DOI: 10.1002/adsc.200700345

Rhodium-Catalyzed Asymmetric Transfer Hydrogenation of Aryl Alkyl Ketones Employing Ligands Derived from Amino Acids

Jenny Wettergren,[a] Alexey B. Zaitsev,[a] and Hans Adolfsson[a,*]

[a] Department of Organic Chemistry, the Arrhenius Laboratory, Stockholm University, SE-10691 Stockholm, Sweden
Fax: (+46)-8-154-908; e-mail: hansa@organ.su.se

Received: July 13, 2007; Published online: November 21, 2007

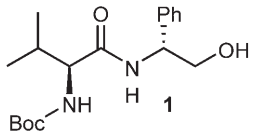
Dedicated to Professor Jan-E. Bäckvall on the occasion of his 60th birthday.

Abstract: The combination of (pentamethylcyclopentadienyl)rhodium dichloride dimer [{$RhCl_2Cp^*$}$_2$] and pseudodipeptide ligands, formed from *N*-Boc protected amino acids and amino alcohols, resulted in efficient and selective catalysts for the asymmetric transfer hydrogenation of ketones in 2-propanol. A number of different secondary alcohols was obtained in high yields and in excellent enantioselectivity using these *in situ* formed catalysts. Deuterium-labeling experiments showed that the hydride transfer reaction occurs *via* the monohydridic route.

Keywords: amino acid ligands; asymmetric transfer hydrogenation; ketones; reductions; rhodium

Introduction

Asymmetric transfer hydrogenation (ATH) employing transition-metal[1–14] or purely organic[15–22] catalysts is a very useful process allowing for enantioselective reduction of prochiral ketones, imines and activated alkenes. This process provides an easy access to enantiomerically enriched chiral compounds and is especially attractive on a laboratory or small industrial scale, since it avoids the use of molecular hydrogen and hence often expensive specialized high pressure equipment. However, further improvement in terms of scope, selectivity and turnover frequency is required to make the process competitive with conventional hydrogenations using molecular hydrogen. Studies uncovering structural features which are essential for high catalytic activity and selectivity are important for facilitating further catalyst design. Ru(II) and Rh(III) half-sandwich complexes are generally thought to form active catalysts for ATH when combined with 1,2-amino alcohols or monotosylated 1,2-diamines, containing a basic primary or secondary amino group in the β-position to a relatively acidic OH or NH group.[23] *N*-Boc-protected amino acid hydroxyamide (in our previous papers and later on in this study referred to as pseudodipeptide) ligands (**1**)[24–29] previously developed by us represent a different class of ligands without an explicit basic nitrogen center. Instead, we have demonstrated that alkali ions play a crucial role in the hydrogen transfer step employing catalysts derived from such ligands.[30] Hence, the combination of a pseudodipeptide ligand with [{$RuCl_2$(*p*-cymene)}$_2$] and alkali base form an efficient catalyst for highly enantioselective ATH of aromatic ketones in 2-propanol. On the other hand, the corresponding rhodium complex [{$RhCl_2Cp^*$}$_2$] in combination with pseudodipeptide **1** gave only 80% *ee* in the



1

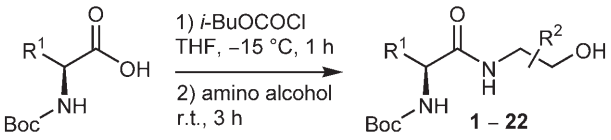
ATH of acetophenone *versus* 95% *ee* obtained with the ruthenium complex.[25]

This result appeared to be in discrepancy with several studies[31–36] on the ATH of aromatic ketones using the [{$RhCl_2Cp^*$}$_2$]-aminoindanol or monotosylated diamine system, where results matching those obtained using the corresponding ruthenium precursor were achieved. Herein we describe how the highly modular nature of pseudodipeptides can be used for fine-tuning of the ligand structure, which has eventually lead to rhodium catalysts giving high conversion and excellent enantioselectivity in the ATH of aromatic ketones.

Results and Discussion

Ligand Synthesis

The pseudodipeptide ligands were prepared in a straightforward fashion from vicinal amino alcohols and *N*-protected amino acids (Scheme 1) according to



R^1 = Me, *i*-Pr, *i*-Bu, *s*-Bu, *t*-Bu, Bn, Ph; R^2 = Me, Ph

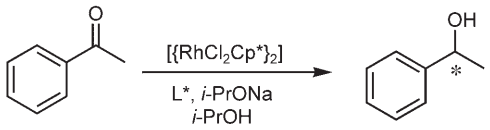
Scheme 1.

