# *Supplementary Information*

## Stereodivergent Propargylic Alkylation of Enals via Cooperative NHC and Copper Catalysis

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# 1. Supplementary Notes

**General data:**

NMR spectra were recorded on Bruker-400 MHz spectrometer or Bruker-500 MHz spectrometer. Chemical shifts (δ) are given in ppm relative to TMS. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm).

Enantiomeric excesses were measured on Waters-Alliance (2998. Photodiode Array Detector, UV detection monitored at220 nm, 230 nm, 254 nm or 270 nm). Chiralpak IA, IC, IE and IG columns were purchased from Daicel Chemical Industries, LTD.

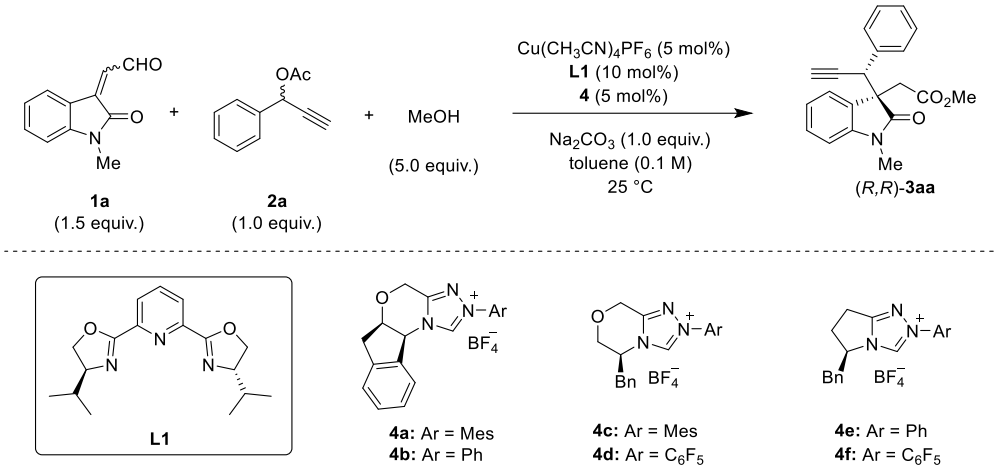
Melting points were determined with a SWG X-4 melting apparatus. The high resolution mass spectra were recorded on a Thermo LTQ Orbitrap XL (ESI+) or a P-SIMS-Gly of Bruker DaltonicsInc (EI+). Infrared spectra were recorded on a Nicolet MX-1E FT-IR spectrometer. Optical rotations were measured at 589 nm (sodium D line) by using a Perkin-Elmer 343 polarimeter.

**Materials:**

All starting materials, reagents and solvents were purchased from commercial suppliers (Aldrich, Alfa, TCI, Daicel, etc.) and used as supplied unless otherwise stated. The isatin-derived enals **1**[1,2], propargylic acetates **2**[3,4], NHC precatalysts **4**[5,6], and Pybox ligand **L6**[7] were synthesized in accordance with the procedures in literatures. Tetrahydrofuran and toluene were dried over Na and distilled prior to use.

## 2. Supplementary Discussion

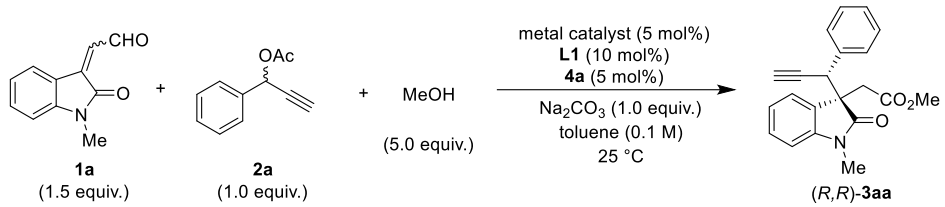
**Supplementary Table 1.** Effect of NHC precatalyst on the reaction[a]

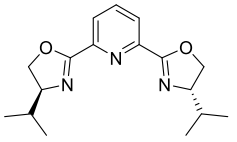



| entry | **4** | yield (%) | d.r. | e.e. (%) |
|---|---|---|---|---|
| 1 | **4a** | 70 | 93:7 | 96 |
| 2 | **4b** | 20 | 87:13 | 94 |
| 3 | **4c** | 76 | 92:8 | 92 |
| 4 | **4d** | 74 | 67:33 | 29 |
| 5 | **4e** | 22 | 71:29 | 59 |
| 6 | **4f** | 83 | 50:50 | 18 |

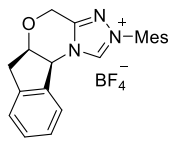
[a]Unless noted, reaction conditions: $Cu(CH_3CN)_4PF_6$ (5 mol%) and pyridine bisoxazoline ligand **L1** (10 mol%) were stirred in toluene (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4** (5 mol%), **1a** (0.15 mmol), **2a** (0.1 mmol), MeOH (0.5 mmol), $Na_2CO_3$ (0.1 mmol) and toluene (0.5 mL) were added to the reaction mixture and stirred at 25 ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1H$ NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC.

**Supplementary Table 2.** Effect of copper catalyst on the reaction[a]



L1

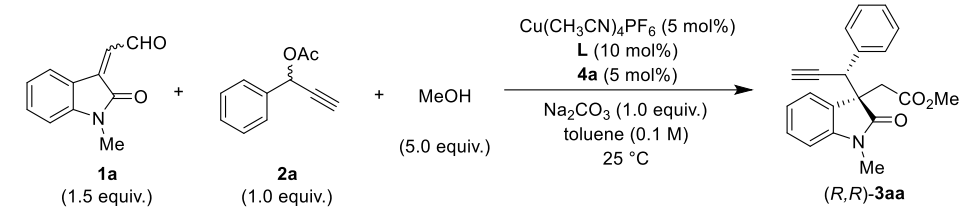


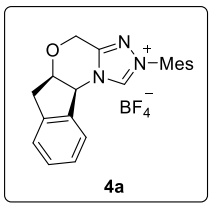

4a

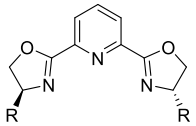
| entry | metal catalyst | yield (%) | d.r. | e.e.(%) |
|---|---|---|---|---|
| 1 | $Cu(CH_3CN)_4PF_6$ | 70 | 93:7 | 96 |
| 2 | $Cu(CH_3CN)_4BF_4$ | 32 | 75:25 | 88 |
| 3 | CuI | <5 | - | - |
| 4 | $Cu(OTf)_2$ | 52 | 88:12 | 94 |
| 5 | $Cu(OAc)_2$ | 43 | 67:33 | 88 |

[a]Unless noted, reaction conditions: copper catalyst (5 mol%) and pyridine bisoxazoline ligand **L1** (10 mol%) were stirred in toluene (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4a**(5 mol%), **1a** (0.15 mmol), **2a** (0.1 mmol), MeOH (0.5 mmol), $Na_2CO_3$ (0.1 mmol) and toluene (0.5 mL) were added to the reaction mixture and stirred at 25 ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1H$ NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC. n.d. = not detected.

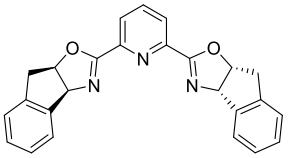
**Supplementary Table 3.** Effect of ligand on the reaction[a]



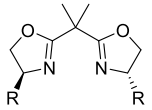



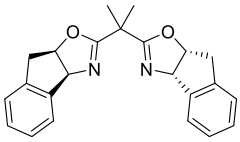
**L1**: R = $^{i}$Pr
**L2**: R = $^{t}$Bu
**L3**: R = Ph
**L4**: R = Bn



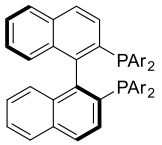
**L-S1**



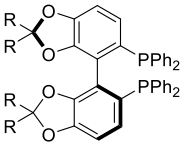
**L-S2**: R = $^{i}$Pr
**L-S3**: R = $^{t}$Bu
**L-S4**: R = Ph
**L-S5**: R = Bn



**L-S6**




**L-S7**: Ar = Ph
**L-S8**: Ar = 3,5-$Me_2$-$C_6H_3$

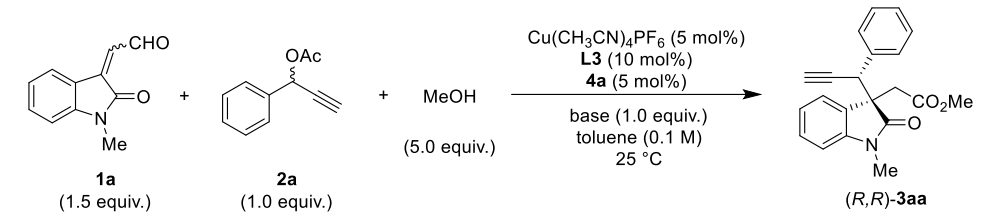


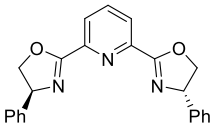

**L-S9**: R = H
**L-S10**: R = F

| entry | L | yield (%) | d.r. | e.e. (%) |
|---|---|---|---|---|
| 1 | **L1** | 70 | 93:7 | 96 |
| 2 | **L2** | 42 | 60:40 | 73 |
| 3 | **L3** | 51 | >95:5 | 99 |
| 4 | **L4** | 39 | 81:19 | 87 |
| 5 | **L-S1** | 16 | 78:22 | - |
| 6 | **L-S2** | <5 | - | - |
| 7 | **L-S3** | <5 | - | - |
| 8 | **L-S4** | 15 | 78:22 | 90 |
| 9 | **L-S5** | 41 | 85:15 | 97 |
| 10 | **L-S6** | 15 | 84:16 | 94 |
| 11 | **L-S7** | <5 | - | - |
| 12 | **L-S8** | <5 | - | - |
| 13 | **L-S9** | <5 | - | - |
| 14 | **L-S10** | <5 | - | - |

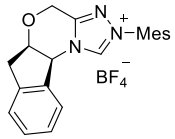
[a]Unless noted, reaction conditions: $Cu(CH_3CN)_4PF_6$ (5 mol%) and ligand **L** (10 mol%) were stirred in toluene (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4a** (5 mol%), **1a** (0.15 mmol), **2a** (0.1 mmol), MeOH (0.5 mmol), $Na_2CO_3$ (0.1 mmol) and toluene (0.5 mL) were added to the reaction mixture and stirred at 25 ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1$H NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC.

**Supplementary Table 4.** Effect of base on the reaction[a]




L3

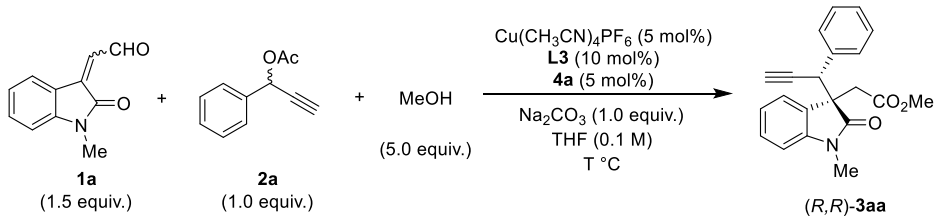


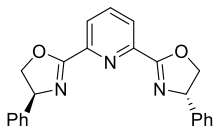

4a

| entry | base | yield (%) | d.r. | e.e. (%) |
|---|---|---|---|---|
| 1 | $Na_2CO_3$ | 51 | >95:5 | 99 |
| 2 | $K_2CO_3$ | <5 | - | - |
| 3 | $Cs_2CO_3$ | n.d. | - | - |
| 4 | NaOAc | 11 | 92:8 | - |
| 5 | $NaHCO_3$ | 9 | 95:5 | - |
| 6 | $^{i}Pr_2NEt$ | 51 | 93:7 | 96 |
| 7 | $NEt_3$ | 60 | 95:5 | 98 |
| 8 | DMAP | 16 | 73:27 | - |
| 9 | DABCO | 30 | 80:20 | 98 |
| 10 | TMEDA | 44 | 86:14 | 95 |

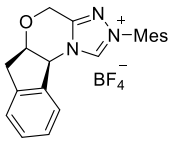
[a]Unless noted, reaction conditions: $Cu(CH_3CN)_4PF_6$ (5 mol%) and pyridine bisoxazoline ligand **L3** (10 mol%) were stirred in toluene (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4a** (5 mol%), **1a** (0.15 mmol), **2a** (0.1 mmol), MeOH (0.5 mmol), base (0.1 mmol) and toluene (0.5 mL) were added to the reaction mixture and stirred at 25 ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1$H NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC. DMAP = 4-dimethylaminopyridine; DABCO = triethylene diamine; TMEDA = *N*,*N*,*N*',*N*'-tetramethylethylenediamine.

**Supplementary Table 5.** Effect of temperature on the reaction[a]




L3

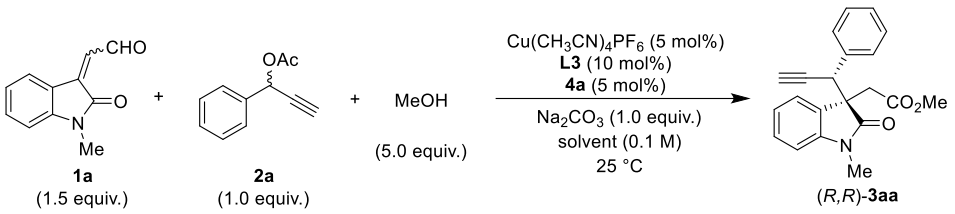


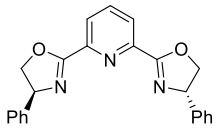

4a

| entry | T (℃) | yield (%) | d.r. | e.e. (%) |
|---|---|---|---|---|
| 1 | 40 | 65 | >95:5 | 99 |
| 2 | 30 | 66 | >95:5 | 99 |
| 3 | 25 | 79 | >95:5 | >99 |
| 4[b] | 10 | 64 | >95:5 | 99 |
| 5[b] | 0 | 32 | >95:5 | 99 |

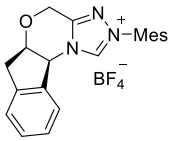
[a]Unless noted, reaction conditions: $Cu(CH_3CN)_4PF_6$ (5 mol%) and pyridine bisoxazoline ligand **L3** (10 mol%) were stirred in THF (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4a**(5 mol%), **1a** (0.15 mmol), **2a** (0.1 mmol), MeOH (0.5 mmol), $Na_2CO_3$ (0.1 mmol) and THF (0.5 mL) were added to the reaction mixture and stirred at T ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1H$ NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC. [b]For 3 days.

**Supplementary Table 6.** Effect of solvent on the reaction[a]




L3



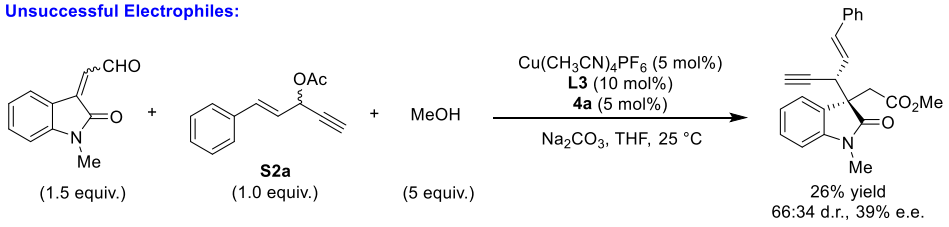

4a

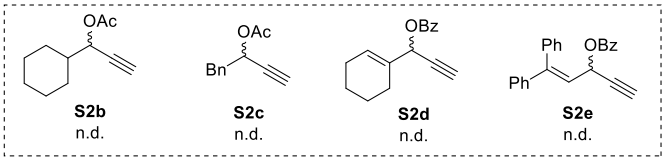
| entry | solvent | yield (%) | d.r. | e.e. (%) |
|---|---|---|---|---|
| 1 | toluene | 51 | >95:5 | 99 |
| 2 | DCM | 47 | >95:5 | 99 |
| 3 | THF | 79 | >95:5 | >99 |
| 4 | DCE | 45 | >95:5 | 98 |
| 5 | DMSO | n.d. | - | - |
| 6 | MeOH | 22 | 73:27 | 84 |
| 7 | EtOAc | 40 | >95:5 | 99 |
| 8 | $CH_3CN$ | 53 | 80:20 | 48 |
| 9 | 1,4-dioxane | 57 | >95:5 | 99 |

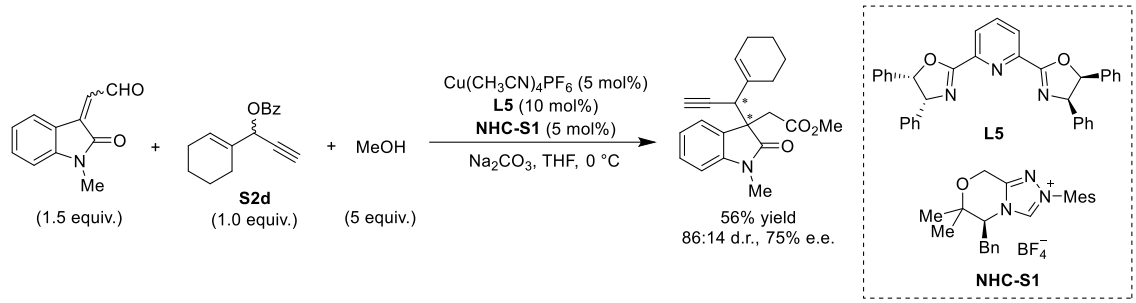
[a]Unless noted, reaction conditions: $Cu(CH_3CN)_4PF_6$ (5 mol%) and pyridine bisoxazoline ligand **L3** (10 mol%) were stirred in solvent (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4a**(5 mol%), **1a** (0.15 mmol), **2a** (0.1 mmol), MeOH (0.5 mmol), $Na_2CO_3$ (0.1 mmol) and solvent (0.5 mL) were added to the reaction mixture and stirred at 25 ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1H$ NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC.DCM = dichloromethane; DCE = 1,2-dichloroethane; THF =tetrahydrofuran; DMSO = dimethyl sulfoxide.

**Supplementary Table 7.** Unsuccessful substrates
Incompatible substratesare shown below:

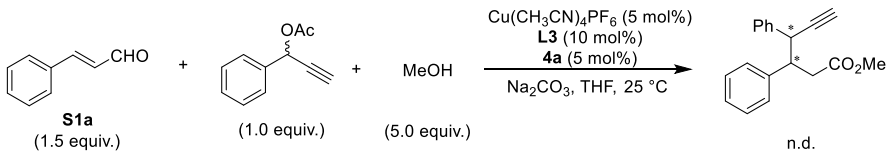
**Unsuccessful Electrophiles:**

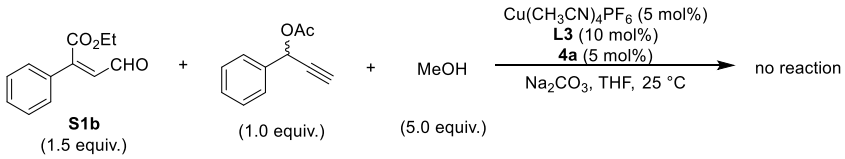


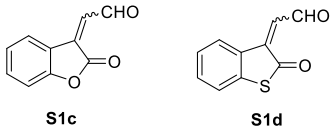




**Unsuccessful Nucleophiles:**

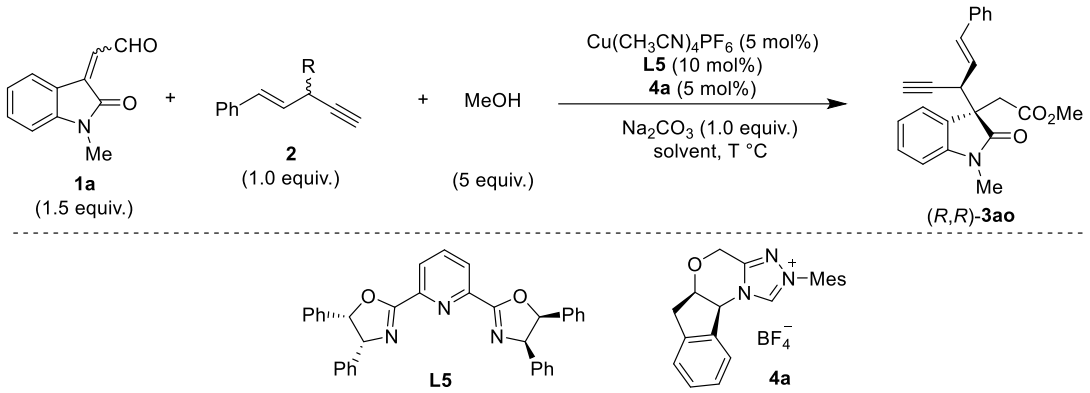



**Failed to synthesize:**



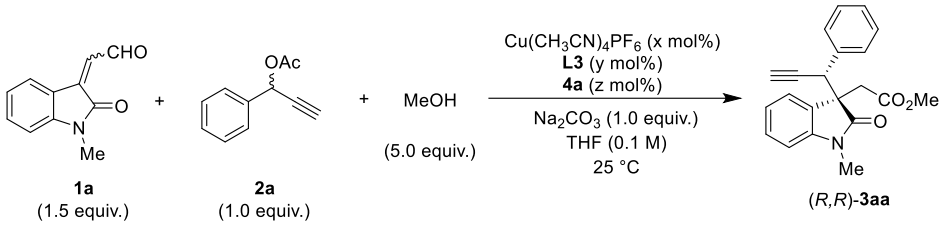
**Supplementary Table 8.** Condition optimization for styryl-substituted propargylic substrates[a]

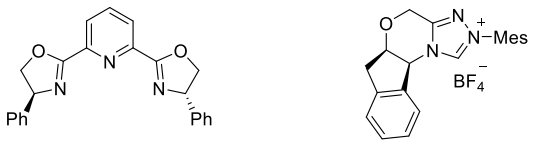



| entry | R | solvent | T | yield (%) | d.r. | e.e. (%) |
|---|---|---|---|---|---|---|
| 1 | OBz | THF | 25 | 40 | 86:14 | 85 |
| 2 | OPiv | THF | 25 | 26 | 68:32 | 64 |
| 3 | $OC(O)C_6F_5$ | THF | 25 | 8 | 66:34 | n.d. |
| 4[b] | OBz | THF | 25 | 32 | 86:14 | 89 |
| 5[b] | OBz | THF | 35 | 35 | 81:19 | 89 |
| 6[b] | OBz | THF | 15 | 34 | 89:11 | 96 |
| 7[b] | OBz | toluene | 15 | 26 | >95:5 | >99 |
| 8[b] | OBz | DCM | 15 | 32 | >95:5 | >99 |
| 9[c] | OBz | DCM | 15 | 44 | >95:5 | 99 |

[a]Unless noted, reaction conditions: $Cu(CH_3CN)_4PF_6$ (5 mol%) and pyridine bisoxazoline ligand **L5** (10 mol%) were stirred in solvent (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4a** (5 mol%), **1a** (0.15 mmol), **2** (0.1 mmol), MeOH (0.5 mmol), $Na_2CO_3$ (0.1 mmol) and solvent (0.5 mL) were added to the reaction mixture and stirred at T ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1H$ NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC. DCM = dichloromethane; THF = tetrahydrofuran. [b]with **4a** (7.5 mol%). [c]with $Cu(CH_3CN)_4PF_6$ (7.5 mol%), **L5** (15 mol%), **4a** (7.5 mol%), and $Na_2CO_3$ (0.2 mmol).

**Supplementary Table 9.** Effect of Cu/Ligand/NHC ratio on the reaction[a]



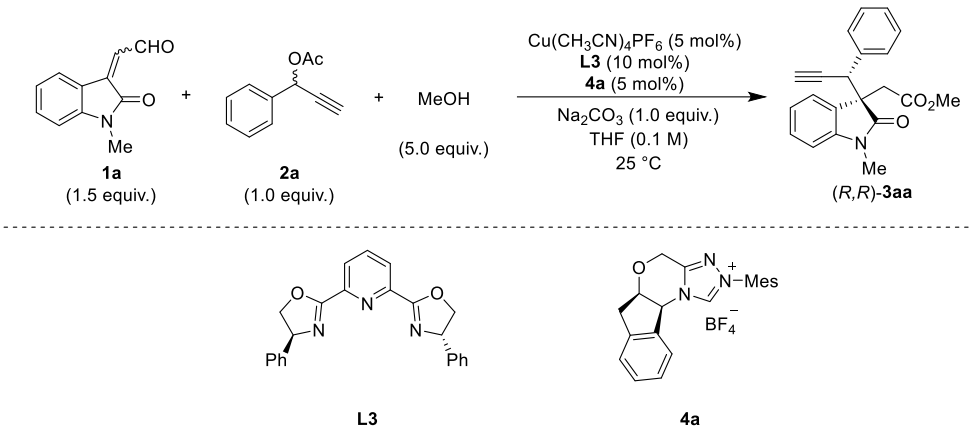




| entry | x | y | z | yield (%) | d.r. | e.e. (%) |
|---|---|---|---|---|---|---|
| 1 | 5 | 5 | 5 | 64 | >95:5 | >99 |
| 2 | 5 | 10 | 5 | 79 | >95:5 | >99 |
| 3 | 10 | 20 | 5 | 73 | >95:5 | >99 |
| 4 | 20 | 40 | 5 | 63 | >95:5 | >99 |
| 5 | 30 | 60 | 5 | 62 | >95:5 | >99 |
| 6 | 50 | 100 | 5 | 50 | >95:5 | >99 |

[a]Unless noted, reaction conditions: $Cu(CH_3CN)_4PF_6$ (x mol%) and pyridine bisoxazoline ligand **L3** (y mol%) were stirred in THF (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4a** (z mol%), **1a** (0.15 mmol), **2a** (0.1 mmol), MeOH (0.5 mmol), $Na_2CO_3$ (0.1 mmol) and THF (0.5 mL) were added to the reaction mixture and stirred at 25 ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1H$ NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC.

# 3. Supplementary Methods

## Gram Scale Reaction



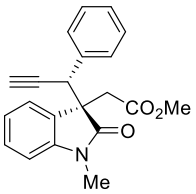

To a flame-dried and $N_2$-purged Schlenk tube were added $Cu(CH_3CN)_4PF_6$ (0.2 mmol, 74.5 mg) and pyridine bisoxazoline ligand **L3** (0.4 mmol, 147.8 mg). The vial was sealed, purged and backfilled with $N_2$ three times before adding THF (20.0 mL) at 25℃. The resulting solution was stirred at 25℃ for 1 hour. Then, isatin-derived enal **1a** (6.0 mmol, 1123.2 mg), NHC precatalyst **4a** (0.2 mmol, 83.8 mg), $Na_2CO_3$ (4.0 mmol, 424.0 mg), MeOH (20.0 mmol, 800 μL) and a solution of propargylic acetate **2a** (4.0 mmol, 696.8 mg) in THF (20.0 mL) were added. The resulting solution was stirred at 25℃ for 12 hours and then quenched with saturated $NH_4Cl$ aqueous solution (10.0 mL). The resulting solution was extracted with ethyl acetate (15.0 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated in vacuo. The diastereomeric ratio was determined by $^1H$ NMR analysis of the crude reaction mixture. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate= 5:1-2:1) to afford the desired product (*R*,*R*)-**3aa** (1.0 g, 75% yield, > 95:5 d.r., >99% e.e.).

**General Procedure**

To a flame-dried and $N_2$-purged Schlenk tube were added $Cu(CH_3CN)_4PF_6$ (0.005 mmol, 5 mol%) and pyridine bisoxazoline ligand **L3** (or *ent*-**L3**) (0.01 mmol, 10 mol%). The vial was sealed, purged and backfilled with $N_2$ three times before adding THF (0.5 mL) at 25 ℃. The resulting solution was stirred at 25 ℃ for 1 hour. Then, isatin-derived enal **1** (0.15 mmol), NHC precatalyst **4a** (or *ent*-**4a**) (0.005 mmol, 5 mol%), $Na_2CO_3$ (0.1 mmol), MeOH (0.5 mmol) and a solution of propargylic acetate **2** (0.1 mmol) in THF (0.5 mL) were added. The resulting solution was stirred at 25 ℃ for 12 hours and then quenched with saturated $NH_4Cl$ aqueous solution (5.0 mL). The resulting solution was extracted with ethyl acetate (5.0 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated in vacuo. The diastereomeric ratio was determined by $^1H$ NMR analysis of the crude reaction mixture. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate = 5:1-2:1) to afford the desired product **3**.

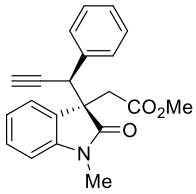
**Characterization Data of Products**

**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3aa)**




White solid, m.p. 73-75 ℃; 77% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.30 – 7.18 (m, 4H), 7.15 – 7.11 (m, 2H), 6.97 (td, *J* = 7.5, 1.0 Hz, 1H), 6.85 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.71 (d, *J* = 7.7 Hz, 1H), 4.16 (d, *J* = 2.6 Hz, 1H), 3.42 (s, 3H), 3.28 (d, *J* = 16.5 Hz, 1H), 3.12 (s, 3H), 2.89 (d, *J* = 16.5 Hz, 1H), 2.20 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.4, 170.1, 145.1, 134.9, 129.9, 128.9, 128.2, 128.0, 127.9, 124.1, 121.8, 107.9, 81.0, 73.2, 53.1, 51.8, 45.0, 39.2, 26.3. **IR** (KBr, $cm^{-1}$) $\gamma$ 3291, 3058, 3029, 2952, 2925, 2853, 1715, 1613, 1494, 1471, 1377, 1354, 1262, 1198, 1176, 1091, 1028, 752, 702, 543, 489. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{19}NO_3Na)^+$: 356.1257, found: 356.1270; **$[\alpha]^{20}_D$** = +37.4 (*c* = 0.50, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (major) = 11.26 min, $t_R$ (minor) = 16.01 min.

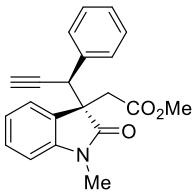
**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*S*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*S*)-3aa)**




White solid, m.p. 66 ℃; 55% yield; 91:9 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.64 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.21 (td, *J* = 7.8, 1.3 Hz, 1H), 7.10 – 7.02 (m, 2H), 7.01 – 6.95 (m, 2H), 6.86 – 6.81 (m, 2H), 6.48 – 6.43 (m, 1H), 4.13 (d, *J* = 2.6 Hz, 1H), 3.58 (d, *J* = 16.6 Hz, 1H), 3.45 (s, 3H), 3.28 (d, *J* = 16.7 Hz, 1H), 2.77 (s, 3H), 2.51 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.0, 170.3, 144.4, 134.5, 128.9, 128.8, 127.8, 127.7, 127.3, 123.9, 122.0, 107.7, 82.3, 74.2, 53.6, 51.8, 45.1, 39.7, 25.9. **IR** (KBr, $cm^{-1}$) $\gamma$ 3289, 3058, 3031, 2924, 2853, 1742, 1713, 1613, 1494, 1471, 1377, 1355, 1255, 1199, 1177, 1092, 1028, 752, 699, 683, 543, 487. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{19}NO_3Na)^+$: 356.1257, found: 356.1257; **$[\alpha]^{20}_D$** = -51.2 (*c* = 0.59, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 270

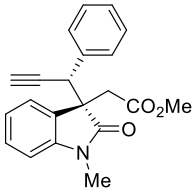
nm), $t_R$ (major) = 8.74 min, $t_R$ (minor) = 10.81 min.

**Methyl 2-((*S*)-1-methyl-2-oxo-3-((*S*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*S*,*S*)-3aa)**



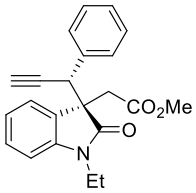

White solid; 74% yield; >95:5 d.r.; Spectral data were in agreement with those of the enantiomer reported above. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{19}NO_3Na)^+$: 356.1257, found: 356.1255; **$[\alpha]^{20}_D$** = -40.1 (*c* = 0.48, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (minor) = 11.46 min, $t_R$ (major) = 15.42 min.

**Methyl 2-((*S*)-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*S*,*R*)-3aa)**




White solid; 60% yield; 92:8 d.r.; Spectral data were in agreement with those of the enantiomer reported above. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{19}NO_3Na)^+$: 356.1257, found: 356.1263; **$[\alpha]^{20}_D$** = +53.7 (*c* = 0.25, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 270 nm), $t_R$ (minor) = 9.30 min, $t_R$ (major) = 10.79 min.

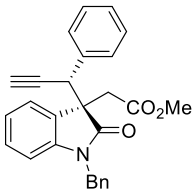
**Methyl 2-((*R*)-1-ethyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3ba)**




Yellow solid, m.p. 91-92 ℃; 79% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.27 – 7.24 (m, 1H), 7.24 – 7.18 (m, 3H), 7.17 – 7.11 (m, 2H), 6.97 (td, *J* = 7.5, 1.0 Hz, 1H), 6.90 (dd, *J* = 7.5, 1.4 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 4.18 (d, *J* = 2.6 Hz, 1H), 3.78 (dq, *J* = 14.5, 7.3 Hz, 1H), 3.59 (dq, *J* = 14.3, 7.2 Hz, 1H), 3.40 (s, 3H), 3.27 (d, *J* = 16.4 Hz, 1H), 2.90 (d, *J* = 16.4 Hz, 1H), 2.21 (d, *J* = 2.6 Hz, 1H), 1.11 (t, *J* = 7.2 Hz, 3H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 176.8, 170.1, 144.2, 135.0, 129.9, 128.8, 128.5, 128.0, 127.9, 124.4, 121.6, 108.0, 81.1, 73.4, 52.7, 51.7, 44.9, 39.5, 34.7, 12.2. **IR** (KBr,

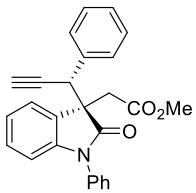
cm$^{-1}$) $\gamma$ 3299, 2961, 2926, 2853, 1712, 1612, 1489, 1467, 1369, 1261, 1201, 1174, 1135, 1098, 1022, 799, 753, 700. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_3Na)^+$: 370.1414, found: 370.1417; **$[\alpha]^{20}_D$** = +35.7 (*c* = 0.53, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 10.57 min, $t_R$ (minor) = 16.33 min.

**Methyl 2-((*R*)-1-benzyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3ca)**




Yellow solid, m.p. 93 ℃; 81% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.32 – 7.11 (m, 11H), 6.99 – 6.91 (m, 2H), 6.58 (d, *J* = 7.8 Hz, 1H), 4.88 (d, *J* = 15.8 Hz, 1H), 4.77 (d, *J* = 15.8 Hz, 1H), 4.25 (d, *J* = 2.7 Hz, 1H), 3.39 (s, 3H), 3.36 (d, *J* = 16.4 Hz, 1H), 2.96 (d, *J* = 16.4 Hz, 1H), 2.18 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.4, 170.0, 144.4, 135.9, 135.0, 130.0, 128.8, 128.6, 128.3, 128.1, 128.0, 127.7, 127.5, 124.2, 121.9, 109.1, 81.2, 73.6, 52.9, 51.8, 44.9, 44.3, 39.9. **IR** (KBr, cm$^{-1}$) $\gamma$ 3297, 3029, 2954, 2924, 1715, 1613, 1488, 1467, 1454, 1355, 1261, 1197, 1080, 1173, 1014, 800, 753, 699. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{27}H_{23}NO_3Na)^+$: 432.1570, found: 432.1577; **$[\alpha]^{20}_D$** = +29.9 (*c* = 0.60, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 18.93 min, $t_R$ (minor) = 25.23 min.

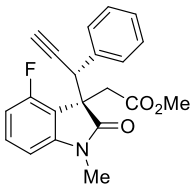
**Methyl 2-((*R*)-2-oxo-1-phenyl-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3da)**




Yellow solid, m.p. 130 ℃; 73% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.48 (t, *J* = 7.8 Hz, 2H), 7.41 – 7.36 (m, 1H), 7.32 – 7.22 (m, 5H), 7.21 – 7.14 (m, 3H), 7.01 (td, *J* = 7.5, 1.0 Hz, 1H), 6.93 (dd, *J* = 7.5, 1.3 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 4.24 (d, *J* = 2.6 Hz, 1H), 3.47 (s, 3H), 3.46 (d, *J* = 16.7 Hz, 1H), 2.98 (d, *J* = 16.6 Hz, 1H), 2.31 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 176.7, 170.1, 145.3, 134.9, 134.7, 130.0, 129.6, 128.8, 128.1, 128.1, 128.0, 126.8, 124.2, 122.2, 109.1, 81.0, 77.4, 73.7,

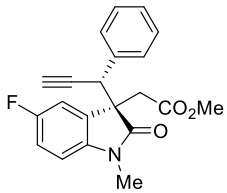
53.0, 51.9, 45.3, 39.8. **IR** (KBr, $cm^{-1}$) $\gamma$ 3301, 3011, 2954, 2923, 2853, 1723, 1611, 1595, 1503, 1465, 1377, 1261, 1200, 1174, 1114, 1027, 800, 752, 700, 594. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{26}H_{21}NO_3Na)^+$: 418.1414, found: 418.1425; $[\alpha]^{20}_D$ = +1.9 (*c* = 0.55, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IE, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 16.91 min, $t_R$ (minor) = 32.05 min.

**Methyl 2-((*R*)-4-fluoro-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3ea)**




Yellow solid, m.p. 97 ℃; 60% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.19 – 7.01 (m, 6H), 6.67 (ddd, *J* = 9.3, 8.4, 0.7 Hz, 1H), 6.30 (dd, *J* = 7.8, 0.7 Hz, 1H), 4.21 (d, *J* = 2.7 Hz, 1H), 3.74 (d, *J* = 17.0 Hz, 1H), 3.48 (s, 3H), 3.27 (d, *J* = 17.0 Hz, 1H), 2.94 (s, 3H), 2.45 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 175.6, 170.5, 158.8 (d, *J* = 245.6 Hz), 146.5 (d, *J* = 9.6 Hz), 134.9, 130.7 (d, *J* = 8.8 Hz), 128.7, 127.9, 127.7, 114.3 (d, *J* = 18.8 Hz), 109.6 (d, *J* = 20.8 Hz), 104.0 (d, *J* = 2.9 Hz), 80. 6, 74.4, 53.3 (d, *J* = 3.0 Hz), 51.9, 43.8, 38.5, 26.4. **$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -120.06. **IR** (KBr, $cm^{-1}$) $\gamma$ 3293, 2921, 2851, 1723, 1629, 1477, 1455, 1358, 1260, 1235, 1200, 1147, 1050, 776, 701, 577, 542. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1171; $[\alpha]^{20}_D$ = +70.7 (*c* = 0.39, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 8.00 min, $t_R$ (minor) = 9.23 min.

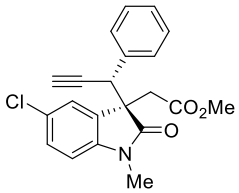
**Methyl2-((*R*)-5-fluoro-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3fa)**




White solid, m.p. 84 ℃; 50% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.32 – 7.23 (m, 3H), 7.19 – 7.13 (m, 2H), 6.97 (ddd, *J* = 9.3, 8.5, 2.6 Hz, 1H), 6.65 (dd, *J* = 8.5, 4.2 Hz, 1H), 6.61 (dd, *J* = 8.1, 2.6 Hz, 1H), 4.15 (d, *J* = 2.6 Hz, 1H), 3.45 (s, 3H), 3.27 (d, *J* = 16.9 Hz, 1H), 3.12 (s, 3H), 2.85 (d, *J* = 16.8 Hz, 1H), 2.20 (d, *J* = 2.6 Hz,

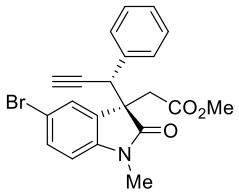
1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.1, 170.0, 158.6 (d, *J* = 239.9 Hz), 141.2, 134.5, 129.9 (d, *J* = 8.3 Hz), 129.8, 128.3, 128.0, 115.4 (d, *J* = 23.3 Hz), 112.2 (d, *J* = 25.2 Hz), 108.2 (d, *J* = 8.2 Hz), 80.6, 73.4, 53.4 (d, *J* = 1.9 Hz), 52.0, 44.8, 39.0, 26.5. **$^{19}$F NMR (471 MHz, $CDCl_3$)** δ -121.05. **IR** (KBr, $cm^{-1}$) *γ* 3303, 3009, 2956, 2922, 2852, 1715, 1659, 1625, 1496, 1469, 1359, 1262, 1200, 1177, 1111, 1023, 811, 755, 701, 664, 561. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1179; **$[\alpha]^{20}_D$** = +29.6 (*c* = 0.22, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 9.99 min, $t_R$ (minor) = 18.36 min.

**Methyl 2-((*R*)-5-chloro-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3ga)**




Yellow oil; 84% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.30 – 7.21 (m, 4H), 7.18 – 7.12 (m, 2H), 6.79 (d, *J* = 2.1 Hz, 1H), 6.65 (d, *J* = 8.3 Hz, 1H), 4.13 (d, *J* = 2.6 Hz, 1H), 3.46 (s, 3H), 3.28 (d, *J* = 16.9 Hz, 1H), 3.12 (s, 3H), 2.85 (d, *J* = 17.0 Hz, 1H), 2.21 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.0, 169.9, 143.8, 134.4, 130.0, 129.8, 128.8, 128.3, 128.1, 127.0, 124.6, 108.7, 80.5, 73.5, 53.2, 52.0, 44.9, 39.0, 26.4. **IR** (KBr, $cm^{-1}$) *γ* 3296, 3029, 2957, 2925, 1717, 1610, 1492, 1454, 1358, 1261, 1201, 1177, 1100, 1023, 809, 750, 702. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}ClNO_3Na)^+$: 390.0867, found: 390.0874; **$[\alpha]^{20}_D$** = +70.4 (*c* = 0.58, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254nm), $t_R$ (major) = 9.18 min, $t_R$ (minor) = 15.87 min.

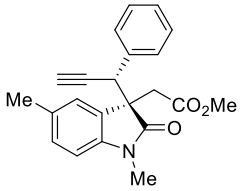
**Methyl 2-((*R*)-5-bromo-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3ha)**




Yellow oil; 81% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.39 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.30 – 7.24 (m, 3H), 7.17 – 7.11 (m, 2H), 6.91 (d, *J* = 2.0 Hz, 1H), 6.61 (d, *J* = 8.3 Hz, 1H), 4.12

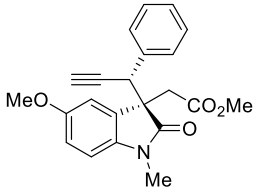
(d, *J* = 2.6 Hz, 1H), 3.46 (s, 3H), 3.28 (d, *J* = 17.0 Hz, 1H), 3.11 (s, 3H), 2.84 (d, *J* = 17.0 Hz, 1H), 2.20 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 176.9, 169.9, 144.3, 134.4, 131.7, 130.3, 129.8, 128.3, 128.1, 127.3, 114.3, 109.3, 80.5, 73.5, 53.1, 52.0, 44.9, 39.0, 26.4. **IR** (KBr, $cm^{-1}$) *γ* 3296, 3028, 2952, 2925, 2853, 1715, 1608, 1491, 1366, 1204, 1177, 1099, 1024, 809, 750, 702. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}BrNO_3Na)^+$: 434.0362, found: 434.0368; **$[\alpha]^{20}_D$** = +76.0 (*c* = 0.60, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 9.52 min, $t_R$ (minor) = 14.99 min.

**Methyl 2-((*R*)-1,5-dimethyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl) acetate ((*R*,*R*)-3ia)**




Yellow oil; 79% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.27 – 7.20 (m, 3H), 7.16 – 7.12 (m, 2H), 7.07 – 7.03 (m, 1H), 6.63 (d, *J* = 1.7 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 1H), 4.15 (d, *J* = 2.6 Hz, 1H), 3.43 (s, 3H), 3.27 (d, *J* = 16.7 Hz, 1H), 3.10 (s, 3H), 2.86 (d, *J* = 16.7 Hz, 1H), 2.28 (s, 3H), 2.19 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.3, 170.1, 142.7, 134.9, 131.1, 129.9, 129.1, 128.1, 128.0, 127.8, 125.0, 107.5, 81.0, 73.1, 53.0, 51.8, 44.9, 39.1, 26.3, 21.3. **IR** (KBr, $cm^{-1}$) *γ* 3288, 3028, 2923, 1740, 1715, 1621, 1603, 1501, 1454, 1358, 1199, 1175, 1096, 1032, 809, 754, 702, 661. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_3Na)^+$: 370.1414, found: 370.1417; **$[\alpha]^{20}_D$** = +69.5 (*c* = 0.52, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 10.19 min, $t_R$ (minor) = 16.93 min.

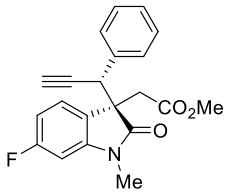
**Methyl 2-((*R*)-5-methoxy-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3ja)**




Yellow oil; 69% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.29 – 7.22 (m, 3H), 7.17 (dd, *J* = 6.3, 2.7 Hz, 2H), 6.78 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.45 (d, *J* = 2.5 Hz,

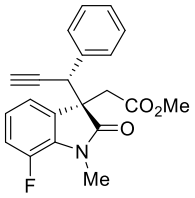
1H), 4.16 (d, *J* = 2.5 Hz, 1H), 3.72 (s, 3H), 3.43 (s, 3H), 3.25 (d, *J* = 16.6 Hz, 1H), 3.10 (s, 3H), 2.84 (d, *J* = 16.6 Hz, 1H), 2.19 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.1, 170.1, 155.3, 138.8, 134.9, 130.0, 129.5, 128.1, 127.9, 113.1, 111.8, 108.1, 81.0, 73.1, 55.8, 53.4, 51.8, 44.9, 39.2, 26.4. **IR** (KBr, $cm^{-1}$) $\gamma$ 3288, 3004, 2924, 2852, 1739, 1709, 1601, 1498, 1367, 1288, 1234, 1201, 1175, 1115, 1033, 888, 807, 753, 701. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_4Na)^+$: 386.1363, found: 386.1369; **$[\alpha]^{20}_D$** = +5.0 (*c* = 0.43, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IA, hexane/*i*-PrOH = 85/15, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (minor) = 12.89 min, $t_R$ (major) = 13.84 min.

**Methyl 2-((*R*)-6-fluoro-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3ka)**



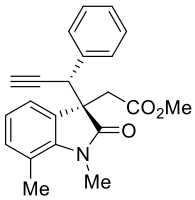

White solid; 88% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.29 – 7.22 (m, 3H), 7.16 – 7.11 (m, 2H), 6.74 (dd, *J* = 8.2, 5.4 Hz, 1H), 6.64 (ddd, *J* = 9.4, 8.2, 2.3 Hz, 1H), 6.47 (dd, *J* = 8.9, 2.3 Hz, 1H), 4.12 (d, *J* = 2.6 Hz, 1H), 3.43 (s, 3H), 3.26 (d, *J* = 16.7 Hz, 1H), 3.12 (s, 3H), 2.84 (d, *J* = 16.7 Hz, 1H), 2.20 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 177.8, 170.0, 163.5 (d, *J* = 245.4 Hz), 146.7 (d, *J* = 11.7 Hz), 134.7, 129.8, 128.2, 128.0, 125.1 (d, *J* = 9.9 Hz), 123.4 (d, *J* = 2.9 Hz), 107.8 (d, *J* = 22.4 Hz), 96.8 (d, *J* = 27.5 Hz), 80.7, 73.3, 52.7, 51.9, 44.9, 39.1, 26.4. **$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -111.19. **IR** (KBr, $cm^{-1}$) $\gamma$ 3301, 3029, 2953, 2926, 2853, 1723, 1615, 1504, 1454, 1382, 1198, 1178, 1085, 837, 755, 702. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1171; **$[\alpha]^{20}_D$** = +31.5 (*c* = 0.49, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 9.35 min, $t_R$ (minor) = 13.58 min.

**Methyl 2-((*R*)-7-fluoro-1-methyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3la)**



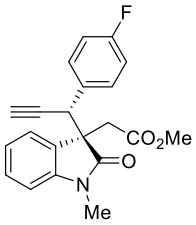
White solid, m.p. 127-129 ℃; 78% yield; >95:5 d.r.; **$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.31 – 7.20 (m, 3H), 7.14 – 7.08 (m, 2H), 6.98 (ddd, *J* = 11.5, 8.4, 1.1 Hz, 1H), 6.89 (ddd, *J* = 8.4, 7.4, 4.5 Hz, 1H), 6.60 (dd, *J* = 7.3, 1.1 Hz, 1H), 4.11 (d, *J* = 2.6 Hz, 1H), 3.44 (s, 3H), 3.33 (d, *J* = 2.7 Hz, 3H), 3.32 (d, *J* = 16.8 Hz, 1H), 2.86 (d, *J* = 16.8 Hz, 1H), 2.25 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 177.1, 170.0, 147.6 (d, *J* = 243.3 Hz), 134.5, 131.7 (d, *J* = 8.2 Hz), 131.3 (d, *J* = 3.6 Hz), 129.8, 128.2, 128.0, 122.2 (d, *J* = 6.3 Hz), 119.8 (d, *J* = 3.2 Hz), 116.9 (d, *J* = 19.4 Hz), 80.6, 73.5, 53.4 (d, *J* = 2.0 Hz), 51.9, 45.1, 39.3, 28.7 (d, *J* = 5.9 Hz). **$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -136.67. **IR** (KBr, $cm^{-1}$) $\gamma$ 3300, 3030, 2924, 2853, 1720, 1631, 1598, 1484, 1454, 1437, 1374, 1240, 1200, 1116, 1057, 925, 778, 733, 702. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1171; **$[\alpha]^{20}_D$** = +51.2 (*c* = 0.44, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 8.38 min, $t_R$ (minor) = 10.36 min.

**Methyl 2-((*R*)-1,7-dimethyl-2-oxo-3-((*R*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R*,*R*)-3ma)**



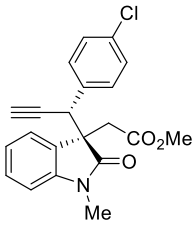
White solid, m.p. 109 ℃; 80% yield; >95:5 d.r.; **$^{1}$H NMR (500 MHz, $CDCl_3$)** δ 7.25 – 7.18 (m, 3H), 7.11 – 7.05 (m, 2H), 6.97 (d, *J* = 7.2 Hz, 1H), 6.85 (t, *J* = 7.6 Hz, 1H), 6.67 (dd, *J* = 7.4, 1.3 Hz, 1H), 4.10 (d, *J* = 2.6 Hz, 1H), 3.44 (s, 3H), 3.36 (s, 3H), 3.33 (d, *J* = 16.7 Hz, 1H), 2.87 (d, *J* = 16.7 Hz, 1H), 2.45 (s, 3H), 2.25 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 178.0, 170.2, 142.9, 134.8, 132.6, 129.8, 128.8, 128.0, 127.7, 121.8, 121.7, 119.4, 81.1, 73.3, 52.4, 51.8, 45.4, 39.3, 29.6, 19.2. **IR** (KBr, $cm^{-1}$) $\gamma$ 3360, 3303, 2922, 2852, 1742, 1712, 1632, 1601, 1455, 1369, 1262, 1198, 1114, 1077, 747, 701, 666. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{21}NO_3Na)^+$: 370.1414, found: 370.1421; **$[\alpha]^{20}_D$** = +9.7 (*c* = 0.09, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (major) = 10.71 min, $t_R$ (minor) = 14.86 min.

**Methyl 2-((*R*)-3-((*R*)-1-(4-fluorophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R,R*)-3ab)**




White solid, m.p. 55 ℃; 76% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.29 – 7.22 (m, 1H), 7.10 – 7.03 (m, 2H), 6.99 (td, *J* = 7.5, 1.0 Hz, 1H), 6.92 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.90 – 6.85 (m, 2H), 6.69 (d, *J* = 7.7 Hz, 1H), 4.16 (d, *J* = 2.6 Hz, 1H), 3.44 (s, 3H), 3.29 (d, *J* = 16.7 Hz, 1H), 3.08 (s, 3H), 2.93 (d, *J* = 16.6 Hz, 1H), 2.27 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 176.9, 170.1, 162.5 (d, *J* = 247.0 Hz), 145.0, 131.3 (d, *J* = 8.1 Hz), 130.7 (d, *J* = 3.2 Hz), 129.0, 128.3, 123.8, 121.9, 114.7 (d, *J* = 21.6 Hz), 108.0, 80.8, 73.7, 53.0, 51.9, 44.2, 39.1, 26.2. **$^{19}$F NMR (471 MHz, $CDCl_3$)** δ -114.28. **IR** (KBr, $cm^{-1}$) *γ* 3299, 3010, 2953, 2925, 2853, 1715, 1612, 1508, 1494, 1470, 1377, 1353, 1224, 1176, 1160, 1091, 827, 753, 568, 543. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1172; **$[\alpha]^{20}_D$** = +44.7 (*c* = 0.54, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 10.21 min, $t_R$ (minor) = 12.80 min.

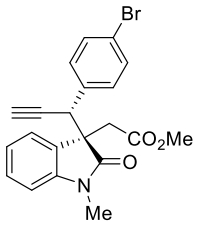
**Methyl 2-((*R*)-3-((*R*)-1-(4-chlorophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R,R*)-3ac)**




Yellow oil; 74% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.30 – 7.23 (m, 1H), 7.20 – 7.14 (m, 2H), 7.06 – 7.02 (m, 2H), 6.99 (td, *J* = 7.5, 1.0 Hz, 1H), 6.93 – 6.88 (m, 1H), 6.71 (dt, *J* = 7.8, 0.8 Hz, 1H), 4.15 (d, *J* = 2.6 Hz, 1H), 3.44 (s, 3H), 3.28 (d, *J* = 16.6 Hz, 1H), 3.09 (s, 3H), 2.91 (d, *J* = 16.5 Hz, 1H), 2.26 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 176.9, 170.0, 144.9, 133.9, 133.5, 131.0, 129.1, 128.0, 128.0, 123.8, 122.0, 108.1, 80.5, 73.8, 52.9, 51.9, 44.2, 39.1, 26.3. **IR** (KBr, $cm^{-1}$) *γ* 3298, 3055, 3011, 2952, 2925, 2853, 1715, 1613, 1493, 1470, 1377, 1352, 1198, 1175, 1091, 1016, 819, 753, 651, 592, 543, 491. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}ClNO_3Na)^+$: 390.0867, found: 390.0870; **$[\alpha]^{20}_D$** = +36.4 (*c* = 0.50, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e.

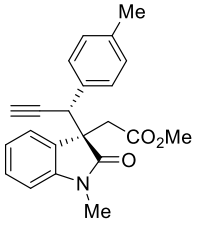
(CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (major) = 10.60 min, $t_R$ (minor) = 13.93 min.

**Methyl 2-((*R*)-3-((*R*)-1-(4-bromophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*R*)-3ad)**




Yellow oil; 74% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.36 – 7.30 (m, 2H), 7.29 – 7.23 (m, 1H), 7.02 – 6.95 (m, 3H), 6.93 – 6.87 (m, 1H), 6.71 (dt, *J* = 7.8, 0.7 Hz, 1H), 4.14 (d, *J* = 2.6 Hz, 1H), 3.44 (s, 3H), 3.27 (d, *J* = 16.5 Hz, 1H), 3.09 (s, 3H), 2.91 (d, *J* = 16.6 Hz, 1H), 2.25 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 176.9, 170.0, 144.9, 134.0, 131.4, 131.0, 129.1, 128.0, 123.9, 122.2, 122.0, 108.1, 80.4, 73.8, 52.8, 51.9, 44.3, 39.0, 26.3. **IR** (KBr, $cm^{-1}$) $\gamma$ 3295, 3011, 2952, 2925, 2853, 1715, 1613, 1488, 1470, 1377, 1352, 1199, 1175, 1091, 1012, 816, 753, 643, 543. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}BrNO_3Na)^+$: 434.0362, found: 434.0364; **$[\alpha]^{20}_D$** = +28.3 (*c* = 0.54, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (major) = 11.44 min, $t_R$ (minor) = 13.93 min.

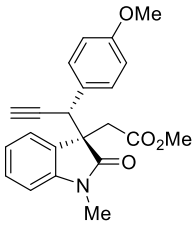
**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*R*)-1-(*p*-tolyl)prop-2-yn-1-yl)indolin-3-yl) acetate ((*R*,*R*)-3ae)**




White solid, m.p. 52 ℃; 75% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.29 – 7.24 (m, 1H), 7.04 (m, 4H), 6.96 (td, *J* = 7.5, 1.1 Hz, 1H), 6.82 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 4.12 (d, *J* = 2.6 Hz, 1H), 3.40 (s, 3H), 3.24 (d, *J* = 16.5 Hz, 1H), 3.15 (s, 3H), 2.86 (d, *J* = 16.6 Hz, 1H), 2.31 (s, 3H), 2.15 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.6, 170.1, 145.2, 137.8, 131.9, 129.8, 128.8, 128.6, 128.3, 124.2, 121.7, 107.8, 81.2, 72.9, 53.1, 51.8, 44.6, 39.2, 26.3, 21.2. **IR** (KBr, $cm^{-1}$) $\gamma$ 3290, 3009, 2952, 2924, 2854, 1715, 1613, 1496, 1470, 1377, 1352, 1261, 1197, 1175, 1091, 1022, 811, 753, 667, 642, 543. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_3Na)^+$: 370.1414, found: 370.1418; **$[\alpha]^{20}_D$** = +16.1 (*c* = 0.50, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IA,

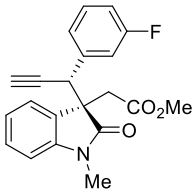
hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (minor) = 5.96 min, $t_R$ (major) = 7.44 min.

**Methyl 2-((*R*)-3-((*R*)-1-(4-methoxyphenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*R*)-3af)**




White solid, m.p. 85 ℃; 76% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.29 – 7.23 (m, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.97 (td, *J* = 7.5, 1.1 Hz, 1H), 6.85 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.76 (d, *J* = 8.7 Hz, 2H), 6.73 (d, *J* = 7.8 Hz, 1H), 4.11 (d, *J* = 2.6 Hz, 1H), 3.78 (s, 3H), 3.41 (s, 3H), 3.25 (d, *J* = 16.5 Hz, 1H), 3.13 (s, 3H), 2.87 (d, *J* = 16.5 Hz, 1H), 2.18 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.5, 170.1, 159.4, 145.2, 130.9, 128.8, 128.3, 126.9, 124.1, 121.7, 113.3, 107.9, 81.2, 73.0, 55.4, 53.2, 51.8, 44.2, 39.2, 26.3. **IR** (KBr, $cm^{-1}$) *γ* 3288, 3005, 2954, 2926, 2852, 1715, 1612, 1511, 1494, 1170, 1377, 1353, 1257, 1177, 1031, 825, 753, 667, 543. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_4Na)^+$: 386.1363, found: 386.1376; **$[\alpha]^{20}_D$** = +15.5 (*c* = 0.50, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 16.39 min, $t_R$ (minor) = 18.68 min.

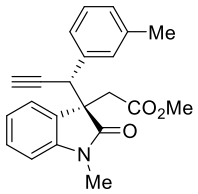
**Methyl 2-((*R*)-3-((*R*)-1-(3-fluorophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*R*)-3ag)**




White solid, m.p. 50-60 ℃; 77% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.30 – 7.24 (m, 1H), 7.17 (td, *J* = 7.9, 6.1 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 6.97 – 6.93 (m, 1H), 6.91 (d, *J* = 7.7 Hz, 2H), 6.85 (dd, *J* = 10.0, 2.3 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 4.18 (d, *J* = 2.6 Hz, 1H), 3.44 (s, 3H), 3.27 (d, *J* = 16.5 Hz, 1H), 3.10 (s, 3H), 2.92 (d, *J* = 16.5 Hz, 1H), 2.25 (d, *J* = 2.4 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 176.9, 170.0, 162.3 (d, *J* = 246.2 Hz), 145.0, 137.5 (d, *J* = 7.3 Hz), 129.2 (d, *J* = 8.2 Hz), 129.1, 128.1, 125.5 (d, *J* = 3.1 Hz), 123.9, 122.0, 116.8 (d, *J* = 22.5 Hz), 115.0 (d, *J* = 21.1 Hz), 108.0, 80.4, 73.8, 52.9, 51.9, 44.6 (d, *J* = 1.9 Hz), 39.1, 26.3. **$^{19}$F NMR (471 MHz, $CDCl_3$)** δ -113.14. **IR** (KBr, $cm^{-1}$) *γ* 3299, 3016, 2953, 2925, 2853, 1715, 1613,

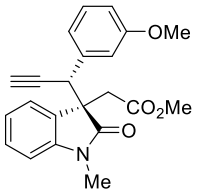
1589, 1493, 1470, 1377, 1352, 1261, 1205, 1177, 1131, 1090, 1027, 764, 754, 693, 650, 542. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1172; $[\alpha]^{20}_D$ = +37.8 (*c* = 0.59, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 9.87 min, $t_R$ (minor) = 13.97 min.

**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*R*)-1-(*m*-tolyl)prop-2-yn-1-yl)indolin-3-yl) acetate ((*R*,*R*)-3ah)**




White solid, m.p. 98 ℃; 66% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.29 – 7.23 (m, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 6.99 – 6.91 (m, 3H), 6.83 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 4.12 (d, *J* = 2.5 Hz, 1H), 3.41 (s, 3H), 3.26 (d, *J* = 16.5 Hz, 1H), 3.13 (s, 3H), 2.87 (d, *J* = 16.5 Hz, 1H), 2.28 (s, 3H), 2.17 (d, *J* = 2.4 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.5, 170.1, 145.2, 137.6, 134.8, 130.6, 128.8, 128.7, 128.3, 127.8, 127.0, 124.2, 121.6, 107.8, 81.1, 73.0, 53.1, 51.8, 44.9, 39.2, 26.3, 21.4. **IR** (KBr, $cm^{-1}$) *γ* 3289, 3021, 2952, 2924, 2853, 1715, 1613, 1494, 1470, 1377, 1353, 1261, 1203, 1176, 1091, 795, 755, 701, 543, 487. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_3Na)^+$: 370.1414, found: 370.1419; $[\alpha]^{20}_D$ = +36.7 (*c* = 0.44, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 85/15, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 17.39 min, $t_R$ (minor) = 27.59 min.

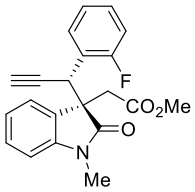
**Methyl 2-((*R*)-3-((*R*)-1-(3-methoxyphenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*R*)-3ai)**




White solid, m.p. 58-64 ℃; 75% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.29 – 7.23 (m, 1H), 7.15 (t, *J* = 7.9 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.4 Hz, 1H), 6.81 – 6.76 (m, 2H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.63 (d, *J* = 2.1 Hz, 1H), 4.14 (d, *J* = 2.5 Hz, 1H), 3.69 (s, 3H), 3.42 (s, 3H), 3.25 (d, *J* = 16.5 Hz, 1H), 3.12 (s, 3H), 2.90 (d, *J* = 16.5 Hz, 1H), 2.19 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.4, 170.1, 159.1,

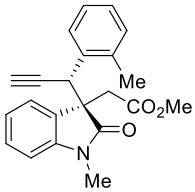
145.2, 136.4, 128.9, 128.9, 128.3, 124.2, 122.3, 121.7, 115.2, 114.0, 107.9, 80.9, 73.2, 55.3, 53.1, 51.8, 45.0, 39.2, 26.3. **IR** (KBr, $cm^{-1}$) $\gamma$ 3286, 2962, 2853, 1712, 1610, 1469, 1434, 1376, 1350, 1261, 1090, 1025, 865, 797, 754, 697, 542, 487. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_4Na)^+$: 386.1363, found: 386.1372; $[\alpha]^{20}_D$ = +34.7 (*c* = 0.58, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 14.03 min, $t_R$ (minor) = 20.86 min.

**Methyl 2-((*R*)-3-((*S*)-1-(2-fluorophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*S*)-3aj)**




White solid, m.p. 105 ℃; 60% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.35 (td, *J* = 7.6, 1.7 Hz, 1H), 7.27 (q, *J* = 5.9, 4.3 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.00 – 6.93 (m, 2H), 6.86 (d, *J* = 7.4 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 4.59 (d, *J* = 2.6 Hz, 1H), 3.37 (d, *J* = 17.5 Hz, 4H), 3.21 (s, 3H), 2.85 (d, *J* = 16.6 Hz, 1H), 2.12 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.3, 170.1, 160.2 (d, *J* = 247.3 Hz), 145.1, 131.7 (d, *J* = 3.0 Hz), 130.0 (d, *J* = 8.3 Hz), 129.0, 127.8, 124.4, 123.9 (d, *J* = 3.7 Hz), 122.6 (d, *J* = 13.8 Hz), 121.7, 115.2 (d, *J* = 22.7 Hz), 107.8, 80.5, 72.5, 53.1, 51.8, 38.4 (d, *J* = 2.5 Hz), 36.9 (d, *J* = 2.8 Hz), 26.4. **$^{19}$F NMR (471 MHz, $CDCl_3$)** δ -115.00. **IR** (KBr, $cm^{-1}$) $\gamma$ 3269, 3056, 3011, 2924, 2853, 1715, 1613, 1613, 1491, 1470, 1377, 1352, 1198, 1094, 1029, 802, 754, 677. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1171; $[\alpha]^{20}_D$ = +8.2 (*c* = 0.33, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IC, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 10.49 min, $t_R$ (minor) = 13.34 min.

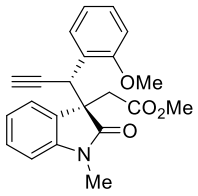
**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*R*)-1-(*o*-tolyl)prop-2-yn-1-yl)indolin-3-yl) acetate ((*R*,*R*)-3ak)**




White solid, m.p. 130 ℃; 52% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.39 – 7.34 (m, 1H), 7.30 – 7.24 (m, 1H), 7.18 – 7.14 (m, 2H), 7.11 – 7.07 (m, 1H), 7.02 (dd, *J* = 7.4, 1.5 Hz, 1H), 6.97 (dd, *J*

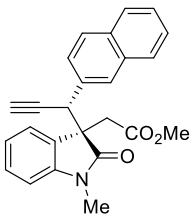
= 8.0, 6.8 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 4.46 (d, *J* = 2.6 Hz, 1H), 3.36 (s, 3H), 3.27 (d, *J* = 16.3 Hz, 1H), 3.21 (s, 3H), 2.85 (d, *J* = 16.2 Hz, 1H), 2.30 (s, 3H), 2.11 (d, *J* = 2.4 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.8, 170.1, 145.1, 136.4, 133.9, 130.6, 130.5, 129.0, 128.3, 128.0, 125.7, 124.8, 121.5, 107.8, 82.1, 72.2, 53.7, 51.8, 40.1, 38.2, 26.4, 20.3. **IR** (KBr, $cm^{-1}$) *γ* 3289, 3054, 3020, 2925, 2853, 1715, 1612, 1493, 1470, 1436, 1377, 1351, 1262, 1197, 1175, 1090, 1028, 894, 753, 543, 488. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_3Na)^+$: 370.1414, found: 370.1419; **$[\alpha]^{20}_D$** = -7.2 (*c* = 0.34, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 97% e.e. (CHIRALPAK IA, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 10.46 min, $t_R$ (minor) = 11.57 min.

**Methyl 2-((*R*)-3-((*R*)-1-(2-methoxyphenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*R*)-3al)**



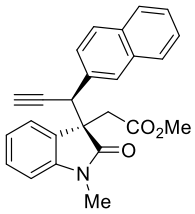

White solid, m.p. 141-146 ℃; 48% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.30 – 7.23 (m, 3H), 6.93 (q, *J* = 7.6 Hz, 2H), 6.84 (d, *J* = 7.4 Hz, 1H), 6.79 (dd, *J* = 16.6, 8.0 Hz, 2H), 4.81 (d, *J* = 2.6 Hz, 1H), 3.79 (s, 3H), 3.40 (d, *J* = 16.7 Hz, 1H), 3.35 (s, 3H), 3.23 (s, 3H), 2.74 (d, *J* = 16.7 Hz, 1H), 2.02 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 178.0, 170.5, 156.8, 145.3, 131.4, 129.4, 128.7, 128.3, 124.7, 123.8, 121.3, 120.2, 110.4, 107.6, 81.9, 71.5, 55.3, 53.5, 51.6, 38.3, 36.5, 26.4. **IR** (KBr, $cm^{-1}$) *γ* 3290, 2961, 2924, 2853, 1713, 1612, 1493, 1469, 1176, 1351, 1261, 1091, 1026, 799, 752, 665, 607, 542, 490. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_4Na)^+$: 386.1363, found: 386.1374; **$[\alpha]^{20}_D$** = -27.1 (*c* = 0.31, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 98% e.e. (CHIRALPAK IA, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (major) = 4.94 min, $t_R$ (minor) = 5.71 min.

**Methyl 2-((*R*)-1-methyl-3-((*R*)-1-(naphthalen-2-yl)prop-2-yn-1-yl)-2-oxoindolin-3-yl)acetate ((*R*,*R*)-3am)**



White solid, m.p. 150-153 ℃; 87% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.82 – 7.78 (m, 1H), 7.77 – 7.73 (m, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 1.8 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.32 – 7.21 (m, 2H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 7.4 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 4.35 (d, *J* = 2.6 Hz, 1H), 3.41 (s, 3H), 3.34 (d, *J* = 16.5 Hz, 1H), 3.11 (s, 3H), 2.93 (d, *J* = 16.5 Hz, 1H), 2.25 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.4, 170.1, 145.2, 133.0, 132.9, 132.5, 129.1, 128.9, 128.2, 128.1, 127.6, 127.6, 127.4, 126.4, 126.3, 124.2, 121.8, 107.9, 81.0, 73.4, 53.3, 51.8, 45.1, 39.3, 26.3. **IR** (KBr, $cm^{-1}$) *γ* 3292, 3056, 3012, 2952, 2925, 2853, 1715, 1613, 1494, 1470, 1436, 1376, 1352, 1201, 1176, 1090, 1018, 818, 751, 654, 543, 480. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{25}H_{21}NO_3Na)^+$: 406.1414, found: 406.1420; **$[\alpha]^{20}_D$** = +2.6 (*c* = 0.49, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 15.75 min, $t_R$ (minor) = 22.76 min.

