JOC The Journal of Organic Chemistry

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Organocatalytic Asymmetric Michael Addition of Oxindoles to Nitroolefins for the Synthesis of 2,2-Disubstituted Oxindoles Bearing Adjacent Quaternary and Tertiary Stereocenters

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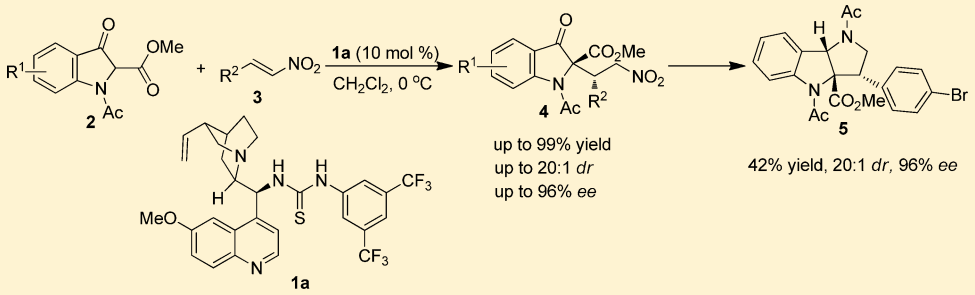
Supporting Information



ABSTRACT: A bifunctional thiourea-catalyzed Michael addition of activated indolin-3-ones to nitroolefins has been developed. The synthetically useful 2,2-disubstituted indolin-3-one derivatives with vicinal chiral quaternary−tertiary stereocenters were obtained in high yields with excellent stereoselectivities. The adduct can be readily transformed into a structurally interesting heterocyclic architecture by means of further synthetic elaboration.

Indolin-3-ones with a quaternary stereocenter at the 2-position are commonly found in a wide range of biologically active natural alkaloids such as brevianamide A,[1] austamide,[2] and fluorocurine[3] (Figure 1). Thus, the development of

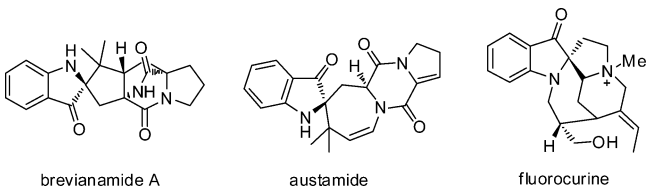


Figure 1. Biologically active molecules containing indolin-3-ones with a quaternary stereocenter at the 2-position.

efficient methods for the construction of functionalized indolin-3-one building blocks with structural complexity and skeleton diversity would provide new opportunities for the synthesis of new kinds of biologically active molecules. Despite the fruitful achievements toward the enantioselective construction of quaternary carbon-incorporated indolin-2-ones,[4] the catalytic asymmetric synthesis of indolin-3-ones with a quaternary center at the 2-position had been rarely explored, and it remained a challenging task.[5]

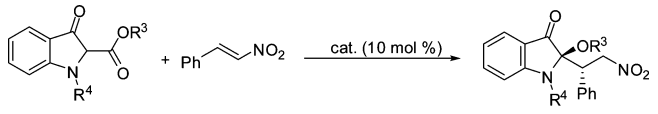
The Michael addition reaction is one of the most fundamental, yet important, methods for carbon−carbon bond formation in modern organic synthesis. Over the past decade, various organocatalytic asymmetric Michael addition reactions have been developed by employing new catalysts and activation modes via efficient combination of diverse nucleophiles and electrophiles.[6,7] Although the organocatalytic Michael addition of highly reactive trisubstituted carbon nucleophiles to nitroalkenes to generate quaternary carbons are well-documented,[8] to our knowledge, the organocatalytic strategy exploiting 2-substituted indolin-3-ones as pronucleophiles to construct a quaternary carbon at the 2-position in a highly stereocontrolled manner has not been reported. With our ongoing interest in the study of indolin-3-one chemistry,[9] we report here an efficient method for the synthesis of 2,2-disubstituted oxindoles bearing adjacent quaternary and tertiary stereocenters via a bifunctional thiourea-catalyzed the Michael addition reaction of methyl 1-acetyl-3-oxoindoline-2-carboxylate[10] to nitroalkenes.

Initially, the Michael addition reaction of methyl 1-acetyl-3-oxoindoline-2-carboxylate **2** with *β*-nitrostyrene **3a** in the presence of catalyst **1a** (10 mol %) in toluene was investigated.[11] To our delight, the Michael addition reaction proceeded smoothly to afford the desired product **4a** in excellent yield and stereoselectivity (91% yield, 94% ee, 20:1 dr) after 30 h (Table 1, entry 1). Various promising bifunctional base/Brønsted acid catalysts were tested (Table 1, entries 2−6), and it was found that the cinchonine- and quinidine-derived bifunctional thiourea **1b**, **1f**, Takemoto catalyst **1d**, and amino acid-derived catalyst **1c** could also

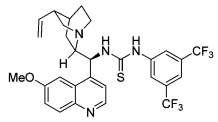
Received: August 31, 2012
Published: November 20, 2012

   dx.doi.org/10.1021/jo301886j | J. Org. Chem. 2012, 77, 11307−11312

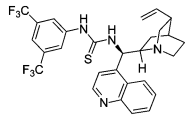
Table 1. Screening of the Reaction Conditions[a]