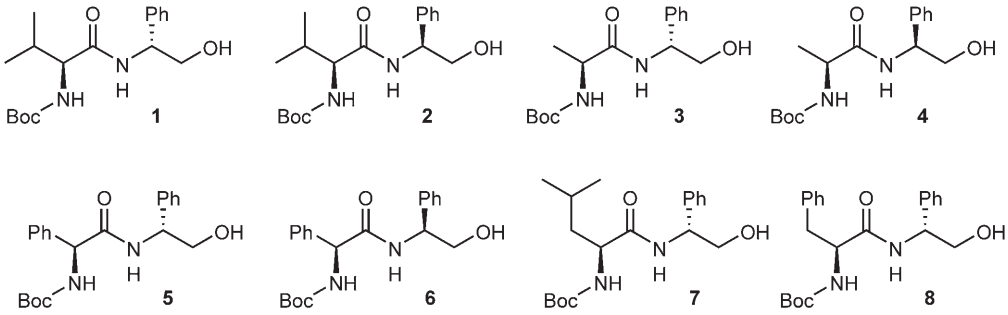
the procedure described previously.[25] Ligands based on amino acid derivatives have previously been studied by several different research groups in transfer hydrogenation processes.[37–49]

Ligand Screening

We decided to exploit the highly modular nature of pseudodipeptides in order to investigate if fine-tuning of the ligand structure can significantly improve the performance of the $[\{RhCl_2Cp^*\}_2]$-pseudodipeptide catalytic system in the ATH of acetophenone. First, we studied the catalytic system using the first-generation pseudodipeptides **1**–**8** (Table 1). A considerably more pronounced matched-mismatched behavior of the ligands in terms of enantioselectivity was observed using the rhodium system as compared to the ruthenium counterpart. For example, diastereomeric ligand pairs **1**, **2** and **3**, **4** gave around 95% *ee* in combination with $[\{RuCl_2(p\text{-cymene})\}_2]$, whereas significantly different enantioselectivities were achieved using the $[\{RhCl_2Cp^*\}_2]$ catalyst precursor (Table 1). The bulkier substituents on the amino acid moiety, the larger was the difference in *ee* obtained on going from one diastereomer to another. Enantioselectivities up to 88% were achieved using the leucine- and phenylalanine-derived ligands **7** and **8**. As observed in the Ru case, the absolute configuration of the product phenylethanol, appeared to be strongly influenced by

Table 1. Effect of structural variations in the first generation pseudodipeptides on the performance of the $[\{RhCl_2Cp^*\}_2]$-pseudodipeptide-catalyzed ATH of acetophenone.[a]