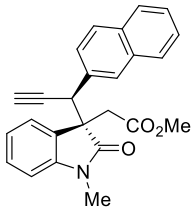
**Methyl 2-((*R*)-1-methyl-3-((*S*)-1-(naphthalen-2-yl)prop-2-yn-1-yl)-2-oxoindolin-3-yl)acetate ((*R*,*S*)-3am)**



White solid, m.p. 145-151 ℃; 67% yield; 95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.71 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.68 – 7.65 (m, 1H), 7.59 (dd, *J* = 7.1, 2.3 Hz, 1H), 7.44 (d, *J* = 8.6 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.34 (d, *J* = 1.9 Hz, 1H), 7.17 (td, *J* = 7.7, 1.3 Hz, 1H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 6.94 (dd, *J* = 8.6, 1.9 Hz, 1H), 6.37 – 6.32 (m, 1H), 4.31 (d, *J* = 2.6 Hz, 1H), 3.63 (d, *J* = 16.7 Hz, 1H), 3.46 (s, 3H), 3.34 (d, *J* = 16.7 Hz, 1H), 2.66 (s, 3H), 2.57 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.0, 170.3, 144.4, 132.7, 132.0, 129.0, 128.1, 128.0, 127.8, 127.4, 126.7, 126.5, 126.0, 125.9, 123.9, 122.1, 107.8, 82.3, 74.5, 53.6, 51.9, 45.1, 39.8, 25.9. **IR** (KBr, $cm^{-1}$) *γ* 3293, 3056, 3012, 2960, 2923, 2852, 1740, 1712, 1613, 1494, 1470, 1377, 1353, 1261, 1200, 1177, 1092, 1027, 859, 816, 752, 682, 543, 479. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{25}H_{21}NO_3Na)^+$: 406.1414, found: 406.1413; **$[\alpha]^{20}_D$** = +23.7 (*c* = 0.43, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e.

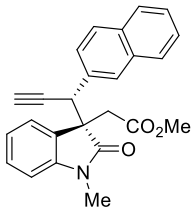
(CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 11.34 min, $t_R$ (minor) = 13.08 min.

**Methyl 2-((*S*)-1-methyl-3-((*S*)-1-(naphthalen-2-yl)prop-2-yn-1-yl)-2-oxoindolin-3-yl)acetate ((*S,S*)-3am)**



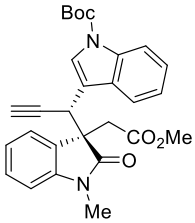

White solid, m.p. 150-153 ℃; 87% yield; >95:5 d.r.; Spectral data were in agreement with those of the enantiomer reported above. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{25}H_{21}NO_3Na)^+$: 406.1414, found: 406.1418; $[\alpha]^{20}_D$ = -3.9 (c = 0.55, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (minor) = 15.83 min, $t_R$ (major) = 21.04 min.

**Methyl 2-((*S*)-1-methyl-3-((*R*)-1-(naphthalen-2-yl)prop-2-yn-1-yl)-2-oxoindolin-3-yl)acetate ((*S,R*)-3am)**




White solid, m.p. 145-151 ℃; 63% yield; 95:5 d.r.; Spectral data were in agreement with those of the enantiomer reported above. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{25}H_{21}NO_3Na)^+$: 406.1414, found: 406.1422; $[\alpha]^{20}_D$ = -29.3 (*c* = 0.42, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (minor) = 11.36 min, $t_R$ (major) = 12.99 min.

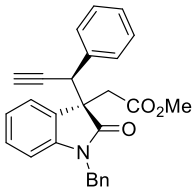
***tert*-Butyl 3-((*R*)-1-((*R*)-3-(2-methoxy-2-oxoethyl)-1-methyl-2-oxoindolin-3-yl) prop-2-yn-1-yl)-1*H*-indole-1-carboxylate ((*R,R*)-3an)**




Yellow oil; 66% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 8.12 (d, *J* = 8.3 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.38 (s, 1H), 7.32 – 7.27 (m, 2H), 7.23 – 7.15 (m, 1H), 6.95 (q, *J* = 4.1, 3.5 Hz, 2H), 6.79 (d, *J* = 7.8 Hz, 1H), 4.44 (d, *J* = 2.7 Hz, 1H), 3.38 (s, 3H), 3.27 (d, *J* = 16.4 Hz, 1H), 3.18 (s, 3H), 2.93 (d, *J* = 16.4 Hz, 1H), 2.11 (d, *J* = 2.6 Hz, 1H), 1.67 (s, 9H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.7, 170.0, 149.5, 145.3, 135.2, 129.5, 129.0, 128.5, 126.5, 124.7, 124.2, 122.7, 121.8, 120.2, 115.3, 115.0, 107.9, 84.1, 80.5,

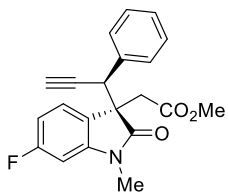
72.1, 53.3, 51.7, 39.1, 36.5, 28.3, 26.4. **IR** (KBr, $cm^{-1}$) $\gamma$ 3304, 3054, 3008, 2929, 2854, 1732, 1613, 1564, 1494, 1470, 1452, 1359, 1308, 1255, 1156, 1084, 1020, 854, 750, 666, 543, 487. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{28}H_{28}N_2O_5Na)^+$: 495.1890, found: 495.1894; $[\alpha]^{20}_D$ = +50.8 (*c* = 0.55, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 9.31 min, $t_R$ (minor) = 22.57 min.

**Methyl 2-((*R*)-1-benzyl-2-oxo-3-((*S*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R,S*)-3ca)**




Yellow solid, m.p. 86 ℃; 62% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.74 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.21 – 7.11 (m, 4H), 7.11 – 7.01 (m, 4H), 6.93 – 6.89 (m, 2H), 6.67 (dd, *J* = 7.4, 2.1 Hz, 2H), 6.30 (dd, *J* = 7.4, 1.3 Hz, 1H), 4.65 (d, *J* = 16.1 Hz, 1H), 4.49 (d, *J* = 16.1 Hz, 1H), 4.21 (d, *J* = 2.6 Hz, 1H), 3.65 (d, *J* = 16.4 Hz, 1H), 3.42 (s, 3H), 3.33 (d, *J* = 16.4 Hz, 1H), 2.53 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 177.2, 170.1, 144.0, 135.5, 134.9, 129.2, 128.9, 128.6, 127.9, 127.8, 127.7, 127.2, 126.8, 124.1, 122.2, 109.2, 82.6, 74.2, 53.4, 51.8, 45.0, 44.0, 40.7. **IR** (KBr, $cm^{-1}$) $\gamma$ 3290, 3060, 3030, 2923, 2853, 1741, 1716, 1613, 1488, 1467, 1455, 1355, 1262, 1198, 1175, 1101, 1079, 1013, 800, 753, 697, 651, 552. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{27}H_{23}NO_3Na)^+$: 432.1570, found: 432.1574; $[\alpha]^{20}_D$ = -11.1 (*c* = 0.53, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IE, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 9.57 min, $t_R$ (minor) = 12.03 min.

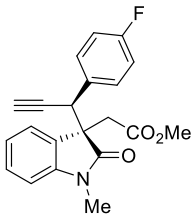
**Methyl 2-((*R*)-6-fluoro-1-methyl-2-oxo-3-((*S*)-1-phenylprop-2-yn-1-yl)indolin-3-yl)acetate ((*R,S*)-3ka)**




White solid, m.p. 55 ℃; 56% yield; 91:9 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.57 (dd, *J* = 8.2, 5.4 Hz, 1H), 7.12 – 7.06 (m, 1H), 7.05 – 6.98 (m, 2H), 6.87 – 6.82 (m, 2H), 6.74 (ddd, *J* = 9.5, 8.2, 2.4 Hz, 1H), 6.21 (dd, *J* = 8.9, 2.3 Hz, 1H), 4.10 (d, *J* = 2.7 Hz, 1H),

3.56 (d, *J* = 16.8 Hz, 1H), 3.47 (s, 3H), 3.27 (d, *J* = 16.8 Hz, 1H), 2.75 (s, 3H), 2.52 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.3, 170.2, 163.7 (d, *J* = 245.3 Hz), 146.0, (d, *J* = 11.8 Hz).134.2, 128.7, 127.8, 127.5, 124.9, 123.2 (d, *J* = 3.1 Hz), 108.2, 96.6 (d, *J* = 27.6 Hz), 82.1, 74.4, 53.3, 51.9, 45.0, 39.7, 26.0. **$^{19}$F NMR (471 MHz, $CDCl_3$)** δ -111.24. **IR** (KBr, $cm^{-1}$) *γ* 3297, 3063, 3031, 2956, 2923, 2853, 1721, 1615, 1504, 1437, 1380, 1261, 1246, 1198, 1177, 1086, 1024, 972, 936, 834, 797, 758, 699, 544. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1172; **$[\alpha]^{20}_D$** = -46.8 (*c* = 0.44, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 12.91 min, $t_R$ (minor) = 14.82 min.

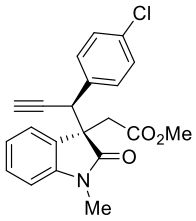
**Methyl 2-((*R*)-3-((*S*)-1-(4-fluorophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*S*)-3ab)**




White solid, m.p. 86 ℃; 64% yield; 95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.63 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.22 (td, *J* = 7.7, 1.3 Hz, 1H), 7.06 (td, *J* = 7.5, 1.0 Hz, 1H), 6.81 (dd, *J* = 8.7, 5.4 Hz, 2H), 6.67 (t, *J* = 8.7 Hz, 2H), 6.49 (d, *J* = 7.8 Hz, 1H), 4.12 (d, *J* = 2.7 Hz, 1H), 3.56 (d, *J* = 16.6 Hz, 1H), 3.44 (s, 3H), 3.26 (d, *J* = 16.7 Hz, 1H), 2.81 (s, 3H), 2.53 (d, *J* = 2.7 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 176.8, 170.0, 162.2 (d, *J* = 246.4 Hz), 144.3, 130.3 (d, *J* = 8.1 Hz), 130.2 (d, *J* = 3.2 Hz), 129.0, 127.4, 123.7, 122.0, 114.1 (d, *J* = 21.4 Hz), 107.7, 81.9, 74.4, 53.4, 51.7, 44.1, 39.6, 25.9. **$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -114.68. **IR** (KBr, $cm^{-1}$) *γ* 3299, 3012, 2922, 2852, 1741, 1710, 1612, 1508, 1469, 1376, 1354, 1224, 1177, 1160, 1093, 1028, 839, 753, 681, 567, 542. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}FNO_3Na)^+$: 374.1163, found: 374.1168; **$[\alpha]^{20}_D$** = -52.7 (*c* = 0.38, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 6.49 min, $t_R$ (minor) = 7.17 min.

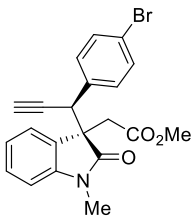
**Methyl 2-((*R*)-3-((*S*)-1-(4-chlorophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-**

**yl)acetate ((*R*,*S*)-3ac)**



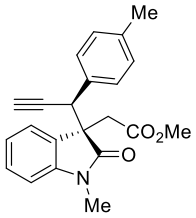

Yellow oil; 51% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.62 (d, *J* = 7.4 Hz, 1H), 7.23 (td, *J* = 7.7, 1.3 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.99 – 6.93 (m, 2H), 6.82 – 6.75 (m, 2H), 6.51 (d, *J* = 7.8 Hz, 1H), 4.11 (d, *J* = 2.6 Hz, 1H), 3.55 (d, *J* = 16.7 Hz, 1H), 3.44 (s, 3H), 3.26 (d, *J* = 16.7 Hz, 1H), 2.83 (s, 3H), 2.52 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 176.84, 170.11, 144.37, 133.62, 133.15, 130.14, 129.15, 127.53, 127.44, 123.87, 122.18, 107.96, 81.82, 74.60, 53.47, 51.87, 44.35, 39.76, 26.02. **IR** (KBr, $cm^{-1}$) *γ* 3294, 3055, 2953, 2925, 2853, 1742, 1713, 1613, 1493, 1470, 1376, 1352, 1260, 1199, 1177, 1092, 1016, 832, 753, 678, 542, 468. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}ClNO_3Na)^+$: 390.0867, found: 390.0875; **$[\alpha]^{20}_D$** = -20.9 (*c* = 0.34, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (major) = 6.98 min, $t_R$ (minor) = 7.85 min.

**Methyl 2-((*R*)-3-((*S*)-1-(4-bromophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*S*)-3ad)**



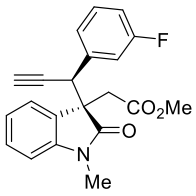

Yellow oil; 50% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.62 (d, *J* = 7.4 Hz, 1H), 7.23 (td, *J* = 7.8, 1.3 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.74 – 6.69 (m, 2H), 6.52 (d, *J* = 7.8 Hz, 1H), 4.09 (d, *J* = 2.6 Hz, 1H), 3.55 (d, *J* = 16.6 Hz, 1H), 3.44 (s, 3H), 3.25 (d, *J* = 16.7 Hz, 1H), 2.83 (s, 3H), 2.52 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 176.82, 170.09, 144.37, 133.68, 131.39, 130.49, 129.16, 127.41, 123.87, 122.19, 121.84, 107.99, 81.75, 74.61, 53.40, 51.87, 44.41, 39.77, 26.03. **IR** (KBr, $cm^{-1}$) *γ* 3293, 3055, 3009, 2953, 2924, 2853, 1742, 1712, 1613, 1489, 1470, 1376, 1352, 1260, 1200, 1177, 1192, 1073, 1012, 810, 753, 667, 542. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{18}BrNO_3Na)^+$: 434.0362, found: 434.0367; **$[\alpha]^{20}_D$** = -9.5 (*c* = 0.40, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (major) = 7.30 min, $t_R$ (minor) = 8.49 min.

**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*S*)-1-(*p*-tolyl)prop-2-yn-1-yl)indolin-3-yl) acetate ((*R*,*S*)-3ae)**




White solid, m.p. 50-55 ℃; 50% yield; 92:8 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.63 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.21 (td, *J* = 7.7, 1.3 Hz, 1H), 7.05 (td, *J* = 7.5, 1.0 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 2H), 6.74 – 6.69 (m, 2H), 6.48 (d, *J* = 7.7 Hz, 1H), 4.09 (d, *J* = 2.6 Hz, 1H), 3.56 (d, *J* = 16.7 Hz, 1H), 3.44 (s, 3H), 3.26 (d, *J* = 16.7 Hz, 1H), 2.80 (s, 3H), 2.49 (d, *J* = 2.6 Hz, 1H), 2.17 (s, 3H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.1, 170.3, 144.5, 137.3, 131.5, 128.8, 128.6, 128.1, 127.9, 123.9, 122.0, 107.7, 82.5, 74.0, 53.5, 51.8, 44.7, 39.8, 26.0, 21.1. **IR** (KBr, $cm^{-1}$) *γ* 3287, 3055, 3009, 2922, 2852, 1743, 1714, 1613, 1512, 1494, 1470, 1437, 1377, 1354, 1259, 1199, 1177, 1093, 1023, 811, 753, 682, 543. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{22}H_{21}NO_3Na)^+$: 370.1414, found: 370.1421; **$[\alpha]^{20}_D$** = -27.5 (*c* = 0.33, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 7.30 min, $t_R$ (minor) = 9.21 min.

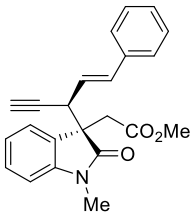
**Methyl 2-((*R*)-3-((*S*)-1-(3-fluorophenyl)prop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl)acetate ((*R*,*S*)-3ag)**




White solid, m.p. 68 ℃; 50% yield; 94:6 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.62 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.23 (td, *J* = 7.8, 1.3 Hz, 1H), 7.07 (td, *J* = 7.5, 1.0 Hz, 1H), 6.98 (td, *J* = 8.0, 6.0 Hz, 1H), 6.77 (tdd, *J* = 8.4, 2.6, 1.0 Hz, 1H), 6.70 (dt, *J* = 7.7, 1.3 Hz, 1H), 6.56 – 6.47 (m, 2H), 4.13 (d, *J* = 2.6 Hz, 1H), 3.56 (d, *J* = 16.6 Hz, 1H), 3.45 (s, 3H), 3.26 (d, *J* = 16.6 Hz, 1H), 2.82 (s, 3H), 2.54 (d, *J* = 2.6 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 176.8, 170.1, 161.9 (d, *J* = 245.4 Hz), 144.4, 137.1 (d, *J* = 7.6 Hz), 129.2, 128.7 (d, *J* = 8.1 Hz), 127.5, 124.7 (d, *J* = 2.9 Hz), 123.8, 122.2, 115.7 (d, *J* = 22.7 Hz), 114.6 (d, *J* = 21.2 Hz), 107.8, 81.7, 74.7, 53.5, 51.9, 44.6 (d, *J* = 1.9 Hz), 39.7, 26.0. **$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -113.89. **IR** (KBr, $cm^{-1}$) *γ* 3299, 3057, 3010, 2922, 2852, 1741, 1713, 1614, 1589, 1494, 1471, 1450, 1377, 1355, 1263, 1204, 1178, 1135, 1092, 872, 753, 691, 542, 522. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for

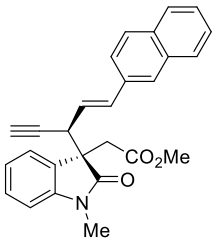
($C_{21}H_{18}FNO_3Na$)$^+$: 374.1163, found: 374.1172; **[α]$^{20}_D$** = -55.7 (*c* = 0.34, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 7.09 min, $t_R$ (minor) = 7.70 min.

**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*R,E*)-1-phenylpent-1-en-4-yn-3-yl)indolin-3-yl) acetate ((*R,R*)-3ao)**




colorless liquid; 44% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.54 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.30 (td, *J* = 7.8, 1.3 Hz, 1H), 7.25 – 7.12 (m, 3H), 7.18 – 7.02 (m, 3H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.46 (d, *J* = 15.7 Hz, 1H), 5.49 (dd, *J* = 15.7, 8.1 Hz, 1H), 3.71 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 3.44 (d, *J* = 16.5 Hz, 1H), 3.44 (s, 3H), 3.17 (d, *J* = 16.7 Hz, 1H), 3.15 (s, 3H), 2.47 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 177.4, 170.2, 144.6, 136.5, 134.3, 129.0, 128.5, 128.2, 127.8, 126.5, 123.7, 122.8, 122.4, 108.0, 81.3, 74.5, 52.4, 51.8, 42.4, 39.7, 26.5. **IR** (KBr, $cm^{-1}$) γ 2929, 2387, 1959, 1713, 1613, 1494, 1470, 1435, 1377, 1350, 1176, 1091, 753, 697, 451, 434, 425. **HRMS** (ESI) m/z (M+Na)$^+$: calculated for ($C_{23}H_{21}NO_3Na$)$^+$: 382.1414, found: 382.1424; **[α]$^{20}_D$** = -67.0 (*c* = 0.21, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 10.68 min, $t_R$ (minor) = 11.74 min.

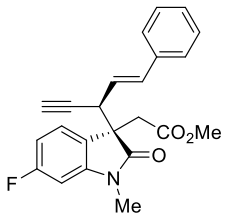
**Methyl 2-((*R*)-1-methyl-3-((*R,E*)-1-(naphthalen-2-yl)pent-1-en-4-yn-3-yl)-2-oxoindolin-3-yl)acetate ((*R,R*)-3ap)**




colorless liquid; 40% yield; >95:5 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.73 (td, *J* = 7.2, 2.5 Hz, 2H), 7.66 (d, *J* = 8.6 Hz, 1H), 7.58 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.53 – 7.50 (m, 1H), 7.42 (tt, *J* = 6.9, 5.1 Hz, 2H), 7.30 (td, *J* = 7.7, 1.2 Hz, 1H), 7.23 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.09 (td, *J* = 7.6, 1.0 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.61 (d, *J* = 15.6 Hz, 1H), 5.63 (dd, *J* = 15.7, 8.1 Hz, 1H), 3.77 (dt, *J* = 8.1, 1.6 Hz, 1H), 3.46 (d, *J* = 16.6 Hz, 1H), 3.46 (s, 3H), 3.20 (d, *J* = 16.6 Hz, 1H), 3.14 (s, 3H), 2.50 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.4, 170.2, 144.6, 134.4, 133.9, 133.5, 133.1, 129.1,

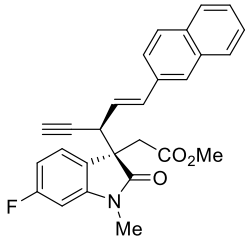
128.2, 128.1, 127.7, 126.6, 126.4, 126.1, 123.8, 123.5, 123.1, 122.5, 108.0, 81.3, 74.5, 52.5, 51.9, 42.5, 39.7, 26.4. **IR** (KBr, $cm^{-1}$) $\gamma$ 3461, 2924, 1959, 1713, 1613, 1494, 1469, 1378, 1261, 1203, 1179, 1092, 810, 754, 476. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{27}H_{23}NO_3Na)^+$: 432.1570, found: 432.1752; $[\alpha]^{20}_D$ = -11.0 (*c* = 0.26, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (minor) = 16.43 min, $t_R$ (minor) = 18.12 min.

**Methyl 2-((*R*)-6-fluoro-1-methyl-2-oxo-3-((*R,E*)-1-phenylpent-1-en-4-yn-3-yl) indolin-3-yl)acetate ((*R,R*)-3ko)**




colorless liquid; 41% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.48 (dd, *J* = 8.2, 5.4 Hz, 1H), 7.25 – 7.16 (m, 3H), 7.13 – 7.06 (m, 2H), 6.74 (ddd, *J* = 9.6, 8.2, 2.4 Hz, 1H), 6.53 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.46 (d, *J* = 15.7 Hz, 1H), 5.49 (dd, *J* = 15.7, 8.0 Hz, 1H), 3.68 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 3.47 (s, 3H), 3.42 (d, *J* = 16.7 Hz, 1H), 3.15 (d, *J* = 16.7 Hz, 1H), 3.13 (s, 4H), 2.47 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 177.7, 170.1, 163.7 (d, *J* = 245.5 Hz), 146.2 (d, *J* = 11.8 Hz), 136.4, 134.6, 128.6, 128.0, 126.5, 124.8 (d, *J* = 9.8 Hz), 123.5, 122.5, 108.5 (d, *J* = 22.3 Hz), 97.0 (d, *J* = 27.7 Hz), 81.1, 74.6, 52.1, 51.9, 42.4, 39.8, 26.6. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -111.16. **IR** (KBr, $cm^{-1}$) $\gamma$ 3467, 2962, 1959, 1720, 1618, 1503, 1467, 1382, 1261, 1180, 1089, 938, 802, 695, 545. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{23}H_{20}FNO_3Na)^+$: 400.1319, found: 400.1327; $[\alpha]^{20}_D$ = -55.0 (*c* = 0.20, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 8.10 min, $t_R$ (minor) = 9.19 min.

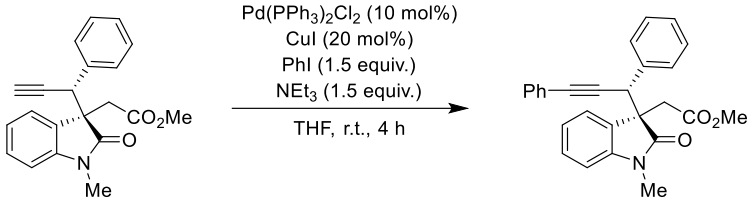
**Methyl 2-((*R*)-6-fluoro-1-methyl-3-((*R,E*)-1-(naphthalen-2-yl)pent-1-en-4-yn-3-yl) -2-oxoindolin-3-yl)acetate ((*R,R*)-3kp)**




colorless liquid; 41% yield; >95:5 d.r.; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.74 (dd, *J* = 8.4, 5.9 Hz, 2H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.47 – 7.38 (m, 2H), 7.26 – 7.22 (m, 1H),

6.76 (ddd, *J* = 9.6, 8.2, 2.3 Hz, 1H), 6.61 (d, *J* = 15.7 Hz, 1H), 6.52 (dd, *J* = 8.9, 2.3 Hz, 1H), 5.62 (dd, *J* = 15.7, 8.1 Hz, 1H), 3.74 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 3.48 (s, 3H), 3.45 (d, *J* = 16.6 Hz, 1H), 3.18 (d, *J* = 16.6 Hz, 1H), 3.12 (s, 3H), 2.50 (d, *J* = 2.5 Hz, 1H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 177.8, 170.1, 163.7 (d, *J* = 245.6 Hz), 146.2 (d, *J* = 11.7 Hz), 134.6, 133.7, 133.5, 133.2, 128.3, 128.1, 127.7, 126.7, 126.5, 126.2, 124.8 (d, *J* = 9.8 Hz), 123.5 (d, *J* = 3.0 Hz), 123.4, 122.7, 108.5 (d, *J* = 22.2 Hz), 97.0 (d, *J* = 27.5 Hz), 81.1, 74.7, 52.2, 51.9, 42.5, 39.7, 26.6. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -111.08. **IR** (KBr, $cm^{-1}$) *γ* 3466, 2925, 1959, 1720, 1612, 1504, 1453, 1381, 1264, 1171, 1088, 938, 812, 757, 666, 576, 545, 478. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{27}H_{23}FNO_3Na)^+$: 450.1476, found: 450.1479; **$[\alpha]^{20}_D$** = -8.2 (*c* = 0.20, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (minor) = 11.57 min, $t_R$ (major) = 13.18 min.

**Synthetic Applications**

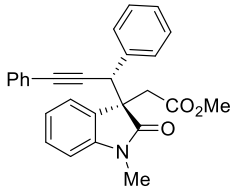



(*R*,*R*)-**3aa**
>99% e.e.

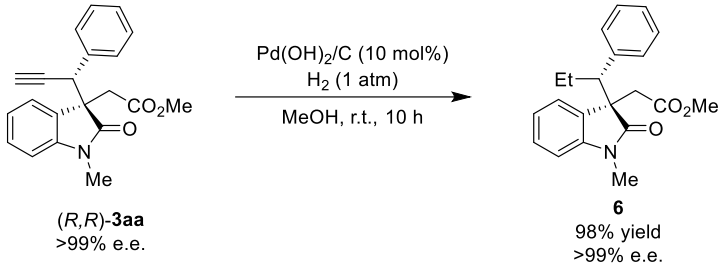
**5**
95% yield
>99% e.e.

To a flame-dried and $N_2$-purged Schlenk tube were added (*R*,*R*)-**3aa** (33.3 mg, 0.10 mmol, 1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (7.0 mg, 0.01 mmol, 10 mol%), and CuI (3.8 mg, 0.02 mmol, 20 mol%). The vial was then sealed, purged and backfilled with $N_2$ three times before adding $NEt_3$ (21 μL, 0.15 mmol, 1.5 equiv.), PhI (17 μL, 0.15 mmol, 1.5 equiv.) and THF (1.0 mL) at room temperature. The resulting mixture was stirred at room temperature under nitrogen atmosphere for 4 hours. After concentrated under reduced pressure, the residue was purified by column chromatography on silica gel to give **5** (38.9 mg, 95% yield, >99% e.e.).

**Methyl 2-((*R*)-3-((*S*)-1,3-diphenylprop-2-yn-1-yl)-1-methyl-2-oxoindolin-3-yl) acetate (5)**




Colorless oil; 95% yield; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.31 – 7.18 (m, 11H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.84 – 6.81 (m, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 4.33 (s, 1H), 3.41 (s, 3H), 3.31 (d, *J* = 16.5 Hz, 1H), 3.15 (s, 3H), 2.88 (d, *J* = 16.5 Hz, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.8, 170.1, 145.3, 135.5, 131.7, 130.1, 128.9, 128.4, 128.2, 128.1, 128.0, 128.0, 124.2, 123.1, 121.7, 107.8, 86.6, 85.2, 53.6, 51.8, 45.9, 39.1, 26.4. **IR** (KBr, $cm^{-1}$) $\gamma$ 3058, 3029, 2954, 2926, 2854, 1741, 1716, 1613, 1492, 1470, 1377, 1353, 1261, 1198, 1175, 1081, 1028, 801, 756, 700, 605, 543. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{27}H_{23}NO_3Na)^+$: 432.1570, found: 432.1569; **$[\alpha]^{20}_D$** = +131.3 (*c* = 0.72, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IA, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (minor) = 6.77 min, $t_R$ (major) = 7.78 min.

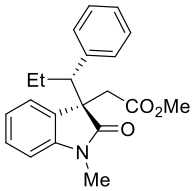



(*R*,*R*)-**3aa**
>99% e.e.

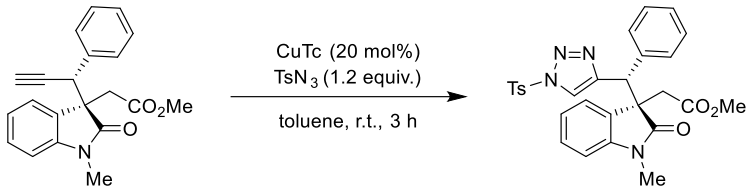
**6**
98% yield
>99% e.e.

To a stirring solution of (*R*,*R*)-**3aa** (33.3 mg, 0.10 mmol, 1.0 equiv.) in MeOH (5.0 mL) was slowly added palladium hydroxide-onactivated charcoal (10%; 20.0 mg) at room temperature. The resulting mixture was stirred at room temperature in an atmosphere of hydrogen gas for 6 hours. The mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give **6** (33.0 mg, 98% yield, >99%e.e.).

**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*R*)-1-phenylpropyl)indolin-3-yl)acetate (6)**

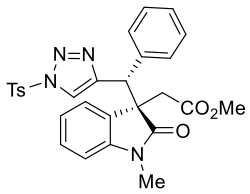



Colorless oil; 98% yield; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.31 – 7.21 (m, 4H), 7.09 (d, *J* = 6.5 Hz, 2H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.88 (dd, *J* = 7.3, 1.2 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 3.33 (s, 3H), 3.23 (s, 3H), 3.11 (d, *J* = 16.3 Hz, 1H), 3.01 (dd, *J* = 12.1, 3.6 Hz, 1H), 2.62 (d, *J* = 16.3 Hz, 1H), 1.55 (dqd, *J* = 14.6, 7.3, 3.5 Hz, 1H), 1.45 (ddq, *J* = 14.2, 12.1, 7.2 Hz, 1H), 0.59 (t, *J* = 7.3 Hz, 3H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 179.7, 170.4, 144.9, 138.2, 130.2, 129.5, 128.3, 128.0, 127.3, 124.5, 121.7, 107.8, 54.5, 53.5, 51.6, 40.7, 26.4, 21.2, 12.1. **IR** (KBr, $cm^{-1}$) $\gamma$ 3057, 3027, 2962, 2932, 2875, 1743, 1712, 1612, 1493, 1469, 1377, 1350, 1252, 1197, 1176, 1126, 1094, 1027, 755, 702, 679, 603, 543, 488. **$[\alpha]^{20}_D$** = -11.2 (*c* = 0.73, $CHCl_3$); **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{21}H_{23}NO_3Na)^+$: 360.1570, found: 360.1569; The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (minor) = 7.32 min, $t_R$ (major) = 9.08 min.

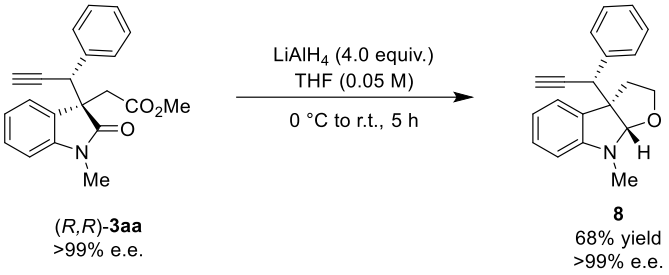



To a flame-dried and $N_2$-purged Schlenk tube were added (*R*,*R*)-**3aa** (33.3 mg, 0.10 mmol, 1.0 equiv.) and CuTc (3.8 mg, 0.02 mmol, 20 mol%). The vial was then sealed, purged and backfilled with $N_2$ three times before adding $TsN_3$ (23.7 mg, 0.12 mmol, 1.2 equiv.) and toluene (1.0 mL) at room temperature. The resulting mixture was stirred at room temperature under nitrogen atmosphere for 3 hours. After concentrated under reduced pressure, the residue was purified by column chromatography on silica gel to give **7** (47.2 mg, 89% yield, >99%e.e.).

**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*R*)-phenyl(1-tosyl-1*H*-1,2,3-triazol-4-yl)methyl) indolin-3-yl)acetate (7)**



White solid, m.p. 85-93 ℃; 89% yield; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 8.29 (s, 1H), 7.96 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.22 (td, *J* = 7.7, 1.3 Hz, 1H), 7.17 (d, *J* = 7.3 Hz, 1H), 7.15 – 7.06 (m, 5H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.53 (d, *J* = 7.8 Hz, 1H), 4.74 (s,1H), 3.34 (s, 3H), 2.99 (d, *J* = 16.4 Hz, 1H), 2.87 (s, 3H), 2.82 (d, *J* = 16.5 Hz, 1H), 2.43 (s, 3H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 177.7, 170.0, 147.3, 145.3, 144.4, 135.70, 133.2, 130.5, 129.7, 129.1, 129.0, 128.8, 128.0, 127.7, 123.8, 122.8, 122.3, 108.0, 52.9, 51.8, 50.8, 39.9, 26.0, 21.9. **IR** (KBr, $cm^{-1}$) *γ* 3012, 2926, 2854, 1741, 1707, 1613, 1496, 1471, 1381, 1356, 1202, 1174, 1122, 1033, 1009, 816, 753, 702, 682, 568, 490**. HRMS** (ESI) m/z $(M+H)^+$: calculated for $(C_{28}H_{27}N_4O_5S)^+$: 531.1697, found: 531.1707; **$[\alpha]^{20}_D$** = +77.8 (*c* = 0.73, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IA, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (minor) = 9.92 min, $t_R$ (major) = 11.81 min.

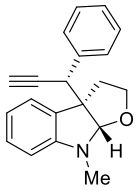



(*R,R*)-**3aa**
>99% e.e.

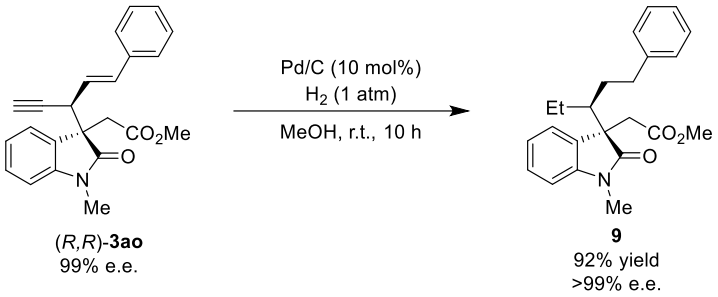
**8**
68% yield
>99% e.e.

Under nitrogen atmosphere, a solution of $LiAlH_4$ (15.2 mg, 0.4 mmol, 4.0 equiv.) in anhydrous THF (1.0 ml) was added dropwise to a solution of (*R,R*)-**3aa** (33.3 mg, 0.10 mmol, 1.0 equiv.) in anhydrous THF (1.0 mL) at 0 ℃. The resulting mixture was stirred at room temperature under nitrogen atmosphere for 5 hours. The reaction mixture was quenched with $Na_2SO_4$•$10H_2O$, filtered and extracted with ethyl acetate (10.0 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give **8** (19.6 mg, 68% yield, >99% e.e.).

**(*3aR,8aS*)-8-methyl-3a-((*R*)-1-phenylprop-2-yn-1-yl)-3,3a,8,8a-tetrahydro-2*H*-furo[2,3-*b*]indole (8)**

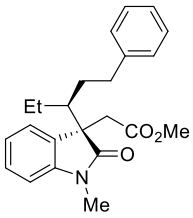



White solid, m.p. 96-100 ℃; 68% yield; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.21 (tt, *J* = 7.4, 3.1 Hz, 5H), 7.07 (td, *J* = 7.6, 1.3 Hz, 1H), 6.96 (dd, *J* = 7.3, 1.3 Hz, 1H), 6.63 (td, *J* = 7.4, 0.9 Hz, 1H), 6.23 (d, *J* = 7.8 Hz, 1H), 5.35 (s, 1H), 4.08 (d, *J* = 2.6 Hz, 1H), 3.96 (ddd, *J* = 8.5, 7.2, 1.2 Hz, 1H), 3.42 (ddd, *J* = 11.3, 8.5, 4.7 Hz, 1H), 2.78 (s, 3H), 2.65 (td, *J* = 11.5, 7.3 Hz, 1H), 2.34 (d, *J* = 2.5 Hz, 1H), 2.17 – 2.10 (m, 1H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 151.9, 137.0, 130.1, 129.2, 128.9, 127.8, 127.5, 124.3, 116.9, 105.3, 101.2, 83.5, 72.7, 67.5, 60.7, 44.4, 38.3, 31.1. **IR** (KBr, $cm^{-1}$) $\gamma$ 3290, 3054, 3029, 2924, 2870, 1659, 1607, 1495, 1453, 1390, 1303, 1262, 1220, 1156, 1108, 1011, 931, 913, 799, 750, 702, 648, 601. **HRMS** (ESI) m/z $(M+H)^+$: calculated for $(C_{20}H_{20}NO)^+$: 290.1539, found: 290.1538; **$[\alpha]^{20}_D$**=-141.2 (*c* = 0.38, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 80/20, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 4.38 min, $t_R$ (major) = 4.74 min.

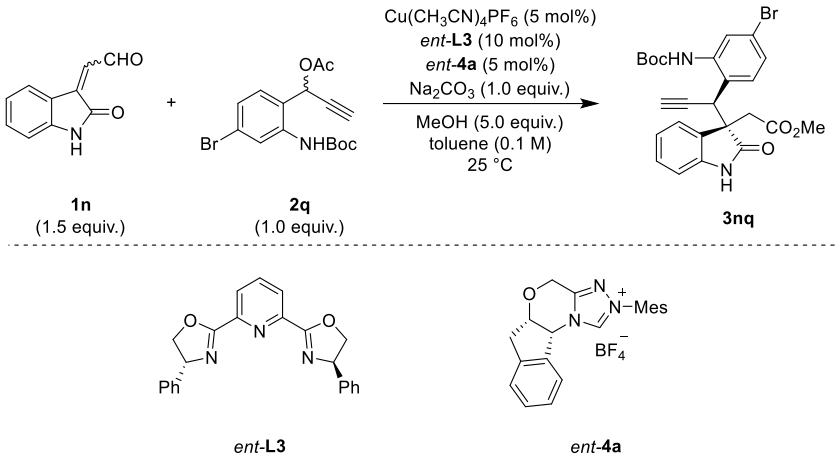



To a stirring solution of (*R*,*R*)-**3ao** (35.9 mg, 0.10 mmol, 1.0 equiv.) in MeOH (5.0 mL) was slowly added palladium onactivated charcoal (10%, 20.0 mg) at room temperature. The resulting mixture was stirred at room temperature in an atmosphere of hydrogen gas for 10 hours. The mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give **9** (33.6 mg, 92% yield, >99%e.e.).

**Methyl 2-((*R*)-1-methyl-2-oxo-3-((*S*)-1-phenylpentan-3-yl)indolin-3-yl)acetate (9)**

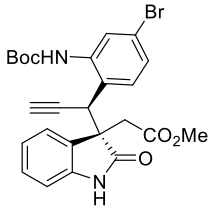


Colorless liquid; 92% yield; >95:5 d.r.; **$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.33 – 7.21 (m, 3H), 7.20 – 7.12 (m, 2H), 7.10 – 7.04 (m, 2H), 7.01 (td, *J* = 7.5, 1.1 Hz, 1H), 6.89 – 6.80 (m, 1H), 3.39 (s, 3H), 3.25 (s, 3H), 3.08 (d, *J* = 16.0 Hz, 1H), 2.99 (d, *J* = 16.0 Hz, 1H), 2.47 (dd, *J* = 9.6, 7.4 Hz, 2H), 1.80 (ddd, *J* = 8.6, 6.7, 3.5 Hz, 1H), 1.71 – 1.54 (m, 2H), 1.46 – 1.34 (m, 1H), 1.28 (ddt, *J* = 14.4, 10.3, 7.3 Hz, 1H), 0.92 (t, *J* = 7.4 Hz, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 179.5, 170.6, 144.9, 142.5, 130.8, 128.4, 128.4, 125.8, 123.3, 122.2, 108.0, 53.1, 51.7, 47.0, 40.2, 34.8, 31.8, 26.4, 23.1, 13.4. **IR** (KBr, $cm^{-1}$) *γ* 3470, 2929, 1959, 1709, 1611, 1492, 1452, 1343, 1260, 1168, 1091, 1026, 814, 755, 701, 544. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{23}H_{27}NO_3Na)^+$: 388.1883, found: 388.1892; **$[\alpha]^{20}_D$** = +10.9 (*c* = 0.61, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: >99% e.e. (CHIRALPAK IG, hexane/*i*-PrOH = 85/15, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$(major) = 17.73 min, $t_R$ (minor) = 19.15 min.



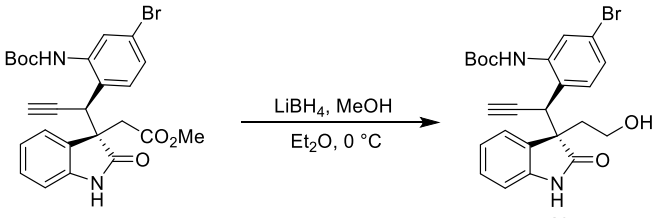

To a flame-dried and $N_2$-purged Schlenk tube were added $Cu(CH_3CN)_4PF_6$ (0.15 mmol, 55.9 mg) and pyridine bisoxazoline ligand *ent*-**L3** (0.3 mmol, 110.9 mg). The vial was sealed, purged and back filled with $N_2$ three times before adding toluene (15.0 mL) at 25 ℃. The resulting solution was stirred at 25 ℃ for 1 hour. Then, isatin-derived enal **1n** (4.5 mmol, 779.3 mg), NHC precatalyst **4a** (0.15 mmol, 62.9 mg) $Na_2CO_3$ (3.0mmol, 318.0 mg), MeOH (15.0 mmol, 600 μL) and a solution of propargylic acetate **2q** (3.0 mmol, 1104.7 mg) in toluene (15.0 mL) were added. The resulting solution was stirred at 25 ℃ for 12 hours and then quenched with saturated $NH_4Cl$ aqueous solution (10.0 mL). The resulting solution was extracted with ethyl acetate (15.0 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated in vacuo. The diastereomeric ratio was determined by $^1H$ NMR analysis of the crude reaction mixture. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate = 3:1-2:1) to afford desired product **3nq** (0.94 g, 82:18 d.r., 93% e.e.).

**Methyl 2-((*S*)-3-((*S*)-1-(4-bromo-2-((*tert*-butoxycarbonyl)amino)phenyl)prop-2-yn-1-yl)-2-oxoindolin-3-yl)acetate (3nq)**



White solid, m.p. 90-96 ℃; 61% yield; 82:18 d.r.; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 8.35 (s, 1H), 7.78 (s, 1H), 7.20 (td, *J* = 7.7, 1.3 Hz, 1H), 7.09 (m, 3H), 6.98 (td, *J* = 7.5, 1.0 Hz, 2H), 6.80 (d, *J* = 7.8 Hz, 1H), 4.38 (d, *J* = 2.6 Hz, 1H), 3.44 (s, 3H), 3.28 (d, *J* = 16.5 Hz, 1H), 2.99 (d, *J* = 16.4 Hz, 1H), 2.38 (d, *J* = 2.6 Hz, 1H), 1.48 (s, 9H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 179.2, 170.1, 153.0, 141.9, 137.7, 133.0, 129.2, 128.5, 127.1, 124.3,

122.4, 122.1, 110.1, 80.9, 80.0, 74.5, 53.4, 51.8, 40.2, 38.7, 28.3. **IR** (KBr, $cm^{-1}$) $\gamma$ 3299, 2964, 2928, 1716, 1621, 1575, 1506, 1472, 1438, 1367, 1261, 1235, 1158, 1051, 1024, 870, 804, 755, 666, 580, 492. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{25}H_{25}BrN_2O_5Na)^+$: 535.0833, found: 535.0844; **$[\alpha]^{20}_D$** = -31.2 (*c* = 0.87, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 93% e.e. (CHIRALPAK IA, hexane/*i*-PrOH = 85/15, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 13.58 min, $t_R$ (minor) = 16.16 min.

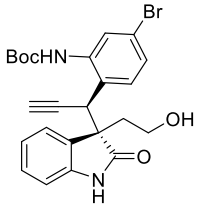



**3nq**
93% e.e.

**10**
60% yield
94% e.e.

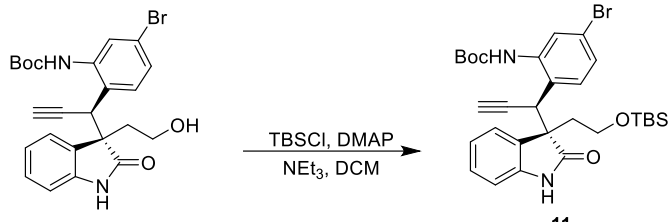
A flame-dried Schlenk tube equipped with a magnetic stir bar was charged with **3nq** (51.3 mg, 93% e.e., 0.1 mmol, 1.0 equiv.), and 2.0 mL of $Et_2O$ was added to the Schlenk tube under argon. After cooling down to 0 ℃, $LiBH_4$ (21.8mg, 1.0 mmol, 10.0 equiv.) and methanol (40 μL, 1.0 mmol, 10.0 equiv.) were added subsequently. The mixture was stirred at 0 ℃ until the starting materials were consumed (monitoring by TLC). The reaction mixture was quenched with water (5.0 mL). The resulting solution was extracted with ethyl acetate (5.0 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated in vacuo. The crude material was purified by column chromatography to afford compound **10** (29.1 mg, 60% yield, 94% e.e.).

***tert*-Butyl (5-bromo-2-((*S*)-1-((*S*)-3-(2-hydroxyethyl)-2-oxoindolin-3-yl)prop-2-yn -1-yl)phenyl)carbamate (10)**




White solid, m.p. 109-111 ℃; 60% yield; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 8.84 (s, 1H), 7.75 (br, 1H), 7.24 – 7.05 (m, 3H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 4.41 (s, 1H), 3.38 (m, *J* = 11.8, 7.1, 3.7 Hz, 1H), 3.13 (s, 1H), 2.54 (m, *J* = 7.2 Hz, 1H), 2.15 (s, 1H), 1.90 (m, *J* = 14.5, 4.5 Hz, 1H), 1.46 (s, 9H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 181.2, 142.1, 138.2, 133.3, 128.9, 128.3, 127.2, 125.4,

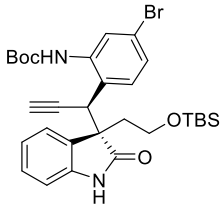
110.4, 81.2, 81.0, 59.1, 55.6, 40.5, 36.9, 28.4. **IR** (KBr, $cm^{-1}$) $\gamma$ 3298, 2927, 2854, 1713, 1621, 1592, 1576, 1514, 1471, 1408, 1392, 1368, 1235, 1158, 1050, 1021, 870, 804, 754, 665, 575, 493. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{24}H_{25}BrN_2O_4Na)^+$: 504.0890, found: 507.0897; $[\alpha]^{20}_D$ = -6.7 (*c* = 0.65, $CHCl_3$); The product was analyzed by HPLC to determine the enantiomeric excess: 94% e.e. (CHIRALPAK IA, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 254 nm), $t_R$ (major) = 4.44 min, $t_R$ (minor) = 5.90 min.




**10** **11** 80% yield

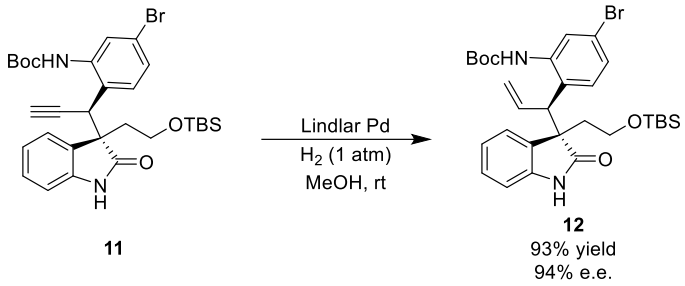
To a flame-dried and $N_2$-purged Schlenk tube were added **10** (48.5 mg, 94% e.e., 0.10 mmol, 1.0 equiv.), DMAP (1.2 mg, 0.01 mmol, 10 mol%) and TBSCl (45.2 mg, 0.3 mmol, 3.0 equiv.). The vial was then sealed, purged and backfilled with $N_2$ three times before adding $NEt_3$ (42 μL, 0.3 mmol, 3.0 equiv.) and DCM (2.0 mL) at room temperature. The resulting mixture was stirred at room temperature under nitrogen atmosphere until the reaction completed (monitoring by TLC). After concentrated under reduced pressure, the residue was purified by column chromatography on silica gel to give **11** (48.0 mg, 80% yield).

***tert*-Butyl (5-bromo-2-((*S*)-1-((*S*)-3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-oxoindolin-3-yl)prop-2-yn-1-yl)phenyl)carbamate (11)**



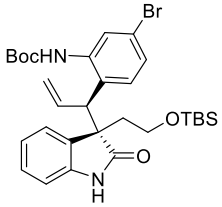

White solid, m.p. 90-97 ℃; 80% yield; **$^1$H NMR (400 MHz, $CDCl_3$)** δ 8.46 (s, 1H), 7.89 (s, 1H), 7.21 (td, *J* = 7.7, 1.3 Hz, 1H), 7.16 – 7.01 (m, 2H), 6.98 (td, *J* = 7.5, 1.1 Hz, 1H), 6.91 (d, *J* = 7.4 Hz, 1H), 6.84 (dt, *J* = 7.7, 0.8 Hz, 1H), 4.26 (d, *J* = 2.7 Hz, 1H), 3.27 (qdd, *J* = 10.2, 7.7, 5.2 Hz, 2H), 2.50 (dt, *J* = 13.4, 7.8 Hz, 1H), 2.25 (d, *J* = 2.5 Hz, 1H), 2.00 (ddd, *J* = 13.4, 6.0, 4.3 Hz, 1H), 1.47 (s, 9H), 0.74 (s, 9H), -0.19 (s, 3H), -0.21 (s, 3H). **$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 180.3, 152.9, 141.9, 138.0, 133.5, 128.9, 128.1, 126.7, 125.3, 122.4, 122.1, 110.1, 80.9, 80.6, 74.3, 59.4, 55.2, 37.0, 28.4,

25.9, 18.3, -5.7, -5.7. **IR** (KBr, $cm^{-1}$) $\gamma$ 3303, 2955, 2928, 2856, 1712, 1619, 1592, 1577, 1509, 1473, 1408, 1382, 1368, 1340, 1250, 1158, 1110, 1051, 1022, 853, 754, 663, 491. **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{30}H_{39}BrN_2O_4SiNa)^+$: 621.1755, found: 621.1763; $[\alpha]^{20}_D$ = -11.5 (*c* = 0.62, $CHCl_3$).




To a stirring solution of **11** (60.0 mg, 0.10 mmol, 1.0 equiv.) in MeOH (5.0 mL) was slowly added Lindlar Pd (5%, 20.0 mg) at room temperature. The resulting mixture was stirred at room temperature in an atmosphere of hydrogen gas until the reaction completed (monitoring by TLC). The mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give **12** (56.0 mg, 93% yield, 94% e.e.).

***tert*-Butyl (5-bromo-2-((*S*)-1-((*S*)-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-2-oxoindolin-3-yl)allyl)phenyl)carbamate(12)**




White solid; 93% yield; **$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.87 (s, 1H), 7.69 (s, 1H), 7.18 (td, *J* = 7.5, 1.6 Hz, 1H), 7.11 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.06 – 6.93 (m, 3H), 6.74 (d, *J* = 7.7 Hz, 1H), 6.31 (s, 1H), 6.16 (dt, *J* = 17.8, 9.6 Hz, 1H), 5.15 (dd, *J* = 16.8, 1.6 Hz, 1H), 5.09 (dd, *J* = 10.0, 1.5 Hz, 1H), 3.85 (d, *J* = 9.4 Hz, 1H), 3.32 – 3.18 (m, 2H), 2.44 (dt, *J* = 13.6, 7.9 Hz, 1H), 1.88 (ddd, *J* = 13.6, 6.2, 4.1 Hz, 1H), 1.53 (s, 9H), 0.74 (s, 9H), -0.18 (s, 3H), -0.22 (s, 3H). **$^{13}$C NMR (126 MHz, $CDCl_3$)** δ 180.7, 153.2, 141.4, 137.0, 135.0, 131.0, 129.4, 128.7, 127.4, 124.7, 122.0, 121.0, 118.8, 109.9, 81.0, 59.4, 55.2, 51.1, 37.8, 28.5, 25.9, 18.3, -5.7. **IR** (KBr, $cm^{-1}$) $\gamma$ 2956, 2927, 2855, 1707, 1619, 1592, 1572, 1509, 1472, 1367, 1258, 1159, 1090, 1050, 1022, 923, 836, 806, 776, 755, 666, 492. $[\alpha]^{20}_D$ = +44.6 (*c* = 0.26, $CHCl_3$); **HRMS** (ESI) m/z $(M+Na)^+$: calculated for $(C_{30}H_{41}BrN_2O_4SiNa)^+$: 623.1911, found: 623.1927; The product was analyzed by HPLC to determine the enantiomeric excess: 94% e.e.

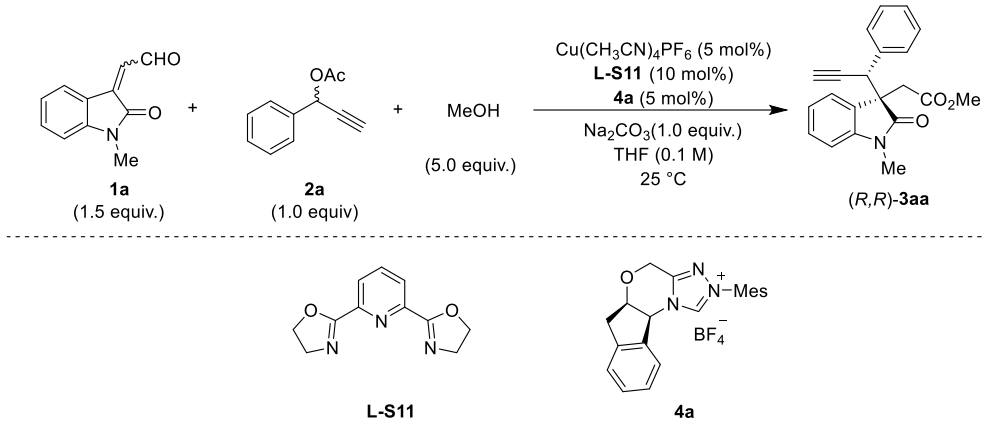
(CHIRALPAK IA, hexane/*i*-PrOH = 98/2, flow rate: 1.0 mL/min, T = 30 ℃, 220 nm), $t_R$ (minor) = 23.47 min, $t_R$ (major) = 32.21 min.

**Nonlinear Effect Studies**

The non-linear effect study were conducted by building a relationship between the e.e. value of the NHC precatalyst **4a** and that of the product (*R*,*R*)-**3aa**. The specified e.e. values of NHC precatalyst **4a** was made by mixing certain amounts of optically pure NHC precatalyst **4a** with optically pure NHC precatalyst *ent*-**4a**. Six reactions containing NHC precatalyst of racemic, 21%, 34%, 60%, 80%, and 99% optical purity were run in parallel.

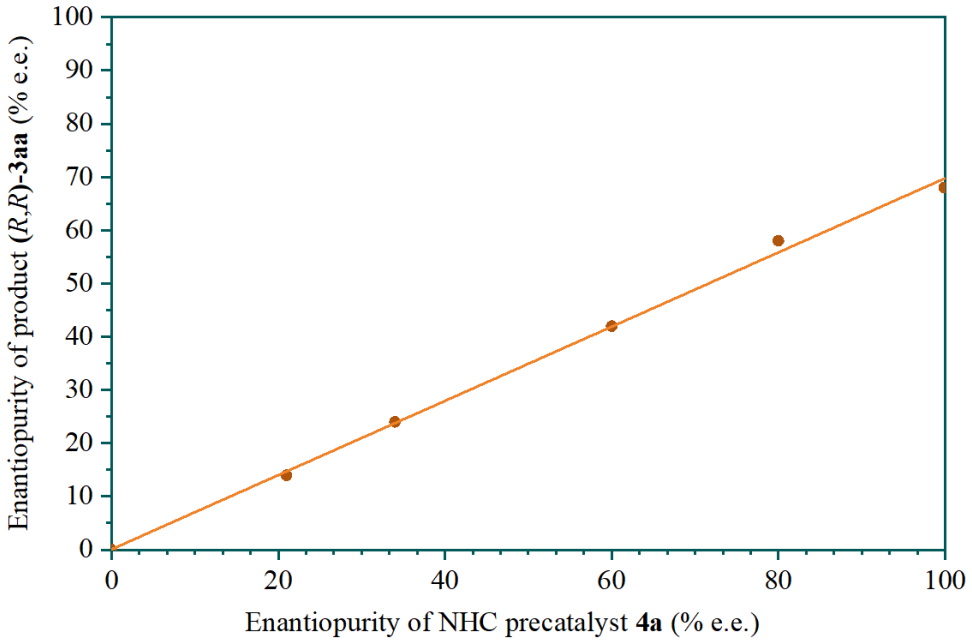
To a flame-dried and $N_2$-purged Schlenk tube were added $Cu(CH_3CN)_4PF_6$ (0.005 mmol, 5 mol%) and pyridine bisoxazoline ligand **L-S11** (0.01 mmol, 10 mol%). The vial was sealed, purged and backfilled with $N_2$ three times before adding THF (0.5 mL) at 25 ℃. The resulting solution was stirred at 25 ℃ for 1 hour. Then, isatin-derived enal **1a** (0.15 mmol), NHC precatalyst **4a** with different e.e. values (0.005 mmol, 5 mol%), $Na_2CO_3$ (0.1mmol), MeOH (0.5 mmol) and propargylic acetate **2a** (0.1 mmol) in THF (0.5 mL) were added. The resulting solution was stirred at 25 ℃ for 12 hours and then quenched with saturated aqueous $NH_4Cl$ solution (5.0 mL). The resulting solution was extracted with ethyl acetate (5.0 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated in vacuo. The diastereomeric ratio was determined by $^1H$ NMR analysis of the crude reaction mixture. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate = 5:1-2:1) to afford desired product (*R*,*R*)-**3aa**. The product was analyzed by HPLC (CHIRALPAK IG, hexane/*i*-PrOH = 70/30, flow rate: 1.0 mL/min, T = 30 ℃, 230 nm), $t_R$ (major) = 11.26 min, $t_R$ (minor) = 16.01 min. A graph of e.e. of product vs. e.e. of catalyst was then plotted.

**Supplementary Table 10.** Nonlinear experiments



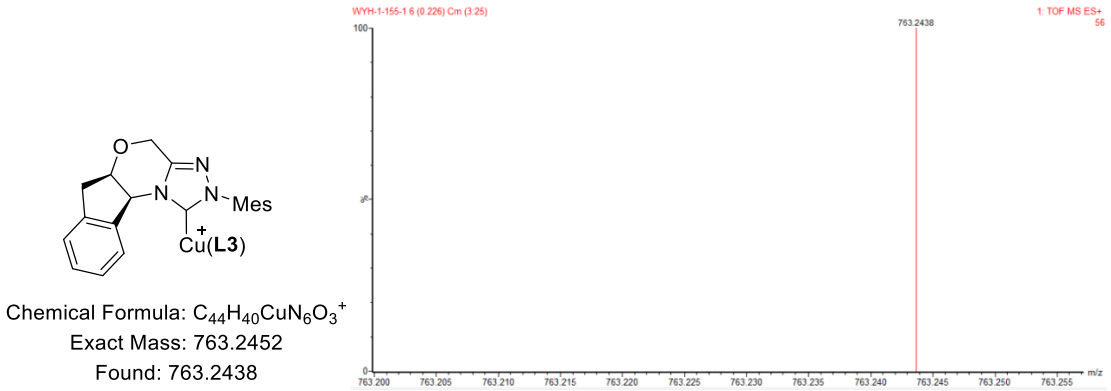

| entry[a] | e.e. of NHC precatalyst **4a**(%) | yield (%) | d.r. | e.e. of (*R*,*R*)-**3aa**(%) |
|---|---|---|---|---|
| 1 | 0 | 70 | 82:18 | 0 |
| 2 | 21 | 73 | 82:18 | 14 |
| 3 | 34 | 72 | 82:18 | 24 |
| 4 | 60 | 74 | 81:19 | 42 |
| 5 | 80 | 74 | 81:19 | 58 |
| 6 | 99 | 71 | 80:20 | 68 |

[a]Unless noted, reaction conditions: $Cu(CH_3CN)_4PF_6$ (5 mol%), pyridine bisoxazoline ligand **L-S11** (10 mol%) were stirred in THF (0.5 mL) at 25 ℃ for 1 h under $N_2$, then NHC precatalyst **4a**(5 mol%), **1a** (0.15 mmol), **2a** (0.1 mmol), MeOH (0.5 mmol), $Na_2CO_3$ (0.1 mmol) and THF (0.5 mL) were added to the reaction mixture and stirred at 25 ℃ for 12 h under $N_2$. The yield and diastereomeric ratio (d.r.) were determined by $^1H$ NMR spectroscopy. The enantiomeric excess (e.e.) was determined by HPLC.



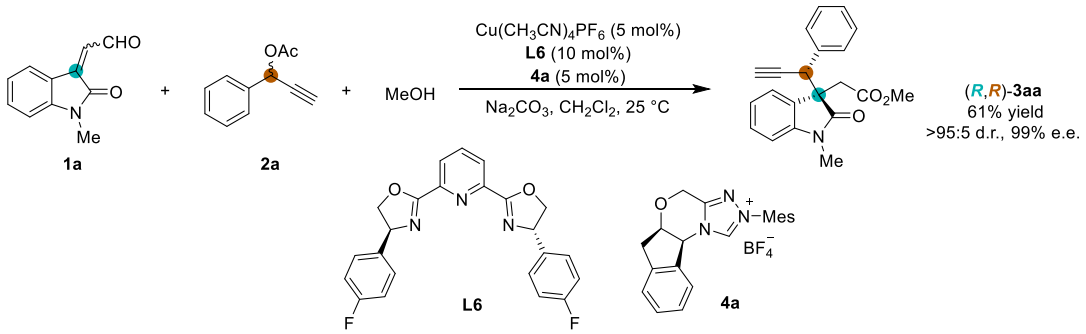
## ESI-MS Analysis

HRMS analysis of $Cu^{I}$(**L3**)(**4a**)$^{+}$



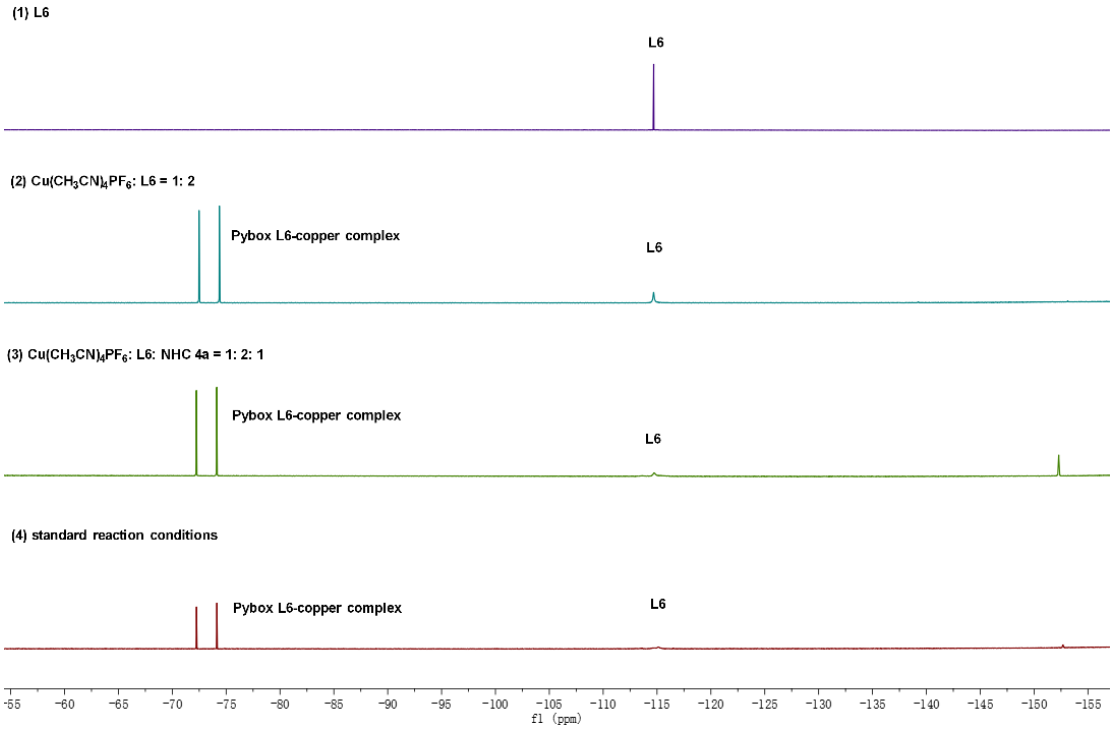

To a flame-dried and $N_2$-purged Schlenk tube were added $Cu(CH_3CN)_4PF_6$ (0.005 mmol, 5 mol%) and pyridine bisoxazoline ligand **L3** (0.01 mmol, 10 mol%). The vial was sealed, purged and backfilled with $N_2$ three times before adding THF (0.5 mL) at 25 ℃. The resulting solution was stirred at 25 ℃ for 1 hour. Then, isatin-derived enal **1a** (0.15 mmol), NHC precatalyst **4a** (0.005 mmol, 5 mol%), $Na_2CO_3$ (0.1mmol), MeOH (0.5 mmol) and a solution of propargylic acetate **2a** (0.1 mmol) in THF (0.5 mL) were added. The resulting solution was stirred at 25 ℃ for 1 hour. HRMS analysis of the reaction mixture showed the presence of $Cu^{I}$(**L3**)(**4a**)$^{+}$.

## NMR Studies




$^{19}F$ NMR studies (in $CD_2Cl_2$) on the coordination effect of copper salt $Cu(CH_3CN)_4PF_6$, a fluorine-substituted Pybox ligand **L6** (2,6-bis((*S*)-4-(4-fluorophenyl)-4,5-dihydrooxazol-2-yl)pyridine),[7] and an NHC catalyst **4a** were carried out. The $^{19}F$ NMR spectra of Pybox **L6** and Pybox **L6**-copper complex were collected and are shown in (1) and (2) (Supplementary Figure 1). The $^{19}F$ NMR spectrum of the catalyst system of $Cu(CH_3CN)_4PF_6$, Pybox

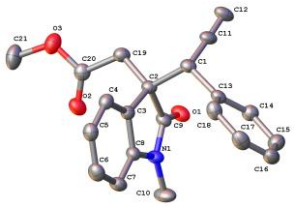
**L6**, and NHC **4a** in a ratio of 1:2:1 found that a considerable amount of the Pybox **L6**-copper complex was formed (Supplementary Figure 1, (3)). The same result was observed under the standard reaction conditions (Supplementary Figure 1, (4)). We speculated that the copper complex including NHC-**4a** as a ligand cannot be detected in our catalytic system via NMR analysis, which may be due to the instability or extremely low concentration (can be detected via ESI-MS Analysis) of the complex.

