Tetrahedron: *Asymmetry* 21 (2010) 703–710

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

A modular design of ruthenium(II) catalysts with chiral C_2-symmetric phosphinite ligands for effective asymmetric transfer hydrogenation of aromatic ketones

Murat Aydemir *, Nermin Meric, Akın Baysal, Bahattin Gümgüm, Mahmut Toğrul, Yılmaz Turgut

Department of Chemistry, Dicle University, TR-21280 Diyarbakır, Turkey

ARTICLE INFO

Article history:
Received 2 March 2010
Accepted 6 April 2010
Available online 11 May 2010

ABSTRACT

Hydrogen-transfer reduction processes are attracting increasing interest from synthetic chemists in view of their operational simplicity. The new chiral C_2-symmetric ligands *N,N′*-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **1** and *N,N′*-bis-[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)-ethyl]ethanediamide, **2** and the corresponding ruthenium complexes **3** and **4** have been prepared and their structures have been elucidated by a combination of multi-nuclear NMR spectroscopy, IR spectroscopy, and elemental analysis. ^{1}H–^{31}P NMR, DEPT, ^{1}H–^{13}C HETCOR, or ^{1}H–^{1}H COSY correlation experiments were used to confirm the spectral assignments. The catalytic activity of complexes **3** and **4** in transfer hydrogenation of acetophenone derivatives by *iso*-PrOH has also been studied. Under optimized conditions, these chiral ruthenium complexes serve as catalyst precursors for the asymmetric transfer hydrogenation of acetophenone derivatives in *iso*-PrOH and act as excellent catalysts, giving the corresponding chiral alcohols in 99% yield and up to 75% ee. This transfer hydrogenation is characterized by low reversibility under these conditions.

1. Introduction

Among the most spectacular recent developments in catalytic asymmetric synthesis, asymmetric transfer hydrogenation is an attractive method for the preparation of optically active alcohols.[1] Chiral alcohols are very important building blocks and synthetic intermediates in organic synthesis and the pharmaceutical industry.[2] Catalytic reduction is preferred to stoichiometric reduction for large-scale industrial processes involving ketone hydrogenations and they are well known.[3] Hydrogen gas presents considerable safety hazards especially for large-scale reactions.[4] The use of a solvent that can donate hydrogen overcomes these difficulties. 2-propanol is a popular reactive solvent for transfer hydrogenation reactions since it is easy to handle (bp 82 °C) and is relatively nontoxic, environmentally benign, and inexpensive.

In general, the most successful chiral ligands used in asymmetric hydrogenation reactions are rigid chelating diphosphines possessing a C_2-symmetry axis thus reducing the number of diastereomeric transition states.[5] In addition, most of them bear at least two aryl substituents on their phosphorus atoms. If one analyzes the structures of these ligands,[6] several design principles can be identified which might lead to good enantiocontrol. Generally speaking, these measures create the necessary flexibility of the ligand to give high turnover rates and impart sufficient rigidity to control stereoselectivity. It has to be stressed that there are always examples where just the opposite is true. A ligand is more likely to induce high enantioselectivity if it has a C_2 symmetry[7] (first example: diop) or is very strongly unsymmetrical[8] (e.g., josiphos) in order to reduce the number of possible isomeric catalyst–substrate complexes.

Phosphine ligands have found wide-spread applications in transition metal-catalyzed asymmetric transformations.[9] Phosphinites provide different chemical, electronic, and structural properties compared to phosphines. The metal–phosphorus bond is often stronger for phosphinites compared to the related phosphine due to the presence of electron-withdrawing P-OR group. In addition, the empty σ^*-orbital of the phosphinite $P(OR)R_2$ is stabilized and it makes the phosphinite a better acceptor.[10] The most important advantage of chiral phosphinite ligands over the corresponding phosphine ligands is the easiness of preparation. From a practical standpoint, it is of substantial interest to develop highly effective chiral phosphinite ligands for asymmetric catalysis. The excellent catalytic performance of phosphinite-based transition metal complexes[11] prompted us to develop new Ru(II) complexes with well-shaped ligands. On this subject, herein, we report the synthesis and characterization of new C_2-symmetric chiral phosphinite ligands *N,N′*-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl] ethanediamide, **1** and *N,N′*-bis-[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **2** and corresponding Ru(II) complexes **3** and **4**. These compounds were also fully characterized by elemental analysis, FT-IR, and multi-nuclear NMR spectroscopies. We also report the catalytic activity of ruthenium(II) complexes as a

* Corresponding author.
E-mail address: aydemir@dicle.edu.tr (M. Aydemir).

0957-4166/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2010.04.002

pre-catalyst in asymmetric transfer hydrogenation reactions of acetophenone derivatives with *iso*-PrOH.

2. Results and discussion

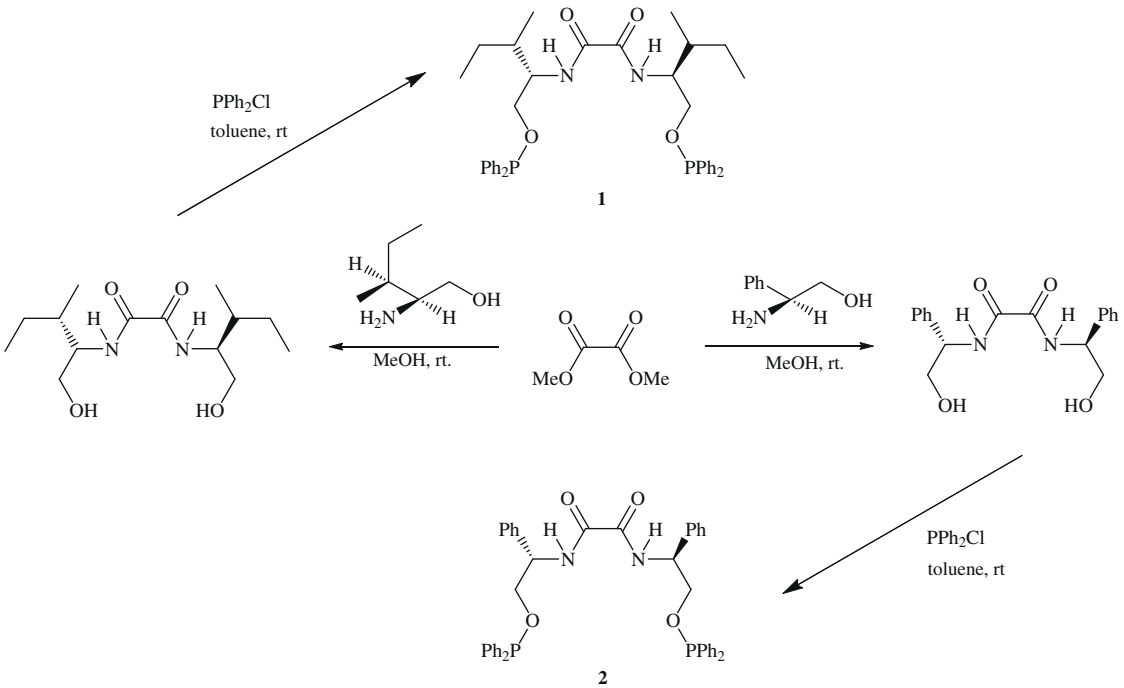
2.1. Synthesis of chiral ligands, 1 and 2 and their corresponding Ru(II) complexes

The synthetic procedure for the preparation of the ligands is shown in Scheme 1. Bis(phosphinite) ligands, *N,N′*-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **1**, and *N,N′*-bis-[(1*S*)-1-phenyl-2-*O,O′*-(diphenylphosphinite)ethyl]ethanediamide, **2** were synthesized by hydrogen abstraction from the described chiral bis(aminoalcohol) oxalamides *N,N′*-bis[(1*S*)-1-*sec*-butyl-2-hydroxyethyl]ethanediamide and *N,N′*-bis[(1*S*)-1-phenyl-2-hydroxyethyl]ethanediamide, respectively, by a base (Et_3N) and the subsequent reaction with 2 equiv of chlorodiphenylphosphine, in anhydrous toluene and inert atmosphere (Ar). The ammonium salt was separated by filtration and the ligands were obtained in high yields (91% **1** and 95% **2**, respectively).

