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Asymmetric Hydrogenation of Unprotected Indoles Catalyzed by η⁶-Arene/ *N*-Me-sulfonyldiamine-Ru(II) Complexes

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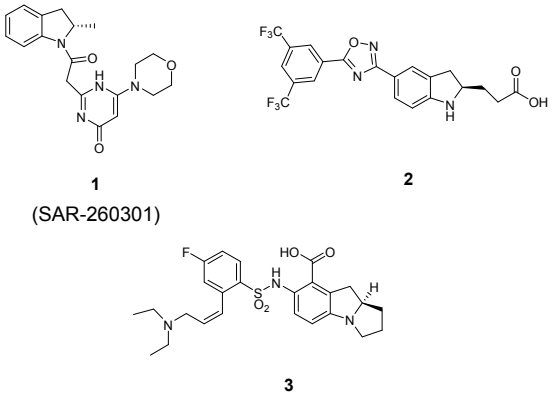
KEYWORDS: Asymmetric Hydrogenation · Indole · Indoline · Ru Complexes · N-Me-sulfonyldiamine Ligand · Halogen Atom · Protecting Groups · Derivatization of chiral indolines

ABSTRACT: Protecting group-free transformation is a challenging and important issue in atom-economical organic synthesis. The η⁶-arene/*N*-Me-sulfonyldiamine-Ru(II)-BF_4 complex-catalyzed asymmetric hydrogenation of 2-substituted unprotected indoles in weakly acidic hexafluoroisopropanol gives optically active indoline compounds with up to >99% ee. Under mild reaction media, halogen atoms and synthetically important protecting groups (e.g. silyl ether, acetal, benzyl ether, and ester) on indoles are maintained, which is advantageous for the synthesis of further complex indoline molecules.

INTRODUCTION

Chiral indolines are important structural motifs in naturally occurring alkaloids and numerous bioactive compounds.[1-3] For example, the antitumor agent SAR-260301 (**1**)[1h-i] is an *N*-amide of (*S*)-2-methylindoline, and the anti-inflammatory agent **2**[1j] and antitumor agent **3**[1k] also contain the chiral indoline skeleton (Figure 1).

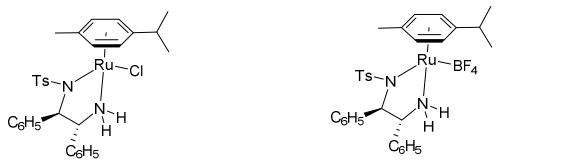
FIGURE 1. Examples of Chiral Indoline-Containing Biologically Active Compounds



Among the various methods that are available for the synthesis of chiral indolines,[2] the direct asymmetric hydrogenation of 2-substituted indoles is the simplest, most practical and atom-efficient.[3]

The η⁶-arene/sulfonyldiamine-Ru(II) complexes pioneered by Noyori and Ikariya[4] have been shown to exhibit excellent catalytic activity in a wide range of asymmetric transfer hydrogenations of ketones or imines (Figure 2). Ohkuma reported the cationic Ru(OTf)(TsDPEN)(*p*-cymene) complex (**5a**), which works efficiently in methanol for the catalytic asymmetric hydrogenation of ketonic substrates.[5] The BF_4 analog ((*R*,*R*)-**5b**) has also been shown to exhibit similar catalytic activity.[6a]

FIGURE 2. η⁶-Arene/sulfonyldiamine-Ru(II) Complexes



Through the use of η⁶-arene/sulfonyldiamine-Ru(II) complexes, transfer hydrogenation and H_2-hydrogenation of prochiral ketones,[4,5] imines, quinolones, and quinoxalines have been widely investigated, as summarized in Scheme 1.[6] For example, 2-methylquinoline and 2-methylquinoxaline can be suc-

cessfully reduced by (*R*,*R*)-**4** with formic acid as the hydrogen source [Method A].[6h] In the reduction of an imine substrate, 2,3,3-trimethylindolenine is smoothly obtained by (*R*,*R*)-**5b** in methanol with hydrogen gas as a hydrogen source [Method B].[6b, d, e, g, j, k] However, the reduction of indoles is difficult to achieve with Ru complexes under these conditions.