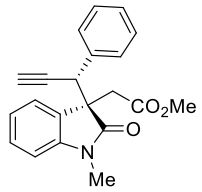



**Supplementary Figure 1.** $^{19}F$ NMR studies.

**X-ray Single Crystal Data**

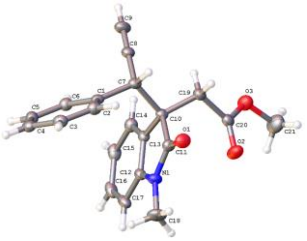
(*R*,*R*)-**3aa**

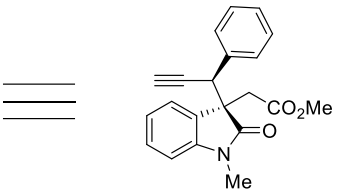





| | |
|---|---|
| Empirical formula | $C_{21}H_{19}NO_3$ |
| Formula weight | 333.37 |
| Temperature/K | 192.99 |
| Wavelength/Å | 1.34139 |
| Crystal system | Hexagonal |
| Space group | $P6_1$ |
| a/Å | 9.47499(10) |
| b/Å | 9.47499(10) |
| c/Å | 70.0389(7) |
| α/° | 90 |
| β/° | 90 |
| γ/° | 120 |
| Volume/Å$^3$ | 5445.37(13) |
| Z | 12 |
| $\rho_{calc}$ Mg/m$^3$ | 1.220 |
| μ/mm$^{-1}$ | 0.423 |
| F(000) | 2112 |
| Crystal size/mm$^3$ | 0.08 x 0.05 x 0.03 |
| 2Θ range for data collection/° | 3.294 to 54.891 |
| Index ranges | -10<=h<=11, -11<=k<=9, -85<=l<=85 |
| Reflections collected | 79418 |
| Independent reflections | 6910 [R(int) = 0.0377] |
| Data/restraints/parameters | 6910 / 1 / 455 |
| Goodness-of-fit on F$^2$ | 1.031 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0332, $wR_2$ = 0.0790 |
| Final R indexes [all data] | $R_1$ = 0.0398, $wR_2$ = 0.0840 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.187 and -0.200 |
| Absolute structure parameter | 0.13(6) |

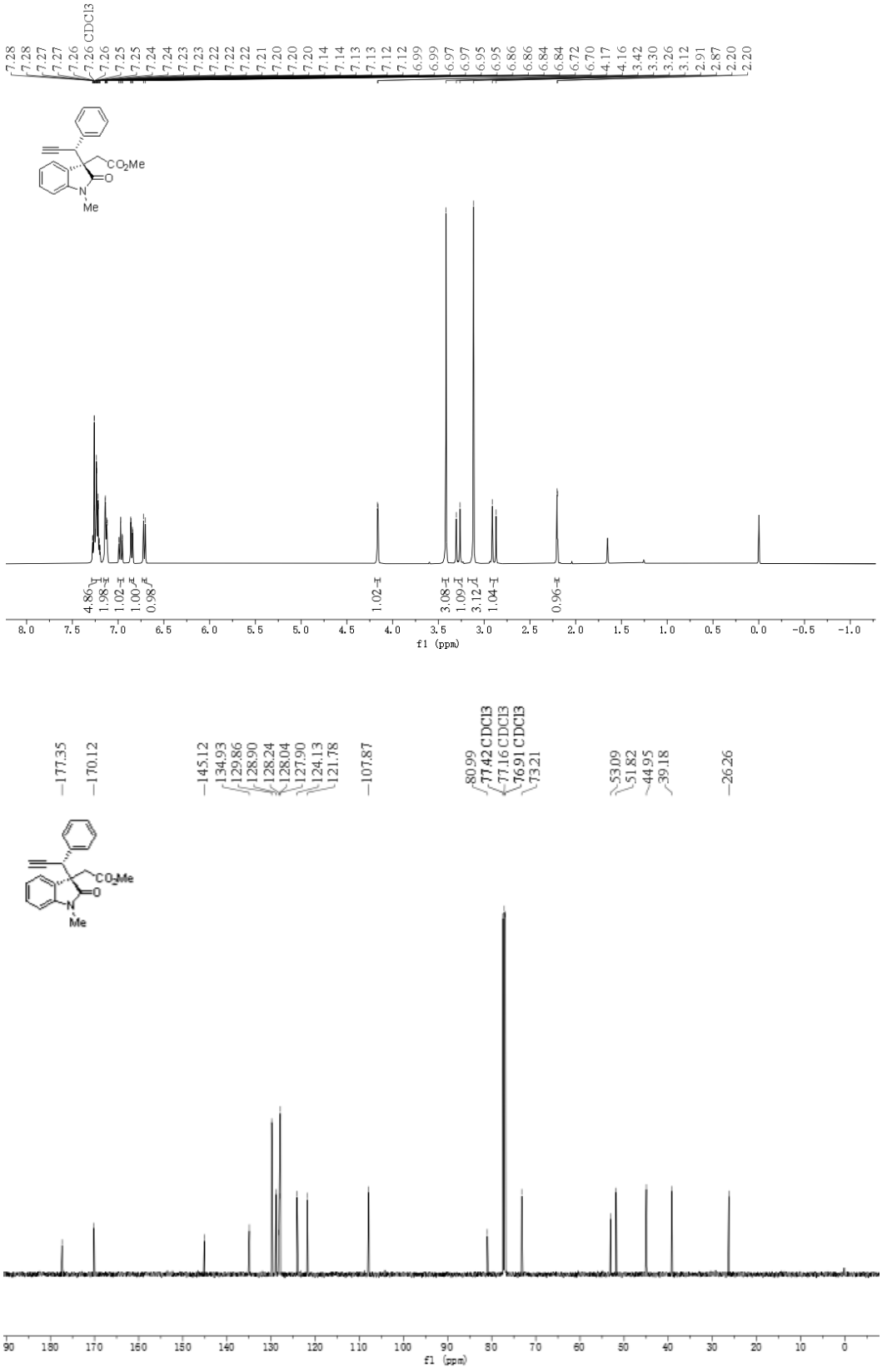
(*R*,*S*)-**3aa**



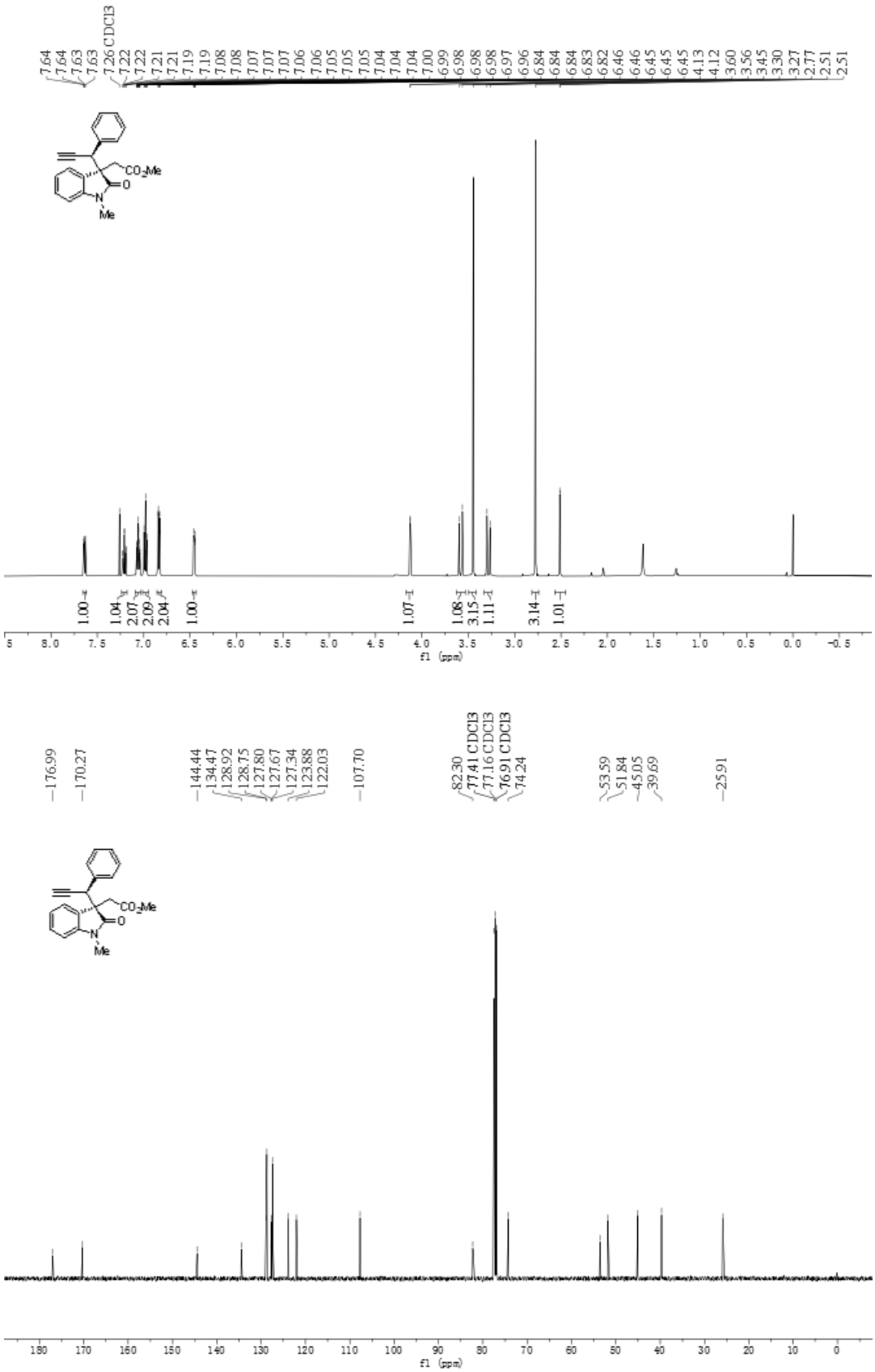



| | |
|---|---|
| Empirical formula | $C_{21}H_{19}NO_3$ |
| Formula weight | 333.37 |
| Temperature/K | 173.0 |
| Wavelength/Å | 1.34139 |
| Crystal system | Monoclinic |
| Space group | P1 21 1 |
| a/Å | 8.81790(10) |
| b/Å | 9.00430(10) |
| c/Å | 22.8050(3) |
| α/° | 90 |
| β/° | 97.2030 |
| γ/° | 90 |
| Volume/$Å^3$ | 1796.40(13) |
| Z | 4 |
| $\rho_{calc}$ $Mg/m^3$ | 1.233 |
| $\mu/mm^{-1}$ | 0.427 |
| F(000) | 704 |
| Crystal size/$mm^3$ | 0.07 x 0.06 x 0.05 |
| 2Θ range for data collection/° | 3.399 to 54.939 |
| Index ranges | -10<=h<=10, -10<=k<=10, -26<=l<=27 |
| Reflections collected | 27020 |
| Independent reflections | 6758 [R(int) = 0.0310] |
| Data/restraints/parameters | 6758 / 1 / 455 |
| Goodness-of-fit on $F^2$ | 1.084 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0322, $wR_2$ = 0.0834 |
| Final R indexes [all data] | $R_1$ = 0.0341, $wR_2$ = 0.0852 |
| Largest diff. peak/hole / e $Å^{-3}$ | 0.181 and -0.131 |
| Absolute structure parameter | 0.04(6) |

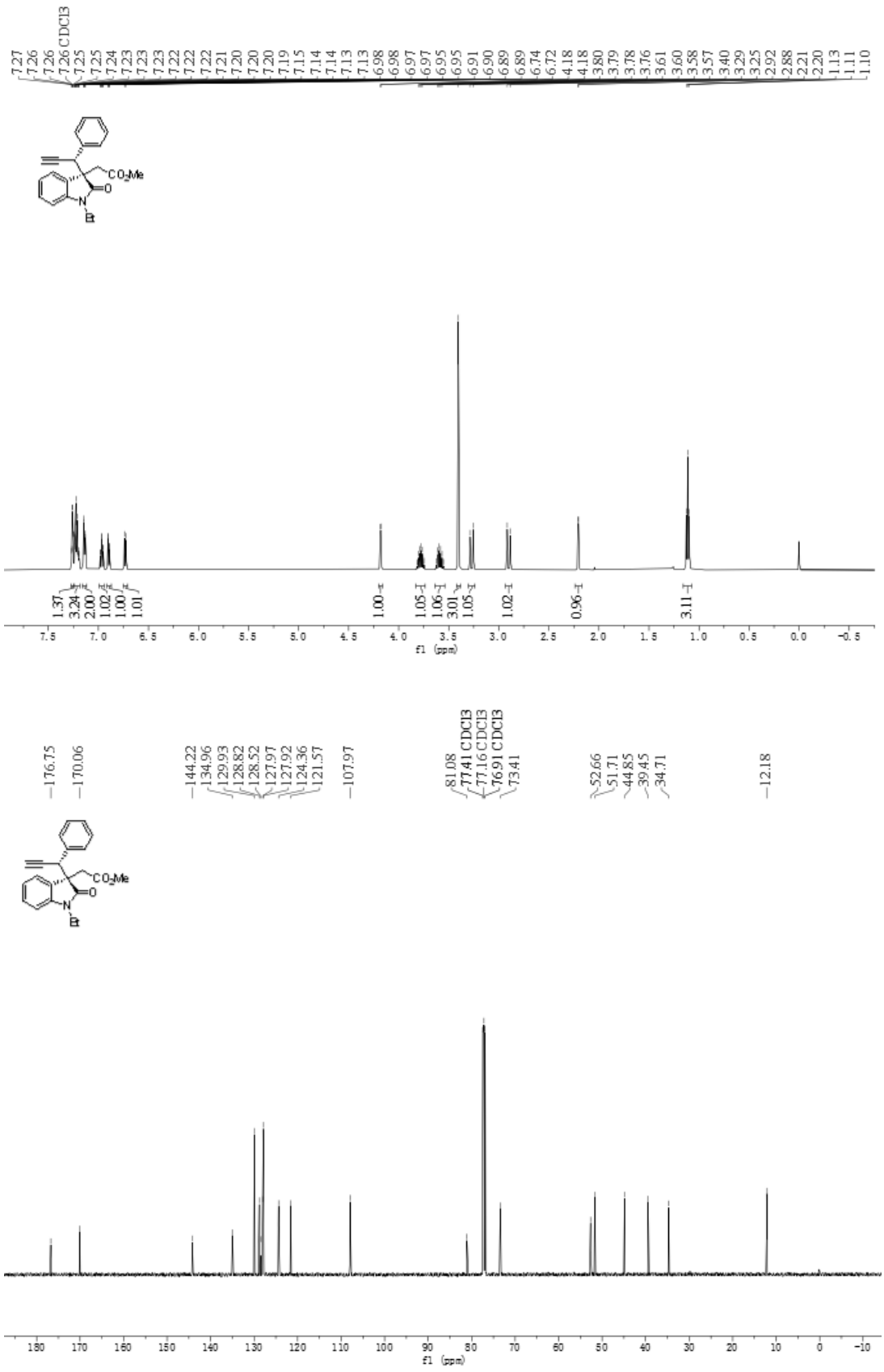
## Supplementary Figures
## NMR Spectra



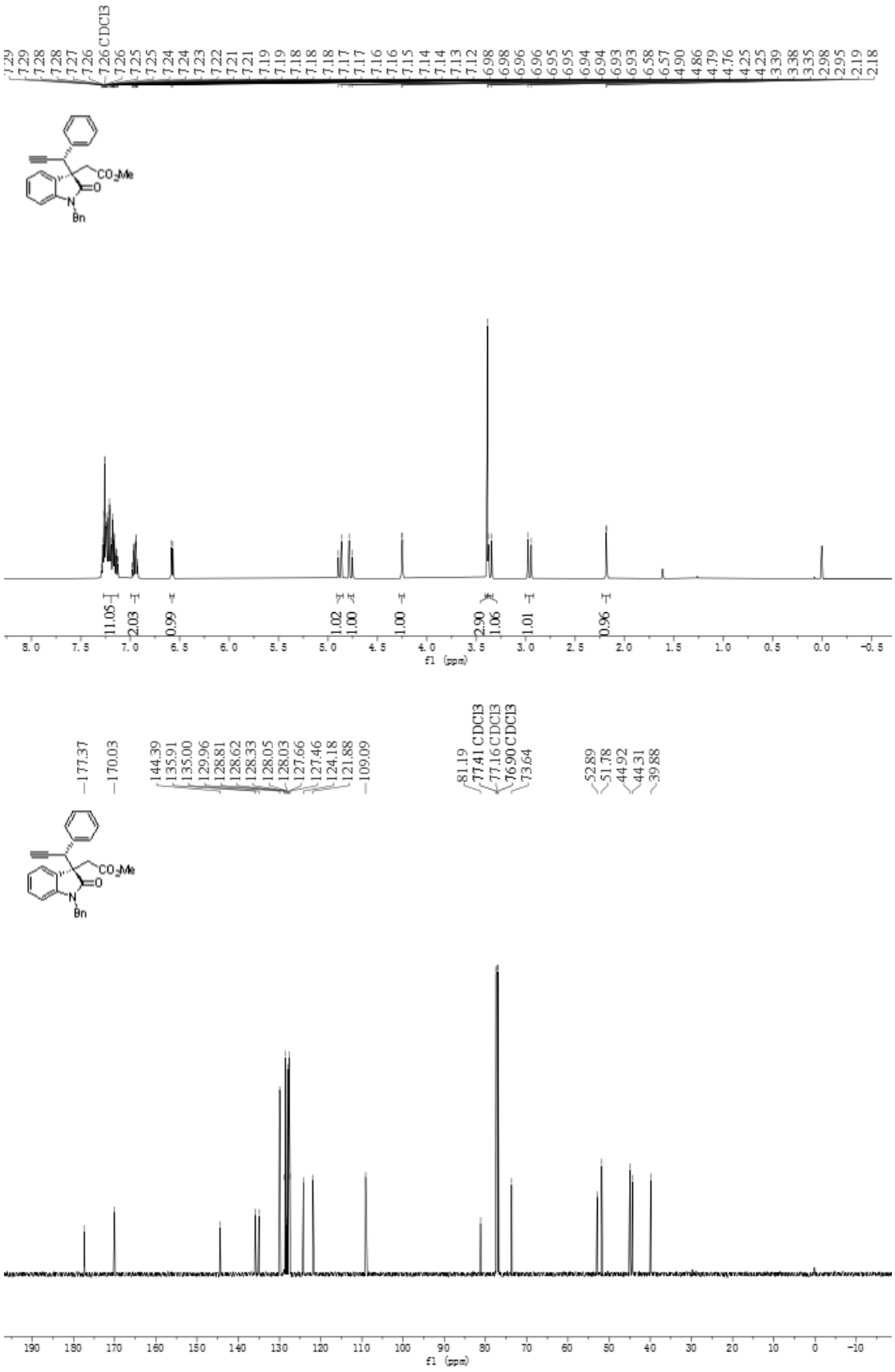

**Supplementary Fig. 2.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3aa**



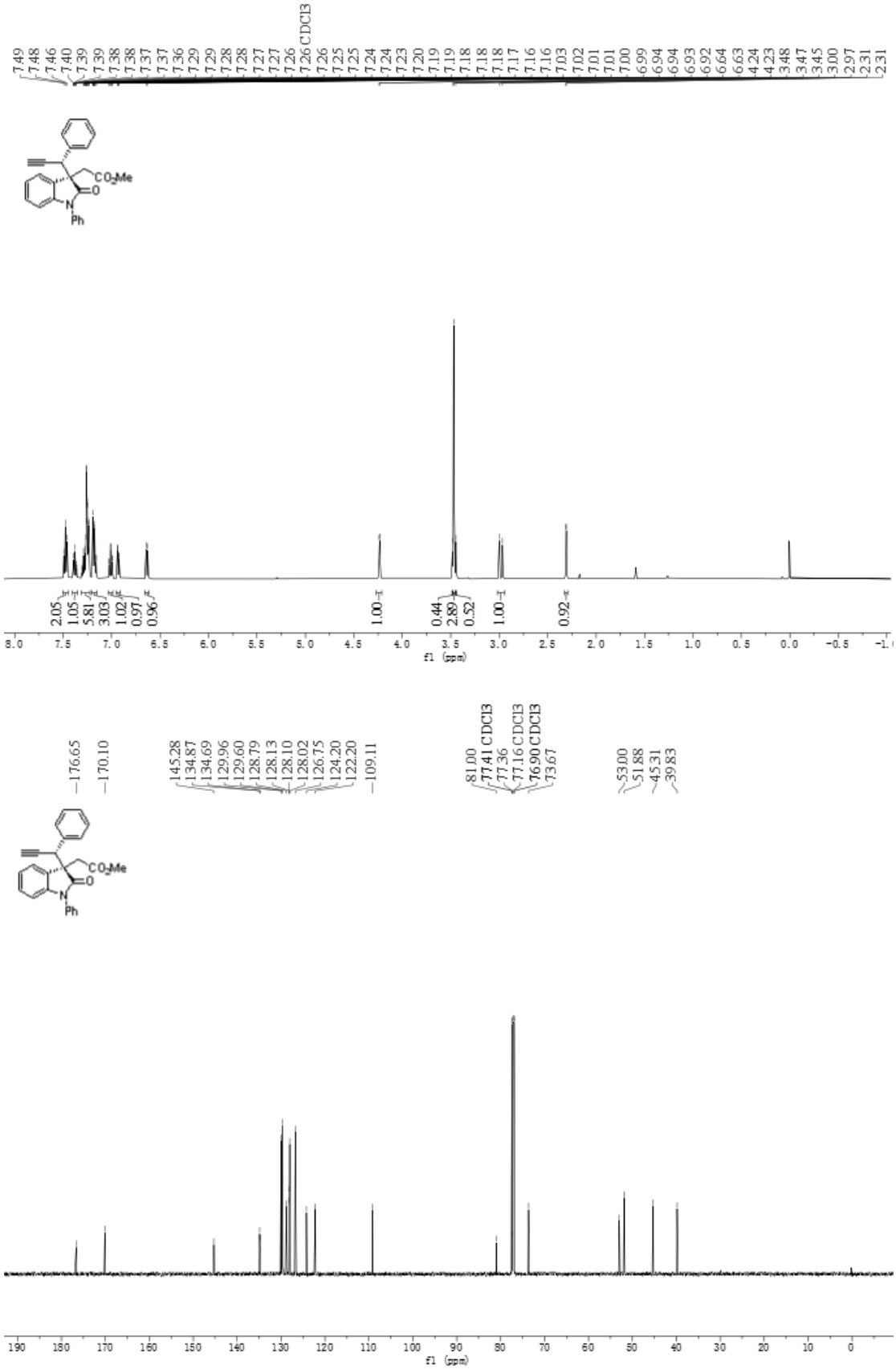

**Supplementary Fig. 3.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*S*)-**3aa**



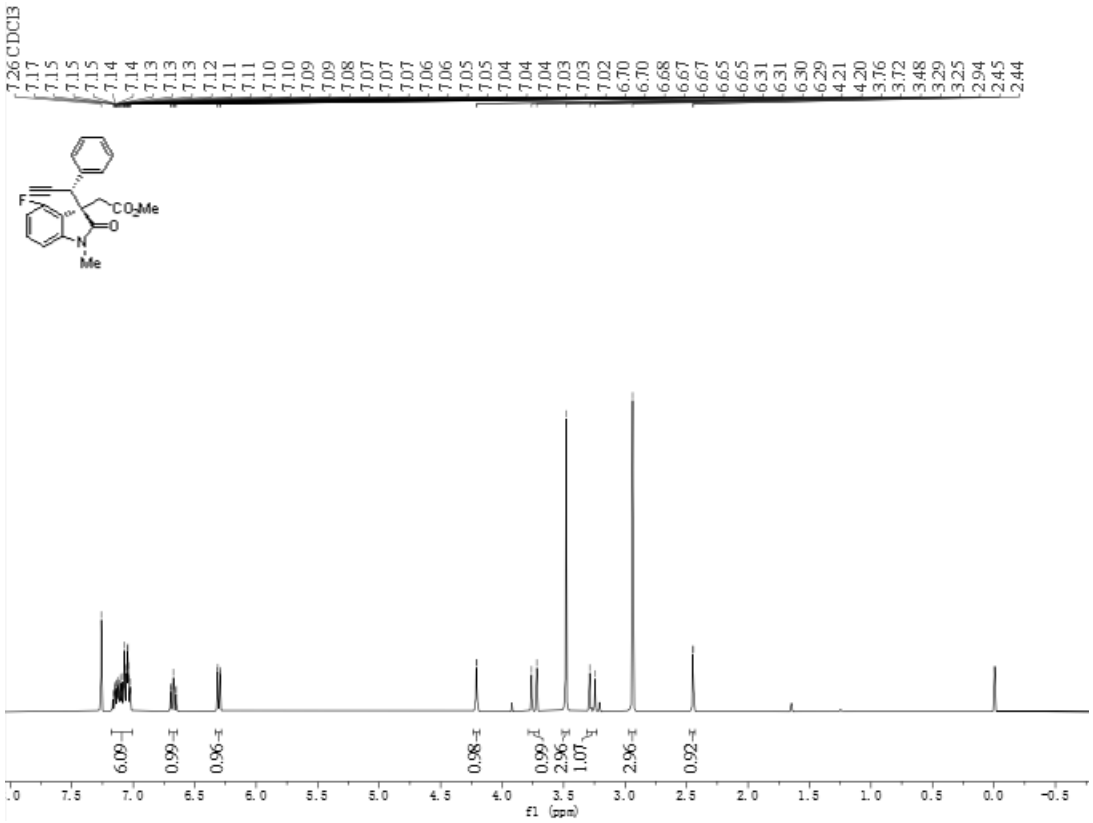

**Supplementary Fig. 4.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ba**

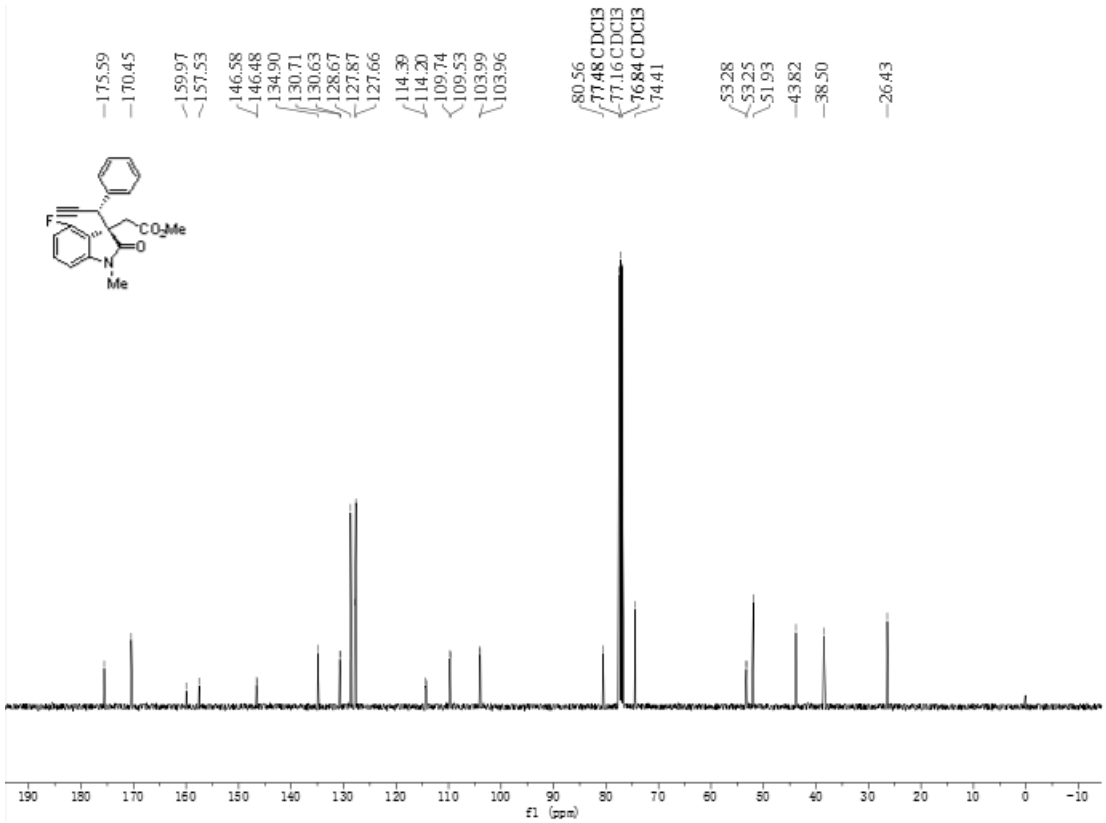


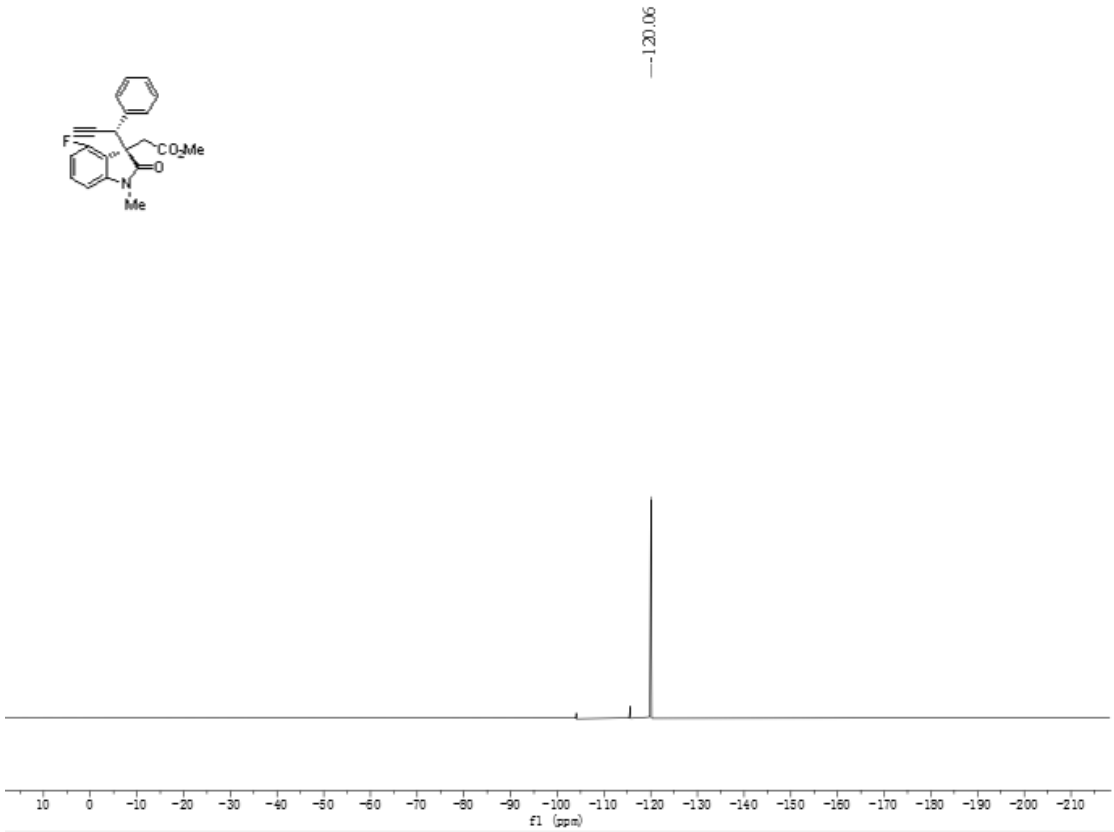

**Supplementary Fig. 5.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ca**



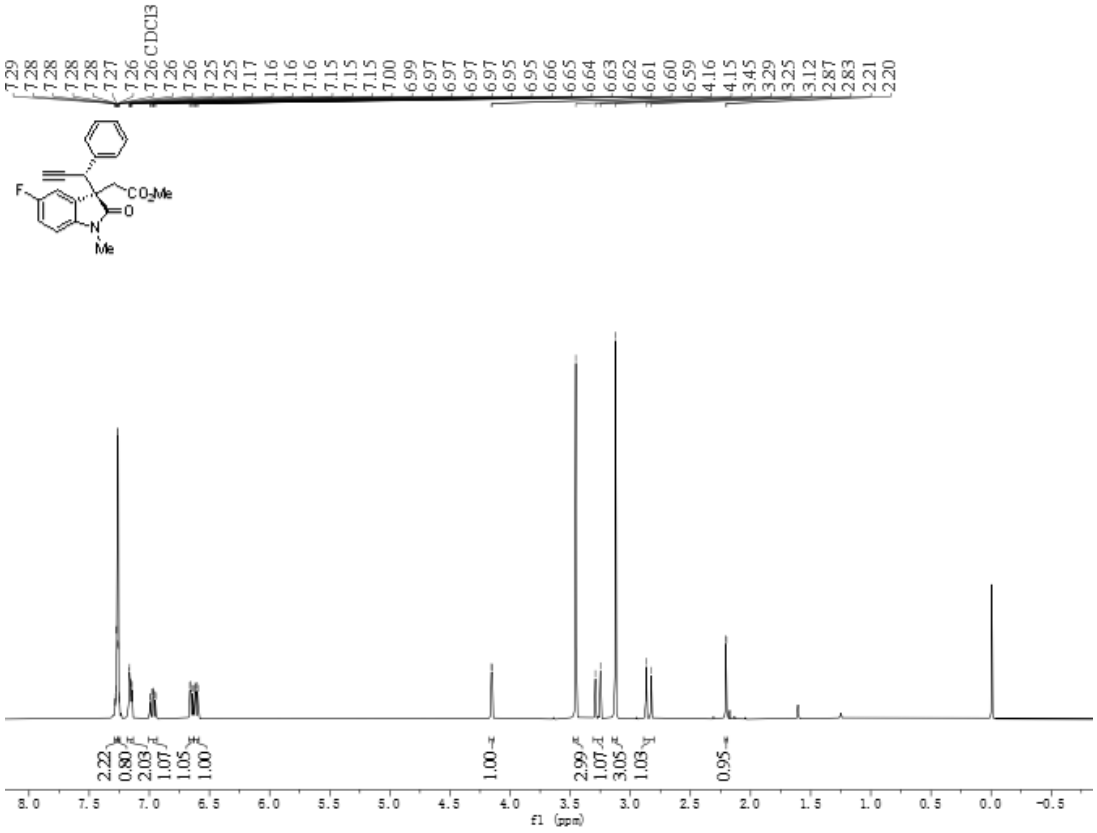

**Supplementary Fig. 6.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3da**

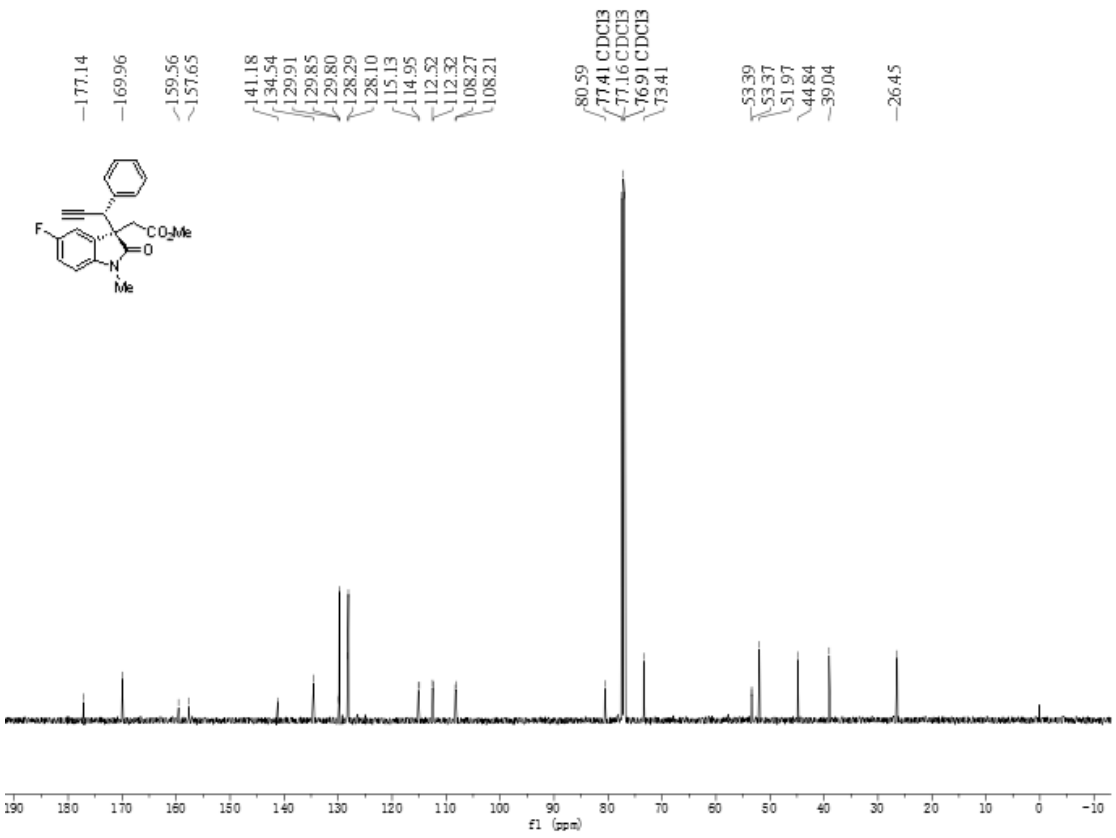

7.26 CDCl3
7.17
7.15
7.15
7.15
7.14
7.14
7.13
7.13
7.13
7.12
7.11
7.11
7.10
7.10
7.09
7.09
7.08
7.07
7.07
7.07
7.06
7.06
7.05
7.05
7.04
7.04
7.04
7.03
7.03
7.02
6.70
6.70
6.68
6.67
6.67
6.65
6.65
6.31
6.31
6.30
6.29
4.21
4.20
3.76
3.72
3.48
3.29
3.25
2.94
2.45
2.44
F
CO2Me
O
N
Me
6.09
0.99
0.96
0.98
0.99
2.96
1.07
2.96
0.92
f1 (ppm)

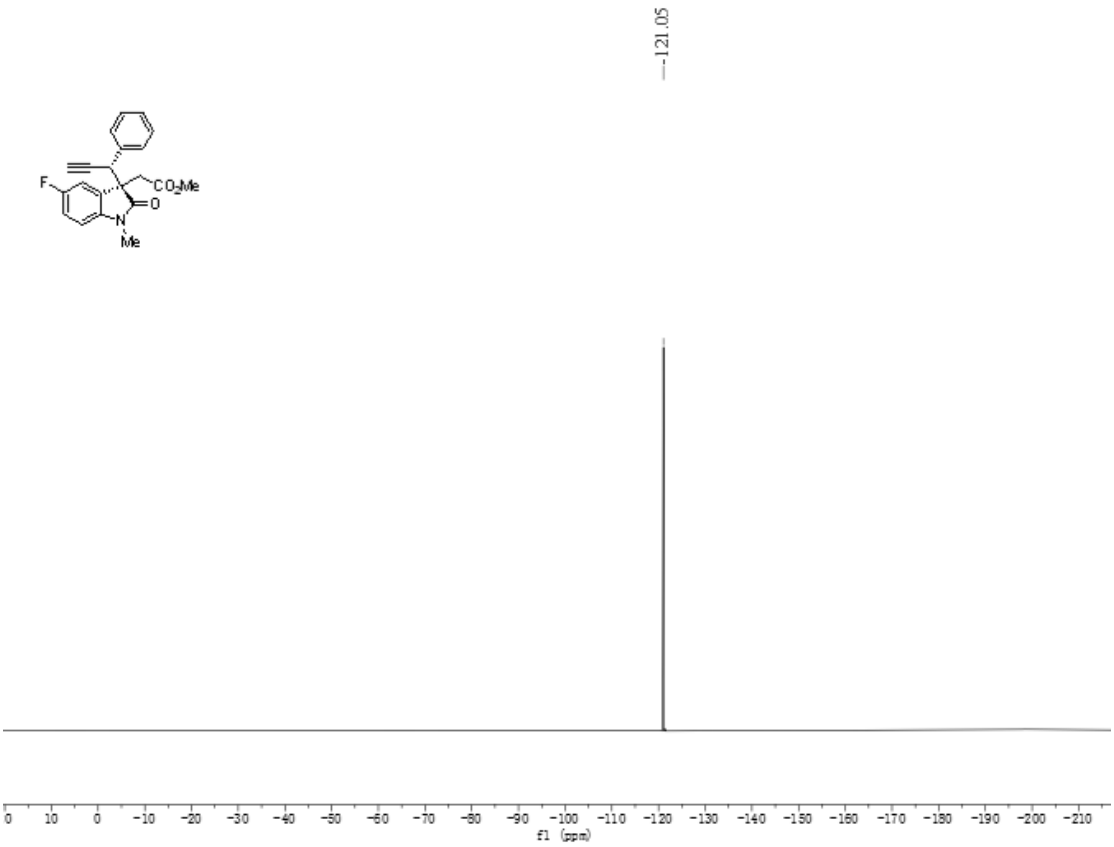

175.59
170.45
159.97
157.53
146.58
146.48
134.90
130.71
130.63
128.67
127.87
127.66
114.39
114.20
109.74
109.53
103.99
103.96
80.56
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
74.41
53.28
53.25
51.93
43.82
38.50
26.43
F
CO2Me
O
N
Me
f1 (ppm)



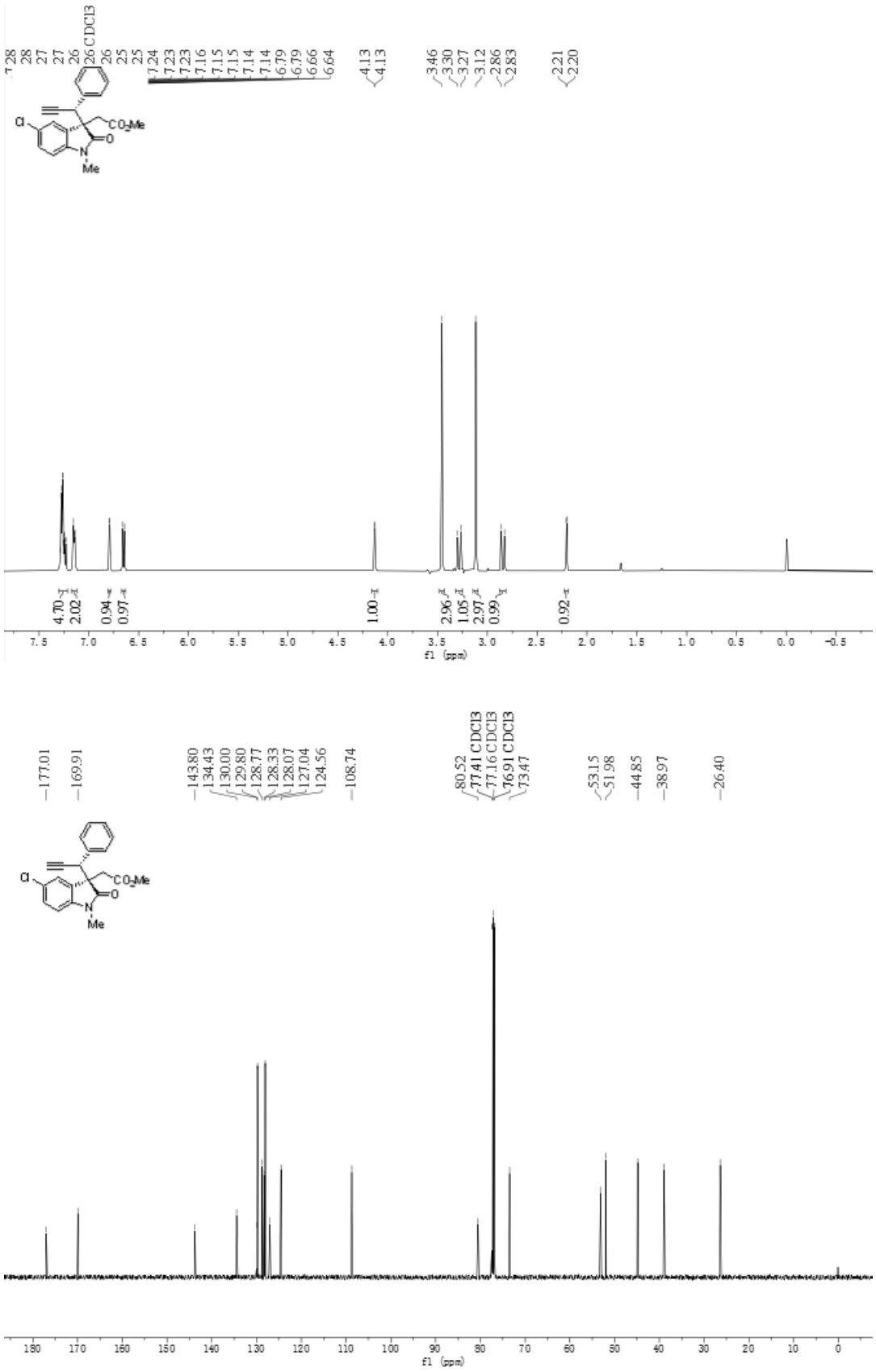

**Supplementary Fig. 7.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*R*)-**3ea**


7.29
7.28
7.28
7.28
7.28
7.27
7.26 CDCl3
7.26
7.26
7.25
7.25
7.17
7.16
7.16
7.16
7.15
7.15
7.15
7.00
6.99
6.97
6.97
6.97
6.97
6.95
6.95
6.66
6.65
6.64
6.63
6.62
6.61
6.60
6.59
4.16
4.15
3.45
3.29
3.25
3.12
2.87
2.83
2.21
2.20
F
CO2Me
O
N
Me
2.22
0.80
2.03
1.07
1.05
1.00
1.00
2.99
1.07
3.05
1.03
0.95
f1 (ppm)

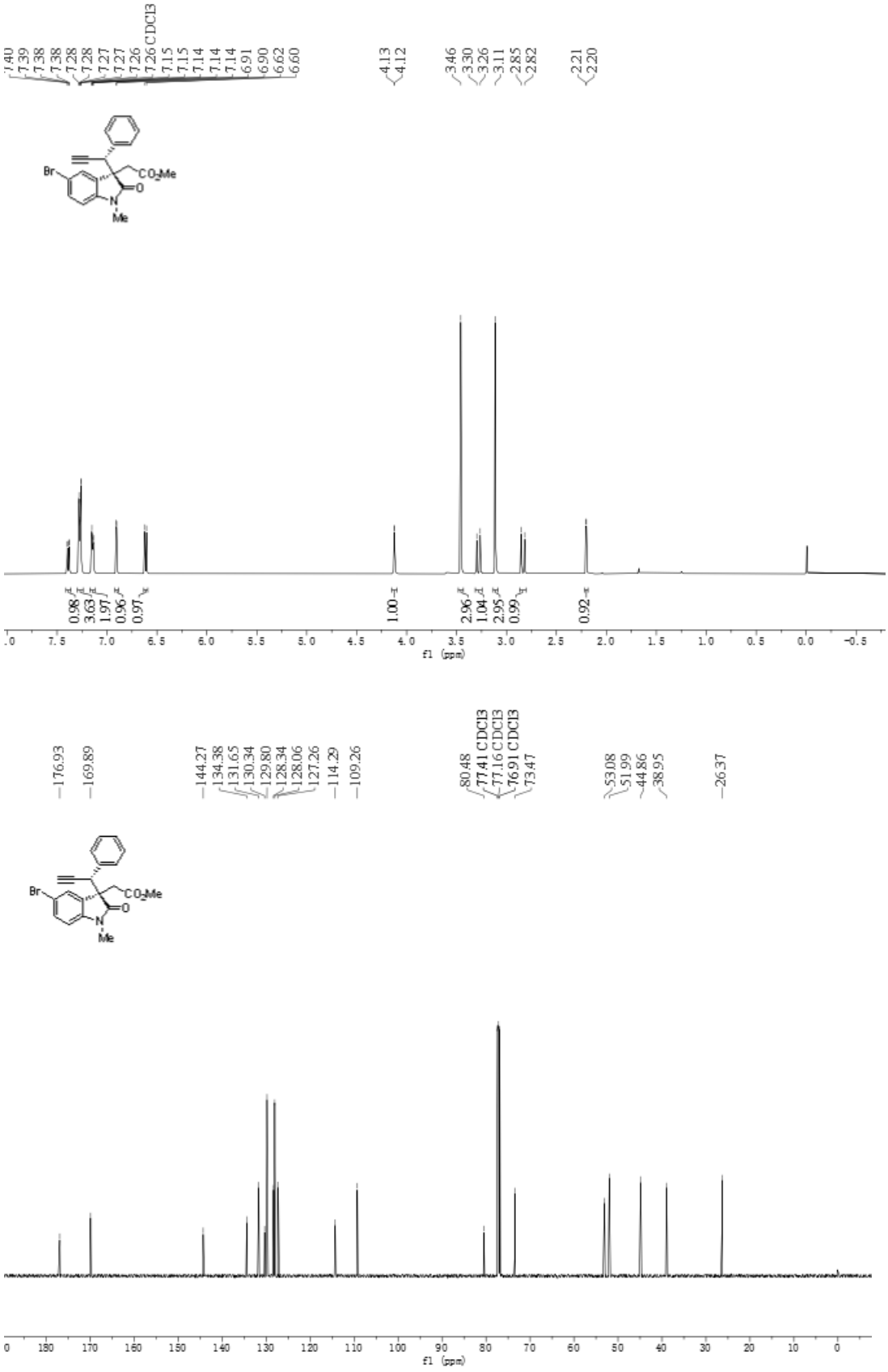

177.14
169.96
159.56
157.65
141.18
134.54
129.91
129.85
129.80
128.29
128.10
115.13
114.95
112.52
112.32
108.27
108.21
80.59
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
73.41
53.39
53.37
51.97
44.84
39.04
26.45
F
CO2Me
O
N
Me
f1 (ppm)



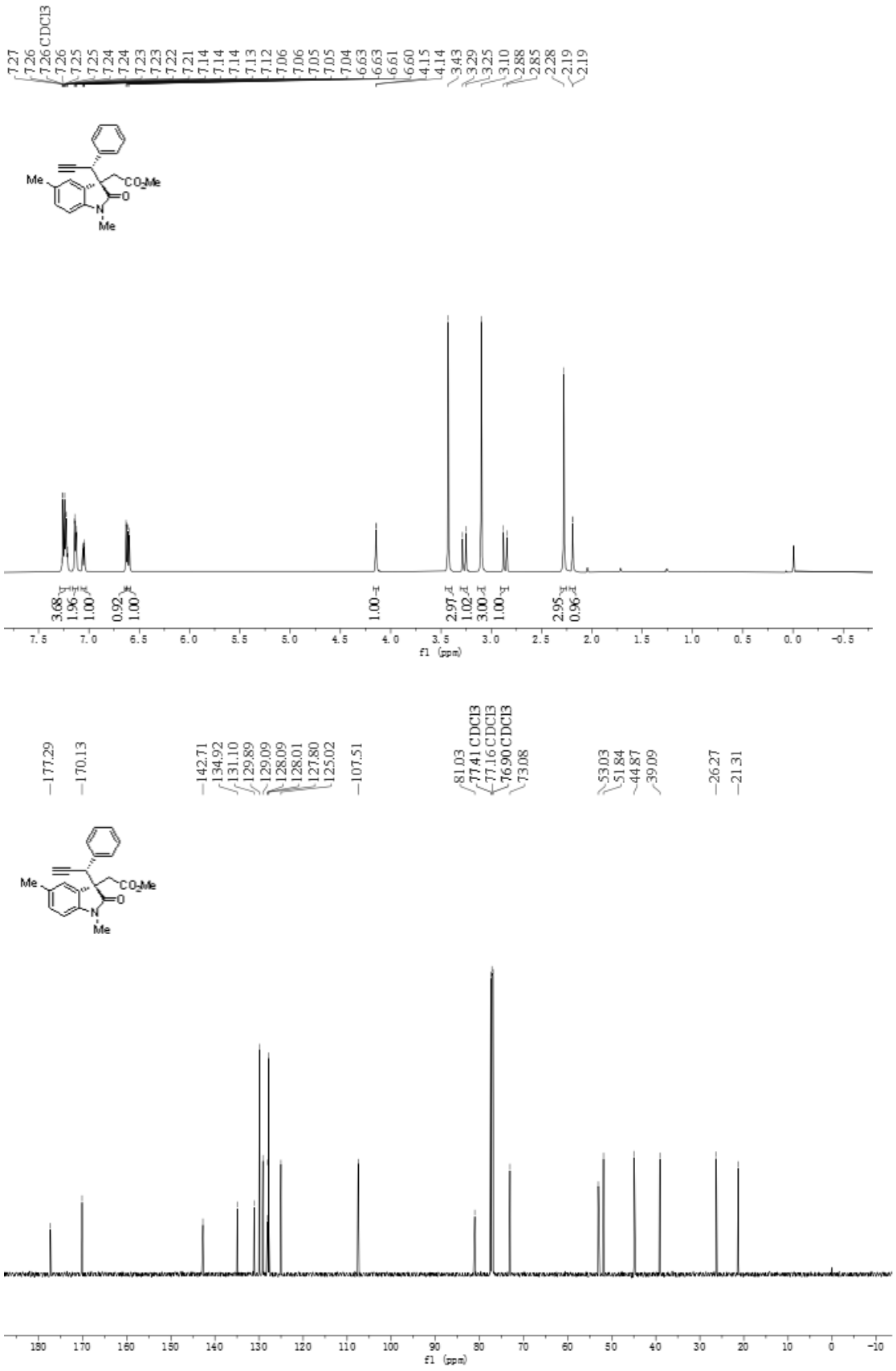

**Supplementary Fig. 8.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*R*)-**3fa**



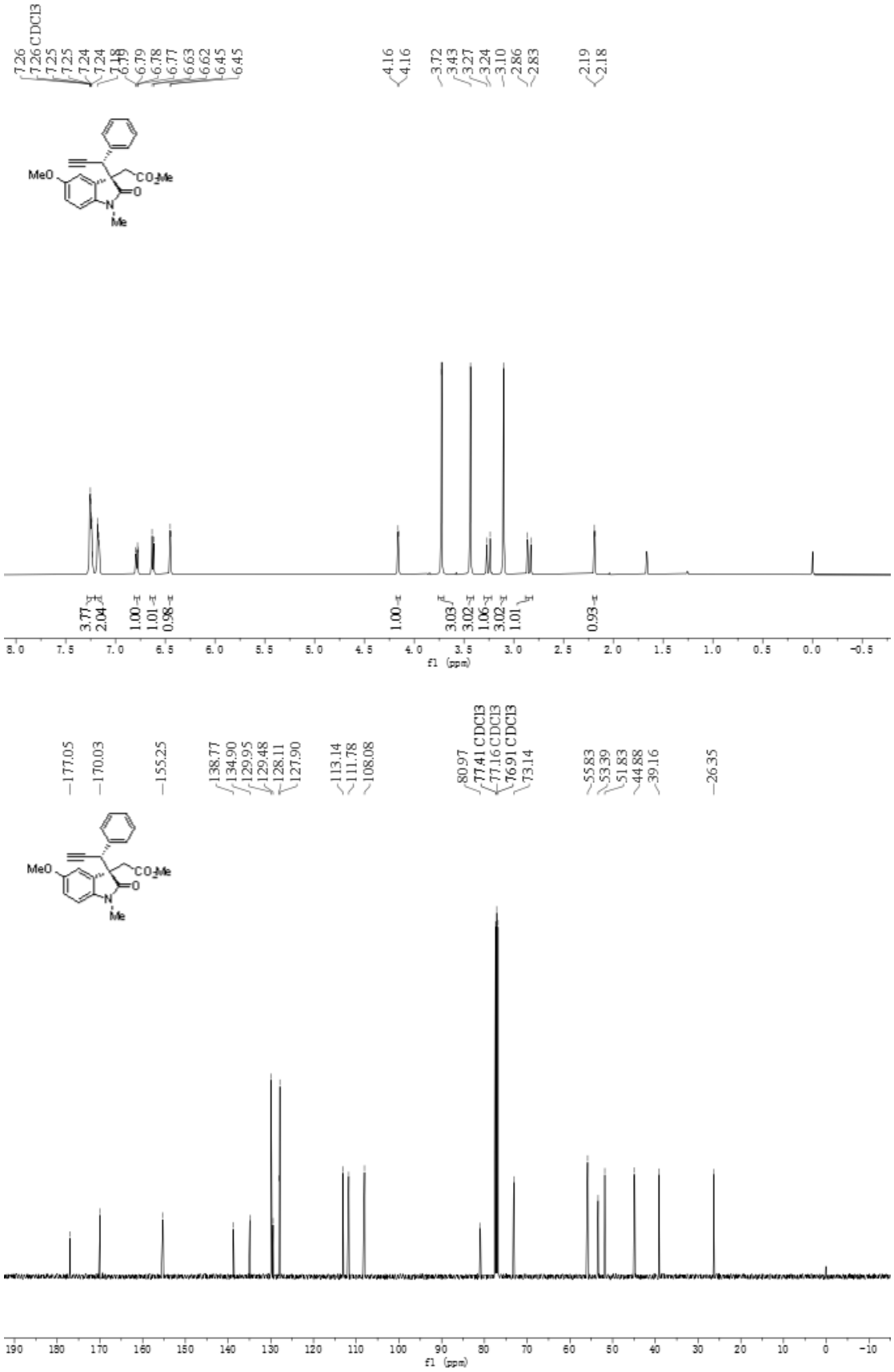
**Supplementary Fig. 9.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ga**



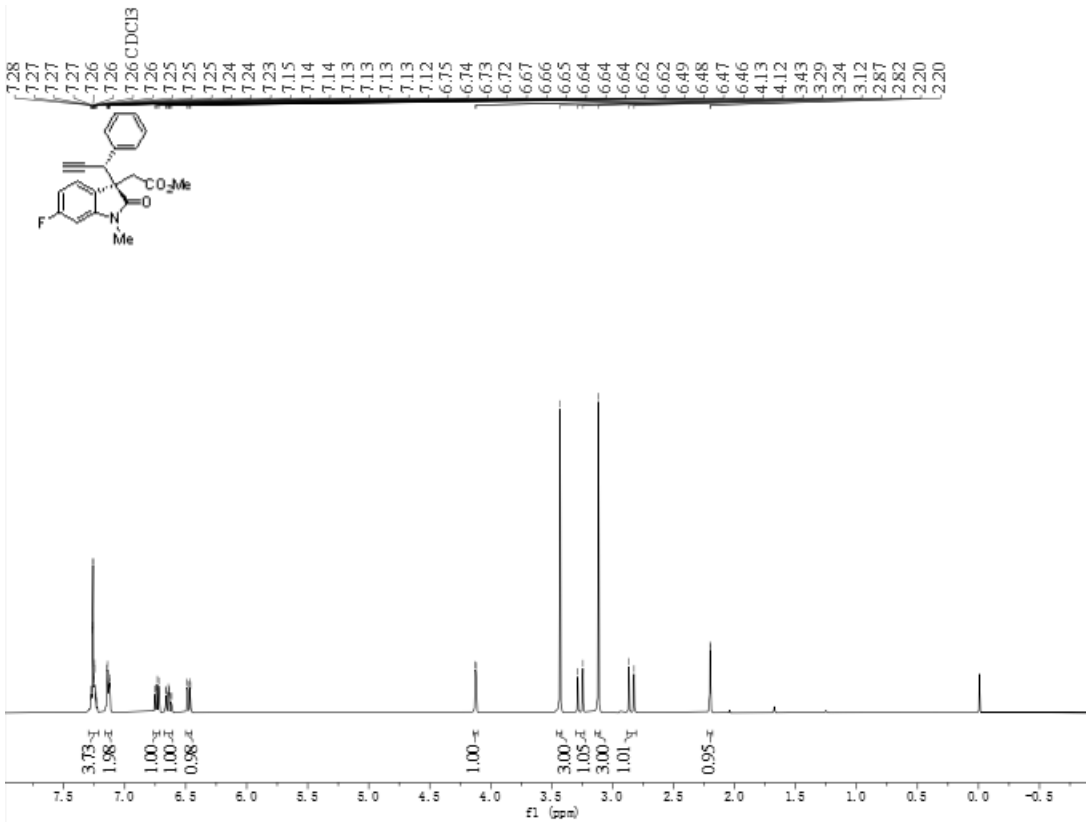

**Supplementary Fig. 10.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ha**

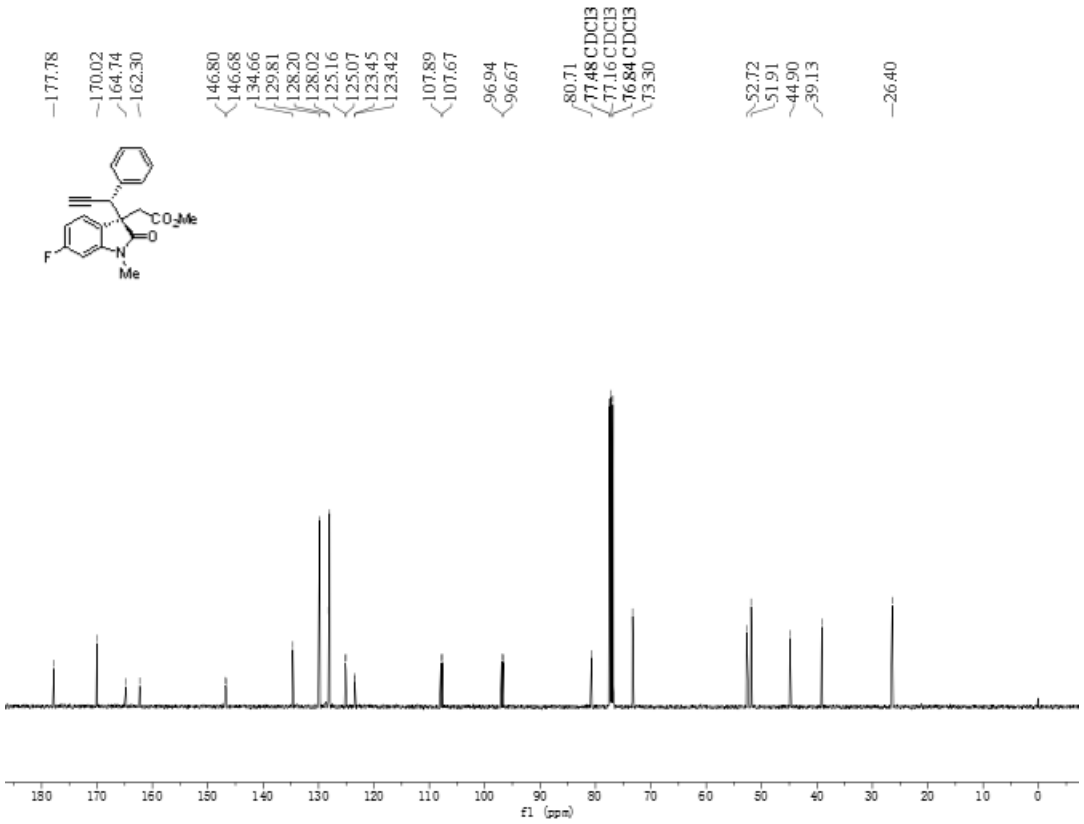


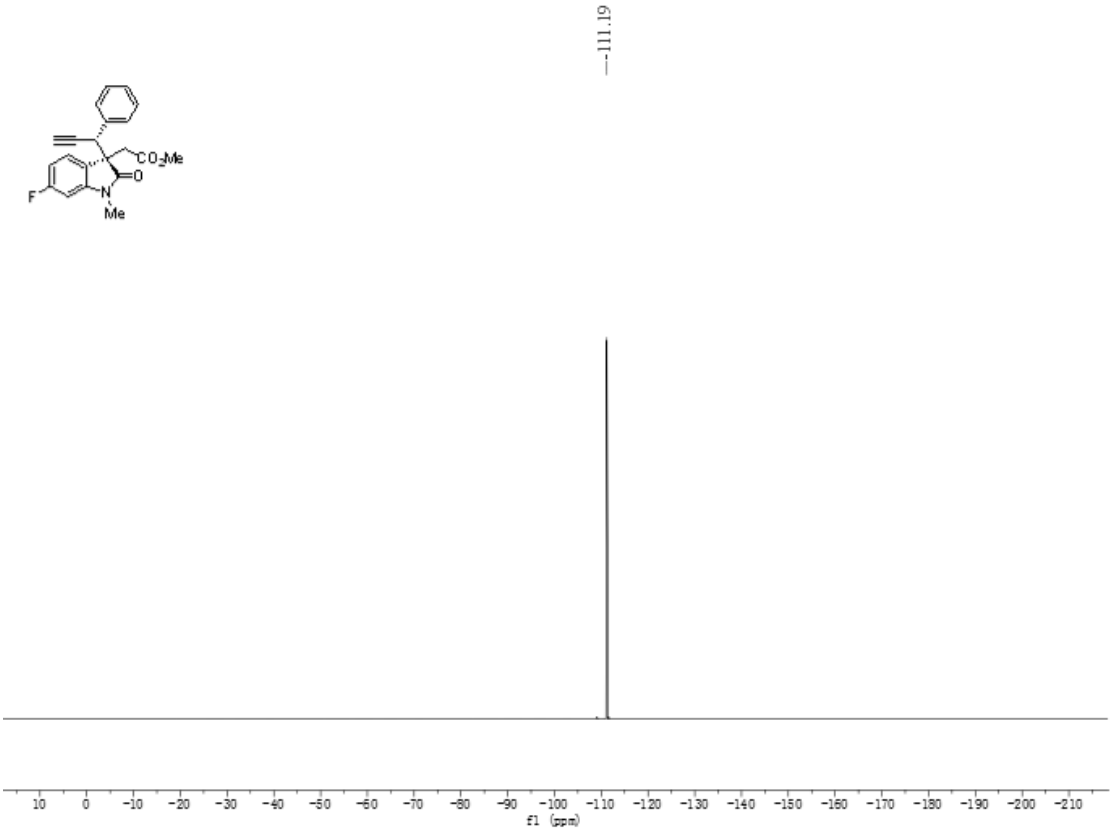

**Supplementary Fig. 11.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ia**



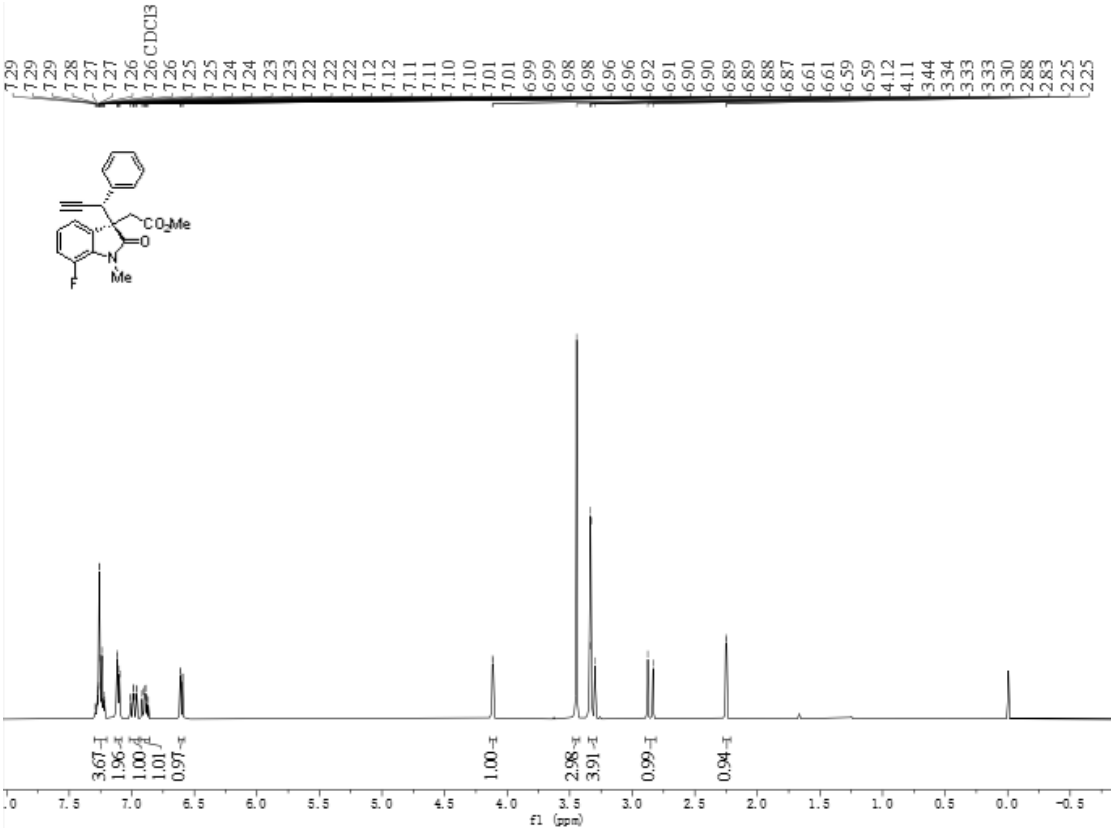

**Supplementary Fig. 12.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ja**

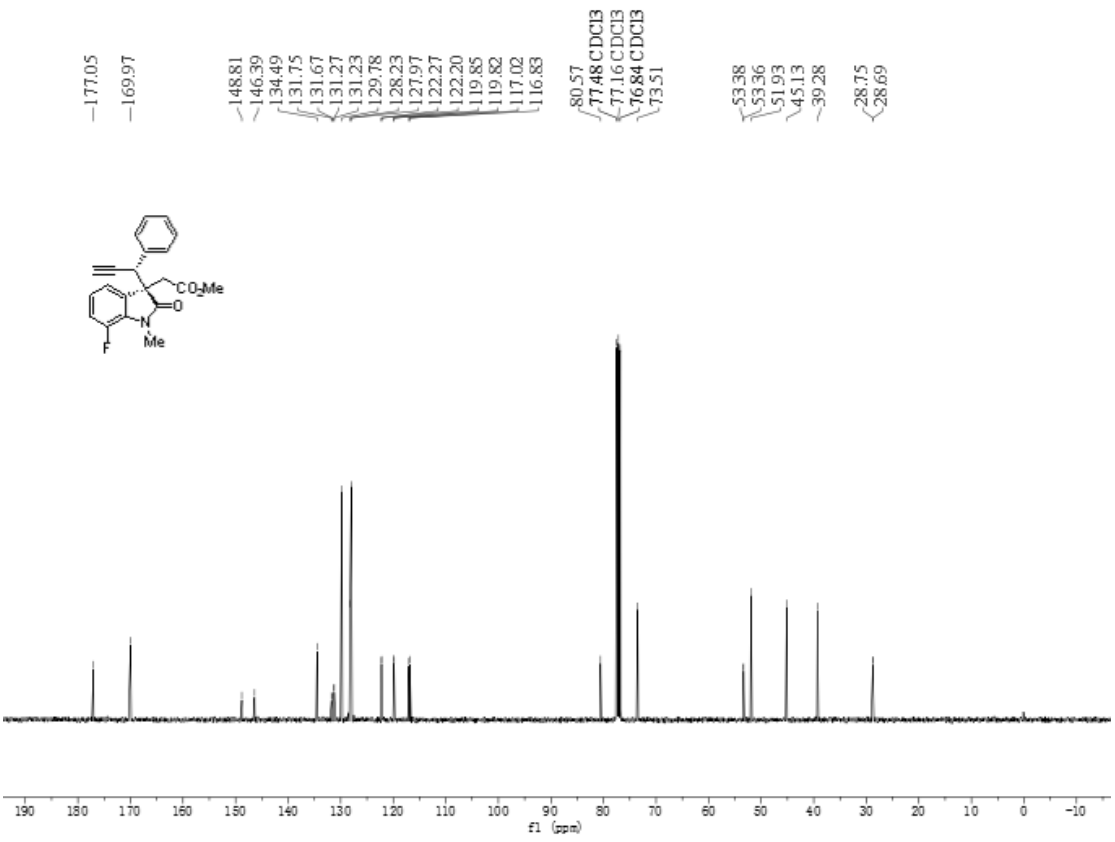

7.28 7.27 7.27 7.27 7.26 7.26 CDCl3 7.26 7.25 7.25 7.25 7.24 7.24 7.23 7.15 7.14 7.14 7.13 7.13 7.13 7.12 6.75 6.74 6.73 6.72 6.67 6.66 6.65 6.64 6.64 6.64 6.62 6.62 6.49 6.48 6.47 6.46 4.13 4.12 3.43 3.29 3.24 3.12 2.87 2.82 2.20 2.20
CO2Me
O
F
N
Me
3.73 1.98 1.00 1.00 0.98 1.00 3.00 1.05 3.00 1.01 0.95
f1 (ppm)

