Enantioselective Synthesis of Tryptophan Derivatives by a Tandem Friedel–Crafts Conjugate Addition/Asymmetric Protonation Reaction

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Supporting Information 1 (Experimental):

Table of Contents

1. Materials and Methods. Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Methylene chloride, deuterated methylene chloride, dioxane, ether, tetrahydrofuran, and toluene were dried by passing through activated alumina. Dichloroethane and chloroform were distilled over calcium hydride. Powdered 4Å molecular sieves were flame-dried under vacuum immediately prior to use. Potassium carbonate was dried for 12 h at 130 °C under vacuum and 2,6-lutidine was distilled over $AlCl_3$. All other commercially obtained reagents were used as received unless specifically indicated. (*R*)-BINOL (**9a**), 2-phenylindole (**6a**) and 2-methylindole (**6r**) were purchased from Alfa Aesar, *N*-methyl-2-phenylindole (**6b**) was obtained from Sigma-Aldrich, and 1 M $SnCl_4$ in CH_2Cl_2 was purchased from Acros Organics. (*R*)-3,3'-diphenyl-BINOL (**9b**),[1] (*R*)-3,3'-dimethyl-BINOL (**9c**),[2] (*R*)-3,3'-dichloro-BINOL (**9e**)[3], (*R*)-3,3'-dibromo-BINOL (**9f**),[4] (*R*)-3,3'-dimethoxy-BINOL (**9g**),[4] (*R*)-6,6'-dimethyl-BINOL (**9i**)[5] and (*R*)-6,6'-dibromo-BINOL (**9j**)[6] were prepared according to literature procedures. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel column chromatography was performed either as described by Still et al. (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem*. **1978**, *43*, 2923.) using silica gel (particle size 0.032-0.063) purchased from Silicycle or using pre-packaged RediSep®Rf columns on a CombiSilica gel Rf system (Teledyne ISCO Inc.). Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^{1}H and ^{13}C NMR were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz respectively) or a Varian Inova 600 (at 600 MHz and 150 MHz respectively) and are reported relative to internal chloroform (^{1}H, δ = 7.26, ^{13}C, δ = 77.0) or internal acetonitrile (^{1}H, δ = 1.94, ^{13}C, δ = 1.32). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system with Chiralcel AD-H, OD-H, AS-H, OB-H, and OJ-H

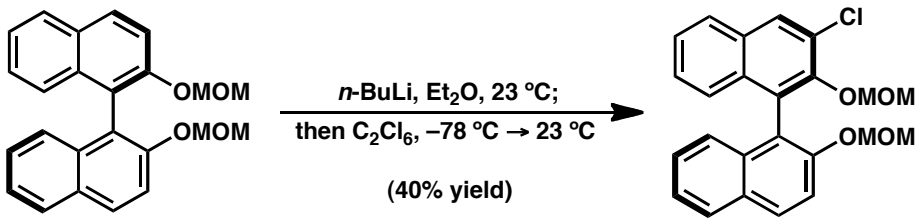
[1] Zhang, X. *PCT Int. Appl.* WO 2002040491, 2002.
[2] Wu, T. R.; Shen, L.; J. M. Chong., J. M. *Org. Lett.* **2004**, *6*, 2701.
[3] Ito, K.; Takahashi, M.; Hoshino, T.; Nishiki, M.; Ohba. Y. *Lett. Org. Chem.* **2006**, *3*, 735.
[4] Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 5139.
[5] Verga, D.; Percivalle, C.; Doria, F.; Porta, A.; Freccero, M. *J. Org. Chem.* **2011**, *76*, 2319.
[6] Rueping, M.; Sugiono, E.; Steck, A.; Thiessmann, T. *Adv. Synth. Catal.* **2010**, *352*, 281.

columns (4.6 mm x 25 cm). HRMS were acquired using either an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI) or mixed (MM) ionization mode, or obtained from the Caltech Mass Spectral Facility.

Abbreviations used: BINOL – 1,1'-bi(2-naphthol); IPA – isopropanol; Et_2O – diethyl ether; PhMe – toluene; EtOAc – ethyl acetate; DCE – dichloroethane; DCM – dichloromethane; MeCN – acetonitrile; ee – enantiomeric excess

2. Catalyst and Substrate Preparation.

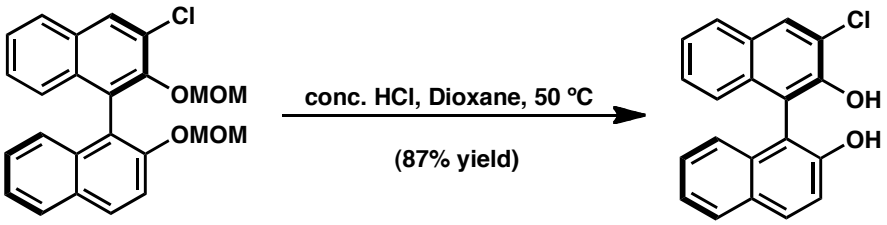
Preparation of (*R*)-3-chloro-BINOL (9d)



S1 **S2**

To a flame-dried 100 mL flask containing MOM–protected (*R*)-BINOL **S1**[2] (748 mg, 2.00 mmol, 1.00 equiv) was added Et_2O (45 mL), followed by dropwise addition of *n*-BuLi as a solution in hexanes (2.5 M, 960 μL, 2.40 mmol, 1.20 equiv) at room temperature. The mixture was then stirred at room temperature for 3 h and subsequently cooled to –78 ºC, followed by addition of C_2Cl_6 (569 mg, 2.40 mmol, 1.20 equiv) in one portion. The reaction mixture was allowed to warm to room temperature over 3 h, then diluted with EtOAc (15 mL) and washed with saturated aqueous NH_4Cl (50 mL). The aqueous layer was extracted with EtOAc (45 mL) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated. The crude yellow oil was purified by silica gel chromatography (0:100 to 12:88 EtOAc:hexanes) to yield 328 mg (40% yield) of **S2** as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.97 (d, J = 9.0 Hz, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.59 (d, J = 9.1 Hz, 1H), 7.42 (ddd, J = 8.1, 6.7, 1.3 Hz, 1H), 7.37 (ddd, J = 8.1, 6.8, 1.2 Hz, 1H), 7.28 (ddd, J = 8.2, 6.8, 1.3 Hz, 1H), 7.24 (ddd, J = 8.5, 6.7, 1.3 Hz, 1H), 7.18 (dddd, J = 8.6, 1.3, 0.7, 0.7 Hz, 1H), 7.16 (ddd, J = 8.5, 1.8, 0.8 Hz, 1H), 5.15 (d, J = 7.0 Hz, 1H), 5.04 (d, J = 7.0 Hz, 1H), 4.80 (d, J = 5.6 Hz, 1H), 4.75 (d, J = 5.6 Hz, 1H), 3.19 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 148.9,

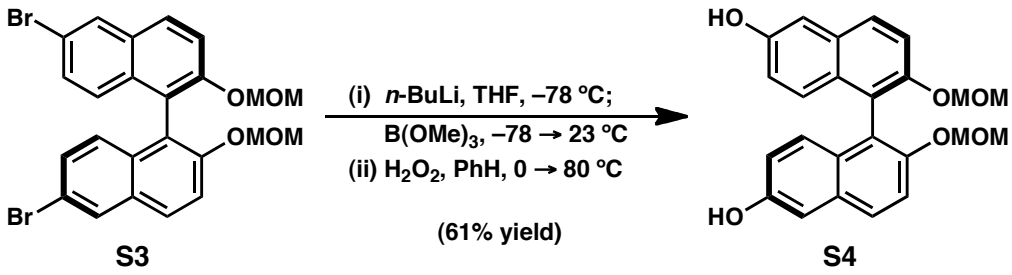
133.8, 132.6, 131.1, 130.0, 129.5, 128.8, 128.0, 127.9, 127.8, 127.0, 126.7, 126.4, 126.1, 125.8, 125.5, 124.2, 119.9, 116.3, 98.8, 94.9, 56.5, 55.9; IR (NaCl/thin film): 2955, 2902, 1594, 1508, 1354, 1241, 1159, 1149, 1034, 1014, 961, 922 cm^{-1}; $[\alpha]_D^{25}$ = +69.1 (*c* = 0.90, $CHCl_3$). HRMS (FAB+) calc'd for M^+ 408.1128, found 408.1128.



S2 **9d**

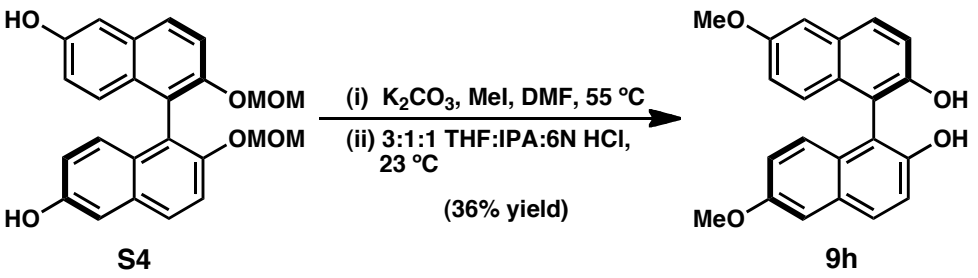
A 10 mL flask was charged with **S2** (305 mg, 0.75 mmol, 1.00 equiv), dioxane (3.7 mL) and aqueous HCl (12 M, 130 μL, 1.58 mmol, 2.10 equiv), then heated to 50 ºC for 2 h. The mixture was cooled to room temperature, then diluted with H_2O (30 mL) and extracted with EtOAc (6 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography (0:100 to 20:80 EtOAc:hexanes) to yield 210 mg (87% yield) of (*R*)-3-chloro-BINOL (**9d**) as a white foam, which was dried over P_2O_5 under vacuum. ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.97 (d, *J* = 8.9 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.45 – 7.35 (m, 3H), 7.34 – 7.28 (m, 2H), 7.16 (d, *J* = 8.5 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 1H), 5.60 (s, 1H), 4.94 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 148.3, 133.1, 132.4, 131.3, 129.7, 129.32, 129.26, 128.4, 127.7, 127.5, 127.3, 125.1, 124.6, 124.1, 123.9, 122.4, 117.7, 113.6, 111.7; IR (NaCl/thin film): 3503, 3057, 1620, 1596, 1502, 1451, 1379, 1265, 1212, 1184, 1146, 828 cm^{-1}; $[\alpha]_D^{25}$ = +55.4 (*c* = 1.01, $CHCl_3$). HRMS (MM) calc'd for $[M-H]^-$ 319.0531, found 319.0549.

Preparation of (*R*)-6,6'-dimethoxy-BINOL (9h)



S3 S4

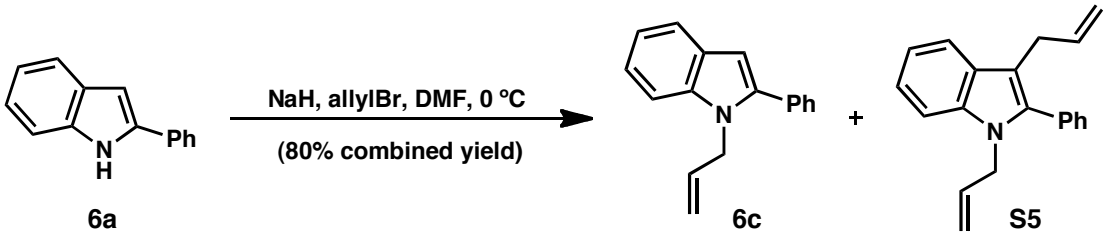
(*R*)-6,6'-dimethoxy-BINOL (**9h**) was prepared following a procedure adapted from a reported synthesis of (*R*)-3,3'-dimethoxy-BINOL (**9g**).[4] To a 25 mL flask containing MOM–protected (*R*)-6,6'-dibromo-BINOL **S3**[6] (1.10 g, 2.07 mmol, 1.00 equiv) was added THF (6.3 mL). The flask was cooled to –78 ºC, followed by dropwise addition of *n*-BuLi as a solution in hexanes (2.5 M, 2.50 mL, 6.20 mmol, 3.00 equiv). After stirring 1 hour at –78 ºC, $B(OMe)_3$ (645 mg, 6.20 mmol, 3.00 equiv) was added and the reaction was allowed to warm to room temperature. After 14 hours, the reaction mixture was concentrated to give the crude borate intermediate, which was suspended in benzene (7.2 mL) and cooled to 0 ºC, followed by dropwise addition of aqueous hydrogen peroxide (30 wt %, 0.61 mL, 5.98 mmol, 2.89 equiv). The suspension was heated to reflux for 4 hours, then cooled to room temperature, poured into ice-cold saturated aqueous $NaSO_3$ (20 mL), and extracted with EtOAc (3 x 15 mL). The combined organics were washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography (0:100 to 50:50 EtOAc:hexanes) to yield 512 mg (61% yield) of **S4** as a light yellow foam. ^{1}H NMR (500 MHz, CD_3CN) δ 7.80 (ddd, J = 9.1, 0.8, 0.4 Hz, 2H), 7.51 (d, J = 9.1 Hz, 2H), 7.20 (ddd, J = 2.5, 0.5, 0.5 Hz, 2H), 7.09 (br s, 2H), 6.93 (ddd, J = 9.1, 0.7, 0.7 Hz, 2H), 6.87 (dd, J = 9.1, 2.5 Hz, 2H), 5.02 (d, J = 6.7 Hz, 2H), 4.94 (d, J = 6.7 Hz, 2H), 3.11 (s, 6H) ; ^{13}C NMR (125 MHz, CD_3CN) δ 154.4, 151.6, 132.1, 129.6, 128.4, 127.8, 122.1, 119.6, 118.7, 110.1, 96.0, 56.1; IR (NaCl/thin film): 3368, 2914, 1624, 1599, 1511, 1240, 1196, 1148, 1023 cm^{-1}; $[\alpha]_D^{25}$ = +87.1 (*c* = 1.00, MeCN). HRMS (MM) calc'd for $[M-H]^-$ 405.1344, found 405.1350.



S4 **9h**

A 15 mL flask was charged with **S4** (200 mg, 0.493 mmol, 1.00 equiv) and K_2CO_3 (177 mg, 1.28 mmol, 2.60 equiv). DMF (2 mL) was added, followed by MeI (123 μL, 1.97 mmol, 4.00 equiv) dropwise. The reaction was then heated to 55 ºC for 22 hours, then cooled to room temperature and quenched with saturated aqueous NH_4Cl (2 mL) and Et_3N (3 drops). The mixture was stirred at room temperature for 6 hours, then diluted with H_2O (15 mL) and extracted with EtOAc (3 x 10 mL). The combined organics were washed with brine (15 mL), dried (Na_2SO_4), and concentrated. THF (28 mL) and IPA (9.5 mL) were added to the crude residue, followed by dropwise addition of aqueous HCl (6.0 M, 9.4 mL). The reaction was stirred at room temperature for 3 hours, then diluted with H_2O (70 mL) and extracted with EtOAc (3 x 30 mL). The combined organics were washed with saturated aqueous $NaHCO_3$ (2 x 45 mL) and brine (45 mL), then dried (Na_2SO_4), filtered, and concentrated. The crude oil was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 62 mg (36% yield) of (*R*)-6,6'-dimethoxy-BINOL **(9h)** as a light brown solid, which was dried over P_2O_5 under hi-vacuum. Spectral data are in agreement with the literature.[7]

Preparation of 1-allyl-2-phenylindole (6c)



6a **6c** **S5**

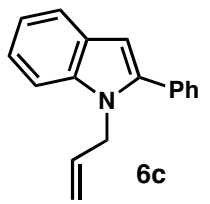
To a 50 mL flask was added NaH (620 mg, 15.5 mmol, 3.00 equiv) and DMF (8 mL) and the suspension was cooled to 0 ºC in an ice bath. A solution of 2-phenylindole **6a** (1.00 g, 5.18 mmol, 1.00 equiv) in DMF (3 mL) was added slowly to the suspension over 15 minutes and the reaction mixture was further stirred at 0 ºC for 20 minutes, followed by dropwise addition of

[7] Yu, H.-B.; Hu, Q.-S.; Pu, L. *J. Am. Chem. Soc.* **2000**, *122*, 6500.

allyl bromide (670 μL, 7.77 mmol, 1.50 equiv). The ice bath was then removed and the mixture was stirred for 15 minutes, then quenched by addition of saturated aqueous NH_4Cl (5 mL) and Et_3N (5 drops). After 2 hours, the reaction was diluted with H_2O (40 mL) and extracted with EtOAc (3 x 30 mL). The combined organics were washed with brine (120 mL), dried (Na_2SO_4), filtered, and concentrated. The crude was then purified by reverse phase preparatory HPLC (55:45 to 95:5 MeCN:H_2O) using an Agilent 1200 Series HPLC with an Agilent XDB-C18 5 μM column (9.4 x 250 mm and 21.2 x 150 mm) to yield 687 mg (57% yield) of 1-allyl-2-phenylindole (**6c**) as a yellow solid and 331 mg (23% yield) of 1,3-diallyl-2-phenylindole (**S5**) as a yellow oil.

1-allyl-2-phenylindole (6c):

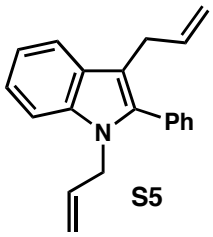
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (ddd, *J* = 7.8, 1.2, 0.8 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.48 – 7.43 (m, 2H), 7.42 – 7.38 (m, 1H), 7.33 (br d, *J* = 8.2 Hz, 1H), 7.22 (ddd, *J* = 7.0, 7.0, 1.3 Hz, 1H), 7.15 (ddd, *J* = 7.0, 7.0, 1.0 Hz, 1H), 6.60 (br s, 1H), 6.02 (ddt, *J* = 17.2, 10.5, 4.4 Hz, 1H), 5.22 (dtd, *J* = 10.5, 1.8, 1.1 Hz, 1H), 5.00 (dtd, *J* = 17.1, 2.0, 1.2 Hz, 1H), 4.74 (dt, *J* = 4.2, 1.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 137.8, 133.8, 132.7, 129.1, 128.5, 128.1, 128.0, 121.7, 120.5, 120.0, 116.5, 110.3, 102.0, 46.5; IR (NaCl/thin film): 3055, 2917, 1602, 1462, 1443, 1392, 1345, 1317, 1162 cm^{-1}; HRMS (APCI) calc'd for $[M+H]^+$ = 234.1277, found 234.1284.



6c

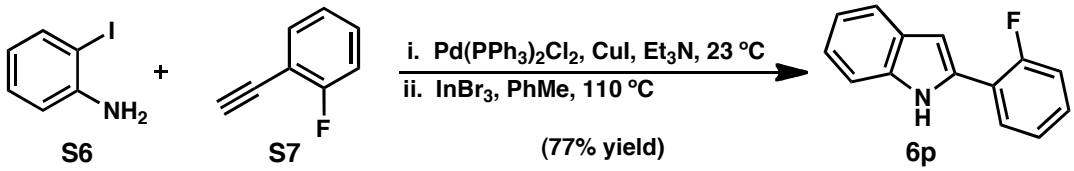
1,3-diallyl-2-phenylindole (S5):

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (ddd, *J* = 7.8, 1.2, 0.7 Hz, 1H), 7.50 – 7.40 (m, 5H), 7.33 (ddd, *J* = 8.1, 0.9, 0.9 Hz, 1H), 7.24 (ddd, *J* = 7.0, 7.0, 1.2 Hz, 1H), 7.16 (ddd, *J* = 7.0, 7.0, 1.1 Hz, 1H), 6.05 (ddt, *J* = 17.0, 10.1, 5.9 Hz, 1H), 5.91 (ddt, *J* = 17.1, 10.4, 4.7 Hz, 1H), 5.14 (dtd, *J* = 10.4, 1.8, 1.2 Hz, 1H), 5.08 – 5.02 (m, 2H), 4.92 (dtd, *J* = 17.1, 1.9, 1.3 Hz, 1H), 4.62 (dt, *J* = 4.6, 1.9 Hz, 2H), 3.46 (dt, *J* = 6.0, 1.7 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 137.9, 136.7, 133.9, 131.8, 130.4, 128.3, 128.2, 128.1, 128.0, 121.7, 119.34, 119.30, 116.2, 114.6, 110.9, 110.1, 46.4, 29.2; IR (NaCl/thin film): 3056, 2915, 1637, 1463, 1443, 1408, 1360, 1340, 1191 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ = 274.1590, found 274.1591.



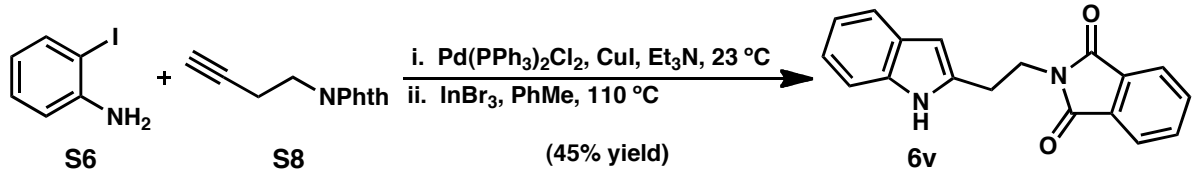
S5

Preparation of 2-(2-fluorophenyl)indole (6p)



2-(2-fluorophenyl)indole (**6p**) was prepared by an analogous procedure to that reported by Sakai et. al.[8] A flame-dried flask was charged with 2-iodoaniline (**S6**, 200 mg, 0.90 mmol, 1.00 equiv), ethynyl-2-fluorobenzene (**S7**, 133 mg, 1.10 mmol, 1.20 equiv), $Pd(PPh_3)_2Cl_2$ (13 mg, 0.02 mmol, 0.02 equiv), copper (I) iodide (2.0 mg, 0.025 mmol, 0.01 equiv) and Et_3N (4 mL). The mixture was stirred overnight at room temperature, then filtered through a plug of silica, concentrated and redissolved in PhMe (5 mL). $InBr_3$ (16 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was heated to 110 ºC for 5 h, then cooled to room temperature, filtered through celite, and concentrated. The crude residue was purified by silica gel chromatography (10:90 EtOAc:hexanes) to yield 148 mg (77% yield) of 2-(2-fluorophenyl)indole (**6p**) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (br s, 1H), 7.80 (ddd, J = 7.8, 7.8, 1.8 Hz, 1H), 7.66 (dddd, J = 2.5, 1.3, 0.8, 0.8 Hz, 1H), 7.43 (ddd, J = 8.1, 1.5, 0.8 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.26 – 7.16 (m, 3H), 7.14 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 6.97 (d, J = 1.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3 (d, $J_{C\text{-}F}$= 246.4 Hz), 134.6 (d, $J_{C\text{-}F}$ = 501.8 Hz), 128.8 (d, $J_{C\text{-}F}$ = 8.8 Hz), 128.1, 128.0 (d, $J_{C\text{-}F}$ = 4.1 Hz), 124.8 (d, $J_{C\text{-}F}$ = 3.2 Hz), 122.7, 120.6, 120.2, 119.9 (d, $J_{C\text{-}F}$ = 11.0 Hz), 116.6, 116.4, 111.0, 101.6 (d, $J_{C\text{-}F}$ = 3.0 Hz); IR (NaCl/thin film): 3469, 3042, 2918, 2848, 1577, 1472, 1460, 1212, 1178, 1109, 928 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 212.0870, found 212.0869.

Preparation of 2-(ethylphthalimide)indole (6v)



2-(ethylphthalimide)indole (**1v**) was prepared by an analogous procedure to that reported by Sakai et. al.[8] A flame-dried flask was charged with 2-iodoaniline (**S6**, 500 mg, 2.30 mmol, 1.00 equiv), 2-(but-3-yn-1-yl)isoindoline-1,3-dione (**S8**, 550 mg, 2.75 mmol, 1.20 equiv),

[8] Sakai, N.; Annaka, K.; Fujita, A.; Sato, A.; Konakahara, T. *J. Org. Chem.* **2008**, *73*, 4160.

$Pd(PPh_3)_2Cl_2$ (32 mg, 0.05 mmol, 0.02 equiv), copper (I) iodide (4.5 mg, 0.025 mmol, 0.01 equiv) and Et_3N (8 mL). The mixture was stirred overnight at room temperature, then filtered through a plug of silica, concentrated and redissolved in PhMe (10 mL). $InBr_3$ (40 mg, 0.1 mmol, 0.05 equiv) was added in one portion and the mixture was heated to 110 ºC for 5 h, then cooled to room temperature, filtered through celite and concentrated. The crude residue was purified by silica gel chromatography (60:40 EtOAc:hexanes) to yield 302 mg (45% yield) of 2-(ethylphthalimide)indole (**6v**) as a light yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (br s, 1H), 7.83 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.51 (d, J = 7.8 Hz, 1H), 7.33 (d, J = 8.1 Hz, 1H), 7.13 (ddd, J = 8.2, 7.1, 1.2 Hz, 1H), 7.06 (ddd, J = 7.5, 7.5, 1.0 Hz, 1H), 6.33 (d, J = 1.2 Hz, 1H), 4.06 (t, *J* = 7.5 Hz, 2H), 3.21 (t, J = 7.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 136.1, 134.9, 134.1, 131.9, 128.6, 123.4, 121.4, 120.0, 119.7, 110.6, 101.1, 37.1, 27.4.; IR (NaCl/thin film): 3366, 1772, 1707, 1653, 1617, 1466, 1395, 1363, 1293 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 291.1128, found 291.1138.

3. Optimization of Reaction Parameters.

a. General Procedure 1

An oven-dried vial was charged with 2-phenylindole (**6a**, 0.20 mmol, 1.00 equiv), the acrylate (0.24 mmol, 1.20 equiv) and an (*R*)-BINOL derivative and pumped into a glove box. The vial was charged with solvent to an indole concentration of 0.12 M, and $SnCl_4$ (1.00 equiv, as a 1.0 M solution in DCM) was added. The reaction was stirred at 20 °C for 2 hours, after which time it was removed from the glove box and quenched by dilution with 1 M HCl (5 mL) and MeCN (1 mL). The aqueous layer was extracted with EtOAc (2 x 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (5 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography.

Additive screens. Reactions were performed following General Procedure 1 using 0.20 equiv (*R*)-BINOL. After the vial was pumped into the glove box, one of the following additives was added:

- flame-dried powdered 4Å molecular sieves (200 wt % relative to indole)
- K_2CO_3 (1.00 equiv)

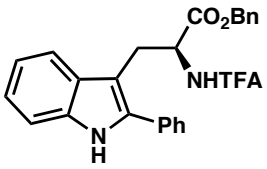
- 2,6-lutidine (1.00 equiv)

Upon addition of the additive, DCM was added to an indole concentration of 0.12 M and the reaction was further conducted as described above.

Catalyst screens. Reactions were performed following General Procedure 1 using flame-dried powdered 4Å molecular sieves (200 wt % relative to indole) as an additive and DCM as a solvent.

b. Characterization Data

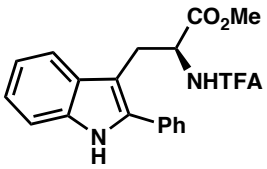
(*S*)-N_α-Trifluoroacetyl-2-phenyltryptophan benzyl ester (7a)



Prepared from benzyl 2-trifluoroacetamidoacrylate[9] (**2a**, 65.5 mg, 0.24 mmol) following General Procedure 1. The crude residue was purified by silica gel chromatography (30:70 to 70:30 DCM:hexanes) to yield 11.1 mg (12% yield) of **7a** as a yellow solid. The enantiomeric excess was determined to be 35% by chiral SFC analysis (OB-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R(major) = 11.0 min, t_R(minor) = 12.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (br s, 1H), 7.57 (ddd, *J* = 7.9, 1.8, 0.7 Hz, 1H), 7.54 – 7.50 (m, 2H), 7.50 – 7.45 (m, 2H), 7.42 – 7.36 (m, 2H), 7.34 – 7.29 (m, 3H), 7.24 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 7.16 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 7.11 – 7.07 (m, 2H), 6.67 (br d, *J* = 7.6 Hz, 1H), 4.95 (d, *J* = 12.2 Hz, 1H), 4.88 (dt, *J* = 7.8, 6.0 Hz, 1H), 4.53 (d, *J* = 12.2 Hz, 1H), 3.65 – 3.56 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 156.6 (q, $J_{C\text{-}F}$ = 37.8 Hz), 136.3, 135.6, 134.6, 132.4, 129.2, 128.9, 128.5, 128.44, 128.38, 128.2, 128.1, 122.8, 120.3, 118.6, 115.3 (q, $J_{C\text{-}F}$ = 287.9 Hz), 111.0, 105.6, 67.5, 53.3, 26.7; IR (NaCl/thin film): 3391, 3061, 2924, 1714, 1542, 1457, 1210, 1173 cm^{-1}; $[\alpha]_D^{25}$ = +3.5 (*c* = 0.44, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 467.1577, found 467.1580.

[9] Synthesis of benzyl 2-trifluoroacetamidoacrylate (**2a)**: Crossley, M.; Stamford, A. *Aust. J. Chem.* **1994**, *47*, 1695.

(*S*)-N_α-Trifluoroacetyl-2-phenyltryptophan methyl ester (7b)



Prepared from methyl 2-trifluoroacetamidoacrylate[10] (**2b**, 47.3 mg, 0.24 mmol) following General Procedure 1. The crude residue was purified by silica gel chromatography (0:100 to 5:95 EtOAc:toluene, then 0:100 to 20:80 EtOAc:hexanes) to yield 9.0 mg (12% yield) of **7b** as a yellow solid. The enantiomeric excess was determined to be 42% by chiral SFC analysis (AS-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 8.7 min, t_R(minor) = 7.7 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (br s, 1H), 7.58 – 7.52 (m, 3H), 7.52 – 7.47 (m, 2H), 7.43 – 7.39 (m, 1H), 7.38 (ddd, *J* = 8.1, 0.9, 0.9 Hz, 1H), 7.23 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.16 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 6.65 (br d, *J* = 7.3 Hz, 1H), 4.83 (dt, *J* = 7.8, 5.6 Hz, 1H), 3.66 – 3.56 (m, 2H), 3.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 156.6 (q, $J_{C\text{-}F}$ = 37.7 Hz), 136.3, 135.6, 132.5, 129.2, 129.0, 128.4, 128.2, 122.8, 120.3, 118.5, 115.3 (q, $J_{C\text{-}F}$= 287.7 Hz), 111.0, 105.5, 53.2, 52.5, 26.4; IR (NaCl/thin film): 3391, 3057, 2917, 2849, 1718, 1542, 1458, 1449, 1211, 1170 cm^{-1} ; $[\alpha]_D^{25}$ = +22.3 (*c* = 0.39, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 391.1264, found 391.1267.

[10] Synthesis of methyl 2-trifluoroacetamidocacrylate (**2b**): Navarre, L.; Martinez, R.; Genet, J.; Darses, S. *J. Am. Chem. Soc.* **2008**, *130*, 6159.

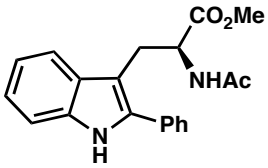
3. Optimized Conjugate Addition/Asymmetric Protonation.

a. General Procedure 2

An oven-dried vial was charged with the indole (1.00 equiv), methyl 2-acetamidoacrylate (**2c**, 1.20 equiv)[11] and (*R*)-3,3'-dibromo-BINOL (**9f**, 0.20 equiv) and pumped into a glove box. To the vial was added flame-dried powdered 4Å molecular sieves (200 wt % relative to indole). The vial was charged with DCM to an indole concentration of 0.12 M, and $SnCl_4$ (1.00 equiv unless specifically indicated, as a 1 M solution in DCM) was added. The reaction was stirred at 20 °C for 2 hours, after which time it was removed from the glove box and quenched by dilution with 1 M HCl (5 mL) and MeCN (1 mL). The aqueous layer was extracted with EtOAc (2 x 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (5 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography.

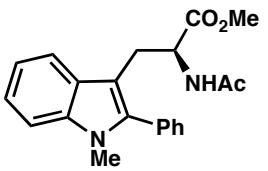
b. Characterization Data

(*S*)-N_α-Acetyl-2-phenyltryptophan methyl ester (7c)



Prepared from 2-phenylindole (**6a**, 19.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 25.6 mg (76% yield) of **7c** as a white foam. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm). t_R(major) = 5.7 min, t_R(minor) = 6.9 min. $[\alpha]_D^{25}$ = +37.7 (*c* = 0.94, $CHCl_3$). Spectral data matches that reported in the literature.[12]

(*S*)-N_α-Acetyl-1-methyl-2-phenyltryptophan methyl ester (7d)



Prepared from 1-methyl-2-phenylindole (**6b**, 41.4 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (0:100 to 55:45 EtOAc:hexanes) to yield 43.4 mg (63% yield) of **7d** as a yellow solid. The enantiomeric excess was

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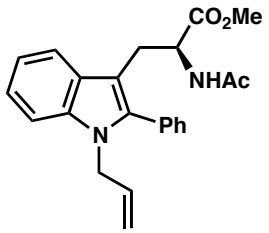
[11] Methyl 2-acetamidoacrylate (**2c**) is commercially available, or can be prepared according to Crestey, F.; Collot, V.; Steibing, S.; Rault, S. *Synthesis* **2006**, *20*, 3506.

[12] Angelini, E.; Balsamini, C.; Bartoccini, F.; Lucarini, S.; Piersanti, G. *J. Org. Chem.* **2008**, *73*, 5654.

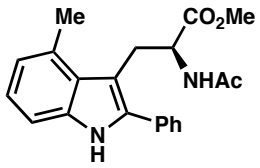
determined to be 85% by chiral SFC analysis (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(major) = 4.6 min, t_R(minor) = 3.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (ddd, *J* = 7.9, 1.2, 0.7 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.48 – 7.44 (m, 1H), 7.42 – 7.38 (m, 2H), 7.34 (ddd, *J* = 8.2, 0.9, 0.9 Hz, 1H), 7.26 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.17 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 5.72 (br d, *J* = 7.8 Hz, 1H), 4.74 (dt, *J* = 8.0, 5.6 Hz, 1H), 3.57 (s, 3H), 3.39 (s, 3H), 3.41 (dd, *J* = 14.7, 5.7 Hz, 1H), 3.34 (dd, *J*=14.8, 5.6 Hz, 1H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.5, 139.2, 136.9, 131.6, 130.7, 128.7, 128.4, 127.9, 122.0, 119.7, 118.7, 109.5, 106.7, 52.8, 52.0, 30.8, 26.6, 23.0.; IR (NaCl/thin film): 3288, 3055, 2950, 1743, 1657, 1539, 1469, 1441, 1368, 1238, 1212 cm^{-1}; $[\alpha]_D^{25}$ = +21.3 (*c* = 0.91, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1708.

