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Palladium-Catalyzed Asymmetric Hydrogenation of Unprotected 3-Substituted Indoles

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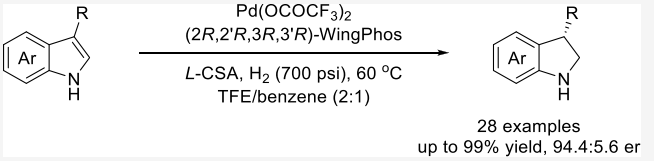
ABSTRACT: A palladium-catalyzed asymmetric hydrogenation of unprotected 3-substituted indoles was developed, providing a series of 3-substituted indolines in excellent yields with ≤94.4:5.6 er. The large sterically hindered bisphosphine ligand played a crucial role in the enantioselective control. In addition, the gram-scale hydrogenation experiment and product derivatizations were performed successfully.



The chiral indoline skeleton is a ubiquitous structural unit that is present in natural products, biologically active molecules, and organic synthesis.[1] Therefore, a series of methods for synthesizing chiral indolines have been developed.[2] One of the most efficient approaches to accessing chiral indolines is direct asymmetric reduction of the corresponding indoles.[3] Over the past several decades, the asymmetric hydrogenation (AH) of N-protected indoles, including N-protected 2-substituted, 2,3-disubstituted, and 3-substituted indoles, was developed using chiral rhodium,[4] ruthenium,[5] and iridium[6] catalytic systems with good to excellent enantioselectivities. Subsequently, the transition-metal-catalyzed[7−10] asymmetric hydrogenation of unprotected 2-substituted and 2,3-disubstituted indoles was successfully developed for the synthesis of the corresponding chiral indolines with excellent enantioselectivities using the strong Brønsted acid as an activator. Later, the organo-catalyzed asymmetric reduction of unprotected 2-substituted and 2,3-disubstituted indoles was also developed with trichlorosilane and borane as the reductants.[11] These methodologies provide an effective approach for the synthesis of chiral indolines.

Despite the great advances in asymmetric reduction of unprotected 2-substituted and 2,3-disubstituted indoles, the asymmetric reduction of unprotected simple 3-substituted indoles for the synthesis of chiral 3-substituted indolines remains a challenge, which has been rarely explored to date. In 2011, the chiral Lewis base-catalyzed asymmetric hydrosilylation of unprotected 3-substituted indoles was developed by Chen's group to obtain 3-substituted indolines with up to moderate 77.5:22.5 er[11a] (Scheme 1a). Subsequently, palladium diphosphine[7e] and ruthenium diamine[9a] catalytic systems were reported by Zhang and Fan, respectively, in their achievement of asymmetric hydrogenation of unprotected 3-substituted indoles, but only ≤83:17 er (Scheme 1b) was observed. In 2020, Du achieved an asymmetric transfer hydrogenation of ethyl 2-(1*H*-indol-3-yl)acetate catalyzed by a frustrated Lewis pair derived from $HB(C_6F_5)_2$ and (*S*)-*tert*-butyl-sulfinamide,[11d] giving the desired product with 64:36 er (Scheme 1c). Therefore, developing an efficient and atom-economic method for synthesizing unprotected 3-substituted indolines with high enantioselectivity is still desirable in organic synthesis and drug research.

In general, asymmetric hydrogenation of unprotected 2,3-disubstituted indoles under acidic conditions involves two steps: the protonation of a C=C bond to form dearomative iminium salts and asymmetric hydrogenation of the iminium salt (it is, in fact, a dynamic kinetic resolution process).[7a] The high enantioselectivity of the asymmetric hydrogenation of unprotected 2,3-disubstituted indoles was obtained because of the steric hindrance at position 2, which made the enantioselectivity easier to control. However, an unprotected 3-substituted indole does not have the steric hindrance effect of the position 2 substituent, and the position 3 substituent of indole is remote from the chiral environment of the palladium catalyst. These issues render highly enantioselective hydrogenation of unprotected 3-substituted indoles highly challenging. In connection with our previous work on palladium-catalyzed asymmetric hydrogenation of indoles,[7a,b,f] we envisioned the introduction of a large sterically hindered chiral ligand for forming a deep chiral pocket that affects position 3 of indole during the hydrogenation process, thus achieving highly enantioselective hydrogenation of unprotected 3-substituted indoles (Scheme 1d). Herein, we report a palladium-catalyzed asymmetric hydrogenation of unprotected 3-substituted indoles using a large sterically hindered chiral ligand to access 3-substituted indolines with ≤94.4:5.6 er.

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Scheme 1. Asymmetric Reduction of Unprotected 3-Substituted Indoles

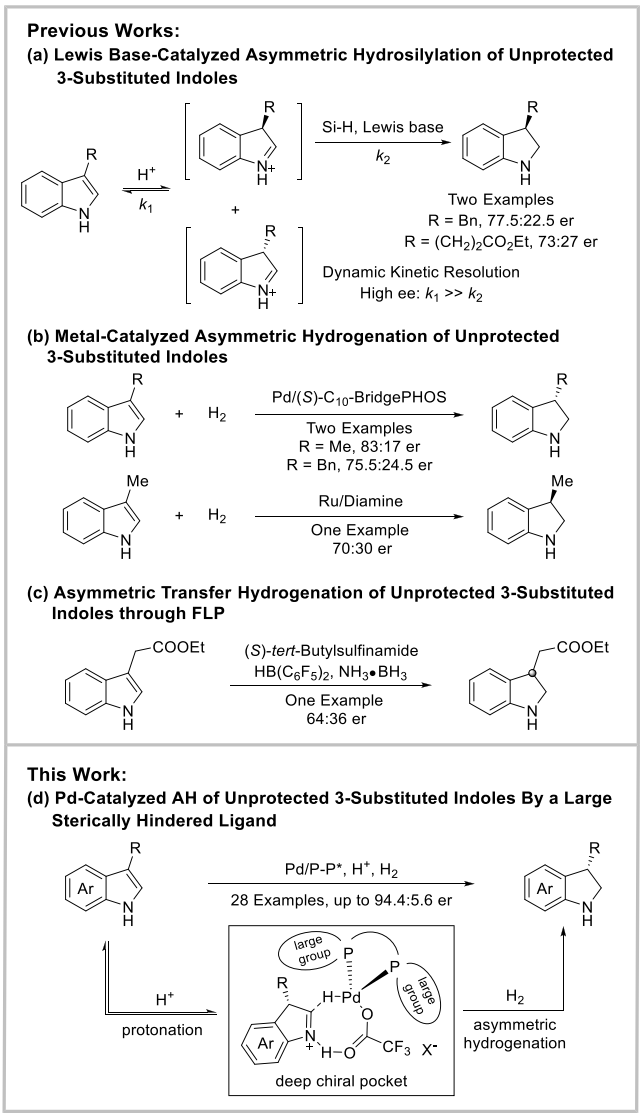
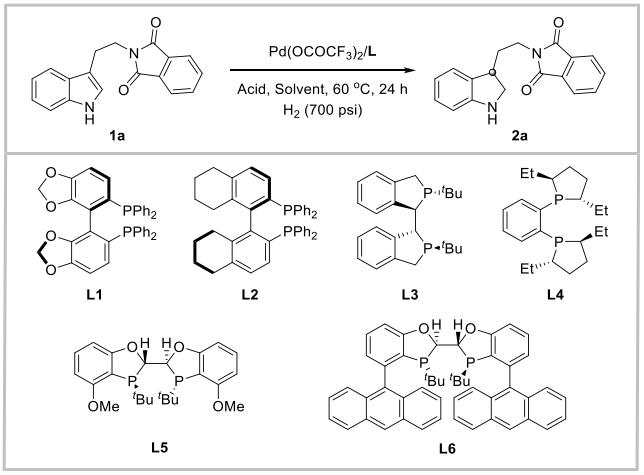


Table 1. Optimization of the Reaction Parameters[a]



entry	solvent	acid	L	yield of **2a** (%)[b]	er of **2a** (%)[c]
1	TFE	D-CSA	**L1**	72	71.7:28.3 (*R*)
2	DCE	D-CSA	**L1**	59	60.6:39.4 (*R*)
3	benzene	D-CSA	**L1**	36	75.5:24.5 (*R*)
4	TFE/benzene (1:1)	D-CSA	**L1**	82	72.7:27.3 (*R*)
5	TFE/benzene (2:1)	D-CSA	**L1**	81	73.7:26.3 (*R*)
6	TFE/benzene (3:1)	D-CSA	**L1**	81	74.0:26.0 (*R*)
7	TFE/benzene (2:1)	L-CSA	**L1**	>95	75.1:24.9 (*R*)
8	TFE/benzene (2:1)	$TsOH·H_2O$	**L1**	>95	67.8:32.2 (*R*)
9	TFE/benzene (2:1)	CF_3SO_3H	**L1**	20	64.1:35.9 (*R*)
10	TFE/benzene (2:1)	$PhSO_3H$	**L1**	66	67.8:32.2 (*R*)
11	TFE/benzene (2:1)	L-CSA	**L2**	92	74.9:25.1 (*R*)
12	TFE/benzene (2:1)	L-CSA	**L3**	59	52.8:47.2 (*R*)
13	TFE/benzene (2:1)	L-CSA	**L4**	84	50.0:50.0
14	TFE/benzene (2:1)	L-CSA	**L5**	53	57.3:42.7 (*R*)
15	TFE/benzene (2:1)	L-CSA	**L6**	>95	92.6:7.4 (*S*)
16[d]	TFE/benzene (2:1)	L-CSA	**L6**	>95 (99)[e]	92.6:7.4 (*S*)

