# "Ether-Linked" Organometallic Catalysts for Ketone Reduction Reactions

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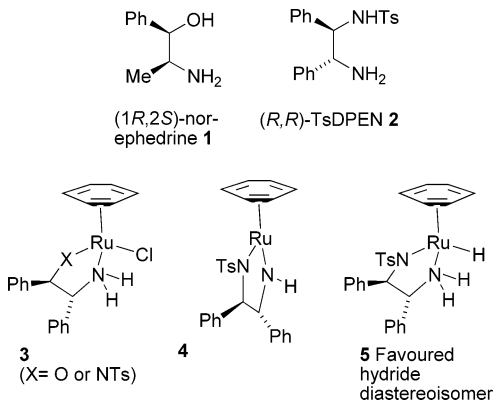
*Received June 20, 2007*

The synthesis and applications to asymmetric ketone hydrogenation of a series of novel Ru(II) catalysts is described. The design of the ligands ensures that the configuration at the metal atom is retained and cannot invert during the catalytic cycle. The catalysts generate alcohols in moderate to good enantiomeric excess and conversion.

## Introduction

Many ligands have been reported for the asymmetric transfer hydrogenation (ATH) of ketones, most commonly with either rhodium, iridium, or ruthenium metals.[1−4] The two main classes of ligand used are $\beta$-amino alcohols[2] **1** and monotosylated 1,2-diamines **2**.[3,4] The structure of the catalyst is completed with a halide such as chloride, and an $\eta^6$-arene ring (when Ru(II) is used) to give an 18 electron system **3**.[1−5]




Elimination of HCl from the 18-electron "precatalyst" complex **3** upon treatment with an appropriate base results in formation of a 16-electron species **4**, which abstracts two hydrogen atoms from the donor (isopropanol or formic acid) forming the hydride **5**.[5] These are then transferred to the ketone substrate to deliver the product in a process which also regenerates the 16-electron species **4**. Noyori has demonstrated

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(1) (a) Palmer, M.; Wills, M. *Tetrahedron: Asymmetry* **1999**, *10*, 2045. (b) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97. (c) Clapham, S. E.; Hadzovic, A.; Morris, R. H. *Coord. Chem. Rev.* **2004**, *248*, 2201. (d) Gladiali, S.; Alberico, E. *Chem. Soc. Rev.* **2006**, *35*, 226. (e) Ikariya, T.; Murata, K.; Noyori, R. *Org. Biomol. Chem.* **2006**, *4*, 393.

(2) (a) Takehara, J.; Hashiguchi, S.; Fujii, A.; Inoue, S.-I.; Ikariya, T.; R. Noyori, R. *Chem. Commun.* **1996**, 233. (b) Palmer, M.; Walsgrove, T.; Wills, M. *J. Org. Chem.* **1997**, *62*, 5226. (c) Alonso, D. A.; Nordin, S. J.; Roth, P.; Tarnai, T.; Andersson, P. G. *J. Org. Chem.* **2000**, *65*, 3116. (d) Everaere, K.; Mortreaux, A.; Carpentier, J.-F. *Adv. Synth Catal.* **2003**, *345*, 67. (e) Nordin, S. J. M.; Roth, P.; Tarnai, T.; Alonso, D. A.; Brandt, P.; Andersson, P. G. *Chem. Eur. J.* **2001**, *7*, 1431. (f) Hennig, M.; Püntener, K.; Scalone, M. *Tetrahedron: Asymmetry* **2000**, *11*, 1849. (g) Hansen, K. B.; Chilenski, J. R.; Desmond, R.; Devine, P. N.; Grabowski, E. J. J.; Heid, R.; Kubryk, M.; Mathre, D. J.; Varsolona, R. *Tetrahedron: Asymmetry* **2003**, *14*, 3581. (h) Liu, P. N.; Chen, Y. C.; Li, X. Q.; Tu, Y. Q.; Deng, J. G.; *Tetrahedron: Asymmetry* **2003**, *14*, 2481. (i) Schiffers, I.; Rantanen, T.; Schmidt, F.; Bergmans, W.; Zani, L.; Bolm, C. *J. Org. Chem.* **2006**, *71*, 2320. (j) Wisman, R. V.; de Vries, J. G.; Deelman, B.-J.; Heeres, H. J. *Org. Proc. Res. Dev.* **2006**, *10*, 423. (k) Bastin, S.; Eaves, R. J.; Edwards, C. W.; Ichihara, O.; Whittaker, M.; Wills, M. *J. Org. Chem.* **2004**, *69*, 5405. (l) Ursini, C. V.; Dias, G. H. M.; Rodrigues, J. A. R. *J. Organomet. Chem.* **2005**, *690*, 3176.

(3) (a) Fujii, A.; Hashiguchi, S.; Uematsu, N.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 2521. (b) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562. (c) Haack, K. J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed.* **1997**, *36*, 285. (d) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738. (e) Watanabe, M.; Murata, K.; Ikariya, T. *J. Org. Chem.* **2002**, *67*, 1712. (f) Li, M; O'Doherty, G. A. *Tetrahedron Lett.* **2004**, *45*, 6407. (g) Marshall, J. A.; Ellis, K. *Tetrahedron Lett.* **2004**, *45*, 1351. (h) Yamano, Y.; Shimizu, Y.; Ito, M. *Chem. Pharm. Bull.* **2003**, *51*, 878. (i) Cheung, F. K.; Hayes, A. M.; Morris, D. J.; Wills, M. *Org. Biomol. Chem.* **2007**, *5*, 1093. (j) Mogi, M.; Fuji, K.; Node, M. *Tetrahedron: Asymmetry* **2004**, *15*, 3715. (k) Vandyck, K.; Matthys, B.; Van der Eycken, J. *Tetrahedron Lett.* **2005**, *46*, 75. (l) Bogliotti, N.; Dalko, P. I.; Cossy, J. *Tetrahedron Lett.* **2005**, *46*, 6915. (m) Maki, M.; Motoki, R.; Fujii, K.; Kanai, M.; Kobayashi, T.; Tamura, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 17111. (n) Ros, A.; Magriz, A.; Dietrich, H.; Fernández, R.; Alvarez, E.; Lassaletta, J. M. *Org. Lett.* **2006**, *8*, 127. (o) Lennon, I. C.; Ramsden, J. A. *Org. Proc. Res. Dev.* **2005**, *9*, 110. (p) Hayes, A. M.; Clarkson, G.; Wills, M. *Tetrahedron: Asymmetry* **2004**, *15*, 2079. (q) Sterk, D.; Stephan, M.; Mohar, B. *Org. Lett.* **2006**, *8*, 5935.