(*S*)-N_α-Acetyl-1-allyl-2-phenyltryptophan methyl ester (7e)



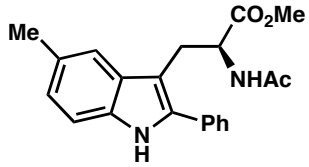
Prepared from 1-allyl-2-phenylindole (**6c**, 46.6 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (0:100 to 55:45 EtOAc:hexanes) to yield 51.3 mg (68% yield) of **7e** as a yellow foam. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AS-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 2.9 min, t_R(minor) = 2.4 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (ddd, *J* = 7.8, 1.0, 1.0 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.47 – 7.42 (m, 1H), 7.42 – 7.37 (m, 2H), 7.30 (ddd, *J* = 8.1, 0.9, 0.9 Hz, 1H), 7.23 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.17 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 5.85 (ddt, *J* = 17.1, 10.3, 4.7 Hz, 1H), 5.76 (br d, *J* = 7.9 Hz, 1H), 5.11 (dtd, *J* = 10.4, 1.7, 1.2 Hz, 1H), 4.82 (dtd, *J* = 17.1, 1.9, 1.3 Hz, 1H), 4.76 (dt, *J* = 8.0, 5.8 Hz, 1H), 4.56 (dt, *J* = 4.7, 1.8 Hz, 2H), 3.39 (s, 3H), 3.36 (dd, *J* = 14.7, 5.7 Hz, 1H), 3.29 (dd, *J* = 14.7, 5.9 Hz, 1H), 1.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.5, 139.0, 136.3, 133.5, 131.5, 130.5, 128.7, 128.5, 128.1, 122.0, 119.8, 118.8, 116.3, 110.2, 107.2, 52.8, 52.0, 46.3, 26.8, 23.0; IR (NaCl/thin film): 3435, 3287, 3056, 2950, 2926, 2851, 1744, 1658, 1538, 1500, 1408, 1367, 1219, 1196, 1134; $[\alpha]_D^{25}$ = +13.8 (*c* = 2.96, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 377.1860, found 377.1865.

(*S*)-N_α-Acetyl-4-methyl-2-phenyltryptophan methyl ester (7f)



Prepared from 4-methyl-2-phenylindole[13] (**6d**, 21.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 30.8 mg (88% yield) of **7f** as a white foam. The enantiomeric excess was determined to be 96% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 9.9 min, t_R(minor) = 8.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (br s, 1H), 7.55 – 7.45 (m, 4H), 7.44 – 7.37 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.08 (m, 1H), 6.91 (m, 1H), 5.44 (br d, J = 7.6 Hz, 1H), 4.63 (td, *J* = 8.2, 5.0 Hz, 1H), 3.69 – 3.45 (m, 2H), 3.44 (s, 3H), 2.78 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 169.7, 136.3, 136.1, 133.1, 130.5, 129.2, 128.9, 128.3, 126.9, 122.5, 122.3, 109.0, 107.6, 54.2, 52.1, 27.6, 22.8, 20.5; IR (NaCl/thin film): 3295, 3052, 2952, 1741, 1659, 1602, 1547, 1514, 1492, 1449, 1372, 1218; $[\alpha]_D^{25}$ = -29.0 (*c* = 0.63, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1698.

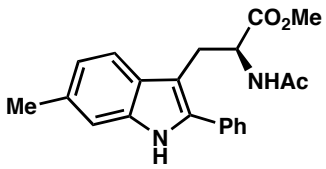
(*S*)-N_α-Acetyl-5-methyl-2-phenyltryptophan methyl ester (7g)



Prepared from 5-methyl-2-phenylindole[8] (**6e**, 42.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (30:70 to 100:0 EtOAc:hexanes) to yield 58.0 mg (83% yield) of **7g** as a white foam. The enantiomeric excess was determined to be 95% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 4.9 min, t_R(minor) = 6.4 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (br s, 1H), 7.54 (ddd, *J* = 10.1, 6.1, 4.2 Hz, 2H), 7.50 – 7.43 (m, 2H), 7.40 – 7.33 (m, 2H), 7.24 (d, *J* = 8.3 Hz, 1H), 7.06 – 7.00 (m, 1H), 5.78 (br d, *J* = 8.1 Hz, 1H), 4.83 (dt, *J* = 8.1, 5.4 Hz, 1H), 3.53 – 3.51 (m, 2H), 3.31 (s, 3H), 2.46 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.5, 136.1, 134.0, 133.3, 129.7, 129.2, 129.1, 128.2, 128.0, 124.1, 118.6, 110.6, 106.3, 52.7, 51.2, 26.5, 22.8, 21.5; IR (NaCl/thin film): 3379, 3365, 2948, 1737, 1658, 1439, 1372, 1306, 1217 cm^{-1}; $[\alpha]_D^{25}$ = +33.8 (*c* = 0.26, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1680.

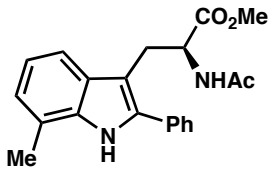
[13] Zhao, J.; Zhang, Y.; Cheng, K. *J. Org. Chem.* **2008**, *73*, 7428.

(*S*)-N_α-Acetyl-6-methyl-2-phenyltryptophan methyl ester (7h)



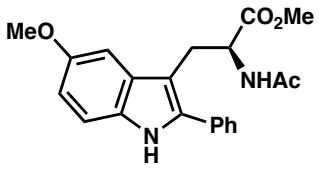
Prepared from 6-methyl-2-phenylindole[13] (**6f**, 21.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 27.9 mg (80% yield) of **7h** as a colorless oil. The enantiomeric excesses was determined to be 89% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 9.1 min, t_R(minor) = 10.1 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (br s, 1H), 7.55 (ddd, J = 5.8, 4.0, 2.1 Hz, 2H), 7.48 – 7.44 (m, 3H), 7.39 – 7.33 (m, 1H), 7.14 (s, 1H), 6.97 (dd, J = 8.3, 1.5 Hz, 1H), 5.78 (br d, J = 7.8 Hz, 1H), 4.83 (dt, J = 8.0, 5.4 Hz, 1H), 3.55 – 3.49 (m, 2H), 3.30 (s, 3H), 2.47 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 172.1, 169.6, 136.1, 135.2, 133.3, 132.4, 129.1, 128.2, 127.9, 127.3, 121.8, 118.5, 110.9, 106.5, 52.7, 52.0, 26.6, 22.9, 21.7; IR (NaCl/thin film): 3292, 3052, 2958, 2908, 1741, 1658, 1545, 1530, 1511, 1446, 1375, 1216; $[\alpha]_D^{25}$ = +39.3 (c = 0.38, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1698.

(*S*)-N_α-Acetyl-7-methyl-2-phenyltryptophan methyl ester (7i)



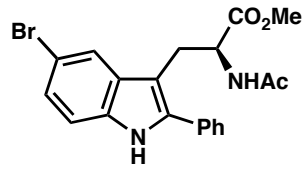
Prepared from 7-methyl-2-phenylindole[13] (**6g**, 21.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (30:70 to 100:0 EtOAc:hexanes) to yield 33.0 mg (94% yield) of **7i** as a white foam. The enantiomeric excess was determined to be 94% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 5.6 min, t_R(minor) = 5.0 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (br s, 1H), 7.61 – 7.54 (m, 2H), 7.51 – 7.45 (m, 2H), 7.42 (d, J = 8.1 Hz, 1H), 7.40 – 7.35 (m, 1H), 7.11 – 7.04 (m, 1H), 7.03 – 6.97 (m, 1H), 5.79 (br d, J = 8.1 Hz, 1H), 4.82 (dt, J = 8.1, 5.7 Hz, 1H), 2.55 (dd, J = 12.5, 3.1 Hz, 1H), 3.51 (dd, J = 12.5, 3.1 Hz, 1H), 3.30 (s, 3H), 2.50 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.6, 135.8, 135.3, 133.3, 129.1, 128.9, 128.4, 128.0, 123.1, 120.20, 120.18, 116.5, 107.1, 52.7, 51.9, 26.6, 22.8, 16.6; IR (NaCl/thin film): 3283, 3053, 2950, 1736, 1659, 1518, 1438, 1372, 1306, 1266, 1219, 1137, 1043; $[\alpha]_D^{25}$ = +26.5 (c = 0.20, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1708.

(*S*)-N_α-Acetyl-5-methoxy-2-phenyltryptophan methyl ester (7j)



Prepared from 5-methoxy-2-phenylindole[13] (**6h**, 45.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 62.0 mg (85% yield) of **7j** as a colorless oil. The enantiomeric excess was determined to be 91% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 4.7 min, t_R(minor) = 6.5 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (br s, 1H), 7.58 – 7.49 (m, 2H), 7.50 – 7.41 (m, 2H), 7.36 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.24 (d, J = 8.7 Hz, 1H), 7.05 (d, J = 2.3 Hz, 1H), 6.90 – 6.80 (m, 1H), 5.82 (br d, J = 7.9 Hz, 1H), 4.82 (td, J = 7.9, 5.4 Hz, 1H), 3.87 (s, 3H), 3.49 (m, 2H), 3.29 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.6, 154.4, 136.7, 133.2, 130.8, 129.8, 129.1, 128.2, 128.0, 112.7, 111.7, 106.5, 100.5, 55.9, 52.7, 52.0, 26.6, 22.9; IR (NaCl/thin film): 3291, 3057, 2926, 1739, 1652, 1558, 1539, 1520, 1483, 1455, 1374, 1218, 1178; $[\alpha]_D^{25}$ = +32.6 (*c* = 0.93, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 367.1652, found 367.1658.

(*S*)-N_α-Acetyl-5-bromo-2-phenyltryptophan methyl ester (7k)

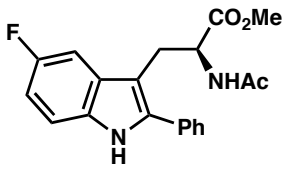


Prepared from 5-bromo-2-phenylindole[14] (**6i**, 54.0 mg, 0.20 mmol) with 1.6 equiv $SnCl_4$ following General Procedure 2. The crude residue was purified by silica gel chromatography (30:70 to 100:0 EtOAc:hexanes) to yield 49.5 mg (60% yield) of **7k** as a white foam. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 5.3 min, t_R(minor) = 7.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (br s, 1H), 7.66 (d, *J* = 2.0 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.49 – 7.43 (m, 2H), 7.42 – 7.34 (m, 1H), 7.28 – 7.24 (m, 1H), 7.22 – 7.18 (m, 1H), 5.75 (br d, *J* = 8.1 Hz, 1H), 4.82 (dt, *J* = 8.1, 5.7 Hz, 1H), 3.53 (dd, J = 14.9, 5.5 Hz, 1H), 3.46 (dd, J = 14.9, 4.8 Hz, 1H), 3.36 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 169.6, 137.2, 134.2, 132.6, 131.1, 129.2, 128.3, 128.2, 125.2, 121.6, 113.1, 112.4, 106.4, 52.6, 52.1, 26.5, 22.8; IR (NaCl/thin film): 3417, 3369, 3282, 1734, 1654, 1521, 1466, 1437, 1374, 1215; $[\alpha]_D^{25}$ = +47.2 (*c* = 1.04, $CHCl_3$).

[14] Prepared from 4-bromo-2-iodoaniline by an analogous procedure to that reported by Sakai et. al. (reference 8). Spectral data matches that reported in the literature: Homes, T. P.; Mattner, F.; Keller, P. A.; Katsifis, A. *Bioorg. Med. Chem.* **2006**, *14*, 3938.

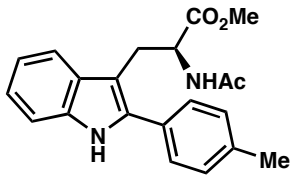
HRMS (MM) calc'd for $[M+H]^+$ 415.0652, found 415.0653.

(*S*)-N_α-Acetyl-5-fluoro-2-phenyltryptophan methyl ester (7l)



Prepared from 5-fluoro-2-phenylindole[13] (**6j**, 42.0 mg, 0.20 mmol) with 1.6 equiv $SnCl_4$ following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 44.7 mg (63% yield) of **7l** as a colorless oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 3.8 min, t_R(minor) = 5.2 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (br s, 1H), 7.60 – 7.52 (m, 2H), 7.50 – 7.43 (m, 2H), 7.42 – 7.34 (m, 1H), 7.27 – 7.24 (m, 1H), 7.21 (dd, *J* = 9.8, 2.6 Hz, 1H), 6.94 (ddd, *J* = 9.0, 9.0, 2.6 Hz, 1H), 5.77 (br d, *J* = 7.8 Hz, 1H), 4.82 (dt, *J* = 8.1, 5.4 Hz, 1H), 3.53 (dd, J = 14.9, 5.6 Hz, 1H), 3.47 (dd, J = 14.9, 5.0 Hz, 1H), 3.35 (s, 3H), 1.64 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 169.8, 168.3, 135.6, 134.2, 132.5, 131.9, 128.6, 123.5, 121.8, 119.7, 118.2, 110.8, 107.4, 52.9, 52.4, 37.0, 27.0, 25.3, 23.1; IR (NaCl/thin film): 3275, 3062, 2952, 1733, 1652, 1584, 1558, 1539, 1520, 1486, 1456, 1436, 1374, 1266, 1217, 1180; $[\alpha]_D^{25}$ = +49.9 (*c* = 1.25, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1455.

(*S*)-N_α-Acetyl-2-(4-methylphenyl)tryptophan methyl ester (7m)

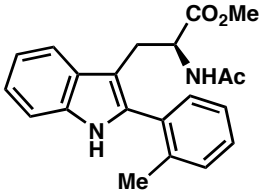


Prepared from 2-(4-methylphenyl)indole[15] (**6k**, 41.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 60.1 mg (86% yield) of **7m** as a white foam. The enantiomeric excess was determined to be 94% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm). t_R(major) = 6.6 min, t_R(minor) = 8.8 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (br s, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 8.1, 2H), 7.34 (d, *J* = 8.1, 1H), 7.28 (d, *J* = 8.1, 2H), 7.19 (ddd, *J* = 7.8, 7.1, 1.2 Hz, 1H), 7.15 – 7.09 (m, 1H), 5.77 (br d, *J* = 8.1, 1H), 4.82 (dt, *J* = 7.8, 5.5 Hz, 1H), 3.54 (dd, J = 13.1, 4.0 Hz, 1H), 3.50 (dd, J = 13.1, 3.7 Hz, 1H), 3.33 (s, 3H), 2.40 (s,

[15] Prepared from 2-iodoaniline by an analogous procedure to that reported by Sakai et. al. (reference 8). Spectral data matches that reported in the literature: Shen, M.; Leslie, B. E.; Driver, T. G. *Angew. Chem., Int. Ed.* **2008**, *47*, 5056.

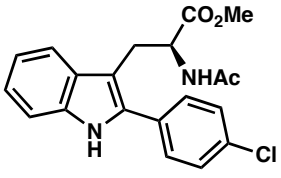
3H), 1.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.6, 138.0, 136.1, 135.6, 130.2, 129.8, 129.4, 128.1, 122.3, 119.9, 118.7, 110.9, 106.4, 52.8, 52.0, 26.6, 22.8, 21.2; IR (NaCl/thin film): 3365, 3271, 3052, 2951, 1737, 1657, 1519, 1460, 1439, 1375, 1305, 1217 cm^{-1}; $[\alpha]_D^{25}$ = 43.2 (*c* = 0.74, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1700.

(*S*)-*N*$_\alpha$-Acetyl-2-(2-methylphenyl)tryptophan methyl ester (7n)



Prepared from 2-(2-methylphenyl)indole[16] (**6l**, 21.0 mg, 0.1 mmol) following General Procedure 2. The crude residue was purified by flash chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 9.2 mg (26% yield) of **7n**. The enantiomeric excess was determined to be 87% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 4.3 min, t_R(minor) = 4.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.62 – 7.55 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.38 – 7.32 (m, 4H), 7.31 – 7.27 (m, 1H), 7.22 (ddd, J = 8.1, 5.6, 2.1 Hz, 1H), 7.16 (ddd, J = 7.1, 5.6, 1.1 Hz, 1H), 5.71 (br d, J = 7.9 Hz, 1H), 4.82 – 4.68 (dt, *J* = 7.9, 5.4 Hz, 1H), 3.38 – 3.29 (m, 4H), 3.28 – 3.16 (m, 1H), 2.28 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.6, 137.3, 135.8, 135.5, 132.1, 130.9, 130.8, 128.9, 128.7, 126.0, 122.3, 119.9, 118.8, 110.8, 107.6, 52.8, 52.0, 26.6, 23.0, 20.0; IR (NaCl/thin film): 3385, 3271, 3062, 2924, 2853, 1734, 1653, 1559, 1539, 1521, 1457, 1437, 1374; $[\alpha]_D^{25}$ = +21.5 (*c* = 0.29, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1709.

(*S*)-*N*$_\alpha$-Acetyl-2-(4-chlorophenyl)tryptophan methyl ester (7o)

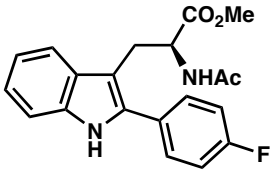


Prepared from 2-(4-chlorophenyl)indole[13] (**6m**, 45.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 55.2 mg (75% yield) of **7o** as a colorless oil. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 6.1 min, t_R(minor) = 7.0 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (br s, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.43 – 7.37 (m, 2H), 7.33 (ddd, *J* = 8.1, 8.1, 1.0

[16] Prepared from 2-iodoaniline by an analogous procedure to that reported by Sakai et. al. (reference 8). Spectral data matches that reported in the literature: Zhao, J.; Zhang, Y.; Cheng, K. *J. Org. Chem.* **2008**, *73*, 7428.

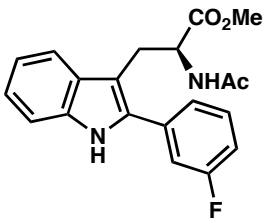
Hz, 1H), 7.23 – 7.18 (m, 1H), 7.14 (ddd, J = 8.0, 7.1, 1.1 Hz, 1H), 5.85 (br d, J = 8.1 Hz, 1H), 4.83 (dt, J = 8.1, 5.5 Hz, 1H), 3.55 – 3.38 (m, 2H), 3.34 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.6, 135.8, 134.6, 133.9, 131.5, 129.4, 129.3, 122.7, 120.1, 118.9, 111.1, 107.1, 52.8, 52.1, 29.6, 26.7, 22.9; IR (NaCl/thin film): 3280, 3058, 2948, 1737, 1657, 1519, 1487, 1458, 1439, 1373, 1310, 1216, 1093 cm^{-1}; $[\alpha]_D^{25}$ = +40.8 (c = 0.96, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 371.1157, found 371.1158.

(*S*)-*N*$_\alpha$-Acetyl-2-(4-fluorophenyl)tryptophan methyl ester (7p)



Prepared from 2-(4-fluorophenyl)indole[8] (**6n**, 42.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc/hexanes) to yield 55.6 mg (78% yield) of **7p** as a colorless oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 6.1 min, t_R(minor) = 6.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 47.9 Hz, 1H), 7.57 (dd, J = 7.9, 1.1 Hz, 1 H), 7.54 – 7.51 (m, 2H), 7.36 (ddd, J = 8.1, 8.1, 0.9 Hz, 1H), 7.23 – 7.10 (m, 4H), 5.82 (d, J = 8.1 Hz, 1H), 4.83 (dt, J = 8.1, 5.5 Hz, 1H), 3.55 – 3.40 (m, 2H), 3.34 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.5, 135.6, 135.0, 130.1, 130.1, 129.4, 122.7, 120.2, 118.9, 116.2, 116.1, 110.9, 106.9, 52.8, 52.0, 26.7, 22.9.; IR (NaCl/thin film): 3364, 3271, 3061, 2925, 2853, 1738, 1661, 1553, 1505, 1460, 1440, 1373, 1221, 1158; $[\alpha]_D^{25}$ = +38.2 (c = 0.65, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1460.

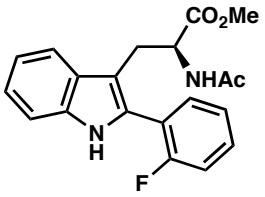
(*S*)-*N*$_\alpha$-Acetyl-2-(3-fluorophenyl)tryptophan methyl ester (7q)



Prepared from 2-(3-fluorophenyl)indole[15] (**6o**, 42.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 ethyl acetate/hexanes) to yield 50.6 mg (76% yield) of **7q** as a white foam. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 3.8 min, t_R(minor) = 4.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (br s, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.33-7.31 (m, 2H), 7.27-7.24 (m, 1H), 7.19 (ddd, J = 8.2, 7.0, 1.0 Hz, 1H), 7.13 (ddd, J = 7.9, 7.0, 1.0 Hz, 1H), 7.07 – 7.03 (m,

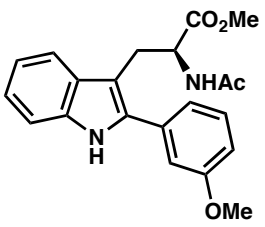
1H), 5.89 (br d, J = 8.1 Hz, 1H), 4.84 (dt, J = 8.1, 5.5 Hz, 1H), 3.53 (dd, J = 13.6, 4.7 Hz, 1H), 3.49 (dd, J = 13.6, 4.2 Hz, 1H), 3.34 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.7, 162.9 (d, $J_{C\text{-}F}$ = 246.3 Hz), 135.8, 135.2 (d, $J_{C\text{-}F}$ = 7.5 Hz), 134.5 (d, $J_{C\text{-}F}$ = 2.5 Hz), 130.6 (d, $J_{C\text{-}F}$ = 8.8 Hz), 129.2, 123.9 (d, $J_{C\text{-}F}$ = 3.8 Hz), 122.8, 120.0, 118.9, 115.1 (d, $J_{C\text{-}F}$ = 21.2 Hz), 114.7 (d, $J_{C\text{-}F}$ = 21.2 Hz), 111.1, 107.3, 52.8, 52.0, 26.7, 22.8; IR (NaCl/thin film): 3370, 3275, 3060, 2952, 1735, 1655, 1614, 1585, 1522, 1438, 1374, 1266, 1200, 1155 cm^{-1}; $[\alpha]_D^{25}$ = +37.6 (*c* = 1.21, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1450.

(*S*)-N_α-Acetyl-2-(2-fluorophenyl)tryptophan methyl ester (7r)



Prepared from 2-(2-fluorophenyl)indole (**6p**, 21.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 12.4 mg (35% yield) of **7r**. The enantiomeric excesses was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 9.5 min, t_R(minor) = 8.4 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.55 (ddd, J = 7.5, 7.5, 1.8 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.29 (ddd, J = 7.5, 7.5, 1.2 Hz, 1H), 7.25 – 7.20 (m, 1H), 7.19 – 7.10 (m, 1H), 5.83 (br d, J = 7.6 Hz, 1H), 4.85 (dt, J = 7.9, 5.5 Hz, 1H), 3.55 – 3.39 (m, 2H), 3.36 (s, 2H), 1.73 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.5, 159.8 (d, $J_{C\text{-}F}$ = 246.3 Hz), 135.9, 131.4 (d, $J_{C\text{-}F}$ = 3.8 Hz) 130.2 (d, $J_{C\text{-}F}$ = 8.8 Hz), 129.73, 128.65, 124.8 (d, $J_{C\text{-}F}$ = 3.8 Hz), 122.84, 120.6 (d, $J_{C\text{-}F}$ = 15.0 Hz), 120.0, 119.0, 116.4 (d, $J_{C\text{-}F}$ = 21.3 Hz), 111.0, 108.8, 52.5, 52.0, 26.8, 26.8, 22.9; IR (NaCl/thin film): 3275, 3058, 2925, 2853, 1734, 1653, 1523, 1490, 1457, 1437, 1374, 1245, 1216, 1130, 1104; $[\alpha]_D^{25}$ = +39.8 (*c* = 0.41, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1463.

(*S*)-N_α-Acetyl-2-(3-methoxyphenyl)tryptophan methyl ester (7s)

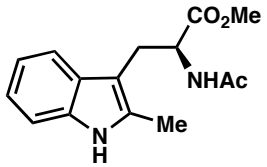


Prepared from 2-(3-methoxyphenyl)indole[17] (**6q**, 45.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (30:70 to 100:0 EtOAc:hexanes) to yield 65.0 mg

[17] Prepared from 2-iodoaniline by an analogous procedure to that reported by Sakai et. al. (reference 8). Spectral data matches that reported in the literature: Yang, S.-D.; Sun, C. L.; Fang, Z.; Li, B.-J.; Li, Y.-Z.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 1473.

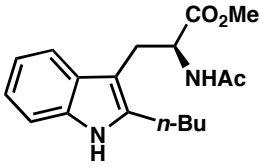
(88% yield) of **7s** as a colorless oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 5.9 min, t_R(minor) = 7.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (br s, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.19 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 7.16 – 7.10 (m, 2H), 7.08 (dd, J = 2.6, 1.6 Hz, 1H), 6.91 (ddd, J = 8.3, 2.6, 0.8 Hz, 1H), 5.82 (br d, J = 7.8 Hz, 1H), 4.83 (dt, J = 7.8, 5.5 Hz, 1H), 3.85 (s, 3H), 3.57 – 3.49 (m, 2H), 3.35 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.6, 160.0, 135.8, 135.6, 134.4, 130.2, 129.3, 122.5, 120.6, 119.9, 118.8, 113.8, 113.5, 111.0, 106.7, 55.4, 52.8, 52.0, 26.6, 22.8; IR (NaCl/thin film): 3282, 3058, 2951, 1738, 1658, 1603, 1520, 1462, 1439, 1373, 1218, 1040; $[\alpha]_D^{25}$ = +40.3 (c = 1.16, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 367.1652, found 367.1656.

(*S*)-*N*$_\alpha$-Acetyl-2-methyltryptophan methyl ester (7t)



Prepared from 2-methylindole (**6r**, 26.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (50:50 to 100:0 EtOAc:hexanes) to yield 31.0 mg (61% yield) of **7t** as a white foam. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 3.9 min, t_R(minor) = 2.7 min. $[\alpha]_D^{25}$ = +25.9 (c = 0.99, $CHCl_3$). Spectral data matches that reported in the literature.[9]

(*S*)-*N*$_\alpha$-Acetyl-2-butyltryptophan methyl ester (7u)

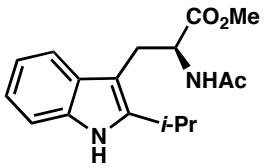


Prepared from 2-butylindole[18] (**6s**, 35.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 45.8 mg (72% yield) of **7u** as a colorless oil. The enantiomeric excess was determined to be 91% by chiral SFC analysis (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(major) = 5.1 min, t_R(minor) = 4.2 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.46 – 7.40 (m, 1H), 7.31 – 7.24 (m, 1H), 7.15 – 6.99 (m, 2H), 6.00 (br d, J = 7.8 Hz, 1H), 4.88 (dt, J = 8.1, 5.7 Hz,

[18] Prepared from 2-iodoaniline by an analogous procedure to that reported by Sakai et. al. (reference 8). Spectral data matches that reported in the literature: Ambrogio, I.; Cacchi, S.; Fabrizi, G.; Prastaro, A. *Tetrahedron* **2009**, *65*, 8916.

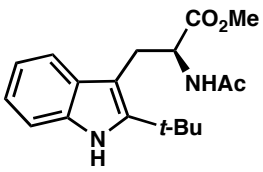
1H), 3.65 (s, 3H), 3.26 (dd, *J* = 5.7, 0.9 Hz, 2H), 2.69 (td, *J* = 7.8 2.2 Hz, 2H), 1.93 (s, 3H), 1.66 – 1.57 (m, 2H), 1.45 – 1.31 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 169.6, 137.4, 135.2, 128.8, 121.3, 119.5, 117.9, 110.4, 105.26, 105.29, 53.0, 52.3, 31.8, 26.8, 25.7, 23.2, 22.6, 13.9; IR (NaCl/thin film): 3296, 3058, 2955, 2871, 1737, 1658, 1562, 1530, 1463, 1439, 1376, 1217, 1129; $[\alpha]_D^{25}$ = +16.3 (*c* = 0.83, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 317.1860, found 317.1855.

(*S*)-*N*$_\alpha$-Acetyl-2-isopropyltryptophan methyl ester (7v)



Prepared from 2-isopropylindole[19] (**6t**, 32.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 39.6 mg (66% yield) of **7v** as a colorless oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm). t_R(major) = 6.4 min, t_R(minor) = 5.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (br s, 1H), 7.48 – 7.41 (m, 1H), 7.30 – 7.27 (m, 1H), 7.15 – 7.02 (m, 2H), 6.04 (br d, *J* = 8.0 Hz, 1H), 4.89 (dt, *J* = 8.1, 5.7 Hz, 1H), 3.66 (s, 3H), 3.29 (dd, J = 12.7, 4.0 Hz, 1H), 3.26 (dd, J = 12.7, 3.4 Hz, 1H), 3.18 (m, 1H), 1.93 (s, 3H1.31 (d, J = 3.3 Hz, 3H), 1.30 (d, J = 3.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 169.7, 142.7, 135.2, 128.7, 121.3, 119.5, 117.9, 110.6, 103.6, 53.0, 52.3, 26.7, 25.3, 23.2, 23.0; IR (NaCl/thin film): 3305, 2962, 1734, 1700, 1653, 1559, 1539, 1506, 1457, 1436, 1374, 1299, 1217 cm^{-1}; $[\alpha]_D^{25}$ = +22.2 (*c* = 0.35, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 303.1703, found 303.1709.

(*S*)-*N*$_\alpha$-Acetyl-2-(tert-butyl)tryptophan methyl ester (7w)

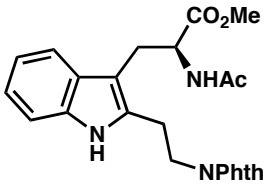


Prepared from 2-(tert-butyl)indole[13] (**6u**, 35.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 18.1 mg (29% yield) of **7w** as a yellow oil. The enantiomeric excess was determined to be 84% by chiral SFC analysis (OD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) =

[19] Prepared from 2-iodoaniline by an analogous procedure to that reported by Sakai et. Al (reference 8). Spectral data matches that reported in the literature: Smith, A. B.; Visnick, M.; Haseltine, J. N.; Sprengeler, P. A. *Tetrahedron* **2007**, *42*, 2957.

12.8 min, t_R(minor) = 14.2 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (br s, 1H), 7.47 (dd, J = 14.0, 7.1 Hz, 1H), 7.27 (dd, J = 5.8, 4.8 Hz, 1H), 7.15 – 7.03 (m, 2H), 6.06 (br d, J = 7.4 Hz, 1H), 4.84 (m, 1H), 3.54 (s, 3H), 3.38 – 3.29 (m, 2H), 1.86 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 169.6, 143.4, 133.9, 129.8, 121.3, 119.4, 117.7, 110.4, 104.3, 53.7, 52.2, 33.2, 30.7, 28.6, 23.0; IR (NaCl/thin film): 3326, 3047, 2961, 2918, 2868, 1734, 1653, 1539, 1457, 1436, 1374, 1303, 1254, 1211, 1128; $[\alpha]_D^{25}$ = +12.4 (*c* = 0.36, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 317.1860, found 317.1856.

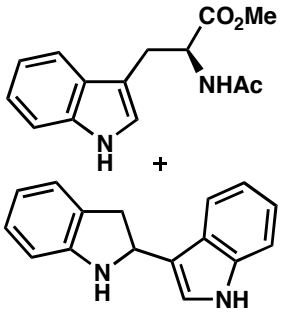
(*S*)-*N*$_\alpha$-Acetyl-2-(ethylphthalimide)tryptophan methyl ester (7x)



Prepared from 2-(ethylphthalimide)indole (**6v**, 29.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (70:30 to 100:0 EtOAc:hexanes) to yield 34.6 mg (80% yield) of **7x** as a yellow foam. The enantiomeric excess was determined to be 90% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 7.3 min, t_R(minor) = 6.3 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (br s, 1H), 7.83 (dd, *J* = 5.4, 2.9 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.31 (ddd, *J* = 8.1, 8.1, 1.0 Hz, 1H), 7.13 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.07 (ddd, *J* = 10.5, 5.8, 2.2 Hz, 1H), 6.13 (br d, *J* = 8.1 Hz, 1H), 4.92 (dt, *J* = 8.2, 6.0 Hz, 1H), 4.05 – 3.89 (m, 2H), 3.66 (s, 3H), 3.33 – 2.98 (m, 4H), 1.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 169.8, 168.3, 135.6, 134.2, 132.5, 131.9, 128.6, 123.5, 121.8, 119.7, 118.2, 110.8, 107.4, 52.9, 52.4, 37.0, 27.0, 25.3, 23.1; IR (NaCl/thin film): 3369, 3280, 3052, 2948, 1770, 1738, 1711, 1659, 1530, 1438, 1397, 1371; $[\alpha]_D^{25}$ = +14.8 (*c* = 0.96, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1455.

(*S*)-N_α-Acetyltryptophan methyl ester and indole dimer

Prepared from indole (23.4 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (0:100 to 100:0 EtOAc:hexanes) to yield 17.9 mg



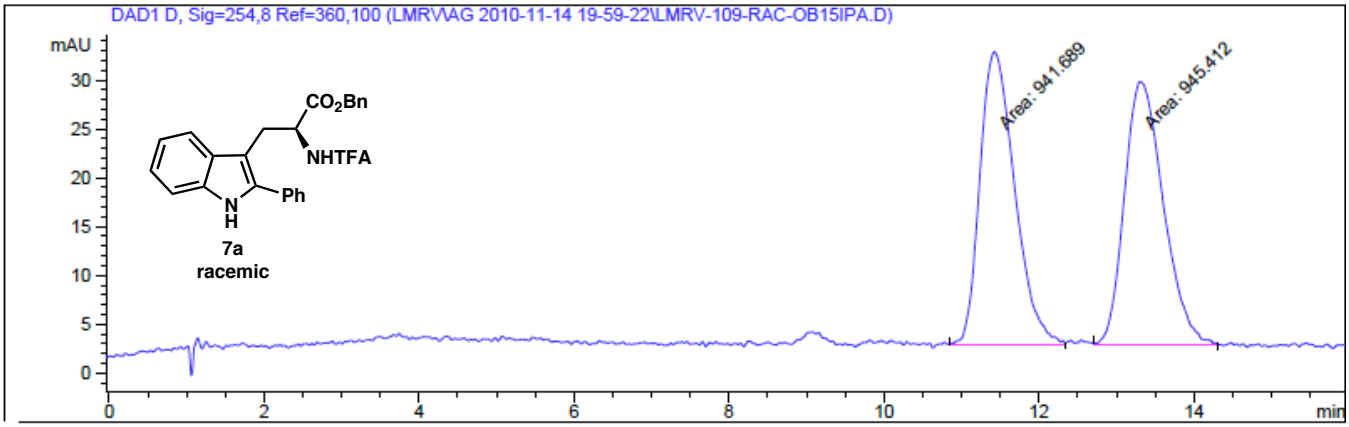
(contains 9 wt % EtOAc, 31% corrected yield) of (*S*)-N_α-acetyltryptophan methyl ester as a light pink oil and 7.0 mg (30% yield) of an indole dimer as a light yellow oil. The enantiomeric excess of (*S*)-N_α-acetyltryptophan methyl ester was determined to be 67% by chiral SFC analysis (OD-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R(major) = 11.4 min, t_R(minor) = 10.6 min. $[\alpha]_D^{25}$ = +39.3 (*c* = 0.83, $CHCl_3$). Spectral data for both (*S*)-N_α-acetyltryptophan methyl ester[20] and the indole dimer[21] are in agreement with the literature.

[20] Ruis-Rodríguez, J.; Albericio, F.; Lavilla, R. *Chem. Eur. J.* **2010**, *16*, 1124.
[21] Xu, X.-H.; Liu, G.-K.; Azuma, A.; Tokunaga, E.; Shibata, N. *Org. Lett.* **2011**, *13*, 4854.

