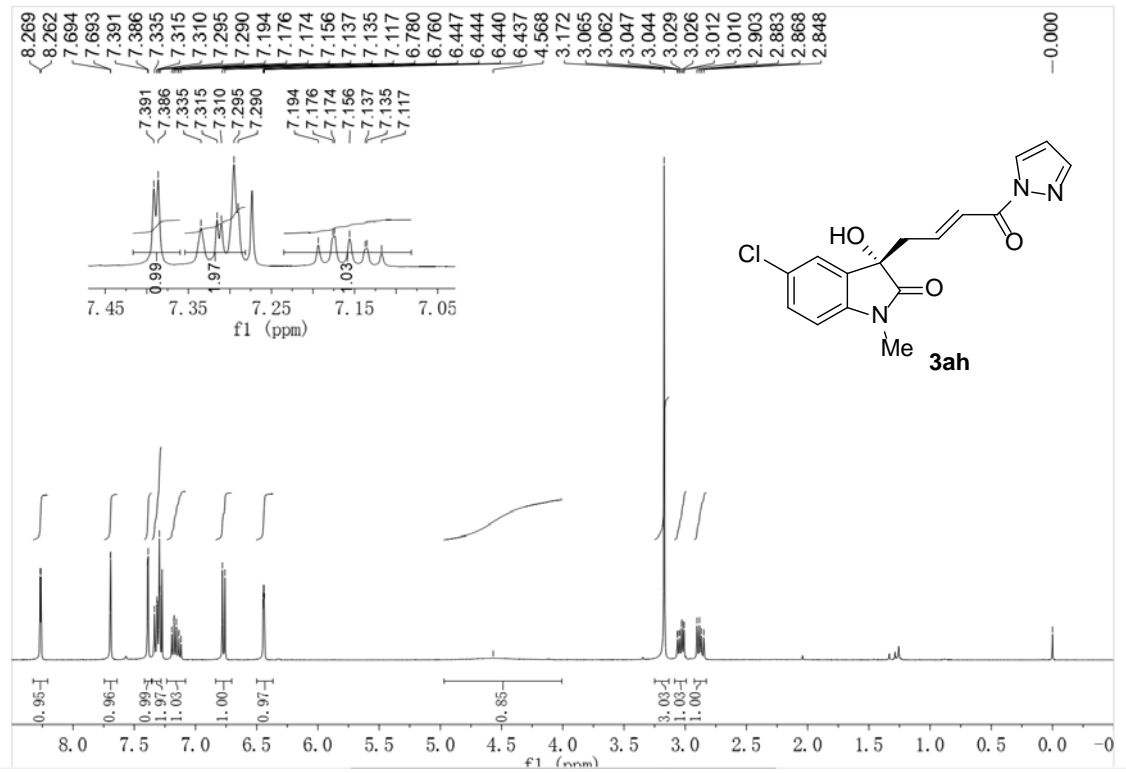


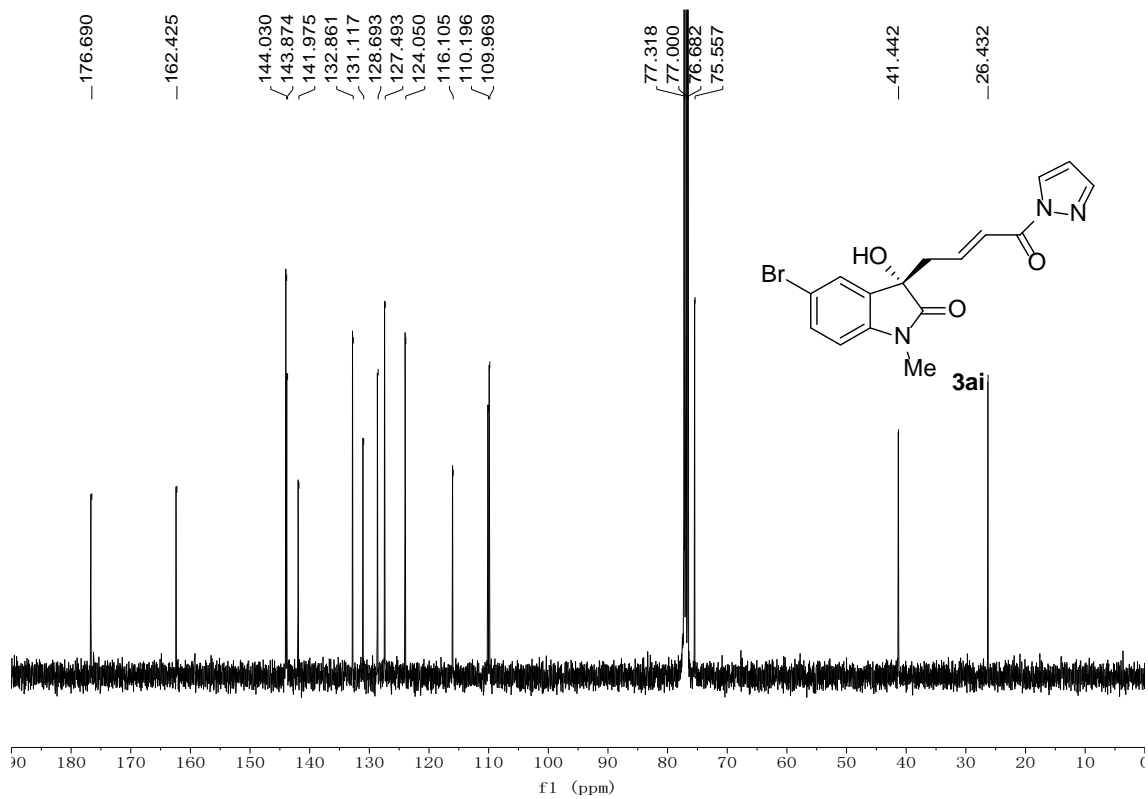
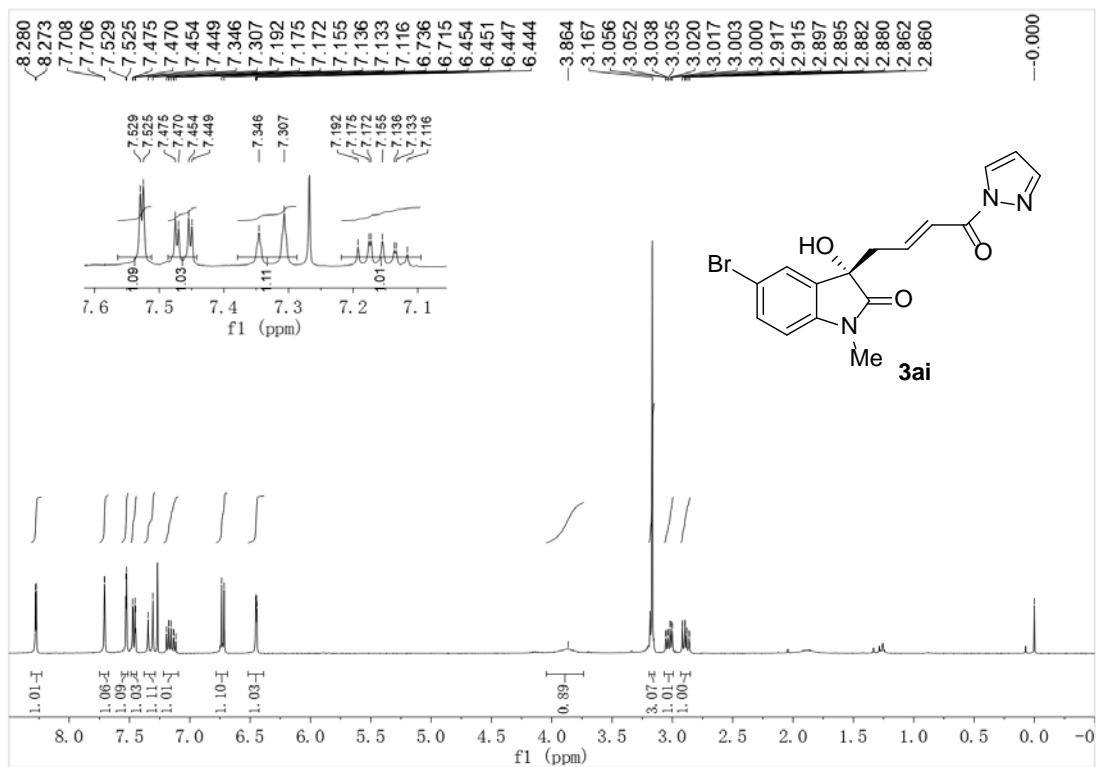


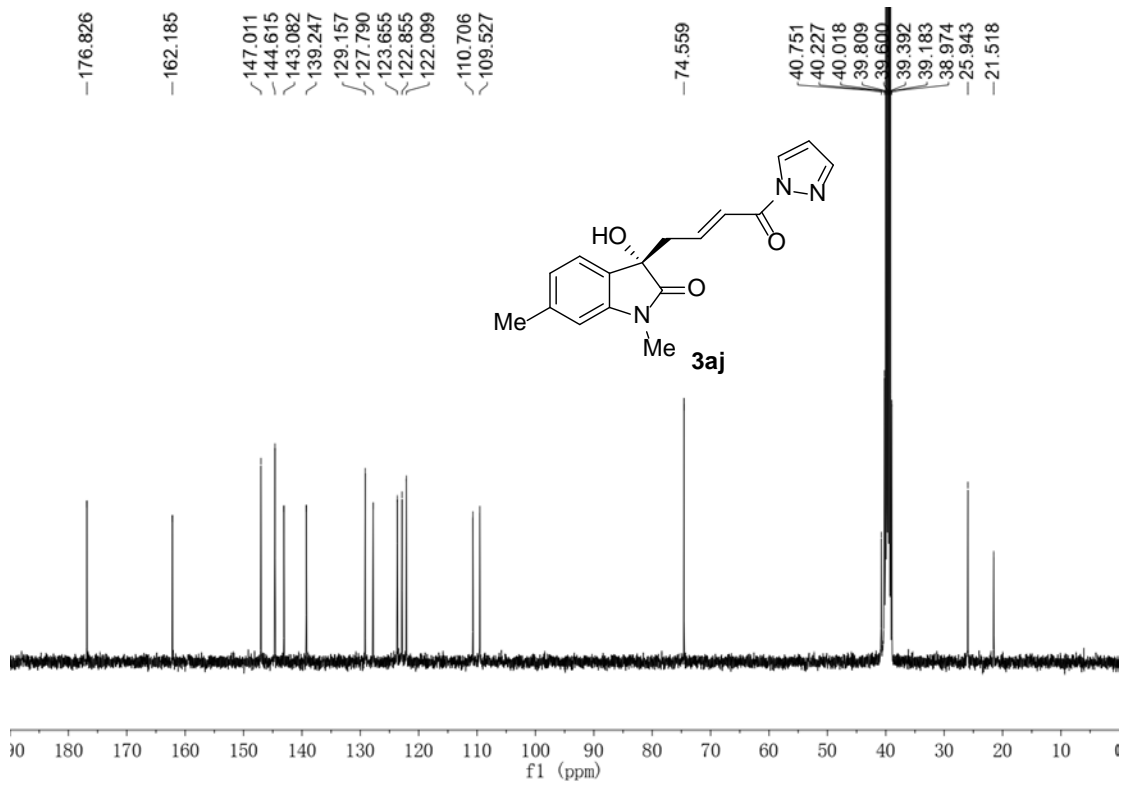
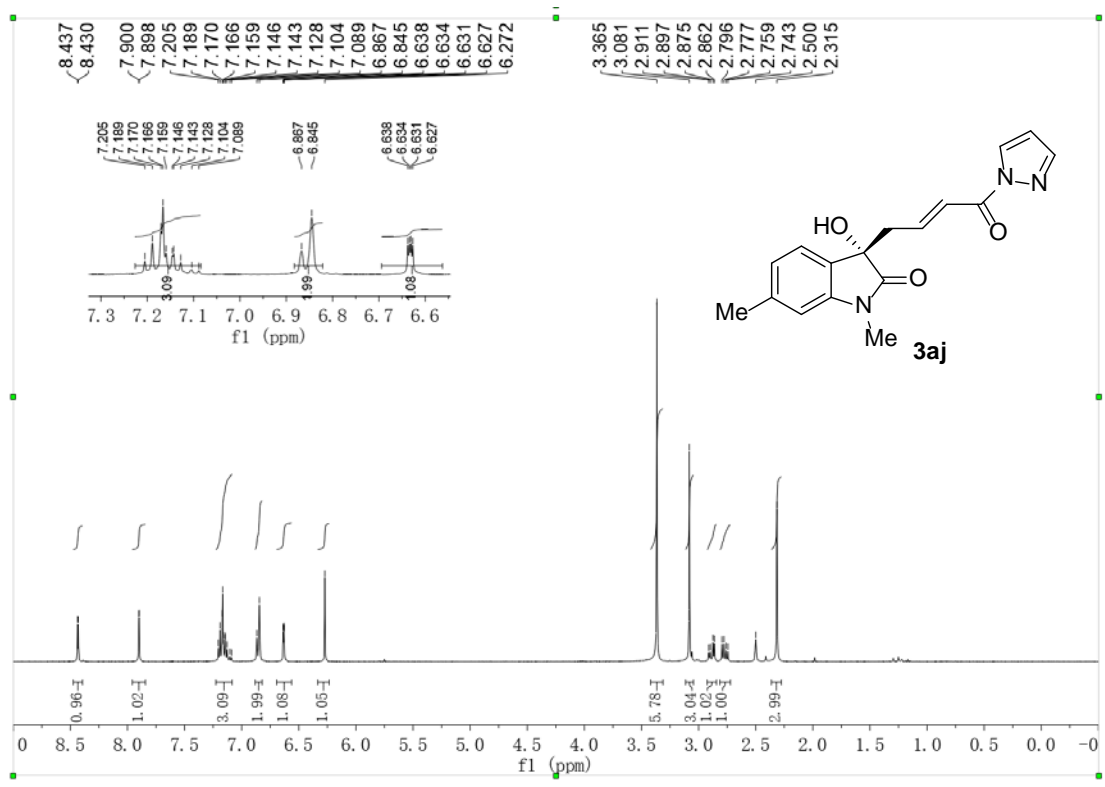


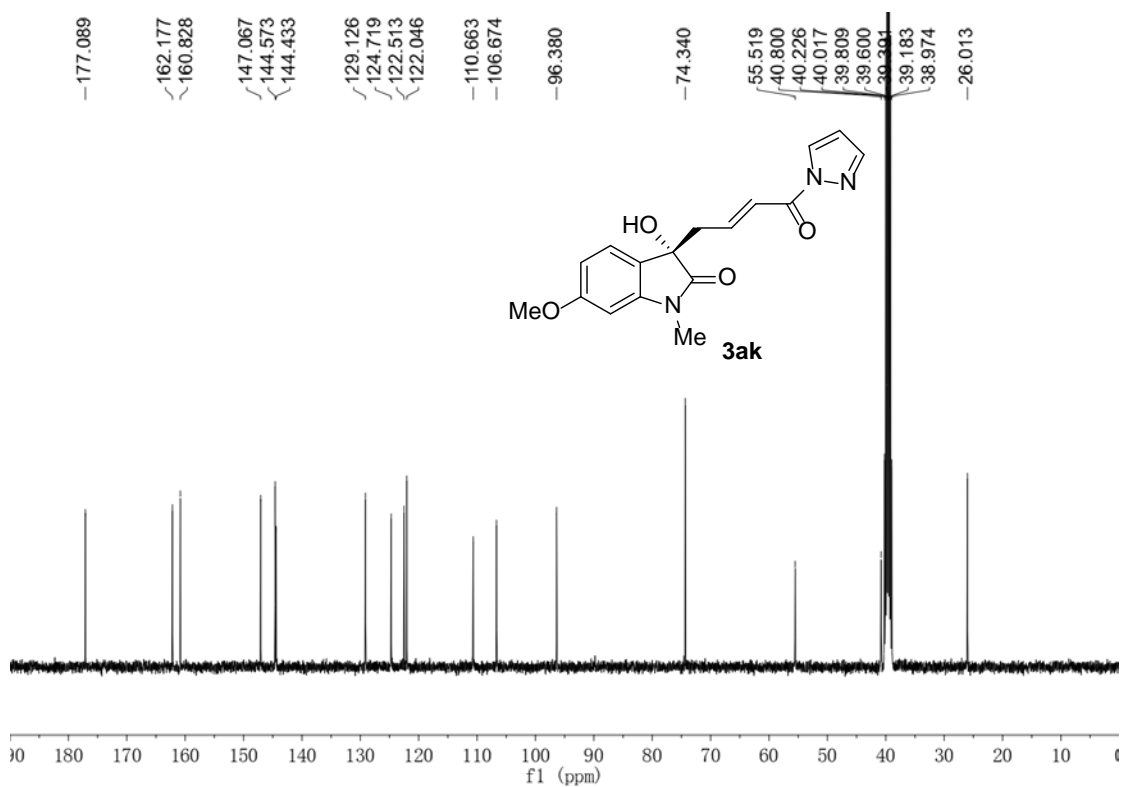
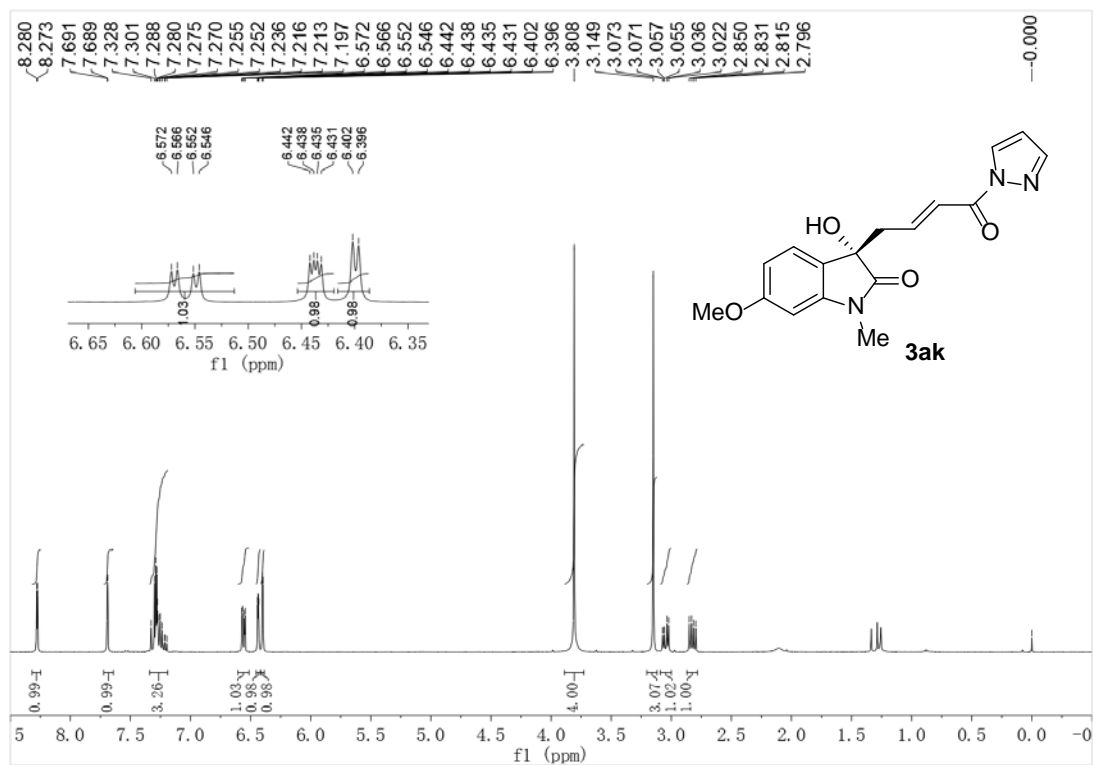


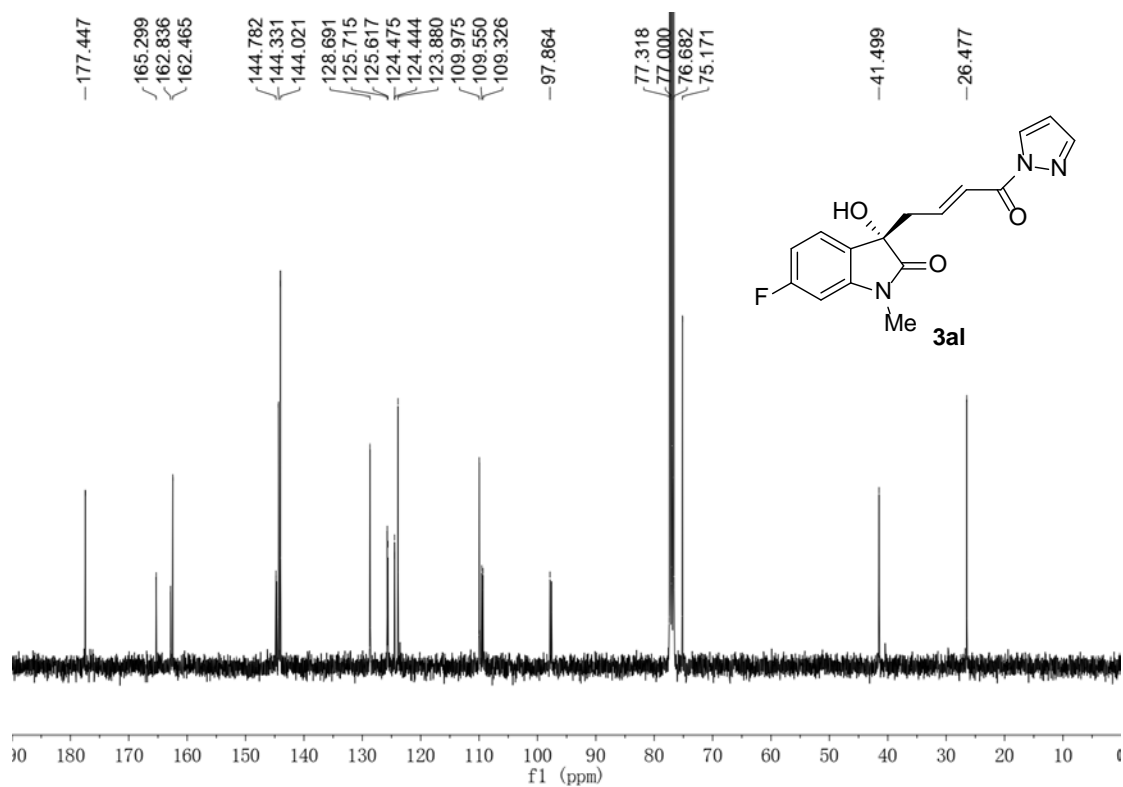
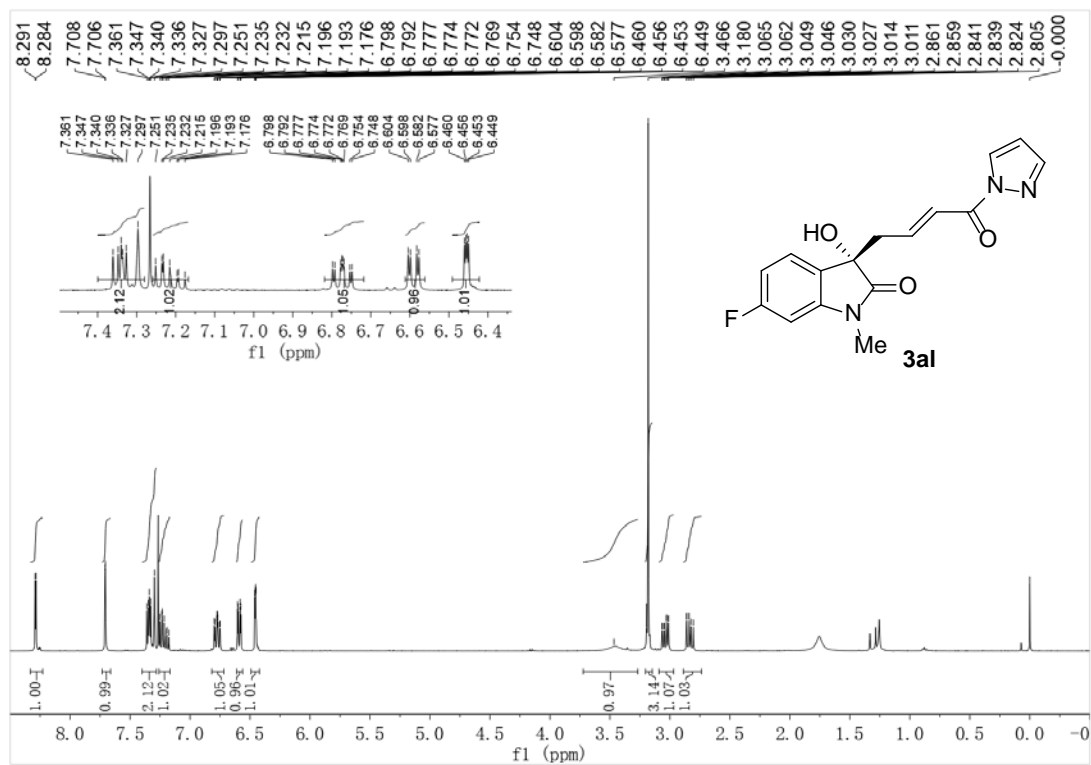


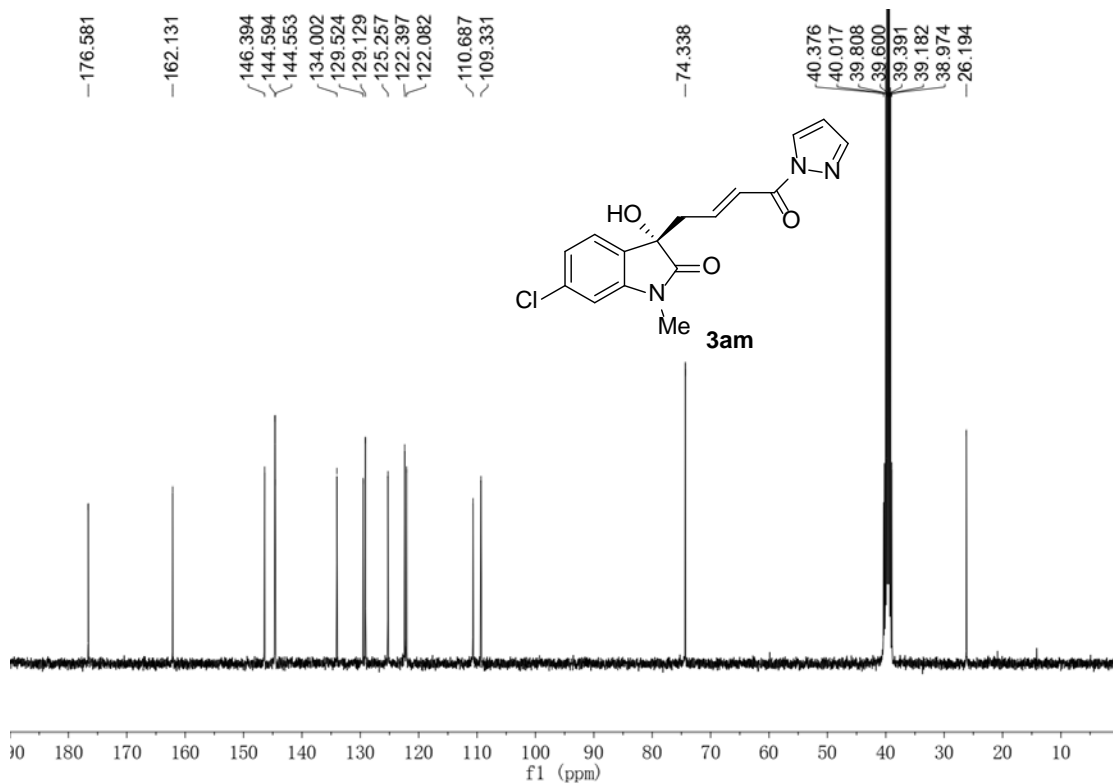
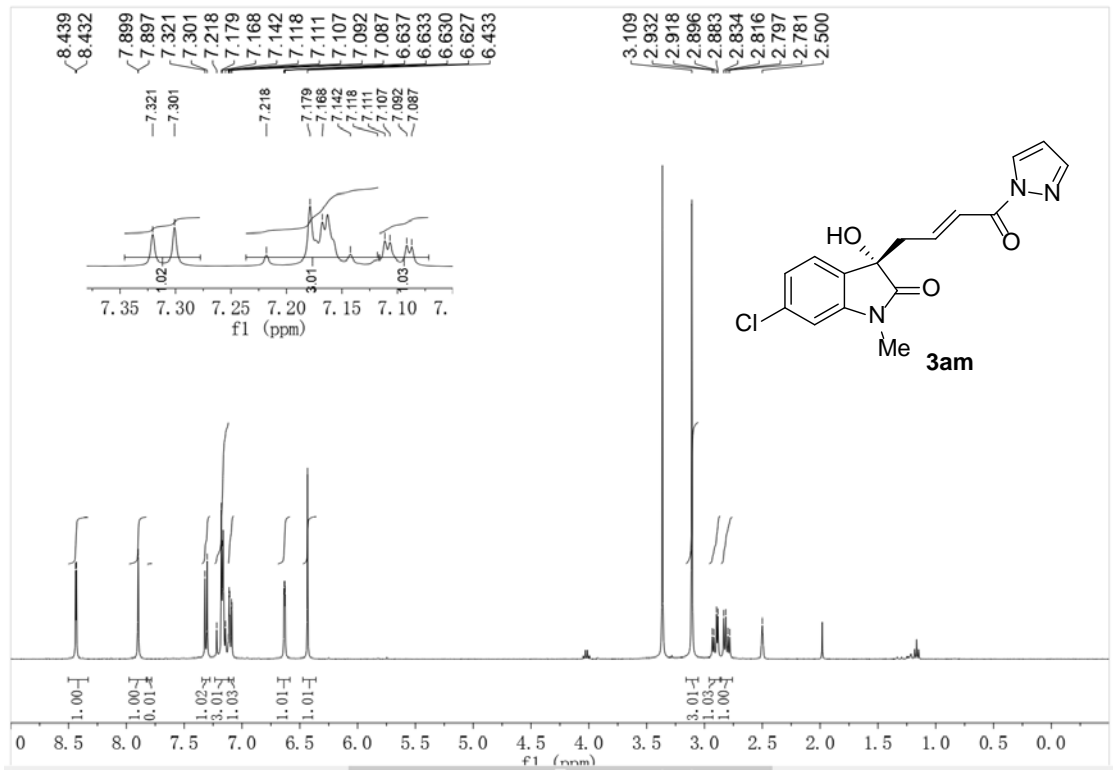


