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A class of readily available optically pure 7,7′-disubstituted BINAPs for asymmetric catalysis

Wei-Cheng Yuan [a,*], Lin-Feng Cun [a], Ai-Qiao Mi [a], Yao-Zhong Jiang [a], Liu-Zhu Gong [a,b,*]

[a] Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu 610041, China
[b] Hefei National Laboratory for Physical Sciences at the Microscale and Department of Chemistry, University of Science and Technology of China, Hefei 230026, China

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ABSTRACT

A class of optically pure 7,7′-disubstituted BINAPs have been prepared starting with a catalytic asymmetric oxidative coupling reaction. A general, concise, and straightforward synthetic procedure has been established, and is suitable for all optically pure 7,7′-disubstituted BINAPs **1a–h**, regardless of the substituents' structure in the 7,7′-positions. The catalytic potential of this class of ligands has been investigated in the highly enantioselective Rh-catalyzed 1,4-addition of aryl boronic acids to enones (up to 99.8% ee), and Ru-catalyzed asymmetric hydrogenation of simple aromatic ketones (up to *S*/*C*=100,000, up to 98% ee) and β-ketoesters (up to *S*/*C*=10,000, up to 99.8% ee), respectively.

1. Introduction

Transition metal-catalyzed asymmetric transformation plays a very important role in modern organic chemistry, in which searching for highly efficient chiral ligands is the key objective to obtain high reactivity and enantioselectivity.[1] Over the past four decades, thousands of chiral ligands have been synthesized for a variety of catalytic asymmetric reactions in both academic research and industrial production.[1,2] Among them, chiral phosphorus ligands have received much more attention since Knowles and Sabacky[3a] and Horner and co-workers[3b] pioneered the asymmetric hydrogenation with rhodium complexes of chiral phosphorus ligands in the late 1960s. In the history of chiral phosphorus ligands, BINAP (2,2′-bis(diphenylphosphino)-1,1′-bi-naphthyl), discovered by Noyori and co-workers in 1980,[4a] appears to be the most frequently applied ligand for asymmetric catalysis.[2,4] Indeed, many asymmetric transformations can be carried out with metal complexes of chiral BINAP ligand in very good enantioselectivity since this particular ligand exhibits atropoisomerism.[2,4,5] Many modified BINAP derivatives have also been developed by fine-tuning both the steric and electronic properties of BINAP scaffold in order to obtain higher efficiency and selectivity.[6] For example, H_8-BINAP provides better enantioselectivity than BINAP in Ru-catalyzed hydrogenation of unsaturated carboxylic acids,[7] and the chiral biaryl bisphosphine ligand SEGPHOS provides greater enantioselectivities than BINAP in Ru-catalyzed hydrogenation of a wide variety of carbonyl compounds.[8] In addition, 3,3′-, 4,4′-, 5,5′-, and 6,6′-disubstituted BINAPs have been synthesized and exhibit different enantiocontrol ability from mother BINAP in some catalytic asymmetric reactions.[6b]

The subtle modulation of the dihedral angle and electronic properties of BINAP maybe lead to an improvement of catalytic behavior of the ligand. In principal, introducing substituents at 7,7′-positions of BINAP should alter the dihedral angle and electronic properties to a certain degree. Therefore, we envisioned that the 7,7′-disubstituted BINAPs would exhibit different catalytic behavior from the mother BINAP in asymmetric catalysis. However, in sharp contrast to numerous studies on 3,3′-, 4,4′-, 5,5′-, and 6,6′-disubstituted BINAP derivatives,[6] there are few reports on synthesizing and using optically pure 7,7′-disubstituted BINAPs in catalytic asymmetric reactions so far.[9] This may be resulted from lacking convenient methods to synthesize them. To the best of our knowledge, the preparation of 7,7′-disubstituted BINAPs mainly subjected to the indispensable tedious resolution of 7,7′-disubstituted BINOLs.[9] Thus developing easily accessible approach to 7,7′-disubstituted BINAPs is still a challenge. Recently, we have discovered three types of chiral oxovanadium complexes for catalytic asymmetric oxidative coupling of 2-naphthols, and very high enantioselectivity has been achieved.[10] Based on this procedure, a class of optically pure 7,7′-disubstituted BINOLs were conveniently prepared and applied in catalytic asymmetric addition of phenylacetynylzincs to aldehdyes with excellent

* Corresponding authors. Fax: +86 28 8522 3978.
E-mail address: yuanwc@cioc.ac.cn (W.-C. Yuan).

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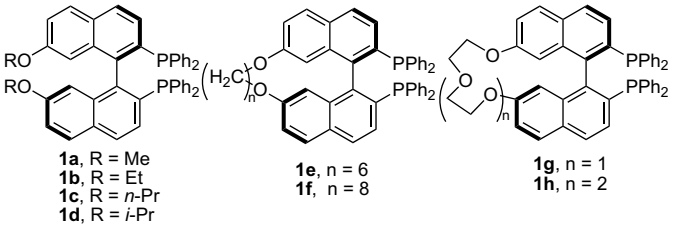
enantioselectivities.[11] As a logical extension, we decided to prepare 7,7′-disubstituted BINAPs (7,7′-disubstituted-2,2′-bis(diphenylphosphino)-1,1′-binaphthyls) starting from optically pure 7,7′-disubsituted BINOLs, and further investigate their catalytic potential in asymmetric reactions.

We have previously communicated the syntheses of a series of ligands **1a**, **1e**–**h** (Scheme 1) and their applications in Rh-catalyzed highly enantioselective 1,4-additions of aryl boronic acids to enones.[12] In this article, we will give full details of the syntheses of the optically pure 7,7′-disubstituted BINAPs ligands and provide a general, concise, and straightforward synthetic procedure suitable for all ligands **1a**–**h**, regardless of the substituents' structure in the 7,7′-positions. In addition to previously reported Rh-catalyzed 1,4-addition reactions of aryl boronic acids to enones, evaluations of this class of 7,7′-disubstituted BINAPs ligands in Ru-catalyzed hydrogenation reaction of simple aromatic ketones and β-ketoesters are also discussed.



Scheme 1. The chiral ligands evaluated in this study.

2. Results and discussion

2.1. Synthesis of chiral 7,7′-disubstituted BINAPs ligands 1a–h

Starting from an asymmetric oxidative coupling reaction of readily accessible 7-alloxyl-2-naphthol **2** in the presence of 5 mol % chiral oxovanadium catalyst,[10] optically pure 7,7′-disubstituted BINOLs **4a**–**h** were conveniently obtained (Scheme 2).[11] According to the literature procedure,[13] treatment of **4a**–**h** with triflic anhydride (Tf_2O) and pyridine in CH_2Cl_2 afforded 7,7′-disubstituted-binaphthols ditriflates **5a**–**h** in almost quantitative yields. The ditriflates **5a**–**d** were then coupled with diphenylphosphine in the presence of 10 mol % nickel(II) catalyst and DABCO as base in DMF at 100 °C for 2–3 days afforded optically pure 7,7′-disubstituted BINAPs ligands **1a**–**d** in 73%, 70%, 61%, and 66% yields, respectively. However, ligands **1e**–**h** were not obtained under the same conditions even for prolonged reaction time (Scheme 2). This difference between **5a**–**d** and **5e**–**h** presumably arises from the steric properties of the substituents at 7,7′-positions. In the cases of preparing **1e**–**h**, 7,7′-positions of **5e**–**h** are linked by an alkyl or crown ether forming cyclic substituents, which maybe have some effects on the dihedral angle of BINAP scaffold and thus inhibited the coupling reactions.

Since the phosphination steps of **5e**–**h** with diphenylphosphine in the presence of Ni(dppe)Cl_2 failed to directly give the desired products, an indirect synthetic pathway was attempted (Scheme 3).[14] Monophosphination of **5g** with diphenylphosphine oxide in the presence of 5 mol % of palladium complex generated in situ from palladium acetate and 1,4-bis(diphenylphosphino)butane (dppb) gave compound **6**, which was subsequently reduced into **7** with trichlorosilane (Cl_3SiH). Compound **8** was obtained by the phosphination of intermediate **7** with diphenylphosphine oxide under similar conditions to those of the preparation of **6** from **5g**, and subsequently was reduced by Cl_3SiH to afford the desired ligand **1g**. Although this synthetic process included several steps, it was noteworthy that the purification of all intermediates **6**, **7**, and **8** was normally unnecessary and the optically pure ligand **1g** was obtained by recrystallization from dry toluene/methanol at 0 °C with an overall 56% yield from **5g**. Unfortunately, partial racemization took place during the course of preparing ligands **1e**, **1f**, and **1h** with the same process as described in Scheme 3.

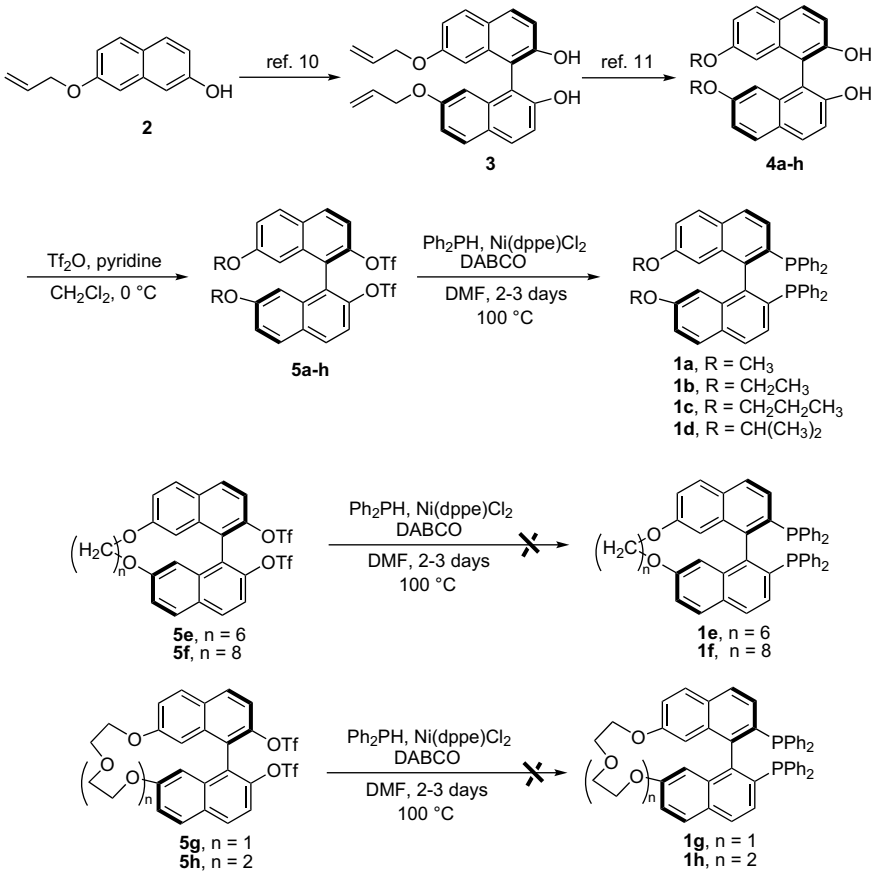
The partial racemization was determined by ^{31}P NMR spectrum of the complexes formed from [$RuCl_2$(benzene)]$_2$, (*R*,*R*)-1,2-diphenylenediamine (DPEN), and ligands **1e**, **1f**, and **1h**, respectively. We chose ligand **1h** as one example to elaborate the partial racemization (Fig. 1). The Ru-complex of optically pure ligand (*R*)-**1g** showed sole peak at 46.00 ppm in ^{31}P NMR spectrum (Fig. 1, C), and the similar Ru-complex of racemic ligand (±)-**1g** showed a couple of same absorption intensity peaks at 46.04 ppm and 45.69 ppm in ^{31}P NMR spectrum (Fig. 1, B). However, one stronger peak at 46.04 ppm and one weaker peak at 45.70 ppm were showed in the ^{31}P NMR spectrum of the Ru-complex of ligand **1g**, this one ligand was synthesized through the procedure as described in Scheme 3. It can be seen from Figure 1 that the stronger peak (46.04 ppm, Fig. 1, A), the left peak (46.04 ppm, Fig. 1, B), and the sole peak (46.00 ppm Fig. 1, C) should be assigned to Ru-complex of (*R*)-isomer **1h**. Meanwhile, the weaker peak (45.70 ppm, Fig. 1, A), the right peak (45.69 ppm, Fig. 1, B) belong to Ru-complex of (*S*)-isomer **1h**. From these, we concluded that ligand **1h** had partial racemized during the course of preparation, but the cause of partial racemization in synthesizing ligands **1e**, **1f**, and **1h** through the procedure as described in Scheme 3 is unclear.

