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Anion Effect in Enantioselective Oxidative NHC Catalysis: Highly Efficient Kinetic Resolution of Tertiary alcohols

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Supporting Information

Contents

1. General Information.....S3
2. Synthesis of azolium chloride.....S5
3. General procedure for the anion exchange reaction. S6
4. General procedure for the synthesis of N-benzyl Isatin derivations.....S8
5. General procedure A for the synthesis of 3-Hydroxy-3-Substituted Oxindoles.....S9
6. General Procedures for Kinetic Resolution of 3-Hydroxy-3-Substituted Oxindoles S10
7. General procedure B for the synthesis of 3-Hydroxy-3-Substituted Oxindoles.....S11
8. Table 1. Screening different additives for kinetic resolution of substate **1e**.....S13
9. General Procedures B for Kinetic Resolution of 3-Hydroxy-3-Substituted Oxindoles…….. .....S14
10. Characterization of compounds. S15
11. Reference S31
12. NMR Spectrum S32

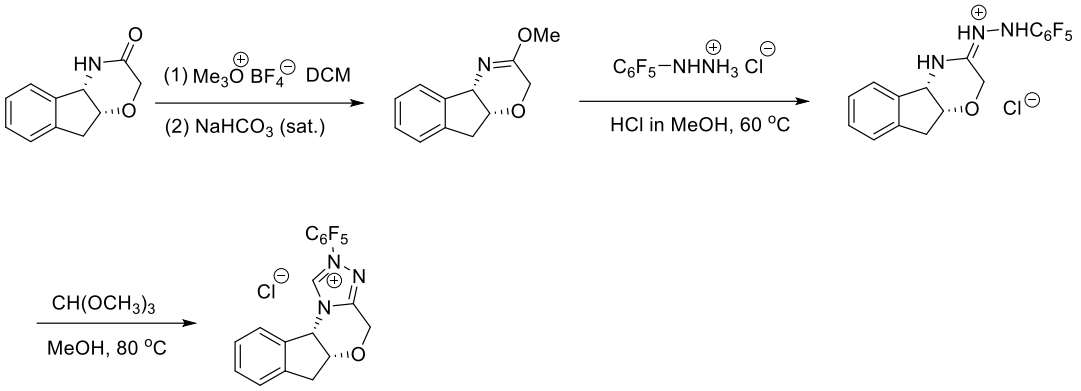
1. General Information

^{1}H and **^{13}C NMR** spectra were recorded on a Bruker ACF300 (300 MHz) or AMX500 (500 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26, acetone δ 2.05, dimethyl sulfoxide δ 2.50), carbon (chloroform δ 77.0, acetone δ 29.84, dimethyl sulfoxide δ 39.6) or tetramethylsilane (TMS δ 0.00) was used as a reference. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), bs (broad singlet). Coupling constants were reported in Hertz (Hz). Low resolution mass spectra were obtained on a Finnigan/MAT LCQ spectrometer in ESI mode, and a Finnigan/MAT 95XL-T mass spectrometer in EI mode. All high resolution mass spectra (**HRMS**) were obtained on a Finnigan/MAT 95XL-T spectrometer. For thin layer chromatography (**TLC**), Merck pre-coated TLC plates (Merck 60 F254) were used, and compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine, or potassium permanganate solution followed by heating using a heat gun. Flash chromatography separations were performed on Merck 60 (0.040-0.063 mm) mesh silica gel. **Optical rotations** were measured using an Anton Paar MCP-150 digital polarimeter using a 1 cm glass cell. **The enantiomeric excess** (ee) of products were determined by chiral phase HPLC analysis on on ThermoFisher HPLC units, or Agilent HPLC units, including the following instruments: pump, LPG-3400SDN; detector, VWD-3400RS; column, Chiralcel OD-H, Chiralpak AS-H, IA, or IC.

All reactions were carried out under nitrogen atmosphere. All commercially available reagents were used as received for the reactions without any purification. All solvents were dried on alumina columns using a solvent dispensing system. Sodium hydride, benzyl bromide, cinnamaldehyde, indole-3-propionic acid, 5-methoxyisatin, isatin, tetrabutyl ammonium

bromide, triethyl phosphite, malonic acid, pyridine, thionyl chloride were purchased from Aldrich or Fluka and used directly.

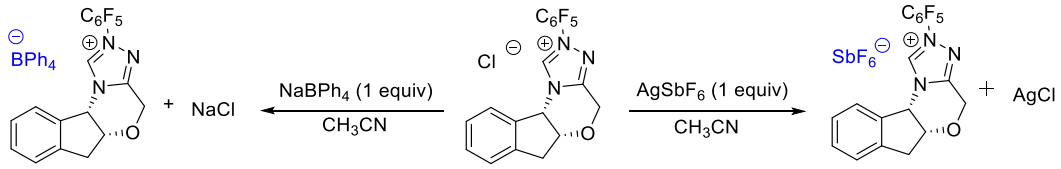
2. Synthesis of the azolium chloride



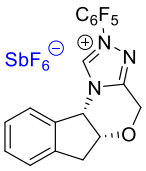
The synthesis is an adaption of literature procedures[1,2] from Rovis procedure. Methylation of (4*aS*,9*aR*)-4,4a,9,9a-tetrahydroindeno[2,1-b][1,4]oxazin-3(*2H*)-one with Meerwein's reagent, followed by liberation of the free base by treatment with sodium bicarbonate gave imino ether. Reaction of the imino ether with an equimolar amount of Pentafluorophenylhydrazine hydrochloride and a catalytic amount of anhydrous hydrochloric acid in methanol afforded amidrazone hydrochloride. Treatment of amidrazone with excess trimethylorthoformate in MeOH at 80 °C for 36 hours provided the crude product which subsequent precipitation from acetonitrile by the addition of diethyl ether. The azolium chloride was obtained as a white solid.

White solid. 45% yield, **MP:** 210 - 212 °C. **^{1}H NMR** (500 MHz, DMSO) δ 11.89 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.42 (dt, *J* = 14.7, 7.3 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 6.18 (d, *J* = 3.6 Hz, 1H), 5.36 (d, *J* = 16.2 Hz, 1H), 5.10 (d, *J* = 16.2 Hz, 1H), 4.99 (t, *J* = 4.5 Hz, 1H), 3.49 (dd, *J* = 17.0, 4.9 Hz, 1H), 3.17 (d, *J* = 17.1 Hz, 1H). **^{13}C NMR** (126 MHz, DMSO) δ 151.3, 147.5, 143.7 (m), 141.6 (m), 141.1, 139.2 (m), 137.2 (m), 135.8, 129.9, 127.5, 125.9, 124.9, 77.3, 62.2, 60.0, 37.3. **^{19}F NMR** (471 MHz, DMSO) δ -145.35 (d, J = 20.0 Hz), -147.85, -159.99 (d, J = 25.0 Hz). **HRMS (ESI)** m/z Calcd for $[C_{18}H_{11}F_5N_3O, M - Cl]^+$: 380.0817; Found: 380.0819.

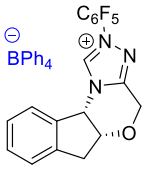
3. General procedure for the anion exchange reaction.[2,3]



To a suspension of azolium chloride (0.1 mmol) in CH_3CN (1 mL) was added $AgSbF_6$ or $NaBPh_4$ (0.1 mmol). After being stirred for 12 h at 24 °C, the reaction mixture was filtered through silica gel and the solvent was removed under reduced pressure. Recrystallization from Hexanes/Ethyl acetate gave the desired product as white solid.



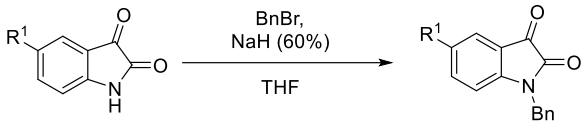
White solid. 82% yield, **MP:** 221 - 223 °C. **^{1}H NMR** (500 MHz, Acetone) δ 11.29 (s, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.48-7.43 (m, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 6.38 (d, *J* = 3.4 Hz, 1H), 5.44 (d, *J* = 16.4 Hz, 1H), 5.28 (d, *J* = 16.4 Hz, 1H), 5.21 (t, *J* = 4.5 Hz, 1H), 3.57 (dd, *J* = 17.1, 5.0 Hz, 1H), 3.33 (d, *J* = 17.1 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 151.7, 146.1, 143.9 (m), 141.9 (m), 140.8, 139.4 (m), 137.3 (m), 135.1, 129.7, 127.2, 125.7, 124.2, 77.3, 62.7, 59.9, 37.0. **^{19}F NMR** (471 MHz, Acetone) δ -146.65 (d, *J* = 18.6 Hz), -149.45 (t, *J* = 22.2 Hz), -161.41 – -161.55 (m). **HRMS (ESI)** m/z Calcd for $[C_{18}H_{11}F_5N_3O, M - SbF_6]^+$: 380.0817; Found: 380.0820.



White solid. 70% yield, **MP:** 216 - 218 °C. **^{1}H NMR** (500 MHz, Acetone) δ 10.77 (s, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.40 – 7.29 (m, 9H), 6.95 (t, *J* = 7.4 Hz, 8H),

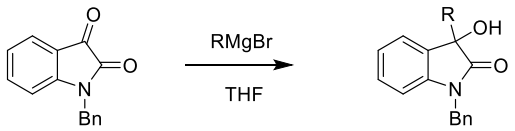
6.81 (t, *J* = 7.2 Hz, 4H), 6.05 (d, *J* = 4.1 Hz, 1H), 5.26 (t, *J* = 21.0 Hz, 1H), 5.10 – 4.98 (m, 1H), 4.91 (t, *J* = 4.5 Hz, 1H), 3.46 – 3.33 (m, 1H), 3.23 (d, *J* = 17.2 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 164.0 (dd, *J* = 98.7, 49.4 Hz), 151.7, 145.8, 143.9 (m), 141.8 (m), 140.8, 139.4 (m), 137.4 (m), 136.1 (d, *J* = 1.4 Hz), 134.8, 129.7, 127.1, 125.7, 125.2 (m), 124.1, 121.4, 77.2, 62.5, 59.8, 36.9. **^{19}F NMR** (471 MHz, Acetone) δ -146.36 (d, *J* = 17.0 Hz), -148.74 (t, *J* = 20.0 Hz), -160.68 – -161.51 (m). **HRMS (ESI)** m/z Calcd for $[C_{18}H_{11}F_5N_3O, M - BPh_4]^+$: 380.0817; Found: 380.0824.

4. General procedure for the synthesis of *N*-benzyl Isatin derivations



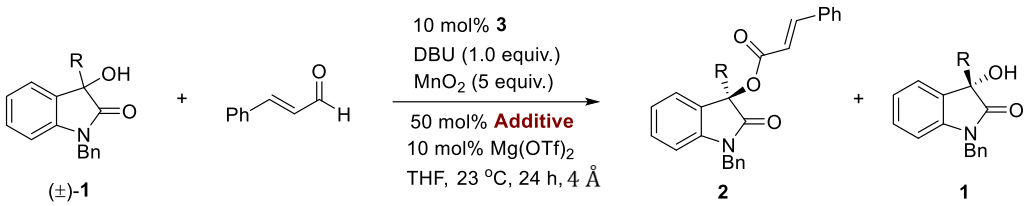
A solution of isatin (5.0 g, 34 mmol) in DMF (60 mL) was cooled to 0 ^{o}C (ice bath). NaH (60% dispersion in mineral oil, 1.4 g, 36 mmol) was added portion wise to the orange solution. The colour of the solution turned to deep purple. When the gas evolution stopped, benzyl bromide (6.7 g, 39 mmol) was added slowly, upon which the mixture turned red-brown. After the reaction mixture was stirred for 15 min at room temperature, ice water (300 mL) was introduced to precipitate the product. After suction filtration, the product was washed with hexane to afford 1-benzylindoline-2,3-dione after drying.

5. General procedure A for the synthesis of 3-Hydroxy-3-Substituted Oxindoles.[4]



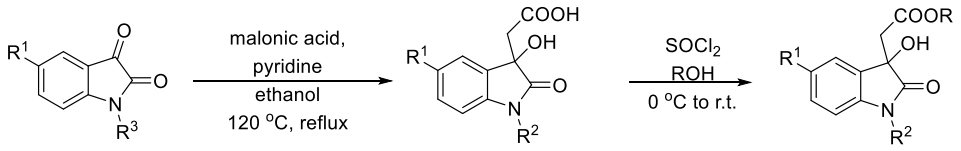
The isatin derivative (20 mmol) was dissolved in anhydrous THF (60 mL) and cooled to -78 ^{o}C followed by dropwise addition of a 2.0 M solution of RMgBr in THF (12.0 ml, 24.0 mmol). Then, the reaction warmed to room temperature, and the reaction was stirred under N_2 for 30 min at which point TLC analysis indicated consumption of the starting material. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (20 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered, concentrated, and the residue was purified by silica gel chromatography with EtOAc/Hexane to afford desired product.

6. General procedure for the kinetic resolution of 3-Hydroxy-3-Substituted Oxindoles through NHC-Catalyzed Oxidative Esterification

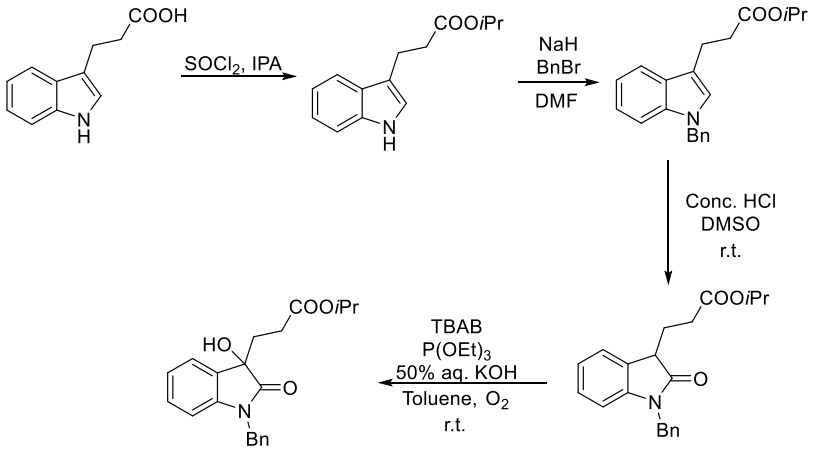


To a 4 mL vial was added alcohol (0.15 mmol), triazolium salt **3** (0.015 mmol), Manganese (IV) oxide activated (0.75 mmol), additive (0.075 mmol). In glovebox Magnesium trifluoromethanesulfonate (0.015 mmol), cinnamaldehyde (48 μL, 0.375 mmol), 100 mg 4Å, anhydrous THF (0.3 mL) were added, and after 10 min DBU (23 μL,, 0.15 mmol) were added. The mixture was stirred at 23 °C for 24 h, and purified by column chromatography on silica gel with hexane/ethyl acetate (10:1 v/v) as eluent to afford the annulation product. Racemic products were synthesized *via* similar procedure using achiral triazolium salt.

7. General procedure B for the synthesis of 3-Hydroxy-3-Substituted Oxindoles.[5]



To a solution of *N*-protected isatin derivative (6 mmol) in pyridine (8 mL) and ethanol (24 mL), malonic acid (956 mg, 9.2 mmol) was added. The reaction mixture was refluxed for 20 h, after which TLC revealed the complete consumption of the starting material. The reaction mixture was quenched with 2M HCl (25 mL), extracted with dichloromethane (3 x 25 mL), and concentrated under reduced pressure to yield a solid residue. The crude product was then dissolved in 30 mL of the alcohol and cooled to 0 °C with an ice bath. Thionyl chloride (2.2 mL) was added dropwise to the solution and left to stir overnight at room temperature. The resulting tertiary alcohol was quenched with sodium carbonate to bring the solution to pH 8, extracted with DCM, dried over Na_2SO_4, evaporated in vacuo and purified by column chromatography with Hexane/Ethyl acetate as eluent.



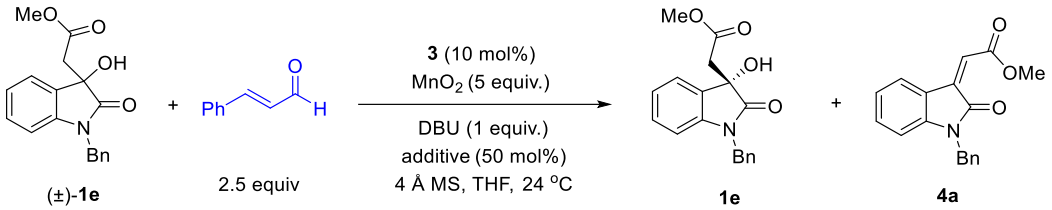
To a solution of 3-(1H-indol-3-yl)propanoic acid (6 mmol) in IPA was added $SOCl_2$ (2.2 mL) at 0 °C and warmed to room temperature and stirred overnight. The reaction was quenched with sodium carbonate to bring the solution to pH 8, extracted with DCM, dried over Na_2SO_4, evaporated *in vacuo* and purified by column chromatography with hexanes/ethyl acetate as

eluent to yield the ester product. Benzylation of the product was performed as above procedures to yield isopropyl 3-(1-benzyl-1*H*-indol-3-yl)proponoate.

The benzylated ester product (2 g, 6.2 mmol) was dissolved in DMSO (10 mL) and to it was added dropwise conc. HCl (14 mL) at r.t. The resulting dark solution was stirred overnight, and poured into ice-water (120 mL). Aqueous $NaHCO_3$ was added slowly to bring the pH of the solution to ~7, and extracted with extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography with hexanes/ethyl acetate (8:1) as eluent.

The purified isopropyl 3-(1-benzyl-2-oxoindolin-3-yl)propanoate (900 mg, 2.7 mg) was dissolved in toluene (20 mL). Tetra-n-butylammonium bromide (TBAB) (150 mg, 0.53 mmol), $P(OEt)_3$ (0.9 mL, 5.3 mmol) and 50% aqueous KOH (6 mL) was added. Reaction was stirred at r.t. overnight in air, after which the reaction mixture was diluted with EtOAc and water. Aqueous layer was extracted EtOAc (2 x 15 mL) and combined organic extracts was dried over Na_2SO_4, concentrated under reduced pressure and residue was purified by column chromatography with hexane/ethyl acetate as eluent to yield the racemic version of **1i**.

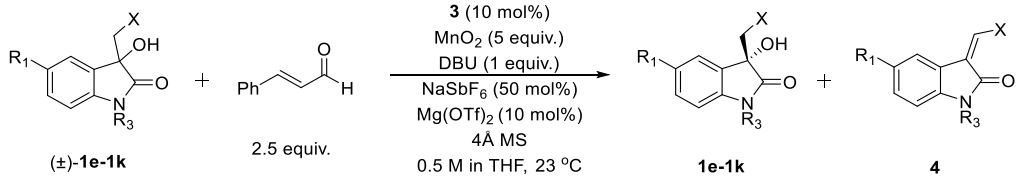
8. Table 1. Screening different additives for kinetic resolution of substate 1e[a]



entry	Additive	ee_{1e}[b]	Conv.[c]	k_{rel}[c]
1	none	49	45	6
2	$LiBF_4$	48	43	7
3	$NaBF_4$	45	40	8
4	KBF_4	40	42	5
5	$NaPF_6$	59	50	7
6	$NaSbF_6$	72	48	17
7	$NaBPh_4$	65	47	12
8[d]	$NaSbF_6$	84	50	30

[a]The reaction was carried out at 0.15 mmol scale using **1e** (1.0 equiv.), cinnamaldehyde (2.5 equiv.), NHC precursor **3** (10 mol%), DBU (1.0 equiv.), MnO_2 (5 equiv.), 4 Å MS (100 mg) and one of the additives (50 mol%) in THF (0.5 M). [b]Determined by HPLC. [c]Conv. was indicated by ^1H NMR using 1,1,2,2-tetrachloroethane as the internal standard. $k_{rel} = \ln[(1-Conv.)(1-ee_{1e})] / \ln[(1-Conv.)(1+ee_{1e})]$. [d]Reaction was carried out with 10 mol% of $Mg(OTf)_2$.

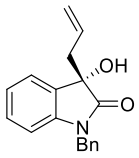
9. General Procedures B for Kinetic Resolution of 3-Hydroxy-3-Substituted Oxindoles



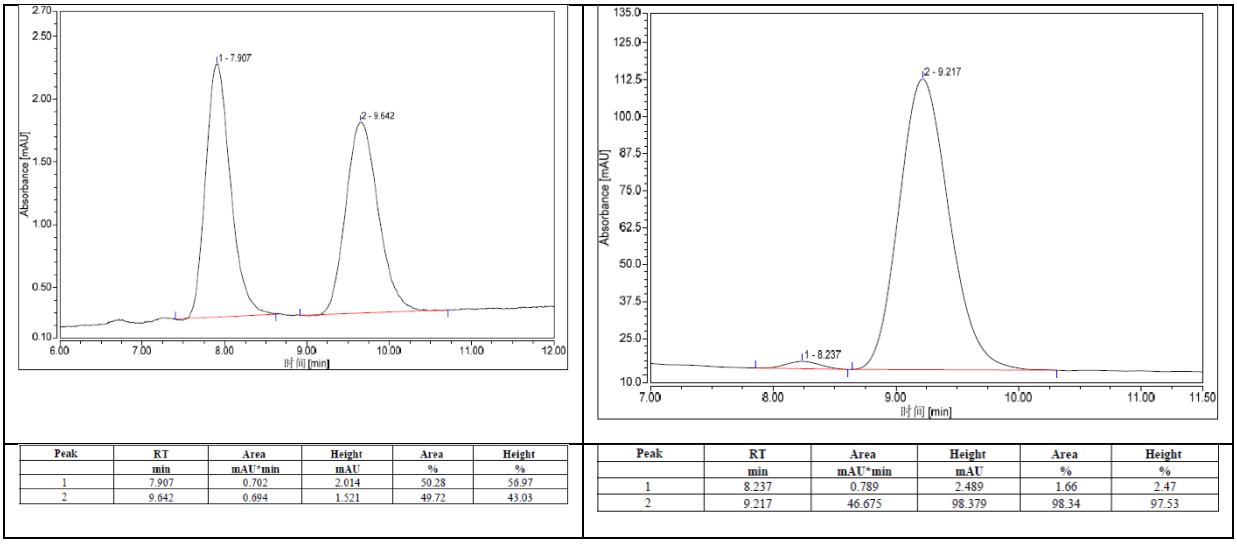
To a 4 mL vial was added the (±)-**1e-1k** (0.15 mmol), **3** (0.015 mmol), activated manganese (IV) oxide (0.75 mmol), $NaSbF_6$ (0.075 mmol) and 4Å molecular sieves (100mg). The mixture was taken into the glovebox, where magnesium trifluoromethanesulfonate (0.015 mmol), cinnamaldehyde (50 μL, 0.375 mmol) and anhydrous THF (300 μL) were added. The reaction mixture was taken outside the glovebox, and DBU (23 μL, 0.15 mmol) was added using a micropipette. The reaction vial was then sealed and allowed to stir at ambient temperature overnight, and filtered over a short column of silica gel with dichloromethane as eluent. The filtrate was concentrated under reduced pressure and the conversion was indicated by ^{1}H NMR using 1,1,2,2-tetrachloroethane as the internal standard. The crude reaction mixture was directly purified by silica gel column chromatography with hexanes/ethyl acetate (10:1 v/v) as eluent to afford the ester product and recovered the tertiary alcohol in pure form.

10. Characterization of compounds.

(*S*)-3-allyl-1-benzyl-3-hydroxyindolin-2-one (Scheme 3, **1a).**



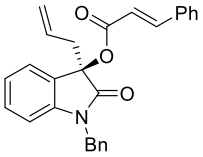
Recovered starting material: colorless syrup, 45 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.3 Hz, 1H), 7.37 – 7.26 (m, 5H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 5.66 (dddd, *J* = 14.7, 10.1, 8.4, 6.3 Hz, 1H), 5.17 (d, *J* = 17.1 Hz, 1H), 5.12 (d, *J* = 10.1 Hz, 1H), 5.05 (d, *J* = 15.7 Hz, 1H), 4.76 (d, *J* = 15.7 Hz, 1H), 3.55 (br, 1H), 2.85 (dd, *J* = 13.2, 6.2 Hz, 1H), 2.74 (dd, *J* = 13.0, 8.4 Hz, 1H). **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 178.0, 142.4, 135.3, 130.5, 129.7, 129.4, 128.6, 127.6, 127.2, 124.1, 123.0, 120.3, 109.4, 76.0, 43.7, 42.9. **IR** *v* (cm^{-1}): 2465, 2344, 2282, 2115, 2038, 1850, 1681, 1621, 799, 757. The NMR date were consistent with that reported in the literature.[6] **Specific Rotation**: $[\alpha]^{25}_{D}$ -36.0 (*c* = 0.10, $CHCl_3$). The absolute configuration of **1a** was assigned by comparing its specific rotation with that of the same compound reported in the literature.[4] 97% ee (HPLC condition: Chiralpak IC column, *n*-Hexane/*i*-PrOH = 80:20, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 8.24 min for minor isomer, t_R = 9.22 min for major isomer).