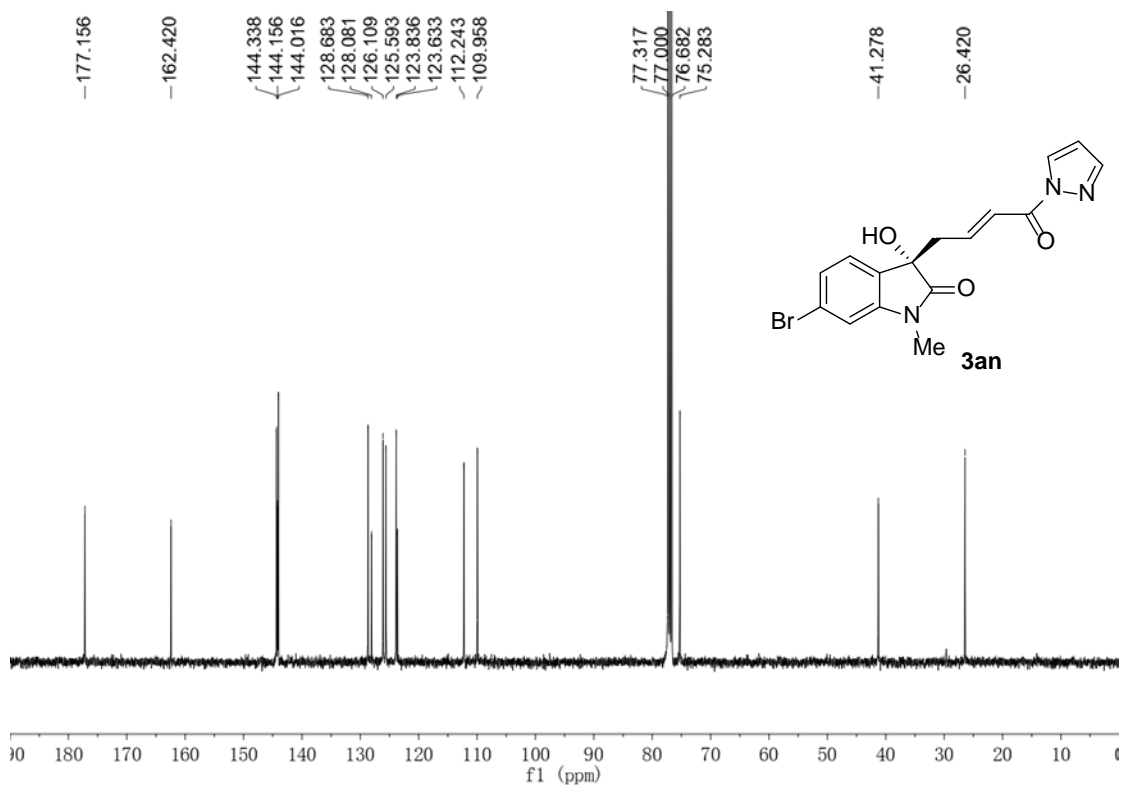
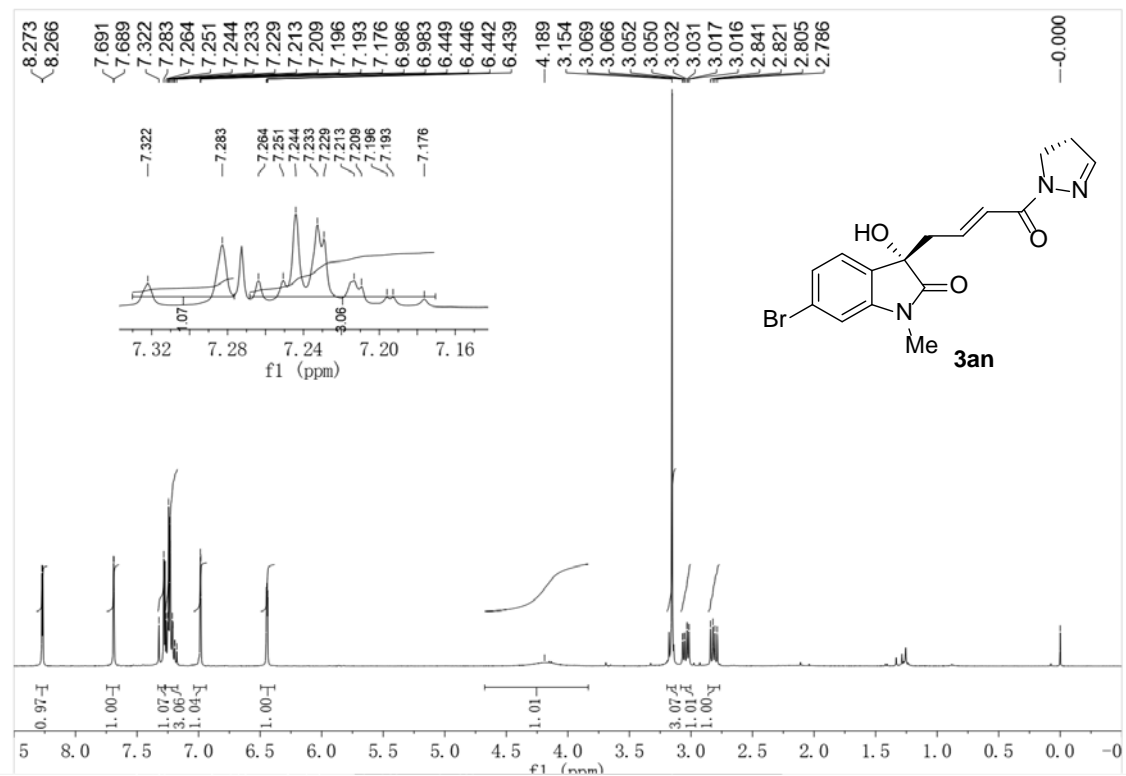


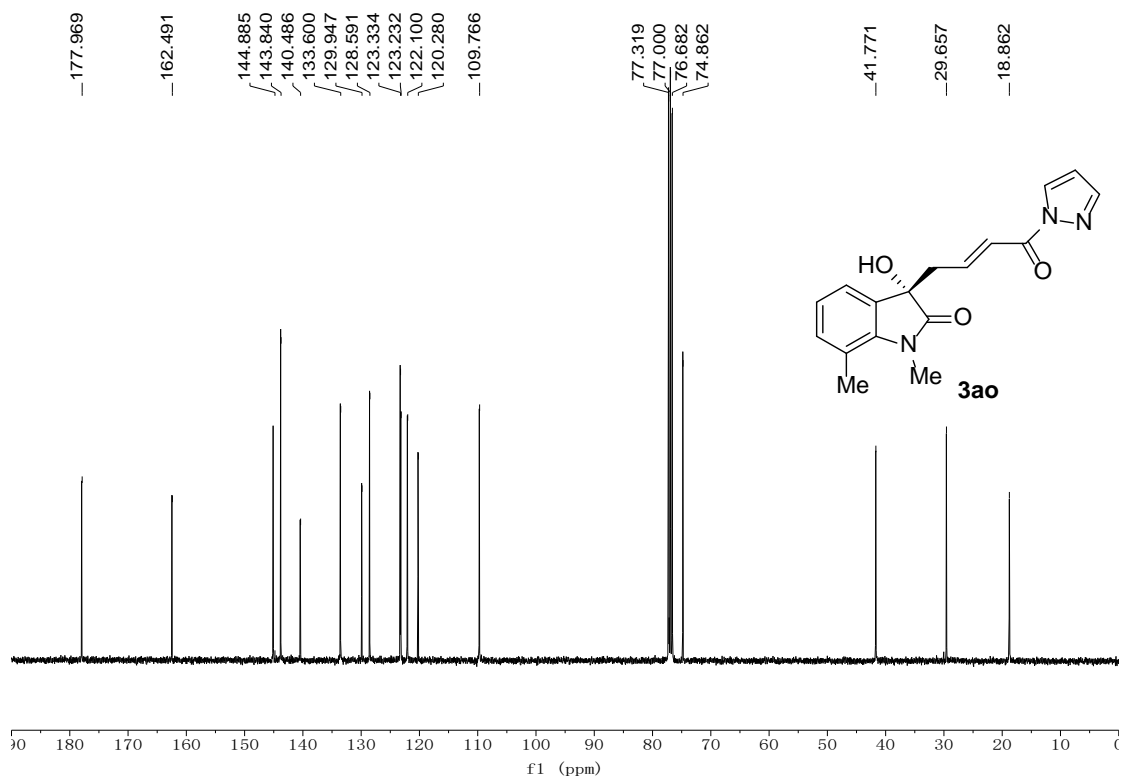
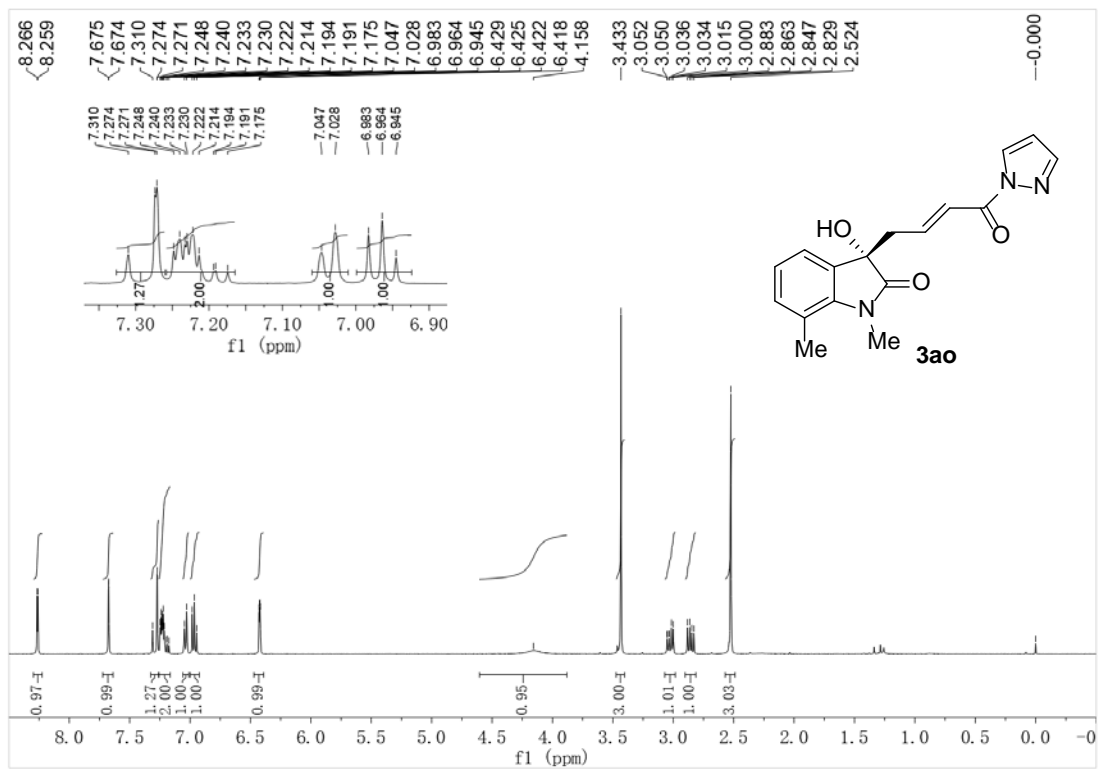


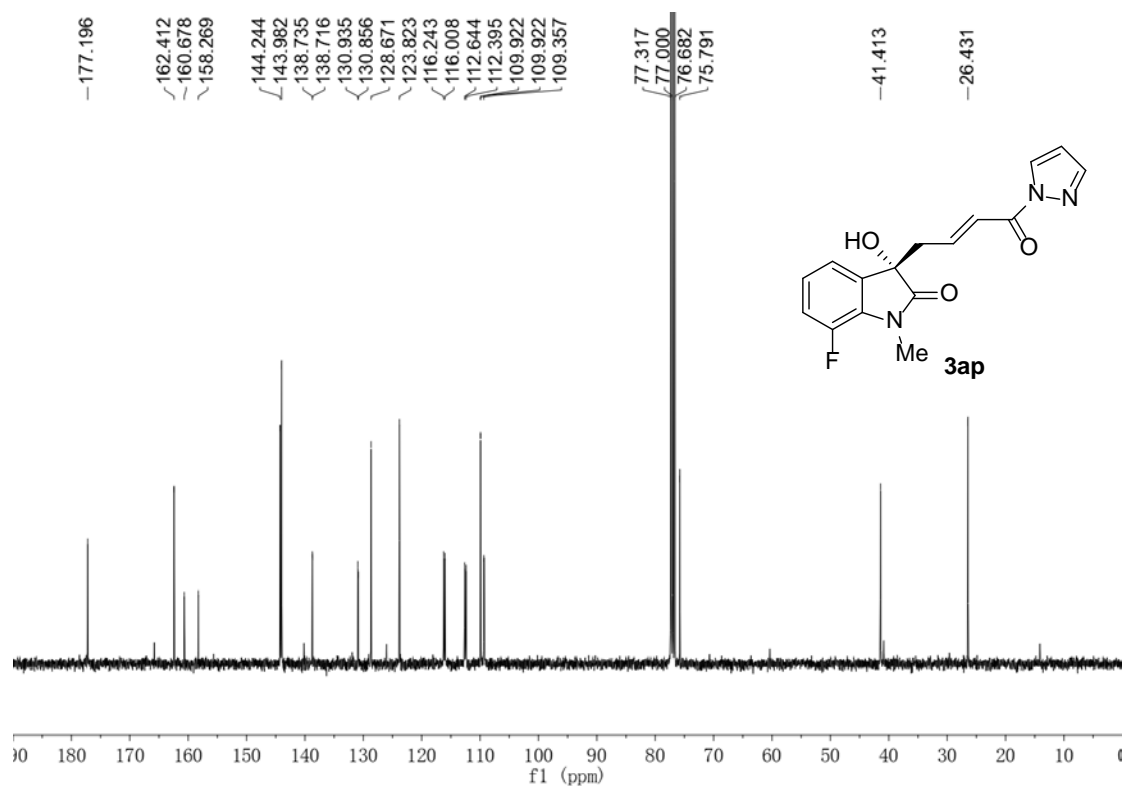
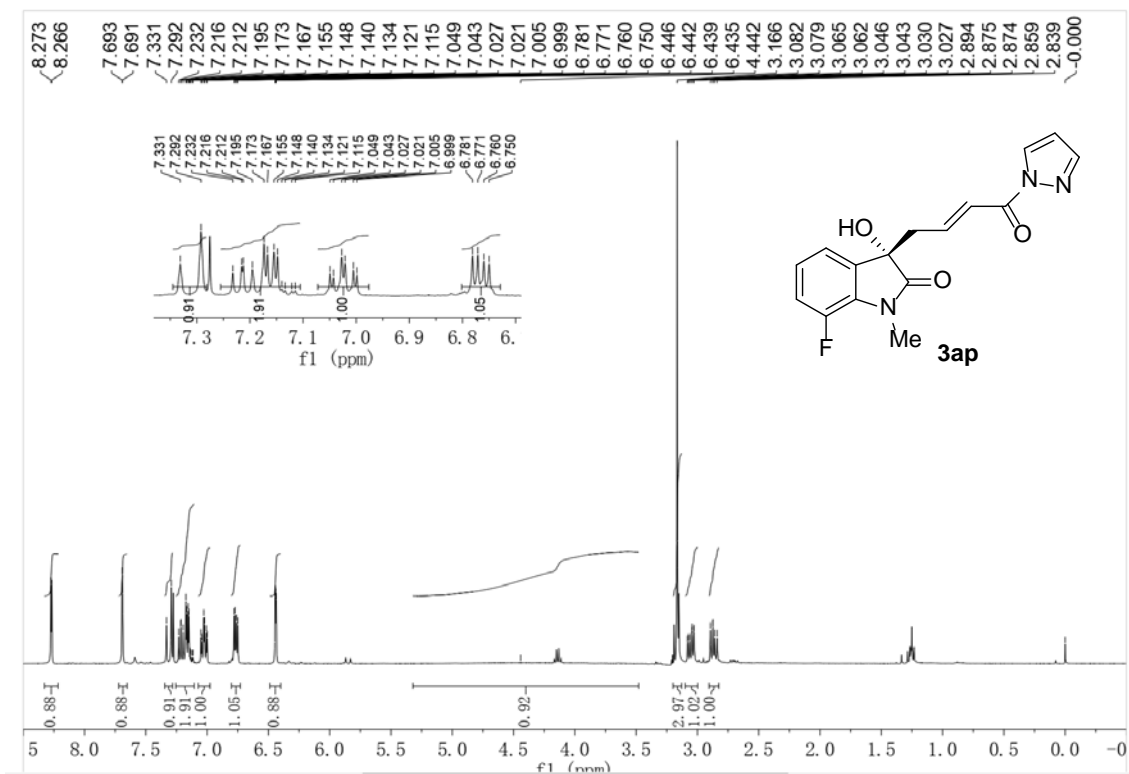


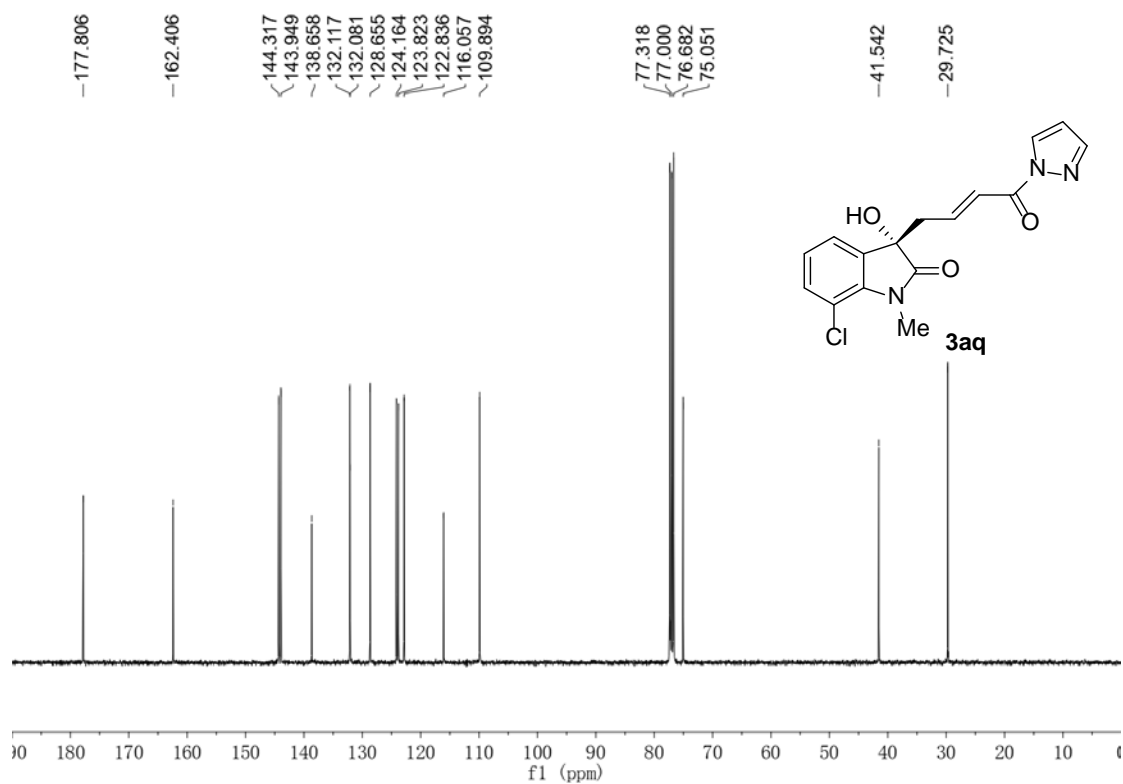
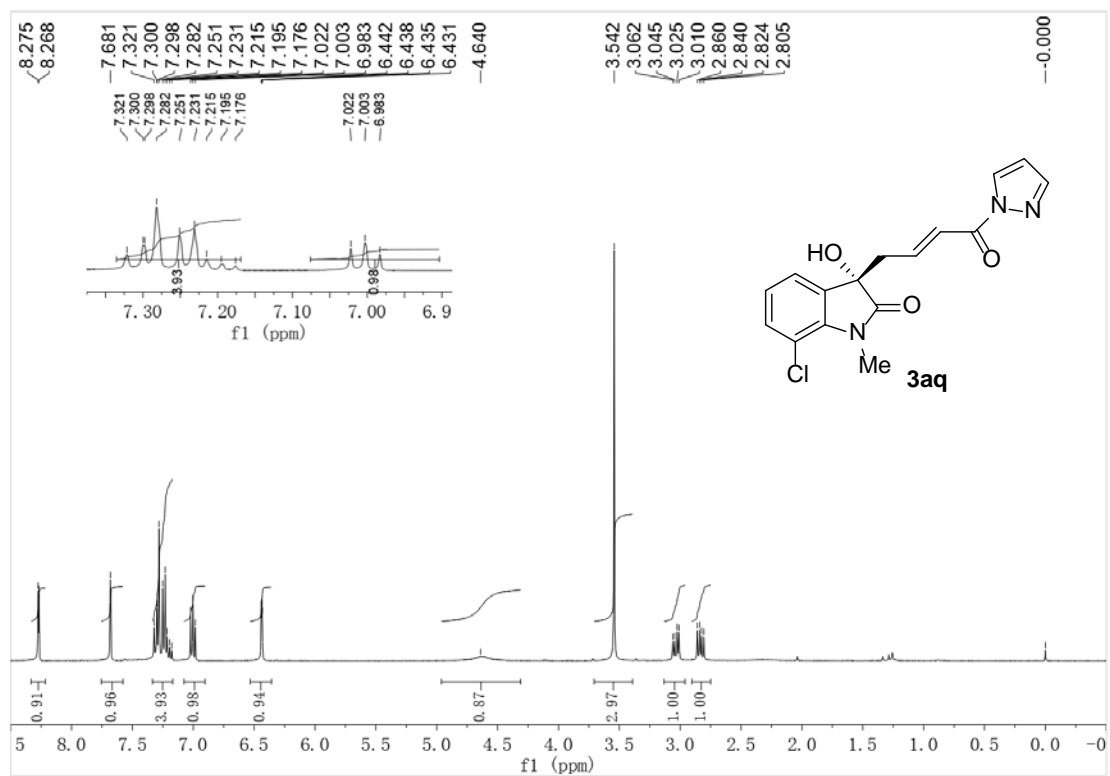


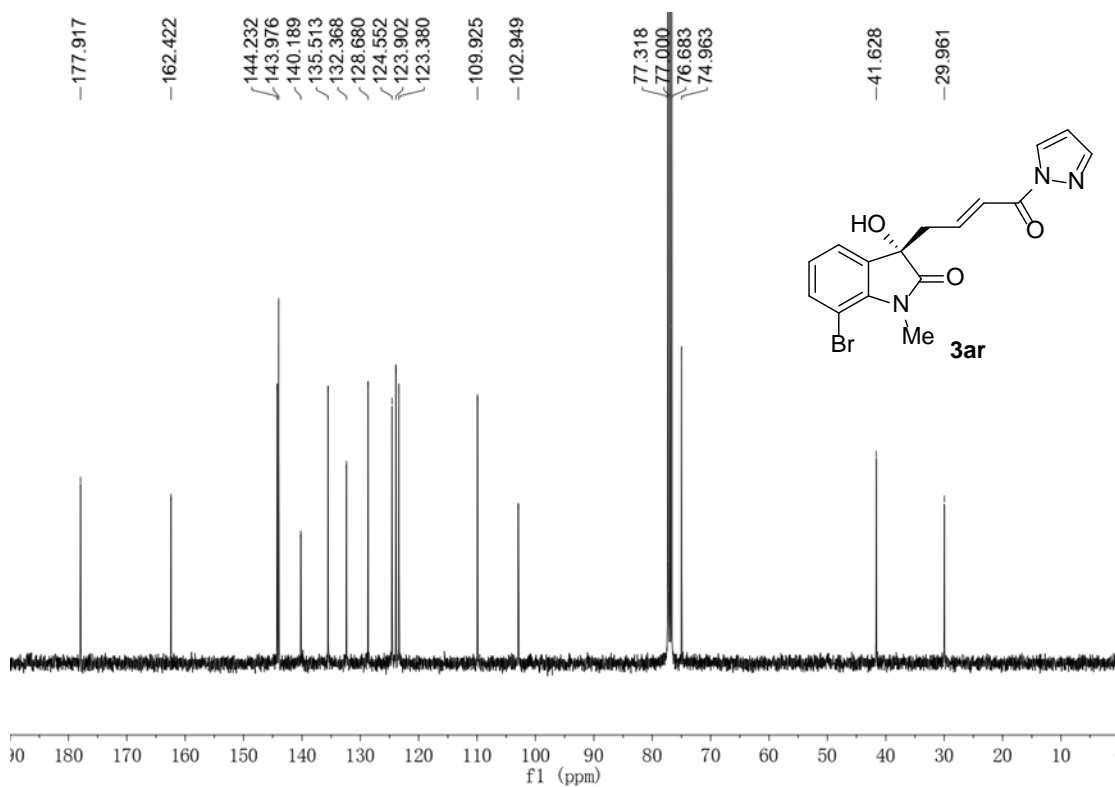
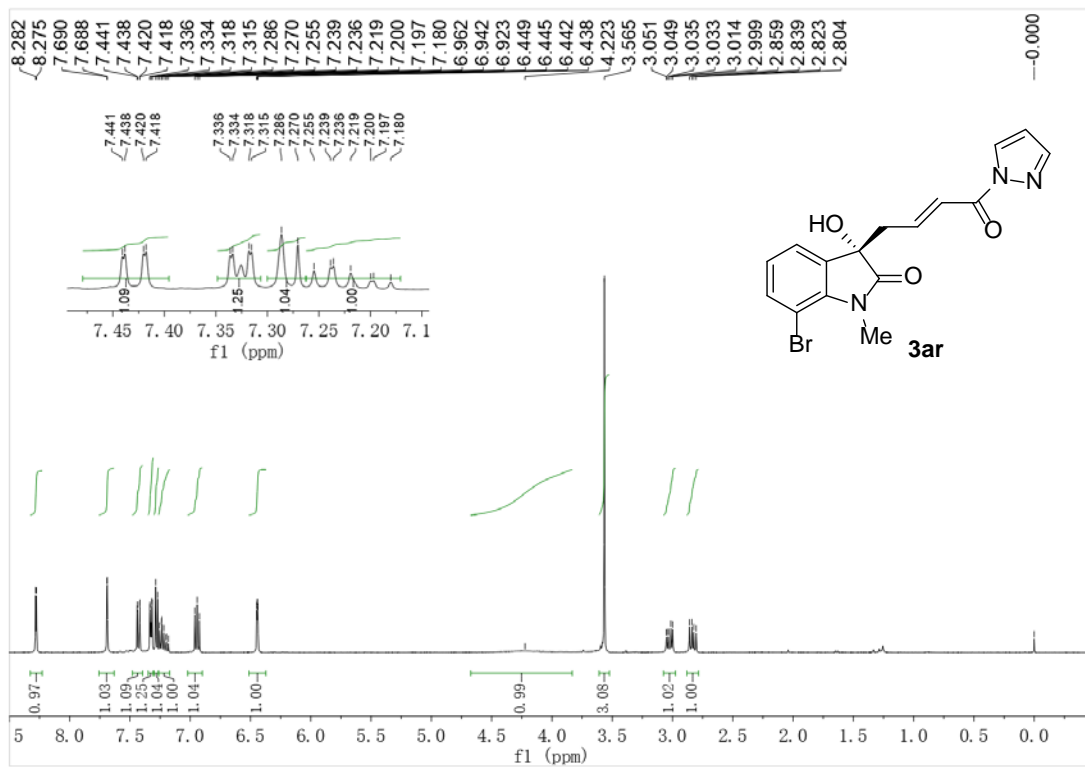


