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Modular synthesis of the ClickFerrophos ligand family and their use in rhodium- and ruthenium-catalyzed asymmetric hydrogenation

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ABSTRACT

A series of diphosphine ClickFerrophos ligands (CF), based on a triazoleferrocene backbone, was synthesized in a four-step sequence via click chemistry methodology. In addition to the four previously synthesized ligands **CF1**, **CF4**, **CF7** and **CF10**, six novel CF ligands **CF2–3** and **CF5–8** were prepared. Hydrogenation reactions of alkenes and ketones were significantly improved upon by using CF ligands as rhodium- or ruthenium-complexes in which the % ee values can be optimized by choosing the appropriate CF ligand depending on the substrate.

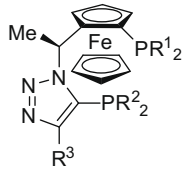
1. Introduction

Ferrocenylphosphines constitute a well-established class of ligands for transition metals which often catalyze asymmetric reactions with high enantioselectivity.[1] In previous papers, we reported on a class of ferrocenyl-triazole-based 1,5-diphosphine ligands (ClickFerrophos ligands, **CF1**–**10**, Chart 1),[2] which were readily prepared by click chemistry methodology.[3] Subsequently, these ligands were found to be highly effective for rhodium- and ruthenium-catalyzed asymmetric hydrogenations of alkenes and ketones giving high enantioselectivities of up to 99.7% and 99% ee, respectively.[2a] In addition to hydrogenations, ClickFerrophos ligands were successfully applied towards the copper-catalyzed asymmetric 1,3-dipolar addition of azomethine ylide with electron-deficient alkenes[2b] and towards the reductive aldol reaction of ethyl acrylate with ketones.[2c] Studies have shown that the phosphino substituents of the ClickFerrophos ligands affect the enantioselectivity of the reactions. Diphenylphosphine derivative **CF1** was the most effective for the hydrogenation and 1,3-dipolar addition reactions with azomethine ylides, whereas the dicyclohexylphosphine derivative **CF7** was the most effective for reductive aldol reactions. The modularity within the family of ClickFerrophos ligands, therefore, can allow for the specific fine tuning of the catalytic properties depending on the reactions. In addition to modifications of the phosphino substituents, the 4-aryl group on the triazole ring can be varied by using various terminal aryl acetylenes in the click reactions. The key intermediate for this ligand family is the enantiomerically pure ligand framework; the triazole backbone **4** can be obtained via *click chemistry* from *ortho*-bromoferrocenylethyl azide **3**, which is prepared from Ugi's amine **1**[4] (Scheme 1). Herein we report the synthesis and reactivities of ten representative ClickFerrophos ligands **CF1**–**10** with various steric and electronic environments of the 4-aryl group (R^3) and the phosphino substituents (R^1 and R^2). The effectiveness of the ligands **CF1**-**10** was evaluated in the hydrogenation of alkenes and ketones with respect to enantioselectivities.

2. Results and discussion

2.1. Synthesis of ClickFerrophos ligands

As shown in Scheme 1, Ugi's amine **1** was subjected to *ortho*-lithiation, then trapped with bromine (using 1,2-dibromo-1,1,2,



ClickFerrophos

CF1: $R^1 = R^2 = R^3 = Ph$
CF2: $R^1 = R^2 = Ph$, $R^3 = o\text{-}MeC_6H_4$
CF3: $R^1 = R^2 = Ph$, $R^3 = o\text{-}FC_6H_4$
CF4: $R^1 = R^2 = Ph$, $R^3 = H$
CF5: $R^1 = R^2 = 3,5\text{-xyl}$, $R^3 = Ph$
CF6: $R^1 = R^2 = 3,5\text{-xyl}$, $R^3 = o\text{-}FC_6H_4$
CF7: $R^1 = R^2 = Cy$, $R^3 = Ph$
CF8: $R^1 = R^3 = Ph$, $R^2 = 3,5\text{-xyl}$
CF9: $R^1 = R^3 = Ph$, $R^2 = 3,5\text{-}(CF_3)_2C_6H_3$
CF10: $R^1 = R^3 = Ph$, $R^2 = Cy$

Chart 1. ClickFerrophos (CF) family.

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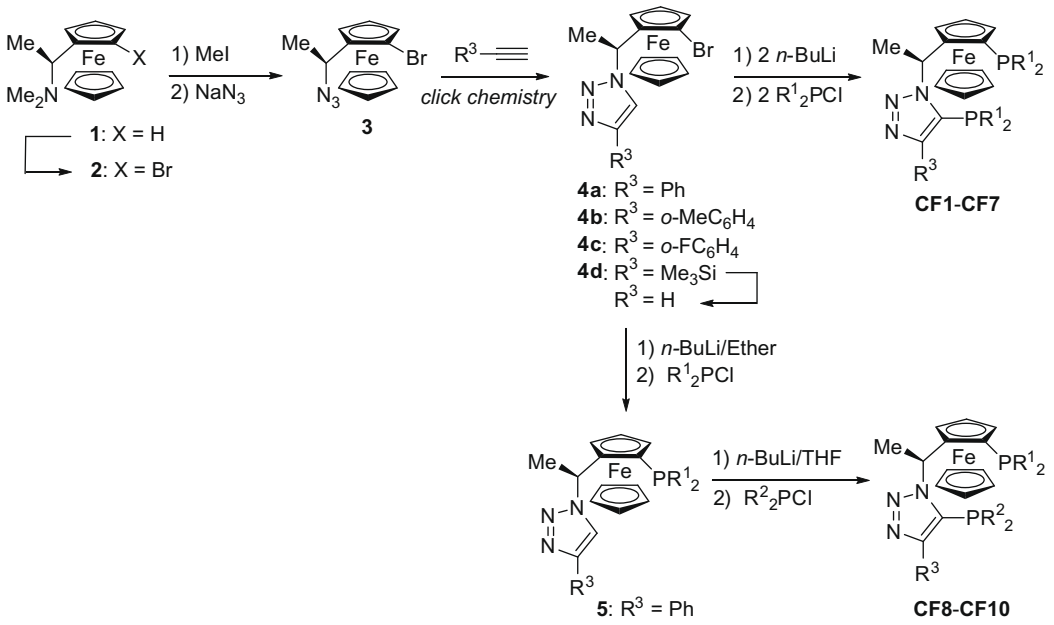


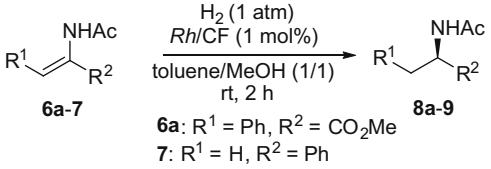
Scheme 1. Synthesis of ClickFerrophos **CF1**–**CF10**.