Yokozawa and Saito recently developed the phosphination reaction of BINOL ditriflate with diphenylphosphine catalyzed by a Pd-complex generated in situ from $Pd_2(dba)_3\cdot CHCl_3$ and dppp, and achieved optically active BINAP in high yield.[9c] Based on this literature procedure,[9c] the phosphination reactions of 7,7′-disubstituted BINOL ditriflates **5e**, **5f**, and **5h** with diphenylphosphine were conducted in the presence of 5 mol % palladium catalyst generated in situ from $Pd_2(dba)_3\cdot CHCl_3$ and dppp using DMF as solvent at 100 °C (Scheme 4). We were pleased to find that not only this method smoothly provided the desired products but also this approach tolerated a wide range of substrates regardless of the substituents' structure in the 7,7′-positions. Thus, all the chiral ligands **1a**–**h** were obtained in good yields without any racemization (Scheme 4). This new family of optically pure 7,7′-disubstituted BINAPs were smoothly prepared from corresponding 7,7′-disubstituted BINOLs obtained from the catalytic asymmetric oxidative coupling reaction. To the best of our knowledge, this synthetic route is the most concise and straightforward to prepare 7,7′-disubstituted BINAPs ligand to date.

2.2. Rh-catalyzed 1,4-addition of aryl boronic acids to enones

Among the catalytic asymmetric carbon–carbon bond formation reactions catalyzed by chiral transition metal complexes, the catalytic asymmetric 1,4-addition reaction holds a prominent position because it is frequently used in organic synthesis.[15] Considerable efforts have been recently made on the asymmetric 1,4-addition of organometallic reagents to electron deficient olefins and the important progress has been achieved in this field.[16] One of the significant cases, Rh-catalyzed highly enantioselective 1,4-addition addition of aryl boronic acids to enones was reported by Hayashi and co-workers in 1998.[17]

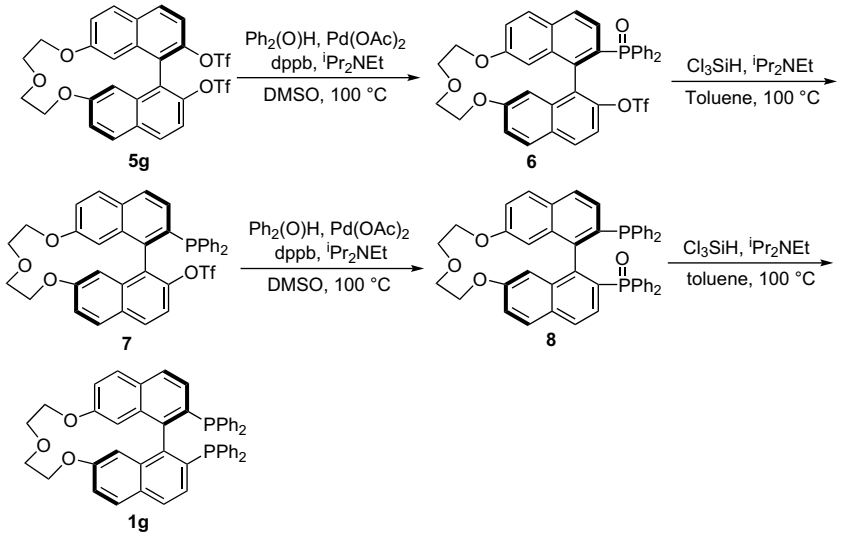
To evaluate the catalytic potential of ligands **1a**–**h** in the asymmetric catalysis, we first explored Rh-catalyzed enantioselective 1,4-addition of aryl boronic acids to enones. A model reaction of cyclohexenone **9a** with phenyl boronic acid **10a** was carried out in the presence of Ru-complex in situ generated from Rh(acac)$(C_2H_4)_2$ and either of ligands **1a**–**h** according to the literature reaction conditions.[17] As shown in Table 1, all the ligands were excellent for the 1,4-addition reaction, good to excellent yields with high enantioselectivities were obtained. High to 98% and 99% ees



Scheme 2. The synthesis of ligands **1a–d**.

were obtained with **1b** or **1c** as chiral ligand, respectively (Table 1, entries 2 and 3), but ligand BINAP gave 97% ee.[17] Ligand **1g** resulted in the corresponding adduct in nearly quantitative yield and 97% ee under the same condition (Table 1, entry 7). Ligands **1a**, **1d–1f**, and **1h** all resulted in very high catalytic activity and enantioselectivity (Table 1, entries 1, 4–6, and 8). These observations indicate that the substituents at 7,7′-positions of the ligands have some effect on the ligand's stereocontrol ability. Notably, decreasing the catalyst loading from 3 mol % to 1 mol %, product **11a** was obtained in 97% ee and 92% yield (Table 1, entry 9). Further decreasing the catalyst loading to 0.5 mol %, product **11a** was obtained in 92% ee and 75% yield with a slightly prolonged reaction time (Table 1, entry 10). Electron-donating groups at 7 and 7′ positions of BINAP scaffold may increase the electron density of the phosphine atom comparing that of mother BINAP. The electron rich phosphorus may therefore contribute to the higher activity.

Ligand **1g** was chosen to perform the further study because it provided the very comparable results to BINAP under the same reaction.[17] The 1,4-additions of a range of aryl boronic acids bearing either electron-donating or -withdrawing groups to cyclohexenone



Scheme 3. The synthesis of ligand **1g**.

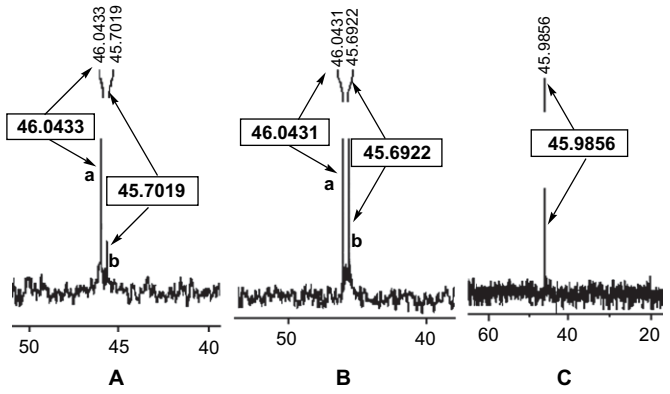


Figure 1. The ^{31}P NMR spectra of Ru-complexes for different purity ligands **1h**. A: The ligand **1h** synthesized by procedure as described in Scheme 3; (major *R* and minor *S*)-**1h**–$RuCl_2$–(*RR*)DPEN, peak **a**, $\delta \approx 46.04$ ppm; peak **b**, $\delta \approx 45.70$ ppm. B: (*rac*)-**1h**–$RuCl_2$–(*RR*)DPEN, peak **a**, $\delta \approx 46.04$ ppm; peak **b**, $\delta \approx 45.69$ ppm. C: (*R*)-**1h**–$RuCl_2$–(RR)DPEN, single peak $\delta \approx 46.00$ ppm.

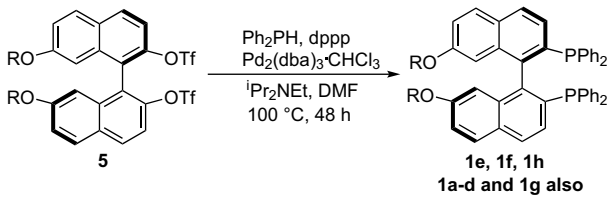
were conducted. As shown in Table 2, excellent ee values ranging from 94% to 99.8% were obtained and all the reactions successfully proceeded in 5 h and gave the corresponding adducts in very high yields. 4-*tert*-Butylboronic acid **10e** and 4-trifluorometyhlboronic acid **10f** both underwent the catalytic asymmetric additions and the resulting adducts were obtained in even over 99% ee (Table 2, entries 5 and 6). It is obvious from the results in Table 2 that the catalyst Rh(I)–**1g** possesses very high activity and stereocontrol ability in the 1,4-addition of aryl boronic acids **10a**–**g** to cyclohexenone **9a** and these results are comparable to BINAP in these reactions.[17]

The optimized protocol was then extended to different types of α,β-unsaturated ketones. The results were summarized in Table 3. Rh(I)–**1g** exhibited high enantioselectivities for various α,β-unsaturated ketones. Comparing with cyclohexenone **9a** (Table 2, entry 1), cyclopentenone **9b** and cycloheptenone **9c** resulted in slightly lower, but still high, up to 90% ee values, respectively (Table 2, entries 2 and 3), which were similar to the results provided with BINAP served as catalyst in the same reaction.[17] However, phenyl boronic acid added to a linear enone substrate **9d** furnishing **11da** in 88% yield and a 97% ee (Table 2, entry 4). This result also is similar to that of Rh(I)–BINAP catalyzed same reaction.[17]

In term of all the results summarized in Tables 1–3, 7,7′-disubstituted BINAPs ligands **1a**–**h** demonstrated the considerable catalytic potential for catalytic asymmetric 1,4-addition reactions of aryl boronic acids to both cyclic and linear enones with high activities and enantioselectivites. These results were comparable to the best results observed with BINAP as ligand in this reaction.

