Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 1943–1955

TETRAHEDRON: *ASYMMETRY*

Optically active palladacycles containing imines derived from 1-(1-naphthyl)ethylamine: new resolving agents for P-chiral phosphines

Joan Albert,[a] J. Magali Cadena,[a] Jaume R. Granell,[a,*] Xavier Solans[b] and Mercè Font-Bardia[b]

[a]*Departament de Química Inorgànica, Universitat de Barcelona, Diagonal 647, 08028 Barcelona, Spain*
[b]*Departament de Cristallografia, Mineralogia i Dipòsits Minerals, Universitat de Barcelona, Martí i Franquès s/n, 08028 Barcelona, Spain*

Received 10 March 2000; accepted 6 April 2000

Abstract

The synthesis of the new palladium metallacycles containing imines derived from 1-(1-naphthyl)ethylamine is reported. These new organometallic complexes have been used to resolve the P-chiral ligand benzylcyclohexylphenylphosphine. The absolute configuration of (R_C,S_P)-[PdCl{2-[HC=N-CH(Me)$C_{10}H_6$]-3-ClC_6H_3}(PBzCyPh)] has been determined by single crystal X-ray analysis. © 2000 Elsevier Science Ltd. All rights reserved.

1. Introduction

Enantiomerically pure cyclopalladated compounds are of great interest as a consequence of their useful applications in many areas such as the determination of enantiomeric excess[1] and absolute configuration of chiral compounds,[2] the asymmetric synthesis of optically active organic molecules[3] and the resolution of Lewis bases.[4] *Ortho*-palladated derivatives of the tertiary amines *N*,*N*-dimethyl-1-(1-naphthyl)ethylamine and *N*,*N*-dimethyl-α-methylbenzylamine have been used in nearly all the stereochemical applications of such compounds; however, only over the last few years has the application of other new cyclometallated compounds in these fields been explored.[1b,1c,5] In contrast to the wide use of these metallacycles for the resolution of bi- and polydentate ligands few agents have been found for the resolution of monodentate P-chiral ligands, in spite of the interest of such phosphines since metal complexes featuring marked

* Corresponding author. Fax: 34-934907725; e-mail: jgranell@kripto.qui.ub.es

PII: S0957-4166(00)00143-9

asymmetry near the catalytic center are considered to be excellent stereoselectivity inducers.[6] It should be noted that the resolution of any monodentate Lewis base by enantiomerically pure cyclopalladated compounds requires a more efficient resolving agent, compared to that required for the bidentate analogues.[5f] In this paper we describe the synthesis of novel chiral cyclopalladated compounds containing enantiomerically pure imine ligands and their use for the resolution of the P-chiral ligand benzylcyclohexylphenylphosphine, which has been shown to be a very useful ligand for the catalytic asymmetric hydrovinylation of vinyl aromatic derivatives.[5a]

2. Results and discussion

Imines can undergo metallation on different carbon atoms, giving organometallic complexes of different structures: *endo*-metallacycles, if the C=N bond is included in the metallacycle, or *exo*-derivatives (Fig. 1). In addition, imines can exist as *E*- or *Z*-isomers, but in general, *N*-substituted aldimines adopt the more stable *E*-form.[7] *Endo*- or *exo*-metallacycles can be obtained from imines in the *E*-form but *exo*-metallacycles only can be formed from the *Z*-isomer.

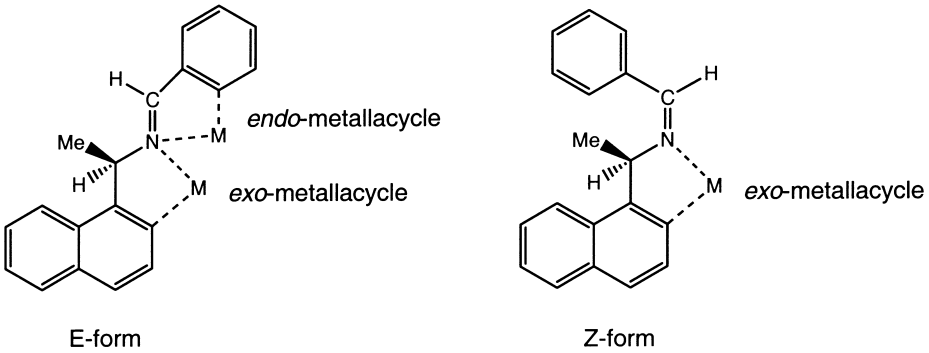


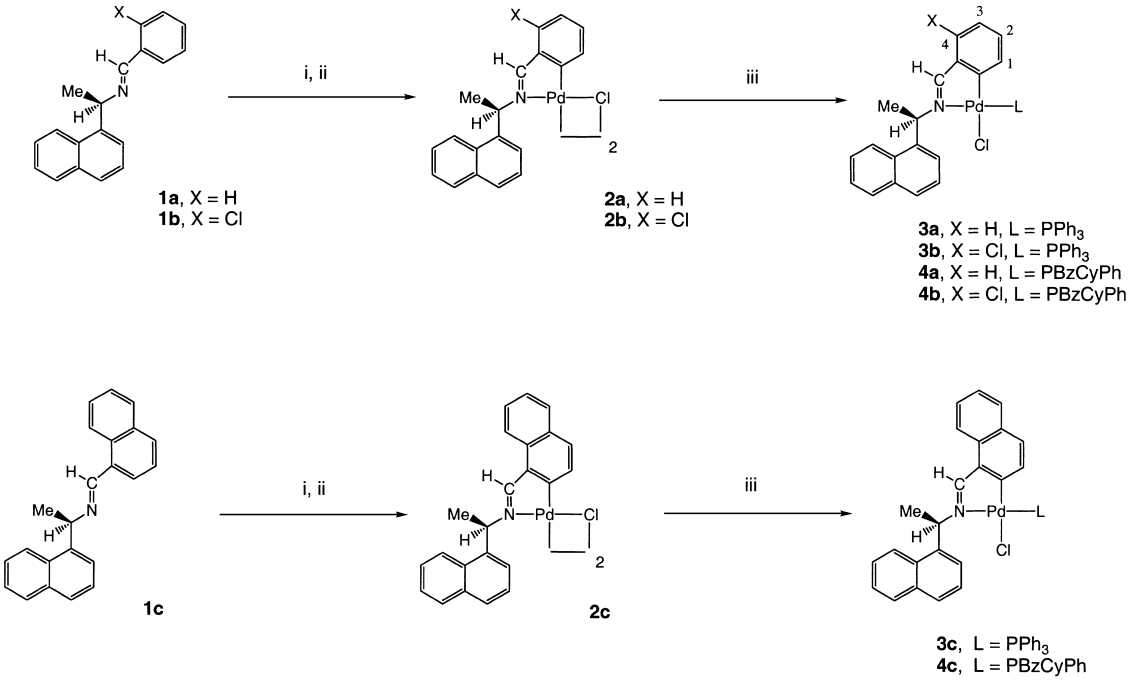
Figure 1.

