
Supplementary information

Catalytic atroposelective synthesis of C–N axially chiral 5-pyrazolyl indoles via multicomponent tandem cycloaddition

Yu-Yu Chen, Jia Xue, Yu-Chen Zhang, Feng Shi

Contents

1. General information	S2
2. Synthetic procedures and characterization data of substrates 1-3	S3
3. Procedure for the synthesis of products 4 and characterization data.....	S6
4. Study on the configurational stability	S19
5. Procedure for 1-mmol-scale reaction	S20
6. Synthetic procedures and characterization data of products 6-10	S21
7. NMR spectra of substrates 1	S26
8. NMR spectra of substrates 4	S33
9. NMR spectra of substrates 6-10.....	S68
10. HPLC traces of products 4.....	S73
11. HPLC traces of products 7-10	S105
12. X-ray single-crystal data for compounds 4aag.....	S109
13. Theoretical calculations on the rotational barriers.....	S111

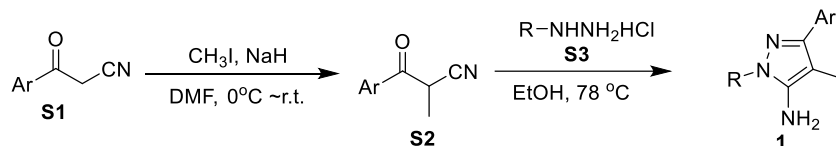
1. General information

¹H NMR spectra (400 MHz), ¹³C NMR spectra (100 MHz), ³¹P NMR spectra (162 MHz) and ¹⁹F NMR spectra (376 MHz) were recorded on commercial instruments. The solvents used for NMR spectroscopy were CDCl₃ and Acetone-*d*₆, using tetramethylsilane as the internal reference. High resolution mass spectra (HRMS) were performed on AB SCIEX TripleTOF 4600. Enantiomeric excesses (*ee*) were determined by chiral high-performance liquid chromatography (chiral HPLC). The chiral columns used for the determination of enantiomeric excesses by chiral HPLC were Chiralpak columns. Optical rotation values were measured with instruments operating at $\lambda = 589$ nm, corresponding to the sodium D line at the temperatures indicated. The X-ray source used for the single crystal X-ray diffraction analysis of compound **4aag** were GaK α ($\lambda = 1.34139$), and the thermal ellipsoid was drawn at the 50% probability level. Analytical grade solvents for the column chromatography were distilled before use. All starting materials commercially available were used directly. Chiral catalysts (*R*)-**5d** are known compounds and were synthesized according to the literature procedures.¹

2. Synthetic procedures and characterization data of substrates 1-3

Substrates **1a–1e**, **1g–1i**, **1m**, **1p–1r**, **1t** are known compounds, and the identities of these compounds were confirmed by comparing the measured spectroscopic and physical data with the literature data.² Substrates **1f**, **1j–1l**, **1n**, **1o**, **1s** were synthesized as follows.³ Substrates **2** commercially available are used directly. Substrates **3a**⁴, **3b–3k**⁵ are known compounds, and the identities of these compounds were confirmed by comparing the measured spectroscopic and physical data with the literature data.

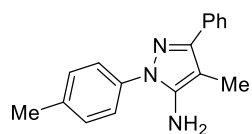
Synthetic procedures and characterization data of **1f**, **1j–1l**, **1n**, **1o**, **1s**



At 0 °C, NaH (15 mmol, 1.5 equiv) was slowly added to DMF (20 mL), followed by the addition of **S1** (10 mmol, 1.0 equiv). The mixture was stirred at room temperature for 30 minutes. Then, CH₃I (11 mmol, 1.1 equiv) was slowly added via syringe at 0 °C, after which the mixture was stirred at room temperature until the starting material was completely consumed. At 0 °C, H₂O (2 mL) was added to quench the reaction, and the pH was adjusted to 7 with HCl (2 M, 60 mL). The mixture was extracted with EtOAc (30 mL × 3), and the combined organic phases were washed with saturated aqueous sodium bicarbonate and brine. After drying over anhydrous sodium sulfate, filtration, and concentration under reduced pressure, the residue crude was purified by flash column chromatography on silica gel to afford the crude product **S2**.

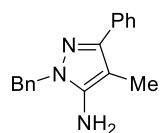
In a 50 mL round-bottom flask, a mixture of substituted hydrazine hydrochlorides **S3** (11 mmol, 1.1 equiv) and **S2** was dissolved in EtOH (20 mL). The reaction mixture was heated to 78 °C in an oil bath and stirred for 16 h. The reaction progress was monitored by TLC until completion. Upon completion, the mixture was quenched with H₂O (60 mL) and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The mixture was directly purified by flash column chromatography on silica gel to afford the pure product **1**.

4-methyl-3-phenyl-1-(*p*-tolyl)-1*H*-pyrazol-5-amine (1f):



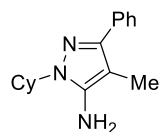
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 10/1); 76% yield (2.0 g); pale yellow solid; m.p. 95.5-96.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 7.6 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.39 (m, 2H), 7.36 – 7.31 (m, 1H), 7.30 – 7.27 (m, 2H), 3.63 (s, 2H), 2.40 (s, 3H), 2.11 (s, 3H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 150.5, 142.8, 137.2, 136.4, 134.3, 130.0, 128.4, 127.7, 127.5, 124.0, 96.9, 21.2, 8.8; IR (KBr): 2379, 2324, 1749, 1716, 1646, 1507, 1489, 1456, 1275, 750 cm⁻¹; HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₁₈N₃ 264.1495; Found 264.1499.

1-benzyl-4-methyl-3-phenyl-1*H*-pyrazol-5-amine (1j):



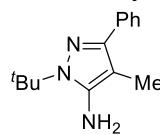
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 10/1); 72% yield (1.9 g); pale yellow solid; m.p. 114.5-115.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 7.6 Hz, 2H), 7.46 – 7.39 (m, 2H), 7.38 – 7.27 (m, 4H), 7.25 – 7.19 (m, 2H), 5.28 (s, 2H), 3.18 (s, 2H), 2.07 (s, 3H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 148.9, 142.5, 137.0, 134.7, 128.9, 128.4, 127.8, 127.5, 127.2, 127.0, 98.5, 52.0, 9.0; IR (KBr): 2924, 1621, 1568, 1454, 1377, 1261, 1136, 1016, 749, 699 cm⁻¹; HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₁₈N₃ 264.1495; Found 264.1491.

1-cyclohexyl-4-methyl-3-phenyl-1*H*-pyrazol-5-amine (1k):



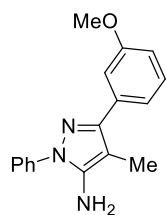
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 10/1); 67% yield (1.7 g); pale yellow solid; m.p. 109.5-110.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J* = 7.6 Hz, 2H), 7.42 – 7.35 (m, 2H), 7.32 – 7.27 (m, 1H), 4.04 – 3.95 (m, 1H), 3.24 (s, 2H), 2.06 (s, 3H), 2.03 – 1.89 (m, 6H), 1.71 (d, *J* = 11.8 Hz, 1H), 1.44 – 1.26 (m, 3H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 148.2, 141.1, 135.1, 128.3, 127.6, 126.9, 98.3, 56.5, 32.4, 25.9, 25.3, 8.8; IR (KBr): 2932, 2857, 1621, 1507, 1447, 1275, 1261, 1157, 750, 700 cm⁻¹; HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₂₂N₃ 256.1808; Found 256.1807.

1-(*tert*-butyl)-4-methyl-3-phenyl-1*H*-pyrazol-5-amine (1l):



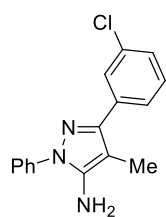
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 10/1); 70% yield (1.6 g); pale yellow solid; m.p. 96.5-97.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, *J* = 7.2 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.32 – 7.27 (m, 1H), 3.32 (s, 2H), 2.07 (s, 3H), 1.71 (s, 9H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 146.4, 142.2, 135.2, 128.4, 127.5, 126.9, 100.1, 58.7, 29.5, 8.9; IR (KBr): 2981, 1615, 1489, 1363, 1275, 1150, 750, 700, 649, 599 cm⁻¹; HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₄H₂₀N₃ 230.1652; Found 230.1647.

3-(3-methoxyphenyl)-4-methyl-1-phenyl-1*H*-pyrazol-5-amine (1n):



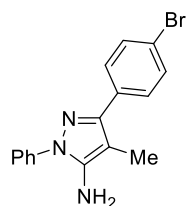
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 10/1); 75% yield (2.1 g); pale yellow solid; m.p. 78.5-79.4 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, $J = 8.0$ Hz, 2H), 7.49 – 7.44 (m, 2H), 7.37 – 7.28 (m, 4H), 6.92 – 6.86 (m, 1H), 3.85 (s, 3H), 3.67 (s, 2H), 2.10 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 159.7, 150.6, 142.9, 139.0, 135.6, 129.5, 129.4, 127.2, 123.9, 120.3, 113.5, 112.9, 97.3, 55.3, 8.9; IR (KBr): 2926, 1597, 1508, 1489, 1374, 1259, 1026, 864, 750, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{18}\text{N}_3\text{O}$ 280.1445; Found 280.1447.

3-(3-chlorophenyl)-4-methyl-1-phenyl-1H-pyrazol-5-amine (10):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 10/1); 78% yield (2.2 g); pale yellow solid; m.p. 76.5-77.4 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.72 (s, 1H), 7.63 – 7.56 (m, 3H), 7.51 – 7.46 (m, 2H), 7.38 – 7.28 (m, 3H), 3.78 (s, 2H), 2.11 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 149.2, 143.2, 138.6, 135.9, 134.3, 129.7, 129.6, 127.7, 127.6, 125.8, 124.0, 97.3, 8.8; IR (KBr): 2924, 1597, 1508, 1455, 1370, 1150, 1077, 967, 764, 694 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{15}\text{ClN}_3$ 284.0949; Found 284.0950.

3-(4-bromophenyl)-4-methyl-1-phenyl-1H-pyrazol-5-amine (1s):

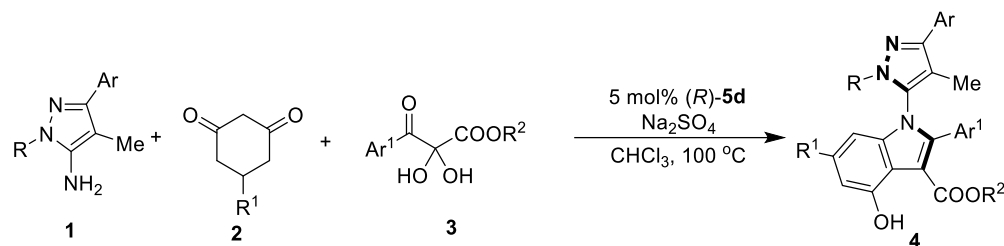


Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 10/1); 70% yield (2.3 g); pale yellow solid; m.p. 96.5-97.4 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.61 – 7.51 (m, 6H), 7.49 – 7.43 (m, 2H), 7.37 – 7.31 (m, 1H), 4.00 (s, 2H), 2.05 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 149.4, 143.3, 138.5, 133.0, 131.6, 129.6, 129.3, 127.5, 124.0, 121.7, 97.1, 8.8; IR (KBr): 2923, 1597, 1509, 1488, 1454, 1370, 1072, 1007, 831, 762 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{15}\text{BrN}_3$ 328.0444; Found 328.0427.

References:

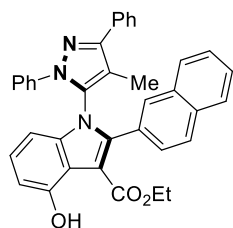
- (1) Lancaster BMJ, White AJP, Braddock DC. Fortuitous enantiomeric self-rectification of an unreported partial racemisation in the synthesis of a chiral phosphoric acid: A warning to practitioners. *Chem Eur J.* 2024;30(72):e202403318. [10.1002/chem.202403318]
- (2) Chen YY, Xue J, Shi Q, Zhang YC, Shi F. Catalytic atroposelective synthesis of C–N axially chiral pyrazolyl pyrroles via de novo construction of a pyrrole ring. *Org Lett.* 2026; [10.1021/acs.orglett.5c05409]
- (3) Bai L, Wei JS, Zhong LY, Ma AQ, Wang J, Du ZQ, et al. Enantioselective α -amination of amides by one-pot organo-/iodine sequential catalysis. *Org Lett.* 2024;26(1):258–263. [10.1021/acs.orglett.3c03925]
- (4) Sha Q, Armanb H, Doyle MP. Asymmetric synthesis of 1H-pyrrol-3(2H)-ones from 2,3-diketooesters by combination of aldol condensation with benzilic acid rearrangement. *Chem Commun.* 2016;52(1):108–111. [10.1039/C5CC07780J]
- (5) Wang L, Zhong J, Lin X. Atroposelective phosphoric acid catalyzed three-component cascade reaction: Enantioselective synthesis of axially chiral N-arylindoles. *Angew Chem Int Ed.* 2019;58(44):15824–15828. [10.1002/ange.201909855]

3. Procedure for the synthesis of products 4 and characterization data



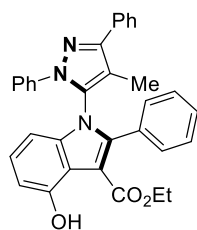
In a sealed tube were added 5-aminopyrazole **1** (0.1 mmol, 1 equiv), cyclohexanedione **2** (0.1 mmol, 1 equiv), 2,3-diketoester precursor **3** (0.1 mmol, 1 equiv), chiral phosphoric acid catalyst (*R*)-**5d** (5 mol%, 0.05 equiv), and Na₂SO₄ (50 mg). Subsequently, CHCl₃ (1 mL) was added, and the sealed tube was stirred at 100 °C for 15 h. The reaction progress was monitored by thin-layer chromatography (TLC). Upon completion of the reaction, the crude mixture was purified by flash column chromatography on silica gel to afford the pure product **4**.

(*R_a*)-ethyl 4-hydroxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-(naphthalen-2-yl)-1*H*-indole-3-carboxylate (**4aaa**):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 96% yield (54.2 mg); white solid; m.p. 93.5-94.4 °C; [α]_D²⁰ = -8.1 (c = 5.29, acetone); ¹H NMR (400 MHz, CDCl₃) δ 11.49 (s, 1H), 7.86 – 7.78 (m, 3H), 7.65 – 7.43 (m, 6H), 7.41 – 7.34 (m, 2H), 7.32 – 7.28 (m, 2H), 7.25 – 7.19 (m, 3H), 7.00 – 6.97 (m, 1H), 6.89 – 6.85 (m, 1H), 6.78 (d, *J* = 8.0 Hz, 2H), 4.13 – 3.95 (m, 2H), 2.27 (s, 3H), 0.73 – 0.61 (m, 3H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 168.2, 152.2, 150.2, 146.1, 139.6, 138.4, 133.3, 133.1, 132.8, 132.2, 129.3, 128.7, 128.3, 128.2, 127.7, 127.6, 127.5, 127.4, 127.0, 126.9, 126.4, 122.6, 115.4, 114.3, 109.5, 107.8, 102.1, 61.4, 13.4, 9.5; IR (KBr): 3058, 1655, 1601, 1500, 1415, 1386, 1156, 1042, 909, 763 cm⁻¹; HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₃₇H₃₀N₃O₃ 564.2282; Found 564.2264; The enantiomeric excess: 93%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 4.776 (major), t_R = 5.696 (minor).

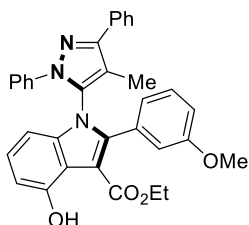
(*R_a*)-ethyl 4-hydroxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (**4aab**):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 80% yield (41.3 mg); pale white solid; m.p. 194.5-195.4 °C; [α]_D²⁰ = -7.4 (c = 0.83, acetone); ¹H NMR (400 MHz, CDCl₃) δ 11.33 (s, 1H), 7.79 (d, *J* = 7.6 Hz, 2H), 7.49 – 7.43 (m, 2H), 7.40 – 7.35 (m, 1H), 7.33 – 7.28 (m, 1H), 7.25 – 7.15 (m, 5H), 7.12 – 7.00 (m, 2H), 6.89 – 6.86 (m, 1H), 6.79 – 6.74 (m, 3H), 6.71 – 6.60 (m, 1H), 4.11 – 4.00 (m, 2H), 2.16 (s, 3H), 0.86 – 0.78 (m, 3H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 168.2, 151.9, 150.1, 146.1, 139.3, 138.2, 133.3, 132.6, 130.1, 129.2, 128.9, 128.7, 128.1, 127.3, 127.2, 126.7, 122.4, 115.2, 114.3, 109.3, 107.3, 102.0, 61.3, 13.3,

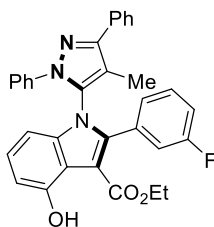
9.4; IR (KBr): 3060, 1655, 1600, 1500, 1384, 1257, 1194, 1043, 760, 696 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{27}\text{N}_3\text{O}_3\text{Na}$ 536.1944; Found 536.1944; The enantiomeric excess: 93%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_{R} = 6.763 (major), t_{R} = 7.746 (minor).

(*R*_a)-ethyl 4-hydroxy-2-(3-methoxyphenyl)-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-1*H*-indole-3-carboxylate (4aac):



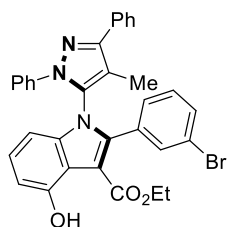
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 59% yield (31.9 mg); white solid; m.p. 152.2-153.1 °C; $[\alpha]_{\text{D}}^{20}$ = -7.4 (c = 0.64, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.32 (s, 1H), 7.79 (d, J = 7.6 Hz, 2H), 7.50 – 7.42 (m, 2H), 7.42 – 7.36 (m, 1H), 7.33 – 7.27 (m, 1H), 7.25 – 7.15 (m, 4H), 7.05 – 6.96 (m, 1H), 6.91 – 6.85 (m, 1H), 6.81 – 6.75 (m, 4H), 6.33 – 6.12 (m, 1H), 4.16 – 4.00 (m, 2H), 3.55 (s, 3H), 2.17 (s, 3H), 0.91 – 0.82 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 158.4, 152.0, 150.1, 145.7, 139.2, 138.3, 133.2, 132.6, 131.2, 129.2, 128.7, 128.3, 128.1, 127.3, 126.8, 122.3, 115.3, 115.2, 114.3, 109.3, 107.3, 102.0, 61.3, 55.1, 13.4, 9.4; IR (KBr): 2982, 1655, 1601, 1383, 1320, 1263, 1192, 1156, 763, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_4\text{Na}$ 566.2050; Found 566.2044; The enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_{R} = 6.039 (major), t_{R} = 7.096 (minor).

(*R*_a)-ethyl 2-(3-fluorophenyl)-4-hydroxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-1*H*-indole-3-carboxylate (4aad):



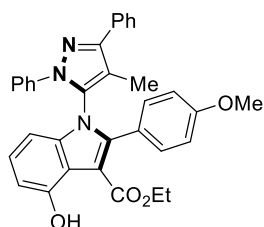
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 89% yield (47.1 mg); white solid; m.p. 192.6-193.5 °C; $[\alpha]_{\text{D}}^{20}$ = -6.5 (c = 0.94, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.27 (s, 1H), 7.80 (d, J = 7.2 Hz, 2H), 7.49 – 7.44 (m, 2H), 7.42 – 7.36 (m, 1H), 7.34 – 7.29 (m, 1H), 7.25 – 7.20 (m, 3H), 7.11 – 7.03 (m, 1H), 6.99 – 6.93 (m, 1H), 6.90 – 6.88 (m, 1H), 6.82 – 6.75 (m, 3H), 6.69 – 5.74 (m, 2H), 4.17 – 3.99 (m, 2H), 2.17 (s, 3H), 0.90 – 0.82 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 167.8, 161.5 (d, J = 244.9 Hz), 152.0, 150.3, 144.1, 144.1, 139.3, 138.1, 133.1, 132.3, 132.1 (d, J = 8.5 Hz), 129.3, 128.9 (d, J = 8.2 Hz), 128.7, 128.2, 127.5, 127.3, 127.1, 122.3, 115.9 (d, J = 20.9 Hz), 115.1, 114.3, 109.5, 107.7, 102.1, 61.5, 13.3, 9.3; ^{19}F NMR (376 MHz, CDCl_3) δ -113.8; IR (KBr): 2983, 1656, 1599, 1502, 1472, 1442, 1323, 1261, 1207, 763 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{FN}_3\text{O}_3\text{Na}$ 554.1850; Found 554.1852; The enantiomeric excess: 91%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_{R} = 5.256 (major), t_{R} = 5.936 (minor).

(*R*_a)-ethyl 2-(3-bromophenyl)-4-hydroxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-1*H*-indole-3-carboxylate (4aae):



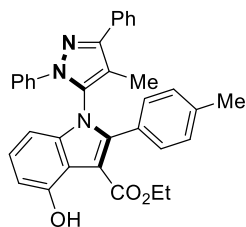
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 77% yield (45.7 mg); white solid; m.p. 177.2-178.1 °C; $[\alpha]_D^{20} = -9.9$ ($c = 0.88$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.28 (s, 1H), 7.80 (d, $J = 7.6$ Hz, 2H), 7.52 – 7.44 (m, 2H), 7.42 – 7.36 (m, 2H), 7.35 – 7.27 (m, 3H), 7.25 – 7.20 (m, 1H), 7.07 – 6.79 (m, 4H), 6.75 – 6.70 (m, 2H), 6.64 – 6.41 (m, 1H), 4.21 – 3.91 (m, 2H), 2.18 (s, 3H), 0.93 – 0.85 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 167.8, 152.0, 150.3, 143.9, 139.3, 138.0, 133.1, 132.3, 132.0, 131.9, 129.4, 128.8, 128.7, 128.2, 127.6, 127.4, 127.1, 122.4, 121.1, 115.1, 114.2, 109.5, 107.7, 102.0, 61.5, 13.4, 9.3; IR (KBr): 2982, 1656, 1600, 1501, 1469, 1383, 1321, 1257, 1194, 763 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{BrN}_3\text{O}_3\text{Na}$ 614.1050; Found 614.1060; The enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 5.423$ (major), $t_R = 6.119$ (minor).

(*R*_a)-ethyl 4-hydroxy-2-(4-methoxyphenyl)-1-(4-methyl-1,3-diphenyl-1H-pyrazol-5-yl)-1H-indole-3-carboxylate (4aaf):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 75% yield (40.5 mg); white solid; m.p. 190.2-191.1 °C; $[\alpha]_D^{20} = -1.9$ ($c = 0.81$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.37 (s, 1H), 7.82 (d, $J = 7.6$ Hz, 2H), 7.51 – 7.45 (m, 2H), 7.43 – 7.37 (m, 1H), 7.32 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 6.89 – 6.85 (m, 1H), 6.81 – 6.76 (m, 3H), 6.64 – 6.57 (m, 3H), 4.20 – 4.01 (m, 2H), 3.78 (s, 3H), 2.17 (s, 3H), 0.95 – 0.87 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.3, 160.0, 151.9, 150.1, 146.1, 139.2, 138.3, 133.3, 132.8, 129.1, 128.7, 128.1, 127.3, 126.6, 122.3, 122.2, 115.3, 114.2, 112.7, 109.2, 107.2, 102.0, 61.3, 55.3, 13.6, 9.4; IR (KBr): 1654, 1600, 1488, 1418, 1383, 1255, 1194, 1042, 764, 694 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_4\text{Na}$ 566.2050; Found 566.2051; The enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 6.606$ (major), $t_R = 8.016$ (minor).

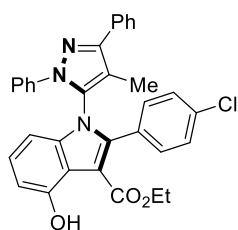
(*R*_a)-ethyl 4-hydroxy-1-(4-methyl-1,3-diphenyl-1H-pyrazol-5-yl)-2-(*p*-tolyl)-1H-indole-3-carboxylate (4aag):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 88% yield (46.3 mg); white solid; m.p. 172.2-173.1 °C; $[\alpha]_D^{20} = -2.3$ ($c = 0.93$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.35 (s, 1H), 7.70 (d, $J = 8.0$ Hz, 2H), 7.34 – 7.27 (m, 4H), 7.25 – 7.17 (m, 4H), 7.12 – 7.05 (m, 2H), 6.91 – 6.88 (m, 1H), 6.82 – 6.75 (m, 3H), 6.71 – 6.49 (m, 1H), 4.14 – 3.98 (m, 2H), 2.42 (s, 3H), 2.17 (s, 3H), 0.88 – 0.80 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 151.9, 150.1, 146.1, 139.3, 138.3, 138.0, 132.5, 130.4, 130.1, 129.3, 129.1, 128.8, 127.2, 126.7, 122.4, 115.2, 114.1, 109.3, 107.3, 102.1, 61.3, 21.4, 13.3, 9.4; IR (KBr): 2982, 1654, 1600, 1487, 1416, 1320, 1193, 1156, 763, 694 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{34}\text{H}_{30}\text{N}_3\text{O}_3$ 528.2282; Found 528.2281; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 5.926$ (major), $t_R =$

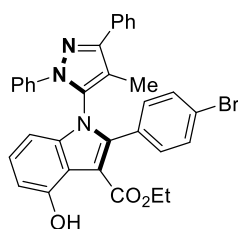
7.006 (minor).

(*R_a*)-ethyl 2-(4-chlorophenyl)-4-hydroxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-1*H*-indole-3-carboxylate (4aah):



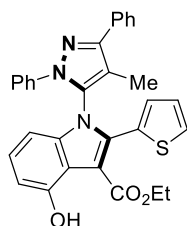
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 85% yield (46.8 mg); white solid; m.p. 181.2-182.1 °C; $[\alpha]_D^{20} = -4.4$ ($c = 0.94$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.29 (s, 1H), 7.82 (d, $J = 7.6$ Hz, 2H), 7.52 – 7.46 (m, 2H), 7.44 – 7.38 (m, 1H), 7.34 – 7.27 (m, 2H), 7.24 – 7.20 (m, 3H), 7.11 – 7.03 (m, 2H), 6.92 – 6.88 (m, 1H), 6.82 – 6.76 (m, 3H), 6.64 – 6.53 (m, 1H), 4.15 – 4.05 (m, 2H), 2.18 (s, 3H), 0.93 – 0.85 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 167.9, 152.0, 150.2, 144.4, 139.3, 138.2, 135.1, 133.1, 132.3, 129.3, 128.7, 128.2, 127.6, 127.5, 127.3, 127.0, 122.3, 115.1, 114.3, 109.5, 107.7, 102.1, 61.5, 13.5, 9.4; IR (KBr): 2982, 1657, 1600, 1384, 1256, 1193, 1155, 764, 694, 600 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{ClN}_3\text{O}_3\text{Na}$ 570.1555; Found 570.1554; The enantiomeric excess: 93%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 5.456$ (major), $t_R = 6.256$ (minor).

(*R_a*)-ethyl 2-(4-bromophenyl)-4-hydroxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-1*H*-indole-3-carboxylate (4aai):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 86% yield (51.1 mg); white solid; m.p. 173.2-174.1 °C; $[\alpha]_D^{20} = -3.1$ ($c = 1.02$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.28 (s, 1H), 7.83 (d, $J = 7.6$ Hz, 2H), 7.51 – 7.45 (m, 2H), 7.43 – 7.38 (m, 1H), 7.36 – 7.27 (m, 2H), 7.25 – 7.17 (m, 5H), 6.91 – 6.88 (m, 1H), 6.82 – 6.76 (m, 3H), 6.60 – 6.47 (m, 1H), 4.17 – 4.05 (m, 2H), 2.17 (s, 3H), 0.93 – 0.85 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 167.9, 152.0, 150.2, 144.4, 139.3, 138.2, 133.1, 132.3, 130.5, 129.3, 129.1, 128.7, 128.2, 127.5, 127.3, 127.0, 123.4, 122.3, 115.2, 114.3, 109.5, 107.7, 102.1, 61.5, 13.5, 9.4; IR (KBr): 2981, 1656, 1599, 1500, 1472, 1414, 1320, 1257, 1194, 763 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{BrN}_3\text{O}_3\text{Na}$ 614.1050; Found 614.1056; The enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 5.566$ (major), $t_R = 6.336$ (minor).

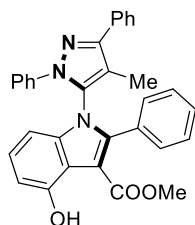
(*R_a*)-ethyl 2-(thiophen-2-yl)-4-hydroxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-1*H*-indole-3-carboxylate (4aaj):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 52% yield (26.9 mg); white solid; m.p. 177.2-178.1 °C; $[\alpha]_D^{20} = 6.9$ ($c = 0.54$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.31 (s, 1H), 7.82 (d, $J = 7.6$ Hz, 2H), 7.50 – 7.45 (m, 2H), 7.41 – 7.37 (m, 1H), 7.32 – 7.27 (m, 2H), 7.23 – 7.18 (m, 3H), 6.89 – 6.84 (m, 3H), 6.82 – 6.78 (m, 1H), 6.76 – 6.72 (m, 1H), 6.44 – 6.40 (m, 1H), 4.19 – 4.12 (m, 2H), 2.13 (s, 3H), 1.01 – 0.96 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.0, 151.9, 150.2, 139.5, 138.3, 138.2, 133.3, 132.4, 130.5, 129.2, 128.7, 128.5, 128.1, 127.4, 127.3, 127.2, 126.1, 122.1, 115.3, 114.9, 109.3, 109.1, 102.0,

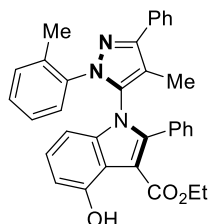
61.5, 13.5, 9.3; IR (KBr): 2983, 1655, 1600, 1429, 1383, 1256, 1155, 763, 694, 601 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{31}\text{H}_{25}\text{N}_3\text{O}_3\text{SNa}$ 542.1509; Found 542.1510; The enantiomeric excess: 85%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 $^{\circ}\text{C}$, 254 nm): t_{R} = 5.633 (major), t_{R} = 6.839 (minor).

(*R*_a)-methyl 4-hydroxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (4aak):



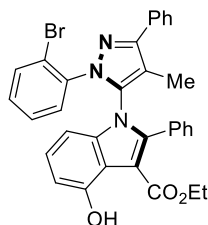
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 57% yield (28.7 mg); white solid; m.p. 183.2-184.1 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20}$ = -8.9 (c = 0.57, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.29 (s, 1H), 7.81 (d, J = 7.6 Hz, 2H), 7.50 – 7.45 (m, 2H), 7.42 – 7.37 (m, 1H), 7.33 – 7.27 (m, 2H), 7.25 – 7.16 (m, 4H), 7.13 – 7.05 (m, 2H), 6.91 – 6.88 (m, 1H), 6.81 – 6.78 (m, 1H), 6.73 (d, J = 8.0 Hz, 2H), 6.70 – 6.59 (m, 1H), 3.57 (s, 3H), 2.18 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.7, 151.9, 150.1, 146.0, 139.3, 138.2, 133.3, 132.6, 129.9, 129.2, 128.9, 128.7, 128.1, 127.3, 126.8, 122.3, 115.2, 114.3, 109.4, 106.9, 102.1, 52.1, 9.4; IR (KBr): 2952, 1659, 1600, 1444, 1384, 1257, 1200, 1155, 759, 696 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{32}\text{H}_{26}\text{N}_3\text{O}_3$ 500.1969; Found 500.1969; The enantiomeric excess: 91%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 $^{\circ}\text{C}$, 254 nm): t_{R} = 5.946 (major), t_{R} = 7.303 (minor).

(*R*_a)-ethyl 4-hydroxy-1-(4-methyl-3-phenyl-1-(*o*-tolyl)-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (4bab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 78% yield (41.0 mg); white solid; m.p. 214.2-215.1 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20}$ = 60.0 (c = 0.82, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.30 (s, 1H), 7.82 (d, J = 7.6 Hz, 2H), 7.49 – 7.43 (m, 2H), 7.40 – 7.35 (m, 1H), 7.33 – 7.27 (m, 2H), 7.20 – 7.13 (m, 3H), 7.12 – 7.08 (m, 1H), 6.91 – 6.72 (m, 5H), 6.44 – 6.38 (m, 1H), 4.10 – 3.95 (m, 2H), 2.25 (s, 3H), 1.51 (s, 3H), 0.86 – 0.78 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.3, 151.9, 150.0, 146.4, 139.3, 138.8, 138.3, 133.3, 132.8, 129.1, 128.7, 128.1, 127.9, 127.3, 127.1, 126.6, 122.4, 115.2, 114.2, 109.2, 107.2, 102.0, 61.3, 21.4, 13.4, 9.4; IR (KBr): 1651, 1622, 1470, 1384, 1258, 1155, 764, 750, 654, 599 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_3\text{Na}$ 550.2101; Found 550.2100; The enantiomeric excess: 93%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 $^{\circ}\text{C}$, 254 nm): t_{R} = 5.819 (major), t_{R} = 7.333 (minor).

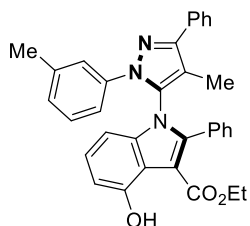
(*R*_a)-ethyl 1-(1-(2-bromophenyl)-4-methyl-3-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4cab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 74% yield (44.0 mg); white solid; m.p. 218.2-219.1 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20}$ = 51.8 (c = 0.88, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.26 (s, 1H), 7.82 (d, J = 7.6 Hz, 2H), 7.51 – 7.42 (m, 3H), 7.39 – 7.30 (m, 2H), 7.25 – 7.18 (m, 4H), 7.13 – 7.08 (m, 1H), 7.01 – 6.96 (m, 1H), 6.83 – 6.75 (m, 3H), 6.45 – 6.40 (m, 1H), 4.10 – 3.96 (m, 2H), 2.19 (s, 3H), 0.86 –

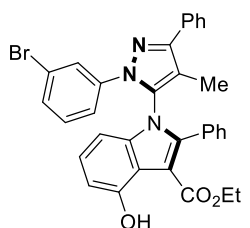
0.78 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 151.8, 150.1, 145.7, 139.6, 136.7, 134.0, 133.6, 133.2, 130.0, 129.9, 129.3, 128.7, 128.2, 127.8, 127.4, 126.5, 121.4, 115.1, 113.7, 109.2, 107.3, 102.6, 61.3, 13.4, 9.7; IR (KBr): 2926, 1651, 1484, 1466, 1262, 1193, 1156, 764, 696, 600 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{BrN}_3\text{O}_3\text{Na}$ 614.1050; Found 614.1049; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30\text{ }^\circ\text{C}$, 254 nm): $t_{\text{R}} = 6.463$ (major), $t_{\text{R}} = 8.289$ (minor).

(*R*_a)-ethyl 4-hydroxy-1-(4-methyl-3-phenyl-1-(*m*-tolyl)-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (4dab):



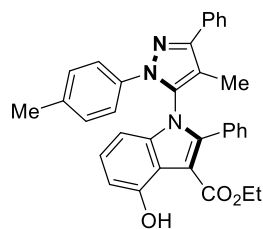
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 90% yield (47.4 mg); white solid; m.p. 210.2-211.1 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{20} = -11.2$ ($c = 0.95$, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.30 (s, 1H), 7.78 (d, $J = 7.6$ Hz, 2H), 7.47 – 7.42 (m, 2H), 7.39 – 7.34 (m, 1H), 7.31 – 7.27 (m, 1H), 7.25 – 7.19 (m, 2H), 7.09 – 6.99 (m, 4H), 6.89 – 6.82 (m, 1H), 6.80 – 6.73 (m, 1H), 6.67 – 6.62 (m, 2H), 6.41 – 6.37 (m, 1H), 4.12 – 3.98 (m, 2H), 2.20 (s, 3H), 2.15 (s, 3H), 0.85 – 0.77 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 151.9, 150.0, 146.1, 139.4, 139.2, 138.0, 133.3, 132.7, 130.1, 128.8, 128.6, 128.2, 128.1, 127.4, 127.1, 126.7, 123.9, 118.9, 115.2, 114.1, 109.2, 107.2, 102.1, 61.3, 21.3, 13.3, 9.4; IR (KBr): 3060, 2983, 1655, 1598, 1484, 1384, 1258, 1192, 770, 696 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_3\text{Na}$ 550.2101; Found 550.2099; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, $T = 30\text{ }^\circ\text{C}$, 254 nm): $t_{\text{R}} = 7.599$ (major), $t_{\text{R}} = 10.473$ (minor).

(*R*_a)-ethyl 1-(1-(3-bromophenyl)-4-methyl-3-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4eab):



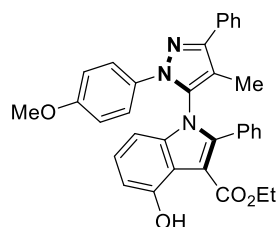
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 92% yield (54.5 mg); white solid; m.p. 211.2-212.1 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{20} = -25.9$ ($c = 0.76$, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.34 (s, 1H), 7.81 (d, $J = 8.4$ Hz, 2H), 7.51 – 7.46 (m, 2H), 7.44 – 7.36 (m, 2H), 7.34 – 7.27 (m, 3H), 7.17 – 7.11 (m, 2H), 7.09 – 7.06 (m, 1H), 7.04 – 6.99 (m, 1H), 6.92 – 6.88 (m, 1H), 6.80 – 6.64 (m, 2H), 6.49 – 6.44 (m, 1H), 4.15 – 4.03 (m, 2H), 2.19 (s, 3H), 0.90 – 0.82 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 152.0, 150.7, 145.7, 139.2, 139.1, 132.9, 132.8, 130.3, 129.9, 129.0, 128.7, 128.4, 127.4, 126.9, 126.6, 122.9, 119.9, 115.2, 114.8, 109.5, 107.5, 101.9, 61.4, 13.4, 9.4; IR (KBr): 1655, 1484, 1385, 1262, 1192, 1155, 1118, 750, 697, 600 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{BrN}_3\text{O}_3\text{Na}$ 614.1050; Found 614.1049; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, $T = 30\text{ }^\circ\text{C}$, 254 nm): $t_{\text{R}} = 7.903$ (major), $t_{\text{R}} = 8.979$ (minor).

(*R*_a)-ethyl 4-hydroxy-1-(4-methyl-3-phenyl-1-(*p*-tolyl)-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (4fab):



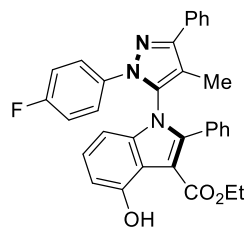
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 83% yield (43.6 mg); white solid; m.p. 196.2-197.1 °C; $[\alpha]_D^{20} = -13.8$ ($c = 0.82$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.32 (s, 1H), 7.78 (d, $J = 7.6$ Hz, 2H), 7.48 – 7.43 (m, 2H), 7.39 – 7.35 (m, 1H), 7.31 – 7.27 (m, 2H), 7.24 – 7.21 (m, 1H), 7.12 – 7.06 (m, 2H), 7.02 – 6.98 (m, 2H), 6.89 – 6.86 (m, 1H), 6.78 – 6.75 (m, 1H), 6.72 – 6.62 (m, 3H), 4.09 – 4.02 (m, 2H), 2.33 (s, 3H), 2.14 (s, 3H), 0.87 – 0.79 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 151.9, 149.8, 146.2, 139.4, 137.3, 135.9, 133.4, 132.5, 130.2, 129.7, 128.9, 128.6, 128.0, 127.3, 127.2, 126.7, 122.3, 115.2, 114.0, 109.2, 107.2, 102.1, 61.3, 21.1, 13.3, 9.3; IR (KBr): 2983, 1656, 1515, 1471, 1384, 1257, 1193, 1156, 770, 697 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_3\text{Na}$ 550.2101; Found 550.2099; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IB, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 4.863$ (major), $t_R = 5.263$ (minor).

(*R_a*)-ethyl 4-hydroxy-1-(1-(4-methoxyphenyl)-4-methyl-3-phenyl-1H-pyrazol-5-yl)-2-phenyl-1H-indole-3-carboxylate (4gab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 84% yield (45.4 mg); white solid; m.p. 202.2-203.1 °C; $[\alpha]_D^{20} = -10.8$ ($c = 0.91$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.32 (s, 1H), 7.78 (d, $J = 7.6$ Hz, 2H), 7.48 – 7.43 (m, 2H), 7.39 – 7.34 (m, 1H), 7.32 – 7.27 (m, 2H), 7.25 – 7.22 (m, 1H), 7.15 – 7.06 (m, 2H), 6.89 – 6.85 (m, 1H), 6.79 – 6.65 (m, 6H), 4.12 – 4.01 (m, 2H), 3.78 (s, 3H), 2.15 (s, 3H), 0.87 – 0.79 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 158.8, 151.9, 149.6, 146.2, 139.4, 133.4, 132.5, 131.5, 130.2, 128.9, 128.6, 128.0, 127.3, 127.2, 126.7, 124.0, 115.2, 114.2, 113.8, 109.2, 107.2, 102.0, 61.3, 55.5, 13.3, 9.4; IR (KBr): 3059, 1653, 1514, 1472, 1384, 1257, 1193, 1155, 834, 697 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_4\text{Na}$ 566.2050; Found 566.2051; The enantiomeric excess: 91%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 10.153$ (major), $t_R = 12.359$ (minor).

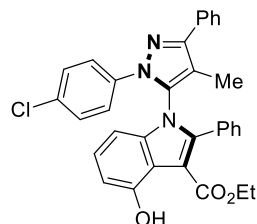
(*R_a*)-ethyl 1-(1-(4-fluorophenyl)-4-methyl-3-phenyl-1H-pyrazol-5-yl)-4-hydroxy-2-phenyl-1H-indole-3-carboxylate (4hab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 95% yield (50.6 mg); white solid; m.p. 218.2-219.1 °C; $[\alpha]_D^{20} = -3.7$ ($c = 1.01$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.33 (s, 1H), 7.78 (d, $J = 7.6$ Hz, 2H), 7.50 – 7.44 (m, 2H), 7.42 – 7.36 (m, 1H), 7.32 – 7.27 (m, 2H), 7.25 – 7.22 (m, 1H), 7.14 – 7.07 (m, 2H), 6.93 – 6.86 (m, 3H), 6.78 – 6.66 (m, 4H), 4.15 – 3.98 (m, 2H), 2.17 (s, 3H), 0.90 – 0.79 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 161.6 (d, $J = 247.8$ Hz), 152.0, 150.2, 145.8, 139.2, 134.4 (d, $J = 3.0$ Hz), 133.1, 132.6, 130.1, 129.0, 128.7, 128.2, 127.3, 126.9, 124.3 (d, $J = 8.5$ Hz), 116.0 (d, $J = 22.9$ Hz), 115.2, 114.3, 109.4, 107.4, 101.9, 61.4, 13.4, 9.4; $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -113.9; IR (KBr): 2983, 1656, 1511, 1384, 1257, 1193, 1155, 839, 697, 593 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{FN}_3\text{O}_3\text{Na}$ 554.1850; Found 554.1851; The enantiomeric excess: 93%, determined by HPLC (Daicel

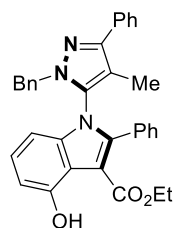
Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.669 (major), t_R = 7.323 (minor).

(*R*_a)-ethyl 1-(1-(4-chlorophenyl)-4-methyl-3-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4iab):



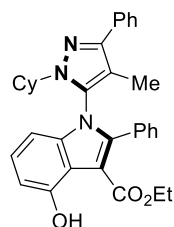
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 84% yield (46.3 mg); white solid; m.p. 221.2-222.1 °C; $[\alpha]_D^{20}$ = -30.8 (c = 0.93, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.33 (s, 1H), 7.77 (d, J = 7.6 Hz, 2H), 7.49 – 7.44 (m, 2H), 7.42 – 7.36 (m, 1H), 7.32 – 7.27 (m, 2H), 7.25 – 7.22 (m, 1H), 7.20 – 7.16 (m, 2H), 7.13 – 7.07 (m, 2H), 6.91 – 6.85 (m, 1H), 6.79 – 6.66 (m, 4H), 4.15 – 4.04 (m, 2H), 2.16 (s, 3H), 0.88 – 0.80 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 152.0, 150.5, 145.8, 139.1, 136.8, 133.0, 132.6, 130.0, 129.3, 129.0, 128.7, 128.3, 127.4, 127.3, 126.9, 123.4, 115.2, 114.7, 109.5, 107.5, 101.9, 61.4, 13.3, 9.4; IR (KBr): 2984, 1656, 1623, 1498, 1470, 1409, 1193, 1093, 768, 697 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{ClN}_3\text{O}_3\text{Na}$ 570.1555; Found 570.1557; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.029 (major), t_R = 5.776 (minor).

(*R*_a)-ethyl 1-(1-(benzyl-4-methyl-3-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4jab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 84% yield (44.2 mg); white solid; m.p. 215.5-216.4 °C; $[\alpha]_D^{20}$ = 18.7 (c = 0.88, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.29 (s, 1H), 7.69 (d, J = 7.6 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.35 – 7.29 (m, 2H), 7.22 – 7.09 (m, 6H), 7.08 – 7.00 (m, 2H), 6.91 – 6.86 (m, 2H), 6.80 – 6.77 (m, 1H), 6.31 – 6.26 (m, 1H), 4.89 (s, 2H), 4.17 – 4.10 (m, 2H), 1.94 (s, 3H), 0.95 – 0.87 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.3, 151.6, 148.9, 146.1, 139.2, 135.3, 133.7, 133.1, 130.4, 130.0, 129.2, 128.6, 128.5, 127.9, 127.7, 127.6, 127.1, 126.3, 115.0, 112.4, 109.0, 107.3, 102.0, 61.4, 53.0, 13.5, 9.5; IR (KBr): 2982, 1651, 1623, 1479, 1384, 1323, 1262, 769, 697, 601 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_3\text{Na}$ 550.2101; Found 550.2104; The enantiomeric excess: 86%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.409 (major), t_R = 6.653 (minor).

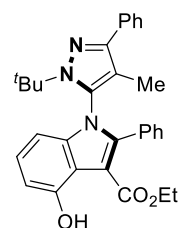
(*R*_a)-ethyl 1-(1-(cyclohexyl-4-methyl-3-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4kab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 87% yield (45.1 mg); white solid; m.p. 209.2-210.1 °C; $[\alpha]_D^{20}$ = 7.1 (c = 0.90, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.32 (s, 1H), 7.71 (d, J = 7.6 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.37 – 7.28 (m, 6H), 7.21 – 7.16 (m, 1H), 6.86 – 6.79 (m, 1H), 6.53 – 6.46 (m, 1H), 4.26 – 4.09 (m, 2H), 3.36 – 3.26 (m, 1H), 2.03 (s, 3H), 1.89 – 1.52 (m, 7H), 1.19 – 1.03 (m, 3H), 0.99 – 0.93 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.3, 151.8, 148.4, 146.0, 139.7, 134.1, 131.6, 130.6, 129.3,

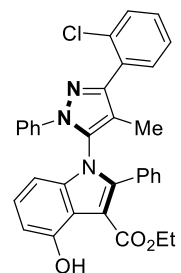
128.5, 127.7, 127.5, 127.2, 126.4, 115.2, 111.4, 109.0, 107.1, 101.8, 61.4, 57.1, 33.8, 31.7, 25.6, 25.4, 25.0, 13.5, 9.3; IR (KBr): 2935, 1653, 1623, 1477, 1384, 1324, 1261, 1194, 1155, 769 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{33}\text{N}_3\text{O}_3\text{Na}$ 542.2414; Found 542.2415; The enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 $^\circ\text{C}$, 254 nm): $t_{\text{R}} = 4.673$ (major), $t_{\text{R}} = 5.579$ (minor).

(*R_a*)-ethyl 1-(1-(tert-butyl)-4-methyl-3-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4lab):



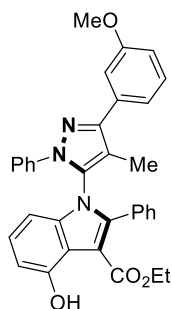
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 67% yield (33.0 mg); white solid; m.p. 193.2-194.1 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{20} = 53.3$ (c = 0.61, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.31 (s, 1H), 7.74 (d, $J = 7.6$ Hz, 2H), 7.45 – 7.41 (m, 2H), 7.36 – 7.29 (m, 6H), 7.21 – 7.16 (m, 1H), 6.81 – 6.78 (m, 1H), 6.46 – 6.42 (m, 1H), 4.23 – 4.07 (m, 2H), 1.97 (s, 3H), 1.21 (s, 9H), 0.98 – 0.90 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.4, 151.8, 147.1, 146.2, 140.4, 134.1, 131.5, 130.7, 130.5, 129.2, 128.5, 127.6, 127.5, 127.0, 126.4, 115.0, 113.5, 108.8, 107.3, 102.2, 61.6, 61.4, 29.4, 13.5, 9.5; IR (KBr): 2980, 1651, 1472, 1384, 1263, 1186, 1155, 769, 697, 652 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{31}\text{H}_{31}\text{N}_3\text{O}_3\text{Na}$ 516.2257; Found 516.2254; The enantiomeric excess: 85%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 $^\circ\text{C}$, 254 nm): $t_{\text{R}} = 6.743$ (major), $t_{\text{R}} = 8.173$ (minor).

(*R_a*)-ethyl 1-(3-(2-chlorophenyl)-4-methyl-1-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4mab):



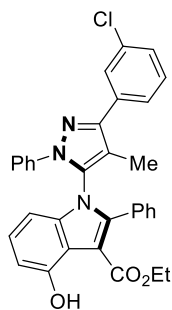
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 70% yield (38.6 mg); white solid; m.p. 230.2-231.1 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{20} = -36.3$ (c = 0.74, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.33 (s, 1H), 7.52 – 7.44 (m, 2H), 7.41 – 7.27 (m, 4H), 7.25 – 7.13 (m, 4H), 7.12 – 7.04 (m, 2H), 6.91 – 6.86 (m, 1H), 6.85 – 6.78 (m, 1H), 6.75 – 6.66 (m, 3H), 4.15 – 4.00 (m, 2H), 1.93 (s, 3H), 0.88 – 0.82 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 152.0, 149.9, 146.0, 139.1, 138.0, 134.1, 132.2, 132.0, 131.7, 130.0, 129.7, 129.1, 128.8, 127.4, 127.2, 126.8, 126.7, 122.3, 116.4, 115.3, 109.3, 107.1, 102.0, 61.3, 13.4, 8.5; IR (KBr): 1655, 1600, 1483, 1385, 1261, 1193, 1155, 757, 695, 600 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{ClN}_3\text{O}_3\text{Na}$ 570.1555; Found 570.1555; The enantiomeric excess: 95%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 $^\circ\text{C}$, 254 nm): $t_{\text{R}} = 9.203$ (major), $t_{\text{R}} = 12.459$ (minor).

(*R_a*)-ethyl 4-hydroxy-1-(3-(3-methoxyphenyl)-4-methyl-1-phenyl-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (4nab):



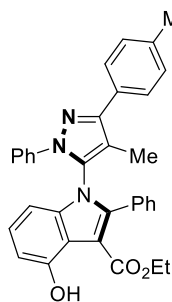
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 84% yield (45.9 mg); white solid; m.p. 188.2-189.1 °C; $[\alpha]_D^{20} = -4.4$ (c = 0.92, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.34 (s, 1H), 7.40 – 7.35 (m, 3H), 7.32 – 7.27 (m, 2H), 7.24 – 7.18 (m, 4H), 7.11 – 7.05 (m, 2H), 6.96 – 6.92 (m, 1H), 6.90 – 6.86 (m, 1H), 6.81 – 6.71 (m, 4H), 4.11 – 4.01 (m, 2H), 3.87 (s, 3H), 2.17 (s, 3H), 0.87 – 0.79 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 159.9, 152.0, 149.9, 146.1, 139.3, 138.2, 134.6, 132.6, 130.1, 129.7, 129.2, 128.9, 127.4, 127.3, 126.8, 122.4, 119.8, 115.2, 114.4, 113.9, 112.7, 109.3, 107.3, 102.0, 61.3, 55.4, 13.3, 9.4; IR (KBr): 2983, 1656, 1600, 1479, 1384, 1259, 1192, 1044, 763, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_4\text{Na}$ 566.2050; Found 566.2051; The enantiomeric excess: 91%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): $t_R = 6.829$ (major), $t_R = 8.476$ (minor).

(R_a)-ethyl 1-(3-(3-chlorophenyl)-4-methyl-1-phenyl-1H-pyrazol-5-yl)-4-hydroxy-2-phenyl-1H-indole-3-carboxylate (4oab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 73% yield (40.0 mg); white solid; m.p. 190.2-191.1 °C; $[\alpha]_D^{20} = -10.6$ (c = 0.80, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.32 (s, 1H), 7.80 (s, 1H), 7.70 – 7.64 (m, 1H), 7.41 – 7.33 (m, 2H), 7.31 – 7.28 (m, 1H), 7.25 – 7.16 (m, 5H), 7.12 – 7.03 (m, 2H), 6.90 – 6.86 (m, 1H), 6.78 – 6.65 (m, 4H), 4.13 – 3.98 (m, 2H), 2.16 (s, 3H), 0.86 – 0.78 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 152.0, 148.7, 146.0, 139.2, 138.1, 135.0, 134.6, 132.8, 130.1, 129.9, 129.2, 128.9, 128.1, 127.6, 127.3, 126.8, 125.3, 122.4, 115.2, 114.4, 109.4, 107.4, 101.9, 61.3, 13.3, 9.3; IR (KBr): 1656, 1598, 1417, 1384, 1327, 1257, 1194, 1155, 763, 696 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{ClN}_3\text{O}_3\text{Na}$ 570.1555; Found 570.1555; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): $t_R = 9.293$ (major), $t_R = 10.263$ (minor).

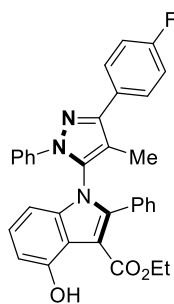
(R_a)-ethyl 4-hydroxy-1-(4-methyl-1-phenyl-3-(p-tolyl)-1H-pyrazol-5-yl)-2-phenyl-1H-indole-3-carboxylate (4pab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 81% yield (43.0 mg); white solid; m.p. 177.2-178.1 °C; $[\alpha]_D^{20} = -1.4$ (c = 0.86, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.35 (s, 1H), 7.70 (d, $J = 6.8$ Hz, 2H), 7.33 – 7.27 (m, 4H), 7.25 – 7.17 (m, 4H), 7.13 – 7.02 (m, 2H), 6.91 – 6.88 (m, 1H), 6.83 – 6.64 (m, 4H), 4.12 – 4.02 (m, 2H), 2.43 (s, 3H), 2.16 (s, 3H), 0.86 – 0.81 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 151.9, 149.3, 145.8, 139.7, 136.5, 135.8, 133.5, 133.3, 131.4, 130.2, 129.1, 128.6, 128.5, 128.0, 127.4, 127.2, 126.6, 126.3, 124.7, 115.1, 113.0, 109.2, 107.1, 102.0, 61.2, 18.1, 13.3, 9.6; IR (KBr): 2982, 1656, 1600, 1483, 1384, 1257, 1193, 1156, 763, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_3\text{Na}$ 550.2101; Found 550.2101; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254

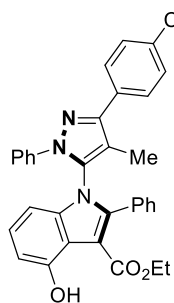
nm): $t_R = 7.949$ (major), $t_R = 9.486$ (minor).

(*R_a*)-ethyl 1-(3-(4-fluorophenyl)-4-methyl-1-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4qab):



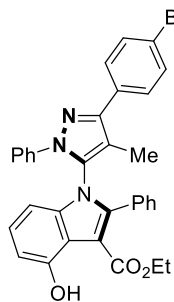
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 79% yield (42.0 mg); white solid; m.p. 184.2-185.1 °C; $[\alpha]_D^{20} = -11.3$ ($c = 0.84$, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.37 (s, 1H), 7.84 – 7.77 (m, 2H), 7.42 – 7.27 (m, 4H), 7.25 – 7.04 (m, 6H), 6.94 – 6.91 (m, 1H), 6.87 – 6.69 (m, 4H), 4.16 – 4.04 (m, 2H), 2.18 (s, 3H), 0.91 – 0.83 (m, 3H); ^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 162.7 (d, $J = 246.1$ Hz), 152.0, 149.3, 146.0, 139.2, 138.2, 132.7, 130.1, 129.4 (d, $J = 3.2$ Hz), 129.2, 129.1 (d, $J = 8.1$ Hz), 128.9, 127.4, 127.3, 126.8, 122.4, 115.6 (d, $J = 21.3$ Hz), 115.2, 114.0, 109.3, 107.4, 102.0, 61.3, 13.3, 9.3; ^{19}F NMR (376 MHz, CDCl_3) δ -113.6; IR (KBr): 2983, 1656, 1502, 1385, 1257, 1193, 1156, 753, 695, 601 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{FN}_3\text{O}_3\text{Na}$ 554.1850; Found 554.1850; The enantiomeric excess: 91%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 6.606$ (major), $t_R = 7.636$ (minor).

(*R_a*)-ethyl 1-(3-(4-chlorophenyl)-4-methyl-1-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4rab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 69% yield (37.6 mg); white solid; m.p. 165.2-166.1 °C; $[\alpha]_D^{20} = 0.7$ ($c = 0.75$, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.32 (s, 1H), 7.73 (d, $J = 8.4$ Hz, 2H), 7.42 (d, $J = 8.4$ Hz, 2H), 7.32 – 7.27 (m, 1H), 7.25 – 7.16 (m, 5H), 7.14 – 7.00 (m, 2H), 6.89 – 6.86 (m, 1H), 6.79 – 6.60 (m, 4H), 4.10 – 4.00 (m, 2H), 2.14 (s, 3H), 0.85 – 0.79 (m, 3H); ^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 152.0, 149.0, 146.0, 139.2, 138.1, 134.0, 132.8, 131.8, 130.1, 129.2, 128.9, 128.8, 128.5, 127.5, 127.3, 126.8, 122.4, 115.2, 114.2, 109.4, 107.4, 102.0, 61.3, 13.3, 9.4; IR (KBr): 2983, 1655, 1600, 1501, 1385, 1257, 1194, 1156, 763, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{ClN}_3\text{O}_3\text{Na}$ 570.1555; Found 570.1555; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_R = 6.143$ (major), $t_R = 6.939$ (minor).

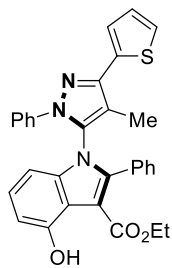
(*R_a*)-ethyl 1-(3-(4-bromophenyl)-4-methyl-1-phenyl-1*H*-pyrazol-5-yl)-4-hydroxy-2-phenyl-1*H*-indole-3-carboxylate (4sab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 94% yield (55.7 mg); white solid; m.p. 186.2-187.1 °C; $[\alpha]_D^{20} = 5.5$ ($c = 1.11$, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.33 (s, 1H), 7.67 (d, $J = 8.0$ Hz, 2H), 7.57 (d, $J = 8.4$ Hz, 2H), 7.32 – 7.27 (m, 1H), 7.25 – 7.15 (m, 5H), 7.13 – 6.97 (m, 2H), 6.89 – 6.86 (m, 1H), 6.81 – 6.58 (m, 4H), 4.10 – 3.99 (m, 2H), 2.14 (s, 3H), 0.84 – 0.79 (m, 3H); ^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 152.0, 149.0, 146.0, 139.2, 138.1, 132.8, 132.2, 131.8, 130.1, 129.2, 128.9, 128.8, 127.5, 127.3, 126.8, 122.4, 122.2, 115.2, 114.2, 109.4, 107.4,

101.9, 61.3, 13.3, 9.4; IR (KBr): 2983, 1656, 1599, 1500, 1417, 1321, 1257, 1194, 1007, 763 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{26}\text{BrN}_3\text{O}_3\text{Na}$ 614.1050; Found 614.1044; The enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 $^{\circ}\text{C}$, 254 nm): $t_{\text{R}} = 7.833$ (major), $t_{\text{R}} = 8.966$ (minor).

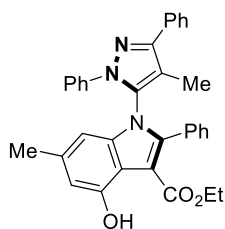
(*R*_a)-ethyl 4-hydroxy-1-(4-methyl-1-phenyl-3-(thiophen-2-yl)-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (4tab):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 79% yield (40.9 mg); white solid; m.p. 64.2-65.1 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20} = -9.8$ (c = 0.82, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.34 (s, 1H), 7.46 – 7.42 (m, 1H), 7.36 – 7.33 (m, 1H), 7.32 – 7.27 (m, 2H), 7.25 – 7.18 (m, 4H), 7.15 – 7.05 (m, 3H), 6.91 – 6.87 (m, 1H), 6.78 – 6.73 (m, 3H), 6.69 – 6.60 (m, 1H), 4.12 – 3.99 (m, 2H), 2.19 (s, 3H), 0.87 – 0.79 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.1, 151.9, 146.0, 145.5, 139.3, 138.0, 136.0, 132.6, 130.0, 129.2, 128.9,

127.6, 127.4, 127.3, 126.8, 125.3, 124.9, 122.4, 115.2, 113.7, 109.4, 107.4, 102.0, 61.3, 13.3, 9.2; IR (KBr): 2983, 1655, 1599, 1481, 1383, 1321, 1258, 1192, 1156, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{31}\text{H}_{25}\text{N}_3\text{O}_3\text{SNa}$ 542.1509; Found 542.1510; The enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 $^{\circ}\text{C}$, 254 nm): $t_{\text{R}} = 9.479$ (major), $t_{\text{R}} = 12.086$ (minor).

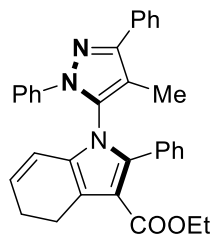
(*R*_a)-ethyl 4-hydroxy-6-methyl-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (4abb):



Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 78% yield (41.1 mg); white solid; m.p. 64.2-65.1 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20} = 0.1$ (c = 0.82, acetone); ^1H NMR (400 MHz, CDCl_3) δ 11.21 (s, 1H), 7.81 (d, $J = 7.6$ Hz, 2H), 7.48 – 7.43 (m, 2H), 7.40 – 7.36 (m, 1H), 7.25 – 7.24 (m, 1H), 7.23 – 7.17 (m, 4H), 7.11 – 7.00 (m, 2H), 6.86 – 6.65 (m, 4H), 6.56 (s, 1H), 4.09 – 3.99 (m, 2H), 2.42 (s, 3H), 2.17 (s, 3H),

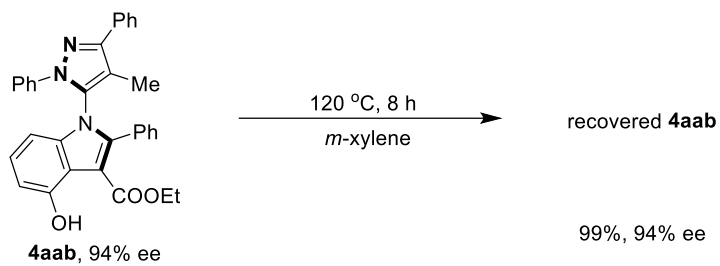
0.84 – 0.79 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 168.2, 151.4, 150.0, 145.5, 139.6, 138.3, 137.3, 133.3, 132.7, 130.2, 129.1, 128.7, 128.6, 128.1, 127.3, 127.2, 122.4, 114.2, 113.1, 110.8, 107.2, 102.1, 61.2, 21.9, 13.3, 9.4; IR (KBr): 2981, 1657, 1600, 1500, 1373, 1331, 1231, 1155, 764, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_3\text{Na}$ 550.2101; Found 550.2101; The enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 $^{\circ}\text{C}$, 254 nm): $t_{\text{R}} = 5.443$ (major), $t_{\text{R}} = 6.583$ (minor).

(*R*_a)-ethyl 1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-phenyl-4,5-dihydro-1*H*-indole-3-carboxylate (4acb):



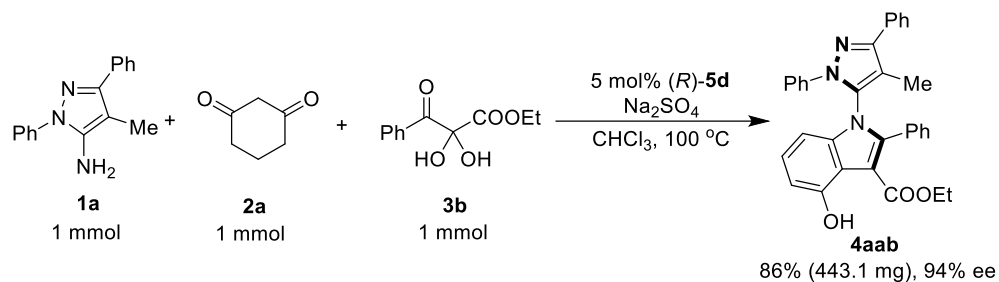
Purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 20/1); 50% yield (25.2 mg); white solid; m.p. 94.2-95.1 °C; $[\alpha]_{\text{D}}^{20} = -18.8$ ($c = 0.50$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.77 (d, $J = 7.6$ Hz, 2H), 7.47 – 7.42 (m, 2H), 7.39 – 7.34 (m, 1H), 7.25 – 7.19 (m, 3H), 7.15 – 7.10 (m, 1H), 7.05 – 6.99 (m, 2H), 6.85 – 6.77 (m, 2H), 6.69 (d, $J = 7.6$ Hz, 2H), 6.15 – 6.07 (m, 1H), 5.87 – 5.79 (m, 1H), 4.16 – 4.04 (m, 2H), 3.17 – 3.00 (m, 2H), 2.56 – 2.45 (m, 2H), 2.17 (s, 3H), 1.13 – 1.06 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 165.0, 149.8, 138.3, 133.4, 133.2, 130.8, 130.4, 129.9, 129.0, 128.6, 128.0, 127.8, 127.3, 127.2, 127.0, 126.2, 122.1, 120.2, 116.2, 113.4, 113.3, 59.6, 24.2, 21.0, 14.0, 9.3; IR (KBr): 2923, 1704, 1630, 1599, 1473, 1369, 1252, 1132, 758, 694 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{33}\text{H}_{30}\text{N}_3\text{O}_2$ 500.2333; Found 500.2324; The enantiomeric excess: 74%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_{\text{R}} = 4.003$ (major), $t_{\text{R}} = 4.607$ (minor).

4. Study on the configurational stability



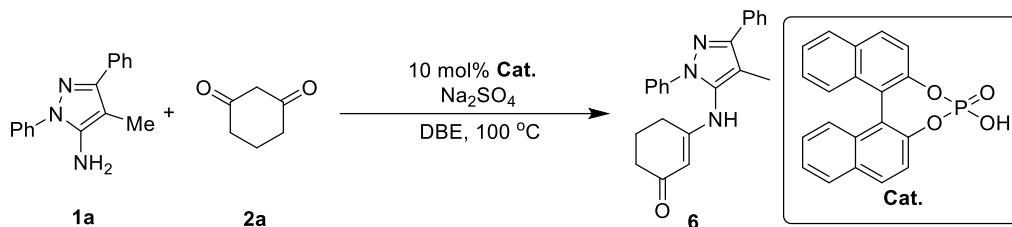
To a reaction tube were added compound **4aab** (51.4 mg, 0.1 mmol) and *m*-xylene (1.0 mL). The mixture was then stirred at 120 °C for 8 hours. Compound **4aab** was recovered in 99% yield with 94% ee.