The air sensitivity of the free ligands **1** and **2** is a limitation. Both compounds are unstable in air and decompose rapidly on exposure to air or moisture. So, the synthesis and isolation of the products must be carried out with rigorous exclusion of air, in order to avoid oxidation of the phosphinite groups. The $^{31}P–\{^1H\}$ NMR spectra of compounds **1** and **2** show single resonances due to phosphinite at 116.17 and 117.44 ppm, respectively, indicating the symmetric nature of the molecules (Fig. 1). Our results agree with the chemical shifts for other phosphinites reported in the literature[12] The $^{31}P–\{^1H\}$ NMR spectra also display formation of PPh_2PPh_2 and $P(O)Ph_2PPh_2$, as indicated by signals at about δ −14.0 ppm as singlet and δ 36.4 ppm and δ −22.8 ppm as doublets with $^1J_{(PP)}$ 226 Hz, respectively.[13] ^1H NMR spectral data **1** and **2** are consistent with the structures proposed. Furthermore, in the ^{13}C NMR spectra of all phosphinite ligands prepared showed characteristic $J_{(31P\text{-}13C)}$ coupling constants of the carbons of the phenyl rings (including *i*-, *o*-, *m*-, and *p*-carbons of phenyl rings, consistent with the literature data.[14]

The starting ruthenium(II) complex was [Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$, which was prepared from the reaction of the commercially available α-phellandrene (5-isopropyl-2-methylcyclohexa-1,3-diene) with $RuCl_3$.[15] The whole reactions with [Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$ with ligands **1** and **2** are depicted in Scheme 2. The reactions of [Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$ with 2 equiv of **1** and **2** in toluene at room temperature gave the red compounds **3** and **4** in high yields.

The reactions between Ru(II) precursor and bis(phosphinite) ligands, **1** and **2** are not affected by the molar ratio of [Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$ as well as the steric and electronic properties of the donor phosphorus atoms. The initial color change, that is, from clear orange to deep red, can be attributed to the dimer cleavage most probably by the bis(phosphinite) ligand.[16] [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl] ethanediamide))]chloride, **3** and [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide))] chloride, **4** were isolated as indicated by singlets in the $^{31}P–\{^1H\}$ NMR spectra at (δ) 115.69 and 116.28 ppm, respectively, in line with the values previously observed for similar compounds (Fig. 1).[17] It is significant to remark that $^{31}P–\{^1H\}$ NMR signals of ligands and complexes do not differ significantly.[18] These complexes are highly soluble CH_2Cl_2 and slightly in hexane and they can be crystallized from CH_2Cl_2/hexane solutions. The structure of the P-coordinated complexes **3** and **4** is supported by elemental analyses and spectroscopic data (IR and ^1H and ^{13}C NMR). ^1H NMR spectral data of complexes are consistent with the structures proposed and their ^1H NMR spectra differ from the spectra of compounds **1** and **2**. ^1H NMR spectra of complexes display signals of the η^6-*p*-cymene ligand together with the resonances of the hydrogens of the P-coordinated ligands. The arene signals are well resolved and show only H–H coupling, as found in the previously reported mononuclear η^6-*p*-cymene compounds.[19] Furthermore, in the ^1H NMR spectra, **3** and **4** are characterized by isopropyl methyl doublets of *p*-cymene groups, at δ 1.05 ppm (d, 6H,



Scheme 1. Synthesis of the *N,N′*-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide **1** and *N,N′*-bis-[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl] ethanediamide **2**.

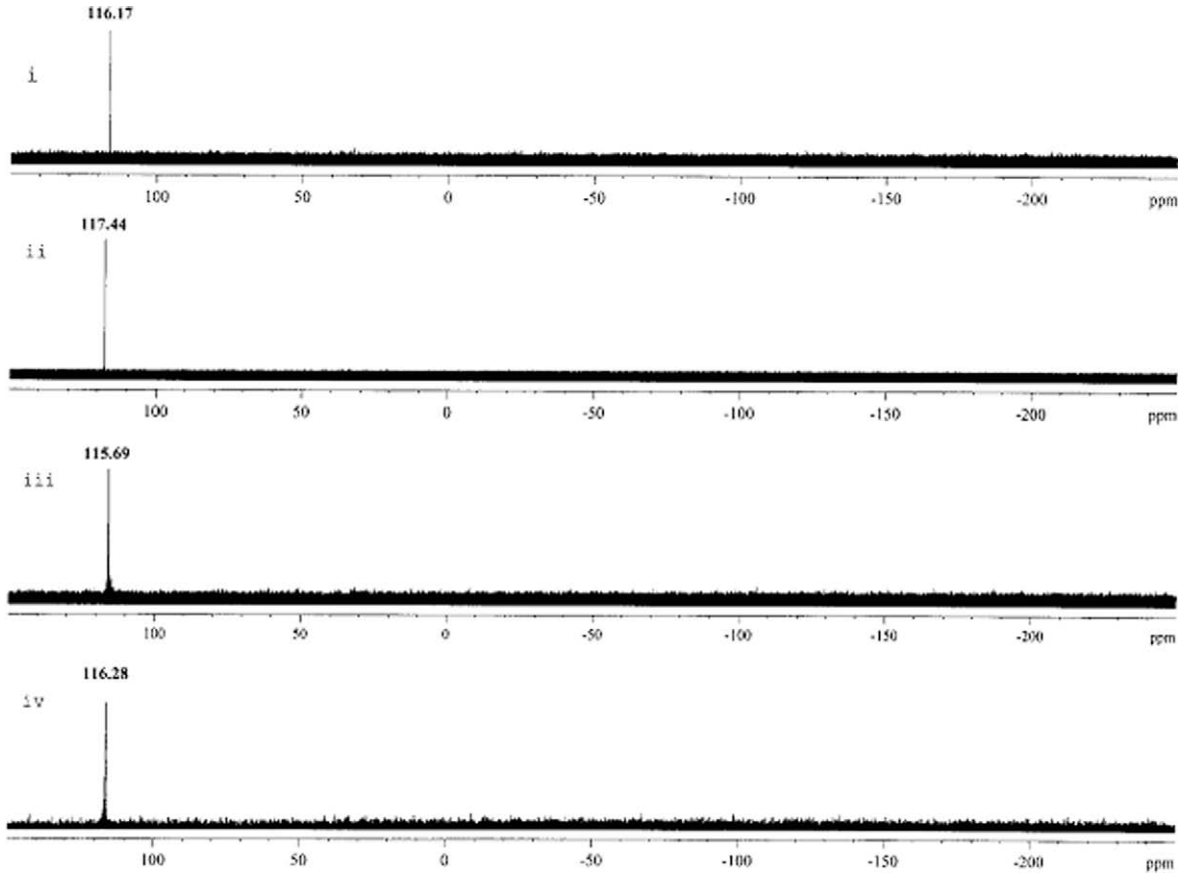
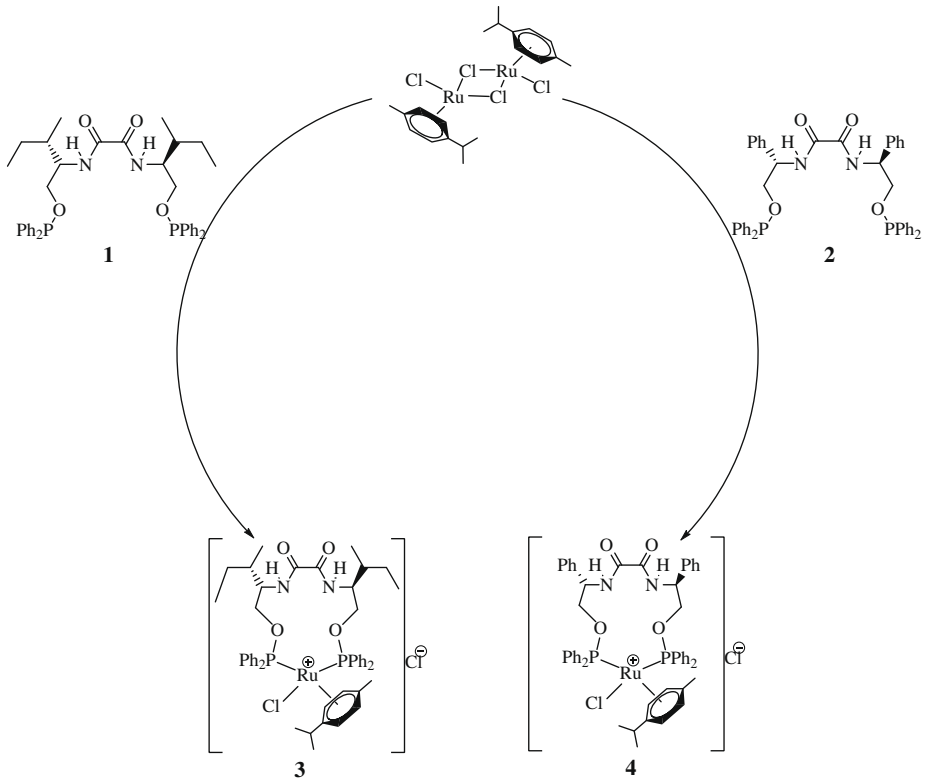


