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# Transfer Hydrogenation of Activated C=C Bonds Catalyzed by Ruthenium Amido Complexes: Reaction Scope, Limitation, and Enantioselectivity

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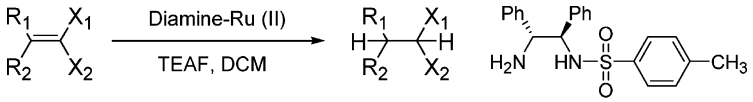


$R_1$, $R_2$ = H, alkyl, aryl; $X_1$, $X_2$ = functional groups

**2a** (*R*,*R*)-TsDPEN

It was found that the chemoselectivity could be completely switched from C=O to C=C bonds in the transfer hydrogenation of activated α,*β*-unsaturated ketones catalyzed by diamine−ruthenium complex. Moreover, this addition via metal hydride had been applied to the reduction of various activated olefins. The electron-withdrawing ability of functional groups substituted on C=C bonds at the α- or *β*-position had strong influence on the reactivity. In addition, a wide variety of chiral diamine−Ru(II)−(arene) systems was investigated to explore the asymmetric transfer hydrogenation of prochiral α,α-dicyanoolefins. Two parameters had been systematically studied, (i) the structure of the *N*-sulfonylated chiral diamine ligands, in which several chiral diamines substituted on the benzene ring of DPEN were first reported, and (ii) the structure of the metal precursors, and high enantioselectivitiy (up to 89% ee) at the *β*-carbon was obtained.

## Introduction

The reduction of C=C double bonds is one of the most fundamental synthetic transformations and plays a key role in the manufacturing of a wide variety of bulk and fine chemicals. Hydrogenation of olefins can be achieved readily with molecular hydrogen in many cases, but transfer hydrogenation methods using suitable donor molecules such as formic acid or alcohols are receiving increasing attention as possible synthetic alternatives as they require no special equipment and avoid the handling of potentially hazardous gaseous hydrogen.[1] Highly stereoselective methods have emerged from transfer hydrogenation techniques based on the use of suitable chiral transition metal complexes in homogeneous solution.[2] Especially, chiral phosphine−rhodium complexes have proven effective for transfer hydrogenation of C=C double bonds.[3] Recently, Noyori has achieved highly enantioselective transfer hydrogenation of ketones and imines by using chiral TsDPEN−Ru(II) catalysts[4] and proposes a concerted mechanism of hydrogen transfer involving metal-to-ligand "bifunctional" hydrogen activation.[5,6] *Besides this, another notable feature of these catalysts is that the transfer hydrogenation reaction is highly chemoselective for the C=O function and tolerant of alkenes.*[4b,6] Excellent results have been obtained in the kinetic

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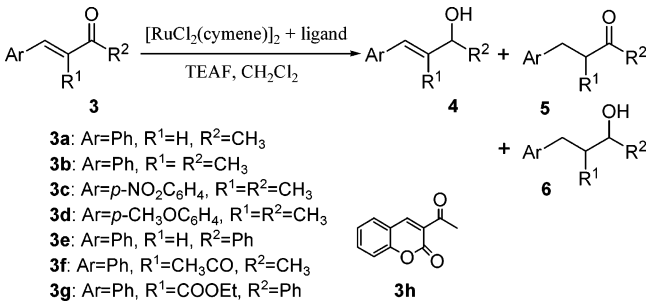
**TABLE 1. Switched Chemoselectivity in Transfer Hydrogenation of α,β-Unsaturated Ketones**[a]




| entry | substrate | ligand | *T* (h) | product | yield (%)[b]/ ee (%) |
|---|---|---|---|---|---|
| 1 | 3a | 1 | 30 | 4a | 90 |
| 2 | 3a | 2a | 28 | 4a | 89/39[c] |
| 3 | 3b | 2a | 45 | 4b | 85/76[c] |
| 4 | 3c | 2a | 52 | 4c | 98/38[c] |
| 5 | 3d | 2a | 72 | 4d | 61/69[c] |
| 6 | 3e | 2a | 48 | 5e | 75 |
| | | | | 6e | 23/93[c] |
| 7 | 3f | 1 | 5.5 | 5f | 90 |
| 8 | 3g | 1 | 9 | 5g | 94 |
| 9 | 3h | 1 | 2 | 5h | 91 |

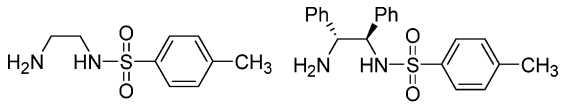
[a] The ligand and Ru precursor were initially heated in methanol. Reactions were conducted at 30 °C in 0.5 mL of $CH_2Cl_2$, S/C = 200. [b] Isolated yield. [c] Percent ee was determined by HPLC on a chiral column.

resolution of allylic alcohols using acetone as hydrogen acceptor.[7] Moreover, α,β-acetylenic ketones were also selectively reduced to give chiral propargylic alcohols in excellent enantioselectivity.[8] On the contrary, in our continuous study on transfer hydrogenation reactions catalyzed by these coordinately saturated monosulfonylated diamine−Ru(II) complexes,[9] we found that the chemoselectivity could be completely switched from C=O to C=C bonds through further polarization of the olefins.[10]

## Results and Discussion

Table 1 shows the representative results for the transfer hydrogenation of various α,β-unsaturated ketones **3** catalyzed by ruthenium complexes [$RuCl_2$(cymeme)]$_2$−TsEN [**1**, TsEN = *N*-(*p*-toluenesulfonyl)-1,2-ethylenediamine] and [$RuCl_2$(cymeme)]$_2$−(*R,R*)-TsDPEN

**SCHEME 1**




[**2a**, TsDPEN = *N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine] (Scheme 1), using the azeotrope of formic acid and triethylamine (5:2) as hydrogen source under established conditions.[4,9] Like the kinetic resolution of allylic alcohols reported early,[7] for simple enones **3a**−**d** (Table 1, entries 1−5), the only detected reduction products were the corresponding allylic alcohols **4a**−**d** with low to moderate enantioselectivities when chiral ligand **2a** was used (entries 2−5). When chalcone **3e** was employed (entry 6), however, saturated ketone **5e** and alcohol **6e** were isolated.[11] We inferred that the switched chemoselectivity was due to the further activation of the C=C bond by the benzene ring, so introduction of an electron-withdrawing group at the α-position would strengthen this effect.[12] We were pleased to find that the activated olefins **3f**−**h** displayed much higher reactivity toward the C=C bond in the presence of the diamine−Ru(II) complex. The chemoselectivity was indeed completely switched from C=O to C=C bonds in the transfer hydrogenation of these activated enones (entries 7−9), and saturated ketones **5f**−**h** were isolated in excellent yields in much shorter time. In the $^1$H and $^{13}$C NMR spectra (see Supporting Information), partial and complete enolization of resulted ketones **5f** and **5h** was observed, and the α-H of **5g** could be partially deuterated with $D_2O$ in the presence of triethylamine. Thus, asymmetric transfer hydrogenation of **3g** and **3h** was not further investigated.