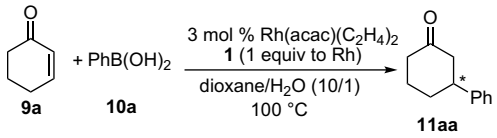
2.3. Ru-catalyzed enantioselective hydrogenation of simple aromatic ketones

Among the extraordinary advances achieved in catalytic asymmetric reactions, asymmetric hydrogenation remains to be an attractive method to prepare chiral material due to the fact that it provides a powerful, efficient, and atom economic avenue for biologically active compounds and advanced materials.[2a,18] The



Scheme 4. The synthesis of ligands **1e**, **1f**, and **1h**.

Table 1
1,4-Addition of phenyl boronic acid to cyclohexenone catalyzed by ligands **1**–Rh(I) complexes[a]



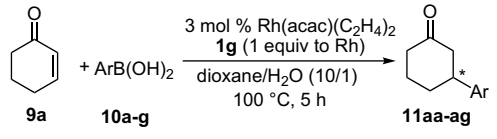
Entry	Ligand	Time (h)	Yield[b] (%)	ee[c] (%)
1	**1a**	5	83	94
2	**1b**	5	93	98
3	**1c**	5	90	99
4	**1d**	5	85	96
5	**1e**	5	90	91
6	**1f**	5	82	92
7	**1g**	5	99	97
8	**1h**	5	92	97
9	**1g**	5	92	97[d]
10	**1g**	8	75	92[e]

[a] For a general reaction procedure, see Experimental section.
[b] Isolated yield based on cyclohexenone **9a**.
[c] The ee values were determined by HPLC and the absolute configuration was *R* assigned by comparison of the sign of the optical rotation with reported data.[17]
[d] In the presence of 1.0 mol % catalyst.
[e] In the presence of 0.5 mol % catalyst.

catalytic asymmetric hydrogenation of prochiral simple aromatic ketones appears to be the most facile route to produce enantiomerically enriched secondary alcohols, which are important building blocks for the synthesis of many natural products and pharmaceutical compounds. This reaction has been also extensively used as a model reaction to evaluate various diphosphine ligands in asymmetric hydrogenation.[19] Our further exploration of 7,7′-disubstituted BINAPs ligands **1a**–**h** in asymmetric catalysis was focused on applying Ru-complex of this class of ligands to this hydrogenation reaction. These reactions were performed with the literature catalytic system developed by Noyori and co-workers.[20]

The catalysts were easily prepared according to the following procedure. The reaction mixture of ligands **1a**–**h** and 0.5 equiv $[RuCl_2(benzene)]_2$ in anhydrous and degassed DMF was stirred for 10 min at 100 °C, followed by addition of 1.0 equiv of (*R*,*R*)-1,2-diphenylethylenediamine (DPEN) to the reddish solution at room temperature. The resulting mixture was stirred for 3–4 h at room temperature. The solvent was removed under high vacuum at 50 °C and the light brown complex was used for hydrogenation reaction without further purification. All the catalysts showed single signal in the ^{31}P NMR spectrum and the chemical shift values (δ) were listed in Table 4.

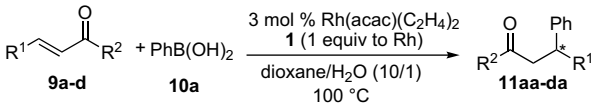
Table 2
Asymmetric 1,4-addition of arylboronic acids to cyclohexenone catalyzed by ligands Rh(I)–**1g** complex[a]

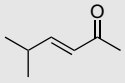


Entry	$ArB(OH)_2$	Ar	Yield[b] (%)	ee[c] (%)
1	**10a**	Ph	99	97
2	**10b**	4-ClC_6H_4	85	98
3	**10c**	4-$MeOC_6H_4$	90	96
4	**10d**	3-$MeOC_6H_4$	92	96
5	**10e**	4-$^tBuC_6H_4$	86	99
6	**10f**	4-$CF_3C_6H_4$	84	99.8
7	**10g**	4-$CH_3C_6H_4$	97	94

[a] For a general reaction procedure, see Experimental section.
[b] Isolated yields based on cyclohexenone **9a**.
[c] The ee values were determined by HPLC and the absolute configuration was *R* assigned by comparison of the sign of the optical rotation with reported data.[17]

Table 3
Asymmetric 1,4-addition of phenyl boronic acids to enones **11** catalyzed by ligands **1g**–Rh(I) complex[a]



Entry	Enones **9**	Time (h)	Yield[b] (%)	ee[c] (%)
1	 **9a**	5	99	97
2	 **9b**	5	90	90[d]
3	 **9c**	5	82	90
4	 **9d**	5	88	97

[a] For a general reaction procedure, see Experimental section.
[b] Isolated yield based on unsaturated ketones **9a**–**d**.
[c] The ee values were determined by HPLC and the absolute configuration was *R* assigned by comparison of the sign of the optical rotation with reported data.[17]
[d] The ee value was determined by GC and the absolute configuration was *R* assigned by comparison of the sign of the optical rotation with reported data.[17]

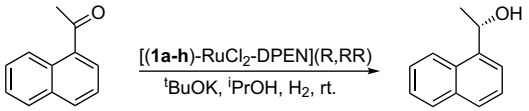
With these optically active catalysts in hand, 1-acetonaphthone **12a** was chosen as a model substrate to optimize ligands and reaction conditions. The results were summarized in Table 5. As can be seen in Table 5, 1-acetonaphthone **12a** could be smoothly reduced to alcohol **13a** in 8 h with very high enantioselectivies with the catalysts formed from ligands **1a**–**h** (Table 5, entries 1–8). The best results, 100% conversion and 98% ee, were obtained with the catalyst generated from ligand **1c** under 40 atm of hydrogen pressure and a catalyst loading of 0.05 mol % at room temperature (Table 5, entry 3). This result is slight better than that obtained with complex [$RuCl_2$\{(*R*)-BINAP\}\{(*R*,*R*)-DPEN\}] as a precatalyst.[20] To further examine the catalytic potential, we found that more than 99% conversion and 97% ee were obtained in 10 h by decreasing the catalyst loading to 0.02 mol % (Table 5, entry 9). The catalyst loading was decreased to 0.01 mol % without loss of enantioselectivity, but the reaction required prolonged time of 16 h (Table 5, entry 10). It is noteworthy that the catalyst was further decreased to 0.001 mol %, to get the same results, we only need to prolong the reaction to 30 h and elevate the reaction temperature to 60 °C (Table 5, entry 11).

The optimized protocol was then extended to a variety of aromatic ketones in order to further examine the ligands. The hydrogenation reactions were conducted with 0.05% loading of Ru-complex formed from ligand **1c** under 40 atm of hydrogen pressure at room temperature. The results are summarized in Table 6. It was

Table 4
The chemical shift values (δ) of ^{31}P NMR signal of catalysts derived from ligands **1a**–**h**

Entry	1	2	3	4	5	6	7	8
Ligand	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**
δ (ppm)	45.70	45.72	45.70	45.67	46.41	45.90	46.68	46.00

Table 5
Enantioselective hydrogenation of 1-acetonaphthone (**12a**) to alcohol **13a**[a]



Entry	Ligand	*S*/*C*[b]	Time (h)	Conv[c] (%)	ee[d] (%)
1	**1a**	2000	8	100	96
2	**1b**	2000	8	100	96
3	**1c**	2000	8	100	98
4	**1d**	2000	8	100	96
5	**1e**	2000	8	100	92
6	**1f**	2000	8	100	96
7	**1g**	2000	8	100	91
8	**1h**	2000	8	100	94
9	**1c**	5000	10	>99	97
10	**1c**	10,000	16	>99	97
11	**1c**	100,000	30	>99	97[e]

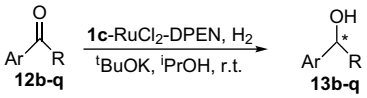
[a] Unless otherwise stated, the reaction was conducted at 25–28 °C with a 1.0 M solution of substrate (2 mmol) in 2-propanol in the presence of $(CH_3)_3COK$ (base/catalyst=70:1). H_2 pressure was 40 atm.
[b] The molar ratio of substrate to catalyst.
[c] Determined by GC on CP-Cyclodex β-236M column or crude ^1H NMR.
[d] Determined by GC on CP-Cyclodex β-236M column. Absolute configuration is *S* and assigned by the sign of rotation.
[e] The solution concentration was 2.0 M. and temperature was 60 °C.

found that methyl ketone substrates containing an electron-donating or -withdrawing group at *ortho*-position of phenyl ring were the better substrates for asymmetric hydrogenation (Table 6, entries 1, 12, and 16), while containing *meta*- or *para*-substituent substrates gave lower enantioselectivites than that containing *ortho*-substituent substrates. For instance, substrate **12m** was hydrogenated to give the product in 94% ee, whereas **12n** gave only 71% ee under the same conditions (Table 6, entries 12 and 13). Analogous examples, substrates **12b** and **12h** gave the products in 90% and 81% ee under identical conditions, respectively (Table 6, entries 1 and 7). The reduction of 2′-acetonaphthone **12k** gave only 77% ee (Table 6, entry 10), but the model substrate 1′-acetonaphthone **12a** afforded 98% ee (Table 5, entry 3). Comparing *meta*-*para*-disubstituted substrate **12o** with *ortho*-*para*-disubstituted substrate **12p**, the former afforded 77% ee but the latter afforded 90% ee under the same conditions. These results suggest the *ortho*-substituted group has important effects on the enantioselectivity (Table 6, entries 14 and 15). Interestingly, substrates **12f** and **12g** bearing the same substituent group in the phenyl ring were smoothly reduced under the same conditions but exhibited different enantioselectivity, which may be due to the different electronic effect resulted from the positions' difference of substituents in phenyl ring (Table 6, entries 5 and 6).

We also found that the size of the alkyl substituent in aromatic ketones **12** was another factor to influence the enantioselectivity. Only a slight drop was observed comparing propiophenone **12i** with benzylphenone **12e** (Table 6, entries 8 and 4), but an apparent ee value decrease from 88% to 73% was observed by comparing isopropylphenone **12j** with benzylphenone **12e** (Table 6, entries 4 and 9). Since 1-ferrocenylethanol is a crucial starting material in the synthesis of many chiral ferrocene compounds such as ferrocenylethylamines and ferrocenylphosphines,[21] we subjected acetylferrocene **12l** under the optimized conditions and it was reduced to (*S*)-1-ferrocenylethanol in 79% ee at *S*/*C*=1000 (Table 6, entry 11).

