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Tetrahedron: *Asymmetry* 14 (2003) 1467–1472

TETRAHEDRON: *ASYMMETRY*

New efficient *P,N,O*-tridentate ligands for Ru-catalyzed asymmetric transfer hydrogenation

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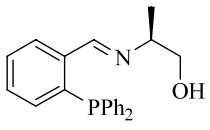
Received 15 January 2003; accepted 8 April 2003

Abstract—New chiral *P,N,O* Schiff base ligands derived from substituted salicylaldehyde and (*R*)-1-[(*S*)-2-(diphenylphosphino)-ferrocenyl]ethylamine[(R,S_{Fc})-PPFNH$_2$] have been prepared and employed in ruthenium catalyzed asymmetric transfer hydrogenation of simple ketones. Up to 94% e.e. with 99% conversion was obtained when the electron-withdrawing 3,5-dinitro substituted ligand **2f** was used.

1. Introduction

The development of new chiral transition metal catalysts for enantioselective reactions has been the subject of many investigations in recent years.[1,2] Ruthenium-catalyzed asymmetric transfer hydrogenation of prochiral ketones is an efficient method for the preparation of chiral secondary alcohols.[3–22] This method holds great promise because it is simple and does not require the use of molecule hydrogen and high-pressure equipment. Chiral Schiff base complexes are very effective catalysts for a wide range of reactions, such as epoxidation,[23] epoxide ring opening reaction,[24] Diels–Alder reaction[25] and aldol reaction,[26] however, there are only a few examples using Schiff bases as chiral ligands for asymmetric transfer hydrogenation of ketones. Recently, Kwong and co-workers described a *P,N,O* ligand **1** for transfer hydrogenation with 81% e.e.[27] More recently, Kim et al. reported a new ferrocene-based ligand **2a** ($R_1 = R_2 = H$) for the asymmetric addition of diethylzinc to aromatic aldehydes with 98% e.e.[28] Herein, we report a series of *P,N,O* ligands **2** for the ruthenium catalyzed asymmetric transfer hydrogenation of simple ketones with up to 94% e.e.



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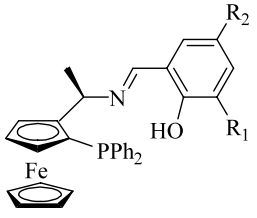

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2. Results and discussion

2.1. Preparation of *P,N,O* type ligands

The synthesis of ferrocene based *P,N,O* type ligands is outlined in Scheme 1. According to the literature procedure,[29] (R,S_{Fc})-PPFA **3** was reacted with Ac_2O at 100°C for 2 h followed by the treatment with a large excess of ammonia in methanol in an autoclave at 80°C to afford the key primary amine (R,S_{Fc})-PPFNH$_2$ **5**. The target ligand **2a** was then prepared by condensation of (R,S_{Fc})-PPFNH$_2$ **5** with salicylaldehyde in ethanol under reflux in the presence of anhydrous $MgSO_4$. 91.8% yield was obtained. The ^{1}H NMR spectrum of ligand **2a** was consistent with the target molecule structure, and the ^{31}P NMR spectrum showed the expected single peak at −23.78 ppm in accordance with one phosphino group. In a similar procedure, the ligands **2b–j** were also prepared with the corresponding salicylaldehydes.

The ligands (R,R_{Fc})-**2a** and (R,R_{Fc})-**2f** with reverse planar chirality compared with that of (R,S_{Fc})-**2a** and (R,S_{Fc})-**2f** were also prepared according to the literature method.[30]

