

Supporting information

Catalytic Enantioselective Synthesis of Chiral 4-Hydroxy 4'-Substituted Pyrazolones by Vinylogous Aldol Reaction of Pyrazole-4,5-diones with 3-Alkylidene-2-Oxindoles

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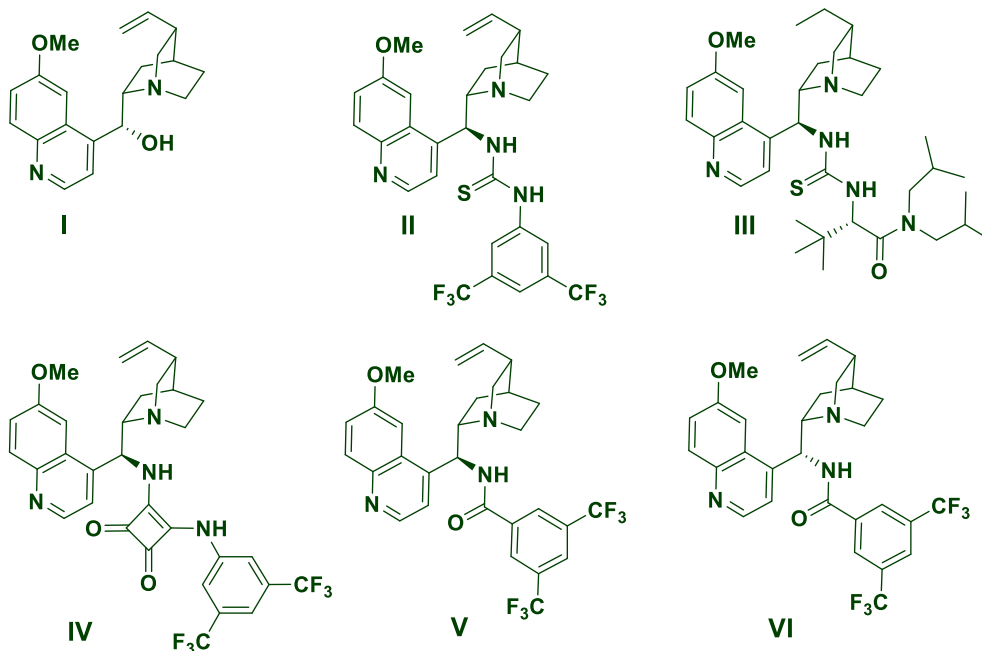
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1. General Information

^1H and ^{13}C NMR spectra were recorded on a Bruker AV-300 instrument (300/400MHz and 75/100MHz, respectively) and internally referenced to Tetramethylsilane signal or residual protonated solvent signals. Data for ^1H NMR are reported as follows: chemical shift (δ , ppm), multiplicity (s- singlet; d- doublet; t- triplet; q- quartet; m- multiplet), integration, coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ , ppm). Perkin Elmer FT-IR Spectrometer was used to record infrared spectra and is reported in frequency of absorption. MS-TOF mass spectrometer and ESI mass spectrometer were used to record low resolution and high resolution mass spectra. Column chromatographic separations were carried out on silica gel (230–400 mesh). High performance liquid chromatography (HPLC) analysis was performed on a Agilent 1220 Infinity LC instrument equipped with a quaternary pump, using a Chiralpak IB-H, ID-H, IE-H, AD-H Column (250 x 4.6mm). UV absorption was monitored at 225 nm.

2. General procedure preparation of the catalysts:

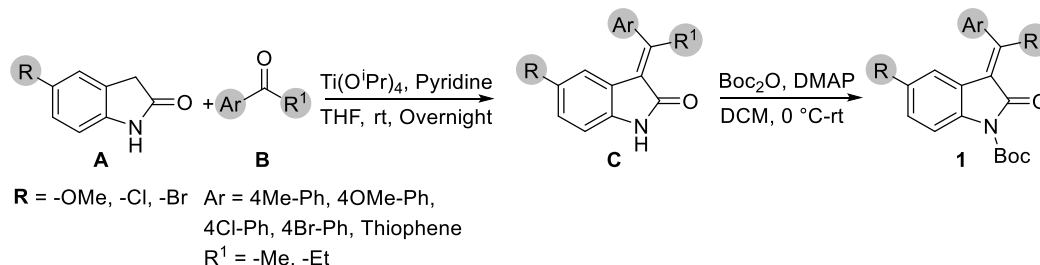
Catalysts **I** were purchased from Sigma Aldrich and used without further purification. Catalyst **IV-V** was prepared according to known literature procedure.¹



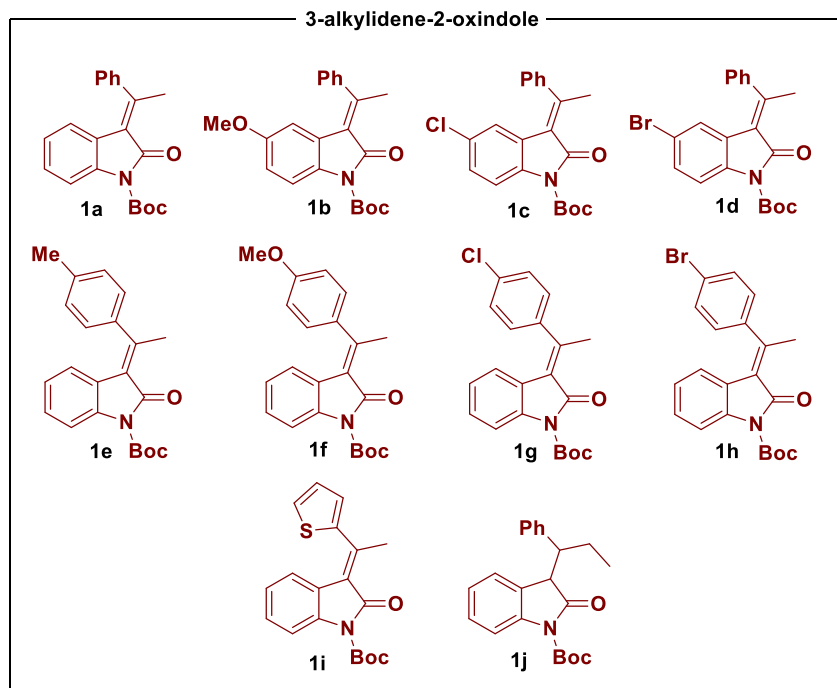
2.1. General procedure for the preparation of starting materials:

2.2. General procedure for the synthesis of 3-alkylidene oxindole (1)

3-alkylidene oxindole (D) were prepared by following the reported literature procedure.²



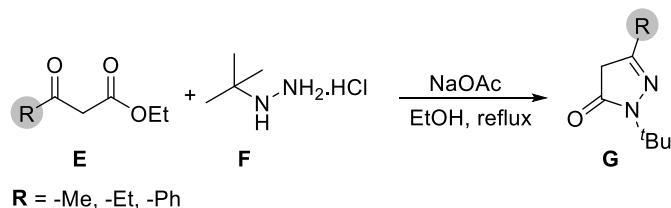
To a solution of 2-oxindole **A** (1.0 equiv.), acetophenone **B** (1.2 equiv.) in dry THF (0.5 M) was added pyridine (2.0 equiv.) and stirred for 10 min. Then titanium isopropoxide (3.0 equiv.) was added to the mixture and stirred at room temperature for overnight. After completion, reaction mixture was diluted with ethyl acetate and wash with 1(N) HCL, NaHCO₃, and brine. The organic layer was dried over Na₂SO₄, concentrated in *vacuo*, and purified by flash column chromatography to afford **C**. Then compound **C** was dissolved in 0.2 (M) DCM and treated with boc-anhydride (1.2 equiv.), along with DMAP (0.5 equiv.) at 0 °C. The resulting solution was then kept to room temperature for 4 h. After completion reaction mixture was quenched with water and extracted with ethyl acetate. Organic phase was then washed with water, brine and dried over Na₂SO₄, solvent was removed in vacuum. The resulting residue was purified by flash chromatography on silica gel to afford **1**.



2.3. General procedure for the synthesis of Pyrazole-4,5-dione (**J**)

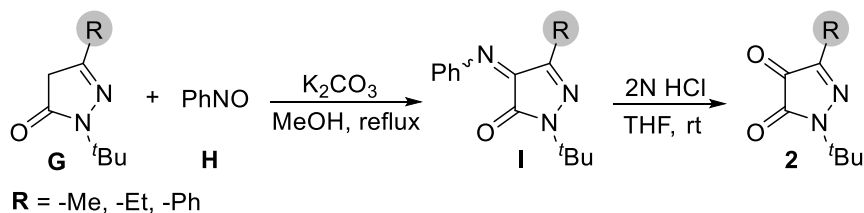
Pyrazole-4,5-dione (**J**) were prepared by following steps.³

2.3.1. Step 1: Synthesis of pyrazolones (**G**)



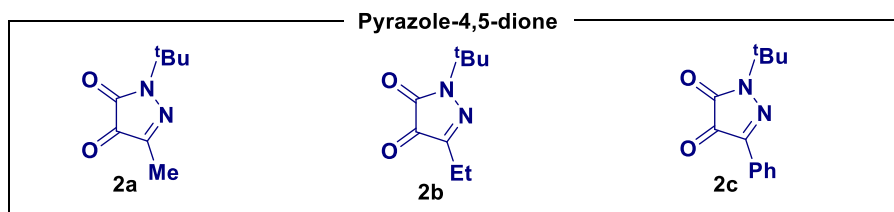
Tert-butylhydrazine hydrochloride **F** (2.0 equiv.) and NaOAc (2.0 equiv.) was added to a solution of ethyl acetoacetate **E** (1.0 equiv.) in ethanol (0.87 M). The reaction mixture was then refluxed for overnight under argon atmosphere. After completion of reaction, the mixture was diluted with DCM and washed with water and brine, dried over Na₂SO₄, and concentrated to give a yellow solid. The resulting compound was then washed with cold Et₂O (3 x 50 mL) and dried in *vacuo* to afford **G** as white solid.

2.3.2. Step 2: Synthesis of pyrazole-4,5-dione (**2**):

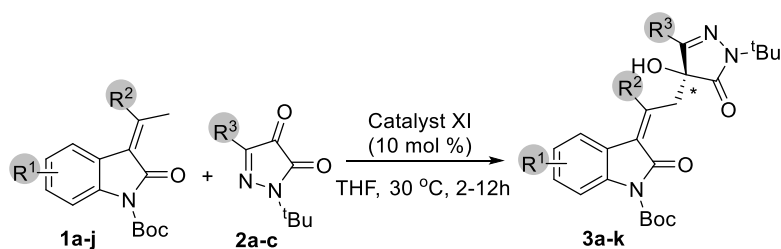


To a solution of pyrazolone **G** (1.0 equiv.) in MeOH (0.6 M) at room temperature were added Nitrosobenzene **H** (1.0 equiv.) and K₂CO₃ (0.2 equiv.). The reaction mixture was then charged with reflux condenser and refluxed for 3 h. The solvent was removed under reduced pressure, and the residue was dissolved in ethyl acetate and washed three times with water, brine and dried over Na₂SO₄. After removing the solvent in vacuum, the crude product was purified by flash column chromatography to afford ketimine (**I**).

Ketimine **I** was then dissolved in THF (0.13 M), and an aqueous HCl (2.0 N) solution (25 mL) was added to it at room temperature. After completion of the reaction checked by TLC, the mixture was diluted with water and organic layer was extracted three times with DCM. The combined organic layers were dried over Na₂SO₄, solvent was removed in vacuum. The crude product was then purified by flash column chromatography to afford **2**.

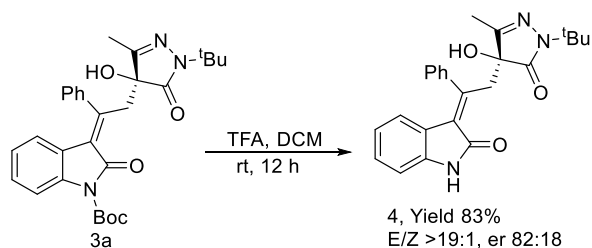


3. General procedure for asymmetric vinylogous aldol reaction of 3-alkylidene-2-oxindole with pyrazolones



To a solution of catalyst **V**/**VI** (0.01mmol, 10 mol%) in THF (1.0 mL) was added pyrazole-4,5-dione (**2a-c**) (0.12 mmol). In the resulting homogenous mixture 3-alkylidene-2-oxindole (**1a-j**) (0.1 mmol) was added at room temperature and it was kept at rt until the completion of the reaction. The reaction mixture was directly processed for the purification by silica gel column chromatography (eluent: EtOAc/Petroleum ether = 3/10, v/v) without any workup. Racemic reaction were performed as racemic thiourea [1-(3,5-bis(trifluoromethyl)phenyl)-3-(2-(dimethylamino)ethyl)thiourea] (7.46 mg, 0.2equiv., 0.02 mmol) was added to a homogenous mixture 3-alkylidene-2-oxindole (0.1 mmol) and pyrazolone (0.12 mmol) in THF (1.0 ml) at room temperature until the reaction completion. Purification of the racemic adduct was done similar to chiral reaction condition.

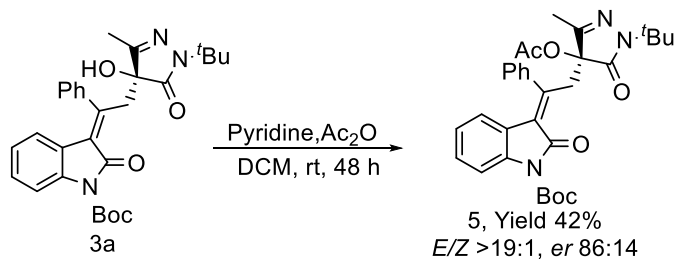
4. General procedure for N-Boc deprotection of compound **3a**:



Compound **3a** (50.3 mg, 0.10 mmol, 1.0 equiv) was dissolved in anhydrous DCM (1.0 mL) and trifluoroacetic acid (TFA) (1.00mmol, 77 μ L, 10.0 equiv.) was added in the reaction mixture. The reaction mixture was then stirred at room temperature for 12 h. After completion of reaction checked by TLC, it was quenched with saturated NaHCO_3 . The organic layer was separated and the aqueous layer was washed with DCM (3 x 3 mL). The combined organic layer was dried over Na_2SO_4 , filtered and concentrated. The crude mixture was purified by

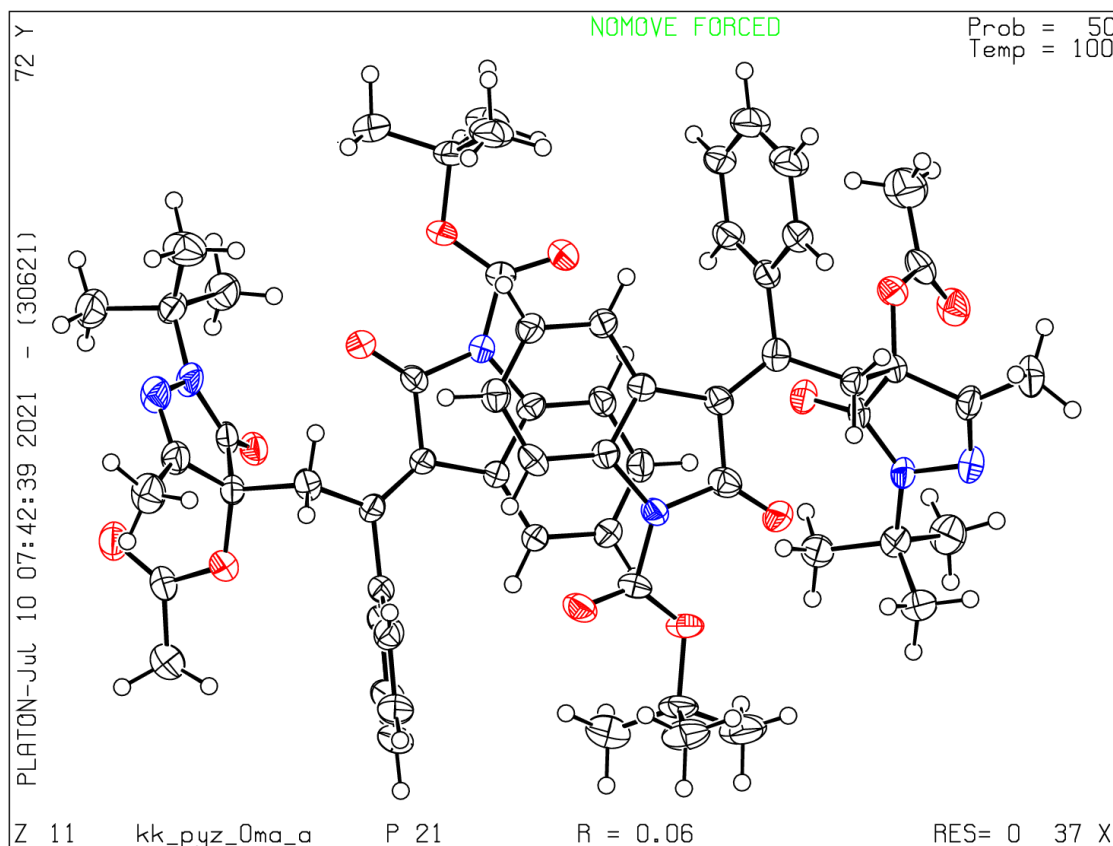
flash chromatography (silica gel, hexane/ethyl acetate = 70/30) to give the product as a yellow sticky solid.

5. General procedure for -O acylation of compound **3a**:



Compound **3a** (50.3 mg, 0.10 mmol, 1.0 equiv) was dissolved in anhydrous DCM (1.0 mL) and pyridine (0.1 mmol, 1.0 equiv.) was added in the reaction mixture followed by addition of acetic anhydride (0.15 mmol, 1.5 equiv.). The reaction mixture was then stirred at room temperature for 48 h. After completion of reaction checked by TLC and the reaction mixture was directly processed for the purification by silica gel column chromatography. The combined organic layer was dried over Na₂SO₄, filtered and concentrated. The crude mixture was purified by flash chromatography (silica gel, hexane/ethyl acetate = 93/7) to give the product as a yellow solid.

6. Crystal Structure of 5:



Bond precision:

C-C = 0.0086 Å

Wavelength=0.71073

Cell:

a=6.5527(6)

b=23.763(2)

c=22.007(2)

alpha=90

beta=90.081(3)

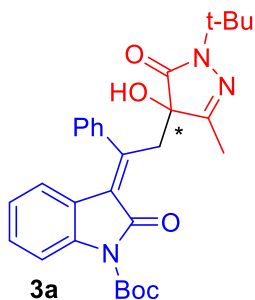
gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	3426.8(5)	3426.8(5)
Space group	P 21	P 21
Hall group	P 2yb	P 2yb
Moiety formula	C ₃₁ H ₃₅ N ₃ O ₆ [+ solvent]	C ₃₁ H ₃₅ N ₃ O ₆ [+ solvent]
Sum formula	C ₃₁ H ₃₅ N ₃ O ₆ [+ solvent]	C ₃₁ H ₃₅ N ₃ O ₆ [+ solvent]

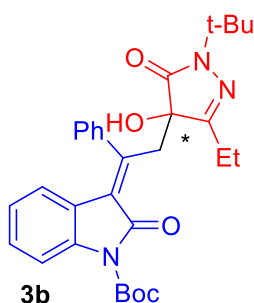
Mr	545.62	545.62
Dx,g cm-3	1.058	1.058
Z	4	4
Mu (mm-1)	0.074	0.074
F000	1160.0	1160.0
F000'	1160.55	
h,k,lmax	7,28,26	7,28,26
Nref	12073[6196]	12073
Tmin,Tmax	0.984,0.988	
Tmin'	0.982	
Correction method= Not given		
Data completeness= 1.95/1.00	Theta(max)= 25.000	
R(reflections)= 0.0618(7898)	wR2(reflections)= 0.1763(12069)	
S = 1.096	Npar= 738	

***tert*-Butyl (*E*)-3-(2-(1-(*tert*-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1*H*-pyrazol-4-yl)-1-phenylethylidene)-2-oxoindoline-1-carboxylate (**3a**):**



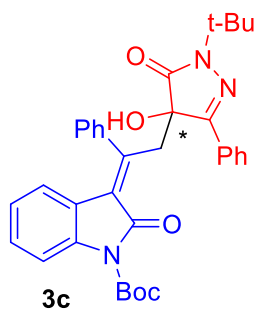
light yellow solid (48 mg, 95% yield). **R_f** = 0.4 (ethyl acetate/petroleum ether = 3/7). **HPLC**: The *er* of the **3a** was determined to be 86:14 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 90:10, 1mL/min, λ = 225 nm, t (major) = 8.051 min, t (minor) = 6.977 min]. **Optical Rotation**: $[\alpha]^{D25} = +59.36^\circ$ (c 0.47, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.79 (d, *J* = 8.2 Hz, 1H), 7.64 – 7.51 (m, 2H), 7.49-7.41 (m, 3H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.71 (t, *J* = 7.7 Hz, 1H), 6.18 (d, *J* = 7.8 Hz, 1H), 4.10 (d, *J* = 13.1 Hz, 1H), 3.29 (d, *J* = 13.2 Hz, 1H), 3.12 (s, 1H), 2.02 (s, 3H), 1.64 (s, 9H), 1.41 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 173.1, 166.2, 158.0, 151.3, 149.3, 141.6, 138.8, 129.6, 129.5, 129.4, 129.1, 127.8, 126.1, 123.4, 123.0, 122.8, 114.5, 84.2, 80.6, 57.2, 40.7, 28.1, 27.9, 13.0. **HRMS ESI**: [M+Na]⁺, Calcd for C₂₉H₃₃N₃NaO₅: 526.2318; found 526.2301.