5. SFC traces for racemic and enantioenriched tryptophan derivatives.

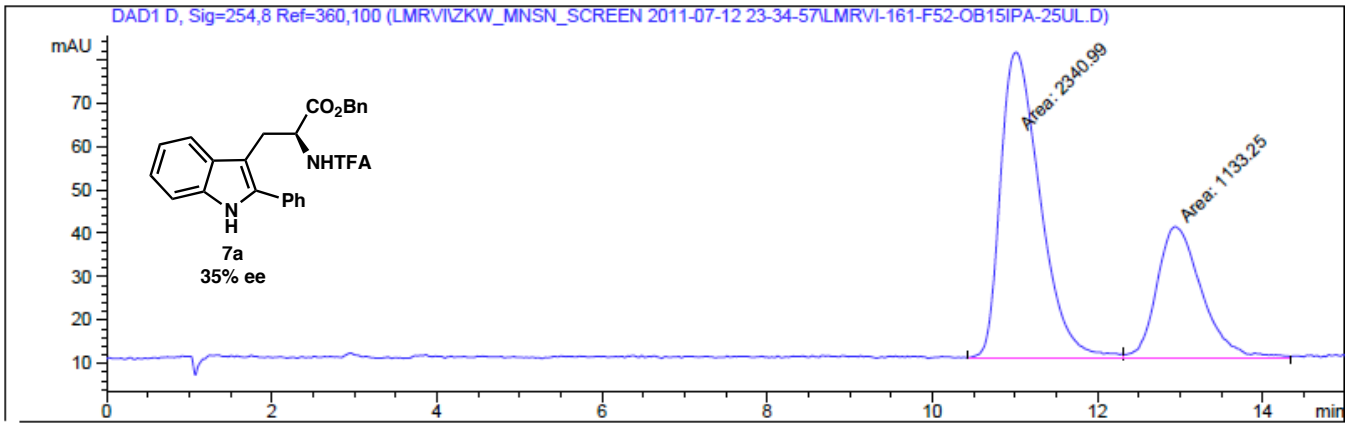
Optimization of Reaction Parameters

7a (Table 2, entry 1): racemic



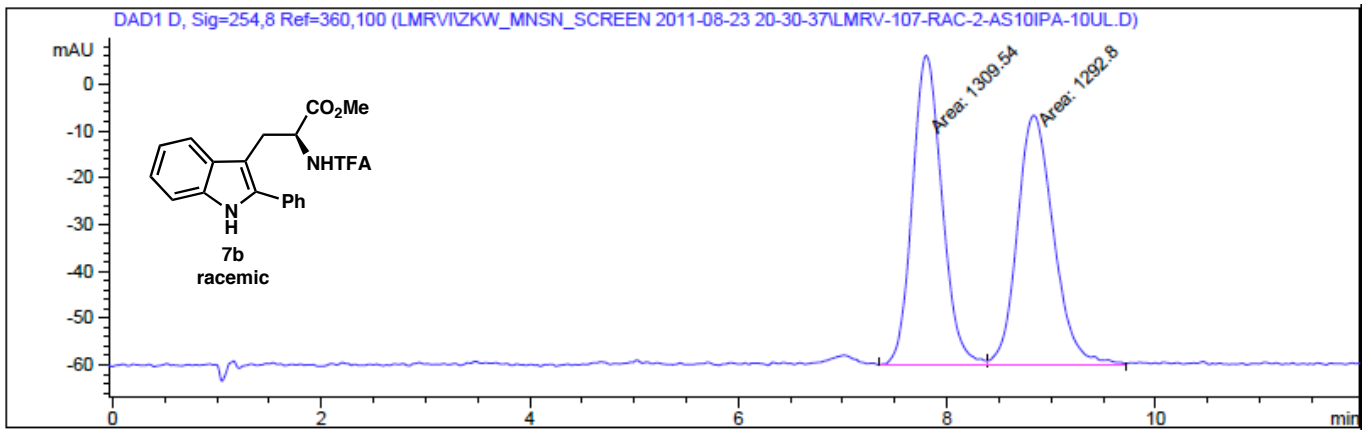
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.427	MM	0.5219	941.68884	30.07461	49.9014
2	13.305	MM	0.5837	945.41193	26.99413	50.0986

7a (Table 2, entry 1): enantioenriched, 35% ee



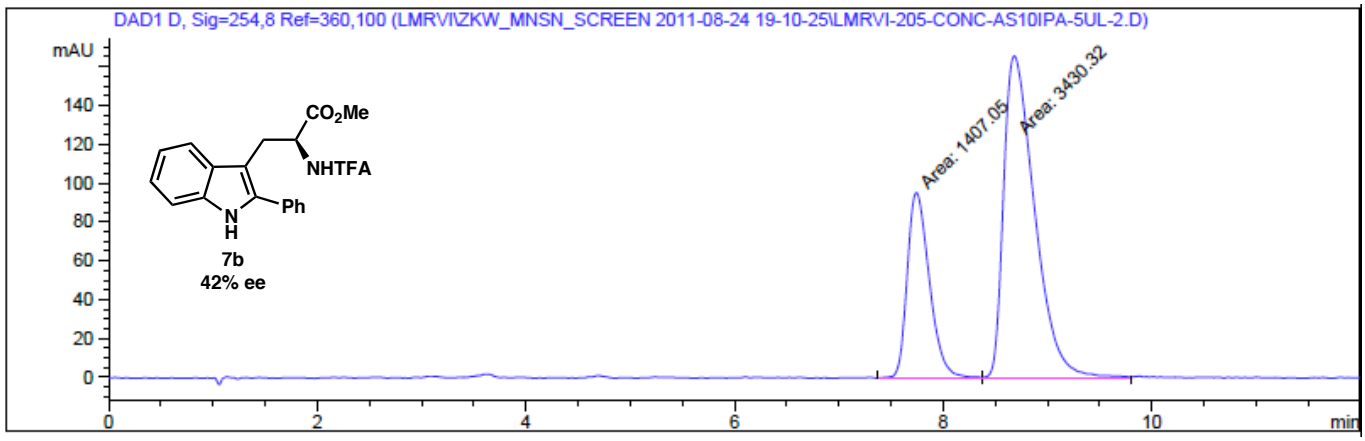
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.016	MM	0.5552	2340.98975	70.28041	67.3814
2	12.949	MM	0.6247	1133.24951	30.23348	32.6186

7b (Table 2, entry 2): racemic



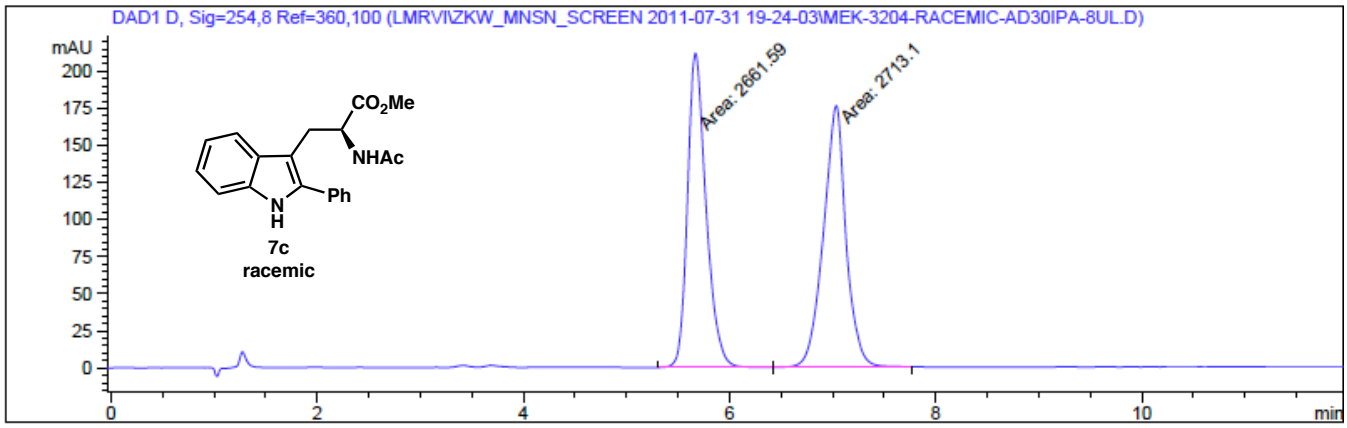
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.800	MM	0.3300	1309.54053	66.13437	50.3216
2	8.832	MM	0.4035	1292.80322	53.39447	49.6784

7b (Table 2, entry 2): enantioenriched, 42% ee



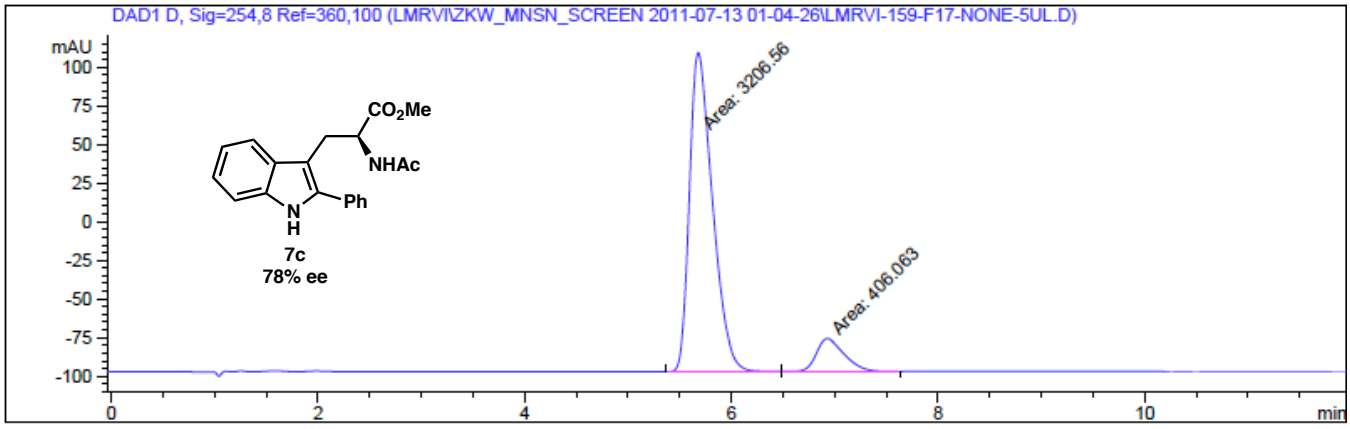
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.744	MM	0.2458	1407.04663	95.40716	29.0870
2	8.683	MM	0.3450	3430.32251	165.69673	70.9130

7c: racemic



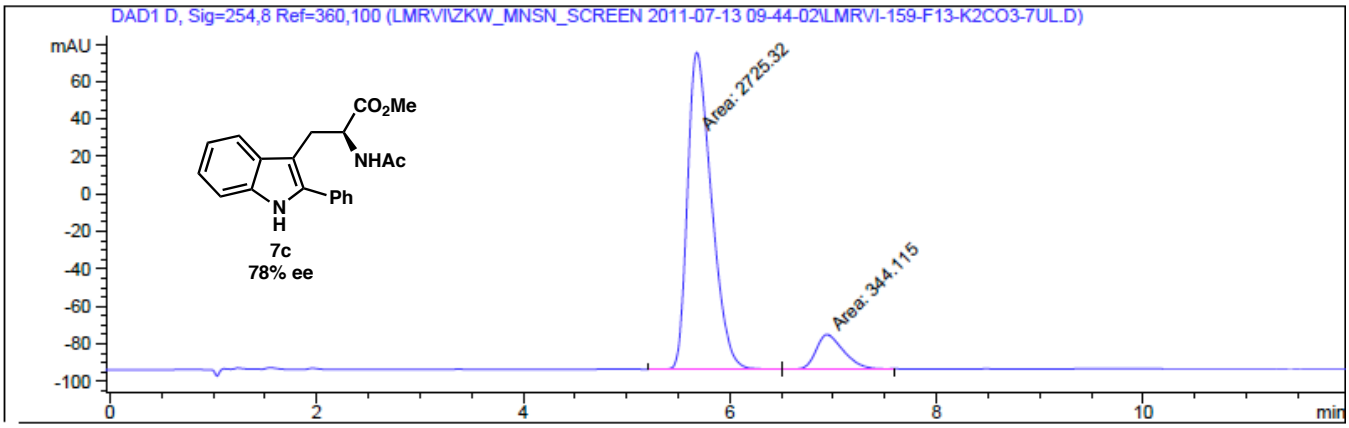
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.669	MM	0.2091	2661.59399	212.13072	49.5208
2	7.035	MM	0.2559	2713.10010	176.69841	50.4792

7c (Table 2, entry 3, no additive, DCM as solvent**):** enantioenriched, 78% ee



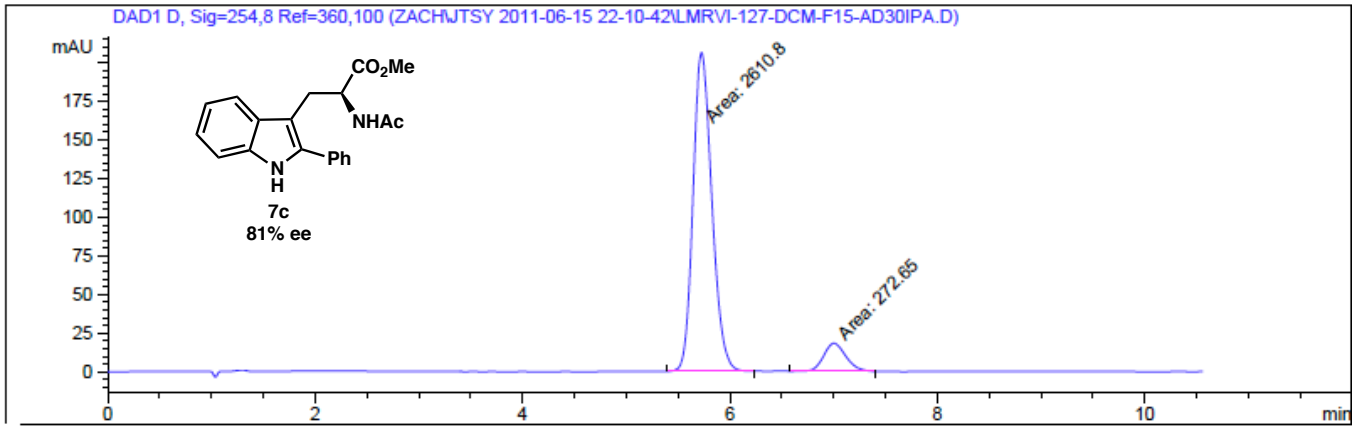
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.680	MM	0.2586	3206.56348	206.67487	88.7599
2	6.931	MM	0.3155	406.06302	21.44969	11.2401

7c (Table 2, entry 6, with K_2CO_3, DCM as solvent**):** enantioenriched, 78% ee



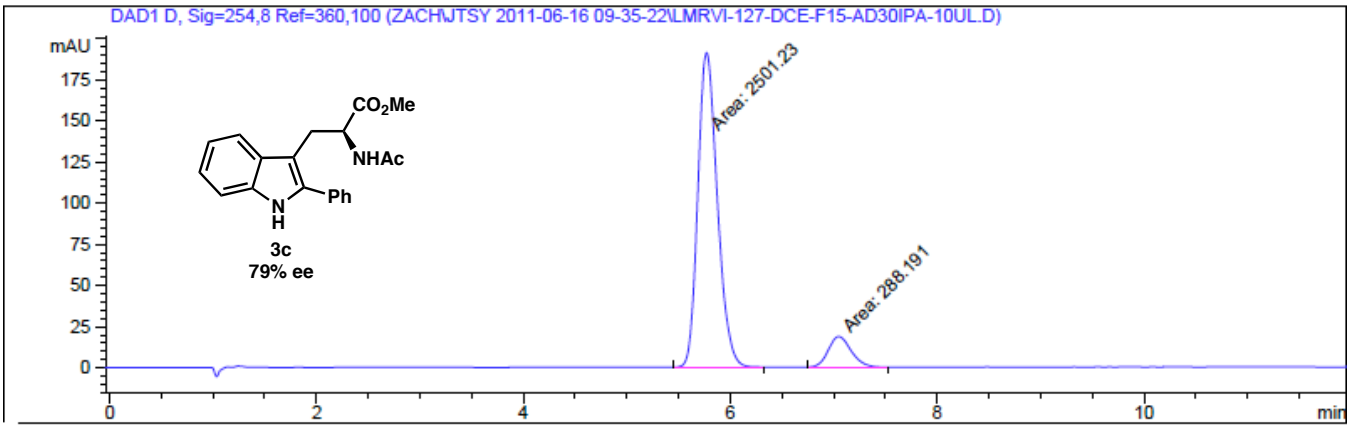
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.680	MM	0.2687	2725.31787	169.06570	88.7890
2	6.940	MM	0.3096	344.11493	18.52597	11.2110

7c (Table 2, entry 8, with 4Å MS, DCM as solvent**):** enantioenriched, 81% ee



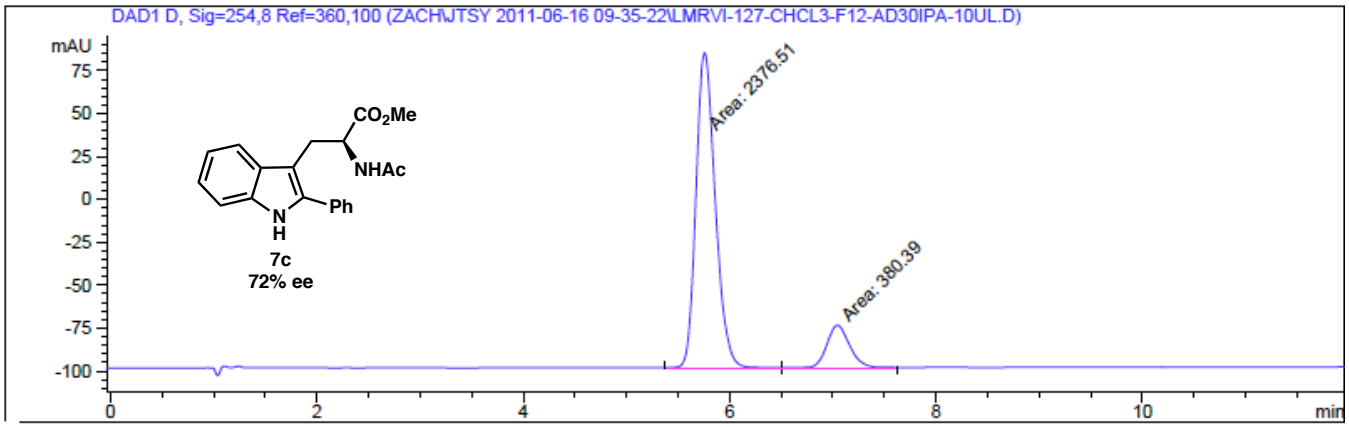
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.727	MM	0.2106	2610.80005	206.59111	90.5443
2	7.003	MM	0.2491	272.64963	18.24538	9.4557

7c (Table 2, entry 9, with 4Å MS, DCE as solvent**):** enantioenriched, 79% ee



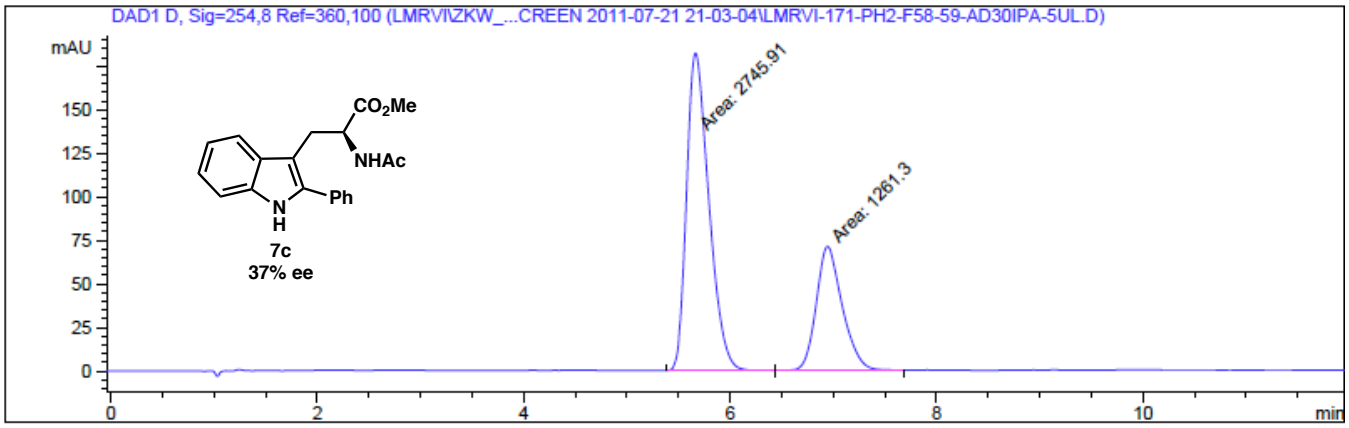
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.770	MM	0.2179	2501.22583	191.34946	89.6684
2	7.046	MM	0.2574	288.19092	18.66254	10.3316

7c (Table 2, entry 10, with 4Å MS, $CHCl_3$ as solvent**):** enantioenriched, 72% ee



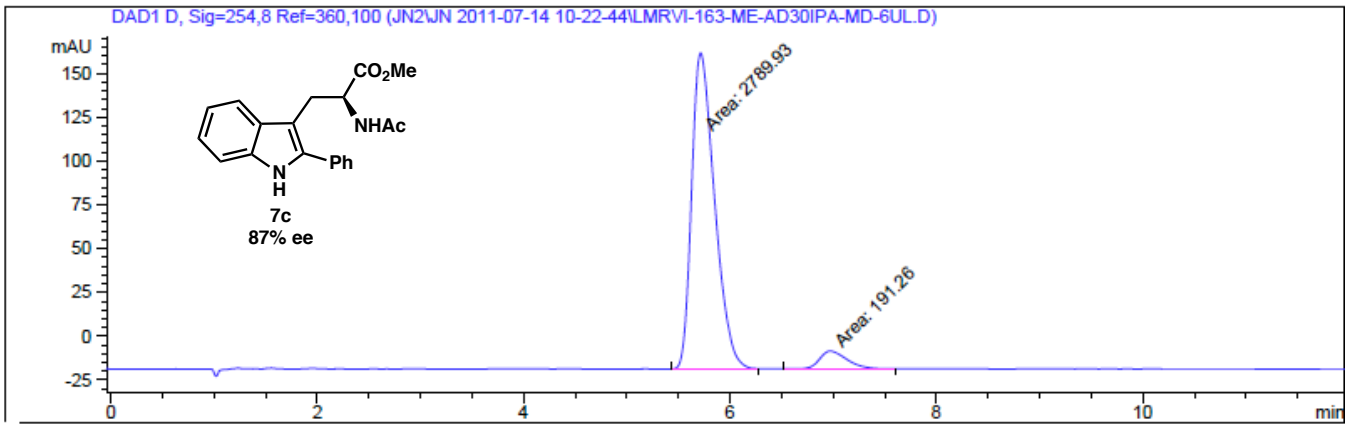
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.758	MM	0.2156	2376.51440	183.68063	86.2023
2	7.046	MM	0.2564	380.39029	24.72798	13.7977

7c (Table 3, entry 2, (*R*)-3,3'-diphenyl-BINOL (**9b**))**:** enantioenriched, 37% ee



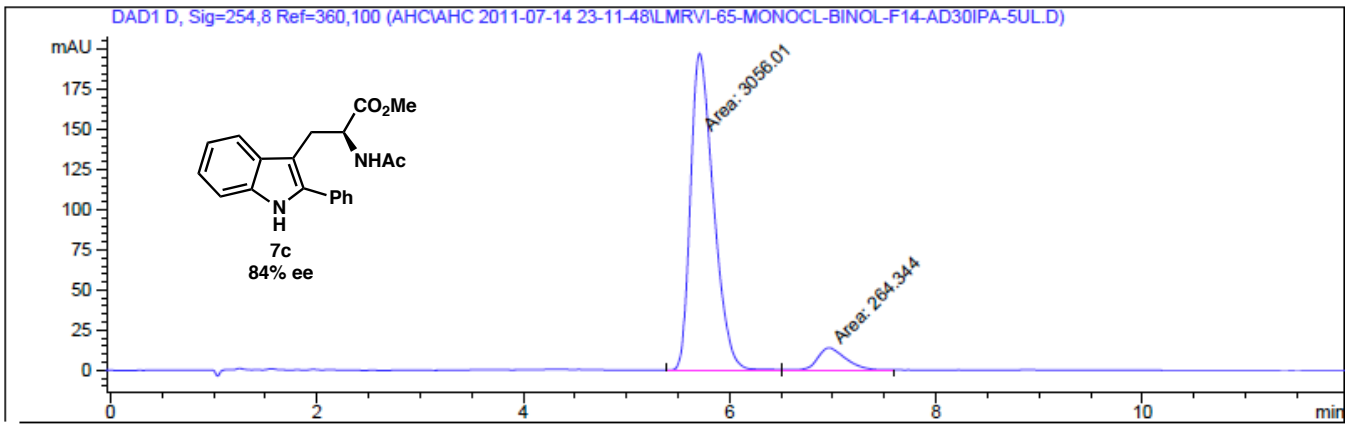
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.665	MM	0.2511	2745.91113	182.26123	68.5243
2	6.944	MM	0.2946	1261.29749	71.36543	31.4757

7c (Table 3, entry 3, (*R*)-3,3'-dimethyl-BINOL (**9c**))**:** enantioenriched, 87% ee



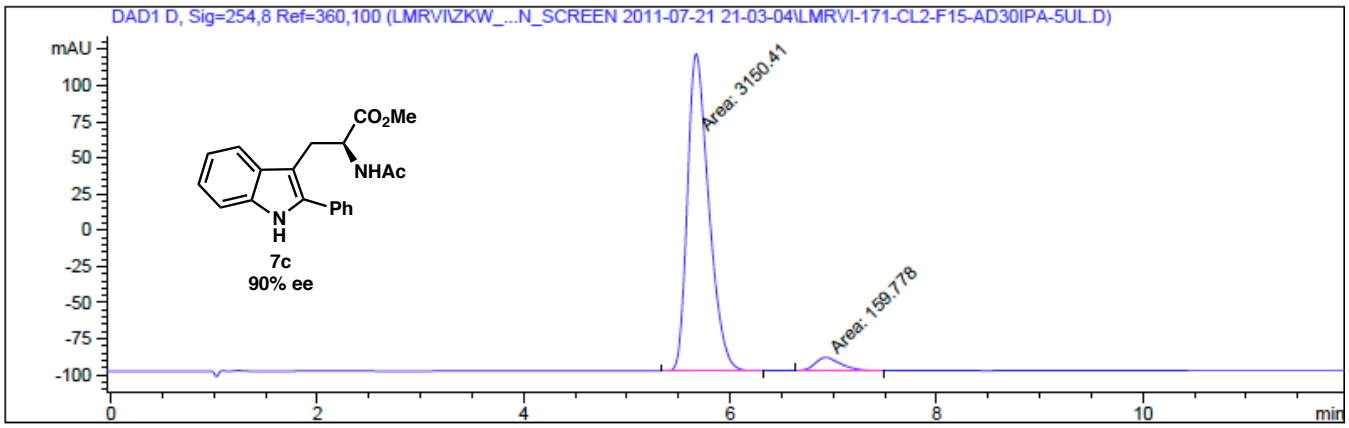
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.716	MM	0.2577	2789.92920	180.42043	93.5844
2	6.976	MM	0.3109	191.26035	10.25464	6.4156

7c (Table 3, entry 4, (*R*)-3-chloro-BINOL (**9d**)**):** enantioenriched, 84% ee



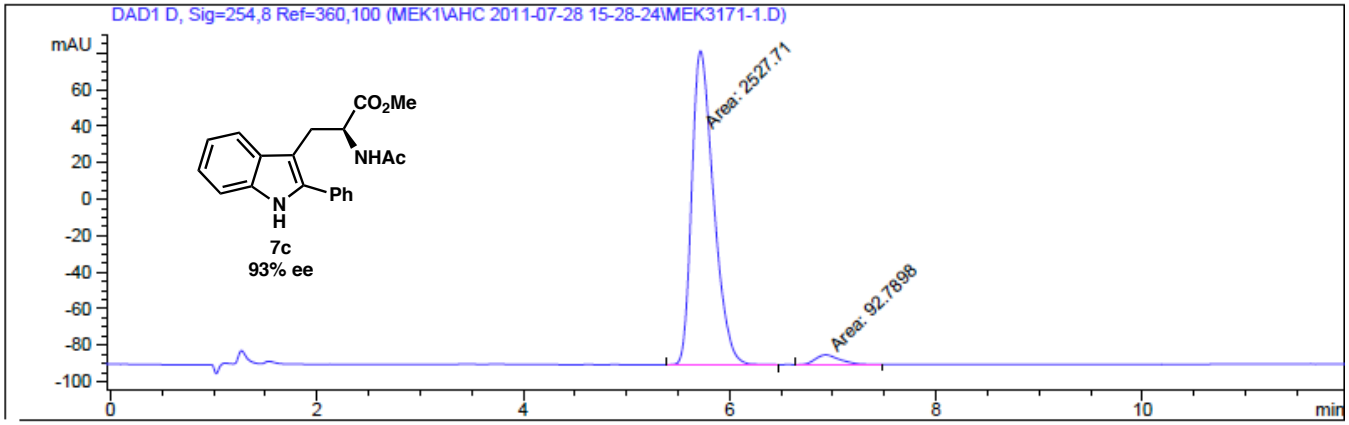
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.709	MM	0.2580	3056.00586	197.42212	92.0387
2	6.963	MM	0.3156	264.34421	13.95930	7.9613

7c (Table 3, entry 5, (*R*)-3,3'-dichloro-BINOL (**9e**)**):** enantioenriched, 90% ee



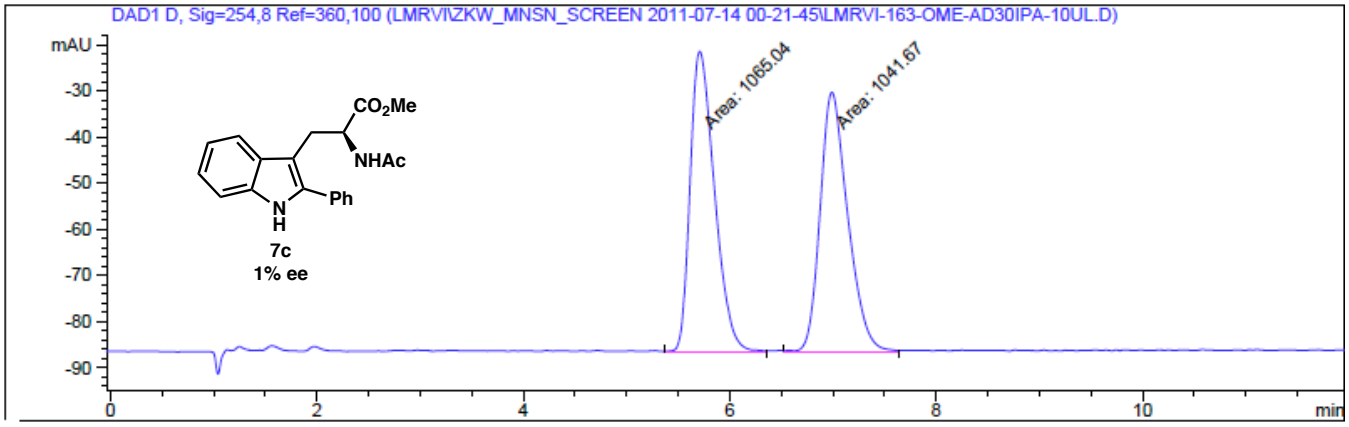
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.671	MM	0.2398	3150.40820	218.99393	95.1731
2	6.928	MM	0.2902	159.77843	9.17721	4.8269

7c (Table 3, entry 6, (*R*)-3,3'-dibromo-BINOL (9f)): enantioenriched, 93% ee



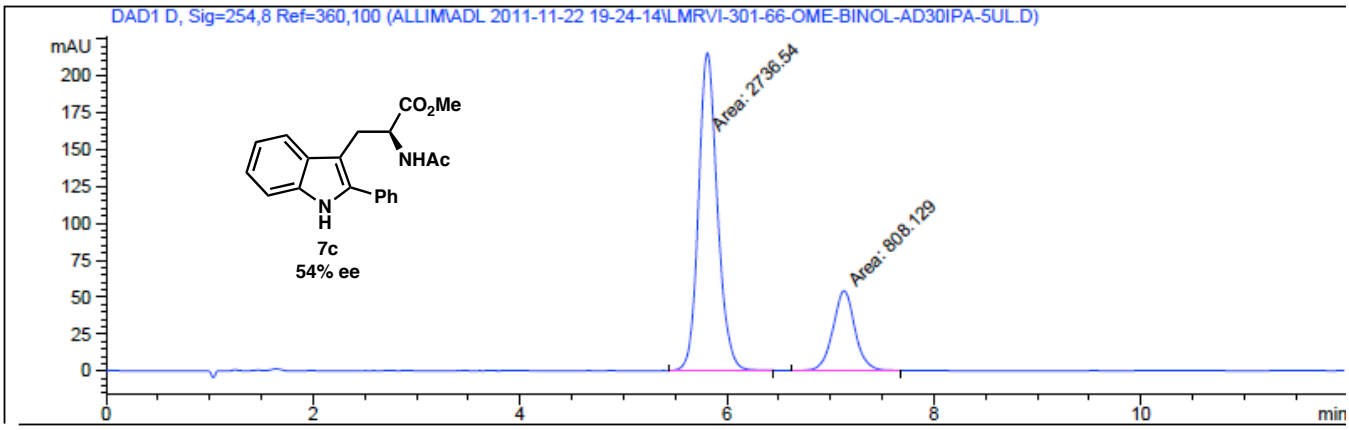
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.718	MM	0.2447	2527.71191	172.14331	96.4591
2	6.930	MM	0.2860	92.78983	5.40752	3.5409

7c (Table 3, entry 7, (*R*)-3,3'-dimethoxy-BINOL (9g)): enantioenriched, 1% ee



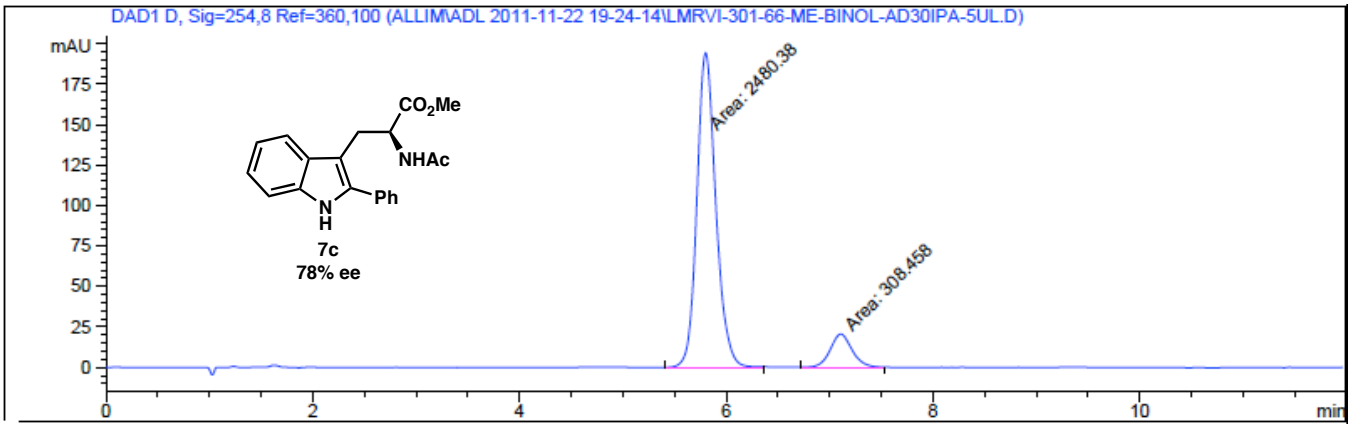
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.709	MM	0.2729	1065.04150	65.04519	50.5546
2	6.989	MM	0.3090	1041.67273	56.18153	49.4454