SCHEME 1. Asymmetric Reduction of *N*-Hetero Aromatic Compounds with η^6-Arene/sulfonyldiamine-Ru(II) Complexes[7]

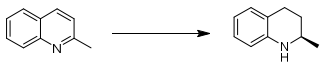
[Method A] *Asymmetric Transfer Hydrogenation*

cat. (*R*,*R*)-**4** (1 mol %), HCOOH-Et_3N (5:2), 60 °C, 8 h

[Method B] *Asymmetric Hydrogenation*

cat. (*R*,*R*)-**5b** (1 mol %), H_2 (3 MPa), MeOH, 40 °C, 18 h

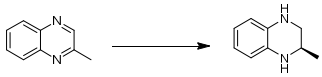
(a) 2-Methylquinoline



[Method A] 55% yield, 65% ee

[Method B] >99% yield, 95% ee

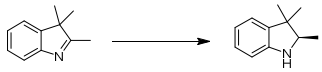
(b) 2-Methylquinoxaline



[Method A] 79% yield, 83% ee

[Method B] 92% yield, 26% ee

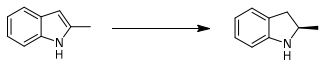
(c) 2,3,3-Trimethylindolenine



[Method A] 43% yield, 39% ee

[Method B] >99% yield, 89% ee

(d) 2-Methylindole



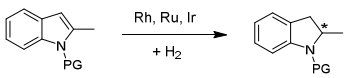
[Method A] No Reaction

[Method B] <1% yield

Kuwano and Ito reported the first hydrogenation of the olefin-portion of *N*-protected indoles using Rh and a Ru/PhTRAP complex under basic conditions.[8a-d] Feringa[8e] and Pfaltz[8f] also reported the asymmetric hydrogenation of *N*-protected indoles with the use of Rh and Ir/N,P catalysts (Scheme 2, eq. (1)). In contrast, the hydrogenation of unprotected indoles is still an unsolved challenge. Zhang, Zhou and co-workers approached this problem by changing the reduction of the olefin-portion of indole[9a-b] (a) to the reduction of an iminium ion intermediate (b), which is generated with the assistance of a Brϕnsted acid. While the chiral diphosphine-Pd catalyst reduced the iminium ion intermediate, a stoichiometric amount of a strong Brϕnsted acid (e.g., camphorsulfonic acid) was required as an *activator* (Scheme 2, eq. (2)).

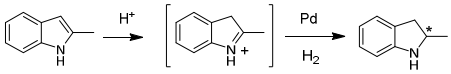
SCHEME 2. Classification of the Asymmetric Hydrogenation of Indoles.

(a) hydrogenation of olefin of protected indole



(Kuwano, Ito, Pfaltz, Feringa) PG = Boc, Ac, Ts (1)

(b) hydrogenation of imine generated from unprotected indole



(X. Zhang, Y-G. Zhou) (2)

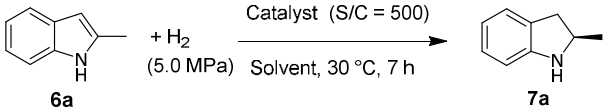
There has been limited success in the catalytic asymmetric reduction of unprotected indoles, and there is no previous report on the Ru-catalyzed reduction of unprotected indoles. We report here the first chiral Ru(II) complex-catalyzed hydrogenation of unprotected indoles under mild reaction conditions in protic solvent.

RESULTS AND DISCUSSION

Initial Screening of Asymmetric Hydrogenation of 2-Methylindole.

Based on the work of Zhang and Zhou, we considered that the iminium intermediate is a *key point* for the reduction of indole derivatives with the use of η^6-arene/sulfonyldiamine-Ru(II)-type complexes. Based on these pioneering works,[9a-b] η^6-arene/sulfonyldiamine-Ru(II) complexes were applied to the asymmetric hydrogenation of unprotected 2-methylindole (**6a**) (Table 1). For the reaction with a substrate/catalyst molar ratio (S/C) = 500 under H_2 (5.0MPa) at 30 °C, although neither the RuCl complex (*R*,*R*)-**4** nor the $RuBF_4$ complex (*R*,*R*)-**5b** promoted the hydrogenation of **6a** in MeOH, toluene or THF, (*R*,*R*)-**5b** catalyzed the reaction in 2,2,2-trifluoroethanol (TFE) to give the 2-methylindoline (**7a**) in 32% yield with 88% ee (entry 6). The use of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) as a fluorinated solvent further improved the catalytic performance of (*R*,*R*)-**5b** to give **7a** in 65% yield with a higher stereoselectivity of 94% ee (entry 7).