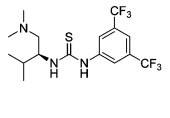
2 3a 4



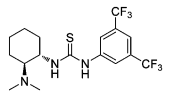
1a



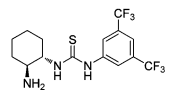
1b



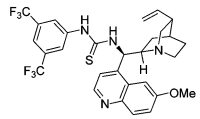
1c



1d



1e



1f

entry	cat.	solvent	R^3	R^4	T (°C)	time (h)	yield (%)	dr[b]	ee (%)[c]
1	**1a**	toluene	Me	Ac	0	30	91	20:1	94
2	**1b**	toluene	Me	Ac	0	30	91	20:1	−92
3	**1c**	toluene	Me	Ac	0	30	93	20:1	92
4	**1d**	toluene	Me	Ac	0	30	92	20:1	−91
5	**1e**	toluene	Me	Ac	0	30	90	20:1	55
6	**1f**	toluene	Me	Ac	0	30	92	20:1	−93
7	**1a**	CH_2Cl_2	Me	Ac	0	24	90	20:1	95
8	**1a**	THF	Me	Ac	0	72	<30	20:1	79
9	**1a**	$CHCl_3$	Me	Ac	0	24	90	20:1	94
10	**1a**	CH_3OH	Me	Ac	0	42	84	20:1	11
11	**1a**	CH_2Cl_2	Me	Ac	−10	42	91	20:1	94
12	**1a**	CH_2Cl_2	Me	Boc	0	42	87	20:1	95
13	**1a**	CH_2Cl_2	*i*-Pr	Ac	0	42	91	20:1	91

[a]Unless otherwise noted, the reactions were carried out with **2** (0.1 mmol), **3a** (0.2 mmol), and catalyst **1** (0.01 mmol) in solvent (1.0 mL) at 0 °C. [b]Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c]Determined by HPLC on a chiral stationary phase.

give good results albeit with slightly lower enantioselectivities in contrast to catalyst **1a**. However, primary aminothiourea catalyst **1e** gave a significantly decreased enantioinduction. Subsequently, the solvent effect was investigated, and CH_2Cl_2 was identified as the solvent of choice in comparison with the protonic and polar solvents (Table 1, entries 7−10). When the reaction temperature was dropped to −10 °C, no obviously beneficial effect on the stereoselctivity and yield was observed (Table 1, entry 11). Further optimization with modified substrates also revealed that bulkyl isopropyl ester and *N*-Boc-protected nucleophile were also suitable reaction partners.

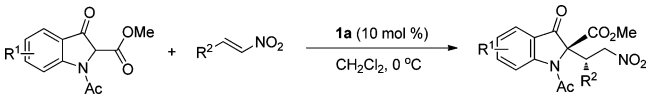
With the reaction conditions optimized, we next examined the substrate scope of the reaction (Table 2). The results showed that a wide range of nitroalkenes could be used in this reaction. Aromatic groups bearing electron-withdrawing or -donating groups were well tolerated as well as aromatic rings substituted in the *para*, *meta* and *ortho* positions. A heteroaromatic group, such as furan, could also be successfully employed to afford the desired product. Notably, despite the structural difference of nitroalkenes, the Michael adducts were obtained with excellent yields, dr values, and ee values in most cases. However, the steric hindrance of the *o*-methoxy-substituted aromatic ring of nitroolefin resulted in lower diastereoselectivity compared with other substituted aromatic substrates (8:1 dr, Table 2, entry 10). Alkyl substrates, on the other hand, did not perform well in the reaction; *n*-butyl-substituted nitroolefin proceeded slowly under the optimized reaction conditions (Table 2, entry 17). However, with a modification to our optimal method by raising the reaction temperature to 20 °C, the Michael reaction proceeded well to give the product in 87% yield, 20:1 dr, albeit with 75% ee. Furthermore, indolin-2-ones with different substituents on the aryl ring were also tolerated and afforded the desired products with good results (Table 2, entries 18−20). The absolute and relative configuration of the product was determined based on single-crystal X-ray diffraction of **4e** (see the Supporting Information).[12]

As a further example illustrative of the power of this reaction, the product **4e** was readily converted to a structurally diverse heterocyclic architecture. When **4e** was reduced with Zn/HCl in EtOH followed by treatment with AcCl/Et_3N in CH_2Cl_2, the desired substituted hexahydropyrrolo[3,2-*b*]indole **5** was obtained in moderate yields and high enantioselectivity (Scheme 1). The structure and configuration of **5** was determined by X-ray diffraction (see the Supporting Information).[12]

Based on the observed reactivity and experimental results of these Michael addition reactions, we propose that the reaction proceeds via a double activation model.[13] As shown in Figure 2, the thiourea moiety of the catalyst **1a** interacts via hydrogen bonding with the nitro group of the nitroalkene and enhances its electrophilicity while the tertiary amine deprotonates an acidic proton of the methyl 1-acetyl-3-oxoindoline-2-carboxylate, generating a ternary complex. The proposed activation model explains the stereochemical outcome of these Michael reactions and why *Si*-face attack at the nitroolefin is favored.

dx.doi.org/10.1021/jo301886j | J. Org. Chem. 2012, 77, 11307−11312

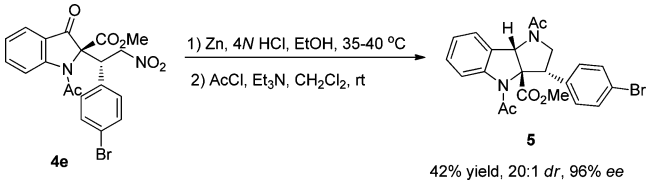
Table 2. Investigating the Scope of the Reaction[a]