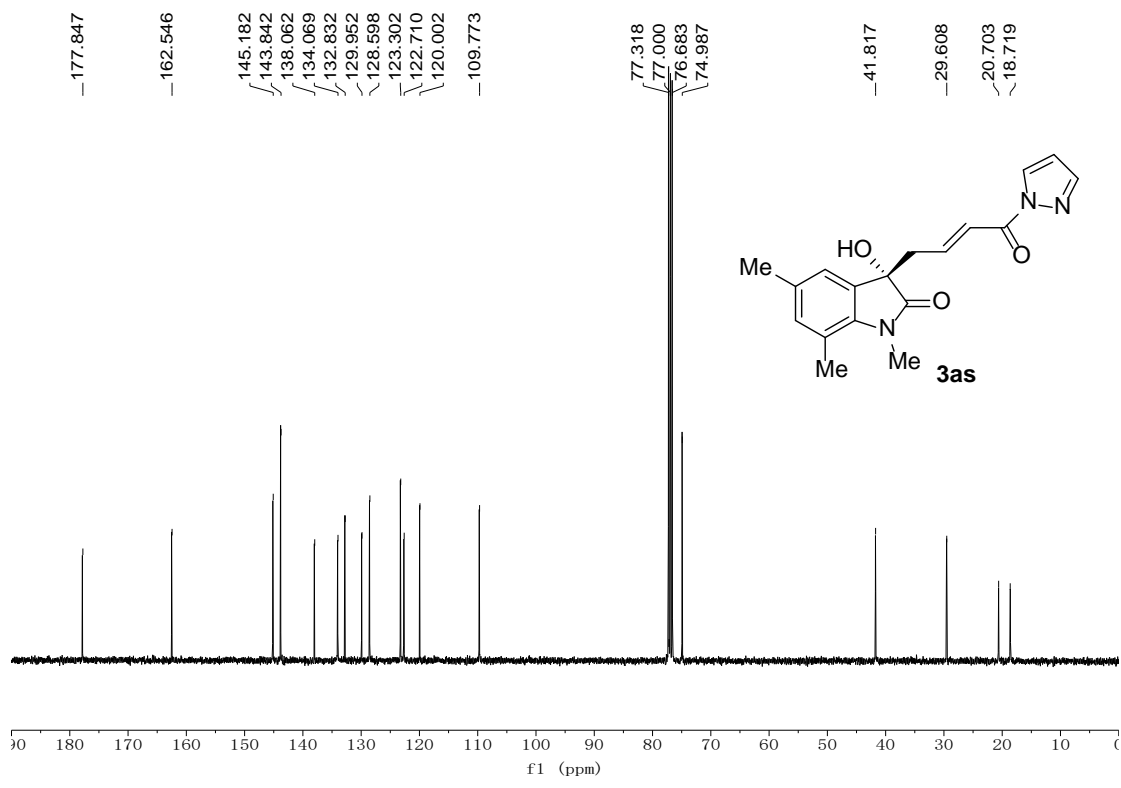
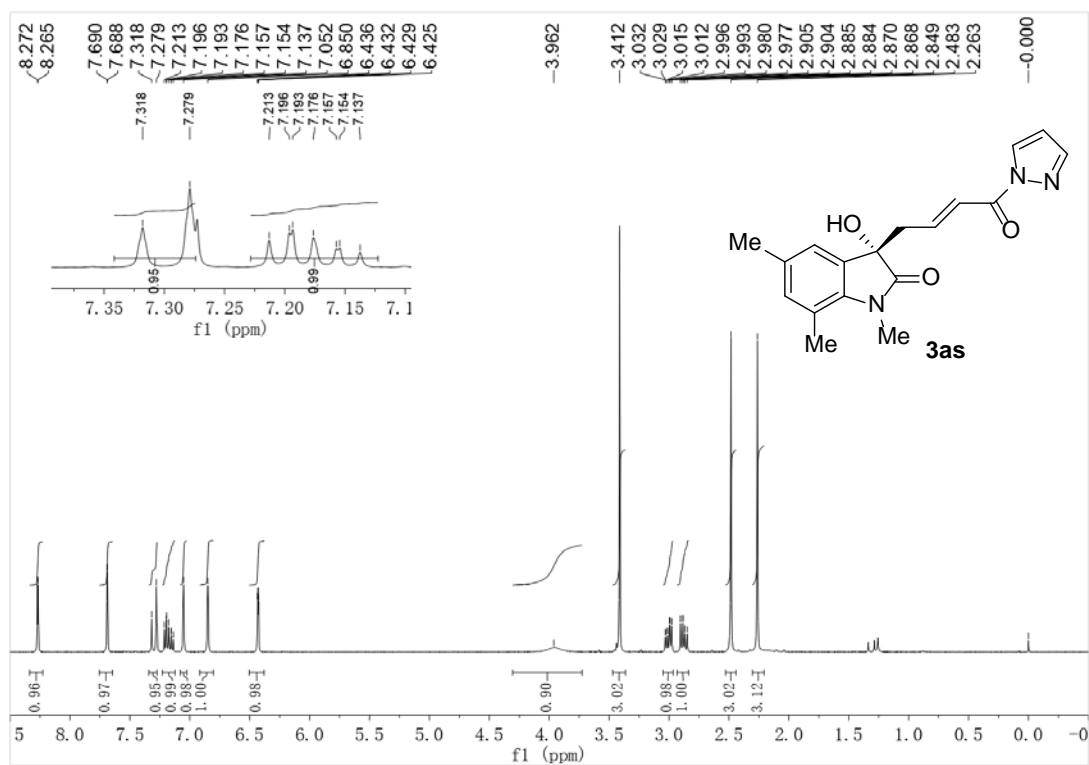


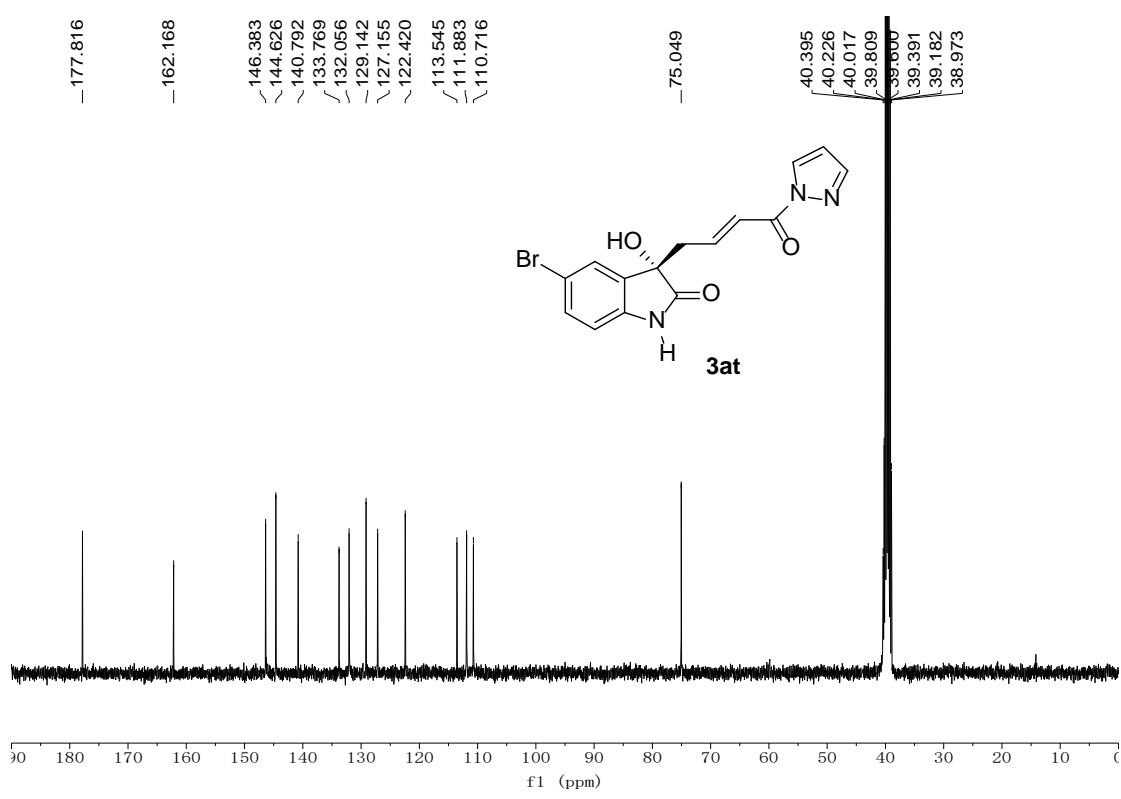
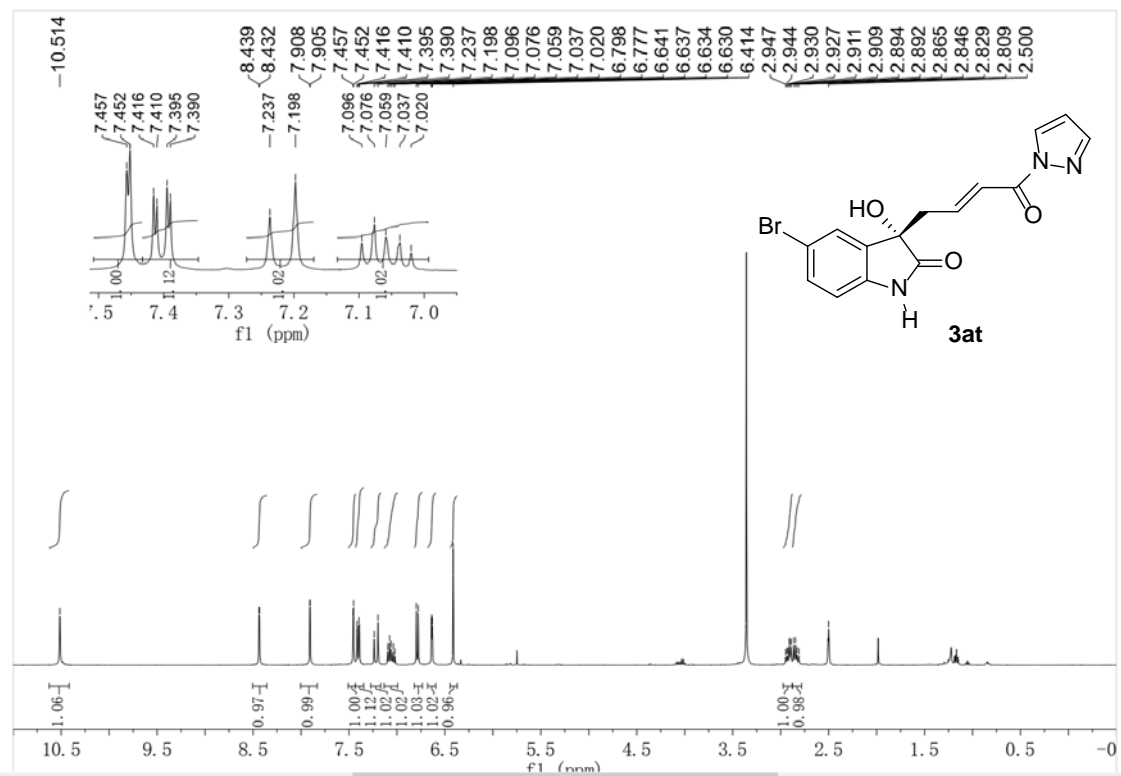


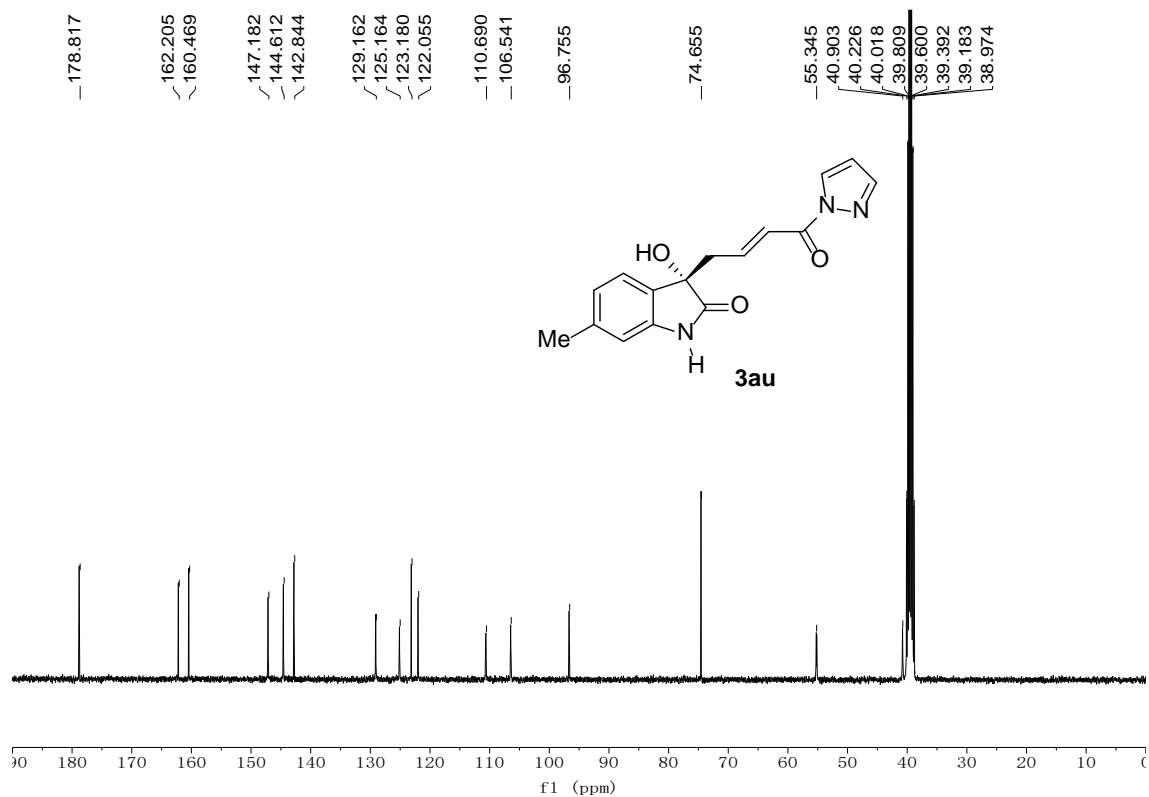
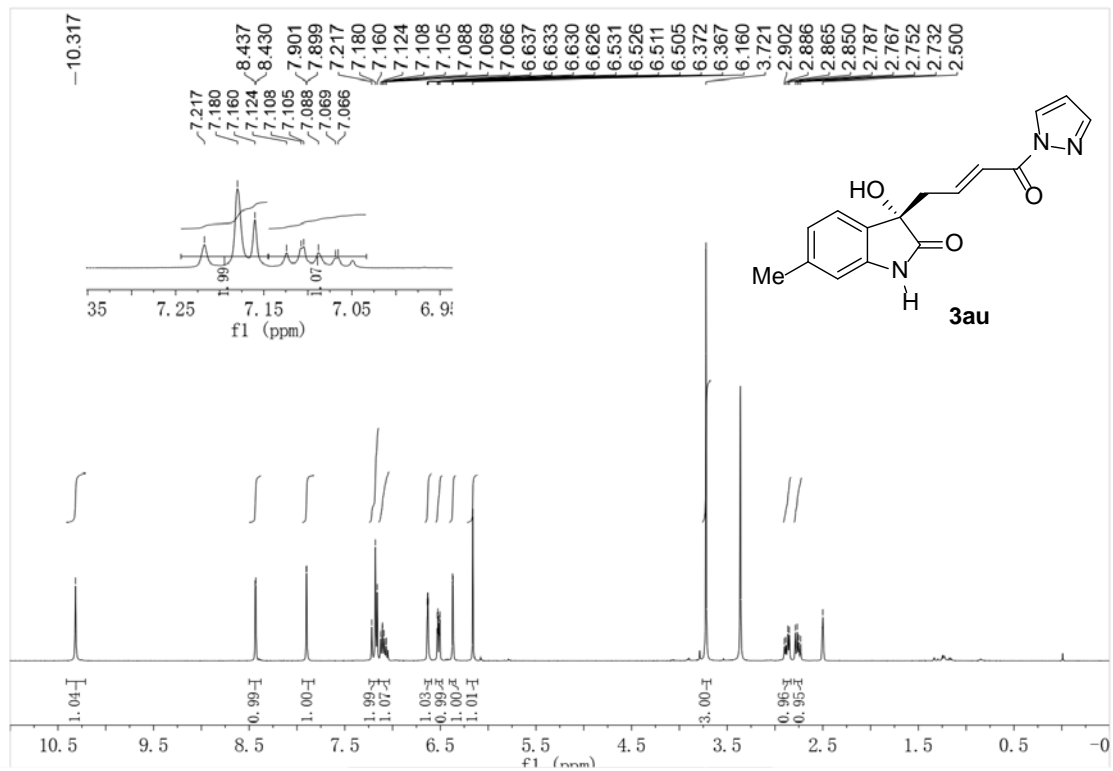


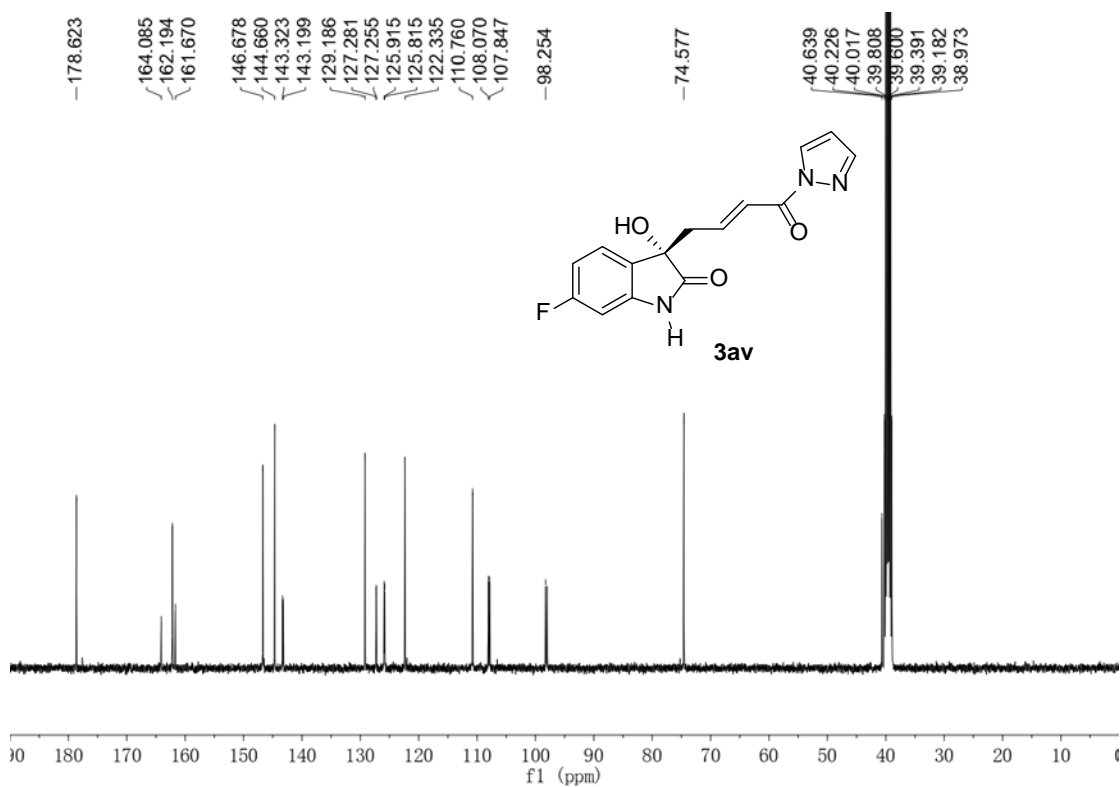
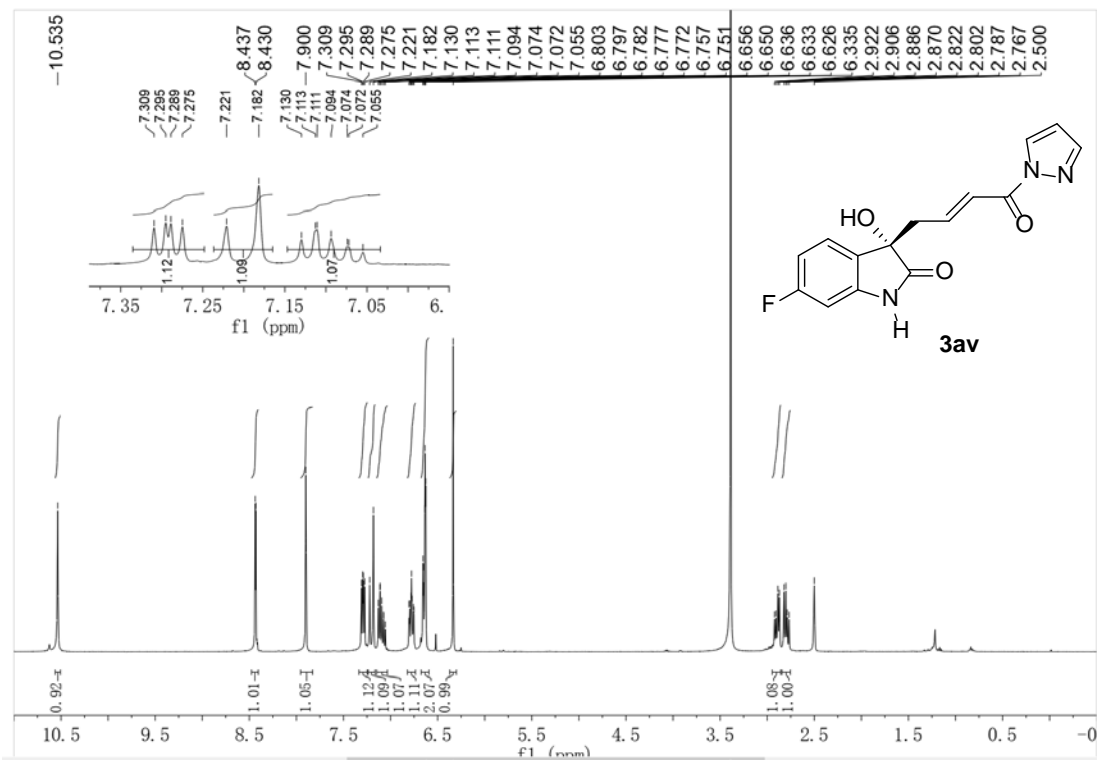


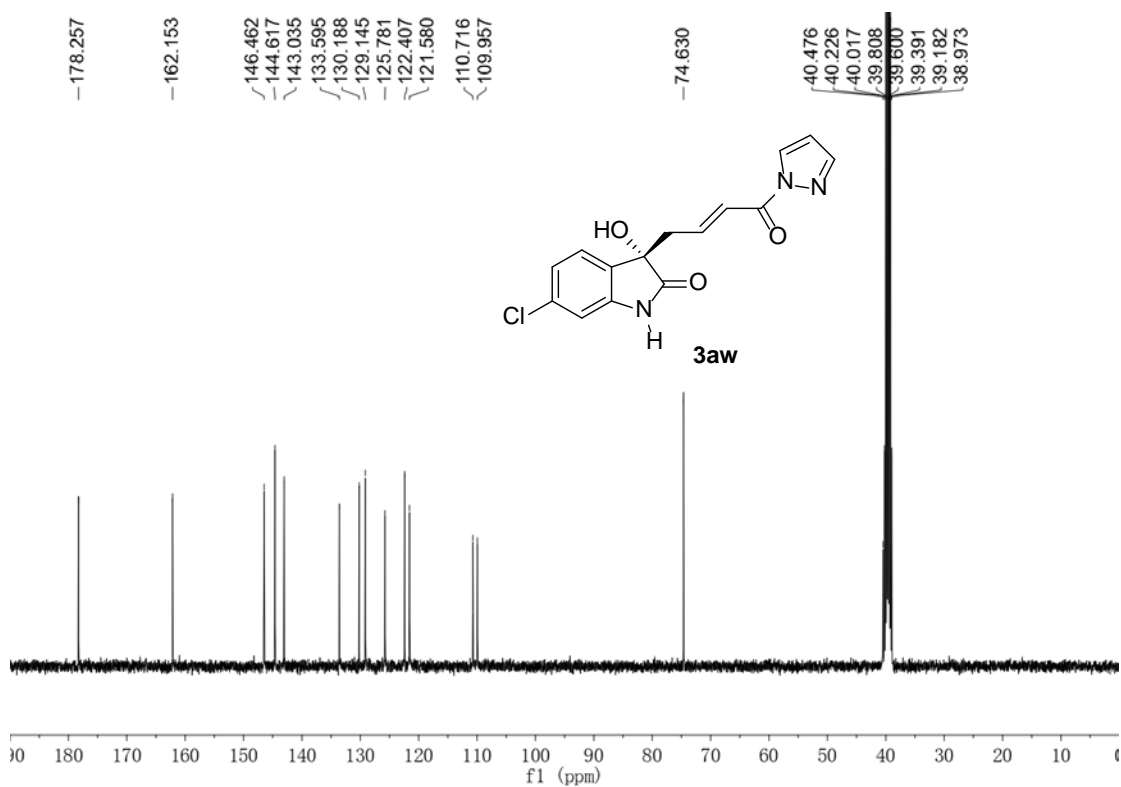
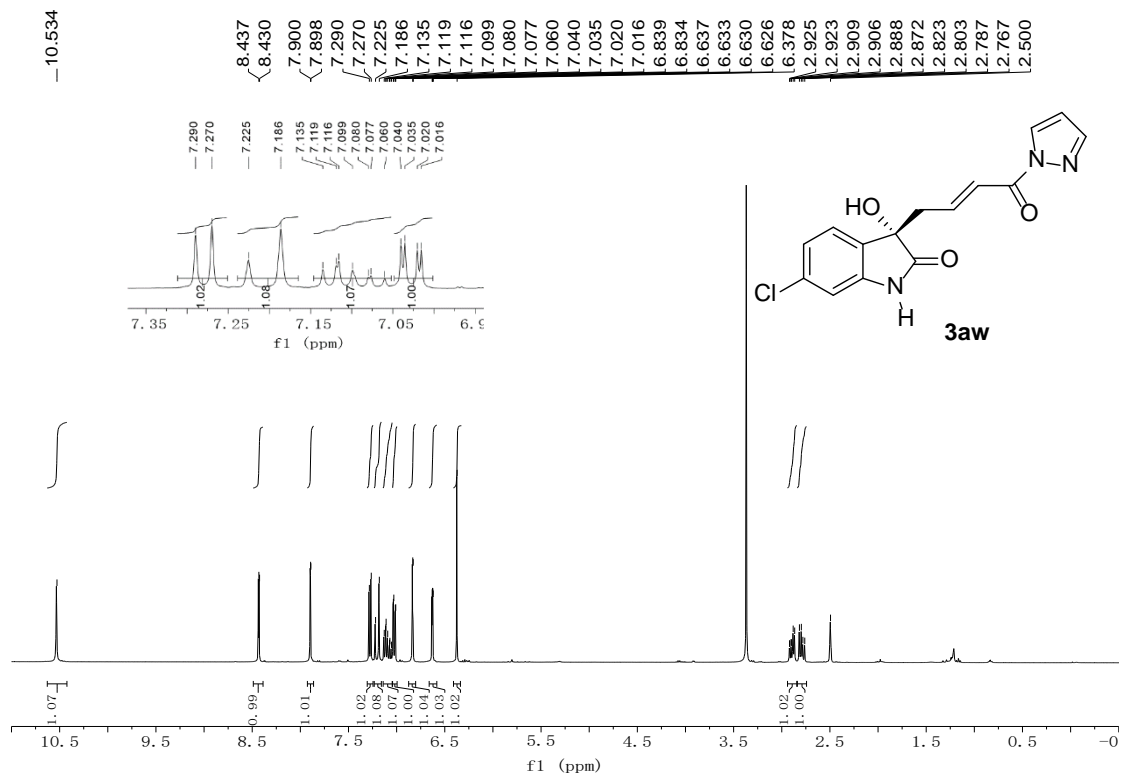


