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Catalytic asymmetric hydrogenation of indoles using a rhodium complex with a chiral bisphosphine ligand PhTRAP

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This paper is dedicated to Professor Jack Halpern on the occasion of his 80th birthday

Abstract—Highly enantioselective hydrogenation of N-protected indoles was successfully developed by use of the rhodium catalyst generated in situ from $[Rh(nbd)_2]SbF_6$ and the chiral bisphosphine PhTRAP, which can form a *trans*-chelate complex with a transition metal atom. The PhTRAP–rhodium catalyst required a base (e.g., Cs_2CO_3) for the achievement of high enantioselectivity. Various 2-substituted *N*-acetylindoles were converted into the corresponding chiral indolines with up to 95% ee. The hydrogenations of 3-substituted *N*-tosylindoles yielded indolines possessing a stereogenic center at the 3-position with high enantiomeric excesses (up to 98% ee).

1. Introduction

Catalytic asymmetric hydrogenation of prochiral unsaturated compounds is regarded as a versatile method in synthetic organic chemistry.[1] The enantioselective hydrogenations of olefins, ketones, and imines have been intensively studied and are widely utilized for preparing optically active compounds in industrial production as well as on a laboratory scale. Meanwhile, catalytic asymmetric hydrogenation of aromatic functionality is expected to be useful for organic synthesis.[2,3] In particular, the asymmetric reduction of heteroaromatics could offer a straightforward approach to various optically active heterocycles, if it could be conducted successfully on a routine basis. Chiral heterocyclic skeletons are often found in biologically active compounds.[4] However, such an asymmetric hydrogenation has been rare despite its potential usefulness.

In 1998, Bianchini reported the iridium-catalyzed asymmetric hydrogenation of 2-methylquinoxaline, which was converted into 1,2,3,4-tetrahydro-2-methylquinoxaline with 90% ee.[5] To the best of our knowledge, this is the first example of highly enantioselective hydrogenation of aromatic functionality, but the asymmetric catalysis was proven effective for the hydrogenation of 2-methylquinoxaline only. Furthermore, the yield of the chiral heterocyclic product was not satisfactory. In a preliminary communication, we reported the rhodium-catalyzed asymmetric hydrogenation of 2-substituted indoles.[6] Characteristically, the asymmetric reaction proceeded with high enantioselectivity only when *trans*-chelate chiral bisphosphine PhTRAP[7] (Fig. 1) was used as a chiral ligand. A wide range of indoles, including 3-substituted ones,[8] were transformed into chiral indolines with high ee values by the PhTRAP–rhodium catalyst. Subsequently, 2-substituted quinolines[9] and *N*-iminopyridinium ylides[10] were successfully hydrogenated with high stereoselectivity by means of asymmetric catalysis.[11] Herein, we report the asymmetric hydrogenation of 2- and 3-substituted indoles catalyzed by PhTRAP–rhodium catalyst. Previously, we reported that the hydrogenation of *N*-acyl indoles was promoted with high efficiency by a rhodium catalyst generated from Rh(acac)(cod) and triphenylphosphine.[12] The present

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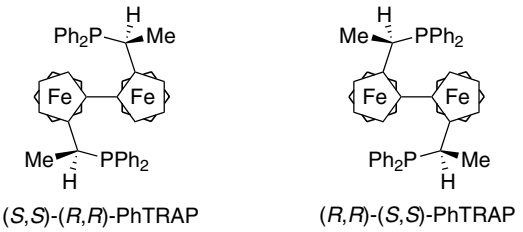


Figure 1. Structure of PhTRAP.

asymmetric hydrogenation of indoles is based on the Rh(acac)(cod)–PPh_3 catalyst.

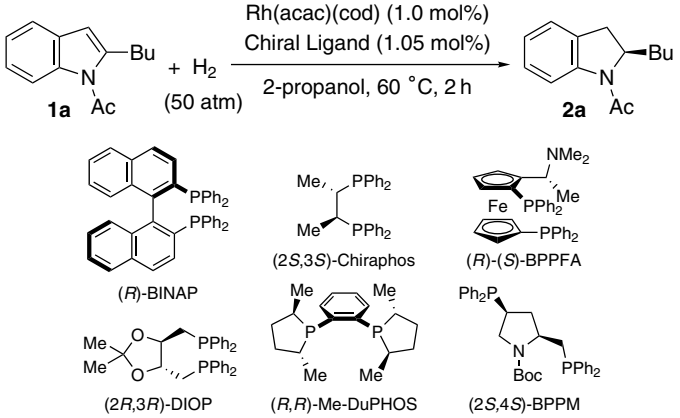
2. Results and discussion

2.1. Development of asymmetric catalysis for hydrogenation of indoles

Toward the development of highly enantioselective hydrogenation of indoles, we evaluated a broad range of chiral bidentate phosphine ligands for the asymmetric hydrogenation of *N*-acetyl-2-butylindole **1a** by using Rh(acac)(cod). The evaluation of chiral ligands was conducted with 1 mol % rhodium at 60 °C for 2 h. The representative results are shown in Table 1. The hydrogenation of **1a** quantitatively gave 2-butylindoline **2a** by use of various commercially available chiral phosphines, but the product was almost racemic in every case (entries 1–6). However, only the (*S*,*S*)-(*R*,*R*)-PhTRAP ligand, able to form a *trans*-chelate metal complex, was found to exhibit high enantioselectivity (entry 7).

Table 2 summarizes the effects of the rhodium catalyst precursor and additive on the hydrogenation of **1a** using the (*S*,*S*)-(*R*,*R*)-PhTRAP ligand. When $[Rh(nbd)_2]SbF_6$ and $[RhCl(cod)]_2$ were used as a catalyst precursor with no additives, the hydrogenation of **1a** scarcely proceeded to give a small amount of **2a** with very low enantioselectivity (entries 1 and 2). In contrast, (hydroxo)rhodium complex produced (*R*)-**2a** with a good ee value as well as Rh(acac)(cod) did (entry 3). These findings suggest that the basicity of the hydroxo or acetylacetonato ligand might be essential for achieving a high level of asymmetric induction as well as the catalytic activity of PhTRAP–rhodium catalyst. The ee values of **2a** were enhanced to 93% when the catalytic hydrogenation was conducted in the presence of 10% cesium carbonate and PhTRAP–Rh(acac)(cod) catalyst (entry 4). In the presence of a base, $[Rh(diene)_2]^+$ and $[RhCl(diene)]_2$ worked as good catalyst precursors, and gave **2a** with high enantiomeric excess (entries 5–8). 2,5-Norbornadiene-ligated rhodium complexes exhibited somewhat higher catalytic activity than 1,5-cyclooctadiene-ligated ones, whereas the diene ligand scarcely influenced the enantioselectivity. Cesium carbonate merely acted as a base because the PhTRAP–rhodium catalyst gave **2a** with 92–94% ee in the presence of other bases, including tertiary amines (entries 9, 11, and 12). However, the use of potassium carbonate or diisopropylamine resulted in lower enantioselectivities (entries 10 and 13). It is possible that the insolubility of potassium carbonate obstructed the generation of the catalyst species. The active hydrogen of the secondary amine might cause the formation of an undesirable rhodium species in the latter case. No consumption of **1a** was observed during hydrogenation using pyridines as an additive (entries 14 and 15). The tight coordination of pyridine to rhodium

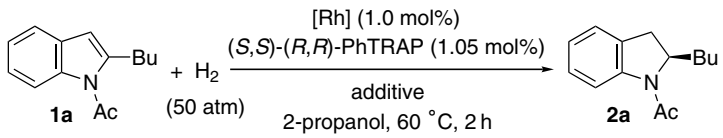
Table 1. Evaluation of chiral ligands for the hydrogenation of 2-butylindole **1a**



Entry	Chiral ligand	Yield (%)[a]	ee (%)[b]
1	(*R*)-BINAP	100	1 (*S*)
2	(2*S*,3*S*)-Chiraphos	100	1 (*S*)
3	(*R*)-(*S*)-BPPFA	100	0
4	(−)-(2*R*,3*R*)-DIOP	100	0
5	(*R*,*R*)-Me-DuPHOS	100	0
6	(2*S*,4*S*)-BPPM	100	0
7	(*S*,*S*)-(*R*,*R*)-PhTRAP	77	85 (*R*)

[a] Yields were determined by ^1H NMR spectra of crude mixture.
[b] ees were determined by chiral HPLC. Absolute configurations are given in parentheses.

Table 2. Effects of rhodium catalyst precursor and additive



Entry	[Rh]	Additive[a]	Yield (%)[b]	ee (%)[c]
1	$[Rh(nbd)]_2SbF_6$	—	<5	7 (*S*)
2	$[RhCl(cod)]_2$	—	9	33 (*R*)
3	$[Rh(OH)(cod)]_2$	—	53	85 (*R*)
4	Rh(acac)(cod)	Cs_2CO_3 (10)	100	93 (*R*)
5	$[RhCl(cod)]_2$	Cs_2CO_3 (10)	68	94 (*R*)
6	$[RhCl(nbd)]_2$	Cs_2CO_3 (10)	86	95 (*R*)
7	$[Rh(cod)_2]BF_4$	Cs_2CO_3 (10)	55	94 (*R*)
8	$[Rh(nbd)_2]SbF_6$	Cs_2CO_3 (10)	100 (94)	94 (*R*)
9	$[Rh(nbd)_2]SbF_6$	K_3PO_4 (10)	100	93 (*R*)
10	$[Rh(nbd)_2]SbF_6$	K_2CO_3 (10)	44	76 (*R*)
11	$[Rh(nbd)_2]SbF_6$	Et_3N (10)	100	94 (*R*)
12	$[Rh(nbd)_2]SbF_6$	*i*-Pr_2NEt (10)	100	92 (*R*)
13	$[Rh(nbd)_2]SbF_6$	*i*-Pr_2NH (10)	99	78 (*R*)
14	$[Rh(nbd)_2]SbF_6$	Pyridine (10)	0	—
15	$[Rh(nbd)_2]SbF_6$	DMAP (10)	0	—
16	$[Rh(nbd)_2]SbF_6$	Cs_2CO_3 (20)	100	94 (*R*)
17	$[Rh(nbd)_2]SbF_6$	Cs_2CO_3 (5)	100	95 (*R*)
18	$[Rh(nbd)_2]SbF_6$	Cs_2CO_3 (1)	100	94 (*R*)

[a] Equivalents of additive to rhodium are given in parentheses.
[b] Yields were determined by ^1H NMR spectra of crude mixture. Isolated yield is shown in parentheses.
[c] ees were determined by chiral HPLC. Absolute configurations are given in parentheses.

might prohibit the indole substrate from interacting with the rhodium. The ratio of base to rhodium was not essential for high enantioselectivity (entries 16–18).

The hydrogenation of **1a** proceeded in solvents other than 2-propanol, but the use of toluene, 1,2-dichloroethane, or THF diminished slightly the enantiomeric excess of **2a** (Table 3, entries 1–3). No hydrogenation occurred in methanol, which caused the alcoholysis of *N*-acetyl group in **1a** (entry 4). The catalytic hydrogenation of **1a** can be conducted at a lower hydrogen pressure (10 atm) without any significant loss of reaction rate and enantioselectivity (entry 5). The catalyst loading was successfully reduced to 0.1 mol % when the hydrogenation was conduced at 100 atm of hydrogen pressure (entry 6).