While having discovered that diamine−Ru(II) complexes had high catalytic activity in the transfer hydrogenation of activated olefins, a series of activated α,β-unsaturated substrates was employed to investigate the reaction scope using achiral catalyst **1**−Ru(II). The results are summarized in Table 2, which showed that this reaction could be successfully extended to a wide range of activated olefins and C=C-bond-reduced products **8** were isolated in excellent yields, *suggesting a potential synthetic application of this catalyst system for reduction of activated olefins under mild conditions*.[13] The electron-withdrawing ability of functional groups substituted on C=C bonds had strong influence on the reactivity. **7a** and **7b** (entries 1 and 2) had different reactivity owing to different electron-withdrawing power of COOMe (Hammett substituent parameter $\sigma = 0.45$) and $NO_2$ ($\sigma = 0.78$).[14] For the substrates condensed from aromatic, aliphatic aldehydes and ketones with various 1,3-

(6) Hydrogenation catalysts Noyori's Binap/1,2-diamine−Ru(II) and hydroxycyclopentadienylruthenium hydride are also proposed to react with a similar mechanism and show high chemoselectivity for carbonyl over olefins, see: (a) Sandoval, C. A.; Ohkuma, T.; Muñiz, K.; Noyori, R. *J. Am. Chem. Soc.* **2003**, *125*, 13490. (b) Abdur-Rashid, K.; Clapham, S. E.; Hadzovic, A.; Harvey, J. N.; Lough, A. J.; Morris, R. H. *J. Am. Chem. Soc.* **2002**, *124*, 15104 and references therein. (c) Casey, C. P.; Singer, S. W.; Powell, D. R.; Hayashi, R. K.; Kavana, M. *J. Am. Chem. Soc.* **2001**, *123*, 1090. (d) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40.

(7) Hashiguchi, S.; Fujii, A.; Haack, K.-J.; Matsumura, K.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed*. **1997**, *36*, 288.

(8) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc*. **1997**, *119*, 8738.

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(10) For primary communication, see: Chen, Y.-C.; Xue, D.; Deng, J.-G.; Cui, X.; Zhu, J.; Jiang, Y.-Z. *Tetrahedron Lett*. **2004**, *45*, 1555.

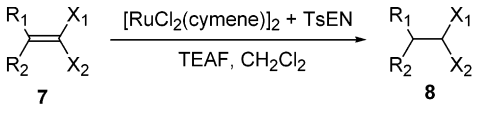
(11) Recently Wills reported that chalcone was reduced with TsDPEN−ruthenium complex to give saturated ketone in low yield, see: Hannedouche, J.; Kenny, J. A.; Walsgrove, T.; Wills, M. *Synlett* **2002**, 263.

(12) The theoretical calculation by Noyori predicts that the reactivity of unsaturated compounds toward the Ru hydride depends on the polarity of the double bonds and, by a concerted mechanism, ethylene possesses much higher activation energy and also is entropically much less favorable. See ref 5d.

(13) For a recent example of reducing the activated olefins using indium metal, see: Ranu, B. C.; Dutta, J.; Guchhait, S. K.*Org. Lett*. **2001**, *3*, 2603.

(14) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

**TABLE 2. Transfer Hydrogenation of Activated Olefins Catalyzed by TsEN−Ru(II) Complex[a]**




7 8

**7a** : $R_1$=H, $R_2$=Ph, $X_1$=COOMe, $X_2$ =H
**7b** : $R_1$=H, $R_2$=Ph, $X_1$=$NO_2$, $X_2$ =H
**7c** : $R_1$=H, $R_2$=Ph, $X_1$=Ph, $X_2$ =$NO_2$
**7d** : $R_1$=H, $R_2$=Ph, $X_1$=*p*-$ClC_6H_5$, $X_2$ =CN
**7e** : $R_1$=H, $R_2$=Ph, $X_1$=COOMe, $X_2$ =COOMe
**7f** : $R_1$=H, $R_2$=Ph, $X_1$=COOEt, $X_2$ =CN
**7g** : $R_1$=H, $R_2$=Ph, $X_1$=COOEt, $X_2$ =$NO_2$
**7h** : $R_1$=H, $R_2$=*p*-$NO_2C_6H_4$, $X_1$=COOEt, $X_2$ =CN
**7i** : $R_1$=H, $R_2$=*p*-$CH_3OC_6H_4$, $X_1$=COOEt, $X_2$ =CN
**7j** : $R_1$=H, $R_2$=*n*-$C_5H_{11}$, $X_1$=COOEt, $X_2$ =CN
**7k** : $R_1$=H, $R_2$=Ph, $X_1$=CN, $X_2$ =CN
**7l** : $R_1$=H, $R_2$=Ph, $X_1$=COOMe, $X_2$ =NHAc
**7m** : $R_1$=H, $R_2$=H, $X_1$=Ph, $X_2$ =COOH
**7n** : $R_1$=H, $R_2$=H, $X_1$=Ph, $X_2$ =COOEt
**7o** : $R_1$=H, $R_2$=PhCH=CH, $X_1$=CN, $X_2$ =CN
**7p** : $R_1$=H, $R_2$=2-Py, $X_1$=COOEt, $X_2$ =CN
**7q** : $R_1$=$CH_3$, $R_2$=Ph, $X_1$=COOMe, $X_2$ =COOMe
**7r** : $R_1$=$CH_3$, $R_2$=Ph, $X_1$=CN, $X_2$ =CN
**7s** : $R_1$=$CH_3$, $R_2$=Ph, $X_1$=COOEt, $X_2$ =CN

| entry | substrate | *T* (h) | yield (%)[b] | entry | substrate | *T* (h) | yield (%)[b] |
|---|---|---|---|---|---|---|---|
| 1 | 7a | 24 | NR[c] | 11 | 7k | 2 | 99 |
| 2 | 7b | 4 | 89 | 12 | 7l | 24 | NR[c,15] |
| 3 | 7c | 4.5 | 99 | 13 | 7m | 2 | 97 |
| 4 | 7d | 13 | 98 | 14 | 7n | 5 | 98 |
| 5 | 7e | 5 | 99 | 15 | 7o | 2 | d |
| 6 | 7f | 2 | 99 | 16 | 7p | 2 | d |
| 7 | 7g | 4 | 87 | 17 | 7q | 24 | NR[c,15] |
| 8 | 7h | 2 | 99 | 18 | 7r | 2 | 93 |
| 9 | 7i | 2 | 99 | 19 | 7s | 24 | NR[c,15] |
| 10 | 7j | 2 | 83 | | | | |