Based on all of the above observations, we can easily conclude that Ru-complexes (*RRR*)-[(**1a**–**h**)–$RuCl_2$–DPEN] are highly active and efficient in catalytic asymmetric hydrogenation of simple aromatic ketones. Almost quantitative yields and moderate to excellent enantioselectivities are furnished throughout all the substrates

Table 6
Enantioselective hydrogenation reactions of aromatic ketones catalyzed by (*RRR*)-**1c**–$RuCl_2$–DPEN complex[a]



Entry	Ketone	Ar	R	Time (h)	Conv[b] (%)	ee[c] (%)
1	**12b**	*o*-$CH_3C_6H_5$	CH_3	8	100	90
2	**12c**	C_6H_5	CH_3	8	>99	81
3	**12d**	C_6H_5	$(CH_2)_3CH_3$	8	>99	87
4	**12e**	C_6H_5	CH_2Ph	8	>99	88[d]
5	**12f**	*m*-$CH_3OC_6H_5$	CH_3	8	100	88
6	**12g**	*p*- $CH_3OC_6H_5$	CH_3	8	>99	78
7	**12h**	*p*-$CH_3C_6H_5$	CH_3	8	>99	81
8	**12i**	C_6H_5	CH_2CH_3	8	100	85
9	**12j**	C_6H_5	$CH(CH_3)_2$	8	>99	73
10	**12k**	2′-Naphthyl	CH_3	8	100	77
11	**12l**	Ferrocenyl	CH_3	12	>99	79[d,e]
12	**12m**	*o*-ClC_6H_5	CH_3	10	100	94
13	**12n**	*m*-ClC_6H_5	CH_3	10	100	71
14	**12o**	3,4-$(CH_3O)_2C_6H_5$	CH_3	8	>99	77
15	**12p**	2,4-$(Cl)_2C_6H_5$	CH_3	10	100	90
16	**12q**	*o*-BrC_6H_5	CH_3	15	>99	94[e]

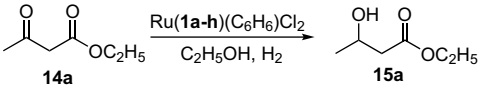
[a] Unless otherwise stated, the reaction was conducted at 25–28 °C with 1.0 M solution of substrate (2 mmol) in 2-propanol in the presence of $(CH_3)_3COK$ (base/catalyst=70:1). H_2 pressure was 40 atm. The molar ratio of substrate to catalyst is 2000.
[b] Determined by GC on CP-Cyclodex β-236 M column or ^1H NMR.
[c] Determined by GC on CP-Cyclodex β-236 M column. Absolute configuration was *S* and determined by the sign of rotation.
[d] The ee values were determined by HPLC and the absolute configuration was *S*.
[e] *S*/*C*=1000. The solution concentration was 2.0 M and the temperature was 60 °C.

examined, in addition, these results obtained herein are slight better or similar to those provided by their analogue complex $RuCl_2$[(*R*)-BINAP][(*R*,*R*)-DPEN] in the same hydrogenation reaction.[20]

2.4. Ru-catalyzed enantioselective hydrogenation of β-ketoesters

Optically pure β-hydroxyl ester belongs to a very important class of compound, because they are widely used for natural products synthesis.[22] To the best of our knowledge, among the studies reported, one of the most successful protocols is the asymmetric hydrogenation of β-ketoesters using chiral Ru-complex of phosphine ligand as catalyst.[1a,18a,23] Initially, Noyori and co-workers successfully reported that the chiral ruthenium catalyst of BINAP was efficient for this reaction.[23a] To further investigate the utility of ligands **1a**–**h** in the asymmetric catalysis, another asymmetric

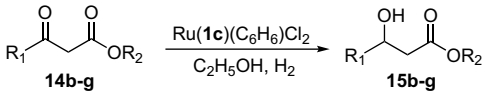
Table 7
Asymmetric hydrogenation of ethyl acetoacetate with **1a**–**h** as the ligands[a]

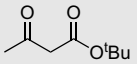
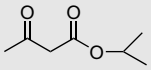
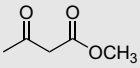
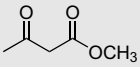
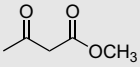
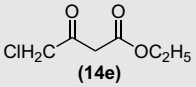
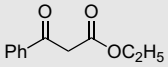
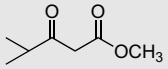


Entry	Ligand	*T* (°C)	*P* (atm)	Conv[b] (%)	ee[c] (%)
1	**1a**	50	30	100	98
2	**1b**	50	30	100	97
3	**1c**	50	30	100	98
4	**1d**	50	30	100	97
5	**1e**	50	30	100	97
6	**1f**	50	30	100	97
7	**1g**	50	30	100	96
8	**1h**	50	30	100	98
9	**1c**	85	30	100	98
10	**1c**	50	60	100	98

[a] Unless otherwise stated, the reaction was carried out in EtOH with 1.0 M solution of substrate (2 mmol) for 12 h. The molar ratio of substrate to catalyst was 1000.
[b] Determined by GC on β-225 capillary column or crude ^1H NMR.
[c] Determined by GC on β-225 capillary column.

Table 8
Asymmetric hydrogenation of β-ketoesters with **1c** as the ligand[a]



Entry	Substrate	*S*/*C*[b]	Time (h)	Conv[c] (%)	ee[d] (%)
1	 **(14b)**	1000	12	>99	96
2	 **(14c)**	1000	12	>99	98
3	 **(14d)**	1000	12	100	99
4	 **(14d)**	5000	15	100	98
5	 **(14d)**	10,000	20	>99	98
6	 **(14e)**	1000	12	>99	91[e]
7	 **(14f)**	1000	26	>99	85[f]
8	 **(14g)**	1000	12	100	99.8

[a] Unless otherwise stated, the reaction was carried out in EtOH with 1.0 M solution of substrate (2 mmol) and 30 atm of hydrogen pressure at 50 °C.
[b] The molar ratio of substrate to catalyst.
[c] Determined by GC on a β-225 capillary column or crude ^1H NMR.
[d] Determined by GC on a β-225 capillary column.
[e] Product was acylated to 3-acetoxy-4-chloro-butyric acid ethyl ester **15e** in pyridine and acetic anhydride for ee value determination by GC analysis.
[f] The conversion and ee value were determined by HPLC on Chiralpak OD-H column. Additive is HI, substrate/[Ru(benzene)Cl_2]/ligand/adductive=1000:1:1.1:1.5.

hydrogenation reaction was examined with these ligands. Herein, we present the results of apply ligands **1a**–**h** in catalytic asymmetric hydrogenation of β-ketoesters to chiral β-hydroxyl esters according to the literature procedure.[23a]

Initial studies were aimed at determining the most optimal reaction conditions for the asymmetric hydrogenation of β-ketoesters using ethyl acetoacetate **14a** as a standard substrate. The experimental results are summarized in Table 7. It was found that all of the catalysts, which were in situ generated from [$RuCl_2$(benzene)]$_2$ and 2 equiv of ligands **1a**–**h**, exhibited high activity and gave excellent enantioselectivity under the mild conditions (*S*/*C*=1000, 50 °C, 30 atm, and EtOH as solvent) (Table 7, entries 1–8). Under the optimized reaction conditions, we found that elevating temperature from 50 °C to 85 °C under 30 atm of H_2 pressure (Table 7, entry 9) or increasing H_2 pressure from 30 atm to 60 atm at 50 °C (Table 7, entry 10) both using **1c** as ligand, the conversion and ee values were maintained. Based on these preliminary results, we chose ligand **1c**, reaction temperature 50 °C, *S*/*C*=1000, and 30 atm of hydrogen pressure as the set of optimized conditions.

As a reasonable extension of the optimized procedure, hydrogenation reactions of a variety of β-ketoesters were then performed

and all the results are listed in Table 8. The results indicated that very high enantioselectivities and almost complete conversions were achieved with Ru-complex formed from ligand **1c** in all cases (Table 8). We also found that ligand **1c** proceeded well in the asymmetric reduction of alkyl acetoacetates regardless of the bulkiness of the alkyl group (Table 8, entries 1–3). Ligand **1c** exhibited excellent stereocontrol ability in the asymmetric hydrogenation of not only linear alkyl-substituted β-keto methyl ester **14e** (Table 8, entry 6) but also branched alkyl-substituted β-keto ethyl ester **14g** with excellent 99.8% ee (Table 8, entry 8). Substrate methyl acetoacetate (**14d**) was reduced in 99% ee value and 100% conversion under the standard set of reaction conditions (Table 8, entry 3). Notably, increasing the substrate-to-catalyst ratio to 5000 and 10,000, respectively, the reactions also proceeded smoothly and afforded 98% ee values with slightly prolonging the reaction times to 15 h and 20 h (Table 8, entries 4 and 5). When substrate 3-oxo-3-phenyl-propionic acid ethyl ester **14f** was subjected to hydrogenation reaction, the product was obtained in 85% ee, and HI was required as an additive under the optimized reaction conditions (Table 8, entry 7). This 85% ee value was same as what was observed when BINAP used as ligand in this reacion.[23a]

In summary, a series of 7,7′-disubstituted BINAPs **1a**–**h** were applied in Ru-catalyzed enantioselective hydrogenation of aryl- and alkyl-substituted β-ketoesters. We found these catalysts formed from ligands **1a**–**h** behaved very well under mild and concise reaction conditions, and these reactions afforded the corresponding reductive products in excellent conversions and very good enantioselectivity up to 99.8% ee. These 7,7′-disubstituted BINAPs ligands showed the comparable catalytic activity and enantiocontrol potential to BINAP ligand in the same hydrogenation of β-ketoesters.[23a]

3. Conclusion

In summary, starting from chiral oxovanadium complex catalyzed asymmetric oxidative coupling reaction, a class of optically pure 7,7′-disubstituted BINAPs **1a**–**h** have been prepared via different synthetic routes due to the 7,7′-disubstitutents' difference from each other in their 7,7′-positions. Furthermore, a general, concise, and straightforward approach that is suitable to prepare all optically pure 7,7′-disubstituted BINAPs **1a**–**h**, regardless of the substituents' structure in the 7,7′-positions, has been successfully developed for the first time. Their catalytic potential also has been demonstrated in the highly enantioselective Rh-catalyzed 1,4-additions of aryl boronic acids to α,β-unsaturated ketones and Ru-catalyzed asymmetric hydrogenation of both simple aromatic ketones and β-ketoesters with high activity and selectivity.

4. Experimental

4.1. General remarks

All reactions and manipulations were performed in an argon-filled glovebox or using standard Schlenk techniques. Ru(acac)$(C_2H_4)_2$, enone, $Ph_2P(O)H$, dppb, $Pb(OAc)_2$, Ph_2PH, Ni(dppe)Cl_2, aromatic ketones, and β-ketoesters and others were purchased from Aldrich or Acros chemical company. Anhydrous toluene and dioxane were distilled from sodium benzophenone ketyl. CH_2Cl_2, DMSO, ^{i}PrOH, and C_2H_5OH were freshly distilled from calcium hydride. ^{1}H, ^{13}C, ^{31}P NMR spectra were recorded on a Brucker-300 MHz spectrometer. Optical rotations were measured on a Perkin–Elmer 241 Polarimeter. HPLC analysis was performed on BECKMAN (110B Solvent Delivery Module and 168 Detector). GC analysis was performed using a Hewlett Packard Model HP 6890 Series. IR spectra were recorded on NICOLET MX-1E FT-IR. ESI MS spectra were recorded on Bruker BIO TPF Q.

