Asymmetric Hydrogenation of Unprotected Indoles Catalyzed by η^6-Arene/*N*-Me-sulfonyldiamine-Ru(II) complexes

η^6-Arene/*N*-Me-sulfonyldiamine-ルテニウム(II) 錯体を用いた
無保護インドール類の不斉水素化反応の開発

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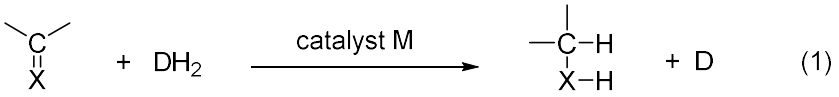
Efficient Access to Chiral Benzohydrols via Asymmetric Transfer Hydrogenation of Unsymmetrical Benzophenones with Bifunctional Oxo-tethered Ruthenium Catalysts

Chapter 1.

General Introduction of η⁶-Arene/sulfonyldiamine-Ru(II) complexes

Asymmetric reduction of C=O and C=N bonds producing chiral alcohols and amines is the most fundamental and powerful molecular transformations. In nature, oxidoreductases such as horse liver alcohol dehydrogenase catalyze transfer hydrogenation of carbonyl compounds to alcohols using cofactors like NADH or NADPH. Such biochemical reactions are generally very stereoselective. However, organic synthesis needed economically and technically more beneficial methods. A reaction using nonhazardous organic molecules (eq 1) provides a useful complement to catalytic reduction using molecular hydrogen.

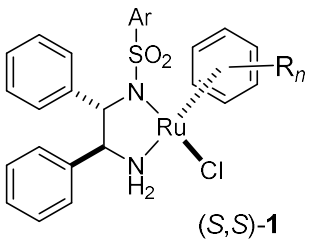


X = O, NR
DH_2 = hydrogen donor

Asymmetric transfer hydrogenation is operationally simple, and the selectivities including functional group differentiation may be different from those of H_2-hydrogenation.

In 1995, Noyori et al. developed practical and outstanding catalysts for asymmetric transfer hydrogenation. They found that *N*-sulfonyl ethylenediamine is an excellent promoter of the Ru catalyzed transfer hydrogenation[1]. In fact they found that a chiral Ru complex represented as **1** acts as an excellent catalyst for asymmetric transfer hydrogenation of aromatic ketones in 2-propanol. Experimental results proposed that the (*S*,*S*)-**1a**-catalyzed reaction of acetophenone proceeds with an excellent enantioface differentiation, k_{Re}/k_{si} = 99, and that the resulting (*S*)-alcohol is more susceptible to the reverse reaction by a factor of 99. Because of the occurrence of the reverse process, the level of enantioselection decreases with increasing conversion of the ketone reductions.

Figure 1. η⁶-Arene/sulfonyldiamine-Ru(II) complexes

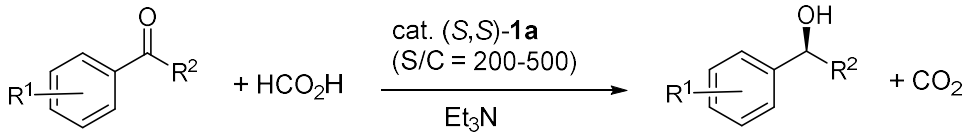


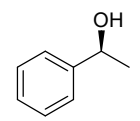
(*S*,*S*)-**1**

a: Ar = 4-$CH_3C_6H_4$: η⁶-arene = mesitylene
b: Ar = 4-$CH_3C_6H_4$: η⁶-arene = *p*-cymene
c: Ar = 4-$CH_3C_6H_4$: η⁶-arene = benzene
d: Ar = 2,4,6-$(CH_3)_3C_6H_2$: η⁶-arene = *p*-cymene
e: Ar = 2,4,6-$(CH_3)_3C_6H_2$: η⁶-arene = benzene
f: Ar = 1-naphthyl: η⁶-arene = benzene

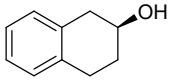
On the other hand, formic acid is other well-behaving, inexpensive reducing agent. The asymmetric reduction using this hydrogen donor, an adduct of H_2 and CO_2, in place of 2-propanol must proceed irreversibly with truly kinetic enantioselection. In this reaction conditions, reaction will be a 100% conversion in principle. In fact the reaction with a 5:2 formic acid-triethylamine azeotropic mixture, in the presence of the chiral Ru catalyst **1a** has provided a simple solution to this longstanding problem. Although Ru(II) complexes generally catalyze the reversible process $HCO_2H \rightleftarrows H_2 + CO_2$, molecular hydrogen does not participate in the ketone reduction under these catalytic conditions. As summarized in Table 1, many kinds of aromatic ketones are reduced to the corresponding secondary alcohols with higher yield and ee[1b].

Table 1. Asymmetric Transfer Hydrogenation of Ketones Using (*S*,*S*)-**1**

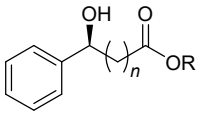




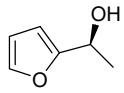
>99%, 96% ee



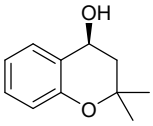
70%, 82% ee



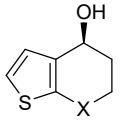
R = CH_3; *n* = 3 99%, 95% ee
R = C_2H_5; *n* = 1 98%, 93% ee
R = $CH(CH_3)_2$; *n* = 0 94%, 75% ee



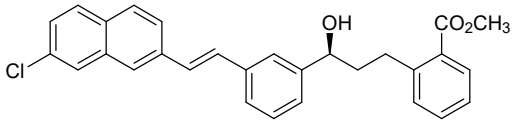
>99%, 98% ee



47%, 97% ee



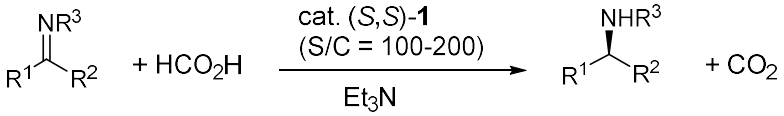
X = S 95%, 99% ee
X = SO_2 95%, 98% ee

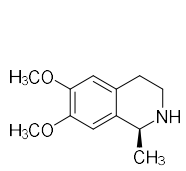


68%, 92% ee

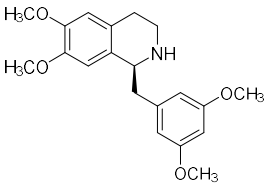
The arene-Ru(II) complexes of type **1** possessing some suitable chiral 1,2-diamine ancillaries also efficiently catalyze asymmetric reduction of imines with a formic acid-triethylamine axeotropic mixure. The reaction can be conducted with a formic acid-triethylamine mixture with an S/C ratio of 100-200 at room temperature in various polar solvents, such as acetonitrile, acetone, dichloromethane, DMF and DMSO [1f] (Table 2).

Table 2. Asymmetric Transfer Hydrogenation of Imines Using (*S*,*S*)-**1**

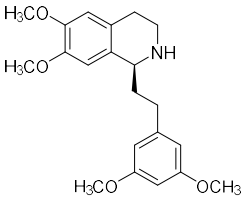




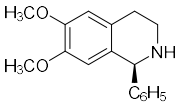
cat. **1b**
>99%, 95% ee



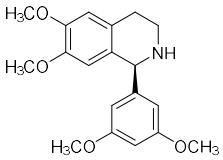
cat. **1d**
90%, 95% ee



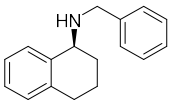
cat. **1d**
99%, 92% ee



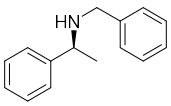
cat. **1f**
99%, 84% ee



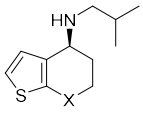
cat. **1f**
96%, 84% ee



cat. **1f**
90%, 89% ee



cat. **1e**
72%, 77% ee

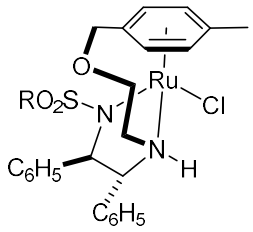


cat. **1e**
X = S 82%, 83% ee
X = SO_2 84%, 88% ee

In 2011, Touge and Ikariya developed oxo-tethered ruthenium complexs **3** and **4** [2] (Figure 2). The asymmetric transfer hydrogenation of ketones was successfully performed in 5:2 formic acid/ trimethylamine azeotoropic mixture. Remarkably corresponding chiral alcohols bearing a broad scope of substituents were enantioselectively synthesized with low catalyst loading, down to S/C = 30,000 (Table 3).

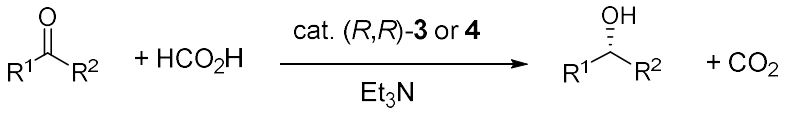
In this reported "oxo-tethered" ruthenium−arene catalysts, both the persistent inflicted coordination of the otherwise labile η^6-arene and the strong chelation of the sulfonamido-amine anchor led to prolonged life span of the active catalytic species. This resulted in a reinforced congregative three-point ligation of the conjugate ligand to the ruthenium metal core, thereby decreasing the overall structure flexibility and rigidifing the stereoarray of the catalyst. These factors can explain the enhanced catalytic performances.

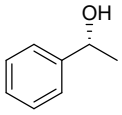
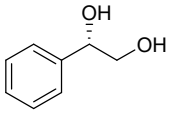
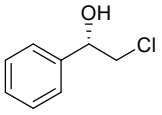
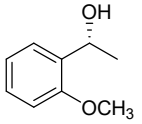
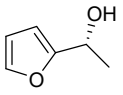
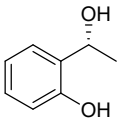
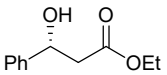
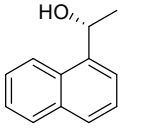
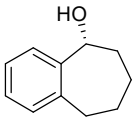
Figure 2. Structure of Oxo-Tethered Ruthenium(II) Catalysts



SO_2R = Ts (*R*,*R*)-**3** **(Ts-DENEB)**
Ms (*R*,*R*)-**4** **(Ms-DENEB)**

Table 3. Asymmetric Transfer Hydrogenation of Ketones Using (*R*,*R*)-**3** or (*R*,*R*)-**4**

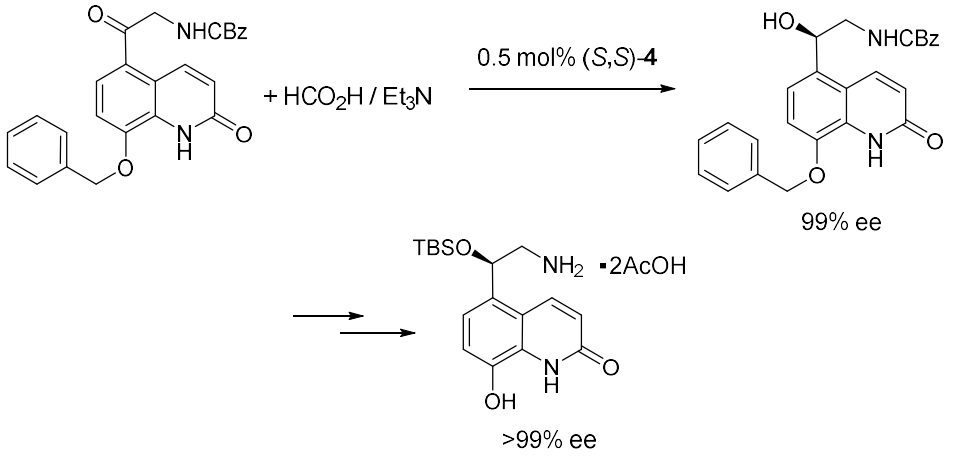


				
(*R*,*R*)-**3** (S/C = 30,000)	(*R*,*R*)-**3** (S/C = 1,000)	(*R*,*R*)-**3** (S/C = 1,000)	(*R*,*R*)-**3** (S/C = 1,000)	(*R*,*R*)-**3** (S/C = 1,000)
95%, 97% ee	98%, 96% ee	95%, 97% ee	99%, 93% ee	99%, 98% ee
				
(*R*,*R*)-**3** (S/C = 1,000)	(*R*,*R*)-**3** (S/C = 1,000)	(*R*,*R*)-**4** (S/C = 1,000)	(*R*,*R*)-**4** (S/C = 1,000)	
95%, 96% ee	99%, 96% ee	96%, 97% ee	85%, 98% ee	

In industrial aspects, oxo-tethered ruthenium complexes **3** and **4** are using for the synthesis of some active pharmaceutical ingrediants.

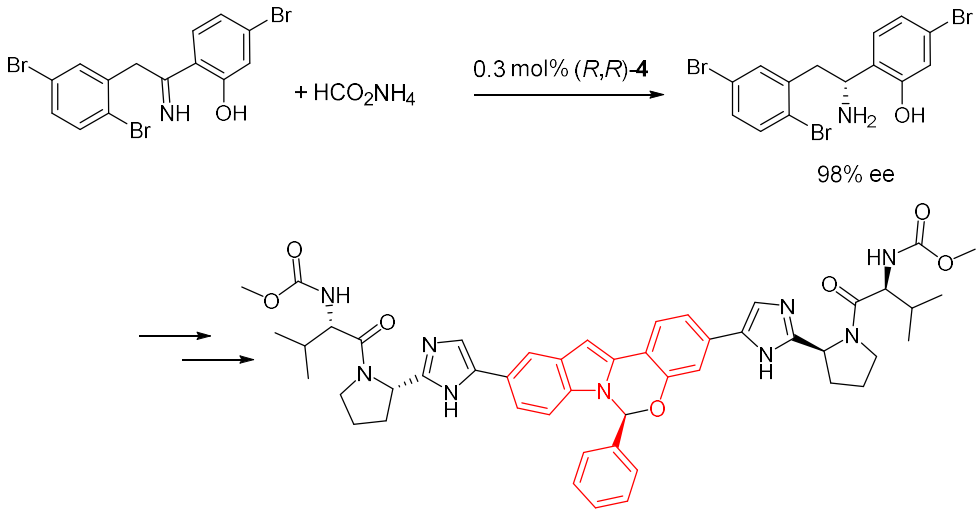
For example, in Teijin Pharma, an efficient and scalable enantioselective synthesis of the intermediate for a β2-adrenergic receptor agonist has been developed. This synthesis features an enantioselective reduction of α-amino-acetophenone derivative using the (*S*,*S*)-**4** (Ms-DENEB). Effective asymmetric transfer hydrogenation of the ketone substrate to the chiral alcohol afforded the primary amine in >99% ee [6].

Scheme 1. Asymmetric Synthesis of a Key Intermediate for the β2-Adrenergic Receptor Agonist (Teijin Pharma)



In Merck, a concise, enantioselective synthesis of MK-8742, a potent and selective NS5a inhibitor for the treatment of chronic HCV infection, has been developed. This approach features a highly enantioselective asymmetric hydrogenation of NH-imine using (*R*,*R*)-**4** (Ms-DENEB) and following a directed stereochemical relay strategy that leverages a dynamic diastereoselective condensation to produce the challenging hemiaminal stereocenter [7].

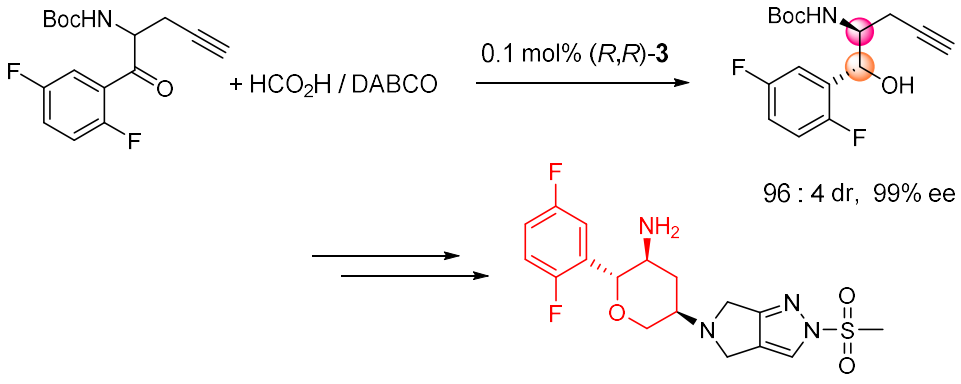
Scheme 2. Asymmetric Synthesis of a Key Intermediate for Elbasvir (MK-8742, Merck)



Elbasvir (MK-8742)

In Merck, development of a convergent synthesis of Omarigliptin (Marizev, MK-3102), a long-acting DPP‑4 inhibitor for the treatment of Type 2 Diabetes, the synthesis of the pyranone relies on (*R*,*R*)-**3** (Ts-DENEB)-catalyzed asymmetiric transfer hydrogenation *via* DKR reduction of a *rac*-*α*-aminoketone to set the two contiguous stereogenic centers [8].

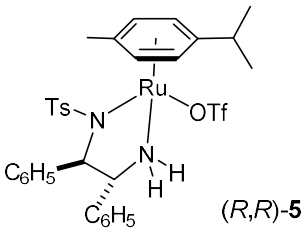
Scheme 3. Asymmetric Synthesis of a Key Intermediate for the Marizev (MK-3102, Merck)



Marizev (MK-3102)

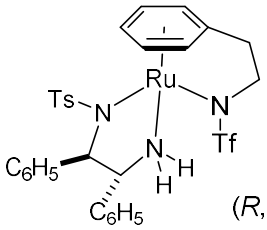
Chiral ruthenium η^6-arene/*N*-sufonyldiamine complexes, excellent catalysts for the asymmetric transfer hydrogenation of ketones, are also efficient catalysts for the H_2-hydrogenation of ketones under neutral or acidic conditions. Cationic ruthenium complex **5** developed by Ohkuma and co-workers including chiral Ts-DPEN ligand show high activity and enantioselectivity in the H_2-hydrogenation of 4-chromanones, and providing the corresponding chiral alcohols with 95-98% ee and up to 7,000 TON in the absence of a base [4a] (Scheme 4, eq 1). Catalyst **5** also gives high enantioselectivity in the H_2-hydrogenation of α-chloro aromatic ketones [4b]. The well-defined triflylamido ruthenium complex **6** developed by Ikariya and co-workers with a carbon-chain tether also affords high enantioselectivity (91-98% ee) in the H_2-hydrogenation of aromatic ketones, however, the turnover number of the catalyst was only 1,000 [5] (eq 2). The oxo-tethered ruthenium complex **3** and its dehydrochlorinated complex **3-16e**$^-$ developed by Touge and Ikariya give >99% ee in the H_2-hydrogenation of several aromatic cyclic ketones including 4-chromanone, and turnover numbers of up to 5,000. Furthemore this catalyst could be used in the hydrogenation of ester such as γ-butyrolactone under basic conditions (eq 3－5).

Figure 3. η^6-Arene/sulfonyldiamine-Ru(II) Complexes for Asymetric H_2-Hydrogenation



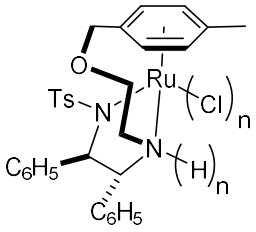
(*R*,*R*)-**5**

(Ohkuma, 2006)



(*R*,*R*)-**6**

(Ikariya, 2008)



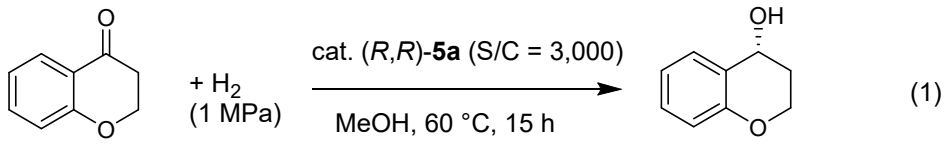
n = 1 (*R*,*R*)-**3** **(Ts-DENEB)**

n = 0 (*R*,*R*)-**3-16e**$^-$ **(Ts-DENEB-16e**$^-$**)**

(Touge, Ikariya, 2011)

Scheme 4. Asymmetric H_2-Hydrogenation of Ketones and Ester by Using η^6-Arene/sulfonyldiamine-Ru(II) complexes

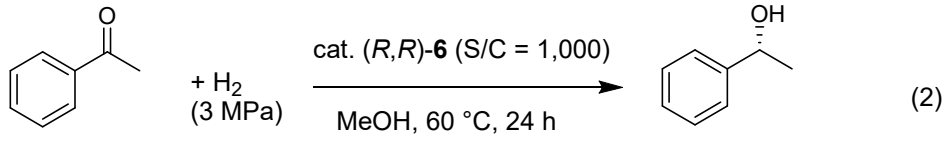
(Ohkuma *et al.* **2006**)



(1)

100% yield, 97% ee

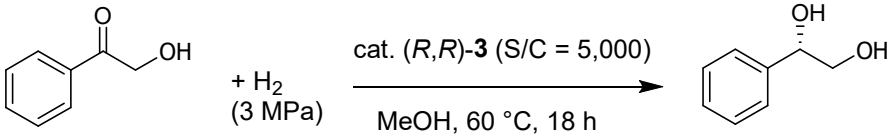
(Ikariya *et al.* **2008**)



(2)

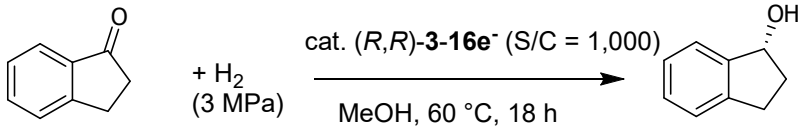
96% yield, 92% ee

(Touge, Ikariya *et al.* **2011**)



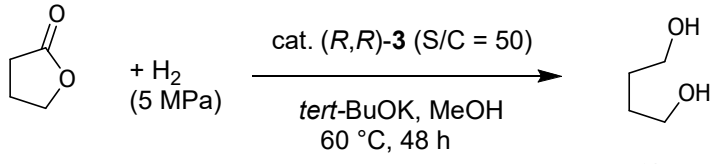
(3)

99% yield, 93% ee



(4)

97% yield, 98% ee



(5)

99% yield

References

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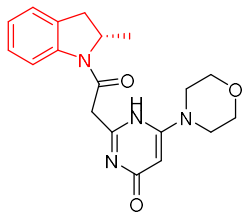
Chapter 2.

Asymmetric Hydrogenation of Unprotected Indoles Catalyzed by η^6-Arene/*N*-Me-sulfonyldiamine-Ru(II) complexes

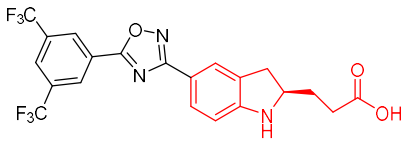
1. Introduction

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).

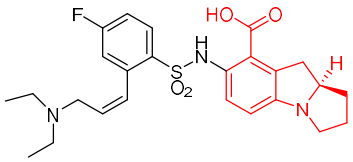
Figure 1. Examples of Biologically Active Compounds Containing Chiral Indoline



1
(SAR-260301)



2

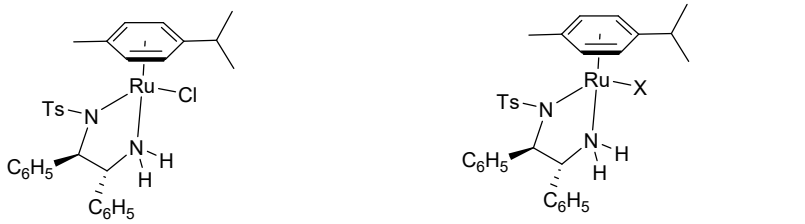


3

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 η^6-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 (Scheme 1).[5] The BF_4 analog ((*R*,*R*)-**5b**) has also been shown to exhibit similar catalytic activity.[6a]

Figure 2. η^6-Arene/sulfonyldiamine-Ru(II) Complexes

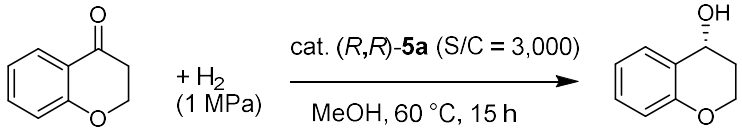


(*R*,*R*)-**4**
Noyori
Ikariya
(1996)

(*R*,*R*)-**5a** X = TfO
Ohkuma
(2006)

(*R*,*R*)-**5b** X = BF_4

Scheme 1. Example of the Reaction Using Complex (*R*,*R*)-5a



100% yield, 97% ee

(Ohkuma *et al.* **2006**)

Through the use of η^6-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 2.[6] For example, 2-methylquinoline and 2-methylquinoxaline can be successfully 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 2. Asymmetric Reduction of *N*-Hetero Aromatic Compounds with η^6-Arene/sulfonyldiamine-Ru(II) Complexes[7]

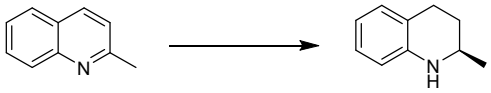
[Method A] *Asymmetric Transfer Hydrogenation*

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

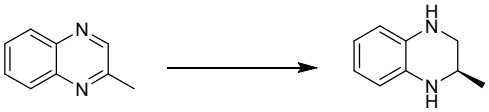
(a) 2-Methylquinoline



[Method A] 55% yield, 65% ee

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

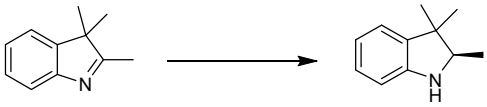
(b) 2-Methylquinoxaline



[Method A] 79% yield, 83% ee

[Method B] 92% yield, 26% ee

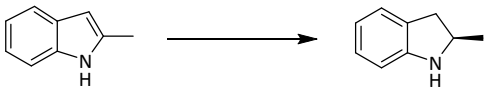
(c) 2,3,3-Trimethylindolenine



[Method A] 43% yield, 39% ee

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

(d) 2-Methylindole

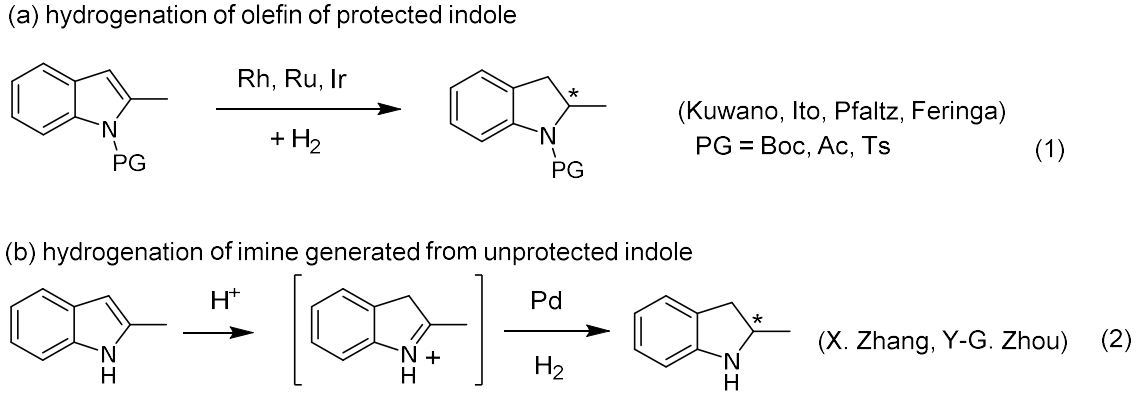


[Method A] No Reaction

[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 3, 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 3, eq. (2)).

Scheme 3. Classification of the Asymmetric Hydrogenation of Indoles.



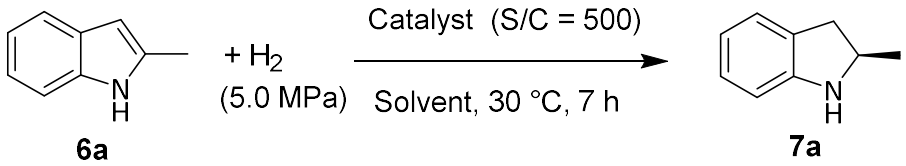
There has been limited success in the catalytic asymmetric reduction of unprotected indoles, and there is no previous report on the Ru-catalyzed reduction of unprotected indoles. We report here the first chiral Ru(II) complex-catalyzed hydrogenation of unprotected indoles under mild reaction conditions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

2. Results and Discussions

2.1 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



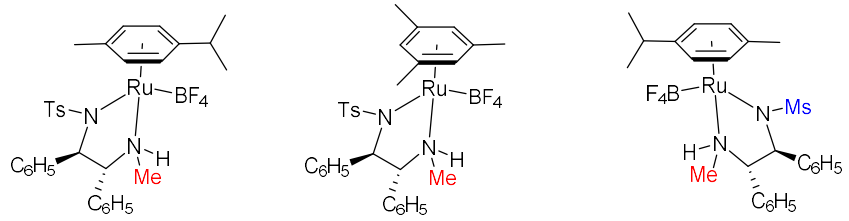
entry	catalyst	solvent[a]	yield (%)[b]	ee (%)[c]
1	(*R*,*R*)-**4**	MeOH	<0.1	-
2	(*R*,*R*)-**4**	Toluene	<0.1	-
3	(*R*,*R*)-**5b**	MeOH	<1	-
4	(*R*,*R*)-**5b**	Toluene	1	-
5	(*R*,*R*)-**5b**	THF	<1	-
6	(*R*,*R*)-**5b**	TFE[d]	32	88(*R*)
7	(*R*,*R*)-**5b**	HFIP[e]	65	94.1(*R*)

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

2.2 Synthesis of New Cationic η⁶-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 η⁶-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, the author newly prepared a series of *N*-methylated $RuBF_4$ complexes (**8-10**) (Figure 3).

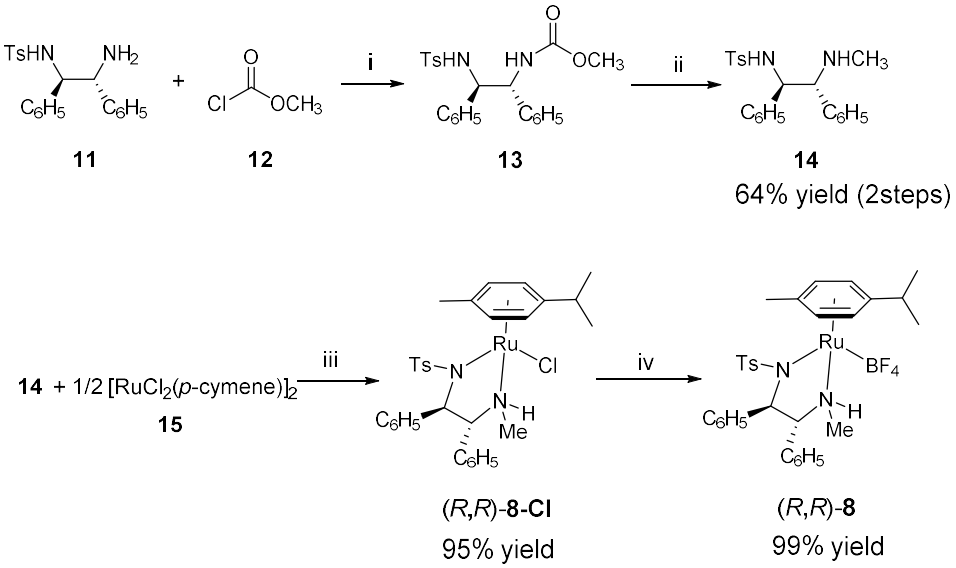
Figure 3. New Cationic η⁶-Arene/*N*-Me-sulfonyldiamine-Ru(II) Complexes



(*R*,*R*)-**8** (*R*,*R*)-**9** (*S*,*S*)-**10**

New genenation

Scheme 4. Preparation of New Cationic η⁶-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 the 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).

Figure 4. ^{1}H NMR of (*R*,*R*)-**8** (400 MHz, CD_3OD)

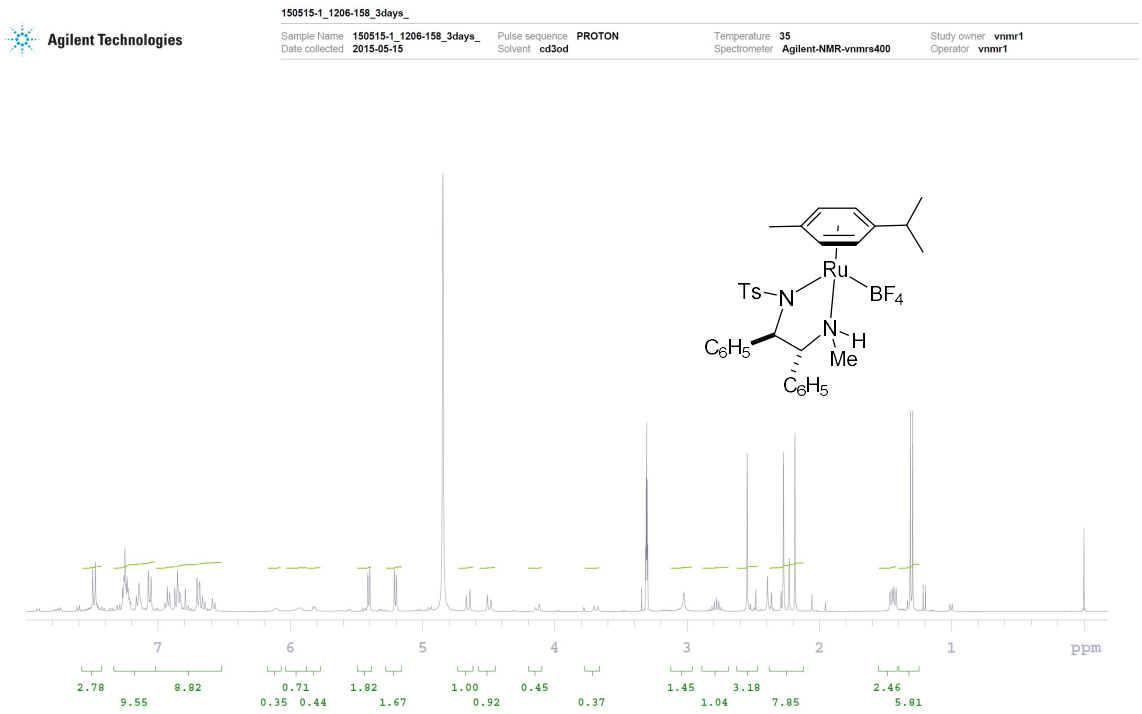


Figure 5. ^{13}C NMR of (*R*,*R*)-**8** (125 MHz, CD_3OD)

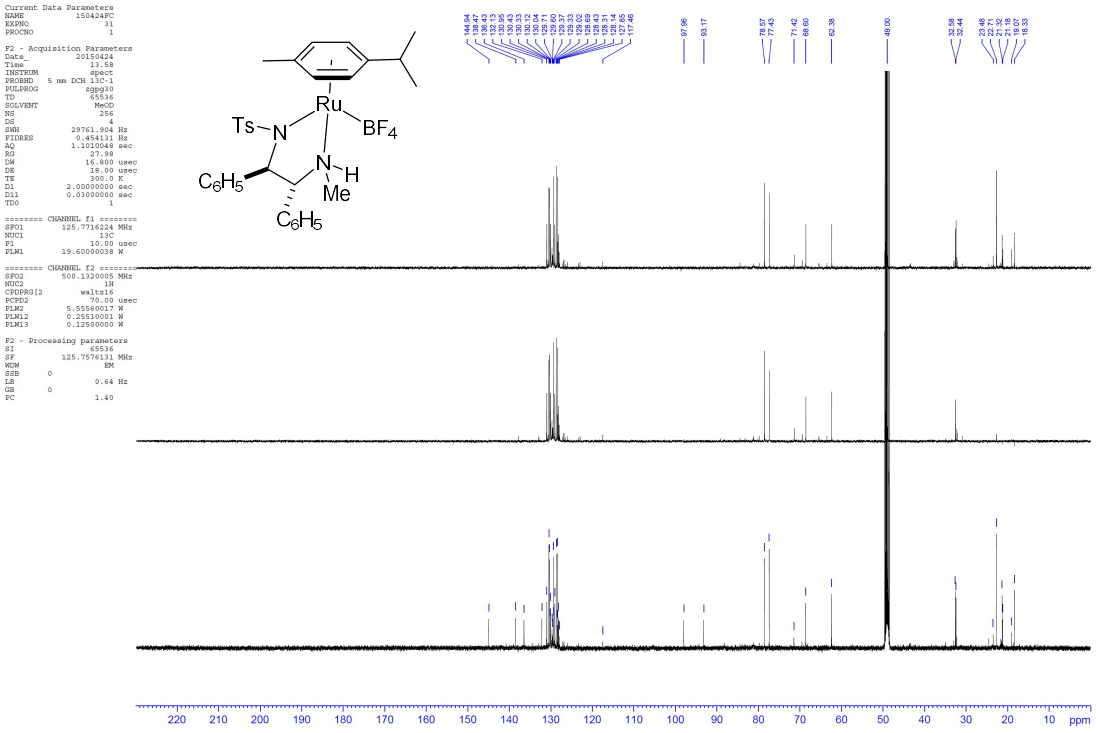


Figure 6. ^{1}H-^{1}H COSY of (*R*,*R*)-**8** (500 MHz, CD_3OD)

