CHAPTER 3

Conjugate Addition/in situ Reduction for the Synthesis of Indolines[*]

3.1 Introduction

In addition to the pyrroloindolines discussed in Chapters 1 and 2, there are a great number of structurally distinct natural products that incorporate an indoline moiety. These compounds feature diverse substitution about the heterocyclic core, and several exhibit promising biological activities (see Figure 1 for representative examples).[1] Many groups have developed methods for the stereoselective preparation of non-pyrroloindoline indolines, including transformations starting from tryptophan, as well as catalytic asymmetric reactions using organo- or transition metal catalysts.

Mechanistic studies on the formal (3 + 2) cycloaddition to prepare enantioenriched pyrroloindolines (described in Chapter 2) revealed that the initial product of this reaction is an indolinium ion (**119)**, and that cyclization to form the pyrroloindoline (**121**) does not occur until aqueous work-up. Thus, we proposed that these intermediates could be trapped with an external hydride source (Figure 2). This chapter describes the development of this approach for the preparation of indoline-

[*] Portions of this chapter have been reproduced from a published study (see reference 13) and the supporting information found therein. The research presented in this chapter was completed in collaboration with Haoxuan Wang, a graduate student in the Reisman group.

containing amino acid derivatives bearing an all-carbon quaternary stereocenter at the C3 position (**120**).

Figure 1. Selected indoline natural products.

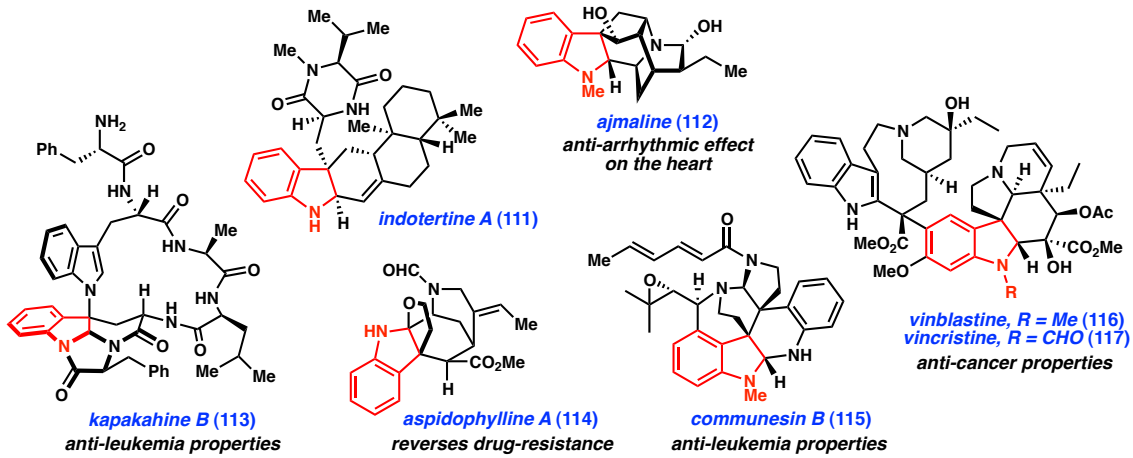
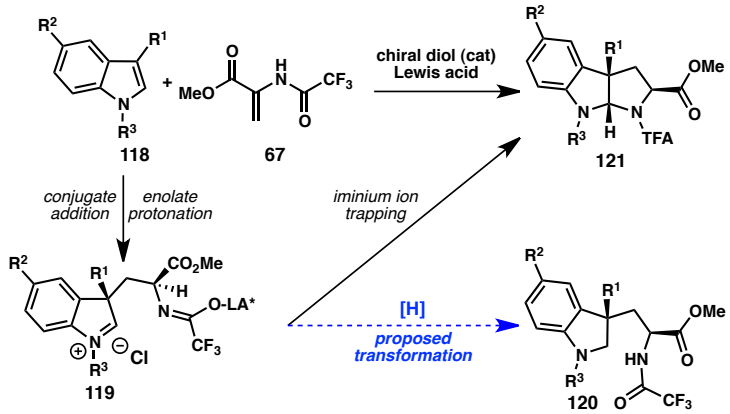


Figure 2. Proposed in situ reduction of an iminium ion intermediate to generate indolines.

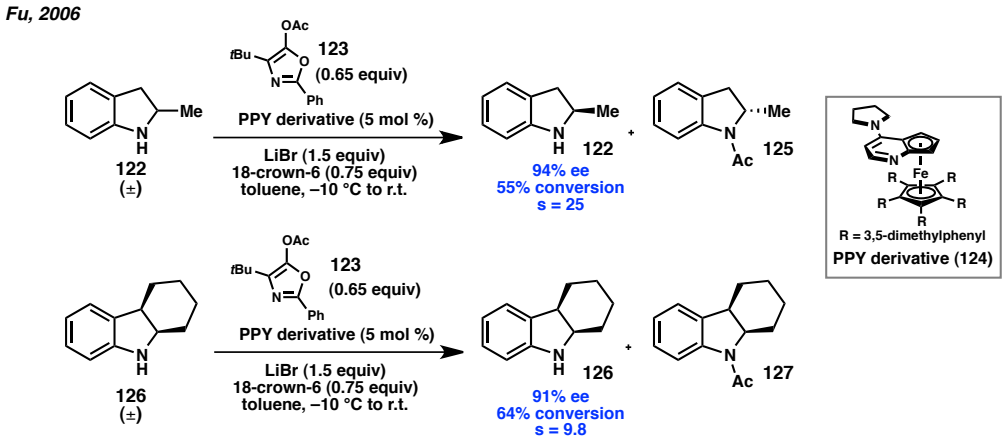


3.1.1 Methods for the Enantioselective Preparation of Indolines

Several methods to access enantioenriched indolines have been developed. One such approach is to effect a kinetic resolution of racemic indolines. Fu and coworkers

achieved this goal using a planar-chiral PPY derivative (**124**) as the catalyst (Figure 3).[2] High selectivity factors were achieved by employing a catalyst possessing a highly sterically-demanding C_5Ar_5 group.

Figure 3. Kinetic resolution of indolines



Besides resolutions, there are also several catalytic, asymmetric methods to prepare indolines; these can be divided into two classes: (a) those that start from a related nitrogen-containing heterocycle, such as indoles or oxindoles, and (b) those that directly form the indoline framework. In the first class, a common approach to prepare indolines from indoles or oxindoles is *via* asymmetric reduction. For example, Zhang and coworkers achieved the asymmetric hydrogenation of unprotected indoles (e.g., **128**) with a palladium catalyst and chiral phosphine ligand (Figure 4).[3] Protonation of the indole by a Brønsted acid forms an indolinium ion (**130**), which is more readily reduced. A dynamic kinetic resolution occurs to afford 2,3-disubstituted indolines (**131**) with high enantiomeric excess. An organocatalyzed version of this reaction was developed by Chen and coworkers (Figure 4).[4] In this transformation, in situ-generated HCl effects C3

protonation to give the indolinium followed by chiral Lewis base mediated enantioselective hydrosilylation.

Figure 4. Enantioselective indoline synthesis by hydrogenation of indoles.

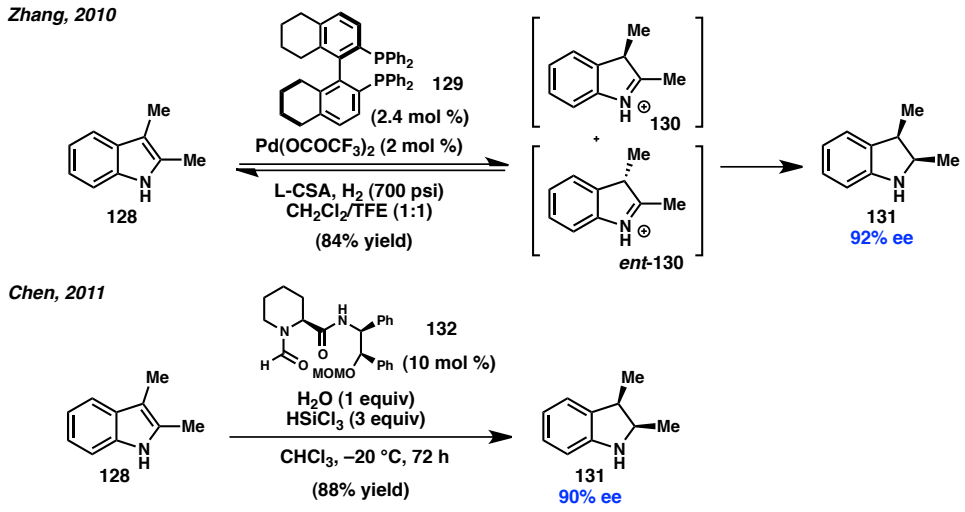
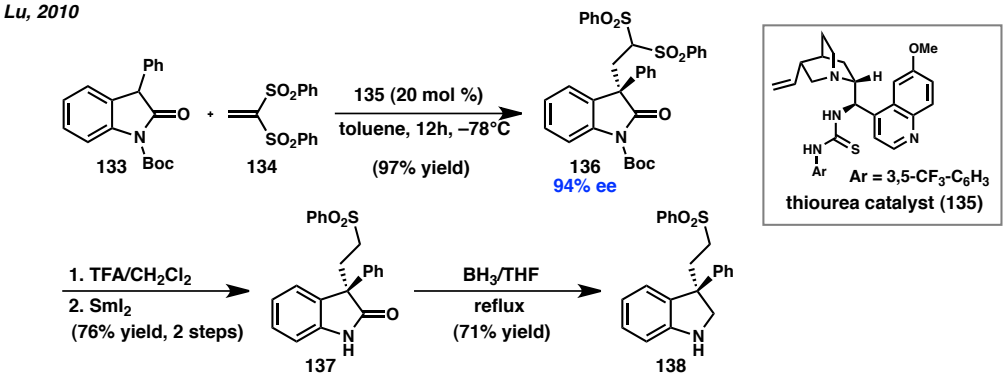


Figure 5. Enantioselective indoline synthesis by reduction of oxindoles.

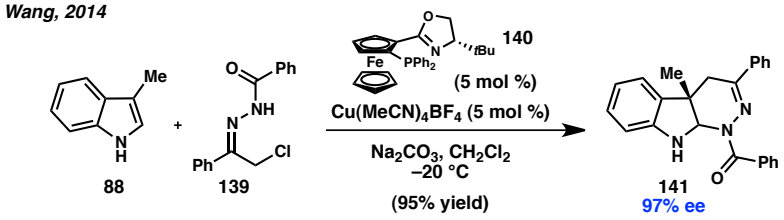


The Lu laboratory reported the enantioselective preparation of indolines with an all-carbon quaternary center by reduction of the corresponding oxindole (Figure 5).[5] Thiourea-catalyzed asymmetric conjugate of oxindole **133** to vinyl sulfone **134** generates

the C3 stereocenter. While direct reduction of oxindole **136** led to the formation of retro-Michael side products, one aryl sulfone group can be selectively removed with SmI_2 to allow subsequent reduction with BH_3 to afford the corresponding indoline (**138**).

