Dalton Transactions

Cite this: *Dalton Trans.*, 2012, **41**, 5391

www.rsc.org/dalton

PAPER

Chiral cyclopalladated complex promoted asymmetric synthesis of diester-substituted *P,N*-ligands *via* stepwise hydrophosphination and hydroamination reactions†

Ke Chen, Sumod A. Pullarkat, Mengtao Ma, Yongxin Li and Pak-Hing Leung*

Received 9th December 2011, Accepted 9th February 2012
DOI: 10.1039/c2dt12379g

A series of enantiomerically pure 1,2-diester substituted *P,N*-ligands incorporating two chiral carbons in the backbone were generated in high yields and high stereoselectivity from acetylenedicarboxylate *via* initial hydrophosphination using diphenylphosphine followed by hydroamination with various primary and secondary amines. The reactions were activated and stereochemically controlled by the organopalladium complex containing *ortho*-palladated (*S*)-(1-(dimethylamino)ethyl)naphthalene under mild conditions. The absolute stereochemistry and the coordination chemistry of *P,N*-products were determined by the single crystal X-ray diffraction analysis. All the chiral *P,N*-ligands could be liberated from the palladium template without loss of optical purity. Subsequent recomplexation to selected chiral palladium centers confirmed the optical purity of the new functionalized chiral *P,N*-ligands.

Introduction

It has been well established that bidentate *P,N* ligands play important roles in the areas of coordination chemistry and catalysis. For example, heterobidentate *P,N*-type ligands, by virtue of the fact that they have soft phosphorus and hard nitrogen donor atoms, can provide a crucial hybrid environment in a catalytic process. *P,N*-type ligands can furthermore stabilize intermediate oxidation states or geometries during a catalytic cycle in a metal catalyzed reaction.[1] The stereochemistry of such a reaction can also be controlled by the utilization of a suitable chiral heterobidentate *P,N*-ligand. Over the past decades, *P,N*-ligands have been successfully applied in various catalysis reactions including allylic alkylations,[2,3] hydrogenation,[4,5] hydrosilylation,[6] and hydroamination reactions.[7,8] Among this class of chiral ligands, 1,2-*P,N*-bidentates were most commonly employed, perhaps due to the formation of the corresponding stable 5-membered metal chelates. When coupled to suitable metal ions, these ligands have shown significant catalytic activities.[2,4,6,7,9–11] Currently, however, there are only limited chiral 1,2-*P,N*-bidentates available and their preparation mainly depend on the resolution from natural chiral pool sources and subsequent synthetic modifications.[2a,4a,c,9a,b,12–16] Accordingly, the development of the methodologies for the synthesis of structurally designed chiral 1,2-*P,N* derivatives is an area of research that has received much attention in recent years.

In this article, we report the synthesis of a series of diester substituted chiral 1,2-*P,N* ligands from acetylenedicarboxylate *via* the stepwise hydrophosphination and hydroamination reaction employing the *ortho*-palladated (*S*)-(1-(dimethylamino) ethyl)naphthalene as chiral auxiliary and reaction promoter. The initial hydrophosphination reaction produces the palladium coordinated prochiral vinylic phosphine species. The subsequent hydroamination step, however, generates two stereogenic carbon centers on the ligand backbone. It is interesting to note that the simultaneous generation of two stereogenic carbon centers *via* a single hydroamination reaction is a stereochemically demanding novel strategy that has not been reported previously. It is also noteworthy in this context that phosphine ligands containing ester functional groups are important reagents for cancer-chemotherapy.[17]

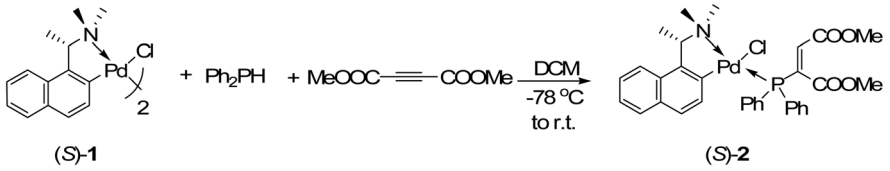
Results and discussion

Hydrophosphination and formation of the coordinated prochiral diphenylphosphino maleate