2-tetrafluoroethane) to afford **2**. Retentive displacement of the amino group by an azide group afforded *ortho*-bromoferrocenyl azide **3**,[4a] which was subjected to click chemistry[5] to give the triazole backbones **4** in good yields. In a previous paper, we used the *ortho*-iodo analogue of ferrocenyl azide **3**; the click reaction of the azide to the triazole was improved from 75% to 85–90% by using the *ortho*-bromo ferrocenes.[6] The 4-(2-substituted phenyl) triazole derivatives with electron-donating (R^3 = *o*-MeC_6H_4) and electron-withdrawing (R^3 = *o*-FC_6H_4) groups were prepared using the corresponding 2-substituted phenylacetylenes. Di-lithiation of **4** at the 5-triazole and 2-ferrocenyl positions, followed by trapping with R_2PCl afforded **CF1**–**3** and **CF5**–**7**. In contrast, **CF4** was prepared using trimethylsilylacetylene instead of the phenylacetylenes, and involved an extra step to remove the silyl group prior to di-phosphination.[2c,d] As shown in Scheme 1, **CF8**–**10** were obtained via successive phosphinations of firstly the *ortho*-cyclopentadienyl ring to afford mono-phosphine **5**, followed by the 5-triazole ring. It should be noted that the phosphino groups (R^1, R^2) of **CF8**–**10** are dissimilar to each other.

2.2. Hydrogenation of enamides

Ligands (*S*,*Rp*)-**CF1**–**10** were evaluated as rhodium complexes in the hydrogenation of enamides such as methyl α-acetamidocinnamate **6a** (R^1 = Ph, R^2 = CO_2Me) and α-acetamidostyrene (**7**: R^1 = H, R^2 = Ph).[7] After generating the rhodium catalysts in situ using $[Rh(nbd)_2]BF_4$ (1 mol % loading), the hydrogenations were carried out in toluene/MeOH (1:1) at rt for 2 h under hydrogen (atmospheric pressure). The resulting enantioselectivities (% ee) of the reactions are listed in Table 1. The hydrogenation reactions of **6a** and **7** proceeded to give **8a** and **9**, respectively, in good to quantitative yields except for **CF7** and **CF9**. In the case of **6a**, the original **CF1** (entry 1) was the most effective and afforded the highest enantioselectivity (99% ee *R*).[2a] For **7**, the sterically hindered phosphine **CF5** (entry 5) was the most effective with an enantioselectivity of 90% ee. The use of **CF2** (entry 2), with an electron-donating group (*o*-MeC_6H_4), gave lower values of ee for both **6a** (86% ee) and **7** (54% ee), whereas the use of **CF3** (entry 3), with an electron-withdrawing group (*o*-FC_6H_4), gave values of ee that were comparable as those of **CF1** for both **6a** (98% ee) and **7** (88% ee).

Table 1
Enantioselective hydrogenation of enamides[a]



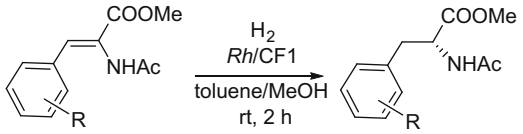
Entry	Ligand	Enamide			
		6a		**7**	
		Conv. (%)	ee (%)[b]	Conv. (%)	ee (%)[b]
1	**CF1**	99	99	99	84
2	**CF2**	99	86	99	54
3	**CF3**	99	98	99	88
4	**CF4**	99	93	99	86
5	**CF5**	99	95	99	90
6	**CF6**	99	98	99	85
7	**CF7**	Trace	—	60	27
8	**CF8**	99	90	99	81
9	**CF9**	50	83	35	35
10	**CF10**	99	67	99	11

[a] Enamide (1 mmol), $[Rh(nbd)_2]BF_4$ (0.010 mol), ligand (0.011 mol), toluene/MeOH (2/2 mL); rt, H_2 (1 atm).
[b] Determined by HPLC (Chiralcel AD-H).

In the absence of a 4-aryl group (**CF4**, entry 4), the ee was lower for **6a** but comparable to that of **CF1** for **7**. Sterically hindered **CF5** with two di(3,5-xylyl)phosphine units and **CF8** with one di(3,5-xylyl)phosphine unit, were efficient in the hydrogenation reactions with high ee values, while **CF9**, with one di(3,5-$(CF_3)_2C_6H_3$)phosphine unit, generated a less active catalyst.

Consequently, for hydrogenations of substituted methyl (*Z*)-α-acetamidocinnamates **6a**–**6i**, **CF1** was chosen as the ligand due to its effectiveness and facile preparation. The reactions were carried out under the same conditions as described above, and the results are summarized in Table 2. In all cases, the reactions proceeded quantitatively with excellent enantioselectivities—every product possessed the *R*-configuration [using (*S*,*Rp*)-**CF1**] regardless of the electronic nature or position of the substituents on the aromatic

Table 2
Asymmetric hydrogenation of substituted methyl α-acetamidocinnamate[a]



6a-6i **8a-8i**

Entry	Substrate (R)	Conv (%)	ee (%) (Config)[b]
1	**6a** (H)	99	98 (*R*)
2	**6b** (*p*-Me)	99	98 (*R*)
3	**6c** (*o*-Me)	99	97 (*R*)
4	**6d** (*p*-MeO)	99	97 (*R*)
5	**6e** (*p*-Cl)	99	98 (*R*)
6	**6f** (*p*-F)	99	98 (*R*)
7	**6g** (*m*-F)	99	98 (*R*)
8	**6h** (*o*-F)	99	98 (*R*)
9	**6i** (*p*-NO_2)	99	99 (*R*)

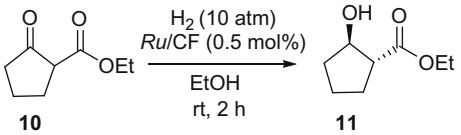
[a] Enamide (1 mmol), $[Rh(nbd)_2]BF_4$ (0.010 mol), ligand (0.011 mol), toluene/MeOH (2/2 mL); rt, H_2 (1 atm).
[b] Determined by HPLC (Chiralcel AD-H).

ring. For example, both *p*-MeO and *p*-NO_2 substituents gave excellent enantioselectivities (entries 4 and 9, respectively). Our results indicate that the rhodium–**CF1** complex can function as a general catalyst for the asymmetric hydrogenation of substituted (*Z*)-α-acetamidocinnamates giving enantiomerically pure amino acids. Additionally, the excellent catalytic activities of rhodium–**CF1** complexes towards asymmetric hydrogenations of other substituted alkenes, such as itaconic acid/ester and α-acetamido acrylic acid/ester,[2a] further support the utilization of the rhodium-**CF** catalysts in the hydrogenation of alkenes.

2.3. Hydrogenation of ketones

Ligands **CF1**–**8** were evaluated as ruthenium complexes in the asymmetric hydrogenation of 2-carboethoxycyclopentanone **10**.[8] The hydrogenation was carried out using 0.5 mol % of [Ru(cod)(metallyl)$_2$]/HBr and (*S*,*Rp*)-CF ligand in EtOH under hydrogen (10 atm) at 50 °C for 24 h. As listed in Table 3, the reactions proceeded quantitatively to afford product (*R*,*R*)-**11** diastereoselectively (92–97% de). The ruthenium–**CF2** complex (entry 2), with a 4-*o*-MePh substituent, was the most effective catalyst with a high enantioselectivity of 92% ee, whereas the rhodium–**CF2** complex was less effective for the hydrogenation of enamides (Table 1, entry 2). **CF2** was also effective for dibenzoylmethane **12** giving (*S*,*S*)-1,3-diphenyl-1,3-propanediol **13** in >99% ee, while it was not so effective for ethyl benzoylacetate **14** (96% ee) although **CF1** (98% ee) still afforded high% ee (Scheme 2). Sterically hindered phosphines **CF5**, **CF6** and **CF8** were also effective in yielding high enantioselectivities (88–90% ee). **CF5** was revealed to be the most effective ligand considering that it gave the highest de value although the ee value was slightly lower than that of **CF2** (entry 5). Thus, by using the family of our new CF ligands, the enantioselectivities were improved upon compared to that of **CF1** (84% ee). The **CF4** complex, without a substituent at the 4-position, was the least effective in the hydrogenation of **10** with an enantioselectivity of merely 48% ee—in contrast, it was effective in the hydrogenation of enamides.