Imines **1** were treated with palladium acetate in acetic acid for 24 h at 60°C. Subsequent treatment of the reaction residues with LiCl in ethanol afforded, after purification by SiO_2 column chromatography, the corresponding chloro-bridged cyclopalladated dimers **2**. Overall NMR data showed that only the *endo*-derivative was formed, in agreement with studies reporting the strong tendency of imines to form *endo*-metallacycles.[8] The aromaticity of the five-membered metallacycle, involving the two conjugated bonds C=C, C=N and the filled *d* orbital of the metal of appropriate symmetry has been proposed to explain the greater stability of endocyclic compounds.[9]

The ^1H NMR spectra of **2** showed two series of signals, assigned to the metallated ligands (experimental), which can be explained by the existence of a mixture of *cis*- and *trans*-isomers of these dinuclear derivatives, as has been reported for the cyclopalladated compound containing the *N*,*N*-dimethyl-1-(1-naphthyl)ethylamine.[4a] Reaction of dimers **2** with PPh_3 afforded the mononuclear complexes [PdCl(C-N)(PPh_3)] **3** (C-N being the metallated imine). The high-field shift of the aromatic protons of the palladated ring in **3**, due to the aromatic rings of the phosphine, indicates the *cis* disposition of the phosphorus relative to the metallated carbon atom and the

chemical shift of the phosphorus confirms this arrangement.[10] This arrangement is usual in cyclopalladated compounds containing phosphines.[11]

Reaction of dimers **2** with the coordination compound dichlorobis[(±)-benzylcyclohexylphenylphosphine]nickel(II) afforded the mononuclear complexes [PdCl(C-N)(PBzCyPh)], as a 1:1 mixture of diastereomers (R_C,R_P)-**4** and (R_C,S_P)-**4** (Scheme 1). NMR data of **4** show the *cis* disposition of phosphorus relative to the metallated carbon. It should be noted that H^1 and H^2 resonances are more high field shifted in **4** than in their PPh_3 analogues **3**. This fact has been explained by the restricted rotation around the Pd–P bond and suggests that the rotamers with the phenyl group in the proximity of the metallacycle are predominant.[5f]



Scheme 1. (i) $PdAc_2$, AcH, 60°C, 24 h; (ii) LiCl, EtOH, 20°C; (iii) PPh_3, acetone, 20°C, 30 min, or $[NiCl_2(PBzCyPh)_2]$, THF, 45 min

All the new organometallic compounds obtained were characterized by elemental analysis, IR spectra, and ^1H and ^{31}P NMR spectra. In some cases, 2D NMR experiments and positive FAB-mass spectra, were carried out to complete the characterization. The *H*CMe methinic proton signal appeared shifted to low field in relation to free imines for all the organometallic compounds. This downfield shift can be explained by the paramagnetic anisotropy of the metal[12] and suggests that these compounds adopt a conformation in which this proton is close to the metal atom, which minimizes steric repulsions.

For all the compounds containing a chlorine substituent in an *ortho* position on the aromatic ring (compounds **b**) the HC=N proton resonance appeared at lower fields than for the non-substituted derivatives, indicating an intramolecular interaction between the atoms, as has been found for related palladium and platinum metallacycles.[5d,13] The crystal structure determination of (R_C,R_P)-**4b** confirms this, see Figure 2.

2.1. Resolution of the phosphine

The elution of the mixture of (R_C,R_P)-**4** and (R_C,S_P)-**4** through a SiO_2 column allowed the separation of the first diastereomer eluted (R_C,S_P)-**4** with a *d.e.* higher than 95% (Table 1), with the three cyclopalladated imines (see below for the assignment of absolute configuration). Otherwise, recrystallization of a saturated solution of a mixture of (R_C,R_P)-**4a** and (R_C,S_P)-**4a** or a mixture of (R_C,R_P)-**4b** and (R_C,S_P)-**4b** in ether afforded the diastereomers (R_C,R_P)-**4a** and (R_C,R_P)-**4b**, respectively, with a *d.e.* higher than 95% in both cases.

Table 1
Separation of diastereomers **4**

Compound	*Column chromatography*		*Recrystallization*	
	Yield (%)	*d.e. (%)*	*Yield (%)*	*d.e. (%)*
(R_C,S_P)-**4a**	31	>95	-	-
(R_C,R_P)-**4a**	47	62	85	>95
(R_C,S_P)-**4b**	34	>95	-	-
(R_C,R_P)-**4b**	36	85	85	>95
(R_C,S_P)-**4c**	72	>95	–	–
(R_C,R_P)-**4c**	47	79	–	–

To evaluate the enantiomeric excess of such mixtures the $^{31}P\{^1H\}$ NMR spectra should be used because the ^1H NMR spectra of each pair of diastereomers **4** are very similar. This is an unusual result, since cyclopalladated compounds are usually good agents for the determination of enantiomeric purities of phosphines because the ^1H NMR spectra of the monomeric compounds [Pd(C-N)XL] show a good diastereomeric peak separation.[1] The crystal structure of (R_C,R_P)-**4b** can explain the similarity of the proton NMR spectra of diastereomers **4** (see below).

The absolute configuration of the phosphine in (R_C,R_P)-**4b** was determined by X-ray crystallography (Fig. 2). The X-ray analysis of this diastereomer reveals the presence of two crystallographically independent molecules (labelled A and B) in the asymmetric unit and both molecules have the same absolute configuration of the two stereogenic centers. For clarity, only molecule B is depicted in Fig. 2; the ORTEP plot of molecule A has been deposited as supplementary material. There are slight differences in the bond distances and angles between both molecules and these values are similar to those reported for related metallacycles[10,14] (Table 2). The palladium atom is in a square-planar environment, coordinated to carbon, chlorine, nitrogen and phosphorus atoms. The coordination plane shows a tetrahedral distortion, the deviation from the mean plane being: –0.120, –0.149, +0.083 and 0.114 Å for Cl, C1, P and N, respectively. The phosphorus and nitrogen atoms adopt a *trans* arrangement and the absolute configuration of the phosphine ligand in this diastereomer is *R*. The metallacycle contains the C=N bond and it is roughly planar, the deviation from the mean plane being: 0.091, –0.097, 0.043, 0.075 and –0.111Å for Pd, N, C1, C2 and C3, respectively.