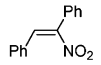
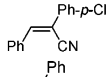
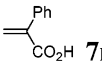
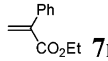
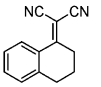
[a] The ligand and Ru precursor were initially heated in methanol. Reactions were conducted at 30 °C in 0.5 mL of $CH_2Cl_2$, S/C = 200. [b] Isolated yield. [c] No reaction. [d] A complicate mixture was obtained.

bifunctional compounds, the reactivity of the substrate reflected the polarity of double bonds. α-(Acetylamino) acrylate **7l**[15] (entry 12) was totally inactive under the same conditions, probably due to the weak electron-withdrawing effect of the acetylamino group ($\sigma = 0.00$).[14] Conjugate olefin **7o**[16] (entry 15) and heteroaromatic substrate **7p** (entry 16) gave complicate mixtures. The substituent on the C=C bond at the $\beta$-position also had subtle effects on the reactivity. α,$\beta$-Unsaturated carboxylic acid **7m** and its ester **7n**, which are unsubstituted at the $\beta$-position, had high reactivity (entries 13 and 14). On the other hand, **7q** and **7s**, which are the $\beta$-methyl analogue of **7e** and **7f**, respectively, were inactive even at higher temperature, owing to the electron-donating effect of $CH_3$ ($\sigma = -0.17$)[14] (entry 17 vs 5 and 19 vs 6). While **7r**, the $\beta$-methyl analogue of **7k**, was reduced within 2 h due to the strong electron-withdrawing ability of the di-CN substituents ($\sigma = 0.66$),[14] which made the kinetic barrier to attack the double bond easier to overcome (entry 18 vs 11). Interestingly, in the case of

(15) No reaction was found in $CH_3OH$, $(CH_3)_2COH$, or DMSO, and no product was determined even in DMF at refluxing temperature.

(16) Recently the selective reduction of the α,$\beta$-C=C double bond by $InCl_3$−$NaBH_4$ was reported, see: Ranu, B. C.; Samanta, S. *J. Org. Chem.* **2003**, *68*, 7130.

**TABLE 3. Asymmetric Transfer Hydrogenation of Prochiral Activated Olefins Catalyzed by (*R*,*R*)-TsDPEN−Ru(II) Complex[a]**

| Entry | Substrate | T (h) | Yield (%)[b] | Ee (%)[c] |
|---|---|---|---|---|
| 1 |  **7c** | 4 | 96 | 0 |
| 2 |  **7d** | 13 | 99 | 0 |
| 3 |  **7m** | 2 | 97 | 7 |
| 4 |  **7n** | 5 | 98 | 20 |
| 5 |  **7r** | 2 | 94 | 49 |
| 6 |  **10a** | 4 | 98 | 54 |

[a] The ligand and $[RuCl_2(cymene)]_2$ were initially heated in methanol. Reaction was conducted in 0.5 M of DCM solution, S/C = 100. [b] Isolated yield. [c] Percent ee was determined by HPLC on chiral column.

the highly active substrate **7k**, simple $[RuCl_2(cymene)]_2$ without ligand could also catalyze the transfer hydrogenation but at a much lower rate.[17] Nevertheless, an experiment with **7k** in 2-propanol catalyzed by TsEN−Ru(II) revealed that 2-propanol cannot serve as a successful hydrogen source.

Since several types of α- and $\beta$-prochiral olefins could be successfully reduced with diamine−Ru(II) complex as catalyst, we investigated the potential application of this methodology for the asymmetric reduction of prochiral olefins. Complete racemic products were obtained for the transfer hydrogenation of α-prochiral olefins **7c** and **7d** (Table 3, entries 1 and 2) catalyzed by (*R*,*R*)-TsDPEN−Ru(II) complex,[18] which is a good catalyst for the asymmetric transfer hydrogenation of ketones and imines.[2a] Moreover, only low enantioselectivity was generated in the reduction of α-phenylacrylic acid **7m** and its ester **7n** (entries 3 and 4). On the other hand, moderate enantioselectivity (49% ee, entry 5) could be obtained in the asymmetric reduction of $\beta$-prochiral 1-phenylethylidenemalononitrile **7r**[19] with the same catalyst. The cyclic 1,2,3,4-tetrahydro-1-naphthylidenemalononitrile **10a** gave higher enantioselectivity (54% ee, entry 6). Thus, the olefin **10a** was used as the model substrate for the optimization of the asymmetric catalytic conditions.

Solvents were found to have mild effects on the enantioselectivity, while the best results were obtained in THF.[10] Then, a wide variety of diamine(arene)−Ru(II) systems was investigated to explore the effects on

(17) When $[RuCl_2(cymene)]_2$ alone was used as catalyst, 7% and 65% conversions were obtained in 2 and 24 h, respectively, under the same conditions.

(18) The α-H of **8f** and **8k** is highly active and could be completely deuterated with $D_2O$ catalyzed by triethylamine, while no deuterium incorporation was observed for **8c** and **8d** under same conditions, and this implies that the racemic products were not produced from the racemization of the α-carbon of **8c** and **8d**.

(19) For previous work on reduction of **7r** with NADH model compounds, see: (a) Ohno, A.; Ikeguchi, M.; Kimura, T.; Oka, S. *J. Am. Chem. Soc.* **1979**, *101*, 7036. (b) Seki, M.; Baba, N.; Oda, J.; Inouye, Y. *J. Org. Chem.* **1983**, *48*, 1370. (c) Zhang, B.-L.; Zhu, X.-Q.; Lu, J.-Y.; He, J.-Q.; Wang, P. G.; Cheng, J.-P. *J. Org. Chem.* **2003**, *68*, 3295.

**SCHEME 2**

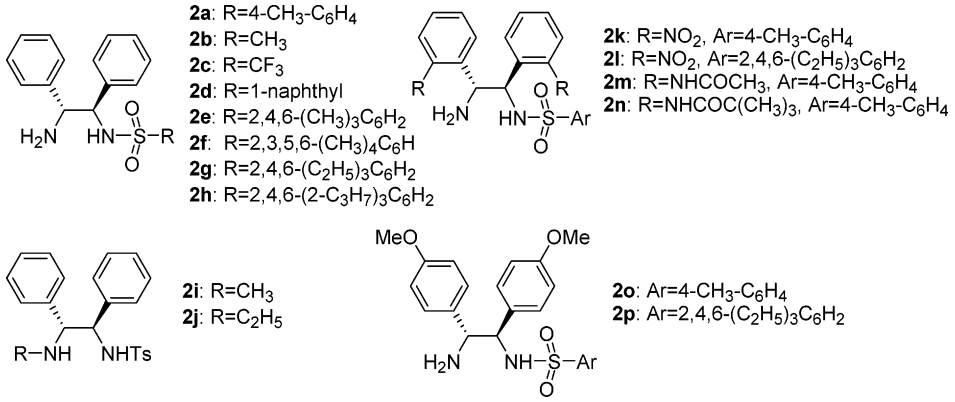
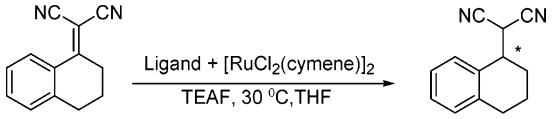