***tert*-Butyl (*E*)-3-(2-(1-(*tert*-butyl)-3-ethyl-4-hydroxy-5-oxo-4,5-dihydro-1*H*-pyrazol-4-yl)-1-phenylethylidene)-2-oxoindoline-1-carboxylate (**3b** & **3b'**):**



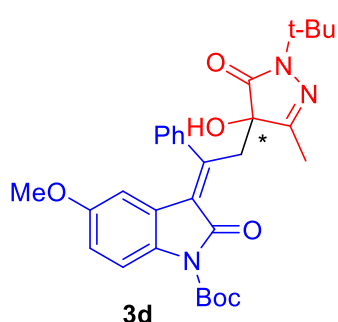
light yellow solid (49 mg, 95% yield). **R_f** = 0.6 (ethyl acetate/petroleum ether = 3/7). **HPLC**: The *er* of the **3b** (**Catalyst V**) was determined to be 78:22 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 95:5, 1mL/min, λ = 225 nm, t (major) = 22.40 min, t (minor) = 16.37 min] and **3b'** (**Catalyst VI**) was determined to be 75:25 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 95:5, 1mL/min, λ = 225 nm, t (major) = 16.09 min, t (minor) = 22.71 min]. **Optical Rotation**: $[\alpha]^{D25} = +50.20^\circ$ (c 0.49, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.78 (d, *J* = 8.2 Hz, 1H), 7.66 – 7.50 (m, 2H), 7.48-7.40 (m, 3H), 7.15 (t, *J* = 8 Hz, 1H), 6.70 (t, *J* = 7.5 Hz, 1H), 6.16 (d, *J* = 7.8 Hz, 1H), 4.11 (d, *J* = 13.1 Hz, 1H), 3.29 (d, *J* = 13.2 Hz, 1H), 3.03 (s, 1H), 2.39 (m, 2H), 1.64 (s, 9H), 1.42 (s, 9H), 1.19 (t, *J* = 7.4 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃): δ 173.3, 166.2, 161.6, 151.5, 149.3, 141.6, 138.7, 129.6, 129.5, 129.3, 129.0, 127.8, 126.0, 123.4, 123.0, 122.8, 114.5, 84.2, 80.9, 77.2, 57.3, 40.9, 28.1, 27.9, 20.7, 9.3. **HRMS ESI**: [M+Na]⁺, Calcd for C₃₀H₃₅N₃KO₅: 556.2214; found 556.2289.

***tert*-Butyl (*E*)-3-(2-(1-(*tert*-butyl)-4-hydroxy-5-oxo-3-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-1-phenylethylidene)-2-oxoindoline-1-carboxylate (**3c** & **3c'**):**



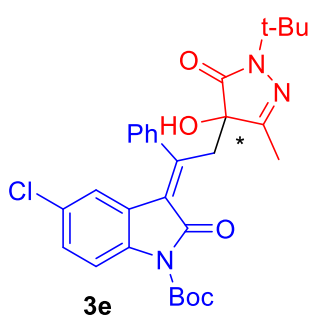
light yellow solid (52 mg, 92% yield). $R_f = 0.6$ (ethyl acetate/petroleum ether = 3/7). **HPLC:** The *er* of the **3c** (**Catalyst V**) was determined to be 65:35 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 95:5, 1mL/min, $\lambda = 225$ nm, t (major) = 29.14 min, t (minor) = 17.02 min] and **3c'** (**Catalyst VI**) was determined to be 62:38 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 95:5, 1mL/min, $\lambda = 225$ nm, t (major) = 16.49 min, t (minor) = 28.49 min]. **Optical Rotation:** $[\alpha]^{D25} = +56.73^\circ$ (c 0.52, CHCl_3). **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ 8.01 – 7.92 (m, 2H), 7.81 (d, $J = 8.1$ Hz, 1H), 7.68 – 7.56 (m, 2H), 7.56 – 7.43 (m, 3H), 7.42 – 7.36 (m, 3H), 7.18 (t, $J = 8.1$ Hz, 1H), 6.73 (t, $J = 8.2$ Hz, 1H), 6.63 (d, $J = 8.2$ Hz, 1H), 6.20 (d, $J = 7.6$ Hz, 1H), 4.29 (d, $J = 13.5$ Hz, 1H), 3.54 (d, $J = 13.5$ Hz, 1H), 3.33 (bs, 1H), 1.67 (s, 9H), 1.55 (s, 9H); **$^{13}\text{C NMR}$** (100 MHz, CDCl_3): δ 173.4, 166.0, 155.3, 151.2, 149.3, 141.8, 138.7, 130.4, 129.8, 129.7, 129.5, 129.3, 129.0, 128.6, 128.0, 127.8, 126.7, 126.1, 123.4, 123.0, 122.8, 114.5, 84.1, 81.2, 58.0, 42.1, 28.2, 28.0. **HRMS ESI:** $[\text{M}+\text{Na}]^+$, Calcd for $\text{C}_{34}\text{H}_{35}\text{N}_3\text{NaO}_5$: 588.2474; found 588.2521.

tert-Butyl (E)-3-(2-(1-(tert-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-1-phenylethylidene)-5-methoxy-2-oxoindoline-1-carboxylate (3d):



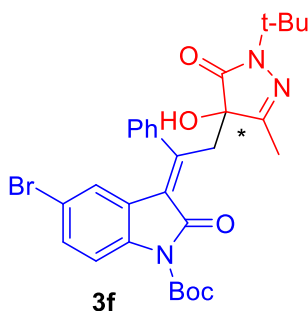
light yellow solid (52 mg, 98% yield). $R_f = 0.5$ (ethyl acetate/petroleum ether = 3/7). **HPLC:** The *er* of the **3d** was determined to be 81:19 [determined by HPLC, Chiralpak ID, hexane: isopropanol = 95:5, 0.75mL/min, $\lambda = 225$ nm, t (major) = 20.31 min, t (minor) = 18.20 min]. **Optical Rotation:** $[\alpha]^{D25} = +79.80^\circ$ (c 0.52, CHCl_3). **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ 7.69 (d, $J = 9.0$ Hz, 1H), 7.64 – 7.50 (m, 2H), 7.50 – 7.39 (m, 3H), 6.70 (dd, $J = 9.0, 2.7$ Hz, 1H), 5.70 (d, $J = 2.6$ Hz, 1H), 4.05 (d, $J = 13.1$ Hz, 1H), 3.35 (s, 3H), 3.31 (d, $J = 13.1$ Hz, 1H), 2.01 (s, 3H), 1.62 (s, 9H), 1.39 (s, 9H). **$^{13}\text{C NMR}$** (100 MHz, CDCl_3): δ 173.2, 166.4, 158.2, 155.6, 151.5, 149.3, 141.4, 132.6, 129.6, 129.4, 129.3, 128.0, 127.9, 126.4, 123.6, 115.5, 115.5, 107.9, 84.0, 80.6, 57.2, 55.0, 40.6, 28.1, 27.9, 25.3, 13.0. **HRMS ESI:** $[\text{M}+\text{Na}]^+$, Calcd for $\text{C}_{30}\text{H}_{34}\text{N}_3\text{O}_6$: 534.2604; found 534.2632.

tert-Butyl (E)-3-(2-(1-(tert-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-1-phenylethylidene)-5-chloro-2-oxoindoline-1-carboxylate (3e):



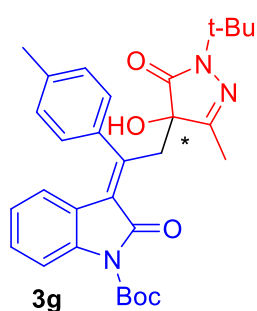
light yellow solid, (50 mg, 94% yield). **R_f** = 0.6 (ethyl acetate/petroleum ether = 3/7). **HPLC:** The *er* of the **3e** was determined to be 81:19 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 95:5, 1mL/min, λ = 225 nm, t (major) = 14.06 min, t (minor) = 12.35 min]. **Optical Rotation:** $[\alpha]^{D25}$ (**3e**) = +61.40° (c 0.5, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.78 (d, *J* = 8.7 Hz, 1H), 7.62 (m, 2H), 7.54 (m, 2H), 7.42 (d, *J* = 7.2 Hz, 1H), 7.15 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.08 (d, *J* = 2.1 Hz, 1H), 4.17 (d, *J* = 13.0 Hz, 1H), 3.25 (d, *J* = 13.1 Hz, 1H), 2.88 (s, 1H), 2.04 (s, 3H), 1.65 (s, 9H), 1.45 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 173.0, 165.4, 158.0, 153.2, 149.2, 141.0, 137.1, 129.9, 129.8, 129.6, 128.9, 128.7, 127.6, 127.5, 125.2, 124.2, 123.0, 115.7, 84.5, 80.5, 57.3, 40.5, 28.1, 27.9, 13.0. **HRMS ESI:** [M+Na]⁺, Calcd for C₂₉H₃₃N₃O₅Cl: 538.2109; found 538.2098.

tert-Butyl (E)-5-bromo-3-(2-(1-(tert-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-1-phenylethylidene)-2-oxoindoline-1-carboxylate (3f):



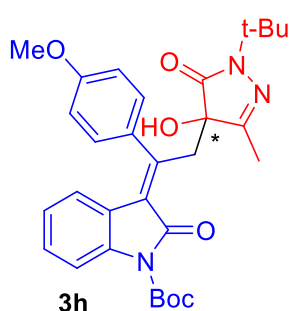
light yellow sticky (53 mg, 92% yield). **R_f** = 0.6 (ethyl acetate/petroleum ether = 3/7). **HPLC:** The *er* of the **3f** was determined to be 67:33 [determined by HPLC, Chiralpak IB, hexane: isopropanol = 95:5, 1mL/min, λ = 225 nm, t (major) = 7.39 min, t (minor) = 5.75 min]. **Optical Rotation:** $[\alpha]^{D25}$ = +20.28° (c 0.53, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.70 (d, *J* = 8.7 Hz, 1H), 7.57 (d, *J* = 11.3 Hz, 2H), 7.55 – 7.45 (m, 2H), 7.38 (d, *J* = 7.2 Hz, 1H), 7.26 (dd, *J* = 8.6, 2.1 Hz, 1H), 6.18 (d, *J* = 1.9 Hz, 1H), 4.15 (d, *J* = 13.1 Hz, 1H), 3.22 (d, *J* = 13.1 Hz, 1H), 2.94 (bs, 1H), 2.00 (s, 3H), 1.62 (s, 9H), 1.41 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 172.9, 165.3, 158.0, 153.3, 149.1, 141.0, 137.6, 131.6, 129.8, 129.8, 129.6, 127.6, 127.5, 125.9, 125.1, 124.6, 116.5, 116.1, 84.5, 80.5, 57.3, 40.5, 28.1, 27.9, 13.0. **HRMS ESI:** [M+Na]⁺, Calcd for C₂₉H₃₂N₃NaO₅Br: 604.1423; found 604.1471.

tert-Butyl (E)-3-(2-(1-(tert-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-1-(p-tolyl)ethylidene)-2-oxoindoline-1-carboxylate (3g):



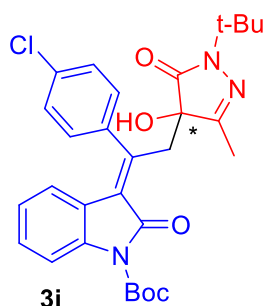
light yellow sticky (51 mg, 98% yield). R_f = 0.5 (ethyl acetate/petroleum ether = 3/7). **HPLC:** The *er* of the **3g** was determined to be 78:22 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 80:20, 1mL/min, λ = 225 nm, *t* (major) = 9.12 min, *t* (minor) = 7.71 min]. **Optical Rotation:** $[\alpha]^{D_{25}}$ (**3g**) = +53.60° (c 0.5, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.79 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 6.7 Hz, 1H), 7.29 (dd, *J* = 27.0, 8.6 Hz, 3H), 7.21 – 7.11 (m, 1H), 6.73 (t, *J* = 7.7 Hz, 1H), 6.30 (d, *J* = 7.8 Hz, 1H), 4.13 (d, *J* = 13.1 Hz, 1H), 3.24 (d, *J* = 13.2 Hz, 1H), 2.43 (s, 3H), 2.00 (s, 3H), 1.64 (s, 9H), 1.41 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 173.2, 166.2, 158.1, 151.6, 149.3, 139.6, 138.6, 138.4, 130.3, 130.2, 128.9, 127.9, 125.8, 123.4, 123.0, 122.9, 114.5, 84.1, 80.5, 60.4, 57.2, 40.6, 28.1, 27.9, 21.4, 14.2, 13.0. **HRMS ESI:** $[M+Na]^+$, Calcd for C₃₀H₃₆N₃O₅: 518.2655; found 518.2623.

***tert*-Butyl (*E*)-3-(2-(1-(*tert*-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1*H*-pyrazol-4-yl)-1-(4-methoxyphenyl)ethylidene)-2-oxoindoline-1-carboxylate (**3h**):**



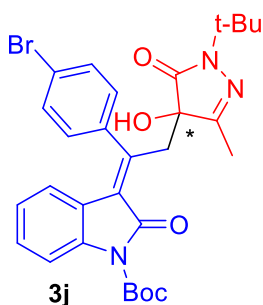
light yellow sticky (52 mg, 97% yield). R_f = 0.5 (ethyl acetate/petroleum ether = 3/7). **HPLC:** The *er* of the **3h** was determined to be 71:29 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 95:5, 1mL/min, λ = 225 nm, *t* (major) = 48.46 min, *t* (minor) = 33.49 min]. **Optical Rotation:** $[\alpha]^{D_{25}}$ (**3h**) = +45.57° (c 0.52, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.78 (dd, *J* = 7.7, 2.5 Hz, 1H), 7.48 (s, 1H), 7.35 (s, 1H), 7.20– 7.09 (m, 1H), 7.07 – 6.86 (m, 2H), 6.79 – 6.68 (m, 1H), 6.43 – 6.32 (m, 1H), 4.08 (d, *J* = 13.2 Hz, 1H), 3.87 (s, 3H), 3.38 (bs, 1H), 3.28 (d, *J* = 13.2 Hz, 1H), 1.99 (s, 3H), 1.62 (s, 9H), 1.39 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 173.3, 166.4, 160.6, 158.2, 151.6, 149.3, 138.5, 133.2, 129.8, 128.9, 125.7, 123.4, 123.1, 122.7, 114.8, 114.5, 84.2, 80.5, 57.2, 55.4, 40.6, 28.1, 27.9, 13.0. **HRMS ESI:** $[M+Na]^+$, Calcd for for C₃₀H₃₃N₃NaO₆: 556.2424; found 556.2591.

***tert*-Butyl (*E*)-3-(2-(1-(*tert*-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1*H*-pyrazol-4-yl)-1-(4-chlorophenyl)ethylidene)-2-oxoindoline-1-carboxylate (**3i**):**



give light yellow sticky (53 mg, 98% yield). R_f = 0.5 (ethyl acetate/petroleum ether = 3/7). **HPLC:** The *er* of the **3i** was determined to be 78:22 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 95:5, 1mL/min, λ = 225 nm, *t* (major) = 7.95 min, *t* (minor) = 6.88 min]. **Optical Rotation:** $[\alpha]^{D25}$ (**3i**) = +85.19° (c 0.52, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.78 (d, *J* = 8.2 Hz, 1H), 7.57 – 7.54 (m, 2H), 7.44 – 7.30 (m, 2H), 7.18 (t, *J* = 8.1 Hz, 1H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.24 (d, *J* = 7.9 Hz, 1H), 4.03 (d, *J* = 13.2 Hz, 1H), 3.26 (d, *J* = 13.2 Hz, 1H), 2.01 (s, 3H), 1.63 (s, 9H), 1.39 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 173.1, 166.1, 158.3, 149.9, 149.2, 139.8, 138.8, 135.3, 129.8, 129.6, 129.3, 126.4, 123.6, 122.9, 122.5, 114.7, 84.4, 80.5, 57.3, 40.4, 28.1, 27.9, 25.3, 13.0. **HRMS ESI:** $[M+Na]^+$, Calcd for C₂₉H₃₃N₃O₅Cl: 538.2109; found 538.2091.

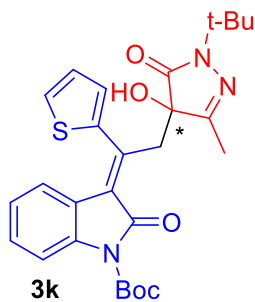
tert-Butyl (E)-3-(1-(4-bromophenyl)-2-(1-(tert-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)ethylidene)-2-oxoindoline-1-carboxylate (3j):



light yellow sticky (56 mg, 96% yield). R_f = 0.6 (ethyl acetate/petroleum ether = 3/7). **HPLC:** The *er* of the **3j** was determined to be 83:17 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 95:5, 1mL/min, λ = 225 nm, *t* (major) = 13.10 min, *t* (minor) = 10.66 min]. **Optical Rotation:** $[\alpha]^{D25}$ (**3j**) = +97.30° (c 0.52, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.78 (d, *J* = 8.2 Hz, 1H), 7.69 – 7.39 (m, 3H), 7.26 (s, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.75 (t, *J* = 7.7 Hz, 1H), 6.24 (d, *J* = 7.8 Hz, 1H), 4.07 (dd, *J* = 13.5, 4.6 Hz, 1H), 3.23 (d, *J* = 13.2 Hz, 1H), 2.00 (s, 3H), 1.62 (s, 9H), 1.38 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 173.2, 166.1, 149.8, 149.2, 140.3, 138.8, 132.7, 132.5, 129.9, 129.7, 126.3, 123.6, 123.5, 122.9, 122.5, 114.7, 84.3, 64.4, 57.3, 40.3, 28.1, 27.9, 25.3, 13.0. **HRMS ESI:** $[M+Na]^+$, Calcd for C₂₉H₃₃N₃O₅Br: 582.1604; found 582.1588.