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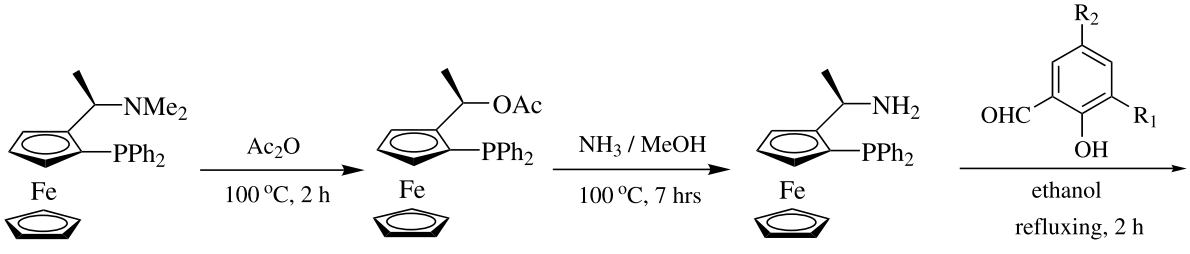
0957-4166/03/$ - see front matter
doi:10.1016/S0957-4166(03)00320-3

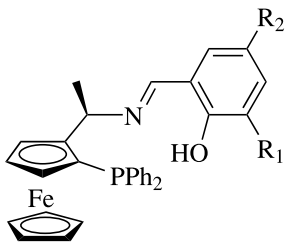
2.2. Asymmetric transfer hydrogenation of ketones with 2-propanol

2.2.1. Asymmetric transfer hydrogenation of acetophenone using Ru(II)-2a. The Ru(II)-**2a** catalyst was generated in situ by refluxing **2a** (2 mol%) with $Ru(DMSO)_4Cl_2$ (1 mol%) in 2-propanol at 80°C under argon for 1 h. Transfer hydrogenation occurred immediately when acetophenone and *tert*-BuOK was added to the above catalyst solution. 1-Phenylethanol was formed as the only product favoring *R* configuration from GC analysis, 81% conversion and 50% e.e. were obtained after 30 min at 80°C (entry 2, Table 1). Prolonging reaction time led to higher conversion but relatively lower e.e. (entry 5, Table 1, 98% conversion, 35% e.e.).

The influence of **2a**/Ru ratio and reaction temperature on the catalytic activity and enantioselectivity was investigated (Table 1). Under the same reaction conditions, different **2a**/Ru ratios were used in the reaction (entries 1–4, Table 1). With **2a**/Ru ratios increasing from 1 to 4, the conversion was slightly increased, while the enantioselectivity increased greatly (from 27 to 50%



(*R*, S_{Fc})-PPFA **3** (*R*, S_{Fc})-PPFOAc **4** (*R*, S_{Fc})-PPFNH$_2$ **5**

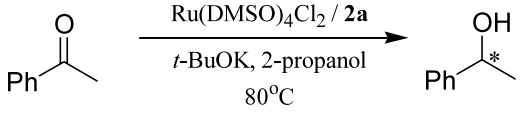


(*R*, S_{Fc})-**2**

2a: R_1= H; R_2= H;
2b: R_1= CH_3; R_2= H;
2c: R_1= F; R_2= H;
2d: R_1= Cl; R_2= H;
2e: R_1= Br; R_2= H;
2f: R_1= NO_2; R_2= NO_2;
2g: R_1= Cl; R_2= Cl;
2h: R_1= Br; R_2= Br;
2i: R_1= CH_3; R_2= Bu-*t*;
2j: R_1= Bu-*t*; R_2= NO_2;

Scheme 1.

Table 1. Asymmetric transfer hydrogenation of acetophenone using Ru(II)-**2a** catalyst



Entry	Ru precursor	**2a**/Ru	*T* (°C)	Time	Conv. (%)[b]	E.e. % (config.)[c,d]
1	$Ru(DMSO)_4Cl_2$	1	80	30 min	80	27 (*R*)
2	$Ru(DMSO)_4Cl_2$	2	80	30 min	81	50 (*R*)
3	$Ru(DMSO)_4Cl_2$	2.5	80	30 min	85	51 (*R*)
4	$Ru(DMSO)_4Cl_2$	4	80	30 min	87	50 (*R*)
5	$Ru(DMSO)_4Cl_2$	2	80	2 h	98	35 (*R*)
6	$Ru(DMSO)_4Cl_2$	4	25	2 h	35	45 (*R*)
7	$Ru(DMSO)_4Cl_2$	2.5	0	24 h	30	50 (*R*)
8	$Ru(DMSO)_4Cl_2$	4	80	1 h	80	49 (*R*)
9[a]	$Ru(PPh_3)_3Cl_2$	4	80	1 h	70	45 (*R*)
10	$Ru(cymene)_2Cl_2$	4	80	1 h	78	40 (*R*)