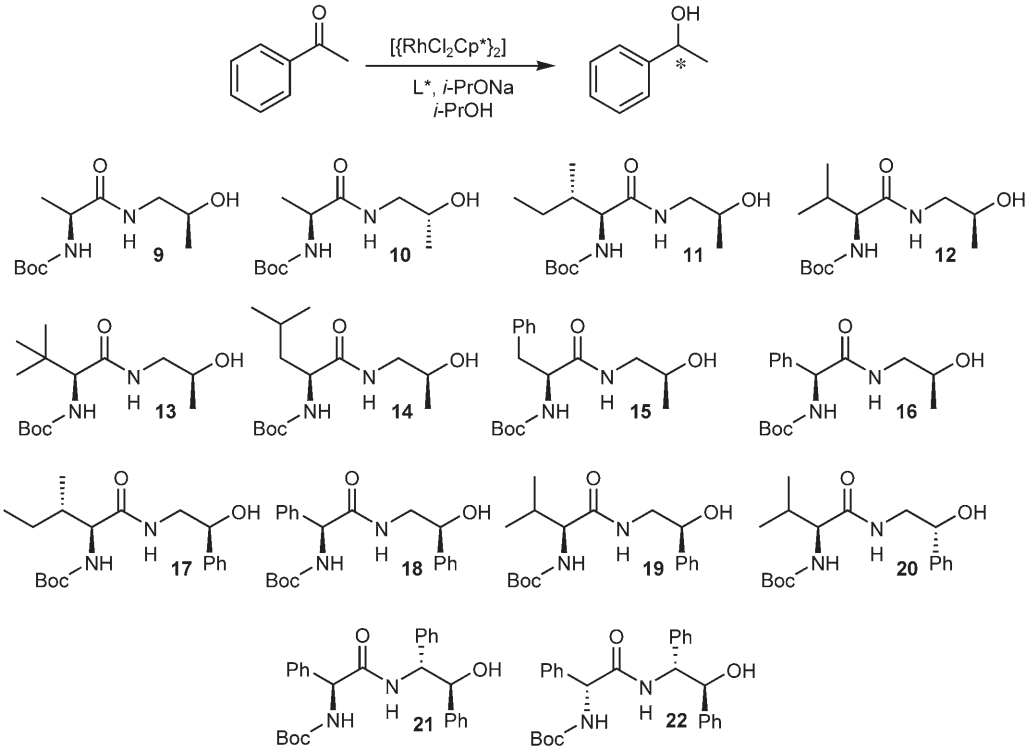




Entry	Ligand	Time [h]	Conversion [%][b]	*ee* [%][b]
1	**1**	2	37	76 (*S*)
2	**2**	2	10	24 (*S*)
3	3	2	86	81 (*S*)
4	**4**	2	42	71 (*S*)
5	**5**	2	56	82 (*S*)
6	**6**	2	42	9 (*S*)
7	**7**	2	79	**88** (*S*)
8	**8**	2	62	**88** (*S*)

[a] *Reaction conditions:* acetophenone (1 equiv., 0.2 M in 2-propanol), $[\{RhCl_2Cp^*\}_2]$ (0.5 mol%), ligand (1.1 mol%) and *i*-PrONa (5 mol%), room temperature.
[b] Conversion and enantioselectivity were determined by GLC (CP Chirasil DEXCB).

Table 2. Effect of structural variations in the second generation pseudodipeptides on the performance of the [{$RhCl_2Cp^*$}$_2$]-pseudodipeptide-catalyzed ATH of acetophenone.[a]



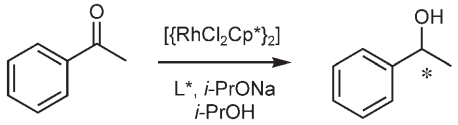
Entry	Ligand	Time [h]	Conversion [%][b]	*ee* [%][b]
1	**9**	0.5[c]	78	92 (*S*)
2	**10**	0.5	41	30 (*S*)
3	**11**	2	**84**	**96** (*S*)
4	**12**	2	**81**	**95** (*S*)
5	**13**	2	68	94 (*S*)
6	**14**	2	84	92 (*S*)
7	**15**	2	**88**	**96** (*S*)
8	**16**	0.5[c]	**89**	**95** (*S*)
9	**17**	2	81	92 (*S*)
10	**18**	0.5[c]	84	92 (*S*)
11	**19**	2	79	88 (*S*)
12	**20**	2	44	29 (*S*)
13	**21**	2	25	22 (*S*)
14	**22**	2	31	62 (*R*)

[a] *Reaction conditions:* acetophenone (1 equiv., 0.2 M in 2-propanol), [{$RhCl_2Cp^*$}$_2$] (0.5 mol%), ligand (1.1 mol%) and *i*-PrONa (5 mol%), room temperature.
[b] Conversion and enantioselectivity were determined by GLC (CP Chirasil DEXCB).
[c] The reaction time had to be decreased due to higher reaction rates leading to a relatively fast achievement of the equilibrium product concentration (*ca.* 91%) and, hence, erosion of the *ee*.

the configuration of the amino acid moiety in the ligand. Thus, the *S*-isomer was obtained regardless of the configuration on the stereogenic center present in the amino alcohol region.

More promising results both in terms of conversion and enantioselectivity were obtained using the second generation pseudodipeptides **9**–**22** (Table 2). Enantioselectivities up to 96% were achieved using ligands **11**, **12**, **15**, **16** prepared from (*S*)-1-amino-2-propanol and isoleucine, valine, phenylalanine and phenylglycine, respectively. The use of the second generation ligands resulted in more active catalysts as compared to their first generation congeners, and in several cases significantly shorter reaction times were required for arriving at high conversions. The increase of steric bulkiness of the substituents in the α-position of the amino acid moiety led to a drop in catalytic activity. The use of ligands derived from (*S*)-2-amino-1-

Table 3. Effect of additives on the [{$RhCl_2Cp^*$}$_2$]-pseudodipeptide-catalyzed ATH of acetophenone.[a]