4.2. General procedure for synthesis of 7,7′-disubstituted-binaphthols ditriflate 5a–h

To a solution of **4a**–**h** (20.0 mmol) in 50 mL of CH_2Cl_2 was added pyridine (3.9 g, 4.1 mL, 50.0 mmol) and followed by dropwise addition of triflic anhydride Tf_2O (13.0 g, 7.8 mL, 46 mmol) at 0 °C. The mixture was stirred at room temperature for 5 h. The mixture was diluted with CH_2Cl_2 and then washed with 2.0 M aqueous HCl, saturated $NaHCO_3$, and brine. The organic layer was extracted and dried over anhydrous sodium sulfate, concentrated under reduced pressure, then passed through a silica gel plug (eluted with CH_2Cl_2) to give the corresponding products **5a**–**h**.

*4.2.1. (R)-Trifluoro-methanesulfonic acid 7,7′-dimethoxy-2′-trifluoromethanesulfonyloxy-1,1′-binaphthalenyl-2-yl ester (**5a**)*

White foam solid, yield 97%. Mp 106.7–107.9 °C. $[\alpha]_D^{20}$ −292.3 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.52 (s, 6H), 6.52 (d, *J*=2.4 Hz, 2H), 7.23 (dd, *J*=9.0, 2.4 Hz, 2H), 7.46 (d, *J*=9.0 Hz, 2H), 7.89 (d, *J*=9.0 Hz, 2H), 8.04 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.2, 105.0, 116.0, 116.7, 120.1, 122.2, 127.8, 129.9, 131.5, 134.5, 146.0, 159.1. IR (KBr) 3085.6, 2952.5, 2831.0, 1625.8, 1586.2, 1506.6, 1465.6, 1244.9, 1226.6, 992.3, 869.8 cm^{-1}. HRMS (ESI) calcd for $(C_{24}H_{16}F_6O_8S_2+Na)^+$: *m*/*z* 633.0191, found *m*/*z* 633.0199.

*4.2.2. (R)-Trifluoro-methanesulfonic acid 7,7′-diethoxy-2′-trifluoromethanesulfonyloxy-1,1′-binaphthalenyl-2-yl ester (**5b**)*

White foam solid, yield 98%. Mp 66.8–67.6 °C. $[\alpha]_D^{20}$ −306.4 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 (t, *J*=6.9 Hz, 6H), 3.62–3.76 (m, 4H), 6.52 (d, *J*=1.8 Hz, 2H), 7.23 (dd, *J*=9.0, 1.8 Hz, 2H), 7.43 (d, *J*=9.0 Hz, 2H), 7.89 (d, *J*=9.0 Hz, 2H), 8.04 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 63.2, 105.7, 116.0, 116.6, 120.4, 122.2, 127.8, 129.8, 131.4, 134.6, 145.9, 158.4. IR (KBr) 3073.1, 2980.0, 2933.2, 1623.7, 1507.1, 1482.1, 1453.0, 1424.3, 1394.0, 1221.6, 1164.9, 1141.5, 1042.9, 916.7, 868.8, 839.0 cm^{-1}. HRMS (ESI) calcd for $(C_{26}H_{20}F_6O_8S_2+Na)^+$: *m*/*z* 661.0504, found *m*/*z* 661.0502.

*4.2.3. (R)-Trifluoro-methanesulfonic acid 7,7′-dipropoxy-2′-trifluoromethanesulfonyloxy-1,1′-binaphthalenyl-2-yl ester (**5c**)*

Colorless oil, yield 98%. $[\alpha]_D^{20}$ −310.7 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, *J*=6.3 Hz, 6H), 1.59–1.66 (m, 4H), 3.54–3.67 (m, 4H), 6.52 (d, *J*=1.5 Hz, 2H), 7.22–7.26 (m, 2H), 7.44–7.47 (m, 2H), 7.89 (d, *J*=9.0 Hz, 2H), 8.04 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.3, 22.1, 69.3, 105.7, 116.0, 116.6, 120.3, 120.4, 122.2, 127.8, 129.8, 131.4, 134.6, 146.0, 158.6. IR (film) 2968.6, 2939.5, 2880.3, 1623.5, 1585.2, 1506.5, 1451.6, 1421.7, 1389.4, 1246.8, 1223.9, 1165.0, 1140.8, 969.5, 879.8, 836.0 cm^{-1}. HRMS (ESI) calcd for $(C_{28}H_{24}F_6O_8S_2+Na)^+$: *m*/*z* 689.0817, found *m*/*z* 689.0811.

*4.2.4. (R)-Trifluoro-methanesulfonic acid 7,7′-diisopropoxy-2′-trifluoromethanesulfonyloxy-1,1′-binaphthalenyl-2-yl ester (**5d**)*

White foam solid, yield 93%. Mp 138.7–139.9 °C. $[\alpha]_D^{20}$ −379.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.99 (d, *J*=6.0 Hz, 6H), 1.15 (d, *J*=6.0 Hz, 6H), 4.11–4.19 (m, 2H), 6.49 (d, *J*=2.4 Hz, 2H), 7.19 (dd, *J*=9.0, 2.4 Hz, 2H), 7.88 (d, *J*=9.0 Hz, 2H), 8.02 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 21.7, 69.8, 107.5, 116.0, 116.6, 120.3, 121.0, 122.1, 127.6, 129.9, 131.4, 134.6, 145.9, 157.3. IR (KBr) 3049.5, 2962.4, 2933.3, 2874.7, 1618.1, 1584.4, 1501.9, 1432.3, 1387.2, 1267.6, 1219.0, 1106.9, 1067.1, 1024.8, 989.7, 838.4, 741.4, 694.4 cm^{-1}. HRMS (ESI) calcd for $(C_{28}H_{24}F_6O_8S_2+Na)^+$: *m*/*z* 689.0817, found *m*/*z* 689.0800.

*4.2.5. (R)-Trifluoro-methanesulfonic acid 7,7′-cyclohexyloxy-2′-trifluoromethanesulfonyloxy-1,1′-binaphthalenyl-2-yl ester (**5e**)*

White foam solid, yield 94%. Mp 71.1–72.4 °C. $[\alpha]_D^{20}$ −259.4 (*c* 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26–1.29 (m, 4H), 1.30–1.36 (m, 2H), 1.40–1.51 (m, 2H), 3.82–3.89 (m, 2H), 4.00–4.07 (m,

2H), 6.66 (d, J=2.4 Hz, 2H), 7.26 (dd, J=9.0, 2.4 Hz, 2H), 7.45 (d, J=9.0 Hz, 2H), 7.90 (d, J=9.0 Hz, 2H), 8.03 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.0, 27.3, 66.8, 109.7, 116.1, 117.2, 120.0, 122.0, 1278.0, 130.1, 131.6, 134.1, 146.2, 157.6. IR (KBr) 3033.5, 2934.2, 2861.9, 1623.6, 1582.3, 1504.4, 1452.0, 1422.2, 1245.4, 1214.7, 1140.5, 984.7, 870.8 cm^{-1}. HRMS (ESI) calcd for $(C_{28}H_{22}F_6O_8S_2+Na)^+$: m/z 687.0660, found m/z 687.0665.

*4.2.6. (R)-Trifluoro-methanesulfonic acid 7,7′-cyclooctyloxy-2′-trifluoromethanesulfonyloxy-1,1′-binaphthalenyl-2-yl ester (**5f**)*

White foam solid, yield 93%. Mp 64.0–65.7 °C. $[\alpha]_D^{20}$ −259.5 (c 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06–1.08 (m, 2H), 1.17–1.19 (m, 2H), 1.26–1.53 (m, 8H), 3.70–3.78 (m, 2H), 3.83–3.88 (m, 2H), 6.60 (d, J=2.4 Hz, 2H), 7.24 (dd, J=9.0, 2.4 Hz, 2H), 7.44 (d, J=9.0 Hz, 2H), 7.90 (d, J=9.0 Hz, 2H), 8.03 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1, 27.0, 27.1, 66.6, 107.0, 116.0, 116.9, 119.9, 122.1, 127.8, 130.0, 131.5, 134.3, 146.1, 158.1. IR (KBr) 3083.7, 2933.8, 2860.0, 1623.4, 1505.1, 1422.0, 1245.4, 1217.5, 1140.1, 957.8, 873.3 cm^{-1}. HRMS (ESI) calcd for $(C_{30}H_{26}F_6O_8S_2+Na)^+$: m/z 715.0973, found m/z 715.0960.

*4.2.7. (R)-Trifluoro-methanesulfonic acid 7,7′-2crown-2′-trifluoromethanesulfonyloxy-1,1′-binaphthalenyl-2-yl ester (**5g**)*

White foam solid, yield 90%. Mp 121.7–122.3 °C. $[\alpha]_D^{20}$ −263.7 (c 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.44–3.55 (m, 4H), 3.83–3.89 (m, 2H), 4.29–4.34 (m, 2H), 7.03 (d, J=2.4 Hz, 2H), 7.20 (dd, J=9.0, 2.4 Hz, 2H), 7.40 (d, J=9.0 Hz, 2H), 7.84 (d, J=9.0 Hz, 2H), 8.00 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 65.9, 73.1, 108.2, 117.0, 120.3, 121.6, 122.1, 127.9, 129.5, 131.5, 134.0, 146.2, 158.5. IR (KBr) 3069.2, 2956.4, 2868.6, 1623.4, 1504.7, 1422.6, 1245.6, 1215.1, 1140.9, 992.9, 862.7 cm^{-1}. HRMS (ESI) calcd for $(C_{26}H_{18}F_6O_9S_2+Na)^+$: m/z 675.0296, found m/z 675.0290.

*4.2.8. (R)-Trifluoro-methanesulfonic acid 7,7′-3crown-2′-trifluoromethanesulfonyloxy-1,1′-binaphthalenyl-2-yl ester (**5h**)*

White foam solid, yield 91%. Mp 79.5–80.9 °C. $[\alpha]_D^{20}$ −276.0 (c 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.43–3.62 (m, 8H), 3.91–3.98 (m, 4H), 6.61 (d, J=2.4 Hz, 2H), 7.29 (dd, J=9.0, 2.4 Hz, 2H), 7.45 (d, J=9.0 Hz, 2H), 7.90 (d, J=9.0 Hz, 2H), 8.04 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 67.9, 69.0, 71.1, 107.0, 116.0, 117.1, 120.5, 122.1, 127.9, 130.1, 131.6, 134.1, 146.1, 158.0. IR (KBr) 3069.2, 2924.6, 2869.6, 1623.6, 1585.2, 1505.2, 1446.0, 1421.4, 1246.0, 1220.3, 1164.0, 1139.7, 911.4, 867.2, 837.7 cm^{-1}. HRMS (ESI) calcd for $(C_{28}H_{22}F_6O_{10}S_2+Na)^+$: m/z 719.0559, found m/z 719.0548.

4.3. A general procedure for synthesis of 7,7′-disubstituted BINAPs ligands 1a–d catalyzed by $NiCl_2$(dppe)

A solution of [$NiCl_2$(dppe)] (0.4 mmol, 106 mg) in anhydrous DMF (3.0 mL) was degassed. Ph_2PH (1.5 mmol, 0.26 mL) was added and the mixture was heated at 100 °C for 1 h. A degassed solution containing the bistriflate of **5a–d** (2 mmol) and DABCO (8 mmol, 0.9 g) in DMF (5.0 mL) was added to the mixture solution. The mixture was heated at 100 °C and three additional portions of Ph_2PH (1.5 mmol, 0.26 mL) were added after 1, 3, and 7 h. The reaction was maintained at 100 °C for 3 days. After the solution was cooled to room temperature, the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (eluted with hexane/ether=15:1) to afford the corresponding products **1a–d** as white powder solid.

