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Transition metal complexes with the C_1-symmetric diphosphines (*R*)-(*R*)-3-benzyl-2,4-bis(diphenylphosphino)pentane and (*R*)-(*R*)-3-benzyl(*p*-sulphonate)-2,4-bis(diphenylphosphino)pentane sodium salt. Applications to enantioselective catalysis in different phase systems

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Dedicated to Professor Henri Brunner, a pioneer in asymmetric catalysis, on the occasion of his 65th birthday

Abstract

The C_1-symmetric diphosphine (*R*)-(*R*)-3-benzyl-2,4-bis(diphenylphosphino)pentane [(*R*)-(*R*)-BDPBzP] has been employed, in combination with Ru(II), Rh(I), Ir(I) and Pd(II) ions, in a variety of homogeneous asymmetric reactions spanning from the hydrogenation of dimethyl itaconate, methyl 2-acetamidocinnamate, 2-methylquinoxaline, methyl pyruvate and dihydro-4,4-dimethyl-2,3-furandione, to the hydroboration of styrene, to the allylic alkylation of (*rac*)-(*E*)-3-acetoxy-1,3-diphenyl-1-propene with dimethyl malonate. The aqueous-biphase hydrogenation of dimethyl itaconate has been accomplished with Rh(I) and Ir(I) complexes containing the monosulphonated derivative (*R*)-(*R*)-3-benzyl(*p*-sulphonate)-2,4-bis(diphenylphosphino)pentane [(*R*)-(*R*)-BDPBzPSO$_3^-$]. Irrespective of the phase variation system, the catalyst precursors generally feature good activity and good to modest enantioselectivity.

Keywords: C_1-symmetric diphosphines; Asymmetric catalysis; Aqueous biphase catalysis

1. Introduction

In a recent paper, we described the synthesis of the C_1-symmetric chiral diphosphine ligand (*R*)-(*R*)-3-benzyl-2,4-bis(diphenylphosphino)pentane [(*R*)-(*R*)-BDPBzP] [1] and of its monosulphonated derivative (*R*) - (*R*) - 3 - benzyl(*p* - sulphonate) - 2,4 - bis(diphenylphosphino)pentane sodium salt [(*R*)-(*R*)-BDPBzPSO$_3^-$ Na$^+$] [2]. This latter compound was obtained by regioselective sulphonation of the benzyl ring of (*R*)-(*R*)-BDPBzP with concentrated H_2SO_4 at 100°C (Fig. 1).

A single-crystal X-ray analysis on the *p*-cymene complex [(*R*)-(*R*)-BDPBzP)Ru(*p*-cymene)I]I·2CH$_2$Cl$_2$ and the NMR characteristics of some Ru(II) complexes [1] indicate that six-membered metallarings containing (*R*)-(*R*)-BDPBzP prefer to adopt a distorted chair conformation such as that shown in Fig. 2. In this conformation, two phenylphosphino rings are axial and two are equatorial, one methyl substituent is axial and the other one is equatorial, the benzyl CH$_2$ group is equatorial while its phenyl ring lies in the same portion of space as the two axial phenylphosphino rings.

^{1}H-NOESY experiments carried out on CDCl$_3$ solutions of [(*R*)-(*R*)-BDPBzP)Ru(*p*-cymene)I]I·2CH$_2$Cl$_2$ and [(*R*)-(*R*)-(BDPBzP)(DMSO)Ru(μ-Cl)$_3$RuCl(*R*)-(*R*)-(BDPBzP)] (**6**) showed that the six-membered chelated ring adopts in solution the primary conformation found in the solid state [1]. Moreover, no detectable line-width narrowing was observed by variable-temperature ^{1}H-NMR spectroscopy (from 273 to 313 K) thus suggesting the absence of conformational equilibria.

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Besides reducing the ligand flexibility, the introduction of a benzyl substituent on the central carbon atom of the 2,4-bis(diphenylphosphino)pentane (BDPP) backbone has apparently two other major effects: it removes the C_2 symmetry and disfavours the skew conformation which is preferred by optically active BDPP (Fig. 2) [3]. Reduced flexibility, C_1-symmetry and chair conformation make any correlation between BDPP and (*R*)-(*R*)-BDPBzP catalysts quite improper, and also do not allow one to forecast the stereodifferentiation ability of (*R*)-(*R*)-BDPBzP metal complexes by simply taking into account the knowledge developed on chiral diphosphine ligands over many years. Indeed, if ligand rigidity often provides superior properties in asymmetric catalysis by limiting the number of competing conformations, the chair form for the chelate BBP-BzP metallaring, with two axial and two equatorial phenyl rings, is expected to be less efficient in controlling the coordination of the substrate [3,4]. On the other hand, dissymmetry may be very important when intermediates in catalytic cycles lack the intrinsic symmetry of the ligand [5]. In conclusion, the chiral transfer ability of (*R*)-(*R*)-BDPBzP seems to be governed by a complex web of steric (and eventually electronic) effects. Accordingly, only a large amount of experimental work will enable a serious evaluation of the stereodifferentiation properties of (*R*)-(*R*)-BDPBzP in asymmetric catalysis.