[a]Conditions: **1a** (0.20 mmol), $Pd(OCOCF_3)_2$ (2.0 mol %), **L** (2.4 mol %), acid (0.24 mmol), solvent (3.0 mL), H_2 (700 psi), 60 °C, 24 h. [b]Determined by ^1H NMR analysis using dibromomethane as the internal standard. [c]Determined by chiral HPLC analysis. [d]**1a** (0.30 mmol), $Pd(OCOCF_3)_2$ (1.0 mol %), **L6** (1.2 mol %), L-CSA (0.36 mmol). [e]Isolated yield.

To begin our investigation, 2-[2-(1*H*-indol-3-yl)ethyl]-isoindoline-1,3-dione **1a** was chosen as the model substrate. We tested asymmetric hydrogenation of **1a** with Pd-$(OCOCF_3)_2$/(*R*)-SegPhos[12a] as the catalyst and D- camphorsulfonic acid (D-CSA) as the activator in 2,2,2-trifluoroethanol (TFE) under hydrogen gas (700 psi) at 60 °C. The reaction proceeded to give product **2a** in 72% NMR yield and 71.7:28.3 er (Table 1, entry 1), and hydrogenation did not occur without an acid. Subsequently, the effect of solvents on the activity and enantiomeric ratio was examined (entries 2−6), and a TFE/benzene mixture in a volume ratio of 2:1 gave the best result in terms of both yield and enantiomeric ratio (entry 5). Furthermore, different Brønsted acids were evaluated (entries 7−10), and a slightly higher enantiomeric ratio and excellent NMR yield were obtained with L-camphorsulfonic acid (L-CSA) (entry 7). Next, a series of chiral bisphosphine ligands[12b−e] were examined (entries 11−15). To our delight, the enantiomeric ratio increased dramatically from 75.1:24.9 to 92.4:7.6 when the large sterically hindered ligand (2*R*,2′*R*,3*R*,3′*R*)-WingPhos (**L6**) originally developed by Tang's group[12f] was employed (entry 15). We speculated that the large sterically hindered bisphosphine ligand formed a deep chiral pocket[12] that affects position 3 of indole during the hydrogenation process. Gratifyingly, a 99% isolated yield and a 92.4:7.6 er were obtained on a 0.30 mmol scale, even with the catalyst loading decreased from 2.0 to 1.0 mol % (entry 16). Therefore, the optimal conditions were established [Pd-$(OCOCF_3)_2$, **L6**, L-CSA, 2:1 TFE/benzene, H_2 (700 psi), and 60 °C].

With the optimized conditions in hand, we evaluated the substrate generality of asymmetric hydrogenation of unprotected 3-substituted indoles (Scheme 2). Initially, various

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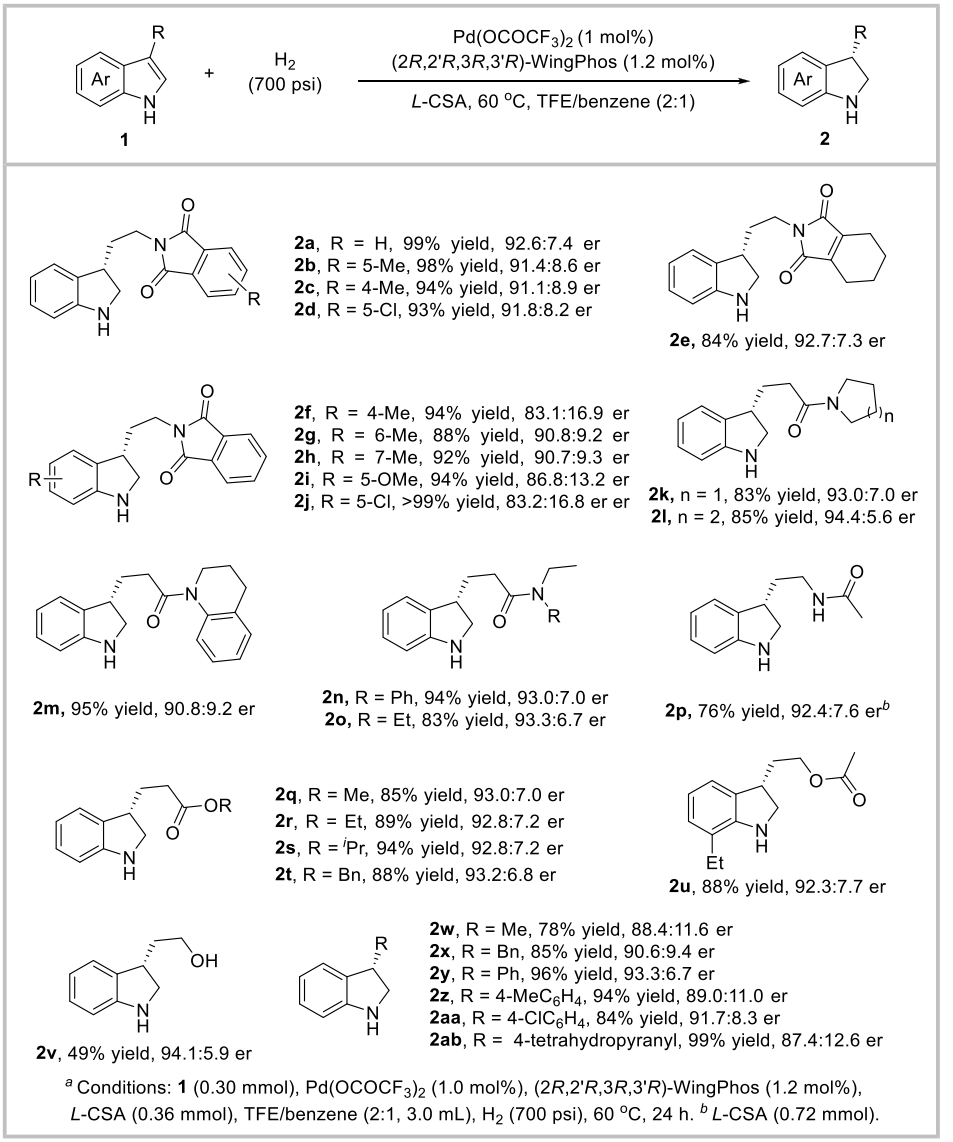
Scheme 2. Substrate Scope for Unprotected 3-Substituted Indoles



[a] Conditions: **1** (0.30 mmol), $Pd(OCOCF_3)_2$ (1.0 mol%), (2*R*,2'*R*,3*R*,3'*R*)-WingPhos (1.2 mol%), *L*-CSA (0.36 mmol), TFE/benzene (2:1, 3.0 mL), H_2 (700 psi), 60 °C, 24 h. [b] *L*-CSA (0.72 mmol).

substituents on the phenyl ring of the phthalimide were examined. The steric hindrance and electronic properties of the phenyl group had a marginal effect on the enantiomeric ratio and activity (**2b**–**d**). Product **2e** with 84% yield and 92.7:7.3 er was obtained when the benzene ring of the phthalimide was replaced with an alkyl ring. Moreover, various aromatic substituted indoles could react smoothly in this palladium-catalyzed asymmetric hydrogenation to furnish the products (**2f**–**j**) in good yields (88–99%). We found that the position of the substituent has an obvious influence on the enantiomeric ratio. The introduction of methyl at position 4 (**2f**) and methoxyl (**2i**) or chloro (**2j**) at position 5 of the indole would reduce the enantiomeric ratios.

