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Asymmetric transfer hydrogenation of aromatic ketones with the ruthenium(II) catalyst derived from C_2 symmetric *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide

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Dedicated to Prof. Dr. Bahattin Gümgüm on the occasion of 60th birthday

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ABSTRACT

Asymmetric transfer hydrogenation of ketones with chiral molecular catalysts is realized to be one of the most magnificent tools to access chiral alcohols in organic synthesis. A new chiral phosphinite compound *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (**1**), has been synthesized by the reaction of chlorodiphenylphosphine with *N,N′*-bis[(1*S*)-1-benzyl-2-hydroxyethyl]ethanediamide under argon atmosphere. The oxidation of **1** with aqueous hydrogen peroxide, elemental sulfur or grey selenium in toluene gave the corresponding oxide **1a**, sulfide **1b** and selenide **1c**, respectively. Pd, Pt and Ru complexes were obtained by the reaction of **1** with $[MCl_2(cod)]$ (M: Pd **1d**, Pt **1e**) and $[Ru(p\text{-cymene})Cl_2]_2$ **1f**, respectively. All these new complexes were characterized by using NMR, FT-IR spectroscopies and microanalysis. Additionally, as a demonstration of their catalytic reactivity, the ruthenium complex **1f** was tested as catalyst in the asymmetric transfer hydrogenation reactions of acetophenone derivatives with *i*PrOH was also investigated.

1. Introduction

The use of chiral transition metal complex catalysis is a powerful and economically feasible tool for the preparation of optically active compounds on both laboratory and industrial scales [1–3]. Nowadays, there is an immense interest in obtaining enantiomerically pure compounds as building blocks for pharmaceuticals and bioactive agents. The preparation of optically active hydroxy compounds by the catalytic asymmetric hydrogenation of prochiral ketones is a well-known method that possesses a great significance for the research in enantioselective organometallic catalysis [4].

Noyori and co-workers devoted much effort for the asymmetric catalytic hydrogenation [5–7] and asymmetric transfer hydrogenation of simple ketones [8,9] which are the most common unsaturated substrates used in organic synthesis. This extensive effort has been receiving increased attention as well and has led to extend the concept of molecular catalysts and to new catalysts system both in academia and industry. In particular, the metals coordinated by one or more chiral phosphorus ligands exhibit exciting enantioselectivity and reactivity. Among the phosphorus based ligands, phosphines and phosphinites are the most commonly used ligands because of their wide range of steric and electronic properties. Phosphinites provide different chemical, electronic and structural properties compared to phosphines. The metal–phosphorus bonds are often stronger for phosphinites than that of phosphines due to the presence of the electron withdrawing P–OR group [10]. Already more than a thousand of chiral nonracemic bis(phosphines), striking examples include L-DOPA [11], L-menthol [12,13], and dissymmetric phosphine ligand BINAP [14], have been synthesized. Recently, phosphine [15–17], phosphite [18], bis(phosphinites) [19–21], and aminophosphine-phosphinite [22–24] (abbreviated as AMPP) compounds have been of great interest and widely used in asymmetric transfer hydrogenation reactions.

In general, the most successful chiral ligands used in the asymmetric hydrogenation reactions are rigid chelating diphosphines possessing a C_2 symmetry axis thus reducing the number of diastereomeric transition states [25–28]. In addition, most of them bear at least two aryl substituents on their phosphorus atoms. If one analyzed the structures of these ligands [29], 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 though 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 [30,31] (first example: diop) or is very strongly

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unsymmetrical [32] (e.g. josiphos) in order to reduce the number of possible isomeric catalyst-substrate complexes.

As part of our research program on this subject, herein, we report the synthesis of a new C_2 symmetric chiral phosphinite ligand *N,N′*-bis[(1S)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl] ethanediamide (**1**), and corresponding oxide, sulfide and selenide as well as its complexes with selected transition metal ions (Pd^{2+}, Pt^{2+}, Ru^{2+}). The compounds were fully characterized using elemental analysis, FT-IR and multi-nuclear NMR spectroscopies. We also report the catalytic activity of ruthenium(II) complex as a pre-catalyst in asymmetric transfer hydrogenation reactions of acetophenone derivatives with *i*PrOH.

