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Synthesis and characterization of a new chiral phosphinothiol ligand and its palladium(II) complexes

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Abstract—The chiral ligand (1-diphenylphosphino-3-benzyloxy)propane-2-thiol **3** has been prepared both in racemic and enantiomerically enriched (92% e.e.) form. Addition of 2 equiv. of ligand **3** to a solution of $[Pd(PPh_3)_4]$ gave the diastereoisomeric bischelate complexes [Pd(phosphinothiolato)$_2$] **4** which exhibit a *cis–trans* equilibrium in solution. Formation of the diastereoisomeric complexes **4** allows the determination of the enantiomeric purity of ligand **3** by ^{31}P NMR spectroscopy. Addition of 1 equiv. of ligand **3** to a solution of $[PdCl_2(PPh_3)_2]$ gave the enantiomeric complexes [PdCl(phosphinothiolate)(PPh_3)] **5**, which can be converted to the bischelate complexes **4** by addition of a second equivalent of ligand **3**. This process allows the selective preparation of the two diastereoisomeric forms of complex **4**.

1. Introduction

Chelating chiral diphosphines are classical ligands extensively used in metal-catalysed enantioselective processes.[1] Besides the asymmetry introduced by the chelate ring, many of these diphosphines have two donor atoms with similar electronic and steric properties (e.g. DIOP,[2] BINAP[3]). In order to decrease the symmetry of the bidentate ligand, diphosphines with different substituents at each phosphorus have been synthesized (e.g. DIPAMP[4]), and some chemical changes in the phosphorous group have been introduced (e.g. BINAPHOS[5]). Marked differentiation between the coordinating groups is achieved with a change in the chemical nature of one of the donor atoms, as in the case of phosphinooxazolines[6] where a phosphorous donor atom is replaced by nitrogen, a harder first period atom.

Phosphinothiolates are asymmetric chelating ligands where one of the donor atoms, sulfur, supports a formal negative charge and, once bound to the metal, can act as a π-donor owing to the two non-bonding electron pairs on sulfur. Moreover, the thiolate group has only one substituent, the chain that connects it to the phosphino group. Conversely, phosphorous is neutral and once bound to the metal it does not support any non-bonding electron pairs, acting as a classical π-acceptor ligand. Chirality in phosphinothiolate ligands can be introduced in different ways. It can be achieved by means of the addition of a substituent in the chelate chain, as in the case of 1-methyl-2-(diphenylphosphino)ethane-1-thiol,[7] or by the use of a phosphino group with different substituents, as in the case of 2-(phenylmethylphosphino)ethane-1-thiol.[8] But in both cases these ligands were obtained as racemic mixtures. And only the latter phosphinothiolate ligand was used to prepare a metal complex, the bischelate bis{2-(phenylmethylphosphino)ethane-1-thiolato}palladium(II), which proved to contain a mixture of all structural possibilities in solution due to the racemic nature of the ligand used.

As part of a project on the use of phosphinothiolate complexes of the Group 10 metals as homogenous catalysts,[9,10] we have synthesized a new class of palladium(II) complexes using (1-diphenylphosphino-3-benzyloxy)propane-2-thiol **3**, both in racemic and enantiomerically enriched form.

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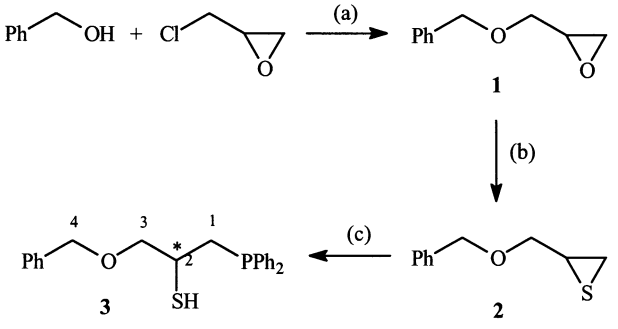
2. Synthesis of chiral phosphinothiol ligands

The ligand (1-diphenylphosphino-3-benzyloxy)propane-2-thiol **3** was prepared in a three-step synthesis according to Scheme 1. In the first step, reaction of benzyl alcohol and epichlorohydrin gave the benzyl glycidyl ether **1** in good yield (85%) upon treatment with aqueous potassium hydroxide in the presence of a small amount of tetrabutylammonium bromide as phase transfer catalyst. It has been determined that the phase transfer agent is an important additive for this reaction to proceed to completion. Compound **1** was converted into the corresponding episulfide, the benzyl thioglycidyl ether **2**, using thiourea as the sulfur exchange agent (58%). Treatment of compound **2** with 1 equiv. of potassium diphenylphosphide in THF at 0°C gave (1-diphenylphosphino-3-benzyloxy)propane-2-thiol **3**, in a 75% yield.

Compounds **1**–**3** were characterized by NMR spectroscopy. In the ^{1}H NMR spectrum, compound **3** shows the resonance of the thiol proton as a doublet from coupling to the hydrogen on the stereogenic carbon atom. The proton attached to the stereogenic center appears as a multiplet due coupling with six different nuclei ($2CH_2$, SH, ^{31}P). The methylenic protons near the phosphine group are diastereotopic and show a ^{2}J coupling constant with the phosphorous atom, as it can be seen in the $^{1}H\{^{31}P\}$ NMR spectrum. In the $^{13}C\{^{1}H\}$ NMR spectrum all carbon signals appear as doublets by coupling with the phosphorous atom, with the exception of the methylenic carbon of the benzyl group. In the $^{31}P\{^{1}H\}$ NMR spectrum, compound **3** shows a single resonance at −20.53 ppm. Enantiomerically enriched forms of compound **3** can be obtained by the same synthetic process using commercial benzyl (*R*)-(−)-glycidyl ether and benzyl (*S*)-(+)-glycidyl ether as starting materials. Thiiranes may be stereoselectively synthesized from the corresponding oxiranes using different agents: phosphine sulfides,[11] benzothiazole-2-thiones[12] and thiourea.[13] For all these methods a mechanism involving two *Walden* inversions, one for each oxirane carbon has been proposed, indicating that for terminal chiral oxiranes, as in our case, the stereochemistry of the resulting episulfide is opposite to that of the starting material. Reaction of thiirane **2** with potassium diphenylphosphide in THF at 0°C was found to be a regioselective process where only the S_N2 product was observed. The resulting phosphinothiol ligand has the opposite stereochemistry to the starting oxirane, but the same absolute configuration (*S* or *R*) due to a change in the C.I.P. substituent order of precedence.[14]



Scheme 1. Synthesis of (1-diphenylphosphino-3-benzyloxy)-propane-2-thiol **3**. (a) $NaOH/H_2O$, n-Bu_4NBr. (b) $SC(NH_2)_2$/$EtOH/H_2O$. (c) (i) $KPPh_2$, (ii) NH_4Cl.