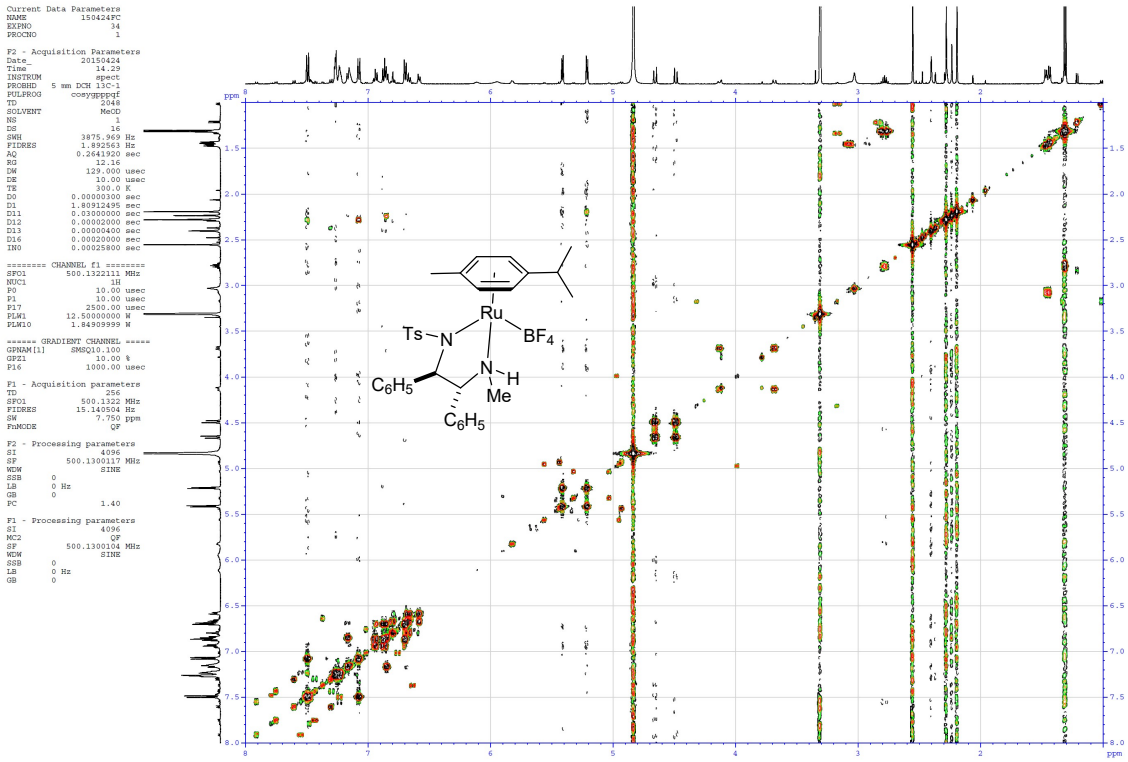


Figure 7. HSQC of (*R*,*R*)-**8** (500 MHz, CD_3OD)

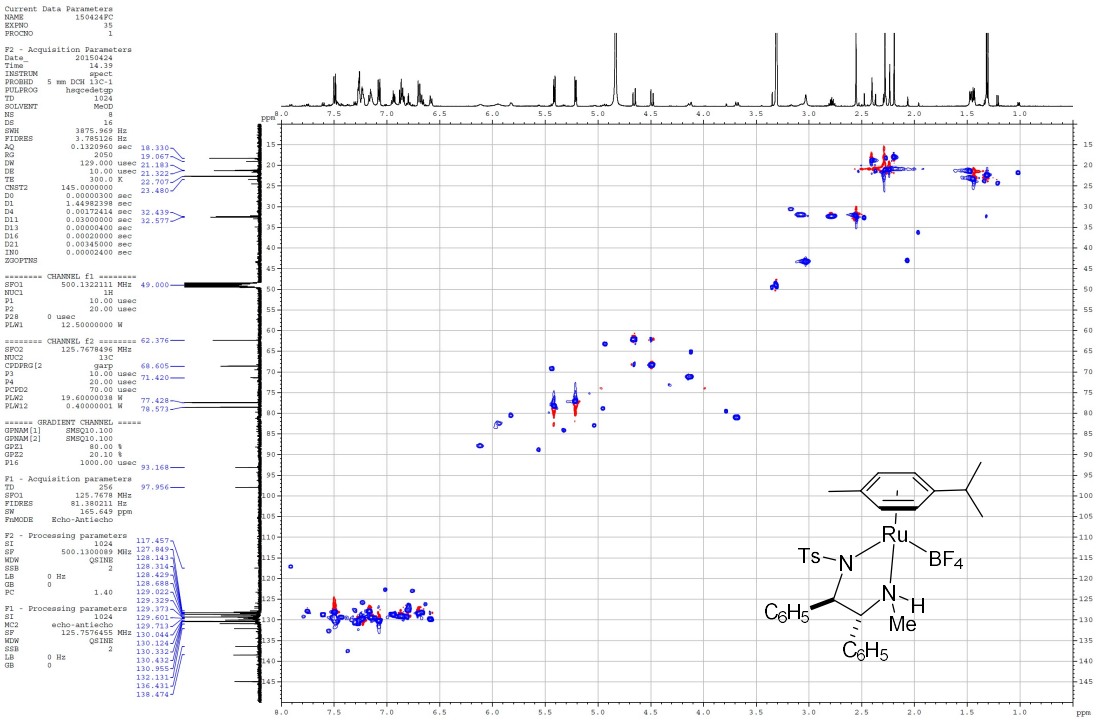


Figure 8. HMBC of (*R*,*R*)-**8** (500 MHz, CD_3OD)

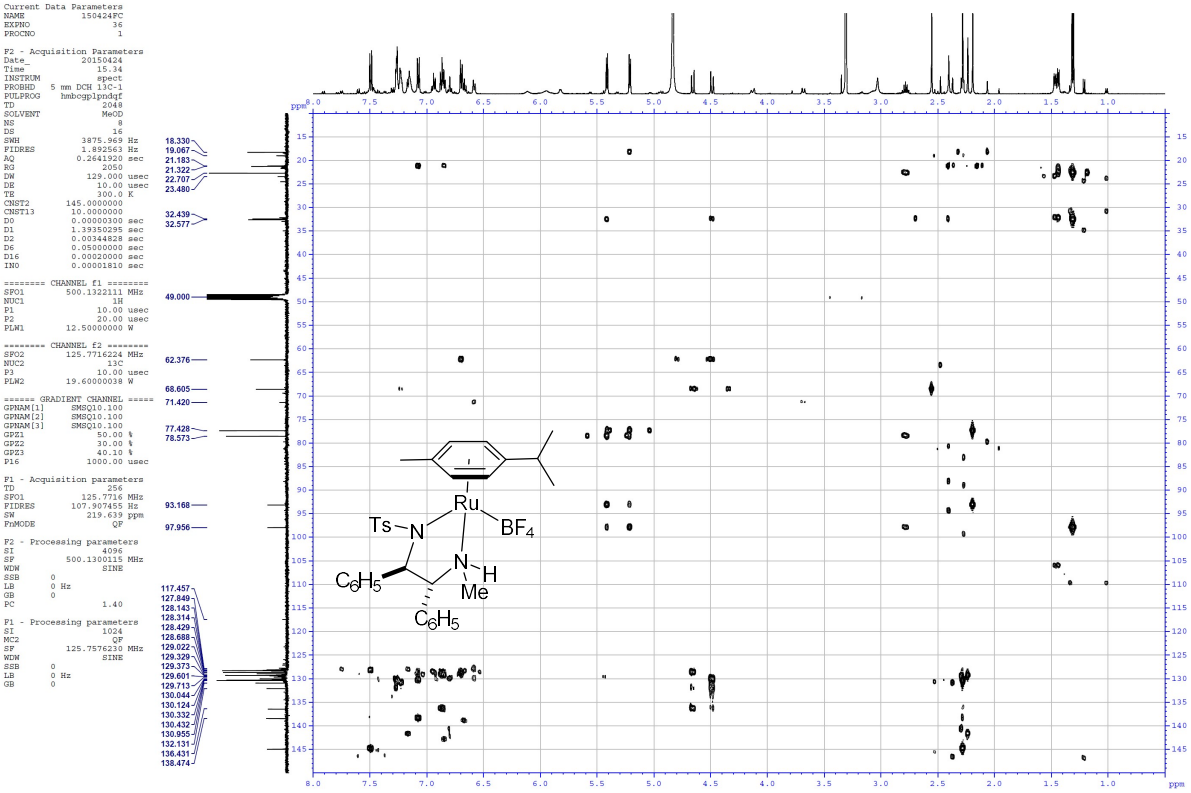
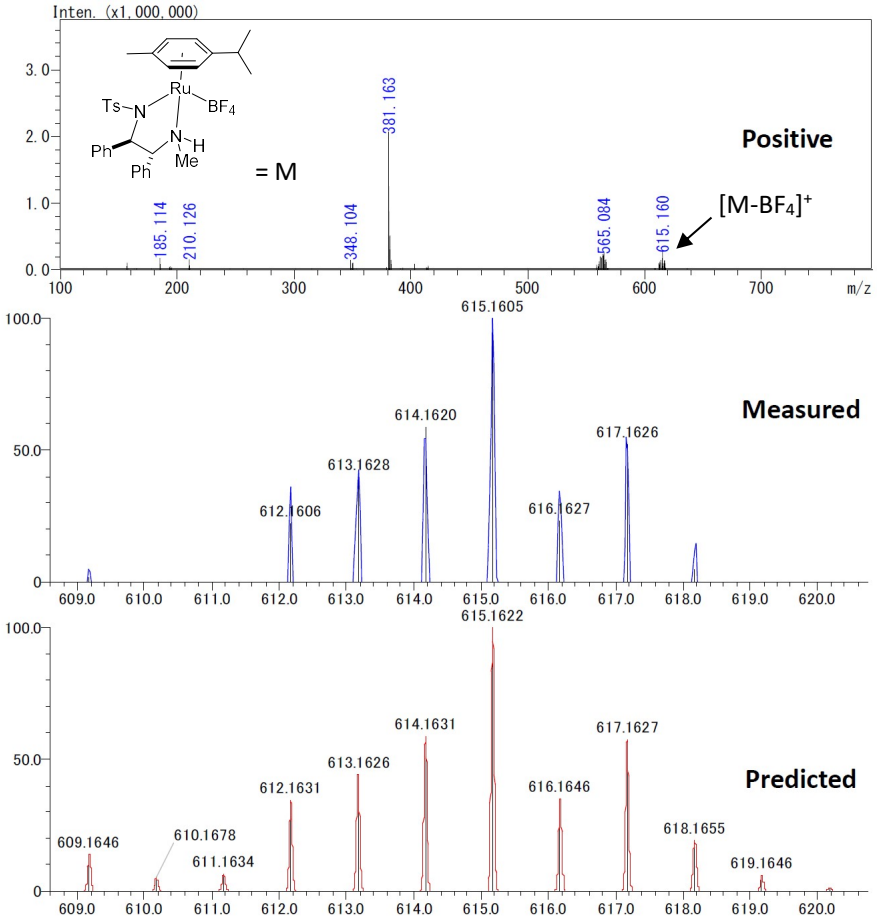
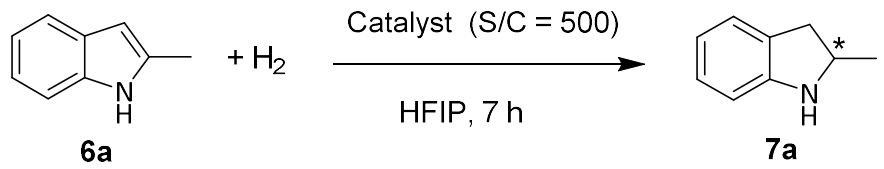


Figure 9. ESI-MS of (*R*,*R*)-**8**



Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Diff (mDa)	Diff (ppm)	DBE	Pred. (M)
77.83	C32 H37 N2 O2 S Ru	M+	615.1605	615.1622	-1.7	-2.76	15.5	615.1627

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



6a **7a**

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*)

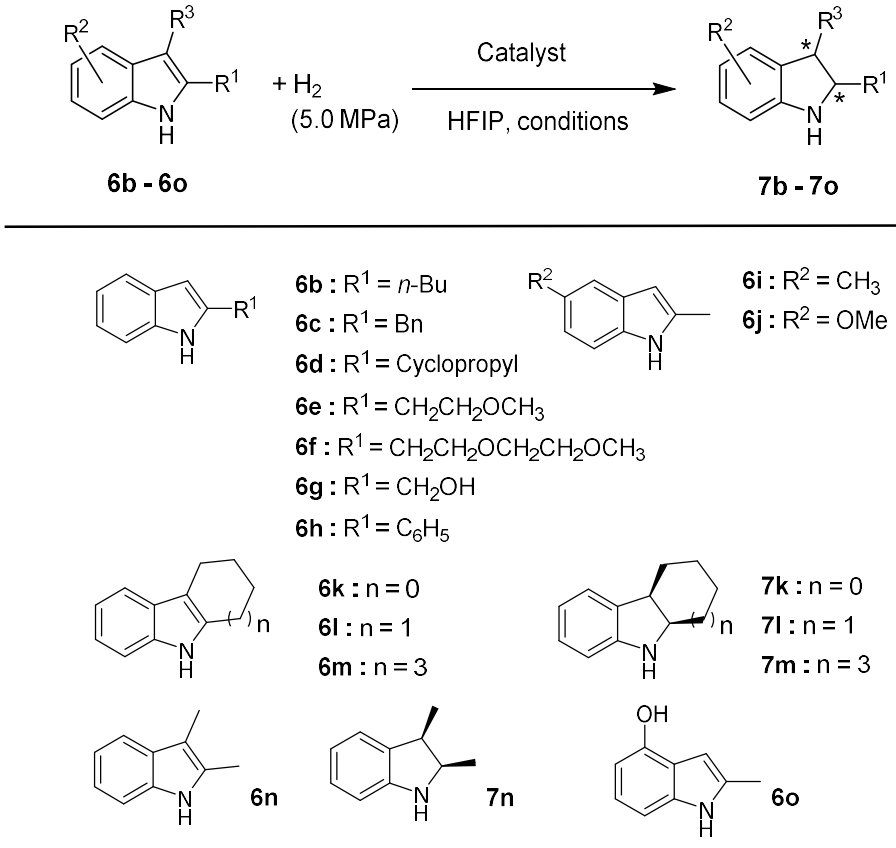
[a] Using 0.7mL/100mg substrate of solvent. [b] GC yield. [c] Determined by HPLC analysis. [d] S/C = 1000, 30 h. [e] Isolated yield was 99%. [f] S/C=100, HFIP (1.0 equiv. of 6a), without the other solvent, 18 h.

Now new series of catalysts **8**-**10** are in hand, asymmetric hydrogenation of 2-methylindole was investigated with new catalysts and results were summarized in Table 2. 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 = 1000 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).

2.3 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]



entry	substrate	catalyst	S/C	Temp (°C)	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**	2000	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(+)

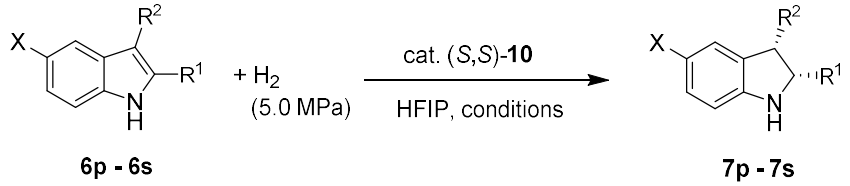
[a] Using 0.7mL/100mg substrate of solvent. [b] Isolated yield. [c] Determined by GC or HPLC analysis. [d] Only *cis* form products (7k-7m) were obtained. [e] Major product was the *cis* isomer (7n) (84.0% de (*cis*), and the ee of the *trans* isomer was 99% ee.)

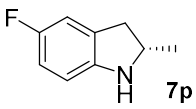
Under the optimized conditions, 2-alkylated indoles were smoothly hydrogenated to give the corresponding indolines in high conversion with high to excellent ees (entries 1,2). The cyclopropyl ring remained intact in (*R*,*R*)-**8**-catalysis to give **7d** with 83% ee. (*1H*-Indol-2-yl)methanol (**6g**) was also smoothly hydrogenated for the first time directly to 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 = 2000 (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).

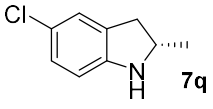
2.4 Asymmetric Hydrogenation of Halogenated Indoles.

Table 4. Asymmetric Hydrogenation of Halogenated Indoles [a]

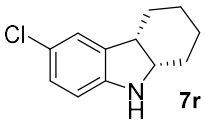




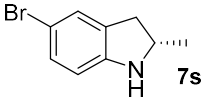
0.2 mol %
(10 °C, 31 h)
95% Yield, 94% ee



1 mol % **(3g scale)**
(20 °C, 20 h)
99% Yield, 95% ee



1 mol %
(30 °C, 12 h)
99% Yield, 90% ee



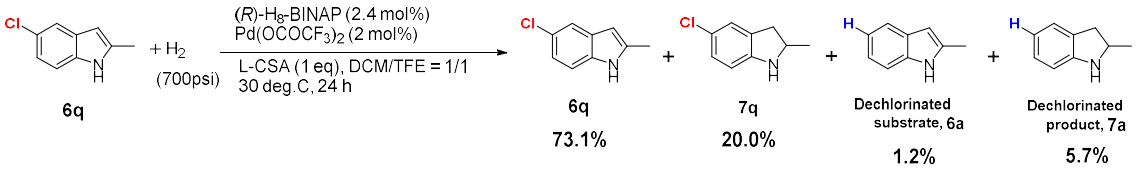
1 mol %
(10 °C, 30 h)
94% Yield, 96% ee

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

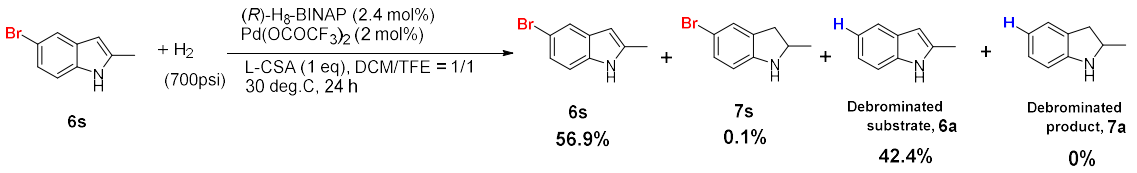
The (*S*,*S*)-**10**-catalyzed asymmetric hydrogenation is also useful for the reduction of indoles having electron-withdrawing substituents. The 5-fluoro-2-methylindole was successfully converted to the 5-fluoro-2-methylindoline with 94% ee. Furthermore, the reduction of chloro- or bromo-substituted 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**. On the other hands, previously reported H_8-BINAP-Pd catalysis in CSA[9a,b] gave small amount of product, and generated dehalogenated compounds **6a** or **7a** as a by-product considerably (Scheme 5)

Scheme 5. Comparison of Catalyst Activity with H_8-BINAP-Pd Complex [a][b][2]

(a) Asymmetric hydrogenation of 5-Chloro-2-methylindole **(6q)**



(b) Asymmetric hydrogenation of 5-Bromo-2-methylindole **(6s)**

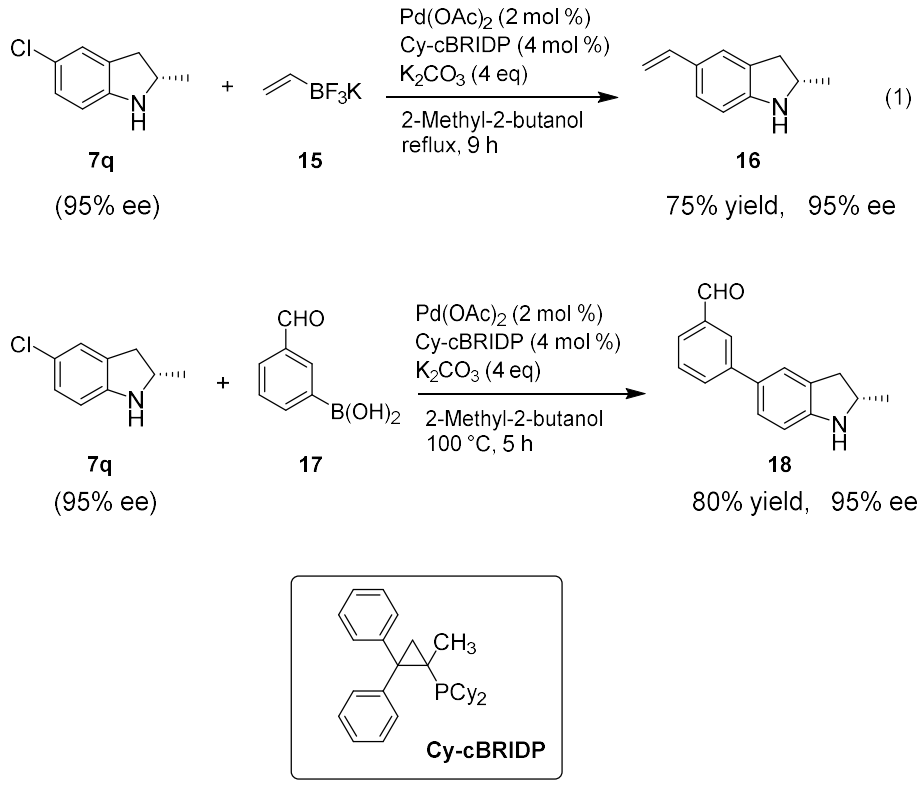


[a] Yield were determined by GC analysis. [b] Standard reaction conditions: substrate (0.25 mmol), L-CSA (0.25 mmol), $Pd(OCOCF_3)_2$ (2mol %), H_8-BINAP (2.4 mol %), H_2 (700 psi), 3 mL of solvent, 24 h, RT.

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

The synthetic utility of the chiral (*S*)-5-chloro-2-methylindoline (**7q**) is shown in Scheme 6. 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 without a loss of enantioselectivity. The successful introduction of a hydrogenation-sensitive vinyl group or formyl group demonstrates the advantage of the current halogen-tolerant catalytic asymmetric reduction.

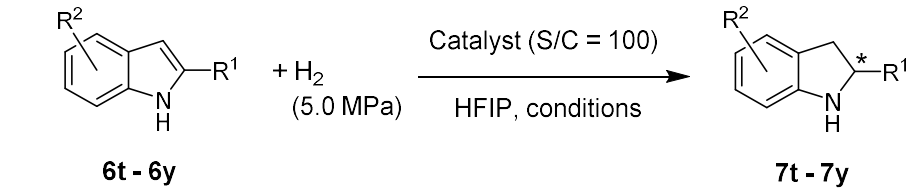
Scheme 6. Derivatizations of (*S*)-5-chloro-2-methylindoline to 2-methyl-5-vinylindoline and (*S*)-5-(3-formylphenyl)-2-methylindoline.



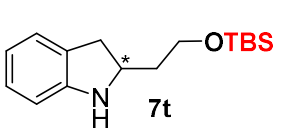
2.6 Asymmetric Hydrogenation of Indoles with Protecting Groups.

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]

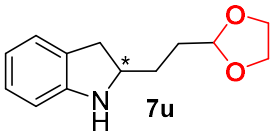


6t - 6y **7t - 7y**



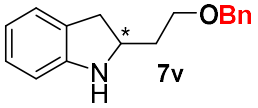
7t

cat. (*S*,*S*)-**10,** 30 °C, 7 h
94% Yield, 92% ee



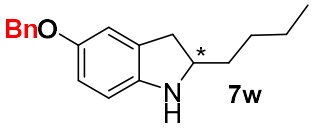
7u

cat. (*S*,*S*)-**10,** 30 °C, 7 h
90% Yield, 90% ee



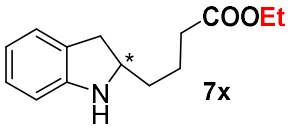
7v

cat. (*R*,*R*)-**8,** 30 °C, 7 h
94% Yield, 84% ee



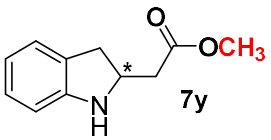
7w

cat. (*R*,*R*)-**8,** 10 °C, 29 h
93% Yield, 97% ee



7x

cat. (*S*,*S*)-**10,** 10 °C, 30 h
95% Yield, 91% ee



7y

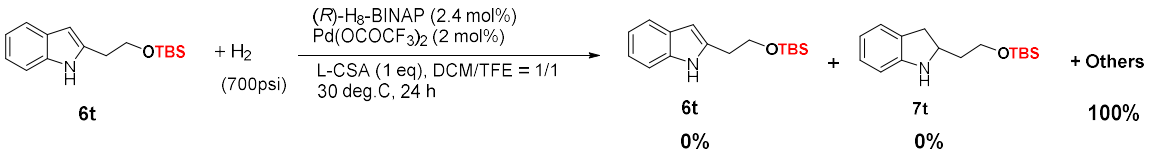
cat. (*S*,*S*)-**10,** 30 °C, 27 h
91% Yield, 72% ee

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

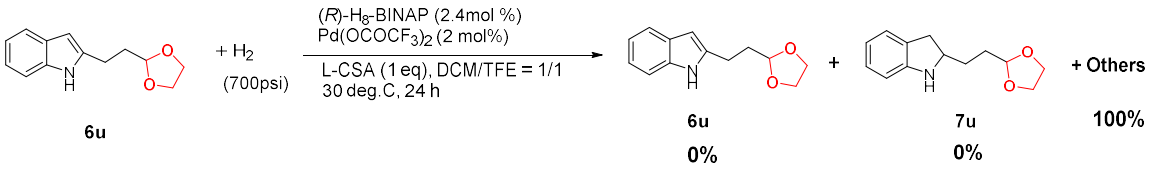
In weakly acidic HFIP reaction media (pH = 4–5), the acid-sensitive *tert*-butyldimethylsilyl (TBS) protecting group of a primary alcohol and ethylene acetal of an aliphatic aldehyde were tolerated in the (*S*,*S*)-**10**-catalyzed hydrogenation to give **7t** in 94% yield with 92% ee and **7u** in 90% 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 (Scheme 7), these results demonstrate the advantages of the current ruthenium catalysis directed toward the synthesis of further complex indoline-derived compounds.

Scheme 7. Comparison of Catalyst Activity with H_8-BINAP-Pd Complex [a][b][2]

(a) Asymmetric hydrogenation of indole containing silyl protecting group **(6s)**



(b) Asymmetric hydrogenation of indole containing acetal protecting group **(6t)**



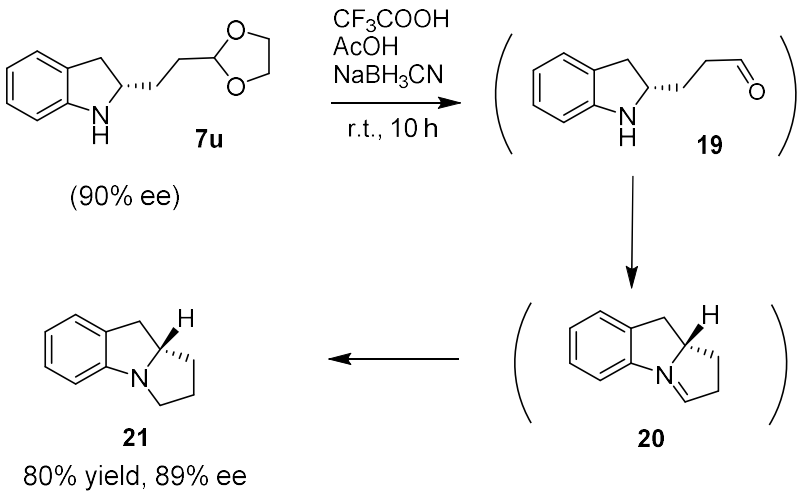
[a] Yield were determined by GC analysis. [b] Standard reaction conditions: substrate (0.25 mmol), L-CSA (0.25 mmol), $Pd(OCOCF_3)_2$ (2mol %), H_8-BINAP (2.4 mol %), H_2 (700 psi), 3 mL of solvent, 24 h, RT.

2.7 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 8. 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.

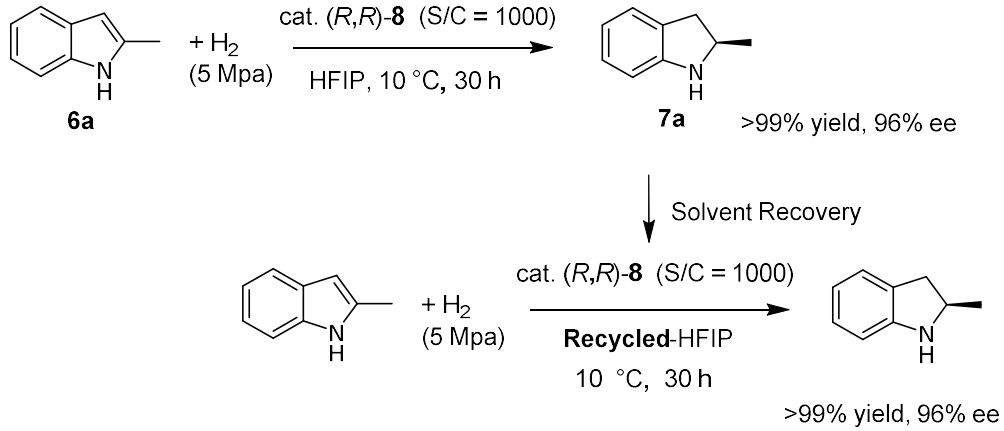
Scheme 8. Derivatization of Chiral Indoline to Tetrahydro-*1H*-pyrroloindole



2.8 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 9).

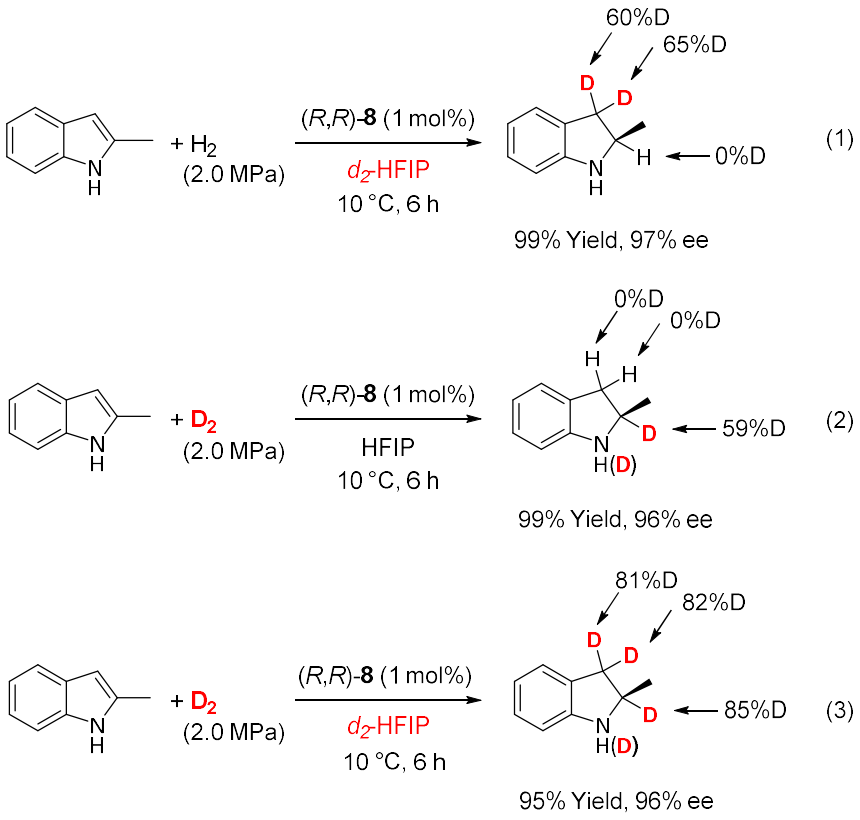
Scheme 9. Reuse of HFIP Solvent for Asymmetric Hydrogenation of 2-Methylindole



2.9 Mechanistic Study by Using Isotopic Labeling Experiments.

To elucidate the reaction mechanism, asymmetric hydrogenation was run in HFIP-d_2 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. 1, Scheme 10).

Scheme 10. Isotopic Labeling Experiments Using D_2 and HFIP-d_2

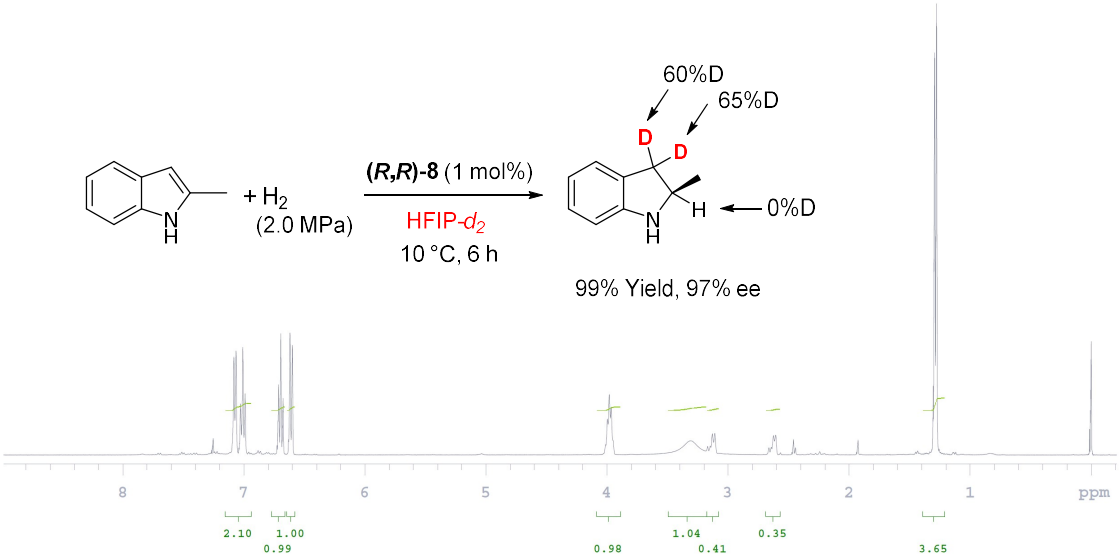


In contrast, when hydrogenation was performed with D_2 and HFIP, the incorporation of deuterium was observed only at the 2-position and the amine of the indoline (eq. 2, Scheme 10). These experimental results prove that unprotected indoles are activated in the weakly acidic HFIP solvent to form an iminium 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 isotopic labeling at 2-position in eq. 2 was discussed later in the reaction mechanism section, and was improved by carrying out the reaction using both D_2 and HFIP-d_2 (eq. 3). In addition,

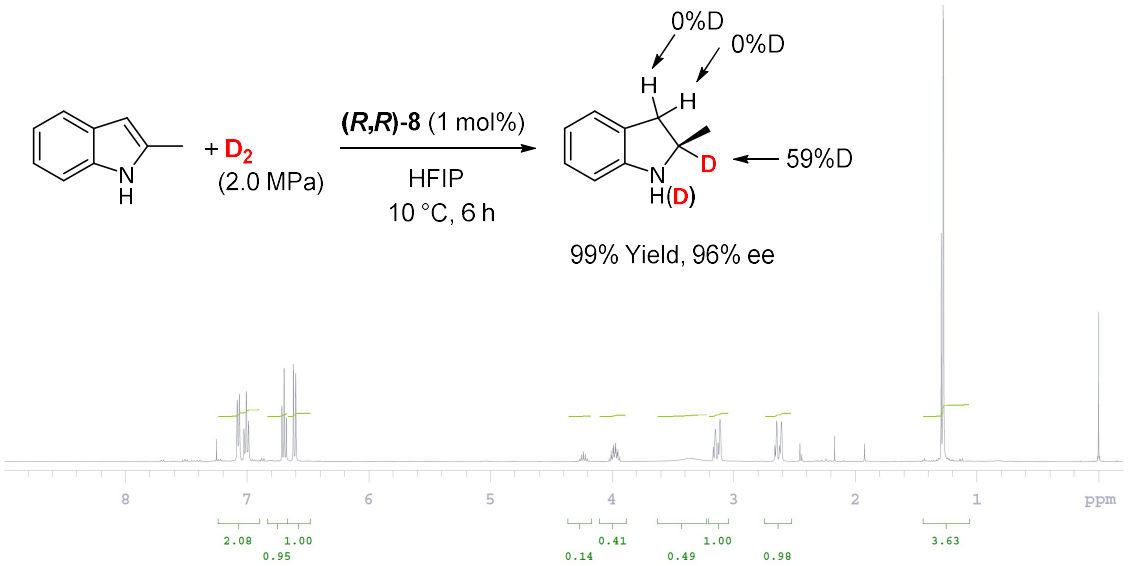
according to eq. 1, the incorporation of deuterium at 3-position was observed without catalyst. (i.e. the incorporation of deuterium at 3-position was occurred just mixed the 2-methylindole substrate and HFIP.)

Figure 10. The Results of Isotopic Labeling Experiments and Proposed Pathway of Hydrogenation of Indoles

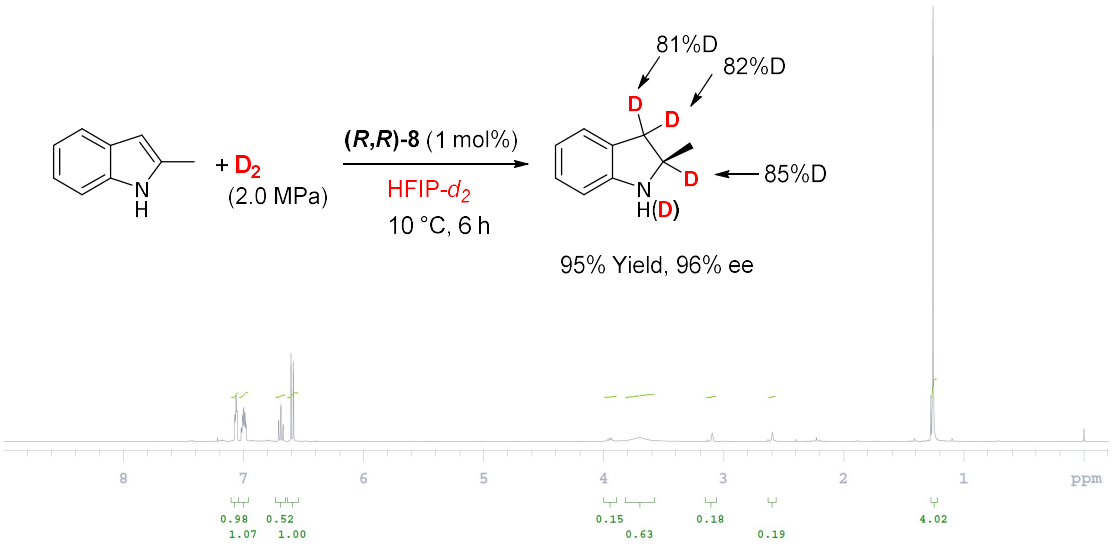
(a) Asymmetric Hydrogenation of 2-Methylindole by using H_2 and HFIP-d_2



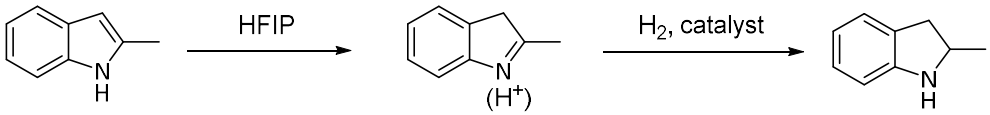
(b) Asymmetric Hydrogenation of 2-Methylindole by using D_2 and HFIP



(c) Asymmetric Hydrogenation of 2-Methylindole by using D_2 and HFIP-d_2



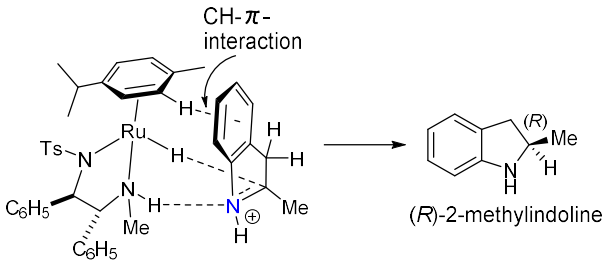
(d) Proposed Pathway of Hydrogenation of Indoles



2.10 Proposed Transition State.

In the reaction of ketonic or imine substrates with η^6-arene/sulfonyldiamine-Ru(II) complexes, a CH/π interaction occurs between a hydrogen atom on the η^6-arene and the aromatic ring of a substrate.[10c-d,13] Furthermore, hydrogen-bonding interaction between the substrates with NH-proton of ligand is important for facilitating 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 12 (a)). 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 ring transition state.[10d] If the proton is dissociated from the iminium intermediate, the hydrogen-bonding interaction using imine would strongly stabilize the 6-membered ring transition state. Further discussion including other possible transition states and why we excluded these other possibilities were described in Figure 11.