2. Results and discussion

2.1. Synthesis of chiral ligand

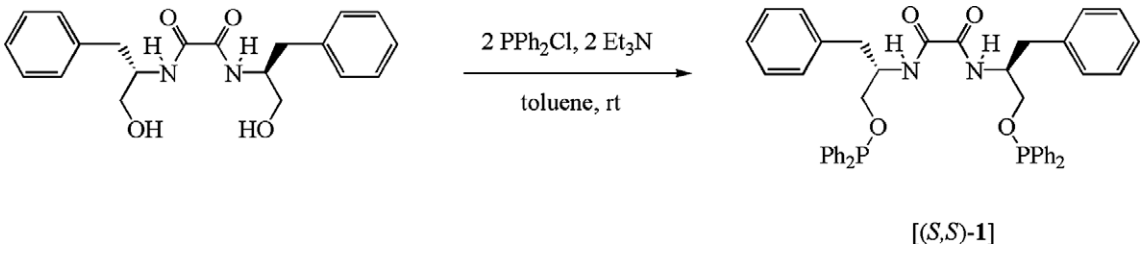
N,N′-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (**1**) with a high yield (94%), was prepared from the reaction of *N,N′*-bis[(1*S*)-1-benzyl-2-hydroxyethyl]ethanediamide [33] with 2 equiv of chlorodiphenylphosphine in the presence of Et_3N at room temperature under argon atmosphere (Scheme 1). The $^{31}P–\{^1H\}$ NMR spectrum of compound **1** shows a single resonance due to phosphinite at 121.1 ppm, indicating that two phosphorus atoms in the molecule are equivalent [34]. The $^{31}P–\{H\}$ NMR spectrum also displays formation of PPh_2PPh_2 and $P(O)Ph_2PPh_2$ which give signals at δ −14.3 ppm as singlet and δ 37.4 ppm and δ −22.5 ppm as doublets with $^1J_{(PP)}$ 220 Hz, respectively [35]. These by products were easily eliminated by washing the solid residue with copious amounts of dried diethyl ether. Solution of **1** in $CDCl_3$, prepared under anaerobic conditions, is unstable and decomposes gradually to give oxide and bis(diphenylphosphino)monoxide [$P(O)Ph_2PPh_2$] derivatives. Compound **1** is also not stable in the solid state and decomposes rapidly when it exposes to air or moisture. In the ^{13}C NMR spectra characteristic $J_{(31_{P}-13_{C})}$ coupling constants of the carbons of the phenyl rings were observed (including *i*-, *o*-, *m*-, *p*-carbons of phenyl rings, for details see Section 4), which are consistent with the literature values [36]. The FT-IR spectrum of **1** gives characteristic bands at 3310, 1658, and 951 cm^{-1} due to ν(N–H), ν(C=O) and ν(P–O) stretching, respectively and ν(O–H) stretching band was not observed. The compound **1** could be isolated as analytically pure solid material and fully characterized microanalysis as well, and found to be in good agreement with the theoretical values.

2.2. Synthesis of chalcogenides

The corresponding oxidized derivatives of **1**, with aqueous hydrogen peroxide, elemental sulfur or grey selenium gave the corresponding oxide **1a**, sulfide **1b** or selenide **1c** derivatives, respectively (Scheme 2). The $^{31}P–\{H\}$ NMR spectra of **1a**, 1b and **1c** display one singlet at 33.8, 84.9 and 88.7 ppm ($^1J_{(PSe)}$ = 805 Hz for **1c**) [34,37,38], respectively. The oxidation reaction using aqueous hydrogen peroxide was very rapid and takes place spontaneously under ambient conditions. A small amount of hydrolysis product $Ph_2P(O)H$ was also formed as evidenced by the signal at about 20.0 ppm in the $^{31}P–\{^1H\}$ NMR spectra [39]. In contrast, the oxidations with elemental sulfur and selenium were slow compared with **1a** and had to be carried out under reflux conditions. This is not surprising since elemental sulfur and selenium are weaker oxidizing agents than hydrogen peroxide. In the $^{13}C–\{1H\}$ NMR spectra of oxide, sulfide and selenide, $J_{31_{P}-13_{C}}$ coupling constants of the carbons of the phenyls rings were observed, which are in agreement with the literature values [36]. Furthermore, the coupling between the *i*-carbon and phosphorus in the oxidized P(V) compounds is quite large $^1J_{PC}$ = 136.0, 110.0 and 95.5 Hz, respectively, corresponding to O, S and Se oxidized species [40]. The FT-IR spectra of **1a–c** consist of characteristic bands at 1192, 650, and 579 cm^{-1} due to ν(P=O), ν(P=S) and ν(P=Se) stretching, respectively [37]. The structures of the oxidized derivative **1a**, sulfide **1b** and selenide **1c** were further confirmed by microanalysis and found to be in good agreement with the theoretical values.

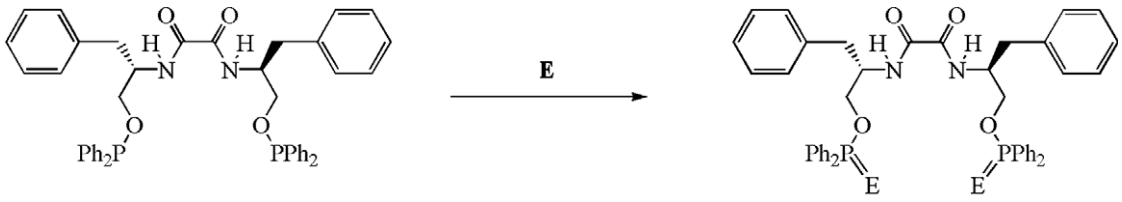
2.3. Synthesis of metal complexes

In the reaction of [M(cod)Cl_2] (M = Pd, Pt; cod = 1,5-cyclooctadiene) with 1 equiv of **1** in toluene, cod is replaced by the



[(*S,S*)-**1**]