Entry	Ligand	Additive	Time [h]	Conversion [%][b,c]	*ee* [%][b,c]
1	**9**	LiCl	0.5[c]	84 (78)	88 (92, *S*)
2	**10**	LiCl	0.5	75 (41)	54 (30, *S*)
3	**19**	LiCl	2	88 (79)	80 (88, *S*)
4	**20**	LiCl	2	72 (44)	17 (29, *S*)
5	**3**	LiCl	2	90 (86)	73 (81, *S*)
6	**4**	LiCl	2	81 (42)	70 (71, *S*)
7	**11**	LiCl	2	89 (84)	89 (96, *S*)
8	**11**	LiOAc	2	80	92 (*S*)
9	**11**	15-crown-5	2	39	83 (*S*)
10	**11**	*t*-BuOK[d]	2	77	95 (*S*)

[a] *Reaction conditions:* acetophenone (1 equiv., 0.2 M in 2-propanol), [{$RhCl_2Cp^*$}$_2$] (0.5 mol%), ligand (1.1 mol%) and *i*-PrONa (5 mol%), room temperature.
[b] Conversion and enantioselectivity were determined by GLC (CP Chirasil DEXCB).
[c] The corresponding conversion and enantioselectivity obtained without additives are presented in parentheses.
[d] *t*-BuOK (5 mol%) was used as base instead of *i*-PrONa.

phenylethanol (**17**–**20**) resulted in slightly lower enantioselectivity (Table 1). Surprisingly, ligand **21** for which the phenyl substituents on the amino alcohol part were expected to act in a complimentary fashion (*cf.* ligands **5** and **18**) gave a considerably lower conversion and enantioselectivity as compared to the seemingly doubly mismatched ligand **22**.

Modification of the [{$RhCl_2Cp^*$}$_2$]-pseudodipeptide catalytic system with LiCl was attempted in order to increase enantioselectivity of the process as was previously observed with the analogous [{$RuCl_2$(*p*-cymene)}$_2$] catalyst. Unexpectedly, an opposite behavior was observed with the Rh system. Addition of LiCl to the system led to a significant decrease in enantioselectivity when matched ligands were used, and the opposite was true for mismatched ligands (Table 3 entries 1–7). Such a deviation in the behavior of the Rh and Ru catalytic systems might be due to such intrinsic differences between [{$RhCl_2Cp^*$}$_2$] and [{$RuCl_2$(*p*-cymene)}$_2$] as a higher oxidation state of rhodium and (or) the presence of the negatively charged aromatic Cp* ligand in the Rh complex. These factors may be disadvantageous for the enantiodiscrimination in the transition state involving Li ions. To rule out that the observed behavior of the catalytic system upon lithium chloride addition is not an effect of the halide anion, we performed reductions in the presence of lithium acetate (Table 3, entry 8). The addition of LiOAc resulted in slightly lower conversion to, and enantiomeric excess of 1-phenylethanol, hence in line with the above observations for LiCl additions. This result is further strengthened by the fact that addition of silver triflate to the "standard" catalytic set-up (i.e.. no additional additives) showed no influence on the product enantioselectivity. We can therefore conclude that chloride ions are not directly involved in the enantiodiscriminating step.

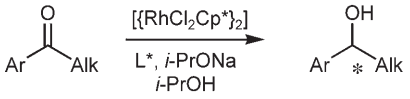
The use of *t*-BuOK as a base only slightly decreases enantioselectivity, whereas complexation of sodium by 15-crown-5 led to a dramatic drop of conversion and enantioselectivity (Table 3, entries 9 and 10). Thus, "un-coordinated" sodium ions seem to be optimal for efficient enantiodiscrimination by the active complex.

Substrate Scope

To assess the practical usefulness of the catalytic system, we evaluated a number of different substrates in ATH in 2-propanol employing the [{$RhCl_2Cp^*$}$_2$]-ligand **15** catalytic system (Table 4), which gave the best results in ATH of acetophenone (see above). High isolated yields and enantioselectivities up to 98% were obtained for most of the substrates studied. Particularly good results were achieved in the case of electron-deficient ketones (entries 1–6). Substrates with electron-releasing substituents provided the same level of enantioselectivity, though the conversions in most cases were somewhat lower due to less favorable position of the equilibrium in reduction with 2-propanol (entries 10–12).