In contrast to methods to access indolines by the reduction of indoles, Wang and coworkers developed an asymmetric inverse-electron-demand aza-Diels–Alder reaction of indoles and azoalkenes.[6] This reaction is catalyzed by a Cu^I/*t*Bu-Phosferrox complex to give [2,3]-fused indoline tetrahydropyridazine heterocycles (Figure 6). The azoalkenes are formed in situ from α-halogeno hydrazones in the presence of a base; coordination to a copper complex enhances its reactivity compared to the uncatalyzed background reaction.

Figure 6. Indoline synthesis via Diels–Alder cycloaddition.

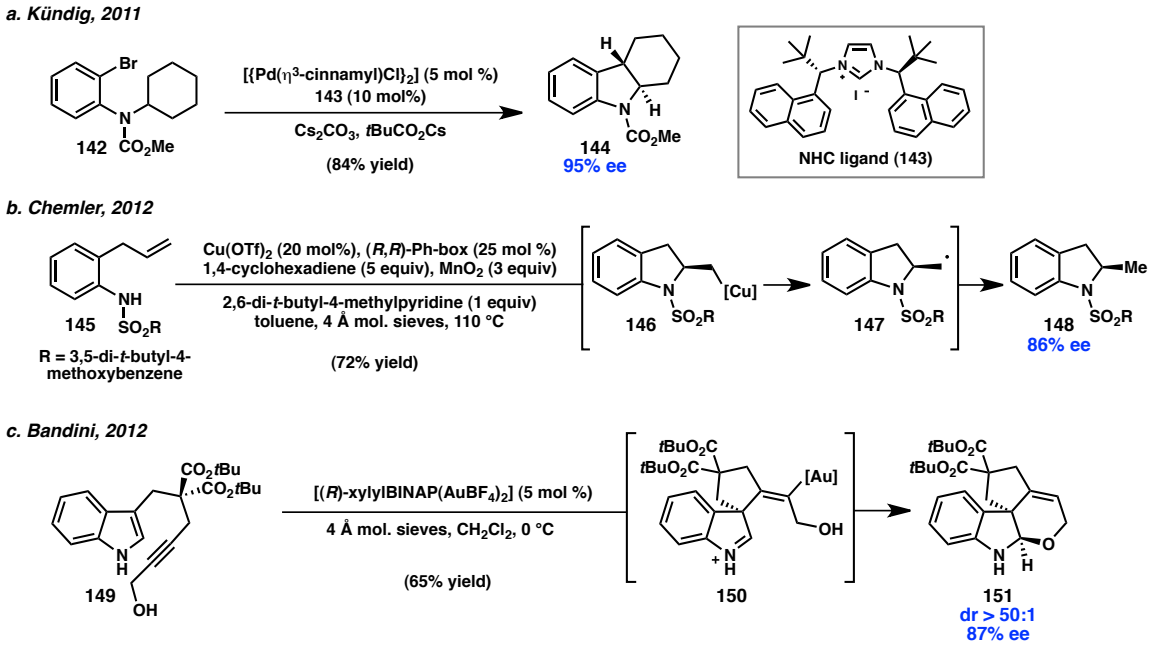


The second class of methods to access indolines involves direct preparation of the heterocyclic framework. Of these methods, several transition metal-catalyzed cyclization reactions have been developed. Kündig and coworkers prepared enantioenriched, *trans*-fused indolines by palladium-catalyzed activation of enantiotopic methylene C–H bonds (Figure 7).[7] This reaction utilizes NHC ligands derived from chiral *o*-substituted α-alkylphenethyl amines.

The Chemler laboratory disclosed an enantioselective, intramolecular copper-catalyzed alkene hydroamination to afford indolines (Figure 7).[8] This reaction is thought to occur *via* initial *cis* aminocupration, resulting in an unstable organocopper(II) intermediate (**146**) that undergoes homolysis to generate a primary organic radical (**147**) and copper(I). Hydrogen atom abstraction from 1,4-cyclohexadiene provides the net hydroamination product.

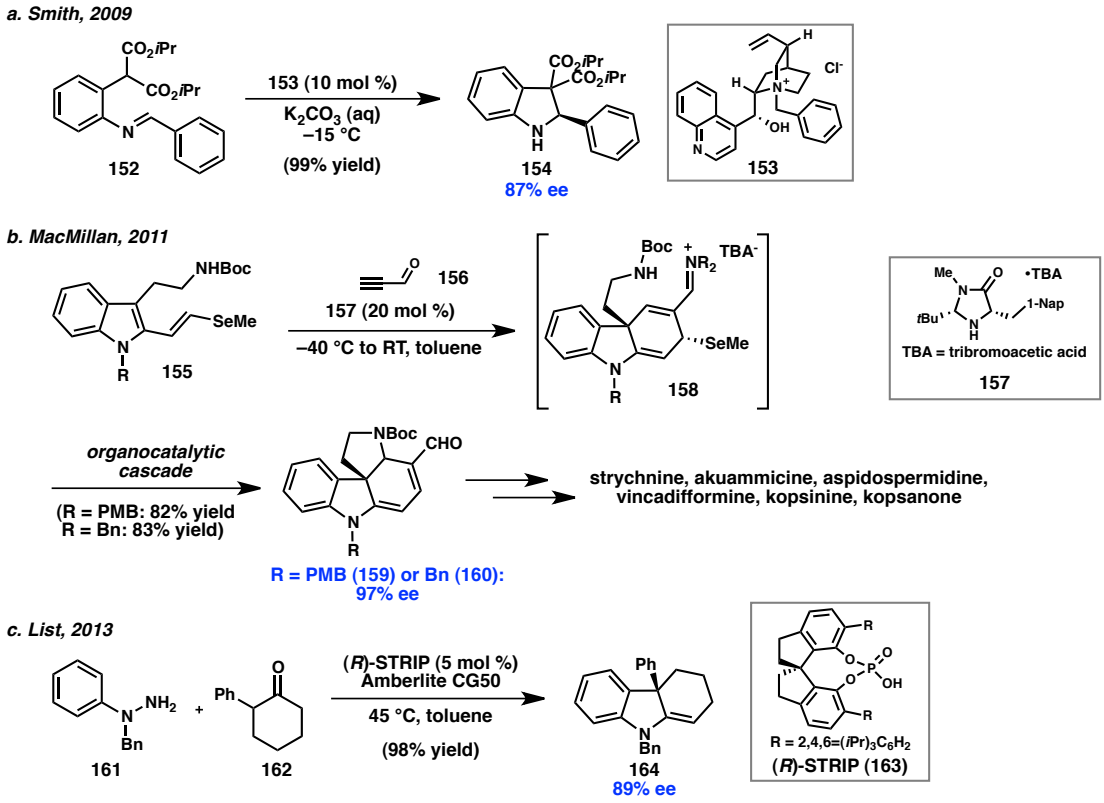
Bandini and coworkers reported a gold-catalyzed cascade reaction of functionalized propargylic alcohols (e.g. **149**) yielding indoline products (Figure 7).[9] The authors propose that this reaction involves hydroindolination of the triple bond and subsequent iminium trapping. 5-*exo-dig* cyclization was observed exclusively when a carbon-based tether between the indole and alkyne was utilized.

Figure 7. Enantioselective indoline synthesis by transition metal catalyzed (a) C–H activation, (b) hydroamination, and (c) alkyne cyclization.



In contrast to these transition-metal-catalyzed transformations, several organocatalytic methods for the direct prepartion of indolines have been reported. The Smith laboratory employed a chiral phase transfer catalyst to promote a cyclization reaction to prepare indolines (Figure 8).[10] The authors propose two possible mechanisms for this reaction: an intramolecular Mannich reaction, or an electrocyclization. These possibilities could not be distinguished by the stereochemical outcome of the reaction, because the substrates reported did not include the appropriate substituents to probe the stereospecificity that is diagnostic of pericyclic processes.

Figure 8. Organocatalytic indoline syntheses: (a) electrocyclization, (b) cascade for total syntheses of indoline natural products, and (c) Fischer indolization.



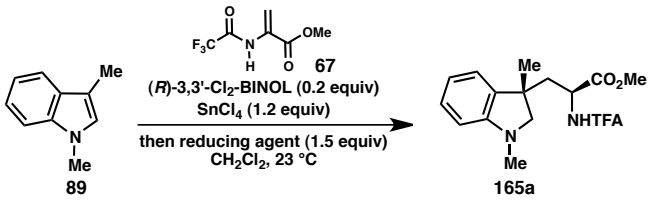
On the other hand, the MacMillan laboratory utilized an organocatalyst to promote a [4+2] cycloaddition: exposure of tryptamine derivative **155** to an imidazolidinone catalyst (**157**) results in a Diels–Alder reaction with propynal (Figure 8).[11] Incorporation of an organoselenide facilitates further cascade reactions to afford indolines **159** and **160** in excellent yield and enantioselectivity. This functionalized intermediate was further elaborated to complete highly efficient total syntheses of six structurally diverse natural products.

Another organocatalytic approach was developed by List and coworkers, in which a chiral phosphoric acid catalyzed an asymmetric Fischer indolization (Figure 8).[12] Upon condensation of α-substituted cyclic ketone **162** with phenylhydrazine (**161**), the Brønsted acid promotes the [3,3]-sigmatropic rearrangement, leading to enantioenriched fused indolines.

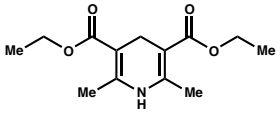
3.2 Development of the Indoline Synthesis

To assess the feasibility of our proposed indoline synthesis, indole **89** and acrylate **67** were exposed to the optimized conditions for the formal (3 + 2) cycloaddition (Chapter 2), along with a reductant (Table 1). Whereas weaker reductants such as triethylsilane and sodium triacetoxy borohydride proved ineffective, we were pleased to find that use of Hantzsch ester **166** did provide the indoline product, albeit in low yield (entry 3). Alternatively, use of sodium borohydride furnished **165a** in good yield, 15:1 dr, 92% ee (entry 5). The more soluble reducing agent lithium borohydride provided a lower yield of the desired product along with a greater amount of byproducts. The limited solubility of $NaBH_4$ and $LiBH_4$ in methylene chloride likely contributes to the compatibility of all the reagents, allowing the reaction to be carried out in one pot.

Table 1. Screen of reducing agents.