The crystal structure of (R_C,R_P)-**4b** shows that the three substituents of the phosphine are placed away from the naphthyl group of the imine. In addition, the benzyl group of the phosphine is oriented towards the chloro ligand but, in contrast, the phenyl and cyclohexyl groups are located in the proximity of the metallacycle (see Fig. 3). It is reasonable to assume that in the diastereomer

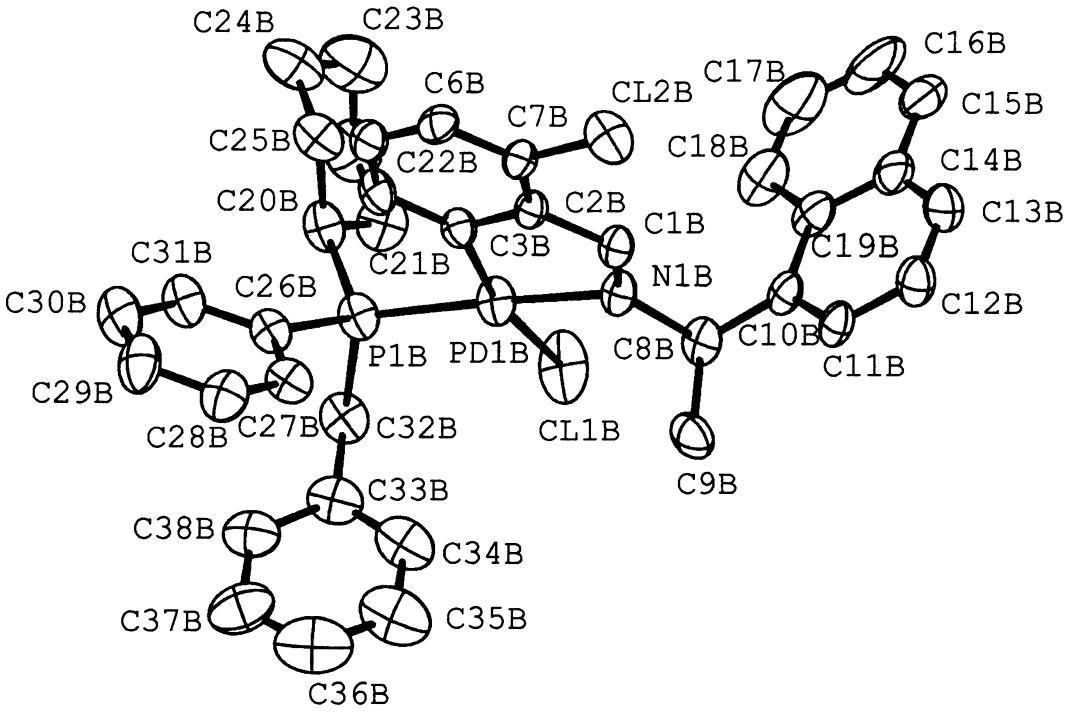


Figure 2. ORTEP plot of the structure of (R_C,R_P)-**4b**

Table 2
Selected bond lengths [Å] and angles [deg] for (R_C,R_P)-**4b**

Pd(1A)-C(3A)	2.012(4)	Pd(1B)-C(3B)	2.026(5)
Pd(1A)-N(1A)	2.104(4)	Pd(1B)-N(1B)	2.103(4)
Pd(1A)-P(1A)	2.275(2)	Pd(1B)-P(1B)	2.278(2)
Pd(1A)-Cl(1A)	2.3823(14)	Pd(1B)-Cl(1B)	2.385(2)
N(1A)-C(1A)	1.270(6)	N(1B)-C(1B)	1.273(6)
N(1A)-C(8A)	1.493(6)	N(1B)-C(8B)	1.497(6)
C(1A)-C(2A)	1.441(7)	C(1B)-C(2B)	1.456(7)
C(2A)-C(3A)	1.431(6)	C(2B)-C(3B)	1.410(7)
C(3A)-Pd(1A)-N(1A)	81.2(2)	C(3B)-Pd(1B)-N(1B)	80.6(2)
C(3A)-Pd(1A)-P(1A)	96.42(13)	C(3B)-Pd(1B)-P(1B)	96.5(2)
N(1A)-Pd(1A)-Cl(1A)	90.38(11)	N(1B)-Pd(1B)-Cl(1B)	91.73(12)
P(1A)-Pd(1A)-Cl(1A)	92.21(6)	P(1B)-Pd(1B)-Cl(1B)	91.78(7)

(R_C,S_P)-**4b** the benzyl group should also be oriented towards the chloro ligand, and the main structural change would be the exchange of the positions of cyclohexyl and phenyl groups which should have a slight effect on the proton NMR.[15]

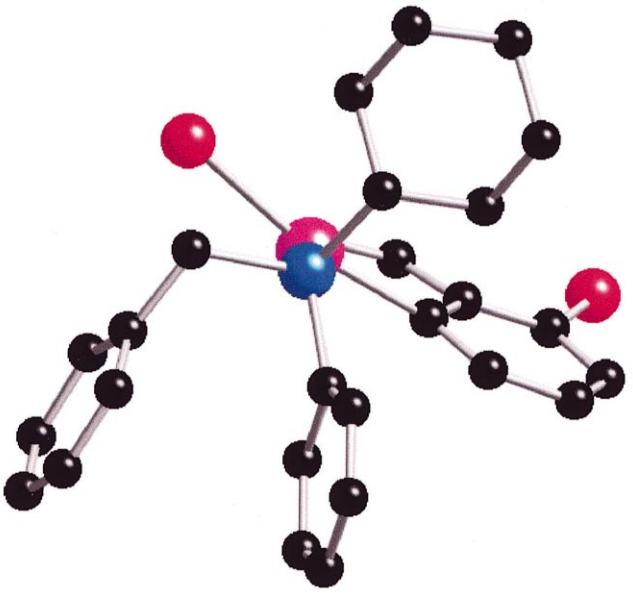


Figure 3. Structure of (R_C,R_P)-**4b**. The naphthyl and CHMe groups have been omitted for clarity

The distance between the HC=N carbon atom and the chlorine substituent in an *ortho* position on the imine is 3.077(6) and 3.091(6), for molecules A and B, respectively, showing the existence of an intramolecular interaction between these groups.[5d,13]

Reaction of 1,2-bis(diphenylphosphino)ethane (dppe) with the enantiomerically pure cyclopalladated derivatives **4** liberated the enantiopure free phosphine PBzCyPh (^{31}P NMR: $\delta = -6.1$). The displacement proceeds with a retention of the configuration at phosphorus as verified by the quantitative regeneration of the starting material **4** from the free ligand and the corresponding dinuclear cyclopalladated derivative **2**. The addition of dppe to solutions of each one of the different diastereomers of **4a** or **4c** and subsequent reaction of the free phosphine formed with the cyclopalladated compound **2b** permitted the determination of the absolute configuration of the phosphine in all the diastereomers by ^{31}P NMR.