TABLE 1. Initial Screening for the Asymmetric Hydrogenation of 2-Methylindole



6a **7a**

entry	catalyst	solvent[a]	yield (%)[b]	ee (%)[c]
1	(*R*,*R*)-**4**	MeOH	<0.1	-
2	(*R*,*R*)-**4**	Toluene	<0.1	-
3	(*R*,*R*)-**5b**	MeOH	<1	-

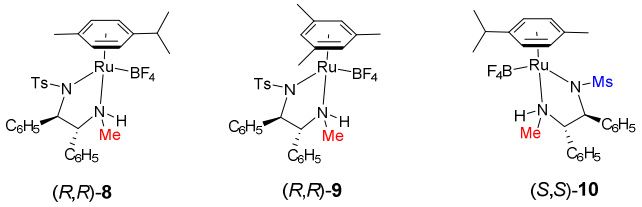
4	(*R*,*R*)-**5b**	Toluene	1	-
5	(*R*,*R*)-**5b**	THF	<1	-
6	(*R*,*R*)-**5b**	TFE[d]	32	88(*R*)
7	(*R*,*R*)-**5b**	HFIP[e]	65	94.1(*R*)

[a] 0.7mL/100mg substrate of solvent was used. [b] GC yield. [c] Determined by HPLC analysis. [d] 2,2,2-Trifluoroethanol [e] 1,1,1,3,3,3-Hexafluoroisopropanol

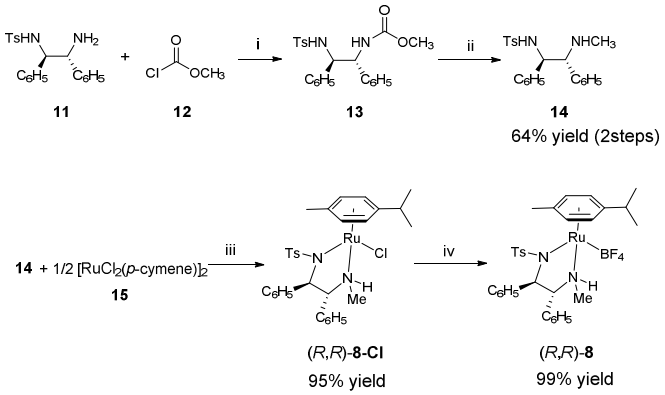
Synthesis of New Cationic η^6-Arene/*N*-Me-sulfonyldiamine-Ru(II) Complexes and Its Application for Asymmetric Hydrogenation of 2-Methylindole.

Ikariya and Wills reported that the catalytic activity of η^6-arene/sulfonyldiamine-Ru(II) complexes could be enhanced with the use of a secondary amino analogue.[10] Based on a consideration of the ease of preparation and the practical utility of related cationic complexes, we newly prepared a series of *N*-methylated $RuBF_4$ complexes (**8-10**) (Figure 3).

FIGURE 3. New Cationic η^6-Arene/*N*-Me-sulfonyldiamine-Ru(II) Complexes



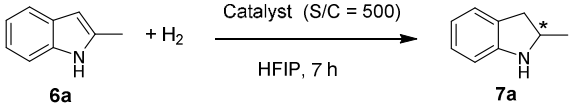
SCHEME 3. Preparation of New Cationic η^6-Arene/*N*-Me-sulfonyldiamine-Ru(II) Complexes (*R*,*R*)-**8**



Conditions:
i) K_2CO_3, THF-H_2O, r.t., 2 h
ii) Vitride®, Toluene, reflux, 2 h, 64% yield (2 steps)
iii) Et_3N, 2-Propanol, 80 °C, 1 h, 95% yield
iv) $AgBF_4$, MeOH-CH_2Cl_2, r.t., 2 h, 99% yield

N-Methylated TsDPEN ligand (**14**) was prepared by the treatment of (*R*,*R*)-TsDPEN (**11**) with methyl chloroformate (**12**) under Schotten-Baumann reaction conditions (i) and subsequent reduction using Vitride® (ii) in 64% yield in two steps. Complexation of ligand (**14**) with $[RuCl_2(p\text{-cymene})]_2$ (**15**) easily afforded the parent RuCl complex ((*R*,*R*)-**8-Cl**) (iii) and cationic $RuBF_4$ complex ((*R*,*R*)-**8**) was prepared by the anion exchange reaction using $AgBF_4$ in quantitative yield (iv).