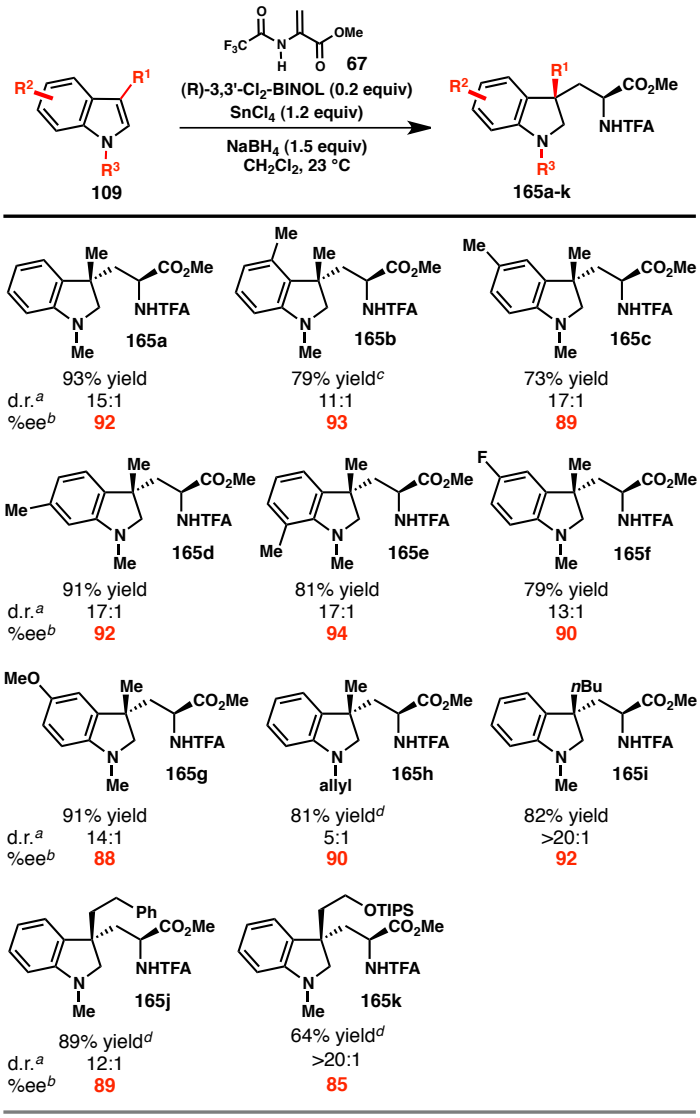
Entry	Reducing Agent	Yield (%)
1	Et_3SiH	0
2	$NaBH(OAc)_3$	0
3	Hantzsch ester **25**	3
4	$LiBH_4$	85
5	$NaBH_4$	93



3.2.1 Substrate Scope of Indoline Synthesis

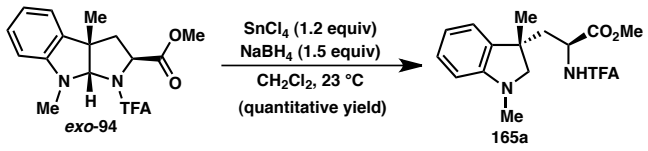
Having identified the optimal reducing agent, a survey of indole substrates was conducted (Figure 9).[13] Indoles with either electron-donating or –withdrawing substituents are good substrates for the reaction. At the 3-position, *n*-butyl and phenylethyl groups are tolerated, but reactivity decreases with increasing steric bulk and 1.6 equivalents of $SnCl_4$ are required to achieve good reactivity with the phenylethyl substrate. Whereas the cleavage of the protecting group was observed when TBS-protected tryptophol was employed, use of the TIPS-protected tryptophol furnished **165k** in good yield. The indole nitrogen can also be protected with an allyl group, which would be useful when an *N*-Me functionality is not desired in the product.

Figure 9. In situ reduction for the synthesis of indolines.



[a] Determined by ^{1}H NMR of crude reaction mixture. [b] Determined by SFC using chiral stationary phase. [c] Isolated yield of *exo*-diastereomer. [d] 1.6 equiv. $SnCl_4$ was employed.

Figure 10. Re-exposure of pyrroloindoline ***exo-94*** *to $SnCl_4$ and $NaBH_4$.*



The reduced products **165** are formed with the same diastereomeric and enantiomeric ratios as the corresponding pyrroloindolines, suggesting that iminium reduction does not affect the selectivities of the other steps. When a methylene chloride solution of pyrroloindoline ***exo*-94** and $SnCl_4$ was re-exposed to $NaBH_4$, the pyrroloindoline was reduced to indoline **165a** in quantitative yield (Figure 10). This is consistent with amide cyclization being reversible in the presence of the Lewis acid.

3.3 Concluding Remarks

Mechanistic insight into the (*R*)-BINOL•$SnCl_4$-catalyzed formal (3 + 2) cycloaddition (Chapter 1) has led to the development of a method for the preparation of enantioenriched indoline-containing amino acid derivatives with all-carbon quaternary centers at C3. It was determined that the intially-formed product of the formal (3 + 2) cycloaddition is an iminium ion, and that cyclization by the pendant amide to provide the pyrroloindoline does not occur until aqeous work-up. Thus, we proposed that the addition of external nucleophiles will allow access to a variety of indoline structures. This chapter explores the use of reducing agents to effect the in situ reduction of this iminium intermediate. Of the reagents screened, sodium borohydride was found to be optimal. This one-pot procedure tolerates a variety of substitution on the backbone or at C3 of the indole substrate.

3.4 Experimental Section

3.4.1 Materials and Methods

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), and toluene were dried by passing through activated alumina columns. Deuterated methylene chloride (CD_2Cl_2) was dried by passing through a plug of activated alumina in a glovebox. Dimethylformamide (DMF) was dried over activated molecular sieves, and dichloroethane (DCE) was distilled over calcium hydride. All other commercially obtained reagents were used as received unless specifically indicated. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Flash column chromatography was performed either as described by Still et al. (Still, W. C., Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.) using silica gel (partical size 0.032-0.063) purchased from Silicycle or using pre-packaged RediSep®Rf columns on a CombiFlash Rf system (Teledyne ISCO Inc.). Diastereomeric ratios were determined by integration of NMR spectra or HPLC or SFC analysis. 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 spectra were recorded on a Varian Mercury 300 (at 300 MHz and 75 MHz, respectively), a Varian 400 (at 400 MHz and 100 MHz, respectively) or a Varian Inova 500 (at 500 MHz and 125 MHz respectively), and are reported relative to internal chloroform (^{1}H, δ = 7.26, ^{13}C, δ = 77.0). 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, app = apparent. IR spectra were recorded on a

Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Preparatory HPLC was performed with either an Agilent 1100 or 1200 Series HPLC utilizing an Agilent Zorbax RX-SIL 5μm column (9.4 x 250 mm). Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing Chiralcel AD or OD-H columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd, with visualization at 254 nm. Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system with Chiralcel AD-H, OJ-H columns (4.6 mm x 25 cm). Melting points were determined using a Büchi B-545 capillary melting point apparatus and the values reported are uncorrected. 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.

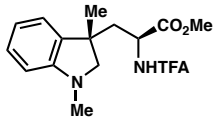
3.4.2 General Procedure: Formal (3 + 2) Cycloaddition/in situ Reduction.

To a flame-dried flask was added indole (0.20 mmol, 1.00 equiv), acrylate (0.20 mmol, 1.00 equiv), and (*R*)-3,3'-dichloro-BINOL (0.04 mmol, 0.20 equiv). The flask was charged with CH_2Cl_2 (1.5 mL), followed by addition of $SnCl_4$ (0.24 mmol, 1.20 equiv unless specifically indicated, 1 M in CH_2Cl_2). $NaBH_4$ (0.30 mmol, 1.50 equiv) was then added, and the reaction was stirred at room temperature for 24 h (unless specifically indicated). The reaction was quenched by diluting with 1 mL MeCN and 1 mL 1 M HCl, followed by addition of 5 mL H_2O. The aqueous layer was extracted with ethyl acetate (3 x 15 mL) and the combined organic layers were washed with saturated $NaHCO_{3(aq)}$ (10 mL). The aqueous layer was extracted with ethyl acetate (10 mL). The combined organic

layers were dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by flash chromatography.

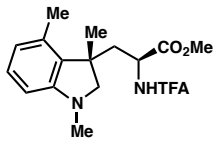
3.4.3 Indoline Products

Indoline 165a.



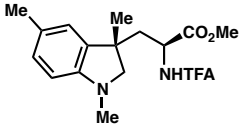
Prepared from 1,3-dimethyl-1*H*-indole [14] and methyl 2-trifluoroacetamidoacrylate using the general procedure. The diastereomeric ratio was determined to be 15:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (5→25% ethyl acetate/hexanes) to yield 64.1 mg (93% yield) of **165a**, a pale yellow oil. The enantiomeric excess of the major diastereomer was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R(major) = 9.9 min t_R(minor) = 5.9 min. The major diastereomer was separated by flash chromatography (5% ethyl acetate/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (br d, J = 5.9 Hz, 1H), 7.14 (td, J = 7.7, 1.2 Hz, 1H), 6.99 (dd, J = 7.3, 0.8 Hz, 1H), 6.76 (td, J = 7.4, 0.8 Hz, 1H), 6.54 (d, J = 7.9 Hz, 1H), 4.27 (br td, J = 7.7, 4.7 Hz, 1H), 3.65 (s, 3H), 3.31 (d, J = 9.1 Hz, 1H), 2.98 (d, J = 9.1 Hz, 1H), 2.74 (s, 3H), 2.21 (dd, J = 14.7, 4.7 Hz, 1H), 2.15 (dd, J = 14.7, 8.2 Hz, 1H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 156.6 (q, $J_{C\text{-}F}$ = 37.5 Hz), 152.1, 153.3, 128.5, 122.4, 119.0, 115.6 (q, $J_{C\text{-}F}$ = 287.9 Hz), 108.4, 68.3, 52.7, 51.2, 42.8, 42.1, 35.8, 26.1; IR (NaCl/thin film): 3319, 2956, 2858, 2811, 1751, 1718, 1607, 1559, 1491, 1452, 1209, 1179, 744 cm^{-1}; $[\alpha]_D^{25}$ = +79.6 (c = 1.32, CH_2Cl_2). HRMS (MM) calc'd for $[M+H]^+$ 345.1421, found 345.1423.

Indoline 165b.



Prepared from 1,3,4-trimethyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure. The diastereomeric ratio was determined to be 11:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (5→25% ethyl acetate/hexanes) to yield 56.8 mg (79% yield, yellow oil) of **165b** as a single diastereomer. The enantiomeric excess of the major diastereomer was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 6% IPA in CO_2, λ = 254 nm): t_R(major) = 3.9 min t_R(minor) = 3.5 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (br d, J = 4.9 Hz, 1H), 7.06 (t, J = 7.7 Hz, 1H), 6.54 (d, J = 7.6 Hz, 1H), 6.42 (d, J = 7.9 Hz), 4.10 (ddd, J = 9.0, 6.5, 4.2 Hz, 1H), 3.65 (s, 3H), 3.32 (d, J = 9.3 Hz, 1H), 2.95 (d, J = 9.2 Hz, 1H), 2.71 (s, 3H), 2.45 (dd, J = 15.0, 4.0 Hz, 1H), 2.30 (s, 3H), 2.13 (dd, J = 14.8, 8.9 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 156.7 (q, $J_{C\text{-}F}$ = 37.5 Hz), 152.8, 134.5, 131.5, 128.8, 122.4, 115.6 (q, $J_{C\text{-}F}$ = 287.9 Hz), 106.7, 68.6, 52.7, 51.7, 43.7, 40.9, 35.9, 26.6, 18.7; IR (NaCl/thin film): 3315, 2956, 2812, 1750, 1710, 1593, 1559, 1484, 1457, 1209, 1179, 774 cm^{-1}; $[\alpha]_D^{25}$ = +66.0 (c = 1.04, CH_2Cl_2). HRMS (MM) calc'd for $[M+H]^+$ 359.1577, found 359.1591.

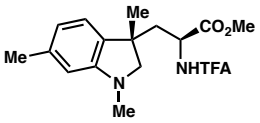
Indoline 165c.