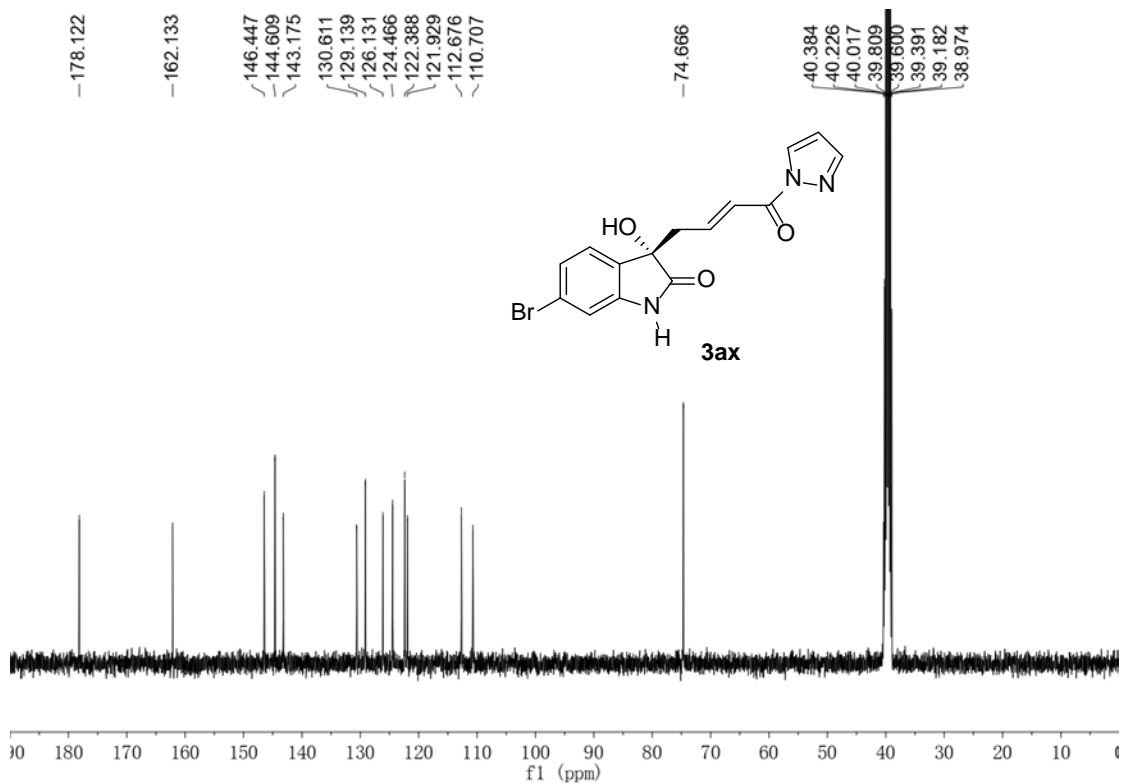
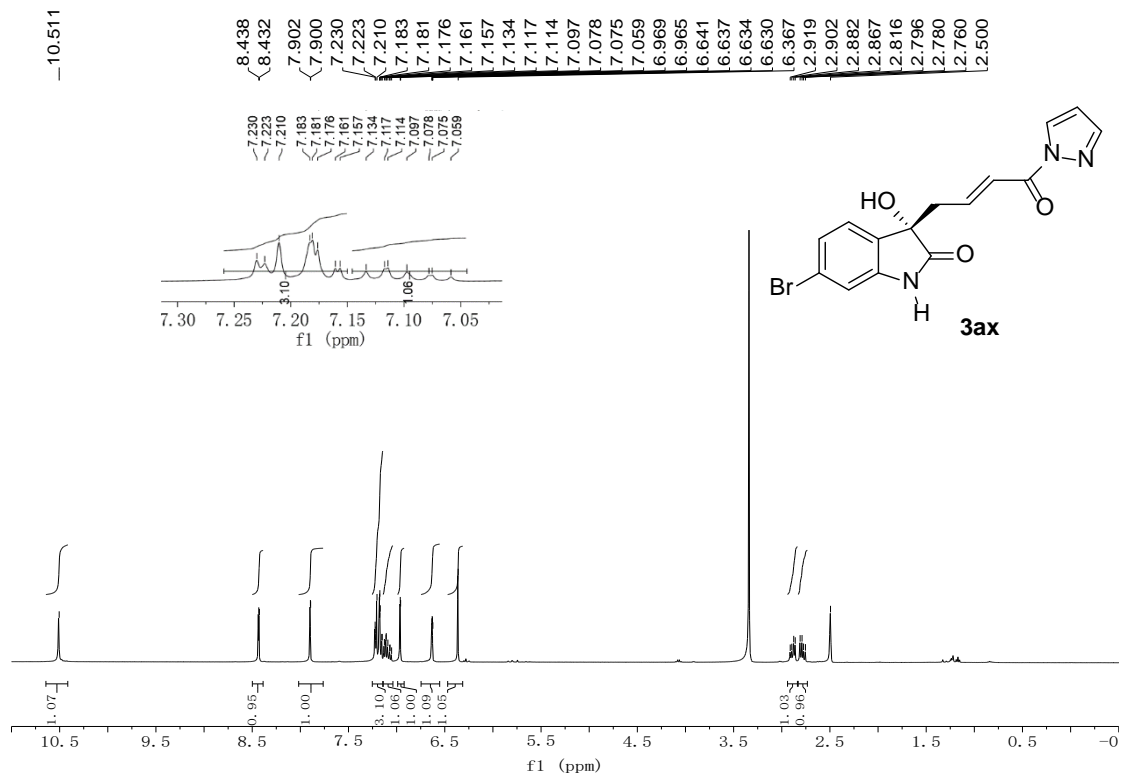


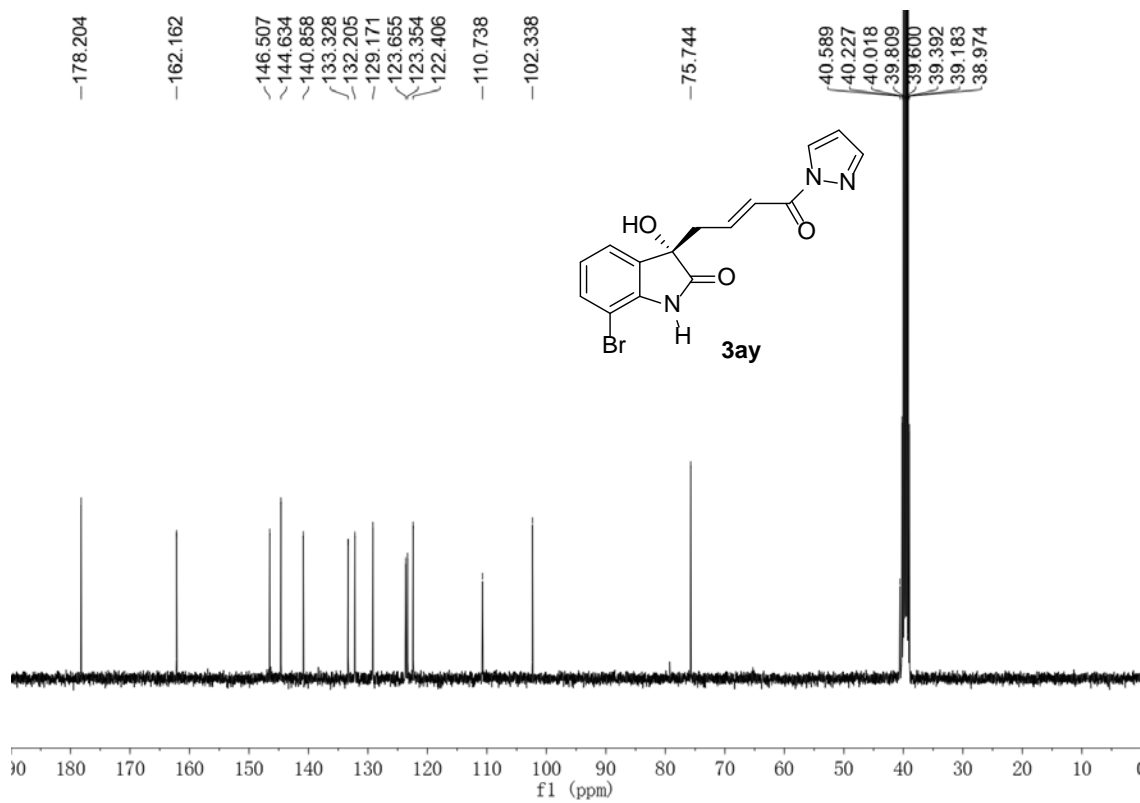
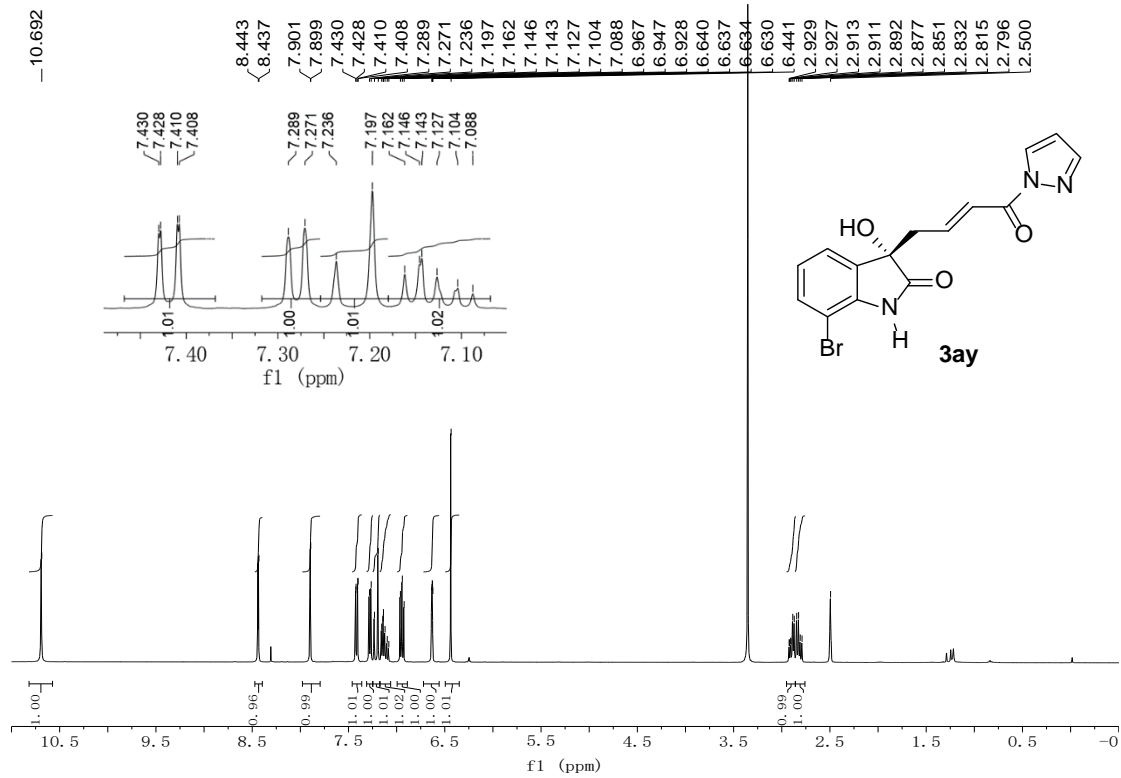


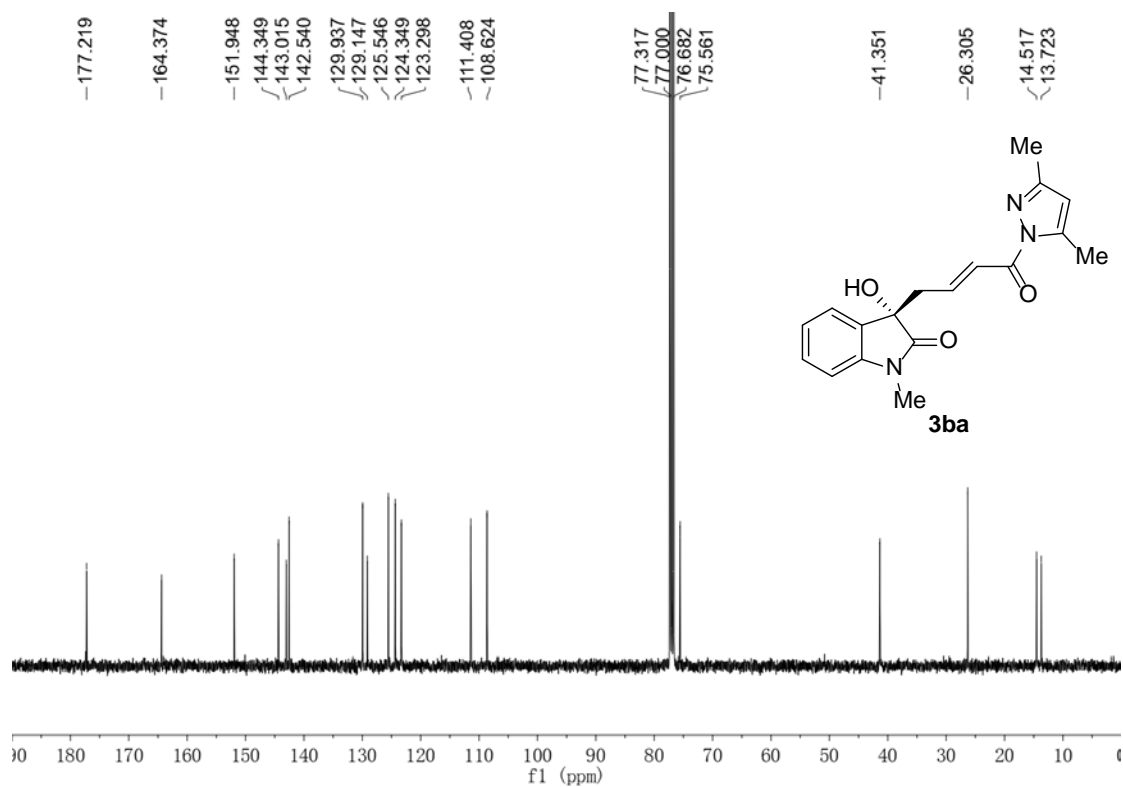
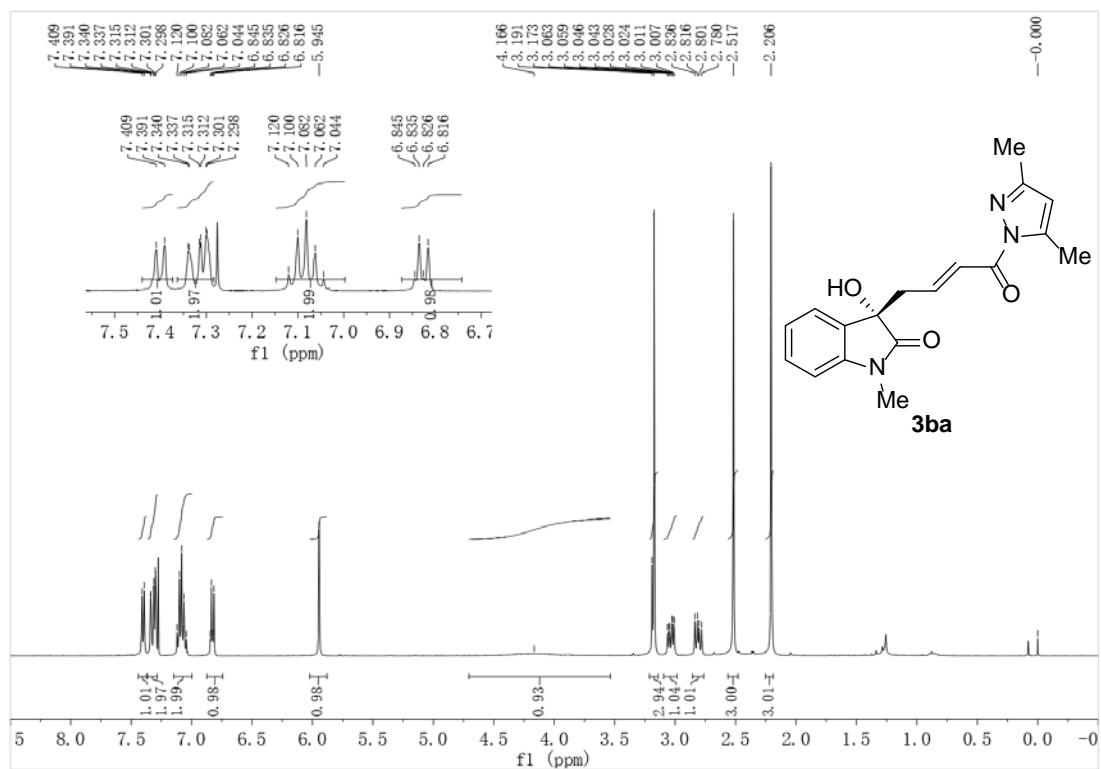


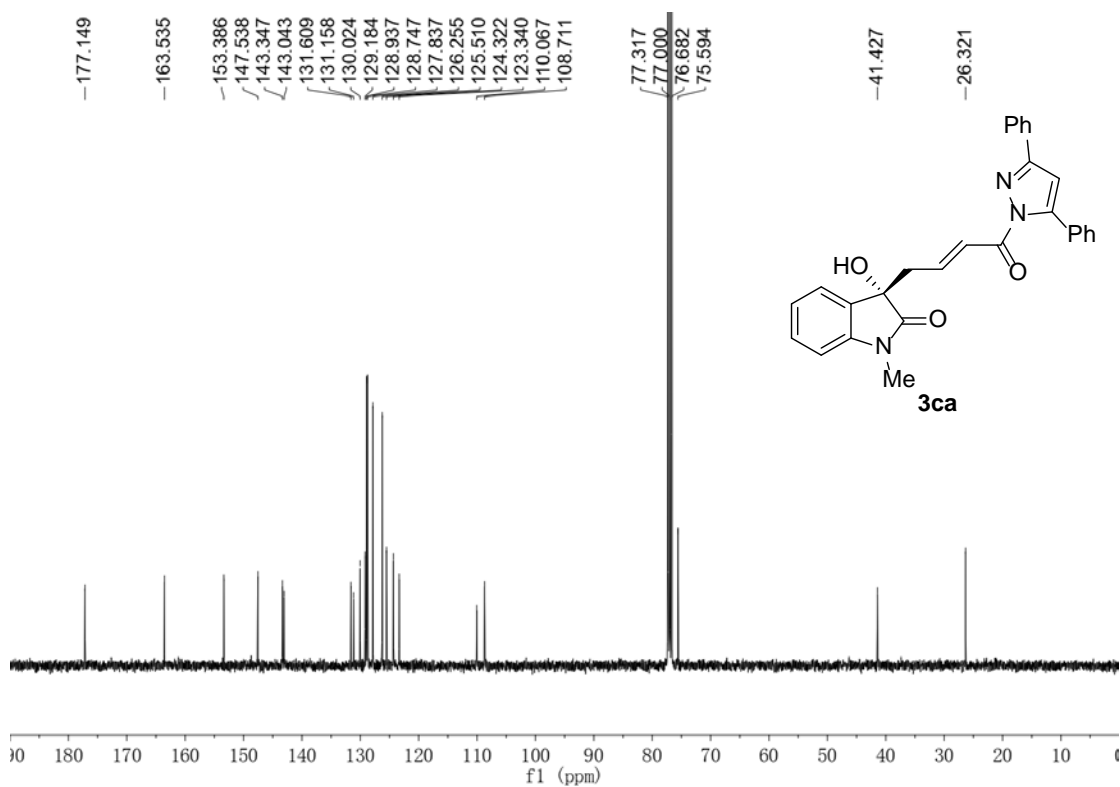
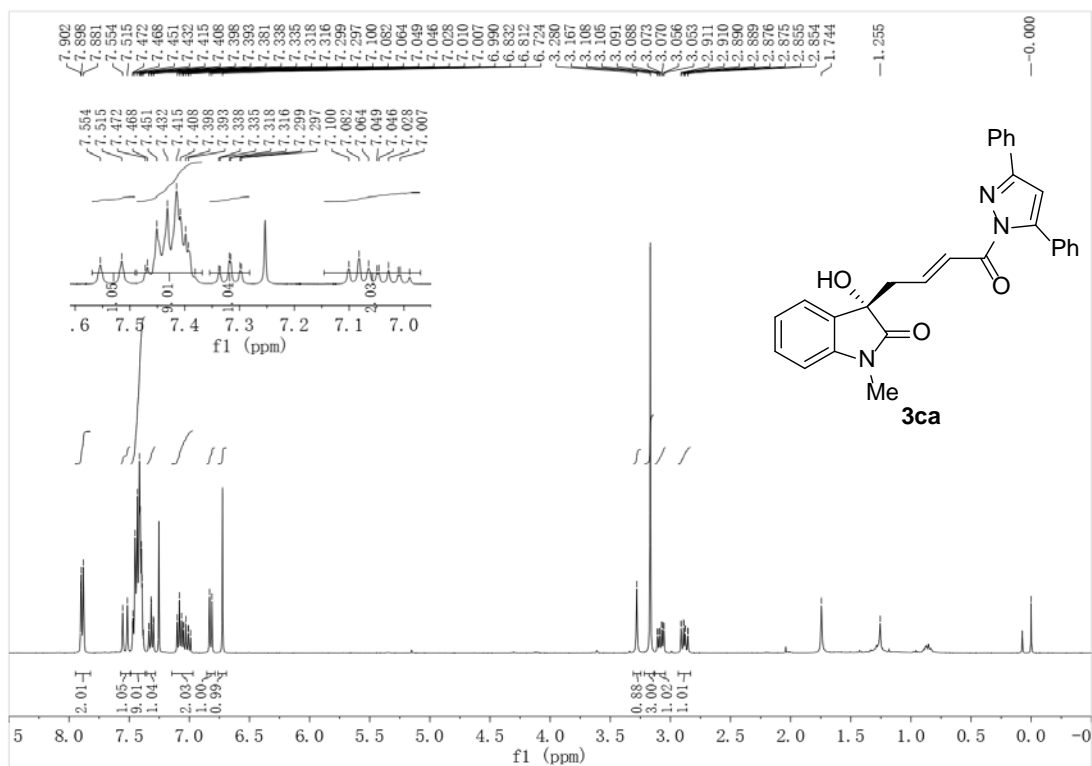


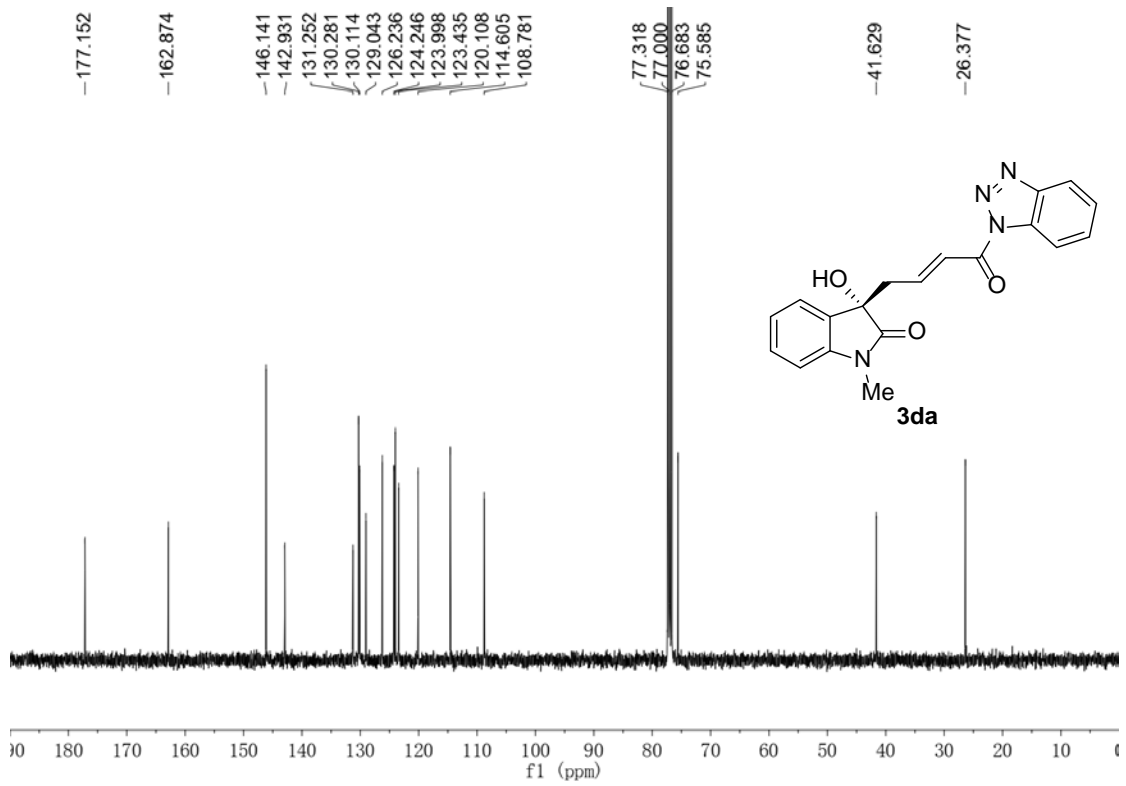
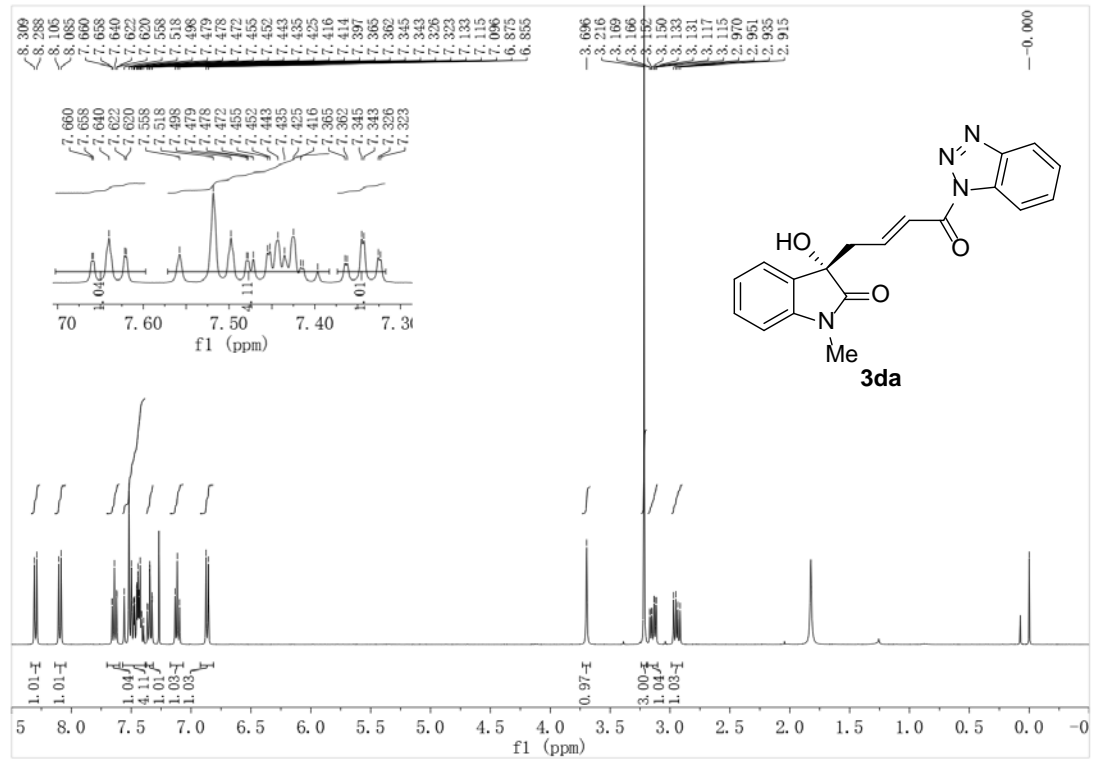