Figure 1. The $^{31}P-\{^{1}H\}$ NMR spectra of complexes; (i) *N,N′*-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide; (ii) *N,N′*-bis-[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite) ethyl]ethanediamide; (iii) [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide))]chloride; (iv) [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide))]chloride.

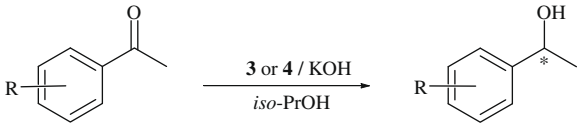


Scheme 2. Synthesis of the Ru{chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)}] **3** and [Ru{chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)}] **4**.

J = 6.8 Hz) and 1.06 ppm (d, 6H, J = 7.2 Hz), respectively. In the $^{13}C–\{^1H\}$ NMR spectra of compounds **3** and **4**, $J(^{31}P–^{13}C)$ coupling constants of the carbons of the phenyl rings were observed, which are consistent with the literature values.[20] In the compounds **3** and **4**, the coupling between *i*-carbons and the phosphorus is relatively large, $^1J(PC)$ 49.3 and 50.3 Hz, while the coupling between *o*-carbon and the phosphorus is relatively small $^2J(PC)$ 15.4; 22.0 and 12.1; 14.2 Hz, respectively. The most relevant signals of $^{13}C–\{^1H\}$ NMR spectra of complexes **3** and **4** are those corresponding to arene ligands (*p*-cymene). Carbon atoms of the arene rings in *p*-cymene ligands are observed as four signals at 87.19, 88.30, 89.87, and 88.13 ppm in complex **3** and 87.68, 88.05, 89.81, and 90.30 ppm in complex **4**.

2.2. Asymmetric transfer hydrogenation of prochiral ketones

In a preliminary study, the synthesized complexes **3** and **4** were evaluated as a precursor for the catalytic transfer hydrogenation of the acetophenone by *iso*-PrOH/KOH as a reducing system. In all the reactions, these complexes catalyzed the reduction of acetophenone to the 1-phenylethanol via hydrogen transfer from *iso*-PrOH (Scheme 3) and the results are summarized in Table 1.



R: H, 4-F, 4-Cl, 4-Br, 2-CH_3O, 4-CH_3O

Scheme 3. Hydrogen transfer from *iso*-PrOH to acetophenone derivatives.

Based on our results, these complexes catalyzed the reduction of acetophenone to corresponding alcohol ((*R*)- or (*S*)-1-phenylethanol) with KOH as a promoter. At room temperature, transfer hydrogenation of acetophenone occurred very slowly[21] with low conversion (3% after 1 h, entries 1 and 2) in all the reactions. But, at 50 °C (Table 1, entries 3 and 4), this reaction of acetophenone occurred slowly with high conversion (<98% after 70 h) and high enantioselectivity (up to 73% ee). In addition, the ees do not vary with the time, as indicated by the catalytic results collected with **3** and **4.** Reduction of acetophenone into 1-phenylethanol could be achieved in high yield by increasing the temperature up to 82 °C. The negligible catalytic activity of $[Ru(p\text{-cymene})Cl_2]_2$ was observed under the applied experimental conditions.[22] It should be also pointed out that complexes **3** and **4** are more active catalyst than the corresponding precursor: $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-}Cl)Cl]_2$ (41% maximum yield in 24 h) with a 1/14 complex/NaOH ratio.[23] When the temperature was increased to 82 °C smooth reduction of acetophenone into 1-phenylethanol occurred with conversion ranging from 65% to 67% after 30 min for **3** and **4**. The catalytic activities of **3** and **4** are comparable, with the TOF values referred to 30 min of 130 h^{-1} and 134 h^{-1}, respectively. These reactions were carried out under Ar atmosphere at 82 °C and reached the maximum conversion within 1 h (Table 1, entries 5 and 6). In these cases conversions higher than 30% have always been obtained (TOFs up to 120 h^{-1}), indicating that the reactions start immediately after the addition of base without any induction time. Furthermore, as can be inferred from Table 1 (entries 7 and 8), the precatalysts and the presence of base are necessary to observe appreciable conversions and the absence of base leads to the deactivation of the catalysts.[24] The choice of base, such as KOH and NaOH, had little influence on the conversion or enantioselectivity. The base facilitates the formation of ruthenium alkoxide by abstracting proton of the alcohol and subsequently alkoxide undergoes β-elimination to give ruthenium hydride, which is an active species in this reaction. This is the mechanism proposed by several workers on the studies of ruthenium-catalyzed transfer hydrogenation reaction by metal hydride intermediates.[25] In addition, optimization studies of the catalytic reduction of acetophenone in *iso*-PrOH showed that good activity was obtained with a base/cat. ratio of >5:1. Although the yields gradually decreased on increasing the mole ratios of [acetophenone]/[Ru] from 100/1 to 500/1 or 1000/1, the enantioselectivity was still high (Table 1, entries 9–12). That is to say, the ee remained unchanged when the molar ratio of substrate to catalyst was increased.