7c (Table 3, entry 8, (*R*)-6,6'-dimethoxy-BINOL (**9h**))**:** enantioenriched, 54% ee



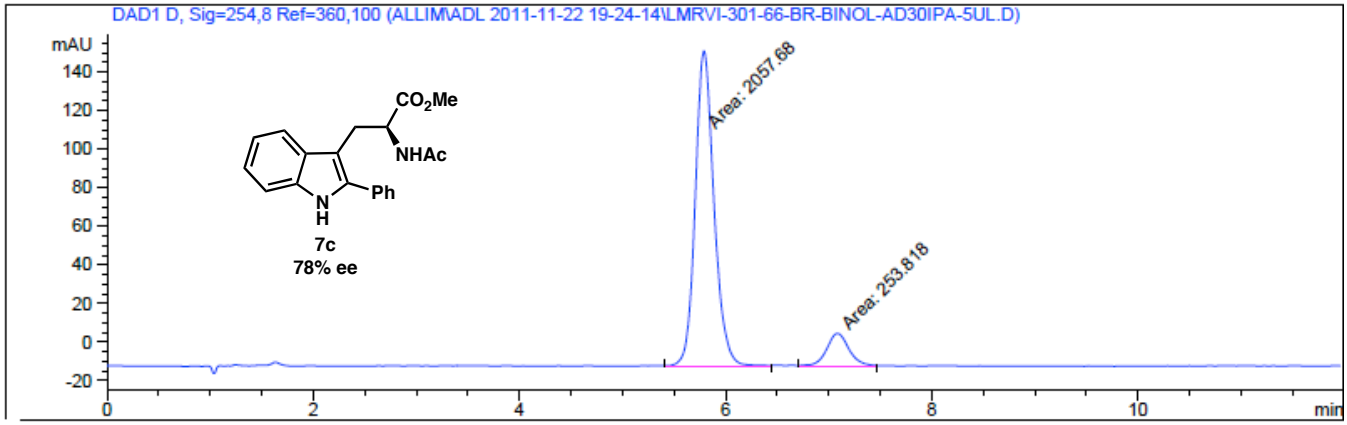
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.811	MM	0.2116	2736.53906	215.56961	77.2016
2	7.134	MM	0.2481	808.12903	54.27740	22.7984

7c (Table 3, entry 9, (*R*)-6,6'-dimethyl-BINOL (**9i**))**:** enantioenriched, 78% ee



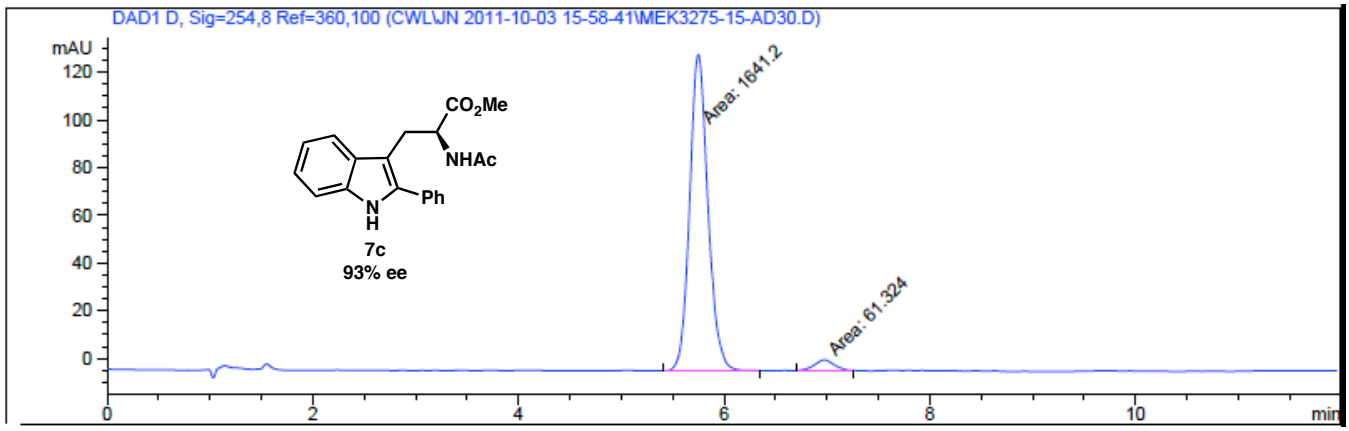
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.801	MM	0.2122	2480.38086	194.82515	88.9395
2	7.108	MM	0.2484	308.45816	20.69525	11.0605

7c (Table 3, entry 10, (*R*)-6,6'-dibromo-BINOL (**9j**)**):** enantioenriched, 78% ee



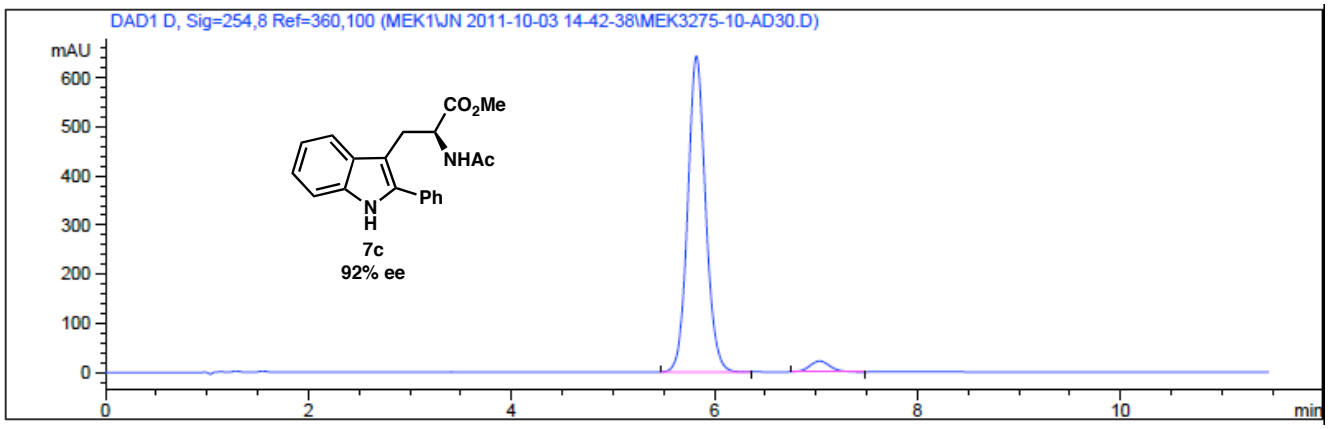
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.791	MM	0.2099	2057.68115	163.40929	89.0193
2	7.089	MM	0.2512	253.81812	16.83896	10.9807

7c (Table 3, entry 12, 15 mol % **9f):** enantioenriched, 93% ee



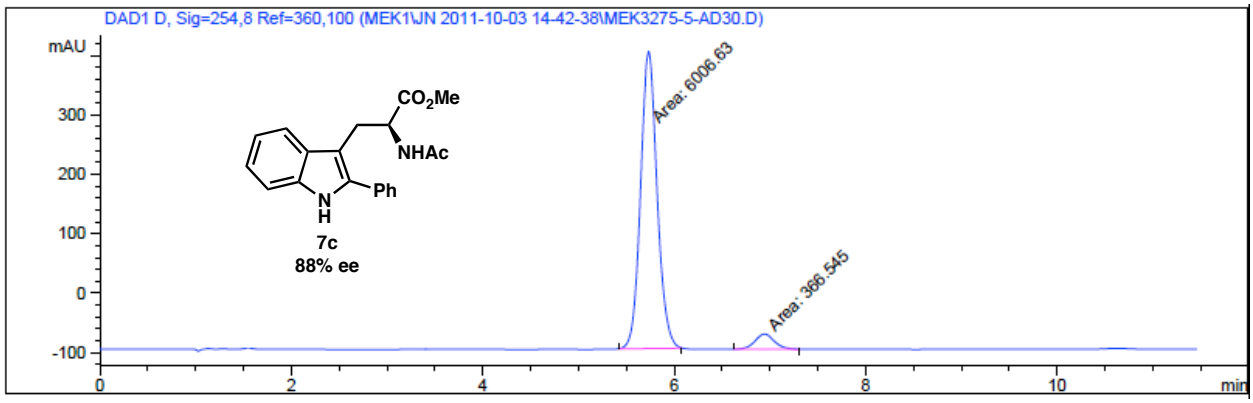
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.749	MM	0.2058	1641.20337	132.90843	96.3981
2	6.976	MM	0.2267	61.32397	4.50806	3.6019

7c (Table 3, entry 13, 10 mol % **9f):** enantioenriched, 92% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.823	BB	0.1872	7899.69922	643.65857	96.1676
2	7.036	BB	0.2153	314.81149	22.49169	3.8324

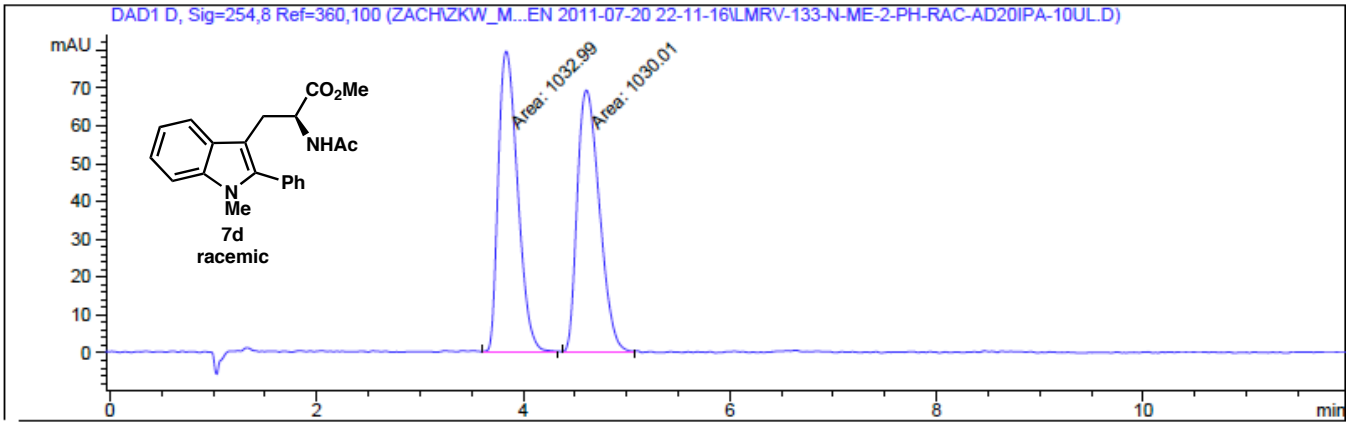
7c (Table 3, entry 14, 5 mol % **9f):** enantioenriched, 88% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.732	MM	0.1999	6006.63232	500.90204	94.2486
2	6.943	MM	0.2375	366.54471	25.72305	5.7514

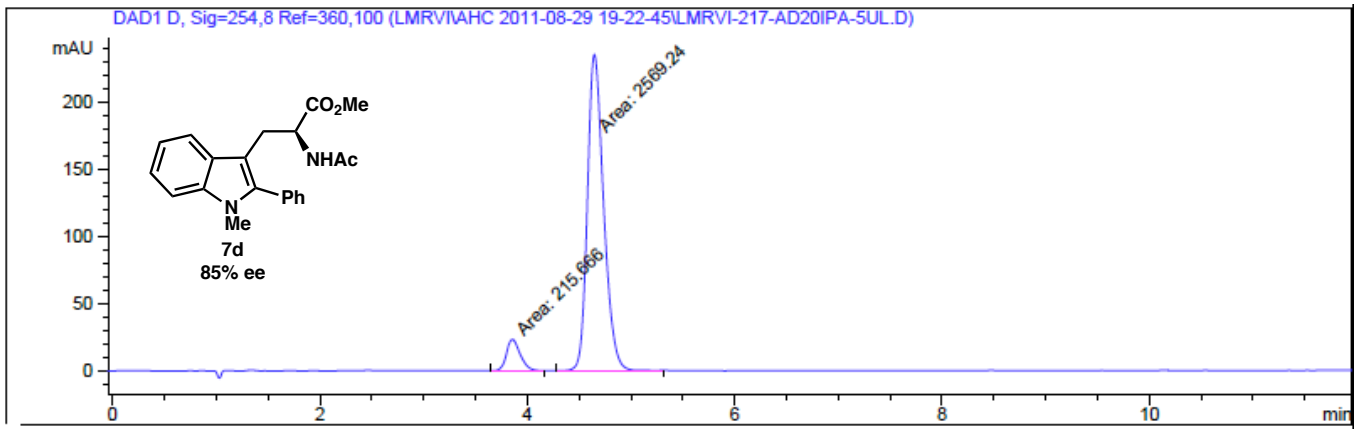
Substrate scope of the conjugate addition/asymmetric protonation

7d (Table 4, entry 2): racemic



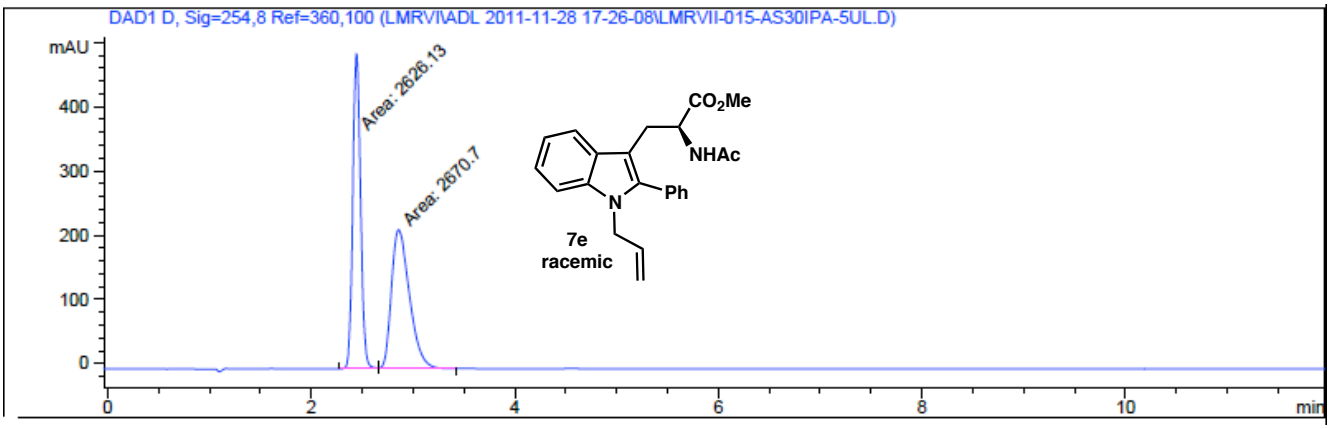
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.836	MM	0.2168	1032.99182	79.40057	50.0722
2	4.612	MM	0.2483	1030.01440	69.12988	49.9278

7d (Table 4, entry 2): enantioenriched, 85% ee



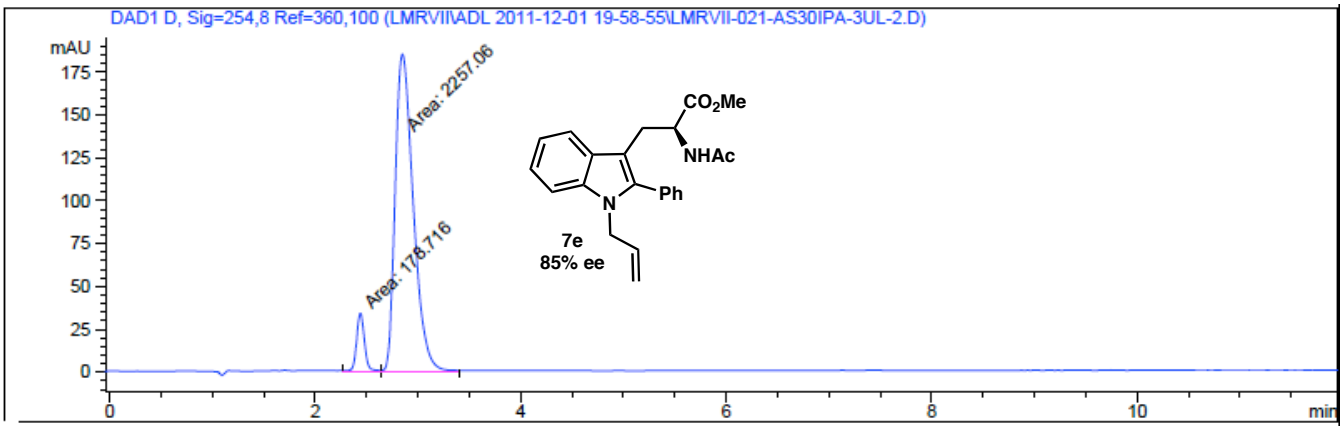
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.857	MM	0.1536	215.66585	23.40283	7.7441
2	4.648	MM	0.1816	2569.23853	235.83917	92.2559

7e (Table 4, entry 3): racemic



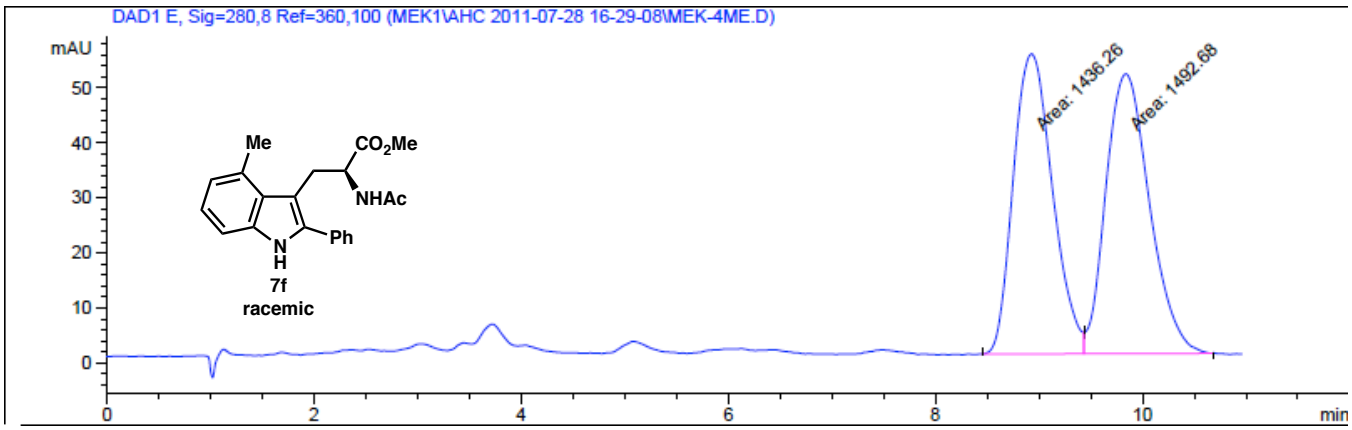
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.445	MM	0.0885	2626.12964	494.64706	49.5793
2	2.860	MM	0.2054	2670.69971	216.69223	50.4207

7e (Table 4, entry 3): enantioenriched, 85% ee



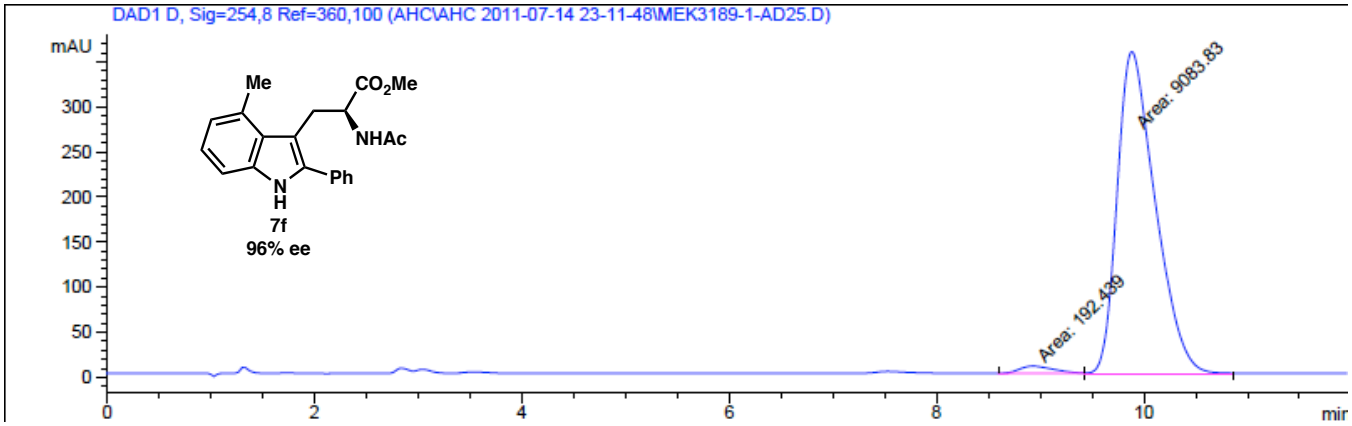
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.440	MM	0.0877	178.71585	33.96154	7.3371
2	2.850	MM	0.2033	2257.05518	185.04457	92.6629

7f (Table 4, entry 4): racemic



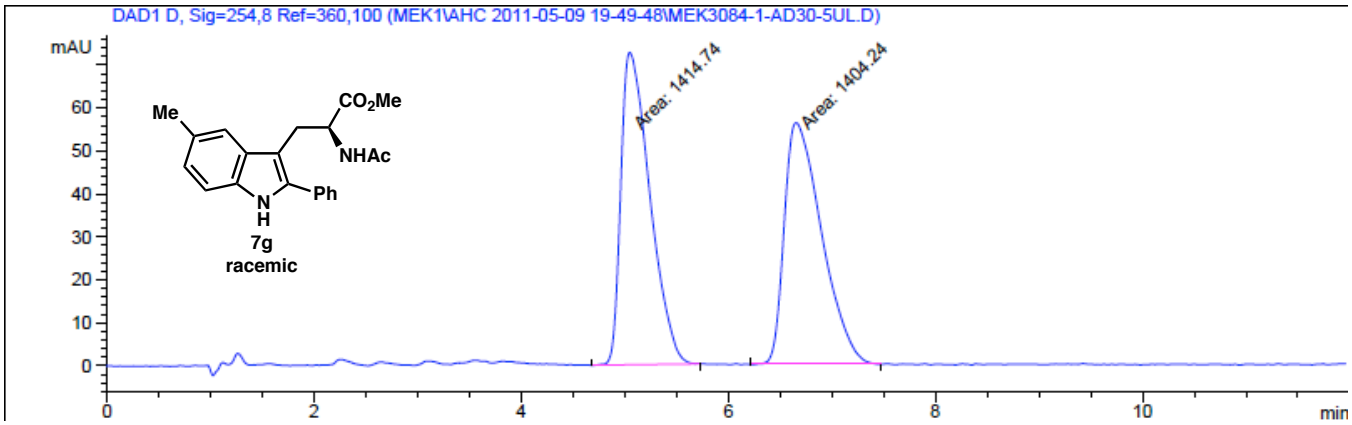
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.929	MF	0.4389	1436.26184	54.54070	49.0370
2	9.840	FM	0.4892	1492.67529	50.85297	50.9630

3e (Table 2, entry 3): enantioenriched, 96% ee



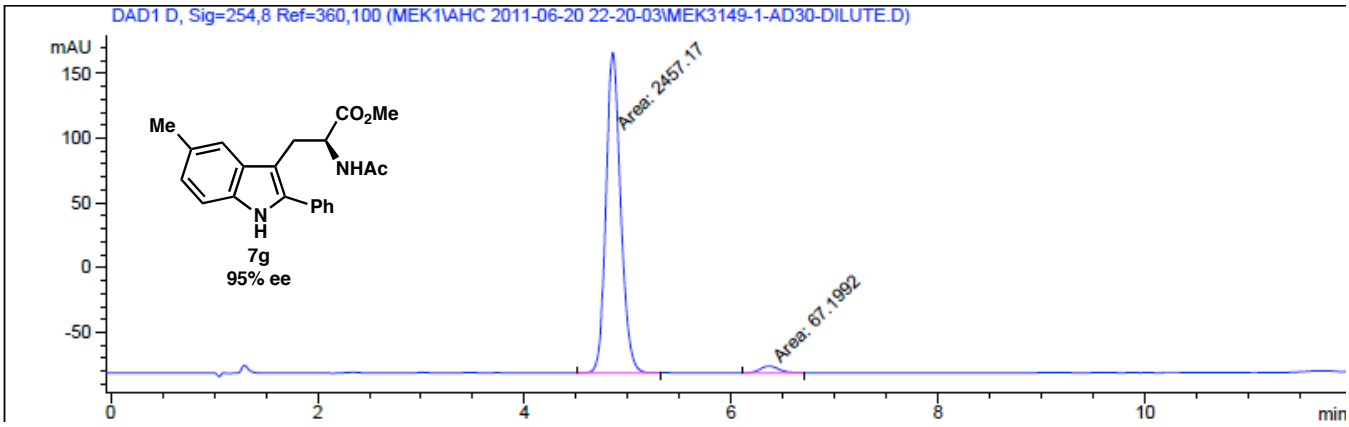
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.934	MF	0.3836	192.43893	8.36206	2.0745
2	9.884	FM	0.4243	9083.83105	356.81247	97.9255

7g (Table 4, entry 5): racemic



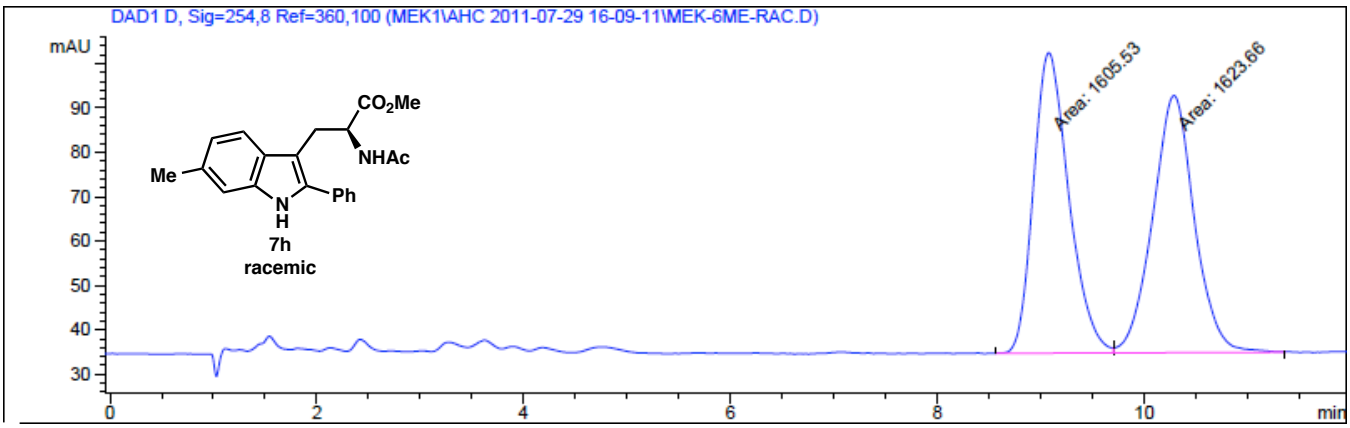
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.050	MM	0.3239	1414.74487	72.79134	50.1863
2	6.656	MM	0.4167	1404.24048	56.16964	49.8137

7g (Table 4, entry 5): enantioenriched, 95% ee



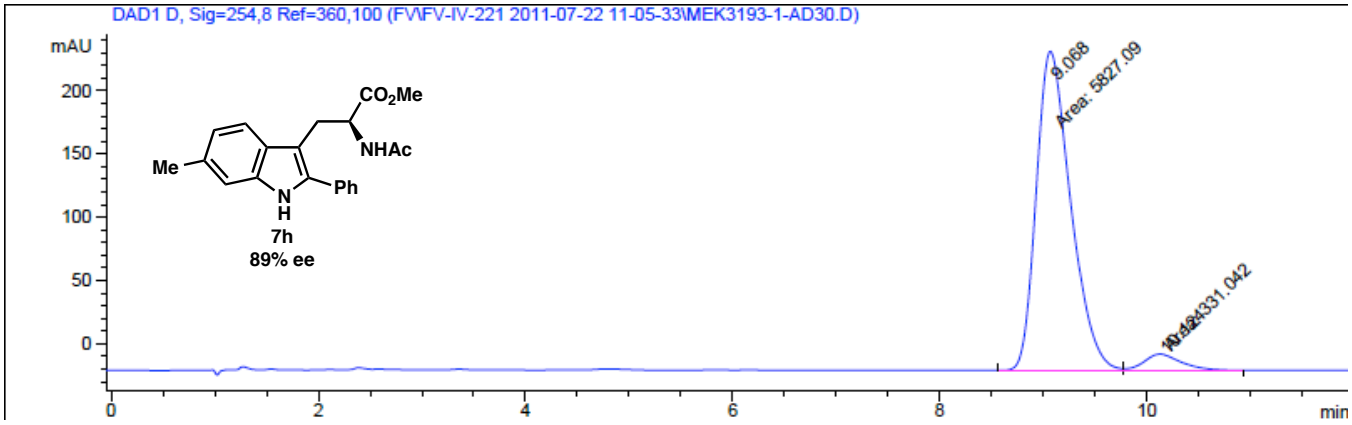
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.854	MM	0.1651	2457.17432	248.06091	97.3380
2	6.363	MM	0.2091	67.19923	5.35534	2.6620

7h (Table 4, entry 6): racemic



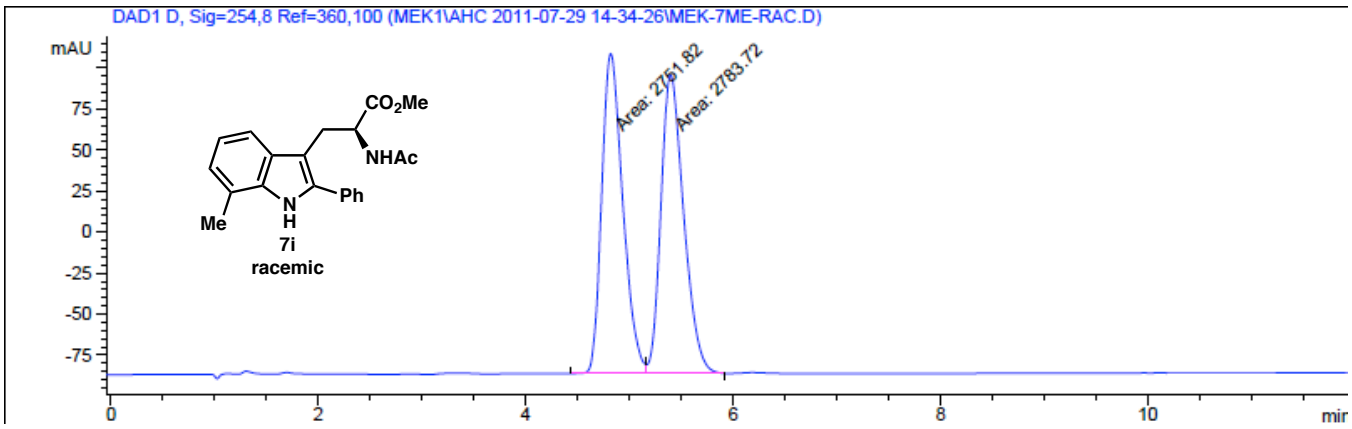
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.077	MF	0.3956	1605.53394	67.64597	49.7194
2	10.287	FM	0.4674	1623.65698	57.89628	50.2806

7h (Table 4, entry 6): enantioenriched, 89% ee



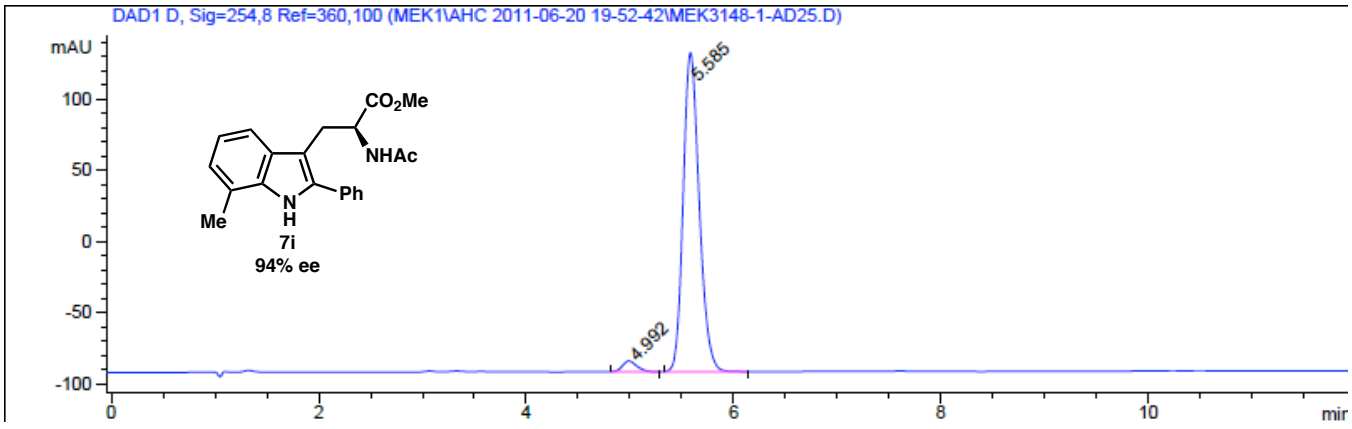
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.068	MF	0.3850	5827.08984	252.25751	94.6243
2	10.124	FM	0.4240	331.04230	13.01276	5.3757

7i (Table 4, entry 7): racemic



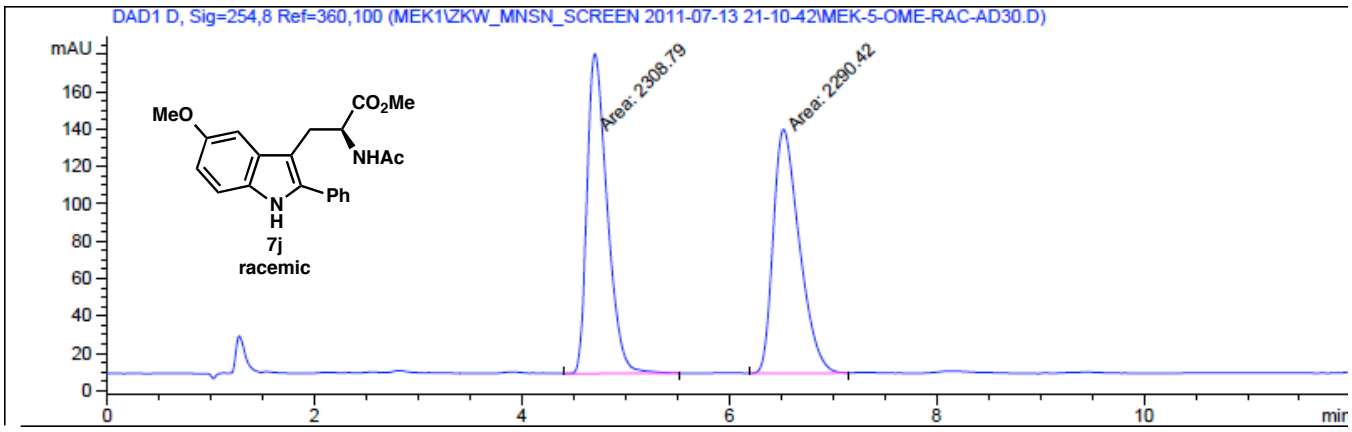
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.820	MF	0.2351	2751.81982	195.09174	49.7119
2	5.397	FM	0.2547	2783.71802	182.13214	50.2881