[a] After catalyst was formed, free PPh_3 and **2a** were washed out with diethyl ether before adding acetophenone and *tert*-BuOK.
[b] Conversion was determined by GC analysis.
[c] The enantiomeric excesses were determined by GC using a capillary chiral column (cyclodex-β,2-,3-,6-methylated, 30 m×0.25 mm (i.d.)).
[d] The absolute configuration was determined by comparison of the retention time of the enantiomers on the GC analysis with literature values.

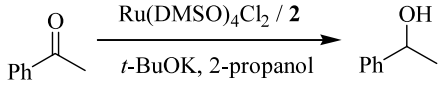
with **2a**/Ru ratio increasing from 1 to 2). However, only slight increasing of enantioselectivity was observed with **2a**/Ru ratio increasing further from 2 to 4 (entries 2–4, Table 1). The reaction was performed at 0, 25 and 80°C, respectively. With reaction temperature decreasing, the conversion decreased sharply. When the reaction was performed at 0°C, the conversion was only 30% (entry 7, Table 1). These results indicate that the reaction temperature plays an important role on the catalytic property of **2a**/Ru. The catalyst exhibited high activity and enantioselectivity at 80°C with **2a**/Ru ratio of 2. The following reactions were carried out under the above-optimized conditions.

$Ru(PPh_3)_3Cl_2$ and $Ru(cymene)_2Cl_2$ was also chosen as ruthenium precursors. Under typical reaction conditions, $Ru(PPh_3)_3Cl_2$-**2a** and $Ru(cymene)_2Cl_2$-**2a** exhibited lower activity and enantioselectivity than that of $Ru(DMSO)_4Cl_2$-**2a** (entries 9 and 10, Table 1).

2.2.2. The influence of substituents of phenyl moiety in *P,N,O*-ligand on catalytic property. The steric and electronic properties of the catalyst play a significant role in the catalytic reactions, so it is very important to introduce easily tunable groups on the ligand when designing new ligands.[31] One of the advantages of the salicylaldehyde structure lies in the easy modification of the ligand using different substituents R_1 and R_2. The ligands **2a**–**j** were prepared by introducing substituents with different electron-withdrawing and electron-donating character to the salicyaldehyde backbone. The results of asymmetric transfer hydrogenation of acetophenone by Ru(II)/**2a**–**j** are listed in Table 2. The Ru(II)-**2** catalysts with an electron-withdrawing substituent R_1 resulted in significantly higher activity and enantioselectivity compared with electron-donating ligands, for example, when Ru/**2d** was used as catalyst, 90% conversion and 68% e.e. were obtained after 30 min (entry 5, Table 2). However, an electron-donating group R_1 led to lower activity and enantioselectivity ($R_1=CH_3$, 17% conversion with 18% e.e. entry 3, Table 2). The introduction of two electron-withdrawing substituents ($R_1=R_2$) on the salicyaldehyde backbone results in significant increase of both the conversion and the enantioselectivity (entries 7, 9, 10, Table 2). Up to 92% e.e. was achieved with Ru(II)-**2f** ($R_1=R_2=NO_2$). On the contrary, the introduction of two electron-donating substituents (Ru(II)-**2i**, $R_1=CH_3$, $R_2=$*tert*-Bu) caused a sharp decrease of activity and enantioselectivity (8% conversion with 10% e.e. entry 11, Table 2). Concluded from the above data, the ligands with electron-withdrawing substituents on salicyaldehyde ring exhibit higher catalytic activity and enantioselectivity. The catalytic activity and enantioselectivity decreased in the following order: NO_2>Cl>Br>F>H>CH_3>*tert*-Bu.