**TABLE 4. Catalytic Effects of the *N*-Sulfonylated Chiral Diamine Ligands**[a]



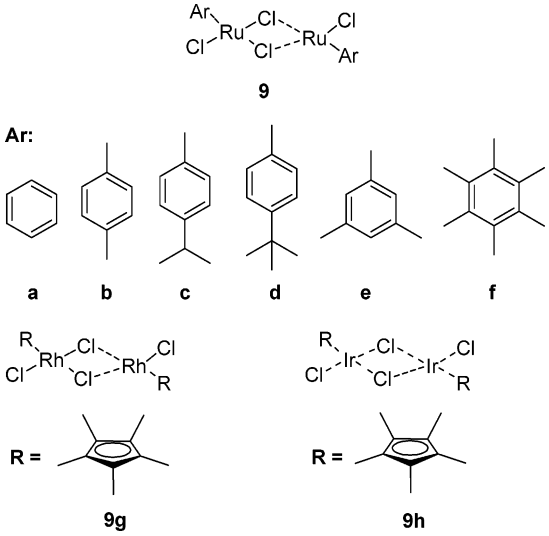

| entry | ligand | *T* (h) | yield (%)[b] | ee (%)[c] | entry | ligand | *T* (h) | yield (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 2a | 4 | 98 | 61 | 9 | 2i | 3.5 | 97 | 52 |
| 2 | 2b | 3 | 98 | 32 | 10 | 2j | 10 | 96 | 47 |
| 3 | 2c | 6 | 93 | 71 | 11 | 2k | 4 | 93 | 60 |
| 4 | 2d | 6 | 96 | 81 | 12 | 2l | 4 | 98 | 75 |
| 5 | 2e | 3.5 | 98 | 84 | 13 | 2m | 4 | 90 | 58 |
| 6 | 2f | 4 | 98 | 84 | 14 | 2n | 4 | 85 | 53 |
| 7 | 2g | 4 | 99 | 85 | 15 | 2o | 2 | 88 | 66 |
| 8[d] | 2h | 4 | 97 | 81 | 16 | 2p | 4 | 85 | 85 |

[a] The ligand and Ru precursor were initially heated in THF at 65 °C for 2 h, S/C = 100. [b] Isolated yield. [c] Percent ee was determined by HPLC on chiral OD column. [d] Ligand and Ru precursor were previously heated in 2-propanol at 85 °C.

the enantioselectivity and the catalytic activity. Two parameters have been systematically studied: (i) the structure of the *N*-sulfonylated chiral diamine ligands and (ii) the structure of the metal precursors.

For the promotion of the enantioselectivity, we fine-tuned the substitution on the *N*-sulfonylated chiral diamine ligands (Scheme 2), and Table 4 shows the representative results. While electron-withdrawing triflate ligand **2c** slightly increased the enantioselectivity (entry 3, 71% ee), 1-Naphthysulfonyl-DPEN gave a much better result (entry 4, 81% ee). When more bulky 2,4,6-mesitylenesulfonyl-DPEN was used, the enantioselectivity was increased to 84% ee with high catalytic activity (entry 5). Through fine-tuning of the substituents on the benzene ring of *N*-sulfonyl group, the highest enantioseletivity (85% ee) was achieved while 2,4,6-triethylbenzenesulfonyl-DPEN was used (entry 7). Monoalkylation of the $NH_2$ group on TsDPEN decreased both enantioselectivity and activity (entries 9 and 10). On the other hand, though 1,2-diphenylethylenediamine is an important chiral ligand in asymmetric transfer hydrogenation,[2a,b] up to now, there was scarce literature references[20] reported the effect of substituents on the benzene ring of DPEN on asymmetric transfer hydrogenation. Here, we synthesized a series of phenyl-substituted chiral 1,2-diphenylethylenediamines and studied the effect on the

**SCHEME 3**

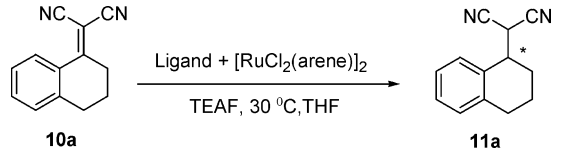



enantioselectivity and reactivity for the reduction of activated olefins. When a $NO_2$ group was introduced at the ortho-position of phenyl groups of DPEN, it had little effects on the enantioselectivity and activity (entry 11), and moderate enantioselectivity (75%) was obtained while bulky *N*-sulfonylated ligand **2l** was used (entry 12). The introduction of an amido group on the benzene rings decreased the enantioselectivity (entries 13 and 14). It was noted that the introduction of a methoxy group at the para-position of the phenyl groups gave higher enantioselectivity compared with TsDPEN **2a** (entry 15 vs 1), while the bulky 2,4,6-triethylbenzene-sulfonylated ligand **2p** gave similar results compared with ligand **2g** (entry 16 vs 7).

Preliminary observation revealed that substituent on the Ru−arene ring may also have a significant influence on the performance of the catalyst system. This effect was investigated by in situ combination of 2 equiv of *N*-arylsulfonyl-DPEN and $[RuCl_2(arene)]_2$ precursor (Scheme 3). The Ru(II) dimers were easily prepared by reaction of $RuCl_3 \cdot 3H_2O$ with 1,4-dienes,[21] which are available by Birch reduction of the corresponding arenes. Table 5

(20) For the diamines substituted on the benzene ring of DPEN, see: (a) Ma, Y.-P.; Liu, H.; Cui, X.; Zhu, J.; Deng, J.-G. *Org. Lett.* **2003**, *5*, 2013. (b) Itsuno, S.; Tsuji, A.; Takahashi, M. *Tetrahedron Lett.* **2003**, *44*, 3825. (c) Li, X.; Chen, W. P.; Hems, W.; King, F.; Xiao, J. *Tetrahedron Lett.* **2004**, *45*, 951. (d) Li, X.; Wu, X.; Chen, W.; Hancock, F. E.; King, F.; Xiao, J. *Org. Lett.* **2004**, *6*, 3321.