(4) (a) Chen, Y.-C.; Wu, T.-F.; Jiang, L.; Deng, J.-G.; Liu, H.; Zhu, J.; Jiang, Y.-Z. *J. Org. Chem.* **2005**, *70*, 1006. (b) Liu, W.; Cui, X.; Cun, L.; Zhu, J.; Deng, J. G. *Tetrahedron: Asymmetry* **2005**, *16*, 2525. (c) Liu, P.-N.; Gu, P.-M.; Deng, J. G.; Tu; Y.-Q.; Ma, Y.-P. *Eur. J. Org. Chem.* **2005**, *70*, 3221. (d) Li, X.; Chen, W.; Hems, W.; King, F.; Xiao, J. *Tetrahedron Lett.* **2004**, *45*, 951. (e) Arakawa, Y.; Haraguchi, N.; Itsuno, S. *Tetrahedron Lett.* **2006**, *47*, 3239. (f) Severin, K.; Polborn, K. *Chem. Eur. J.* **2000**, *6*, 4604. (g) Li, Y.; Li, Z.; Wang Q.; Tao, F. *Org. Biol. Chem.* **2005**, 2513. (h) Wu, X.; Li, X.; King, F.; Xiao, J. *Angew. Chem., Int Ed.* **2005**, *44*, 3407. (i) Wu, X.; Vinci, D.; Ikariya, T.; Xiao, J. *Chem. Commun.* **2005**, 4447. (j) Wu, X.; Li, X.; McConville, M.; Saidi, O.; Xiao, J. *J. Mol. Catal. A* **2006**, *247*, 153. (k) Li, X.; Blacker, J.; Houson, I.; Wu, X.; Xiao, J. *Synlett* **2006**, 1155. (l) Tanis, S. P.; Evans, B. R.; Nieman, J. A.; Parker, T. T.; Taylor, W. D.; Heasley, S. E.; Herrinton, P. M.; Perrault, W. R.; Hohler, R. A.; Dolak, L. A.; Hester, M. R.; E. P. Seest, E. P. *Tetrahedron: Asymmetry* **2006**, *17*, 2154. (m) Letondor, C.; Pordea, A.; Humbert, N.; Ivanova, A.; Mazurek, S.; Novic, M.; Ward, T. R. *J. Am. Chem. Soc.* **2006**, *128*, 8320.

(5) (a) Alonso, D. A.; Brandt, P.; Nordin, S. J. M.; Andersson, P. G. *J. Am. Chem. Soc.* **1999**, *121*, 9580. (b) Yamakawa, M.; Ito, H.; Noyori, R. *J. Am. Chem. Soc.* **2000**, *122*, 1466. (c) Noyori, R.; Yamakawa, M.; Hashiguchi, S.; *J. Org. Chem.* **2001**, *66*, 7931. (d) Yamakawa, M.; Yamada, I.; Noyori, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 2818. (e) Brandt, P.; Roth, P.; Andersson, P. G. *J. Org. Chem.* **2004**, *69*, 4885. (f) Hayes, A.; Clarkson, G.; Wills, M. *Tetrahedron: Asymmetry* **2004**, *15*, 2079.

10.1021/om700610y CCC: $37.00 
Publication on Web 09/22/2007

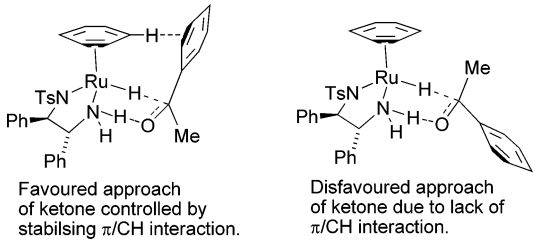



**Figure 1.** Stereocontrol in asymmetric transfer hydrogenations.

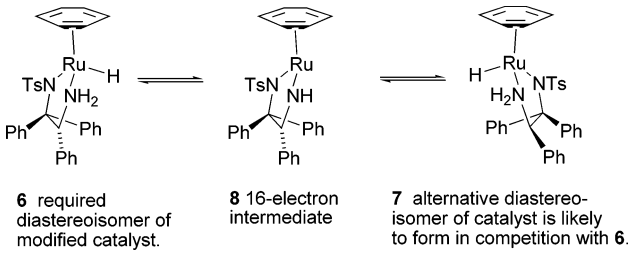



**Figure 2.** Modified ligand may exist as two diastereoisomers.

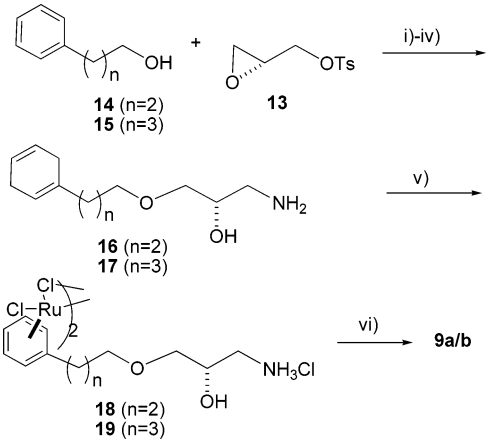
that both **3** and **5** exist predominantly in the diastereoisomeric form illustrated (through X-ray crystallography and molecular modeling).[5] This diastereoisomeric preference also extends to the amino alcohol systems. Thus, the chiral ligand renders the metal center a single configuration.

In each "2H" transfer process, the absolute stereochemistry is controlled via a six-membered transition state (Figure 1). Approach of the substrate to the metal hydride is favored through the conformation in which its aromatic ring is adjacent to the arene group on the metal. The interaction of the aromatic ring of acetophenone (substrate) with the $\eta^6$-arene component on the catalytic species through a favorable $\pi$/CH interaction is indicated.[5] This accounts for the observation that asymmetric reduction only proceeds in high ee when with aryl/alkyl ketones are used as substrates, but not dialkyl ketones, as no comparable $\pi$/CH interactions can exist.

A possible limitation of these complexes is that there is a potential for diastereomer interchange in the mechanism. Since the reduction mechanism proceeds through a speculated "16-electron" intermediate **4** to which hydride (from isopropanol or formic acid) may be added from either face. In practice this is not a significant problem when using ligands such as **1** and **2** because the hydride transfer is generally diastereoselective and strongly in favor of the diastereoisomer indicated in structure **5**.