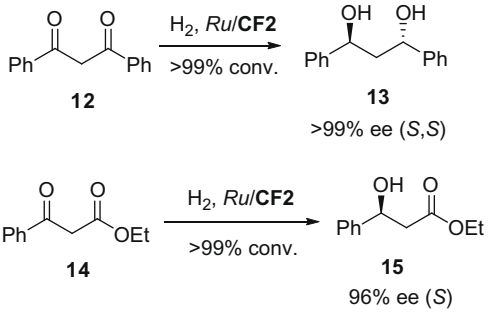
Table 3
Enantioselective hydrogenation of 2-carboethoxycyclopentanone by a Ru/CF complex[a]



10 **11**

Entry	Ligand	de (%)[b]	ee (%) (Config)[b]
1	**CF1**	95	84 (*R*,*R*)
2	**CF2**	94	92 (*R*,*R*)
3	**CF3**	93	85 (*R*,*R*)
4	**CF4**	92	48 (*R*,*R*)
5	**CF5**	97	90 (*R*,*R*)
6	**CF6**	93	89 (*R*,*R*)
8	**CF8**	97	88 (*R*,*R*)

[a] Ketone (2 mmol), [Ru(cod)(metallyl)$_2$]/HBr(0.010 mol), ligand (0.011 mol), EtOH (4 mL); 50 °C, H_2 (10 atm).
[b] Determined by GC (CP-Chirasil-Dex CB).



Scheme 2. Hydrogenation of dibenzoylmethane and ethyl benzoylacetate.

3. Conclusion

Our studies have demonstrated that the fine tuning of CF ligands, as rhodium- or ruthenium-complexes, can optimize (maximize) the enantioselectivities of asymmetric hydrogenations. Compared to the original **CF1**, the use of sterically hindered phosphine **CF5** significantly improves the efficiencies and enantiomeric excesses for the hydrogenations of α-acetamidostyrene **7** and 2-carboethoxycyclopentanone **10**. The choice of the most suitable ligand was essential for substrates to obtain the highest enantioselectivity.[9] The sterically demanding ligand **CF5** seemed to be the ligand of choice amongst the ClickFerrophos family.

4. Experimental

4.1. General

The ^1H and ^{13}C NMR spectra were recorded using a Varian Mercury 300 NMR (300 MHz) spectrometer as solutions in $CDCl_3$. The chemical shifts are reported in δ units downfield from the internal reference, Me_4Si. The optical rotations were determined by a JASCO P-2200 instrument. The HPLC analyses were carried out on a JASCO PU-1580 apparatus equipped with a multi-wavelength detector (MD 2010) using chiral columns (Chiralcel AD-H, OJ-H). Preparative TLC was conducted using a 20 × 20 cm glass sheet coated with a 2 mm thick layer of Merck Kieselgel 60 PF_{254}. All products of asymmetric reactions were reported compounds and characterized by spectroscopic methods by reference to the literature.

4.2. Preparation of (*S*,*Rp*)-(*Rp*)-1-bromo-2-[(*S*)-1-azidoethyl]-ferrocene 3

A 100mL round-bottomed flask equipped with a condenser was charged with (*S*,*Rp*)-(1*Rp*)-bromo-2-(1*S*-dimethylaminoethyl)ferrocene

2 (1.01 g, 3.00 mmol),[5] methyl iodide (0.7 mL, 12.0 mmol) and dry acetone (25 mL). An aqueous solution (25 mL) of sodium azide (0.98 g, 15.0 mmol) was then added to the flask and the resulting mixture was heated at reflux with magnetic stirring for 1 h. The mixture was allowed to cool to room temperature and stirred overnight. The reaction was quenched with water and the resulting solution was extracted with CH_2Cl_2 (20×3 mL). The combined extracts were washed (brine), dried ($MgSO_4$) and the solvent was removed on a rotary evaporator to leave a reddish brown residue. The residue was subjected to column chromatography on silica gel (hexane/ethyl acetate = 4/1 as eluent) to give pure **3**. Dark red oil; yield, 0.90 g, 2.67 mmol, 90%; $[\alpha]_D^{25} = +74$ (*c* 0.34, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.67 (d, 3H, *J* = 6.9 Hz), 4.17 (s, 1H), 4.19 (s, 6H), 4.53 (s, 1H), 4.61 (q, 1H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$) δ = 19.0, 55.3, 64.2, 66.5, 70.9, 71.3, 79.0, 86.0. HRMS: calcd for $C_{12}H_{12}BrFeN_3$ (M+H$^+$) 332.9560, found 332.9584.

4.3. General procedure for the preparation of (*S*,*Rp*)-(*Rp*)-1-bromo-2-{(*S*)-1-[4-aryl-1*H*1,2,3-triazol-1-yl]ethyl}ferrocene 4

A 100mL round-bottomed flask containing a magnetic stirring bar was charged with **3** (156 mg, 0.47 mmol), 2-methylphenylacetylene (66 μL, 0.52 mmol), *t*-butanol (1 mL) and water (1 mL). Sodium ascorbate (24 mg, 0.10 mmol) was added to the flask followed by $CuSO_4{\cdot}5H_2O$ (13 mg, 0.05 mmol) and the resulting mixture was magnetically stirred for 24 h. The mixture was then extracted with CH_2Cl_2 (10×3 mL). The combined extracts were washed (brine), dried ($MgSO_4$) and the solvent was removed on a rotary evaporator to leave a yellow residue. The residue was subjected to column chromatography on silica gel (hexane/ethyl acetate = 2/1 as eluent) to give pure **4b** (R^3 = *o*-MeC_6H_4). Yellow solid; yield, 185 mg, 0.41 mmol, 87%; mp = 118 °C. $[\alpha]_D^{25} = +118$ (*c* 0.34, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.00 (d, 3H, *J* = 7.0 Hz), 2.37 (s, 3H), 4.21 (s, 5H+1H), 4.39 (s, 1H), 4.50 (s, 1H), 5.86 (q, 1H, *J* = 7.0 Hz), 7.25–7.34 (m, 3H), 7.39 (s, 1H), 7.6–7.7 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 20.6, 21.3, 55.0, 65.0, 66.9, 71.1, 71.5, 79.1, 84.7, 120.3, 125.8, 127.8, 128.7, 130.0, 130.6, 135.4, 146.1. HRMS (ESI): calcd for $C_{21}H_{20}BrFeN_3$ (M+H) 450.0265, found 450.0269.