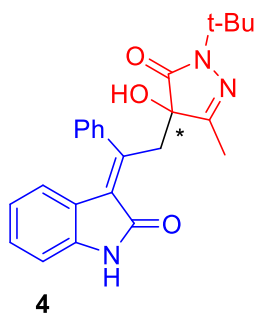
tert-Butyl (E)-3-(2-(1-(tert-butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-1-(thiophen-2-yl)ethylidene)-2-oxoindoline-1-carboxylate (3k):

light yellow sticky (46 mg, 90% yield). R_f = 0.5 (ethyl acetate/petroleum ether = 3/7); **HPLC:** The *er* of the **3k** was determined to be 78:22 [determined by HPLC, Chiralpak AD-H,



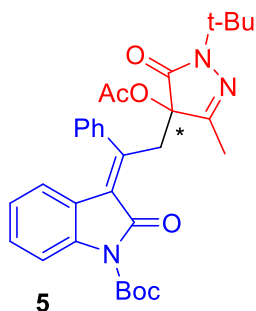
hexane: isopropanol = 95:5, 1mL/min, $\lambda = 225$ nm, t (major) = 10.41 min, t (minor) = 8.00 min]. **Optical Rotation:** $[\alpha]^{25}$ (**3k**) = +116.30° (c 0.46, CHCl₃). **¹H NMR** (400 MHz, CDCl₃): δ 7.79 (d, $J = 8.2$ Hz, 1H), 7.55 (dd, $J = 4.1, 0.9$ Hz, 1H), 7.41 – 7.32 (m, 1H), 7.19 (t, $J = 7.8$ Hz, 1H), 7.17 – 7.10 (m, 1H), 6.81 (t, $J = 7.7$ Hz, 1H), 6.69 (d, $J = 7.9$ Hz, 1H), 3.96 (d, $J = 13.4$ Hz, 1H), 3.73 (bs, 1H), 3.31 (d, $J = 13.4$ Hz, 1H), 2.00 (s, 3H), 1.62 (s, 9H), 1.42 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 173.3, 166.2, 158.2, 149.1, 143.7, 142.7, 138.8, 129.5, 129.1, 129.0, 128.2, 127.6, 123.6, 122.7, 122.6, 114.7, 84.4, 80.4, 28.1, 27.9, 25.3, 13.0. **HRMS ESI:** $[M+Na]^+$, Calcd for C₂₇H₃₁N₃NaO₅S: 532.1882; found 532.2579

(E)-3-(2-(1-(tert-Butyl)-4-hydroxy-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-1-



phenylethylidene)indolin-2-one (4): light yellow sticky (33 mg, 83% yield). **R_f** = 0.4 (ethyl acetate/petroleum ether = 4/6); **HPLC:** The *er* of the **3k** was determined to be 82:18 [determined by HPLC, Chiralpak ID, hexane: isopropanol = 70:30, 1mL/min, $\lambda = 225$ nm, t (major) = 12.12 min, t (minor) = 6.24 min]. **¹H NMR** (400 MHz, CDCl₃): δ 9.37 (s, 1H), 7.53 (s, 1H), 7.46 (s, 3H), 7.39 (s, 1H), 7.07 (t, $J = 7.6$ Hz, 1H), 6.93 – 6.85 (m, 1H), 6.58 (t, 1H), 6.25 – 6.14 (m, 1H), 5.70 (s, 1H), 3.88 (dd, $J = 13.3, 5.3$ Hz, 1H), 3.56 (dd, $J = 13.3, 5.1$ Hz, 1H), 2.03 (s, 3H), 1.34 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃): δ 174.8, 171.0, 160.1, 151.2, 141.0, 140.1, 129.3, 129.1, 128.4, 127.8, 123.4, 123.1, 121.9, 110.2, 81.3, 57.1, 41.1, 29.8, 27.9, 13.3.

tert-butyl (E)-3-(2-(4-acetoxy-1-(tert-butyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-

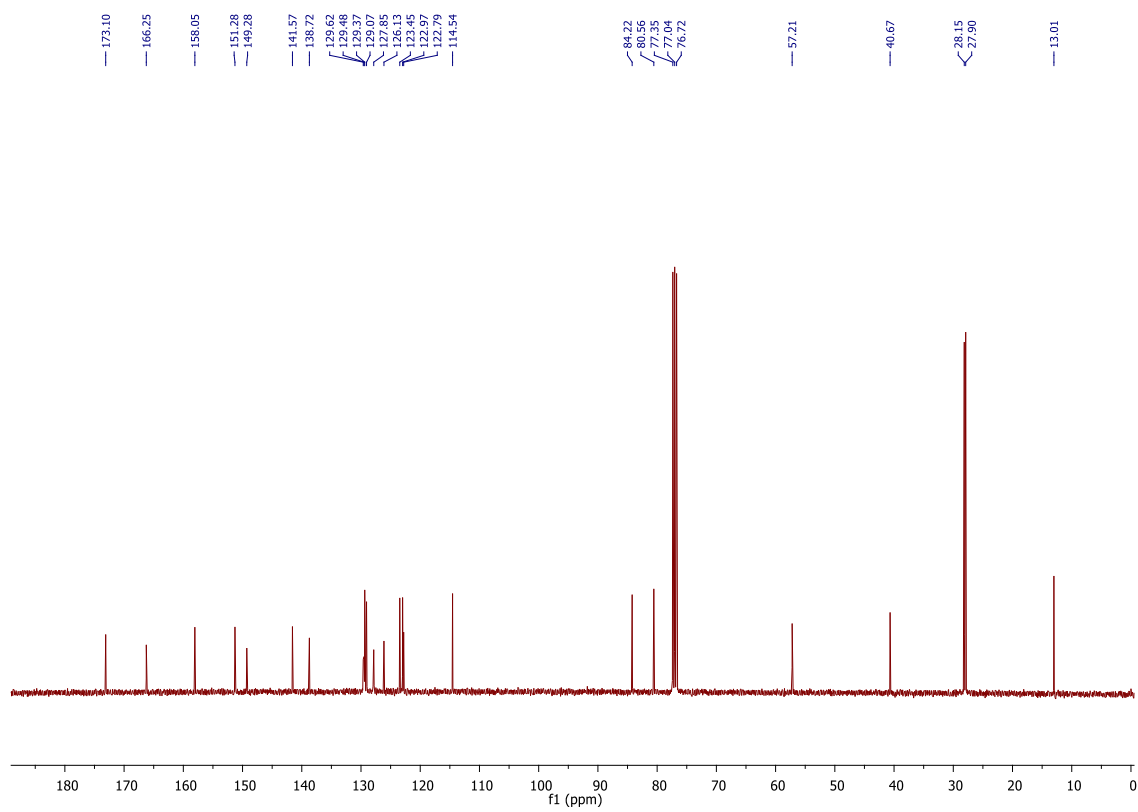
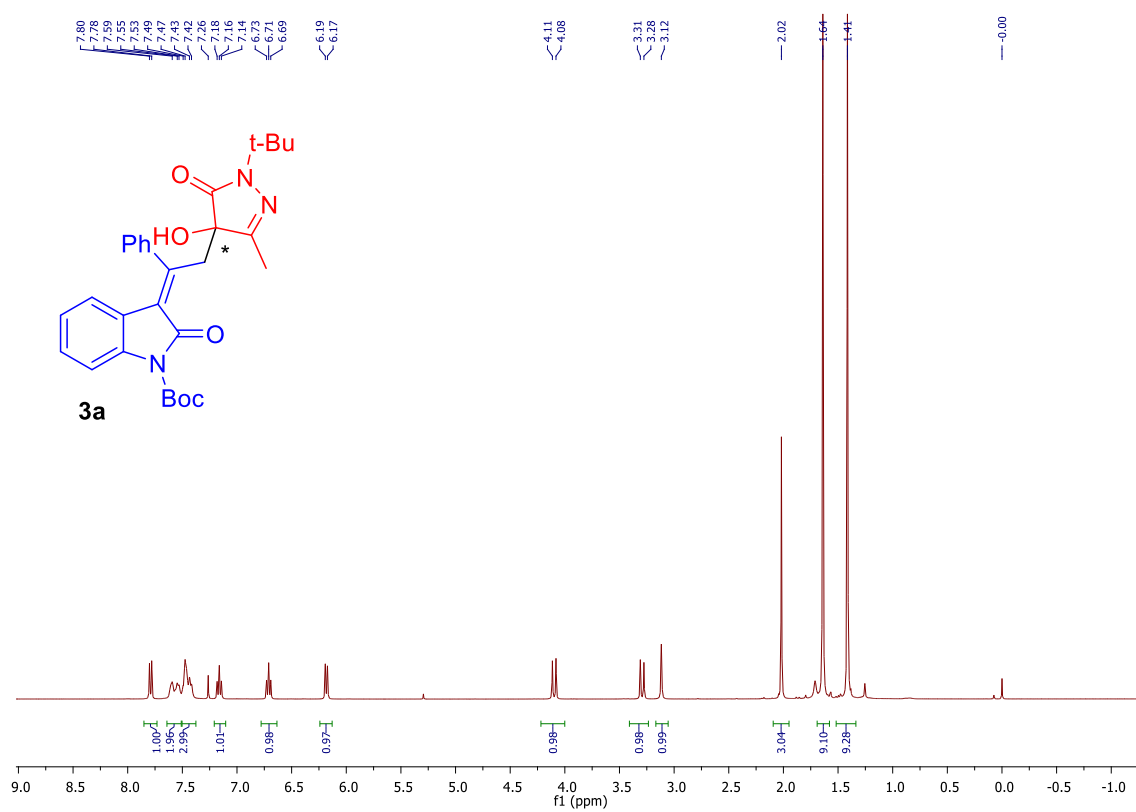


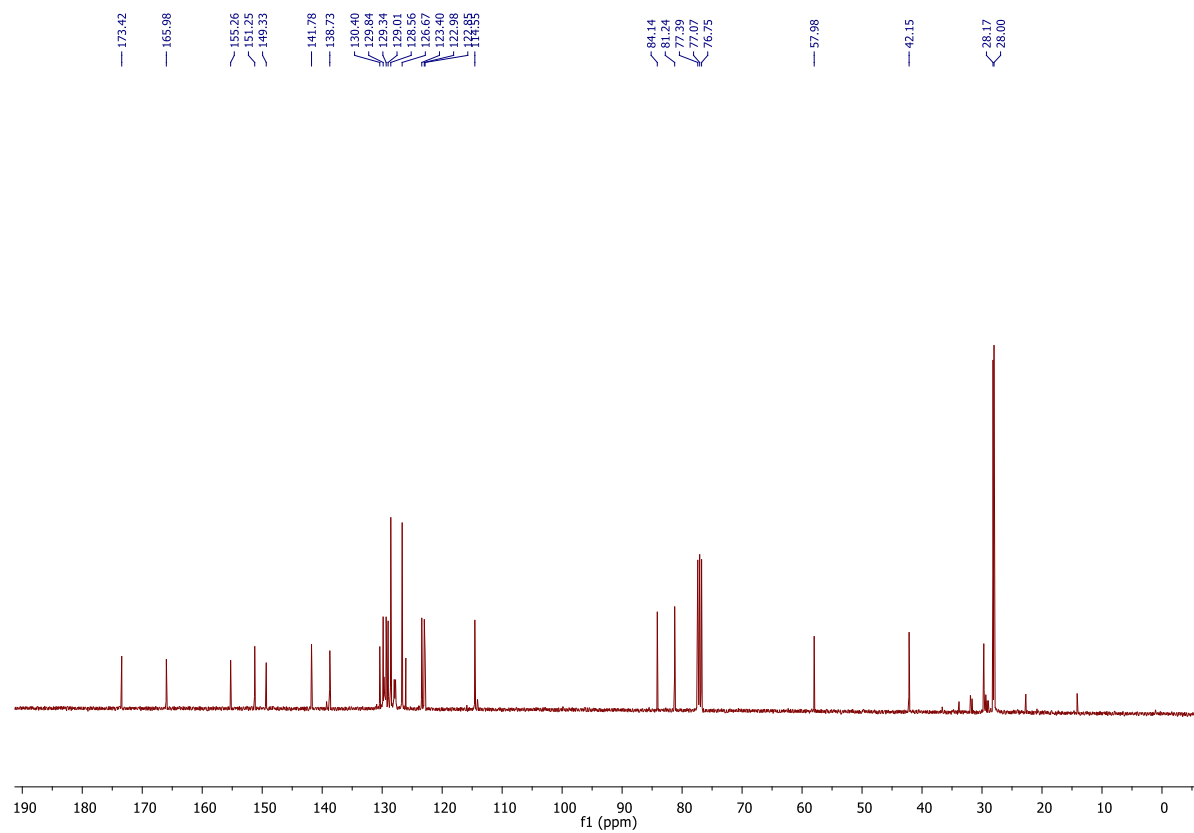
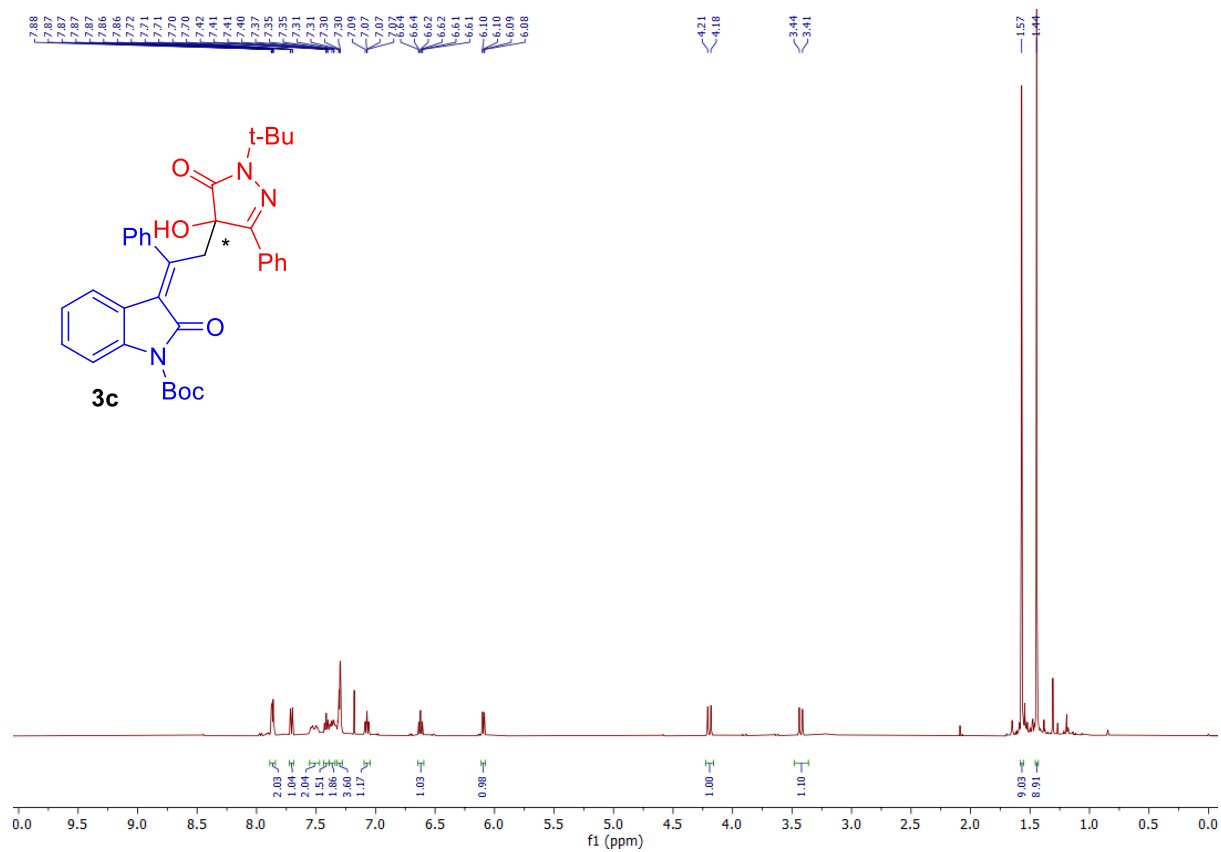
yl)-1-phenylethylidene)-2-oxoindoline-1-carboxylate (5): light yellow (23 mg, 42% yield). **R_f** = 0.4 (ethyl acetate/petroleum ether = 1/10); **HPLC:** The *er* of the **5** was determined to be 86:14 [determined by HPLC, Chiralpak IE, hexane: isopropanol = 97:03, 0.5mL/min, $\lambda = 225$ nm, t (major) = 19.78 min, t (minor) = 16.41 min]. **¹H NMR** (500 MHz, CDCl₃) δ 7.74 (d, $J = 8.2$ Hz, 1H), 7.60 (d, $J = 6.9$ Hz, 1H), 7.46 (t, $J = 7.2$ Hz, 1H), 7.40 – 7.33 (m, 2H), 7.19 (s, 1H), 7.08 (t, $J = 7.9$ Hz, 1H), 6.62 (t, $J = 7.7$ Hz, 1H), 6.07 (d, $J = 7.9$ Hz, 1H), 4.46 (d, $J = 13.3$ Hz, 1H), 2.94 (d, $J = 13.3$ Hz, 1H), 1.84 (s, 3H), 1.56 (s, 9H), 1.51 (s, 3H), 1.43 (s, 9H). **¹³C NMR** (126 MHz, CDCl₃) δ 169.5, 168.3, 165.3, 153.0, 149.8, 149.5, 142.0, 138.9, 129.4, 129.0, 128.5, 128.4, 126.3, 126.1, 123.3, 122.9, 114.5, 83.96, 82.8, 57.6, 36.9, 28.2, 27.8, 19.7, 13.0.