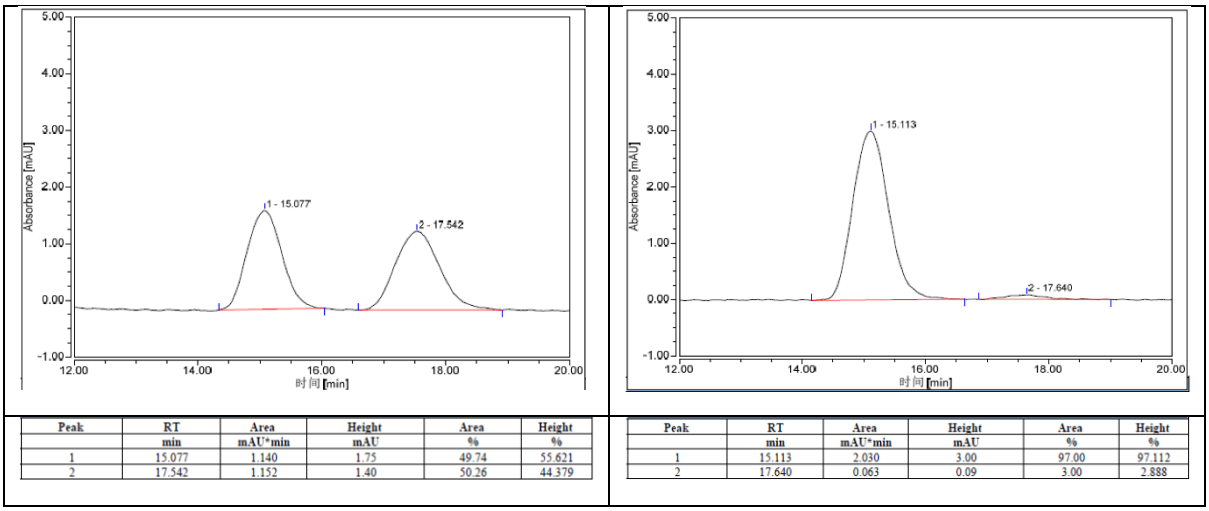
Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	7.907	0.702	2.014	50.28	56.97
2	9.642	0.694	1.521	49.72	43.03

Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	8.237	0.789	2.489	1.66	2.47
2	9.217	46.675	98.379	98.34	97.53

(*R*)-3-allyl-1-benzyl-2-oxoindolin-3-yl cinnamate (Scheme 3, **2a).**



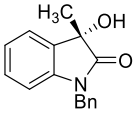
Product: colorless syrup, 48 % yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 16.0 Hz, 1H), 7.55 - 7.52 (m, 2H), 7.45 - 7.36 (m, 7H), 7.32 - 7.28 (m, 2H), 7.22 (td, *J* = 7.5, 1.0 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 7.5 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 5.74 - 5.65 (m, 1H), 5.21- 5.15 (m, 2H), 5.08 (d, *J* = 16.0 Hz, 1H), 4.97 (d, *J* = 16.0 Hz, 1H), 3.03 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.79 (dd, *J* = 13.5, 8.5 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 174.3, 164.7, 146.4, 142.9, 135.6, 134.1, 130.5, 129.5, 129.5, 128.8, 128.6, 128.1, 127.4, 127.2, 127.1, 122.9, 122.5, 120.7, 116.6, 109.4, 79.4, 44.0, 41.2. **HRMS (ESI)** m/z Calcd for [$C_{27}H_{23}NNaO_3$, M + Na]$^+$: 432.1570; Found: 432.1572. **IR** *v* (cm^{-1}): 2463, 2310, 2113, 1989, 1885, 1671, 1599, 806, 757. **Specific Rotation**: $[\alpha]^{25}_D$ -35.0 (*c* = 0.10, $CHCl_3$). 94% ee (HPLC condition: Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 80:20, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 15.11 min for major isomer, t_R = 17.64 min for minor isomer).



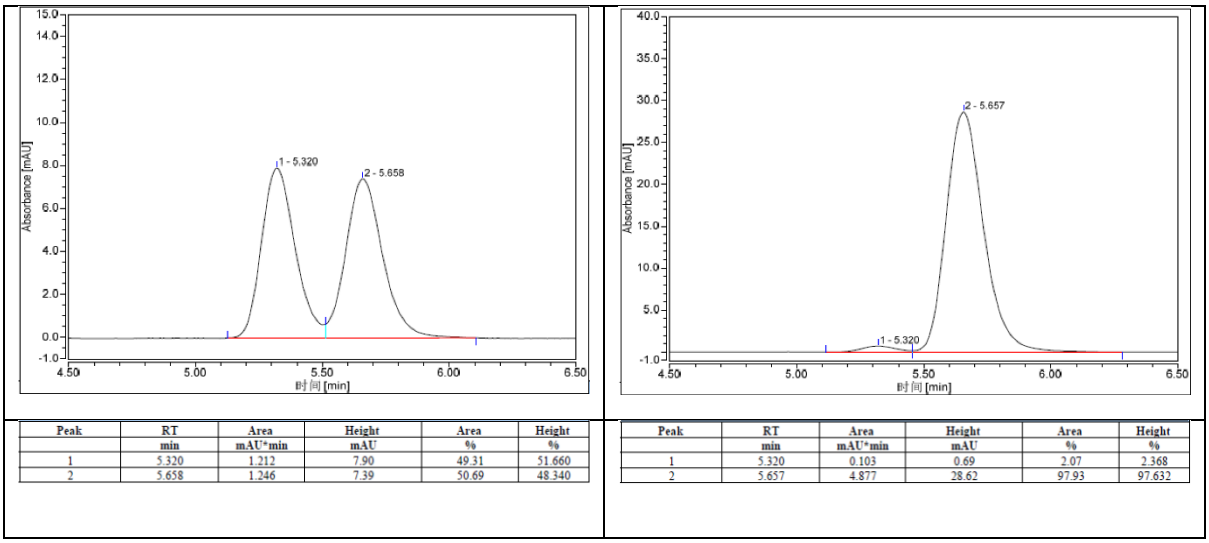
Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	15.077	1.140	1.75	49.74	55.621
2	17.542	1.152	1.40	50.26	44.379

Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	15.113	2.030	3.00	97.00	97.112
2	17.640	0.063	0.09	3.00	2.888

(*S*)-1-benzyl-3-hydroxy-3-methylindolin-2-one (Scheme 3, **1b).**



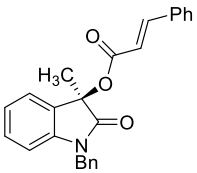
Recovered starting material: colorless syrup, 44 % yield.**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.2 Hz, 1H), 7.27 - 7.35 (m, 5H), 7.24 (td, *J* = 7.5, 1.2 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 4.99 (d, *J* = 15.7 Hz, 1H), 4.84 (d, *J* = 15.7 Hz, 1H), 3.44 (br, 1H), 1.70 (s, 3H). **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 178.9, 141.8, 141.7, 135.4, 131.6, 129.4, 129.3, 128.8, 127.6, 127.1, 123.4, 123.2, 109.5, 73.7, 43.6, 25.0. The NMR date were consistent with that reported in the literature.[6] **IR** *v* (cm^{-1}): 2426, 2358, 2282, 2145, 1976, 1855, 1676, 1625, 1175, 734, 483. **Specific Rotation**: $[\alpha]^{25}_{D}$ -55.0 (*c* = 0.10, $CHCl_3$). The absolute configuration of **1b** was assigned by analogy to **1a**. 96% ee (HPLC condition: Chiralpak IC column, *n*-Hexane/*i*-PrOH = 70:30, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 5.32 min for minor isomer, t_R = 5.66 min for major isomer).



Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	5.320	1.212	7.90	49.31	51.660
2	5.658	1.246	7.39	50.69	48.340

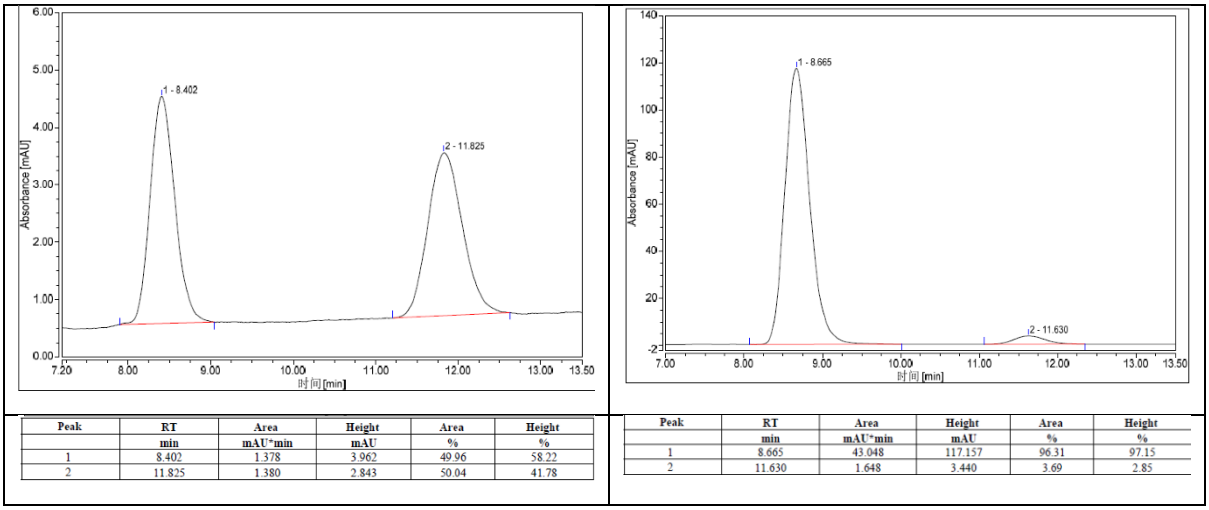
Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	5.320	0.103	0.69	2.07	2.368
2	5.657	4.877	28.62	97.93	97.632

(*R*)-1-benzyl-3-methyl-2-oxoindolin-3-yl cinnamate (Scheme 3, **2b).**



Product: colorless syrup, 47 % yield. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.71 (d, *J* = 16.0 Hz, 1H), 7.54 - 7.52 (m, 2H), 7.45 - 7.37 (m, 7H), 7.32 - 7.28 (m, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.04 (t,

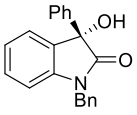
J = 7.5 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 5.04 (s, 2H), 1.80 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 175.2, 164.8, 146.3, 142.3, 135.6, 134.1, 130.5, 129.4, 129.2, 128.8, 128.7, 128.1, 127.5, 127.1, 122.8, 122.0, 116.7, 109.5, 77.4, 44.0, 23.7. **HRMS (ESI)** m/z Calcd for $[C_{25}H_{21}NNaO_3, M + Na]^+$: 406.1414; Found: 406.1391. **IR** *v* (cm^{-1}): 2467, 2412, 2291, 2115, 1978, 1876, 1676, 1588, 748, 671. **Specific Rotation**: $[\alpha]^{25}_D$ - 45.0 (*c* = 1.00, $CHCl_3$). 93% ee (HPLC condition: Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 70:30, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 8.67 min for major isomer, t_R = 11.63 min for minor isomer).



Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	8.402	1.378	3.962	49.96	58.22
2	11.825	1.380	2.843	50.04	41.78

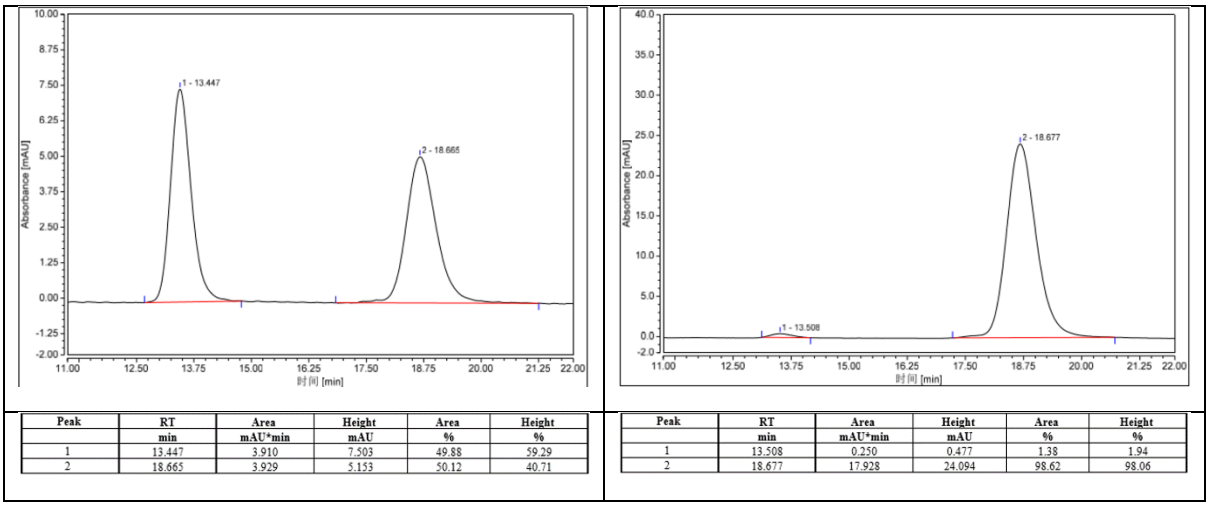
Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	8.665	43.048	117.157	96.31	97.15
2	11.630	1.648	3.440	3.69	2.85

(*S*)-1-benzyl-3-hydroxy-3-phenylindolin-2-one (Scheme 3, **1c).**



Recovered starting material: colorless syrup, 43 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.43 (m, 2H), 7.40 – 7.33 (m, 6H), 7.33 – 7.28 (m, 2H), 7.25 (td, *J* = 7.8, 1.1 Hz, 1H), 7.07 (dd, *J* = 10.9, 4.2 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 5.07 (d, *J* = 15.6 Hz, 1H), 4.85 (dd, *J* = 15.7, 1.8 Hz, 1H), 3.73 (br, 1H). **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 177.7, 142.5, 140.2, 135.4, 131.8, 129.6, 128.8, 128.5, 128.1, 127.7, 127.2, 125.3, 124.9, 123.5, 109.7, 77.9, 43.9. The

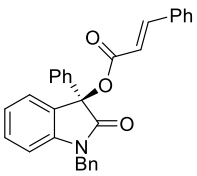
NMR date were consistent with that reported in the literature.[6] **IR** *v* (cm^{-1}): 2486, 2430, 2277, 2076, 2082, 1743, 1985, 1616, 762. **Specific Rotation**: $[\alpha]^{25}_D$ -32.5 (*c* = 1.00, $CHCl_3$). The absolute configuration of **1c** was assigned by analogy to **1a**. 97% ee (HPLC condition: Chiralpak AS-H column, *n*-Hexane/*i*-PrOH = 70:30, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 13.51 min for minor isomer, t_R = 18.68 min for major isomer).



Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	13.447	3.910	7.503	49.88	59.29
2	18.665	3.929	5.153	50.12	40.71

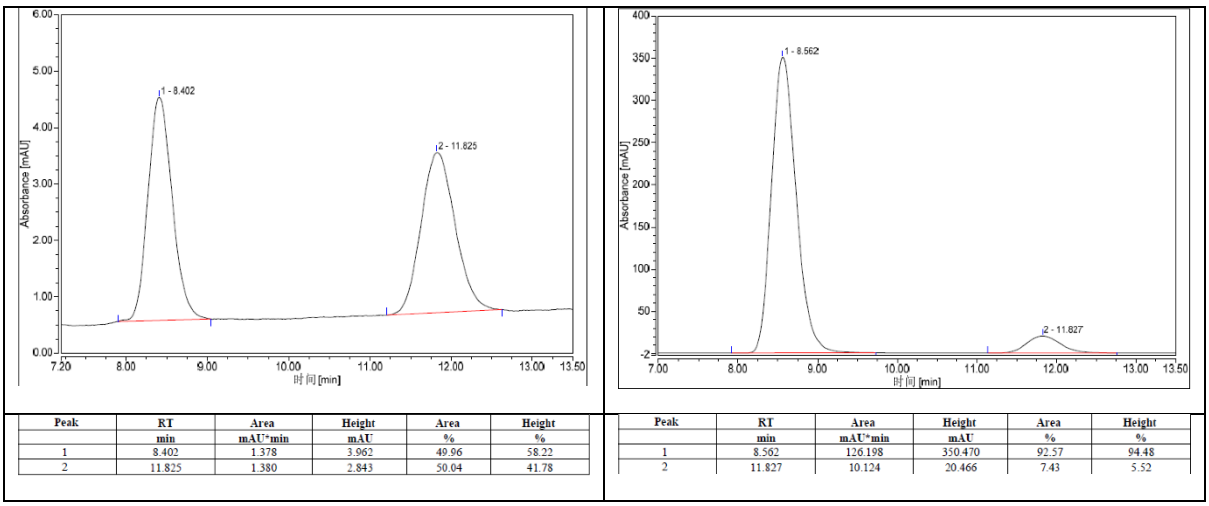
Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	13.508	0.250	0.477	1.38	1.94
2	18.677	17.928	24.094	98.62	98.06

(*R*)-1-benzyl-2-oxo-3-phenylindolin-3-yl cinnamate (Scheme 3, **2c).**



product: colorless syrup, 50 %. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.79 (d, *J* = 16.0 Hz, 1H), 7.57 - 7.56 (m, 2H), 7.51 - 7.49 (m, 2H), 7.43-7.27 (m, 13H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.62 (d, *J* = 16.0 Hz, 1H), 5.05 (d, *J* = 16.0 Hz, 1H), 4.97 (d, *J* = 16.0 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 174.0, 165.0, 146.6, 143.6, 136.8, 135.6, 134.1, 130.6, 129.9, 128.9, 128.9, 128.7, 128.6, 128.2, 127.5, 127.2, 126.4, 124.1, 123.0, 116.8, 109.7, 81.3, 44.3. **HRMS (ESI)** m/z Calcd for $[C_{30}H_{23}NNaO_3, M + Na]^+$: 468.1570; Found: 468.1557. **IR** *v* (cm^{-1}): 2488, 2319, 2122, 1999, 1857, 1676, 1607, 799, 752. **Specific Rotation**: $[\alpha]^{25}_D$ -12.2 (*c* = 0.10, $CHCl_3$). 85% ee (HPLC condition: Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 70:30,

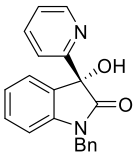
flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 8.56 min for major isomer, t_R = 11.83 min for minor isomer).



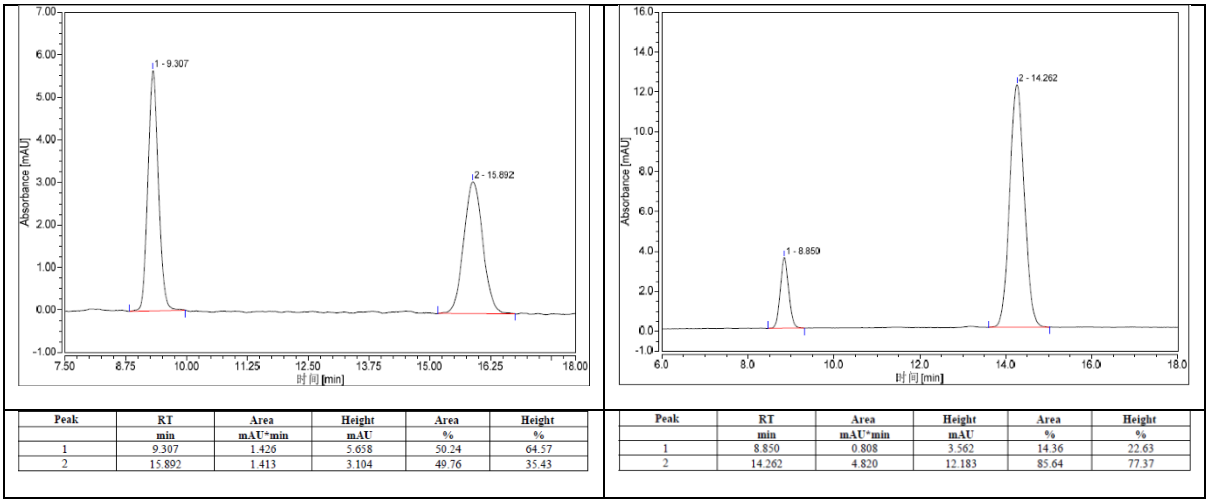
Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	8.402	1.378	3.962	49.96	58.22
2	11.825	1.380	2.843	50.04	41.78

Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	8.562	126.198	350.470	92.57	94.48
2	11.827	10.124	20.466	7.43	5.52

(*R*)-1-benzyl-3-hydroxy-3-(pyridin-2-yl)indolin-2-one (Scheme 3, **1d).**



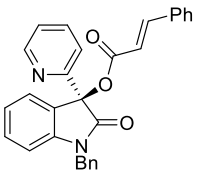
Recovered starting material: colorless syrup, 51 % yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.6 Hz, 1H), 7.64 (td, *J* = 7.7, 1.3 Hz, 1H), 7.43 – 7.23 (m, 8H), 7.19 (d, *J* = 7.3 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 7.9 Hz, 1H), 6.83 (d, *J* = 7.9 Hz, 1H), 6.30 (s, 1H), 5.09 (d, *J* = 15.7 Hz, 1H), 4.84 (d, *J* = 15.7 Hz, 1H). **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 176.6, 156.6, 148.1, 143.6, 137.4, 135.5, 130.9, 130.0, 128.8, 127.6, 127.3, 124.7, 123.4, 119.9, 109.6, 77.7, 44.0. The NMR date were consistent with that reported in the literature.[6] **IR** *v* (cm^{-1}): 2484, 2323, 2117, 2001, 1676, 1595, 801, 755, 648. **Specific Rotation**: $[\alpha]^{25}_D$ -15.0 (*c* = 0.10, $CHCl_3$). The absolute configuration of **1d** was assigned by analogy to **1a**. 71% ee (HPLC condition: Chiralpak IC column, *n*-Hexane/*i*-PrOH = 70:30, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 8.85 min for minor isomer, t_R = 14.26 min for major isomer).



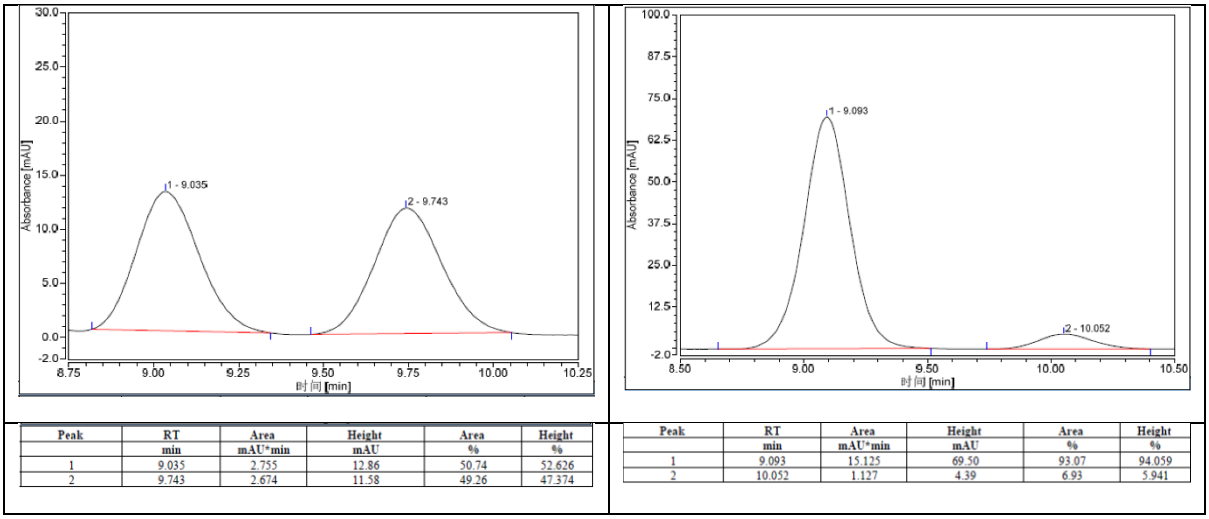
Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	9.307	1.426	5.658	50.24	64.57
2	15.892	1.413	3.104	49.76	35.43

Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	8.850	0.808	3.562	14.36	22.63
2	14.262	4.820	12.183	85.64	77.37

(*S*)-1-benzyl-2-oxo-3-(pyridin-2-yl)indolin-3-yl cinnamate (Scheme 3, **2d).**



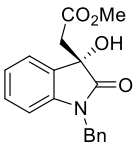
Product: colorless syrup, 41 % yield. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 8.56 (d, *J* = 3.5 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.84 (td, *J* = 8.0, 1.5 Hz, 1H), 7.79 (d, *J* = 16.0 Hz, 1H), 7.58 - 7.54 (m, 4H), 7.43- 7.37 (m, 5H), 7.32-7.26 (m, 2H), 7.23-7.20 (m, 2H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.74 (t, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 16.0 Hz, 1H), 5.22 (d, *J* = 16.0 Hz, 1H), 5.02 (d, *J* = 16.0 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 173.7, 164.6, 156.9, 149.6, 146.9, 144.0, 137.1, 135. 6, 134.1, 130.7, 129.8, 128.9, 128.8, 128.7, 128.3, 127.4, 127.2, 123.5, 123.3, 122.8, 120.6, 116.6, 109.8, 82.4, 44.3. **HRMS (ESI)** m/z Calcd for $[C_{29}H_{22}N_2NaO_3, M + Na]^+$: 469.1523; Found: 469.1511. **IR** *v* (cm^{-1}): 2470, 2351, 2291, 2113, 1982, 1857, 1669, 1607, 810, 750. **Specific Rotation**: $[\alpha]^{25}_D$ -13.6 (*c* = 1.00, $CHCl_3$). 86% ee (HPLC condition: Chiralpak AD-H column, *n*-Hexane/*i*-PrOH = 60:40, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 9.09 min for major isomer, t_R = 10.05 min for minor isomer).