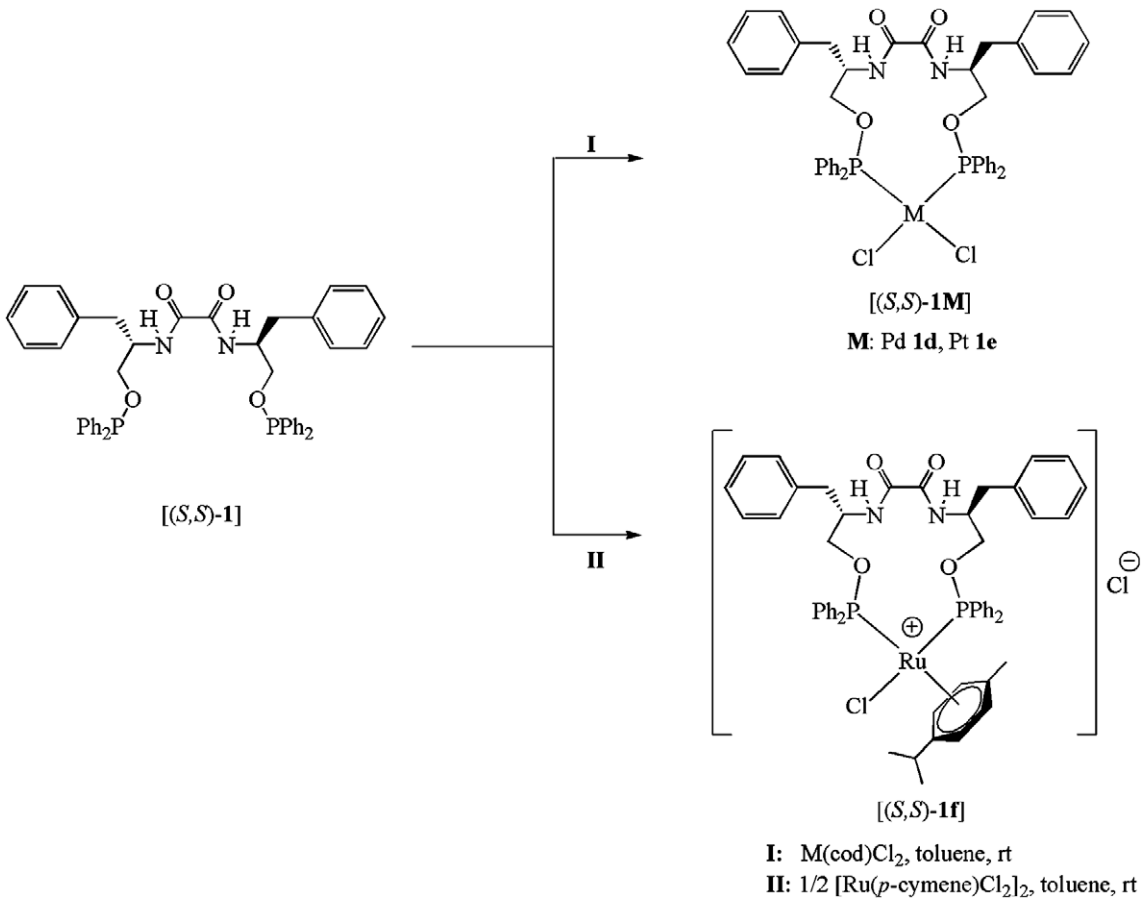
Scheme 1. Synthesis of *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)-ethyl]ethanediamide (**1**).



[(*S,S*)-**1**] [(*S,S*)-**1E**]

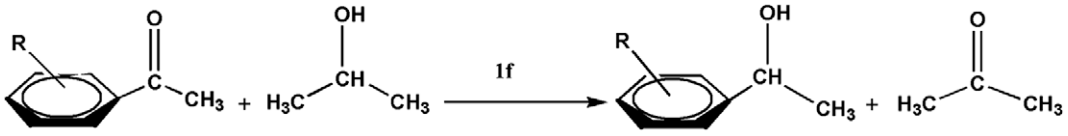
E: O **1a**, S **1b**, Se **1c**

Scheme 2. Oxidation of *N,N′*-bis[(1S)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (**1**) with aqueous H_2O_2 (**1a**), elemental sulfur (**1b**) and grey selenium (**1c**).



Scheme 3. Reactions of *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (**1**) with M(cod)Cl_2 (M: Pd (**1d**), Pt (**1e**)) and [Ru(*p*-cymene)Cl_2]$_2$ in toluene.

N,N′-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (1) as bidentate ligand yielding the respective [M(*N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)-Cl_2] complexes **1d**, **1e**, (M: Pd, Pt, respectively). The reaction of [Ru(*p*-cymene) Cl_2]$_2$ with 2 equiv of **1** gives the expected complex [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide)] chloride **1f**, these reactions are summarized in Scheme 3. The synthesis of compounds **1d** and **1e** were followed by ^{31}P–{1H} NMR spectroscopy. The ^{31}P–{1H} NMR spectra of **1d** and **1e** show single resonances at δ 112.9 and 85.6 ppm, respectively [10,41]. The complex **1e** shows large $^{1}J_{PtP}$ coupling ($^{1}J_{31_{P}-195_{Pt}}$ = 4189 Hz) which is characteristics for phosphines having mutually *cis*-disposition [42,43]. In the ^{13}C NMR spectra a long range P–C coupling was observed [44]. Furthermore, ^{1}H NMR spectral data of **1d** and **1e** are in agreement with the structures proposed which were also confirmed by elemental analysis. We also examined simple coordination chemistry of **1** with [Ru(*p*-cymene)Cl_2]$_2$in which the coordination to ruthenium being carried out at room temperature. The ^{31}P–{1H} NMR chemical shift of **1f** is also within the expected range, 115.3 ppm for structurally similar complexes [45–47]. ^{1}H NMR analysis reveals that this compound to be diamagnetic, exhibiting signals apart from phosphinite ligand consisting of two doublets centered at 5.40 and 5.35 ppm are due to the presence of the aromatic protons in the *p*-cymene group and at 2.27 and 0.92 ppm due to the CH and CH_3 of the *iso*-propyl group of the *p*-cymene moiety and a signal due to the methyl group in the *p*-cymene group is observed at 1.60 ppm. Characteristic $J_{31_{P}-13_{C}}$ coupling constants of the carbons of the phenyls rings were observed in the ^{13}C NMR spectra. Furthermore ^{1}H, ^{13}C NMR, IR spectra and microanalysis values of **1f** confirmed the proposed structure (for details see Section 4). ^{31}P–{1H} NMR spectra show that all complexes, **1d–f**, are quite stable in the solid state, when they expose to air or moisture for several months.