(R,R_{Fc})-**2a** and (R,R_{Fc})-**2f** with reverse planar chirality are the diastereomers of (R,S_{Fc})-**2a** and (R,S_{Fc})-**2f**, respectively. When they were used in the transfer hydrogenation of acetophenone with *tert*-BuOK, the 1-phenylethanol formed favored *S* configuration from GC analysis (entries 2, 8, Table 2). The catalytic activity and enantioselectivity of (R,R_{Fc})-type ligand were comparable to that of (R,S_{Fc})-type ligand. Further studies are underway.

Table 2. The influence of the substituents' properties on asymmetric transfer hydrogenation of acetophenone with 2-propanol[a]



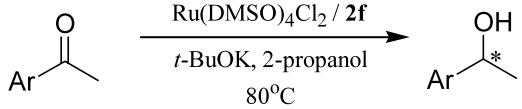
Entry	Ligand	% Conv.[b]	% E.e. (config.)[c,d]
1	**2a**	85	51 (*R*)
2	**2a**-[(*R*)-(*R*)-type]	86	49 (S)
3	**2b**	17	18 (*R*)
4	**2c**	87	55 (*R*)
5	**2d**	90	68 (*R*)
6	**2e**	90	63 (*R*)
7	**2f**	99	92 (*R*)
8	**2f**-[(*R*)-(*R*)-type]	99	90 (S)
9	**2g**	98	87 (*R*)
10	**2h**	98	85 (*R*)
11	**2I**	8	10 (*R*)
12	**2j**	70	61 (*R*)

[a] Reactions were carried out in a period of 30 min at 80°C in the presence of 2.0 mmol acetophenone, 1 mol% $Ru(DMSO)_4Cl_2$, 2 mol% **2** and 15 mol% *tert*-BuOK.
[b] Conversion was determined by GC.
[c] The enantiomeric excesses were determined by GC using a capillary chiral column (cyclodex-β,2-,3-,6-methylated, 30 m×0.25 mm (i.d.)).
[d] The absolute configuration was determined by comparison of the retention time of the enantiomers on GC analysis with literature values.

2.2.3. Asymmetric transfer hydrogenation of different ketone substrates. Due to its efficiency in transfer hydrogenation of acetophenone, ligand **2f** was chosen as a model ligand for thorough study of the transfer hydrogenation of various methyl aryl ketones. The results were summarized in Table 3.

Ru(II)-**2f** showed high activity and enantioselectivity in transfer hydrogenations of various ketones. The activity and enantioselectivity were found to be related to the substituent electronic factor of ketones. The introduction of electron-withdrawing substituents, such as F, Cl, Br and NO_2, in the *para* position of the aryl ring, resulted in higher activities and enantioselectivities (entries 3–6, Table 3). Decreasing activity and enantioselectivity was observed for ligands with electron-donating substituents on aromatic ring, but the enantioselectivity was reasonable (entries 1, 2, Table 3). 1-Acetonaphthone and 2-acetonaphthone were also reduced with high activity and enantioselectivity. 1-Acetonaphthone gave the highest enantioselectivity reported in this study (94%). Compared with other *P,N,O*-Ru systems previously reported by Mathieu[32] and Kwong,[27] the e.e. obtained in this study is the highest among *P,N,O*-ligands based catalysts so far.

Table 3. Catalytic asymmetric transfer hydrogenation with $Ru(DMSO)_4Cl_2$/**2f** for acetophenones with 2-propanol[a]



Entry	Ar	Time (h)	% Conv.[b]	% e.e.[c,d]
1	4-MeC_6H_4	1	98	83 (*R*)
2	4-$MeOC_6H_4$	2	95	54 (*R*)
3	4-FC_6H_4	0.5	98	90 (*R*)
4	4-ClC_6H_4	0.5	99	91 (*R*)
5	4-BrC_6H_4	0.5	99	89 (*R*)
6	4-$NO_2C_6H_4$	0.5	100	90 (*R*)
7	1-Naphthyl	1.5	99	94 (*R*)
8	2-Naphthyl	1.5	98	87 (*R*)

[a] Reactions were carried out at 80°C in the presence of 2.0 mmol ketone, 1 mol% $Ru(DMSO)_4Cl_2$, 2 mol% **2f** and 15 mol% *t*-BuOK.
[b] The conversion was determined by GC.
[c] The enantiomeric excesses were determined by GC using a capillary chiral column [cyclodex-β,2-,3-,6-methylated, 30 m×0.25 mm (i.d.)].
[d] The absolute configuration was determined by comparison of the retention time of the enantiomers on GC analysis with literature values.