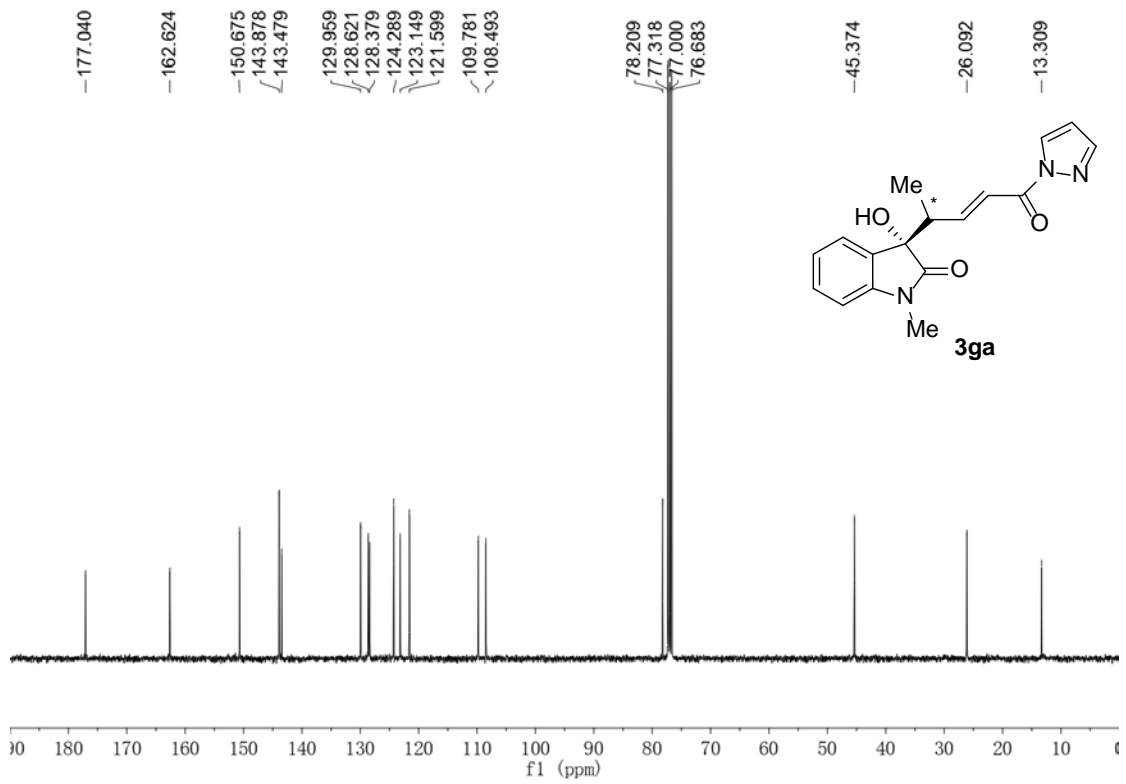
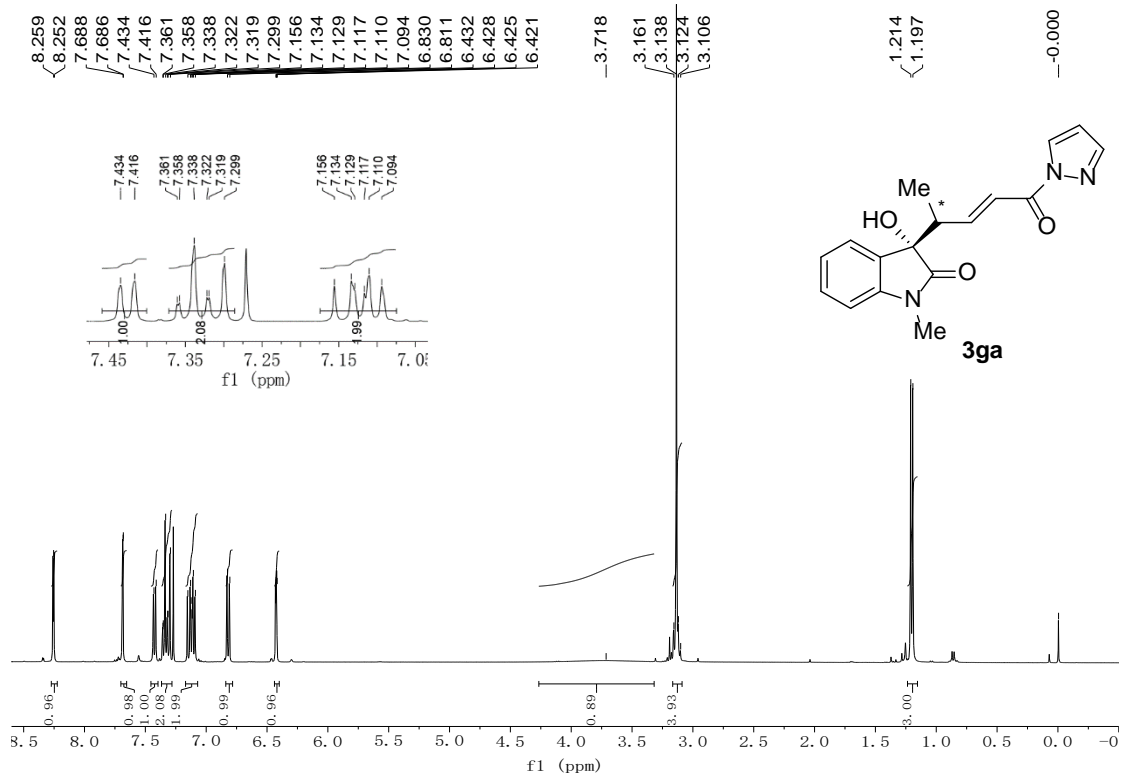


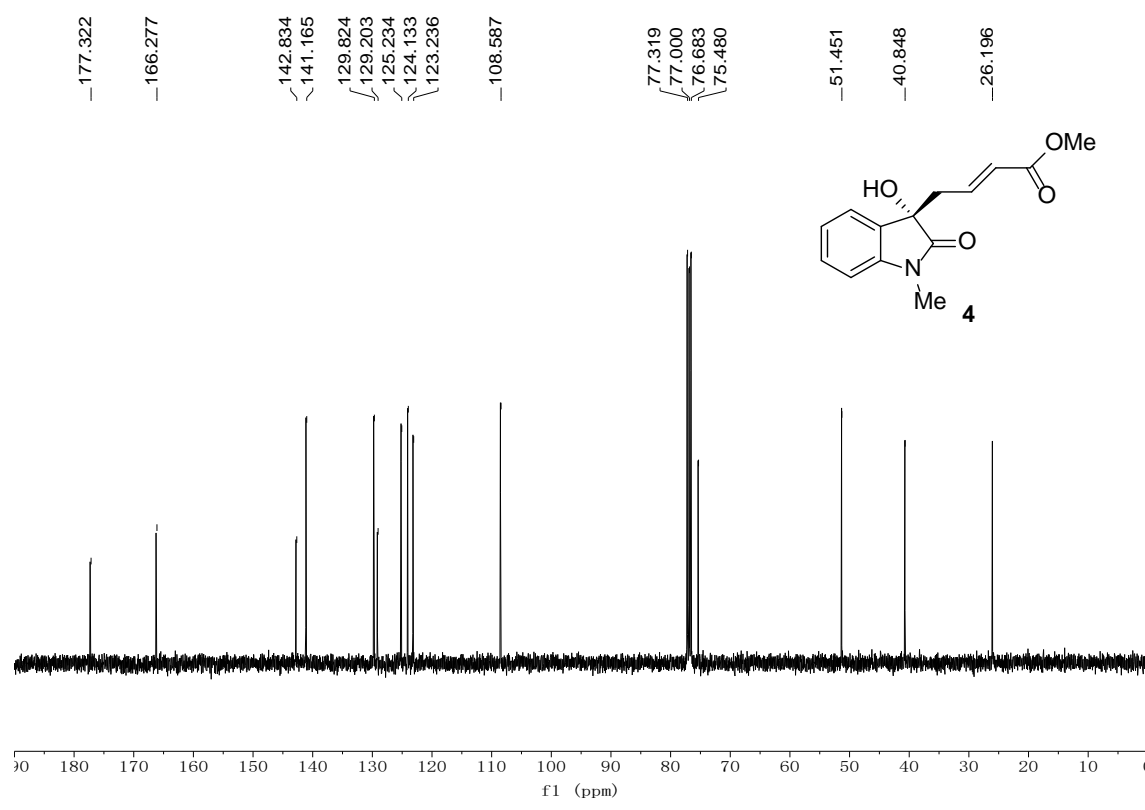
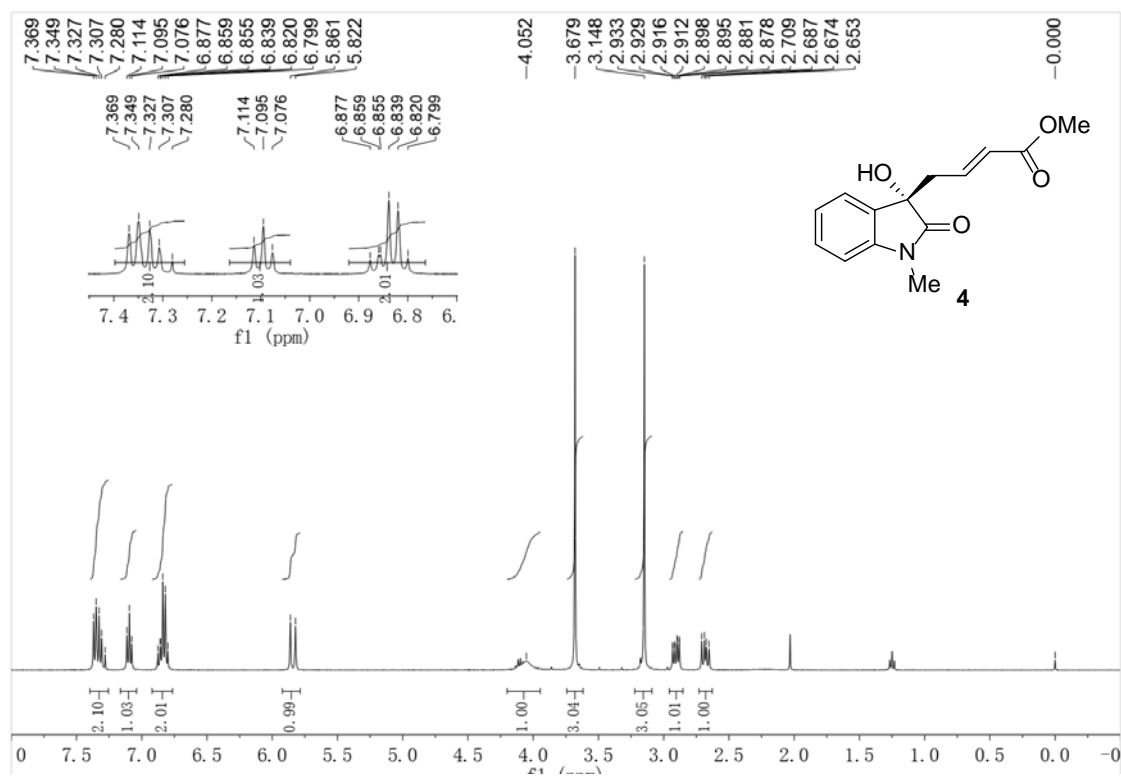


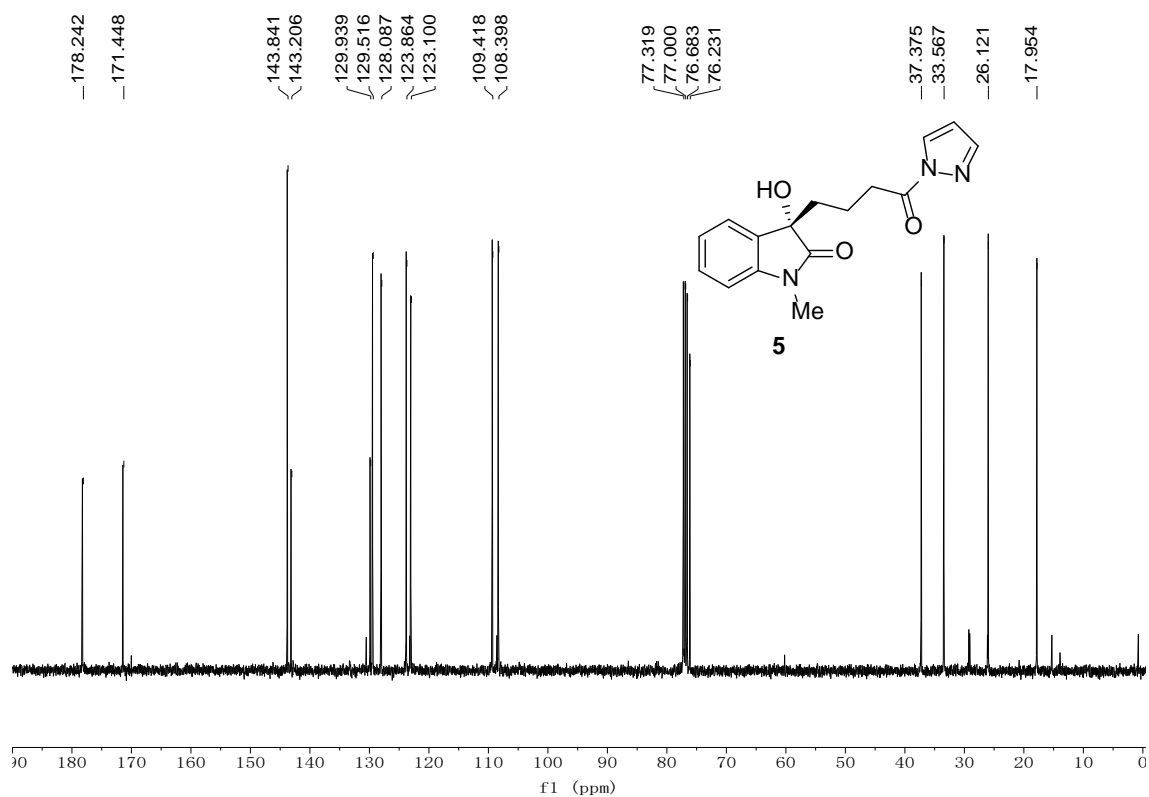
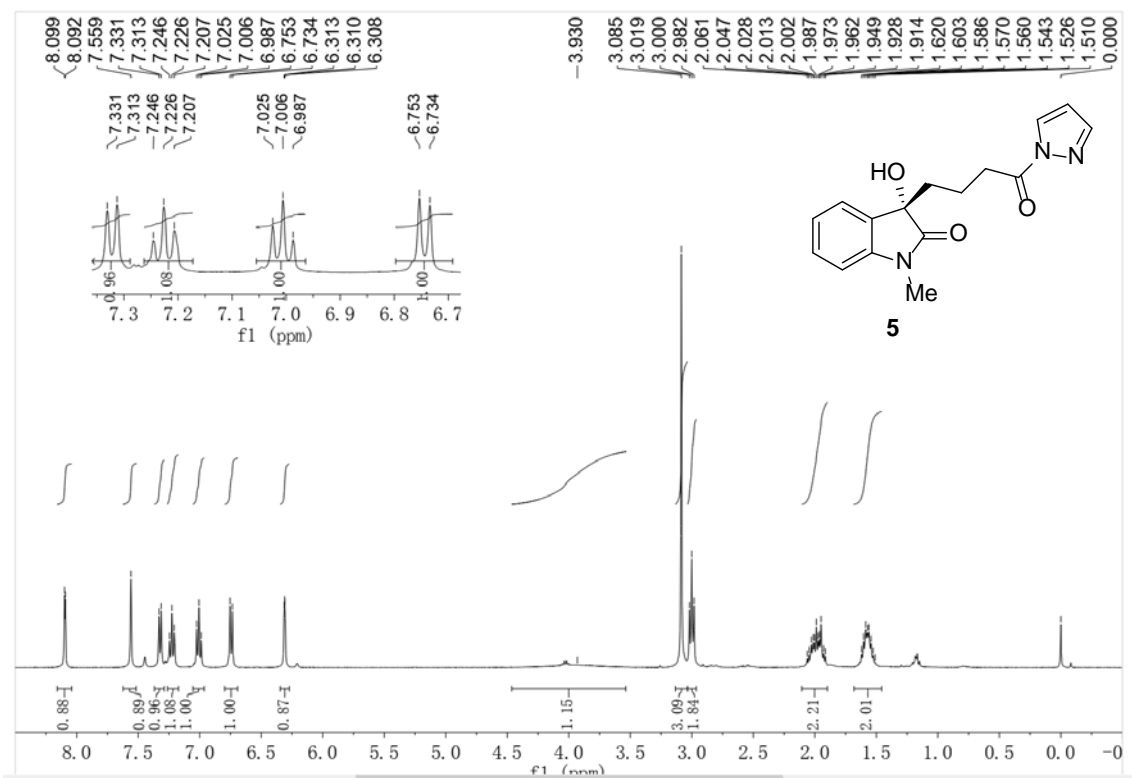


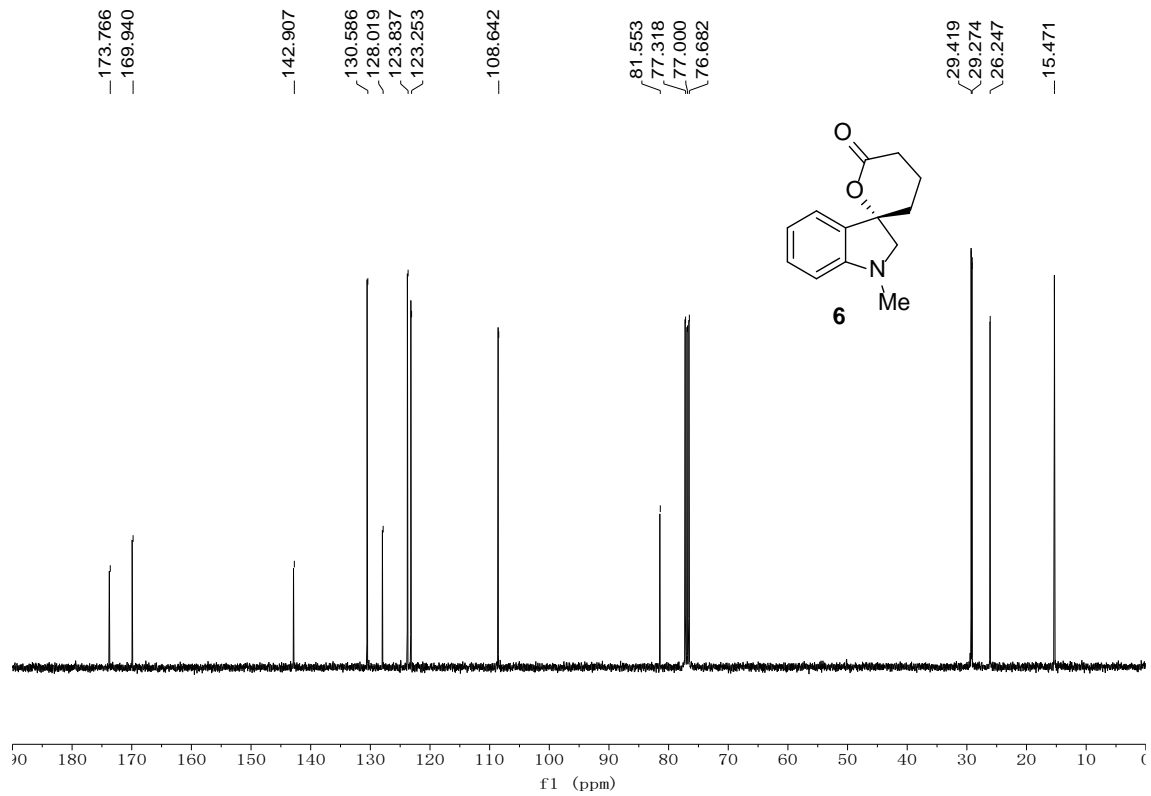
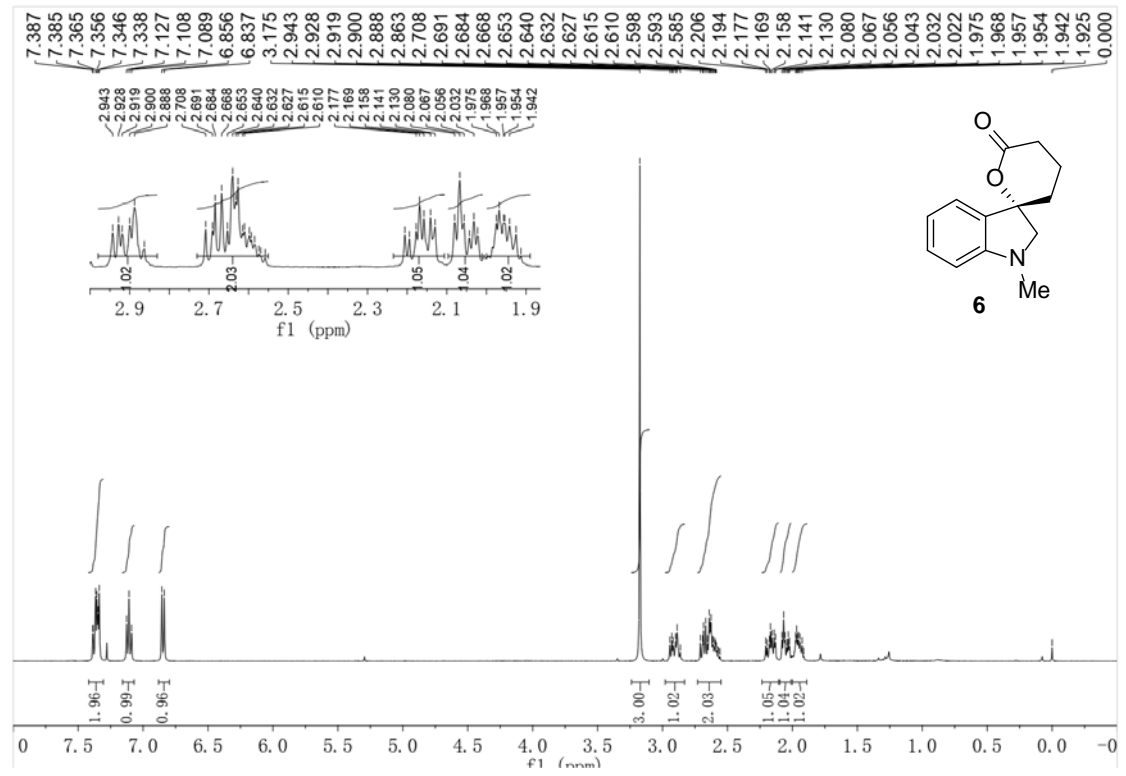


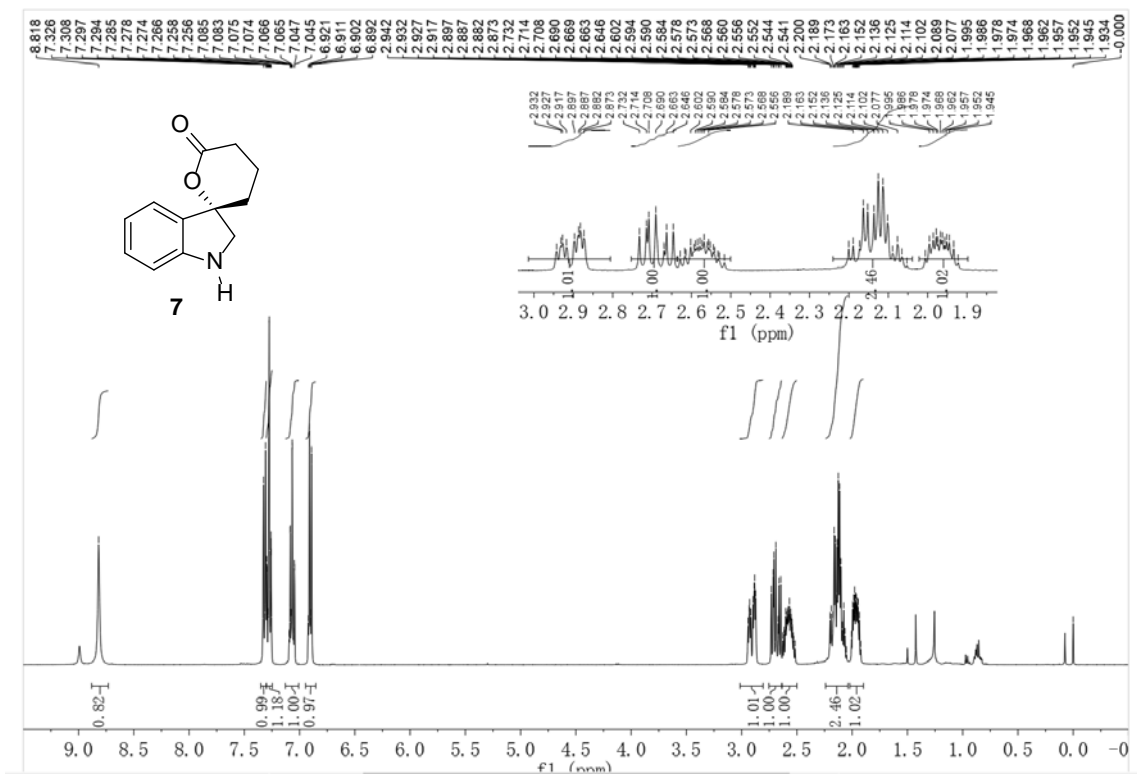




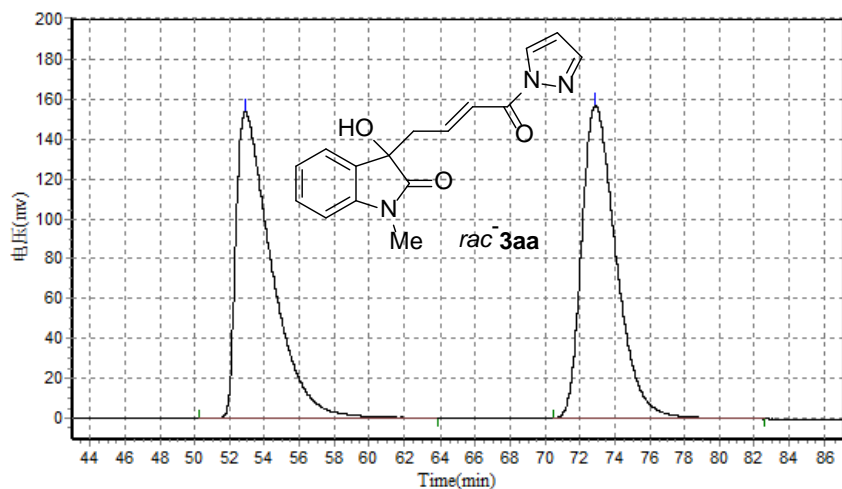






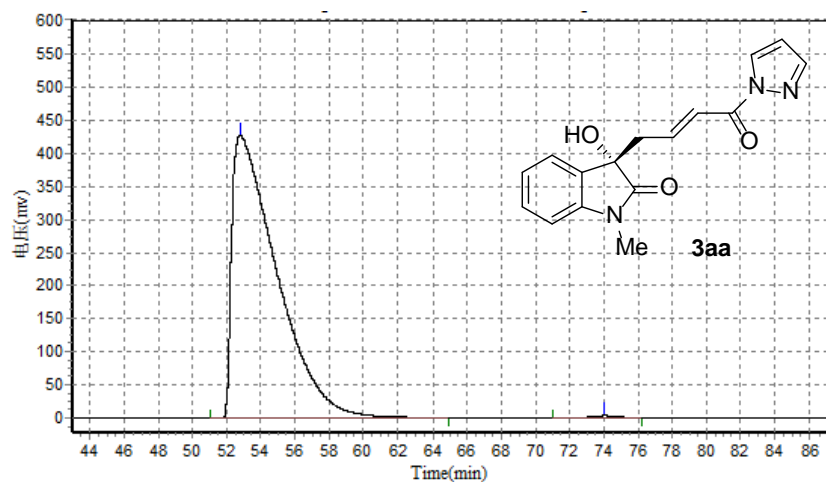


8. Copies of HPLC Spectra for the Product 3-7



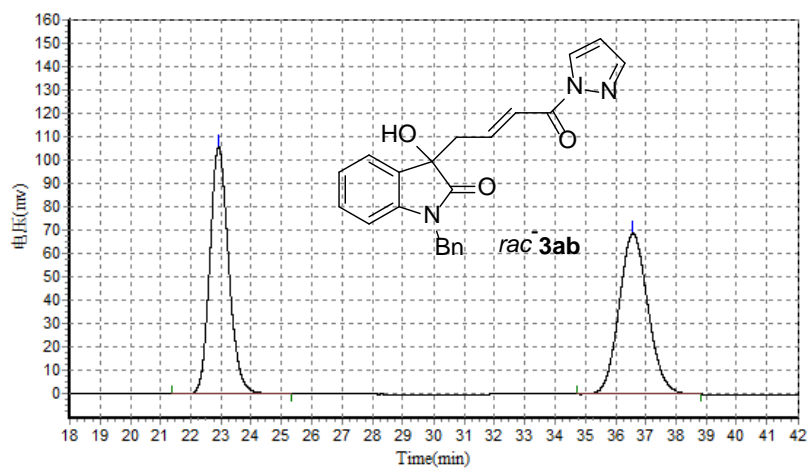
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		52.927	153506.453	21771754.000	50.2048
2		72.882	157139.234	21594142.000	49.7952
Total			310645.688	43365896.000	100.0000



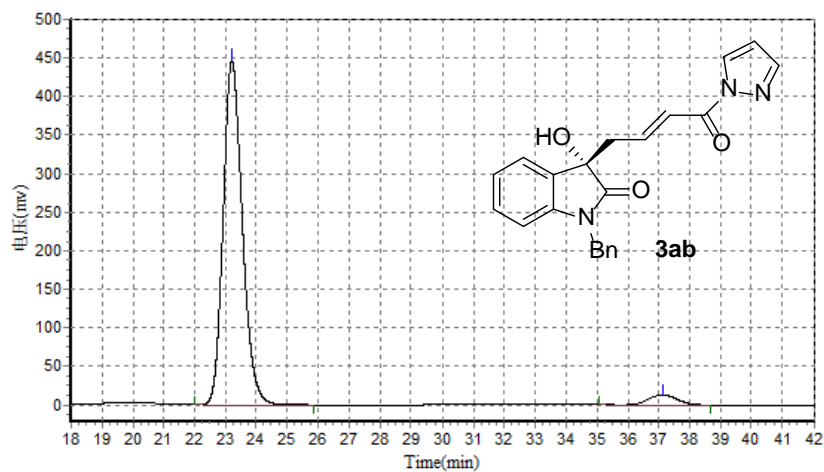
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		52.787	427313.031	78144656.000	99.4518
2		74.002	3756.249	430748.688	0.5482
Total			431069.280	78575404.688	100.0000