4.4. A general procedure for synthesis of 7,7′-disubstituted BINAPs ligands catalyzed by $Pd_2(dba)_3\cdot CHCl_3$

Under a nitrogen atmosphere, to a DMF solution containing the bistriflate of **5a–h** (2.0 mmol), $Pd_2(dba)_3\cdot CHCl_3$ (0.1 mmol, 103.5 mg), 1,3-bisdiphenylphosphinopropane (0.22 mmol, 90.7 mg), diisopropylethylamine (3.0 mmol, 0.52 mL) added Ph_2PH (4.4 mmol, 0.82 g, 0.77 mL) through syringe at 100 °C and the mixture was stirred for 48 h at the same temperature. After the solution was cooled to room temperature, the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (eluted with hexane/ether=15:1) to afford corresponding products **1a–h** as white powder solid.

*4.4.1. (R)-2,2′-Bis-diphenylphosphanyl-7,7′-dimethoxy-1,1′-binaphthalenyl (**1a**)*

White powder solid, yield 73%. Mp 269.0–270.0 °C. $[\alpha]_D^{20}$ 251.0 (c 0.1, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.12 (s, 6H), 6.05 (d, J=2.4 Hz, 2H), 7.02 (dd, J=9.0, 2.5 Hz, 2H), 7.12–7.20 (m, 20H), 7.38–7.41 (m, 2H), 7.74 (d, J=9.0 Hz, 2H), 7.83 (d, J=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 54.6, 105.6, 119.1, 127.4, 127.8, 128.0, 128.1, 128.3, 128.6, 128.8, 129.2, 132.5, 132.6, 132.7, 134.4, 134.5, 134.7, 134.8, 144.3, 157.4. ^{31}P NMR (121 MHz, $CDCl_3$): δ −14.50 (s). IR (KBr) 3069.2, 2998.8, 2966.0, 2916.9, 2848.4, 1617.1, 1549.5, 1501.2, 1431.9, 1264.2, 1220.5, 1029.1, 746.9, 696.5 cm^{-1}. HRMS (ESI) calcd for $(C_{46}H_{36}O_2P_2+H)^+$: m/z 683.2191, found m/z 683.2199.

*4.4.2. (R)-2,2′-Bis-diphenylphosphanyl-7,7′-diethoxy-1,1′-binaphthalenyl (**1b**)*

White powder solid, yield 71%. Mp 268.6–269.6 °C. $[\alpha]_D^{20}$ 250.8 (c 0.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.10 (t, J=6.9 Hz, 6H), 3.08–3.30 (m, 4H), 6.05 (d, J=2.1 Hz, 2H), 7.02 (dd, J=9.0, 2.4 Hz, 2H), 7.13–7.38 (m, 20H), 7.74 (d, J=9.0 Hz, 2H), 7.83 (d, J=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 62.7, 106.6, 118.4, 119.3, 127.3, 127.7, 127.9, 128.2, 128.4, 128.7, 129.1, 132.5, 132.6, 132.7, 134.4, 134.5, 134.7, 135.1, 136.1, 137.8, 138.7, 143.8, 144.4, 156.9. ^{31}P NMR (121 MHz, $CDCl_3$): δ −14.58 (s). IR (KBr) 3046.1, 2980.7, 2927.5, 1617.7, 1501.8, 1477.3, 1433.1, 1391.2, 1266.6, 1219.0, 1107.9, 1088.9, 1048.7, 1025.8, 975.6, 839.9, 696.1 cm^{-1}. HRMS (ESI) calcd for $(C_{48}H_{40}O_2P_2+H)^+$: m/z 711.2504, found m/z 711.2508.

*4.4.3. (R)-2,2′-Bis-diphenylphosphanyl-7,7′-dipropoxy-1,1′-binaphthalenyl (**1c**)*

White powder solid, yield 60%. Mp 100.1–101.3 °C. $[\alpha]_D^{20}$ 242.9 (c 0.4, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (t, J=7.5 Hz, 6H), 1.47–1.54 (m, 4H), 3.01–3.25 (m, 4H), 6.08 (d, J=2.1 Hz, 2H), 7.05 (dd, J=9.0, 2.4 Hz, 2H), 7.03–7.40 (m, 20H), 7.76 (d, J=9.0 Hz, 2H), 7.84 (d, J=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.4, 22.2, 68.5, 105.7, 106.6, 119.3, 127.3, 127.7, 128.0, 128.2, 128.5, 128.7, 129.1, 132.5, 132.6, 132.7, 134.3, 134.5, 134.6, 136.0, 137.8, 138.6, 143.9, 144.4, 157.1. ^{31}P NMR (121 MHz, $CDCl_3$): δ −14.60 (s). IR (KBr) 3048.5, 2961.6, 2931.9, 2874.0, 1617.7, 1501.6, 1477.5, 1477.5, 1432.3, 1387.0, 1267.5, 1218.5, 1106.9, 1067.0, 1024.8, 989.7, 838.4, 741.3, 694.4 cm^{-1}. HRMS (ESI) calcd for $(C_{50}H_{44}O_2P_2+H)^+$: m/z 739.2817, found m/z 739.2811.

*4.4.4. (R)-2,2′-Bis-diphenylphosphanyl-7,7′-diisopropoxy-1,1′-binaphthalenyl (**1d**)*

White powder solid, yield 70%. Mp 239.3–240.7 °C. $[\alpha]_D^{20}$ 267.2 (c 0.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.74 (d, J=6.0 Hz, 6H), 1.05 (d, J=6.0 Hz, 6H), 3.71–3.75 (m, 2H), 6.06 (d, J=2.4 Hz, 2H), 6.99 (dd, J=9.0, 2.4 Hz, 2H), 7.08–7.34 (m, 20H), 7.72 (d, J=9.0 Hz, 2H), 7.80 (d, J=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.4, 22.3, 69.0, 107.4, 108.5, 119.7, 127.4, 127.7, 127.9, 128.0, 128.4, 128.5, 129.1, 129.9, 131.4, 132.6, 132.7, 132.9, 134.1, 134.2, 134.4, 134.5, 138.3, 143.4, 155.5. ^{31}P NMR (121 MHz, $CDCl_3$): δ −14.27 (s). IR (KBr) 3049.7, 2974.8, 2926.9, 1616.0, 1499.9, 1477.0, 1432.9, 1382.6, 1268.0, 1218.4, 1138.4, 1113.7, 1218.4, 1138.4, 1113.7, 982.2, 838.8, 741.8, 695.8 cm^{-1}. HRMS (ESI) calcd for $(C_{50}H_{44}O_2P_2+H)^+$: m/z 739.2817, found m/z 739.2825.

*4.4.5. (R)-2,2′-Bis-diphenylphosphanyl-7,7′-cyclohexyloxy-1,1′-binaphthalenyl (**1e**)*

White powder solid, yield 54%. Mp 245.0–247.0 °C. $[\alpha]_D^{20}$ 276.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89–1.01 (m, 4H), 1.14–1.18 (m, 4H), 3.59–3.64 (m, 2H), 3.81–3.88 (m, 2H), 6.04 (d, *J*=2.1 Hz, 2H), 6.97–7.01 (m, 10H), 7.05–7.07 (m, 2H), 7.28–7.32 (m, 8H), 7.39–7.43 (m, 4H), 7.68 (d, *J*=9.0 Hz, 2H), 7.78 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.2, 27.2, 66.9, 110.3, 119.7, 127.8, 127.9, 128.1, 128.4, 128.5, 129.0, 129.4, 133.2, 133.3, 133.5, 134.1, 134.5, 134.7, 134.8, 137.7, 138.3, 155.6. ^{31}P NMR (121 MHz, $CDCl_3$): δ −11.39 (s). IR (KBr) 3052.8, 2928.9, 2886.0, 1618.6, 1583.7, 1499.3, 1432.3, 1266.4, 1223.6, 1205.0, 1195.6, 887.1, 842.0, 741.8, 693.6 cm^{-1}. HRMS (ESI) calcd for $(C_{50}H_{42}O_2P_2+H)^+$: *m*/*z* 737.2660, found *m*/*z* 737.2669.

*4.4.6. (R)-2,2′-Bis-diphenylphosphanyl-7,7′-cyclooctyloxy-1,1′-binaphthalenyl (**1f**)*

White powder solid, yield 61%. Mp 251.0–253.2 °C. $[\alpha]_D^{20}$ 254.0 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04–1.08 (m, 4H), 1.18–1.29 (m, 8H), 3.46–3.51 (m, 2H), 3.59–3.64 (m, 2H), 6.01 (d, *J*=2.4 Hz, 2H), 6.99–7.04 (m, 12H), 7.21–7.36 (m, 12H), 7.70 (d, *J*=9.0 Hz, 2H), 7.78 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.3, 27.1, 27.2, 66.1, 107.3, 119.4, 127.5, 127.7, 127.8, 128.0, 128.1, 128.4, 128.5, 129.2, 132.8, 132.9, 133.0, 134.2, 134.3, 134.5, 134.6, 142.9, 156.1. ^{31}P NMR (121 MHz, $CDCl_3$): δ −13.20 (s). IR (KBr) 3065.3, 2926.8, 2855.1, 1617.4, 1584.3, 1500.4, 1432.2, 1259.4, 1216.6, 1202.2, 1025.0, 837.8, 740.9, 694.5 cm^{-1}. HRMS (ESI) calcd for $(C_{52}H_{46}O_2P_2+H)^+$: *m*/*z* 765.2973, found *m*/*z* 765.2988.

*4.4.7. (R)-2,2′-Bis-diphenylphosphanyl-7,7′-2crown-[1,1′]-binaphthalenyl (**1g**)*

White powder solid, yield 60%. Mp 254.7–255.9 °C. $[\alpha]_D^{20}$ −238.3 (*c* 0.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.22–3.37 (m, 4H), 3.66–3.70 (m, 2H), 3.91–3.99 (m, 2H), 6.39 (d, *J*=2.4 Hz, 2H), 6.84–6.91 (m, 10H), 6.93–6.94 (m, 2H), 7.19–7.39 (m, 12H), 7.60 (d, *J*=9.0 Hz, 2H), 7.72 (d, *J*=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 66.1, 73.1, 109.4, 120.3, 127.6, 127.7, 128.0, 128.3, 128.4, 128.7, 128.8, 133.3, 133.5, 133.6, 133.8, 134.5, 134.6, 134.8, 138.2, 141.5, 156.3. ^{31}P NMR (121 MHz, $CDCl_3$): δ −9.74 (s). IR (KBr) 3049.0, 2973.7, 2855.1, 1618.6, 1585.2, 1500.5, 1432.8, 1214.8, 1204.4, 1126.5, 1089.8, 1067.9, 1026.9, 965.0, 955.7, 839.3, 694.8 cm^{-1}. HRMS (ESI) calcd for $(C_{48}H_{38}O_3P_2+H)^+$: *m*/*z* 725.2296, found *m*/*z* 725.2301.