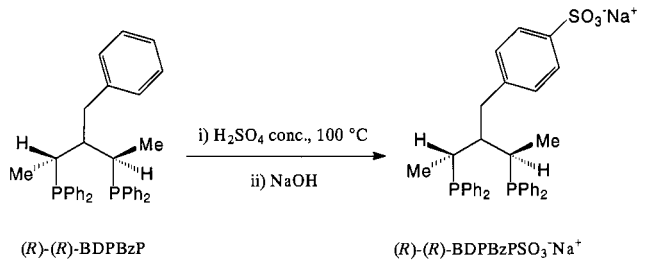


Fig. 1. Sketches of (*R*)-(*R*)-BDPBzP and (*R*)-(*R*)-BDPBzP$SO_3^-Na^+$.

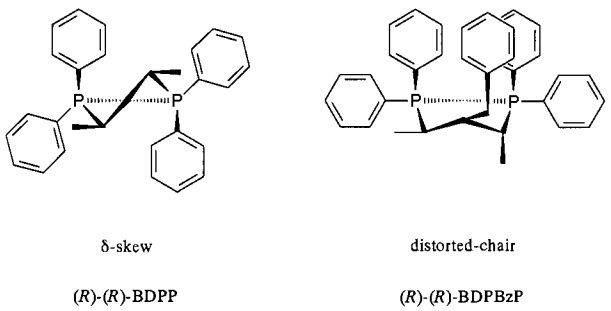


Fig. 2. Preferred skew and chair conformations adopted by (*R*)-(*R*)-BDPP and (*R*)-(*R*)-BDPBzP, respectively.

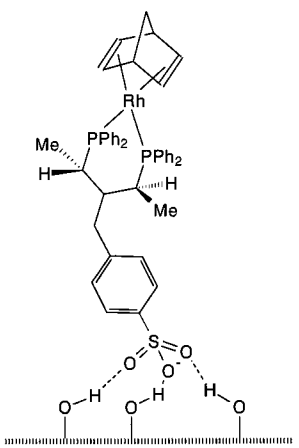


Fig. 3. The supported-hydrogen bonded complex [(*R*)-(*R*)-BDPBzPSO_3^-]Rh(NBD) (**5**).

Some mono- and dinuclear Ru(II) complexes containing the diphosphine (*R*)-(*R*)-BDPBzP have already been tested as catalyst precursors for the enantioselective hydrogenation of acetylacetone to (*R*)-(*R*)-2,4-pentandiol [1]. Enantiomeric excesses (ee) as high as 99% were obtained, while the catalytic activities were found to be from good to modest, which is in line with the remarkable rigidity of (*R*)-(*R*)-BDPBzP [6].

The heterogeneous hydrogenation of prochiral olefins (dimethyl itaconate, ethyl *trans*-β-(methyl)cinnamate and methyl α-(acetamido)acrylate) has also been reported to occur in *n*-heptane using the Rh(I) complex [(*R*)-(*R*)-BDPBzPSO_3^-]Rh(NBD) tethered to silica via hydrogen bonding (Fig. 3) [2]. In this case, rather low values of ee were observed (10–50%), which, however, were comparable to those of analogous heterogenized (+)-DIOP and (*S*)-BINAP Rh catalysts in the same experimental conditions.

In this paper, we describe the synthesis and characterization of new (*R*)-(*R*)-BDPBzP complexes with Ir(I), Rh(I) and Pd(II) metal ions and report on the performance of various catalysts in the following reactions: Pd-catalysed allylic alkylation, Rh-catalysed hydroboration, Rh and Ir-catalysed hydrogenation of olefins and imines, and Ru-catalysed hydrogenation of activated ketones. Also, we present a preliminary study on the potential of (*R*)-(*R*)-BDPBzP$SO_3^-Na^+$ in aqueous-biphase catalysis in combination with Rh(I) and Ir(I) ions.