entry	R^1	R^2	time (h)	yield (%)	dr[b]	ee[c] (%)
1	H	Ph	24	90 (**4a**)	>20:1	95
2	H	3-ClC_6H_4	24	99 (**4b**)	>20:1	94
3	H	4-ClC_6H_4	24	98 (**4c**)	>20:1	94
4	H	3-BrC_6H_4	24	94 (**4d**)	>20:1	95
5	H	4-BrC_6H_4	24	92 (**4e**)	>20:1	94
6	H	4-FC_6H_4	24	95 (**4f**)	>20:1	95
7	H	3-$NO_2C_6H_4$	24	95 (**4g**)	>20:1	94
8	H	4-$NO_2C_6H_4$	24	93 (**4h**)	>20:1	92
9	H	4-$CF_3C_6H_4$	24	90 (**4i**)	>20:1	94
10	H	2-$MeOC_6H_4$	72	90 (**4j**)	8:1	96
11	H	3-$MeOC_6H_4$	72	98 (**4k**)	>20:1	87
12	H	3,4-$(OCH_2O)C_6H_3$	24	95 (**4l**)	>20:1	93
13	H	4-MeC_6H_4	24	97 (**4m**)	>20:1	96
14	H	3,4-$(CH_3)_2C_6H_3$	36	93 (**4n**)	>20:1	92
15	H	2-naphthyl	24	95 (**4o**)	>20:1	93
16	H	2-furyl	24	93 (**4p**)	>20:1	90
17[d]	H	*n*-Bu	48	87 (**4q**)	>20:1	75
18	5-Br	Ph	48	94 (**4r**)	>20:1	90
19	6-Cl	Ph	48	95 (**4s**)	16:1	91
20	7-Me	Ph	48	88 (**4t**)	12:1	91

[a]Unless otherwise noted, the reactions were carried out with **2** (0.1 mmol), **3** (0.2 mmol), and catalyst **1a** (0.01 mmol) in 1.0 mL of CH_2Cl_2 at 0 °C. [b]Determined by ^1H NMR spectroscopic analysis of the crude reaction mixture. [c]Determined by HPLC on a chiral stationary phase. [d]The reaction was performed at 20 °C.

Scheme 1. Synthetic Transformation



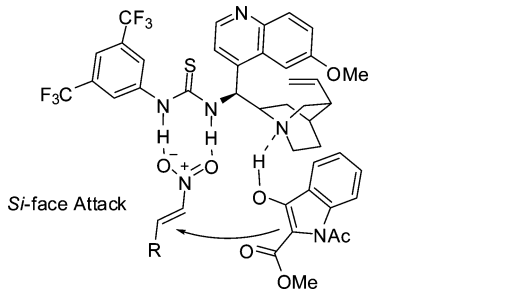


Figure 2. Proposed transition-state model in the Michael addition.

In conclusion, we have developed a bifunctional base/Brønsted acid-catalyzed asymmetric Michael addition reaction of methyl 1-acetyl-3-oxoindoline-2-carboxylate to nitroolefins affording indolin-3-ones with vicinal quaternary and tertiary stereocenters in excellent yields with high diastereo- and enantioselectivities. The corresponding product could be readily converted to a structurally interesting heterocyclic architecture without loss of enantioselectivities.

EXPERIMENTAL SECTION

Typical Procedure for Michael Addition of Methyl 1-Acetyl-3-oxoindoline-2-carboxylate to Nitroolefins (Table 2). To a solution of *β*-nitrostyrene **3a** (30.0 mg, 0.2 mmol) and catalyst **1a** (6.0 mg, 0.01 mmol) in dry CH_2Cl_2 (1.0 mL) was added methyl 1-acetyl-3-oxoindoline-2-carboxylate **2** (24.0 mg, 0.1 mmol) at 0 °C. The reaction mixture was stirred at 0 °C until **2** was consumed as monitored by TLC. Then the reaction mixture was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel using petroleum ether/EtOAc as eluting reagent to afford the desired product **4a** 34.4 mg, in 90% yield. Unless otherwise specified, all products were synthesized according to the typical procedure.