Table 1
Transfer hydrogenation of acetophenone with *iso*-PrOH catalyzed by [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide))] chloride, **3**, and [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethane diamide))] chloride, **4**

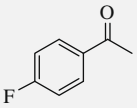
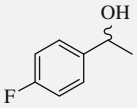
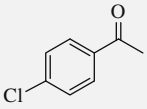
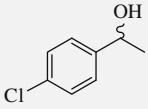
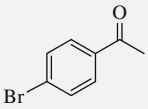
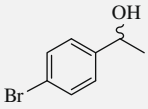
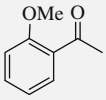
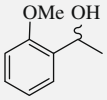
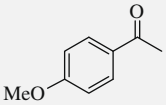
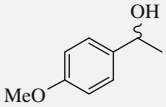
Entry	Catalyst	s/c	Time	Conversion (%)[i]	ee[j] %	Configuration[k]	TOF[l] (h^{-1})
1	3[a]	100:1	1 h	<3	—	—	—
2	4[a]	100:1	1 h	<3	—	—	—
3	3[b]	100:1	48 h (70 h)	75 (98)	72 (73)	*S*	<2
4	4[b]	100:1	48 h (70 h)	74 (97)	69 (72)	*S*	<2
5	3[c]	100:1	30 min (1 h)	65 (98)	60 (62)	*S*	130 (98)
6	4[c]	100:1	30 min (1 h)	67 (99)	63 (64)	*S*	134 (99)
7	3[d]	100:1	1 h	—	—	—	—
8	4[d]	100:1	1 h	—	—	—	—
9	3[e]	500:1	5 h	98	73	*S*	98
10	4[e]	500:1	5 h	99	71	*S*	99
11	3[f]	1000:1	9 h	99	74	*S*	110
12	4[f]	1000:1	9 h	98	75	*S*	109
13	3[g]	100:1	3 h	98	71	*S*	33
14	4[g]	100:1	3 h	99	70	*S*	33
15	3[h]	100:1	8 h	97	66	*S*	12
16	4[h]	100:1	8 h	98	63	*S*	12

Reaction conditions: [a] at room temperature; acetophenone/Ru/KOH, 100:1:5. [b] At 50 °C; acetophenone/Ru/KOH, 100:1:5. [c] Refluxing in *iso*-PrOH; acetophenone/Ru/KOH, 100:1:5. [d] In the absence of base. [e] Refluxing in *iso*-PrOH; acetophenone/Ru/KOH, 500:1:5. [f] Refluxing in *iso*-PrOH; acetophenone/Ru/KOH, 1000:1:5. [g] Added 0.1 mL H_2O. [h] Carried out (refluxing) the reaction in air. [i] Determined by GC (three independent catalytic experiments). [j] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column. [k] Determined by comparison of the retention times of the enantiomers on the GC traces with the literature values. [l] Referred at the reaction time indicated in column; TOF = (mol product/mol Ru(II) Cat.) × h^{-1}.

For the transfer hydrogenation of acetophenone, the catalyst system showed high activity and moderate selectivity even in the presence of small amount of water. When we increased the amount of water in the reaction system, the high conversion with the same enantioselectivity remained intact (Table 1, entries 13 and 14). Performing the reaction in air slowed down the reaction but did not affect enantioselectivity (65–70% ee, Table 1, entries 15 and 16). Under identical conditions, the differences in enantioselectivities between the Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide))]chloride, **3** and [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide))]chloride, **4** were quite small and (*S*) configuration was obtained in all experiments.

With the cationic ruthenium complexes, [Ru{chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl] ethanediamide)}]chloride, **3** and [Ru{chloro(*p*-cymene)(*N,N′*-bis [(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)}] chloride, **4**, a variety of aromatic ketones were transformed to the corresponding secondary alcohols and it is noteworthy that **3** and **4** complexes display the same catalytic activities and selectivities in the transfer hydrogenation of acetophenone derivatives (Table 2).

Table 2
Asymmetric transfer hydrogenation results for substituted acetophenones with the catalyst systems prepared from [Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$ and *N*,*N*′-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **3**, and *N*,*N*′-bis-[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **4**[a]

Entry	Catalyst	Substrate	Product	Conversion[b] (%)	ee[c] (%)	Configuration[d]
1	3			99	62	*S*
2	4			98	64	*S*
3	3			98	58	*S*
4	4			98	60	*S*
5	3			96	61	*S*
6	4			97	58	*S*
7	3			93	77	*S*
8	4			94	75	*S*
9	3			90	68	*S*
10	4			91	70	*S*

[a] Catalyst (0.005 mmol), substrate (0.5 mmol), *iso*-PrOH (5 mL), KOH (0.025 mmol %), 82 °C, 1.0 h for **3** and **4**, the concentration of acetophenone is 0.1 M.
[b] Purity of compounds is checked by NMR and GC (three independent catalytic experiments), yields are based on methyl aryl ketone.
[c] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column (30 m × 0.32 mm I.D. × 0.25 μm film thickness).
[d] Determined by comparison of the retention times of the enantiomers on the GC traces with the literature values.

Replacing a *sec*-butyl moiety by a phenyl group induced no significant increase of the conversion and enantioselectivity.

The catalytic reductions of acetophenone derivatives were all tested with the conditions optimized for acetophenone. Complexes **3** and **4** showed very high activity for most of the ketones. The introduction of electron-withdrawing substituents, such as F, Cl, and Br to the *para*-position of the aryl ring of the ketone decreased the electron density of the C=O bond so that the activity was improved giving rise to easier hydrogenation.[26] An electron-withdrawing group such as fluoro group to the *para*-position was helpful to obtain excellent conversion and good enantioselectivity (up to 65% ee, Table 2, entries 1 and 2), while the introduction of an electron-donating substituents such as methoxy group to the *para*-position tended to higher enantioselectivity while maintaining sat-