Compound **4c**: Yellow solid; yield, 85%; mp = 78 °C. $[\alpha]_D^{25} = +116$ (*c* 0.34, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.06 (d, 3H, *J* = 7.0 Hz), 4.25 (s, 5H+1H), 4.44 (s, 1H), 4.53 (s, 1H), 5.91 (q, 1H, *J* = 7.0 Hz), 7.03–7.26 (m, 3H), 7.68 (s, 1H), 8,24–8.29 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 20.8, 55.3, 65.0, 66.9, 71.2, 71.5, 79.1, 84.6, 115.4 (d, *J* = 21.6 Hz), 118.7 (d, *J* = 12.2 Hz), 121.0 (d, *J* = 12.8 Hz), 124.4 (d, *J* = 3.1 Hz), 127.6 (d, *J* = 3.6 Hz), 128.9 (d, *J* = 8.4 Hz), 140.3 (d, *J* = 1.7 Hz), 159.0 (d, *J* = 247.6 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ −115.1 (s). HRMS (ESI): calcd for $C_{20}H_{17}BrFeN_3$ (M+H) 454.0014, found 454.0069.

4.4. General procedure for preparation of ClickFerrophos CF1–CF7

A 20 mL Schlenk tube containing a magnetic stirring bar was charged with triazole ferrocene **4b** (135 mg, 0.30 mmol) and dry THF (3 mL) under a slight pressure of nitrogen. The flask was cooled at −78 °C, and a hexane solution of *n*-BuLi (0.5 mL, 0.8 mmol, 1.6 M) was then added using a syringe through the septum with magnetic stirring. After 10 min, Ph_2PCl (140 μL, 0.8 mmol) was injected into the mixture at −78 °C. When the addition was completed, the mixture was allowed to warm to room temperature and then stirred for an additional 2 h. The reaction was quenched with saturated NH_4Cl, and the solution was then extracted with diethyl ether (30 mL × 3). The combined extracts were washed (brine), dried (Na_2SO_4), filtered and the solvent was removed on a rotary evaporator to leave a yellow solid. The crude product was purified by recrystallization from hexane/dichloromethane to give pure **CF2**. Yellow solid; yield, 170 mg, 0.23 mmol, 77%; mp = 226 °C. $[\alpha]_D^{25} = +220$ (*c* 0.32, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.93 (d, 3H, *J* = 6.8 Hz), 4.00 (s, 5H+1H), 4.52 (s, 1H), 4.95 (s, 1H), 6.28 (d, 1H, *J* = 7.6 Hz), 6.5–7.6 (m, 24H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.6, 22.7, 54.0 (dd, *J* = 9.1 Hz, 15.8 Hz), 69.8, 70.6, 71.0 (d, *J* = 5.1 Hz), 71.7 (d, *J* = 4.6 Hz), 75.5 (d, *J* = 11.8 Hz), 93.2 (d, *J* = 28.2 Hz), 124.1, 127.1, 127.2 (d, *J* = 7.9 Hz), 127.4, 127.5 (d, *J* = 5.2 Hz), 127.8 (d, *J* = 5.2 Hz), 128.0 (d, *J* = 8.2 Hz), 128.3, 128.4, 128.7, 129.1 (d, *J* = 20.9 Hz), 129.4, 130.6, 130.9, 131.1 (d, *J* = 16.0 Hz), 131.5 (d, *J* = 4.2 Hz), 132.6 (d, *J* = 19.2 Hz), 133.3, 133.8 (d, *J* = 4.6 Hz), 135.7 (d, *J* = 21.9 Hz), 137.9, 138.1 (d, *J* = 7.5 Hz), 140.1 (d, *J* = 8.1 Hz), 151.7 (d, *J* = 3.5 Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −36.2 (d, *J* = 29.6 Hz), −24.7 (d, *J* = 33.3 Hz). HRMS (ESI): calcd for $C_{45}H_{39}FeN_3P_2$ (M+H$^+$) 740.2042, found 740.2078.

4.5. ClickFerrophos CF1[2a]

Yield, 81%. Yellow solid; mp = 190–191 °C. $[\alpha]_D^{25} = +183$ (*c* 0.31, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.76 (d, 3H, *J* = 6.9 Hz), 3.86 (s, 1H), 4.06 (s, 5H), 4.48 (t, 1H, *J* = 2.6 Hz), 4.92 (s, 1H), 6.53 (q, 1H, *J* = 6.9 Hz), 6.6–7.1 (m, 14H), 7.3–7.6 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 54.0 (dd, *J* = 9.3, 17.7), 69.7, 70.3, 71.0 (d, *J* = 3.8 Hz), 71.7 (d, *J* = 5.1 Hz), 75.2 (d, *J* = 10.4 Hz), 92.8 (d, *J* = 26.8 Hz), 126.8, 127.0 (d, *J* = 12.8 Hz), 127.6 (d, *J* = 11.8 Hz), 127.7, 127.9 (d, *J* = 7.7 Hz), 128.0, 128.7 (d, *J* = 7.2 Hz), 129.0, 129.2 (d, *J* = 7.2 Hz), 131.1 (d, *J* = 16.9), 131.8 (d, *J* = 18.5 Hz), 133.2 (d, 23.1 Hz), 135.5 (d, J = 21.2 Hz), 137.4 (d, *J* = 9.4 Hz), 139.8 (d, *J* = 7.6 Hz), 151.8. ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −35.1 (d, *J* = 34.4 Hz), −23.8 (d, *J* = 34.4 Hz). HRMS (ESI): cacld for $C_{44}H_{37}FeN_3P_2$ (M+H$^+$) 726.1875, found 726.1865.

4.6. ClickFerrophos CF3

Yield, 74%. Yellow solid; mp = 236 °C. $[\alpha]_D^{25} = +175$ (*c* 0.33, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75 (d, 3H, *J* = 7.0), 3.85 (s, 1H), 4.05 (s, 5H), 4.48 (s, 1H), 4.94 (s, 1H), 6.12 (t, 1H, *J* = 7.5 Hz), 6.5–7.11 (m, 14H), 7.38–7.60 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.1, 54.1 (dd, *J* = 9.9 Hz, 15.7 Hz), 69.8, 70.5, 71.2 (d, *J* = 2.5 Hz), 71.8 (d, *J* = 5.2 Hz), 75.3 (d, *J* = 11.3 Hz), 93.0 (d, *J* = 25.7 Hz), 114.6 (d, *J* = 21.9 Hz), 119.6 (d, *J* = 15.5 Hz), 122.7 (d, *J* = 3.5 Hz), 127.1, 127.5 (d, *J* = 7.1 Hz), 127.9 (d, *J* = 5.5 Hz), 128.1 (d, *J* = 8.0 Hz), 128.4, 128.5 (d, *J* = 7.4 Hz), 129.2, 129.3, 129.4, 131.0, 131.2 (d, *J* = 11.5 Hz), 132.1 (d, *J* = 5.5 Hz), 132.3, 132.6 (d, *J* = 20.3 Hz), 133.6 (d, *J* = 2.9 Hz), 133.8 (d, *J* = 2.3 Hz), 135.7 (d, *J* = 21.3 Hz), 137.6 (d, 8.6 Hz), 140.6 (d, *J* = 9.1 Hz), 146.0 (d, *J* = 4.0 Hz), 159.8 (d, *J* = 247.6 Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −34.9 (d, *J* = 40.7 Hz), −24.0 (d, *J* = 40.7 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ −110.9 (s). HRMS (ESI): calcd for $C_{44}H_{36}FeFN_3P_2$ (M+H$^+$) 743.1719, found 743.1712.