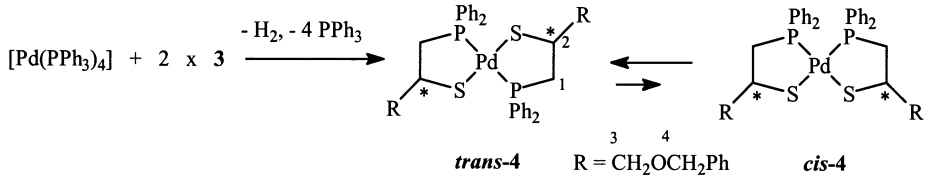
3. Synthesis of bis(phosphinothiolate)palladium(II) complexes

3.1. Use of the racemic ligand

The complex bis{1-diphenylphosphino-3-benzyloxy)-propane-2-thiolato}palladium(II) **4** can be obtained in good yield (86%) via oxidative addition of 2 equiv. of racemic ligand **3** to a solution of $[Pd(PPh_3)_4]$ at room temperature (Scheme 2).[9] Bischelate complex **4** exists as a mixture of the *cis* and *trans* isomers in solution, which are present in different amounts owing to their relative stabilities. Phosphorous NMR spectroscopy proved to be the best tool to analyze the composition of the isomeric mixtures, because *cis*–*trans* interconversion equilibria are kinetically slow.

The isomeric *trans*/*cis*-**4** complexes were characterized by NMR spectroscopy. Freshly prepared CD_2Cl_2 solutions of **4** show four resonances at 55.54, 54.45, 50.56 and 47.55 ppm in a 95:95:5:5 intensity ratio (Fig. 1a) in the $^{31}P\{^{1}H\}$ spectrum. The two larger phosphorous signals and the smaller ones show an equilibration process at room temperature leading to an intensity ratio of 66:66:34:34 (Fig. 1b) after 24 h. This dynamic process is inverted by crystallization of the product and it can also be frozen by cooling the solution to −22°C. These observations are attributed to the chemical equilibrium between *trans* and *cis* geometries of the complexes and has been described for other bis(phosphinothiolato) complexes of palladium(II).[8,15]

This equilibrium exists only in solution, in the solid state complex **4** adopts a *trans* geometry.[9,16] The *trans* geometry of the two major diastereomers is also con-



Scheme 2. Synthesis of chiral bis(phosphinothiolato)palladium(II) complexes **4**.

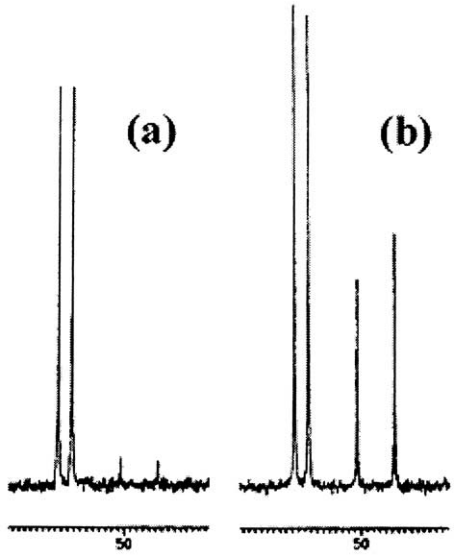
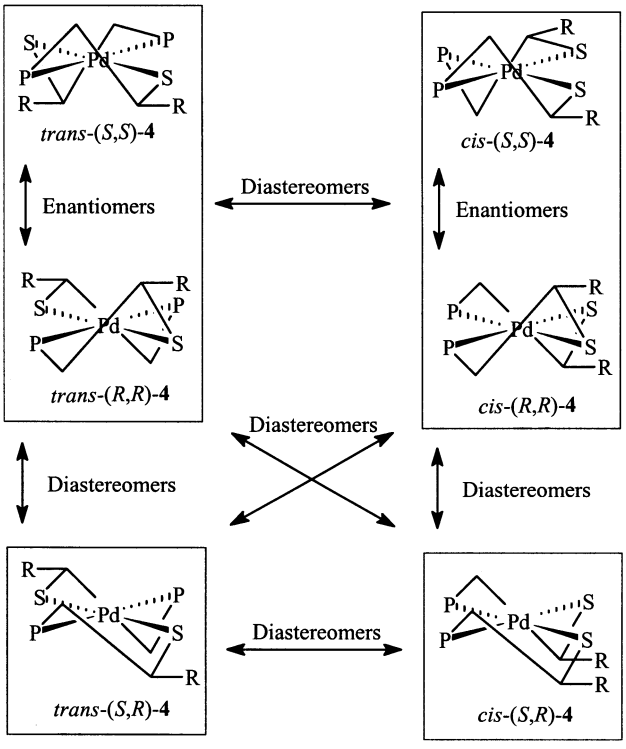


Figure 1. $^{31}P\{^{1}H\}$ NMR spectra of **4** obtained using racemic ligand **3**. (a) Freshly prepared CD_2Cl_2 solution. (b) After 24 h in solution.

firmed by the $^{13}C\{^{1}H\}$ spectrum, where the absorptions of three aliphatic carbons of the ligand chain appear as triplets owing to coupling with the 2 equiv. phosphorous centers mutually in *trans* positions.[9,16] Only the secondary carbons corresponding to the benzyl groups appear as singlets.



Scheme 3. Conformational analysis for complexes **4**.