However, it would be of some interest to induce modifications of the chiral space in the region of the transition state which lies below the Ru−H bond. For example, the introduction of a large group, such as phenyl ring, in the position occupied by the hydrogen adjacent to the NTs group provides a means by which the steric demand in this region can be dramatically increased (i.e., in catalyst **6**, Figure 2). This catalyst may be more sensitive to ketones with groups of different sizes flanking the carbonyl (e.g., unsymmetrical alkyl/alkyl ketones). Unfortunately the introduction of this group will undoubtedly disrupt the delicately balanced diastereoselectivity currently observed in, and essential to, the existing hydride transfer process, by competitively forming **7** via 16-electron species **8** (Figure 2). We have previously demonstrated that the *trans*-1,2-diphenyl substitution pattern in the diamine ligand is essential to both activity and enantioselectivity. If the *cis*-1,2-diphenyl ligand is used instead, for example, the ee decreases significantly (from 98 to 70%), and the reaction time is greatly extended (from 22 to 220 h).[5f]

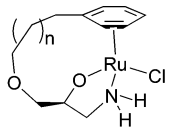
**Scheme 1. Synthesis of Catalysts 9a/b**[a]

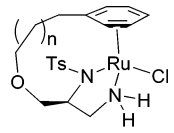


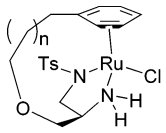

[a] Reagents and conditions: (i) $BF_3{\cdot}Et_2O$, DCM, 0 °C, 71% for $n = 2$, 33% for $n = 3$; (ii) $K_2CO_3$, MeOH, −10 °C, 83% for $n = 2$, 24% for $n = 3$; (iii) $NaN_3$, DMF, 40 °C, 13% for $n = 2$, 67% for $n = 3$; (iv) Na, $NH_3$, EtOH, −78 °C, 58% for $n = 2$, 47% for $n = 3$; (v) 2 M $HCl{\cdot}Et_2O$, then $RuCl_3{\cdot}3H_2O$, EtOH, reflux, 58% for $n = 2$, 28% for $n = 3$; (vi) base (in situ in reaction).

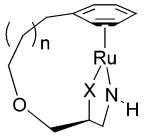
## Results and Discussion

A solution to this problem may be obtained by tethering the ligand to the arene ring in such a manner that the ligand is "held over" to one side. Catalysts **9**−**11** possess such a structural feature. In these complexes the tether is designed to be sufficiently long to allow the ligand to complex successfully, and for the intermediate 16-electron species **12** to form, yet also be rigid enough for an inversion of configuration at Ru to be prohibited. In effect, the ligands can readily form only one diastereoisomer of complex, rendering the ruthenium atom a single configuration, which is a prerequisite for high enantioselectivity in the reduction. In this paper we describe the synthesis and application to ATH of catalysts **9**−**11**.




To prepare **9a/b**, we chose an approach in which the Birch reduction and azide reduction were carried out together. This serves to minimize the number of steps involved in the synthetic route (Scheme 1). Tosylate **13**[6] was reacted with 3-phenyl 1-propanol **14** or 4-phenyl 1-butanol **15** in the presence of the Lewis acid trifluoroborane etherate to give an intermediate which was then treated with azide to introduce a nitrogen function. Although we employed a two-step process, that is, via the epoxide, it was also possible to complete both steps in

(6) Klunder, J. M.; Ko, Y. S.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 3710−3712.

**Table 1. Ketone Reductions Using Catalysts 9−11**

| entry | catalyst[a] | substrate | *T*/°C | time/h | conversion % | ee % |
|---|---|---|---|---|---|---|
| 1 | **9a** (**18**) | acetophenone | 40 | o/n | 15 | 12 (*R*) |
| 2 | **9b** (**19**) | acetophenone | 28 | 1 | 22 | 72 (*R*) |
| 3 | **9b** (**19**) | acetophenone | 28 | 27 | 22 | 69 (*R*) |
| 4 | **9b** (**19**) | acetophenone | 40 | 17.5 | 7.4 | 68 (*R*) |
| 5 | **9b** (**19**) | acetophenone | 10 | 17.5 | 56 | 72 (*R*) |
| 6 | **9b** (**19**) | cyclohexyl methyl ketone | 40 | 17.5 | 0 | |
| 7 | *rac*-**10a** (**23**) | acetophenone | 28 | o/n | 0 | |
| 8 | *rac*-**10** (**23**) | acetophenone | 40 | o/n | 1 | |
| 9 | **11a** (**28a**) | acetophenone | 28 | o/n | 13 | 20 (*R*) |
| 10 | **11a** (**28a**) | acetophenone | 40 | o/n | 40 | 41 (*R*) |
| 11 | **11b** (**28b**) | acetophenone | 20 | o/n | 32 | 50 (*R*) |
| 12 | **11b** (**28b**) | acetophenone | 40 | 3 | 79 | 31 (*R*) |
| 13 | **11b** (**28b**) | acetophenone | 40 | o/n | 100 | 29 (*R*) |
| 14[b] | **11b** (**28b**) | acetophenone | 28 | o/n | 19 | 28 (*R*) |
| 15 | **11b** (**28b**) | *o*-chloro-acetophenone | 40 | o/n | 100 | 10 (*R*) |
| 16 | **11b** (**28b**) | cyclohexyl methyl ketone | 40 | o/n | 65 | 16 (*S*) |

[a] All reactions using **9a/b** carried out in isopropanol/KOH; all reactions using **10a** and **11a/b** carried out in formic acid/triethylamine azeotropic mixture unless otherwise stated. [b] Reaction in 0.1 M KOH in 2-propanol. S/C = 200.

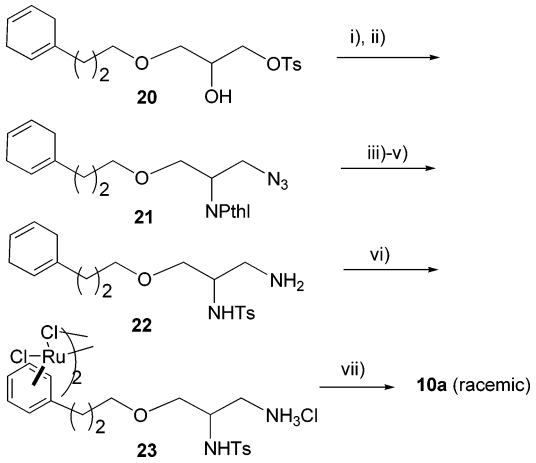
a one-pot process. This was followed by Birch reduction[7] which served to reduce both the aryl group and the azide in one pot, furnishing **16** and **17**, respectively. The catalyst dimers **18** and **19** were prepared by reaction of the protonated amino alcohols with ruthenium trichloride in ethanol under reflux. Attempts were not made to isolate the monomers **9a** and **9b**, as these are known to form under the ATH conditions (isopropanol and alkoxide base), in analogy with the in-situ formation of the untethered compounds under the same conditions.[8]

The aminoalcohol tethered catalysts **9a/b** were first evaluated for ATH with acetophenone and cyclohexyl methyl ketone in isopropanol/KOH (Table 1). Using **9a** at 40 °C gave the alcohol in 15% conversion and 12% ee; however, the catalyst was poorly soluble in iPrOH. Cosolvents were used in the reactions in attempt to increase the solubility of the catalyst. Acetophenone was used as the substrate; however, only a trace of reduction was evident in each case. Reduction was also attempted with acetophenone and cyclohexyl methyl ketone in 5:2 formic acid/triethylamine solution. In this solution, the dimer was fully dissolved; however, no reduction was evident, as is commonly the case for aminoalcohol/Ru(II) catalysts.