Prepared from 1,3,5-trimethyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure. The diastereomeric ratio was determined to be 17:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (10→25% ethyl acetate/hexanes) to yield 52.6 mg (73% yield) of **165c**,

a yellow oil. The enantiomeric excess of the major diastereomer was determined to be 89% by chiral SFC analysis (AD-H, 2.5 mL/min, 6% IPA in CO_2, λ = 254 nm): t_R(major) = 4.8 min t_R(minor) = 3.4 min. The major diastereomer was separated by flash chromatography (7% ethyl acetate/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (br d, *J* = 4.8 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.81 (s, 1H), 6.47 (d, *J* = 7.9 Hz, 1H), 4.16 (q, *J* = 6.5 Hz, 1H), 3.67 (s, 3H), 3.27 (d, *J* = 9.1 Hz, 1H), 2.91 (d, *J* = 9.1 Hz, 1H), 2.70 (s, 3H), 2.25 (s, 3H), 2.17 (d, *J* = 6.5 Hz, 2H), 1.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 156.7 (q, $J_{C\text{-}F}$ = 37.5 Hz), 150.0, 135.5, 128.9, 128.8, 123.3, 115.6 (q, $J_{C\text{-}F}$ = 287.9 Hz), 108.7, 69.0, 52.7, 51.5, 42.7, 42.1, 36.4, 26.07, 20.7; IR (NaCl/thin film): 3326, 2955, 2922, 2863, 2806, 1752, 1719, 1555, 1499, 1452, 1209, 1163, 806 cm^{-1}; $[\alpha]_D^{25}$ = -+42.3 (*c* = 0.87, CH_2Cl_2). HRMS (MM) calc'd for $[M+H]^+$ 359.1577, found 359.1565.

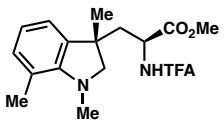
Indoline 165d.



Prepared from 1,3,6-trimethyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure. The diastereomeric ratio was determined to be 17:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (5→30% ethyl acetate/hexanes) to yield 65.0 mg (91% yield) of **165d**, a yellow oil. The enantiomeric excess of the major diastereomer was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R(major) = 11.1 min t_R(minor) = 5.0 min. The major diastereomer was separated by flash chromatography (5% ethyl acetate/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 5.7 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 6.37 (s, 1H), 4.22 (td, *J* = 7.5, 4.9 Hz), 3.66 (s, 3H), 3.29 (d, *J* = 9.1 Hz, 1H), 2.96 (d, *J* = 9.1 Hz, 1H), 2.72 (s, 3H), 2.30 (s, 3H), 2.20-2.11

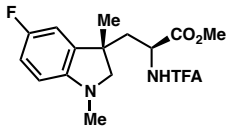
(m, 2H), 1.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 156.6 (q, $J_{C\text{-}F}$ = 37.5 Hz), 152.3, 138.6, 132.5, 122.2, 119.8, 115.6 (q, $J_{C\text{-}F}$ = 287.8 Hz), 109.3, 68.6, 52.7, 51.4, 42.5, 42.2, 35.8, 26.2, 21.6; IR (NaCl/thin film): 3321, 2956, 2923, 2870, 2804, 1750, 1716, 1615, 1557, 1497, 1455, 1208, 1179, 802 cm^{-1}; $[\alpha]_D^{25}$ = +76.0 (*c* = 1.56, CH_2Cl_2). HRMS (MM) calc'd for $[M+H]^+$ 359.1577, found 359.1577.

Indoline 165e.



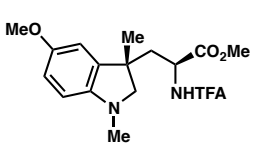
Prepared from 1,3,7-trimethyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure. The diastereomeric ratio was determined to be 17:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (5→30% ethyl acetate/hexanes) to yield 58 mg (81% yield) of **165e**, a pale yellow oil. The enantiomeric excess of the major diastereomer was determined to be 94% by chiral SFC analysis (AD-H, 2.5 mL/min, 6% IPA in CO_2, λ = 254 nm): t_R(major) = 4.3 min t_R(minor) = 3.3 min. The major diastereomer was separated by flash chromatography (5% ethyl acetate/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 4.7 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 7.4 Hz, 1H), 6.73 (t, *J* = 7.4 Hz, 1H), 4.14-4.08 (m, 1H), 3.66 (s, 3H), 3.29 (d, *J* = 9.6 Hz, 1H), 2.97 (d, *J* = 9.6 Hz, 1H), 2.93 (s, 3H), 2.37 (s, 3H), 2.17-2.06 (m, 2H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 156.7 (q, $J_{C\text{-}F}$ = 37.5 Hz), 149.9, 136.1, 131.8, 121.2, 120.4, 120.3, 115.6 (q, $J_{C\text{-}F}$ = 287.8 Hz), 69.7, 52.7, 51.3, 42.8, 42.3, 39.5, 26.6, 19.5; IR (NaCl/thin film): 3322, 2959, 2924, 1750, 1713, 1557, 1480, 1456, 1412, 1208, 1180, 1071, 750 cm^{-1}; $[\alpha]_D^{25}$ = +84.9 (*c* = 1.20, CH_2Cl_2). HRMS (APCI) calc'd for $[M+H]^+$ 359.1577, found 359.1595.

Indoline 165f.



Prepared from 5-fluoro-1,3-dimethyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure. The diastereomeric ratio was determined to be 13:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (10→30% ethyl acetate/hexanes) to yield 57.0 mg (79% yield) of **165f**, a pale yellow oil. The enantiomeric excess of the major diastereomer was determined to be 90% by chiral SFC analysis (AD-H, 2.5 mL/min, 6% IPA in CO_2, λ = 254 nm): t_R(major) = 3.9 min t_R(minor) = 2.9 min. The major diastereomer was separated by preparatory TLC (40% CH_2Cl_2/hexanes then 50% CH_2Cl_2/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (br d, J_{C-H} = 5.8 Hz, 1H), 6.83 (td, J_{C-H} = 8.8, 2.6 Hz, 1H), 6.72 (dd, J_{C-H} = 8.2, 2.6 Hz, 1H), 6.44 (dd, J_{C-H} = 8.5, 4.1 Hz, 1H), 4.25 (td, J_{C-H} = 7.7, 4.8 Hz, 1H), 3.68 (s, 3H), 3.31 (d, J_{C-H} = 9.2 Hz, 1H), 2.97 (d, J_{C-H} = 9.2 Hz, 1H), 2.70 (s, 3H), 2.21 (dd, J_{C-H} = 14.7, 4.8 Hz, 1H), 2.12 (dd, J_{C-H} = 14.7, 8.1 Hz, 1H), 1.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 157.2 (d, J_{C-F} = 237.2 Hz), 156.6 (q, J_{C-F} = 37.8 Hz), 148.4, 137.1 (d, J_{C-F} = 7.1 Hz), 116.7, 114.5 (d, J_{C-F} = 23.3 Hz), 110.1 (d, J_{C-F} = 24.0 Hz), 108.8 (d, J_{C-F} = 8.1 Hz), 68.6, 52.8, 51.1, 42.8, 42.0, 36.4, 26.1; IR (NaCl/thin film): 3319, 2958, 2866, 2811, 1745, 1711, 1552, 1494, 1468, 1267, 1210, 1179, 808 cm^{-1}; $[\alpha]_D^{25}$ = +63.7 (*c* = 0.62, CH_2Cl_2). HRMS (ESI) calc'd for $[M+H]^+$ 363.1326, found 363.1334.

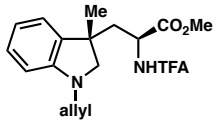
Indoline 165g.



Prepared from 5-methoxy-1,3-dimethyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure. The reaction was allowed to run for 18.5 h. The diastereomeric ratio was determined to be

14:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (10→30% ethyl acetate/hexanes) to yield 68.5 mg (91% yield) of **XX**, a yellow oil. The enantiomeric excess of the major diastereomer was determined to be 88% by chiral SFC analysis (AD-H, 2.5 mL/min, 7% IPA in CO_2, λ = 254 nm): t_R(major) = 7.1 min t_R(minor) = 3.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (br d, $J_{C\text{-}H}$ = 5.0 Hz, 1H), 6.70 (dd, $J_{C\text{-}H}$ = 8.4, 1.9 Hz, 1H), 6.62 (d, $J_{C\text{-}H}$ = 1.8 Hz, 1H), 6.50 (d, $J_{C\text{-}H}$ = 8.3 Hz, 1H), 4.01 (dd, $J_{C\text{-}H}$ = 13.1, 6.3 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.28 (d, $J_{C\text{-}H}$ = 8.6 Hz, 1H), 2.89 (d, $J_{C\text{-}H}$ = 9.1 Hz, 1H), 2.68 (s, 3H), 2.23-2.08 (m, 2H), 1.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 156.8 (q, $J_{C\text{-}F}$ = 37.5 Hz), 154.1, 146.1, 137.0, 115.6 (q, $J_{C\text{-}F}$ = 287.8 Hz), 113.1, 110.8, 109.6, 69.0, 55.8, 52.7, 51.5, 43.0, 42.0, 36.9, 26.2; IR (NaCl/thin film): 3319, 2955, 2804, 1751, 1718, 1555, 1496, 1468, 1214, 1179, 1031 cm^{-1}; $[\alpha]_D^{25}$ = +26.3 (*c* = 1.24, CH_2Cl_2). HRMS (APCI) calc'd for $[M+H]^+$ 375.1526, found 375.1542.

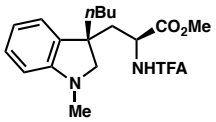
Indoline 165h.



Prepared from 1-allyl-3-methyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure, except the formal (3 + 2) cycloaddition was allowed to run for 24 h before adding $NaBH_4$. After adding $NaBH_4$, the reaction was allowed to run for another 24 h. The diastereomeric ratio was determined to be 5:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (5→20% ethyl acetate/hexanes) to yield 60.0 mg (81% yield) of **XX**, a yellow oil. The enantiomeric excess of the major diastereomer was determined to be 90% by chiral SFC analysis (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R(major) = 7.2 min t_R(minor) = 6.2 min. Isolated as a 5:1

mixture of diastereomers; the major diastereomer is denoted by *, minor diastereomer denoted by §. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (br d, *J* = 8.5 Hz, 1H§), 7.16-7.05 (m, 2H*, 1H§), 6.98 (ddd, *J* = 7.4, 1.2, 0.5 Hz, 1H*, 1H§), 6.78 (td, *J* = 7.4, 1.0 Hz, 1H§), 6.72 (td, *J* = 7.4, 1.0 Hz, 1H*), 6.64 (d, *J* = 7.9 Hz, 1H§), 6.56 (d, *J* = 7.9 Hz, 1H*), 5.93-5.83 (m, 1H*, 1H§), 5.32-5.20 (m, 1H*, 1H§), 4.81-4.75 (m, 1H§), 4.40 (td, *J* = 7.6, 5.0, 1H*), 3.79 (ddt, *J* = 15.0, 5.9, 1.4 Hz, 1H*, 1H§), 3.73-3.70 (m, 1H§), 3.65-3.59 (m, 1H*), 3.63 (s, 3H*), 3.42 (s, 3H§), 3.31 (d, *J* = 9.3 Hz, 1H*), 3.28 (d, *J* = 9.6 Hz, 1H§), 3.07 (d, *J* = 9.6 Hz, 1H§), 3.05 (d, *J* = 9.3 Hz, 1H*), 2.35 (ddd, *J* = 14.8, 5.9, 0.6 Hz, 1H§), 2.23 (dd, *J* = 14.6, 4.9 Hz, 1H*), 2.18 (dd, *J* = 14.9, 4.6 Hz, 1H§), 2.13 (dd, *J* = 14.7, 7.8 Hz, 1H*), 1.41 (s, 3H§), 1.38 (s, 3H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2*, 170.1§, 156.6* (q, $J_{C\text{-}F}$ = 37.6 Hz), 150.8*, 135.4*, 133.3*, 132.4§, 128.6§, 128.4*, 123.3§, 122.5*, 119.4§, 118.9§, 118.7*, 118.1*, 115.5* (q, $J_{C\text{-}F}$ = 287.9 Hz), 109.9§, 108.4*, 65.2§, 65.1*, 52.7*, 52.5§, 52.1§, 51.8*, 50.9*, 50.5§, 42.7§, 42.6*, 42.5§, 42.1*, 27.8§, 26.1*; IR (NaCl/thin film): 3316, 2957, 2923, 1750, 1718, 1605, 1554, 1487, 1460, 1437, 1209, 1165, 744 cm^{-1}; $[\alpha]_D^{25}$ = +33.412 (*c* = 1.62, CH_2Cl_2). HRMS (MM) calc'd for $[M+H]^+$ 371.1577, found 371.1582.