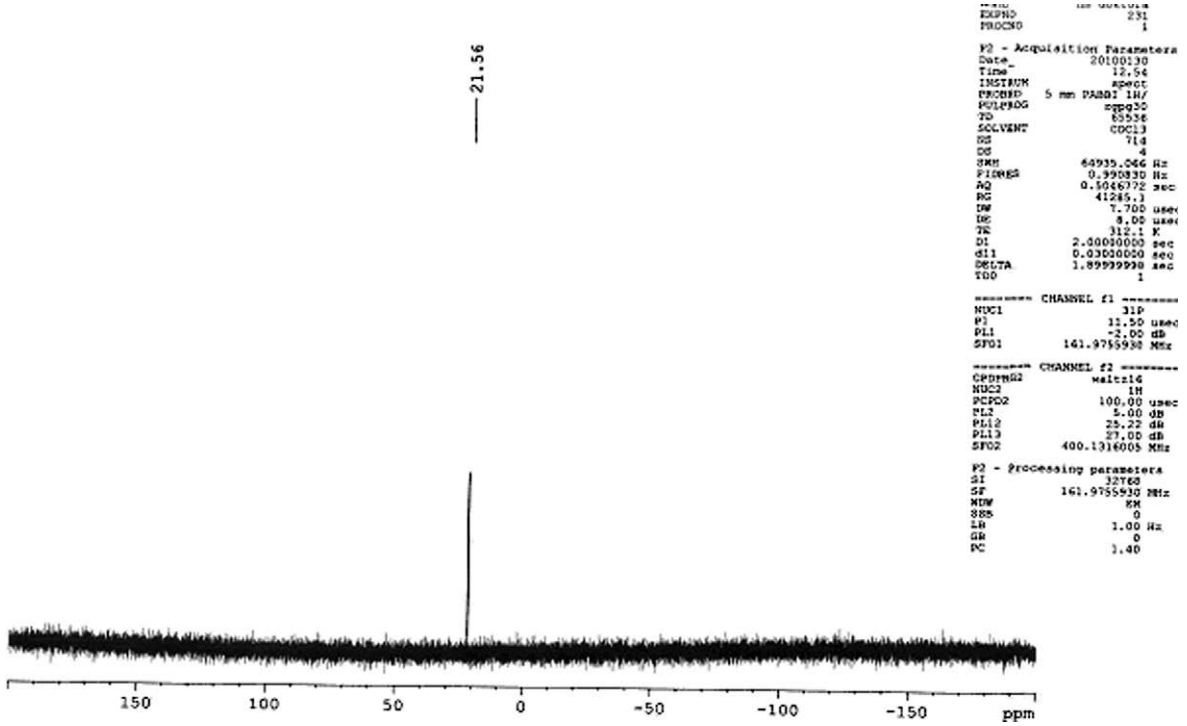


Figure 2. The $^{31}P–\{^1H\}$ NMR spectrum of the hydrolysis product diphenylphosphinous acid, $Ph_2P(O)H$.

isfactory activity (entries 9 and 10). The position and electronic property of the ring substituents also influenced hydrogenation results. The introduction of an electron-donating group methoxy group to the *para*-position decelerates the reaction, but that to the *ortho*-position increases the rate, however, improves the enantioselectivity (Table 2, entries 7–10). Among all the selected ketones, the best result was obtained in the reduction of *ortho*-methoxyacetophenone giving 75% and 77% ee (entries 7 and 8). The results (Table 2) indicated that a strong electron-withdrawing substituent, such as fluoro or chloro, was capable of higher conversion but with slightly lower enantiomeric purity. Conversely, the most electron-donating substituent ($-OCH_3$) led to lower conversion with higher ee. In order to investigate the evolution of the catalyst, **3** or **4,** $^{31}P-\{^1H\}$ NMR spectrum was recorded immediately after the catalytic reaction. The observed singlet at 21.6 ppm (Fig. 2) in the spectrum is corresponding to hydrolysis product diphenylphosphinous acid, $Ph_2P(O)H$.[27]

3. Conclusions

In conclusion, we have developed an effective, modular catalytic system for the asymmetric transfer hydrogenation of ketones. High conversion and moderate to good enantioselectivity were obtained in the catalytic reaction. Amazingly, the reaction was not affected in the air or with the addition of water. This may imply industrial applications. Future work will focus on finding the structure of the real catalyst and improving the enantioselectivity of the catalytic system.

4. Experimental

4.1. Materials and methods

Unless otherwise stated, all reactions were carried out under an atmosphere of argon using conventional Schlenk glass-ware, solvents were dried using established procedures and distilled under argon immediately prior to use. Analytical grade and deuterated solvents were purchased from Merck. The starting materials PPh_2Cl and Et_3N are purchased from Fluka and were used as received. $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$[15] and *N,N′*-bis[(1*S*)-1-*sec*-butyl-2-hydroxyethyl]ethanediamide[28] were prepared according to the literature procedures.

4.2. Spectroscopic analyses

The IR spectra were recorded on a Mattson 1000 ATI UNICAM FT-IR spectrometer as KBr pellets. ^1H (400.1 MHz), ^{13}C NMR, (100.6 MHz) and $^{31}P-\{^1H\}$ NMR (162.0 MHz) spectra were recorded on a Bruker Avance 400 spectrometer, with δ referenced to external TMS and 85% H_3PO_4, respectively. Elemental analysis was carried out on a Fisons EA 1108 CHNS-O instrument. Melting points were recorded by Gallenkamp Model apparatus with open capillaries.

4.3. GC analyses

GC analyses were performed on a HP 6890N Gas Chromatograph equipped with cyclodex B (Agilent) capillary column (30 m × 0.32 mm I.D. × 0.25 μm film thickness). The GC parameters for asymmetric transfer hydrogenation of ketones were as follows; initial temperature, 50 °C; initial time 1, 1 min; solvent delay, 4.48 min; temperature ramp 1, 3 °C/min; final temperature, 150 °C; initial time 2, 2 min; temperature ramp 2, 15 °C/min; final temperature, 250 °C; initial time 3, 3 min; final time, 44.33 min; injector port temperature, 200 °C; detector temperature, 200 °C, injection volume, 2.0 μL.

4.4. General procedure for the transfer hydrogenation of ketones

Typical procedure for the catalytic hydrogen-transfer reaction: a solution of the ruthenium complexes [Ru{chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)}]chloride, **3** or [Ru{chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)}]chloride, **4** (0.005 mmol), KOH (0.025 mmol), and the corresponding ketone (0.5 mmol) in degassed *iso*-PrOH (5 mL) was refluxed for one hour. After this time a sample of the reaction mixture is taken off, diluted with acetone, and analyzed immediately by GC, yields obtained are related to the residual unreacted ketone.