More promising results were obtained using catalyst **9b**, which has a longer hydrocarbon chain. Low temperature and high catalyst loadings, however, were required for reasonable conversions (56%) to be obtained while the enantiomeric excess was maintained at 72% (*R*) even at high S/C. In a separate experiment at S/C = 200, 28 °C, the conversion and ee were monitored using acetophenone as the substrate. It was found that the initial ee (72%) did not change significantly, decreasing slightly to 69% after 27 h, while the initial conversion (22%) after 1 h did not increase. These results suggest that, in contrast to **9a**, the longer chain in **9b** allows the catalyst to shuttle between the speculated 18- and 16-electron species. Although the catalyst is initially active and moderately enantioselective, it appears to rapidly decompose.

Two classes of monotosylated diamine derivatives, **10** and **11**, can be envisaged, depending on the position of the sulfonamide relative to the tether. The synthetic route to racemic **10a** is shown in Scheme 2. Alcohol **20**, prepared by reaction of the precursor cyclohexyldiene alcohol with racemic **13**, provides a convenient starting material. After the displacement of the tosylate group by azide, the alcoholic functionality was replaced by a pthtalimide group under Mitsunobu reaction conditions[9] to give **21**. Hydrazinolysis of **21** gave an amine, which was tosylated. The desired ligand **22** was obtained by reduction of the azide moiety with $LiAlH_4$. The complexation step afforded dimer **23** which was directly used in catalytic reductions, as the active catalyst **10a** will be formed in situ.[8]

**Scheme 2. Racemic Synthesis of Catalyst 10a[a]**




[a] Reagents and conditions: (i) $NaN_3$, DMF, 40 °C 22%; (ii) pthalimide, $Ph_3P$, DTBAD, THF, 65%; (iii) hydrazine monohydrate, EtOH, reflux. 81%; (iv) TsCl, $Et_3N$, DCM, −10 °C, 81%; (v) $LiAlH_4$, THF, reflux, 20%; (vi) 2 M HCl·$Et_2O$, then $RuCl_3$·$3H_2O$, EtOH, reflux, 69%; (vii) base (in situ in reaction).

Catalyst dimer **10a** was tested in the reduction of acetophenone (in 5:2 $HCO_2H/Et_3N$, S/C = 200). The results were very poor: when the reaction was conducted at room temperature there was no conversion, and even at 40 °C the conversion was lower than 1%. This may reflect an unfavorable steric clash between the tosyl group and the new side chain. It was therefore decided not to proceed with the synthesis of the enantiomerically pure form of this catalyst or of **10b**.

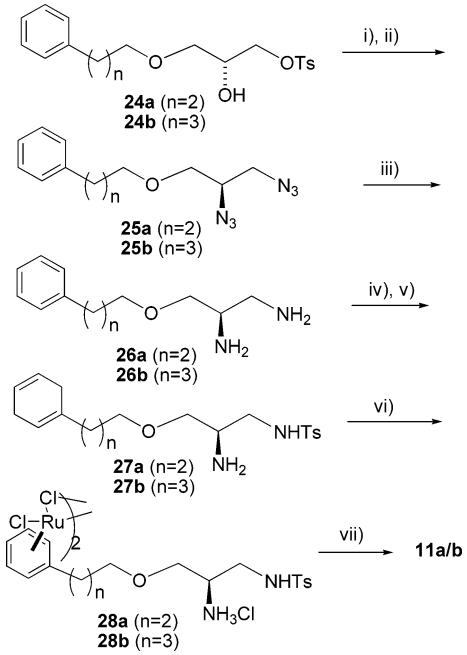
Catalysts **11a** and **11b** differ from **10a** in that the Ts group is distant from the connecting chain. These were initially prepared in racemic form and gave encouraging results in ATH,

(7) Subba Rao, G. S. R. *Pure Appl. Chem.* **2003**, *75*, 1443.

(8) (a) Hayes, A. M.; Morris, D. J.; Clarkson, G. J.; Wills, M. *J. Am. Chem. Soc.* **2005**, *127*, 7318. (b) Hannedouche, J.; Clarkson, G. J.; Wills, M. *J. Am. Chem. Soc.* **2004**, *126*, 986. (c) Cheung, F. K.; Hayes, A. M.; Hannedouche, J.; Yim, A. S. Y.; Wills, M. *J. Org. Chem.* **2005**, *70*, 3188. (d) Morris, D. J.; Hayes, A. M.; Wills, M. *J. Org. Chem.* **2006**, *71*, 7035.

(9) Thomas, E. W.; Cudahy, M. M.; Spilman, C. H.; Dinh, D. M.; Watkins, T. L.; Vidmar, T. J. *J. Med. Chem.* **1992**, *35*, 1233.

**Scheme 3. Asymmetric Synthesis of Catalysts 11a/b**[a]




[a] Reagents and conditions: (i) TsCl, $Et_3N$, DCM, −10 °C, 92% for $n = 1$, 82% for $n = 2$; (ii) $NaN_3$, DMF, 40 °C, 88% for $n = 2$, 87% for $n = 3$; (iii) $LiAlH_4$, room temp, o/n, 46% for $n = 2$, 53% for $n = 3$; (iv) Na, $NH_3$, EtOH, THF, −78 °C, 43% for $n = 2$, 73% for $n = 3$. (v) TsCl, $Et_3N$, DCM, −10 °C, 36% for $n = 2$, 67% for $n = 3$. (vi) 2 M HCl·$Et_2O$, then $RuCl_3$·$3H_2O$, EtOH, reflux, 93% for $n = 2$, 40% for $n = 3$; (vii) base (in situ in reaction).

they were also prepared in enantiomerically pure form through the route illustrated in Scheme 3. Starting from enantiomercially pure **24a/b**, tosylation and double azide displacement gave diazides **25a/b**. These were reduced to diamines **26a/b** using $LiAlH_4$. Birch reduction[7] was next employed to generate the 1,4-dienes which were N-tosylated selectively at the terminal amine to give **27a/b**. Complexation was completed using the normal procedure to furnish **28a/b** which were again used as the dimers, but known to be converted in-situ to the monomers **11a/b**. An alternative procedure which involved the direct conversion of **25a/b** to **27a/b** through the use of reducing metal was investigated, but this gave only very low yields of the required products.