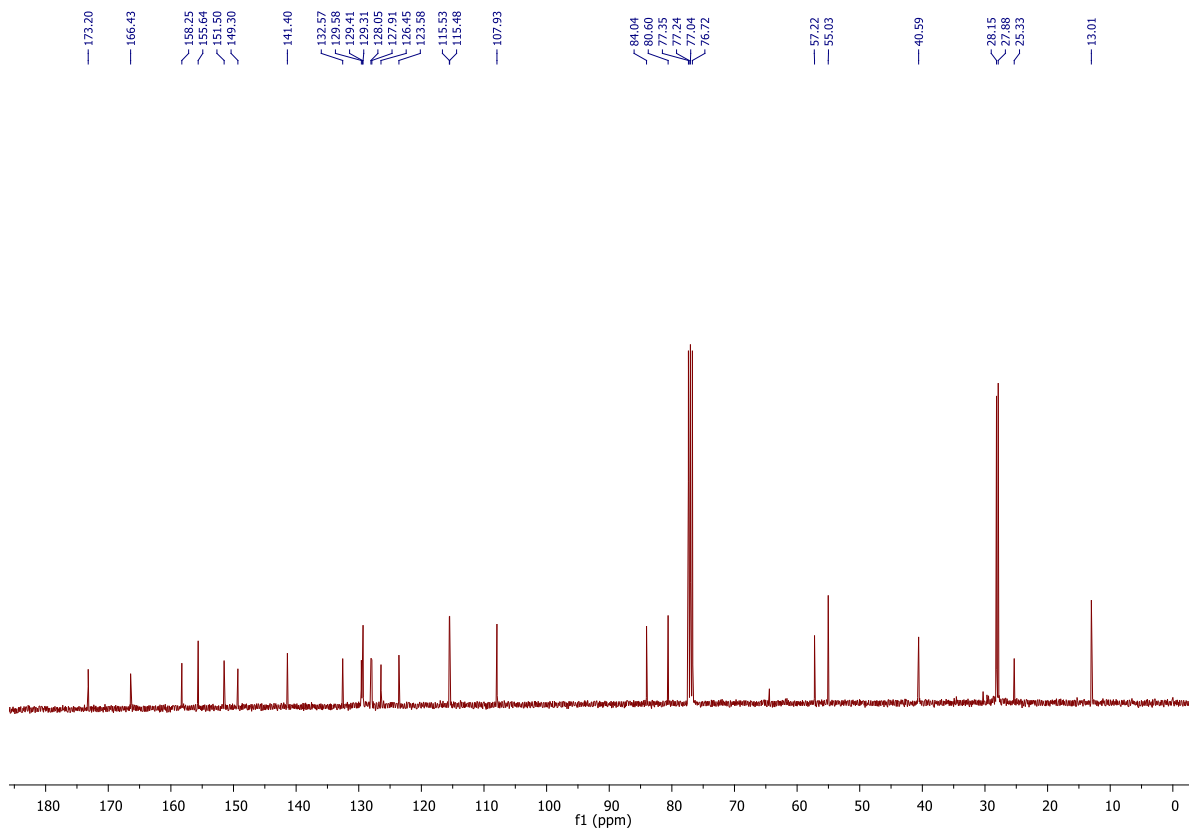
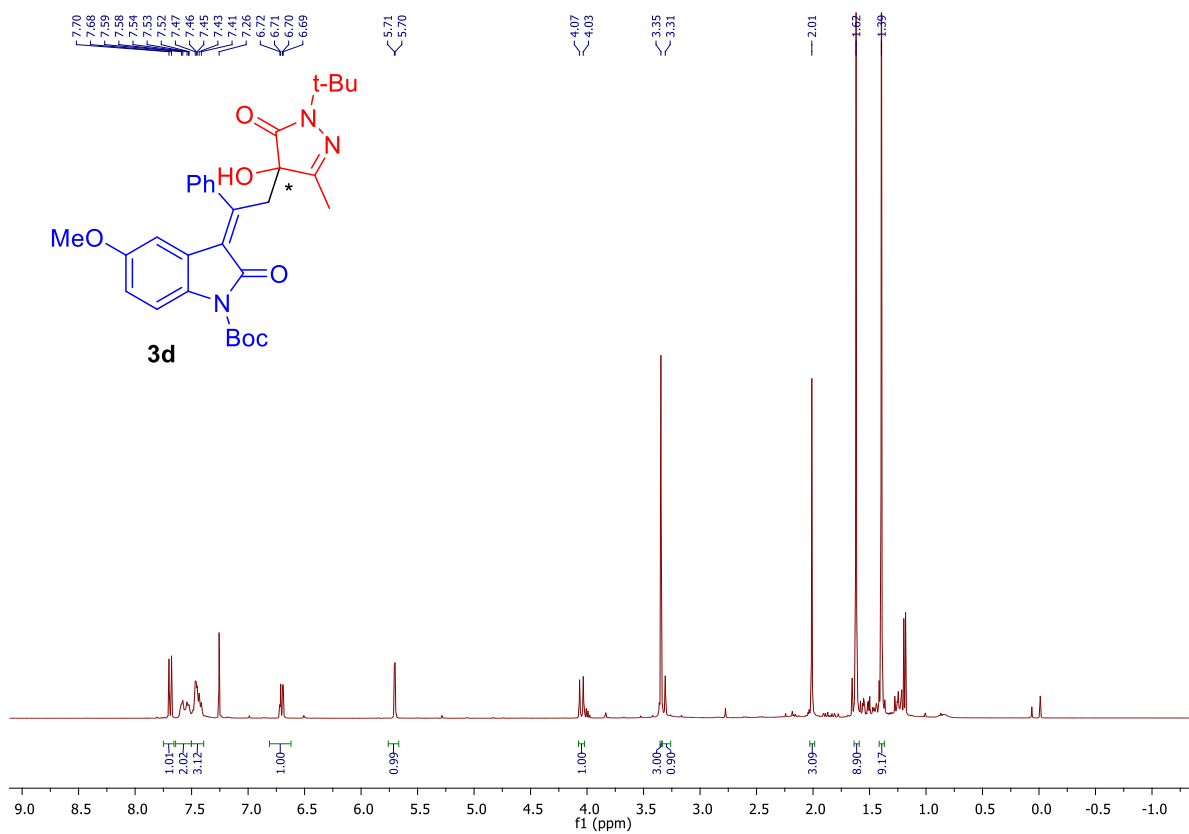
5. References:

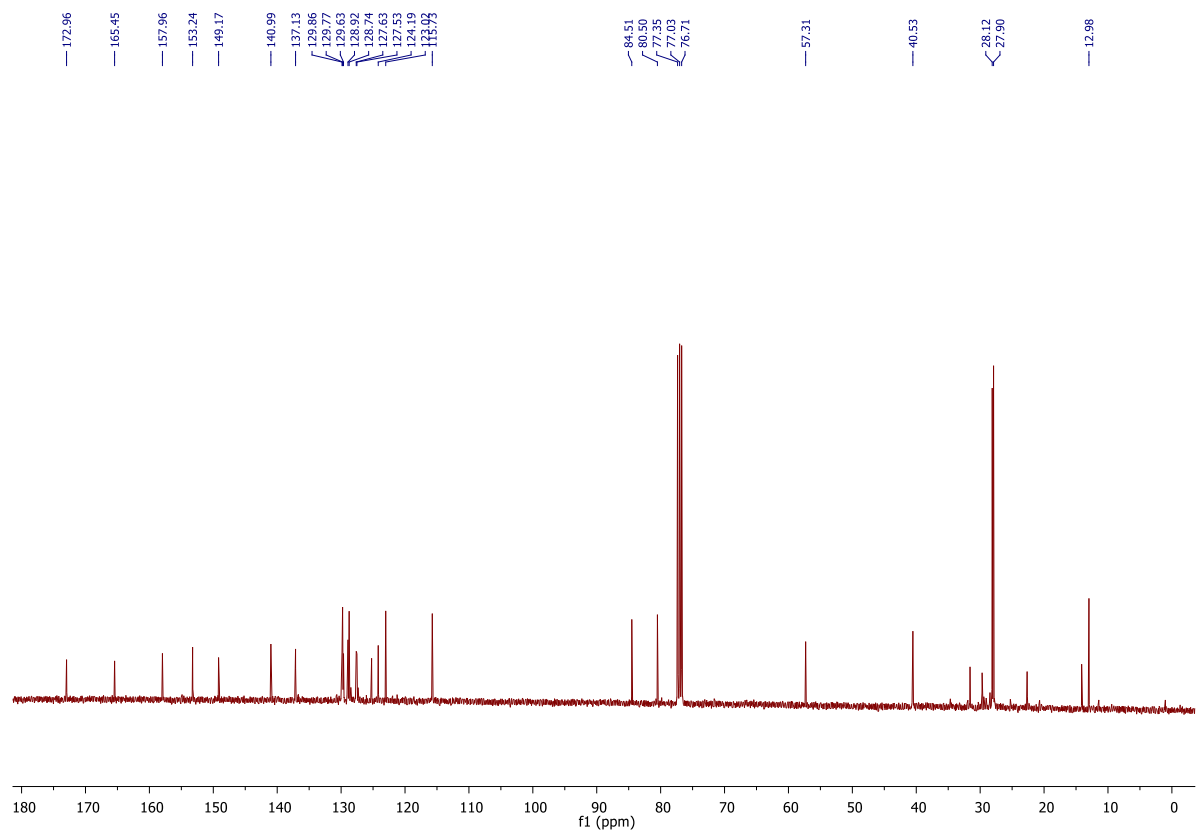
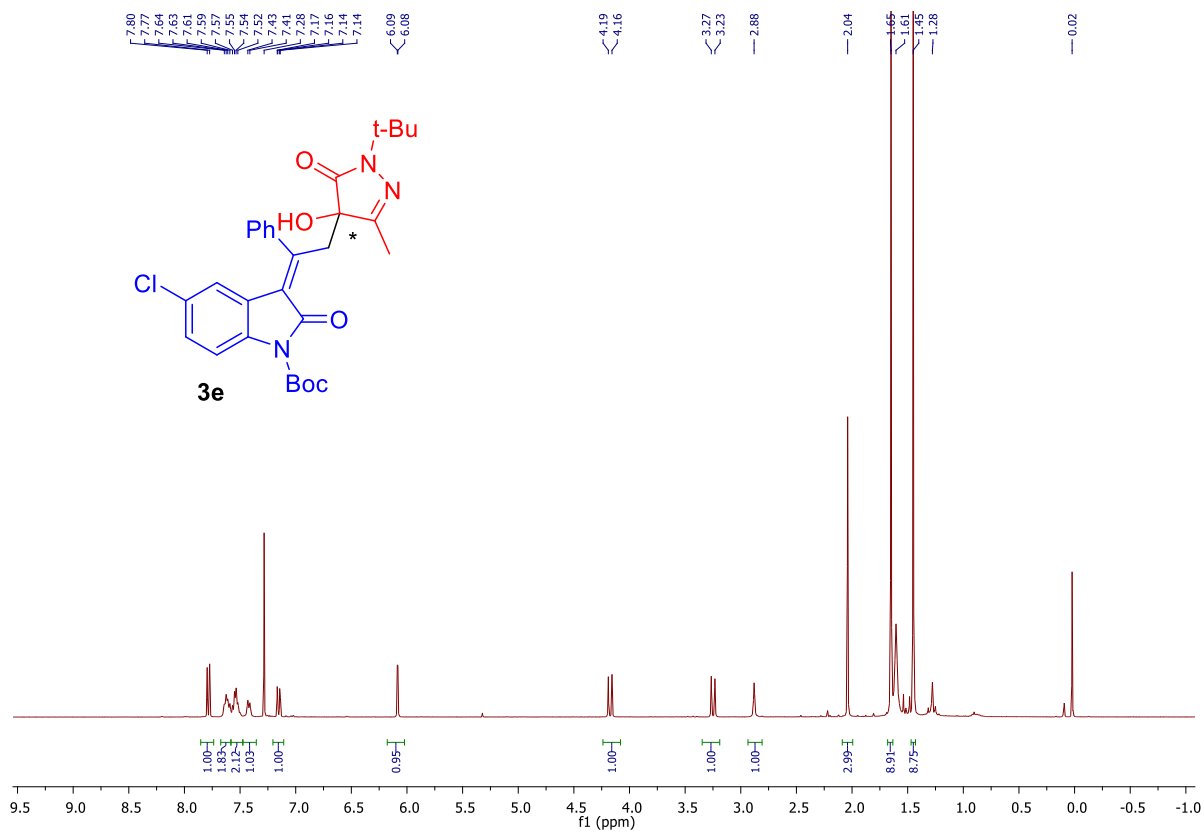
1. (a) C. Cassani, R. Martín-Rapún, E. Arceo, F. Bravo and P. Melchiorre, *Nature Protocols*, 2013, **8**, 325–344; (b) J. P. Malerich, K. Hagihara and V. H. Rawal, *J. Am. Chem. Soc.*, 2008, **130**, 14416–14417; (c) T. Sekikawa, T. Kitaguchi, H. Kitaura, T. Minami and Y. Hatanaka, *Org. Lett.*, 2015, **17**, 3026–3029. (d) L. Roiser and M. Waser, *Org. Lett.*, 2017, **19**, 2338–2341.
2. Y. Liu, Y. Yang, Y. Huang, X.-H. Xu and F.-L. Qing, *Synlett*, 2015, **26**, 67-72.
3. (a) J. P. Phelan and J. A. Ellman, *Adv. Synth. Catal.*, 2016, **358**, 1713–1718; (b) P. Chauhan, S. Mahajan, U. Kaya, A. Peuronen, K. Rissanen and D. Enders, *J. Org. Chem.*, 2017, **82**, 7050–7058.

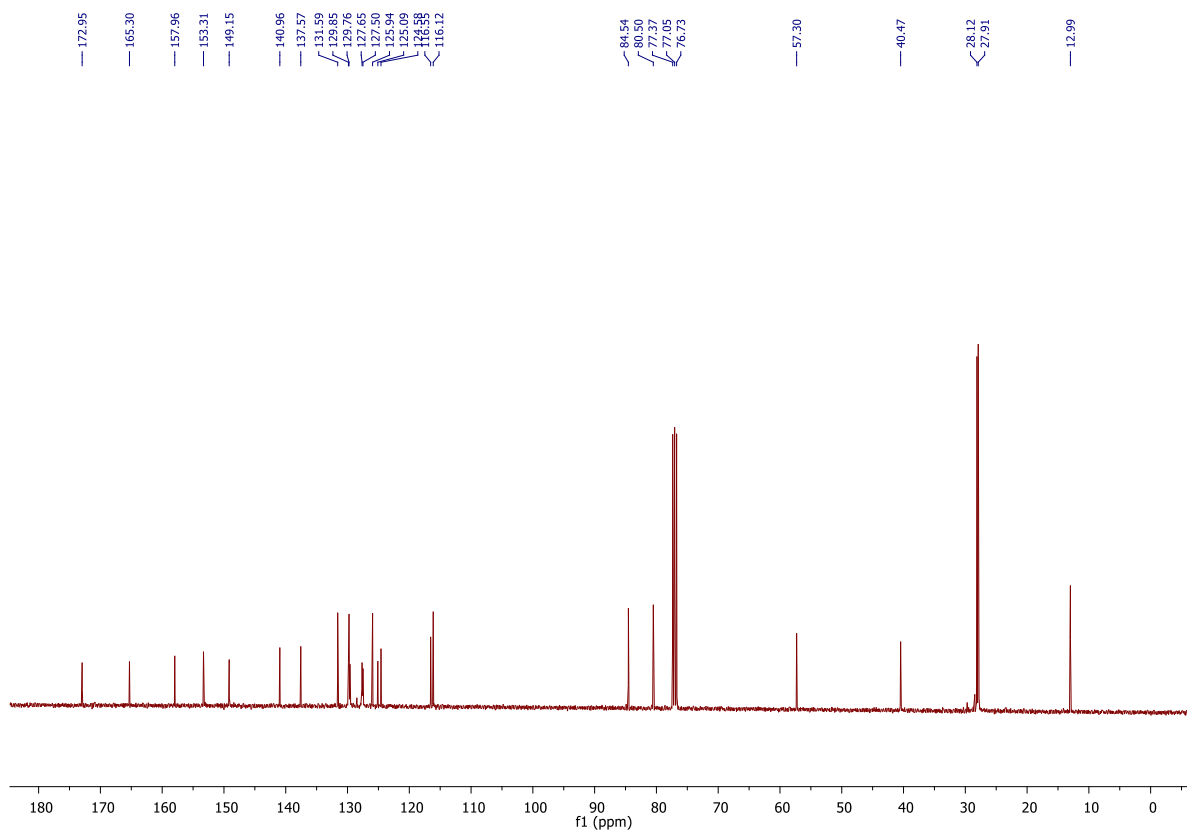
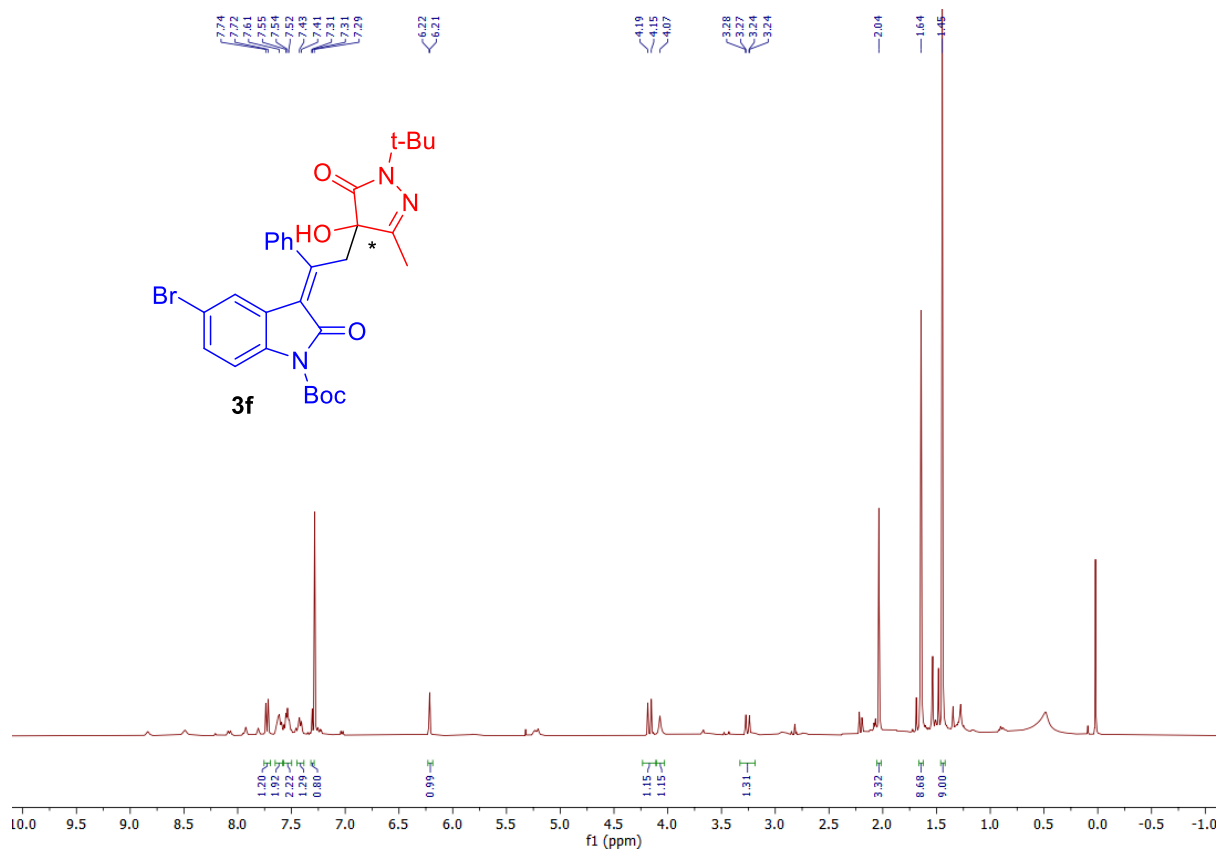
6. Copies of ^1H , ^{13}C and HPLC spectra