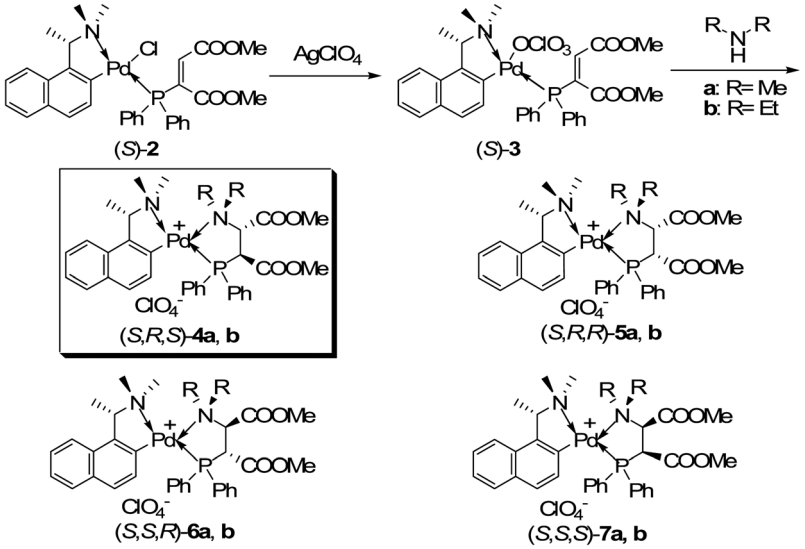
As illustrated in Scheme 1, hydrophosphination of dimethyl acetylenedicarboxylate with diphenylphosphine promoted by the chiral metal template (*S*)-**1** gave the neutral complex (*S*)-**2** regioselectively. The $^{31}P\{^{1}H\}$ NMR spectrum of the crude reaction mixture in $CDCl_3$ exhibited only one singlet signal at δ 41.7, indicating that only one phosphine product was formed quantitatively. Therefore the crude monophosphine complex, (*S*)-**2**, could be used directly for the subsequent hydroamination reaction. However, for storage and characterization purposes, it could be

Division of Chemistry and Biological Chemistry, School of Physical & Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore. E-mail: pakhing@ntu.edu.sg; Fax: +65 63166984; Tel: +65 63168905

†CCDC 857605–857607. For crystallographic data in CIF format for complexes (*R,S*)-**8a**, (*S,R,S*)-**10g**, (*R,S*)-**14f** and (*R,S*)-**14′f** see DOI: 10.1039/c2dt12379g



Scheme 1



Scheme 2

isolated as a stable complex *via* silica gel column chromatography in 75% yield. The regiospecific coordination of the "soft" phosphine ligand ion in the position *trans* to the NMe_2 moiety of the chiral template is due to the well established electronic directing effects originating from the σ-donating nitrogen and the strong π-accepting aromatic carbon of the organopalladium ring.[18]