4-Cyanoacetophenone reacted significantly slower, as compared to other electron-deficient ketones, and provided low enantioselectivity (entry 7). This behav-

Table 4. Substrate scope of the [{$RhCl_2Cp^*$}$_2$]-catalyzed transfer hydrogenation using pseudodipeptide **15** as ligand.[a]



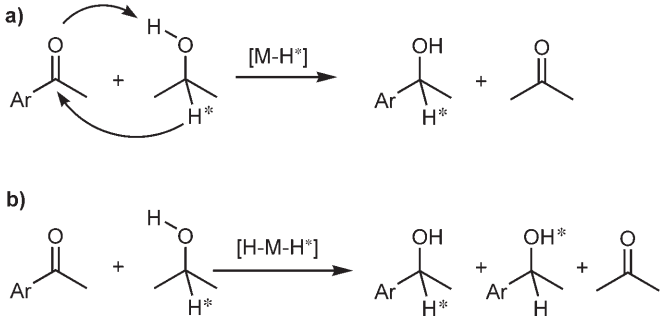
Entry	Ar	Alk	Time [h]	Conversion [%][b]	Isolated yield [%]	*ee* [%][b]
1	3′-CF_3-C_6H_4	Me	2	98	83	96 (*S*)
2	4′-CF_3-C_6H_4	Me	2	93	87	95 (*S*)
3	3′-Br-C_6H_4	Me	1	93	91	97 (*S*)
4	4′-Br-C_6H_4	Me	2	98	93	94 (*S*)
5	2′-F-C_6H_4	Me	2	72	63	90 (*S*)
6	3′-Pyridyl	Me	2	96	95	94 (*S*)
7	4′-CN-C_6H_4	Me	2	48	-	61 (*S*)
8	Ph	Me	2	72	71	97 (*S*)
9	Ph	Et	2	63	58	95 (*S*)
10	4′-Me-C_6H_4	Me	2	57	53	97 (*S*)
11	3′-MeO-C_6H_4	Me	2	75	74	98 (*S*)
12	3′,4′-dimethoxyphenyl	Me	2	46	-	95 (*S*)

[a] *Reaction conditions:* acetophenone (1 equiv., 0.2 M in 2-propanol), [{$RhCl_2Cp^*$}$_2$] (0.5 mol%), ligand (1.1 mol%) and *i*-PrONa (5 mol%), room temperature.
[b] Conversion and enantioselectivity were determined by GLC (CP Chirasil DEXCB).

ior might be due to a relatively high affinity of the cyano substituent to the rhodium center, which can compete with the substrate carbonyl group and the pseudodipeptide ligand in coordination to the active catalyst. The occurrence of such coordination obviously leads to the formation of less selective catalytic species. Attempts to reduce alkyl alkyl ketones resulted in poor conversion and in low stereoselectivity. Thus, the quest to find an efficient and selective catalyst system for this considerably more challenging substrate class remains.

Mechanistic Considerations

Transition metal-catalyzed hydrogen transfer reactions are typically progressing *via* either of two different hydridic mechanisms, the monohydridic route (Scheme 2a) or the dihydridic route (Scheme 2b).[50]

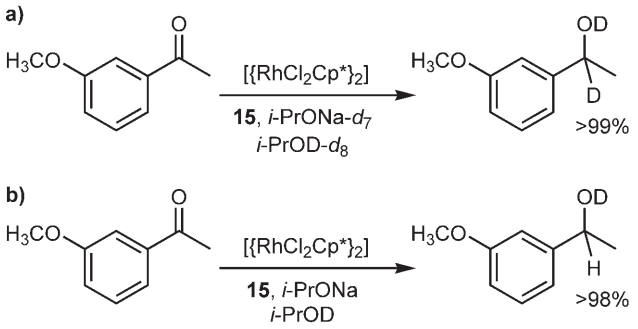


Scheme 2. Reaction outcome in transfer hydrogenations. a) Monohydridic route. b) Dihydridic route.

In the monohydridic route, the intermediate metal hydride forms *via* abstraction of a hydrogen atom from the carbon on the donor, and the hydride is subsequently transferred exclusively to the carbonyl carbon of the acceptor. When the dihydridic route is operating, the hydrogen atoms which are transferred from the donor completely loose their identity since both the "hydride" and the "proton" end up coordinating to the metal. Consequently, the transfer of hydrides from the intermediate metal dihydride to the acceptor occurs with complete scrambling and no prediction on the origin of a specific hydrogen atom can be made.