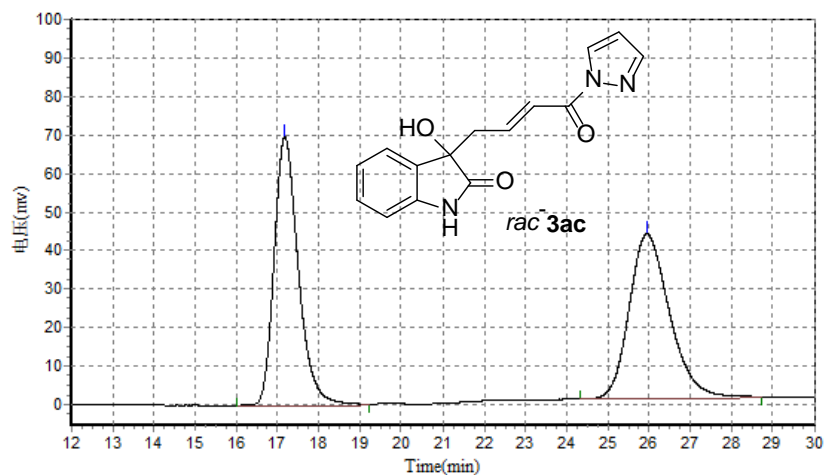
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.922	105893.891	4550180.500	49.8687
2		36.575	68925.500	4574133.000	50.1313
Total			174819.391	9124313.500	100.0000



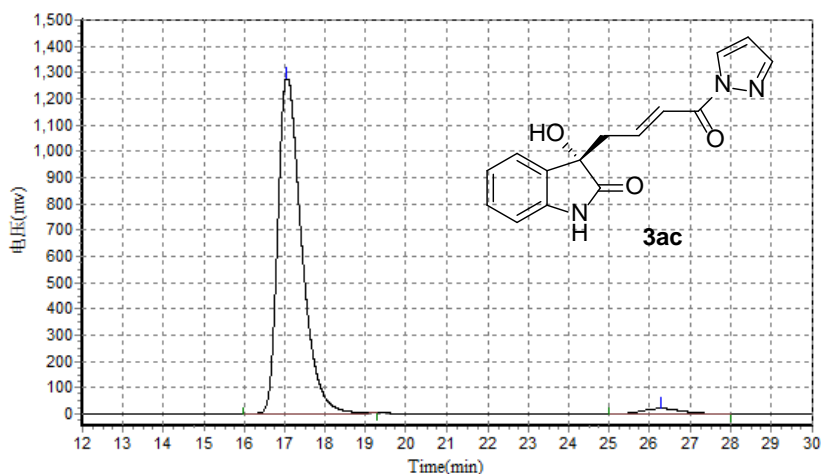
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		23.210	445985.844	19231278.000	95.7620
2		37.112	13421.620	851098.375	4.2380
Total			459407.464	20082376.375	100.0000



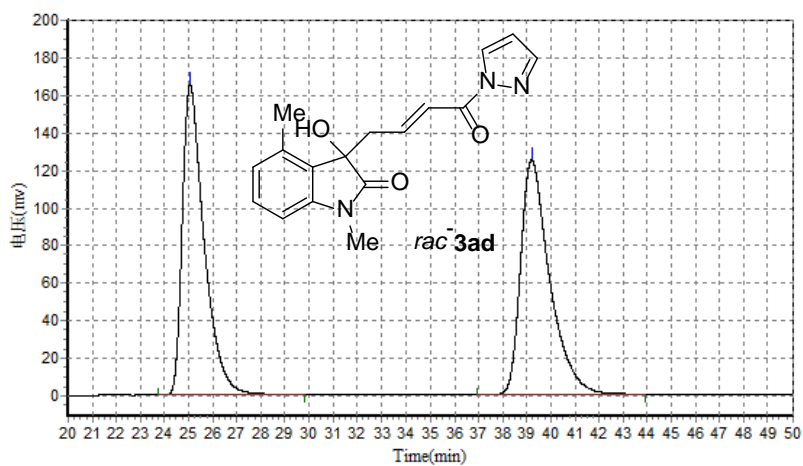
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.177	69609.977	2824763.000	49.4856
2		25.950	42567.582	2883485.000	50.5144
Total			112177.559	5708248.000	100.0000



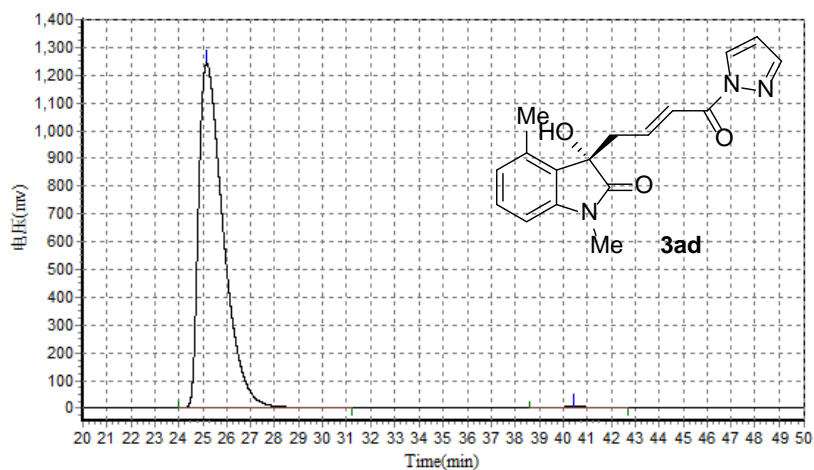
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.025	1270693.500	52179548.000	97.3975
2		26.267	20522.543	1394268.125	2.6025
Total			1291216.043	53573816.125	100.0000



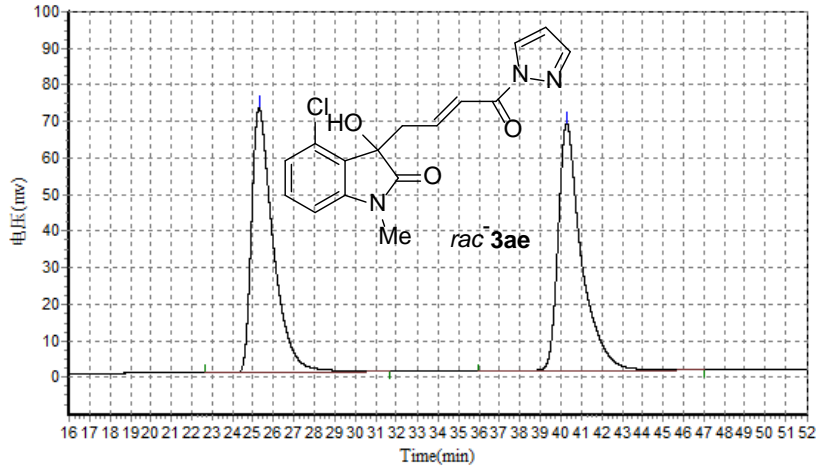
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.058	165389.641	10354877.000	49.8566
2		39.192	124996.297	10414444.000	50.1434
Total			290385.938	20769321.000	100.0000



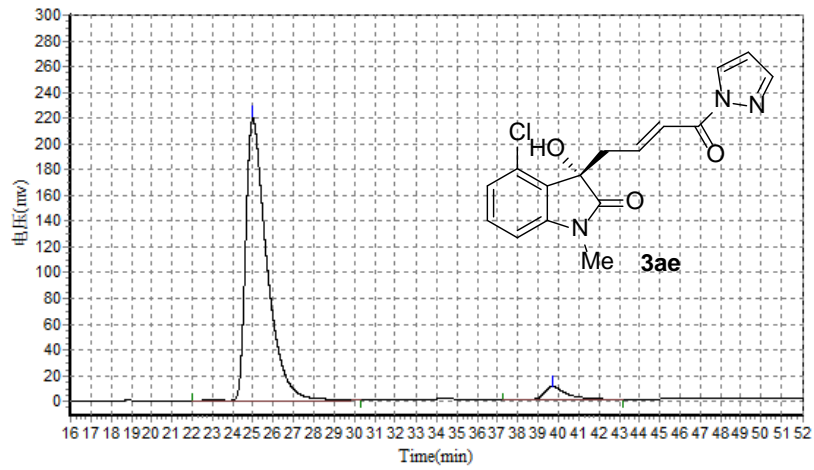
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.170	1242418.375	88704712.000	99.4494
2		40.427	6226.643	491126.500	0.5506
Total			1248645.018	89195838.500	100.0000



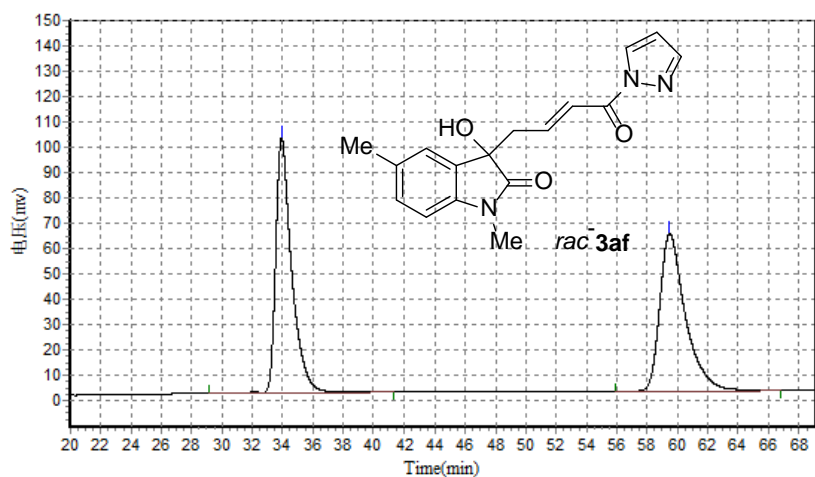
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.292	72303.344	5314339.500	49.9955
2		40.285	67477.125	5315300.000	50.0045
Total			139780.469	10629639.500	100.0000



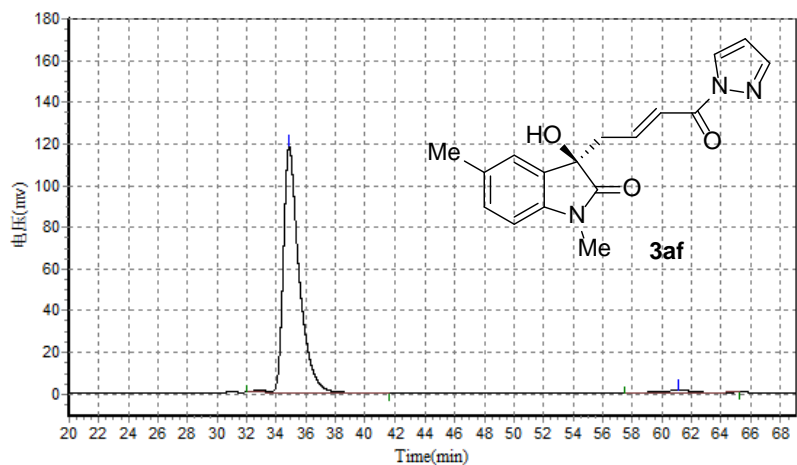
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		24.988	219262.438	15738429.000	95.4882
2		39.723	10098.634	743645.438	4.5118
Total			229361.071	16482074.438	100.0000



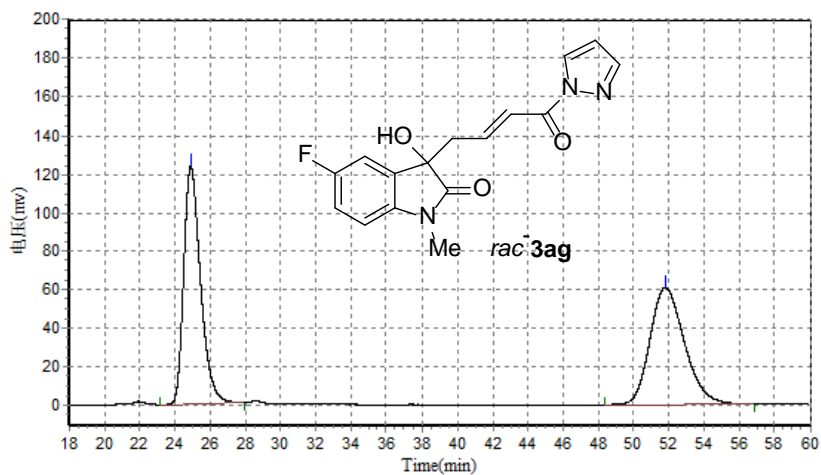
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		33.940	100819.203	7362127.000	50.3781
2		59.493	62289.703	7251617.500	49.6219
Total			163108.906	14613744.500	100.0000



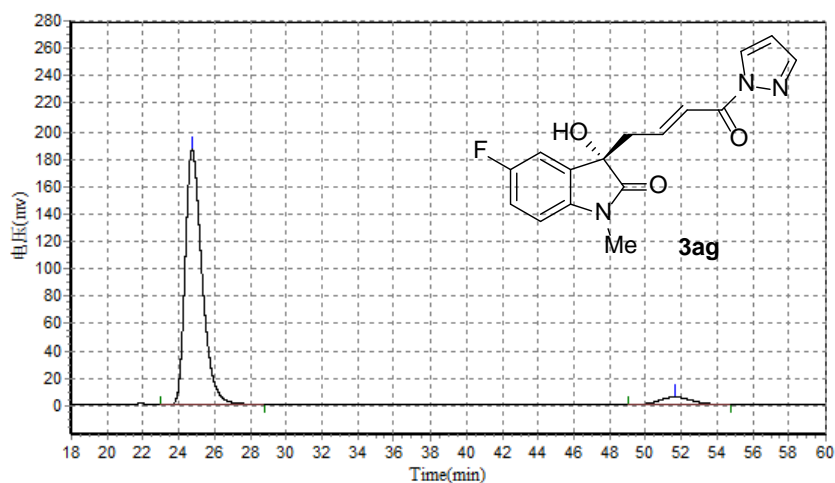
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		34.875	118001.289	8733882.000	98.3860
2		61.105	1338.307	143274.594	1.6140
Total			119339.596	8877156.594	100.0000



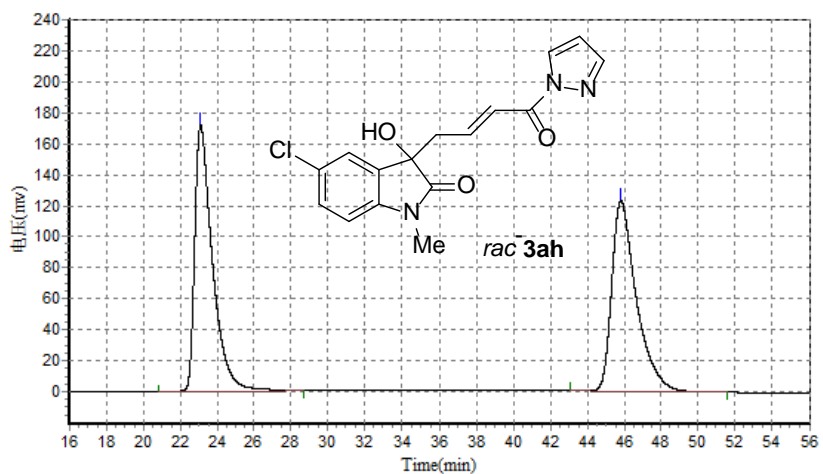
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		24.895	123399.375	8197191.500	49.8212
2		51.795	60744.172	8256040.500	50.1788
Total			184143.547	16453232.000	100.0000



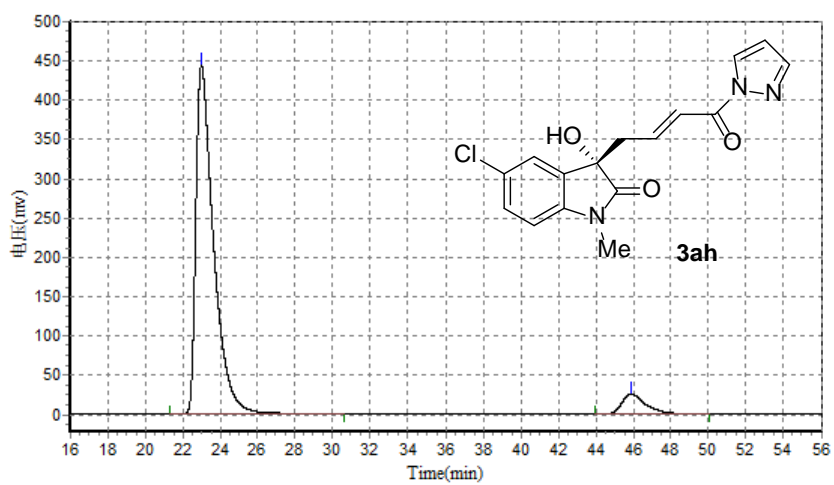
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		24.745	186357.859	12167291.000	94.1544
2		51.622	5657.717	755402.750	5.8456
Total			192015.576	12922693.750	100.0000



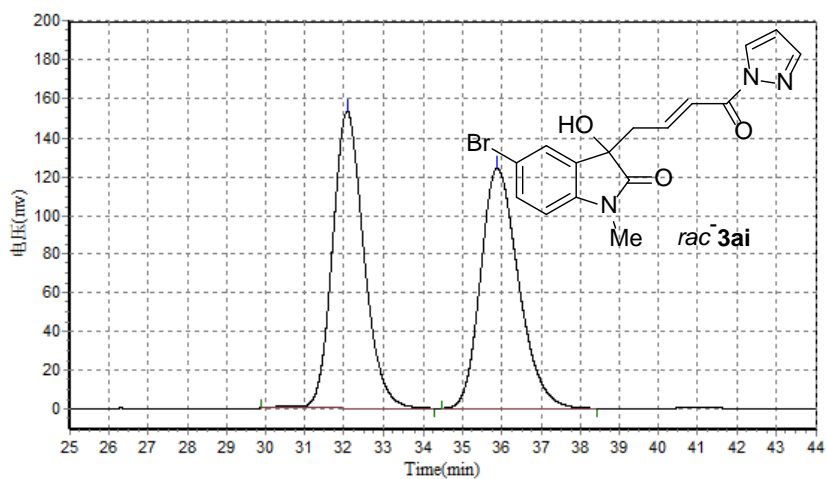
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		23.098	171791.063	11433211.000	50.1159
2		45.820	122846.305	11380328.000	49.8841
Total			294637.367	22813539.000	100.0000



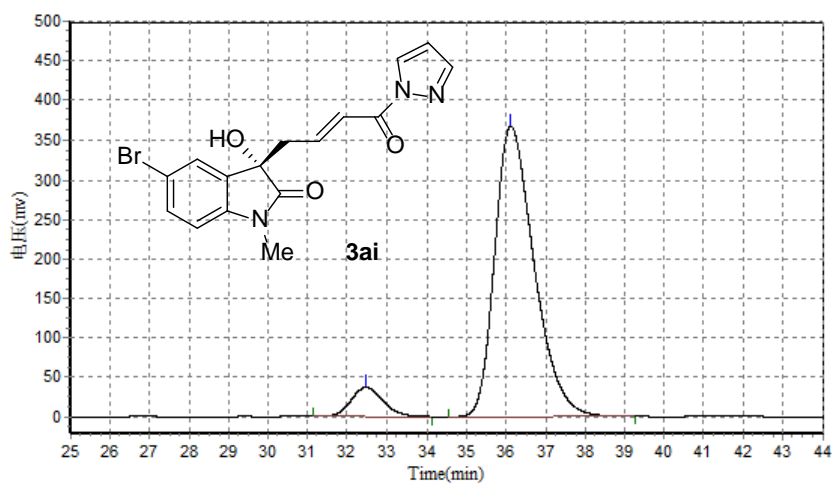
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.990	444707.281	29205324.000	92.6963
2		45.883	25602.506	2301141.250	7.3037
Total			470309.787	31506465.250	100.0000



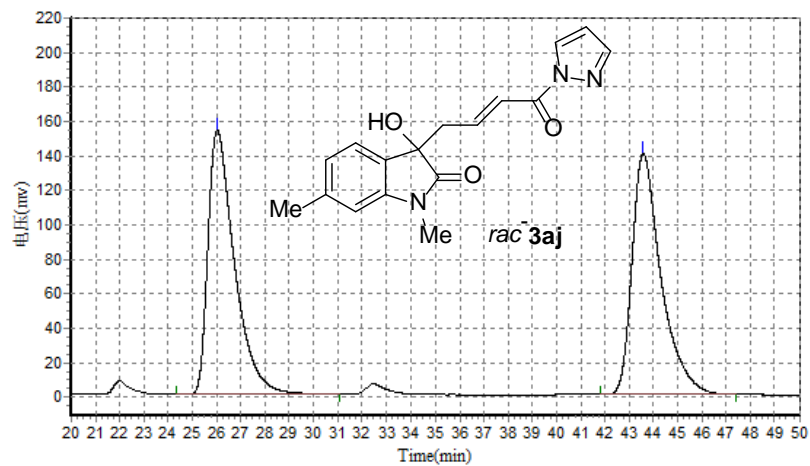
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		32.080	152922.891	8510596.000	50.4496
2		35.882	124385.633	8358897.000	49.5504
Total			277308.523	16869493.000	100.0000



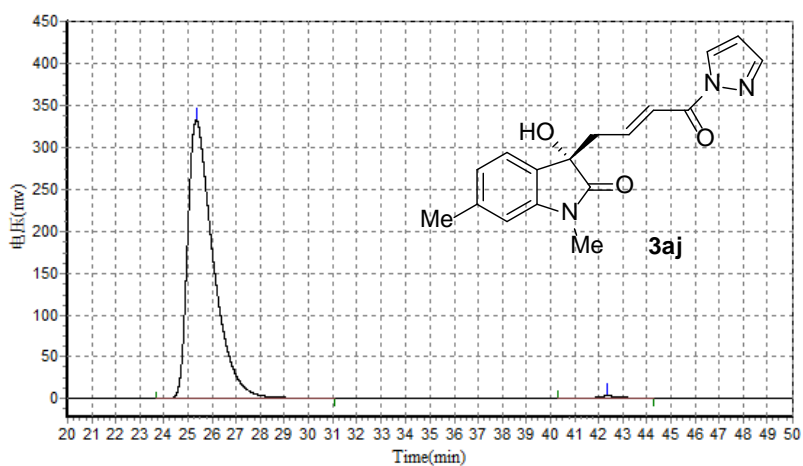
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		32.480	36940.172	2058230.750	7.4536
2		36.118	367964.344	25555574.000	92.5464
Total			404904.516	27613804.750	100.0000



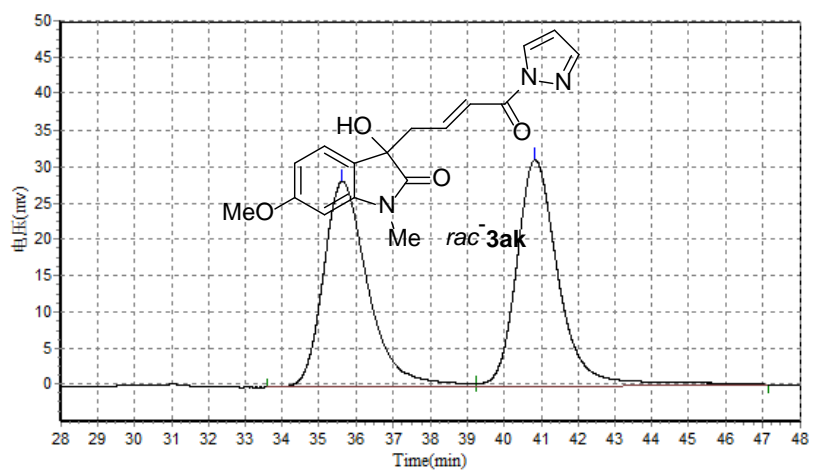
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		26.027	153375.875	11662809.000	50.0363
2		43.580	139826.109	11645878.000	49.9637
Total			293201.984	23308687.000	100.0000



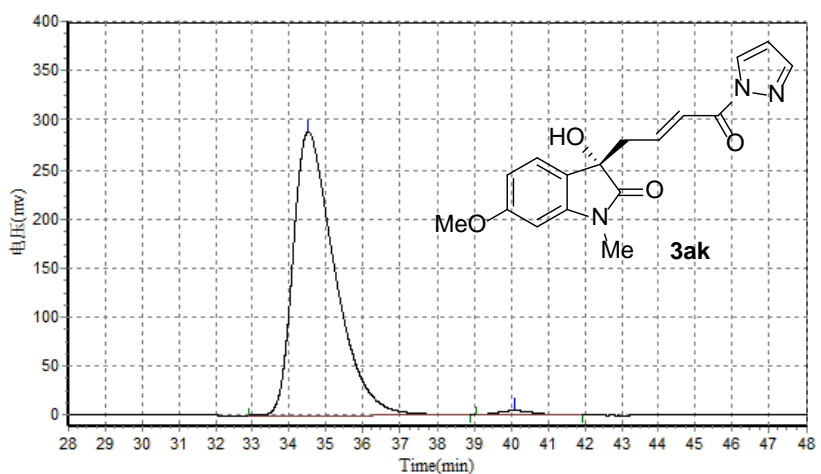
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.348	331715.188	24457648.000	99.1860
2		42.355	2842.697	200726.250	0.8140
Total			334557.884	24658374.250	100.0000



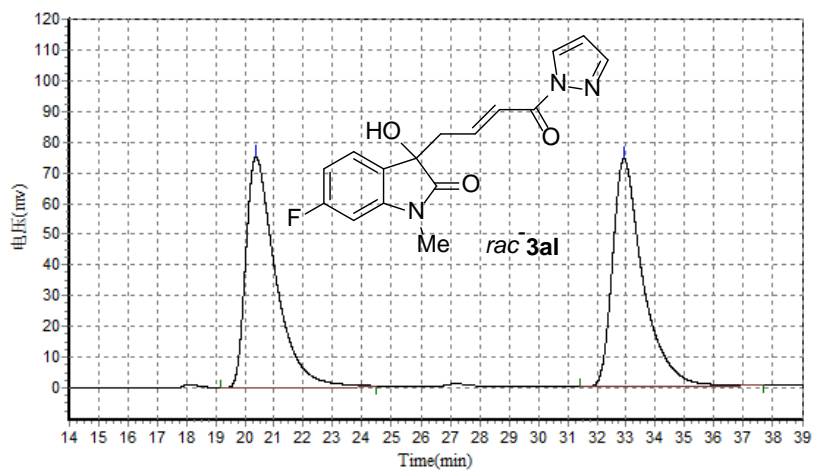
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		35.633	28340.332	2369282.250	49.0613
2		40.837	31219.906	2459946.000	50.9387
Total			59560.238	4829228.250	100.0000



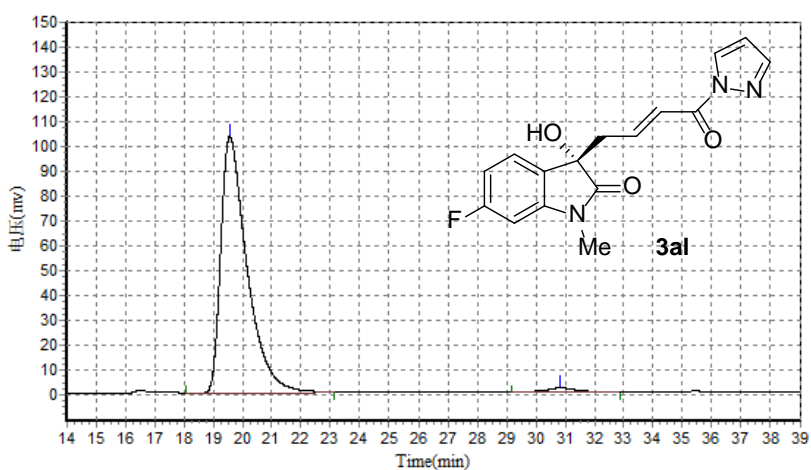
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		34.513	288336.906	22622818.000	98.7234
2		40.093	4274.730	292539.188	1.2766
Total			292611.636	22915357.188	100.0000



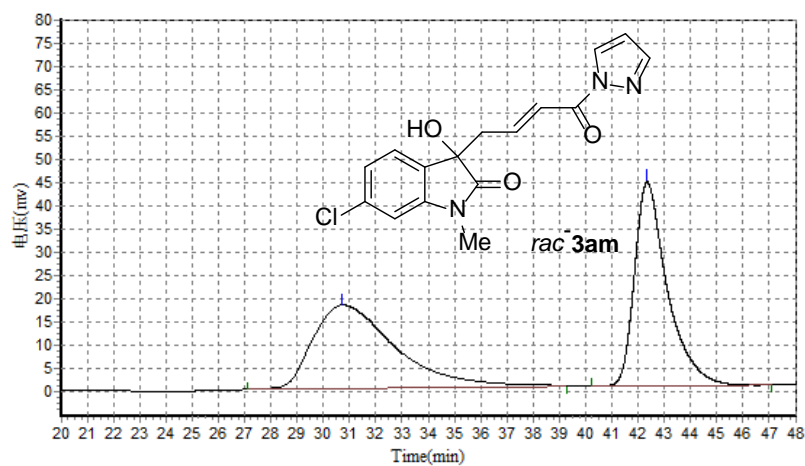
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		20.382	75042.164	5299524.000	49.7163
2		32.925	74155.430	5360014.000	50.2837
Total			149197.594	10659538.000	100.0000