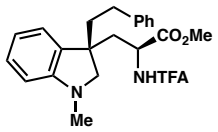
Indoline 165i.



Prepared from 3-butyl-1-methyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure. The diastereomeric ratio was determined to be >20:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (5→20% ethyl acetate/hexanes) to yield 63.4 mg (82% yield) of **XX**, a pale yellow oil. The enantiomeric excess of the major diastereomer was determined to be 92% by chiral SFC analysis (AD-

H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R(major) = 7.2 min t_R(minor) = 5.3 min. The major diastereomer was separated by flash chromatography (5% ethyl acetate/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (br d, $J_{C\text{-}H}$ = 5.5 Hz, 1H), 7.13 (td, $J_{C\text{-}H}$ = 7.7, 1.2 Hz, 1H), 6.96 (dd, $J_{C\text{-}H}$ = 7.3, 0.7 Hz, 1H), 6.75 (t, $J_{C\text{-}H}$ = 7.3 Hz, 1H), 6.53 (d, $J_{C\text{-}H}$ = 7.8 Hz, 1H), 4.22-4.15 (m, 1H), 3.64 (s, 3H), 3.24 (d, $J_{C\text{-}H}$ = 9.3 Hz, 1H), 3.08 (d, $J_{C\text{-}H}$ = 9.3 Hz, 1H), 2.74 (s, 3H), 2.23 (dd, $J_{C\text{-}H}$ = 14.7, 8.4 Hz, 1H), 2.17 (dd, $J_{C\text{-}H}$ = 14.7, 4.7 Hz, 1H), 1.86-1.77 (m, 1H), 1.69-1.57 (m, 1H), 1.40-1.24 (m, 3H), 1.19-1.08 (m, 1H), 0.89 (t, $J_{C\text{-}H}$ = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 156.6 (q, $J_{C\text{-}F}$ = 37.5 Hz), 152.3, 134.3, 128.6, 123.0, 119.0, 115.5 (q, $J_{C\text{-}F}$ = 287.8 Hz), 108.4, 66.4, 52.7, 51.2, 46.2, 40.6, 39.3, 35.9, 26.5, 23.2, 14.0; IR (NaCl/thin film): 3319, 2956, 2932, 2860, 2809, 1751, 1718, 1606, 1559, 1491, 1465, 1207, 1178, 743 cm^{-1}; $[\alpha]_D^{25}$ = +62.0 (*c* = 1.15, CH_2Cl_2). HRMS (ESI) calc'd for $[M+H]^+$ 387.1890, found 387.1902.

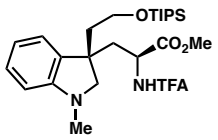
Indoline 165j.



Prepared from 1-methyl-3-phenethyl-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure, except the formal (3 + 2) cycloaddition was allowed to run for 24 h before adding $NaBH_4$. After adding $NaBH_4$, the reaction was allowed to run for another 24 h. The diastereomeric ratio was determined to be 12:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (5→20% ethyl acetate/hexanes) to yield 77.6 mg (89% yield) of **XX**. The enantiomeric excess of the major diastereomer was determined to be 89% by chiral SFC analysis (AD-H, 2.5 mL/min, 7% IPA in CO_2, λ = 254 nm): t_R(major) = 9.5 min t_R(minor) = 8.1 min. The major diastereomer was separated by flash chromatography (10% ethyl acetate/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ

7.30-7.22 (m, 3H), 7.21-7.11 (m, 4H), 6.99 (dd, $J_{C\text{-}H}$ = 7.4, 1.0 Hz, 1H), 6.75 (td, $J_{C\text{-}H}$ = 7.4, 0.7 Hz, 1H), 6.55 (d, $J_{C\text{-}H}$ = 7.9 Hz, 1H), 4.27 (dt, $J_{C\text{-}H}$ = 12.6, 6.4 Hz, 1H), 3.63 (s, 3H), 3.30 (d, $J_{C\text{-}H}$ = 9.3 Hz, 1H), 3.17 (d, $J_{C\text{-}H}$ = 9.3 Hz, 1H), 2.76 (s, 3H), 2.68 (td, $J_{C\text{-}H}$ = 13.0, 5.0 Hz, 1H), 2.47 (td, $J_{C\text{-}H}$ = 12.9, 4.7 Hz, 1H), 2.34-2.22 (m, 2H), 2.13 (ddd, $J_{C\text{-}H}$ = 13.7, 12.3, 5.1 Hz, 1H), 1.97 (ddd, $J_{C\text{-}H}$ = 13.8, 12.6, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 156.6 (q, $J_{C\text{-}F}$ = 37.5 Hz), 152.4, 141.7, 133.5, 128.7, 128.5, 128.2, 126.0, 122.9, 119.0, 115.5 (q, $J_{C\text{-}F}$ = 287.8 Hz), 108.4, 66.0, 52.7, 51.1, 46.3, 41.5, 40.7, 35.8, 30.8; IR (NaCl/thin film): 3317, 2951, 2858, 2812, 1749, 1716, 1606, 1555, 1494, 1453, 1208, 1178, 745 cm^{-1}; $[\alpha]_D^{26}$ = +23.1 (*c* = 0.87, CH_2Cl_2). HRMS (MM) calc'd for $[M+H]^+$ 435.1890, found 435.1882.

Indoline 165k.

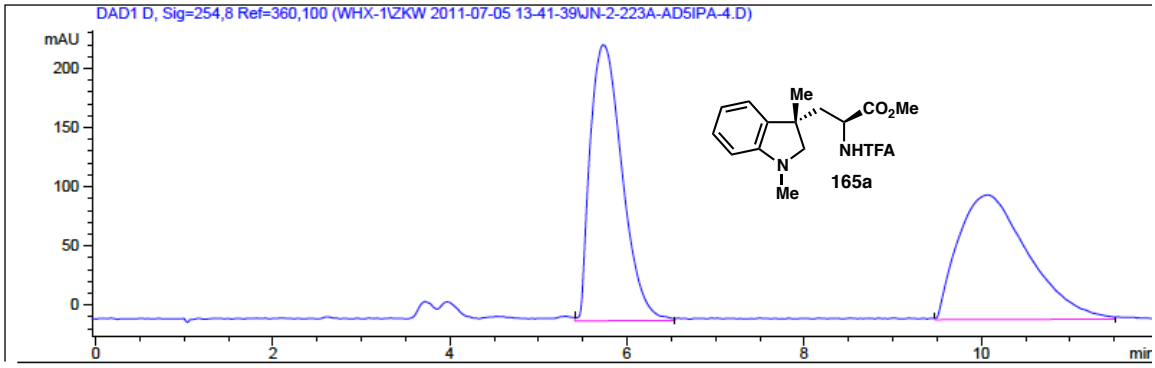


Prepared from 1-methyl-3-(2-((triisopropylsilyl)oxy)ethyl)-1*H*-indole and methyl 2-trifluoroacetamidoacrylate using the general procedure, except the formal (3 + 2) cycloaddition was allowed to run for 20.5 h before adding $NaBH_4$. After adding $NaBH_4$, the reaction was allowed to run for another 24 h. The diastereomeric ratio was determined to be >20:1 by ^{1}H NMR analysis of the crude reaction mixture. The crude residue was purified by flash chromatography (5→30% ethyl acetate/hexanes) to yield 68.3 mg (64% yield) of **XX**, a yellow oil. The enantiomeric excess of the major diastereomer was determined to be 85% by chiral SFC analysis (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R(major) = 8.7 min t_R(minor) = 7.5 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (br s, 1H), 7.15 (t, $J_{C\text{-}H}$ = 7.6 Hz, 1H), 7.00 (d, $J_{C\text{-}H}$ = 7.2 Hz, 1H), 6.75 (t, $J_{C\text{-}H}$ = 7.1 Hz, 1H), 6.54 (d, $J_{C\text{-}H}$ = 7.3 Hz, 1H), 4.22-4.15 (m, 1H), 3.81 (dd, $J_{C\text{-}H}$ = 6.96, 5.35 Hz, 2H), 3.64 (s, 3H), 3.34-3.26 (m, 1H), 3.26-3.18 (m, 1H), 2.74

(s, 3H), 2.46-2.36 (m, 1H), 2.24 (dd, $J_{C\text{-}H}$ = 14.7, 3.7 Hz, 1H), 2.11-1.94 (m, 2H), 1.08-1.03 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 156.7 (q, $J_{C\text{-}F}$ = 37.6 Hz), 152.1, 134.3, 128.7, 123.0, 118.9, 115.6 (q, $J_{C\text{-}F}$ = 287.8 Hz), 108.5, 67.6, 60.0, 52.6, 51.2, 45.3, 41.2, 39.5, 18.0, 18.0, 11.9; IR (NaCl/thin film): 3323, 2943, 2866, 1719, 1606, 1552, 1491, 1463, 1207, 1175, 1104, 882, 742 cm^{-1}; $[\alpha]_D^{25}$ = +27.4 (*c* = 0.85, CH_2Cl_2). HRMS (APCI) calc'd for $[M+H]^+$ 531.2860, found 531.2883.