2.2. Catalytic asymmetric hydrogenation of 2-substituted indoles

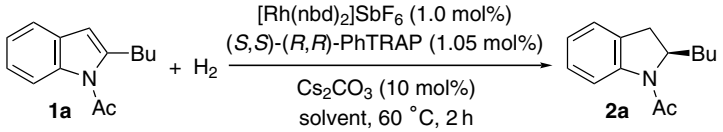
As shown in Table 4, various 2-substituted indoles **1** were subjected to asymmetric hydrogenation with the PhTRAP–rhodium–Cs_2CO_3 catalyst system. Indole **1b** possessing a β-branched primary alkyl group was hydrogenated into indoline **2b** with high enantiomeric excess (entry 1). However, the secondary alkyl group at the 2-position of **1c** hindered the catalytic hydrogenation, and the product **2c** was obtained with low ee value (entry 2). The reactions of **1d** and **1e** proceeded with 87% and 79% ee, respectively (entries 3 and 4). In the case of **1e**, a higher temperature and hydrogen pressure (100 °C, 100 atm) were favorable to achieving higher enantioselectivity. Moreover, the enantioselectivity was successfully improved to 95% ee by using triethylamine in place of cesium carbonate (entry 5). The ee values of **2** were scarcely affected by the steric and electronic properties of the substituent on the fused aromatic ring of **1** (entries 6–9).

The protective group on the nitrogen of **1** was crucial for high enantioselection by the PhTRAP–rhodium catalyst. When 2-alkylindole protected by *p*-toluenesulfonyl or *tert*-butoxycarbonyl group was used as a substrate, the asymmetric hydrogenation yielded the corresponding N-protected 2-alkylindoline with 77–78% ee (entries 10 and 11). A sulfonyl group on the nitrogen seemed to cause diminution of the reaction rate.

2.3. Catalytic asymmetric hydrogenation of 3-substituted indoles

Next, we challenged the catalytic asymmetric hydrogenation of 3-substituted indoles. The hydrogenation of *N*-acetyl-3-methylindole **3a** was conducted in 2-propanol at 80 °C for 2 h by means of the (*S*,*S*)-(*R*,*R*)-PhTRAP–$[Rh(nbd)_2]SbF_6$–Cs_2CO_3 catalyst system, which is the most effective for the reaction of 2-substituted indoles. The chiral rhodium catalyst promoted the hydrogenation of **3a** with good enantioselectivity (Scheme 1). However, the hydrogenation competed with undesirable alcoholysis of the *N*-acetyl group, which gave 3-methylindole **5** in 58% yield. Therefore, our initial effort was focused on suppressing the solvolysis of the N-protecting group. The undesired reaction can be suppressed by the use of organic or insoluble bases (triethylamine, potassium carbonate, etc.), but the ee values

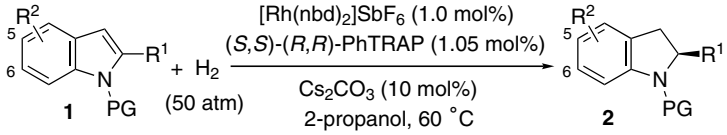
Table 3. Effect of reaction conditions



Entry	Solvent	H_2 pressure (atm)	Yield (%)[a]	ee (%)[b]
1	Toluene	50	92	91 (*R*)
2	$ClCH_2CH_2Cl$	50	53	87 (*R*)
3	THF	50	52	84 (*R*)
4	MeOH	50	0	—
5	*i*-PrOH	10	100 (94)	92 (*R*)
6[c]	*i*-PrOH	100	100 (92)	93 (*R*)

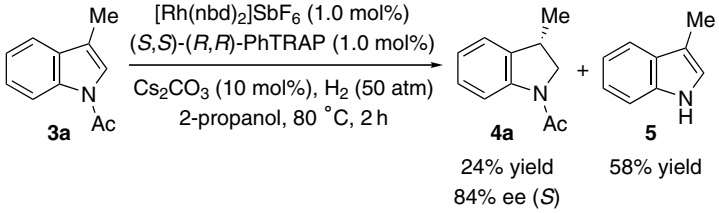
[a] Yields were determined by ^1H NMR spectra of crude mixture. Isolated yields are given in parentheses.
[b] ees were determined by chiral HPLC. Absolute configurations are given in parentheses.
[c] The reaction was conducted in the presence of 0.1 mol % PhTRAP–rhodium catalyst.

Table 4. Catalytic asymmetric hydrogenation of 2-substituted indoles **1**



Entry	Substrate				Time (h)	Product		
	R^1	R^2	PG	**1**		**2**	Yield (%)[a]	ee (%)[b]
1	*i*-Bu	H	Ac	**1b**	2	**2b**	91	91
2	*c*-C_6H_{11}	H	Ac	**1c**	3	**2c**	(27)	19
3	Ph	H	Ac	**1d**	1	**2d**	91	87
4	CO_2Me	H	Ac	**1e**	2	**2e**	86	79 (*S*)
5[c]	CO_2Me	H	Ac	**1e**	0.5	**2e**	95	95 (*S*)
6	Bu	5-Me	Ac	**1f**	2	**2f**	94	94
7	Bu	5-CF_3	Ac	**1g**	2	**2g**	84	92
8	Bu	6-CF_3	Ac	**1h**	2	**2h**	83	92
9	Bu	6-MeO	Ac	**1i**	2	**2i**	98	94
10	Me	H	Ts	**1j**	2	**2j**	45	78 (*R*)
11	Bu	H	Boc	**1k**	2	**2k**	94	77[d] (*R*)

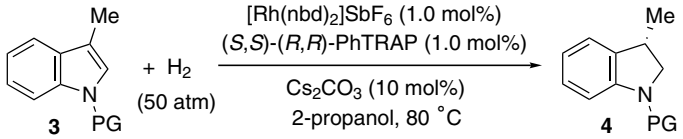
[a] Isolated yield. Yield in parentheses was estimated by ^1H NMR spectrum of the crude reaction mixture.
[b] ees were determined by chiral HPLC.
[c] The reaction was conducted at 100 °C and 100 atm. Triethylamine was used in place of cesium carbonate.
[d] The enantiomeric excess was determined by HPLC analysis of **2a** derived from the hydrogenation product **2k**.



Scheme 1. Hydrogenation of *N*-acetyl-3-methylindole **3a**.

of the resulting products were lower than 10% ee. No hydrogenation occurred in aprotic solvent such as acetonitrile, THF, toluene, and so on. When indole **3b** protected by *tert*-butoxycarbonyl was employed as a substrate, no deprotection of the N-protective group was observed even in the presence of cesium carbonate but the enantiomeric excess of indoline **4b** was only 16% (Table 5, entry 1). The use of sulfonyl protective groups dramatically improved the enantiomeric excess as well as the yield of the desired product. Tosyl-protected 3-methylindole **3c** was converted into (*S*)-3-methyl-*N*-tosylindoline **4c** with 97% ee in 31% yield after 2 h, with no formation of **5** (entry 2). Furthermore, the yield of **4c** was improved to 96% without the loss of the ee value by prolonging the reaction time to 24 h (entry 3). The antipode (*R*)-**4c** was obtained with 98% ee when

Table 5. Hydrogenation of 3-methylindoles **3**



Entry	PG (**3**)	Time (h)	Product	Yield (%)[a]	ee (%)[b]
1	Boc (**3b**)	2	**4b**	14	16
2	Ts (**3c**)	2	**4c**	31	97 (*S*)
3	Ts (**3c**)	24	**4c**	100 (96)	98 (*S*)
4[c]	Ts (**3c**)	24	**4c**	100 (98)	98 (*R*)
5	Ms (**3d**)	24	**4d**	92 (83)	94
6	Tf (**3e**)	24	**4e**	100 (93)	94

[a] Yields were determined by ^{1}H NMR spectra of crude mixture. Isolated yields are given in parentheses.
[b] ees were determined by chiral HPLC. Absolute configurations are given in parentheses.
[c] (*R*,*R*)-(*S*,*S*)-PhTRAP was used.

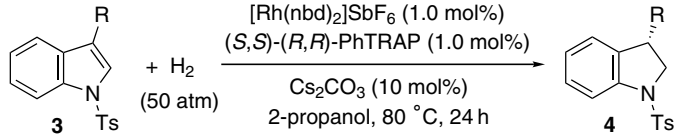
(*R*,*R*)-(*S*,*S*)-PhTRAP was used as a chiral ligand (entry 4). Indoles **3d** and **3e** protected with other sulfonyl groups were also transformed into the corresponding indolines with high enantiomeric excesses by using the PhTRAP–rhodium catalyst (entries 5 and 6). In contrast to the hydrogenation of 2-substituted indoles **1**, no hydrogenation of **3c** occurred in the presence of the rhodium catalysts generated from other phosphine ligands, for example, triphenylphosphine and cis-chelating bisphosphine ligand BINAP.

As shown in Table 6, the hydrogenations of various 3-substituted *N*-tosylindoles were attempted by means of the (*S*,*S*)-(*R*,*R*)-PhTRAP–rhodium catalyst. The indoles **3f** and **3g** possessing a bulky substituent at the 3-position underwent highly enantioselective hydrogenation (entries 1 and 2). The catalytic asymmetric hydrogenation was compatible with a silyl-protected alcohol, Boc-protected amine, and *tert*-butyl ester (entries 3–5). Although the hydrogenation of methyl ester **3k** proceeded with 97% ee, the product **4k** was obtained in low yield (entry 6). The reaction was accompanied by ester exchange of **3k** with 2-propanol, and isopropyl 3-(*N*-tosylindol-3-yl)propionate **3k′** was formed as a side product in 34% yield. This undesirable side reaction may deactivate the PhTRAP–rhodium catalyst, because no hydrogenation product of the isopropyl ester **3k′** was detected by ^{1}H NMR analysis of the crude reaction mixture. (Indol-3-yl)acetate **3l** was converted into **4l** with moderate enantiomeric excess in low yield (entry 7). The enolizable hydrogens of **3l** might cause a decrease in enantioselectivity as well as catalyst turnover number. When 3-acetyl-*N*-tosylindole was used as a substrate, the PhTRAP–rhodium catalyst reduced the ketone carbonyl as well as the indole ring to give 1-(*N*-tosylindolin-3-yl)ethanol quantitatively. The hydrogenation product was obtained as a mixture of two diastereomers (73:27), which were racemic.

2.4. Stereochemistry in the catalytic asymmetric hydrogenation of indoles

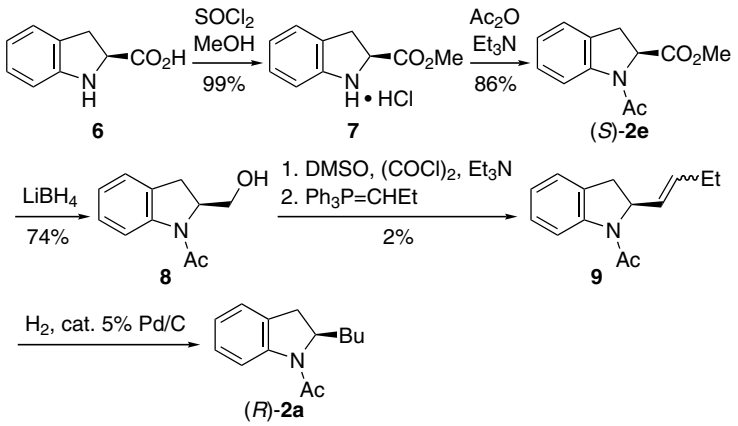
The absolute configurations of the hydrogenation products (−)-**2a** and (−)-**2e** were assigned by comparison with the chiral HPLC data of their authentic samples. The authentic samples were prepared from commercially available (*S*)-indoline-2-carboxylic acid **6** (Scheme 2). The esterification of **6** with methanol and thionyl

Table 6. Catalytic asymmetric hydrogenation of 3-substituted indoles **3**



Entry	R (**3**)	Product	Yield (%)[a]	ee (%)[b]
1[c]	*i*-Pr (**3f**)	**4f**	94	97
2[d]	Ph (**3g**)	**4g**	93	96
3	CH_2CH_2OTBS (**3h**)	**4h**	94	98
4	CH_2CH_2NHBoc (**3i**)	**4i**	71	95
5	$CH_2CH_2CO_2$(*t*-Bu) (**3j**)	**4j**	93	97
6	$CH_2CH_2CO_2Me$ (**3k**)	**4k**	(32)	97
7[d]	CH_2CO_2(*t*-Bu) (**3l**)	**4l**	(29)	62

[a] Isolated yield. Yields in parentheses were estimated by ^{1}H NMR spectrum of the crude reaction mixture.
[b] ees were determined by chiral HPLC.
[c] The reaction was conducted for 48 h.
[d] The reactions were conducted with 2 mol % catalyst.