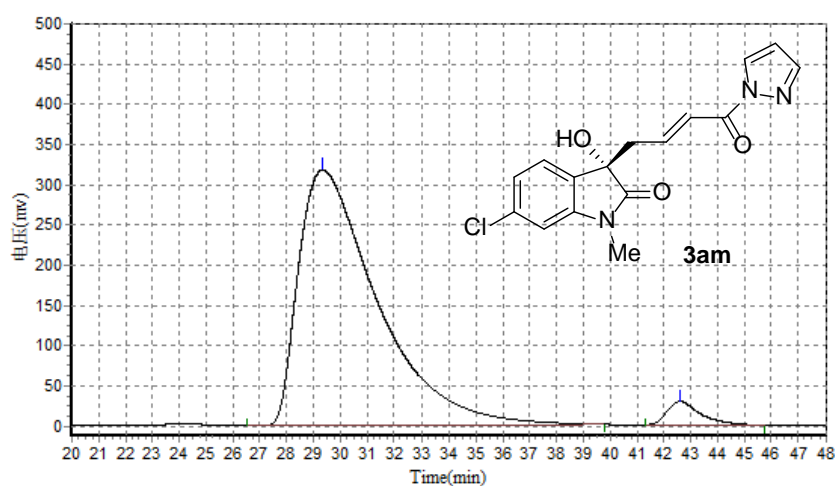
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.568	103225.992	6396701.500	97.9870
2		30.820	1817.137	131408.938	2.0130
Total			105043.129	6528110.438	100.0000



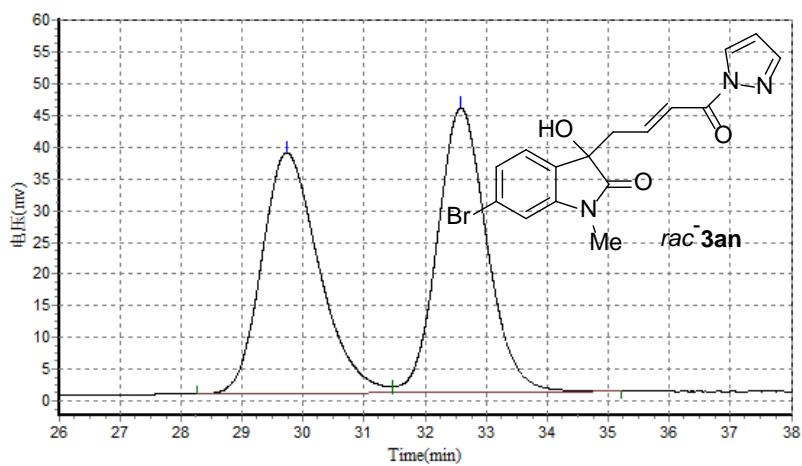
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		30.737	17927.072	3874674.250	50.5846
2		42.357	43802.074	3785116.000	49.4154
Total			61729.146	7659790.250	100.0000



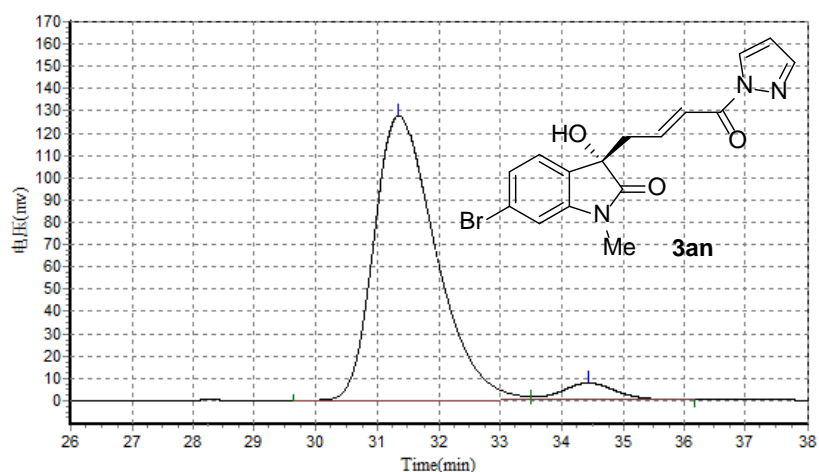
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		29.343	317300.656	64548512.000	96.2700
2		42.575	29269.391	2500953.000	3.7300
Total			346570.047	67049465.000	100.0000



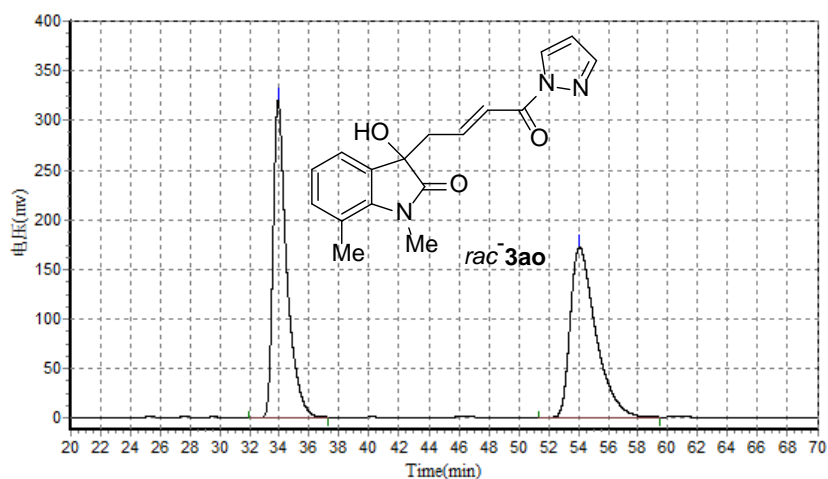
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		29.740	37827.883	2476533.000	49.5508
2		32.578	44756.848	2521437.000	50.4492
Total			82584.730	4997970.000	100.0000



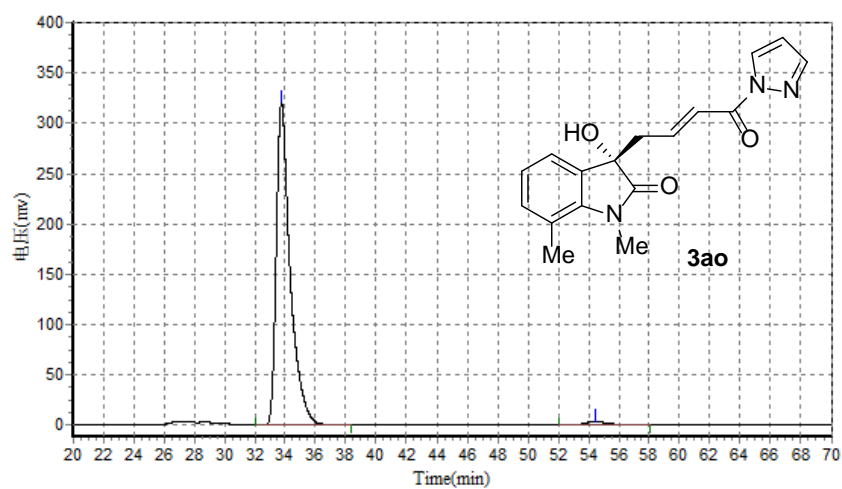
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		31.350	127582.773	8802284.000	95.1965
2		34.428	7431.411	444153.000	4.8035
Total			135014.185	9246437.000	100.0000



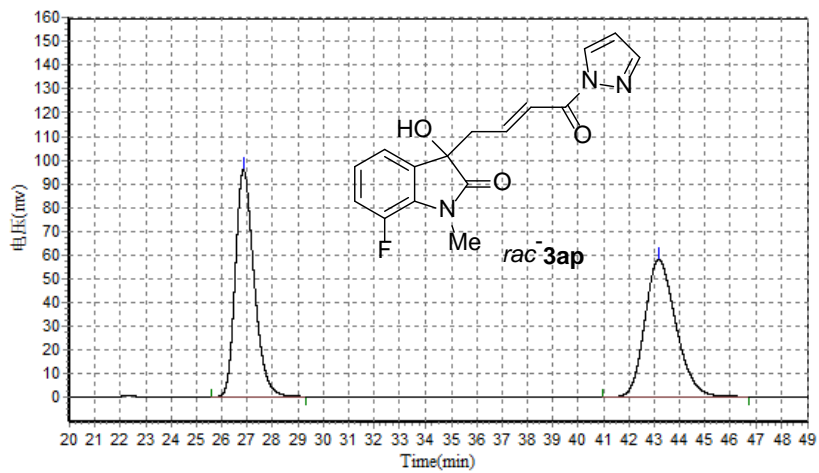
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		33.922	319357.250	20328916.000	50.0081
2		54.068	171321.609	20322356.000	49.9919
Total			490678.859	40651272.000	100.0000



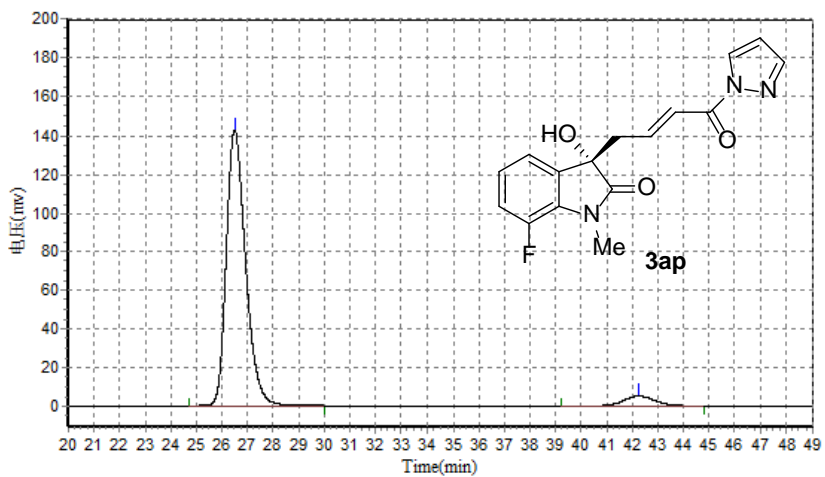
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		33.763	320222.375	20345584.000	98.0635
2		54.400	3657.798	401769.250	1.9365
Total			323880.173	20747353.250	100.0000



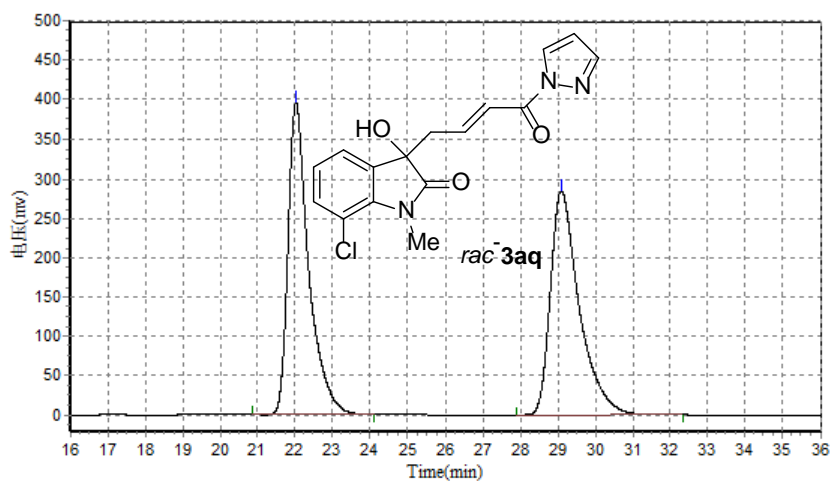
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		26.855	95901.648	4908006.500	49.9451
2		43.168	57912.453	4918806.000	50.0550
Total			153814.102	9826812.500	100.0000



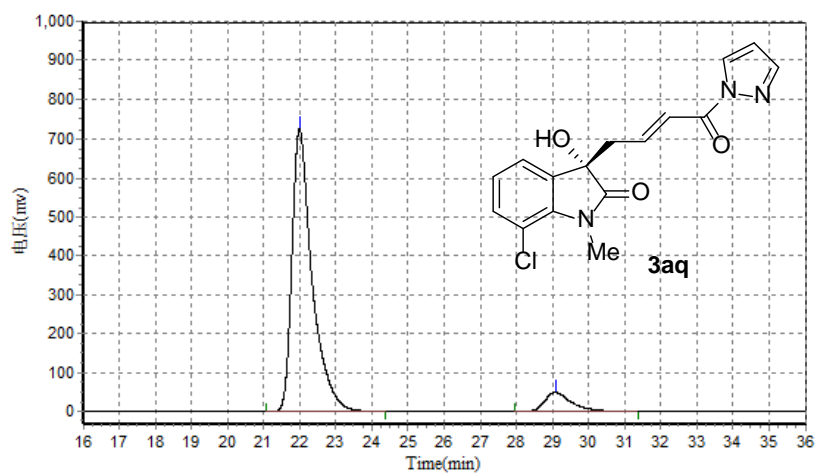
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		26.495	142476.891	7456825.000	94.4759
2		42.245	5119.101	436008.781	5.5241
Total			147595.991	7892833.781	100.0000



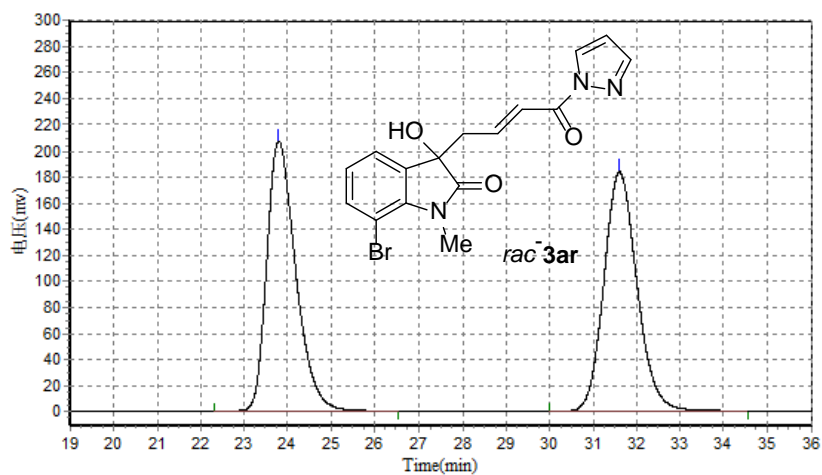
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.025	395740.281	15221214.000	49.9588
2		29.090	284586.219	15246341.000	50.0412
Total			680326.500	30467555.000	100.0000



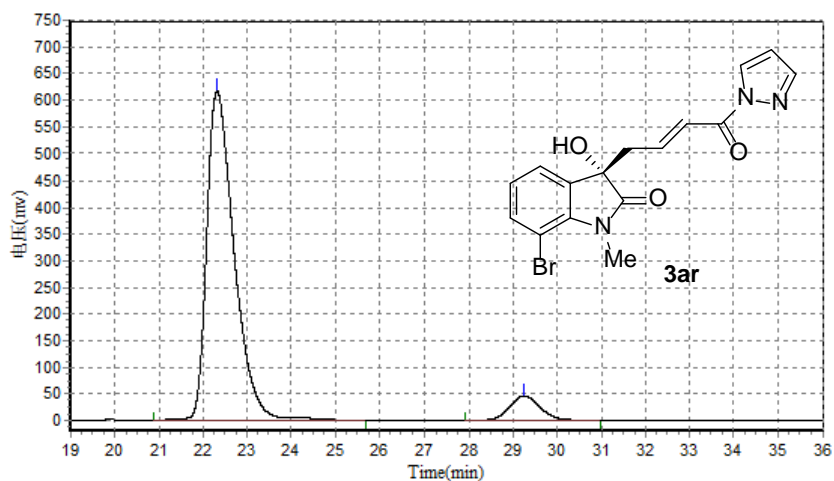
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.997	726918.625	28045564.000	91.8116
2		29.075	48851.684	2501313.750	8.1884
Total			775770.309	30546877.750	100.0000



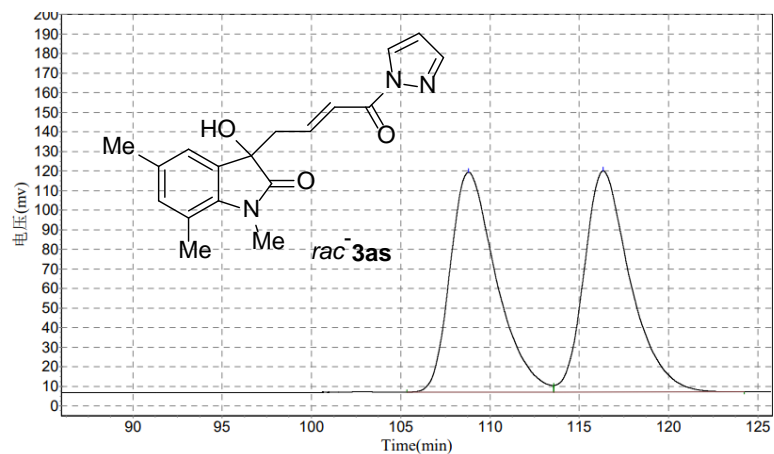
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		23.795	207517.469	9599314.000	49.4542
2		31.602	184482.516	9811212.000	50.5458
Total			391999.984	19410526.000	100.0000



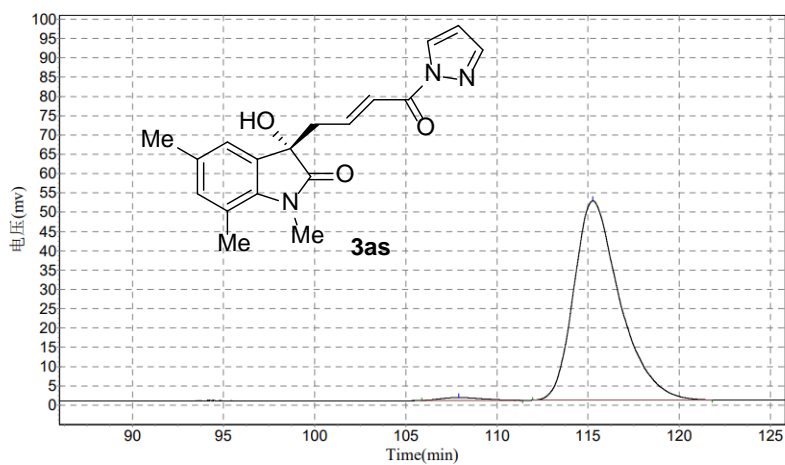
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.318	617302.313	26633330.000	92.5593
2		29.243	45390.262	2141003.000	7.4407
Total			662692.574	28774333.000	100.0000



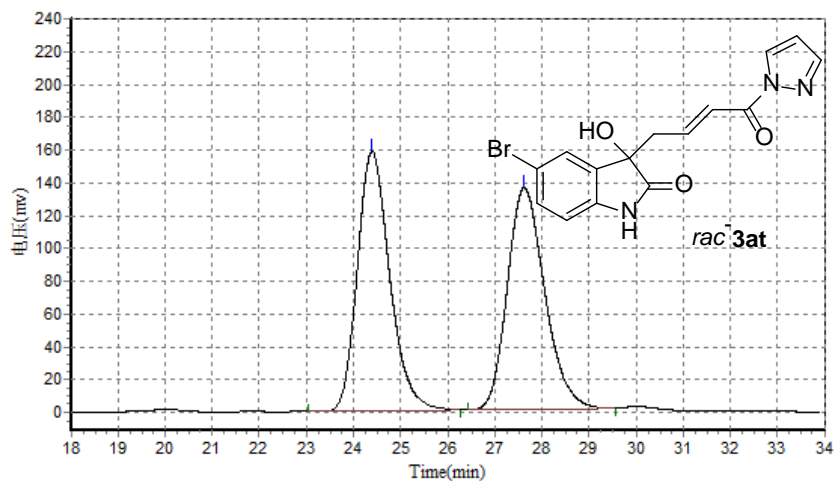
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		108.805	112287.422	20080312.000	49.8481
2		116.330	112895.422	20202694.000	50.1519
Total			225182.844	40283006.000	100.0000



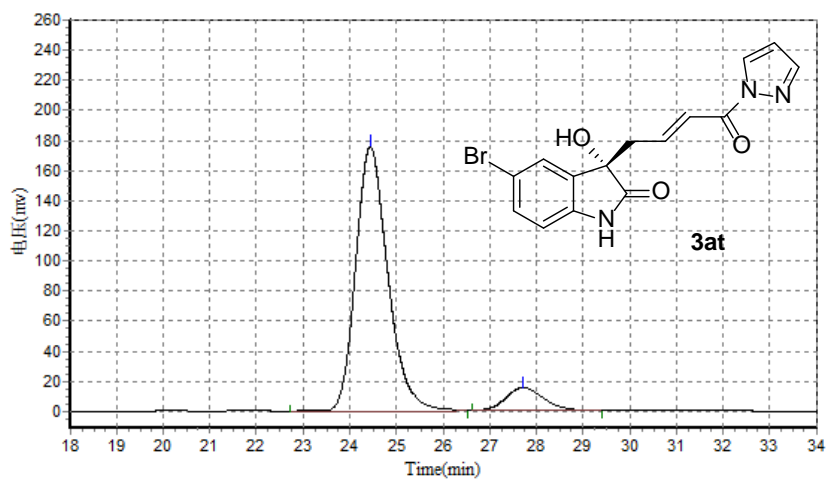
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		107.908	765.990	119499.414	1.3048
2		115.268	51679.797	9038896.000	98.6952
Total			52445.787	9158395.414	100.0000



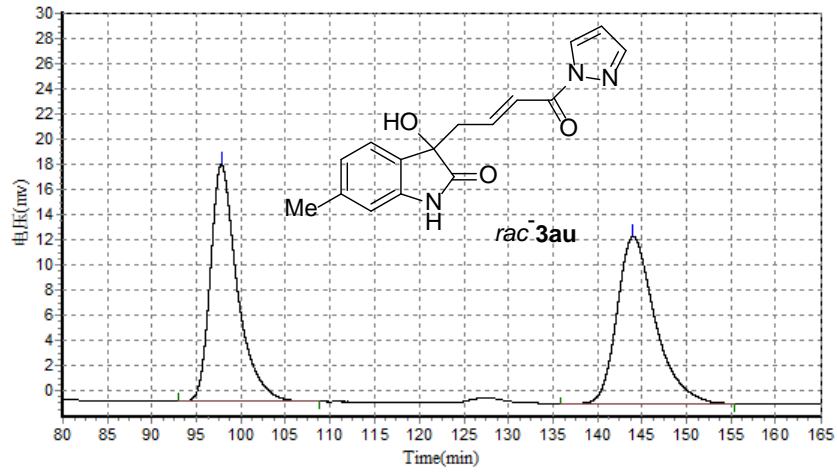
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		24.403	157949.547	7565719.500	50.2898
2		27.612	135302.938	7478522.000	49.7102
Total			293252.484	15044241.500	100.0000



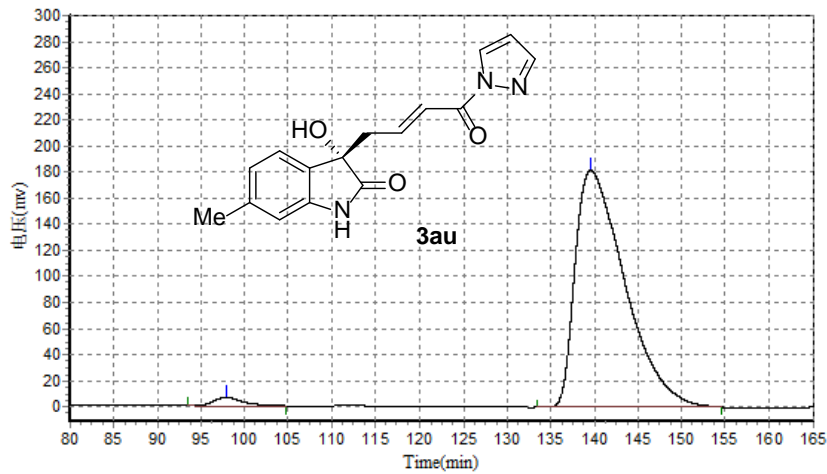
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		24.443	174744.375	8380856.500	90.8035
2		27.718	15223.012	848810.125	9.1965
Total			189967.387	9229666.625	100.0000



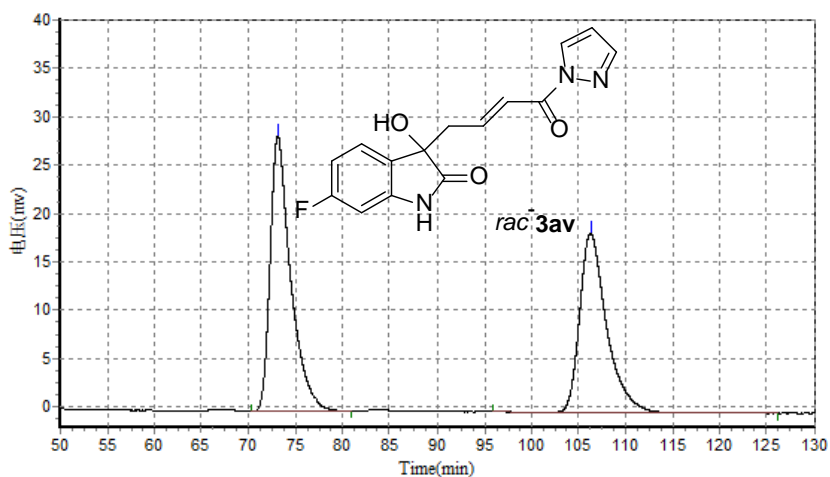
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		97.815	18884.381	3961220.000	49.9608
2		143.977	13291.020	3967428.250	50.0392
Total			32175.400	7928648.250	100.0000



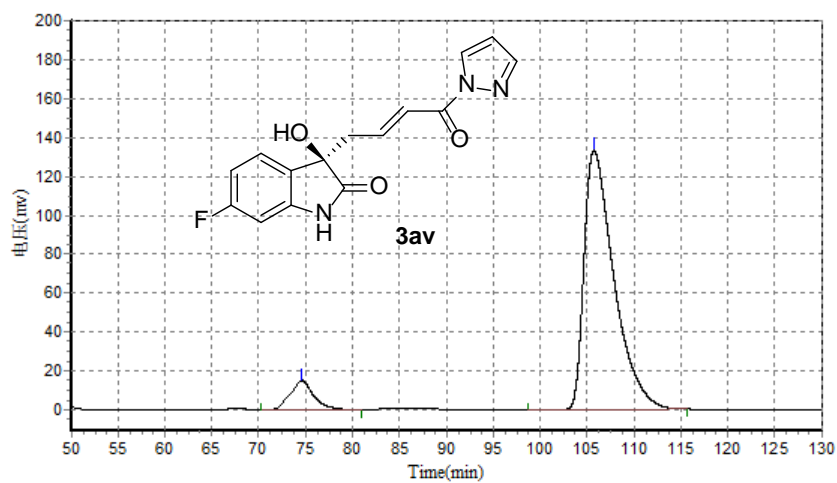
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		97.872	6205.766	1399736.750	1.9100
2		139.610	181452.672	71884424.000	98.0900
Total			187658.438	73284160.750	100.0000



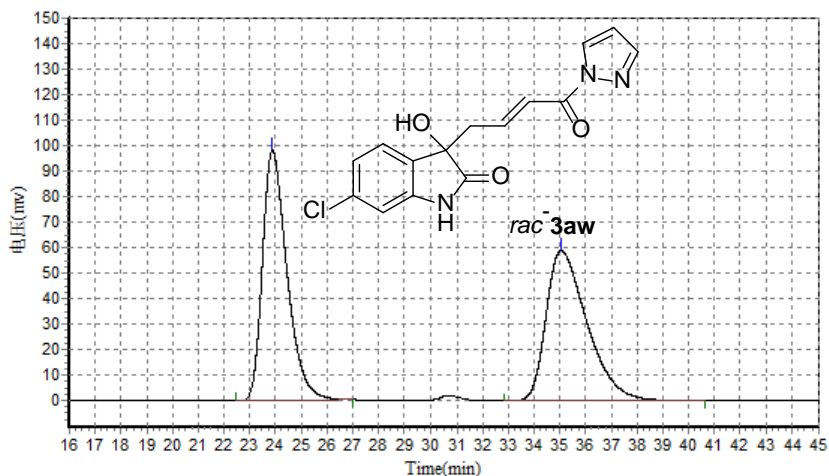
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		73.130	27207.719	3800213.750	51.1185
2		106.270	18512.527	3633907.250	48.8815
Total			45720.246	7434121.000	100.0000



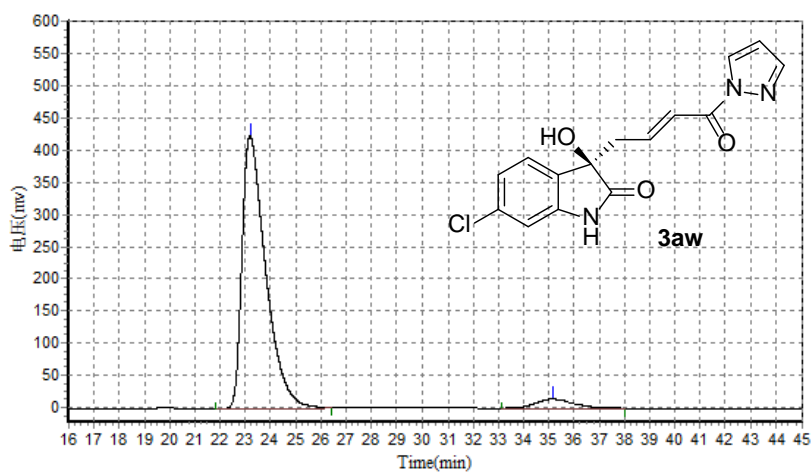
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		74.608	15033.543	2634599.750	8.1868
2		105.750	133015.594	29546406.000	91.8132
Total			148049.137	32181005.750	100.0000