In conclusion, optically active palladacycles, containing imines derived from 1-(1-naphthyl)-ethylamine, are good resolution agents for monodentate phosphines. The diastereomers formed when these cyclopalladated complexes react with [$NiCl_2$(PBzCyPh)$_2$] (used as a storage agent for this easily oxidable phosphine) can be easily separated, with a *d.e.* higher than 95%. Subsequent reaction of the pure diastereomers with dppe, under nitrogen, affords the free enantiomerically pure phosphine. These imine cyclopalladated derivatives are better resolution agents for this phosphine than the primary or tertiary metallated amines previously reported,[5a] because the yields for the separation process are better than the yields obtained when the amine complexes are used.[16] Furthermore, the separation of the diastereomers can also be accomplished by recrystallization when the imine derivatives are used, whereas column chromatography is essential for the separation of the diastereomers containing metallated amines.

3. Experimental

^{1}H NMR spectra at 200 MHz were recorded on a Varian Gemini 200 spectrometer, and ^{1}H NMR at 500 MHz and ^{31}P{^{1}H} at 101.26 MHz were recorded, respectively, on a Varian VXR 500 or a Bruker DRX 250 spectrometer. Chemical shifts (in ppm) were measured relative to $SiMe_4$ for ^{1}H and to 85% H_3PO_4 for ^{31}P. Microanalyses were performed at the Institut de Química Bio-Orgànica de Barcelona and the Serveis Científico-Tècnics de la Universitat de Barcelona. Infrared spectra were recorded as KBr disks on a Nicolet 520 FT-IR spectrometer. The optical rotations of the complexes (c = g/100 mL, in $CHCl_3$) were determined at 20°C using a Perkin–Elmer 241-MC polarimeter. Mass spectra were recorded on a Fisons VG-Quattro spectrometer. The samples were introduced in a matrix of 2-nitrobenzylalcohol for FAB analysis and then bombarded with cesium atoms.

3.1. Materials and synthesis

All the reactions involving free PBzCyPh were carried out using Schlenk techniques under nitrogen atmosphere. All solvents were dried and degassed by standard methods. Tetrahydrofuran was distilled over sodium–benzophenone, under a nitrogen atmosphere, before use. All chemicals were of commercial grade and used as received. [$NiCl_2$(PBzCyPh)$_2$] was prepared according to the procedure described elsewhere.[5a]

3.2. Synthesis of imines *1a–c*

A mixture of (*R*)-(+)-1-(1-naphthyl)ethylamine and the corresponding aldehyde was refluxed in ethanol for 3 h. The resulting solution was concentrated in vacuo and the oil obtained was characterized by IR and ^{1}H NMR spectra and was used without further purification.

^{1}H NMR (200 MHz, $CDCl_3$) data for **1a**: δ = 8.42 (s, 1H, *H*C=N), 8.21 (d, 1H, J_{HH} = 7.8 Hz, *Ar*), 7.85–7.78 (m, 5H, *Ar*), 7.58–7.40 (m, 6H, *Ar*), 5.40 (q, J_{HH} = 6.6 Hz, 1H, *H*CMe), 1.75 (d, J_{HH} = 6.6 Hz, 3H, *Me*). IR (cm^{-1}): 1641 (C=N).

^{1}H NMR (200 MHz, $CDCl_3$) data for **1b**: δ = 8.9 (s, 1H, *H*C=N), 8.27 (d, J_{HH} = 8.0 Hz, 1H, *Ar*), 8.19 (m, 1H, *Ar*), 7.9–7.74 (m, 3H, *Ar*), 7.56–7.44 (m, 3H, *Ar*), 7.36–7.31 (m, 3H *Ar*), 5.41 (q, J_{HH} = 6.6 Hz, 1H, *H*CMe), 1.75 (d, J_{HH} = 6.6 Hz, 3H, *Me*). IR (cm^{-1}): 1637 (C=N).

^{1}H NMR (200 MHz, $CDCl_3$) data for **1c**: δ = 9.06 (s, 1H, *H*C=N), 9.0 (d, J_{HH} = 8.4 Hz, 1H, *Ar*), 8.35 (d, J_{HH} = 8.4 Hz, 1H, *Ar*), 7.92–7.85 (m, 4H, *Ar*), 7.78 (d, J_{HH} = 8.2 Hz, 2H, *Ar*), 7.62–7.40 (m, 6H, *Ar*), 5.40 (q, J_{HH} = 6.6 Hz, 1H, *H*CMe), 1.80 (d, J_{HH} = 6.6 Hz, 3H, *Me*). IR (cm^{-1}): 1637 (C=N).

3.3. Synthesis of *2*

A stirred suspension of Pd(O_2CMe)$_2$ (2.23 mmol, 0.5 g) in acetic acid (30 mL) was treated with the corresponding imine (2.23 mmol) at 60°C for 24 h. The resulting solution was concentrated in vacuo and the residue was treated with 4.44 mmol (186 mg) of LiCl in ethanol for 30 min. The brown solid formed was isolated by filtration and purified by column chromatography over SiO_2, with $CHCl_3$:MeOH (100:2) as eluent to obtain compounds **2** in 40–45% yield.

Characterization data for **2a**: anal. (%) calcd for $C_{38}H_{32}N_2Cl_2Pd_2$: C, 57.02; H, 4.03; N, 3.50. Found: C, 56.8; H, 4.2; N, 3.3. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 8.33$ (d, $J_{HH} = 8.4$ Hz, 2H, *Ar*), 7.90 (d, $J_{HH} = 8.0$ Hz, 4H, *Ar*), 7.69–7.42 (m, 12H, *Ar*, HC=N), 6.90 (m, 6H, *Ar*), 6.09 (m, 2H, *H*CMe), 2.00 (d, $J_{HH} = 7.0$ Hz, 3H, *Me*), 1.94 (d, $J_{HH} = 6.6$ Hz, 3H, *Me*).

Characterization data for **2b**: anal. (%) calcd for $C_{38}H_{30}N_2Cl_4Pd_2$: C, 52.48; H, 3.45; N, 3.22. Found: C, 52.25; H, 3.65; N, 3.28. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 8.30$ (d, $J_{HH} = 8.4$ Hz, 2H, *Ar*), 7.90–7.80 (m, 6H, *H*C=N, *Ar*), 7.65–7.2 (m, 10H, *Ar*), 6.90–6.86 (m, 4H, *Ar*), 6.10 (m, *H*CMe), 2.00 (d, $J_{HH} = 6.6$ Hz, 3H, *Me*), 1.90 (d, $J_{HH} = 7.0$ Hz, 3H, *Me*).

Characterization data for **2c**: anal. (%) calcd for $C_{46}H_{36}N_2Cl_2Pd_2$: C, 61.35; H, 4.03; N, 3.11. Found: C, 61.1; H, 4.0; N, 3.3. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 8.40$ (d, $J_{HH} = 7.5$ Hz, 2H, *Ar*), 8.19 (s, 2H, *H*C=N), 7.9–7.2 (m, 24H, *Ar*), 6.20 (m, 2H, *H*CMe), 2.09 (d, $J_{HH} = 7.0$ Hz, 3H, Me), 2.00 (d, $J_{HH} = 6.4$ Hz, 3H, *Me*).