5. Procedure for 1-mmol-scale reaction



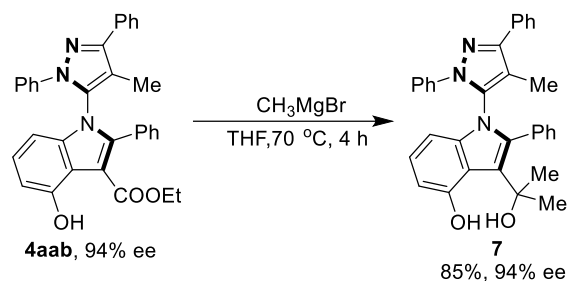
In a sealed tube were added **1a** (249.3 mg, 0.1 mmol, 1 equiv), **2a** (112.1 mg, 0.1 mmol, 1 equiv), **3b** (224.21 mg, 0.1 mmol, 1 equiv), chiral phosphoric acid catalyst (*R*)-**5d** (35.0 mg, 5 mol%, 0.05 equiv), and Na_2SO_4 (500 mg). Subsequently, CHCl_3 (10 mL) was added, and the sealed tube was stirred at 100 °C for 15 hours. After the reaction was confirmed to be complete by TLC analysis, the mixture was directly purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to afford the pure product **4aab** in 86% yield (443.1 mg) with 94% ee.

6. Synthetic procedures and characterization data of products 6-10



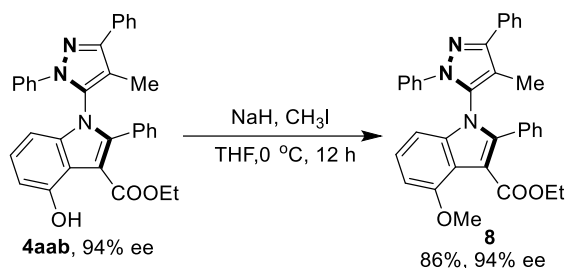
3-((4-methyl-1,3-diphenyl-1H-pyrazol-5-yl)amino)cyclohex-2-en-1-one (**6**):

In the reaction tube were added 5-aminopyrazole **1a** (1 mmol, 1 equiv), cyclohexanedione **2a** (1 mmol, 1 equiv), **Cat.** (10 mol%, 0.1 equiv), and Na_2SO_4 (500 mg). Subsequently, 1,2-dibromoethane (10 mL) was added, and the reaction tube was stirred at $100\text{ }^\circ\text{C}$ for 15 hours. After the completion of the reaction which was indicated by TLC, the reaction mixture was concentrated and the residue was purified by flash column chromatography through silica gel (petroleum ether/ethyl acetate = 10/1) to afford pure product **6** in 78% yield (267.9 mg) as a pale yellow solid. m.p. $174.2\text{--}175.1\text{ }^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 8.14 (s, 1H), 7.55 (d, $J = 7.2\text{ Hz}$, 2H), 7.39 – 7.27 (m, 6H), 7.25 – 7.22 (m, 1H), 7.20 – 7.14 (m, 1H), 4.91 (s, 1H), 2.14 – 2.02 (m, 2H), 2.02 – 1.96 (m, 2H), 1.85 (s, 3H), 1.73 – 1.62 (m, 2H); ^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 198.6, 165.2, 150.5, 138.4, 134.6, 133.3, 129.1, 128.6, 127.9, 127.5, 127.4, 123.4, 111.9, 100.3, 36.2, 27.8, 21.7, 9.0; IR (KBr): 2950, 1597, 1500, 1361, 1241, 1188, 1140, 915, 764, 695 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{22}\text{H}_{21}\text{N}_3\text{ONa}$ 366.1577; Found 366.1577.



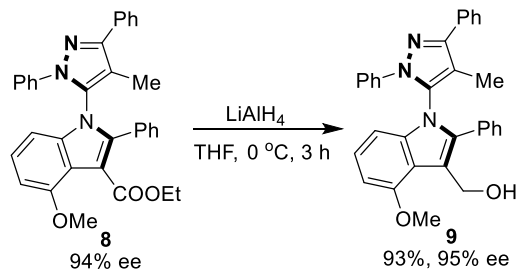
(*R*)-3-(2-hydroxypropan-2-yl)-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indol-4-ol (7):

Under argon atmosphere, CH_3MgBr (0.2 mL, 3 mol/mL, 6 equiv) was added to a Schlenk tube. Then, the solution of **4aab** (51.4 mg, 0.1 mmol, 1 equiv) in anhydrous THF (1 mL) was added dropwise to the Schlenk tube at 0 °C. Subsequently, the reaction mixture was stirred at 70 °C for 4 hours. After the completion of the reaction indicated by TLC, the reaction mixture was quenched by saturated ammonium chloride aqueous solution and extracted by ethyl acetate for three times. The combined organic layers were dried and concentrated under reduced pressure to give a residue. Finally, the residue was purified by preparative thin layer chromatography (PE:EA = 4:1) on silica gel to afford pure products **7** in 85% yield (42.5 mg) as a white solid. m.p. 209.2-210.1 °C; $[\alpha]_{\text{D}}^{20} = -2.4$ ($c = 0.67$, acetone); $^1\text{H NMR}$ (400 MHz, Acetone- d_6) δ 11.20 (s, 1H), 7.84 (d, $J = 7.6$ Hz, 2H), 7.48 – 7.44 (m, 2H), 7.39 – 7.35 (m, 1H), 7.31 – 7.28 (m, 3H), 7.25 – 7.17 (m, 4H), 7.04 – 6.99 (m, 1H), 6.93 – 6.88 (m, 2H), 6.75 – 6.68 (m, 2H), 6.33 (s, 1H), 6.26 – 6.22 (m, 1H), 2.13 (s, 3H), 1.51 (s, 3H), 1.39 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, Acetone- d_6) δ 151.7, 149.3, 139.7, 139.1, 134.1, 133.8, 133.5, 132.2, 130.9, 130.4, 128.9, 128.7, 128.5, 127.8, 127.7, 127.4, 127.3, 127.0, 126.9, 125.2, 123.0, 121.7, 116.2, 114.2, 107.7, 101.1, 71.0, 32.0, 31.0, 8.8; IR (KBr): 2927, 1600, 1576, 1500, 1473, 1366, 1251, 1150, 748, 699 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{33}\text{H}_{30}\text{N}_3\text{O}_2$ 500.2333; Found 500.2322; The enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_{\text{R}} = 11.069$ (major), $t_{\text{R}} = 8.109$ (minor).



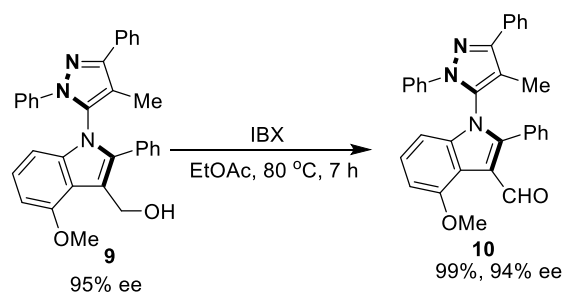
(*R*)-ethyl 4-methoxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carboxylate (8**):**

NaH (60% in oil, 12 mg, 0.3 mmol, 3 equiv) and THF (2 mL) were added to a reaction tube at 0 °C. A solution of compound **4aab** (102.7 mg, 0.2 mmol, 1 equiv) in THF (1 mL) was then added to the reaction mixture, followed by stirring at room temperature for 30 minutes. Afterward, CH₃I (18.7 μL, 0.3 mmol, 3 equiv) was added to the solution at 0 °C, and the reaction mixture was stirred at 0 °C for 12 hours. After the completion of the reaction indicated by TLC, the reaction mixture was quenched by water and extracted by ethyl acetate for three times. The combined organic layers were dried over anhydrous Na₂SO₄ and then concentrated under reduced pressure. The residue was purified through flash column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) to afford pure product **8** in 86% yield (90.3 mg) as a white solid. m.p. 184.2-185.1 °C; $[\alpha]_D^{20} = 2.9$ (c = 0.81, acetone); ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, *J* = 7.6 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.41 – 7.36 (m, 1H), 7.31 – 7.27 (m, 1H), 7.21 – 7.11 (m, 4H), 7.10 – 7.05 (m, 2H), 6.93 – 6.89 (m, 1H), 6.80 – 6.74 (m, 3H), 6.72 – 6.65 (m, 2H), 4.23 – 4.14 (m, 2H), 4.01 (s, 3H), 2.19 (s, 3H), 1.13 – 1.05 (m, 3H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 165.8, 153.9, 150.1, 140.9, 138.6, 138.3, 133.5, 133.4, 129.8, 129.3, 129.0, 128.6, 128.4, 128.0, 127.7, 127.4, 127.1, 125.3, 122.2, 116.2, 113.8, 110.0, 104.0, 103.2, 60.7, 55.7, 14.0, 9.5; IR (KBr): 1723, 1599, 1500, 1361, 1256, 1194, 1086, 1045, 759, 695 cm⁻¹; HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₃₄H₂₉N₃O₃Na 550.2101; Found 550.2100; The enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 11.679 (major), t_R = 13.166 (minor).



(*R*)-4-methoxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indol-3-yl)methanol (9**):**

LiAlH₄ (75.9 mg, 2 mmol, 10 equiv) and 1.5 mL THF were added to a reaction tube. Then, the solution of compound **8** (105.5 mg, 0.2 mmol, 1 equiv) in 0.5 mL THF was added to the reaction mixture, which was stirred at 0 °C for 3 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was quenched with 10 mL H₂O and the aqueous layer was extracted with EtOAc (3×5 mL). The combined organic layers were dried over anhydrous Na₂SO₄ and then concentrated under reduced pressure. The residue was purified through flash column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to afford pure product **9** in 93% yield (90.3 mg) as a white solid. m.p. 112.2-113.1 °C; [α]_D²⁰ = 13.6 (c = 1.03, acetone); ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 7.6 Hz, 2H), 7.52 – 7.45 (m, 2H), 7.43 – 7.37 (m, 1H), 7.30 – 7.27 (m, 1H), 7.23 – 7.18 (m, 1H), 7.17 – 7.06 (m, 5H), 6.98 – 6.93 (m, 1H), 6.81 – 6.72 (m, 3H), 6.67 (d, *J* = 7.6 Hz, 2H), 4.84 – 4.66 (m, 2H), 4.09 (s, 3H), 3.31 (s, 1H), 2.21 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 153.3, 150.1, 139.1, 138.4, 137.0, 134.2, 133.7, 129.7, 128.9, 128.6, 128.0, 127.4, 126.9, 124.5, 122.2, 118.0, 116.0, 113.3, 104.7, 101.8, 57.1, 55.8, 9.5; IR (KBr): 1600, 1498, 1473, 1363, 1252, 1183, 1118, 1086, 759, 696 cm⁻¹; HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₃₂H₂₇N₃O₂Na 508.1995; Found 508.1998; The enantiomeric excess: 95%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.066 (major), t_R = 6.209 (minor).

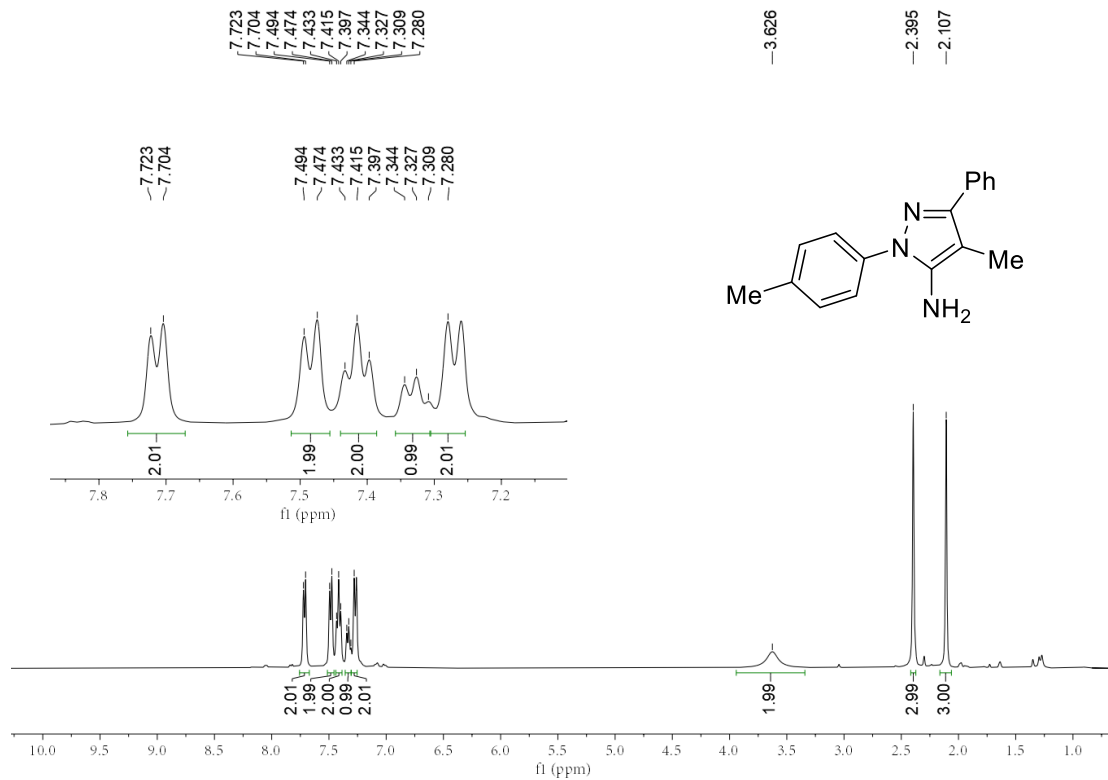


(*R*)-4-methoxy-1-(4-methyl-1,3-diphenyl-1*H*-pyrazol-5-yl)-2-phenyl-1*H*-indole-3-carbaldehyde (10**):**

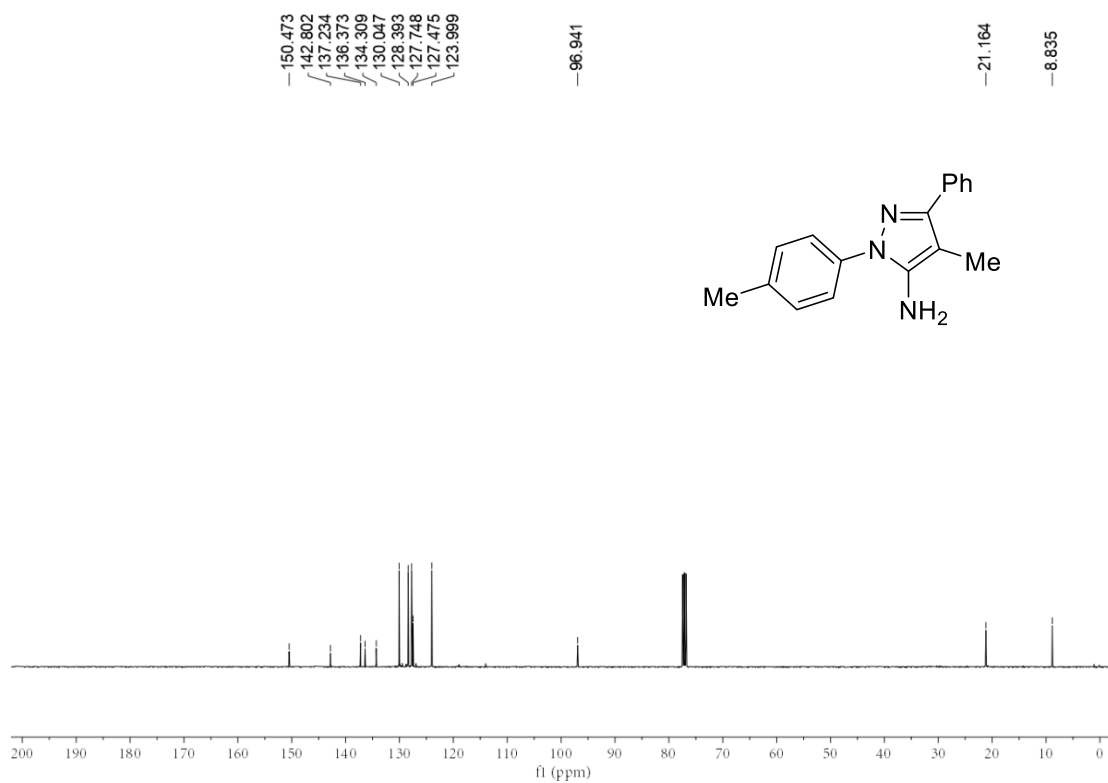
Compound **9** (48.6 mg, 0.1 mmol, 1 equiv) and EtOAc (2.0 mL) were added to a reaction tube. Then, 2-iodoxybenzoic acid (IBX) (56 mg, 0.2 mmol, 2 equiv) was added to the reaction mixture, which was stirred at 80 °C for 7 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was filtered and concentrated under reduced pressure. The residue was purified through preparative thin layer chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to afford pure product **10** in 99% yield (48.0 mg) as a white solid. m.p. 178.2-179.1 °C; $[\alpha]_{\text{D}}^{20} = -87.6$ ($c = 0.96$, acetone); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.50 (s, 1H), 7.83 (d, $J = 7.6$ Hz, 2H), 7.50 – 7.45 (m, 2H), 7.42 – 7.33 (m, 2H), 7.25 – 7.22 (m, 1H), 7.20 – 7.16 (m, 1H), 7.15 – 7.09 (m, 4H), 6.98 – 6.94 (m, 1H), 6.90 – 6.87 (m, 1H), 6.81 (d, $J = 7.6$ Hz, 2H), 6.65 (d, $J = 8.8$ Hz, 2H), 4.08 (s, 3H), 2.21 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 187.8, 154.9, 150.3, 145.5, 139.0, 138.0, 133.3, 132.6, 129.9, 129.3, 129.1, 128.7, 128.2, 127.7, 127.4, 125.7, 122.2, 117.0, 116.5, 114.0, 104.3, 104.2, 55.7, 9.4; IR (KBr): 1673, 1600, 1500, 1363, 1254, 1084, 964, 759, 694, 601 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{32}\text{H}_{26}\text{N}_3\text{O}_2$ 484.2020; Found 484.2009; The enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, $T = 30$ °C, 254 nm): $t_{\text{R}} = 9.109$ (major), $t_{\text{R}} = 10.389$ (minor).

7. NMR spectra of substrates 1

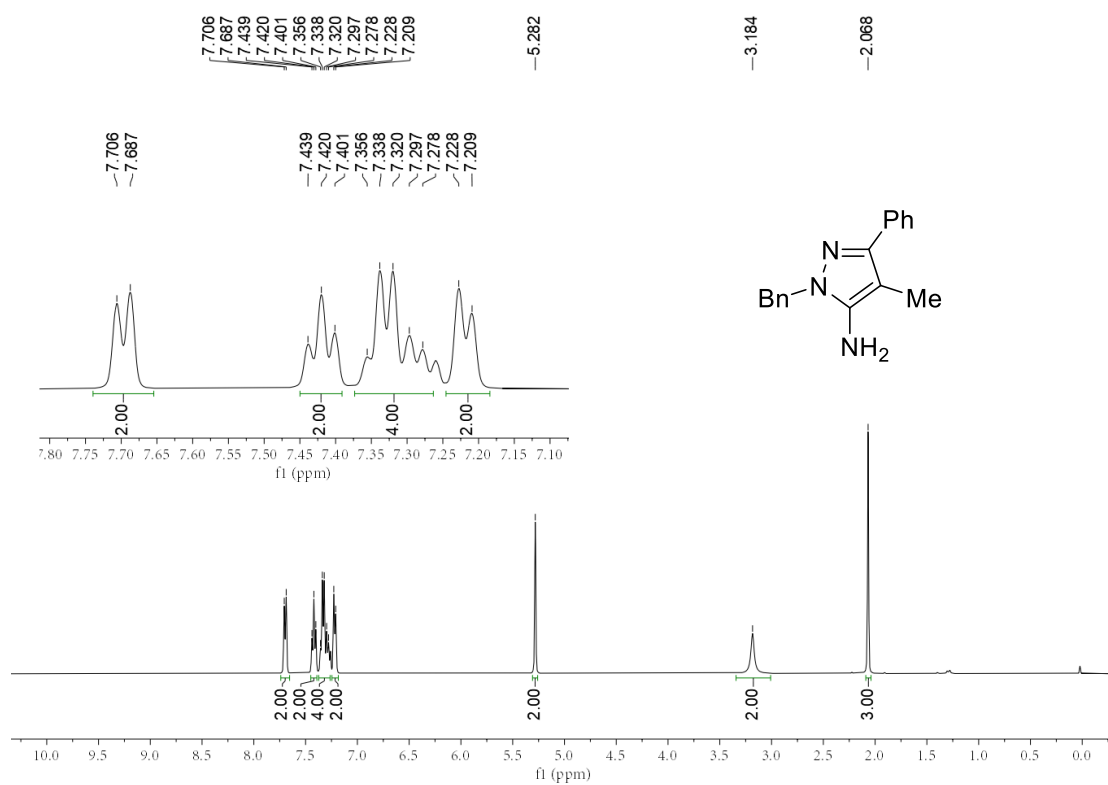
^1H NMR (400 MHz, CDCl_3) of compound **1f**:



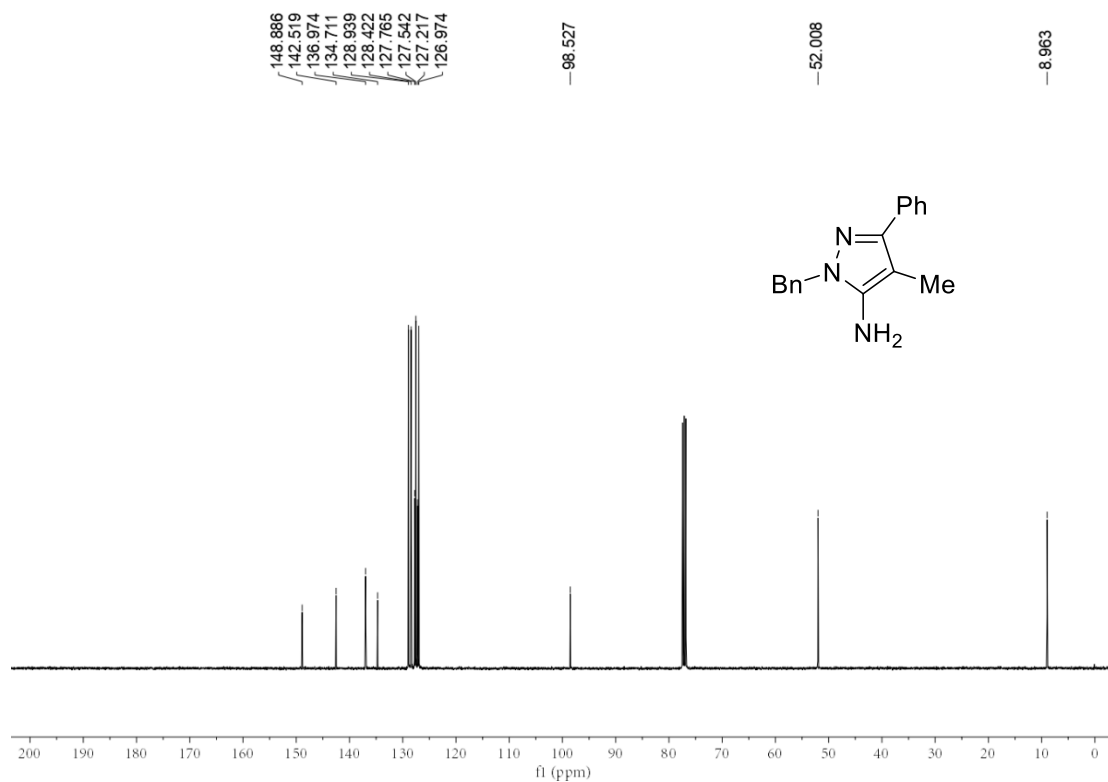
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **1f**:



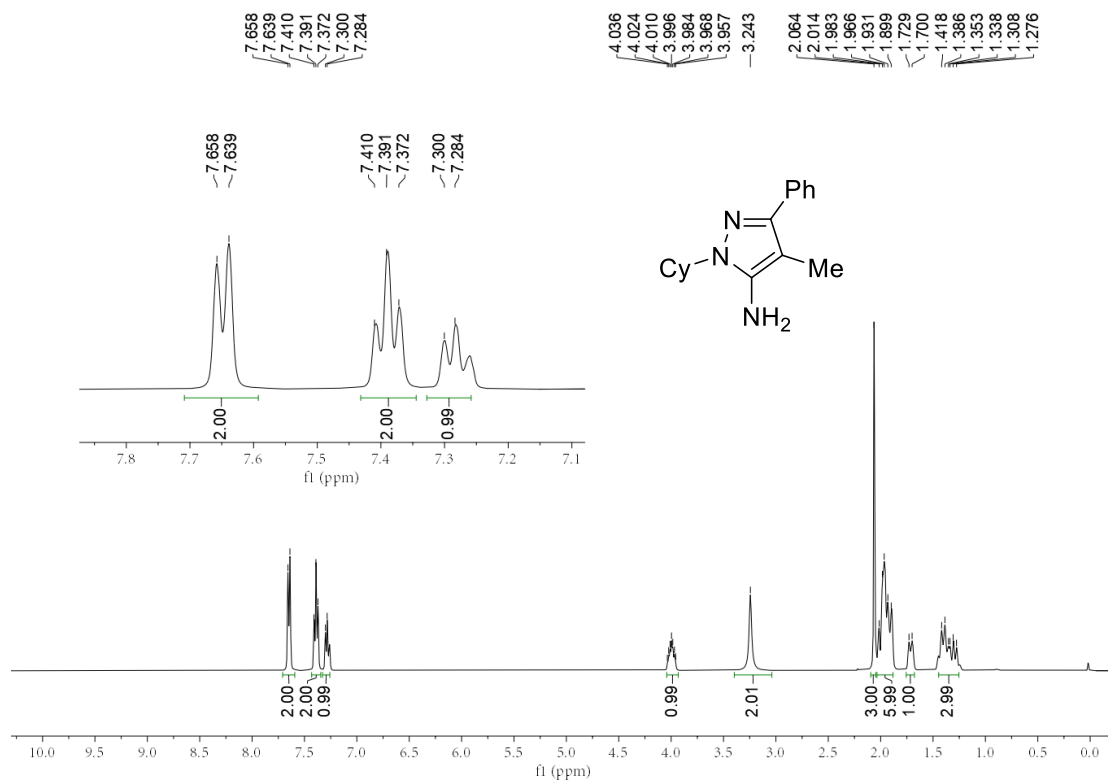
^1H NMR (400 MHz, CDCl_3) of compound **1j**:



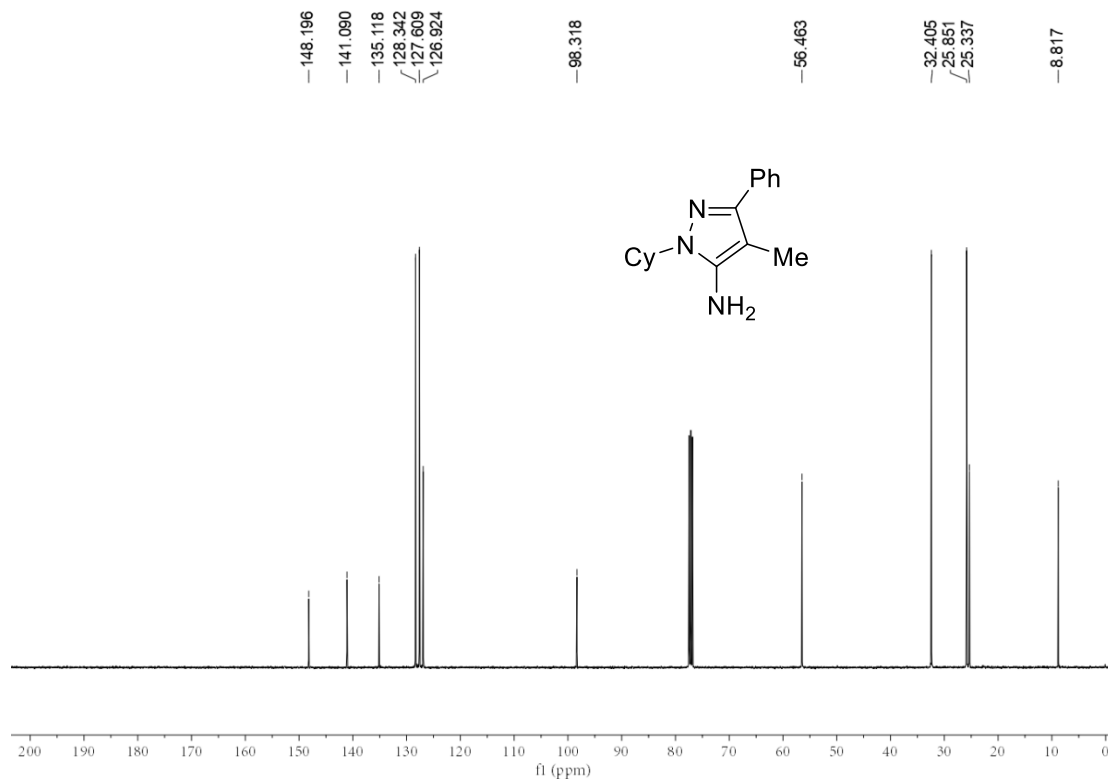
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **1j**:



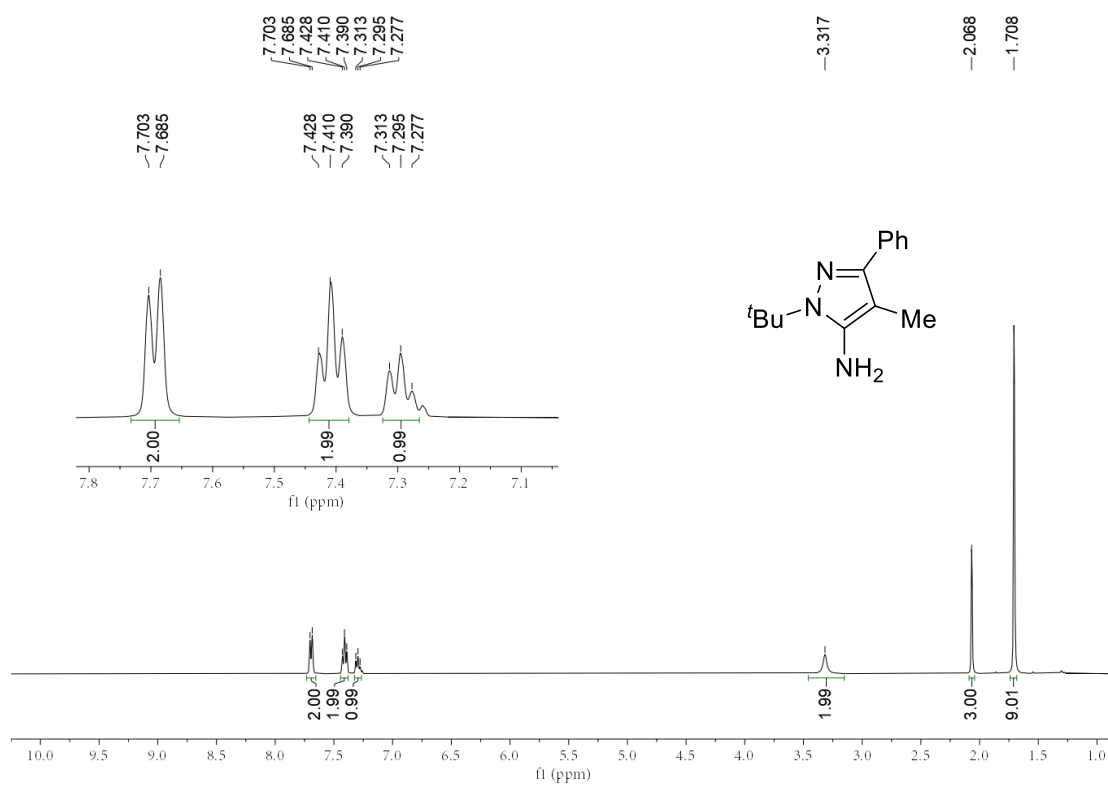
^1H NMR (400 MHz, CDCl_3) of compound **1k**:



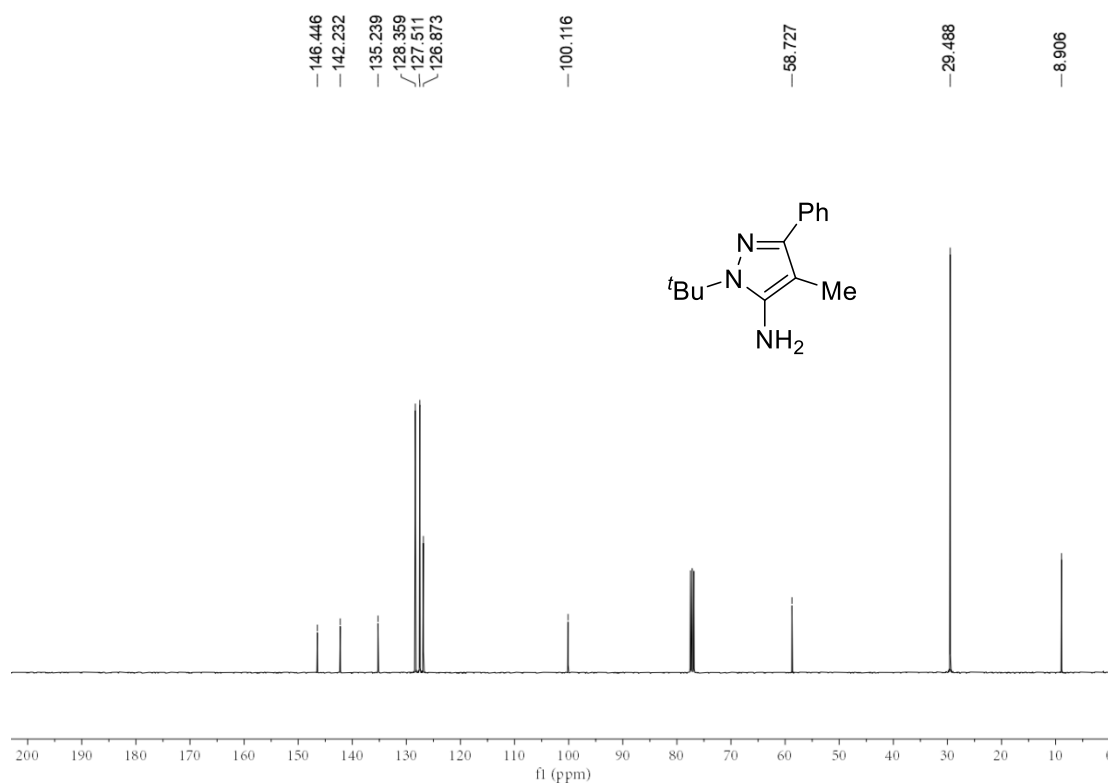
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of compound **1k**:



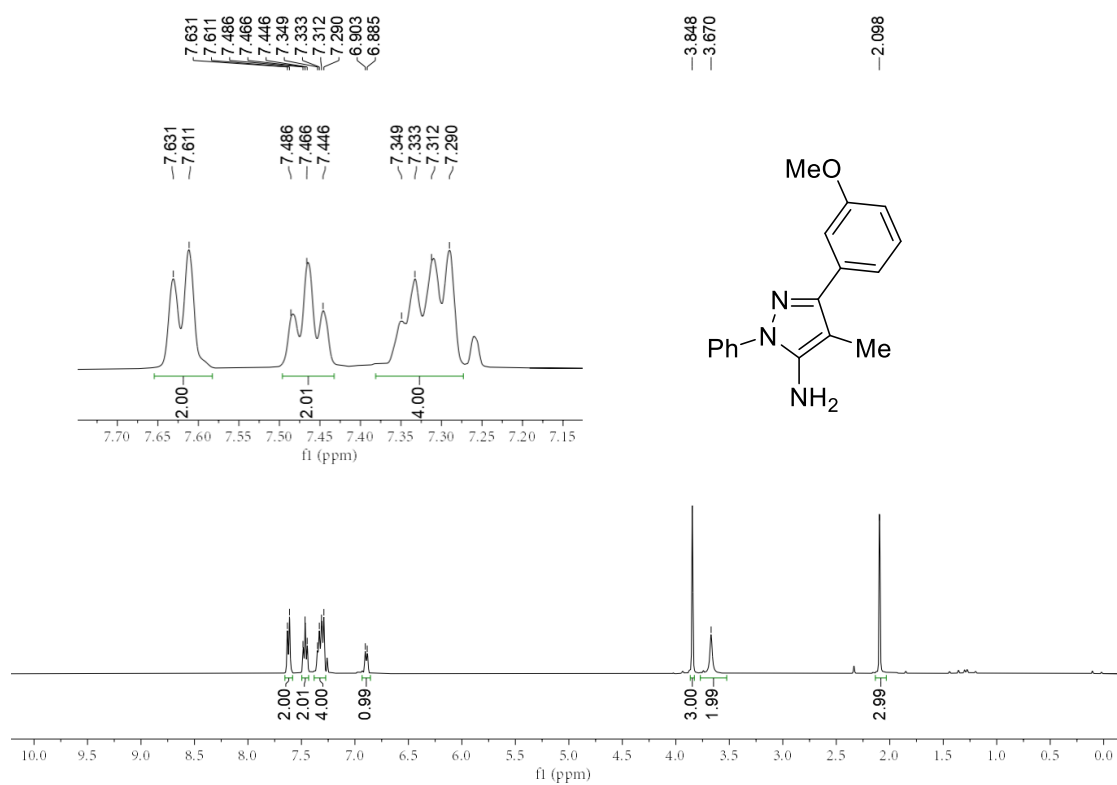
^1H NMR (400 MHz, CDCl_3) of compound **11**:



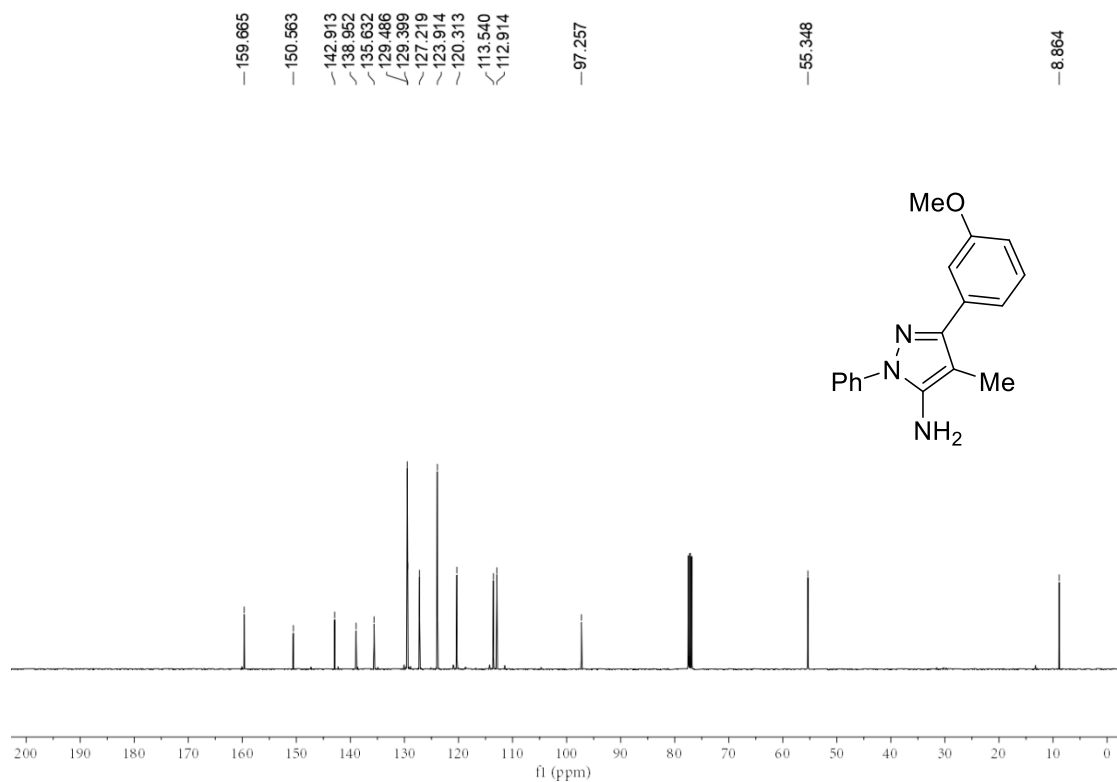
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **11**:



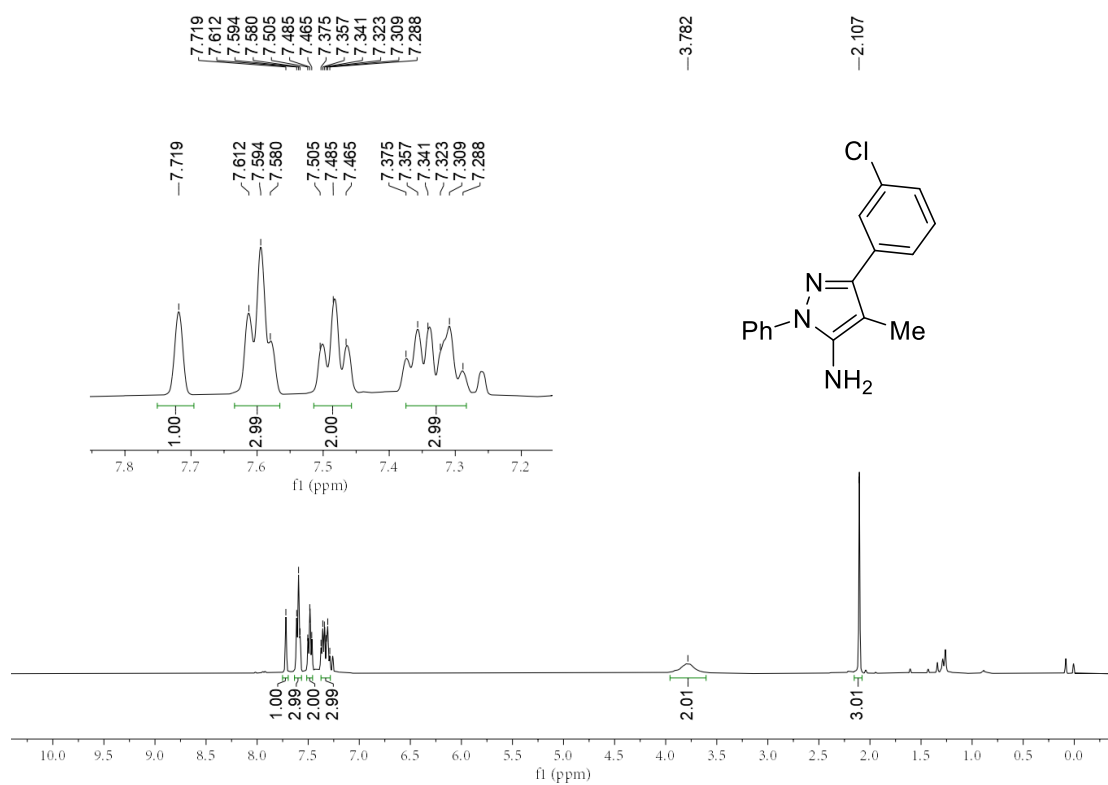
^1H NMR (400 MHz, CDCl_3) of compound **1n**:



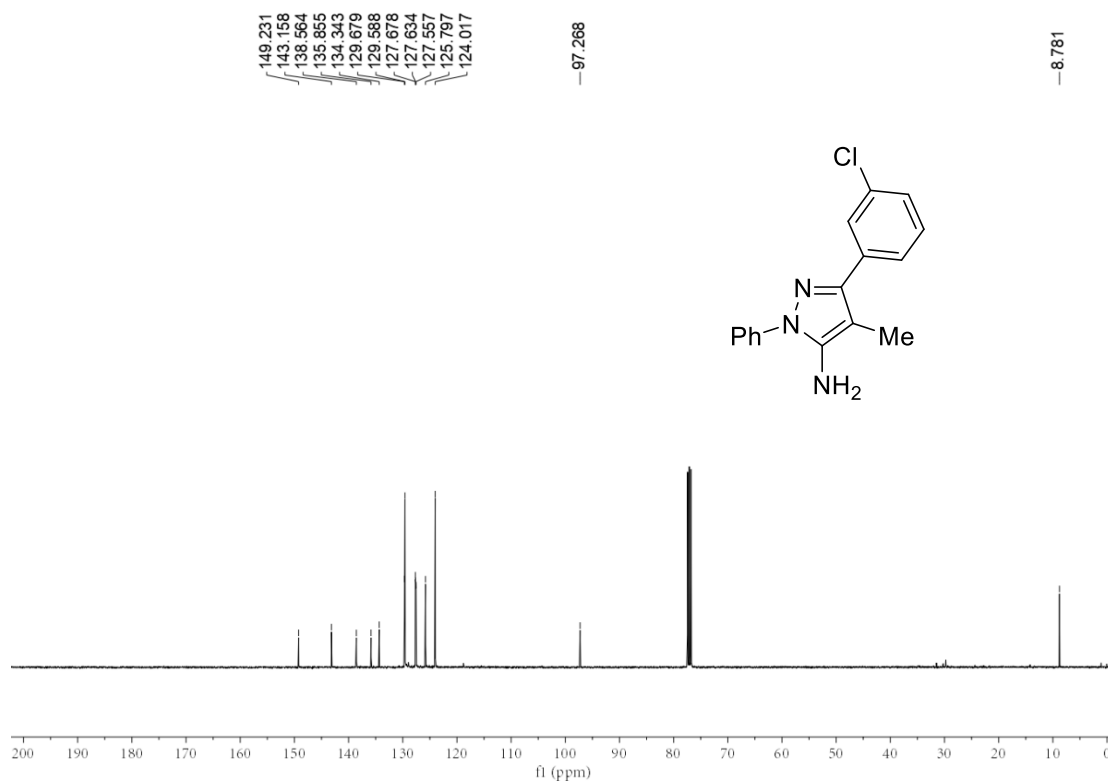
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **1n**:



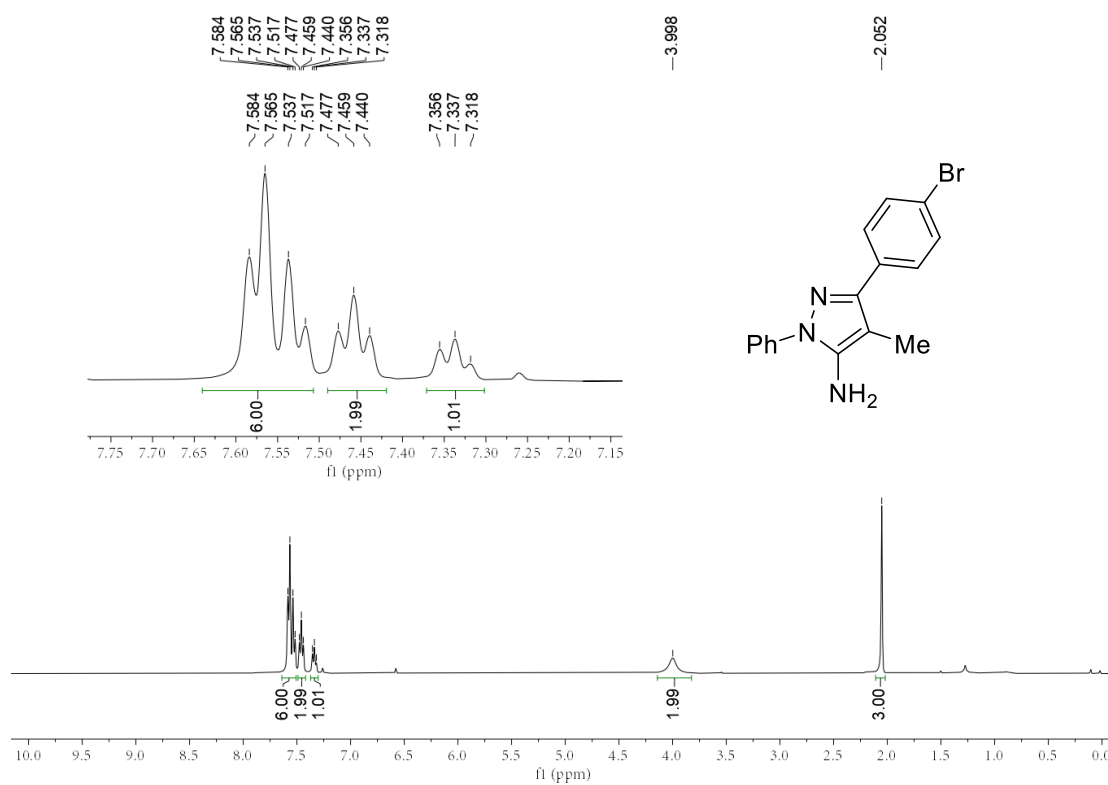
^1H NMR (400 MHz, CDCl_3) of compound **1o**:



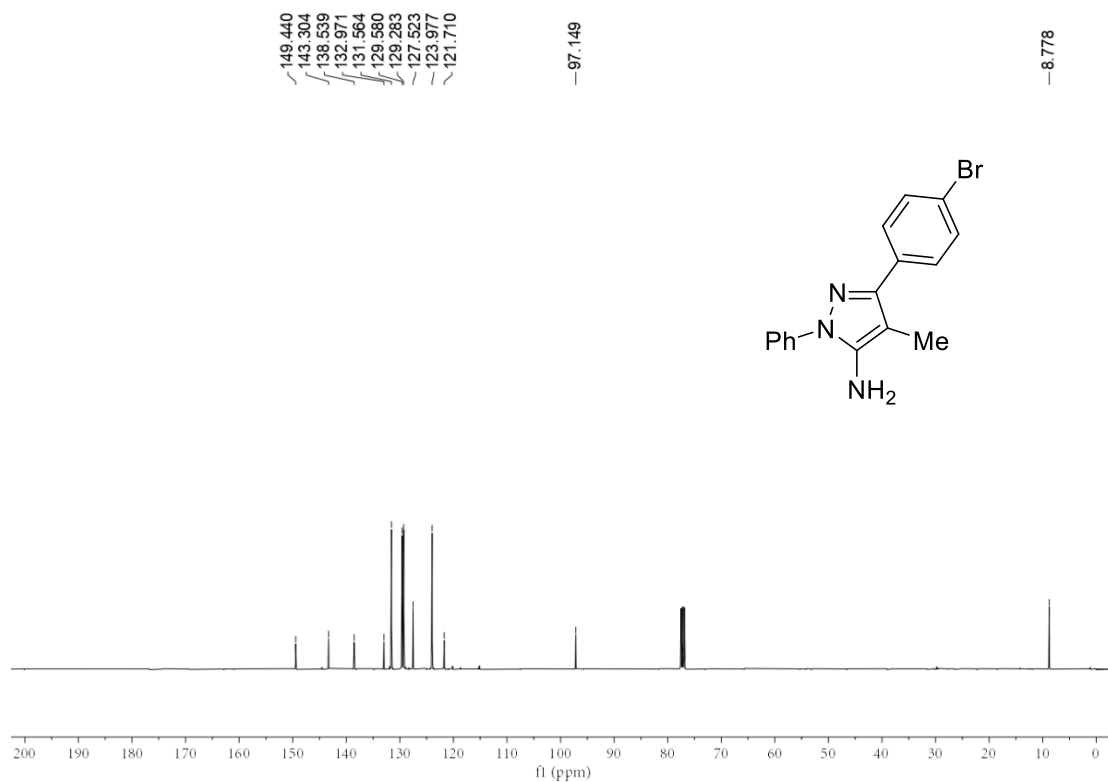
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **1o**:



^1H NMR (400 MHz, CDCl_3) of compound **1s**:

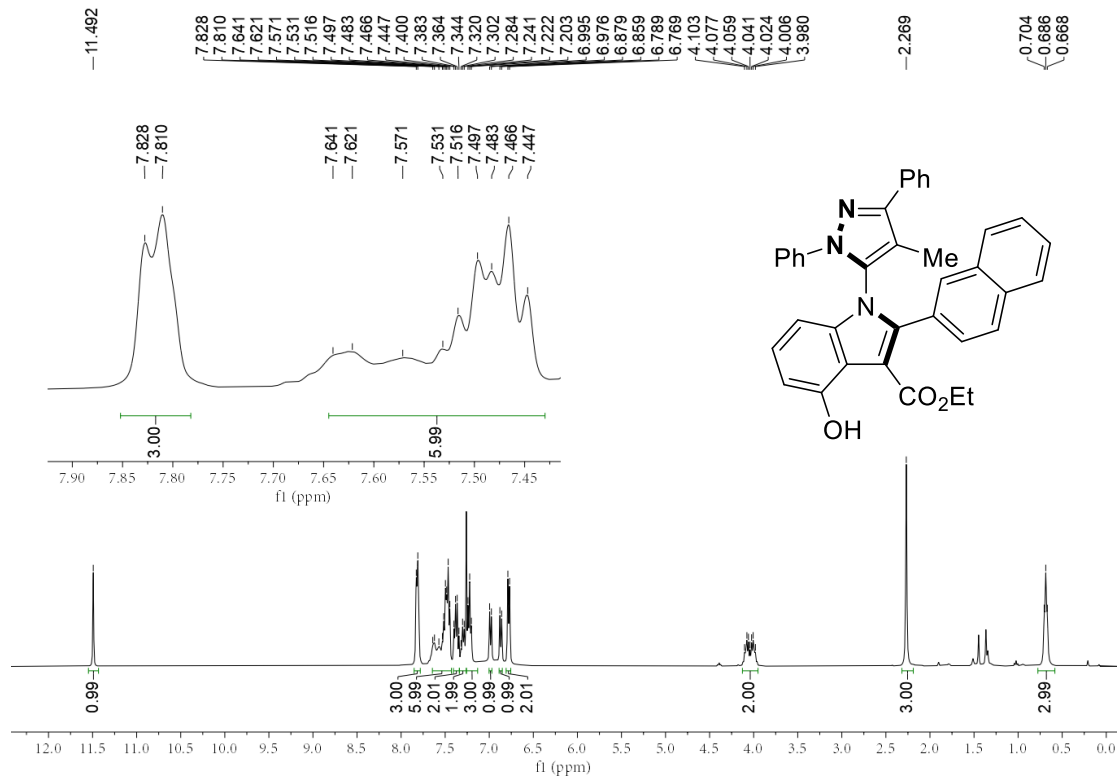


$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **1s**:

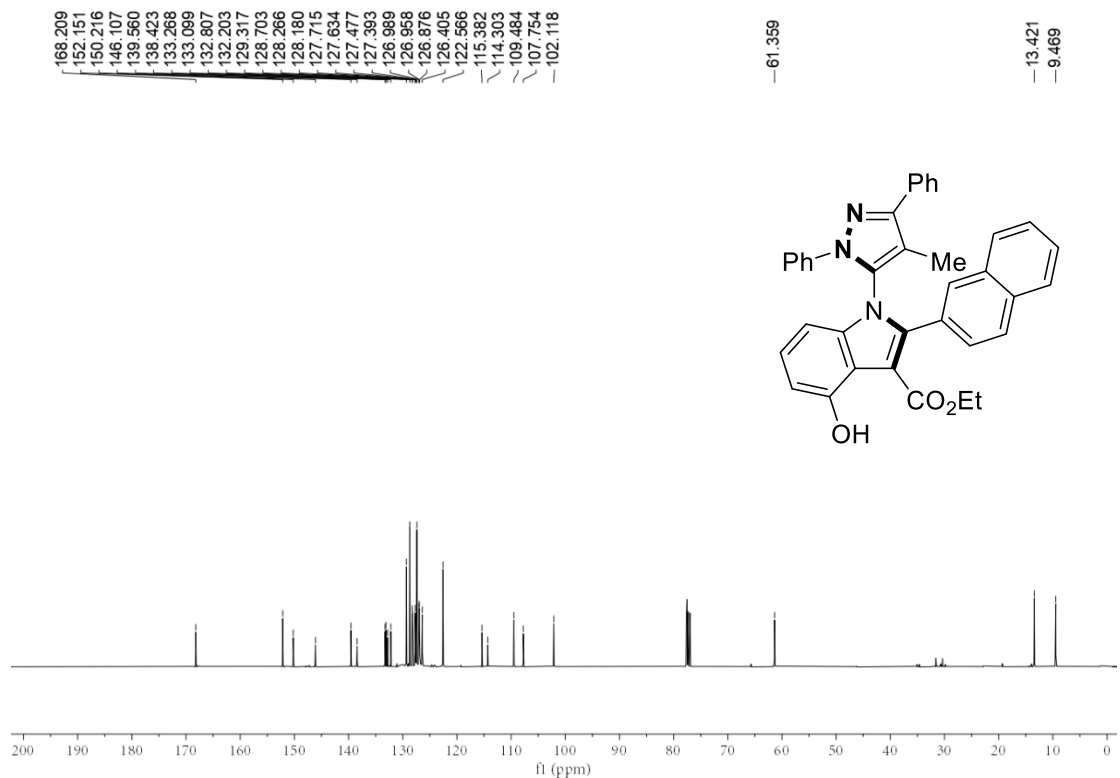


8. NMR spectra of substrates 4

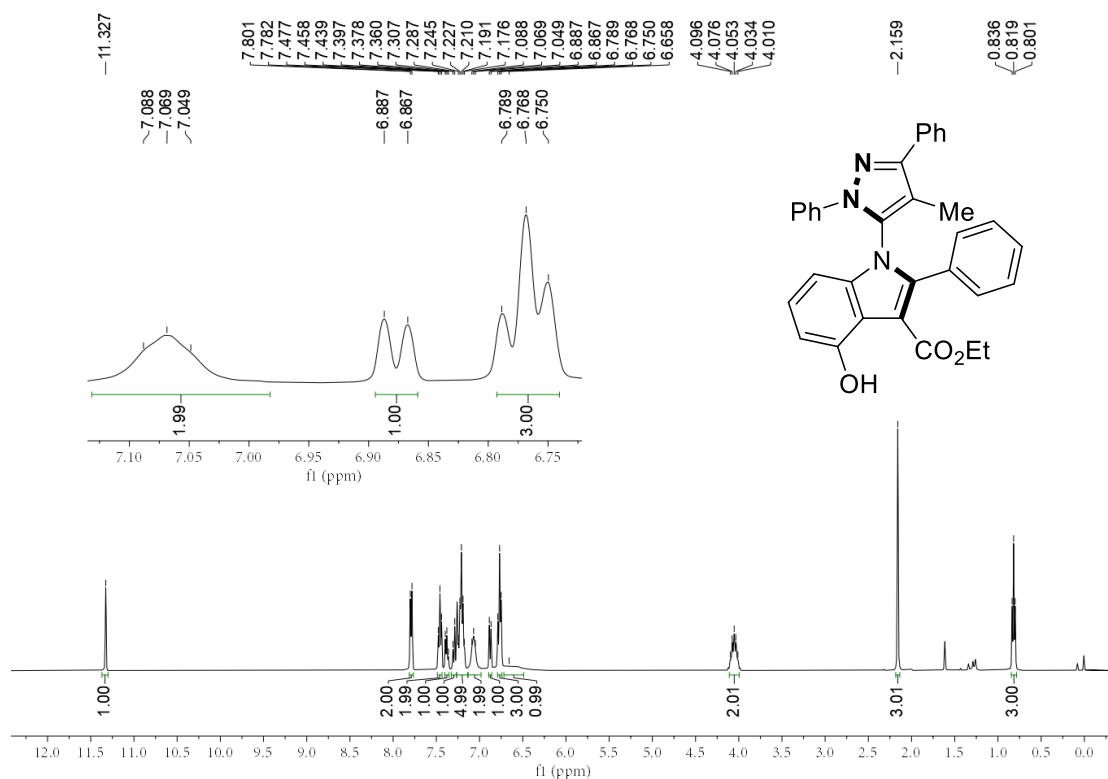
^1H NMR (400 MHz, CDCl_3) of compound **4aaa**:



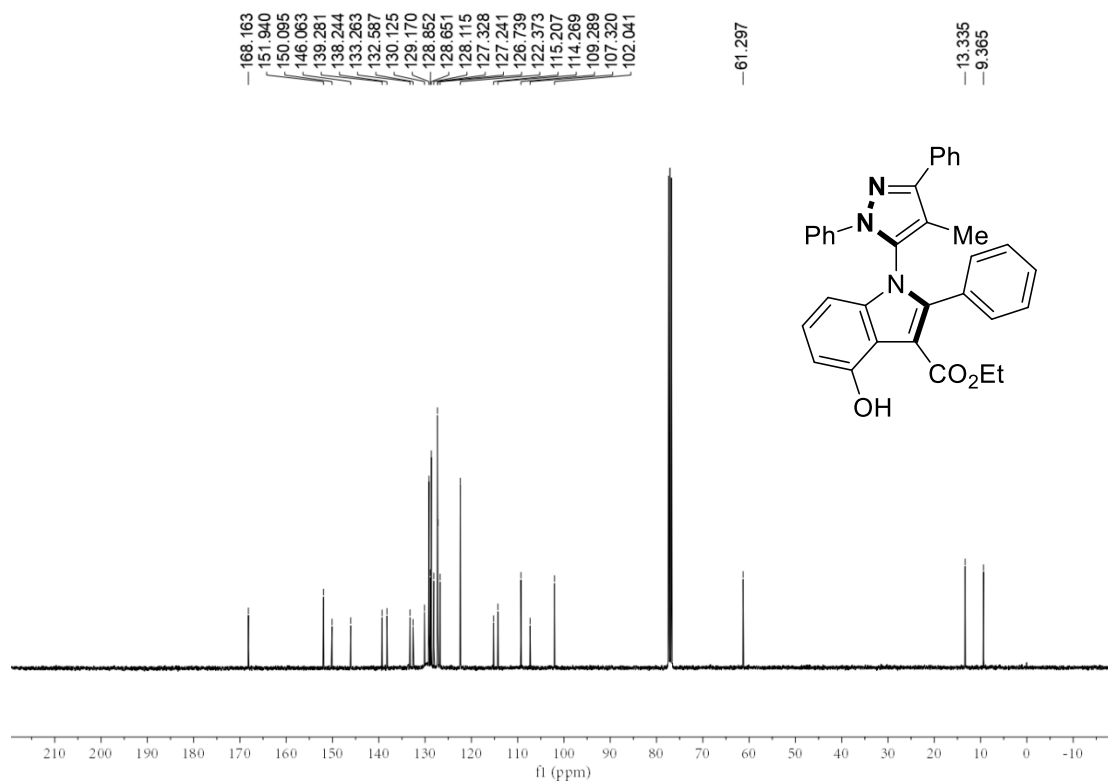
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aaa**:



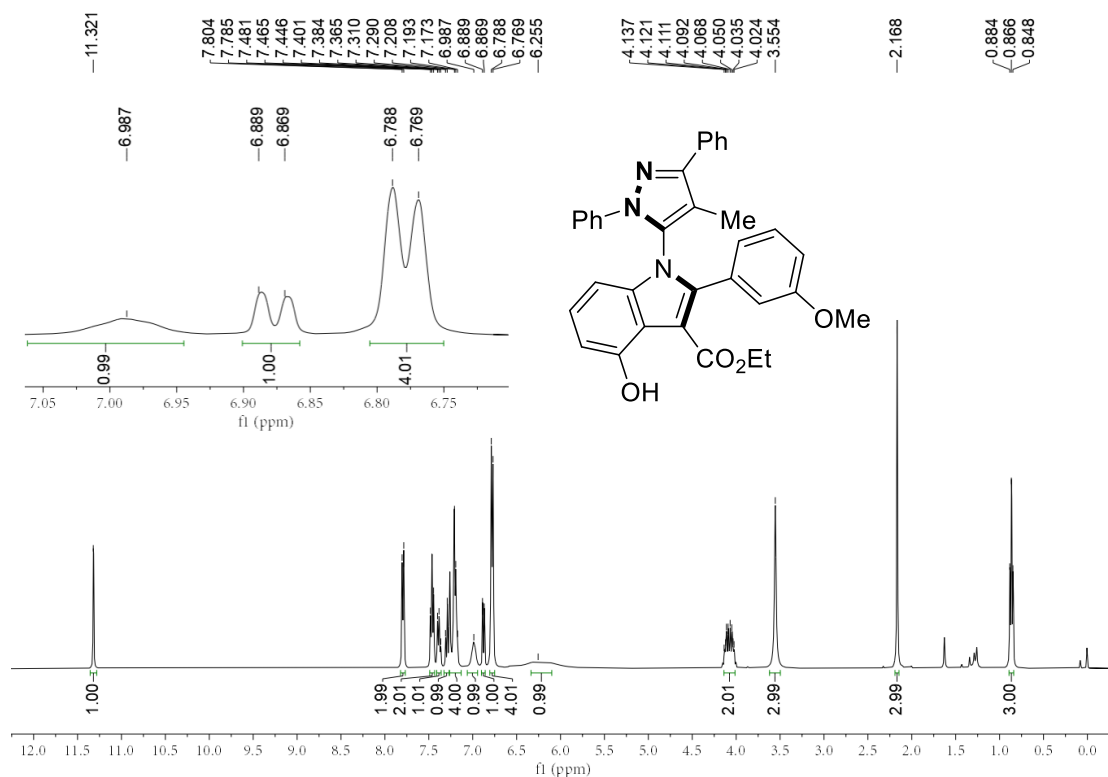
^1H NMR (400 MHz, CDCl_3) of compound **4aab**:



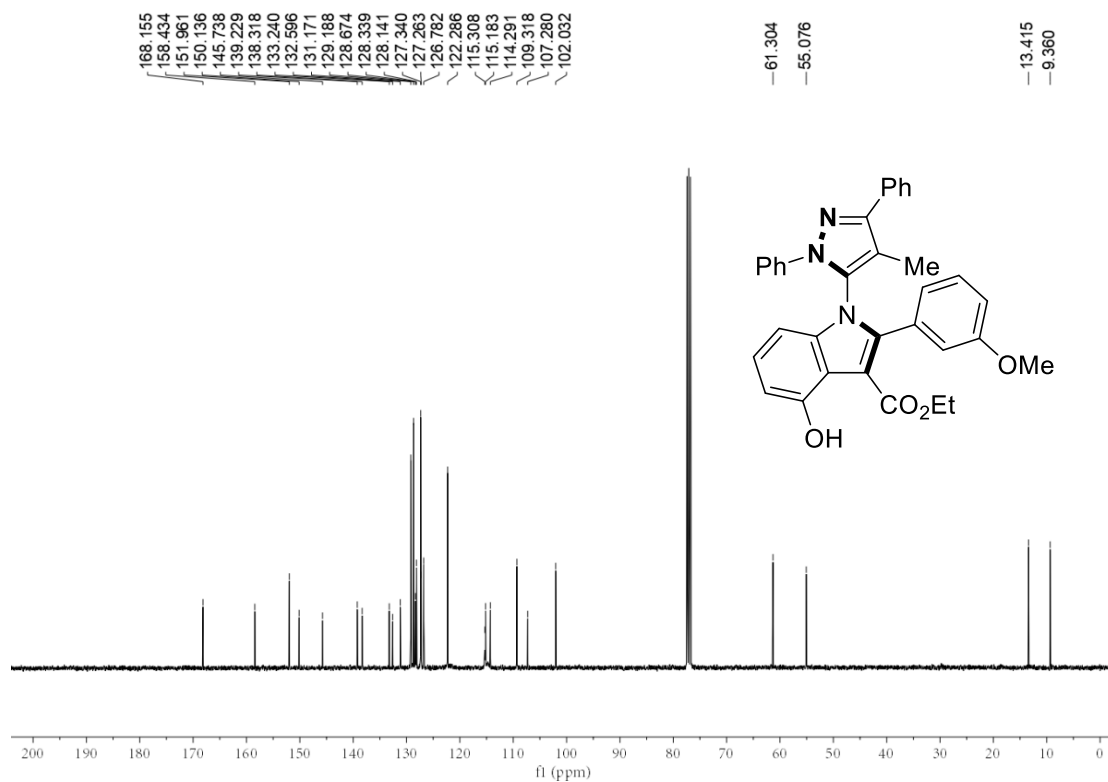
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aab**:



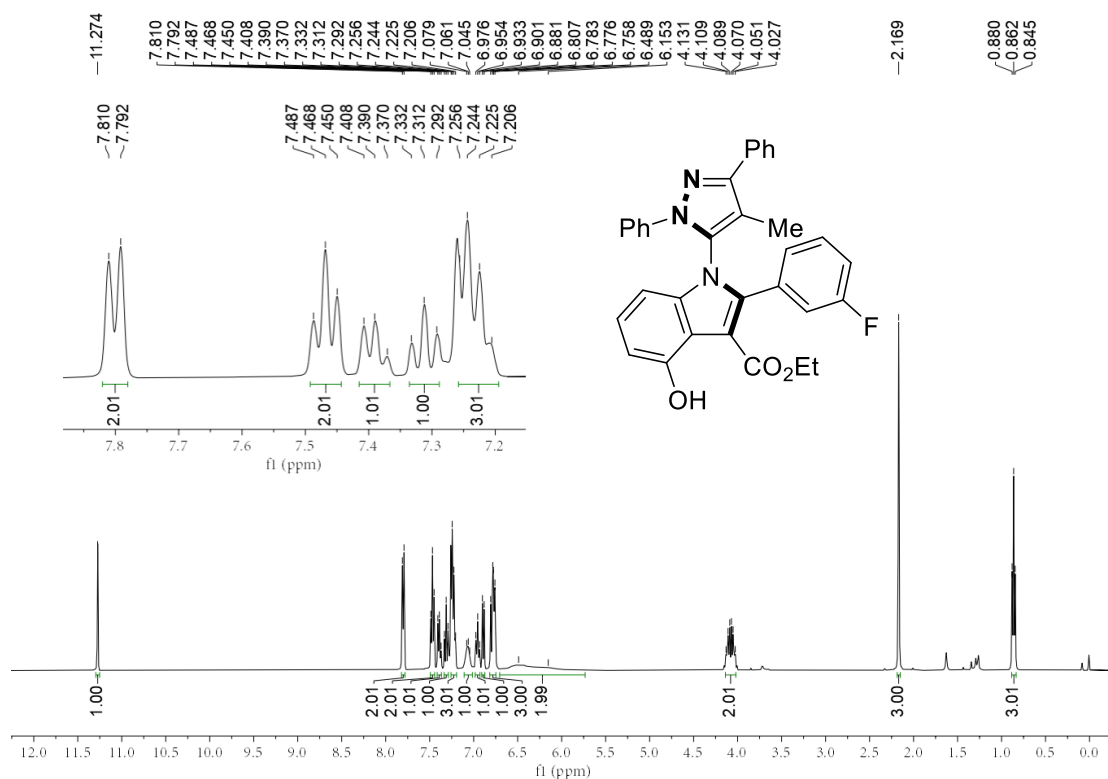
^1H NMR (400 MHz, CDCl_3) of compound **4aac**:



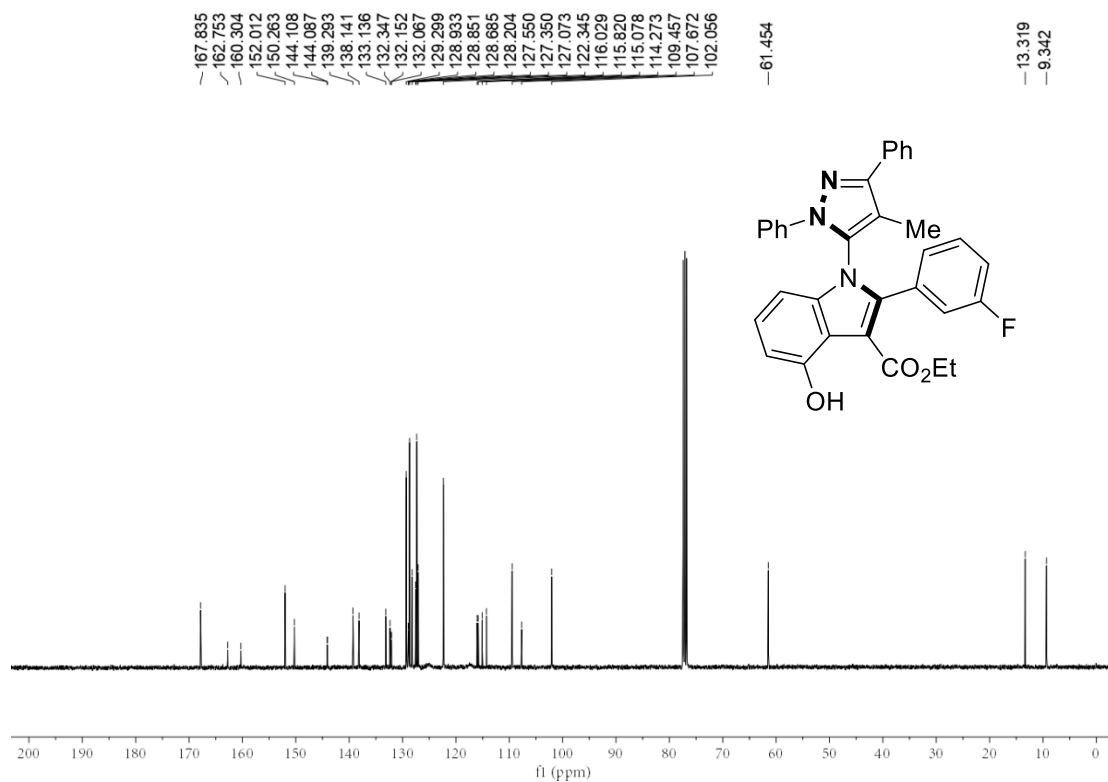
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aac**:



^1H NMR (400 MHz, CDCl_3) of compound **4aad**:

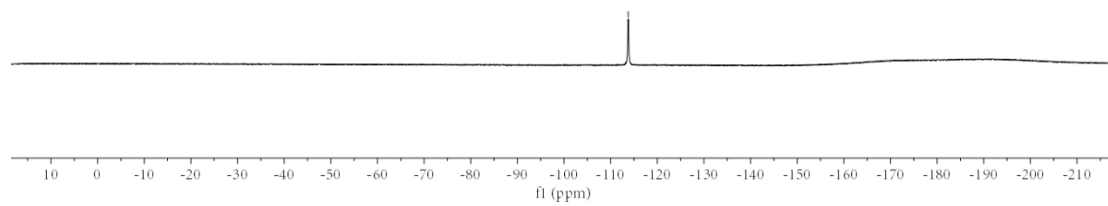
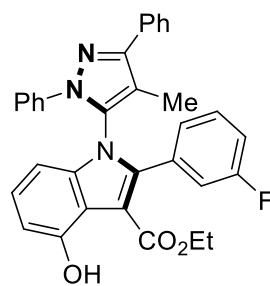


$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aad**:

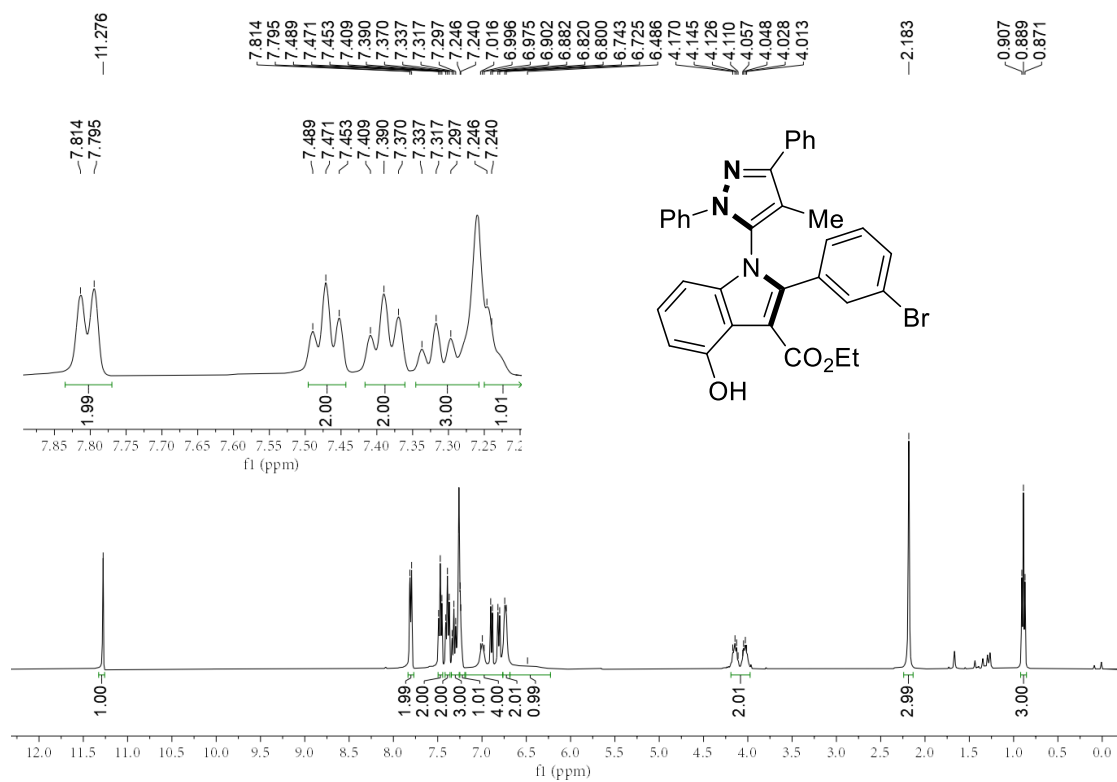


^{19}F NMR (376 MHz, CDCl_3) of compound **4aad**:

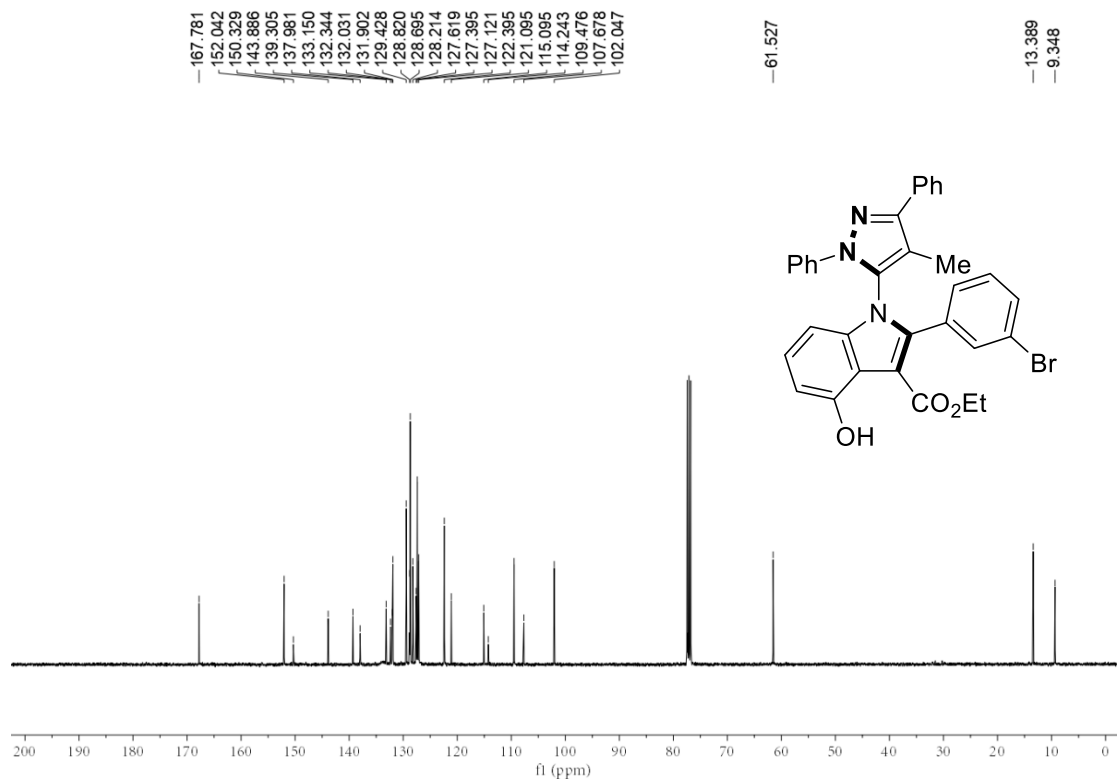
—113.769



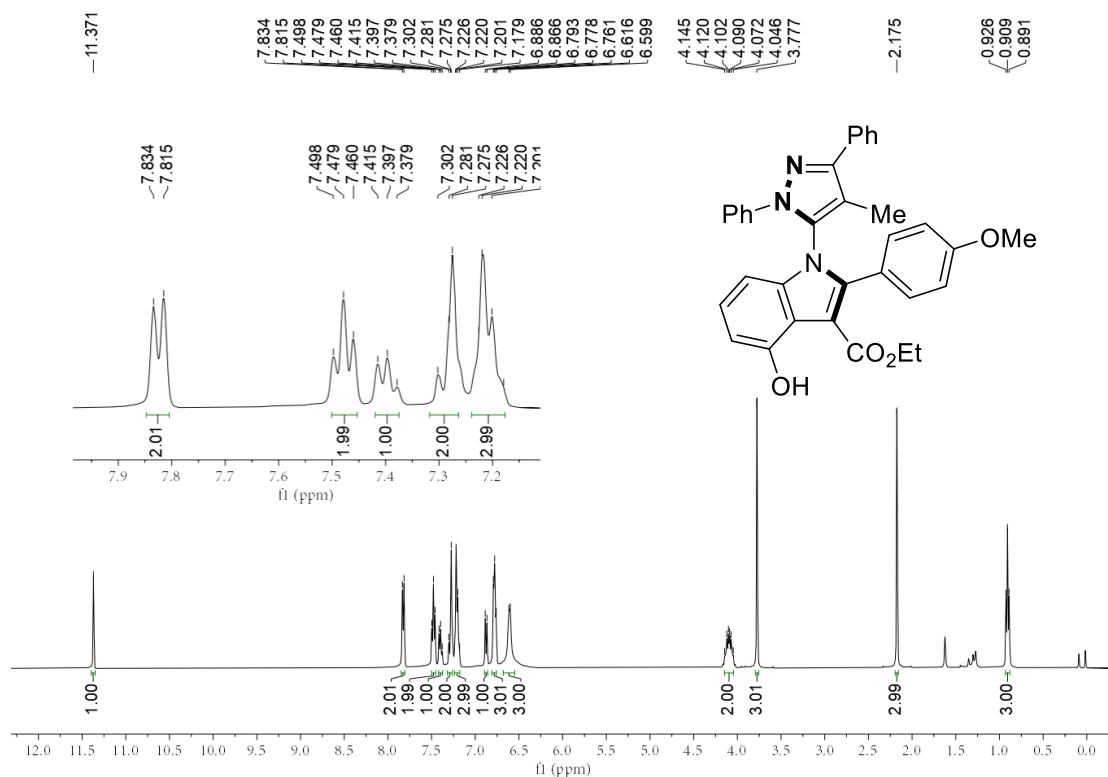
^1H NMR (400 MHz, CDCl_3) of compound **4aae**:



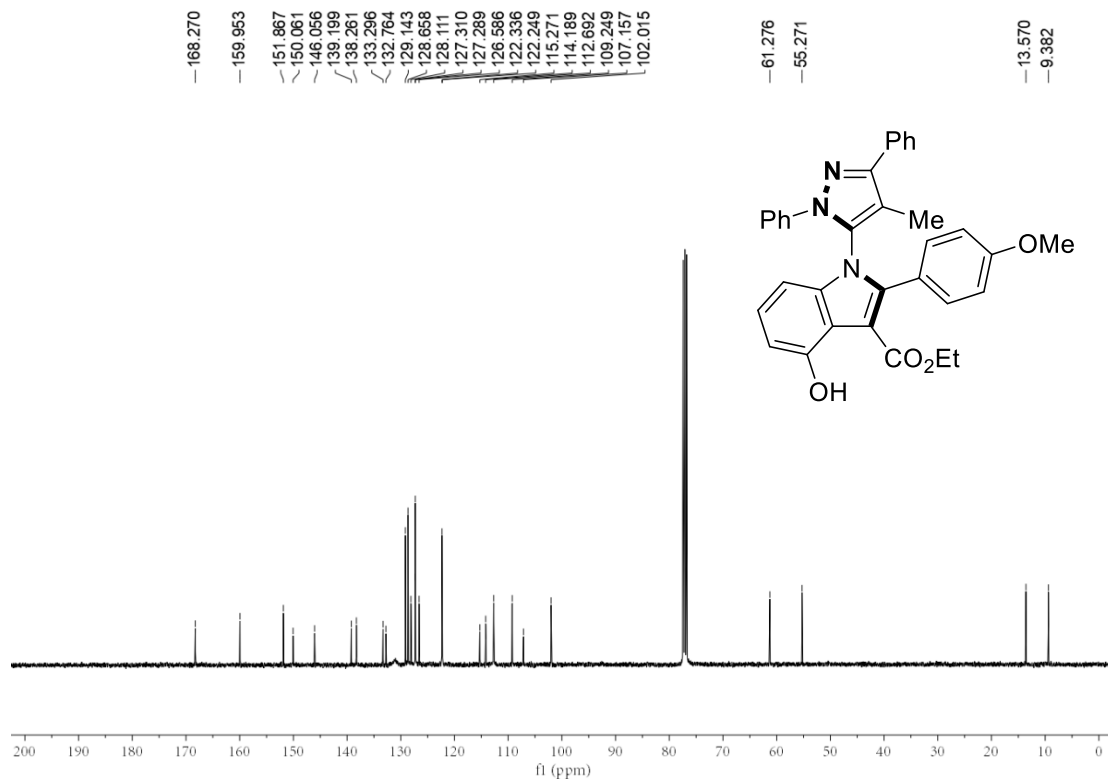
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aae**:



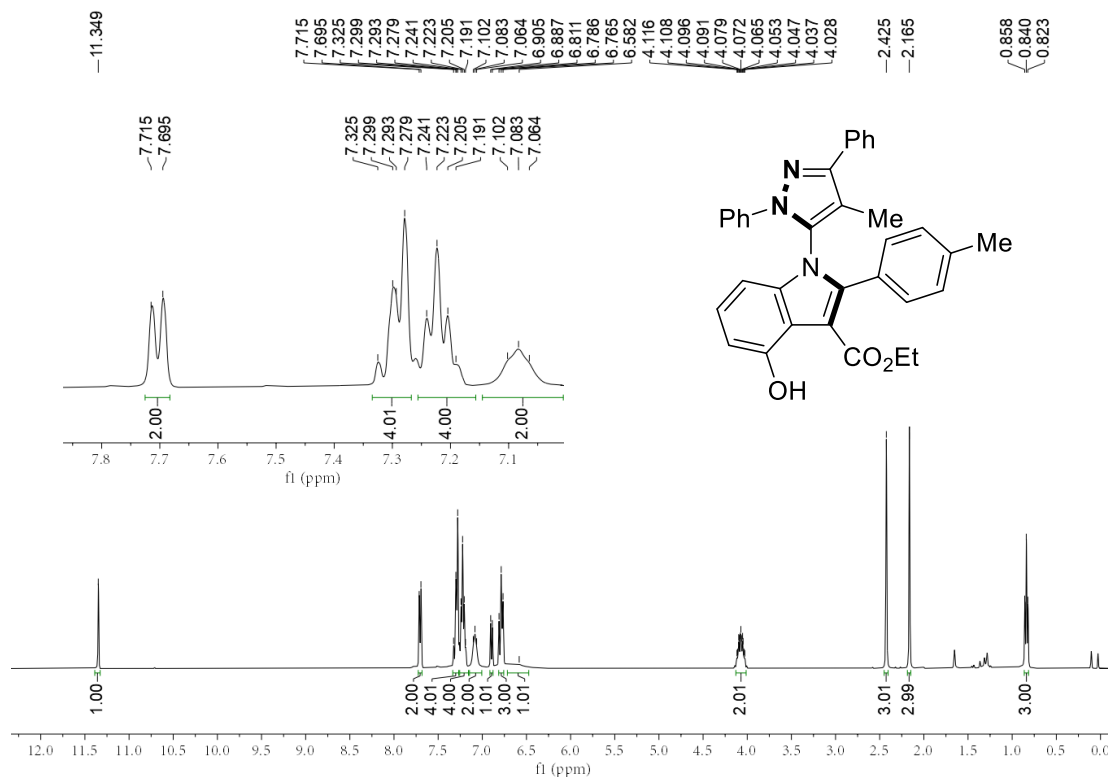
^1H NMR (400 MHz, CDCl_3) of compound **4aaf**:



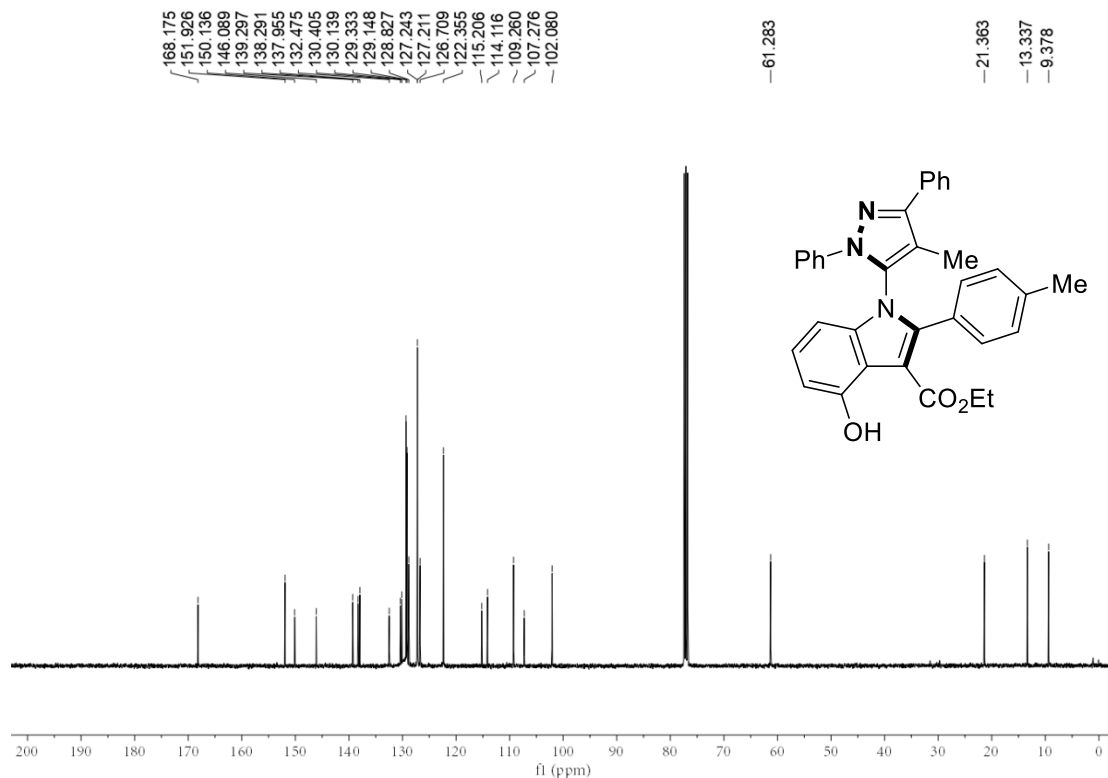
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aaf**:



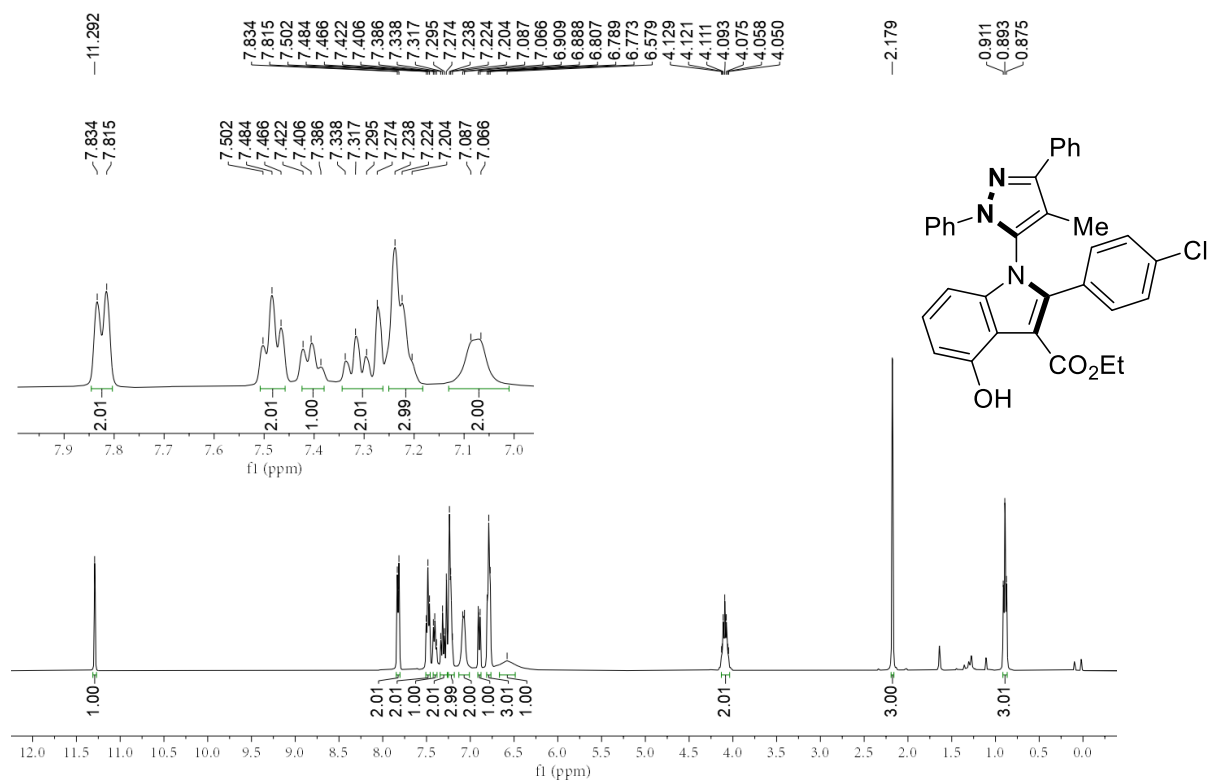
^1H NMR (400 MHz, CDCl_3) of compound **4aag**:



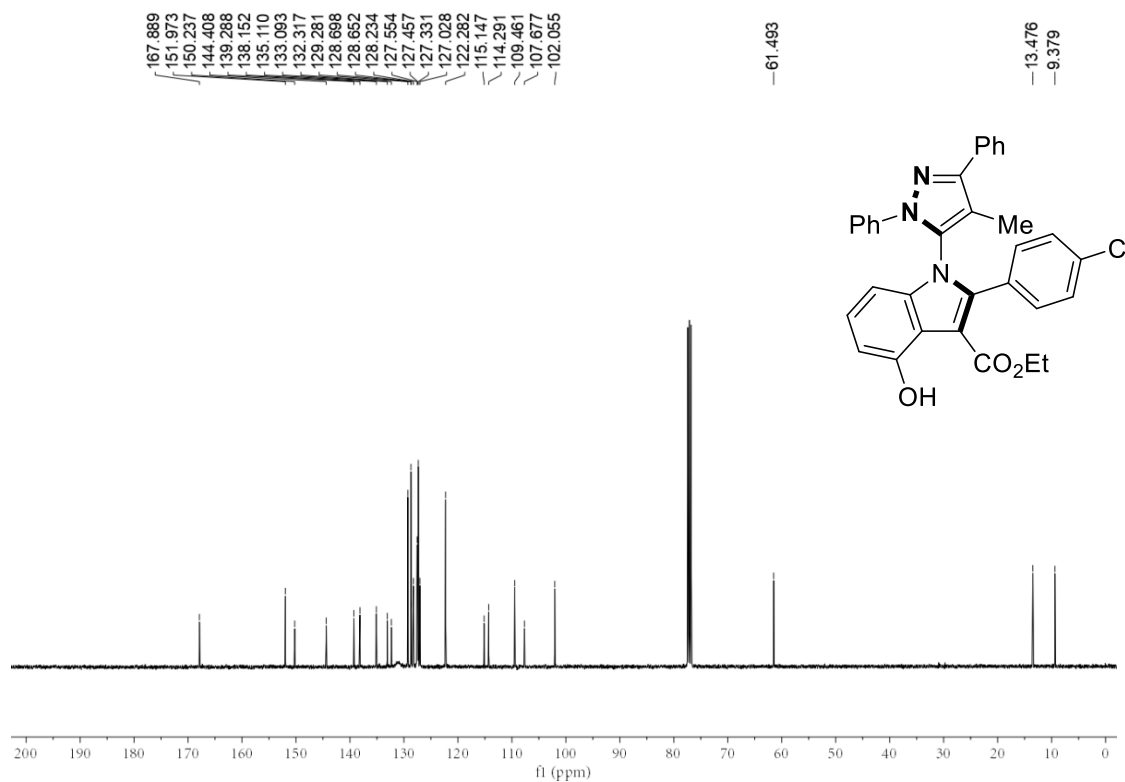
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aag**:



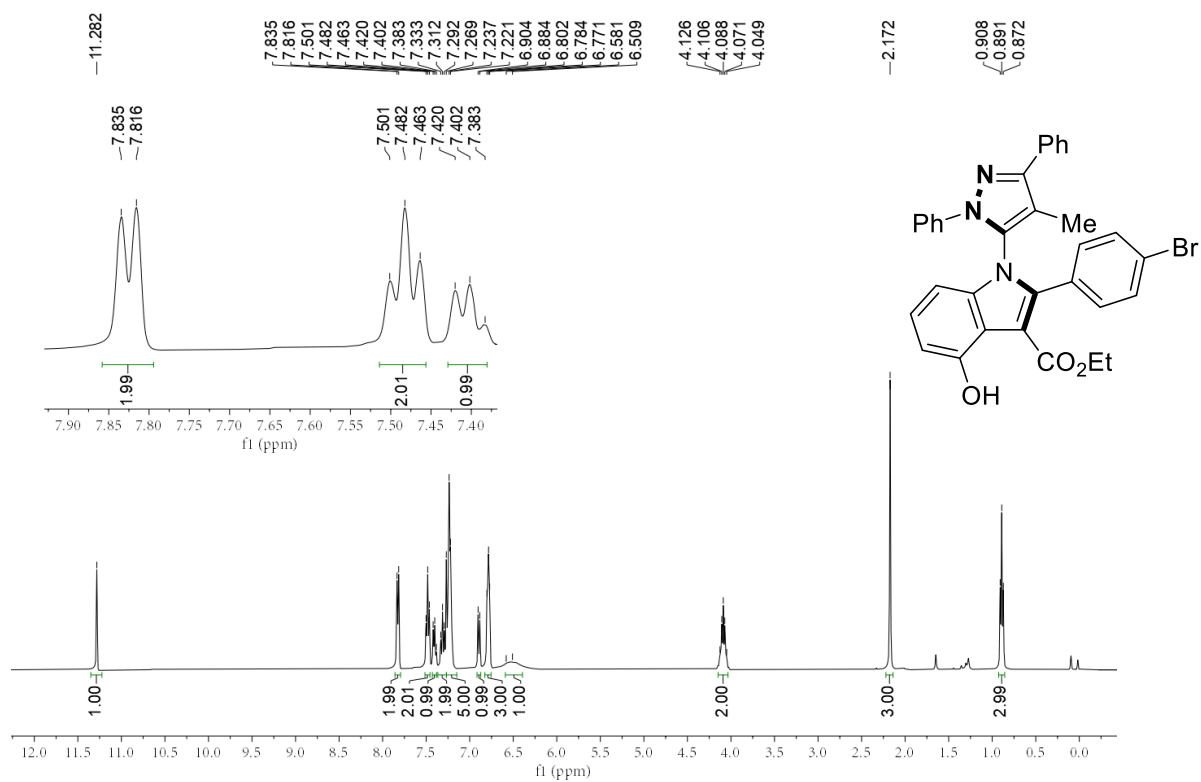
^1H NMR (400 MHz, CDCl_3) of compound **4aah**:



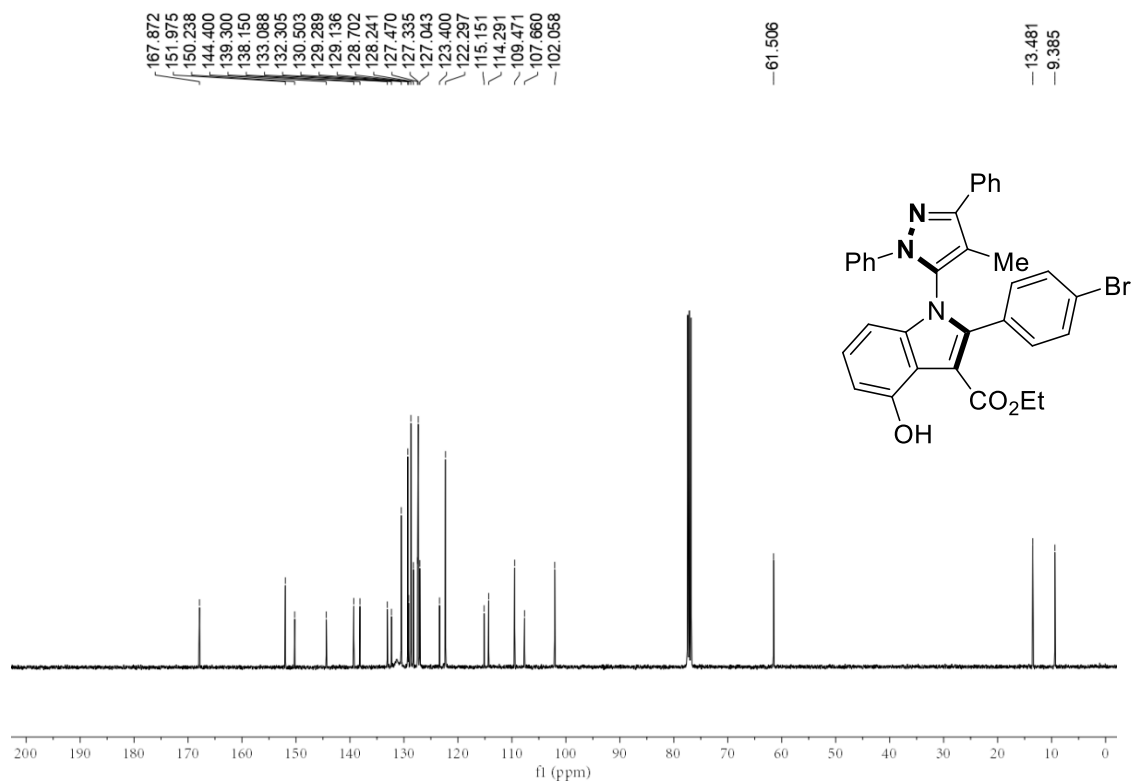
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aah**:



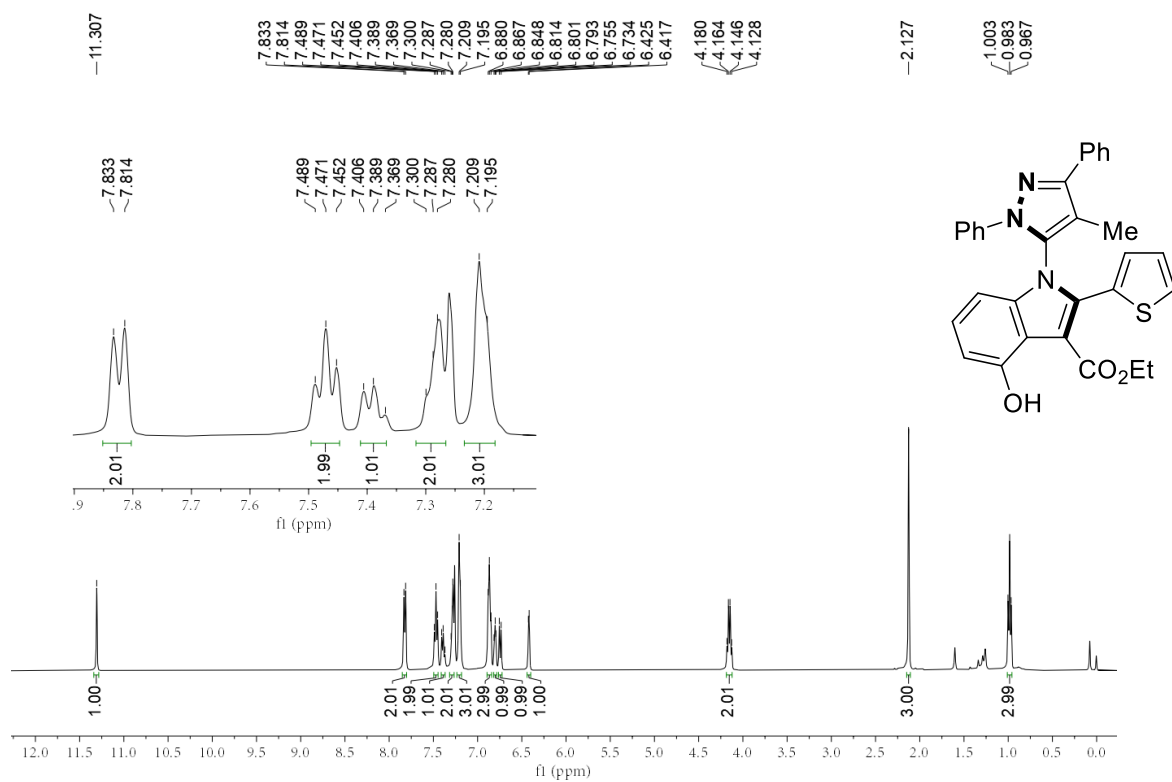
^1H NMR (400 MHz, CDCl_3) of compound **4aai**:



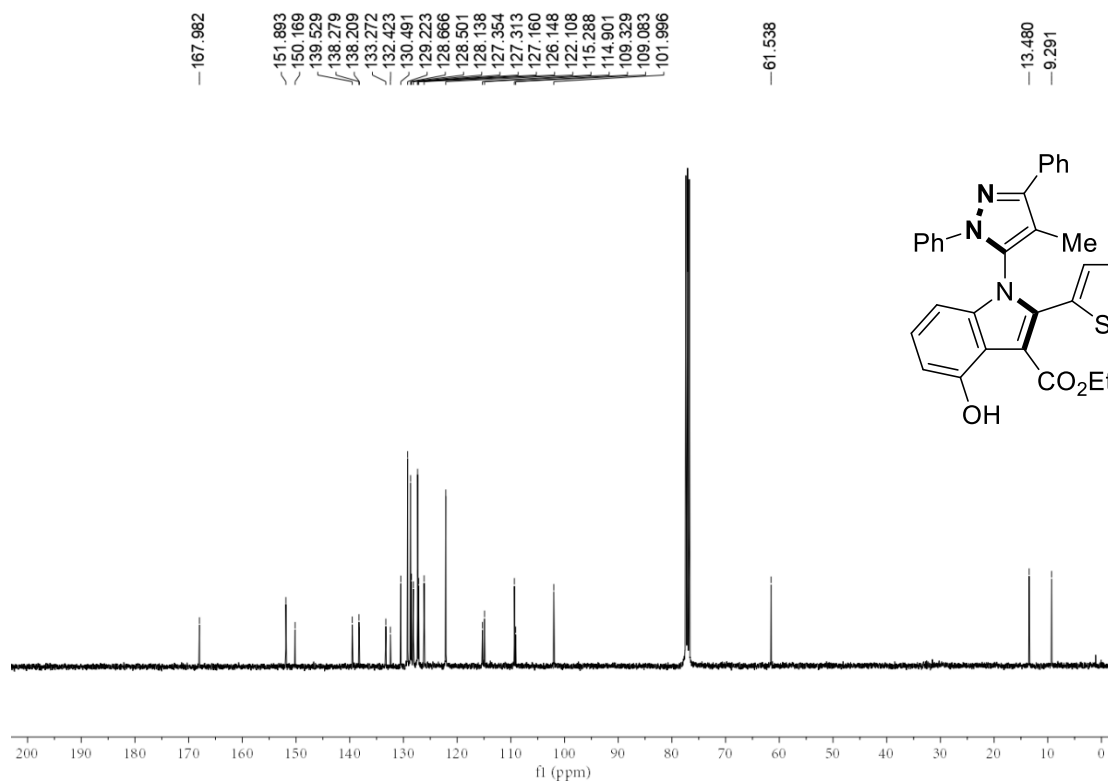
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aai**:



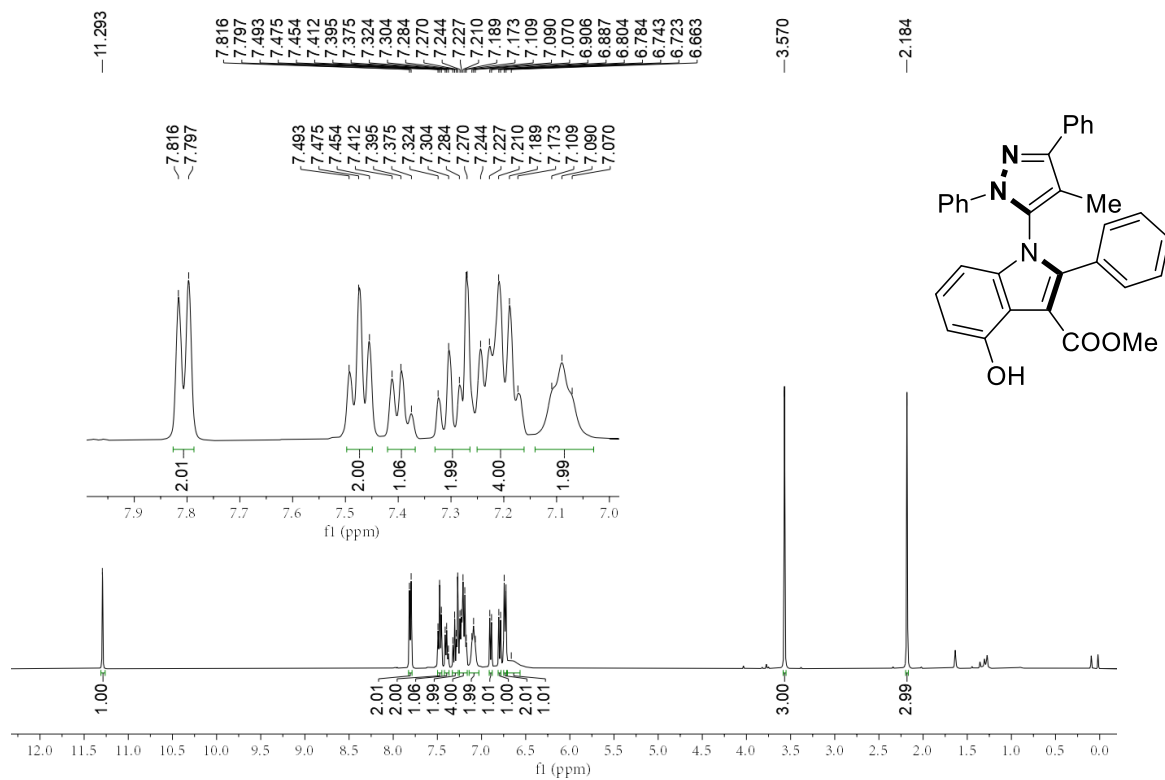
^1H NMR (400 MHz, CDCl_3) of compound **4aaj**:



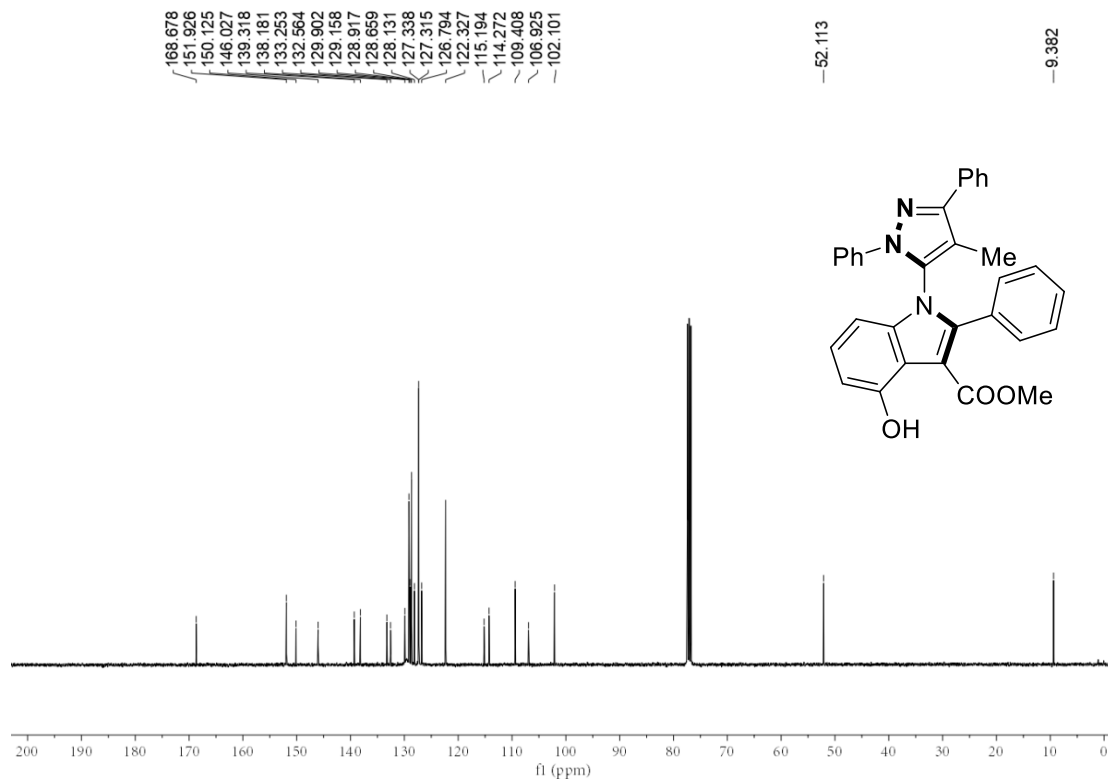
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aaj**:



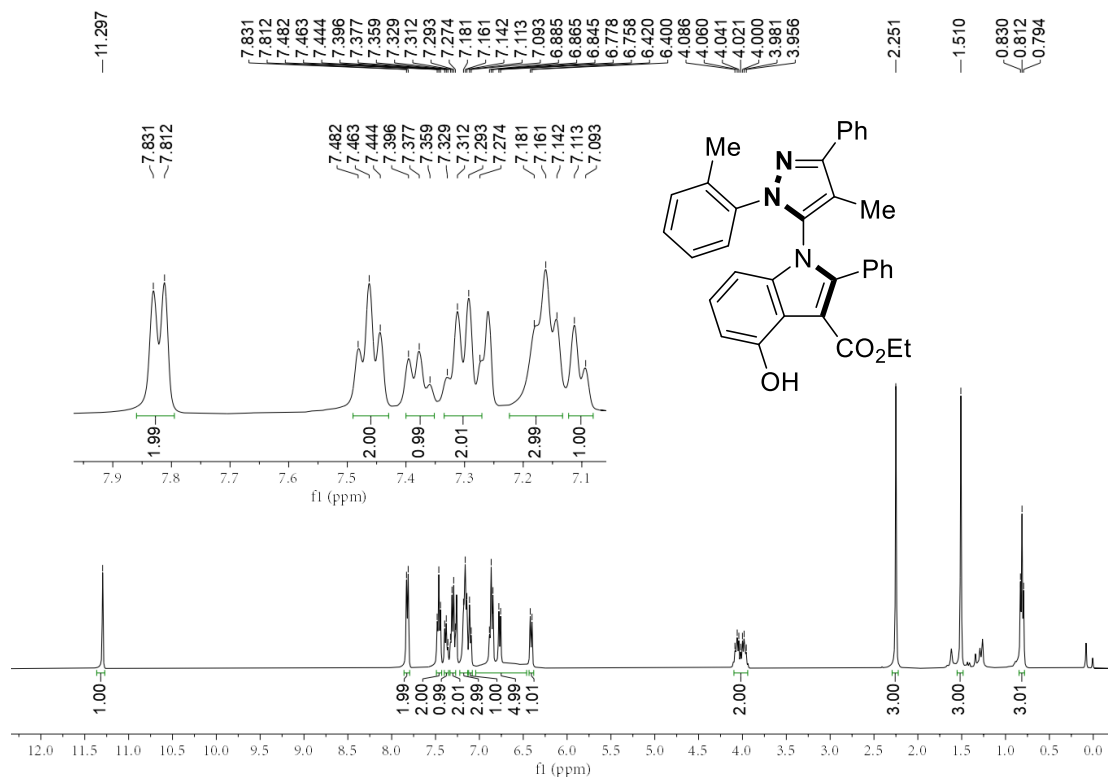
^1H NMR (400 MHz, CDCl_3) of compound **4aak**:



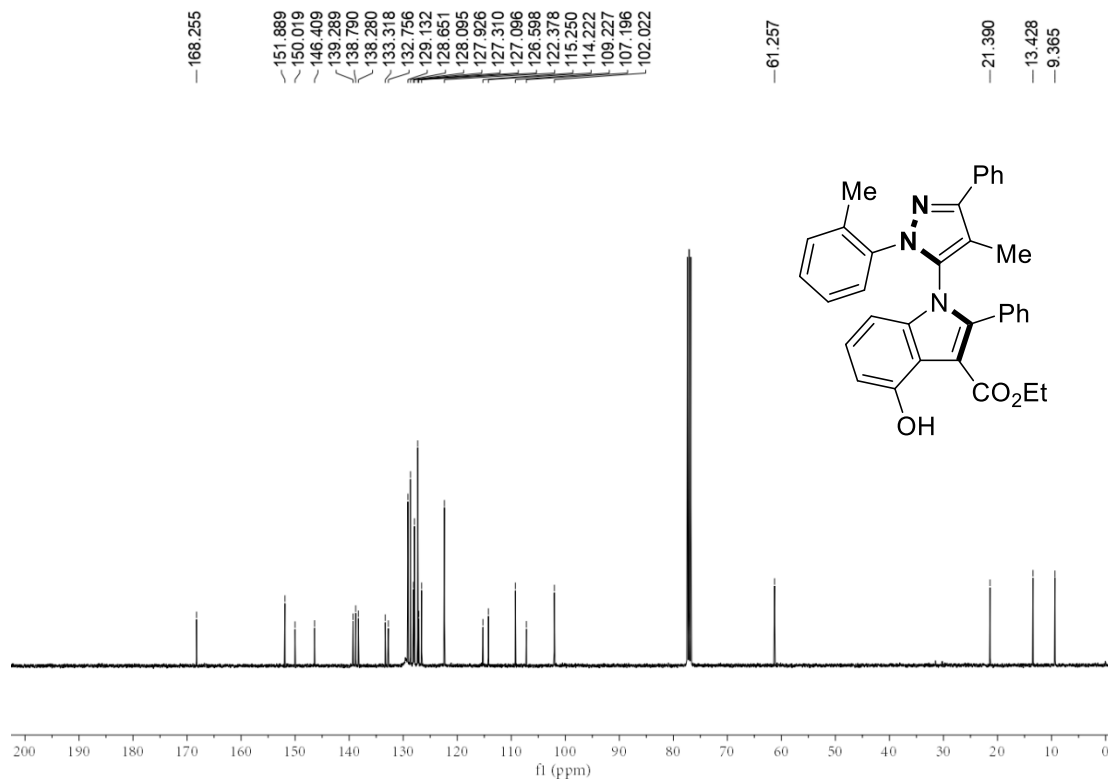
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4aak**:



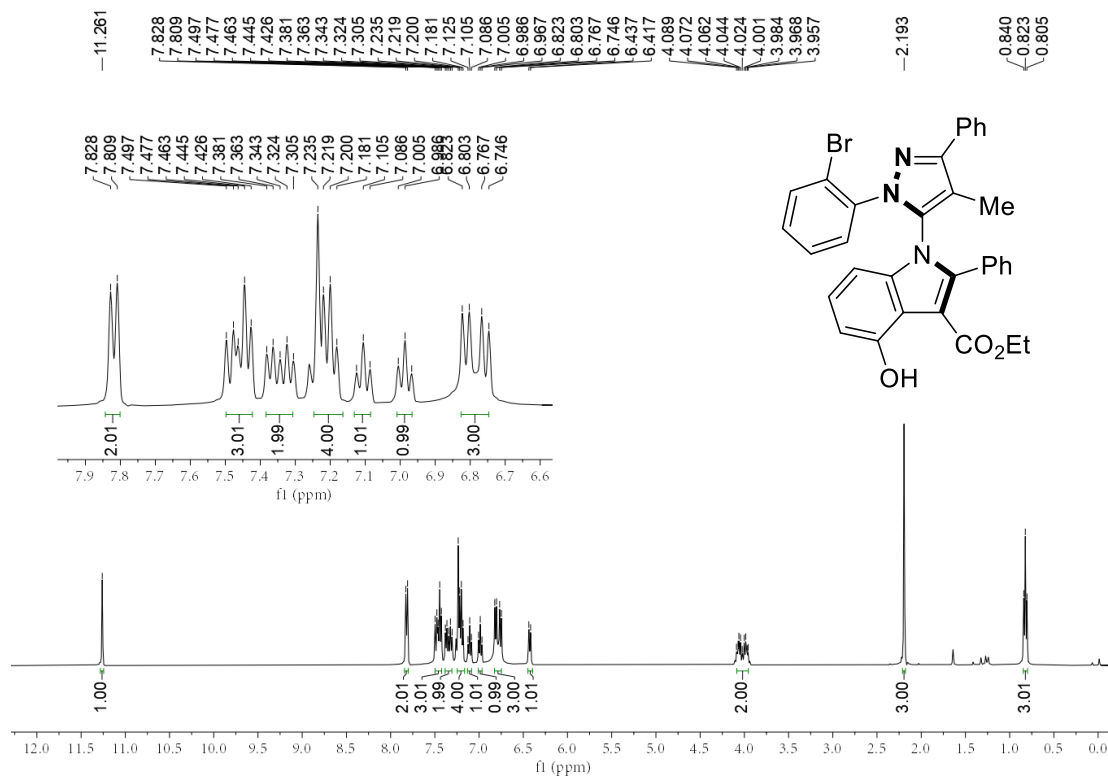
^1H NMR (400 MHz, CDCl_3) of compound **4bab**:



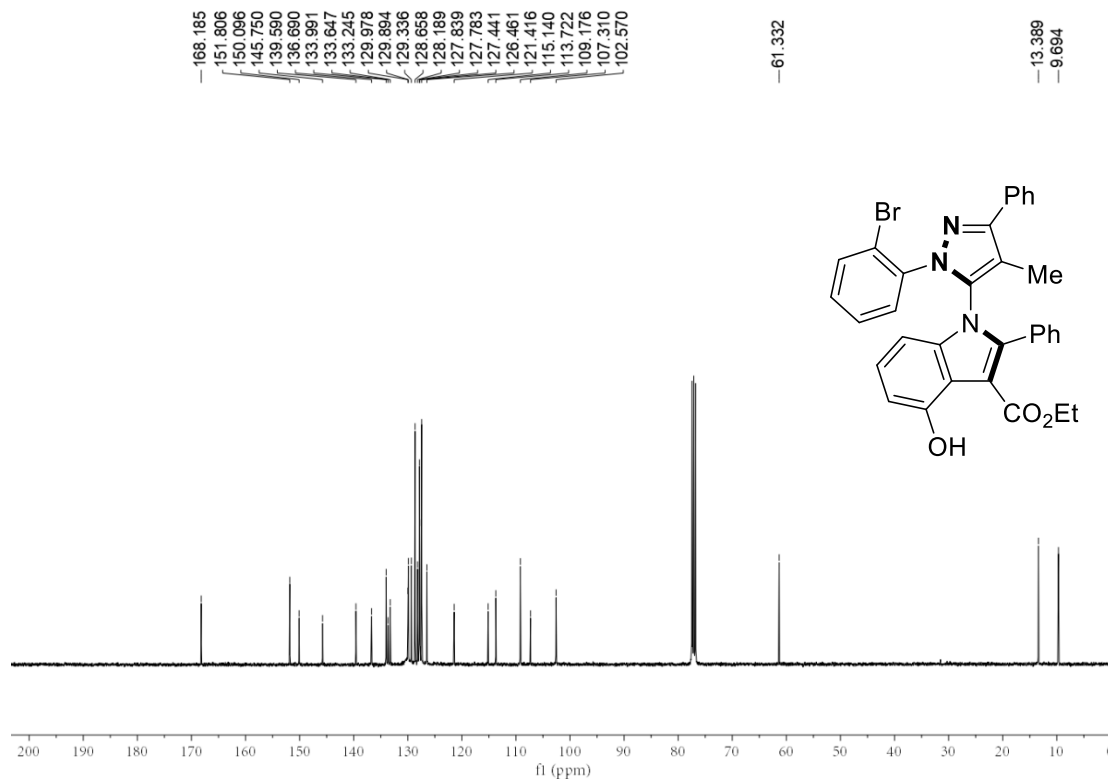
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4bab**:



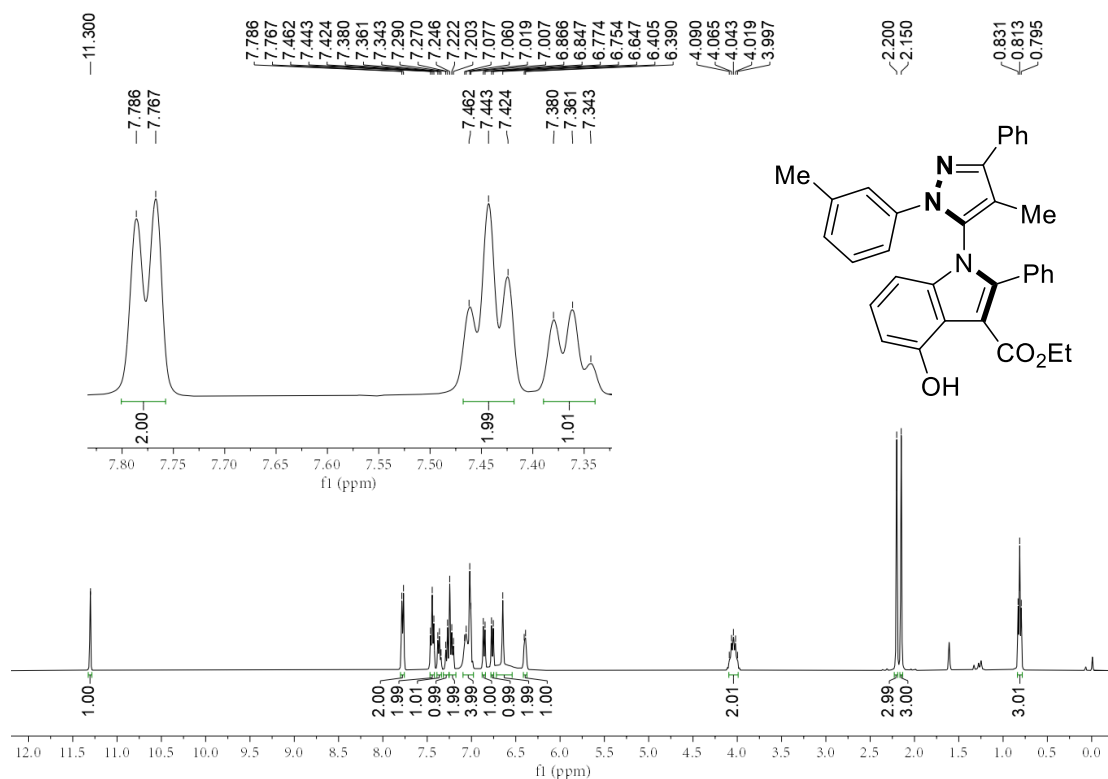
^1H NMR (400 MHz, CDCl_3) of compound **4cab**:



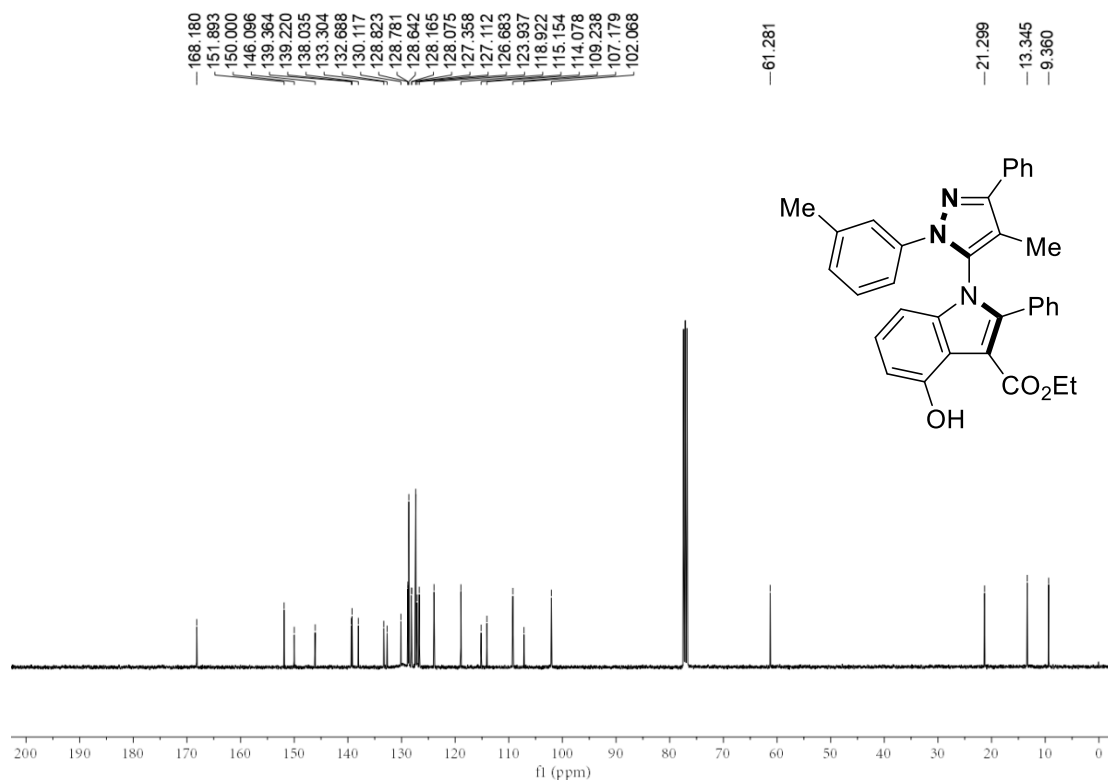
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4cab**:



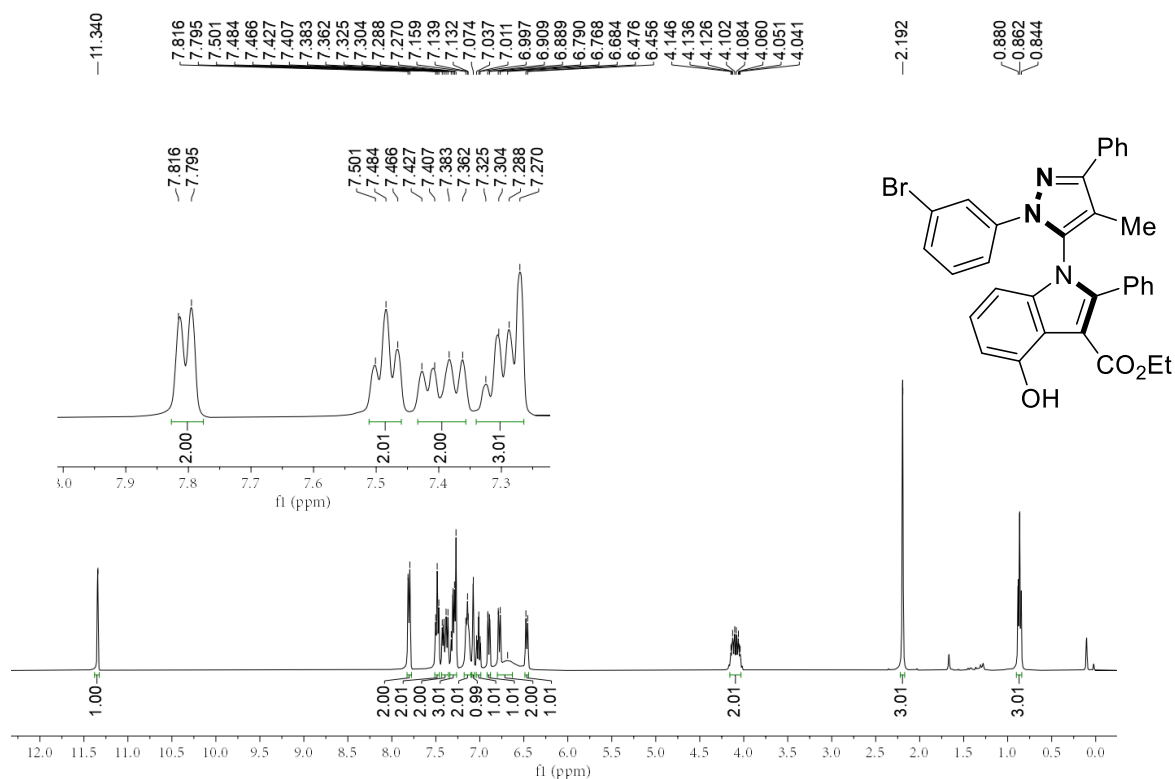
^1H NMR (400 MHz, CDCl_3) of compound **4dab**:



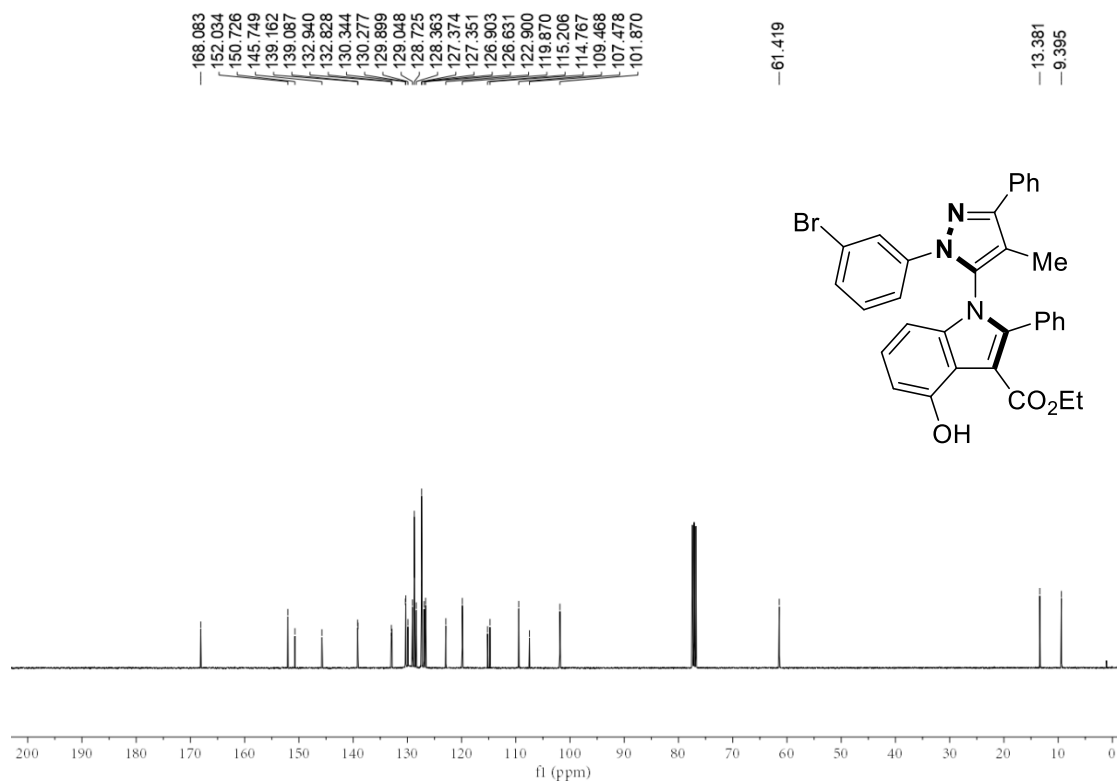
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4dab**:



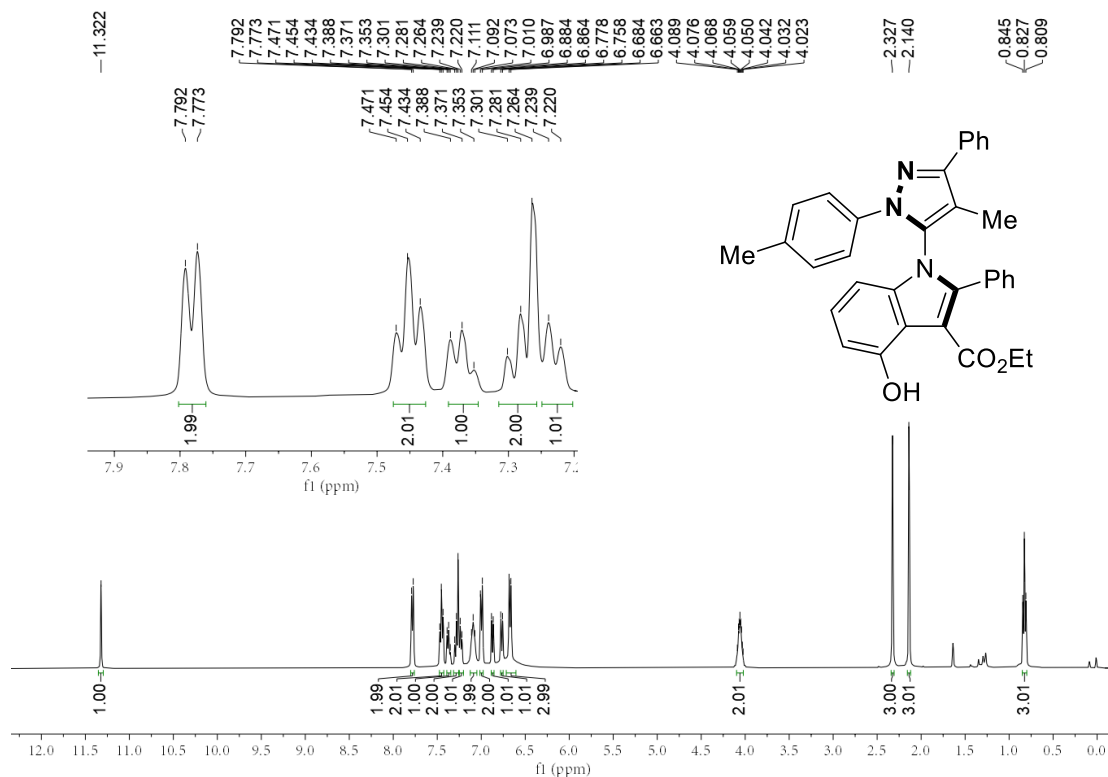
^1H NMR (400 MHz, CDCl_3) of compound **4eab**:



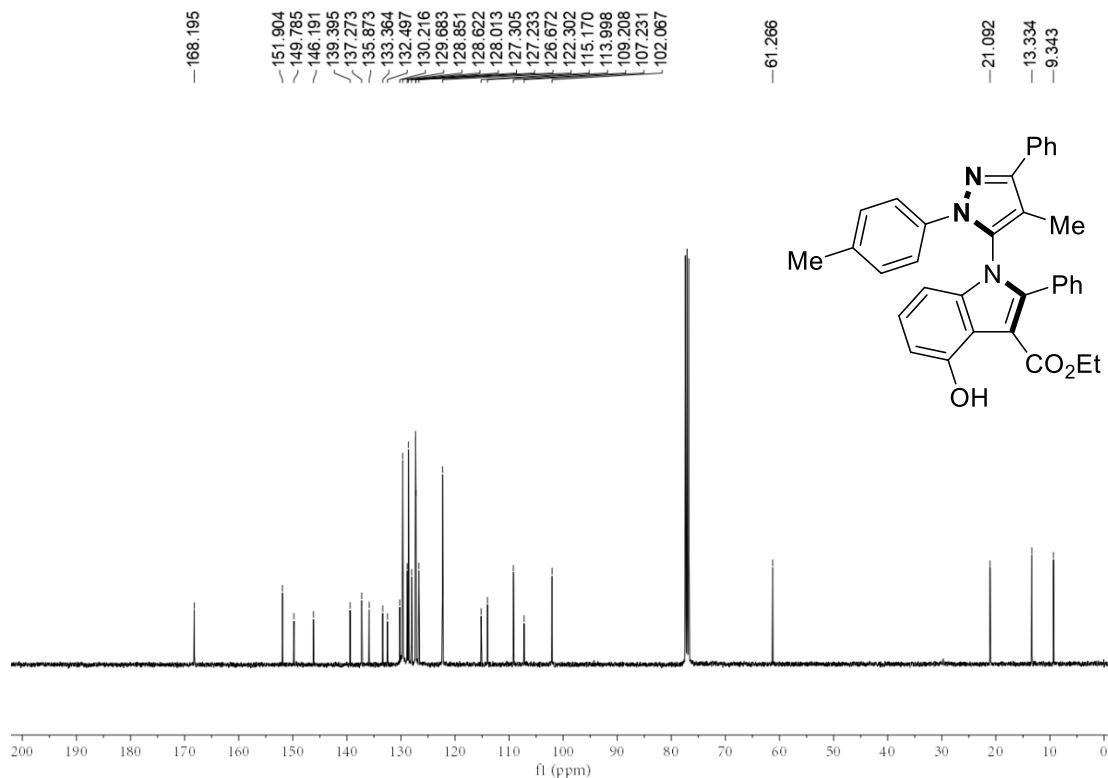
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4eab**:



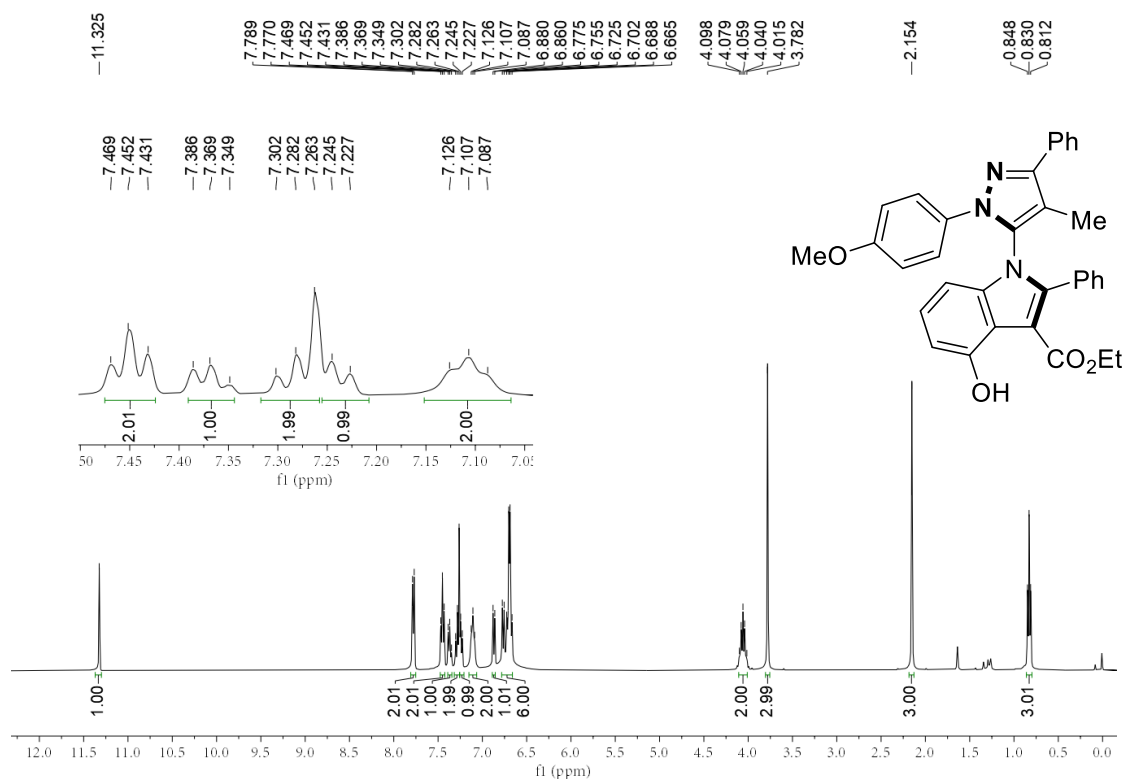
^1H NMR (400 MHz, CDCl_3) of compound **4fab**:



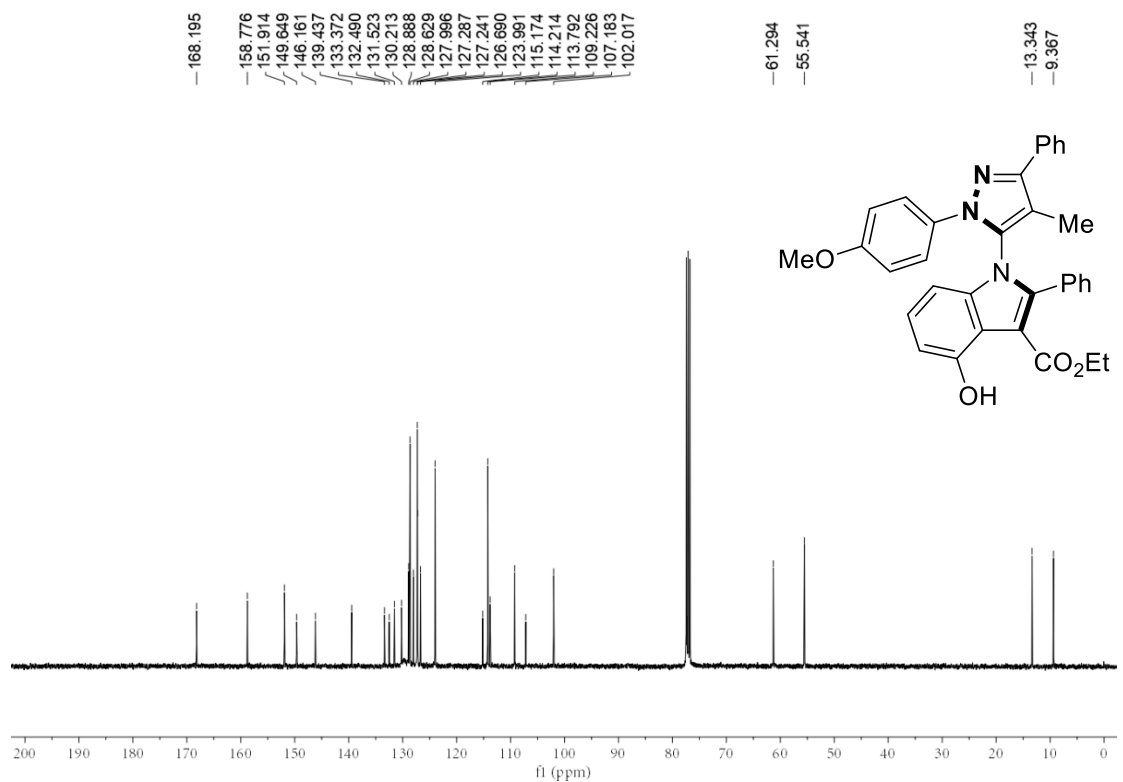
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4fab**:



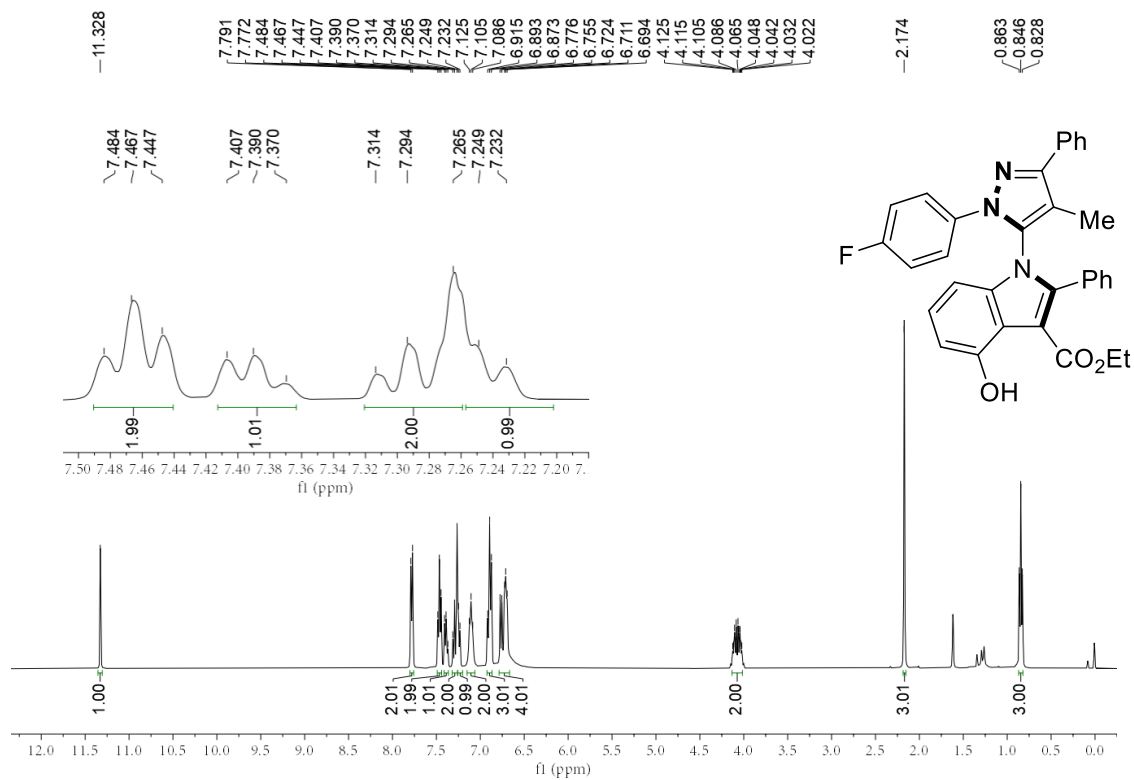
^1H NMR (400 MHz, CDCl_3) of compound **4gab**:



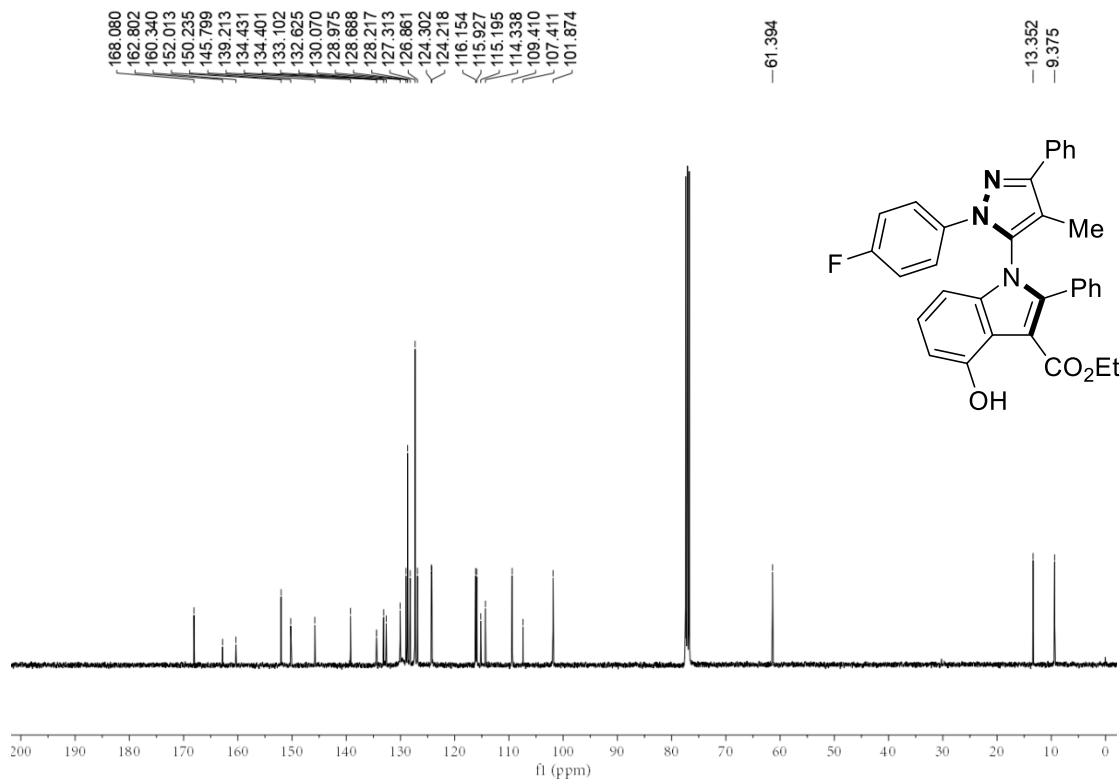
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4gab**:



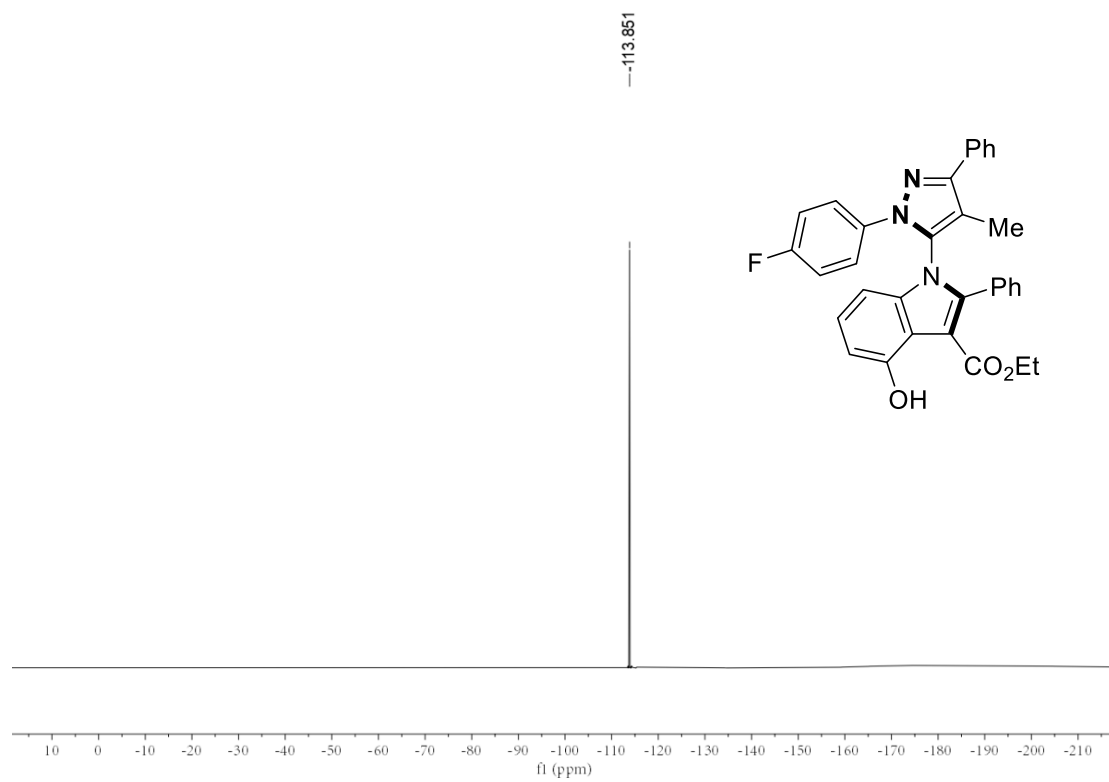
^1H NMR (400 MHz, CDCl_3) of compound **4hab**:



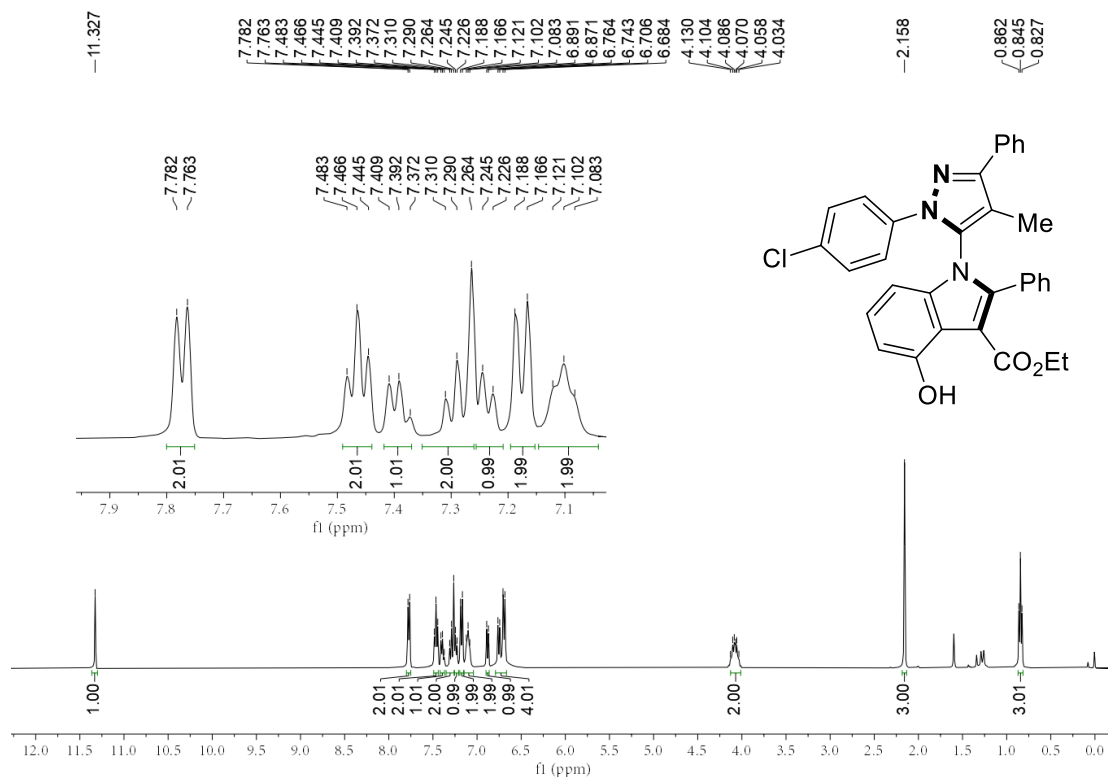
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4hab**:



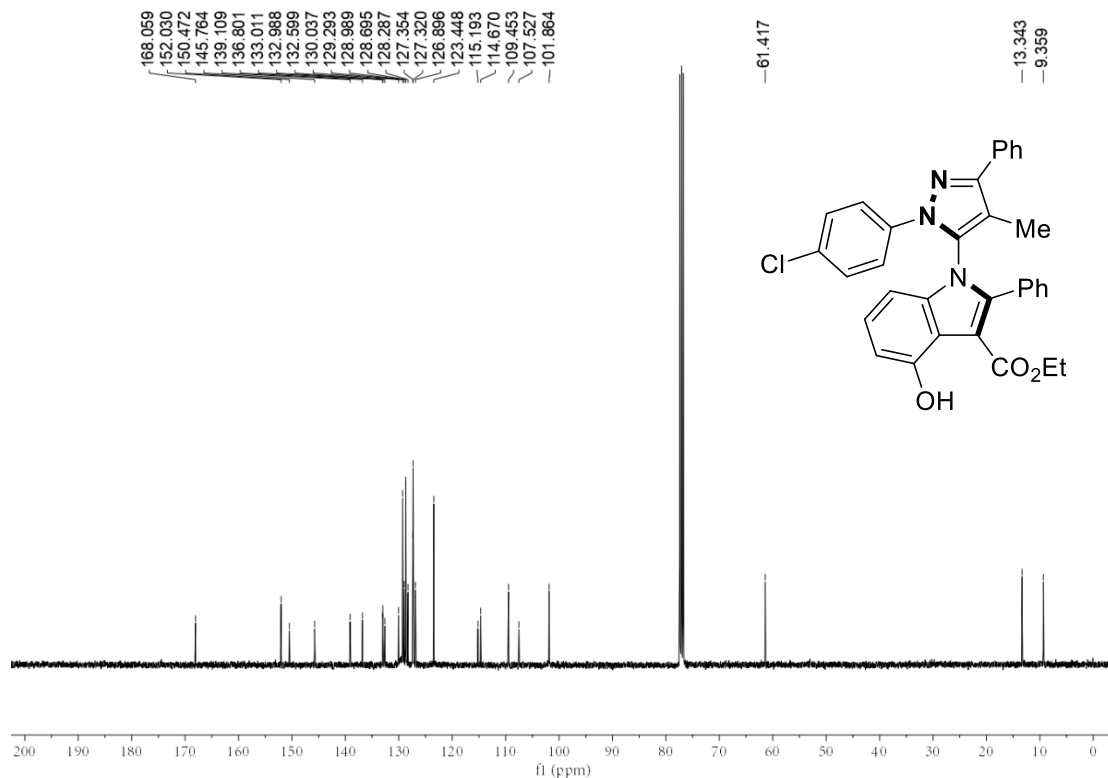
^{19}F NMR (376 MHz, CDCl_3) of compound **4hab**:



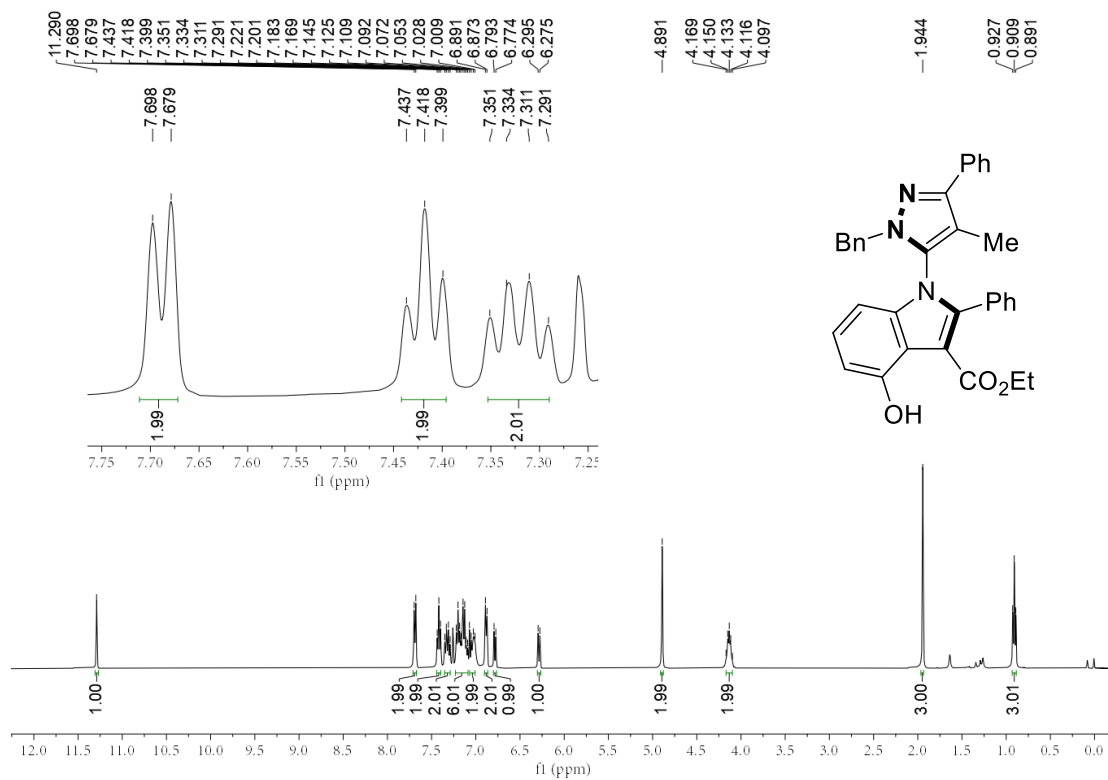
^1H NMR (400 MHz, CDCl_3) of compound **4iab**:



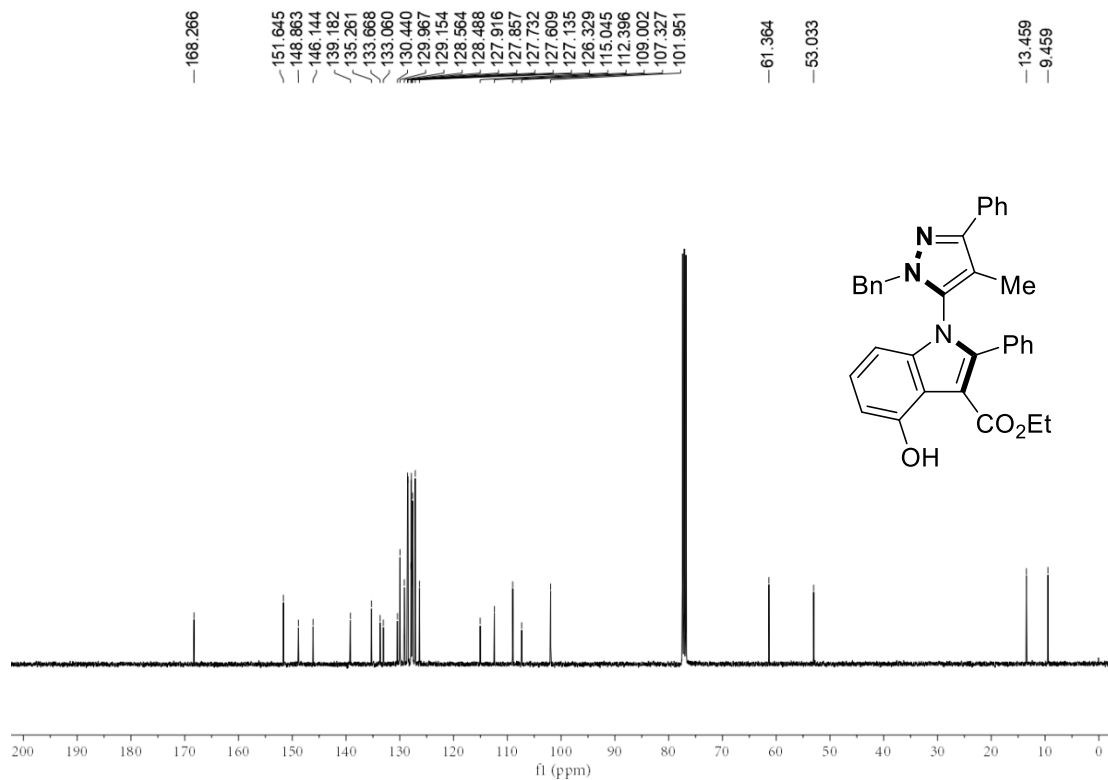
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4iab**:



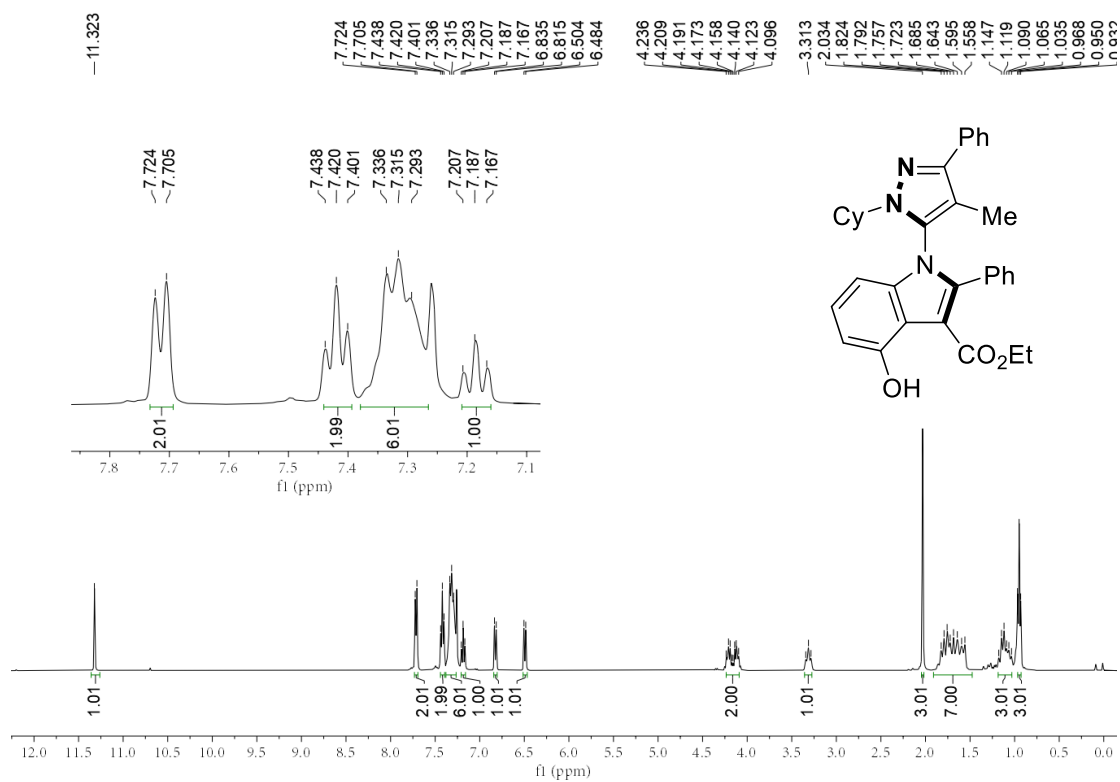
^1H NMR (400 MHz, CDCl_3) of compound **4jab**:



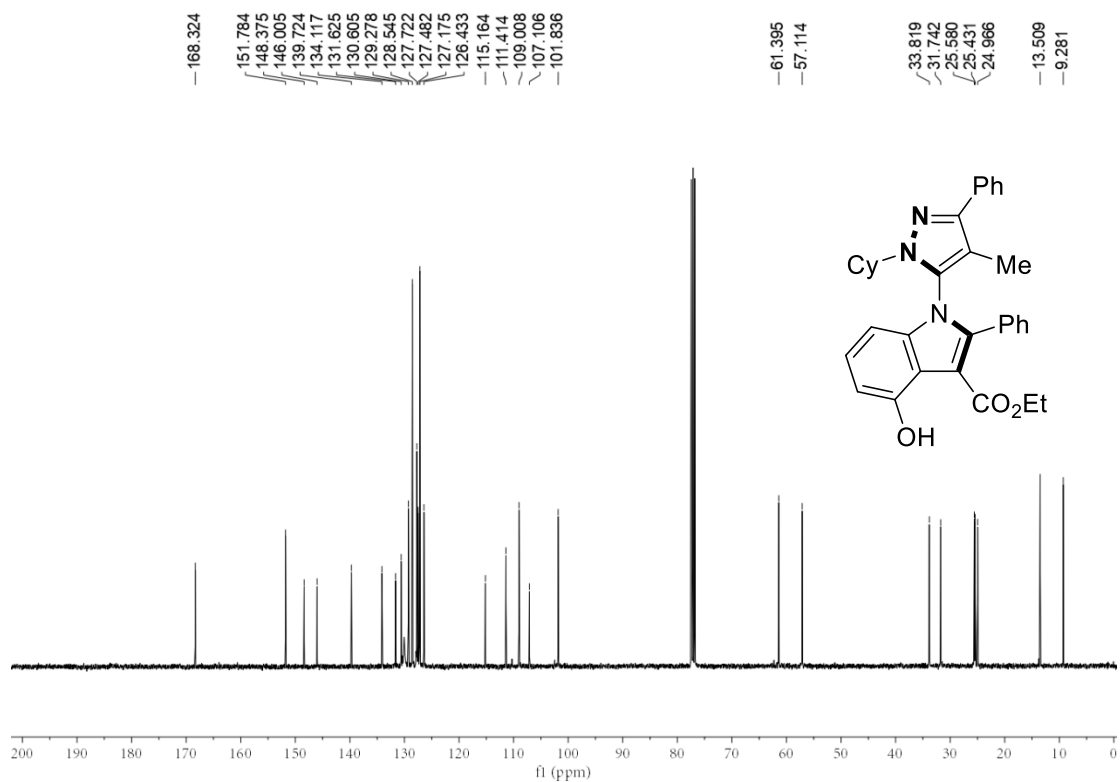
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4jab**:



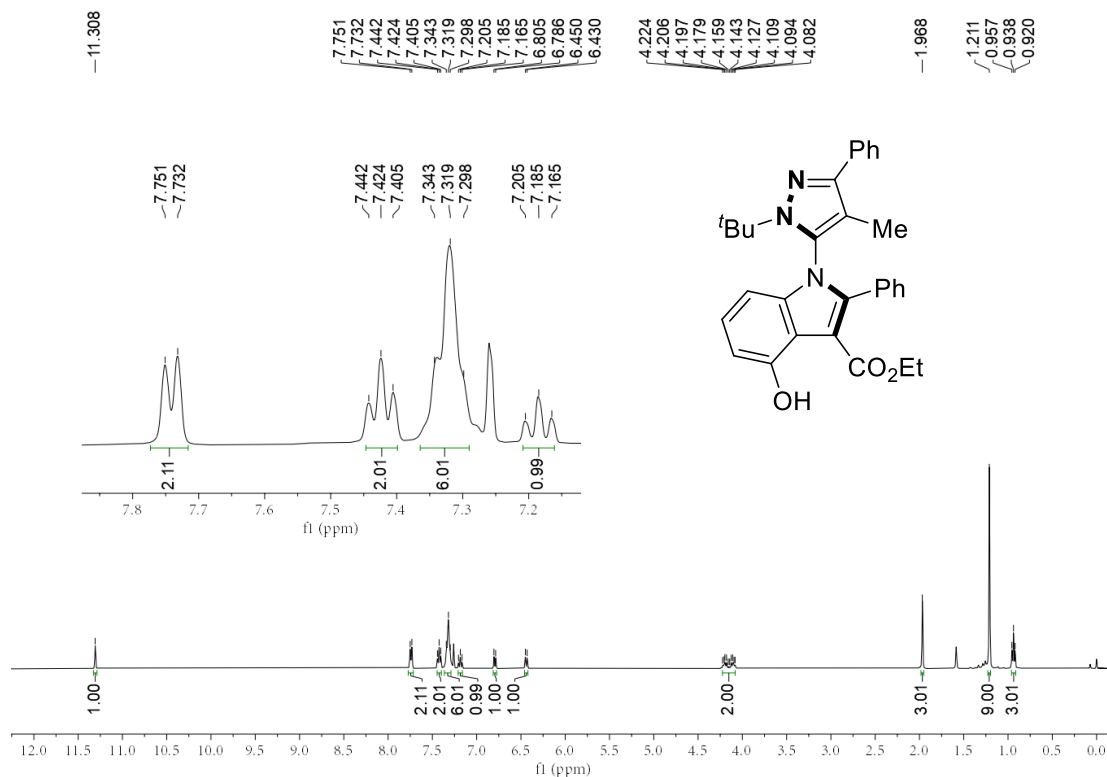
^1H NMR (400 MHz, CDCl_3) of compound **4kab**:



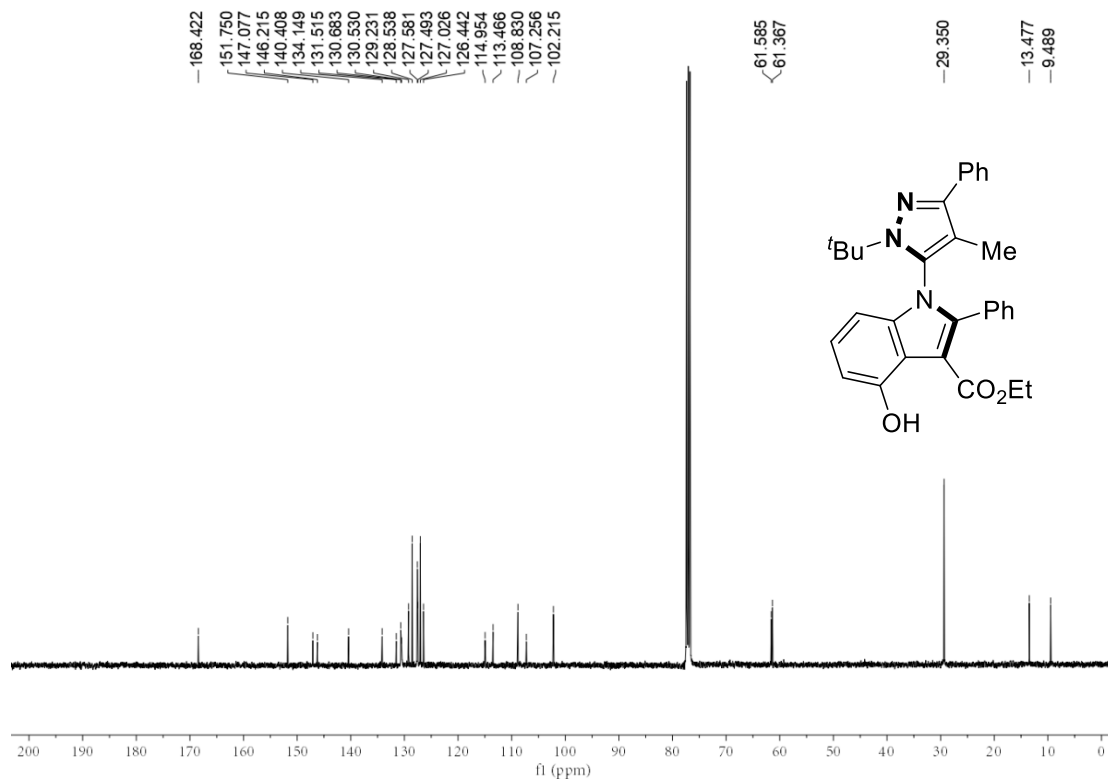
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4kab**:



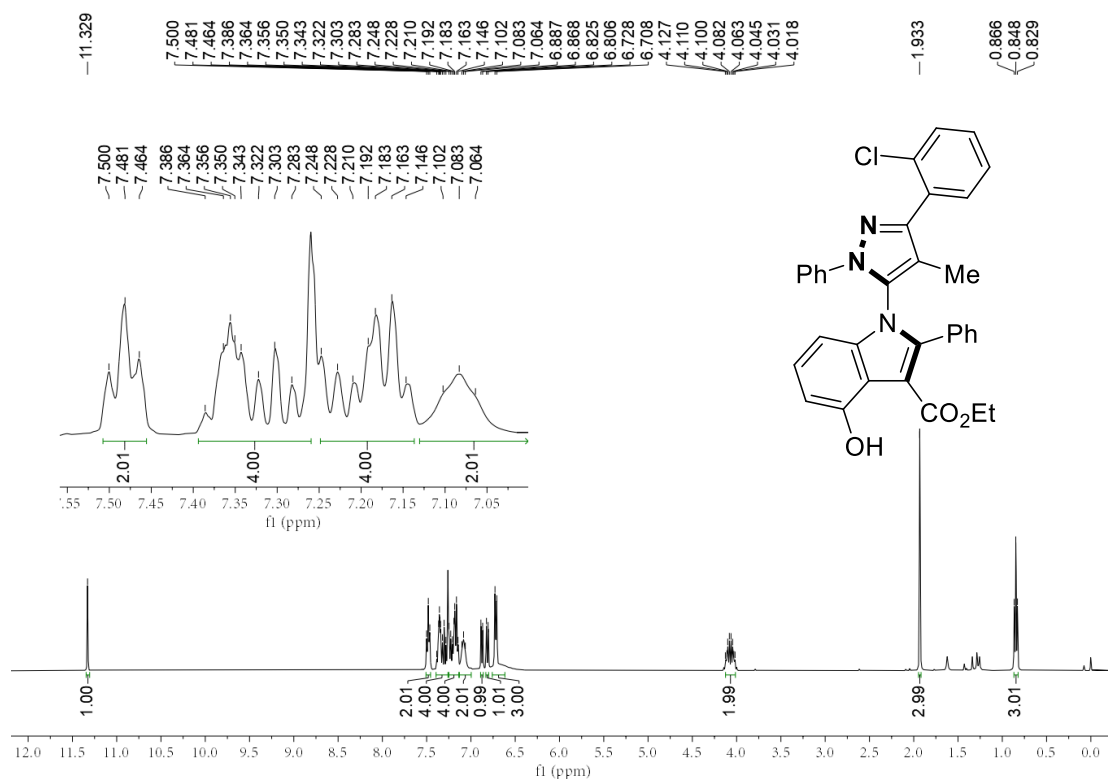
^1H NMR (400 MHz, CDCl_3) of compound **4lab**:



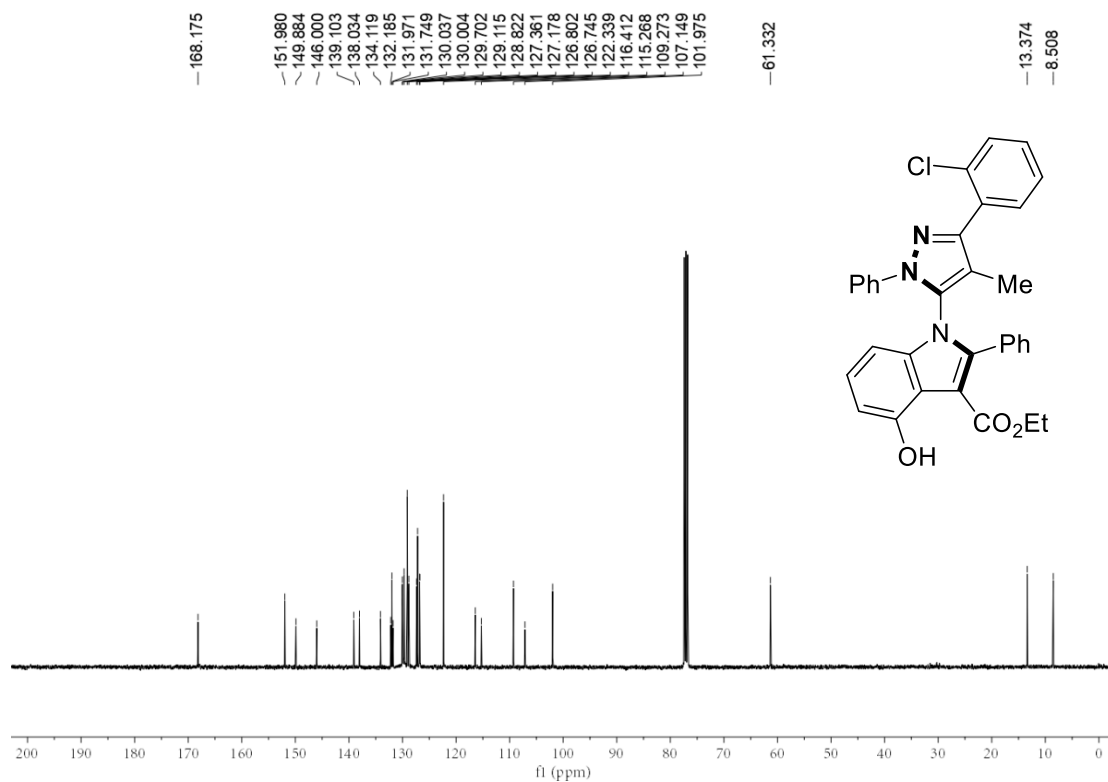
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4lab**:



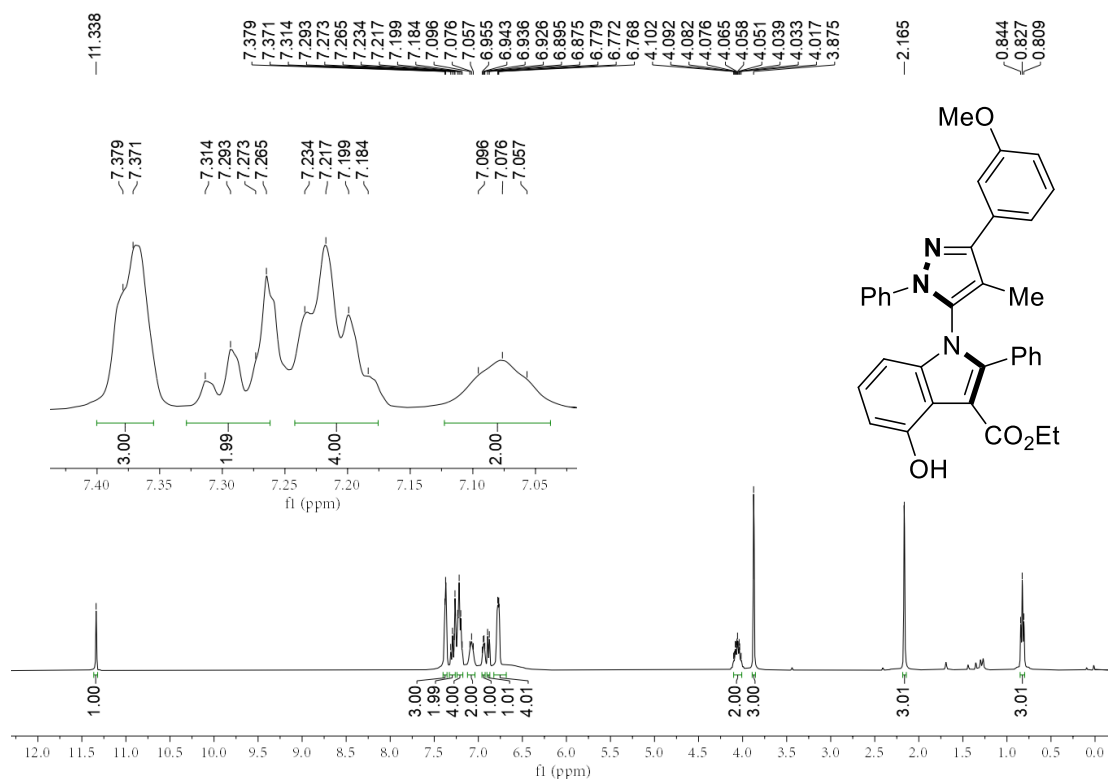
^1H NMR (400 MHz, CDCl_3) of compound **4mab**:



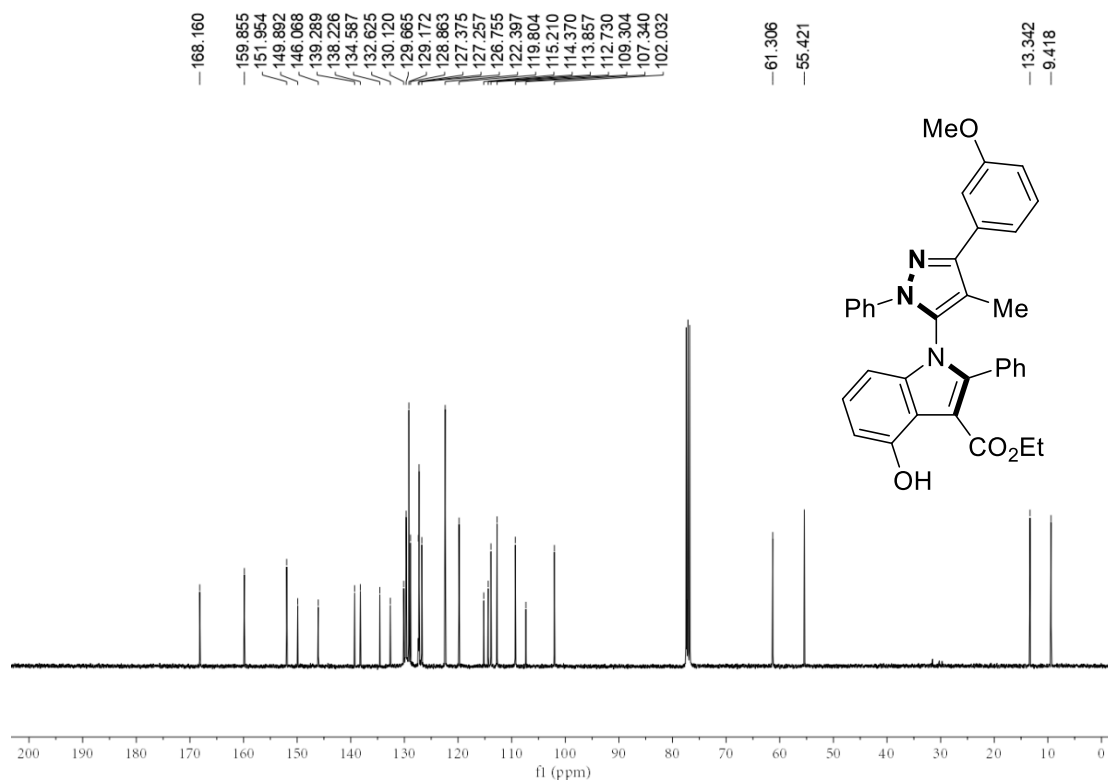
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4mab**:



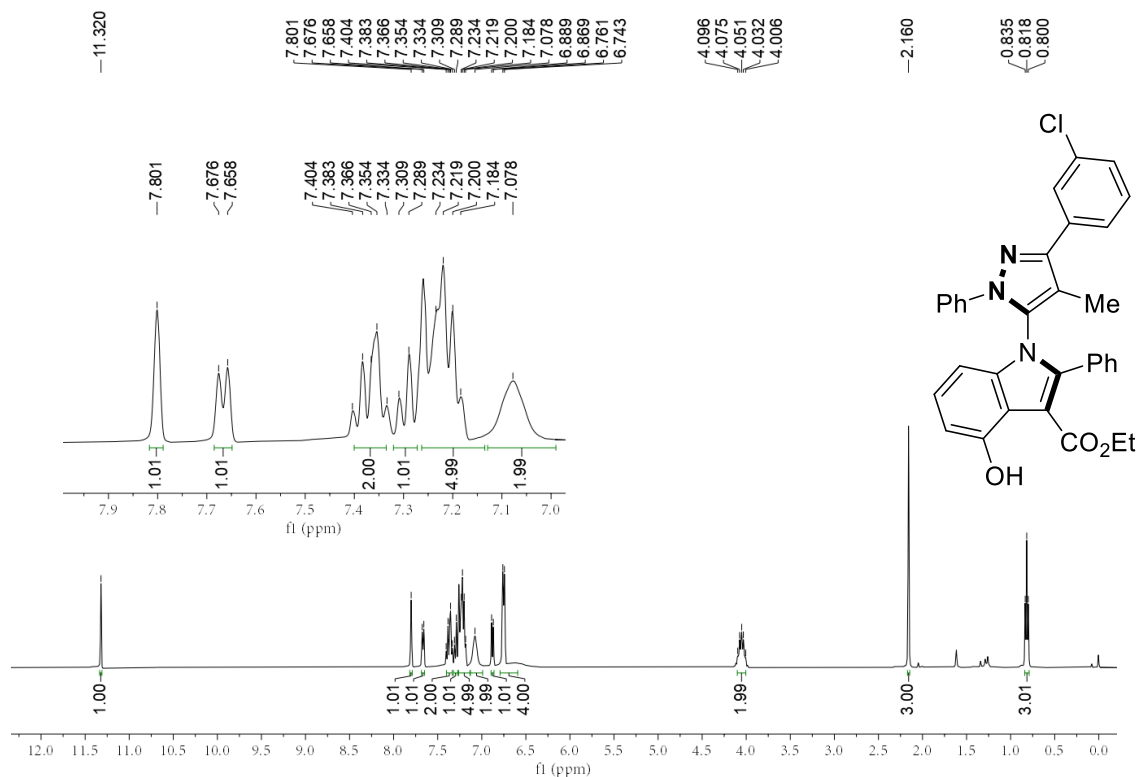
^1H NMR (400 MHz, CDCl_3) of compound **4nab**:



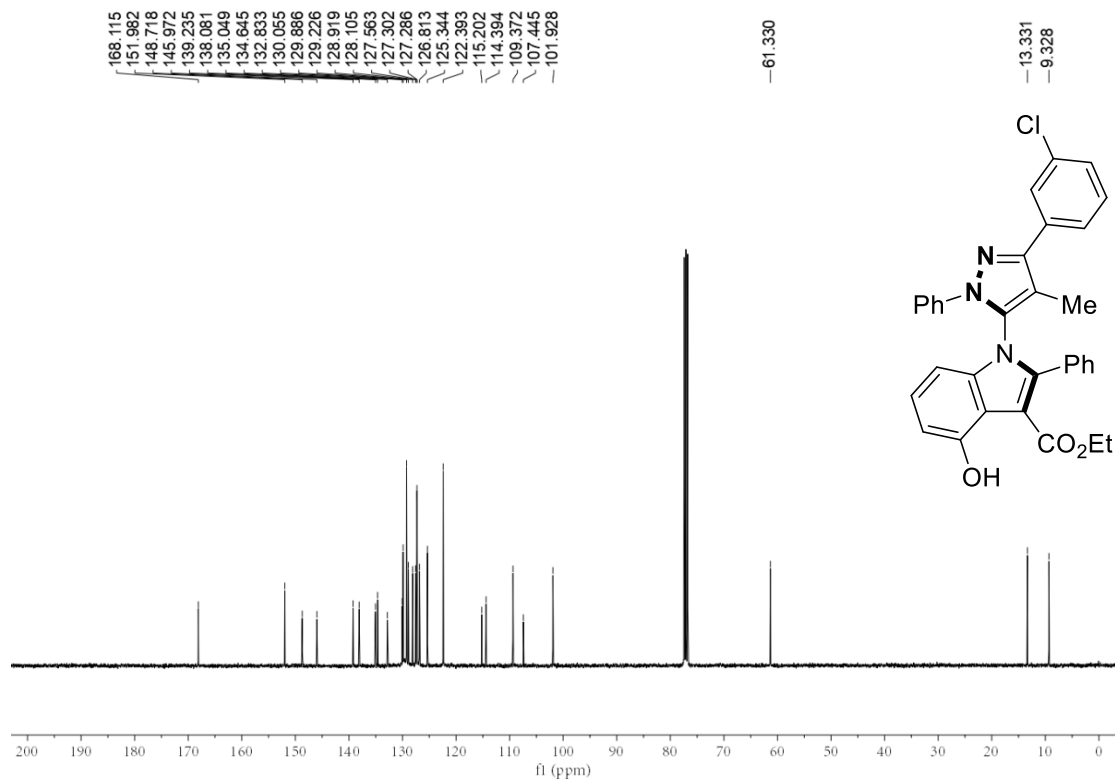
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4nab**:



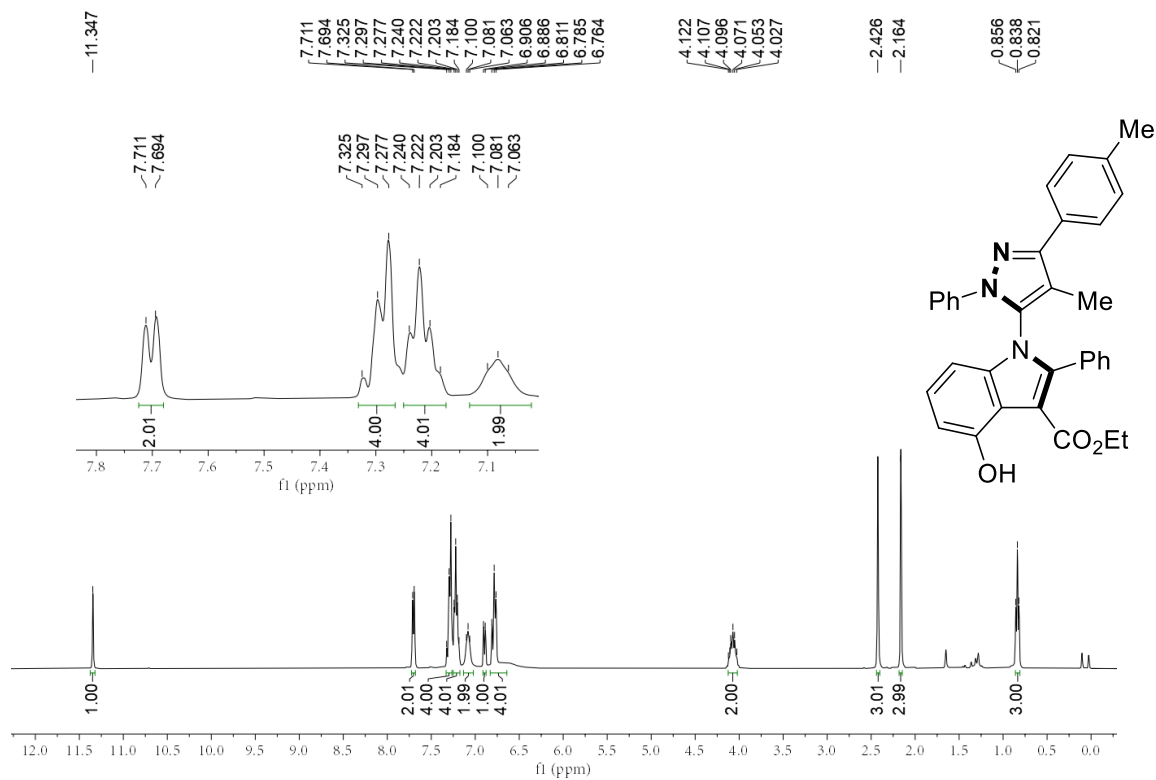
^1H NMR (400 MHz, CDCl_3) of compound **4oab**:



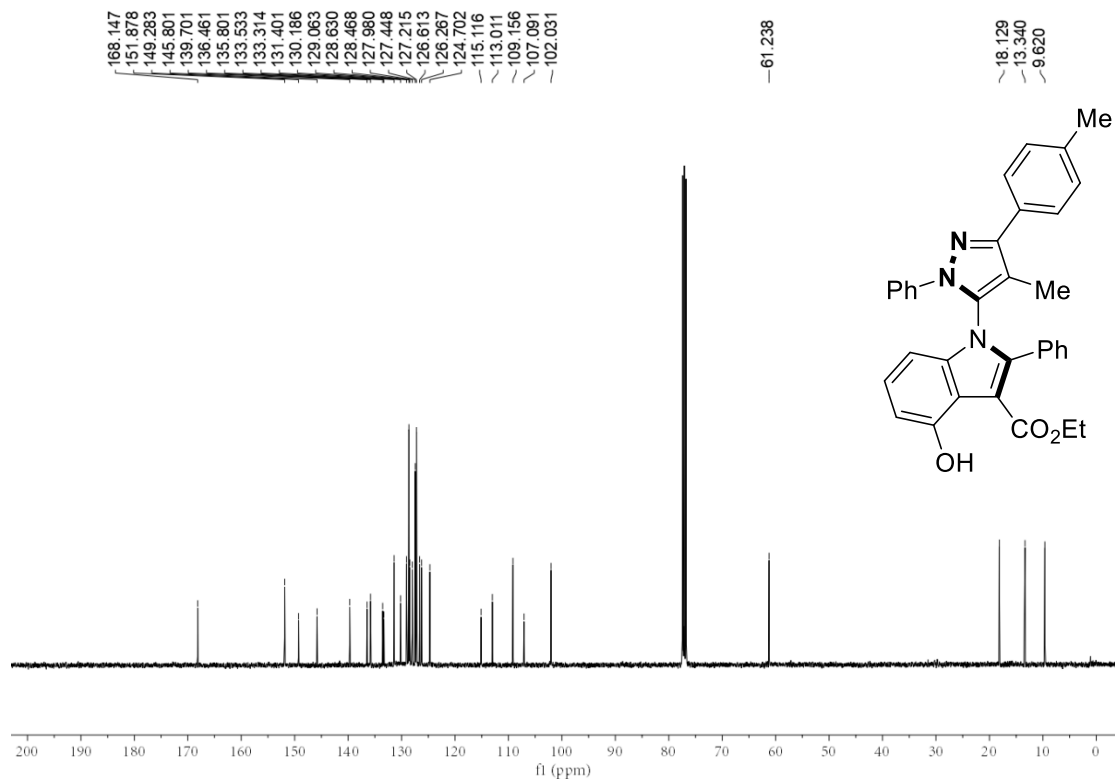
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4oab**:



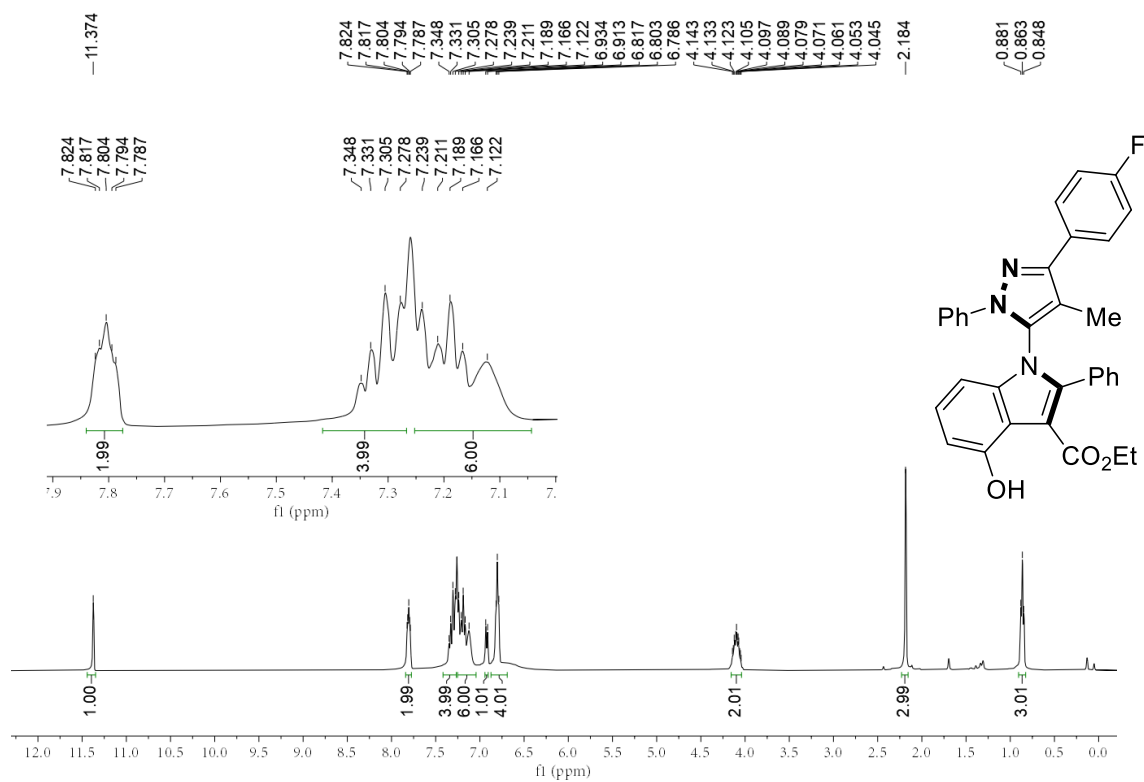
^1H NMR (400 MHz, CDCl_3) of compound **4pab**:



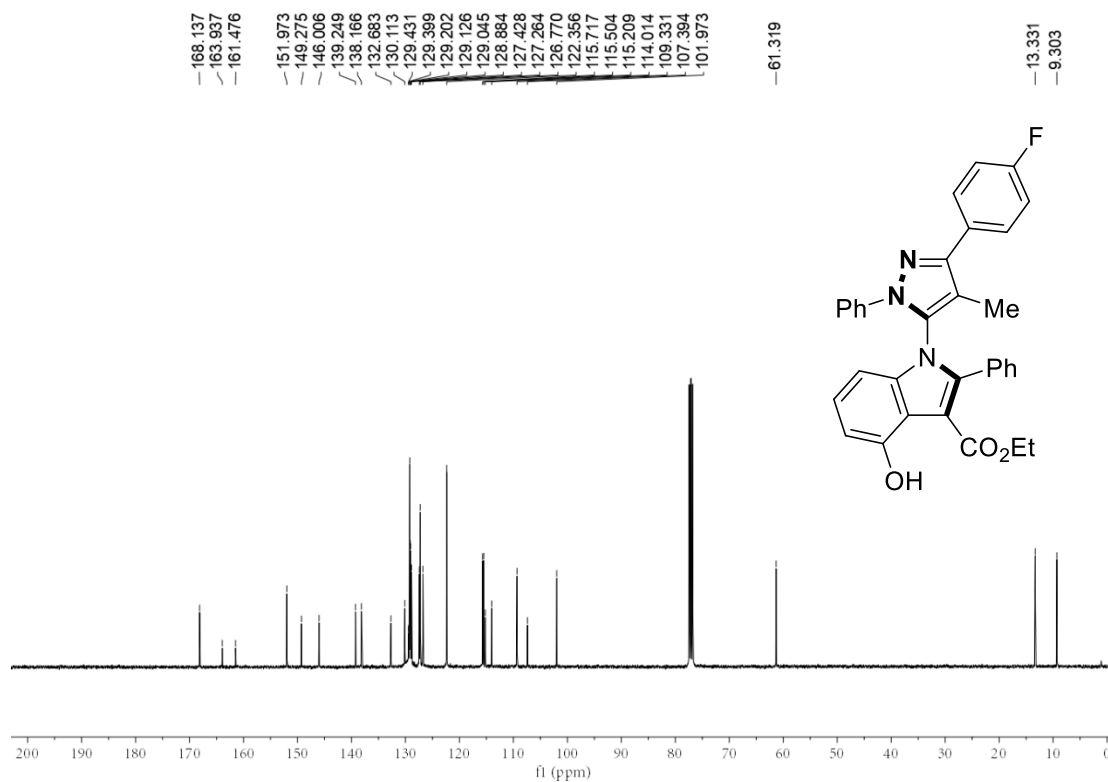
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4pab**:



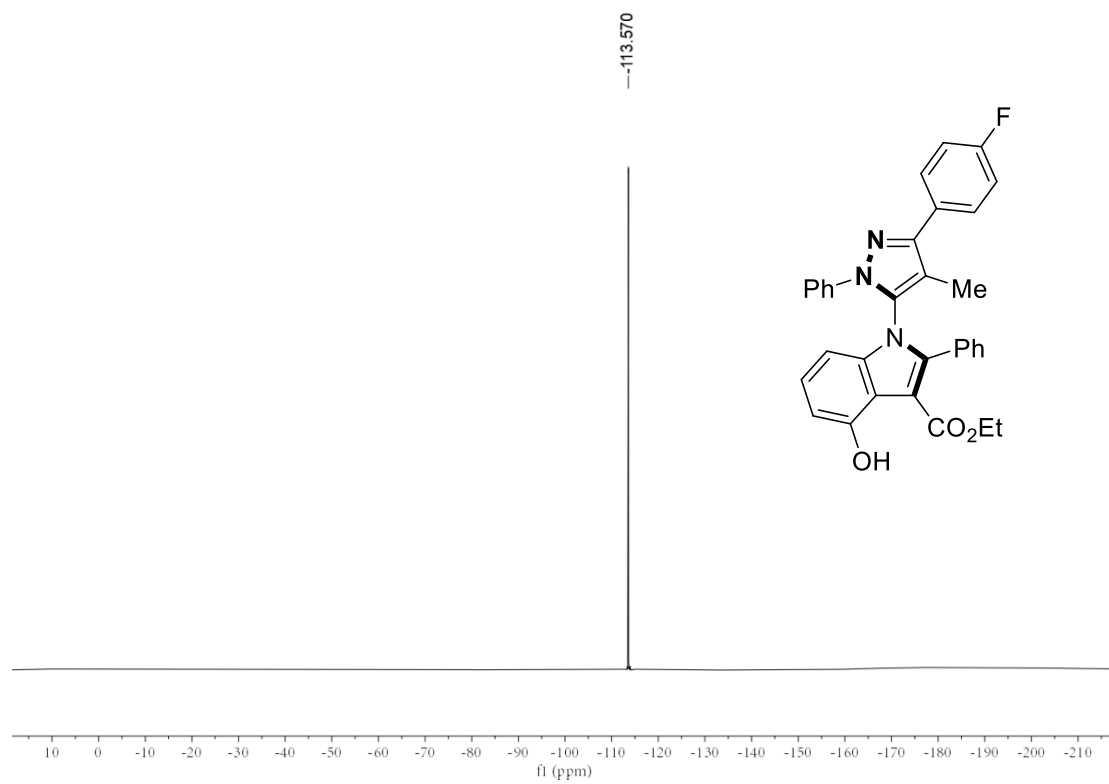
^1H NMR (400 MHz, CDCl_3) of compound **4qab**:



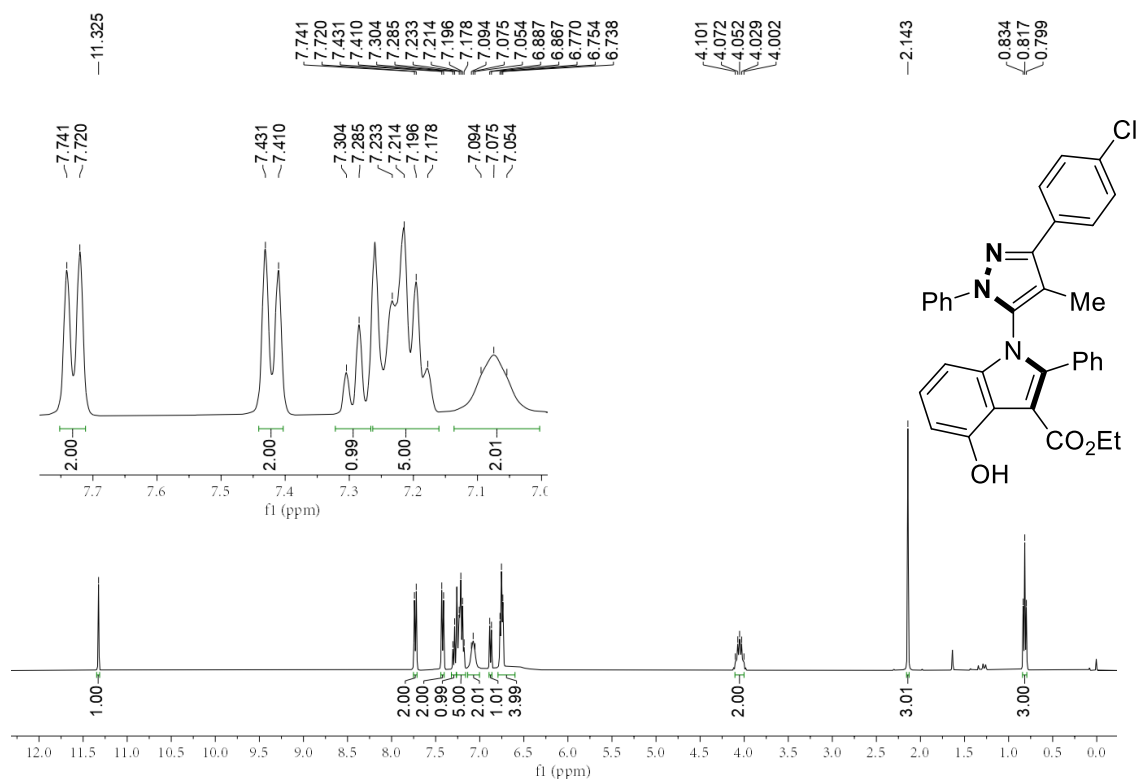
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4qab**:



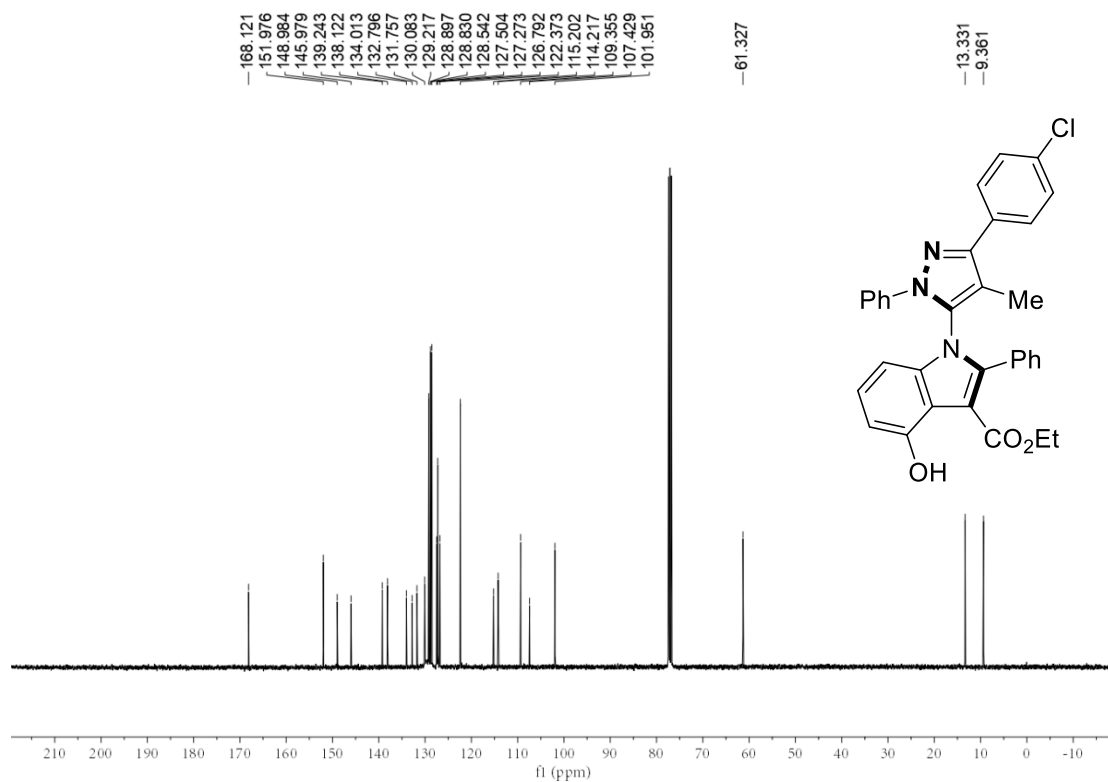
^{19}F NMR (376 MHz, CDCl_3) of compound **4qab**:



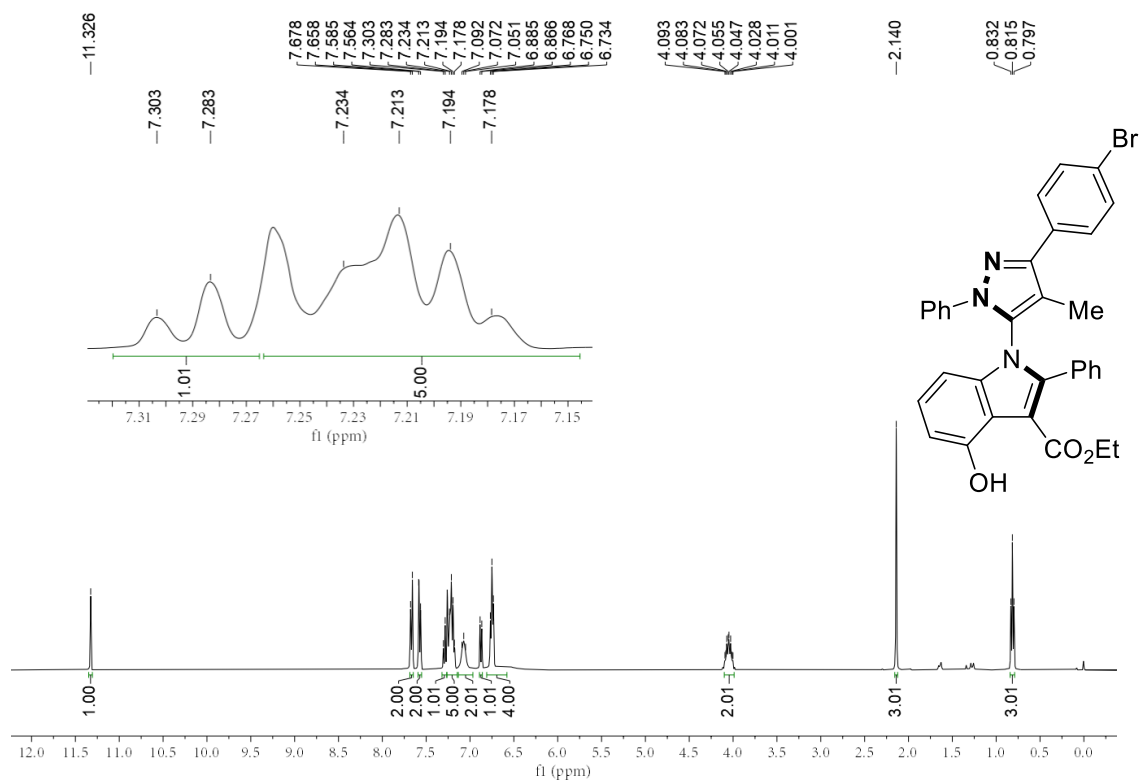
^1H NMR (400 MHz, CDCl_3) of compound **4rab**:



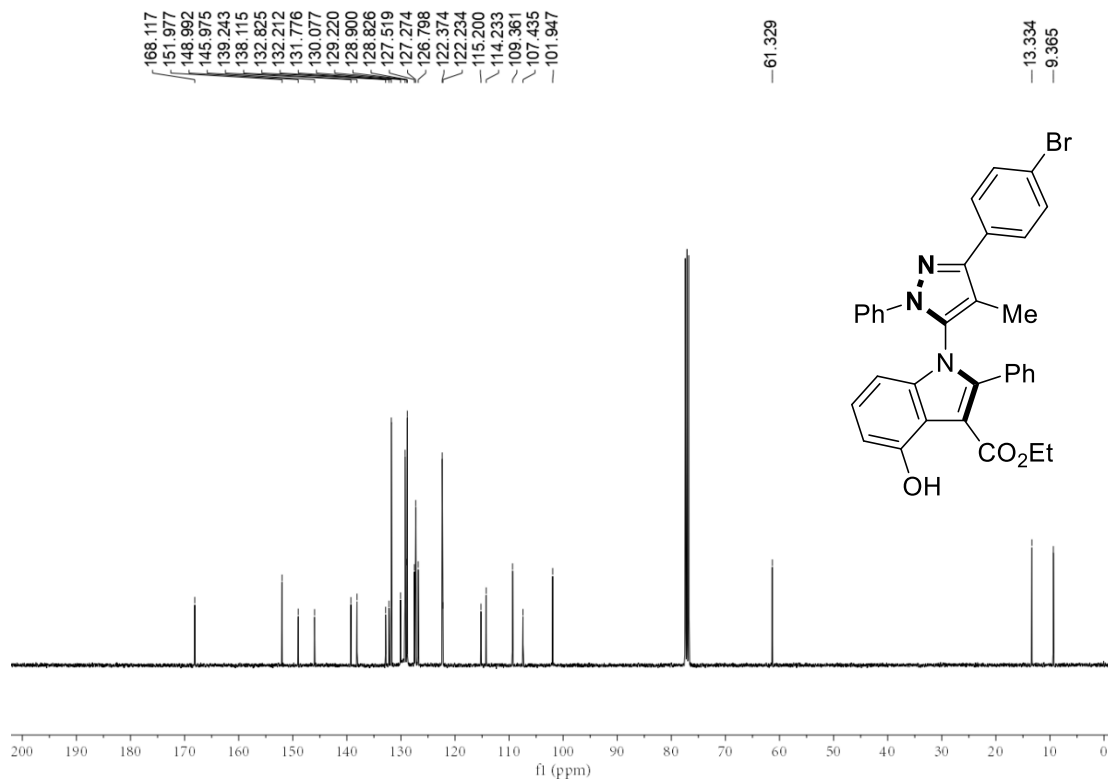
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4rab**:



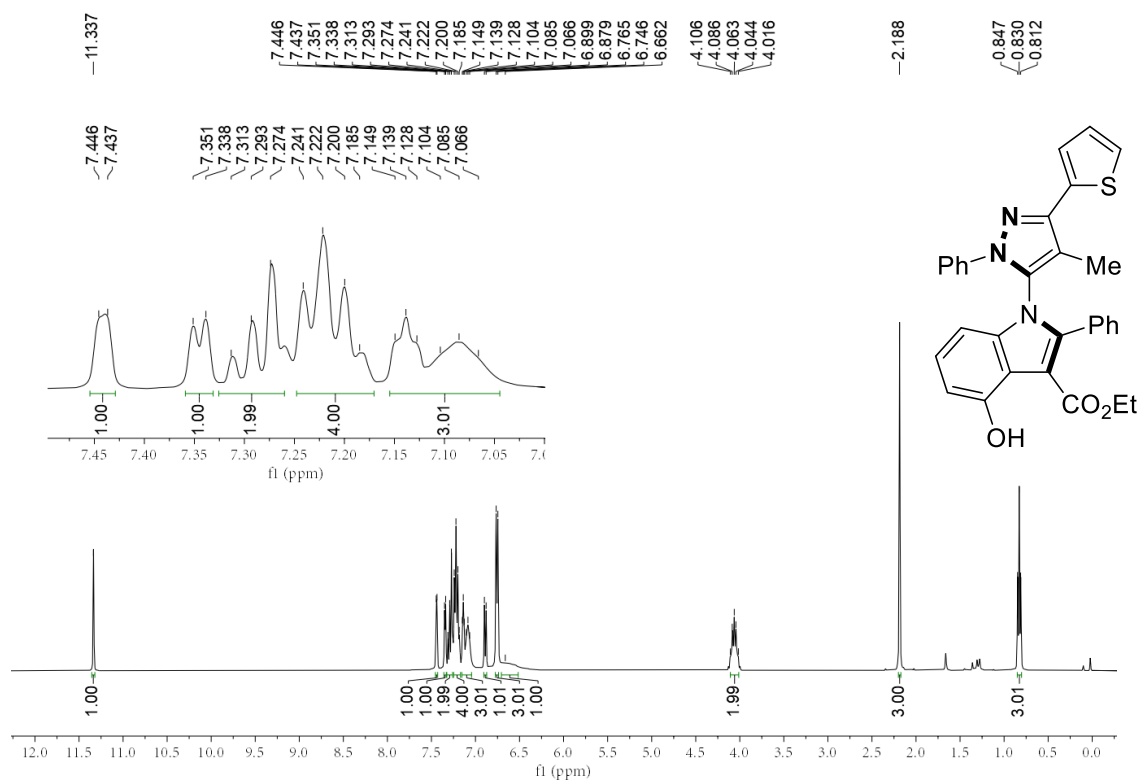
^1H NMR (400 MHz, CDCl_3) of compound **4sab**:



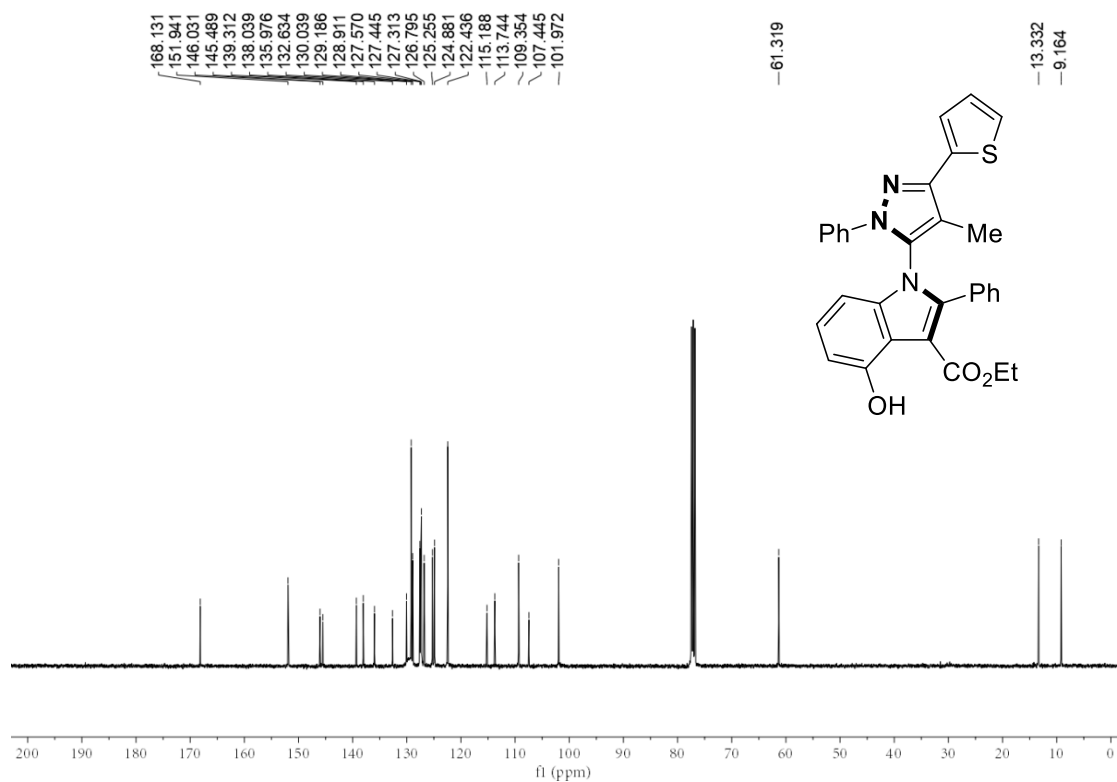
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4sab**:



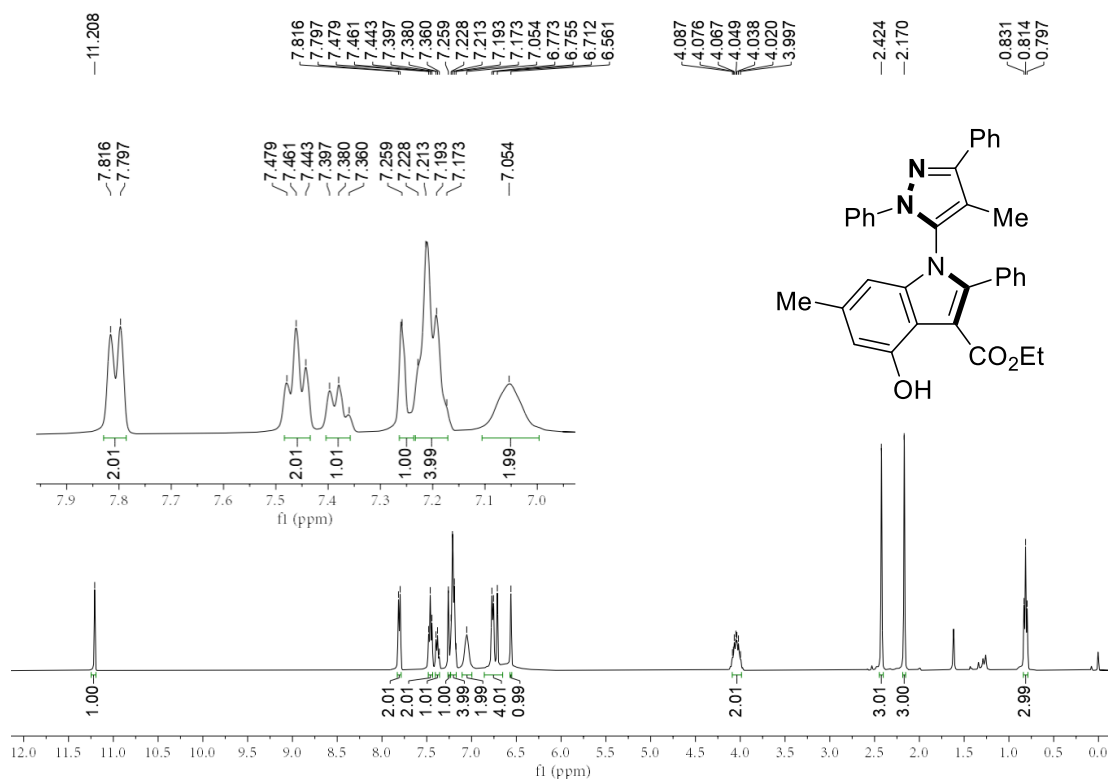
¹H NMR (400 MHz, CDCl₃) of compound **4tab**:



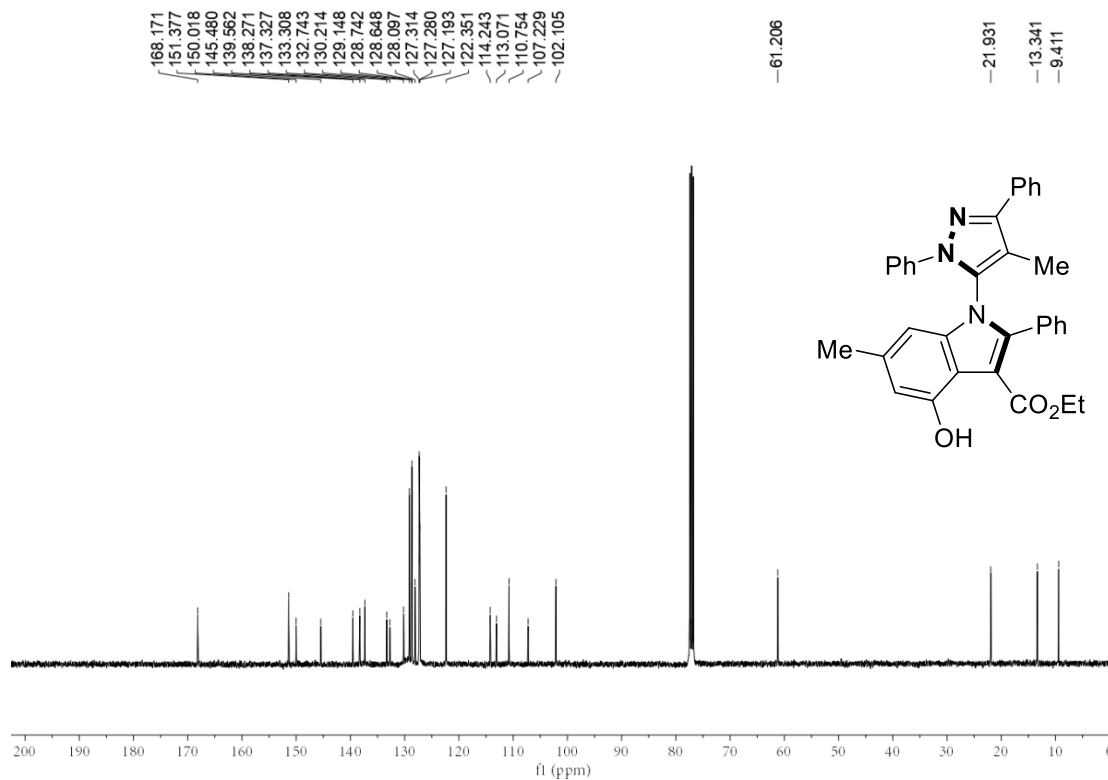
¹³C{¹H} NMR (100 MHz, CDCl₃) of compound **4tab**:



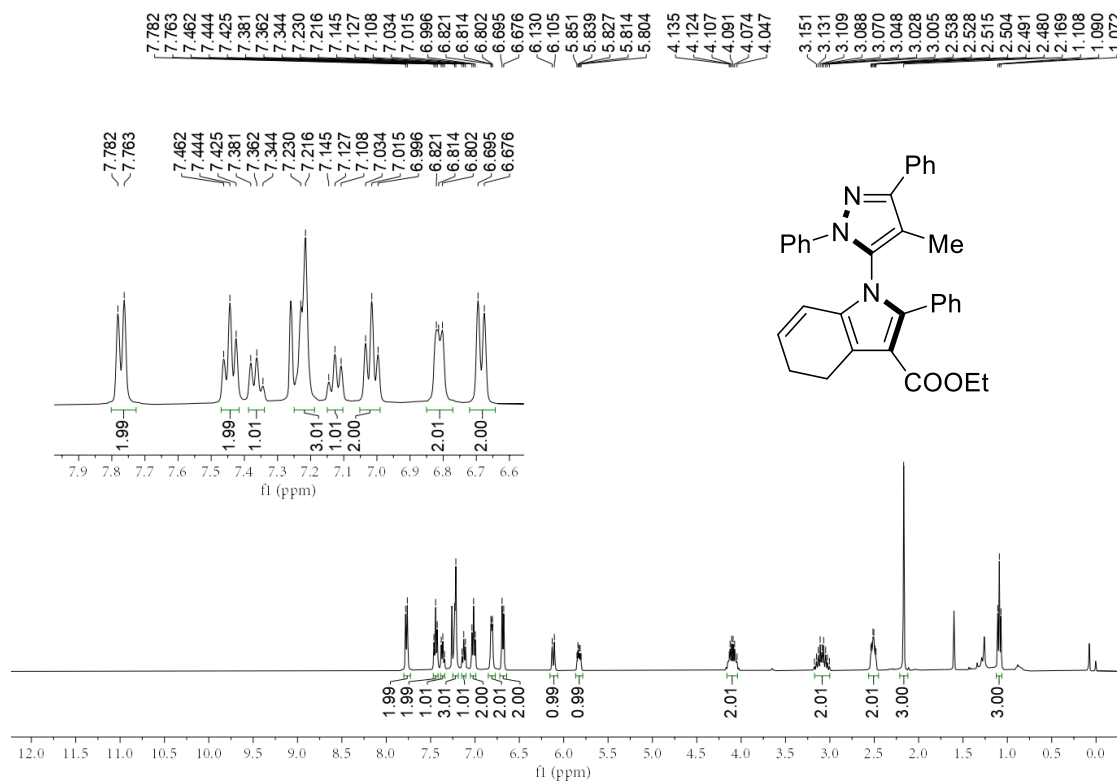
^1H NMR (400 MHz, CDCl_3) of compound **4abb**:



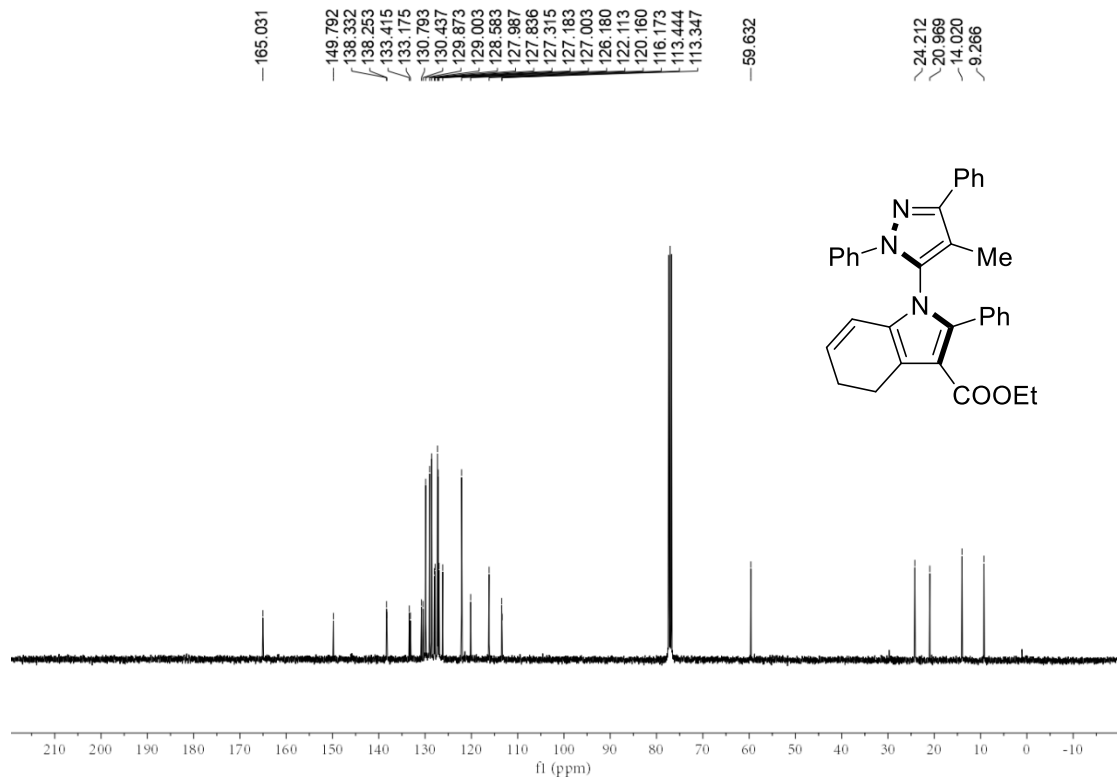
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **4abb**:



^1H NMR (400 MHz, CDCl_3) of compound **4acb**:

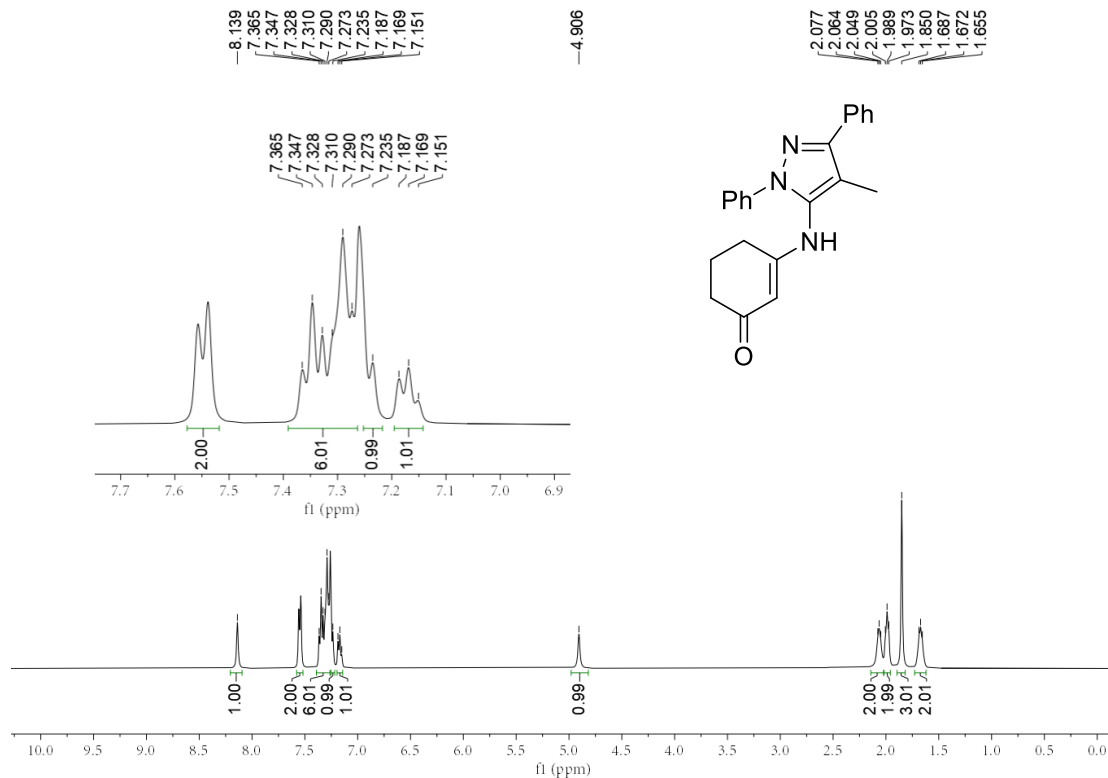


^{13}C { ^1H } NMR (100 MHz, CDCl_3) of compound **4acb**:

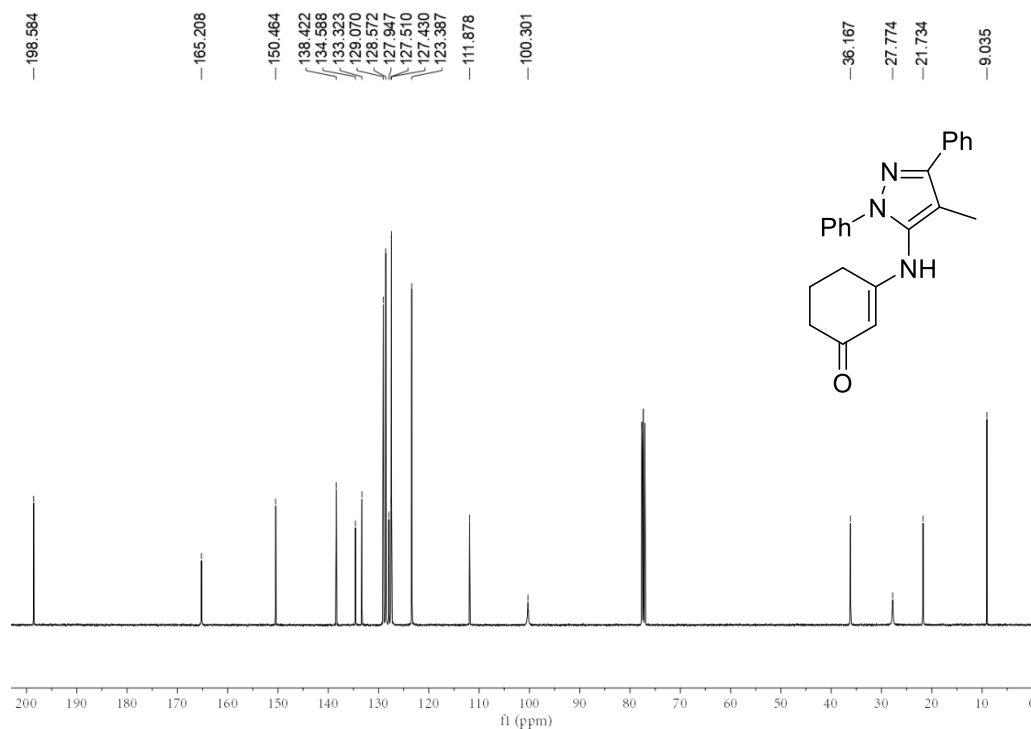


9. NMR spectra of substrates 6-10

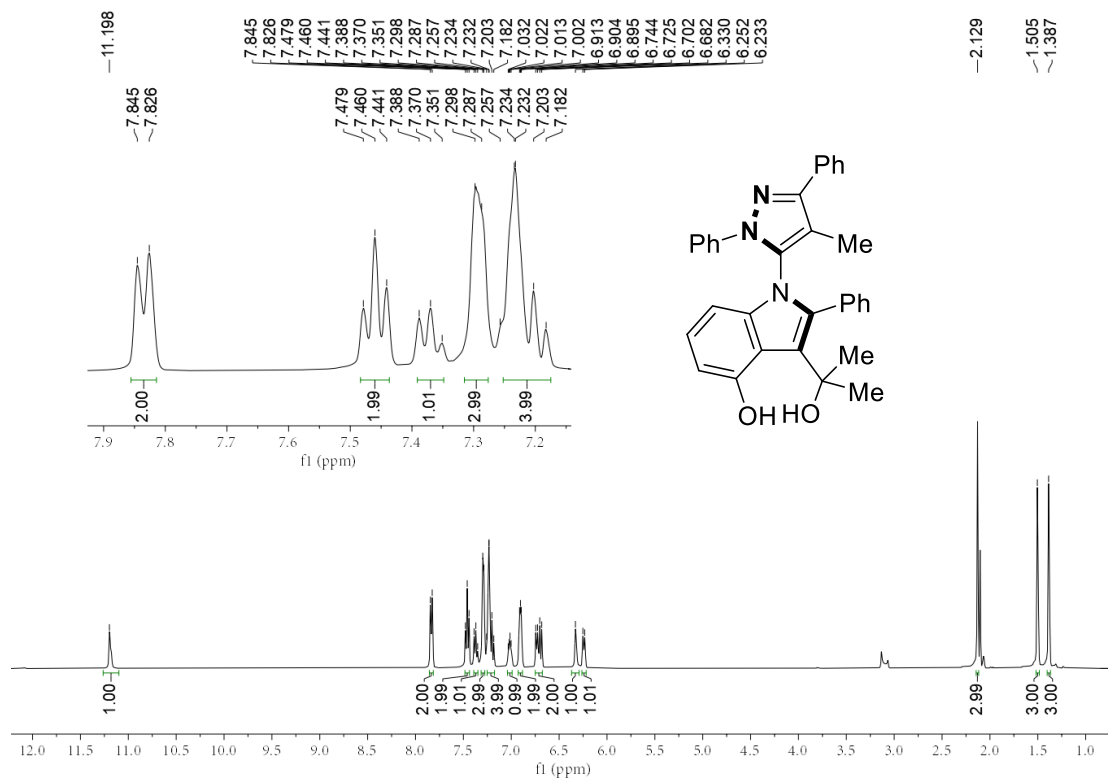
^1H NMR (400 MHz, CDCl_3) of compound **6**:



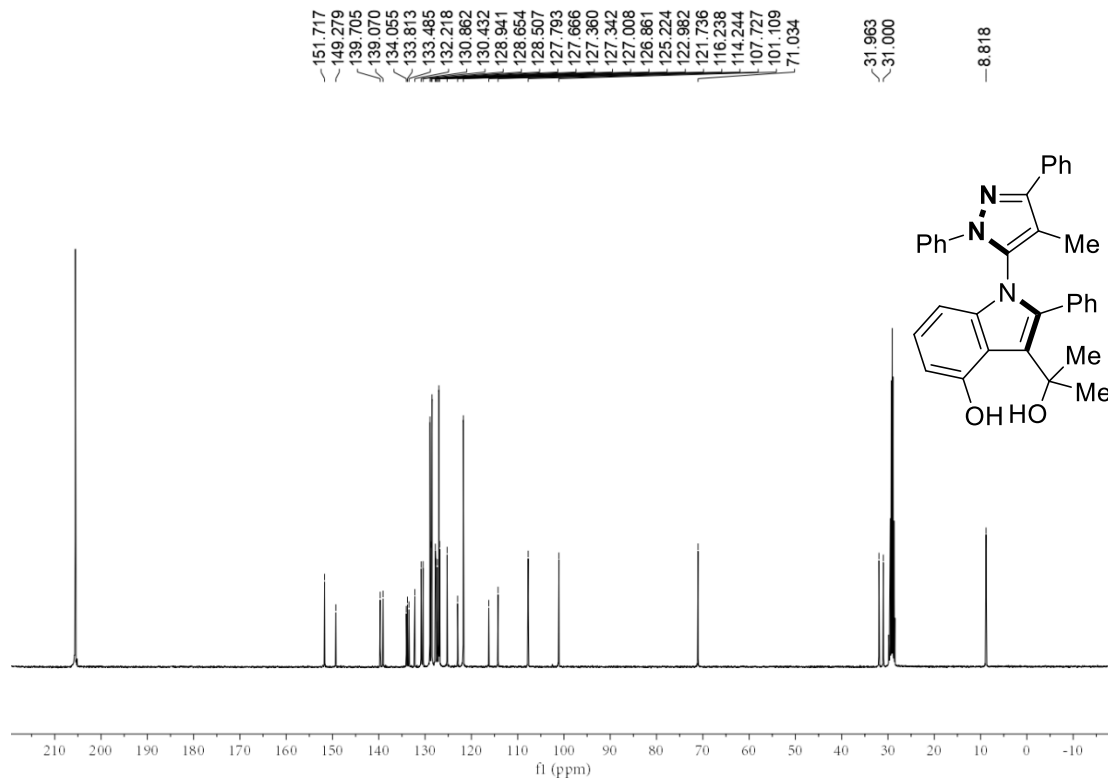
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of compound **6**:



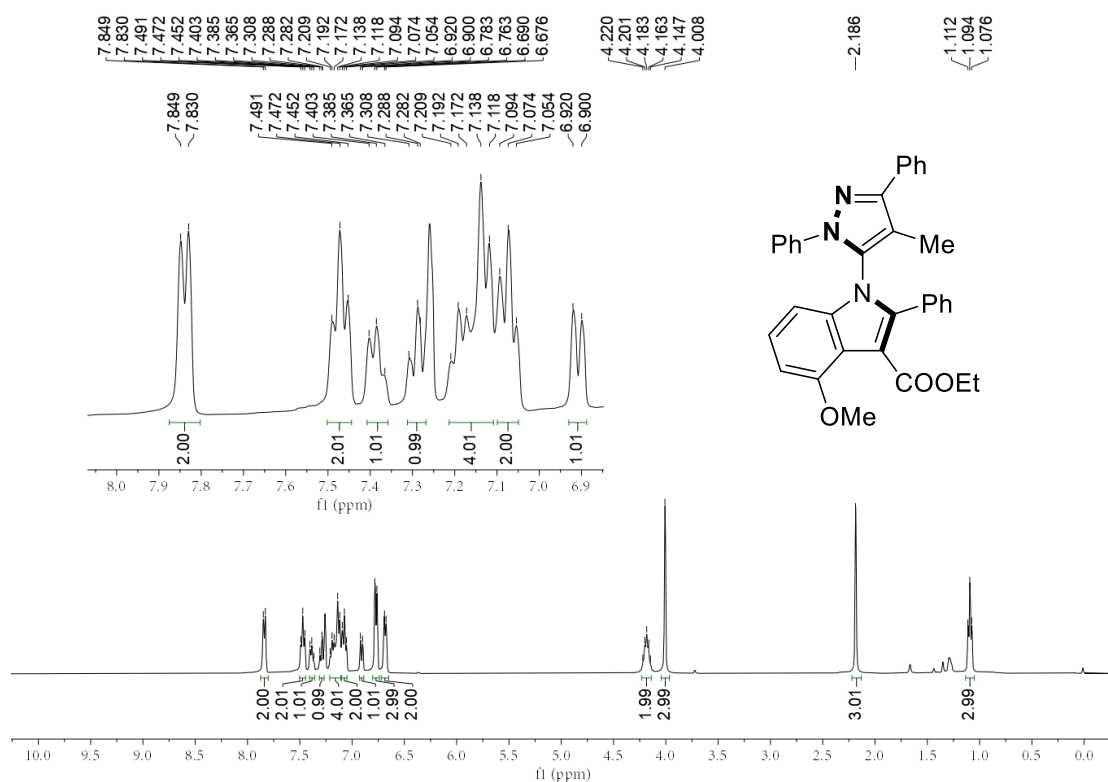
^1H NMR (400 MHz, Acetone- d_6) of compound 7:



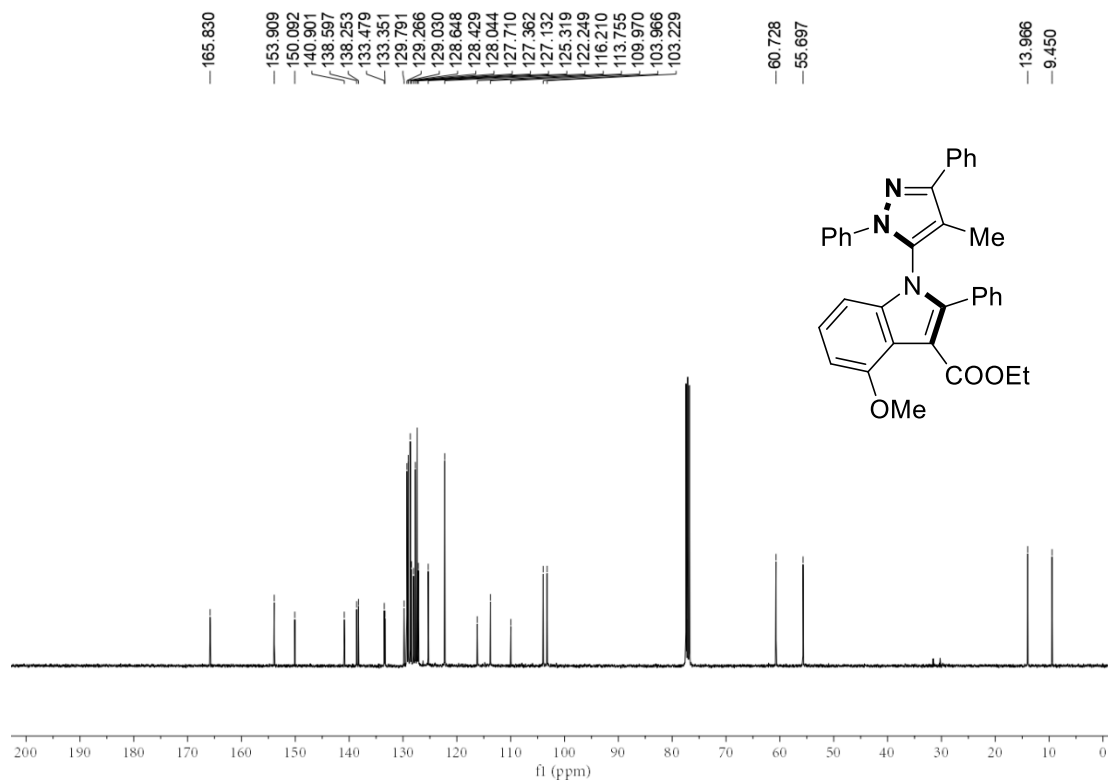
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, Acetone- d_6) of compound 7:



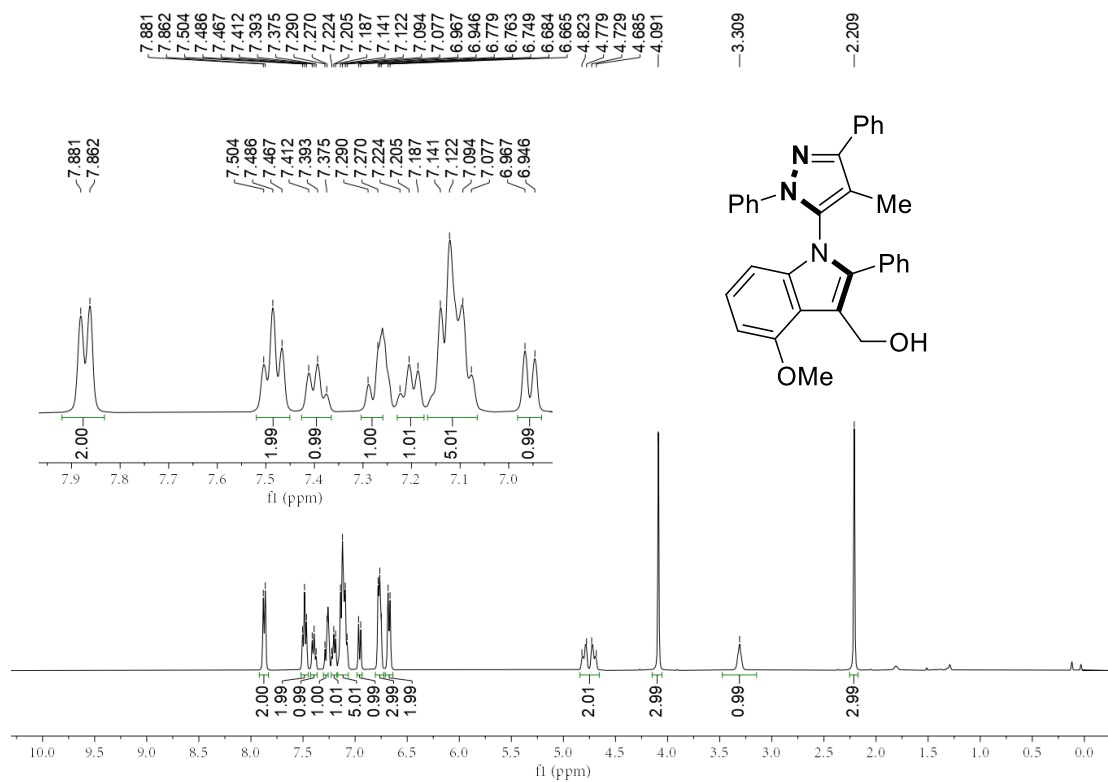
^1H NMR (400 MHz, CDCl_3) of compound **8**:



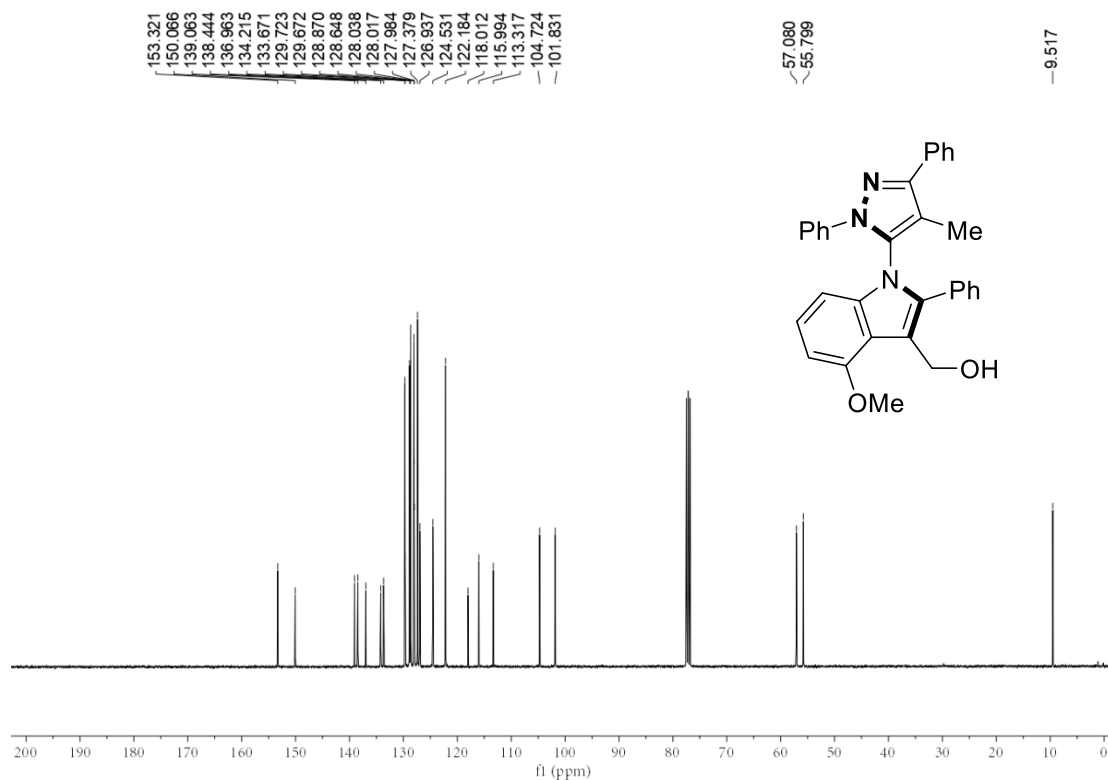
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of compound **8**:



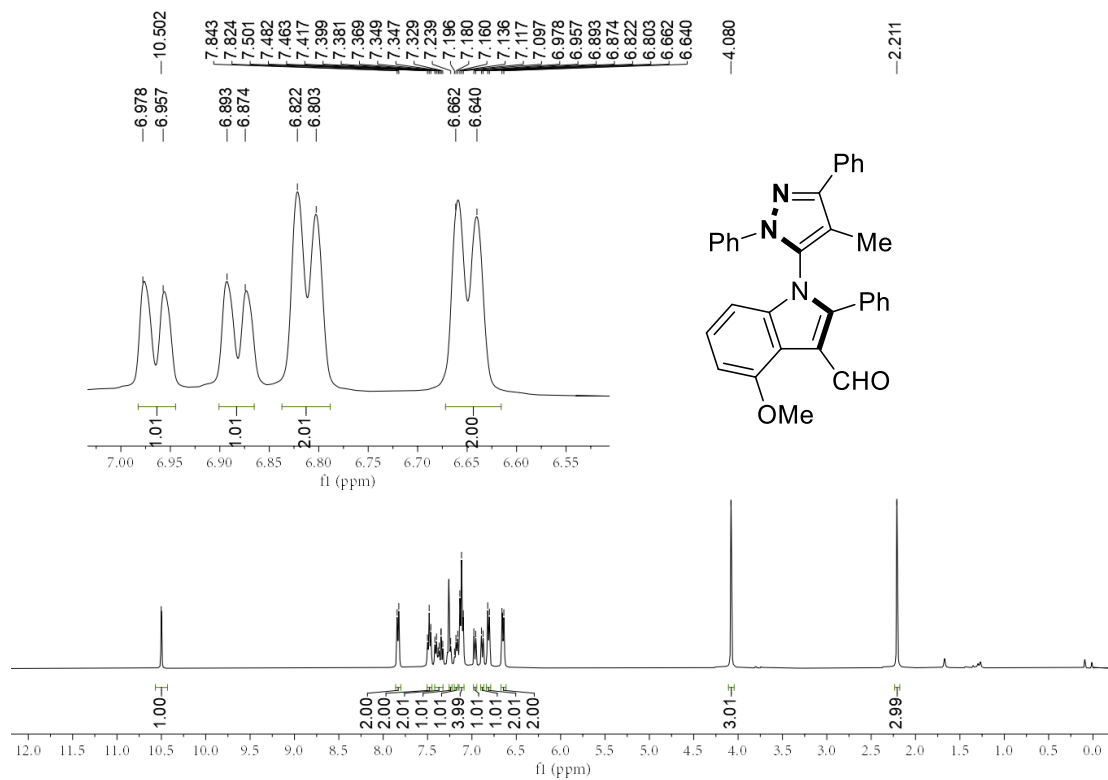
^1H NMR (400 MHz, CDCl_3) of compound **9**:



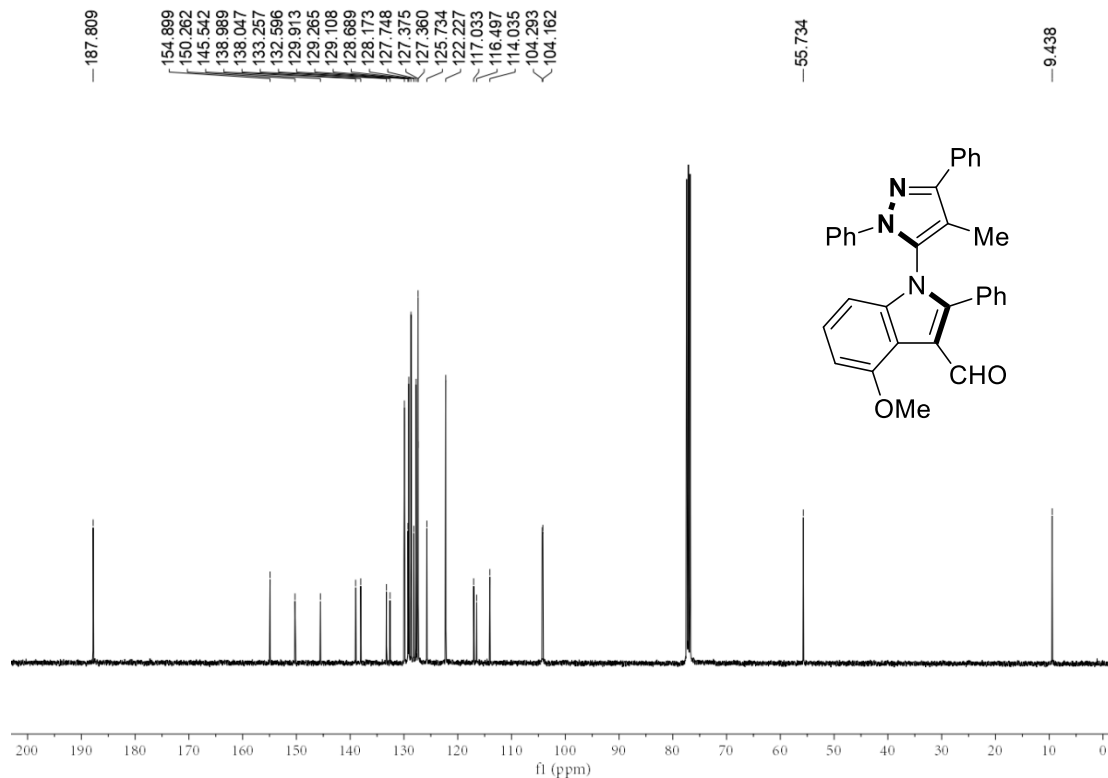
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of compound **9**:



^1H NMR (400 MHz, CDCl_3) of compound **10**:



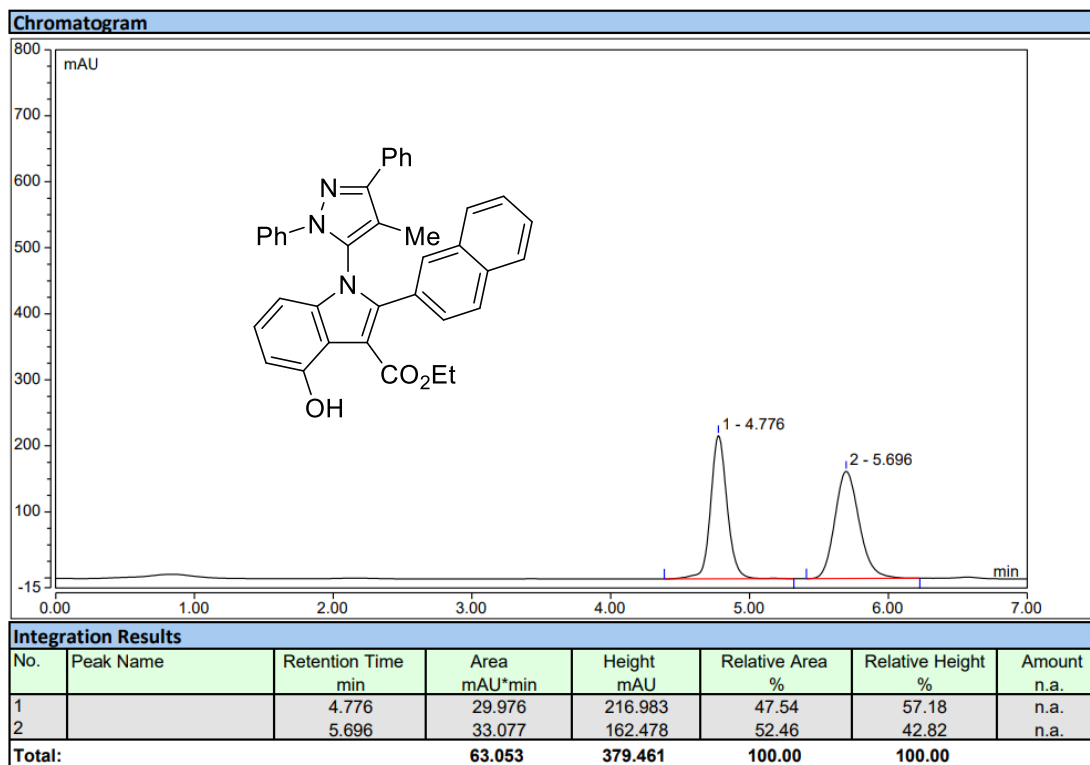
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of compound **10**:



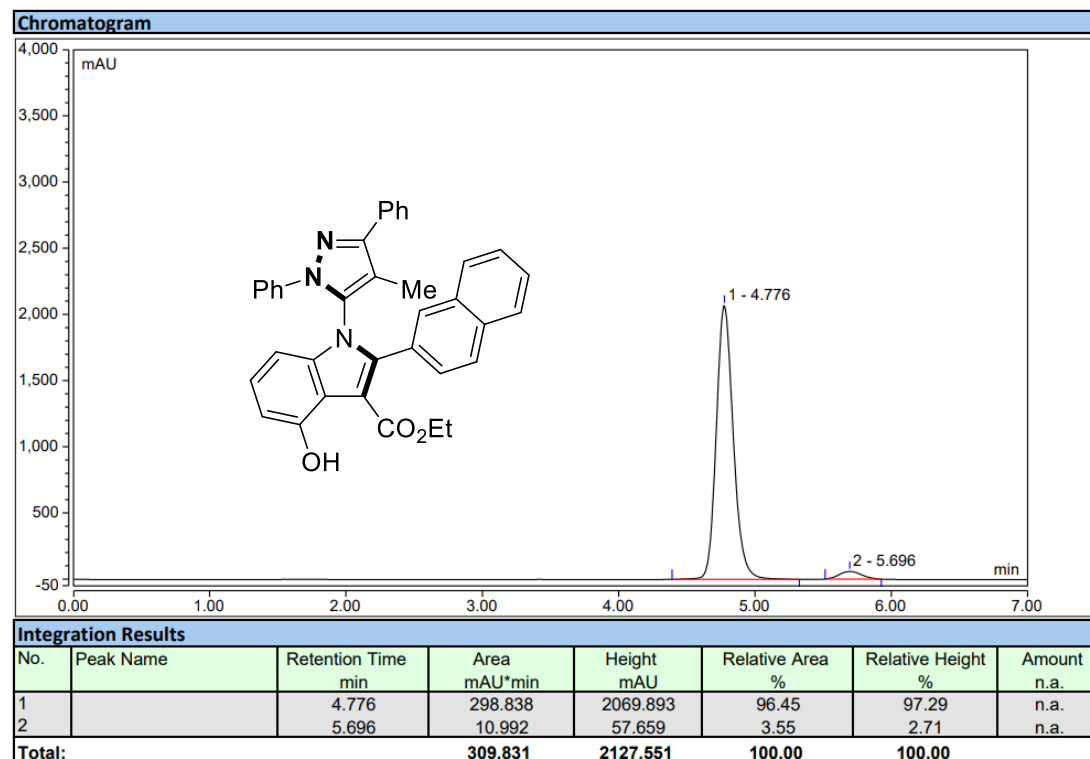
10. HPLC traces of products 4

4aaa

Racemic:

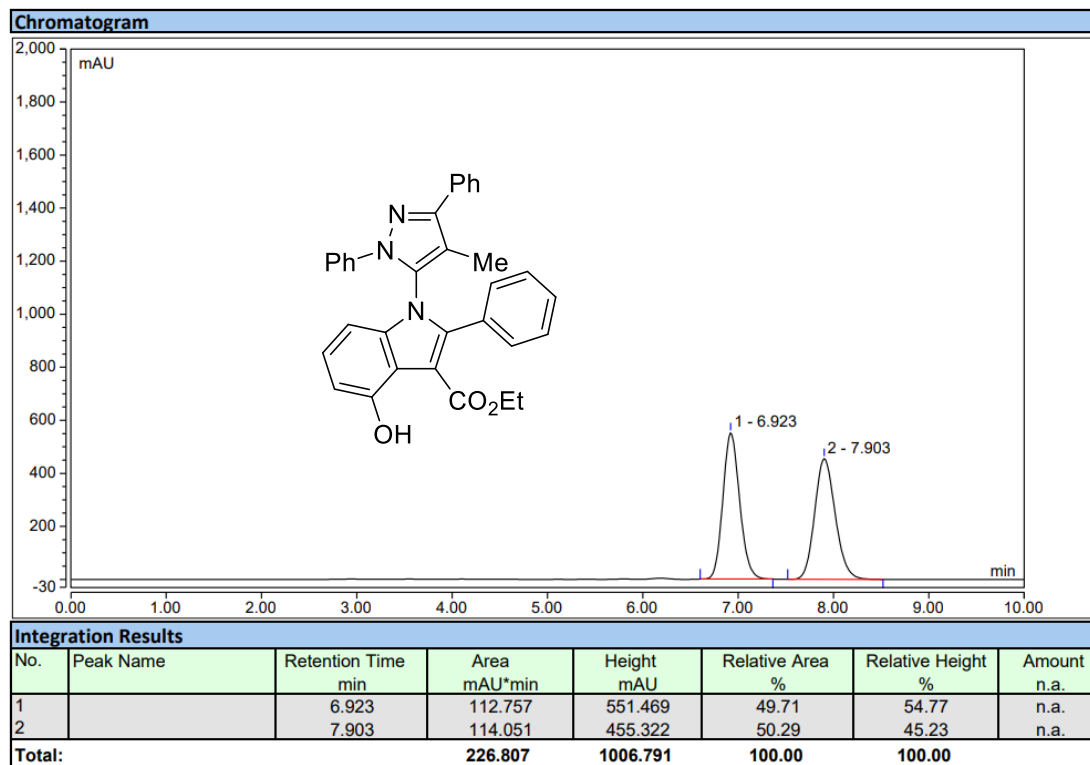


Enantioselective:

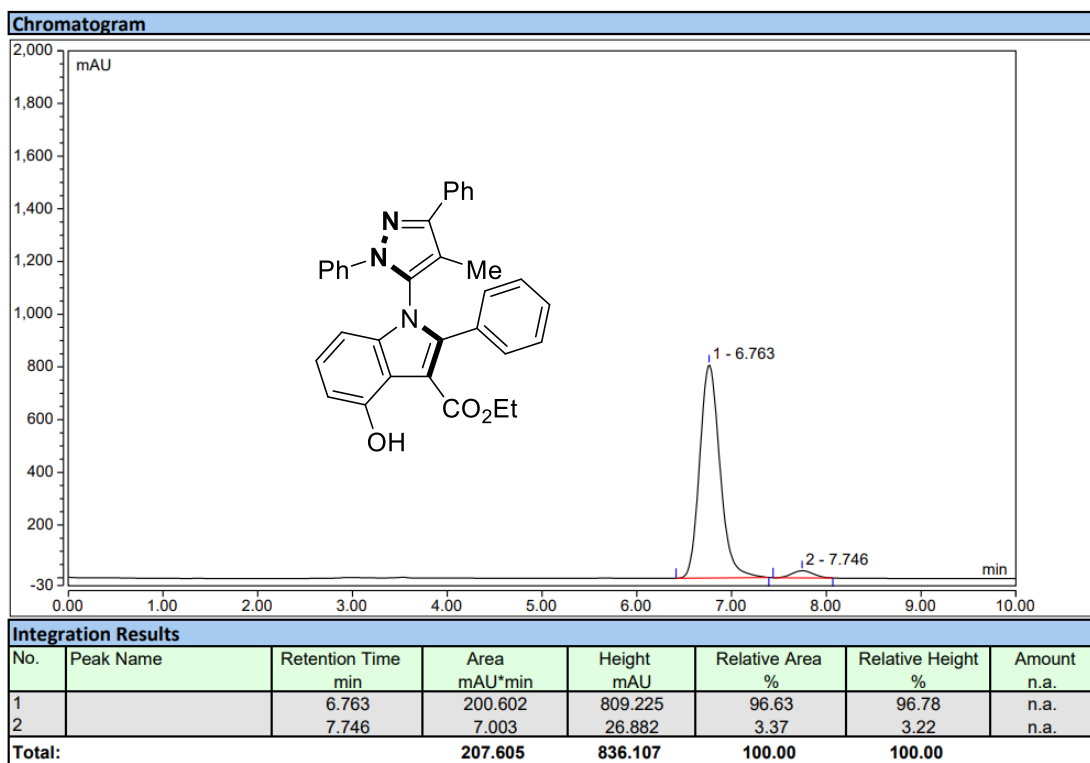


4aab

Racemic:

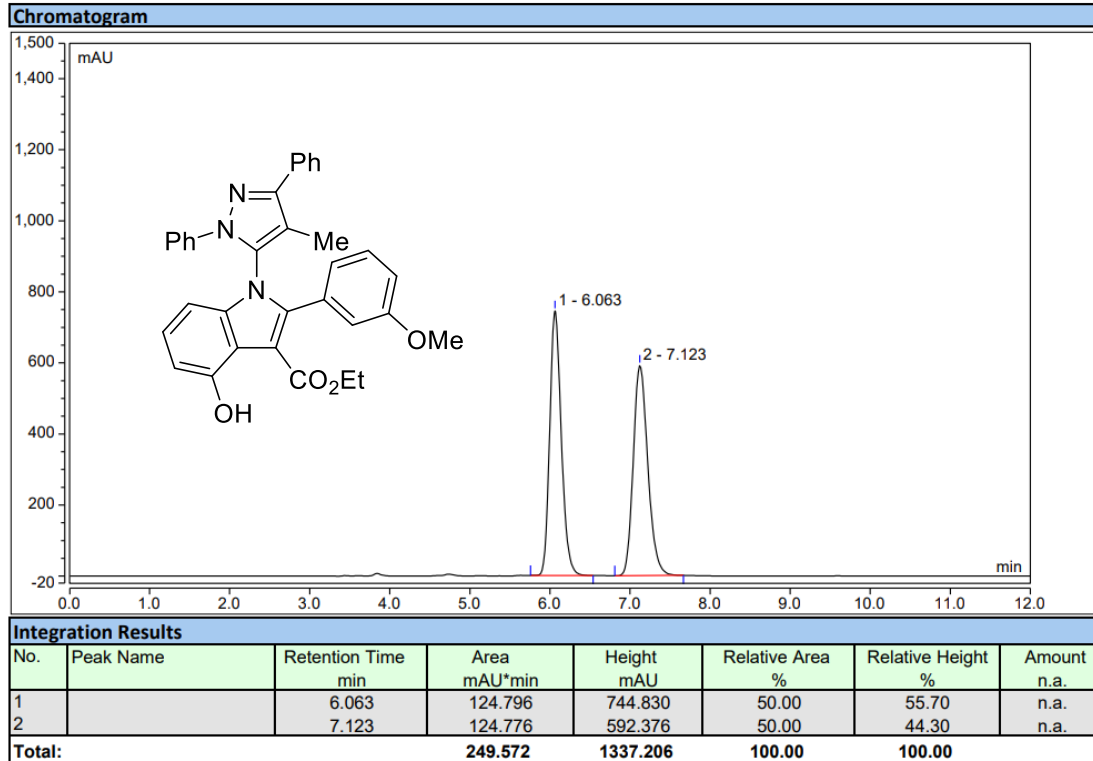


Enantioselective:

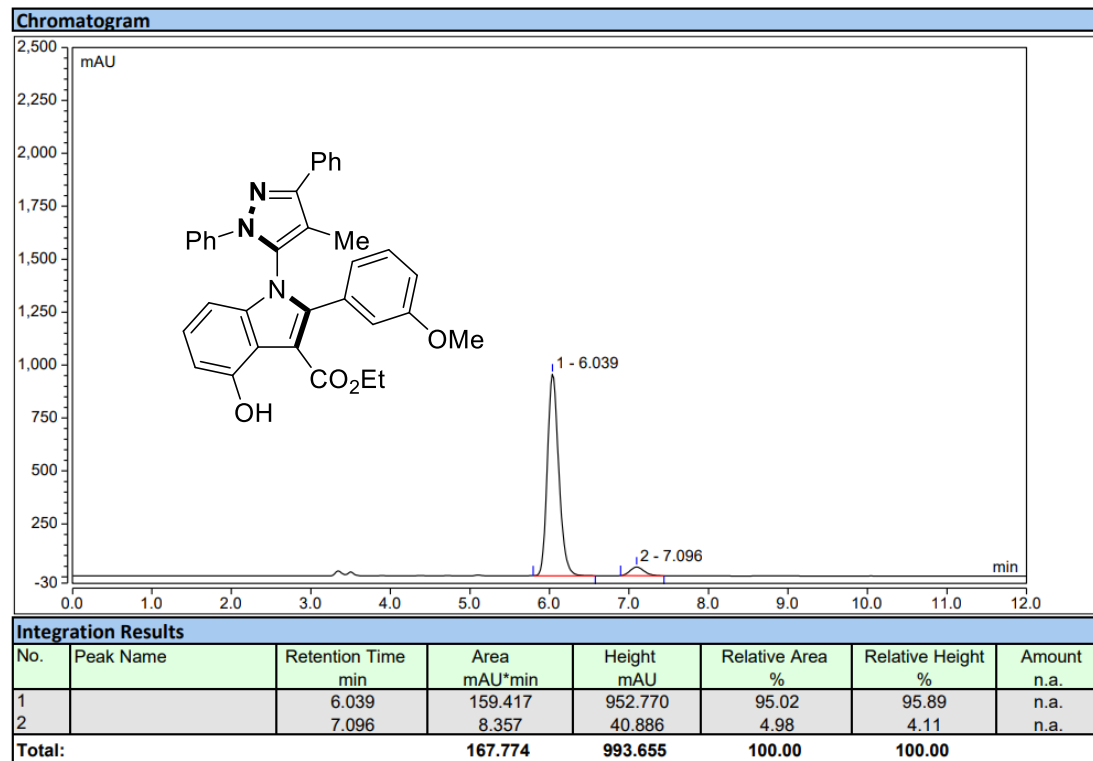


4aac

Racemic:

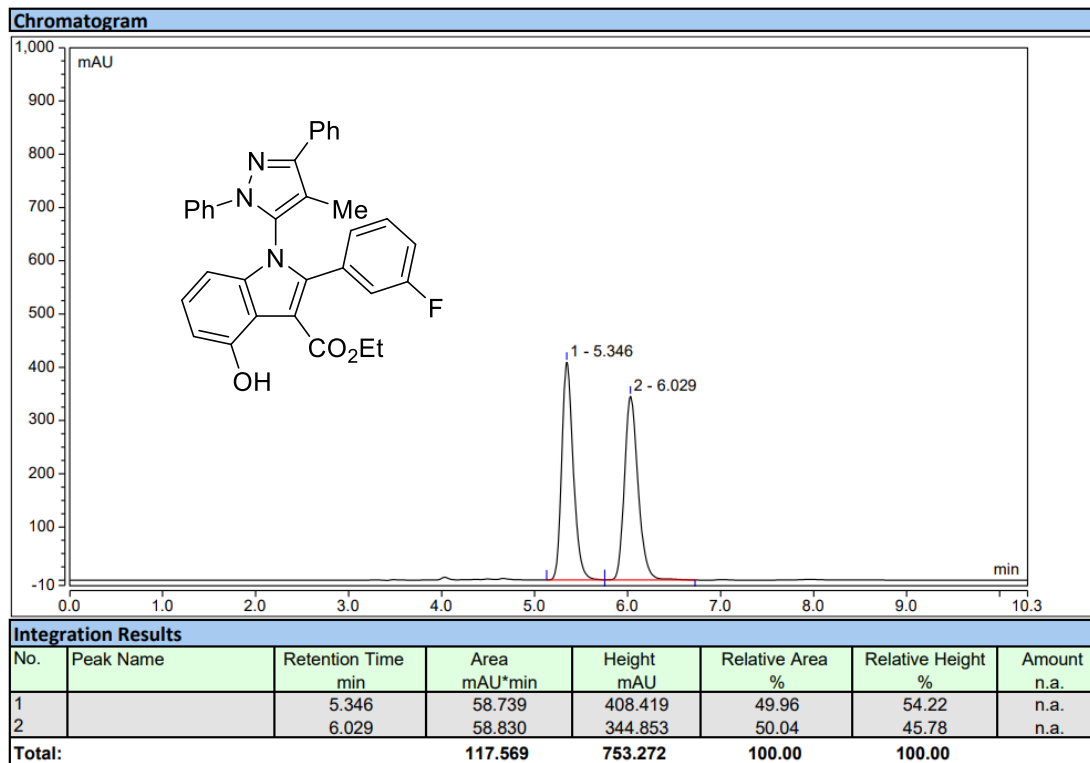


Enantioselective:

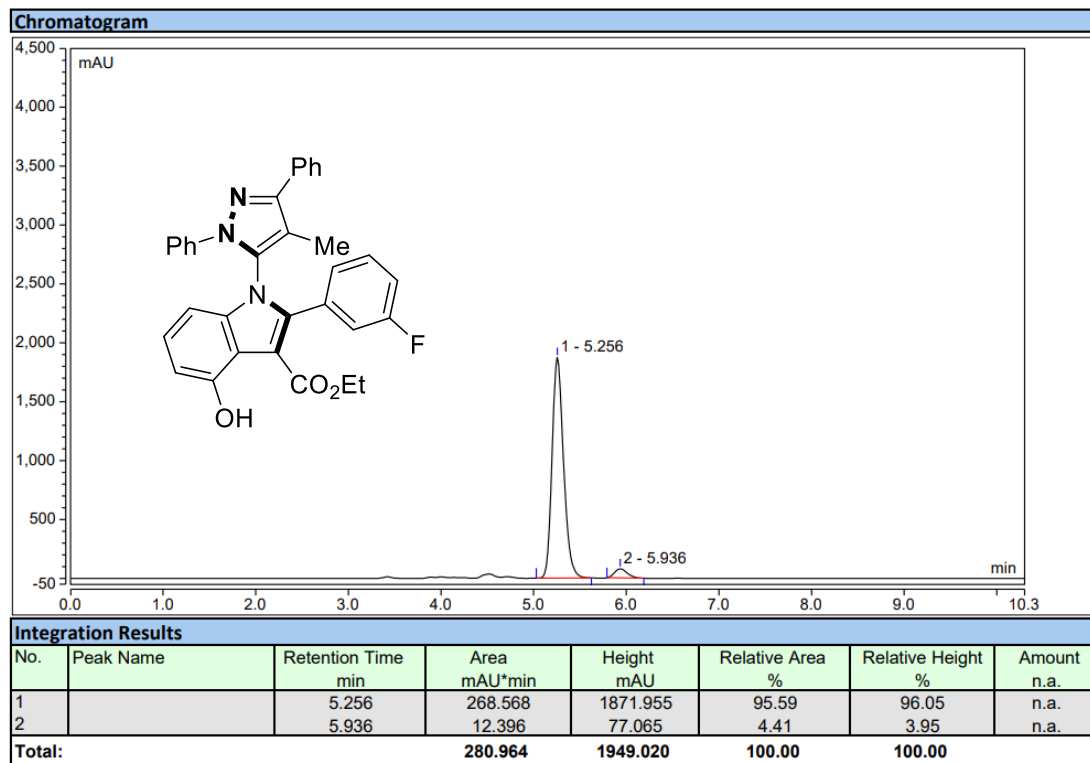


4aad

Racemic:

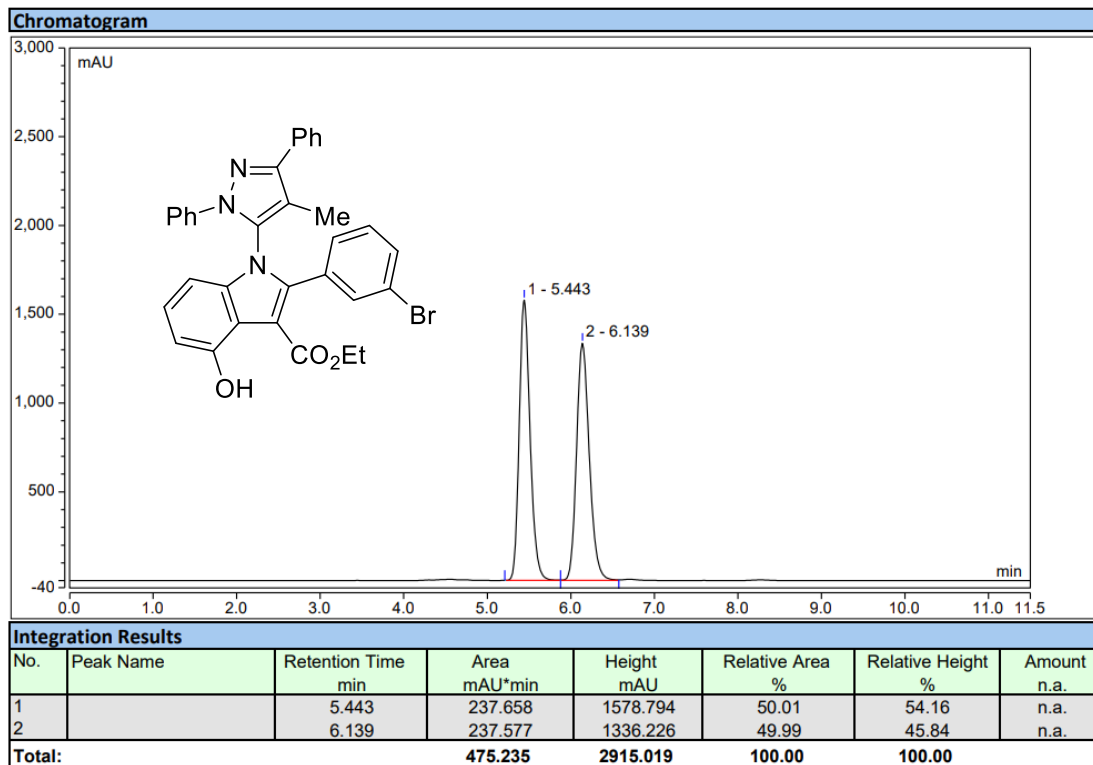


Enantioselective:

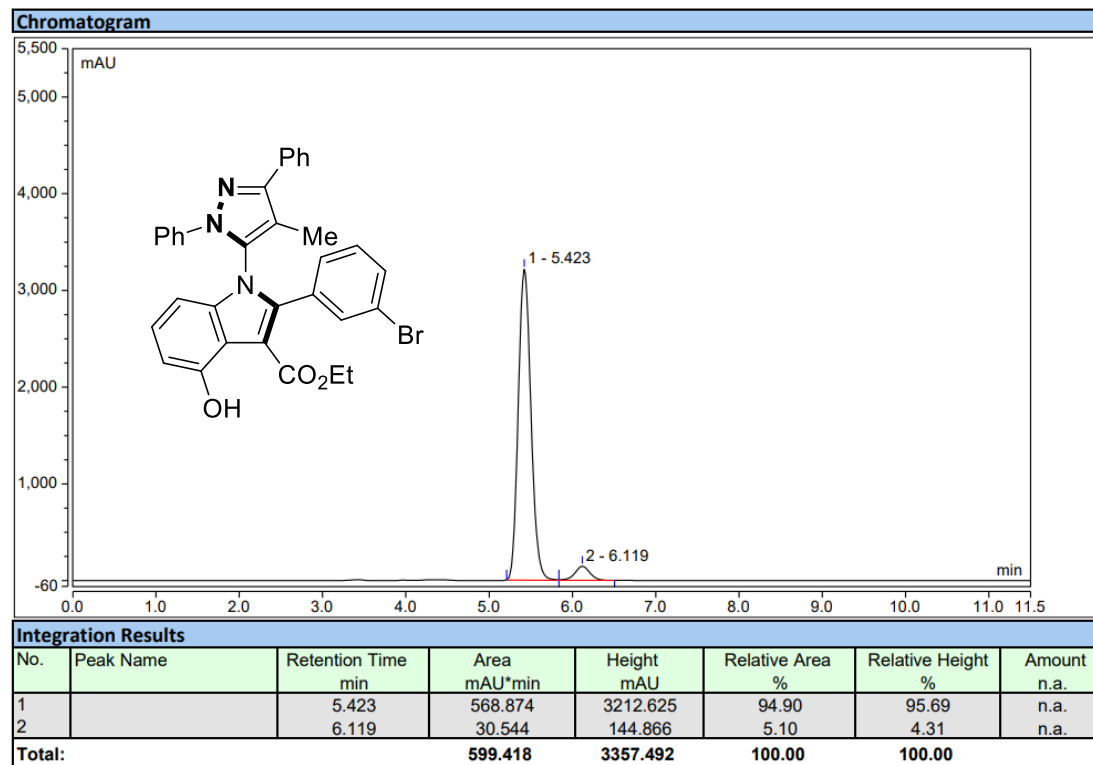


4aae

Racemic:

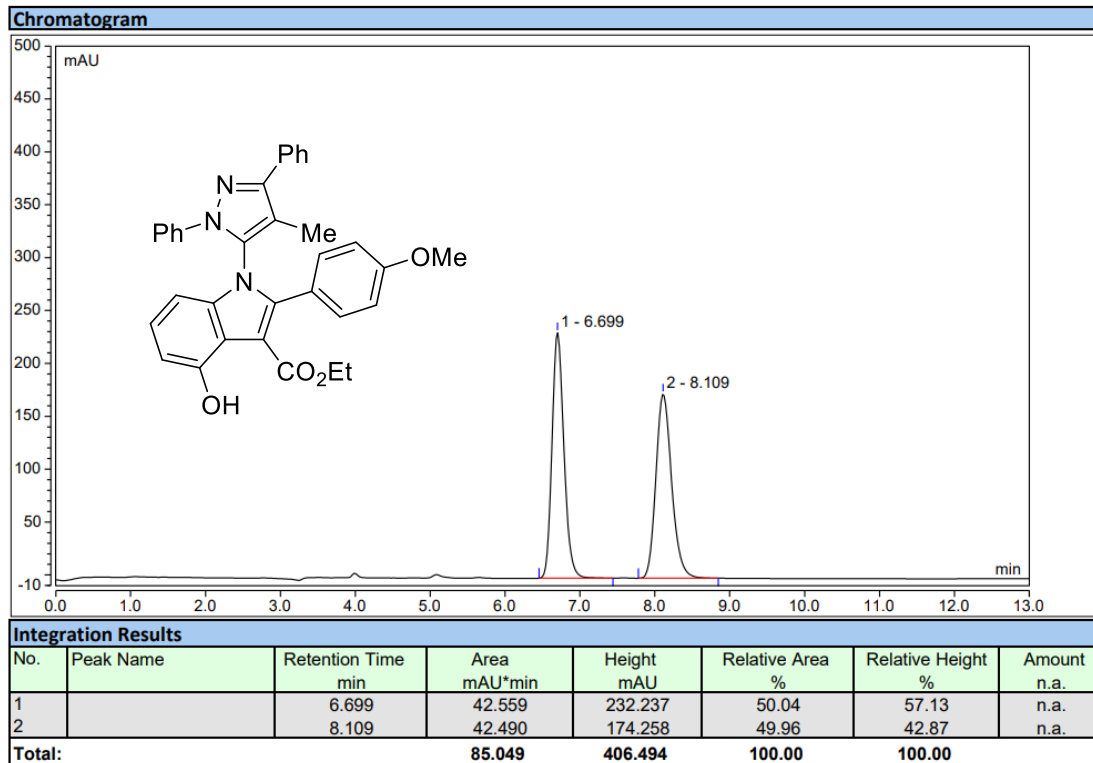


Enantioselective:

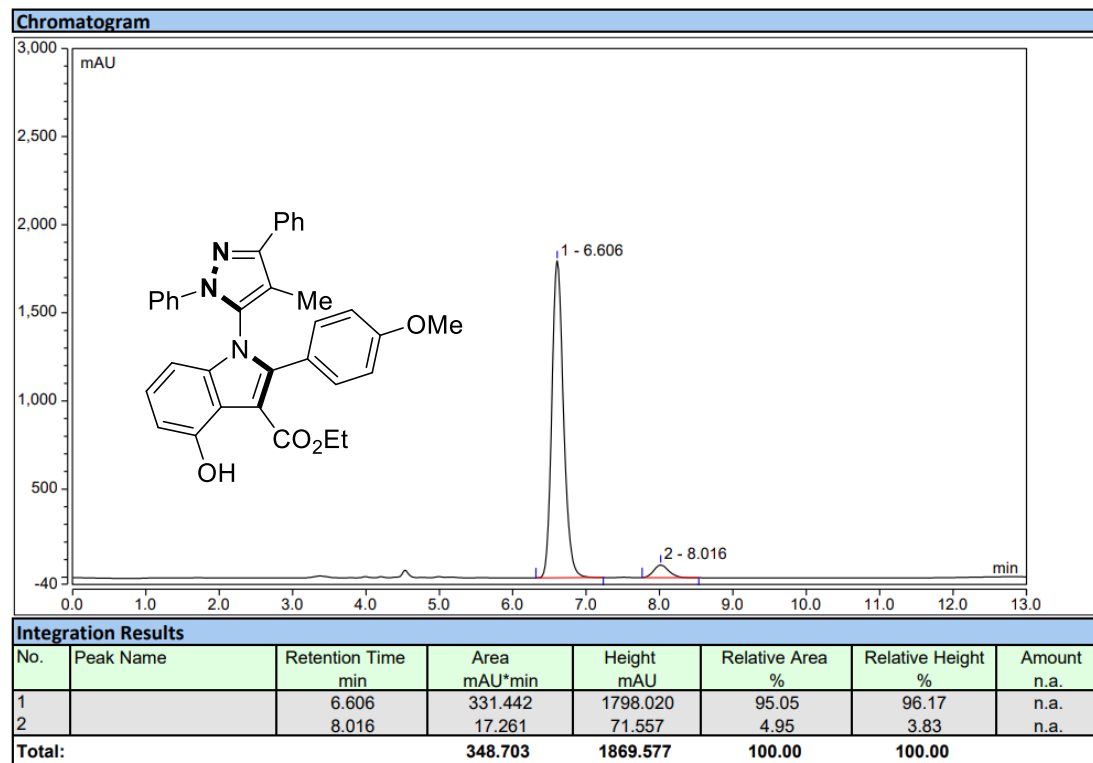


4aaf

Racemic:

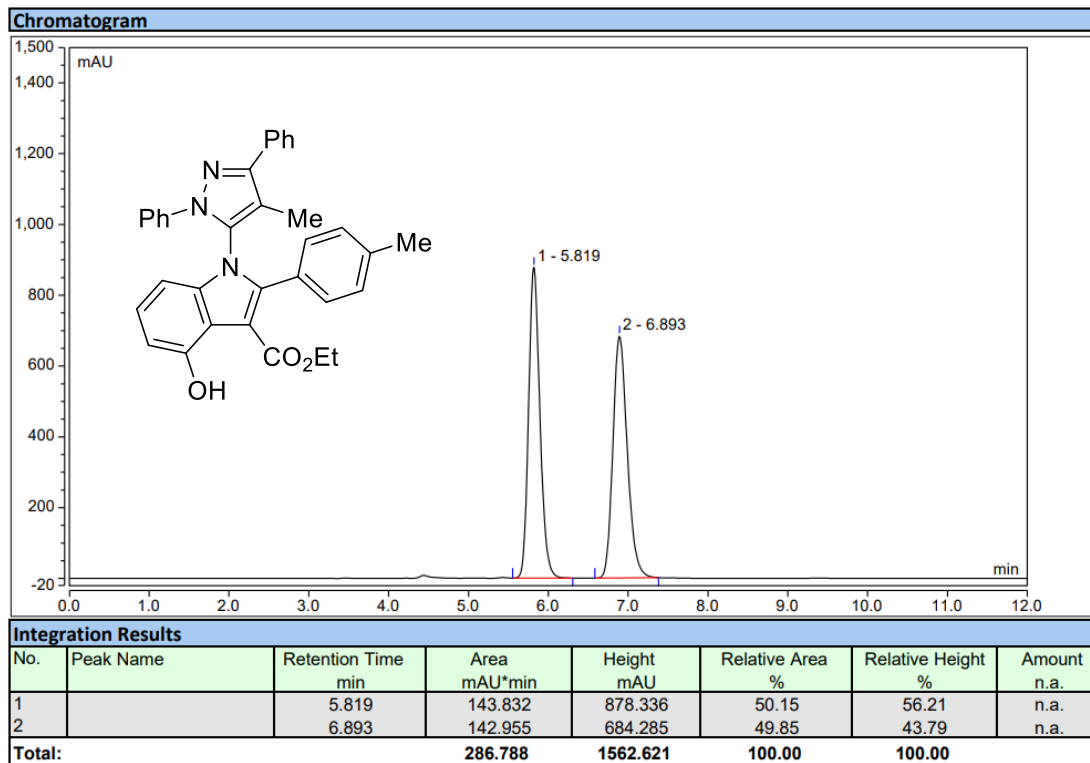


Enantioselective:

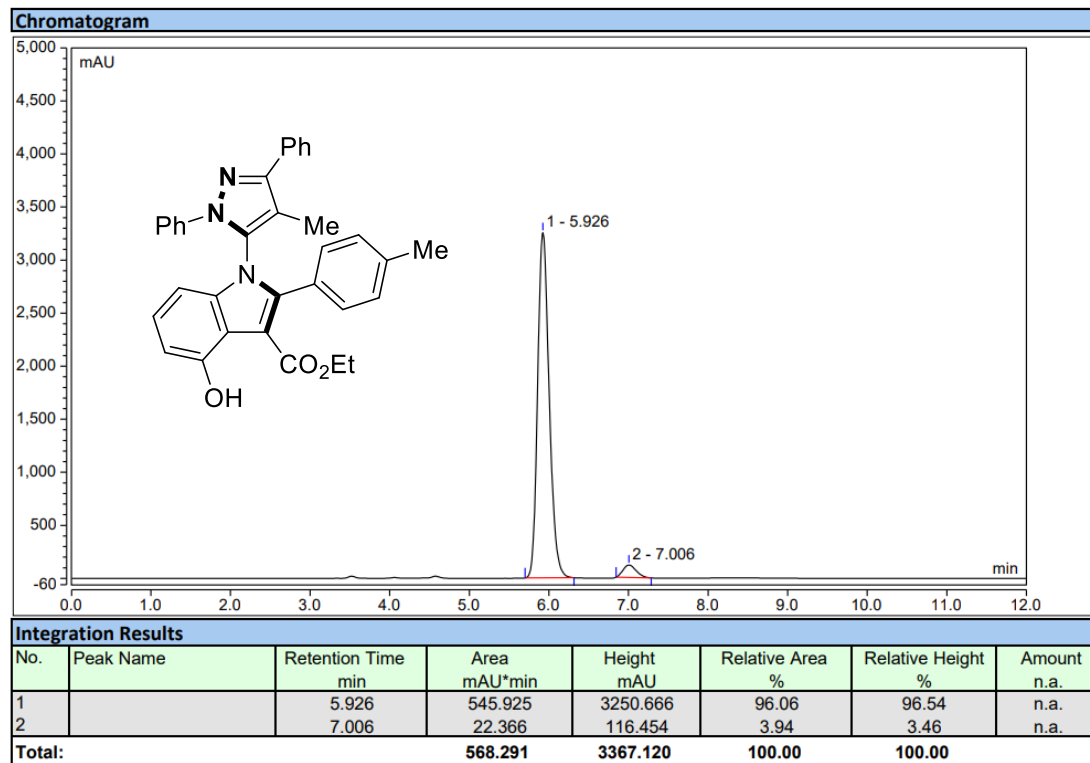


4aag

Racemic:

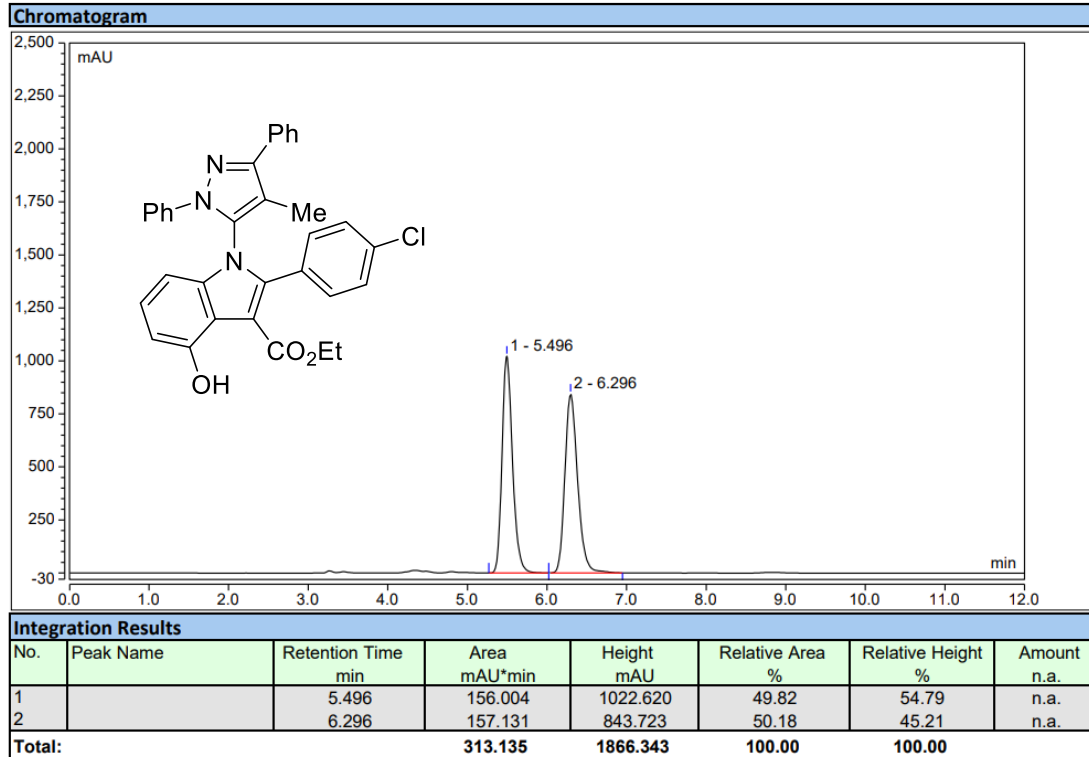


Enantioselective:

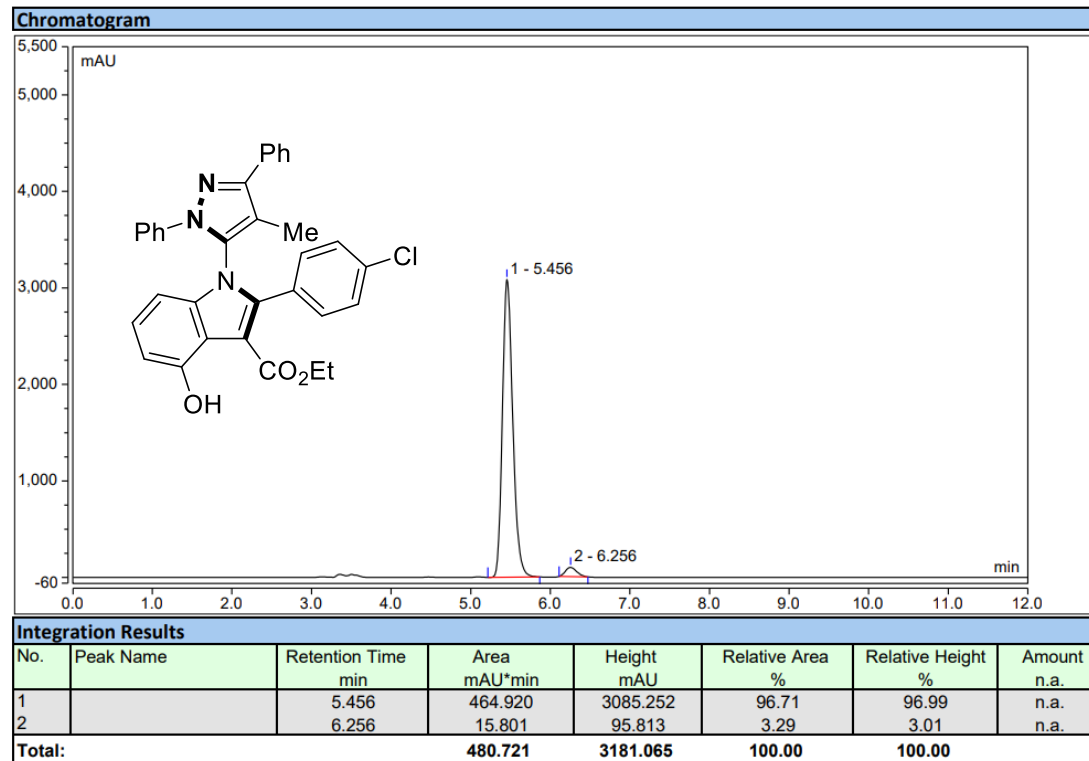


4aah

Racemic:

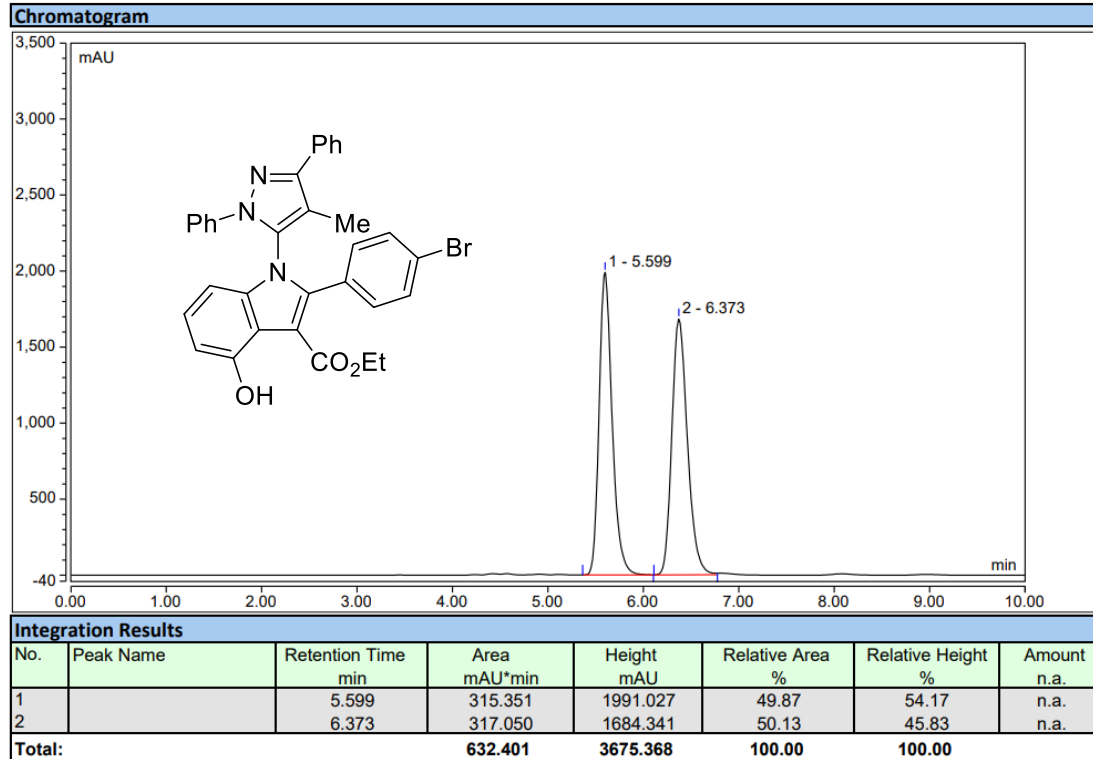


Enantioselective:

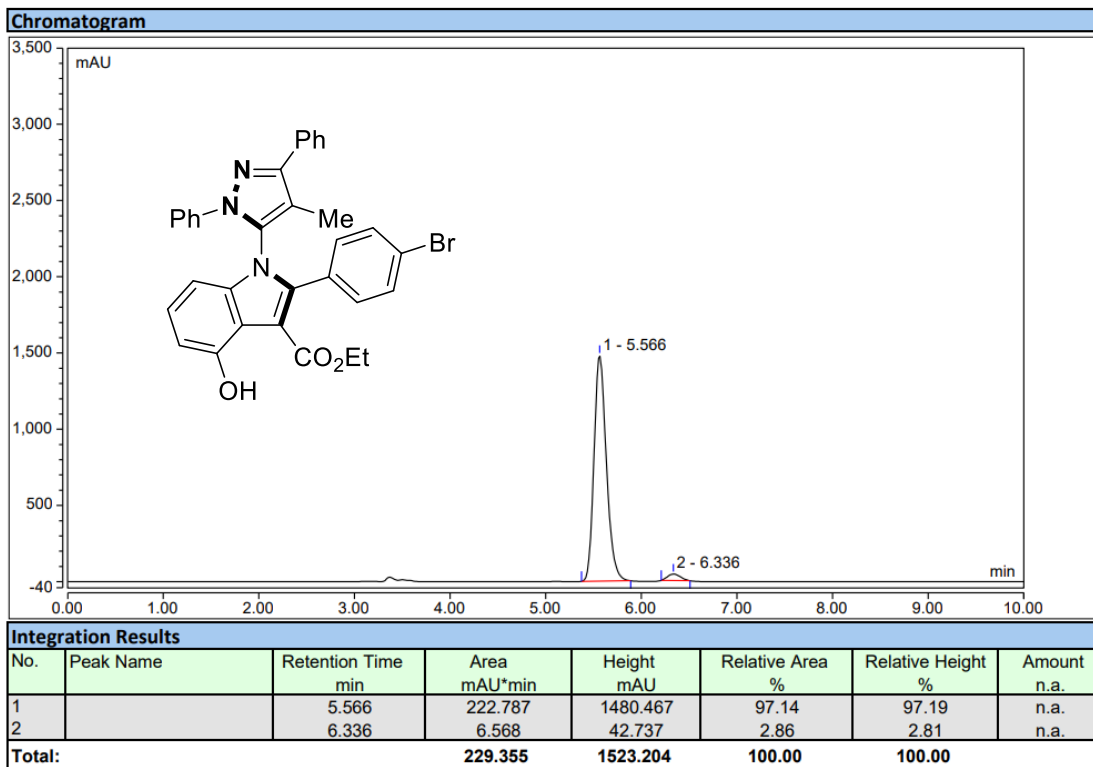


4aai

Racemic:

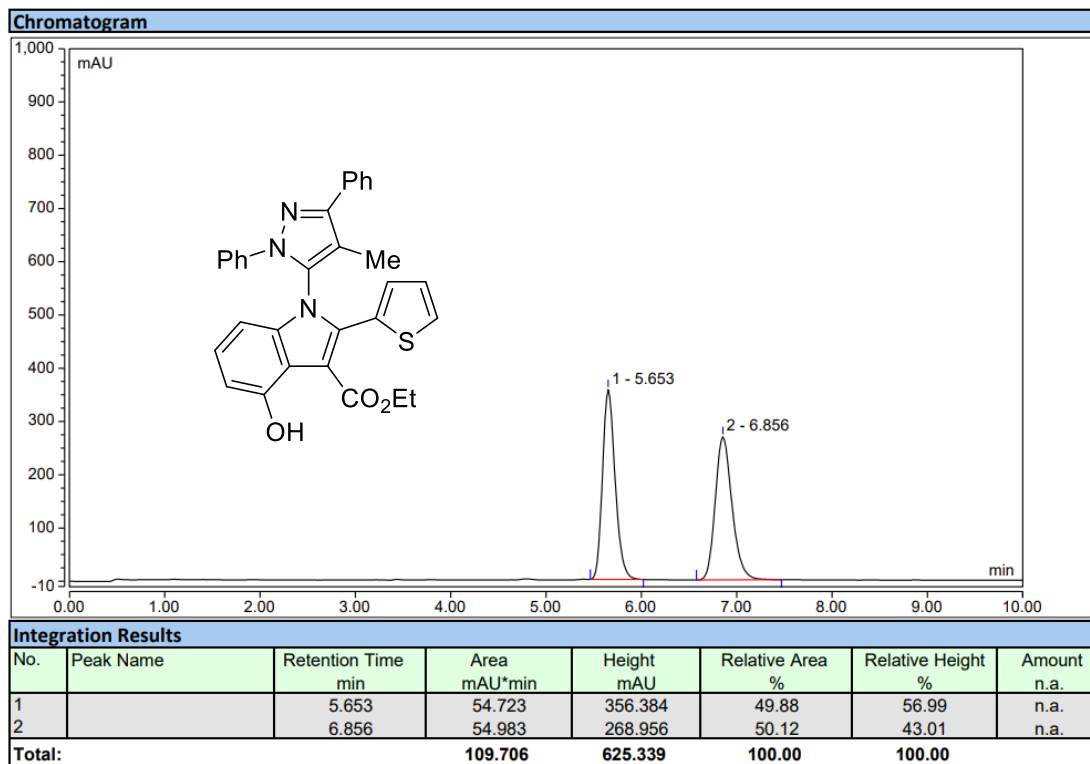


Enantioselective:

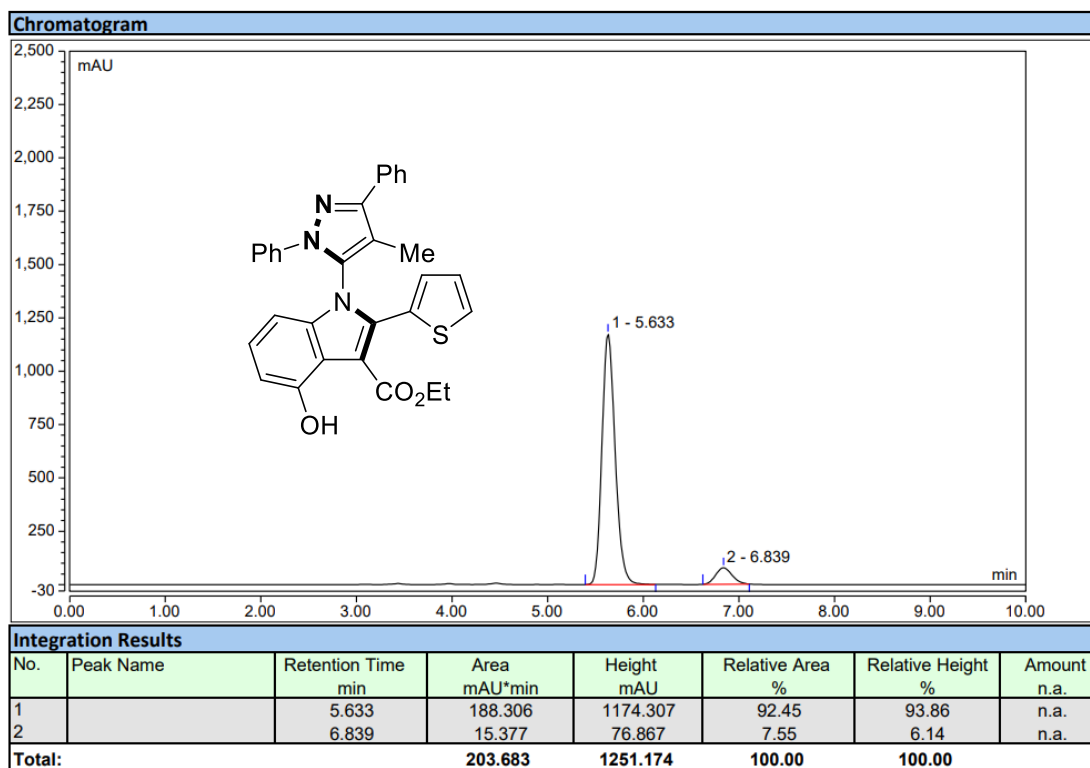


4aaj

Racemic:

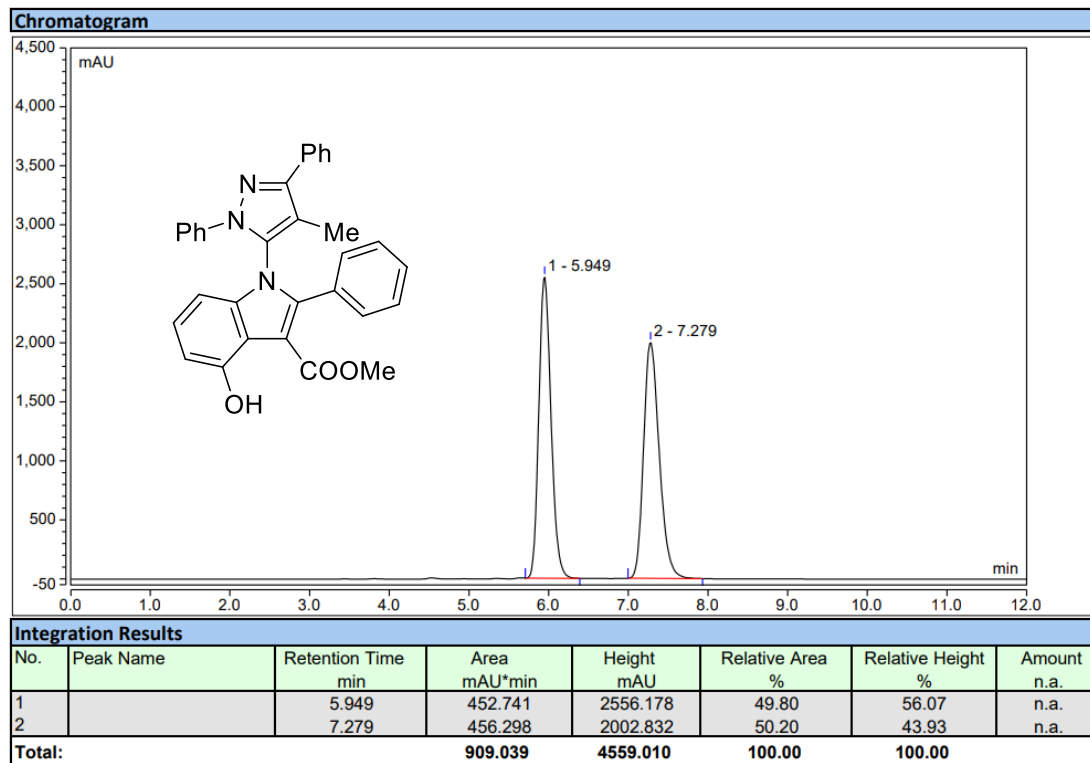


Enantioselective:

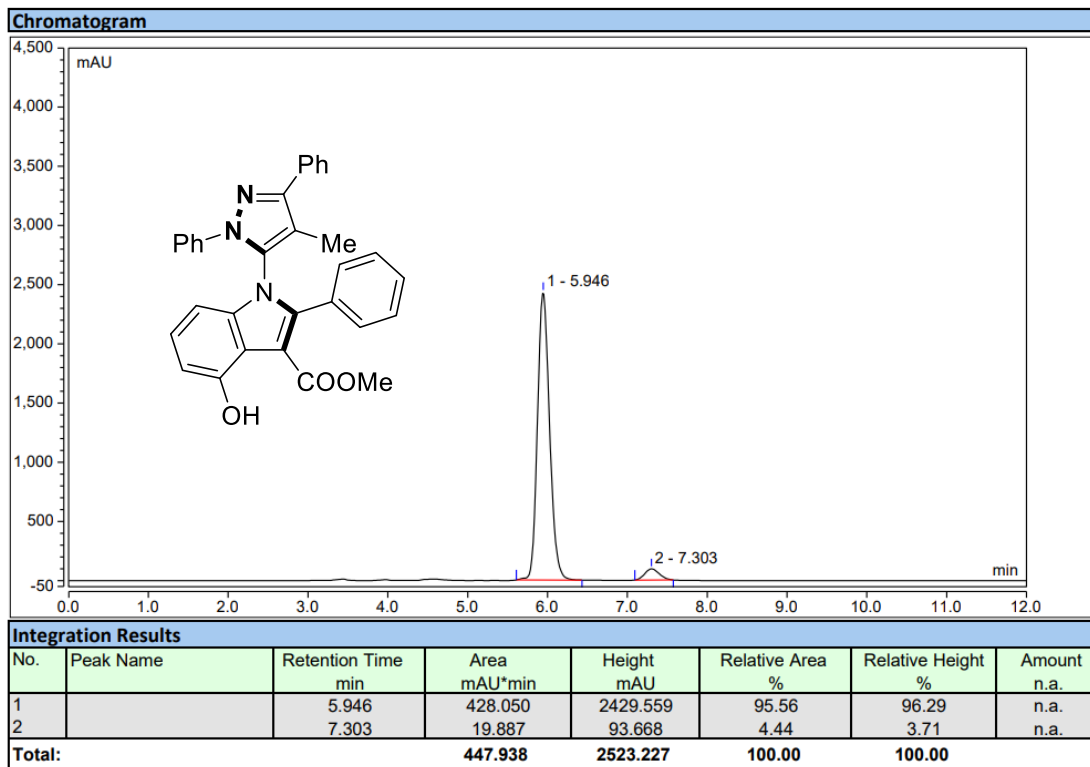


4aak

Racemic:

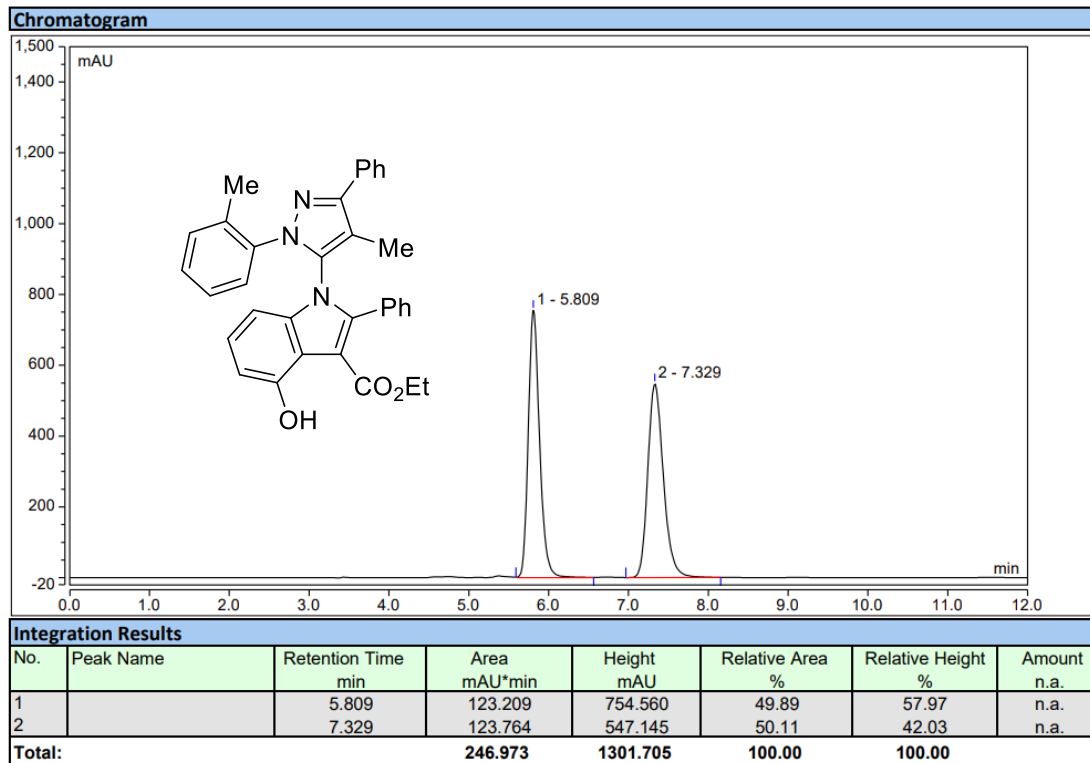


Enantioselective:

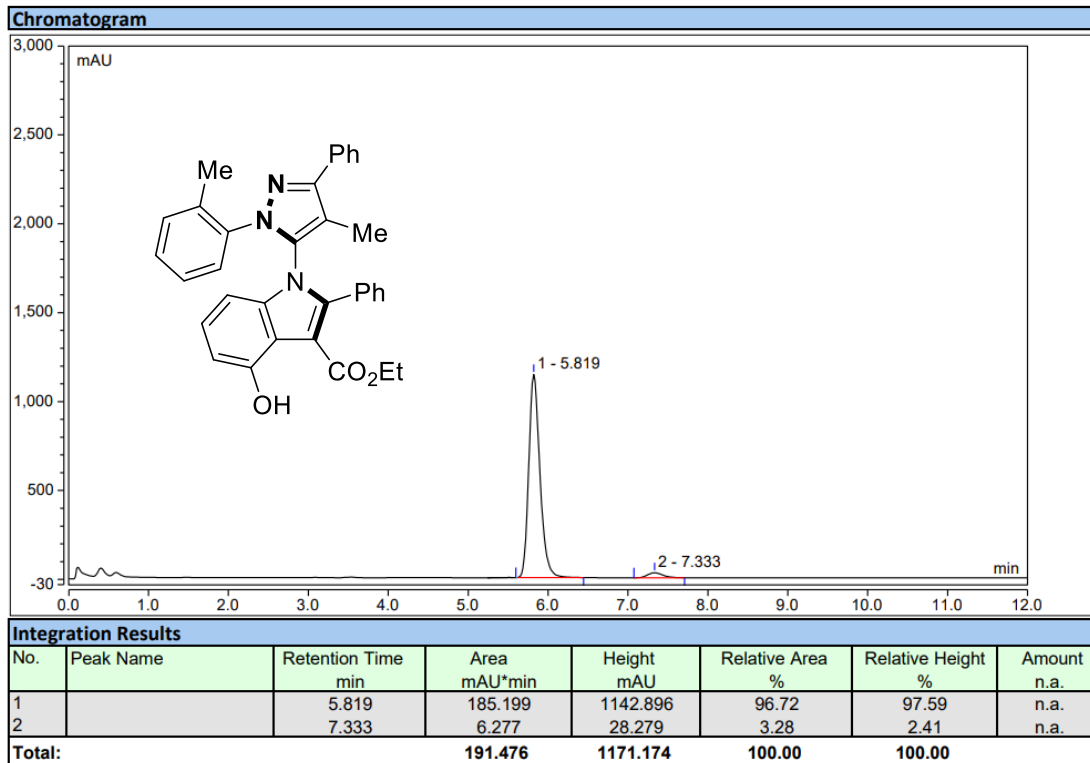


4bab

Racemic:

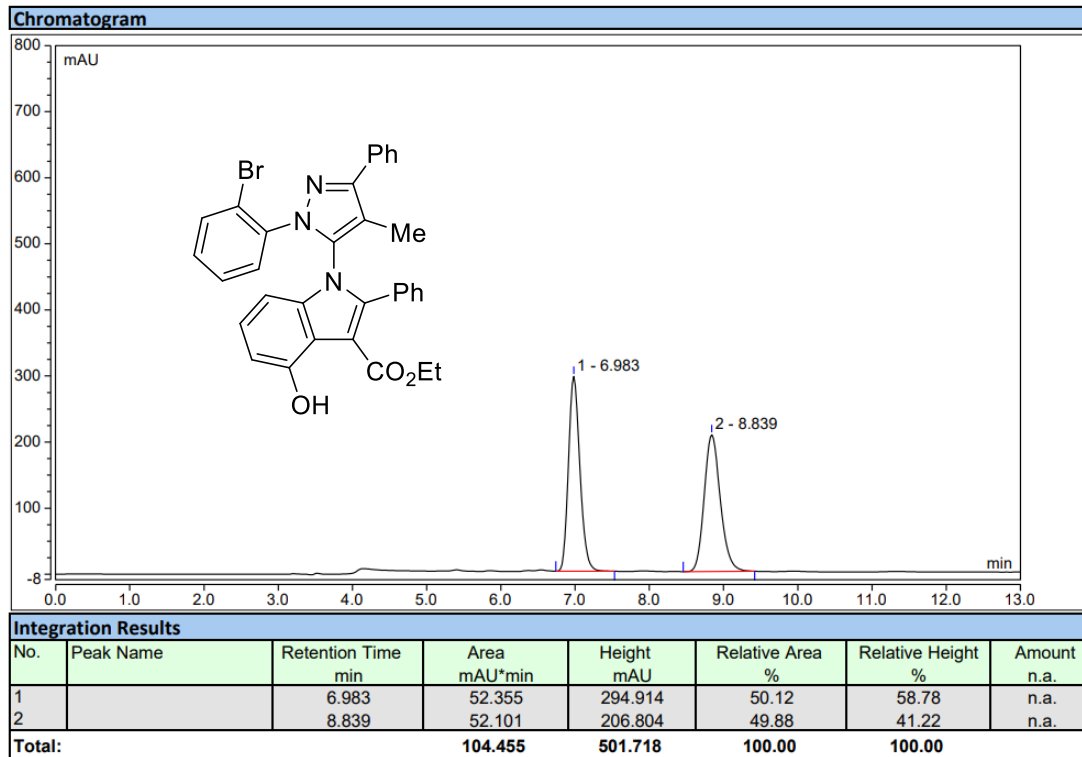


Enantioselective:

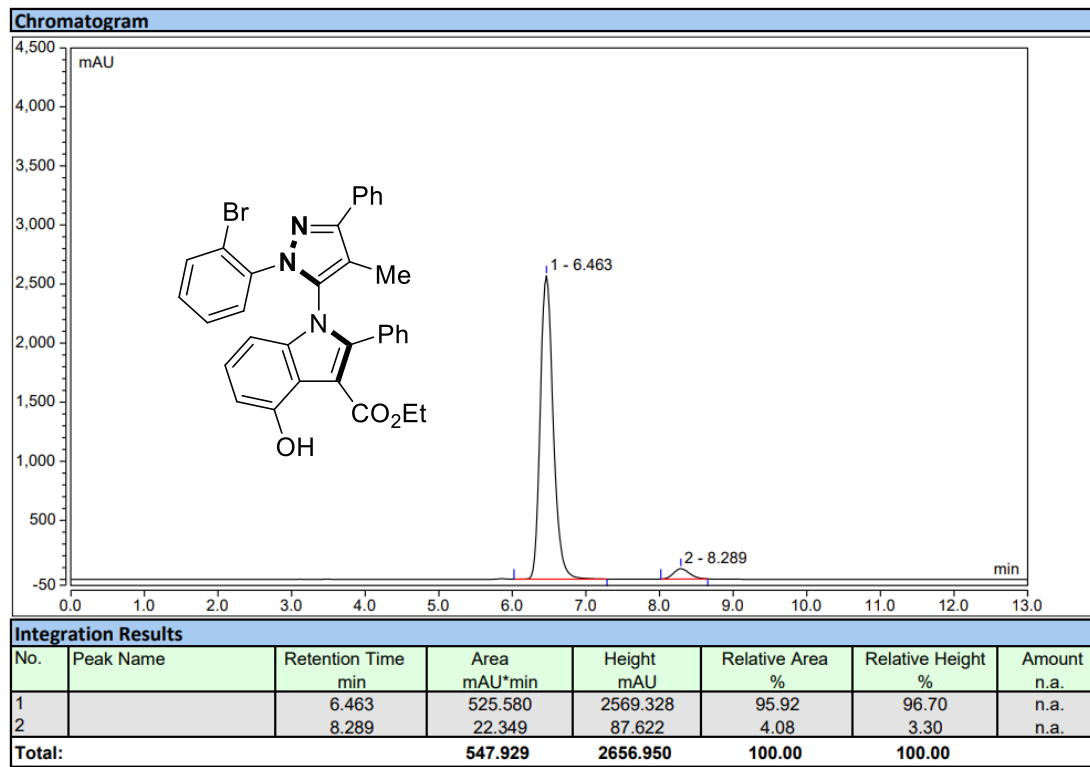


4cab

Racemic:

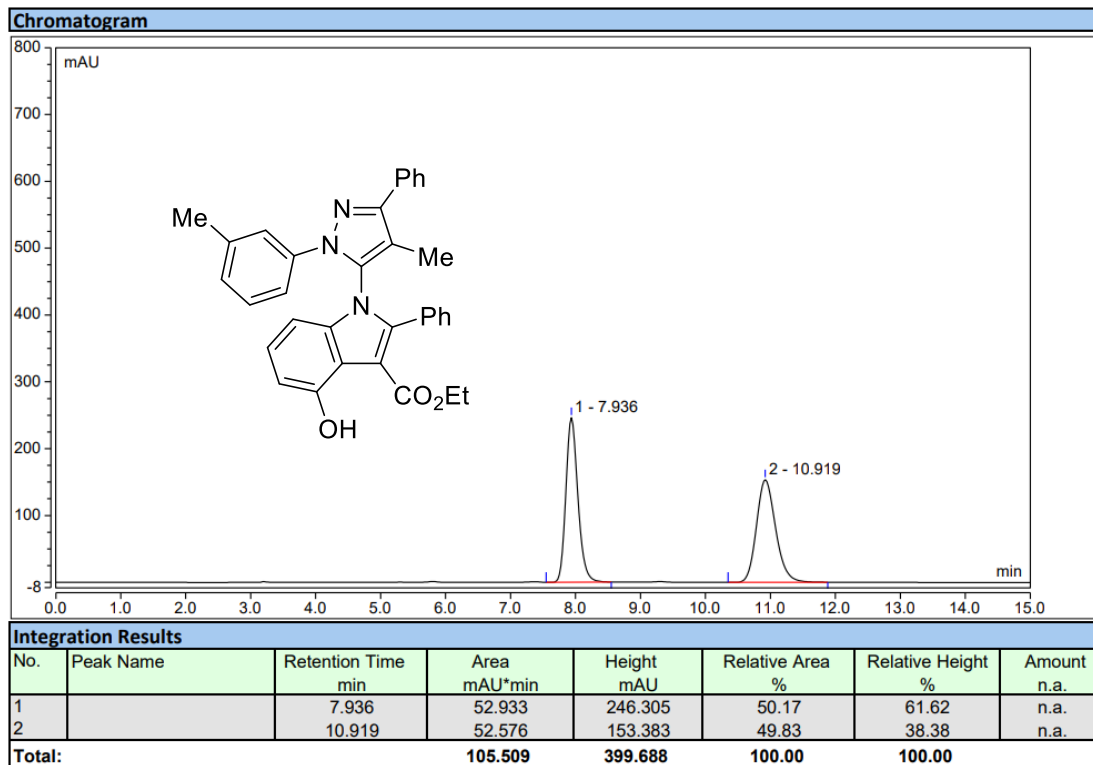


Enantioselective:

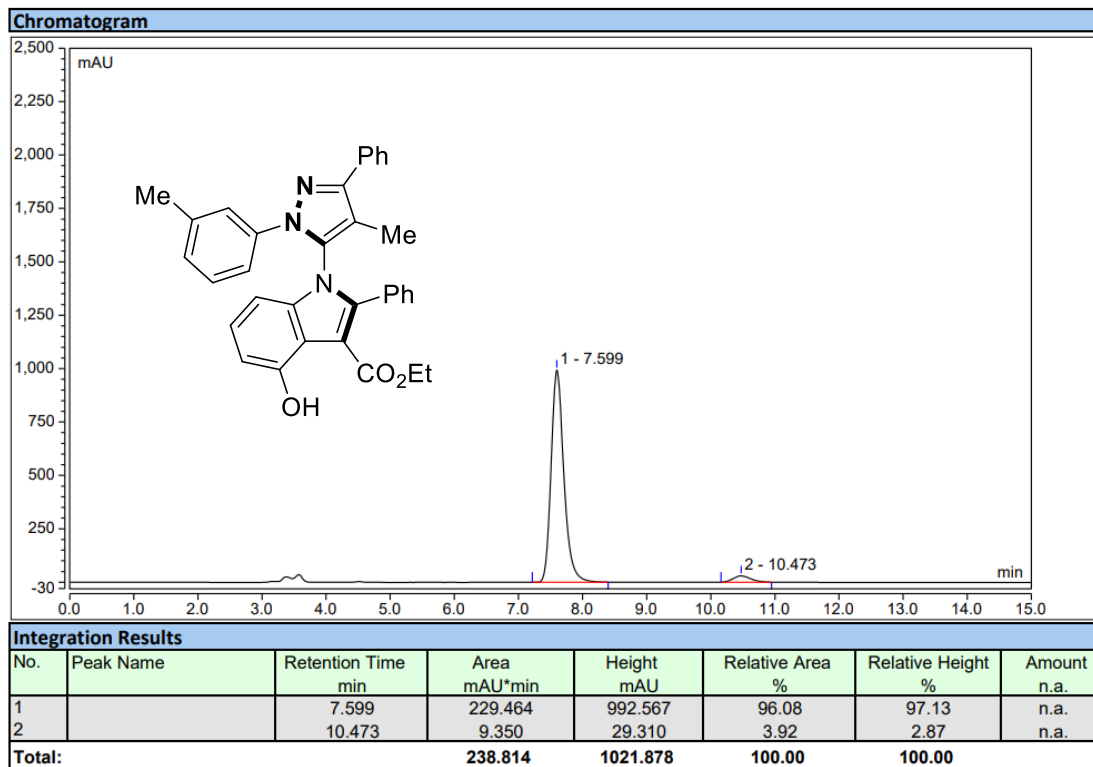


4dab

Racemic:

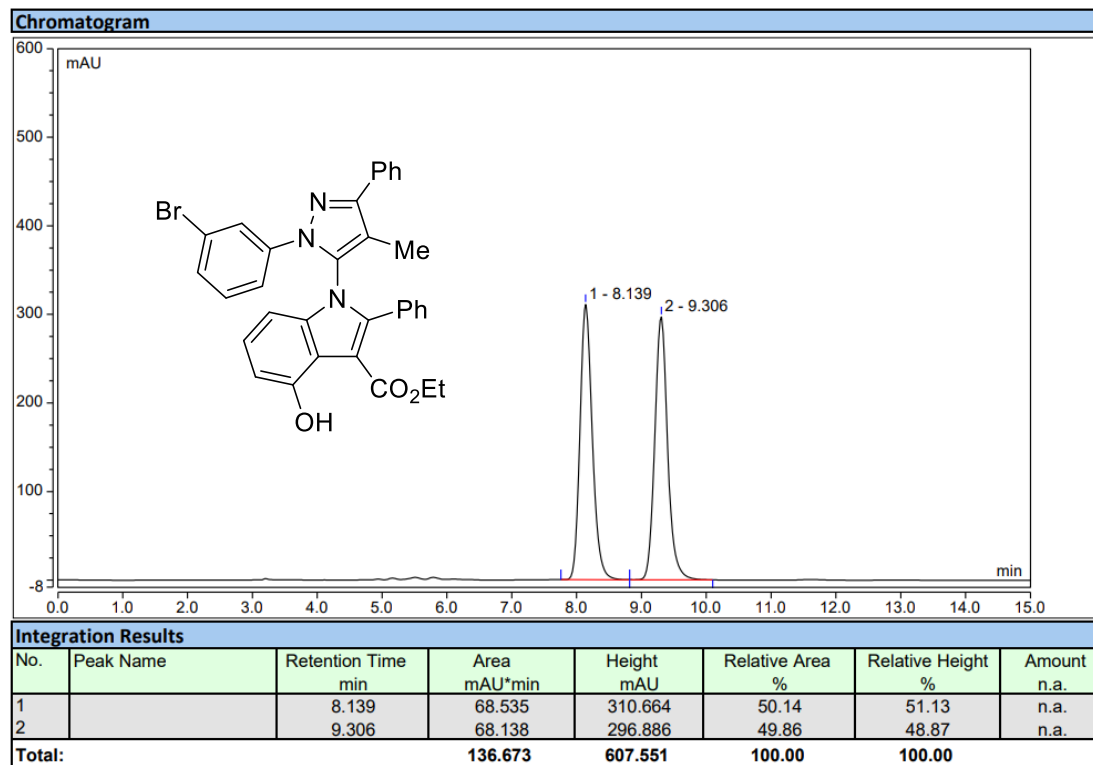


Enantioselective:

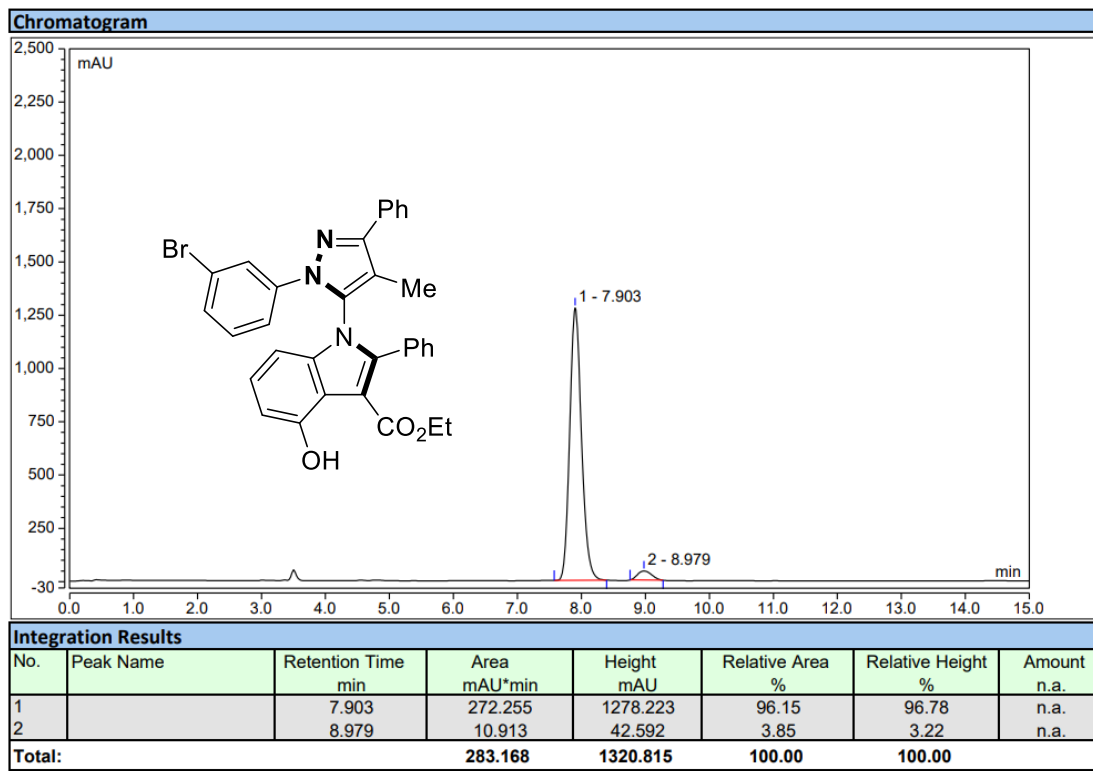


4eab

Racemic:

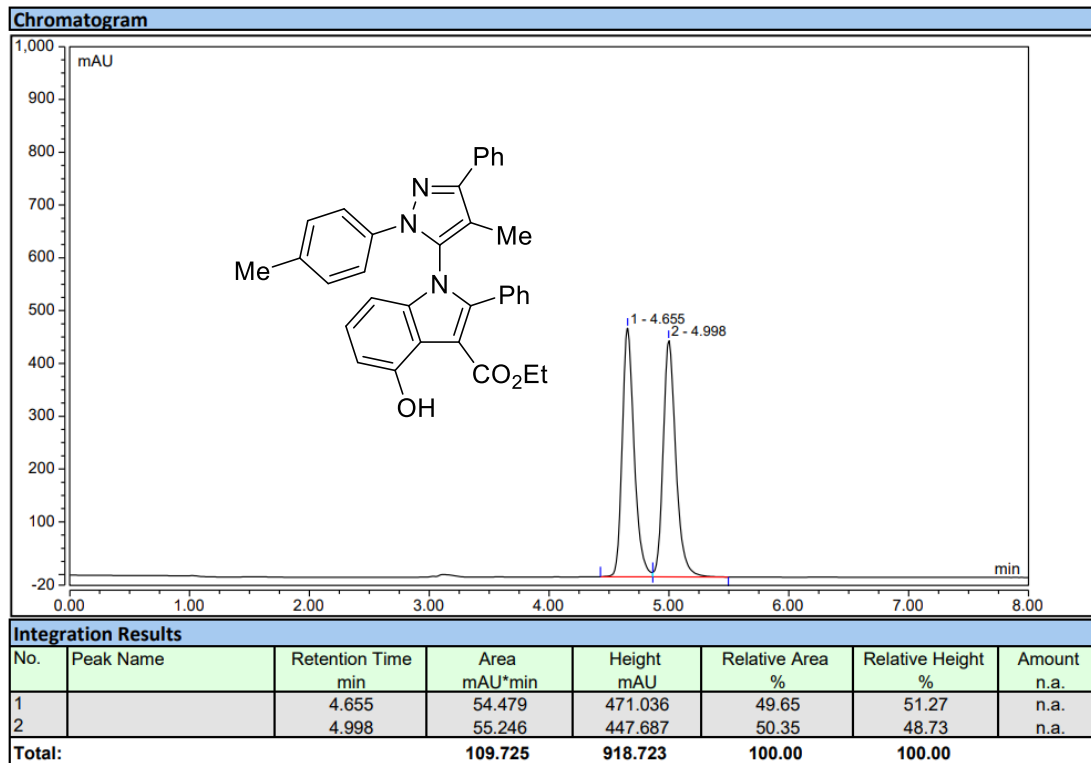


Enantioselective:

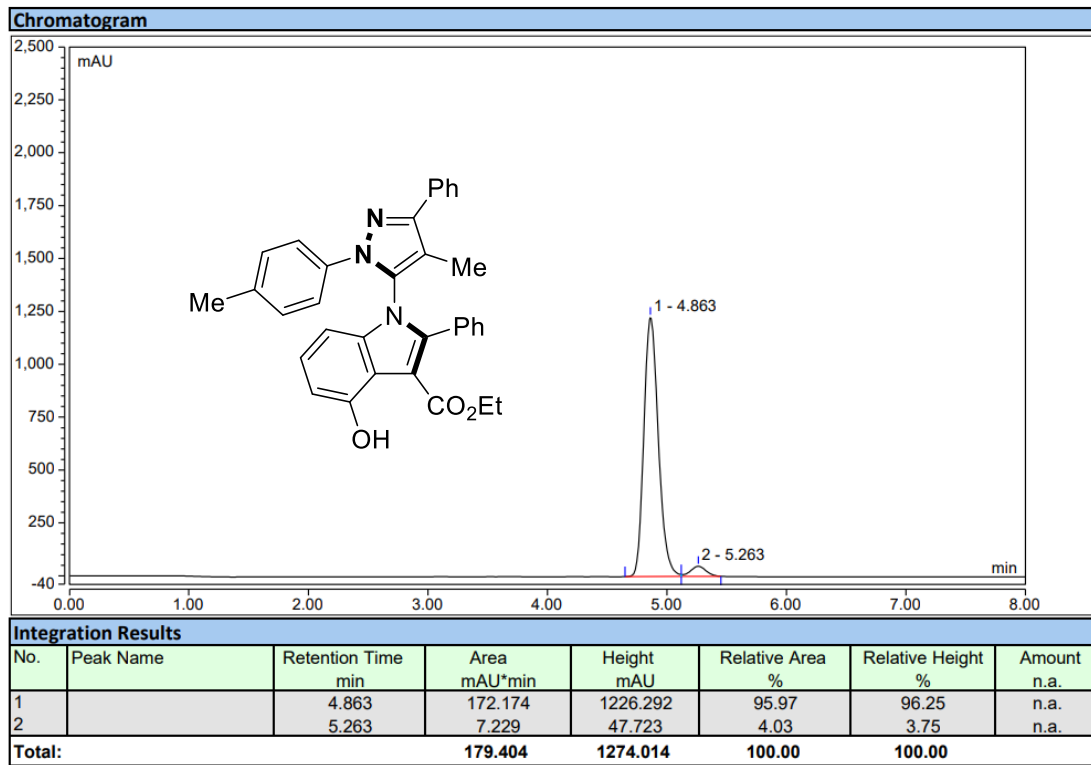


4fab

Racemic:

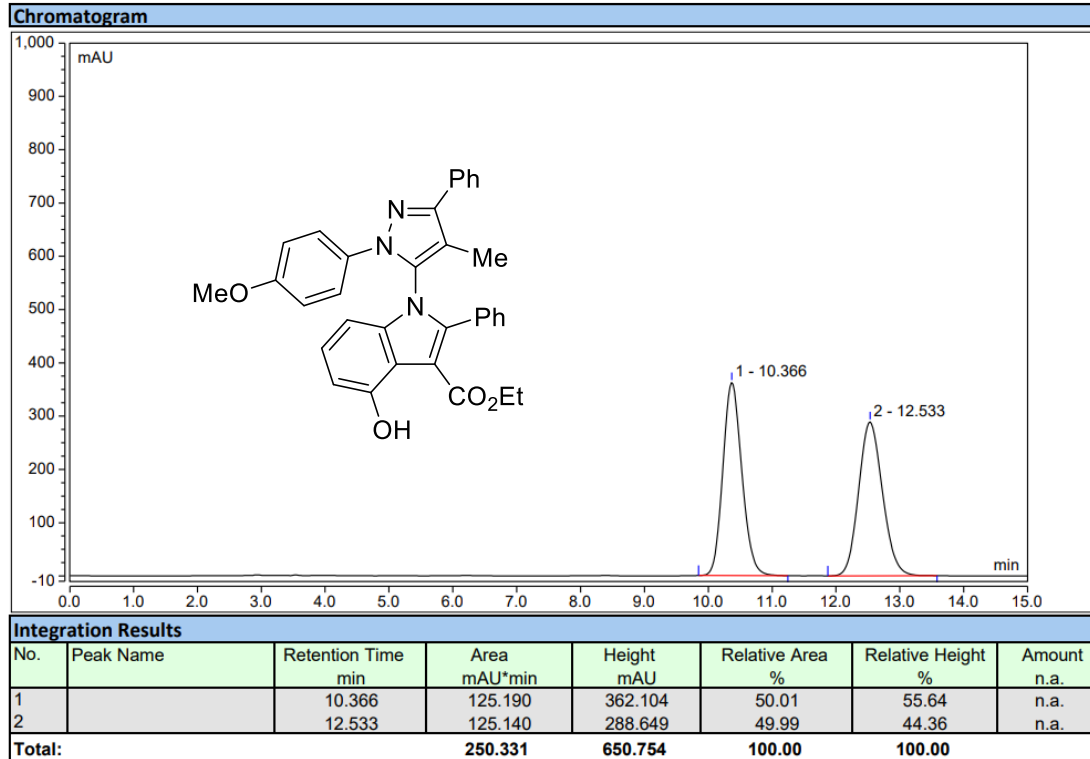


Enantioselective:

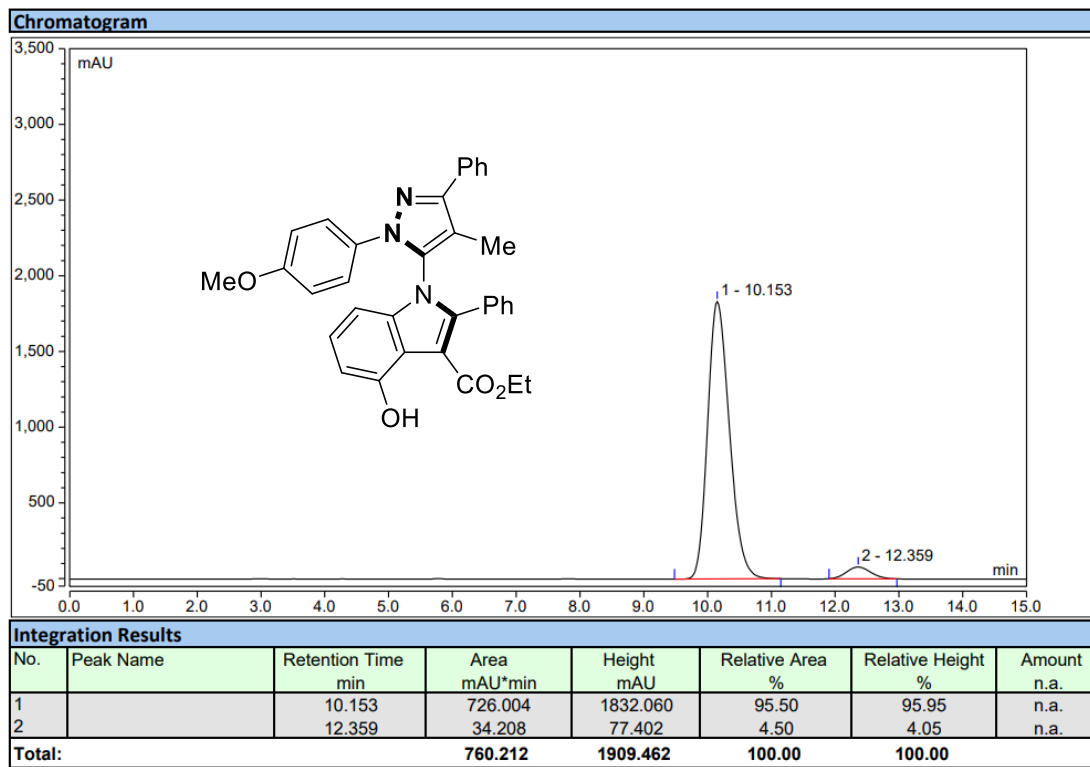


4gab

Racemic:

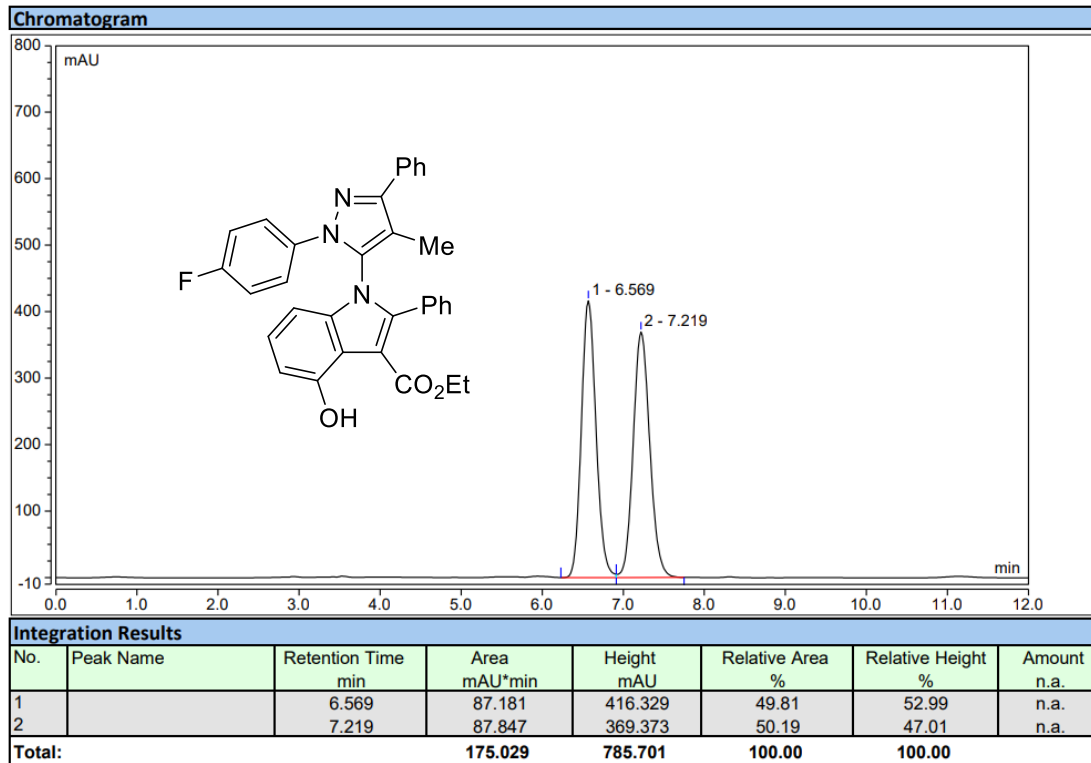


Enantioselective:

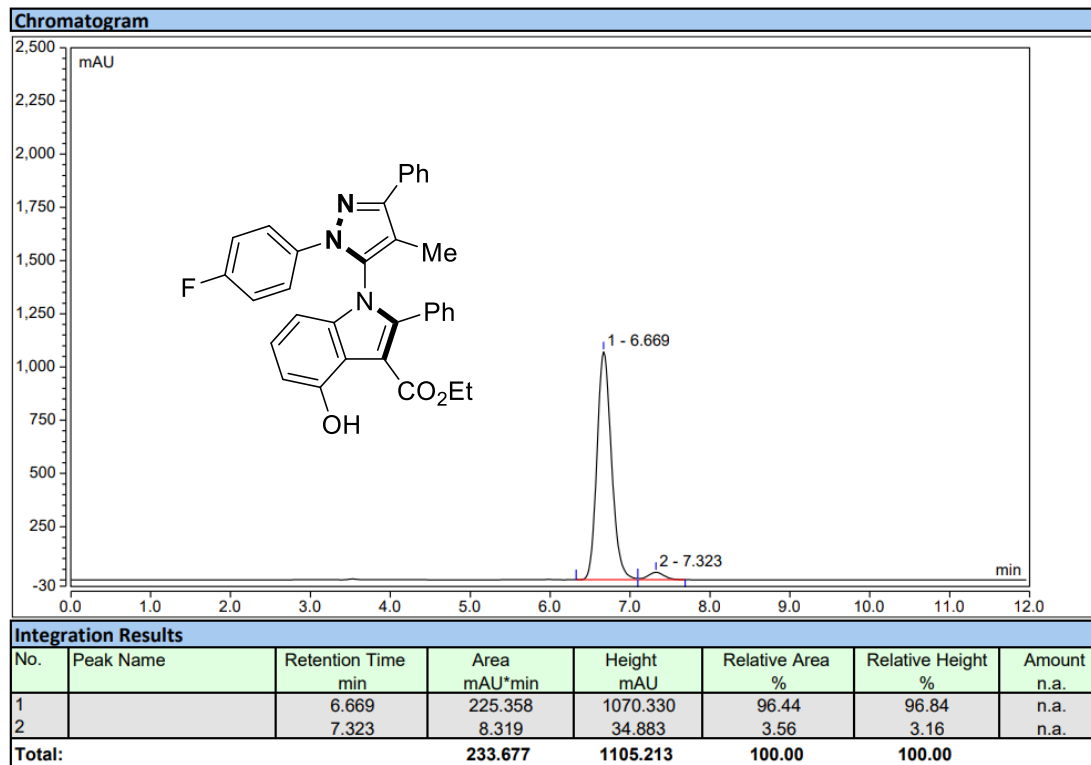


4hab

Racemic:

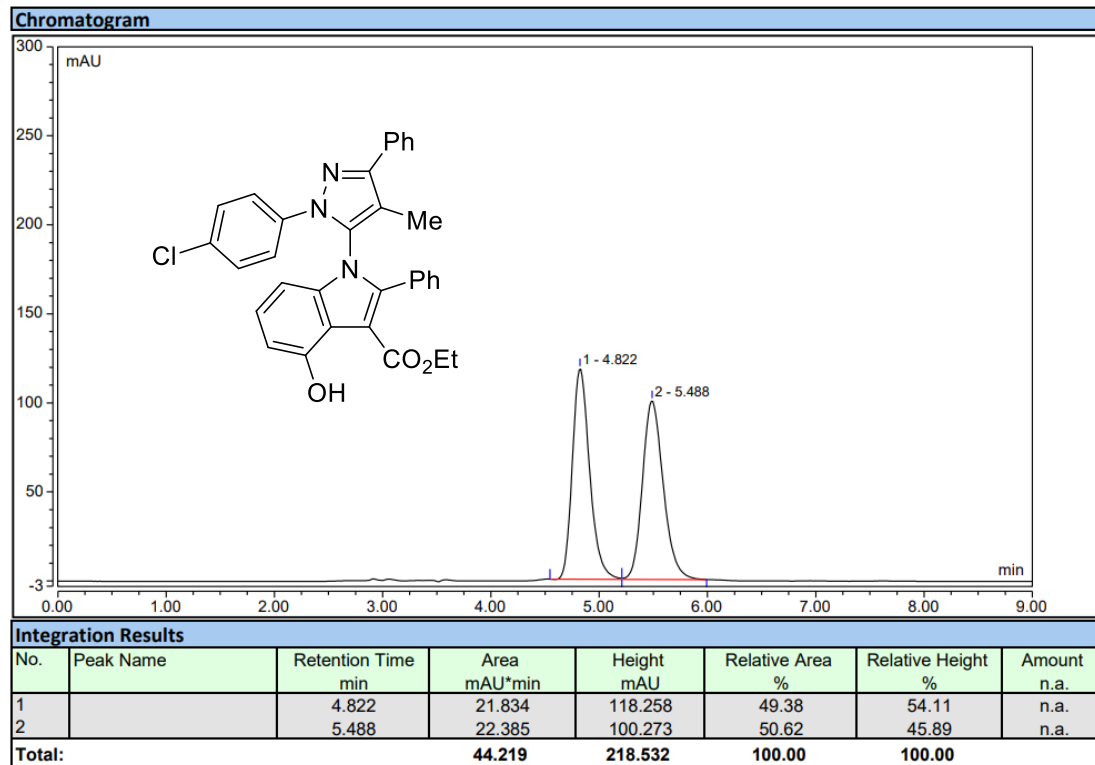


Enantioselective:

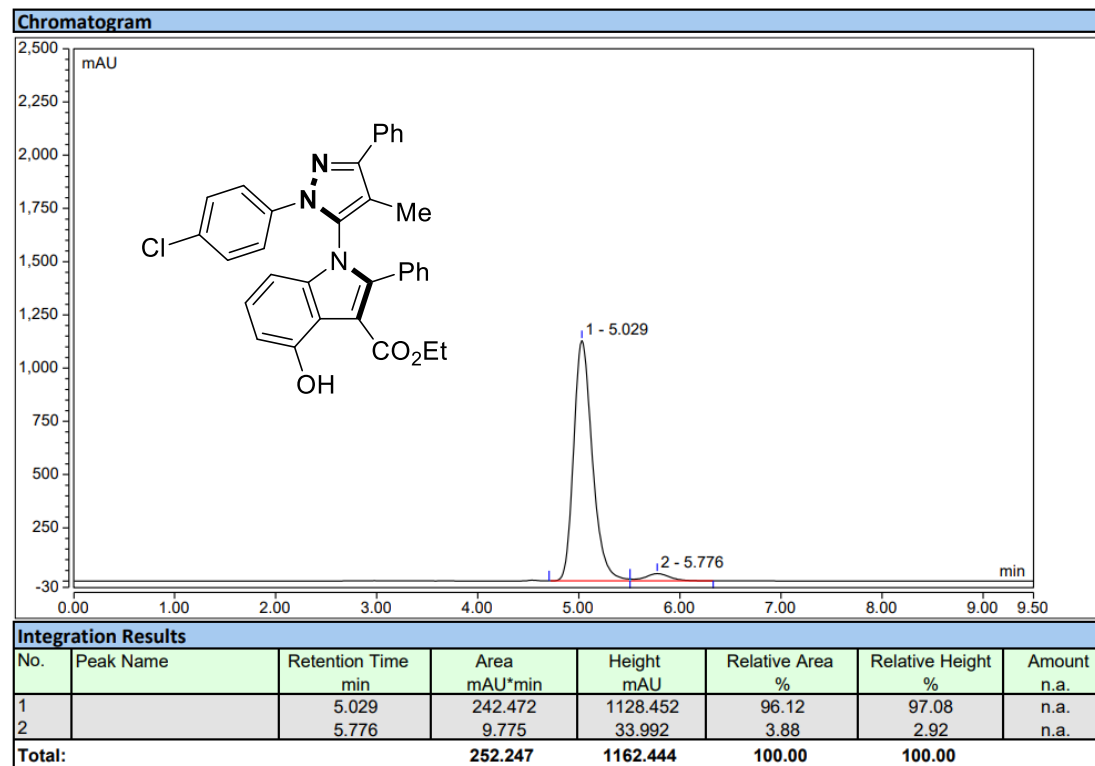


4iab

Racemic:

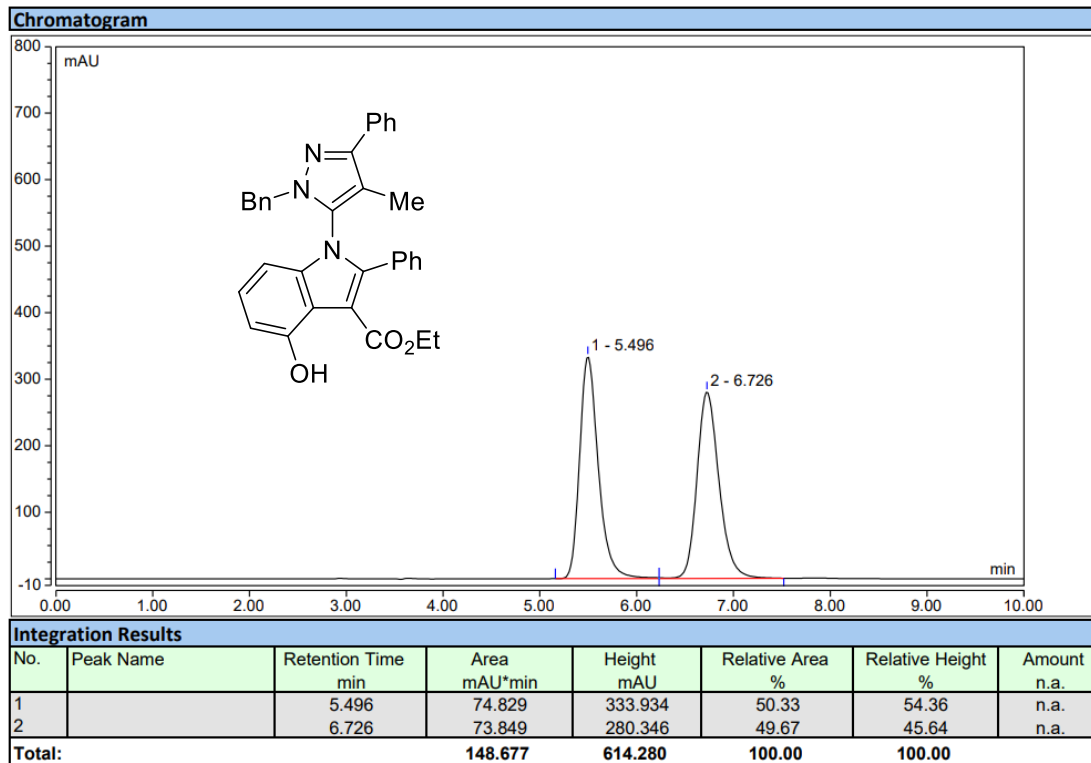


Enantioselective:

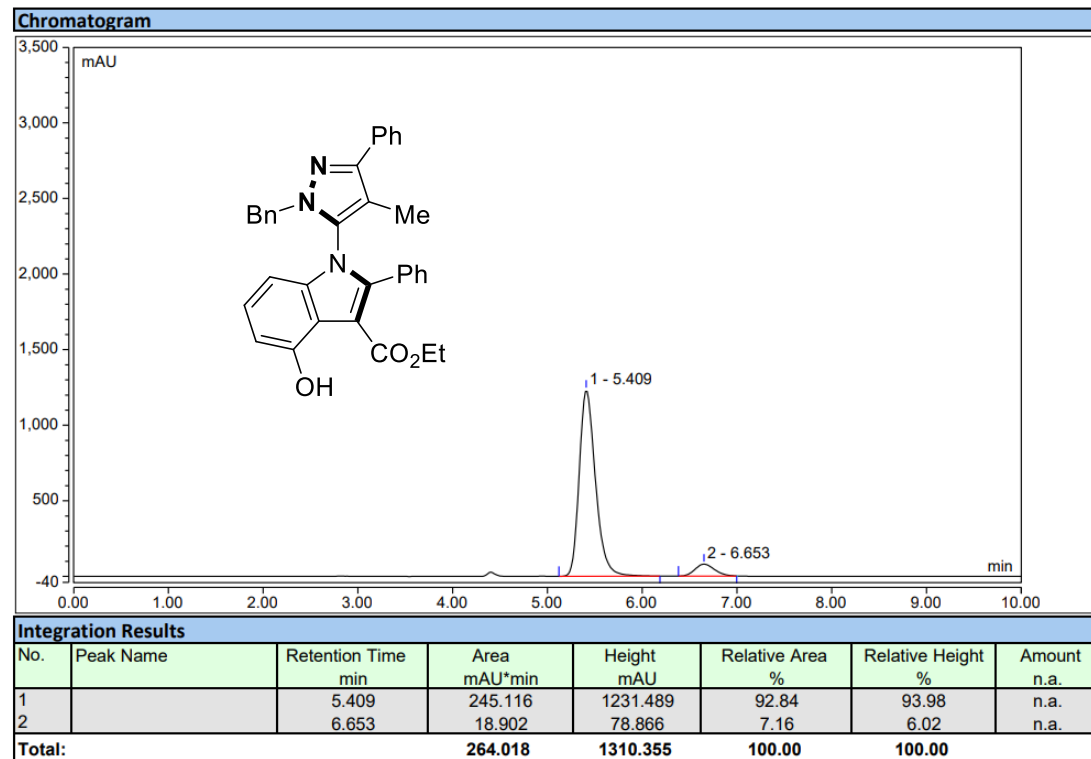


4jab

Racemic:

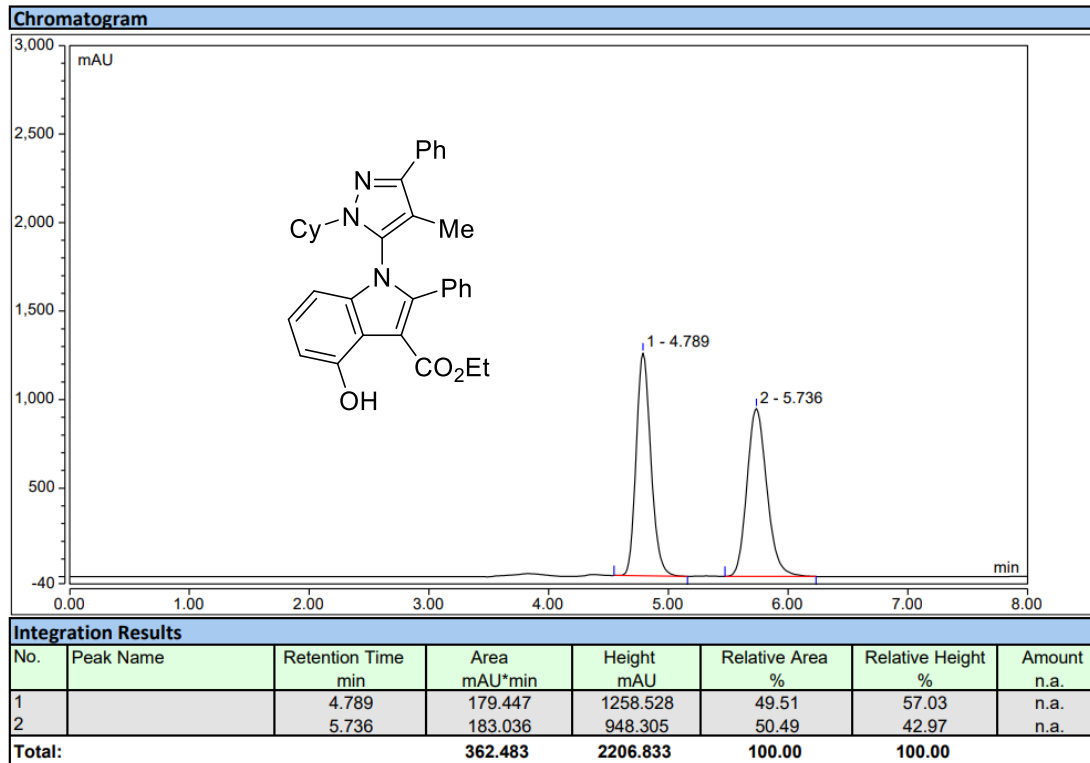


Enantioselective:

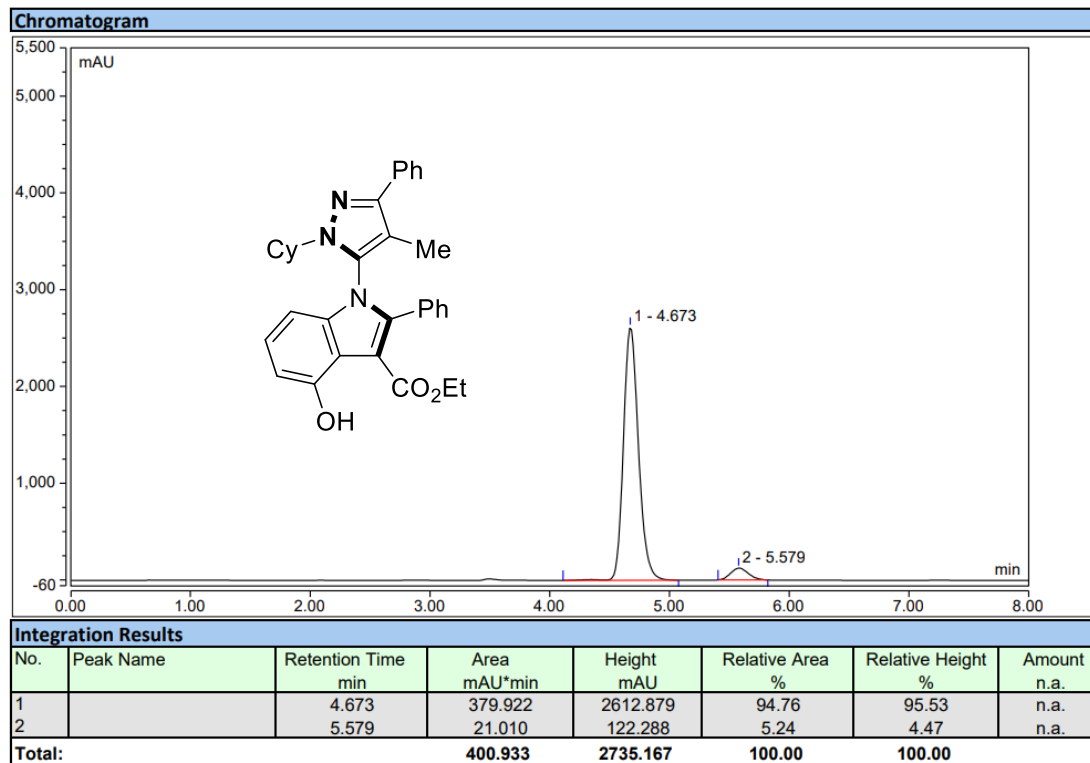


4kab

Racemic:

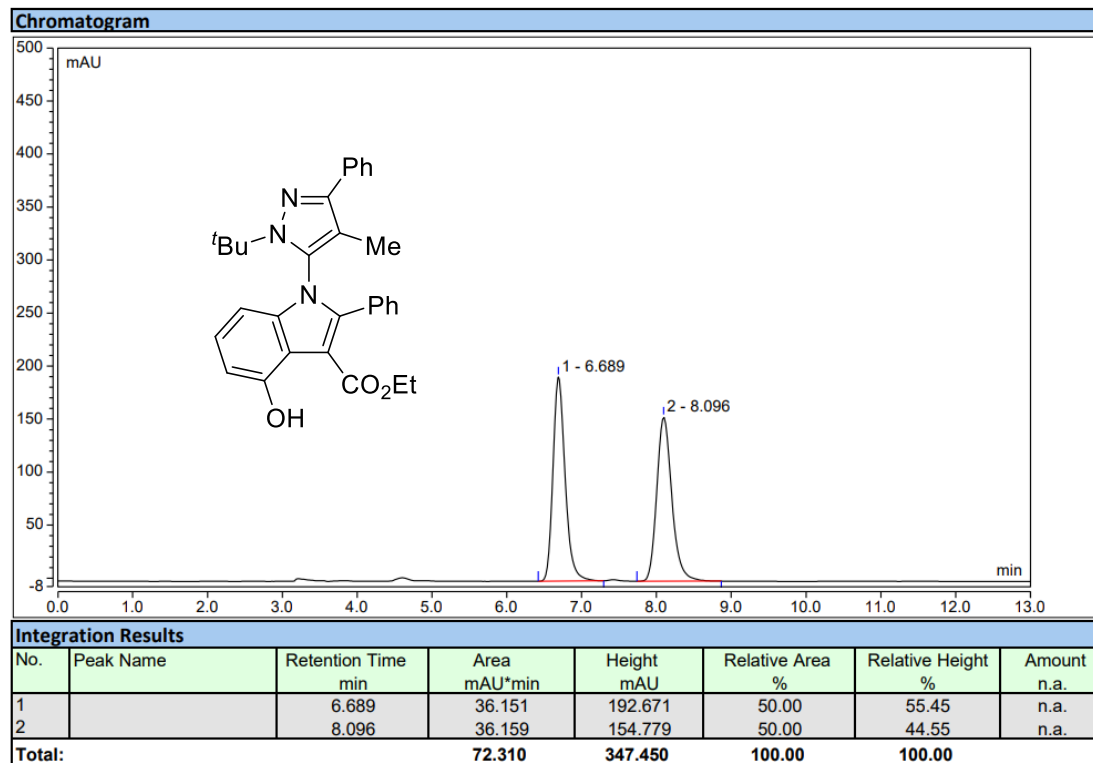


Enantioselective:

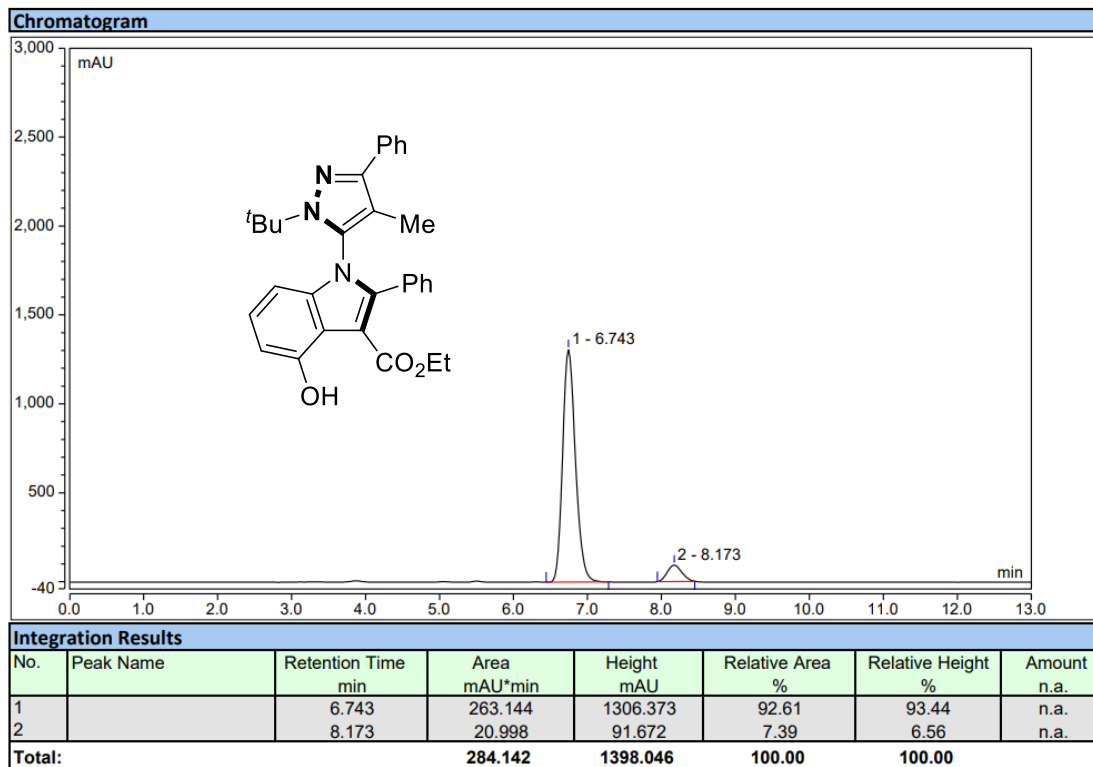


4lab

Racemic:

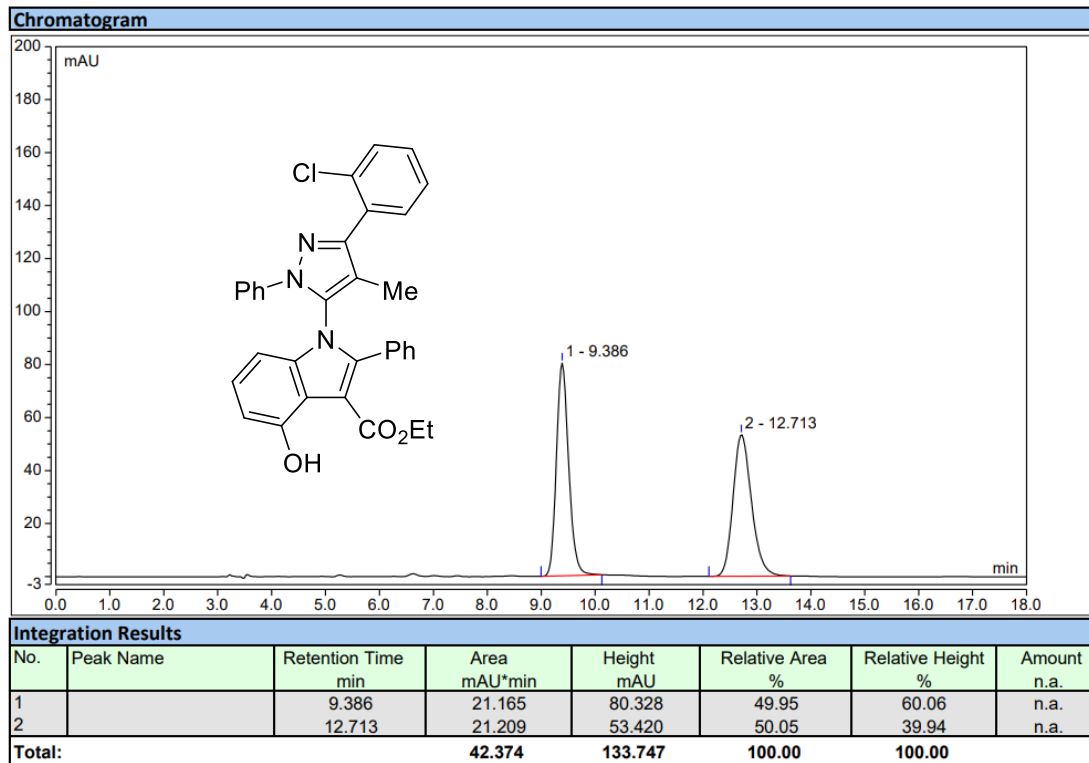


Enantioselective:

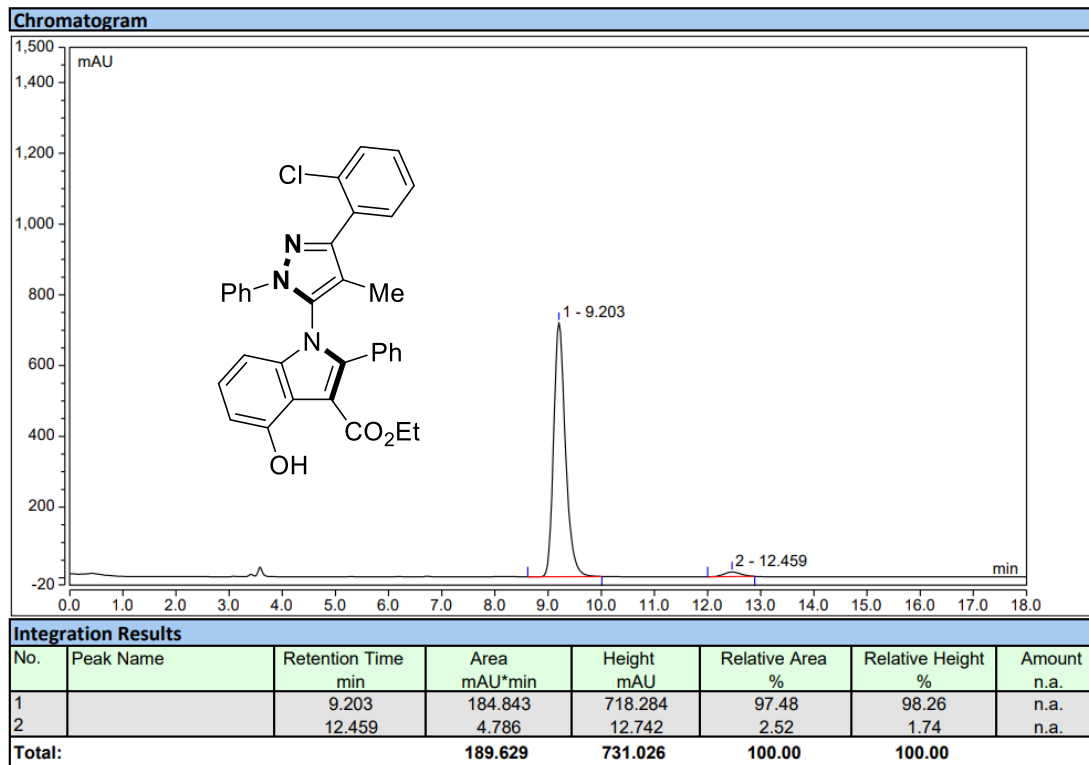


4mab

Racemic:

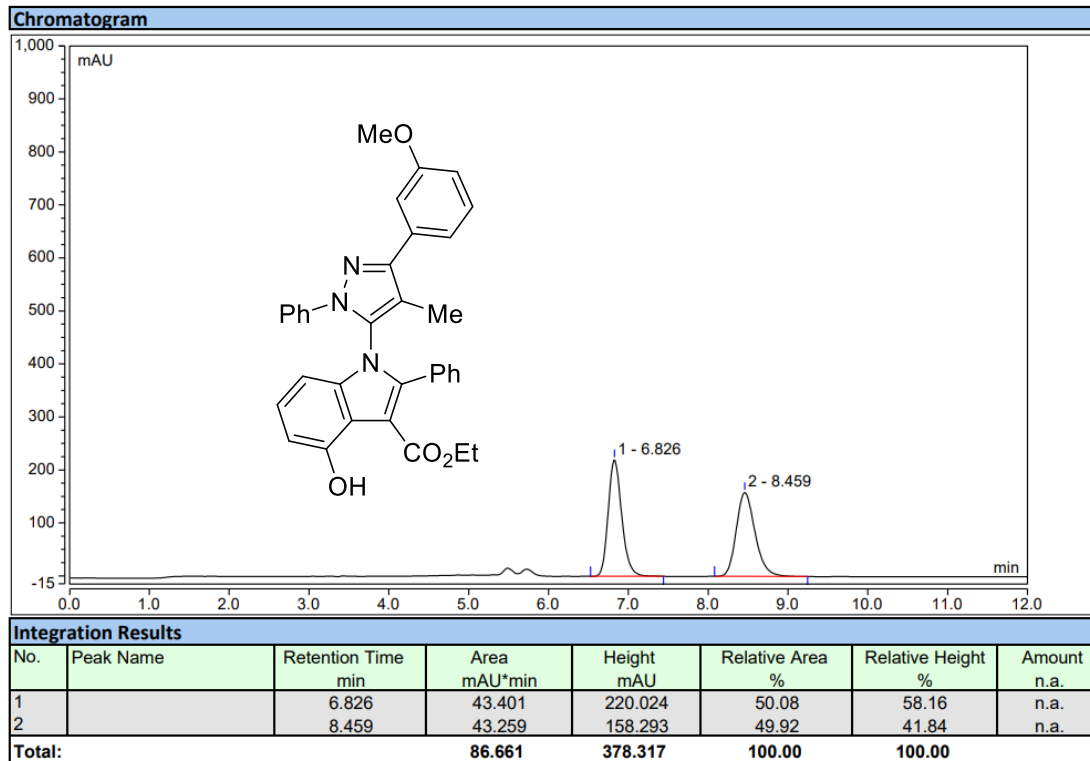


Enantioselective:

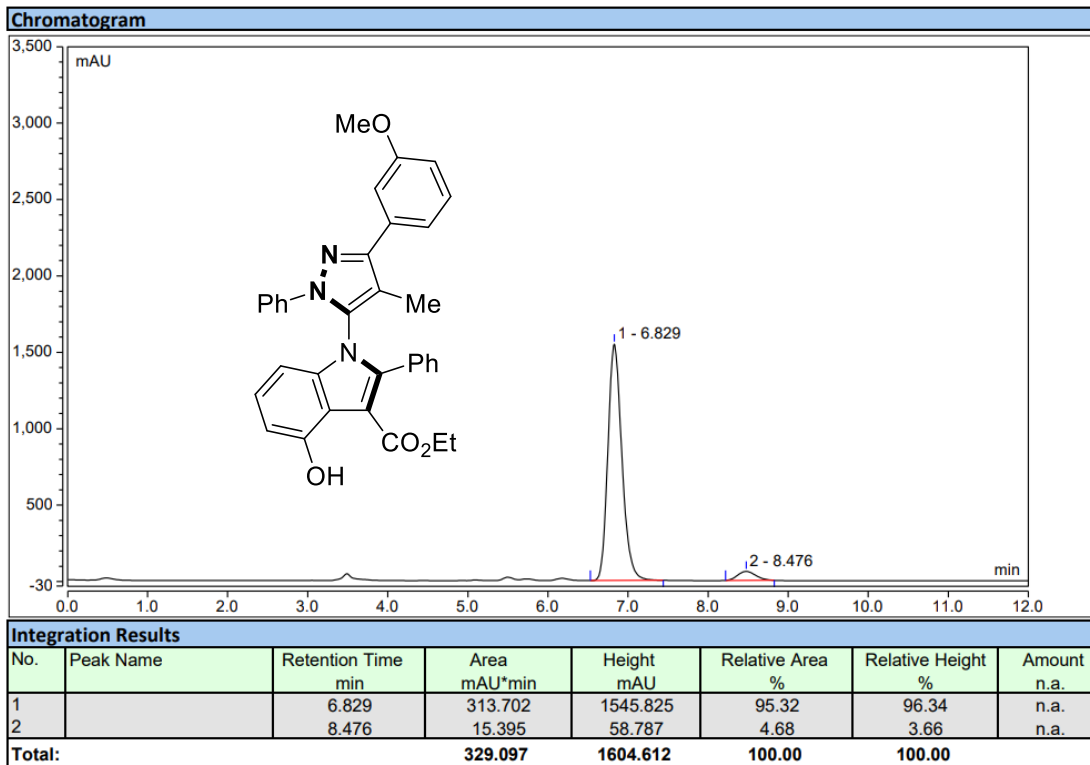


4nab

Racemic:

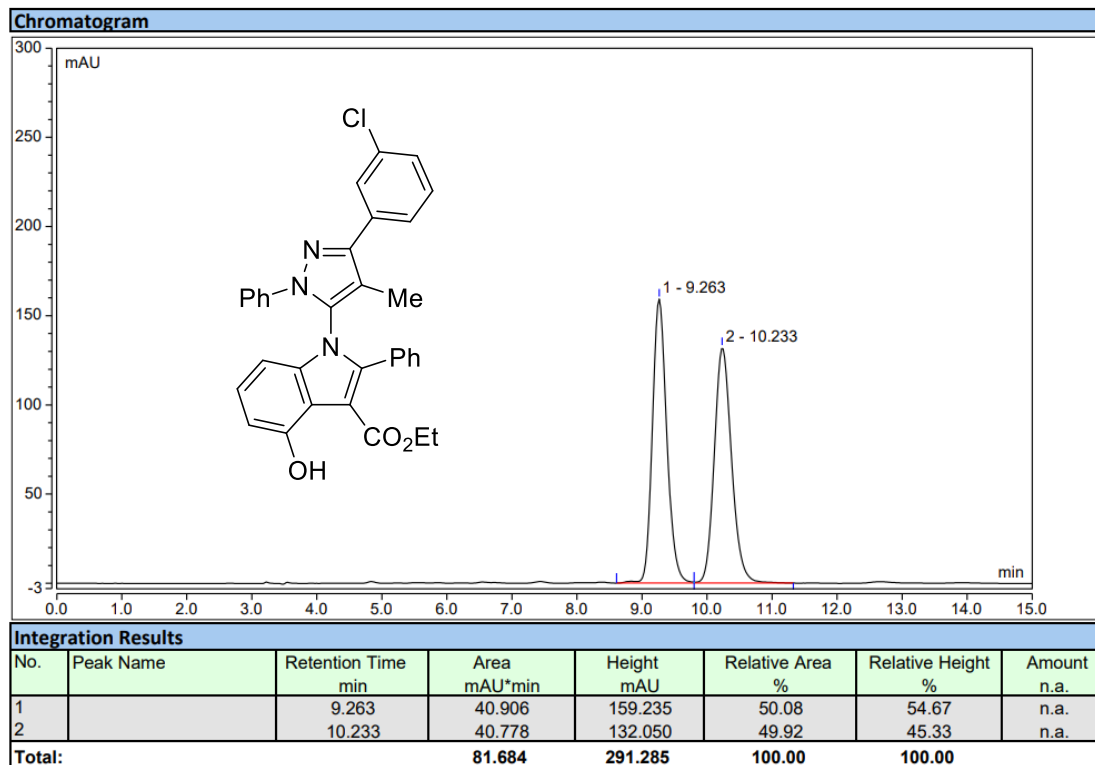


Enantioselective:

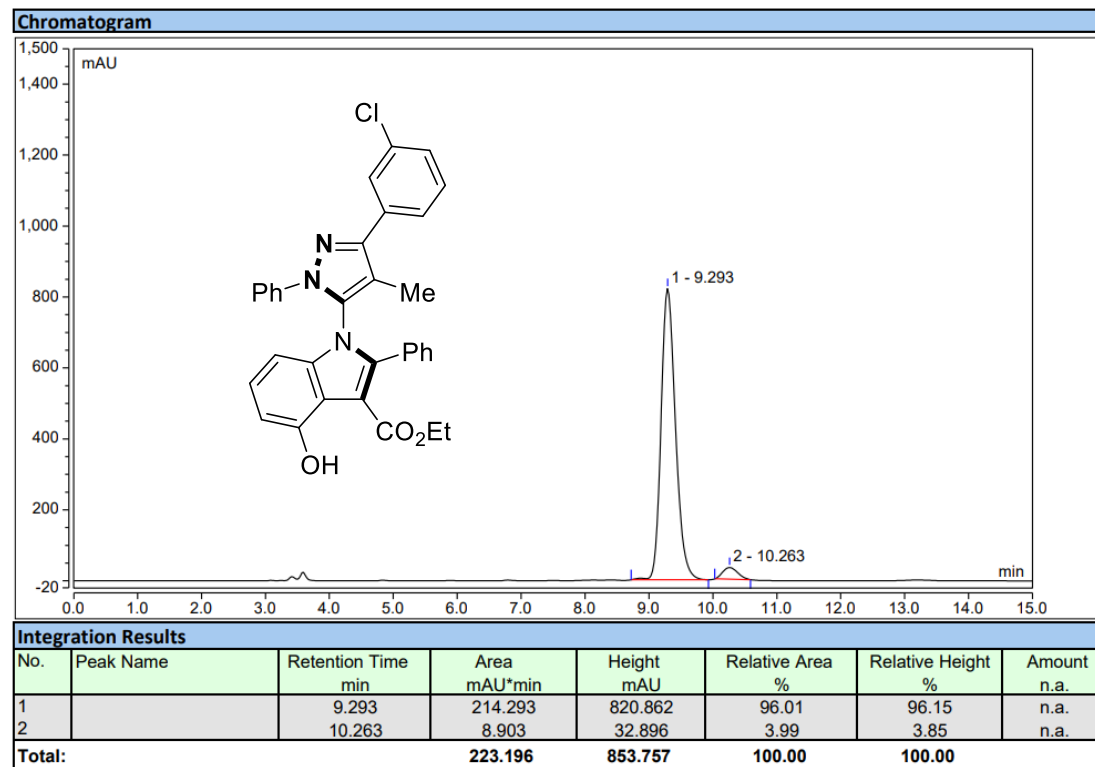


4oab

Racemic:

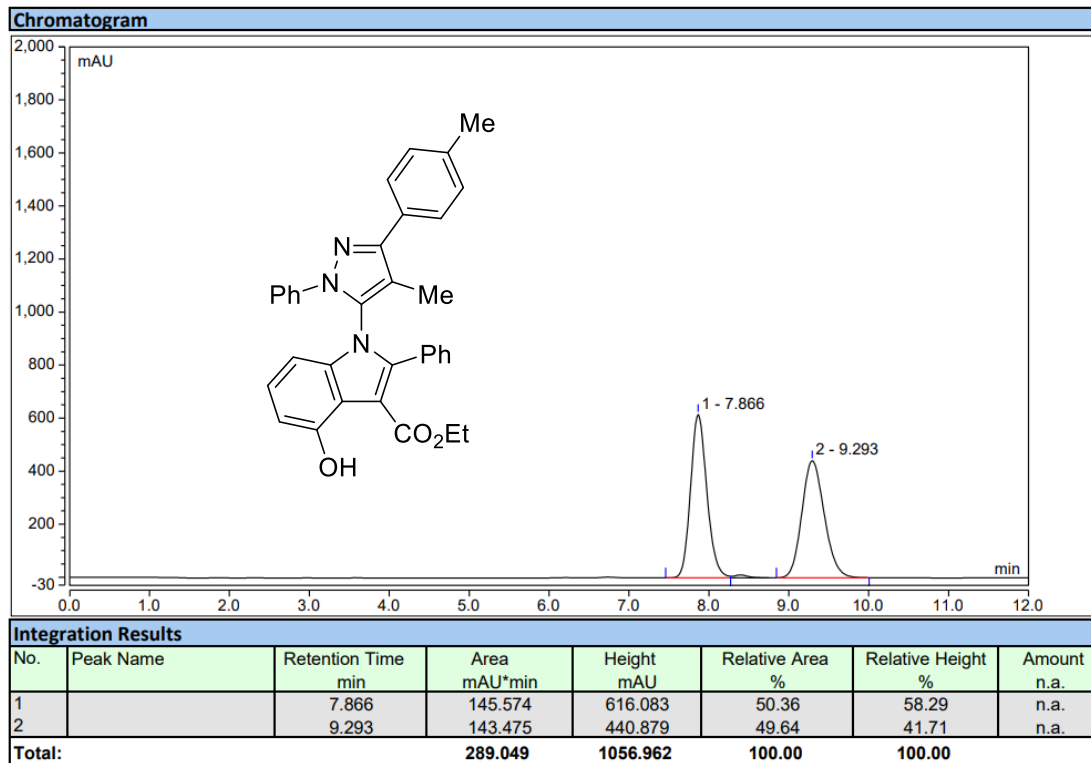


Enantioselective:

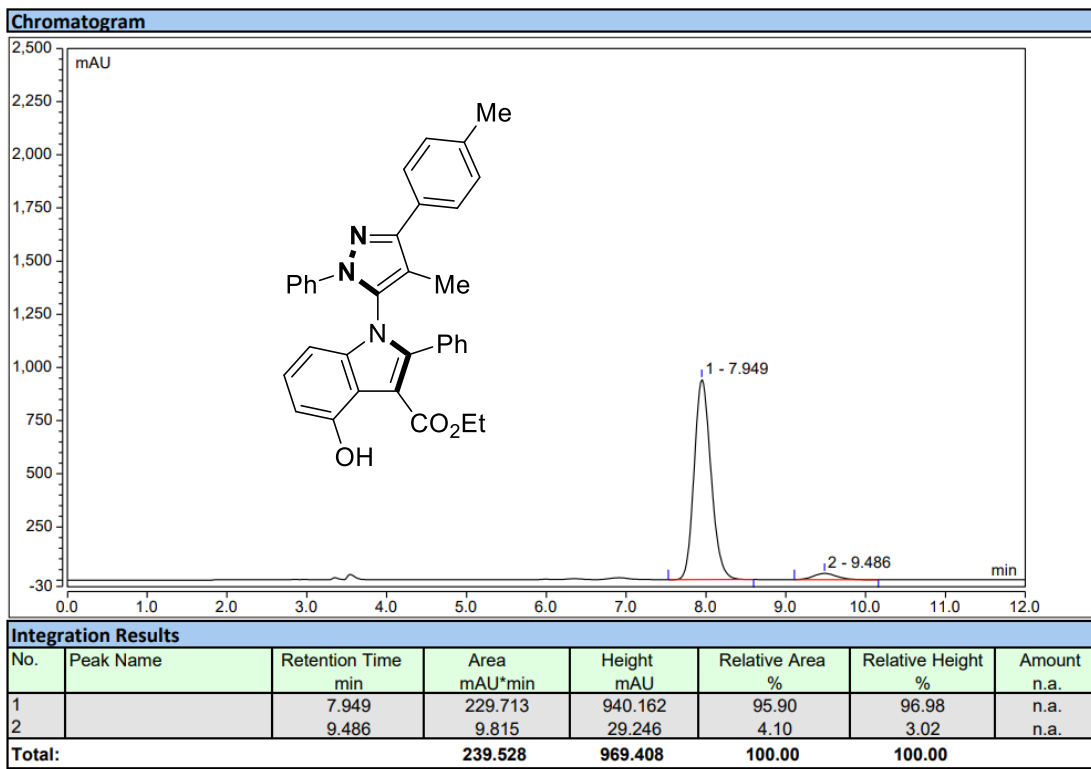


4pab

Racemic:

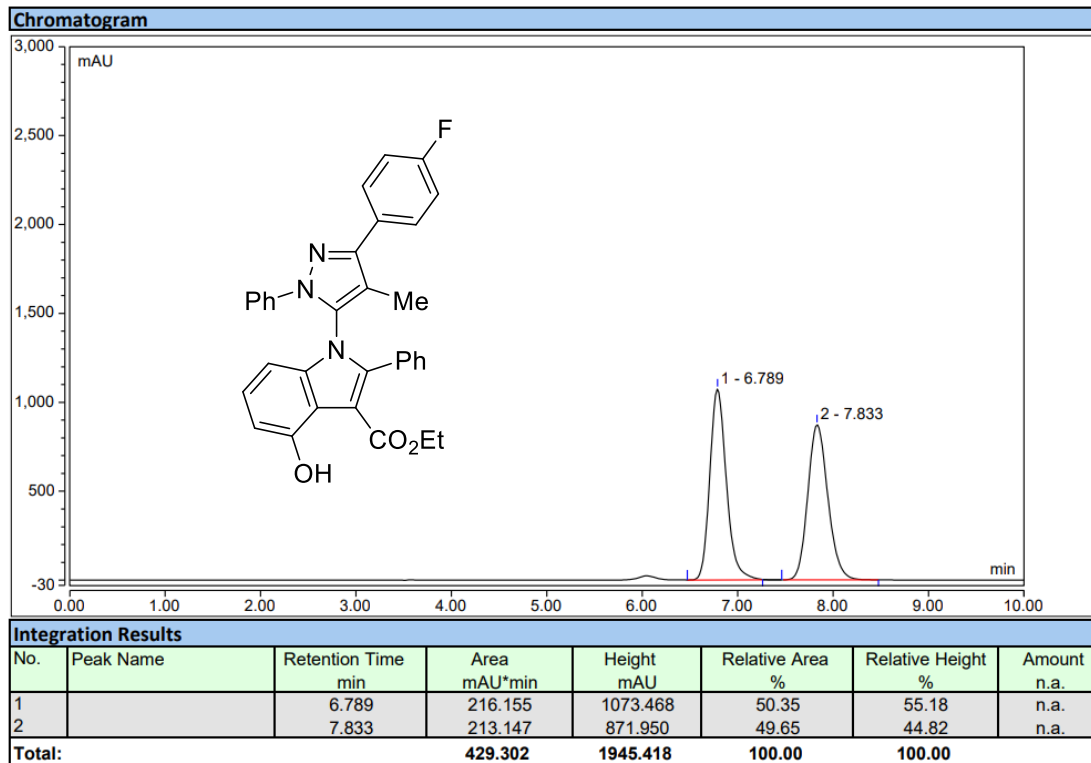


Enantioselective:

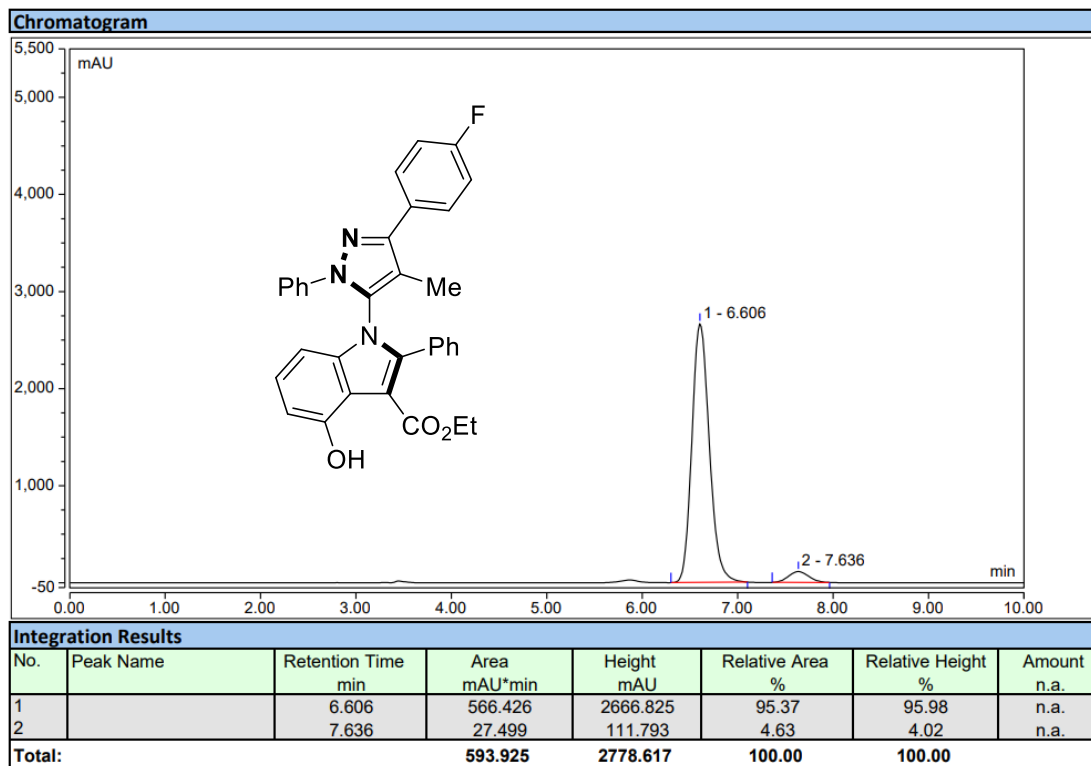


4qab

Racemic:

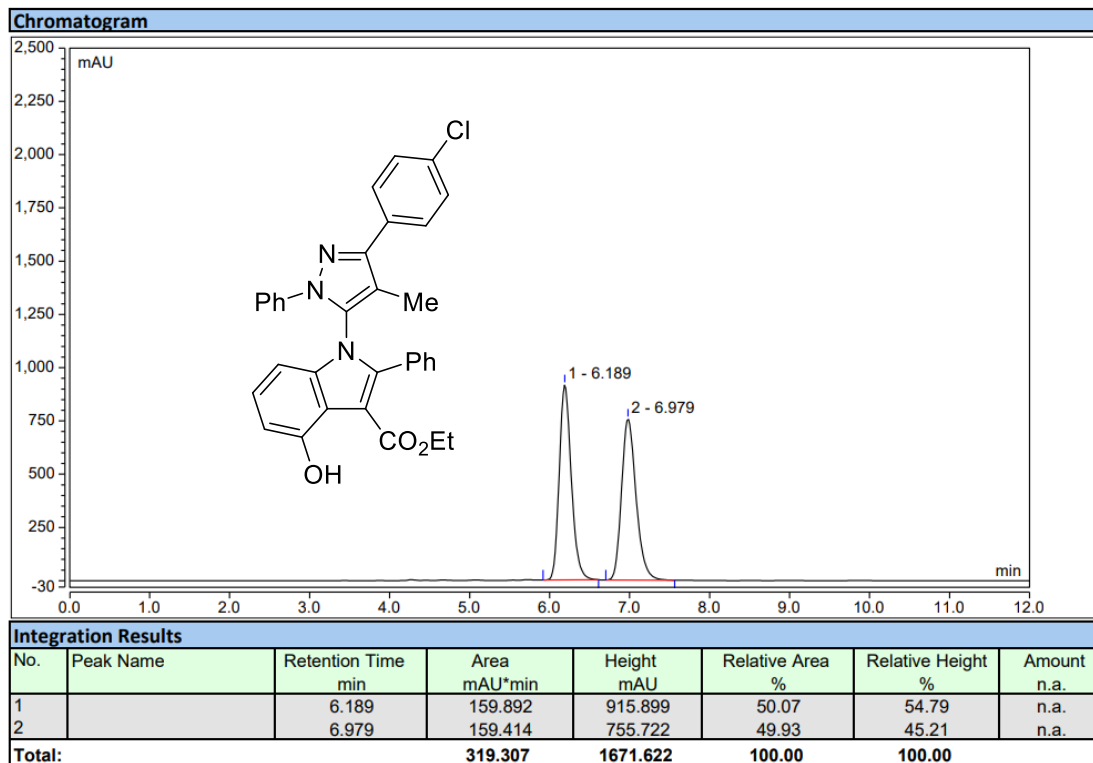


Enantioselective:

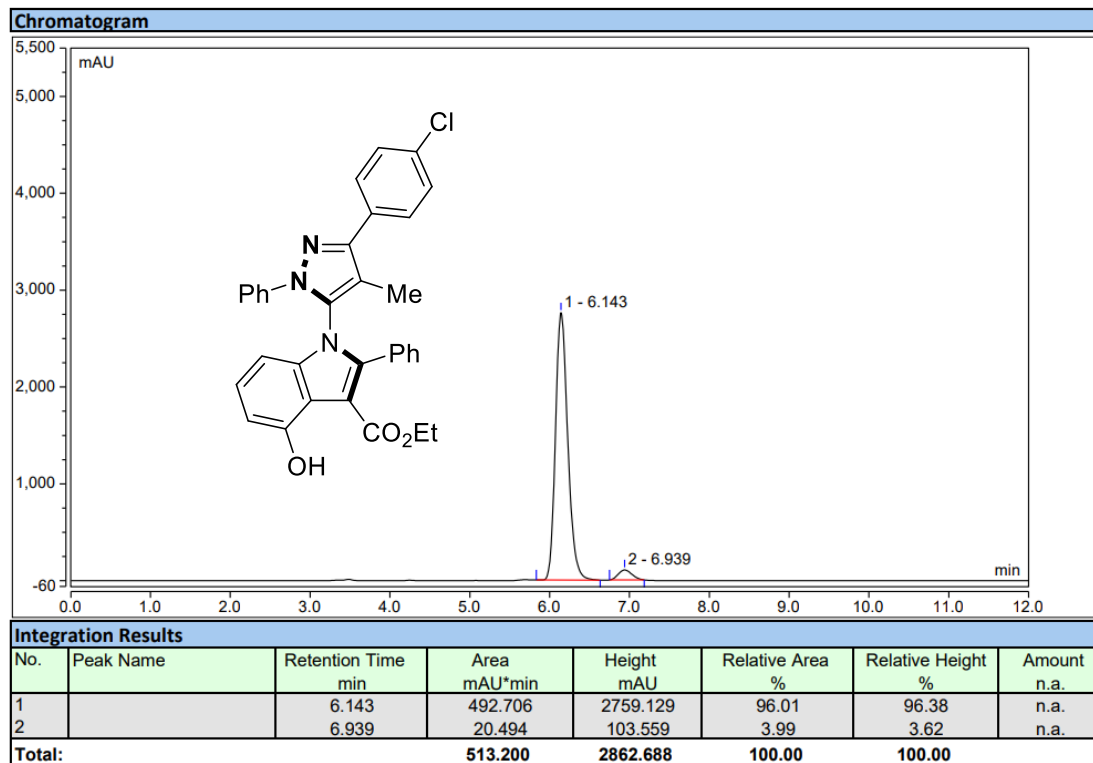


4rab

Racemic:

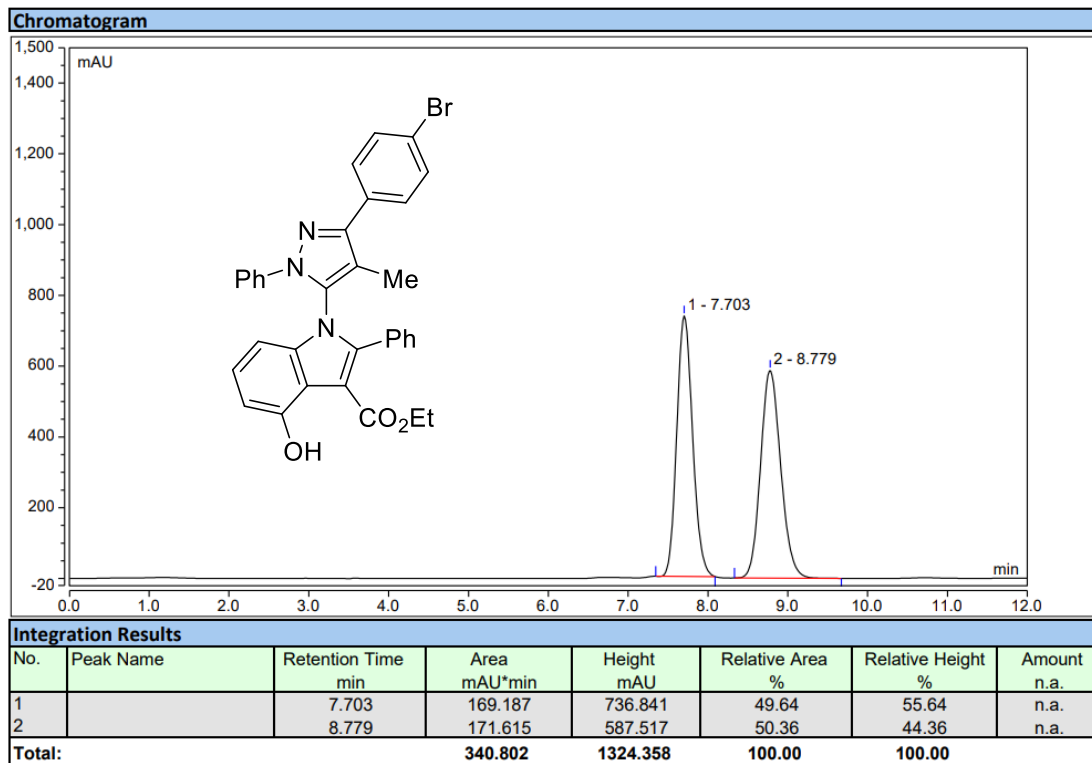


Enantioselective:

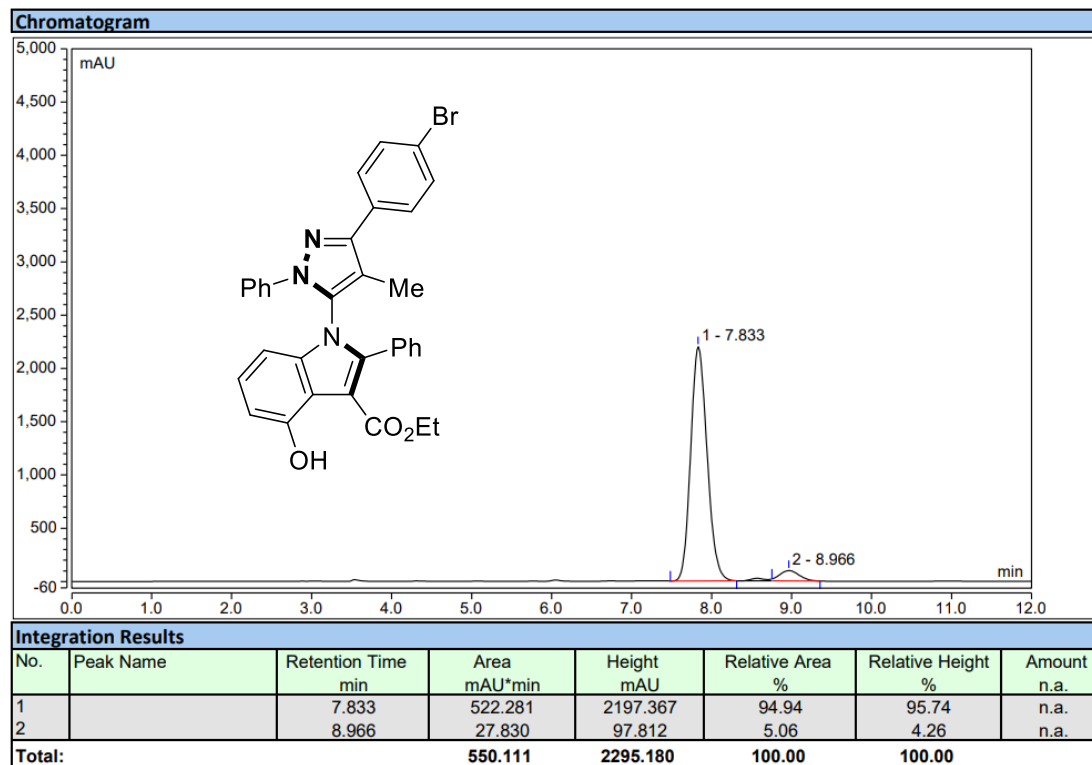


4sab

Racemic:

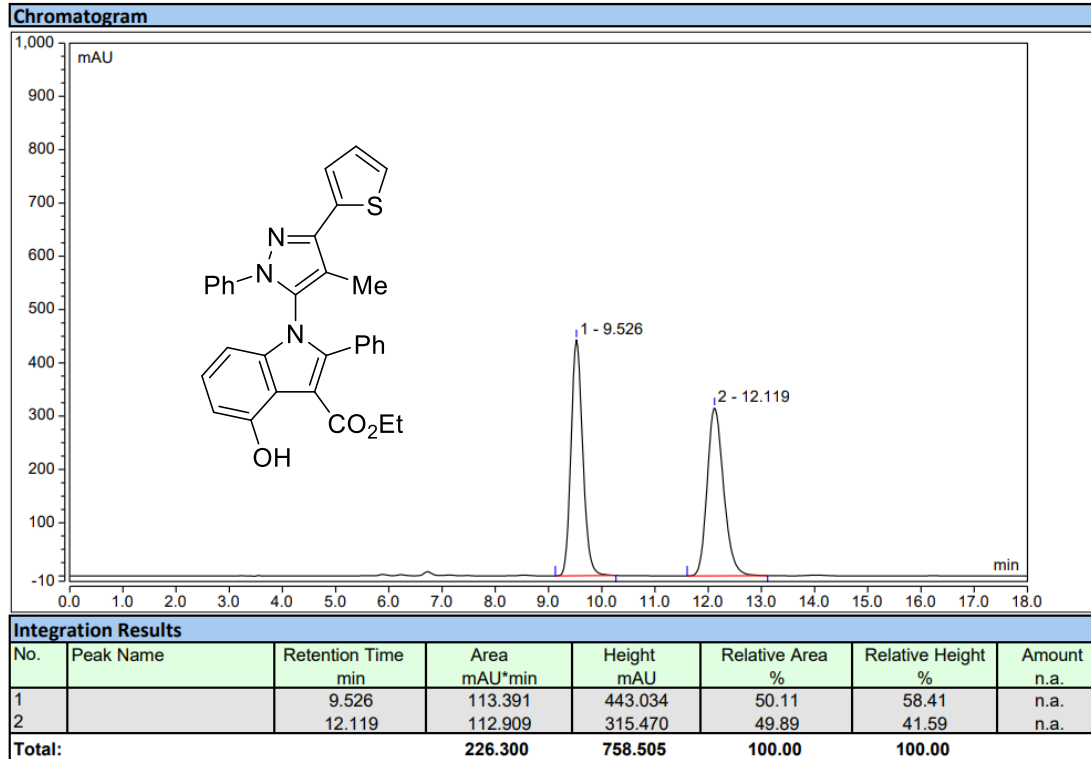


Enantioselective:

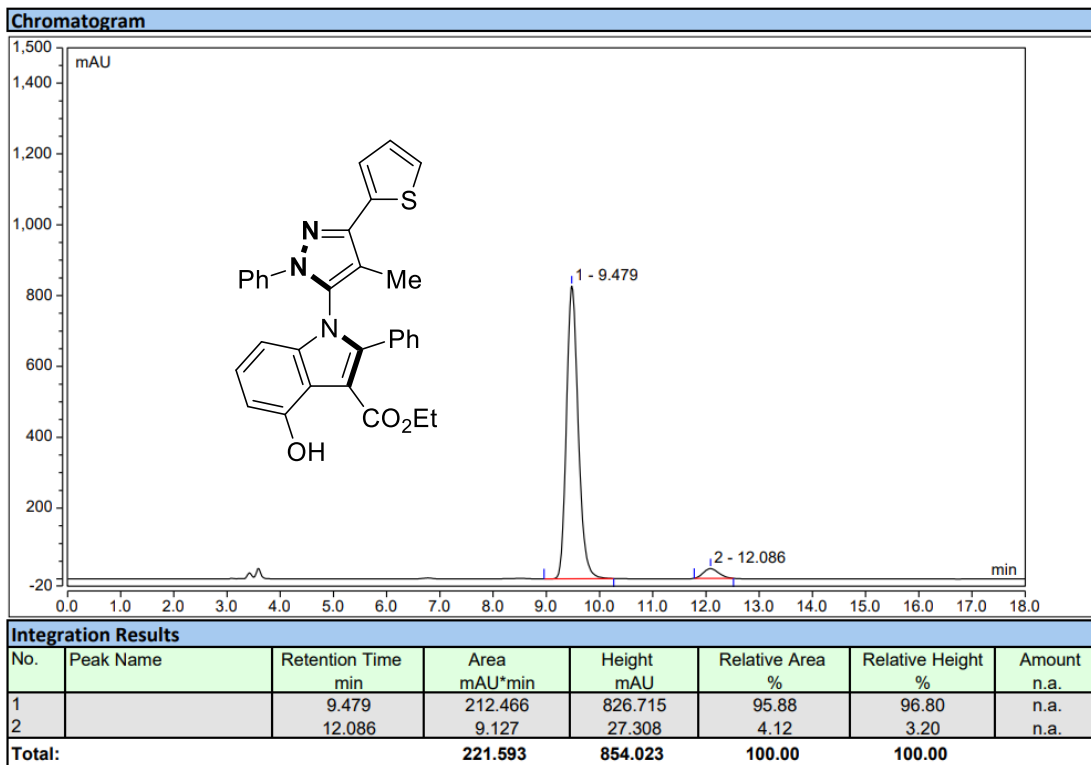


4tab

Racemic:

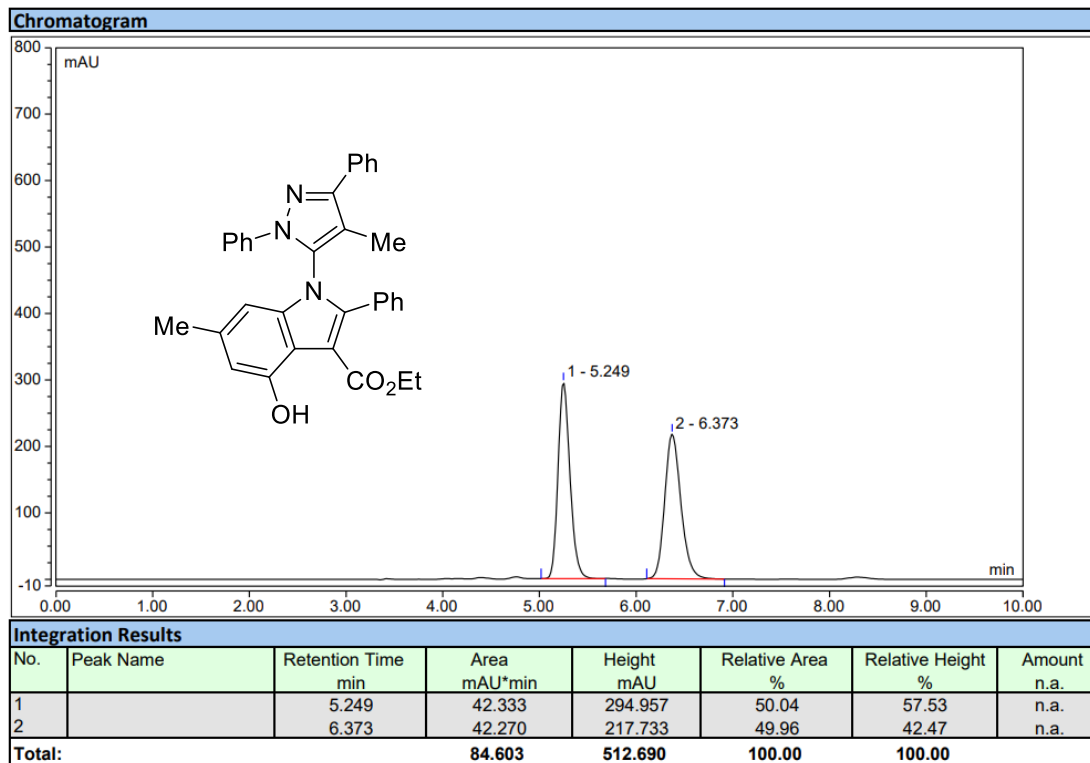


Enantioselective:

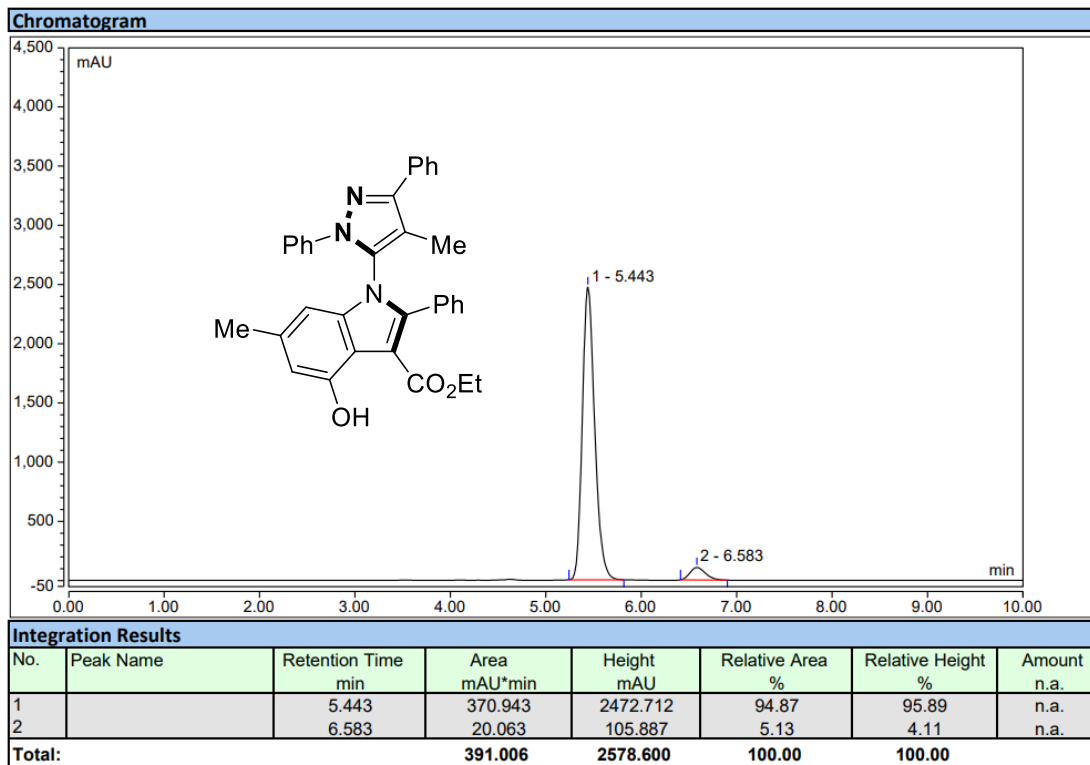


4abb

Racemic:

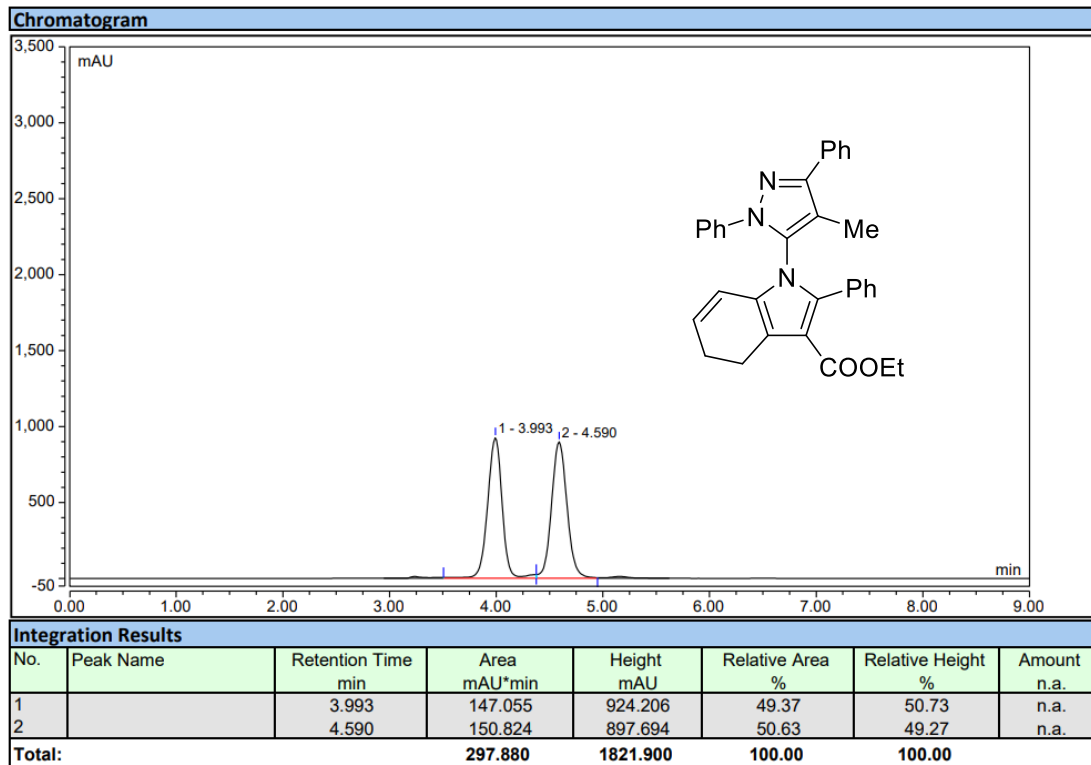


Enantioselective:

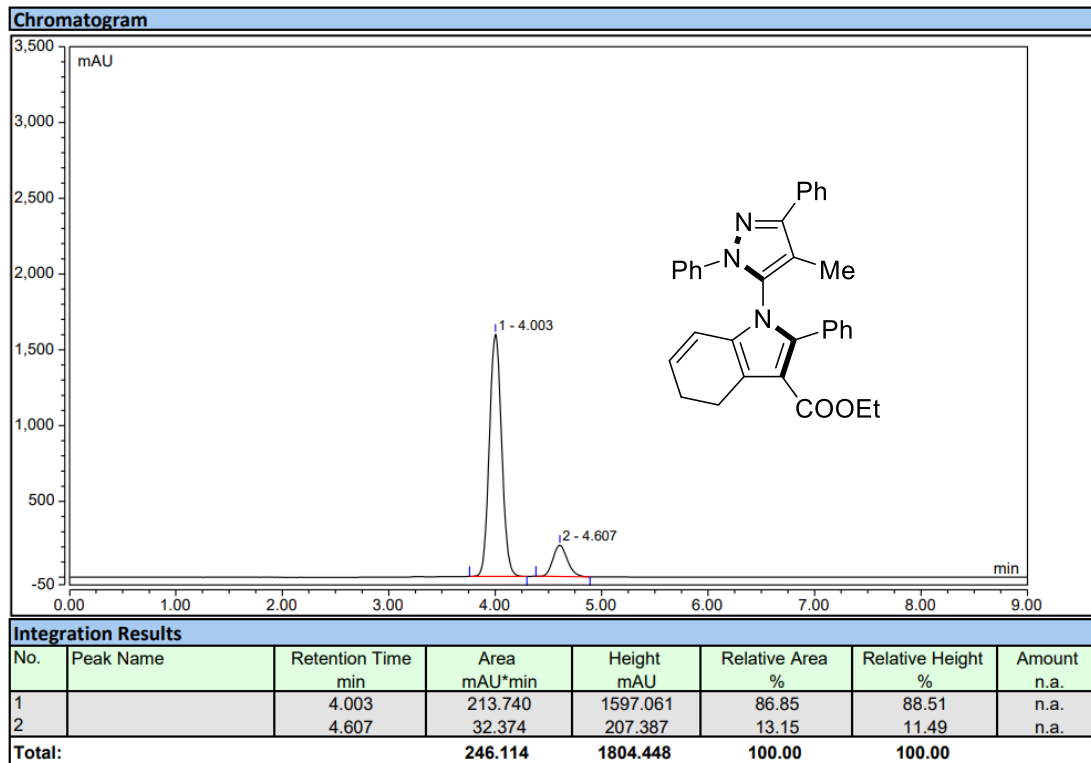


4acb

Racemic:



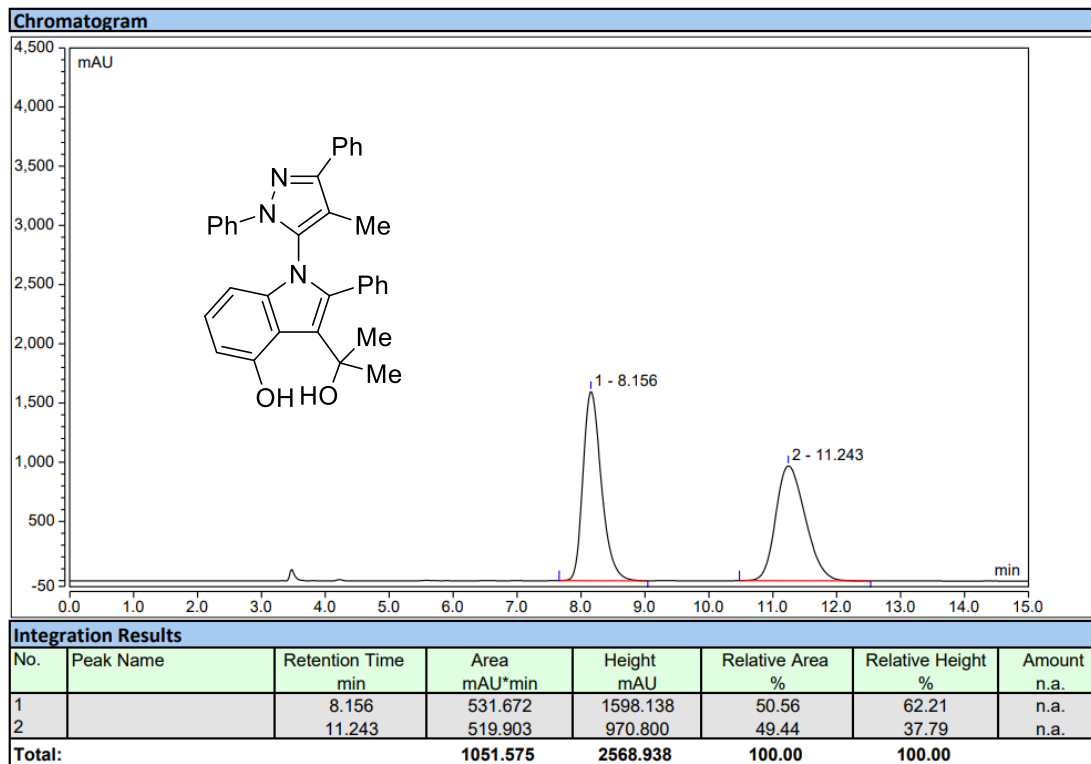
Enantioselective:



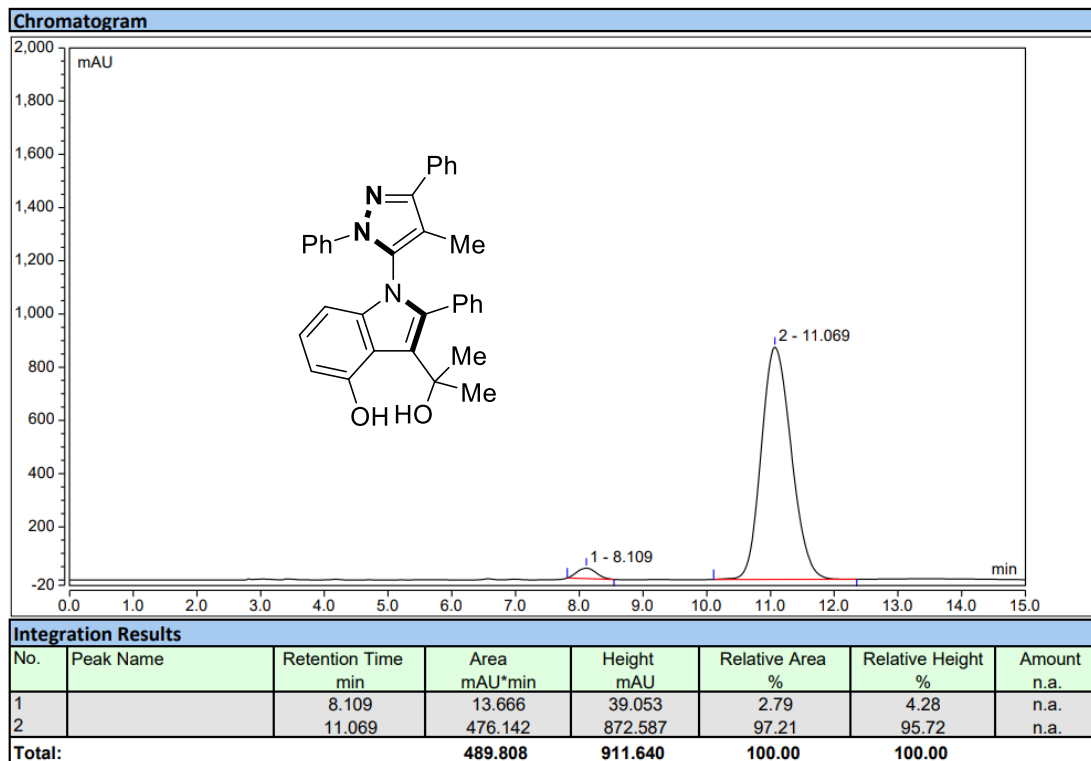
11. HPLC traces of products 7-10

7

Racemic:

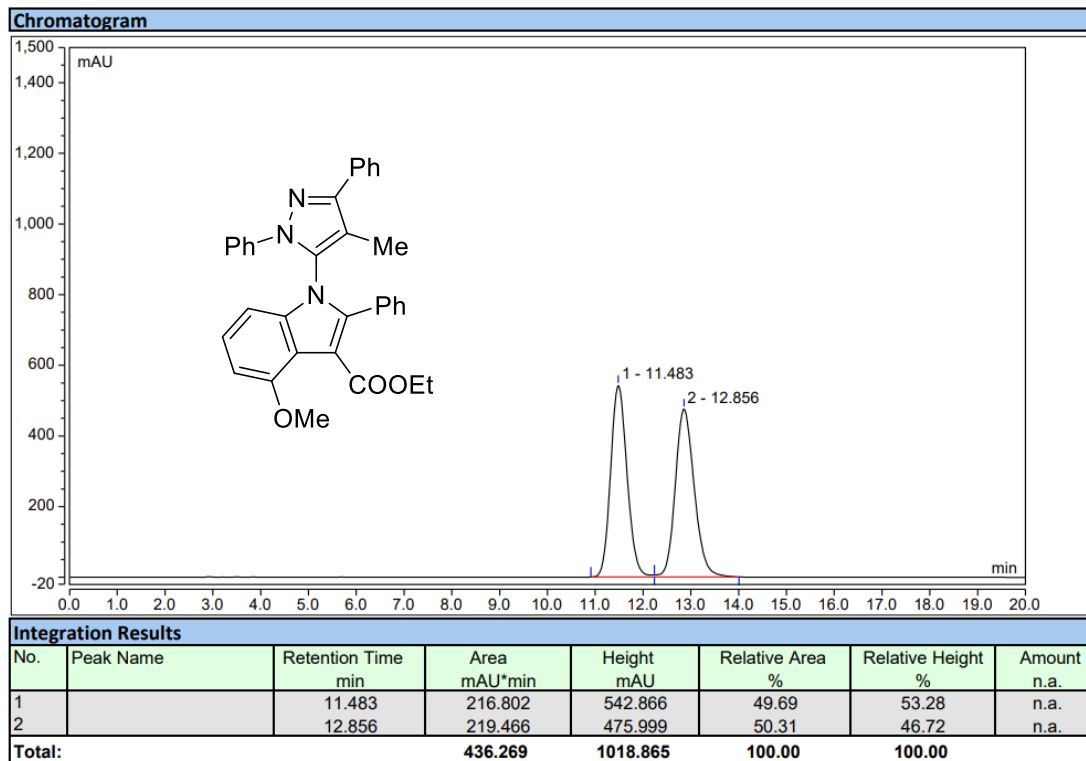


Enantioselective:

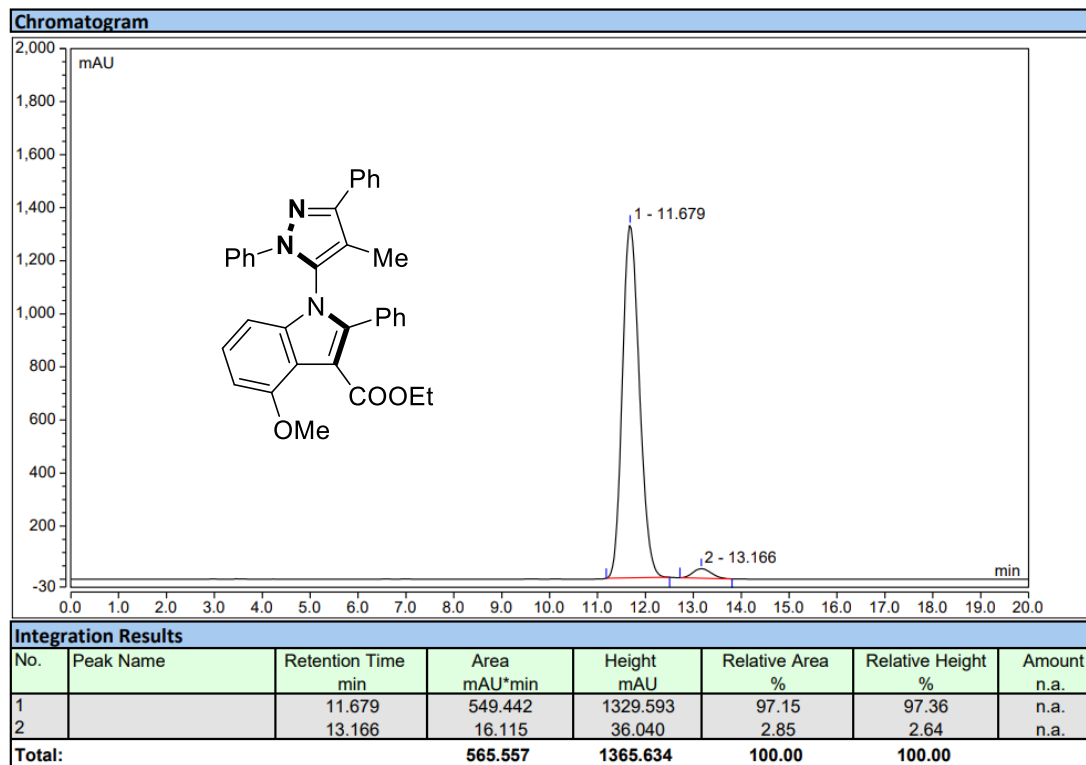


8

Racemic:

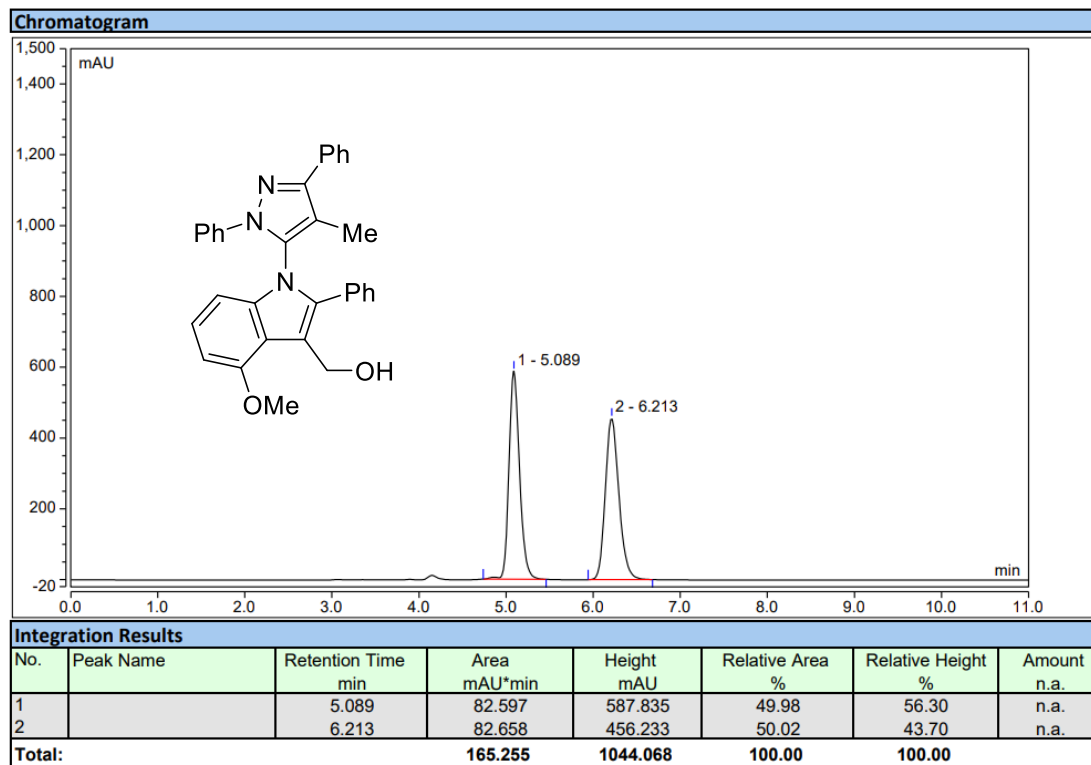


Enantioselective:

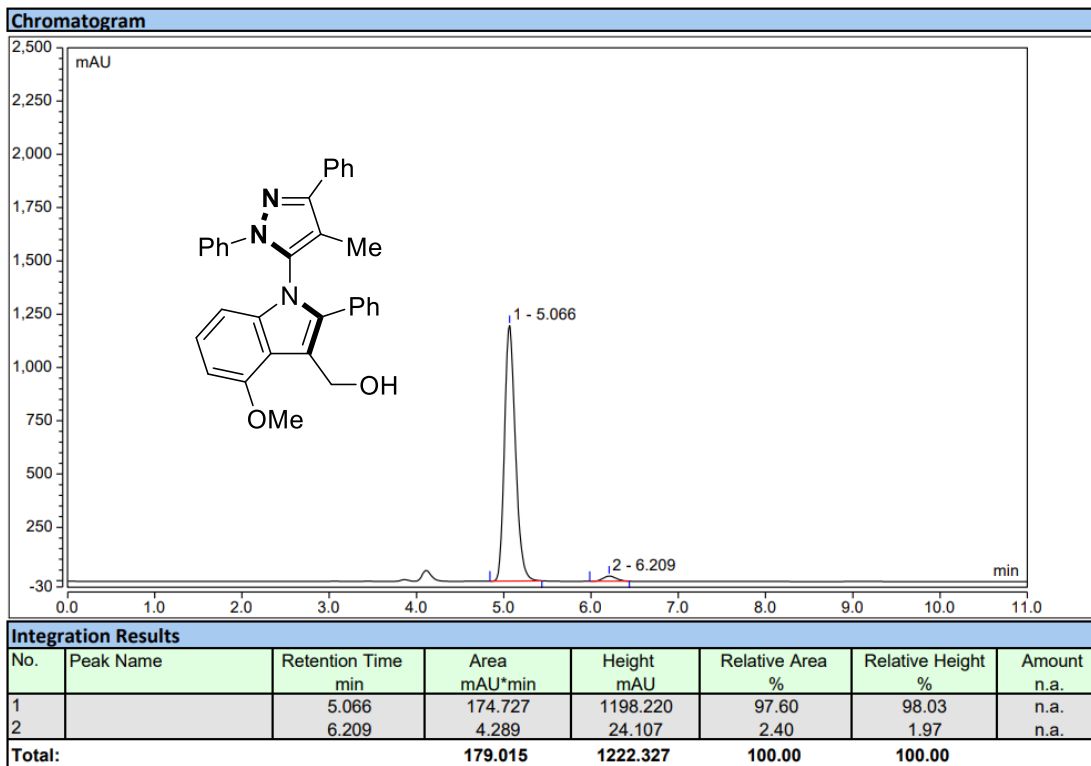


9

Racemic:

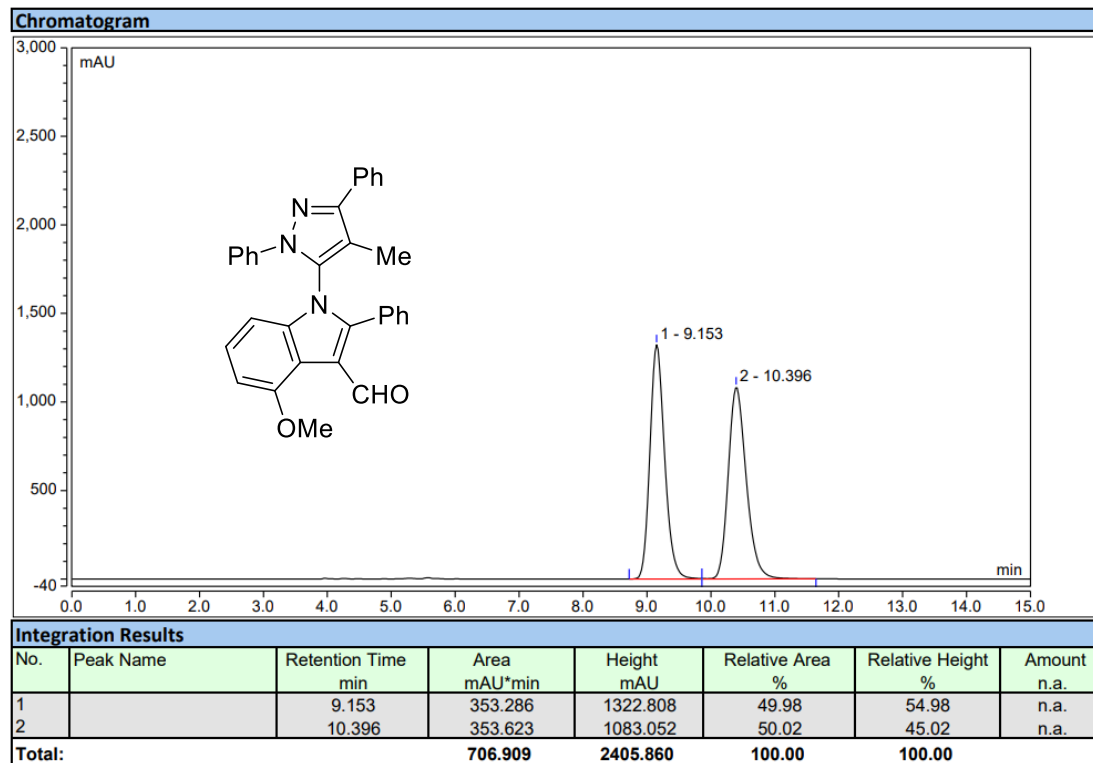


Enantioselective:

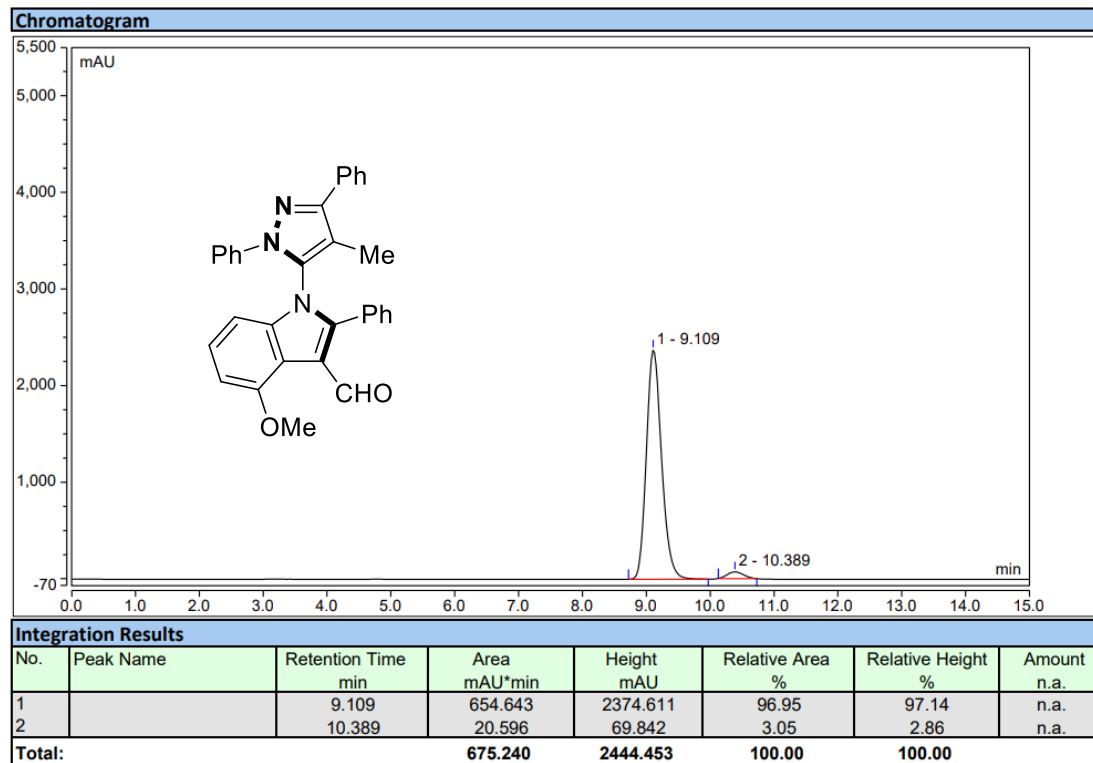


10

Racemic:

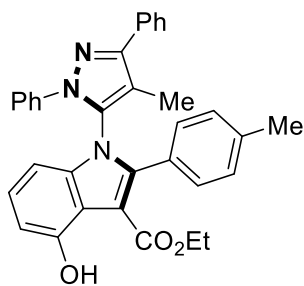


Enantioselective:

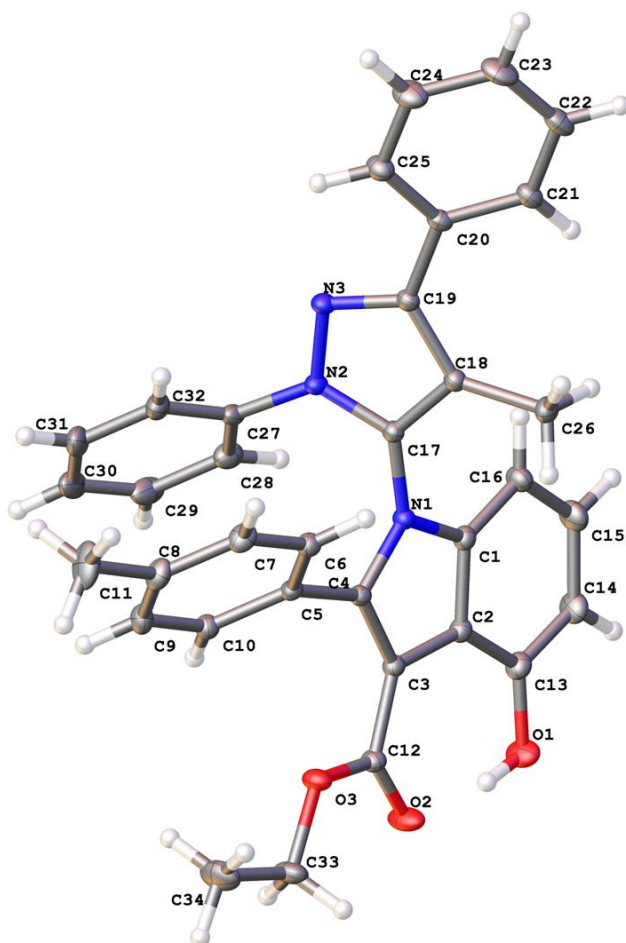


12. X-ray single-crystal data for compounds 4aag

Crystal growth: 50 mg of compound **4aag** was dissolved in the solvent (acetone, 2 mL). Then, *n*-hexane (18 mL) was added to the sample bottle. Single crystals were formed slowly within 3 days. The thermal ellipsoid was drawn at the 50% probability level.



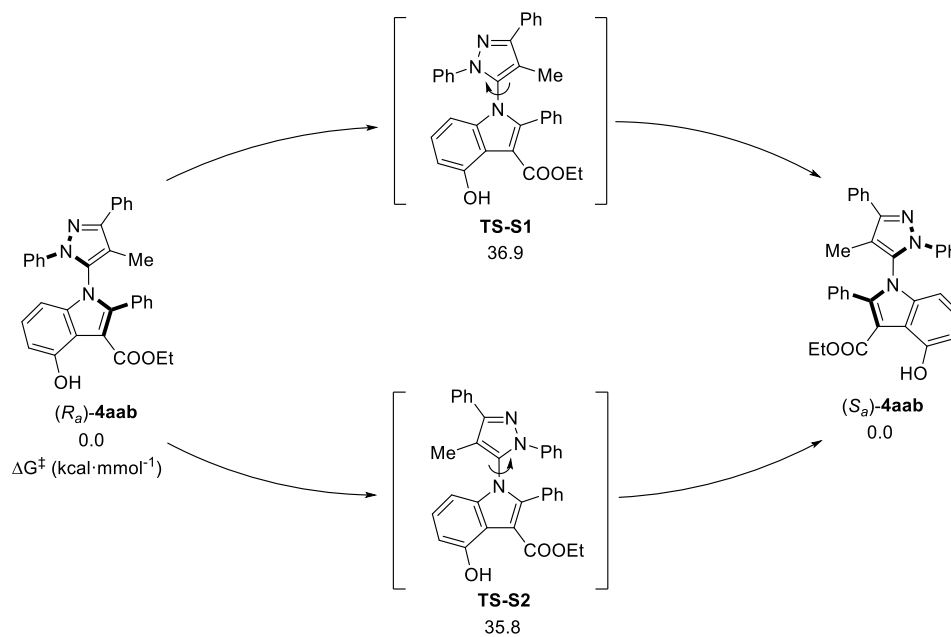
4aag



Empirical formula	$C_{34}H_{29}N_3O_3$	
Formula weight	527.60	
Temperature	170.00 K	
Wavelength	1.34139 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	$a = 7.87600(10)$ Å	$\alpha = 90^\circ$.
	$b = 11.9351(2)$ Å	$\beta = 90^\circ$.
	$c = 29.7692(5)$ Å	$\gamma = 90^\circ$.
Volume	$2798.33(8)$ Å ³	
Z	4	
Density (calculated)	1.252 Mg/m ³	
Absorption coefficient	0.427 mm ⁻¹	
F(000)	1112	
Crystal size	0.17 x 0.11 x 0.05 mm ³	
Theta range for data collection	3.471 to 63.553°.	
Index ranges	$-10 \leq h \leq 10$, $-15 \leq k \leq 15$, $-39 \leq l \leq 39$	
Reflections collected	54301	
Independent reflections	6931 [R(int) = 0.0383]	
Completeness to theta = 53.594°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7523 and 0.6684	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	6931 / 0 / 365	
Goodness-of-fit on F ²	1.037	
Final R indices [I > 2σ(I)]	R1 = 0.0304, wR2 = 0.0799	
R indices (all data)	R1 = 0.0309, wR2 = 0.0802	
Absolute structure parameter	0.00(5)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.227 and -0.159 e.Å ⁻³	

13. Theoretical calculations on the rotational barriers

All calculations were performed using Gaussian 16, Revision A.03 package.⁶ All of the reactants, intermediates, transition states, products were optimized by the DFT with the B3LYP-D3 functional.⁷ For geometry optimizations and frequency calculations, BS-I basis set system was employed. In BS-I, we employed 6-31G(d) basis sets for C, H, O and N. All the stationary structures were characterized with no imaginary frequency and the transition state structures (TSs) were characterized with a single imaginary frequency. Intrinsic reaction coordinate (IRC) calculations were performed on the TSs. The solvent effect of *m*-xylene was evaluated through the SMD method,⁸ in which a better basis system BS-II was used. In BS-II, we employed 6-311++G(d, p) basis sets for all atoms. All reported energies are free energies at a concentration of 1 M and a temperature of 298.15 K.



Cartesian coordinates of the optimized structures:

(R_o)-4aab

E = -1663.86823324 a.u.

0 1

O	14.66013300	-6.36639800	12.44396400
H	14.95769900	-7.23854400	12.08281100
O	15.66588000	-8.74208200	11.78366900
O	17.10172600	-10.25593800	12.61020200
N	16.99193100	-8.06706900	16.16571400
N	16.90631300	-9.17075300	18.33997900
N	17.56327800	-9.17359800	19.52017400
C	16.24944000	-6.96574300	15.72096800
C	15.86553600	-7.22388500	14.38524500
C	16.40756400	-8.53216100	14.04180600
C	17.07764700	-9.02239000	15.15892100
C	17.73854900	-10.30923700	15.42983300
C	19.03754800	-10.34794400	15.95489100
H	19.58295500	-9.42245500	16.10614600
C	19.62895700	-11.56763800	16.28136300
H	20.63603300	-11.58475300	16.68745100
C	18.92930000	-12.75914100	16.08715400
C	17.63323200	-12.72678600	15.56587300
H	17.07529000	-13.64883200	15.43144000
C	17.04060300	-11.51113800	15.24177200
H	16.02243700	-11.47895700	14.87247200
C	16.33979000	-9.15988200	12.72762900
C	15.09210400	-6.24442200	13.71306900
C	14.74747300	-5.08377100	14.41497100
H	14.15119900	-4.34259000	13.89341300
C	15.14214500	-4.87771900	15.74288900
H	14.84184900	-3.96256200	16.24487800
C	15.90370500	-5.81726400	16.43247100
H	16.21132600	-5.67621600	17.46204600
C	17.42719000	-8.22669200	17.48816700
C	18.43868000	-7.56456600	18.15688300
C	18.48072400	-8.20081800	19.43569500
C	19.38506200	-7.95063300	20.56722500
C	19.99425200	-6.70141400	20.76166900
H	19.78005100	-5.88340100	20.08331400
C	20.85190700	-6.49016800	21.84108100
H	21.31199400	-5.51548100	21.97771500
C	21.11011700	-7.51950300	22.74624800
H	21.77901100	-7.35421300	23.58605300
C	20.49905600	-8.76375900	22.56747600

H	20.69196600	-9.57023000	23.26958100
C	19.64687200	-8.97891000	21.48894700
H	19.17112300	-9.94253900	21.34207700
C	19.31065400	-6.49947500	17.56877400
H	19.00974400	-5.49304500	17.88557100
H	19.25126400	-6.52116300	16.47585300
H	20.35601300	-6.63803700	17.86281400
C	15.89457200	-10.12951200	18.07596500
C	14.77478300	-9.78065000	17.31605200
H	14.64261100	-8.76243100	16.96873100
C	13.82580600	-10.75760800	17.01761800
H	12.95809200	-10.49026400	16.42199000
C	13.97909400	-12.06134100	17.49271500
C	15.08839900	-12.38759400	18.27697300
H	15.21180300	-13.39888700	18.65313200
C	16.05296100	-11.42694500	18.56708700
H	16.93407200	-11.66345400	19.15076900
C	17.05298700	-10.95761600	11.35005900
H	17.35431700	-10.27295100	10.55159100
H	16.01942900	-11.26131900	11.15548800
C	17.98808100	-12.14483100	11.47746900
H	17.68157200	-12.79242800	12.30443600
H	19.01252200	-11.81139500	11.66966700
H	19.38872100	-13.70858100	16.34703800
H	13.23439500	-12.81678600	17.26014100
H	17.97909900	-12.72808000	10.55060100

TS-S1

E = -1663.80821717 a.u.

0 1

O	15.21415200	-5.99960500	12.49778000
H	14.86160300	-6.91619100	12.39574600
O	14.77226900	-8.60768000	12.29558100
O	16.21363400	-10.29821000	12.60082900
N	17.43520700	-8.17885300	16.06849500
N	18.03611500	-9.58117800	17.99866700
N	18.54527700	-9.42644100	19.28320200
C	17.25836500	-6.91263500	15.44624200
C	16.40913100	-7.08768800	14.33026500
C	16.25947700	-8.52250700	14.15426500
C	16.93673700	-9.16212500	15.18247700
C	17.37425800	-10.56976600	15.20736000
C	18.74803700	-10.84448300	15.26189100
H	19.45048300	-10.02486100	15.37098700

C	19.20698900	-12.15723400	15.17296800
H	20.27371800	-12.35768700	15.21492400
C	18.30046300	-13.20744600	15.02583600
C	16.92998400	-12.93830600	14.97175100
H	16.21703800	-13.75237700	14.87998700
C	16.47099700	-11.62958300	15.05784800
H	15.40788800	-11.42123700	15.03509700
C	15.67330900	-9.12950100	12.95359200
C	16.06022700	-5.96032200	13.54601800
C	16.65110600	-4.73238500	13.85779100
H	16.39164800	-3.87660600	13.24379100
C	17.59919600	-4.62722000	14.87843700
H	18.10311700	-3.67857600	15.03862800
C	17.92661800	-5.71308000	15.68685000
H	18.70608300	-5.63869400	16.42786300
C	17.74757700	-8.32429600	17.44383600
C	17.96476000	-7.37468100	18.43911400
C	18.51377600	-8.13625200	19.53227300
C	19.05490700	-7.62763400	20.81270700
C	18.25947300	-6.91318500	21.71988400
H	17.21159100	-6.73888500	21.49604300
C	18.79317700	-6.46226400	22.92643700
H	18.16356000	-5.91495800	23.62227800
C	20.12673500	-6.72432900	23.24532500
H	20.54198600	-6.37134100	24.18504300
C	20.92119700	-7.44966900	22.35574000
H	21.95707500	-7.66575900	22.60178600
C	20.38859200	-7.89922200	21.14840000
H	20.99903800	-8.46663200	20.45311600
C	17.63907900	-5.91380200	18.58018900
H	16.86361100	-5.58895700	17.88900100
H	18.50882300	-5.25928500	18.44659100
H	17.27718100	-5.73576900	19.59512300
C	17.09444800	-10.67488100	18.00658600
C	15.72430100	-10.41810700	17.93882900
H	15.37201700	-9.39958700	17.81326200
C	14.82244300	-11.47844000	18.02777300
H	13.75613600	-11.28100800	17.96388400
C	15.28684400	-12.78046400	18.21457000
C	16.66023200	-13.01830400	18.31695600
H	17.02760300	-14.02907300	18.46776300
C	17.56798200	-11.96855000	18.21466300
H	18.63557200	-12.13465000	18.28773300
C	15.63783300	-10.97185500	11.45912900

H	15.61991100	-10.27941300	10.61306800
H	14.60207300	-11.23590300	11.69723000
C	16.49678300	-12.19277300	11.19353400
H	16.52809100	-12.84332700	12.07212700
H	17.52254400	-11.89733800	10.95234600
H	18.65754300	-14.23141900	14.96252300
H	14.58389700	-13.60512100	18.28787200
H	16.08911800	-12.75697700	10.34797700

TS-S2

E = -1663.81032376 a.u.

0 1

O	16.21574300	-9.17741500	11.67573300
H	16.56071400	-8.25458400	11.62121000
O	16.78779800	-6.59869500	11.90289400
O	16.01920300	-5.10603500	13.38841600
N	16.65146100	-8.14368800	16.27915700
N	17.01552000	-9.51108300	18.29615400
N	17.35842600	-9.33325800	19.62328700
C	16.26929100	-9.18609700	15.38301800
C	16.37274100	-8.68039700	14.06472000
C	16.59622200	-7.25044600	14.18757000
C	16.70237800	-6.94418500	15.53583400
C	16.57239800	-5.61814800	16.16067600
C	15.56812300	-5.41612000	17.11810200
H	14.94002400	-6.24995400	17.41407000
C	15.37897700	-4.15770000	17.68737700
H	14.59799400	-4.01520400	18.42857800
C	16.18567900	-3.08509600	17.30238600
C	17.18397000	-3.27855000	16.34291900
H	17.82232800	-2.45126900	16.04596500
C	17.37471600	-4.53496800	15.77739300
H	18.16149600	-4.69024500	15.04645700
C	16.49227600	-6.31303100	13.06351300
C	16.09207300	-9.53558400	12.96997000
C	15.63469700	-10.82686800	13.24298000
H	15.41226300	-11.47326900	12.40070600
C	15.40854100	-11.24563200	14.55567800
H	14.98096400	-12.22744200	14.73519000
C	15.71008800	-10.43644400	15.64693600
H	15.48412100	-10.76715900	16.64549500
C	17.16679500	-8.30565500	17.59190800
C	17.73420400	-7.38810300	18.47657100
C	17.75428400	-8.08069100	19.73461600

C	18.17492700	-7.55738300	21.04649900
C	17.95321100	-6.21925800	21.40440900
H	17.45225600	-5.55351500	20.70909500
C	18.34583100	-5.74715000	22.65646800
H	18.16503800	-4.70901300	22.92104900
C	18.95907800	-6.60610600	23.56927700
H	19.26632700	-6.23740300	24.54390900
C	19.17246500	-7.94366000	23.22541100
H	19.64654000	-8.61820500	23.93297500
C	18.78440600	-8.41651900	21.97480900
H	18.94512000	-9.45287300	21.69723800
C	18.48505300	-6.10416500	18.26648700
H	17.89000300	-5.19721000	18.39445300
H	18.93596100	-6.06917100	17.27386600
H	19.29702000	-6.06918200	18.99983200
C	17.46048400	-10.80526100	17.84571800
C	16.91092500	-11.94092400	18.44221400
H	16.15663300	-11.81992400	19.21170000
C	17.34066700	-13.20169500	18.03641800
H	16.90949800	-14.08716500	18.49438000
C	18.31472500	-13.32986000	17.04205900
C	18.87467500	-12.18704300	16.47180400
H	19.63936200	-12.27623300	15.70600800
C	18.46056500	-10.92007100	16.88212500
H	18.89263400	-10.02769900	16.44267100
C	15.94532700	-4.12472800	12.32965100
H	15.36607200	-4.54304100	11.50187800
H	16.95851500	-3.92980100	11.96296500
C	15.29951500	-2.88802300	12.92332200
H	15.88279500	-2.51263900	13.76908300
H	14.28952300	-3.11330300	13.27935400
H	16.04037100	-2.10540400	17.74821100
H	18.63835100	-14.31491300	16.71949100
H	15.23325800	-2.10251500	12.16307800

(S_a)-4aab

E = -1663.86782468 a.u.

0 1

O	18.74853000	-6.90460100	11.58305200
H	18.13590800	-7.66330500	11.41306700
O	17.03705300	-8.94425400	11.49201600
O	15.73707200	-10.12170800	12.89269400
N	17.71403200	-8.15948300	16.00256600
N	18.45943600	-9.34913800	17.99527900

N	18.36181800	-9.27413300	19.33949500
C	18.46530900	-7.25008600	15.24693100
C	18.22708200	-7.53330400	13.88247500
C	17.30210500	-8.65856700	13.84597900
C	17.02316500	-9.02207000	15.15985800
C	16.23838200	-10.12569800	15.73671400
C	16.52269300	-11.45173000	15.37996100
H	17.30722100	-11.64849300	14.65876100
C	15.83384000	-12.50297800	15.97577600
H	16.07526200	-13.52616000	15.70304200
C	14.85476600	-12.24456600	16.93865000
C	14.56917300	-10.92804900	17.30226300
H	13.81111300	-10.72025900	18.05163700
C	15.25791100	-9.87277000	16.70567700
H	15.03470000	-8.84901900	16.98724500
C	16.70903700	-9.23305000	12.64479800
C	18.88701700	-6.73893200	12.91170100
C	19.74290200	-5.72714800	13.36176200
H	20.24724000	-5.12812900	12.61093600
C	19.95649300	-5.49138200	14.72568200
H	20.63644600	-4.69811300	15.02234100
C	19.32272800	-6.25033000	15.70604000
H	19.48179500	-6.08482000	16.76531600
C	17.81729100	-8.29231400	17.39490700
C	17.31286100	-7.48108400	18.39274300
C	17.68564900	-8.14739900	19.60139200
C	17.45666800	-7.74995900	20.99880500
C	16.40195100	-6.89936600	21.36463300
H	15.71501200	-6.53166700	20.61153700
C	16.20772900	-6.54188400	22.69880600
H	15.38423900	-5.88421900	22.96300200
C	17.05840200	-7.03143300	23.68970200
H	16.90719700	-6.75070900	24.72814500
C	18.10538500	-7.88736600	23.33688700
H	18.77270800	-8.27470400	24.10185300
C	18.30461100	-8.24210500	22.00640000
H	19.11786300	-8.90205200	21.72464200
C	16.56129200	-6.20419800	18.17420500
H	16.70516800	-5.84578600	17.15097500
H	16.90110400	-5.42068400	18.85943100
H	15.48230200	-6.32999600	18.33257700
C	19.04071300	-10.48802100	17.37881700
C	18.82852800	-11.74364100	17.95204600
H	18.24290900	-11.81336900	18.86056700

C	19.35528800	-12.87319500	17.33206200
H	19.18746900	-13.85147500	17.77281500
C	20.07804200	-12.75429800	16.14222200
C	20.29375600	-11.49233200	15.58568500
H	20.86918000	-11.38827800	14.67069200
C	19.78820000	-10.35043300	16.20619700
H	19.97912400	-9.36886500	15.78828500
C	15.13026900	-10.76655900	11.75326300
H	15.90876800	-11.28769000	11.18699100
H	14.70026400	-10.00099200	11.10042100
C	14.08160800	-11.71630300	12.29956900
H	13.31787300	-11.16820200	12.85983300
H	14.53592700	-12.44876400	12.97359300
H	14.32212800	-13.06646200	17.40852100
H	20.47787000	-13.63935100	15.65619300
H	13.59506000	-12.24915800	11.47575100

References:

- (6) Gaussian 16, Revision A.03, Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, et al. Gaussian, Inc., Wallingford CT, 2016.
- (7) Grimme S, Ehrlich S, Goerigk L. Effect of the damping function in dispersion corrected density functional theory. *J Comp Chem.* 2011;32(7):1456-65. [10.1002/jcc.21759]
- (8) Marenich AV, Cramer CJ, Truhlar DG. Universal solvation model based on solute electron density and on a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions. *J Phys Chem B.*, 2009;113(18):6378–6396. [10.1021/jp810292n]