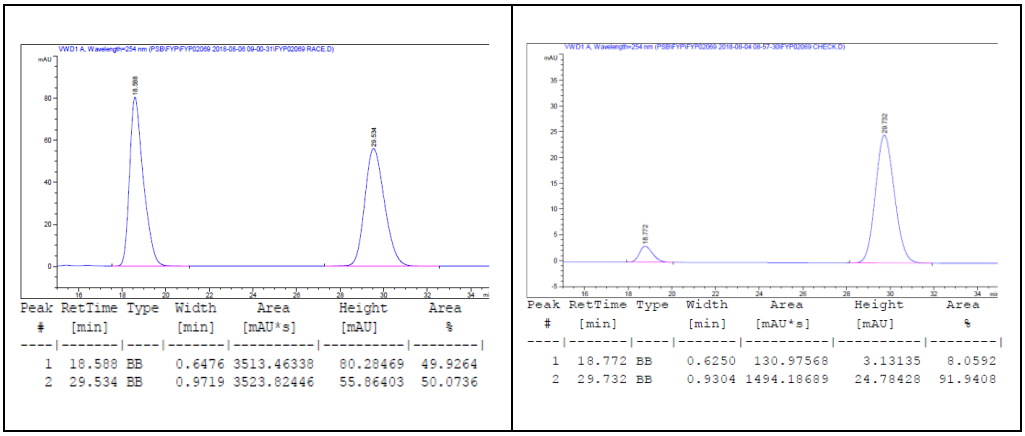
Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	9.035	2.755	12.86	50.74	52.626
2	9.743	2.674	11.58	49.26	47.374

Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	9.093	15.125	69.50	93.07	94.059
2	10.052	1.127	4.39	6.93	5.941

methyl (S)-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetate, (Scheme 4, **1e**)



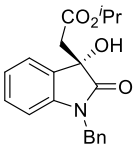
Recovered starting material: 45% yield. **^{1}H NMR (400 Mhz)** δ 7.31 (dd, *J* = 9.0 Hz, 1H), 7.23 – 7.19, (m, 5H), 7.14 (td, *J* = 7.8, 1.2 Hz, 1H), 6.97 (td, *J* = 7.6, 0.8 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.77 (d, *J* = 15.6 Hz, 1H), 4.03 (br, 1H), 3.59 (s, 3H), 2.92 (d, *J* = 2.4 Hz, 2H). **^{13}C NMR (100 MHz)** δ 176.2, 170.8, 142.6, 135.3, 130.1, 129.2, 128.8, 127.7, 127.3, 123.9, 123.2, 109.7, 73.5, 52.1, 43.9, 41.0. **HRMS (ESI)** m/z Calcd for $[C_{18}H_{17}NNaO_4, M + Na]^+$: 334.1050; Found: 334.1049. **IR** *v* (cm^{-1}): 2460, 2347, 2268, 1987, 1859, 1597, 1175, 799, 757. **Specific Rotation**: $[\alpha]^{25}_D$ +10.70 (*c* = 0.1, $CHCl_3$). The absolute configuration of **1e** was assigned by analogy to **1k**. 84% ee (HPLC condition: Chiralpak IC column, *n*-Hexane/*i*-PrOH = 80:20, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 18.77 min for minor isomer, t_R = 29.73 min for major isomer).



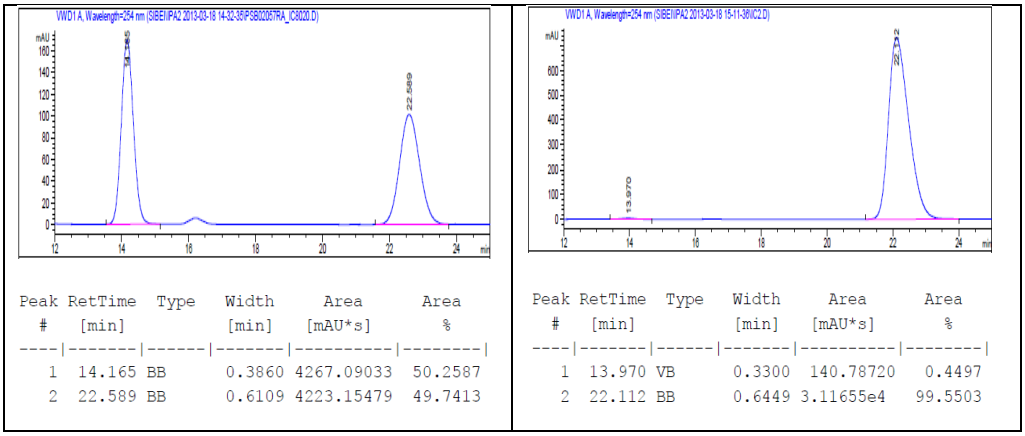
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.588	BB	0.6476	3513.46338	80.28469	49.9264
2	29.534	BB	0.9719	3523.82446	55.86403	50.0736

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.772	BB	0.6250	130.97568	3.13135	8.0592
2	29.732	BB	0.9304	1494.18689	24.78428	91.9408

Isopropyl 2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetate, (Scheme 5, **1f**)



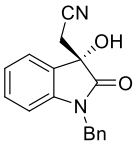
Recovered starting material: 42% yield. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.5 Hz, 1H), 7.31 - 7.25 (m, 5H), 7.19 (dd, *J* = 8.0 Hz, 1H) 7.04 (dd, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 7.5 Hz, 1H), 5.03 (h, *J* = 6.4, 6.2 Hz, 1H), 4.89 (d, *J* = 1.5 Hz, 2H), 2.93 (s, 2H), 1.73 (br, 1H), 1.23 (dd, *J* = 6.4, 6.2 Hz, 6 H). **^{13}C NMR** (300 MHz, $CDCl_3$): δ 176.2, 170.0, 142.6, 135.3, 129.9, 129.3, 128.8, 127.6, 127.2, 123.9, 123.1, 109.6, 73.6, 68.9, 43.8, 41.4, 21.6. **HRMS (ESI)** m/z Calcd for $[C_{20}H_{21}NNaO_4, M + Na]^+$: 362.1363; Found: 362.1369. **IR** *v* (cm^{-1}): 2486, 2410, 2317, 2293, 2117, 2003, 1783, 1671, 1599, 752, 666. **Specific Rotation**: $[\alpha]^{25}_D$ +12.00 (*c* = 0.1, $CHCl_3$). The absolute configuration of **1f** was assigned by analogy to **1k**. 99% ee (HPLC condition: Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 85:15, flow rate = 0.5 mL/min, wave length = 254 nm, t_R = 13.97 min for minor isomer, t_R = 12.11 min for major isomer).



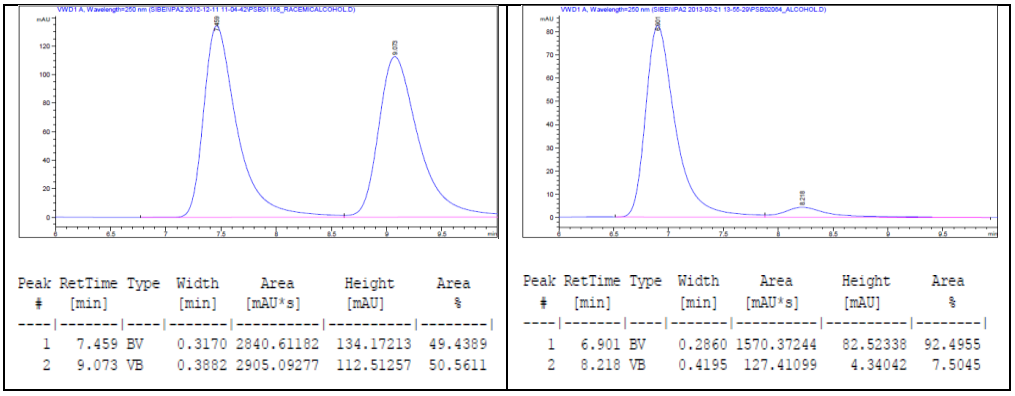
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	14.165	BB	0.3860	4267.09033	50.2587
2	22.589	BB	0.6109	4223.15479	49.7413

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	13.970	VB	0.3300	140.78720	0.4497
2	22.112	BB	0.6449	3.11655e4	99.5503

2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetonitrile, (Scheme 5, **1g)**



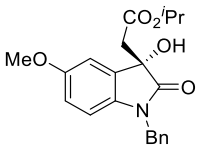
Recovered starting material: 39% yield. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 7.5 Hz, 1 H), 7.34 – 7.26 (m, 6 H), 7.14, (dd, *J* = 7.5 Hz, 1 H), 6.78 (d, *J* = 7.5 Hz, 1 H), 4.90 (d, *J* = 15.5 Hz, 1 H), 4.84 (d, *J* = 15.5 Hz, 1 H), 3.13 (d, *J* = 16.5 Hz, 1 H), 2.80 (d, *J* = 16.5 Hz, 1 H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 175.2, 142.1, 134.6, 130.9, 128.9, 128.0, 127.3, 127.2, 124.3, 123.9, 115.2, 110.1, 72.5, 44.1, 27.5. **HRMS (ESI)** m/z Calcd for $[C_{17}H_{14}N_2NaO_2, M + Na]^+$: 301.0947; Found: 301.0946. **IR** *v* (cm^{-1}): 2486, 2347, 2314, 2117, 1996, 1848, 1674, 1597, 762, 715. **Specific Rotation**: $[\alpha]^{25}_D$ +18.60 (*c* = 0.1, $CHCl_3$). The absolute configuration of **1g** was assigned by analogy to **1k**. 85% ee (HPLC condition: Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 70:30, flow rate = 2.0 mL/min, wave length = 254 nm, t_R = 6.90 min for major isomer, t_R = 8.22 min for minor isomer).



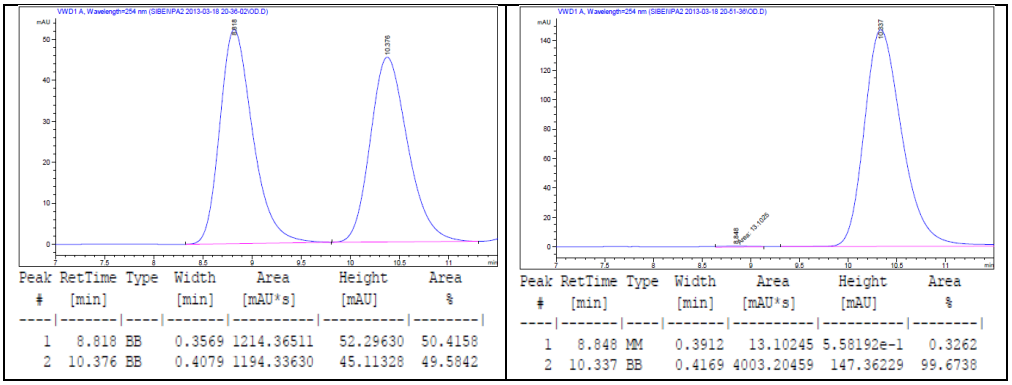
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.459	BV	0.3170	2840.61182	134.17213	49.4389
2	9.073	VB	0.3882	2905.09277	112.51257	50.5611

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.901	BV	0.2860	1570.37244	82.52338	92.4955
2	8.218	VB	0.4195	127.41099	4.34042	7.5045

Isopropyl 2-(1-benzyl-3-hydroxy-5-methoxy-2-oxoindolin-3-yl)acetate, (Scheme 5, **1h)**



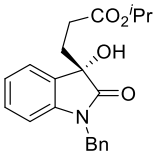
Recovered starting material: 36% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 5 H), 7.06 (d, 2.4 Hz, 1 H), 6.74, (dd, *J* = 8.4, 2.4 Hz, 1 H), 6.61 (d, *J* = 8.4 Hz, 1 H), 5.08 (h, *J* = 6.0 Hz, 1H), 4.89 (s, 2 H), 4.51 (s, 1 H), 3.77 (s, 3 H), 2.93 (d, *J* = 0.4 Hz, 2 H), 1.23 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.9, 170.1, 156.3, 135.8, 135.4, 130.5, 128.8, 127.6, 127.2, 114.5, 111.1, 110.1, 76.6, 74.0, 69.0, 55.8, 43.9, 41.4, 21.6. **HRMS (ESI)** m/z Calcd for $[C_{21}H_{23}NNaO_5, M + Na]^+$: 392.1468; Found: 392.1470. **IR** *v* (cm^{-1}): 2470, 2386, 2293, 2096, 1971, 1841, 1750, 1614, 1595, 1159, 752, 702. **Specific Rotation**: $[\alpha]^{25}_D$ +13.30 (*c* = 0.1, $CHCl_3$). The absolute configuration of **1h** was assigned by analogy to **1k**. 99% ee (HPLC condition: Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 85:15, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 8.85 min for minor isomer, t_R = 10.34 min for major isomer).



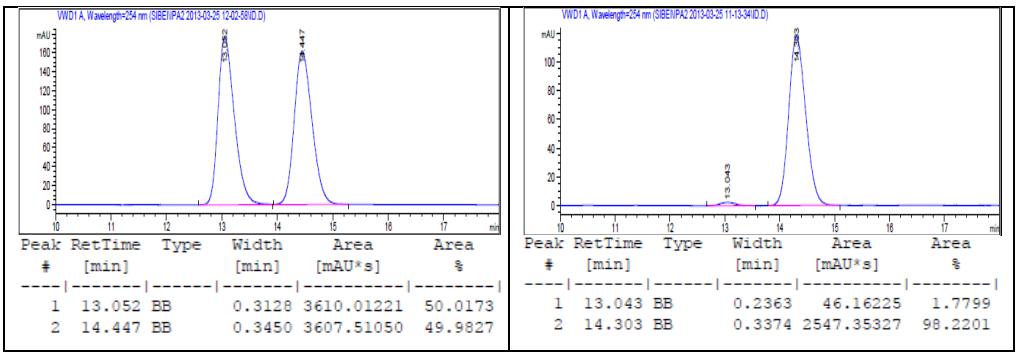
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.818	BB	0.3569	1214.36511	52.29630	50.4158
2	10.376	BB	0.4079	1194.33630	45.11328	49.5842

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.848	MM	0.3912	13.10245	5.58192e-1	0.3262
2	10.337	BB	0.4169	4003.20459	147.36229	99.6738

Isopropyl 3-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)propanoate, (Scheme 5, **1i)**



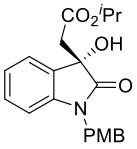
Recovered starting material: 43%. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.32 (dd, *J* = 7.6, 0.8 Hz, 1 H), 7.25 – 7.20, (m, 5 H), 7.13 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.01 (dd, *J* = 7.6, 0.8 Hz, 1 H), 6.64 (d, *J* = 7.6 Hz, 1 H), 4.86 – 4.83 (m, 3 H), 2.57 – 2.53 (m, 2 H), 2.33 – 2.26 (m, 2H), 1.12 (d, *J* = 6.0 Hz, 3 H), 1.07 (d, *J* = 6.0 Hz, 3 H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 173.6, 171.3, 141.7, 135.0, 130.3, 128.9, 128.9, 127.8, 127.1, 124.4, 123.5, 109.8, 68.1, 64.0, 44.1, 34.0, 29.7, 21.7, 21.7. **HRMS (ESI)** m/z Calcd for $[C_{21}H_{23}NNaO_4, M + Na]^+$: 376.1519; Found: 376.1515. **IR** *v* (cm^{-1}): 2484, 2275, 2029, 1836, 1614, 803, 752, 725. **Specific Rotation**: $[\alpha]^{25}_D$ +22.00 (*c* = 0.1, $CHCl_3$). The absolute configuration of **1i** was assigned by analogy to **1k**. 96% ee (HPLC condition: Chiralpak ID column, *n*-Hexane/*i*-PrOH = 80:20, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 13.04 min for minor isomer, t_R = 14.30 min for major isomer).



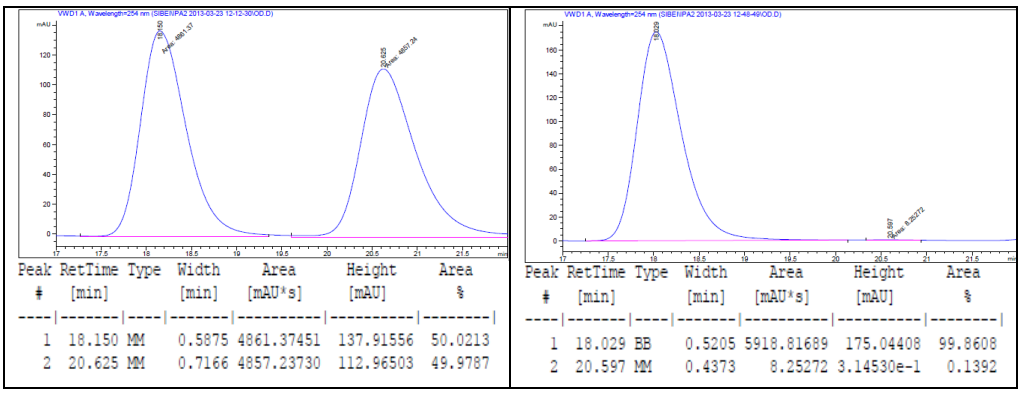
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	13.052	BB	0.3128	3610.01221	50.0173
2	14.447	BB	0.3450	3607.51050	49.9827

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	13.043	BB	0.2363	46.16225	1.7799
2	14.303	BB	0.3374	2547.35327	98.2201

Isopropyl 2-(3-hydroxy-1-(4-methoxybenzyl)-2-oxoindolin-3-yl)acetate, (Scheme 5, **1j)**



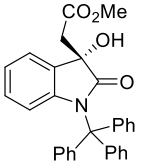
Recovered starting material: 40%, **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.40 (dd, *J* = 7.5 Hz, 1 H), 7.26 – 7.19 (m, 3 H), 7.03 (dd, *J* = 7.5 Hz, 1 H), 6.84 (d, *J* = 8.5 Hz, 2 H), 6.72 (d, *J* = 7.5 Hz, 1 H), 5.04 – 4.99 (m, 1 H), 4.86 – 4.79 (m, 2 H), 3.76 (s, 3H), 2.94 (s, 2 H), 1.17 – 1.15 (m, 6 H),. **^{13}C NMR** (125 MHz): δ 176.2, 169.9, 159.0, 142.6, 129.9, 129.3, 128.6, 127.3, 123.8, 123.0, 114.1, 109.5, 73.6, 68.8, 55.2, 43.3, 41.5, 21.5, 21.5. **HRMS (ESI)** m/z Calcd for $[C_{21}H_{23}NNaO_5, \ M + Na]^+$: 392.1468; Found: 392.1468. **IR** *v* (cm^{-1}): 2474, 2384, 2354, 2092, 1982, 1676, 1616, 1161, 736, 708. **Specific Rotation**: $[\alpha]^{25}_D$ +24.00 (*c* = 0.1, $CHCl_3$). The absolute configuration of **1j** was assigned by analogy to **1k**. 99% ee (HPLC condition: Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 85:15, flow rate = 0.5 mL/min, wave length = 254 nm, t_R = 18.03 min for major isomer, t_R = 20.60 min for minor isomer).



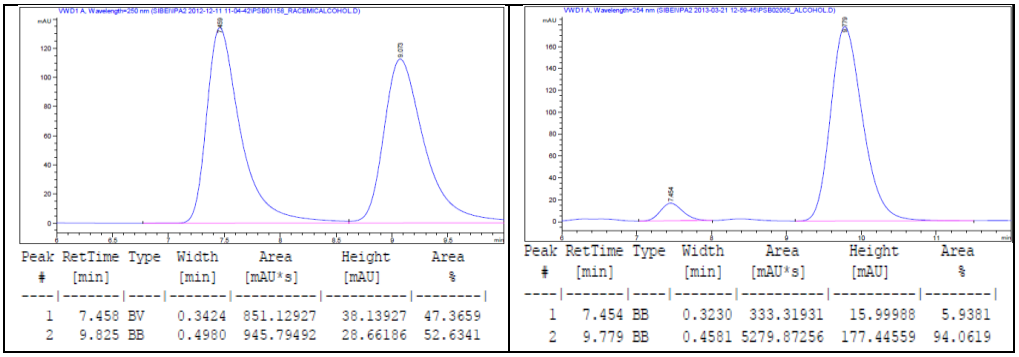
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.150	MM	0.5875	4861.37451	137.91556	50.0213
2	20.625	MM	0.7166	4857.23730	112.96503	49.9787

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.029	BB	0.5205	5918.81689	175.04408	99.8608
2	20.597	MM	0.4373	8.25272	3.14530e-1	0.1392

Isopropyl 2-(3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetate, (Scheme 5, **1k)**



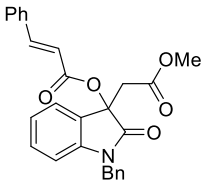
Recovered starting material: 43% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.40 – 7.38 (m, 5H), 7.27 – 7.25 (m, 1H), 7.20-7.10 (m, 10 H), 6.90 – 6.84 (m, 2H), 6.24 – 6.22 (m, 1H), 3.74 (br, 1h), 3.57 (s, 3H), 2.94 (d, *J* = 15.2 Hz, 1H), 2.88 (d, *J* = 15.2 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 177.8, 170.2, 143.2, 141.8, 129.2, 128.5, 127.9, 127.6, 126.9, 123.2, 122.6, 116.3, 74.5, 73.3, 52.0, 42.1. **HRMS (ESI)** m/z Calcd for $[C_{30}H_{25}NNaO_4, M + Na]^+$: 486.1676; Found: 486.1680. **IR** *v* (cm^{-1}): 2493, 2284, 2117, 2031, 1920, 1769, 1678, 1602, 750. **Specific Rotation**: $[\alpha]^{25}_D$ + 24.20 (*c* = 0.1, CH_2Cl_2). The absolute configuration of **1k** was assigned by comparing its specific rotation with that of the enantiomer reported in the literature.[7] 88% ee (HPLC condition: Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 85:15, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 7.45 min for minor isomer, t_R = 9.78 min for major isomer).



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.458	BV	0.3424	851.12927	38.13927	47.3659
2	9.825	BB	0.4980	945.79492	28.66186	52.6341

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.454	BB	0.3230	333.31931	15.99988	5.9381
2	9.779	BB	0.4581	5279.87256	177.44559	94.0619

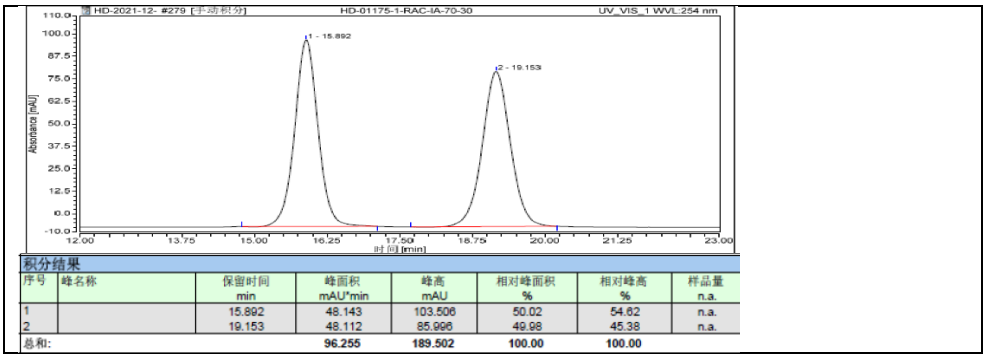
1-benzyl-3-(2-methoxy-2-oxoethyl)-2-oxoindolin-3-yl cinnamate, (Scheme 4b, **2e)**



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 16.0 Hz, 1H), 7.58 – 7.36 (m, 10H), 7.31 (dd, *J* = 14.6, 7.3 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.48 (d, *J* = 15.9 Hz, 1H), 5.07 (d, *J* = 15.8 Hz, 1H), 5.02 (d, *J* = 15.9 Hz, 1H), 3.58 (s, 3H), 3.37 (d, *J* = 15.4 Hz, 1H), 3.17 (d, *J* = 15.4 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.7,

168.2, 164.4, 146.7, 143.8, 135.6, 134.1, 130.6, 130.2, 128.9, 128.8, 128.2, 127.5, 127.4, 126.0, 123.8, 122.7, 116.6, 109.6, 77.1, 51.8, 44.5, 41.2. **HRMS (ESI)** m/z Calcd for [$C_{27}H_{23}NNaO_5$, M + Na]$^+$: 464.1468; Found: 464.1467. **IR** *v* (cm^{-1}): 2479, 2423, 2310, 1987, 1781, 1595, 1168, 813, 752

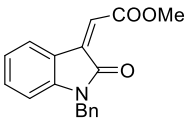
(HPLC condition: Chiralcel AD column, *n*-Hexane/*i*-PrOH = 70:30, flow rate = 1.0 mL/min, wave length = 254 nm, t_R = 15.89 min for one isomer, t_R = 19.15 min for the other isomer).