To investigate which of the two proposed mechanisms is operating in the [{$RhCl_2Cp^*$}$_2$]-pseudodipeptide catalyst system, we performed a number of experiments using deuterium-labeled 2-propanol. In an initial experiment we carried out the reduction of acetophenone in fully deuterium labeled 2-propanol, which resulted in the incorporation of deuterium in the former carbonyl carbon as well as in the α-methyl group of the substrate. The incorporation of deuterium atoms in the methyl group is probably the result of a simple acid-base reaction involving the intermediate enol or enolate of the ketone. The deuterium exchange in the α-methyl group turned out to be problematic, since that particular methyl group is the natural "^{1}H NMR marker" to which the level of deuterium or hydrogen addition to the carbonyl carbon is compared. The analysis of the reaction outcome using differently deuterium-labeled 2-propanols would therefore be significantly more difficult when such a "side-reaction" can occur. To overcome this problem we instead performed transfer hydrogenations on 3′-methoxyacetophenone. This particular substrate con-

tains an additional methyl group in which no deuterium exchange can take place, and a simple analysis of the reaction outcome can therefore accurately be made even if deuterium atoms end up in the α-methyl group of the substrate. Thus, when 3′-methoxyacetophenone was subjected to the reduction using the [{$RhCl_2Cp^*$}$_2$]-pseudodipeptide catalyst system in 2-propanol-d_8 we obtained, as expected, a product with the exclusive incorporation of deuterium in the former carbonyl group (Scheme 3 a).[51] Changing the



Scheme 3. Deuterium incorporation into 3′-methoxyacetophenone. **a)** Reaction performed in 2-propanol-d_8. **b)** Reaction performed in 2-PrOD.

solvent to 2-propanol-d_1 where the only deuterium is situated on the hydroxy group (2-PrOD), otherwise keeping the reaction conditions unchanged, resulted in the almost exclusive formation (>98%) of a product containing a hydrogen atom on the former carbonyl carbon (Scheme 3 b). The absence of deuterium incorporation on the carbonyl carbon in the latter experiment strongly suggests that the reaction follows the monohydridic route. We can therefore conclude that the ketone reduction occurs *via* a hydride transfer from the rhodium metal and a proton or alkali transfer from the ligand (*cf.* the mechanistic suggestion presented in ref.[32]). Attempts to isolate rhodium complexes containing pseudodipeptide ligands have so far been unsuccessful and we cannot therefore provide further details on the catalyst structure.

Conclusions

We have demonstrated that the modular nature of pseudodipeptides effectively could be used for fine-tuning of the structure of novel rhodium catalysts, and thereby obtain a highly selective ATH process for aromatic ketones in 2-propanol. High conversions (isolated yields) and enantioselectivities up to 98% were obtained using the [{$RhCl_2Cp^*$}$_2$] catalyst precursor in combination with pseudodipeptide ligands derived from (*S*)-1-amino-propan-2-ol and isoleucine, valine, phenylalanine or phenylglycine, respectively. The performance of the rhodium system is comparable with the corresponding [{$RuCl_2$(*p*-cymene)}$_2$] system. However, in each of the systems there are different structural requirements on the ligand for obtaining high catalytic activity and selectivity. The addition of lithium salts to the rhodium catalytic system causes a decrease in enantioselectivity with matched ligands, which is in contrast to the behavior of the ruthenium counterpart. In comparison to other catalytic transfer hydrogenations systems based on [{$RhCl_2Cp^*$}$_2$] (i.e., protocols using 1,2-aminoindanol or TsCYDN/TsDPEN ligands) with 2-propanol as hydrogen source, the herein described method gives better enantioselectivity than the 1,2-aminoindanol protocol for the reduction of aryl alkyl ketones. Moreover, the use of pseudodipeptide ligands gives catalysts with significantly higher activity in comparison to the TsCYDN/TsDPEN system. The high modularity of the pseudodipeptide ligand system, along with the low cost for ligand production represents additional advantages. In conclusion, the [{$RhCl_2Cp^*$}$_2$]-pseudodipeptide catalytic system, which operates via the monohydridic route, has a wide substrate scope that allows for high conversions and enantioselectivities in ATH of various aromatic ketones in 2-propanol.

Experimental Section

General Procedure for the Synthesis of Ligands 1–22

N-Methylmorpholine (NMM, 1.1 mmol) and isobutyl chloroformate (1 mmol) were slowly added to a solution of *N*-Boc-amino acid (1 mmol) in THF (5 mL) cooled to −15 °C (a white solid was formed upon the addition of *i*-BuO-COCl). The reaction mixture was stirred for 1 h at −15 °C, and then an amino alcohol (1 mmol) was added and the resulting mixture was stirred at room temperature for an additional 3 h. The mixture was filtered through a plug of silica (3×4 cm) and eluted with ethyl acetate (80 mL). The solvent was evaporated under vacuum to give a pure product. For spectroscopic characterization of the synthesized ligands see refs.[25,26, 29]

