Facile Synthesis of Enantioenriched C^{γ}-Tetrasubstituted α-Amino Acid Derivatives via an Asymmetric Nucleophilic Addition/Protonation Cascade

Shu-Wen Duan, Jing An, Jia-Rong Chen* and Wen-Jing Xiao*

Contents

1. General Information

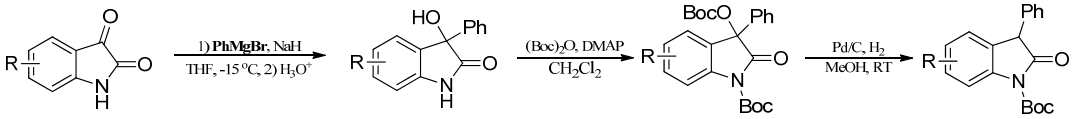
Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Flash column chromatography was performed using 200-300 mesh silica gel. ^{1}H NMR spectra were recorded on Varian Mercury 400/600 (400/600 MHz) spectrophotometers. Chemical shifts (δ) are reported in ppm from the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR spectra were recorded on Varian Mercury 400/600 (100/150 MHz) with complete proton decoupling spectrophotometers ($CDCl_3$: 77.0 ppm). Mass spectra were measured on a Finnigan Trace MS spectrometer (EI) or API 2000 LC/MS/MS (ESI-MS). Enantiomeric ratios were determined by chiral HPLC on Agilent 1100 series with chiral columns (chiralpak AS-H column, chiralpak AD-H column or chiralcel OD-H column) with hexane and *i*-PrOH as solvents. Optical rotations were measured with JASCO P-1020 polarimeter.

2. Preparation and Spectral Data of Substrates

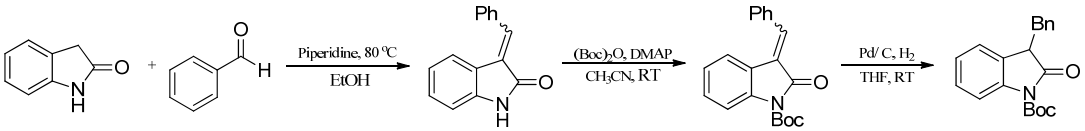
2.1 Preparation of Michael donors.

3-Substituted oxindoles **1a**, **1b** were prepared by following the procedure Route **1** in reference[1a, b]. 3-Benzyl oxindole **1l** was prepared by Route **2**[1a].

*Route **1***



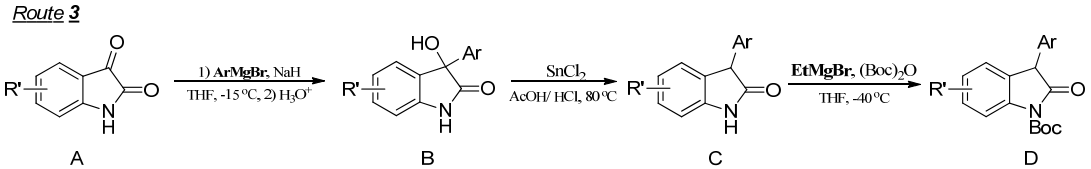
*Route **2***



*Oxindoles **1c-1k** were obtained by following procedure Route **3***

To a solution of oxindole **A** (8.3 mmol) in THF (20 ml), NaH (10.0 mmol) was added at –15 °C and stirred for 30 min. ArMgBr (10.0 mmol) in ether was then added dropwise to the reaction mixture and allowed to warm to rt. A solution of 2N HCl. (30 ml) was added and the mixture was extracted with ether. The organic phase was washed with sat.Na_2CO_3 and brine. The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. Purification by recrystallization (petroleum ether: ethyl acetate) was carried out to give **B** as light orange solid.

*Route **3***

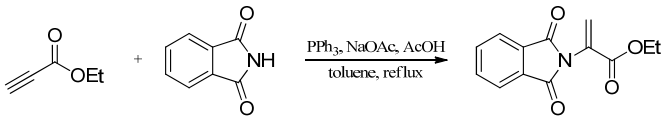


To a solution of **B** (6.6 mmol) in AcOH/HCl (30mL/2 ml), $SnCl_2$ (13.2 mmol) was added at rt. Then the mixture was heated to reflux for 1h. The mixture was diluted with H_2O and extracted with ether. The organic phase was washed with aqueous sodium hydroxide solution and brine. The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. Purification by recrystallization (petroleum ether: ethyl acetate) was carried out to give **C** as white solid.

To a solution of **C** (5.8 mmol) in THF (20 ml), EtMgBr (7.0 mmol) in ether was added dropwise at –40 °C followed by adding $(Boc)_2O$ in one portion. The mixture was stirred at the same temperature for 30 min and warmed to rt. Then the mixture was diluted with ether and quenched with sat.NH_4Cl and extracted with ether. The combined organic layers were washed with H_2O and brine and dried over Na_2SO_4. Purification by flash silica-gel column chromatography (petroleum ether: ethyl acetate) was carried out to give **D** as white solid.

2.2 Preparation of Michael acceptor.

2-phthalimidoacrylate was prepared according to literatures [2].



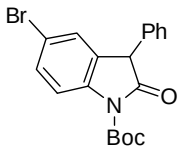
Reference

(1) (a) Ishimaru, T.; Shibata, N.; Nagai, J.; Nakamura, S.; Toru, T.; Kanemasa, S. *J. Am. Chem. Soc.* **2006**, *128*, 16488. (b) Huang, A.; Kodanko, J.; Overman, L. E. *J. Am. Chem. Soc.* **2004**, *126*, 14043.

(2) (a) Trost, B. M.; Dake, G. R. *J. Am. Chem. Soc.* **1997**, *119*, 7595. (b) Leow, D.; Lin, S.-S.; Chittimalla, S. K.; Fu, X.; Tan, C.-H. *Angew. Chem. Int. Ed.* **2008**, *47*, 5641.

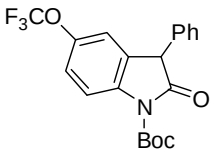
2.3 Spectral Data of Substrates

***tert*-butyl 5-bromo-2-oxo-3-phenylindoline-1-carboxylate (1d)**



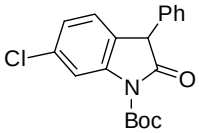
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.84 (d, *J* = 8.7 Hz, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.34 (t, *J* = 8.2 Hz, 4H), 7.17 (d, *J* = 6.7 Hz, 2H), 4.70 (s, 1H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.91, 149.06, 139.40, 135.43, 131.52, 129.23, 128.48, 128.05, 127.93, 117.48, 116.69, 84.70, 52.24, 27.95. MS: m/z = 388.97 (M^+).

***tert*-butyl 2-oxo-3-phenyl-5-(trifluoromethoxy)indoline-1-carboxylate (1e)**



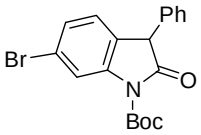
^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.99 (d, *J* = 8.9 Hz, 1H), 7.99 (d, *J* = 8.9 Hz, 1H), 7.64 – 7.30 (m, 4H), 7.42 – 7.29 (m, 4H), 7.30 – 7.08 (m, 5H), 7.21 (dd, *J* = 23.3 Hz, 8.2, 3H), 7.05 (s, 1H), 7.05 (s, 1H), 4.74 (s, 1H), 4.74 (s, 1H), 1.62 (s, 10H), 1.62 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 173.12, 149.13, 145.91, 138.99, 135.29, 128.67, 128.12, 126.56, 121.53, 118.33, 116.20, 84.81, 52.42, 27.96. MS: m/z = 393.02 (M^+).

***tert*-butyl 6-chloro-2-oxo-3-phenylindoline-1-carboxylate (1f)**



^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 8.02 (d, *J* = 1.7 Hz, 1H), 7.33 (m, 3H), 7.20 – 7.13 (m, 3H), 7.08 (d, *J* = 8.0 Hz, 1H), 4.69 (s, 1H), 1.63 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 173.25, 149.01, 141.24, 135.64, 134.27, 128.91, 128.43, 127.97, 125.82, 125.66, 124.59, 115.74, 84.80, 52.01, 27.91. MS: m/z = 343.03 (M^+).

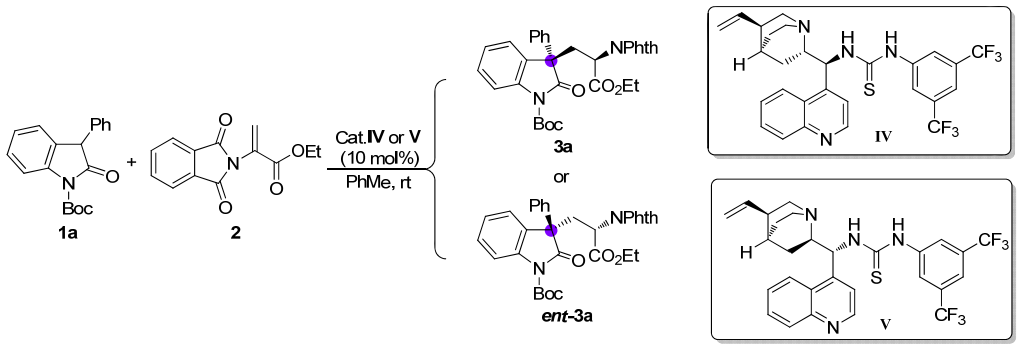
***tert*-butyl 6-bromo-2-oxo-3-phenylindoline-1-carboxylate (1g)**



^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 8.17 (d, *J* = 1.5 Hz, 1H), 7.38 – 7.30 (m, 4H), 7.17 (d, *J* = 6.9 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 4.66 (s, 1H), 1.62 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 173.11, 148.99, 141.38, 135.52, 128.90, 128.42, 127.97, 127.48, 126.19, 122.12, 118.51, 84.81, 52.05, 27.93. MS: m/z = 388.90 (M^+).

3. General Procedure and Spectral Data of Products

3.1 General Procedure

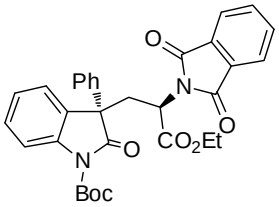


A mixture of *tert*-butyl 2-oxo-3-phenylindoline-1-carboxylate **1a** (0.24 mmol, 74.2 mg), **2** (0.2 mmol, 49.0 mg) and catalyst **IV** (0.02 mmol, 11.3 mg) in toluene (1 mL) was stirred at room temperature for 10

h. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 10:1~8:1) to give the desired product **3a** as a white solid.

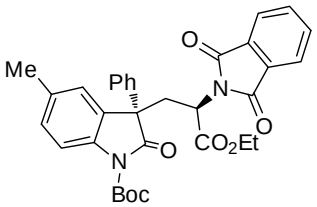
3.2 Spectral Data of Products

***tert*-butyl 3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-2-oxo-3-phenylindoline-1 carboxylate (3a)**



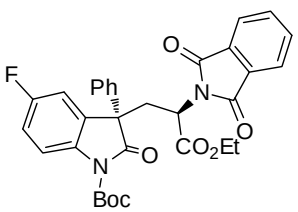
Prepared according to the general procedure from **1a** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 10 h to provide the title compound as a white solid (93% yield, 94% ee, 91:9 dr). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.68 – 7.54 (m, 5H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.17 – 7.11 (m, 2H), 6.77-6.66 (m, 2H), 5.03 (dd, *J* = 10.1 Hz, 4.8, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.44 – 3.30 (m, 2H), 1.69 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.78, 168.19, 166.66, 148.94, 139.19, 133.56, 131.25, 129.14, 128.49, 127.56, 126.55, 124.37, 123.94, 122.80, 115.53, 84.26, 62.09, 54.83, 48.75, 34.99, 27.95, 13.94. Calcd for $C_{32}H_{30}N_2O_7$ [M+Na]: 577.1945. Found: 577.1952. $[\alpha]_D^{14}$= -36.56 (C = 1.02, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 95:5, 0.7 mL/min; 254 nm, 25 ^{o}C, t_1 = 35.30 min, t_2 = 46.65 min, t_3 = 50.42 min, t_4 = 70.33 min).

***tert*-butyl 3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-5-methyl-2-oxo-3-phenylindoline-1-carboxylate (3b)**



Prepared according to the general procedure from **1b** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 10 h to provide the title compound as a white solid (90% yield, 93% ee, 89:11 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.62 (d, *J* = 6.5 Hz, 4H), 7.51 (d, *J* = 8.3 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.1 Hz, 1H), 6.83 (s, 1H), 6.47 (d, *J* = 8.3 Hz, 1H), 4.97 (d, *J* = 11.9 Hz, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.51 – 3.24 (m, 2H), 1.85 (s, 3H), 1.69 (s, 9H), 1.20 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 176.00, 168.22, 166.54, 149.01, 139.61, 136.97, 133.54, 131.22, 129.16, 128.52, 128.17, 127.53, 126.49, 124.83, 122.66, 115.55, 84.12, 62.08, 55.01, 48.82, 34.65, 27.98, 20.45, 13.93. Calcd for $C_{33}H_{32}N_2O_7$ [M+Na]: 591.2102. Found: 591.2104. $[\alpha]_D^{18}$= -19.21 (C = 0.95, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 95:5, 0.7 mL/min; 254 nm, 25 ^{o}C, t_1 = 35.87 min, t_2 = 38.56 min, t_3 = 44.00 min, t_4 = 56.33 min).

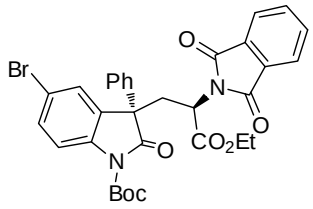
***tert*-butyl 3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-5-fluoro-2-oxo-3-phenylindoline-1-carboxylate (3c)**



Prepared according to the general procedure from **1c** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 2 h to provide the title compound as a white solid (96% yield, 96% ee, 91:9 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.64 (d, *J* = 4.4 Hz, 5H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.25 (t, *J* = 10.6 Hz, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 6.87 – 6.82 (m, 1H), 6.39 (t, *J* = 8.8 Hz, 1H), 5.00 (dd, J_1 = 11.6 Hz, J_2 = 3.0 Hz, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.46 – 3.29 (m, 2H), 1.68 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150

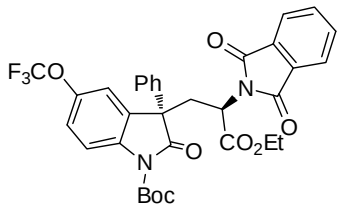
MHz, $CDCl_3$) δ (ppm) 175.33, 168.07, 166.70, 159.97, 158.34, 148.95, 138.74, 135.28, 133.81, 131.20, 128.71, 127.81, 126.40, 122.93, 117.09, 114.18, 112.00, 111.83, 84.56, 62.22, 55.17, 48.69, 34.88, 27.99, 13.98. Calcd for $C_{32}H_{29}FN_2O_7$ [M+Na]: 595.1851. Found: 595.1842. $[\alpha]_D^{16}$= -32.84 (C = 0.98, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 95:5, 0.7 mL/min; 254 nm, 25 °C, t_1 = 28.28 min, t_2 = 37.62 min, t_3 = 42.13 min, t_4 = 46.91 min).

***tert*-butyl 5-bromo-3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-2-oxo-3-phenylindoline-1-carboxylate (3d)**



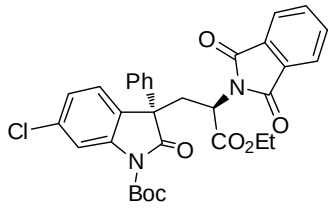
Prepared according to the general procedure from **1d** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 2 h to provide the title compound as a white solid (94% yield, 97% ee, 89:11 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.66 (s, 4H), 7.54 (d, *J* = 8.8 Hz, 1H), 7.28 (d, *J* = 7.5 Hz, 5H), 7.22 (d, *J* = 6.9 Hz, 1H), 7.16 (s, 1H), 6.79 (d, *J* = 8.8 Hz, 1H), 4.95 (d, *J* = 12.0 Hz, 1H), 4.24 – 4.14 (m, 2H), 3.46 – 3.27 (m, 2H), 1.68 (s, 9H), 1.21 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 174.96, 168.04, 166.69, 148.83, 138.85, 138.44, 133.83, 131.59, 131.00, 130.62, 128.79, 127.91, 127.36, 126.39, 123.10, 117.31, 84.76, 62.23, 55.03, 48.59, 28.42, 28.99, 13.84. Calcd for $C_{32}H_{29}BrN_2O_7$ [M+Na]: 655.1050. Found: 655.1065. $[\alpha]_D^{20}$= -13.65 (C = 0.98, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 95:5, 0.7 mL/min; 254 nm, 25 °C, t_1 = 31.26 min, t_2 = 36.56 min, t_3 = 39.23 min, t_4 = 79.57 min).

***tert*-butyl 3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-2-oxo-3-phenyl-5-(trifluoromethoxy)indoline-1-carboxylate (3e)**



Prepared according to the general procedure from **1e** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 2 h to provide the title compound as a white solid (94% yield, 97% ee, 91:9 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.71 (d, *J* = 8.9 Hz, 1H), 7.63 (d, *J* = 2.7 Hz, 4H), 7.32 – 7.23 (m, 4H), 7.19 (t, *J* = 7.1 Hz, 1H), 7.03 (s, 1H), 6.64 (d, J_1 = 8.9 Hz, 1H), 5.01 (dd, J_1 = 11.7 Hz, J_2 = 2.9 Hz, 1H), 4.18 (dd, J_1 = 6.7 Hz, J_2= 4.0 Hz, 2H), 3.48 – 3.31 (m, 2H), 1.69 (s, 9H), 1.19 (t, *J* = 7.0, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 175.11, 168.02, 166.72, 148.82, 145.33, 138.58, 137.76, 133.84, 131.26, 131.02, 128.77, 127.89, 126.38, 123.01, 120.89, 120.11, 119.18, 117.54, 116.65, 84.81, 62.24, 55.10, 48.73, 35.22, 27.95, 13.95. Calcd for $C_{33}H_{29}F_3N_2O_8$ [M+Na]: 661.1768. Found: 661.1754. $[\alpha]_D^{16}$= -35.33 (C = 1.00, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 90:10, 1.0 mL/min; 254 nm, 25 °C, t_1 =7.88 min, t_2 = 10.50 min).

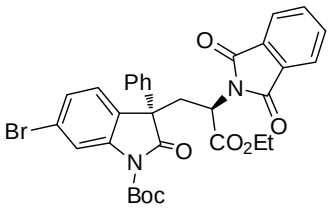
***tert*-butyl 6-chloro-3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-2-oxo-3-phenylindoline-1-carboxylate (3f)**



Prepared according to the general procedure from **1f** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 2 h to provide the title compound as a white solid (93% yield, 97% ee, 92:8 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.74

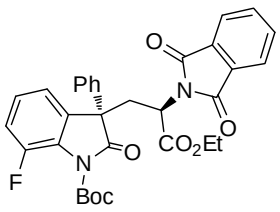
(s, 1H), 7.65 (t, *J* = 6.8 Hz, 4H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 4.99 (dd, J_1 = 11.9 Hz, J_2 = 1.9 Hz, 1H), 4.18 (q, *J* = 7.0 Hz, 2H), 3.45 – 3.25 (m, 2H), 1.69 (s, 9H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 175.22, 168.05, 166.75, 148.77, 140.22, 138.80, 133.95, 131.13, 128.68, 127.76, 126.45, 125.23, 124.07, 122.95, 116.26, 84.86, 77.20, 76.99, 76.77, 62.20, 54.68, 48.70, 34.95, 27.96, 13.97. Calcd for $C_{32}H_{29}ClN_2O_7$ [M+Na]: 611.1555. Found: 611.1552. $[\alpha]_D^{14}$= -55.12 (C = 0.99, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 90:10, 1.0 mL/min; 254 nm, 25 °C, t_1 = 7.98 min, t_2 = 11.12 min, t_3 = 14.24 min, t_4 = 18.84 min).

tert-butyl 6-bromo-3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-2-oxo-3-phenylindoline-1-carboxylatee (3g)



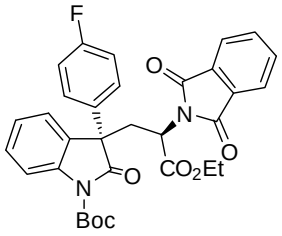
Prepared according to the general procedure from **1g** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 2 h to provide the title compound as a white solid (94% yield, 96% ee, 90:10 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 1.5 Hz, 1H), 7.70 – 7.62 (m, 4H), 7.29 (d, *J* = 7.7 Hz, 2H), 7.25 (t, *J* = 7.7 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.80 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 4.98 (dd, J_1 = 12.1 Hz, J_2 = 3.0 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.29-3.41 (m, 2H), 1.69 (s, 9H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 175.11, 168.06, 166.77, 148.79, 140.40, 138.81, 134.11, 131.17, 128.71, 128.35, 127.83, 127.06, 126.45, 125.56, 122.99, 121.79, 119.04, 84.88, 62.21, 54.78, 48.74, 34.90, 27.99, 13.99. Calcd for $C_{32}H_{29}BrN_2O_7$ [M+Na]: 655.1050. Found: 655.1065. $[\alpha]_D^{20}$= -50.95 (C = 0.99, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 90:10, 1.0 mL/min; 254 nm, 25 °C, t_1 = 8.05 min, t_2 = 11.71 min, t_3 = 14.80 min, t_4 = 20.85 min).

tert-butyl 3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-7-fluoro-2-oxo-3-phenylindoline-1-carboxylate (3h)



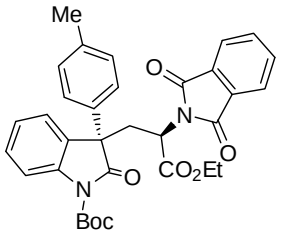
Prepared according to the general procedure from **1h** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 2 h to provide the title compound as a white solid (95% yield, 95% ee, 93:7 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.74 (s, 1H), 7.64 (s, 4H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.19 (t, *J* = 7.8 Hz, 2H), 7.14 – 7.02 (m, 2H), 6.70-6.74 (m, 1H), 6.68 – 6.59 (m, 1H), 5.02 (dd, J_1 = 11.7 Hz, J_2 = 2.9 Hz, 1H), 4.18 (q, *J* = 7.0 Hz, 2H), 3.33-3.41 (m, 2H), 1.63 (s, 9H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 175.07, 168.12, 166.67, 149.31, 147.64, 147.04, 138.23, 133.78, 132.25, 131.29, 128.58, 127.66, 126.36, 124.90, 122.90, 120.62, 116.27, 116.13, 84.91, 62.24, 55.51, 48.76, 35.16, 27.61, 13.96. Calcd for $C_{32}H_{29}FN_2O_7$ [M+]: 595.1851. Found: 595.1842. $[\alpha]_D^{20}$= -77.30 (C = 1.01, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 90:10, 1.0 mL/min; 254 nm, 25 °C, t_1 = 23.81 min, t_2 = 26.66 min, t_3 = 33.67 min, t_4 = 49.85 min).