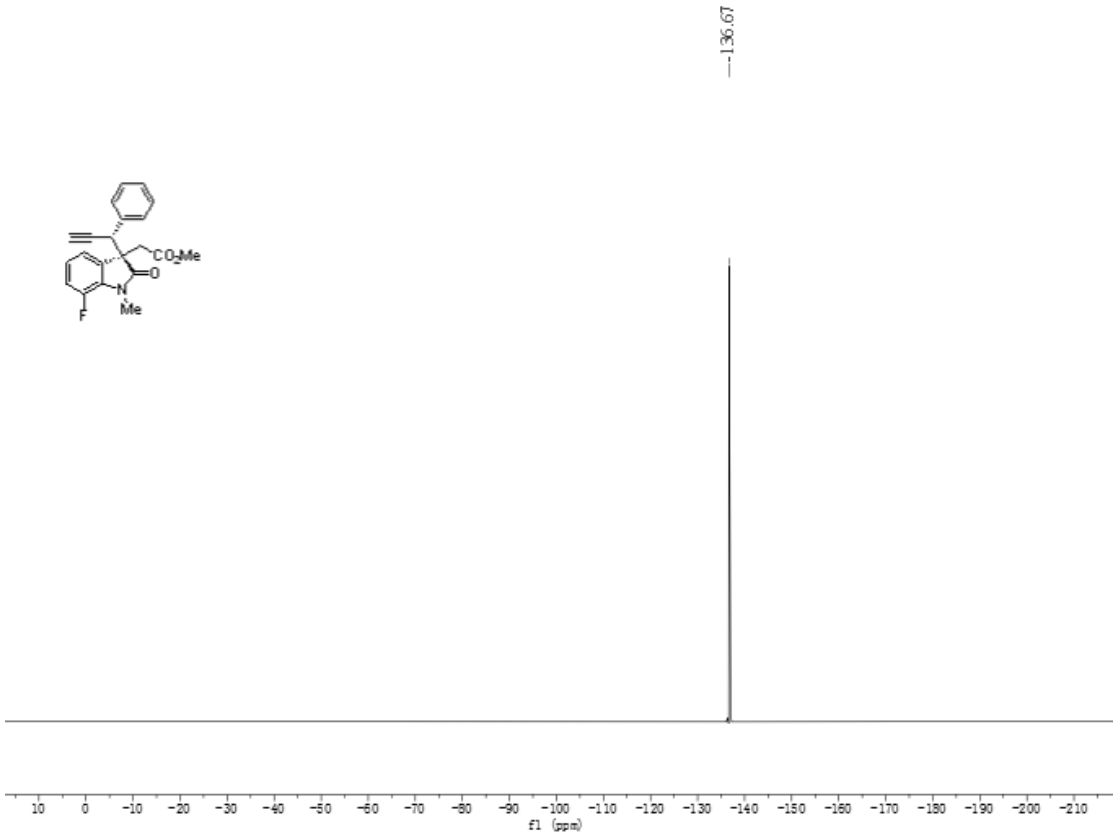

177.78 170.02 164.74 162.30 146.80 146.68 134.66 129.81 128.20 128.02 125.16 125.07 123.45 123.42 107.89 107.67 96.94 96.67 80.71 77.48 CDCl3 77.16 CDCl3 76.84 CDCl3 73.30 52.72 51.91 44.90 39.13 26.40
CO2Me
O
F
N
Me
f1 (ppm)



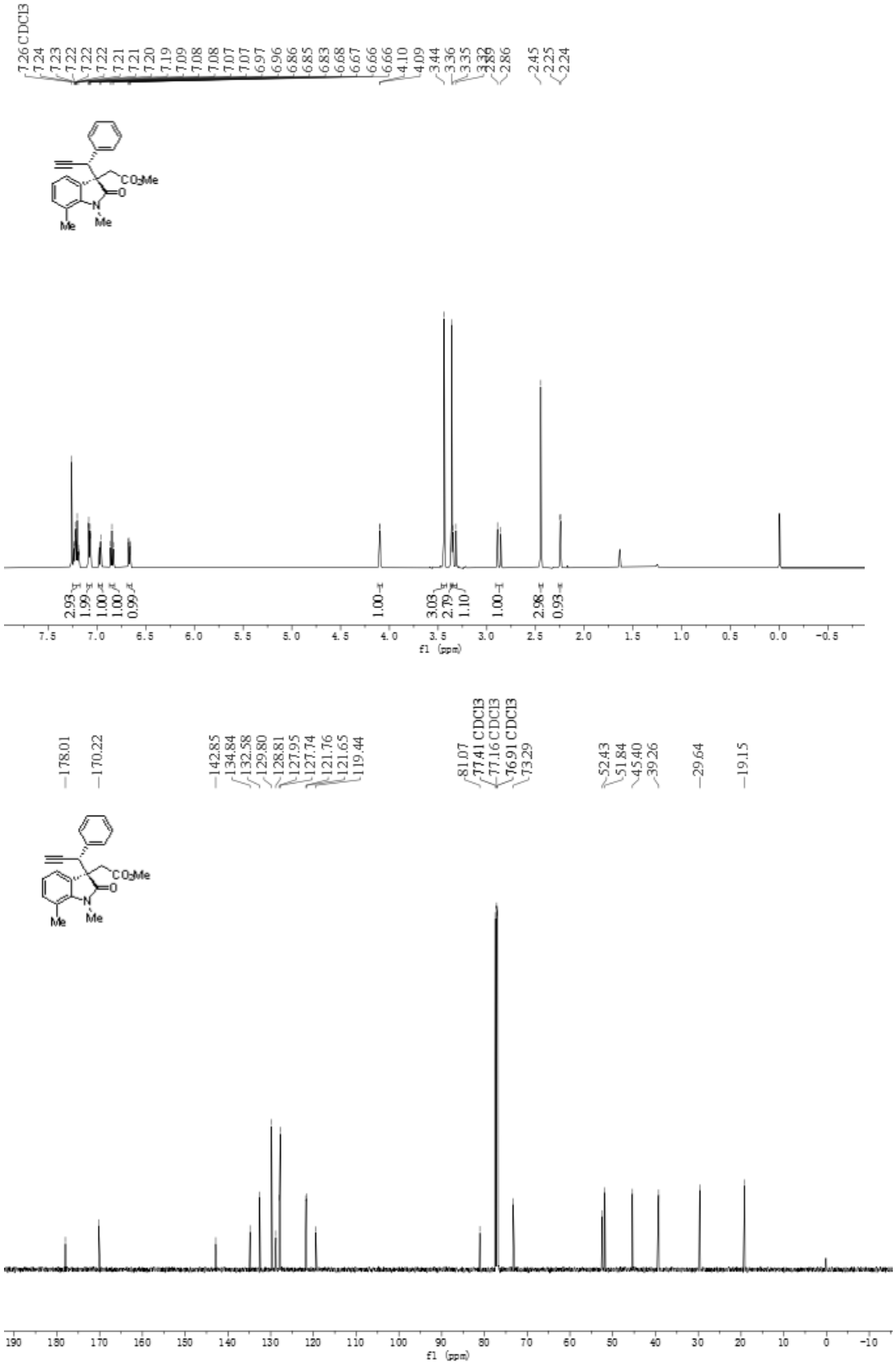

**Supplementary Fig. 13.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*R*)-**3ka**


7.29 7.29 7.29 7.28 7.27 7.27 7.26 7.26 CDCl3 7.26 7.25 7.24 7.24 7.23 7.23 7.22 7.22 7.22 7.12 7.12 7.11 7.11 7.10 7.10 7.01 7.01 6.99 6.99 6.98 6.98 6.96 6.96 6.92 6.91 6.90 6.90 6.89 6.89 6.88 6.87 6.61 6.61 6.59 6.59 4.12 4.11 3.44 3.34 3.33 3.33 3.30 2.88 2.83 2.25 2.25
CO2Me
O
N
Me
F
3.67 1.96 1.00 1.01 0.97 1.00 2.98 3.91 0.99 0.94
f1 (ppm)

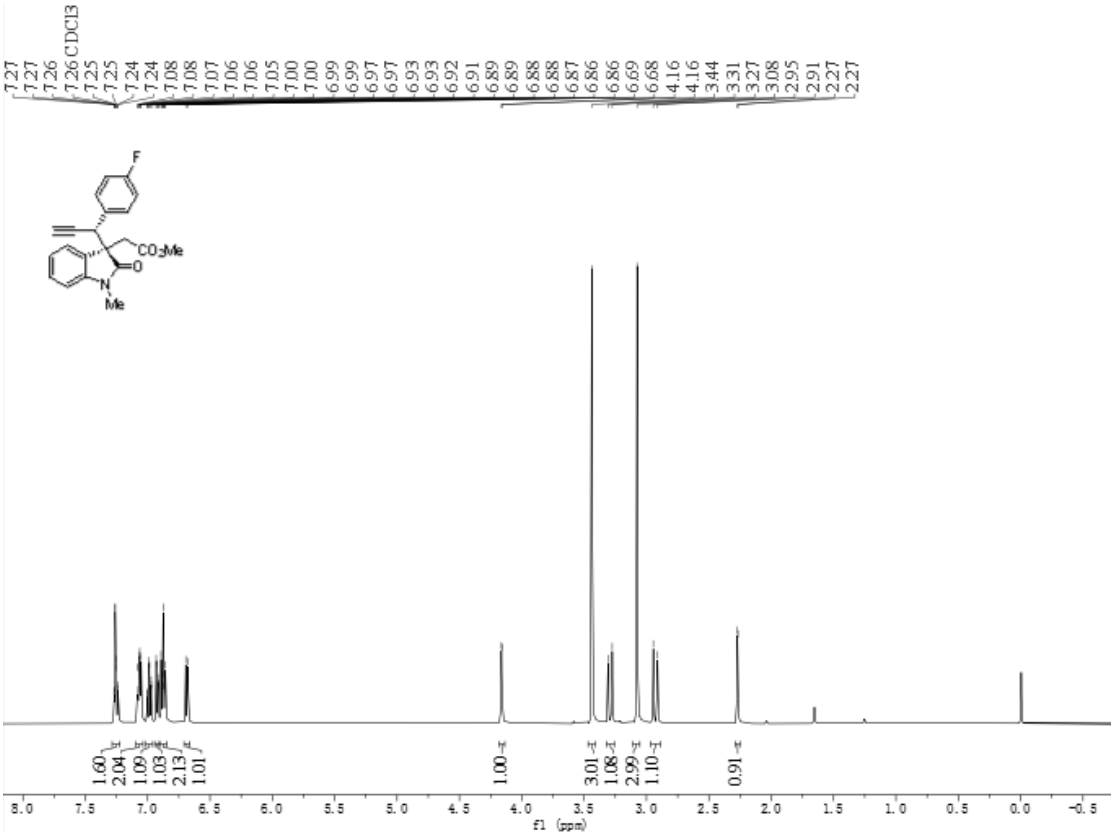

177.05 169.97 148.81 146.39 134.49 131.75 131.67 131.27 131.23 129.78 128.23 127.97 122.27 122.20 119.85 119.82 117.02 116.83 80.57 77.48 CDCl3 77.16 CDCl3 76.84 CDCl3 73.51 53.38 53.36 51.93 45.13 39.28 28.75 28.69
CO2Me
O
N
Me
F
f1 (ppm)

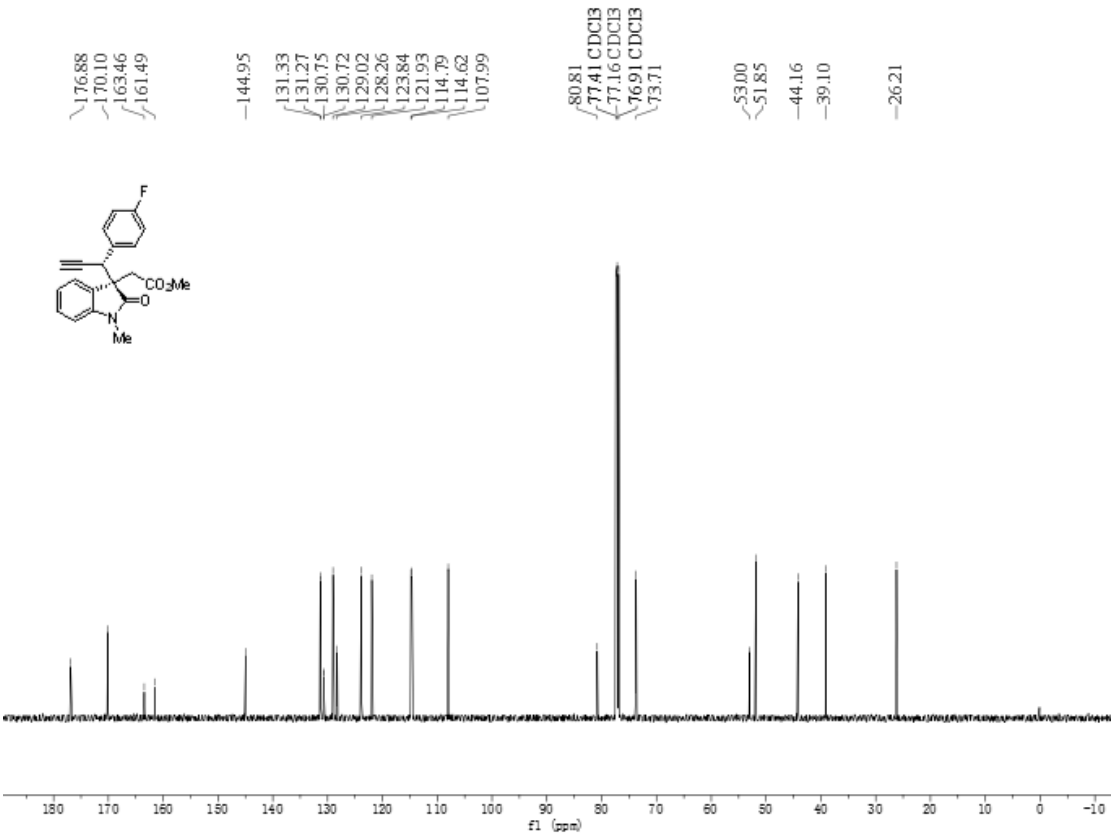


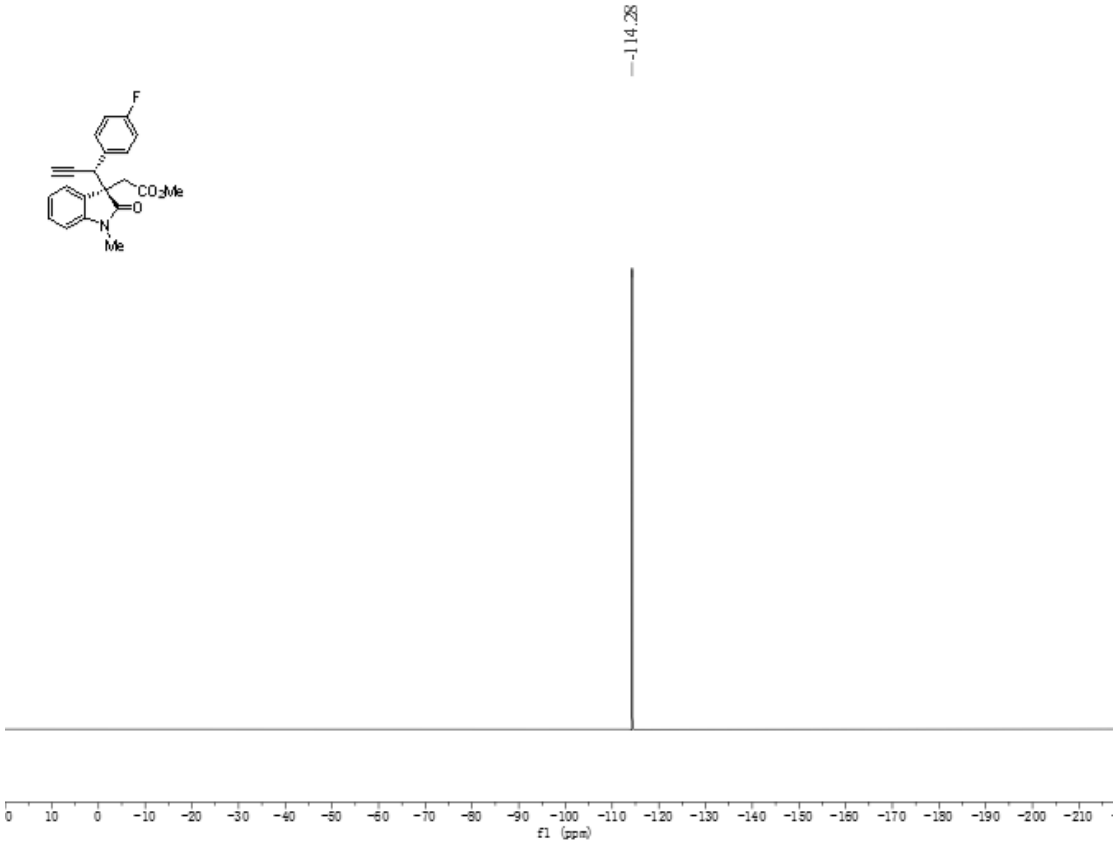

**Supplementary Fig. 14.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*R*)-**3la**



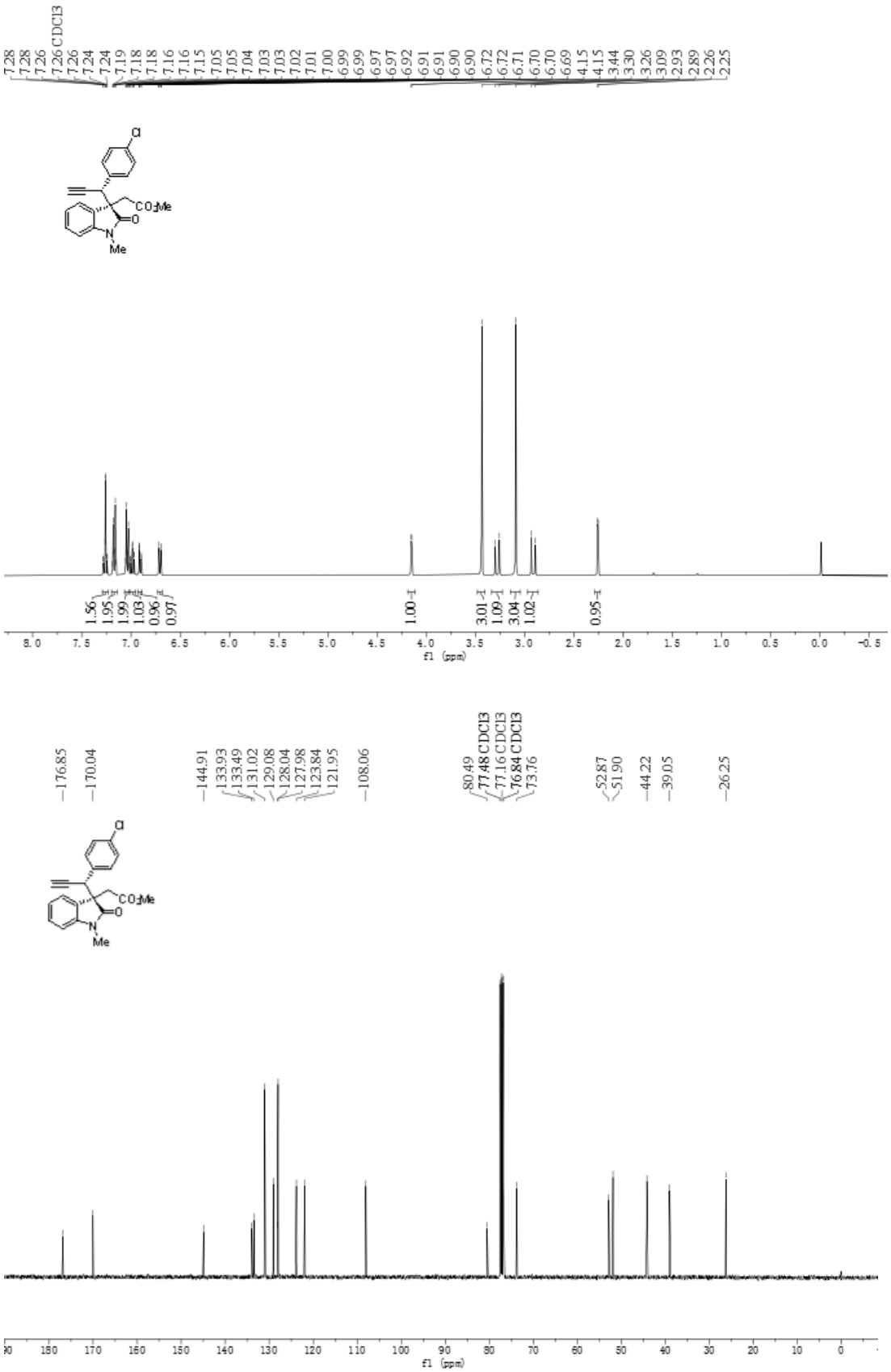

**Supplementary Fig. 15.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ma**


7.27
7.27
7.26
7.26 CDCl3
7.25
7.25
7.24
7.24
7.08
7.08
7.07
7.06
7.06
7.05
7.00
7.00
6.99
6.99
6.97
6.97
6.93
6.93
6.92
6.91
6.89
6.89
6.88
6.88
6.87
6.86
6.86
6.69
6.68
4.16
4.16
3.44
3.31
3.27
3.08
2.95
2.91
2.27
2.27
F
CO2Me
O
N
Me
1.60
2.04
1.09
1.03
2.13
1.01
1.00
3.01
1.08
2.99
1.10
0.91
f1 (ppm)

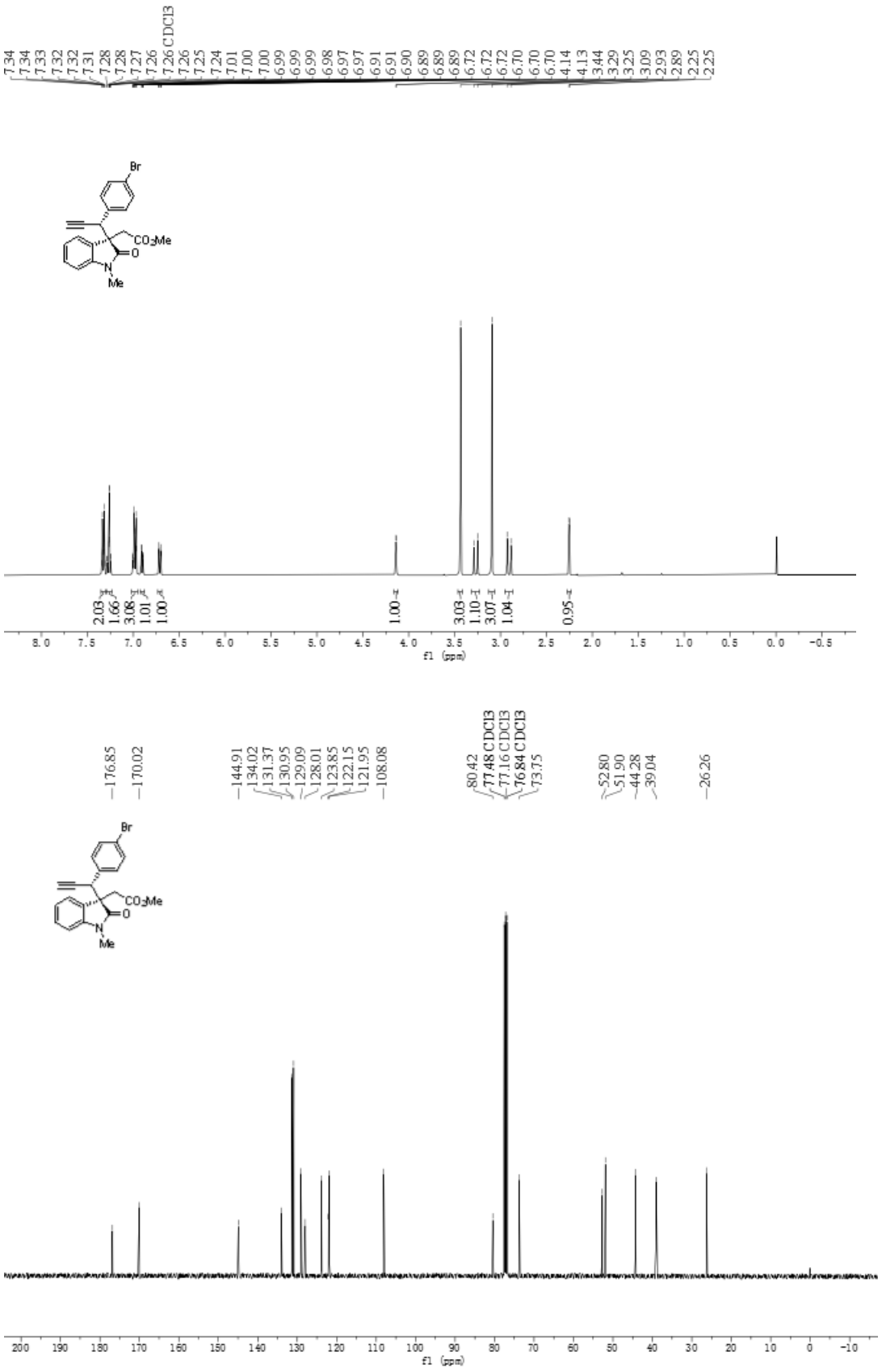

176.88
170.10
163.46
161.49
144.95
131.33
131.27
130.75
130.72
129.02
128.26
123.84
121.93
114.79
114.62
107.99
80.81
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
73.71
53.00
51.85
44.16
39.10
26.21
F
CO2Me
O
N
Me
f1 (ppm)



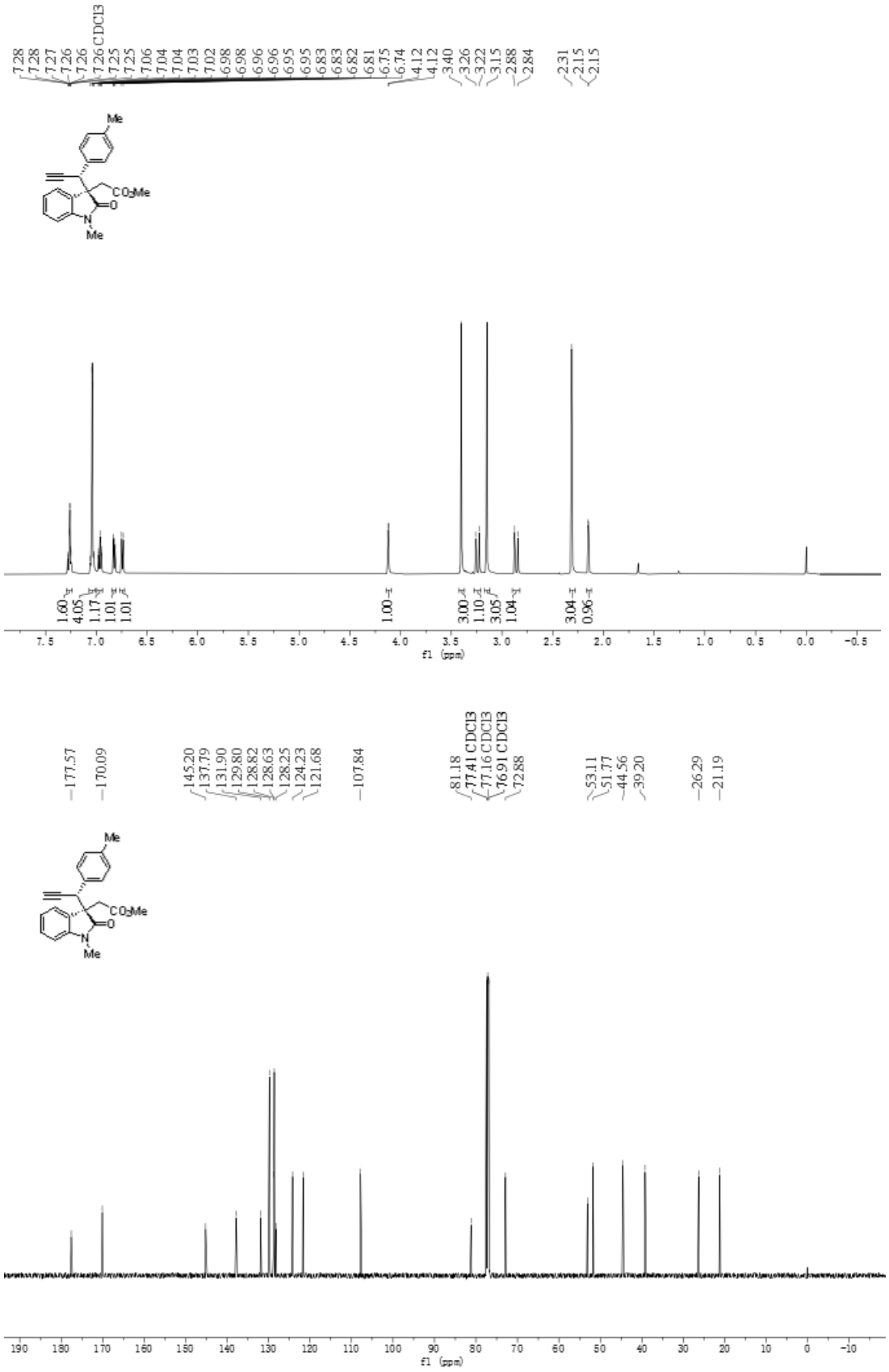

**Supplementary Fig. 16.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*R*)-**3ab**



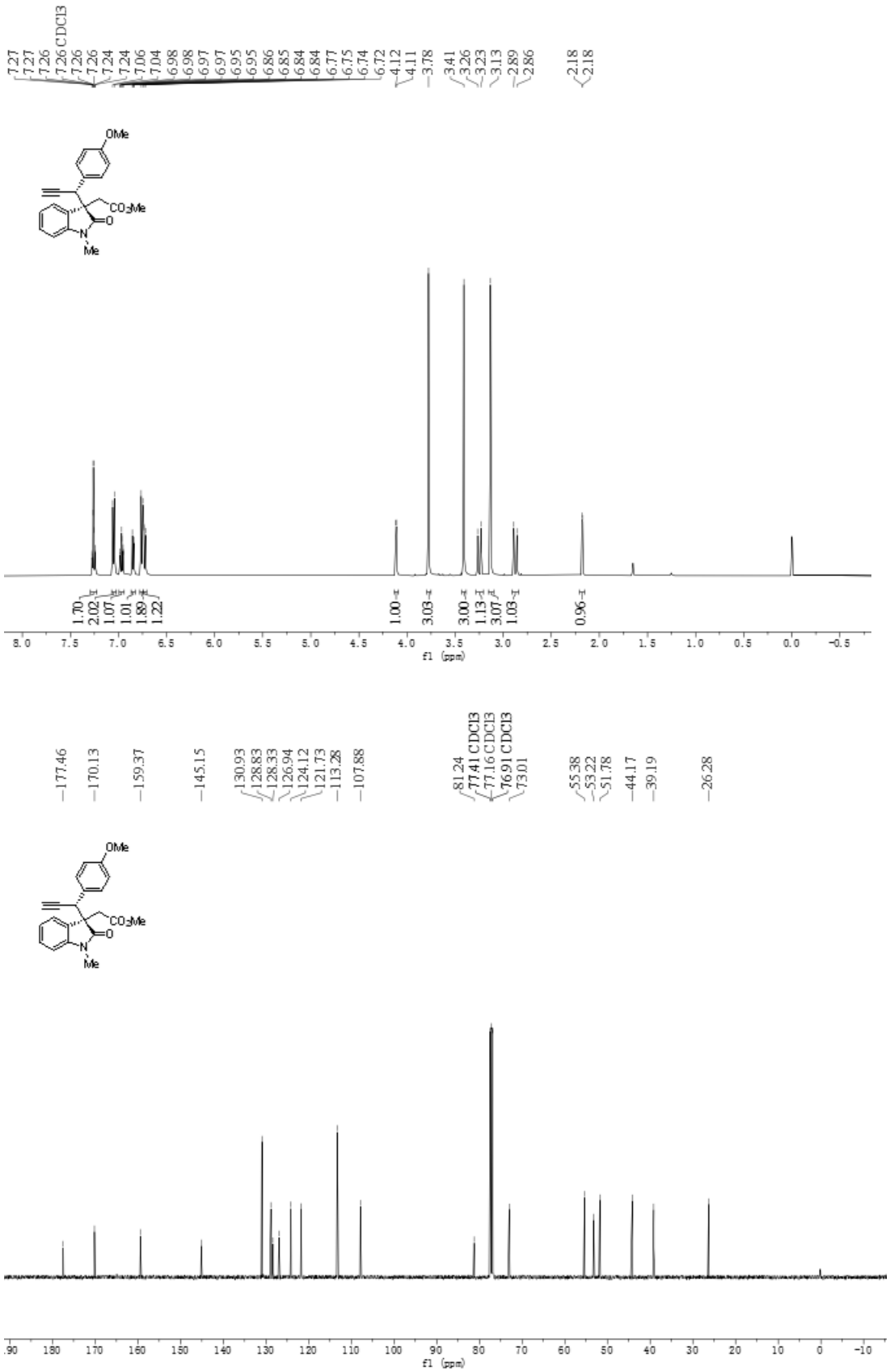

**Supplementary Fig. 17.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ac**



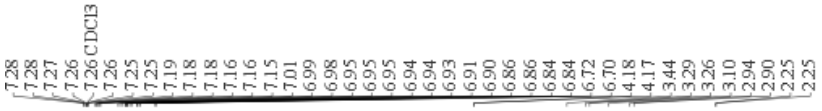

**Supplementary Fig. 18.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ad**

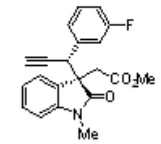


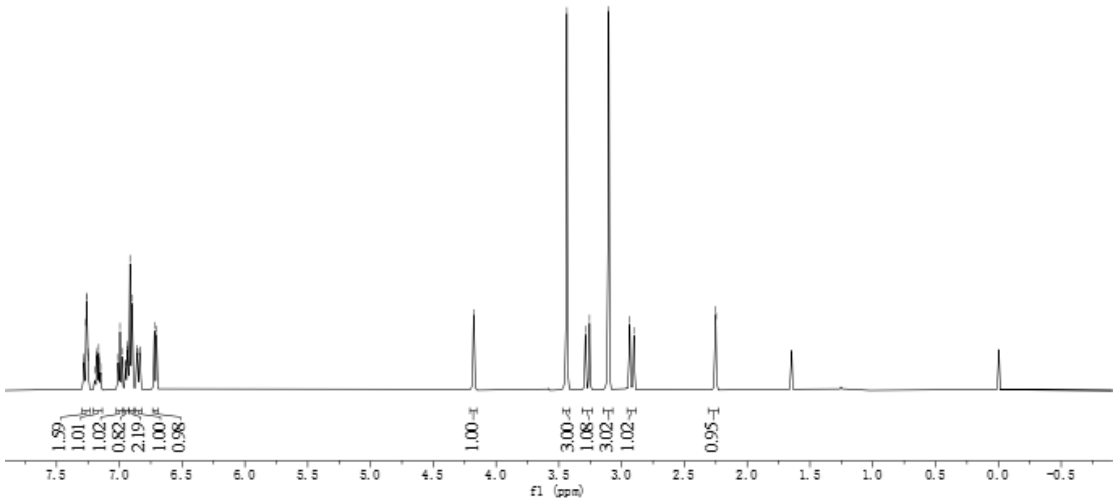

**Supplementary Fig. 19.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ae**



**Supplementary Fig. 20.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3af**

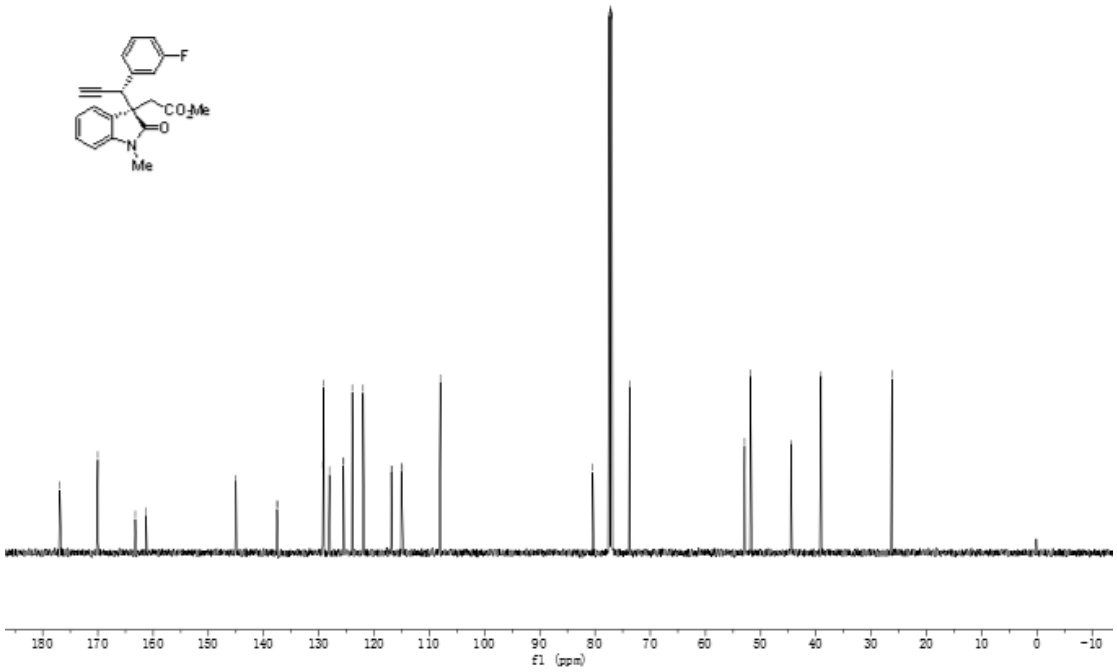

7.28
7.28
7.27
7.26 CDCl3
7.26
7.25
7.25
7.19
7.18
7.18
7.16
7.16
7.15
7.01
6.99
6.98
6.95
6.95
6.95
6.94
6.94
6.93
6.91
6.90
6.86
6.86
6.84
6.84
6.72
6.70
4.18
4.17
3.44
3.29
3.26
3.10
2.94
2.90
2.25
2.25

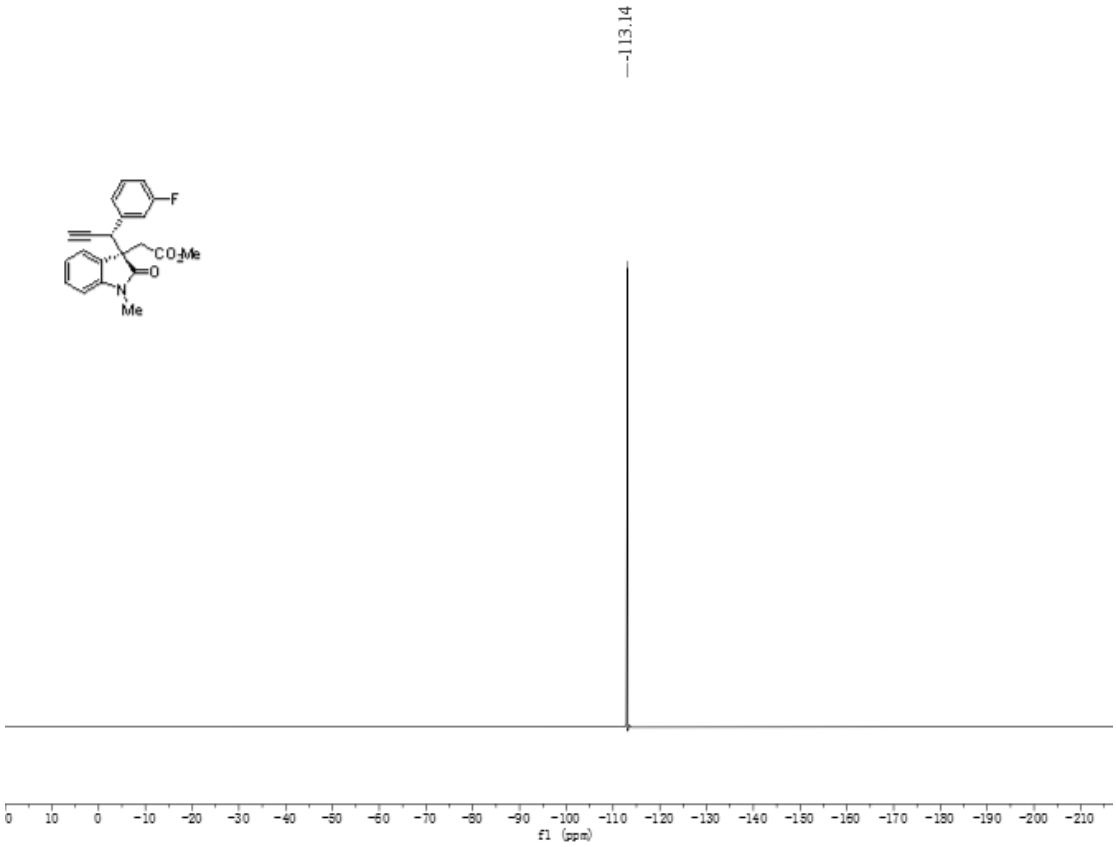

F
CO2Me
O
N
Me


1.99
1.01
1.02
0.82
2.19
1.00
0.98
1.00
3.00
1.08
3.02
1.02
0.95
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

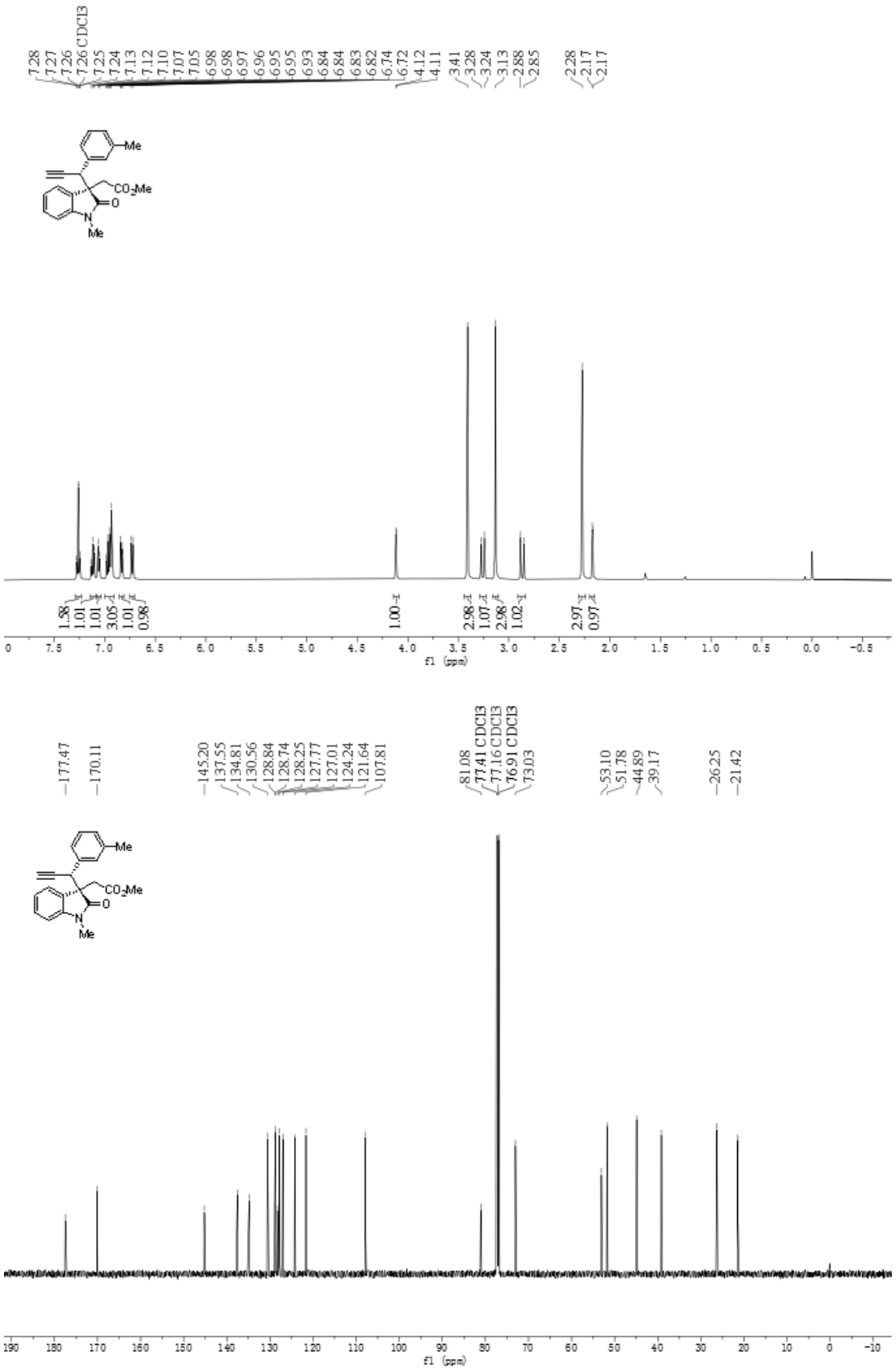

176.89
170.02
163.23
161.27
145.01
137.56
137.50
129.27
129.20
129.10
128.08
125.54
125.52
123.94
121.98
116.87
116.69
115.07
114.90
108.00
80.41
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
73.75
52.93
51.86
44.56
44.54
39.09
26.26


F
CO2Me
O
N
Me

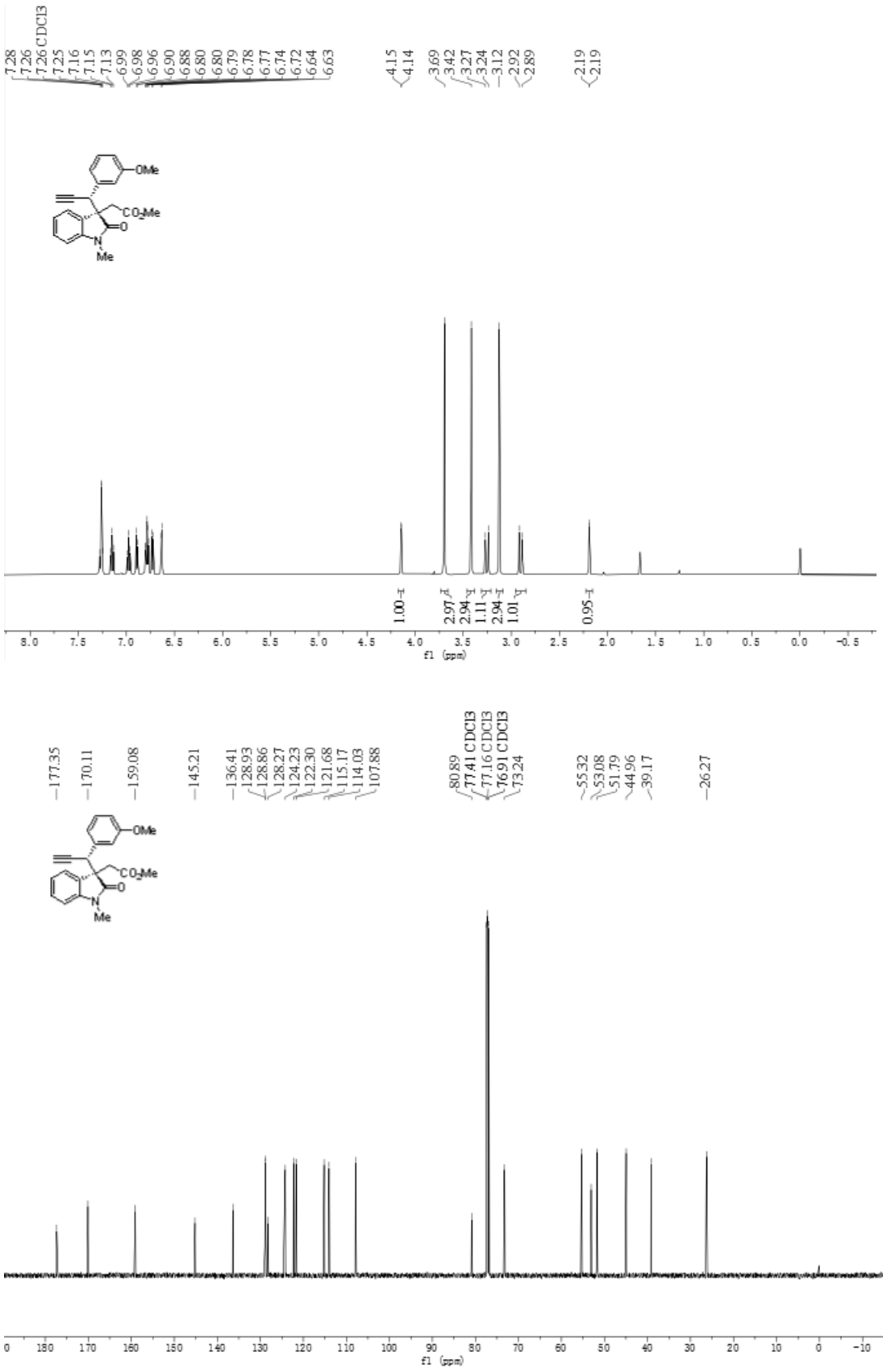

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



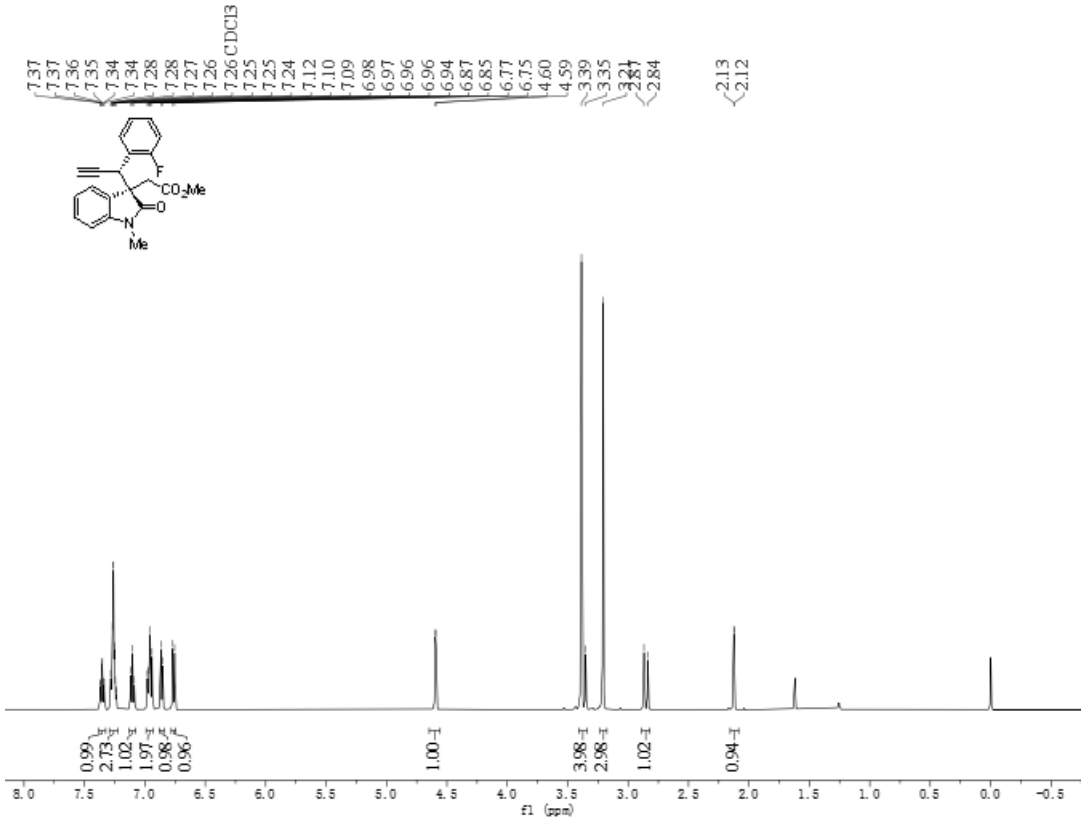

**Supplementary Fig. 21.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*R*)-**3ag**

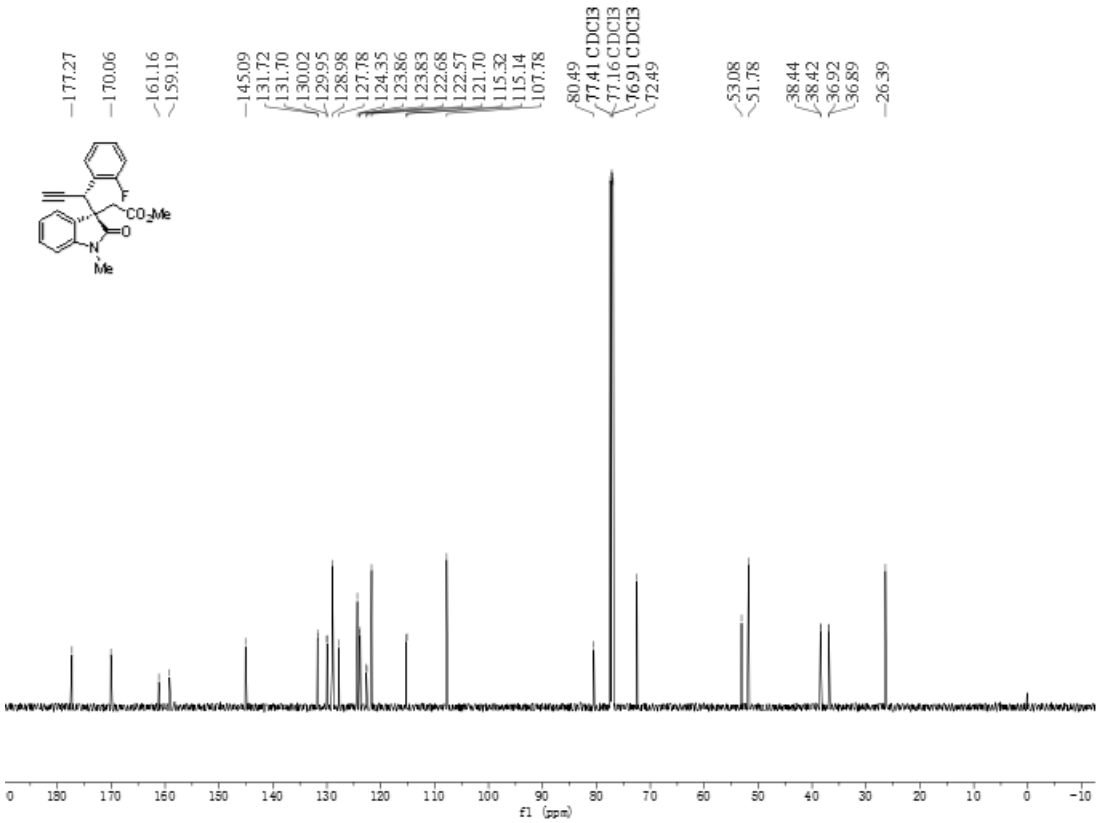


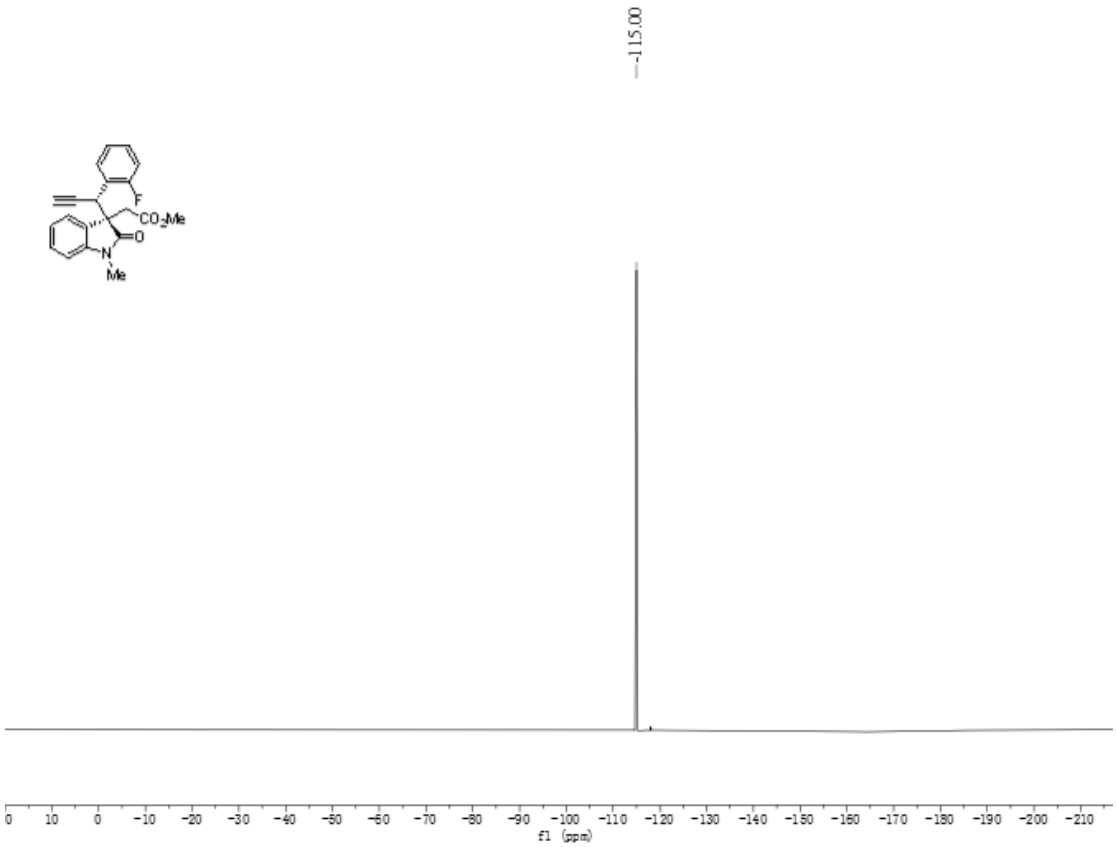

**Supplementary Fig. 22.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ah**



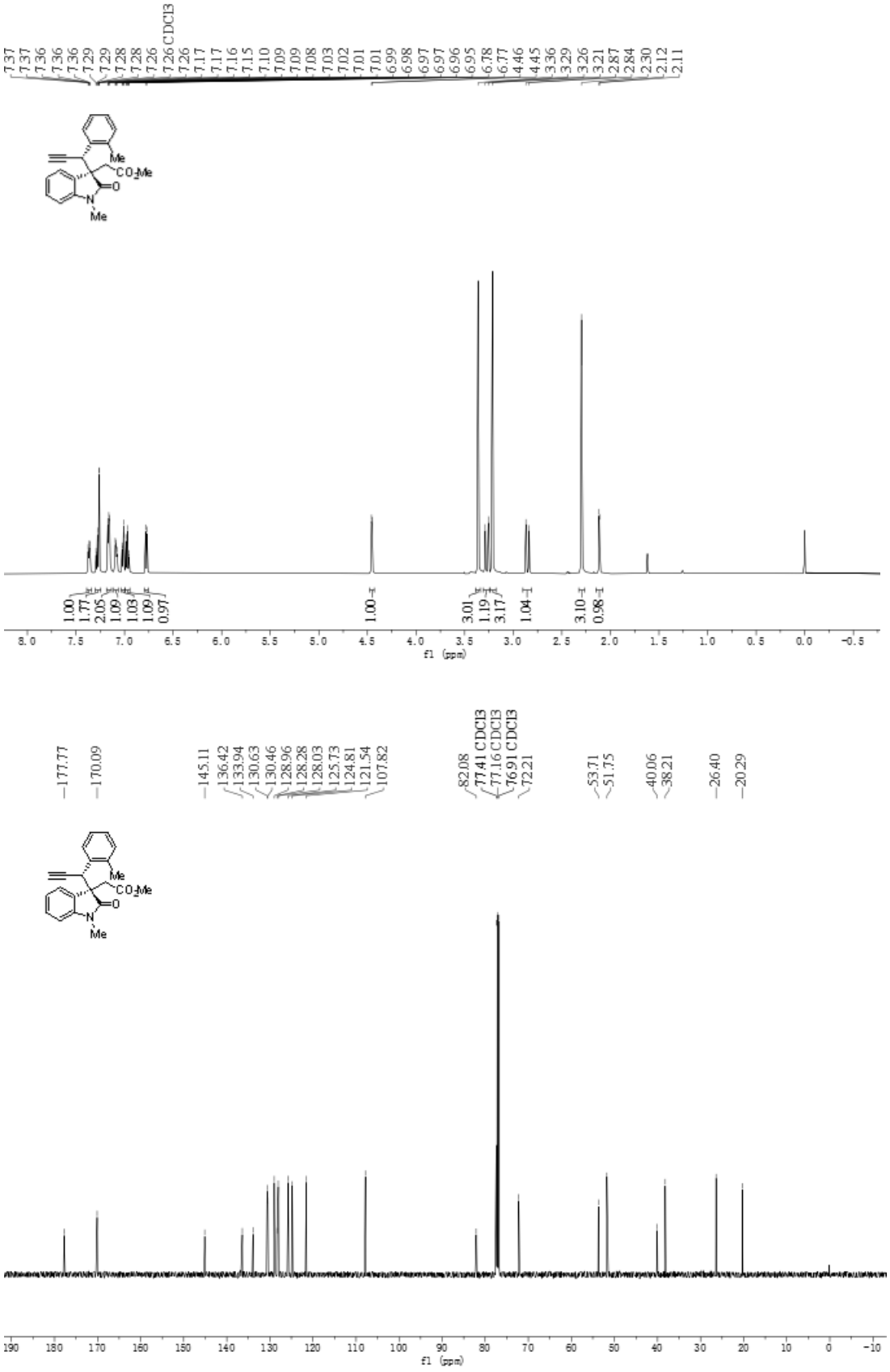

**Supplementary Fig. 23.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ai**


7.37
7.37
7.36
7.35
7.34
7.34
7.28
7.28
7.27
7.26
7.26 CDCl3
7.25
7.25
7.24
7.12
7.10
7.09
6.98
6.97
6.96
6.96
6.94
6.87
6.85
6.77
6.75
4.60
4.59
3.39
3.35
3.21
2.87
2.84
2.13
2.12
F
CO2Me
O
N
Me
0.99
2.73
1.02
1.97
0.98
0.96
1.00
3.98
2.98
1.02
0.94
f1 (ppm)

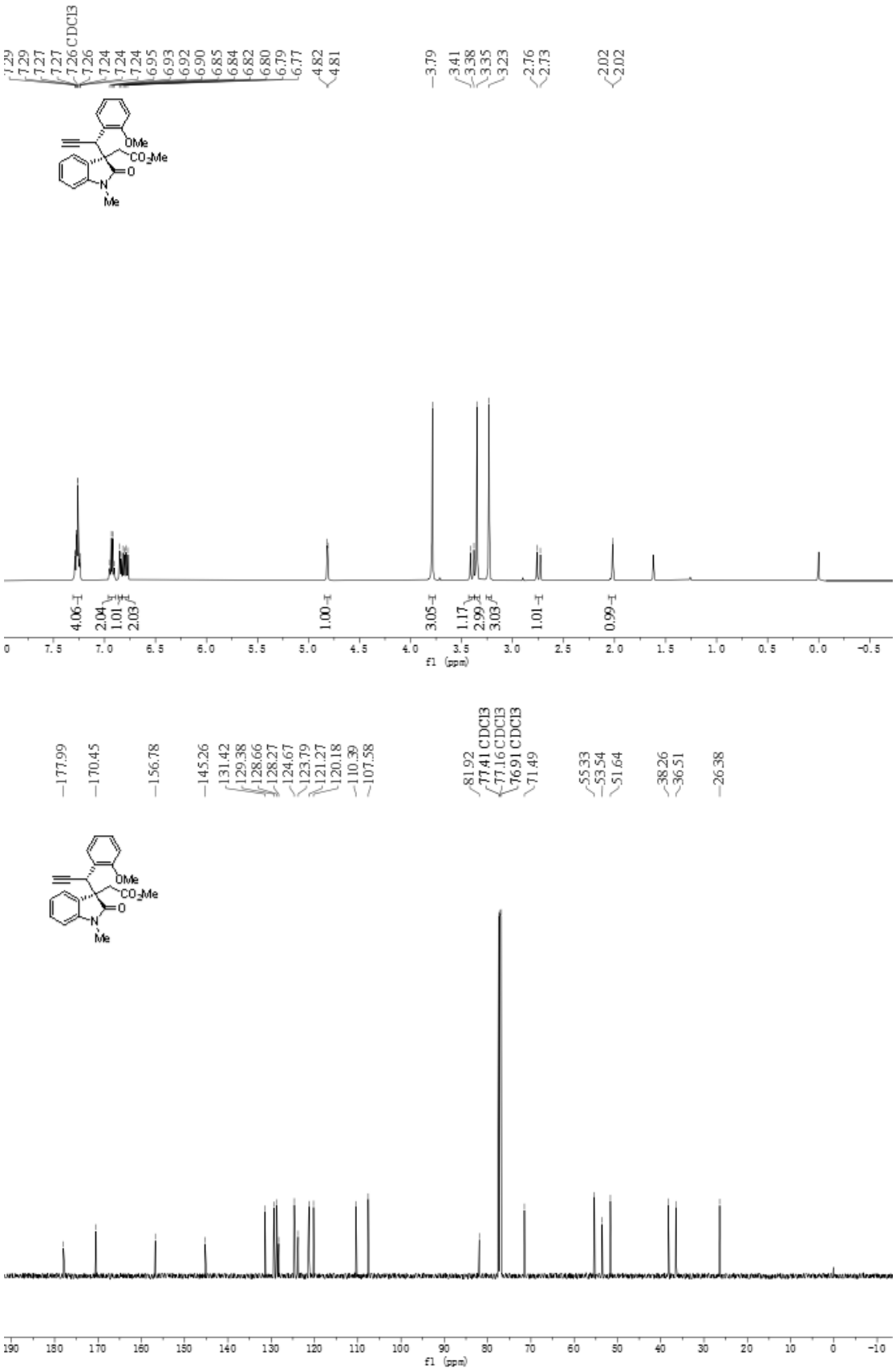

177.27
170.06
161.16
159.19
145.09
131.72
131.70
130.02
129.95
128.98
127.78
124.35
123.86
123.83
122.68
122.57
121.70
115.32
115.14
107.78
80.49
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
72.49
53.08
51.78
38.44
38.42
36.92
36.89
26.39
F
CO2Me
O
N
Me
f1 (ppm)