3. Conclusion

In conclusion, a new class of *P*,*N*,*O*-Schiff bases ligands was synthesized, the catalyst generated in situ by mixing these ligands with $Ru(DMSO)_4Cl_2$ were found to be effective catalysts for the asymmetric transfer hydrogenation of methyl aryl ketones with 2-propanol as the hydrogen donor. A significant influence of substituents on the chiral induction was observed, electron-withdrawing substituents proved to benefit the activity and enantioselectivity. Up to 94% e.e. was obtained using Ru(II)–**2f** as the catalyst.

4. Experimental

4.1. General methods

Optical rotations were measured on a HORIBA SEPA-200 High Sensitive Polarimeter. ^1H NMR spectra were recorded on Bruker DRX-400 NMR spectrometer with TMS as an internal standard. ^{31}P NMR spectra were referenced to external 85% H_3PO_4. The conversions and e.e. values were determined by GC analysis with a chiral capillary column (cyclodex-β,2-,3-,6-methylated, 30 m×0.25 mm (i.d.)). Elemental analysis was carried out on a Fisous EA 1110. All melting points were measured in single sealed tubes. Racemic samples of alcohols were obtained by reduction of the corresponding ketones with $NaBH_4$ and used as the authentic samples for e.e. determination. Column chromatography was carried out on silica gel (200–300 mesh) using ethyl acetate/petroleum ether as eluent. Unless otherwise mentioned, all reactions were carried out under an argon atmosphere. (*R*)-1-[(*S*)-2-(Diphenylphosphino)-ferrocenyl]ethylamine[(R,S_{Fc})-$PPFNH_2$] was synthesized according to the literature method.[29]

4.2. General procedure for preparation of ligands 2a–j

A mixture of salicylaldehyde (140 mg, 1.1 mmol), [(R,S_{Fc})-$PPFNH_2$] (413 mg, 1.0 mmol) and $MgSO_4$ (500 mg, 4.2 mmol) in absolute ethanol was stirred under reflux for 2 h. The solid was filtered off and the resulting orange solution was evaporated to dryness under reduced pressure. The residue was recrystallized from *n*-hexane to afford **2a** (475 mg, 91.8%) as an orange crystal. Similar procedure was employed for the synthesis of ligands **2b–j** using the corresponding salicylaldehydes.

2a: Orange crystals; mp: 106–107°C; $[\alpha]_D^{20}$ −48.7 (*c* 0.61, $CHCl_3$); ^1H NMR (DMSO-d^6) δ 1.68 (d, $J=8.0$ Hz, 3H), 3.73 (s, 1H), 4.06 (s, 5H), 4.32 (s, 1H), 4.58 (s, 1H), 4.71 (m, 1H), 6.59–7.51 (m, 14H), 8.87 (s, 1H), 13.13 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −23.78. Anal. calcd for $C_{31}H_{28}FeNOP$: C, 71.95; H, 5.41; N, 2.71. Found: C, 71.75; H, 5.45; N, 2.76.

2a-[(R,R_{Fc})-type]: Orange crystals; 82% yield; mp: 102–103°C; $[\alpha]_D^{20}$ +46.2 (*c* 0.61, $CHCl_3$); ^1H NMR (DMSO-d^6) δ 1.68 (d, $J=8.0$ Hz, 3H), 3.71 (s, 1H), 4.11 (s, 5H), 4.36 (s, 1H), 4.62 (s, 1H), 4.76 (m, 1H), 6.61–7.58 (m, 14H), 8.92 (s, 1H), 13.10 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −23.62. Anal. calcd for $C_{31}H_{28}FeNOP$: C, 71.95; H, 5.41; N, 2.71. Found: C, 71.73; H, 5.42; N, 2.75.