Scheme 2. Transformation of **6** to authentic (*S*)-**2e** and (*R*)-**2a**.

chloride gave α-amino ester **7** quantitatively. Authentic (*S*)-**2e** was obtained by the N-acetylation of **7** in 86% yield. The ester group of (*S*)-**2e** was reduced with $LiBH_4$. The resulting primary alcohol **8** was subjected to Swern oxidation followed by Wittig olefination. Although the productivity of these processes was very low, 2-substituted indoline **9** was successfully obtained in an amount large enough for HPLC analysis. The hydrogenation of **9** yielded authentic (*R*)-**2a**. The retention times of the authentic (*R*)-**2a** and (*S*)-**2e** in HPLC analysis revealed the configurations of (−)-**2a** and (−)-**2e** produced by the (*S*,*S*)-(*R*,*R*)-PhTRAP–rhodium catalyst to be *R* and *S*, respectively.

The absolute configuration of (+)-**2j**, which was obtained from the (*S*,*S*)-(*R*,*R*)-PhTRAP–rhodium-catalyzed hydrogenation of N-tosyl-protected indole **1j**, was determined by means of an HPLC analysis as mentioned above. An authentic sample of (*R*)-**2j** was prepared by the removal of the Boc group from (*R*)-*N*-Boc-2-methylindoline[13] followed by the reaction of the resulting secondary amine with tosyl chloride. The retention time of the authentic (*R*)-**2j** in HPLC analysis indicated the configuration of (+)-**2j** to be *R*. These stereochemistries of the hydrogenation products **2** indicate that the prochiral face of the indole reacting with hydrogen was not inverted by the N-protecting group or by the substituent at the 2-position of **1**.

In order to determine the stereochemistry of the asymmetric hydrogenation of 3-substituted indoles, the hydrogenation product **4c** was transformed into *N*-benzyl-3-methylindoline, whose correlation between the absolute configuration and specific rotation had been established by Groth.[14] The *N*-tosyl group of (+)-**4c**, which was yielded by the (*S*,*S*)-(*R*,*R*)-PhTRAP–rhodium catalyst, was removed by treatment with sodium bis(methoxyethoxy)aluminum dihydride. Optically active 3-methylindoline was obtained with no racemization at the 3-position.[15] The chiral indoline in hand was alkylated with benzyl chloride to give (+)-*N*-benzyl-3-methylindoline. The sign of the specific rotation indicates that the configuration at the 3-position of (+)-**4c** is *S*. It is noteworthy that the enantioface of **3c** reacting with hydrogen was opposite to that of the 2-substituted indoles **1**. Although the mechanism of the asymmetric hydrogenation remains to be further investigated, the reaction pathway of the reduction of 3-substituted indoles may be different from that of 2-substituted ones.

3. Conclusion

The highly enantioselective hydrogenation of indoles was successfully developed by using a trans-chelating chiral bisphosphine PhTRAP ligand. The rhodium complex generated in situ from $[Rh(nbd)_2]SbF_6$ and PhTRAP in the presence of Cs_2CO_3 was the best catalyst for the asymmetric hydrogenation of indoles. A wide range of 2- and 3-substituted indoles were converted with high enantioselectivities into the indolines possessing a chiral center at their 2- or 3-position. The use of PhTRAP was crucial for achieving the high enantioselectivity in the hydrogenation of indoles. The hydrogenation of 2-substituted indoles **1** proceeded with no stereoselectivity when other chiral bisphosphine ligands were used in place of PhTRAP. In the case of 3-substituted indoles **3**, no hydrogenation occurred in the presence of rhodium complexes modified with other phosphine ligands. To our surprise, the enantiofaces of **1** and **3** reacting with hydrogen were opposite to each other. The observation suggests that the asymmetric hydrogenation of **3** may proceed through a different reaction pathway from that of **1**.

At this stage, the enantioselectivity was significantly affected by the substituent on the nitrogen of the substrate. Acetyl and tosyl groups were the protecting groups of choice for the reaction of 2- and 3-substituted indoles, respectively. However, removal of these protecting groups from the indoline products **2** and **4** usually requires harsh reaction conditions, which is disadvantage for the application of the present hydrogenation to organic synthesis of complex molecules. We will direct our interest to the development of the highly enantioselective hydrogenation of indoles protected with Boc group, which is removable under mild acidic conditions.

4. Experimental

4.1. General

Optical rotations were measured with a JASCO P-1020 polarimeter. NMR spectra were measured with Varian GEMINI-2000 (7.0 T magnet), VXR-200 (4.7 T magnet), or Bruker AVANCE 400 (9.4 T magnet) spectrometer. Flash column chromatographies and preparative TLCs were performed with silica gel 60 (230–400 mesh, Merck) and silica gel 60 PF_{254} (Merck), respectively.

All reactions were conducted under a nitrogen atmosphere unless otherwise noted. Methanol was dried with $Mg(OMe)_2$. Dichloromethane, *N*,*N*-dimethylacetamide (DMA), *N*,*N*-dimethylformamide (DMF), and 2-propanol were dried with CaH_2. Diethyl ether, 1,4-dioxane, tetrahydrofuran (THF), and toluene were dried with sodium-benzophenone ketyl. These dry solvents were distilled under a nitrogen atmosphere before use. N-Acetyl-2-substituted indoles **1a**–**1d**, **1f**–**1i** were prepared from the gold-catalyzed cyclizations of *N*-acetyl-2-(1-alkynyl)anilines.[16] PhTRAP,[7b] $[Rh(nbd)_2]SbF_6$,[17] *N*-Boc-indoles **1k** and **3b**[18] were prepared by the literature procedure. Other materials were commercially available and were used without further purification.

4.2. Methyl *N*-acetylindole-2-carboxylate 1e

Thionyl chloride (21.2 g, 0.18 mol) was added dropwise to dry methanol (50 ml) at 0 °C for 20 min. After 10 min, racemic indoline-2-carboxylic acid (8.16 g, 50 mmol) was added carefully to the solution in small portions for 5 min. The mixture was stirred at room temperature for 21 h, and then evaporated. The residue was crystallized in diethyl ether to give methyl indoline-2-carboxylate hydrochloride (9.75 g, 91%): colorless crystals; ^{1}H NMR (200 MHz, CD_3OD) δ 3.51 (dd, $J = 7.6$, 16.4 Hz, 1H), 3.71 (dd, $J = 9.4$, 16.4 Hz, 1H), 3.89 (s, 3H), 5.09 (dd, $J = 7.6$, 9.4 Hz, 1H), 7.37–7.54 (m, 4H). Triethylamine (4.65 g, 46 mmol) was added to a suspension of methyl indoline-2-carboxylate hydrochloride (4.27 g, 20 mmol) in dry THF (20 ml) at room temperature. After 10 min, acetic anhydride (2.46 g, 24 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (24.4 mg, 0.20 mmol) were added to the suspension. The mixture was stirred at room temperature for 10 h, and then at 40 °C for 3 h. Water was added to the mixture, and then the mixture was extracted with EtOAc. The organic layer was washed with 10% citric acid aq, with saturated Na_2CO_3 aq, then with brine, dried over Na_2SO_4, and was evaporated. The residue was recrystallized from hexane–EtOAc to give methyl *N*-acetylindoline-2-carboxylate (3.89 g, 89%): colorless crystals; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.18 and 2.49 (a pair of br s, 3H), 3.00–3.67 (br m, 2H), 3.77 and 3.74 (a pair of br s, 3H), 4.84–4.98 and 5.10–5.23 (a pair of br m, 1H), 7.03 (t, $J = 7.9$ Hz, 1H), 7.09–7.31 (m, 2H), 8.22 (br d, $J = 7.8$ Hz, 1H). A mixture of methyl *N*-acetylindoline-2-carboxylate (3.89 g, 18 mmol) and DDQ (6.03 g, 27 mmol) in dry toluene (90 ml) was stirred under reflux for 24 h. The mixture was then allowed to cool to room temperature. After the resulting precipitate was filtered off, the filtrate was evaporated. The residue was purified with a flash column chromatography on silica gel (EtOAc/hexane) to give **1e** (3.27 g, 85%): pink solid; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.62 (s, 3H), 3.95 (s, 3H), 7.29 (ddd, $J = 1.0$, 7.1, 7.8 Hz, 1H), 7.33 (d, $J = 0.7$ Hz, 1H), 7.45 (ddd, $J = 1.4$, 7.1, 8.5 Hz, 1H), 7.63 (ddd, $J = 0.7$, 1.4, 7.8 Hz, 1H), 8.13 (dd, $J = 1.0$, 8.5 Hz, 1H).

4.3. 2-Methyl-*N*-tosylindole 1j

The N-tosylations of indoles were carried out by a modified Wenkert procedure.[19] Aqueous sodium hydroxide solution (50%, 7.2 g, 90 mmol) was added to a solution of 2-methylindole (459 mg, 3.5 mmol) and tetrabutylammonium hydrogensulfate (119 mg, 0.35 mmol) in dichloromethane (17.5 ml). A solution of *p*-toluenesulfonyl chloride (1.17 g, 6.1 mmol) in dichloromethane (2.8 ml) was added dropwise to the reaction mixture for 30 min. The two-phase solution was stirred vigorously at room temperature for 5 h, and was poured into water. The resulting mixture was extracted five times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by MPLC (EtOAc/hexane) after passing through a short column on silica gel (EtOAc/hexane = 1/5), giving **1j** (372 mg, 37%): pale pink oil; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.34 (s, 3H), 2.60 (s, 3H), 6.34 (s, 1H), 7.17–7.27 (m, 4H), 7.39 (d, $J = 7.6$ Hz, 1H), 7.66 (d, $J = 8.4$ Hz, 2H), 8.15 (d, $J = 8.3$ Hz, 1H).

4.4. 3-Methyl-*N*-(*p*-toluenesulfonyl)indole 3c (typical procedure of N-tosylation of 3-substituted indoles)

Aqueous potassium hydroxide solution (50%, 10.0 g, 89 mmol) was added dropwise for 20 min to a solution of 3-methylindole (1.31 g, 10.0 mmol), *p*-toluenesulfonyl chloride (2.10 g, 11.0 mmol), and tetrabutylammonium hydrogensulfate (340 mg, 1.0 mmol) in benzene (30 ml). The two-phase solution was stirred vigorously at room temperature for 1 h, and then was poured into water. The resulting mixture was extracted three times with EtOAc. The combined organic layer was washed with brine, dried with Na_2SO_4, and evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving **3c** (2.15 g, 75%): pale brown solid; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.24 (d, $J = 1.2$ Hz, 3H), 2.32 (s, 3H), 7.19 (d, $J = 8.3$ Hz, 2H), 7.20–7.26 (m, 1H), 7.28–7.33 (m, 2H), 7.44 (d, $J = 7.6$ Hz, 1H), 7.74 (d, $J = 8.3$ Hz, 2H), 7.98 (d, $J = 8.2$ Hz, 1H).