积分结果

序号	峰名称	保留时间 min	峰面积 mAU*min	峰高 mAU	相对峰面积 %	相对峰高 %	样品量 n.a.
1		15.892	48.143	103.506	50.02	54.62	n.a.
2		19.153	48.112	85.996	49.98	45.38	n.a.
总和:			96.255	189.502	100.00	100.00	

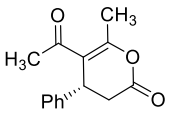
(Z)-methyl 2-(1-benzyl-2-oxoindolin-3-ylidene)acetate, (Scheme 4a**, 4a)**



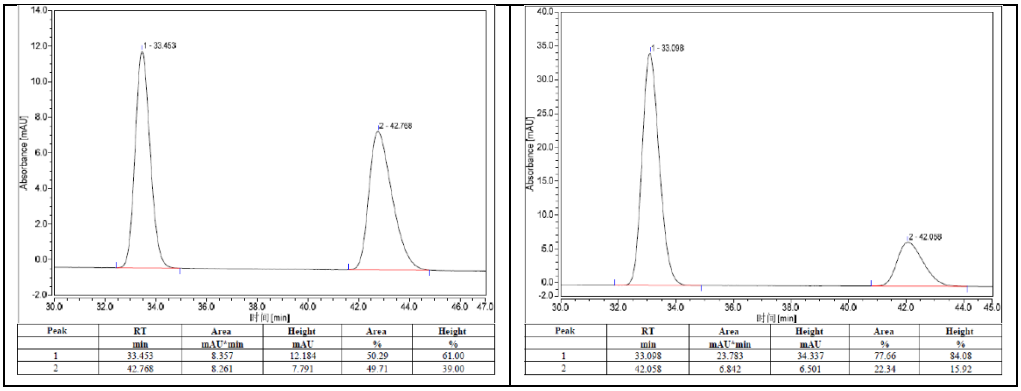
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 7.7 Hz, 1H), 7.37 – 7.26 (m, 6H), 7.06 (td, *J* = 7.7, 0.8 Hz, 1H), 7.01 (s, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 4.96 (s, 2H), 3.91 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.6, 166.1, 145.1, 137.9, 135.4, 132.4, 128.8, 127.7, 127.2, 122.9, 122.2, 119.9, 109.2, 52.2, 43.8. **IR** *v* (cm^{-1}): 2474, 2356. 2298, 1980, 1848, 1774, 1681, 1173, 796, 762

The NMR date were consistent with that reported in the literature.[8]

(*R*)-5-acetyl-6-methyl-4-phenyl-3,4-dihydro-2*H*-pyran-2-one, (Scheme 6b, **7)**



42% yield, **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 10.8, 3.9 Hz, 2H), 7.32 – 7.26 (m, 1H), 7.17 (d, *J* = 7.6 Hz, 2H), 4.17 (d, *J* = 6.8 Hz, 1H), 2.99 (ddd, *J* = 15.6, 7.2, 1.4 Hz, 1H), 2.86 (dd, *J* = 15.7, 2.4 Hz, 1H), 2.45 (s, 3H), 2.14 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.9, 165.6, 160.2, 139.7, 129.4, 127.9, 126.6, 117.3, 38.8, 37.2, 29.7, 19.1. **IR** *v* (cm^{-1}): 2484, 2417, 2312, 2261, 1989, 1662, 1590, 1166, 810, 7552. The NMR date were consistent with that reported in the literature.[8] **Specific Rotation**: $[\alpha]^{25}_{D}$ - 64.00 (*c* = 1.0, $CHCl_3$). The absolute configuration of **7** was assigned by comparing its specific rotation with that of the same compound reported in the literature.[9] 55% ee (HPLC condition: Chiralpak AD-H column, *n*-Hexane/*i*-PrOH = 99:1, flow rate = 1 mL/min, wave length = 254 nm, t_R = 33.10 min for major isomer, t_R = 42.06 min for minor isomer).



Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	33.453	8.357	12.184	50.29	61.00
2	42.768	8.261	7.791	49.71	39.00

Peak	RT	Area	Height	Area	Height
	min	mAU*min	mAU	%	%
1	33.098	23.783	34.337	77.66	84.08
2	42.058	6.842	6.501	22.34	15.92

11. Reference

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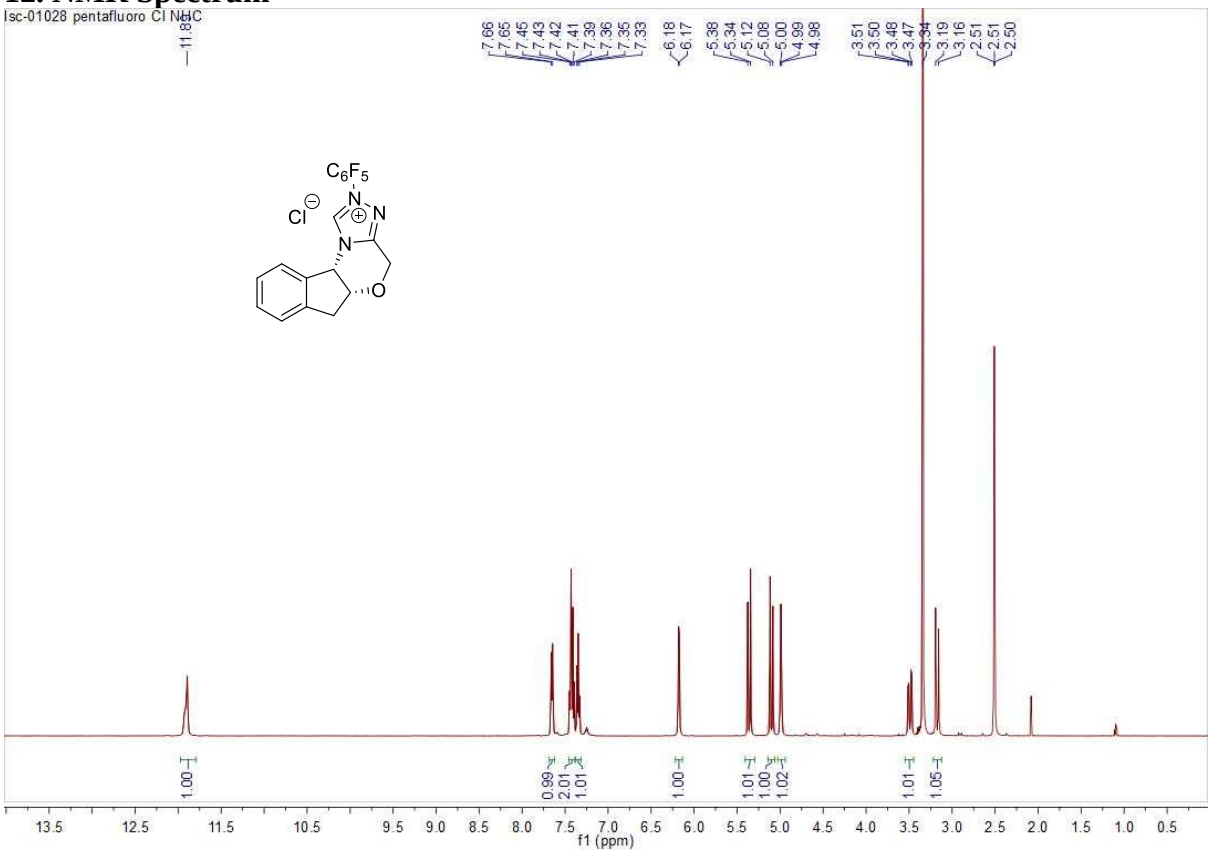
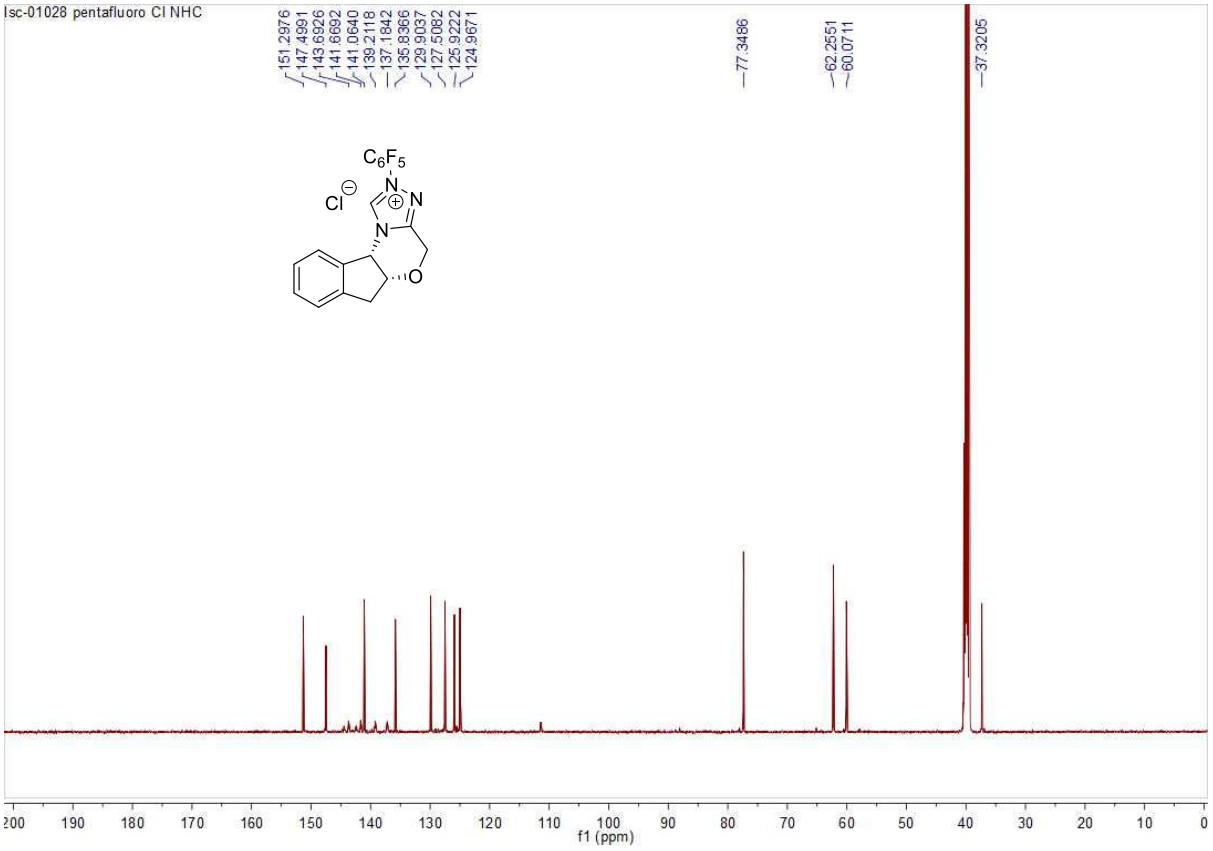
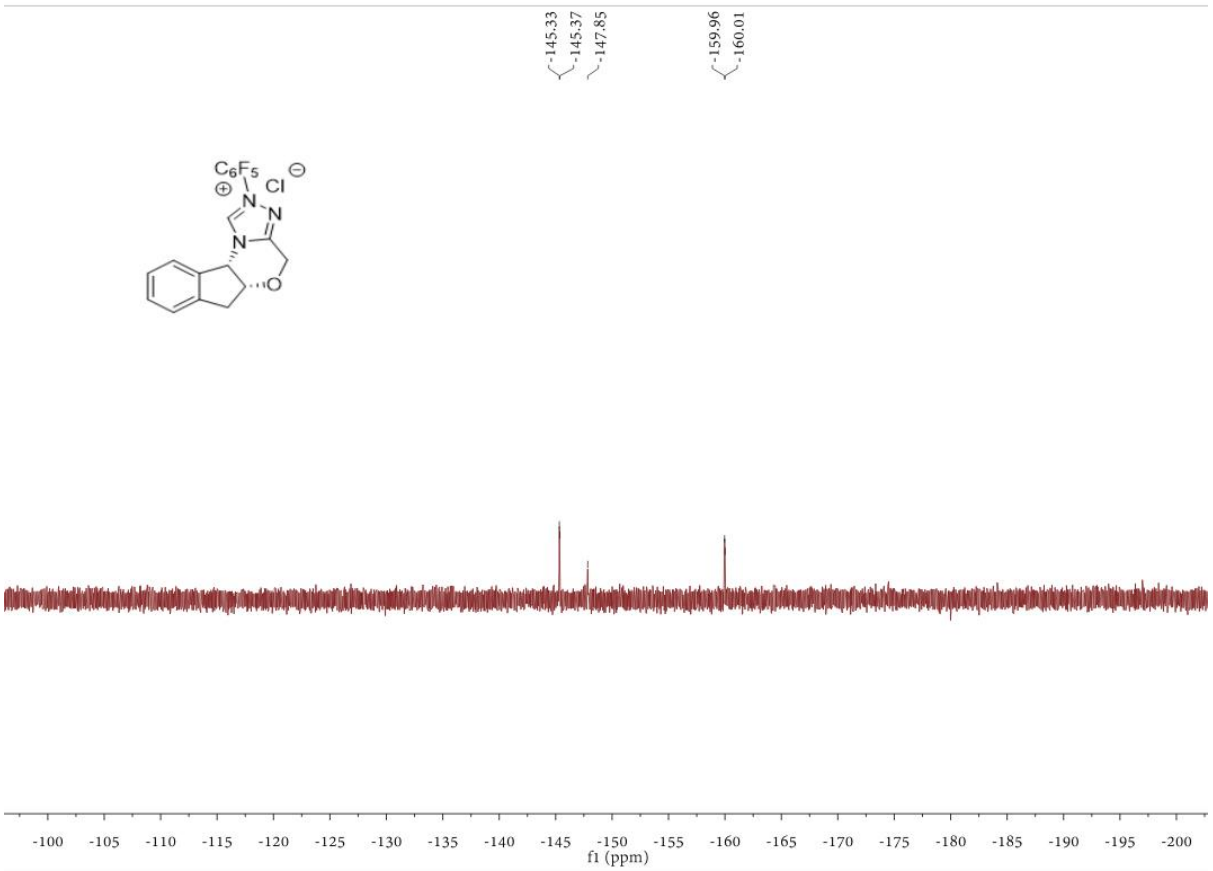
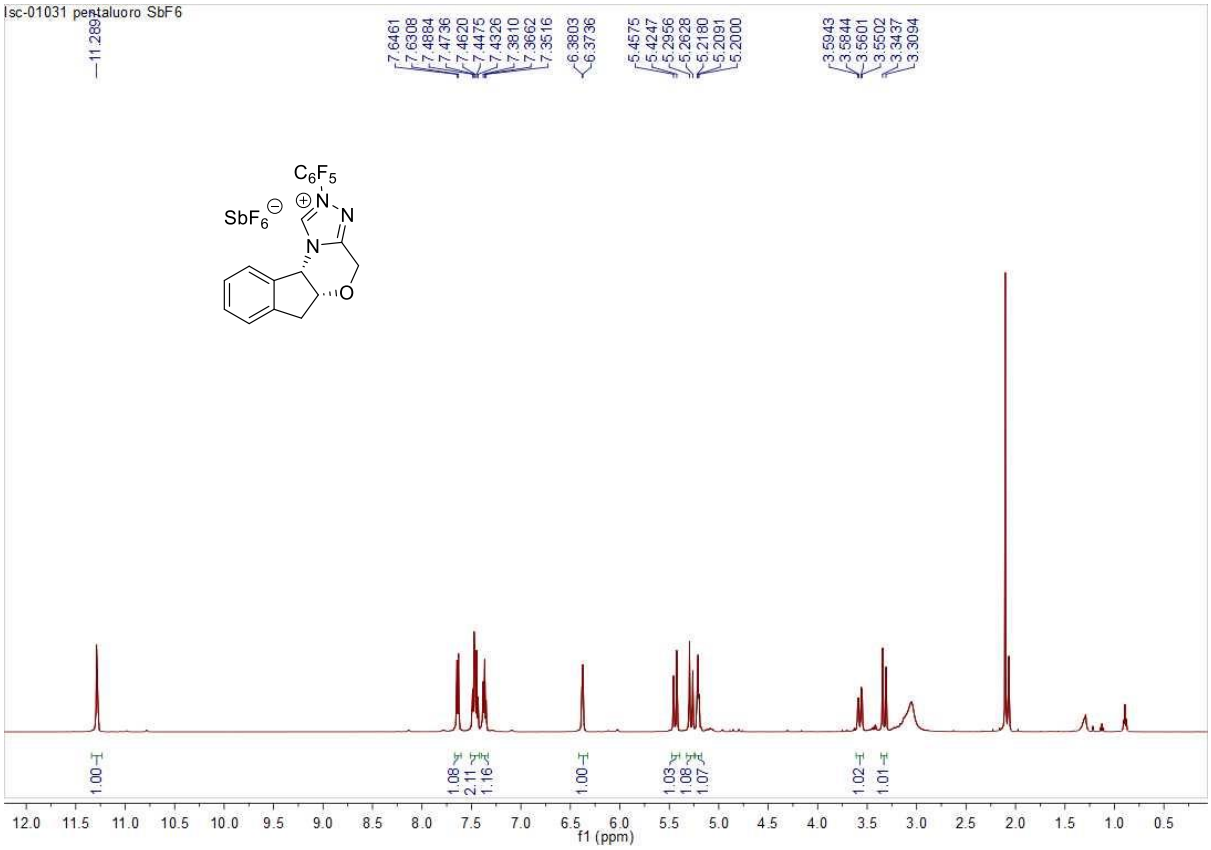
(9) Z.-Q. Rong, M.-Q. Jia and S.-L. You, *Org. Lett*., 2011, **13**, 4080−4083.

12. NMR Spectrum






-145.33
-145.37
-147.85
-159.96
-160.01
C6F5
Cl
N
N
N
O
-100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200
f1 (ppm)