R: H, *p*-F, *p*-Cl, *p*-Br, *o*-OCH_3, *p*-OCH_3

Scheme 4. Hydrogen transfer from *i*PrOH to acetophenone derivatives.

2.4. Asymmetric transfer hydrogenation of prochiral ketones

The outstanding catalytic performance of phosphinite based transition metal complexes in the asymmetric hydrogenation [22 and references there in] prompted us to develop new chiral phosphinite based ruthenium(II) complex. The catalytic activity of **1f** was tested in transfer hydrogenation of acetophenone derivatives in which *i*PrOH/NaOH used as the reducing system as described in Scheme 4.

2-Propanol was selected as the conventional hydrogen source because of its well-know advantages: (i) having stable, (ii) easy to handle, (iii) nontoxic, (iv) environmentally benign, (v) inexpensive, (vi) dissolves in many organic solvents [47]. The catalytic activity of **1f** was tested under different reaction conditions in transfer hydrogenation of acetophenone and the results are collected in Table 1.

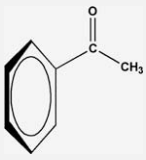
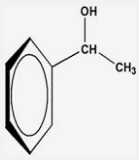
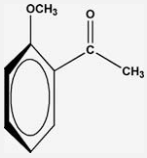
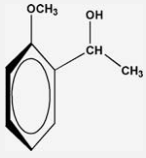
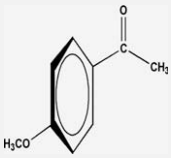
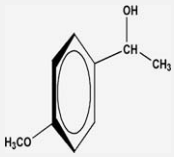
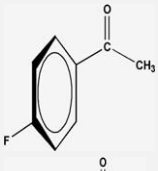
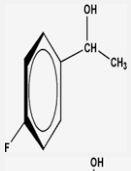
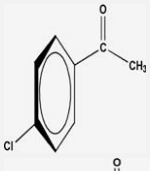
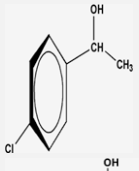
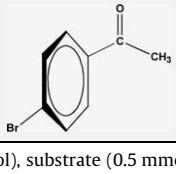
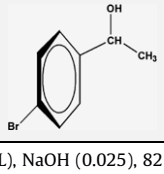
The formation of 1-phenylethanol was found to be negligible at room temperature and proceeds slowly even at 50 °C. However, reduction of acetophenone into 1-phenylethanol could be achieved in high yield by increasing the temperature up to 82 °C. The negligible catalytic activity of $[Ru(p\text{-cymene})Cl_2]_2$ was observed under the applied experimental conditions at room temperature. It should be also pointed out that complex **1f** is 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 [48]. The results obtained from the optimization of reaction conditions indicate that the high conversion and high TOF value can be achieved in the reduction of acetophenone into 1-phenylethanol by using **1f** as a pre-catalyst (1 equiv.) in a system that contains 100 equiv. of acetophenone in *i*PrOH containing 0.025 mmol of NaOH at 82 °C (see Table 2). Catalyst prepared from ruthenium

Table 1
Transfer hydrogenation of acetophenone catalyzed by **1f.**

Entry	Catalyst	S/C/NaOH	Time (h)	Temperature (°C)	Conversion (%)[a]	TOF (h^{-1})[b,c]
1	**1f**	100:1:5	1	25	3<	
2	**1f**	100:1:5	24	50	32	
3	**1f**	100:1:5	0.5	82	81	162
			(1)	82	97	97
4	**1f**	100:1	1	82		
5	**1f**	500:1:5	4	82	96	120
6	**1f**	1000:1:5	2 (7)	82	30 (100)	150 (143)
7	**1f**[d]	100:1:5	1 (4)	82	64 (100)	64 (25)
8	**1f**[e]	100:1:5	6	82	95	16

[a] Determined by GC (three independent catalytic experiments).
[b] Referred at the reaction time indicated in column; TOF: (mol product/mol **1f**) × h^{-1}.
[c] No significant ee was observed.
[d] Added 0.1 mL H_2O.
[e] Carried out (refluxing) the reaction in air.

Table 2
Catalytic transfer hydrogenation of acetophenone derivatives with *i*PrOH catalyzed by **1f**.

Entry	Substrate	Product	Time (h)	Conversion (%)[a,b]	TOF (h^{-1})[c]
1			1	97	97
2			1	92	92
3			1	91	91
4			1	98	98
5			1	95	95
6			1	92	92

[a] Catalyst (0.005 mmol), substrate (0.5 mmol), *i*PrOH (5 mL), NaOH (0.025), 82 °C.
[b] Purity of compounds is checked by NMR and GC, yields are based on methyl aryl ketone.
[c] TOF: (mol product/mol **1f**) × h^{-1}, No significant ee was observed.

precursor and xanthene derived diphosphonite ligand which is reported by Reetz and Li shows remarkable catalytic activity (with 88% conversion) and high stereoselectivity (97% ee) for the reduction of acetophenone by *i*PrOH at 40 °C within 20 h in the presence of NaOH as base [48]. However, we obtained the highest ee value (16%) in the reduction of acetophenone to (*S*), (*R*)-1-phenylethanol catalyzed by **1f**. As seen from Table 1 (entry 4) NaOH is necessary to observe appreciable conversions and a lower concentration of substrate gives a higher conversion of the alcohol. Furthermore, for the asymmetric transfer hydrogenation of acetophenone, the catalyst showed high activity in the presence of small amount (0.1 mL) of water and under ambient conditions. Under the optimized conditions, reaction of acetophenone, *p*-fluoroacetophenone, *p*-chloroacetophenone, *p*-bromoacetophenone, *p*-methoxyacetophenone, *o*-methoxyacetophenone with *i*PrOH gave high yields within 1 h in the absence of induction time period by using **1f** (Table 2). In order to investigate the evolution of the catalyst, **1f**, 31P–{1H} NMR spectrum was recorded immediately after the catalytic reaction.