4.5. 3-(2-Propyl)-*N*-(*p*-toluenesulfonyl)indole 3f

The procedure for the preparation of **3c** was carried out with 3-(2-propyl)indole[20] (768 mg, 4.8 mmol). The crude product was purified by a flash column chromatography on silica gel (EtOAc/hexane) and recrystallization from EtOAc/hexane, giving **3f** (574 mg, 38%): colorless crystal; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.32 (d,

$J = 6.9$ Hz, 6H), 2.33 (s, 3H), 3.08 (septet, $J = 6.9$ Hz, 1H), 7.18–7.31 (m, 5H), 7.52 (d, $J = 7.7$ Hz, 1H), 7.74 (d, $J = 8.4$ Hz, 2H), 7.96 (d, $J = 8.2$ Hz, 1H).

4.6. 3-Phenyl-*N*-(*p*-toluenesulfonyl)indole 3g

A mixture of 3-bromo-*N*-triisopropylsilylindole[21] (3.51 g, 10 mmol), phenylboronic acid (1.46 g, 12 mmol), cesium carbonate (10.8 g, 33 mmol), $Pd(dba)_2$ (115 mg, 0.20 mmol), and tri(*tert*-butyl)phosphonium tetrafluoroborate[22] (139 mg, 0.48 mmol) in dry THF (20 ml) was stirred under reflux for 18 h. The mixture was diluted with water, and then extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. Tetrabutylammonium fluoride (1.0 M in THF solution, 10 ml, 10 mmol) was added at 0 °C to a solution of the residue in dry THF (30 ml). The reaction mixture was stirred at 0 °C for 20 min and at room temperature for 50 min. The mixture was diluted with water, and then extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving 3-phenylindole (1.74 g, 90%) as a colorless solid. The procedure for the preparation of **3c** was followed with 3-phenylindole (1.70 g, 8.8 mmol) to give **3g** (2.90 g, 95%): colorless crystal; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.34 (s, 3H), 7.23 (d, $J = 8.3$ Hz, 2H), 7.25–7.31 (m, 1H), 7.34–7.39 (m, 2H), 7.43–7.49 (m, 2H), 7.58–7.62 (m, 2H), 7.69 (s, 1H), 7.76–7.83 (m, 3H), 8.06 (d, $J = 8.3$ Hz, 1H).

4.7. 3-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-*N*-(*p*-toluenesulfonyl)indole 3h

tert-Butyldimethylchlorosilane (1.24 g, 8.2 mmol) was added at 0 °C to a solution of 3-(2-hydroxyethyl)indole (1.12 g, 7.0 mmol) and imidazole (1.18 g, 17.3 mmol) in dry DMF (3.0 ml). The solution was stirred for 19 h at room temperature, and then poured into water. The resulting mixture was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. ^{1}H NMR spectrum indicated that the residue was almost pure 3-[2-(*tert*-butyldimethylsilyloxy)ethyl]indole (1.92 g, 100%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 0.00 (s, 6H), 0.87 (s, 9H), 2.96 (t, $J = 7.5$ Hz, 2H), 3.85 (t, $J = 7.5$ Hz, 2H), 6.98 (d, $J = 2.2$ Hz, 1H), 7.03–7.19 (m, 2H), 7.27–7.34 (m, 1H), 7.54–7.61 (m, 1H), 7.96–8.16 (br, 1H). A solution of the silyl-protected compound (1.65 g, 6.0 mmol) in dry THF (12 ml) was added at 0 °C to a suspension of sodium hydride (60% in oil, 299 mg, 7.5 mmol) in dry THF (36 ml). After the mixture was stirred at room temperature for 1 h, a solution of *p*-toluenesulfonyl chloride (1.21 g, 6.4 mmol) in dry THF (12 ml) was added at room temperature to the reaction mixture. After 24 h, the mixture was monitored by TLC and ^{1}H NMR analysis. Until no unreacted starting material was detected in the mixture, addition of sodium hydride and *p*-toluenesulfonyl chloride as mentioned above was repeated (two or three times). The resulting mixture was diluted with water, and extracted three times with EtOAc. The combined organic layer was washed with saturated Na_2CO_3 aq, with brine, dried over $MgSO_4$, and evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving **3h** (2.34 g, 91%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ –0.02 (s, 6H), 0.87 (s, 9H), 2.33 (s, 3H), 2.87 (t, $J = 6.8$ Hz, 2H), 3.86 (t, $J = 6.8$ Hz, 2H), 7.16–7.36 (m, 4H), 7.39 (s, 1H), 7.49 (dd, $J = 1.1$, 6.7 Hz, 1H), 7.75 (d, $J = 8.4$ Hz, 2H), 7.98 (d, $J = 7.2$ Hz, 1H).

4.8. 3-[2-(*tert*-Butoxycarbonylamino)ethyl]-*N*-(*p*-toluenesulfonyl)indole 3i

$(Boc)_2O$ (12.1 g, 55 mmol) was added to a solution of tryptamine (8.01 g, 50 mmol) and triethylamine (13.9 ml, 100 mmol) in dry 1,4-dioxane (80 ml). The reaction mixture was stirred at room temperature for 4 h, and then evaporated. After water was added to the residue, the mixture was extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. ^{1}H NMR spectrum indicated that the residue was almost pure 3-[2-(*tert*-butoxycarbonylamino)ethyl]indole (13.0 g, 100%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 1.44 (s, 9H), 2.95 (t, $J = 6.8$ Hz, 2H), 3.46 (br q, $J = 6.4$ Hz, 2H), 4.55–4.72 (br, 1H), 7.01 (s, 1H), 7.07–7.26 (m, 2H), 7.36 (d, $J = 7.6$ Hz, 1H), 7.61 (d, $J = 7.8$ Hz, 1H), 8.04–8.30 (br, 1H). The procedure for the preparation of **3c** was followed with the Boc-protected amine (5.28 g, 20 mmol) to give **3i** (7.99 g, 95%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 1.45 (s, 9H), 2.33 (s, 3H), 2.86 (t, $J = 6.9$ Hz, 2H), 3.41 (q, $J = 6.6$ Hz, 2H), 4.49–4.66 (br, 1H), 7.16–7.38 (m, 5H), 7.46–7.52 (m, 1H), 7.75 (d, $J = 8.4$ Hz, 2H), 7.98 (d, $J = 7.8$ Hz, 1H).

4.9. *tert*-Butyl 3-[*N*-(*p*-toluenesulfonyl)indol-3-yl]propionate 3j

2-Bromo-2-methylpropane (21.4 g, 156 mmol) was added at 55 °C to a suspension of 3-(3-indolyl)propionic acid (757 mg, 4.0 mmol), benzyltriethylammonium chloride (910 mg, 4.0 mmol), and potassium carbonate (14.4 g, 104 mmol) in dry DMA (31 ml). After the mixture was stirred at 55 °C for 5 h, water was added to the mixture. The resulting mixture was extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and then evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving *tert*-butyl 3-(3-indolyl)propionate (643 mg, 65% yield): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 1.42 (s, 9H), 2.62 (t, $J = 7.8$ Hz, 2H), 3.05 (t, $J = 7.8$ Hz, 2H), 6.92 (d, $J = 2.4$ Hz, 1H), 7.04–7.21 (m, 2H), 7.29 (d, $J = 7.2$ Hz, 1H), 7.60 (d, $J = 7.6$ Hz, 1H), 7.94–8.16 (br, 1H). The procedure for the preparation of **3c** was followed with the *tert*-butyl ester (594 mg, 2.4 mmol) to give **3j** (593 mg, 61%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 1.43 (s, 9H), 2.32 (s, 3H), 2.60 (t, $J = 7.5$ Hz, 2H), 2.95 (d, $J = 7.5$ Hz, 2H), 7.14–7.37 (m, 5H), 7.49 (d, $J =$

7.4 Hz, 1H), 7.73 (d, $J = 8.2$ Hz, 2H), 7.97 (d, $J = 8.2$ Hz, 1H).

4.10. Methyl 3-[*N*-(*p*-toluenesulfonyl)indol-3-yl]propionate 3k

A suspension of 3-(3-indolyl)propionic acid (3.69 g, 19.5 mmol) and Amberlyst 15 (H^+ form) (3.94 g) in methanol (39 ml) was stirred at room temperature for 16 h. The mixture was filtered through a Celite pad, and then the filtrate evaporated. ^{1}H NMR spectrum indicates that the residue was almost pure methyl 3-(3-indolyl)propionate (3.85 g, 97%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.72 (t, $J = 7.6$ Hz, 2H), 3.10 (t, $J = 7.6$ Hz, 2H), 3.66 (s, 3H), 6.96 (d, $J = 2.0$ Hz, 1H), 7.06–7.23 (m, 2H), 7.32 (d, $J = 7.2$ Hz, 1H), 7.59 (dd, $J = 0.9$, 7.5 Hz, 1H), 7.91–8.12 (br, 1H). The procedure for the preparation of **3c** was followed with the methyl ester (2.03 g, 10 mmol) to give **3k** (2.88 g, 81%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.33 (s, 3H), 2.69 (t, $J = 7.6$ Hz, 2H), 3.00 (t, $J = 7.6$ Hz, 2H), 3.67 (s, 3H), 7.14–7.39 (m, 5H), 7.48 (d, $J = 7.8$ Hz, 1H), 7.73 (d, $J = 8.4$ Hz, 2H), 7.97 (d, $J = 7.6$ Hz, 1H).

4.11. *tert*-Butyl [*N*-(*p*-toluenesulfonyl)indol-3-yl]acetate 3l

A suspension of (3-indolyl)acetic acid (17.5 g, 100 mmol) and Amberlyst 15 (H^+ form) (20.0 g) in methanol (200 ml) was stirred at room temperature for 16 h. The mixture was filtered through a Celite pad, and then the filtrate evaporated. ^{1}H NMR spectrum indicated that the residue was almost pure methyl (3-indolyl)acetate (18.7 g, 99%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 3.70 (s, 3H), 3.79 (s, 2H), 7.08–7.26 (m, 3H), 7.36 (d, $J = 7.0$ Hz, 1H), 7.62 (d, $J = 7.6$ Hz, 1H), 7.91–8.25 (m, 1H). The procedure for the preparation of **3c** was followed with the methyl ester (3.79 g, 20 mmol). The reaction mixture was washed three times with EtOAc. The aqueous layer was acidified with 10% HCl aq, and then was extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving [*N*-(*p*-toluenesulfonyl)indol-3-yl]acetic acid (1.75 g, 26%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.32 (s, 3H), 3.73 (s, 2H), 7.14–7.38 (m, 4H), 7.45–7.52 (m, 1H), 7.58 (s, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.97 (d, $J = 7.6$ Hz, 1H). 2-Bromo-2-methylpropane (39.2 g, 286 mmol) was added at 55 °C to a suspension of the carboxylic acid (1.97 g, 6.0 mmol), benzyltriethylammonium chloride (1.36 g, 6.0 mmol), and potassium carbonate (21.4 g, 155 mmol) in dry DMA (46 ml). After the mixture was stirred at 55 °C for 4 h, water was added to the mixture. The resulting mixture was extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving **3l** (2.04 g, 89% yield): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 1.41 (s, 9H), 2.33 (s, 3H), 3.58 (s, 2H), 7.14–7.36 (m, 4H), 7.45–7.55 (m, 2H), 7.75 (d, $J = 8.4$ Hz, 2H), 7.97 (d, $J = 7.6$ Hz, 1H).

4.12. 3-Acetyl-*N*-(*p*-toluenesulfonyl)indole

The procedure for the preparation of **3c** was followed with 3-acetylindole (955 mg, 6.0 mmol) to give the desired compound (1.83 g, 97%): ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.37 (s, 3H), 2.57 (s, 3H), 7.24–7.43 (m, 4H), 7.79–7.98 (m, 3H), 8.20 (s, 1H), 8.28–8.39 (m, 1H).