In keeping with the conformational analysis of compounds *trans*-**4** and *cis*-**4** (Scheme 3), the preferred conformation for the chiral chelate ring depends on the configuration of the stereogenic carbon of the ligand chain. In this way, the ligand with *R* configuration adopts the λ conformation, which places the substituent of the chelate ring in equatorial position. For the same reasons, the ligand with *S* configuration adopts the δ conformation. As a result of these conformational preferences, complexes with the same geometry carrying two ligands with the same configuration, *trans*-(*R*,*R*)-**4** and *trans*-(*S*,*S*)-**4** or *cis*-(*R*,*R*)-**4** and *cis*-(*S*,*S*)-**4** are enantiomers producing a single $^{31}P\{^{1}H\}$ NMR signal even at low temperatures. Furthermore, these complexes are diastereomers of the corresponding complexes carrying one ligand in each configuration, *trans*-(*R*,*S*)-**4** and *cis*-(*R*,*S*)-**4**. This conformational analysis allows us to assign the two major $^{31}P\{^{1}H\}$ signals, one to the *trans*-(*R*,*S*)-**4** complex and the other to a mixture of *trans*-(*R*,*R*)-**4** and *trans*-(*S*,*S*)-**4** complexes. It is also possible to assign the two minor $^{31}P\{^{1}H\}$ signals, one to the *cis*-(*R*,*S*)-**4** complex and the other to a mixture of *cis*-(*R*,*R*)-**4** and *cis*-(*S*,*S*)-**4** complexes. The assignment of each $^{31}P\{^{1}H\}$ signal to their corresponding complex will be possible after the preparation of complexes **4** using enantiomerically enriched ligands.

3.2. Use of enantiomerically enriched ligands

Addition of 2 equiv. of enantiomerically enriched ligand **3** to a solution of complex $[Pd(PPh_3)_4]$ at room temperature gave a product **4** showing the same NMR spectra independently of the configuration of the ligand used. Freshly prepared CD_2Cl_2 solutions of the product show three resonances at 55.54, 54.45 and 47.55 ppm in

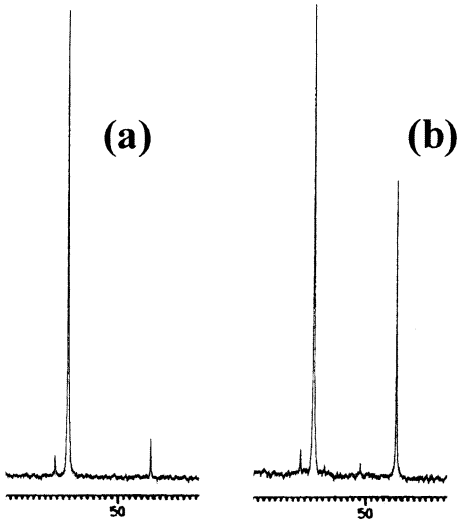


Figure 2. $^{31}P\{^{1}H\}$ NMR spectra of **4** obtained using enantiomerically enriched ligand **3**. (a) Freshly prepared CD_2Cl_2 solution. (b) After 24 h in solution.

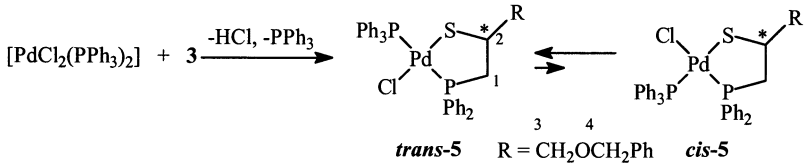
a 4:91:5 intensity ratio in the $^{31}P\{^1H\}$ spectrum (Fig. 2a). The main phosphorous signal and the small resonance at 47.55 ppm show the equilibration process already observed using the racemic ligand, leading to an intensity ratio of 66:34, respectively, after 24 h at room temperature (Fig. 2b).

These observations lead to the assignment of the signals at 54.45 and 47.55 ppm to a mixture of *trans*-(*R*,*R*)-**4** and *trans*-(*S*,*S*)-**4** enantiomeric complexes and to a mixture of *cis*-(*R*,*R*)-**4** and *cis*-(*S*,*S*)-**4** enantiomeric complexes, respectively. The signal at 55.54 ppm was then assigned to the *meso* complex *trans*-(*R*,*S*)-**4**, which also shows an equilibration process with a new signal appearing at 50.56 ppm after 24 h in solution at room temperature. This new absorption is then assigned to the *meso* complex *cis*-(*R*,*S*)-**4**. An important observation is that the intensity ratio between the major $^{31}P\{^1H\}$ signal at 54.45 ppm, and the minor absorption due to *trans*-(*R*,*S*)-**4** at 55.54 ppm, remains constant (96:4) after 48 h at room temperature. This suggests that racemization of the ligand does not occur. Under the right conditions the integration of the NMR signals obtained provides an excellent method to calculate the enantiomeric purity (92% e.e.) of the phosphinothiolate ligands coordinated to palladium.[17] The comparison of the ^1H and $^{13}C\{^1H\}$ NMR spectra of complexes **4** carrying either racemic ligands or enantiomerically enriched ligands allows the assignment of the corresponding signals for *trans*-(*R*,*S*)-**4** and for the enantiomers *trans*-(*R*,*R*)-**4** and *trans*-(*S*,*S*)-**4**.

4. Synthesis of chiral {chloro(phosphinothiolato)-triphenylphosphine}palladium(II) complexes

Addition of 1 equiv. of racemic ligand **3** to a solution of $[PdCl_2(PPh_3)_2]$ at room temperature in the absence of base produced the corresponding chloro complexes [PdCl(phosphinothiolate)(PPh_3)] **5** in good yield (70%) (Scheme 4).[9] The complexes were isolated as orange solids and were characterized by NMR spectroscopy. In solution, complex **5** exhibits an equilibrium between the *trans* and *cis* geometries, as can be seen in the $^{31}P\{^1H\}$ NMR spectrum (Fig. 3).