***tert*-butyl 3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-3-(4-fluorophenyl)-2-oxoindoline-1-carboxylate (3i)**



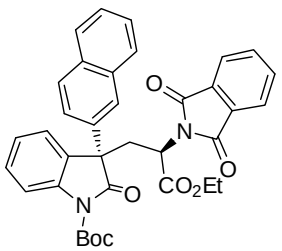
Prepared according to the general procedure from **1i** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 10 h to provide the title compound as a white solid (94% yield, > 99% ee, 90:10 dr). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.67 – 7.57 (m, 6H), 7.42 – 7.10 (m, 3H), 7.05 – 6.62 (m, 5H), 5.00 (dd, *J* = 8.7, 6.4 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 3H), 3.36 – 3.30 (m, 2H), 1.69 (s, 10H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.71, 168.17, 166.73, 163.28, 160.82, 148.93, 139.30, 134.79, 133.68, 131.29, 128.84, 128.55, 127.90, 124.46, 124.09, 122.90, 115.71, 115.43, 115.21, 84.50, 62.22, 54.30, 48.75, 35.37, 28.00, 13.98. Calcd for $C_{33}H_{32}N_2O_7$ [M+]: 572.1959. Found: 572.1960. $[\alpha]_D^{16}$= -70.47 (C = 1.02, $CHCl_3$). HPLC (Chiralpak OD-H column, hexane/2-propanol = 90:10, 1.0 mL/min; 254 nm, 25 ^{o}C, t_1 = 12.36 min, t_2 = 13.32 min, t_3 = 15.64 min, t_4 = 24.12 min).

***tert*-butyl 3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-2-oxo-3-(p-tolyl)indoline-1-carboxylate (3j)**



Prepared according to the general procedure from **1j** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 10 h to provide the title compound as a white solid (94% yield, 94% ee, 89:11 dr). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.52 (s, 4H), 7.08-7.14 (m, 4H), 6.93 (d, *J* = 7.9 Hz, 2H), 6.59-6.69 (m, 2H), 4.94 (t, *J* = 7.5 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.27 (d, *J* = 7.5 Hz, 2H), 2.10 (s, 3H), 1.60 (s, 10H), 1.11 (t, *J* = 7.1 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.90, 168.26, 166.72, 149.05, 139.26, 137.38, 136.12, 133.54, 131.34, 129.18, 127.60, 126.49, 124.43, 123.95, 123.40, 122.83, 115.53, 84.22, 62.11, 54.54, 48.82, 35.00, 27.98, 20.73, 13.97. Calcd for $C_{33}H_{32}N_2O_7$ [M+Na]: 591.2102. Found: 591.2090. $[\alpha]_D^{16}$= -55.55 (C = 1.00, $CHCl_3$). HPLC (Chiralpak OD-H column, hexane/2-propanol = 90:10, 1.0 mL/min; 254 nm, 25 ^{o}C, t_1 = 8.86 min, t_2 = 10.36 min, t_3 = 11.67 min).

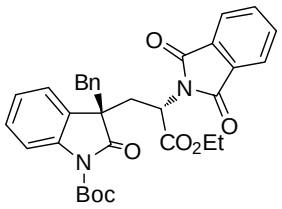
***tert*-butyl 3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-3-(naphthalen-2-yl)-2-oxoindoline-1-carboxylate (3k)**



Prepared according to the general procedure from **1k** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 10 h to provide the title compound as a white solid (94% yield, > 99% ee, 91:9 dr). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.63-7.77 (m, 6H), 7.57 – 7.44 (m, 5H), 7.43 – 7.33 (m, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 6.74-6.84 (m, 2H), 5.11 (dd, J_1 = 10.9 Hz, J_2 = 4.0 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.60 – 3.39 (m, 2H), 1.69 (s, 9H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.74, 168.23, 166.69, 148.94, 139.24, 136.18, 133.76, 132.70, 132.23, 131.10, 129.15, 128.37, 127.78, 127.11, 126.13, 125.67, 124.58, 124.08, 123.25, 122.66, 115.57, 84.33, 62.12, 54.89, 48.71, 34.81, 27.93, 13.93. Calcd for $C_{36}H_{32}N_2O_7$ [M+Na]: 627.2102. Found: 627.2096. $[\alpha]_D^{18}$= -14.09 (C = 0.97,

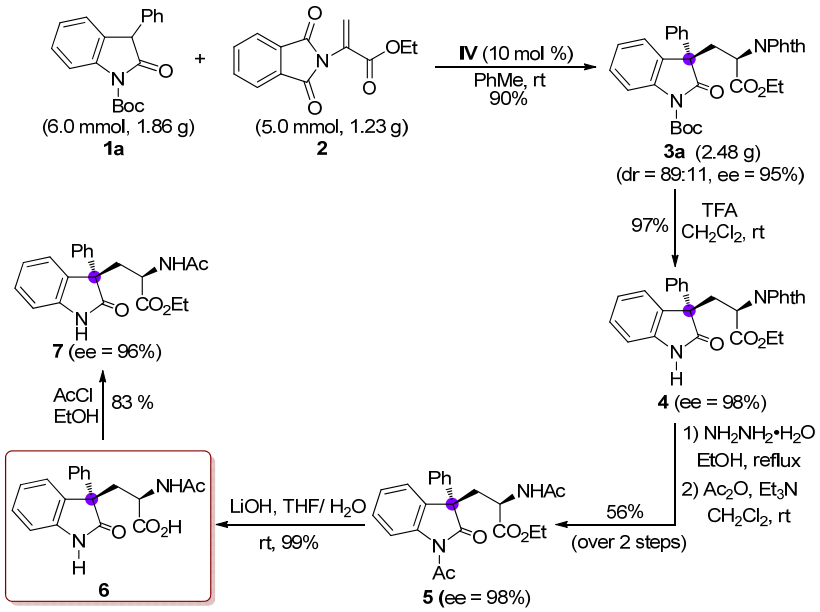
$CHCl_3$). HPLC (Chiralpak OD-H column, hexane/2-propanol = 90:10, 1.0 mL/min; 254 nm, 25 °C, t_1 = 14.08 min, t_2 = 17.51 min).

***tert*-butyl 3-benzyl-3-(2-(1,3-dioxoisoindolin-2-yl)-3-ethoxy-3-oxopropyl)-2-oxoindoline-1-carboxylate (3l)**



Prepared according to the general procedure from **1l** (0.24 mmol), **2** (0.2 mmol), toluene (1 mL) at rt for 48 h to provide the title compound as a light yellow oil (90% yield, 87% ee, 52:48 dr). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.80-7.82 (m, 2H), 7.70 – 7.73 (m, 2H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.30 – 7.35 (m, 1H), 7.23-7.28 (m, 2H), 6.97-7.07 (m, 3H), 6.72 (d, *J* = 7.2 Hz, 2H), 4.37 (dd, *J* = 11.8, 2.2 Hz, 1H), 4.13 (m, 2H), 3.34 (dd, *J* = 14.7, 11.9 Hz, 1H), 3.14 (d, *J* = 12.8 Hz, 1H), 3.07 – 2.91 (m, 2H), 1.22 (s, 9H), 1.15 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.28, 168.61, 166.86, 148.10, 140.18, 134.00, 131.77, 129.89, 128.91, 127.58, 126.81, 124.37, 123.40, 123.12, 115.14, 83.13, 62.12, 53.13, 48.59, 46.13, 34.99, 27.57, 13.96. Calcd for $C_{33}H_{32}N_2O_7$ [M+Na]: 591.2102. Found: 591.2106. $[\alpha]_D^{14}$= -58.10 (C = 0.98, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 90:10, 1.0 mL/min; 254 nm, 25 °C, t_1 = 10.35 min, t_2 = 14.93 min, t_3 = 17.20 min, t_4 = 24.51 min).

4. Derivatizations of adduct 3a.



Procedure: A mixture of *tert*-butyl 2-oxo-3-phenylindoline-1-carboxylate **1a** (6.0 mmol, 1.86 g), **2** (5.0 mmol, 1.23 g) and catalyst **IV** (0.5 mmol) in toluene (25 mL) was stirred at room temperature for 10 h. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 10:1~8:1) to give the desired product **3a** as a white solid. The two stereoisomers were seperated by silica gel chromatography.

To a solution of **3a** (1.0 mmol) in CH_2Cl_2 (20 mL) was added TFA (5.0 mmol) at rt. The mixture was stirred at the same temperature for 4 h. It was then diluted with DCM and washed with sat. Na_2CO_3. The

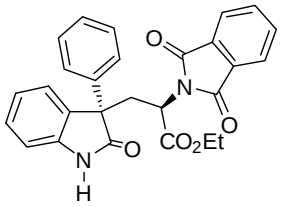
aqueous phase was extracted with CH_2Cl_2 and the combined organic phase was dried over Na_2SO_4. Then the crude product was purified by flash silica gel chromatography to afford the product **4** as white solid in 97 % yield with 98% ee.

Hydrazinemonohydrate (20 mmol, 20.0 equiv) was added to a solution of **4** (1.0 mmol, 1 equiv) in a ethanol (5mL) at 23 °C and the mixture was heated to reflux. The resulting white suspension was filtered, and were concentrated under reduced pressure to afford the crude primary amine as a yellow oil. The yellow residue was dissolved in dichloromethane (5 mL) at 23 °C. Triethylamine (10.0 mmol, 10.0 equiv) was added followed by Ac_2O (10.0 mmol, 10.0 equiv). After 24 h, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (eluent: acetone/ petrolem ether) to afford the product **5** as a white solid (56% for 2 steps).

To a solution of **5** (1.0 mmol) in a mixture of THF (5 mL) and H_2O was added $LiOH \cdot H_2O$ (10.0 mmol) at rt. The mixture was stirred at the same temperature for 4 h. It was then acidfied with 2N HCl. The aqueous phase was extracted with CH_2Cl_2 and the combined organic phase was dried over Na_2SO_4 to give **6** as a white solid in 99 % yield.

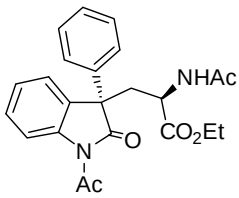
In order to confirm the stereoselectivity of compound **6**, the ersterfication was conducted with AcCl in disted. EtOH under reflux. To a stirred solution of **6** (0.3 mmol) in disted. EtOH (15 mL) AcCl (3.0 mmol) was added dropwise at rt. The mixture was heated to reflux for 2h and the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (eluent: acetone/ petrolem ether) to afford the product **7** as a white solid (83% isolated yield).

***(R)*-ethyl 2-(1,3-dioxoisoindolin-2-yl)-3-((*S*)-2-oxo-3-phenylindolin-3-yl)propanoate(4)**



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.43 (s, 1H), 7.68 – 7.57 (m, 4H), 7.48 – 7.38 (m, 2H), 7.33 – 7.01 (m, 4H), 6.50 – 6.78 (m, 3H), 5.16 (dd, J_1 = 12.1, J_2 = 2.4, 1H), 4.18 (q, J = 6.8, 2H), 3.60 – 3.25 (m, 2H), 1.19 (t, J = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 179.88, 168.50, 167.00, 140.61, 139.21, 133.60, 131.23, 128.45, 127.50, 127.35, 126.36, 124.57, 122.83, 122.05, 110.59, 62.10, 55.16, 49.16, 34.23, 13.95. Calcd for $C_{27}H_{22}N_2O_5$ [M+K]: 493.1166. Found: 493.1146. $[\alpha]_D^{20}$= -67.33 (C = 1.00, $CHCl_3$). HPLC (Chiralpak OD-H column, hexane/2-propanol = 70:30, 1.0 mL/min; 254 nm, 25 ^{o}C, t_1 = 10.16 min, t_2 = 15.92 min).

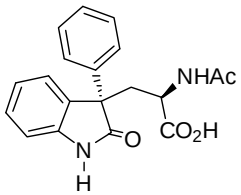
***(R)*-ethyl 2-amino-3-((*S*)-2-oxo-3-phenylindolin-3-yl)propanoate (5)**



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.33 (d, J = 7.9 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.30 (q, J = 8.5 Hz, 7H), 5.82 (d, J = 8.2 Hz, 1H), 4.71 (dd, J = 14.4, 7.6 Hz, 1H), 4.18 – 4.11 (m, 1H), 4.02 – 3.93 (m, 1H), 3.11 (dd, J = 14.4, 6.1 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.64 (s, 3H), 1.63 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150

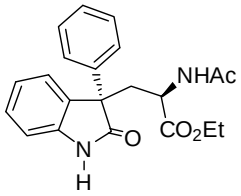
MHz, $CDCl_3$) δ (ppm) 178.20, 171.23, 170.85, 169.32, 140.18, 139.50, 130.00, 129.29, 128.81, 127.90, 126.47, 125.08, 116.92, 61.65, 54.76, 49.65, 39.30, 26.50, 22.51, 13.78. Calcd for $C_{23}H_{24}N_2O_5$ [M+Na]: 431.1583. Found: 431.1567. $[\alpha]_D^{21}$= -51.49 (C = 1.03, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 80:20, 1.0 mL/min; 254 nm, 25 °C, t_1 = 9.84 min, t_2 = 10.99 min, t_3 = 13.24 min, t_4 = 18.76 min).

(*R*)-2-acetamido-3-((*S*)-2-oxo-3-phenylindolin-3-yl)propanoic acid (6)



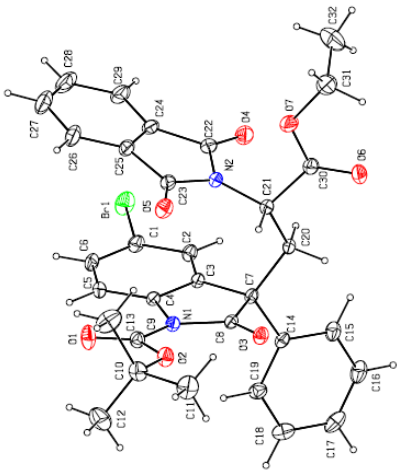
^{1}H NMR (400 MHz, DMSO) δ (ppm) 12.67 (s, 1H), 10.61 (s, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.41 – 7.27 (m, 5H), 7.27 – 7.15 (m, 2H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 4.25 – 4.06 (m, 1H), 2.66 (m, 2H), 1.34 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ (ppm) 178.83, 173.40, 168.50, 142.00, 140.91, 131.62, 128.59, 128.09, 127.19, 126.50, 125.94, 121.46, 110.01, 55.47, 49.28, 37.47, 22.02. Calcd for $C_{19}H_{18}N_2O_4$ [M+Na]: 361.1164. Found: 361.1141. $[\alpha]_D^{22}$= -24.36 (C = 1.00, CH_3OH).

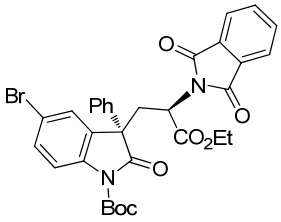
(*R*)-ethyl 2-acetamido-3-((*S*)-2-oxo-3-phenylindolin-3-yl)propanoate (7)



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.71 (s, 1H), 7.46 – 7.38 (m, 2H), 7.35 – 7.26 (m, 3H), 7.25 – 7.18 (m, 2H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.7 Hz, 1H), 6.24 (d, *J* = 8.3 Hz, 1H), 4.74 (m, 1H), 4.18 – 3.94 (m, 2H), 3.04 – 2.91 (m, 1H), 2.73 (dd, *J* = 14.4, 9.4 Hz, 1H), 1.53 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) 180.18, 171.82, 169.94, 141.25, 139.72, 131.64, 128.49, 127.42, 126.42, 125.27, 122.32, 110.63, 61.58, 55.13, 50.06, 38.06, 22.28, 13.88. Calcd for $C_{21}H_{22}N_2O_4$ [M+Na]: 389.1477. Found: 389.1469. $[\alpha]_D^{21}$= -21.24 (C = 1.00, $CHCl_3$). HPLC (Chiralpak AD-H column, hexane/2-propanol = 70:30, 1.0 mL/min; 254 nm, 25 °C, t_1 = 9.17 min, t_2 = 17.60 min).

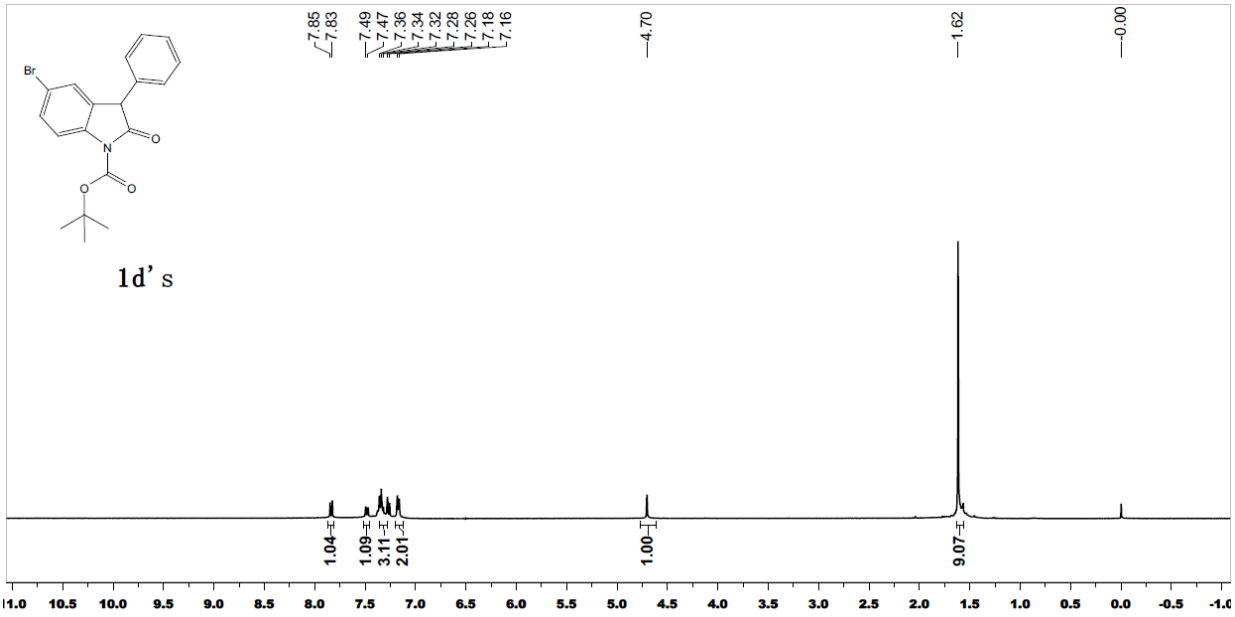
5. X-Ray structure of 3d.