The observed singlet at 21.6 ppm in the spectrum is corresponding to hydrolysis product diphenylphosphinous acid, $Ph_2P(O)H$ [39].

3. Conclusions

In conclusion, we have synthesized a new chiral phosphinite ligand *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]-ethanediamide (**1**). Additionally, its corresponding oxidized derivatives and Pd(II), Pt(II) and Ru(II) complexes were also synthesized and characterized successfully. It was found that the use of [Ru(-chloro(*p*-cymene)((*S*,*S*)-1)] chloride, **1f** as a catalyst in the transfer hydrogenation of aromatic ketones provides secondary alcohols with high conversion and notable TOF values.

4. Experimental

All reactions and manipulations were performed under argon atmosphere unless otherwise stated. Ph_2PCl and $[Ru(p\text{-cymene})Cl_2]_2$ were purchased from Fluka and used directly. Analytical grade and deuterated solvents were purchased from Merck. The starting materials $[MCl_2(cod)]$ (M = Pd [49], Pt [50], cod = 1,5-cyclooctadiene) and *N,N′*-bis[(1*S*)-1-benzyl-2-hydroxyethyl]-ethanediamide [33] were prepared according to literature procedures. Solvents were dried using the appropriate reagents and distilled prior to use. Infrared spectra were recorded as KBr pellet in the range 4000–400 cm^{-1} on a Mattson 1000 ATI UNICAM FT-IR spectrometer. ^1H (400.1 MHz), ^{13}C NMR (100.6 MHz) and ^{31}P–{1H} NMR spectra (162.0 MHz) were recorded on a Bruker Avance 400 spectrometer, with δ referenced to external TMS and 85% H_3PO_4, respectively. Optical rotations were taken on a Perkin Elmer 341 model polarimeter. Elemental analysis was carried out on a Fisons EA 1108 CHNS-O instrument. Melting points were determined by Gallenkamp Model apparatus with open capillaries.

4.1. GC analysis

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, 110 °C; initial time, 1 min; solvent delay, 4.48 min; temperature ramp 80 °C/min; final temperature, 200 °C; final time, 21.13 min; injector port temperature, 200 °C; detector temperature, 200 °C; injection volume, 2.0 μL.

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

Chlorodiphenylphosphine (0.26 g, 1.12 mmol) was added dropwise over a period of 20 min to a solution of *N,N′*-bis[(1*S*)-1-benzyl-2-hydroxyethyl]ethanediamide (0.20 g, 0.56 mmol) and triethylamine (1.16 g, 1.12 mmol) in toluene (40 mL) at room temperature with vigorous stirring. The mixture was stirred for 8 h, and then the white precipitate (triethylamine hydrogen chloride) was filtered off under argon and the solvent removed in vacuum. The remaining solid was washed with cold diethyl ether (3 × 10 mL) and dried in vacuum to produce a white solid compound **1** (Yield: 0.38 g, 94 %); mp: 71–73 °C. $[\alpha]_D^{27} = -43$ (c 0.025, CH_2Cl_2). ^1H NMR (DMSO) δ(ppm): 2.84 (dd, 2H, J = 7.2 and 10.4 Hz, C*H*$_2$Ar (a)), 2.81 (dd, 2H, J = 7.2 and 10.4 Hz, C*H*$_2$Ar (b)), 3.72 (m, 4H, C*H*$_2$O), 4.21 (m, 2H, C*H*–N), 7.03–7.23 (m, 10H, CH_2*Ar*), 7.30 (m, 8H, *m*-protons of phenyls), 7.42 (m, 4H, *p*-protons of phenyls), 7.70 (dd, 8H, J = 5.1 and 10.8 Hz, *o*-protons of phenyls), 8.46 (br, 2H, NH). ^{13}C–{1H} NMR (DMSO) δ(ppm): 36.09 (*C*H$_2$Ar), 51.96 (*C*H–N), 68.97 (*C*H$_2$O), 126.74, 128.60, 129.3, 134.29 ($CH_2C_6H_5$), 129.70 (d, $^3J_{31_P-13_C}$ = 7.0 Hz, *m*-carbons of phenyls), 130.75 (d, $^2J_{31_P-13_C}$ = 11.1 Hz, *o*-carbons of phenyls), 132.61 (d, $^4J_{31_P-13_C}$ = 2.0 Hz, *p*-carbons of phenyls), 140.13 (d, $^1J_{31_P-13_C}$ = 20.1 Hz, *i*-carbons of phenyls), 157.95 (s, C=O), assignment was based on the ^1H–13C HETCOR and ^1H–1H COSY spectra. ^{31}P–{1H} NMR (DMSO) δ(ppm): 121.1 (s). Selected IR, ν (cm^{-1}): 3310 (N–H), 3013, 3049 (Ar–H), 1658 (C=O), 1099 (C–O), 951 (P–O). Anal. Calc. for $C_{44}H_{42}N_2O_4P_2$: C, 72.92; H, 5.84; N, 3.87. Found: C, 72.75; H, 5.68; N, 3.77%.