3.4. Synthesis of *3*

A stirred suspension of compounds **2** (0.25 mmol) was treated with PPh_3 (0.5 mmol, 0.13 g) in acetone (30 mL) for 30 min at room temperature and then filtered. The filtrate was concentred in vacuo and the solid formed was purified by column chromatography over SiO_2, with $CHCl_3$:MeOH as eluent (100:2 for **3a** and 100:1 for **3b** and **3c**) to obtain compounds **3**. The yields of the products were 70, 45 and 35% for **3a**, **3b** and **3c**, respectively.

Characterization data for **3a**: anal. (%) calcd for $C_{37}H_{31}NClPPd$: C, 67.08; H, 4.71; N, 2.11. Found: C, 66.8; H, 4.5; N, 2.0. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 8.50$ (d, $J_{HH} = 8.4$ Hz, 1H, *Ar*), 7.90–7.30 (m, 22H, *H*C=N, *Ar*), 6.90 (m, 2H, *H*CMe, H^4), 6.75 (t, $J_{HH} = 6.6$ Hz, 1H, H^3), 6.40 (m, 2H, H^1, H^2), 1.90 (d, $J_{HH} = 6.6$ Hz, 3H, *Me*). ^{31}P NMR (101.26 MHz, $CDCl_3$): $\delta = 41.90$ s.

Characterization data for **3b**: anal. (%) calcd for $C_{37}H_{30}NCl_2PPd$: C, 63.77; H, 4.34; N, 2.00. Found: C, 63.4; H, 4.1; N, 1.9. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 8.50$ (d, $J_{HH} = 8.4$ Hz, 1H, *Ar*), 8.22 (d, $J_{HH} = 8.4$ Hz, 1H, *H*C=N), 7.80–7.30 (m, 21H, *Ar*), 6.90 (q, $J_{HH} = 6.6$ Hz, 1H, *H*CMe), 6.70 (d, $J_{HH} = 7.6$ Hz, 1H, H^3), 6.30 (t, $J_{HH} = 7.8$ Hz, 1H, H^2), 6.2 (t, $J_{HH} = 7.6$ Hz, 1H, H^1), 1.92 (d, $J_{HH} = 6.6$ Hz, 3H, *Me*). ^{31}P NMR (101.26 MHz, $CDCl_3$): $\delta = 41.39$ s.

Characterization data for **3c**: anal. (%) calcd for $C_{41}H_{33}NClPPd$: C, 69.11; H, 4.66; N, 1.96. Found: C, 68.8; H, 4.7; N, 2.0. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 8.60$ (m, 2H, *Ar*), 7.90–7.75 (m, 9H, *H*C=N, *Ar*), 7.63–7.34 (m, 14H, *Ar*), 7.22–7.17 (m, 2H, *Ar*), 6.90 (br, 2H, *H*CMe, H^2), 6.60 (dd, $J_{HH} = 8.4$ Hz, $J_{PH} = 5.8$ Hz, 1H, H^1), 1.98 (d, $J_{HH} = 6.6$ Hz, 3H, *Me*). ^{31}P NMR (101.26 MHz, $CDCl_3$): $\delta = 42.11$ s.

3.5. Synthesis of *4a*

A suspension formed by 0.24 mmol of **2a**, 0.24 mmol (165 mg) of dichlorobis[(±)-benzylcyclohexylphenylphosphine]nickel(II) and 30 mL of THF was stirred at room temperature for 45 min and the resulting solution was concentrated in vacuo. The solid obtained was eluted by SiO_2 column chromatography with $CHCl_3$:acetone 100:3 as eluent. The 1:1 mixture of diastereomers (R_C,R_P)-**4a** and (R_C,S_P)-**4a** was isolated as a yellow solid in a yield of 80%. Characterization data for **4a**: anal. (%) calcd for $C_{38}H_{39}NClPPd$: C, 66.86; H, 5.75; N, 2.05. Found: C, 67.1; H, 5.7; N, 2.0. ^{31}P NMR (101.26 MHz, $CDCl_3$): $\delta = 40.57$ s, 40.09 s. MS-positive FAB: 646 [$(M–Cl)^+$].

3.6. Synthesis of **4b**

With **2b** as starting material the synthesis of **4b** was analogous to the preparation of **4a**. The solid obtained was eluted by SiO_2 column chromatography with $CHCl_3$:acetone 100:1 as eluent. The 1:1 mixture of diastereomers (R_C,R_P)-**4b** and (R_C,S_P)-**4b** was isolated as a yellow solid in a yield of 85%. Characterization data for **4b**: anal. (%) calcd for $C_{38}H_{38}NCl_2PPd$: C, 63.65; H, 5.34; N, 1.95. Found: C, 63.8; H, 5.2; N, 1.9. ^{31}P NMR (101.26 MHz, $CDCl_3$): $\delta = 40.54$ s, 40.85 s. MS-positive FAB: 681 [(M–Cl)$^+$].

3.7. Synthesis of **4c**

With **2c** as starting material the synthesis of **4c** was analogous to the preparation of **4a**. The solid obtained was eluted by SiO_2 column chromatography with a mixture of $CHCl_3$:acetone 100:2 as eluent. The 1:1 mixture of diastereomers (R_C,R_P)-**4c** and (R_C,S_P)-**4c** was isolated as a yellow solid in a yield of 75%. Characterization data for **4c**: anal. (%) calcd for $C_{42}H_{41}NClPPd$: C, 68.85; H, 5.64; N, 1.91. Found: C, 68.6; H, 5.4; N, 1.8. ^{31}P NMR (101.26 MHz, $CDCl_3$): $\delta = 41.02$ s, 40.74 s. MS-positive FAB: 696 [(M–Cl)$^+$].