4.5. Procedure for the preparation of the chiral ligands and ruthenium complexes

4.5.1. Synthesis of *N,N′*-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, 1

PPh_2Cl (0.16 g, 0.70 mmol) was slowly added to a solution of *N,N′*-bis[(1*S*)-1-*sec*-butyl-2-hydroxyethyl]ethanediamide (0.10 g, 0.35 mmol) and triethylamine (0.07 g, 0.70 mmol) in 25 mL of toluene at room temperature. The mixture was stirred for 2 h and triethylammonium chloride was filtered off. Evaporation of the solvent in vacuo gave *N,N′*-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **1** as a white solid. (Yield: 0.21 g, 91%); mp: 83–85 °C. $[\alpha]_D^{25} = +33.6$ (*c* 1.0, DMSO). [$C_{38}H_{46}N_2O_4P_2$] (mw: 656.74 g/mol); Anal. Calcd: C, 69.49; H, 7.06; N, 4.27. Found: C, 69.35; H 7.01; N 4.22%. Selected IR, ν (cm^{-1}): 3325 (N–H), 2967, 2934 (Ar-H), 1658 (C=O, first amide band), 1510 (C=O, second amide band), 1074 (C–O), 1041 (P–O). ^1H NMR ($CDCl_3$) δ (ppm): 0.91 (t, 6H, *J* = 7.4 Hz, $-CH_2CH_3$), 0.96 (d, 6H, *J* = 6.8 Hz, $-CHCH_3$), 1.14 ((m, 2H, $-CH_2CH_3$), (a)), 1.43 ((m, 2H, $-CH_2CH_3$), (b)), 1.78 (m, 2H, $CHCH_3$), 3.92 ((m, 2H, $-CH_2O-P$, (a)), 3.98 ((m, 2H, $-CH-N$ and 2H, $-CH_2O-$, (b)), 7.36–7.52 (m, 20H, *o*-, *m*- *and* *p*-protons of phenyls), 8.61 (b, 2H, N*H*). $^{13}C-\{^1H\}$ NMR ($CDCl_3$) δ (ppm): 11.26 ($-CH_2CH_3$), 15.47 ($-CHCH_3$), 24.16 ($-CH_2CH_3$), 34.37 ($-CHCH_3$), 55.08 (d, $^3J_{31P-13C}$ = 8.0 Hz, –CH–N), 68.96 (d, $^2J_{31P-13C}$ = 18.0 Hz, $-CH_2O-P$), 128.43 (d, $^3J_{31P-13C}$ = 8.4 Hz, *m*-carbons of phenyls), 129.54 (s, *p*-carbons of phenyls), 130.50 (d, $^2J_{31P-13C}$ = 22.0 Hz, *o*-carbons of phenyls), 140.26 (d, $^1J_{31P-13C}$ = 18.1 Hz, *i*-carbons of phenyls), 158.39 (s, C=O), assignment was based on the $^1H-^{13}C$ HETCOR and $^1H-^1H$ COSY spectra. $^{31}P-\{^1H\}$ NMR ($CDCl_3$) δ (ppm): 116.17 (s, O–*P*–(C_6H_5)$_2$).

4.5.2. Synthesis of *N,N′*-bis-[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, 2

PPh_2Cl (0.14 g, 0.60 mmol) was slowly added to a solution of *N,N′*-bis[(1*S*)-1-phenyl-2-hydroxyethyl]ethanediamide[29] (0.10 g, 0.30 mmol) and triethylamine (0.06 g, 0.60 mmol) in 25 mL of toluene at room temperature. The mixture was stirred for 3 h and triethylammonium chloride was filtered off. Evaporation of the solvent in vacuo gave *N,N′*-bis-[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **2** as a white solid. (Yield: 0.20 g, 95%); $[\alpha]_D^{25} = -35.2$ (*c* 1.0, DMSO). [$C_{42}H_{38}N_2O_4P_2$] (mw: 696.72 g/mol); Anal. Calcd: C, 72.41; H, 5.50; N, 4.02. Found: C, 72.29; H, 5.43; N, 3.94. Selected IR, ν (cm^{-1}): 3293 (N–H), 3050, 2966 (Ar-H), 1688 (C=O, first amide band), 1515 (C=O, second amide band), 1099 (C–O), 1029 (P–O). ^1H NMR ($CDCl_3$) δ (ppm): 4.12 (m, 4H, $-CH_2O-P$), 5.18 (m, 2H, $-CH-N$), 7.25–7.58 (m, 20H, *o*-, *m*- and *p*-protons of phenyls and 10 protons of $CH(C_6H_5)$), 8.03 (d, 2H, *J* = 8.0 Hz, N*H*). $^{13}C-\{^1H\}$ NMR ($CDCl_3$) δ (ppm): 54.72 (d, $^3J_{31P-13C}$ = 9.0 Hz, –CH–N), 71.62 (d, $^2J_{31P-13C}$ = 18.0 Hz, $-CH_2O-$

P), 126.95, 127.99, 128.68, 137.83 (carbons of CH(C_6H_5)), 128.36 (d, $^3J_{31P-13C}$ = 7.6 Hz, *m*-carbons of phenyls), 129.54 (d, $^4J_{31P-13C}$ = 3.0 Hz, *p*-carbons of phenyls), 130.47 (d, $^2J_{31P-13C}$ = 22.0 Hz, *o*-carbons of phenyls), 140.04 (d, $^1J_{31P-13C}$ = 17.6 Hz, *i*-carbons of phenyls), 158.04 (s, C=O), assignment was based on the ^{1}H–^{13}C HETCOR and ^{1}H–^{1}H COSY spectra. ^{31}P–{^{1}H} NMR ($CDCl_3$) δ (ppm): 117.44 (s, O–*P*–(C_6H_5)$_2$).

4.5.3. Synthesis of [Ru{chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)}] chloride, 3

[Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$ (0.05 g, 0.08 mmol) and *N,N′*-bis-[(1*S*)-1-*sec*-butyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **1** (0.10 g, 0.15 mmol) were dissolved in 25 mL of toluene and stirred for 4 h at room temperature. The volume was concentrated to ca. 1–2 mL under reduced pressure and addition of diethyl ether (20 mL) gave **3** as a clear red solid. The product was collected by filtration and dried in vacuum. (Yield: 0.13 g, 86%); mp: 202–204 °C. $[\alpha]_D^{25} = +38.2$ (*c* 1.0, DMSO). [$C_{48}H_{60}N_2O_4P_2RuCl_2$] (mw: 962.94 g/mol); Anal. Calcd: C, 59.87; H, 6.28; N, 2.91. Found: C, 59.78; H, 6.23; N, 2.86. Selected IR, ν (cm^{-1}): 3396 (N–H), 3057, 2973 (Ar-H), 1666 (C=O, first amide band), 1504 (C=O, second amide band), 1097 (C–O), 1026 (P–O). ^{1}H NMR ($CDCl_3$) δ (ppm): 0.76 (m, 6H, –CHC*H*$_3$ and 6H, –CH$_2$C*H*$_3$), 1.05 (d, 6H, *J* = 6.8 Hz, (C*H*$_3$)$_2$CHPh of *p*-cymene), 1.30 ((m, 2H, –C*H*$_2$CH$_3$), (a)), 1.40 ((m, 2H, –C*H*$_2$CH$_3$), (b)), 1.62 (m, 2H, –C*H*CH$_3$), 1.76 (s, 3H, C*H*$_3$-Ph of *p*-cymene), 2.55 (m, 1H, –C*H*CH$_3$– of *p*-cymene), 3.79 (m, 4H, –C*H*$_2$O–P and 2H, –C*H*–N), 5.04, 5.08, 5.16, 5.23 (4s, 4H, aromatic C*H* protons of *p*-cymene), 7.32–7.84 (m, 20H, *o*-, *m*- and *p*-protons of phenyls), 8.73 (br, 2H, N*H*). ^{13}C–{^{1}H} NMR ($CDCl_3$) δ (ppm): 11.32 (–CH$_2$CH$_3$), 15.41 (–CHCH$_3$), 17.60 (*C*H$_3$Ph of *p*-cymene), 22.01 ((*C*H$_3$)$_2$CHPh of *p*-cymene), 25.07 ((–*C*H$_2$CH$_3$), 35.63 (–*C*HCH$_3$), 54.79 (d, $^3J_{31P-13C}$ = 8.0 Hz –*C*H–N), 67.11 (–CH$_2$O–P), (87.19 (d, $^2J_{31P-13C}$ = 5.0 Hz), 88.30 (d, $^2J_{31P-13C}$ = 6.0 Hz), 89.87 (d, $^2J_{31P-13C}$ = 4.5 Hz), 91.31 (d, $^2J_{31P-13C}$ = 4.0 Hz), aromatic carbons of *p*-cymene), 97.26, 111.97 (quaternary carbons of *p*-cymene), 128.19 (t, $^3J_{31P-13C}$ = 10.1 Hz, *m*-carbons of phenyls), 131.30 (d, $^4J_{31P-13C}$ = 6.6 Hz, *p*-carbons of phenyls), 132.81 (dd, $^4J_{31P-13C}$ = 15.4 Hz and $^2J_{31P-13C}$ = 22.0 Hz, *o*-carbons of phenyls), 136.22 (d, $^1J_{31P-13C}$ = 49.3 Hz, *i*-carbons of phenyls), 159.41 (s, C=O), assignment was based on the ^{1}H–^{13}C HETCOR and ^{1}H–^{1}H COSY spectra. ^{31}P–{^{1}H} NMR ($CDCl_3$) δ (ppm): 115.69 (s, O–*P*–(C_6H_5)$_2$).