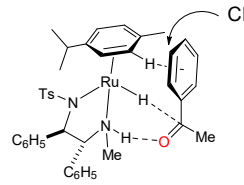
Figure 11. Proposed Transition State

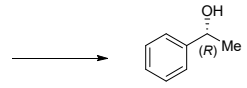


In the asymmetric hydrogenation of 2-methylindole, conceivable various transition state were depicted in Figure 12 (b)-(e).

In the asymmetric hydrogenation of 2-methylindole, the obtained enantiomer was (*R*)-isomer.
This fact would suggest the analogous CH/π interaction between a hydrogen atom on the η^6-arene and the aromatic ring of an indole substrate and could exclude the possibility of Cyclic '*non*-CH/π' mechanism. In addition, Cationic '*anti*' mechanism (d) is also excluded because this transition state yields *incorrect* (*S*)-indoline enantiomer.

On the other hand, non-Cyclic 'CH-π' & Cationic mechanism (Figure 12 (e)) produces *correct* (*R*)-indoline enantiomer. However this transition state would compete with Cationic '*anti*' mechanism (d) by flipping approach of substrate. In this asymmetric hydrogenation, ee value is very high (ca. 96%), so this result would support nitrogen atom of iminium intermediate interacts with N-H bond of catalyst and constructs the 6-membered ring transition state (Cyclic 'CH-π' mechanism (Figure 12 (b)). While the possibility of the solvent like HFIP is involved in transition state could not be excluded.
Figure 12. Possible Transision State

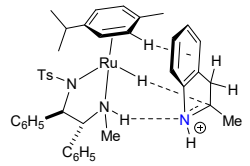


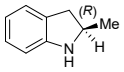


(a) Cyclic 'CH/π' mechanism

(*R*)-Phenylethanol (*ca.* 97% ee)

(*R*)-alcohol from (*R*,*R*)-catalyst

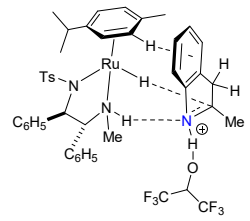


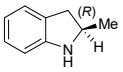


(b) Cyclic 'CH/π' mechanism

(*R*)-2-methylindoline (*ca.* 96% ee)

Produces *correct* product enantiomer
(*R*)-indoline from (*R*,*R*)-catalyst

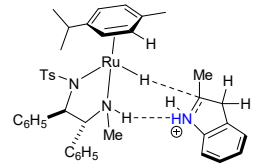


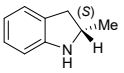


(b') Cyclic 'CH/π' mechanism
with solvent involvement

(*R*)-2-methylindoline

Produces *correct* product enantiomer
(*R*)-indoline from (*R*,*R*)-catalyst

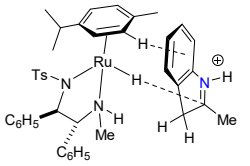


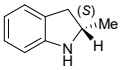


(c) Cyclic '*non*-CH/π' mechanism

(*S*)-2-methylindoline

Produces *incorrect* product enantiomer
(*S*)-indoline from (*R*,*R*)-catalyst

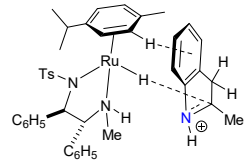


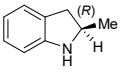


(d) Cationic '*anti*' mechanism

(*S*)-2-methylindoline

Produces *incorrect* product enantiomer
(*S*)-indoline from (*R*,*R*)-catalyst





(e) non-Cyclic 'CH/π'
& Cationic mechanism

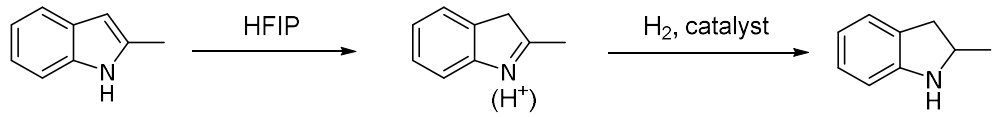
(*R*)-2-methylindoline

Produces *correct* product enantiomer
(*R*)-indoline from (*R*,*R*)-catalyst

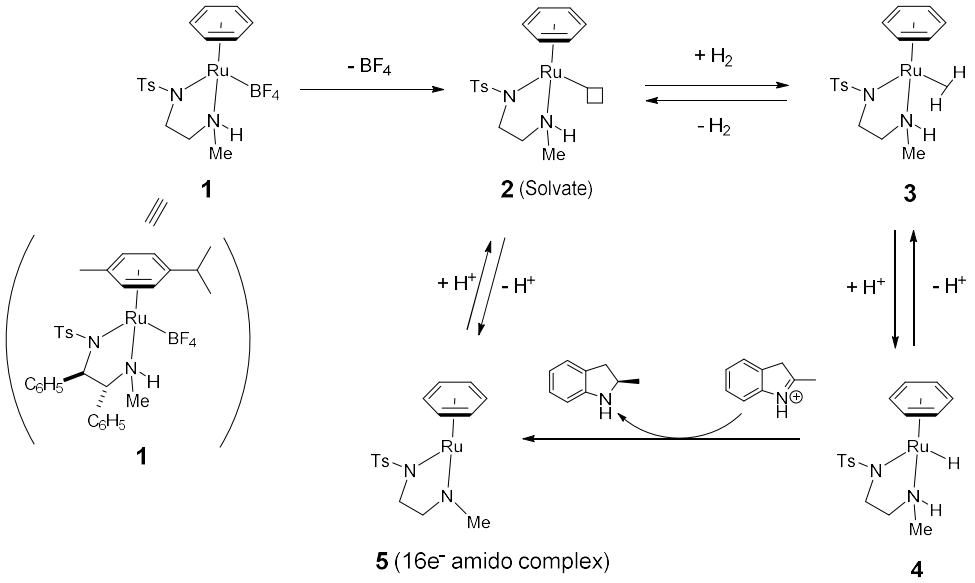
2.11 Proposed Reaction Mechanism.

Figure 13. Possible Reaction Mechanism.

(e) Proposed Pathway for Hydrogenation of Indoles

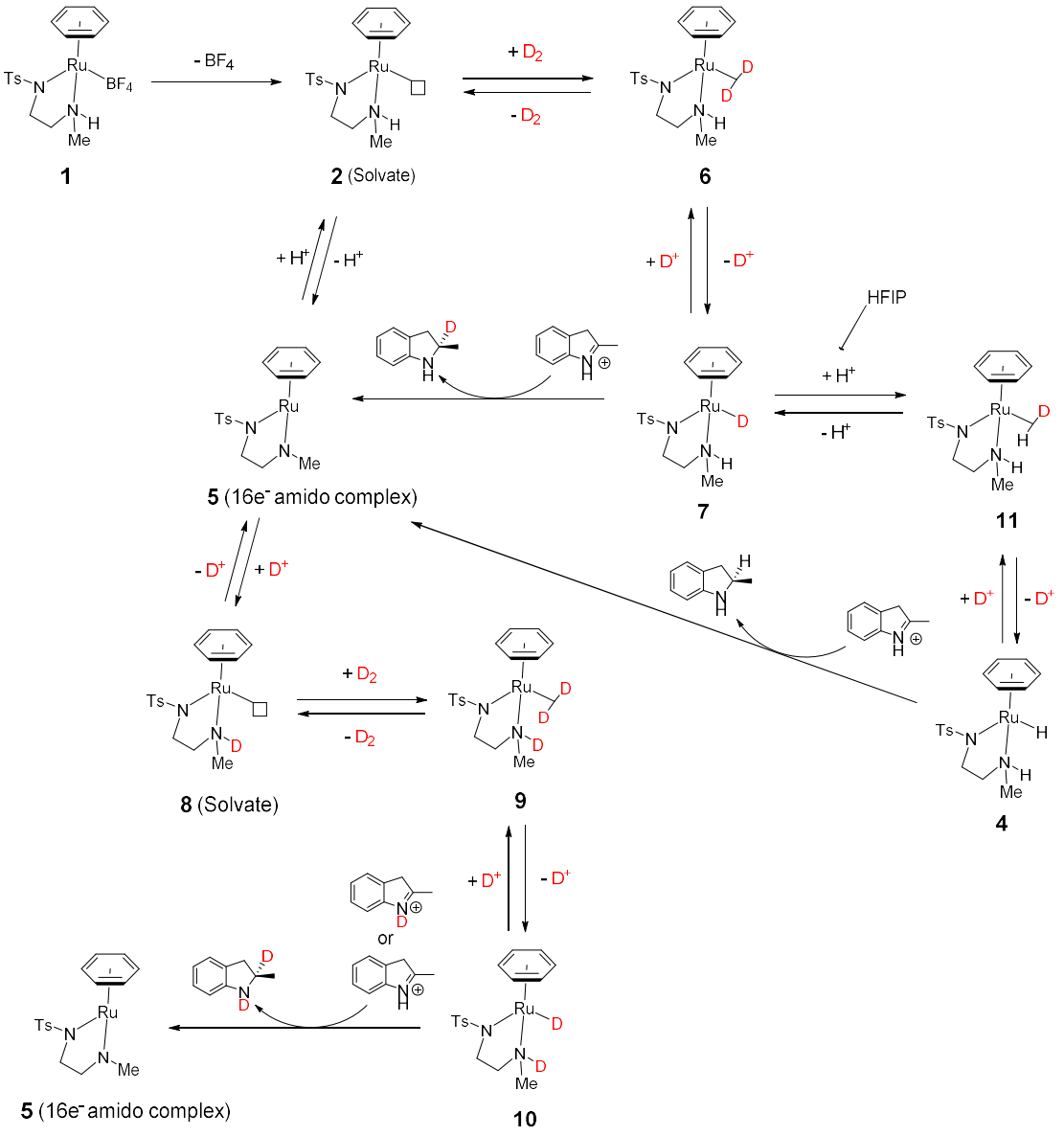


(b) Proposed Reaction Mechanism of Asymmetric Hydrogenation by H_2 and HFIP



This Figure 13 (b) is a basical realization of the asymmetric hydrogenation using Ru catalysts [4]. The cationic Ru species **2** is generated by ionization of complex **1**. The resulting cationic 16e⁻ amido Ru complex **2** (Solvate) can accept reversibly a H_2 molecule to form the η^2-H_2 complex **3**, whose deprotonation leads to RuH **4** as a common reductive species. This complex **4** can reduce indoles to indolines and generate 16e⁻ amido complex **5**. Protonation of complex **5** regenerates complex **2**.

(c) Proposed Reaction Mechanism of Asymmetric Hydrogenation by D_2 in HFIP



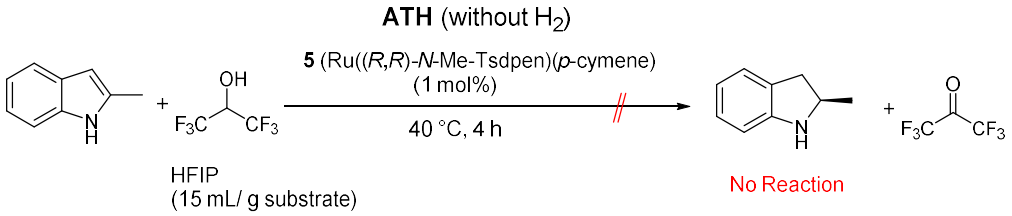
In the asymmetric hydrogenation by D_2 in HFIP, reductive speices Ru-D complex **7** is generated in the same way with Figure 13 (b). This complex **7** reduces indoles to 2-deutero-indolines and generates 16e$^-$ amido complex **5**. By receiving H^+ from HFIP, complex **7** is converted to η^2-H-D complex **11**. If this complex **11** releases D^+, Ru-H complex **4** would generate. The resulting Ru-H complex **4** reduce indoles to corporate hydrogen at the 2-position of indoline products. Besides, complex **5** would be protonated by D^+, which would be suppried in a step **6**→**7**, to generate *N*-D 16e$^-$ amido complex **8** (Solvate). Reductive speices Ru-D (*N*-D) complex **10** would generate from complex **8** by the D_2 addition and following D^+ elimination. Resulting complex **10** reduces indoles to 2-deutero-*N*-deutero-indolines and regenerates complex **5**.

(d) Possibility of ATH Path

In the asymmetric hydrogenation of indoles using HFIP medium, the possibility of asymmetric transfer hydrogenation (ATH) can not be excluded. If ATH reaction was proceeded in certain amount, the deuteraetion value at 2-position of indolines would decrease at the hydrogenation by using D_2 and HFIP system.

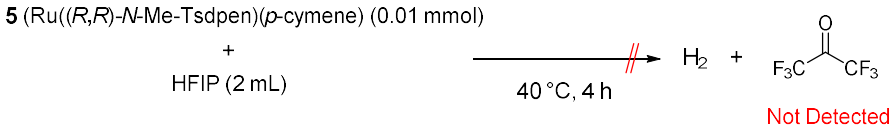
To verify this reaction, following two experiments were conducted.

Condition 1

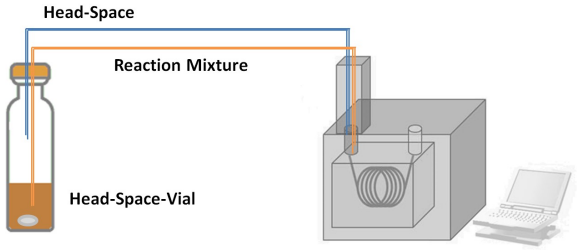


In 10 mL head-space vial, 2-Methylindole and 16e$^-$ amido Ru complex **5** were stirred in HFIP solvent at 40 ^{o}C for 4 h. However, no indoline product was detected by GC analysis. Additionally, although the head spaces of reaction vessel and reaction mixture were checked by (HS)-GC-MS, hexafluoroacetone and its hydrate were not detected at all.

Condition 2



In 10 mL head-space vial, 16e$^-$ amido Ru complex **5** was stirred in HFIP solvent at 40 ^{o}C for 4 h (without indole substrate). Although the head spaces of reaction vessel and reaction mixture were checked by (HS)-GC-MS, hexafluoroacetone and its hydrate were not detected at all.



GC-MS

Condition 1

5 [Ru((*R*,*R*)-*N*-Me-Tsdpen)
(*p*-cymene) (0.01 mmol)]
+ HFIP (2 mL) + 2-Methylindole (0.5 mmol)
40℃, 4 h

Condition 2

5 [Ru((*R*,*R*)-*N*-Me-Tsdpen)
(*p*-cymene) (0.01 mmol)]
+ HFIP (2 mL) 40℃, 4 h

From these results, ATH reaction was not occurred in this HFIP solvent system.

3. 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 and retained the halogen atoms. From the 5-halo-2-methylindoles, cross coupling reactions were accomplished. Some acid-sensitive protecting groups were also tolerant using the mild η^6-arene/*N*-Me-sulfonyldiamine-Ru(II)-BF_4 catalyses. With these fascinating and powerful hydrogenations, further applications toward the synthesis of advanced indoline molecules are now being examined by our group.

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5. Experimental Section

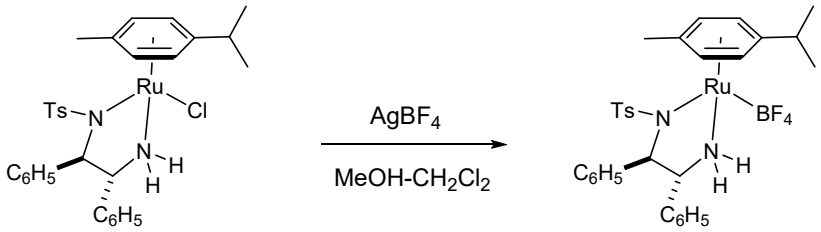
A. General Information

All reactions and manipulations were conducted under a nitrogen atmosphere unless otherwise noted. Synthesis of complexes was performed in commercial anhydrous solvents. NMR Spectra were obtained on Agilent 400-MR DD2 and Bruker BioSpin Avance Ⅲ 500 Systems. NMR chemical shifts are reported in ppm relative to $CHCl_3$ (7.26 ppm for ^1H, and 77.0 ppm for ^{13}C), CH_2Cl_2 (5.32 ppm for ^1H, and 53.1 ppm for ^{13}C), or CH_3OH (3.30 ppm for ^1H, and 49.0 ppm for ^{13}C). Optical rotations were obtained on a JASCO P-1020 Polarimeter. Mass spectra were recorded on SHIMADZU LCMS-IT-TOF and JEOL JMS-T100GCV. High performance liquid chromatography (HPLC) analysis was performed using a system comprised of a GL-Science GL-7400 series; column oven: GL-7430, a gradient unit, a pump, degasser: GL-7430, a UV detector: GL-7450, an auto sampler: GL-7420.Splitting patterns were reported as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

Indoles (**6a**, **6h**, **6i**, **6j**, **6k**, **6n**, **6q**) were perchased from TCI (Tokyo chemical industry Co., LTD), indole (**6o**) was perchased from Wako Pure Chemical Industries, Ltd., indoles (**6g**, **6k**, **6l**, **6r**) were perchased from Sigma-Aldrich, indole (**6m**) was perchased from Alfa Aesar, indole (**6d**) was perchased from Beijing Kaida. Catalyst (*R*,*R*)**-4** was perchased from Takasago International Corporation. Catalyst (*R*,*R*)**-5a** was perchased from Kanto Chemical Co. Inc.

B. Synthesis of Catalysts

(a) Synthesis of $RuBF_4$((*R*,*R*)-Tsdpen)(*p*-cymene) ((*R*,*R*)-5b))

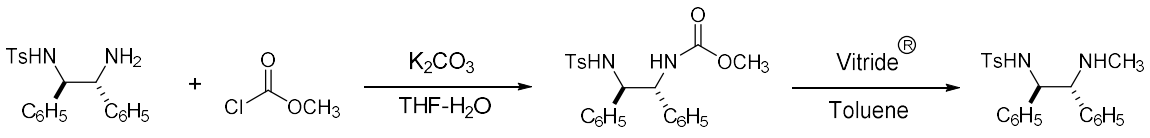


(*R*,*R*)-4 **(*R*,*R*)-5b**

To a stirred solution of **(*R*,*R*)-4** (1.00 g, 1.57 mmol) in dry CH_2Cl_2 (20 mL), a solution of $AgBF_4$ (0.37 g, 1.89 mmol) in dry MeOH (5mL) was added dropwise. After being stirred for 2h at room temperature, the precipitated salt was filtered through Celite. Then, the filtrate was concentrated with an evaporator, and dried under reduced pressure to give the desired complex **(*R*,*R*)-5b**. Yield 1.08 g (99%).

^{1}H NMR (400 MHz, CD_3OD) δ 7.43–6.60 (m, 14H), 5.40 (d, *J* = 6.4 Hz, 2H), 5.21 (d, *J* = 6.4 Hz, 2H), 4.62 (d, *J* = 11.2 Hz, 1H), 4.50 (d, *J* = 11.2 Hz, 1H), 2.82–2.75 (m, 1H), 2.25 (s, 3H), 2.18 (s, 3H), 1.30 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 144.7, 138.6, 136.5, 134.7, 130.9, 130.3, 129.9, 129.5, 129.4, 128.9, 128.7, 128.4, 128.1, 127.2, 97.9, 93.1, 78.6, 77.4, 63.0, 60.8, 32.5, 22.7, 21.3, 18.3; HRMS (ESI) calcd for $C_{31}H_{35}N_2O_2SRu$ $[M–BF_4]^+$ 601.1465, found 601.1461.

(b) Synthesis of 4-Methyl-*N*-((1*R*,2*R*)-2-(methylamino)-1,2-diphenylethyl)benzene-sulfonamide ((*R*,*R*)-*N*-Me-TsDPEN (14)) [1]



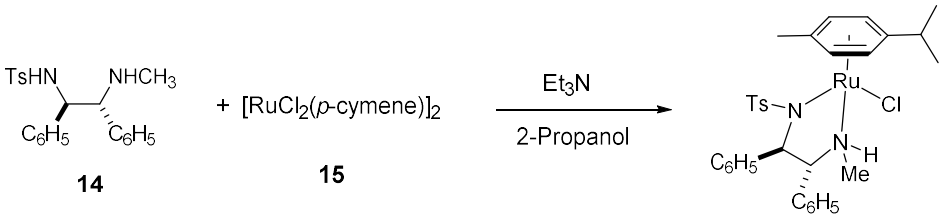
11 **12** **13** **14**

To a solution of (*R*,*R*)-TsDPEN (**11**) (10.0 g, 27.29 mmol) in THF (50 mL), methyl chloroformate (**12**) (4.22 mL, 54.57 mmol), K_2CO_3 (11.3 mL, 81.86 mmol) and H_2O (50 mL) were added. After being stirred for 2h at room temperature, the mixture was washed with water (50 mL), and then, extracted with toluene (3 x 50 mL). The solvent was removed to afford the product (**13**) as a white solid (11.6 g, quantitative yield).
To a stirred solution of amide precursor (**13**) (11.5 g, 27.1 mmol) in dry THF (500 mL), a Vitride® (70% solution in toluene) (21.1 mL, 82.9 mmol) was added dropwise. After refluxing for 2 hours, water (100 mL) was added slowly to quench the reaction. The product was extracted with chloroform (3 x 100 mL), and the combined organic layer was washed with brine (2 x 100 mL), and dried over $MgSO_4$. The $MgSO_4$ was removed by a filtration, and the filtrate was concentrated to afford the crude product. The crude product was purified by silica gel column chromatography to afford the product (**14**) as a white

solid (7.3 g, 64%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.35 (m, 2H), 7.15–7.13 (m, 3H), 7.06–7.00 (m, 5H), 6.94–6.91 (m, 4H), 6.23 (br, 1H), 4.26 (d, *J* = 8.0 Hz, 1H), 3.53 (t, *J* = 8.0 Hz, 1H), 2.33 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.7, 138.8, 138.3, 137.1, 129.1, 128.3, 127.9, 127.6, 127.5, 127.5, 127.3, 127.1, 69.7, 63.0, 34.1, 21.4; HRMS (ESI) calcd for $C_{22}H_{25}N_2O_2S$ $[M+H]^+$ 381.1631, found 381.1648.

(c) Synthesis of RuCl((*R*,*R*)-*N*-Me-Tsdpen)(*p*-cymene) ((*R*,*R*)-8-Cl))

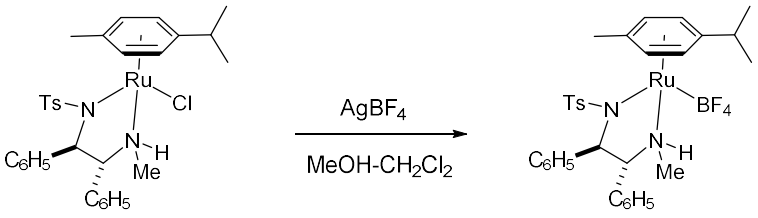


14 **15** **(*R*,*R*)-8-Cl**

A mixture of $[RuCl_2(p\text{-cymene})]_2$ (**15**) (1.19 g, 3.94 mmol), (*R*,*R*)-*N*-Me-TsDPEN (**14**) (1.50 g, 3.94 mmol), and triethylamine (1.11 mL, 7.88 mmol) in 2-propanol (30 mL) was heated at 80 ºC for 1 h. The orange solution was concentrated and a small amount of water was added. The resulting solid was collected by filtration. The crude mixture was washed with a small amount of water and dried under reduced pressure to give the desired complex **(*R*,*R*)-8-Cl**. Yield 2.43 g (95%).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.12–7.07 (m, 5H), 6.81–6.77 (m, 4H), 6.69–6.65 (m, 3H), 6.57–6.55 (m, 2H), 5.72 (d, *J* = 6.0 Hz, 1H), 5.51 (d, *J* = 6.0 Hz, 1H), 5.46–5.42 (m, 2H), 4.03 (d, *J* = 11.2 Hz, 1H), 4.01 (br, 1H), 3.46 (d, *J* = 11.2 Hz, 1H), 3.24–3.19 (m, 1H), 2.79 ((d, *J* = 6.0 Hz, 1H), 2.41 (s, 3H), 2.24 (s, 3H), 1.40 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 139.4, 139.2, 136.7, 129.4, 128.8, 128.4, 128.1, 127.3, 127.2, 126.5, 105.5, 95.0, 87.0, 81.5, 81.3, 80.9, 79.9, 70.3, 42.9, 30.9, 22.9, 21.5, 21.1, 19.2; HRMS (ESI) calcd for $C_{32}H_{37}N_2O_2SRu$ $[M–Cl]^+$ 615.1622, found 615.1616.

(d) Synthesis of $RuBF_4$((*R*,*R*)-*N*-Me-Tsdpen)(*p*-cymene) ((*R*,*R*)-8))



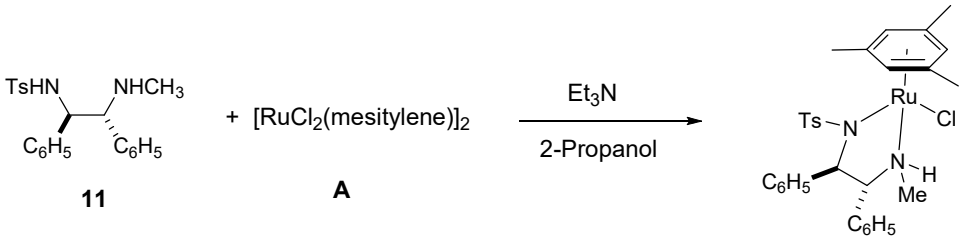
(*R*,*R*)-8-Cl **(*R*,*R*)-8**

To a stirred solution of **(*R*,*R*)-8-Cl** (1.11 g, 1.80 mmol) in dry CH_2Cl_2 (20 mL), a solution of $AgBF_4$ (0.41 g, 2.10 mmol) in dry MeOH (5mL) was added dropwise. After being stirred

for 2h at room temperature, the precipitated salt was filtered through Celite. Then, the filtrate was concentrated with an evaporator, and dried under reduced pressure to give the desired complex **(*R*,*R*)-8**. Yield 1.15 g (99%).

^{1}H NMR (400 MHz, CD_3OD) δ 7.50–6.58 (m, 14H), 5.41 (d, *J* = 6.4 Hz, 2H), 5.21 (d, *J* = 6.4 Hz, 2H), 4.66 (d, *J* = 11.2 Hz, 1H), 4.50 (d, *J* = 11.2 Hz, 1H), 2.81–2.72 (m, 1H), 2.55 (s, 3H), 2.27 (s, 3H), 2.19 (s, 3H),1.30 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 144.9, 138.5, 136.4, 132.1, 130.4, 130.1, 129.7, 129.4, 129.0, 128.4, 128.1, 117.5, 98.0, 93.2, 78.6, 77.4, 68.6, 62.4, 32.4, 23.5, 22.7, 21.2, 18.3; HRMS (ESI) calcd for $C_{32}H_{37}N_2O_2SRu$ $[M–BF_4]^+$ 615.1622, found 615.1605.

(e) Synthesis of RuCl((*R*,*R*)-*N*-Me-Tsdpen)(mesitylene) ((*R*,*R*)-9-Cl))

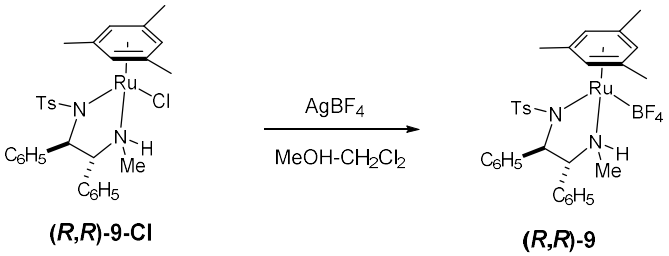


(*R*,*R*)-9-Cl

A mixture of $[RuCl_2(mesitylene)]_2$ (**A**) (0.76 g, 2.60 mmol), (*R*,*R*)-*N*-Me-TsDPEN (**11**) (1.00 g, 2.60 mmol), and triethylamine (0.73 mL, 5.26 mmol) in 2-propanol (20 mL) was heated at 80 ºC for 1 h. The orange solution was concentrated and a small amount of water was added. The resulting solid was collected by filtration. The crude mixture was washed with a small amount of water and dried under reduced pressure to give the desired complex **(*R*,*R*)-9-Cl**. Yield 1.54 g (93%).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.24 (d, *J* = 8.0 Hz, 2H), 7.16–6.70 (m, 10H), 6.64 (d, *J* = 8.0 Hz, 2H), 5.43 (s, 3H), 3.93 (d, *J* = 10.8 Hz, 1H), 3.84 (br, 1H), 3.61 (t, *J* = 10.8 Hz, 1H), 2.72 (d, *J* = 6.4 Hz, 3H), 2.35 (s, 9H), 2.25 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 142.4, 140.2, 139.7, 136.7, 129.1, 128.8, 128.5, 128.1, 127.9, 127.4, 126.6, 125.2, 95.5, 84.0, 81.6, 69.8, 41.7, 21.2, 19.3; HRMS (ESI) calcd for $C_{31}H_{35}N_2O_2SRu$ $[M–Cl]^+$ 601.1465, found 601.1452.

(f) Synthesis of $RuBF_4$((*R*,*R*)-*N*-Me-Tsdpen)(*p*-cymene) ((*R*,*R*)-9))

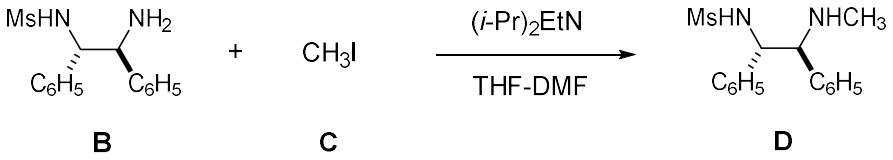


(*R*,*R*)-9-Cl **(*R*,*R*)-9**

To a stirred solution of **(*R*,*R*)-9-Cl** (1.15 g, 1.80 mmol) in dry CH_2Cl_2 (20 mL), a solution of $AgBF_4$ (0.41 g, 2.10 mmol) in dry MeOH (5 mL) was added dropwise. After being stirred for 2h at room temperature, the precipitated salt was filtered through Celite. Then, the filtrate was concentrated with an evaporator, and dried under reduced pressure to give the desired complex **(*R*,*R*)-9**. Yield 1.23 g (99%).

^{1}H NMR (400 MHz, CD_3OD) δ 7.50–6.65 (m, 14H), 5.82 (s, 3H), 4.19 (d, J = 11.2 Hz, 1H), 3.84 (d, J = 11.2 Hz, 1H), 2.97 (s, 3H), 2.34 (s, 9H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 144.9, 142.3, 138.5, 136.5, 130.4, 130.1, 129.7, 129.3, 128.7, 128.4, 92.8, 78.5, 68.7, 62.4, 32.5, 19.2, 18.1; HRMS (ESI) calcd for $C_{31}H_{35}N_2O_2SRu$ $[M–BF_4]^+$ 601.1465, found 601.1460.

(g) Synthesis of *N*-((1*S*,2*S*)-2-(methylamino)-1,2-diphenylethyl)methanesulfonamide) ((*S*,*S*)-*N*-Me-MsDPEN) (D))

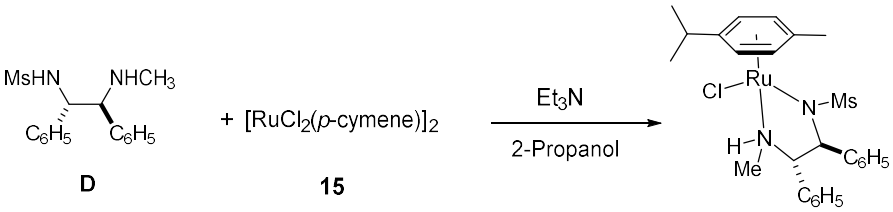


B **C** **D**

To a stirred solution of **(*S*,*S*)-Ms-DPEN (B)** (3.00 g, 10.33 mmol) in dry THF (20 mL) and dry DMF (5 mL), diisopropylethylamine (3.60 mL, 20.7 mmol) and iodomethane (**C**) (0.45mL, 7.23 mmol) was added. After the reaction was heated at 50 ºC for 10 h, water (50 mL) and chloroform (50 mL) was added. The product was extracted with chloroform (2 x 25 mL), and the combined organic fractions were washed with brine (2 x 100 mL), and dried over $MgSO_4$. The $MgSO_4$ was removed by a filtration, and the filtrate was concentrated to give the crude product. The crude product was purified by silica gel column chromatography to afford the product (**D**) as a white solid (1.4 g, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.18 (m, 8H), 7.12–7.09 (m, 2H), 4.48 (d, J = 8.0 Hz, 1H), 3.66 (d, J = 7.6 Hz, 1H), 2.34 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 138.7, 128.5, 128.4, 127.9, 127.7, 127.6, 127.6, 69.2, 63.0, 41.2, 34.0; HRMS (FI) calcd for $C_{16}H_{20}N_2O_2S$ $[M]^+$ 304.1246, found 304.1234.

(h) Synthesis of RuCl((*S*,*S*)-*N*-Me-Msdpen)(*p*-cymene) ((*S*,*S*)-10-Cl))



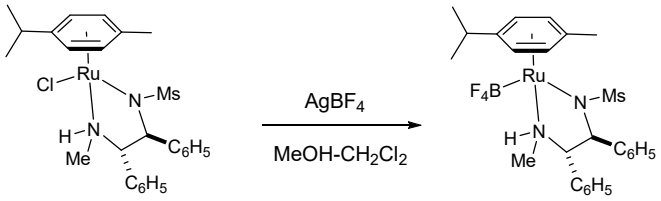
D **15**

(*S*,*S*)-10-Cl

A mixture of $[RuCl_2(p\text{-cymene})]_2$ (**15**) (0.58 g, 1.90 mmol), (*S*,*S*)-*N*-Me-MsDPEN (**D**) (0.60 g, 1.90 mmol), and triethylamine (0.53 mL, 3.80 mmol) in 2-propanol (15 mL) was heated at 80 ºC for 1 h. The reaction was stopped by adding water (15 mL), and the product was extracted with chloroform (2 x 15 mL). The combined organic layer was dried over $MgSO_4$. After removal of $MgSO_4$, concentrion under reduced pressure gave the desired complex **(*S*,*S*)-10-Cl**. Yield 0.8 g (73%).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.24 (d, *J* = 8.0 Hz, 2H), 7.40–6.80 (m, 10H), 5.58 (d, *J* = 6.8 Hz, 1H), 5.42–5.40 (m, 2H), 5.32 (d, *J* = 6.0 Hz, 1H), 3.98 (d, *J* = 11.2 Hz, 1H), 3.94 (br, 1H), 3.58 (t, *J* = 11.2 Hz, 1H), 3.13–3.06 (m, 1H), 2.80 (d, *J* = 6.0 Hz, 1H), 2.35 (s, 3H) , 2.33 (s, 3H), 1.38–1.35 (m, 6H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 141.6, 140.5, 136.7, 129.2, 129.1, 128.9, 128.6, 127.9, 127.2, 126.9, 104.7, 95.6, 86.5, 82.2, 80.8, 80.3, 80.2, 70.4, 66.2, 43.2, 43.0, 31.0, 23.1, 21.3, 19.2; HRMS (ESI) calcd for $C_{26}H_{33}N_2O_2SRu$ $[M–Cl]^+$ 539.1307, found 539.1327.

(i) Synthesis of $RuBF_4$((*S*,*S*)-*N*-Me-Msdpen)(*p*-cymene) ((*S*,*S*)-10))



(*S*,*S*)-10-Cl **(*S*,*S*)-10**

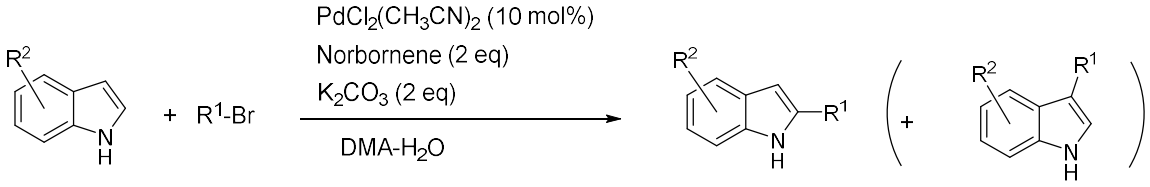
To a stirred solution of **(*S*,*S*)-10-Cl** (0.88 g, 1.53 mmol) in dry CH_2Cl_2 (15 mL), a solution of $AgBF_4$ (0.36 g, 1.84 mmol) in dry MeOH (3 mL) was added dropwise. The reaction left to stir 2h at room temperature, and the precipitated salt was filtered through Celite. Then, the filtrate was concentrated under reduced pressure to give the desired complex **(*S*,*S*)-10**. Yield 0.95 g (99%).

^{1}H NMR (400 MHz, CD_3OD) δ 7.40–7.02 (m, 10H), 5.99–5.97 (m, 1H), 5.90–5.86 (m, 2H), 5.77–5.76 (m, 1H), 4.13 (d, *J* = 11.2 Hz, 1H), 3.92 (t, *J* = 11.2 Hz, 1H), 3.07 (d, 3H), 3.00–2.96 (m, 1H), 2.38 (s, 3H), 2.22 (s, 3H), 1.44–1.29 (m, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 142.0, 140.4, 137.7, 136.7, 130.4, 129.9, 129.4, 127.6, 87.4, 82.7, 80.6, 70.9, 62.2, 44.5, 41.4, 32.3, 22.4, 19.2; HRMS (ESI) calcd for $C_{26}H_{33}N_2O_2SRu$ $[M–BF_4]^+$ 539.1307, found 539.1330.