7i (Table 4, entry 7): enantioenriched, 94% ee



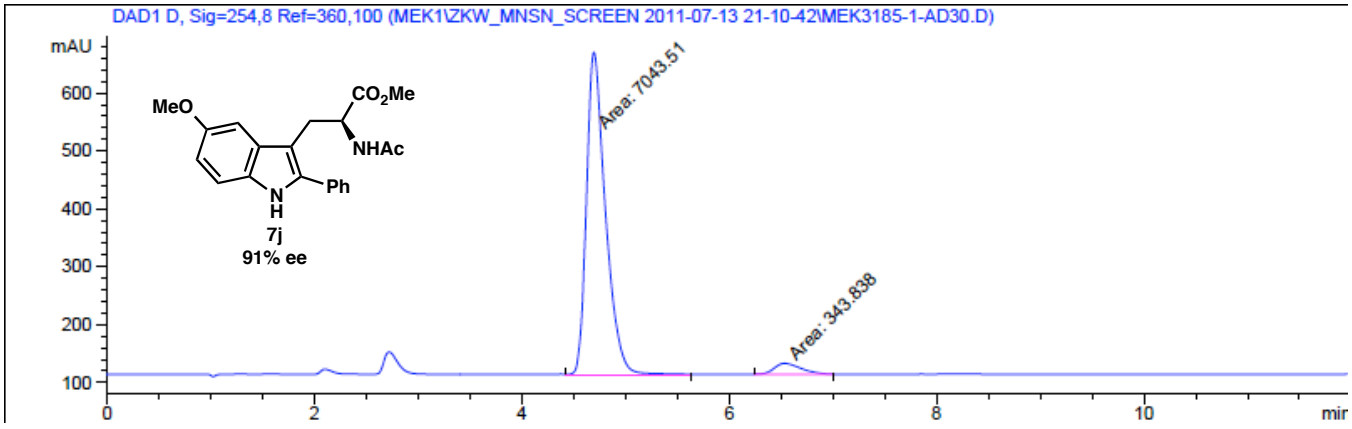
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.992	BB	0.1485	73.50820	7.62170	2.9637
2	5.585	BB	0.1651	2406.73779	224.39053	97.0363

7j (Table 4, entry 8): racemic



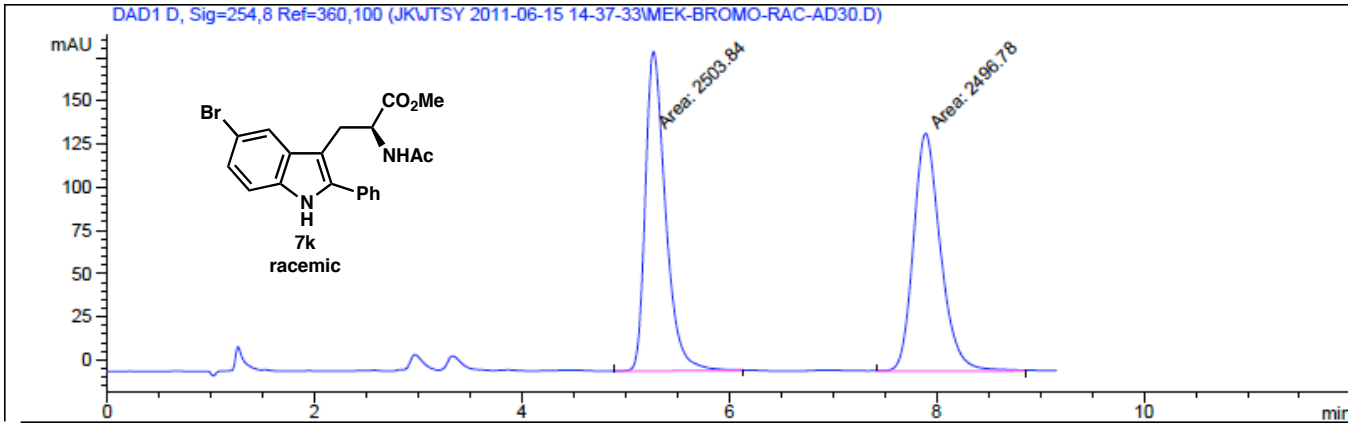
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.705	MM	0.2251	2308.79272	170.98026	50.1998
2	6.524	MM	0.2925	2290.41650	130.51103	49.8002

7j (Table 4, entry 8): enantioenriched, 91% ee



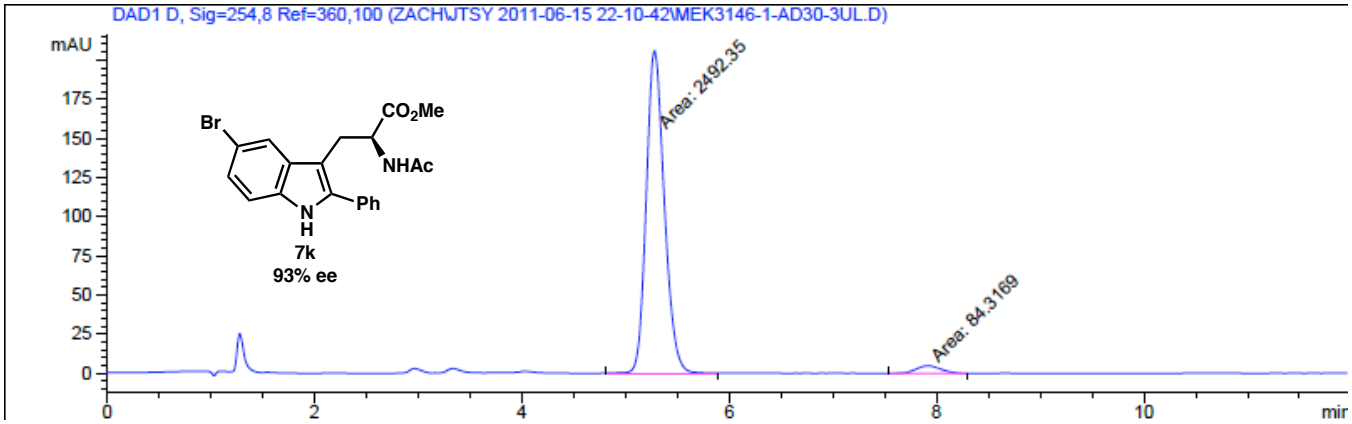
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.696	MM	0.2109	7043.50879	556.51990	95.3456
2	6.537	MM	0.3008	343.83807	19.05145	4.6544

7k (Table 4, entry 9): racemic



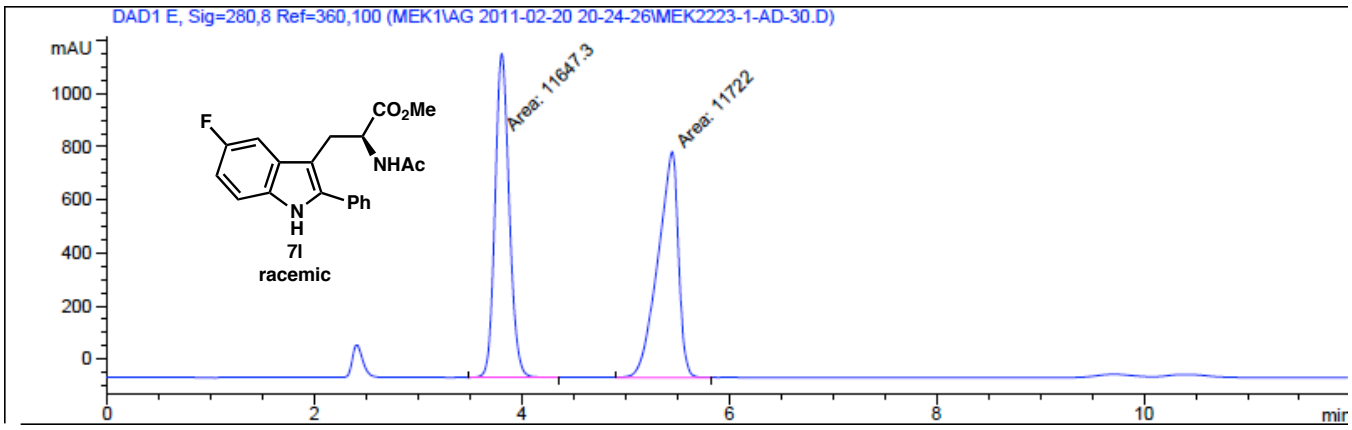
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.271	MM	0.2255	2503.83789	185.02051	50.0705
2	7.894	MM	0.3023	2496.78491	137.64893	49.9295

7k (Table 4, entry 9): enantioenriched, 93% ee



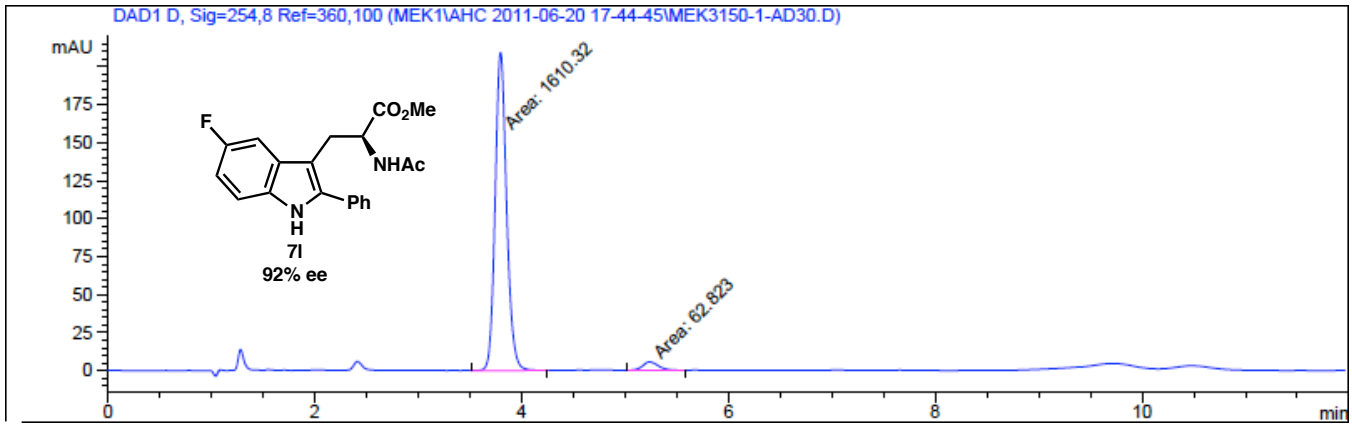
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.280	MM	0.2015	2492.35010	206.16266	96.7277
2	7.908	MM	0.2847	84.31690	4.93608	3.2723

7l (Table 4, entry 10): racemic



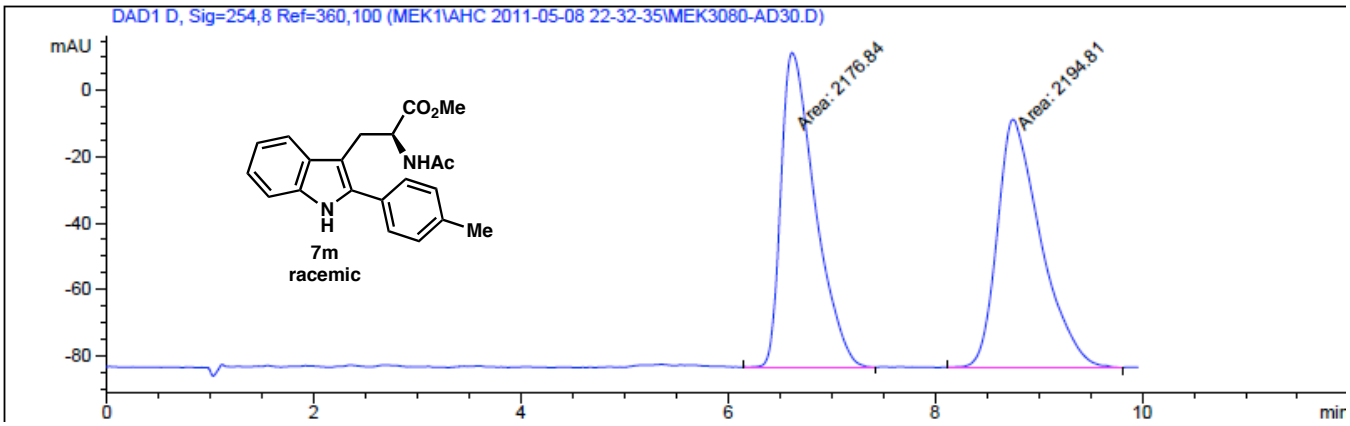
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.808	MM	0.1587	1.16473e4	1223.43835	49.8401
2	5.451	MM	0.2288	1.17220e4	853.89844	50.1599

7l (Table 4, entry 10): enantioenriched, 92% ee



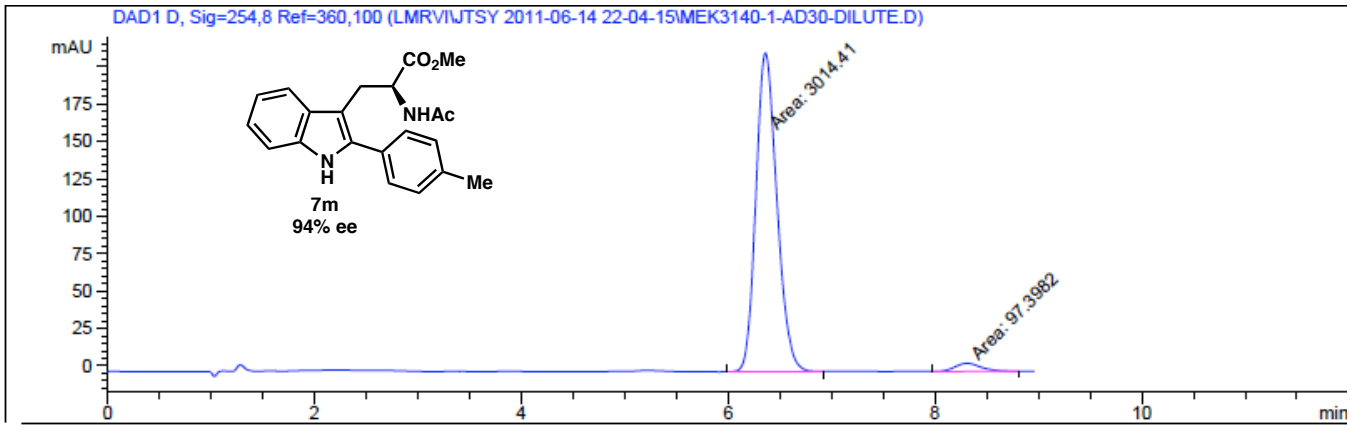
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.798	MM	0.1277	1610.32483	210.17332	96.2452
2	5.237	MM	0.1839	62.82299	5.69236	3.7548

7m (Table 4, entry 11): racemic



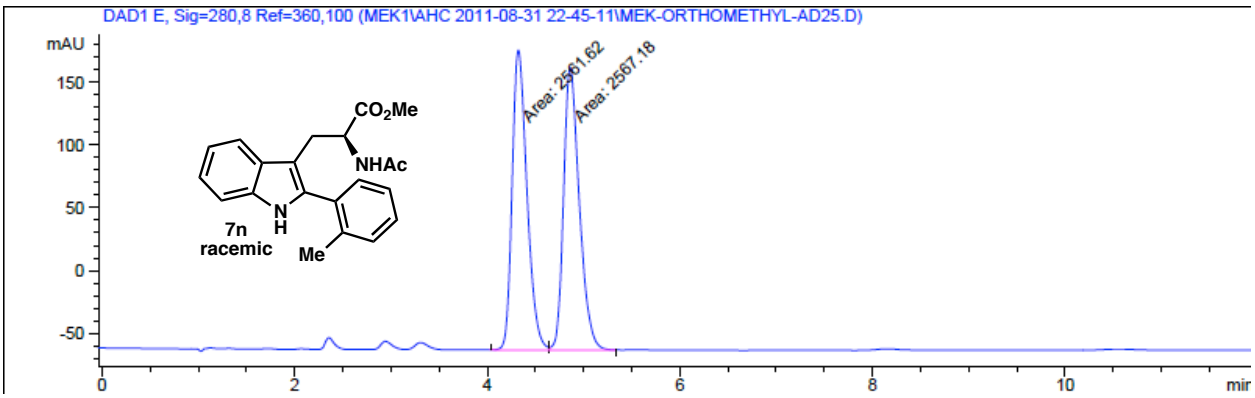
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.621	MM	0.3814	2176.84033	95.11774	49.7945
2	8.753	MM	0.4879	2194.80835	74.98085	50.2055

7m (Table 4, entry 11): enantioenriched, 94% ee



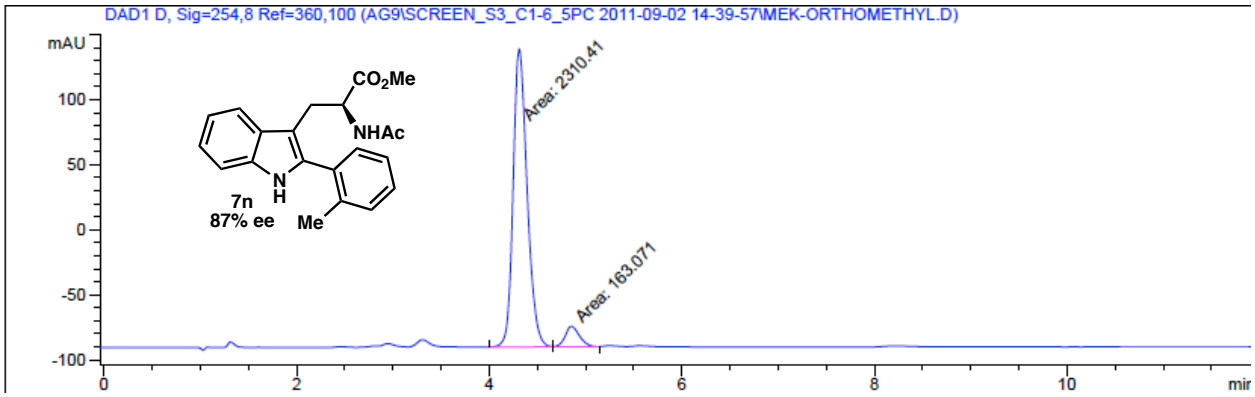
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.362	MM	0.2356	3014.40527	213.28644	96.8700
2	8.308	MM	0.2940	97.39824	5.52150	3.1300

7n (Table 4, entry 12): racemic



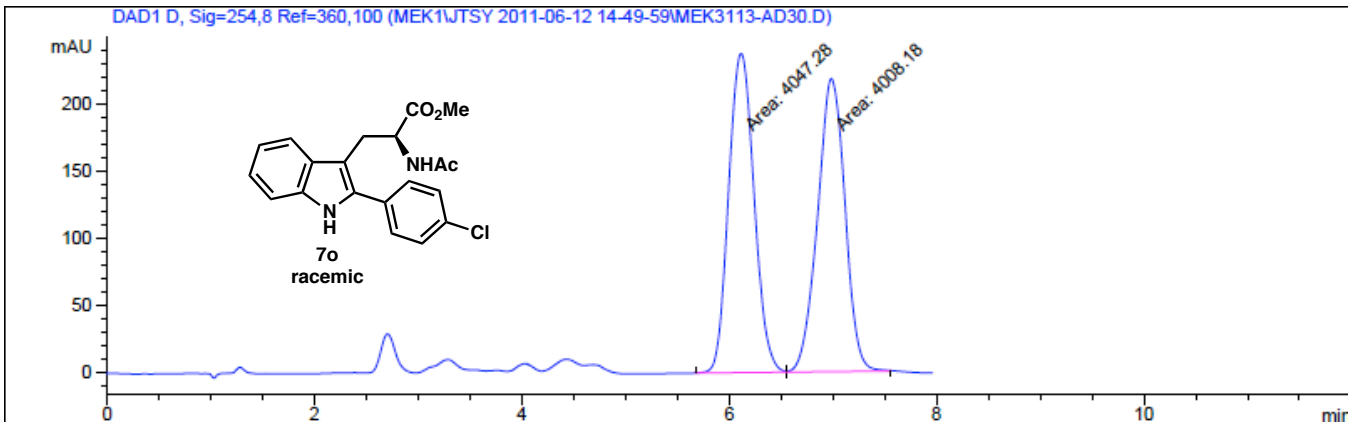
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.324	MF	0.1781	2561.61523	239.71214	49.9458
2	4.862	FM	0.1897	2567.17676	225.56844	50.0542

7n (Table 4, entry 12): enantioenriched, 87% ee



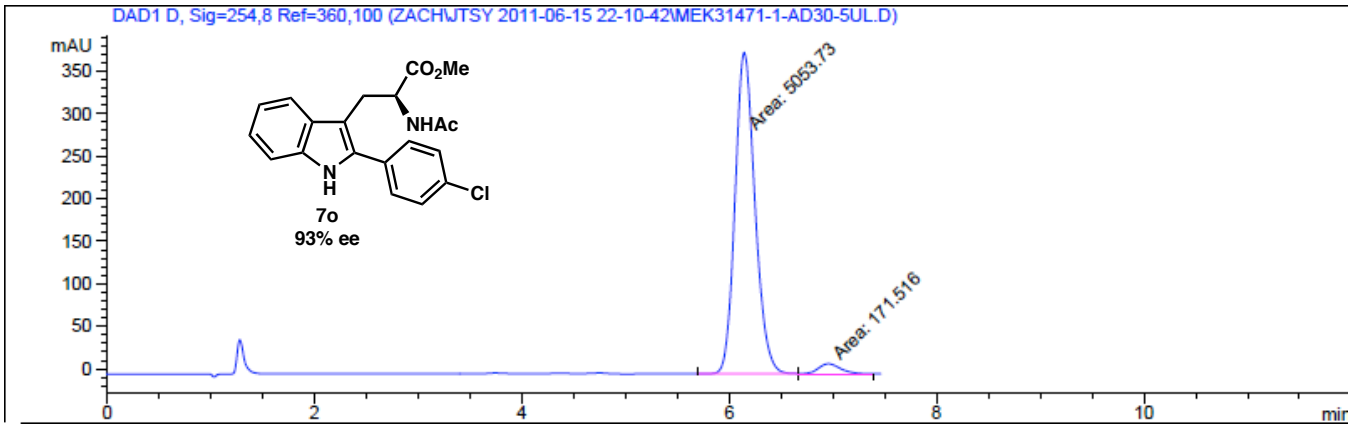
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.312	MF	0.1680	2310.40869	229.23323	93.4072
2	4.854	FM	0.1724	163.07098	15.76543	6.5928

7o (Table 4, entry 13): racemic



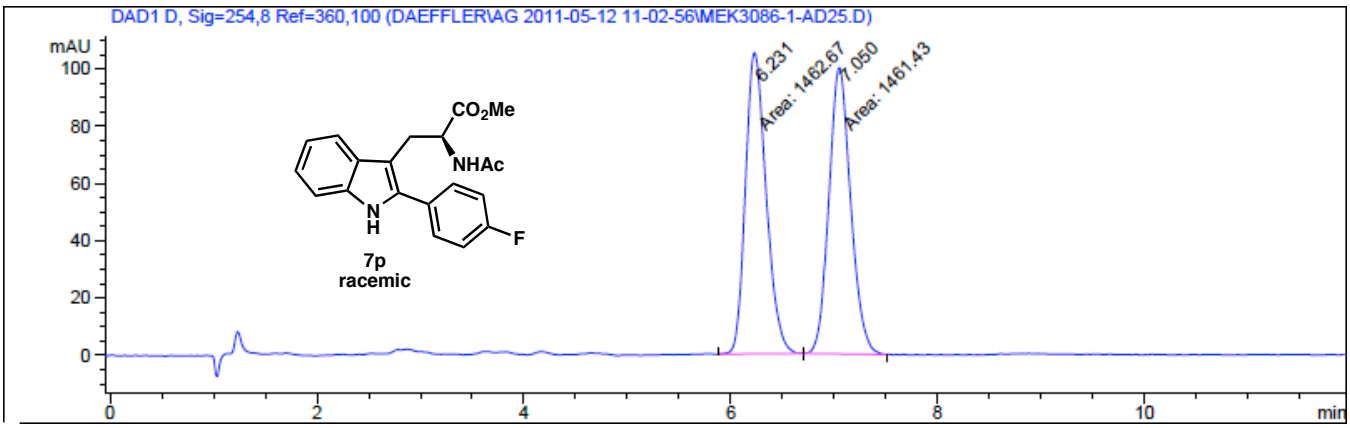
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.115	MF	0.2839	4047.27661	237.58223	50.2427
2	6.986	FM	0.3061	4008.18091	218.21001	49.7573

7o (Table 4, entry 13): enantioenriched, 93% ee



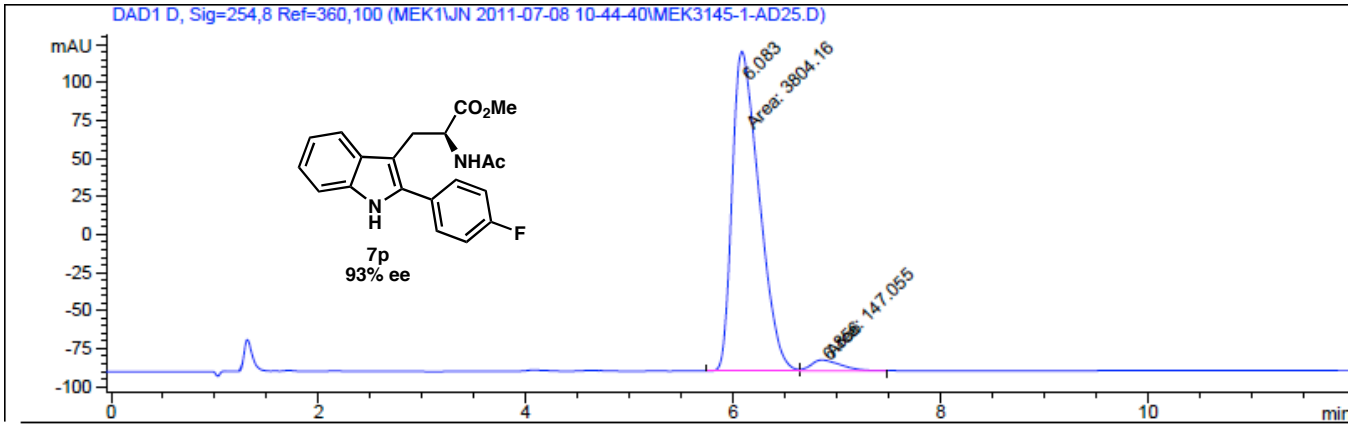
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.146	MF	0.2229	5053.73291	377.91241	96.7176
2	6.960	FM	0.2433	171.51614	11.74924	3.2824

7p (Table 4, entry 14): racemic



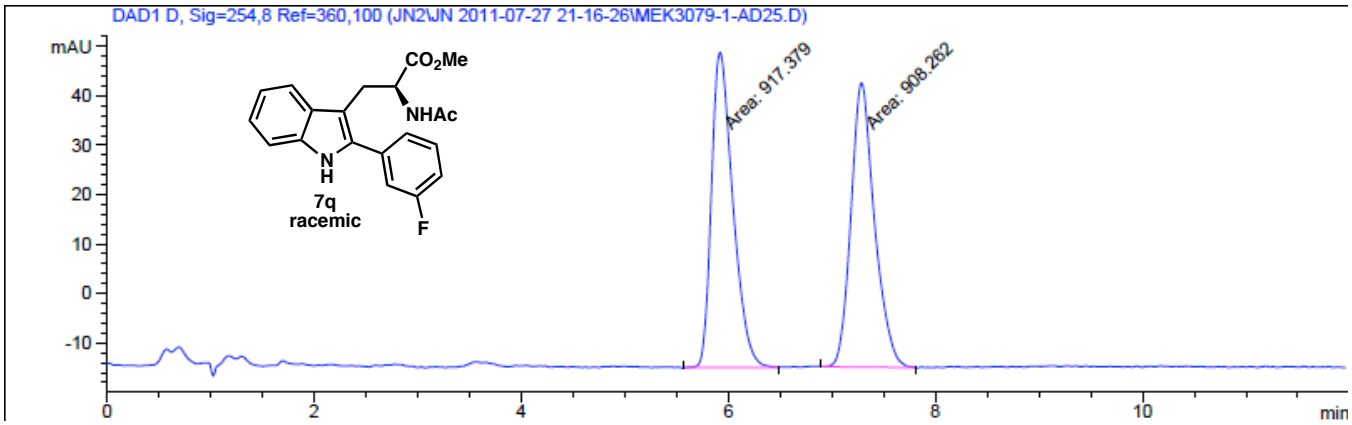
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.231	MM	0.2319	1462.67285	105.12125	50.0213
2	7.050	MM	0.2437	1461.42761	99.94221	49.9787

7p (Table 4, entry 14): enantioenriched, 93% ee



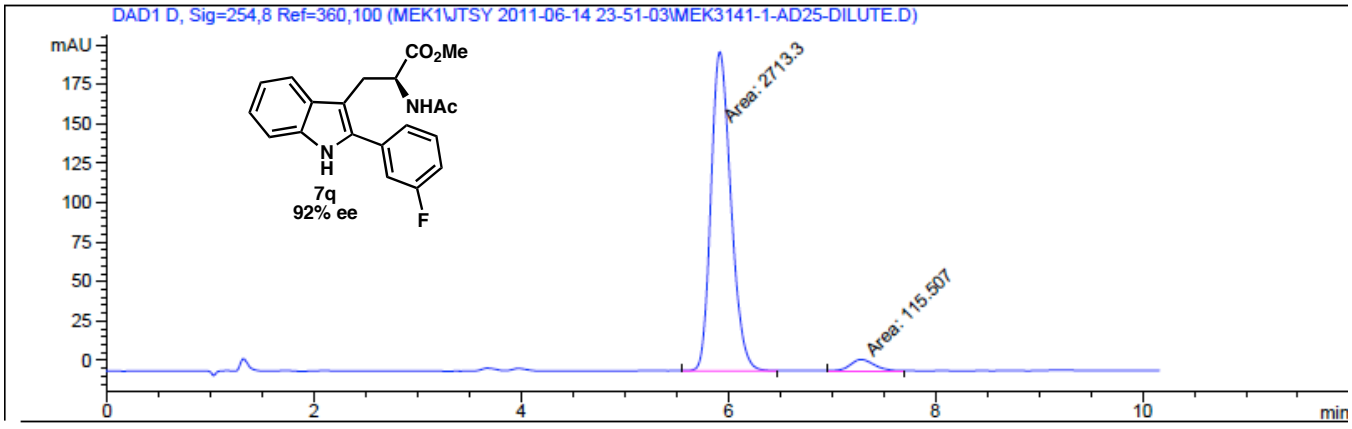
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.083	MF	0.3018	3804.16431	210.09053	96.2782
2	6.856	FM	0.3379	147.05510	7.25396	3.7218

7q (Table 4, entry 15): racemic



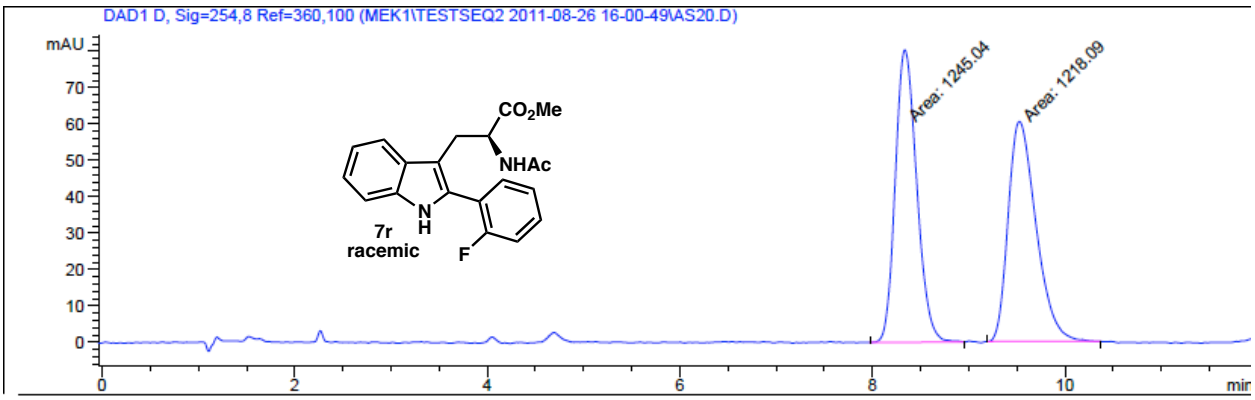
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.921	MM	0.2396	917.37872	63.80575	50.2497
2	7.287	MM	0.2632	908.26233	57.51292	49.7503

7q (Table 4, entry 15): enantioenriched, 92% ee



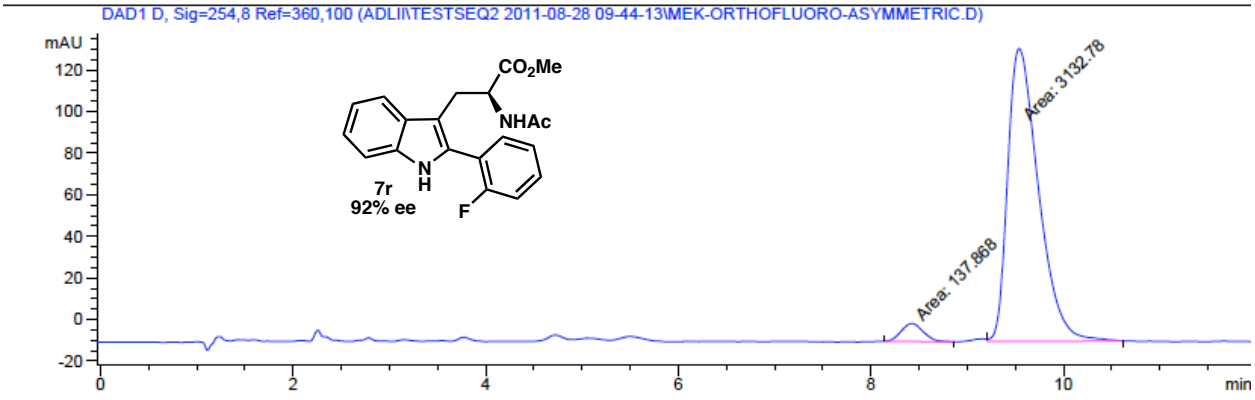
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.919	MM	0.2233	2713.30493	202.51631	95.9167
2	7.288	MM	0.2660	115.50748	7.23739	4.0833