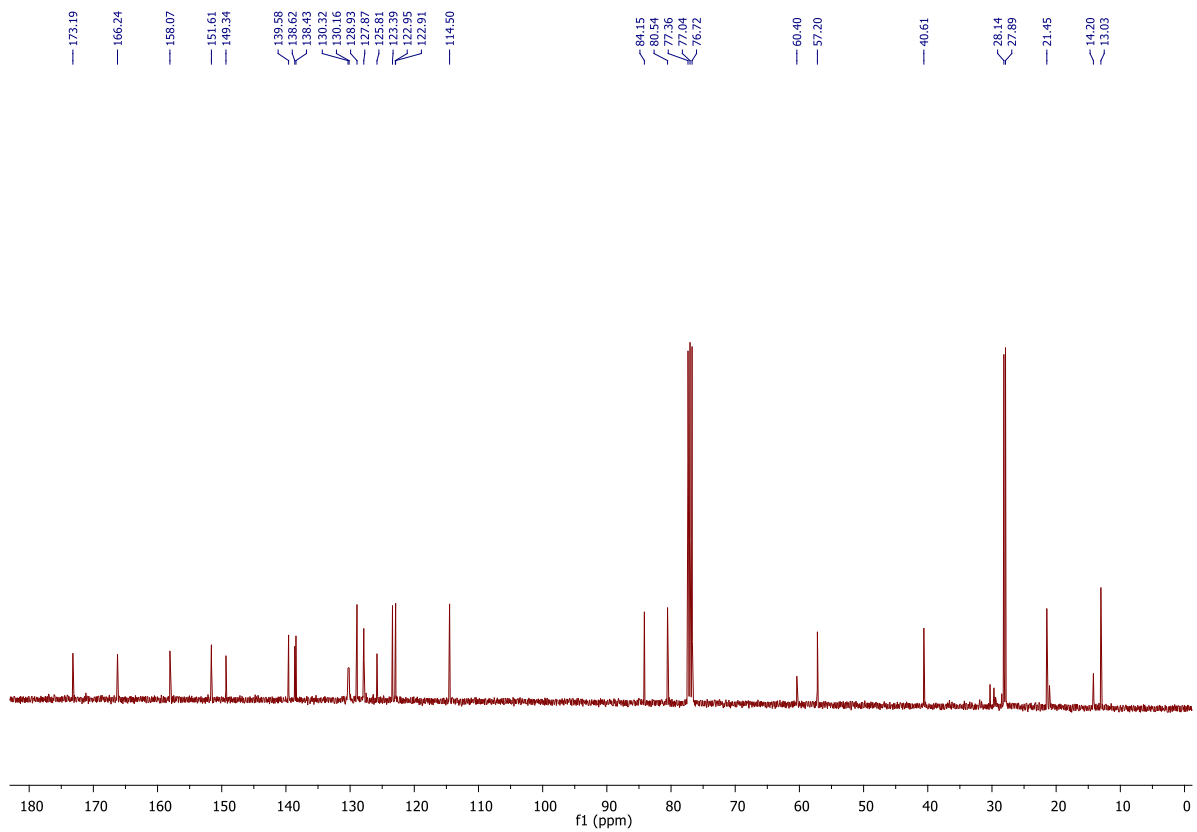
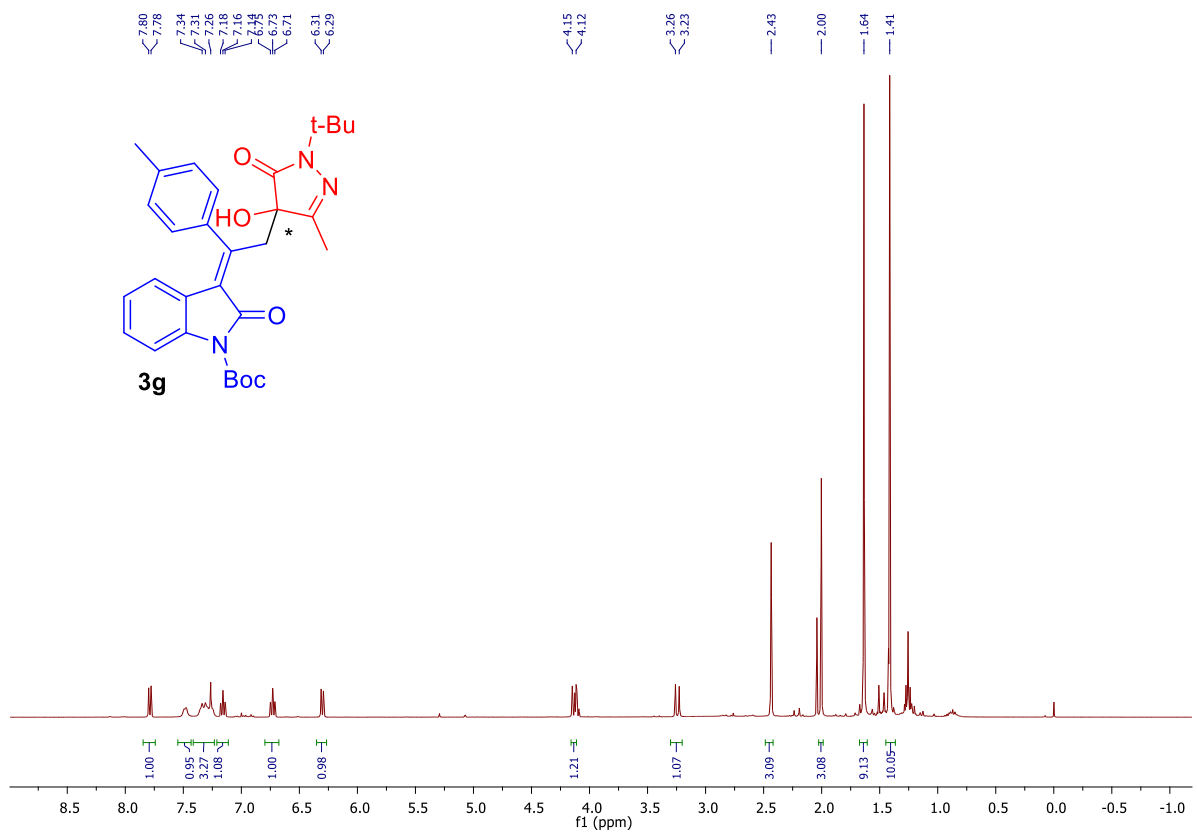


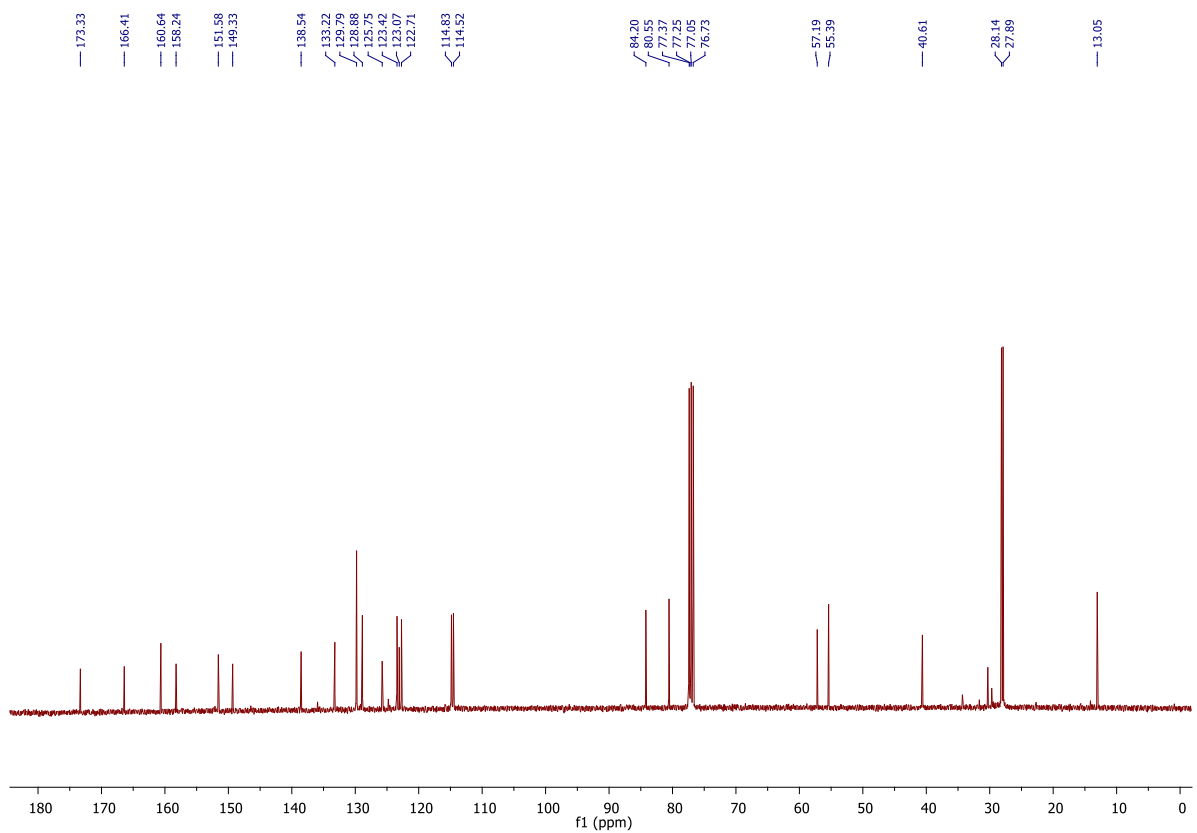
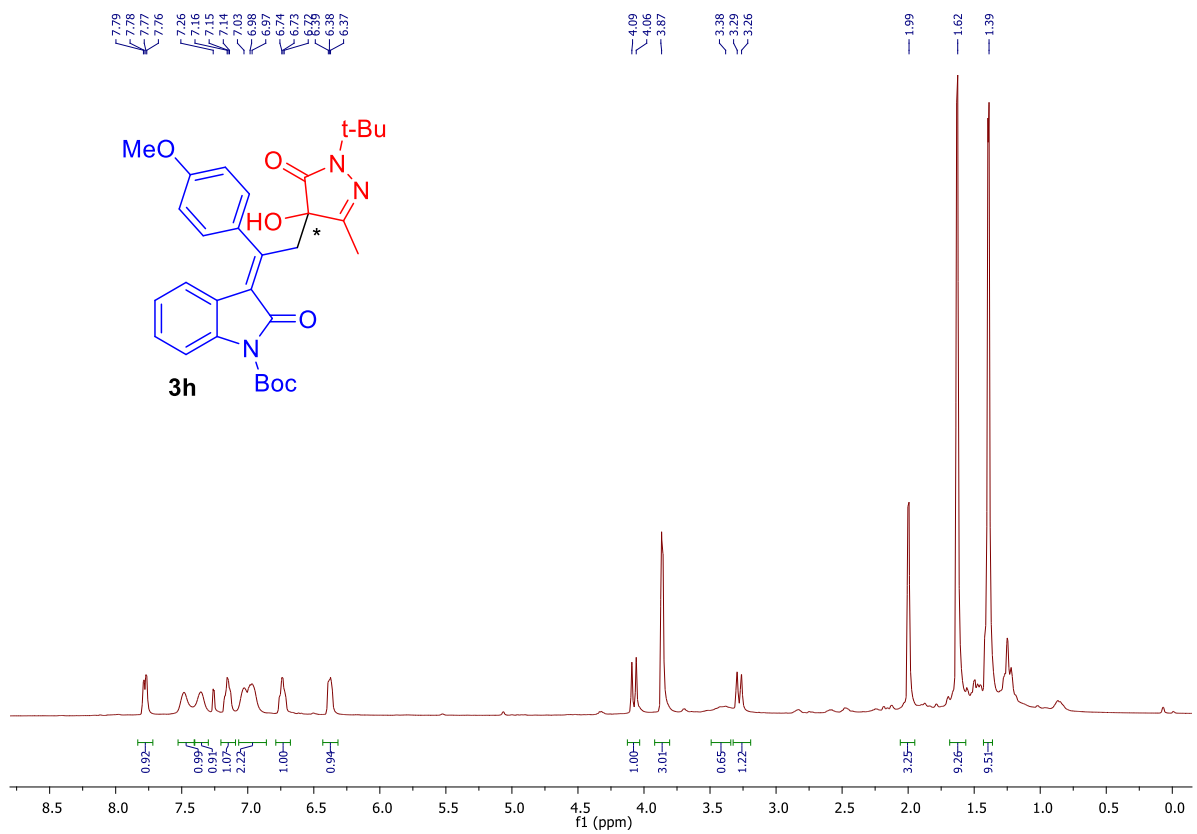


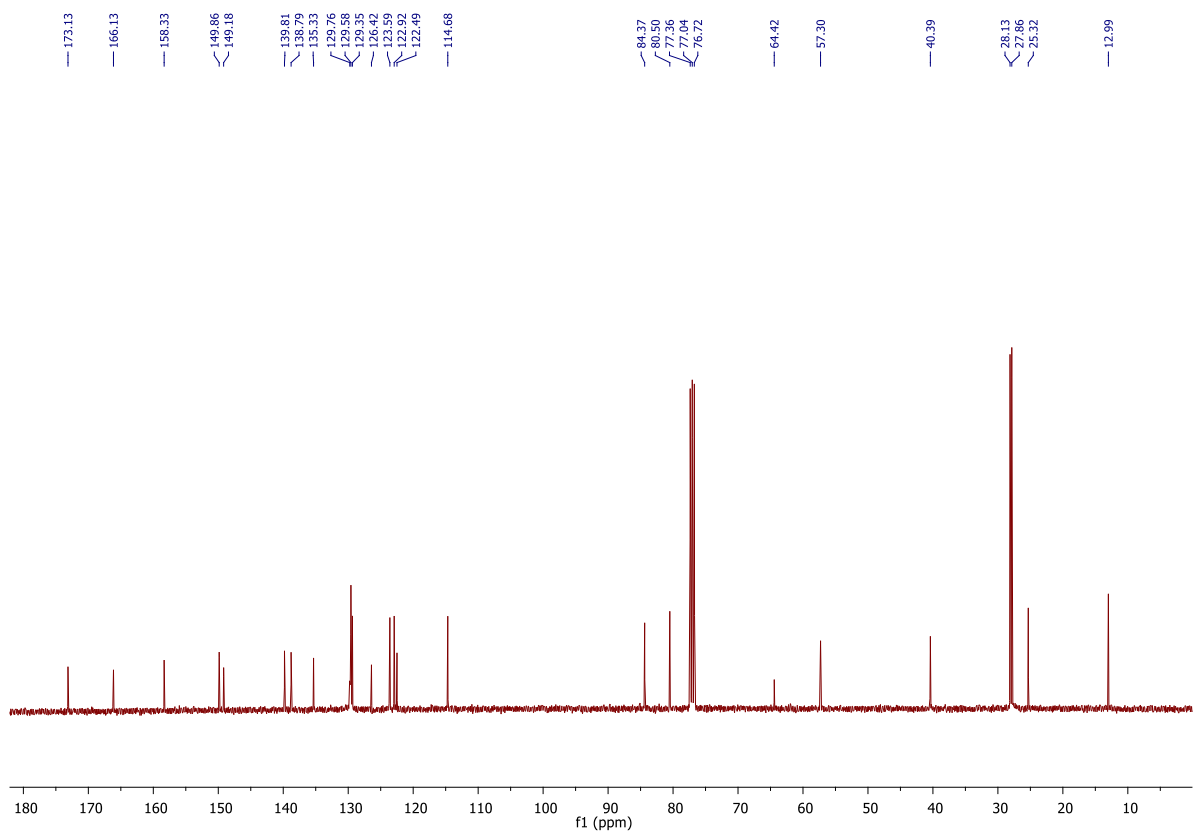
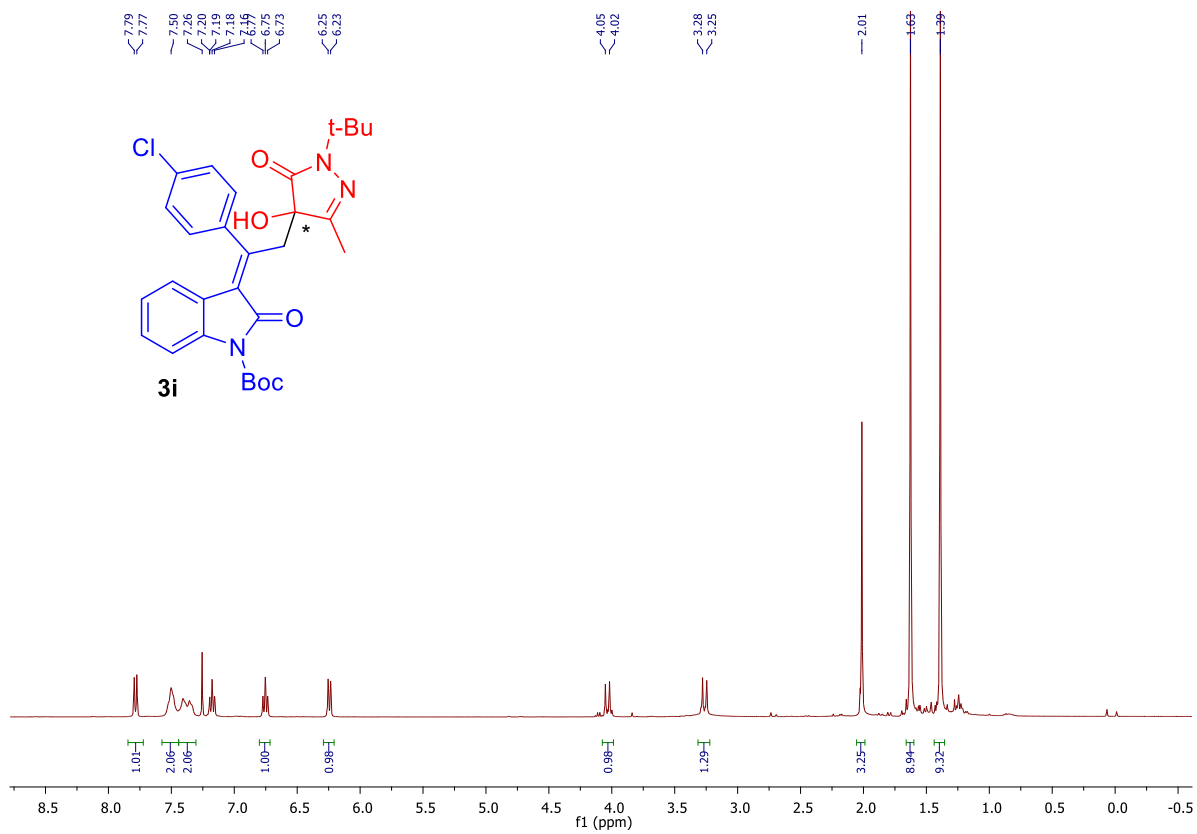


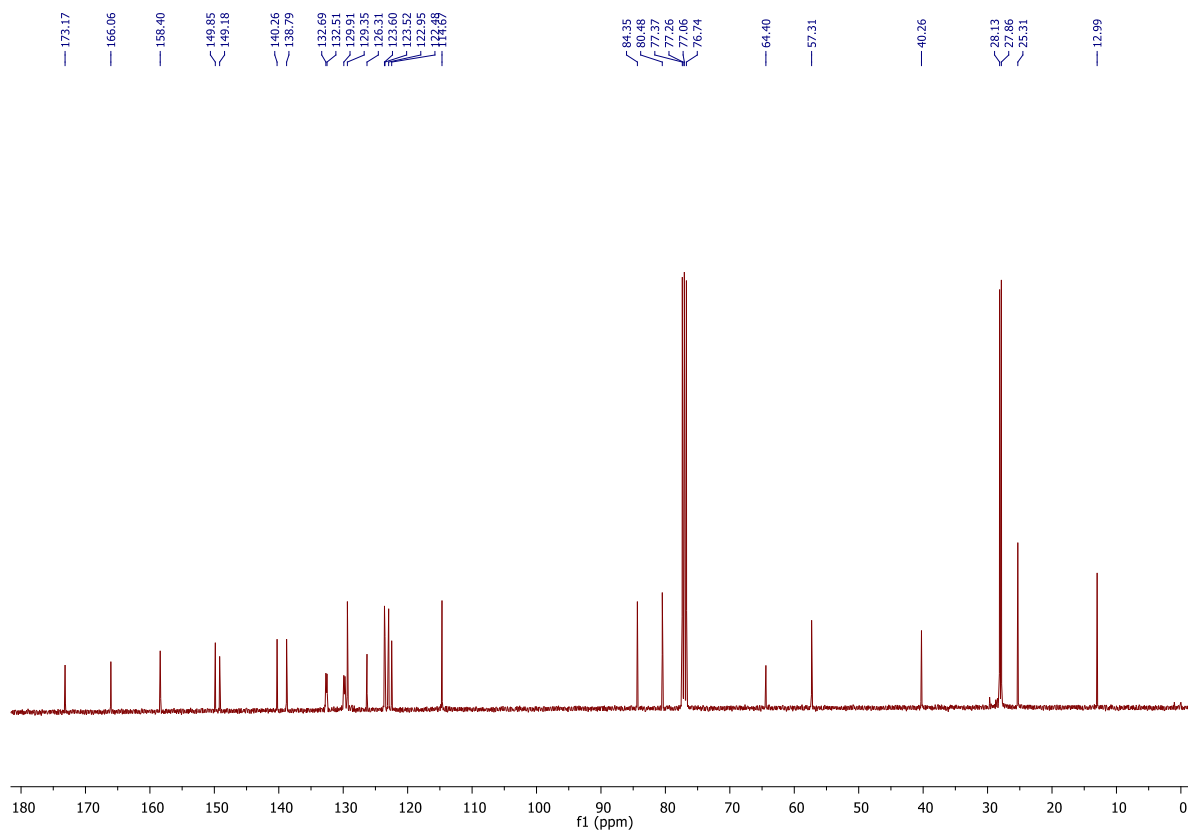
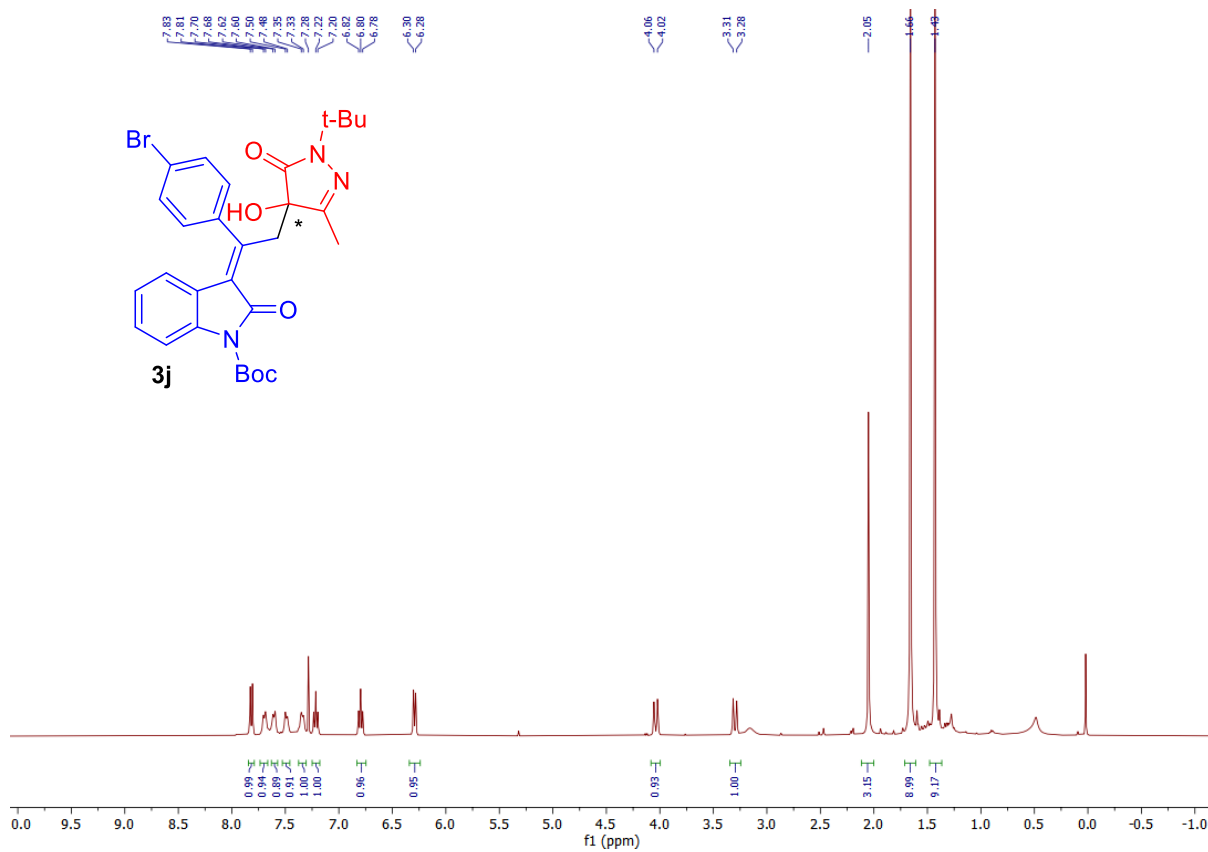