This equilibrium is strongly displaced toward the *trans* form (95%). The use of enantiomerically enriched ligands **3** in the synthesis of complexes **5** gave a product with identical NMR spectra, independently of the configuration of the ligand used, pointing to the simple existence of a pair of enantiomers. In keeping with the conformational analysis of complexes **5** (Scheme 5), much as for bischelate complexes **4**, the preferred conformation of the chelate ring depends on the configuration of the stereogenic carbon of the ligand. The chelate ring with *R* configuration adopts the λ conformation, which places the substituent in an equatorial disposition. For the same reasons, the chelate ring with the



Scheme 4. Synthesis of chiral {chloro(phosphinothiolato)triphenylphosphine}palladium(II) complexes **5**.

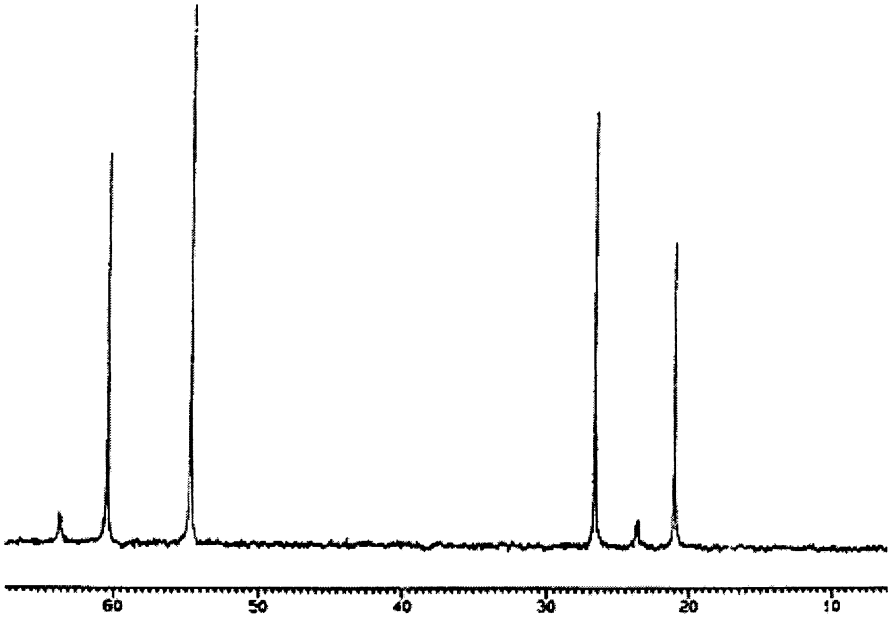
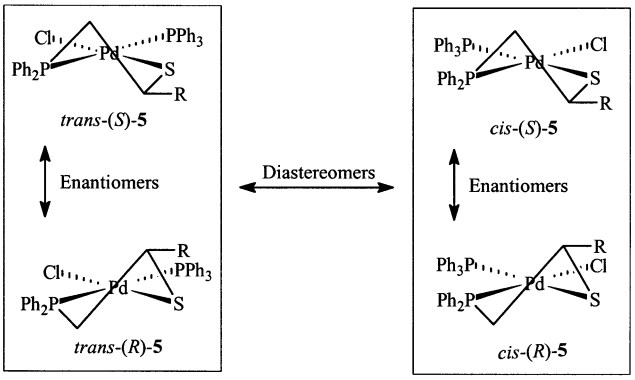


Figure 3. $^{31}P\{^1H\}$ NMR spectra of **5** obtained using both enantiomerically enriched or racemic ligand **3**.



Scheme 5. Conformational analysis for complexes **5**.

(*S*)-configuration adopts a δ conformation. As a result of these conformational preferences, complexes with the same geometry and different configuration of the stereogenic carbon of the chelate ring, *trans*-(*R*)-**5** and *trans*-(*S*)-**5** or *cis*-(*R*)-**5** and *cis*-(*S*)-**5**, are enantiomers producing the same NMR signals. In this case, the introduction of a single stereogenic carbon into the complex does not produce diastereoisomeric differentiation.

5. Interconversion between bischelate and chloro complexes

The bischelate complexes **4** could be converted into chloro complexes **5** in good yield (>90%), by a simple, albeit slow metathesis reaction with an equivalent of $[PdCl_2(PPh_3)_2]$ in refluxing toluene over 24 h (Scheme 6). In a faster reaction, the reverse process allowed the preparation of bischelate complexes **4** by the addition of 1 equiv. of ligand **3** to a solution of the chloro complexes **5** at room temperature.[9]

The synthesis of bischelate complexes from chloro complexes provides a method to prepare the *meso* complex *trans*-(*R*,*S*)-**4** by addition of 1 equiv. of ligand **3** in the (*R*)-enantiomerically enriched form to a solution of complex *trans*-(*S*)-**5**, as depicted in Scheme 7. Freshly prepared CD_2Cl_2 solutions of the recovered product show the signal assigned to complex *trans*-(*R*,*S*)-**4** as the major one in the $^{31}P\{^1H\}$ spectrum (Fig. 4a). Complex *trans*-(*R*,*S*)-**4** equilibrates rapidly with the *trans*-