4.3. Synthesis of *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenyloxophosphinite) ethyl]ethanediamide (1a)

Aqueous hydrogen peroxide (30%, w/w, 0.06 mL, 0.56 mmol) was added dropwise to a suspension of *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (1), (0.20 g, 0.28 mmol) in toluene and the mixture was stirred for 1 h at room temperature. The volume was concentrated in vacuum to ca. 1–2 mL and addition of *n*-hexane (20 mL) gave **1a** as a white solid which was collected by filtration (yield: 0.18 g, 88%); mp: 83–85 °C. $[\alpha]_D^{27} = -40$ (c 0.025, CH_2Cl_2). ^1H NMR (DMSO) δ(ppm): 2.87 (m, 4H, CH_2Ar (a)), 3.92 (m, 4H, C*H*$_2$Ar (b)), 3.92 (br, 4H, C*H*$_2$O), 4.30 (m, 2H, C*H*–N), 7.13–7.22 (m 10H, CH_2*Ar*), 7.43–7.52 (m, 12 H, *m*-, *p*-protons of phenyls), 7.73 (dd, 8H, J = 6.4 Hz and 11.4 Hz *o*-protons of phenyls) 8.88 (d, 2H, J = 9.2 Hz, NH). ^{13}C–{1H} NMR (DMSO) δ(ppm): 35.53 (*C*H$_2$Ar), 45.58 (*C*H–N), 65.10 (*C*H$_2$O), 126.18, 128.17, 128.85, 137.89 ($CH_2C_6H_5$), 128.71 (d, $^3J_{31_P-13_C}$ = 13.1 Hz, *m*-carbons of phenyls), 131.21 (d, $^2J_{31_P-13_C}$ = 10.0 Hz, *o*-carbons of phenyls), 132.28 (d, $^4J_{31_P-13_C}$ = 2.3 Hz, *p*-carbons of phenyls), 131.25 (d, $^1J_{31_P-13_C}$ = 136.0 Hz, *i*-carbons of phenyls), 159.90 (s, C=O), assignment was based on the ^1H–13C HETCOR and ^1H–1H COSY spectra. ^{31}P–{1H} NMR (DMSO) δ(ppm): 33.9 (s). Selected IR, ν (cm^{-1}): 3294 (N–H), 3034, 3063 (Ar–H), 1664 (C=O), 1118 (C–O), 1192 (P=O), 998 (P–O). Anal. Calc. for $C_{44}H_{42}N_2O_6P_2$: C, 69.83; H, 5.59; N, 3.70. Found: C, 69.75; H 5.48; N 3.57%.

4.4. Synthesis of *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylthiophosphinite) ethyl]ethanediamide (1b)

N,N′-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (1), (0.20 g, 0.28 mmol) and elemental sulfur (0.018 g, 0.56 mmol) were heated to reflux in toluene (20 mL) for 1 h. After allowing the mixture to cool room temperature, the white solid **1b** was collected by filtration and dried in vacuum (yield: 0.20 g, 91%); mp: 120–122 °C. $[\alpha]_D^{27} = -32$ (c 0.025, CH_2Cl_2). ^1H NMR (DMSO)

δ(ppm): 2.90 (m, 4H, CH_2Ar), 3.93 (m, 4H, CH_2O), 4.33 (m, 2H, C*H*–N), 7.14–7.43 (m, 10H, CH_2Ar), 7.43–7.53 (m, 12H, *m*-, *p*-protons of phenyls), 7.81 (dd, 8H, *J* = 6.9 and 13.2 Hz, *o*-protons of phenyls), 8.90 (d, 2H, *J* = 9.2 Hz, NH). ^{13}C–{1H} NMR (DMSO) δ(ppm): 35.39 (*C*H_2Ar), 50.89 (*C*H–N), 65.32 (*C*H_2O), 126.19, 128.16, 128.88, 137.92 ($CH_2C_6H_5$), 128.64 (d, $^3J_{31_{P-13_C}}$ = 12.1 Hz, *m*-carbons of phenyls), 130.68 (d, $^2J_{31_{P-13_C}}$ = 11.5 Hz, *o*-carbons of phenyls), 132.11 (d, *p*-carbons of phenyls), 133.70 (d, $^1J_{31_{P-13_C}}$ = 110.0 Hz, *i*-carbons of phenyls), 159.56 (s, C=O), assignment was based on the ^{1}H–13C HETCOR and ^{1}H–1H COSY spectra. ^{31}P–{1H} NMR (DMSO) δ(ppm): 84.9 (s). Selected IR, *ν* (cm^{-1}): 3286 (N–H), 3030, 3057 (Ar–H), 1658 (C=O), 1113 (C–O), 650 (P=S), 911 (P–O). Anal. Calc. for $C_{44}H_{42}N_2O_4S_2P_2$: C, 66.99; H, 5.37; N, 3.57; S, 8.13. Found: C, 66.83; H, 5.48; N, 3.48; S, 8.01%.