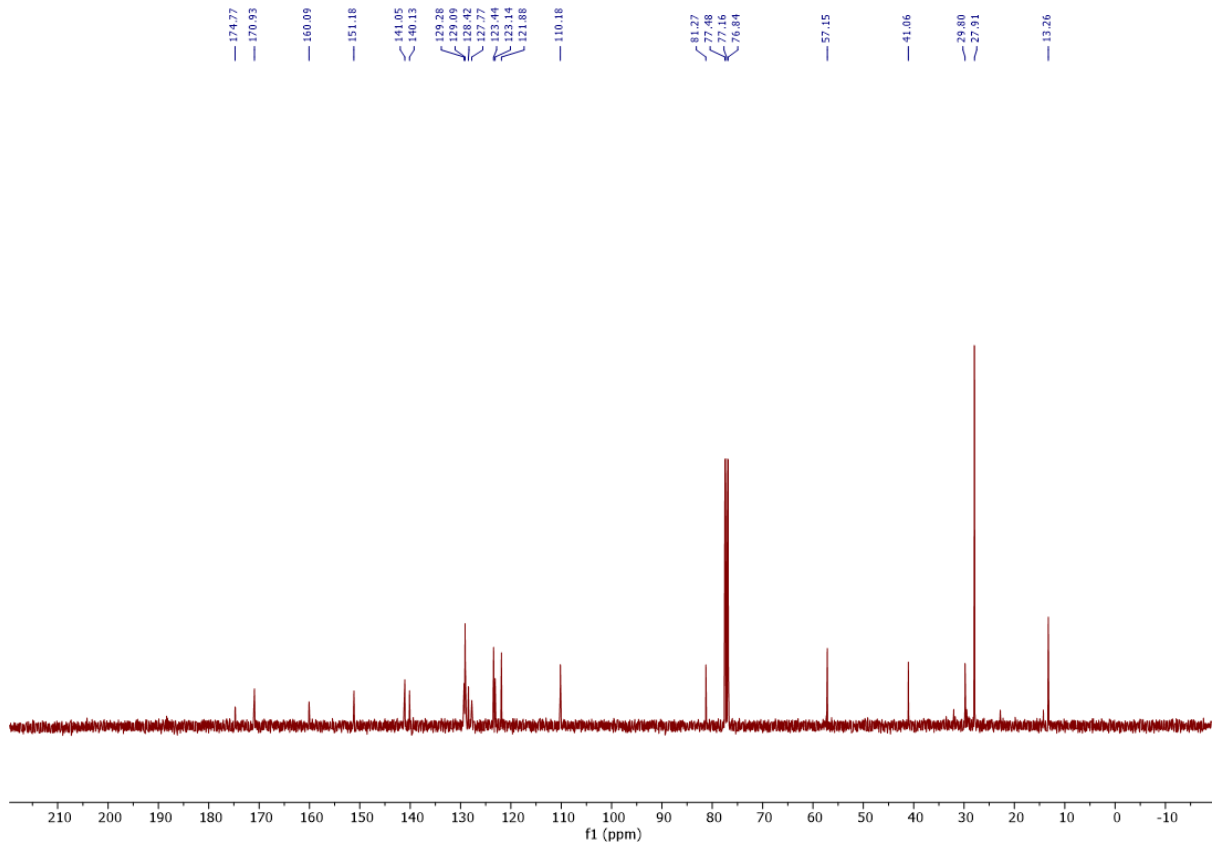
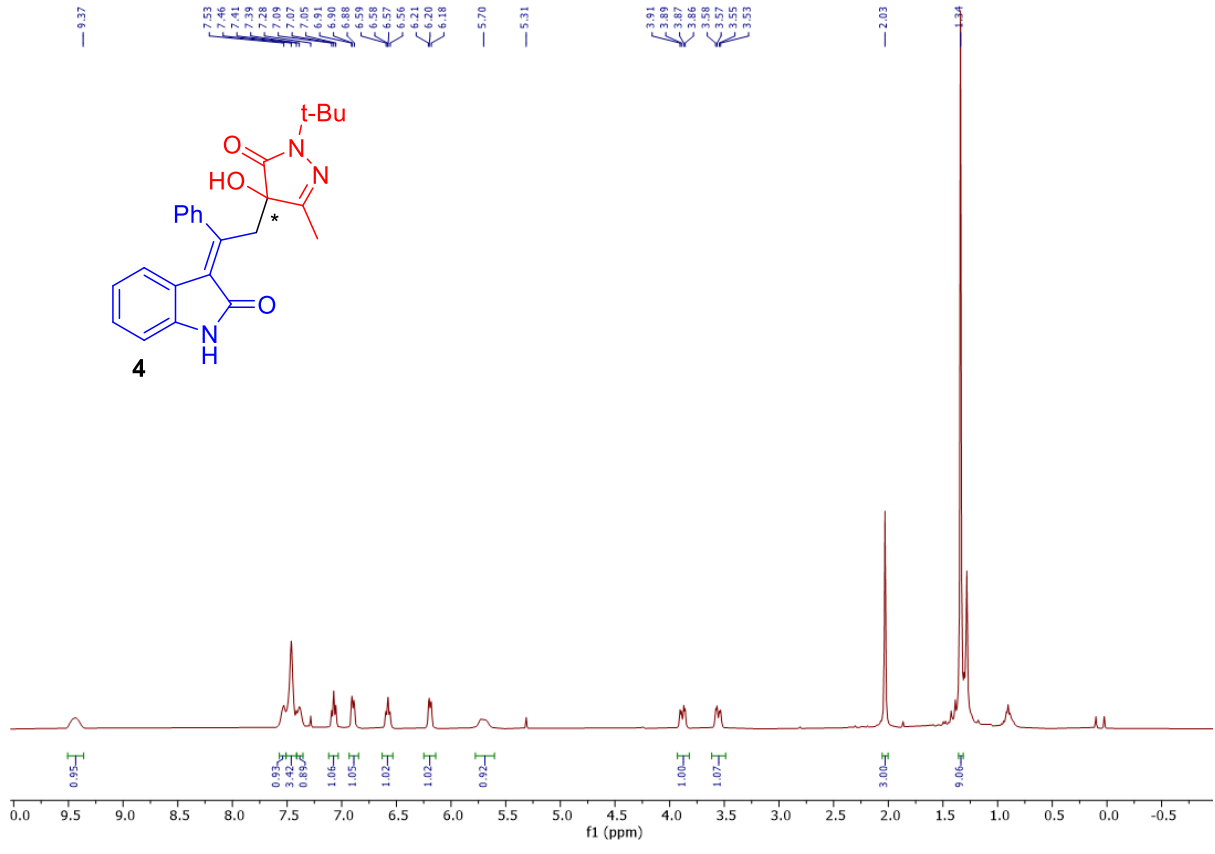


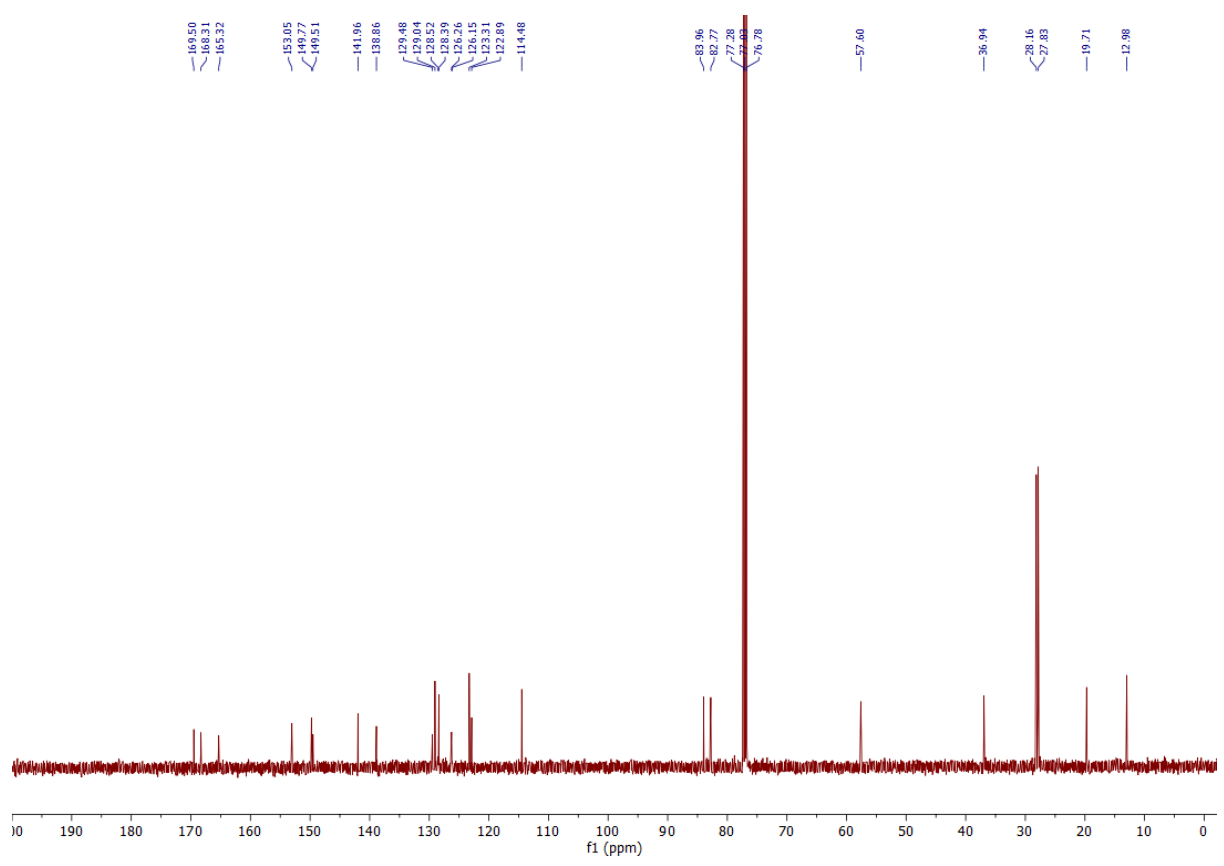
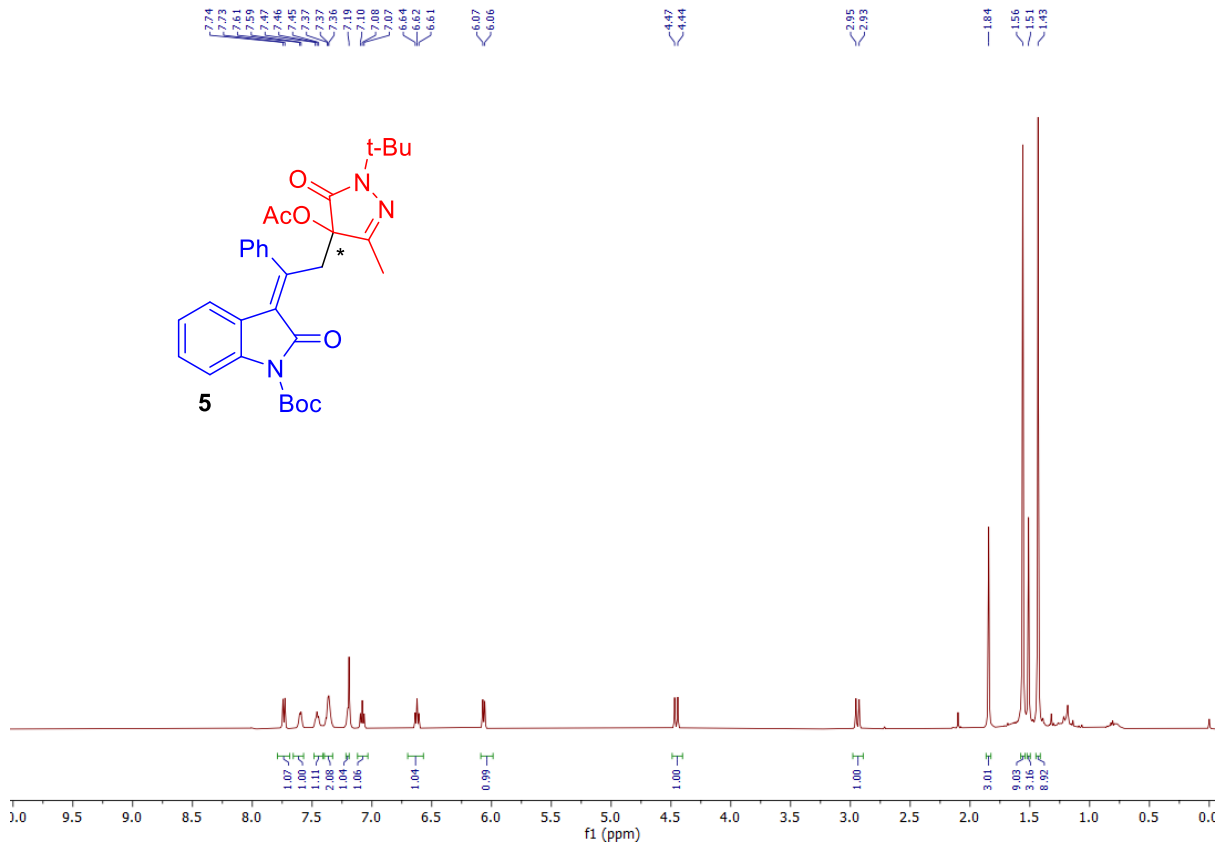




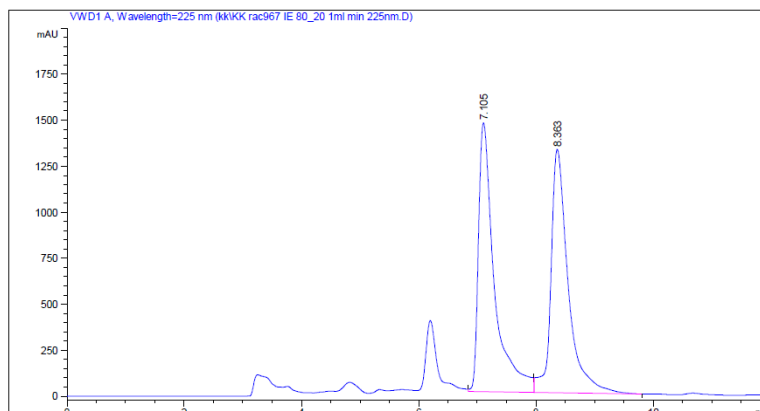
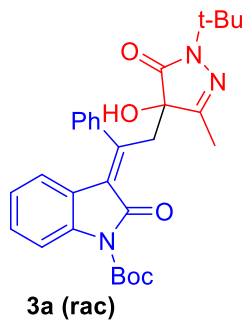








HPLC, Chiralpak IE, hexane: isopropanol = 80:20, 1 mL/min, $\lambda = 225$ nm

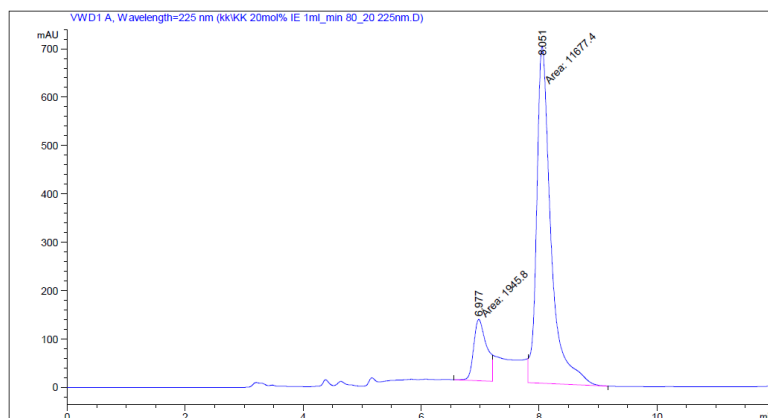
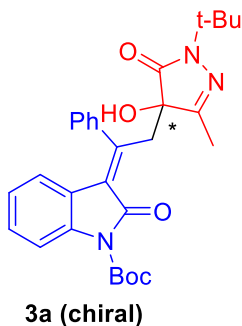


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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: Vwd1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.105	VV	0.2746	2.74940e4	1460.49182	50.4824
2	8.363	VB	0.2988	2.69686e4	1323.32690	49.5176



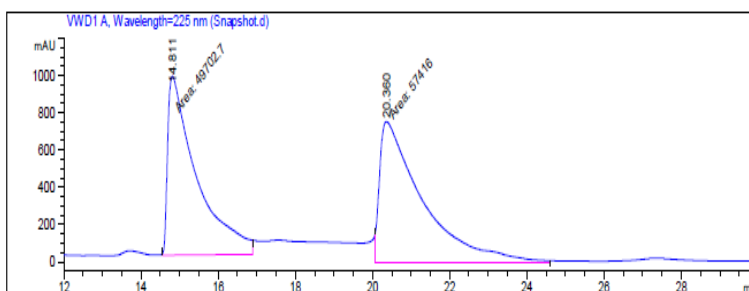
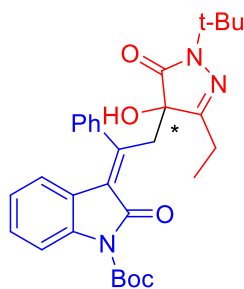
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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: Vwd1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.977	MF	0.2561	1945.80078	126.64944	14.2830
2	8.051	FM	0.2793	1.16774e4	696.76556	85.7170