*(S)-Methyl 1-acetyl-2-((S)-2-nitro-1-phenylethyl)-3-oxoindoline-2-carboxylate (**4a**):* 34.4 mg (90% yield); white solid; mp 146−148 °C; $[\alpha]_D^{20}$ = −222 (*c* 1.00, $CHCl_3$, 95% ee); IR (KBr) 3418, 1751, 1710, 1672, 1610, 1552, 1474, 1374, 1321, 1256, 1200, 997, 754, 698, 673, 596 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.77 (d, *J* = 7.2 Hz, 1H), 7.52−7.48 (m, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.07−6.98 (m, 4H), 6.89 (d, *J* = 6.8 Hz, 2H), 5.95−5.85 (m, 1H), 5.11−5.01 (m, 2H), 3.73 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 193.1, 167.6, 166.0, 151.9, 137.8, 134.1, 128.4, 128.1, 127.8, 125.1, 124.6, 124.1, 114.3, 75.7, 75.1, 53.5, 45.4, 25.4; HRMS (ESI) *m*/*z* calcd for $[C_{20}H_{22}N_3O_6]^+$ $[M + NH_4]^+$ 400.1503, found 400.1490. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 8.2 min, minor enantiomer t_R = 10.9 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(3-chlorophenyl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4b**):* 41.2 mg (99% yield); white solid; mp 120−122 °C; $[\alpha]_D^{20}$ = −199 (*c* 1.00, $CHCl_3$, 94% ee); IR (KBr) 3411, 2955, 1754, 1713, 1665, 1608, 1553, 1472, 1376, 1344, 1246, 1202, 1082, 999, 946, 790, 764, 700, 588, 514 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.78 (d, *J* = 7.6 Hz, 1H), 7.57−7.53 (m, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.06−7.04 (m, 2H), 6.96−6.92 (m, 2H), 6.80 (d, *J* = 7.6 Hz, 1H), 5.92−5.88 (m, 1H), 5.09−4.98 (m, 2H), 3.73 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 192.7, 167.7, 165.8, 151.8, 138.1, 136.2, 134.1, 129.4, 128.6, 125.2, 124.5, 124.4, 114.3, 75.3, 74.8, 53.6, 45.0, 25.4; HRMS (ESI) *m*/*z* calcd for $[C_{20}H_{21}ClN_3O_6]^+$ $[M + NH_4]^+$ 434.1113, found 434.1115. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 80:20), 1.0 mL/min; major enantiomer t_R = 12.6 min, minor enantiomer t_R = 16.1 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(4-chlorophenyl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4c**):* 40.8 mg (98% yield); white solid; mp 140−142 °C; $[\alpha]_D^{20}$ = −208 (*c* 1.00, $CHCl_3$, 94% ee); IR (KBr) 3404, 2952, 1752, 1712, 1668, 1609, 1555, 1473, 1377, 1286, 1245, 1086, 984, 838, 764, 628, 527 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.78 (d, *J* = 7.2 Hz, 1H), 7.58−7.54 (m, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.91−5.87 (dd, *J* = 2.8 Hz, 13.6 Hz, 1H), 5.11−4.96 (m, 2H), 3.72 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 192.8, 167.7, 165.8, 151.9, 138.1, 134.3, 132.8, 129.2, 128.4, 125.3, 124.4, 114.5, 75.6, 74.9, 53.6, 44.9, 25.5; HRMS (ESI) *m*/*z* calcd for $[C_{20}H_{21}ClN_3O_6]^+$ $[M + NH_4]^+$ 434.1113, found 434.1114. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 9.0 min, minor enantiomer t_R = 11.4 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(3-bromophenyl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4d**):* 43.2 mg (94% yield); white solid; mp 160−162 °C; $[\alpha]_D^{20}$ = −175 (*c* 1.00, $CHCl_3$, 95% ee); IR (KBr) 3401, 2954, 1750, 1712, 1664, 1607, 1558, 1473, 1432, 1375, 1249, 1089, 1057, 986, 939, 900, 765, 700, 631, 588, 510 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.79 (d, *J* = 7.6 Hz, 1H), 7.57−7.53 (m, 1H), 7.22−7.18 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.90 (t, *J* = 7.6 Hz, 2H), 5.90 (m, 1H), 5.07−4.97 (m, 2H), 3.73 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 192.7, 167.7, 165.8, 151.7, 138.1, 136.4, 131.5, 129.6, 125.3, 124.5, 124.4, 122.2, 114.3, 75.2, 74.8, 53.6,

dx.doi.org/10.1021/jo301886j | J. Org. Chem. 2012, 77, 11307−11312

44.9, 25.4; HRMS (ESI) m/z calcd for $[C_{20}H_{21}BrN_3O_6]^+$ $[M + NH_4]^+$: 478.0608, found 478.0607. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 90:10), 1.0 mL/min; major enantiomer t_R = 25.0 min, minor enantiomer t_R = 31.6 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(4-bromophenyl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4e**):* 42.3 mg (92% yield); white solid; mp 150−152 °C; $[\alpha]_D^{20}$ = −185 (*c* 1.00, $CHCl_3$, 94% ee); IR (KBr) 3408, 2950, 1752, 1712, 1667, 1609, 1554, 1473, 1376, 1285, 1244, 1073, 1006, 982, 835, 760, 628, 523, 417 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.78 (d, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.90−5.86 (dd, *J* = 2.8 Hz, 13.2 Hz, 1H), 5.09−4.96 (m, 2H), 3.73 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.8, 167.7, 165.8, 151.8, 138.2, 133.3, 131.4, 129.5, 125.3, 124.4, 122.5, 114.5, 75.6, 74.8, 53.6, 44.9, 25.5; HRMS (ESI) m/z calcd for $[C_{20}H_{21}BrN_3O_6]^+$ $[M + NH_4]^+$ 478.0608, found 478.0593. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 9.2 min, minor enantiomer t_R = 11.5 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(4-fluorophenyl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4f**):* 38.0 mg (95% yield); white solid; mp 130−132 °C; $[\alpha]_D^{20}$ = −126 (*c* 1.00, $CHCl_3$, 95% ee); IR (KBr) 3415, 2957, 2924, 1754, 1714, 1670, 1608, 1553, 1511, 1473, 1376, 1345, 1232, 1162, 1106, 995, 843, 756, 629, 598, 533, 421 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.78 (d, *J* = 7.6 Hz, 1H), 7.57−7.53 (m, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.89 (t, *J* = 6.4 Hz, 2H), 6.71 (t, *J* = 8.4 Hz, 2H), 5.91−5.87 (dd, *J* = 2.8 Hz, 13.6 Hz, 1H), 5.11−4.97 (m, 2H), 3.73 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.9, 167.7, 165.9, 162.4 (d, *J* = 246.2 Hz), 151.8, 138.1, 130.0, 129.5, 125.2, 124.4, 124.3, 115.2 (d, *J* = 21.8 Hz), 114.4, 75.7, 75.0, 53.6, 44.7, 25.5; HRMS (ESI) m/z calcd for $[C_{20}H_{21}FN_3O_6]^+$ $[M + NH_4]^+$: 418.1409, found 418.1410. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 9.1 min, minor enantiomer t_R = 12.4 min.