4.7. ClickFerrophos CF4[2c]

Yield, 73%. Yellow solid; mp = 167–168 °C. $[\alpha]_D^{25} = +95$ (*c* 0.34, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.61 (d, 3H, *J* = 6.8 Hz), 3.81 (s, 1H), 4.10 (s, 5H), 4.45 (t, 1H, *J* = 2.6 Hz), 4.90 (s, 1H), 6.30 (m, 1H), 6.6–7.6 (m, 21H). ^{13}C NMR ($CDCl_3$) δ 21.6, 53.9 (dd, *J* = 9.2, 11.7), 69.8, 70.2, 70.8 (d, *J* = 3.7 Hz), 71.8 (d, *J* = 4.9 Hz), 75.3 (d, *J* = 10.2 Hz), 92.4 (d, *J* = 26.0 Hz), 127.0, 127.7 (d, *J* = 5.5 Hz), 127.9 (d, *J* = 8.1 Hz), 128.1 (d, *J* = 6.8 Hz), 128.3 (d, *J* = 7.2 Hz), 128.7, 128.8, 129.5 (d, *J* = 42.5 Hz), 130.9 (d, *J* = 16.9 Hz), 132.4 (d, *J* = 18.6), 133.1 (d, *J* = 7.2), 133.4 (d, *J* = 2.5 Hz), 133.5 (d, *J* = 7.9), 134.0 (d, 21.5 Hz), 135.4 (d, *J* = 21.1 Hz), 137.1 (d, *J* = 8.5 Hz), 138.6, 139.1 (d, *J* = 9.6 Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −40.4 (d, *J* = 37.0 Hz), −24.5 (d, *J* = 37.0 Hz). HRMS (ESI): calcd for $C_{38}H_{33}FeN_3P_2$ (M+H$^+$) 650.1577, found 650.1573.

4.8. ClickFerrophos CF5

Yield, 63%. Yellow solid; mp = 91 °C. $[\alpha]_D^{25} = +161$ (*c* 0.36, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 1.74 (d, 3H, *J* = 7.0 Hz), 1.90 (s, 6H), 2.07 (s, 6H), 2.29 (s, 6H), 2.32 (s, 6H), 3.89 (s, 1H), 4.00 (s, 5H), 4.44 (s, 1H), 4.86 (s, 1H), 6.28, d, 2H, *J* = 7.3 Hz), 6.37 (d, 2H, *J* = 8.6 Hz), 6.45–6.46 (m, 1H), 6.5–6.6 (m, 4H), 6.83 (t, 2H, *J* = 7.4 Hz), 6.9–7.0 (m, 5H), 7.23 (d, 2H, *J* = 8.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 21.2, 21.2, 21.3, 21.9, 52.7 (dd, *J* = 8.6 Hz, 16.7 Hz), 69.7, 70.1, 70.5 (d, *J* = 4.0 Hz), 71.8 (d, *J* = 4.9 Hz), 76.4 (d, 12.5 Hz), 93.3 (d, *J* = 26.9 Hz), 126.5, 126.8, 127.1 (d, *J* = 21.9 Hz), 128.6 (d, 16.3 Hz), 129.0, 129.1, 130.1, 130.7 (d, *J* = 19.4 Hz), 130.9 (d, *J* = 11.9 Hz), 131.0, 131.2, 131.4 (d, *J* = 5.3 Hz), 131.7, 133.3, 133.4 (d, *J* = 21.6 Hz), 136.7 (d, *J* = 9.8 Hz), 136.8 (d, *J* = 11.7 Hz), 137.2 (d, *J* = 7.8 Hz), 137.5 (d, *J* = 8.3 Hz), 138.0 (d, *J* = 7.6 Hz), 139.5 (d, *J* = 9.0 Hz), 151.5. ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −34.6 (d, *J* = 40.7 Hz), −24.2 (d, *J* = 40.7 Hz). HRMS (ESI): calcd for $C_{52}H_{53}FeN_3P_2$ ($M+H^+$) 838.3138, found 838.3140.

4.9. ClickFerrophos CF6

Yield, 51%. Yellow solid; mp: decomp. >190 °C. $[\alpha]_D^{25} = +160$ (*c* = 0.31, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 1.69 (d, 3H, *J* = 6.8 Hz), 1.91 (s, 6H), 2.11 (s, 6H), 2.30 (s, 6H), 2.34 (s, 6H), 3.87 (s, 1H), 4.01 (s, 5H), 4.45 (t, 1H, *J* = 2.5 Hz), 4.88 (s, 1H), 5.89 (dt, 1H, *J* = 1.7, 7.5 Hz)), 6.32–6.70 (m, 9H), 6.89–7.06 (m, 5H), 7.23 (d, 2H, *J* = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 21.2, 21.3, 21.3, 21.7, 53.8 (dd, *J* = 8.2 Hz, 16.6 Hz), 69.8, 70.3, 70.6 (d, *J* = 4.0 Hz), 71.9 (d, *J* = 4.6 Hz), 76.4, 93.3 (d, *J* = 27.2 Hz), 114.2 (d, *J* = 21.7 Hz), 120.0 (d, *J* = 15.4 Hz), 122.1 (d, *J* = 3.7 Hz), 128.7 (d, *J* = 16.4 Hz), 128.9 (d, *J* = 19.5 Hz), 129.0, 130.5, 130.9, 131.0, 131.1, 131.2, 131.3 (d, *J* = 2.6 Hz), 131.6 (d, *J* = 2.5 Hz), 132.4 (d, *J* = 2.6 Hz), 132.6 (d, *J* = 7.6 Hz), 133.4 (d, *J* = 21.9 Hz), 136.8 (d, *J* = 15.0 Hz), 136.9, 137.2 (d, *J* = 8.5 Hz), 137.6 (d, *J* = 8.5 Hz), 138.0 (d, *J* = 7.8 Hz), 139.7 (d, *J* = 9.0 Hz), 145.6 (d, *J* = 2.7 Hz), 160.1 (d, *J* = 248.1 Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −35.5 (d, *J* = 48.1 Hz), −24.1 (d, *J* = 48.1 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ −111.7 (s). HRMS (ESI): calcd for $C_{52}H_{52}FeFN_3P_2$ ($M+H^+$) 855.2971, found 855.2970.

4.10. ClickFerrophos CF7[2c]

Yield, 71%. Yellow solid; mp = 100–101 °C. $[\alpha]_D^{25} = +97$ (*c* 0.31, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 0.9–2.3 (m, 47H) including 2.04 (d, 3H, *J* = 6.9 Hz), 4.19 (s, 1H), 4.29 (s, 5H+1H), 4.33 (s, 1H), 6.17 (m, 1H), 7.3–7.4 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.6 (d, *J* = Hz), 26–36 (several cyclohexyl signals), 54.2, 68.5, 69.7, 71.2, 71.3, 78.4 (d, *J* = 25.3 Hz), 95.3 (d, *J* = 24.8), 127.9, 128.1, 128.4 (d, *J* = 30. 0 Hz), 129.3,133.2, 151.6. ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −28.7 (s), −18.0 (s). HRMS (ESI): calcd for $C_{44}H_{61}FeN_3P_2$ ($M+H^+$) 750.3768, found 750.3767.