lsc-01031 pentaluoro SbF6
11.289
7.6461
7.6308
7.4884
7.4736
7.4620
7.4475
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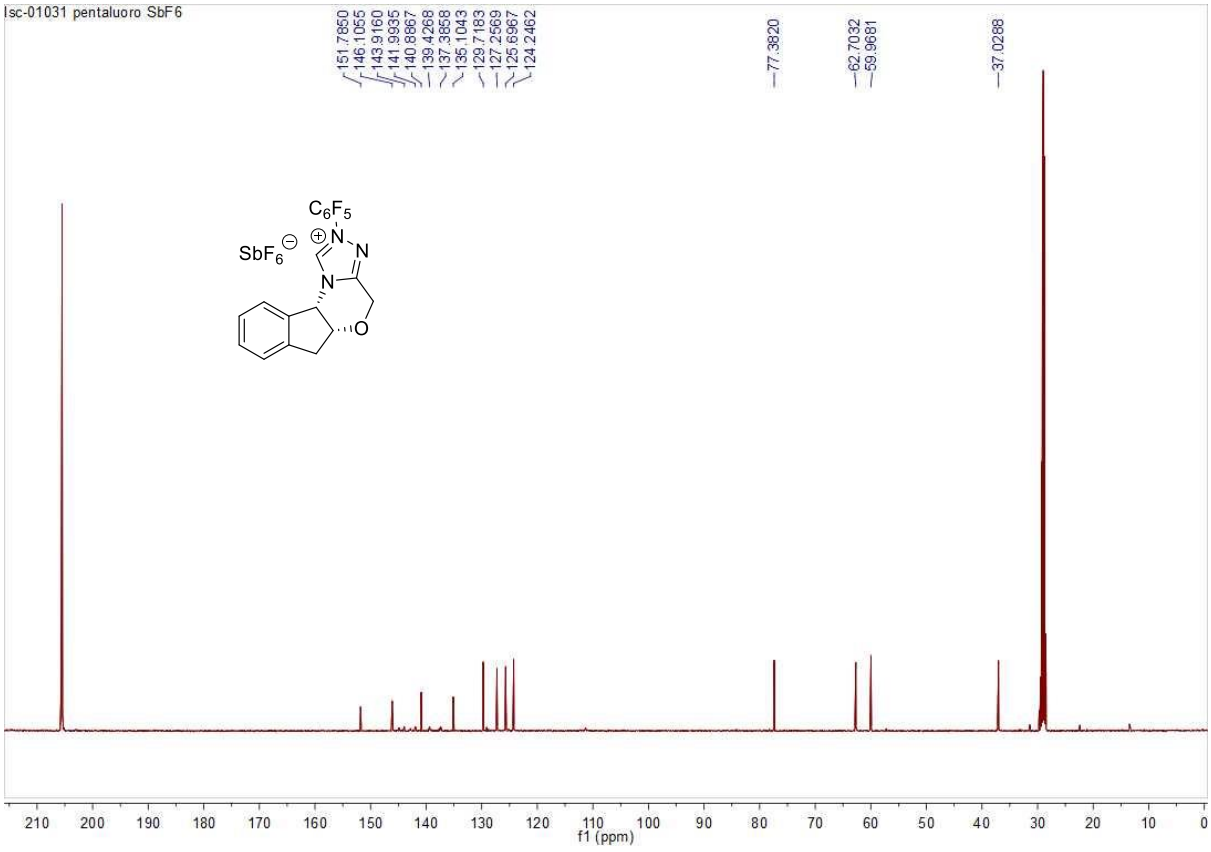
7.3662
7.3516
6.3803
6.3736
5.4575
5.4247
5.2956
5.2628
5.2180
5.2091
5.2000
3.5943
3.5844
3.5601
3.5502
3.3437
3.3094
C6F5
SbF6
N
N
O
1.00
1.08
2.11
1.16
1.00
1.03
1.08
1.07
1.02
1.01
f1 (ppm)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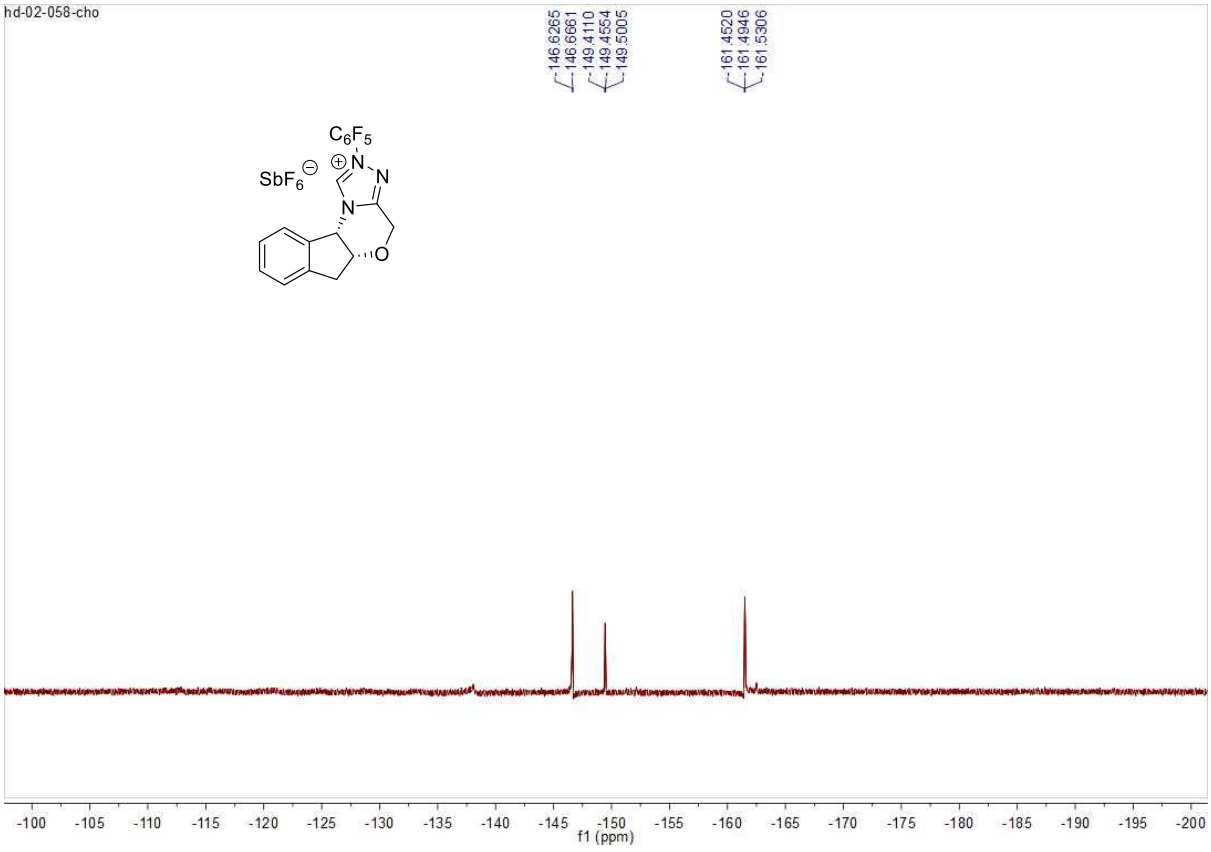
146.1055
143.9160
141.9935
140.8867
139.4268
137.3858
135.1043
129.7183
127.2569
125.6967
124.2462
77.3820
62.7032
59.9681
37.0288
C6F5
SbF6
N
N
O
f1 (ppm)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149.4110
149.4554
149.5005
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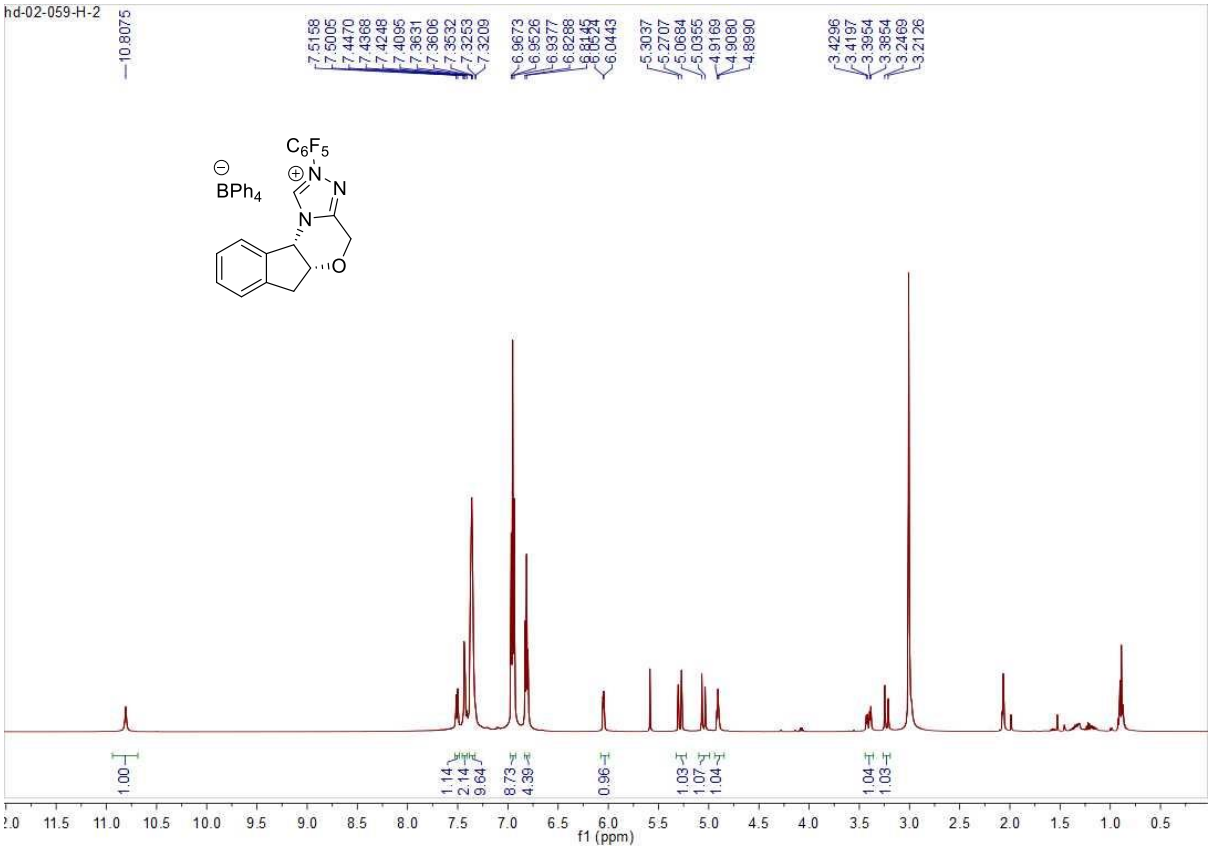
161.5306
C6F5
SbF6
N
N
N
O
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170
-175
-180
-185
-190
-195
-200
f1 (ppm)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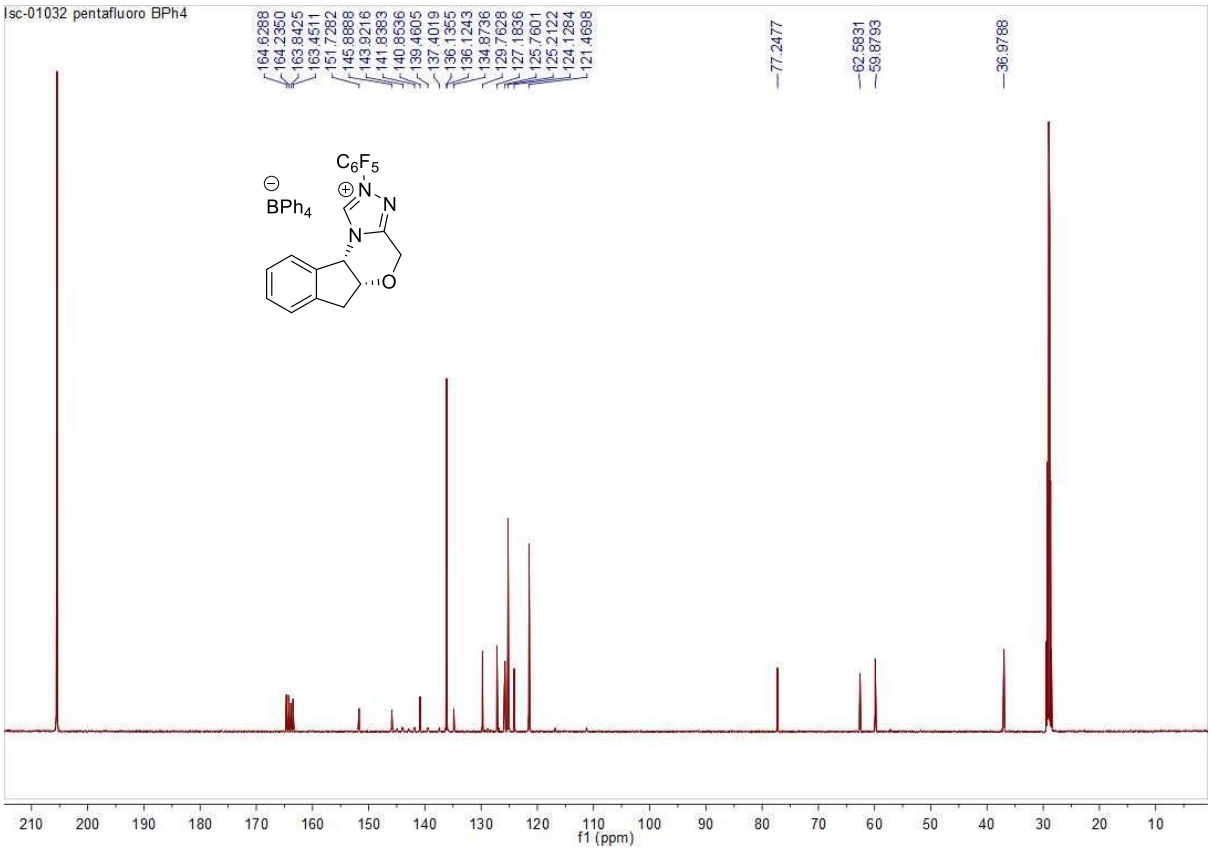
7.5005
7.4470
7.4368
7.4248
7.4095
7.3631
7.3606
7.3532
7.3253
7.3209
6.9673
6.9526
6.9377
6.8298
6.0443
5.3037
5.2707
5.0684
5.0355
4.9169
4.9080
4.8990
3.4296
3.4197
3.3954
3.3854
3.2469
3.2126
1.00
1.14
2.14
9.64
8.73
4.39
0.96
1.03
1.07
1.04
1.04
1.03
f1 (ppm)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164.2350
163.8425
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139.4605
137.4019
136.1355
136.1243
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129.7628
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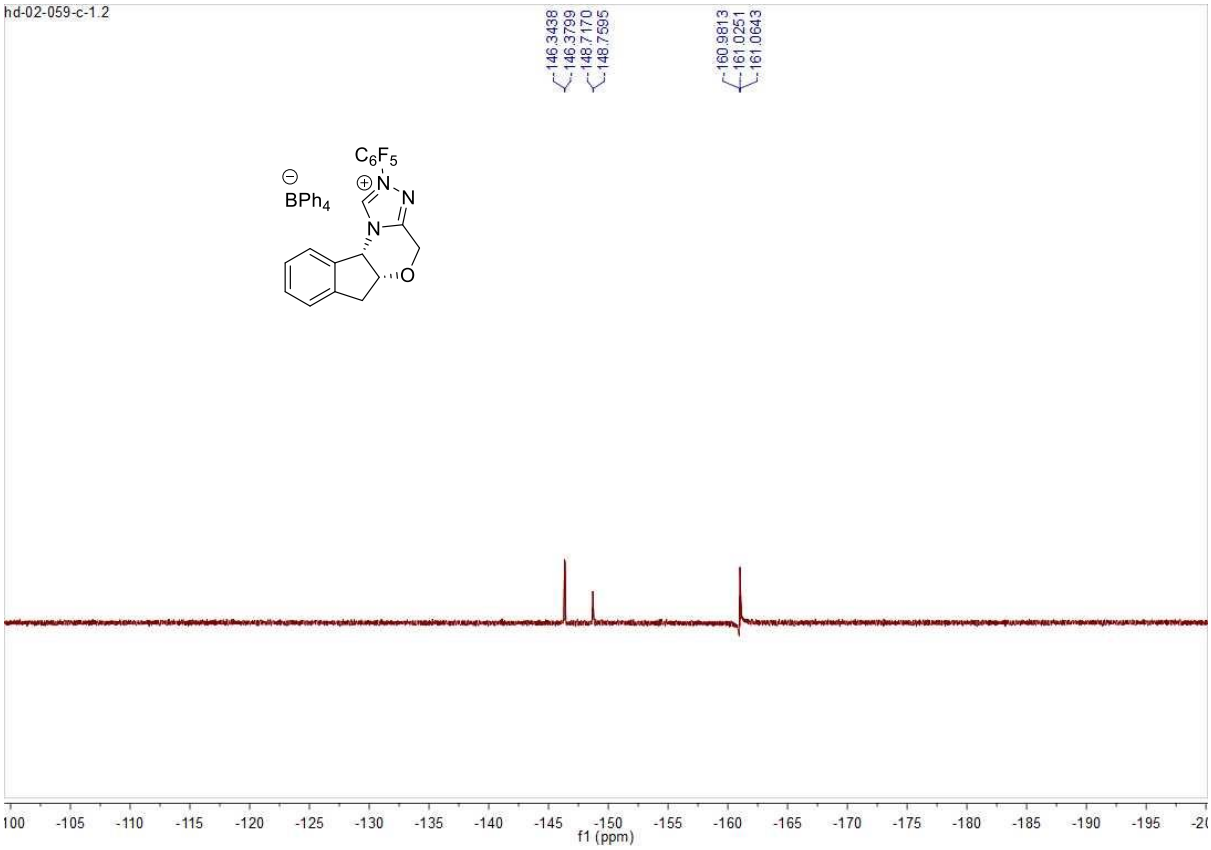
59.8793
36.9788
f1 (ppm)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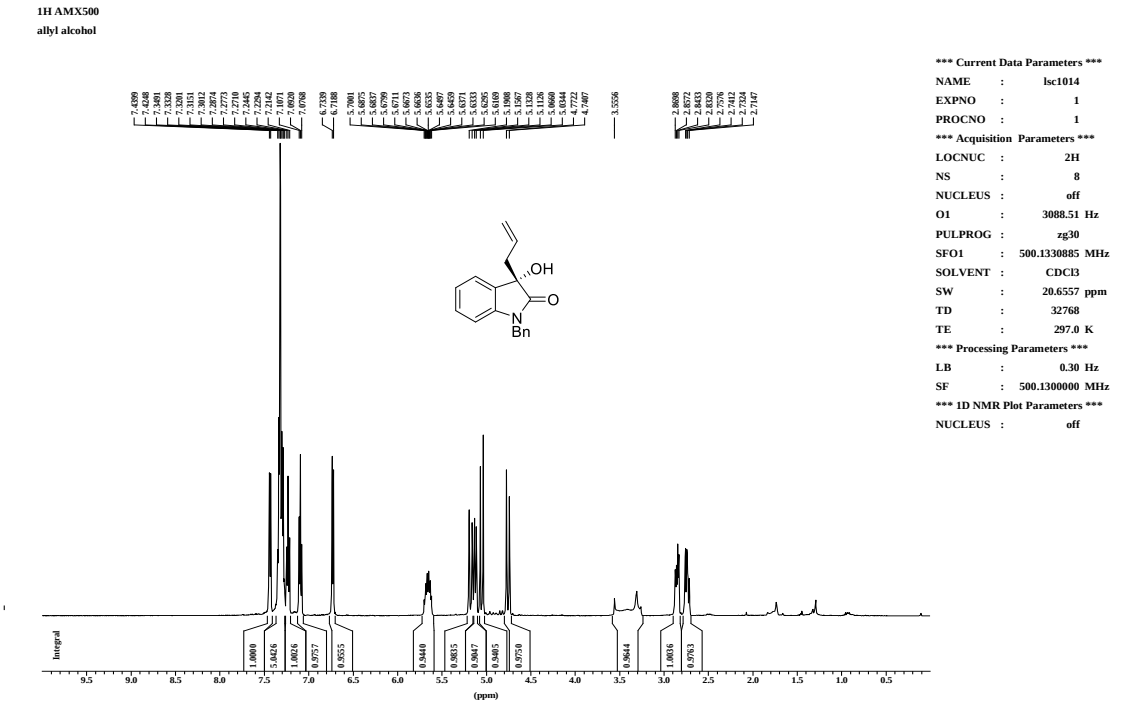
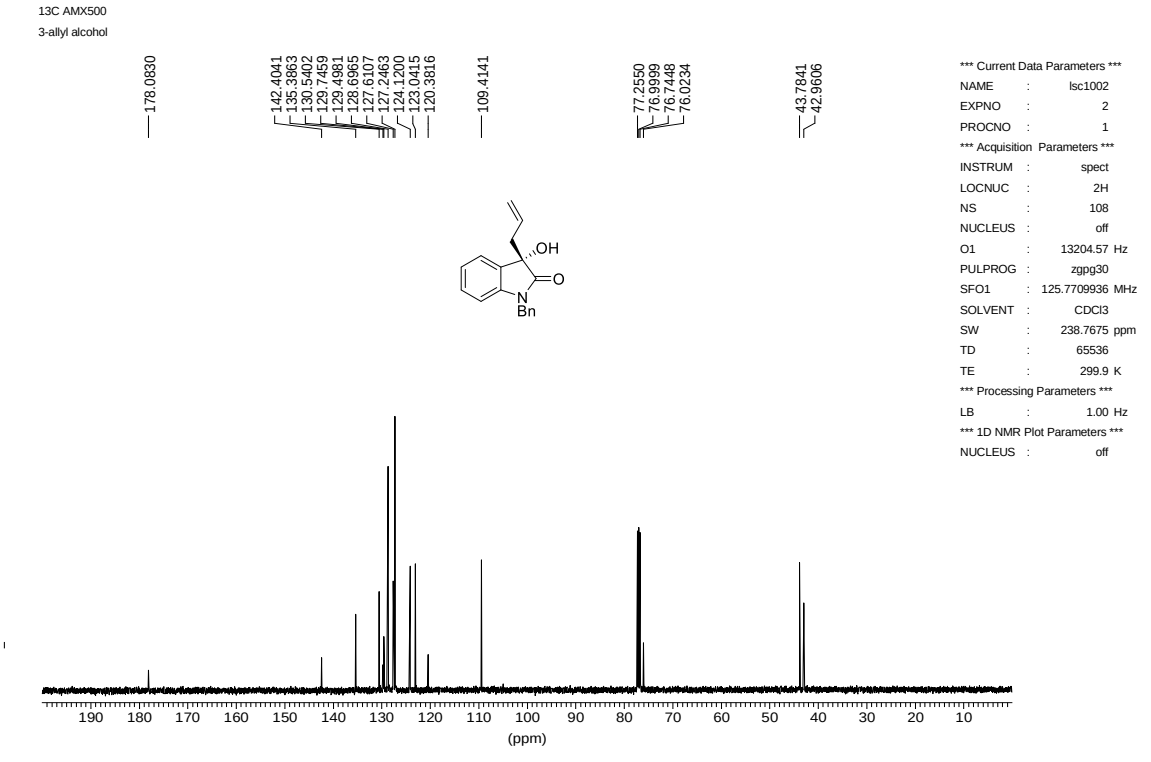
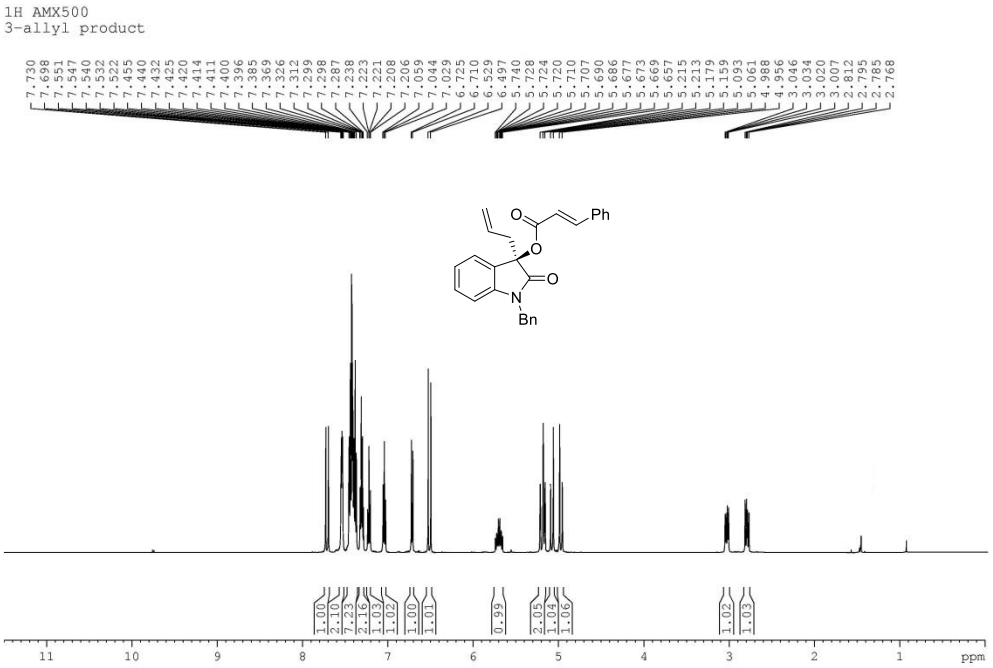
C_6F_5
BPh_4
N
N
N
O
100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195
f1 (ppm)

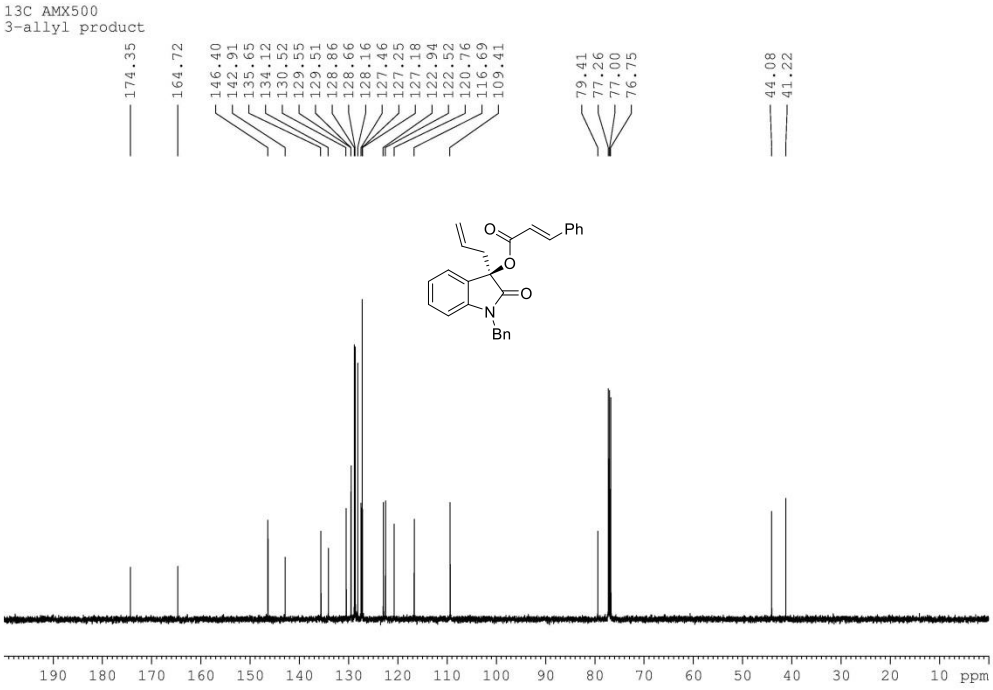
(*S*)-3-allyl-1-benzyl-3-hydroxyindolin-2-one (Scheme 3, **1a).**



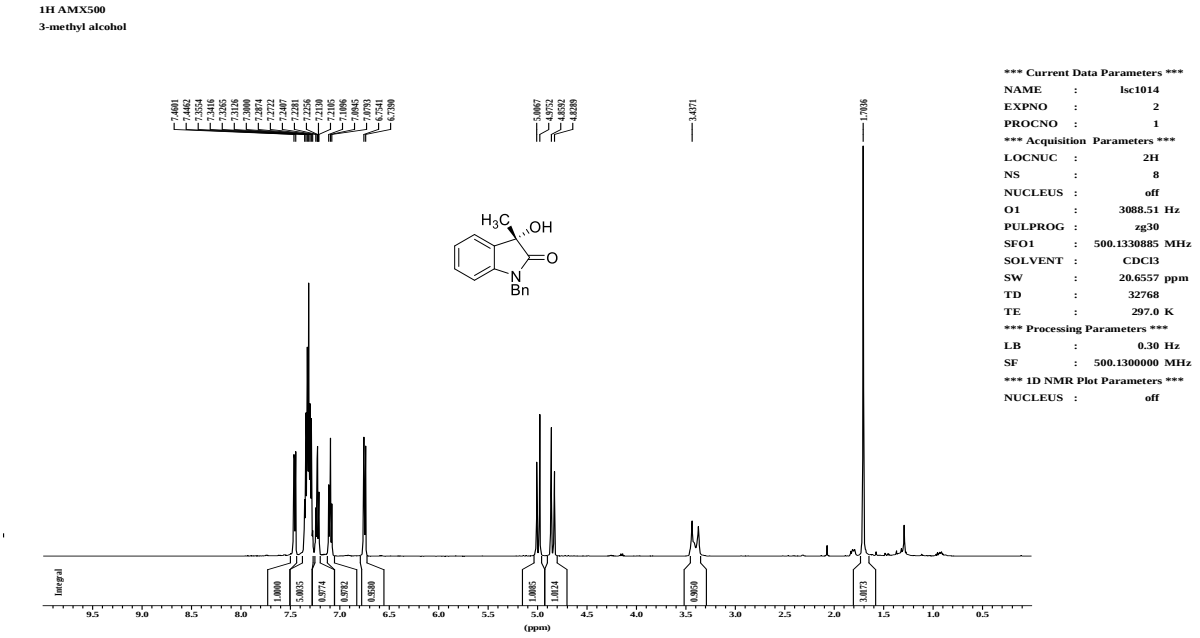


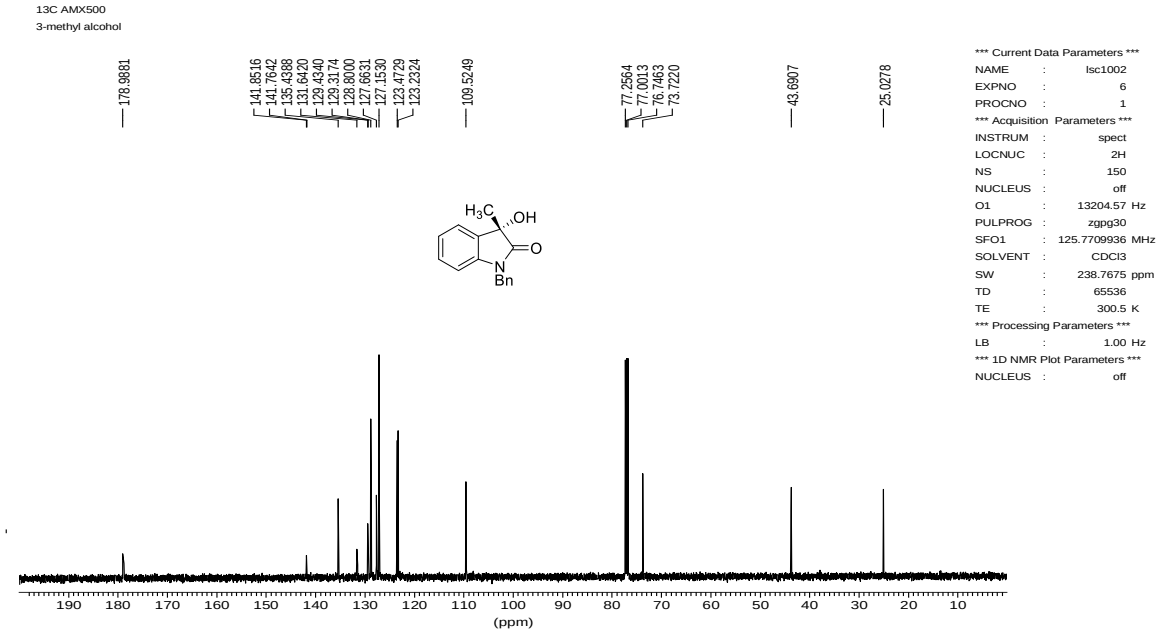
(*R*)-3-allyl-1-benzyl-2-oxoindolin-3-yl cinnamate (Scheme 3, **2a).**



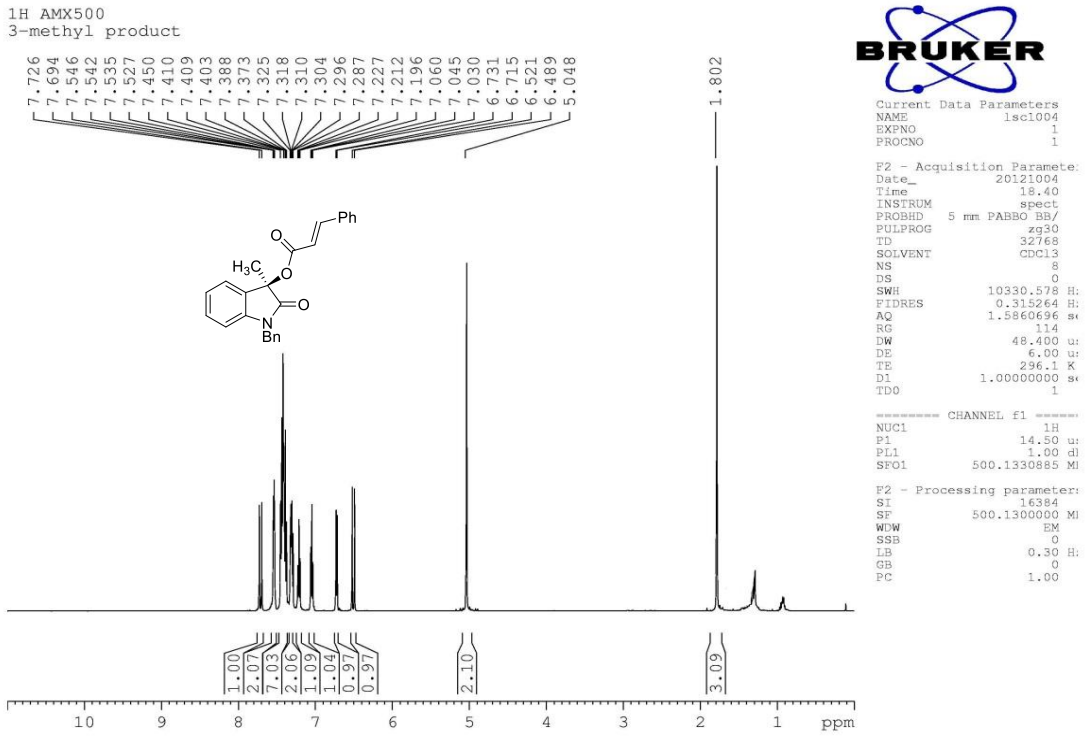


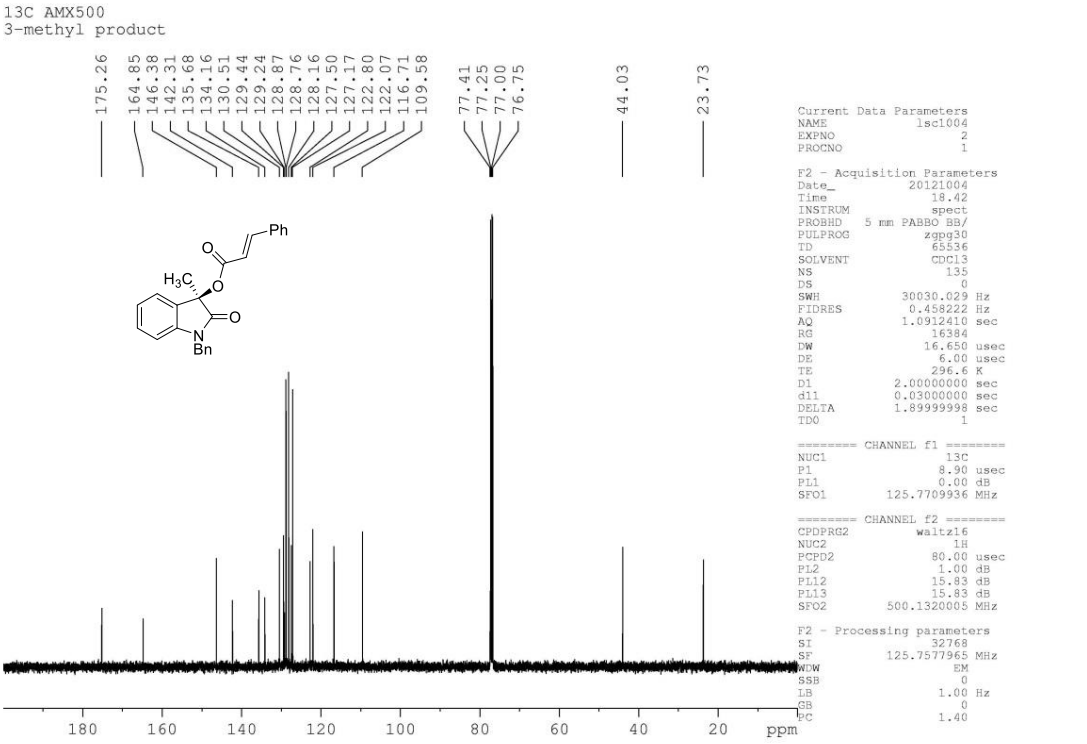
(*S*)-1-benzyl-3-hydroxy-3-methylindolin-2-one (Scheme 3, **1b).**