2. Experimental

2.1. General information

All manipulations were performed under a pure nitrogen atmosphere unless otherwise stated. Freshly distilled, dry solvents were used throughout. $[Rh(NBD)Cl]_2$ [7], $[Ir(COD)Cl]_2$ [8], $[(\eta^3\text{-}C_3H_5)PdCl]_2$ [9], [(*R*)-(*R*)-(BDPBzP)(DMSO)Ru(μ-Cl)$_3$RuCl(*R*)-(*R*)-(BDPBzP)] (**6**) [1], ((*R*)-(*R*)-BDPBzPSO_3^-)Rh(NBD) (**5**)

[2], (*R*)-(*R*)-BDPBzP [1], (*R*)-(*R*)-BDPBzPSO$_3^-$Na$^+$ [2] and (*rac*)-(*E*)-3-acetoxy-1,3-diphenyl-1-propene [10] were synthesized as previously reported. All the other chemicals were commercial products and were used as received without further purification. The solid compounds were collected on sintered glass frits before being dried in a stream of nitrogen.

^{31}P{^{1}H}-NMR spectra were recorded either on a Bruker 200-ACP spectrometer operating at 81.01 MHz or on a Bruker Avance DRX-500 spectrometer operating at 202.46 MHz. Chemical shifts are relative to external 85% H_3PO_4 with downfield values reported as positive. ^{1}H-NMR spectra were recorded at 200.13 MHz on a Bruker 200-ACP spectrometer or at 500.13 MHz on a Bruker Avance DRX-500 spectrometer. Chemical shifts are relative to tetramethylsilane as external reference or calibrated against solvent resonances. Unambiguous assignment of the NMR signals was provided by ^{1}H homonuclear decoupling experiments, ^{1}H-COSY and proton detected ^{1}H–^{31}P correlations using degassed non-spinning samples. 2D-NMR spectra were recorded using pulse sequences suitable for phase-sensitive representations using TPPI. The ^{1}H–^{31}P correlations [11] were recorded using the standard HMQC sequence with no decoupling during acquisition.

Merck silica gel 60, 230-400 mesh ASTM was used for column chromatography. Thin-layer chromatography was performed with Macherey–Nagel Polygram SIL G/UV254 precoated plastic sheets.

Reactions under a controlled pressure of hydrogen were performed with a stainless steel autoclave (100 ml internal volume) constructed at ISSECC-CNR (Florence, Italy) and equipped with a magnetic stirrer, a glass inset and a pressure controller. The temperature control was achieved by an oil bath thermostat accurate to $\pm$ 0.2°C. Hydrogenation reactions in two phase systems were performed with a stainless steel Parr 4565 reactor (100 ml) equipped with a mechanical stirrer and a Parr 4842 temperature and pressure controller.

GC analyses were performed either on a Shimadzu GC-14A gas-chromatograph equipped with a flame ionization detector and a 30 m (0.25 mm ID, 0.25 μm FT) SPB-1 Supelco fused silica capillary column and coupled with a C-R6A Chromatopac operating in the corrected area method or with a Shimadzu GC-17A gas chromatograph equipped with a flame ionization detector and a 40 m $\times$ 0.25 mm ID Chiraldex G-TA capillary column and coupled with a Shimadzu C-R7A Chromatopac. GC/MS analyses were performed on a Shimadzu QP 2000 apparatus equipped with a column identical to that used for GC analyses (SPB-1). The organic compounds were identified by their GC-MS spectra.

HPLC analyses were performed with a Shimadzu LC-8A liquid chromatograph coupled with a Shimadzu SPD-M6A photodiode array UV–Vis detector operating in the 200–350 nm wavelength range and equipped with a Daicel Chiralcel OD-H 0.46 $\times$ 25 cm column.

2.2. Synthesis of the complexes

2.2.1. [((R)-(R)-BDPBzP)Ir(COD)]OTf (1)

Solid [Ir(COD)Cl]$_2$ (0.13 g, 0.19 mmol) was added to a solution of (*R*)-(*R*)-BDPBzP (0.20 g, 0.38 mmol) in CH_2Cl_2 (20 ml). AgOTf (0.10 g, 0.38 mmol) was then added with stirring to the yellow solution causing a colour change to deep red. After AgCl was filtered off, the addition of diethyl ether (20 ml) led to the separation of a red oil which was decanted, washed with diethyl ether (3 $\times$ 30 ml) and dried in vacuo to give solid **1** in 82% yield. Anal. Calc. for $C_{45}H_{48}F_3IrO_3P_2S$: C, 55.15; H, 4.94. Found: C, 55.24; H, 4.82%. ^{1}H-NMR ($CDCl_3$, 296 K, 200.13 MHz): 7.4–7.8 (*m*, 15H, Ph), 7.2–7.4 (*m*, 6H, Ph), 7.08 (*m*, 2H, Ph), 6.83 (*m*, 2H, Ph), 4.12 (*bs*, 3H, CH=CH, COD), 3.97 (*bs*, 1H, CH=C, COD), 3.10 (*dq*, 1H, CH*H*, BDPBzP, $J = 7.4$, $J = 14.1$ Hz), 2.6–2.9 (*m*, 2H), 2.43 (*m*, 2H), 1.9–2.3 (*m*, 8H), 1.56 (*dd*, 3H, CH_3, $J = 15.7$, $J = 7.1$ Hz), 1.22 (*dd*, 3H, CH_3, $J = 13.9$, $J = 7.0$ Hz).