HPLC, Chiralpak IE, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

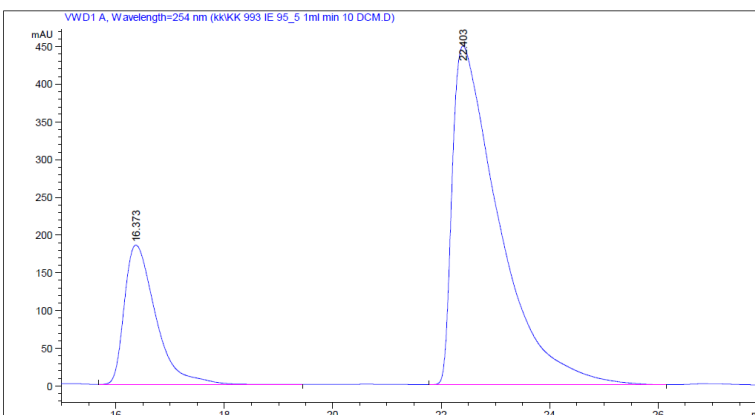
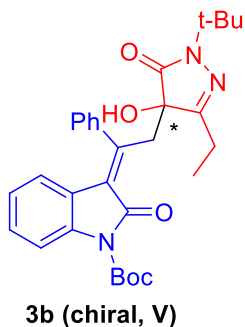


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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: WVD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.811	MM	0.8636	4.97027e4	959.21716	46.3996
2	20.360	MM	1.2713	5.74160e4	752.69354	53.6004



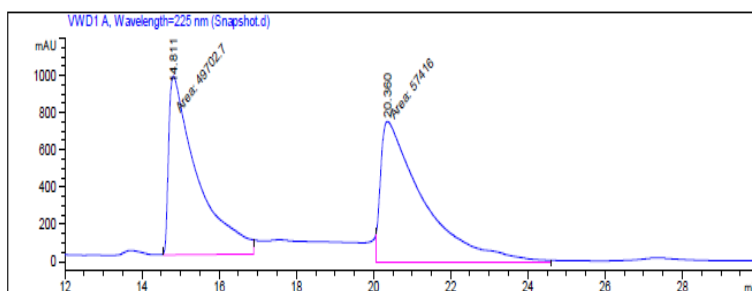
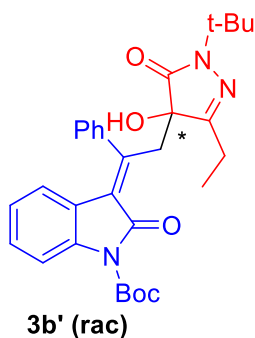
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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: WVD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.373	BB	0.6128	7389.46436	184.68953	21.6250
2	22.403	BB	0.8852	2.67815e4	448.81207	78.3750

HPLC, Chiralpak IE, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

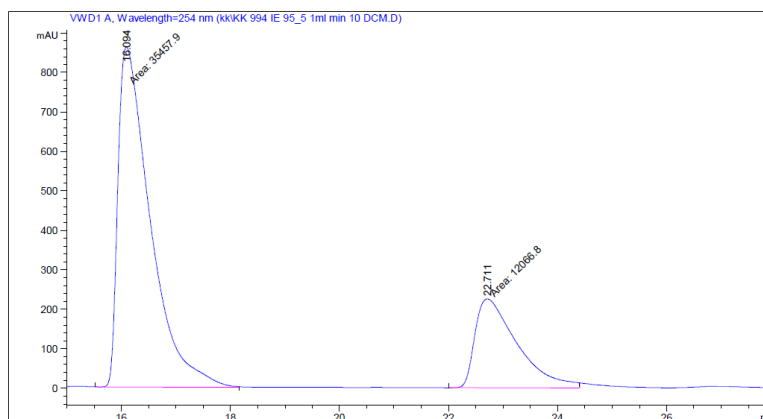
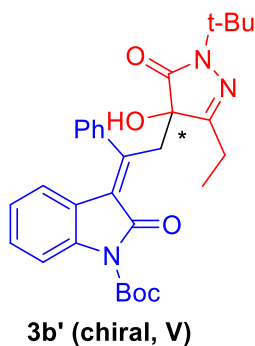


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.811	MM	0.8636	4.97027e4	959.21716	46.3996
2	20.360	MM	1.2713	5.74160e4	752.69354	53.6004



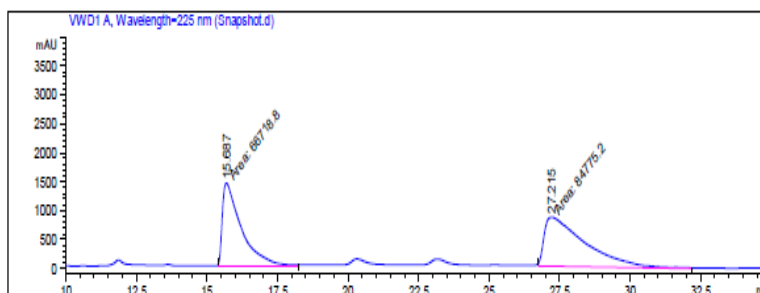
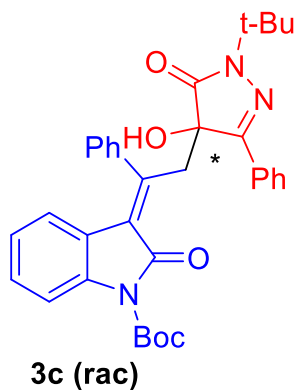
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.094	FM	0.6854	3.54579e4	862.16968	74.6095
2	22.711	MF	0.8927	1.20668e4	225.27863	25.3905

HPLC, Chiralpak IE, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

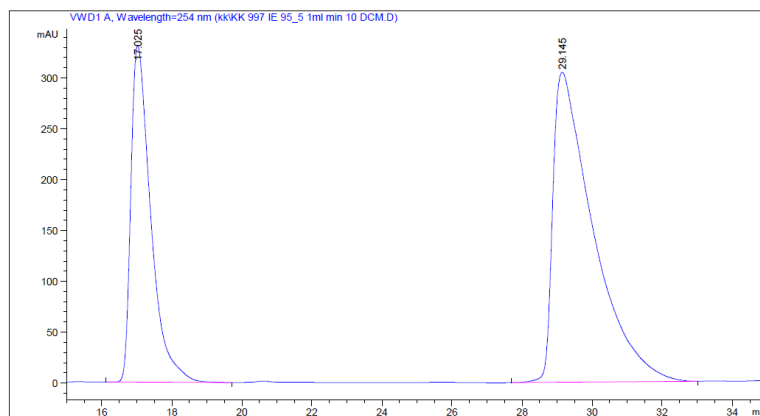
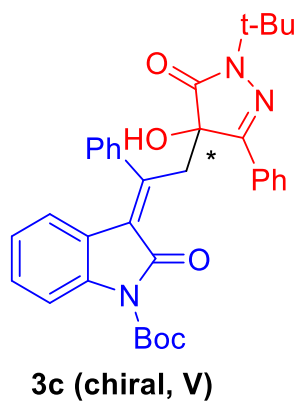


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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.687	MM	0.7785	6.67188e4	1428.38293	44.0406
2	27.215	MM	1.6762	8.47752e4	842.95227	55.9594



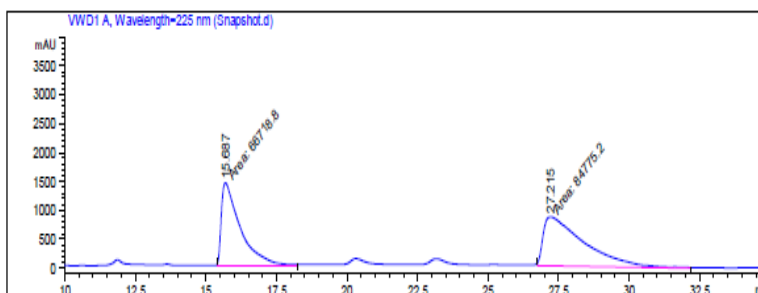
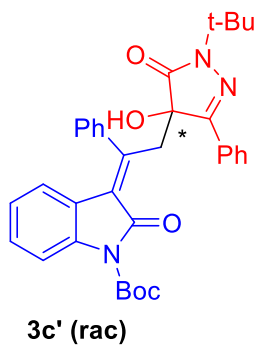
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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.025	BB	0.5951	1.30753e4	330.83969	34.9612
2	29.145	BB	1.0850	2.43241e4	304.80530	65.0388

HPLC, Chiralpak IE, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

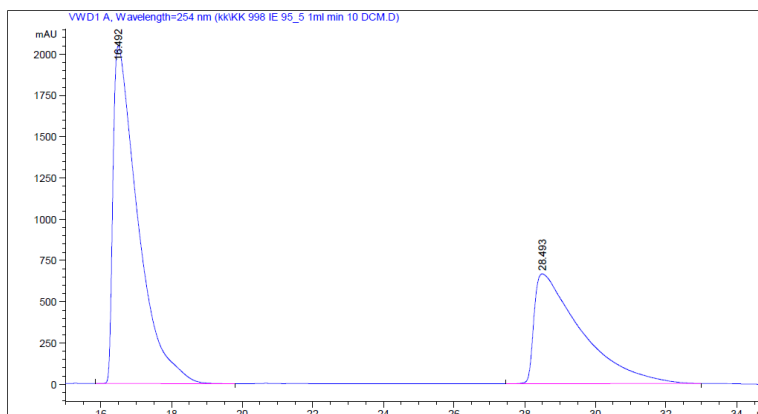
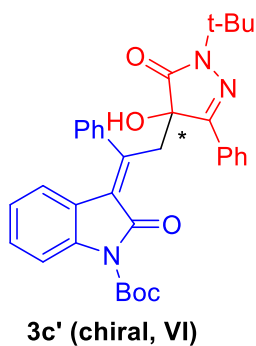


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.687	MM	0.7785	6.67188e4	1428.38293	44.0406
2	27.215	MM	1.6762	8.47752e4	842.95227	55.9594



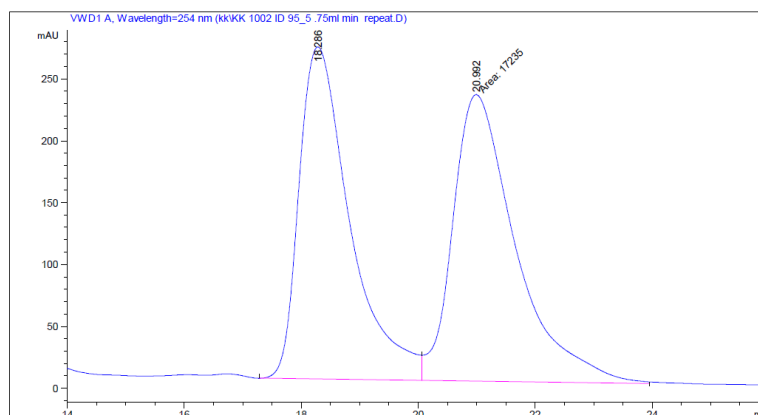
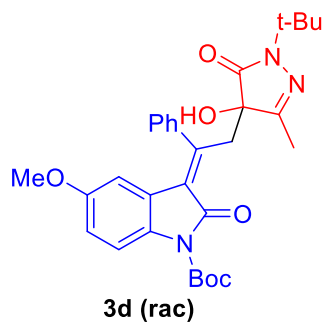
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.492	BB	0.7079	9.94396e4	2046.33875	61.7797
2	28.493	BB	1.2576	6.15187e4	666.01727	38.2203

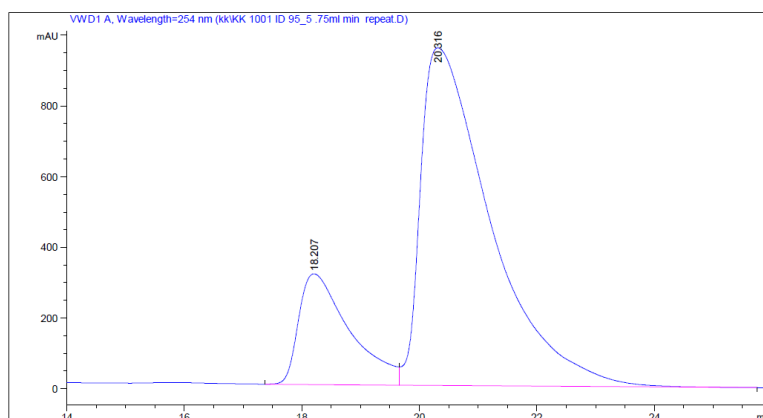
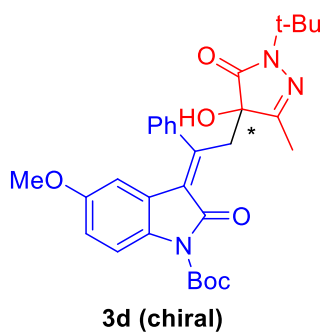
HPLC, Chiralpak IE, hexane: isopropanol = 95:05, 0.75 mL/min, $\lambda = 225$ nm



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 Area Percent Report
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 Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.286	BV	0.9106	1.62291e4	268.33615	48.4971
2	20.992	MF	1.2411	1.72350e4	231.45508	51.5029

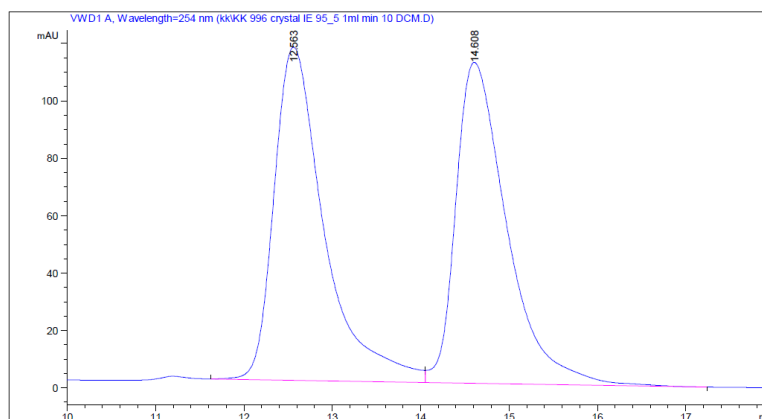
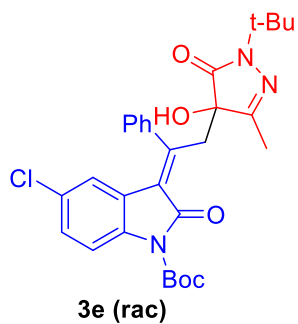


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 Area Percent Report
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 Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.207	BV	0.8769	1.87603e4	313.18530	19.2631
2	20.316	VB	1.2215	7.86298e4	955.07318	80.7369

HPLC, Chiralpak IE, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

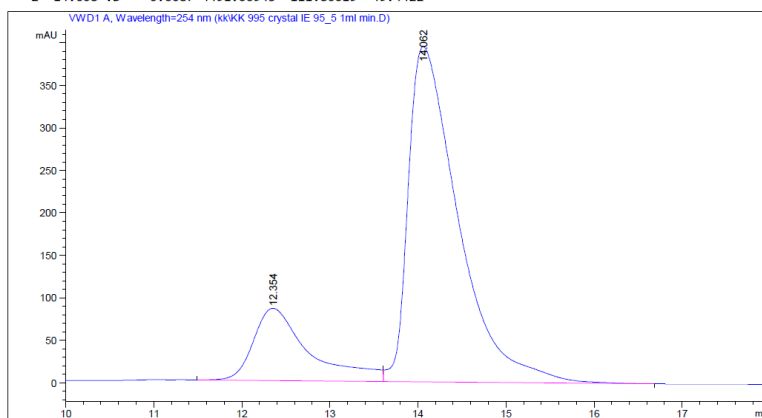
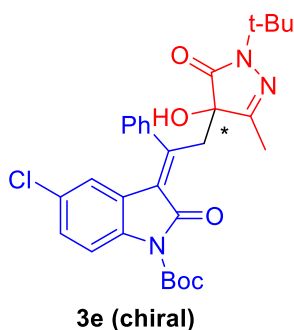


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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.563	BV	0.5926	4593.00928	116.09092	50.5578
2	14.608	VB	0.6087	4491.66943	111.80619	49.4422



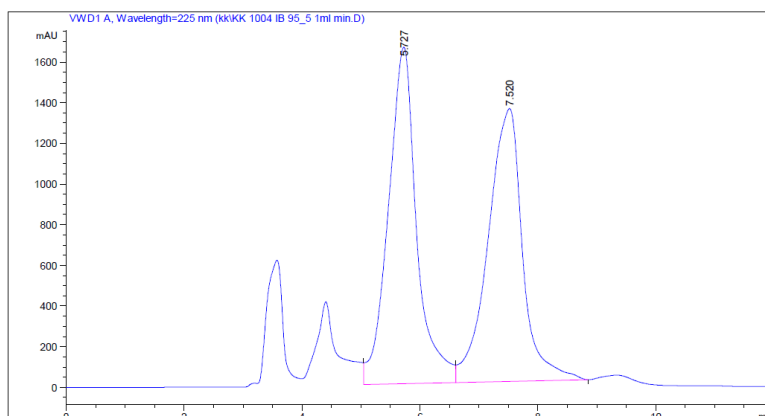
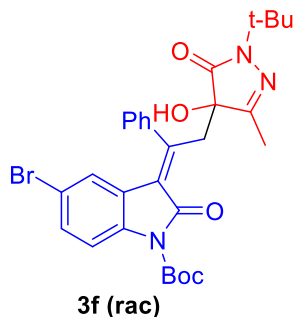
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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.354	BV	0.6370	3735.60547	85.12174	19.3706
2	14.062	VB	0.5997	1.55494e4	394.64352	80.6294

HPLC, Chiralpak IB, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

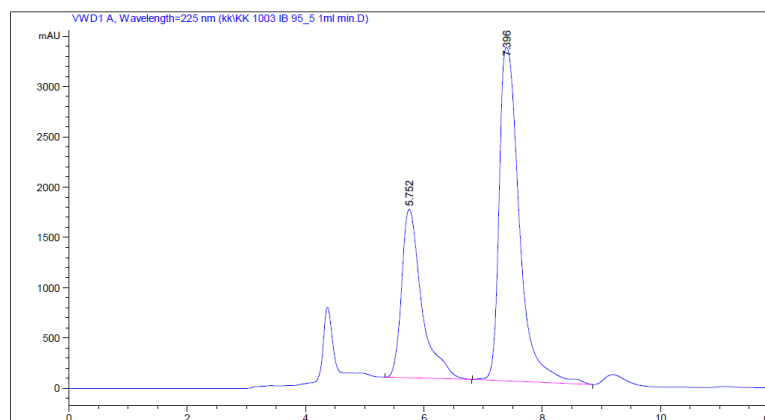
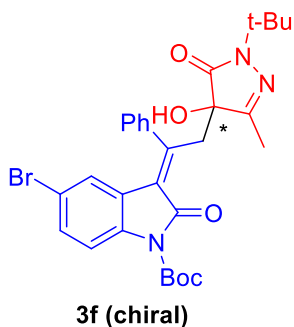


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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.727	VV	0.4748	5.51738e4	1655.62341	50.3024
2	7.520	VB	0.6101	5.45105e4	1341.42908	49.6976