3.8. Separation of **4a** diastereomers

A 1:1 mixture of diastereomers (R_C,R_P)-**4a** and (R_C,S_P)-**4a** (200 mg) was carefully eluted at room temperature, in a SiO_2 column (30×400 mm, 30 g SiO_2) with $CHCl_3$:acetone (100:2) as eluent. The eluted solution was collected in fractions of 15 mL, concentrated in vacuo and checked by $^{31}P\{^1H\}$ NMR spectroscopy (101.26 MHz). The diastereomer (R_C,S_P)-**4a** was obtained in 31% yield (31 mg), with a *d.e.* higher than 95%. The recrystallization of a 1:1 mixture of diastereomers (R_C,R_P)-**4a** and (R_C,S_P)-**4a** (200 mg) from a saturated solution of ethyl ether at 20°C afforded (R_C,R_P)-**4a** in 85% yield (85 mg), with a *d.e.* higher than 95%. ^1H NMR data (500 MHz, $CDCl_3$) for (R_C,S_P)-**4a**: $\delta = 8.50$ (d, $^3J_{HH} = 8.0$ Hz, 1H, *Ar*), 7.86 (m, 2H, *Ar*), 7.60–7.10 (m, 15H, *H*C=N, *Ar*), 6.90 (q, $^3J_{HH} = 6.5$ Hz, 1H, *H*CMe), 6.84 (d, $^3J_{HH} = 7.5$ Hz, 1H, H^4), 6.70 (t, $^3J_{HH} = 7.5$ Hz, 1H, H^3), 6.40 (t, $^3J_{HH} = 7.5$ Hz, 1H, H^2), 6.08 (dd, $^3J_{HH} = 7.0$ Hz, $^4J_{PH} = 5.5$ Hz, 1H, H^1), 3.90 (m, 2H, CH_2Ph), 2.5–1.2 (m, 11H, *Cy*), 1.91 (d, $^3J_{HH} = 6.5$ Hz, 3H, *Me*). ^{31}P NMR (101.26 MHz, $CDCl_3$): $\delta = 40.57$ s. $[\alpha]_D^{20} = +109.35$ deg cm^2 g^{-1}, $c = 10.1$ mg/mL. ^1H NMR data (500 MHz, $CDCl_3$) for (R_C,R_P)-**4a**: $\delta = 8.58$ (d, $^3J_{HH} = 8.2$ Hz, 1H, *Ar*), 7.86 (d, 2H, *Ar*), 7.70–7.05 (m, 15H, *H*C=N, *Ar*), 6.95 (m, 1H, *H*CMe), 6.86 (d, $^3J_{HH} = 7.4$ Hz, 1H, H^4), 6.70 (t, $^3J_{HH} = 7.4$ Hz, 1H, H^3), 6.41 (t, $^3J_{HH} = 7.4$ Hz, 1H, H^2), 6.09 (dd, $^3J_{HH} = 7.2$ Hz, $^4J_{PH} = 4.6$ Hz, 1H, H^1), 3.90 (m, 2H, CH_2Ph), 2.60–1.20 (m, 11H, *Cy*), 1.93 (d, $^3J_{HH} = 6.6$ Hz, 3H, *Me*). ^{31}P NMR (101.26 MHz, $CDCl_3$): $\delta = 40.09$ s.

3.9. Separation of **4b** diastereomers

The separation of diastereomers **4b** was analogous to the separation of **4a**, using a mixture of $CHCl_3$:CH_2Cl_2 (100:4) as eluent. The diastereomer (R_C,S_P)-**4b** was obtained in 34% yield (34 mg), with a *d.e.* higher than 95%.The recrystallization of a 1:1 mixture of diastereomers (R_C,R_P)-**4b** and (R_C,S_P)-**4b** (200 mg) from a saturated solution of ethyl ether at 20°C afforded (R_C,R_P)-**4b** in 85% yield (85 mg), with a *d.e.* higher than 95%. ^1H NMR data (500 MHz, $CDCl_3$) for (R_C,S_P)-**4b**: $\delta = 8.52$ (d, $J_{HH} = 8.4$ Hz, 1H, *Ar*), 8.19 (d, $J_{HH} = 8.0$ Hz, 1H, *H*C=N), 7.86 (m, 2H, *Ar*), 7.70–7.10

(m, 14H, *Ar*), 6.98 (m, 1H, *H*CMe), 6.62 (d, J_{HH} = 7.4 Hz, 1H, H^3), 6.30 (t, J_{HH} = 8.0 Hz, 1H, H^2), 5.90 (dd, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 5.4 Hz, 1H, H^1), 4.00–3.69 (m, 2H, CH_2Ph), 2.60–1.10 (m, 11H, *Cy*), 1.92 (d, $^3J_{HH}$ = 6.6 Hz, 3H, *Me*). ^{31}P (101.26 MHz, $CDCl_3$): δ = 40.85 s. ^{1}H NMR data (500 MHz, $CDCl_3$) for (R_C,R_P)-**4b**: δ = 8.60 (d, J_{HH} = 8.4 Hz, 1H, *Ar*), 8.20 (d, J_{HH} = 8.0 Hz, 1H, *H*C=N), 7.85 (dd, 2H, *Ar*), 7.70–7.10 (m, 14H, *Ar*), 6.99 (m, 1H, *H*CMe), 6.62 (d, J_{HH} = 8.0 Hz,

Table 3
Crystal data and structure refinement for (R_C,R_P)-**4b**

Empirical formula	$C_{38}H_{38}Cl_2NPPd$
Formula weight	716.96
Temperature	293(2) K
Wavelength	0.71069 A
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 13.8903(14) Å α = 90 deg. b = 12.759(8) Å β = 92.51(2) deg. c = 19.719(7) Å γ = 90 deg.
Volume	3491(3) Å^3
Z	4
Density (calculated)	1.364 Mg/m^3
Absorption coefficient	0.757 mm^{-1}
F(000)	1472
Crystal size	0.1 x 0.1 x 0.1 mm
Theta range for data collection	2.07 to 29.95 deg.
Index ranges	-19<=h<=19, -5<=k<=17, -6<=l<=27
Reflections collected	8602
Independent reflections	8319 [R(int) = 0.0168]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8269 / 1 / 933
Goodness-of-fit on F^2	1.043
Final R indices [I>2σ(I)]	R1 = 0.0394, wR2 = 0.0776
R indices (all data)	R1 = 0.0477, wR2 = 0.0901
Absolute structure parameter	-0.01(2)
Largest diff. peak and hole	0.661 and -0.510 e.A^{-3}

1H, H^3), 6.30 (t, $J_{HH}=7.8$ Hz, 1H, H^2), 5.87 (dd, $J_{HH}=7.6$ Hz, $J_{PH}=5.2$ Hz, 1H, H^1), 3.93–3.82 (m, 2H, CH_2Ph), 2.70–1.20 (m, 11H, *Cy*), 1.93 (d, $^3J_{HH}=6.6$ Hz, 3H, *Me*). ^{31}P (101.26 MHz, $CDCl_3$): $\delta=40.54$ s.