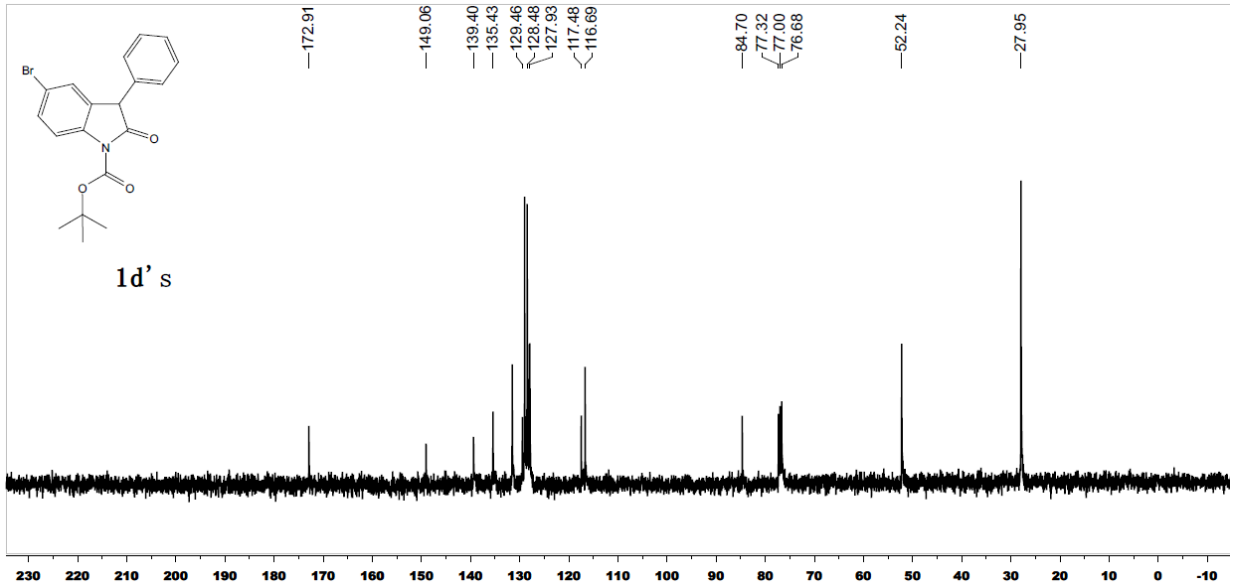


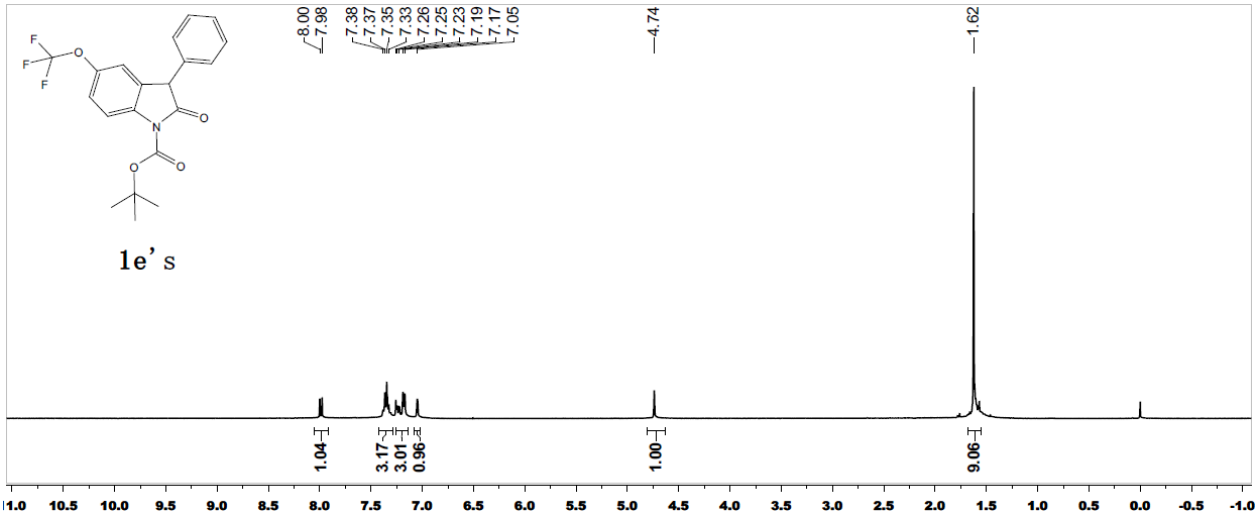


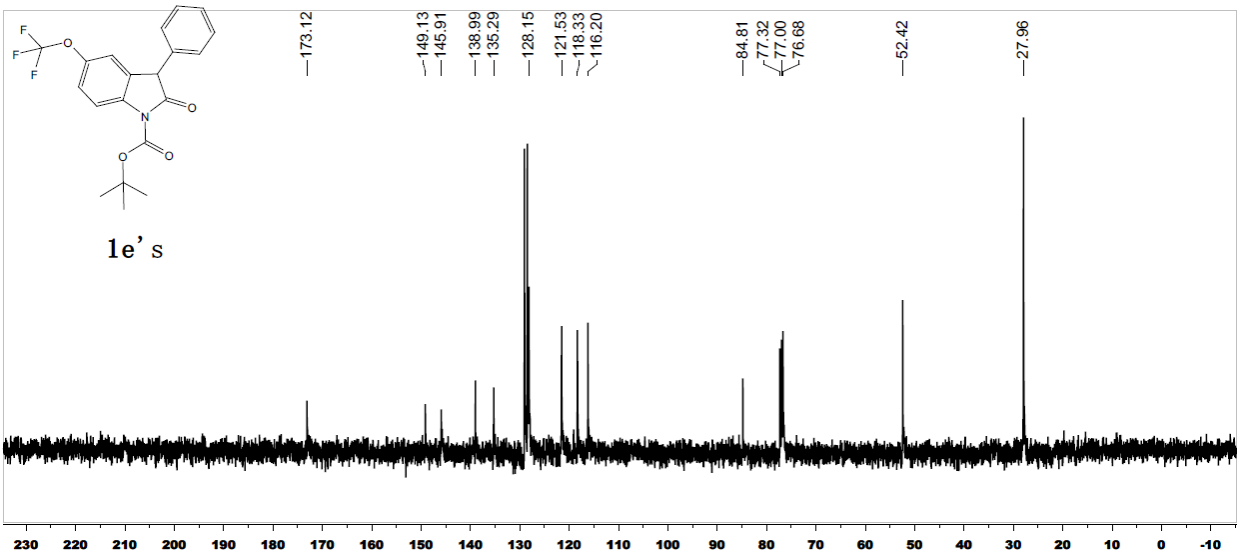
3d

6. Copies of ^{1}H NMR and ^{13}C NMR Spectrums





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138.99
135.29
128.15
121.53
118.33
116.20
84.81
77.32
77.00
76.68
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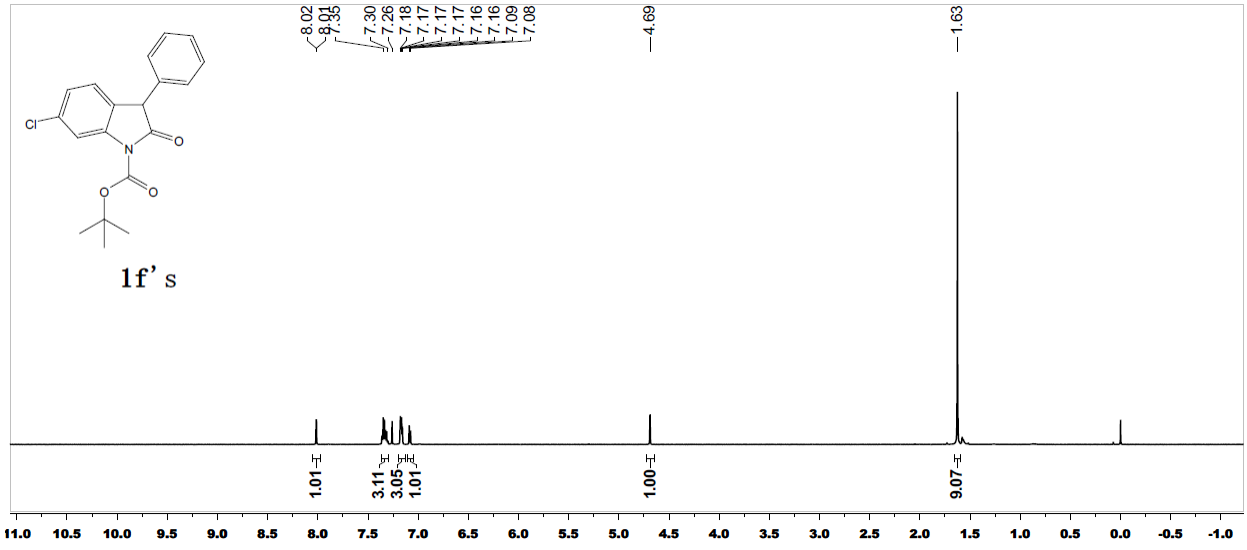
27.96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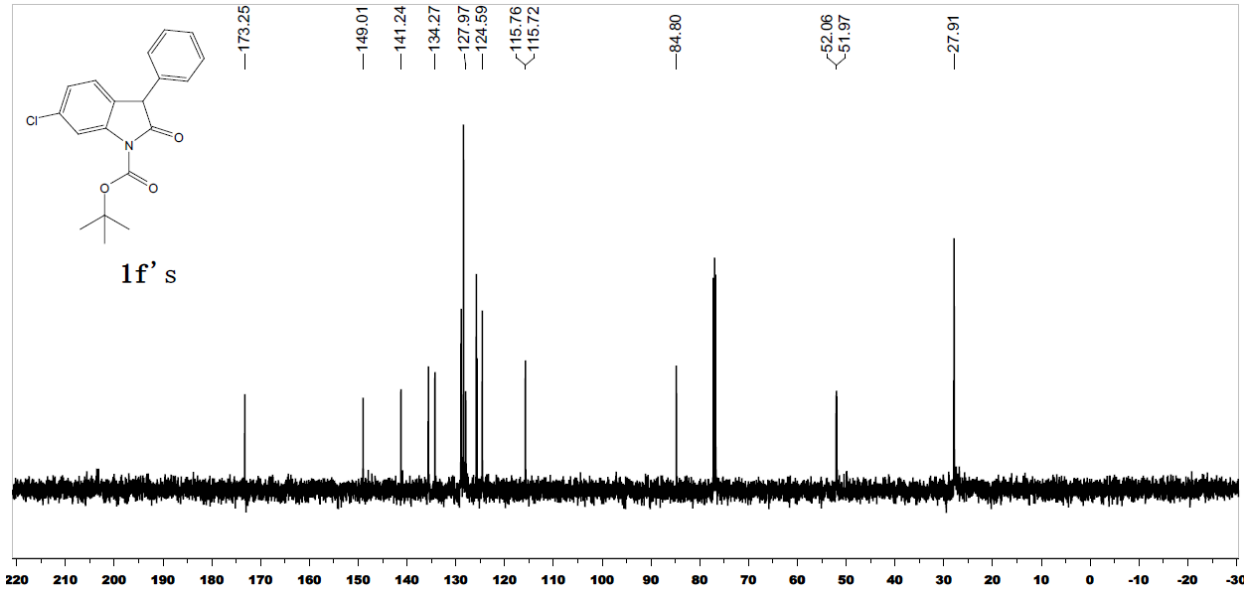
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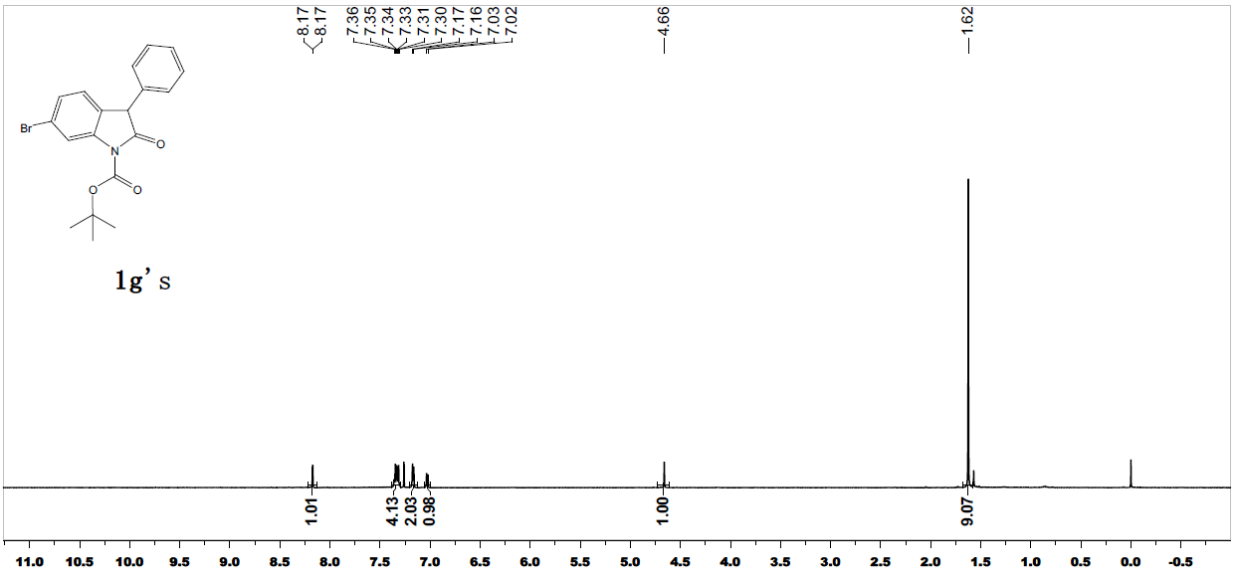
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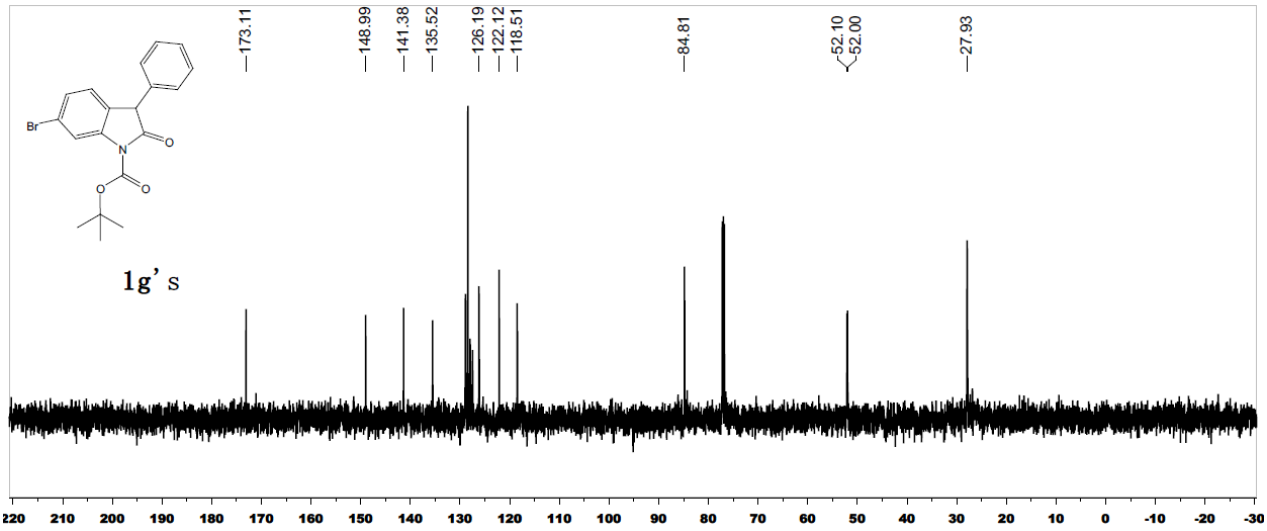
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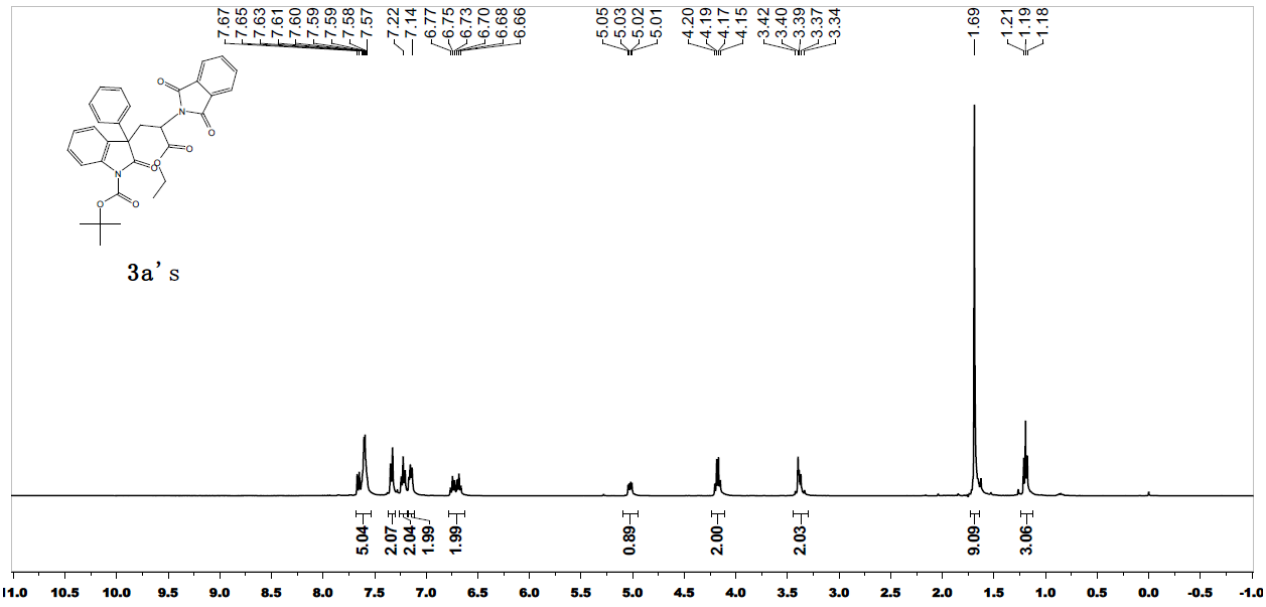
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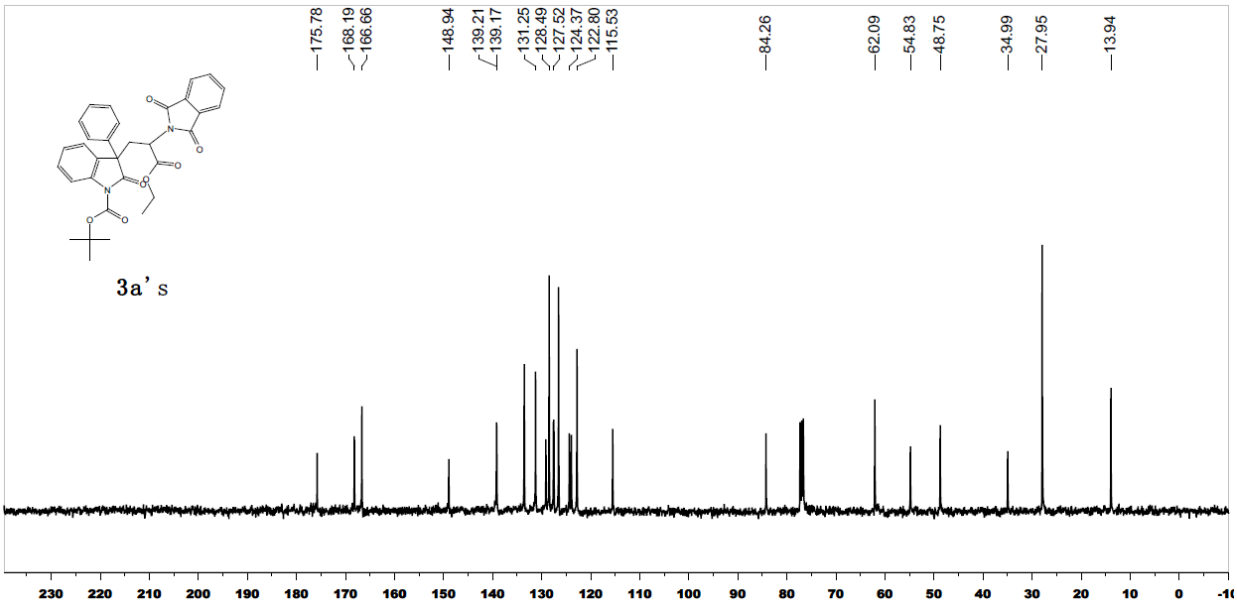
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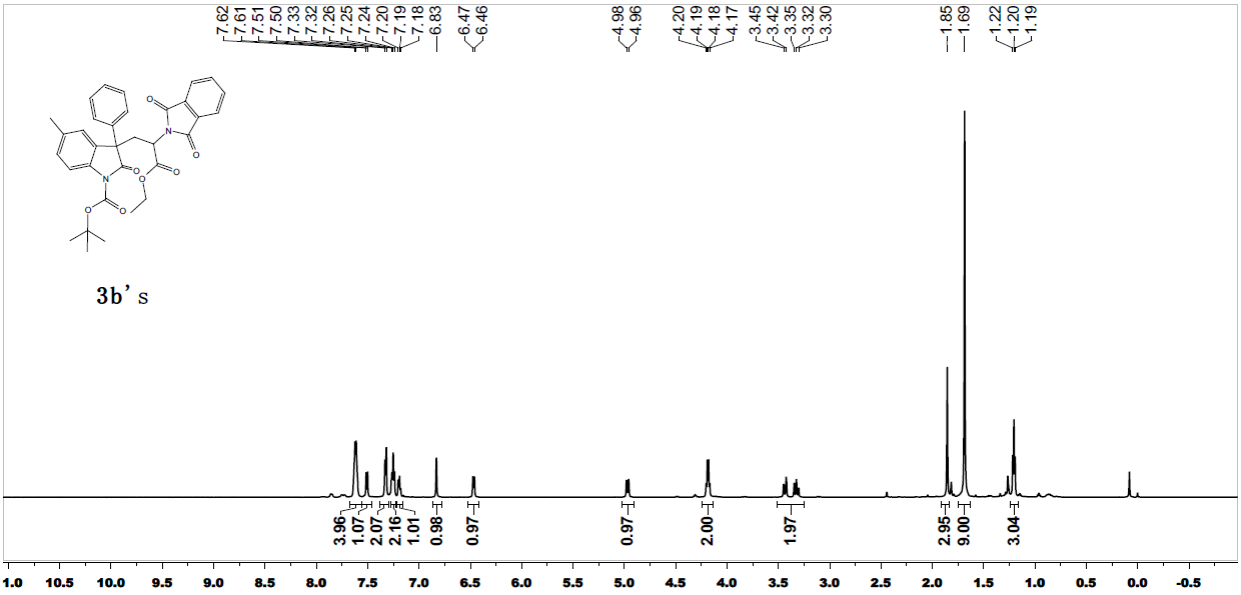
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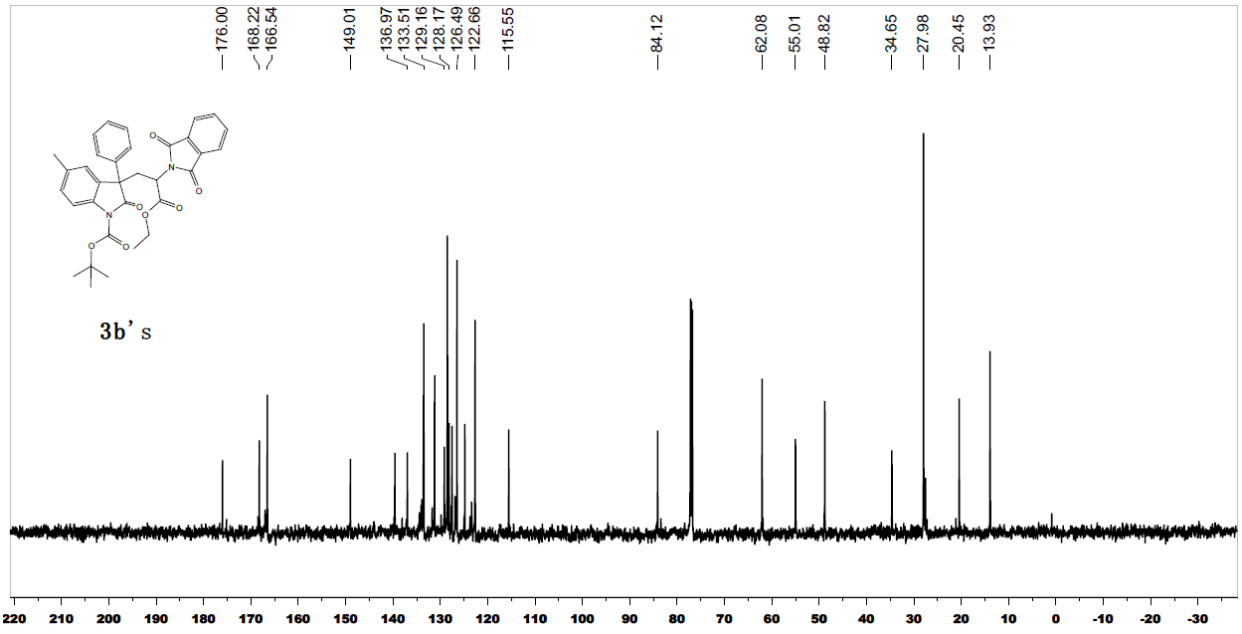
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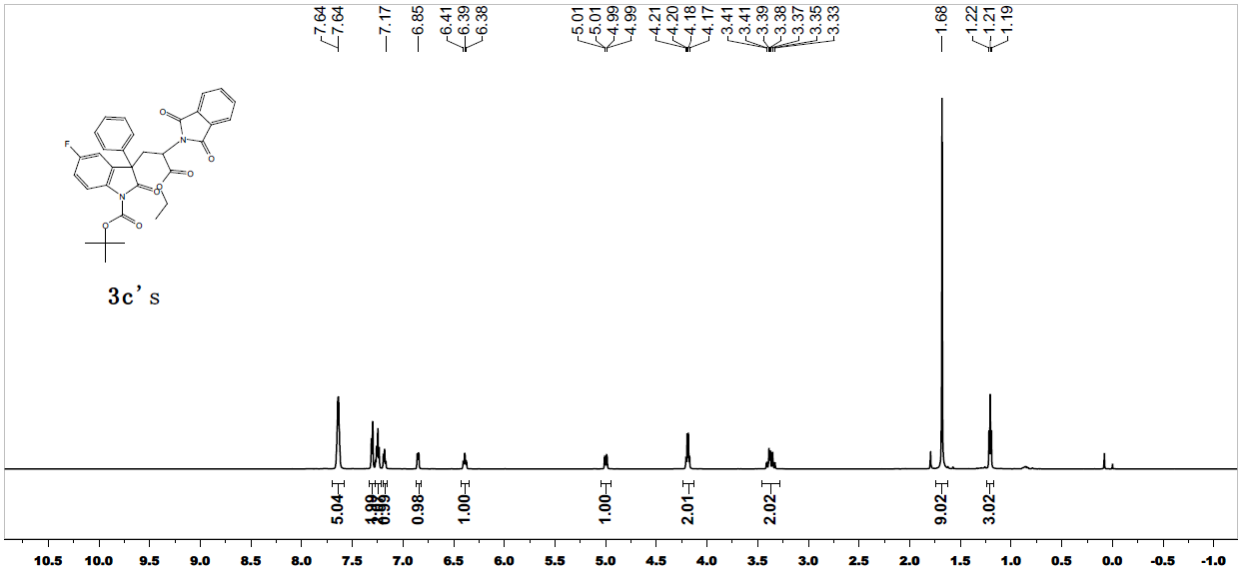
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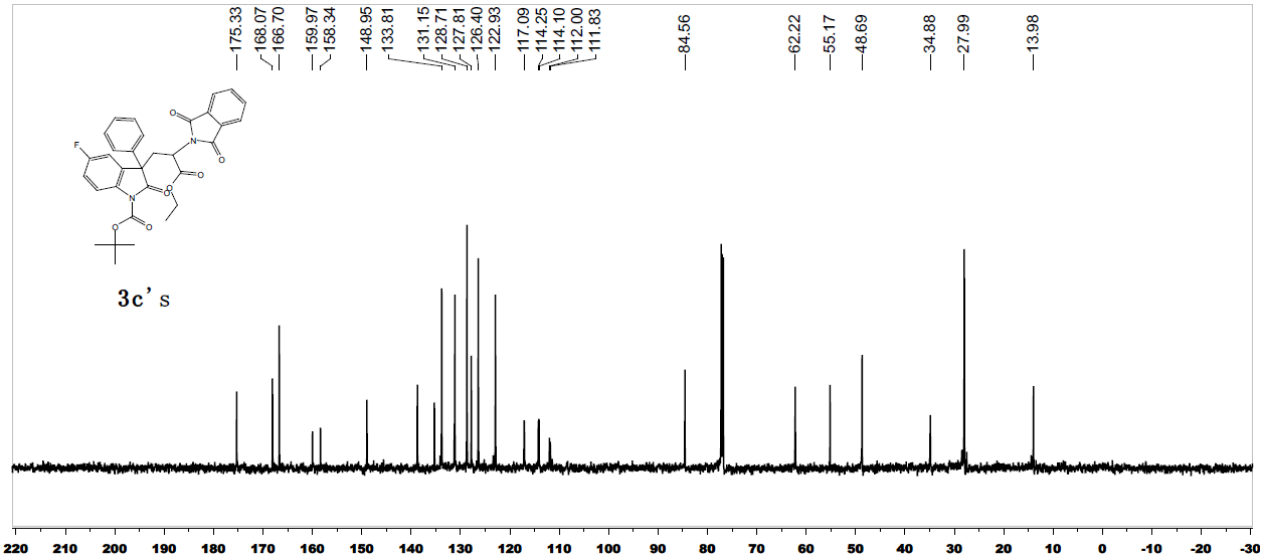
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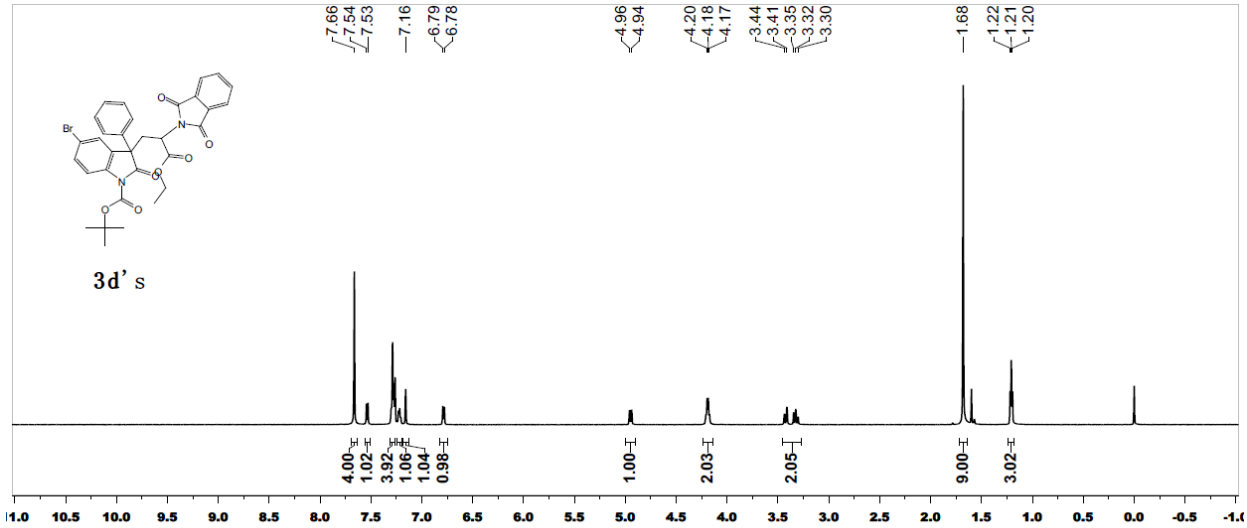
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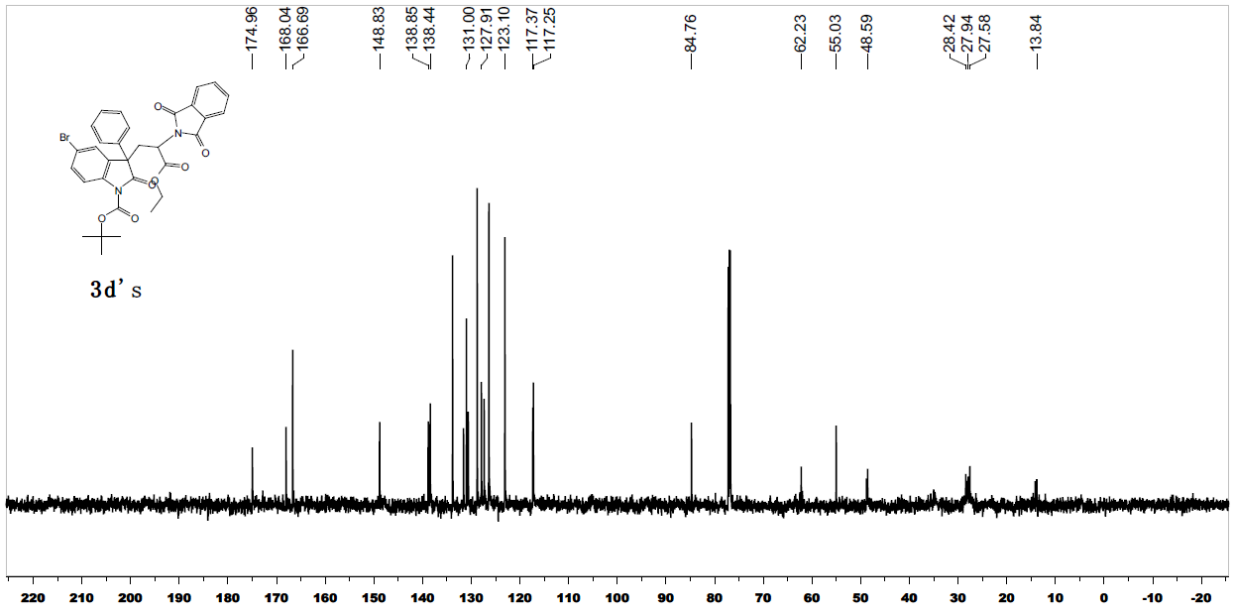
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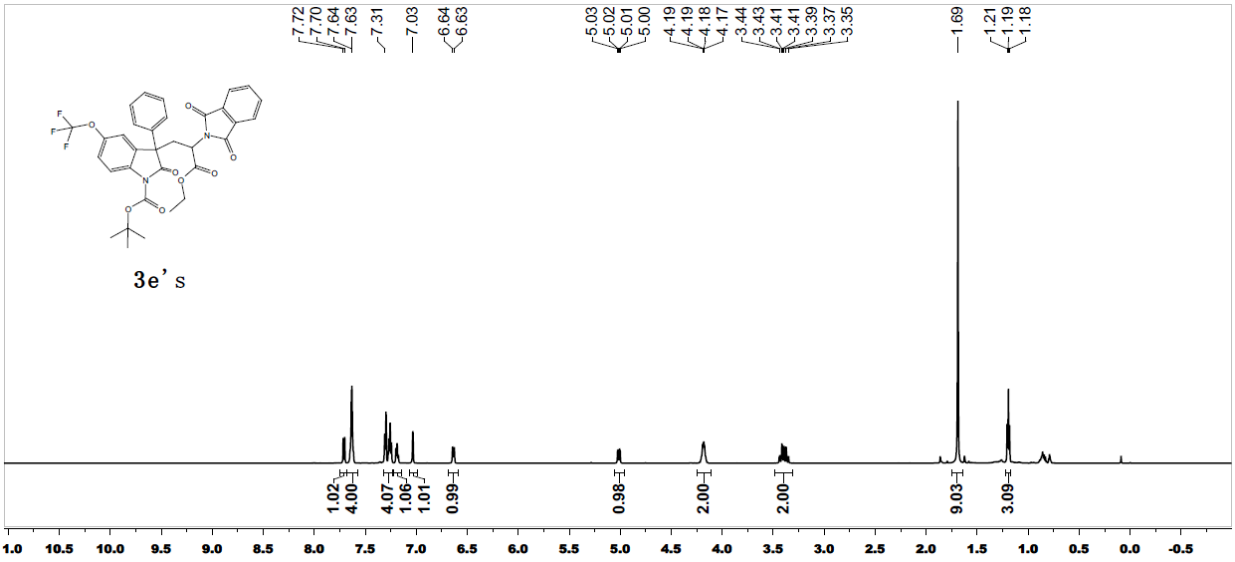