Stereoselective hydroamination with secondary amines

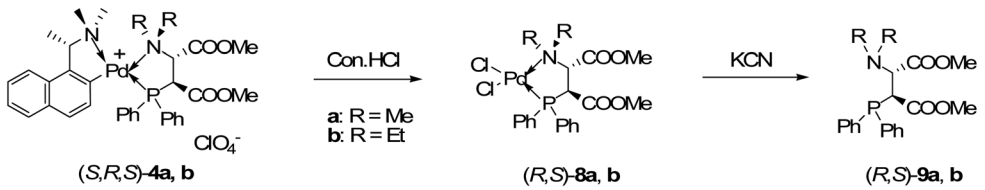
We have previously reported the palladium complex promoted hydroamination of alkynyl-phosphines to form the corresponding imino-phosphines.[19] Therein it was observed that the hydroamination reaction required both the alkynylphosphine and the amine to be coordinated simultaneously onto the palladium ion. In this current work, however, the chloro ligand in the monochloro complex (*S*)-**2** is thermodynamically and kinetically stable and it cannot be efficiently displaced by most incoming monodentate ligands, including phosphines and amines.[19,20] Therefore, as expected, no reaction was observed between the chloro complex (*S*)-**2** and various primary and secondary amines. Accordingly it was indeed necessary to replace the strong chloro ligand with the very weakly coordinated perchlorato counterpart in order to create a potential vacant site for the desired asymmetric hydroamination reaction. Complex (*S*)-**3** could be obtained quantitatively *via* the treatment of (*S*)-**2** with silver perchlorate. This perchlorato complex can also be isolated for storage and characterization purposes. We have previously reported the isolation and the single crystal X-ray structure of a similar perchlorato species.[21] In routine syntheses, however, the reactive perchlorato species (*S*)-**3** need not be isolated and can be used directly for subsequent hydroamination reactions (Scheme 2). The intramolecular hydroamination reaction between the perchlorato complex (*S*)-**3** and dimethylamine proceeded smoothly at −40 °C in dichloromethane. After 12 h the 162 MHz ^{31}P NMR spectrum of the crude reaction product in $CDCl_3$ showed only one singlet at δ 46.1. No other ^{31}P NMR signal was detected, indicating that the reaction produced stereoselectively only one of the four possible diastereomers *viz* (*S*,*R*,*S*)-**4a** was formed. Similarly the pure *P*,*N*-complex (*S*,*R*,*S*)-**4b** could be obtained efficiently from the reaction between (*S*)-**3** and diethylamine (Table 1). On the other hand, no hydroamination reaction was observed when (*S*)-**3** was treated with the diisopropylamine, presumably due to the steric hindrances offered by this bulky amine to the approach of the chiral reaction promoter.

Table 1 Asymmetric hydroamination of alkyl amines[a]

Amines	Products	$^{31}P\{^1H\}$ NMR (δ)	dr (%)[b]
$HNMe_2$	(*S*,*R*,*S*)-**4a**	46.1	99
$HNEt_2$	(*S*,*R*,*S*)-**4b**	45.1	95
$HN(i\text{-}Pr)_2$	N.R	—	—

[a] Reactions were performed using (*S*)-**2** (0.15 mmol) and amine (0.15 mmol) in CH_2Cl_2 (5 mL) at −40 °C for 12 h. [b] dr was determined by ^{31}P NMR.

Single crystals of complexes (*S*,*R*,*S*)-**4a,b** that are suitable for X-ray structural analyses could not be obtained. Hence the



Scheme 3

hydroamination products were treated directly with concentrated hydrochloric acid to remove the chiral naphthylamine auxiliary chemoselectively (Scheme 3). Interestingly, the structural integrity of the *P,N*-metal chelate was not affected by this strong acid treatment. The neutral dichloro complexes (*R*,*S*)-**8a,b** thus obtained is highly crystalline. The coordination chemistry and the absolute stereochemistry of complex (*R*,*S*)-**8a** was determined by X-ray crystallography (Fig. 1). The geometry at palladium center of (*R*,*S*)-**8a** is distorted square planar with angles of 87.3(1)°–92.7(1)° and 174.5(1)°–179.2(1)° (Fig. 1). The absolute stereochemistry at the C(5) and C(6) stereogenic centers are *R* and *S*, respectively. The five membered *P,N* chelate ring adopts the conformation with both ester functional groups occupying the sterically favorable equatorial positions. The difference between the two Pd–Cl bond distances [2.381(1) and 2.294(1) Å], with the bond *trans*- to the phosphorus being noticeably longer, is consistent with the fact that phosphorus has stronger *trans*-electronic influence than the nitrogen. The C(6)–P(1) [1.849(2) Å] and C(9)–P(1) [1.802(2) Å] distances are typical for C–P bonds. The C(5)–N(1) [1.518(3) Å] and C(5)–C(6) [1.531(3) Å] distances are typical for C–N and C–C bonds, respectively. The C(4)–O(1) [1.201(3)) Å] and C(4)–O(2) [1.328 (3) Å] distances are typical for C═O and C–O bonds, respectively (Table 2).