3.10. Separation of **4c** diastereomers

The separation of diastereomers **4c** was analogous to the separation of **4a**, using a mixture of $CHCl_3$:acetone (100:1) as eluent. The diastereomer (R_C,S_P)-**4c** was obtained in 72% yield (72 mg), with a *d.e.* higher than 95%. ^{1}H NMR data (500 MHz, $CDCl_3$) for (R_C,S_P)-**4c**: $\delta=8.50$ (m, 2H, *Ar*), 7.92–7.06 (m, 20H, *H*C=N, *Ar*), 7.02 (m, 1H, *H*CMe), 6.80 (d, $J_{HH}=8.5$ Hz, 1H, H^2), 6.30 (dd, $J_{HH}=8.5$ Hz, $J_{PH}=5.2$ Hz, 1H, H^1), 3.80 (dd, 2H, CH_2P), 2.70–1.10 (m, 11H, *Cy*), 1.98 (d, $^3J_{HH}=6.6$ Hz, 3H, *Me*). ^{31}P (101.26 MHz, $CDCl_3$): $\delta=41.02$ s. $[\alpha]_D^{20}=+56.39$ deg cm^2 g^{-1}, $c=6.8$ mg/mL. ^{1}H NMR data (500 MHz, $CDCl_3$) for (R_C,R_P)-**4c**: $\delta=8.60$ (d, $J_{HH}=8.4$ Hz, 1H, *Ar*), 8.50 (d, $J_{HH}=8.0$ Hz, 1H, *Ar*), 7.90–7.05 (m, 21H, *H*C=N, *Ar*, *H*CMe), 6.87 (d, $J_{HH}=8.8$ Hz, 1H, H^2), 6.30 (dd, $J_{HH}=8.8$ Hz, $J_{HH}=5.4$ Hz, 1H, H^1), 3.90 (m, 2H, CH_2P), 2.70–1.20 (m, 11H, *Cy*), 1.90 (d, $^3J_{HH}=6.6$ Hz, 3H, *Me*). ^{31}P (101.26 MHz, $CDCl_3$): $\delta=40.74$.

3.11. Crystallographic studies

A pale yellow prismatic crystal (0.1×0.1×0.2 mm) was selected and mounted on an Enraf–Nonius CAD4 four-circle diffractometer. Unit cell parameters were determined from automatic centering of 25 reflections ($12\leq\theta\leq21^\circ$) and refined by the least-squares method. Intensities were collected with graphite monochromatized MoKα radiation, using the $\omega/2\theta$-scan technique. 8602 reflections were measured in the range $2.07\leq\theta\leq29.95$; 8319 of which were non-equivalent by symmetry {R_{int} (on I) = 0.016} and 7341 were assumed as observed applying the condition $I\geq2\sigma(I)$. Three reflections were measured every 2 h as orientation and intensity control, significant intensity decay was not observed. Corrections were made for Lorentz-polarization but not for absorption. A summary of experimental details is given in Table 3.

The structure was solved by Patterson synthesis, using the SHELXS computer program[17] and refined by the full-matrix least-squares method, with the SHELX93 computer program,[18] using 8269 reflections (very negative intensities were not assumed). The function minimized was $\Sigma w[|Fo|^2-|Fc|^2]^2$, where $w=[\sigma^2(I)+(0.0414P)^2+0.3064P]^{-1}$, and $P=(|Fo|^2+2|Fc|^2)/3$; f, f' and f'' were taken from the *International Tables of X-Ray Crystallography*.[19] The chirality of the structure was defined from the Flack coefficient, which is equal to –001(2) for the given results.[20] Thirty-eight atoms were located from a difference synthesis and refined with an overall isotropic temperature factor and 38 atoms were computed and refined with an overall isotropic temperature factor using a riding model.

Supporting information available: Crystallographic data (excluding structure factors) for (R_C,R_P)-**4b** is available from the Cambridge Crystallographic Data Centre.

Acknowledgements

This work was supported by the DGICYT and by the Comissionat per a Universitats i Recerca (project: 1997SGR 00174). J.M.C. thanks the Agencia Española de Cooperación Internacional for a fellowship.