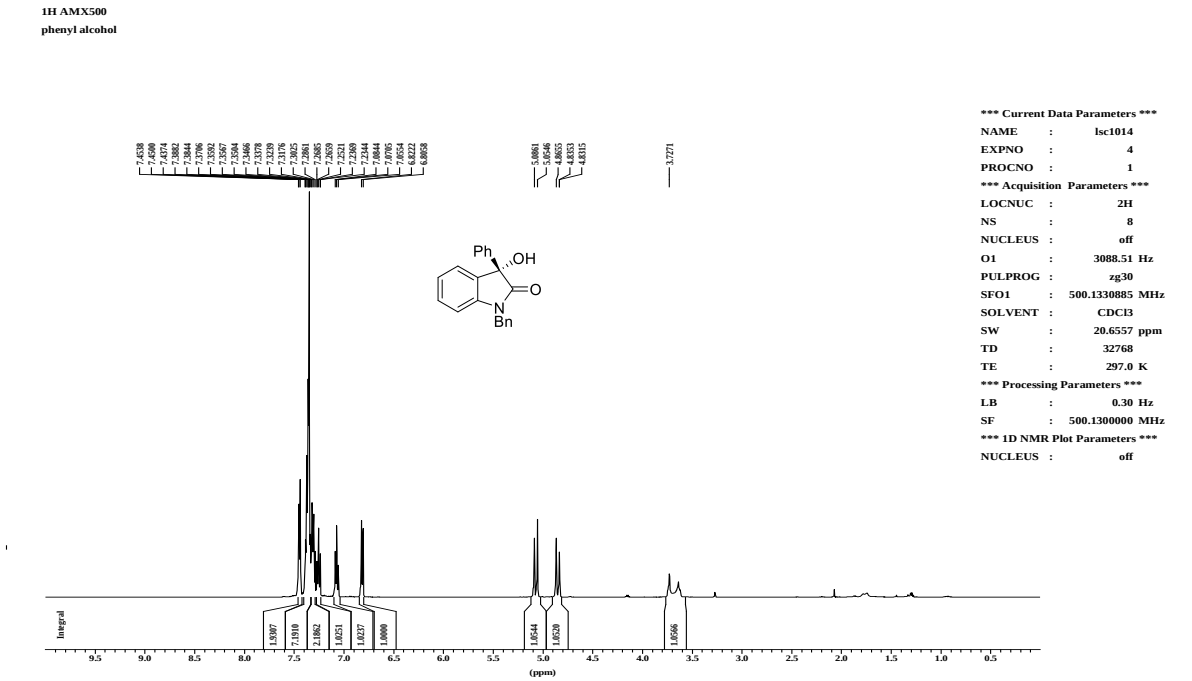


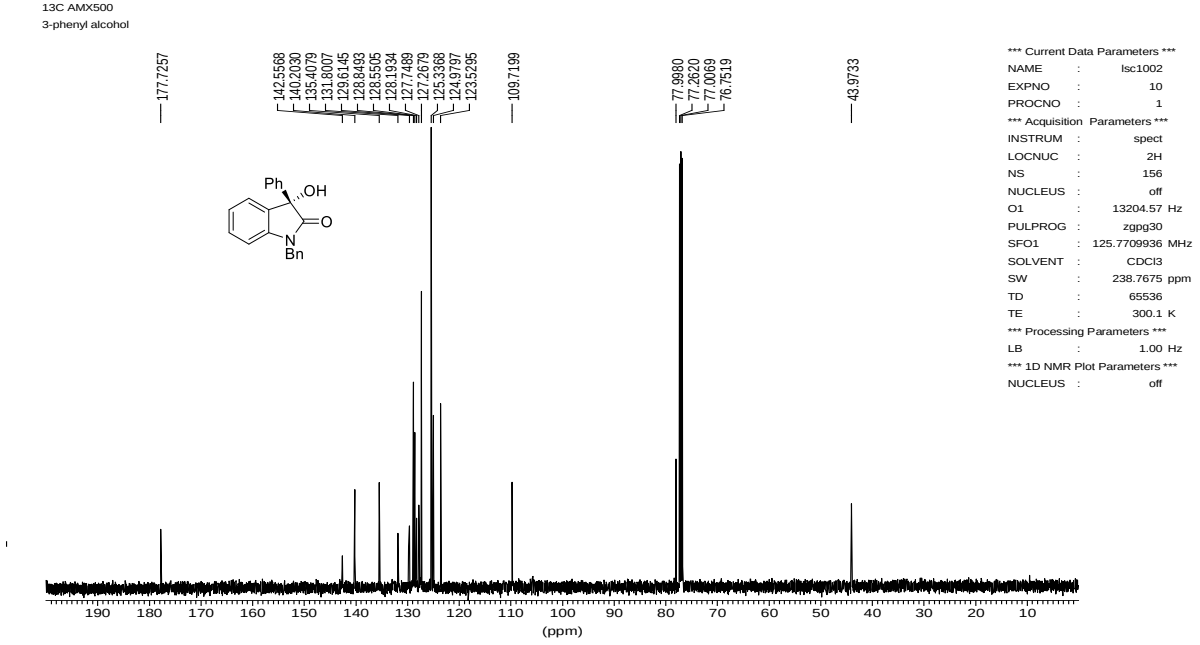
(*R*)-1-benzyl-3-methyl-2-oxoindolin-3-yl cinnamate (Scheme 3, **2b).**



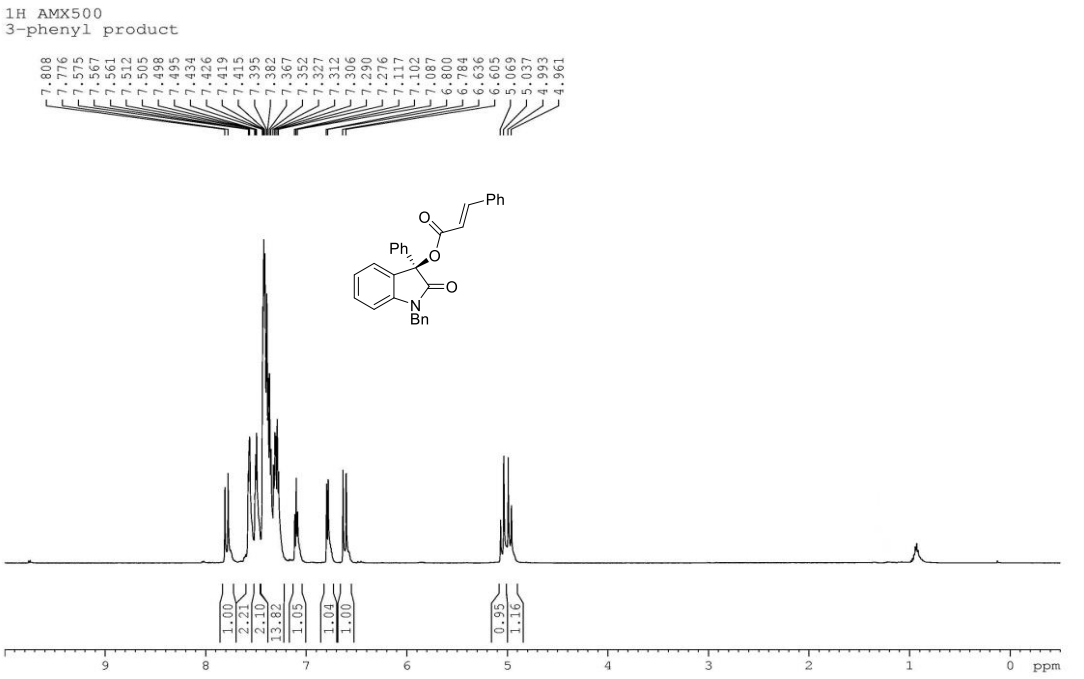


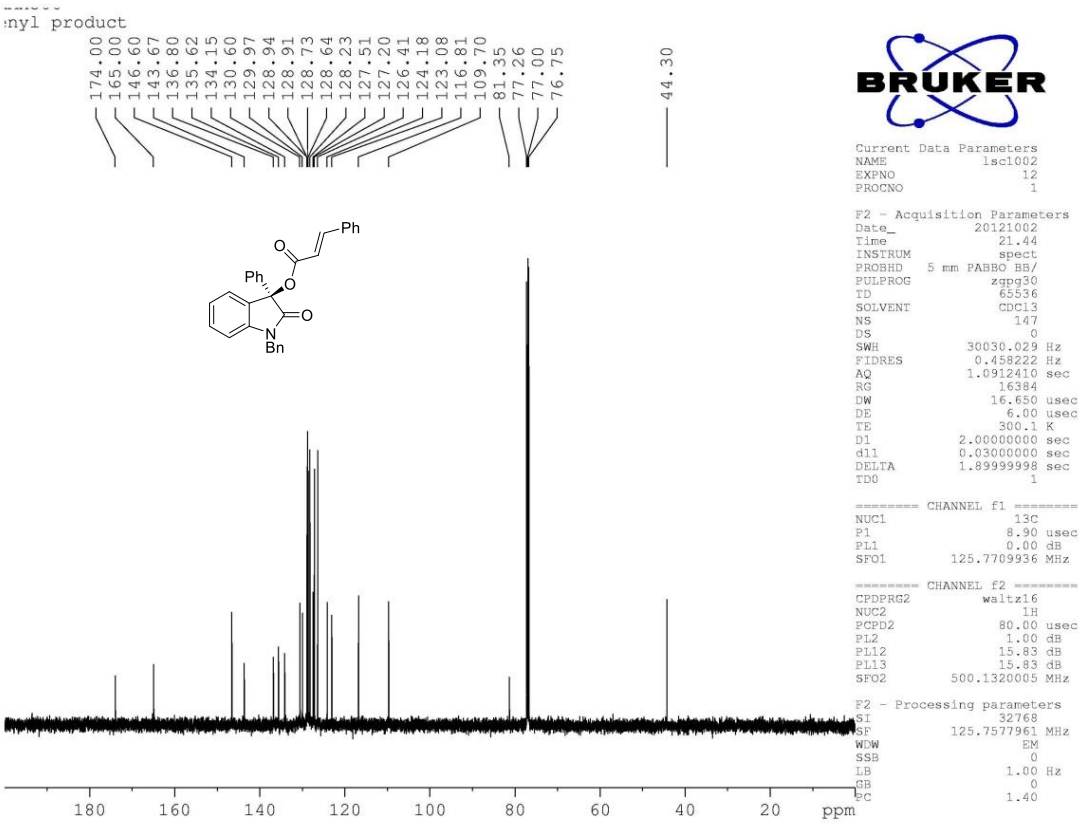
(*S*)-1-benzyl-3-hydroxy-3-phenylindolin-2-one (Scheme 3, **1c).**



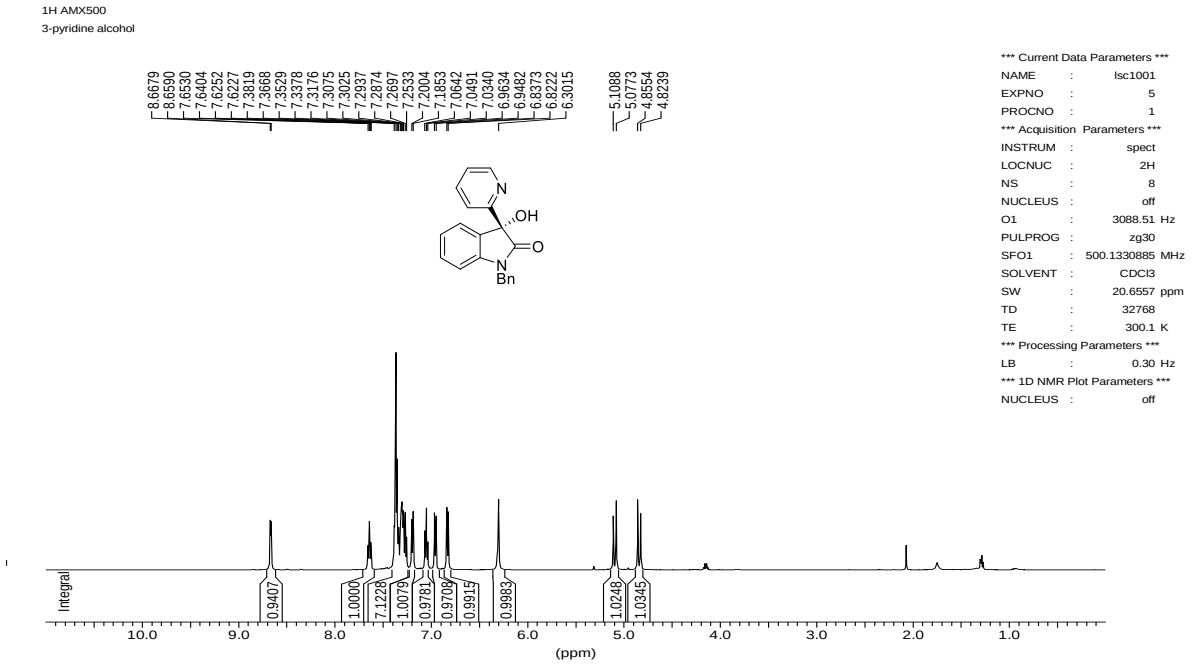


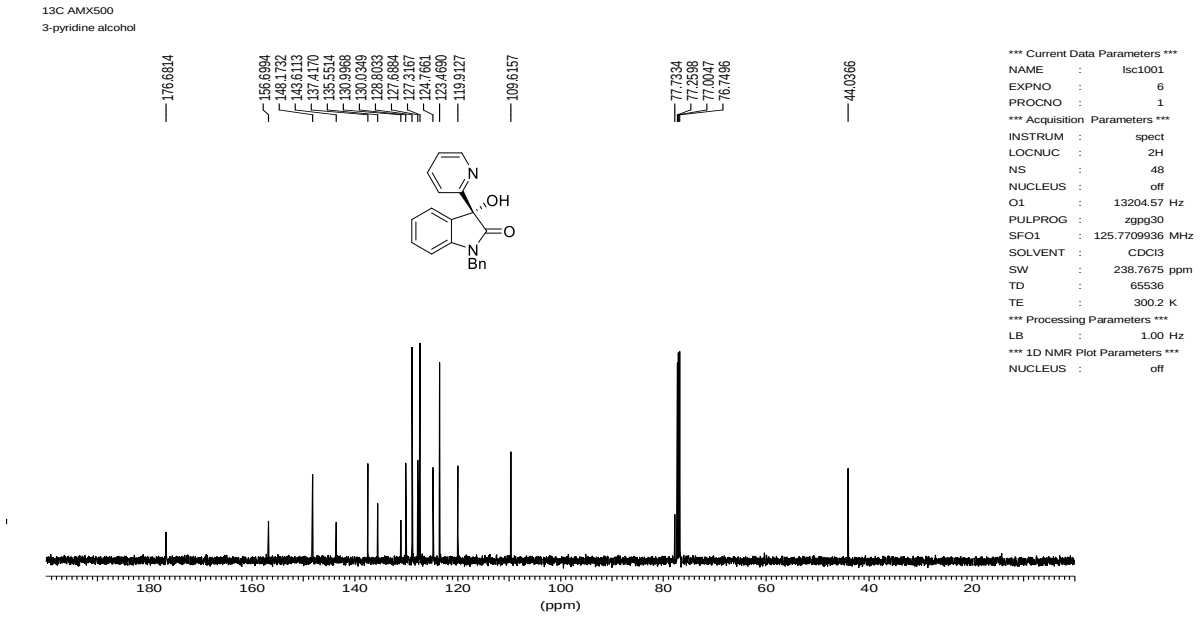
(*R*)-1-benzyl-2-oxo-3-phenylindolin-3-yl cinnamate (Scheme 3, **2c).**



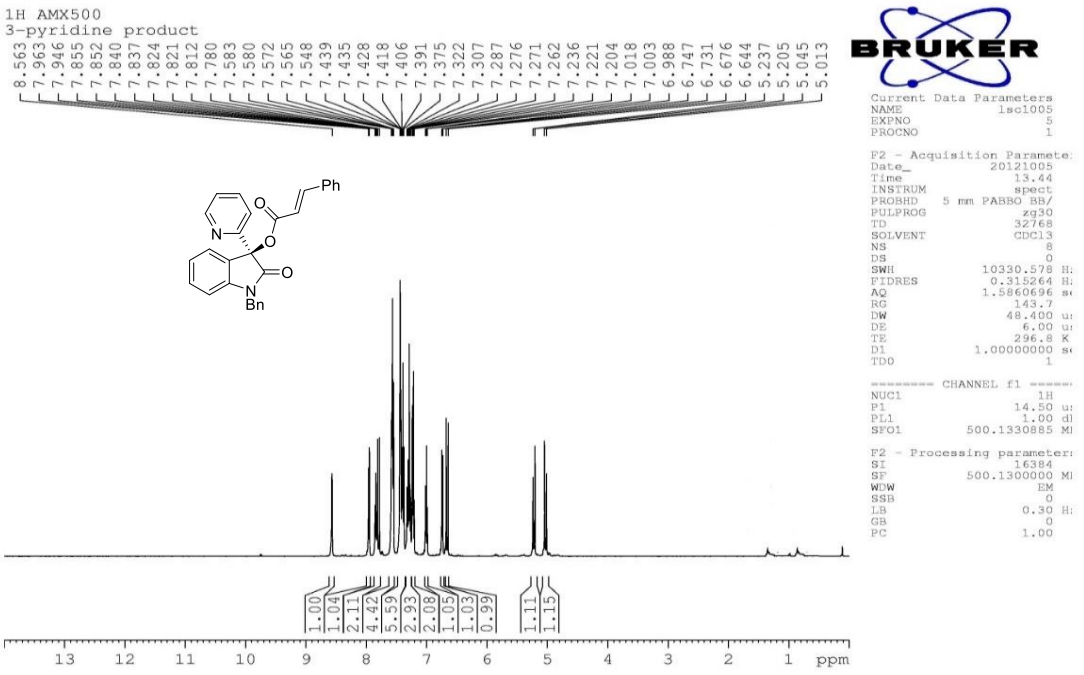


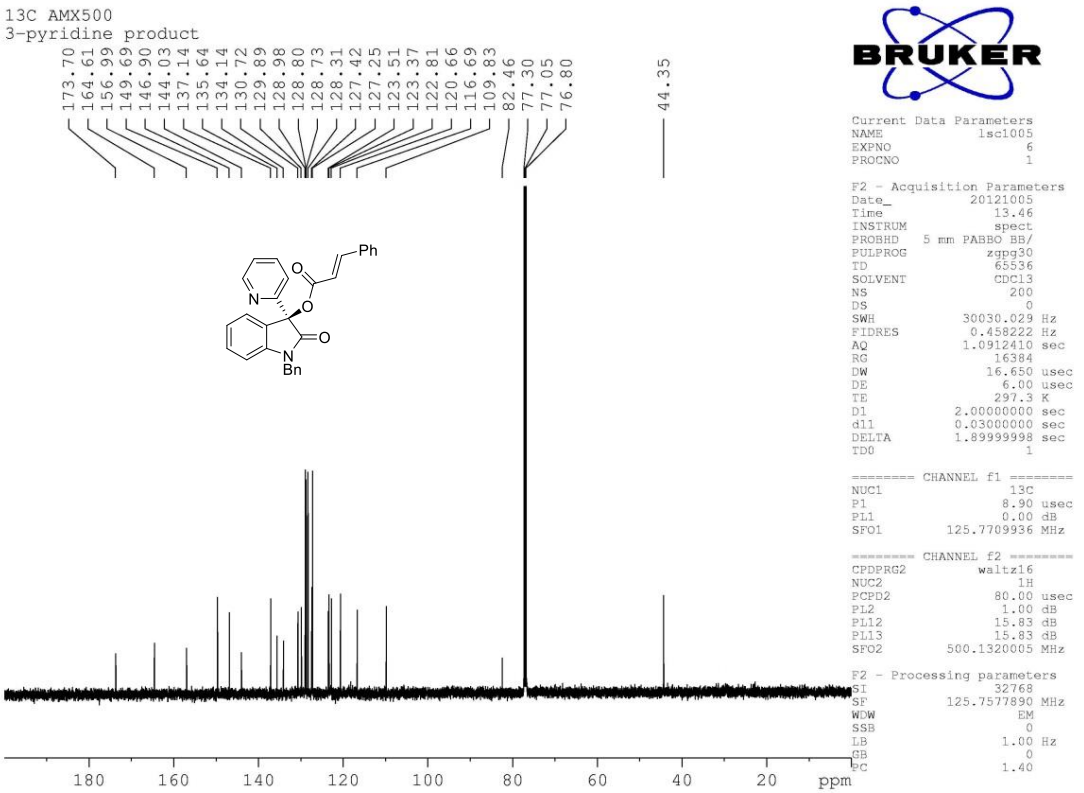
(*R*)-1-benzyl-3-hydroxy-3-(pyridin-2-yl)indolin-2-one (Scheme 3, **1d).**



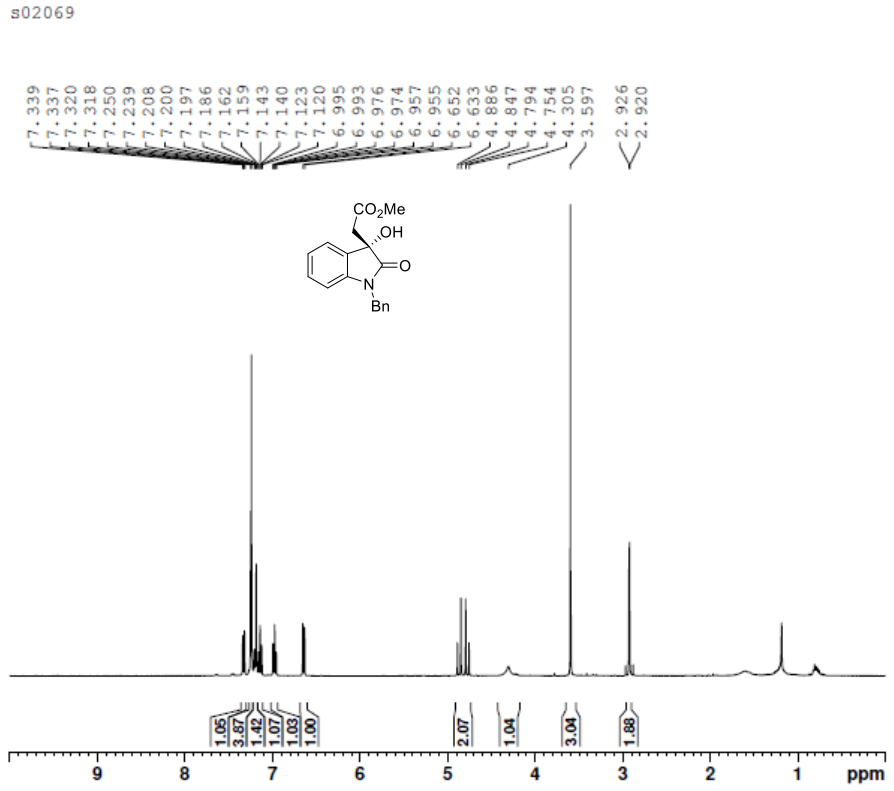


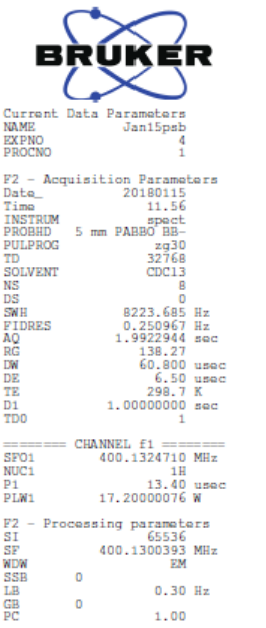
(*S*)-1-benzyl-2-oxo-3-(pyridin-2-yl)indolin-3-yl cinnamate (Scheme 3, **2d)**