4.11. Preparation of (*S*,*Rp*)-(*Rp*)-1-(diphenylphosphino)-2-[(*S*)-1-[4-phenyl-1*H*-1,2,3-triazol-1-yl]ethyl]ferrocene 5

To a 50 mL Schlenk tube containing a magnetic stirring bar were added **4** (0.20 g, 0.41 mmol) and dry diethyl ether (20 mL) under a slight pressure of nitrogen. The flask was cooled at −78 °C, and a hexane solution of *n*-BuLi (0.3 mL, 0.48 mmol, 1.6 M) was then added using a syringe through the septum with magnetic stirring. After 2 h, Ph_2PCl (84 μL, 0.46 mmol) was injected into the mixture at −78 °C. When the addition was completed, the mixture was allowed to warm to room temperature and then stirred for 2 h. The reaction was quenched with saturated NH_4Cl, and the solution was then extracted with diethyl ether (30 mL × 3). The combined extracts were washed (brine), dried (Na_2SO_4), filtered and the solvent was removed on a rotary evaporator to leave a yellow residue. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 1/1) to give pure **5** as a yellow solid. Yield, 0.17 g, 0.64 mmol, 80%; mp = 203 °C. $[\alpha]_D^{25} = +280$ (*c* 0.31, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 2.01 (d, 3H, *J* = 7.0 Hz), 3.89 (s, 1H), 4.10 (s, 5H), 4.43 (t, 1H, *J* = 2.5 Hz), 4.78 (s, 1H), 6.10 (dq, 1H, *J* = 7.0, 3.4 Hz), 6.7–6.9 (m, 5H), 7.11 (s, 1H), 7.2–7.5 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 55.2 (d, *J* = 11.0 Hz), 69.5 (d, *J* = 3.9 Hz), 69.9, 70.0, 72.1 (d, *J* = 4.9 Hz), 76.7, 91.6 (d, *J* = 24.0 Hz), 118.1, 125.5, 127.3, 127.7, 127.8, 128.0, 128.2, 129.1, 130.7, 131.9 (d, *J* = 19.2 Hz), 134.7 (d, *J* = 20.9 Hz), 136.4 (d, *J* = 7.6 Hz), 137.4 (d, *J* = 6.2 Hz), 146.3. ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −26.1. HRMS (ESI): calcd for $C_{32}H_{28}FeN_3P$ ($M+H^+$) 542.1406, found 542.1404.

4.12. General procedure for preparation of CF8–CF10

To a 20 mL Schlenk tube containing a magnetic stirring bar were added **5** (135 mg, 0.25 mmol) and dry THF (2 mL) under a slight pressure of nitrogen. The flask was cooled at −78 °C, and a hexane solution of *n*-BuLi (0.19 mL, 0.30 mmol, 1.6 M) was then added using a syringe through the septum with magnetic stirring. After 10 min, (3,5-dimethylphenyl)$_2$PCl (80 μL, 0.30 mmol) was injected into the mixture at −78 °C and stirred for 1 h. The mixture was allowed to warm to room temperature and then stirred for an additional 2 h. The reaction was quenched with saturated NH_4Cl, and the solution was then extracted with diethyl ether (10 mL × 3). The combined extracts were washed (brine), dried ($NaSO_4$), filtered and the solvent was removed on a rotary evaporator to leave a yellow residue. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 2/1) to give pure **CF8** as a yellow solid. Yield, 73 mg, 0.09 mmol, 37%; mp = 101 °C. $[\alpha]_D^{25} = +160$ (*c* 0.26, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 1.71 (d, 3H, *J* = 7.0 Hz), 1.91 (s, 6H), 2.30 (s, 6H), 3.84 (s, 1H), 4.04 (s, 5H), 4.46 (s, 1H), 4.85 (s, 1H), 6.27 (d, 2H, *J* = 8.8 Hz), 6.41 (m, 1H), 6.5–7.6 (m, 19H). ^{13}C NMR ($CDCl_3$) δ 20.9, 21.3, 21.9, 54.0 (dd, *J* = 8.5 Hz, 16.1 Hz), 69.8, 70.2, 71.0 (d, *J* = 4.3 Hz), 71.8 (d, *J* = 4.6 Hz), 75.6 (d, *J* = 11.8 Hz), 93.3 (d, *J* = 25.4 Hz), 126.6, 126.8, 127.0 (d, *J* = 13.1 Hz), 127.7 (d, *J* = 20.0 Hz), 127.9 (d, *J* = 23.0 Hz), 129.2, 129.3, 130.2, 130.3 (d, *J* = 19.4 Hz), 131.1, 131.2 (d, *J* = 22.4 Hz), 131.3, 131.6, 132.8 (d, *J* = 7.5 Hz), 135.6 (d, *J* = 21.9 Hz), 137.1 (d, *J* = 7.3 Hz), 137.6 (d, *J* = 7.7 Hz), 138.0 (d, *J* = 7.7 Hz), 139.5 (d, *J* = 9.4 Hz), 151.5. ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −34.7 (d, *J* = 33.3 Hz), −24.3 (d, *J* = 33.3 Hz). HRMS (ESI): calcd for $C_{48}H_{45}FeN_3P_2$ ($M+H^+$) 781.2439, found 781.2434.

4.13. ClickFerrophos CF9

Yellow solid; yield, 89 mg, 0.09 mmol, 44%; mp = 153 °C. $[\alpha]_D^{25} = +140$ (*c* 0.31, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 1.82 (d, 3H, *J* = 6.9 Hz), 3.96 (s, 1H), 4.05 (s, 5H), 4.53 (s, 1H), 4.96 (s, 1H), 6.31 (d, 2H, *J* = 8.0 Hz), 6.47–6.51 (m, 1H), 6.6–7.0 (m, 9H), 7.15 (d, 2H, *J* = 7.4 Hz), 7.4–7.6 (m, 6H), 7.71 (d, 1H, *J* = 6.7 Hz), 7.99 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 22.0, 54.9 (dd, *J* = 9.5 Hz, 15.6 Hz), 69.9, 70.7, 70.8 (d, *J* = 3.6 Hz), 72.1 (d, *J* = 4.9 Hz), 75.7 (d, *J* = 9.9 Hz), 92.3 (d, *J* = 27.8 Hz), 122.5 (q, *J* = 273.3 Hz), 122.7 (q, *J* = 273.8), 122.8 (d, *J* = 13.8), 123.5(m), 123.9 (m), 128.0 (d, *J* = 5.1 Hz), 128.1, 128.2 (d, *J* = 5.9 Hz), 129.3, 129.7, 130.2, 130.8 (d, *J* = 16.3 Hz), 131.5 (dq, *J* = 7.3, 33.6 Hz), 132.6 (dq, *J* = 6.2, 33.4 Hz), 132.7 (m), 133.0 (m), 133.8 (d, *J* = 11.4 Hz), 135.4 (d, *J* = 21.8 Hz), 136.2 (d, *J* = 14.1 Hz), 136.9 (d, *J* = 5.7 Hz), 139.2 (d, *J* = 7.1 Hz), 152.6 (d, *J* = 226.3 Hz). ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −35.1 (d, *J* = 35.1 Hz), −24.8 (d, *J* = 40.7 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ −63.1 (s), −63.3 (s). HRMS (ESI): calcd for $C_{48}H_{33}FeF_{12}N_3P_2$ ($M+H^+$) 997.1309, found 997.1302.