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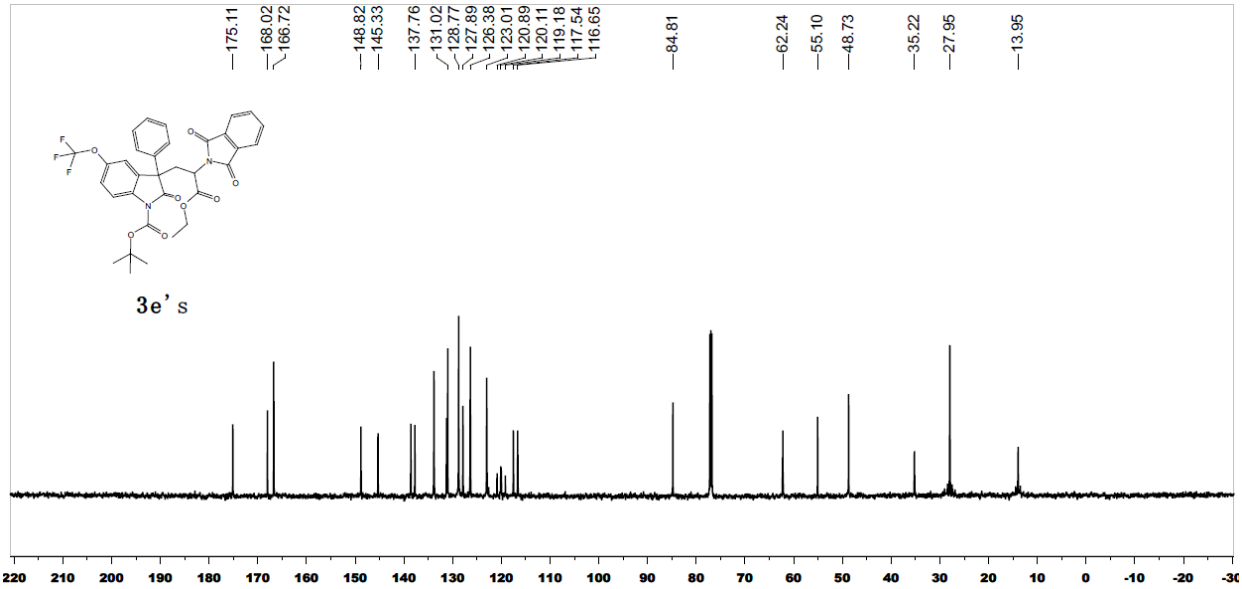
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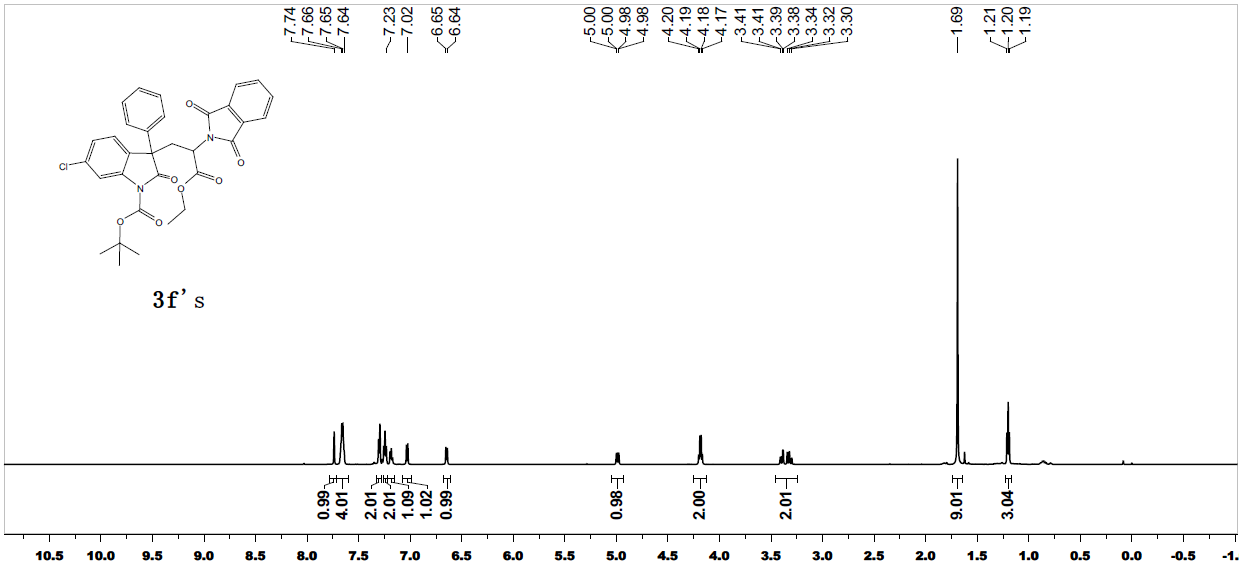
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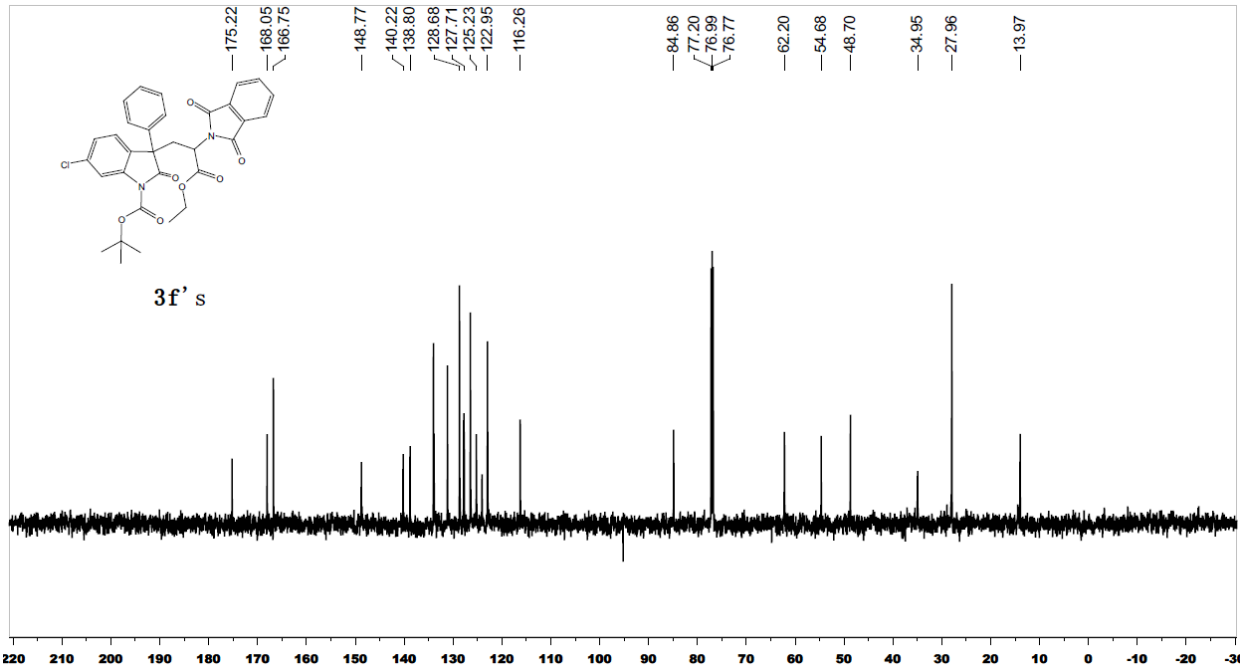
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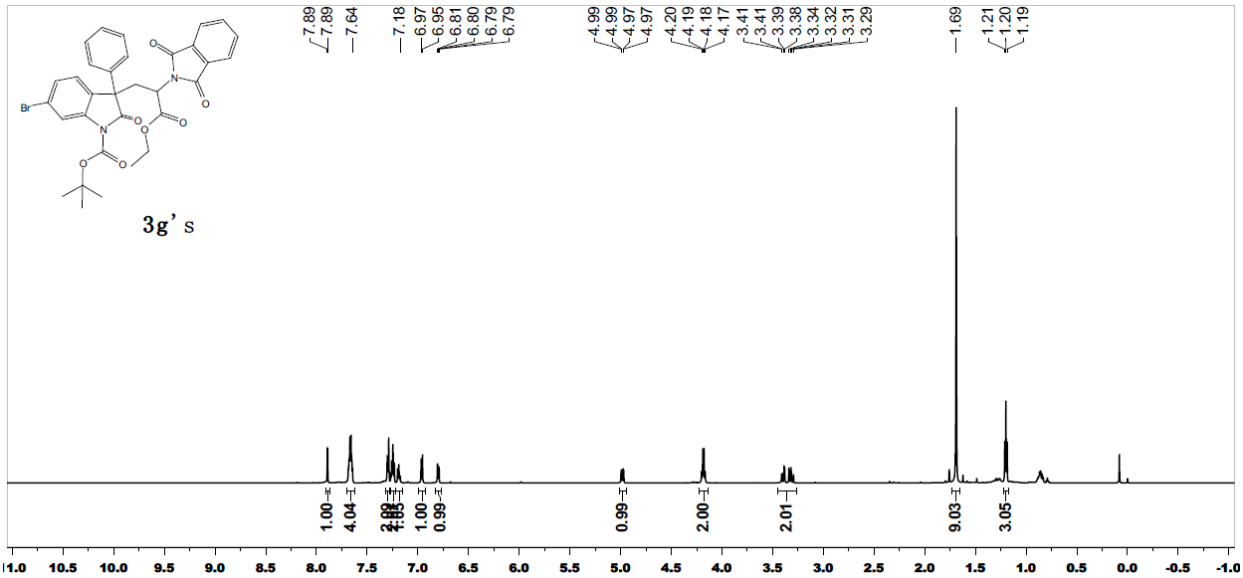
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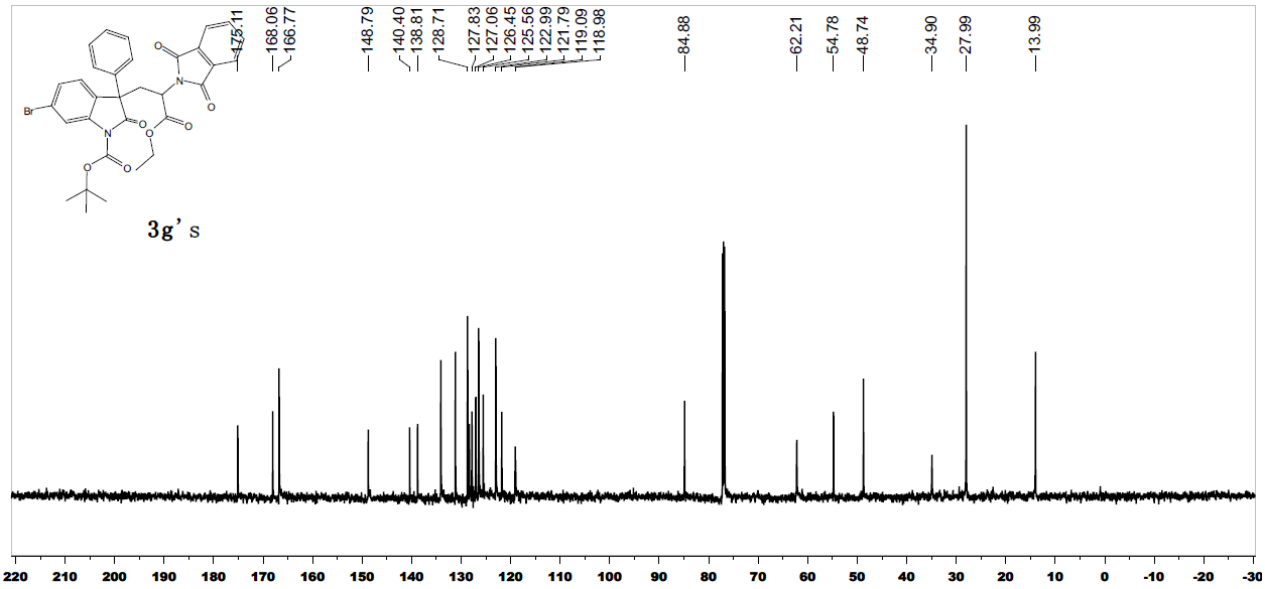
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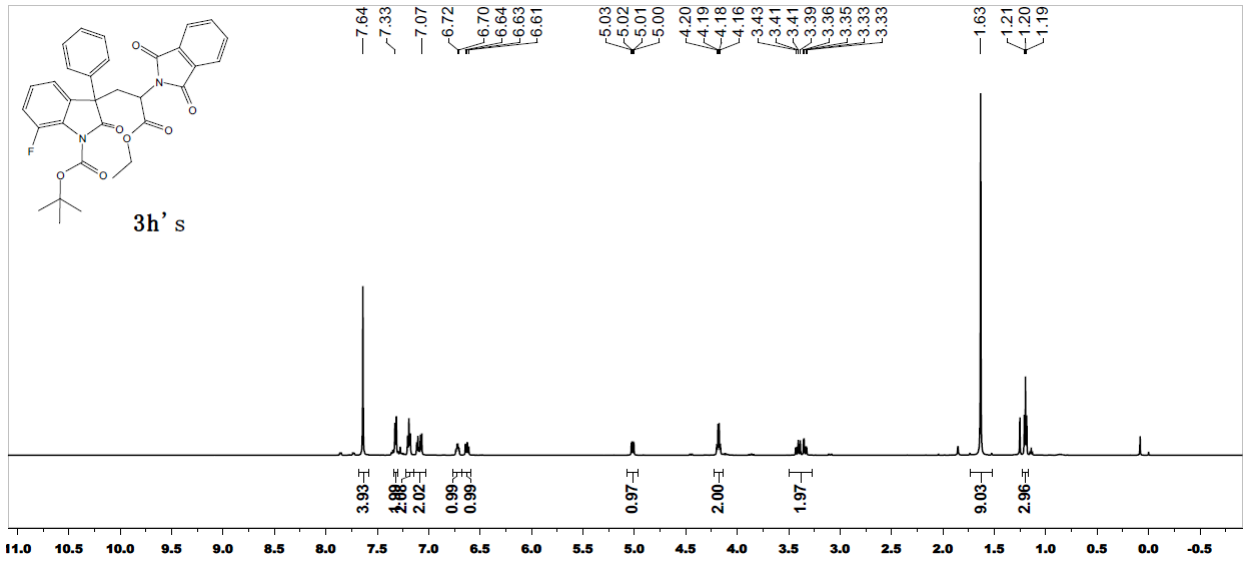
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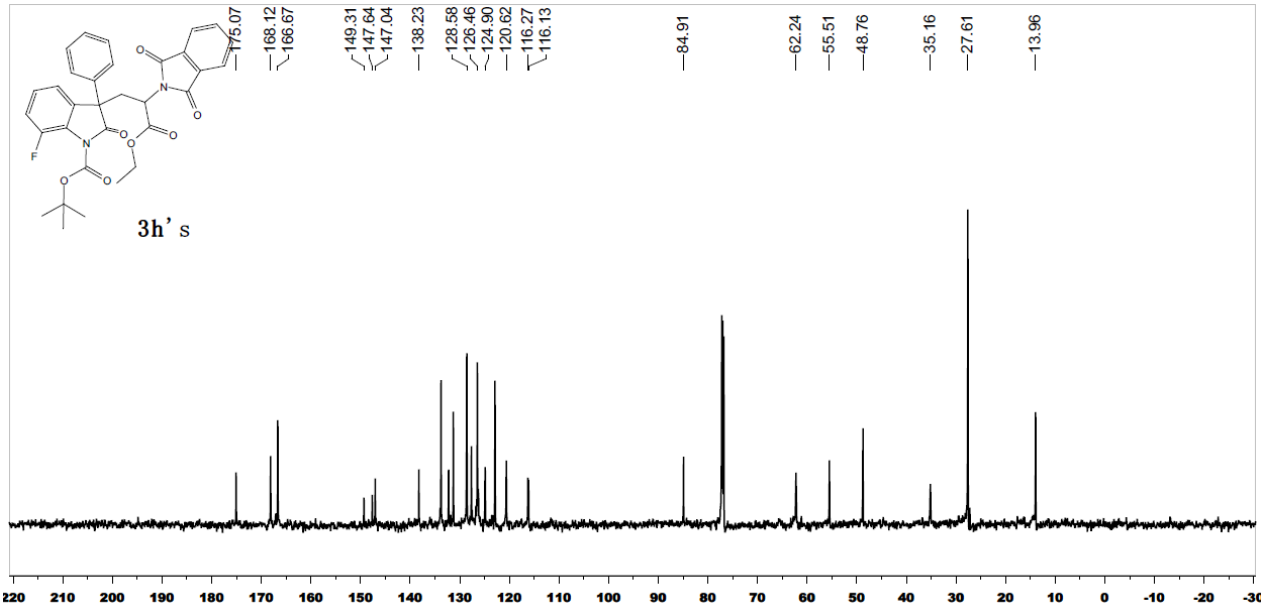
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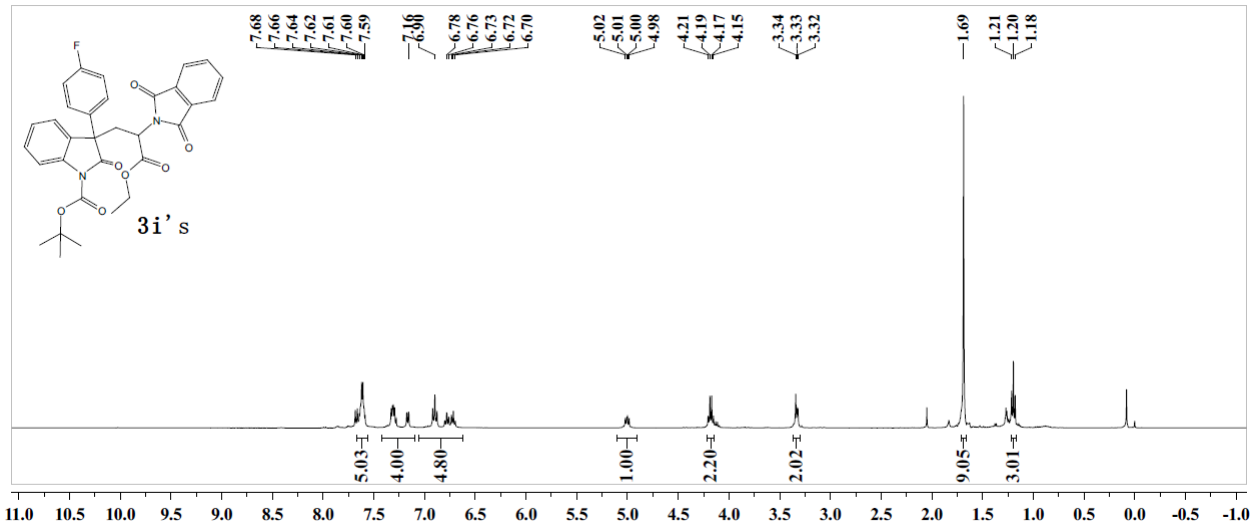
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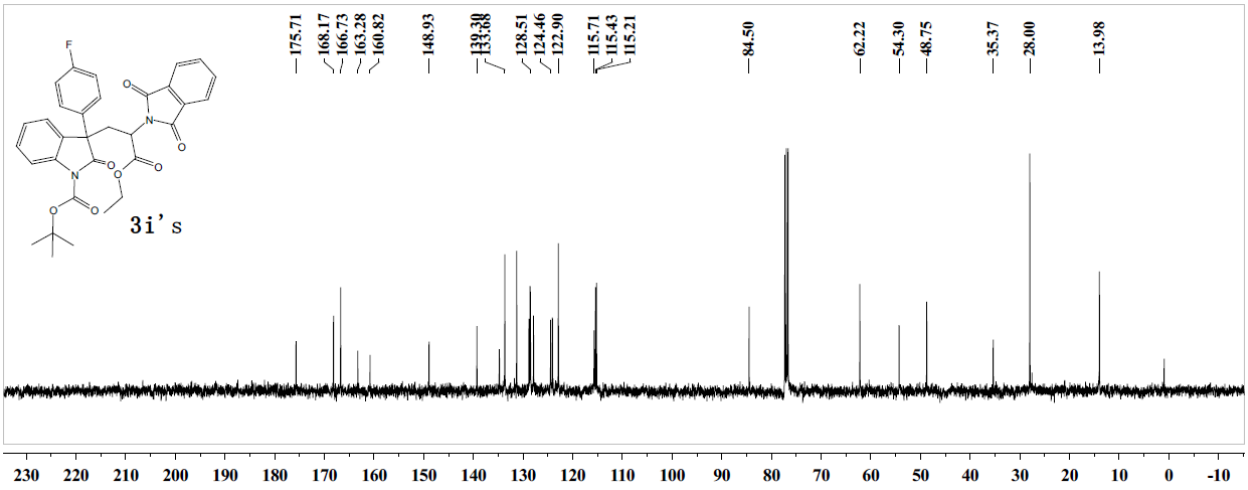
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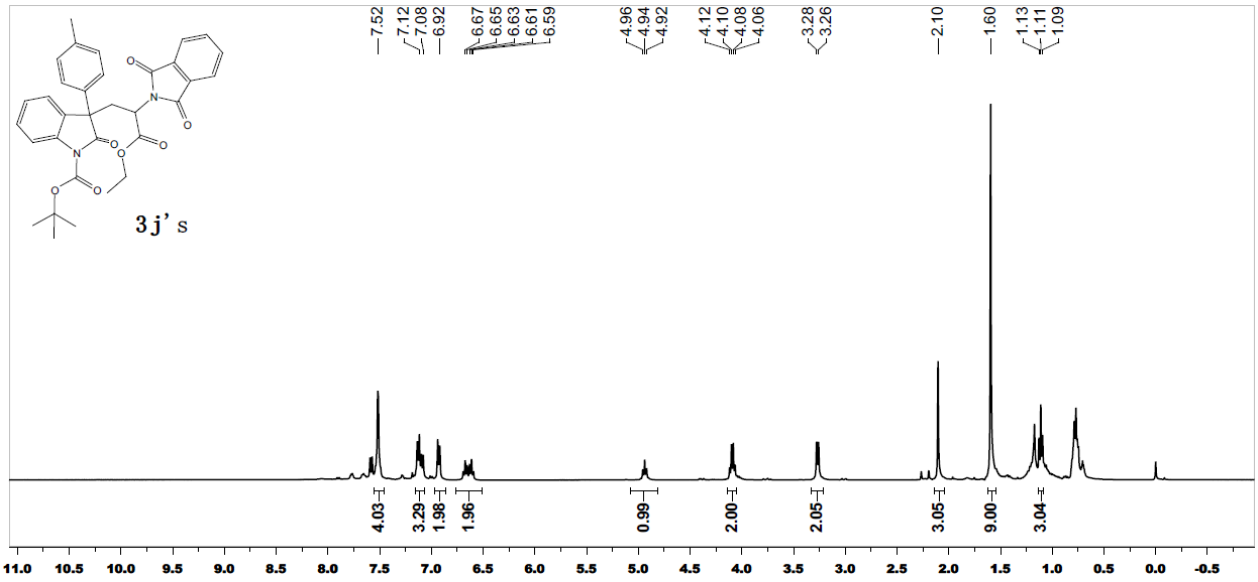
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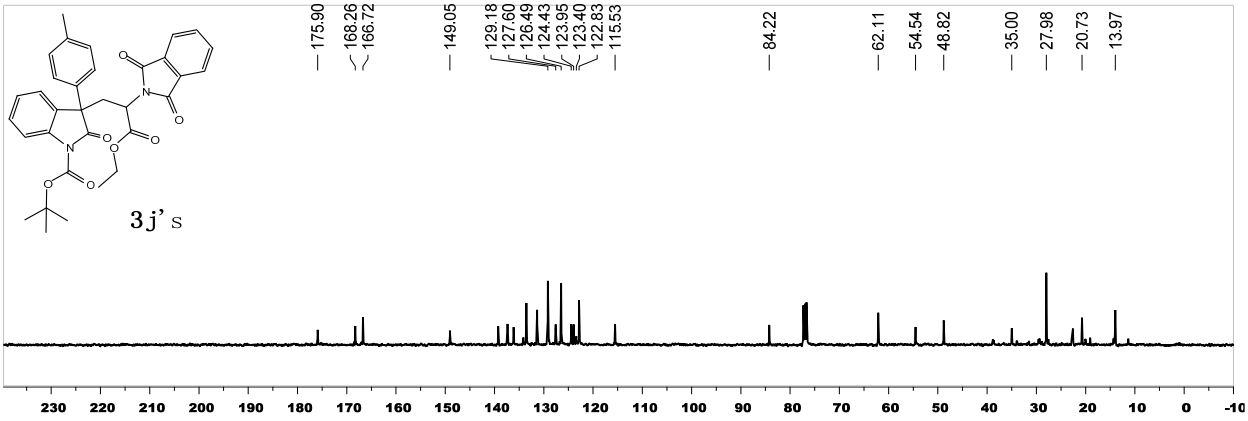
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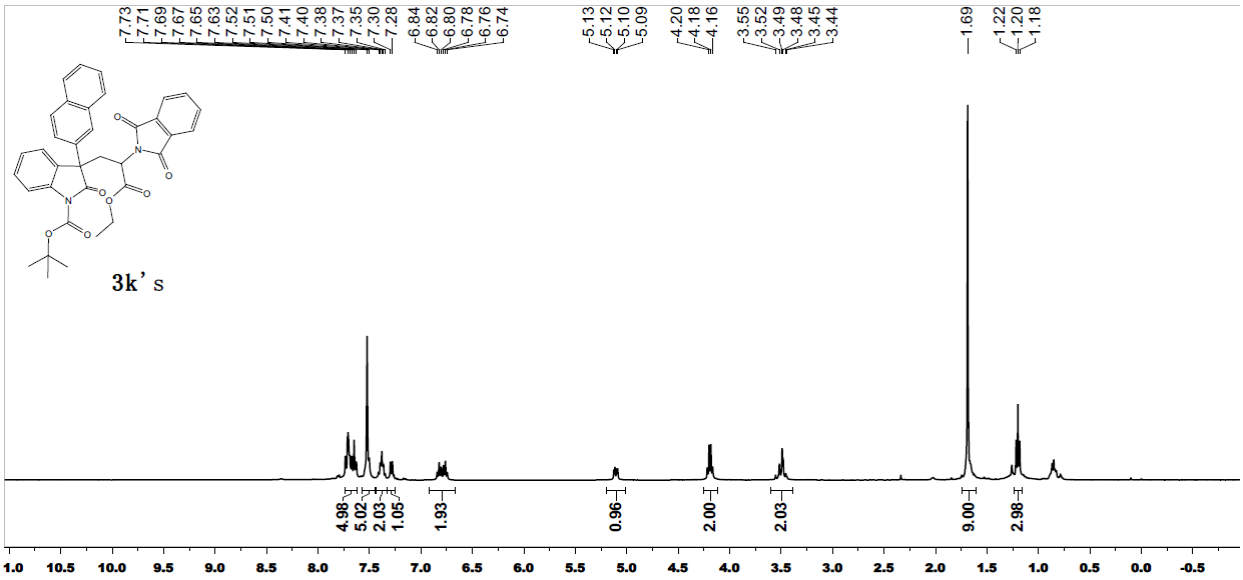
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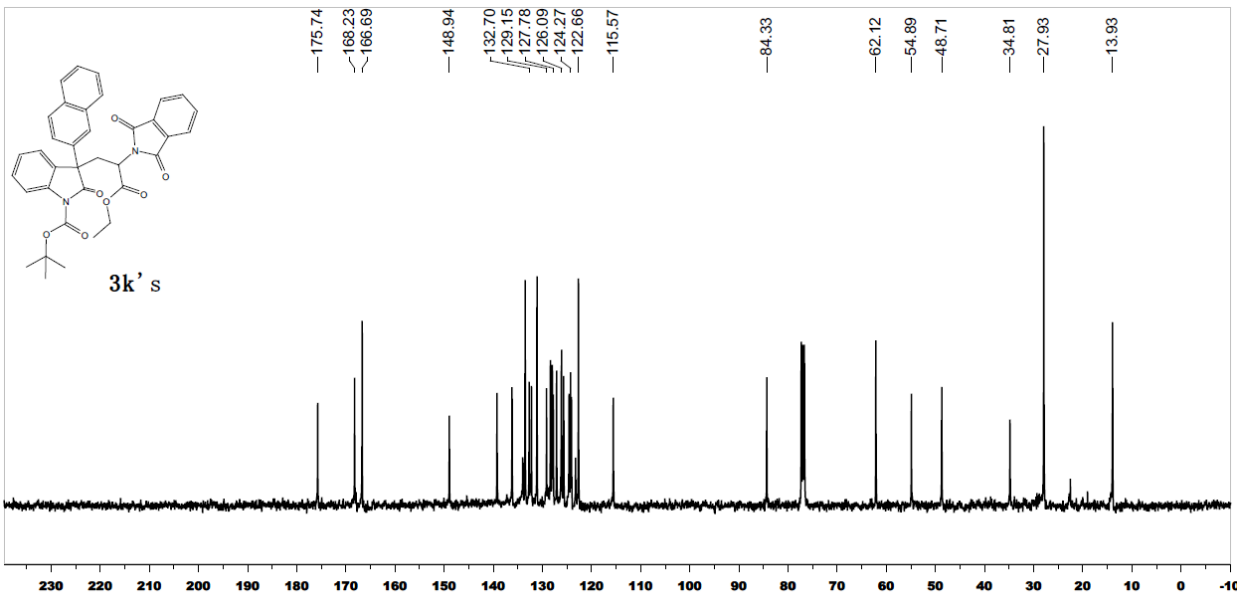
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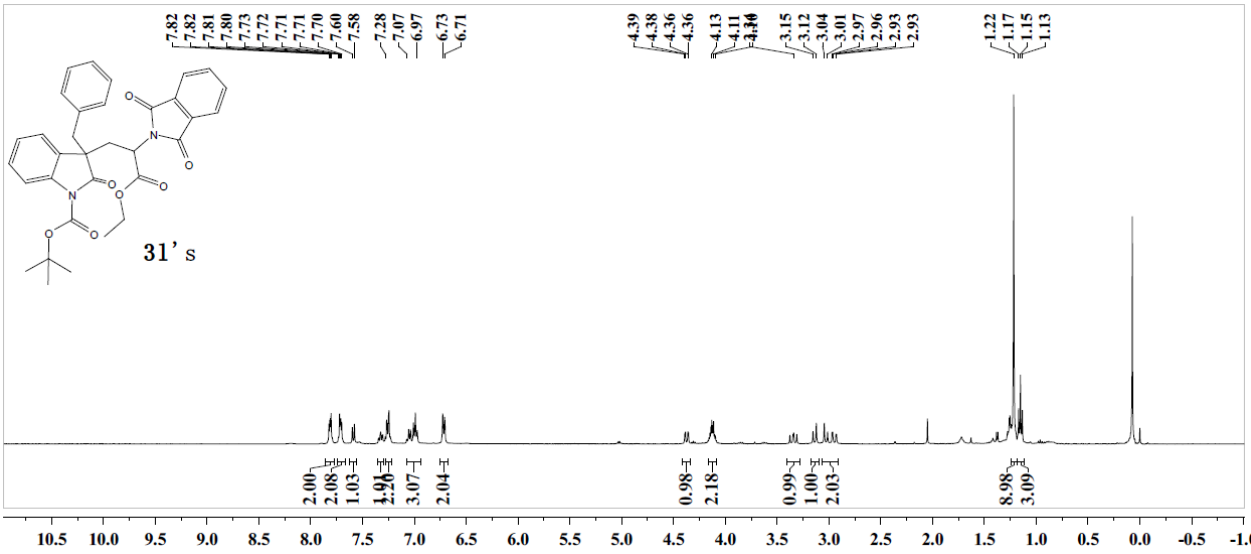
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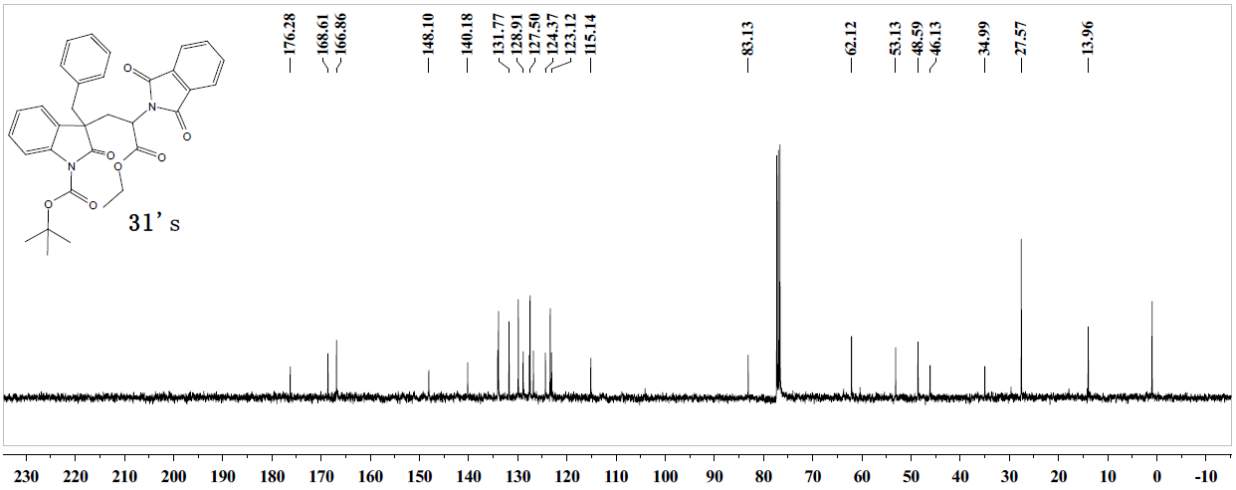
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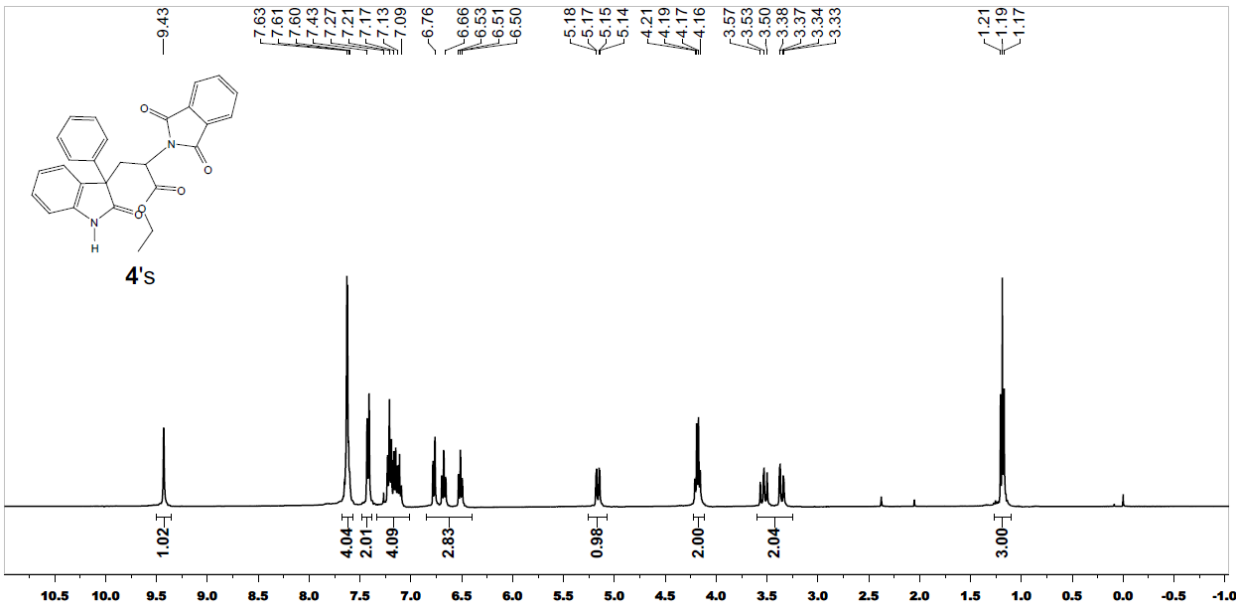
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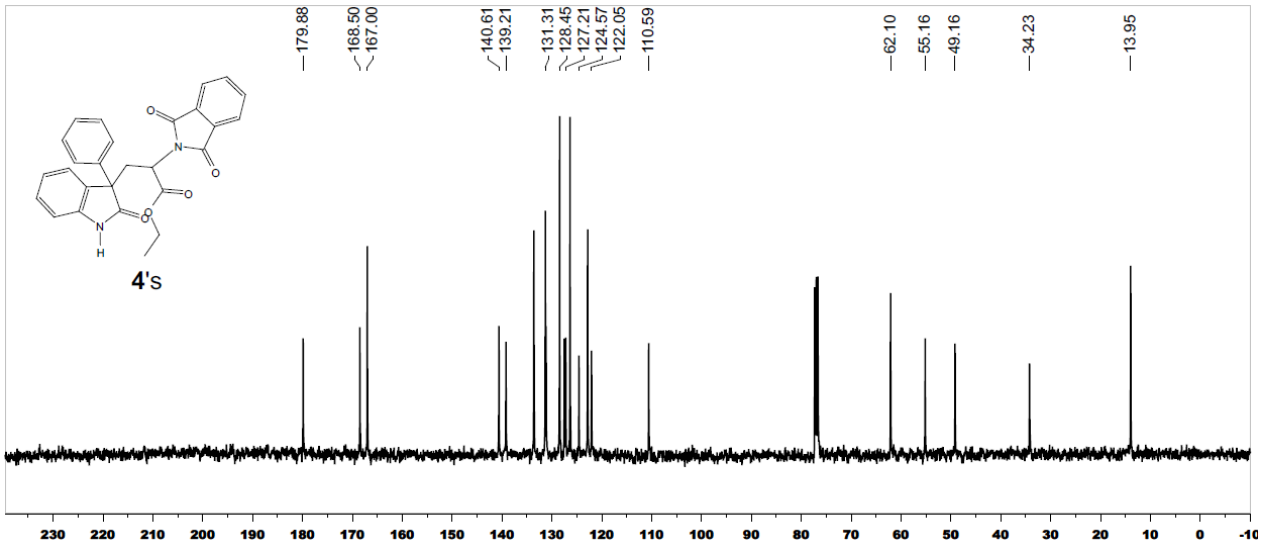