Using catalyst **11a**, a successful ATH reaction was achieved. Unfortunately, the enantioselectivity of acetophenone reduction was quite low, at only 41% ee, and with 88% conversion. Lowering the temperature not only reduced the conversion (only 13% after an overnight reaction) but also the e.e. While simple models suggest that the octahedral complex **11a** should be able to form without substantial strain being introduced, it is possible that the three carbon tether is not long enough to allow formation of the '16e' species. This would prevent the catalytic process from operating efficiently in the case of **11a**. This speculation is supported by our observation that better results were achieved using **11b**, in which the longer tether permits 18e and 16e species to form relatively readily. Indeed it was possible to achieve 100% conversion in an overnight reaction using this catalyst, which suggests that the tether is of a sufficient length to permit the required structural changes. However the ee values were very low, not exceeding 29% at full conversion. This could be increased to 50% at lower temperature, but the reaction rate dropped sharply. Cyclohexyl/methyl ketone was reduced in only 16% ee.

## Conclusion

In summary, we have developed new routes to a series of potential catalysts for transfer hydrogenation which contain a stereochemically well-defined structure that controls the configuration at the metal. Of the catalysts examined, **11b** proved to be the most active, although products were obtained in low ee. This suggests that the tether length is sufficient to provide the 18/16-electron shuttle for the catalytic mechanism to operate, but that the catalyst was lacking the elements which affect the enantioselectivity of ketone reduction. Catalysts such as **9**−**11** may have further potential applications as, for example, chiral Lewis acids, and further studies are ongoing in this area.

## Experimental Section

For general reaction conditions see the Supporting Information. All reactions were carried out under an atmosphere of nitrogen in flame or oven dried glassware (round-bottomed flasks or Schlenk tubes).

**Synthesis of (*S*)-1-Amino-3-(3-(cyclohexa-1,4-dienyl)-propoxy)-propan-2-ol 16**. To a stirred and refluxing solution of ammonia (50 $cm^3$) was slowly added a solution of (*S*)-1-azido-3-(3-phenyl-propoxy)propan-2-ol (1.60 g, 6.81 mmol) in ethanol (4 $cm^3$) at −78 °C while stirring. Small pieces of cleaned sodium were added to the reaction mixture until the blue color persisted. During the addition of sodium, a small amount of ethanol was added several times to facilitate stirring. After the addition of sodium over the course of 1 h, the reaction mixture was left to evaporate the ammonia overnight. An aqueous saturated solution of ammonium chloride (70 $cm^3$) was added to the reaction. The product was then extracted with dichloromethane (3 × 120 $cm^3$), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under vacuum to give the crude product. The residue was added to 1.2 M $HCl_{(aq)}$, and the mixture was washed with EtOAc. The aqueous layer was adjusted to pH 12 with 3 M $NaOH_{(aq)}$, and the product was extracted with DCM, dried ($MgSO_4$), filtered, and concentrated under vacuum to afford the desired product **16** (0.83 g, 58%) as an orange oil: $[\alpha]^{22}_D$ −2.7 (*c* 1.10, $CHCl_3$). $\nu_{max}/cm^{-1}$ (thin film); 1592, 1648, 2818, 2851, 3296, 3357. $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$): 1.15 (2H, brs), 1.71 (2H, quintet, *J* 7.0), 2.02 (2H, t, *J* 7.5), 2.57−2.66 (2H, m), 2.66−2.76 (2H, m), 2.79−2.87 (2H, m), 3.37−3.39 (1H, m), 3.40−3.49 (3H, m), 3.69−3.75 (1H, m), 5.43 (1H, s), 5.71 (2H, s). $\delta_C$(100.6 MHz; $CDCl_3$; $Me_4Si$): 26.7 ($CH_2$), 27.2 ($CH_2$), 28.9 ($CH_2$), 33.9 ($CH_2$), 44.5 ($CH_2$), 71.1 (*C*H), 71.2 ($CH_2$), 73.2 ($CH_2$), 118.6 (*C*H), 124.3 (*C*H), 124.3 (*C*H), 134.3 (*C*). *m*/*z* (EI) 211 ($[M]^+$, 39%), 210 (100), 91 (70), 79 (40), 77 (28), 60 (21). Found (EI): 210.1502 $[M-H]^+$; $C_{12}H_{20}O_2N$ requires 210.1494 (−4.0 ppm error).

**Synthesis of the 3-Carbon Chloro-Bridged $\eta^6$-arene Ruthenium(II) Dimer 18**. To a stirred solution of (*S*)-1-amino-3-(3-(cyclohexa-1,4-dienyl)propoxy)propan-2-ol **16** (0.78 g, 3.68 mmol) in DCM (30 $cm^3$) was added a 2 M solution of hydrochloric acid in diethyl ether (30 $cm^3$) at room temperature. The reaction mixture was stirred for 2 h at room temperature and concentrated under vacuum to give an orange residue. To a suspension of the residue in ethanol (50 $cm^3$) was added hydrate ruthenium(III) trichloride (0.77 g, 2.94 mmol). The reaction mixture was stirred at reflux overnight and filtered to give green solid residue. The residue was washed with anhydrous dichloromethane and ethanol to afford a green solid **18** (0.89 g, 58%); mp 210 °C (dec). $\nu_{max}/cm^{-1}$ (solid): 620, 669, 870, 1038, 1110, 1148, 1449, 1578, 2343, 2359, 2921, 3064. $\delta_H$(400 MHz; $d_6$-DMSO; $Me_4Si$): 1.85−1.88 (2H, m), 2.50 (2H, m), 2.68−2.74 (1H, m), 2.91−2.95 (1H, m), 3.33−3.39 (4H, m), 3.82 (1H, m), 5.76−5.78 (3H, m), 6.00−6.02 (2H, m), 7.71 (3H, m). $\delta_C$(100.6 MHz; $d_6$-DMSO; $Me_4Si$): 29.1 ($CH_2$), 29.8 ($CH_2$), 56.2 ($CH_2$), 66.3 (*C*H), 70.3 ($CH_2$), 72.7 ($CH_2$), 84.1 (*C*H),

85.9 (2 × *C*H), 107.6 (*C*). *m*/*z* (FAB) M+ not detected however strong evidence of $C_{12}H_{20}NO_2{}^{35}Cl_2{}^{102}Ru$ (382) within predicted isotopic pattern.