*(S)-Methyl 1-Acetyl-2-((S)-2-nitro-1-(3-nitrophenyl)ethyl)-3-oxoindoline-2-carboxylate (**4g**):* 40.6 mg (95% yield); white solid; mp 122−124 °C; $[\alpha]_D^{20}$ = −120 (*c* 1.00, $CHCl_3$, 94% ee); IR (KBr) 3420, 3046, 2956, 1754, 1667, 1608, 1554, 1534, 1472, 1435, 1377, 1348, 1248, 1089, 999, 945, 802, 763, 694, 632, 607, 519 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.94 (d, *J* = 7.6 Hz, 1H), 7.83−7.81 (m, 1H), 7.76 (s, 1H), 7.55−7.51 (m, 1H), 7.35−7.33 (d, *J* = 8.0 Hz, 1H), 7.29−7.27(m, 1H), 7.22−7.18 (m, 1H), 7.05−7.01 (m, 1H), 5.99−5.95 (dd, *J* = 3.2 Hz, 14.4 Hz, 1H), 5.25−5.22 (dd, *J* = 2.0 Hz, 11.6 Hz, 1H), 5.12−5.05 (m, 1H), 3.75 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.3, 167.9, 165.5, 151.6, 147.7, 138.3, 136.5, 134.1, 129.3, 125.5, 124.7, 124.3, 123.4, 122.5, 114.3, 75.0, 74.6, 53.7, 45.0, 25.3; HRMS (ESI) m/z calcd for $[C_{20}H_{21}N_4O_8]^+$ $[M + NH_4]^+$ 445.1354, found 445.1359. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 15.8 min, minor enantiomer t_R = 22.1 min.

*(S)-Methyl 1-Acetyl-2-((S)-2-nitro-1-(4-nitrophenyl)ethyl)-3-oxoindoline-2-carboxylate (**4h**):* 39.7 mg (93% yield); white solid; mp 160−162 °C; $[\alpha]_D^{20}$ = −129 (*c* 1.00, $CHCl_3$, 92% ee); IR (KBr) 3432, 2956, 2925, 1750, 1704, 1665, 1606, 1557, 1526, 1474, 1377, 1530, 1289, 1250, 1207, 1112, 1001, 982, 857, 759, 699, 629, 599 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.90 (d, *J* = 8.8 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.59−7.54 (m, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.13(t, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.98−5.94 (dd, *J* = 3.2 Hz, 14.4 Hz, 1H), 5.27 (t, *J* = 3.2 Hz, 1H), 5.09−5.03 (m, 1H), 3.74 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.3, 167.9, 165.5, 151.7, 147.7, 141.9, 138.5, 129.0, 125.5, 124.7, 124.2, 123.3, 114.4, 75.2, 74.6, 53.8, 45.2, 25.4; HRMS (ESI) m/z calcd for $[C_{20}H_{21}N_4O_8]^+$ $[M + NH_4]^+$ 445.1354, found 445.1365. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 50:50), 1.0 mL/min; major enantiomer t_R = 8.3 min, minor enantiomer t_R = 16.3 min.

*(S)-Methyl 1-Acetyl-2-((S)-2-nitro-1-(4-(trifluoromethyl)phenyl)-ethyl)-3-oxoindoline-2-carboxylate (**4i**):* 40.5 mg (90% yield); white solid; mp 50−52 °C; $[\alpha]_D^{20}$ = −55 (*c* 1.00, $CHCl_3$, 94% ee); IR (KBr) 3413, 2959, 2923, 1757, 1715, 1675, 1609, 1557, 1472, 1434, 1376, 1326, 1285, 1248, 1169, 1123, 1068, 993, 847, 759, 630, 527 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.79 (d, *J* = 7.6 Hz, 1H), 7.56−7.52 (m, 1H), 7.29 (d, *J* = 9.2 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.07−7.01 (m, 1H), 5.96−5.91 (dd, *J* = 3.2 Hz, 14 Hz, 1H), 5.19 (d, *J* = 10 Hz, 1H), 5.09−5.02 (m, 1H), 3.74 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.6, 167.8, 165.7, 151.7, 138.4, 138.2, 130.6 (q, *J* = 32.6 Hz), 128.4, 125.3, 125.1(q, *J* = 3.6 Hz), 124.5, 124.4, 123.7 (q, *J* = 272.5 Hz), 114.4, 75.3, 74.7, 53.7, 45.2, 25.4; HRMS (ESI) m/z calcd for $[C_{21}H_{21}F_3N_3O_6]^+$ $[M + NH_4]^+$: 468.1377, found 468.1382. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 7.7 min, minor enantiomer t_R = 10.4 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(2-methoxyphenyl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4j**):* 37.1 mg (90% yield); white solid; mp 170−172 °C; $[\alpha]_D^{20}$ = −120 (*c* 1.00, $CHCl_3$, 96% ee); IR (KBr) 3415, 2924, 2848, 1757, 1717, 1663, 1603, 1556, 1471, 1378, 1253, 1121, 1022, 987, 921, 763, 603, 549, 515, 424 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.82 (d, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.12−7.07 (m, 3H), 6.80 (t, *J* = 7.2 Hz, 1H), 6.44 (d, *J* = 8.0 Hz, 1H), 5.71 (d, *J* = 10.8 Hz, 1H), 5.21−5.12 (m, 2H), 3.72 (s, 3H), 3.07 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.9, 167.4, 167.0, 156.8, 150.4, 136.7, 133.6, 129.7, 125.1, 124.8, 123.6, 122.6, 120.5, 114.3, 109.7, 74.4, 74.3, 53.5, 53.2, 45.7, 25.1; HRMS (ESI) m/z calcd for $[C_{21}H_{24}N_3O_7]^+$ $[M + NH_4]^+$ 430.1609, found 430.1597. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 73:30), 1.0 mL/min; major enantiomer t_R = 8.8 min, minor enantiomer t_R = 11.3 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(3-methoxyphenyl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4k**):* 40.4 mg (98% yield); white solid; mp 154−156 °C; $[\alpha]_D^{20}$ = −171 (*c* 1.00, $CHCl_3$, 87% ee); IR (KBr) 3413, 2962, 1755, 1713, 1663, 1609, 1553, 1473, 1377, 1284, 1254, 1163, 1057, 997, 888, 762, 704, 642, 592, 517, 402 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.78 (d, *J* = 7.6 Hz, 1H), 7.55−7.51 (m, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.91 (t, *J* = 8.0 Hz, 1H), 6.61−6.59 (dd, *J* = 2 Hz, 8.0 Hz, 1H), 6.48 (d, *J* = 6.8 Hz, 1H), 6.41 (s, 1H), 5.93−5.83 (m, 1H), 5.05−4.99 (m, 2H), 3.72 (s, 3H), 3.53 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.1, 167.6, 166.0, 159.2, 152.0, 137.9, 135.5, 129.1, 125.1, 124.6, 124.1, 114.4, 75.8, 75.0, 55.0, 53.5, 45.5, 25.5; HRMS (ESI) m/z calcd for $[C_{21}H_{24}N_3O_7]^+$ $[M + NH_4]^+$ 430.1609, found 430.1606. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 9.0 min, minor enantiomer t_R = 11.0 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(benzo[d][1,3]dioxol-5-yl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4l**):* 40.5 mg (95% yield); white solid; mp 82−84 °C; $[\alpha]_D^{20}$ = −174 (*c* 1.00, $CHCl_3$, 93% ee); IR (KBr) 3412, 2960, 2901, 1758, 1714, 1675, 1608, 1555, 1472, 1377, 1239, 1039, 995, 934, 814, 752, 643, 591, 517, 421 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.78 (d, *J* = 7.6 Hz, 1H), 7.59−7.55 (m, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.50−6.38 (m, 3H), 5.87 (t, *J* = 11.2 Hz, 1H), 5.82−5.76 (m, 2H), 5.02−4.94 (m, 2H), 3.71 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.1, 167.7, 166.0, 152.0, 147.4, 147.4, 137.9, 127.6, 125.2, 124.5, 124.2, 121.4, 114.4, 107.8, 101.1, 76.0, 75.2, 53.5, 45.1, 25.5; HRMS (ESI) m/z calcd for $[C_{21}H_{22}N_3O_8]^+$ $[M + NH_4]^+$ 444.1401, found 444.1392. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 12.0 min, minor enantiomer t_R = 14.8 min.