**TABLE 5. Catalytic Effect of Metal Precursor[a]**




| entry | ligand | metal precursor | $T$ (h) | yield (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|
| 1 | 2g | 9a | 3 | 91 | 35 |
| 2 | 2g | 9b | 4 | 94 | 80 |
| 3 | 2g | 9c | 4 | 98 | 85 |
| 4 | 2g | 9d | 7 | 84 | 72 |
| 5 | 2a | 9e | 5 | NR[d] | |
| 6 | 2a | 9f | 10 | NR[d] | |
| 7 | 2f | 9b | 4 | 98 | 80 |
| 8 | 2d | 9b | 4 | 98 | 82 |
| 9 | 2a | 9g | 1 | 91 | 0 |
| 10 | 2a | 9h | 10 | NR[d] | |

[a] The ligand and Ru precursor were initially heated in THF at 65 °C for 2 h, S/C = 100. [b] Isolated yield. [c] Percent ee was determined by HPLC on chiral column. [d] No reaction.

showed the representative results. When $[RuCl_2(benzene)]_2$ was used, low enantioselectivity was obtained (entry 1), while the introduction of substitutes on the benzene ring gave much higher enantioselectivities (entries 2−4). The highest enantioselectivity was obtained when $[RuCl_2(cymene)]_2$−**2g** was used (entry 3). It was surprising that the combination of $[RuCl_2(mesitylene)]_2$ or $[RuCl_2(HMB)]_2$ and **2a** could not catalyze the reaction (entries 5 and 6) owing to the different electronic properties of the arene ligands. In addition, Rh−amido complex could catalyze this reaction with high reactivity but no enantioselectivity (entry 9). However, the Ir−amido complex was inactive in this reaction (entry 10).

According to above investigation, we found that the best catalytic system was the combination of ligand **2g** and metal precursor $[RuCl_2(cymene)]_2$ (**9c**). The reaction scope was assessed with various substrates **7r** and **10a**−**j** as described in Scheme 4. As noted in Table 6, all substrates were rapidly reduced within 5 h, and high isolated yields were obtained. Activated olefins **10c**−**e** condensed from chromanones and malononitrile were reduced with high enantioselectivity (entries 3−6). Unlike the transfer hydrogenation of aromatic ketones, the substituent on the arene ring had little effect on the reactivity, and a slightly higher enantioselectivity was obtained for **10e** with an electron-donating substituent. A similar result was seen in the reduction of **10e**, when the crowded ligand **2h**−$[RuCl_2(cymeme)]_2$ complex was used (entry 6). Moreover, it was noticeable that optically pure compound **11e** could be obtained via recrystallization from EtOAc/petroleum ether with 82% overall yield (entry 5). A thiochromanone derivative **10f** was quantitatively reduced with good enantioselectivity (entry 7). Great improvement in enantioselectivity was also observed with **2g** as ligand in comparison to **2a** (73% ee vs 49% ee, entry 8) in the reduction of **7r**, and only low to moderate enantioselectivities were obtained for **10g**−**i** derived from acyclic aromatic ketones and malononitrile (entries 9−11). Substrate **10j** derived from acyclic aliphatic ketone gave low enantioselectivity (27% ee) but high yield (entry 12).

**SCHEME 4**

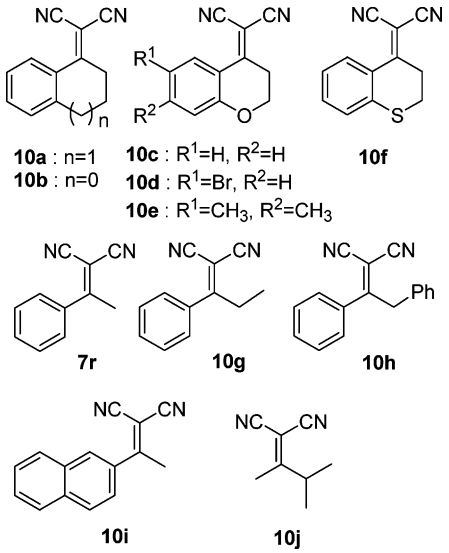



**TABLE 6. Asymmetric Transfer Hydrogenation of Activated Olefins Catalyzed by (*R*,*R*)-2g-$[RuCl_2(cymene)]_2$ Complex[a]**

| entry | substrate | $T$ (h) | yield (%)[b] | ee (%)[c] (rot. sign) |
|---|---|---|---|---|
| 1 | 10a | 4 | 98 | 85 (−) |
| 2 | 10b | 3 | 37 | 58 (−) |
| 3 | 10c | 3 | 96 | 88 (−) |
| 4 | 10d | 3 | 93 | 83 (−) |
| 5 | 10e | 3 | 95 (82)[d] | 89 (99)[d] (−) |
| 6 | 10e[e] | 3 | 94 | 88 (−) |
| 7 | 10f | 4 | 99 | 82 (+) |
| 8 | 7r | 2.5 | 74 | 73 (−, *S*)[f] |
| 9 | 10g | 4 | 82 | 43 (−) |
| 10 | 10h | 4 | 84 | 15 (−) |
| 11 | 10i | 3 | 85 | 59 (−) |
| 12 | 10j | 5 | 95 | 27 (−) |

[a] **2g** and Ru precursor were initially heated in 2-propanol at 85 °C for 2 h. [b] Isolated yield. [c] Percent ee was determined by HPLC on chiral column. [d] After a single recrystallization from EtOAc−petroleum ether (v/v, 1:8). [e] **2h** as the chiral ligand. [f] The absolute configuration was determined by the rotation comparison with literature report.[19a,b]

In regard to the reaction mechanism, the transfer hydrogenation of C=C bond catalyzed by chiral rhodium phosphine complexes with formic acid as hydrogen source has been studied in detail by Brunner and co-workers.[22] But there were few reports on ruthenium−phosphine complexes[23] and ruthenium−nitrogen complexes. Recently, Ikariya and co-workers reported mechanistic aspects of the formation of chiral ruthenium hydride complexes from 16-electron ruthenium−amido complexes and formic acid.[24] To give some useful information on the mechanism of this reaction, we conducted a series of

(21) Bennett, M. A.; Smith, A. K. *J. Chem. Soc., Dalton Trans.* **1974**, 233.

(22) (a) Lange, S.; Leitner, W. *J. Chem. Soc., Dalton Trans*. **2002**, 752. (b) Leitner, W.; Brown, J. M.; Brunner, H. *J. Am. Chem. Soc.* **1993**, *115*, 152.

(23) For asymmetric reduction of unsatutrated compounds catalyzed by ruthenium−phosphine complexes, see: (a) Brown, J. M.; Brunner, H.; Leitner, W.; Rose, M. *Tetrahedron: Asymmetry* **1991**, *2*, 331. (b) Saburi, M.; Ohnuki, M.; Ogasawara, M.; Takahashi, T.; Uchida, Y. *Tetrahedron Lett.* **1993**, *33*, 5783.