2b: Yellow powder; 73% yield; mp: 111–112°C; $[\alpha]_D^{20}$ −45.8 (*c* 0.12, $CHCl_3$); ^1H NMR (DMSO-d^6) δ 1.22 (s, 3H), 1.64 (d, $J=6.8$ Hz, 3H), 3.34 (s, 1H), 4.09 (s, 5H), 4.39 (s, 1H), 4.62 (s, 1H), 4.77 (m, 1H), 6.60–7.49 (m, 13H), 8.05 (s, 1H), 13.01 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −26.38. Anal. calcd for $C_{32}H_{30}FeNOP$: C, 72.32; H, 5.65; N, 2.64. Found: C, 72.18; H, 5.47; N, 2.82.

2c: Orange crystals; 75% yield; mp: 115–117°C; $[\alpha]_D^{20}$ −43.6 (*c* 0.21, $CHCl_3$); ^1H NMR (DMSO-d^6) δ 1.64 (d, $J=8.2$ Hz, 3H), 3.34 (s, 1H), 4.09 (s, 5H), 4.37 (s, 1H), 4.45 (s, 1H), 4.71 (m, 1H), 6.60–7.49 (m, 13H), 8.05 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −26.41. Anal. calcd for $C_{31}H_{27}FFeNOP$: C, 69.53; H, 5.05; N, 2.61. Found: C, 69.72; H, 5.11; N, 2.58.

2d: Orange crystals; 85% yield; mp: 119–120°C; $[\alpha]_D^{20}$ −40.3 (*c* 0.17, $CHCl_3$); ^1H NMR (DMSO-d^6) δ 1.67 (d, $J=8.0$ Hz, 3H), 3.77 (s, 1H), 4.09 (s, 5H), 4.17 (s, 1H), 4.35 (s, 1H), 4.59 (m, 1H), 6.43–7.75 (m, 13H), 9.98 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −25.14; Anal. calcd for $C_{31}H_{27}ClFeNOP$: C, 67.45; H, 4.89; N, 2.54. Found: C, 67.17; H, 5.08; N, 2.65.

2e: Orange crystals; 87% yield; mp: 125–127°C; $[\alpha]_D^{20}$ −44.5 (*c* 0.20, $CHCl_3$); ^1H NMR (DMSO-d^6) δ 1.68 (d, $J=8.4$ Hz, 3H), 3.75 (s, 1H), 4.07 (s, 5H), 4.25(s, 1H), 4.57 (s, 1H), 4.75 (m, 1H3), 6.61–7.76 (m, 13H), 13.16 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −24.43. Anal. calcd for $C_{31}H_{27}BrFeNOP$: C, 62.42; H, 4.53; N, 2.35. Found: C, 62.40; H, 4.56; N, 2.37.

2f: Red powder; 88% yield; mp: 180°C (dec); $[\alpha]_D^{20}$ −98.1 (*c* 0.15, $CHCl_3$); ^1H NMR (DMSO-d^6) δ 1.87 (d, $J=8.4$

Hz, 3H), 3.72 (s, 1H), 4.12 (s, 5H), 4.49 (s, 1H), 4.52 (s, 1H), 4.62 (m, 1H), 6.80–7.62 (m, 12H), 8.83 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −26.48; Anal. calcd for $C_{31}H_{26}FeN_3O_5P$: C, 61.28; H, 4.28; N, 6.92. Found: C, 61.18; H, 4.15; N, 6.78.

2f-[(R,R_{Fc})-type]: Red crystals; 80% yield; mp: 186–187°C (dec); $[\alpha]_D^{20}$ +95.6 (c 0.15, $CHCl_3$); ^{1}H NMR (DMSO-d^6) δ 1.67 (d, J=8.0 Hz, 3H), 3.68 (s, 1H), 4.16 (s, 5H), 4.42 (s, 1H), 4.58 (s, 1H), 4.66 (m, 1H), 6.68–7.52 (m, 12H), 8.96 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −26.22; Anal. calcd for $C_{31}H_{26}FeN_3O_5P$: C, 61.28; H, 4.28; N, 6.92. Found: C, 61.18; H, 4.15; N, 6.78.