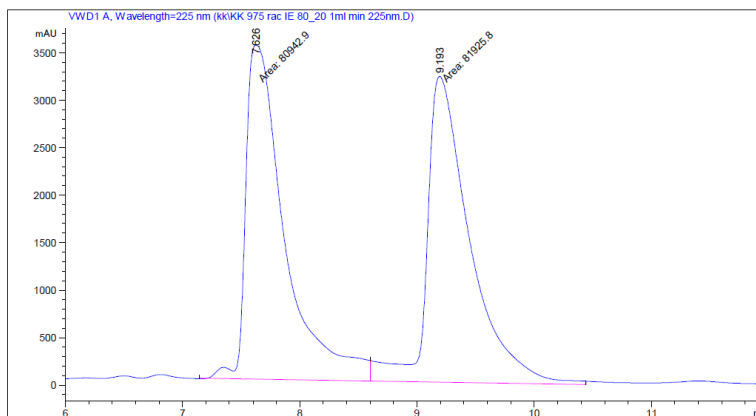
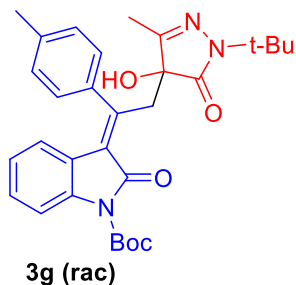
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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.752	BB	0.3511	3.93689e4	1675.55469	33.3669
2	7.396	BV R	0.3629	7.86190e4	3317.52466	66.6331

HPLC, Chiralpak IB, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

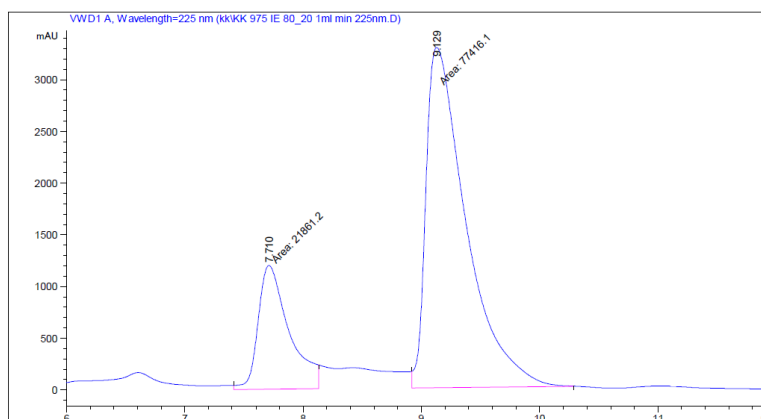
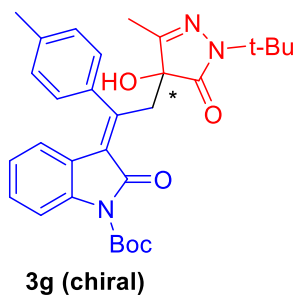


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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.626	MF	0.3834	8.09429e4	3518.21631	49.6983
2	9.193	FM	0.4241	8.19258e4	3219.31396	50.3017



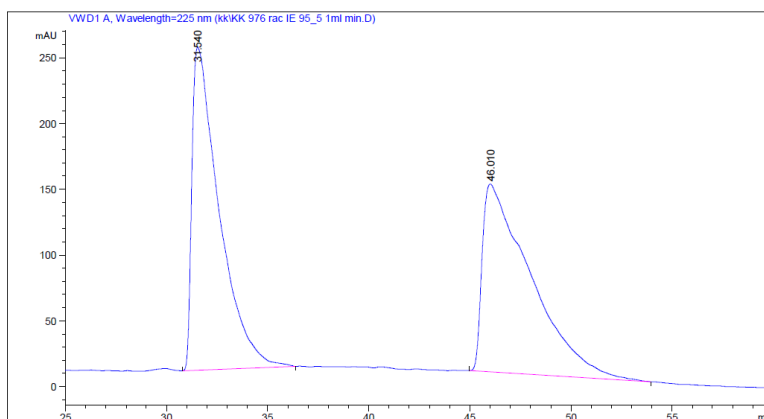
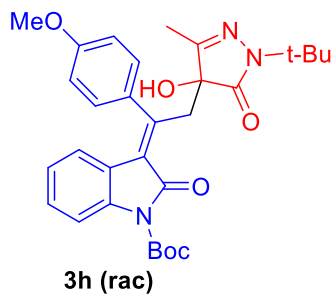
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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.710	MF	0.3044	2.18612e4	1196.93115	22.0203
2	9.129	FM	0.3923	7.74161e4	3289.37891	77.9797

HPLC, Chiralpak IE, hexane: isop ropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

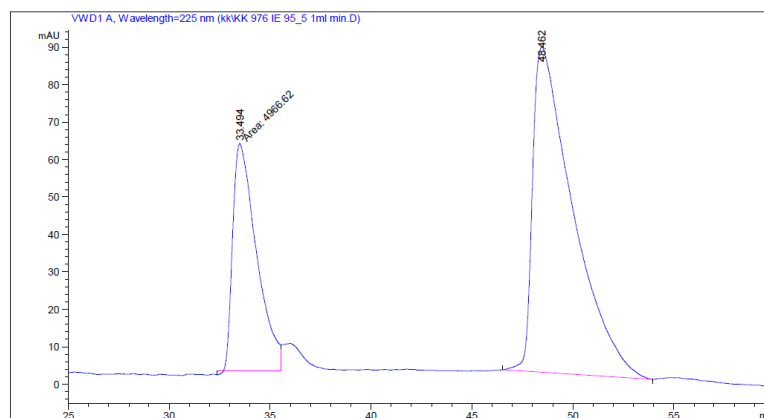
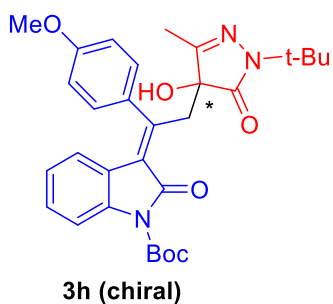


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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.540	BB	1.2986	2.30366e4	245.76431	49.1155
2	46.010	BB	2.1461	2.38664e4	142.93210	50.8845



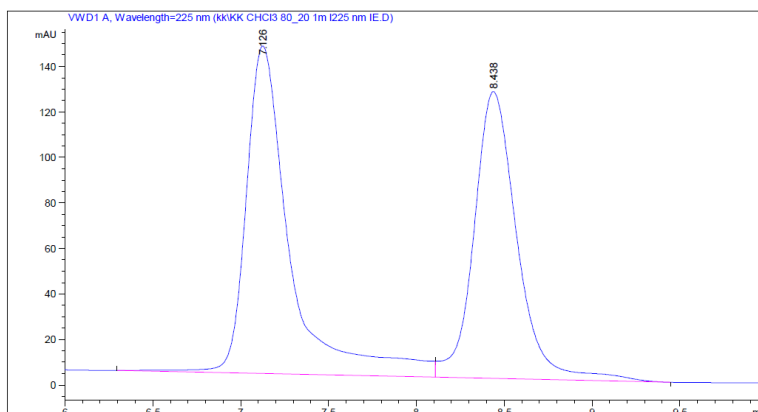
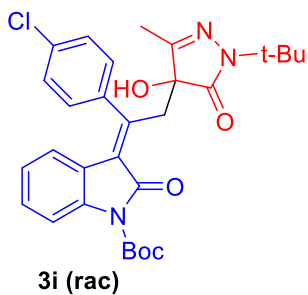
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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.494	MF	1.3652	4966.62305	60.63529	29.1695
2	48.462	BB	1.8017	1.20601e4	86.81453	70.8305

HPLC, Chiralpak IE, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

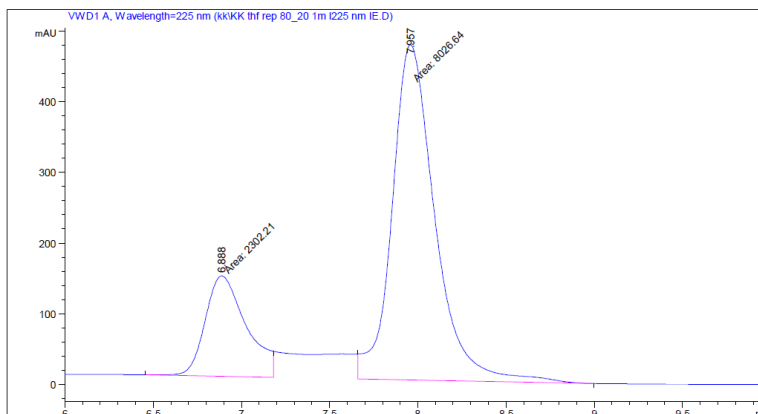
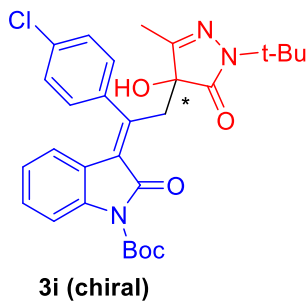


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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.126	BV	0.2564	2509.12646	143.88728	53.8299
2	8.438	VB	0.2582	2152.08789	126.01990	46.1701



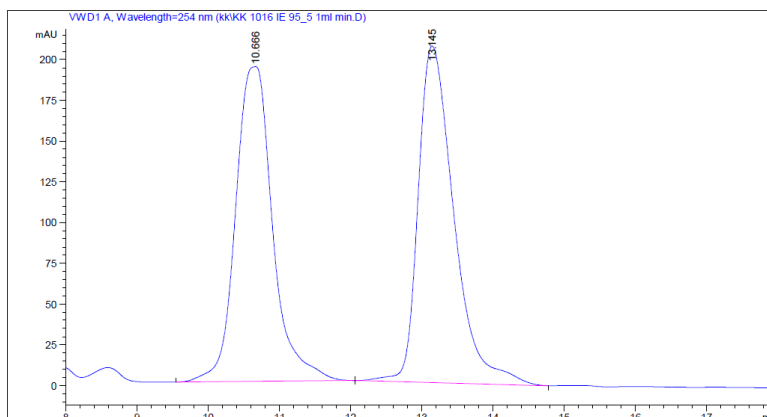
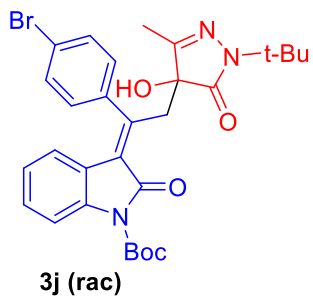
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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.888	MF	0.2702	2302.20923	141.98106	22.2891
2	7.957	FM	0.2824	8026.64453	473.64035	77.7109

HPLC, Chiralpak IE, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

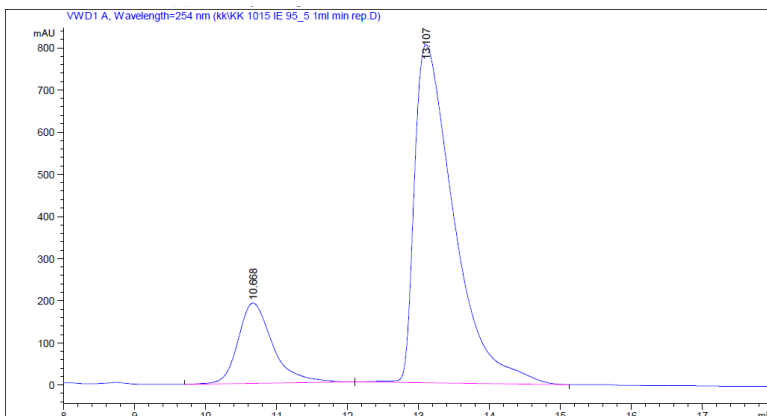
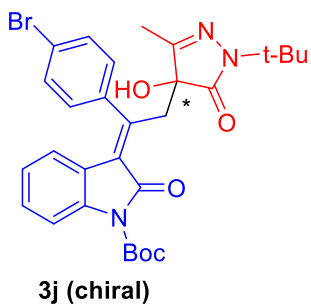


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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.666	BB	0.4811	6991.02490	193.21878	49.2289
2	13.145	BB	0.5370	7210.02295	206.65179	50.7711



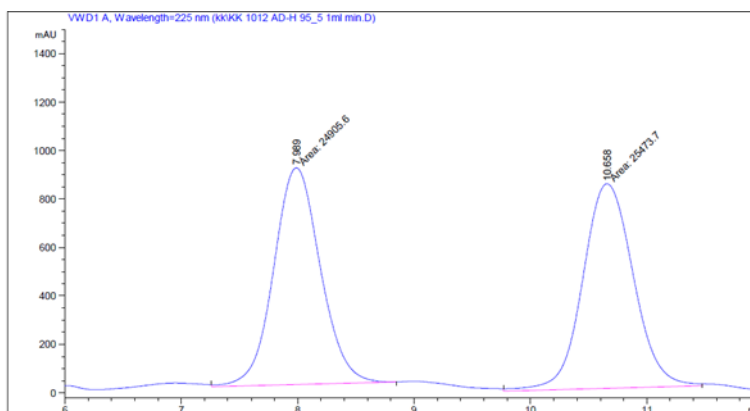
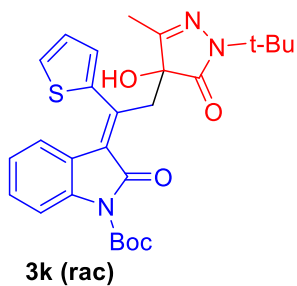
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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.668	BB	0.5202	6436.85547	190.49062	17.2469
2	13.107	BB	0.5824	3.08850e4	801.80225	82.7531

HPLC, Chiralpak AD-H, hexane: isopropanol = 95:05, 1 mL/min, $\lambda = 225$ nm

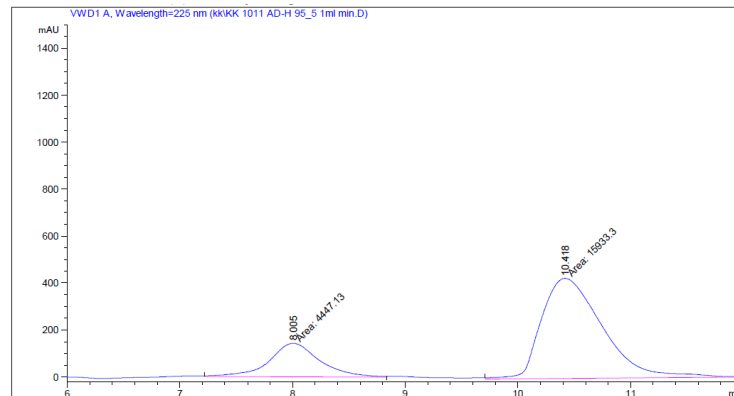
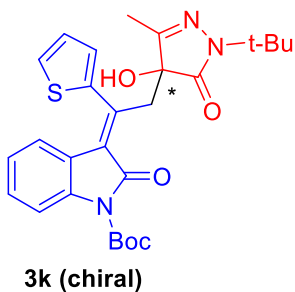


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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.989	MM	0.4643	2.49056e4	894.03729	49.4362
2	10.658	MM	0.5032	2.54737e4	843.69562	50.5638



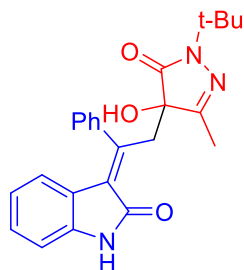
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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

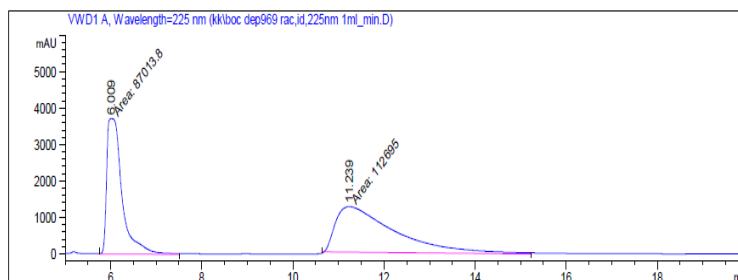
Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.005	MM	0.5200	4447.13281	142.52573	21.8206
2	10.418	MM	0.6234	1.59333e4	425.95026	78.1794

HPLC, Chiralpak ID, hexane: isopropanol = 70: 30, 1mL/min, $\lambda = 225$ nm



4 (rac)

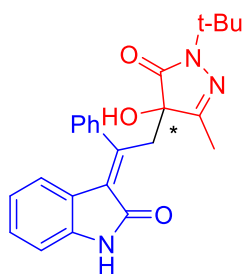


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Area Percent Report
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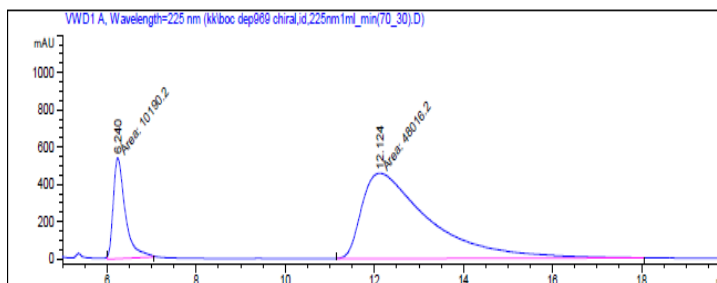
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: WVD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.009	MM	0.3905	8.70138e4	3713.54980	43.5703
2	11.239	MM	1.5048	1.12695e5	1248.14160	56.4297



4 (chiral)



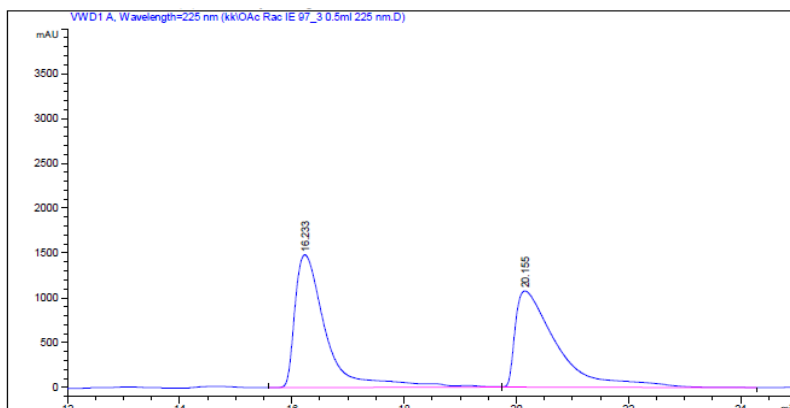
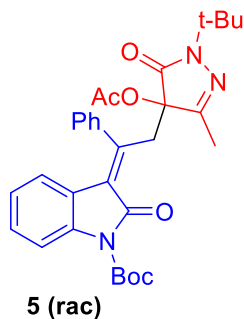
=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: WVD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.240	MM	0.3144	1.01902e4	540.24963	17.5069
2	12.124	MM	1.7471	4.80162e4	458.04709	82.4931

HPLC, Chiralpak IE, hexane: isopropanol = 97: 03, 0.5mL/min, $\lambda = 225$ nm

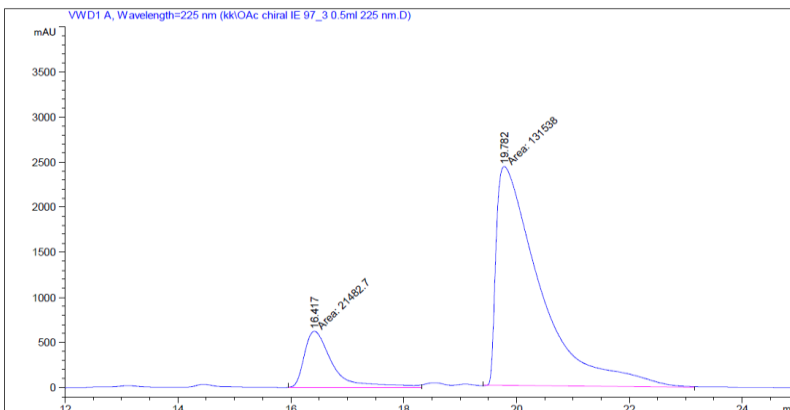
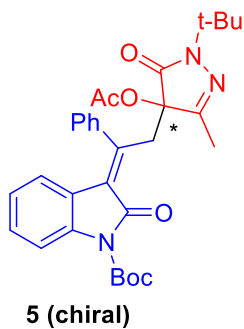


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.233	BV R	0.5826	5.79507e4	1481.98560	51.0557
2	20.155	BB	0.7340	5.46915e4	1070.62488	48.9443



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=225 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.417	MM	0.5779	2.14827e4	619.53278	14.0391
2	19.782	MM	0.9041	1.31538e5	2424.92065	85.9609