(24) Koike, T.; Ikariya, T. *Adv. Synth. Catal*. **2004**, *346*, 37.

**SCHEME 5. Proposed Mechanism of the Reduction of C=C Bonds**

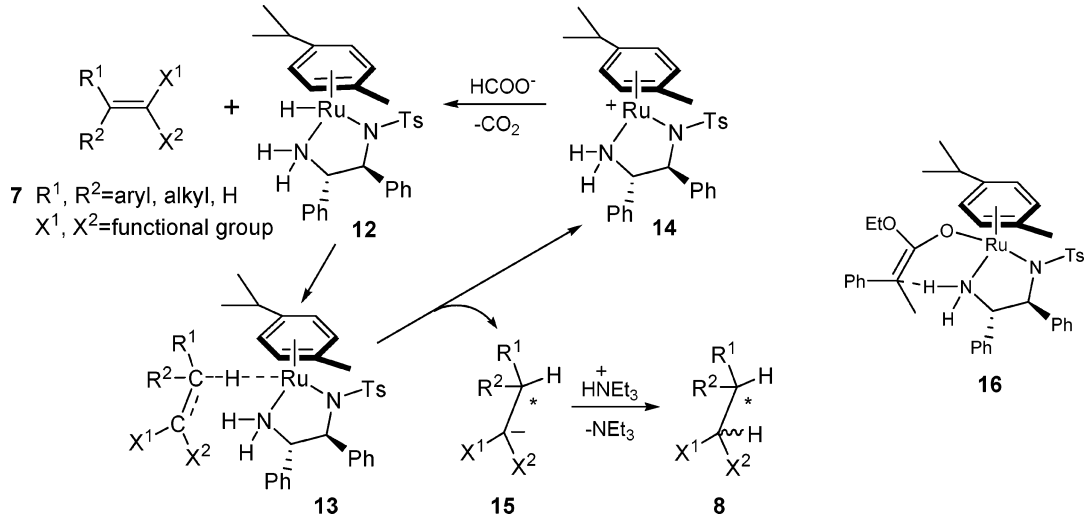
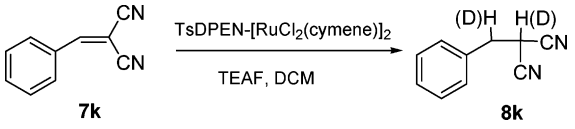



**TABLE 7. Transfer Hydrogenation of 7k with Deuterium-Labeled Formic Acid**[a]




| hydrogen source | | HCOOD | DCOOH | DCOOD |
|---|---|---|---|---|
| relative deuterium distribution[b] | α | 0 | 0 | 0 |
| | β | 0 | 99 | 99 |

[a] 30 °C, 1 M DCM solution, S/C = 100. [b] Determined by $^1$H NMR using mesitylene as internal standard.

deuterium label experiments[25] for the reduction of α,α-dicyanoolefin **7k** with labeled formic acid. The relative deuterium incorporation of substrate was summarized in Table 7.

When formyl-D acid was used, 99% deuterium was labeled on the β-carbon, which provided strong evidence that the hydrogen from the formyl position of formic acid was directly transferred to ruthenium[24] and subsequently the ruthenium hydride attacked the electron-deficient β-carbon of C=C bond. However, no deuterium labeling was observed in the α-position for all formic acids. We speculated that the rapid H−D exchange on the acidic α-H of **8k** in the presence of a base during the workup would account for the phenomena. In fact, it was verified that the α-H of **8k** is highly active and could be completely deuterated with $D_2O$ catalyzed by triethylamine, while no deuterium incorporation could occur in the absence of a base.[18] Therefore, considering the characteristics of activated olefins and the hydridic amido−ruthenium complex (RuH), which is a coordinately saturated complex,[5,24] the reduction of the polarized α,β-unsaturated compounds is proposed to proceed in a stepwise conjugate reduction procedures (Scheme 5),[26] rather than in a concerted mechanism in the transfer hydrogenation of ketones.[5] After a RuH conjugate addition to the β-carbon of the C=C bond (asymmetry generated step), the intermediate **15** might eliminate from the metal complex and subsequently catches another proton rapidly from the excess $NEt_3H^+$ in the reaction mixture.[27] Thus, no asymmetric induction could be generated in the α-carbon center of **8c** and **8d** (Table 3, entries 1 and 2). In the reduction of **7m** and **7n** (Table 3, entries 3 and 4), we consider that a different protonation step might be involved. After a conjugate hydride transfer from the RuH to the β-carbon of the C=C bond, the formation of a chiral ruthenium enolate intermediate **16**[28] may contribute to the generation of low enantioselectivities. An asymmetric protonation of the α-carbon in **16** may preferentially occur from the acidic NH group of TsDPEN via a six-member transition state besides catching a proton from the reaction mixture (Scheme 5).

In conclusion, we demonstrate that the chemoselectivity can be completely switched from C=O to C=C bonds in the transfer hydrogenation of activated α,β-unsaturated ketones catalyzed by the amido−ruthenium hydride complexes. This reaction has been applied to C=C bond reduction of extensively activated α,β-unsaturated compounds, and high enantioselectivity (up to 89% ee) was obtained in the asymmetric transfer hydrogenation of prochiral α,α-dicyanoolefins by screening a variety of ruthenium complexes of arenes and chiral diamines. Moreover, a stepwise conjugate reduction mechanism was

(25) For deuterium labeling experiments on transfer hydrogenation using labeled formic acid as deuterium source, see: (a) Wu, X. F.; Li, X. G.; Hems, W.; King, F.; Xiao, J. L. *Org. Biomol. Chem*. **2004**, 1818. (b) Yu, J.; Spencer, J. B. *Chem. Commun.* **1998**, 1935. (c) Yu, J.; Spencer, J. B. *Chem. Eur. J*. **1999**, *5*, 2237. (d) Tanchoux, N.; de Bellefon, C. *Eur. J. Inorg. Chem.* **2000**, 1495. Also see ref 22.

(26) For selected reports on other metallic hydride mediated asymmetric conjugate reductions, see: (a) Misun, M.; Pfaltz *Helv. Chim. Acta* **1996**, *79*, 961 and references therein. (b) Yamada, T.; Ohtsuka, Y.; Ikeno, T. *Chem. Lett.* **1998**, 1129. (c) Chiu, P.; Szeto, C.-P.; Geng, Z.; Cheng, K.-F. *Org. Lett*. **2001**, *3*, 1901. (d) Kamenecha, T. M.; Overman, L. E.; Ly Sakata, S. K. *Org. Lett*. **2002**, *4*, 79. (e) Zhao, C.-X.; Duffey, M. O.; Taylor, S. J.; Morken, J. P. *Org. Lett*. **2001**, *3*, 1829 and references therein. (f) Jurkauskas V.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 2892 and references therein. (g) Lipshutz, B. H.; Servesko, J. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4789 and references therein. (h) Czekelius, C.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4793.