To further explore the substrate scope of this methodology, a myriad of substrates containing different functional groups were investigated. The substrates containing amide groups could also perform well under the standard conditions, giving the desired products with excellent yields and 90.8:9.2–94.4:5.6 er (**2k**–**p**). The reaction system was also compatible with the ester group, affording the desired products with good yields and enantiomeric ratios (**2q**–**t**). Furthermore, the introduction of an ethyl group at position 7 of the indole ring had little effect on the yield and enantiomeric ratio (**2u**). Interestingly, *de*-Boc product **2v** with 94.1:5.9 er was obtained when *O*-Boc-protected tryptophol was used as a substrate in this catalytic system, which might be ascribed to the strong Brønsted acid-promoted *de*-Boc. However, no desired product was obtained via direct hydrogenation of tryptophol, and the reaction system was messy. It is worth noting that 3-methylindole **1w** and 3-benzylindole **1x** could be hydrogenated with 88.4:11.6 er and 90.4:9.6 er, respectively. In addition, a variety of 3-arylindoles were examined in this reaction, and the target products were obtained with good yields and enantiomeric ratios (**2y**–**aa**). The catalytic system could also tolerate the substrate containing a 4-tetrahydropyranyl group at position 3 of the indole, giving the desired product with excellent yield and 87.4:12.6 er (**2ab**). The broad scope of functional groups adopted in the asymmetric hydrogenation provided a versatile platform for further transformations of the hydrogenative products. The absolute configuration of hydrogenation products **2w** and **2x** was determined to be *S* upon comparison to the known optical rotation data of 3-

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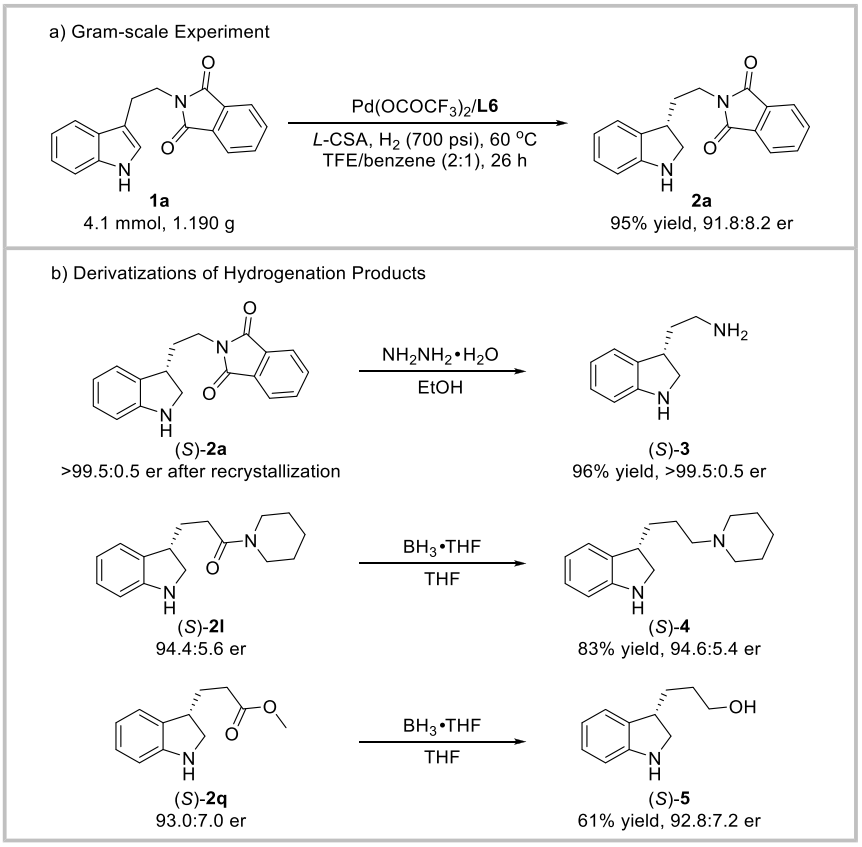
Scheme 3. Gram-Scale Experiment and Derivatizations of Hydrogenation Products



methylindoline[4b] and 3-benzylindoline[11a] in the literature, respectively.

To demonstrate the practicality of this methodology, a gram-scale experiment was carried out on a 4.1 mmol scale (1.190 g) under 0.5 mol % catalyst loading (Scheme 3a). To our delight, the desired 3-substituted indoline **2a** was obtained without a significant loss of activity or enantiomeric ratio (95% yield, 91.8:8.2 er). To further expand the scope of application of our methodology, derivatizations of hydrogenation products were conducted. The phthaloyl protective group of (*S*)-**2a** (recrystallized from dichloromethane/*n*-hexane to increase the er to >99.5:0.5) could be removed upon treatment with hydrazine monohydrate to afford the chiral amine (*S*)-**3** in 96% yield without a loss of optical purity. Reduction of amide (*S*)-**2l** and ester (*S*)-**2q** using borane gave the corresponding reductive products (*S*)-**4** and (*S*)-**5** while maintaining optical purity in 83% and 61% yields, respectively (Scheme 3b).

In summary, we have developed a direct and highly efficient strategy for palladium-catalyzed asymmetric hydrogenation of unprotected 3-substituted indoles with (2*R*,2′*R*,3*R*,3′*R*)-Wing-Phos as the large sterically hindered chiral bisphosphine ligand. This methodology shows good functional group tolerance and provides a rapid route to a series of chiral 3-substituted indolines with excellent yields and ≤94.4:5.6 er. In addition, the gram-scale experiment and derivatizations of products could be carried out well. Further investigations of asymmetric hydrogenation of other aromatic heterocycles are ongoing in our laboratory.

EXPERIMENTAL SECTION

All reactions were carried out under a nitrogen atmosphere using the standard Schlenk techniques, unless otherwise noted. Solvents were treated prior to use according to the standard methods. ^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ on a 400 MHz instrument with TMS as the internal standard. The enantiomeric excess was determined by HPLC analysis, using the chiral column described below in detail. Optical rotations were measured with a polarimeter. Flash column chromatography was performed on silica gel (200−300 mesh). The heat source for all heating reactions was an oil bath. High-resolution mass spectrometry was performed on an electrospray ionization (ESI) apparatus using time-of-flight (TOF) mass spectrometry. Commercially available reagents and solvents were used throughout without further purification.

The 3-substituted indole substrates **1** could be prepared according to the known procedures. Among them, **1a**,[13a] **1f−h**,[13] **1i** and **1j**,[13a] **1k−n**,[14] **1o**,[15] **1p**,[16] **1q−s**,[17] **1t**,[18] **1x**,[19] **1y**,[20] **1z** and **1aa**,[21] and **1ab**[22] are the known compounds. Substrates **1b−e**,[13a] **1u**,[18] and **1v**[23] were prepared according to the known method.

Procedure for the Synthesis of 3-Substituted Indole Substrates 1b−e. To a solution of tryptamine (10.0 mmol, 1.0 equiv) in toluene (50 mL) was added acid anhydride (10.0 mmol, 1.0 equiv). Then the solution was heated to reflux. After the reaction had reached completion (monitored by TLC), the volatiles were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel using an eluent of hexanes, dichloromethane, and ethyl acetate to afford products **1b−e**.

*2-[2-(1H-Indol-3-yl)ethyl]-5-methylisoindoline-1,3-dione (**1b**).* 2.616 g, 86% yield (10.0 mmol scale); yellow solid; mp 167−168 °C; new compound; R_f = 0.72 (3:1:1 hexanes/ethyl acetate/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.72 (dd, J = 14.8, 7.7 Hz, 2H), 7.62 (s, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.21−7.15 (m, 1H), 7.15−7.10 (m, 1H),

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7.09−7.06 (m, 1H), 4.02−3.95 (m, 2H), 3.17−3.11 (m, 2H), 2.49 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.7, 168.6, 145.2, 136.3, 134.5, 132.7, 129.7, 127.5, 123.8, 123.2, 122.2 (d), 119.6, 119.0, 112.5, 111.2, 38.6, 24.6, 22.1; HRMS calcd for $C_{19}H_{17}N_2O_2$ $[M + H]^+$ 305.1285, found 305.1286.

*2-[2-(1H-Indol-3-yl)ethyl]-4-methylisoindoline-1,3-dione (**1c**).* 2.197 g, 98% yield (7.4 mmol scale); yellow solid; mp 159−160 °C; new compound; R_f = 0.73 (3:1:1 hexanes/ethyl acetate/dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.66 (d, J = 7.3 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.23−7.16 (m, 1H), 7.16−7.07 (m, 2H), 4.03−3.93 (m, 2H), 3.19−3.10 (m, 2H), 2.70 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.3, 168.5, 137.9, 136.4, 133.5, 132.7, 129.0, 127.5, 122.2 (d), 120.9, 119.6, 119.0, 112.6, 111.2, 38.4, 24.7, 17.7; HRMS calcd for $C_{19}H_{17}N_2O_2$ $[M + H]^+$ 305.1285, found 305.1284.