TABLE 2. Catalyst Development for the Asymmetric Hydrogenation of 2-Methylindole[a]



entry	catalyst	H_2 (MPa)	temp (ºC)	yield (%)[b]	ee (%)[c]
1	(*R*,*R*)-**5b**	5.0	30	65	94.1(*R*)
2	(*R*,*R*)-**8**	5.0	30	>99	95.6(*R*)
3	(*R*,*R*)-**9**	5.0	30	92	91.7(*R*)
4	(*S*,*S*)-**10**	5.0	30	>99	95.4(*S*)
5	(*R*,*R*)-**8**	5.0	20	>99	96.0(*R*)
6	(*R*,*R*)-**8**	5.0	10	98	96.2(*R*)
7	(*R*,*R*)-**8**	5.0	0	96	96.4(*R*)
8	(*R*,*R*)-**8**	3.0	10	96	96.0(*R*)
9	(*R*,*R*)-**8**	1.0	10	96	95.9(*R*)
10[d]	(*R*,*R*)-**8**	5.0	10	>99[e]	96.2(*R*)
11[f]	(*R*,*R*)-**8**	5.0	10	93	90.0(*R*)

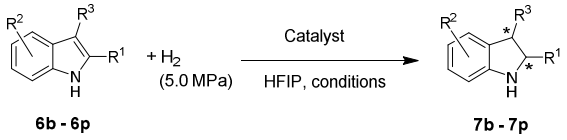
[a] 0.7mL/100mg substrate of solvent was used. [b] GC yield. [c] Determined by HPLC analysis. [d] S/C = 1 000, 30 h. [e] Isolated yield was 99%. [f] S/C=100, HFIP (1.0 eq. to **6a**), without the other solvent, 18 h.

The *N*-methylated $RuBF_4$ complexes (*R*,*R*)-**8** and (*S*,*S*)-**10** furnished the full conversion of **6a** to give (*R*)-**7a** with 95.6% ee and (*S*)-**7a** with 95.4% ee, respectively. For the (*R*,*R*)-**8**-catalyzed hydrogenation, the reaction carried out at 0 ºC gave **7a** in up to 96.4 % ee, and the reaction could be conducted under a lower hydrogen pressure (3 or 1 MPa), which would be particularly important for industrial application. Finally, the catalyst loading could be successfully reduced to S/C = 1 000 for full conversion while maintaining the enantiomeric excess of **7a** (96.2% ee), though the reaction time was prolonged (entry 10). When the amount of HFIP was reduced to 1 eq. to **6a**, **7a** was obtained in 93% yield with 90% ee (entry 11).

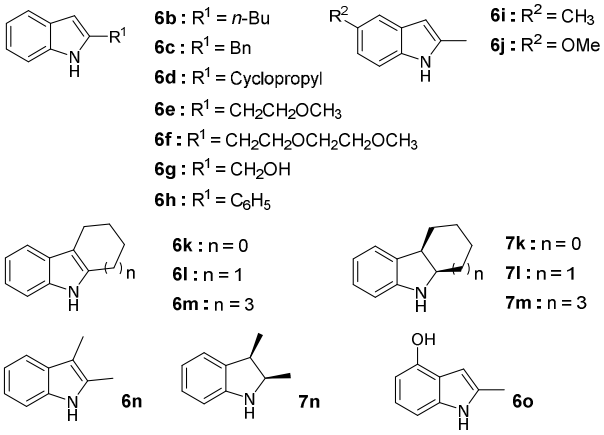
Asymmetric Hydrogenation of Various Unprotected Indoles.

With the ruthenium catalysts (*R*,*R*)-**8**, **9**, and (*S*,*S*)-**10**, the generality of the asymmetric hydrogenation of indoles was examined, and the results with the use of appropriate catalysts for particular substrates are summarized in Table 3.

TABLE 3. Asymmetric Hydrogenation of Unprotected Indoles[a]



6b - 6p **7b - 7p**



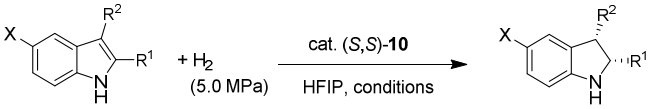
entry	substrate	catalyst	S/C	temp (ºC)	time (h)	yield[b] (%)	ee[c] (%)
1	**6b**	(*R*,*R*)-**8**	100	0	30	>99	97(*R*)
2	**6c**	(*R*,*R*)-**8**	250	10	27	96	97(*R*)
3	**6d**	(*R*,*R*)-**8**	100	0	7	93	83(*S*)
4	**6e**	(*S*,*S*)-**10**	100	30	30	99	83(-)
5	**6f**	(*R*,*R*)-**8**	100	10	25	84	86(+)
6	**6g**	(*R*,*R*)-**8**	100	10	30	98	73(*S*)
7	**6h**	(*S*,*S*)-**10**	100	60	20	38	42(+)
8	**6i**	(*S*,*S*)-**10**	500	10	7	>99	96(*S*)
9	**6j**	(*S*,*S*)-**10**	500	10	7	>99	95(+)
10[d]	**6k**	(*R*,*R*)-**9**	2 000	0	30	97	91(*R*,*R*)
11[d]	**6l**	(*R*,*R*)-**8**	250	30	31	96	96(*R*,*R*)
12[d]	**6m**	(*R*,*R*)-**8**	100	30	27	59	>99(+)
13[e]	**6n**	(*R*,*R*)-**8**	100	10	23	92	97 (*R*,*R*)
14	**6o**	(*R*,*R*)-**8**	250	10	28	>99	99(+)