*(S)-Methyl 1-Acetyl-2-((S)-2-nitro-1-(p-tolyl)ethyl)-3-oxoindoline-2-carboxylate (**4m**):* 38.4 mg (97% yield); white solid; mp 124−126 °C; $[\alpha]_D^{20}$ = −229 (*c* 1.00, $CHCl_3$, 96% ee); IR (KBr) 3409, 2951, 2924, 1752, 1713, 1663, 1609, 1554, 1473, 1377, 1245, 982, 760, 629, 529 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (pp m) 7.77 (d, *J* = 7.6 Hz, 1H), 7.54−7.49 (m, 1H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.81−6.75 (m, 4H), 5.91−5.83 (m, 1H), 5.06−4.99 (m, 2H), 3.72 (s, 3H), 2.31 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.1, 167.6, 166.1, 151.9, 138.1, 137.8, 130.9, 128.8, 127.7,

dx.doi.org/10.1021/jo301886j | *J. Org. Chem.* 2012, 77, 11307−11312

125.1, 124.6, 124.0, 114.4, 75.9, 75.2, 53.4, 45.1, 25.5, 20.9; HRMS (ESI) m/z calcd for $[C_{21}H_{24}N_3O_6]^+$ $[M + NH_4]^+$ 414.1660, found 414.1675. The enantiomeric excess was determined by HPLC with an AD-H column (hexane/*i*-PrOH = 80:20), 1.0 mL/min; major enantiomer t_R = 12.1 min, minor enantiomer t_R = 15.3 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(3,4-dimethylphenyl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4n**):* 38.1 mg (93% yield); white solid; mp 158−160 °C; $[\alpha]_D^{20}$ = −175 (*c* 1.00, $CHCl_3$, 92% ee); IR (KBr) 3403, 2954, 2924, 1747, 1708, 1676, 1607, 1556, 1475, 1434, 1376, 1321, 1248, 1203, 1109, 1056, 999, 941, 816, 757, 717, 640, 611, 514, 419 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.77 (d, *J* = 8.0 Hz, 1H), 7.52−7.48 (m, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 6.61 (s, 2H), 5.89−5.82 (dd, *J* = 9.2 Hz, 20 Hz, 1H), 5.04−4.97 (m, 2H), 3.72 (s, 3H), 2.30 (s, 3H), 2.02 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.2, 167.5, 166.1, 151.9, 137.7, 136.6, 136.3, 131.2, 129.3, 125.0, 124.7, 123.9, 114.3, 75.9, 75.2, 53.4, 45.0, 25.4, 19.3, 19.2; HRMS (ESI) m/z calcd for $[C_{22}H_{26}N_3O_6]^+$ $[M + NH_4]^+$ 428.1816, found 428.1811. The enantiomeric excess was determined by HPLC with an OJ-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 15.7 min, minor enantiomer t_R = 10.7 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(naphthalen-2-yl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4o**):* 41.0 mg (95% yield); white solid; mp 148−150 °C; $[\alpha]_D^{20}$ = −186 (*c* 1.00, $CHCl_3$, 93% ee); IR (KBr) 3422, 2956, 1755, 1715, 1666, 1611, 1548, 1475, 1377, 1346, 1288, 1242, 1207, 1056, 1001, 950, 822, 756, 599, 480, 480 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.79 (d, *J* = 7.6 Hz, 1H), 7.64−7.61 (m, 1H), 7.55(s, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.39−7.32 (m, 4H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.83 (d, *J* = 8.4 Hz,1H), 6.00−5.95 (dd, *J* = 3.2 Hz, 13.6 Hz, 1H), 5.28−5.12 (m, 2H), 3.74 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.1, 167.7, 166.1, 151.8, 137.8, 132.8, 132.7, 131.5, 127.9, 127.6, 127.4, 126.3, 126.3, 125.1, 124.5, 124.1, 114.3, 75.9, 75.2, 53.5, 45.5, 25.4; HRMS (ESI) m/z calcd for $[C_{24}H_{24}N_3O_6]^+$ $[M + NH_4]^+$ 450.1660, found 450.1657. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 17.0 min, minor enantiomer t_R = 13.1 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-(furan-2-yl)-2-nitroethyl)-3-oxoindoline-2-carboxylate (**4p**):* 34.6 mg (93% yield); white solid; mp 132−134 °C; $[\alpha]_D^{20}$ = −181 (*c* 1.00, $CHCl_3$, 90% ee); IR (KBr) 3411, 2965, 1751, 1710, 1675, 1606, 1555, 1474, 1375, 1284, 1206, 1148, 1081, 998, 940, 914, 755, 596, 516, 416 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.77 (d, *J* = 7.6 Hz, 1H), 7.62−7.58 (m, 1H), 7.21 (t, *J* = 7.6 Hz, 2H), 6.90 (s, 1H), 6.08−6.04 (m, 2H), 5.82−5.78 (dd, *J* = 2.8 Hz, 14 Hz, 1H), 5.22 (d, *J* = 10.0 Hz, 1H), 5.01−4.91 (m, 1H), 3.72 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.3, 167.6, 165.8, 151.4, 148.3, 142.4, 137.6, 125.4, 124.1, 114.3, 110.2, 109.8, 74.1, 53.5, 39.5, 25.5; HRMS (ESI) m/z calcd for $[C_{18}H_{20}N_3O_7]^+$ $[M + NH_4]^+$ 390.1296, found 390.1293. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 8.4 min, minor enantiomer t_R = 12.4 min.

*(S)-Methyl 1-Acetyl-2-((S)-1-nitropentan-2-yl)-3-oxoindoline-2-carboxylate (**4q**):* 30.3 mg (87% yield); white solid; mp 156−158 °C; $[\alpha]_D^{20}$ = −140 (*c* 1.00, $CHCl_3$, 75% ee); IR (KBr) 3432, 2964, 1755, 1707, 1669, 1607, 1552, 1473, 1377, 1338, 1262, 1104, 997, 760, 625, 591, 421 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.80−7.77 (dd, *J* = 2.8 Hz, 7.6 Hz, 2H), 7.29 (m, 1H), 5.73 (d, *J* = 14.8 Hz, 1H), 4.36−4.31 (dd, *J* = 6.8 Hz, 15.2 Hz, 1H), 3.86 (s, 1H), 3.68 (s, 3H), 2.55 (s, 3H), 1.30−1.16 (m, 4H), 1.08−1.00 (m, 1H), 0.75 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.4, 168.0, 166.3, 138.2, 125.4, 124.6, 75.3, 53.4, 39.2, 30.8, 25.5, 19.8, 13.9; HRMS (ESI) m/z calcd for $[C_{17}H_{20}NaN_2O_6]^+$ $[M + Na]^+$ 371.1290, found 371.1293. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 33.6 min, minor enantiomer t_R = 40.0 min.

*(S)-Methyl 1-Acetyl-5-bromo-2-((S)-2-nitro-1-phenylethyl)-3-oxoindoline-2-carboxylate (**4r**):* 43.2 mg 94% yield; white solid; mp 156−158 °C; $[\alpha]_D^{20}$ = −246 (*c* 1.00, $CHCl_3$, 90% ee); IR (KBr) 3077, 2963, 1751, 1707, 1673, 1601, 1553, 1469, 1373, 1335, 1263, 1195, 1063, 995, 822, 704, 646, 601, 467 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.87 (s, 1H), 7.58−7.56 (dd, *J* = 2.0 Hz, 8.8 Hz, 1H), 7.11−7.03 (m, 3H), 6.89 (d, *J* = 6.8 Hz, 3H), 5.86 (d, *J* = 10.8 Hz, 1H), 5.08−4.99 (m, 2H), 3.72 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.8, 167.4, 165.5, 150.7, 140.3, 133.8, 128.6, 128.3, 127.6, 126.0, 117.1, 115.8, 75.5, 53.6, 45.5, 25.4; HRMS (ESI) m/z calcd for $[C_{20}H_{21}BrN_3O_6]^+$ $[M + NH_4]^+$ 478.0611, found 478.0608. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 70:30), 1.0 mL/min; major enantiomer t_R = 7.8 min, minor enantiomer t_R = 10.6 min.