C. Synthesis of Indoles

Indole **6c** was synthesized according to the literature procedure. [2]

2-Substituted indoles **6b, 6e, 6f, 6s, 6t, 6u, 6v, 6w, 6x** were prepared following known methods. [3]



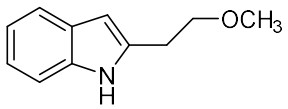
2-Alkylated indoles were obtained by previously reported procedure. [3]

A 500mL four neck flask equipped with a magnetic stirring bar was charged with indole substrate (1 equiv.), norbornene (2 equiv.), K_2CO_3 (2 equiv.), and $PdCl_2(CH_3CN)_2$ (10 mol %). A solution of water in dimethylacetamide (DMA) (0.5M) was added as the solvent to prepare a 0.2 M solution of the substrate. Then the resulting solution was briefly evacuated and then backfilled with argon (5 times), and then the alkyl bromide (1 equiv.) was added via syringe. The reaction mixture was then placed in a preheated oil bath at 80 °C. Vigorous stirring was applied and the reaction was monitored by TLC. Upon completion, the reaction mixture was cooled to room temperature, diluted with *tert*-butylmethylether, and filtered. The filtrate was concentrated by evaporator in a water bath (70°C, 5-10 mmHg) to remove *tert*-Butylmethylether and DMA. The residue was directly submitted to flash column chromatograph (by dry loading) to afford the 2-alkylindole product (30-50 % yield). (Small amount of 3-alkylindole was obtained as a byproduct depending on substrates.)

^{1}H- and ^{13}C-NMR of indoles of **6b**, **6s**, **6t**, **6w** were matched previously reported data.

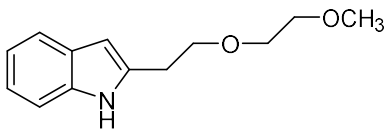
Following this method, unknown indoles **6e**, **6f**, **6u**, **6v**, **6x** were synthesized.

2-(2-Methoxyethyl)-1*H*-indole (6e)



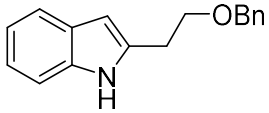
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (br, 1H), 7.54–7.51 (m, 1H), 7.30–7.27 (m, 1H), 7.13–7.03 (m, 2H), 6.23–6.22 (m, 1H), 3.68–3.65 (m, 2H), 3.41 (s, 1H), 3.00–2.97 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.8, 136.0, 128.4, 121.9, 121.0, 119.8, 110.5, 99.7, 72.2, 58.8, 28.5; HRMS (FI) calcd for $C_{11}H_{13}NO$ $[M]^+$ 175.0997, found 175.0989.

2-(2-(2-Methoxyethoxy)ethyl)-1*H*-indole (6f)



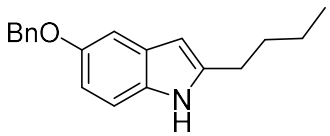
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (br, 1H), 7.53–7.51 (m, 1H), 7.29–7.27 (m, 1H), 7.11–7.02 (m, 2H), 6.22–6.21 (m, 1H), 3.79–3.76 (m, 2H), 3.68–3.65 (m, 2H), 3.62–3.59 (m, 2H), 3.50 (s, 3H), 3.03–3.00 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 136.3, 128.2, 120.8, 119.6, 119.2, 110.6, 99.5, 71.7, 70.6, 69.7, 58.9, 28.2; HRMS (FI) calcd for $C_{13}H_{17}NO_2$ $[M]^+$ 219.1259, found 219.1273.

2-(2-(Benzyloxy)ethyl)-1*H*-indole (6v)



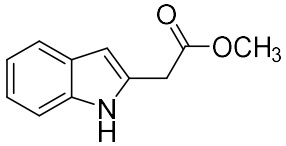
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (br, 1H), 7.54–7.51 (m, 1H), 7.37–7.25 (m, 6H), 7.11–7.05 (m, 2H), 6.24–6.23 (m, 1H), 4.57 (s, 2H), 3.78 (t, J = 6.0 Hz, 2H), 3.04 (t, J = 6.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 137.7, 136.0, 128.6, 128.4, 127.9, 127.8, 121.0, 119.8, 119.5, 110.5, 99.9, 73.4, 70.0, 28.6; HRMS (FI) calcd for $C_{17}H_{17}NO$ $[M]^+$ 251.1310, found 251.1305.

5-(Benzyloxy)-2-butyl-1*H*-indole (6w)



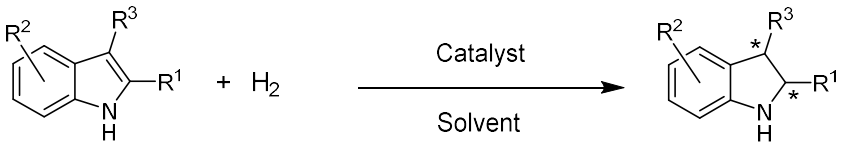
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (br, 1H), 7.47–7.42 (m, 2H), 7.40–7.28 (m, 3H), 7.14–7.07 (m, 2H), 6.85–6.80 (m, 1H), 6.14–6.13 (m, 1H), 5.08 (s, 2H), 2.70–2.65 (m, 2H), 1.69–1.62 (m, 2H), 1.43–1.35 (m, 2H), 0.96–0.91 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 140.9, 137.9, 131.1, 129.3, 128.4, 127.6, 127.5, 111.5, 110.8, 103.6, 99.3, 71.0, 31.3, 28.0, 22.4, 13.8; HRMS (FI) calcd for $C_{19}H_{21}NO$ $[M]^+$ 279.1623, found 279.1626.

Methyl 2-(1*H*-indol-2-yl)acetate (6y)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (br, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.9 Hz, 1H), 6.35–6.34 (m, 1H), 3.83 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 136.3, 130.3, 128.2, 121.8, 120.1, 119.8, 110.8, 101.9, 52.3, 33.7; HRMS (FI) calcd for $C_{13}H_{17}NO$ $[M]^+$ 219.1259, found 219.1273.

D. Asymmetric Hydrogenation of Indoles Using η^6-Arene/ *N*-Me-sulfonyldiamine -Ru(II) complexes

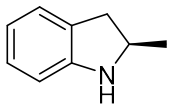


General procedures under the conditions of S/C = 500, 10 °C for 7 h.

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 ºC for 7 h. The product was obtained by silica gel chromatography. Optical purities of the products were determined by Chiral-GC or HPLC analysis.

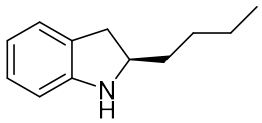
E. Characterization Data for Reduction Products

(*R*)- 2-Methylindoline (7a)



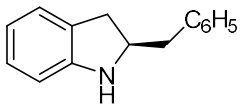
Following the general procedure (cat. **(*R*,*R*)-8**), **7a** was obtained as clear oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 7.2 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 1H), 4.00–3.95 (m, 1H), 3.60 (br, 1H), 3.13 (dd, *J* = 15.6, 8.4 Hz, 1H), 2.62 (dd, *J* = 15.4, 7.8 Hz, 1H), 1.28 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 128.9, 127.2, 124.7, 118.5, 109.1, 55.2, 37.7, 22.2; All characterization data are in agreement with previously reported data[2].
HRMS (FI) calcd for $C_9H_{11}N$ $[M]^+$ 133.0892, found 133.0883.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, Hexane/2-propanol 97:3, 0.8 mL/min, 254 nm, 30 ºC, t_{major}=9.8 min.((*R*)-enantiomer) , t_{minor}=10.9 min.((*S*)-enantiomer); $[\alpha]_D^{20}$ +5.76 (c 2.1 in $CHCl_3$) 96% ee (*R*) (lit. [2] $[\alpha]_D^{RT}$ +6.96 (c 0.63 in benzene) 91% ee (*R*))

(*R*)- 2-Butylindoline (7b)



Following the general procedure (cat. **(*R*,*R*)-8**), **7b** was obtained as clear oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 7.2 Hz, 1H), 7.01–6.97 (m, 1H), 6.66 (t, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 3.85–3.78 (m, 1H), 3.80 (br, 1H), 3.10 (dd, *J* = 15.4, 8.6 Hz, 1H), 2.66 (dd, *J* = 15.6, 8.8 Hz, 1H), 1.62–1.55 (m, 2H), 1.40–1.35 (m, 4H), 0.95–0.85 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 128.9, 127.1, 124.6, 118.4, 109.0, 60.0, 36.5, 36.1, 28.7, 22.7, 14.1; All characterization data are in agreement with previously reported data[2].
HRMS (FI) calcd for $C_{12}H_{17}N$ $[M]^+$ 175.1361, found 175.1364.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, Hexane/2-propanol 99:1, 1.0 mL/min, 254 nm, 30 ºC, t_{major}=8.4 min. ((*R*)-enantiomer), t_{minor}=11.9 min. ((*S*)-enantiomer); $[\alpha]_D^{20}$ +8.70 (c 0.92 in $CHCl_3$) 97% ee (*R*) (lit. [2] $[\alpha]_D^{RT}$ +12.6 (c 1.1 in $CHCl_3$) 93% ee (*R*))

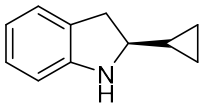
(*R*)- 2-Benzylindoline (7c)



Following the general procedure (cat. **(*R*,*R*)-8**), **7c** was obtained as pale yellow oil.

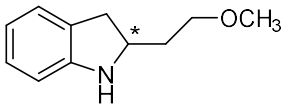
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.30 (m, 2H), 7.23–7.20 (m, 3H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 7.8 Hz, 1H), 6.68 (t, *J* = 7.6 Hz, 1H), 6.56 (t, *J* = 7.8 Hz, 1H), 4.10–4.02 (m, 1H), 3.80 (br, 1H), 3.13 (dd, *J* = 15.4, 8.6 Hz, 1H), 2.93–2.76 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.5, 139.1, 129.1, 128.6, 128.4, 127.3, 126.4, 124.8, 118.5, 109.1, 61.0, 42.7, 35.9; All characterization data are in agreement with previously reported data[2].
HRMS (FI) calcd for $C_{15}H_{15}N$ $[M]^+$ 209.1205, found 209.1216.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, Hexane/2-propanol 99:1, 1.0 mL/min, 254 nm, 30 ºC, t_{major}=12.0 min. ((*R*)-enantiomer), t_{minor}=13.8 min. ((*S*)-enantiomer); $[\alpha]_D^{20}$ +75.6 (c 3.4 in $CHCl_3$) 97% ee (*R*) (lit. [2] $[\alpha]_D^{RT}$ +80.2 (c 1.00 in $CHCl_3$) 95% ee (*R*))

(*S*)- 2-Cyclopropylindoline (7d)



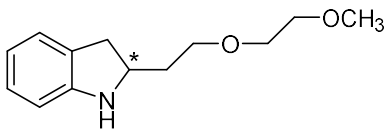
Following the general procedure (cat. **(*R*,*R*)-8**), **7d** was obtained as clear oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, *J* = 7.0 Hz, 1H), 7.00 (t, *J* = 7.8 Hz, 1H), 6.67 (d, *J* = 7.0 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 3.65 (br, 1H), 3.20–3.08 (m, 2H), 2.93–2.83 (m, 1H), 1.10–1.00 (m, 1H), 0.53–0.43 (m, 2H), 0.30–0.19 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.7, 128.7, 127.2, 124.6, 118.4, 109.1, 64.9, 36.0, 16.6, 3.1, 2.1; All characterization data are in agreement with previously reported data [12] .
HRMS (FI) calcd for $C_{11}H_{13}N$ $[M]^+$ 159.1048, found 159.1046.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 140 ºC, P = 20 psi, t_{minor}=11.3 min. ((*R*)-enantiomer), t_{major}=12.3 min. ((*S*)-enantiomer); $[\alpha]_D^{20}$ +49.0 (c 0.7 in $CHCl_3$) 83% ee (*R*) (lit. [12] $[\alpha]_D^{25}$ +61.7 (c 1.0 in $CHCl_3$) >99% ee (*S*))

(-)- 2-(2-Methoxyethyl)indoline (7e)



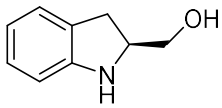
Following the general procedure (cat. **(*S*,*S*)-10**), **7e** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 7.4 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 6.67 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 4.20 (br, 1H), 3.54–3.50 (m, 2H), 3.35 (s, 1H), 3.15 (dd, *J* = 15.6, 8.8 Hz, 1H), 2.69 (dd, *J* = 15.4, 8.2 Hz, 1H), 1.95–1.88 (m, 1H), 1.85–1.78 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 128.5, 127.2, 124.5, 118.3, 109.1, 71.0, 58.8, 58.2, 36.4, 36.3
HRMS (FI) calcd for $C_{11}H_{15}NO$ $[M]^+$ 177.11536, found 177.1162.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, Hexane/2-propanol 95:5, 1.0 mL/min, 254 nm, 30 ºC, t_{minor} =7.1 min. ((+)-enantiomer), t_{major}=8.8 min. ((-)-enantiomer); $[\alpha]_D^{20}$ -15.5 (c 0.84 in $CHCl_3$) 82% ee

(+)- 2-(2-(2-Methoxyethoxy)ethyl)indoline (7f)



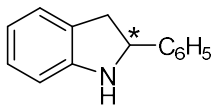
Following the general procedure (cat. **(*R*,*R*)-8**), **7f** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.0 Hz, 1H), 6.98 (t, *J* = 7.7 Hz, 1H), 6.65 (t, *J* = 7.0 Hz, 1H), 6.56 (d, *J* = 7.7 Hz, 1H), 4.00–3.95 (m, 1H), 3.65–3.50 (m, 6H), 3.40 (s, 1H), 3.13 (dd, *J* = 15.6, 8.8 Hz, 1H), 2.68 (dd, *J* = 15.6, 8.4 Hz, 1H), 1.95–1.90 (m, 1H), 1.85–1.78 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 128.5, 127.1, 124.4, 118.1, 108.9, 71.9, 70.0, 69.5, 58.9, 58.2, 36.4, 36.0
HRMS (FI) calcd for $C_{13}H_{19}NO_2$ $[M]^+$ 221.14158, found 221.1415.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, 250 × 4.6 mm column, Hexane/2-propanol 90:10, 1.0 mL/min, 254 nm, 30 ºC, t_{minor} =10.8 min. ((-)-enantiomer), t_{major}=13.8 min. ((+)-enantiomer); $[\alpha]_D^{20}$ +14.1 (c 1.95 in $CHCl_3$) 97% ee

(*S*)- Indolin-2-ylmethanol (7g)



Following the general procedure (cat. **(*R*,*R*)-8**), **7g** was obtained as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.72 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.08–4.00 (m, 1H), 3.74–3.70 (m, 1H), 3.60–3.56 (m, 1H), 3.11 (dd, *J* = 15.6, 9.2 Hz, 1H), 2.83 (dd, *J* = 15.6, 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.5, 128.8, 127.4, 124.8, 119.2, 109.9, 65.2, 60.3, 32.0; All characterization data are in agreement with previously reported data [13] .
HRMS (FI) calcd for $C_9H_{11}NO$ $[M]^+$ 149.08406, found 149.0839.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-H, 250 × 4.6 mm column, Hexane/2-propanol 95:5, 1.0 mL/min, 254 nm, 30 ºC, t_{major}=18.3 min. ((*S*)-enantiomer), t_{minor}=21.0 min. ((*R*)-enantiomer); $[\alpha]_D^{20}$ +40.6 (c 1.2 in EtOH) 73% ee (*S*) (lit. [13] $[\alpha]_D^{28}$ +53.6 (c 0.89 in EtOH) (*S*))

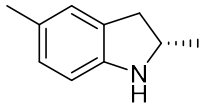
(+)- 2-Phenylindoline (7h)



Following the general procedure (cat. **(*S*,*S*)-10**), **7h** was obtained as a light pink solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.38 (m, 2H), 7.37–7.23 (m, 3H), 7.18–7.13 (m, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.92 (t, *J* = 9.2 Hz, 1H), 4.10 (br, 1H), 3.42 (dd, *J* = 15.6, 9.2 Hz, 1H), 2.96 (dd, *J* = 15.6, 8.8 Hz, 1H); ^{13}C NMR (125 MHz,

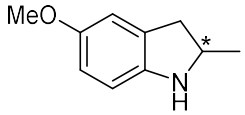
$CDCl_3$) δ 150.9, 144.6, 128.5, 128.0, 127.5, 127.3, 126.2, 124.5, 118.8, 108.8, 63.5, 39.5; All characterization data are in agreement with previously reported data [6] .
HRMS (FI) calcd for $C_{14}H_{13}N$ $[M]^+$ 195.1048, found 195.1058.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 170 ºC, P = 20 psi, t_{minor}=17.3 min. ((-)-enantiomer), t_{major}=18.2 min. ((+)-enantiomer); $[\alpha]_D^{20}$ +32.5 (c 1.2 in $CHCl_3$) 42% ee.

(*S*)- 2,5-Dimethylindoline (7i)



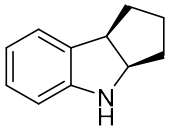
Following the general procedure (cat. **(*S*,*S*)-10**), **7i** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 1H), 4.00–3.93 (m, 1H), 3.09 (dd, *J* = 15.6, 8.4 Hz, 1H), 2.59 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.24 (s, 3H), 1.27 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 129.3, 127.9, 127.5, 125.5, 109.2, 55.4, 37.8, 22.2, 20.8; All characterization data are in agreement with previously reported data[2].
HRMS (FI) calcd for $C_{10}H_{13}N$ $[M]^+$ 147.1048, found 147.1043.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 130 ºC, P = 20 psi, t_{major}=7.7 min. ((*S*)-enantiomer), t_{minor}=8.2 min. ((*R*)-enantiomer); $[\alpha]_D^{20}$ -12.5 (c 1.5 in $CHCl_3$) 96% ee (*S*) (lit. [2] $[\alpha]_D^{RT}$ +12.4 (c 1.10 in $CHCl_3$) 84% ee (*R*))

(-)- 5-Methoxy-2-methylindoline (7j)



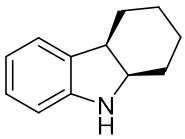
Following the general procedure (cat. **(*S*,*S*)-10**), **7j** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71–6.70 (m, 1H), 6.59–6.51 (m, 2H), 4.00–3.90 (m, 1H), 3.73 (s, 1H), 3.40 (br, 1H), 3.10 (dd, *J* = 15.6, 8.4 Hz, 1H), 2.60 (dd, *J* = 15.4, 7.6 Hz, 1H), 1.27 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 144.7, 130.6, 112.0, 111.6, 109.8, 55.9, 55.6, 38.2, 22.1
HRMS (FI) calcd for $C_{10}H_{13}$ ClNO $[M]^+$ 163.0997, found 163.1003.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 130 ºC, P = 20 psi, t_{major}=17.3 min. ((-)-enantiomer), t_{minor}=18.0 min. ((+)-enantiomer); $[\alpha]_D^{20}$ -8.47 (c 1.2 in $CHCl_3$) 95% ee

(2*R*,3*R*)- 1,2,3,3*a*,4,8*b*-Hexahydrocyclopenta[*b*]indole (7k)



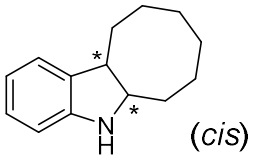
Following the general procedure (cat. **(*R*,*R*)-8**), **7k** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J* = 7.3 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 1H), 4.40–4.35 (m, 1H), 3.80–3.75 (m, 1H), 3.73 (br, 1H), 2.00–1.87 (m, 1H), 1.80–1.50 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.3, 133.3, 127.3, 124.5, 118.2, 108.4, 63.3, 47.2, 36.9, 34.9, 24.4; All characterization data are in agreement with previously reported data [14] .
HRMS (FI) calcd for $C_{11}H_{13}N$ $[M]^+$ 159.1048, found 159.1049.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 150 ºC, P = 20 psi, t_{minor}=9.6 min. ((*S*,*S*)-enantiomer), t_{major}=10.8 min. ((*R*,*R*)-enantiomer); $[\alpha]_D^{20}$ +41.8 (c 3.1 in $CHCl_3$) 91% ee (2*R*,3*R*) (lit. [14] $[\alpha]_D^{20}$ +33.3 (c 0.33 in $CHCl_3$) 70% ee (2*R*,3*R*))

(2*R*,3*R*)- 2,3,4,4*a*,9,9*a*-Hexahydro-1*H*-carbazole (7l)



Following the general procedure (cat. **(*R*,*R*)-8**), **7l** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 3.72 (q, *J* = 6.8 Hz, 1H), 3.60 (br, 1H), 3.09 (q, *J* = 6.8 Hz, 1H), 1.80–1.73 (m, 2H), 1.70–1.50 (m, 3H), 1.45–1.30 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.7, 133.5, 127.0, 123.1, 118.7, 110.1, 59.6, 40.9, 29.2, 26.9, 22.5, 21.6; All characterization data are in agreement with previously reported data[2].
HRMS (FI) calcd for $C_{12}H_{15}N$ $[M]^+$ 173.1205, found 173.1203.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 160 ºC, P = 20 psi, t_{minor}=9.2 min. ((*S*,*S*)-enantiomer), t_{major}=10.5 min. ((*R*,*R*)-enantiomer); $[\alpha]_D^{20}$ +16.7 (c 2.8 in $CHCl_3$) 96% ee (2*R*,3*R*) (lit. [2] $[\alpha]_D^{RT}$ +23.4 (c 1.20 in CHCl3) 91% ee (2*R*, 3*R*))

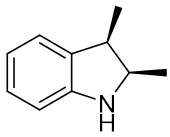
(+)- 5*a*,6,7,8,9,10,11,11*a*-Octahydro-5*H*-cycloocta[*b*]indole (7m)



Following the general procedure (cat. **(*R*,*R*)-8**), **7m** was obtained as white solid.

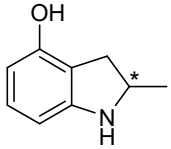
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.4 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 6.68 (t, *J* = 7.4 Hz, 1H), 6.54 (d, *J* = 7.8 Hz, 1H), 3.88–3.80 (m, 1H), 3.60 (br, 1H), 3.22–3.17 (m, 1H), 2.10–1.85 (m, 2H), 1.80–1.40 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.4, 135.3, 127.2, 124.2, 118.5, 108.5, 63.8, 46.1, 30.2, 30.0, 28.6, 27.5, 25.7, 25.4
HRMS (FI) calcd for $C_{14}H_{19}N$ $[M]^+$ 201.15175, found 201.1523.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AS-H, 250 × 4.6 mm column, Hexane/2-propanol 99:1, 0.5 mL/min, 254 nm, 30 ºC, t_{minor}=12.2 min. ((-)-enantiomer), t_{major}=13.2 min. ((+)-enantiomer)); $[\alpha]_D^{20}$ +6.8 (c 0.9 in $CHCl_3$) >99% ee

(2*R*, 3*R*)- 2,3-Dimethylindoline (7n)



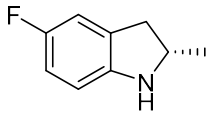
Following the general procedure (cat. **(*R*,*R*)-8**), **7n** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07–7.00 (m, 2H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.60 (t, *J* = 7.6 Hz, 1H), 3.96–3.91 (m, 1H), 3.50 (br, 1H), 3.28–3.24 (m, 1H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.13 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.1, 134.2, 127.2, 123.8, 118.7, 109.3, 58.3, 39.4, 16.3, 13.6; All characterization data are in agreement with previously reported data[2].
HRMS (FI) calcd for $C_{10}H_{13}N$ $[M]^+$ 147.1048, found 147.1055.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 130 ºC, P = 20 psi, t=6.5, 6.7 min. (*trans*- isomer), t_{minor}=7.8 min (*cis*- (*S*,*S*) enantiomer), t_{major}=8.7 min. (*cis*- (*R*,*R*) enantiomer); $[\alpha]_D^{20}$ +32.9 (c 0.3 in $CHCl_3$) 97% ee (2*R,* 3*R*) (92 : 8 diasteromer mixture (*cis* major)) (lit.[2] $[\alpha]_D^{RT}$ +26.6 (c 0.83 in $CHCl_3$) 92% ee (2*R,* 3*R*))

(+)- 2-Methylindolin-4-ol (7o)



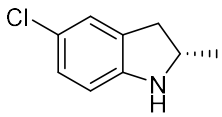
Following the general procedure (cat. **(*R*,*R*)-8)**, **7o** was obtained as a pale yellow crystal.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (t, *J* = 8.0 Hz, 1H), 6.23 (d, *J* = 8.0 Hz, 1H), 6.15 (d, *J* = 8.0 Hz, 1H), 4.50 (br, 1H), 4.15–3.98 (m, 1H), 3.10 (dd, *J* = 15.0, 8.6 Hz, 1H), 2.56 (dd, *J* = 15.2, 7.2 Hz, 1H), 1.28 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.7, 152.4, 128.7, 113.7, 106.3, 102.6, 55.3, 34.1, 22.4
HRMS (FI) calcd for $C_9H_{11}NO$ $[M]^+$ 149.08406, found 149.0842.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 150 ºC, P = 20 psi, t_{major}=22.9 min. ((+)-enantiomer), t_{minor}=24.0 min. ((-)-enantiomer); $[\alpha]_D^{20}$ +24.3 (c 0.82 in $CHCl_3$) 99% ee

(*S*)- 5-Fluoro-2-methylindoline (7p)



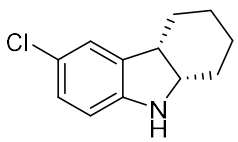
Following the general procedure (cat. **(*S*,*S*)-10**), **7p** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81–6.78 (m, 1H), 6.70–6.63 (m, 1H), 6.50–6.47 (m, 1H), 4.10–3.90 (m, 1H), 3.60 (br, 1H), 3.11 (dd, *J* = 15.6, 8.4 Hz, 1H), 2.61 (dd, *J* = 15.6, 8.0 Hz, 1H), 1.28 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0 (d, *J* = 233 Hz), 146.9, 130.6 (d, *J* = 8.8 Hz), 113.1 (d, *J* = 23.8 Hz), 112.1 (d, *J* = 23.8 Hz), 109.3 (d, *J* = 8.8 Hz), 55.9, 38.0 (d, *J* = 1.2 Hz), 22.1; All characterization data are in agreement with previously reported data[2].
HRMS (FI) calcd for $C_9H_{10}FN$ $[M]^+$ 151.0797, found 151.0799.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, Hexane/2-propanol 97:3, 0.8 mL/min, 254 nm, 30 ºC, t_{minor}=8.0 min. ((*R*)-enantiomer), t_{major}=11.2 min. ((*S*)-enantiomer); $[\alpha]_D^{20}$ -12.0 (c 0.25 in $CHCl_3$) 94% ee (*S*) (lit. [2] $[\alpha]_D^{RT}$ +7.56 (c 0.80 in $CHCl_3$) 88% ee (*R*))

(*S*)- 5-Chloro-2-methylindoline (7q)



Following the general procedure (cat. **(*S*,*S*)-10**), **7q** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01–7.00 (m, 1H), 6.96–6.93 (m, 1H), 6.48 (d, *J* = 8.4 Hz, 1H), 4.03–3.96 (m, 1H), 3.70 (br, 1H), 3.11 (dd, *J* = 15.6, 8.4 Hz, 1H), 2.60 (dd, *J* = 15.6, 7.6 Hz, 1H), 1.27 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 130.8, 126.9, 124.9, 122.9, 109.7, 55.6 37.6, 22.1
HRMS (FI) calcd for $C_9H_{10}ClN$ $[M]^+$ 167.0502, found 167.0508.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 140 ºC, P = 20 psi, t_{major}=12.6 min. ((*S*)-enantiomer), t_{minor}=13.3 min. ((*R*)-enantiomer)
$[\alpha]_D^{20}$ -10.6 (c 1.6 in $CHCl_3$) 94% ee
Absolute configuration was determined by comparison with 2-methylindoline (**7a**): Dechlorination product of (*S*)-**7q** matched (*S*)-**7a** by Chiral-GC analysis.

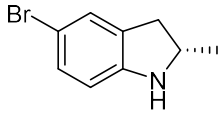
(4*aS*,9*aS*)-6-chloro-2,3,4,4*a*,9,9*a*-hexahydro-1*H*-carbazole (7r)



Following the general procedure (cat. **(*S*,*S*)-10**), **7r** was obtained as white solid.

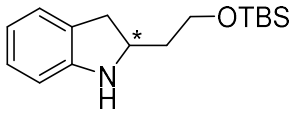
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02–7.01 (m, 1H), 6.98–6.95 (m, 1H), 6.57–6.55 (m, 1H), 3.75–3.71 (m, 1H), 3.60 (br, 1H), 3.11–3.06 (m, 1H), 1.78–1.72 (m, 2H), 1.72–1.45 (m, 3H), 1.43–1.30 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.3, 135.4, 126.7, 123.5, 123.3, 10.8, 60.0, 41.0, 29.1, 26.7, 22.4, 21.5
HRMS (FI) calcd for $C_{12}H_{14}ClN$ $[M]^+$ 207.08148, found 207.08188.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-H, 250 × 4.6 mm column, Hexane/2-propanol 95:5, 1.0 mL/min, 254 nm, 30 ºC, t_{minor}=6.2 min. ((*R*)-enantiomer), t_{major}=7.0 min. ((*S*)-enantiomer)) ; $[\alpha]_D^{20}$ -13.7 (c 1.0 in $CHCl_3$) 90% ee

(*S*)- 5-Bromo-2-methylindoline (7s)



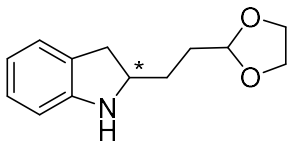
Following the general procedure (cat. **(*S*,*S*)-10**), **7s** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–7.14 (m, 1H), 7.09–7.07 (m, 1H), 6.45 (d, *J* = 8.4 Hz, 1H), 4.02–3.96 (m, 1H), 3.70 (br, 1H), 3.12 (dd, *J* = 15.6, 8.8 Hz, 1H), 2.61 (dd, *J* = 16.0, 7.6 Hz, 1H), 1.26 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.9, 131.2, 129.8, 127.7, 110.3, 109.9, 55.5, 37.5, 22.1; All characterization data are in agreement with previously reported data [14] .
HRMS (FI) calcd for C_9H_{10} BrN $[M]^+$ 210.9997, found 210.9994.
The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 160 ºC, P = 20 psi, t_{major}=8.6 min. ((*S*)-enantiomer), t_{minor}=8.9 min. ((*R*)-enantiomer)); $[\alpha]_D^{20}$ -7.75 (c 1.3 in $CHCl_3$) 96% ee (*S*) (lit. [14] $[\alpha]_D^{20}$ +17.1 (c 1.54 in $CHCl_3$) 85% ee (*R*))

(-)- 2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)indoline (7t)



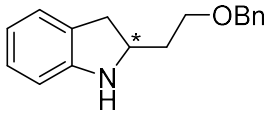
Following the general procedure (cat. **(*S*,*S*)-10**), **7t** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, *J* = 7.3 Hz, 1H), 7.00 (t, *J* = 7.8 Hz, 1H), 6.68 (t, *J* = 7.3 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 4.10–3.95 (m, 1H), 3.82–3.75 (m, 1H), 3.17 (dd, *J* = 15.4, 8.6 Hz, 1H), 2.70 (dd, *J* = 15.6, 7.6 Hz, 1H), 1.90–1.82 (m, 1H), 1.75–1.70 (m, 1H), 0.95 (s, 9H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 128.6, 127.2, 124.6, 118.3, 109.1, 61.5, 58.2, 39.0, 36.5, 25.9, 18.2
HRMS (FI) calcd for $C_{16}H_{27}NOSi$ $[M]^+$ 277.18619, found 277.1854.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, Hexane/2-propanol 99:1, 0.5 mL/min, 254 nm, 30 ºC, t_{minor}=9.5 min. ((+)-enantiomer), t_{major}=11.7 min. ((-)-enantiomer)); $[\alpha]_D^{20}$ -24.7 (c 0.6 in $CHCl_3$) 92% ee

(-)- 2-(2-(1,3-Dioxolan-2-yl)ethyl)indoline (7u)



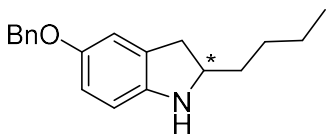
Following the general procedure (cat. **(*S*,*S*)-10**), **7u** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 7.2 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 6.66 (t, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 7.8 Hz, 1H), 4.91–4.89 (m, 1H), 4.00–3.82 (m, 5H), 3.13 (dd, *J* = 15.6, 8.8 Hz, 1H), 2.68 (dd, *J* = 15.6, 8.4 Hz, 1H), 1.80–1.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 128.7, 127.2, 124.6, 118.4, 109.1, 104.3, 64.9, 59.6, 36.1, 30.9, 30.7
HRMS (FI) calcd for $C_{13}H_{17}NO_2$ $[M]^+$ 219.12593, found 219.1249.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, Hexane/2-propanol 90:10, 1.0 mL/min, 254 nm, 30 ºC, t_{major}=23.2 min. ((-)-enantiomer), t_{minor}=26.4 min. ((+)-enantiomer); $[\alpha]_D^{20}$ -8.89 (c 0.9 in $CHCl_3$) 92% ee

(+)- 2-(2-(Benzyloxy)ethyl)indoline (7v)



Following the general procedure (cat. **(*R*,*R*)-8**), **7v** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.25 (m, 5H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.99 (t, *J* = 7.8 Hz, 1H), 6.63 (t, *J* = 7.2 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 4.52 (s, 2H), 4.10 (br, 1H), 4.05–3.98 (m, 1H), 3.63–3.60 (m, 2H), 3.14 (dd, *J* = 15.2, 8.8 Hz, 1H), 2.68 (dd, *J* = 15.4, 8.2 Hz, 1H), 2.00–1.81 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 138.3, 128.6, 128.4, 127.7, 127.6, 127.2, 124.6, 118.4, 109.1, 73.1, 68.3, 58.1, 36.4
HRMS (FI) calcd for $C_{17}H_{19}NO$ $[M]^+$ 253.1467, found 253.1478.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, Hexane/2-propanol 95:5, 1.0 mL/min, 254 nm, 30 ºC, t_{major}=10.4 min. ((+)-enantiomer), t_{minor}=13.9 min. ((-)-enantiomer)); $[\alpha]_D^{20}$ +6.17 (c 1.6 in $CHCl_3$) 84% ee

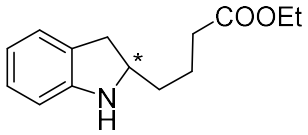
(+)- 5-(Benzyloxy)-2-butylindoline (7w)



Following the general procedure (cat. **(*R*,*R*)-8**), **7w** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.15 (m, 5H), 6.78–6.77 (m, 1H), 6.66–6.63 (m, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 4.98 (s, 2H), 3.85–3.78 (m, 1H), 3.08 (dd, *J* = 15.4, 8.6 Hz, 1H), 2.65 (dd, *J* = 15.6, 8.4 Hz, 1H), 1.62–1.58 (m, 2H), 1.40–1.32 (m, 4H), 0.90–0.85 (m, 3H);

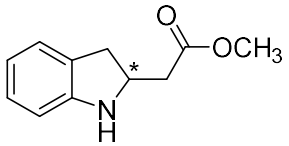
^{13}C NMR (125 MHz, $CDCl_3$) δ 137.7, 131.0, 129.0, 128.5, 128.2, 127.7, 127.5, 113.4, 112.8, 109.7, 71.1, 60.6, 36.7, 36.5, 28.8, 22.8, 14.1
HRMS (FI) calcd for $C_{19}H_{23}NO$ $[M]^+$ 281.1780, found 281.1780.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-H, 250 × 4.6 mm column, Hexane/2-propanol 90:10, 0.8 mL/min, 254 nm, 30 ºC, t_{major}=7.9 min. ((+)-enantiomer), t_{minor}=10.0 min. ((-)-enantiomer); $[\alpha]_D^{20}$ +8.60 (c 0.5 in $CHCl_3$) 97% ee

(-)- Ethyl 4-(indolin-2-yl)butanoate (7x)



Following the general procedure (cat. **(*S*,*S*)-10**), **7x** was obtained as pale yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.3 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.57 (d, *J* = 7.6 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.85–3.78 (m, 1H), 3.70 (br, 1H), 3.11 (dd, *J* = 15.6, 8.8 Hz, 1H), 2.69 (dd, *J* = 15.4, 8.6 Hz, 1H), 2.38–2.33 (m, 2H) , 1.73–1.60 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 150.8, 128.5, 124.6, 127.1, 124.5, 118.4, 109.0, 60.2, 59.4, 36.2, 35.9, 34.1, 21.7, 14.1
HRMS (FI) calcd for $C_{14}H_{19}NO_2$ $[M]^+$ 233.1416, found 233.1427.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, 250 × 4.6 mm column, Hexane/2-propanol 90:10, 1.0 mL/min, 254 nm, 30 ºC, t_{major}=15.3 min. ((-)-enantiomer), t_{minor}=21.2 min. ((+)-enantiomer); $[\alpha]_D^{20}$ -2.32 (c 1.5 in $CHCl_3$) 91% ee

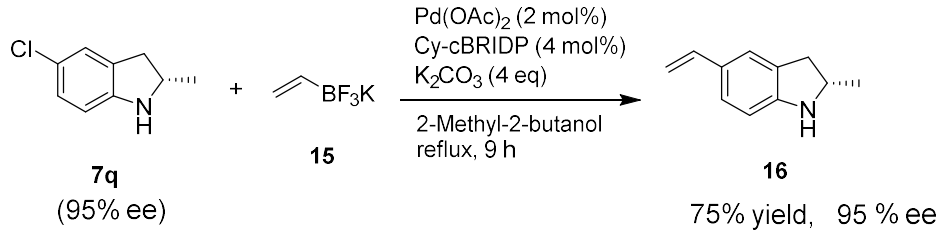
(-)- Methyl 2-(indolin-2-yl)acetate (7y)



Following the general procedure (cat. **(*S*,*S*)-10**), **7y** was obtained as a clear oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.9 Hz, 1H), 6.68 (t, *J* = 7.5 Hz, 1H), 6.60 (d, *J* = 7.9 Hz, 1H), 4.41 (br, 1H), 4.25–4.18 (m, 1H), 3.71 (s, 3H), 3.18 (dd, *J* = 15.4, 8.6 Hz, 1H), 2.66 (dd, *J* = 15.6, 8.4 Hz, 1H), 2.63 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 150.5, 127.8, 127.5, 124.6, 118.7, 109.2, 55.7, 51.7, 40.6, 35.8
HRMS (FI) calcd for $C_{11}H_{13}NO_2$ $[M]^+$ 191.09463, found 191.0953.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AS-H, 250 × 4.6 mm column, Hexane/2-propanol 97:3, 1.0 mL/min, 254 nm, 30 ºC, t_{major}=9.8 min. ((-)-enantiomer), t_{minor}=10.9 min. ((+)-enantiomer); $[\alpha]_D^{20}$ -53.1 (c 0.5 in $CHCl_3$) 72% ee

K. Derivatizations of Chiral Indolines

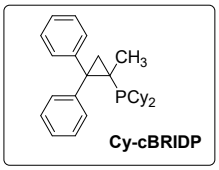
(a) Synthesis of (*S*)-2-Methyl-5-vinylindoline (16)



7q
(95% ee)

15

16
75% yield, 95 % ee

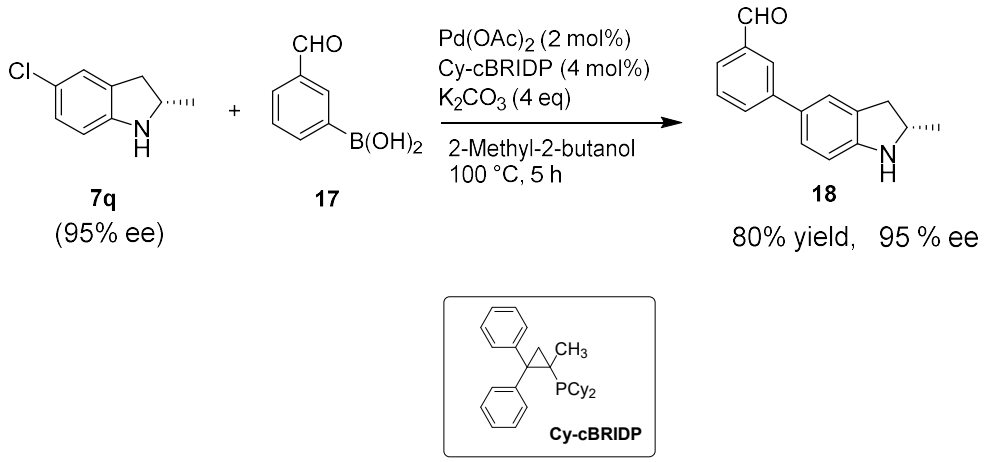


A 50mL schlenk flask equipped with a magnetic stirring bar was charged with (*S*)-5-Chloro-2-methylindoline (**7q**) (0.30 g, 1.789 mmol), potassium vinyltrifluoroborate (**15**) (0.36 g, 2.684 mmol), Cy-cBRIDP (29.0 mg, 0.072 mmol), $Pd(OAc)_2$ (8.0 mg, 0.036 mmol), K_2CO_3 aquaous solution (2.22M) (3.24 mL, 22.00 mmol) and 2-Methyl-2-butanol (*tert*-AmOH) (3.0 mL). Then the resulting solution was briefly evacuated and then backfilled with argon (5 times). The reaction mixture was then placed in a preheated oil bath at 110 °C. Vigorous stirring was applied and the reaction was monitored by GC and TLC. After stirred at 9 h, the reaction mixture was cooled to room temperature, diluted with $CHCl_3$ and water (5 mL each) and separated organic layer. Aquaous layer was extracted by $CHCl_3$ (3 × 5 mL) and combined organic layer was dried over $MgSO_4$. After removal of organic solvents, the residue was purified by silica gel column chromatography (Hexane/AcOEt = 15/1) gave **16** as a clear liquid in 75% yield (0.21 g).

