JOC The Journal of Organic Chemistry

Article

Development of Ferrocene-Based Diamine-Phosphine-Sulfonamide (f-Diaphos) Ligands for Iridium Catalyzed Asymmetric Hydrogenation of Ketones

Fei Ling, Sanfei Nian, Jiachen Chen, Wenjun Luo, Ze Wang, Yaping Lv, and Weihui Zhong

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b01276 • Publication Date (Web): 31 Jul 2018

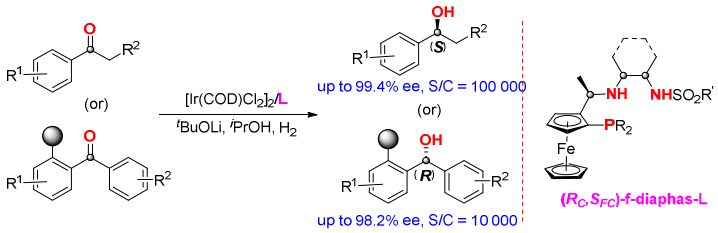
ACS Publications

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Development of Ferrocene-Based Diamine-Phosphine-Sulfonamide (f-Diaphos) Ligands for Iridium Catalyzed Asymmetric Hydrogenation of Ketones

Fei Ling, Sanfei Nian, Jiachen Chen, Wenjun Luo, Ze Wang, Yaping Lv and Weihui Zhong*

Key Laboratory for Green Pharmaceutical Technologies and Related Equipment of Ministry of Education, College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, People's Republic of China

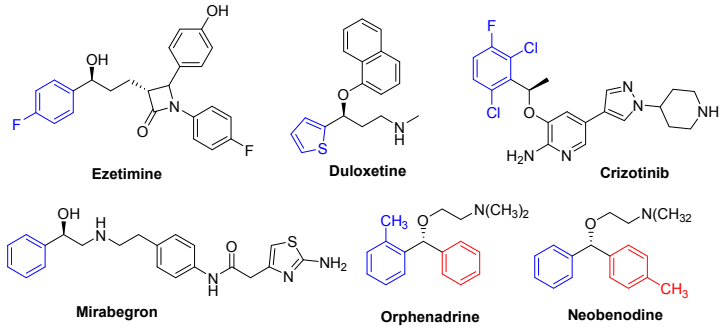


ABSTRACT: A series of air stable, easily accessible tridentate ferrocene-based diamine-phosphine sulfonamide (f-diaphos) ligands were successfully developed for iridium-catalyzed asymmetric hydrogenation of ketones. The f-diphos ligands exhibited excellent enantioselectivity and superb reactivity in Ir-catalyzed asymmetric hydrogenation of ketones (for arylalkyl ketones, (*S*)-selectivity, up to 99.4% ee and 100 000 TON; for diaryl ketones, (*R*)-selectivity, up to 98.2% ee and 10 000 TON). This protocol could be easily conducted on gram scale, thereby providing a chance to various drugs.

INTRODUCTION:

Enantioenriched chiral alcohols are prevalent skeletons, not only existing in many physiologically or/and biologically active molecules,[1] such as in selective cholesterol absorption inhibitor ezetimine,[2] antidepressant duloxetine,[3] c-Met/HGFR inhibitor crizotinib,[4] selective β_3-adrenoceptor agonist mirabegron,[5] antihistamines orphenadrine[6] and neobenodine,[7] but also representing versatile building blocks in organic synthesis.[8] Owing to their great importance, the development of efficient systems for the catalytic enantioselective synthesis of chiral alcohols is of substantial interest to both the academic community and the industrial sector.

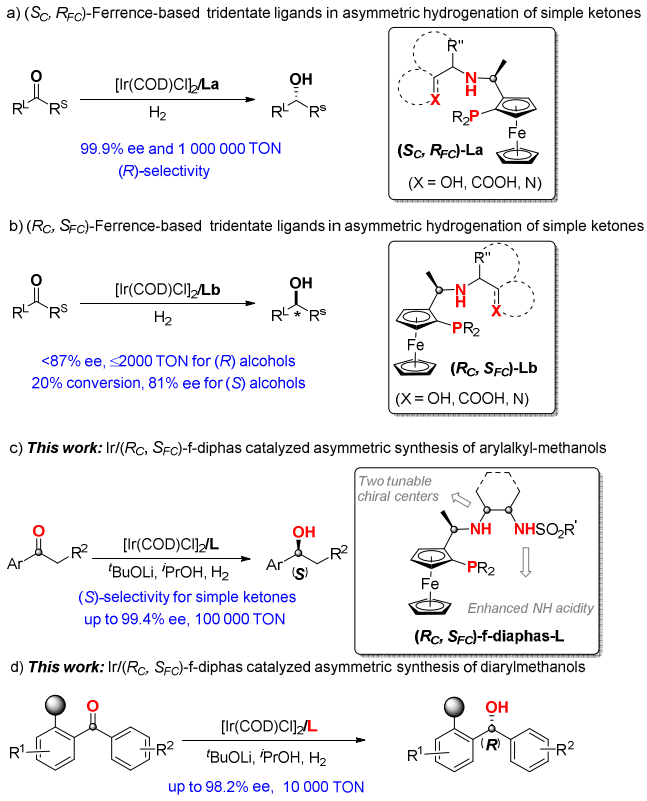
Figure 1. Related chiral pharmaceuticals containing chiral alcohols



Transition-metal-catalyzed asymmetric hydrogenation has emerged as a powerful tool for accessing chiral alcohols from various ketones.[9] The pioneering research work was disclosed by Noyori and Ohkuma in the 1990s, who developed a highly efficient [$RuCl_2$(diphosphine)-(1,2-diamine)] catalytic system for asymmetric hydrogenation of ketones with high reactivity and moderate enantioselectivity.[10] Inspired by this fundamental work, continues efforts have been devoted to creating new types of chiral ligands. In this context, tridentate ligands exhibit unique reactivity and excellent enantioselectivity, owing to their deeper chiral concave pockets around the metal center.[11] For example, Zhou and coworkers have developed a series of axially tridentate spiro P-N-N and P-N-S ligands, and applied them in the iridium-catalyzed reduction of ketones, affording alkyl alcohols with up to 99.9% ee and 4 550 000 TON (Scheme 1, a).[11b,11c] Similarly, Kitamura and cowoker's have created a set of tridentate binan-Py-PPh_2 ligands and also achieved excellent results.[11d,11e] Despite their great success that has been achieved, multistep complicated reactions were employed to synthesize these axially tridentate ligands. Recently, ferrocene-based tridentate ligands have received much attention as powerful ligands for asymmetric hydrogenation of ketones, because of their various advantages such as potential planar and central chiralities, cheapness, readily availability and easy modification. Remarkably, Zhang and coworkers developed a set of privileged tridentate ligands derived from (S_C, R_{FC})-ferrocene and amino acid derivatives, and simple ketones could be hydrogenated to (*R*)-alcohols in up to 99.9% ee and 1 000 000 TON (Scheme 1a).[12] However, in previous studies, (R_C, S_{FC})-ferrocene-based tridentate ligands are far less efficient to produce chiral alcohols (<97% ee, and ≤2000 TON for (*R*)-alcohols; 81%ee and 20% conversion for (*S*)-alcohols) (Scheme 1b).[13,12b] This distinct performance of (S_C, R_{FC})- and (R_C, S_{FC})-ferrocene skeletons made it difficult to obtain both enantioenriched (*R*)- and (*S*)-alcohols with one type of ligands, which remains an unsolved challenge. Despite their low efficiency, (R_C, S_{FC})-ferrocene-based tridentate ligands are potential to give enantioenriched (*S*)-alcohols, which are important structures in pharmaceutical products, albeit in low efficiency (Figure 1)[2-5].

Recently, our studies were focused on developing ferrocene-based organocatalysts for asymmetric transformations.[14] Encouraged by these basic researches, we are interested in designing new ferrocene-based tridentate ligands, especially (R_C, S_{FC})-ferrocene-based tridentate ligands, thereby achieving both alcohol enantiomers at one stroke. We are pleased to find that *C2*-symmetric 1,2-diamine derivatives are competent to this challenging task, owing to their two tunable chiral centers and enhanced NH acidity (Scheme 1c). Herein, we successfully developed a set of novel ferrocene-diamine-phosphine-sulfonamide (f-diaphos) ligands and applied them in iridium-catalytic asymmetric hydrogenation of ketones. Arylalkyl ketones could be hydrogenated to (*S*)-alcohols with (R_C, S_{FC})-f-diphos **L8** in up to 99.4% ee and 100 000 TON (Scheme 1c), while acetophenone was reduced to (*R*)-1-phenylethanol with good results using ligand **L11** as the ligand, which is an enantiomer of (R_C, S_{FC})-f-diaphos **L1** (Scheme 6, 95.4% ee, and 10 000 TON). Furthermore, this protocol could be employed for the asymmetric hydrogenation of more challenging diaryl ketones, affording enantioenriched diaryl methanols with up to 98.2% ee, and 10 000 TON (Scheme 1d).

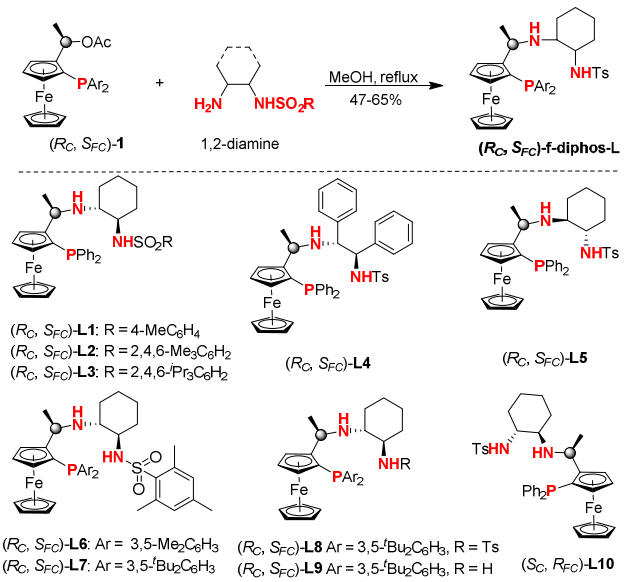
Scheme 1. Ferrocene-based Tridentate Ligands for Asymmetric Hydrogenation of Ketones



RESULT AND DISCUSSION

The current developed f-diaphos ligands **L1−L9** could be easily obtained in 47-65% yield by treatment of acetates (S_C, R_{FC})-**1** with 1,2-diamines in MeOH under reflux conditions (Scheme 2). In addition, we also synthesized ligand **L10**, which is the diasteroisomer of ligand **L1** to investigate the relationship between enantioselectivity and configuration of ligand.

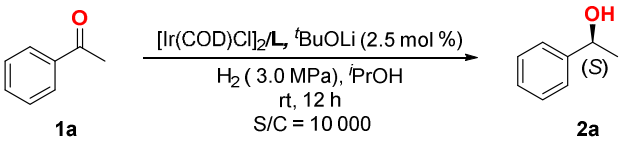
Scheme 2. Synthetic Route of f-Diaphos Ligands L1−L10



With the chiral f-diaphos ligands **L1−L10** in hand, we began our studies by screening them for asymmetric hydrogenation of acetophenone (**1a**) serving as the model substrate with the catalyst generated in situ by mixing $[Ir(COD)Cl]_2$ with ligands **L1−L10** (S/C = 10 000) in ^{i}PrOH (more details on investigations of solvents, bases and temperature see SI). As shown in Table 1, majority of the f-diaphos ligands exhibited extreme high reactivity and excellent enatioselectivity, giving access to (*S*)-1-phenylethanol (**2a**) in >99% conversion with up to 97.7% ee. With an increase in steric hindrance on the benzene ring of the sulfonyl group from **L1** to **L2** by switching 4-methyl to 2,4,6-trimethyl, the enantiomeric selectivity of the reaction increased from 94.3% to 97.4% ee (Table 1, entry 2). Nevertheless, further increasing the steric hindrance from 2,4,6-trimethyl to 2,4,6-triiso-propionyl resulted in a decrease on ee value (Table 1, entry 3). Moreover, relatively lower enantioselectivity was observed when the reaction was conducted with the use of 1,2-diphenylethane-1,2-diamine-based ligand **L4** (Table 1, entry 4). It was noteworthy that replacing the counterparts from (*R*, *R*)-1,2-diaminocyclohexane to its enantiomer led to a significantly reduced enantioselectivity with opposite configuration of the product (**L1**, 94.3% ee vs **L5**, -18.2% ee). In addition, the

substituents on the P-phenyl ring had a little influence on the enantioselectivity, and **L8** was found to afforded the best result with >99% conversion and 97.7% ee (Table 1, entries 6−8). On contrast, upsetting results were obtained when ligand **L9** bearing free NH_2 moiety was applied into this transformation (Table 1, entry 9, 79% conversion, 40% ee). Notably, (S_C, R_{FC})-ferrocene-based ligand **L10** which is the diastereoisomer of ligand **L1** displayed low enantioselectivity and moderate reactivity (Table 1, entry 10, 86% conversion, 16.3% ee). These results indicated that the sulfonyl group and the configuration of the ligand are very critical for enantioselectivity and reactivity.