4.13. General procedure for asymmetric hydrogenation of 2-substituted indoles 1

A mixture of $[Rh(nbd)_2]SbF_6$ (2.6 mg, 5.0 μmol) and (*S*,*S*)-(*R*,*R*)-PhTRAP (4.2 mg, 5.3 μmol) in dry 2-propanol (2.0 ml) was stirred at room temperature for 10 min. The resulting orange suspension was transferred by a cannula to a mixture of **1** (0.50 mmol) and Cs_2CO_3 (16.2 mg, 50 μmol). The mixture was moved into a nitrogen-filled 50 ml stainless steel autoclave. Hydrogen was introduced into the autoclave until the pressure gauge indicated over 50 atm, and then the pressure was carefully released to 1 atm. This procedure was repeated twice, and finally the inside of the autoclave was pressurized with hydrogen to 50 atm. The reaction mixture was stirred at 60 °C for 2 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane) to give **2**. The enantiomeric excess of **2** was determined by chiral HPLC analysis.

4.13.1. (*R*)-*N*-Acetyl-2-butylindoline 2a (Table 2, entry 8). The general procedure was followed with *N*-acetyl-2-butylindole **1a** (108 mg, 0.50 mmol) to give (*R*)-**2a** (102 mg, 94%): pale yellow oil; $[\alpha]_D^{20} = -94.0$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.80–0.99 (br, 3H), 1.19–1.41 (br, 4H), 1.51–1.79 (br, 2H), 2.28 and 2.38 (a pair of br s, 3H), 2.57–2.88 (br m, 1H), 3.12–3.40 (br m, 1H), 4.16–4.41 and 4.63–4.90 (a pair of br, 1H), 7.02 (t, $J = 7.5$ Hz, 1H), 7.05–7.28 (m, 2H), 8.14 (br d, $J = 6.9$ Hz, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 13.9, 22.5, 23.3, and 24.3 (a pair of s), 27.2, 33.8, and 32.7 (a pair of s), 35.0, 60.6, and 59.8 (a pair of s), 117.8 and 115.1 (a pair of s), 123.8, 124.7, and 126.0 (a pair of s), 127.4, 130.6, and 133.4 (a pair of s), 142.4 and 141.4 (a pair of s), 168.4; Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.38; H, 8.93; N, 6.24. The enantiomeric excess of **2a** was determined to be 94% ee by HPLC analysis with CHIRALPAK AD (4.6 mm ∅ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (*R*) $t_1 = 24.8$ min, (*S*) $t_2 = 27.0$ min.

4.13.2. (−)-*N*-Acetyl-2-(2-methylpropyl)indoline 2b (Table 4, entry 1). The general procedure was followed with *N*-acetyl-2-(2-methylpropyl)indole **1b** (108 mg, 0.50 mmol) to give **2b** (99 mg, 91%): pale yellow oil; $[\alpha]_D^{20} = -79.5$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.94 (d, $J = 6.3$ Hz, 3H), 1.01 (br d, $J = 6.3$ Hz, 3H), 1.18–1.80 (br m, 3H), 2.27 and 2.37 (a pair of br s, 3H), 2.56–2.88 (br m, 1H), 3.11–3.40 (br m, 1H), 4.23–4.46 and 4.73–5.01 (a pair of br, 1H), 7.02 (t, $J = 7.4$ Hz, 1H), 7.14–7.36 (m, 2H), 8.14 (br d, $J = 6.9$ Hz, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ

21.3, 23.3, 23.7, 24.6, 33.7, and 32.9 (a pair of s), 43.9 and 42.7 (a pair of s), 59.1 and 58.4 (a pair of s), 117.8 and 115.3 (a pair of s), 123.7, 124.9, and 126.0 (a pair of s), 127.4, 130.4, and 133.4 (a pair of s), 142.2 and 141.5 (a pair of s), 168.1; Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.39; H, 8.96; N, 6.50. The enantiomeric excess of **2b** was determined to be 91% ee by HPLC analysis with CHIRALCEL OD-H (4.6 mm ∅ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 = 18.1$ min, (−) $t_2 = 29.0$ min.

4.13.3. *N*-Acetyl-2-cyclohexylindoline 2c (Table 4, entry 2). The general procedure was followed with *N*-acetyl-2-cyclohexylindole **1c** (121 mg, 0.50 mmol). ^{1}H NMR analysis of the resulting reaction mixture indicated that **2c** was formed in 27%. The enantiomeric excess of **2e** was determined to be 19% ee by HPLC analysis of the crude mixture with CHIRALCEL OD-H (4.6 mm ∅ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, $t_1 = 19.1$ min, $t_2 = 23.5$ min.

4.13.4. (−)-*N*-Acetyl-2-phenylindoline 2d (Table 4, entry 3). The general procedure was followed with *N*-acetyl-2-phenylindole **1d** (117 mg, 0.50 mmol) to give **2d** (108 mg, 91%): pale yellow oil; $[\alpha]_D^{20} = -148.1$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS, at 50 °C) δ 1.57–2.40 (br, 3H), 2.96 (br d, $J = 16.0$ Hz, 1H), 3.76 (br dd, $J = 10.2$, 16.0 Hz, 1H), 5.14–5.64 (br, 1H), 7.03 (t, $J = 7.5$ Hz, 1H), 7.08–7.45 (m, 7H), 8.02–8.51 (br, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$, at 50 °C) δ 24.0, 38.8, 63.5, 117.0, 124.0, 124.9, 125.1, 127.8, 129.1, 143.3, 143.4, 169.4; Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.69; H, 6.25; N, 5.82. The enantiomeric excess of **2d** was determined to be 87% ee by HPLC analysis with CHIRALPAK AD (4.6 mm ∅ × 250 mm): 10% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (−) $t_1 = 16.9$ min, (+) $t_2 = 19.4$ min.

4.13.5. Methyl (*S*)-*N*-acetylindoline-2-carboxylate 2e (Table 4, entry 5). The general procedure was followed with methyl *N*-acetylindole-2-carboxylate **1e** (109 mg, 0.50 mmol). Triethylamine was used as an additive in place of Cs_2CO_3 and the hydrogenation was conducted at 100 °C and 100 atm of hydrogen pressure for 30 min. The reaction gave **2e** (104 mg, 95%): colorless solid; $[\alpha]_D^{20} = -126.1$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.18 and 2.49 (a pair of s, 3H), 3.27 and 3.11 (a pair of br d, $J = 17.1$ Hz and 16.5 Hz, 1H), 3.38–3.69 (br m, 1H), 3.77 and 3.74 (a pair of s, 3H), 4.92 and 5.17 (a pair of br d, $J = 10.5$ Hz and 7.8 Hz, 1H), 7.03 (t, $J = 7.7$ Hz, 1H), 7.10–7.32 (m, 2H), 8.23 (br d, $J = 8.1$ Hz, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 23.5 and 24.4 (a pair of s), 33.4 and 31.4 (a pair of s), 52.8 and 52.3 (a pair of s), 61.3 and 60.1 (a pair of s), 117.3 and 113.8 (a pair of s), 124.0 and 123.4 (a pair of s), 124.2 and 125.7 (a pair of s), 127.9, 128.4, and 130.8 (a pair of s), 142.6 and 141.3 (a pair of s), 168.9 and 168.5 (a pair of s), 171.9; HRMS (FAB) Calcd for $C_{12}H_{13}NO_3$: 219.0895. Found: 219.0892 (M^+). The enantiomeric excess of **2e** was determined to be 95% ee by HPLC analysis with CHIRALPAK AS (4.6 mm ∅ × 250 mm): 20% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (*R*) $t_1 = 22.1$ min, (*S*) $t_2 = 25.3$ min.

4.13.6. (−)-*N*-Acetyl-2-butyl-5-methylindoline 2f (Table 4, entry 6). The general procedure was followed with *N*-acetyl-2-butyl-5-methylindole **1f** (115 mg, 0.50 mmol) to give **2f** (109 mg, 94%): pale yellow oil; $[\alpha]_D^{20} = -98.2$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.77–0.97 (br, 3H), 1.17–1.76 (br m, 6H), 2.26 and 2.37 (a pair of br s, 3H), 2.30 (s, 3H), 2.52–2.80 (br m, 1H), 3.08–3.35 (br m, 1H), 4.18–4.32 and 4.67–4.82 (a pair of br, 1H), 6.88–7.06 (m, 2H), 8.01 (br d, $J = 8.1$ Hz, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 13.8, 20.9, 22.5, 23.1, and 24.2 (a pair of s), 27.1, 33.7, and 32.5 (a pair of s), 34.9 and 33.4 (a pair of s), 60.7 and 59.8 (a pair of s), 117.4 and 114.8 (a pair of s), 125.4 and 126.7 (a pair of s), 127.8, 130.7, 133.4, 140.0, and 139.2 (a pair of s), 168.0; Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.65; H, 9.37; N, 6.05. The enantiomeric excess of **2f** was determined to be 94% ee by HPLC analysis with CHIRALPAK AD (4.6 mm ∅ × 250 mm): 20% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (−) $t_1 = 13.9$ min, (+) $t_2 = 21.6$ min.

4.13.7. (−)-*N*-Acetyl-2-butyl-5-(trifluoromethyl)indoline 2g (Table 4, entry 7). The general procedure was followed with *N*-acetyl-2-butyl-5-(trifluoromethyl)indole **1g** (142 mg, 0.50 mmol) to give **2g** (119 mg, 84%): pale yellow oil; $[\alpha]_D^{20} = -61.6$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS, at 50 °C) δ 0.90 (br t, $J = 6.6$ Hz, 3H), 1.21–1.46 (br, 4H), 1.46–1.74 (br, 2H), 2.31 (s, 3H), 2.83 (br d, $J = 16.0$ Hz, 1H), 3.34 (br dd, $J = 9.0$, 16.0 Hz, 1H), 4.15–4.74 (br, 1H), 7.41 (s, 1H), 7.46 (d, $J = 8.4$ Hz, 1H), 7.76–8.52 (br, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$, at 50 °C) δ 13.8, 22.4, 23.3, 27.0, 33.4, 34.9, 60.9, 117.3, 121.9, 124.4 (q, $J = 272$ Hz), 125.2, 125.7 (q, $J = 32$ Hz), 131.3, 145.2, 168.8; Anal. Calcd for $C_{15}H_{18}NOF_3$: C, 63.15; H, 6.36; N, 4.91. Found: C, 63.29; H, 6.36; N, 4.92. The enantiomeric excess of **2g** was determined to be 92% ee by HPLC analysis with CHIRALPAK AD (4.6 mm ∅ × 250 mm): 20% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (−) $t_1 = 16.5$ min, (+) $t_2 = 30.3$ min.

4.13.8. (−)-*N*-Acetyl-2-butyl-6-(trifluoromethyl)indoline 2h (Table 4, entry 8). The general procedure was followed with *N*-acetyl-2-butyl-6-(trifluoromethyl)indole **1h** (141 mg, 0.50 mmol) to give **2h** (118 mg, 83%): pale yellow oil; $[\alpha]_D^{20} = -45.0$ (*c* 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS, at 50 °C) δ 0.90 (br t, $J = 6.8$ Hz, 3H), 1.15–1.46 (br m, 4H), 1.46–1.74 (br, 2H), 2.30 (s, 3H), 2.83 (br d, $J = 15.8$ Hz, 1H), 3.34 (br dd, $J = 8.9$, 15.8 Hz, 1H), 4.16–4.66 (br, 1H), 7.17–7.36 (m, 2H), 8.11–8.66 (br, 1H); ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$, at 50 °C) δ 13.8, 22.4, 23.2, 27.0, 33.7, 35.0, 60.9, 114.6, 120.8, 124.3 (q, $J = 273$ Hz), 124.9, 129.9 (q, $J = 32$ Hz), 134.6, 142.8, 168.7; Anal. Calcd for $C_{15}H_{18}NOF_3$: C, 63.15; H, 6.36; N, 4.91. Found: C, 63.22; H, 6.40; N, 4.93. The enantiomeric excess of **2h**

was determined to be 92% ee by HPLC analysis with CHIRALPAK AD (4.6 mm ∅ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 = 16.1$ min, (−) $t_2 = 17.9$ min.