[a] 0.7mL/100mg substrate of solvent was used. [b] Isolated yield. [c] Determined by GC or HPLC analysis. [d] Only *cis*-form products (**7k-7m**) were obtained. [e] Major product was the *cis* isomer (**7n**) (84.0% de (*cis*), and the ee of the *trans* isomer was 99% ee.)

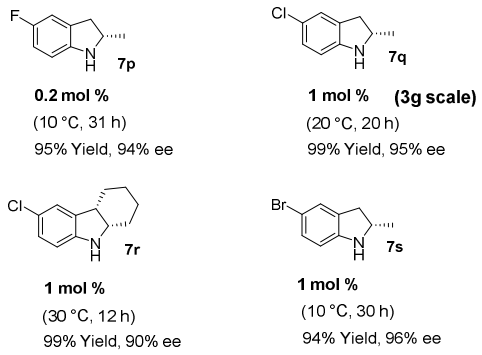
Under the optimized conditions, 2-alkylated indoles were smoothly hydrogenated to give the corresponding indolines in high conversion with high to excellent ees (entries 1,2). The cyclopropyl ring remained intact in (*R*,*R*)-**8**-catalysis to give **7d** with 83% ee. The (*1H*-indol-2-yl)methanol (**6g**) was also smoothly hydrogenated for the first time to directly access the chiral 2-hydroxymethtyl indoline (**7g**) with 73% ee. For methoxy ethyl-substituted **6e**, (*R*,*R*)-**8** gave **7e** with 74% ee, though (*S*,*S*)-**10** gave better results for **7e** with 83% ee. 2-Phenylindole (**6h**) was slowly converted to **7h** with moderate ee (entry 7). For 2-methylindoles with substituents at the 5-position, typically, (*S*,*S*)-**10** showed better results than (*R*,*R*)-**8** (entries 8,9). Ring-fused substrates (**6k**-**m**) that were connected between the 2- and 3-positions of indole were sufficient for the ruthenium-catalyzed asymmetric hydrogenation. The hydrogenation of 5-membered ring-fused substrate (**6k**) was smoothly catalyzed by (*R*,*R*)-**9** even with a catalyst loading of S/C = 2 000 (entry 10). The 8-membered system to give **6m** achieved >99% ee with (*R*,*R*)-**8** (entry 12). Although only *cis*-isomers were obtained for these ring-fused substrates, when 2,3-dimethylindole was subjected to hydrogenation, the *trans*-isomer was detected (*cis*: *trans* = 92 : 8), and both isomers showed a very high enantiomeric excess (97% ee for *cis* and 99% ee for *trans*) (entry 13). Interestingly, a substrate bearing a phenolic hydroxyl group at the 4-position of 2-methylindole was reduced by (*R*,*R*)-**8** with high yield and excellent ee (99% ee) (entry 14).

Asymmetric Hydrogenation of Halogenated Indoles.

TABLE 4. Asymmetric Hydrogenation of Halogenated Indoles [a]



6p - 6s **7p - 7s**



[a] 0.7 mL/100 mg substrate of solvent was used. [b] The results by using **(*R*,*R*)-8** catalyst were shown in *Supporting Information* (Table S2).

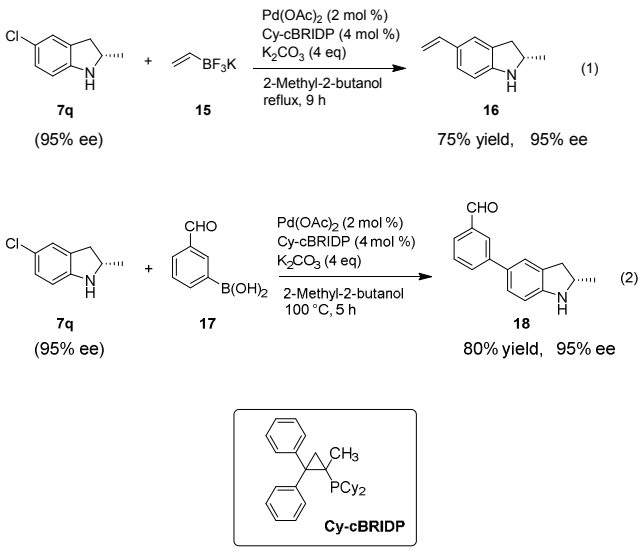
The (*S*,*S*)-**10**-catalyzed asymmetric hydrogenation is also useful for the reduction of indoles having electron-withdrawing substituents. The 5-fluoro-2-methylindole was successfully