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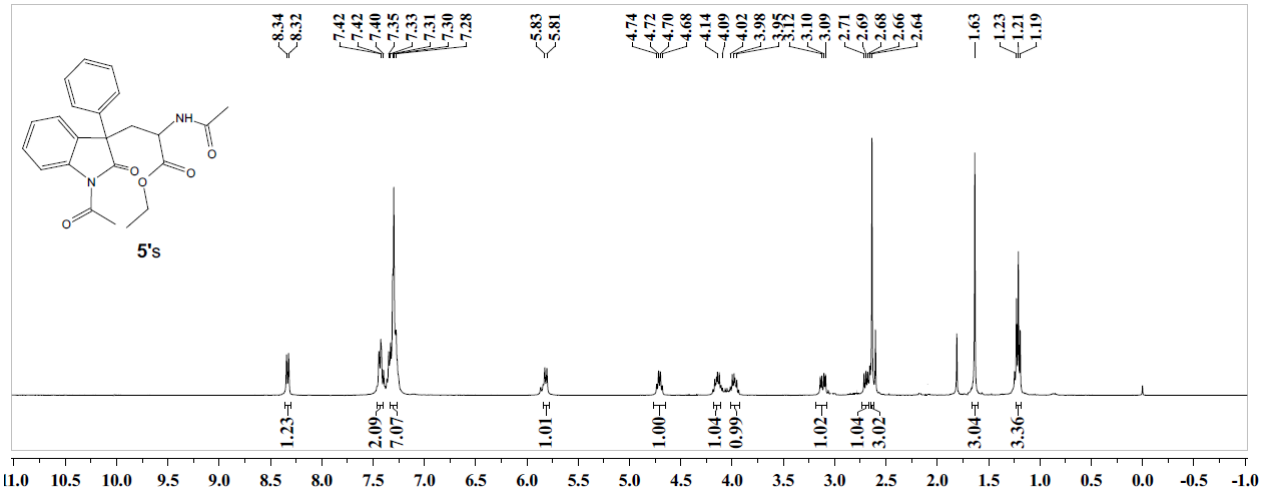
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5.81
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4.72
4.70
4.68
4.14
4.09
4.02
3.98
3.95
3.12
3.10
3.09
2.71
2.69
2.68
2.66
2.64
1.63
1.23
1.21
1.19
1.23
2.09
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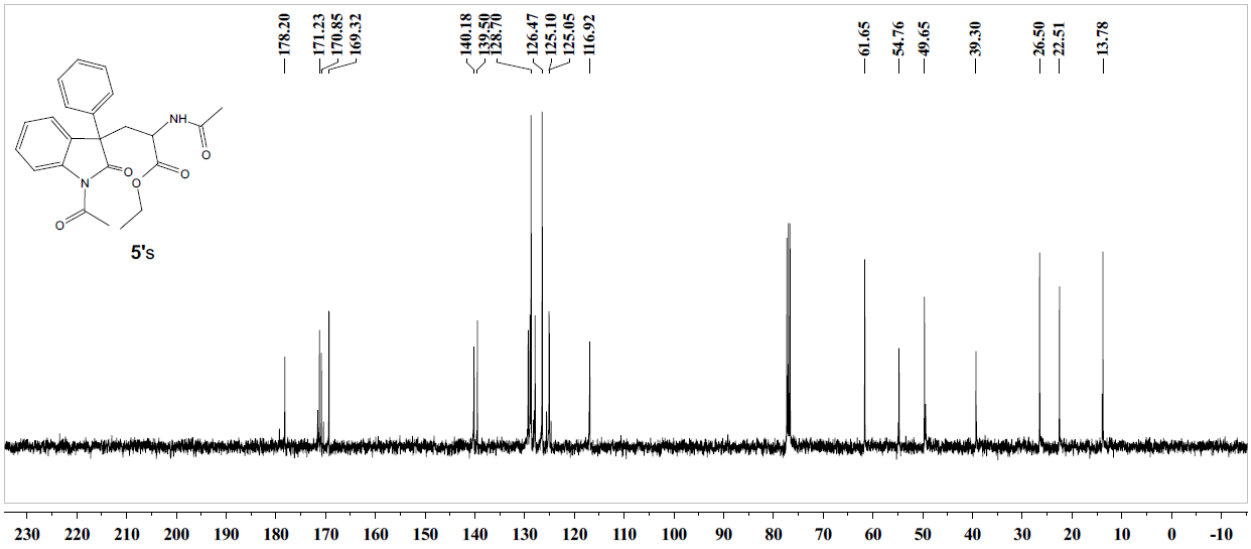
1.01
1.00
1.04
0.99
1.02
1.04
3.02
3.04
3.36
5's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126.47
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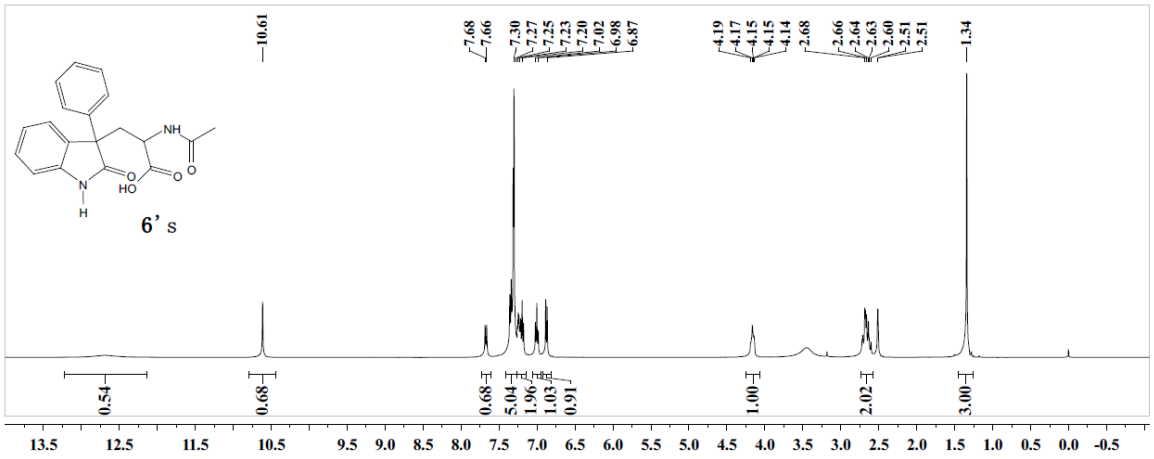
54.76
49.65
39.30
26.50
22.51
13.78
5's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6.98
6.87
4.19
4.17
4.15
4.14
2.68
2.66
2.64
2.63
2.60
2.51
2.51
1.34
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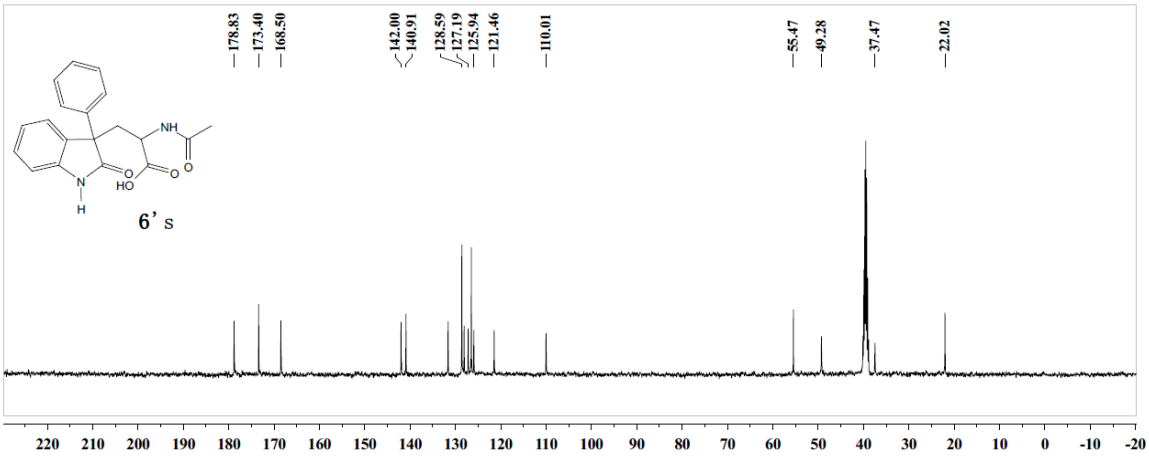
0.68
0.68
5.04
1.96
1.03
0.91
1.00
2.02
3.00
6' s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110.01
55.47
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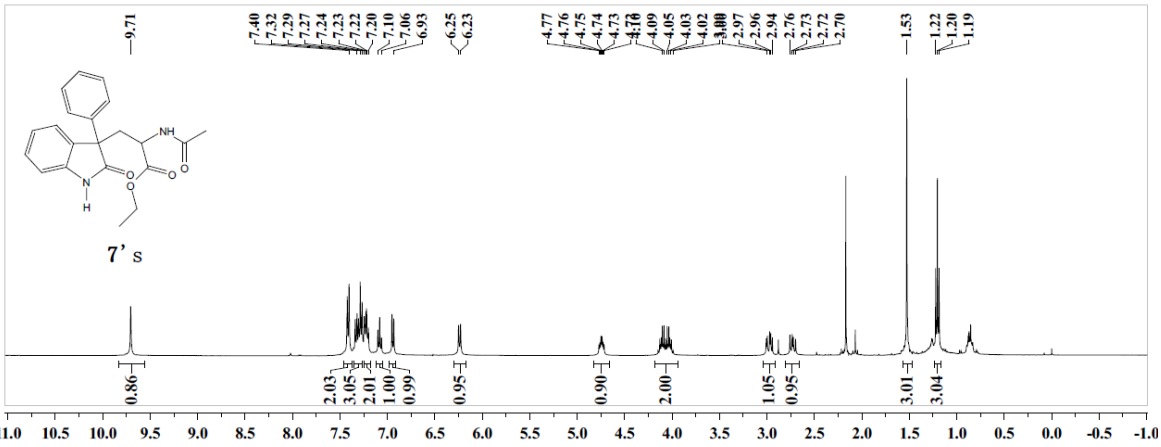
37.47
22.02
6' s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2.94
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2.03
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2.00
1.05
0.95
3.01
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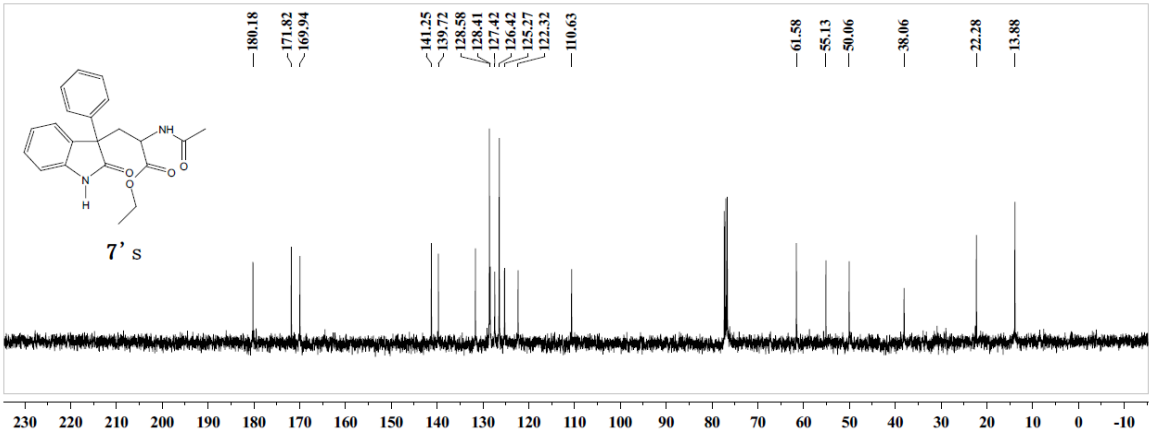
7' s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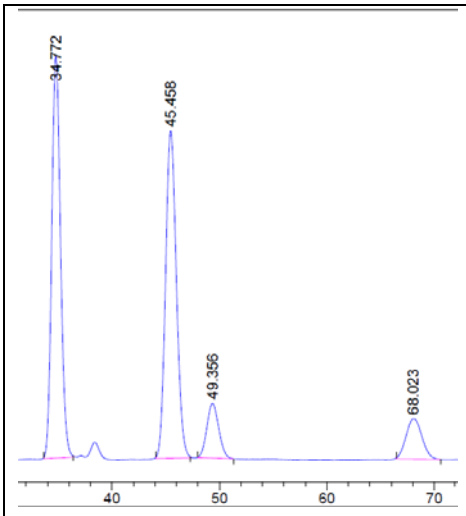
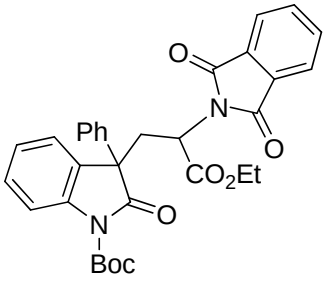
61.58
55.13
50.06
38.06
22.28
13.88
7' s