4.5. Synthesis of N,N′-bis[(1S)-1-benzyl-2-O-(diphenylselenophosphinite) ethyl]ethanediamide (1c)

N,N′-Bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (1) (0.20 g, 0.28 mmol) and grey selenium (0.044 g, 0.56 mmol) were heated to reflux in toluene (20 mL) for 1 h. After allowing the mixture to cool room temperature the dirty white solid **1c** was collected by filtration and dried in vacuum (yield: 0.21 g, 85%); mp: 145–147 °C. $[\alpha]_D^{27}$ = −41 (c 0.025, CH_2Cl_2). ^{1}H NMR (DMSO) δ(ppm): 2.92 (dd, 2H, *J* = 10.6 and 22.8 Hz, CH_2Ar (a)), 2.86 (dd, 2H, *J* = 12.6 and 20.8 Hz, CH_2Ar (b)), 3.93 (m, 4H, CH_2O), 4.34 (m, 2H, C*H*–N), 7.14–7.23 (m 10H, CH_2Ar), 7.40–7.52 (m, 12H, *m*-, *p*-protons of phenyls), 7.79 (dd, 8H, *J* = 6.40 and 12.8 Hz, *o*-protons of phenyls), 8.92 (d, 2H, *J* = 9.2 Hz, NH). ^{13}C–{1H} NMR (DMSO) δ(ppm): 36.09 (*C*H_2Ar), 51.21 (*C*H–N), 66.82 (*C*H_2O), 126.70, 128.66, 129.39, 138.40 ($CH_2C_6H_5$), 129.10 (d, $^3J_{31_{P-13_C}}$ = 13.1 Hz, *m*-carbons of phenyls), 131.22 (d, $^2J_{31_{P-13_C}}$ = 11.9 Hz, *o*-carbons of phenyls), 132.71 (d, *p*-carbons of phenyls), 134.83 (d, $^1J_{1_{P-13_C}}$ = 95.5 Hz, *i*-carbons of phenyls), 160.06 (s, C=O), assignment was based on the ^{1}H–13C HETCOR and ^{1}H–1H COSY spectra. ^{31}P–{1H} NMR (DMSO) δ(ppm): 88.7 [(s), $^1J_{31_{P-13_{Se}}}$ = 805.1 Hz] Selected IR, *ν* (cm^{-1}): 3286 (N–H), 3024, 3049 (Ar–H), 1664 (C=O), 1105 (C–O), 579 (P=Se), 888 (P–O). Anal. Calc. for $C_{44}H_{42}N_2O_4Se_2P_2$: C, 59.87; H, 4.80; N, 3.18. Found: C, 59.96; H, 4.68; N, 3.02%.

4.6. Synthesis of N,N′-bis[(1S)-1-benzyl-2-O-(diphenylphosphinite)-ethyl]ethanediamidepalladium(II)chloride (1d)

[Pd(cod)Cl_2] (0.08 g, 0.28 mmol) and *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (1), (0.20 g, 0.28 mmol) were dissolved in toluene (30 mL) 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 (25 mL) gave **1d** as a yellow solid. The product was collected by filtration and dried in vacuum (yield: 0.23 g, 92%); mp: 157–159 °C. $[\alpha]_D^{27}$ = −37 (c 0.025, CH_2Cl_2). ^{1}H NMR (DMSO) δ(ppm): 2.77–2.81 (m, 4H, CH_2Ar), 4.16 (m, 6H, CH_2O and C*H*–N), 7.18–7.26 (m 10H, CH_2Ar), 7.46–7.52 (m, 12H, *m*-, *p*-protons of phenyls), 7.74 (dd, 8H, *J* = 6.8 and 12.60 Hz, *o*-protons of phenyls), 8.78 (d, 2H, *J* = 8.4 Hz, NH). ^{13}C–{1H} NMR (DMSO) δ(ppm): 36.48 (*C*H_2Ar), 51.12 (*C*H–N), 72.04 (*C*H_2O), 126.36, 128.18, 128.87, 137.32 ($CH_2C_6H_5$), 128.41 (br, *m*-carbons of phenyls), 131.16 (s, *p*-carbons of phenyls), 132.16 (d, $^2J_{31_{P-13_C}}$ = 22.5 Hz, *o*-carbons of phenyls), 136.98 (br, *i*-carbons of phenyls), 158.74 (s, C=O), assignment was based on the ^{1}H–13C HETCOR and ^{1}H–1H COSY spectrum. ^{31}P–{1H} NMR (DMSO) δ(ppm): 112.9 (s). Selected IR, *ν* (cm^{-1}): 3300 (N–H), 3063, 3040 (Ar–H), 1670 (C=O), 1113 (C–O), 886 (P–O). Anal. Calc. for $C_{44}H_{42}N_2O_4P_2PdCl_2$: C, 58.58; H, 4.69; N, 3.11. Found: C, 58.65; H, 4.56; N, 3.05%.