*2-[2-(1H-Indol-3-yl)ethyl]-5-chloroisoindoline-1,3-dione (**1d**).* 2.386 g, 73% yield (10.0 mmol scale); yellow solid; mp 170−171 °C; new compound; R_f = 0.80 (3:1:1 hexanes/ethyl acetate/dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.82−7.78 (m, 1H), 7.76 (d, J = 7.9 Hz, 1H), 7.71 (d, J = 7.9 Hz, 1H), 7.68−7.63 (m, 1H), 7.35 (d, J = 8.1 Hz, 1H), 7.22−7.15 (m, 1H), 7.15−7.09 (m, 1H), 7.09−7.06 (m, 1H), 4.03−3.96 (m, 2H), 3.18−3.11 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.5, 167.2, 140.7, 136.3, 134.0, 133.9, 130.3, 127.5, 124.5, 123.8, 122.3, 122.2, 119.7, 118.9, 112.3, 111.3, 38.9, 24.5; HRMS calcd for $C_{18}H_{14}ClN_2O_2$ $[M + H]^+$ 325.0738 (^{35}Cl) and 327.0715 (^{37}Cl), found 325.0736 (^{35}Cl) and 327.0709 (^{37}Cl).

*2-[2-(1H-Indol-3-yl)ethyl]-4,5,6,7-tetrahydro-1H-isoindole-1,3(2H)-dione (**1e**).* 2.551 g, 87% yield (10.0 mmol scale); yellow solid; mp 191−192 °C; new compound; R_f = 0.78 (3:1:1 hexanes/ethyl acetate/dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.21−7.15 (m, 1H), 7.15−7.10 (m, 1H), 7.09−7.05 (m, 1H), 3.83−3.76 (m, 2H), 3.08−3.01 (m, 2H), 2.35−2.26 (m, 4H), 1.78−1.69 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.4, 141.6, 136.3, 127.6, 122.2, 122.1, 119.6, 119.0, 112.8, 111.2, 38.2, 24.7, 21.5, 20.1; HRMS calcd for $C_{18}H_{19}N_2O_2$ $[M + H]^+$ 295.1441, found 295.1442.

Synthesis of 2-(7-Ethyl-1*H*-indol-3-yl)ethyl Acetate (1u). A solution of 4-(dimethylamino)pyridine (0.244 g, 2.0 mmol) and 7-ethyl tryptophol (1.893 g, 10.0 mmol) in dichloromethane (20 mL) was added to a solution of acetic acid (HOAc, 0.57 mL, 10.0 mmol) in dichloromethane (20 mL) at 0 °C. Then, dicyclohexylcarbodiimide (DCC, 2.166 g, 10.5 mmol) was added to the reaction mixture at 0 °C. The mixture was allowed to warm to room temperature and stirred overnight. The formed precipitate was filtered off and washed with dichloromethane. The combined filtrate was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel using dichloromethane as the eluent to afford product **1u**: 1.938 g, 84% yield; pale yellow oil; new compound; R_f = 0.68 (dichloromethane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 7.1 Hz, 1H), 6.99−6.95 (m, 1H), 4.34 (t, J = 7.2 Hz, 2H), 3.08 (t, J = 7.2 Hz, 2H), 2.81 (q, J = 7.6 Hz, 2H), 2.05 (s, 3H), 1.33 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.4, 135.1, 127.3, 126.7, 121.8, 120.6, 119.8, 116.6, 112.4, 64.8, 25.0, 24.0, 21.2, 13.9; HRMS calcd for $C_{14}H_{18}NO_2$ $[M + H]^+$ 232.1332, found 232.1334.

Synthesis of 2-(1*H*-Indol-3-yl)ethyl *tert*-Butyl Carbonate (1v). A solution of di-*tert*-butyl dicarbonate (2.619 g, 12.0 mmol) in tetrahydrofuran (20 mL) was added to a solution of tryptophol (1.612 g, 10.0 mmol), 4-(dimethylamino)pyridine (0.244 g, 2.0 mmol), and triethylamine (2.7 mL, 20.0 mmol) in tetrahydrofuran (30 mL) at room temperature. After the reaction had reached completion (monitored by TLC), the volatiles were removed under reduced pressure. The residue was purified by flash chromatography on silica gel using an eluent of hexanes and ethyl acetate to afford product **1v**: 0.385 g, 15% yield; yellow oil; new compound; R_f = 0.44 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.19−7.14 (m, 1H), 7.13−7.08 (m, 1H), 6.95−6.90 (m, 1H), 4.33 (t, J = 7.4 Hz, 2H), 3.11 (t, J = 7.4 Hz, 2H), 1.47 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.7, 136.3, 127.4, 122.4, 122.1, 119.4, 118.8, 111.4, 111.3, 82.1, 67.1, 27.9, 25.0; HRMS calcd for $C_{15}H_{20}NO_3$ $[M + H]^+$ 262.1438, found 262.1431.

Procedure for Pd-Catalyzed Asymmetric Hydrogenation of 3-Substituted Indoles. (2*R*,2′*R*,3*R*,3′*R*)-WingPhos (2.7 mg, 0.0036 mmol, 1.2 mol %) and palladium trifluoroacetate (1.0 mg, 0.003 mmol, 1.0 mol %) were placed in a dried Schlenk tube under a nitrogen atmosphere, and degassed anhydrous acetone was added. The mixture was stirred at room temperature for 1 h. The solvent were removed under reduced pressure to give the catalyst. In a glovebox, L-CSA (83.6 mg, 0.36 mmol) and 3-substituted indoles **1** (0.3 mmol) were stirred in 1.0 mL of a mixed solvent [2,2,2-trifluoroethanol and benzene mixed in a 2:1 (v/v) ratio before use] at room temperature for 5 min. Subsequently, the catalyst solution described above together with 2.0 mL of the mixed solvent was added to the reaction mixture, and then the mixture was transferred to an autoclave, which was charged with hydrogen gas (700 psi). The autoclave (300 mL volume, 2.5 in. inner diameter, and 4.0 in. inner depth) was stirred with a magnetic bar at a rate of 450 rpm at 60 °C for 24 h. After the hydrogen gas had been carefully released, the mixture was concentrated under vacuum and dissolved in a saturated aqueous sodium bicarbonate solution (5 mL). After the mixture had been stirred for 10 min, the aqueous phase was extracted with dichloromethane (3 × 5 mL). The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography to give chiral reductive products **2**. Note that other aromatic solvents (toluene, *p*-xylene, chlorobenzene, etc.) have enantioselectivities lower than that of benzene.

The enantiomeric excesses of the chiral reductive products were determined by HPLC with chiral columns. Racemates of **2** were prepared by the hydrogenation of the corresponding 3-substituted indoles using (±)-BINAP and $Pd(OCOCF_3)_2$ as the catalyst.

*(+)-(S)-2-[2-(Indolin-3-yl)ethyl]isoindoline-1,3-dione (**2a**).* 87.3 mg, 99% yield; yellow solid; known compound;[24] R_f = 0.51 (2:1:1 hexanes/ethyl acetate/dichloromethane); 92.6:7.4 er; $[\alpha]^{20}_D$ = +61.65 (c 1.06, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.88−7.80 (m, 2H), 7.75−7.68 (m, 2H), 7.15 (d, J = 7.3 Hz, 1H), 7.01 (t, J = 7.6 Hz, 1H), 6.70 (t, J = 7.4 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 3.94−3.46 (m, 4H), 3.39−3.26 (m, 2H), 2.27−2.16 (m, 1H), 2.00−1.87 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.4, 151.3, 134.0, 132.2, 131.8, 127.8, 124.0, 123.3, 118.8, 109.7, 53.1, 39.7, 36.1, 32.7; HPLC Chiralcel OD-H column, 230 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 17.6 and 20.7 min (major).

*(+)-(S)-2-[2-(Indolin-3-yl)ethyl]-5-methylisoindoline-1,3-dione (**2b**).* 90.4 mg, 98% yield; yellow oil; new compound; R_f = 0.59 (2:1:1 hexanes/ethyl acetate/dichloromethane); 91.4:8.6 er; $[\alpha]^{20}_D$ = +56.96 (c 1.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 1H), 7.63 (s, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.14 (d, J = 7.3 Hz, 1H), 7.01 (t, J = 7.6 Hz, 1H), 6.70 (t, J = 7.4 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 3.81−3.73 (m, 3H), 3.56 (s, 1H), 3.37−3.25 (m, 2H), 2.50 (s, 3H), 2.26−2.16 (m, 1H), 1.97−1.86 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.6, 168.5, 151.3, 145.3, 134.5, 132.6, 131.9, 129.6, 127.7, 124.0, 123.9, 123.2, 118.8, 109.6, 53.1, 39.7, 36.1, 32.8, 22.1; HPLC Chiralcel OD-H column, 230 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 18.7 and 24.8 min (major); HRMS calcd for $C_{19}H_{19}N_2O_2$ $[M + H]^+$ 307.1441, found 307.1441.