Table 1. Screening Ligands for Asymmetric Hydrogenation of 1a[a]



1a **2a**

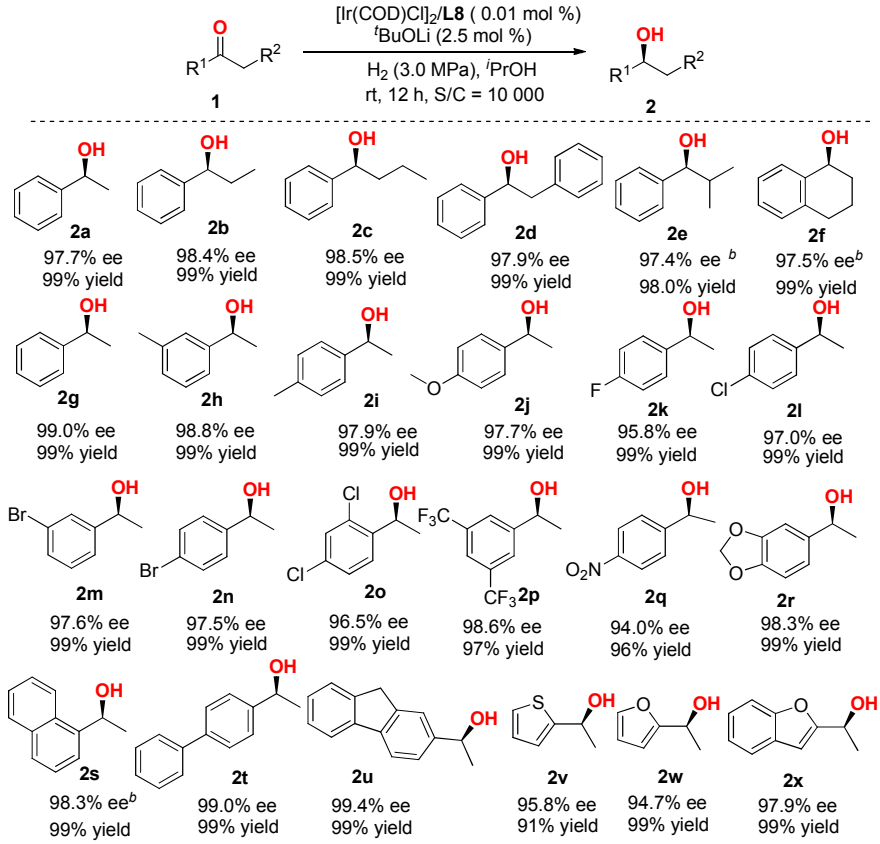
entry	ligand	conv. (%)[b]	ee (%)[c]
1	**L1**	>99	94.3
2	**L2**	>99	97.4
3	**L3**	>99	89.3
4	**L4**	>99	86.1
5	**L5**	>99	-18.2
6	**L6**	>99	97.3
7	**L7**	>99	95.9
8	***L8***	***>99***	***97.7***
9	**L9**	79	40.0
10	**L10**	86	16.3

[a]Reaction conditions: 2 mmol scale, [substrate] = 0.2 M, 0.005 mol % $[Ir(COD)Cl]_2$, 0.0105 mol % ligand **L**, 2.5 mol % ^{t}BuOLi, 10 mL of ^{i}PrOH, room temperature (25−30 ^{o}C). [b]Determined by GC analysis. [c]Determined by HPLC analysis.

After identifying the optimum reaction conditions (Ir-**L8**/30 atm H_2/2.5 mol % ^{t}BuOLi, S/C = 10 000/rt), we next set out to determine the versatility of this reaction system in the asymmetric hydrogenation of arylalkyl ketones. Various (*S*)-alcohols were obtained in almost quantitative yields with 94.0−99.4% ee (Scheme 3). Substrates bearing ethyl and propyl groups on the vicinity of the benzylic position were hydrogenated smoothly to yield the desired alcohols in 98.4% and 98.5% ees, respectively. However, introduction of steric hindered substituent at the benzylic position resulted in a slight reduced ee (**2d**, 97.9% ee and **2e**, 97.4% ee). Notably, tetralone was also compatible with the Ir-**L8** catalytic system, leading to the corresponding product **2f** in 99% yield with 97.5% ee. On the other hand, the substrates bearing electron-donating groups (**1g−1j**) and electron-withdrawing

groups (**1k−1p**) on the phenyl ring were hydrogenated well with excellent results (almost all products in up to >97% ee, 99% yield). An exception was found when the nitro-substituted ketone **1q** was used, delivering the corresponding alcohol **2q** in 94% ee. In addition, the position of the substituent on the phenyl ring had slight influence on the reaction outcome, and *ortho*-substituted ketones gave better results than that of meta- or para-substituted compounds (**2g**, 99.0% ee vs **2h**, 98.8% ee or **2i**, 97.9% ee). In addition, the benzene ring could be effectively replaced by other aromatic substituents like benzo[*d*][1,3]dioxol-5-yl (**1r**), naphthyl (**1s**), 1,1'-biphenyl-4-yl (**1t**) to forge the corresponding alcohols in 98.3−99.0% ee. The best result (99% yield with up to 99.4% ee) was observed when using 9*H*-fluoren-2-yl substituted ketone (**1u**) as the substrate. It indicates that the amplified asymmetric bias between the alkyl and aryl groups offers better results. Delightfully, current protocol also tolerated with heterocyclic aromatic ketones to produce the targeted products (**2v−2x**) in good enatioselectivities.

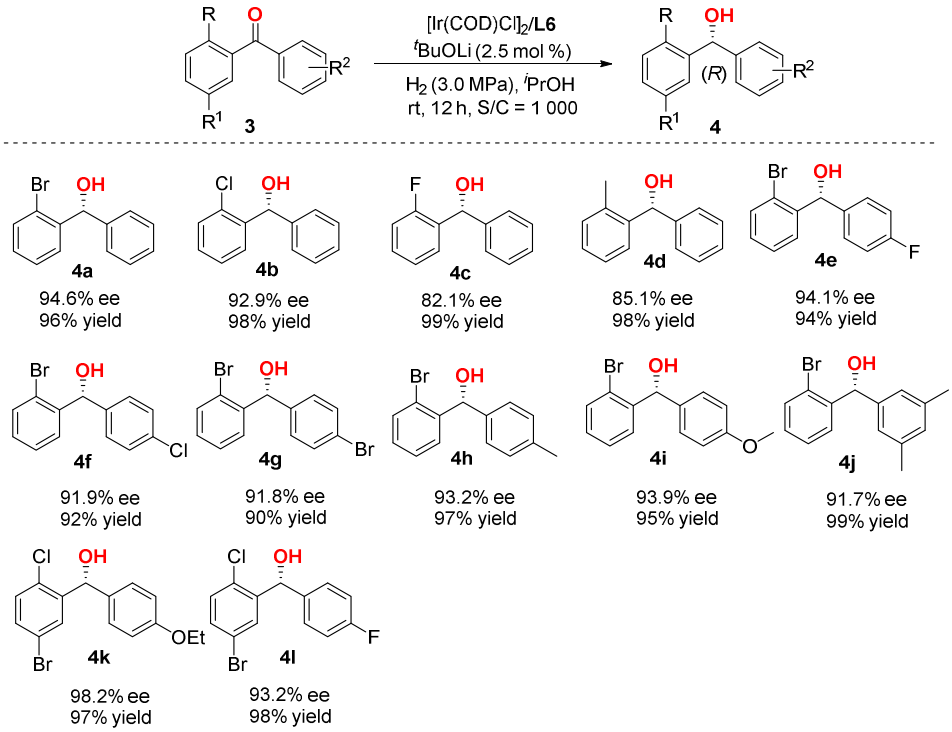
Scheme 3. Ir-L8 Catalysis for the Asymmetric Hydrogenation of 1[a]



[a]Reaction conditions were the same as those listed in Table 1, entry 8. Isolated yields. The ee was determined by HPLC analysis. [b]at 60 °C.

Intriguingly, these privileged f-diaphos ligands could be further applied into the Ir-catalyzed asymmetric hydrogenation of *ortho*-substituted diaryl ketones, leading to a variety of chiral diaryl methanols in 82.1−98.2% ee (Scheme 4). 2-Bromobenzophenone was initially hydrogenated under 0.1 mol % of the Ir-**L6** catalytic system for 12 h, giving (*R*)-(2-bromophenyl)(phenyl)methanol **4a** in 96% yield with 94.6% ee (more details on optimization of reaction conditions, see SI). Notably, the ortho substituent greatly affected the reaction, asymmetric bias between the two aryl groups. Thereby, the introduction of *o*-bromo or *o*-chloro unit was conductive to higher ee values (**4a**, 94.6% ee; **4b**, 92.7% ee) than that of *o*-fluoro or *o*-methyl unit (**4c**, 82.1% ee and **4d**, 85.1% ee). Moreover, the results of the high-performance liquid chromatographic (HPLC) analysis with a chiral stationary phase indicated that the products were (*R*)-isomers. In addition, *o*-Br-phenyl aryl ketones that contained electron-deficient (**3e−3g**) and electron-rich (**3h−3j**) aryl groups furnished the corresponding unsymmetrical diarylmethanols with sufficient yields and ees, which indicating that f-diaphos **L6** can precisely recognize the *ortho*-substituted phenyl group. Furthermore, excellent ees, exceeding 98.2%, were obtained when (5-bromo-2-chlorophenyl)(4-ethoxyphenyl)methanone and (5-bromo-2-chlorophenyl)(4-florophenyl)methanone were employed as the substrates.

Scheme 4. Ir-L6 Catalysis for the Asymmetric Hydrogenation of 3

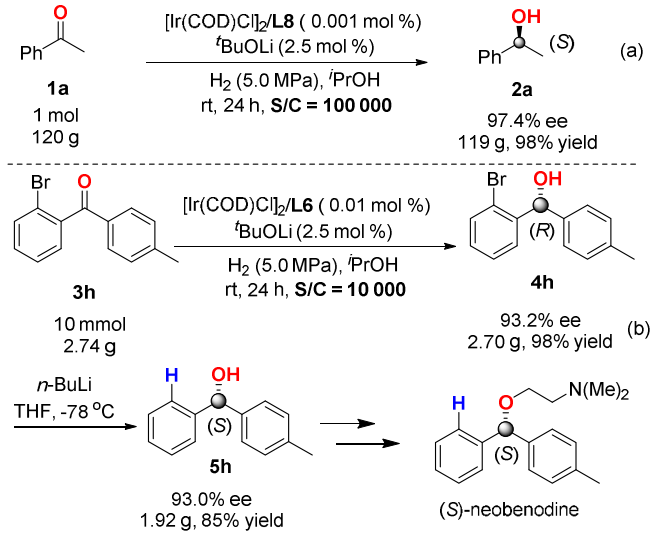


[a]Reaction conditions: 1 mmol scale, [substrate] = 0.2 M, 0.05 mol % $[Ir(COD)Cl]_2$, 0.105 mol % ligand **L6**, 2.5

mol % ^{t}BuOLi, 10 mL of ^{i}PrOH, room temperature (25−30 °C). Isolated yields. The ee was determined by HPLC analysis.

In order to demonstrate the utility of this method, several gram-scale reactions with lower catalyst loading were conducted, as shown in scheme 5. To our delight, Ir-**L8** complex exhibited good stability and excellent reactivity. When the catalyst loading was decreased to 0.001 mol % (S/C=100 000), the asymmetric hydrogenation still underwent smoothly with 120 g of acetophenone **1a** to afford the product (*S*)-**2a** in 117 g, 98% isolated yield and 97.4% ee within only 24 h at room temperature under hydrogen pressure of 50 atm (Scheme 5a). In addition, a gram-scale reduction of (2-bromophenyl)(*p*-tolyl)methanone **3h** was also accomplished with our catalytic system (0.01 mol % Ir-**L6**, S/C=10 000), and the (*R*)-(2-bromophenyl)(*p*-tolyl)methanol **4h** was obtained in 93.2% ee (Scheme 5b). Subsequently debromination of **4h** resulted in the formation of (*S*)-phenyl(*p*-tolyl)methanol **5h**, which is the key intermediate of (*S*)-neobenodine.[15] Furthermore, the debromination of **4f** and **4l** also underwent smoothly to produce (*S*)-(4-chlorophenyl)(phenyl)methanol **5f** (81% yield, >99% ee) and (*R*)-(2-chlorophenyl)(4-fluorophenyl)methanol **5l** (83% yield, 97% ee).

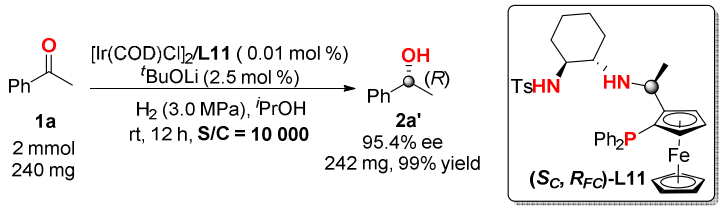
Scheme 5. Gram-Scale Reaction and Further Transformation



To the best of our knowledge, there's no example of controllable asymmetry hydrogenation of aryl alkyl ketones to offer two enantiomers by using ferrocene-based tridentate ligands. We are interested to see whether current developed chiral f-diaphos ligands could achieve this goal. Thus, **L11**, an enantiomer of (R_C, S_{FC})-f-diaphos **L1**, was synthesized and displayed high enantioselectivity and superb reactivity in the Iridium-catalyzed asymmetry hydrogenation of acetophenone (**1a**). (*R*)-1-phenylethanol (**2a'**) could be

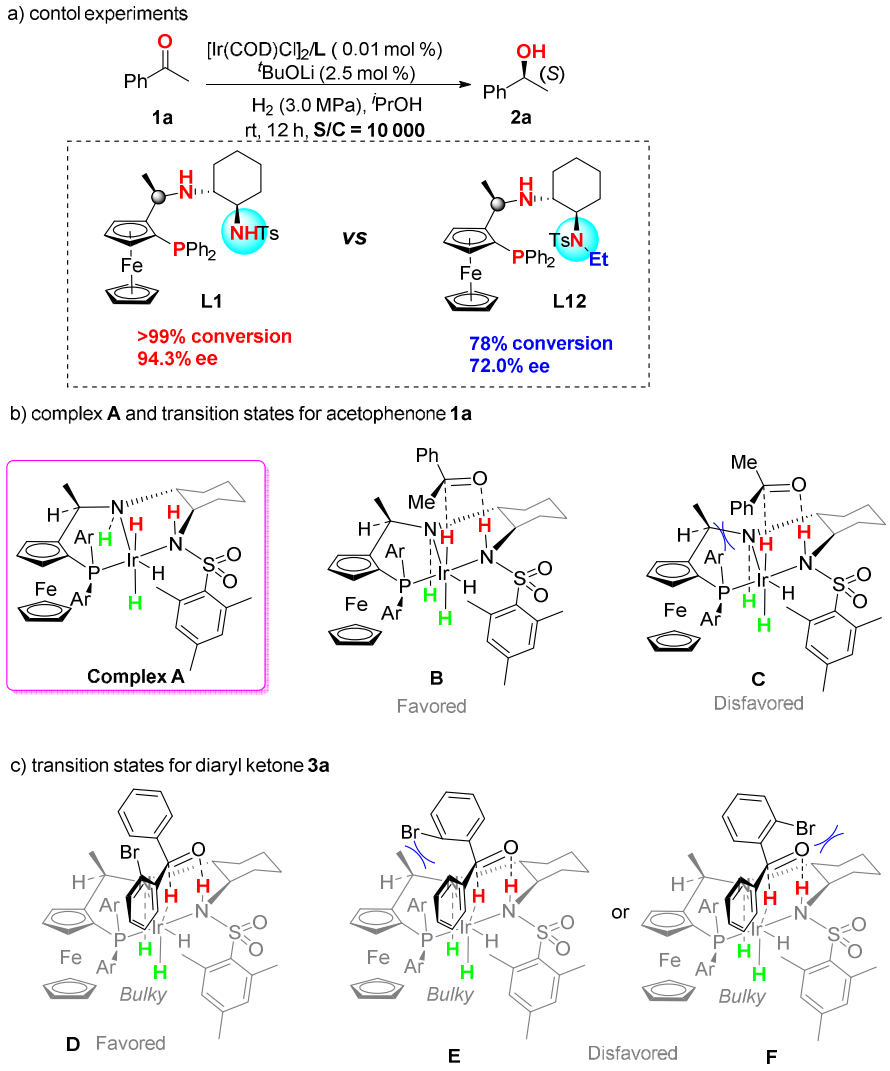
obtained in 99% yield with 95.4% ee (Scheme 6). This result indicates the current developed f-diaphos ligands are capable of affording both (*R*) and (*S*) aryl alkyl methanols in high yields with excellent enantioselectivities.