The enantiomeric excess of **16** was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 140 ºC, P = 20 psi, t_{major}=12.0 min. ((*S*)-enantiomer), t_{minor}=12.8 min. ((*R*)-enantiomer), 95% ee.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (s, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.62 (dd, *J* = 17.6, 10.8 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 1H), 5.51 (d, *J* = 17.6 Hz, 1H), 5.00 (d, *J* = 10.8 Hz, 1H), 4.03–3.97 (m, 1H), 3.80 (br, 1H), 3.13 (dd, *J* = 15.4, 8.6 Hz, 1H), 2.62 (dd, *J* = 15.4, 8.6 Hz, 1H), 1.28 (d, *J* = 4.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 137.1, 129.2, 128.6, 126.3, 122.2, 109.2, 108.6, 55.4, 37.5, 22.3
HRMS (FI) calcd for $C_{11}H_{13}N$ $[M]^+$ 159.1048, found 159.1053.
$[\alpha]_D^{20}$ -6.71 (c 0.60 in $CHCl_3$) 95% ee

(b) Synthesis of (*S*)-3-(2-Methylindolin-5-yl)benzaldehyde (18)

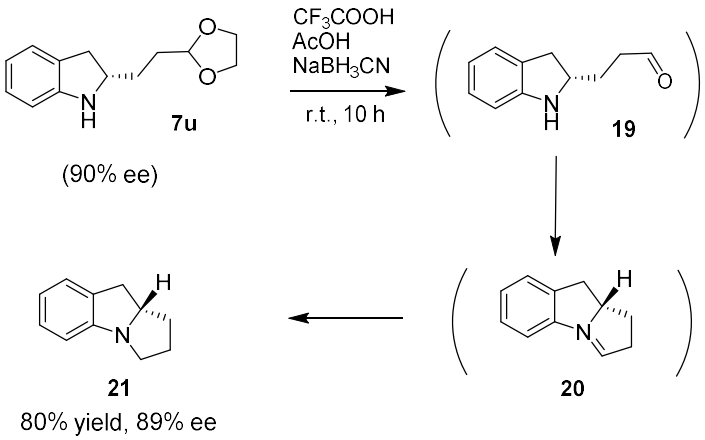


A 50mL schlenk flask equipped with a magnetic stirring bar was charged with (*S*)-5-Chloro-2-methylindoline (**7q**) (0.30 g, 1.789 mmol), 3-formylphenylboronic acid (**17**) (0.36 g, 2.684 mmol), Cy-cBRIDP (29.0 mg, 0.072 mmol), $Pd(OAc)_2$ (8.0 mg, 0.036 mmol), K_2CO_3 aquaous solution (2.22M) (3.24 mL, 22.00 mmol) and 2-Methyl-2-butanol (*tert*-AmOH) (3.0 mL). Then the resulting solution was briefly evacuated and then backfilled with argon (5 times). The reaction mixture was then placed in a preheated oil bath at 100 °C. Vigorous stirring was applied and the reaction was monitored by GC and TLC. After stirred at 5 h, the reaction mixture was cooled to room temperature, diluted with $CHCl_3$ and water (5 mL each) and separated organic layer. Aquaous layer was extracted by $CHCl_3$ (3 × 5 mL) and combined organic layer was dried over $MgSO_4$. After removal of organic solvents, the residue was purified by silica gel column chromatography (Hexane/AcOEt = 10/1) gave **18** as a pale yellow solid in 80% yield (0.34 g).

The enantiomeric excess of **18** was determined by HPLC analysis (Chiralpak AD-H, 250 × 4.6 mm column, Hexane/2-propanol 95:5, 1.0 mL/min, 254 nm, 30 ºC, t_{minor}=19.5 min. ((*R*)-enantiomer), t_{major}=24.0 min. ((*S*)-enantiomer), 95% ee.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.04–8.03 (m, 1H), 7.81–7.74 (m, 2H), 7.54 (t, *J* = 7.8 Hz,1H), 7.38–7.29 (m, 2H), 6.66 (d, *J* = 7.8 Hz, 1H), 4.10–4.04 (m, 1H), 3.90 (br, 1H), 3.21 (dd, *J* = 15.8, 8.0 Hz, 1H), 2.70 (dd, *J* = 15.8, 8.0 Hz, 1H), 1.32 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.6, 151.1, 142.6, 136.8, 132.2, 130.0, 129.7, 129.2, 127.4, 127.3, 126.4, 123.5, 109.0, 55.4, 37.5, 22.3
HRMS (FI) calcd for $C_{16}H_{15}NO$ $[M]^+$ 2387.1154, found 137.1164.
$[\alpha]_D^{20}$ -8.20 (c 0.75 in $CHCl_3$) 95% ee

(c) Synthesis of Tetrahydro-*1H*-pyrroloindole (21)



To a solution of (*S*)-2-(2-(1,3-dioxolan-2-yl)ethyl)indoline (**7u**) (0.30 g, 1.36 mmol) in AcOH (2.0 mL) were added CF_3COOH (3.11g, 2.03 mL, 27.3 mmol, 20eq vs **7u**). After the mixture was stirred for 1 h at room temperature, $NaBH_3CN$ (0.256 g, 4.08 mmol) was added. After stried for 10 h, $CHCl_3$ (10mL) and aqueous $NaHCO_3$ solution (30 mL) was added and separated the organic layer. The aqueous phase was extracted with $CHCl_3$ (2 × 20 mL), and the combined organic portions were dried over $MgSO_4$, and concentrated to give a crude liquid. After removal of organic solvents, the residue was purified by silica gel column chromatography (Hexane/AcOEt = 5/1) gave **21** as a clear liquid in 80% yield (0.17 g).

The enantiomeric excess was determined by GC analysis (CHIRALSIL-DEX-CB 0.25 × 25 m, T = 140 ºC, P = 20 psi, t_{major}=8.8 min. ((*S*)-enantiomer), t_{minor}=9.4 min. ((*R*)-enantiomer), 89% ee.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11–7.08 (m, 2H), 6.75 (t, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 7.2 Hz, 1H), 3.96–3.84 (m, 1H), 3.45–3.38 (m, 1H), 3.23–3.10 (m, 2H), 2.98–2.93 (m, 1H), 1.95–1.78 (m, 3H), 1.40–1.20 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7, 129.9, 127.5, 124.8, 119.3, 111.0, 65.3, 52.3, 33.9, 31.3, 25.8
HRMS (FI) calcd for $C_{11}H_{13}N$ $[M]^+$ 159.1048, found 159.1056.
$[\alpha]_D^{20}$ -9.42 (c 0.50 in $CHCl_3$) 89% ee

L. References in Experimental Section

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Chapter 3.

Efficient Access to Chiral Benzohydrols via Asymmetric Transfer Hydrogenation of Unsymmetrical Benzophenones with Bifunctional Oxo-tethered Ruthenium Catalysts

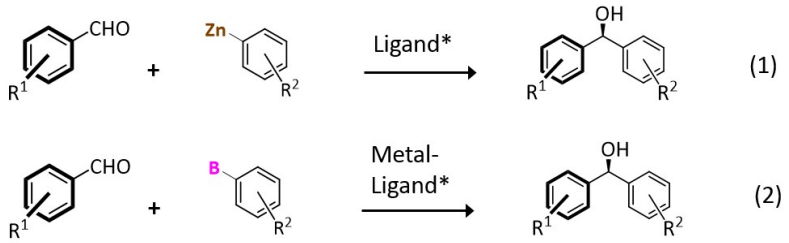
6. Introduction

Catalytic asymmetric synthesis of secondary alcohols from ketones has attracted considerable interest as a reliable method. Since a string of Ru catalysts with 1,2-diamine scaffolds was established for asymmetric H_2-hydrogenation or transfer hydrogenation of acetophenone derivatives in the mid-1990s,[1,2] the utility of metal/NH cooperation has been highlighted via advances in redox transformations of carbonyl or alcoholic compounds.[3] Because of breakthrough developments of the bifunctional catalysts, the scope of ketone substrates has been extensively broadened; however, a high level of stereo-controlling ability of the chiral catalysts is needed to access post-challenging targets.

Among aromatic ketones, unsymmetrical benzophenones have been less frequently subjected to enantioselective reduction, in which a catalyst must discern structural differences in the two aromatic rings.[4-8] The catalytic hydrogenation offers straightforward access to biologically and pharmaceutically valuable benzhydrols without producing stoichiometric amounts of metal waste, compared with the asymmetric catalytic addition of nucleophilic arylmetals to aromatic aldehydes.[9] Ohkuma and Noyori reported that the Ru/(*S*)-Xylbinap/(*S*)-daipen catalyst can effectively promote H_2-hydrogenation of substituted benzophenones in the presence of *tert*-BuOK under mild pressure (8 atm) and temperature conditions.[4a] Although *ortho*-substituted benzophenones were successfully converted to the corresponding diarylmethanols with a maximum of 99% ee, the enantiomeric excesses obtained from *meta*- and *para*-substituted substrates were lower (<47% ee). In other asymmetric H_2-hydrogenation,[4b–f] hydroboration,[5] hydrosilylation,[6] and transfer hydrogenation[7] systems with reasonable enantioselectivity, the substrate scope remains primarily limited to *ortho*-functionalized and mono-substituted benzophenones.[10]

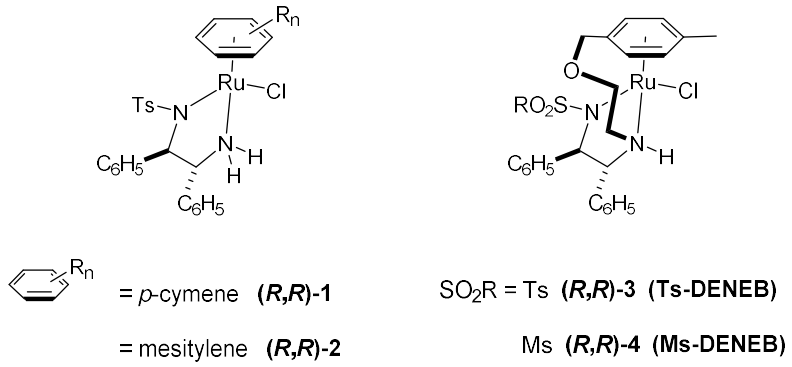
According to other examples to obtaining chiral diarylmethanol, addition of appropriate reagents to aldehyde are widely known. For example, addition of aryl zinc reagent into aldehyde with chiral ligands affords corresponding chiral diarylmethanols (Scheme 1, eq. 1). Furthermore the addition of aryl boron compounds such as aryl boronic acid derivatives into aldehyde with chiral ligands and appropriate metal also affords diarylmethanols (Scheme 1, eq. 2)

Scheme 1. Other examples for obtaining chiral diarylmethanols



Using a systematic approach to structural tuning of the bifunctional catalysts derived from sulfonylated 1,2-diphenylethylenediamine (DPEN), we designed a new family of oxo-tethered Ru complexes—(*R*,*R*)-**3** and (*R*,*R*)-**4**—that exhibit excellent catalytic performance for the asymmetric transfer hydrogenation of simple ketones.[11,17] The persistent three-point coordination obtained by introducing the covalently tethered unit[12] enhanced catalyst longevity and produced the highest activity of a series of the prototypic (η^6-arene)Ru/Ts-DPEN catalysts, including (*R*,*R*)-**1** and (*R*,*R*)-**2**. Regarding the imposed coordination, conformational rigidity also supported the stereodiscrimination ability of the bifunctional catalysts. In this paper, the author reports the substantial enantioselectivity of the oxo-tethered Ru complexes in the catalytic transfer hydrogenation of diaryl ketones with a variety of substituents at *ortho* positions and/or other positions.

Figure 1. **Structure of non-tethered and tethered Ru-DPEN catalysts**

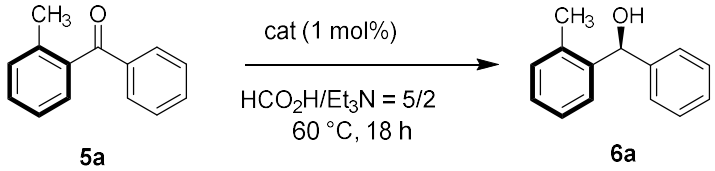


7. Results and Discussions

(ア) Asymmetric Transfer Hydrogenation of 2-Substituted Benzophenones

We initially examined asymmetric transfer hydrogenation of 2-methylbenzophenone using 1 mol% of the DPEN-derived Ru complexes in an azeotropic mixture of formic acid and triethylamine at 60 °C. As listed in Table 1, the corresponding (*S*)-alcohol was obtained in 86-98% ees after the 18 h reaction. Compared to the prototype catalyst of (*R*,*R*)-**1** and (*R*,*R*)-**2** (entries 1 and 2), the oxo-tethered Ru(II) complexes (*R*,*R*)-**3**, (*R*,*R*)-**4** exhibited superior activities (entries 3 and 4), and the former Ts-derivative showed optimal catalytic performance in terms of the yield and enantioselectivity. The attained optical purity is as high as those with a ketoreductase eznyme.[8b]

Table 1. Asymmetric transfer hydrogenation of 2-methylbenzophenone[a]

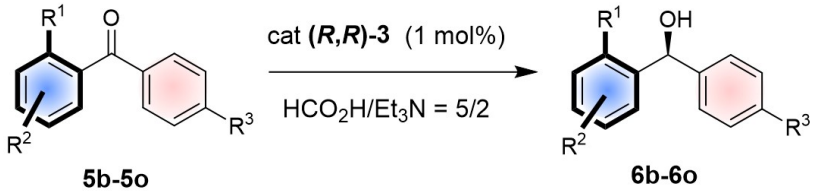


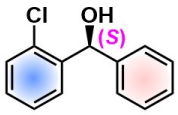
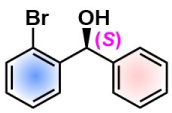
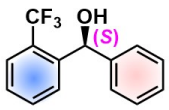
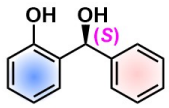
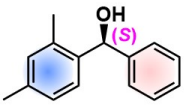
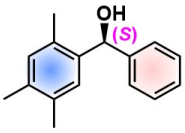
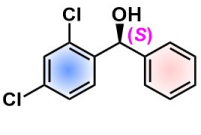
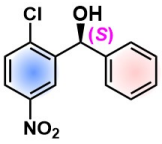
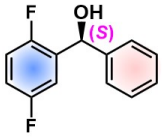
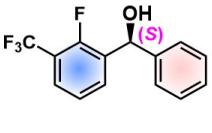
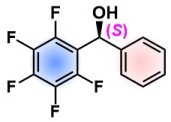
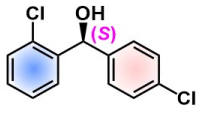
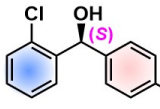
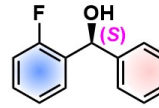
entry	catalyst	% yield	% ee[b]
1	(*R*,*R*)-**1**	22	86 (*S*, +)
2	(*R*,*R*)-**2**	45	90 (*S*, +)
3	(*R*,*R*)-**3**	98	98 (*S*, +)
4	(*R*,*R*)-**4**	94	94 (*S*, +)

[a] Typical reaction condition: catalyst (0.01 mmol), substrate (1.0 mmol), HCO_2H/Et_3N=5/2 azeotropic mixture (0.5 mL) [b] Determined by HPLC analysis.

A variety of 2-substituted benzophenones was shown to be applicable to asymmetric transfer hydrogenation with (*R*,*R*)-**3**, which displayed enhanced enantioselectivities relative to the asymmetric hydrogenation with chiral Ru catalysts,[4a–f] as listed in Table 2.

Table 2. Asymmetric transfer hydrogenation of 2-substituted benzophenones[a,b]



				
6b (40 °C, 17 h)	**6c** (60 °C, 8 h)	**6d** (60 °C, 12 h)	**6e** (40 °C, 13 h) [c,d]	**6f** (60 °C, 17 h)
99% yield, 98% ee	>99% yield, 99% ee	99% yield, >99% ee	94% yield, 77% ee	94.0% yield, 97% ee
				
6g (60 °C, 23 h)	**6h** (30 °C, 18 h)	**6i** (40 °C, 7 h)	**6j** (10 °C, 40 h)	**6k** (30 °C, 7 h)
98% yield, 98% ee	97% yield, 99% ee	>99% yield, 99% ee	91% yield, 91% ee	>99% yield, 90% ee
				
6l (60 °C, 5 h)	**6m** (30 °C, 18 h)	**6n** (40 °C, 17 h)	**6o** (30 °C, 15 h)	
>99% yield, >99% ee	97% yield, 99% ee	99% yield, 97% ee	98% yield, 76% ee	

[a] Typical reaction condition: catalyst (0.01 mmol), substrate (1.0 mmol), HCO_2H/Et_3N=5/2 azeotropic mixture (0.5 mL) [b] Ee values were determined by HPLC analysis. [c] (*R*,*R*)-**4** was employed as a catalyst. [d] Comparable yield (99%) and ee (70%) were obtained by using (*R*,*R*)-**3** under identical conditions.

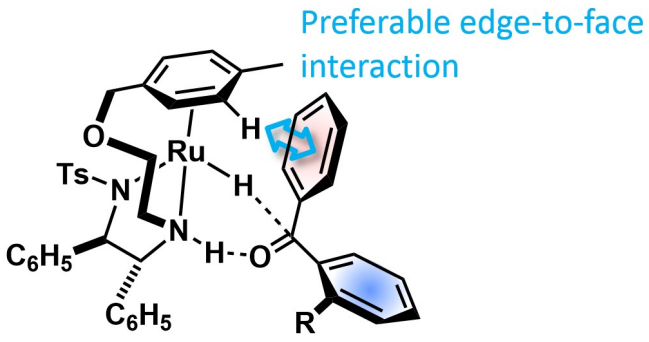
Mono-substituted benzophenones bearing chloro, bromo, and trifluoromethyl groups at the *ortho* position were smoothly reduced with almost complete conversions and excellent ees, exceeding 98% (**6b**–**6d**). The results of the high-performance liquid chromatographic (HPLC) analysis with a chiral stationary phase indicated that the products were (*S*)-isomers. In contrast to the asymmetric hydrogenation with a diphosphine-diamine-Ru(II) complex,[4a] the oxo-tethered catalyst (*R*,*R*)-**4** tolerated a phenolic ketone—2-hydroxybenzophenone—and provided a satisfactory ee of 77% (**6e**).

Multiply-substituted aryl phenyl ketones, including 2,4-methyl-, 2,4,5-trimethyl-, 2,4-dichloro-, and 2-chloro-5-nitrobenzophenone analogues, were converted into the desired (*S*)-benzhydrols with sufficient conversions and ees (**6f**–**6i**). Although reduction of 2,5-difluoro- and 2-fluoro-3-trifluoromethylbenzophenone produced slightly lower ees of 91% and 90% (**6j** and **6k**), 2,3,4,5,6-pentafluorobenzophenone was completely hydrogenated with outstanding enantioselectivity (**6l**). Transfer hydrogenation of 2,4'-dichloro- and 2-chloro-4'-fluorobenzophenone furnished the corresponding unsymmetrical diarylmethanols in high yields with 97% ee (**6m** and **6n**), indicating that (*R*,*R*)-**3** can precisely recognize the *ortho*-substituted phenyl group.

In a putative outer sphere mechanism involving H^+ and H^- transfer to the C=O moiety, an attractive interaction between the edge of an η^6-arene ligand and the face of an aromatic ring[13] in ketone substrates has been considered to impose their one-sided approach and enable remarkable asymmetric induction.[14] Given that the stereochemistry of all products from 2-substituted diaryl ketones has an *S*-configuration, a sterically favorable edge-to-face interaction away from the *ortho*-substituted phenyl groups is envisaged in the transition state, as depicted in Figure 2. The introduction of the sterically less demanding fluorine atom into the *ortho* position was mildly effective compared with other halogens (**6j**, **6k**, **6o**).

Absolute configuration of new diarylmethanol products were determined by X-ray crystallography of corresponding esters of alcohol products (see details in Experimental Section).

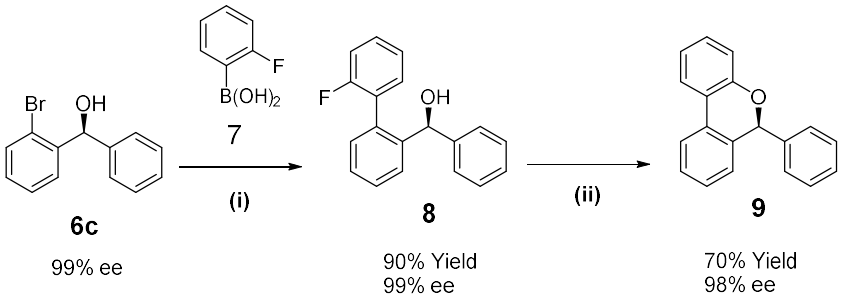
Figure 2. **Proposed interaction between 2-substituted benzophenone and the oxo-tethered Ru(II) complex (*R*,*R*)-**3



2.2 Synthesis of Optically Active 6-Phenyl-6*H*-benzo[*c*]chromene Compound

The chiral benzohydrol product was successfully utilized in the expedient preparation of chiral benzo[*c*]chromene (**9**), for which only few synthetic methods have been reported (Scheme 2).[15] The Suzuki-Miyaura coupling reaction of (*S*)-(2-bromophenyl)(phenyl)methanol (**6c**) with 2-flurorophenylboronic acid (**7**) in the presence of $Pd(PPh_3)_4$ smoothly afforded the corresponding adduct **8** with virtually no loss of optical purity. Subsequent cyclization with *tert*-BuOK in THF yielded the desired benzochromene framework **9** in 70% yield with 98% ee.

Scheme 2. Synthesis of optically active 6-phenyl-6*H*-benzo[*c*]chromene

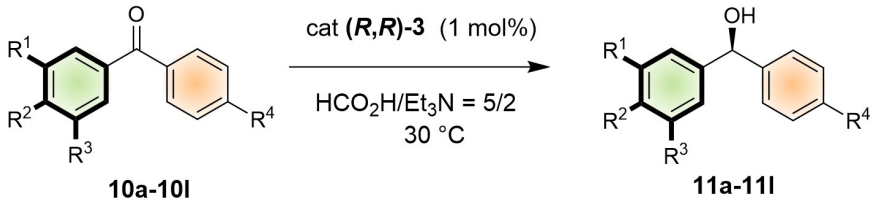


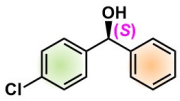
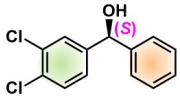
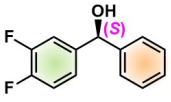
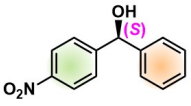
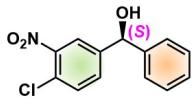
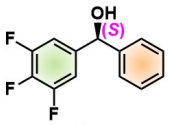
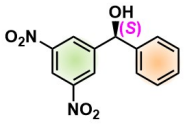
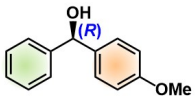
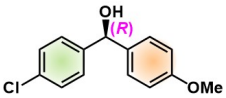
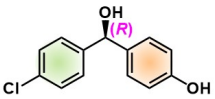
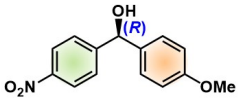
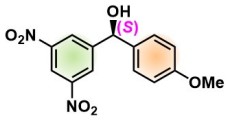
(i) 2-Fluorophenylboronic acid (**7**) (1.5 equiv), $Pd(PPh_3)_4$ (2 mol%), K_2CO_3 (1.5 equiv), Toluene/THF = 1/1, 100 °C, 7 h (ii) *tert*-BuOK (1.0 equiv), THF, 20 °C, 3 h

2.3 Asymmetric Transfer Hydrogenation of Non-*ortho*-Substituted Diaryl Ketones

The utility of (*R*,*R*)-**3** was also demonstrated in the reaction of unsymmetrical diaryl ketones with the exception of 2-substituted benzophenones, as summarized in Table 3.

Table 3. Asymmetric transfer hydrogenation of non-*ortho*-substituted diaryl ketones [a,b]



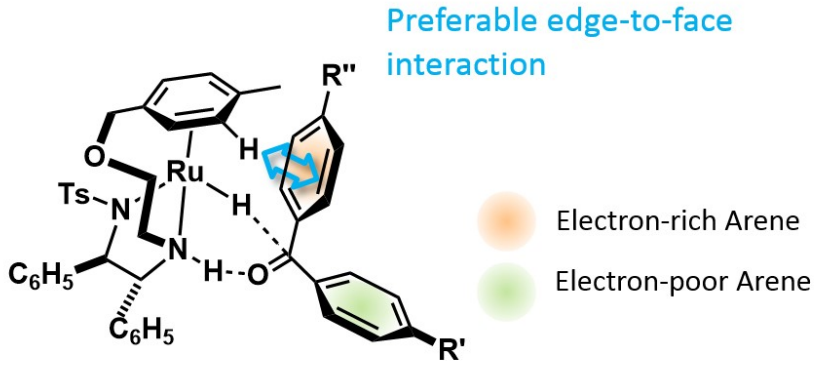
 **11a** (30 °C, 11 h) >99% yield, 48% ee	 **11b** (30 °C, 18 h) >99% yield, 76% ee	 **11c** (10 °C, 17 h) 99% yield, 79% ee	 **11d** (10 °C, 17 h) 99% yield, 79% ee	 **11e** (30 °C, 11 h) >99% yield, 93% ee
 **11f** (10 °C, 16 h) >99% yield, 95% ee	 **11g** (10 °C, 26 h) 90% yield, >99% ee	 **11h** (30 °C, 20 h) 80% yield, 5% ee	 **11i** (30 °C, 21 h) 59% yield, 53% ee	 **11j** (30 °C, 21 h) 59% yield, 53% ee
 **11k** (20 °C, 45 h) >99% yield, 81% ee	 **11l** (30 °C, 9 h) 92% yield, >99% ee			

[a] Typical reaction condition: catalyst (0.01 mmol), substrate (1.0 mmol), HCO_2H/Et_3N=5/2 azeotropic mixture (0.5 mL) [b] Ee values were determined by HPLC analysis.

From 4-chlrorobenzophenone, the corresponding (*S*)-alcohol was formed with a moderate ee of 48% (**11a**). The enantioselectivities can be substantially increased to 76% and 77%

ees by doubly-halogenated substrates at the *meta*- and *para*-positions (**11b** and **11c**). A comparable selectivity of 76% ee was attainable in the reduction of mono-substituted 4-nitrobenzophenone, implying an additional beneficial effect resulting from the incorporation of a strongly electron-withdrawing NO_2 group (**11d**); 3-nitro-4-chlorobenzophenone produced 93% ee with complete conversion (**11e**). When 3,4,5-trifluorobenzophenone and 3,5-dinitrobenzophenone were tested as highly biased diaryl ketones, the expected chiral alcohols (**11f** and **11g**) were obtained with 95% with >99% ees, respectively. In these cases, the (*S*)-enantiomers were formed, possibly via a transition state by avoiding an interaction between the η^6-arene ligand and the relatively electron-deficient ring, as indicated in bold in Figure 3.[16]

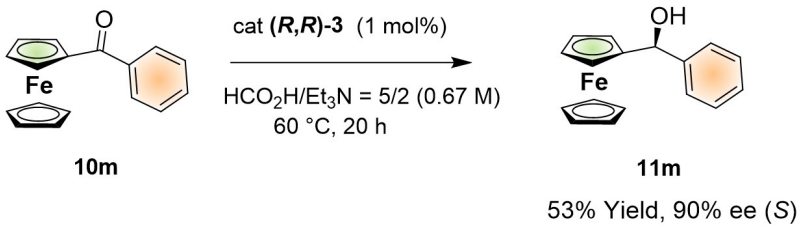
Figure 3. **Plausible transition state in asymmetric transfer hydrogenation of non-*ortho*-substituted benzophenones with (*R*,*R*)-**3



As an intriguing example, 4-methoxybenzophenone produced a low ee (5%) in the *R*-configuration of **11h**, likely because of the arene-arene interaction involving a phenyl ring attached to the electron-donating methoxy group (**11h**). The catalyst molecule can differentiate between two *para*-substituted phenyl groups with opposite electronic character, as observed in the reaction of 4-chloro-4'methoxybenzophenone, which yields a higher ee of **11i**. A comparable ee with complete conversion was achieved in the reduction of 4-chloro-4'-hydroxybenzophenone, and the phenolic OH group remained intact (**11j**). Additional enhancement of enantioselectivity by the nitro group was confirmed in the formation of **11k** and **11l**. The ees of the obtained methoxy-substituted alcohols—**11i** and **11k**—were consistently increased by 3-5 % compared with the stereochemical outcomes of **11a** and **11d**, which were derived from the corresponding aryl phenyl ketones, possibly because the methoxyphenyl ring preferentially interacts with the η^6-arene ligand in the enantio-determining step.

The excellent enantioselectivity was also realized for other aromatic ketones with distinct electronic properties**.** As shown in Schemes 3 and 4, the reaction of benzoylferrocene afforded (*S*)-alcohol (**11m**) in 90% ee via a similar asymmetric induction, albeit producing only a 53% yield after 20 h at 60 °C. In addition, 3-nitrophenyl 2-thienyl ketone was converted to the corresponding (*R*)-product (**11n**) in 96% yield with almost complete enantioselectivity (Scheme 4). These results provide evidence for enantioselective reduction, that is, the chiral oxo-tethered catalyst accurately avoids the sterically demanding and electron-poor ferrocene moiety and establishes the thiophene ring as an electron-rich fragment that can approach the η^6-arene ligand shown in Figure 3.

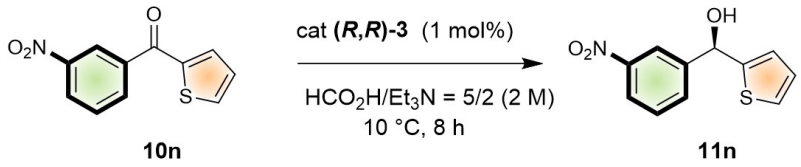
Scheme 3. Asymmetric transfer hydrogenation of benzoylferrocene



10m **11m**

53% Yield, 90% ee (*S*)

Scheme 4. Asymmetric transfer hydrogenation of 3-nitrophenyl 2-thienyl ketone



10n **11n**

96% Yield, 98% ee (*R*)

8. Conclusion

An extensive range of unsymmetrical benzophenone derivatives was successfully reduced with good to excellent ees and in high yields, because the oxo-tethered ligand ensuring precise recognition of *ortho*-substituted phenyl groups as well as differentiation between electron-rich and electron-poor arene rings. Considering the combination of desirable features, including a wide substrate scope, excellent enantioselectivity, mild reaction conditions, and high stability and availability of the catalyst precursor, the author believes that this catalyst system has significant potential for application in a practical streamlined method to obtain chiral diarylmethanols.

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10.Experimental Section

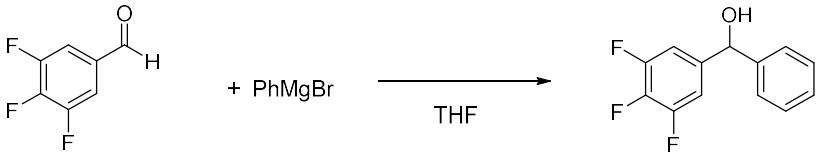
General Information

All reactions and manipulations were conducted under a nitrogen atmosphere unless otherwise noted. Synthesis of ruthenium catalysts was performed in commercial anhydrous solvents. NMR Spectra were obtained on Agilent 400-MR DD2 and Bruker BioSpin Avance Ⅲ 500 Systems. NMR chemical shifts are reported in ppm relative to $CHCl_3$ (7.26 ppm for ^1H, and 77.0 ppm for ^{13}C), or CH_3OH (3.30 ppm for ^1H, and 49.0 ppm for ^{13}C). The following abbreviations were used to designate peak splitting patterns: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Optical rotations were obtained on a JASCO P-1020 Polarimeter. Mass spectra were recorded on SHIMADZU LCMS-IT-TOF and JEOL JMS-T100GCV. Elemental analyses were carried out using a PE2400 Series II CHNS/O Analyser (Perkin Elmer). High performance liquid chromatography (HPLC) analysis was performed using a system comprised of a GL-Science GL-7400 series; column oven: GL-7430, a gradient unit, a pump, degasser: GL-7430, a UV detector: GL-7450, an auto sampler: GL-7420. Recyclable preparative HPLC was performed on a Japan Analytical Industry LC-9225 NEXT system. IR Spectra were obtained on Thermo Fisher Scientific NICOLET iS10.

Ketones (**5a**, **5b**, **5c**, **5e**, **5f**, **5g**, **5h**, **5i**, **5j**, **5l**, **5m**, **5n**, **5o**, **10a**, **10b**, **10c**, **10d**, **10e**, **10h**, **10m**) were purchased from TCI (Tokyo Chemical Industry Co., Ltd.). Ketones (**6d**, **6k**) were purchased froma Sigma-Aldrich. Ketone (**10i**) was purchased from Combi blocks. Ketones (**11j** and **11k**) were purchased from Wako Chemical Ltd. and Alfa Aesar, respectively.

A. Synthesis of Ketones.

(j) Synthesis of Phenyl(3,4,5-trifluorophenyl)methanol ((*rac*)-11f)

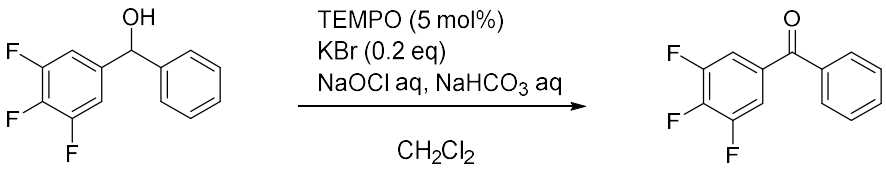


11f

To a stirred mixture of 3,4,5-trifluorobenzaldehyde (4.00 g, 25.0 mmol) in dry THF (100 mL), a solution of phenylmagnesium bromide (26.2 mL 26.23 mmol, 1.0 M in THF) was added dropwise at 0 ºC, and then the reaction temperature was raised to room temperature. After stirring for 2 h, water (50 mL) and EtOAc (50 mL) were added, and HCl conc. (ca. 1 mL) was slowly added to acidify the reaction mixture. The product was extracted with EtOAc (2 × 50 mL) and the combined organic layers were washed with brine (2 × 100 mL), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to afford the crude product. Purification by silica-gel column chromatography gave the product (**11f**) as a colorless oil (4.9 g, 83% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H), 7.00–6.94 (m, 2H), 5.68 (d, J = 2.8 Hz, 1H), 2.51 (d, J = 2.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ151.1 (dd, J = 10.0, 3.8 Hz), , 142.5, 139.9 (m), 137.8 (m), 128.9, 128.4, 126.5, 110.3 (dd, J = 17.5, 5.0 Hz), 74.9.
HRMS (FI) calcd for $C_{13}H_9F_3O$ $[M]^+$: 238.0606. Found: 238.0617.
IR (neat) 3376, 2978, 2876, 1622, 1528, 1447, 1343, 1234, 1036, 758, 704, 613 cm^{-1}.