*(+)-(S)-2-[2-(Indolin-3-yl)ethyl]-4-methylisoindoline-1,3-dione (**2c**).* 86.7 mg, 94% yield; yellow solid; mp 116−117 °C; new compound; R_f = 0.60 (2:1:1 hexanes/ethyl acetate/dichloromethane); 91.1:8.9 er; $[\alpha]^{20}_D$ = +62.83 (c 1.12, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 7.3 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.15 (d, J = 7.3 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.70 (t, J = 7.4 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 3.81−3.73 (m, 3H), 3.57 (s, 1H), 3.38−3.26 (m, 2H), 2.69 (s, 3H), 2.26−2.16 (m, 1H), 1.98−1.87 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.3, 168.5,

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151.4, 138.0, 136.4, 133.5, 132.6, 131.9, 128.9, 127.7, 124.0, 120.9, 118.8, 109.7, 53.1, 39.7, 35.9, 32.8, 17.7; HPLC Chiralcel OD-H column, 230 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 14.1 and 16.1 min (major); HRMS calcd for $C_{19}H_{19}N_2O_2$ $[M + H]^+$ 307.1441, found 307.1440.

(+)-(S)-5-Chloro-2-[2-(indolin-3-yl)ethyl]isoindoline-1,3-dione ***(2d)***. 91.3 mg, 93% yield; yellow oil; new compound; R_f = 0.69 (2:1:1 hexanes/ethyl acetate/dichloromethane); 91.8:8.2 er; $[\alpha]^{20}_D$ = +57.14 (*c* 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.85−7.71 (m, 2H), 7.69−7.63 (m, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.69 (t, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 7.8 Hz, 1H), 3.82−3.73 (m, 3H), 3.54 (s, 1H), 3.37−3.25 (m, 2H), 2.24−2.14 (m, 1H), 1.99−1.88 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.4, 167.1, 151.3, 140.7, 134.1, 133.9, 131.7, 130.2, 127.8, 124.5, 123.9, 123.8, 118.8, 109.7, 53.0, 39.6, 36.4, 32.6; HPLC Chiralcel OD-H column, 230 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 25.0 and 34.0 min (major); HRMS calcd for $C_{18}H_{16}ClN_2O_2$ $[M + H]^+$ 327.0895 (^{35}Cl) and 329.0872 (^{37}Cl), found 327.0895 (^{35}Cl) and 329.0864 (^{37}Cl).

(+)-(S)-2-[2-(Indolin-3-yl)ethyl]-4,5,6,7-tetrahydro-1H-isoindole-1,3(2H)-dione ***(2e)***. 75.0 mg, 84% yield; yellow oil; new compound; R_f = 0.61 (2:1:1 hexanes/ethyl acetate/dichloromethane); 92.7:7.3 er; $[\alpha]^{20}_D$ = +40.33 (*c* 0.95, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 7.3 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 7.8 Hz, 1H), 3.73 (t, *J* = 8.5 Hz, 1H), 3.59 (t, *J* = 7.1 Hz, 2H), 3.34−3.21 (m, 2H), 2.36−2.28 (m, 4H), 2.15−2.06 (m, 1H), 1.90−1.80 (m, 1H), 1.78−1.70 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.3, 151.3, 141.6, 132.0, 127.6, 123.9, 118.7, 109.6, 52.9, 39.5, 35.5, 32.7, 21.4, 20.0; HPLC Chiralcel OD-H column, 230 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 14.7 and 16.9 min (major); HRMS calcd for $C_{18}H_{21}N_2O_2$ $[M + H]^+$ 297.1598, found 297.1599.

(+)-(S)-2-[2-(4-Methylindolin-3-yl)ethyl]isoindoline-1,3-dione ***(2f)***. 86.5 mg, 94% yield; yellow oil; new compound; R_f = 0.57 (2:1:1 hexanes/ethyl acetate/dichloromethane); 83.1:16.9 er; $[\alpha]^{20}_D$ = +21.58 (*c* 1.02, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.87−7.80 (m, 2H), 7.73−7.68 (m, 2H), 6.91 (t, *J* = 7.6 Hz, 1H), 6.48 (dd, *J* = 14.1, 7.6 Hz, 2H), 3.89−3.80 (m, 1H), 3.73−3.63 (m, 2H), 3.57−3.52 (m, 1H), 3.34−3.28 (m, 1H), 2.22 (s, 3H), 2.04−1.89 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.4, 151.1, 134.2, 134.0, 132.2, 130.1, 127.9, 123.3, 120.5, 107.2, 51.6, 38.9, 36.0, 31.2, 18.5; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH; flow rate of 1.0 mL/min, retention times of 16.3 min (major) and 19.9 min; HRMS calcd for $C_{19}H_{19}N_2O_2$ $[M + H]^+$ 307.1441, found 307.1448.

(+)-(S)-2-[2-(6-Methylindolin-3-yl)ethyl]isoindoline-1,3-dione ***(2g)***. 81.2 mg, 88% yield; yellow oil; new compound; R_f = 0.58 (2:1:1 hexanes/ethyl acetate/dichloromethane); 90.8:9.2 er; $[\alpha]^{20}_D$ = +57.28 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.87−7.80 (m, 2H), 7.73−7.68 (m, 2H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.52 (d, *J* = 7.5 Hz, 1H), 6.46 (s, 1H), 3.83−3.73 (m, 3H), 3.68−3.19 (m, 3H), 2.23 (s, 3H), 2.22−2.14 (m, 1H), 1.97−1.87 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.5, 151.6, 137.7, 134.0, 132.2, 129.1, 123.7, 123.3, 119.6, 110.6, 53.3, 39.4, 36.2, 32.9, 21.5; HPLC Chiralpak AD-H column, 254 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 18.9 and 32.8 min (major); HRMS calcd for $C_{19}H_{19}N_2O_2$ $[M + H]^+$ 307.1441, found 307.1442.

(+)-(S)-2-[2-(7-Methylindolin-3-yl)ethyl]isoindoline-1,3-dione ***(2h)***. 84.4 mg, 92% yield; yellow oil; new compound; R_f = 0.47 (2:1:1 hexanes/ethyl acetate/dichloromethane); 90.7:9.3 er; $[\alpha]^{20}_D$ = +54.12 (*c* 1.06, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.90−7.79 (m, 2H), 7.74−7.68 (m, 2H), 7.02 (d, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 7.4 Hz, 1H), 6.65 (t, *J* = 7.4 Hz, 1H), 3.84−3.76 (m, 3H), 3.41−3.31 (m, 2H), 2.26−2.17 (m, 1H), 2.12 (s, 3H), 2.00−1.89 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.5, 149.8, 134.0, 132.3, 131.3, 128.7, 123.3, 121.5, 119.2, 119.1, 53.0, 40.1, 36.2, 32.9, 16.8; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 14.8 and 19.8 min (major); HRMS calcd for $C_{19}H_{19}N_2O_2$ $[M + H]^+$ 307.1441, found 307.1442.

(+)-(S)-2-[2-(5-Methoxyindolin-3-yl)ethyl]isoindoline-1,3-dione ***(2i)***. 91.2 mg, 94% yield; orange oil; new compound; R_f = 0.59 (2:1:1 hexanes/ethyl acetate/dichloromethane); 86.8:13.2 er; $[\alpha]^{20}_D$ = +40.45 (*c* 1.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.85−7.79 (m, 2H), 7.72−7.68 (m, 2H), 6.78 (s, 1H), 6.59−6.53 (m, 2H), 3.83−3.74 (m, 3H), 3.72 (s, 3H), 3.51 (s, 1H), 3.36−3.23 (m, 2H), 2.24−2.14 (m, 1H), 1.99−1.88 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.4, 153.6, 145.0, 134.0, 133.6, 132.1, 123.2, 113.0, 110.5, 56.0, 53.5, 40.2, 36.0, 32.4; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 25.8 and 48.5 min (major); HRMS calcd for $C_{19}H_{19}N_2O_3$ $[M + H]^+$ 323.1390, found 323.1395.

(+)-(S)-2-[2-(5-Chloroindolin-3-yl)ethyl]isoindoline-1,3-dione ***(2j)***. 97.7 mg, >99% yield; yellow solid; mp 133−134 °C; new compound; R_f = 0.19 (5:1 hexanes/ethyl acetate); 83.2:16.8 er; $[\alpha]^{20}_D$ = +44.44 (*c* 0.95, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.86−7.80 (m, 2H), 7.73−7.68 (m, 2H), 7.07 (s, 1H), 6.96−6.86 (m, 1H), 6.54−6.43 (m, 1H), 3.90−3.60 (m, 4H), 3.42−3.34 (m, 1H), 3.33−3.23 (m, 1H), 2.21−2.10 (m, 1H), 1.98−1.88 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.4, 150.0, 134.1, 133.7, 132.1, 127.5, 124.2, 123.3, 123.1, 110.2, 53.2, 39.6, 35.8, 32.5; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 15.8 and 25.6 min (major); HRMS calcd for $C_{18}H_{16}ClN_2O_2$ $[M + H]^+$ 327.0895 (^{35}Cl) and 329.0872 (^{37}Cl), found 327.0894 (^{35}Cl) and 329.0858 (^{37}Cl).