(27) For hydride transfer as the key step in the hydrogenation of iminium ion catalyzed by a P−P* ruthenium hydride complex, see: (a) Magee, M. P.; Norton, J. R. *J. Am. Chem. Soc*. **2001**, *123*, 1778. (b) Rossen, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 4611.

(28) Ruthenium enolates were also proposed as intermediates in the reports, see: (a) Alvarez, S. G.; Hasegawa, S.; Hirano, M.; Komiya, S. *Tetrahedron Lett.* **1998**, *39*, 5209. (b) Chang, S.; Na, Y.; Choi, E.; Kim, S. *Org. Lett.* **2001**, *3*, 2089. (c) Watanabe, M.; Ikagawa, A.; Wang, H.; Murata, K.; Ikariya, T. *J. Am. Chem. Soc.* **2004**, *126*, 11148 and references therein.

proposed following a deuterium labeled experiment and the results of the asymmetric reductions. It is noticeable that the novel chiral diamines substituted on the benzene ring of DPEN were synthesized and first used in asymmetric transfer hydrogenation.[20] Future work to apply this methodology to other asymmetric reductions of activated olefins is actively in progress.

## Experimental Section

**General Methods.** Melting points were determined in open capillaries and were uncorrected. NMR spectra were recorded with tetramethylsilane as the internal standard. Chiral 1,2-diphenylethylenediamine was produced in our laboratory, $[\alpha]^{20}_D$ = +106.7 (*c* 1.0, methanol, *R*,*R*-isomer). All other reagents were used without purification as commercially available.

**General Procedure for Monosulfonylation of Chiral Ligands.** To a stirred solution of (*R*,*R*)-diamine (1.0 mmol) and DIPEA (0.19 mL, 1.1 mmol) in DCM (10 mL) was added a solution of arylsulfonyl chloride (1.1 mmol) in DCM (5 mL) dropwise at 0 °C. The solution was stirred overnight at room temperature. After washed with water, the solution was dried and concentrated, and flash chromatography (DCM/methanol) gave the monosulfonylated ligand.[29]

**Compound 2f**: yield 75%; mp 140−142 °C; $[\alpha]^{28}_D$ +22.2° (*c* 0.36, $CHCl_3$); $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 7.11−6.87 (m, 11H), 4.41 (d, $J$ = 7.4 Hz, 1H), 4.18 (d, $J$ = 6.9 Hz, 1H), 2.32 (s, 6H), 2.10 (s, 6H) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 141.4, 138.3, 138.1, 135.3, 135.1, 134.6, 128.1, 127.6, 127.3, 127.1, 127.0, 126.6, 63.8, 60.3, 20.8, 17.1 ppm; IR (KBr) 3366, 3307, 3201, 1583, 1451, 1317, 1142, 1009 cm$^{-1}$; HRMS (ESI) calcd for $C_{24}H_{28}N_2O_2S$ + H 409.1949, obsd 409.1942.

**Compound 2g**: yield 78%; mp 128−130 °C; $[\alpha]^{28}_D$ +21.3° (*c* 0.40, $CHCl_3$); $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 7.14−6.89 (m, 10H), 6.74 (s, 2H), 4.37 (d, $J$ = 6.7 Hz, 1H), 4.0 (d, $J$ = 6.7 Hz, 1H), 2.91−2.71 (m, 4H), 2.54 (q, $J$ = 7.5 Hz, 2H), 1.22−1.16 (m, 9H) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 143.1, 140.3, 136.9, 133.9, 128.7, 123.9, 123.4, 123.0, 122.8, 122.7, 122.5, 122.3, 121.9, 121.8, 58.8, 55.9, 23.6, 23.5, 11.8, 10.3 ppm; IR (KBr) 3369, 1967, 1600, 1451, 1340, 1155 cm$^{-1}$; HRMS (ESI) calcd for $C_{26}H_{32}N_2O_2S$ + H 437.2262, obsd 437.2257.

**Compound 2k**: yield 44%; mp 183−185 °C; $[\alpha]^{28}_D$ +32.9° (*c* 0.98, $CH_3OH$); $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 8.06−7.98 (m, 4H), 7.59−7.30(m, 6H), 6.97 (d, $J$ = 8.4 Hz, 2H), 6.22 (br.s, NH), 4.53 (d, $J$ = 4.7 Hz, 1H), 4.33 (d, $J$ = 4.7 Hz, 1H), 2.30 (s, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 148.2, 143.5, 142.8, 141.1, 136.6, 133.2, 132.60, 129.6, 129.6, 129.4, 127.9, 127.3, 126.6, 123.8, 122.8, 121.8, 121.4, 62.2, 59.6, 21.3 ppm; IR (KBr) 3278, 3088, 1597, 1526, 1347, 1157, 1091 cm$^{-1}$; HRMS (ESI) calcd for $C_{21}H_{20}N_4O_6S$ + H 457.1176, obsd 457.1164.

**Compound 2l**: yield 74.5%; mp 174−176 °C; $[\alpha]^{25}_D$ +32.7° (*c* 0.31, $CHCl_3$); $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 8.00−7.80 (m, 4H), 7.47−7.21 (m, 4H), 6.67 (s, 2H), 4.64 (d, $J$ = 7.1 Hz, 1H), 4.30 (d, $J$ = 7.1 Hz, 1H), 2.91−2.71 (m, 4H), 2.46 (q, $J$ = 7.6 Hz, 2H), 1.15 (m, 9H) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 148.5, 148.1, 147.8, 144.9, 143.2, 133.7, 133.5, 133.0, 132.6, 129.9, 129.6, 128.9, 122.9, 122.7, 121.9, 121.4, 62.6, 60.3, 28.5, 28.1, 16.7, 16.1, 14.9, 14.6 ppm; IR (KBr) $\nu$ 3450, 3386, 2895, 2933, 2873, 1599, 1529, 1456, 1349, 1154, 904, 877, 807, 742, 692; HRMS (ESI) calcd for $C_{26}H_{30}N_4O_6S$ + H 527.1964, obsd 527.1957.