Scheme 6. Ir-L11 Catalysis for the Synthesis of (*R*)-1-Phenylethanol



In order to further investigate the role of the NHTs group of the f-diaphos ligand, we synthesized ligand **L12** by protecting the NH with ethyl group. Poor conversion and moderate enantioselectivity were observed under the same conditions (**L12**, 78% conversion, 72.0% ee, vs **L1**, >99% conversion, 94.3% ee, Scheme 7a) in the Ir/**L12**-catalyzed asymmetric hydrogenation of acetophenone **1a**. These results indicated that the NHTs group played a crucial role in this asymmetric hydrogenation reaction. Based on the control experiments and previous literatures,[12] two plausible transition state models were proposed to explain the different enantioselectivities in asymmetry hydrogenation of aryl alkyl and diaryl ketones (Scheme 7b and 7c). The common active catalyst was believed to be a Ir(III)-dihydride complex **A** (Scheme 7b), which is derived from reaction of the Ir(I) precursor, **L6** or **L8**, the base, and two H_2 molecules along with dissociation of the COD ligand. For aryl alkyl ketones, the substrate **1a** coordinates to **A** to form transition states **B** or **C** through interaction with two Hs shown in red. The coordination of substrate to the complex **A** through the two Hs shown in green is disfavored due to the steric hinderance caused by the aryl ring and the ferrocene group on P of the ligand and also the large Ar group on NHTS. The transition state **C** has higher energy than transition state **B**, due to the steric repulsion between the Ph ring of the **1a** and the aryl ring of P-centerin transition state **C**. The subsequent step is transfering of proton from the acidic −NHTs group to the substrate, leading to the (*S*)-aryl alcohol with high ee. Similarly, three possible transition state models (**D**, **E** and **F**) were proposed when using *ortho*-bromo diaryl ketone **3a** as a substrate. Transiton state **D** is favored over **E** and **F**, because the increased steric hindrance caused by inner bromo-substituted benzene ring with methyl or cyclohexyl group of the ligand is disfavored in **E** and **F**. Thus, the (*R*)-diaryl methanol **4a** is forming via intermediate **D**. Notably, experiment results are in accordance with this hypothesis: the smaller size of *ortho*-substituent (Br>Cl>Me>F) lead to a decreasement on enantioselectivity (see **4a**−**4d**).

Scheme 7. Control Experiments and Possible Transition States



CONCLUSION

In summary, we have successfully developed a series of novel tridentate ferrocene-based diamine-phosphine sulfonamide (f-diaphos) ligands for iridium-catalytic asymmetric hydrogenation of various arylalkyl ketones and diaryl ketones. Excellent enantioselectivities and superb activities (for arylalkyl ketones, up to 99.4% ee and 100 000 TON; for diaryl ketones, up to 98.2% ee and 10 000 TON) have been achieved using Ir−f-diaphos catalyst. This protocol could be easily conducted on gram scale, thereby provided a chance to synthesis various drugs. Moreover, current process represents the first example that ferrocene-based tridentate ligand

can realize controllable asymmetry hydrogenation of aryl alkyl ketones to produce (*R*)- and (*S*)-alcohols with excellent results.

EXPERIMENTAL SECTION

General information: All reactions were performed in an argon-filled glovebox. Anhydrous THF and toluene were distilled from sodium benzophenoneketyl. Anhydrous MeOH, EtOH and ^{i}PrOH were freshly distilled from magnesium. Hydrogen gas (99.999%), aromatic ketones, $[Ir(COD)Cl]_2$ and other chemical reagents were purchased from commercial suppliers. ^{1}HNMR (400, 500 or 600 MHz), ^{13}C NMR (100, 125 or 150 MHz) and ^{31}P NMR (243 or 202 MHz) spectra were recorded on a Bruker ADVANCE II and III instruments in $CDCl_3$ or DMSO-d_6 with TMS as internal standard. ^{1}H NMR chemical shifts were referenced to tetramethylsilane signal (0 ppm), ^{13}C NMR chemical shifts were referenced to the solvent resonance (77.00 ppm, $CDCl_3$). HRMS spectra were recorded on an Agilent 1200HPLC-6210TOFMS using ESI as ion source. Optical rotations were determined using a AUTOPOL V polarimeter. HPLC analyses were performed using Agilent 1100 equipped with OJ-H, OD-H, AD-H and ID column.

General Procedure for the Preparation of f-diaphos ligands. A solution of (R_c, S_{FC})- or (S_c, R_{FC})-**1** (1 mmol), (*R*, *R*)- or (*S*, *S*)-1,2-diamine (2 mmol) in dry MeOH (1 mL) was stirred at reflux overnight. The reaction mixture was cooled to room temperature, and then the solvent was removed under vacuum. The crude product was purified by column chromatography on silica gel to yield **L1**−**L11**.

*f-Diphos **L1***: Orange solid, 65% yield, 432.0 mg, mp 154−155 °C, $[\alpha]_D^{20}$ = -130.0 (c = 0.5, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.50−7.46 (m, 2H), 7.37−7.34 (m, 3H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.17−7.14 (m, 1H), 7.07−7.03 (m, 4H), 5.89 (s, 1H), 4.49 (s, 1H), 4.34 (t, *J* = 2.4 Hz, 1H), 4.05 (s, 5H), 4.00−3.99 (m, 1H), 3.68 (s, 1H), 2.42 (s, 3H), 2.14−2.06 (m, 2H), 1.91−1.89 (m, 1H), 1.83−1.81 (m, 1H), 1.47−1.42 (m, 2H), 1.33 (d, *J* = 6.0 Hz, 3H), 1.09−0.95 (m, 2H), 0.85−0.77 (m, 1H), 0.06 (brs, 1H), -0.26−-0.40 (m, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.8, 139.9 (d, *J* = 10.5 Hz), 137.2, 136.6 (d, *J* = 9.0 Hz), 135.0 (d, *J* = 21.0 Hz), 132.8 (d, *J* = 19.5 Hz), 129.4, 129.2, 128.3, 128.30, 128.2 (d, *J* = 7.5 Hz), 127.5, 98.1 (d, *J* = 22.5 Hz), 74.3 (d, *J* = 7.5 Hz), 71.2 (d, *J* = 4.5 Hz), 69.7, 69.5 (d, *J* = 4.5 Hz), 69.2, 57.8, 56.9, 32.1, 29.8, 24.8, 24.0, 21.6, 20.1; **^{31}P NMR** (243 MHz, $CDCl_3$) δ -24.73 (s). **HRMS** (ESI) calcd for $C_{37}H_{42}FeN_2O_2PS$ $[M + H]^+$, 665.2049; found: 665.2062.

*f-Diphos **L2***: Orange solid, 48% yield, 333.0 mg, mp 162-164 °C, $[\alpha]_D^{20}$ = -125.2 (c = 0.5, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.51 - 7.47 (m, 2H), 7.38 - 7.35 (m, 3H), 7.16 - 7.11 (m, 1H), 7.03 (t, *J* = 4.4 Hz, 4H), 6.92

(s, 2H), 5.93 (s, 1H), 4.49 (s, 1H), 4.33 (t, *J* = 2.8 Hz, 1H), 4.05 (s, 5H), 4.04-4.02 (m, 1H), 3.69 (s, 1H), 2.59 (s, 6H), 2.31 (s, 3H), 2.15 - 2.04 (m, 2H), 1.91 - 1.86 (m, 1H), 1.77-1.73 (m, 1H), 1.48 - 1.39 (m, 5H), 1.07 - 0.92 (m, 2H), 0.82 - 0.70 (m, 1H), -0.43 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 141.6,140.1 (d, *J* = 11.0 Hz), 139.1, 136.3 (d, *J* = 9.0 Hz), 135.0 (d, *J* = 21.0 Hz), 134.2, 132.6 (d, *J* = 19.0 Hz), 131.8, 129.2, 128.4 (d, *J* = 6.0 Hz), 128.2 (d, *J* = 8.0 Hz), 97.8 (d, *J* = 23.0 Hz), 74.0 (d, *J* = 6.0 Hz), 71.1 (d, *J* = 4.0 Hz), 69.7, 69.4 (d, *J* = 4.0 Hz), 69.2, 57.8, 57.0, 46.3 (d, *J* = 10.0 Hz), 32.0, 29.8, 24.9, 24.0, 23.1, 21.0, 19.9; **^{31}P NMR (162 MHz, $CDCl_3$)** δ -24.94 (s). HRMS (ESI) calcd for $C_{39}H_{46}FeN_2O_2PS$ $[M + H]^+$: 693.2362; Found: 693.2357.

*f-Diphos **L3***: Orange solid, 47% yield, 365 mg, mp 151-152 °C, $[\alpha]_D^{20}$ = -52.4 (c = 0.5, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.49−7.47 (m, 2H), 7.36−7.34 (m, 3H), 7.15 (s, 2H), 7.08 (t, *J* = 7.2 Hz, 3H), 6.96 (t, *J* = 7.2 Hz, 2H), 5.96 (s, 1H), 4.50 (s, 1H), 4.27 (s, 1H), 4.07−4.01 (br, 1H), 4.04 (s, 5H), 3.64 (s, 1H), 2.92 (hept, *J* = 6.6 Hz, 1H), 2.19−1.97 (m, 4H), 1.49 (t, *J* = 9.6 Hz, 2H), 1.39 (d, *J* = 5.4 Hz, 3H), 1.29−1.26 (m, 7H), 1.23 (d, *J* = 6.6 Hz, 6H), 1.17 (d, *J* = 6.6 Hz, 6H), 1.07−0.98 (m, 2H), 0.90−0.82 (m, 2H), 0.14 (s, 1H), -0.19−-0.21 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.1, 150.3, 139.9 (d, *J* = 10.0 Hz), 136.4 (d, *J* = 8.8 Hz), 135.1 (d, *J* = 21.3 Hz), 133.5, 132.6 (d, *J* = 18.8 Hz), 129.2, 128.3 (d, *J* = 6.3 Hz), 128.1 (d, *J* = 7.5 Hz), 123.6, 97.34 (d, *J* = 26.3 Hz), 74.3 (d, *J* = 6.3 Hz), 71.2 (d, *J* = 3.8 Hz), 70.0 (d, *J* = 2.5 Hz), 69.7, 69.1, 57.3 (d, *J* = 17.5 Hz), 46.6 (d, *J* = 8.8 Hz), 34.1, 32.0, 29.8 (d, *J* = 17.5 Hz), 25.1 (d, *J* = 13.8 Hz), 23.9, 23.6 (d, *J* = 25.0 Hz), 19.8; **^{31}P NMR** (243 MHz, $CDCl_3$) δ -24.96 (s). **HRMS** (ESI) calcd for $C_{45}H_{58}FeN_2O_2PS$ $[M + H]^+$, 777.3301; found: 777.3320.

*f-Diphos **L4***: Orange solid, 52% yield, 397 mg, mp 92-94 °C, $[\alpha]_D^{20}$ = -150.0 (c = 0.5, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53−7.50 (m, 2H), 7.40−7.38 (m, 6H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.29−7.28 (m, 2H), 7.13 (t, *J* = 6.6 Hz, 1H), 7.08 (t, *J* = 7.2 Hz, 2H), 7.00 (t, *J* = 7.8 Hz, 3H), 6.93 (t, *J* = 7.2 Hz, 2H), 6.79 (d, *J* = 7.8 Hz, 2H), 6.68 (d, *J* = 6.6 Hz, 2H), 6.45 (s, 1H), 4.37 (s, 1H), 4.30 (s, 1H), 4.02 (d, *J* = 7.8 Hz, 1H), 3.95 (s, 5H), 3.71−3.69 (m, 2H), 3.62 (d, *J* = 5.4 Hz, 1H), 2.34 (s, 3H), 1.51 (s, 1H), 1.16 (d, *J* = 3.0 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.4, 140.6 (d, *J* = 12.0 Hz), 138.6, 137.7, 135.3 (d, *J* = 21.0 Hz), 132.7 (d, *J* = 18.0 Hz), 129.1, 128.9, 128.5, 128.3, 128.1 (d, *J* = 7.5 Hz), 127.70, 127.65, 127.6, 127.4, 127.2, 127.0, 74.2 (d, *J* = 10.5 Hz), 71.5 (d, *J* = 4.5 Hz), 69.8, 69.6, 69.5, 64.7, 63.3, 47.6, 21.5, 19.7; **^{31}P NMR** (202 MHz, $CDCl_3$) δ -23.54 (s). **HRMS** (ESI) calcd for $C_{45}H_{44}FeN_2O_2PS$ $[M + H]^+$, 763.2206; found: 763.2174.