**Synthesis of (*S*)-1-Amino-3-(4-(cyclohexa-1,4-dienyl)-butoxy)-propan-2-ol 17**. To a stirred and refluxing solution of ammonia (100 $cm^3$) was slowly added a solution of (*S*)-1-azido-3-(4-phenylbutoxy)propan-2-ol (3.00 g, 12.0 mmol) in ethanol (7.5 $cm^3$) at −78 °C while stirring. Small pieces of cleaned sodium were added to the reaction mixture until the blue color persisted. During addition of sodium, a small amount of ethanol was added several times to facilitate stirring. After the addition of sodium over the course of 1 h, the reaction mixture was left to evaporate the ammonia overnight. An aqueous saturated solution of ammonium chloride (100 $cm^3$) was added to the reaction. The product was then extracted with dichloromethane (3 × 100 $cm^3$), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under vacuum to give the crude product. The residue was added to 1.2 M $HCl_{(aq)}$, and the mixture was washed with EtOAc. The aqueous layer was adjusted to pH 12 with 3 M $NaOH_{(aq)}$, and the product was extracted with DCM, dried ($MgSO_4$), filtered, and concentrated under vacuum to afford the desired product **17** (2.56 g, 47%) as a orange oil: $[\alpha]^{22}{}_D$ −5.80 (*c* 0.50, $CHCl_3$). $\nu_{max}/cm^{-1}$ (thin film): 1083, 1648, 2856, 2930, 3325, $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$): 1.42−1.47 (2H, m), 1.54−1.57 (2H, m), 1.94−2.00 (2H, m), 2.56−2.59 (2H, m), 2.65−2.67 (2H, m), 2.83 (1H, brs), 2.97 (1H, brs) 3.42−3.44 (4H, m), 3.90 (1H, brs), 5.40 (1H, s), 5.69 (2H, s). $\delta_C$(100.6 MHz; $CDCl_3$; $Me_4Si$): 23.7 (*C*$H_2$), 26.8 (*C*$H_2$), 28.9 (*C*$H_2$), 29.3 (*C*$H_2$), 37.3 (*C*$H_2$), 43.8 (*C*$H_2$), 69.3 (*C*H), 71.6 (*C*$H_2$), 73.0 (*C*$H_2$), 118.5 (*C*H), 124.3 (2 × *C*H), 134.7 (*C*). *m*/*z* (EI) 225 ([M]$^+$, 12%), 224 (99), 104 (22), 92 (30), 91 (100), 83 (69), 79 (30), 77 (22). Found (EI): 224.1647 [M−H]$^+$; $C_{13}H_{22}O_2N$ requires 224.1651 (1.4 ppm error).

**Synthesis of the 4-Carbon Chloro-Bridged $\eta^6$-arene Ruthenium(II) Dimer 19.** To a stirred solution of ((*S*)-1-amino-3-(4-(cyclohexa-1,4-dienyl)butoxy)propan-2-ol **17** (2.56 g, 11.4 mmol) in DCM (100 $cm^3$) was added a 2 M solution of hydrochloric acid in diethyl ether (90 $cm^3$) at room temperature. The reaction mixture was stirred for 2 h at room temperature, and half of the solution was concentrated under vacuum to give an orange residue. To a suspension of the residue in ethanol (70 $cm^3$) was added hydrate ruthenium(III) trichloride (1.15 g, 4.40 mmol). The reaction mixture was stirred at reflux overnight and filtered to give a green solid residue. The residue was washed with anhydrous dichloromethane and ethanol to afford a green solid **19** (1.37 g, 28%): mp 240 °C (dec). $\nu_{max}/cm^{-1}$ (solid): 1112, 1482, 1578, 2359, 2863, 2913, 3430. $\delta_H$(400 MHz; $d_6$-DMSO; $Me_4Si$): 1.61 (4H, m), 2.52 (2H, m), 2.71 (1H, m), 2.93 (1H, m), 3.34−3.45 (4H, m), 3.84 (1H, m), 5.76 (3H, m), 6.00 (2H, mH), 7.75 (3H, brs). $\delta_C$(100.6 MHz; $d_6$-DMSO; $Me_4Si$): 25.9 (*C*$H_2$), 28.9 (*C*$H_2$), 23.5 (*C*$H_2$), 43.3 (*C*$H_2$), 66.2 (*C*H), 70.6 (*C*$H_2$), 72.6 (*C*$H_2$), 83.9 (*C*H), 85.5 (2 × *C*H), 89.9 (2 × *C*H), 107.9 (*C*). *m*/*z* (FAB) complex pattern, M+ not detected however 396 ($C_{13}H_{22}{}^{35}Cl_2NO_2{}^{102}Ru$) within predicted isotopic pattern.

**Synthesis of 3-(3-(Cyclohexa-1,4-dienyl)propoxy)-*N*2-tosyl-propane-1,2-diamine 22**. To a solution of $LiAlH_4$ (50 mg, 1.32 mmol) in anhydrous THF (5 $cm^3$), *N*-(3-azido-1-(3-(cyclohexa-1,4-dienyl)propoxy)propan-2-yl)-4-methyl-benzenesulfonamide (500 mg, 1.28 mmol) was added. The solution was heated at reflux under nitrogen for 2 h. The solution was then allowed to cool to room temperature, then water (0.05 $cm^3$), 10% aqueous NaOH (0.05 $cm^3$), and again water (0.15 $cm^3$) were subsequentially slowly added. The resulting mixture was filtered through celite, and the filtrate was concentrated under reduced pressure. The residue was dissolved in dichloromethane (10 $cm^3$) and extracted with a solution of water plus a few drops of 36% aqueous HCl (2 × 10 $cm^3$). The combined aqueous layers were made basic with aqueous NaOH and extracted with dichloromethane (2 × 10 $cm^3$). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give the crude product **22** as a yellow oil (75 mg, 20%) that was used without any further purification. $\delta_H$(300 MHz; $CDCl_3$; $Me_4Si$): 1.49−1.59 (2H, m), 1.89 (2H, t, *J* 7.5), 2.41 (3 H, s), 2.54 (2 H, d, *J* 8.3), 2.64−2.69 (2 H, m), 2.83−2.96 (2 H, m), 3.16−3.35 (4 H, m), 3.39−3.42 (1 H, m), 4.13 (2 H, brs), 5.36 (1H, brs), 5.70 (2 H, brs), 7.28 (2 H, d, *J* 8.2), 7.79 (2 H, d, *J* 8.2).