General Procedure for the Transfer Hydrogenation of Ketones Employing Ligands 1–22

Ligand (0.011 mmol) and [{$RhCl_2Cp^*$}$_2$] (0.005 mmol) were dried under vacuum in a dry Schlenk tube for 15 min. 2-Propanol (4.5 mL), substrate (1 mmol) and a 0.1 M solution of *i*-PrONa (0.5 mL, 5 mol%) in *i*-PrOH were added under nitrogen. The reaction mixture was stirred at ambient temperature. Aliquots were taken after the reaction times indicated in the Tables and were then passed through a pad of silica using EtOAc as eluent. The resulting solutions were analyzed by GLC (CP Chirasil DEXCB). The isolated yields were obtained from reactions performed on a 5-mmol scale of substrate. Column chromatography on silica was used for isolation of the reaction products. For chromatographic and spectroscopic characterization of the reaction products see refs.[25, 26,29]

Acknowledgements

The Swedish Research Council, the Carl Trygger Foundation and the Wenner-Gren Foundations are thanked for financial support and postdoctoral fellowship, respectively.

References

[1] G. Zassinovich, G. Mestroni, S. Gladiali, *Chem. Rev.* **1992**, *92*, 1051.
[2] C. Bianchini, L. Glendenning, *Chemtracts* **1997**, *10*, 333.
[3] R. Noyori, S. Hashiguchi, *Acc. Chem. Res.* **1997**, *30*, 97.
[4] T. Ohkuma, R. Noyori, in: *Comprehensive Asymmetric Catalysis*, Vol. 1, (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer-Verlag, Berlin, **1999**; p 199.
[5] M. J. Palmer, M. Wills, *Tetrahedron: Asymmetry* **1999**, *10*, 2045.
[6] H.-U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner, M. Studer, *Adv. Synth. Catal.* **2003**, *345*, 103.
[7] K. Everaere, A. Mortreux, J.-F. Carpentier, *Adv. Synth. Catal.* **2003**, *345*, 67.
[8] S. Gladiali, E. Alberico, in: *Transition Metals for Organic Synthesis*, Vol. 2, (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **2004**, p 145.
[9] M. Kitamura, R. Noyori, in: *Ruthenium in Organic Synthesis*, (Ed.: S.-I. Murahashi), Wiley-VCH, Weinheim, **2004**, p 3.
[10] T. Ohkuma, R. Noyori, *Comprehensive Asymmetric Catalysis Supplement*, (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer Verlag, Berlin, **2004**, Vol. 1, p 43.
[11] A. Zanotti-Gerosa, W. Herns, M. Groarke, F. Hancock, *Platinum Met. Rev.* **2005**, *49*, 158.
[12] K. Muñiz, *Angew. Chem. Int. Ed.* **2005**, *44*, 6622.
[13] S. Gladiali, E. Alberico, *Chem. Soc. Rev.* **2006**, *35*, 226.
[14] T. Ikariya, K. Murata, R. Noyori, *Org. Biomol. Chem.* **2006**, *4*, 393.
[15] W. J. Yang, M. T. Hechavarria Fonseca, N. Vignola, B. List, *Angew. Chem. Int. Ed.* **2004**, *43*, 108.
[16] W. J. Yang, M. T. Hechavarria Fonseca, B. List, *Angew. Chem. Int. Ed.* **2004**, *43*, 6660.
[17] S. Hoffmann, A. M. Seayad, B. List, *Angew. Chem. Int. Ed.* **2005**, *44*, 7424.
[18] J. Rosen, *Chemtracts* **2005**, *18*, 65.
[19] S. G. Ouellet, J. B. Tuttle, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 32.
[20] M. Rueping, E. Sugiono, C. Azap, T. Theissmann, M. Bolte, *Org. Lett.* **2005**, *7*, 3781.
[21] H. Adolfsson, *Angew. Chem. Int. Ed.* **2005**, *44*, 3340.
[22] M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem. Int. Ed.* **2006**, *45*, 3683.