(k) Synthesis of Phenyl(3,4,5-trifluorophenyl)methanone (10f)[1]



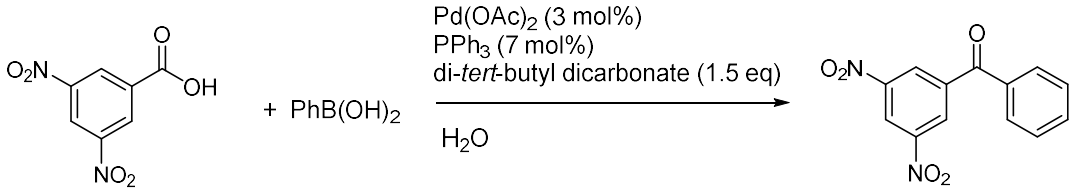
11f **10f**

To a solution of **11f** (2.00 g, 8.39 mmol) in CH_2Cl_2 (73 mL) were added KBr (0.204g, 1.71 mmol), 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) (65.5 mg, 0.419 mmol), and saturated aqueous $NaHCO_3$ (50 mL). The biphasic mixture was vigorously stirred, and aqueous NaOCl (36.7 mL, 0.7 M) was added. The resulting bright orange mixture was stirred for 2 h, and the orange color faded away. The colorless biphasic layers were separated, the aqueous phase was extracted with $CHCl_3$ (2 × 50 mL), and the combined organic portions were dried over $MgSO_4$, and concentrated to give a crude liquid. The

mixture was filtered through a plug of silica gel and concentrated to give the product (**10f)** as a colorless liquid (1.9 g, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.75 (m, 2H), 7.65–7.60 (m, 1H), 7.55–7.40 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.8, 151.9 (dd, *J* = 10.0, 3.8 Hz), 149.9 (dd, *J* = 10.0, 3.8 Hz), 142.7 (m), 136.1, 133.0 (m), 129.8, 128.6, 114.5 (dd, *J* = 16.3, 5.0 Hz).
HRMS (FI) calcd for $C_{13}H_7F_3O$ $[M]^+$: 236.0449. Found: 236.0448.
IR (neat) 3391, 1662, 1596, 1526, 1434, 1344, 1232, 1046, 886, 763, 727, 700, 667 cm^{-1}.
.

(l) Synthesis of (3,5-Dinitrophenyl)(phenyl)methanone (10g)

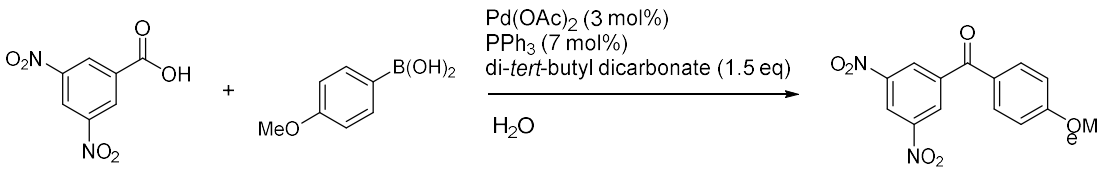


10g

A THF solution (60 mL) containing $Pd(OAc)_2$ (67.2 mg, 0.30 mmol), PPh_3 (184.0 mg, 0.70 mmol), 3,5-dinitrobenzoic acid (2.121 g, 10.0 mmol), phenylboronic acid (1.463 g, 12.0 mmol), di-*tert*-butyl dicarbonate (2.764 g, 15.0 mmol), and H_2O (0.450 mL) was heated under Ar atmosphere at 60 °C for 15 h. After cooling the reaction mixture, the insoluble materials were filtered off through a pad of Florisil. The Florisil was washed with Et_2O (50 mL) and the combined filtrates were washed with a saturated aqueous solution of $NaHCO_3$ (3 × 20 mL), and brine (10 mL), and then dried over $MgSO_4$. After removal of organic solvents, the residue was purified by silica-gel column chromatography (hexane/AcOEt = 6/1), followed by preparative HPLC equipped with JAIGEL-1H and -2H columns using $CHCl_3$ as an eluent at a flow rate of 14 mL min^{-1} gave **10g** as a white solid in 24% yield (0.650 g, 2.39 mmol).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (s, 1H), 8.93 (s, 2H), 7.83–7.80 (m, 2H), 7.78–7.72 (m, 1H), 7.62–7.57 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ191.6, 148.5, 140.7, 135.0, 134.2, 130.0, 129.4, 129.1, 121.5.
HRMS (FI) calcd for $C_{13}H_8N_2O_5$ $[M]^+$: 272.0433. Found: 272.0442.
IR (neat) 3100, 1670, 1545, 1348, 1282, 1079, 916, 809, 710 cm^{-1}.

(d) Synthesis of (3,5-Dinitrophenyl)(4-methoxyphenyl)methanone (10l)

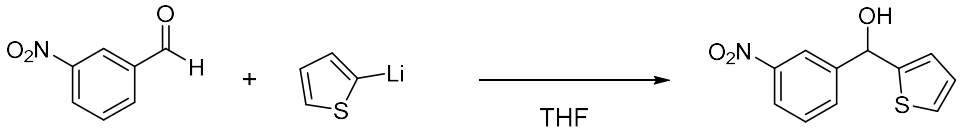


10l

A THF solution (60 mL) containing $Pd(OAc)_2$ (67.2 mg, 0.30 mmol), PPh_3 (184.0 mg, 0.70 mmol), 3,5-dinitrobenzoic acid (2.121 g, 10.0 mmol), 4-methoxyphenylboronic acid (1.824 g, 12.0 mmol), di-*tert*-butyl dicarbonate (2.765 g, 15.0 mmol), and H_2O (0.450 mL) was heated under Ar atmosphere at 60 °C for 18 h. After cooling the reaction mixture, the insoluble materials were filtered off through a pad of Florisil. The Florisil was washed with Et_2O (50 mL) and the combined filtrates were washed with a saturated aqueous solution of $NaHCO_3$ (3 × 20 mL), and brine (10 mL), and then dried over $MgSO_4$. After removal of organic solvents, the residue was purified by silica-gel column chromatography (hexane/AcOEt = 5/1), followed by preparative HPLC equipped with JAIGEL-1H and -2H columns using $CHCl_3$ as an eluent at a flow rate of 14 mL min^{-1} gave **10l** as a white solid in 33% yield (0.976 g, 3.23 mmol).

^1H NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.89 (s, 2H), 7.82 (d, J = 8.8 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 3.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.2, 164.6, 148.5, 141.5, 132.7, 129.1, 127.7, 121.1, 114.5, 55.70.
HRMS (ESI) calcd for $C_{14}H_{10}N_2O_6$ $[M]^+$: 302.0539. Found: 302.0539.
IR (neat) 3092, 1661, 1597, 1546, 1538, 1264, 1165, 1023, 846, 729, 608 cm^{-1}.

(e) Synthesis of (3-Nitrophenyl)(thiophen-2-yl)methanol ((*rac*)-11n)

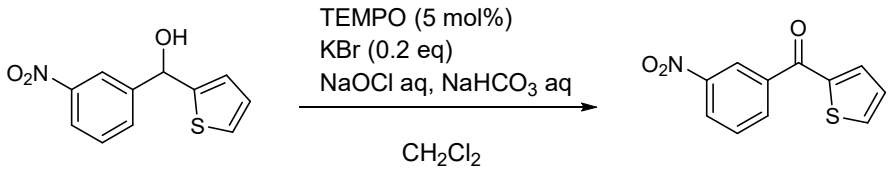


11n

A solution of 3-nitrobenzaldehyde (3.02 g, 20.0 mmol) in dry THF (25 mL) was cooled to 0 °C, and commercially available 2-thienyl lithium (1.0 M in hexane/THF) was carefully added dropwise under Ar atmosphere. The resulting solution was allowed to warm to room temperature followed by stirring for 3 h. After the reaction was quenched with aqueous NH_4Cl (5 mL), the resulting mixture was extracted with Et_2O (3 × 15 mL) and then washed with brine (5 mL). The organic layer was dried over $MgSO_4$ and the volatiles were removed under reduced pressure. The residue was purified by column chromatography on silica gel using hexane/AcOEt = 3/1 as eluents. The following purification by preparative HPLC equipped with JAIGEL-1H and -2H columns using $CHCl_3$ as an eluent at a flow rate of 14 mL min^{-1} gave (3-nitrophenyl)(thiophen-2-yl)methanol (**11n**) as a colorless oil in 48% yield (2.25 g, 9.56 mmol).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32–8.31 (m, 1H), 8.15–8.12 (m, 1H), 7.78–7.76 (m, 1H), 7.54–7.52 (m, 1H), 7.30–7.29 (m, 1H), 6.97–6.94 (m, 2H), 6.15 (s, 1H), 2.83 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.3, 146.6, 145.1, 132.2, 129.4, 126.9, 126.2, 125.5, 122.8, 121.2, 71.1.
HRMS (FI) calcd for $C_{11}H_9NO_3S$ $[M]^+$: 235.0303. Found: 235.0294.
IR (neat) 3392, 2917, 2848, 1529, 1350, 1094, 1022, 811, 760, 707 cm^{-1}.

(f) Synthesis of (3-Nitrophenyl)(thiophen-2-yl)methanone (10n)



11n **10n**

To a solution of **11n** (1.00 g, 4.25 mmol) in CH_2Cl_2 (36 mL) were added KBr (0.102g, 0.86 mmol), 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) (32.8 mg, 0.210 mmol), and saturated aqueous $NaHCO_3$ (25 mL). The biphasic mixture was vigorously stirred, and aqueous NaOCl (18.3 mL, 0.7 M) was added. The resulting bright orange mixture was stirred for 3 h, and the orange color faded away. The colorless biphasic layers were separated, the aqueous phase was extracted with $CHCl_3$ (2 × 25 mL), and the combined organic portions were dried over $MgSO_4$, and concentrated to give a crude liquid. The mixture was filtered through a plug of silica gel and concentrated to give the product (**10n**) as a pale white solid (0.94 g, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72–8.71 (m, 1H), 8.46–8.43 (m, 1H), 8.22–8.19 (m, 1H), 7.82–7.80 (m, 1H) , 7.78–7.75 (m, 1H) , 7.65–7.63 (m, 1H) , 7.22–7.20 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.6, 148.1, 142.4, 139.5, 135.5, 135.3, 134.7, 129.8, 128.4, 126.6, 124.0.
HRMS (FI) calcd for $C_{11}H_7NO_3S[M]^+$: 233.0147. Found: 233.0134.

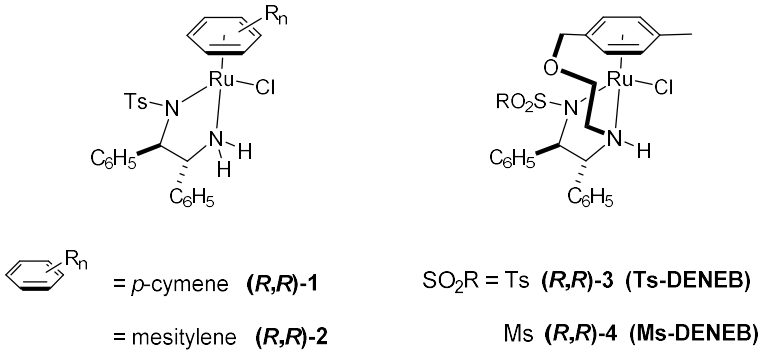
B. Asymmetric Transfer Hydrogenation of Unsymmetrical Benzophenones Using (*R*,*R*)-3 of (*R*,*R*)-4

General procedures under the conditions of S/C = 100, 60 °C, and 5 h.

Under N_2 atmosphere, a mixture of ketone (1.0 mmol) and the Ru catalyst (0.01 mmol) in an azeotrope of formic acid and triethylamine (5:2, 0.5 mL) was stirred at 60 ºC for 5 h. After the reaction completion, water (3 mL) and EtOAc (5 mL) were added. The biphasic layers were separated, the aqueous layer was extracted with EtOAc (3 × 5 mL), and the combined organic portions were washed with brine (3 mL). After drying over $MgSO_4$, filtration, and solvent removal under reduced pressure, the crude residue was purified by silica-gel column chromatography to afford the desired product. The optical purity of

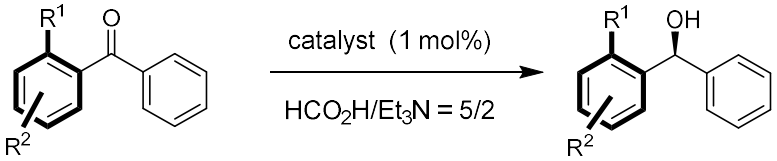
product was determined by chiral HPLC analysis using a Daicel Chiralcel OD-H, OJ-H or Chiralpak AD-H, AS-H column (4.6 mm × 25 cm) with hexane/2-propanol as the eluent where a clear base-line separation was obtained.

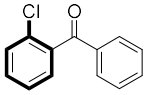
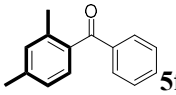
Figure S1. Structure of non-tethered and tethered Ru-DPEN catalysts.



To confirm the advantages of Oxo-tethered complexes, the reactivity and selectivity were compared with Non-tethered conventional type Ru-diamine complex (*R*, *R*)-**1**. The results were summarized in Table S1 and Table S2.

Table S1. Asymmetric transfer hydrogenation of 2-substituted benzophenones



Substrate	Temp. (°C)	Time (h)	Catalyst	
			(*R*,*R*)-3	**(*R*,*R*)-1**
 **5b**	40	17	>99% yield, 98% ee	95% yield, 93% ee
 **5f**	60	17	94% yield, 97% ee	16% yield, 83% ee

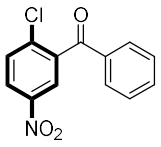
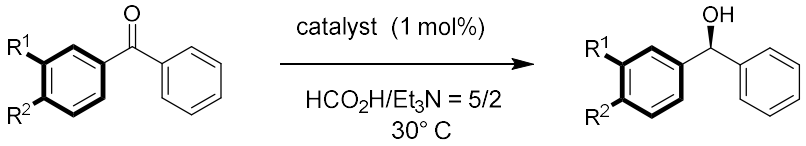
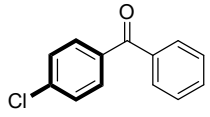
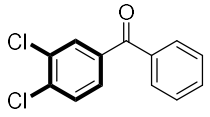
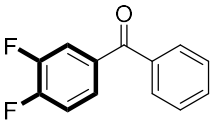
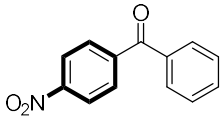
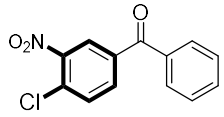
 **5i**	40	7	>99% yield, 99% ee	60% yield, 98% ee

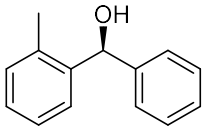
Table S2. Asymmetric transfer hydrogenation of non-*ortho*-substituted diaryl ketones



Substrate	Time (h)	Catalyst	
		(*R*,*R*)-3	**(*R*,*R*)-1**
 **10a**	11	>99% yield, 48% ee	51% yield, 37% ee
 **10b**	18	>99% yield, 76% ee	98% yield, 64% ee
 **10c**	7	>99% yield, 77% ee	86% yield, 64% ee
 **10d**	11	>99% yield, 76% ee	98% yield, 67% ee
 **10e**	7	>99% yield, 93% ee	80% yield, 88% ee

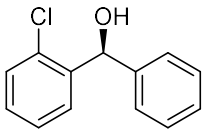
C. Characterization Data for Reduction Products.

(*S*)-Phenyl(*o*-tolyl)methanol (6a)



According to the general procedure (ketone: 0.196 g (1 mmol), cat. **(*R*,*R*)-3**), 0.194 g of **6a** was obtained as a white solid (98% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.50 (m, 1H), 7.33–7.14 (m, 8H), 6.01 (d, *J* = 3.2 Hz, 1H), 2.25 (s, 1H), 2.12 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.9, 141.4, 135.4, 130.5, 128.5, 127.6, 127.5, 127.1, 126.3, 126.1, 73.4, 19.4. All characterization data are in agreement with the previously reported data[2].
HRMS (FI) calcd for $C_{14}H_{14}O$ $[M]^+$: 198.10446. Found: 198.10457.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 15.8 min, (*S*) isomer 17.3 min); $[\alpha]_D^{20}$ +7.3 (c 0.735 in $CHCl_3$) 98% ee (*S*) (lit.[2] $[\alpha]_D^{22}$ +6.38 (c 0.906 in $CHCl_3$) 93% ee (*S*)).
IR (neat) 3375, 3064, 3027, 1492, 1454, 1017, 699, 667 cm^{-1}.

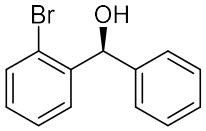
(*S*)-(2-Chlorophenyl)(phenyl)methanol (6b)



According to the general procedure (ketone: 0.216 g (1 mmol), cat. **(*R*,*R*)-3**), 0.217 g of **6b** was obtained as a clear oil (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.57 (m, 1H), 7.39–7.18 (m, 8H), 6.20 (s, 1H), 2.44 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.2, 141.0, 132.5, 129.5, 128.7, 128.5, 128.0, 127.7, 127.0, 126.9, 72.7. All characterization data are in agreement with the previously reported data[2].
HRMS (FI) calcd for $C_{12}H_{11}ClO$ $[M]^+$: 218.04984. Found: 218.05035.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 14.6 min, (*S*)

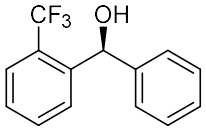
isomer 18.6 min); $[\alpha]_D^{20}$ -15.2 (c 1.51 in $CHCl_3$) 98% ee (*S*) (lit.[2] $[\alpha]_D^{20}$ -21.51 (c 1.136 in $CHCl_3$) 97% ee (*S*)).
IR (neat) 3355, 3064, 3031, 1441, 1183, 1020, 699, 646 cm^{-1}.

(*S*)-(2-Bromophenyl)(phenyl)methanol (6c)



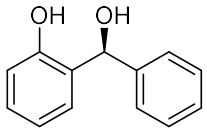
According to the general procedure (ketone: 3.0 g (11.5 mmol), cat. **(*R*,*R*)-3**), 0.301 g of **6c** was obtained as a clear oil (>99% yield).
^1H NMR (400 MHz, $CDCl_3$) δ 7.60–7.53 (m, 2H), 7.42–7.28 (m, 6H), 7.18–7.13 (m, 1H), 6.19 (s, 1H), 2.56 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.5, 142.1, 132.8, 129.1, 128.4, 128.4, 127.7, 127.7, 127.0, 122.8, 74.7. All characterization data are in agreement with the previously reported data[2].
HRMS (FD) calcd for $C_{13}H_{11}BrO$ $[M]^+$: 261.9993. Found: 261.9996.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 15.8 min, (*S*) isomer 22.3 min); $[\alpha]_D^{20}$ -41.6 (c 1.40 in $CHCl_3$) 99% ee (*S*) (lit.[2] $[\alpha]_D^{RT}$ -41.9 (c 1.19 in $CHCl_3$) 96% ee (*S*)).
IR (neat) 3354, 3063, 3030, 1735, 1438, 1184, 1016, 699 cm^{-1}.

(*S*)-Phenyl[2-(trifluoromethyl)phenyl]methanol (6d)



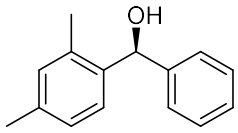
According to the general procedure (ketone: 0.250 g (1 mmol), cat. **(*R*,*R*)-3**), 0.250 g of **6d** was obtained as a clear oil (99% yield).
^1H NMR (400 MHz, $CDCl_3$) δ 7.67–7.62 (m, 2H), 7.58–7.52 (m, 1H), 7.40–7.24 (m, 6H), 6.31 (d, J = 3.2 Hz, 1H), 2.34 (d, J = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.7, 132.3, 129.5, 128.4, 127.8, 127.7, 127.5, 126.4, 125.6, 125.4, 123.3, 70.8.
HRMS (FI) calcd for $C_{14}H_{11}F_3O$ $[M]^+$: 252.07620. Found: 252.07615.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 9.1 min, (*S*) isomer 13.4 min); $[\alpha]_D^{20}$-71.7 (c 1.53 in $CHCl_3$) >99% ee (*S*); the stereochemistry was determined based on the reported literature[9].
IR (neat) 3356, 3066, 3032, 1454, 1313, 1161, 1123, 1037, 767, 737, 700, 649 cm^{-1}.

(*S*)-2-(1'-Hydroxybenzyl)phenol (6e)



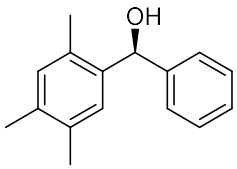
According to the general procedure (ketone: 0.198 g (1 mmol), cat. **(*R*,*R*)-4**), 0.188 g of **6e** was obtained as a clear oil (94% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (br, 1H), 7.35–7.26 (m, 5H), 7.26–7.12 (m, 1H), 6.85–6.76 (m, 3H), 5.92 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 141.8, 129.2, 128.6, 128.2, 128.1, 126.8, 126.7, 120.0, 117.1, 76.7. All characterization data are in agreement with the previously reported data[7].
HRMS (ESI) calcd for $C_{13}H_{12}O_2$ $[M-H]^-$: 199.0765. Found: 199.0766.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 80:20, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 6.0 min, (*S*) isomer 8.0 min); $[\alpha]_D^{20}$ -46.1 (c 1.40 in $CHCl_3$) 77% ee (*R*) (lit.[7] $[\alpha]_D^{25}$ -5.68 (c 0.827 in CH_3CN) 99% ee).
IR (neat) 3347, 3062, 3032, 1587, 1489, 1456, 1014, 699 cm^{-1}.

(*S*)-(2,4-Dimethylphenyl)(phenyl)methanol (6f)



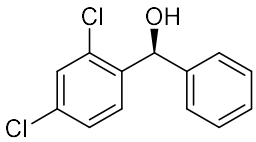
According to the general procedure (ketone: 0.210 g (1 mmol), cat. **(*R*,*R*)-3**), 0.199 g of **6f** was obtained as a white solid (94% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 6H), 7.05–7.02 (m, 2H), 6.96 (s, 1H), 5.97 (s, 1H) , 2.31 (s, 3H) , 2.22 (s, 3H), 2.09 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 138.6, 137.2, 135.3, 131.4, 128.4, 127.4, 126.9, 126.7, 126.4, 73.2, 21.0, 19.3. All characterization data are in agreement with the previously reported data[3].
HRMS (FI) calcd for $C_{15}H_{16}O$ $[M]^+$: 212.12011. Found: 212.11955.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 13.3 min, (*S*) isomer 15.9 min); $[\alpha]_D^{20}$ -2.0 (c 2.93 in $CHCl_3$) 97% ee (*S*) (lit.[3] $[\alpha]_D^{23}$ +8.9 (c 0.80 in $CHCl_3$) 82% ee (*R*)).
IR (neat) 3335, 3061, 3029, 2917, 1615, 1493, 1452, 1187, 1033, 1020, 800, 760, 699, 638 cm^{-1}.

(*S*)-Phenyl(2,4,5-trimethylphenyl)methanol (6g)



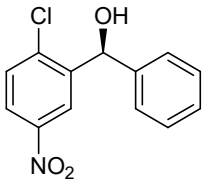
According to the general procedure (ketone: 0.224 g (1 mmol), cat. **(*R*,*R*)-2**), 0.222 g of **6g** was obtained as a white solid (98% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.20 (m, 6H), 6.92 (s, 1H), 5.96 (d, *J* = 2.8 Hz, 1H), 2.23 (s, 3H) , 2.22 (s, 3H) , 2.19 (s, 3H), 2.07 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.2, 138.8, 135.7, 134.1, 132.5, 132.0, 128.4, 127.6, 127.4, 126.9, 73.2, 19.4, 19.2, 18.7.
HRMS (FI) calcd for $C_{16}H_{18}O$ $[M]^+$: 226.13576. Found: 226.13621.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 14.4 min, (*S*) isomer 21.3 min); $[\alpha]_D^{20}$ +24.7 (c 1.02 in $CHCl_3$) 98% ee (*S*).
IR (neat) 3362, 3032, 2968, 2892, 1504, 1452, 1264, 1069, 1012, 869, 746, 703, 687 cm^{-1}.

(*S*)-(2,4-Dichlorophenyl)(phenyl)methanol (6h)



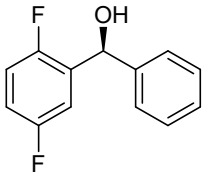
According to the general procedure (ketone: 0.251 g (1 mmol), cat. **(*R*,*R*)-3**), 0.246 g of **6h** was obtained as a clear oil (97% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.35–7.26 (m, 7H), 6.15 (d, *J* = 3.2 Hz, 1H), 2.37 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.8, 139.6, 133.8, 133.1, 129.3, 128.9, 128.6, 128.0, 127.4, 126.9, 72.3. All characterization data are in agreement with the previously reported data[6].
HRMS (FI) calcd for $C_{13}H_{10}Cl_2O$ $[M]^+$: 252.01087. Found: 252.01169.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 14.2 min, (*S*) isomer 16.0 min); $[\alpha]_D^{20}$ -2.82 (c 1.75 in $CHCl_3$) 99% ee (*S*) (lit.[6] $[\alpha]_D^{22}$ -15.4 (c 0.17 in $CHCl_3$) 93% ee (*S*)).
IR (neat) 3336, 3064, 3031, 1589, 1470, 1454, 1381, 1183, 1103, 1033, 1021, 865, 697, 668, 626 cm^{-1}.

(*S*)-(2-Chloro-5-nitrophenyl)(phenyl)methanol (6i)



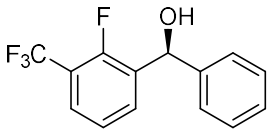
According to the general procedure (ketone: 0.262 g (1 mmol), cat. **(*R*,*R*)-3**), 0.262 g of **6i** was obtained as a clear oil (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 2.4 Hz, 1H), 8.10–8.07 (m, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.40–7.28 (m, 5H), 6.19 (d, *J* = 3.2 Hz, 1H), 2.49 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0, 143.0, 140.9, 138.9, 130.5, 128.9, 128.5, 127.1, 123.4, 123.0 72.5.
HRMS (FI) calcd for $C_{13}H_{10}NClNO_3[M]^+$: 263.03492. Found: 263.03539.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 23.3 min, (*S*) isomer 25.9 min); $[\alpha]_D^{20}$ +169.9 (c 1.53 in $CHCl_3$) >99% ee (*S*).
IR (neat) 3385, 3101, 1609, 1576, 1525, 1456, 1346, 1183, 1023, 918, 836, 768, 743, 699 cm^{-1}.

(*S*)-(2,5-Difluorophenyl)(phenyl)methanol (6j)



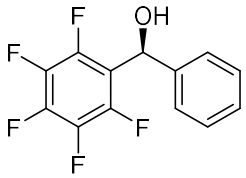
According to the general procedure (ketone: 0.218 g (1 mmol), cat. **(*R*,*R*)-3**), 0.200 g of **6j** was obtained as a clear oil (91% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.23 (m, 6H), 7.00–6.86 (m, 2H), 6.08 (d, *J* = 3.6 Hz, 1H), 2.37 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9 (d, *J* = 240 Hz), 155.6 (d, *J* = 240 Hz), 142.2, 132.7 (dd, *J* = 15.6, 8.0 Hz), 128.7, 128.1, 126.4, 116.4 (dd, *J* = 25.0, 8.0 Hz), 115.3 (dd, *J* = 25.0, 8.0 Hz), 114.1 (dd, *J* = 25.0, 4.0 Hz), 69.8 (d, *J* = 2.0 Hz).
HRMS (FI) calcd for $C_{13}H_{10}F_2O$ $[M]^+$: 220.06997. Found: 220.07077.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 26.7 min, (*S*) isomer 29.3 min); $[\alpha]_D^{20}$ +29.6 (c 2.1 in $CHCl_3$) 91% ee (*S*).
IR (neat) 3354, 3065, 3032, 2916, 2848, 1491, 1429, 1241, 1181, 1134, 1035, 1022, 884, 834, 818, 769, 699 cm^{-1}.

(*S*)-[2-Fluoro-3-(trifluoromethyl)phenyl](phenyl)methanol (6k)



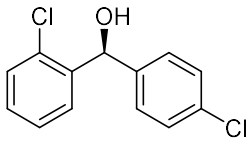
According to the general procedure (ketone: 0.268 g (1 mmol), cat. **(*R*,*R*)-3**), 0.268 g of **6k** was obtained as a white solid (>99% ee).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.78 (m, 1H), 7.58–7.50 (m, 1H), 7.45–7.22 (m, 6H), 6.21 (d, *J* = 4.0 Hz, 1H), 2.36 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.8 (qd, *J* = 260.0, 2.5 Hz) 142.0, 132.6 (d, *J* = 12.5 Hz), 131.6 (d, *J* = 5.0 Hz), 128.8, 128.2, 126.3, 126.3 (q, *J* = 5.0 Hz), 124.1(d, *J* = 3.8 Hz), 122.6 (q, *J* = 270 Hz), 118.3 (qd, *J* = 32.5, 12.5 Hz), 69.5.
HRMS (FI) calcd for $C_{14}H_{10}F_4O$ $[M]^+$: 270.06678. Found: 270.06633.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 15.0 min, (*S*) isomer 16.3 min); $[\alpha]_D^{20}$ +1.90 (c 2.1 in $CHCl_3$) 90% ee (*S*).
IR (neat) 3236, 1623, 1594, 1467, 1326, 1227, 1144, 1110, 1023, 831, 793, 746, 696 cm^{-1}.

(*S*)-(Perfluorophenyl)(phenyl)methanol (6l)



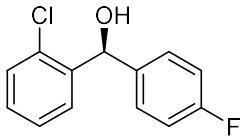
According to the general procedure (ketone: 0.272 g (1 mmol), cat. **(*R*,*R*)-3**), 0.272 g of **6l** was obtained as a white solid (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.30 (m, 5H), 6.24 (d, *J* = 7.2 Hz, 1H), 2.65 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.6 (m), 140.8 (m), 140.6, 137.7 (m), 128.8, 128.3, 125.4 (m), 117.0 (m), 67.6. All characterization data are in agreement with the previously reported data[7].
HRMS (FI) calcd for $C_{13}H_7F_5O$ $[M]^+$: 274.04171. Found: 274.04238.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 254 nm, 30 ºC, (*R*) isomer 9.8 min, (*S*) isomer 12.1 min); $[\alpha]_D^{20}$ -45.0 (c 1.90 in $CHCl_3$) >99% ee (*S*) (lit.[7] $[\alpha]_D^{20}$ +42.0 (c 1.224 in $CHCl_3$) 70% ee (*R*)).
IR (neat) 3275, 1654, 1522, 1505, 1304, 1121, 995, 948, 699, 644 cm^{-1}.

(*S*)-(2-Chlorophenyl)(4-chlorophenyl)methanol (6m)



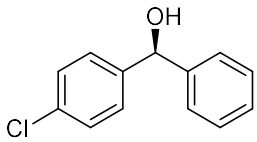
According to the general procedure (ketone: 0.251 g (1 mmol), cat. **(*R*,*R*)-3**), 0.251 g of **6m** was obtained as a clear oil (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.54 (m, 1H), 7.36–7.22 (m, 7H), 6.19 (d, *J* = 3.6 Hz, 1H), 2.40 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.7, 140.6, 133.5, 132.4, 129.6, 129.0, 128.6, 128.3, 127.9, 127.2, 72.0; All characterization data are in agreement with the previously reported data[4].
HRMS (FI) calcd for $C_{13}H_{10}NCl_2O[M]^+$: 252.01087. Found: 252.01037.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 15.6 min, (*S*) isomer 23.6 min); $[\alpha]_D^{20}$ -42.1 (c 1.55 in $CHCl_3$) 97% ee (*S*) (lit.[4] $[\alpha]_D^{23}$ +40.0 (c 1.04 in $CHCl_3$) 96% ee (*R*)).
IR (neat) 3370, 1489, 1438, 1183, 1091, 1056, 1014, 798, 668 cm^{-1}.

(*S*)-(2-Chlorophenyl)(4-fluorophenyl)methanol (6n)



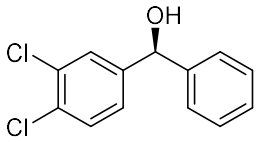
According to the general procedure (ketone: 0.235 g (1 mmol), cat. **(*R*,*R*)-3**), 0.233 g of **6n** was obtained as a clear oil (99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.57 (m, 1H), 7.40–7.20 (m, 5H), 7.03–6.95 (m, 2H), 6.19 (d, *J* = 3.2 Hz, 1H), 2.39 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2 (d, *J* = 245.0 Hz), 140.8, 138.0 (d, *J* = 3.8 Hz), 132.4, 129.6, 128.9, 128.6 (d, *J* = 8.8 Hz), 127.8, 127.2, 115.3 (d, *J* = 21.3 Hz), 72.1. All characterization data are in agreement with the previously reported data[5].
HRMS (FI) calcd for $C_{13}H_{10}NClFO$ $[M]^+$: 236.04042. Found: 1236.04013.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 12.7 min, (*S*) isomer 18.3 min); $[\alpha]_D^{20}$ -15.2 (c 1.51 in $CHCl_3$) 97% ee (*S*) (lit.[5] $[\alpha]_D^{20}$ +9.9 (c 0.82 in $CHCl_3$) 83% ee (*R*)).
IR (neat) 3351, 1604, 1509, 1471, 1441, 1158, 1056, 1023, 842, 813, 668 cm^{-1}.

(*S*)-(4-Chlorophenyl)(phenyl)methanol (11a)



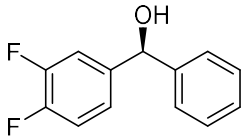
According to the general procedure (ketone: 0.217 g (1 mmol), cat. **(*R*,*R*)-3**), 0.217 g of **11a** was obtained as a white solid (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 9H), 5.79 (d, *J* = 3.2 Hz, 1H), 2.28 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 142.2, 133.3, 128.6, 128.6, 127.9, 126.5, 75.6. All characterization data are in agreement with the previously reported data[2].
HRMS (FI) calcd for $C_{13}H_{11}ClO$ $[M]^+$: 218.04984. Found: 218.05004.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 18.5 min, (*S*) isomer 20.5 min); $[\alpha]_D^{20}$ +8.0 (c 1.51 in $CHCl_3$) 48% ee (*S*) (lit.[2] $[\alpha]_D^{RT}$ +2.77 (c 0.932 in $CHCl_3$) 9% ee (*S*)).
IR (neat) 3370, 3030, 1488, 1454, 1407, 1185, 1090, 1013, 795, 701, 668 cm^{-1}.

(*S*)-(3,4-Dichlorophenyl)(phenyl)methanol (11b)



According to the general procedure (ketone: 0.251 g (1 mmol), cat. **(*R*,*R*)-3**), 0.251 g of **11b** was obtained as a clear oil (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.47 (m, 1H), 7.40–7.13 (m, 7H), 5.72 (d, *J* = 3.2 Hz, 1H), 2.46 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 142.8, 132.5, 131.4, 130.3, 128.8, 128.3, 128.1, 126.5, 125.8, 75.1.
HRMS (FI) calcd for $C_{13}H_{10}Cl_2O$ $[M]^+$: 252.01087. Found: 252.00984.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, 250 × 4.6 mm column, hexane/2-propanol 90:10, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 10.1 min, (*S*) isomer 11.2 min); $[\alpha]_D^{20}$ +31.2 (c 1.70 in $CHCl_3$) 76% ee (*S*).
IR (neat) 3311, 3220, 1495, 1458, 1398, 1269, 1029, 896, 812, 704, 636 cm^{-1}.

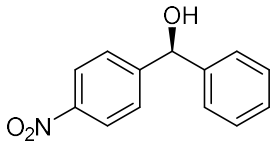
(*S*)-(3,4-Difluorophenyl)(phenyl)methanol (11c)



According to the general procedure (ketone: 0.218 g (1 mmol), cat. **(*R*,*R*)-3**), 0.218 g of **11c** was obtained as a clear oil (>99% yield).

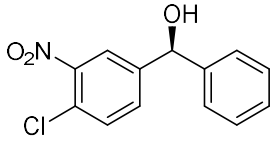
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.05 (m, 8H), 5.77 (d, *J* = 3.2 Hz, 1H), 2.33 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9 (dd, *J* = 12.5, 8.5 Hz), 149.0 (dd, *J* = 12.5, 8.5 Hz), 143.1, 140.7 (t, *J* = 3.8 Hz), 128.7, 128.1, 126.5, 122.3 (dd, *J* = 6.2, 3.8 Hz), 117.1 (d, *J* = 17.5 Hz), 115.5 (d, *J* = 17.5 Hz), 75.2.
HRMS (FI) calcd for $C_{13}H_{10}F_2O$ $[M]^+$: 220.06997. Found: 220.07028.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 22.8 min, (*S*) isomer 26.7 min); $[\alpha]_D^{20}$ +20.7 (c 1.29 in $CHCl_3$) 77% ee (*S*).
IR (neat) 3514, 2961, 2886, 1724, 1287, 1186, 1069, 1036, 957, 931,851, 754 cm^{-1}.

(*S*)-(4-Nitrophenyl)(phenyl)methanol (11d)



According to the general procedure (ketone: 0.227 g (1 mmol), cat. **(*R*,*R*)-3**), 0.227 g of **11d** was obtained as a pale yellow solid (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–8.16 (m, 2H), 7.58–7.55 (m, 2H), 7.40–7.30 (m, 5H), 5.91 (d, *J* = 2.8 Hz, 1H), 2.47 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.7, 147.2, 142.7, 128.9, 128.4, 127.0, 126.7, 123.7, 75.5. All characterization data are in agreement with the previously reported data[6].
HRMS (FI) calcd for $C_{13}H_{11}NO_3$ $[M]^+$: 229.07389. Found: 229.07343.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-H, 250 × 4.6 mm column, hexane/2-propanol 90:10, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 12.3 min, (*S*) isomer 15.4 min); $[\alpha]_D^{20}$ +51.5 (c 1.57 in $CHCl_3$) 76% ee (*S*) (lit.[6] $[\alpha]_D^{22}$ +71.0 (c 0.27 in $CHCl_3$) 92% ee (*S*)).
IR (neat) 3466, 1595, 1515, 1450, 1345, 1190, 1055, 867, 813, 754, 745, 708, 692 cm^{-1}.

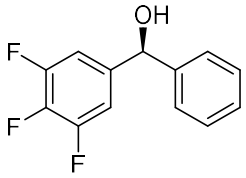
(*S*)-(4-Chloro-3-nitrophenyl)(phenyl)methanol (11e)



According to the general procedure (ketone: 0.261 g (1 mmol), cat. **(*R*,*R*)-3**), 0.262 g of **11e** was obtained as a pale yellow solid (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 1.6 Hz, 1H), 7.53–7.48 (m, 2H), 7.40–7.30 (m, 5H), 5.86 (s, 1H), 2.37 (br, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5, 144.1, 142.3, 131.8, 131.0, 129.1, 128.6, 126.7, 125.7, 123.3, 74.8.
HRMS (FI) calcd for $C_{13}H_{10}ClNO_3$ $[M]^+$: 263.03492. Found: 263.03518.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, 250 × 4.6 mm

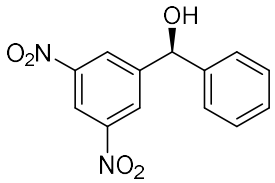
column, hexane/2-propanol 90:10, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 22.7 min, (*S*) isomer 27.1 min); $[\alpha]_D^{20}$ +52.5 (c 1.91 in $CHCl_3$) 96% ee (*S*).
IR (neat) 3578, 3428, 1530, 1454, 1350, 1191, 1048, 1024, 827, 768, 715 cm^{-1}.