**Synthesis of Dimer 23.** To a stirred solution of **22** (70 mg, 0.19 mmol) in diethyl ether (1 $cm^3$) was added a 2 M solution of hydrochloric acid in diethyl ether (0.29 $cm^3$, 0.58 mmol). The reaction mixture was stirred for 2 h and concentrated under reduced pressure. To a suspension of the residue in ethanol (2 $cm^3$) was added trihydrated ruthenium trichloride (32 mg, 0.15 mmol). The reaction mixture was stirred at reflux temperature overnight and filtered to give a dark solid. The residue was washed with anhydrous dichloromethane and ethanol to afford **23** as a dark solid (70 mg, 69%). $\delta_H$(300 MHz; $d_6$-DMSO): 1.58−1.73 (4 H, m), 2.38 (6H, s), 2.91−3.19 (4H, m), 3.35−3.50 (14H, m), 5.77−5.80 (6H, m), 5.98−6.00 (4H, m), 7.43 (4H, d, *J* 7.6), 7.73 (4H, d, *J* 7.6), 7.73−7.82 (6 H, m). $\nu_{max}/cm^{-1}$ (solid) 816, 1089, 1155, 1319, 1448, 1595, 2340, 2358, 2871, 3056. $\delta_C$(100.6 MHz; $d_6$-DMSO) 21.7 (*C*$H_3$), 28.8 (*C*$H_2$), 29.7 (*C*$H_2$), 51.2 (*C*H), 69.6 (*C*$H_2$), 70.0 (*C*$H_2$), 83.6 (*C*H), 85.4 (*C*H), 89.6 (*C*H), 108.1 (*C*), 126.2 (*C*H), 127.0 (2 × *C*H), 128.7 (*C*H), 130.2 (2 × *C*H), 138.5 (*C*), 143.3 (*C*). *m*/*z* (LSIMS) 534 ([monomer], 1.4%), 363 [ligand] (26), 307 (42), 154 (100), 139 (63).

**Synthesis of (*R*)-3-[3-(cyclohexa-1,4-dienyl)propoxy]-*N*1-tosylpropane-1,2-diamine 27a.** To a solution of (*R*)-3-[3-(cyclohexa-1,4-dienyl)propoxy]propane-1,2-diamine (0.14 g, 0.66 mmol) and triethylamine (0.15 $cm^3$, 1.12 mmol) in anhydrous dichloromethane (5 $cm^3$), was added tosyl chloride (0.12 g, 0.61 mmol) at −10 °C. The solution was stirred under nitrogen overnight, washed with brine (5 $cm^3$), dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give the crude product. The residue was purified by flash chromatography (2 → 60% v/v ethyl acetate/hexane) to afford the product **27a** (0.90 g, 36%) as a yellow oil: $[\alpha]^{20}{}_D$ +7.1 (*c* 0.5, $CHCl_3$). $\nu_{max}/cm^{-1}$ (thin film): 749, 812, 923, 998, 1095, 1173, 1363, 1452, 1597, 2868, 2921. $\delta_H$(300 MHz; $CDCl_3$; $Me_4Si$): 1.48−1.62 (2 H, m), 1.89 (2H, t, *J* 7.7), 2.35 (3 H, s), 2.49−2.60 (4H, m), 2.80−3.41 (5H, m), 3.27−3.33 (2H, m), 5.32 (1 H, brs), 5.59−5.66 (2 H, m), 7.22 (2H, d, *J* 8.2), 7.68 (2H, d, *J* 8.2). $\delta_C$(100.6 MHz; $CDCl_3$; $Me_4Si$): 21.5 (*C*$H_3$), 26.8 (*C*$H_2$), 27.2 (*C*$H_2$), 28.9 (*C*$H_2$), 33.8 (*C*$H_2$), 46.0 (*C*$H_2$), 50.4 (*C*H), 71.1 (*C*$H_2$), 72.9 (*C*$H_2$), 118.6 (*C*H), 124.3 (2 × overlapping *C*H), 127.1 (2 × *C*H), 129.7 (2 × *C*H), 134.2 (*C*), 136.9 (*C*), 143.3 (*C*). *m*/*z* (EI) 363 ([M−H]$^+$, 60%), 213 (14), 180 (44), 178 (52), 91 (100). Found (EI): 363.1744 [M−H]$^+$; $C_{19}H_{28}N_2O_3S_1$ requires 363.1742 (−0.4 ppm error).

**Synthesis of (*R*)-3-[4-(cyclohexa-1,4-dienyl)butoxy]-*N*1-tosyl-propane-1,2-diamine 27b.** To a solution of (*R*)-3-[3-(cyclohexa-1,4-dienyl)butoxy]propane-1,2-diamine (0.26 g, 1.17 mmol) and triethlamine (0.27 $cm^3$, 2.0 mmol) in anhydrous dichloromethane (15 $cm^3$), was added tosyl chloride (0.20 g, 1.05 mmol) at −10 °C. The solution was stirred under nitrogen overnight, washed with brine (15 $cm^3$), dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give the crude product. The residue was purified by flash chromatography (2 → 60% v/v ethyl acetate/hexane) to afford the product **27b** (0.30 g, 67%) as a yellow oil: $[\alpha]^{21}{}_D$ +17.5 (*c* 0.07 in $CH_2Cl_2$). $\nu_{max}/cm^{-1}$ (thin film): 752, 815, 902, 936, 1002, 1175, 1373, 1412, 1492, 1583, 2875, 3006. $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$): 1.40−1.55 (4H, m), 1.93−1.97 (2H, m), 2.40 (3H, s), 2.56−2.67 (4H, m), 2.75−2.84 (1H, m), 2.98−3.03 (2H, m), 3.28−3.44 (4 H, m), 5.40 (1H, br s), 5.66−5.74 (2H, m), 7.28 (2H, d, *J* 8.3), 7.73 (2H, d, *J* 8.3). $\delta_C$(100.6 MHz; $CDCl_3$; $Me_4Si$): 21.5 (*C*$H_3$), 23.7 (*C*$H_2$), 26.7 (*C*$H_2$), 28.3 (*C*$H_2$), 29.2 (*C*$H_2$), 37.2 (*C*$H_2$), 46.6 (*C*$H_2$), 50.3 (*C*H), 71.3 (*C*$H_2$), 73.7 (*C*$H_2$), 118.5 (*C*H), 124.3 (2 × overlapping *C*H), 127.0 (2 × *C*H), 129.7 (2 × *C*H), 134.7 (*C*), 137.0 (*C*), 143.2 (*C*); *m*/*z* (EI) 379 ([M+H]$^+$,

34%), 401 (82), 91 (100). Found (LSI-MS): 379.2050 $[M+H]^+$; $C_{20}H_{31}N_2O_3S_1$ requires 379.2055 (1.4 ppm error).