2.2.2. [((R)-(R)-BDPBzP)Rh(NBD)]OTf (2)

Solid [Rh(NBD)Cl]$_2$ (0.09 g, 0.19 mmol) was added to a solution of (*R*)-(*R*)-BDPBzP (0.20 g, 0.38 mmol) in CH_2Cl_2 (20 ml). AgOTf (0.10 g, 0.38 mmol) was then added and the suspension was stirred for 50 min. After AgCl was filtered off, *n*-hexane (20 ml) was added until a red oil separated which was decanted, washed with *n*-hexane (3 $\times$ 30 ml) and dried in vacuo to give solid **2** in 78% yield. Anal. Calc. for $C_{44}H_{44}F_3O_3P_2SRh$: C, 60.42; H, 5.07. Found: C, 60.33; H, 4.92%. ^{1}H-NMR (CD_3COCD_3, 296 K, 200.13 MHz): 6.9–7.9 (*m*, 22H, Ph), 6.95 (*m*, 3H, Ph), 5.03 (*bs*, 2H, CH=CH, NBD), 4.91 (*bs*, 1H, CH=C, NBD), 4.32 (*bs*, 1H, CH=C, NBD), 4.08 (*bs*, 1H, CH, NBD), 3.96 (*bs*, 1H, CH, NBD), 3.1–2.8 (*m*, 3H), 2.62 (*dd*, 1H, CH*H*, BDPBzP, $J = 11.8$, $J = 14.2$ Hz), 2.29 (*m*, 1H), 1.59 (*t*, 1H, CH*H*, NBD, $J = 1.6$ Hz), 1.58 (*dd*, 3H, CH_3, $J = 16.3$, $J = 7.1$ Hz), 1.27 (*s*, 1H, C*H*H, NBD), 1.25 (*dd*, 3H, CH_3, $J = 12.5$, $J = 7.1$ Hz).

2.2.3. [((R)-(R)-BDPBzP)Pd(η^3-C$_3$H$_5$)]PF$_6$ (3)

Solid [(η^3-C_3H_5)PdCl]$_2$ (0.07 g, 0.19 mmol) was added to a solution of (*R*)-(*R*)-BDPBzP (0.20 g, 0.38 mmol) in acetone (15 ml). $TlPF_6$ (0.13 g, 0.38 mmol) was added to the mixture. After stirring for 5 min, TlCl was filtered off and *n*-pentane (20 ml) was added to give a colourless oil which was decanted, washed with *n*-pentane (3 $\times$ 30 ml) and dried in vacuo to give solid **3** in 77% yield. Anal. Calc. for $C_{39}H_{41}F_6P_3Pd$: C, 56.91; H, 5.02. Found: C, 56.84; H, 4.98%. ^{1}H-NMR ($CDCl_3$, 296 K, 200.13 MHz): isomer A, 5.53 (*m*, 1H, central

Table 1
$^{31}P\{^1H\}$-NMR data for L = (*R*)-(*R*)-BDPBzP compounds [a]

Compound	δ P_1	δ P_2	*J*
L [b,c]	−1.24	−10.73	J_{PP} 0.0
[LIr(COD)]OTf (**1**)	16.25	14.07	$^2J_{PP}$ 27.5
[LRh(NBD)]OTf [d] (**2**)	33.10	29.52	$^2J_{PP}$ 49.5, $^1J_{P1Rh}$ 145.6, $^1J_{P2Rh}$ 151.6
[LPd(η^3-C_3H_5)]PF_6 (**3**)			
Isomer A	23.39	21.98	$^2J_{PP}$ 63.5
Isomer B	22.92	21.72	$^2J_{PP}$ 62.3

[a] Chemical shifts in ppm, coupling constants in Hz, 81.01 MHz, 296 K, $CDCl_3$.
[b] 202.46 MHz.
[c] Data from Ref. [1].
[d] CD_3COCD_3.

allyl), 4.15 (*m*, 1H, terminal allyl), 3.66 (*m*, 1H, terminal allyl), 2.51 (*t*, 1H, CH*H*, BDPBzP, $J = 12.3$ Hz); isomer B, 5.97 (*m*, 1H, central allyl), 4.28 (*m*, 1H, terminal allyl), 3.94 (*m*, 1H, terminal allyl), 2.55 (*t*, 1H, C*H*H, BDPBzP, $J = 13.1$ Hz).