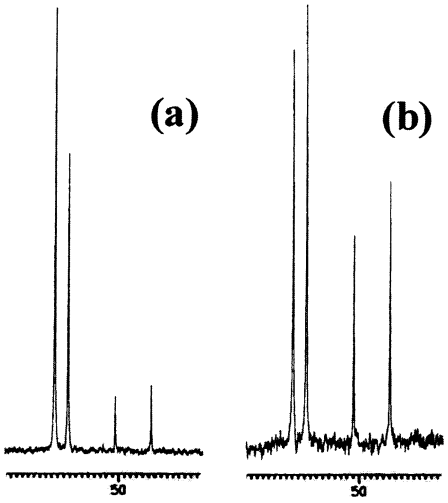
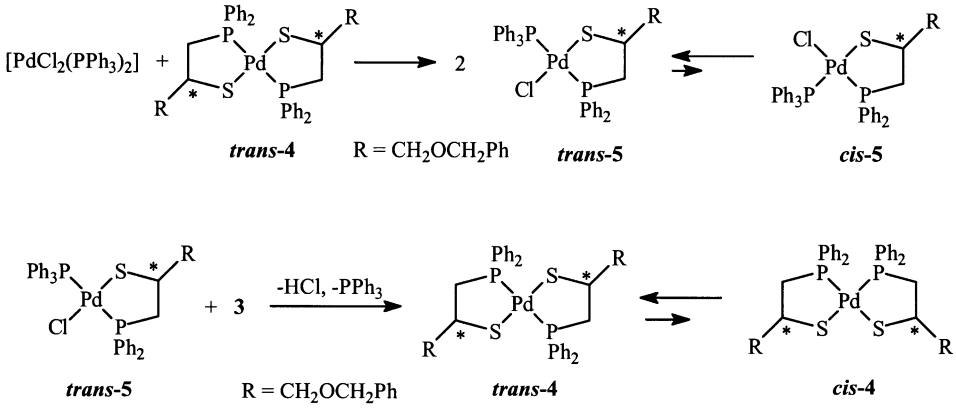
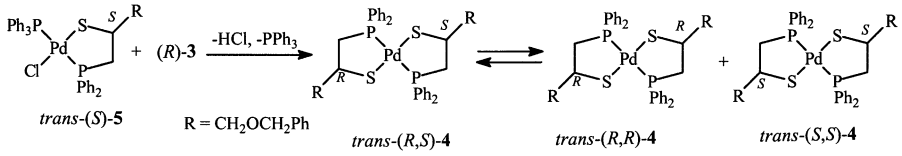


Figure 4. $^{31}P\{^1H\}$ NMR spectra of **4** obtained by addition of 1 equiv. of ligand (*R*)-**3** to complex *trans*-(*S*)-**5**. (a) Freshly prepared CD_2Cl_2 solution. (b) After 2 h in solution.



Scheme 6. Interconversion between bischelate **4** and chloro **5** complexes.



Scheme 7. Selective formation of complex *trans*-(*R*,*S*)-**4**.

(*R*,*R*)-**4** and *trans*-(*S*,*S*)-**4** complexes and after 2 h the two signals have the same intensity (Fig. 4b), pointing to the tendency of the phosphinothiolate ligands in this system towards the exchange process.

6. Crystal structure of *trans*-(*S*,*S*)-4

The X-ray analysis study was carried out on the compound after recrystallization from CH_2Cl_2/hexane (Table 1). Selected distances and angles are listed in Table 2. The structure of *trans*-(*S*,*S*)-**4** (Fig. 5)[18,19] reveals a mononuclear square planar *trans* palladium complex with Pd–S and Pd–P distances of 2.313(2) and 2.281(2) Å, which are consistent with their respective *trans* influences. These values can be compared to those in *trans*-[Pd($PPh_2C_6H_4$-2-S)$_2$], 2.308(2) and 2.291(1) Å, and *cis*-[Pd($PPh_2C_6H_4$-2-S)$_2$], 2.391(1) and 2.282(1) Å, respectively.[15] The Pd–S distance in *cis*-P,S-[PdCl($PPh_2CH_2CH_2S$)(PPh_3)] is shorter (2.270(2) Å) owing to the lower influence of chlorine, but the chelate Pd–P distance is comparable, 2.288(2) Å.[9] Shorter Pd–S (2.253(2) Å) and Pd–P (2.254(2) Å) distances are observed in the nitrogen donor containing cysteine complex *cis*-P,S-[PdCl($SCH_2CH(CO_2Et)NH_2$)(PPh_3)].[10]

The planarity of the PdS_2P_2 group is slightly distorted, owing most probably to packing forces in the solid state. The chelate chain carbons are displaced from the plane, adopting a δ conformation that places the substituents in equatorial positions (Fig. 5).

Table 1. Crystallographic data for complex *trans*-(*S*,*S*)-**4**

Empirical formula	$C_{44}H_{44}O_2P_2PdS_2$
FW	837.25
Temperature (K)	293(2)
Wavelength (Å)	0.71069
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	10.116(1)
b (Å)	9.410(7)
c (Å)	21.331(6)
α (°)	90
β (°)	99.27(2)
γ (°)	90
Volume (Å^3)	2004(2)
Z	2
Calculated density (g cm^{-1})	1.388
Absorption coefficient (mm^{-1})	6.83
Unique data/parameters	3757/388
$R(F_o)$ $[I>2\sigma(I)]$[a]	0.0467
$R_w(F_o^2)$ (all data)[b]	0.1032
Flack parameter	−0.04(4)

[a] $R(F_o)=\Sigma||F_o|-|F_c||/\Sigma|F_o|$.
[b] $R_w(F_o^2)=[\Sigma w(F_o^2-F_c^2)^2/\Sigma(F_o^2)^2]^{1/2}$.

Table 2. Selected bond distances (Å) and angles (°) for complex *trans*-(*S*,*S*)-**4**

Distances			
Pd–P1	2.280(2)	C1–P1	1.851(7)
Pd–P2	2.282(2)	C2–C31	1.533(13)
Pd–S1	2.307(2)	S2–C4	1.824(8)
Pd–S2	2.319(2)	C3–C4	1.522(10)
S1–C2	1.847(8)	C3–P2	1.821(7)
C1–C2	1.504(11)	C4–C61	1.513(9)
Angles			
P1–Pd–P2	178.70(6)	C1–C2–C31	113.5(7)
P1–Pd–S1	86.96(7)	C1–C2–S1	113.1(6)
P2–Pd–S1	94.15(7)	C31–C2–S1	108.9(6)
P1–Pd–S2	92.48(7)	C4–S2–Pd	105.3(2)
P2–Pd–S2	86.44(7)	C4–C3–P2	108.4(5)
S1–Pd–S2	177.4(1)	C61–C4–C3	111.7(7)
C2–S1–Pd	107.6(3)	C61–C4–S2	107.0(5)
C2–C1–P1	112.5(6)	C3–C4–S2	111.6(6)