converted to the 5-fluoro-2-methylindoline with 94% ee. Furthermore, the reduction of chloro- or bromo-substituted indoles was fascinating, since various late-transition metal-mediated reduction caused dehalogenation as a side reaction. 5-Chloro- and 5-bromo-2-methylindole were converted to the corresponding indolines **7q** and **7s** in almost quantitative yields and with high enantioselectivities (95% ee and 96% ee, respectively), while retaining the halogen atoms. In these reactions, dehalogenated products were not observed, and the reaction could be carried out on a 3 g scale to give **7q**.

Derivatization of (*S*)-5-Chloro-2-methylindoline.

The synthetic utility of the chiral (*S*)-5-chloro-2-methylindoline (**7q**) is shown in Scheme 4. The coupling reactions of **7q** with potassium vinyltrifluoroborate (**15**) and 3-formylphenylboronic acid (**17**) were catalyzed by a Pd-Cy-cBRIDP complex[11] to afford the corresponding coupling products **16** and **18** in high yields and without a loss of enantioselectivity. The successful introduction a hydrogenation-sensitive vinyl group or formyl group demonstrates the advantage of the current halogen-tolerant catalytic asymmetric reduction.

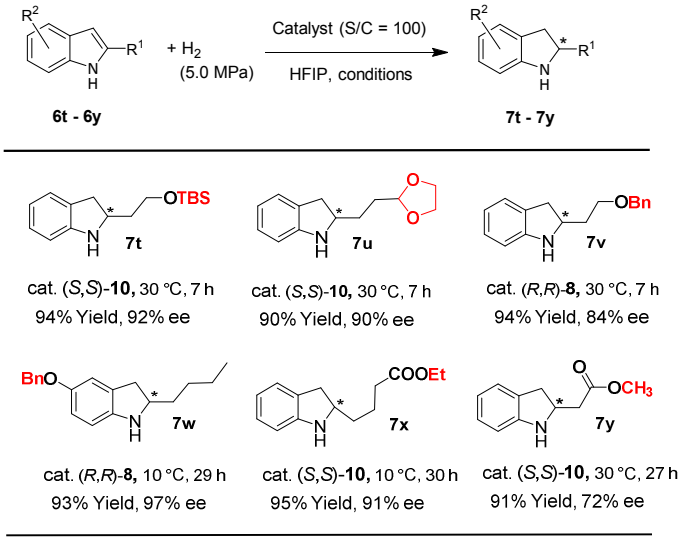
SCHEME 4. Derivatizations of (*S*)-5-chloro-2-methylindoline to 2-methyl-5-vinylindoline and (*S*)-5-(3-formylphenyl)-2-methylindoline.



Asymmetric Hydrogenation of Indoles with Protecting Groups.

Furthermore, the results using indoles with synthetically important protecting groups are fascinating, as shown in Table 5.

TABLE 5. Asymmetric Hydrogenation of Indoles with Protecting Groups[a]



[a] 0.7 mL/100 mg substrate of solvent was used.

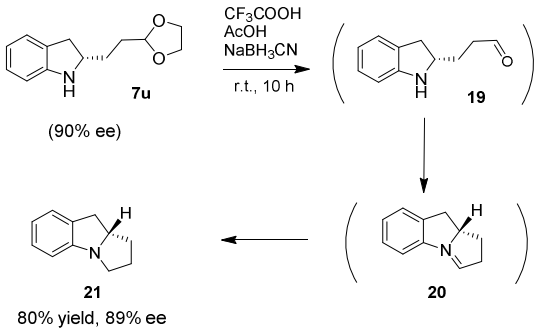
In weakly acidic HFIP reaction media (pH = 4–5), the acid-sensitive *tert*-butyldimethylsilyl (TBS) protecting group of a primary alcohol and ethylene acetal of an aliphatic aldehyde were tolerated in the (*S*,*S*)-**10**-catalyzed hydrogenation to give **7t** in 94% yield with 92% ee and **7u** in 90% yield with 90% ee, respectively. Both benzyl ethers of primary alcohol and phenolic alcohol survived in the (*R*,*R*)-**8**-catalyzed hydrogenation. Ethyl ester was also compatible with the hydrogenation to give **7x** in 95% yield with 91% ee. Since the previously reported H_8-BINAP-Pd catalysis in CSA[9a,b] did not give **7t** or **7u** at all, these results demonstrate the advantages of the current ruthenium catalysis directed toward the synthesis of further complex indoline-derived compounds (see details in the *Supporting Information*).