7r (Table 4, entry 16): racemic



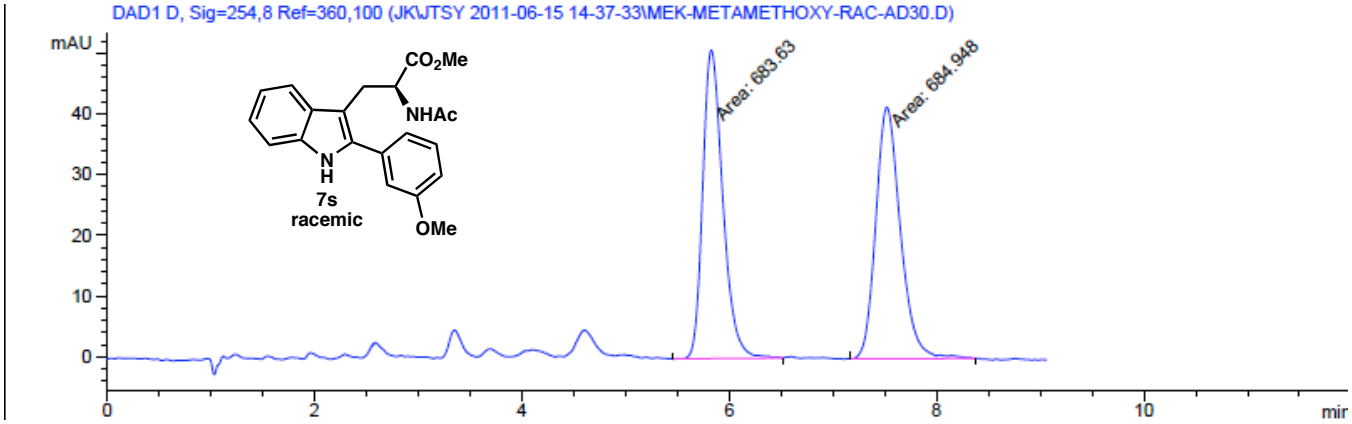
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.337	MM	0.2581	1245.03833	80.40385	50.5471
2	9.527	MM	0.3356	1218.08643	60.50121	49.4529

7r (Table 4, entry 16): enantioenriched, 92% ee



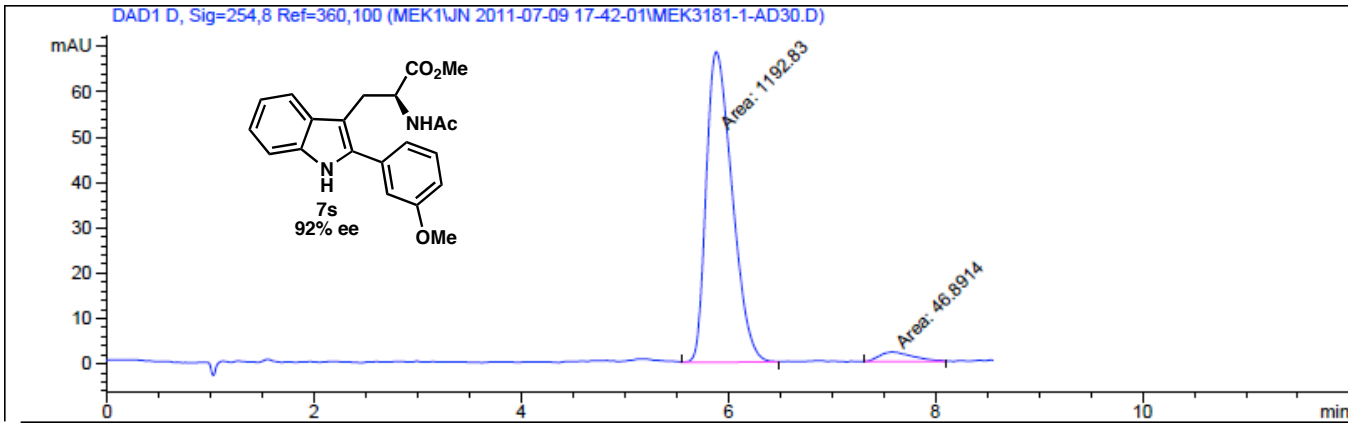
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.424	MM	0.2645	137.86769	8.68627	4.2153
2	9.540	MM	0.3705	3132.78320	140.94464	95.7847

7s (Table 4, entry 17): racemic



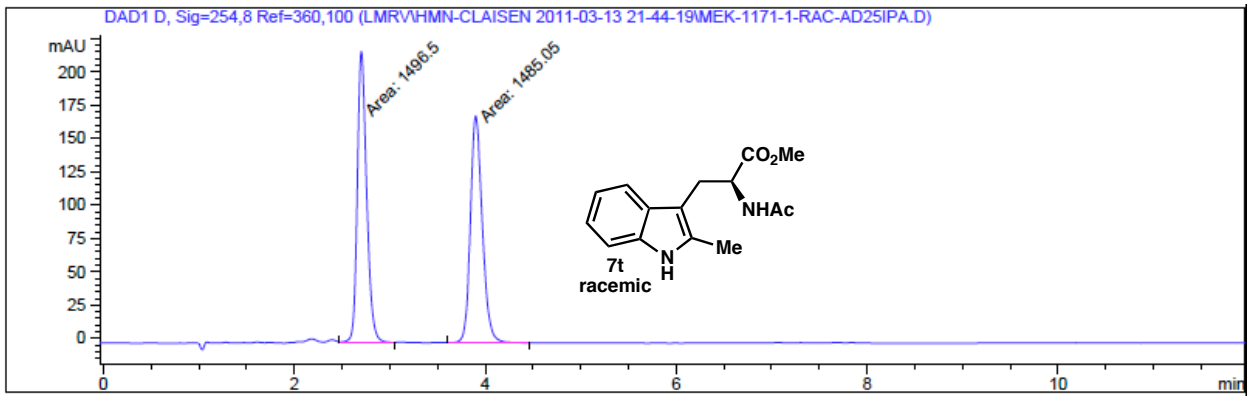
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.829	MM	0.2242	683.62952	50.82516	49.9518
2	7.521	MM	0.2756	684.94781	41.42142	50.0482

7s (Table 4, entry 17): enantioenriched, 92% ee



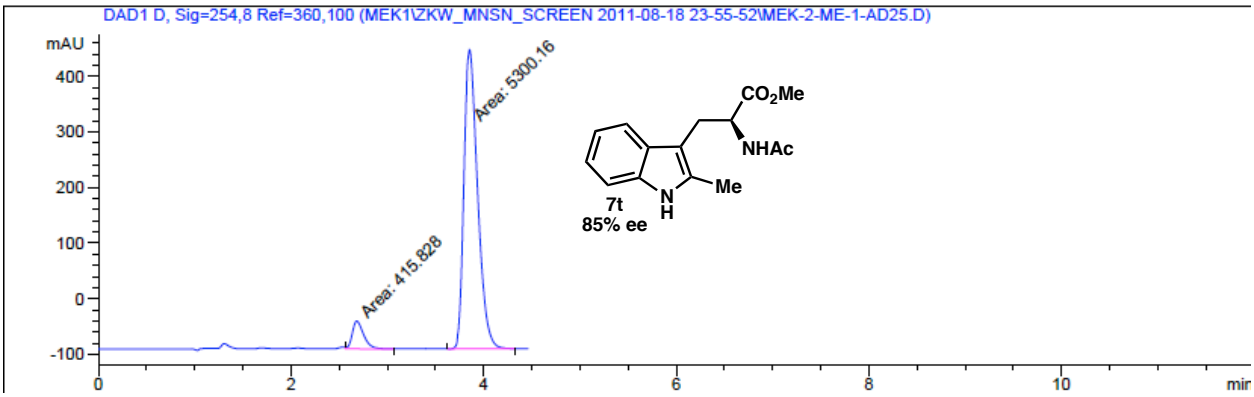
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.885	MM	0.2902	1192.82666	68.51757	96.2176
2	7.580	MM	0.3706	46.89137	2.10879	3.7824

7t (Table 4, entry 18): racemic



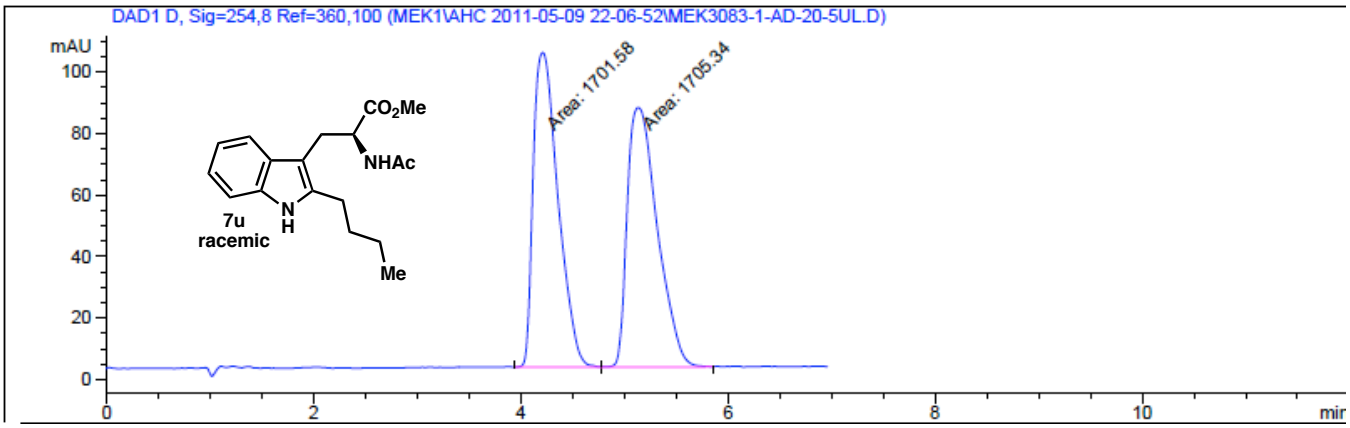
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.704	MM	0.1135	1496.50342	219.75923	50.1920
2	3.902	MM	0.1449	1485.05188	170.80902	49.8080

7t (Table 4, entry 18): enantioenriched, 85% ee



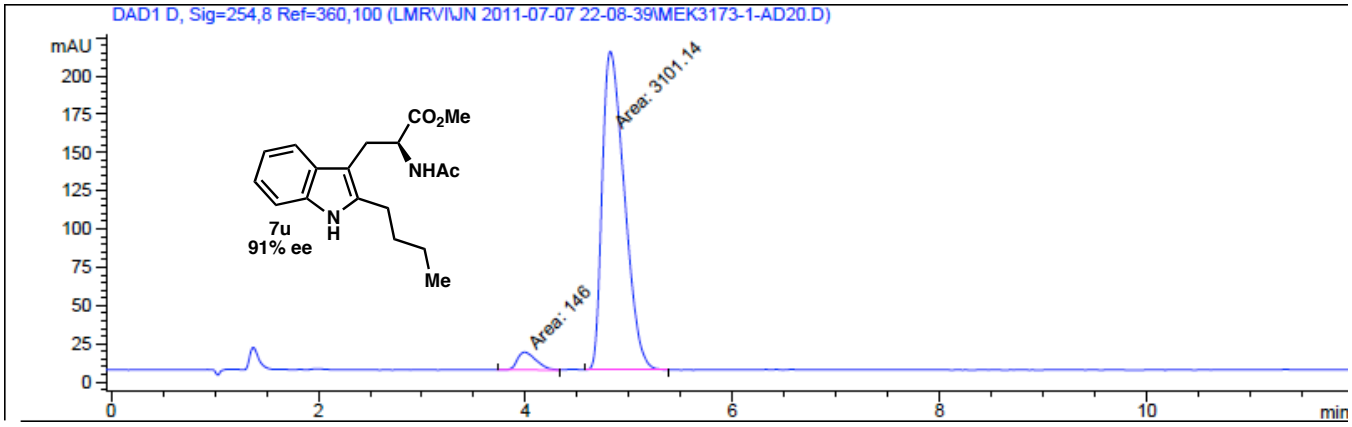
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.683	MM	0.1386	415.82819	49.99455	7.2748
2	3.853	MM	0.1639	5300.16357	538.95465	92.7252

7u (Table 4, entry 19): racemic



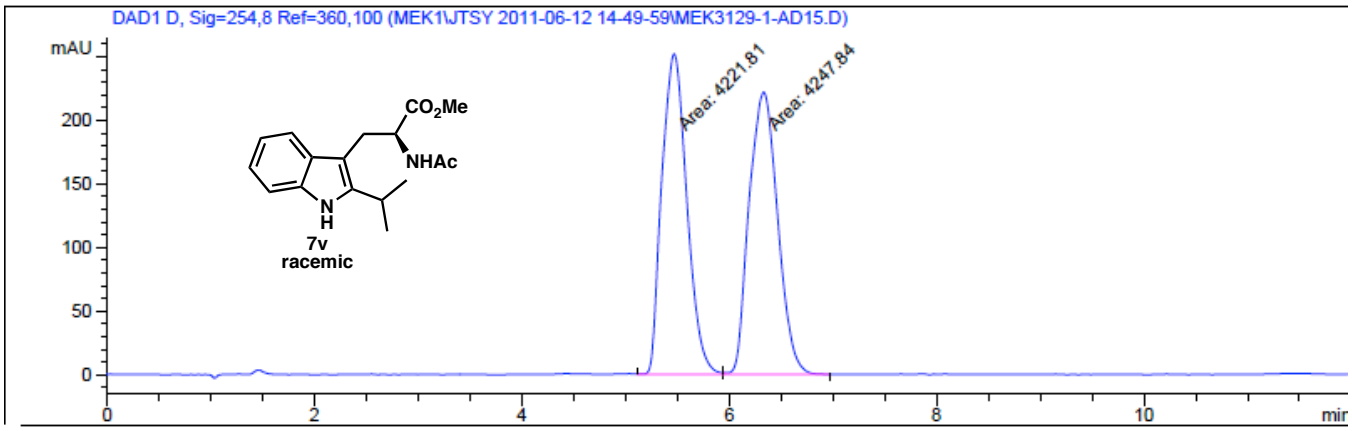
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.212	MM	0.2768	1700.02417	102.35526	50.0010
2	5.137	MM	0.3361	1699.95459	84.29318	49.9990

7u (Table 4, entry 19): enantioenriched, 91% ee



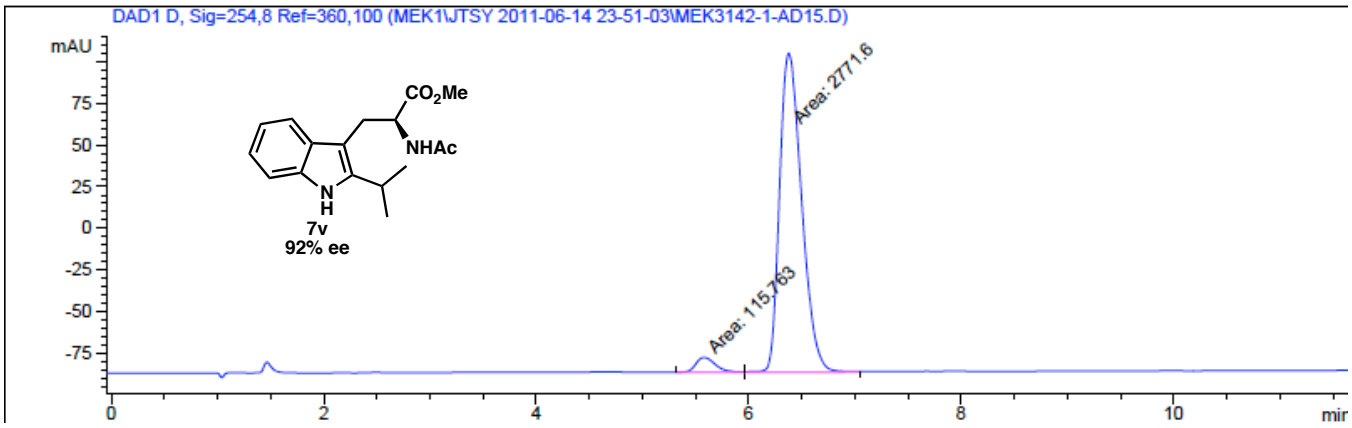
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.989	MM	0.2108	145.99951	11.54476	4.4962
2	4.820	MM	0.2481	3101.14380	208.34941	95.5038

7v (Table 4, entry 20): racemic



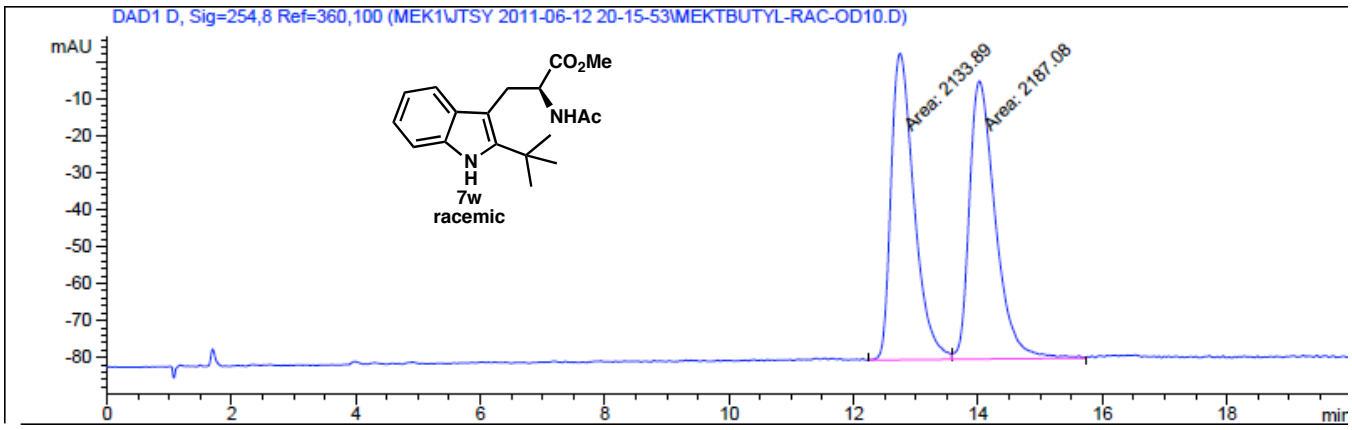
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.470	MF	0.2791	4221.81055	252.11853	49.8463
2	6.333	FM	0.3188	4247.84424	222.08144	50.1537

7v (Table 4, entry 20): enantioenriched, 92% ee



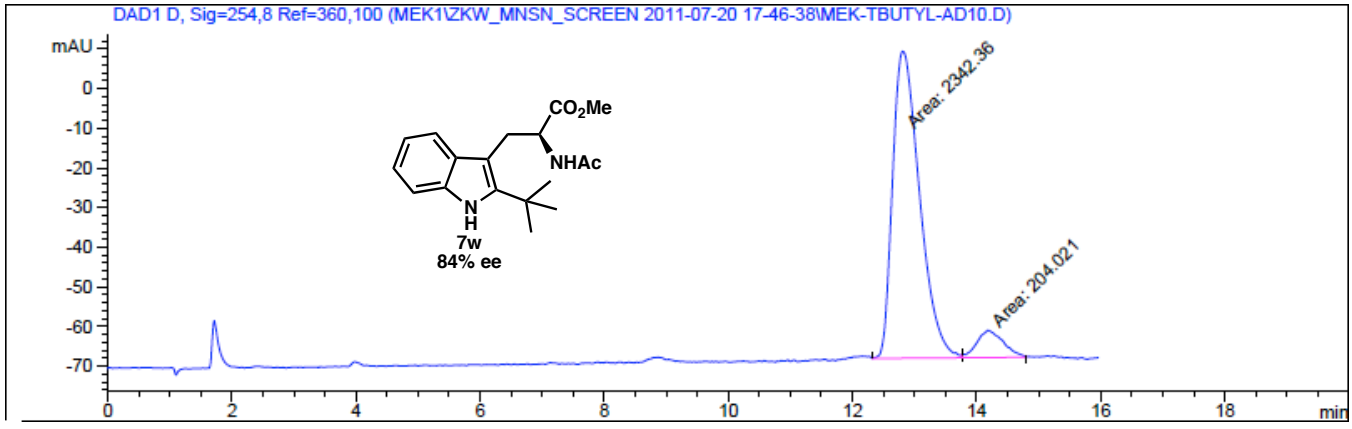
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.579	MF	0.2157	115.76347	8.94554	4.0093
2	6.378	FM	0.2407	2771.60327	191.88481	95.9907

7w (Table 4, entry 21): racemic



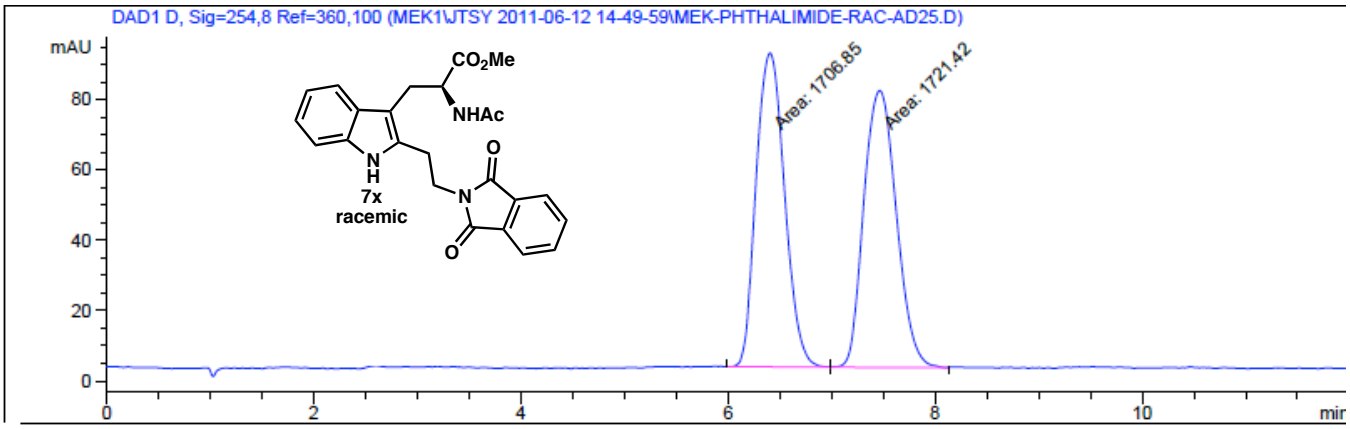
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.747	MF	0.4289	2133.88867	82.91142	49.3845
2	14.022	FM	0.4846	2187.08203	75.22533	50.6155

7w (Table 4, entry 21): enantioenriched, 84% ee



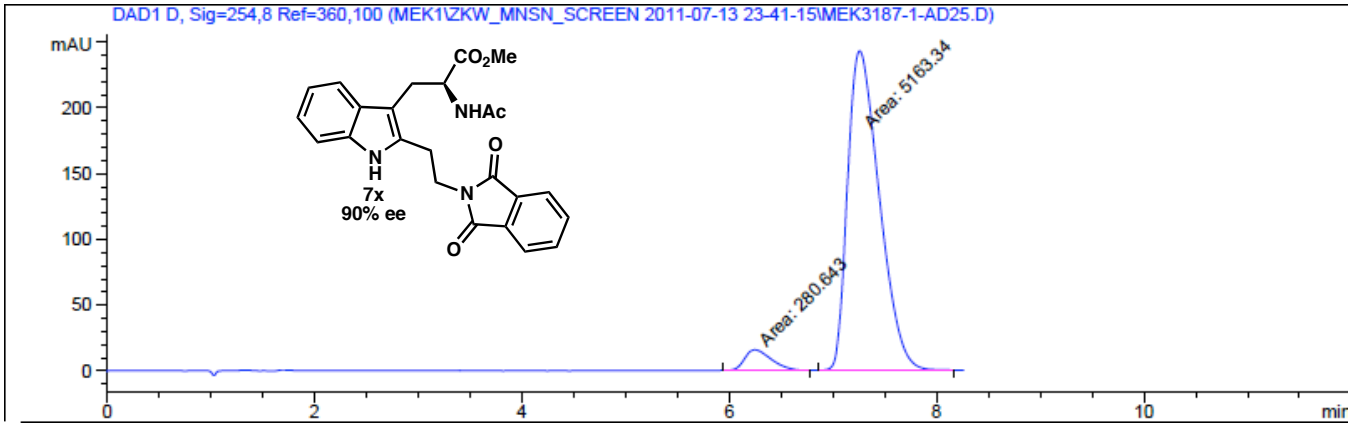
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.811	MF	0.5042	2342.36499	77.42957	91.9878
2	14.185	FM	0.4960	204.02127	6.85510	8.0122

3x (Table 4, entry 22): racemic



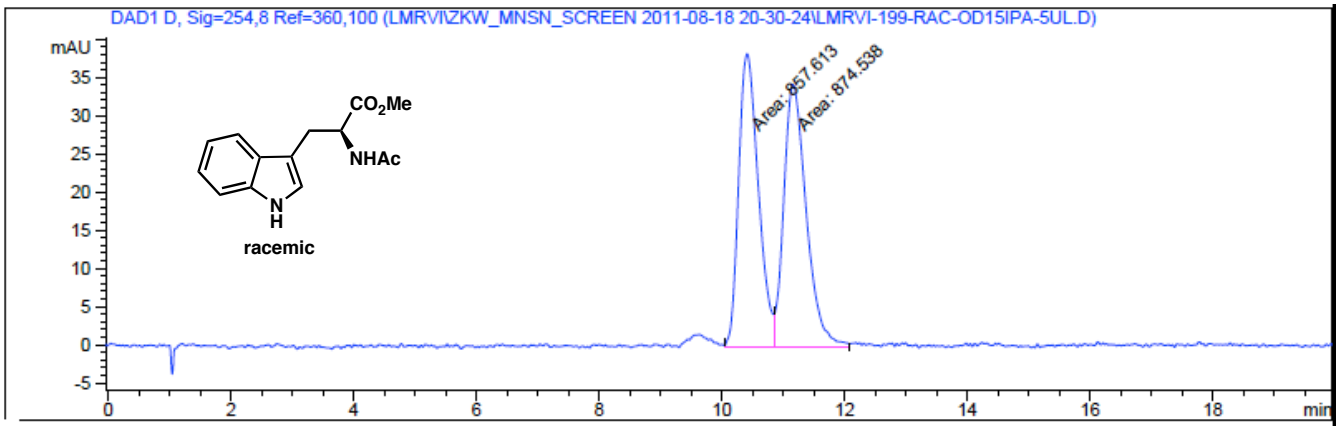
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.408	MF	0.3187	1706.84790	89.26434	49.7874
2	7.465	FM	0.3642	1721.42261	78.76897	50.2126

3x (Table 4, entry 22): enantioenriched, 90% ee



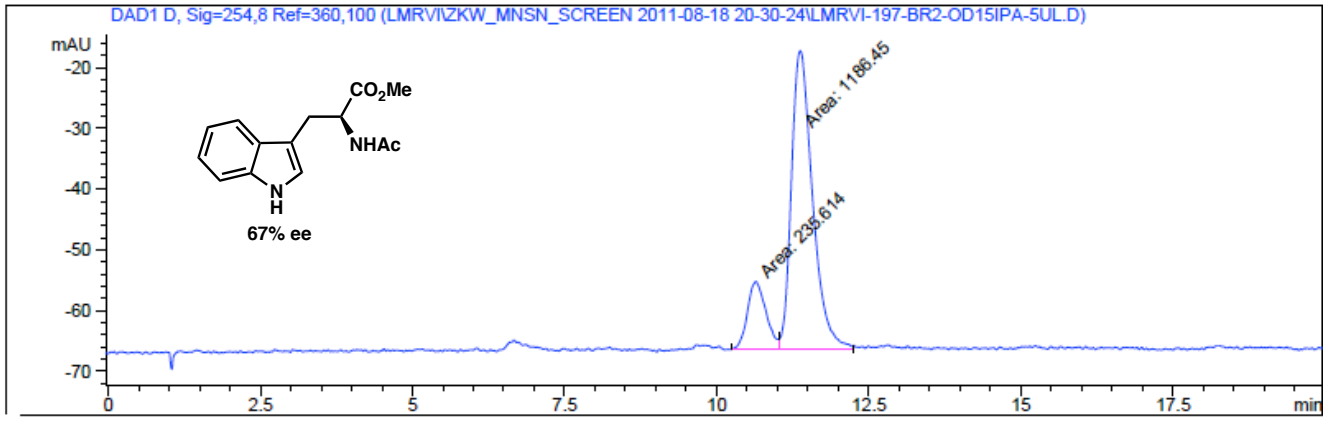
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.251	MM	0.2975	280.64285	15.72261	5.1551
2	7.260	MM	0.3544	5163.33643	242.81979	94.8449

(*S*)-*N*α-Acetyltryptophan methyl ester: racemic



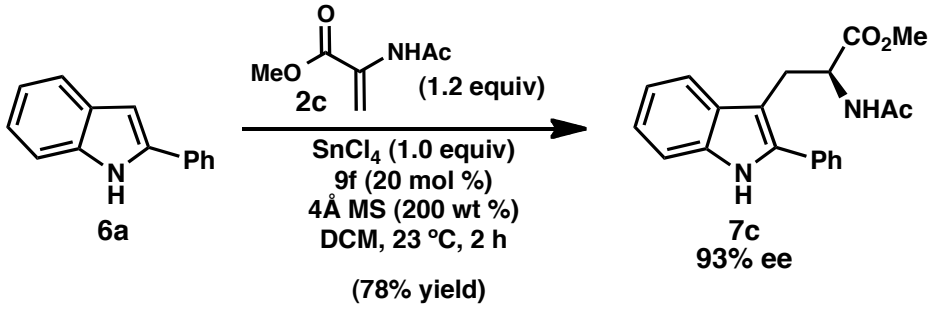
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.415	MM	0.3727	857.61285	38.35357	49.5114
2	11.162	MM	0.4245	874.53839	34.33775	50.4886

(*S*)-*N*α-Acetyltryptophan methyl ester: enantioenriched, 67% ee

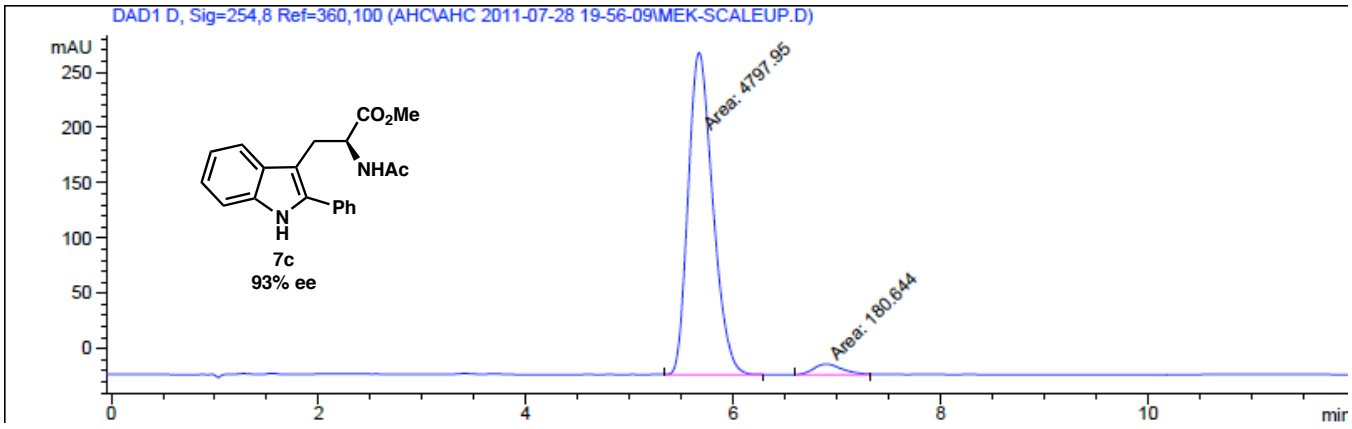


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.642	MM	0.3525	235.61412	11.14041	16.5685
2	11.371	MM	0.4028	1186.44934	49.09745	83.4315

6. Scale-up Procedure.



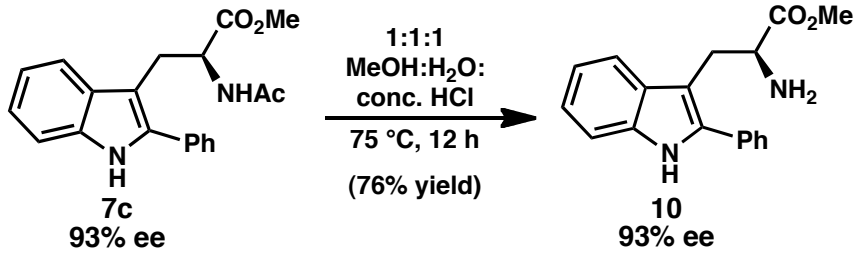
To a flame-dried flask under nitrogen containing freshly activated powdered 4Å molecular sieves (200 wt %) was added 2-phenylindole (**1a**, 1.00 g, 5.20 mmol, 1.00 equiv), methyl 2-acetamidoacrylate (**2c**, 890 mg, 6.20 mmol, 1.20 equiv), and (*R*)-3,3'-dibromo-BINOL (**9f**, 457 mg, 1.00 mmol, 0.20 equiv). The flask was charged with DCM (40 mL) and $SnCl_4$ (1 M in DCM, 5.20 mL, 5.20 mmol, 1.00 equiv) was added. The reaction was stirred at room temperature for 2 hours, then quenched by addition of 1 M HCl (50 mL). The aqueous layer was extracted with EtOAc (2 x 50 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (50 mL), dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 1.33 g (77% yield) of **7c** as a pale yellow foam. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 5.7 min, t_R(minor) = 6.9 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.670	MM	0.2746	4797.95020	291.18689	96.3716
2	6.889	MM	0.3168	180.64430	9.50427	3.6284

7. Functionalization of tryptophans 7c and 7d.

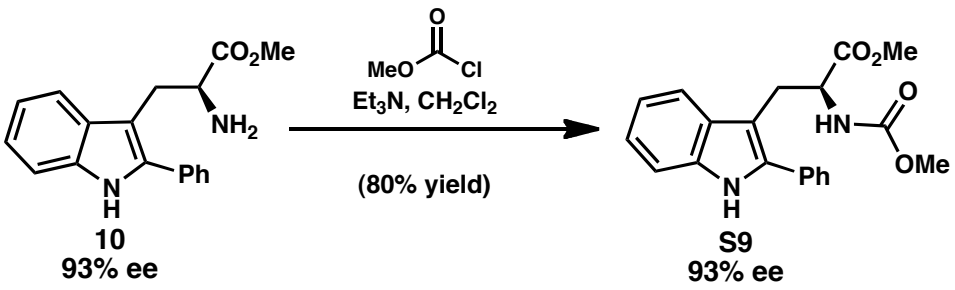
Acetamide hydrolysis of 7c[22]



A vial was charged with (*S*)-N_α-acetyl-2-phenyltryptophan methyl ester (**7c**, 30.0 mg, 0.09 mmol), MeOH (1 mL), H_2O (1 mL) and aqueous HCl (12 M, 1 mL). The reaction was heated to 75 °C for 12 hours, then concentrated, redissolved in DCM (10 mL) and washed with saturated aqueous $NaHCO_3$ (3 X 5 mL). The aqueous layers were combined and extracted with DCM (4 X 5 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography (99:1 CH_2Cl_2:MeOH) to yield 20.0 mg (76% yield) of **10** as a light yellow oil. The enantiomeric excess was determined by chiral SFC analysis of the corresponding methylcarbamate **S9** (see below). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (br s, 1H), 7.67 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.62 – 7.60 (m, 2H), 7.50 – 7.43 (m, 2H), 7.41 – 7.34 (m, 2H), 7.22 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.15 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 3.89 (dd, J = 8.4, 5.0 Hz, 1H), 3.56 (s, 3H), 3.47 – 3.38 (m, 1H), 3.27 – 3.14 (m, 1H), 1.69 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 136.1, 135.8, 132.9, 129.1, 129.0, 128.3, 128.0, 122.5, 119.9, 119.2, 110.9, 108.2, 55.2, 51.9, 30.2; IR (NaCl/thin film): 3367, 3062, 2948, 1732, 1603, 1489, 1457, 1207; $[\alpha]_D^{25}$ = -12.4 (*c* = 0.85, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 295.1441, found 295.1446.