4.13.9. (−)-*N*-Acetyl-2-butyl-6-methoxyindoline 2i (Table 4, entry 9). The general procedure was followed with *N*-acetyl-2-butyl-6-methoxyindole **1i** (123 mg, 0.50 mmol) to give **2i** (121 mg, 98%): pale yellow oil; $[\alpha]_D^{20} = -54.8$ (*c* 1.01, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 0.79–0.95 (br, 3H), 1.17–1.40 (br, 4H), 1.51–1.74 (br, 2H), 2.27 (br s, 3H), 2.72 (br d, $J = 14.7$ Hz, 1H), 3.05–3.32 (br m, 1H), 3.80 (s, 3H), 4.18–4.39 (br, 1H), 6.58 (br dd, $J = 2.0$, 7.9 Hz, 1H), 7.05 (br d, $J = 7.9$ Hz, 1H), 7.77–7.90 (br, 1H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ 13.9, 22.5, 23.3, 27.2, 33.0, 35.0, 55.5, 61.5, 103.7, 110.1, 122.4, 124.8, 143.5, 159.4, 168.5; Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.58; H, 8.64; N, 5.68. The enantiomeric excess of **2i** was determined to be 92% ee by HPLC analysis with CHIRALPAK AD (4.6 mm ∅ × 250 mm): 20% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 =$ 13.5 min, (−) $t_2 = 19.0$ min.

4.13.10. (*R*)-2-Methyl-*N*-(*p*-toluenesulfonyl)indoline 2j (Table 4, entry 10). The general procedure was followed with 2-methyl-*N*-(*p*-toluenesulfonyl)indole **1j** (143 mg, 0.50 mmol) to give **2j** (50 mg, 45%): pale yellow oil; $[\alpha]_D^{27} = +206.8$ (*c* 0.99, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 1.42 (d, $J = 6.5$ Hz, 3H), 2.34 (s, 3H), 2.43 (dd, $J = 2.2$, 16.0 Hz, 1H), 2.89 (dd, $J = 9.4$, 16.0 Hz, 1H), 4.30–4.39 (m, 1H), 6.98–7.06 (m, 2H), 7.13–7.27 (m, 3H), 7.55 (d, $J = 8.1$ Hz, 2H), 7.65 (d, $J = 8.0$ Hz, 1H); ^{13}C {^1H} NMR (100.5 MHz, $CDCl_3$) δ 21.5, 23.3, 36.2, 58.4, 117.1, 124.4, 125.2, 126.9, 127.6, 129.5, 131.6, 135.3, 141.0, 143.7. The enantiomeric excess of **2j** was determined to be 78% ee by HPLC analysis with CHIRALPAK AD-H (4.6 mm ∅ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (*S*) $t_1 = 25.5$ min, (*R*) $t_2 = 32.0$ min.

4.13.11. (*R*)-*N*-(*tert*-Butoxycarbonyl)-2-butylindoline 2k (Table 4, entry 11). The general procedure was followed with *N*-(*tert*-butoxycarbonyl)-2-butylindole **1k** (139 mg, 0.51 mmol) to give **2k** (131 mg, 94%): colorless oil; $[\alpha]_D^{26} = -46.3$ (*c* 1.04, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 0.90 (t, $J = 6.9$ Hz, 3H), 1.23–1.41 (m, 4H), 1.46–1.62 (m, 1H), 1.56 (s, 9H), 1.71–1.81 (m, 1H), 2.72 (dd, $J = 2.1$, 16.0 Hz, 1H), 3.26 (dd, $J = 9.7$, 16.0 Hz, 1H), 4.37 (br, 1H), 6.92 (t, $J = 7.4$ Hz, 1H), 7.10–7.17 (m, 2H), 7.40–7.88 (br, 1H); ^{13}C {^1H} NMR (100.5 MHz, $CDCl_3$) δ 14.1, 22.6, 27.2, 28.5, 33.3, 34.3, 59.4, 80.6, 115.3, 122.2, 124.8, 127.2, 130.5, 142.2, 152.4; Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 6.45. Found: C, 77.39; H, 8.96; N, 6.50. The enantiomeric excess of **2k** was determined to be 77% ee by HPLC analysis of **2a** derived from **2k** with CHIRALPAK AD (4.6 mm ∅ × 250 mm). The procedure of the transformation is as follows: trifluoroacetic acid (0.4 ml) was added at 0 °C to a solution of **2k** (23.5 mg, 0.10 mmol) in CH_2Cl_2 (3.6 ml). The mixture was stirred at room temperature for 1 h, and then was evaporated. After the residue and (*N*,*N*-dimethylamino)pyridine (1.2 mg, 10 μmol) were dissolved in CH_2Cl_2 (0.2 ml), acetic anhydride (12.3 mg, 0.12 mmol) and triethylamine (40.5 mg, 0.40 mmol) were added to the resulting solution at 0 °C. The mixture was stirred for 1 h, and then diluted with EtOAc. The mixture was washed with 3 M HCl aq, with saturated $NaHCO_3$ aq, and with water. The organic layer was dried over Na_2SO_4, and then evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving **2a**.

4.14. General procedure for asymmetric hydrogenation of 3-substituted indoles 3

A mixture of $[Rh(nbd)_2]SbF_6$ (2.6 mg, 5.0 μmol) and (*S*,*S*)-(*R*,*R*)-PhTRAP (4.0 mg, 5.0 μmol) in dry 2-propanol (2.0 ml) was stirred at room temperature for 10 min. The resulting orange suspension was transferred by cannula to a mixture of **3** (0.50 mmol) and Cs_2CO_3 (16.2 mg, 50 μmol). The mixture was moved into a nitrogen-filled 50 ml stainless steel autoclave. Hydrogen was introduced into the autoclave until the pressure gauge indicated over 50 atm. The pressure was then carefully released to 1 atm. This procedure was repeated twice, and finally the inside of the autoclave pressurized with hydrogen to 50 atm. The reaction mixture was stirred at 80 °C for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane) to give **4**. The enantiomeric excess of **4** was determined by chiral HPLC analysis.

4.14.1. (*S*)-3-Methyl-*N*-(*p*-toluenesulfonyl)indoline 4c (Table 5, entry 3). The general procedure was followed with 3-methyl-*N*-(*p*-toluenesulfonyl)indole **3c** (143 mg, 0.50 mmol) to give (*S*)-**4c** (138 mg, 96%): colorless solid; $[\alpha]_D^{20} = +29.4$ (*c* 1.06, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 1.11 (d, $J = 7.0$ Hz, 3H), 2.36 (s, 3H), 3.19 (double quintet, $J = 8.6$, 7.0 Hz, 1H), 3.42 (dd, $J = 7.0$, 10.4 Hz, 1H), 4.08 (dd, $J = 8.6$, 10.4 Hz, 1H), 6.96–7.08 (m, 2H), 7.16–7.26 (m, 3H), 7.64 (d, $J = 8.4$ Hz, 1H), 7.68 (d, $J = 8.4$ Hz, 2H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ 19.4, 21.4, 34.6, 57.5, 114.9, 123.8, 124.0, 127.4, 127.9, 129.7, 134.1, 136.9, 141.6, 144.1; Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.84; H, 5.96; N, 4.73. The enantiomeric excess of **4c** was determined to be 98% ee by HPLC analysis with CHIRALCEL OD-H (4.6 mm ∅ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (*S*) $t_1 = 22.4$ min, (*R*) $t_2 = 25.8$ min.

4.14.2. (*R*)-3-Methyl-*N*-(*p*-toluenesulfonyl)indoline 4c (Table 5, entry 4). The general procedure was followed with 3-methyl-*N*-(*p*-toluenesulfonyl)indole **3c** (285 mg, 1.00 mmol) and (*R*,*R*)-(*S*,*S*)-PhTRAP to give (*R*)-**4c** (280 mg, 98%): colorless solid; $[\alpha]_D^{25} = -32.4$ (*c* 1.54, $CHCl_3$). The enantiomeric excess of **4c** was determined to be 98% ee by HPLC analysis with CHIRALCEL OD-H (4.6 mm ∅ × 250 mm).

4.14.3. (+)-3-(2-Propyl)-*N*-(*p*-toluenesulfonyl)indoline 4f (Table 6, entry 1). The general procedure was followed with the exception of amount of solvent (1 ml) and reaction time (48 h), with 3-(2-propyl)-*N*-(*p*-toluenesulfonyl)indole **3f** (157 mg, 0.50 mmol) to give **4f** (152 mg, 94%): colorless oil; $[\alpha]_D^{20} = -19.1$ (*c* 1.06, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 0.63 (d, $J = 6.8$ Hz, 3H), 0.88 (d, $J = 6.8$ Hz, 3H), 1.87 (double septet, $J = 4.8$, 6.8 Hz, 1H), 2.37 (s, 3H), 3.11 (dt, $J = 10.5$, 5.2 Hz, 1H), 3.73 (dd, $J = 5.5$, 10.5 Hz, 1H), 3.81 (dd, $J = 10.0$, 10.5 Hz, 1H), 6.96 (t, $J = 7.5$ Hz, 1H), 7.06 (d, $J = 7.5$ Hz, 1H), 7.19 (t, $J = 8.0$ Hz, 1H), 7.23 (d, $J = 8.0$ Hz, 2H), 7.64 (d, $J = 8.0$ Hz, 1H), 7.71 (d, $J = 8.0$ Hz, 2H); ^{13}C {^1H} NMR (100.5 MHz, $CDCl_3$) δ 17.3, 20.0, 21.5, 31.3, 45.8, 51.7, 114.1, 123.2, 125.0, 127.3, 127.9, 129.6, 133.9 (2C), 142.2, 144.0; Anal. Calcd for $C_{18}H_{21}NO_2S$: C, 68.54; H, 6.71; N, 4.44. Found: C, 68.47; H, 6.70; N, 4.39. The enantiomeric excess of **4f** was determined to be 97% ee by HPLC analysis with CHIRALCEL OD-H (4.6 mm ∅ × 250 mm), 20% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 = 17.3$ min, (−) $t_2 = 19.3$ min.

4.14.4. (+)-3-Phenyl-*N*-(*p*-toluenesulfonyl)indoline 4g (Table 6, entry 2). The general procedure was followed with 3-phenyl-*N*-(*p*-toluenesulfonyl)indole **3g** (174 mg, 0.50 mmol), $[Rh(nbd)_2]SbF_6$ (5.2 mg, 10 μmol), and (*S*,*S*)-(*R*,*R*)-PhTRAP (8.3 mg, 10.5 μmol) to give **4g** (163 mg, 93%): colorless solid; $[\alpha]_D^{25} = +88.9$ (*c* 1.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 2.39 (s, 3H), 3.74–3.82 (m, 1H), 4.31–4.38 (m, 2H), 6.84–6.89 (m, 3H), 6.97 (t, $J = 7.5$ Hz, 1H), 7.17–7.28 (m, 6H), 7.68 (d, $J = 8.0$ Hz, 2H), 7.74 (d, $J = 8.0$ Hz, 1H); ^{13}C {^1H} NMR (100.5 MHz, $CDCl_3$) δ 21.6, 46.2, 58.5, 114.9, 124.0, 125.6, 127.1, 127.4, 127.7, 128.3, 128.7, 129.7, 133.8, 134.8, 142.1, 142.4, 144.1; Anal. Calcd for $C_{21}H_{19}NO_2S$: C, 72.18; H, 5.48; N, 4.01. Found: C, 71.96; H, 5.46; N, 3.90. The enantiomeric excess of **4g** was determined to be 96% ee by HPLC analysis with CHIRALCEL OD-H (4.6 mm ∅ × 25 cm): 20% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 = 26.4$ min, (−) $t_2 = 31.6$ min.