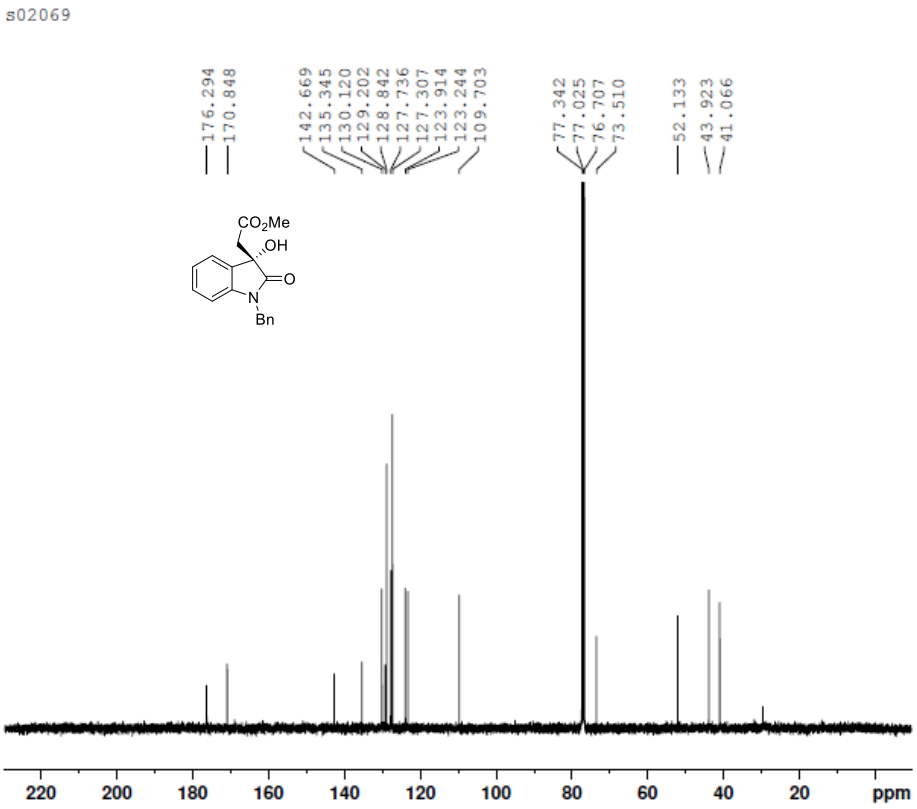


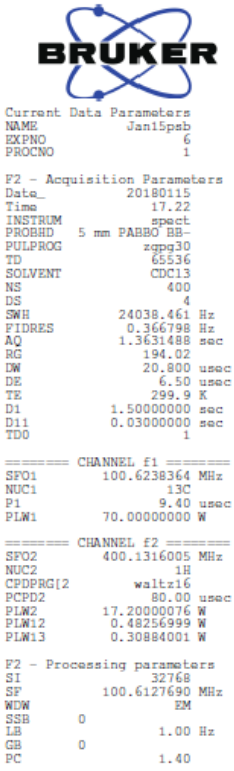


methyl (S)-2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetate, (Scheme 4, **1e**)

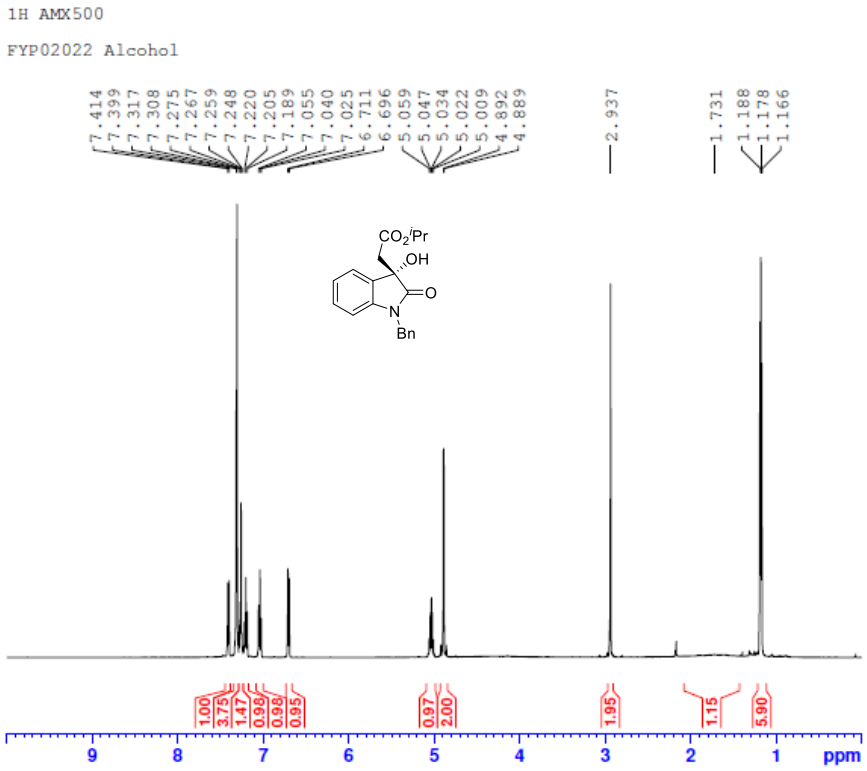


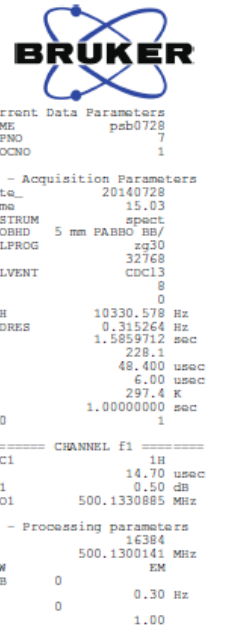


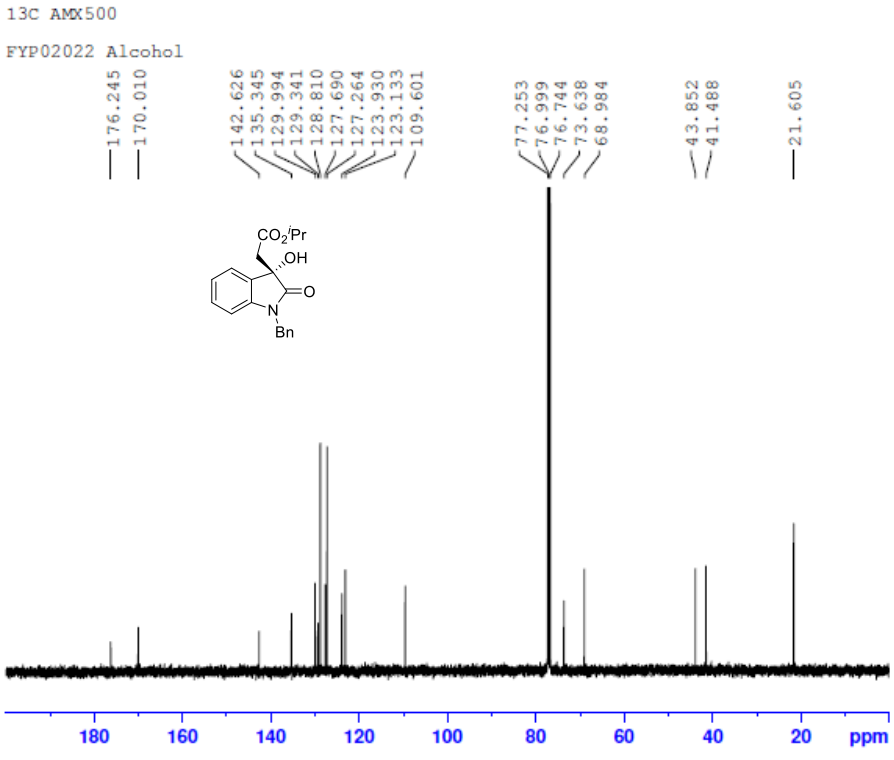


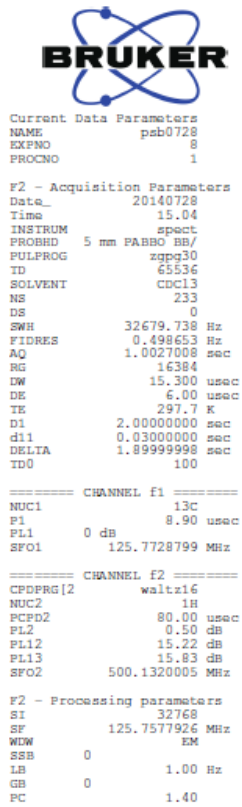


Isopropyl 2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetate, (Scheme 5, **1f**)

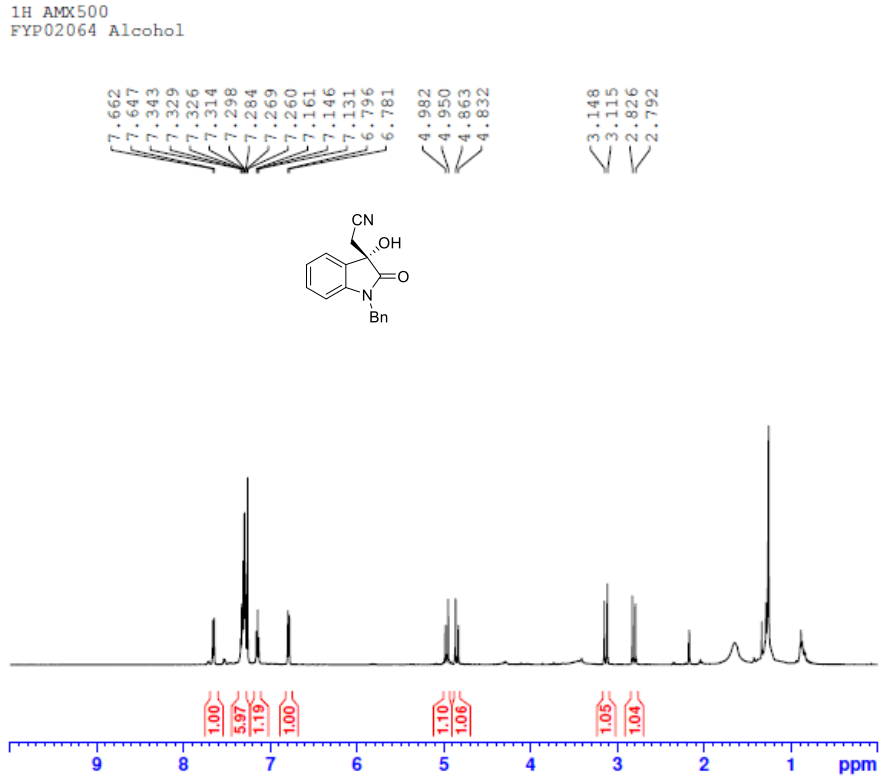


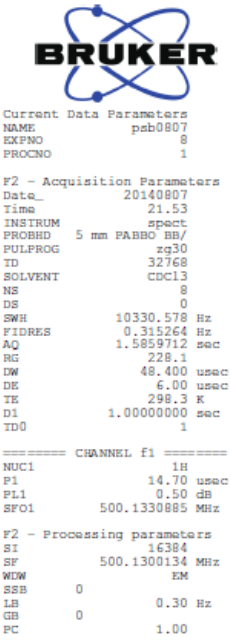


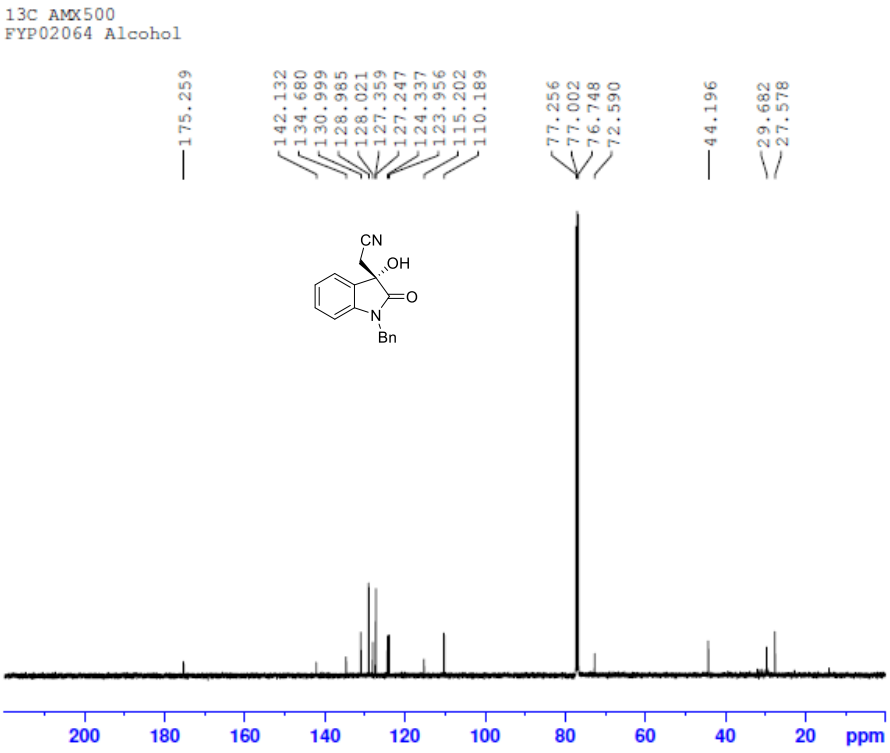


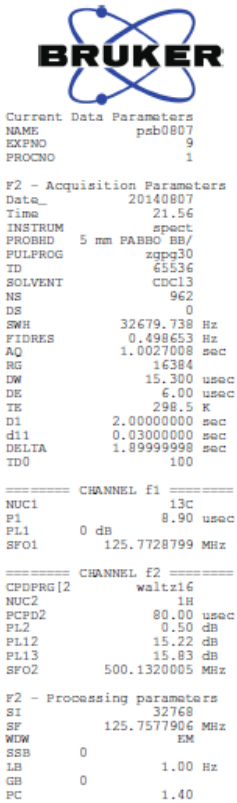


2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetonitrile, (Scheme 5, **1g)**

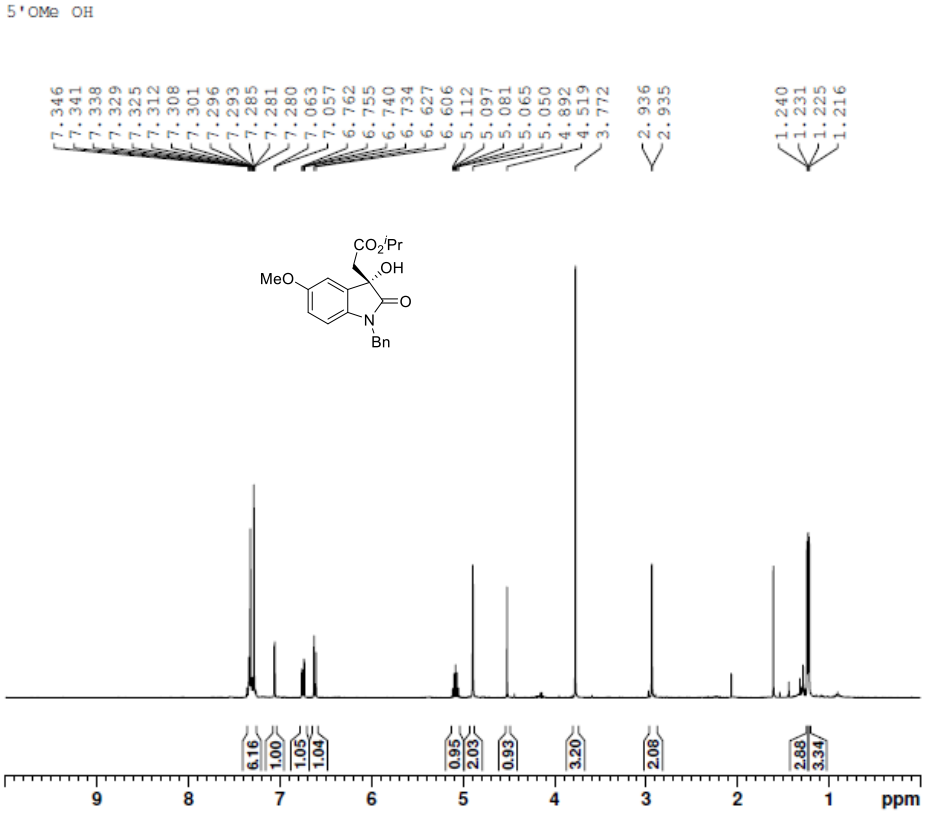








Isopropyl 2-(1-benzyl-3-hydroxy-5-methoxy-2-oxoindolin-3-yl)acetate, (Scheme 5, **1h)**

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PROCNO                  1

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DS                      2
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FIDRES            0.489064 Hz
AQ                2.0447233 sec
RG                  205.55
DW                  62.400 usec
DE                   6.50 usec
TE                  299.7 K
D1                1.00000000 sec
TD0                     1
SFO1            400.2324714 MHz
NUC1                    1H
P1                   14.00 usec
PLW1            13.02400017 W

F2 - Processing parameters
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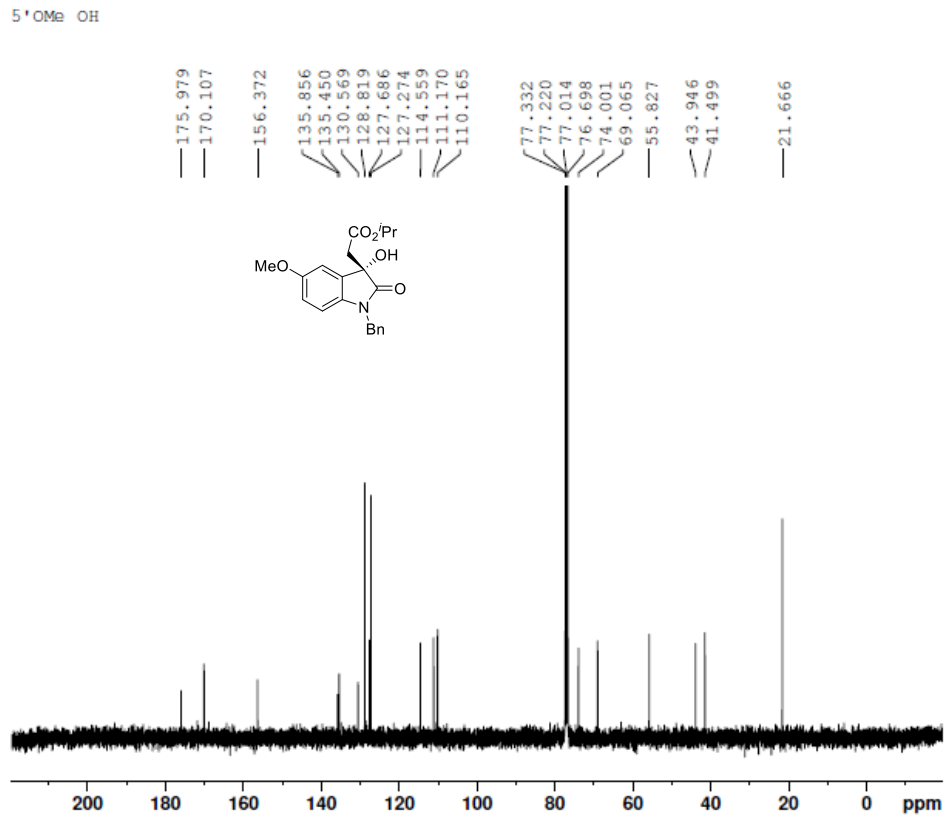


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DW                  20.800 usec
DE                   6.50 usec
TE                  300.9 K
D1                2.00000000 sec
D11               0.03000000 sec
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SFO1            100.6479773 MHz
NUC1                    13C
P1                   15.00 usec
PLW1            26.83600044 W
SFO2            400.2316009 MHz
NUC2                    1H
CPDPRG[2            waltz16
PCPD2                90.00 usec
PLW2            13.02400017 W
PLW12            0.31628889 W
PLW13            0.15852401 W

F2 - Processing parameters
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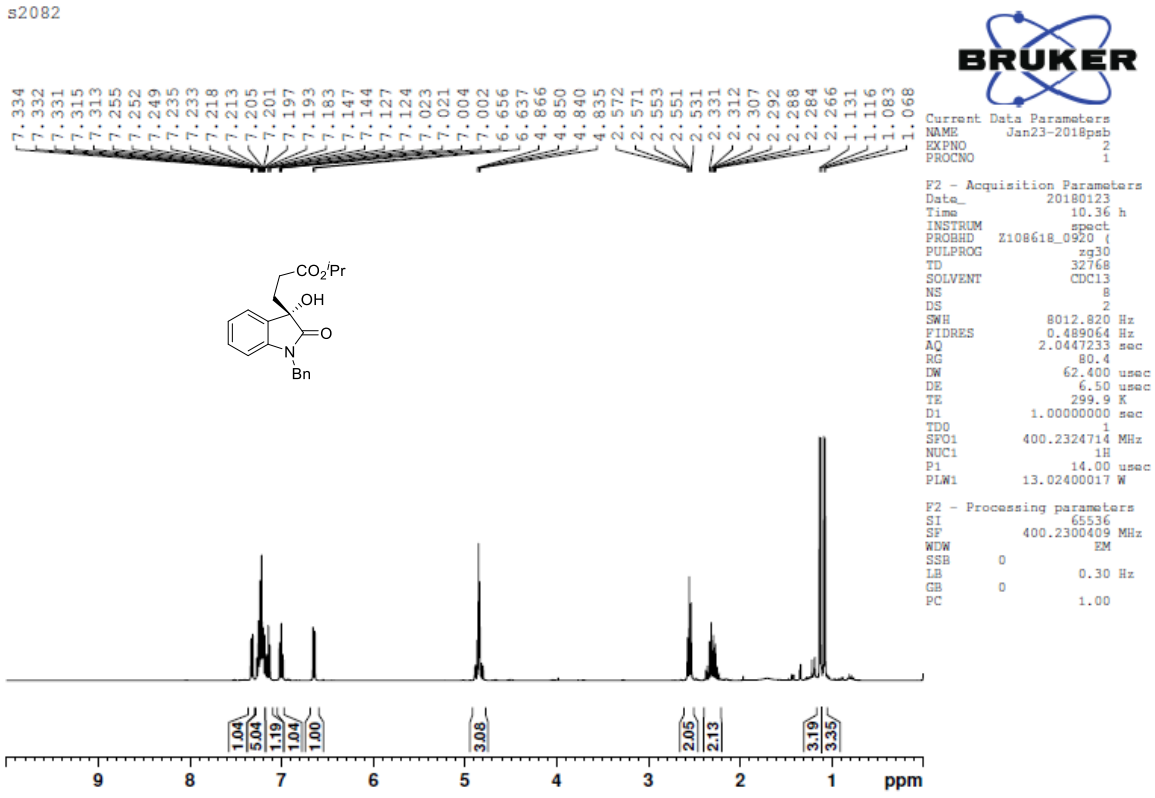
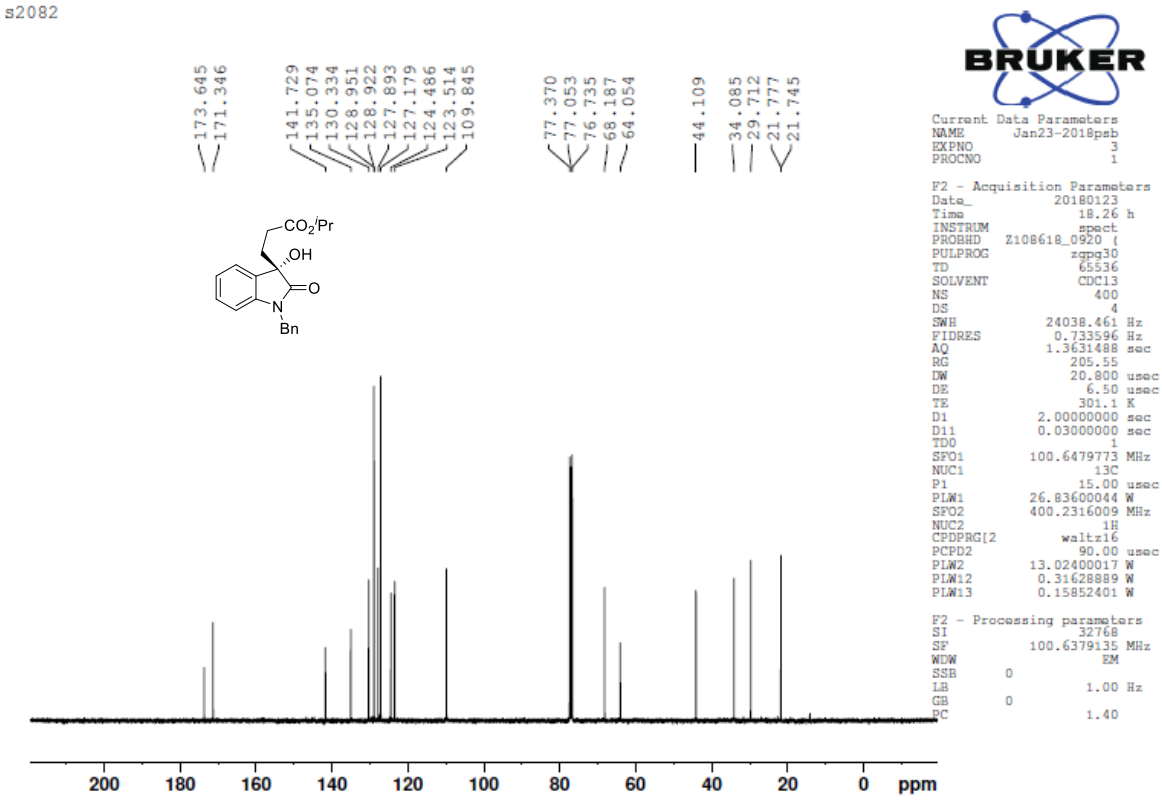
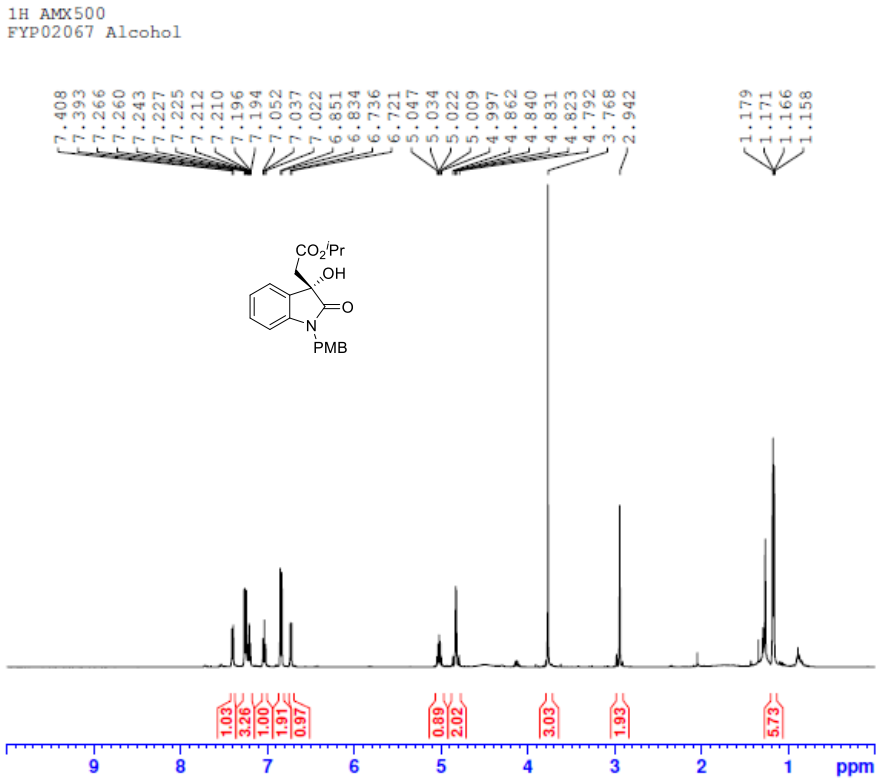
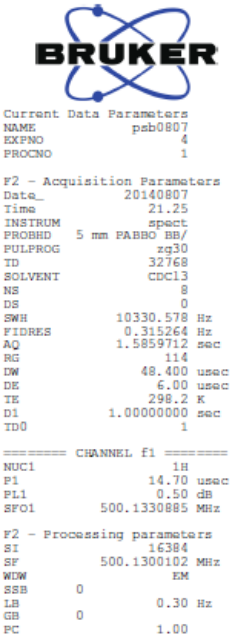
Isopropyl 3-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)propanoate, (Scheme 5, **1i)**