*f-Diphos **L5***: Orange solid, 62% yield, 412 mg, mp 140−142 °C, $[\alpha]_D^{20}$ = -72.8 (c = 0.5, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.8 Hz, 2H), 7.61 (d, *J* = 4.8 Hz, 2H), 7.40 (s, 3H), 7.31−7.26 (m, 7H), 5.10 (s, 1H), 4.44 (d, *J* = 9.0 Hz, 2H), 4.05 (s, 2H), 3.93 (s, 5H), 2.45 (s, 3H), 2.42−2.40 (br, 1H), 2.01−1.93 (m, 1H), 1.83 (d, J_1 = 10.2 Hz, 2H), 1.45 (s, 3H), 1.34 (d, *J* = 13.2 Hz, 1H), 1.27 (d, *J* = 12.0 Hz, 1H), 1.00−0.85 (m, 2H),

0.74−0.69 (m, 2H), 0.50−0.49 (br, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.9, 140.2 (d, *J* = 9.0 Hz), 137.8 (d, *J* = 7.5 Hz), 135.2 (d, *J* = 22.5 Hz), 132.7 (d, *J* = 19.5 Hz), 129.5, 129.2, 128.4 (d, *J* = 6.0 Hz), 128.1 (d, *J* = 3.0 Hz), 128.1, 127.3, 74.1 (d, *J* = 7.5 Hz), 71.0 (d, *J* = 3.0 Hz), 69.9, 69.7, 68.6 (d, *J* = 4.5 Hz), 56.9, 47.6, 31.7, 24.7, 24.0, 23.8, 21.6, 19.2; **^{31}P NMR** (243 MHz, $CDCl_3$) δ -26.91 (s). **HRMS** (ESI) calcd for $C_{37}H_{42}FeN_2O_2PS$ $[M + H]^+$, 665.2095; found: 665.2070.

*f-Diphos **L6***: Orange solid, 51% yield, 382 mg, mp 88−89 °C, $[\alpha]_D^{20}$ = -78.4 (c = 0.5, $CHCl_3$). **^{1}HNMR** (600 MHz, $CDCl_3$) δ 7.14 (d, *J* = 7.8 Hz, 2H), 7.01 (s, 1H), 6.88 (s, 2H), 6.85 (s, 1H), 6.73 (s, 2H), 5.96 (s, 1H), 4.46 (s, 1H), 4.31 (s, 1H), 4.05 (s, 5H), 4.01 (s, 1H), 3.71 (s, 1H), 2.60 (s, 6H), 2.32 (s, 6H), 2.26 (s, 3H), 2.11 (s, 6H), 2.03 (s, 2H), 1.90 (s, 1H), 1.80 (d, *J* = 12.6 Hz, 1H), 1.45−1.38 (m, 5H), 0.98−0.95 (m, 2H), 0.85−0.77 (m, 1H), 0.14 (s, 1H), -0.38 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 141.6, 139.5 (d, *J* = 9.0 Hz), 138.9, 137.9 (d, *J* = 7.5 Hz), 137.5 (d, *J* = 7.5 Hz), 136.2 (d, *J* = 9.0 Hz), 134.7, 132.7 (d, *J* = 21.0 Hz), 131.8, 130.9, 130.6 (d, *J* = 19.5 Hz), 130.1, 75.0 (d, *J* = 7.5 Hz), 71.2, 69.7, 57.6 (d, *J* = 61.5 Hz), 31.3, 29.8, 23.9, 22.9, 21.4, 21.2, 20.9; **^{31}P NMR** (243 MHz, $CDCl_3$) δ -25.04 (s). **HRMS** (ESI) calcd for $C_{43}H_{54}FeN_2O_2PS$ $[M + H]^+$, 749.2988; found: 749.3006.

*f-Diphos **L7***: Orange solid, 47% yield, 431 mg, mp 91−93 °C, $[\alpha]_D^{20}$ = -80.8 (c = 0.5, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.26 (s, 1H), 7.05 (d, *J* = 6.0 Hz, 2H), 6.86 (s, 2H), 6.00 (s, 1H), 4.48 (s, 1H), 4.31 (s, 1H), 4.08 (s, 5H), 4.00 (s, 1H), 3.59 (s, 1H), 2.60 (s, 6H), 2.27 (s, 3H), 2.06-1.99 (m, 2H), 1.89(s, 1H), 1.69 (d, *J* = 13.2 Hz, 1H), 1.45 (s, 3H), 1.37 (s, 2H), 1.27 (s, 19H), 1.14 (s, 18H), 0.98 - 0.94 (m, 2H), 0.79 - 0.70 (m, 1H), -0.52 - -0.55 (m, 1H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 150.7 (d, *J* = 7.5 Hz), 150.1 (d, *J* = 7.5 Hz), 141.3, 138.7, 138.1 (d, *J* = 6.3 Hz), 135.1 (d, *J* = 6.3 Hz), 134.7, 131.8, 129.2 (d, *J* = 21.3 Hz), 127.2 (d, *J* = 20.0 Hz), 122.6 (d, *J* = 47.5 Hz), 97.0 (d, *J* = 22.5 Hz), 76.1 (d, *J* = 5.0 Hz), 70.8 (d, *J* = 2.5 Hz), 69.6, 69.3 (d, *J* = 2.5 Hz), 68.9, 57.8 (d, *J* = 22.5 Hz), 47.2 (d, *J* = 10.0 Hz), 34.8 (d, *J* = 22.5 Hz), 31.4 (d, *J* = 5.0 Hz), 31.1, 30.0, 25.2, 23.8, 22.9, 20.8 (d, *J* = 11.3 Hz); **^{31}P NMR (162 MHz, $CDCl_3$)** δ -24.65 (s). HRMS (ESI) calcd for $C_{55}H_{78}FeN_2O_2PS$ $[M + H]^+$, 917.4879; found: 917.4867.

*f-Diphos **L8***: Orange solid, 50% yield, 444 mg, mp 87−89 °C, $[\alpha]_D^{20}$ = -74.4 (c = 0.5, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.71−7.70 (m, 2H), 7.39 (s, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.26 (s, 1H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.06 (d, *J* = 7.8 Hz, 2H), 5.95 (s, 1H), 4.48 (s, 1H), 4.29 (s, 1H), 4.08 (s, 5H), 3.99−3.98 (m, 1H), 3.58 (s, 1H), 2.40 (s, 3H), 2.06−2.02 (m, 2H), 1.96−1.93 (m, 1H), 1.78 (d, *J* = 12.6 Hz, 1H), 1.45−1.43 (m, 1H), 1.39 (d, *J* = 6.6 Hz, 4H), 1.28 (s, 18H), 1.15 (s, 18H), 1.00−0.92 (m, 2H), 0.81−0.75 (m, 1H), 0.14 (s, 1H), -0.32−-0.44 (q, *J* = 10.8 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 150.7 (d, *J* = 6.0 Hz), 150.1 (d, *J* = 6.0 Hz), 142.6, 138.1 (d, *J* =

7.5 Hz), 135.2 (d, *J* = 7.5 Hz), 129.4, 129.2 (d, *J* = 21.0 Hz), 127.4 (d, *J* = 21.0 Hz), 127.1, 122.8, 122.3, 76.1 (d, *J* = 6.0 Hz), 70.9 (d, *J* = 3.0 Hz), 69.6, 69.5, 68.9, 57.7 (d, *J* = 12.0 Hz), 47.1, 34.9, 34.7, 31.5, 31.4, 31.3, 30.0, 25.1, 23.8, 21.5, 20.8; **^{31}P NMR** (243 MHz, $CDCl_3$) δ -24.42 (s). **HRMS** (ESI) calcd for $C_{53}H_{74}FeN_2O_2PS$ $[M + H]^+$, 889.4554; found: 889.4516.

*f-Diphos **L9***: Orange oil, 56% yield, 412 mg, $[\alpha]_D^{20}$ = -374.4 (c = 0.5, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.34 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 2H), 7.30 (s, 1H), 7.13 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 2H), 4.45 (s, 1H), 4.23 (t, *J* = 2.4 Hz, 1H), 4.14−4.13 (m, 1H), 4.07 (s, 5H), 3.55 (s, 1H), 1.97−1.95 (m, 1H), 1.90−1.86 (m, 1H), 1.70−1.68 (m, 1H), 1.52−1.48 (m, 2H), 1.47−1.44 (m, 1H), 1.37 (d, *J* = 6.0 Hz, 3H), 1.27 (s, 18H), 1.21 (s, 18H), 1.07−1.00 (m, 1H), 0.96−0.83 (m, 3H), -0.086−-0.015 (m, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 150.6 (d, *J* = 6.0 Hz), 150.0 (d, *J* = 7.5 Hz), 138.3 (d, *J* = 7.5 Hz), 135.4 (d, *J* = 7.5 Hz), 129.3 (d, *J* = 19.5 Hz), 127.6 (d, *J* = 16.5 Hz), 122.5 (d, *J* = 64.5 Hz), 98.1 (d, *J* = 21.0 Hz), 76.2 (d, *J* = 4.5 Hz), 70.9 (d, *J* = 4.5 Hz), 69.5, 69.3 (d, *J* = 3.0 Hz), 68.6, 60.6, 55.3, 46.7 (d, *J* = 9.0 Hz), 34.9, 34.8, 34.5, 31.5, 30.2, 25.6, 24.8, 20.0; **^{31}P NMR** (243 MHz, $CDCl_3$) δ -24.22 (s). **HRMS** (ESI) calcd for $C_{46}H_{68}FeN_2P$ $[M + H]^+$, 735.4465; found: 735.4461.

*f-Diphos **L10***: Orange solid, 64% yield, 426 mg, mp 145−146 °C, $[\alpha]_D^{20}$ = +86.0 (c = 0.5, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 2H), 7.60−7.57 (m, 2H), 7.37−7.36 (m, 3H), 7.28−7.22 (m, 7H), 5.14 (s, 1H), 4.41−4.39 (m, 2H), 4.00−3.98 (m, 2H), 3.90 (s, 5H), 2.41 (s, 3H), 2.36 (s, 1H), 1.96−1.93 (m, 1H), 1.80−1.79 (m, 2H), 1.40 (d, *J* = 6.6 Hz, 3H), 1.33−1.23 (m, 3H), 0.89−0.87 (m, 1H), 0.75−0.73 (m, 1H), 0.66−0.60 (m, 1H), 0.53−0.47(m, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.9, 140.2 (d, *J* = 7.5 Hz), 137.8 (d, *J* = 7.5 Hz), 137.7, 135.2 (d, *J* = 22.5 Hz), 132.7 (d, *J* = 18.0 Hz), 129.5, 129.2, 128.3 (d, *J* = 6.0 Hz), 128.1 (d, *J* = 3.0 Hz), 127.3, 100.0 (d, *J* = 27 Hz), 74.1 (d, *J* = 9.0 Hz), 70.9 (d, *J* = 4.5 Hz), 69.9, 69.7, 68.6 (d, *J* = 4.5 Hz), 57.5, 56.8, 47.5 (d, *J* = 9.0 Hz), 32.0, 31.7, 24.8, 24.0, 23.8, 21.6; **^{31}P NMR** (243 MHz, $CDCl_3$) δ -26.78 (s). **HRMS** (ESI) calcd for $C_{37}H_{42}FeN_2O_2PS$ $[M + H]^+$, 665.2049; found: 665.2044.

*f-Diphos **L11***: Orange solid, 61% yield, 406 mg, mp 146−148 °C, $[\alpha]_D^{20}$ = +60.4 (c = 0.5, $CHCl_3$). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.70 (d, *J* = 6.0 Hz, 2H), 7.49−7.47 (m, 2H), 7.37 (s, 3H), 7.24 (d, *J* = 7.2 Hz, 2H), 7.18−7.13 (m, 1H), 7.05 (d, *J* = 3.0 Hz, 4H), 5.89 (s, 1H), 4.49 (s, 1H), 4.34 (d, *J* = 2.4 Hz, 1H), 4.05 (d, *J* = 2.4 Hz, 5H), 3.99 (d, *J* = 6.0 Hz, 1H), 3.68 (s, 1H), 2.43 (d, *J* = 1.2 Hz, 3H), 2.10 (t, *J* = 7.8 Hz, 2H), 1.91 (d, *J* = 12.6 Hz, 1H), 1.81 (t, *J* = 9.0 Hz, 1H), 1.47−1.42 (m, 2H), 1.33 (d, *J* = 4.2 Hz, 3H), 1.09−1.03 (m, 1H), 1.00−0.96 (m, 1H), 0.83−0.77 (m, 1H), 0.46 (brs, 1H), -0.35 (q, *J*= 10.8 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.8, 139.8 (d, *J* = 10.5 Hz), 137.2, 136.6 (d, *J* = 9.0 Hz), 134.9 (d, *J* = 21.0 Hz), 132.7 (d, *J* = 19.5 Hz), 129.4, 129.2, 128.3 (d, *J* = 6.0 Hz), 128.2 (d, *J* = 7.5 Hz), 127.5, 98.1 (d, *J* = 24.0 Hz), 74.3 (d, *J* = 6.0 Hz), 71.1 (d, *J* = 4.5 Hz), 70.4,

69.7, 69.5 (d, *J* = 3.0 Hz), 69.2, 57.8, 56.9, 46.3 (d, *J* = 9.0 Hz), 32.1, 29.8, 24.8, 23.9, 21.6, 20.0; **^{31}P NMR** (202 MHz, $CDCl_3$) δ -24.63 (s). **HRMS** (ESI) calcd for $C_{37}H_{42}FeN_2O_2PS$ $[M + H]^+$, 665.2053; found: 665.2060.

*f-Diphos **L12***: Orange solid, 46% yield, 318 mg, mp 77−78 °C, $[\alpha]_D^{20}$ = -80.6 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.59−7.54 (m, 2H), 7.39−7.36 (m, 3H), 7.24−7.15 (m, 7H), 4.35 (s, 1H), 4.29 (t, *J* = 2.8 Hz, 1H), 4.05−4.01 (m, 1H), 4.00 (s, 5H), 3.75 (s, 1H), 3.15−3.08 (m, 2H), 2.84 (s, 1H), 2.45 (s, 1H), 2.37 (s, 3H), 2.00 (d, *J* = 12.4 Hz, 1H), 1.61−1.45 (m, 3H), 1.42 (d, *J* = 6.4 Hz, 3H), 1.33−1.27 (m, 2H), 1.18 (t, *J* = 6.8 Hz, 3H), 0.93−0.87 (m, 2H), 0.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 140.2 (d, *J* = 10.0 Hz), 138.8, 137.4 (d, *J* = 8.0 Hz), 135.3 (d, *J* = 21.0 Hz), 132.8 (d, *J* = 18.0 Hz), 129.4, 129.1, 128.1 (d, *J* = 3.0 Hz), 128.0 (d, *J* = 2.0 Hz), 127.9, 127.2, 99.7 (d, *J* = 24.0 Hz), 74.2 (d, *J* = 6.0 Hz), 70.8 (d, *J* = 5.0 Hz), 69.6, 69.1, 68.8, 62.8, 54.8, 46.2, 32.4, 31.7, 29.7 (d, *J* = 4.0 Hz), 29.4, 25.7, 24.5, 22.7, 21.6, 20.2, 16.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ -23.55 (s). HRMS (ESI) calcd for $C_{39}H_{46}FeN_2O_2PS$ $[M + H]^+$, 693.2320; found: 693.2343.