2.2.4. ((R)-(R)-BDPBzPSO$_3$)Ir(COD) (4)

Solid $[Ir(COD)Cl]_2$ (0.013 g, 0.19 mmol) was added to a solution of (*R*)-(*R*)-BDPBzP$SO_3^-Na^+$ (0.24 g, 0.38 mmol) in CH_2Cl_2 (15 ml). After stirring for 30 min at room temperature (r.t.), a red solution was obtained. The addition of diethyl ether (30 ml) caused the precipitation of a red oil which solidified on standing. The solid compound was washed with diethyl ether (50 ml), dried in vacuo and recrystallized from CH_2Cl_2–diethyl ether (1:1, vv). Yield 75%. Anal. Calc. for $C_{44}H_{47}IrO_3P_2S$: C, 58.07; H, 5.21. Found: C, 58.12; H, 5.30%. ^{1}H-NMR (CD_3OD, 296 K, 200.13 MHz): 7.2–7.9 (*m*, 20H, Ph), 7.05 (*m*, 2H, Ph), 6.72 (*m*, 2H, Ph), 4.00 (*bm*, 4H, CH=CH, COD), 1.8–3.0 (*bm*, 11H), 1.3–1.5 (*bm*, 5H), 1.18 (*dd*, 3H, CH_3, $J = 11.1$, $J = 6.7$ Hz).

2.3. Enantioselective hydrogenation reactions

The reactions were carried out as previously described [12]. In a typical experiment solid **1** (5 mg, 0.005 mmol) was added to a solution of the unsaturated substrate (0.5 mmol) in methanol (20 ml) under argon. The suspension was stirred at r.t until the complete dissolution of the starting complex occurred (ca. 15 min.). The resulting solution was transferred via a Teflon capillary into a 100 ml autoclave under argon. Argon was then replaced by hydrogen with three cycles 5 bar/normal pressure. The autoclave was finally charged with the desired pressure of H_2 and then heated using a thermostated oil-bath. After the desired time under stirring, the reactor was cooled to room temperature and a sample of the reaction mixture was analysed by GC and GC/MS.

2.4. Enantioselective allylic alkylation reactions

The reactions were carried out using the conditions reported by Pfaltz and co-workers [13]. A representative procedure is reported in Ref. [14].

2.5. Enantioselective hydroboration reactions

The reactions were carried out following a reported procedure [14].

2.6. Aqueous-biphase enantioselective hydrogenation reactions

In a typical reaction, the catalyst precursor ((*R*)-(*R*)-BDPBzPSO_3^-)Rh(NBD) (**5**) (9 mg, 0.011 mmol) was dissolved at r.t. in 1:1 (v/v) water–methanol (10 ml) under a nitrogen atmosphere. A deareated solution of dimethyl itaconate (0.18 g, 1.14 mmol) in *n*-heptane (10 ml) was then added and the mixture was transferred into the autoclave via a Teflon capillary under a nitrogen atmosphere. Nitrogen was then replaced by hydrogen with three cycles 5 bar/normal pressure. The autoclave was finally charged with the desired pressure of H_2 and then heated with stirring (1000 rpm). After the desired time, the reactor was cooled to r.t., the organic and aqueous phases were separated and analysed by GC.

3. Results and discussion

3.1. Synthesis and characterization of the compounds

The new complexes [((*R*)-(*R*)-BDPBzP)Ir(COD)]OTf (**1**), [((*R*)-(*R*)-BDPBzP)Rh(NBD)]OTf (**2**) and [((*R*)-(*R*)-BDPBzP)Pd(η^3-C_3H_5)]PF_6 (**3**) have been prepared in excellent yields by reaction of (*R*)-(*R*)-BDPBzP with suitable metal precursors, $[Ir(COD)Cl]_2$, $[Rh(NBD)Cl]_2$ and $[(\eta^3\text{-}C_3H_5)PdCl]_2$, followed by treatment with AgOTf. No external chloride scavenger is needed to synthesize ((*R*)-(*R*)-BDPBzPSO_3)Ir(COD) (**4**) from $[Ir(COD)Cl]_2$ and (*R*)-(*R*)-BDPBzP$SO_3^-Na^+$ due to the presence of the sodium cation in the diphosphine ligand. The Rh(I) derivative ((*R*)-(*R*)-BDPBzPSO_3^-)-Rh(NBD) (**5**) has recently been prepared in this way [2].

All the metal complexes have been characterized in solution by NMR spectroscopy. $^{31}P\{^1H\}$-NMR data are reported in Tables 1 and 2, while relevant ^{1}H-NMR data are reported in Section 2.

The diene complexes **1** and **2** and the Pd(II)-η^3-allyl complex **3** are soluble and stable in deareated solutions of common organic solvents, while the zwitterionic complexes **4** and **5** are very soluble also in a 1:1 mixture of methanol and water. At room temperature, the solubility of **4** and **5** in pure water is quite low.