**Synthesis of Dimer 28a.** To a stirred solution of (*R*)-*N*-(2-amino-3-(3-(cyclohexa-1,4-dienyl)propoxy)propyl)-4-methylbenzenesulfonamide **27a** (15 mg, 0.041 mmol) in diethyl ether (1 $cm^3$) was added a 2 M solution of hydrochloric acid in diethyl ether (0.06 $cm^3$, 0.6 mmol). The reaction mixture was stirred for 2 h and concentrated under reduced pressure. To a suspension of the residue in ethanol (2 $cm^3$) was added trihydrated ruthenium trichloride (7 mg, 0.03 mmol). The reaction mixture was stirred at reflux temperature overnight and filtered to give a dark solid. The residue was washed with anhydrous dichloromethane and ethanol to afford the product **28a** as a dark solid (20 mg, 93%). $\nu_{max}/cm^{-1}$ (solid): 814, 1089, 1156, 1325, 1447, 1595, 2342, 2359, 2945, 3052. $\delta_H$(300 MHz; $d_6$-DMSO): 1.82−1.85 (4H, m), 2.40 (6H, s), 2.89−2.91 (4H, m), 3.30−3.51 (14H, m), 5.73−5.78 (6H, m), 5.98−6.02 (4H, m), 7.45 (4H, d, *J* 8.2), 7.71 (4H, d, *J* 8.2), 7.89−7.99 (6H, m). $\delta_C$(100.6 MHz; $d_6$-DMSO): 21.4 ($CH_3$), 28.6 ($CH_2$), 29.3 ($CH_2$), 50.3 (*C*H), 56.1 ($CH_2$), 67.7 ($CH_2$), 70.0 ($CH_2$), 83.4 (*C*H), 85.2 (2 × *C*H), 89.5 (2 × *C*H), 107.9 (*C*), 126.8 (2 × *C*H), 130.2 (2 × *C*H), 136.6 (*C*), 143.2 (*C*). *m*/*z* (FAB+) (nb **28a** is a salt ($C_{38}H_{54}{}^{35}Cl_6N_4O_6{}^{102}Ru_2S_2$), MW = 1140 with dication of MW = 1070) 919, 864, 766, 675, 306, 153, 136. Found (FAB+) 535.013 $[0.5M-{}^{35}Cl]^+$; $C_{19}H_{27}{}^{35}Cl_2N_2O_3{}^{102}RuS$ requires 535.016.

**Synthesis of Dimer 28b.** To a stirred solution of (*R*)-3-[4-(cyclohexa-1,4-dienyl)butoxy]-*N*1-tosylpropane-1,2-diamine **27b** (290 mg, 0.766 mmol) in diethyl ether (3 $cm^3$) was added a 2 M solution of hydrochloric acid in diethyl ether (1.15 $cm^3$, 2.30 mmol). The reaction mixture was stirred for 2 h and concentrated under reduced pressure. To a suspension of the residue in ethanol (6 $cm^3$) was added trihydrated ruthenium trichloride (130 mg, 0.627 mmol). The reaction mixture was stirred at reflux temperature overnight and filtered to give a dark solid. The residue was washed with anhydrous dichloromethane and ethanol to afford **28b** as a dark solid (170 mg, 40% yield). $\nu_{max}/cm^{-1}$ (solid): 851, 1036, 1088, 1258, 1397, 1444, 1474, 2340, 2360, 2497, 2603, 2941, 2977. $\delta_H$-(400 MHz; $d_6$-DMSO): 1.58−1.65 (8H, m), 2.42 (6H, s), 2.93−2.93 (4H, m), 3.29−3.55 (14H, m), 5.75−5.79 (6H, m), 6.00−6.03 (4H, m), 7.45 (4H, d, *J* 8.0), 7.71 (4H, d, *J* 8.0), 7.90−7.96 (6H, m). $\delta_C$(100.6 MHz; $d_6$-DMSO): 21.0 ($CH_3$), 26.9 ($CH_2$), 29.9 ($CH_2$), 33.7 ($CH_2$), 45.4 ($CH_2$), 50.0 (*C*H), 67.2 ($CH_2$), 70.1 ($CH_2$), 83.0 (*C*H), 84.8 (*C*H), 89.0 (*C*H), 108.6 (C), 126.7 (*C*H), 126.8 (*C*H), 128.3 (2 × *C*H), 130.0 (2 × *C*H). *m*/*z* (FAB+) (nb **28a** is a salt ($C_{40}H_{58}{}^{35}Cl_6N_4O_6{}^{102}Ru_2S_2$), MW = 1168 with dication of MW = 1098) 919, 766, 613, 550, 307, 154. Found (ESI) 477.0779 $[0.5M-{}^3HCl]^+$; $C_{20}H_{27}N_2O_3{}^{102}RuS$ requires 549.0319.

**Transfer Hydrogenation: General Procedure in Isopropanol/KOH Using Amino Alcohol-Tethered Catalyst Dimer.** To a suspension of amino alcohol-tethered ruthenium(II) dimer **18 or 19** ($4.25 \times 10^{-3}$ mmol) in anhydrous isopropanol (15 $cm^3$) was added a 0.1 M solution of KOH in isopropanol at 28 °C. The mixture was stirred for 15 min, and then substrate was added (1.7 mmol). The mixture was stirred overnight then hexane (30 $cm^3$) was added. The solution was filtered through silica gel and washed with a 1:1 solution of ethyl acetate/hexane (100 $cm^3$). The solution was concentrated under vacuum to afford the reduction product. Conversions and enantiomeric excesses were determined using chiral GC, conditions for which have been reported in a previous paper.[8]

**Transfer Hydrogenation: General Procedure in Formic Acid/Triethylamine Using Monosulfonated Diamine-Tethered Catalyst Dimer.** A suspension of monosulfonated diamine-tethered ruthenium(II) dimer **23**, **28a**, or **28b** ($12.5 \times 10^{-3}$ mmol) in formic acid/triethylamine 5:2 azeotrope (2.5 $cm^3$) was stirred at 28 °C for 30 min, and then substrate was added (5 mmol). The mixture was stirred overnight, and then hexane (30 $cm^3$) was added. The solution was filtered through silica gel and washed with a 1:1 solution of ethyl acetate/hexane (100 $cm^3$). The solution was concentrated under vacuum to afford the reduction product. Conversions and enantiomeric excesses were determined using chiral GC, conditions for which have been reported in a previous paper.[8]

**Acknowledgment.** We thank the BBSRC and AstraZeneca for a CASE postgraduate studentship (to F.K.C.) and the EPSRC for a project studentship (Grant C000927). We thank Dr B. Stein of the EPSRC National Mass Spectroscopic service (Swansea) for HRMS analysis of certain compounds and Arran Chemical (Ireland) for a generous donation of enantiopure diamines. We acknowledge the use of the EPSRC's Chemical Database Service at Daresbury.[10]

**Supporting Information Available:** General experimental details, synthetic procedures, and characterization data precursor molecules and ketone reductions. This material is available free of charge via the Internet at http://pubs.acs.org.

OM700610Y

(10) ) Fletcher, D. A.; McMeeking, R. F.; Parkin, D. *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 746.