(+)-(S)-3-(Indolin-3-yl)-1-(pyrrolidin-1-yl)propan-1-one ***(2k)***. 61.1 mg, 83% yield; pale yellow oil; new compound; R_f = 0.28 (1:1:1 hexanes/ethyl acetate/dichloromethane); 93.0:7.0 er; $[\alpha]^{20}_D$ = +53.43 (*c* 1.02, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 7.3 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 3.68 (t, *J* = 8.7 Hz, 1H), 3.45 (t, *J* = 6.8 Hz, 2H), 3.40−3.32 (m, 3H), 3.26−3.20 (m, 1H), 2.40−2.26 (m, 2H), 2.21−2.11 (m, 1H), 1.98−1.88 (m, 3H), 1.87−1.79 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.3, 151.5, 132.4, 127.6, 124.1, 118.6, 109.6, 53.2, 46.6, 45.7, 41.6, 32.2, 29.1, 26.2, 24.4; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 17.3 min (major) and 19.9 min; HRMS calcd for $C_{15}H_{21}N_2O$ $[M + H]^+$ 245.1648, found 245.1651.

(+)-(S)-3-(Indolin-3-yl)-1-(piperidin-1-yl)propan-1-one ***(2l)***. 65.6 mg, 85% yield; white solid; mp 94−95 °C; new compound; R_f = 0.19 (2:1:1 hexanes/ethyl acetate/dichloromethane); 94.4:5.6 er; $[\alpha]^{20}_D$ = +50.05 (*c* 0.98, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 7.3 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.71 (t, *J* = 7.4 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 3.69 (t, *J* = 8.7 Hz, 1H), 3.58−3.51 (m, 2H), 3.39−3.31 (m, 3H), 3.26−3.20 (m, 1H), 2.45−2.32 (m, 2H), 2.18−2.08 (m, 1H), 1.95−1.84 (m, 1H), 1.67−1.59 (m, 2H), 1.57−1.47 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.0, 151.5, 132.4, 127.6, 124.1, 118.6, 109.6, 53.2, 46.7, 42.7, 41.6, 30.8, 29.6, 26.6, 25.6, 24.6; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 27.0 min (major) and 30.3 min; HRMS calcd for $C_{16}H_{23}N_2O$ $[M + H]^+$ 259.1805, found 259.1803.

(+)-(S)-1-[3,4-Dihydroquinolin-1(2H)-yl]-3-(indolin-3-yl)propan-1-one ***(2m)***. 87.7 mg, 95% yield; pale yellow oil; new compound; R_f = 0.50 (2:1:1 hexanes/ethyl acetate/dichloromethane); 90.8:9.2 er; $[\alpha]^{20}_D$ = +49.30 (*c* 0.93, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.24−7.04 (m, 4H), 7.02−6.95 (m, 2H), 6.66 (t, *J* = 7.4 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 3.79 (t, *J* = 6.5 Hz, 2H), 3.60−3.54 (m, 1H), 3.29−3.22 (m, 1H), 3.16−3.08 (m, 1H), 2.71 (t, *J* = 6.7 Hz, 2H), 2.59 (t, *J* = 7.7 Hz, 2H), 2.21−2.11 (m, 1H), 1.99−1.89 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.6, 151.4, 139.2, 132.2, 128.6, 127.6, 126.2, 125.4, 124.7, 124.1, 118.6, 109.6, 53.2, 41.5, 32.2, 30.2, 26.9, 24.2; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 31.3 min (major) and 34.6 min; HRMS calcd for $C_{20}H_{23}N_2O$ $[M + H]^+$ 307.1805, found 307.1810.

(+)-(S)-N-Ethyl-3-(indolin-3-yl)-N-phenylpropanamide ***(2n)***. 83.1 mg, 94% yield; colorless viscous liquid; new compound; R_f = 0.41 (2:1:1 hexanes/ethyl acetate/dichloromethane); 93.0:7.0 er; $[\alpha]^{20}_D$ = +34.65 (*c* 1.04, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.45−7.38

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(m, 2H), 7.38−7.32 (m, 1H), 7.16−7.11 (m, 2H), 6.97 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 7.3 Hz, 1H), 6.63 (t, J = 7.3 Hz, 1H), 6.57 (d, J = 7.7 Hz, 1H), 3.75 (q, J = 7.1 Hz, 2H), 3.48 (t, J = 8.7 Hz, 1H), 3.20−3.11 (m, 1H), 2.96 (t, J = 8.1 Hz, 1H), 2.16−2.04 (m, 3H), 1.86−1.74 (m, 1H), 1.11 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.2, 151.4, 142.5, 132.4, 129.8, 128.4, 128.0, 127.5, 124.0, 118.6, 109.5, 53.1, 44.1, 41.6, 32.3, 29.8, 13.2; HPLC Chiralcel OJ-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min; retention times of 34.9 min (major) and 56.6 min; HRMS calcd for $C_{19}H_{23}N_2O$ $[M + H]^+$ 295.1805, found 295.1803.

*(+)-(S)-N,N-Diethyl-3-(indolin-3-yl)propanamide (**2o**).* 61.4 mg, 83% yield; white solid; mp 60−61 °C; new compound; R_f = 0.20 (1:1 hexanes/ethyl acetate); 93.3:6.7 er; $[\alpha]^{20}_D$ = +55.23 (c 1.02, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, J = 7.3 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.71 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.7 Hz, 1H), 3.68 (t, J = 8.6 Hz, 1H), 3.59−3.17 (m, 7H), 2.44−2.30 (m, 2H), 2.21−2.11 (m, 1H), 1.97−1.86 (m, 1H), 1.18−1.07 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.8, 151.5, 132.4, 127.6, 124.1, 118.6, 109.6, 53.3, 42.1, 41.6, 40.2, 30.6, 29.6, 14.5, 13.2; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 10.4 min (major) and 11.7 min; HRMS calcd for $C_{15}H_{23}N_2O$ $[M + H]^+$ 247.1805, found 247.1817.

*(+)-(S)-N-[2-(Indolin-3-yl)ethyl]acetamide (**2p**).* 46.3 mg, 76% yield; pale yellow oil; new compound; R_f = 0.24 (1:2:1 hexanes/ethyl acetate/dichloromethane); 92.4:7.6 er; $[\alpha]^{20}_D$ = +61.12 (c 0.93, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J = 7.3 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.71 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.7 Hz, 1H), 6.08 (s, 1H), 3.67 (t, J = 8.7 Hz, 1H), 3.41−3.12 (m, 5H), 2.02−1.94 (m, 1H), 1.93 (s, 3H), 1.78−1.69 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.3, 151.3, 132.1, 127.8, 124.0, 118.8, 109.7, 53.1, 39.7, 37.5, 34.0, 23.3; HPLC Chiralpak AD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 20.0 and 23.0 min (major); HRMS calcd for $C_{12}H_{17}N_2O$ $[M + H]^+$ 205.1335, found 205.1337.

*(+)-Methyl (S)-3-(Indolin-3-yl)propanoate (**2q**).* 52.3 mg, 85% yield; yellow oil; known compound;[25] R_f = 0.40 (5:1 hexanes/ethyl acetate); 93.0:7.0 er; $[\alpha]^{20}_D$ = +67.97 (c 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, J = 7.3 Hz, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.72 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.8 Hz, 1H), 3.70−3.65 (m, 4H), 3.33−3.26 (m, 1H), 3.23−3.18 (m, 1H), 2.45−2.35 (m, 2H), 2.18−2.08 (m, 1H), 1.94−1.84 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.0, 151.5, 132.0, 127.8, 124.2, 118.7, 109.7, 53.1, 51.7, 41.4, 31.8, 29.3; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 15.4 min (major) and 17.6 min.

*(+)-Ethyl (S)-3-(Indolin-3-yl)propanoate (**2r**).* 58.3 mg, 89% yield; yellow oil; known compound;[11a] R_f = 0.69 (2:1:1 hexanes/ethyl acetate/dichloromethane); 92.8:7.2 er; $[\alpha]^{20}_D$ = +66.80 (c 1.00, $CHCl_3$) [lit.[11a] $[\alpha]^{20}_D$ = −32.4 (c 0.55, $CHCl_3$) for 73:27 er]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, J = 7.3 Hz, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.74−6.68 (m, 1H), 6.63 (d, J = 7.8 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 3.67 (t, J = 8.6 Hz, 1H), 3.56−3.23 (m, 2H), 3.23−3.17 (m, 1H), 2.43−2.33 (m, 2H), 2.18−2.07 (m, 1H), 1.93−1.83 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.5, 151.4, 132.0, 127.8, 124.1, 118.7, 109.7, 60.5, 53.1, 41.4, 32.1, 29.3, 14.3; HPLC Chiralcel OD-H column, 230 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 13.4 min (major) and 15.5 min.