4.14.5. (+)-3-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-*N*-(*p*-toluenesulfonyl)indoline 4h (Table 6, entry 3). The general procedure was followed with 3-[2-(*tert*-butyldimethylsilyloxy)ethyl]-*N*-(*p*-toluenesulfonyl)indole **3h** (215 mg, 0.50 mmol) to give **4h** (202 mg, 94%): colorless solid; $[\alpha]_D^{20} = +9.7$ (*c* 1.18, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 0.05 (s, 6H), 0.90 (s, 9H), 1.32–1.45 (m, 1H), 1.70–1.82 (m, 1H), 2.32 (s, 3H), 3.14–3.27 (m, 1H), 3.57 (dd, $J = 6.6$, 10.8 Hz, 1H), 3.58 (t, $J = 6.0$ Hz, 2H), 3.99 (dd, $J = 9.0$, 10.8, 1H), 6.94 (dt, $J = 0.8$, 7.4 Hz, 1H), 7.02 (d, $J = 7.4$ Hz, 1H), 7.12–7.21 (m, 3H), 7.58–7.66 (m, 3H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ −5.5, 18.1, 21.4, 25.8, 37.2, 37.5, 56.0, 60.7, 114.9, 123.7, 124.4, 127.4, 128.0, 129.7, 134.1, 135.7, 141.8, 144.0; Anal. Calcd for $C_{23}H_{33}NO_3SSi$: C, 64.00; H, 7.71; N, 3.24. Found: C, 64.27; H, 7.86; N, 3.33. The enantiomeric excess of **4h** was determined to be 98% ee by HPLC analysis with Ceramospher RU-1 (4.6 mm ∅ × 250 mm), methanol, 0.08 ml/min flow, at 50 °C, UV 254 nm detection, (−) $t_1 = 54.1$ min, (+) $t_2 = 58.0$ min.

4.14.6. (+)-3-[2-{*N*-(*tert*-Butoxycarbonyl)amino}ethyl]-*N*-(*p*-toluenesulfonyl)indoline 4i (Table 6, entry 4). The general procedure was followed with 3-[2-{*N*-(*tert*-butoxycarbonyl)amino}ethyl]-*N*-(*p*-toluenesulfonyl)-indole **3i** (208 mg, 0.50 mmol) to give **4i** (148 mg, 71%): colorless solid; $[\alpha]_D^{20} = +9.0$ (*c* 1.02, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 1.32–1.55 (m, 1H), 1.44 (s, 9H), 1.67–1.80 (m, 1H), 2.37 (s, 3H), 3.05–3.20 (m, 3H), 3.61 (dd, $J = 5.9$, 10.6 Hz, 1H), 4.00 (dd, $J = 9.2$, 10.6 Hz, 1H), 4.48 (br s, 1H), 6.99 (t, $J = 7.4$ Hz, 1H), 7.08 (d, $J = 7.4$ Hz, 1H), 7.17–7.26 (m, 3H), 7.65 (d, $J = 8.1$ Hz, 1H), 7.69 (d, $J = 8.4$ Hz, 2H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ 21.4, 28.3, 29.6, 35.3, 37.6, 38.2, 55.4, 114.9, 123.8, 124.4, 127.4, 128.2, 129.7, 133.9, 134.9, 141.7, 144.2, 155.9; Anal. Calcd for $C_{22}H_{28}N_2O_4S$: C, 63.44; H, 6.78; N, 6.73. Found: C, 63.71; H, 6.83; N, 6.60. The enantiomeric excess of **4i** was determined to be 95% ee by HPLC analysis with CHIRALCEL OC (4.6 mm ∅ × 250 mm), 20% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 = 31.6$ min, (−) $t_2 = 38.8$ min.

4.14.7. *tert*-Butyl (+)-3-[*N*-(*p*-toluenesulfonyl)indolin-3-yl]propionate 4j (Table 6, entry 5). The general procedure was followed with *tert*-butyl 3-[*N*-(*p*-toluenesulfonyl)indol-3-yl]propionate **3j** (201 mg, 0.50 mmol) to give **4j** (187 mg, 93%): colorless solid; $[\alpha]_D^{20} = +15.6$ (*c* 1.06, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 1.43 (s, 9H), 1.47–1.60 (m, 1H), 1.79–1.92 (m, 1H), 2.16 (t, $J = 7.7$ Hz, 2H), 2.36 (s, 3H), 3.08–3.20 (m, 1H), 3.58 (dd, $J = 5.9$, 10.4 Hz, 1H), 3.97 (dd, $J = 9.0$, 10.4 Hz, 1H), 6.99 (dt, $J = 0.9$, 7.5 Hz, 1H), 7.09 (d, $J = 7.5$ Hz, 1H), 7.18–7.26 (m, 3H), 7.65 (d, $J = 8.4$ Hz, 1H), 7.69 (d, $J = 8.1$ Hz, 2H); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ 21.4, 28.0, 29.7, 32.5, 39.0, 55.2, 80.6, 114.8, 123.7, 124.6, 127.3, 128.2, 129.7, 133.8, 134.7, 141.7, 144.2, 172.2; Anal. Calcd for $C_{22}H_{27}NO_4S$: C, 65.81; H, 6.78; N, 3.49. Found: C, 66.03; H, 6.82; N, 3.50. The enantiomeric excess of **4j** was determined to be 97% ee by HPLC analysis with CHIRALPAK AD (4.6 mm ∅ × 250 mm), 4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 = 37.7$ min, (−) $t_2 = 41.6$ min.

4.14.8. Methyl 3-[*N*-(*p*-toluenesulfonyl)indolin-3-yl]propionate 4k (Table 6, entry 6). The general procedure was followed with methyl 3-[*N*-(*p*-toluenesulfonyl)indol-3-yl]propionate **3k** (179 mg, 0.50 mmol). ^1H NMR analysis of the resulting reaction mixture indicated that **4k** was formed in 32%. The enantiomeric excess of **4k** was determined to be 97% ee by HPLC analysis with CHIRALPAK AS (4.6 mm ∅ × 250 mm), 30% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, $t_1 = 23.3$ min, $t_2 = 28.0$ min.

4.14.9. *tert*-Butyl [*N*-(*p*-toluenesulfonyl)indolin-3-yl]acetate 4l (Table 6, entry 7). The general procedure was followed with *tert*-butyl [*N*-(*p*-toluenesulfonyl)indol-3-yl]acetate **3l** (98 mg, 0.25 mmol). ^1H NMR analysis of

the resulting reaction mixture indicated that **4l** was formed in 29%. The enantiomeric excess of **4l** was determined to be 62% ee by HPLC analysis with CHIRALPAK AS (4.6 mm ∅ × 250 mm), 4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, $t_1 = 18.7$ min, $t_2 = 25.8$ min.

4.15. Assignment of the absolute configuration of 2a and 2e

4.15.1. Methyl (*S*)-indoline-2-carboxylate hydrochloride 7. Thionyl chloride (2.6 ml, 36 mmol) was added carefully to dry methanol (10 ml) at −10 °C. After the mixture was stirred for 10 min, (*S*)-indoline-2-carboxylic acid **6** (1.63 g, 10.0 mmol) was added to the resulting solution. The mixture was stirred at room temperature for 53 h, and then evaporated. The residue was crystallized in Et_2O, giving (*S*)-**7** (2.12 g, 99%): colorless crystals; ^{1}H NMR (200 MHz, CD_3OD) δ 3.51 (dd, $J = 7.6$, 16.4 Hz, 1H), 3.71 (dd, $J = 9.4$, 16.4 Hz, 1H), 3.89 (s, 3H), 5.09 (dd, $J = 7.6$, 9.4 Hz, 1H), 7.37–7.54 (m, 4H).

4.15.2. Methyl (*S*)-*N*-acetylindoline-2-carboxylate 2e. Triethylamine (2.54 g, 25 mmol) was added at room temperature to a suspension of (*S*)-**7** (2.12 g, 9.9 mmol) in dry THF (10 ml). After 30 min, acetic anhydride (1.19 g, 12 mmol) was added to the resulting mixture at 0 °C. The mixture was stirred at 0 °C for 10 min and then at room temperature for 17 h. The mixture was diluted with water, and then extracted with EtOAc. The organic layer was washed with 10% HCl aq, then with saturated Na_2CO_3 aq, followed by brine, dried over Na_2SO_4, and then evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving (*S*)-**2e** (1.86 g, 86%): colorless solid; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.18 and 2.49 (a pair of br s, 3H), 3.00–3.67 (br m, 2H), 3.77 and 3.74 (a pair of s, 3H), 4.84–4.98 and 5.10–5.23 (a pair of br m, 1H), 7.03 (t, $J = 7.9$ Hz, 1H), 7.09–7.31 (m, 2H), 8.22 (br d, $J = 7.8$ Hz, 1H). The retention time of the authentic (*S*)-**2e** in HPLC analysis with CHIRALPAK AS revealed the absolute configuration of (−)-**2e** obtained from the asymmetric hydrogenation of **1e** using (*S*,*S*)-(*R*,*R*)-PhTRAP to be *S*.

4.15.3. (*S*)-*N*-Acetyl-2-(hydroxymethyl)indoline 8. Lithium borohydride (205 mg, 9.4 mmol) was added to a solution of (*S*)-**2e** (1.37 g, 6.2 mmol) in dry THF (6.2 ml) at room temperature. After the mixture was stirred for 5 h, 10% HCl aq was carefully added to the reaction mixture. The mixture was extracted twice with EtOAc. The combined organic layer was washed with saturated Na_2CO_3 aq, with brine, dried with Na_2SO_4, and then evaporated. The residue was purified by a flash column chromatography on silica gel (EtOAc/hexane), giving 890 mg (74%) of (*S*)-**8**: ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.18–2.54 (br s, 3H), 2.54–2.96 (br m, 1H), 3.34 (dd, $J = 9.5$, 16.5 Hz, 1H), 3.43–3.85 (m, 2H), 4.35–4.67 and 4.81–5.09 (a pair of br, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 7.11–7.34 and 7.92–8.12 (br, 3H).

4.15.4. (*S*)-*N*-Acetyl-2-(1-butenyl)indoline 9. A solution of dimethyl sulfoxide (78 mg, 1.0 mmol) in dry dichloromethane (0.25 ml) was added dropwise to a solution of oxalyl chloride (70 mg, 0.55 mmol) in dry dichloromethane (0.5 ml) at −60 °C for 30 min. After 5 min, a solution of (*S*)-**8** (95.6 mg, 0.50 mmol) in dry dichloromethane (0.25 ml) was added dropwise to the reaction mixture for 5 min. After 15 min, triethylamine (250 mg, 2.5 mmol) was added. After 5 min, the mixture was warmed to room temperature, and stirred for 10 min. The mixture was diluted with water, and extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was dissolved in dry diethyl ether (1.5 ml). A suspension of the phosphonium ylide, which was prepared by mixing triphenylpropylphosphonium bromide (202 mg, 0.52 mmol) and potassium *tert*-butoxide (73 mg, 0.65 mmol) in dry diethyl ether (1.5 ml) at 0 °C for 2.5 h was added to the solution of the residue at −78 °C. After 1 h, the resulting mixture was warmed to room temperature and stirred for 24 h. After the mixture was diluted with Et_2O, the colorless precipitate was filtered off. The filtrate was evaporated. The residue was purified by a preparative TLC (EtOAc/hexane), giving (*S*)-**9** (1.6 mg, 1.5%): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 1.06 (t, $J = 7.5$ Hz, 3H), 2.08–2.32 (br, 5H), 2.79 (br d, $J = 15.4$ Hz, 1H), 3.56 (br dd, $J = 10.4$, 15.4 Hz, 1H), 5.00–5.18 (br, 1H), 5.36–5.56 (m, 2H), 7.02 (dt, $J = 0.9$, 7.5 Hz, 1H), 7.11–7.29 (m, 2H), 8.20 (br d, $J = 7.6$ Hz, 1H).