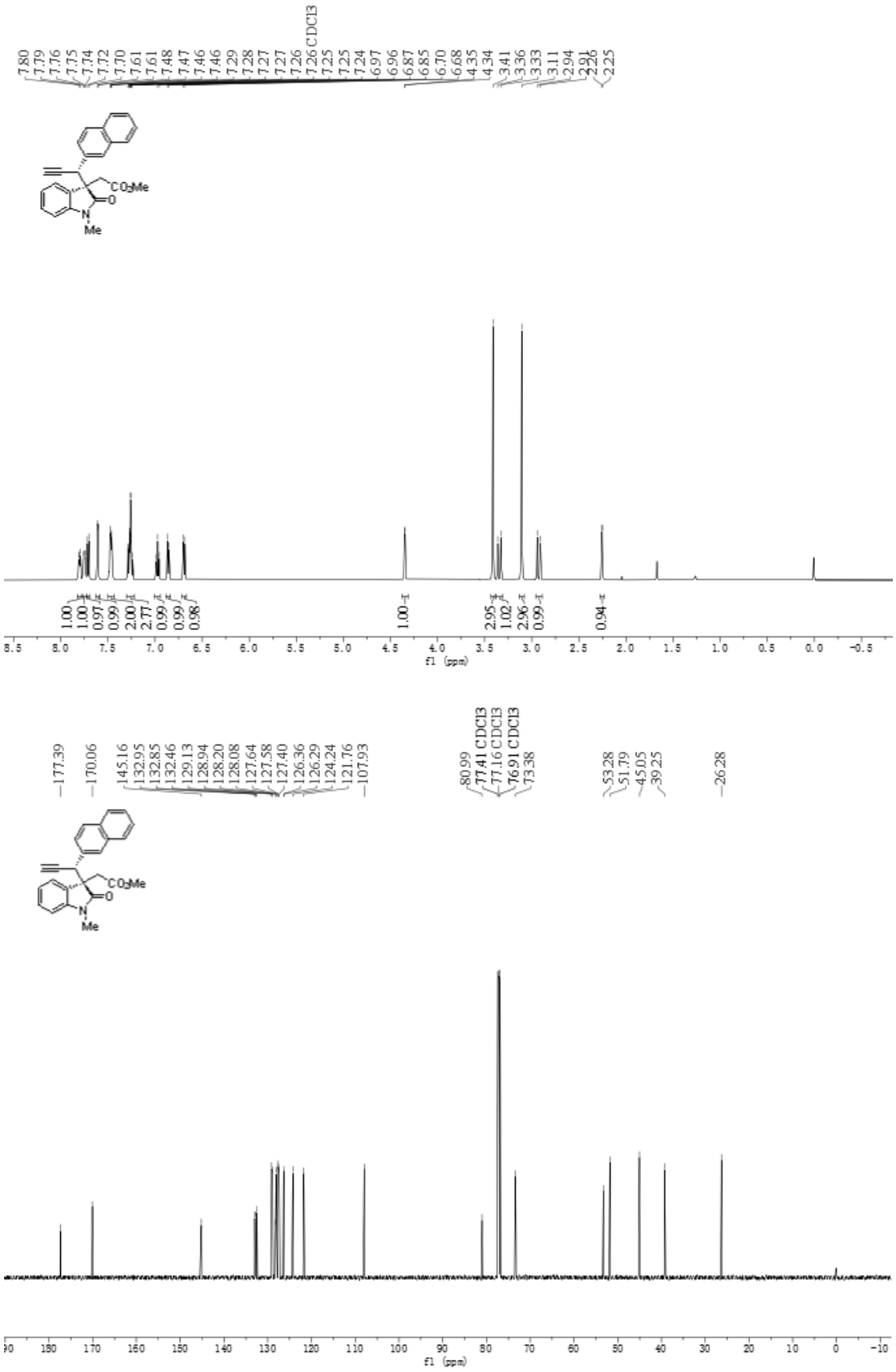

**Supplementary Fig. 24.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*S*)-**3aj**



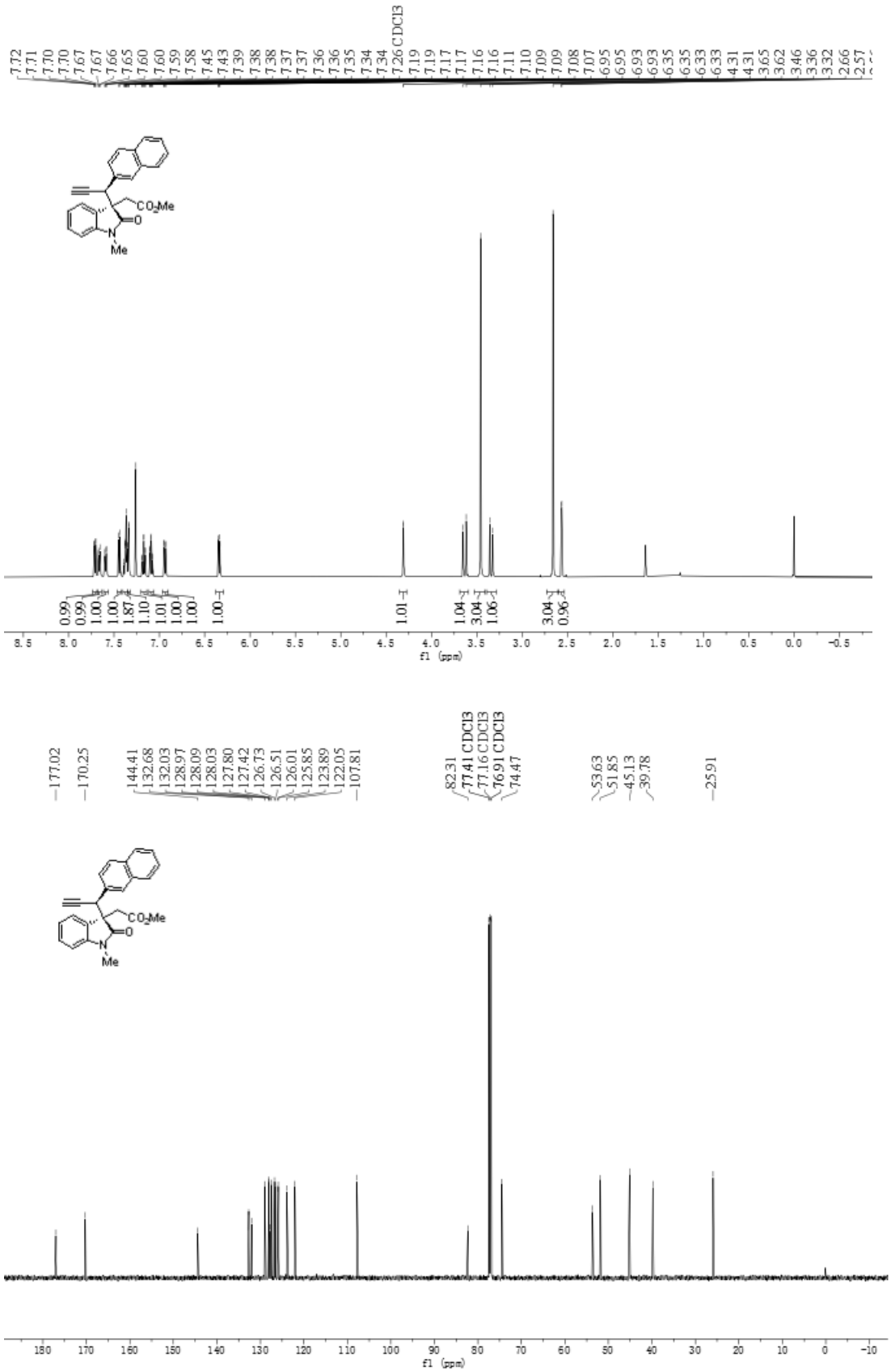

**Supplementary Fig. 25.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ak**



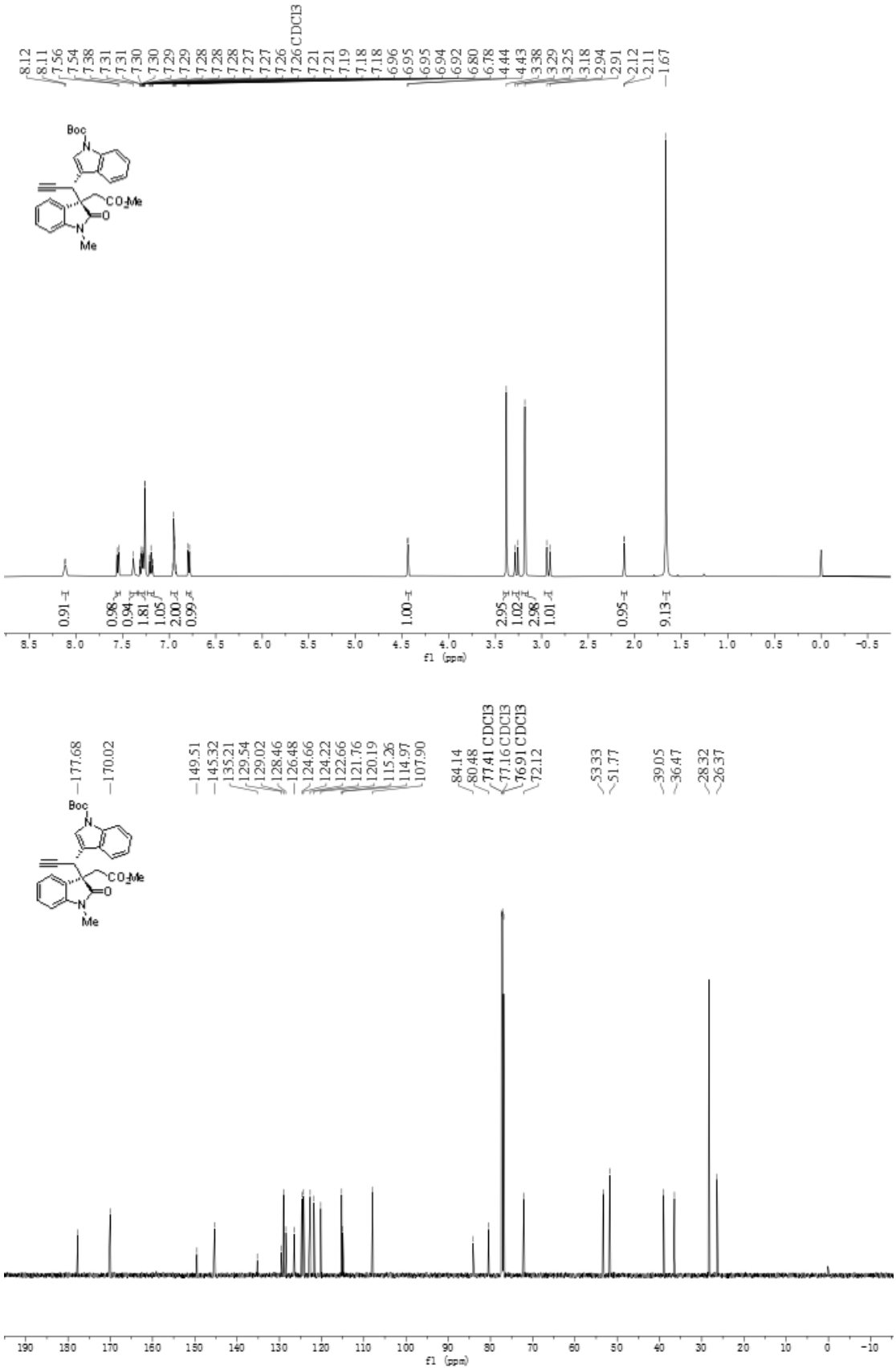

**Supplementary Fig. 26.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3al**



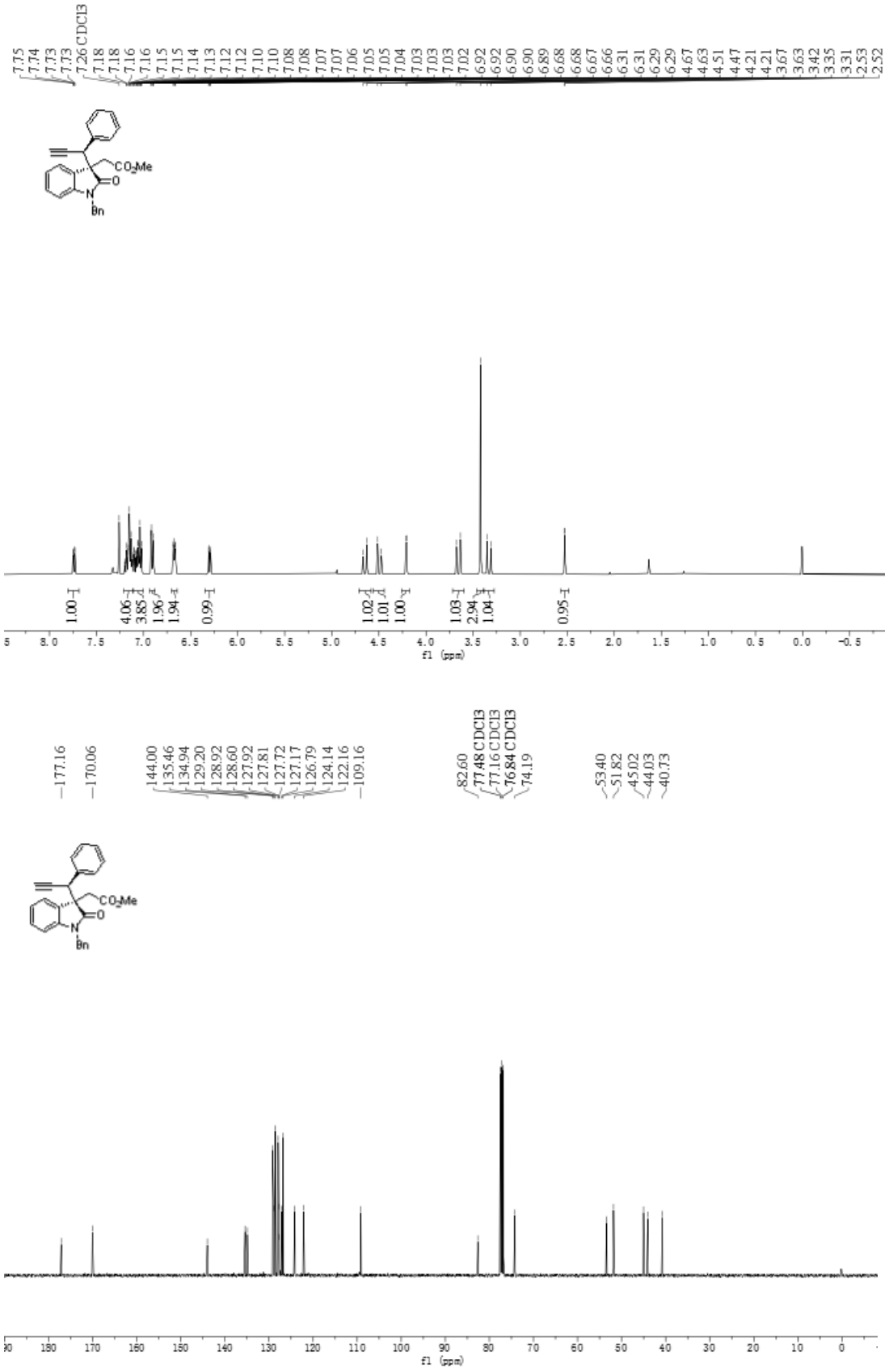

**Supplementary Fig. 27.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3am**



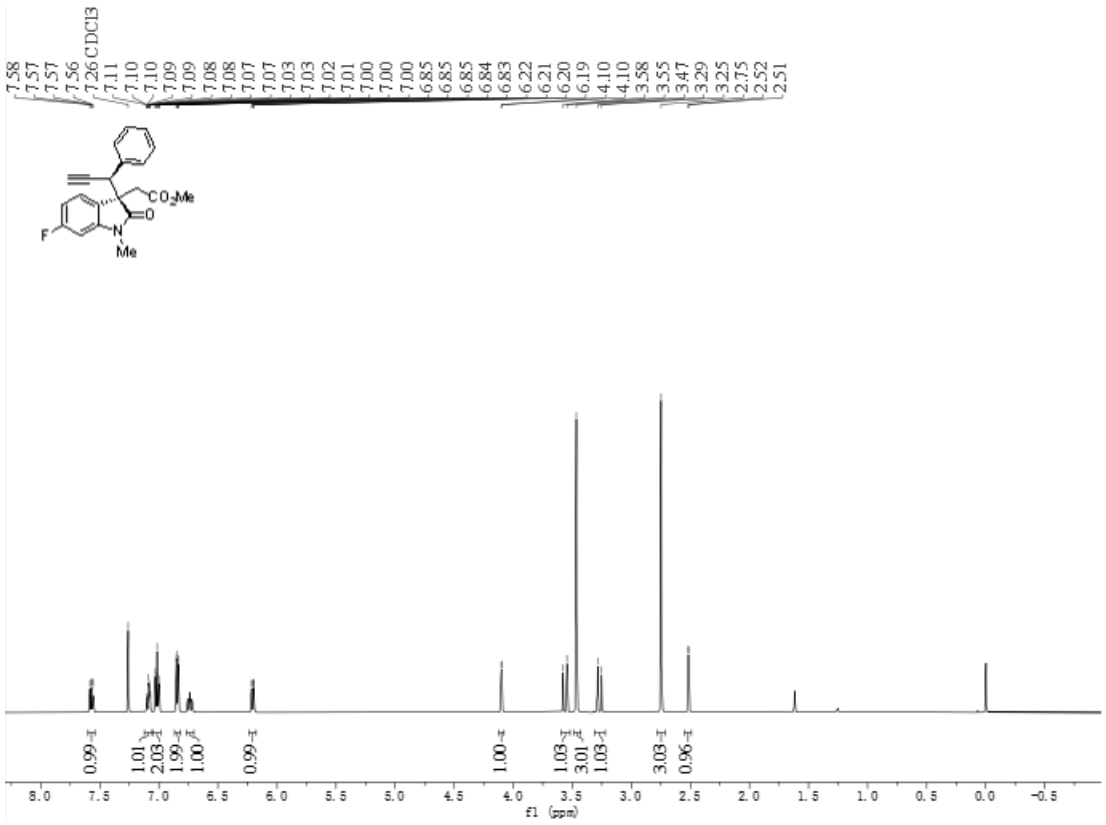
**Supplementary Fig. 28.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*S*)-**3am**

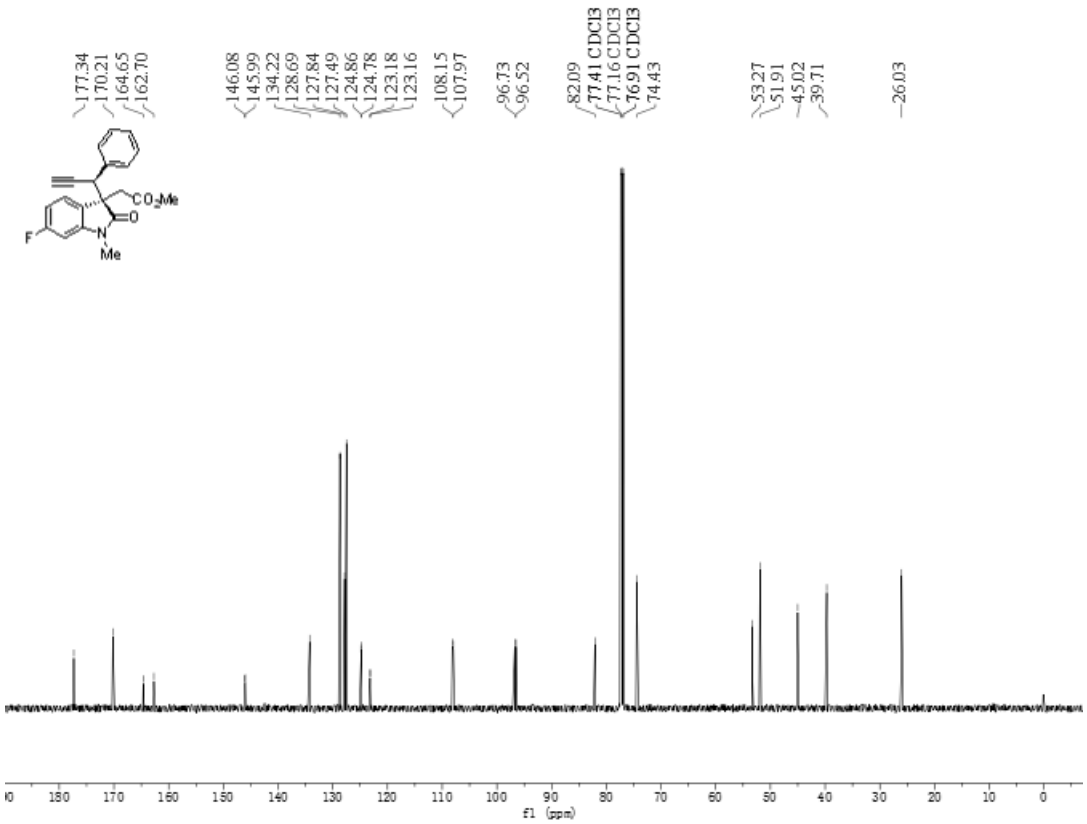


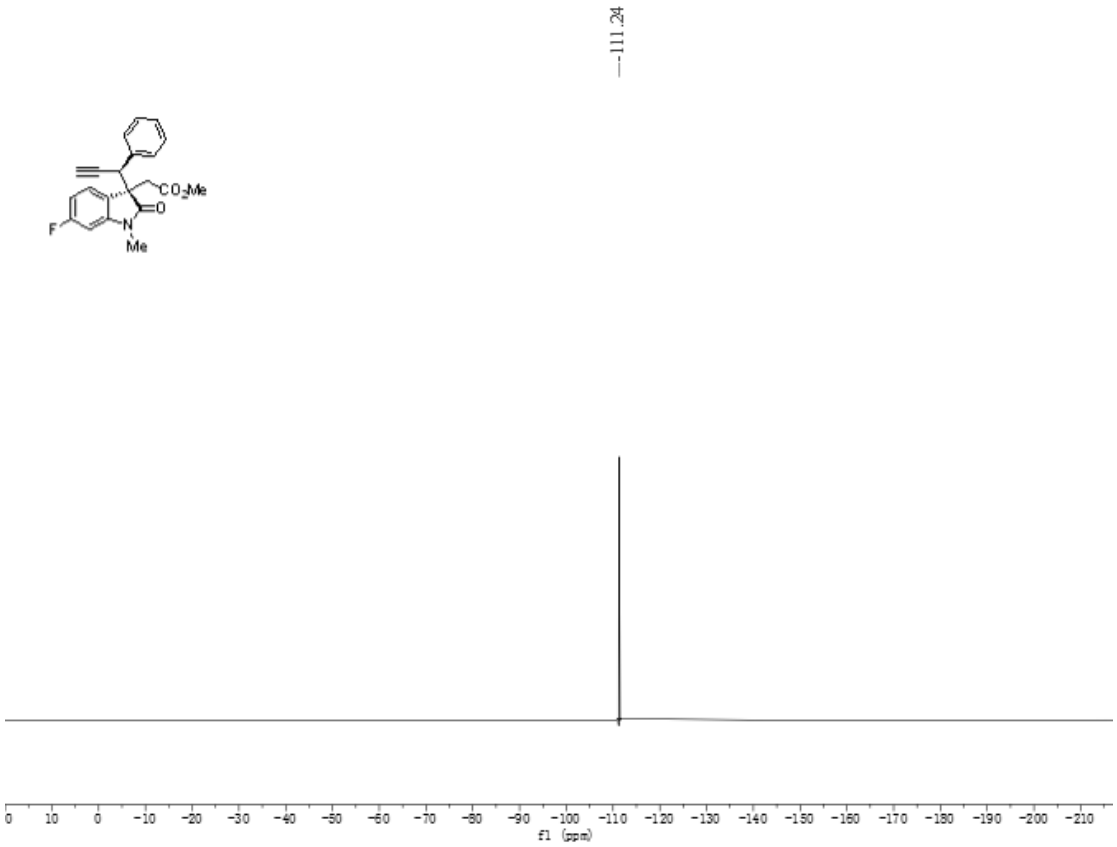

**Supplementary Fig. 29.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3an**



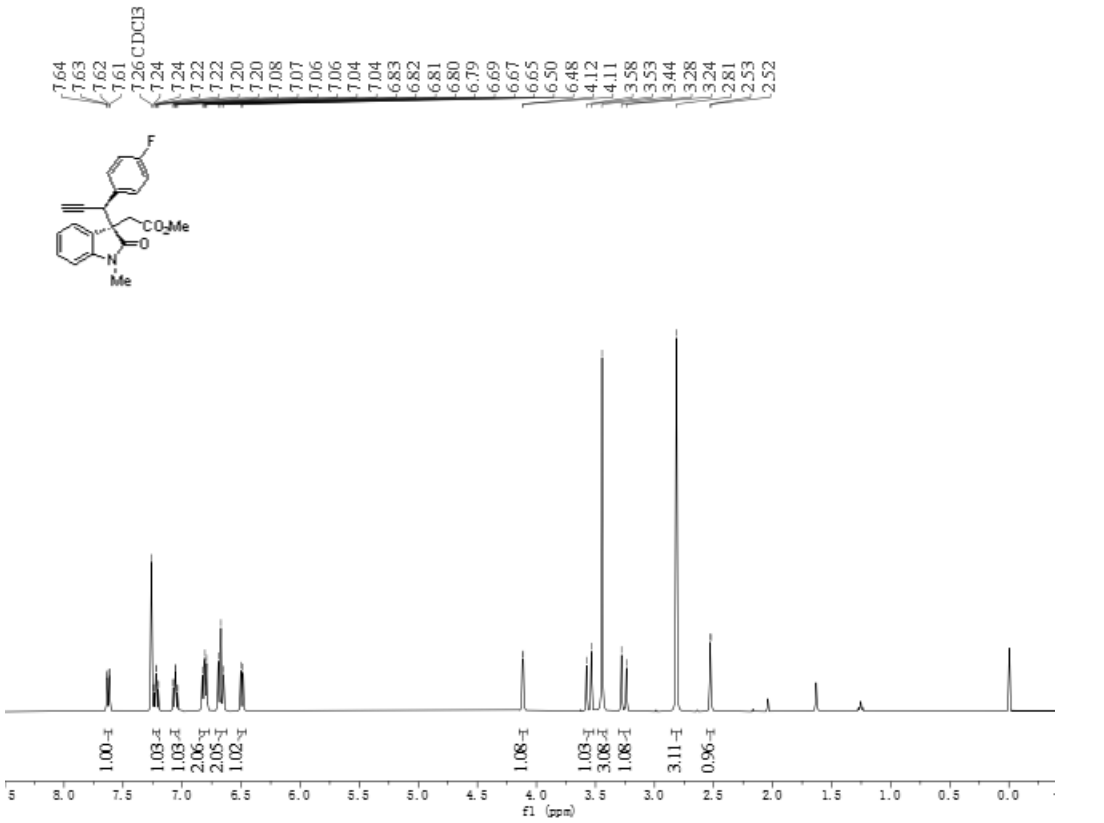

**Supplementary Fig. 30.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*S*)-**3ca**

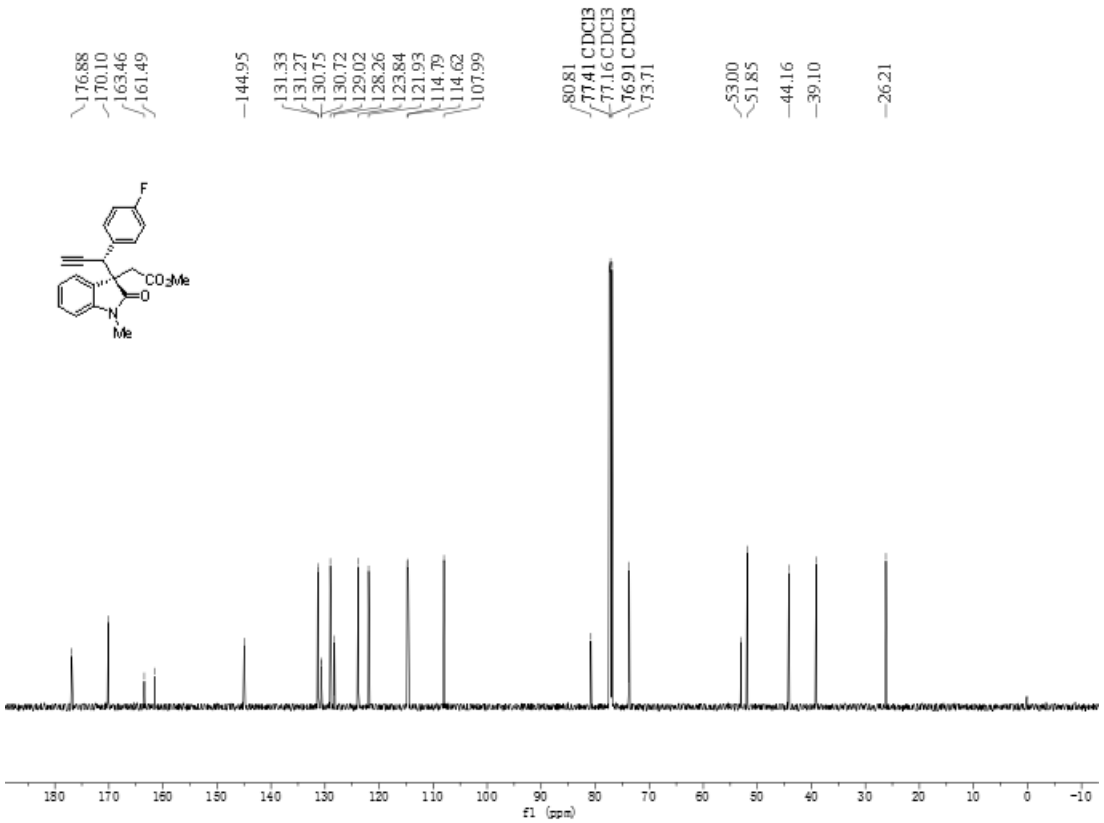

7.58
7.57
7.57
7.56
7.26 CDCl3
7.11
7.10
7.10
7.09
7.09
7.08
7.08
7.07
7.07
7.03
7.03
7.02
7.01
7.00
7.00
7.00
6.85
6.85
6.84
6.83
6.22
6.21
6.20
6.19
4.10
4.10
3.58
3.55
3.47
3.29
3.25
2.75
2.52
2.51
CO2Me
O
F
N
Me
0.99
1.01
2.03
1.99
1.00
0.99
1.00
1.03
3.01
1.03
3.03
0.96
f1 (ppm)

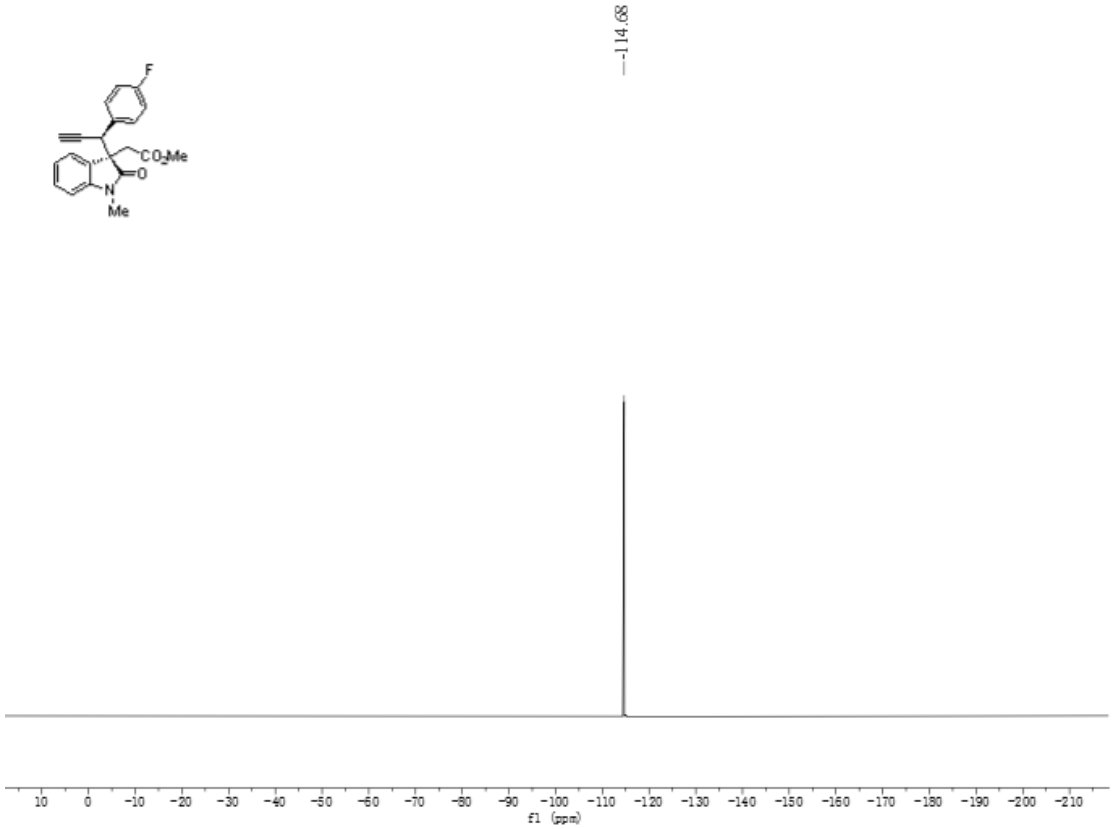

177.34
170.21
164.65
162.70
146.08
145.99
134.22
128.69
127.84
127.49
124.86
124.78
123.18
123.16
108.15
107.97
96.73
96.52
82.09
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
74.43
53.27
51.91
45.02
39.71
26.03
CO2Me
O
F
N
Me
f1 (ppm)



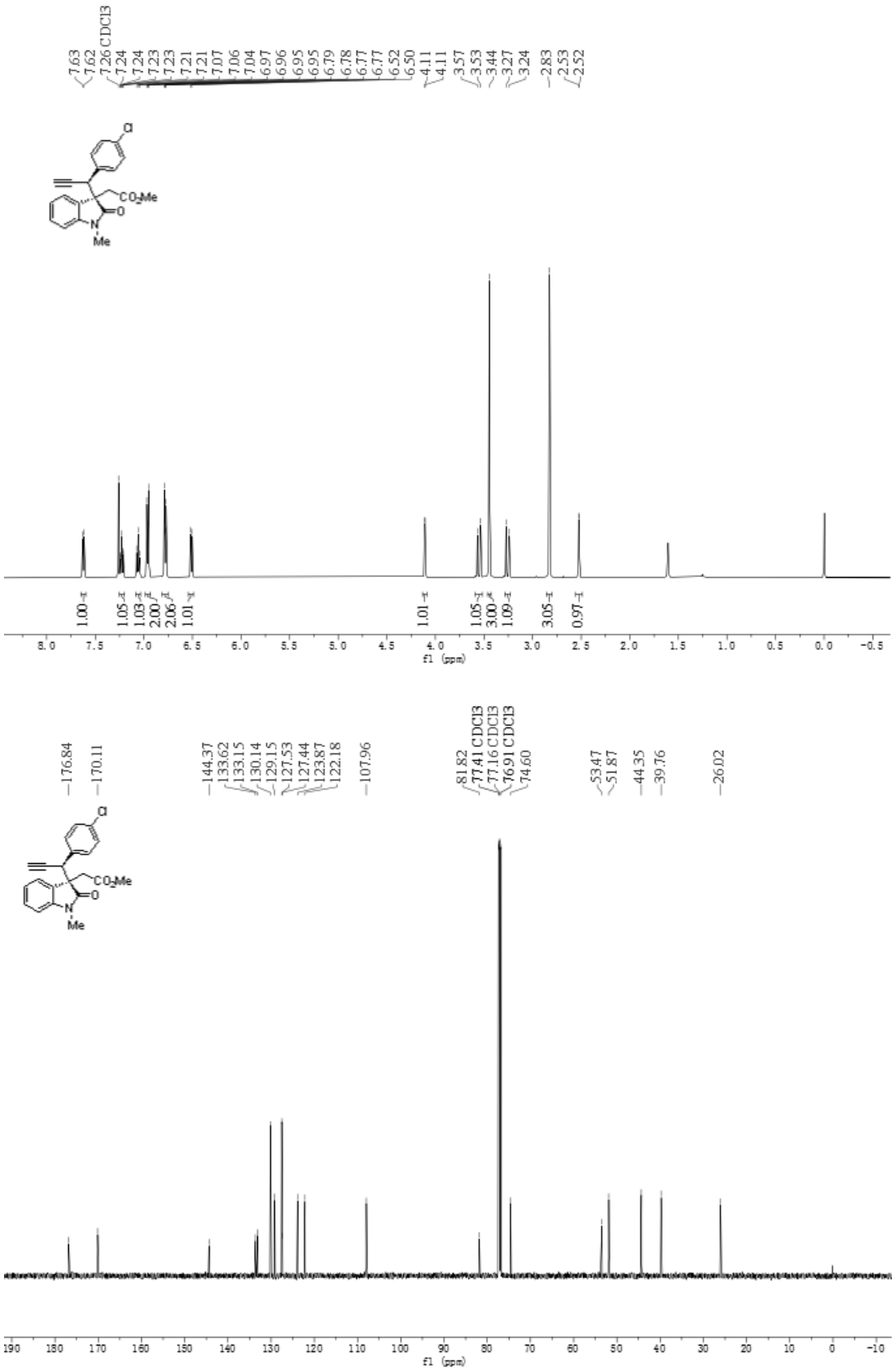

**Supplementary Fig. 31.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*S*)-**3ka**


7.64
7.63
7.62
7.61
7.26 CDCl3
7.24
7.24
7.22
7.22
7.20
7.20
7.08
7.07
7.06
7.06
7.04
7.04
6.83
6.82
6.81
6.80
6.79
6.69
6.67
6.65
6.50
6.48
4.12
4.11
3.58
3.53
3.44
3.28
3.24
2.81
2.53
2.52
F
CO2Me
O
N
Me
1.00
1.03
1.03
2.06
2.05
1.02
1.08
1.03
3.08
1.08
3.11
0.96
f1 (ppm)

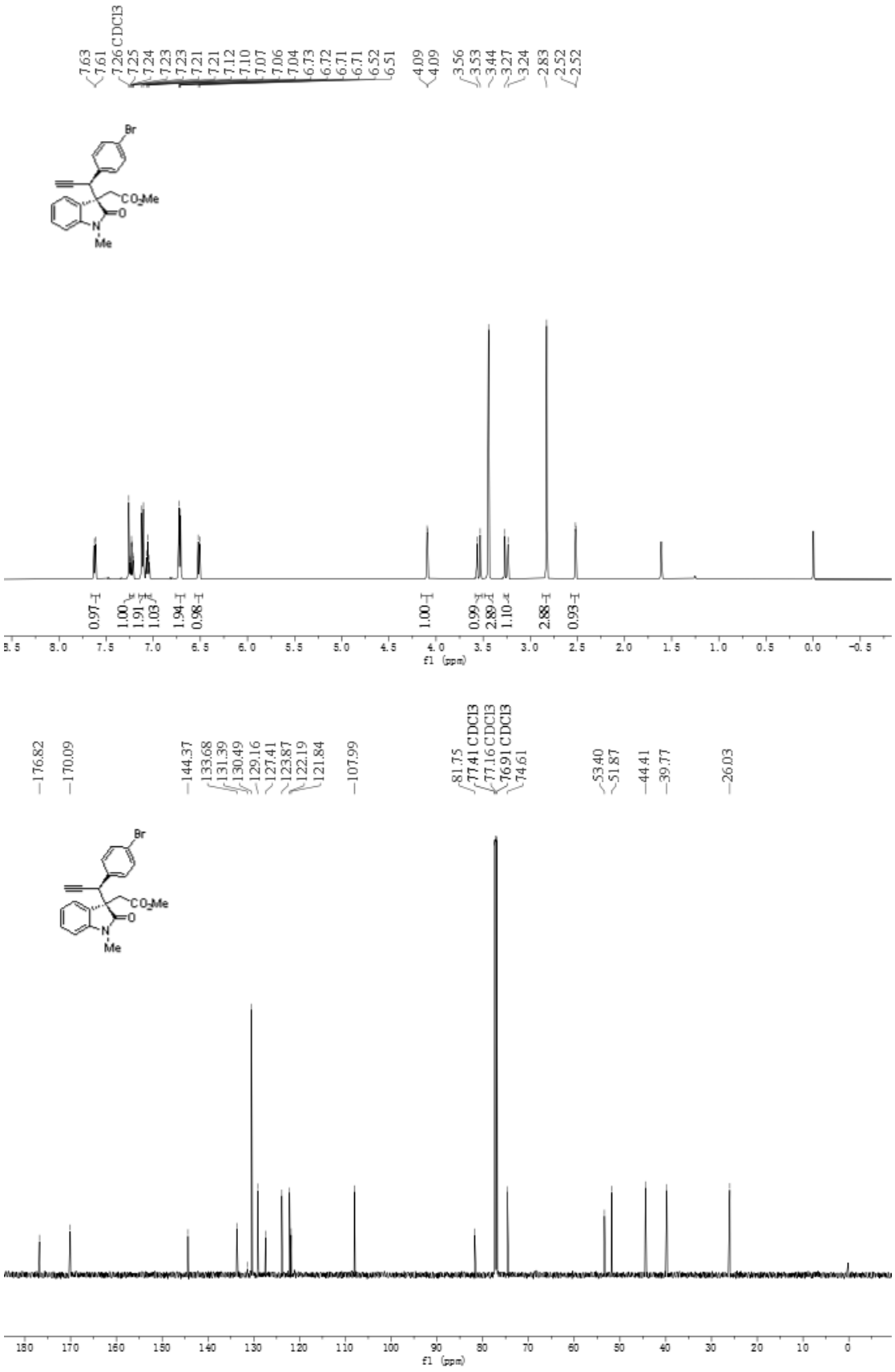

176.88
170.10
163.46
161.49
144.95
131.33
131.27
130.75
130.72
129.02
128.26
123.84
121.93
114.79
114.62
107.99
80.81
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
73.71
53.00
51.85
44.16
39.10
26.21
F
CO2Me
O
N
Me
f1 (ppm)



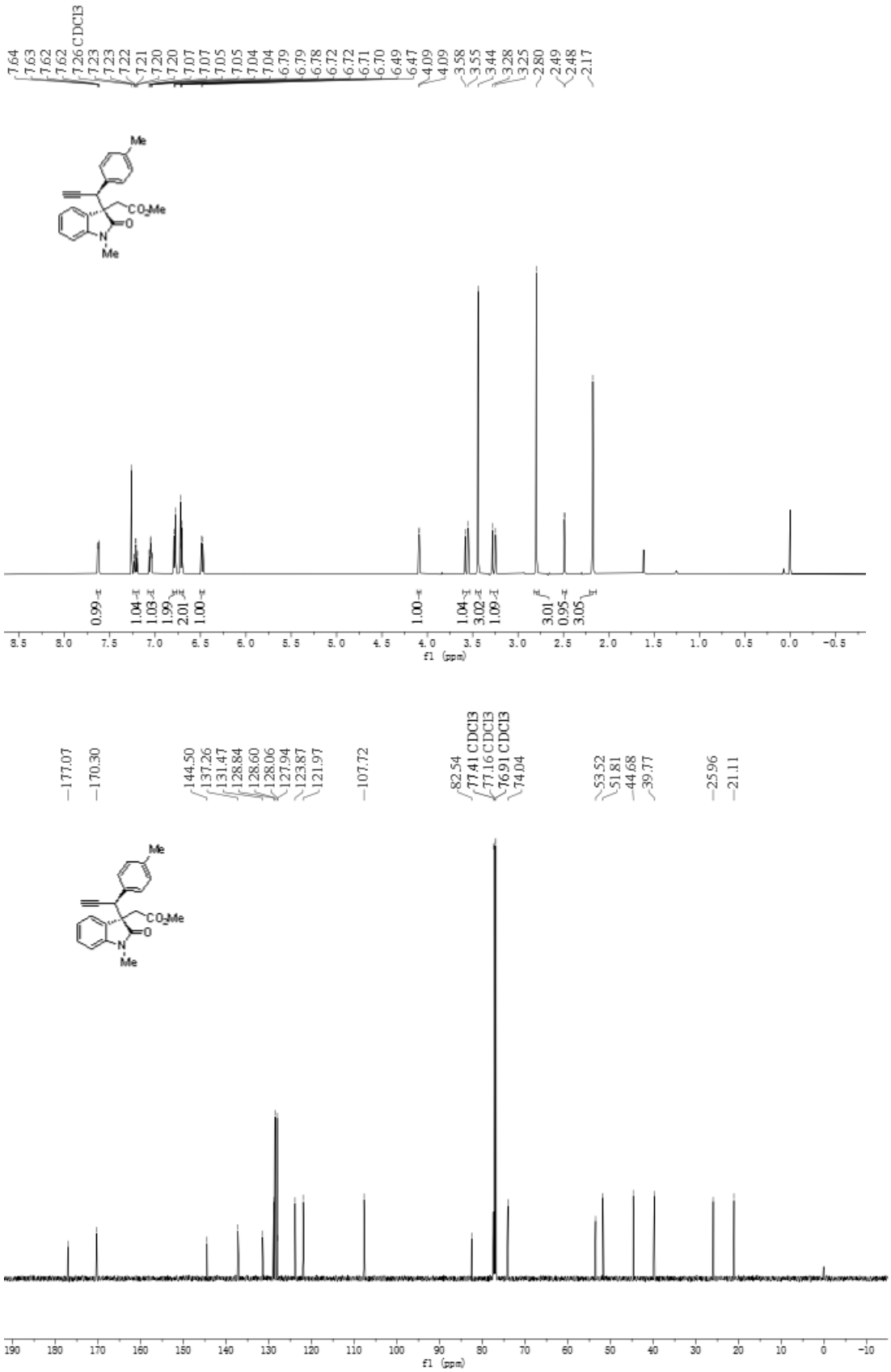

**Supplementary Fig. 32.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*S*)-**3ab**



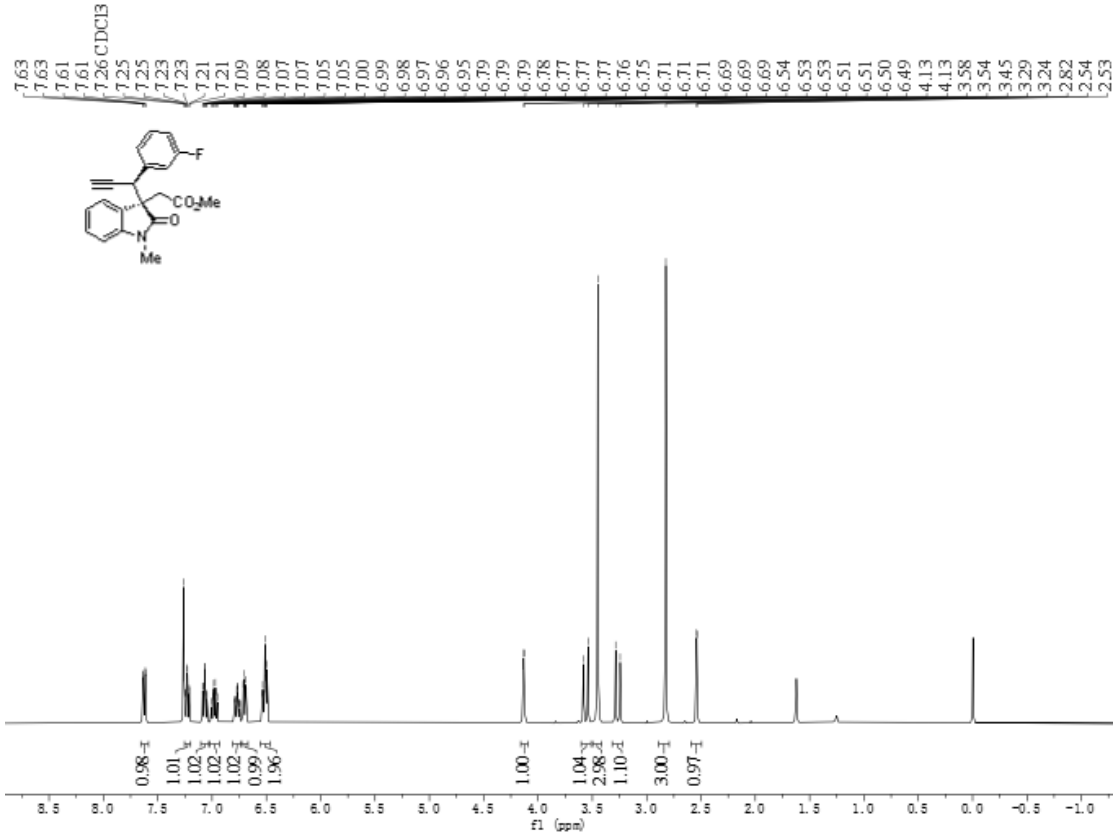

**Supplementary Fig. 33.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*S*)-**3ac**

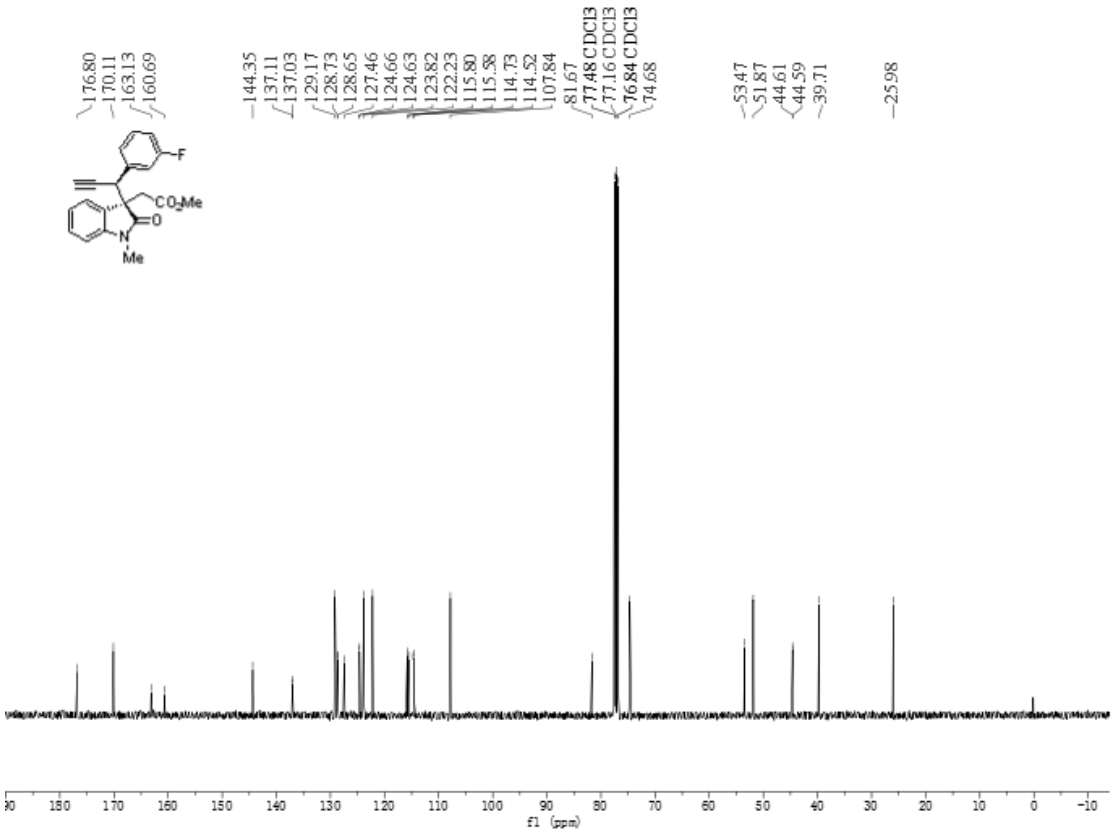


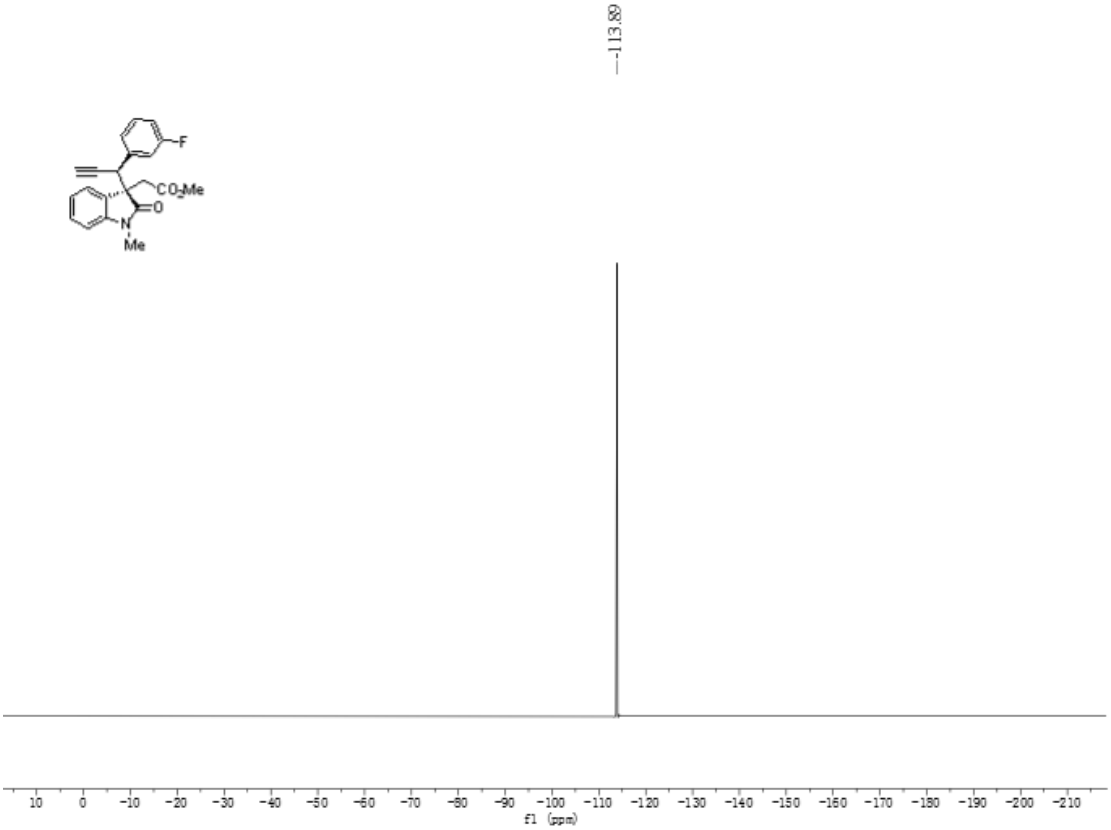

**Supplementary Fig. 34.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*S*)-**3ad**



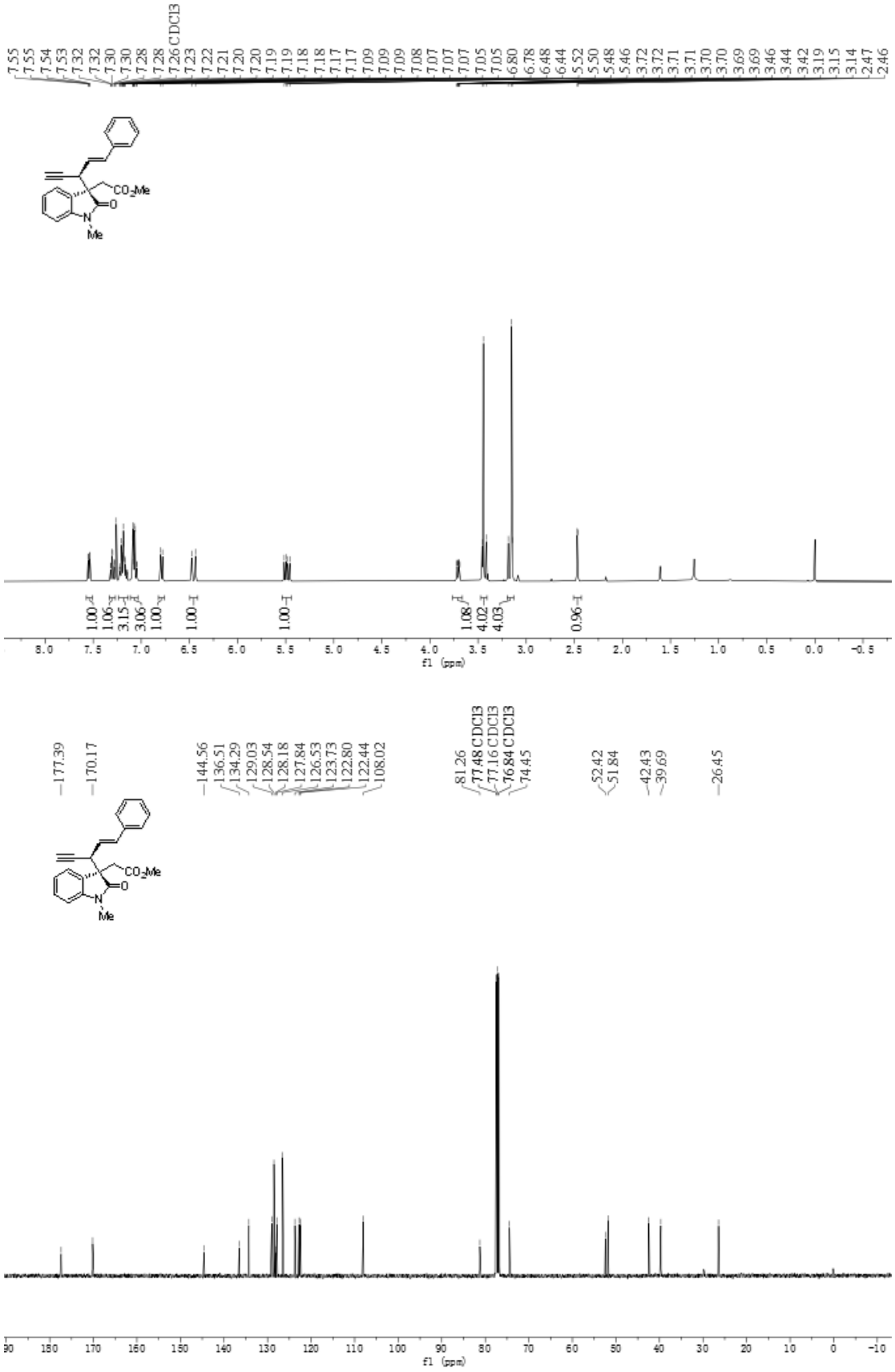

**Supplementary Fig. 35.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*S*)-**3ae**


7.63
7.63
7.61
7.61
7.26 CDCl3
7.25
7.25
7.23
7.23
7.21
7.21
7.09
7.08
7.07
7.07
7.05
7.05
7.00
6.99
6.98
6.97
6.96
6.95
6.79
6.79
6.78
6.77
6.77
6.77
6.76
6.75
6.71
6.71
6.71
6.69
6.69
6.69
6.54
6.53
6.53
6.51
6.51
6.50
6.49
4.13
3.58
3.54
3.45
3.29
3.24
2.82
2.54
2.53
F
CO2Me
O
N
Me
0.98
1.01
1.02
1.02
1.02
0.99
1.96
1.00
1.04
2.98
1.10
3.00
0.97
f1 (ppm)

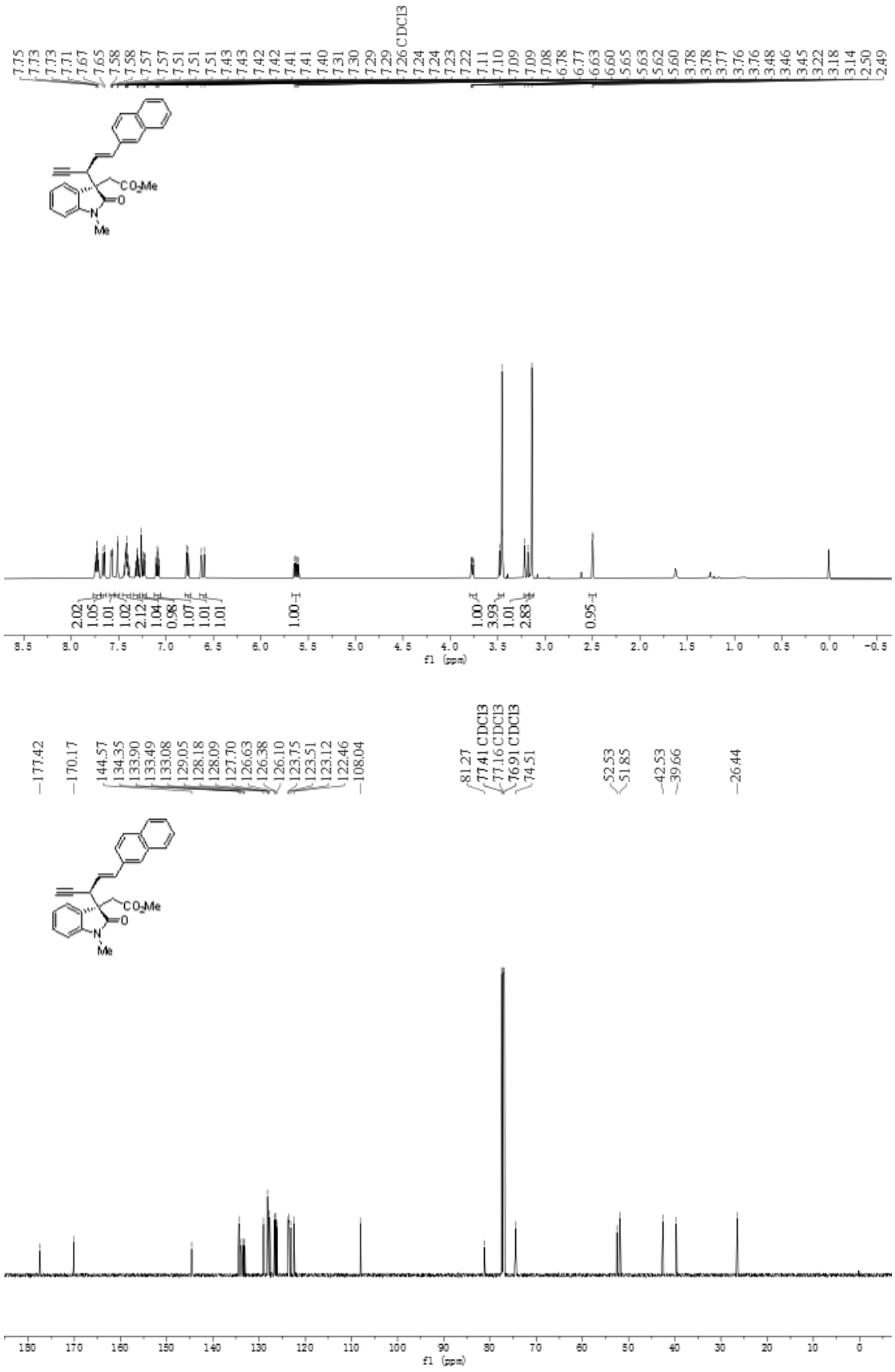

176.80
170.11
163.13
160.69
144.35
137.11
137.03
129.17
128.73
128.65
127.46
124.66
124.63
123.82
122.23
115.80
115.58
114.73
114.52
107.84
81.67
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
74.68
53.47
51.87
44.61
44.59
39.71
25.98
F
CO2Me
O
N
Me
f1 (ppm)



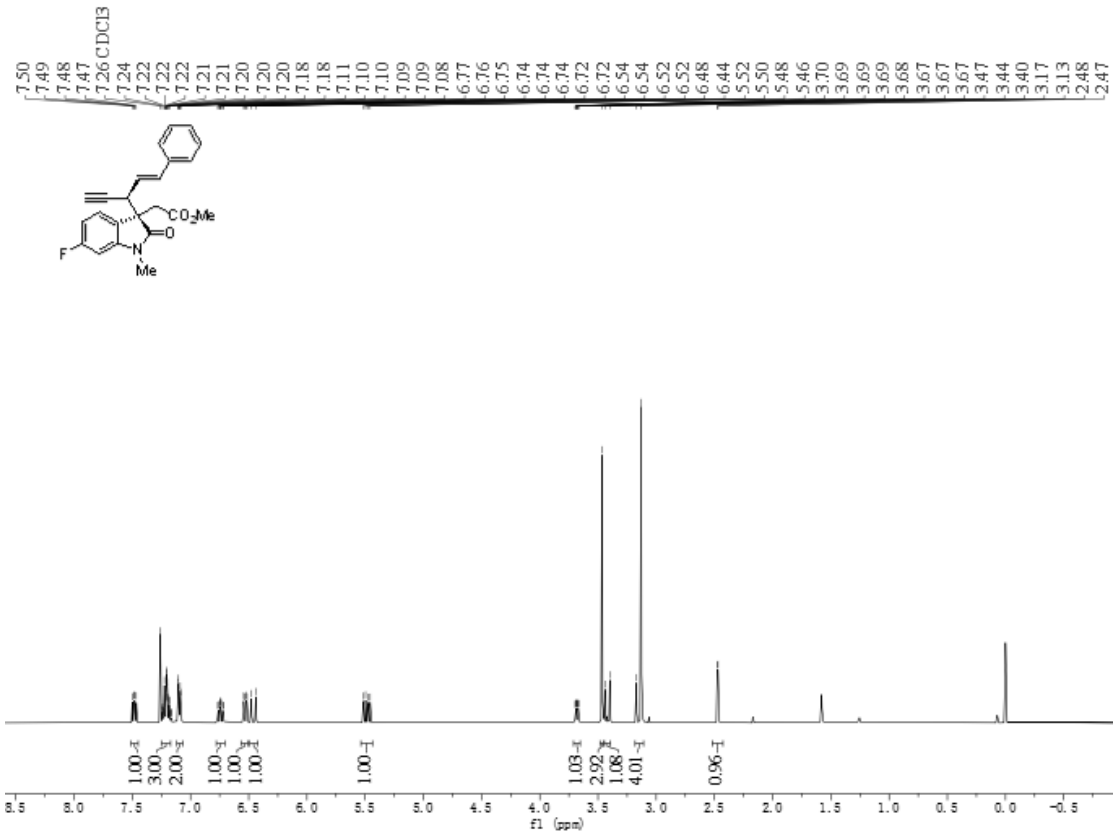

**Supplementary Fig. 36.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*S*)-**3ag**

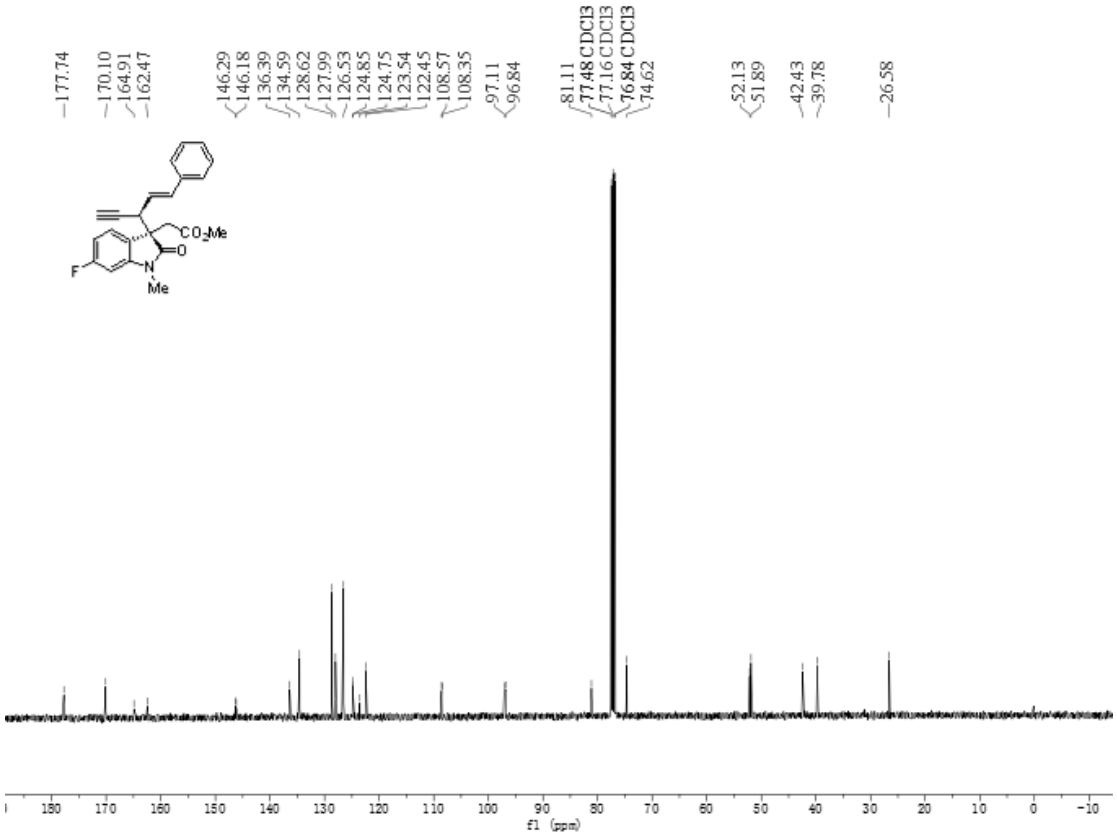


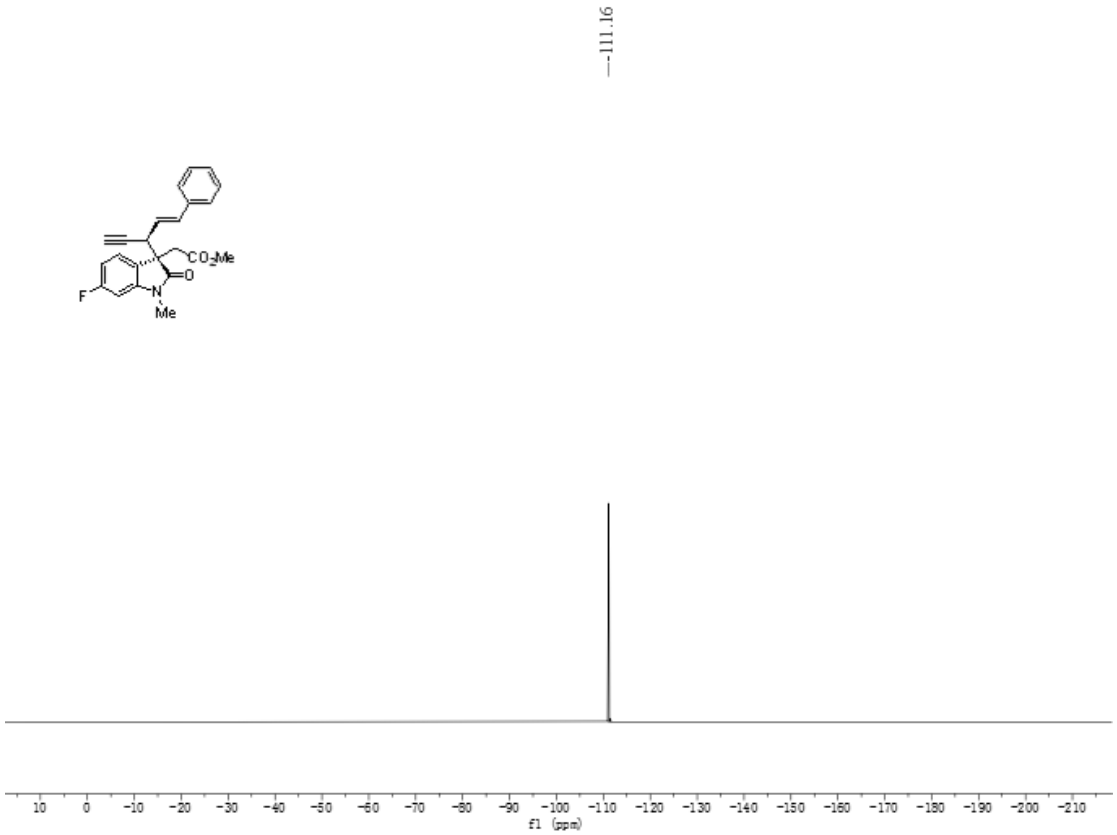

**Supplementary Fig. 37.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ao**



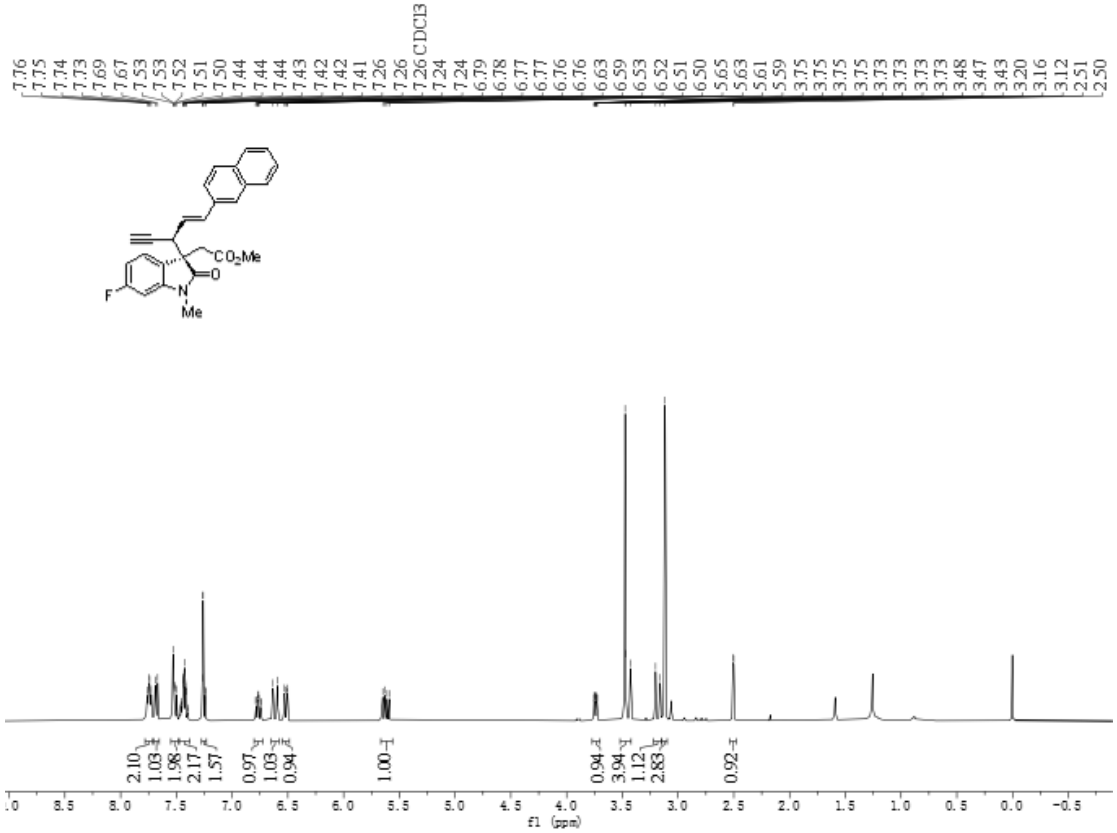

**Supplementary Fig. 38.** $^{1}$H NMR & $^{13}$C NMR spectra of compound (*R*,*R*)-**3ap**

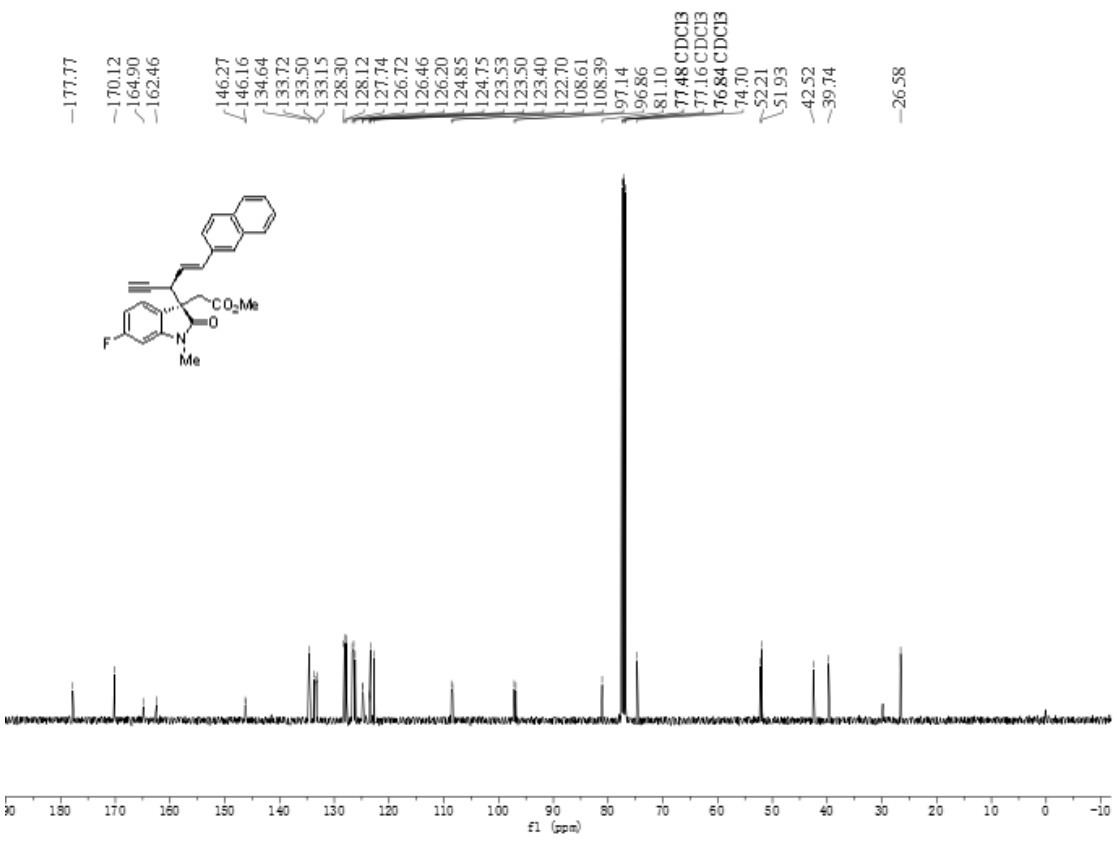

7.50
7.49
7.48
7.47
7.26 CDCl3
7.24
7.22
7.22
7.22
7.21
7.21
7.20
7.20
7.20
7.18
7.18
7.11
7.10
7.10
7.09
7.09
7.08
6.77
6.76
6.75
6.74
6.74
6.74
6.72
6.72
6.54
6.54
6.52
6.52
6.48
6.44
5.52
5.50
5.48
5.46
3.70
3.69
3.69
3.69
3.68
3.67
3.67
3.67
3.47
3.44
3.40
3.17
3.13
2.48
2.47
CO2Me
O
N
Me
F
1.00
3.00
2.00
1.00
1.00
1.00
1.00
1.03
2.92
1.08
4.01
0.96
f1 (ppm)