*(+)-Isopropyl (S)-3-(Indolin-3-yl)propanoate (**2s**).* 65.5 mg, 94% yield; colorless viscous liquid; new compound; R_f = 0.54 (5:1 hexanes/ethyl acetate); 92.8:7.2 er; $[\alpha]^{20}_D$ = +59.19 (c 1.09, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, J = 7.3 Hz, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.72 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.8 Hz, 1H), 5.05−4.96 (m, 1H), 3.67 (t, J = 8.5 Hz, 1H), 3.42 (s, 1H), 3.32−3.25 (m, 1H), 3.23−3.18 (m, 1H), 2.40−2.31 (m, 2H), 2.17−2.07 (m, 1H), 1.92−1.82 (m, 1H), 1.23 (d, J = 6.3 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.0, 151.5, 132.1, 127.8, 124.2, 118.7, 109.7, 67.7, 53.2, 41.4, 32.5, 29.4, 21.9; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 10.0 min (major) and 11.4 min; HRMS calcd for $C_{14}H_{20}NO_2$ $[M + H]^+$ 234.1489, found 234.1488.

*(+)-Benzyl (S)-3-(Indolin-3-yl)propanoate (**2t**).* 74.3 mg, 88% yield; colorless viscous liquid; new compound; R_f = 0.34 (5:1 hexanes/ethyl acetate); 93.2:6.8 er; $[\alpha]^{20}_D$ = +55.32 (c 1.06, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.28 (m, 5H), 7.08 (d, J = 7.3 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.70 (t, J = 7.4 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 5.11 (s, 2H), 3.65 (t, J = 8.6 Hz, 1H), 3.32−3.25 (m, 1H), 3.21−3.16 (m, 1H), 2.50−2.39 (m, 2H), 2.19−2.10 (m, 1H), 1.96−1.85 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.3, 151.5, 136.1, 132.0, 128.7, 128.4, 127.8, 124.2, 118.7, 109.7, 66.4, 53.1, 41.4, 32.0, 29.3; HPLC Chiralpak AD-H column, 254 nm, 30 °C, 80:20 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 8.8 and 9.8 min (major); HRMS calcd for $C_{18}H_{20}NO_2$ $[M + H]^+$ 282.1489, found 282.1492.

*(+)-(S)-2-(7-Ethylindolin-3-yl)ethyl Acetate (**2u**).* 61.3 mg, 88% yield; colorless viscous liquid; new compound; R_f = 0.46 (5:1 hexanes/ethyl acetate); 92.3:7.7 er; $[\alpha]^{20}_D$ = +48.01 (c 1.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.97 (d, J = 7.3 Hz, 1H), 6.92 (d, J = 7.5 Hz, 1H), 6.72 (t, J = 7.4 Hz, 1H), 4.25−4.13 (m, 2H), 3.73 (t, J = 8.7 Hz, 1H), 3.42−3.33 (m, 1H), 3.30−3.24 (m, 1H), 2.48 (q, J = 7.6 Hz, 2H), 2.20−2.12 (m, 1H), 2.06 (s, 3H), 1.93−1.83 (m, 1H), 1.22 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.2, 149.2, 131.6, 126.7, 125.3, 121.5, 119.1, 62.9, 53.4, 39.4, 33.1, 24.1, 21.1, 13.3; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 95:5 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 12.4 and 13.2 min (major); HRMS calcd for $C_{14}H_{20}NO_2$ $[M + H]^+$ 234.1489, found 234.1492.

*(+)-(S)-2-(Indolin-3-yl)ethan-1-ol (**2v**).* 24.0 mg, 49% yield; yellow oil; known compound;[26] R_f = 0.56 (5:2.5:0.1 dichloromethane/ethyl acetate/methanol); 94.1:5.9 er; $[\alpha]^{20}_D$ = +51.33 (c 0.60, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, J = 7.3 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.79−6.72 (m, 1H), 6.67 (d, J = 7.8 Hz, 1H), 3.72−3.65 (m, 2H), 3.63−3.56 (m, 1H), 3.48−3.40 (m, 1H), 3.28 (dd, J = 8.8, 5.9 Hz, 1H), 2.89 (s, 2H), 2.12−2.04 (m, 1H), 1.83−1.74 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.1, 132.6, 127.7, 124.2, 119.3, 110.1, 60.8, 53.7, 39.3, 37.2; HPLC Chiralpak AD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 15.0 and 17.5 min (major).

*(+)-(S)-3-Methylindoline (**2w**).* 31.2 mg, 78% yield; yellow oil; known compound;[4b] R_f = 0.50 (10:1 hexanes/ethyl acetate); 88.4:11.6 er; $[\alpha]^{20}_D$ = +30.25 (c 0.78, $CHCl_3$) [lit.[4b] $[\alpha]^{20}_D$ = −38.8 (c 1.04, $CHCl_3$) for 99:1 er]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, J = 7.3 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.73 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.7 Hz, 1H), 3.68 (t, J = 8.6 Hz, 1H), 3.61−3.15 (m, 2H), 3.09 (t, J = 8.6 Hz, 1H), 1.31 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.3, 134.5, 127.4, 123.5, 118.8, 109.6, 55.5, 36.7, 18.7; HPLC Chiralpak IC column, 254 nm, 30 °C, 95:5 *n*-hexane/*i*-PrOH, flow rate of 0.5 mL/min, retention times of 11.1 and 12.7 min (major).

*(+)-(S)-3-Benzylindoline (**2x**).* 53.4 mg, 85% yield; pale yellow oil; known compound;[11a] R_f = 0.35 (2:1 hexanes/dichloromethane); 90.6:9.4 er; $[\alpha]^{20}_D$ = +63.01 (c 1.07, $CHCl_3$) [lit.[11a] $[\alpha]^{20}_D$ = −18.1 (c 0.81, $CHCl_3$) for 77.5:22.5 er]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.25 (m, 2H), 7.23−7.18 (m, 3H), 7.03 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 7.3 Hz, 1H), 6.68 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.8 Hz, 1H), 3.63−3.55 (m, 1H), 3.55−3.28 (m, 2H), 3.24 (dd, J = 8.7, 6.5 Hz, 1H), 3.09 (dd, J = 13.7, 5.9 Hz, 1H), 2.79 (dd, J = 13.7, 9.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.5, 140.2, 132.5, 129.1, 128.5, 127.8, 126.3, 124.2, 118.6, 109.7, 53.0, 43.7, 40.5; HPLC Chiralpak AD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 7.3 and 8.8 min (major).

*(+)-(S)-3-Phenylindoline (**2y**).* 56.3 mg, 96% yield; pale yellow oil; known compound;[24] R_f = 0.42 (20:1 hexanes/ethyl acetate), 93.3:6.7 er; $[\alpha]^{20}_D$ = +23.38 (c 0.93, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.19 (m, 5H), 7.06 (t, J = 7.6 Hz, 1H), 6.90 (d, J = 7.7 Hz, 1H), 6.70 (t, J = 7.1 Hz, 2H), 4.47 (t, J = 9.0 Hz, 1H), 3.91 (t, J = 9.1 Hz, 1H), 3.58−3.19 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.7, 143.7, 132.5, 128.7, 128.3, 127.9, 126.8, 125.1, 119.2, 109.9, 56.8,

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48.8; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 95:5 *n*-hexane/*i*-PrOH, flow rate of 0.5 mL/min, retention times of 19.3 min (major) and 25.6 min.

*(+)-(S)-3-(p-Tolyl)indoline (**2z**).* 58.9 mg, 94% yield; yellow oil; new compound; R_f = 0.61 (10:1 hexanes/ethyl acetate); 89.0:11.0 er; $[\alpha]^{20}_D$ = +17.31 (*c* 0.98, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.10 (m, 4H), 7.09−7.03 (m, 1H), 6.93−6.87 (m, 1H), 6.75−6.65 (m, 2H), 4.45 (t, *J* = 9.1 Hz, 1H), 3.90 (t, *J* = 9.1 Hz, 1H), 3.46 (t, *J* = 9.0 Hz, 1H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.7, 140.6, 136.3, 132.6, 129.4, 128.2, 127.8, 125.1, 119.1, 109.8, 56.9, 48.4, 21.1; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 95:5 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 9.5 min (major) and 12.2 min; HRMS calcd for $C_{15}H_{16}N$ $[M + H]^+$ 210.1277, found 210.1278.