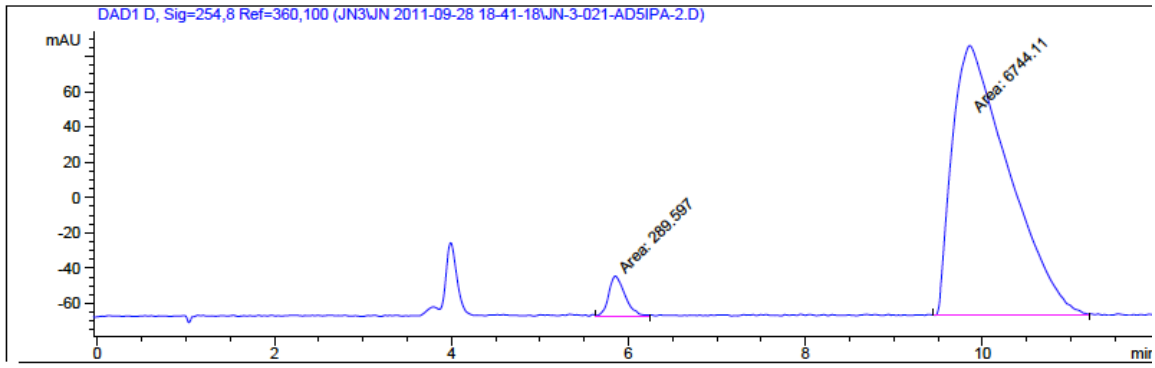
3.4.4 SFC Traces for Racemic and Enantioenriched Products

165a (Figure 9): racemic



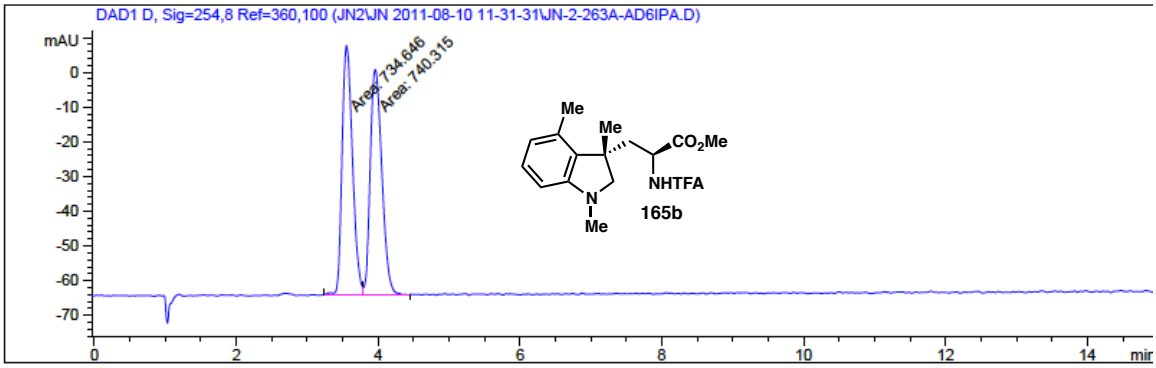
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.733	VV	0.4124	5847.14258	233.31508	50.2291
2	10.073	VV	0.7324	5793.80518	105.22972	49.7709

165a (Figure 9): 92% ee



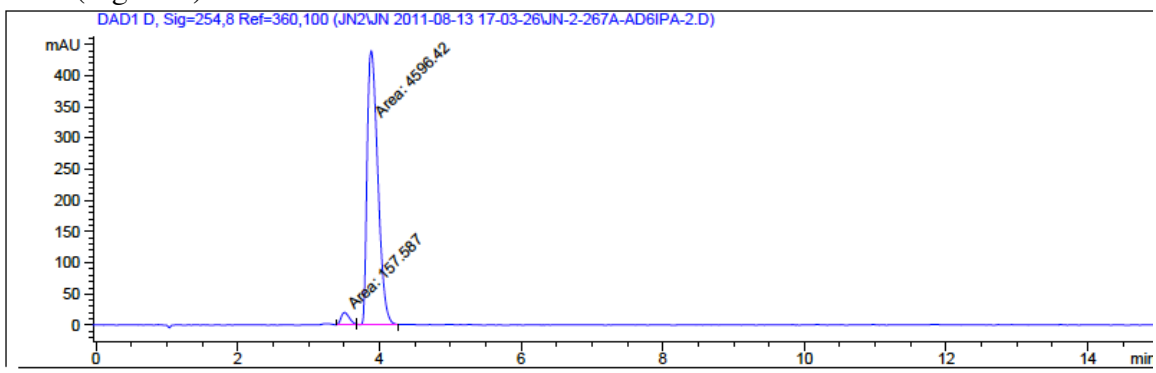
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.852	MM	0.2132	289.59744	22.63515	4.1173
2	9.857	MM	0.7372	6744.11035	152.46228	95.8827

165b (Figure 9): racemic



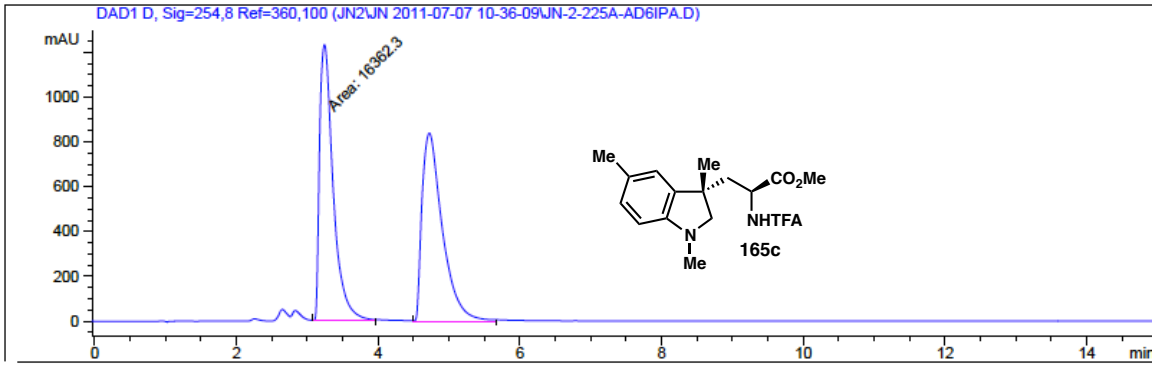
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.555	MM	0.1704	734.64594	71.86649	49.8078
2	3.960	MM	0.1899	740.31531	64.97649	50.1922

165b (Figure 9): 93% ee



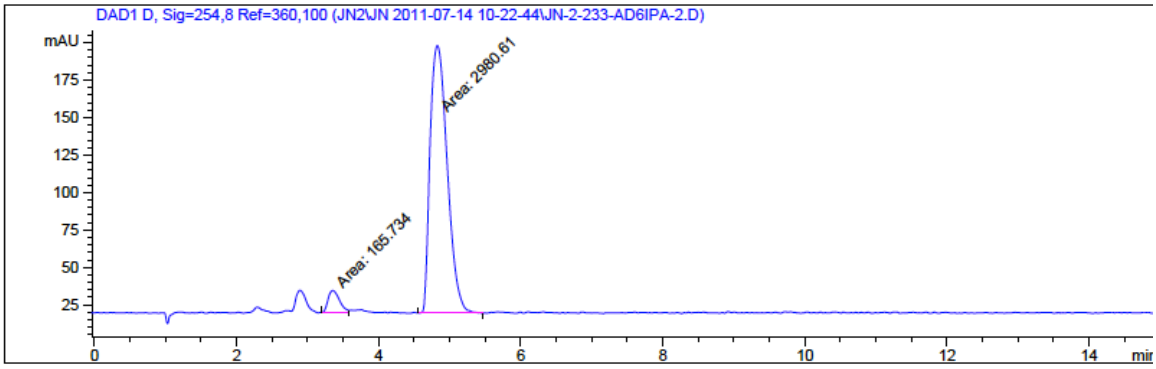
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.510	MM	0.1343	157.58659	19.55832	3.3148
2	3.886	MM	0.1745	4596.41699	439.04443	96.6852

165c (Figure 9): racemic



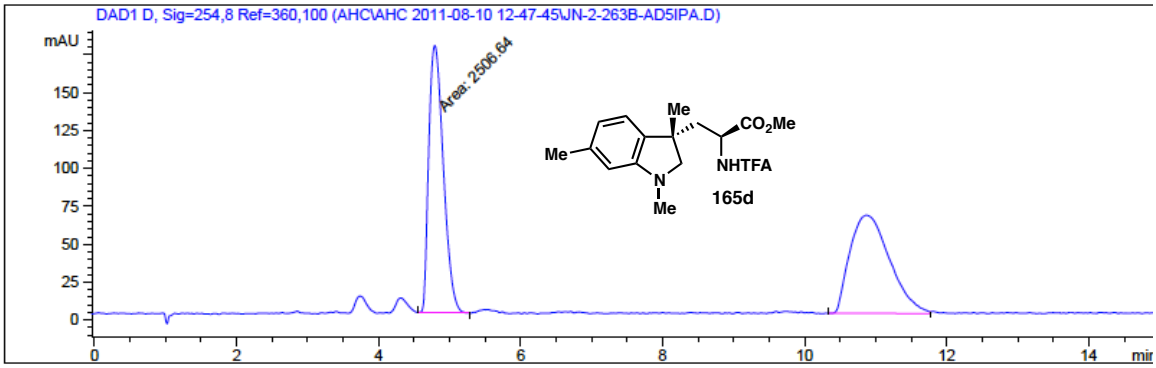
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.242	MM	0.2216	1.63623e4	1230.56165	49.1373
2	4.723	VV	0.3066	1.69368e4	842.43842	50.8627

165c (Figure 9): 89% ee



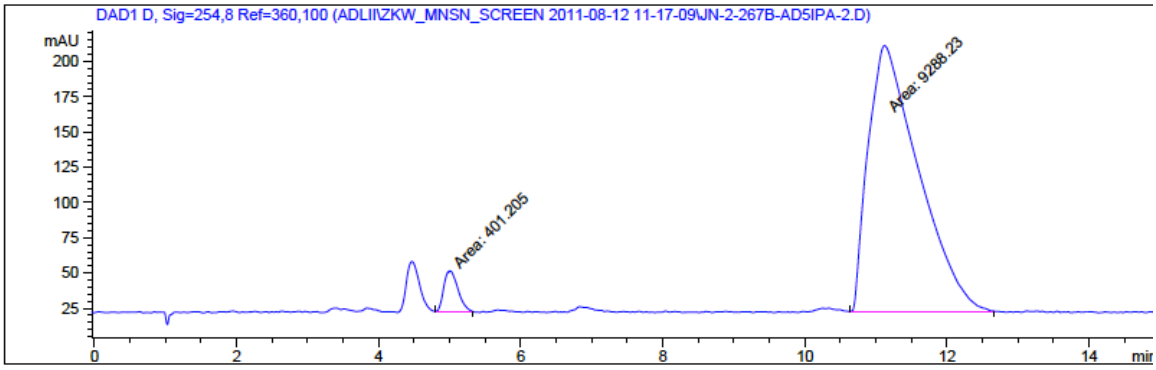
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.356	MM	0.1880	165.73442	14.69443	5.2675
2	4.826	MM	0.2787	2980.60571	178.23856	94.7325