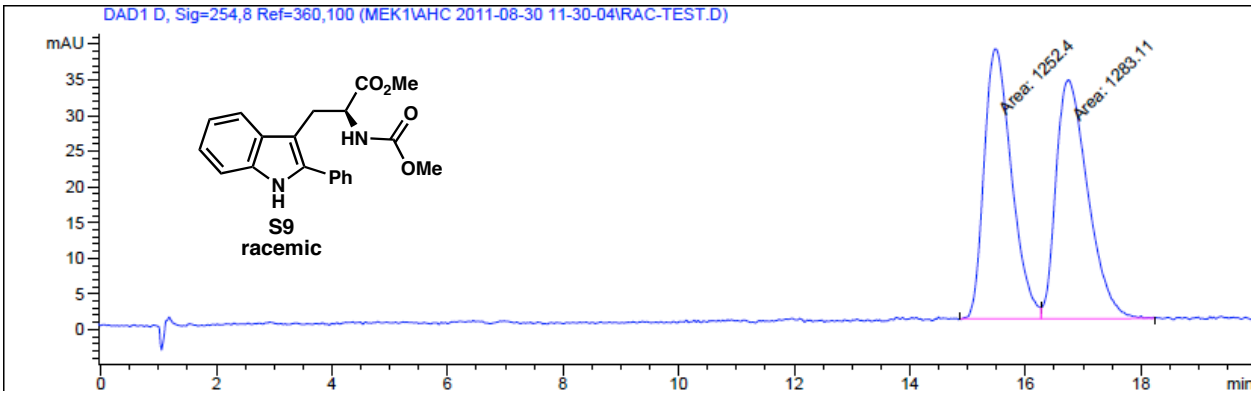
[22] For an analogous hydrolysis procedure, see: Messina, F.; Botta, M.; Corelli, F.; Schneider, M.; Fazio, F. *J. Org. Chem.* **1999**, 64, 3767.

Methylcarbamate Protection



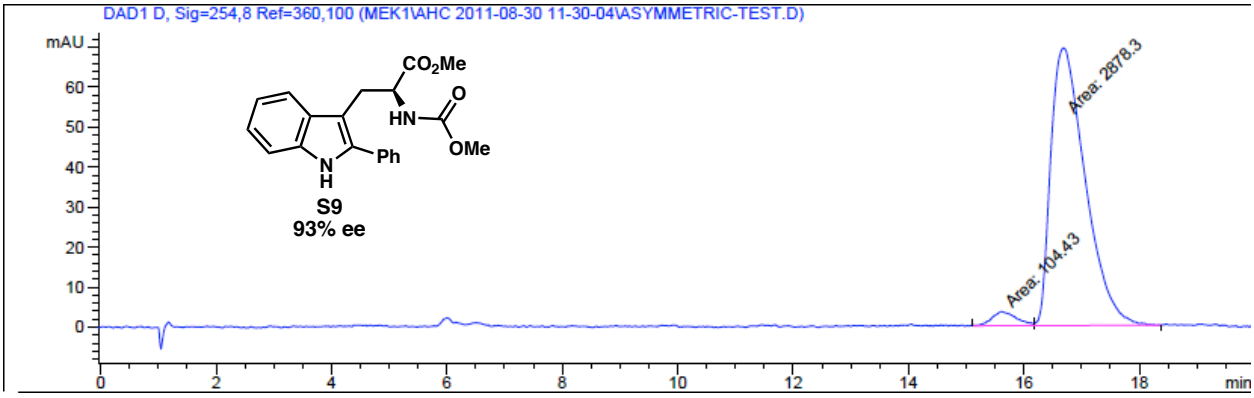
A flame-dried flask was charged with free amine **10** (19.5 mg, 0.70 mmol, 1.00 equiv), Et_3N (19 μL, 0.13 mmol, 2.0 equiv) and DCM (5 mL). Methylchloroformate (6.0 μL, 0.73 mmol, 1.10 equiv) was added and the solution was stirred at room temperature for 3 hours, then quenched with saturated aqueous NH_4Cl (5 mL) and extracted with EtOAc (2 X 5 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography (25:75 EtOAc:hexanes) to yield 18.5 mg (80% yield) of methylcarbamate **S9** as a colorless oil. The enantiomeric excess was determined to be 93% by chiral SFC analysis (OD-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R(major) = 16.7 min, t_R(minor) = 15.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (br s, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.48 – 7.45 (m, 2H), 7.40 – 7.35 (m, 2H), 7.25 – 7.19 (m, 1H), 7.16 (m, 1H), 5.06 (br d, J = 7.7 Hz, 1H), 4.63 – 4.59 (m, 1H), 3.54 (s, 3H), 3.50 (m, 2H), 3.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 156.1, 136.2, 135.7, 132.9, 129.2, 129.0, 128.3, 128.0, 122.5, 120.0, 118.9, 110.9, 106.7, 54.5, 52.12, 52.07, 27.1; IR (NaCl/thin film) 3338, 2953, 2923, 2852, 1718, 1701, 1507, 1457, 1363, 1213, 1072 cm^{-1}; $[\alpha]_D^{25}$ = +22.6 (*c* = 0.10, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 353.1496, found 353.1497.

Methylcarbamate (S9): racemic



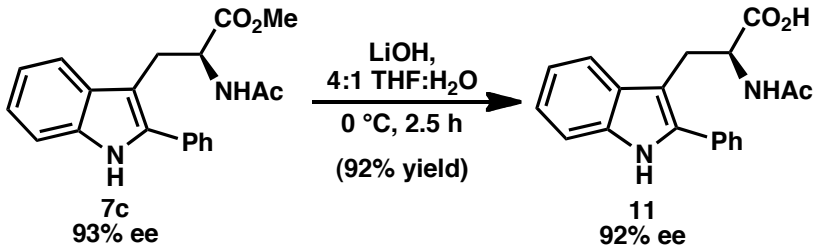
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.480	MF	0.5516	1252.40308	37.84099	49.3945
2	16.749	FM	0.6385	1283.11060	33.49063	50.6055

Methylcarbamate (S9): enantioenriched, 93% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.610	MF	0.4860	104.43002	3.58131	3.5012
2	16.684	FM	0.6913	2878.30273	69.39832	96.4988

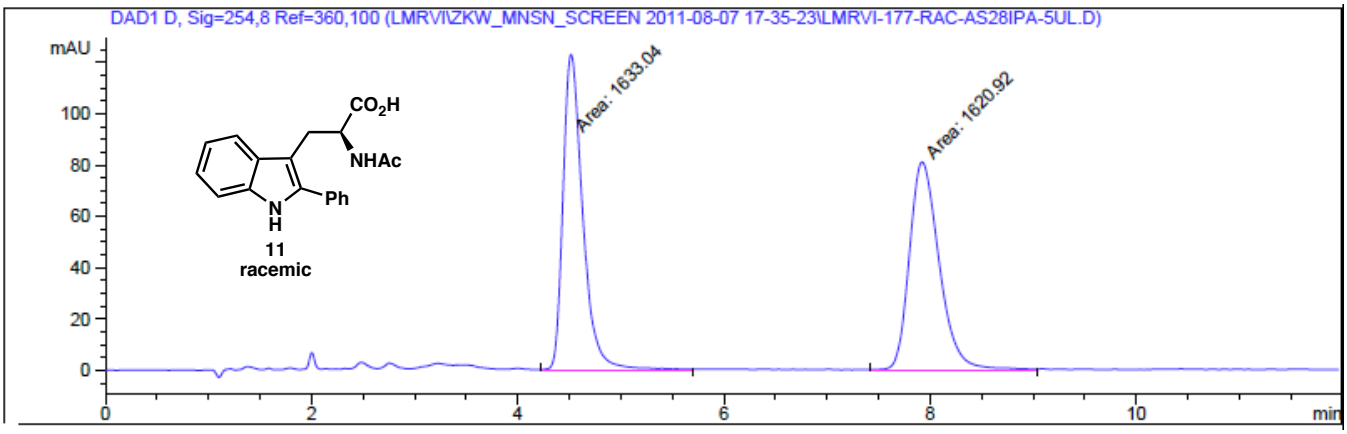
Methyl ester hydrolysis[23]



A 10 mL flask was charged with (*S*)-N_α-acetyl-2-phenyltryptophan methyl ester **7c** (67.2 mg, 0.20 mmol, 1.00 equiv) and THF (0.9 mL) then cooled to 0 ºC, followed by dropwise addition of aqueous LiOH (1.75 M, 230 μL, 0.40 mmol, 2.00 equiv). The reaction was vigorously stirred at 0 ºC for 2 hours, then diluted with H_2O (15 mL) and extracted with EtOAc (2 x 10 mL). The aqueous layer was acidified to pH = 1.5 and extracted with EtOAc (5 x 15 mL). The combined organic layers from the acidic aqueous extraction were dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography (0:99:1 to 15:84:1 MeOH:DCM:AcOH) to yield 59.2 mg (92% yield) of carboxylic acid **11** as a pale yellow foam. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AS-H, 2.5 mL/min, 28% IPA in CO_2, λ = 254 nm): t_R(major) = 4.5 min, t_R(minor) = 8.0 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.47 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.40 (m, 1H), 7.37 (ddd, *J* = 8.0, 0.8, 0.8 Hz, 1H), 7.21 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 7.14 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 5.72 (br d, *J* = 7.4 Hz, 1H), 4.73 (td, *J* = 7.1, 5.4 Hz, 1H), 3.56 (dd, *J* = 14.9, 5.2 Hz, 1H), 3.49 (dd, *J*=15.0, 6.9 Hz, 1H), 1.62 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.7, 170.9, 136.2, 135.7, 132.9, 129.13, 129.05, 128.3, 128.2, 122.6, 120.1, 118.8, 111.0, 106.8, 53.1, 26.2, 22.6; IR (NaCl/thin film): 3391, 3306, 3055, 3011, 2921, 2850, 1717, 1615, 1527, 1457, 1448, 1215 cm^{-1}; $[\alpha]_D^{25}$ = +9.2 (*c* = 1.05, MeCN). HRMS (MM) calc'd for $[M+H]^+$ 323.1390, found 323.1390.

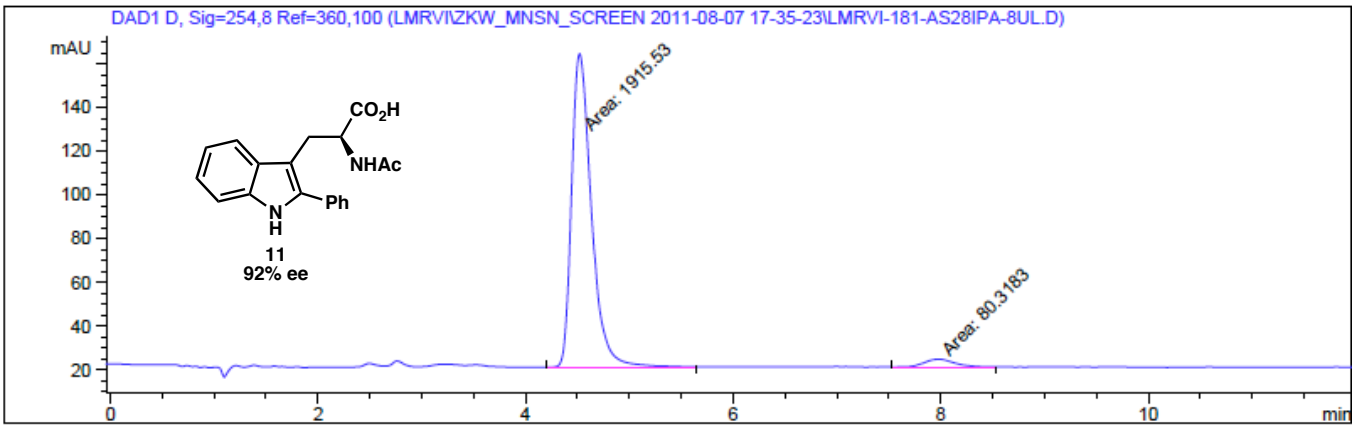
[23] For an analogous hydrolysis procedure, see: Morieux, P.; Stables, J.P.; Kohn, H. *Bioorg. Med. Chem.* **2008**, *16*, 8968.

11: racemic



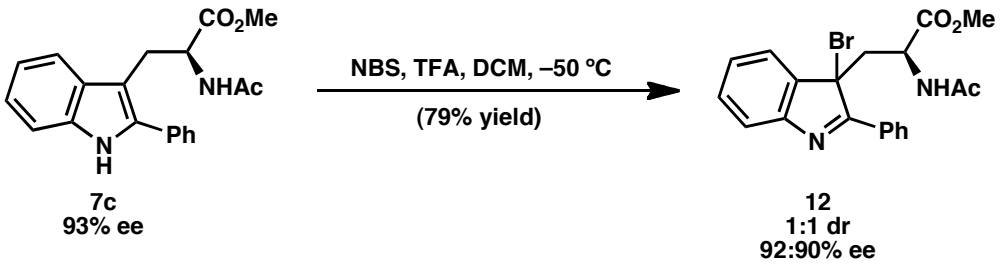
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.517	MM	0.2216	1633.03918	122.81268	50.1863
2	7.923	MM	0.3341	1620.91711	80.86505	49.8137

11: enantioenriched, 92% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.521	MM	0.2225	1915.53430	143.46094	95.9757
2	7.970	MM	0.3592	80.31825	3.72675	4.0243

Preparation of bromo-dehydroindoline 12.

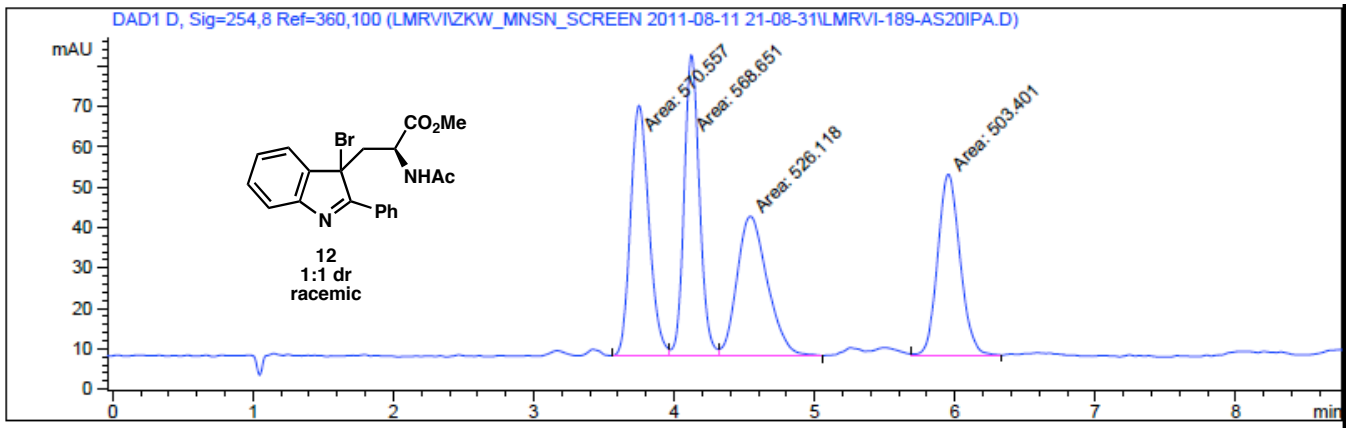


7c
93% ee

12
1:1 dr
92:90% ee

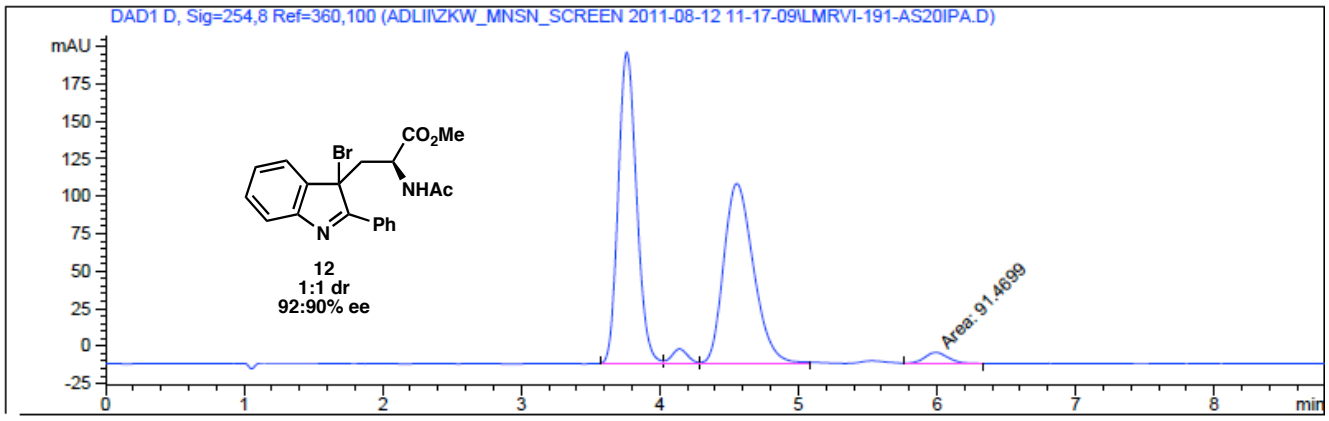
A solution of (*S*)-N_α-acetyl-2-phenyltryptophan methyl ester **7c** (101 mg, 0.30 mmol, 1.00 equiv) in DCM (8.4 mL) was cooled to –50 ºC in an acetonitrile/dry ice bath. NBS (53.4 mg, 0.30 mmol, 1.00 equiv) was then added, followed by TFA (900 μL). The reaction was stirred in the dark at –50 ºC for 3 hours, then poured onto ice, quenched with aqueous ammonia (1.5 mL) and extracted with DCM (3 x 25 mL). The combined organics were washed (40 mL H_2O, then 40 mL brine), dried (Na_2SO_4), filtered, and concentrated. The product **12** was formed in a 1:1 ratio of diastereomers (determined by ^{1}H NMR analysis of the crude reaction mixture) and was purified by silica gel chromatography (30:70 to 70:30 EtOAc:hexanes) to yield 98 mg (79% yield) of the combined diastereomers as a bright yellow foam. The enantiomeric excesses of the two diastereomers were determined to be 92% and 90% by chiral SFC analysis (AS-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(major) = 3.8 min, t_R(minor) = 4.1 min; t_R(major) = 4.6 min, t_R(minor) = 6.0 min. Spectral data and optical rotation are reported for the mixture of diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 – 8.32 (m, 4H), 7.70 – 7.64 (m, 2H), 7.57 – 7.49 (m, 8H), 7.47 – 7.40 (m, 2H), 7.39 – 7.30 (m, 2H), 5.37 (br d, *J* = 7.4 Hz, 1H), 5.05 (br d, *J* = 8.5 Hz, 1H), 4.33 (dt, *J* = 7.5, 5.5 Hz, 1H), 3.95 (td, *J* = 8.9, 4.0 Hz, 1H), 3.56 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.47 – 3.41 (m, 4H), 3.38 – 3.32 (m, 4H), 3.23 (dd, *J* = 14.6, 9.3 Hz, 1H), 1.45 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 174.8, 170.7, 170.0, 169.4, 169.2, 151.82, 151.76, 139.8, 139.6, 131.6, 131.4, 131.3, 130.5, 130.4, 128.81, 128.80, 128.71, 128.70, 127.2, 126.6, 123.2, 122.5, 121.9, 121.7, 59.16, 59.14, 52.5, 52.3, 50.3, 49.8, 41.6, 41.4, 22.3, 22.0; IR (NaCl/thin film): 3271, 3062, 2952, 2924, 2853, 1747, 1661, 1525, 1444, 1372, 1264, 1216 cm^{-1}; $[\alpha]_D^{25}$ = +17.1 (*c* = 0.50, $CHCl_3$). HRMS (MM) calc'd for M^+ 415.0652, found 415.0652.

Bromo-dehydroindoline 12: 1:1 mixture of diastereomers, racemic



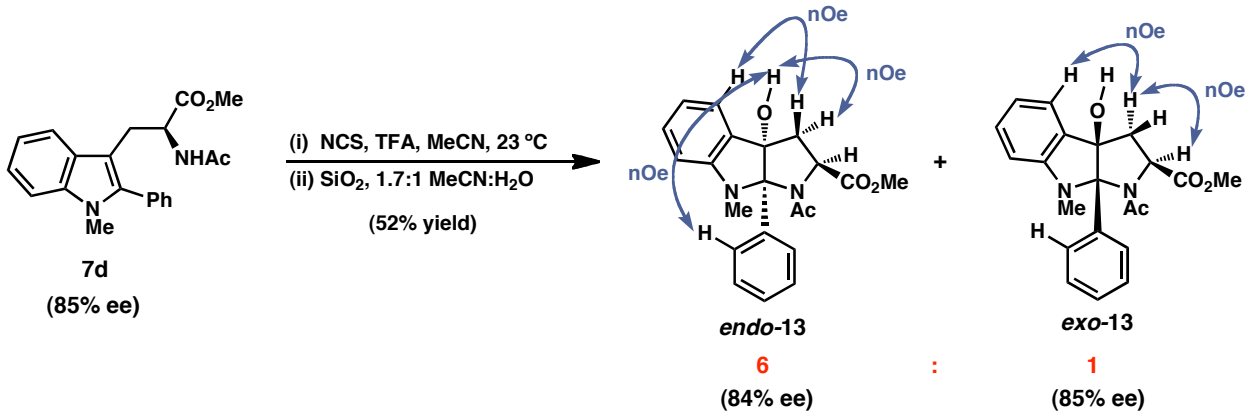
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.750	MM	0.1528	570.55682	62.21929	26.3084
2	4.123	MM	0.1267	568.65100	74.80566	26.2205
3	4.544	MM	0.2530	526.11841	34.66383	24.2593
4	5.953	MM	0.1862	503.40063	45.06438	23.2118

Bromo-dehydroindoline 12: 1:1 mixture of diastereomers, enantioenriched, 92:90% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.762	BV	0.1436	1915.73315	207.78340	49.2377
2	4.143	VV	0.1222	79.59740	9.85449	2.0458
3	4.557	VB	0.2312	1803.98438	120.14987	46.3656
4	5.995	MM	0.2044	91.46992	7.45990	2.3509

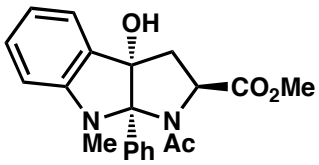
Preparation of 3-hydroxypyrroloindoline 13



A 15 mL flask containing (*S*)-*N*$_\alpha$-acetyl-1-methyl-2-phenyltryptophan methyl ester **7d** (52.5 mg, 0.150 mmol, 1.00 equiv) was flushed with argon and then charged with MeCN (3.3 mL). TFA was added as a solution in MeCN (1.3 M, 125 μL, 0.150 mmol, 1.00 equiv), followed by NCS as a solution in MeCN (0.2 M, 0.75 mL, 0.150 mmol, 1.00 equiv). The flask was then sealed under argon and the solution was stirred in the dark at room temperature. After 3 hours, the reaction was quenched with aqueous ammonia (1.5 mL), poured onto ice, and extracted with DCM (3 x 15 mL). The combined organics were washed (20 mL H_2O, then 20 mL brine), dried (Na_2SO_4), filtered, and concentrated to give the crude mixture of 3-chloropyrroloindoline diastereomers (detected by HRMS direct injection (MM) calc'd for $[M+H]^+$ 385.1313, found 385.1320). The crude residue was redissolved in MeCN (2 mL), then H_2O (1.2 mL) and SiO_2 (2.5 mL) were added. The mixture was vigorously stirred open to air at room temperature for 30 minutes, then filtered through a 1.5 mL silica plug with EtOAc (50 mL), dried (Na_2SO_4), filtered and concentrated. The 3-hydroxypyrroloindoline **13** existed in a 6:1 ratio of diastereomers, favoring the *endo* diastereomer (determined by ^{1}H NMR analysis of the crude reaction mixture) and was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 30.8 mg (contains 18 wt % $CHCl_3$, 46% corrected yield) of the *endo* diastereomer as a yellow oil. The *exo* diastereomer, obtained post chromatography in a mixture with (*S*)-*N*$_\alpha$-acetyl-1-methyl-2-phenyltryptophan methyl ester **7d**, was subjected to reverse phase preparatory HPLC (30:70 to 90:10 MeCN:H_2O) using an Agilent 1200 Series HPLC with an Agilent XDB-C18 5 μM column (9.4 x 250 mm) to yield 3.5 mg (6% yield) of the *exo* diastereomer as a yellow oil.

Endo diastereomer:

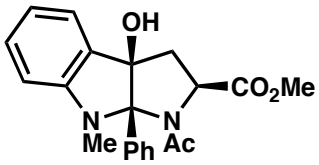
The enantiomeric excess was determined to be 84% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 7.4 min, t_R(minor) = 4.7 min. The relative stereochemistry was assigned by 2D NMR analysis. ^{1}H NMR (500 MHz, CD_3CN; compound exists as a 15:1 mixture of rotamers, the major rotamer is reported) δ 7.40 – 7.35 (m, 2H), 7.34 – 7.26 (m, 3H), 7.20 (ddd, *J* = 7.9, 7.5, 1.3 Hz, 1H), 7.12 (ddd, *J* = 7.2, 1.3, 0.5 Hz, 1H), 6.66 (ddd, *J* = 7.3, 7.3, 1.0 Hz, 1H), 6.51 (d, *J* = 7.9 Hz, 1H), 4.79 (d, *J* = 8.8 Hz, 1H), 3.19 (s, 3H), 2.97 (s, 3H), 2.90 (br s, 1H), 2.82 (d, *J* = 12.7 Hz, 1H), 2.59 (ddd, *J* = 12.7, 8.8, 1.1 Hz, 1H), 1.95 (s, 3H); ^{13}C NMR (125 MHz, CD_3CN; compound exists as a 15:1 mixture of rotamers, the major rotamer is reported) δ 172.0, 171.3, 153.1, 138.0, 131.6, 128.9, 128.6, 128.3, 125.2, 118.0, 107.1, 95.3, 88.3, 61.3, 52.7, 39.0, 32.7, 23.6; IR (NaCl/thin film): 3292, 3010, 2948, 1735, 1653, 1648, 1610, 1491, 1448, 1388, 1313, 1220 cm^{-1}; $[\alpha]_D^{25}$ = +264.0 (*c* = 1.35, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 367.1652, found 367.1650.



***endo*-13**

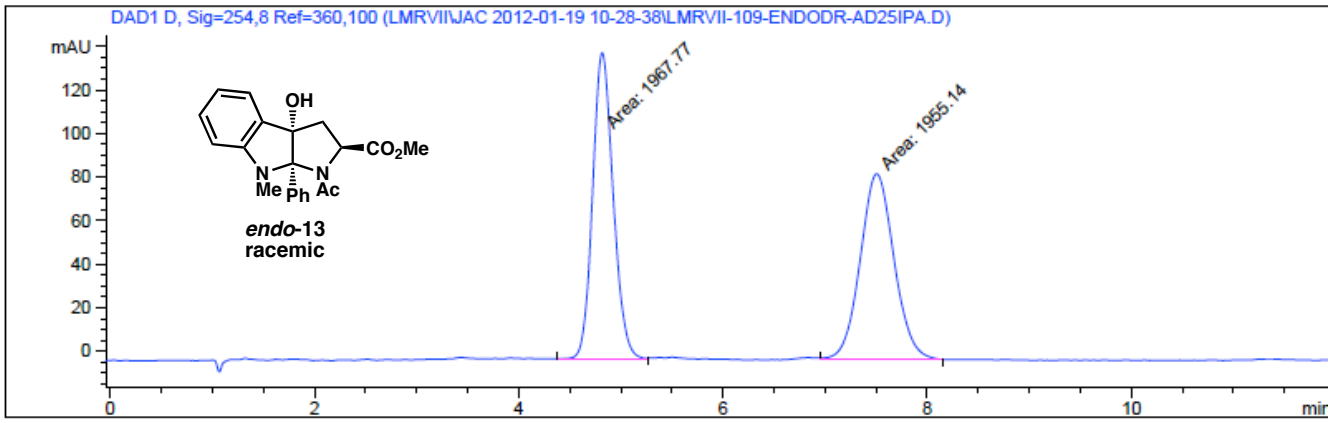
Exo diastereomer:

The enantiomeric excess was determined to be 85% by chiral SFC analysis (OD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(major) = 6.2 min, t_R(minor) = 4.0 min. The relative stereochemistry was assigned by 2D NMR analysis. ^{1}H NMR (500 MHz, CD_3CN; compound exists as a 1.5:1 mixture of rotamers, the major rotamer is denoted by *, the minor rotamer by §) δ 7.60 – 7.22 (m, 6H*, 7H§), 7.17 (ddd, *J* = 7.3, 0.6, 0.6 Hz, 1H*), 6.79 (dd, *J* = 7.5, 7.5 Hz, 1H§), 6.70 (dd, *J* = 7.5, 7.5 Hz, 1H*), 6.65 (d, *J* = 7.9 Hz, 1H§), 6.54 (d, *J* = 7.9 Hz, 1H*), 4.49 (dd, *J* = 8.0, 6.7 Hz, 1H*), 4.07 (dd, *J* = 10.0, 6.9 Hz, 1H§), 3.81 (s, 3H*), 3.71 (s, 3H§), 3.34 (s, 1H§), 3.01 (s, 1H*), 2.963 (s, 3H*), 2.958 (s, 3H§), 2.71 (dd, *J* = 13.0, 8.1 Hz, 1H*), 2.68 (dd, *J* = 12.6, 7.0 Hz, 1H§), 2.34 (dd, *J* = 12.9, 6.7 Hz, 1H*), 2.07 (dd, *J* = 12.7, 10.0 Hz, 1H§), 1.89 (s, 3H*), 1.80 (s, 3H§); ^{13}C NMR (125 MHz, CD_3CN) δ 174.1, 173.6, 172.3, 171.8, 151.2, 151.1, 136.3, 136.2, 131.6, 131.3, 130.3, 129.60, 129.57, 129.4, 128.7, 128.6, 124.4, 123.9, 119.3, 118.2, 108.0, 106.4, 98.8, 96.1, 90.1, 88.5, 61.2, 60.3, 53.3, 52.6, 40.9, 37.2, 33.4, 32.4, 24.6, 23.8; IR (NaCl/thin film): 3305, 2924, 1747, 1646, 1610, 1491, 1448, 1381, 1311, 1207 cm^{-1}; $[\alpha]_D^{25}$ = -138.2 (*c* = 0.33, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 367.1652, found 367.1655.