Table 2
^{31}P-NMR data for L′ = (*R*)-(*R*)-BDPBzPSO$_3^-$Na$^+$ compounds [a]

Compound	δ P$_1$	δ P$_2$	J
L′ [b]	−1.08	−10.80	J_{PP} 0.0
L'Ir(COD) (**4**) [c]	16.31	14.59	J_{PP} 27.0
L'Rh(NBD) (**5**) [c,b]	32.64	29.47	J_{PP} 49.3, J_{P1Rh} 145.9, J_{P2Rh} 151.4

[a] Chemical shifts in ppm, coupling constants in Hz, 81.01 MHz, 296 K, $CDCl_3$.
[b] Data from Ref. [2].
[c] CD_3OD.

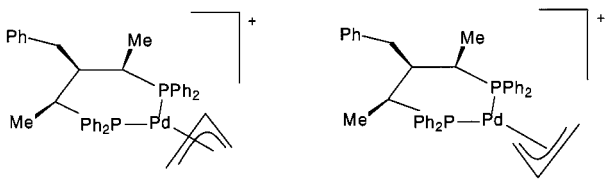


Fig. 4. Sketches of the two *exo* and *endo* isomers of [((*R*)-(*R*)-BDPBzP)Pd(η^3-C_3H_5)]PF_6 (**3**).

The NMR data for **1**, **2** and **4** are consistent with a square-planar coordination geometry around the metal centre with two *cis* phosphorus atoms ($^2J_{PP}$ = 27.0–49.5 Hz) [15,16]. Complex **3** exists in solution as two diastereomeric *exo* and *endo* species, **A** and **B** in Fig. 4 and Table 1, which is a typical feature for Pd-η^3-allyl complexes with chiral diphosphine ligands [10,17,18]. All the NMR assignments were made on the basis of 2D ^{1}H-COSY spectra and ^{1}H–^{31}P correlations. The NMR characteristics of **1**–**4** are rather trivial and do not deserve particular comment.

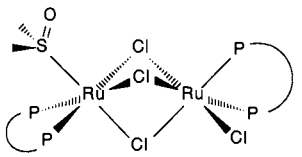
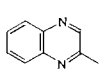
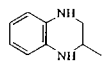
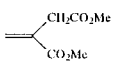
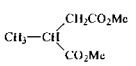
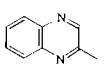
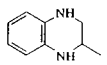
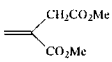
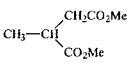
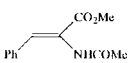
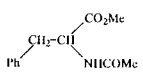
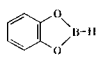
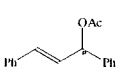
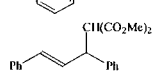
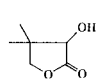


Fig. 5. Structure of [(*R*)-(*R*)-(BDPBzP)(DMSO)Ru(μ-Cl)$_3$RuCl(*R*)-(*R*)-(BDPBzP)] (**6**).

3.2. Asymmetric catalysis

The hydrogenation, hydroboration and allylic alkylation reactions reported in Table 3 were performed using the mononuclear precursors **1**, **2** and **3**, while the dimeric complex [(*R*)-(*R*)-(BDPBzP)(DMSO)Ru(μ-Cl)$_3$RuCl(*R*)-(*R*)-(BDPBzP)] (**6**) was employed to catalyse the reduction of an α-ketoester and a lactone.

Table 3
Asymmetric catalysis using L = (*R*)-(*R*)-BDPBzP complexes [a]

Entry	Complex	Substrate	Solvent	S/C mol. ratio	Temp. (°C)	Time (h)	Reagents	Product	Yield [b] (%)	ee (%)
1	[LIr(COD)]OTf		MeOH	100	40	48	H_2 (290 psi)		40.7	23 [c]
2	[LIr(NBD)]OTf		MeOH	100	40	48	H_2 (15 psi)		47.4	77 [b]
3	[LRh(NBD)]OTf		MeOH	100	r.t.	24	H_2 (290 psi)		93.2	11 [c]
4	[LRh(NBD)]OTf		MeOH	100	r.t.	24	H_2 (15 psi)		100.0	68 [b]
5	[LRh(NBD)]OTf		MeOH	100	r.t.	24	H_2 (15 psi)		100.0	59 [d]
6	[LRh(NBD)]OTf		DME	100	0	3.75	1)  2) H_2O_2, NaOH		28.5	26 [b]
7	[LPd(η^3-C_3H_5)]PF_6		CH_2Cl_2	100	r.t.	22	$CH_2(CO_2Me)_2$		96.0	32 [c]
8	$L_2Ru_2(\mu\text{-}Cl)_3(DMSO)Cl$		EtOH	500	40	48	H_2 (725 psi)		90.7	8 [b]
9	$L_2Ru_2(\mu\text{-}Cl)_3(DMSO)Cl$		EtOH	250	40	48	H_2 (725 psi)		21.4	28 [c]

[a] BDPBzP = 3-benzyl-2,4-bis(diphenylphosphino)pentane.
[b] GC; reaction mixture.
[c] HPLC; isolated product.
[d] ^{1}H NMR, isolated product using the shift reagent (S)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol.