7. Experimental

All complexes were synthesized using standard Schlenk techniques under a nitrogen atmosphere. Solvents were dried by standard methods and distilled and deoxygenated before use. Complexes Pd(PPh_3)$_4$, $PdCl_2$(PPh_3)$_2$ and $PdCl_2$($PhCN$)$_2$ were prepared as previously reported.[20–22] C, H and S analyses were carried out using a Carlo–Erba microanalyser. Infrared spectra (range 4000–400 cm^{-1}) were recorded on a Nicolet 205 spectrophotometer. Deuterated solvents for NMR measurements were dried over molecular sieves. Proton NMR spectra were recorded at 300 and 200 MHz on a Varian Gemini-300 and Bruker DPX-200 spectrometers, respectively. Peak positions are relative to tetramethylsilane as internal reference. $^{31}P\{^1H\}$ NMR spectra were recorded on the same instruments operating at 121.4 and 81.0 MHz, respectively. Chemical shifts are relative to external 85% H_3PO_4, with downfield values reported as positive. $^{13}C\{^1H\}$ NMR spectra were recorded on the same instruments operating at 75.4 and 50.3 MHz, respectively. Chemical shifts are relative to tetramethylsilane as internal reference. Gas chromatography analyses were performed on a Shimatzu GC-17A in a TRB-2 (5% diphenylsilicone–95% dimethylsilicone) column (30 m×0.25 ∅). Flash chromatography was performed on silica gel 60 A CC. Solvents for chromatography were distilled at atmospheric pressure prior to use. Microdistillation procedures were performed on a Buchi GK-R-51. The X-ray analysis study was carried out on a Enraf–Nonius CAD-4 diffractometer at room temperature, graphite monochromatized Mo Kα radiation and the $\omega/2\theta$ scan mode. Cell parameters were determined by least-square refinement on diffractometer parameters for 25 automatically centered reflections. Lp and empirical absorptions corrections were applied.[23] The structures were solved by direct methods using the program SHELXS-86[24] and refined on F^2 for all reflections using SHELXL-97.[25] The non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed at their calculated positions with isotropic temperature factors equal to 1.2 times the U_{eq} values of the corresponding carbons. Benzenic rings were refined as rigid bodies. Crystallographic data and structure refinement parameters are presented in Table 1, and selected distances and angles in Table 2.

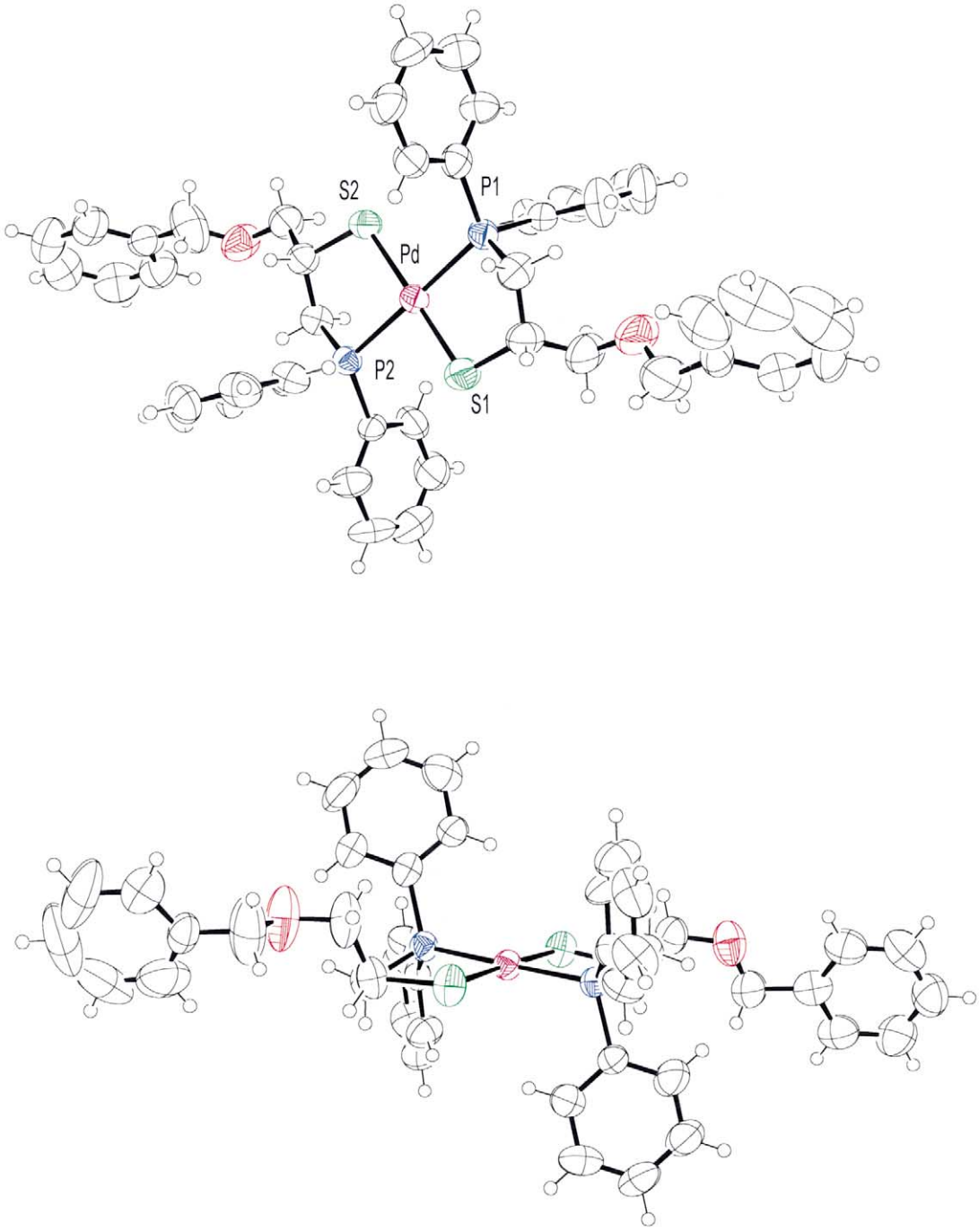


Figure 5. ORTEP plots of *trans*-(*S*,*S*)-**4**.