General Procedure for the asymmetric hydrogenation of aryl alkyl ketones 1. Under argon atomosphere, $[Ir(COD)Cl]_2$ (8.4 mg, 0.012 mmol), **L8** (22.7 mg, 0.025 mmol), anhydrous ^{i}PrOH (3 mL) were added to an oven-dried vial (10 mL) and then stirred at 30 °C for 1.5 h to give a clear yellow solution. An aliquot of the catalyst solution (25 μL, 0.0002 mmol) was transferred into a 20-mL hydrogenation vessel, then ketones (2.0 mmol), ^{t}BuOLi in ^{i}PrOH (0.025 mmol/mL, 2 mL, 0.05 mmol) and anhydrous ^{i}PrOH (8 mL) were added. The vessel was placed in an autoclave which was then charged with 30 atm of H_2 and stirred at 25−30 °C for 12 h (60 °C for **2e**, **2f**, **2s**). After slowly releasing the hydrogen pressure, the solvent was removed, and the mixture was purified by passing through a short column of silica gel to afforded corresponding alcohol. The ee values of all compounds were determined by HPLC with a chiral column.

*(S)-1-Phenylethan-1-ol (**2a**)*: Colorless oil, 99% yield, 242.4 mg; 97.7% ee (*S*); $[\alpha]_D^{20}$ = -71.2 (c = 0.5, $CHCl_3$); lit.[16] $[\alpha]_D^{20}$ = -48 [c = 0.17, $CHCl_3$, 93% ee (*S*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 90:10; flow rate = 0.7 mL/min; UV detection at 210 nm; t_R(*S*) = 11.29 min (major), t_R(*R*) = 12.89 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38−7.34 (m, 1H), 7.29−7.26 (m, 1H), 4.90 (q, *J* = 6.6 Hz, 1H), 1.81 (brs, 1H), 1.50 (d, *J* = 6.6 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 145.8, 128.5, 127.5, 125.4, 70.5, 25.2.

*(R)-1-Phenylethan-1-ol (**2a'**)*: Colorless oil, 99% yield, 242.2 mg; 95.4% ee (*R*); $[\alpha]_D^{20}$ = +65.3 (c = 0.5, $CHCl_3$); lit.[16] $[\alpha]_D^{20}$ = -48 [c = 0.17, $CHCl_3$, 93% ee (*S*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 90:10; flow rate = 0.7 mL/min; UV detection at 210 nm; t_R(*S*) = 11.01 min (minor), t_R(*R*) = 12.51 min (major). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38−7.34 (m, 1H), 7.29−7.26 (m, 1H), 4.90 (q, *J* = 6.6 Hz, 1H), 1.81 (brs, 1H), 1.50 (d, *J* = 6.6 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.8, 127.5, 126.5,

124.4, 69.4, 24.1.

*(S)-1-Phenylpropan-1-ol (**2b**)*: Colorless oil, 99% yield, 270.0 mg; 98.4% ee (*S*). $[\alpha]_D^{20}$ = -40.4 (c = 0.5, $CHCl_3$); lit.[12c] $[\alpha]_D^{20}$ = +46.9 [c = 1.0, $CHCl_3$, >99% ee (*R*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 220 nm; t_R(*S*) = 10.95 min (major), t_R(*R*) = 12.02 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34−7.30 (m, 4H), 7.27−7.24 (m, 1H), 4.56−4.53 (m, 1H), 2.16−2.08 (br, 1H), 1.83−1.69 (m, 2H), 0.892 (t, *J* = 7.8 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.6, 128.4, 127.5, 126.0, 76.0, 31.9, 10.2.

*(S)-1-Phenylbutan-1-ol (**2c**)*: White solid, 99% yield, 149.2 mg, 98.5% ee (*S*). $[\alpha]_D^{20}$ = -33.2 (c = 0.5, $CHCl_3$); lit.[17] $[\alpha]_D^{20}$ = +51.6 [c = 0.94, $CHCl_3$, 96.6% ee (*R*)].The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 97:3; flow rate = 0.5 mL/min; UV detection at 220 nm; t_R(*S*) = 21.61 min (major), t_R(*R*) = 23.44 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35−7.32 (m, 4H), 7.28−7.25 (m, 1H), 4.65 (t, *J* = 7.2 Hz, 1H), 1.94−1.92 (br, 1H), 1.81−1.75 (m, 1H), 1.70−1.64 (m, 1H), 1.47−1.38 (m, 1H), 1.34−1.26 (m, 1H), 0.92 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 145.0, 128.4, 127.5, 125.9, 74.4, 41.3, 19.1, 14.0.

*(S)-1,2-Diphenylethan-1-ol (**2d**)*: White soild, 99% yield, 395.4 mg, 97.9% ee (*S*). $[\alpha]_D^{20}$ = -29.6 (c = 0.5, $CHCl_3$); lit.[18] $[\alpha]_D^{20}$ = +47.6 [c = 0.5, EtOH, 94.0% ee (*R*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 90:10; flow rate = 0.9 mL/min; UV detection at 210 nm; t_R(*R*) = 9.19 min (minor), t_R(*S*) = 10.02 min (major). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36−7.19 (m, 10H), 4.90−4.88 (m, 1H), 3.06−2.97 (m, 2H), 2.04−1.95 (br, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.8, 138.1, 129.6, 128.5, 128.4, 127.7, 126.7, 125.9, 75.4, 46.1.

*(S)-2-Methyl-1-phenylpropan-1-ol (**2e**)*: Colorless oil, 98% yield, 294.4 mg; 97.4% ee (*S*). $[\alpha]_D^{20}$ = -24.8 (c = 0.5, $CHCl_3$); lit.[12c] $[\alpha]_D^{20}$ = +41.6 [c = 1.0, $CHCl_3$, >99% ee (*R*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 98:2; flow rate = 0.8 mL/min; UV detection at 210 nm; t_R(*S*) = 15.26 min (major), t_R(*R*) = 17.85 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34−7.25 (m, 5H), 4.35 (d, *J* = 7.2 Hz, 1H), 1.98−1.92 (m, 1H), 1.89−1.88 (br, 1H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.7, 128.2, 127.4, 126.6, 80.1, 35.3, 19.0, 18.3.

*(S)-1,2,3,4-Tetrahydronaphthalen-1-ol (**2f**)*: Red solid, 99% yield, 295.4 mg, 97.5% ee (*S*). $[\alpha]_D^{20}$ = +33.2 (c = 0.5, $CHCl_3$); lit.[17] $[\alpha]_D^{20}$ = -28.6 (c = 0.88, $CHCl_3$, 94.4% ee (*R*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 13.43 min (major), t_R(*R*) = 16.66 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.45−7.43 (m, 1H), 7.24−7.20 (m, 2H), 7.12 (t, *J* = 4.8 Hz, 1H), 4.76 (t, *J* = 4.8 Hz, 1H), 2.86−2.81 (m, 1H), 2.77−2.71 (m, 1H), 2.19 (s, 1H), 2.02−1.95 (m, 2H),

1.92−1.86 (m, 1H), 1.83−1.76 (m, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.9, 137.1, 129.0, 128.7, 127.6, 126.2, 68.1, 32.3, 29.3, 18.9.

*(S)-1-(o-Tolyl)ethan-1-ol (**2g**)*: Colorless oil, 99% yield, 271.2 mg, 99.0% ee (*S*). $[\alpha]_D^{20}$ = -36.4 (c = 0.5, $CHCl_3$); lit.[12c] $[\alpha]_D^{20}$ = +77.0 [c = 1.0, $CHCl_3$, >99% ee (*R*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 99:1; flow rate = 0.5 mL/min; UV detection at 220 nm; t_R(*S*) = 45.38 min (minor), t_R(*R*) = 47.79 min (major). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.2 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.16 (td, J_1 = 7.8 Hz, J_2 = 1.2 Hz), 7.13−7.12 (d, *J* = 7.8 Hz, 2H), 5.12−5.09 (m, 1H), 2.33 (s, 3H), 1.91−1.86 (br, 1H), 1.45 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.9, 134.2, 130.4, 127.2, 126.4, 124.5, 66.8, 24.0, 18.9.

*(S)-1-(m-Tolyl)ethan-1-ol (**2h**)*: Colorless oil, 99% yield, 270.2 mg, 98.8% ee (*S*). $[\alpha]_D^{20}$ = -36.0 (c = 0.5, $CHCl_3$); lit.[19] $[\alpha]_D^{20}$ = +47.8 [c = 1.0, $CHCl_3$, 96% ee (*R*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 12.94 min (major), t_R(*R*) = 14.31 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.24−7.21 (m, 1H), 7.17 (s, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 4.82 (q, *J* = 6.6 Hz, 1H), 2.35 (s, 3H), 2.12−2.05 (br, 1H), 1.46 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 145.9, 138.2, 128.4, 128.2, 126.2, 122.5, 70.4, 25.1, 21.5.

*(S)-1-(p-Tolyl)ethan-1-ol (**2i**)*: Colorless oil, 99% yield, 270.0 mg, 97.9% ee (*S*). $[\alpha]_D^{20}$ = -27.6 (c = 0.5, $CHCl_3$); lit.[16] $[\alpha]_D^{20}$ = -49.0 [c = 0.33, $CHCl_3$, 85% ee (*S*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 220 nm; t_R(*S*) = 12.60 min (major), t_R(*R*) = 14.88 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 4.84 (q, *J* = 6.6 Hz, 1H), 2.34 (s, 3H), 1.98−1.91 (br, 1H), 1.47 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.9, 137.1, 129.2, 125.4, 70.2, 25.1, 21.1.

*(S)-1-(4-Methoxyphenyl)ethan-1-ol (**2j**):* Colorless oil, 99% yield, 303.4 mg, 97.7% ee (*S*). $[\alpha]_D^{20}$ = -51.6 (c = 0.5, $CHCl_3$); lit.[19] $[\alpha]_D^{20}$ = +56.8 [c = 1.0, $CHCl_3$, 95% ee (*R*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 210 nm; t_R(*R*) = 16.27 min (minor), t_R(*S*) = 18.44 min (major). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 4.78 (q, *J* = 6.0 Hz, 1H), 3.76 (s, 3H), 2.57 (brs, 1H), 1.43 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 158.9, 138.1, 126.7, 113.8, 69.8, 55.3, 25.0.

*(S)-1-(4-Fluorophenyl)ethan-1-ol (**2k**)*: Colorless oil, 99% yield, 279.2 mg, 95.8% ee (*S*). $[\alpha]_D^{20}$ = -29.6 (c = 0.5, $CHCl_3$); lit.[12a] $[\alpha]_D^{20}$ = +49.0 [c = 0.2, CH_2Cl_2, 99.9% ee (*R*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 97:3; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 21.68 min

(major), t_R(*R*) = 23.15 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.32−7.28 (m, 2H), 7.03−6.99 (m, 2H), 4.83 (q, *J* = 6.6 Hz, 1H), 2.38 (s, 1H), 1.44 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.1 (d, $^1J_{C\text{-}F}$ = 244.5 Hz), 141.5 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 127.1 (d, $^3J_{C\text{-}F}$ = 7.5 Hz), 115.3 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 69.8, 25.3.

*(S)-1-(4-Chlorophenyl)ethan-1-ol (**2l**)*: Colorless oil, 99% yield, 310.4 mg, 97.0% ee (*S*). $[\alpha]_D^{20}$ = -5.2 (c = 0.5, $CHCl_3$); lit.[16] $[\alpha]_D^{20}$ = -38 [c = 0.28, $CHCl_3$, 95% ee (*S*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 97:3; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 20.34 min (major), t_R(*R*) = 22.49 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30−7.25 (m, 4H), 4.82 (q, *J* = 6.6 Hz, 1H), 2.40 (s, 1H), 1.43 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.3, 133.0, 128.6, 126.8, 69.7, 25.2.

*(S)-1-(3-Bromophenyl)ethan-1-ol (**2m**)*: Colorless oil, 99% yield, 398.6 mg, 97.6% ee (*S*). $[\alpha]_D^{20}$ = -27.2 (c = 0.5, $CHCl_3$); lit.[16] $[\alpha]_D^{20}$ = -35 [c = 0.32, $CHCl_3$, 99% ee (*S*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 220 nm; t_R(*S*) = 11.64 min (major), t_R(*R*) = 14.01 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.51 (t, *J* = 1.8 Hz, 1H), 7.39−7.37 (m, 1H), 7.26 (d, *J* = 7.8 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 4.82 (q, *J* = 6.6 Hz, 1H), 2.21 (s, 1H), 1.45 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 148.1, 130.5, 130.1, 128.6, 124.0, 122.6, 69.7, 25.3.

*(S)-1-(4-Bromophenyl)ethan-1-ol (**2n**)*: Colorless oil, 99% yield, 398.4 mg, 97.5% ee (*S*). $[\alpha]_D^{20}$ = -17.2 (c = 0.5, $CHCl_3$); lit.[16] $[\alpha]_D^{20}$ = -32 [c = 0.36, $CHCl_3$, 95% ee (*S*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 98:2; flow rate = 0.8 mL/min; UV detection at 210 nm; t_R(*S*) = 35.48 min (major), t_R(*R*) = 39.57 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47−7.45 (m, 2H), 7.25−7.23 (m, 2H), 4.85 (q, *J* = 6.6 Hz, 1H), 1.93 (s, 1H), 1.46 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.8, 131.6, 127.2, 121.2, 69.8, 25.3.