4.5.4. Synthesis of [Ru{chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)}] chloride, 4

[Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$ (0.04 g, 0.07 mmol) and *N,N′*-bis-[(1*S*)-1-phenyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide, **2** (0.10 g, 0.14 mmol) were dissolved in 20 mL of toluene and stirred for 2 h at room temperature. The volume was concentrated to ca. 1–2 mL under reduced pressure and addition of diethyl ether (20 mL) gave **4** as a clear red solid. The product was collected by filtration and dried in vacuum. (Yield: 0.12 g, 85%); mp: 193–195 °C. $[\alpha]_D^{25} = -38.0$ (*c* 1.0, DMSO) [$C_{55}H_{52}N_2O_4P_2RuCl_2$] (mw: 1002.92 g/mol); Anal. Calcd: C, 62.28; H, 5.23; N, 2.79. Found: C, 62.14; H, 5.16; N, 2.68. Selected IR, ν (cm^{-1}): 3415 (N–H), 3057, 2966 (Ar-H), 1670 (C=O, first amide band), 1496 (C=O, second amide band), 1099 (C–O), 1036 (P–O). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.06 (d, 6H, *J* = 7.2 Hz, (C*H*$_3$)$_2$CHPh of *p*-cymene), 1.78 (s, 3H, C*H*$_3$-Ph of *p*-cymene), 2.60 (m, 1H, –C*H*– of *p*-cymene), 4.05 (m, 4H, –C*H*$_2$O–P), 5.03 (d, 2H, *J* = 5.6 Hz, aromatic C*H* protons of *p*-cymene, (a)), 5.18 (m, 2H, aromatic C*H* protons of *p*-cymene, (a) and 2H, –C*H*–N), 7.25–7.38 (m, 20H, *o*-, *m*- and *p*-protons of phenyls and 10 protons of CH(C_6H_5)), 8.29 (d, 2H, *J* = 8.0 Hz, N*H*). ^{13}C-{^{1}H} NMR ($CDCl_3$) δ (ppm): 17.49 (*C*H$_3$Ph of *p*-cymene), 21.88 ((*C*H$_3$)$_2$CHPh of *p*-cymene), 30.08 (–*C*H– of *p*-cymene), 54.39 (–*C*H–N), 69.29 (–*C*H$_2$O–P), (87.68 (d, $^2J_{31P-13C}$ = 6.0 Hz), 88.05 (d, $^2J_{31P-13C}$ = 6.0 Hz), 89.81 (d, $^2J_{31P-13C}$ = 3.0 Hz), 90.30 (d, $^2J_{31P-13C}$ = 4.0 Hz), aromatics carbons of *p*-cymene), 97.84, 112.10 (quaternary carbons of *p*-cymene), 126.92, 127.98, 128.65, 137.85 (carbons of CH(C_6H_5)), 128.10 (d, $^3J_{31P-13C}$ = 10.0 Hz, *m*-carbons of phenyls), 131.16 (d, *p*-carbons of phenyls), 132.48 (dd, $^4J_{31P-13C}$ = 12.1 and $^2J_{31P-13C}$ = 14.2 Hz, *o*-carbons of phenyls), 136.00 (d, $^1J_{31P-13C}$ = 50.3 Hz, *i*-carbons of phenyls), 159.15 (s, C=O), assignment was based on the ^{1}H–^{13}C HETCOR and ^{1}H–^{1}H COSY spectra. ^{31}P–{^{1}H} NMR ($CDCl_3$) δ (ppm): 116.26 (s, O–*P*–(C_6H_5)$_2$).

Acknowledgment

Partial support from Dicle University (Project number: DÜBAP-07-01-22) is gratefully acknowledged.