Derivatization of Chiral Indoline to Tetrahydro-*1H*-pyrroloindole.

A one-pot derivatization of acetal-protected chiral indoline (**7u**) to chiral tetrahydro *1H*-pyrroindole (**21**) is shown in Scheme 5. After the deprotection of acetal **7u** with trifluoroacetic acid, subsequent reduction of the intermediary tetrahydro pyrroloindolium salt using sodium cyanoborohydride gave **21** in high yield and with almost no loss of enantioselectivity.

As shown in Figure 1, chiral tetrahydro-*1H*-pyrroloindole skeletons are found in some biologically active compounds, which have been prepared in multistep syntheses that include optical resolution. This is the first and practical example of the catalytic asymmetric synthesis of tetrahydro-*1H*-pyrroloindole.

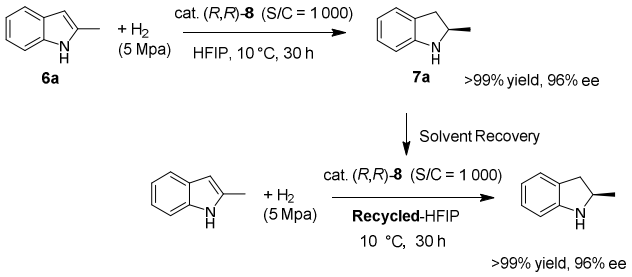
SCHEME 5. Derivatization of Chiral Indoline to Tetrahydro-*1H*-pyrroloindole



Reuse of HFIP Solvent for Asymmetric Hydrogenation.

From the perspective of green chemistry and industrial production, the reuse of solvent is very important. Since the current reaction system of asymmetric hydrogenation does not require the use of co-solvents or additives, the solvent can be easily recovered by simple distillation after the reaction is complete. The HFIP solvent was recovered quantitatively after hydrogenation of 2-methylindole, and the recovered HFIP was reused in the next hydrogenation to give 2-methylindole without a loss of yield or enantioselectivity (Scheme 6).

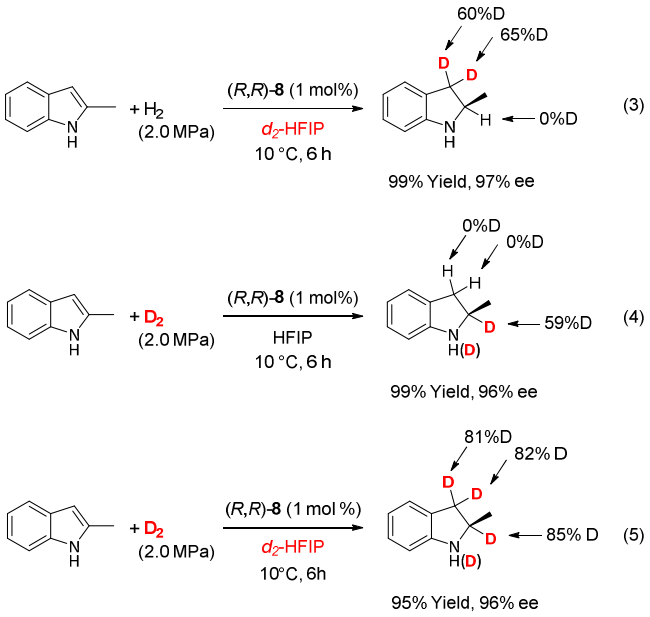
SCHEME 6. Reuse of the HFIP Solvent for Asymmetric Hydrogenation of 2-Methylindole



Mechanistic Study by Using Isotopic Labeling Experiments.

To elucidate the reaction mechanism, the negligible asymmetric transfer hydrogenation (ATH) reaction in this HFIP solvent system was firstly confirmed (see details in the *Supporting Information*). When asymmetric hydrogenation was run in d_2-HFIP and H_2, ^{1}H-NMR analysis showed that two deuterium atoms were introduced at the 3-position, and deuteration at the 2-position was not observed (eq. 3, Scheme 7).