*(S)-1-(2,4-Dichlorophenyl)ethan-1-ol (**2o**):* Colorless oil, 99% yield, 378.0 mg, 96.5% ee (*S*). $[\alpha]_D^{20}$ = -21.6 (c = 0.5, $CHCl_3$); lit.[20] $[\alpha]_D^{25}$ = -52.4 [c = 0.55, $CHCl_3$, 94% ee (*S*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 98:2; flow rate = 0.6 mL/min; UV detection at 210 nm; t_R(*S*) = 22.15 min (major), t_R(*R*) = 24.05 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 1H), 7.29 (d, *J* = 1.8 Hz, 1H), 7.24−7.20 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 5.15 (q, *J* = 6.6 Hz, 1H), 3.02 (s, 1H), 1.40 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 141.7, 133.3, 132.0, 129.0, 127.5, 127.4, 66.5, 23.6.

*(S)-1-(3,5-Bis(trifluoromethyl)phenyl)ethan-1-ol (**2p**)*: White soild, 97% yield, 500.8 mg, 98.6% ee (*S*). $[\alpha]_D^{20}$ = -10.3 (c = 0.5, $CHCl_3$); lit.[19] $[\alpha]_D^{20}$ = +22.7 [c = 1.0, $CHCl_3$, 93% ee (*R*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 98:2; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 10.44 min (major), t_R(*R*) = 11.55 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.84 (s, 2H), 7.79 (s, 1H), 5.04 (q, *J*

= 6.6 Hz, 1H), 2.09 (s, 1H), 1.54 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 148.2, 131.7 (q, $^2J_{C\text{-}F}$ = 33.0 Hz), 125.6 (q, $^4J_{C\text{-}F}$ = 1.5 Hz), 123.3 (q, $^1J_{C\text{-}F}$ = 271.5 Hz), 121.4−121.2 (m), 69.3, 25.5.

*(S)-1-(4-Nitrophenyl)ethan-1-ol (**2q**)*: Brown oil, 96% yield, 320.9 mg, 94.0% ee (*S*). $[\alpha]_D^{20}$ = -18.0 (c = 0.5, $CHCl_3$); lit.[16] $[\alpha]_D^{20}$ = -17.0 [c = 0.65, $CHCl_3$, 80% ee (*S*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 96:4; flow rate = 0.8 mL/min; UV detection at 210 nm; t_R(*S*) = 55.86 min (major), t_R(*R*) = 60.69 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.18 (td, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 2H), 7.54−7.52 (m, 2H), 5.01 (q, *J* = 6.6 Hz, 1H), 2.11 (s, 1H), 1.51 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 153.1, 147.2, 126.1, 123.8, 69.5, 25.5.

*(S)-1-(Benzo[d][1,3]dioxol-5-yl)ethan-1-ol (**2r**)*: Brown oil, 99% yield, 165.3 mg, 98.3% ee (*S*). $[\alpha]_D^{20}$ = -24.8 (c = 0.5, $CHCl_3$); lit.[21] $[\alpha]_D^{20}$ = +32.4 [c = 0.67, CH_2Cl_2, 86% ee (*R*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 230 nm; t_R(*R*) = 18.91 min (minor), t_R(*S*) = 22.78 min (major). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.88 (s, 1H), 6.78 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 2H), 5.94 (s, 2H), 4.80 (q, *J* = 6.6 Hz, 1H), 1.95 (s, 1H), 1.45 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 147.8, 146.8, 140.0, 118.7, 108.1, 106.1, 101.0, 70.2, 25.2.

*(S)-1-(Naphthalen-1-yl)ethan-1-ol (**2s**)*: White soild, 99% yield, 171.2 mg, 98.3% ee (*S*). $[\alpha]_D^{20}$ = -80.4 (c = 0.5, $CHCl_3$); lit.[12a] $[\alpha]_D^{20}$ = +38.4 [c = 0.5, CH_2Cl_2, 94% ee (*R*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 230 nm; t_R(*S*) = 21.29 min (major), t_R(*R*) = 38.27 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 1H), 7.89−7.88 (m, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.54−7.47 (m, 3H), 5.66 (q, *J* = 6.6 Hz, 1H), 2.11 (s, 1H), 1.67 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 141.4, 133.8, 130.3, 128.9, 127.9, 126.1, 125.6, 125.6, 123.2, 122.0, 67.1, 24.4.

*(S)-1-([1,1'-Biphenyl]-4-yl)ethan-1-ol (**2t**)*: White solid, 99% yield, 394.6 mg, 99.0% ee (*S*). $[\alpha]_D^{20}$ = -20.8 (c = 0.5, $CHCl_3$); lit.[22] $[\alpha]_D^{22}$ = -41.9 [c = 1.0, $CHCl_3$, 92% ee (*S*)]. The ee was determined by HPLC on Chiralpak AD−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 254 nm; t_R(*S*) = 15.86 min (major), t_R(*R*) = 17.59 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.61−7.59 (m, 4H), 7.45 (t, *J* = 7.8 Hz, 4H), 7.36 (t, *J* = 7.8 Hz, 1H), 4.96 (q, *J* = 6.6 Hz, 1H), 1.94−1.92 (br, 1H), 1.55 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.9, 140.9, 140.5, 128.8, 127.3, 127.1, 125.9, 70.2, 25.2.

*(S)-1-(9H-Fluoren-2-yl)ethan-1-ol (**2u**):* White solid, 99% yield, 418.0 mg, 99.4% ee (*S*); $[\alpha]_D^{20}$ = -33.2 (c = 0.5, $CHCl_3$); lit.[23] $[\alpha]_D^{25}$ = +44.3 [c = 1.5, $CHCl_3$, 81% ee (*R*)]. The ee was determined by HPLC on Chiralpak AD−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 18.94 min

(major), t_R(*R*) = 22.29 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 2H), 7.40−7.37 (m, 2H), 7.31 (t, *J* = 7.8 Hz, 1H), 4.98 (q, *J* = 6.6 Hz, 1H), 3.89 (s, 2H), 2.00 (s, 1H), 1.56 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.6, 143.6, 143.4, 141.5, 141.2, 126.8, 126.7, 125.1, 124.2, 122.1, 119.9, 119.8, 70.7, 36.9, 25.3.

*(S)-1-(Thiophen-2-yl)ethan-1-ol (**2v**)*: Colorless oil, 91% yield, 233.3 mg, 95.8% ee (*S*). $[\alpha]_D^{20}$ = -32.8 (c = 0.5, $CHCl_3$); lit.[12a] $[\alpha]_D^{20}$ = +14.6 [c = 1.25, $CHCl_3$, 99.9% ee (*R*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 16.94 min (major), t_R(*R*) = 22.46 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.23 (dd, J_1 = 4.8 Hz, J_2 = 1.2 Hz, 1H), 6.96−6.95 (m, 2H), 5.10 (q, *J* = 6.6 Hz, 1H), 2.48 (s, 1H), 1.58 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.0, 126.7, 124.4, 123.2, 66.2, 25.3.

*(S)-1-(Furan-2-yl)ethan-1-ol (**2w**)*: Yellow oil, 99% yield, 111.3 mg, 94.7% ee (*S*). $[\alpha]_D^{20}$ = -31.2 (c = 0.5, $CHCl_3$); lit.[12c] $[\alpha]_D^{20}$ = +16.6 [c = 1.0, $CHCl_3$, 96% ee (*R*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 14.06 min (major), t_R(*R*) = 16.07 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37−7.36 (m, 1H), 6.33 (dd, J_1 = 3.0 Hz, J_2 = 1.8 Hz, 1H), 6.23 (d, *J* = 3.0 Hz, 1H), 4.88 (q, *J* = 6.6 Hz, 1H), 1.97 (s, 1H), 1.54 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 157.6, 141.9, 110.1, 105.1, 63.7, 21.3.

*(S)-1-(Benzofuran-2-yl)ethan-1-ol (**2x**)*: Brown oil, 99% yield, 322.0 mg, 97.9% ee (*S*). $[\alpha]_D^{20}$ = -8.0 (c = 0.5, $CHCl_3$); lit.[24] $[\alpha]_D^{20}$ = +11.6 [c = 1.0, $CHCl_3$, 97% ee (*R*)]. The ee was determined by HPLC on Chiralpak ID column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 215 nm; t_R(*R*) = 8.04 min (minor), t_R(*S*) = 8.43 min (major). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 6.8 Hz, 1H), 7.47−7.46 (m, 1H), 7.28 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz,1H), 7.23−7.21 (m, 1H), 6.60 (s, 1H), 5.01 (q, *J* = 6.6 Hz, 1H), 2.28 (s, 1H), 1.64 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 160.2, 154.8, 128.2, 124.2, 122.8, 121.1, 111.2, 101.8, 64.2, 21.4.

Typical procedure for the asymmetric hydrogenation of diaryl ketones 3: Under argon atomosphere, $[Ir(COD)Cl]_2$ (8.4 mg, 0.012 mmol), **L6** (18.7, 0.025 mmol), anhydrous ^{i}PrOH (3 mL) were added to an oven-dried vial (10 mL) and then stirred at room temperature for 1.5 h to give a clear yellow solution. An aliquot of the catalyst solution (125 μL, 0.001 mmol) was transferred by syringe into a 10-mL vial, then ketones (1 mmol), ^{t}BuOLi in ^{i}PrOH (0.025 mmol/mL, 1.0 mL, 0.025 mmol) and anhydrous ^{i}PrOH (4 mL) were added. The vessel was placed in an autoclave which was then charged with 30 atm of H_2 and stirred at 25−30 ^{o}C for 12 h. After slowly releasing the hydrogen pressure, the solvent was removed, and the mixture was purified by passing through a short column of silica gel to afforded corresponding alcohols **4a−4l**. The ee values of all

compounds were determined by HPLC with a chiral column.

*(R)-(2-Bromophenyl)(phenyl)methanol (**4a**)*: Clear oil, 96% yield, 253.2 mg, 94.6% ee (*R*). $[\alpha]_D^{20}$ = +46.4 (c = 0.5, $CHCl_3$); lit.[25] $[\alpha]_D^{20}$ = -41.6 [c = 1.4, $CHCl_3$, 99% ee (*S*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*R*) = 13.46 min (major), t_R(*S*) = 19.40 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.36−7.33 (m, 3H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 6.21 (s, 1H), 2.43 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.5, 142.2, 132.9, 129.1, 128.5, 127.8, 127.7, 127.1, 122.8, 74.8. **HRMS** (EI) calcd for $C_{13}H_{11}BrO$ $[M]^+$, 261.9993; found: 261.9998.

*(R)-(2-Chlorophenyl)(phenyl)methanol (**4b**)*: Clear oil, 98% yield, 215.4 mg, 92.9% ee (*R*). $[\alpha]_D^{20}$ = +11.6 (c = 0.5, $CHCl_3$); lit.[26] $[\alpha]_D^{20}$ = -15.2 [c = 1.51, $CHCl_3$, 98% ee (*S*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 97:3; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*R*) = 30.65 min (major), t_R(*S*) = 38.41 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.61 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.41−7.40 (m, 2H), 7.36−7.33 (m, 3H), 7.32−7.27 (m, 2H), 7.23 (t, J_1 = 7.8 Hz, J_2 = 1.8 Hz,1H), 6.23 (s, 1H), 2.39 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.3, 141.0, 132.6, 129.6, 128.8, 128.5, 128.1, 127.8, 127.1, 126.9, 72.7. **HRMS** (EI) calcd for $C_{13}H_{11}ClO$ $[M]^+$, 218.0498; found: 218.0506.

*(R)-(2-Fluorophenyl)(phenyl)methanol (**4c**)*: Clear oil, 99% yield, 201.6 mg, 82.1% ee (*R*). $[\alpha]_D^{20}$ = -3.6 (c = 0.5, $CHCl_3$); lit.[26] $[\alpha]_D^{20}$ = -4.6 [c = 0.84, $CHCl_3$, 84% ee (*R*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 97:3; flow rate = 1.0 mL/min; UV detection at 220 nm; t_R(*R*) = 18.24 min (major), t_R(*S*) = 20.26 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53 (t, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.32−7.26 (m, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 6.11 (s, 1H), 3.00 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 160.0 (d, $^1J_{C\text{-}F}$ = 244.5 Hz), 142.8, 131.0 (d, $^3J_{C\text{-}F}$ = 13.5 Hz), 129.2 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 128.6, 127.8, 127.7 (d, $^4J_{C\text{-}F}$ = 4.5 Hz), 126.4, 124.4 (d, $^4J_{C\text{-}F}$ = 4.5 Hz), 115.4 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 70.1 (d, $^4J_{C\text{-}F}$ = 3.0 Hz). **HRMS** (EI) calcd for $C_{13}H_{11}FO$ $[M]^+$, 202.0794; found: 202.0789.

*(R)-Phenyl(o-tolyl)methanol (**4d**)*: White soild, 98% yield, 195.1 mg, 85.1% ee (*R*). $[\alpha]_D^{20}$ = -3.6 (c = 0.5, $CHCl_3$); lit.[25] $[\alpha]_D^{20}$ = +7.3 [c = 0.735, $CHCl_3$, 98% ee (*S*)]. The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 210 nm; t_R(*R*) = 20.83 min (major), t_R(*S*) = 23.26 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 4.2 Hz, 4H), 7.27−7.22 (m, 2H), 7.20−7.18 (m, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 5.97 (s, 1H), 2.23 (s, 3H), 2.18 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.9, 141.5, 135.4, 130.6, 128.5, 127.6, 127.6, 127.1, 126.3, 126.1, 73.4, 19.4. **HRMS** (EI) calcd for $C_{14}H_{14}O$ $[M]^+$, 198.1045; found: 198.1058.

*(R)-(2-Bromophenyl)(4-fluorophenyl)methanol (**4e**):* White soild, 94% yield, 264.6 mg, 94.1% ee (*R*). $[\alpha]_D^{20}$ = +21.6 (c = 0.5, $CHCl_3$); The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*R*) = 11.55 min (major), t_R(*S*) = 17.42 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.54 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.38−7.34 (m, 3H), 7.16 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.02 (t, *J* = 8.4 Hz, 2H), 6.16 (s, 1H), 2.56 (brs, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.3 (d, $^1J_{C\text{-}F}$ = 244.5 Hz), 142.4, 137.9 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 132.9, 129.3, 128.8 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 128.3, 127.8, 122.7, 115.3 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 74.2. **HRMS** (EI) calcd for $C_{13}H_{10}BrFO$ $[M]^+$, 279.9899; found: 279.9911.