(*S*)-Phenyl(3,4,5-trifluorophenyl)methanol (11f)



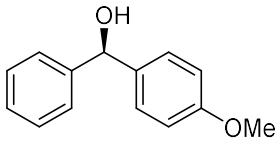
According to the general procedure (ketone: 0.236 g (1 mmol), cat. **(*R*,*R*)-3**), 0.236 g of **11f** was obtained as a clear oil (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H), 7.00–6.94 (m, 2H), 5.68 (d, *J* = 2.8 Hz, 1H), 2.51 (d, *J* = 2.8 Hz, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.1 (dd, *J* = 10.0, 3.8 Hz), , 142.5, 139.9 (m), 137.8 (m), 128.9, 128.4, 126.5, 110.3 (dd, *J* = 17.5, 5.0 Hz), 74.9.
HRMS (FI) calcd for $C_{13}H_9F_3O$ $[M]^+$: 238.0606. Found: 238.0617.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 95:5, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 16.1 min, (*S*) isomer 21.2 min); $[\alpha]_D^{20}$ +52.1 (c 1.46 in $CHCl_3$) 95% ee (*S*).
IR (neat) 3376, 2978, 2876, 1622, 1528, 1447, 1343, 1234, 1036, 758, 704, 613 cm^{-1}.

(*S*)-(3,5-Dinitrophenyl)(phenyl)methanol (11g)



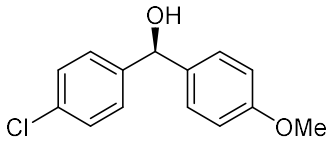
According to the general procedure (ketone: 0.136 g (0.5 mmol), cat. **(*R*,*R*)-3**), 0.123 g of **11g** was obtained as a yellow oil (90% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94–8.92 (m, 1H), 8.61–8.60 (m, 1H), 7.43–7.35 (m, 5H), 6.00 (s, 1H), 2.66 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 148.3, 141.7, 129.4, 129.1, 126.7, 126.4, 117.7, 74.9.
HRMS (FI) calcd for $C_{13}H_{10}N_2O_5$ $[M]^+$: 274.0590. Found: 274.0596.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AS-H, 250 × 4.6 mm column, hexane/2-propanol 90:10, 1.0 mL/min, 220 nm, 30 ºC, (*S*) isomer 17.2 min, (*R*) isomer 18.6 min); $[\alpha]_D^{20}$ +72.8 (c 1.15 in $CHCl_3$) 96% ee (*S*).
IR (neat) 3351, 3106, 1597, 1560, 1541, 1450, 1348, 1266, 1041, 912, 752, 728, 703, 679 cm^{-1}.

(*R*)-(4-Methoxyphenyl)(phenyl)methanol (11h)



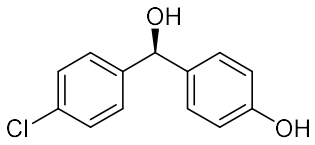
According to the general procedure (ketone: 0.212 g (1 mmol), cat. **(*R*,*R*)-3**), 0.171 g of **11h** was obtained as a white solid (80% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.25 (m, 7H), 6.87–6.80 (m, 2H), 5.80 (s, 1H), 3.78 (s, 3H), 2.18 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 144.0, 136.2, 128.4, 127.9, 127.4, 126.4, 113.9, 55.3. All characterization data are in agreement with the previously reported data[3].
HRMS (FI) calcd for $C_{14}H_{14}O_2$ $[M]^+$: 214.09938. Found: 214.09995.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-H, 250 × 4.6 mm column, hexane/2-propanol 90:10, 0.5 mL/min, 220 nm, 30 ºC, (*R*) isomer 22.5 min, (*S*) isomer 24.3 min); $[\alpha]_D^{20}$ +1.50 (c 1.08 in $CHCl_3$) 5% ee (*R*) (lit.[3] $[\alpha]_D^{29}$ +24.6 (c 0.80 in $CHCl_3$) 90% ee (*R*)).
IR (neat) 3403, 2952, 2837, 1611, 1588, 1516, 1495, 1446, 1305, 1252, 1178, 1034, 1019, 841, 811, 727, 697, 655, 624 cm^{-1}.

(*S*)-(4-Chlorophenyl)(4-methoxyphenyl)methanol (11i)



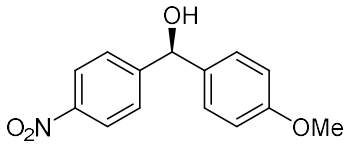
According to the general procedure (ketone: 0.123 g (0.5 mmol), cat. **(*R*,*R*)-3**), 0.073 g of **11i** was obtained as a white solid (59% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.29 (m, 4H), 7.25–7.23 (m, 2H), 6.87–6.85 (m, 2H), 5.76 (d, *J* = 2.8 Hz, 1H), 3.79 (s, 3H), 2.20 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 142.4, 135.8, 133.1, 128.5, 127.9, 127.7, 114.0, 75.2, 55.3. All characterization data are in agreement with the previously reported data[3].
HRMS (FI) calcd for $C_{14}H_{13}ClO_2$ $[M]^+$: 248.06041. Found: 248.06039.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 95:5, 0.5 mL/min, 220 nm, 30 ºC, (*S*) isomer 34.0 min, (*R*) isomer 36.3 min); $[\alpha]_D^{20}$ +16.6 (c 0.73 in $CHCl_3$) 53% ee (*S*) (lit.[3] $[\alpha]_D^{27}$ +36.6 (c 0.80 in $CHCl_3$) 89% ee (*S*)).
IR (neat) 3315, 1611, 1513, 1488, 1253, 1174, 1091, 1035, 1008, 859, 806, 773 cm^{-1}.

(*S*)-4-[(4-Chlorophenyl)hydroxymethyl]phenol (11j)



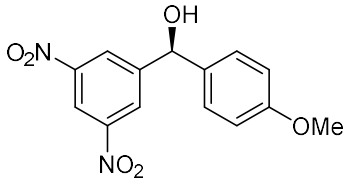
According to the general procedure (ketone: 0.116 g (0.5 mmol), cat. **(*R*,*R*)-4**), 0.116 g of **11j** was obtained as a white solid (>99% yield).
^{1}H NMR (400 MHz, CD_3OD) δ 7.33–7.27 (m, 4H), 7.15–7.12 (m, 2H), 6.74–6.72 (m, 2H), 5.67 (S, 1H), 4.86 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 145.1, 136.5, 133.6, 129.2, 129.1, 116.1, 75.9, 49.0.
HRMS (FI) calcd for $C_{13}H_{11}NClO_2$ $[M]^+$: 234.0448. Found: 234.0454.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 90:10, 1.0 mL/min, 220 nm, 30 ºC, (*S*) isomer 16.3 min, (*R*) isomer 18.8 min); $[\alpha]_D^{20}$ +23.2 (c 0.97 in MeOH) 55% ee (*S*). Absolute configuration was determined by HPLC analysis of a demethylated compound derived from (*S*)-**11i**.
IR (neat) 3384, 3142, 1614, 1598, 1513, 1489, 1455, 1372, 1242, 1172, 1093, 1004, 832, 817 cm^{-1}.

(*R*)-(4-Methoxyphenyl)(4-nitrophenyl)methanol (11k)



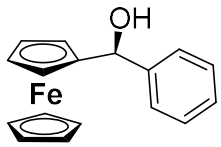
According to the general procedure (ketone: 0.257 g (1 mmol), cat. **(*R*,*R*)-3**), 0.257 g of **11k** was obtained as a pale yellow oil (>99% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 5.85 (s, 1H), 3.78 (s, 3H), 2.50 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 151.1, 147.0, 135.0, 128.1, 126.9, 123.6, 114.2, 75.0, 55.3.
HRMS (FI) calcd for $C_{14}H_{13}NO_4$ $[M]^+$: 259.08446. Found: 259.0853.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AD-H, 250 × 4.6 mm column, hexane/2-propanol 90:10, 1.0 mL/min, 220 nm, 30 ºC, (*S*) isomer 19.5 min, (*R*) isomer 23.9 min); $[\alpha]_D^{20}$ +43.1(c 1.14 in $CHCl_3$) 79% ee (*R*).
IR (neat) 3454, 1068, 1513, 1463, 1347, 1249, 1173, 1109, 1032, 834, 804, 739 cm^{-1}.

(*S*)-(3,5-Dinitrophenyl)(4-methoxyphenyl)methanol (11l)



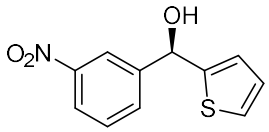
According to the general procedure (ketone: 0.152 g (0.5 mmol), cat. **(*R*,*R*)-3**), 0.141 g of **11l** was obtained as a yellow liquid (92% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91–8.89 (m, 1H), 8.58–8.57 (m, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 5.94 (s, 1H), 3.80 (s, 3H), 2.80 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 148.5, 133.9, 132.6, 128.2, 126.4, 117.5, 114.7, 74.4, 55.4.
HRMS (ESI) calcd for $C_{14}H_{12}N_2O_6$ $[M+Cl]^-$: 339.0389. Found: 339.0382.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, 250 × 4.6 mm column, hexane/2-propanol 85:15, 1.0 mL/min, 220 nm, 30 ºC, (*S*) isomer 68.9 min, (*R*) isomer 85.4 min); $[\alpha]_D^{20}$ +73.9 (c 0.9 in $CHCl_3$) 99% ee (*S*).
IR (neat) 3421, 3107, 2917, 2849, 1598, 1541, 1254, 1174, 1113, 1031, 840, 730 cm^{-1}.

(*S*)-Phenyl(ferrocenyl)methanol (11m)



According to the general procedure (ketone: 0.290 g (1 mmol), cat. **(*R*,*R*)-3**), 0.154 g of **11m** was obtained as a red solid (53% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.23 (m, 5H), 5.47 (d, *J* = 3.2 Hz, 1H), 4.23 (s, 9H), 2.43 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.2, 128.2, 127.4, 126.2, 94.3, 72.0, 68.5, 68.2, 68.1, 67.5, 66.0. All characterization data are in agreement with the previously reported data[8].
HRMS (ESI) calcd for $C_{17}H_{16}OFe$ $[M]^+$: 292.0545. Found: 292.0537.
The enantiomeric excess was determined by HPLC analysis (Chiralpak AS-H, 250 × 4.6 mm column, hexane/2-propanol 95:5, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 9.8 min, (*S*) isomer 10.8 min); $[\alpha]_D^{20}$ +80.8 (c 0.05 in $CHCl_3$) 90% ee (*S*) (lit.[8] $[\alpha]_D$ -94.4 (c 0.016 in $CHCl_3$) 98% ee (*R*)).
IR (neat) 3566, 3415, 3083, 3027, 2957, 2919, 2859, 1731, 1494, 1453, 1409, 1372, 1320, 1182, 1048, 1017, 1000, 823, 720, 700 cm^{-1}.

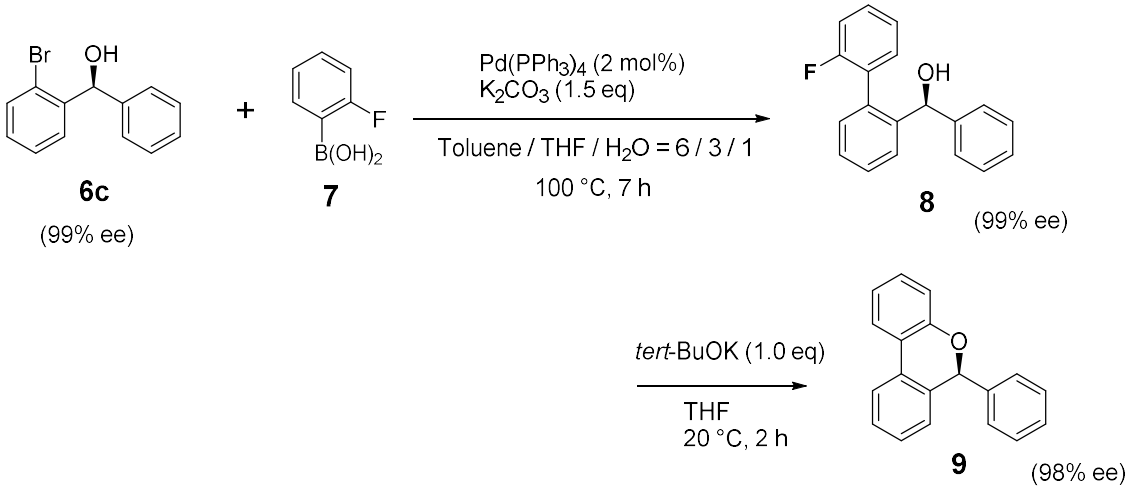
(*R*)-(3-Nitrophenyl)(thiophen-2-yl)methanol (11n)



According to the general procedure (ketone: 0.233 g (1 mmol), cat. **(*R*,*R*)-3**), 0.226 g of **11n** was obtained as a clear oil (96% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32–8.31 (m, 1H), 8.15–8.12 (m, 1H), 7.78–7.76 (m, 1H), 7.54–7.52 (m, 1H), 7.30–7.29 (m, 1H), 6.97–6.94 (m, 2H), 6.15 (s, 1H), 2.83 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.3, 146.6, 145.1, 132.2, 129.4, 126.9, 126.2, 125.5, 122.8,

121.2, 71.1.
HRMS (FI) calcd for $C_{11}H_9NO_3S$ $[M]^+$: 235.0303. Found: 235.0294.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, 250 × 4.6 mm column, hexane/2-propanol 90:10, 1.0 mL/min, 220 nm, 30 ºC, (*S*) isomer 34.9 min, (*R*) isomer 38.9 min); $[\alpha]_D^{20}$ +19.4 (c 1.43 in $CHCl_3$) 98% ee (*R*).
IR (neat) 3392, 2917, 2848, 1529, 1350, 1094, 1022, 811, 760, 707 cm^{-1}.

D. Synthesis of Chiral Benzo[*c*]chromene Compound.



To a solution of **6c** (0.5 g, 1.9 mmol) in toluene (6 mL) and THF (3 mL) were added (2-fluorophenyl)boronic acid (**7**) (0.399 g, 2.85 mmol), $Pd(PPh_3)_4$ (43.9 mg, 0.038 mmol), K_2CO_3 (0.394 g, 2.85 mmol), and H_2O (10 mL). The biphasic mixture was vigorously stirred at 100 ºC for 7 h. The biphasic layers were separated, the aqueous phase was extracted with EtOAc (2 × 10 mL), and the combined organic portions were dried over $MgSO_4$, and concentrated to give a crude liquid of **8**. The crude product was used for the following cyclization reaction without further purification (90% yield).

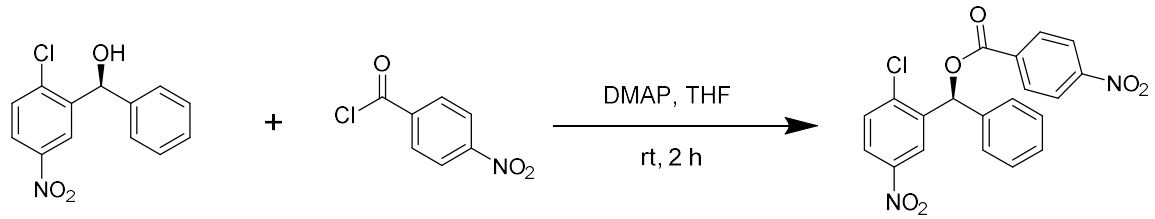
The enantiomeric excess of **8** was determined by HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 97:3, 1.0 mL/min, 254 nm, 30 ºC, (*S*) isomer 10.4 min, (*R*) isomer 11.7 min).

To a solution of crude liquid of **8** (0.05 g, 0.18 mmol) in toluene (1 mL) were added *tert*-BuOK (20.2 mg, 0.18 mmol). After the reaction mixture was stirred at 20 ºC for 2 h, aqueous NH_4Cl (5 mL) was added to acidify the solution. The biphasic layers were separated, the aqueous phase was extracted with EtOAc (3 × 5 mL), and the combined organic portions were washed with brine (2 × 3 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford the crude product which was purified by silica-gel column chromatography to afford the product (**9**) as a white solid (28.9 mg, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78–7.74 (m, 2H), 7.42–7.28 (m, 6H), 7.26–7.18 (m, 2H), 7.08–6.95 (m, 2H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.16 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 139.6, 134.0, 130.0, 129.6, 128.5, 128.5, 128.4, 128.1, 127.6, 126.2, 123.1, 122.8, 122.1, 117.9, 79.6.
HRMS (APCI) calcd for $C_{19}H_{14}O$ $[M]^+$: 258.1039. Found: 258.1019.
The enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, 250 × 4.6 mm column, hexane/2-propanol 98:2, 1.0 mL/min, 220 nm, 30 ºC, (*R*) isomer 17.4 min, (*S*) isomer 20.7 min); $[\alpha]_D^{20}$ -80.7 (c 0.07 in $CHCl_3$) 98% ee (*S*).
IR (neat) 3065, 3033, 2960, 2922, 2852, 1726, 1593, 1486, 1439, 1245, 1010, 722, 699, 612 cm^{-1}.

E. Determination of Absolute Configuration of Products

a) Synthesis of (*S*)-(2-Chloro-5-nitrophenyl)(phenyl)methyl 4-nitrobenzoate (13i)

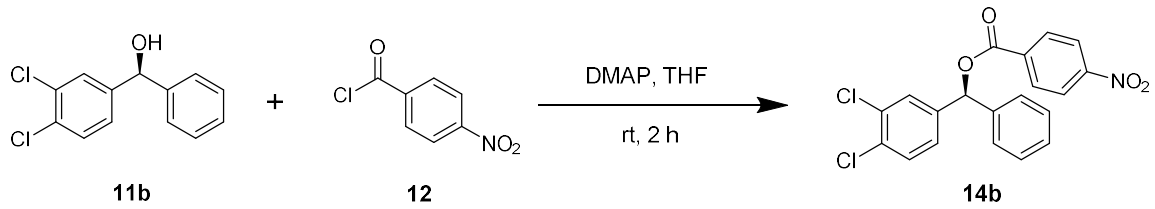


To a mixture of 4-nitrobenzoylchloride (**12**) (400 mg, 2.17 mmol) and *N*,*N*-dimethyl-4-aminopyridine (256 mg, 2.17 mmol) in THF (10 mL) was added alcohol **6i** (0.57 mg, 2.17 mmol) in THF (10 mL). The reaction mixture was stirred for 2 h at room temperature and then quenched by water. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography to give ester **13i** in 90% yield as a white solid. Single crystals were obtained by recrystallization from a slow diffusion of hexane into a THF solution.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 2.8 Hz, 2H), 8.35–8.29 (m, 4H), 8.16 (dd, *J* = 2.8, 8.7 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.48–7.38 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4, 150.9, 147.0, 139.7, 139.4, 136.6, 134.7, 131.2, 131.0, 129.2, 129.1, 127.5, 124.3, 123.8, 123.0, 74.6. HRMS (APCI) calcd for $C_{20}H_{13}N_2O_6Cl$ $[M-H]^-$: 411.0389. Found: 411.0405. Anal. calcd for $C_{20}H_{13}ClN_2O_6$: C, 58.19; H, 3.17; N, 6.79. Found: C, 58.48; H, 3.23; N, 6.62.

IR (neat) 1728, 1522, 1346, 1264, 1249, 1095, 1054, 852, 742, 717 cm^{-1}.

b) Synthesis of (*S*)-(3,4-Dichlorophenyl)(phenyl)methyl 4-nitrobenzoate (14b)

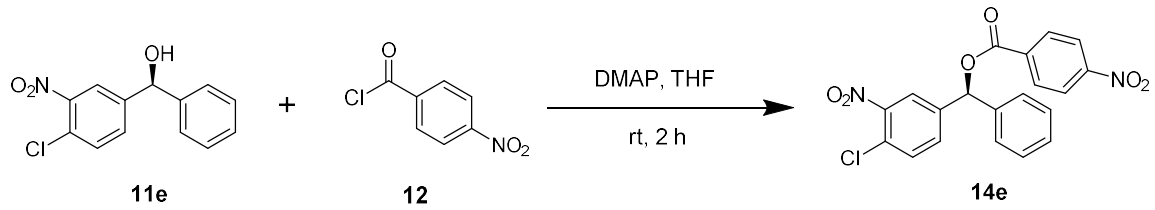


11b **12** **14b**

To a mixture of 4-nitrobenzoylchloride (**12**) (352 mg, 1.90 mmol) and *N*,*N*-dimethyl-4-aminopyridine (232 mg, 1.90 mmol) in THF (10 mL) was added alcohol **11b** (0.50 mg, 1.90 mmol) in THF (10 mL). The reaction mixture was stirred for 2 h at room temperature and then quenched by water. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography to give ester **14b** in 90% yield as a white solid. Single crystals were obtained by recrystallization from an Et_2O-hexane solution.

^1H NMR (400 MHz, $CDCl_3$) δ 8.33–8.27 (m, 4H), 7.51–7.50 (m, 1H), 7.45–7.35 (m, 6H), 7.27–7.25 (m, 1H), 7.06 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.5, 150.8, 139.7, 138.4, 135.1, 132.9, 132.5, 130.9, 130.7, 129.0, 128.9, 128.7, 127.0, 126.5, 123.7, 76.8. HRMS (APCI) calcd for $C_{20}H_{13}NO_4Cl_2$ $[M-H]^-$: 400.0149. Found: 400.0144. Anal. calcd for $C_{20}H_{13}Cl_2NO_4$: C, 59.72; H, 3.26; N, 3.48. Found: C, 59.84; H, 3.35; N, 3.43.
IR (neat) 1724, 1523, 1493, 1469, 1342, 1323, 1302, 1269, 1115, 1030, 1015, 983, 873, 856, 717, 695 cm^{-1}.

c) Synthesis of (*S*)-(4-Chloro-3-nitrophenyl)(phenyl)methyl 4-nitrobenzoate (14e)

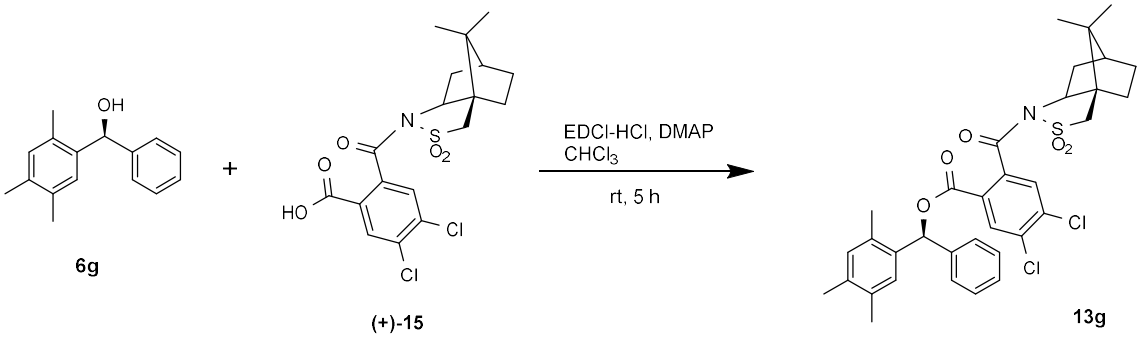


11e **12** **14e**

To a mixture of 4-nitrobenzoylchloride (**12**) (352 mg, 1.90 mmol) and *N*,*N*-dimethyl-4-aminopyridine (232 mg, 1.90 mmol) in THF (10 mL) was added alcohol **11e** (0.50 mg, 1.90 mmol) in THF (10 mL). The reaction mixture was stirred for 2 h at room temperature and then quenched by water. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography to give ester **14e** in 90% yield as a white solid. Single crystals were obtained by recrystallization from a heptane solution.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34–8.28 (m, 4H), 7.93–7.92 (m, 1H), 7.57–7.56 (m, 2H), 7.43–7.40 (m, 5H), 7.13 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.5, 150.9, 148.0, 140.1, 137.7, 134.7, 132.3, 131.7, 130.9, 129.2, 129.1, 127.1, 127.0, 124.1, 123.8, 78.0. HRMS (APCI) calcd for $C_{20}H_{13}N_2O_6Cl$ $[M-H]^-$: 411.0389. Found: 411.0401. Anal. calcd for $C_{20}H_{13}ClN_2O_6$: C, 58.19; H, 3.17; N, 6.79. Found: C, 58.16; H, 2.98; N, 6.60.
IR (neat) 1729, 1535, 1337, 1278, 1117, 1106, 732, 720, 702 cm^{-1}.

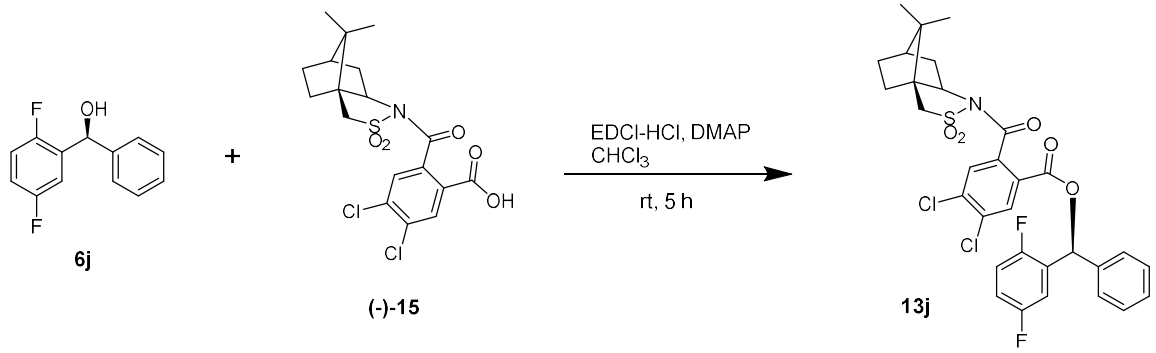
d) Synthesis of (*S*)-Phenyl(2,4,5-trimethylphenyl)methyl 4,5-dichloro -2-((3*aR*,6*S*)-8,8-dimethyl-2,2-dioxidohexahydro-3*H*-3*a*,6-methanobenzo[*c*]isothi azole-1-carbonyl)benzoate[10] (13g)



To a mixture of *N*-(2-carboxy-4,5-dichlorobenzoyl)-(+)-10,2-camphorsultam (**(+)-15**) (500 mg, 1.16 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (220 mg, 1.16 mmol), and *N*,*N*-dimethyl-4-aminopyridine (142 mg, 1.16 mmol) in $CHCl_3$ (3 mL) was added alcohol **6g** (201 mg, 0.89 mmol) in $CHCl_3$ (2 mL). The reaction mixture was stirred for 5 h at room temperature and then quenched by a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography to give ester **13g** in 95% yield as a white solid. Single crystals were obtained by recrystallization from a methanol solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.49 (s, 1H), 7.35–7.27 (m, 5H), 7.12–7.11 (m, 2H), 6.93 (s, 1H), 3.62–3.58 (m, 1H), 3.31–3.21 (m, 2H), 2.42–2.37 (m, 1H), 2.24 (s, 3H), 2.21 (s, 3H), 2.20 (s, 3H), 2.03–1.98 (m, 1H), 1.84–1.82 (m, 3H), 1.30–1.24 (m, 2H), 0.94 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 162.6, 139.0, 136.8, 136.3, 134.9, 134.8, 134.5, 134.1, 133.2, 131.9, 131.9, 131.0, 128.9, 128.5, 128.5, 127.9, 127.6, 76.3, 65.4, 52.8, 48.3, 47.6, 44.7, 37.6, 32.8, 26.4, 20.4, 19.9, 19.4, 19.3, 18.8. HRMS (ESI) calcd for $C_{34}H_{35}NO_5SCl_2$ $[M+Na]^+$: 662.1505. Found: 662.1504. Anal. calcd for $C_{34}H_{35}Cl_2NO_5S$: C, 63.74; H, 5.51; N, 2.19. Found: C, 63.84 H, 5.38; N, 2.38.
IR (neat) 2960, 1727, 1674, 1552, 1461, 1331, 1316, 1301, 1242, 1167, 1139, 1117, 1091, 1067, 753, 703 cm^{-1}.

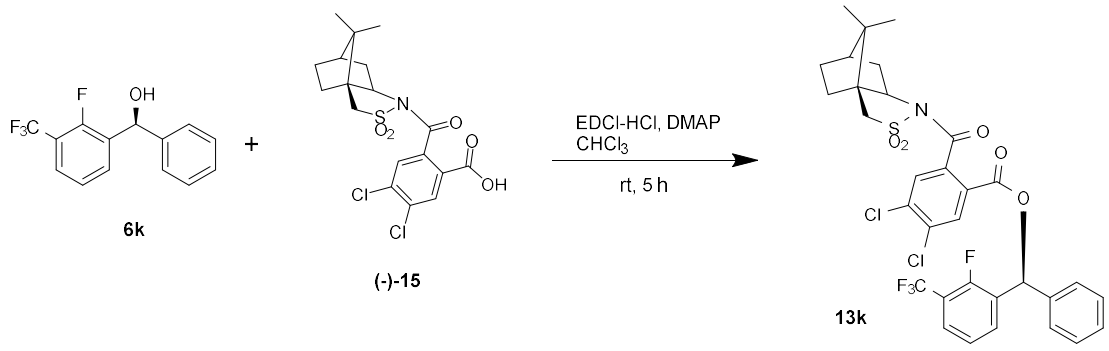
e) Synthesis of (*S*)-(2,5-Difluorophenyl)(phenyl)methyl 4,5-dichloro-2-((3*aS*,6*R*)-8,8-dimethyl-2,2-dioxidohexahydro-3*H*-3a,6-methanobenzo[*c*]isothiazole-1-carbonyl)benzoate[10] (13j)



To a mixture of *N*-(2-carboxy-4,5-dichlorobenzoyl)-(-)-10,2-camphorsultam (**(-)-15**) (406 mg, 0.94 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (180 mg, 0.94 mmol), and *N*,*N*-dimethyl-4-aminopyridine (115 mg, 0.94 mmol) in $CHCl_3$ (2 mL) was added alcohol **6j** (138 mg, 0.63 mmol) in $CHCl_3$ (2 mL). The reaction mixture was stirred for 5 h at room temperature and then quenched by a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography to give ester **13j** in 94% yield as a white solid. Single crystals were obtained by recrystallization from a methanol solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.53 (s, 1H), 7.39–7.32 (m, 5H), 7.18 (s, 1H), 7.18–7.15 (m, 1H), 7.06–6.96 (m, 2H), 3.71–3.68 (m, 1H), 3.39–3.27 (m, 2H), 2.40–2.35 (m, 1H), 2.80–2.20 (m, 1H), 1.89–1.85 (m, 3H), 1.33–1.28 (m, 2H), 1.03 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 162.5, 157.8, 156.8, 155.0, 137.7, 137.1, 135.1, 134.7, 131.8, 131.3, 128.7, 128.5, 128.2, 127.2, 116.9 (dd, J = 23.8, 8.8 Hz), 116.2 (dd, J = 23.8, 8.8 Hz), 114.8 (d, J = 28.8 Hz), 72.5, 65.5, 53.0, 48.4, 47.7, 44.7, 37.6, 32.9, 26.4, 20.5, 19.9. HRMS (ESI) calcd for $C_{31}H_{27}NO_5F_2SCl_2$ $[M+Na]^+$: 656.0847. Found: 656.0831. Anal. calcd for $C_{31}H_{27}Cl_2F_2NO_5S$: C, 58.68; H, 4.29; N, 2.21. Found: C, 59.00; H, 4.31; N, 2.21.
IR (neat) 2959, 1734, 1686, 1496, 1337, 1299, 1243, 1169, 1141, 1116, 1092, 1063, 764 cm^{-1}.

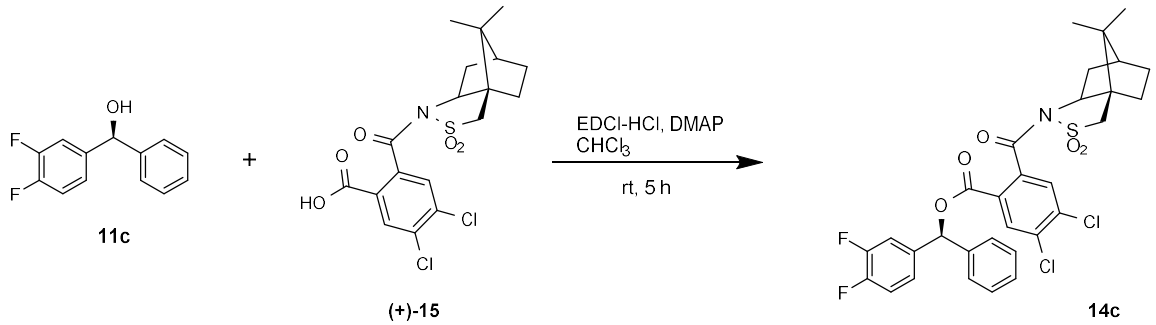
f) Synthesis of (*S*)-(2-Fluoro-3-(trifluoromethyl)phenyl)(phenyl)methyl 4,5-dichloro-2-((3*aS*,6*R*)-8,8-dimethyl-2,2-dioxidohexahydro-3*H*-3*a*,6-methanobenzo[*c*]isothiazole-1-carbonyl)benzoate[10] (13k)



To a mixture of *N*-(2-carboxy-4,5-dichlorobenzoyl)-(-)-10,2-camphorsultam (**(-)-15**) (500 mg, 1.16 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (220 mg, 1.16 mmol), and *N*,*N*-dimethyl-4-aminopyridine (142 mg, 1.16 mmol) in $CHCl_3$ (3 mL) was added alcohol **6k** (240 mg, 0.89 mmol) in $CHCl_3$ (2 mL). The reaction mixture was stirred for 5 h at room temperature and then quenched by a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography to give ester **13k** in 95% yield as a white solid. Single crystals were obtained by recrystallization from a 2-propanol solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.68–7.65 (m, 1H), 7.60–7.56 (m, 1H), 7.51 (s, 1H), 7.39–7.13 (m, 5H), 7.29–7.25 (m, 2H), 3.68–3.65 (m, 1H), 3.36–3.23 (m, 2H), 2.42–2.36 (m, 1H), 2.08–2.02 (m, 1H), 1.88–1.85 (m, 3H), 1.33–1.25 (m, 2H), 1.03 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 162.3, 158.0, 155.9, 137.5 (d, J = 27.5 Hz), 135.0, 134.9, 132.0, 131.7, 131.2, 128.8, 128.7, 128.6, 127.9, 127.3, 127.0 (d, J = 5.0 Hz), 124.3 (d, J = 3.8 Hz), 122.4 (q, J = 270.0 Hz), 118.7 (qd, J = 32.5, 12.5 Hz), 72.2, 65.5, 52.9, 48.4, 47.7, 44.7, 37.5, 32.9, 26.4, 20.5, 19.9. HRMS (ESI) calcd for $C_{32}H_{27}NO_5F_4SCl$ $[M+Na]^+$: 706.0815. Found: 706.0804. Anal. calcd for $C_{32}H_{27}Cl_2F_4NO_5S$: C, 56.14; H, 3.98; N, 2.05. Found: C, 55.78; H, 4.00; N, 2.03.
IR (neat) 2962, 1736, 1685, 1474, 1335, 1296, 1265, 1244, 1165, 1129, 1110, 1094, 1061, 795, 758, 697 cm^{-1}.