*(+)-(S)-3-(4-Chlorophenyl)indoline (**2aa**).* 58.1 mg, 84% yield; pale pink oil; new compound; R_f = 0.5 (10:1 hexanes/ethyl acetate); 91.7:8.3 er; $[\alpha]^{20}_D$ = +36.53 (*c* 0.95, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.24 (m, 2H), 7.21−7.16 (m, 2H), 7.10−7.04 (m, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.74−6.67 (m, 2H), 4.44 (t, *J* = 8.8 Hz, 1H), 3.91 (t, *J* = 9.1 Hz, 1H), 3.43 (t, *J* = 8.7 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.6, 142.3, 132.6, 132.0, 129.6, 128.8, 128.1, 125.0, 119.3, 110.0, 56.6, 48.2; HPLC Chiralcel OD-H column, 254 nm, 30 °C, 95:5 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 14.4 min (major) and 17.6 min; HRMS calcd for $C_{14}H_{13}ClN$ $[M + H]^+$ 230.0731 (^{35}Cl) and 232.0705 (^{37}Cl), found 230.0732 (^{35}Cl) and 232.0701 (^{37}Cl).

*(+)-(S)-3-(Tetrahydro-2H-pyran-4-yl)indoline (**2ab**).* 60.4 mg, 99% yield; pale yellow oil; new compound; R_f = 0.55 (5:1 hexanes/ethyl acetate); 87.4:12.6 er; $[\alpha]^{20}_D$ = +57.89 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 7.8 Hz, 1H), 4.01−3.95 (m, 2H), 3.57 (t, *J* = 9.2 Hz, 1H), 3.44−3.39 (m, 1H), 3.38−3.30 (m, 2H), 3.19−3.13 (m, 1H), 1.89−1.79 (m, 1H), 1.69−1.62 (m, 1H), 1.51−1.39 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.0, 130.6, 127.8, 125.1, 118.4, 109.6, 68.3 (d), 49.7, 47.3, 38.6, 31.0, 29.5; HPLC Chiralpak AS-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min; retention times of 8.2 and 9.9 min (major); HRMS calcd for $C_{13}H_{18}NO$ $[M + H]^+$ 204.1383, found 204.1387.

Experiment on a Gram Scale. Ligand (2*R*,2′*R*,3*R*,3′*R*)-Wing-Phos (18.2 mg, 0.0246 mmol, 0.6 mol %) and palladium trifluoroacetate (6.8 mg, 0.0205 mmol, 0.5 mol %) were placed in a dried Schlenk tube under a nitrogen atmosphere, and degassed anhydrous acetone was added. The mixture was stirred at room temperature for 1 h. The solvents were removed under reduced pressure to give the catalyst. In a glovebox, L-CSA (1.138 g, 4.9 mmol) and 3-substituted indole **1a** (1.190 g, 4.1 mmol) were stirred in 4.0 mL of a mixed solvent [2,2,2-trifluoroethanol and benzene were mixed in a 2:1 (v/v) ratio before use] at room temperature for 5 min. Subsequently, the catalyst solution described above together with 14.0 mL of a mixed solvent was added to the reaction mixture, and then the mixture was transferred to an autoclave, which was charged with hydrogen gas (700 psi). The autoclave (300 mL volume, 2.5 in. inner diameter, and 4.0 in. inner depth) was stirred with a magnetic bar at a rate of 450 rpm at 60 °C for 26 h. After the careful release of hydrogen gas, the resulting mixture was concentrated under vacuum and dissolved in a saturated aqueous sodium bicarbonate solution (25 mL). After the mixture had been stirred for 10 min, the aqueous phase was extracted with dichloromethane (3 × 15 mL). The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography (6:1:1 to 4:1:1 hexanes/ethyl acetate/dichloromethane) to give chiral reductive product (+)-**2a** (1.135 g, 95% isolated yield, and 91.8:8.2 er).

Recovery of Camphorsulfonic Acid. To the extracted aqueous phase was added concentrated hydrochloric acid (3.0 mL, 12 mol/L), and the mixture was concentrated under reduced pressure. To the residue was added acetone (50 mL), and the mixture was filtered through Celite and washed with acetone. The combined filtrate was evaporated under reduced pressure to afford camphorsulfonic acid (1.085 g, 95% yield).

Synthesis of (+)-(*S*)-2-(Indolin-3-yl)ethan-1-amine (3). To a stirred solution of chiral (*S*)-**2a** (58.1 mg, 0.2 mmol, >99.5:0.5 er) (upgrade to >99.5:0.5 er by recrystallization with dichloromethane/*n*-hexane in 38% yield) in ethanol (5.0 mL) was added hydrazine monohydrate (0.24 mL, 4.0 mmol), and the resulting mixture was stirred at 60 °C for 1 h. The cooled mixture was concentrated under reduced pressure, and then water (10 mL) was added to the residue. The aqueous phase was extracted with dichloromethane (3 × 15 mL). The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel using a 10:1 dichloromethane/methanol eluent to afford chiral diamine (*S*)-**3**: 31.1 mg, 96% yield; pale yellow oil; known compound;[27] R_f = 0.40 (10:1 dichloromethane/methanol); >99.5:0.5 er; $[\alpha]^{20}_D$ = +49.87 (*c* 0.78, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 3.68 (t, *J* = 8.6 Hz, 1H), 3.38−3.30 (m, 1H), 3.24−3.18 (m, 1H), 2.80 (t, *J* = 7.4 Hz, 2H), 2.42−1.93 (m, 3H), 1.75−1.65 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.4, 132.8, 127.6, 123.9, 118.8, 109.7, 53.6, 40.3, 39.9, 38.3; er determined by HPLC analysis of the corresponding *N*-Boc derivative; HPLC Chiralcel OJ-H column, 254 nm, 30 °C, 98:2 *n*-hexane/*i*-PrOH, flow rate of 0.8 mL/min; retention times of 16.2 min (major) and 19.3 min.

Synthesis of (+)-(*S*)-3-[3-(Piperidin-1-yl)propyl]indoline (4). To a stirred solution of chiral **2l** (77.2 mg, 0.3 mmol, 94.4:5.6 er) in tetrahydrofuran (2.0 mL) at 0 °C was added a borane−tetrahydrofuran complex (3.0 mL, 1.0 M in tetrahydrofuran), and the mixture was left to stir overnight at room temperature. The reaction was quenched by the addition of methanol, and the volatiles were removed under reduced pressure. The crude residue was purified by column chromatography on silica gel (5:1:1 hexanes/ethyl acetate/dichloromethane) to give the desirable chiral amine (*S*)-**4**: 60.6 mg, 83% yield; colorless viscous oil; new compound; R_f = 0.67 (20:1 dichloromethane/methanol); 94.6:5.4 er; $[\alpha]^{20}_D$ = +34.28 (*c* 0.67, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13−6.97 (m, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.00−3.50 (m, 2H), 3.34−3.19 (m, 2H), 3.13−3.03 (m, 2H), 2.99−2.86 (m, 4H), 1.85−1.49 (m, 10H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.4, 132.5, 127.8, 123.9, 118.7, 109.7, 55.0 (d), 53.3, 41.7, 31.9, 22.7, 20.5, 19.7; HPLC Chiralpak AD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min; retention times of 22.7 and 29.6 min (major); HRMS calcd for $C_{16}H_{25}N_2$ $[M + H]^+$ 245.2012, found 245.2014.

Synthesis of (+)-(*S*)-3-(Indolin-3-yl)propan-1-ol (5). To a stirred solution of chiral **2q** (49.4 mg, 0.24 mmol, 93.0:7.0 er) in tetrahydrofuran (3.0 mL) at 0 °C was added the borane−tetrahydrofuran complex (0.48 mL, 1.0 M in tetrahydrofuran). The mixture was allowed to warm to room temperature. After the reaction had reached completion (monitored by TLC), the reaction was quenched by addition of methanol, and the volatiles were removed under reduced pressure. The residue was purified by column chromatography on silica gel (5:2.5:0.1 dichloromethane/ethyl acetate/methanol) to give the desired (*S*)-**5**: 25.8 mg, 61% yield; yellow viscous oil; known compound;[28] R_f = 0.35 (5:2.5:0.1 dichloromethane/ethyl acetate/methanol): 92.8:7.2 er; $[\alpha]^{20}_D$ = +52.00 (*c* 0.43, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.72 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.7 Hz, 1H), 3.74−3.62 (m, 3H), 3.34−3.18 (m, 2H), 2.42 (s, 2H), 1.94−1.84 (m, 1H), 1.71−1.58 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.4, 133.0, 127.6, 124.0, 118.8, 109.8, 63.0, 53.5, 41.9, 30.6, 30.4; HPLC Chiralpak AD-H column, 254 nm, 30 °C, 90:10 *n*-hexane/*i*-PrOH, flow rate of 1.0 mL/min, retention times of 15.5 and 18.5 min (major).

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.2c00702.

NMR spectra and HPLC spectra of the products (PDF)

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Notes

The authors declare no competing financial interest.

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