Complex **6** has the *transoid* structure illustrated in Fig. 5 [1].

The reaction of 2-methylquinoxaline in MeOH in the presence of 1 mol% of either **1** or **2** under a hydrogen pressure of 290 psi gave (−)-(2*S*)-2-methyl-1,2,3,4-tetrahydroquinoxaline in 93% (24 h, room temperature) and 41% (48 h, 40°C) yield, respectively (Table 3, entries 1, 3). As expected, the Rh precursor was more active than the Ir analogue which, however, gave a higher enantiomeric excess (ee) (23 versus 11% ee). The higher stereoselectivity of Ir versus Rh is most likely kinetic in nature, i.e. the greater kinetic inertness of Ir compounds as compared to Rh analogues may be crucial for the stabilization of the intermediate which undergoes the enantiotopic hydride transfer [19].

The enantioselective hydrogenation of 2-substituted quinoxalines is a difficult task in asymmetric catalysis [20]. Rhodium diphosphine complexes such as [((+)-DIOP)RhH] prepared in situ, are quite efficient but scarcely enantioselective [21], while iridium generally provides much better catalysts. Good ee values for (−)-(2*S*)-2-methyl-1,2,3,4-tetrahydroquinoxaline have recently been obtained with the *o*-metalated dihydride complex *fac-exo*-(*R*)-[$IrH_2\{C_6H_4C^*H(Me)N(CH_2CH_2PPh_2)_2\}$] (90% ee, 5 bar H_2, MeOH, 100°C) [12].

The Rh precursors **1** gave better results when employed for the hydrogenation of dimethyl itaconate (68% ee) or methyl 2-acetamidocinnamate (59% ee) at an initial hydrogen pressure of 15 psi (entries 4 and 5). Like the reduction of 2-methyl quinoxaline, the substitution of iridium for rhodium resulted in a lower conversion and in a better enantioface discrimination (47% yield, 77% ee) (entry 2). Although similar to those obtained with (*S*)-(*S*)-BDPP rhodium catalysts [3b,22], these results are worse than those obtainable with C_2 symmetric chiral diphosphines like BINAP and DUPHOS [23].

The hydroboration of styrene with catecholborane, followed by oxidation with hydrogen peroxide, was carried out using the Rh precursor **2** (1 mol%) in dimethoxyethane at 0°C over a period of 4 h (entry 6). The reaction gave a good regioselectivity as only a very small amount (<1%) of the branched product 2-phenylethanol was formed, but the stereoselectivity in the linear-chain alcohol 1-phenylethanol was rather modest (26% ee) and generally lower than those reported for rhodium complexes with C_2-symmetric chiral diphosphines [24].

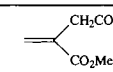
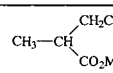
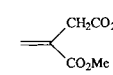
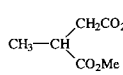
The Pd-η^3-allyl complex **3** behaves as an efficient catalyst precursor for the alkylation reaction of (*rac*)-(*E*)-3-acetoxy-1,3-diphenyl-1-propene by dimethyl malonate. At room temperature, the conversion in CH_2Cl_2 was almost quantitative in 22 h using a 100:1 substrate to catalyst ratio yielding the desired product in 32% ee (entry 7), which is lower than that obtainable with many other catalysts [17,25].

Finally, the *transoid* Ru(II) dimer **6** was employed as catalyst precursor for the asymmetric hydrogenation of the α-ketoester methyl pyruvate and of the lactone dihydro-4,4-dimethyl-2,3-furandione. The chemoselective hydrogenation of the keto group in the ketoester was efficiently performed in ethanol, but the ee was only 8% (entry 8). Under comparable experimental conditions, the cyclic ketoester was more difficult to reduce (21.4% yield) but a slightly better enantioselectivity was observed (28% ee) (entry 9). The formation of acetal by-products did not occur. Other simple ketones behaved similarly, yielding the corresponding chiral alcohols with modest ee values.

It has previously been shown that **6** is an efficient catalyst precursor for the enantioselective hydrogenation of acetylacetone to (*R*)-(*R*)-2,4-pentandiol (up to 99% ee) [1]. A double stereodifferentiation process involving the monohydrogenated (*R*)-4-hydroxypentan-2-one product was invoked to account for the excellent enantioselectivity of **6**. It is, therefore, very likely that the low stereoselectivity observed in the reduction of the ketoester and the lactone with **6** may be due to the lack of efficient chelate effect of the substrate [26].