*(R)-(2-Bromophenyl)(4-chlorophenyl)methanol (**4f**):* Clear oil, 92% yield, 275.3 mg, 91.9% ee (*R*). $[\alpha]_D^{20}$ = +59.6 (c = 0.5, $CHCl_3$); The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*R*) = 12.10 min (major), t_R(*S*) = 19.41 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.55−7.52 (m, 2H), 7.34−7.32 (m, 3H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.16 (td, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 6.16 (s, 1H), 2.53 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.2, 140.6, 133.6, 133.0, 129.4, 128.6, 128.4, 128.4, 127.9, 122.7, 74.1. **HRMS** (EI) calcd for $C_{13}H_{10}BrClO$ $[M]^+$, 295.9604; found: 295.9607.

*(R)-(2-Bromophenyl)(4-bromophenyl)methanol (**4g**):* Clear oil, 90% yield, 305.9 mg, 91.8% ee (*R*). $[\alpha]_D^{20}$ = +13.6 (c = 0.5, $CHCl_3$); The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 97:3; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*R*) = 35.85 min (major), t_R(*S*) = 67.70 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 1H), 7.52 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 2H), 7.18−7.15 (m, 1H), 6.14 (s, 1H), 2.53 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.1, 141.2, 133.0, 131.6, 129.4, 128.8, 128.4, 127.9, 122.7, 121.7, 74.2. **HRMS** (EI) calcd for $C_{13}H_{10}Br_2O$ $[M]^+$, 339.9098; found: 339.9099.

*(R)-(2-Bromophenyl)(p-tolyl)methanol (**4h**):* White soild, 97% yield, 270.2 mg, 93.2% ee (*R*). $[\alpha]_D^{20}$ = +31.6 (c = 0.5, $CHCl_3$); lit.[27] $[\alpha]_D^{20}$ = -30.0 [c = 1.1, $CHCl_3$, 86% ee (S)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*R*) = 10.71 min (major), t_R(*S*) = 13.92 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.62 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.54 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.36−7.34 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.16−7.14 (m, 3H), 6.15 (s, 1H), 2.43 (s, 1H), 2.34 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.7, 139.3, 137.5, 132.8, 129.2, 129.0, 128.4, 127.7, 127.1, 122.8, 74.7, 21.2. **HRMS** (EI) calcd for $C_{14}H_{13}BrO$ $[M]^+$, 276.0150; found: 276.0160.

*(R)-(2-Bromophenyl)(4-methoxyphenyl)methanol (**4i**):* White soild, 95% yield, 280.1 mg, 93.9% ee (*R*). $[\alpha]_D^{20}$ = +11.2 (c = 0.5, $CHCl_3$); lit.[28] $[\alpha]_D^{20}$ = -10.3 [c = 0.63, CH_2Cl_2, 85% ee (S)]. The ee was determined by HPLC on

Chiralpak OD−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*R*) = 17.19 min (major), t_R(*S*) = 22.08 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.64 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.53 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.37−7.34 (m, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.14 (td, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 6.87−6.85 (m, 2H), 6.10 (s, 1H), 3.78 (s, 3H), 2.58 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 159.1, 142.7, 134.4, 132.8, 129.0, 128.5, 128.2, 127.7, 122.7, 113.9, 74.4, 55.3. **HRMS** (EI) calcd for $C_{14}H_{13}BrO_2$ $[M]^+$, 292.0099; found: 292.0111.

*(R)-(2-bromophenyl)(3,5-dimethylphenyl)methanol (**4j**):* White soild, 99% yield, 289.5 mg, 91.7% ee (*R*). $[\alpha]_D^{20}$ = +82.8 (c = 0.5, $CHCl_3$); The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*R*) = 12.48 min (major), t_R(*S*) = 39.68 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.54 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.36−7.33 (m, 1H), 7.15 (td, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.01 (s, 2H), 6.92 (s, 1H), 6.13 (s, 1H), 2.30 (s, 6H), 1.57 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.7, 142.1, 138.0, 132.8, 129.5, 129.0, 128.6, 127.7, 124.8, 122.8, 74.8, 21.4. **HRMS** (EI) calcd for $C_{15}H_{15}BrO$ $[M]^+$, 290.0306; found: 290.0305.

*(R)-(5-Bromo-2-chlorophenyl)(4-ethoxyphenyl)methanol (**4k**):* White soild, 97% yield, 331.7 mg, 98.2% ee (*R*). $[\alpha]_D^{20}$ = -84.6 (c = 0.5, $CHCl_3$); The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 225 nm; t_R(*R*) = 8.80 min (major), t_R(*S*) = 10.17 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 2.0 Hz, 1H), 7.31 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 1H), 6.84−6.81 (m, 2H), 6.01 (s, 1H), 3.99 (q, *J* = 7.0 Hz, 2H), 2.47 (s, 1H), 1.38 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.8, 143.2, 133.6, 131.5, 131.2, 131.0, 130.6, 128.4, 121.0, 114.5, 72.2, 63.5, 14.8. **HRMS** (EI) calcd for $C_{15}H_{14}BrClO_2$ $[M]^+$, 339.9866; found: 339.9856.

*(R)-(5-Bromo-2-chlorophenyl)(4-fluorophenyl)methanol (**4l**):* White soild, 98% yield, 309.5 mg, 93.2% ee (*R*). $[\alpha]_D^{20}$ = -193.2 (c = 0.5, $CHCl_3$); The ee was determined by HPLC on Chiralpak OJ−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 210 nm; t_R(*R*) = 10.95 min (major), t_R(*S*) = 13.05 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 2.4 Hz, 1H), 7.36−7.33 (m, 3H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.04 (t, *J* = 8.4 Hz, 2H), 6.10 (s, 1H), 2.39 (s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.4 (d, $^1J_{C\text{-}F}$ = 244.5 Hz), 142.8, 137.3, 131.9, 131.2, 131.1, 130.7, 128.8 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 121.1, 115.6 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 71.8. **HRMS** (EI) calcd for $C_{13}H_9BrClFO$ $[M]^+$, 313.9509; found: 313.9499.

Typical procedure for the synthesis of compound 5h. To a 5.0-mL vial was added the catalyst precursor $[Ir(COD)Cl]_2$ (8.4 mg, 0.012 mmol), **L6** (18.7, 0.025 mmol) and anhydrous ^{i}PrOH (3 mL) under argon atomosphere. The mixture was stirred for 1 h at room temperature to give a clear yellow solution. An aliquot of

the catalyst solution (125 μL, 0.001 mmol) was transferred into a 100-mL hydrogenation autoclave, then ^{t}BuOLi (20 mg, 0.25 mmol), **3h** (2.74 g, 10 mmol) and anhydrous ^{i}PrOH (20 mL) was added. The autoclave was then charged with 50 atm of H_2 and stirred at 25−30 ^{o}C for 24 h. The work-up was identical to that described for the asymmetric hydrogenation at S/C = 1 000. (*R*)-(2-Bromophenyl)(p-tolyl)methanol (**4h**): > 99% conversion, 93.42% ee (*R*).

To a solution of **4h** (2.70 g, 9.75 mmol) in THF (54 mL) was added *n*-BuLi (12 mL, 2.5 M in n-hexane) under argon atomosphere at -78 °C. After addition was complete, the mixture was stirred for 3.0 h at -78 °C. The mixture was quenched by the addition of H_2O. The aqueous layer was extracted with CH_2Cl_2 (×3). The combined organic portions were dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by column chromatography to give 1.92g **5h** in 85% yield as a white solid. The ee values of the **5h** were determined by HPLC with a chiral column.

*(S)-Phenyl(p-tolyl)methanol (**5h**):* White solid, 85% yield, 192 mg, 93.0% ee (*S*). $[\alpha]_D^{20}$ = -3.6 (c = 0.5, $CHCl_3$); lit.[29] $[\alpha]_D^{30}$ = -4.0 [c = 0.76, $CHCl_3$, 47% ee (*S*)]. The ee was determined by HPLC on Chiralpak OD−H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 12.12 min (major), t_R(*R*) = 13.30 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 3H), 7.16 (d, *J* = 7.8 Hz, 2H), 5.81 (s, 1H), 2.35 (s, 3H), 2.32−2.25 (br, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.0, 141.0, 137.3, 129.2, 128.5, 127.5, 126.6, 126.5, 76.1, 21.1. **HRMS** (EI) calcd for $C_{14}H_{14}O$ $[M]^+$, 198.1045; found: 198.1060.

Compoounds **5f**, **5l** could be prepared under the similar reaction condition.

(*S*)-(4-chlorophenyl)(phenyl)methanol *(**5f**)*: Oil, 81% yield, 176.6 mg, **>99**% ee (*S*). $[\alpha]_D^{20}$ = +42.2 (c = 0.5, $CHCl_3$), lit.[30] $[\alpha]_D^{30}$ = +18.6 (c = 0.40, $CHCl_3$, 87% ee, *S*). The ee was determined by HPLC on Chiralpak AD−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 16.04 min (major), t_R(*R*) = 17.71 min (minor). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33-7.24 (m, 9H), 5.71 (s, 1H), 2.57 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.4, 142.2, 133.3, 128.7, 128.6, 127.92, 127.87, 126.6, 75.6. **HRMS** (EI) calcd for $C_{13}H_{11}ClO$ $[M]^+$, 218.0498; found: 218.0502.

(*R*)-(2-chlorophenyl)(4-fluorophenyl)methanol *(**5l**)*: Oil, 83% yield, 196.3 mg, 97.0% ee (*R*). $[\alpha]_D^{20}$ = +5.2 (c = 0.5, $CHCl_3$), lit.[25] $[\alpha]_D^{20}$ = -15.2 (c = 1.51, $CHCl_3$, 97% ee, *S*). The ee was determined by HPLC on Chiralpak AD−H column, hexane: isopropanol = 95:5; flow rate = 0.8 mL/min; UV detection at 220 nm; t_R(*S*) = 15.74 min (minor), t_R(*R*) = 17.20 min (major). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (dd, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1H), 7.35−7.21 (m, 5H), 7.03−6.97 (m, 2H), 6.12 (s, 1H), 3.02 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.2 (d, *J* =

244.0 Hz), 140.8, 138.0 (d, *J* = 3.0 Hz), 132.4, 129.6, 128.9, 128.7 (d, *J* = 8.0 Hz), 127.8, 127.2, 115.3 (d, *J* = 22.0 Hz), 72.0. **HRMS** (EI) calcd for $C_{13}H_{10}ClFO$ $[M]^+$, 236.0404; found: 236.0406.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.xxxxxxx

Copies of NMR spectra of ligands and products, as well as HPLC charts of products.

AUTHOR INFORMATION

Corresponding Author

*E-mail: weihuizhong@zjut.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (Nos. 21676253 and 21706234) and Project funded by China Postdoctoral Science Foundation (Nos. 2017M612033) for financial support.

REFERENCES

(1) For Selected examples, see: (a) Rogawski, M. A.; Löscher, W. The neurobiology of antiepileptic drugs. *Nat. Rev. Neurosci.* **2004**, *5*, 553–564. (b) Creighton, C. J.; Ramabadran, K.; Ciccone, P. E.; Liu, J.; Orsini, M. J.; Reitz, A. B. Synthesis and biological evaluation of the major metabolite of atomoxetine: elucidation of a partial κ-opioid agonist effect Short communication. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 4083−4085. (c) Almeida, L.; Soares-Da-Silva, P. *Neurotherapeutics* **2007**, *4*, 88−96. (d) Cui, J. J.; Tran-Dubé, M.; Shen, H.; Nambu, M.; Kung, P.-P.; Pairish, M.; Jia, L.; Meng, J.; Funk, L.; Botrous, I.; McTigue, M.; Grodsky, N.; Ryan, K.; Padrique, E.; Alton, G.; Timofeevski, S.; Yamazaki, S.; Li, Q.; Zou, H.; Christensen, J.; Mroczkowski, B.; Bender, S.; Kania, R. S.; Edwards, M. P. Structure Based Drug Design of Crizotinib (PF−02341066), a Potent and Selective Dual Inhibitor of Mesenchymal–Epithelial Transition Factor (c-MET) Kinase and Anaplastic Lymphoma Kinase (ALK). *J. Med. Chem.* **2011**, *54*, 6342−6363.

(2) Rosenblum, S. B.; Huynh, T.; Afonso, A.; Davis, H. R. Jr.; Yumibe, N.; Clader, J. W.; Burnett, D. A. Discovery of 1-(4-Fluorophenyl)-(3R)-[3-(4-fluorophenyl)-(3S)-hydroxypropyl]-(4S)-(4-hydroxyphenyl)-2-azetidinone (SCH 58235): A Designed, Potent, Orally Active Inhibitor of Cholesterol Absorption. *J. Med. Chem*. **1998**, *41*, 973−980.

(3) Wong, D. T.; Robertson, D. W.; Bymaster, F. P.; Krushinski, J. H.; Reid, L. R. LY227942, an inhibitor of serotonin and norepinephrine uptake: Biochemical pharmacology of a potential antidepressant drug. *Life sciences* **1988**, *43*, 2049−2057.

(4) (a) Zou, H. Y.; Li, Q.; Lee, J. H.; Arango, M. E.; McDonnell, S. R.; Yamazaki, S.; Koudriakova, T. B.; Alton, G.; Cui, J. J.; Kung, P.-P.; Nambu, M. D.; Los, G.; Bender, S. L.; Mroczkowski, B.; Christensen, J. G. An Orally Available Small-Molecule Inhibitor of c-Met, PF−2341066, Exhibits Cytoreductive Antitumor Efficacy through Antiproliferative and Antiangiogenic Mechanisms. *Cancer research* **2007**, *67*, 4408−4417. (b) Nishii, H.; Chiba, T.; Morikami, K.; Fukami, T. A.; Sakamoto, H.; Kwangseok, K.; Koyano, H. Discovery of 6-benzyloxyquinolines as c-Met selective kinase inhibitors. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1405−1409.

(5) Takasu, T.; Ukai, M.; Sato, S.; Matsui, T.; Nagase, I.; Maruyama, T.; Sasamata, M.; Miyata, K.; Uchida, H.; Yamaguchi, O. Effect of (R)-2-(2-Aminothiazol-4-yl)-4'-{2-[(2-hydroxy-2-phenyl-ethyl)amino]ethyl} Acetanilide (YM178), a Novel Selective β_3-Adrenoceptor Agonist, on Bladder Function. *J. Pharmacol. Exp. Ther.* **2007**, *321*, 642−647.