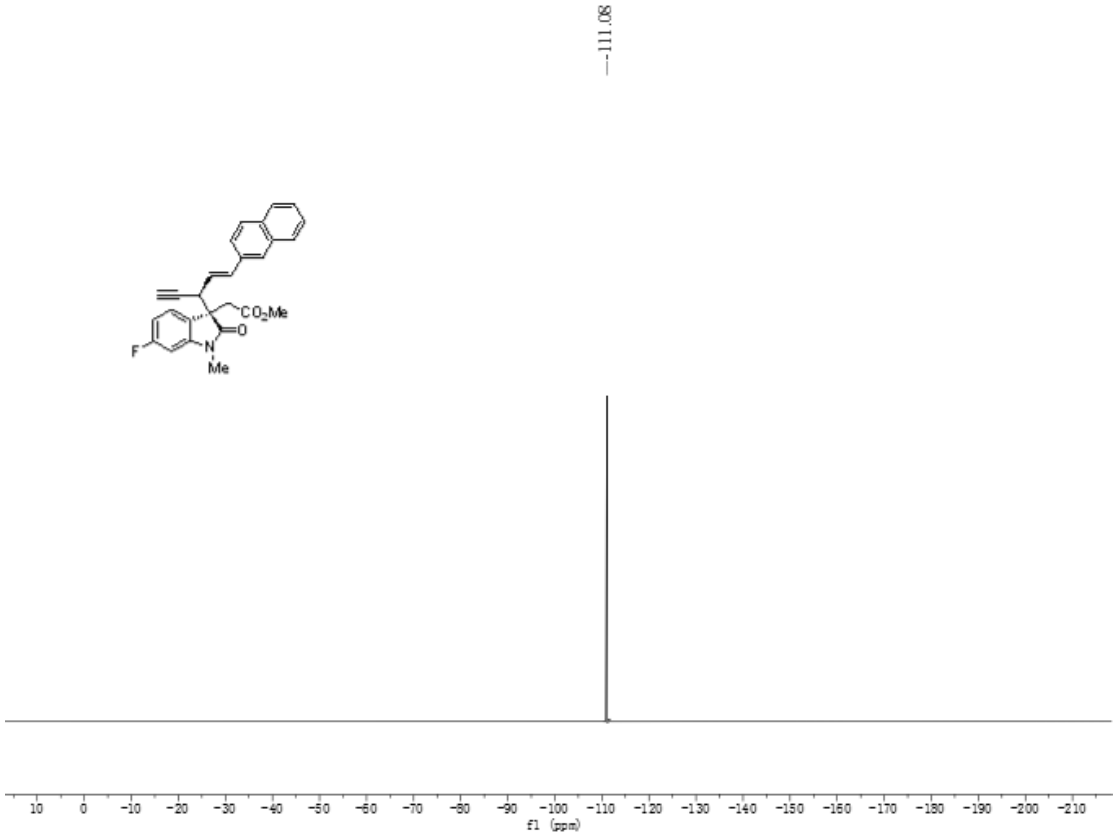

177.74
170.10
164.91
162.47
146.29
146.18
136.39
134.59
128.62
127.99
126.53
124.85
124.75
123.54
122.45
108.57
108.35
97.11
96.84
81.11
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
74.62
52.13
51.89
42.43
39.78
26.58
CO2Me
O
N
Me
F
f1 (ppm)



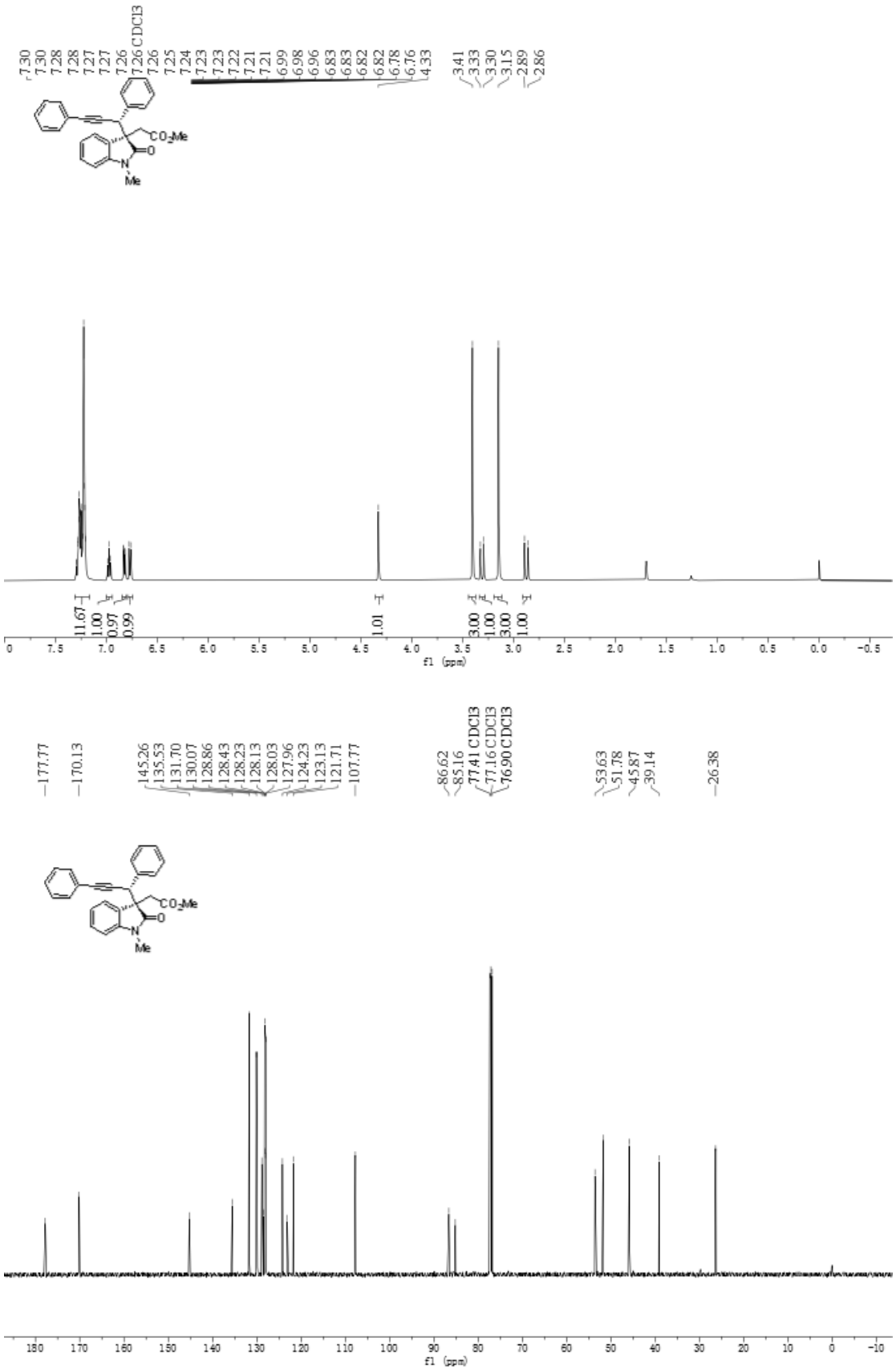

**Supplementary Fig. 39.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*R*)-**3ko**


7.76
7.75
7.74
7.73
7.69
7.67
7.53
7.53
7.52
7.51
7.50
7.44
7.44
7.44
7.43
7.42
7.42
7.41
7.26
7.26
7.26 CDCl3
7.24
7.24
6.79
6.78
6.77
6.77
6.76
6.76
6.63
6.59
6.53
6.52
6.51
6.50
5.65
5.63
5.61
5.59
3.75
3.75
3.75
3.75
3.73
3.73
3.73
3.73
3.48
3.47
3.43
3.20
3.16
3.12
2.51
2.50
CO2Me
O
F
N
Me
2.10
1.03
1.98
2.17
1.57
0.97
1.03
0.94
1.00
0.94
3.94
1.12
2.83
0.92
f1 (ppm)

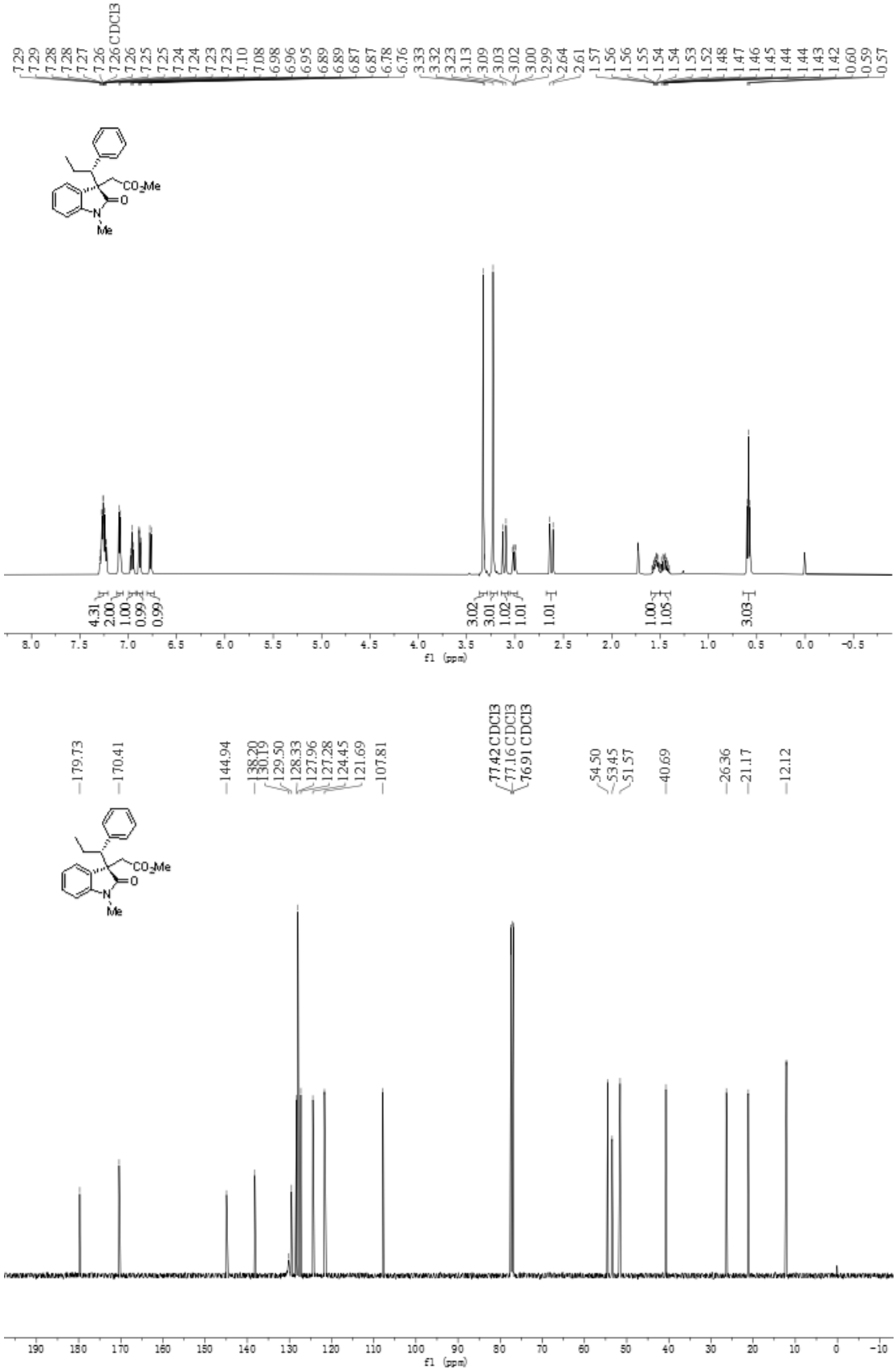

177.77
170.12
164.90
162.46
146.27
146.16
134.64
133.72
133.50
133.15
128.30
128.12
127.74
126.72
126.46
126.20
124.85
124.75
123.53
123.50
123.40
122.70
108.61
108.39
97.14
96.86
81.10
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
74.70
52.21
51.93
42.52
39.74
26.58
CO2Me
O
F
N
Me
f1 (ppm)



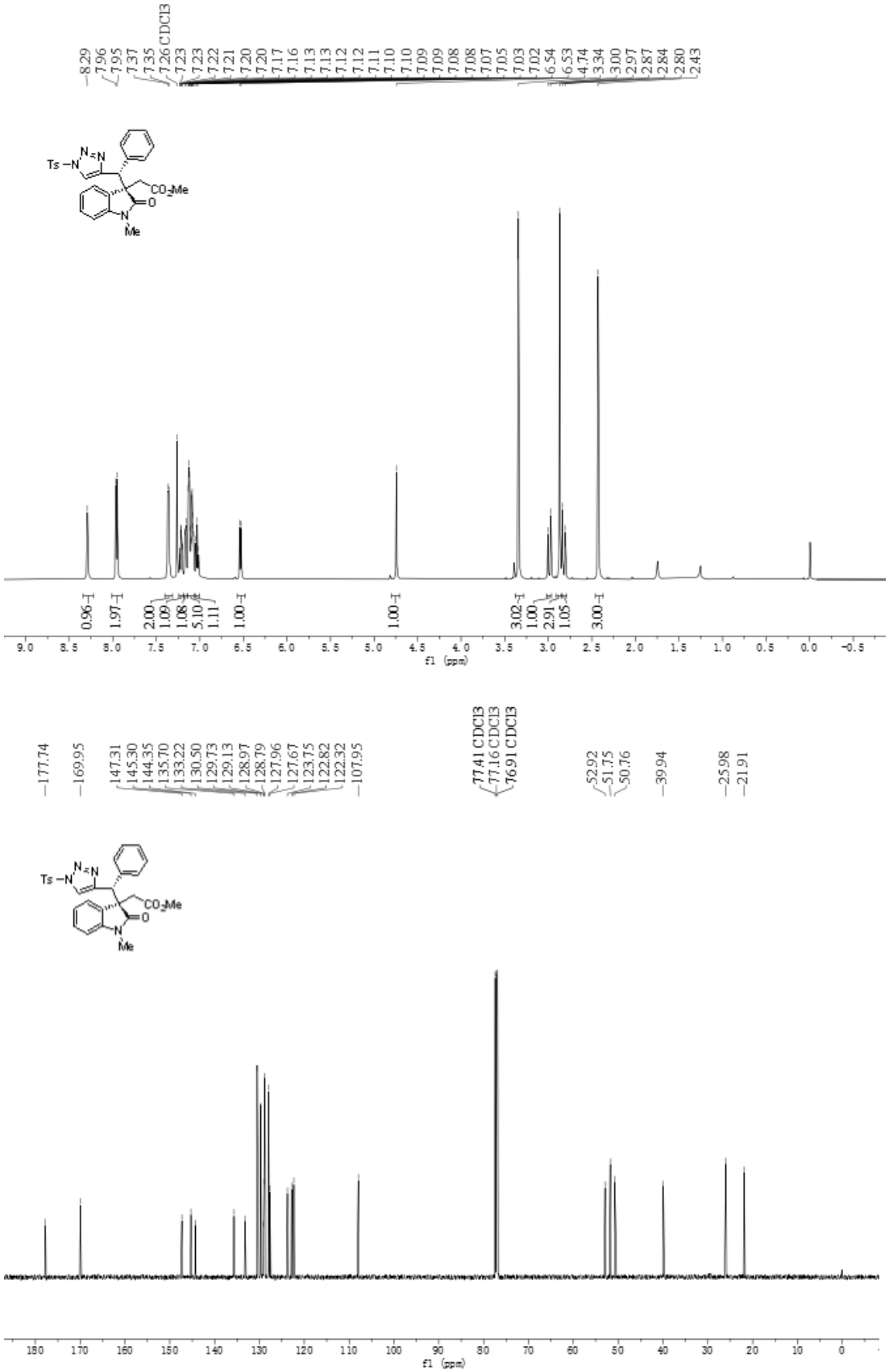

**Supplementary Fig. 40.** $^{1}$H NMR $^{13}$C NMR & $^{19}$F NMR spectra of compound (*R*,*R*)-**3kp**



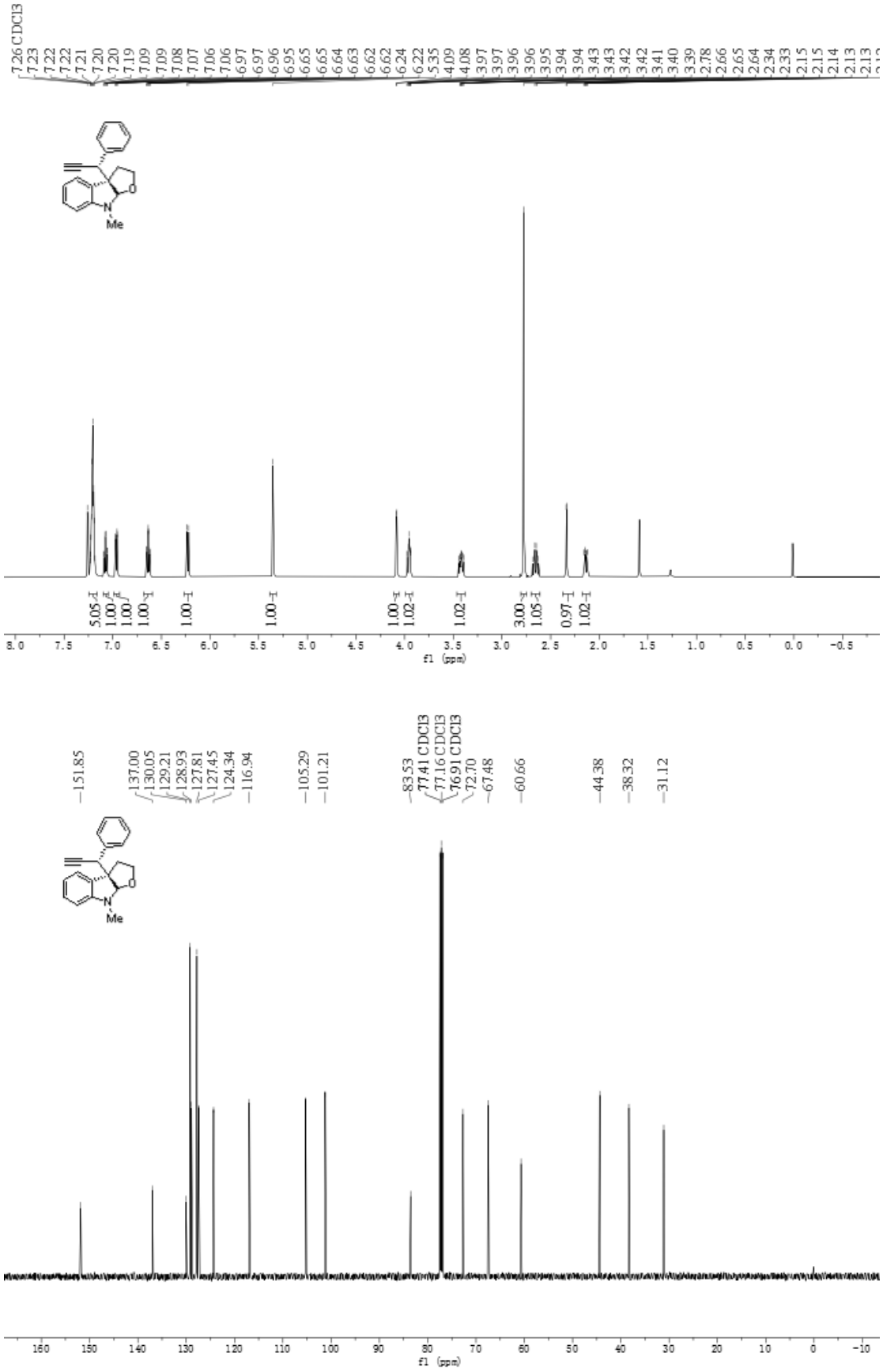

**Supplementary Fig. 41.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **5**



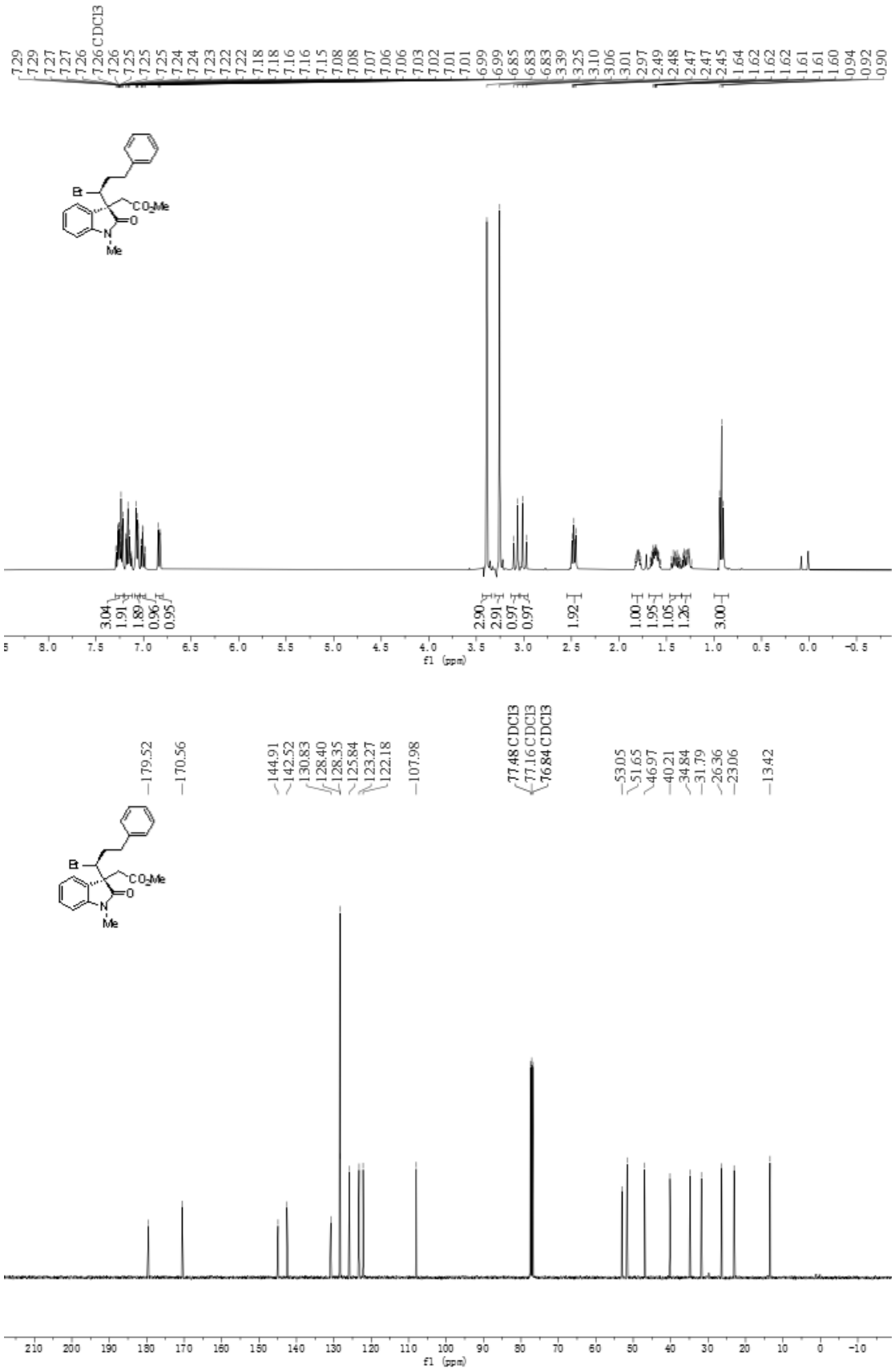

**Supplementary Fig. 42.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **6**



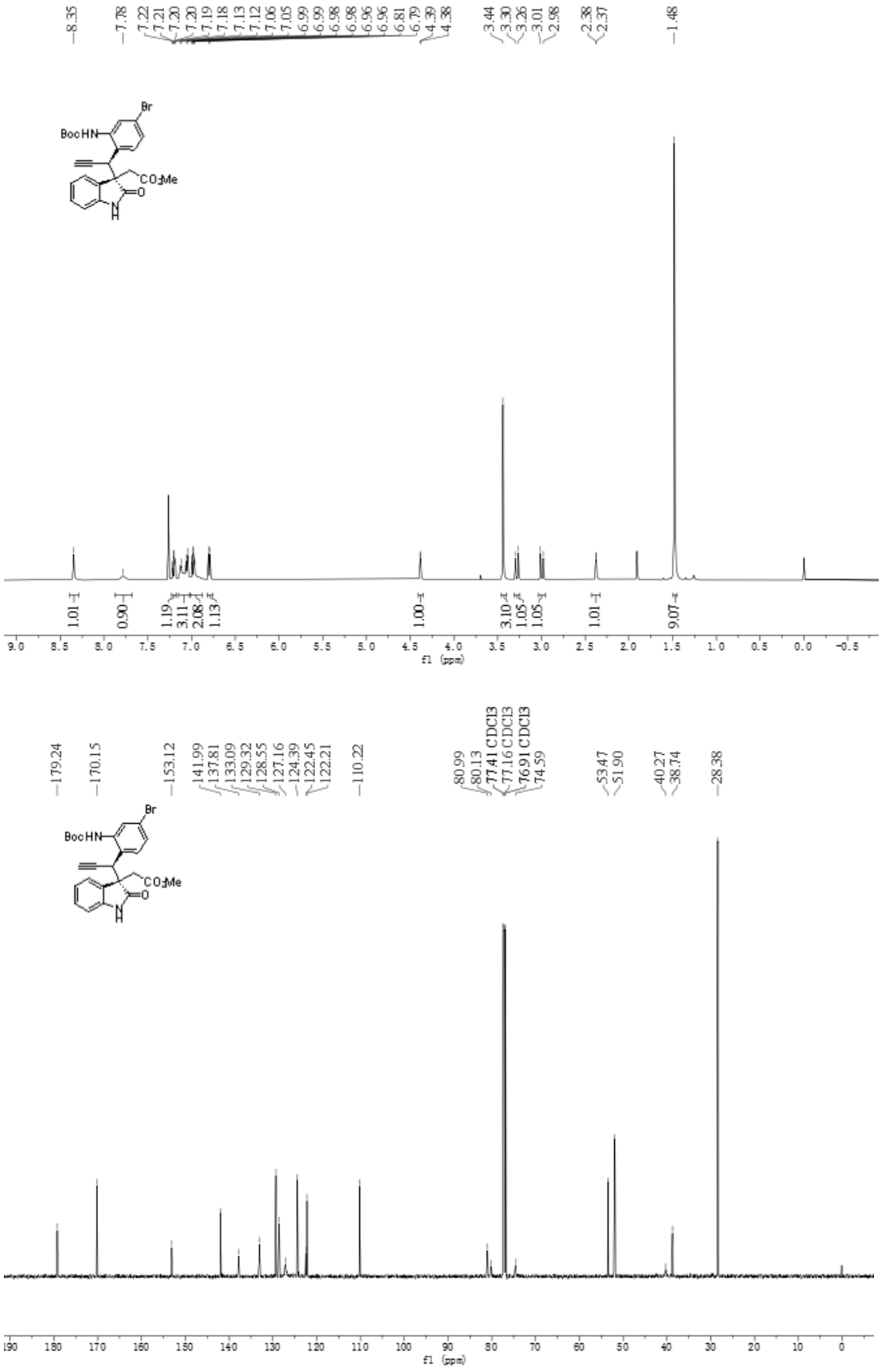

**Supplementary Fig. 43.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **7**



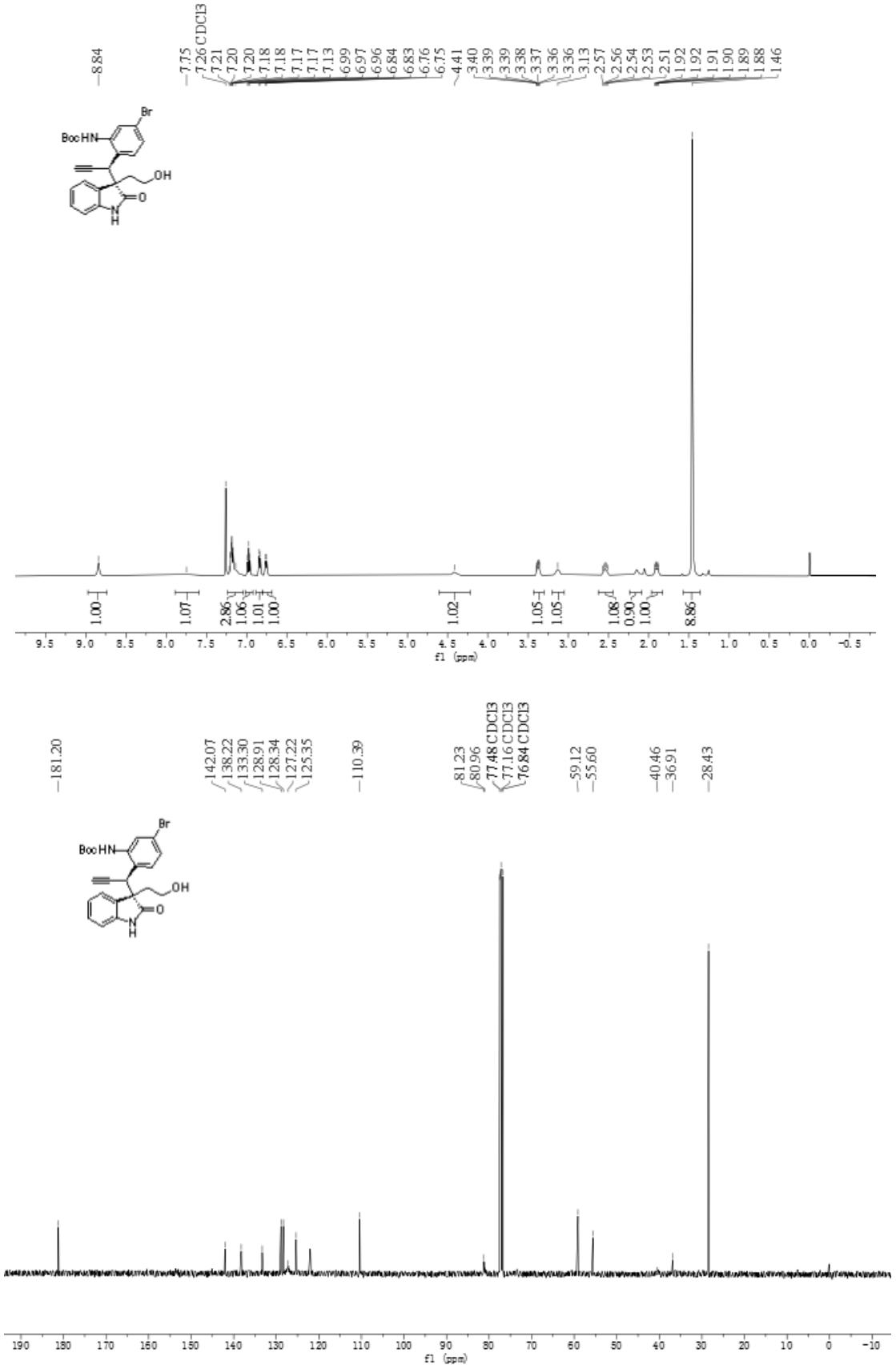

**Supplementary Fig. 44.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **8**



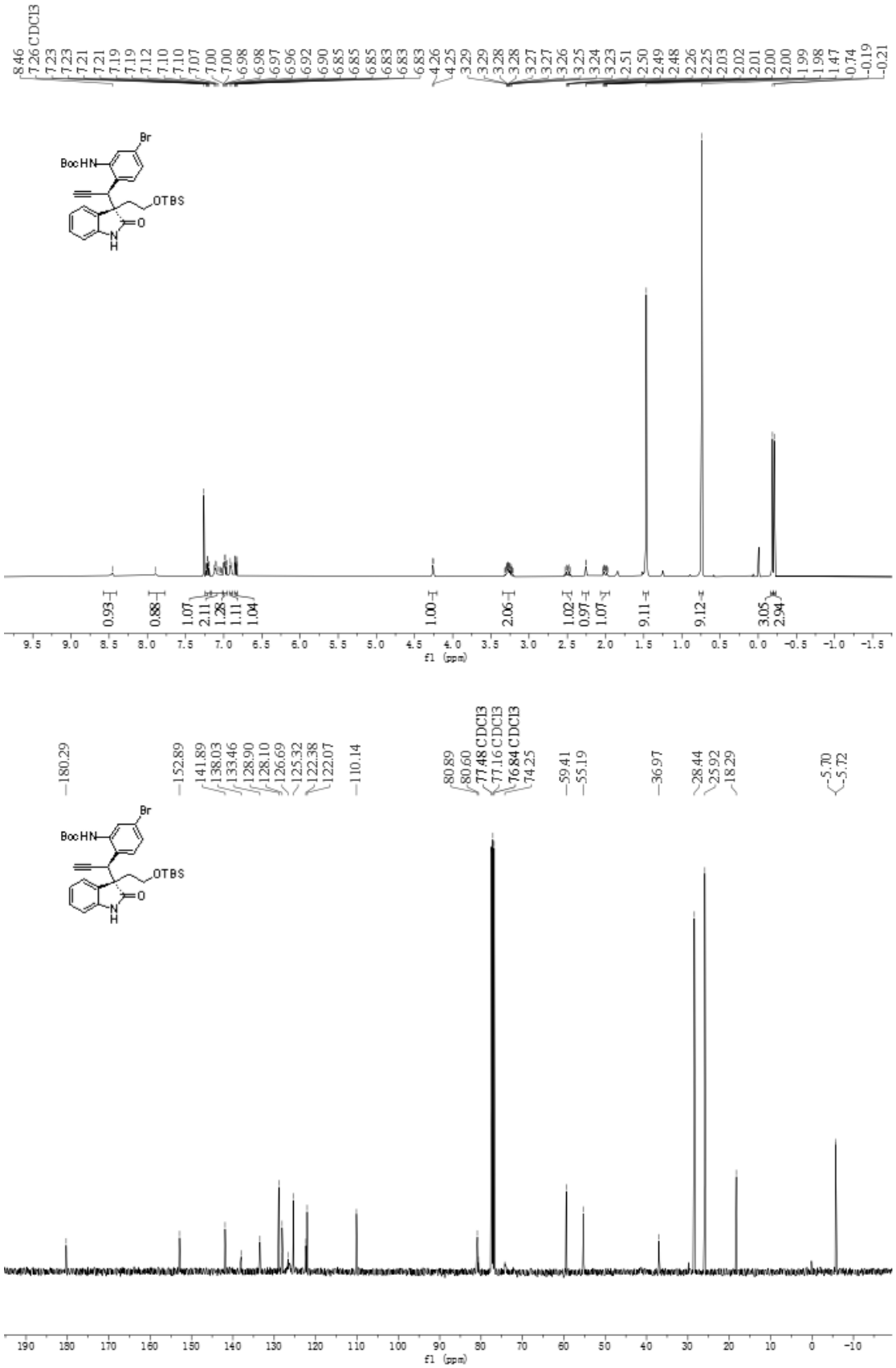

**Supplementary Fig. 45.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **9**



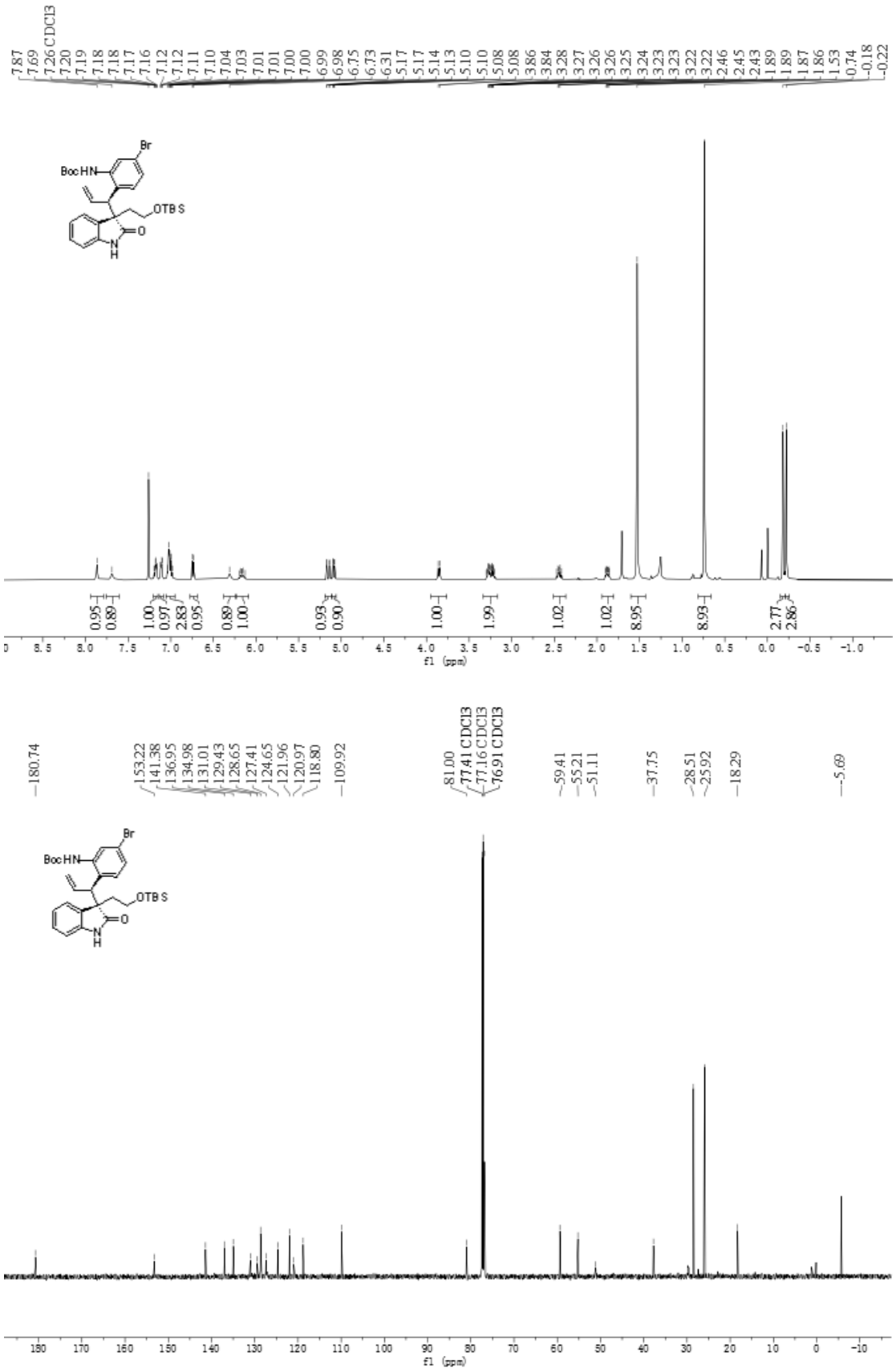

**Supplementary Fig. 46.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **3nq**




**Supplementary Fig. 47.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **10**




**Supplementary Fig.48.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **11**

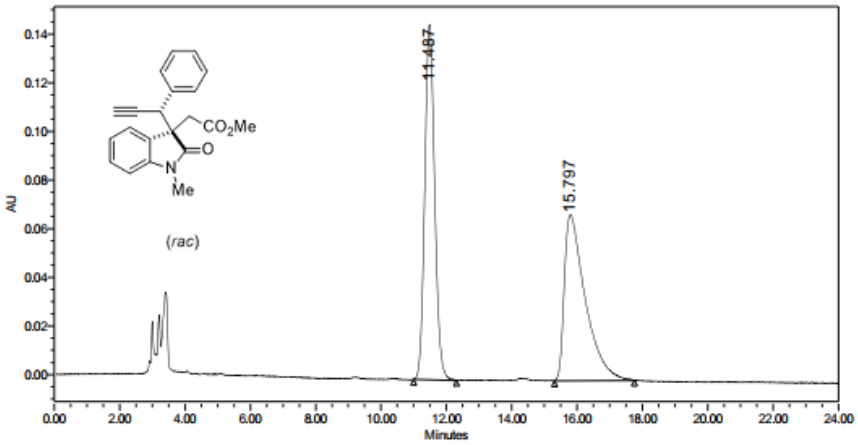



**Supplementary Fig. 49.** $^{1}$H NMR & $^{13}$C NMR spectra of compound **12**

## 13. HPLC of Products

SAMPLE INFORMATION

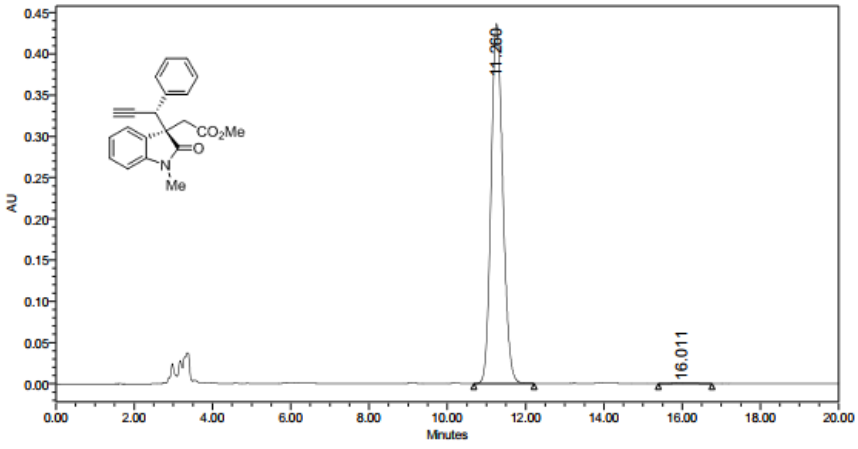
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-167-1-rac-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh16713 |
| Vial: | 51 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 24.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 7/13/2021 5:55:33 PM CST | | |
| Date Processed: | 7/13/2021 7:36:08 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.487 | 3089227 | 50.37 | 145990 |
| 2 | 15.797 | 3043361 | 49.63 | 68143 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-75-1-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1751 |
| Vial: | 32 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 1/5/2021 4:02:00 PM CST | | |
| Date Processed: | 7/14/2021 8:11:35 PM CST | | |

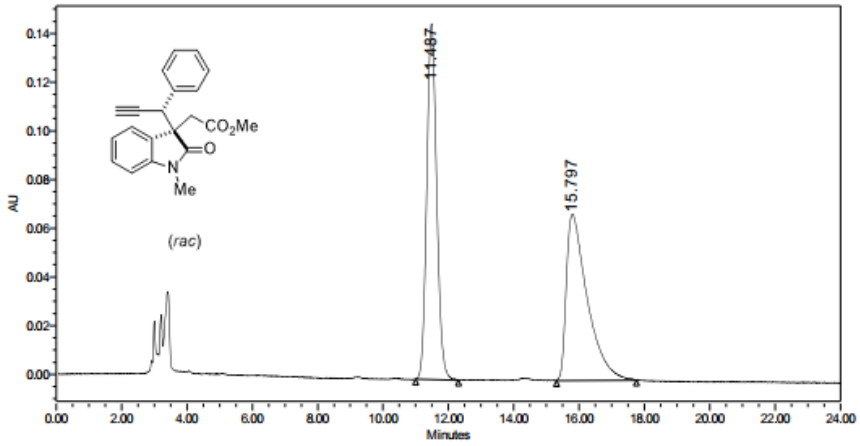



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.260 | 9107741 | 99.75 | 436059 |
| 2 | 16.011 | 22534 | 0.25 | 553 |

**Supplementary Fig. 50.** HPLC spectra of compound **(*R*,*R*)-3aa**

SAMPLE INFORMATION

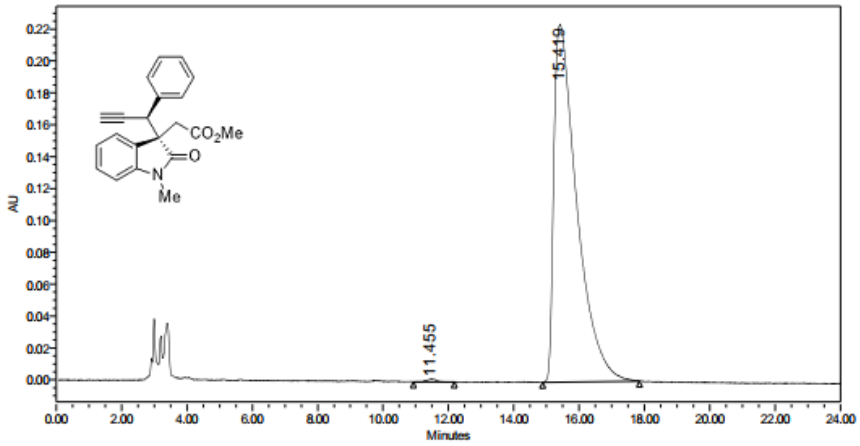
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-167-1-rac-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh16713 |
| Vial: | 51 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 24.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 7/13/2021 5:55:33 PM CST | | |
| Date Processed: | 7/13/2021 7:36:08 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.487 | 3089227 | 50.37 | 145990 |
| 2 | 15.797 | 3043361 | 49.63 | 68143 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh16713 |
| Vial: | 53 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 24.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 7/13/2021 6:44:55 PM CST | | |
| Date Processed: | 7/13/2021 7:37:15 PM CST | | |

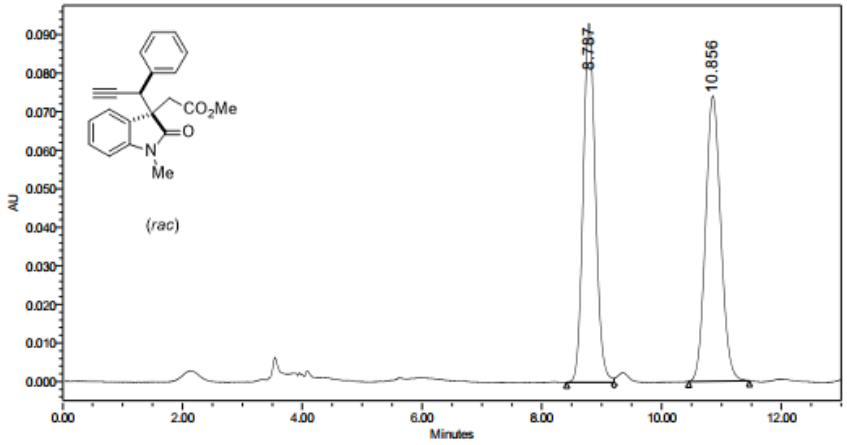



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.455 | 40971 | 0.37 | 1824 |
| 2 | 15.419 | 11001117 | 99.63 | 224374 |

**Supplementary Fig. 51.** HPLC spectra of compound **(*S*,*S*)-3aa**

SAMPLE INFORMATION

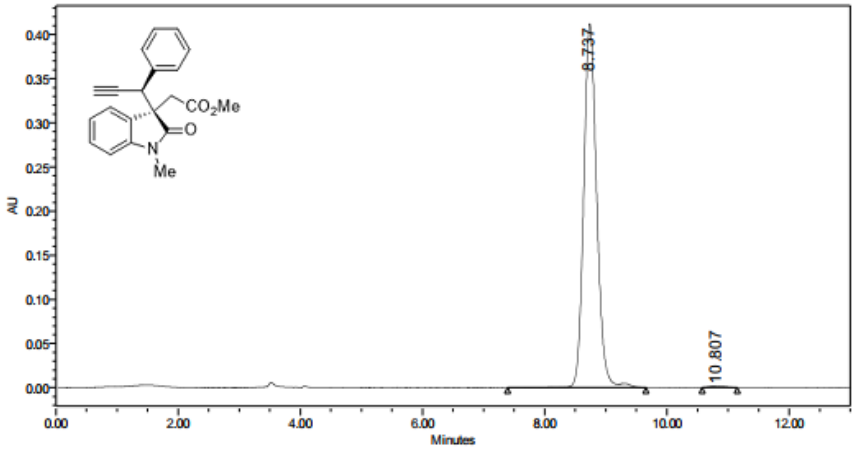
| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh182up |
| Vial: | 12 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 270.0nm |
| Run Time: | 13.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 270.0 nm (2998 |
| Date Acquired: | 3/6/2021 1:01:37 PM CST | | |
| Date Processed: | 3/6/2021 2:41:06 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.787 | 1318498 | 50.20 | 93123 |
| 2 | 10.856 | 1307970 | 49.80 | 74057 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-82-1-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh182up |
| Vial: | 13 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 270.0nm |
| Run Time: | 13.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 270.0 nm (2998 |
| Date Acquired: | 3/6/2021 1:20:26 PM CST | | |
| Date Processed: | 3/6/2021 2:43:32 PM CST | | |

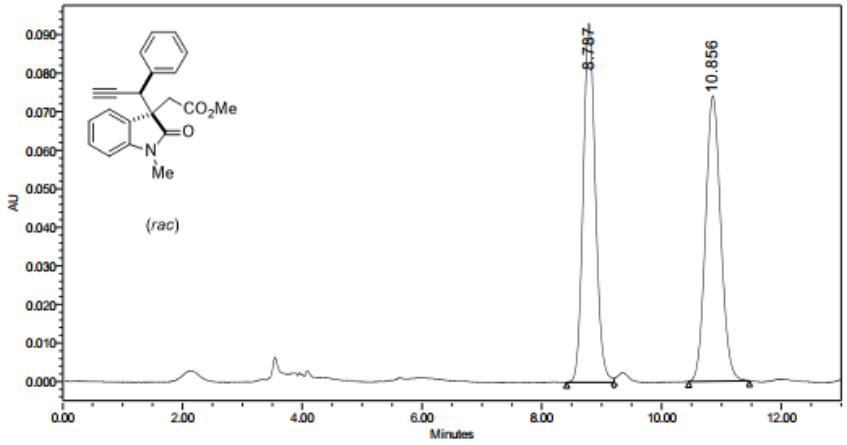



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.737 | 6079519 | 99.57 | 411878 |
| 2 | 10.807 | 26183 | 0.43 | 1625 |

**Supplementary Fig. 52.** HPLC spectra of compound **(*R*,*S*)-3aa**

SAMPLE INFORMATION

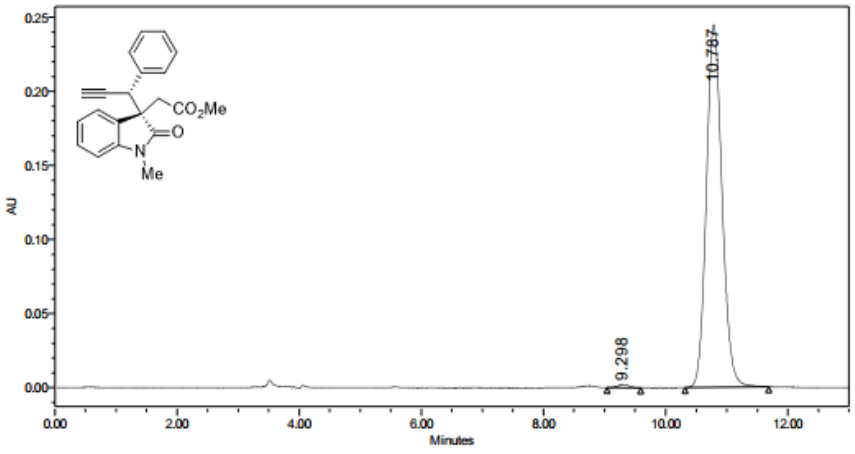
| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh182up |
| Vial: | 12 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 270.0nm |
| Run Time: | 13.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 270.0 nm (2998 |
| Date Acquired: | 3/6/2021 1:01:37 PM CST | | |
| Date Processed: | 3/6/2021 2:41:06 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.787 | 1318498 | 50.20 | 93123 |
| 2 | 10.856 | 1307970 | 49.80 | 74057 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-82-2-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh182up |
| Vial: | 14 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 270.0nm |
| Run Time: | 13.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 270.0 nm (2998 |
| Date Acquired: | 3/6/2021 1:39:19 PM CST | | |
| Date Processed: | 3/6/2021 2:43:00 PM CST | | |

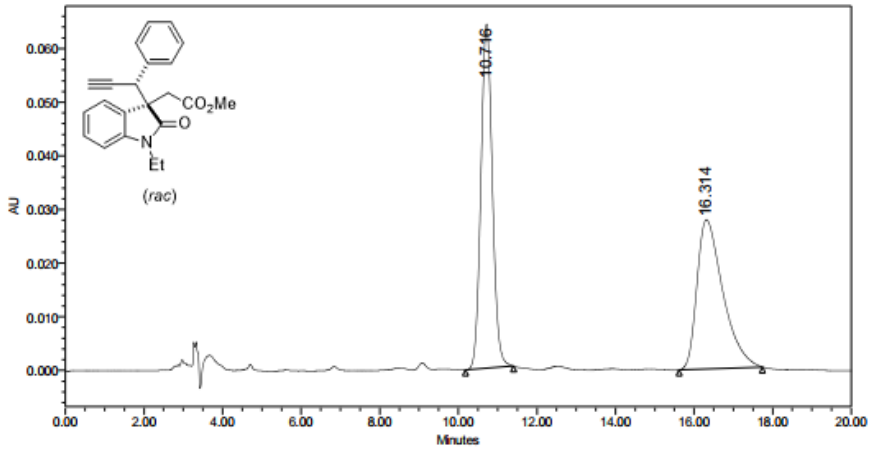



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.298 | 27777 | 0.63 | 2335 |
| 2 | 10.787 | 4386613 | 99.37 | 244641 |

**Supplementary Fig. 53.** HPLC spectra of compound **(*S*,*R*)-3aa**

SAMPLE INFORMATION

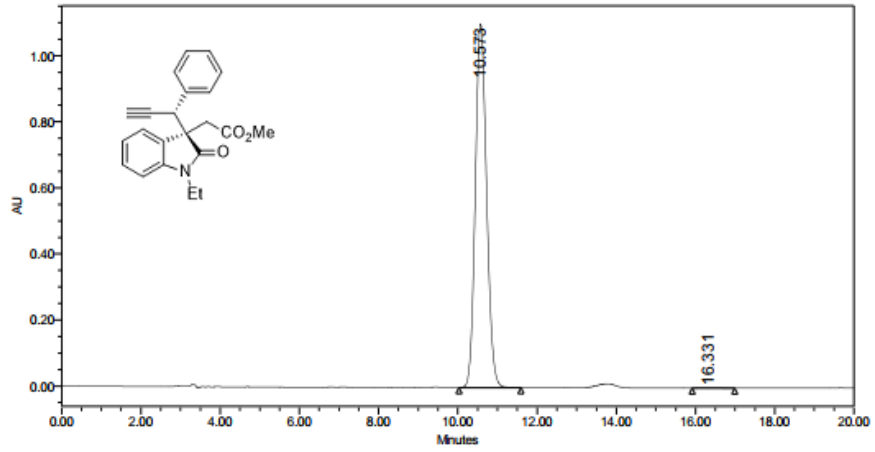
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-74-1-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyhh174 |
| Vial: | 32 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/25/2020 1:26:58 PM CST | | |
| Date Processed: | 12/30/2020 3:37:34 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.716 | 1294232 | 50.37 | 64133 |
| 2 | 16.314 | 1275325 | 49.63 | 27833 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-74-1-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh174 |
| Vial: | 41 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/24/2020 11:13:25 AM CST | | |
| Date Processed: | 12/30/2020 3:38:05 PM CST | | |

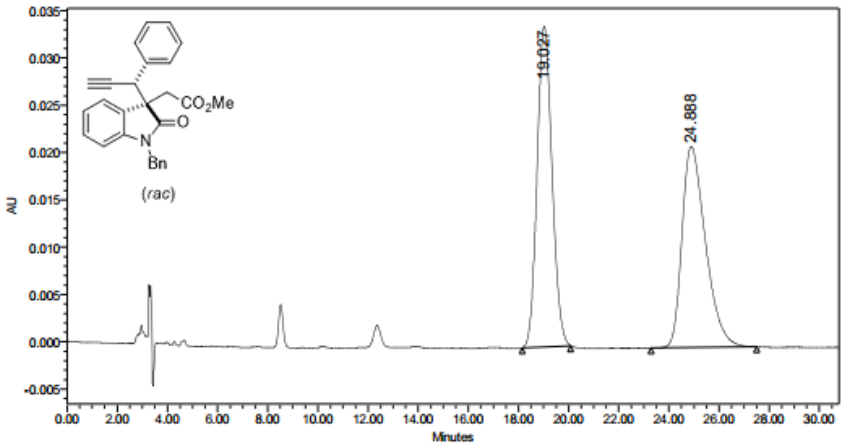



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.573 | 21835641 | 99.91 | 1100912 |
| 2 | 16.331 | 20046 | 0.09 | 533 |

**Supplementary Fig. 54.** HPLC spectra of compound **(*R*,*R*)-3ba**

SAMPLE INFORMATION

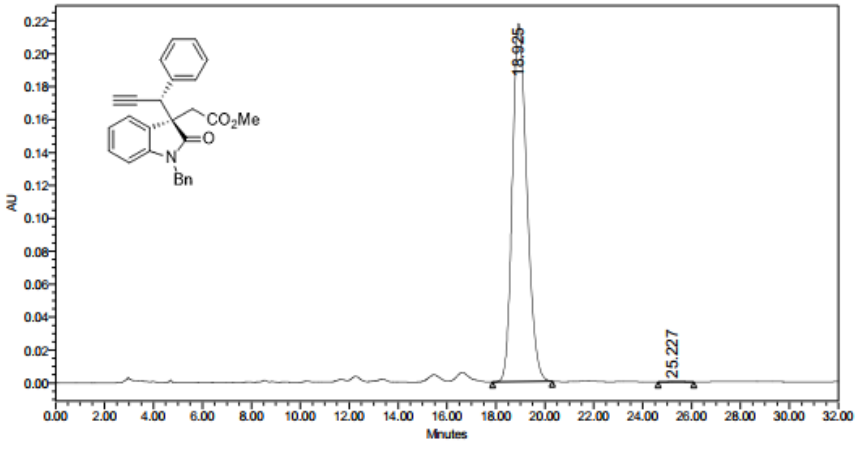
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-74-3-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1743 |
| Vial: | 8 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 32.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/31/2020 4:12:33 PM CST | | |
| Date Processed: | 12/31/2020 5:11:54 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 19.027 | 1398690 | 50.38 | 33886 |
| 2 | 24.888 | 1377494 | 49.62 | 21262 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-74-3-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1743 |
| Vial: | 9 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 32.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/31/2020 4:44:51 PM CST | | |
| Date Processed: | 1/1/2021 5:07:10 PM CST | | |

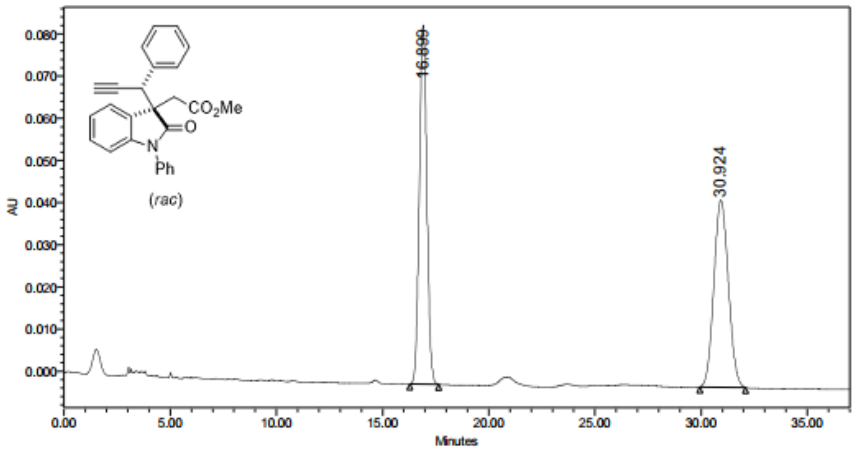



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 18.925 | 8999172 | 99.94 | 217624 |
| 2 | 25.227 | 4996 | 0.06 | 109 |

**Supplementary Fig. 55.** HPLC spectra of compound **(*R*,*R*)-3ca**

SAMPLE INFORMATION

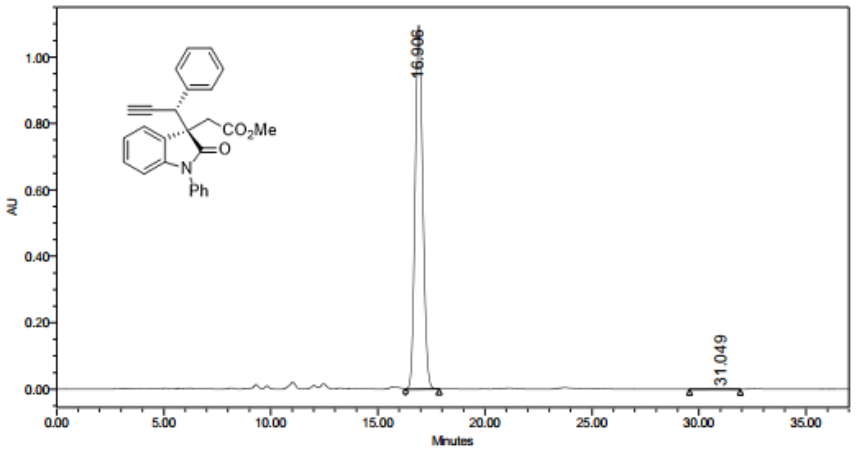
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-74-2-rac-d-IE-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1742 |
| Vial: | 43 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 37.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/30/2020 8:43:58 PM CST | | |
| Date Processed: | 12/30/2020 10:07:48 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 16.899 | 2110483 | 49.99 | 85122 |
| 2 | 30.924 | 2110915 | 50.01 | 44390 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-74-2-asy-IE-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1742 |
| Vial: | 44 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 37.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/30/2020 9:21:42 PM CST | | |
| Date Processed: | 12/30/2020 10:08:48 PM CST | | |

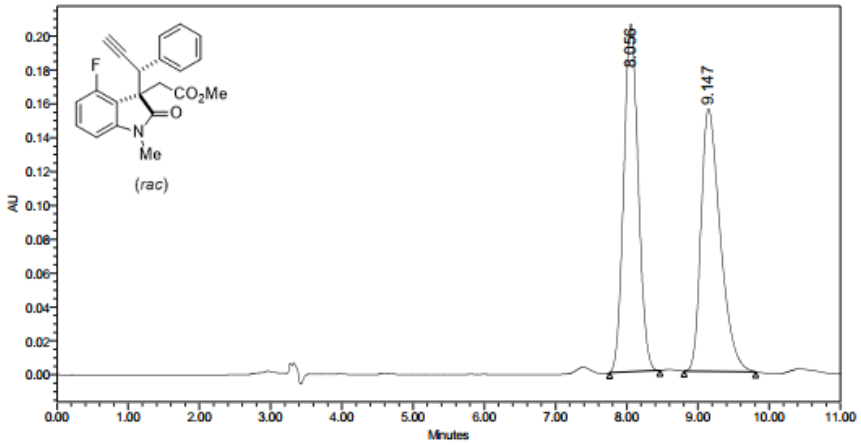



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 16.906 | 27421176 | 99.75 | 1095000 |
| 2 | 31.049 | 68443 | 0.25 | 1349 |