A preliminary investigation of the ability of the sulphonated ligand (*R*)-(*R*)-$BDPBzPSO_3^-Na^+$ in aqueous biphase asymmetric catalysis has been carried out. Indeed, there is much current interest in designing chiral catalysts that can be efficiently recovered after a

Table 4
Asymmetric catalytic hydrogenations in two phase systems using L′ = (*R*)-(*R*)-$BDPBzPSO_3^-$ complexes [a]

Entry	Complex	Solvent	S/C mol. ratio	Temp. (°C)	Time (h)	H_2 (psi)	Substrate	Product [b]	Yield [c] (%)	ee [c] (%)
1	L′Ir(NBD)	MeOH : H_2O : *n*-heptane 1: 1: 2	100	r.t.	48	72			45.3	76
2	L′Rh(NBD)	MeOH : H_2O : *n*-heptane 1: 1: 2	100	r.t	24	72			100.0	66

[a] BDPBzP = 2,4-Bis-(diphenylphosphino)-3-benzyl-pentane. Reaction conditions: metal (0.01 mmol), solvent (20 ml).
[b] Hydrocarbon phase.
[c] GC; reaction mixture.

catalytic run [27]. Catalyst recovery is of paramount importance in fine chemicals production, particularly when sophisticated ligands are used, whose cost often exceeds that of the noble metal employed.

The zwitterionic complexes **4** and **5** have the same primary structure as the parent cationic compounds **1** and **2** as determined by NMR spectroscopy. Unlike **1** and **2**, however, the complexes with the sulphonated diphosphine are very soluble in 1:1 water–MeOH mixtures already at room temperature. This physical feature allows **4** and **5** to be employed as catalyst precursors in a biphase system containing *n*-heptane as the apolar phase.

The hydrogenation of dimethyl itaconate has preliminary been studied in such biphasic system where both the unsaturated substrate and the hydrogenation products are exclusively soluble in the hydrocarbon phase (GC). Using 1% catalyst precursor at an initial hydrogen pressure of 72 psi and at room temperature, the hydrogenation of the C–C double bond was achieved in 45% and 100% yields by Ir and Rh catalysis, respectively (Table 4). Like in the homogeneous phase, iridium (entry 1) forms a better enantioselective catalyst than rhodium (entry 2) (77% versus 66% ee).

After a catalytic run, the polar phase containing either rhodium or iridium was carefully separated from the hydrocarbon phase under an H_2 atmosphere and then was re-used in a second run. This procedure was repeated twice. In either case, no appreciable decay in stereoselectivity was observed, while the activity decreased by ca. 5% only after every run, which we ascribe to catalyst deactivation during the phase separation and autoclave re-charging process.

The aqueous biphase hydrogenation of dimethyl itaconate with catalysts prepared in situ from $[Rh(COD)Cl]_2$ and (*S*)-(*S*)-BDPP carrying 0–4 sulphonate groups has recently been reported by de Vries et al. [28]. Interestingly, the catalyst system that is more similar to **5**, i.e. that containing the monosulphonated BDPP ligand gave the lowest ee (28%). Ee valuse comparable to those given by **5** have more recently been obtained in the Rh-assisted hydrogenation of functionalized chelating olefins using water-soluble diphosphines bearing, like (*R*)-(*R*)-BDPBz-$PSO_3^-Na^+$, the polar group(s) far away from the phosphorus donors [29].

4. Conclusions

The C_1-symmetric diphosphine (*R*)-(*R*)-BDPBzP has been employed, in combination with Ru(II), Rh(I), Ir(I) and Pd(II) ions, in a variety of homogeneous asymmetric reactions ranging from the hydrogenation of prochiral olefins, 2-substituted quinoxalines and activated ketones, to the hydroboration of styrene, to the allylic alkylation of (*rac*)-(*E*)-3-acetoxy-1,3-diphenyl-1-propene. The aqueous-biphase hydrogenation of dimethyl itaconate has been accomplished with Rh(I) and Ir(I) complexes containing the monosulphonated diphosphine (*R*)-(*R*)-BDPBzPSO_3^-. Irrespective of the phase variation system, the catalyst precursors feature good activity and good to modest enantioselectivity. Still acetylacetone remains the substrate that undergoes the most efficient enantioface discrimination by an (*R*)-(*R*)-BDPBzP metal complex in the homogeneous phase [1]. (*R*)-(*R*)-BDPBzP is actually a complex ligand that combines dissymmetry, remarkable skeletal rigidity and preference for the chair conformation of six-membered metallarings. These features, taken altogether, might limit the successful applicability of (*R*)-(*R*)-BDPBzP metal complexes in enantioselective catalysis to a restricted number of suitable prochiral substrates.

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