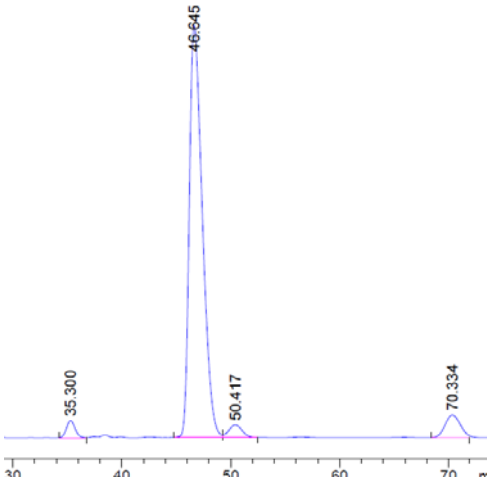
7.The copy of HPLC chromatograms

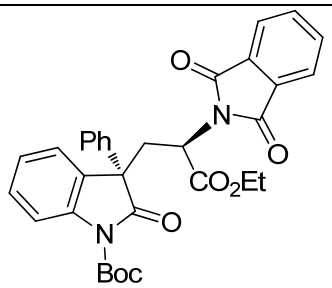




***rac*-3a's**

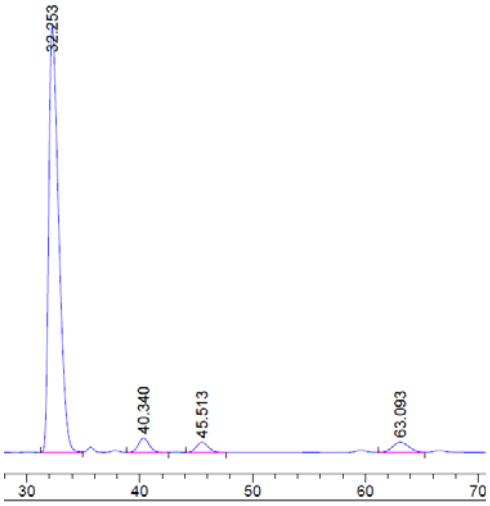
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	34.772	BB	0.8816	1008.14844	17.81303	42.1535
2	45.458	BB	1.0950	1013.26276	14.49732	42.3673
3	49.356	BP	0.9906	186.34465	2.43036	7.7916
4	68.023	BP	1.2158	183.85829	1.78997	7.6876

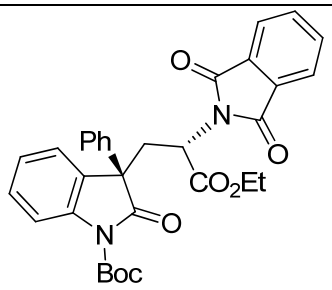




3a's

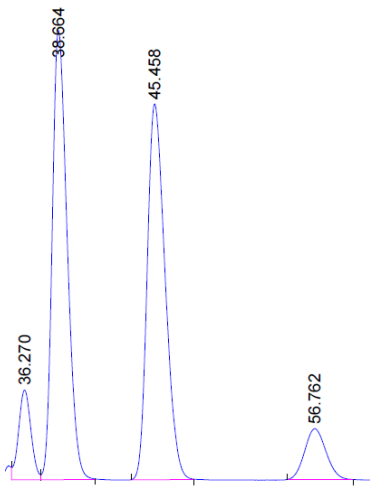
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	35.300	BB	0.8794	393.30270	6.94144	2.5238
2	46.645	BV	1.2784	1.38156e4	166.20982	88.6531
3	50.417	VB	1.2514	451.24500	5.21389	2.8956
4	70.334	BB	1.5373	923.73688	9.23101	5.9275

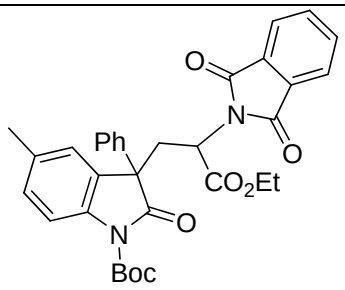




***ent*-3a's**

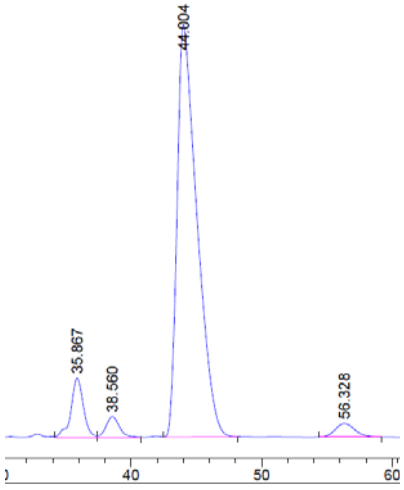
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	32.253	BB	0.9376	1.84095e4	299.85370	90.4251
2	40.340	VP	1.0385	679.68402	10.13670	3.3385
3	45.513	PB	1.1470	531.15454	7.09643	2.6090
4	63.093	VV	1.4835	738.50977	7.26173	3.6275

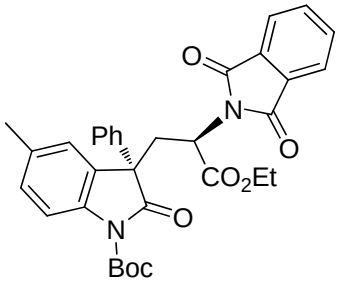




***rac*-3b's**

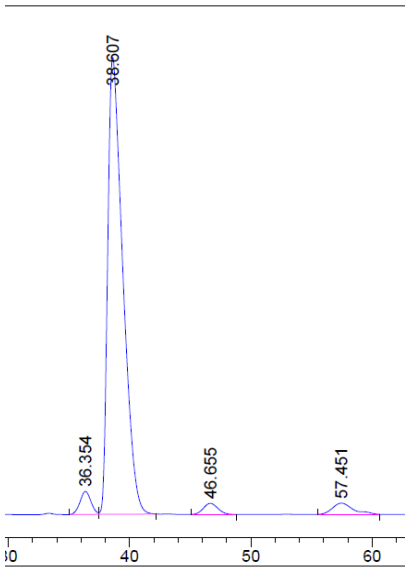
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	36.270	VV	0.9492	1194.19287	19.69297	7.1180
2	38.664	VB	1.1260	7195.13281	98.49303	42.8869
3	45.458	BB	1.3531	7205.44971	82.32357	42.9484
4	56.762	BB	1.5668	1182.23242	11.19634	7.0467

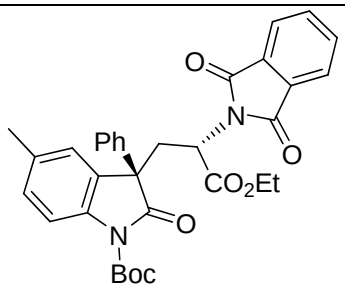




3b's

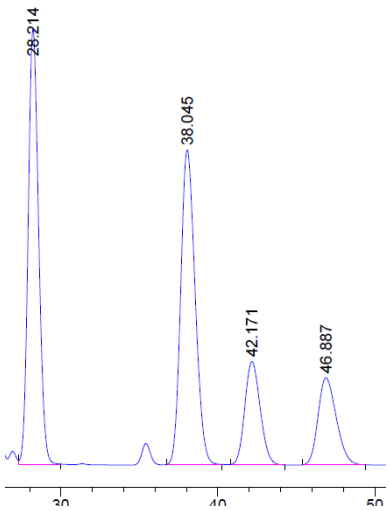
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	35.867	BV	1.0002	2666.17358	40.23814	7.7590
2	38.560	VB	1.0987	1008.75745	14.16581	2.9356
3	44.004	VB	1.5291	2.96666e4	280.25595	86.3346
4	56.328	BB	1.6308	1020.82526	9.40160	2.9708