165d (Figure 9): racemic



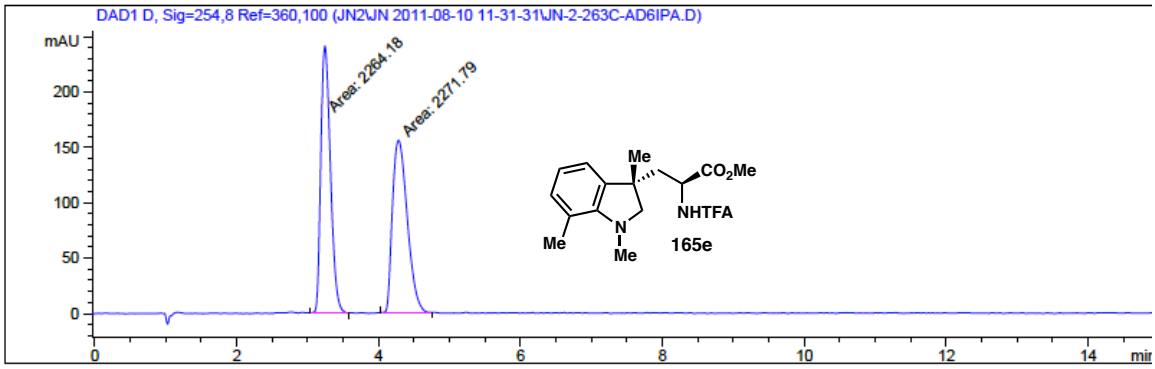
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.791	MM	0.2372	2506.63574	176.10995	49.9313
2	10.862	BV	0.5828	2513.53687	64.75647	50.0687

165c (Figure 9): 92% ee



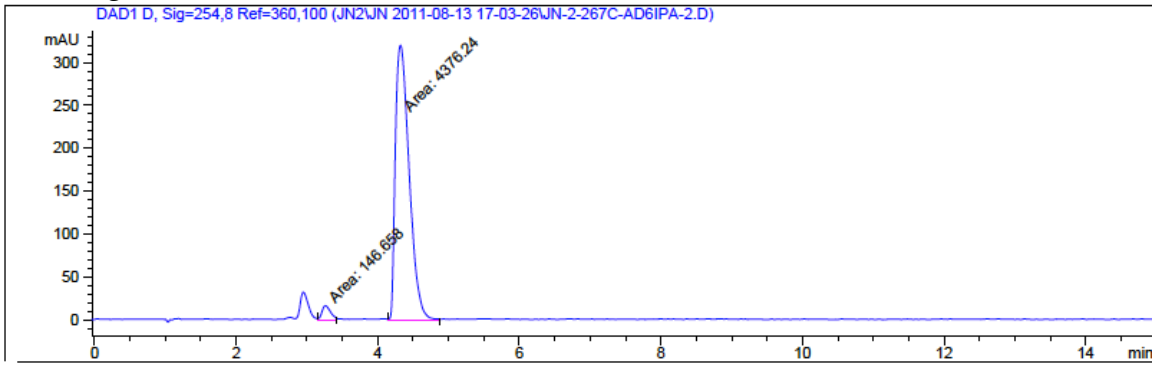
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.005	MM	0.2320	401.20471	28.82077	4.1406
2	11.122	MM	0.8212	9288.23340	188.50002	95.8594

165e (Figure 9): racemic



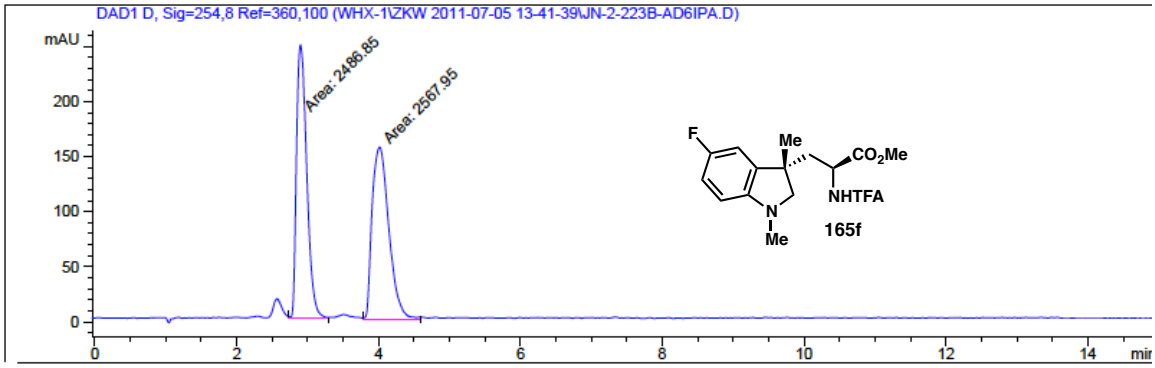
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.241	MM	0.1566	2264.17603	241.04764	49.9161
2	4.280	MM	0.2428	2271.78613	155.94717	50.0839

165e (Figure 9): 94% ee



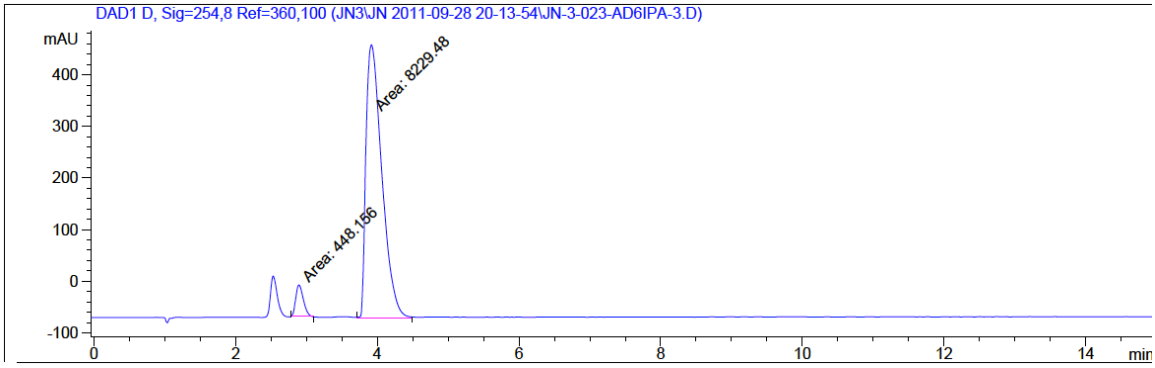
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.261	MM	0.1428	146.65776	17.12008	3.2426
2	4.322	MM	0.2272	4376.23779	321.00308	96.7574

165f (Figure 9): racemic



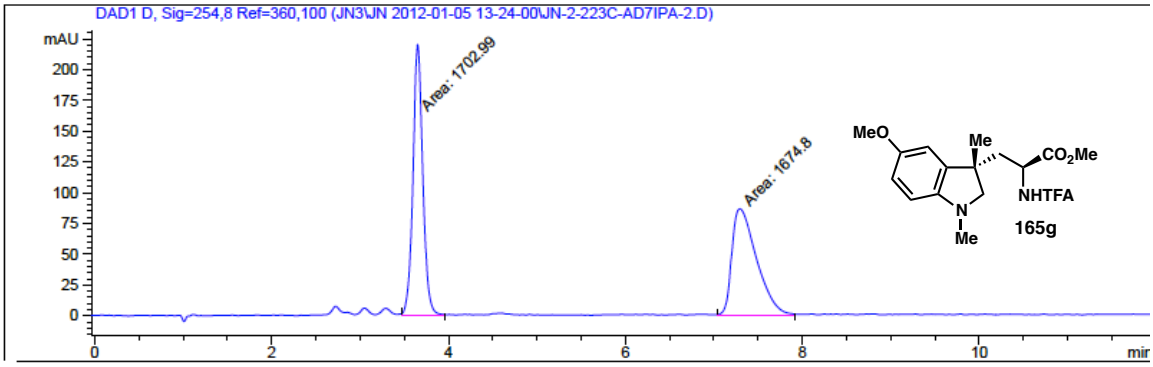
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.900	MM	0.1670	2486.84692	248.18283	49.1978
2	4.015	MM	0.2735	2567.94849	156.45912	50.8022

165f (Figure 9): 90% ee



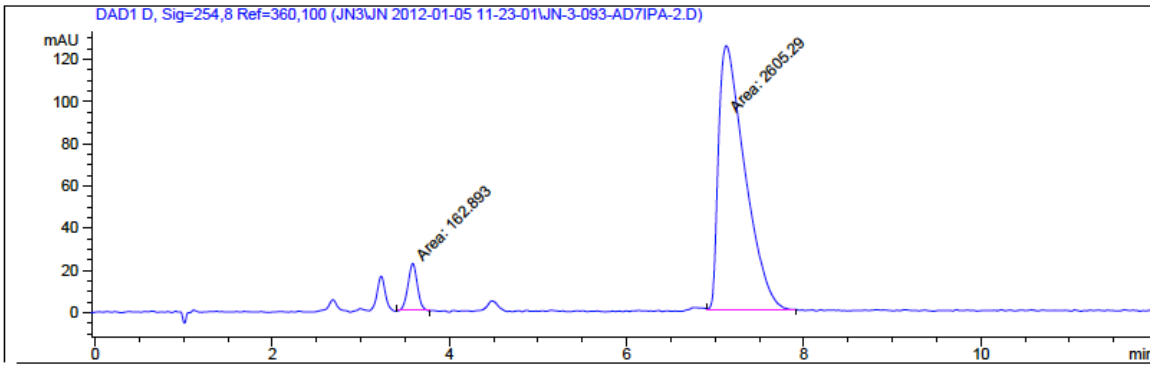
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.894	MM	0.1228	448.15573	60.80370	5.1645
2	3.917	MM	0.2592	8229.47559	529.13312	94.8355

165g (Figure 9): racemic



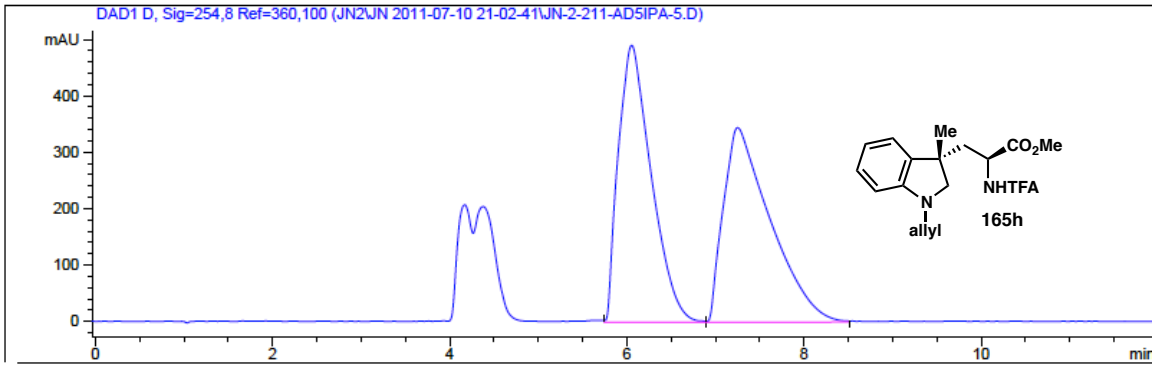
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.651	MM	0.1289	1702.99353	220.23915	50.4173
2	7.294	MM	0.3230	1674.80334	86.42379	49.5827