*4.4.8. (R)-2,2′-Bis-diphenylphosphanyl-7,7′-3crown-1,1′-binaphthalenyl (**1h**)*

White powder solid, yield 62%. Mp 251.1–253.0 °C. $[\alpha]_D^{20}$ 275.7 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.21–3.36 (m, 4H), 3.42–3.49 (m, 4H), 3.78–3.80 (m, 2H), 3.89–3.90 (m, 2H), 6.10 (d, *J*=2.4 Hz, 2H), 7.11–7.13 (m, 10H), 7.14–7.15 (m, 2H), 7.37–7.44 (m, 12H), 7.82 (d, *J*=9.0 Hz, 2H), 7.91 (d, *J*=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 66.9, 68.4, 70.9, 107.1, 119.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.4, 129.3, 132.8, 132.9, 133.1, 134.5, 134.7, 142.6, 155.7. ^{31}P NMR (121 MHz, $CDCl_3$): δ −12.58 (s). IR (KBr) 3066.3, 2959.3, 2917.3, 2849.2, 1619.2, 1584.0, 1501.2, 1432.6, 1261.4, 1217.2, 1208.6, 1138.9, 1106.6, 1093.0, 1061.9, 1025.5, 836.8, 801.2, 742.9, 695.7 cm^{-1}. HRMS (ESI) calcd for $(C_{50}H_{42}O_4P_2+H)^+$: *m*/*z* 769.2558, found *m*/*z* 769.2562.

4.5. The typical experiment for the 1,4-addition of aryl boronic acids to enones

To a Schlenk tube charged with $Rh(acac)(C_2H_4)_2$ (3.1 mg, 12 μmol), **1g** (9.3 mg, 12.6 μmol), and $PhB(OH)_2$ (244 mg, 2.00 mmol) was added 1,4-dioxane (1.0 mL) and the solution was flushed with argon. After the mixture was stirred for 15 min at room temperature, 100 μL water was added and followed by addition of 2-cyclohexenone (39 mg, 40 μL, 0.40 mmol). The resulting mixture was then stirred at 100 °C for 5 h. The solution was cooled to room temperature and dissolved in 5 mL ethyl acetate. The solution was washed with saturated sodium bicarbonate and the aqueous layer is extracted with ethyl acetate (3 mL×3), the organic layer is dried over anhydrous Na_2SO_4, then concentrate the solvent and chromatography on silica gel (petroleum ether/EtOAc=15:1) to give 3-phenylcyclohexanone as colorless oil.

*4.5.1. (R)-3-Phenylcyclohexanone (**11aa**)*

Yield 99%, 97% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.80–1.89 (m, 2H), 2.07–2.16 (m, 2H), 2.39–2.58 (m, 4H), 3.01 (m, 1H), 7.21–7.25 (m, 3H), 7.33–7.35 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.7, 32.9, 41.3, 44.9, 49.1, 126.7, 126.8, 128.5, 144.5, 211.2. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 15:85, flow rate 1.0 mL/min, t_R (major)=7.36 min, t_R (minor)=8.39 min). $[\alpha]_D^{20}$ 20.1 (*c* 0.69, $CHCl_3$).

*4.5.2. (R)-3-Phenyl-cyclopentanone (**11ba**)*

Yield 90%, 90% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.67–2.04 (m, 1H), 2.32–2.51 (m, 4H), 2.65–2.74 (m, 1H), 3.50 (m, 1H), 7.24–7.29 (m, 3H), 7.34–7.39 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.3, 39.0, 42.4, 45.9, 126.9, 128.8, 143.2, 218.5. GC analysis (GAMMA β-DEX 225 column, column temperature=155 °C, H_2=12 psi. N_2 flow 2 mL/min, t_R (minor)=9.47 min, t_R (major)=9.63 min). $[\alpha]_D^{20}$ 89.1 (*c* 0.94, $CHCl_3$).

*4.5.3. (R)-3-Phenyl-cycloheptanone (**11ca**)*

Yield 82%, 90% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.72–1.76 (m, 3H), 2.07–2.17 (m, 3H), 2.57–2.67 (m, 3H), 2.94 (m, 2H), 7.16–7.22 (m, 3H), 7.26–7.32 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.3, 29.4, 39.3, 42.9, 44.1, 51.4, 126.5, 126.6, 128.8, 147.1, 213.7. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 5:95, flow rate 1.0 mL/min, t_R (major)=12.37 min, t_R (minor)=13.22 min). $[\alpha]_D^{20}$ 59.8 (*c* 0.83, $CHCl_3$).

*4.5.4. (R)-5-Methyl-4-phenyl-hexan-2-one (**11da**)*

Yield 88%, 97% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.74 (d, *J*=6.6 Hz, 3H), 0.94 (d, *J*=6.6 Hz, 3H), 1.77–1.86 (m, 1H), 1.97 (s, 3H), 2.78–2.80 (m, 2H), 2.88–2.95 (m, 1H), 7.12–7.20 (m, 3H), 7.24–7.29 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.5, 20.9, 30.7, 33.5, 47.8, 48.2, 126.4, 128.3, 128.4, 143.4, 208.5. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 1:99, flow rate 1.0 mL/min, t_R (major)=7.93 min, t_R (minor)=11.40 min). $[\alpha]_D^{20}$ 32.7 (*c* 0.79, $CHCl_3$).

*4.5.5. (R)-3-(4-Chloro-phenyl)-cyclohexanone (**11ab**)*

Yield 85%, 98% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.77–1.84 (m, 2H), 2.01–2.26 (m, 2H), 2.43–2.55 (m, 4H), 2.99 (m, 1H), 7.15 (d, *J*=8.4 Hz, 2H), 7.29 (d, *J*=8.5 Hz, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 25.5, 32.8, 41.2, 44.2, 48.9, 128.1, 128.9, 132.4, 142.8, 210.6. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 5:95, flow rate 1.0 mL/min, t_R major=11.43 min, t_R (minor)=12.99 min). $[\alpha]_D^{20}$ 19.3 (*c* 0.97, $CHCl_3$).

*4.5.6. (R)-3-(4-Methoxy-phenyl)-cyclohexanone (**11ac**)*

Yield 90%, 96% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.76–1.84 (m, 2H), 2.05–2.14(m, 2H), 2.42–2.56 (m, 4H), 2.96 (m, 1H), 3.80 (s, 3H), 6.87 (d, *J*=6.6 Hz, 2H), 7.14 (d, *J*=6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.6, 33.1, 41.3, 44.1, 49.4, 55.4, 114.1, 127.6, 136.7, 158.4, 211.4. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 5:95, flow rate 1.0 mL/min, t_R (major)=19.72 min, t_R (minor)=26.80 min). $[\alpha]_D^{20}$ 18.6 (*c* 0.89, $CHCl_3$).

*4.5.7. (R)-3-(3-Methoxy-phenyl)-cyclohexanone (**11ad**)*

Yield 92%, 96% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.81–1.89 (m, 2H), 2.06–2.18 (m, 2H), 2.40–2.60 (m, 4H), 3.00 (m, 1H), 3.82 (s, 3H), 6.78–6.84 (m, 3H), 7.28 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.7,

32.9, 41.3, 44.9, 49.1, 55.4, 111.8, 112.9, 119.1, 129.8, 146.2, 160.0, 211.1. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 5:95, flow rate 1.0 mL/min, t_R (major)=15.04 min, t_R (minor)=19.52 min). $[\alpha]_D^{20}$ 15.1 (*c* 0.87, $CHCl_3$).

*4.5.8. (R)-3-(4-tert-Butyl-phenyl)-cyclohexanone (**11ae**)*

Yield 86%, 99% ee. ^1H NMR (300 MHz, $CDCl_3$): δ 1.29 (s, 9H), 1.76–1.85 (m, 2H), 2.04–2.13 (m, 2H), 2.36–2.56 (m, 4H), 2.99 (m, 1H), 7.13 (d, *J*=8.4 Hz, 2H), 7.33 (d, *J*=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.7, 31.5, 32.9, 41.3, 44.4, 49.1, 125.7, 126.3, 141.4, 149.6, 211.4. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 1:99, flow rate 1.0 mL/min, t_R (major)=9.03 min, t_R (minor)=9.92 min). $[\alpha]_D^{20}$ 11.9 (*c* 0.68, $CHCl_3$).

*4.5.9. (R)-3-(4-Trifluoromethyl-phenyl)-cyclohexanone (**11af**)*

Yield 84%, 99.8% ee. ^1H NMR (300 MHz, $CDCl_3$): δ 1.81–1.89 (m, 2H), 2.09–2.11 (m, 2H), 2.45–2.59 (m, 4H), 3.11 (m, 1H), 7.33 (d, *J*=8.1 Hz, 2H), 7.58 (d, *J*=8.1 Hz, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 25.5, 32.6, 41.2, 44.6, 48.7, 125.8, 125.8, 125.9, 127.1, 148.3, 210.4. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 5:95, flow rate 1.0 mL/min, t_R (major)=12.87 min, t_R (minor)=16.17 min). $[\alpha]_D^{20}$ 10.1 (*c* 0.79, $CHCl_3$).

*4.5.10. (R)-3-p-Tolyl-cyclohexanone (**11ag**)*

Yield 97%, 94% ee. ^1H NMR (300 MHz, $CDCl_3$): δ 1.79–1.86 (m, 2H), 2.05–2.16 (m, 2H), 2.33 (s, 3H), 2.36–2.57 (m, 4H), 2.98 (m, 1H), 7.34 (d, *J*=8.4 Hz, 2H), 7.59 (d, *J*=8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 25.7, 33.1, 41.4, 44.5, 49.2, 126.6, 129.5, 136.4, 141.6, 211.4. HPLC analysis (Chiralcel OJ-H column, 2-propanol/hexane 5:95, flow rate 1.0 mL/min, t_R (major)=10.87 min, t_R (minor)=12.24 min). $[\alpha]_D^{20}$ 18.2 (*c* 0.84, $CHCl_3$).

4.6. General procedure for preparation of [(*RRR*)-(1a–h)–$RuCl_2$–DPEN] precatalysts

Ligands **1a**–**h** (0.031 mmol) and $[(C_6H_6)RuCl_2]_2$ (0.015 mmol, 7.5 mg) were dissolved in anhydrous and degassed DMF (3 mL) under nitrogen. The reaction mixture was heated to 100 °C for 20 min, then the reaction mixture was slowly cooled to room temperature followed by the addition of 1,2-diphenylethylenediamine (*RR*-DPEN) (0.031 mmol, 6.6 mg). The solvent was stirred at room temperature for 4 h. The solvent DMF was removed under high vacuum at 50 °C and the residue was used for asymmetric hydrogenation of simple aromatic ketones as precatalyst without further purification.