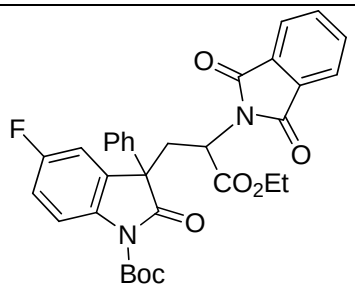




***ent*-3b's**

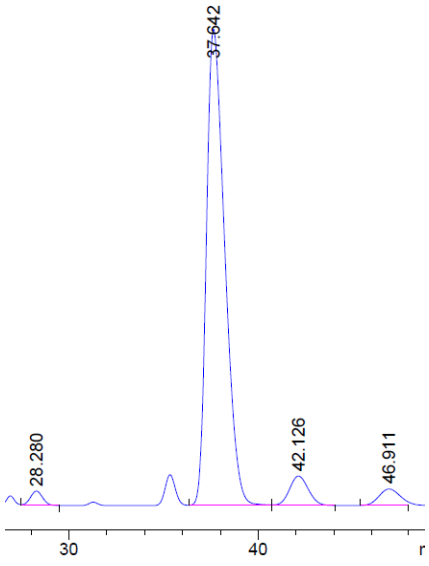
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	36.354	BV	0.9567	771.52252	12.23951	3.3780
2	38.607	VB	1.3391	2.08436e4	242.14435	91.2595
3	46.655	BB	1.2567	493.24014	5.92462	2.1596
4	57.451	BB	1.6169	731.56299	6.02775	3.2030

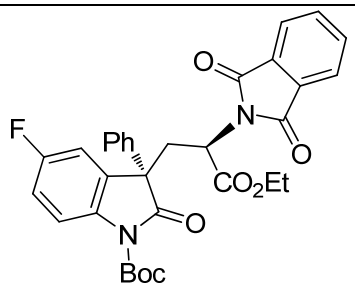




***rac*-3c's**

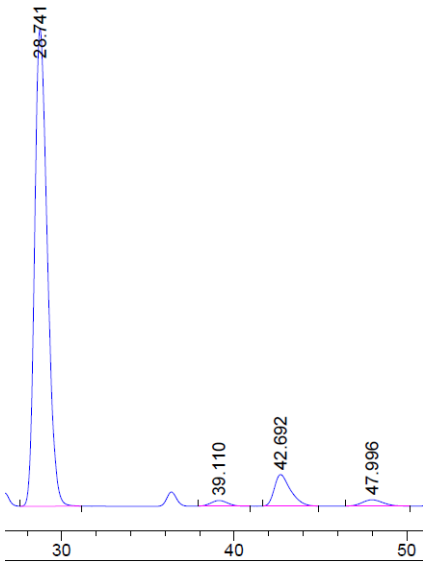
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	28.214	VB	0.7195	7703.85010	166.76460	36.9437
2	38.045	BB	0.9969	7722.15576	120.69139	37.0315
3	42.171	BB	1.0730	2717.44019	39.66395	13.0314
4	46.887	BB	1.2587	2709.51343	33.47735	12.9934

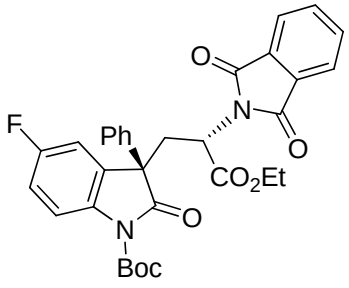




3c's

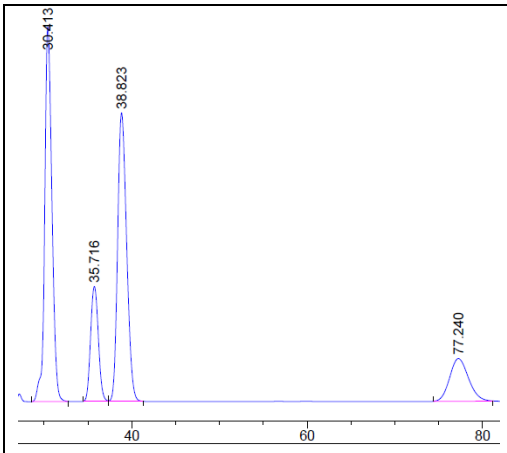
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	28.280	VB	0.7112	474.10678	10.42320	1.8244
2	37.642	VV	1.0468	2.30738e4	343.06104	88.7920
3	42.126	VB	1.0910	1480.43201	21.28465	5.6970
4	46.911	BB	1.2500	958.01373	11.94700	3.6866

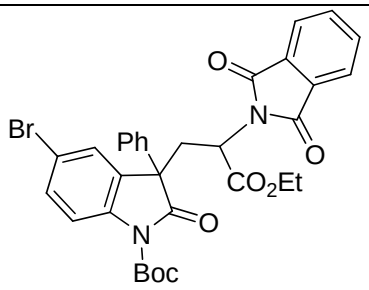




***ent*-3c's**

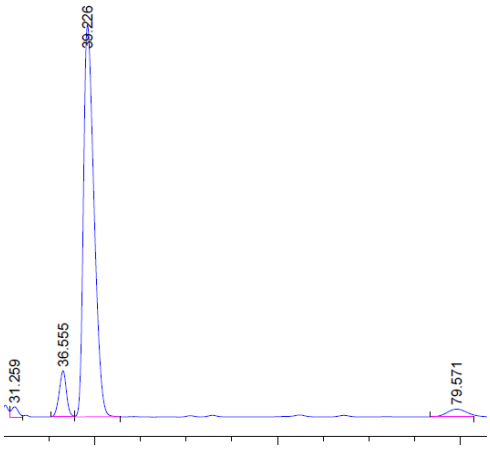
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	28.741	VB	0.7925	1.79361e4	351.96783	89.0373
2	39.110	BB	0.9869	285.31174	4.18854	1.4163
3	42.692	BB	0.9731	1529.85779	23.29139	7.5944
4	47.996	BP	1.2039	393.21387	4.65504	1.9520

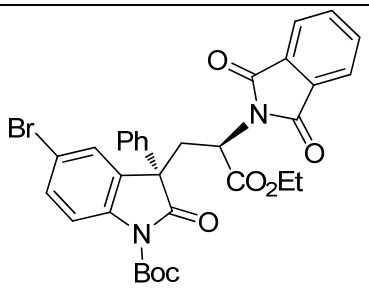




***rac*-3d's**

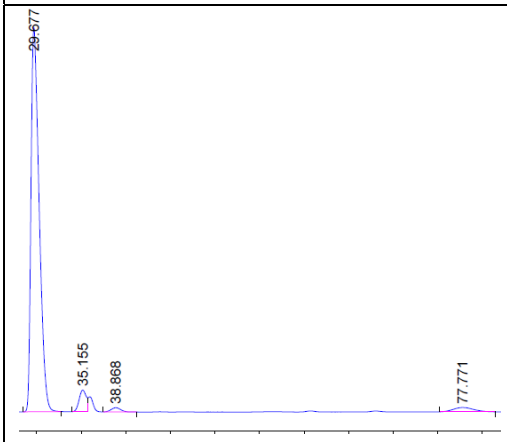
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	30.413	BB	0.8773	1.45310e4	253.92920	38.6095
2	35.716	BV	0.9776	4816.13135	77.89231	12.7967
3	38.823	VB	1.1060	1.39447e4	195.47040	37.0518
4	77.240	BB	2.2320	4343.94580	28.98341	11.5421

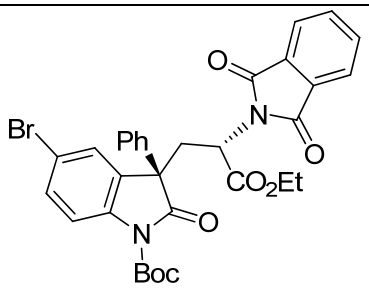




3d's

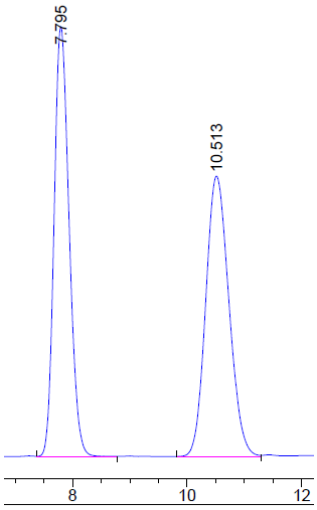
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	31.259	VV	0.8069	650.14020	12.33816	1.4788
2	36.555	BV	0.8425	3140.66724	56.85649	7.1440
3	39.226	VB	1.2288	3.86503e4	483.91364	87.9162
4	79.571	BB	2.3711	1521.53955	9.61113	3.4610

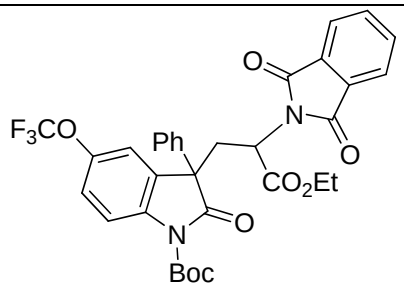




***ent*-3d's**

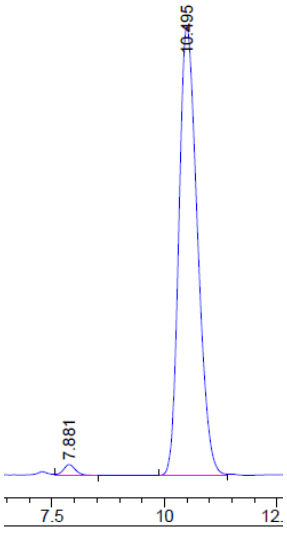
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	29.677	PB	0.9718	3.65054e4	574.19141	91.6604
2	35.155	BV	0.8512	1805.18433	32.38474	4.5326
3	38.868	BP	1.1490	458.12622	6.18853	1.1503
4	77.771	BB	1.9421	1058.07800	6.53252	2.6567

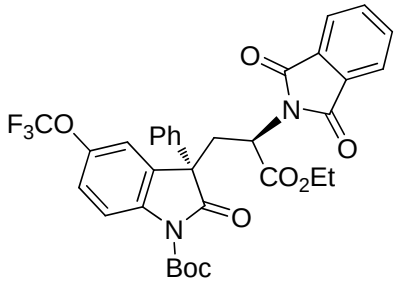




***rac*-3e's**

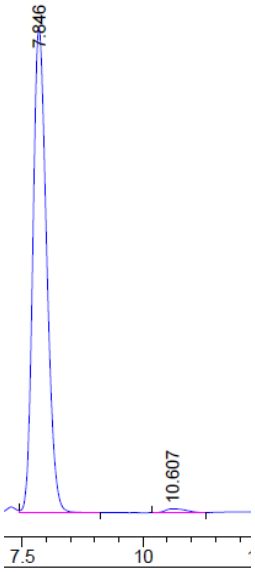
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.795	VB	0.2823	7670.97607	421.30676	49.7839
2	10.513	BV	0.4390	7737.58545	274.90714	50.2161

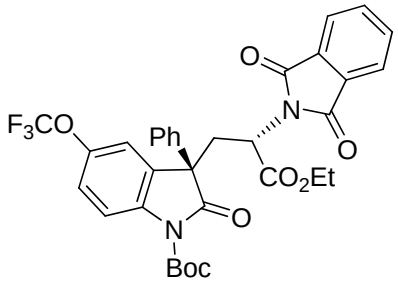




3e's

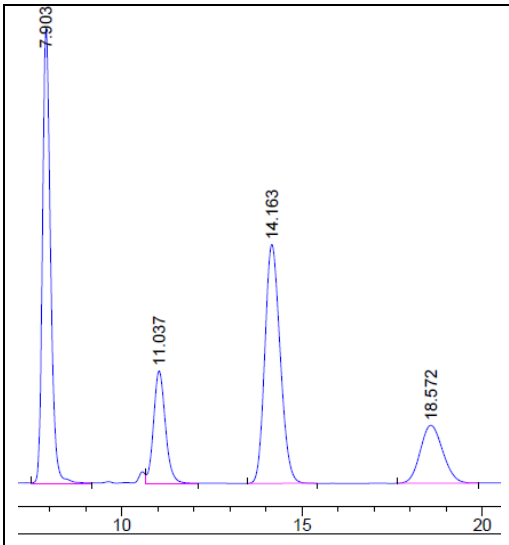
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.881	VB	0.2872	294.58163	15.60914	1.5649
2	10.495	BV	0.4445	1.85293e4	647.47321	98.4351

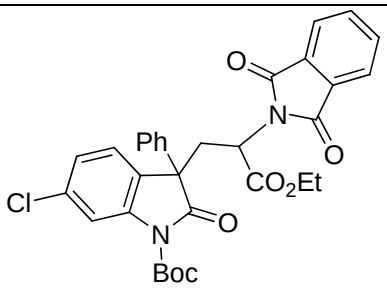




***ent*-3e's**

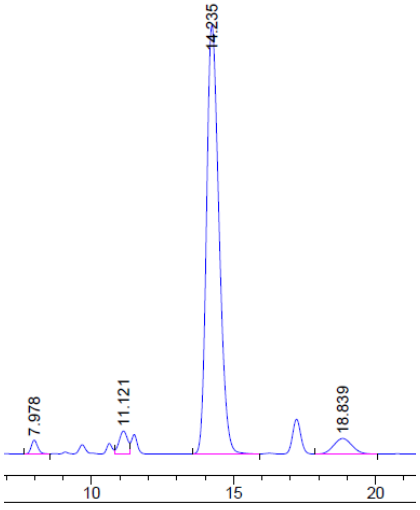
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.846	VB	0.3065	9403.25879	475.43497	98.7560
2	10.607	BV	0.4867	118.45387	3.91814	1.2440

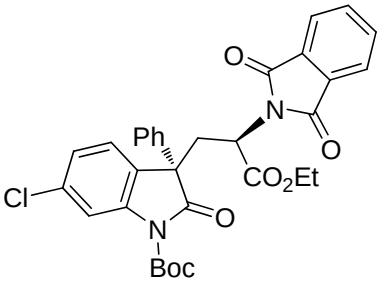




***rac*-3f's**

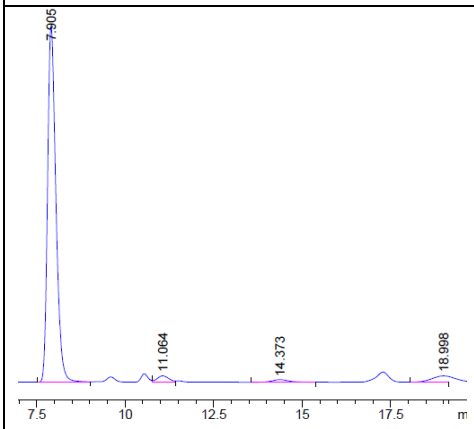
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.903	VB	0.2372	5401.33203	346.46613	36.8642
2	11.037	VP	0.3499	1949.15442	85.68139	13.3030
3	14.163	PP	0.4612	5383.96289	182.20558	36.7456
4	18.572	BP	0.6752	1917.53235	44.18195	13.0872

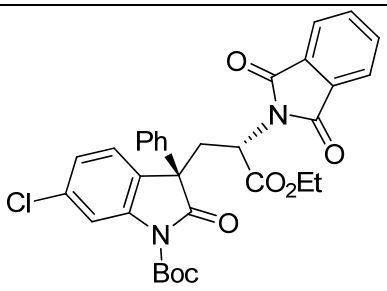




3f's

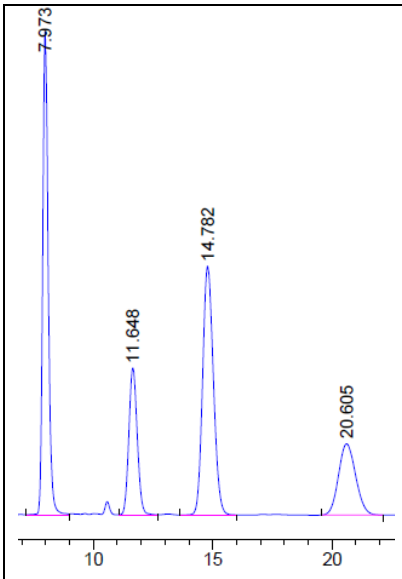
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.978	VB	0.2446	191.14676	11.96448	1.5278
2	11.121	VV	0.3253	414.60913	19.84727	3.3138
3	14.235	BB	0.4720	1.12945e4	370.67981	90.2724
4	18.839	VB	0.7091	611.32495	13.49284	4.8861

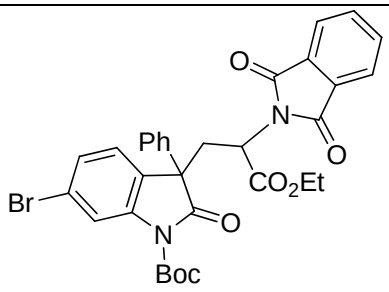




***ent*-3f's**

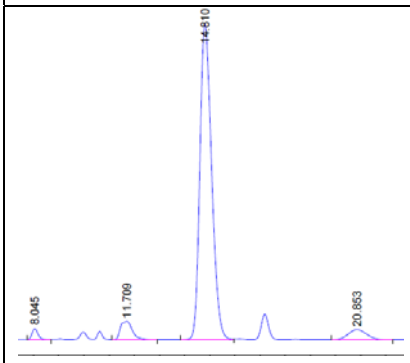
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.905	BV	0.2490	1.05414e4	644.78400	91.5687
2	11.064	VV	0.3573	268.64395	11.61227	2.3336
3	14.373	VB	0.5127	156.71306	4.64885	1.3613
4	18.998	BBA	0.7398	545.24750	11.43336	4.7363

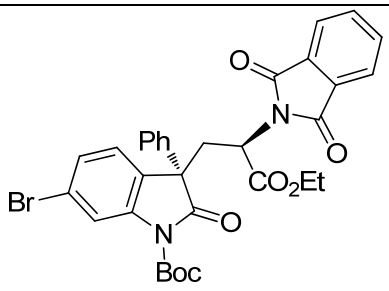




***rac*-3g's**

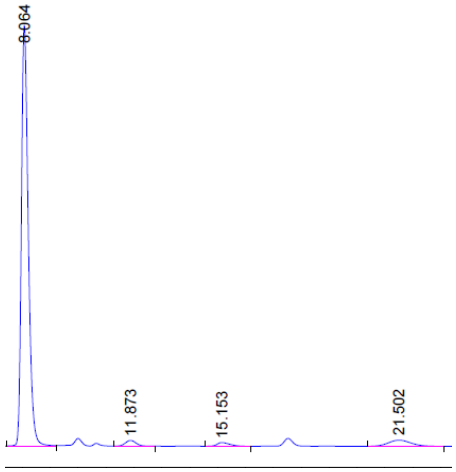
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.973	VV	0.2457	4775.54492	297.18848	34.1202
2	11.648	BB	0.3820	2217.65576	90.50834	15.8447
3	14.782	VB	0.4915	4807.46387	153.11142	34.3483
4	20.605	BB	0.7851	2195.57031	43.84682	15.6869

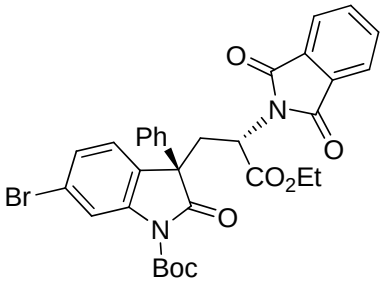




3g's

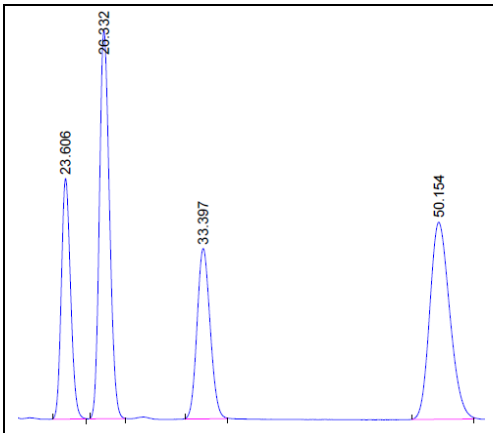
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.045	BV	0.2578	294.44705	17.21502	1.6598
2	11.709	BP	0.4603	928.83417	27.96521	5.2359
3	14.810	BV	0.5055	1.57311e4	486.31155	88.6766
4	20.853	BP	0.7800	785.47864	15.51423	4.4278

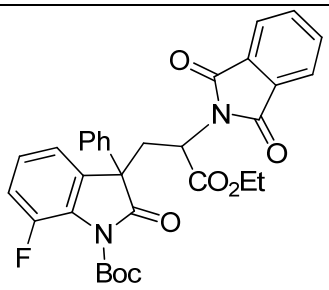




***ent*-3g's**

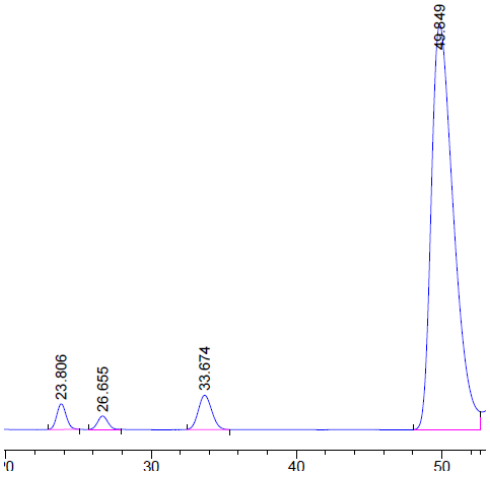
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.064	VV	0.2611	1.92933e4	1125.51379	92.1639
2	11.873	VB	0.4181	421.17496	15.54265	2.0119
3	15.153	VP	0.4504	300.85324	9.90532	1.4372
4	21.502	BB	0.8806	918.35974	16.32311	4.3870

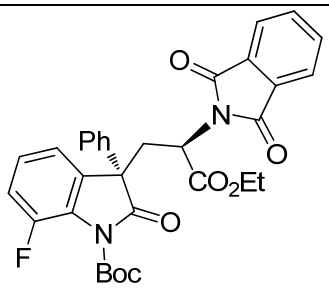




***rac*-3h's**

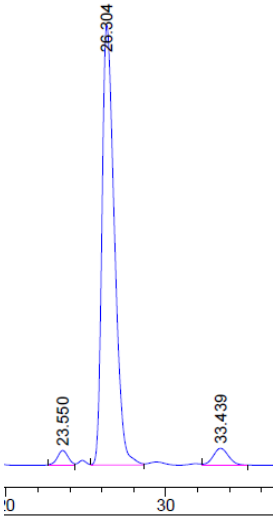
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	23.606	BB	0.7041	1231.84326	26.99862	18.1014
2	26.332	BB	0.7739	2161.34473	43.56816	31.7599
3	33.397	BB	1.0110	1236.76978	19.11837	18.1737
4	50.154	BB	1.4878	2175.29687	22.12472	31.9650