2g: Orange crystals; 81% yield; mp: 166–168°C; $[\alpha]_D^{20}$ −42.8 (c 0.12, $CHCl_3$); ^{1}H NMR (DMSO-d^6) δ 1.67 (d, J=7.8 Hz, 3H), 3.78 (s, 1H), 4.09 (s, 5H), 4.32 (s, 1H), 4.58 (s, 1H), 4.85 (m, 1H), 6.39–7.69 (m, 12H), 14.37 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −24.85. Anal. calcd for $C_{31}H_{26}Cl_2FeNOP$: C, 63.48; H, 4.44; N, 2.39. Found: C, 63.46; H, 4.42; N, 2.36.

2h: Orange crystals; 80% yield; mp: 178–179°C; $[\alpha]_D^{20}$ −43.7 (c 0.11, $CHCl_3$); ^{1}H NMR (DMSO-d^6) δ 1.69 (d, J=8.0 Hz, 3H), 3.78 (s, 1H), 4.10 (s, 5H), 4.24 (s, 1H), 4.35 (s, 1H), 4.67 (m, 1H), 6.54–7.69 (m, 12H), 14.35 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −24.90. Anal. calcd for $C_{31}H_{26}Br_2FeNOP$: C, 55.11; H, 3.85; N, 2.07. Found: C, 55.32; H, 3.67; N, 2.18.

2i: Orange crystals; 72% yield; mp: 119–121°C; $[\alpha]_D^{20}$ −44.7 (c 0.22, $CHCl_3$); ^{1}H NMR (DMSO-d^6) δ 1.24 (s, 3H), 1.37 (s, 9H), 1.64 (d, J=8.0 Hz, 3H), 3.81 (s, 1H), 4.10 (s, 5H), 4.39 (s, 1H), 4.51 (s, 1H), 4.62 (m, 1H), 6.60–7.49 (m, 12H), 8.05 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −25.47. Anal. calcd for $C_{36}H_{38}FeNOP$: C, 73.59; H, 6.47; N, 2.39. Found: C, 73.47; H, 6.25; N, 2.18.

2j: Orange crystals; 71% yield; mp: 164–166°C; $[\alpha]_D^{20}$ −52.7 (c 0.15, $CHCl_3$); ^{1}H NMR (DMSO-d^6) δ 1.41 (s, 9H), δ 1.69 (d, J=10.7 Hz, 3H), 3.74 (s, 1H), 4.08 (s, 5H), 4.32 (s, 1H), 4.45 (s, 1H), 4.68 (m, 1H), 6.25–7.87 (m, 12H), 13.27 (s, 1H); ^{31}P NMR (DMSO-d^6) δ −23.78. Anal. calcd for $C_{35}H_{35}FeN_2O_3P$: C, 67.96; H, 5.66; N, 4.53. Found: C, 67.72; H, 5.48; N, 4.55.

4.3. General procedure for the ruthenium catalyzed transfer hydrogenation with 2-propanol

The catalyst was generated in situ by refluxing ligand **2** (2.0 mol%) with $Ru(DMSO)_4Cl_2$ (1.0 mol%) in 2-propanol at 80°C under argon for 1 h. After cooling down to room temperature, ketone (2.0 mmol) was added, followed by *tert*-BuOK (34 mg, 0.3 mmol) under argon. The transfer hydrogenation was conducted at the desired temperature under argon for the time indicated (monitored by GC). The resulting solution was quenched with 1 M HCl and the organic phase was concentrated in vacuo. The residue was purified by flash chromatography on a silica gel column eluted by petroleum ether/ethyl acetate (9/1).

Acknowledgements

This work was supported by the National Science Foundation of China (29933050).

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