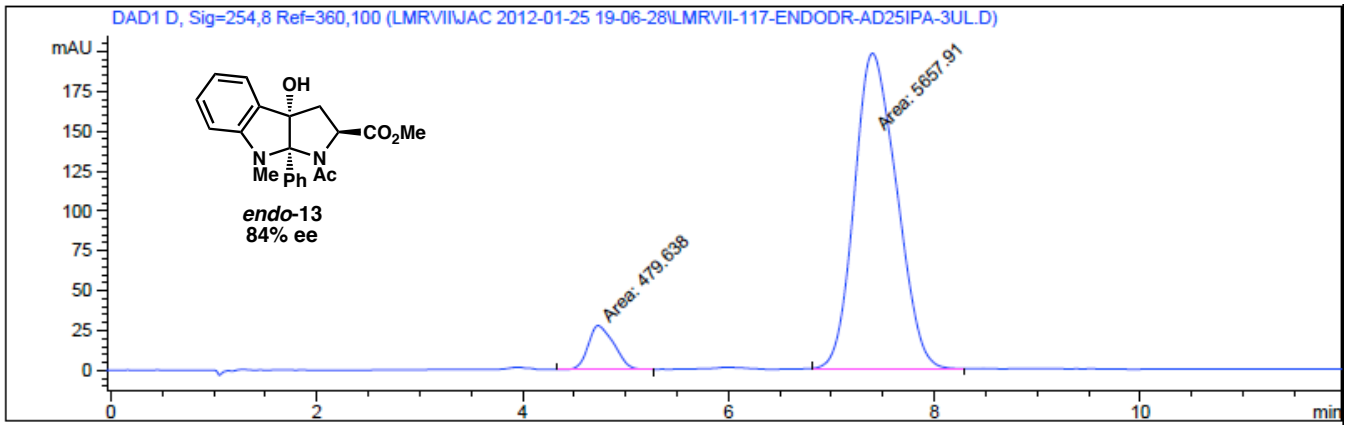
***exo*-13**

***Endo*-13:** racemic



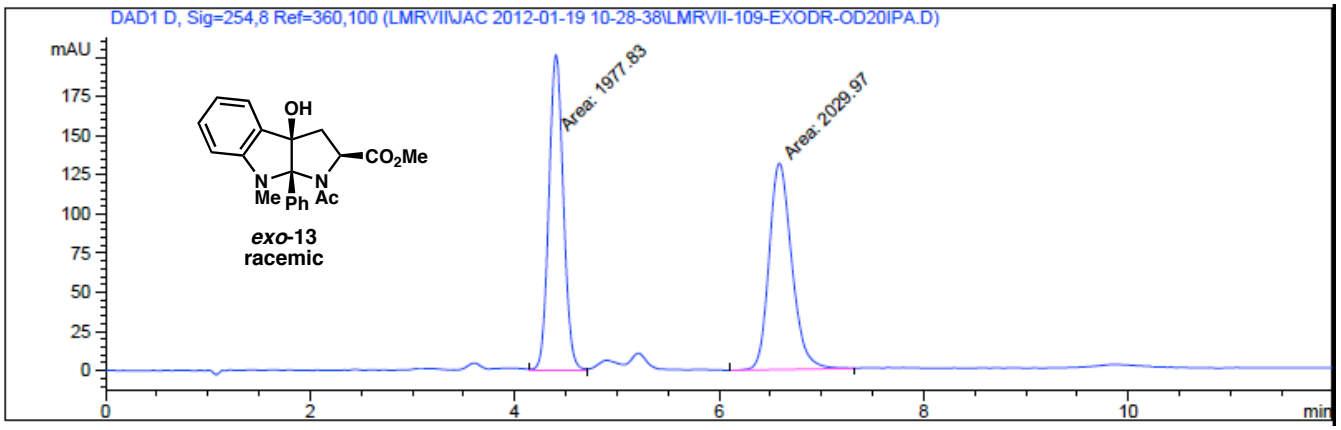
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.817	MM	0.2330	1967.76941	140.72768	50.1610
2	7.506	MM	0.3827	1955.13940	85.15020	49.8390

***Endo*-13:** enantioenriched, 84% ee



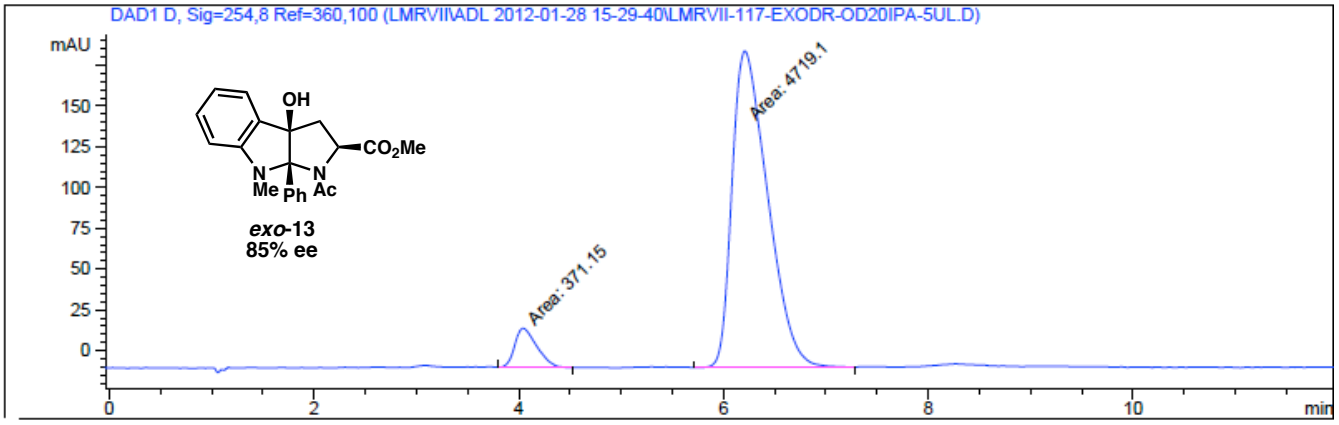
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.733	MM	0.2897	479.63791	27.59108	7.8148
2	7.399	MM	0.4764	5657.91357	197.94064	92.1852

***Exo*-13:** racemic



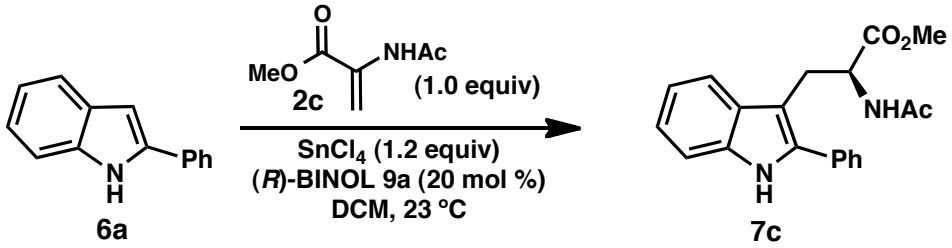
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.404	MM	0.1638	1977.83203	201.27939	49.3495
2	6.589	MM	0.2569	2029.97083	131.71642	50.6505

***Exo*-13:** enantioenriched, 85% ee

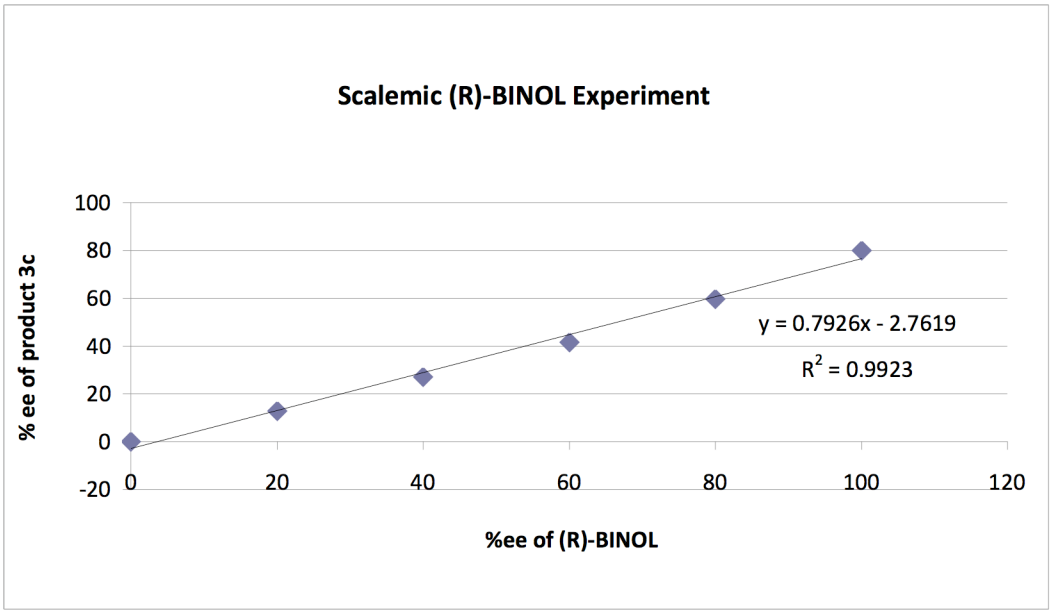


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.042	MM	0.2550	371.15012	24.25386	7.2914
2	6.208	MM	0.4046	4719.09912	194.37576	92.7086

8. Scalemic (*R*)-BINOL Experiment.



A flame-dried flask was charged with 2-phenylindole (**6a**, 19.0 mg, 0.10 mmol, 1.00 equiv) and methyl 2-acetamidoacrylate (**2c**, 14.0 mg, 0.10 mmol, 1.00 equiv). Stock solutions of (*R*)-BINOL (**9a**) and racemic BINOL were prepared (0.0134 M in DCM) and the appropriate volume of each solution was added to the flask (0.02 mmol, 0.20 equiv). The reaction was charged with $SnCl_4$ as a solution in DCM (1 M, 120 µL, 0.12 mmol, 1.20 equiv) and stirred at room temperature for 2 hours, then quenched by dilution with 1 M HCl (5 mL) and MeCN (1 mL). The aqueous layer was extracted with EtOAc (2 x 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (5 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes). The enantiomeric excess of each experiment was determined by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm).

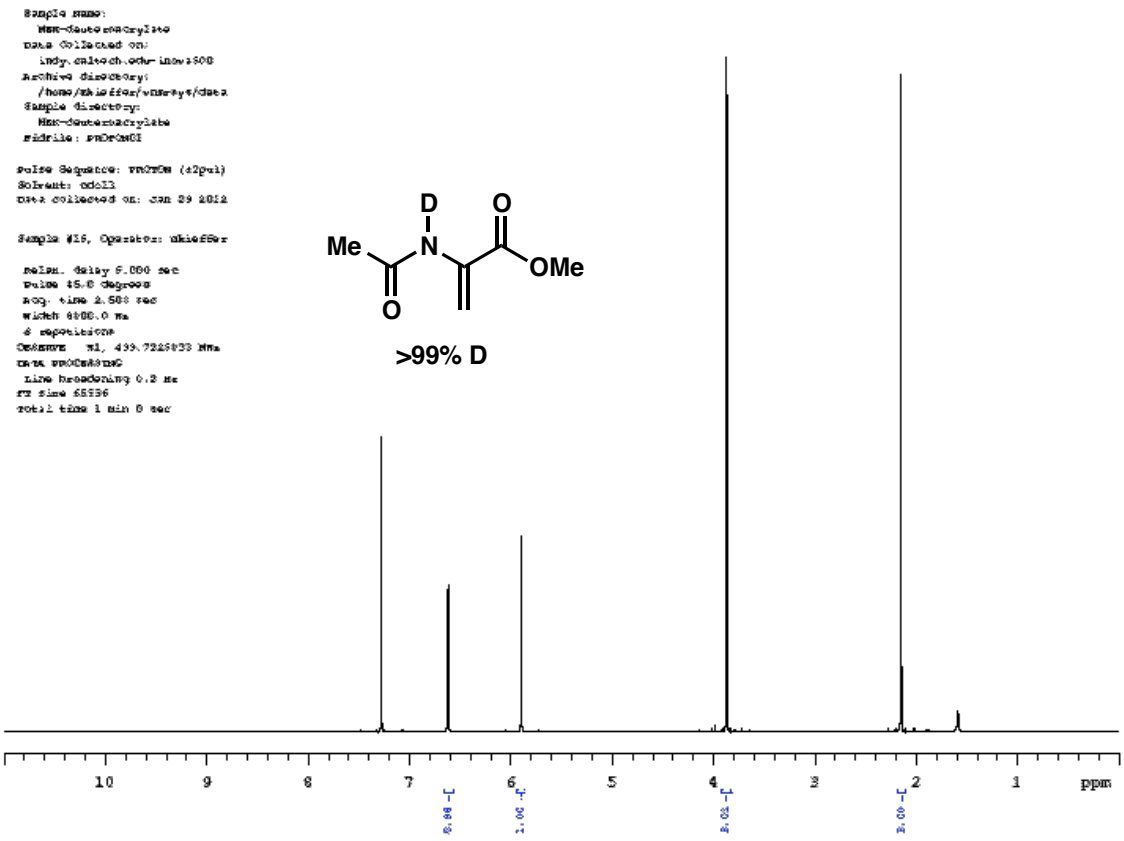


9. Deuterium labeling studies.

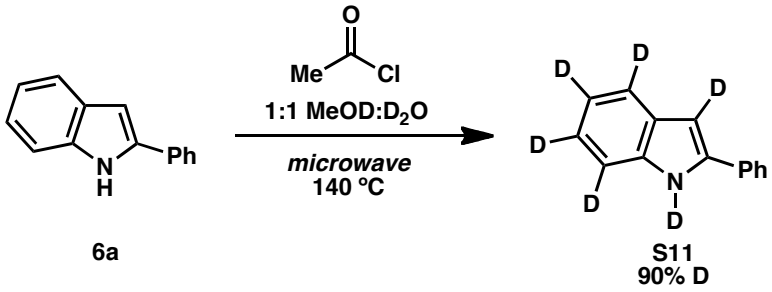
Preparation of *N*-deuteroacrylate (S10).

2c **S10**
>99% D

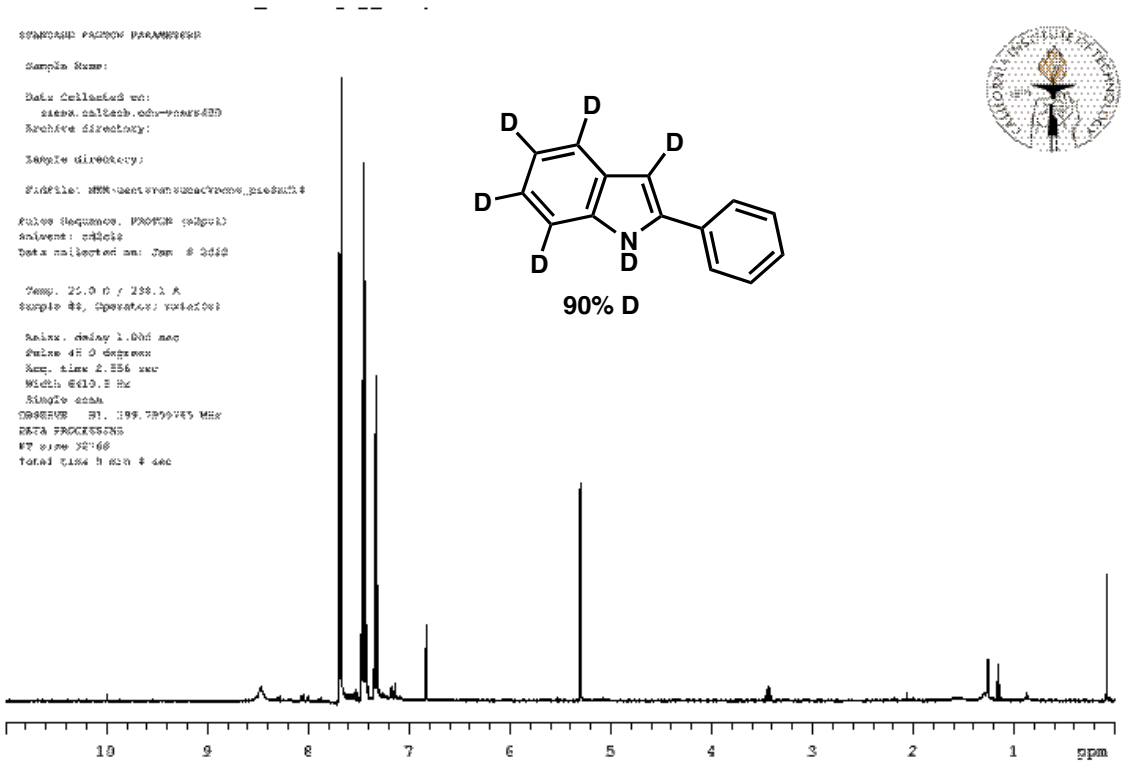
Acrylate **2c** was dissolved in MeOD (1 mL) under nitrogen. After stirring for 1 minute, the solution was concentrated under high vacuum. This procedure was repeated three times to give >99% deuterium incorporation.



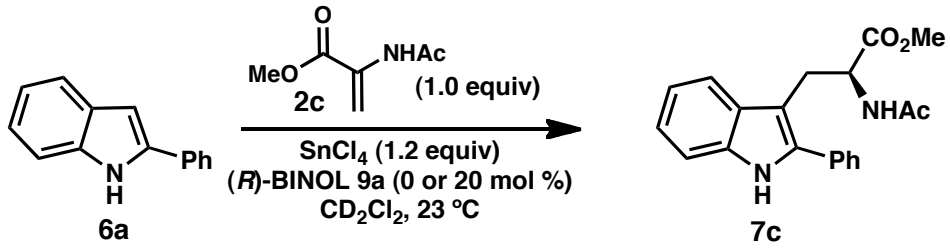
Preparation of per-deutero-2-phenylindole (S11).



To MeOD (1 mL) in a microwave vial was added acetyl chloride (100 μL), followed by 2-phenylindole (**6a**, 50 mg) and D_2O (1 mL). The vial was sealed and heated in a microwave to 140 °C for 1 hour. Upon cooling, the heterogenous solution was diluted with DCM. The phases were separated and the aqueous was extracted with DCM (2 x 5 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated to give per-deutero-2-phenylindole (**S11**) with 90% deuterium incorporation.

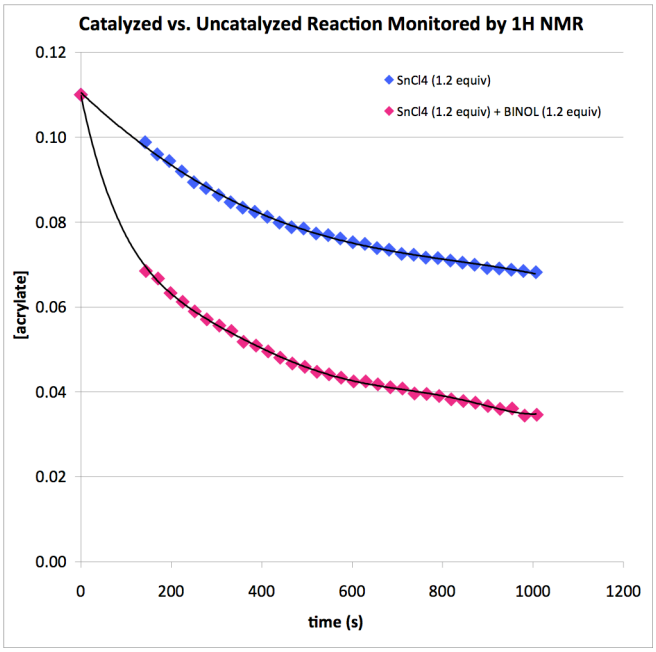


10. ^{1}H NMR Kinetics Experiment for $SnCl_4$ and (*R*)-BINOL (9a)•$SnCl_4$ promoted reaction of 6a and 2c.



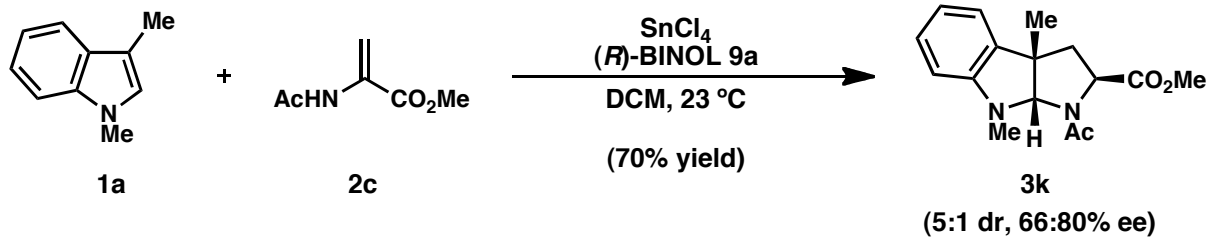
An oven-dried vial was charged with 2-phenylindole (**6a**, 19.0 mg, 0.10 mmol, 1.00 equiv), methyl 2-acetamidoacrylate (**2c**, 14.0 mg, 0.10 mmol, 1.00 equiv), (*R*)-BINOL if necessary (**9a**, 6.0 mg, 0.02 mmol, 0.20 equiv) and 1,4-diethylbenzene (4.7 μL, 0.03 mmol, 0.30 equiv) as the internal standard. The vial was pumped into a glove box and charged with CD_2Cl_2 (0.75 mL, to an indole concentration of 0.12 M), then transferred to a screw-cap NMR tube. A ^{1}H NMR spectrum (1 scan) was taken to determine the inital ratio of acrylate and 1,4-diethylbenzene. $SnCl_4$ (1 M in CD_2Cl_2, 120 μL, 0.12 mmol, 1.20 equiv) was then added through the septum of the screw-cap and the NMR tube was inverted once and quickly inserted into the spectrometer. The concentration of acrylate was monitored by ^{1}H NMR over 9 hours and was determined by integration of its resonance at 3.83 ppm relative to 1,4-diethylbenzene's resonance at 2.74 ppm.

Kinetics Plot



11. Comparison of conditions for pyrroloindoline formation.

Table 5, entry 1:



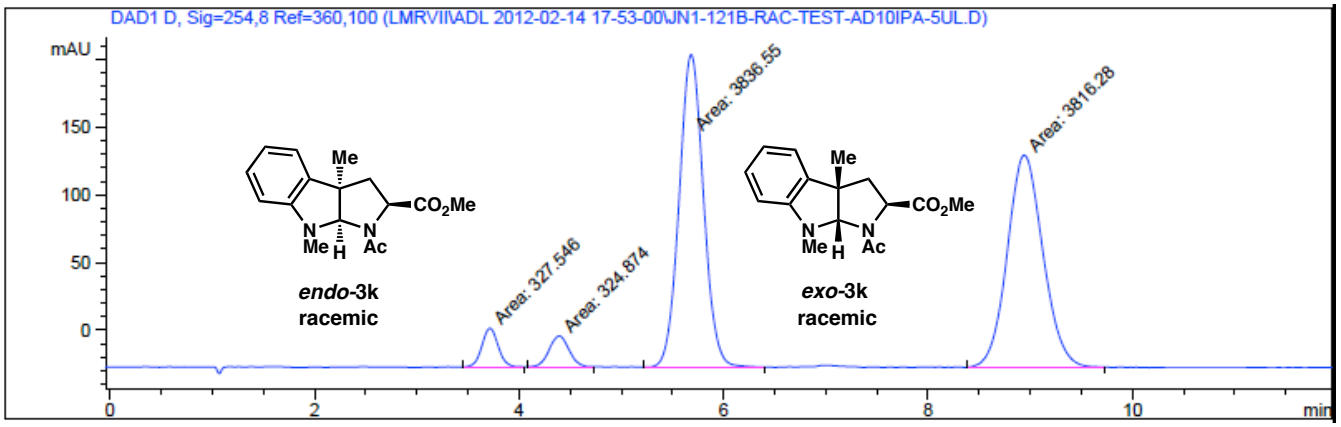
1a **2c** **3k**

(5:1 dr, 66:80% ee)

To a flame-dried 10 mL flask was added 1,3-dimethylindole (**1a**, 29.0 mg, 0.20 mmol, 1.00 equiv), acrylate **2c** (28.6 mg, 0.20 mmol, 1.00 equiv), and (*R*)-BINOL (**9a**, 11.4 mg, 0.04 mmol, 0.20 equiv). The flask was charged with DCM (1.5 mL), followed by addition of $SnCl_4$ (1 M in DCM, 240 μL, 0.24 mmol, 1.20 equiv) and the reaction mixture was stirred at room temperature for 4 hours, then quenched by diluting with MeCN (1 mL) and 1 M HCl (5 mL). The aqueous layer was extracted with EtOAc (3 x 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL). The aqueous layer was back extracted with EtOAc (10 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The product **3k** was formed in a 5:1 ratio of diastereomers favoring the *exo* diastereomer (determined by ^1H NMR analysis of the crude reaction mixture) and purified by silica gel chromatography (0:100 to 100:0 EtOAc:hexanes) to yield 40.1 mg (70% yield) of the combined diastereomers as a yellow oil. The enantiomeric excess of the *exo* diastereomer was determined to be 66% by chiral SFC analysis (AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 9.0 min, t_R(minor) = 5.8 min. The enantiomeric excess of the *endo* diastereomer was determined to be 80% by chiral SFC analysis (AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 3.8 min, t_R(minor) = 4.5 min. Spectral data are in agreement with the literature.[24]

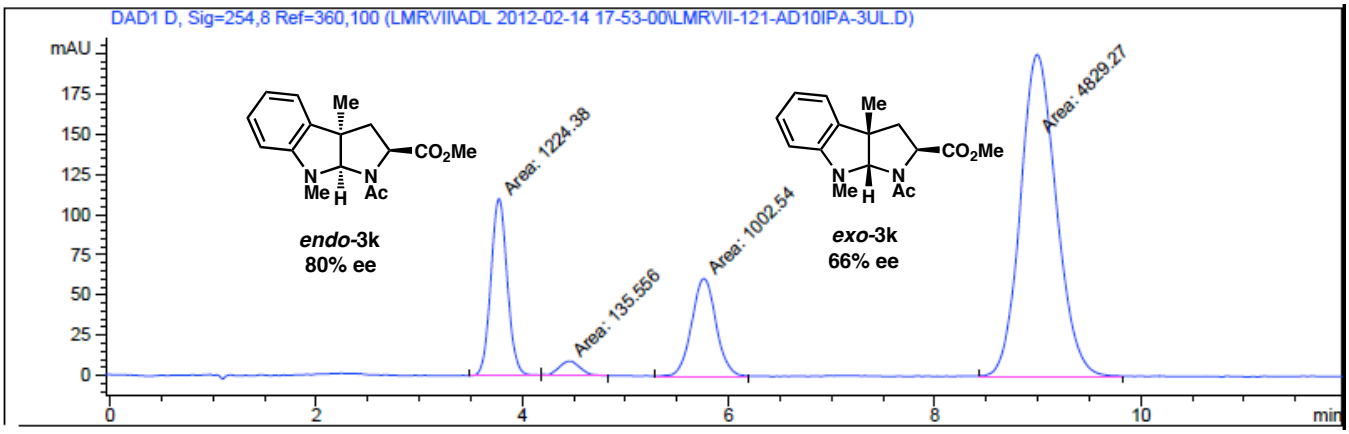
[24] Repka, L. M.; Ni, J.; J. Reisman. S. E. *J. Am. Chem. Soc.* **2010**, *132*, 14418.

3k (Table 5, entries 1-2): racemic



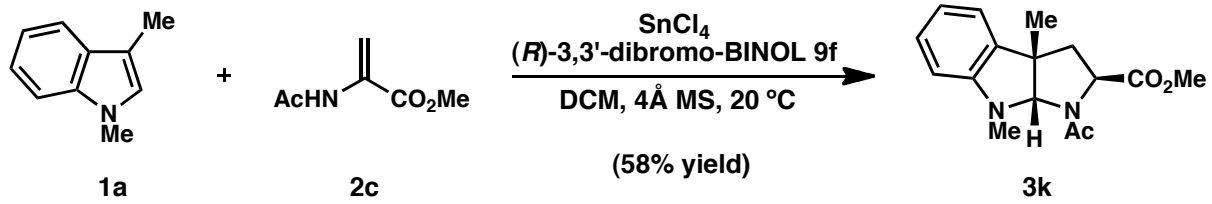
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.716	MM	0.1887	327.54623	28.92616	3.9438
2	4.393	MM	0.2327	324.87354	23.26702	3.9117
3	5.684	MM	0.2766	3836.55249	231.14015	46.1943
4	8.941	MM	0.4056	3816.27661	156.80905	45.9502

3k (Table 5, entry 1): enantioenriched, *exo*: 66% ee, *endo*: 80% ee



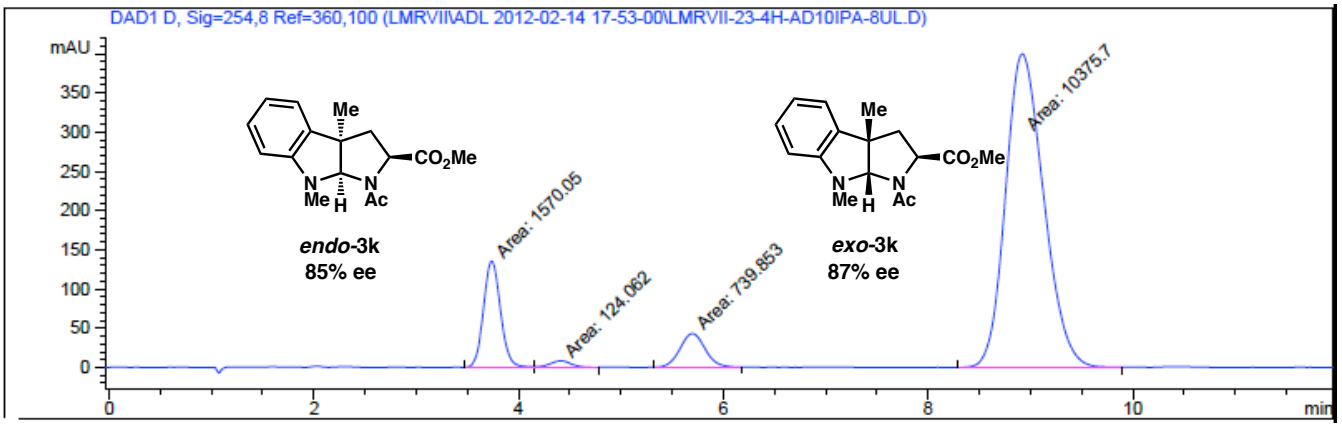
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.774	MM	0.1852	1224.37573	110.17274	17.0248
2	4.454	MM	0.2457	135.55609	9.19677	1.8849
3	5.762	MM	0.2749	1002.53888	60.78873	13.9402
4	8.994	MM	0.4027	4829.26514	199.89325	67.1502

Table 5, entry 2:



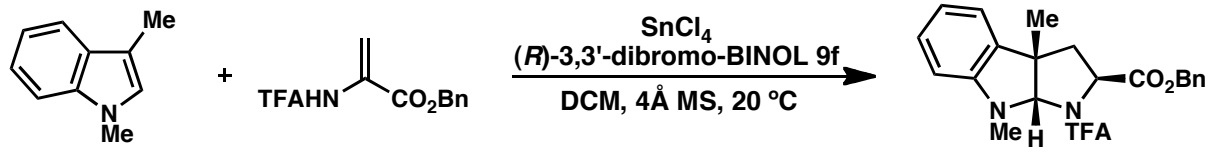
An oven-dried vial was charged with 1,3-dimethylindole (**1a**, 29.0 mg, 0.20 mmol, 1.00 equiv), acrylate **2c** (34.3 mg, 0.24 mmol, 1.20 equiv), and (*R*)-3,3'-dibromo-BINOL (**9f**, 17.8 mg, 0.04 mmol, 0.20 equiv) and pumped into a glove box. To the vial was added flame-dried powdered 4Å molecular sieves (200 wt % relative to **1a**). The vial was charged with DCM (1.5 mL) and $SnCl_4$ (1 M in DCM, 200 μL, 0.20 mmol, 1.00 equiv) was added. The reaction was stirred at 20 °C for 4 hours, after which time it was removed from the glove box and quenched by dilution with 1 M HCl (5 mL) and MeCN (1 mL). The aqueous layer was extracted with EtOAc (3 x 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL). The aqueous was back extracted with EtOAc (10 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The product **3k** was formed in a 8:1 ratio of diastereomers favoring the *exo* diastereomer (determined by ^1H NMR analysis of the crude reaction mixture) and purified by silica gel chromatography (0:100 to 100:0 EtOAc:hexanes) to yield 33.5 mg (58% yield) of the combined diastereomers as a yellow oil. The enantiomeric excess of the *exo* diastereomer was determined to be 87% by chiral SFC analysis (AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 8.9 min, t_R(minor) = 5.7 min. The enantiomeric excess of the *endo* diastereomer was determined to be 85% by chiral SFC analysis (AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 3.7 min, t_R(minor) = 4.4 min. Spectral data are in agreement with the literature.[24]

3k (Table 5, entry 2): enantioenriched, *exo*: 87% ee, *endo*: 85% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.737	MM	0.1930	1570.05005	135.56972	12.2568
2	4.408	MM	0.2459	124.06150	8.40710	0.9685
3	5.698	MM	0.2863	739.85333	43.07298	5.7757
4	8.919	MM	0.4323	1.03757e4	400.02573	80.9990

Table 5, entry 4:[25]



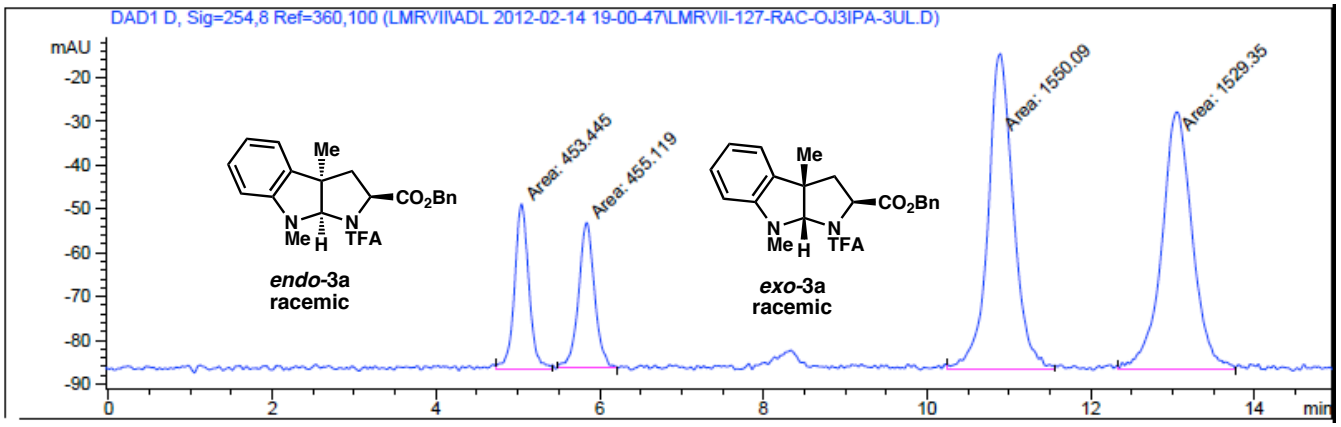
1a **2a** **3a**

(7:1 dr, 98:92% ee)

An oven-dried vial was charged with 1,3-dimethylindole (**1a**, 29.0 mg, 0.20 mmol, 1.00 equiv), acrylate **2a** (65.5 mg, 0.24 mmol, 1.20 equiv), and (*R*)-3,3'-dibromo-BINOL (**9f**, 17.8 mg, 0.04 mmol, 0.20 equiv) and pumped into a glove box. To the vial was added flame-dried powdered 4Å molecular sieves (200 wt % relative to **1a**). The vial was charged with DCM (1.5 mL) and $SnCl_4$ (1 M in DCM, 200 μL, 0.20 mmol, 1.00 equiv) was added. The reaction was stirred at 20 °C for 4 hours, after which time it was removed from the glove box and quenched by dilution with 1 M HCl (5 mL) and MeCN (1 mL). The aqueous layer was extracted with EtOAc (3 x 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL). The aqueous was back extracted with EtOAc (10 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The product **3a** was formed in a 7:1 ratio of diastereomers favoring the *exo* diastereomer (determined by ^1H NMR analysis of the crude reaction mixture) and purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 32.7 mg (39% yield) of the combined diastereomers as a yellow oil. The enantiomeric excess of the *exo* diastereomer was determined to be 98% by chiral SFC analysis (OJ-H, 2.5 mL/min, 3% IPA in CO_2, λ = 254 nm): t_R(major) = 12.5 min, t_R(minor) = 10.9 min. The enantiomeric excess of the *endo* diastereomer was determined to be 92% by chiral SFC analysis (OJ-H, 2.5 mL/min, 3% IPA in CO_2, λ = 254 nm): t_R(major) = 5.8 min, t_R(minor) = 5.0 min. Spectral data are in agreement with the literature.[24]

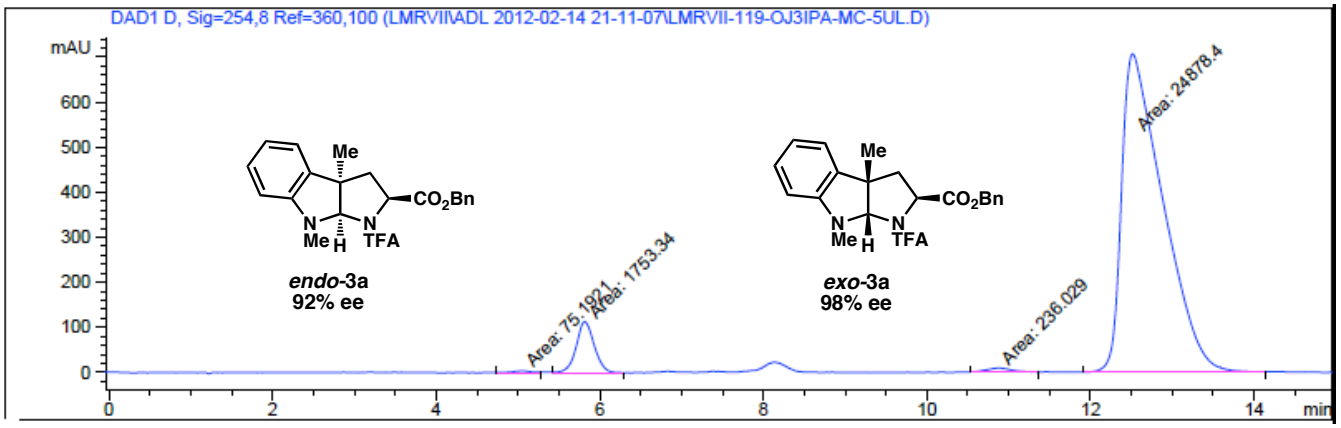
[25] For more information regarding Table 5, entry 3, see reference 24.

3a (Table 5, entry 4): racemic



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.046	MM	0.2006	453.44531	37.66904	11.3702
2	5.841	MM	0.2280	455.11948	33.27365	11.4122
3	10.895	MM	0.3583	1550.08838	72.09877	38.8688
4	13.054	MM	0.4330	1529.35278	58.87241	38.3488

3a (Table 5, entry 4): enantioenriched, *exo*: 98% ee, *endo*: 92% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.047	MM	0.2718	75.19215	4.61071	0.2791
2	5.818	MM	0.2566	1753.34155	113.89976	6.5076
3	10.862	MM	0.3831	236.02933	10.26737	0.8760
4	12.514	MM	0.5861	2.48784e4	707.50366	92.3373