**Supplementary Fig. 56.** HPLC spectra of compound **(*R*,*R*)-3da**

SAMPLE INFORMATION

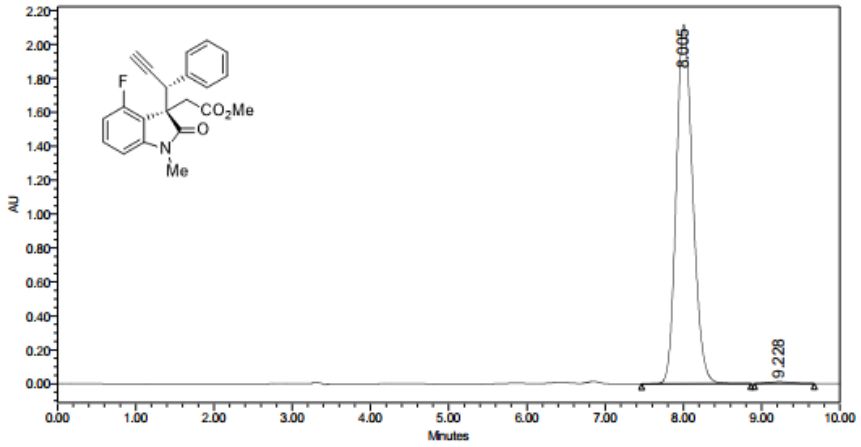
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-1-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh_1_76_123 |
| Vial: | 91 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 11.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/1/2021 4:33:24 PM CST | | |
| Date Processed: | 1/1/2021 5:10:03 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.056 | 2896300 | 49.99 | 205215 |
| 2 | 9.147 | 2896903 | 50.01 | 154854 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-1-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 92 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 10.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/1/2021 9:23:37 PM CST | | |
| Date Processed: | 1/1/2021 9:34:28 PM CST | | |

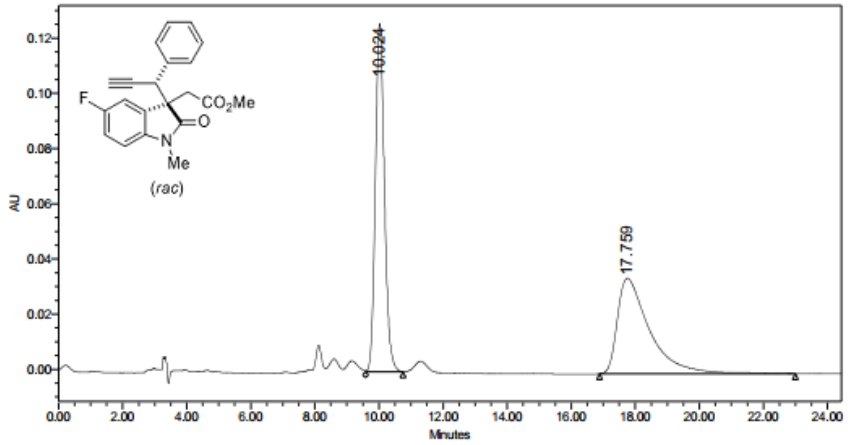



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.005 | 30960952 | 99.30 | 2117349 |
| 2 | 9.228 | 217384 | 0.70 | 11289 |

**Supplementary Fig. 57.** HPLC spectra of compound **(*R*,*R*)-3ea**

SAMPLE INFORMATION

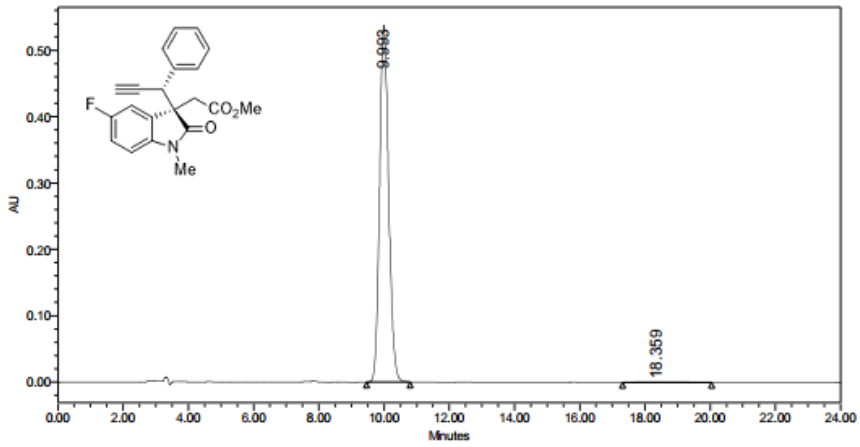
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-6-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 10 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 40.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/6/2021 2:48:50 PM CST | | |
| Date Processed: | 1/6/2021 8:00:35 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.024 | 2472165 | 50.77 | 126221 |
| 2 | 17.759 | 2396769 | 49.23 | 34582 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-6-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17667 |
| Vial: | 28 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 24.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/6/2021 7:07:41 PM CST | | |
| Date Processed: | 1/6/2021 7:59:54 PM CST | | |

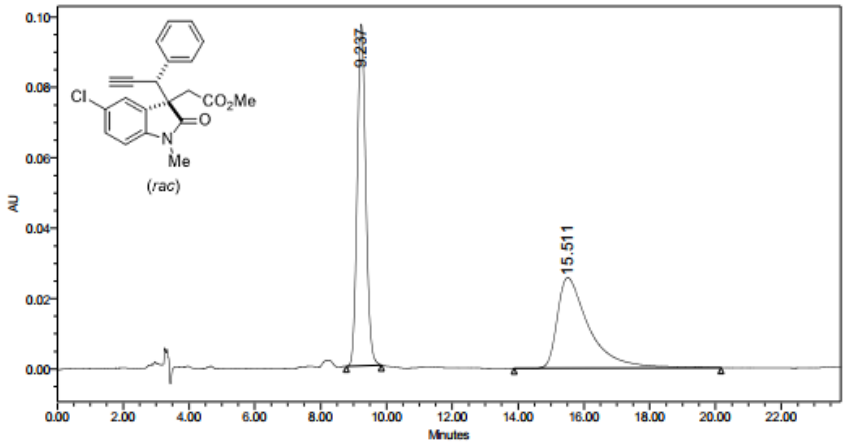



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.993 | 10311953 | 99.65 | 537791 |
| 2 | 18.359 | 36149 | 0.35 | 490 |

**Supplementary Fig. 58.** HPLC spectra of compound **(*R*,*R*)-3fa**

SAMPLE INFORMATION

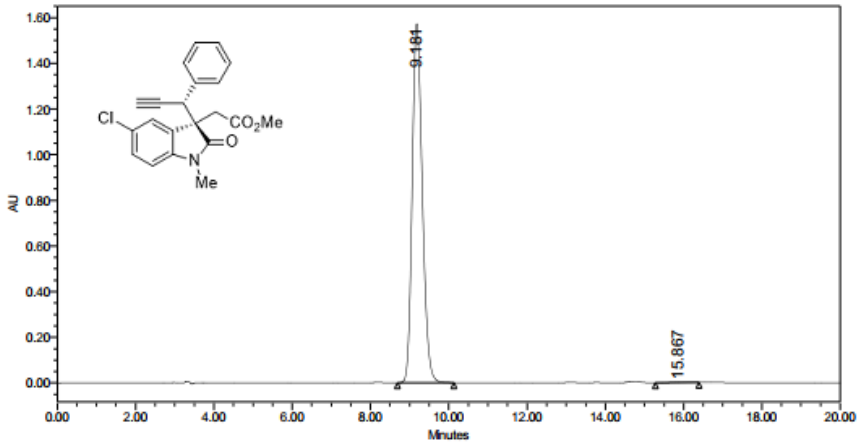
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-7-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 11 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm@1 |
| Run Time: | 40.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/6/2021 3:14:08 PM CST | | |
| Date Processed: | 1/6/2021 3:40:22 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.237 | 1759930 | 50.68 | 97015 |
| 2 | 15.511 | 1713005 | 49.32 | 25701 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-7-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17667 |
| Vial: | 29 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/6/2021 7:32:23 PM CST | | |
| Date Processed: | 1/6/2021 7:57:01 PM CST | | |

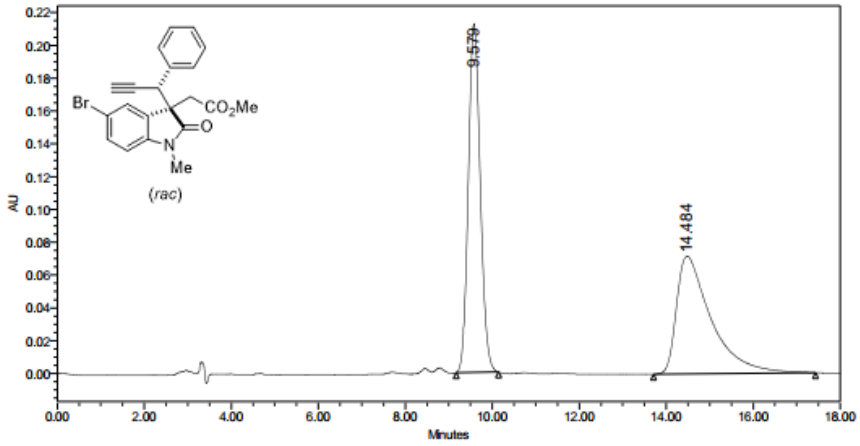



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.181 | 28351847 | 99.88 | 1570425 |
| 2 | 15.867 | 33145 | 0.12 | 914 |

**Supplementary Fig. 59.** HPLC spectra of compound **(*R*,*R*)-3ga**

SAMPLE INFORMATION

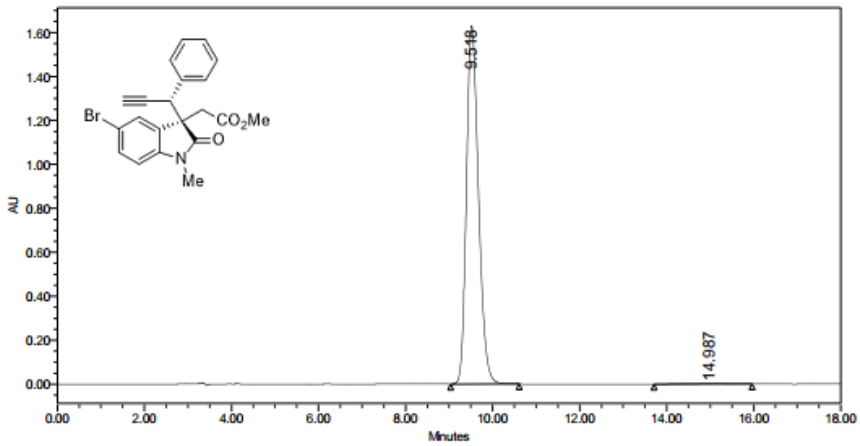
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-2-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh_1_76_123 |
| Vial: | 93 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm@1 |
| Run Time: | 18.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/1/2021 5:02:01 PM CST | | |
| Date Processed: | 1/1/2021 9:27:07 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.579 | 4062612 | 50.72 | 212415 |
| 2 | 14.484 | 3946988 | 49.28 | 71766 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-2-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh_1_76_123 |
| Vial: | 94 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm@1 |
| Run Time: | 18.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/1/2021 5:20:46 PM CST | | |
| Date Processed: | 1/1/2021 9:28:50 PM CST | | |

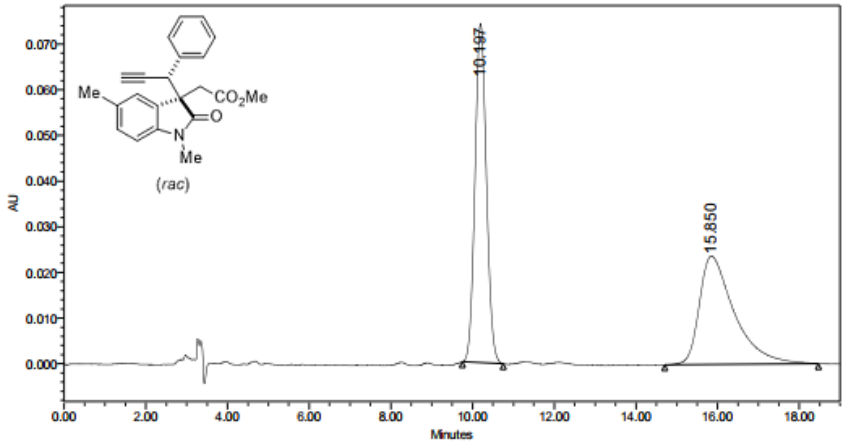



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.518 | 31432586 | 99.62 | 1629903 |
| 2 | 14.987 | 119882 | 0.38 | 2038 |

**Supplementary Fig. 60.** HPLC spectra of compound **(*R*,*R*)-3ha**

SAMPLE INFORMATION

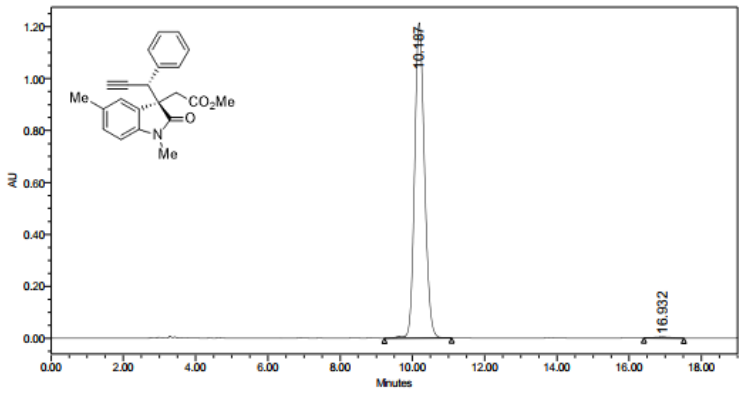
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-3-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | itmustbefinal |
| Vial: | 40 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 19.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/4/2021 5:50:14 PM CST | | |
| Date Processed: | 1/4/2021 6:50:30 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.197 | 1432801 | 50.45 | 74221 |
| 2 | 15.850 | 1407517 | 49.55 | 23716 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-3-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | itmustbefinal |
| Vial: | 41 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 19.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/4/2021 6:09:57 PM CST | | |
| Date Processed: | 7/12/2021 4:45:43 PM CST | | |

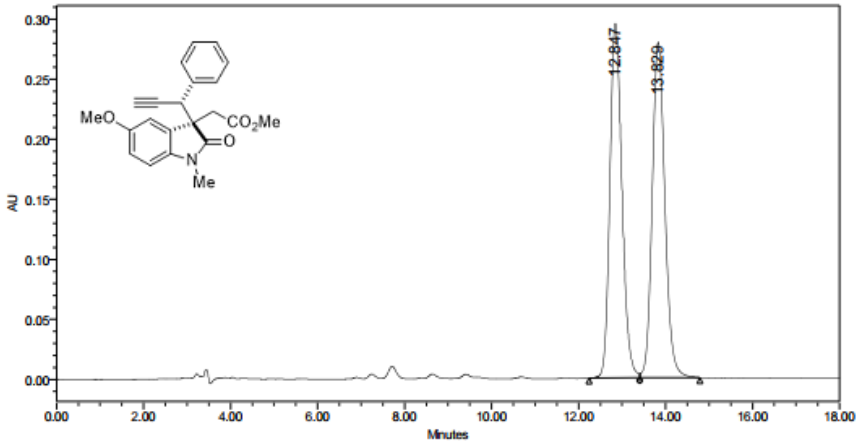



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.187 | 23141433 | 99.48 | 1213865 |
| 2 | 16.932 | 119855 | 0.52 | 4052 |

**Supplementary Fig. 61.** HPLC spectra of compound **(*R*,*R*)-3ia**

SAMPLE INFORMATION

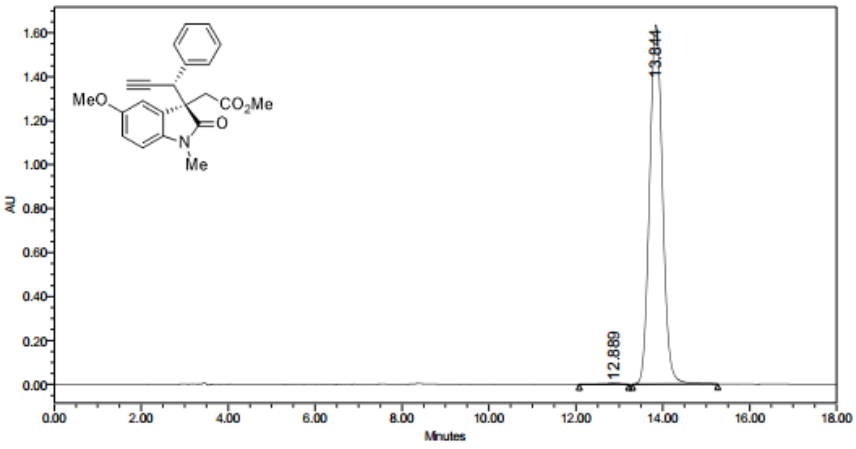
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-9-rac-d-IA-15%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1769 |
| Vial: | 92 | Acq. Method Set: | 15% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 18.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/29/2021 2:49:53 PM CST | | |
| Date Processed: | 1/29/2021 3:30:06 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 12.847 | 5674250 | 49.93 | 295158 |
| 2 | 13.829 | 5689212 | 50.07 | 279436 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-9-asy-IA-15%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1769 |
| Vial: | 93 | Acq. Method Set: | 15% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 18.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/29/2021 3:08:35 PM CST | | |
| Date Processed: | 1/29/2021 3:32:12 PM CST | | |

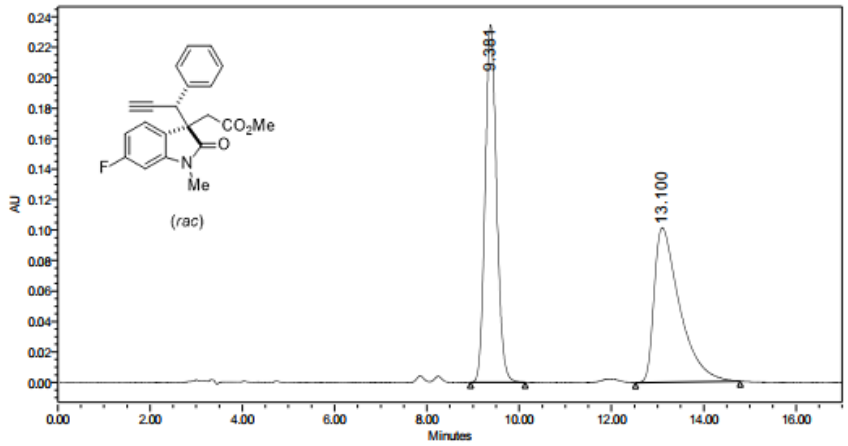



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 12.889 | 108058 | 0.32 | 5399 |
| 2 | 13.844 | 34016725 | 99.68 | 1633558 |

**Supplementary Fig. 62.** HPLC spectra of compound **(*R*,*R*)-3ja**

SAMPLE INFORMATION

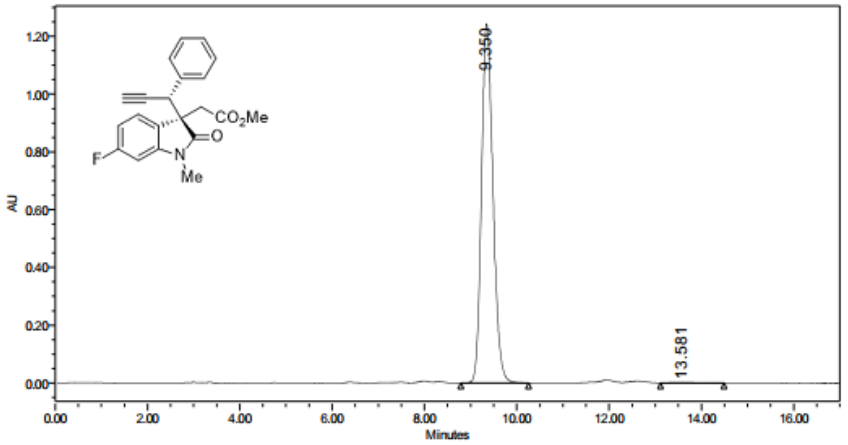
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-167-3-rac-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh16713 |
| Vial: | 54 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm@1 |
| Run Time: | 17.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 7/13/2021 7:09:37 PM CST | | |
| Date Processed: | 7/13/2021 7:46:30 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.381 | 4025654 | 50.72 | 234855 |
| 2 | 13.100 | 3911431 | 49.28 | 101478 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-167-3-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh16713 |
| Vial: | 55 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm@1 |
| Run Time: | 17.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 7/13/2021 7:27:19 PM CST | | |
| Date Processed: | 7/13/2021 7:47:11 PM CST | | |

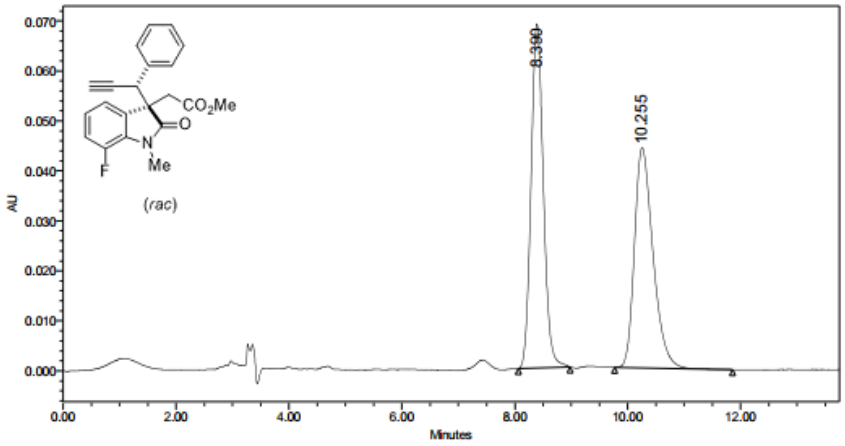



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.350 | 21321429 | 99.81 | 1242968 |
| 2 | 13.581 | 41080 | 0.19 | 1206 |

**Supplementary Fig. 63.** HPLC spectra of compound **(*R*,*R*)-3ka**

SAMPLE INFORMATION

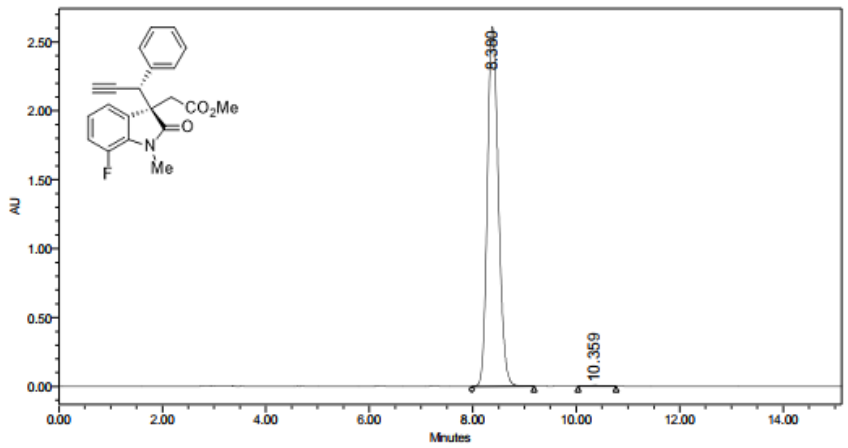
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-5-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 94 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 40.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/3/2021 4:00:18 PM CST | | |
| Date Processed: | 1/3/2021 4:15:48 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.390 | 1040207 | 50.86 | 68815 |
| 2 | 10.255 | 1005115 | 49.14 | 44068 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-5-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 95 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 40.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/3/2021 4:15:06 PM CST | | |
| Date Processed: | 1/3/2021 4:31:28 PM CST | | |

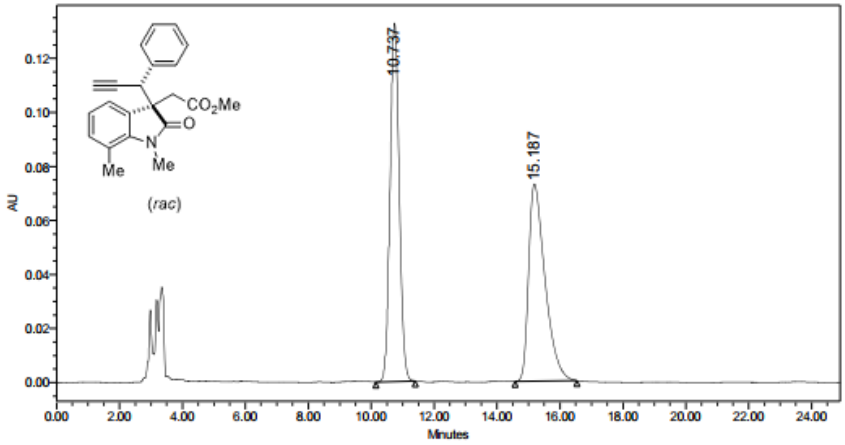



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.380 | 38698850 | 99.76 | 2610008 |
| 2 | 10.359 | 91211 | 0.24 | 4878 |

**Supplementary Fig. 64.** HPLC spectra of compound **(*R*,*R*)-3la**

SAMPLE INFORMATION

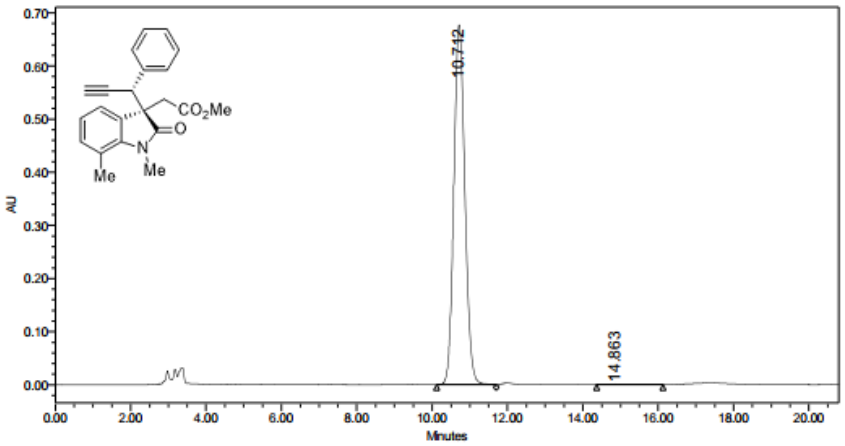
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-8-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 12 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 40.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 1/6/2021 3:38:51 PM CST | | |
| Date Processed: | 1/6/2021 8:17:31 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.737 | 2664485 | 50.05 | 132562 |
| 2 | 15.187 | 2659201 | 49.95 | 72991 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-76-8-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 59 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 40.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 1/6/2021 7:55:34 PM CST | | |
| Date Processed: | 1/6/2021 8:18:38 PM CST | | |

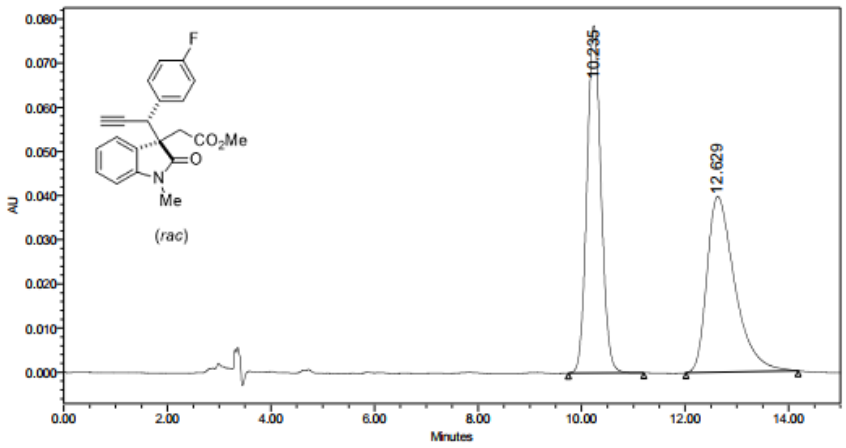



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.712 | 13756777 | 99.77 | 676506 |
| 2 | 14.863 | 31147 | 0.23 | 807 |

**Supplementary Fig. 65.** HPLC spectra of compound **(*R*,*R*)-3ma**

SAMPLE INFORMATION

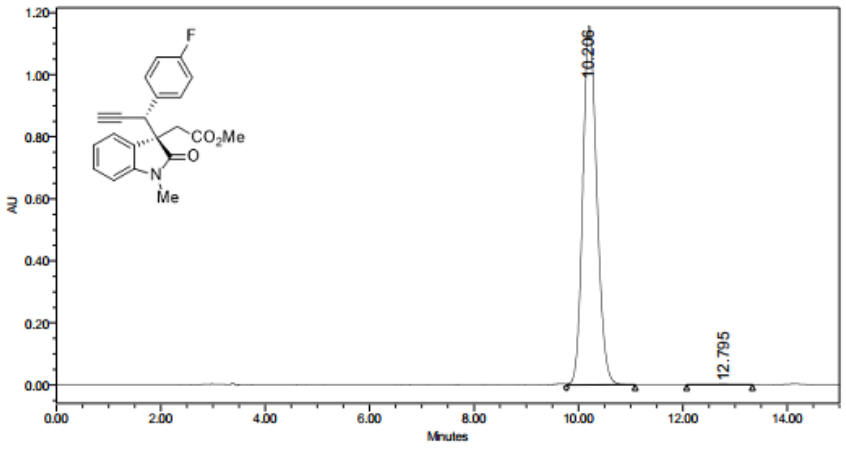
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-3-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1783 |
| Vial: | 57 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 15.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/16/2021 7:33:56 PM CST | | |
| Date Processed: | 1/16/2021 8:07:41 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.235 | 1488308 | 49.96 | 78611 |
| 2 | 12.629 | 1490860 | 50.04 | 39788 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-3-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1783 |
| Vial: | 58 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 15.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/16/2021 7:49:39 PM CST | | |
| Date Processed: | 1/16/2021 8:08:22 PM CST | | |

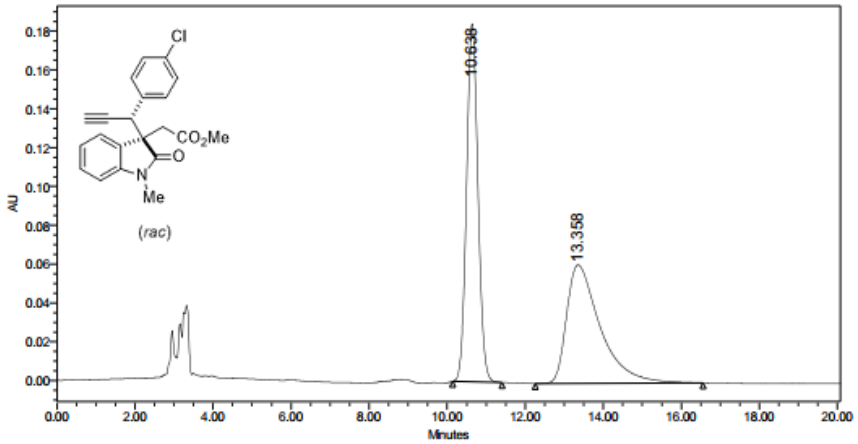



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.206 | 21680665 | 99.84 | 1157434 |
| 2 | 12.795 | 34892 | 0.16 | 1011 |

**Supplementary Fig. 66.** HPLC spectra of compound **(*R*,*R*)-3ab**

SAMPLE INFORMATION

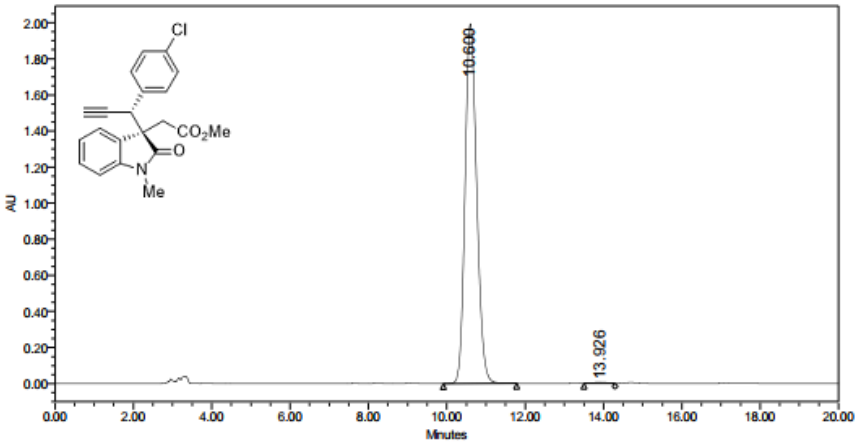
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-1-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1781 |
| Vial: | 77 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 40.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 1/8/2021 9:41:54 AM CST | | |
| Date Processed: | 1/8/2021 11:07:37 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.638 | 3755736 | 50.78 | 184290 |
| 2 | 13.358 | 3639639 | 49.22 | 61008 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-1-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17812 |
| Vial: | 78 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 1/8/2021 10:28:22 AM CST | | |
| Date Processed: | 1/8/2021 11:06:44 AM CST | | |

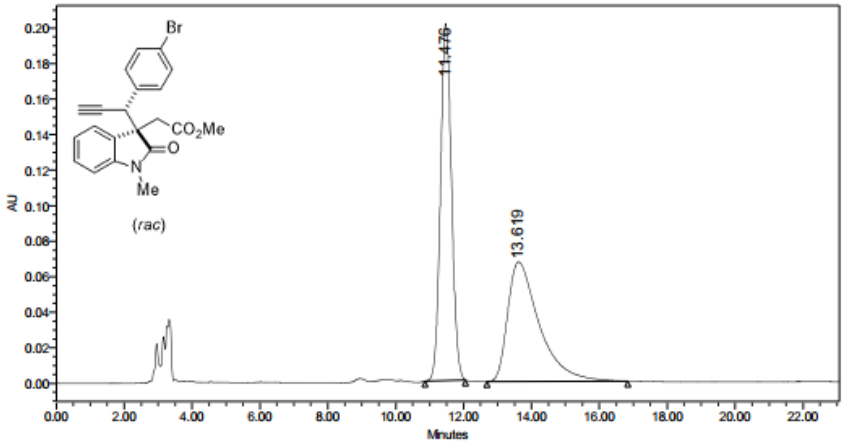



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.600 | 41249361 | 99.70 | 1992212 |
| 2 | 13.926 | 122091 | 0.30 | 5613 |

**Supplementary Fig. 67.** HPLC spectra of compound **(*R*,*R*)-3ac**

SAMPLE INFORMATION

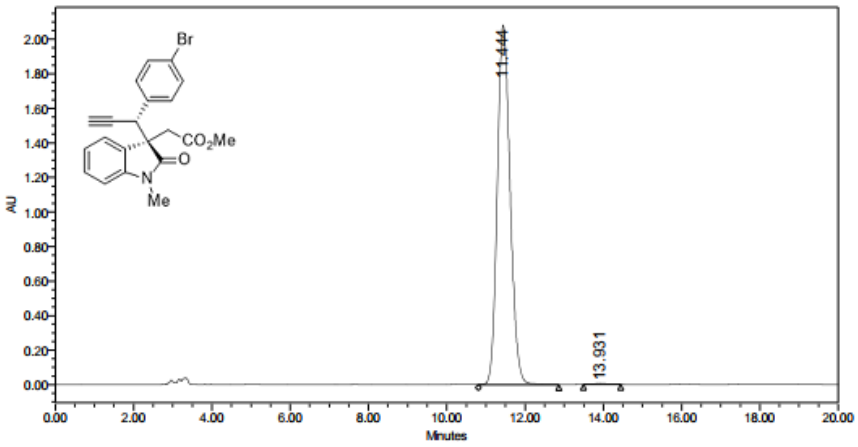
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-2-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 79 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 40.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 1/8/2021 10:03:30 AM CST | | |
| Date Processed: | 1/8/2021 11:10:59 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.476 | 4476860 | 50.75 | 200959 |
| 2 | 13.619 | 4344056 | 49.25 | 67375 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-2-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17812 |
| Vial: | 80 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 1/8/2021 10:49:04 AM CST | | |
| Date Processed: | 1/8/2021 11:11:15 AM CST | | |

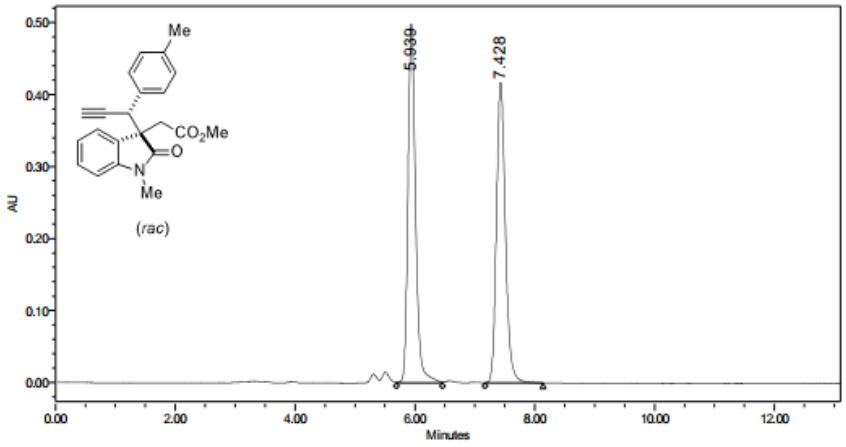



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.444 | 47026853 | 99.74 | 2080336 |
| 2 | 13.931 | 123600 | 0.26 | 5846 |

**Supplementary Fig. 68.** HPLC spectra of compound **(*R*,*R*)-3ad**

SAMPLE INFORMATION

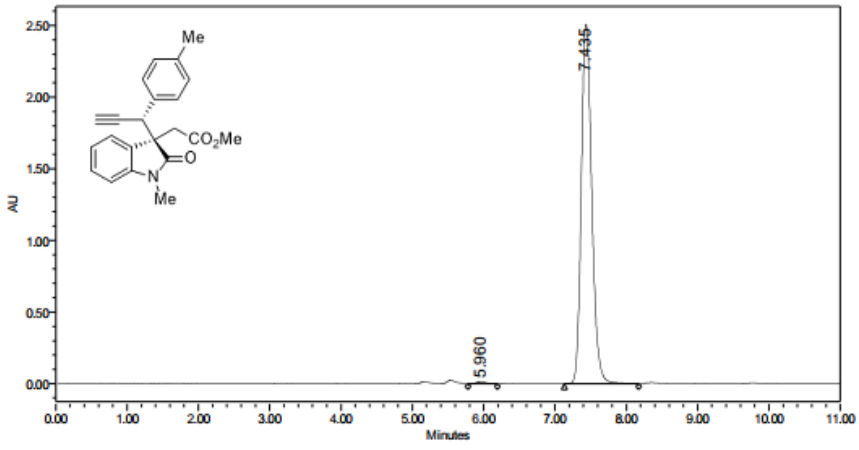
| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh1784racdown |
| Vial: | 49 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/17/2021 5:20:35 PM CST | | |
| Date Processed: | 1/17/2021 6:03:35 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 5.939 | 4396267 | 50.48 | 497966 |
| 2 | 7.428 | 4313244 | 49.52 | 417090 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-4-asy-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | |
| Vial: | 50 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 11.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/17/2021 5:51:33 PM CST | | |
| Date Processed: | 1/17/2021 6:04:02 PM CST | | |

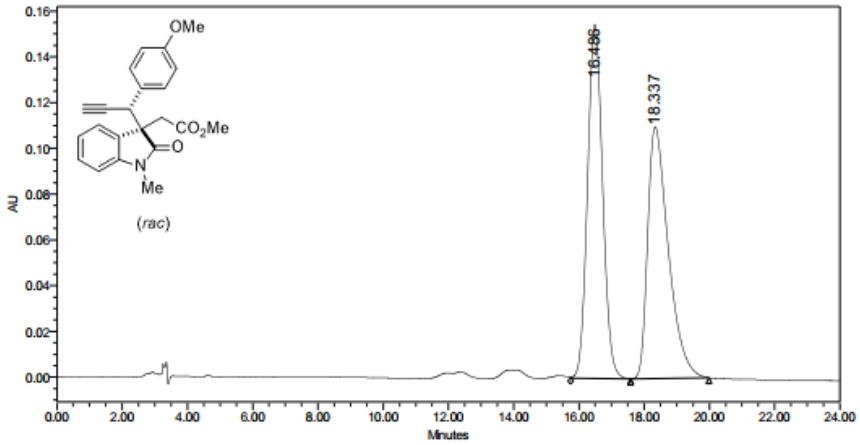



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 5.960 | 111198 | 0.43 | 13336 |
| 2 | 7.435 | 25470899 | 99.57 | 2507009 |

**Supplementary Fig. 69.** HPLC spectra of compound **(*R*,*R*)-3ae**

SAMPLE INFORMATION

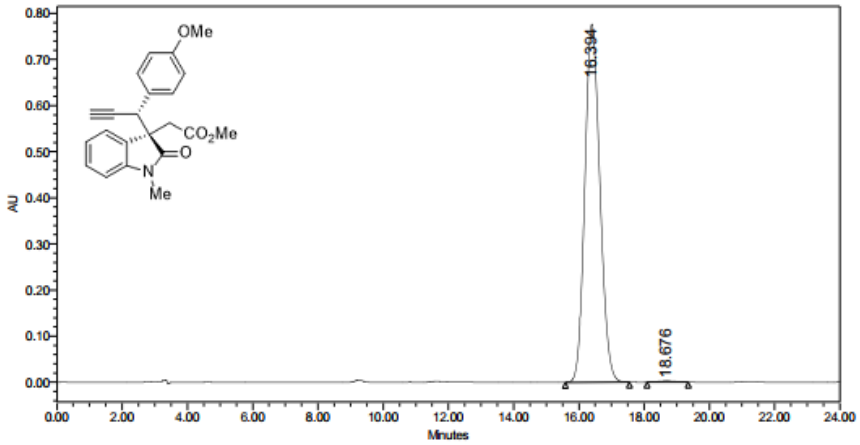
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-5-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh_1_78_5 |
| Vial: | 19 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 24.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/15/2021 1:03:31 PM CST | | |
| Date Processed: | 1/15/2021 2:17:55 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 16.486 | 4992718 | 50.65 | 154628 |
| 2 | 18.337 | 4864342 | 49.35 | 109942 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-5-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh_1_78_5 |
| Vial: | 20 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 24.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/15/2021 1:28:15 PM CST | | |
| Date Processed: | 1/15/2021 2:18:12 PM CST | | |

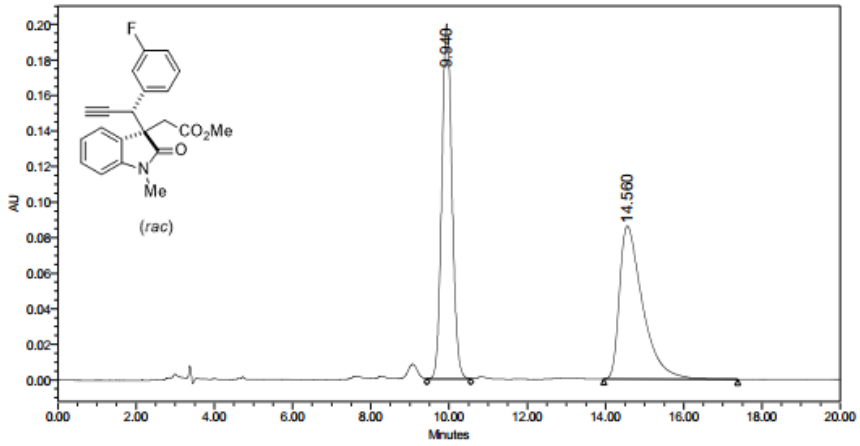



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 16.394 | 25084232 | 99.61 | 776259 |
| 2 | 18.676 | 99206 | 0.39 | 2505 |

**Supplementary Fig. 70.** HPLC spectra of compound **(*R*,*R*)-3af**

SAMPLE INFORMATION

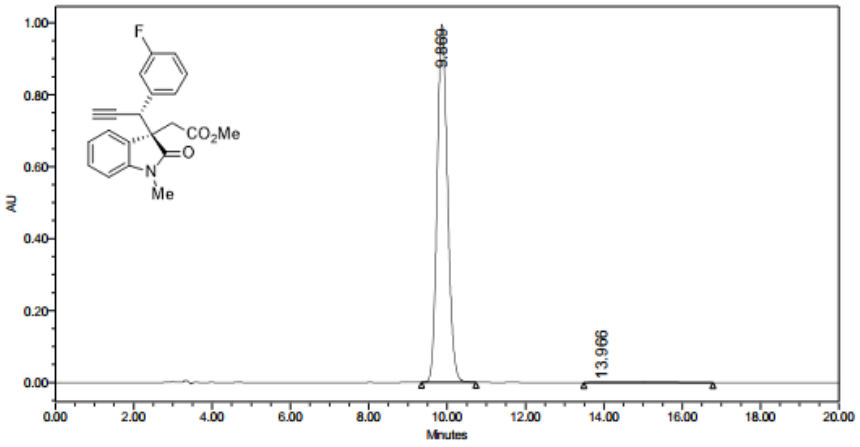
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-9-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh2021123 |
| Vial: | 8 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/23/2021 10:33:21 AM CST | | |
| Date Processed: | 1/24/2021 9:45:25 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.940 | 3578794 | 50.46 | 199591 |
| 2 | 14.560 | 3513676 | 49.54 | 86076 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-9-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1789 |
| Vial: | 5 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/24/2021 9:27:23 PM CST | | |
| Date Processed: | 1/24/2021 9:48:10 PM CST | | |

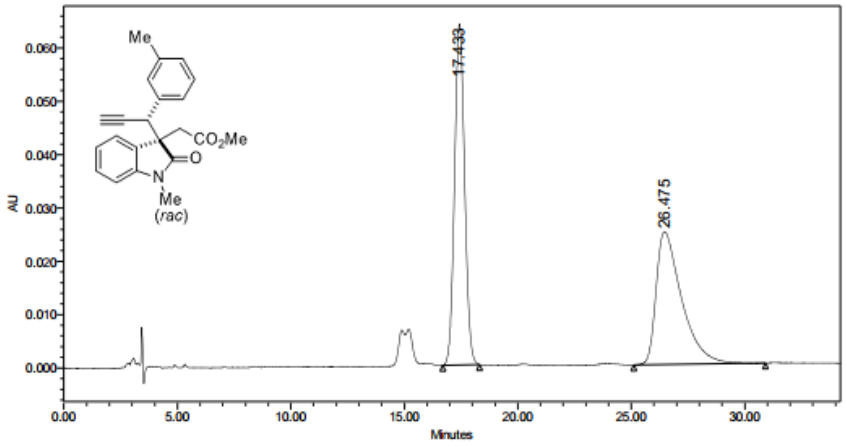



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.869 | 18185456 | 99.65 | 994770 |
| 2 | 13.966 | 62965 | 0.35 | 725 |

**Supplementary Fig. 71.** HPLC spectra of compound **(*R*,*R*)-3ag**

SAMPLE INFORMATION

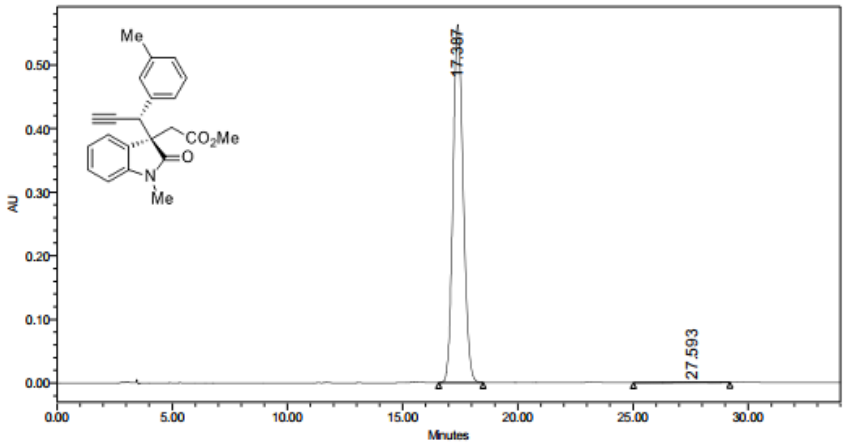
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-6-rac-d-IG-15%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 88 | Acq. Method Set: | 15% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 100.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/16/2021 8:14:32 PM CST | | |
| Date Processed: | 1/16/2021 9:24:36 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 17.433 | 1962375 | 50.28 | 63918 |
| 2 | 26.475 | 1940503 | 49.72 | 24919 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-6-asy-IG-15%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 89 | Acq. Method Set: | 15% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 34.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/16/2021 8:49:48 PM CST | | |
| Date Processed: | 1/16/2021 9:25:43 PM CST | | |

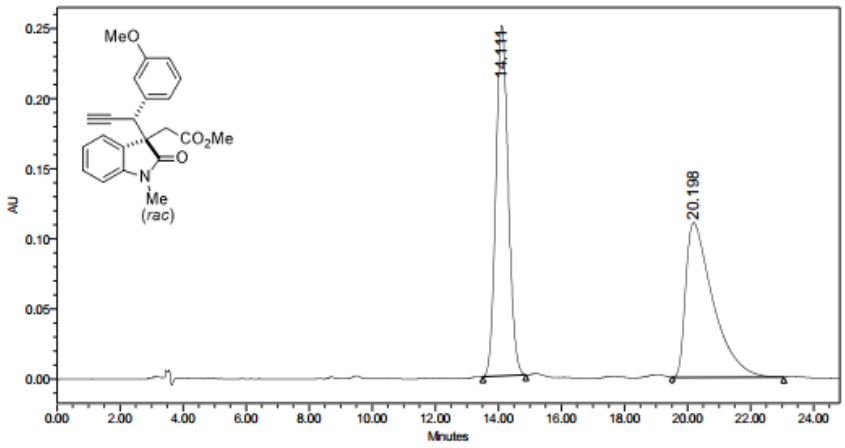



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 17.387 | 17235743 | 99.76 | 562416 |
| 2 | 27.593 | 41009 | 0.24 | 673 |

**Supplementary Fig. 72.** HPLC spectra of compound **(*R*,*R*)-3ah**

SAMPLE INFORMATION

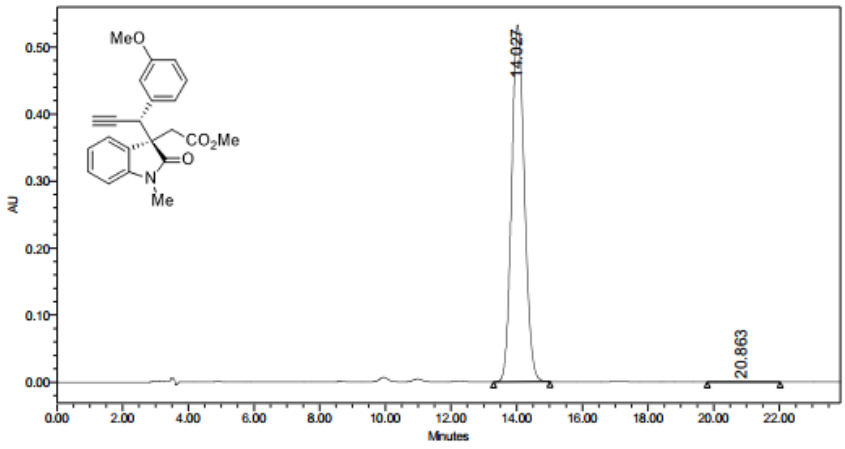
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-10-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17810racdown |
| Vial: | 3 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/21/2021 9:58:55 AM CST | | |
| Date Processed: | 1/21/2021 11:00:38 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 14.111 | 6763591 | 50.70 | 249968 |
| 2 | 20.198 | 6576263 | 49.30 | 110259 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-10-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 5 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm@1 |
| Run Time: | 25.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/21/2021 10:29:34 AM CST | | |
| Date Processed: | 1/21/2021 11:01:07 AM CST | | |

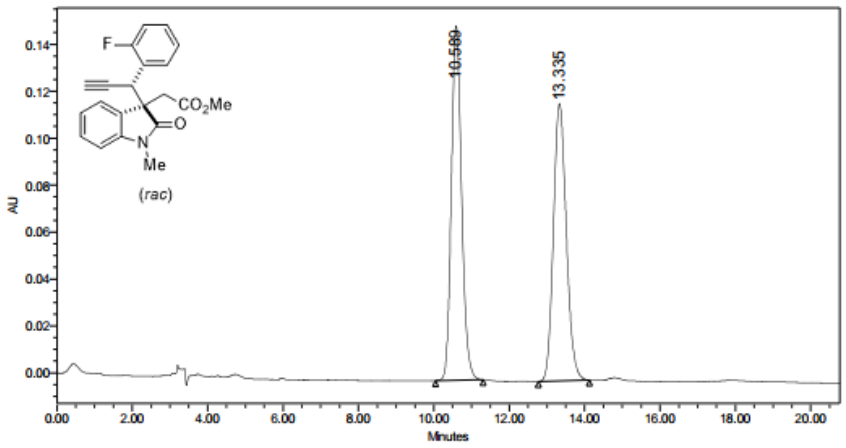



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 14.027 | 14326966 | 99.86 | 532379 |
| 2 | 20.863 | 19388 | 0.14 | 321 |

**Supplementary Fig. 73.** HPLC spectra of compound **(*R*,*R*)-3ai**

SAMPLE INFORMATION

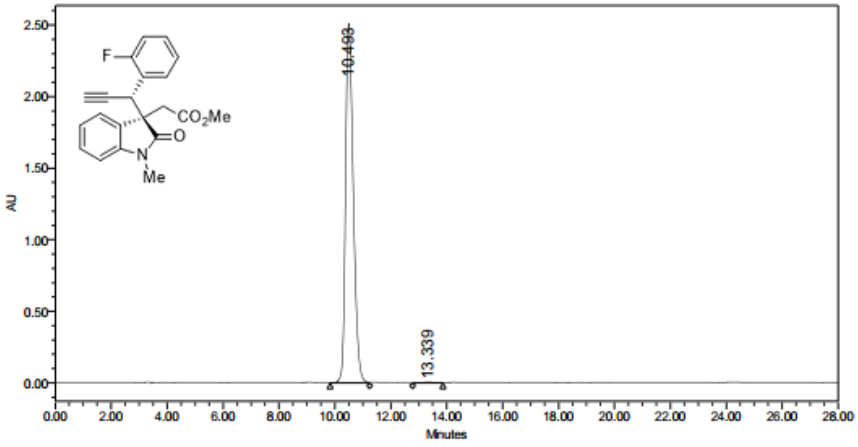
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-11-rac-d-IC-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 24 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/22/2021 6:54:16 PM CST | | |
| Date Processed: | 1/22/2021 7:15:27 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.589 | 2829050 | 50.36 | 150997 |
| 2 | 13.335 | 2788973 | 49.64 | 118080 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-11-asy-IC-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17811asy |
| Vial: | 4 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 28.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/22/2021 11:51:48 AM CST | | |
| Date Processed: | 1/22/2021 7:15:48 PM CST | | |

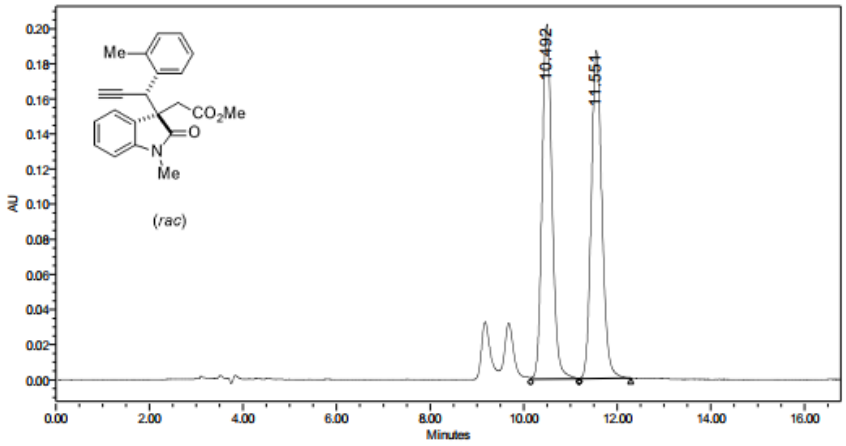



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.493 | 48496476 | 99.76 | 2511254 |
| 2 | 13.339 | 117048 | 0.24 | 4801 |

**Supplementary Fig. 74.** HPLC spectra of compound **(*R*,*S*)-3aj**

SAMPLE INFORMATION

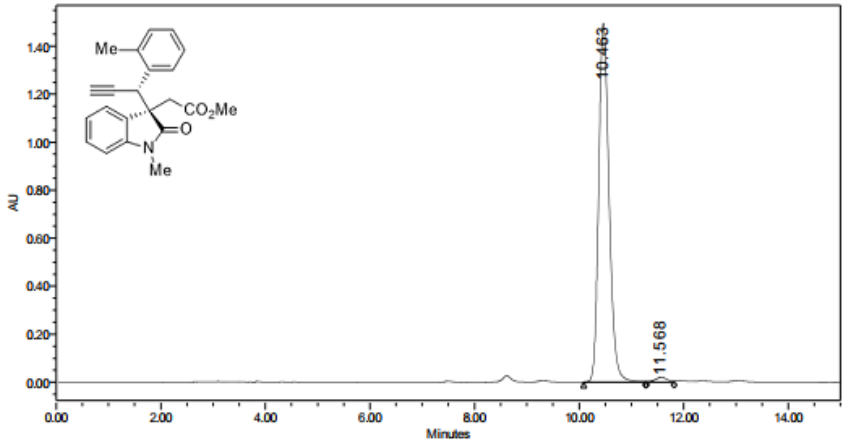
| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh1787racdown |
| Vial: | 51 | Acq. Method Set: | 10% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/17/2021 7:01:54 PM CST | | |
| Date Processed: | 1/17/2021 7:39:47 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.492 | 2942377 | 50.14 | 201948 |
| 2 | 11.551 | 2926496 | 49.86 | 186821 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-7-asy-IA-10%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh1787 |
| Vial: | 52 | Acq. Method Set: | 10% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 15.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/17/2021 7:20:58 PM CST | | |
| Date Processed: | 1/17/2021 7:39:57 PM CST | | |

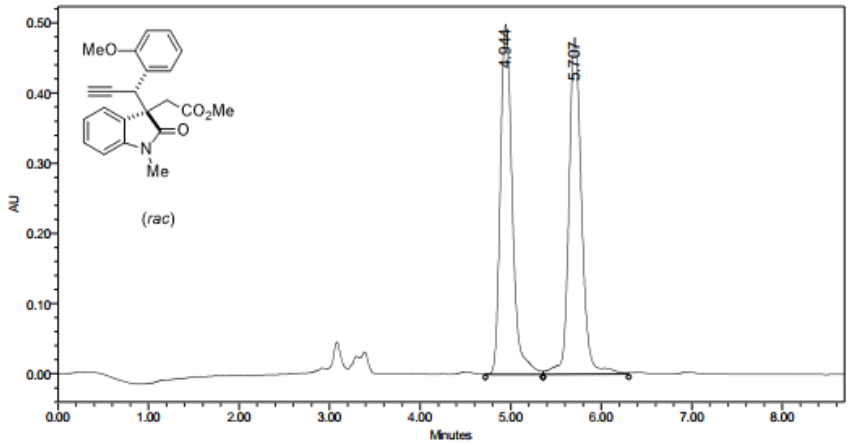



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.463 | 20680670 | 98.49 | 1494485 |
| 2 | 11.568 | 316564 | 1.51 | 19925 |

**Supplementary Fig.75.** HPLC spectra of compound **(*R*,*R*)-3ak**

SAMPLE INFORMATION

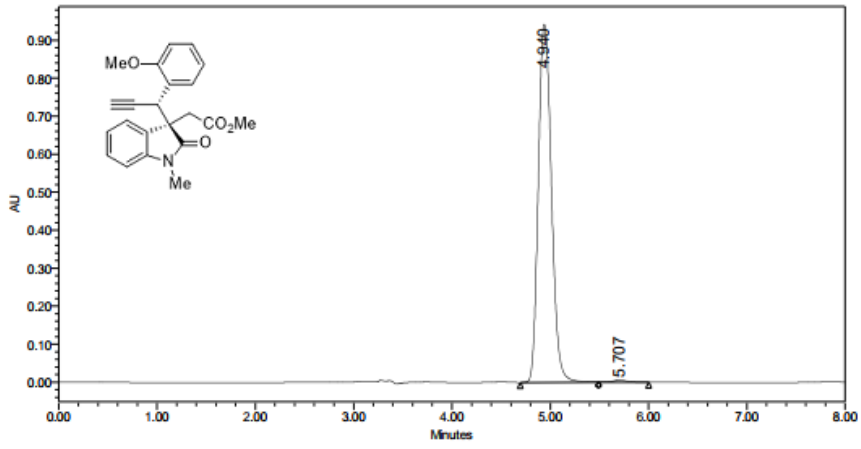
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-12-rac-d-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 68 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 30.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 1/24/2021 8:44:31 PM CST | | |
| Date Processed: | 1/24/2021 8:55:51 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 4.944 | 4541874 | 49.33 | 498260 |
| 2 | 5.707 | 4665923 | 50.67 | 479562 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-12-asy-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17812 |
| Vial: | 60 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 8.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/25/2021 4:31:58 PM CST | | |
| Date Processed: | 1/25/2021 4:43:43 PM CST | | |

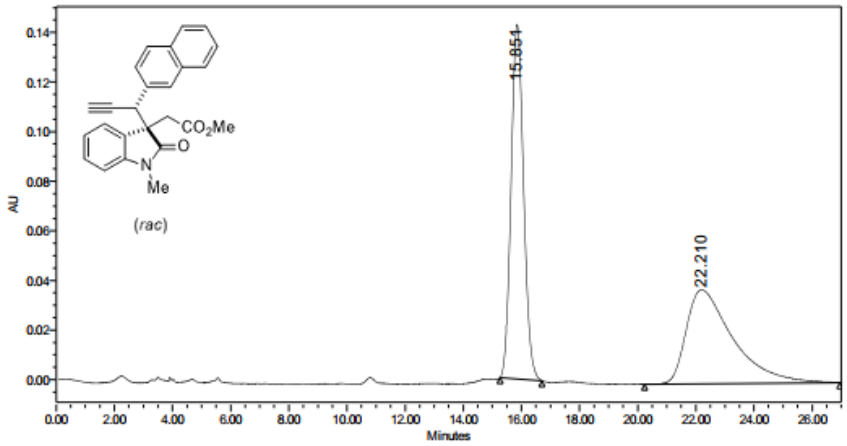



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 4.940 | 8726516 | 99.29 | 942020 |
| 2 | 5.707 | 62633 | 0.71 | 5387 |

**Supplementary Fig.76.** HPLC spectra of compound **(*R*,*R*)-3al**

SAMPLE INFORMATION

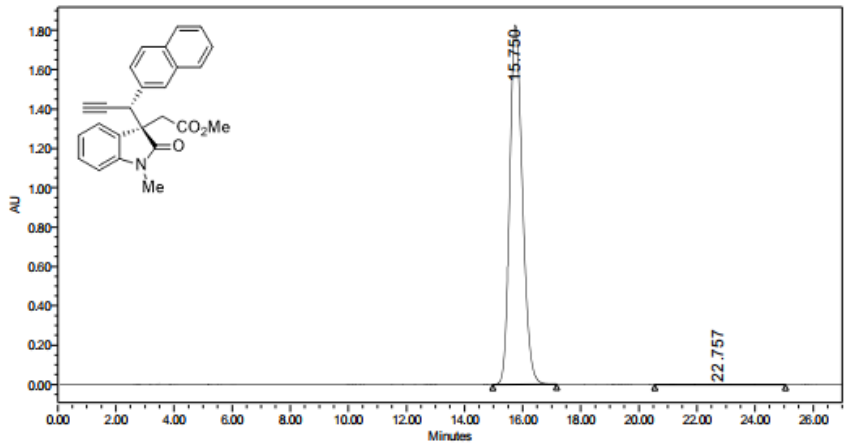
| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyhsgygt |
| Vial: | 9 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 27.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/6/2021 12:59:18 AM CST | | |
| Date Processed: | 3/6/2021 8:54:21 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 15.851 | 4293469 | 50.51 | 142803 |
| 2 | 22.210 | 4206939 | 49.49 | 37815 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-13-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyhsgygt |
| Vial: | 10 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 27.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/6/2021 1:26:58 AM CST | | |
| Date Processed: | 3/6/2021 9:00:32 AM CST | | |

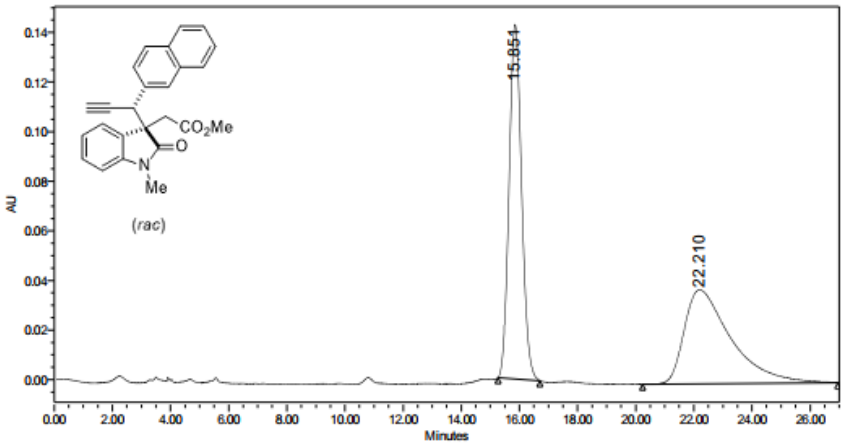



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 15.750 | 55916784 | 99.73 | 1825723 |
| 2 | 22.757 | 153174 | 0.27 | 1338 |

**Supplementary Fig.77.** HPLC spectra of compound **(*R*,*R*)-3am**

SAMPLE INFORMATION

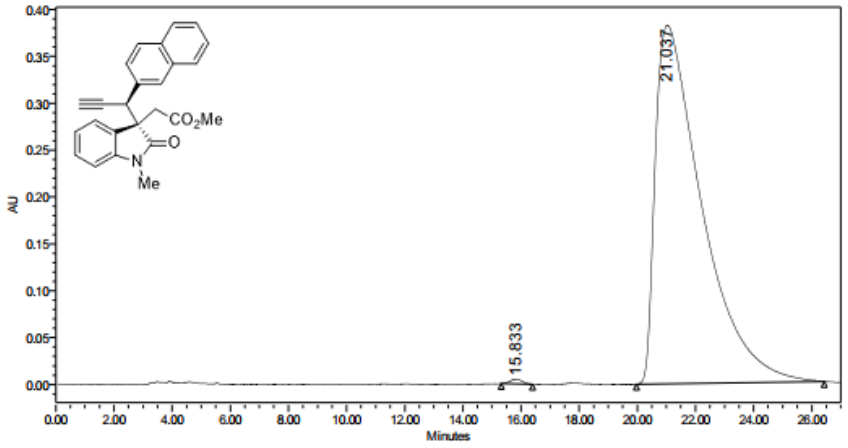
| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyhsgygt |
| Vial: | 9 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 27.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/6/2021 12:59:18 AM CST | | |
| Date Processed: | 3/6/2021 8:54:21 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 15.851 | 4293469 | 50.51 | 142803 |
| 2 | 22.210 | 4206939 | 49.49 | 37815 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-81-2-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyhsgygt |
| Vial: | 11 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 27.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/6/2021 1:54:38 AM CST | | |
| Date Processed: | 3/6/2021 9:00:16 AM CST | | |

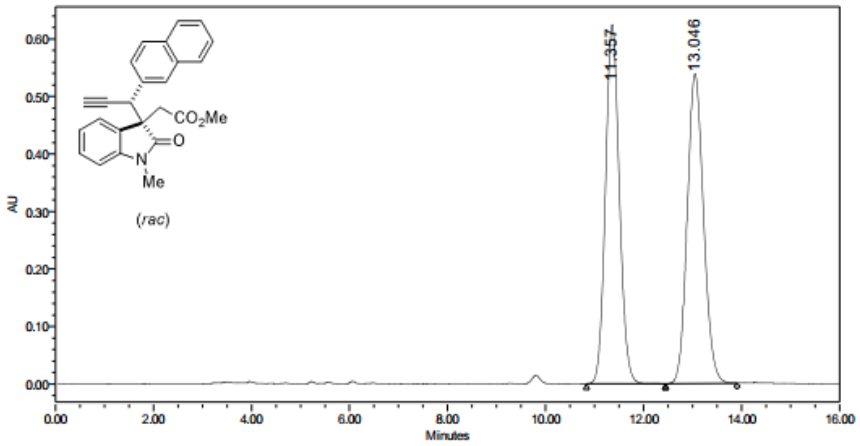



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 15.833 | 149575 | 0.35 | 5216 |
| 2 | 21.037 | 42630567 | 99.65 | 382487 |