Crystallographic data (excluding structure factors) for the structure in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 167715. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

7.1. Preparation of (1-diphenylphosphino-3-benzyloxy)-propane-2-thiol 3

Step 1. A mixture of 50% w/w aqueous potassium hydroxide (60 mL), epichlorohydrin (40 mL) and tetrabutylammonium bromide (1.5 g, 4.7 mmol) was vigorously stirred at room temperature and placed in an ice bath. Benzyl alcohol (10 mL, 96.0 mmol) was gradually added over 10 min, the temperature did not exceed 25°C. The progress of the reaction was monitored by GLC; after 12 h, the reaction was complete and the reaction mixture was poured on ice/water (60 mL). The aqueous phase was extracted with diethyl ether (3×40 mL). The organic phase was washed with brine to neutrality, dried with magnesium sulfate, filtered, evaporated to dryness, and distilled at atmospheric pressure (205–210°C) to yield benzyl glycidyl ether **1** of purity >98% by GLC (13.4 g, 85%). ^{1}H NMR ($CDCl_3$ sol.): δ

2.62 (dd, 1H, $^2J=5.0$ Hz, $^3J=2.7$ Hz); 2.80 (dd, 1H, $^2J=5.0$ Hz, $^3J=4.2$ Hz); 3.19 (m, 1H); 3.44 (dd, 1H, $^2J=11.4$ Hz, $^3J=5.8$ Hz); 3.77 (dd 1H, $^2J=11.4$ Hz, $^3J=3.0$ Hz); 4.59 (m, 2H), 7.0–8.0 (m, 5H). $^{13}C\{^1H\}$ NMR ($CDCl_3$ sol.): δ 44.25 (s, CH_2); 50.82 (s, CH); 70.76 (s, CH_2); 73.28 (s, CH_2); 125.0–130.0 (C arom.).

Step 2. Thiourea (9.3 g, 122.4 mmol), benzyl glycidyl ether **1** (13.4 g, 81.6 mmol), water (8.1 mL) and ethanol (40.8 mL) were introduced in a reactor and vigorously stirred at room temperature. The progress of the reaction was monitored by GLC; after 12 h, the reaction was complete and water (20 mL) was added to the reaction mixture. The aqueous phase was extracted with diethyl ether (3×20 mL). The organic phase was washed with water (20 mL), dried with magnesium sulfate, filtered, evaporated to dryness, and distilled under vacuum (135–145°C, 0.1 Torr) benzyl thioglycidyl ether **2** of purity >98% by GLC was obtained (8.4 g, 58%). ^1H NMR ($CDCl_3$ sol.): δ 2.36 (dd, 1H, $^2J=1.2$ Hz, $^3J=5.5$ Hz); 2.52 (d*pst*, 1H, $^2J=1.2$ Hz, $^3J=6.0$ Hz, $^4J=0.8$ Hz); 3.1 (m, 1H); 3.49 (dd 1H, $^2J=10.6$ Hz, $^3J=6.7$ Hz); 3.69 (ddd 1H, $^2J=10.6$ Hz, $^3J=5.7$ Hz, $^4J=0.8$ Hz); 4.59 (m, 2H), 7.0–8.0 (m, 5H). $^{13}C\{^1H\}$ NMR ($CDCl_3$ sol.): δ 23.79 (s, CH_2); 32.16 (s, CH); 73.12 (s, CH_2); 74.67 (s, CH_2); 125.0–130.0 (C arom.).

Step 3. Benzyl thioglycidyl ether **2** (1.1 g, 6.11 mmol) was slowly added to an ice-cold solution of potassium diphenylphosphide (0.5 M in tetrahydrofuran, 12.2 mL, 6.1 mmol), with stirring under a nitrogen atmosphere. The reaction mixture was then vigorously stirred at room temperature. After 30 min, deoxygenated methanol (4 mL), deoxygenated saturated ammonium chloride aqueous solution (5 mL), and deoxygenated water (10 mL) were consecutively added to the reaction mixture. The aqueous phase was extracted with diethyl ether (3×15 mL). The organic phase was washed with water (15 mL), dried with magnesium sulfate, filtered and evaporated to dryness. Purification of the crude product by flash chromatography (hexane/ethyl acetate: 8/2) afforded (1-diphenylphosphino-3-benzyloxy)propane-2-thiol **3** of purity >98% by NMR (1.67 g, 75%). ^1H NMR ($CDCl_3$ sol.): δ 2.19 (d, SH, $^3J=6.3$ Hz); 2.33 (ddd, 1H, H_1, $^2J=14.0$ Hz, $^3J=8.3$ Hz, $^2J_{H-P}<0.5$ Hz); 2.64 (ddd, 1H, $H_{1'}$, $^2J=14.0$ Hz, $^3J=6.4$ Hz, $^2J_{H-P}=1.2$ Hz); 3.11 (m, 1H, H_2); 3.57 (dd, 1H, H_3, $^2J=9.5$ Hz, $^3J=6.0$ Hz); 3.65 (dd, 1H, $H_{3'}$, $^2J=9.5$ Hz, $^3J=5.8$ Hz); 4.49 (s, 2H, H_4), 7.0–8.0 (m, 15H, $H_{ar.}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$ sol.): δ 34.70 (d, CH, C_2, $^2J_{C-P}=11.3$ Hz); 37.48 (d, CH_2, C_1, $^1J_{C-P}=16.4$ Hz); 72.96 (s, CH_2, C_3); 75.59 (d, CH_2, C_4, $^3J_{C-P}=8.4$ Hz); 125.0–135.0 (C arom.). $^{31}P\{^1H\}$ NMR ($CDCl_3$ sol.): δ –20.53 (s).

Enantiomerically enriched ligands (*R*)-**3** and (*S*)-**3** were obtained through synthetic steps 2 and 3, starting from commercial benzyl (*R*)-(–)-glycidyl ether and benzyl (*S*)-(+)-glycidyl ether, respectively.