4.7. Synthesis of N,N′-bis[(1S)-1-benzyl-2-O-(diphenylphosphinite)ethyl]-ethanediamideplatinum(II)chloride (1e)

[Pt(cod)Cl_2] (0.10 g, 0.28 mmol) and *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]-ethanediamide (1) (0.20 g, 0.28 mmol) were dissolved in dry toluene (30 mL) and stirred for 2 h. The volume was concentrated to ca. 1–2 mL by evaporation under reduced pressure and addition of diethyl ether (25 mL) afforded **1e** as a white solid. The product was collected by filtration and dried in vacuum (yield: 0.24 g, 87%; mp: 205–207 °C. $[\alpha]_D^{27}$ = −35 (c 0.025, CH_2Cl_2). ^{1}H NMR (DMSO) δ(ppm): 2.78–2.85 (m, 4H, CH_2Ar), 4.17 (m, 6H, CH_2O and C*H*–N), 7.01–7.28 (m, 10H, CH_2Ar), 7.46–7.52 (m, 12H, *m*- and *p*-protons of phenyls), 7.74 (dd, 8H, *J* = 6.1 and 10.8 Hz, *o*-protons of phenyls), 8.78 (d, 2H, *J* = 8.4 Hz, NH). ^{13}C–{1H} NMR (DMSO) δ(ppm): 36.51 (*C*H_2Ar), 51.01 (*C*H–N), 70.61 (*C*H_2O), 126.34, 128.15, 128.85, 137.09 ($CH_2C_6H_5$), 128.30 (br, *m*-carbons of phenyls), 131.72 (s, *p*-carbons of phenyls), 132.11 (d, $^2J_{31_{P-13_C}}$ = 39.0 Hz, *o*-carbons of phenyls), 131.09 (br, *i*-carbons of phenyls), 158.80 (s, C=O), assignment was based on the ^{1}H–13C HETCOR and ^{1}H–1H COSY spectrum. ^{31}P–{1H} NMR (DMSO) δ(ppm): 85.6 [s, $^1J_{PPt}$: 4189 Hz]. Selected IR, *ν* (cm^{-1}): 3306 (N–H), 3057, 3043 (Ar–H), 1675 (C=O), 1115 (C–O), 885 (P–O). Anal. Calc. for $C_{44}H_{42}N_2O_4P_2PtCl_2$: C, 53.54; H, 4.27; N, 2.83. Found: C, 53.63; H, 4.16; N, 2.64%.

4.8. Synthesis of [Ru(chloro(p-cymene)(N,N′-bis[(1S)-1-benzyl-2-O-(diphenylphosphinite)ethyl]ethanediamide)] chloride (1f)

[Ru(*p*-cymene)Cl_2]$_2$ (0.08 g, 0.14 mmol) and *N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide (1), (0.20 g, 0.28 mmol) were dissolved in toluene (30 mL) and stirred for 2 h at room temperature. The volume was then concentrated to ca. 1–2 mL under reduced pressure and addition of diethyl ether (25 mL) gave **1f** as a clear red solid. The product was collected by filtration and dried in vacuum (yield: 0.22 g, 78%); mp: 140–141 °C. $[\alpha]_D^{27}$ = −41 (c 0.025, CH_2Cl_2). ^{1}H NMR (DMSO) δ(ppm): 0.92 (d, 6H, *J* = 6.8 Hz, $CH_3C_6H_4CH(CH_3)_2$), 1.60 (s, 3H, $CH_3C_6H_4CH(CH_3)_2$), 2.27 (m, 1H, $CH_3C_6H_4CH(CH_3)_2$), 2.91–2.95 (m, 4H, CH_2Ar), 3.70 (m, 4H, CH_2O), 4.32 (m, 2H, C*H*–N), 5.34 (d, 2H, *J* = 6.4 Hz, aromatic hydrogen of *p*-cymene), 5.38 (d, 2H, *J* = 7.6 Hz, aromatic hydrogen of *p*-cymene), 7.18–7.26 (m, 10H, C^*HCH_2Ar), 7.32–7.40 (m, 12H, *m*- and *p*-protons of phenyls), 7.82 (dd, 8H, *J* = 8.1 and 14.4 Hz, *o*-protons of phenyls), 8.93 (d, 2H, *J* = 8.8 Hz, NH). ^{13}C–{1H} NMR (DMSO) δ(ppm): 17.02, 21.43, 29.58 (aliphatic protons of *p*-cymene) 35.84 (*C*H_2Ar), 51.20 (*C*H–N), 67.47 (*C*H_2O), 87.98, 89.16, 98.32, 109.18, (aromatic carbons of *p*-cymene); 121.17, 127.54, 127.63, 138.11 ($C^*HCH_2C_6H_5$), 127.64 (d, $^3J_{31_{P-13_C}}$ = 9.1 Hz, *m*-carbons of phenyls), 130.57 (d, *p*-carbons of phenyls), 132.07 (d, $^2J_{31_{P-13_C}}$ = 11.1 Hz, *o*-carbons of phenyls), 131.85 (d, $^1J_{31_{P-13_C}}$ = 11.1 Hz, *i*-carbons of phenyls), 159.65 (s, C=O), assignment was based on the ^{1}H–13C HETCOR and ^{1}H–1H COSY spectra. ^{31}P–{1H} NMR (DMSO) δ(ppm): 115.3 (s). Selected IR, *ν* (cm^{-1}): 3391 (N–H), 3063, 3052 (Ar–H), 1677 (C=O), 1099 (C–O), 883 (P–O). Anal. Calc. for ($C_{44}H_{42}N_2O_4P_2$)-$RuCl_2(CH_3C_6H_4CH(CH_3)_2$: C, 51.26; H, 4.11; N, 2.72. Found: C, 51.11; H, 4.08; N, 2.67%.

4.9. General procedure for the transfer hydrogenation of ketones

Typical procedure for the catalytic hydrogen-transfer reaction: a solution of the ruthenium complex [Ru(chloro(*p*-cymene)(*N,N′*-bis[(1*S*)-1-benzyl-2-*O*-(diphenylphosphinite)ethyl]ethanediamide))] chloride **1f** (0.005 mmol), NaOH (0.025 mmol) and the corresponding ketone (0.5 mmol) in degassed *i*PrOH (5 mL) was refluxed for 1 h. 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.

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