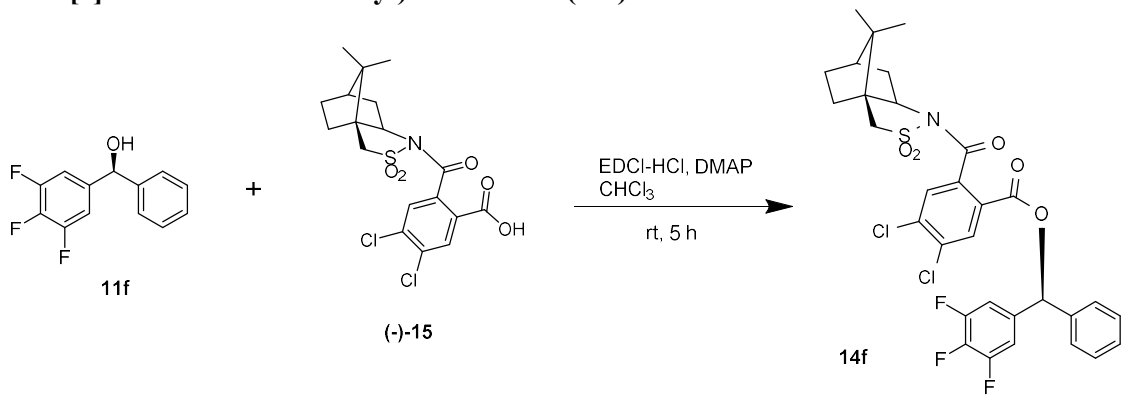
g) Synthesis of (*S*)-(3,4-Difluorophenyl)(phenyl)methyl 4,5-dichloro-2-((3*aR*,6*S*)-8,8-dimethyl-2,2-dioxidohexahydro-3*H*-3*a*,6-methanobenzo[*c*]isothiazole-1-carbonyl)benzoate[10] (14c)



To a mixture of *N*-(2-carboxy-4,5-dichlorobenzoyl)-(+)-10,2-camphorsultam (**(+)-15**) (500 mg, 1.16 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (220 mg, 1.16 mmol), and *N*,*N*-dimethyl-4-aminopyridine (142 mg, 1.16 mmol) in $CHCl_3$ (3 mL) was added alcohol **11c** (196 mg, 0.89 mmol) in $CHCl_3$ (2 mL). The reaction mixture was stirred for 5 h at room temperature and then quenched by a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography to give ester **14c** in 93% yield as a white solid. Single crystals were obtained by recrystallization from a methanol solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.52 (s, 1H), 7.41–7.33 (m, 5H), 7.23–7.19 (m, 1H), 7.16–7.05 (m, 2H), 6.93 (s, 1H), 3.80–3.76 (m, 1H), 3.39–3.30 (m, 2H), 2.42–2.38 (m, 1H), 2.10–2.06 (m, 1H), 1.91–1.88 (m, 3H), 1.34–1.32 (m, 2H), 1.01 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 162.6, 151.1 (dd, *J* = 26.3, 12.5 Hz), 149.1 (d, *J* = 26.3, 12.5 Hz), 138.4, 137.1, 136.4 (m), 135.0, 134.8, 131.4 (m), 128.8, 128.7, 128.2, 127.6, 126.5, 123.3 (m), 117.2 (d, *J* = 18.0 Hz), 116.5 (d, *J* = 18.0 Hz), 77.5, 65.5, 53.0, 48.4, 47.6, 44.7, 37.5, 33.0, 26.4, 20.4, 20.0. HRMS (ESI) calcd for $C_{31}H_{27}NO_5F_2SCl_2$ $[M+Na]^+$: 656.0847. Found: 656.0831. Anal. calcd for $C_{31}H_{27}Cl_2F_2NO_5S$: C, 58.68; H, 4.29; N, 2.21. Found: C, 58.60; H, 4.15; N, 2.36.
IR (neat) 2969, 1732, 1673, 1515, 1328, 1299, 1264, 1244, 1169, 1141, 1114, 1093, 1068, 754, 738, 709 cm^{-1}.

h) Synthesis of (*S*)-Phenyl(3,4,5-trifluorophenyl)methyl 4,5-dichloro-2-((3*aS*,6*R*)-8,8-dimethyl-2,2-dioxidohexahydro-3*H*-3*a*,6-methanobenzo[*c*]isothiazole-1-carbonyl)benzoate[10] (14f)

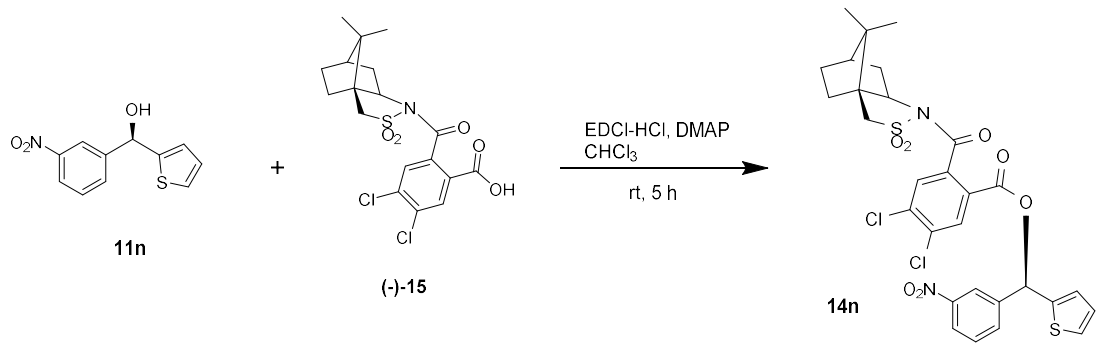


To a mixture of *N*-(2-carboxy-4,5-dichlorobenzoyl)-(-)-10,2-camphorsultam (**(-)-15**) (500 mg, 1.16 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (220 mg, 1.16 mmol), and *N*,*N*-dimethyl-4-aminopyridine (142 mg, 1.16 mmol) in $CHCl_3$ (3 mL) was added alcohol **11f** (212 mg, 0.89 mmol) in $CHCl_3$ (2 mL). The reaction mixture was stirred for 5 h at room temperature and then quenched by a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column

chromatography to give ester **14f** in 95% yield as a white solid. Single crystals were obtained by recrystallization from an ethanol solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 0.5 Hz, 1H), 7.52 (d, *J* = 0.5 Hz, 1H), 7.40–7.32 (m, 5H), 7.03–6.99 (m, 2H), 6.88 (s, 1H), 3.71–3.68 (m, 1H), 3.39–3.26 (m, 2H), 2.40–2.37 (m, 1H), 2.10–2.04 (m, 1H), 1.89–1.88 (m, 3H), 1.33–1.26 (m, 2H), 1.06 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 162.6, 152.2 (d, *J* = 10.0 Hz), 150.2 (d, *J* = 6.3 Hz), 137.9, 137.3, 135.7 (m), 135.2, 134.7, 131.8, 131.3, 128.8, 128.8, 128.0, 127.4, 111.7 (dd, *J* = 16.3, 5.0 Hz), 76.8, 65.5, 53.0, 48.4, 47.7, 44.7, 37.7, 32.9, 26.4, 20.6, 19.9. HRMS (ESI) calcd for $C_{31}H_{26}NO_5F_3SCl_2$ $[M+Na]^+$: 674.0753. Found: 674.0748. Anal. calcd for $C_{31}H_{26}Cl_2F_3NO_5S$: C, 57.06; H, 4.02; N, 2.15. Found: C, 57.32; H, 4.02; N, 2.19.
IR (neat) 2960, 1732, 1684, 1531, 1455, 1338, 1299, 1241, 1169, 1142, 1116, 1091, 1047, 701 cm^{-1}.

i) Synthesis of (*R*)-(3-Nitrophenyl)(thiophen-2-yl)methyl 4,5-dichloro-2-((3*aS*,6*R*)-8,8-dimethyl-2,2-dioxidohexahydro-3*H*-3*a*,6-methanobenzo[*c*]isothiazole-1-carbonyl)benzoate[10] (14n)



To a mixture of *N*-(2-carboxy-4,5-dichlorobenzoyl)-(-)-10,2-camphorsultam (**(-)-15**) (500 mg, 1.16 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (220 mg, 1.16 mmol), and *N*,*N*-dimethyl-4-aminopyridine (142 mg, 1.16 mmol) in $CHCl_3$ (3 mL) was added alcohol **11n** (136 mg, 0.58 mmol) in $CHCl_3$ (2 mL). The reaction mixture was stirred for 5 h at room temperature and then quenched by a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with $CHCl_3$ (×3). The combined organic portions were dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography to give ester **14n** in 92% yield as a white solid. Single crystals were obtained by recrystallization from a 2-propanol solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33–8.32 (m, 1H), 8.23–8.20 (m, 1H), 8.14 (s, 1H), 7.84–7.82 (m, 1H), 7.61–7.57 (m, 1H), 7.16 (s, 1H), 7.37–7.36 (m, 1H), 7.27–7.26 (m, 1H), 7.04–7.03 (m, 1H), 7.02–7.00 (m, 1H), 3.83–3.80 (m, 1H), 3.42–3.29 (m, 2H), 2.44–2.42 (m, 1H), 2.14–2.09 (m, 1H), 1.92–1.86 (m, 3H), 1.36–1.34 (m, 2H), 1.18 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 162.4, 148.4, 141.1, 140.9, 137.4, 135.1, 134.8, 132.8, 131.8, 131.2, 129.8, 127.9, 127.6, 127.2, 127.1, 123.6, 122.3, 73.5, 65.6, 52.9, 48.5, 47.7, 44.8, 37.7, 33.0, 26.4, 20.8, 20.0. HRMS (ESI) calcd for $C_{29}H_{26}N_2O_7S_2Cl_2$ $[M+Na]^+$:

671.0451. Found: 671.0457. Anal. calcd for $C_{29}H_{26}Cl_2N_2O_7S_2$: C, 53.62; H, 4.03; N, 4.31. Found: C, 53.78 H, 3.95; N, 4.23.
IR (neat) 2959, 1732, 1685, 1532, 1339, 1300, 1243, 1169, 1141, 1116, 1090, 1064 cm^{-1}.

X-ray Structure Determination for **13i**, **14b**, **14e**, **13g**, **13j**, **13k**, **14c**, **14f**, and **14n**.
Measurements were made on a Rigaku Saturn CCD area detector equipped with graphite-monochromated Mo-$K\alpha$ radiation (λ = 0.71070 Å) under nitrogen stream at 93 K. Indexing was performed from eighteen images. The crystal-to-detector distance was 45.05 mm. The data were collected to a maximum 2θ value of 55.0°. A total of 720 oscillation images were collected. A sweep of data was carried out using ω scans from –110.0 to 70.0° in 0.5° steps, at χ = 45.0° and ϕ = 0.0°. A second sweep was performed using ω scans from –110.0 to 70.0° in 0.5° steps, at χ = 45.0° and ϕ = 90.0°. Intensity data were collected for Lorentz-polarization effects as well as absorption. Structure solution and refinements were performed with the Crystal Structure program package. The heavy atom positions were determined by direct methods (SIR2002), and the remaining non-hydrogen atoms were found by subsequent Fourier techniques. An empirical absorption correction based on equivalent reflections was applied to all data. All non-hydrogen atoms other than solvent molecules were refined anisotropically by full-matrix least-square techniques based on F^2. All hydrogen atoms were constrained to ride on their parent atom. Relevant crystallographic data are compiled in Tables S3-S5.

Table S3. Crystallographic Data for **13i, 14b, 14e,** and **13g**

	13i	**14b**	**14e**	**13g**
empirical formula	$C_{20}H_{13}ClN_2O_6$	$C_{20}H_{13}Cl_2NO_4$	$C_{20}H_{13}ClN_2O_6$	$C_{34}H_{35}Cl_2NO_5S$
formula weight	412.79	402.23	412.79	640.62
crystal color	Colorless	Colorless	Colorless	Colorless
crystal system	Monoclinic	Monoclinic	Orthorhombic	Orthorhombic
space group	$P2_1$ (#4)	$P2_1$ (#4)	$P2_12_12_1$ (#19)	$P2_12_12_1$ (#19)
a, Å	13.373(4)	5.902(2)	7.210(2)	10.5269(13)
b, Å	7.840(2)	12.201(3)	15.714(4)	11.2332(14)
c, Å	18.471(6)	12.309(3)	15.938(4)	26.231(3)

β, deg	109.497(4)	101.322(4)		
V, Å^3	1815.6(9)	869.2(4)	1805.7(7)	3101.8(7)
Z	4	2	4	4
D_{calcd}, g cm^{-3}	1.510	1.537	1.518	1.372
F_{000}	848.00	412.00	848.00	1344.00
μ, cm^{-1} (MoKα)	2.531	4.006	2.544	3.198
Exposure rate	16.0 sec/°	10.0 sec/°	16.0 sec/°	16.0 sec/°
no. of reflections measured	15140	7112	15014	25817
no. of unique reflections	7694	3893	4139	6996
no. of variables	550	258	276	424
$R1(I>2.00\sigma(I))$	0.0604	0.0422	0.0393	0.0467
w$R2$ (All reflections)	0.1009	0.0977	0.0883	0.1116
GOF on F^2	1.010	1.000	1.000	1.000
Flack parameter	0.09(6)	-0.00(5)	-0.04(6)	-0.06(5)

$R1 = \Sigma\ ||F_o| - |F_c|| / \Sigma\ |F_o|$, w$R2 = [\Sigma(w(F_o^2 - F_c^2)^2)/ \Sigma w(F_o^2)^2]^{1/2}$.

Table S4. Crystallographic Data for **13j, 13k,** and **14c**

	13j	**13k**	**14c**
empirical formula	$C_{31}H_{27}Cl_2F_2NO_5S$	$C_{32}H_{27}Cl_2F_4NO_5S$	$C_{31}H_{27}Cl_2F_2NO_5S$
formula weight	634.52	684.53	634.52
crystal color	Colorless	Colorless	Colorless
crystal system	Monoclinic	Monoclinic	Orthorhombic
space group	*C*2 (#5)	*C*2 (#5)	*C*2 (#5)
a, Å	33.429(9)	24.814(7)	31.304(13)
b, Å	7.746(2)	7.731(2)	7.830(3)
c, Å	12.033(3)	19.580(5)	12.515(6)
β, deg	111.194(4)	126.078(3)	110.626(6)
V, Å^3	2924.3(12)	3035.7(13)	2871(2)
Z	4	4	4
D_{calcd}, g cm^{-3}	1.441	1.498	1.468
F_{000}	1312.00	1408.00	1312.00
μ, cm^{-1} (MoKα)	3.479	3.502	3.544
Exposure rate	6.0 sec/°	10.0 sec/°	4.0 sec/°
no. of reflections measured	12127	12547	11834
no. of unique reflections	5792	6422	6423
no. of variables	407	434	407
$R1(I>2.00\sigma(I))$	0.0437	0.0385	0.0360
w$R2$ (All reflections)	0.1023	0.0906	0.0854
GOF on F^2	1.000	1.000	1.000
Flack parameter	-0.08(6)	-0.03(5)	-0.02(4)

$R1 = \Sigma\ ||F_o| - |F_c|| / \Sigma\ |F_o|$, w$R2 = [\Sigma(w(F_o^2 - F_c^2)^2)/ \Sigma w(F_o^2)^2]^{1/2}$.

Table S5. Crystallographic Data for **14f** and **14n**

	14f	**14n**

empirical formula	$C_{31}H_{26}Cl_2F_3NO_5S$	$C_{29}H_{26}Cl_2N_2O_7S_2$
formula weight	652.51	649.56
crystal color	Colorless	Colorless
crystal system	Monoclinic	Monoclinic
space group	$P2_1$ (#4)	$P2_12_12_1$ (#19)
a, Å	7.590(2)	7.0524(10)
b, Å	33.801(6)	15.8433(22)
c, Å	12.053(2)	25.4267(31)
β, deg	107.278(3)	
V, Å^3	2952.9(10)	2841.0088(0)
Z	4	4
D_{calcd}, g cm^{-3}	1.468	1.519
F_{000}	1344.00	1344.00
μ, cm^{-1} (MoKα)	3.514	4.270
Exposure rate	10.0 sec/°	10.0 sec/°
no. of reflections measured	24300	23544
no. of unique reflections	11664	6486
no. of variables	828	405
$R1(I>2.00\sigma(I))$	0.0402	0.0416
w$R2$ (All reflections)	0.0961	0.0989
GOF on F^2	1.000	1.000
Flack parameter	-0.03(4)	-0.02(5)

$R1 = \Sigma\ ||F_o| - |F_c|| / \Sigma\ |F_o|$, $wR2 = [\Sigma(w(F_o^2 - F_c^2)^2)/ \Sigma w(F_o^2)^2]^{1/2}$.

Figure S2. X-ray crystallographic structure of **13i**.

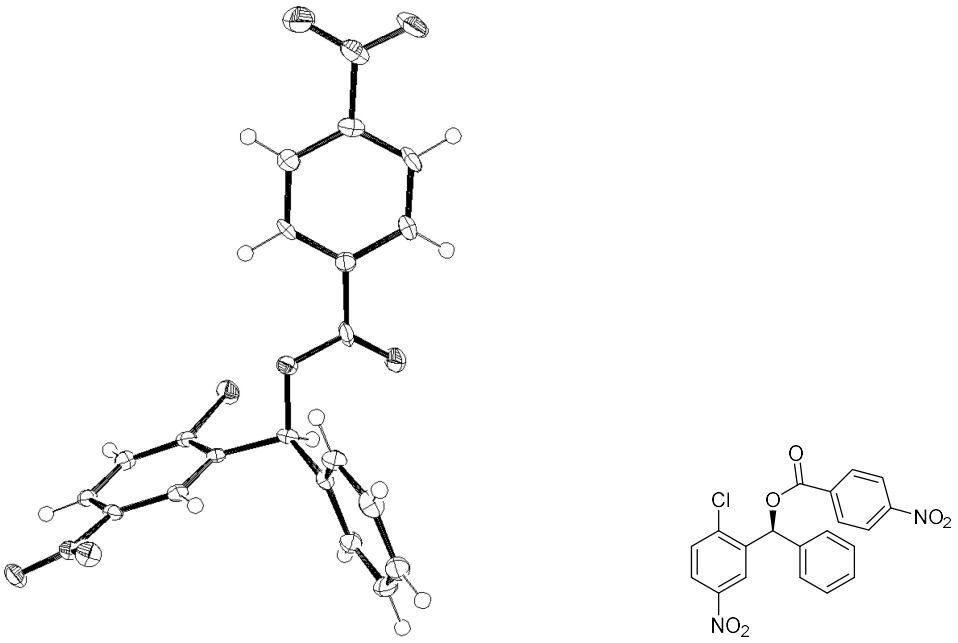


Figure S3. X-ray crystallographic structure of **14b**.

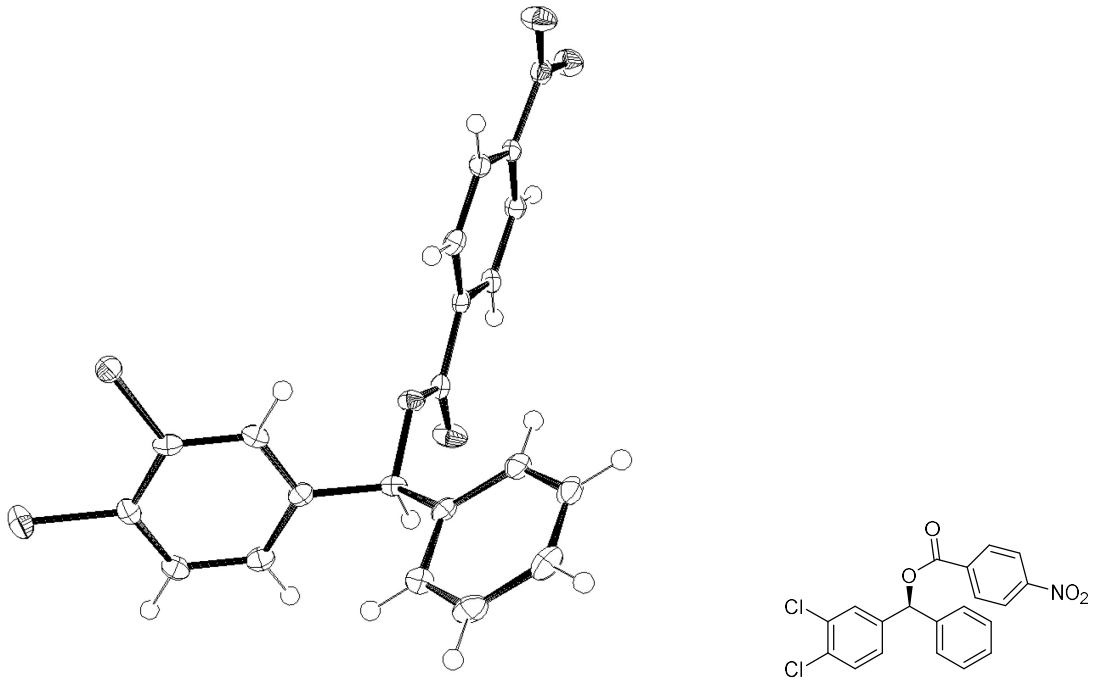


Figure S4. X-ray crystallographic structure of **14e**.

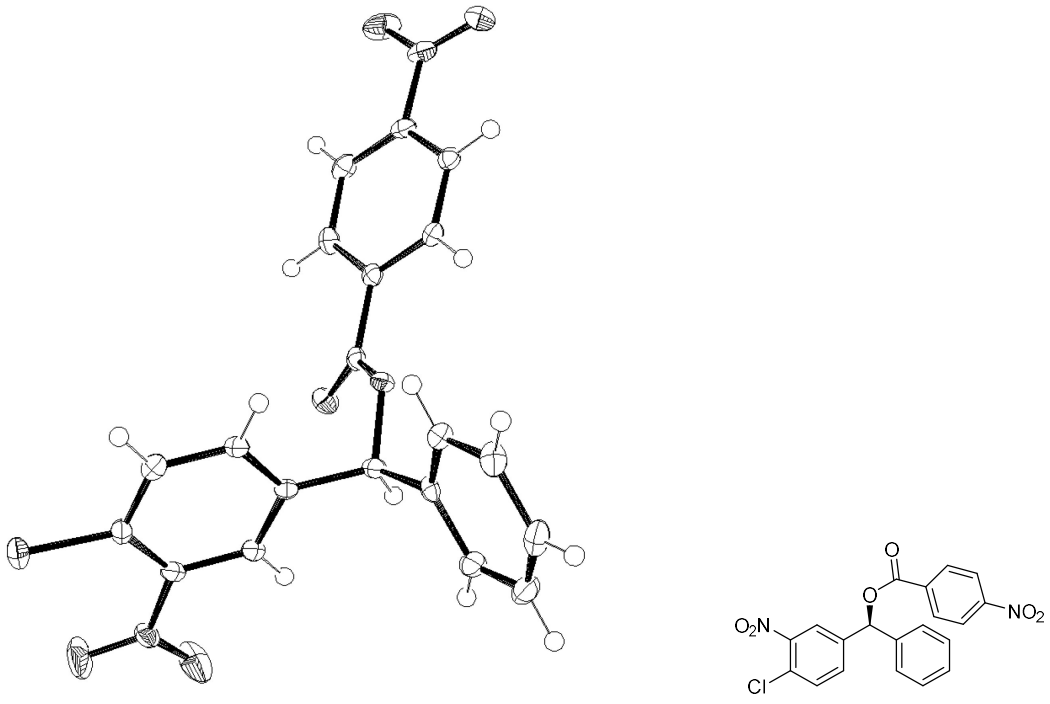


Figure S5. X-ray crystallographic structure of **13g**. All hydrogens except those attached to chiral carbons are omitted for clarity.

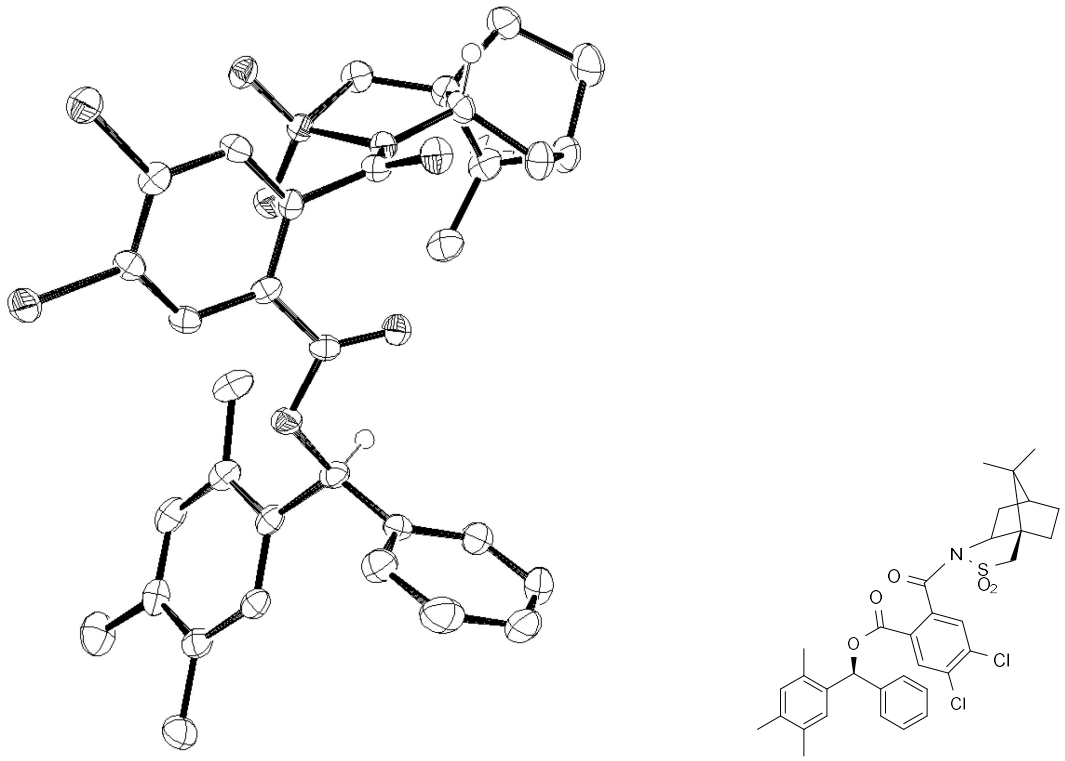


Figure S6. X-ray crystallographic structure of **13j**. All hydrogens except those attached to chiral carbons are omitted for clarity.

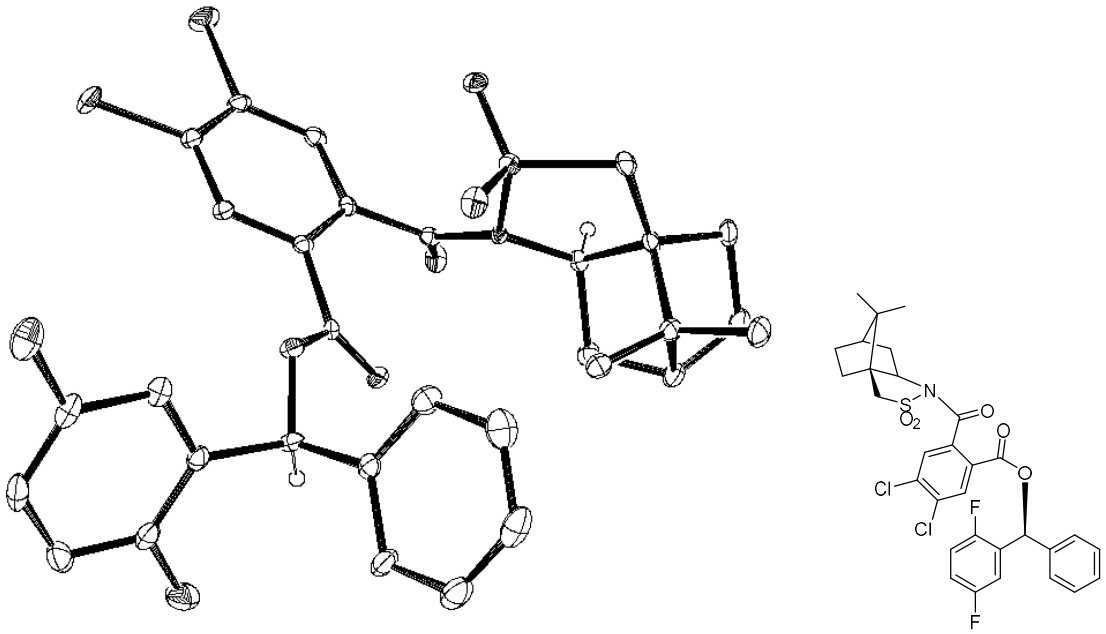


Figure S7. X-ray crystallographic structure of **13k**. All hydrogens except those attached to chiral carbons are omitted for clarity.

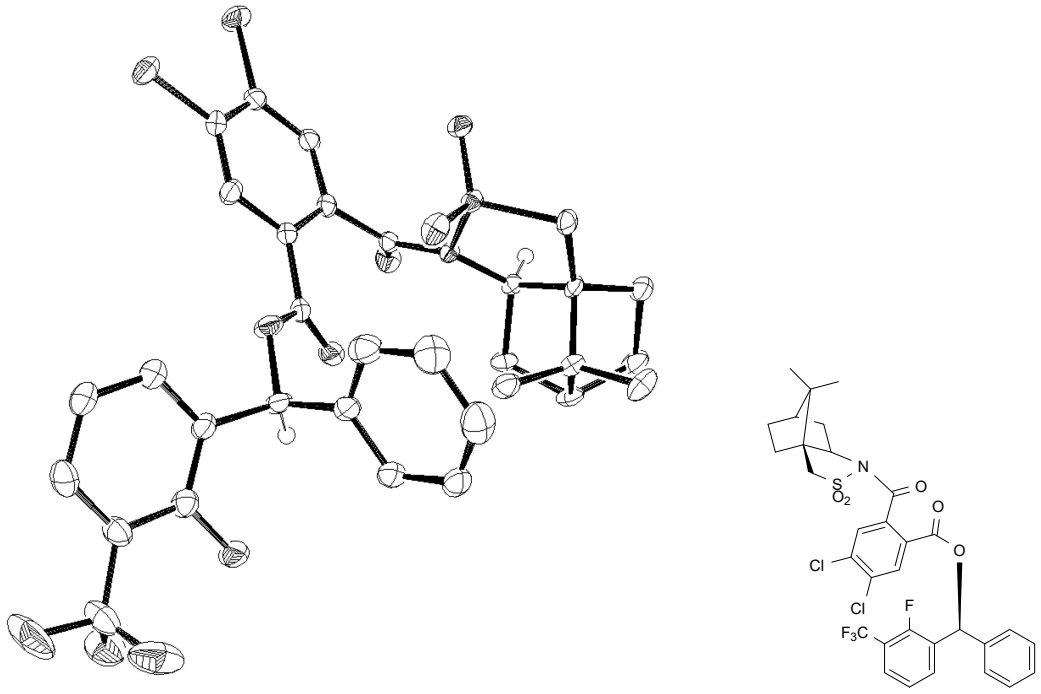


Figure S8. X-ray crystallographic structure of **14c**. All hydrogens except those attached to chiral carbons are omitted for clarity.

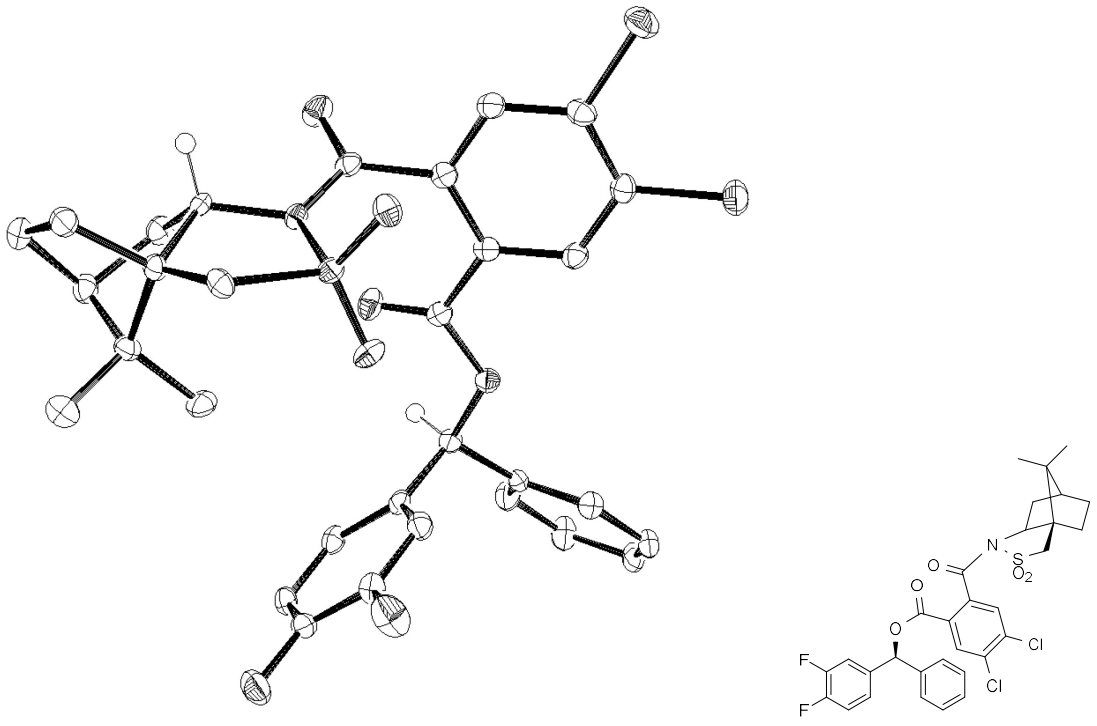


Figure S9. X-ray crystallographic structure of **14f**. All hydrogens except those attached to

chiral carbons are omitted for clarity.

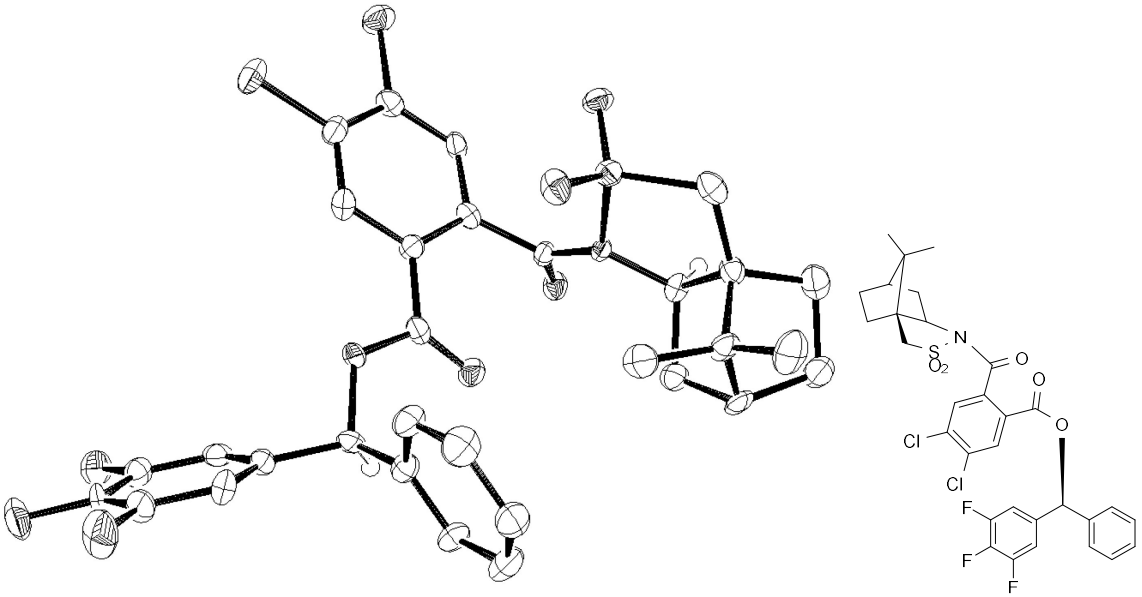
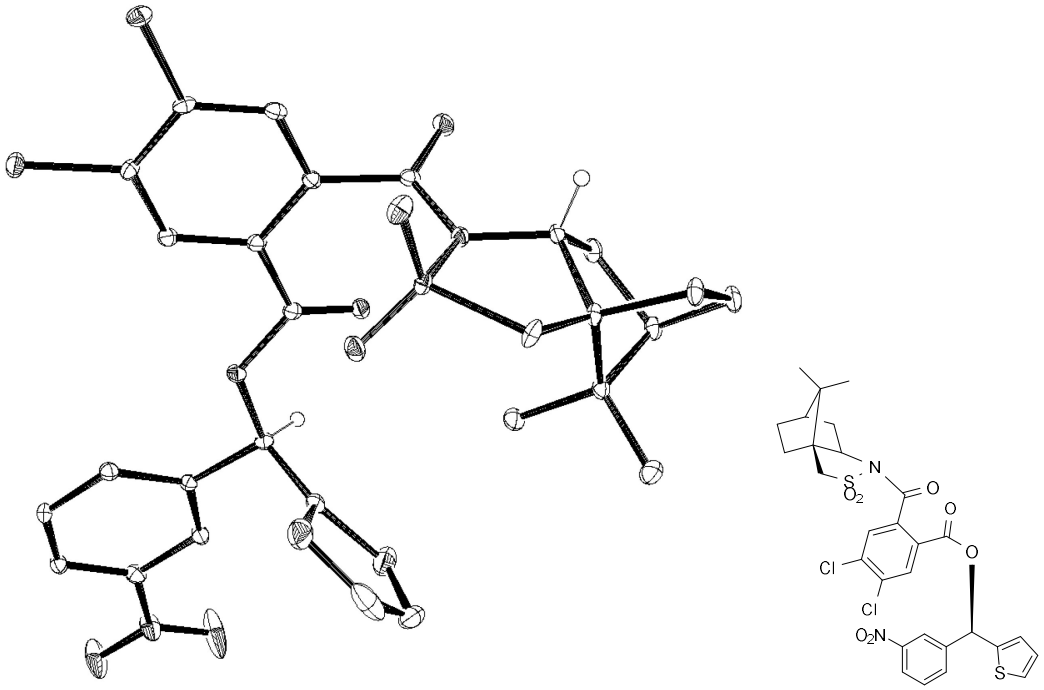


Figure S10. X-ray crystallographic structure of **14n**. All hydrogens except those attached to chiral carbons are omitted for clarity.



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Publication List

1. Oxo-Tethered Ruthenium (II) Complex as a Bifunctional Catalyst for Asymmetric Transfer Hydrogenation and H_2-Hydrogenation

   Touge, T.; Hakamata, T.; Nara, H.; Kobayashi, T.; Sayo, N.; Saito, T.; Kayaki, Y.; Ikariya, T. *J. Am. Chem. Soc.* **2011**, *133*, 14960.

2. Efficient Access to Chiral Benzohydrols via Asymmetric Transfer Hydrogenation of Unsymmetrical Benzophenones with Bifunctional Oxo-tethered Ruthenium Catalysts

   Touge, T.; Nara, H.; Fujiwhara, M.; Kayaki, Y.; Ikariya, T. *J. Am. Chem. Soc.* **2016**, *138*, 10084.
   (Highlighted by SYNFACTS, Synfacts **2016**, *12*, 1171.)

3. Asymmetric Hydrogenation of Unprotected Indoles Catalyzed by η^6-Arene/*N*-Me-sulfonyldiamine-Ru(II) complexes

   Touge, T.; Arai, T. *J. Am. Chem. Soc.* **2016**, *138*, 11299.
   (Highlighted by SYNFACTS, Synfacts **2016**, *12*, 1164.)

Patent List

1. Method for producing ruthenium complex

   JP 2008-279858
   EP 2182001 A1
   US 20100113814
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   AT 516294
   ES 2367952
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2. Ruthenium silyl-arene complex, and method for production thereof

   JP 2009-121013
   US 20100298588 A1
   EP 2258707

   Taichiro Touge, Hideki Nara, Takahiro Fujiwara

3. Preparation of ruthenium diamine complexes as stereoselective transfer hydrogenation catalysts for optically active alcohols and amines

   JP 2009-164712
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4. Ruthenium-diamine complexes and method for producing optically active compounds

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   WO 2012026201 A1

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   JP 2011-95728
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6. Method for preparation of 1,2-diphenylethylenediamine derivatives

   JP 2011-101528
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   Taichiro Touge, Hideki Nara, Tomohiko, Hakamata

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9. Novel diamine compound and metal complexes, and method for producing optically active compounds

   JP 2013-201244
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10. Preparation of optically active compounds by asymmetric reduction of imines or unsaturated heterocyclic compounds in the presence of optically active ruthenium, iridium, or rhodium complexes

    JP 2014-26161
    WO 2015122502 A1

    Taichiro Touge, Hideki Nara

11. Preparation of solid-supported ruthenium-diamine complexes, and method for manufacturing optically active compounds

    JP 2014-208681
    WO 2016056669 A1

    Taichiro Touge, Hideki Nara

Presentation (2015-)

1. The 3rd International Symposim on Process Chemistry
   July 13-15, 2015 Kyoto International Conference Center, KYOTO, JAPAN

2. The 43rd Noyori-Forum (Invited Lecture)
   July 17, 2015 Nagoya University and Nagoya Tokyu Hotel, NAGOYA, JAPAN

3. Chiba University, Molecular Chirality Reserch Center, Regular Meeting (Invited Lecture)
   July 14, 2016 Chiba University, CHIBA, JAPAN

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