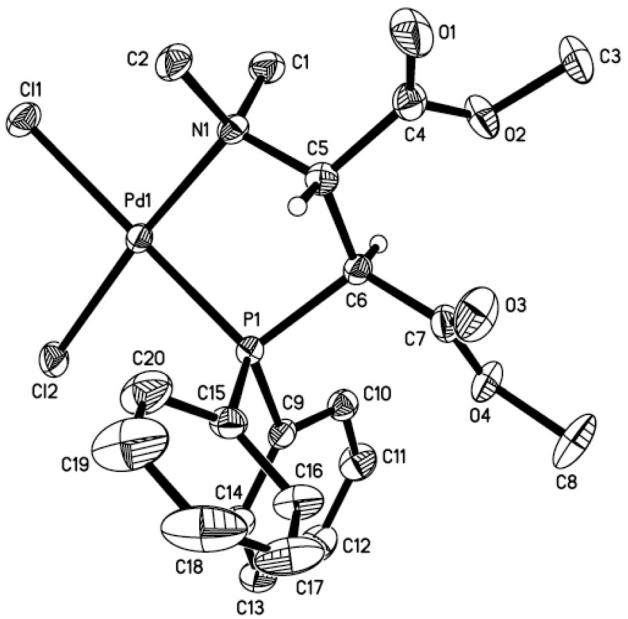


Fig. 1 Structure of (*R*,*S*)-**8a**.

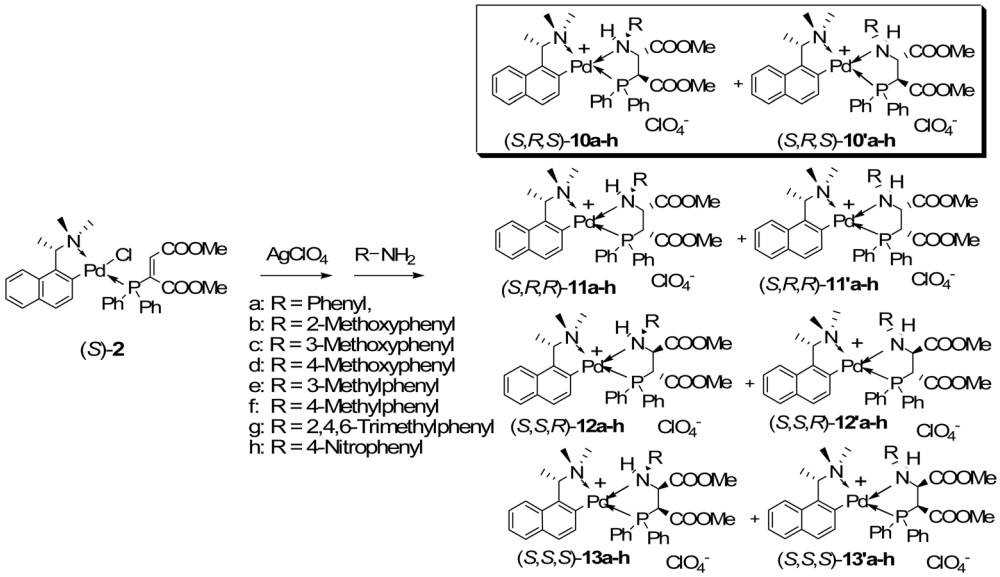
Table 2 Selected bond lengths (Å) and angles (°) of (*R*,*S*)-**8a**

Pd(1)–Cl(1)	2.381(1)	Pd(1)–Cl(2)	2.294(1)
Pd(1)–N(1)	2.133(2)	Pd(1)–P(1)	2.202(1)
C(1)–N(1)	1.486(3)	C(2)–N(1)	1.494(3)
C(4)–O(2)	1.328(3)	C(4)–O(1)	1.201(3)
C(5)–N(1)	1.518(3)	C(5)–C(6)	1.531(3)
C(6)–P(1)	1.849(2)	C(9)–P(1)	1.802(2)
N(1)–Pd(1)–P(1)	87.3(1)	N(1)–Pd(1)–Cl(2)	174.5(1)
P(1)–Pd(1)–Cl(2)	87.2(1)	N(1)–Pd(1)–Cl(1)	92.8(1)
P(1)–Pd(1)–Cl(1)	179.2 (1)	Cl(2)–Pd(1)–Cl(1)	92.7(1)
N(1)–C(5)–C(6)	110.8(2)	C(5)–C(6)–P(1)	105.9(2)
C(1)–N(1)–C(2)	109.7(2)	C(1)–N(1)–Pd(1)	107.1(2)
C(6)–P(1)–Pd(1)	99.9(1)	C(5)–N(1)–Pd(1)	111.0(1)