SCHEME 7. Isotopic Labeling Experiments Using D_2 and d_2-HFIP



In contrast, when hydrogenation was performed with D_2 and HFIP, the incorporation of deuterium was observed only at the 2-position and the amine of the indoline (eq. 4, Scheme 7). These experimental results prove that unprotected indoles are activated in the weakly acidic HFIP solvent to form an iminium intermediate, and the η^6-arene/*N*-Me-sulfonyldiamine-Ru(II)-BF_4 complexes hydrogenate the iminium intermediate quite effectively to provide asymmetric indoline synthesis. This highly efficient asymmetric hydrogenation is believed to occur through cooperation between ruthenium-hydride and amine-NH in the concerto catalysis.[12] The moderate isotropic labeling at 2-position in eq. 4 was discussed in the *Supporting Information*, and was improved by carrying out the reaction using both D_2 and d_2-HFIP (eq. 5).

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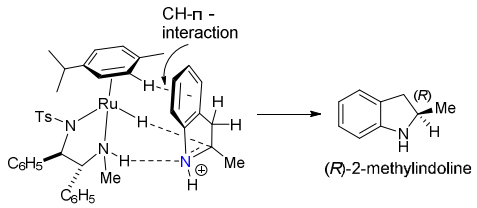
Proposed Transition State.

In the reaction of ketonic or imine substrates with η^6-arene/sulfonyldiamine-Ru(II) complexes, a CH/π interaction between a hydrogen atom on the η^6-arene and the aromatic ring of a substrate has been proposed.[10c-d,13] Furthermore, hydrogen-bonding interaction between the substrates with NH-proton of ligand is believed to facilitate the enantioface selection.[13] With these interactions, acetophenone is reduced to (*R*)-2-phenylethanol by (*R*,*R*)-Ru catalyst. Because (*R*)-enriched indoline was obtained using (*R*,*R*)-**8**, the reaction would proceed via a similar transition state (Figure 4). For the reduction of iminium intermediate, the cationic intermediate would seem to be difficult to receive the assistance of hydrogen-bonding. However, with including π-electron of C=N double bond of the iminium intermediate, the hydrogen-bonding network is workable for constructing the 6-membered transition state.[10d] If the proton is dissociated from the iminium intermediate, the hydrogen-bonding interaction using imine would strongly stabilize the 6-membered transition state. (See further discussion about the other possible transition states in the *Supporting Information* (Figure S4)).

FIGURE 4. Proposed Transition State



CONCLUSION

In conclusion, various unprotected indole compounds were efficiently hydrogenated by η^6-arene/*N*-Me-sulfonyldiamine-Ru(II)-BF_4 catalysts under mildly acidic HFIP, which showed advantages for the synthesis of further complex molecules. The 5-halo-2-methylindoles were converted to the corresponding indolines with retaining the halogen atoms. From the 5-halo-2-methylindoles, cross coupling reactions were accomplished. Some acid-sensitive protective groups were also tolerant under the mild η^6-arene/*N*-Me-sulfonyldiamine-Ru(II)-BF_4 catalyses. With these fascinating and powerful hydrogenation, further applications toward the synthesis of advanced indoline molecules are now being examined by our group.

EXPERIMENTAL DETAILS

General procedure for Asymmetric Hydrogenation of Indoles Using η^6-Arene/*N*-Me-sulfonyldiamine-Ru(II) complexes under the conditions of S/C = 500, 10 °C for 7 h.

Indole (1.5 mmol) and Ru catalyst (0.003 mmol) were placed in a 100 mL stainless steel autoclave equipped with a glass inner tube. The atmosphere was replaced with argon gas, and solvent (1.4 mL) was added to this mixture. Hydrogen was initially introduced into the autoclave at a pressure of 1.0 MPa, before being reduced to 0.1 MPa. This procedure was repeated three times. Then the autoclave was pressurized with H_2 gas (5.0 MPa), and the solution was stirred vigorously at 10 ^{o}C for 7 h. The product was obtained by silica gel chromatography. Optical purities of the products were determined by Chiral-GC or HPLC analysis.

ASSOCIATED CONTENT

Supporting Information

Methods for preparing Ru complexes and indoles, experimental procedures for asymmetric hydrogenation, NMR, MS, chiral-GC and chiral-HPLC data, $[\alpha]_D$ values of products,. This material is available free of charge via the Internet at http://pubs.acs.org.

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Both authors helped to write the manuscript. Both authors have approved the final version of the manuscript. These authors contributed equally.

Notes

The authors declare no competing financial interests.

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ABBREVIATIONS

TsDPEN, (*N*-(*p*-Toluenesulfonyl)-1,2-diphenylethylenediamine

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