References

1. (a) Hannedouche, J.; Clarksom, G. J.; Wills, M. *J. Am. Chem. Soc.* **2004**, *126*, 986–987; (b) Liu, P. N.; Chen, Y. C.; Li, X. Q.; Tu, Y. Q.; Deng, J. G. *Tetrahedron: Asymmetry* **2003**, *14*, 2481–2485; (c) Palmer, M. J.; Wills, M. *Tetrahedron: Asymmetry* **1999**, *10*, 2045–2061.
2. (a) Blaser, H. U.; Malan, C.; Pugin, B.; Spindler, F.; Steiner, H.; Studer, M. *Adv. Synth. Catal.* **2003**, *345*, 103–151; (b) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40–73.
3. (a) Genet, J. P. *Acc. Chem. Res.* **2003**, *36*, 908–918; (b) Yiğit, M.; Yiğit, B.; Özdemir, İ.; Çetinkaya, E.; Çetinkaya, B. *Appl. Organomet. Chem.* **2006**, *20*, 322–327.
4. (a) Zassinovich, G.; Mestroni, G.; Gladiali, S. *Chem. Rev.* **1992**, *92*, 1051–1069; (b) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97–102.
5. (a) Ojima, I.; Clos, N.; Bastos, C. *Tetrahedron* **1989**, *45*, 6901–6939; (b) Kotha, S. *Tetrahedron* **1994**, *50*, 3639–3662; (c) Akutagawa, S. *Appl. Catal., A: Gen.* **1995**, *128*, 171–207; (d) Roucoux, A.; Thieffry, L.; Carpentier, J.-F.; Devocelle, M.; Meliet, C.; Agbossou, F.; Mortreux, A. *Organometallics* **1996**, *25*, 2440–2449.
6. Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581–1590.
7. Dang, T. P.; Kagan, H. B. *Chem. Commun.* **1971**, 481–482.
8. Inoguchi, K.; Sakuraba, S.; Achiwa, K. *Synlett* **1992**, 169–178.
9. (a) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*; Wiley-Interscience: New York, 2001; (b) Kagan, H. B.; Sasaki, M. *Transition Metals for Organic Synthesis*; Wiley-VCH: Weinheim, 1998.
10. Galka, P. W.; Kraatz, H.-B. *J. Organomet. Chem.* **2003**, *674*, 24–31.
11. (a) Yang, H.; Alvarez, M.; Lugan, N.; Mathieu, R. *J. Chem. Soc., Chem. Commun.* **1995**, 1721–1722; (b) Venkatachalam, G.; Ramesh, R. *Inorg. Chem. Commun.* **2005**, *8*, 1009–1013; (c) Claver, C.; Pamies, O.; Dieguez, M. In *Chiral Diphosphinites, Diphosphonites, Diphosphites and Mixed P–O Ligands in Phosphorus Ligands in Asymmetric Catalysis*; Börner, A., Ed.; Wiley: Weinheim, 2008; pp 506–528.
12. (a) Baysal, A.; Aydemir, M.; Durap, F.; Gümgüm, B.; Özkar, S.; Yildırım, L. T. *Polyhedron* **2007**, *26*, 3373–3378; (b) Ceron-Camacho, R.; Gomez-Benitez, V.; Lagadec, R. L.; Morales-Morales, D.; Toscano, R. A. *J. Mol. Catal. A* **2006**, *247*, 124–129; (c) Broger, E. A.; Burkart, W.; Hennig, M.; Scalone, M.; Schmid, R. *Tetrahedron: Asymmetry* **1998**, *9*, 4043–4054.
13. Fei, Z.; Scopelliti, R.; Dyson, P. J. *Eur. J. Org. Chem.* **2004**, 530–537.
14. (a) Majoumo, F.; Lönnecke, P.; Kühl, O.; Hey-Hawkins, E. *Z. Anorg. Allg. Chem.* **2004**, *630*, 305–308; (b) Aydemir, M.; Baysal, A.; Öztürk, G.; Gümgüm, B. *Appl. Organomet. Chem.* **2009**, *23*, 108–113; (c) Aydemir, M.; Baysal, A.; Gümgüm, B. *J. Organomet. Chem.* **2008**, *693*, 3810–3814; (d) Morales-Morales, D.; Redon, R.; Yung, C.; Jensen, C. M. *Chem. Commun.* **2000**, 1619–1620.
15. Bennet, M. A.; Robertson, G. B.; Smith, A. K. *J. Organomet. Chem.* **1972**, *43*, C41.
16. Maj, A. M.; Michal, K. M.; Suisse, I.; Agbossou, F.; Mortreux, A. *Tetrahedron: Asymmetry* **1999**, *10*, 831–835.
17. Balakrishna, M. S.; George, P. P.; Mobin, S. M. *Polyhedron* **2005**, *24*, 475–480.
18. Kostas, I. D.; Steele, B. R.; Trezis, A.; Amosova, S. V. *Tetrahedron* **2003**, *59*, 3467–3473.
19. (a) Yang, H.; Lugan, N.; Mathieu, R. *An. Quim.* **1997**, *93*, 28–38; (b) Moldes, I.; de la Encarnacion, E.; Ros, J.; Alvarez-Larena, A.; Piniella, J. F. *J. Organomet. Chem.* **1998**, *566*, 165–174.
20. (a) Gendre, P. L.; Offenbecher, M.; Bruneau, C.; Dixneuf, P. H. *Tetrahedron: Asymmetry* **1998**, *9*, 2279–2284; (b) Zhang, Q.; Hua, G.; Bhattacharrya, P.; Slawin, A. M. Z.; Woollins, J. D. *J. Chem. Soc., Dalton Trans.* **2003**, 3250–3257.
21. Takehara, J.; Hashiguchi, S.; Fujii, A.; Inoue, S.; Ikariya, T.; Noyori, R. *J. Chem. Soc., Chem. Commun.* **1996**, 233–234.
22. Palegatti, P.; Carcelli, M.; Calbiani, F.; Cassi, C.; Elviri, L.; Pelizzi, C.; Rizzotti, U.; Rogolino, D. *Organometallics* **2005**, *24*, 5836–5844.
23. Tribo, R.; Munoz, S.; Pons, J.; Yanez, R.; Alvarez-Larena, A.; Piniella, J. F.; Ros, *J. Organomet. Chem.* **2005**, *690*, 4072–4079.
24. Pamies, O.; Backvall, J.-E. *Chem. Eur. J.* **2001**, *7*, 5052–5058.
25. (a) Zhang, H.; Yang, B. C.; Li, Y. Y.; Donga, Z. R.; Gao, J. X.; Nakamura, H.; Murata, K.; Ikariya, T. *J. Chem. Soc., Chem. Commun.* **2003**, 142–143; (b) Hannedouche, J.; Clarkson, G. J.; Wills, M. *J. Am. Chem. Soc.* **2004**, *126*, 986–987; (c) Bacchi, A.; Balordi, M.; Cammi, R.; Elviri, L.; Pelizzi, C.; Picchioni, F.; Verdolino, V.; Goubitz, K.; Peschar, R.; Pelagatti, P. *Eur. J. Inorg. Chem.* **2008**, 4462–4473.

26. (a) Chen, J.-S.; Li, Y.-Y.; Dong, Z.-R.; Li, B.-Z.; Gao, J.-X. *Tetrahedron Lett.* **2004**, *45*, 8415–8418; (b) Faller, J. W.; Lavoie, A. R. *Organometallics* **2001**, *20*, 5245–5247; (c) Özdemir, İ.; Yaşar, S. *Transition Met. Chem.* **2005**, *30*, 831–835.
27. (a) Fei, Z.; Scopelliti, R.; Dyson, P. J. *Inorg. Chem.* **2003**, *42*, 2125; (b) Fei, Z.; Scopelliti, R.; Dyson, P. J. *Eur. J. Inorg. Chem.* **2004**, 530–537; (c) Berger, S.; Braun, S.; Kolinowski, H.-O. *NMR-Spektroskopie von Nichtmetallen Band 3, ^{31}P NMR-Spektroskopie*; Georg Theime Verlag: Stuttgart, New York, 1993.
28. Sunkur, M.; Baris, D.; Hosgoren, H.; Togrul, M. *J. Org. Chem.* **2008**, *73*, 2570–2575.
29. Preparation of *N,N′*-bis[(1*S*)-1-phenyl-2-hydroxyethyl]ethanediamide: A solution of L-glisinol (2.5 g, 0.0182 mol) in MeOH (25 mL) was slowly added dropwise over a 30-min period to a solution of dimethyloxalate (1.07 g, 0.009 mol) in MeOH (30 mL) at room temperature. The reaction mixture was stirred for further 5 min and the resulting white solid precipitates were collected and washed with small portion of diethyl ether to give a white solid. (Yield: 1.65 g, 56%); $[\alpha]_D^{25} = -35.2$ (*c* 1.0, DMSO). [$C_{18}H_{20}N_2O_4$] (mw: 328.37 g/mol); Anal. Calcd: C, 65.84; H, 6.09; N, 8.53. Found: C, 65.65; H, 6.04; N, 8.44%. Selected IR, ν (cm^{-1}): 3420 (O–H), 3296 (N–H), 3070, 3043 (Ar-H), 1654 (C=O, first amide band), 1515 (C=O, second amide band), 1042 (C–O). ^{1}H NMR ($CDCl_3$) δ (ppm): 3.50 (br, 2H, CH_2OH), 3.63 (m, 2H, –CH_2–OH, (a)), 3.73 (m, 2H, –CH_2–OH, (b)), 4.88 (m, 2H, –CH–N), 7.21–7.42 (m, 10 protons of CH(C_6H_5)), 9.00 (d, 2H, J = 8.8 Hz, NH). ^{13}C–{^{1}H} NMR ($CDCl_3$) δ (ppm): 56.71 (–CH–N), 64.41 (–CH_2–OH), 127.48, 127.53, 128.64, 140.72 (carbons of CH(C_6H_5)), 160.22 (s, C=O), assignment was based on the ^{1}H–^{13}C HETCOR and ^{1}H–^{1}H COSY spectra.