4.15.5. (*R*)-*N*-Acetyl-2-butylindoline 2a. A mixture of (*S*)-**9** (1.6 mg, 7.4 μmol) and palladium on carbon (5%) (1.3 mg) in dry methanol (1.0 ml) was stirred at room temperature and 50 atm of hydrogen pressure for 3 h. The catalyst was filtered off through Celite, and then the filtrate was evaporated. The residue was passing through a short column on silica gel (EtOAc/hexane = 1/1), giving (*R*)-**2a**. The retention time of the authentic (*R*)-**2a** in chiral HPLC analysis with CHIRALPAK AD revealed the absolute configuration of (−)-**2a** obtained from the asymmetric hydrogenation of **1a** using (*S*,*S*)-(*R*,*R*)-PhTRAP to be *R*.

4.16. Assignment of the absolute configuration of 2j

Trifluoroacetic acid (2.4 ml) was added at 0 °C to a solution of (*R*)–*N*-(*tert*-butoxycarbonyl)-3-methyl indoline[13] (145 mg, 0.62 mmol) in dry dichloromethane (21.6 ml). The reaction mixture was stirred at room temperature for 1 h, and then evaporated. The residue was regarded as 3-methylindoline trifluoroacetic acid salt (153.8 mg). The residue (26.3 mg, 0.11 mmol) and triethylamine (43.2 mg, 0.43 mmol) were added at 0 °C to a solution of *p*-toluenesulfonyl chloride (38.4 mg, 0.20 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (1.2 mg, 10 μmol) in dry dichloromethane (0.1 ml). The reaction mixture was stirred at room temperature for 24 h. After water was added, the resulting mixture was extracted four times with EtOAc. The combined organic layer was washed with 3 M HCl aq, with saturated $NaHCO_3$ aq, dried over Na_2SO_4, and then evaporated. The residue was purified by flash column chromatography on silica gel (EtOAc/hexane), giving the authentic sample of (*R*)-**2j** (10.5 mg, 43%). The retention time of the

authentic (*R*)-**2j** in chiral HPLC analysis with CHIRALPAK AD-H revealed the absolute configuration of (+)-**2j** obtained from the asymmetric hydrogenation of **1j** using (*S*,*S*)-(*R*,*R*)-PhTRAP to be *R*.

4.17. Assignment of the absolute configuration of 4c

Compound (+)-**4c** (72.5 mg, 0.25 mmol), which was obtained from the asymmetric hydrogenation of **3c** using (*S*,*S*)-(*R*,*R*)-PhTRAP, was dissolved in dry toluene (0.5 ml). Sodium bis(2-methoxyethoxy)aluminum dihydride (ca. 70% in toluene) (340 mg, 1.18 mmol) was added to the solution of **4c**. The mixture was stirred under reflux for 16 h. After water was carefully added to the mixture, the resulting suspension was diluted with EtOAc, and then filtered through Celite. The filtrate was extracted three times with EtOAc. The combined organic layer was dried with Na_2SO_4, and evaporated. To a suspension of the residue, K_2CO_3 (57 mg, 0.41 mmol), and KI (4.5 mg, 27 μmol) in dry DMF (0.5 ml) was added benzyl chloride (48 mg, 0.38mmol). After 5 h of stirring at 100 °C, water was added to the resulting mixture. The mixture was extracted ten times with hexanes. The combined organic layer was washed with water, dried with Na_2SO_4, and evaporated. After passing through a column on silica gel, the residue was purified by medium-pressure liquid chromatography (EtOAc/hexane) with C.I.G. pre-packed column CPS-223L-1 (Kusano, Tokyo, Japan), giving (+)-*N*-benzyl-3-methylindoline (26 mg, 46 %) as pale yellow oil: $[\alpha]_D^{26} = +59.0$ (*c* 0.51, CH_2Cl_2), lit.[14] $[\alpha]_D^{20} = -49.7$ (*c* 1, CH_2Cl_2) for 87% ee (*R*); ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 1.30 (d, $J = 6.5$ Hz, 3H), 2.83 (t, $J = 8.5$ Hz, 1H), 3.30 (sextet, $J = 7.5$ Hz, 1H), 3.50 (t, $J = 8.5$ Hz, 1H), 4.11 (d, $J = 15.1$ Hz, 1H), 4.36 (d, $J = 15.1$ Hz, 1H), 6.51 (d, $J = 8.0$ Hz, 1H), 6.70 (t, $J = 7.5$ Hz, 1H), 7.06 (t, $J = 7.0$ Hz, 2H), 7.24–7.36 (m, 5H); ^{13}C {^1H} NMR (100.5 MHz, $CDCl_3$) δ 18.6, 35.2, 53.4, 61.6, 107.0, 117.7, 123.2, 127.0, 127.4, 127.9, 128.4, 135.0, 138.5, 152.1.

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References

1. Recent reviews: (a) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029–3069; (b) Blaser, H.-U.; Malan, C.; Pugin, B.; Spindler, F.; Steiner, H.; Studer, M. *Adv. Synth. Catal.* **2003**, *345*, 103–151; (c) Kitamura, M.; Noyori, R. In *Ruthenium in Organic Synthesis*; Murahashi, S.-i., Ed.; Wiley-VCH: Weinheim, 2004; pp 3–52; (d) Chi, Y.; Tang, W.; Zhang, X. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005; pp 1–31.
2. Hydrogenations of aromatic compounds with a chiral auxiliary have been reported, but gave the products in low yields and/or stereoselectivities, see: (a) Besson, M.; Blanc, B.; Champelet, M.; Gallezot, P.; Nasar, K.; Pinel, C. *J. Catal.* **1997**, *170*, 254–264; (b) Besson, M.; Gallezot, P.; Neto, S.; Pinel, C. *Chem. Commun.* **1998**, 1431–1432; (c) Besson, M.; Delbecq, F.; Gallezot, P.; Neto, S.; Pinel, C. *Chem. Eur. J.* **2000**, *6*, 949–958; (d) Ranade, V. S.; Prins, R. *J. Catal.* **1999**, *185*, 479–486; (e) Ranade, V. S.; Consiglio, G.; Prins, R. *Catal. Lett.* **1999**, *58*, 71–74; (f) Hegedus, L.; Háda, V.; Tungler, A.; Máthé, T.; Szepesy, L. *Appl. Catal. A* **2000**, *201*, 107–114; (g) Kukula, P.; Prins, R. *J. Catal.* **2002**, *208*, 404–411; (h) Douja, N.; Besson, M.; Gallezot, P.; Pinel, C. *J. Mol. Catal. A: Chem.* **2002**, *186*, 145–151; (i) Douja, N.; Malacea, R.; Banciu, M.; Besson, M.; Pinel, C. *Tetrahedron Lett.* **2003**, *44*, 6991–6993; (j) Barbosa, L. A. M. M.; Sautet, P. *J. Catal.* **2003**, *217*, 23–29.
3. Recently, Glorius reported the highly stereoselective hydrogenation of pyridines modified with a chiral oxazolidinone, see: (a) Glorius, F.; Spielkamp, N.; Holle, S.; Goddard, R.; Lehmann, C. W. *Angew. Chem., Int. Ed.* **2004**, *43*, 2850–2852; (b) Scheiper, B.; Glorius, F.; Leitner, A.; Fürstner, A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 11960–11965; (c) Glorius, F. *Org. Biomol. Chem.* **2005**, *3*, 4171–4175.
4. *Comprehensive Natural Products Chemistry*; Barton, D., Nakanish, K., Meth-Cohn, O., Eds.; Elsevier: Oxford, 1999; Vols. 1–9.
5. (a) Bianchini, C.; Barbaro, P.; Scapacci, G.; Farnetti, E.; Graziani, M. *Organometallics* **1998**, *17*, 3308–3310; (b) Henschke, J. P.; Burk, M. J.; Malan, C. G.; Herzberg, D.; Peterson, J. A.; Wildsmith, A. J.; Cobley, C. J.; Casy, G. *Adv. Synth. Catal.* **2003**, *345*, 300–307.
6. Kuwano, R.; Sato, K.; Kurokawa, T.; Karube, D.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7614–7615.
7. (a) Sawamura, M.; Hamashima, H.; Ito, Y. *Tetrahedron: Asymmetry* **1991**, *2*, 593–596; (b) Sawamura, M.; Hamashima, H.; Sugawara, M.; Kuwano, R.; Ito, Y. *Organometallics* **1995**, *14*, 4549–4558.
8. Kuwano, R.; Kaneda, K.; Ito, T.; Sato, K.; Kurokawa, T.; Ito, Y. *Org. Lett.* **2004**, *6*, 2213–2215.
9. (a) Wang, W.-B.; Lu, S.-M.; Yang, P.-Y.; Han, X.-W.; Zhou, Y.-G. *J. Am. Chem. Soc.* **2003**, *125*, 10536–10537; (b) Yang, P.-Y.; Zhou, Y.-G. *Tetrahedron: Asymmetry* **2004**, *15*, 1145–1149; (c) Lu, S.-M.; Han, X.-W.; Zhou, Y.-G. *Adv. Synth. Catal.* **2004**, *346*, 909–912; (d) Xu, L.; Lam, K. H.; Ji, J.; Wu, J.; Fan, Q.-H.; Lo, W.-H.; Chan, A. S. C. *Chem. Commun.* **2005**, 1390–1392.
10. Legault, C. Y.; Charette, A. B. *J. Am. Chem. Soc.* **2005**, *127*, 8966–8967.
11. Catalytic asymmetric hydrogenations of pyridines and furans have been reported but were low enantioselective, see: (a) Blaser, H.-U.; Höning, H.; Studer, M.; Wedemeyer-Exl, C. *J. Mol. Catal. A: Chem.* **1999**, *139*, 253–257; (b) Raynor, S. A.; Thomas, J. M.; Raja, R.; Johnson, B. F. G.; Bell, R. G.; Mantle, M. D. *Chem. Commun.* **2000**, 1925–1926; (c) Studer, M.; Wedemeyer, C.; Spindler, F.; Blaser, H.-U. *Monatsh. Chem.* **2000**, *131*, 1335–1343.
12. Kuwano, R.; Sato, K.; Ito, Y. *Chem. Lett.* **2000**, 428–429.
13. Gross, K. M. B.; Jun, Y. M.; Beak, P. *J. Org. Chem.* **1997**, *62*, 7679–7689.
14. Gil, G. S.; Groth, U. M. *J. Am. Chem. Soc.* **2000**, *122*, 6789–6790.
15. The enantiomeric excess of 3-methylindoline was determined by chiral HPLC analysis of its acetamido derivative, which was prepared by the treatment with acetic anhydride.
16. Iritani, K.; Matsubara, S.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 1799–1802.
17. (a) Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 3089–3091; (b) Schenck, T. G.; Downes, J. M.; Milne,

C. R. C.; Mackenzie, P. B.; Boucher, T. G.; Whelan, J.; Bosnich, B. *Inorg. Chem.* **1985**, *24*, 2334–2337.
18. Coulton, S.; Gilchrist, T. L.; Graham, K. *Tetrahedron* **1997**, *53*, 791–798.
19. Wenkert, E.; Moeller, P. D. R.; Piettre, S. R. *J. Am. Chem. Soc.* **1988**, *110*, 7188–7194.
20. Snyder, H. R.; Smith, C. W. *J. Am. Chem. Soc.* **1943**, *65*, 2452–2454.
21. Choshi, T.; Yamada, S.; Sugino, E.; Kuwada, T.; Hibino, S. *J. Org. Chem.* **1995**, *60*, 5899–5904.
22. Netherton, M. R.; Fu, G. C. *Org. Lett.* **2001**, *3*, 4295–4298.