**Compound 2m**: yield 62.5%; mp 213−215 °C; $[\alpha]^{20}_D$ +80.5° (*c* 0.32, $CH_3OH$); $^1$H NMR ($CD_3OD$, 300 MHz) $\delta$ 7.38−7.31 (m, 4H), 7.13−6.99 (m, 6H), 6.89−6.84 (m, 2H), 6.56 (d, $J$ = 7.8 Hz, 2H,), 4.38 (d, $J$ = 9.1 Hz, 1H), 4.09 (d, $J$ = 9.1 Hz, 1H), 2.26 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H) ppm; $^{13}$C NMR ($CD_3OD$, 75 MHz) $\delta$ 170.3, 142.8, 138.6, 138.5, 128.9, 128.5, 128.1, 126.7, 123.2, 122.9, 119.2, 118.9, 118.4, 64.2, 60.3, 22.5, 20.1 ppm; IR (KBr) 3361, 2925, 1672, 1612, 1556, 1492, 1444, 1373, 1321, 1202, 1158, 1092 cm$^{-1}$; HRMS (ESI) calcd for $C_{25}H_{28}N_4O_4S$ + H 481.1904, obsd 481.1900.

**Compound 2n**: yield 83.6%; mp 115−116 °C; $[\alpha]^{28}_D$ −21.7° (*c* 0.24, $CHCl_3$); $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 7.49−7.25 (m, 8H), 7.14−6.88 (m, 6H), 4.35 (d, $J$ = 4.6 Hz, 1H), 4.14 (d, $J$ = 4.7 Hz, 1H), 2.30 (s, 3H), 1.30 (s, 18H) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 176.9, 176.7, 142.6, 142.0, 140.4, 138.2, 138.1, 129.1, 128.9, 126.8, 122.9, 122.3, 119.5, 119.3, 118.7, 118.3, 62.8, 60.0, 39.6, 27.6, 21.4 ppm; IR (KBr) 3377, 2965, 1662, 1609. 1586, 1537, 1489, 1435, 1316, 1158, 1092 cm$^{-1}$; HRMS (ESI) calcd for $C_{31}H_{40}N_4O_4S$ + H 565.2843, obsd 565.2838.

**Compound 2o**: yield 92%; white solid; mp 188−190 °C; $[\alpha]^{22}_D$ +121.81° (*c* 0.67, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.30 (d, $J$ = 8.2 Hz, 2H), 7.20 (d, $J$ = 8.2 Hz, 2H), 6.84 (dd, $J$ = 8.2, 1.7 Hz, 4H), 6.59 (d, $J$ = 8.6 Hz, 2H), 6.33 (d, $J$ = 8.6 Hz, 2H), 4.84 (d, $J$ = 10.1 Hz, 1H), 4.77 (d, $J$ = 10.1 Hz, 1H), 3.59 (s, 3H), 3.58 (s, 3H), 2.22 (s, 3H) ppm; $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 159.4, 158.6, 142.1, 137.4, 129.7, 129.0, 128.7, 128.4, 127.1, 113.8, 113.2, 61.7, 59.1, 54.9, 21.3 ppm; IR (KBr) 3411, 3037, 2909, 2863, 1613, 1516, 1252, 1159 cm$^{-1}$; HRMS (ESI) calcd for $C_{23}H_{26}N_2O_4S$ + H 427.1692, obsd 427.1686.

**Compound 2p**: yield 87%; solid; mp 108−109 °C; $[\alpha]^{28}_D$ +33.1° (*c* 0.36, $CHCl_3$); $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 6.93 (d, $J$ = 8.6 Hz, 2H), 6.79(d, $J$ = 8.6 Hz, 2H), 6.76 (s, 2H,), 6.66 (d, $J$ = 8.7 Hz, 2H), 6.52 (d, $J$ = 8.7 Hz, 2H), 4.27 (d, $J$ = 6.4 Hz, 1H), 3.91 (d, $J$ = 6.8 Hz,1H), 3.74 (s, 3H), 3.68 (s, 3H), 2.78 (m, 4H), 2.54 (q, $J$ = 7.61 Hz, 2H), 1.18 (m, 9H) ppm; $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 158.8, 158.6, 147.8, 145.1, 133.9, 133.6, 130.8, 128.6, 128.3, 127.5, 113.6, 113.2, 62.9, 60.2, 55.2, 55.1, 28.4, 28.3, 16.6, 15.1 ppm; IR (KBr) $\nu$ 3408, 2965, 2874, 1612, 1515, 1461, 1314, 1250, 1154, 1033, 911, 834, 663, 568; HRMS (ESI) calcd for $C_{28}H_{36}N_2O_4S$ + H 497.2474, obsd 497.2469.

**Procedure for the Transfer Hydrogenation of $\alpha,\beta$-Unsaturated Ketones and Olefins.** Diamine ligand (0.0028 mmol), $[RuCl_2(cymene)]_2$ (0.76 mg, 0.00125 mmol), and triethylamine (0.69 $\mu$L, 0.005 mmol) were heated in methanol (0.5 mL) for 0.5 h. Methanol was then removed under vacuum. Olefin substrate (0.5 mmol) in DCM (0.5 mL) and the azeotrope of formic acid and triethylamine (0.2 mL) were added in turn. The mixture was stirred at 30 °C. After completion, the solution was diluted with EtOAc, washed with water, and dried. Flash chromatography gave the pure products.[30]

**General Procedure for Asymmetric Transfer Hydrogenation of Olefins.** Monosulfonylated chiral ligand (0.0044 mmol), $[RuCl_2(cymene)]_2$ (1.2 mg, 0.002 mmol), and triethylamine (1.1 $\mu$L, 0.008 mmol) were heated in 2-propanol (0.5 mL) for 2 h. Then 2-propanol was removed under vacuum. Olefin substrate (0.4 mmol) in THF (0.4 mL) and the azeotrope of formic acid and triethylamine (0.25 mL) were added in turn. The mixture was stirred at 30 °C. After completion, the solution was diluted with EtOAc, washed with water, and dried. Flash chromatography on silica gel gave the pure products.[30]

**General Procedure for Deuterium Labeling Experiments.** TsDPEN−RuCl(cymene)[5a] (2.6 mg, 0.004 mmol) was dissolved in 0.5 mL of DCM. Activated olefin **7k** (62 mg, 0.4 mmol), triethylamine (112 $\mu$L, 0.8 mmol), and deuterium labeled formic acid (78 $\mu$L, 2.0 mmol) were added in turn. Then the solution was stirred at 30 °C. After completion, the mixture was concentrated, and flash chromatography directly on silica gel gave the reduced product.[30]

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(29) For the details of the synthesis of the chiral ligands and the physical and spectroscopic data of **2c**,**d**,**h**, see the Supporting Information.

(30) For the physical and spectroscopic data of the products, see the Supporting Information.

**Supporting Information Available:** Experimental procedures of the synthesis of the ligands and olefins **7r** and **10a**−**i** and the transfer hydrogenation; characterization data for **2c**−**d**,**h**, **4a**−**d**, **5e**−**h**, **6e**, **8b**−**k**,**m**,**n**,**r**, **11a**−**j**; copies of NMR and MS spectra of ligands **2f**,**g**,**k**−**p** and reduced products **5f**,**h**, **8d**,**e**,**g**,**k**,**r**, and **11a**−**j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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