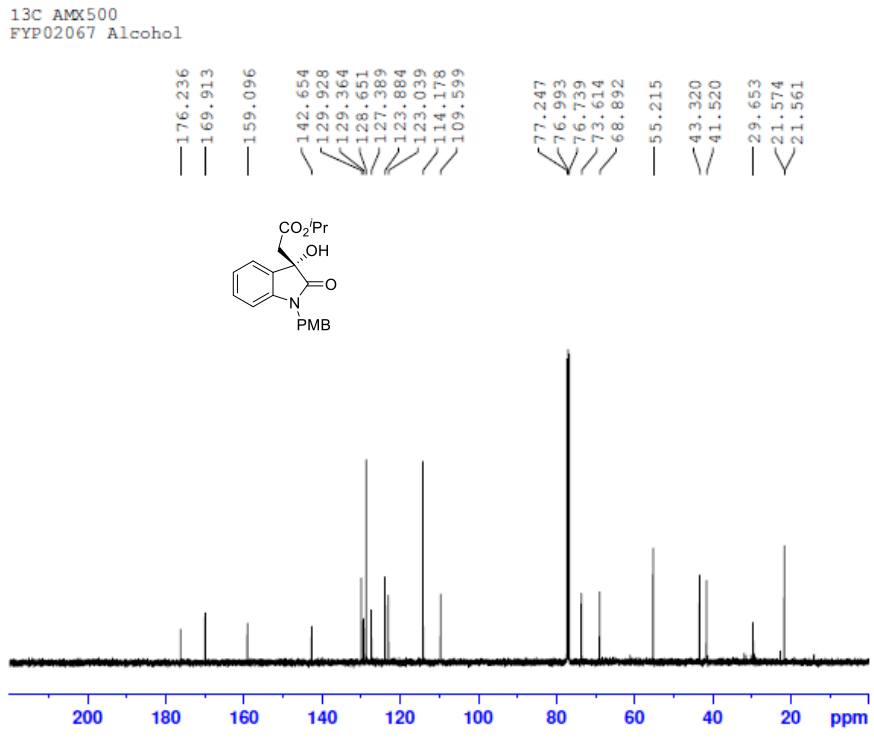


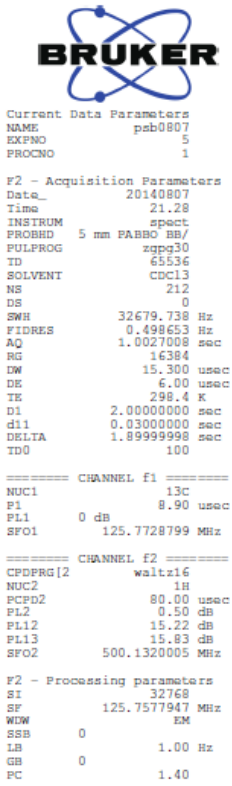


Isopropyl 2-(3-hydroxy-1-(4-methoxybenzyl)-2-oxoindolin-3-yl)acetate, (Scheme 5, **1j)**

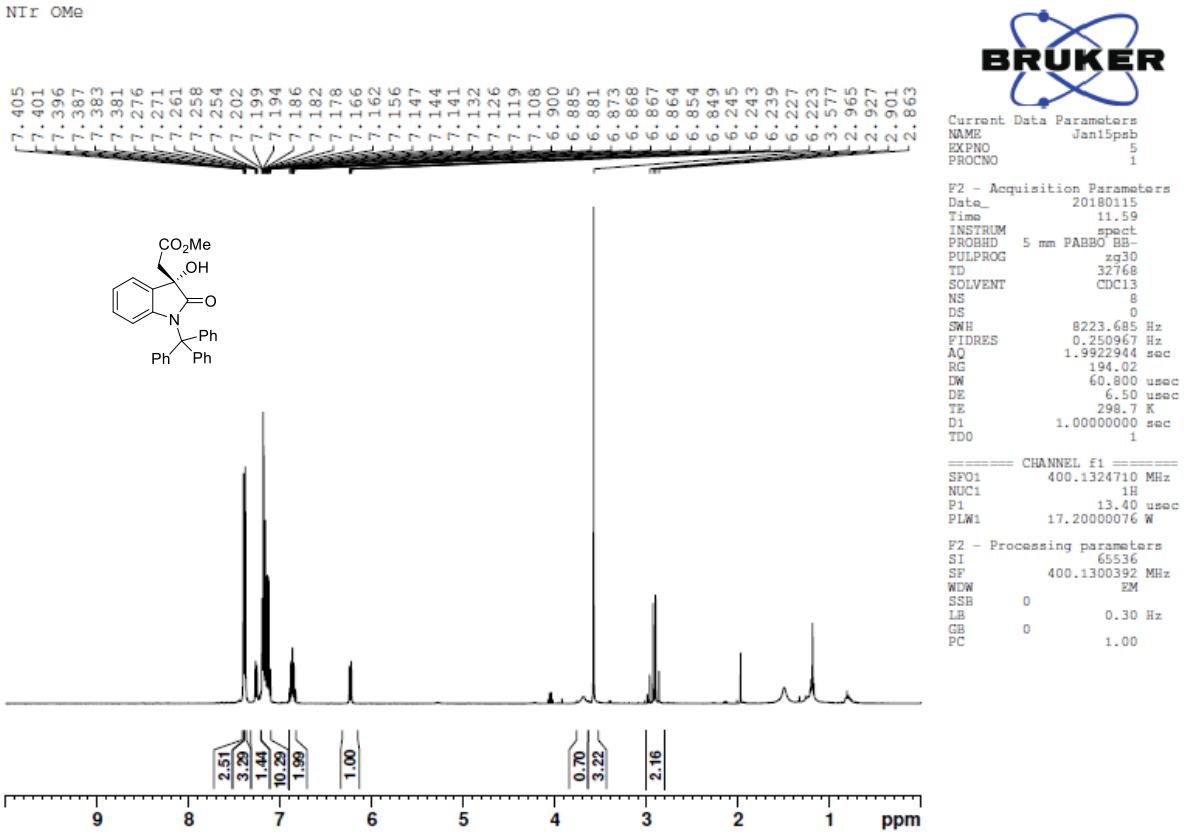


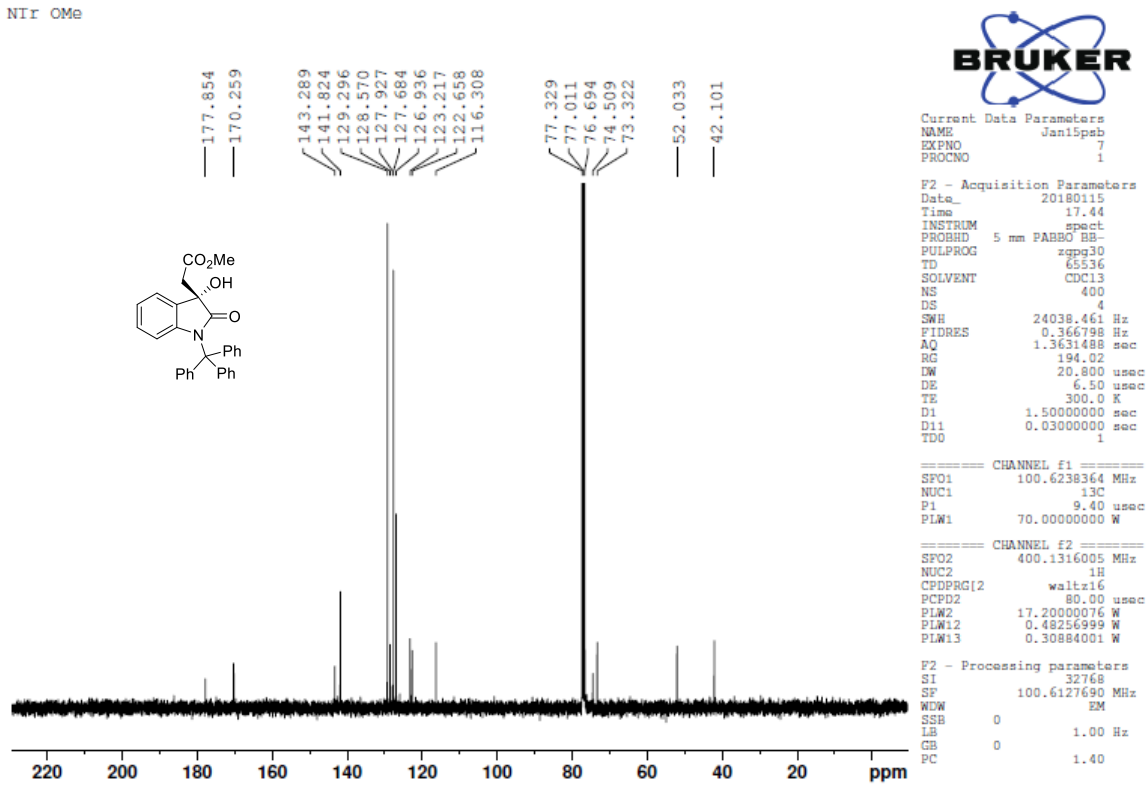




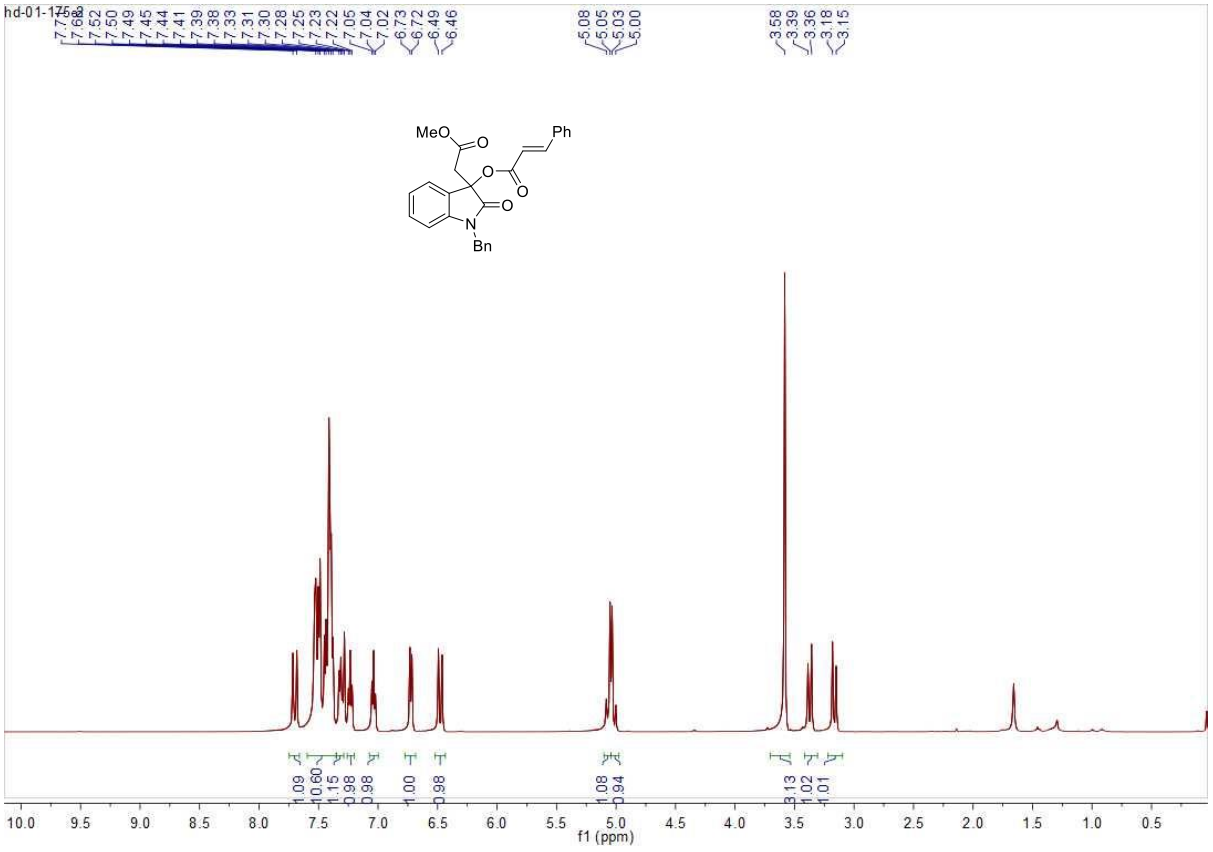


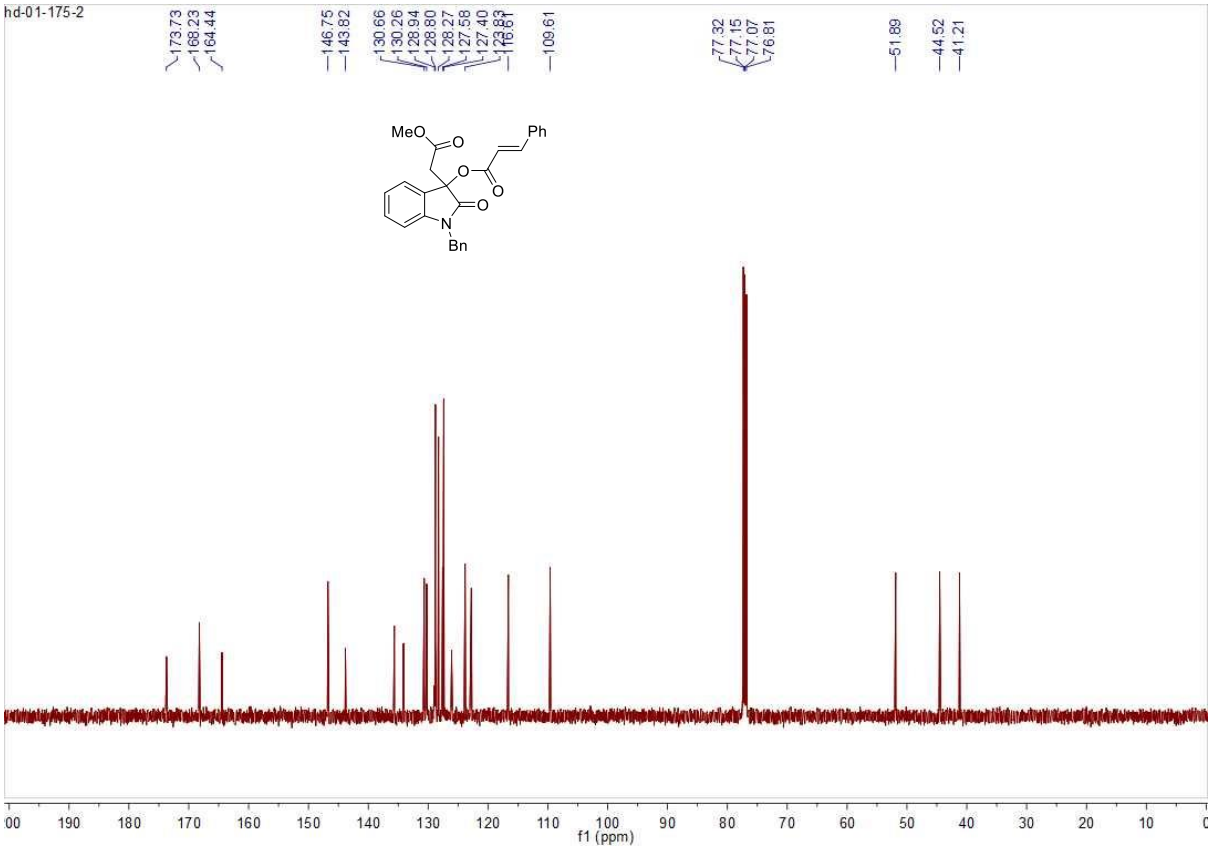
Isopropyl 2-(3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetate, (Scheme 5, **1k)**



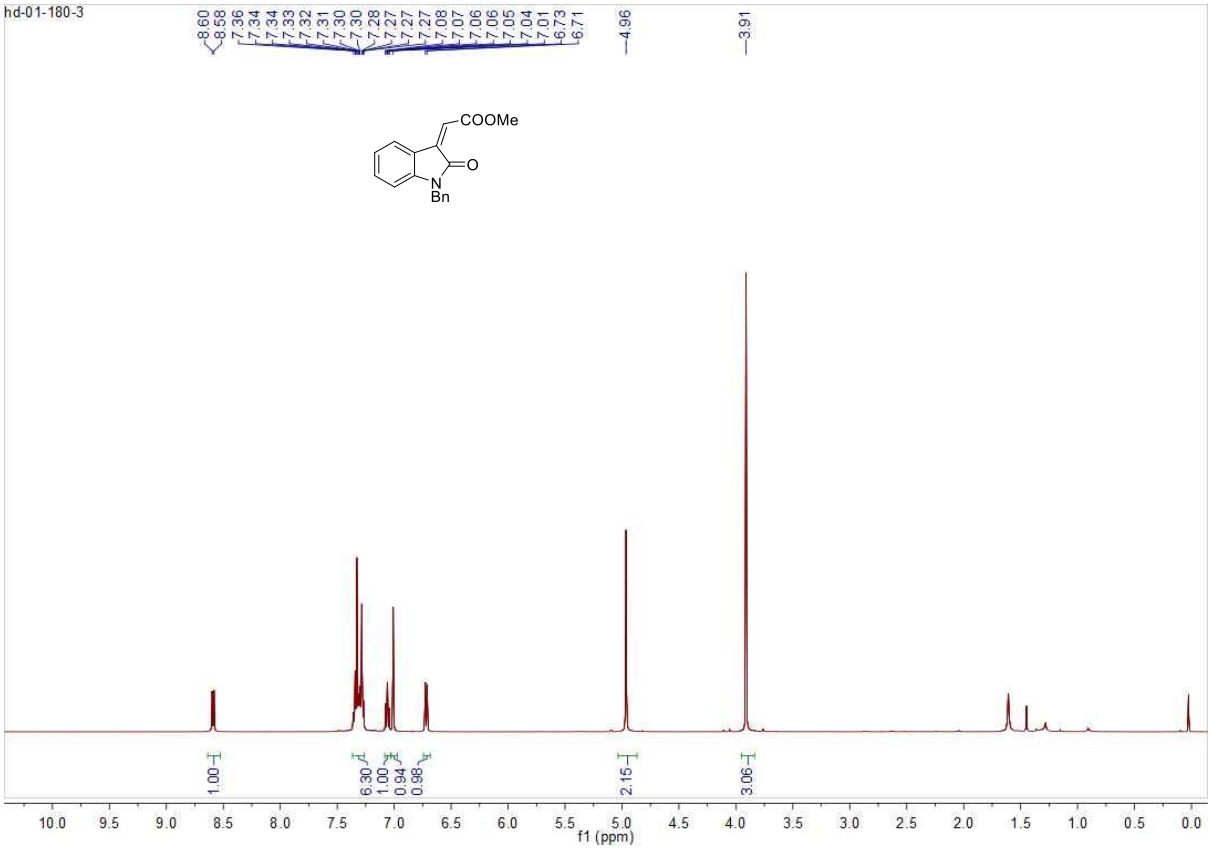


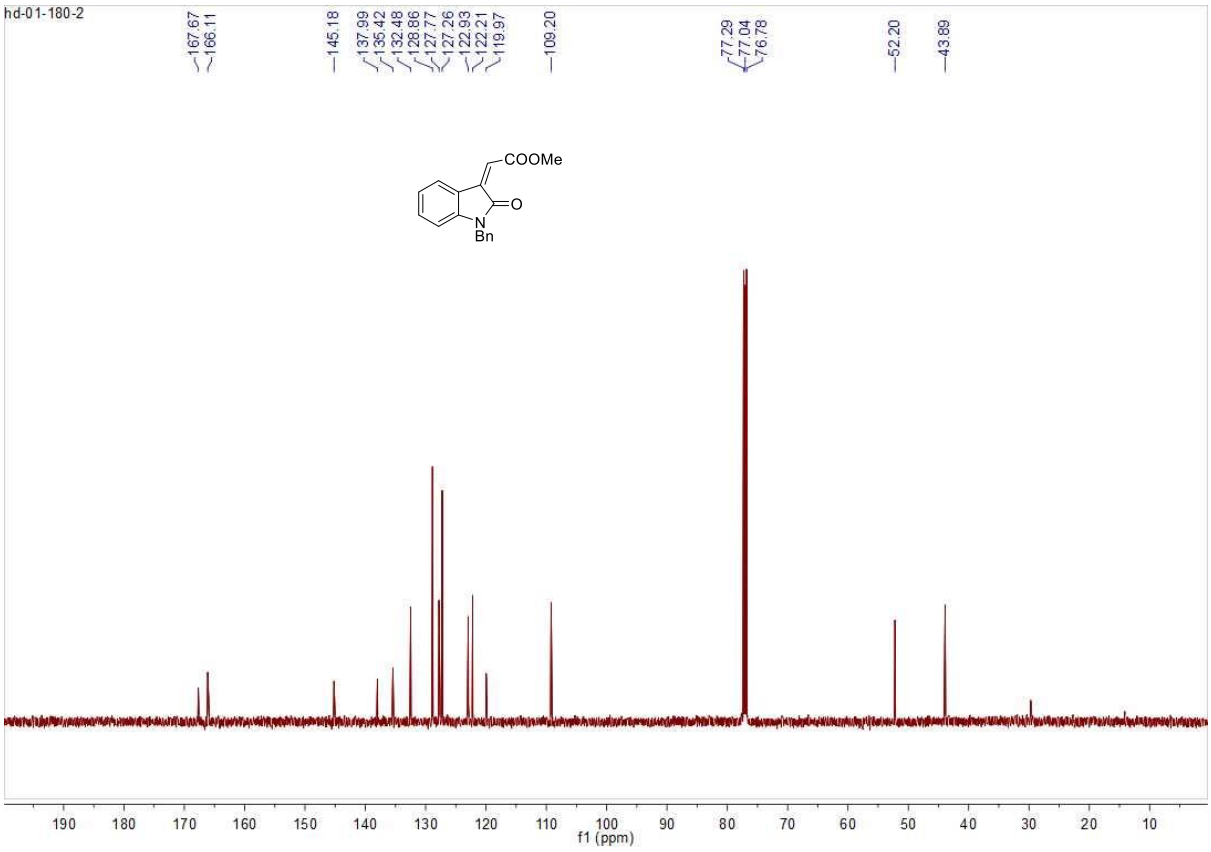
1-benzyl-3-(2-methoxy-2-oxoethyl)-2-oxoindolin-3-yl cinnamate, (Scheme 4b, **2e)**





(Z)-methyl 2-(1-benzyl-2-oxoindolin-3-ylidene)acetate, (Scheme 4a**, 4a)**





(*R*)-5-acetyl-6-methyl-4-phenyl-3,4-dihydro-2*H*-pyran-2-one, (Scheme 6b, **7)**