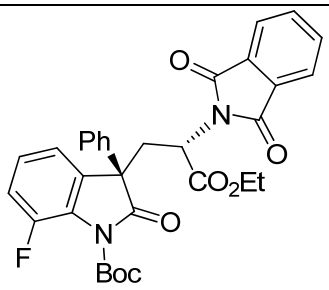




3h's

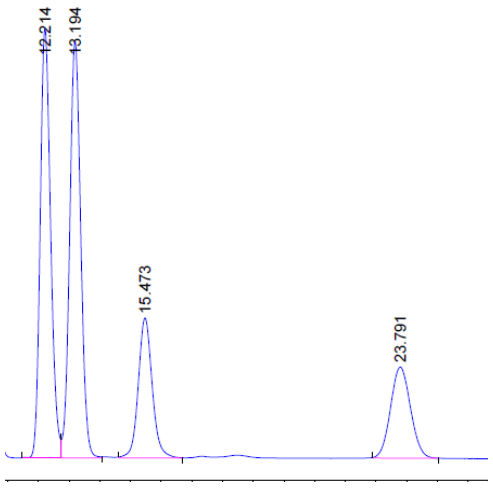
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	23.806	BB	0.7059	397.63440	8.73373	2.4722
2	26.655	BB	0.7617	225.56429	4.59722	1.4024
3	33.674	BB	0.9967	753.79675	11.69371	4.6866
4	49.849	BV	1.6180	1.47071e4	137.79396	91.4388

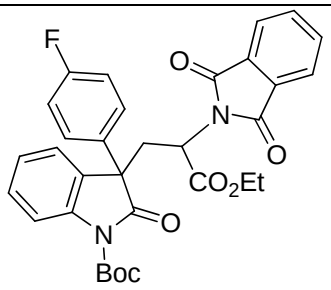




***ent*-3h's**

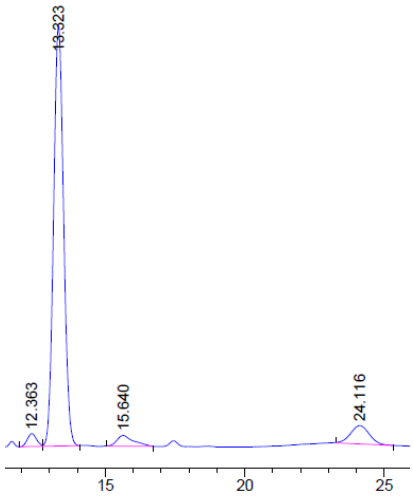
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	23.550	BV	0.6808	158.92760	3.39071	2.6932
2	26.304	VB	0.8311	5486.28320	101.56715	92.9725
3	33.439	BB	0.7881	255.76208	3.87219	4.3342

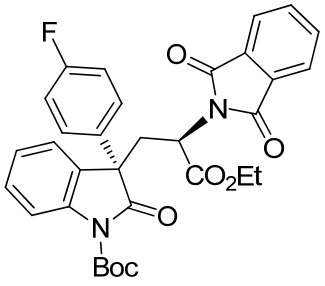




***rac*-3i's**

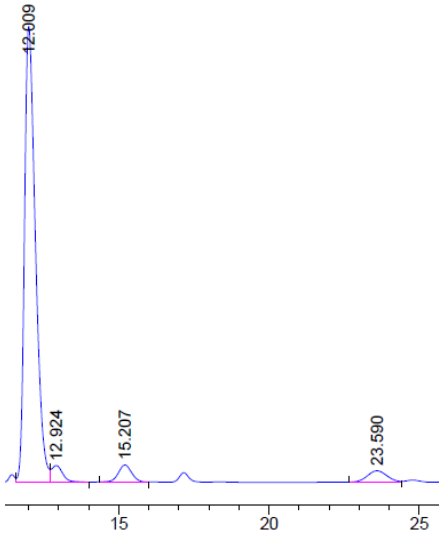
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.214	BV	0.3655	1807.98865	76.65119	34.8414
2	13.194	VB	0.3868	1855.07495	74.44591	35.7488
3	15.473	BB	0.4848	789.39655	25.00112	15.2123
4	23.791	BB	0.7086	736.73743	16.27775	14.1975

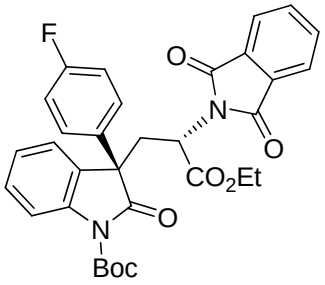




3i's

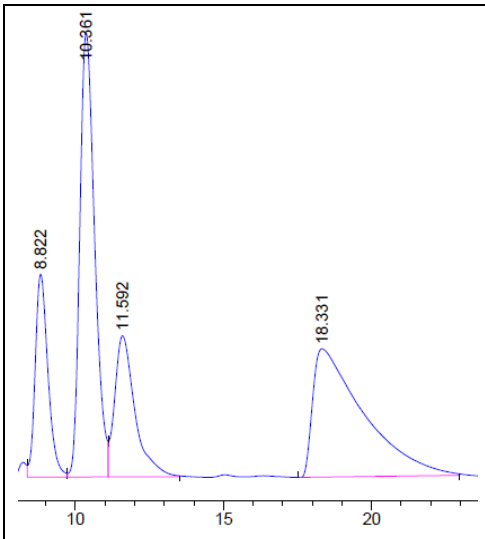
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.363	VV	0.3579	28.08546	1.22427	2.4749
2	13.323	VB	0.3894	983.12793	39.49640	86.6332
3	15.640	BB	0.5565	42.56693	1.02063	3.7510
4	24.116	BP	0.6018	81.03664	1.73009	7.1409

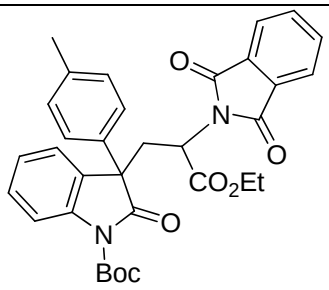




***ent*-3i's**

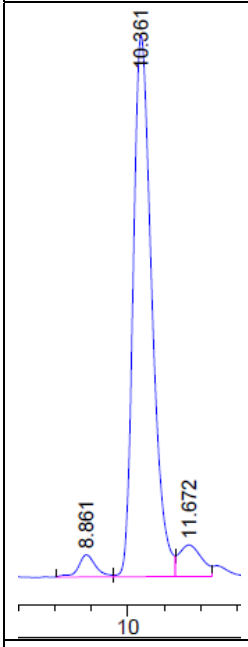
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.009	VV	0.3850	7904.37988	312.89462	88.2053
2	12.924	VB	0.3946	307.16898	11.55427	3.4277
3	15.207	BV	0.4903	387.34827	11.99399	4.3224
4	23.590	BV	0.7241	362.44571	7.86304	4.0445

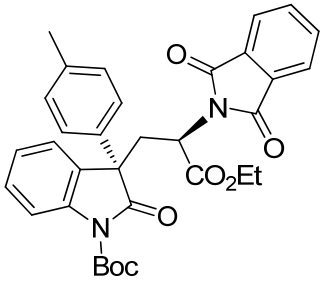




***rac*-3j's**

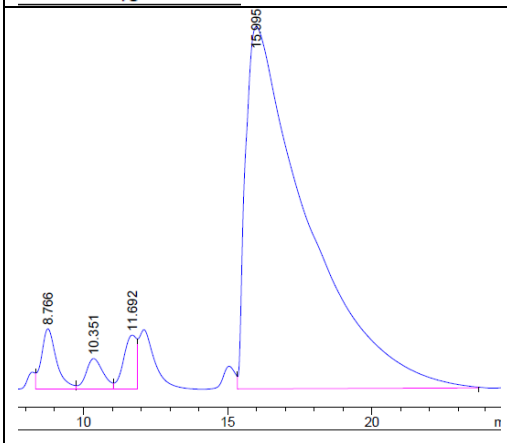
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.822	VV	0.4600	751.53058	25.09801	13.9380
2	10.361	VV	0.5388	1918.66101	54.89978	35.5839
3	11.592	VB	0.7187	831.62317	17.46173	15.4235
4	18.331	PB	1.5552	1890.12134	15.87302	35.0546

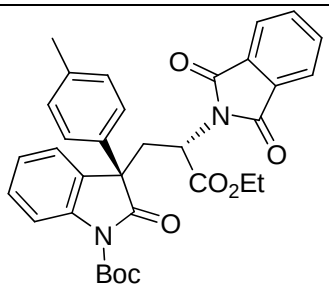




3j's

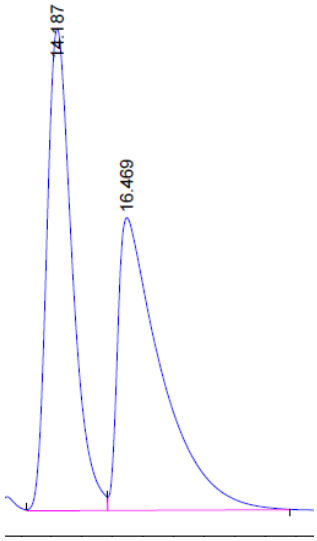
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.861	BV	0.4800	78.48262	2.36730	3.4494
2	10.361	VV	0.5473	2049.86914	57.85296	90.0946
3	11.672	VV	0.6174	146.88887	3.38153	6.4560

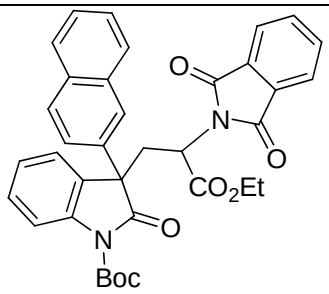




***ent*-3j's**

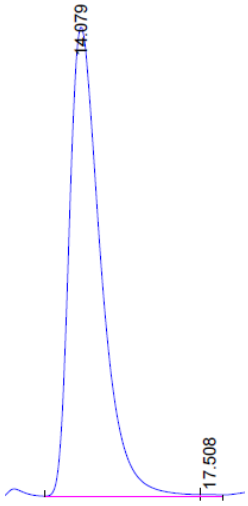
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.766	VV	0.5371	390.07953	10.74471	3.6999
2	10.351	VV	0.6225	223.98207	5.44662	2.1245
3	11.692	VV	0.4798	300.38251	9.64625	2.8491
4	15.995	VB	1.9539	9628.52148	64.72714	91.3265

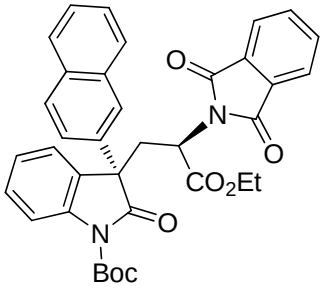




***rac*-3k's**

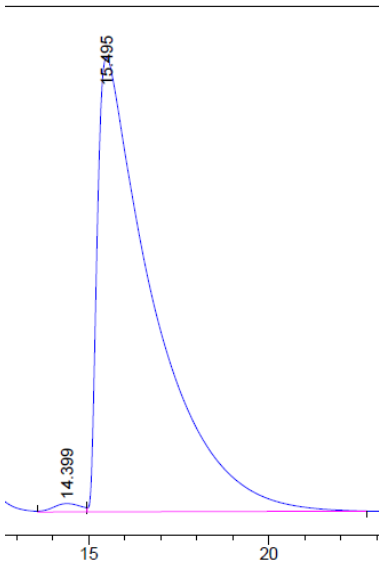
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.214	BV	0.3655	1807.98865	76.65119	34.8414
2	13.194	VB	0.3868	1855.07495	74.44591	35.7488
3	15.473	BB	0.4848	789.39655	25.00112	15.2123
4	23.791	BB	0.7086	736.73743	16.27775	14.1975

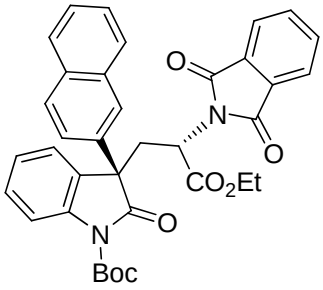




3k's

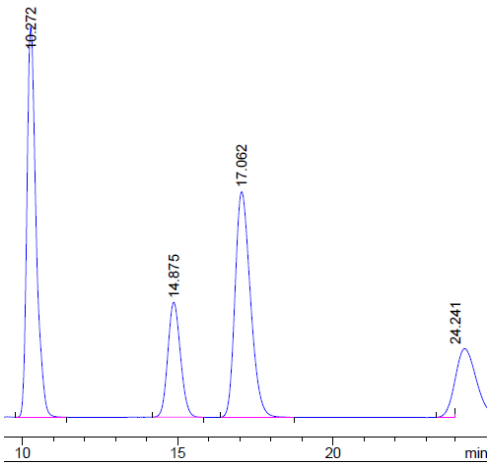
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.079	VV	0.8934	3.98536e4	677.12244	99.7314
2	17.508	VV	0.4648	107.31817	3.17039	0.2686

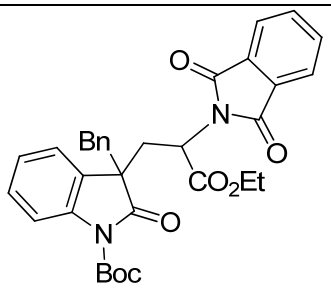




***ent*-3k's**

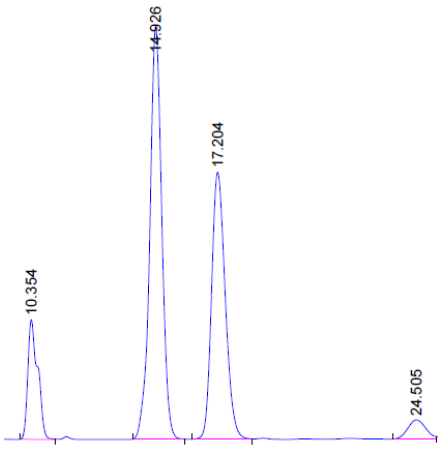
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.399	VV	0.8159	272.01437	5.21016	0.8928
2	15.495	VB	1.4757	3.01964e4	280.20679	99.1072

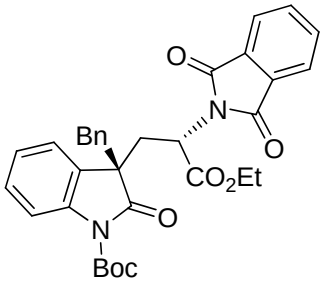




***rac*-3l's**

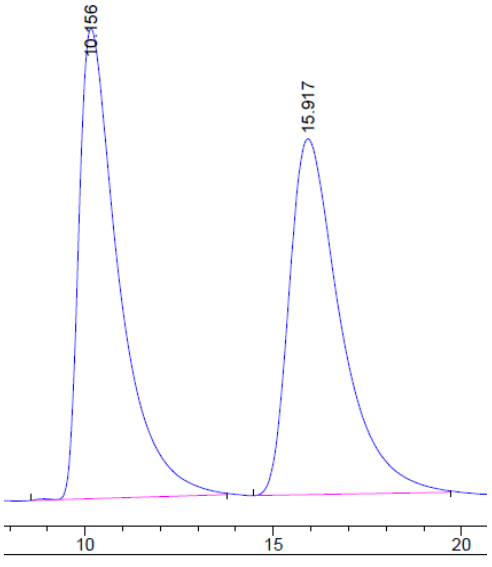
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.272	VB	0.3114	4362.61377	213.27551	36.0659
2	14.875	BB	0.4406	1771.86682	62.64414	14.6481
3	17.062	BB	0.5321	4225.85791	122.93521	34.9354
4	24.241	BBA	0.7265	1735.88049	37.49636	14.3506

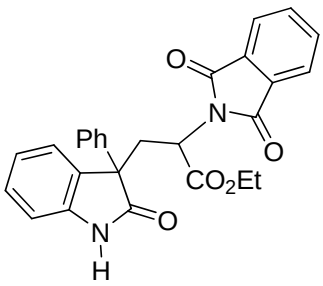




***ent*-3l's**

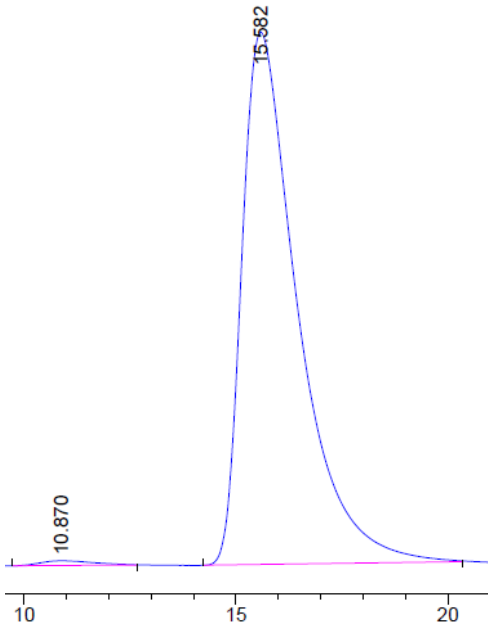
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.354	BB	0.3595	748.97937	29.57887	11.7108
2	14.926	BB	0.4688	3126.94702	101.85064	48.8920
3	17.204	BB	0.5442	2304.75610	66.01456	36.0365
4	24.505	BV	0.6471	214.94107	4.72551	3.3608

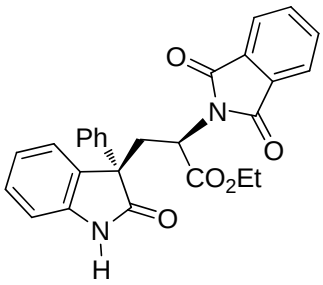




***rac*-4's**

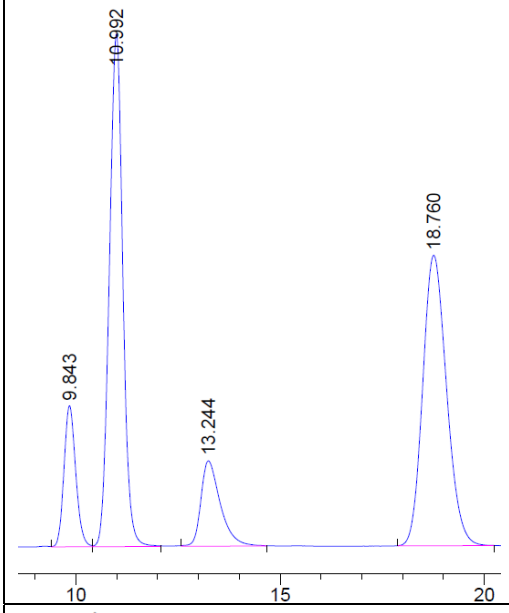
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.156	BB	1.0726	4154.68457	56.36237	50.6381
2	15.917	PB	1.3994	4049.97925	42.63790	49.3619

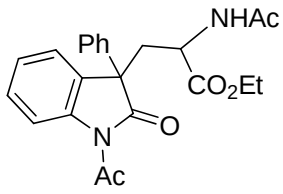




4's

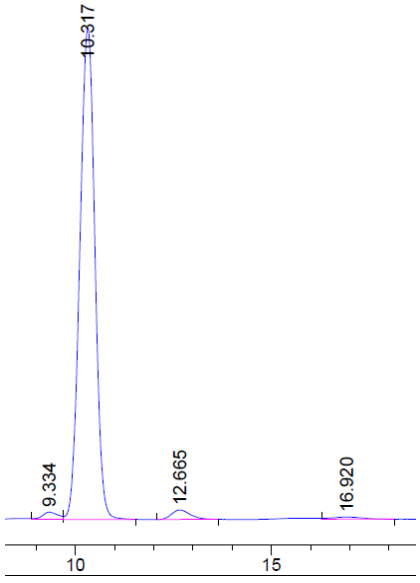
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.870	PB	1.0382	105.45992	1.19510	0.8696
2	15.582	PB	1.3674	1.20225e4	131.39194	99.1304

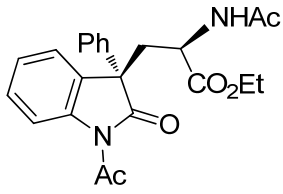




***rac*-5**'s

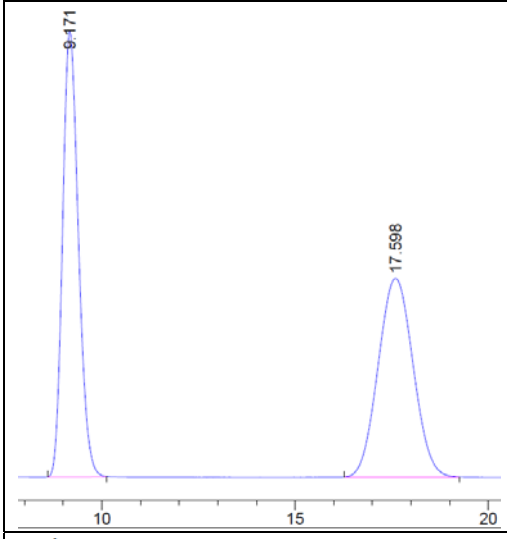
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.843	VV	0.3088	852.97351	42.70146	9.6563
2	10.992	VB	0.3546	3554.49976	155.18039	40.2394
3	13.244	BB	0.4993	854.63812	25.85102	9.6751
4	18.760	BB	0.6309	3571.26440	87.97264	40.4292

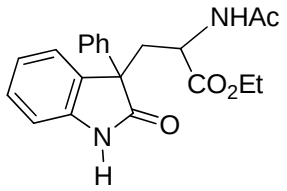




5's

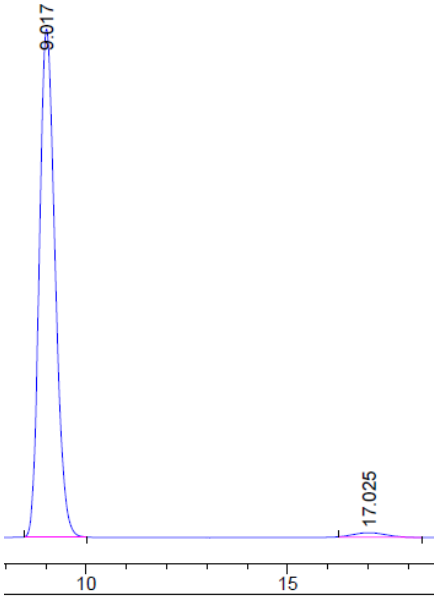
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.334	BV	0.4122	95.46962	3.36860	1.5574
2	10.317	VB	0.4155	5839.53320	219.28169	95.2577
3	12.665	PB	0.5231	143.69739	4.24490	2.3441
4	16.920	BB	0.6902	51.54689	9.34435e-1	0.8409

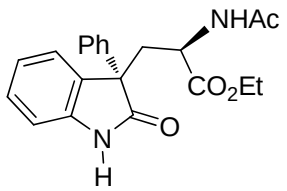




***rac*-7's**

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.171	BB	0.4426	3889.60596	136.71960	50.3286
2	17.598	BB	0.9758	3838.80786	61.01097	49.6714





7's

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.017	BB	0.4215	8040.21338	296.25626	98.2020
2	17.025	BP	0.6828	147.21219	2.62738	1.7980