[23] Tuning the acidities by a subtle change in the ligand structure sometimes result in a dramatic change of enantioselectivity as was observed in: A. B. Zaitsev, H. Adolfsson, *Org. Lett.* **2006**, *8*, 5129.
[24] I. M. Pastor, P. Västilä, H. Adolfsson, *Chem. Commun.* **2002**, 2046.
[25] I. M. Pastor, P. Västilä, H. Adolfsson, *Chem. Eur. J.* **2003**, *9*, 4031.
[26] A. Bøgevig, I. M. Pastor, H. Adolfsson, *Chem. Eur. J.* **2004**, *10*, 294.
[27] P. Västilä, J. Wettergren, H. Adolfsson, *Chem. Commun.* **2005**, 4039.
[28] A. S. Y. Yim, M. Wills, *Tetrahedron* **2005**, *61*, 7994.
[29] J. Wettergren, A. Bøgevig, M. Portier, H. Adolfsson, *Adv. Synth. Catal.* **2006**, *348*, 1277.
[30] P. Västilä, A. B. Zaitsev, J. Wettergren, T. Privalov, H. Adolfsson, *Chem. Eur. J.* **2006**, *12*, 3218.
[31] J. Blacker, B. Mellor, *World Patent* WO9842643, **1997**.
[32] K. Murata, T. Ikariya, R. Noyori, *J. Org. Chem.* **1999**, *64*, 2186.
[33] X. Sun, G. Manos, J. Blacker, J. Martin, A. Gavriilidis, *Org. Process Res. Dev.* **2004**, *8*, 909.
[34] D. G. Blackmond, M. Ropic, M. Stefinovic, *Org. Process Res. Dev.* **2006**, *10*, 457.
[35] D. S. Matharu, D. J. Morris, A. M. Kawamoto, G. J. Clarkson, M. Wills, *Org. Lett.* **2005**, *7*, 5489.
[36] X. Wu, D. Vinci, T. Ikariya, J. Xiao, *Chem. Commun.* **2005**, 4447.
[37] T. Ohta, S.-I. Nakahara, Y. Shigemura, K. Hattori, I. Furukawa, *Chem. Lett.* **1998**, 491.
[38] D. Carmona, F. J. Lahoz, R. Atencio, L. A. Oro, M. P. Lamata, F. Viguri, E. San José, C. Vega, J. Reyes, F. Joó, Á. Kathó, *Chem. Eur. J.* **1999**, *5*, 1544.
[39] Á. Kathó, D. Carmona, F. Viguri, C. D. Remacha, J. Kovács, F. Joó, L. A. Oro, *J. Organomet. Chem.* **2000**, *593–594*, 299.
[40] T. Ohta, S.-I. Nakahara, Y. Shigemura, K. Hattori, I. Furukawa, *Appl. Organomet. Chem.* **2001**, *15*, 699.
[41] J. W. Faller, A. R. Lavoie, *Organometallics* **2001**, *20*, 5245.
[42] H. Y. Rhyoo, Y. A. Yoon, H. J. Park, Y. K. Chung, *Tetrahedron Lett.* **2001**, *42*, 5045.
[43] H. Y. Rhyoo, H.-J. Park, Y. K. Chung, *Chem. Commun.* **2001**, 2064.
[44] D. Carmona, M. P. Lamata, F. Viguri, I. Dobrinovich, F. J. Lahoz, L. A. Oro, *Adv. Synth. Catal.* **2002**, *344*, 499.
[45] D. Carmona, J. Ferrer, E. Lalaguna, M. Lorenzo, F. J. Lahoz, S. Elipe, L. A. Oro, *Eur. J. Inorg. Chem.* **2002**, 259.
[46] H. Y. Rhyoo, H.-J. Park, W. H. Suh, Y. K. Chung, *Tetrahedron Lett.* **2002**, *43*, 269.
[47] P. Pelagatti, M. Carcelli, F. Calbiani, C. Cassi, L. Elviri, C. Pelizzi, U. Rizzotti, D. Rogolino, *Organometallics* **2005**, *24*, 5836.
[48] W. Hoffmueller, H. Dialer, W. Beck, *Z. Naturforsch., B: Chem. Sci.* **2005**, *60*, 1278.
[49] P. Pelagatti, A. Bacchi, F. Calbiani, M. Carcelli, L. Elviri, C. Pelizzi, D. Rogolino, *J. Organomet. Chem.* **2005**, *690*, 4602.
[50] For an excellent review on hydrogen transfer mechanisms, see: J. S. M. Samec, J.-E. Bäckvall, P. G. Andersson, P. Brandt, *Chem. Soc. Rev.* **2006**, *35*, 237.
[51] The reductions of 3′-methoxyacetophenone in deuterium-labeled 2-propanol were performed as described in the general procedure presented in the Experimental Section, however, the catalyst loading was increased to 2 mol% and we used *t*-BuONa instead of *i*-PrONa as base.