References

1. (a) Chooi, S. Y. M.; Leung, P. H.; Lim, C. C.; Mok, K. F.; Quek, G. H.; Sim, K. Y.; Tan, M. K. *Tetrahedron: Asymmetry* **1992**, *3*, 529. (b) Albert, J.; Granell, J.; Muller, G.; Sainz, D.; Font-Bardia, M.; Solans, X. *Tetrahedron: Asymmetry* **1995**, *6*, 325. (c) Dunina, V. V.; Kuz'mina, L. G.; Kazakova, M. Yu.; Grishin, Y. K.; Veits, Yu. A.; Kazakova, E. I. *Tetrahedron: Asymmetry* **1997**, *8*, 2537. (d) Kyba, E. P.; Rines, S. P. *J. Org. Chem.* **1982**, *47*, 4800.
2. Bookham, J. L.; McFarlane, W. *J. Chem. Soc., Chem. Commun.* **1993**, 1352. (b) Jiang, Q.; Rüegger, H.; Venanzi, L. *J. Organomet. Chem.* **1995**, *488*, 233.
3. (a) Leung, P. H.; Liu, A.; Mok, K. F. *Tetrahedron: Asymmetry* **1999**, *10*, 1309. (b) Leung, P. H.; Lang, H.; White, A. J. P.; Williams, D. J. *Tetrahedron: Asymmetry* **1998**, *9*, 2961. (c) Song, Y.; Vittal, J. J.; Chan, S. H.; Leung, P. H. *Organometallics* **1999**, *18*, 650. (d) Leung, P. H.; Loh, S. H.; Mok, K. F.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1996**, 591. (e) Falvello, L. R.; Fernández, S.; Navarro, R.; Urriolabeitia, E. P. *New J. Chem.* **1997**, *21*, 909. (f) Zhao, G.; Wang, Q. G.; Mak, T. C. *Tetrahedron: Asymmetry* **1998**, *9*, 2253. (g) Ryabov, A. D.; Kazankov, G. M.; Kurzeev, S. A.; Samuleev, P. V. *Inorg. Chim. Acta* **1998**, *280*, 57. (h) Gül, N.; Nelson, J. H. *Tetrahedron* **2000**, *56*, 71.
4. (a) Wild, S. B. *Coord. Chem. Rev.* **1997**, *166*, 291. (b) Robin, F.; Mercier, F.; Ricard, L.; Mathey, F.; Spagnol, M. *Chem. Eur. J.* **1997**, *8*, 1365. (c) Dunina, V. V.; Golovan, F. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2747. (d) Leung, P.; Quek, G. H.; Lang, H.; Liu, A. M.; Mok, K. F.; White, A. J.; Williams, D. J.; Rees, N.; McFarlane, W. *J. Chem. Soc., Dalton Trans.* **1998**, 1639. (e) Barclay, C. E.; Deeble, G.; Doyle, R. J.; Elix, S. A.; Salem, G.; Jones, T. L.; Wild, S. B.; Willis, A. C. *J. Chem. Soc., Dalton Trans.* **1995**, 57. (f) Pabel, M.; Willis, A. C.; Wild, S. B. *Inorg. Chem.* **1996**, *35*, 1244. (g) Berens, U.; Brown, J. M.; Long, J.; Selke, R. *Tetrahedron: Asymmetry* **1996**, *7*, 285. (h) Chelucci, G.; Cabras, M. A.; Saba, A.; Sechi, A. *Tetrahedron: Asymmetry* **1996**, *7*, 1027. (i) Gladiali, S.; Dore, A.; Fabbri, D.; De Lucci, O.; Manassero, M. *Tetrahedron: Asymmetry* **1994**, *5*, 511. (j) Chooi, S. Y. M.; Tan, M. K.; Leung, P.; Mok, K. F. *Inorg. Chem.* **1994**, *33*, 3096. (k) Pabel, M.; Willis, A. C.; Wild, S. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2369. (l) He, G.; Mok, K. F.; Leung, P. H. *Organometallics* **1999**, *18*, 4027.
5. (a) Albert, J.; Cadena, J. M.; Granell, J.; Muller, G.; Ordinas, J. I.; Panyella, D.; Puerta, C.; Sañudo, C.; Valerga, P. *Organometallics* **1999**, *18*, 3511**.** (b) Dunina, V. V.; Razmyslova, E. D.; Kuz'mina, L. G.; Churakov, A. V.; Rubina, M. Y.; Grishin, Y. K. *Tetrahedron: Asymmetry* **1999**, *10*, 3147. (c) Benito, M.; López, C.; Solans, X.; Font-Bardia, M. *Tetrahedron: Asymmetry* **1998**, *9*, 4219. (d) Albert, J.; Granell, J.; Mínguez, J.; Muller, G.; Sainz, D.; Valerga, P. *Organometallics* **1997**, *16*, 3561. (e) Albert, J.; Cadena, J. M.; Granell, J. *Tetrahedron: Asymmetry* **1997**, *8*, 991. (f) Dunina, V. V.; Kuz'mina, L. G.; Rubina, M. Yu; Grishin, Y. K.; Veits, Yu. A.; Kazakova, E. I. *Tetrahedron: Asymmetry* **1999**, *10*, 1483. (g) López, C.; Bosque, R.; Sainz, D.; Solans, X.; Font-Bardia, M. *Organometallics* **1997**, *16*, 3261.
6. (a) Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375.
7. (a) Tennant, G. *Comprehensive Organic Chemistry*; Barton, D.; Ollis, W. D., Eds.; Pergamon: Oxford, 1979; Vol. 2, Chapter 8. (b) Patai, S. *The Chemistry of the Carbon–Nitrogen Double Bond*; John Wiley & Sons: Chichester, 1970; pp. 364–372, 405–408.
8. (a) Gómez, M.; Granell, J.; Martínez, M. *J. Chem. Soc., Dalton Trans.* **1998**, 37. (b) Gómez, M.; Granell, J.; Martínez, M. *Organometallics* **1997**, *16*, 2539. (c) De Munno, G.; Ghedini, M.; Neve, F. *Inorg. Chim. Acta* **1995**, *239*, 155. (d) Bosque, R.; López, C.; Sales, J. *J. Organomet. Chem.* **1995**, *498*, 147.
9. (a) Navarro-Raninger, C.; López-Solera, I.; Alvarez-Valdés, A.; Rodríguez-Ramos, J. M.; Masaguer, J. R.; García-Ruano, J. L. *Organometallics* **1993**, *12*, 4104. (b) Crispini, A.; Ghedini, J. *J. Chem. Soc., Dalton Trans.* **1997**, 75. (c) Crespo, M.; Grande, C.; Klein, A.; Font-Bardía, M.; Solans, X. *J. Organomet. Chem.* **1998**, *563*, 179.
10. (a) Albert, J.; Gómez, M.; Granell, J.; Sales, J.; Solans, X. *Organometallics* **1990**, *9*, 1405. (b) Albert, J.; Granell, J.; Sales, J.; Font-Bardia, M.; Solans, X. *Organometallics* **1995**, *14*, 1393.
11. The destabilizing effect of two soft ligands in mutual *trans* positions has been called *antisymbiosis*, see: (a) Davies, J. A.; Hartley, F. R. *Chem. Rev.* **1981**, *81*, 79. (b) Pearson, R. G. *Inorg. Chem.* **1973**, *12*, 712. (c) Navarro, R.; Urriolabeitia, E. P. *J. Chem. Soc., Dalton Trans.* **1999**, 4111. Recently, the term *transphobia* has been proposed to describe the difficulty of coordinating mutually *trans* phosphine and aryl ligands in paladium complexes, see: (d) Vicente, J.; Abad, J. A.; Frankland, A. D.; Ramírez de Arellano, M. C. *Chem. Eur. J.* **1999**, *5*, 3066. (e) Vicente, J.; Arcas, A.; Bautista, D.; Jones, P. G. *Organometallics* **1997**, *16*, 2127.
12. Miller, R. G.; Stauffer, R. D.; Fahey, D. R.; Parnell, D. R. *J. Am. Chem. Soc.* **1970**, *92*, 1511.

13. (a) Bernstein, J. *J. Chem. Soc., Perkin Trans.* **1972**, 946. (b) Inabe, T.; Gaultier-Luneau, I.; Hoshino, N.; Okinawa, K.; Okamoto, H.; Mitani, T.; Nagashima, U.; Maruyama, Y. *Bull. Chem. Soc. Jpn.* **1991**, *801*, 64. (c) Crespo, M.; Martínez, M.; Sales, J.; Solans, X.; Font-Bardia, M. *Organometallics* **1992**, *11*, 1288.
14. (a) Vila, J. M.; Pereira, M. T.; Ortigueira, J. M.; López Torres, M.; Castineiras, J. M.; Lata, D.; Fernández, J. J.; Fernández, A. *J. Organomet. Chem.* **1998**, *556*, 31. (b) Cinelli, M. A.; Gladiali, S.; Minghetti, G.; Stoccoro, S.; Demartin, A. *J. Organomet. Chem.* **1991**, *401*, 371. (c) Vila, J. M.; Suarez, A.; Pereira, M. T.; Gayoso, E.; Gayoso, M. *Polyhedron* **1987**, *6*, 1003.
15. It has been shown that the rotation around Pd–P bonds is rather restricted in cyclopalladated compounds containing monodentate phosphines such as $P(Bu^t)(C_6H_5)(4\text{-}BrC_6H_4)$; see Ref. 5f.
16. The imine cyclopalladated derivatives permit the separation in 85% yield of the corresponding diastereomers containing benzylcyclohexylphenylphosphine coordinated with a *d.e.* higher than 95%. In contrast, when optically active palladacycles containing primary or tertiary amines are used as resolving agents, the maximum yield reported for the resolution of this phosphine is 70%; see Ref. 5a.
17. Sheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467.
18. Sheldrick, G. M. SHELXL, a computer program for crystal structure determination, University of Göttingen, Germany, 1994.
19. *International Tables of X-Ray Crystallography*; Kynoch Press: Birmingham, UK, 1974; Vol. 4, pp. 99–100, 149.
20. Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876.