*(S)-Methyl 1-Acetyl-6-chloro-2-((S)-2-nitro-1-phenylethyl)-3-oxoindoline-2-carboxylate (**4s**):* 39.5 mg 95% yield; white solid; mp 136−138 °C; $[\alpha]_D^{20}$ = −172 (*c* 1.00, $CHCl_3$, 91% ee); IR (KBr) 3401, 2990, 1752, 1711, 1605, 1559, 1553, 1432, 1372, 1273, 1247, 1080, 993, 948, 800, 705, 636, 460 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 8 Hz, 1H), 7.16−7.13 (dd, *J* = 1.6 Hz, 8.0 Hz, 2H), 7.11−7.00 (m, 3H), 6.90 (d, *J* = 7.2 Hz, 2H), 5.89−5.84 (m, 1H), 5.05−5.00 (m, 2H), 3.72 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.7, 167.5, 165.6, 152.3, 144.5, 133.9, 128.6, 128.3, 127.8, 125.9, 124.8, 122.9, 114.7, 75.6, 53.6, 45.3, 25.5; HRMS (ESI) m/z calcd for $[C_{20}H_{21}ClN_3O_6]^+$ $[M + NH_4]^+$ 434.1113, found 434.1111. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 80:20), 1.0 mL/min; major enantiomer t_R = 9.6 min, minor enantiomer t_R = 12.0 min.

*(S)-Methyl 1-Acetyl-7-methyl-2-((S)-2-nitro-1-phenylethyl)-3-oxoindoline-2-carboxylate (**4t**):* 34.8 mg 88% yield; white solid; mp 172−174 °C; $[\alpha]_D^{20}$ = −205 (*c* 1.00, $CHCl_3$, 91% ee); IR (KBr) 3407, 2956, 2925, 1755, 1713, 1673, 1594, 1555, 1437, 1348, 1278, 1246, 1076, 1005, 972, 778, 615, 575 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.57 (d, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.2 Hz, 1H), 6.95 (t, *J* = 6.8 Hz, 2H), 6.87 (s, 2H), 5.80−5.73 (dd, *J* = 10.0 Hz, 20.4 Hz, 1H), 5.03−4.95 (m, 2H), 3.77 (s, 3H), 2.12 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.6, 169.7, 166.6, 152.9, 140.1, 133.9, 128.1, 127.9, 126.6, 125.5, 122.2, 74.8, 53.5, 47.5, 23.5, 19.2; HRMS (ESI) m/z calcd for $[C_{21}H_{21}N_2O_6]^+$ $[M + H]^+$ 397.1396, found397.1394. The enantiomeric excess was determined by HPLC with an OD-H column (hexane/*i*-PrOH = 80:20), 1.0 mL/min; major enantiomer t_R = 10.1 min, minor enantiomer t_R = 14.8 min.

*Experimental Procedure for the Synthesis of Compound **5**.* A 10 mL round-bottom flask with well-stirring was filled with zinc powder (210.0 mg, 0.25 mmol), and then **4e** (94% ee, 115.0 mg, 0.25 mmol) and EtOH (2.5 mL) were added to the flask. After the mixture was stirred at 35 °C for 10 min, 1.5 mL of 4 N HCl aq was added dropwise. The contents were stirred at 35 °C until the reaction was complete (about 4 h as monitored by TLC). After EtOH was removed under reduced pressure, 3 N NaOH aq (5.0 mL) was added, and the solution was stirred for 5 min. After being diluted with 5.0 mL of CH_2Cl_2, the mixture was filtrated through a plug of Celite. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL).The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$ and concentrated. The crude mixture was then dissolved in 2.0 mL of dry CH_2Cl_2, and then Et_3N (55 μL, 0.38 mmol) was added to the solution at 0 °C. After 5 min, AcCl (20 μL, 0.25 mmol) was added dropwise. The mixture was stirred for 4 h and then allowed to warm to room temperature. The solvent was removed by a rotary evaporator and the residue was purified by flash chromatography (petroleum/EtOAc = 2:1) to afford 53.0 mg of pure **5** (42% yield, 20:1 dr, 96% ee).

*(3S,3aS,8bS)-Methyl 1,4-Diacetyl-3-(4-bromophenyl)-1,2,3,3a,4,8b-hexahydropyrrolo[3,2-b]indole-3a-carboxylate (**5**).* 48.0 mg (42% yield); white solid; mp 168−170 °C; $[\alpha]_D^{20}$ = +262 (*c* 1.00, $CHCl_3$, 96% ee); IR (KBr) 2952, 2023, 1744, 1656, 1484, 1383, 1351, 1248, 1011, 988, 831, 759, 520 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.79 (d, *J* = 7.6 Hz, 1H), 7.19−7.12 (m, 3H), 7.08−7.04 (m, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 5.94 (s, 1H), 4.66−4.63 (dd, *J* = 3.2 Hz, 7.6 Hz, 1H), 4.23−4.18 (dd, *J* = 8 Hz, 10.8 Hz, 1H), 3.76 (s, 3H), 3.73−3.70 (dd, *J* = 3.2 Hz, 10.8 Hz, 1H), 2.20 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.0, 170.9, 167.8, 141.0, 137.6, 131.3, 130.5, 130.2, 129.6,

dx.doi.org/10.1021/jo301886j | *J. Org. Chem.* 2012, 77, 11307−11312

128.1, 124.3, 121.2, 112.5, 66.0, 53.6, 53.1, 48.8, 24.5, 22.8; HRMS (ESI) m/z calcd for $[C_{22}H_{22}BrN_2O_4]^+$ $[M + H]^+$ 457.0766, found 457.0757. The enantiomeric excess was determined by HPLC with an AD-H column (hexane/*i*-PrOH = 80:20), 1.0 mL/min; major enantiomer t_R = 12.8 min, minor enantiomer t_R = 10.8 min.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, spectra data for the products, and X-ray crystallographic data of **4e** (CCDC 862138) and **5** (CCDC 862139) (CIF). This materia is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for the NSFC (21032005, 20972058, 21172097), the National Basic Research Program of China (No. 2010CB833203), and the "111" program from MOE of P. R. China.

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