4.7. General procedure for asymmetric hydrogenation simple aromatic ketones

To a vial were added the precatalyst [(*RRR*)-**1c**–$RuCl_2$–DPEN] (0.001 mmol), ^{t}BuOK (0.029 mmol, 3.2 mg), and substrate simple aromatic ketone (2 mmol), then quickly adding new distilled and degassed ^{i}PrOH (1 mL) to the vial and putting the vial into a hydrogenation vessel. The vessel was purged with high purity hydrogen by pressurizing to 10 atm and releasing the pressure. This procedure was repeated five times successively. The vessel was purged with hydrogen and pressurized to 40 atm then making the mixture to stir at room temperature for certain hours. The reaction was stopped and the reaction mixture was filtered through a pad of silica gel and eluted with ethyl acetate to afford the corresponding desired product.

*4.7.1. (S)-1-Naphthalen-1-ethanol (**13a**)*

Conversion 100%, 98% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol, GC analysis (CP-cyclodex β-236 M, column temperature 160 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=11.2 min, t_{R2}=12.0 min.

*4.7.2. (S)-1-o-Tolyl-ethanol (**13b**)*

Conversion 100%, 90% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. GC analysis (CP-cyclodex β-236 M, column temperature 125 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=5.3 min, t_{R2}=6.5 min.

*4.7.3. (S)-1-Phenyl-ethanol (**13c**)*

Conversion >99%, 81% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol, GC analysis (CP-cyclodex β-236 M, column temperature 115 °C, inject temperature 220 °C, N_2 flow 2 mL/min), t_{R1}=5.0 min, t_{R2}=5.3 min.

*4.7.4. (S)-1-Phenyl-pentanol (**13d**)*

Conversion >99%, 87% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol, GC analysis (CP-cyclodex β-236M, column temperature 150 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=24.1 min, t_{R2}=24.3 min.

*4.7.5. (S)-1,2-Diphenyl-ethanol (**13e**)*

Conversion >99%, 88% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol, HPLC analysis (OD column, 2-propanol/hexane 5:95, room temperature, flow rate 1.0 mL/min), t_{R1}=11.7 min, t_{R2}=14.5 min.

*4.7.6. (S)-1-(3-Methoxy-phenyl)-ethanol (**13f**)*

Conversion 100%, 88% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. GC analysis (CP-cyclodex β-236M, column temperature 150 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=4.4 min, t_{R2}=4.6 min.

*4.7.7. (S)-1-(4-Methoxy-phenyl)-ethanol (**13g**)*

Conversion >99%, 78% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol, GC analysis (CP-cyclodex β-236M, column temperature 140 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=5.1 min, t_{R2}=5.4 min.

*4.7.8. (S)-1-p-Tolyl-ethanol (**13h**)*

Conversion >99%, 81% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. GC analysis (CP-cyclodex CB, column temperature 125 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=5.4 min, t_{R2}=6.5 min.

*4.7.9. (S)-1-Phenyl-propan-1-ol (**13i**)*

Conversion 100%, 85% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol, GC analysis (CP-cyclodex β-236M, column temperature 150 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=4.8 min, t_{R2}=5.0 min.

*4.7.10. (S)-2-Methyl-1-phenyl-propan-1-ol (**13j**)*

Conversion >99%, 73% ee. *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. GC analysis (CP-cyclodex β-236M, column temperature 150 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=17.5 min, t_{R2}=18.6 min.

*4.7.11. (S)-1-Naphthalen-2-yl-ethanol (**13k**)*

Conversion 100%, 77% ee, *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. GC analysis (CP-cyclodex β-236M, column temperature 170 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=5.0 min, t_{R2}=5.2 min.

*4.7.12. (S)-1-Ferrocenylethanol (**13l**)*

Conversion >99%, 79% ee, *S*/*C*=1000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. HPLC analysis on AS column, 2-propanol/hexane 5:95, room temperature, flow rate 1.0 mL/min, t_{R1}=11.3 min, t_{R2}=13.7 min.

*4.7.13. (S)-1-(2-Chloro-phenyl)-ethanol (**13m**)*

Conversion 100%, 94% ee, *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. GC analysis (CP-cyclodex CB, column temperature 160 °C, inject temperature 250 °C, N_2 flow 2 mL/min), t_{R1}=2.2 min, t_{R2}=2.4 min.

*4.7.14. (S)-1-(3-Chloro-phenyl)-ethanol (**13n**)*

Conversion 100%, 71% ee, *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. GC analysis (CP-cyclodex β-236M, column temperature 140 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=8.8 min, t_{R2}=9.2 min.

*4.7.15. (S)-1-(3,4-Dimethoxy-phenyl)-ethanol (**13o**)*

Conversion >99%, 77% ee, *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol. GC analysis (CP-cyclodex CB, column temperature 140 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=17.0 min, t_{R2}=17.5 min.

*4.7.16. (S)-1-(2,4-Dichloro-phenyl)-ethanol (**13p**)*

Conversion 100%, 90% ee, *S*/*C*=2000, base/catalyst=70:1, the substrate concentration was 1.0 M in 2-propanol, GC analysis (CP-cyclodex β-236M, column temperature 180 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=4.4 min, t_{R2}=4.6 min.

*4.7.17. (S)-1-(2-Bromo-phenyl)-ethanol (**13q**)*

Conversion >99%, 94% ee, *S*/*C*=1000, base/catalyst=70:1, the substrate concentration was 2.0 M in 2-propanol. GC analysis (CP-cyclodex β-236M, column temperature 180 °C, inject temperature 240 °C, N_2 flow 2 mL/min), t_{R1}=3.4 min, t_{R2}=3.5 min.

4.8. General procedure for asymmetric hydrogenation of β-ketoesters

To a Schlenk tube were added $[(C_6H_6)RuCl_2]_2$ (0.02 mmol, 10.0 mg), ligand **1c** (0.042 mmol), and freshly distilled and degassed EtOH/CH_2Cl_2 (3 mL/3 mL). The solution was stirred at 50 °C for 1 h. The catalyst was dried under reduced pressure and dissolved in degassed EtOH (20 mL). The solution (1 mL) including catalyst was added to each vial containing β-ketoesters (2 mmol), and these vials were taken into a Parr bomb. The reactions were carried out at the desired hydrogen pressure and temperature for 12 h. Taking out the vials and removing the solvent under reduced pressure, the residue was passed through a pad of silica gel and eluted with ethyl acetate to afford the corresponding product.

*4.8.1. (R)-3-Hydroxy-butyric acid ethyl ester (**15a**)*

Conversion 100%, 98% ee, *S*/*C*=1000. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.19 (d, *J*=6.6 Hz, 3H), 1.26 (t, *J*=7.2 Hz, 3H), 2.34–2.48 (m, 2H), 2.93 (br, 1H), 4.17 (q, *J*=7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 22.4, 42.8, 60.6, 64.2, 172.8. GC analysis (column, CP-cyclodex β-225, N_2 flow 2 mL/min, column temperature 70 °C, inject temperature 240 °C), t_{R1}=18.0 min, t_{R2}=18.9 min.

*4.8.2. (R)-3-Hydroxy-butyric acid tert-butyl ester (**15b**)*

Conversion >99%, 96% ee, *S*/*C*=1000. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07 (d, *J*=6.3 Hz, 3H), 1.33 (s, 9H), 2.23–2.32 (m, 2H), 2.35 (br, 1H), 3.97–4.07 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.2, 27.8, 43.8, 64.1, 80.7, 171.9. GC analysis (column, CP-cyclodex β-120, N_2 flow 2 mL/min, column temperature 100 °C, inject temperature 240 °C), t_{R1}=9.2 min, t_{R2}=9.5 min.

*4.8.3. (R)-3-Hydroxy-butyric acid isopropoyl ester (**15c**)*

Conversion >99%, 98% ee, *S*/*C*=1000. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04 (d, *J*=6.3 Hz, 3H), 1.10 (d, *J*=6.3 Hz, 6H), 2.56–2.29 (m, 2H), 3.28 (br, 1H), 4.00–4.08 (m, 1H), 4.84–4.93 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.4, 22.2, 24.9, 43.1, 63.6, 64.0, 67.7, 171.9. GC analysis (column, CP-cyclodex β-225, N_2 flow 2 mL/min, column temperature 70 °C, inject temperature 240 °C), t_{R1}=16.2 min, t_{R2}=16.7 min.

*4.8.4. (R)-3-Hydroxy-butyric acid methyl ester (**15d**)*

Conversion 100%, 99% ee, *S*/*C*=1000. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16 (d, *J*=6.3 Hz, 3H), 1.87–1.95 (m, 2H), 3.22 (br, 1H), 3.63 (s, 3H), 4.08–4.15 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.4, 42.6, 51.5, 64.1, 173.0. GC analysis (column, CP-cyclodex β-225, N_2 flow 2 mL/min, column temperature 70 °C, inject temperature 240 °C), t_{R1}=13.8 min, t_{R2}=15.0 min.

*4.8.5. (R)-4-Chloro-3-hydroxy-butyric acid ethyl ester (**15e**)*

Conversion >99%, 91% ee, *S*/*C*=1000. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.18 (t, *J*=7.5 Hz, 3H), 2.47–2.54 (m, 2H), 3.50 (d, *J*=5.1 Hz, 2H), 3.66 (br, 1H), 4.05 (q, *J*=7.5 Hz, 2H), 4.07–4.14 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 38.5, 47.9, 60.6, 67.6, 171.4. GC analysis (column, CP-cyclodex β-225, N_2 flow 2 mL/min, column temperature 110 °C, inject temperature 240 °C), t_{R1}=8.5 min, t_{R2}=8.8 min.

*4.8.6. (S)-3-Hydroxy-3-phenyl-propionic acid ethyl ester (**15f**)*

Conversion >99%, 85% ee, *S*/*C*=1000. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 (t, *J*=7.2 Hz, 3H), 2.63–2.72 (m, 2H), 3.45 (br, 1H), 4.13 (q, *J*=7.2 Hz, 2H), 5.10 (dd, *J*=4.2, 8.7 Hz, 1H), 7.25–7.36 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 43.3, 60.6, 70.1, 125.5, 127.5, 128.3, 142.6, 172.1. HPLC analysis (column, AD column, eluent 2-propanol/hexane=2:98, temperature, room temperature, flow rate 1.0 mL/min, 254 nm light), t_{R1}=6.5 min, t_{R2}=7.7 min.

*4.8.7. (R)-3-Hydroxy-4-methyl-pentanoic butyric acid methyl ester (**15g**)*

Conversion 100%, 99.8% ee, *S*/*C*=1000. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (d, *J*=6.9 Hz, 6H), 1.54–1.65 (m, 1H), 2.26–2.43 (m, 2H), 3.07 (br, 1H), 3.59 (s, 3H), 3.65–3.71 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.4, 18.1, 33.0, 38.3, 51.4, 72.5, 173.5. GC analysis (column, CP-cyclodex CB, N_2 flow 2 mL/min, column temperature 50 °C, preserving 5 min, then 2.0 °C/min to 150 °C, inject temperature 240 °C), t_{R1}=23.7 min, t_{R2}=23.9 min.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.03.066.

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