165g (Figure 9): 88% ee



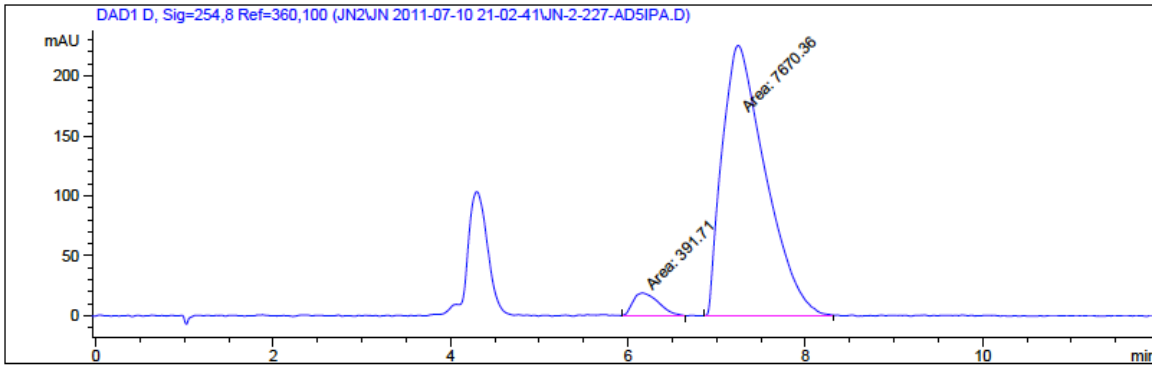
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.585	MM	0.1218	162.89281	22.29179	5.8845
2	7.127	MM	0.3462	2605.29150	125.42136	94.1155

165h (Figure 9): racemic



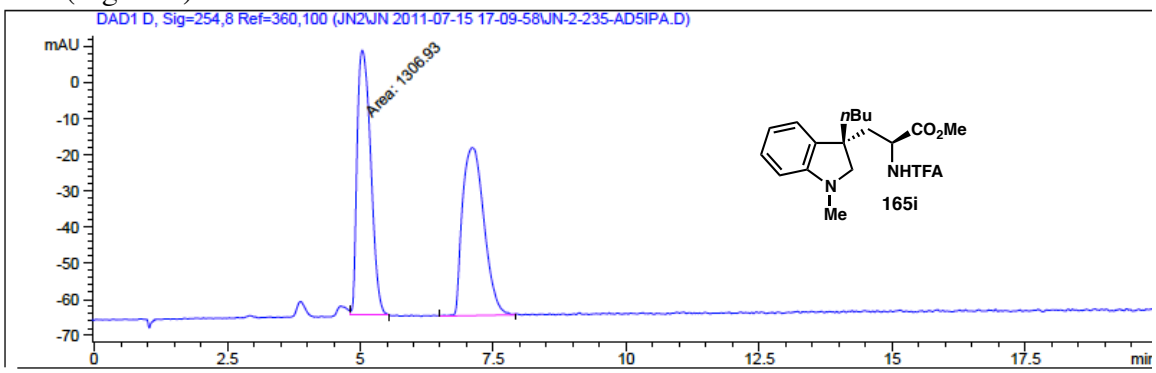
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.054	VV	0.3527	1.26647e4	491.32587	49.9094
2	7.251	VV	0.4860	1.27107e4	344.87524	50.0906

165h (Figure 9): 90% ee



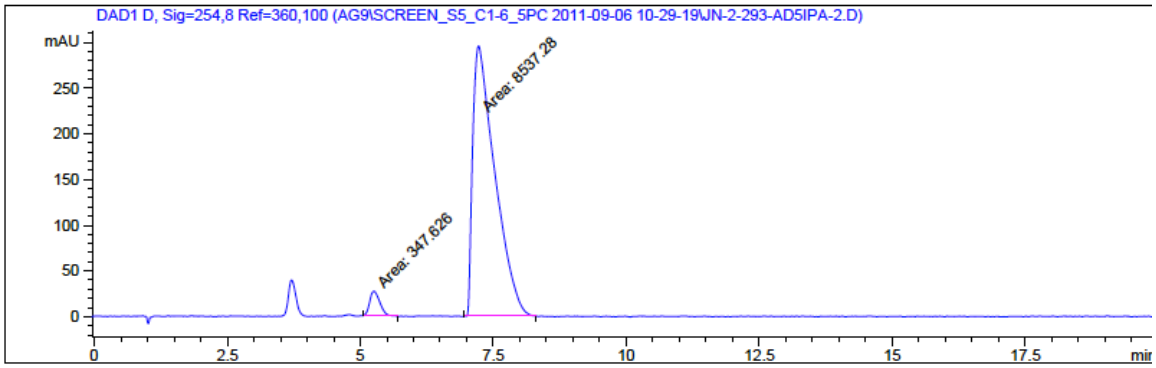
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.163	MM	0.3375	391.71039	19.34439	4.8587
2	7.244	MM	0.5670	7670.36182	225.47943	95.1413

165i (Figure 9): racemic



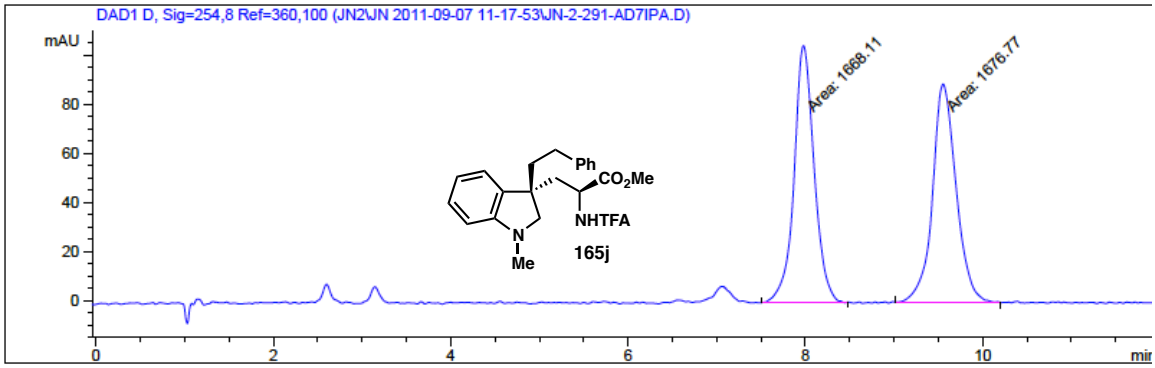
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.038	MM	0.2964	1306.92871	73.49715	49.8219
2	7.100	BB	0.4502	1316.27185	46.51159	50.1781

165i (Figure 9): 92% ee



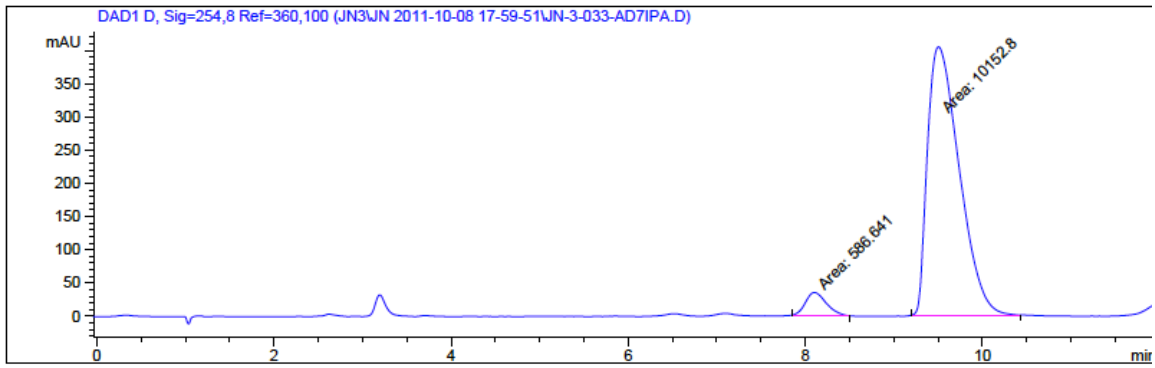
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.257	MM	0.2145	347.62573	27.00829	3.9125
2	7.226	MM	0.4818	8537.27539	295.33777	96.0875

165j (Figure 9): racemic



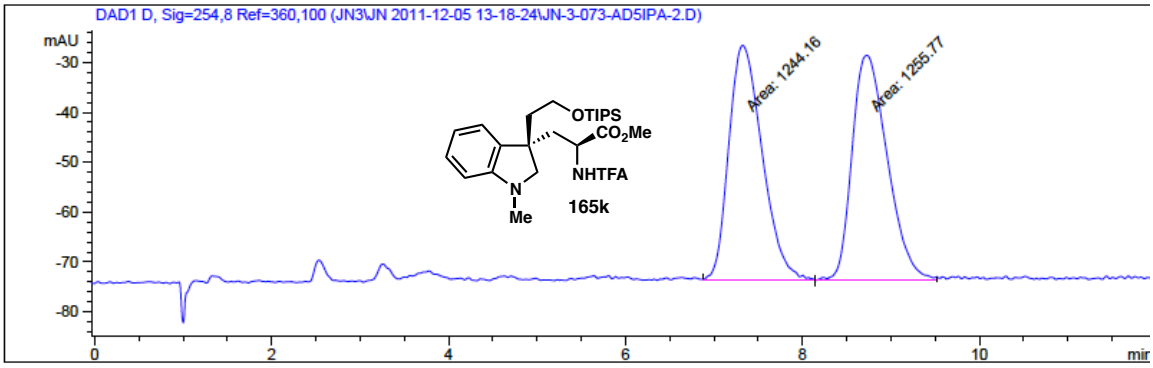
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.978	MM	0.2644	1668.11194	105.15713	49.8706
2	9.552	MM	0.3123	1676.76514	89.49041	50.1294

165j (Figure 9): 89% ee



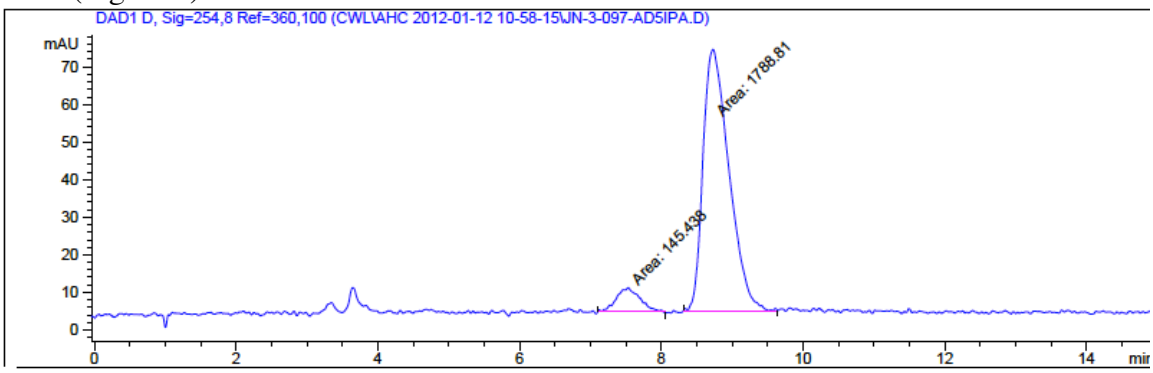
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.105	MM	0.2771	586.64099	35.28017	5.4625
2	9.505	MM	0.4177	1.01528e4	405.11353	94.5375

165k (Figure 9): racemic



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.326	MM	0.4403	1244.16138	47.09854	49.7677
2	8.731	MM	0.4640	1255.77466	45.10927	50.2323

165k (Figure 9): 85% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.535	MM	0.3798	145.43784	6.38237	7.5191
2	8.729	MM	0.4271	1788.81250	69.80029	92.4809

3.5 Notes and References

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