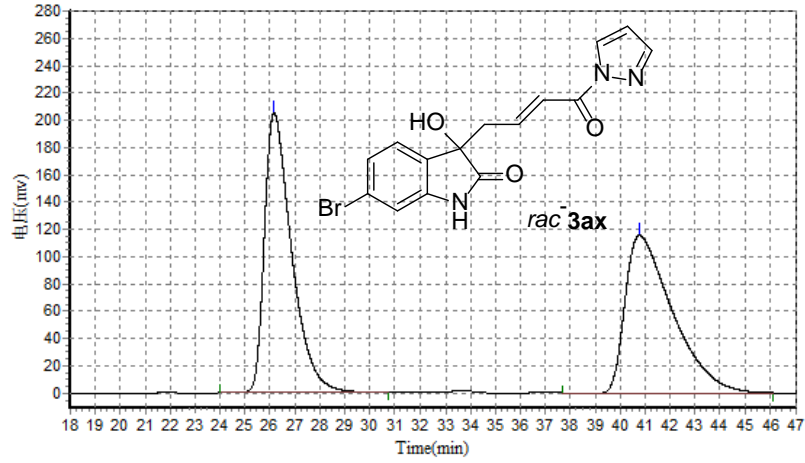
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		23.880	97982.836	6481269.000	49.8976
2		35.050	58980.871	6507872.500	50.1024
Total			156963.707	12989141.500	100.0000



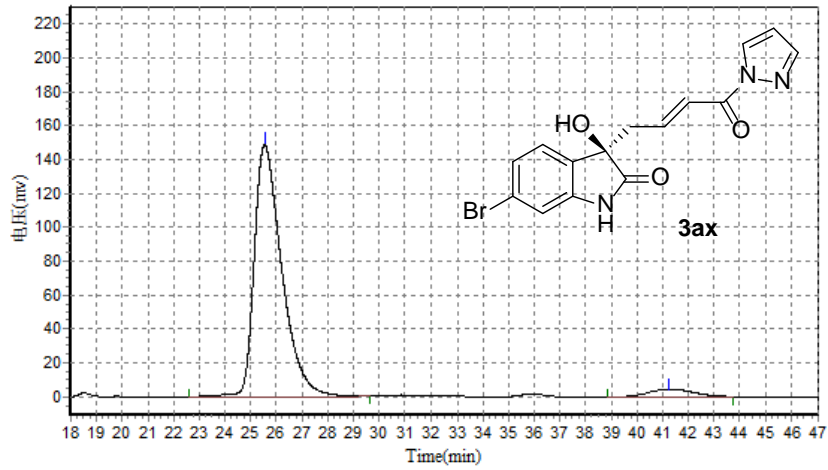
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		23.193	423811.531	27456784.000	94.8116
2		35.135	14117.263	1502518.500	5.1884
Total			437928.794	28959302.500	100.0000



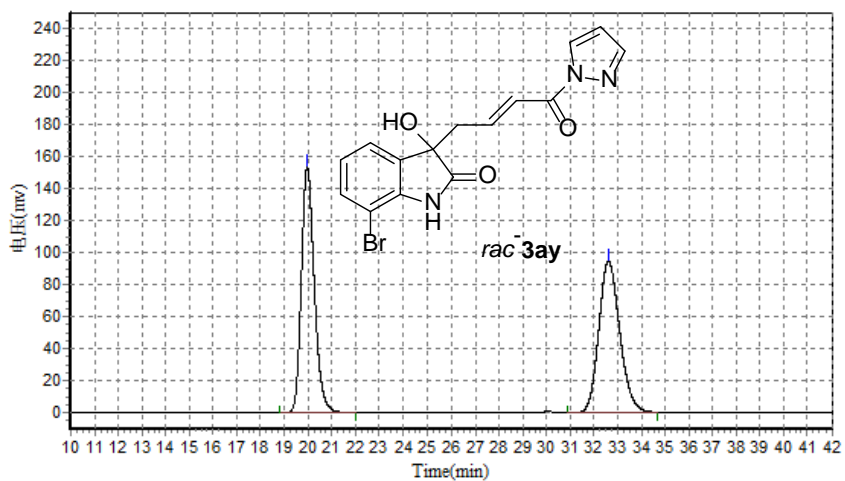
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		26.172	205068.422	15544643.000	50.5325
2		40.782	115476.211	15217005.000	49.4675
Total			320544.633	30761648.000	100.0000



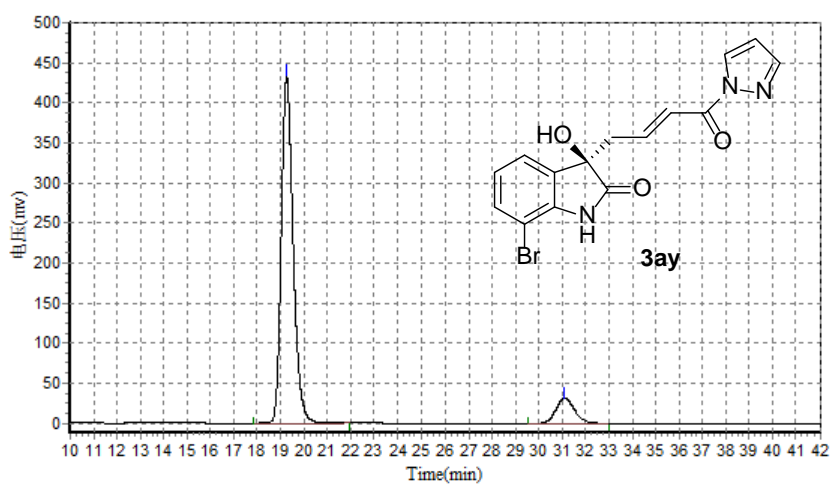
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.547	148882.094	11098267.000	95.1919
2		41.263	4630.260	560568.000	4.8081
Total			153512.354	11658835.000	100.0000



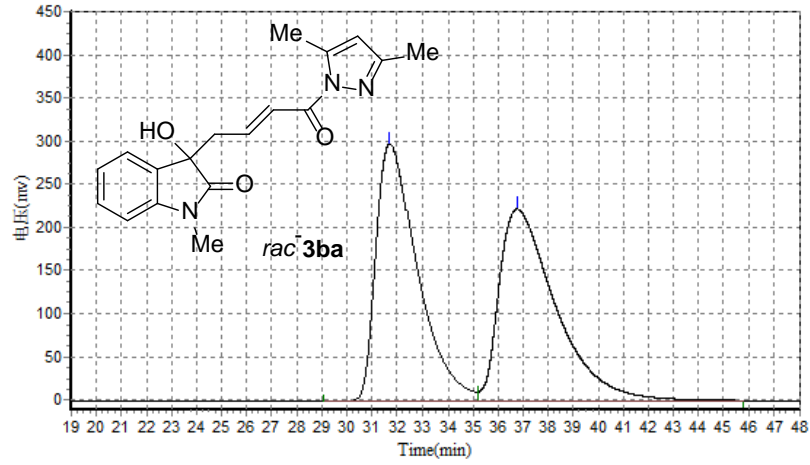
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.968	154140.469	5844029.000	50.1287
2		32.613	95035.633	5814020.000	49.8713
Total			249176.102	11658049.000	100.0000



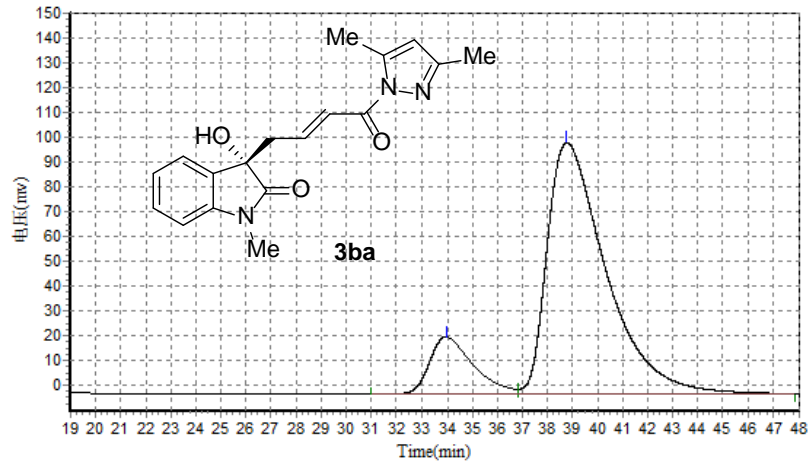
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.260	432633.563	15244854.000	89.5299
2		31.108	31100.912	1782819.500	10.4701
Total			463734.475	17027673.500	100.0000



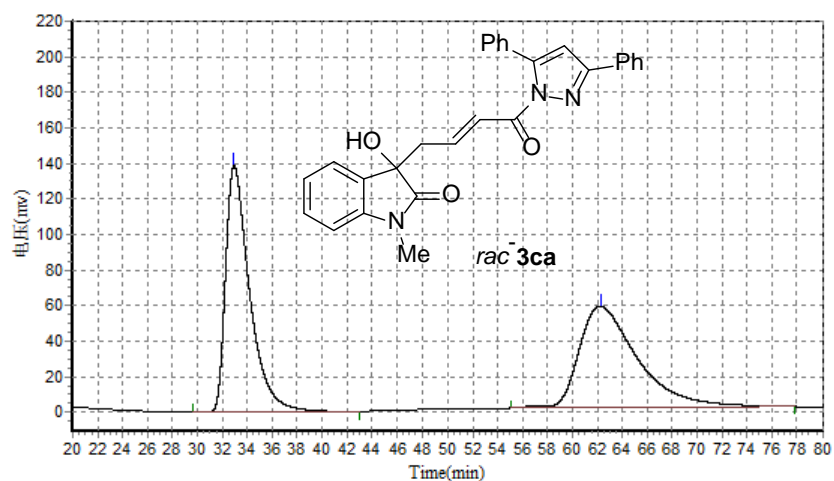
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		31.718	297595.594	33807084.000	49.2333
2		36.745	222260.000	34860028.000	50.7667
Total			519855.594	68667112.000	100.0000



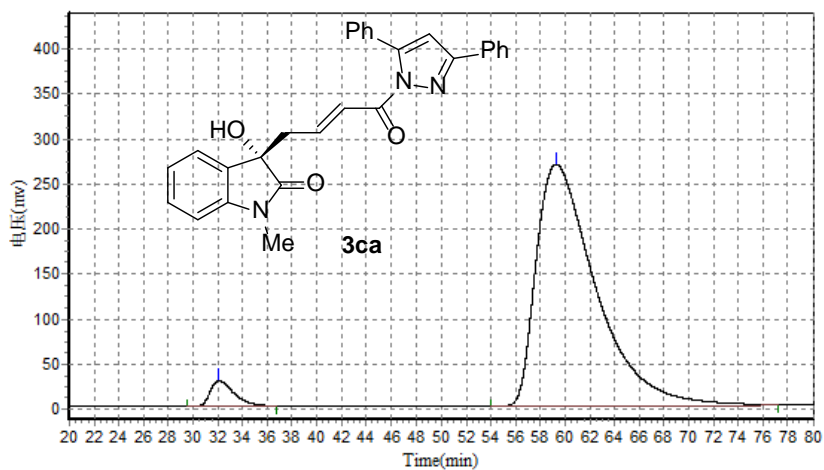
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		33.950	23077.168	2805245.500	14.5334
2		38.765	101191.859	16496749.000	85.4666
Total			124269.027	19301994.500	100.0000



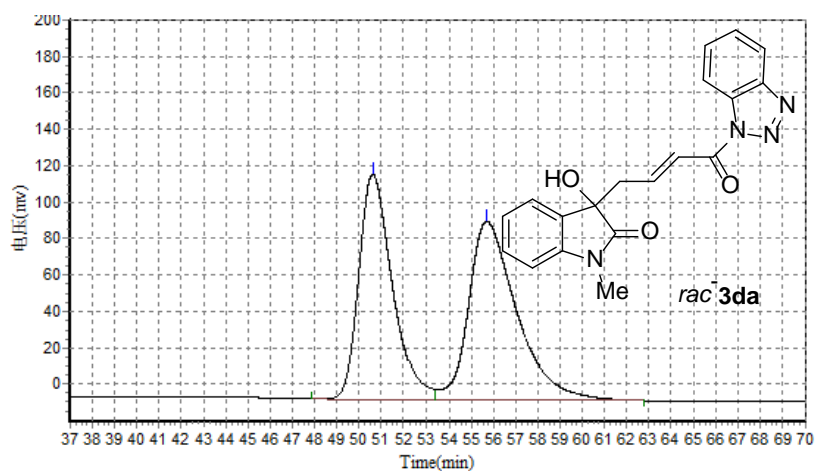
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		32.948	138522.719	18543710.000	49.9717
2		62.232	56875.668	18564728.000	50.0283
Total			195398.387	37108438.000	100.0000



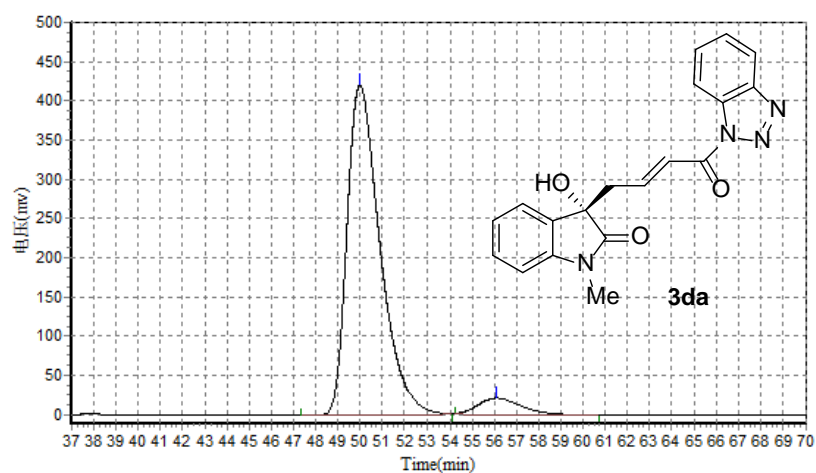
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		32.108	28671.020	3810326.000	4.0641
2		59.245	268471.469	89945096.000	95.9359
Total			297142.488	93755422.000	100.0000



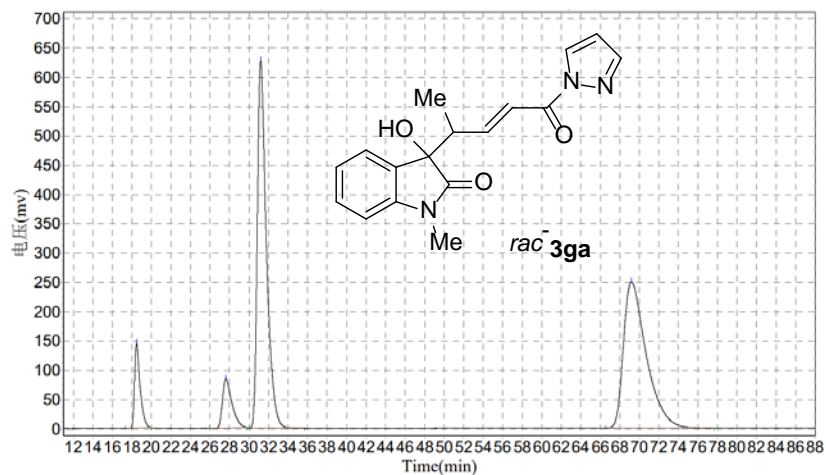
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		50.625	123437.539	12872888.000	50.3314
2		55.695	92669.094	12703346.000	49.6686
Total			216106.633	25576234.000	100.0000



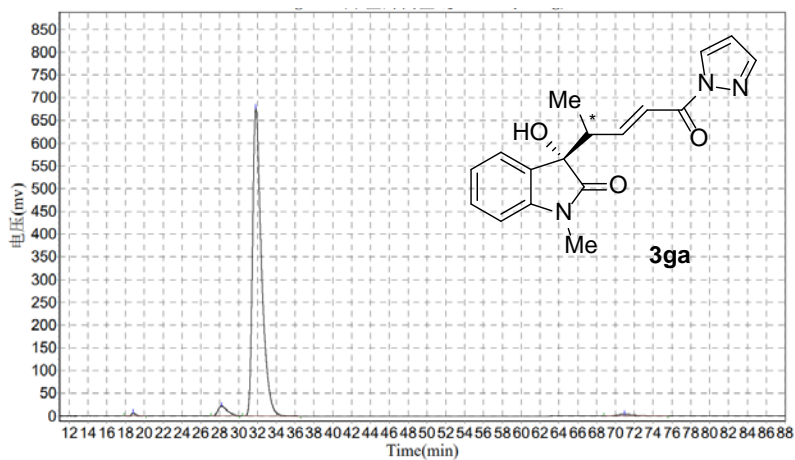
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		49.992	420281.625	43163548.000	94.1428
2		56.110	20238.941	2685493.250	5.8573
Total			440520.566	45849041.250	100.0000



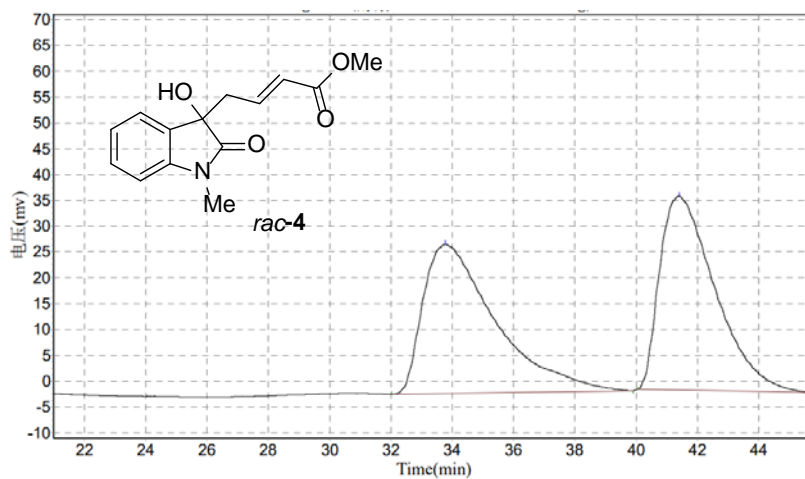
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.478	144970.797	5701830.000	6.1945
2		27.625	84008.375	5568705.500	6.0499
3		31.203	627064.063	40371924.000	43.8606
4		69.202	249688.828	40403524.000	43.8949
Total			1105732.063	92045983.500	100.0000



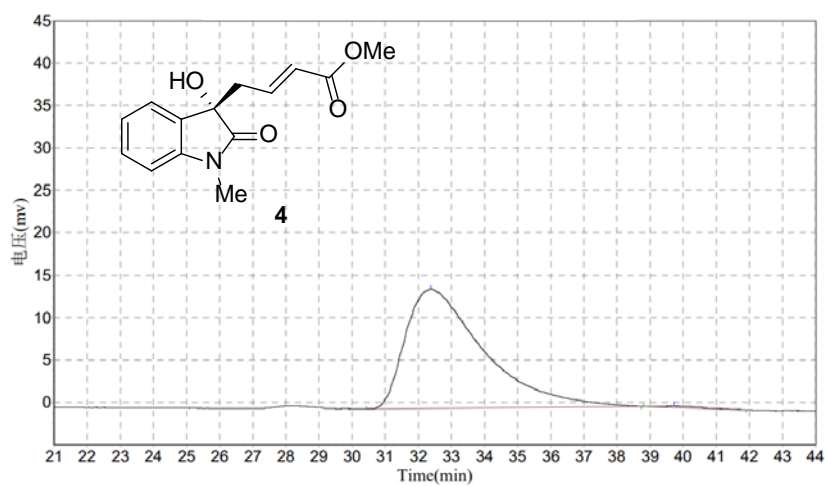
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.797	5641.336	221189.594	0.4736
2		28.182	21584.182	1482099.125	3.1732
3		31.828	676421.250	44499072.000	95.2724
4		70.960	3456.905	504849.938	1.0809
Total			707103.673	46707210.656	100.0000



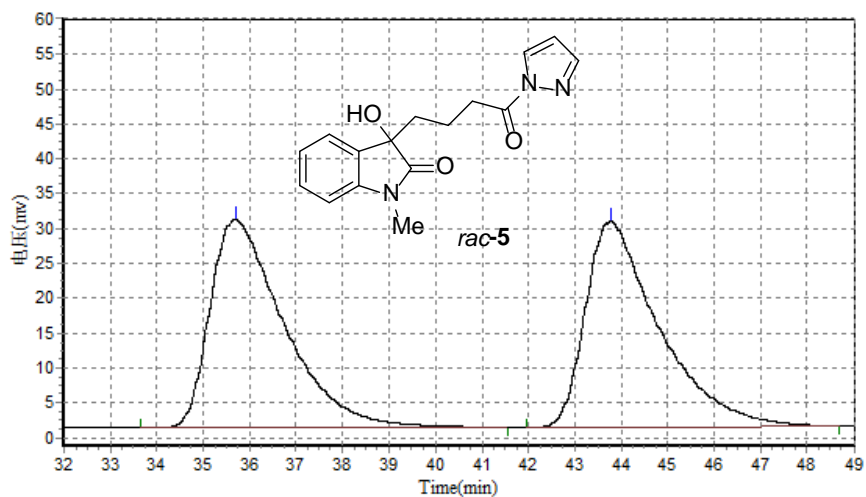
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		33.778	28828.404	4704108.500	50.0089
2		41.408	37585.512	4702439.500	49.9911
Total			66413.916	9406548.000	100.0000



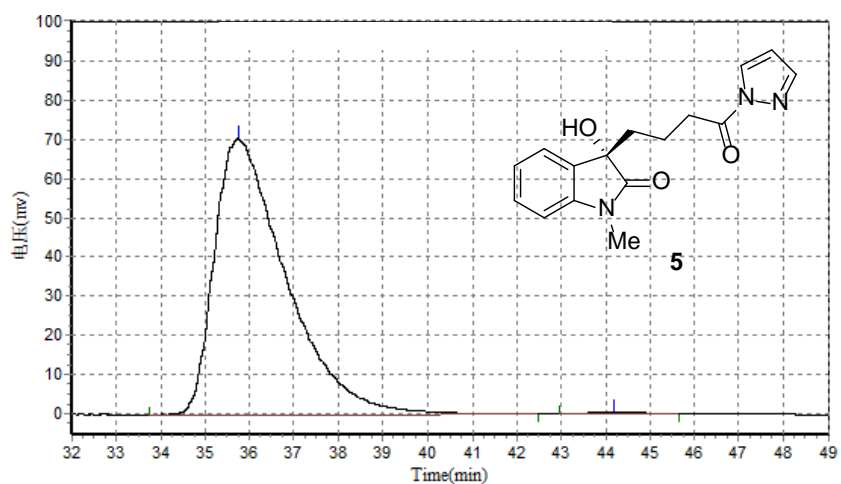
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		32.382	14001.913	2285290.500	99.3399
2		39.732	168.444	15186.409	0.6601
Total			14170.358	2300476.909	100.0000



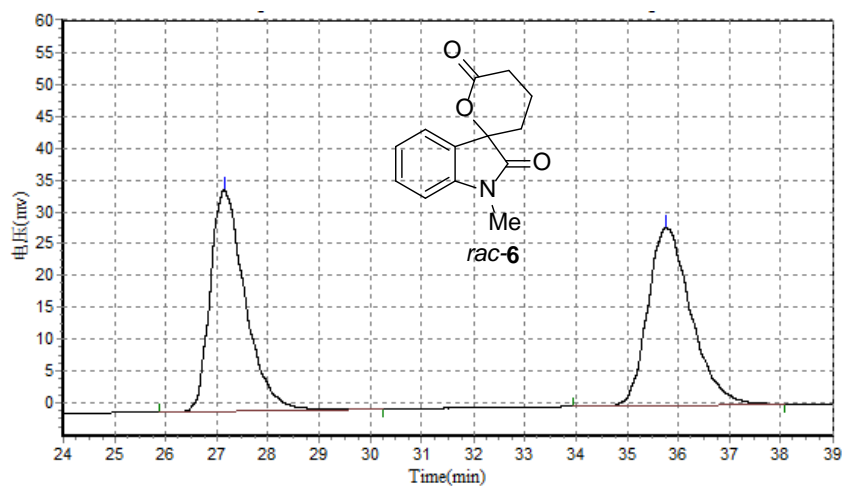
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		35.697	29914.379	3302776.500	50.3930
2		43.763	29551.355	3251256.000	49.6070
Total			59465.734	6554032.500	100.0000



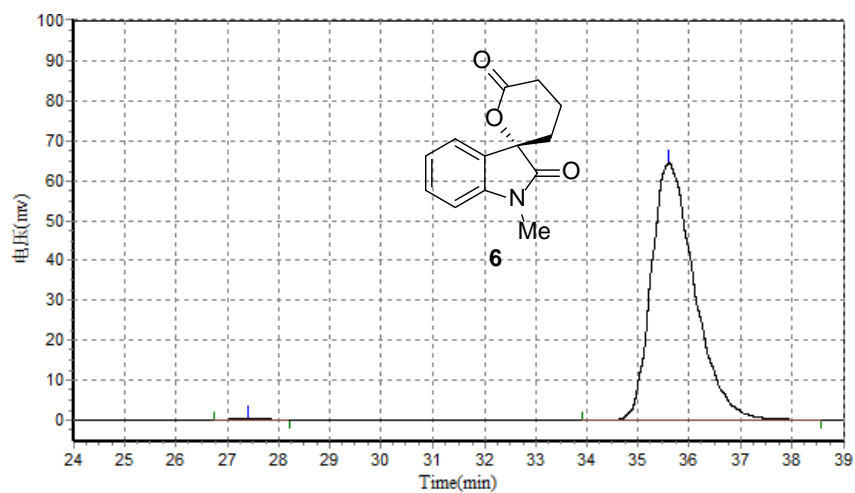
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		35.748	70351.078	7852268.500	99.3968
2		44.185	588.865	47650.699	0.6032
Total			70939.943	7899919.199	100.0000



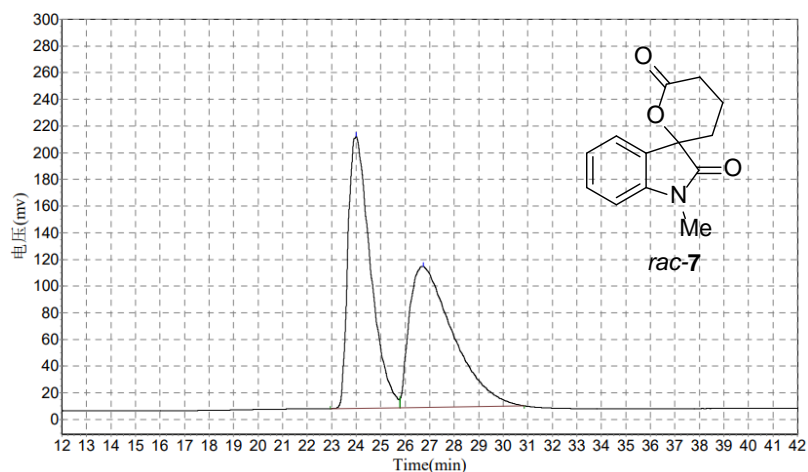
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.140	34734.004	1641941.000	50.0938
2		35.750	27950.576	1635794.500	49.9062
Total			62684.580	3277735.500	100.0000



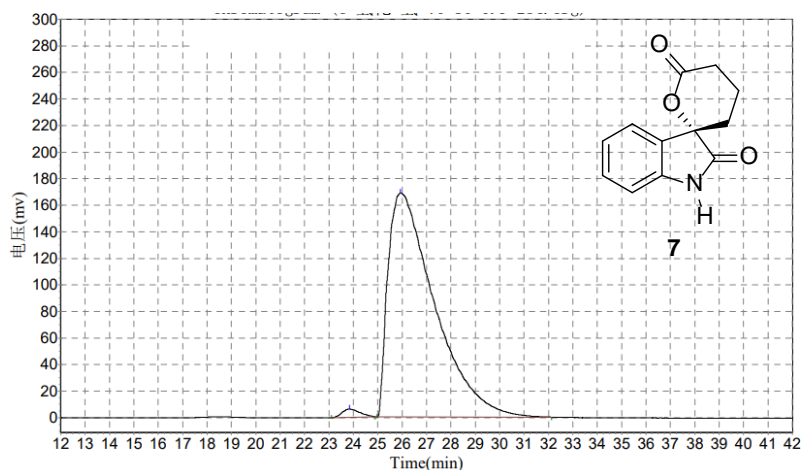
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.405	511.303	21577.701	0.5697
2		35.608	64346.277	3766186.250	99.4303
Total			64857.580	3787763.951	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		24.008	203687.719	12942083.000	49.8135
2		26.733	105729.633	13039004.000	50.1865
Total			309417.352	25981087.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		23.845	6205.409	315397.563	1.3959
2		25.918	168402.453	22279704.000	98.6041
Total			174607.862	22595101.563	100.0000