7.2. General procedure for preparation of bis-{1-diphenylphosphino-3-benzyloxy)propane-2-thiolato}palladium(II) complexes 4

(1-Diphenylphosphino-3-benzyloxy)propane-2-thiol **3** (262.0 mg, 0.57 mmol) was added to a solution of complex $[Pd(PPh_3)_4]$ (300.0 mg, 0.27 mmol) in anhydrous dichloromethane (10 mL) under a nitrogen atmosphere to produce an intense yellow solution. The reaction mixture was stirred at room temperature. After 1 h, the volume was reduced to 5 mL and the product was crystallized by the addition of hexane to afford the complex as orange crystals (187 mg, 86%). Anal. found: C, 63.4; H, 5.45; S, 7.4%. $C_{44}H_{44}P_2PdS_2$ calcd: C, 63.1; H, 5.29; S, 7.7. Complex *trans*-(*R*,*R*)-**4** or *trans*-(*S*,*S*)-**4** ^1H NMR (CD_2Cl_2 sol.): δ 2.76 (m, 1H, H_1); 3.05 (m, 1H, $H_{1'}$); 3.21 (m, 2H, H_3); 3.61 (m, 1H, H_2); 4.30 (m, 2H, H_4); 7.0–8.0 (m, 15H, $H_{ar.}$). $^{13}C\{^1H\}$ NMR (CD_2Cl_2 sol.): δ 41.39 (t, CH, C_2, $J_{C-P}=10.3$ Hz); 42.09 (t, CH_2, C_1, $J_{C-P}=17.4$ Hz); 73.10 (s, CH_2, C_4); 76.59 (t, CH_2, C_3, $J_{C-P}=8.7$ Hz); 125.0–135.0 (C arom.). $^{31}P\{^1H\}$ NMR (CD_2Cl_2 sol): δ 54.45 (s). Complex *cis*-(*R*,*R*)-**4** or *cis*-(*S*,*S*)-**4** $^{31}P\{^1H\}$ NMR (CD_2Cl_2 sol.): δ 47.55 (s). Complex *trans*-(*R*,*S*)-**4** ^1H NMR (CD_2Cl_2 sol.): δ 2.84 (m, 1H, H_1); 3.03 (m, 1H, $H_{1'}$); 3.21 (m, 2H, H_3); 3.63 (m, 1H, H_2); 4.28 (m, 2H, H_4); 7.0–8.0 (m, 15H, $H_{ar.}$). $^{13}C\{^1H\}$ NMR (CD_2Cl_2 sol.): δ 41.60 (t, CH, C_2, $J_{C-P}=10.6$ Hz); 41.95 (t, CH_2, C_1, $J_{C-P}=17.0$); 73.00 (s, CH_2, C_4); 76.52 (t, CH_2, C_3, $J_{C-P}=8.6$ Hz); 125.0–135.0 (C arom.). $^{31}P\{^1H\}$ NMR (CD_2Cl_2 sol.): δ 55.54 (s). Complex *cis*-(*R*,*S*)-**4** $^{31}P\{^1H\}$ NMR (CD_2Cl_2 sol.): δ 50.56 (s).

7.3. General procedure for the preparation of chloro-{(1-diphenylphosphino-3-benzyloxy)propane-2-thiolato)triphenylphosphine}palladium(II) complexes 5

(1-Diphenylphosphino-3-benzyloxy)propane-2-thiol **3** (80.0 mg, 0.21 mmol) was added to a solution of complex $[PdCl_2(PPh_3)_2]$ (150.0 mg, 0.21 mmol) in anhydrous dichloromethane (10 mL) under a nitrogen atmosphere to produce an orange solution. The reaction mixture was stirred at room temperature. After 1 h, the volume was reduced to 3 mL and the product was crystallized by addition of hexane and cooling the mixture to −20°C for 12 h. Complex **5** was obtained as orange crystals (117 mg, 70%). Anal. found: C, 62.3; H, 5.13; S, 4.1%. $C_{40}H_{37}ClP_2PdS$ calcd: C, 62.4; H, 4.84; S, 4.4. Complex *trans*-(*R*)-**5** or *trans*-(*S*)-**5** ^1H NMR (CD_2Cl_2 sol.): δ 2.94 (m, 2H, H_1); 3.17 (m, 2H, H_3); 3.48 (m, 1H, H_2); 4.23 (m, 2H, H_4); 7.0–8.0 (m, 30H, $H_{ar.}$). $^{13}\{^1H\}$ NMR (CD_2Cl_2 sol.): δ 42.44 (d, CH_2, C_1, $J_{C-P}=34.4$ Hz); 43.04 (d, CH, C_2, $J_{C-P}=10.3$ Hz); 73.07 (s, CH_2, C_4); 75.50 (d, CH_2, C_3, $J_{C-P}=18.2$ Hz); 125.0–135.0 (C arom.). $^{31}P\{^1H\}$ NMR (CD_2Cl_2 sol.): δ 23.45 (d, PPh_3, $^2J_{P-P}=463.6$ Hz); 57.56 (d, –PPh_2, $^2J_{P-P}=463.6$ Hz). Complex *cis*-(*R*)-**5** or *cis*-(*S*)-**5** $^{31}P\{^1H\}$ NMR (CD_2Cl_2 sol.): δ 23.64 (d, PPh_3, $^2J_{P-P}=13.4$ Hz); 63.60 (d, –PPh_2, $^2J_{P-P}=13.4$ Hz).

7.4. Interconversion between chloro and bischelate complexes

7.4.1. General procedure for preparation of bischelates from chloro complexes. (1-Diphenylphosphino-3-benzyloxy)propane-2-thiol **3** (48.0 mg, 0.13 mmol) was added to a solution of complex **5** (100.0 mg, 0.13 mmol) in anhydrous dichloromethane (8 mL) under a nitrogen atmosphere to produce an orange solution. The reaction mixture was stirred at room temperature for 2 h. The volume of the mixture was reduced to 5 mL and the product was crystallized by addition of hexane. Complex **4** was obtained as orange crystals (87 mg, 80%).

7.4.2. General procedure for the preparation of chloro complexes from bischelates. A mixture of complex $[PdCl_2(PPh_3)_2]$ (125.7 mg, 0.18 mmol) and bis-{(1-diphenylphosphino-3-benzyloxy)propane-2-thiolato}-palladium(II) complex **4** (150 mg, 0.18 mmol) in toluene (30 mL) was heated under reflux under a nitrogen atmosphere. After 24 h, the volume of the mixture was reduced to 5 mL and the product was crystallized by cooling to −20°C for 12 h. The crude product was filtered and washed with hexane and diethyl ether. Complex **5** was obtained as orange crystals (256 mg, 93%).

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