4.14. ClickFerrophos CF10[2a]

Yellow solid; mp = 183–184 °C. $[\alpha]_D^{25} = +150$ (*c* 0.23, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 0.8–1.8 (m, 20H), 2.08 (d, 3H, *J* = 6.8 Hz), 3.92 (s, 1H), 4.04 (s, 5H), 4.46 (t, 1H, *J* = 2.5 Hz), 4.79 (s, 1H), 6.40 (m, 1H), 6.69 (m, 2H), 7.0–7.6 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9, 25.9–35.4 (several cyclohexyl signals), 53.7 (dd, *J* = 2.5, 10.5), 69.7, 70.4, 71.4 (d, *J* = 5.1 Hz), 71.6 (d, *J* = 4.7 Hz), 75.2 (d, *J* = 11.8 Hz), 94.0 (d, *J* = 26.5 Hz), 126.8–140.4 (several phenyl signals). ^{31}P NMR ($CDCl_3$) δ −28.7 (d, *J* = 11.6 Hz), −23.6 (d, *J* = 11.6 Hz). HRMS (ESI): calcd for $C_{44}H_{49}FeN_3P_2$ ($M+H^+$) 738.2813, found 738.2825.

4.15. General procedure for $[Rh(nbd)_2]BF_4$/CF complex-catalyzed asymmetric hydrogenation of enamide

The following provides a typical experimental procedure of asymmetric hydrogenation of alkenes. In a 20 mL Schlenk tube containing a stirring bar, $[Rh(nbd)_2]BF_4$ (3.7 mg, 1 mol %) and **CF1** (8.0 mg, 1.1 mol %) were dissolved in MeOH/toluene (1:1) (4 mL) and stirred under nitrogen at room temperature. After 30 min, the in situ-formed catalyst solution was transferred to another Schlenk tube containing **6a** (110 mg, 1.0 mmol) using a cannula. The Schlenk tube was connected to vacuum and purged with hydrogen from a balloon and the mixture was stirred at room temperature for the indicated time under hydrogen (1 atm). The GC/MS analysis of the reaction solution revealed that the reaction proceeded quantitatively. The solvent was removed under reduced pressure, and the residue was subjected to PTLC (hexane/ethyl acetate = 1/1 as eluent) to give pure **8a**. The enantiomeric excess was determined by HPLC [Chiralpack AD-H, 25 cm; hexane/*i*-PrOH = 90/10, 0.8 mL/min, t_R (*R*) = 11.8 min, t_R (*S*) = 16.0 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 3.07 (dd, 1H, *J* = 5.9, 13.8 Hz), 3.14 (dd, 1H, *J* = 5.8, 13.8 Hz), 3.71 (s, 3H), 4.87 (ddd, 1H, *J* = 5.8, 5.9, 7.8 Hz), 6.11 (d, 1H, *J* = 7.8 Hz), 7.1–7.3 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9, 37.7, 52.2, 53.0, 127.0, 128.5, 129.1, 135.8, 169.6, 172.1.

4.16. (*R*)-Methyl 2-acetoamido-3-(*p*-methylphenyl)propionate 8b

The enantiomeric excess was determined by HPLC; Chiralpack AD-H, 25 cm; hexane/*i*-PrOH = 90/10, 1.0 mL/min, t_R (*R*) = 11.0 min, t_R (*S*) = 15.0 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.99 (s, 3H), 2.32 (s, 3H), 3.05 (dd, 1H, *J* = 5.5, 13.9 Hz), 3.12 (dd, 1H, *J* = 5.7, 13.9 Hz), 3.74 (s, 3H), 4.86 (ddd, 1H, *J* = 5.6, 5.8, 8.0 Hz), 5.87 (d, 1H, *J* = 8.0 Hz), 6.96 (d, 2H, *J* = 7.8 Hz), 7.10 (d, 2H, *J* = 7.8 Hz). ^{13}C NMR ($CDCl_3$) δ 20.9, 22.9, 37.2, 52.1, 53.0, 128.9, 129.1, 132.6, 136.5, 169.6, 172.2.

4.17. (*R*)-Methyl 2-acetoamido-3-(*o*-methylphenyl)propionate 8c

The enantiomeric excess was determined by HPLC; Chiralpack AD-H, 25 cm; hexane/*i*-PrOH = 90/10, 1.0 mL/min, t_R (*R*) = 8.1 min, t_R (*S*) = 11.0 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 2.33 (s, 3H), 3.04 (dd, 1H, *J* = 6.8, 14.0 Hz), 3.16 (dd, 1H, *J* = 6.7, 14.0 Hz), 3.74 (s, 3H), 4.86 (ddd, 1H, *J* = 6.7, 6.8, 7.1 Hz), 5.87 (d, 1H, *J* = 7.1 Hz), 7.0–7.3 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 22.8, 35.4, 52.1, 52.2, 125.7, 126.9, 129.5, 130.4, 134.2, 136.5, 169.7, 172.5.

4.18. (*R*)-Methyl 2-acetoamido-3-(*p*-methoxyphenyl)propionate 8d

The enantiomeric excess was determined by HPLC; Chiralpack AD-H, 25 cm; hexane/*i*-PrOH = 90/10, 1.0 mL/min, t_R (*R*) = 14.8 min, t_R (*S*) = 20.0 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.99 (s, 3H), 3.03 (dd, 1H, *J* = 5.6, 14.0 Hz), 3.09 (dd, 1H, *J* = 5.8, 14.0 Hz), 3.72 (s, 3H), 3.78 (s, 3H), 4.84 (ddd, 1H, *J* = 5.6, 5.8, 7.1 Hz), 5.97 (d, 1H, *J* = 7.1 Hz), 6.82 (d, 2H, *J* = 8.4 Hz), 7.00 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.7, 36.7, 52.0, 53.1, 54.9, 113.7, 127.7, 130.0, 158.4, 169.6, 172.1.

4.19. (*R*)-Methyl 2-acetoamido-3-(*p*-chlorophenyl)propionate 8e

The enantiomeric excess was determined by HPLC; Chiralpack AD-H, 25 cm; hexane/*i*-PrOH = 90/10, 0.8 mL/min, t_R (*R*) = 12.6 min, t_R (*S*) = 15.9 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.99 (s, 3H), 3.06 (dd, 1H, *J* = 5.4, 13.9 Hz), 3.15 (dd, 1H, *J* = 5.9, 13.9 Hz), 3.74 (s, 3H), 4.87 (ddd, 1H, *J* = 5.4, 5.9, 7.1 Hz), 5.91 (d, 1H, *J* = 7.1 Hz), 7.02 (d, 2H, *J* = 8.3 Hz), 7.27 (d, 2H, *J* = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 37.0, 52.2, 52.9, 128.5, 130.4, 132.8,134.4, 169.9, 171.9.

4.20. (*R*)-Methyl 2-acetoamido-3-(*p*-fluorophenyl)propionate 8f

The enantiomeric excess was determined by HPLC Chiralpack AD-H, 25 cm; hexane/*i*-PrOH = 90/10, 1.0 mL/min, t_R (*R*) = 10.4 min, t_R (*S*) = 12.9 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.89 (s, 3H), 2.95 (dd, 1H, *J* = 6.2, 13.8 Hz), 3.04 (dd, 1H, *J* = 5.9, 13.8 Hz), 3.62 (s, 3H), 4.75 (ddd, 1H, *J* = 5.9, 6.2, 7.4 Hz), 6.33 (d, 1H, *J* = 7.4 Hz), 6.9–7.0 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9, 36.9, 52.2, 53.1, 115.2 (d, *J* = 21.3 Hz), 130.6 (d, *J* = 7.9 Hz), 131.5 (d, *J* = 3.2 Hz), 161.5 (d, *J* = 245 Hz), 169.7, 171.9.