**Supplementary Fig. 78.** HPLC spectra of compound ***(S,S)*-3am**

SAMPLE INFORMATION

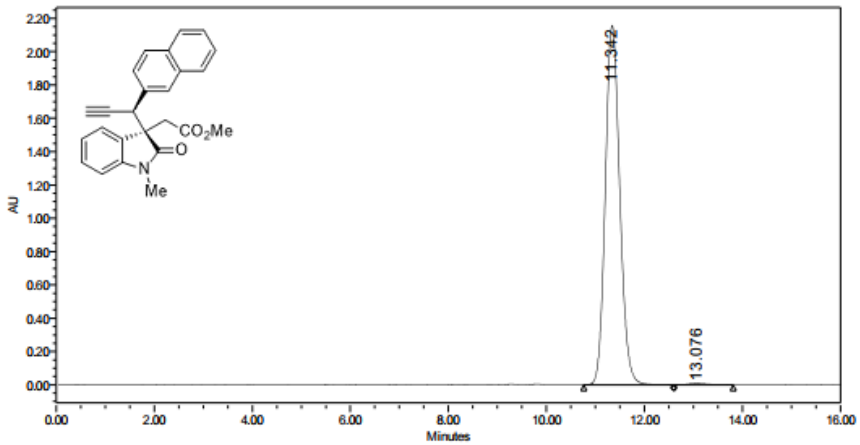
| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh1797 |
| Vial: | 6 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 16.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/6/2021 10:18:15 AM CST | | |
| Date Processed: | 3/6/2021 11:10:53 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.357 | 12358270 | 49.81 | 624155 |
| 2 | 13.046 | 12453815 | 50.19 | 538474 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-7-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh1797asy |
| Vial: | 7 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 16.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/6/2021 11:20:24 AM CST | | |
| Date Processed: | 3/6/2021 11:37:21 AM CST | | |

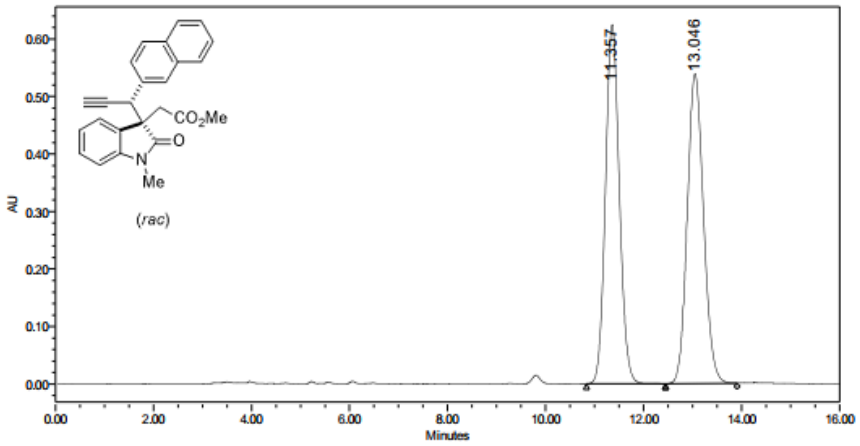



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.342 | 44389796 | 99.54 | 2156068 |
| 2 | 13.076 | 204593 | 0.46 | 7815 |

**Supplementary Fig. 79.** HPLC spectra of compound **(*R*,*S*)-3am**

SAMPLE INFORMATION

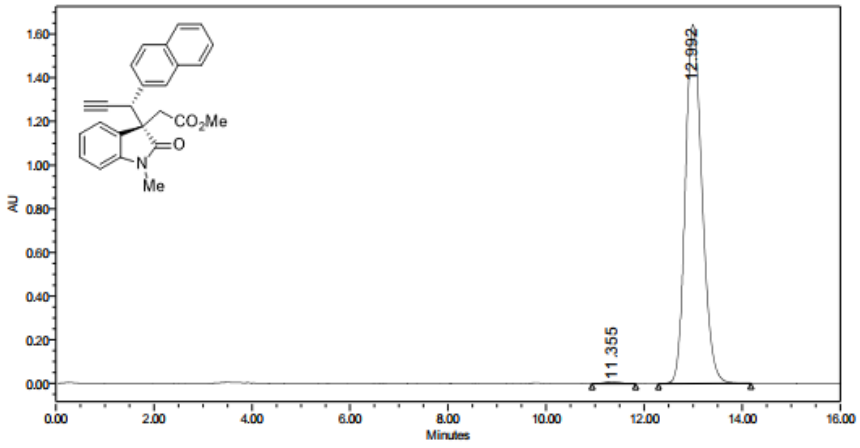
| | | | |
|---|---|---|---|
| Sample Name: | | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh1797 |
| Vial: | 6 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 16.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/6/2021 10:18:15 AM CST | | |
| Date Processed: | 3/6/2021 11:10:53 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.357 | 12358270 | 49.81 | 624155 |
| 2 | 13.046 | 12453815 | 50.19 | 538474 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-81-1-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh1797 |
| Vial: | 8 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm@1 |
| Run Time: | 16.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/6/2021 10:51:34 AM CST | | |
| Date Processed: | 3/6/2021 11:10:41 AM CST | | |

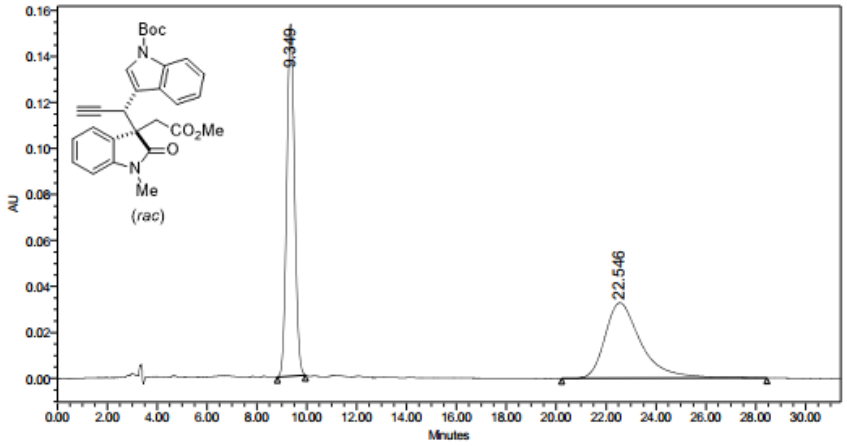



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.355 | 167580 | 0.43 | 8336 |
| 2 | 12.992 | 38868789 | 99.57 | 1644916 |

**Supplementary Fig. 80.** HPLC spectra of compound **(*S*,*R*)-3am**

SAMPLE INFORMATION

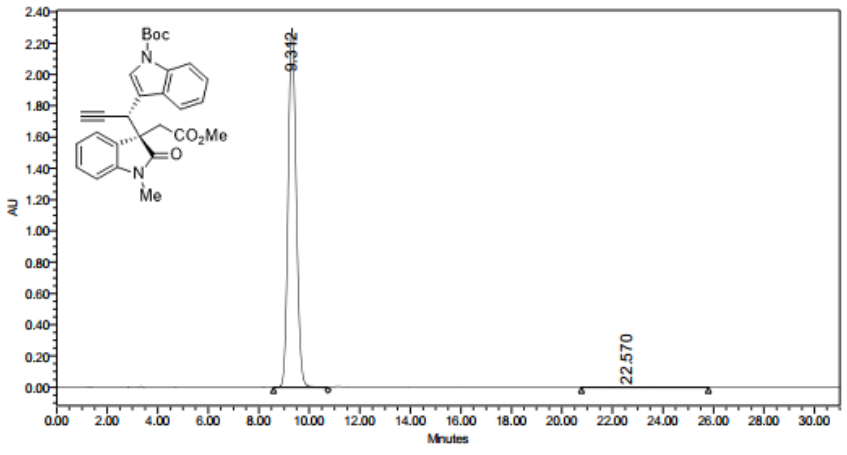
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-8-rac-d-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1788racdown |
| Vial: | 112 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/16/2021 9:35:08 PM CST | | |
| Date Processed: | 1/16/2021 10:07:39 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.349 | 3357364 | 50.65 | 152974 |
| 2 | 22.546 | 3271077 | 49.35 | 32767 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-78-8-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 113 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 31.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 1/16/2021 10:07:49 PM CST | | |
| Date Processed: | 1/16/2021 10:42:50 PM CST | | |

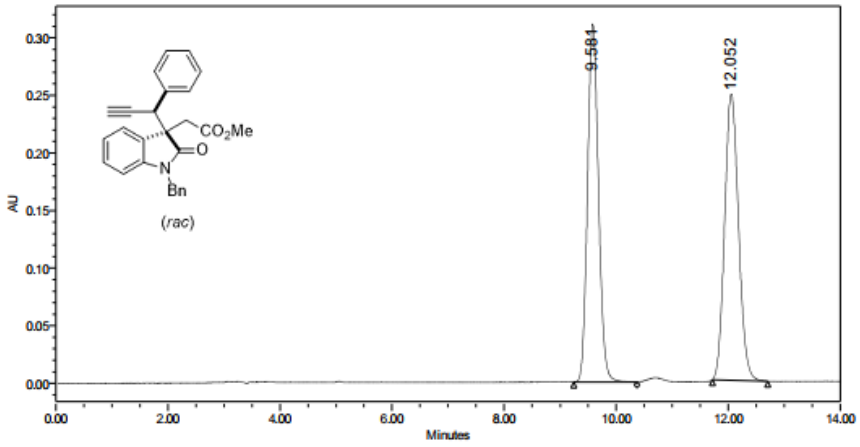



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.312 | 51242671 | 99.54 | 2295437 |
| 2 | 22.570 | 237176 | 0.46 | 2396 |

**Supplementary Fig. 81.** HPLC spectra of compound **(*R*,*R*)-3an**

SAMPLE INFORMATION

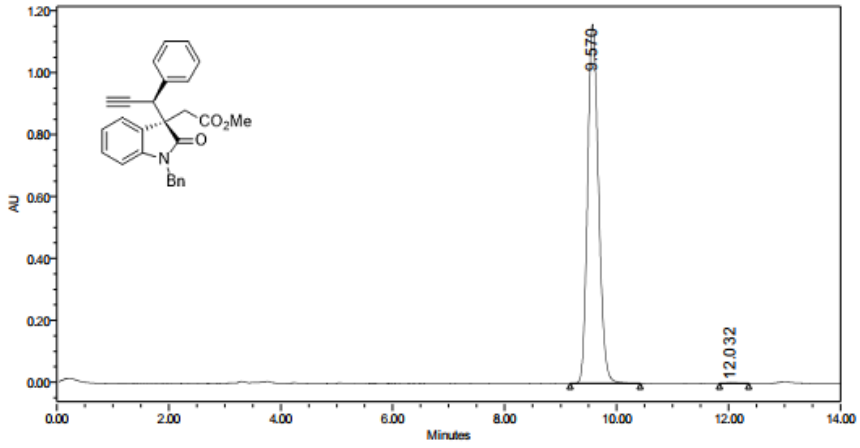
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-167-2-rac-IE-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh11672 |
| Vial: | 61 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 14.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 7/13/2021 5:11:20 PM CST | | |
| Date Processed: | 7/13/2021 7:38:39 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.581 | 4188053 | 49.66 | 310632 |
| 2 | 12.052 | 4245610 | 50.34 | 248490 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-167-2-asy-IE-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh11672 |
| Vial: | 62 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 14.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 7/13/2021 5:26:15 PM CST | | |
| Date Processed: | 7/13/2021 7:39:57 PM CST | | |

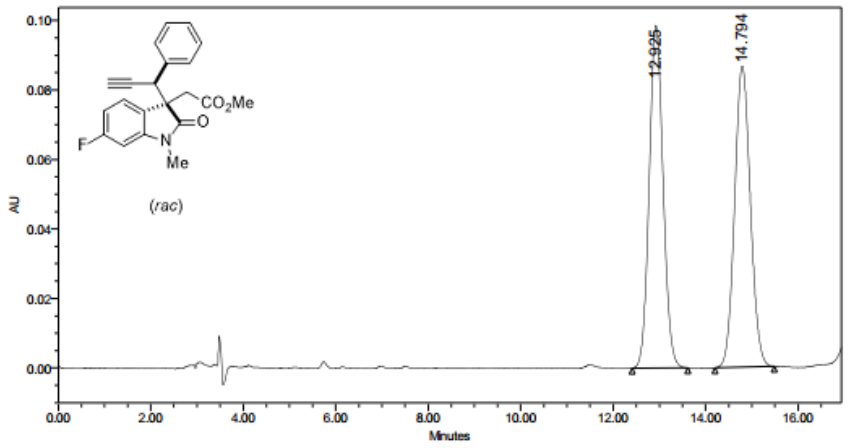



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.570 | 15667461 | 99.91 | 1159870 |
| 2 | 12.032 | 14575 | 0.09 | 942 |

**Supplementary Fig. 82.** HPLC spectra of compound **(*R*,*S*)-3ca**

SAMPLE INFORMATION

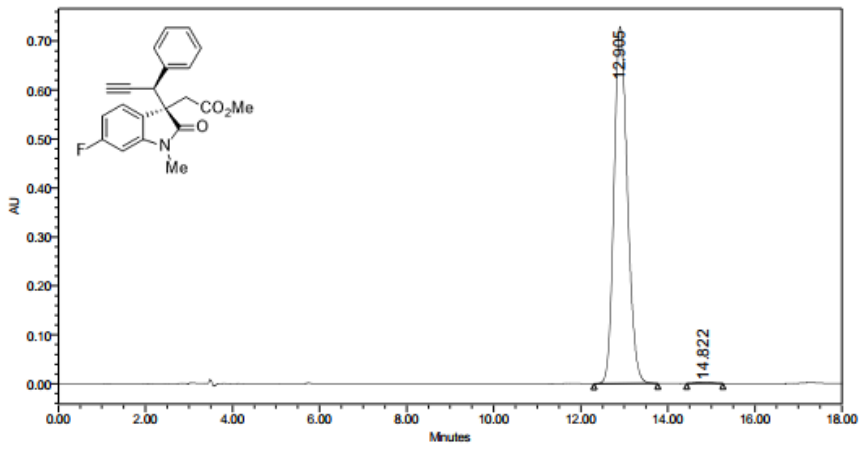
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-11-rac-u-IG-10%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17911 |
| Vial: | 1 | Acq. Method Set: | 10% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 30.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/4/2021 5:45:05 PM CST | | |
| Date Processed: | 3/4/2021 7:19:15 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 12.925 | 2070808 | 50.19 | 98570 |
| 2 | 14.794 | 2054934 | 49.81 | 86600 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-11-asy-IG-10%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17911asy |
| Vial: | 2 | Acq. Method Set: | 10% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 18.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/4/2021 6:14:47 PM CST | | |
| Date Processed: | 3/4/2021 7:19:00 PM CST | | |

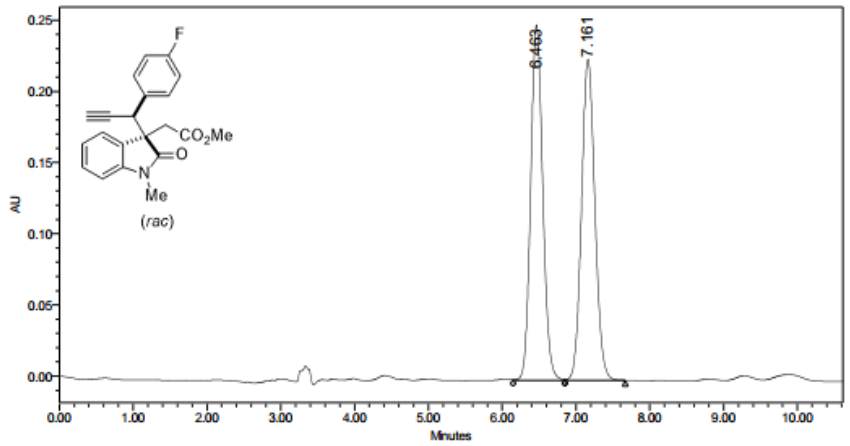



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 12.905 | 15538888 | 99.57 | 729031 |
| 2 | 14.822 | 67286 | 0.43 | 3007 |

**Supplementary Fig. 83.** HPLC spectra of compound **(*R*,*S*)-3ka**

SAMPLE INFORMATION

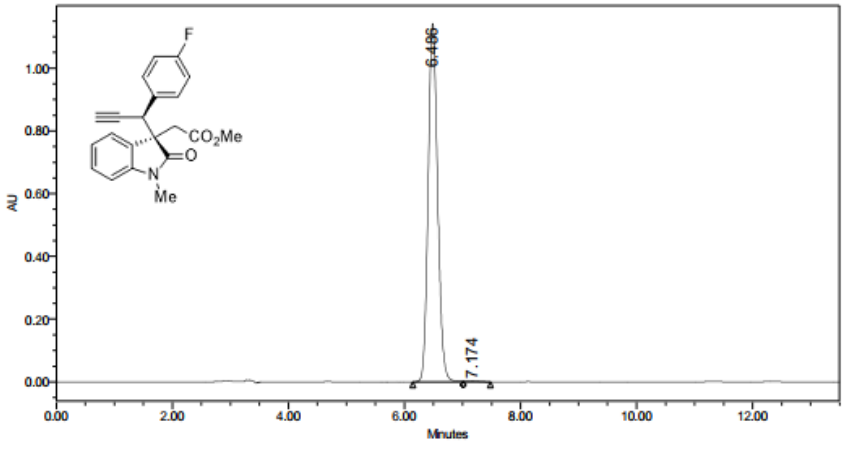
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-5-rac-u-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 49 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 30.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 2/4/2021 12:54:31 PM CST | | |
| Date Processed: | 2/4/2021 1:05:26 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 6.463 | 2844874 | 50.07 | 249568 |
| 2 | 7.161 | 2836586 | 49.93 | 225363 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-5-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 50 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 30.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 2/4/2021 11:40:57 AM CST | | |
| Date Processed: | 2/4/2021 1:01:56 PM CST | | |

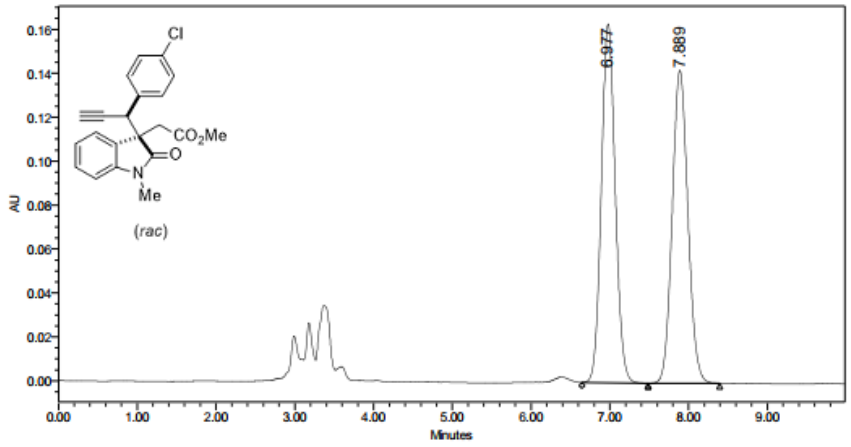



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 6.486 | 12936766 | 99.71 | 1141676 |
| 2 | 7.174 | 37169 | 0.29 | 2530 |

**Supplementary Fig. 84.** HPLC spectra of compound **(*R*,*S*)-3ab**

SAMPLE INFORMATION

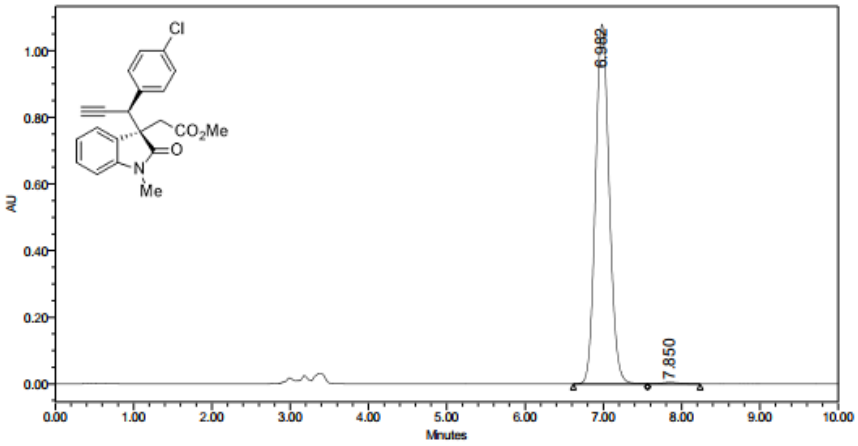
| | | | |
|---|---|---|---|
| Sample Name: | LS-2-4-1-rac-up-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | LS_2_4 |
| Vial: | 7 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 3/14/2021 9:17:59 PM CST | | |
| Date Processed: | 5/7/2021 5:52:53 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 6.977 | 1997021 | 50.28 | 163296 |
| 2 | 7.889 | 1974968 | 49.72 | 142436 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | LS-2-4-1-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | LS_2_4 |
| Vial: | 8 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 10.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 3/14/2021 9:29:07 PM CST | | |
| Date Processed: | 5/7/2021 5:52:42 PM CST | | |

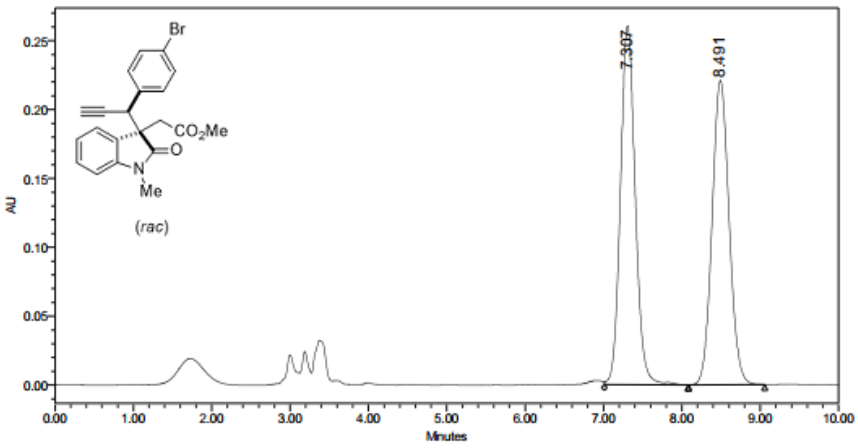



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 6.982 | 13264165 | 99.41 | 1079165 |
| 2 | 7.850 | 78258 | 0.59 | 4800 |

**Supplementary Fig. 85.** HPLC spectra of compound **(*R*,*S*)-3ac**

SAMPLE INFORMATION

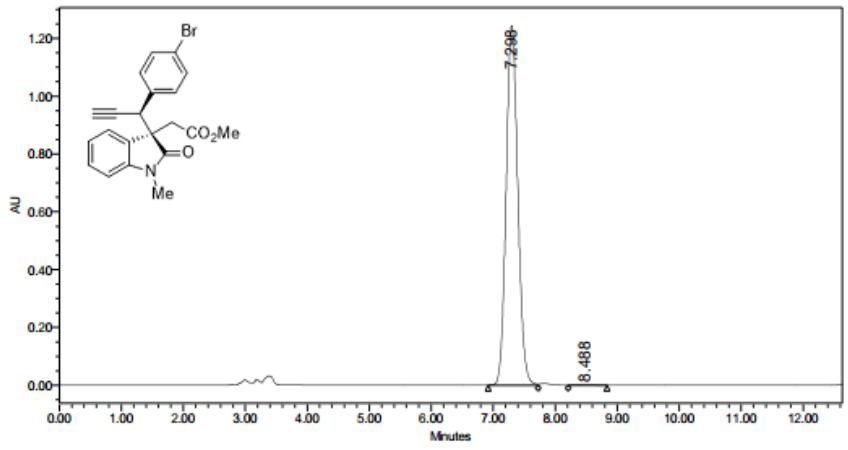
| | | | |
|---|---|---|---|
| Sample Name: | LS-2-4-2-rac-up-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | LS24 |
| Vial: | 9 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 10.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 3/14/2021 10:15:08 PM CST | | |
| Date Processed: | 5/7/2021 5:52:08 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 7.307 | 3410831 | 50.49 | 260433 |
| 2 | 8.491 | 3344450 | 49.51 | 220935 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | LS-2-4-2-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | LS_2_4 |
| Vial: | 10 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 3/14/2021 10:00:32 PM CST | | |
| Date Processed: | 5/7/2021 5:51:54 PM CST | | |

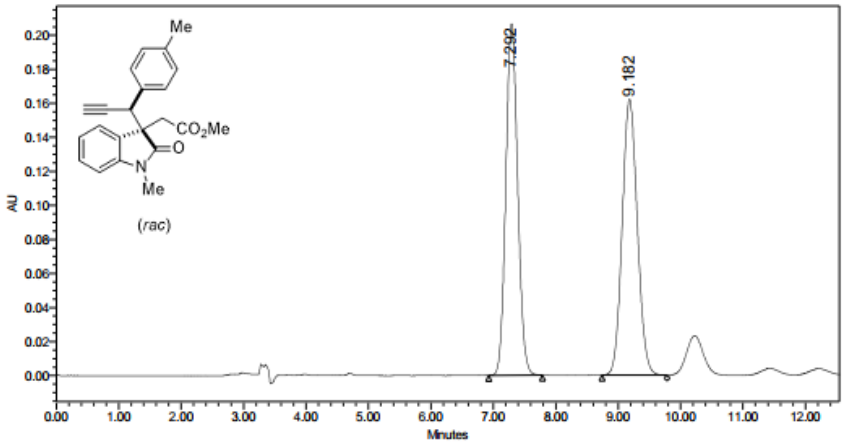



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 7.298 | 16148747 | 99.76 | 1243849 |
| 2 | 8.488 | 38956 | 0.24 | 2485 |

**Supplementary Fig. 86.** HPLC spectra of compound **(*R*,*S*)-3ad**

SAMPLE INFORMATION

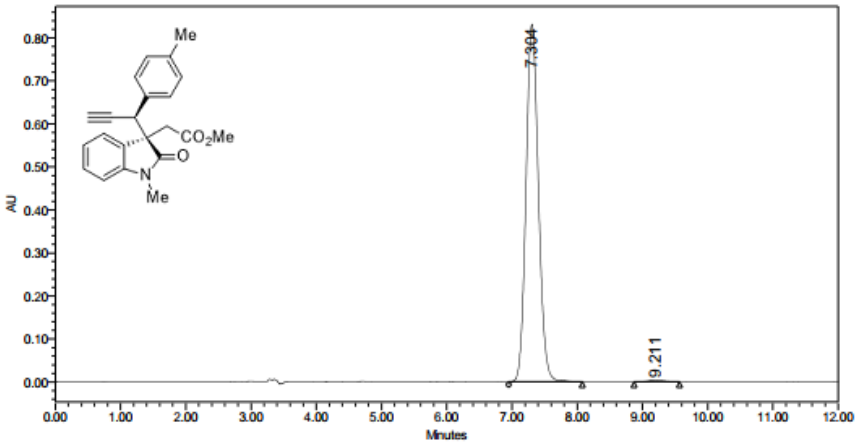
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-12-rac-up | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17912racup |
| Vial: | 1 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/4/2021 9:56:50 AM CST | | |
| Date Processed: | 3/4/2021 10:34:53 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 7.292 | 2707073 | 49.92 | 206422 |
| 2 | 9.182 | 2715675 | 50.08 | 162068 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-12-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh17912asy |
| Vial: | 2 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 12.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 3/4/2021 10:16:43 AM CST | | |
| Date Processed: | 3/4/2021 10:34:27 AM CST | | |

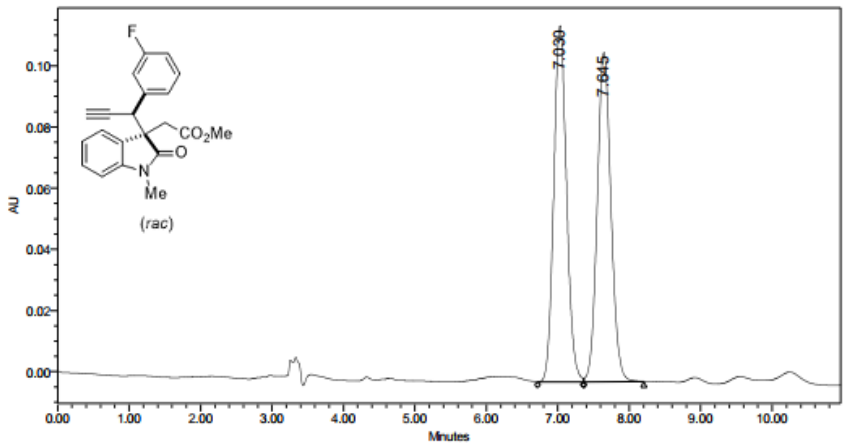



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 7.304 | 11015778 | 99.47 | 830903 |
| 2 | 9.211 | 58365 | 0.53 | 3522 |

**Supplementary Fig. 87.** HPLC spectra of compound **(*R*,*S*)-3ae**

SAMPLE INFORMATION

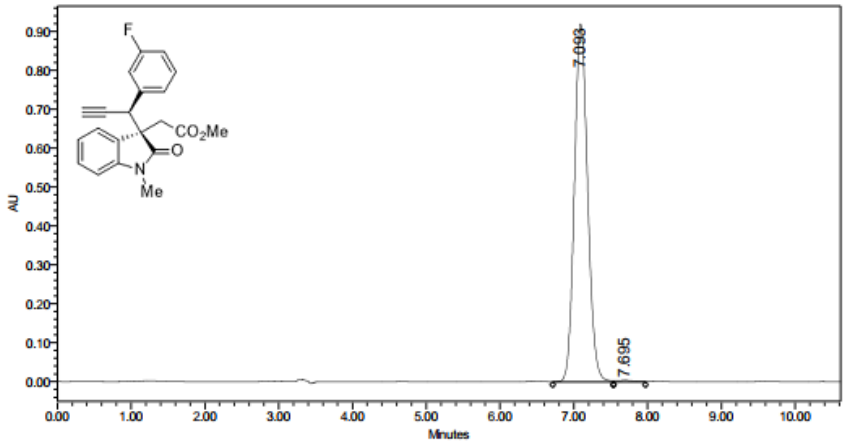
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-6-rac-u-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 49 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 30.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 2/4/2021 10:41:57 AM CST | | |
| Date Processed: | 2/4/2021 11:03:11 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 7.030 | 1443398 | 49.98 | 116353 |
| 2 | 7.645 | 1444832 | 50.02 | 107652 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-79-6-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 50 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 30.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 2/4/2021 10:53:49 AM CST | | |
| Date Processed: | 2/4/2021 11:05:05 AM CST | | |

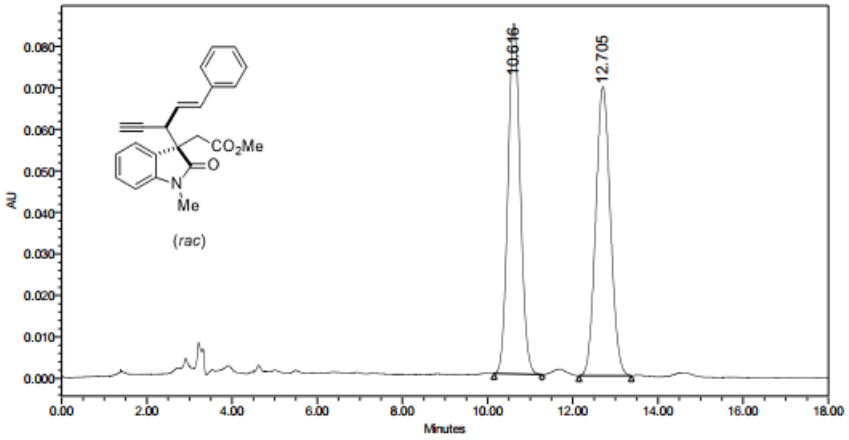



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 7.093 | 11429689 | 99.50 | 919256 |
| 2 | 7.695 | 57547 | 0.50 | 3488 |

**Supplementary Fig. 88.** HPLC spectra of compound **(*R*,*S*)-3ag**

SAMPLE INFORMATION

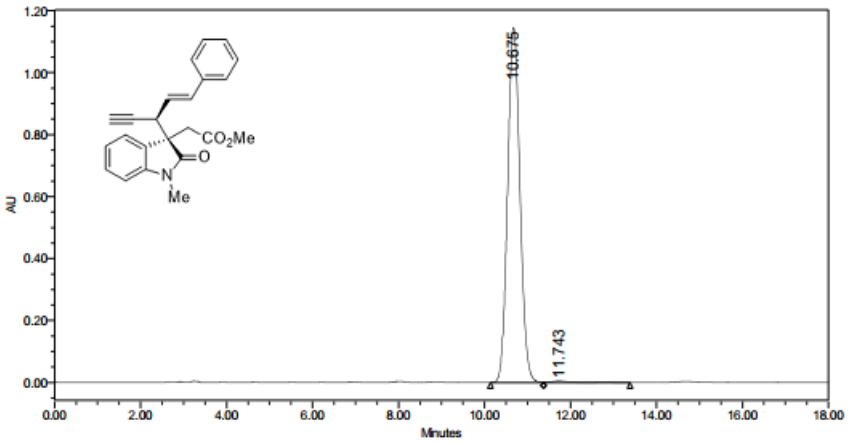
| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-92-2-rac-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | 20211203 |
| Vial: | 18 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 18.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/3/2021 9:23:30 PM CST | | |
| Date Processed: | 12/3/2021 9:46:51 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.616 | 1680172 | 50.19 | 84449 |
| 2 | 12.705 | 1667466 | 49.81 | 69606 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-87-2-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | 20211203 |
| Vial: | 19 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 18.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/3/2021 4:57:16 PM CST | | |
| Date Processed: | 12/3/2021 9:38:45 PM CST | | |

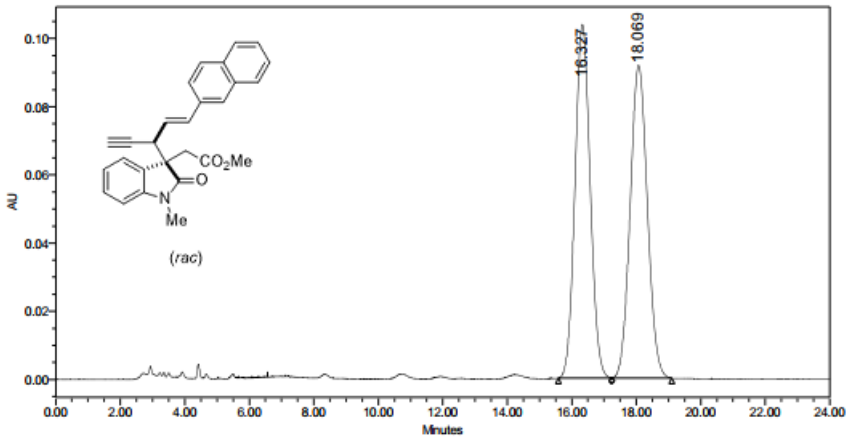



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 10.675 | 22765044 | 99.45 | 1145284 |
| 2 | 11.743 | 125930 | 0.55 | 4446 |

**Supplementary Fig. 89.** HPLC spectra of compound **(*R*,*R*)-3ao**

SAMPLE INFORMATION

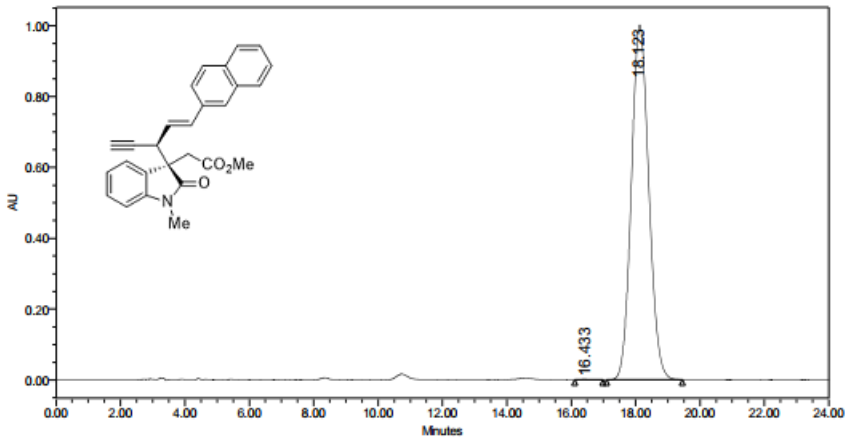
| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-90-2-rac-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh20211127 |
| Vial: | 11 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 24.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 11/27/2021 8:52:32 PM CST | | |
| Date Processed: | 12/3/2021 4:06:04 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 16.327 | 3407568 | 50.01 | 103664 |
| 2 | 18.069 | 3406564 | 49.99 | 91701 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-90-2-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh20211127 |
| Vial: | 12 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 24.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 11/27/2021 9:17:10 PM CST | | |
| Date Processed: | 12/3/2021 4:06:17 PM CST | | |

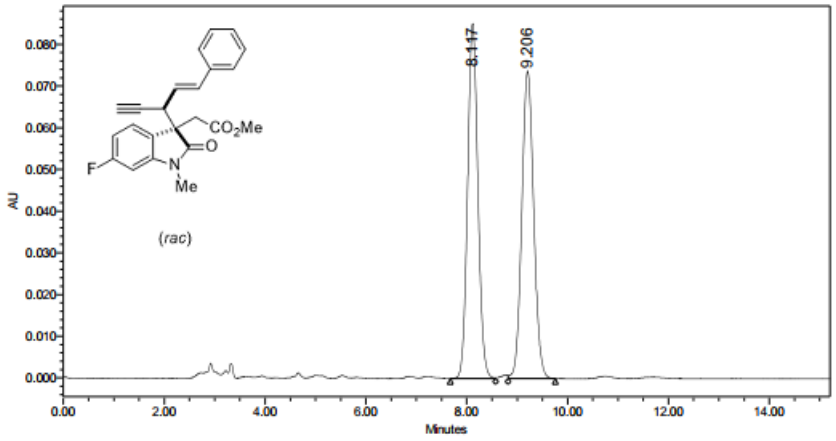



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 16.433 | 19907 | 0.05 | 767 |
| 2 | 18.123 | 37847529 | 99.95 | 1001593 |

**Supplementary Fig. 90.** HPLC spectra of compound **(*R*,*R*)-3ap**

SAMPLE INFORMATION

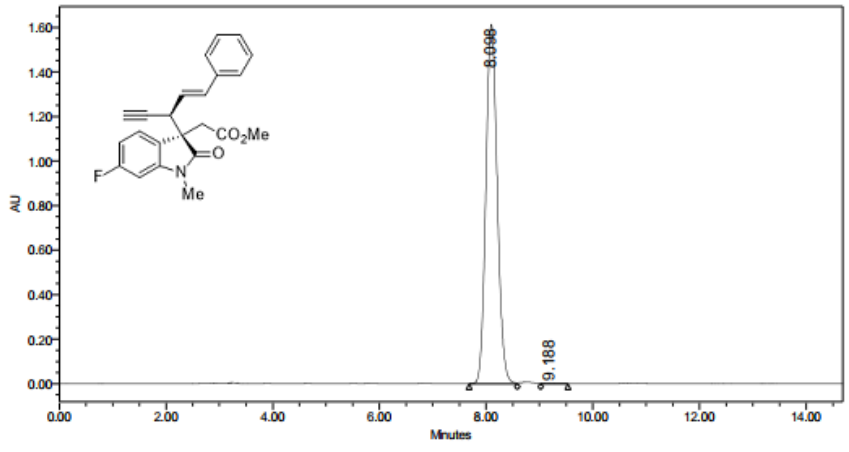
| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-91-1-rac-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 14 | Acq. Method Set: | 30% 1ml |
| Injection #: | 2 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/3/2021 3:22:42 PM CST | | |
| Date Processed: | 12/3/2021 3:56:41 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.117 | 1206081 | 50.03 | 85093 |
| 2 | 9.206 | 1204552 | 49.97 | 73734 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-91-1-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 15 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/3/2021 3:38:49 PM CST | | |
| Date Processed: | 12/3/2021 3:55:47 PM CST | | |

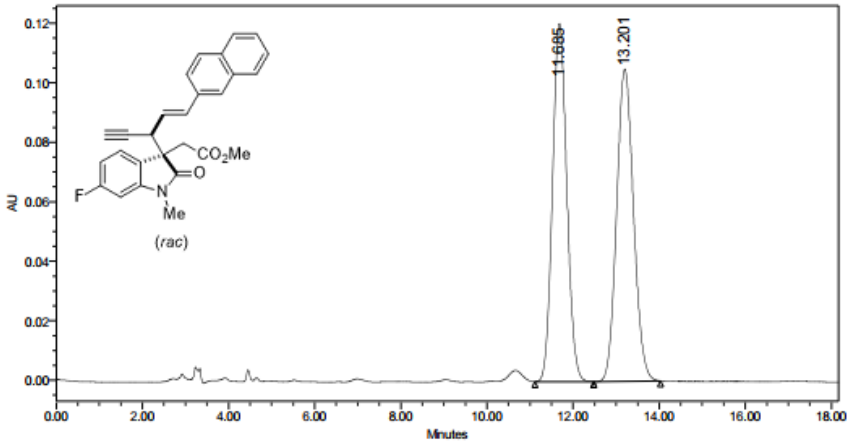



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 8.098 | 23883635 | 99.84 | 1612713 |
| 2 | 9.188 | 39274 | 0.16 | 2371 |

**Supplementary Fig. 91.** HPLC spectra of compound **(*R*,*R*)-3ko**

SAMPLE INFORMATION

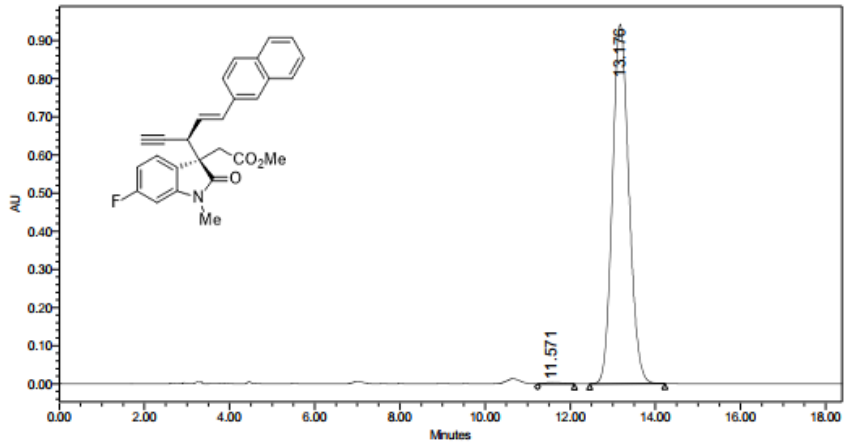
| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-91-2-rac-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 16 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/3/2021 3:55:08 PM CST | | |
| Date Processed: | 12/3/2021 9:35:22 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.685 | 2759531 | 49.22 | 120278 |
| 2 | 13.201 | 2846654 | 50.78 | 104901 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-91-2-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 17 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/3/2021 4:14:07 PM CST | | |
| Date Processed: | 12/3/2021 9:35:34 PM CST | | |

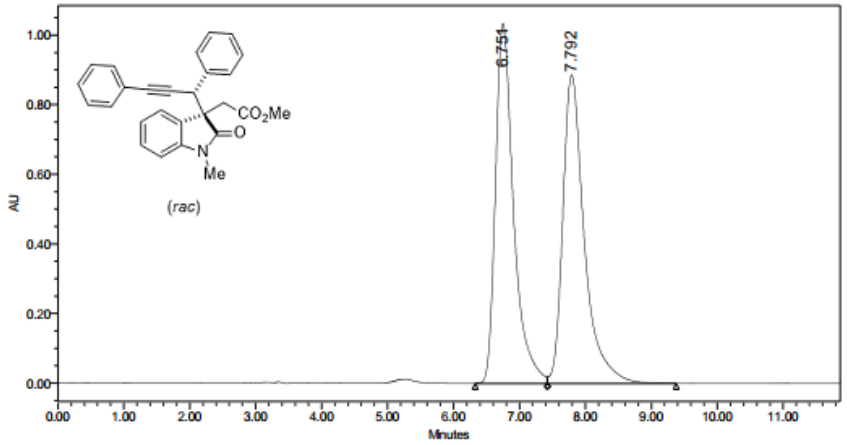



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 11.571 | 71378 | 0.28 | 2958 |
| 2 | 13.176 | 25323224 | 99.72 | 942045 |

**Supplementary Fig. 92.** HPLC spectra of compound **(*R*,*R*)-3kp**

SAMPLE INFORMATION

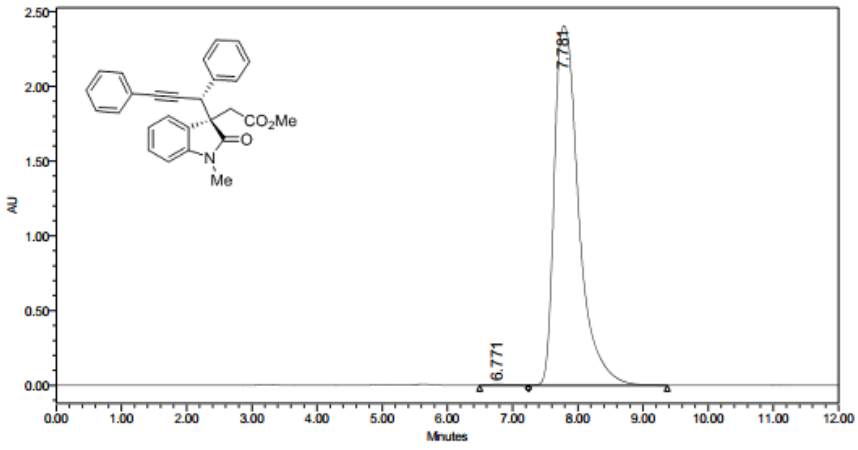
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-158-rac-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh158rac |
| Vial: | 22 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 50.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/25/2021 4:53:09 PM CST | | |
| Date Processed: | 6/27/2021 3:47:20 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 6.751 | 19650870 | 49.55 | 1033599 |
| 2 | 7.792 | 20005071 | 50.45 | 885851 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-158-asy-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | 111 |
| Vial: | 23 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 12.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/25/2021 5:06:46 PM CST | | |
| Date Processed: | 6/27/2021 3:47:35 PM CST | | |

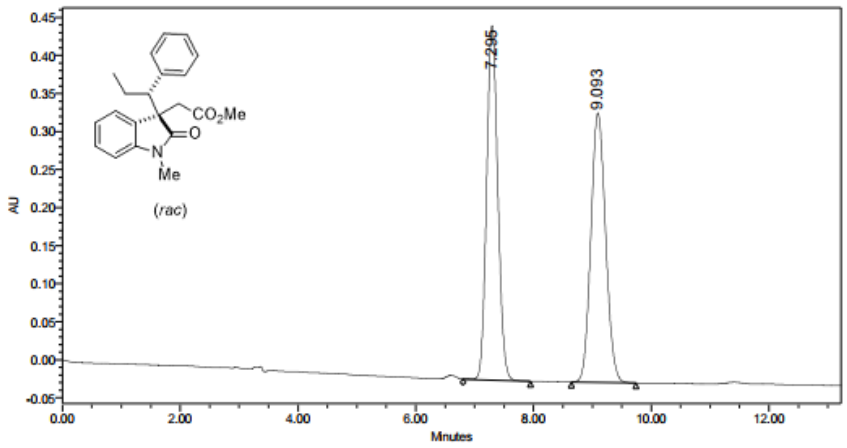



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 6.771 | 123337 | 0.20 | 6518 |
| 2 | 7.781 | 62173725 | 99.80 | 2404716 |

**Supplementary Fig. 93.** HPLC spectra of compound **5**

SAMPLE INFORMATION

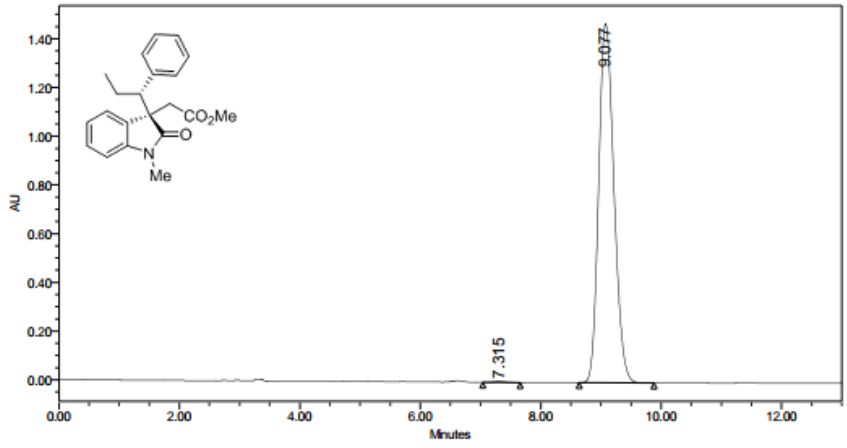
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-159-rac-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1159rac |
| Vial: | 25 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm@1 |
| Run Time: | 30.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/27/2021 3:16:43 PM CST | | |
| Date Processed: | 6/27/2021 3:54:33 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 7.295 | 6158366 | 50.09 | 465846 |
| 2 | 9.093 | 6136651 | 49.91 | 354046 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-159-asy-IG-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1159asy |
| Vial: | 26 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 13.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/27/2021 3:31:27 PM CST | | |
| Date Processed: | 6/27/2021 3:54:56 PM CST | | |

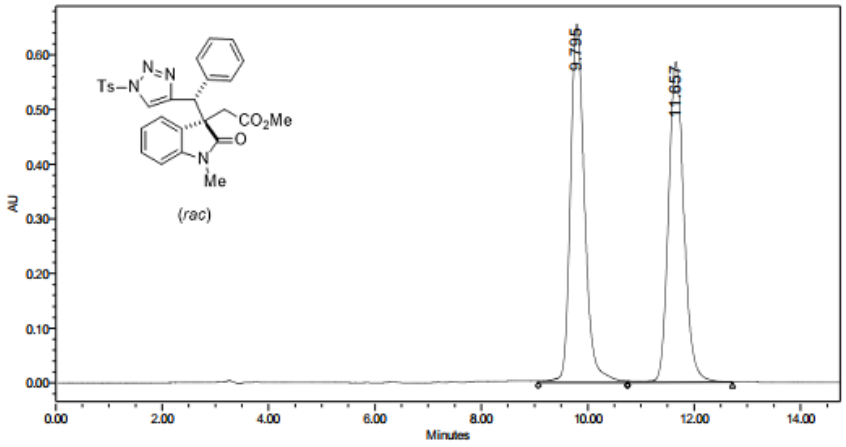



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 7.315 | 49860 | 0.19 | 3788 |
| 2 | 9.077 | 26054486 | 99.81 | 1473643 |

**Supplementary Fig. 94.** HPLC spectra of compound **6**

SAMPLE INFORMATION

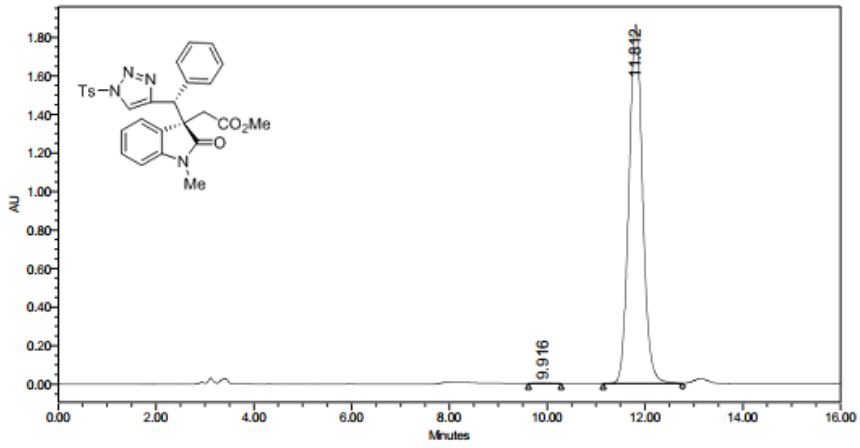
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-157-rac-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name | wyh1157rac |
| Vial: | 21 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 25.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 7/13/2021 9:48:40 PM CST | | |
| Date Processed: | 7/14/2021 9:33:13 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.795 | 12140674 | 50.79 | 655366 |
| 2 | 11.657 | 11764158 | 49.21 | 586102 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-157-asy-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh157asy |
| Vial: | 19 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 230.0nm |
| Run Time: | 16.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 230.0 nm (2998 |
| Date Acquired: | 6/25/2021 10:18:48 PM CST | | |
| Date Processed: | 7/6/2021 9:50:16 AM CST | | |

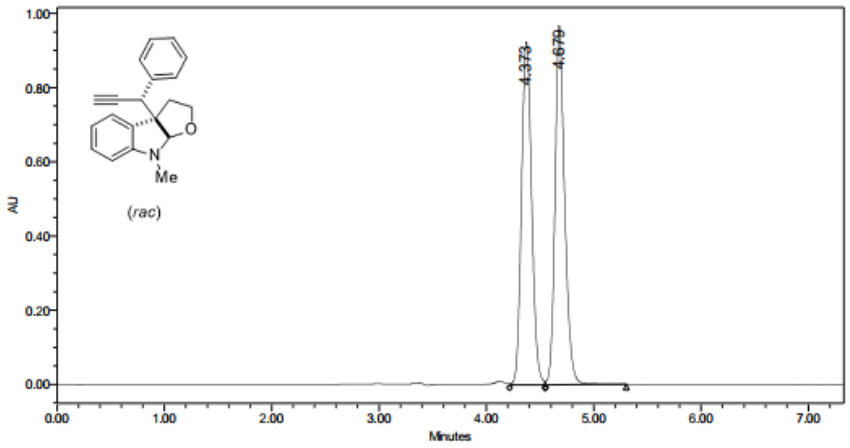



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 9.916 | 39194 | 0.11 | 2247 |
| 2 | 11.812 | 36035727 | 99.89 | 1861785 |

**Supplementary Fig. 95.** HPLC spectra of compound **7**

SAMPLE INFORMATION

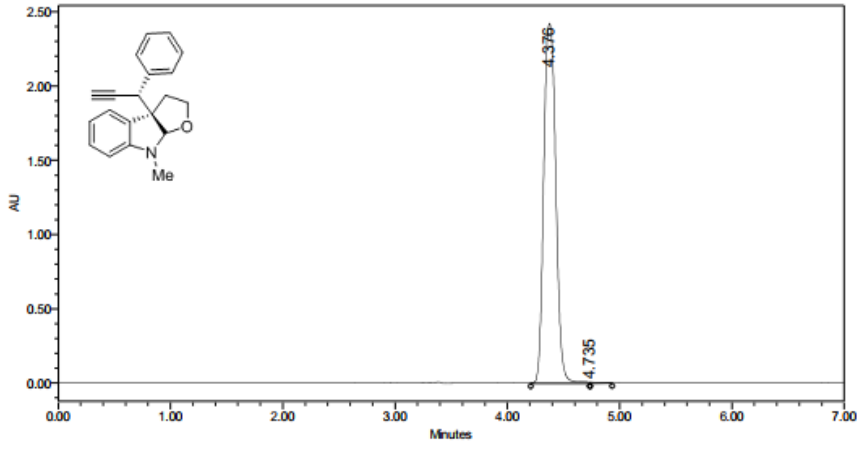
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-160-rac-IG-20%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1160rac |
| Vial: | 31 | Acq. Method Set: | 20% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/30/2021 7:32:35 PM CST | | |
| Date Processed: | 7/1/2021 11:25:32 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 4.373 | 6065317 | 50.01 | 924829 |
| 2 | 4.679 | 6063342 | 49.99 | 968126 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-160-asy-IG-20%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | 111 |
| Vial: | 32 | Acq. Method Set: | 20% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 7.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/30/2021 7:42:11 PM CST | | |
| Date Processed: | 7/1/2021 11:25:53 PM CST | | |

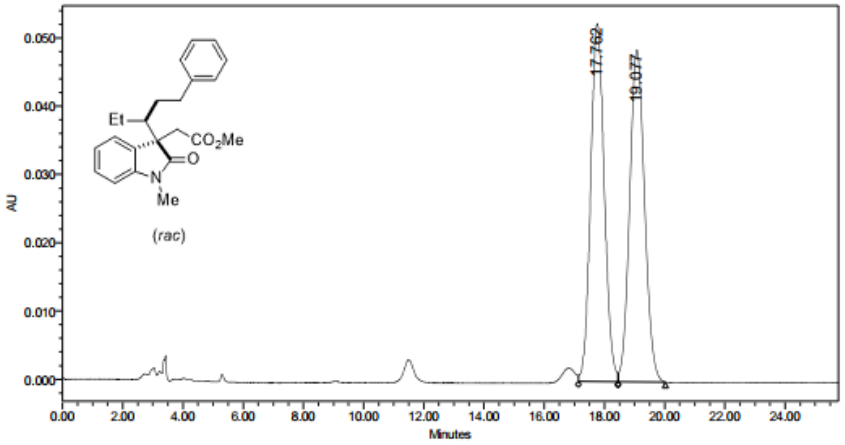



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 4.376 | 18114156 | 99.83 | 2421172 |
| 2 | 4.735 | 31604 | 0.17 | 6167 |

**Supplementary Fig. 96.** HPLC spectra of compound **8**

SAMPLE INFORMATION

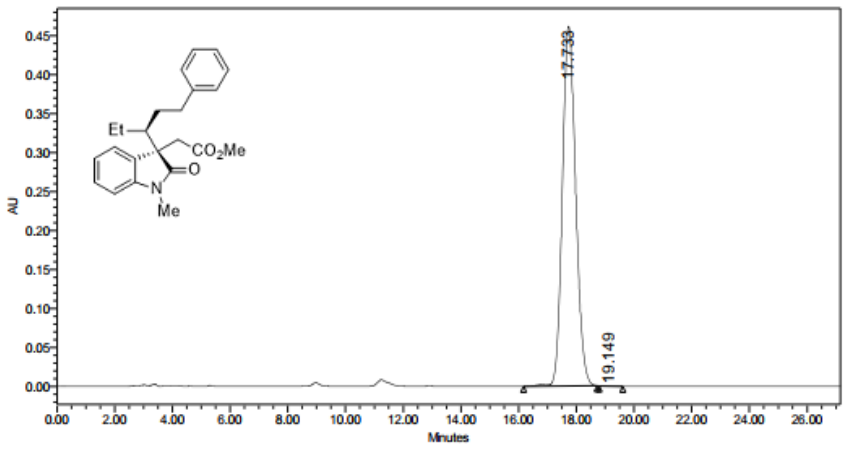
| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-97-rac-IG-15%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 17 | Acq. Method Set: | 15% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/9/2021 3:36:01 PM CST | | |
| Date Processed: | 12/9/2021 4:30:39 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 17.762 | 1656401 | 49.90 | 52435 |
| 2 | 19.077 | 1663372 | 50.10 | 48632 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-2-97-asy-IG-15%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 18 | Acq. Method Set: | 15% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 12/9/2021 4:02:37 PM CST | | |
| Date Processed: | 12/9/2021 4:32:50 PM CST | | |

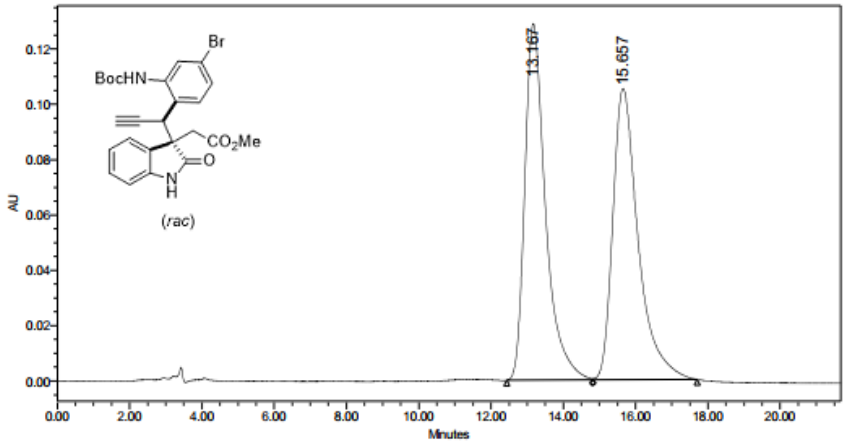



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 17.733 | 14606297 | 99.98 | 461161 |
| 2 | 19.149 | 3149 | 0.02 | 150 |

**Supplementary Fig. 97.** HPLC spectra of compound **9**

SAMPLE INFORMATION

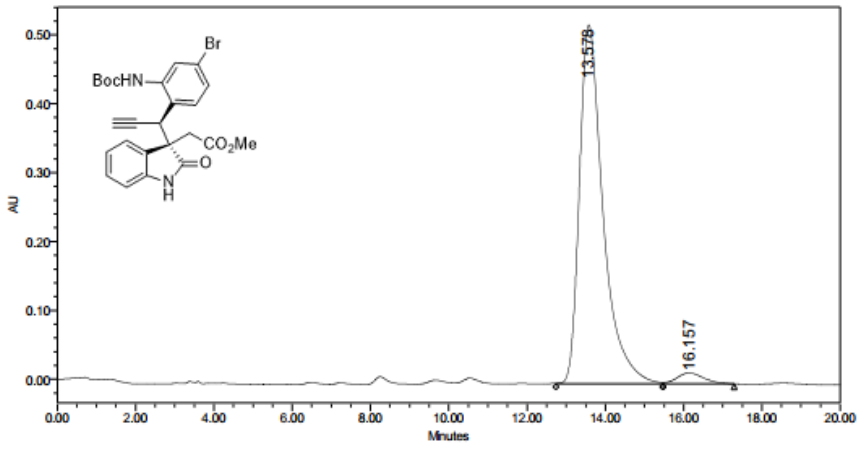
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-139-4-rac-d-IA-15%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 20 | Acq. Method Set: | 15% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/4/2021 10:54:29 AM CST | | |
| Date Processed: | 7/6/2021 9:36:51 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 13.167 | 5158517 | 50.20 | 128896 |
| 2 | 15.657 | 5117450 | 49.80 | 105353 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-big-IA-15%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 27 | Acq. Method Set: | 15% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 20.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/17/2021 7:22:08 PM CST | | |
| Date Processed: | 7/6/2021 9:36:30 AM CST | | |

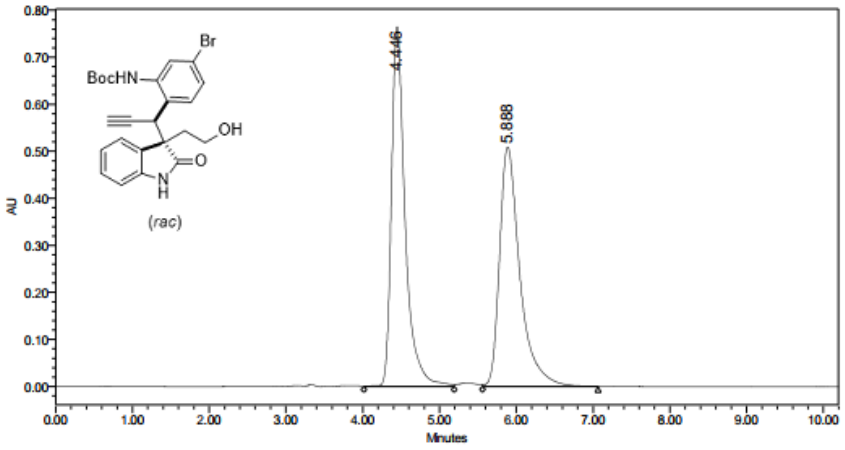



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 13.578 | 21938551 | 96.68 | 520679 |
| 2 | 16.157 | 753318 | 3.32 | 15868 |

**Supplementary Fig. 98.** HPLC spectra of compound **3nq**

SAMPLE INFORMATION

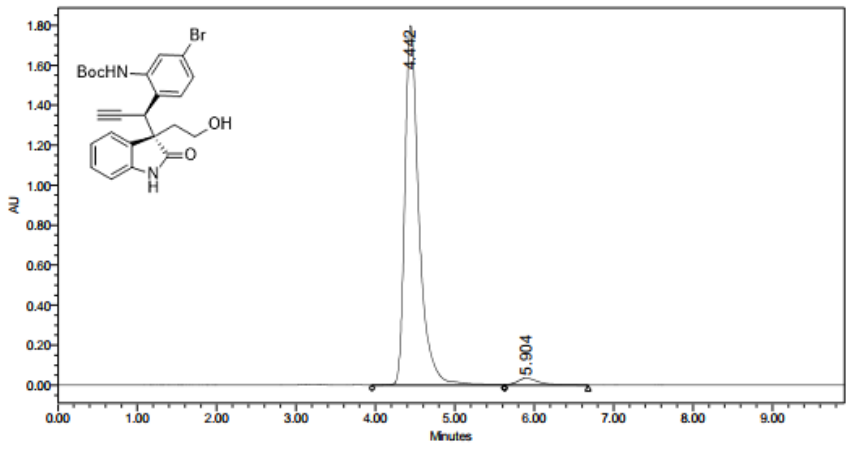
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-OH-rac-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 32 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/23/2021 2:22:06 PM CST | | |
| Date Processed: | 7/6/2021 9:23:24 AM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 4.446 | 9489244 | 50.42 | 764717 |
| 2 | 5.888 | 9331807 | 49.58 | 509137 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-OH-asy-IA-30%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | |
| Vial: | 33 | Acq. Method Set: | 30% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 254.0nm |
| Run Time: | 60.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 254.0 nm (2998 |
| Date Acquired: | 6/23/2021 2:33:11 PM CST | | |
| Date Processed: | 7/6/2021 9:23:12 AM CST | | |

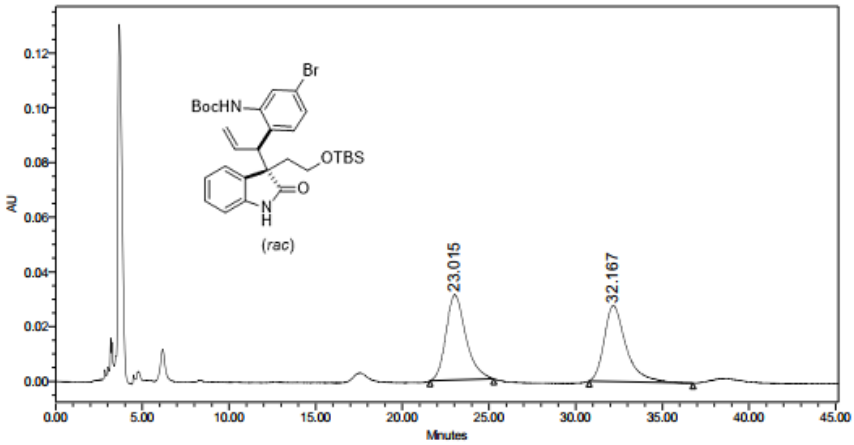



| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 4.442 | 22415861 | 97.23 | 1797071 |
| 2 | 5.904 | 638986 | 2.77 | 34421 |

**Supplementary Fig. 99.** HPLC spectra of compound **10**

SAMPLE INFORMATION

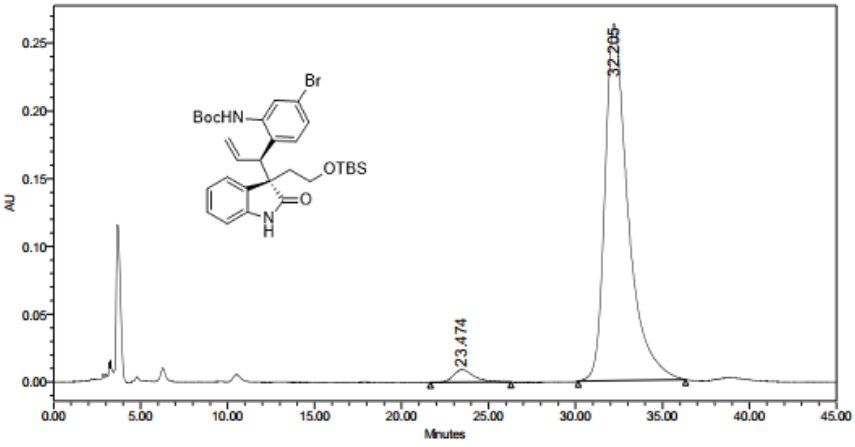
| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-tp-rac-IA-2%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1tprac |
| Vial: | 5 | Acq. Method Set: | 2% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 220.0nm |
| Run Time: | 80.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 220.0 nm (2998 |
| Date Acquired: | 6/26/2021 2:53:18 PM CST | | |
| Date Processed: | 7/14/2021 2:48:50 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 23.015 | 2490961 | 50.61 | 31199 |
| 2 | 32.167 | 2431204 | 49.39 | 27726 |

SAMPLE INFORMATION

| | | | |
|---|---|---|---|
| Sample Name: | wyh-1-tp-asy-IA-2%-1ml/min | Acquired By: | System |
| Sample Type: | Unknown | Sample Set Name: | wyh1tpasy |
| Vial: | 6 | Acq. Method Set: | 2% 1ml |
| Injection #: | 1 | Processing Method: | 1 |
| Injection Volume: | 10.00 ul | Channel Name: | 220.0nm |
| Run Time: | 45.0 Minutes | Proc. Chnl. Descr.: | 2998 PDA 220.0 nm (2998 |
| Date Acquired: | 6/26/2021 3:45:24 PM CST | | |
| Date Processed: | 7/14/2021 5:12:01 PM CST | | |




| | RT | Area | % Area | Height |
|---|---|---|---|---|
| 1 | 23.474 | 762704 | 3.04 | 9274 |
| 2 | 32.205 | 24358883 | 96.96 | 263412 |

**Supplementary Fig. 100.** HPLC spectra of compound **12**

## 4. Supplementary References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