(6) van der Stelt, C.; Heus, W. J.; Nauta, W. T. Resolution in optical isomers of orphenadrine, 4-methyldiphenhydramine and their N-demethyl derivatives. *Arzneim.-Forsch.* **1969**, *19*, 2010−2012.

(7) Rekker, R. F.; Timmerman, H.; Harms, A. F.; Nauta, W. T. Antihistaminic and anticholinergic activities of optically active diphenhydramine derivatives. Concept of complementarity. *Arzneim.-Forsch.* **1971**, *21*, 688−691.

(8) (a) Frkanec, L.; Zinic, M. Chiral bis(amino acid)- and bis(amino alcohol)-oxalamide gelators. Gelation properties, self-assembly motifs and chirality effects. *Chem. Commun*. **2010**, *46*, 522−537. (b) Patti, A.; Pedotti, S. Synthesis and properties of chiral ferrocenylalcohols and diols. *Organometallic Compounds*, 2010, 255−291. (c) Seco, J. M.; Quiñoa, E.; Riguerá, R. Assignment of the Absolute Configuration of Polyfunctional Compounds by NMR Using Chiral Derivatizing Agents. *Chem. Rev.* **2012**, *112*, 4603−4641.

(9). For selected reviews, see: (a) Chen, Q.-A.; Ye, Z.-S.; Duan, Y.; Zhou, Y.-G. Homogeneous palladium-catalyzed asymmetric hydrogenation. *Chem. Soc. Rev.* **2013**, *42*, 497−511. (b) Carroll, M. P.; Guiry, P. J. P, N ligands in asymmetric catalysis. *Chem. Soc. Rev.* **2014**, *43*, 819−833; (c) Xie, J.-H.; Bao, D.-H.; Zhou,

Q.-L. Recent Advances in the Development of Chiral Metal Catalysts for the Asymmetric Hydrogenation of Ketones. *Synthesis* **2015**, *47*, 460−471. (d) Ayad, T.; Phansavath, P.; Ratovelomanana-Vidal, V. Transition-Metal-Catalyzed Asymmetric Hydrogenation and Transfer Hydrogenation: Sustainable Chemistry to Access Bioactive Molecules. *Chem. Rec.* **2016**, *16*, 2754−2771. (e) Ohkuma, T.; Arai, N. Advancement in Catalytic Asymmetric Hydrogenation of Ketones and Imines, and Development of Asymmetric Isomerization of Allylic Alcohols. *Chem. Rec.* **2016**, *16*, 2801−2819. (f) Meemken, F.; Baiker, A. Recent Progress in Heterogeneous Asymmetric Hydrogenation of C=O and C=C Bonds on Supported Noble Metal Catalysts. *Chem. Rev.* **2017**, *117*, 11522−11569. (g) Xie, X.; Lu, B.; Li, W.; Zhang, Z. Coordination determined chemo- and enantioselectivities in asymmetric hydrogenation of multi-functionalized ketones. *Coordin. Chem. Rev.* **2018**, *355*, 39−53. (h) Zhang, Z.; Butt, N. A.; Zhou, M.; Liu, D.; Zhang, W. Asymmetric Transfer and Pressure Hydrogenation with Earth−Abundant Transition Metal Catalysts. *Chin. J. Chem.* **2018**, *36*, 443−454.

(10) (a) Ohkuma, T.; Ooka, H.; Hashiguchi, S.; Ikariya, T.; Noyori, R. Practical Enantioselective Hydrogenation of Aromatic Ketones. *J. Am. Chem. Soc.* **1995**, *117*, 2675−2676. (b) Hashiguchi, S.; Noyori, R. Asymmetric Transfer Hydrogenation Catalyzed by Chiral Ruthenium Complexes. *Acc. Chem. Res.* **1997**, *30*, 97−102. (c) Doucet, H.; Ohkuma, T.; Murata, K.; Yok-ozawa, T.; Kozawa, M.; Katayama, E.; England, A. F.; Ikariya, T.; Noyori, R. trans-[$RuCl_2$(phosphane)$_2$(1,2-diamine)] and Chiral trans-[$RuCl_2$(diphosphane)(1,2-diamine)]: Shelf-Stable Precatalysts for the Rapid, Productive, and Stereoselective Hydrogenation of Ketones. *Angew. Chem., Int. Ed.* **1998**, *37*, 1703−1707. (d) Ohkuma, T.; Koi-zumi, M.; Doucet, H.; Pham, T.; Kozawa, M.; Murata, K.; Katayama, E.; Yokozawa, T.; Ikariya, T.; Noyori, R. Asymmetric Hydrogenation of Alkenyl, Cyclopropyl, and Aryl Ketones. $RuCl_2$(xylbinap)(1,2-diamine) as a Precatalyst Exhibiting a Wide Scope. *J. Am. Chem. Soc.* **1998**, *120*, 13529−13530.

(11) (a) Li, W.; Hou, G.; Wang, C.; Jiang, Y.; Zhang, X. Asymmetric hydrogenation of ketones catalyzed by a ruthenium(II)-indan–ambox complex. *Chem. Commun*. **2010**, *46*, 3979−3981. (b) Xie, J.-H.; Liu, X.-Y.; Xie, J.-B.; Wang, L.-X.; Zhou, Q.-L. An Additional Coordination Group Leads to Extremely Efficient Chiral Iridium Catalysts for Asymmetric Hydrogenation of Ketones. *Angew. Chem., Int. Ed.* **2011**, *50*, 7329−7332. (c) Bao, D.-H.; Wu, H.-L.; Liu, C.-L.; Xie, J.-H.; Zhou, Q.-L. Development of Chiral Spiro P-N-S Ligands for Iridium-Catalyzed Asymmetric Hydrogenation of *β*-Alkyl-*β*-Ketoesters. *Angew. Chem., Int. Ed.* **2015**, *54*, 8791−8794. (d) Yamamura, T.; Nakatsuka, H.; Tanaka, S.; Kitamura, M. Asymmetric Hydrogenation of tert-Alkyl Ketones: DMSO Effect in Unification of Stereoisomeric Ruthenium Complexes. *Angew. Chem., Int. Ed.* **2013**, *52*, 9313−9315. (e) Yamamura, T.; Nakane, S.; Nomura, Y.; Tanaka, S.; Kitamura, M. Development

of an axially chiral $sp^3P/sp^3NH/sp^2N$-combined linear tridentate ligand−fac-selective formation of Ru(II) complexes and application to ketone hydrogenation. *Tetrahedron* **2016**, *72*, 3781−3789.

(12) (a) Wu, W.; Liu, S.; Duan, M.; Tan, X.; Chen, C.; Xie, Y.; Lan, Y.; Dong, X.-Q.; Zhang, X. Iridium Catalysts with f-Amphox Ligands: Asymmetric Hydrogenation of Simple Ketones. *Org. Lett.* **2016**, *18*, 2938−2941. (b) Yu, J.; Duan, M.; Wu, W.; Qi, X.; Xue, P.; Lan, Y.; Dong, X.-Q.; Zhang, X. Readily Accessible and Highly Efficient Ferrocene-Based AminoPhosphine-Alcohol (f-Amphol) Ligands for Iridium-Catalyzed Asymmetric Hydrogenation of Simple Ketones. *Chem. Eur. J.* **2017**, *23*, 970−975. (c) Yu, J.; Jiao, L.; Yang, Y.; Wu, X.; Xue, P.; Chung, W. L.; Dong, X.-Q.; Zhang, X. Iridium-Catalyzed Asymmetric Hydrogenation of Ketones with Accessible and Modular Ferrocene-Based Amino-phosphine Acid (f-Ampha) Ligands. *Org. Lett.* **2017**, *19*, 690−693.

(13) Nie, H.; Zhou, G.; Wang, Q.; Chen, W.; Zhang, S. Asymmetric hydrogenation of aromatic ketones using an iridium(I) catalyst containing ferrocene-based P−N−N tridentate ligands. *Tetrahedron: Asymmetry* **2013**, *24*, 1567−1571.

(14) (a) Luo, W.; Hu, H.; Nian, S.; Qi, L.; Ling, F.; Zhong, W. Phosphine-catalyzed [3 + 2] annulation reaction: highly regio- and diastereoselective synthesis of 2-azaspiro[4.4]nonene-1,3-diones. *Org. Biomol. Chem.* **2017**, *15*, 7523−7526. (b) Zhu, L.; Hu, H.; Qi, L.; Zheng, Y.; Zhong, W. Enantioselective Allylic Substitution of Morita-Baylis-Hillman Adducts Catalyzed by Chiral Bifunctional Ferrocenylphosphines. *Eur. J. Org. Chem.* **2016**, 2139−2144. (c) Hu, H.; Yu, S.; Zhu, L.; Zhou, L.; Zhong, W. Chiral bifunctional ferrocenylphosphine catalyzed highly enantioselective [3 + 2] cycloaddition reaction. *Org. Biomol. Chem.* **2016**, *14*, 752−760. (d) Tu, A.; Hu, H.; Du, T.; Zhong, W. Asymmetric [3+2]-Cycloaddition of Morita–Baylis–Hillman Carbonates with Maleimides Catalyzed by Chiral Ferrocenylphosphines. *Synth. Commun*. **2014**, *44*, 3392−3399. (e) Tang, Q.; Tu, A.; Deng, Z.; Hu, M.; Zhong, W. Progress in Enantioselective Phosphine Organocatalysis. *Chin. J. Org. Chem.* **2013**, *33*, 954−970.

(15) Sui, Y.-Z.; Zhang, X.-C.; Wu, J.-W.; Li, S.; Zhou, J.-N.; Li, M.; Fang, W.; Chan, A. S. C.; Wu, J. Cu^{II}-Catalyzed Asymmetric Hydrosilylation of Diaryl- and Aryl Heteroaryl Ketones: Application in the Enantioselective Synthesis of Orphenadrine and Neobenodine. *Chem. -Eur. J.* **2012**, *18*, 7486−7492.

(16) Süsse, L.; Hermeke, J.; Oestreich, M. The Asymmetric Piers Hydrosilylation. *J. Am. Chem. Soc.* **2016**, *138*, 6940−6943.

(17) Chen, X.; Lu, Z. Iminophenyl Oxazolinylphenylamine for Enantioselective Cobalt-catalyzed Hydrosilylation of Aryl Ketones. *Org. Lett.* **2016**, *18*, 4658−4661.

(18) Xie, J.-B.; Xie, J.-H.; Liu, X.-Y.; Zhang, Q.-Q.; Zhou, Q.-L. Chiral Iridium Spiro Aminophosphine Complexes: Asymmetric Hydrogenation of Simple Ketones, Structure, and Plausible Mechanism. *Chem. Asian J.* **2011**, *6*, 899−908.

(19) Liu, W.-P; Yuan, M.-L; Yang, X.-H; Li, K.; Xie, J.-H; Zhou, Q.-L. Efficient asymmetric transfer hydrogenation of ketones in ethanol with chiral iridium complexes of spiroPAP ligands as catalysts. *Chem. Commun*. **2015**, *51*, 6123−6125.

(20) Salvi, N. A.; Chattopadhyay, S. Asymmetric reduction of halo-substituted arylalkanones with Rhizopus arrhizus. *Tetrahedron: Asymmetry* **2008**, *19*, 1992-1997.

(21) Ma, X.-C.; Zuo, Z.-Q.; Liu, G.-X.; Huang, Z. Manganese-Catalyzed Asymmetric Hydrosilylation of Aryl Ketones. *ACS Omega*. **2017**, *2*, 4688−4692.

(22) Ito, J.; Teshima, T.; Nishiyama, H. Enhancement of enantioselectivity by alcohol additives in asymmetric hydrogenation with bis(oxazolinyl)phenyl ruthenium catalysts. *Chem. Commun.* **2012**, *48*, 1105–1107.

(23) Cherng, Y.-J.; Fang, J.-M.; Lu, T.-J. Pinane-Type Tridentate Reagents for Enantioselective Reactions: Reduction of Ketones and Addition of Diethylzinc to Aldehydes. *J. Org. Chem.* **1999**, *64*, 3207−3212.

(24) Tian, C.; Gong, L.; Meggers, E. Chiral-at-Metal Iridium Complex for Efficient Enantioselective Transfer Hydrogenation of Ketones. *Chem. Commun.* **2016**, *52*, 4207−4210.

(25) Touge, T.; Nara, H.; Fujiwhara, M.; Kayaki, Y.; Ikariya, T. Efficient Access to Chiral Benzhydrols via Asymmetric Transfer Hydrogenation of Unsymmetrical Benzophenones with Bifunctional Oxo-Tethered Ruthenium Catalysts. *J. Am. Chem. Soc.* **2016**, *138*, 10084−10087.

(26) Kokura, A.; Tanaka, S.; Ikeno, T.; Yamada, T. Catalytic Enantioselective Borohydride Reduction of *Ortho*-Fluorinated Benzophenones. *Org. Lett.* **2006**, *8*, 3025–3027.

(27) Schmidt, F.; Rudolph, J.; Bolm, C. Diarylmethanols by Catalyzed Asymmetric Aryl Transfer Reactions onto Aldehydes Using Boronic Acids as Aryl Source. *Adv. Synth. Catal.* **2007**, *349*, 703−708.

(28) Duan, H.-F.; Xie, J.-H.; Shi, W.-J.; Zhang, Q.; Zhou, Q.-L. Enantioselective Rhodium-Catalyzed Addition of Arylboronic Acids to Aldehydes Using Chiral Spiro Monophosphite Ligands. *Org. Lett.* **2006**, *8*, 1479−1481.

(29) Jagt, R. B. C.; Toullec, P. Y.; de Vries, J. G.; Feringa, B. L. ; Minnaard, A. J. Rhodium/phosphoramidite-catalyzed asymmetric arylation of aldehydes with arylboronic acids. *Org. Biomol. Chem.* **2006***, 4*, 773−775.

(30) Morikawa, S.; Michigami, K.; Amii, H. Novel Axially Chiral Phosphine Ligand with a Fluoro Alcohol Moiety for Rh-Catalyzed Asymmetric Arylation of Aromatic Aldehydes. *Org. Lett.* **2010**, *12*, 2520-2523.