4.21. (*R*)-Methyl 2-acetoamido-3-(*m*-fluorophenyl)propionate 7g

The enantiomeric excess was determined by HPLC; Chiralpack AD-H, 25 cm; hexane/*i*-PrOH = 90/10, 1.0 mL/min, t_R (*R*) = 10.8 min, t_R (*S*) = 13.8 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 3H), 3.08 (dd, 1H, *J* = 5.6, 13.9 Hz), 3.17 (dd, 1H, *J* = 5.8, 13.9 Hz), 3.74 (s, 3H), 4.89 (ddd, 1H, *J* = 5.6, 5.8, 6.7 Hz), 6.00 (d, 1H, *J* = 6.7 Hz), 6.9–7.3 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.7, 37.3, 52.2, 52.9, 113.8 (d, *J* = 21.0 Hz), 115.9 (d, *J* = 21.3 Hz), 124.7 (d, *J* = 2.8 Hz), 129.8 (d, *J* = 8.2 Hz), 138.4 (d, *J* = 7.5 Hz), 162.5 (d, *J* = 246 Hz), 169.8, 171.8.

4.22. (*R*)-Methyl 2-acetoamido-3-(*o*-fluorophenyl)propionate 8h

The enantiomeric excess was determined by HPLC; Chiralpack AD-H, 25 cm; hexane/*i*-PrOH = 90/10, 1.0 mL/min, t_R (*R*) = 11.4 min, t_R (*S*) = 14.8 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 3.13 (dd, 1H, *J* = 6.1, 13.9 Hz), 3.22 (dd, 1H, *J* = 6.0, 13.9 Hz), 3.74 (s, 3H), 4.87 (ddd, 1H, *J* = 6.0, 6.1, 7.2 Hz), 6.01 (d, 1H, *J* = 7.2 Hz), 7.0–7.3 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.7, 37.2, 52.2, 52.3, 115.1 (d, *J* = 22.0 Hz), 123.0 (d, *J* = 16.6 Hz), 123.9 (d, *J* = 2.7 Hz), 128.8 (d, *J* = 8.2 Hz), 131.4 (d, *J* = 4.4 Hz), 161.1 (d, *J* = 245 Hz), 169.8, 171.9.

4.23. (*R*)-Methyl 2-acetoamido-3-(*p*-nitrophenyl)propionate 8i

The enantiomeric excess was determined by HPLC; Chiralpack OJ-H, 25 cm; hexane/*i*-PrOH = 90/10, 0.8 mL/min, t_R (*R*) = 52.4 min, t_R (*S*) = 57.0 min]. ^1H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 3H), 3.18 (dd, 1H, *J* = 5.6, 13.7 Hz), 3.31 (dd, 1H, *J* = 5.8, 13.9 Hz), 3.76 (s, 3H), 4.93 (ddd, 1H, *J* = 5.6, 5.8, 8.0 Hz), 5.99 (d, 1H, *J* = 8.0 Hz), 7.30 (d, 2H, *J* = 7.8 Hz), 8.16 (d, 2H, *J* = 7.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 37.6, 52.4, 52.7, 123.5, 130.0, 143.9, 146.9, 169.8, 171.4.

4.24. *N*-Acetyl-1-phenylethylamine 9

The compound was obtained from the hydrogenation with **7**. The enantiomeric excess was determined by GC; CP Chirasil-Dex CB, 25 mm; isotherm 140 °C, t_R (*S*) = 12.0 min, t_R (*R*) = 12.7 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (d, 3H, *J* = 7.0 Hz), 1.82 (s, 3H), 4.98 (quint, 1H, *J* = 7.0 Hz), 6.43 (br s, 1H), 7.23–7.35 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 21.7, 23.0, 48.6, 126.0, 127.0, 128.4, 143.3, 169.3.

4.25. General procedure for [Ru(cod)(2-metallyl)$_2$]/CF complex-catalyzed asymmetric hydrogenation of ketones

The following provides a typical experimental procedure for asymmetric hydrogenation of ketones. In a 20 mL Schlenk tube containing a stirring bar, [Ru(cod)(2-metallyl)$_2$] (1.6 mg, 0.5 mol %), **CF1** (4.0 mg, 0.55 mol %) were dissolved in acetone (2 mL) under nitrogen at room temperature. To the solution was added methanol solution of HBr (0.1 mL, 0.03 mmol, 0.3 M) and stirred at the same temperature for 30 min. Then, the solvent was removed in vacuo and it was replaced by ethanol (4 mL). The substrate **10** (156 mg, 1.0 mmol) was placed in a glass tube containing a magnetic stirring bar in the autoclave. The in situ-formed catalyst solution was added to the substrate using a syringe. The autoclave was purged three times with hydrogen, heated to 50 °C and the hydrogen pressure was placed at 10 atm. The reaction was carried out for 24 h. Then the pressure was released to atmospheric pressure and the solution was transferred to a round-bottomed flask. The solvent was removed on a rotary evaporator to leave the residue, which was subjected to PTLC (hexane/ethyl acetate = 1/1 as eluent) to give pure **11**. The enantiomeric excess was determined by GC [CP-Chirasil-Dex CB, 25 m, isotherm 100 °C, t_R (*S,S*) = 26.7 min, t_R (*R,R*) = 27.3 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, 3H, *J* = 7.1 Hz), 1.5–2.1 (m, 6H), 2.65 (q, 1H, *J* = 8.5 Hz), 4.16 (q, 2H, *J* = 7.1 Hz), 4.38 (q, 1H, *J* = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.0, 27.2, 34.6, 52.5, 60.4, 76.0, 175.1.

4.26. (*R,R*)-2,3-Diphenyl-1,3-propanediol 13

The compound was obtained by hydrogenation with **12**. The enantiomeric excess was determined by HPLC; Chiralcel OD-H, 25 cm; hexane/*i*-PrOH = 90/10, 1.0 mL/min, t_R (*S,S*) = 16.7 min, t_R (*R,R*) = 18.3 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.19 (dd, 2H, *J* = 5.4, 6.2 Hz), 5.0 (t, 2H, *J* = 6.0 Hz), 7.2–7.3 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 46.3, 71.6, 125.5, 127.3, 128.6, 144.3.

4.27. Ethyl 3-hydroxy-3-phenylpropionate 15

The title compound was obtained by hydrogenation with **14**. The enantiomeric excess was determined by HPLC; Chiralcel OD-H, 25 cm; hexane/*i*-PrOH = 95/5, 1.0 mL/min, t_R (*S*) = 11.0 min, t_R (*R*) = 12.2 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.68 (dd, 1H, *J* = 4.3, 16.2 Hz), 2.74 (dd, 1H, *J* = 8.6, 16.2 Hz), 3.45 (br s, 1H), 4.15 (q, 2H, *J* = 7.2 Hz), 5.10 (dd, 1H, *J* = 4.3, 8.6 Hz), 7.2–7.4 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 14.0, 43.3, 60.7, 70.2, 125.6, 127.6, 128.4, 142.4, 172.3.

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