Stereoselective hydroamination with primary amines

The intramolecular hydroamination reaction between the perchlorato complex (*S*)-**3** and primary aryl amines may produce two carbon and one coordinated nitrogen stereogenic centers. Thus the reaction may generate up to eight stereomeric complexes (Scheme 4). Compared with their secondary alkyl amine analogues, primary aryl amines were found to be less reactive towards the hydromination reaction with the vinylphosphine complex (*S*)-**3**. This is an indication that the addition reactions adopted an electrophilic mechanism. As shown in Table 3, the hydroamination reactions with selected primary aryl amines proceeded smoothly at 60 °C to generate the hydroamination products in high yields (Table 3). The $^{31}P\{^{1}H\}$ NMR spectroscopy was used to monitor the asymmetric addition reactions. In all reactions, it was observed that only one major pair of diastereomers (arising from the presence of an additional nitrogen stereogenic centers) were obtained. These complexes are depicted as (*S*,*R*,*S*)-**10a–h** and (*S*,*R*,*S*)-**10′a–h** in Scheme 4. An X-ray structural analysis of complex (*S*,*R*,*S*)-**10g** confirmed the coordination chemistry and the absolute stereochemistry of the new chiral *P,N*-chelate (Fig. 2). Similar to those observed in complex (*R*,*S*)-**8a**, the absolute stereochemistry at the C(24) and C(27) stereogenic centers were *R* and *S*, respectively, with both the ester functional groups occupying the equatorial positions. It is interesting to note that the inter-chelate N(1)–Pd(1)–N(2) angle [99.9 (1)°] in this square-planar complex (Table 4) is clearly larger than the C(1)–Pd(1)–P(1) counterpart [94.9 (1)°], despite the fact that P(1) is bearing two projecting aromatic rings, but only one on N(2). Evidently, the two *ortho*-substituted methyl groups in the N-Ph ring play a significant role in the inter-chelate steric repulsion. Indeed, due to the severe steric hindrances, no hydroamination reaction was observed when (*S*)-**3** was treated with the bulky 2,6-diisopropylaniline.

From a stereochemical point of view, the chirality on the stereogenic nitrogen donors in complexes (*S*,*R*,*S*)-**10** is not a key



Scheme 4

Table 3 Stereoselectivities and yields of asymmetric hydroamination of aryl amines[a]

Amines	Product	^{31}PNMR (δ)	dr [b](%)	Ratio[c]	Yield[d] (%)
$C_6H_5NH_2$	**10a** & **10′a**	49.6 & 46.6	90	3.3 : 1	80
2-$MeOC_6H_4NH_2$	**10b** & **10′b**	49.3 & 48.6	89	1 : 3.1	83
3-$MeOC_6H_4NH_2$	**10c** & **10′c**	50.1 & 46.4	90	2.9 : 1	85
4-$MeOC_6H_4NH_2$	**10d** & **10′d**	49.7 & 45.9	88	3.3 : 1	85
3-$MeC_6H_4NH_2$	**10e** & **10′e**	50.3 & 46.5	87	3.1 : 1	82
4-$MeC_6H_4NH_2$	**10f** & **10′f**	49.5 & 45.9	85	4 : 1	80
2,4,6-$(Me)_3C_6H_2NH_2$	**10g** & **10′g**	54.9 & 44.3	90	1 : 3.1	85
4-$NO_2C_6H_4NH_2$	**10h** & **10′h**	48.0 & 45.4	88	8 : 1	87
2,6-$(iPr)_2C_6H_3NH_2$	—	—	—	—	—

[a] Reactions were performed using (*S*)-**2** (0.15 mmol) and amine (0.15 mmol) in chloroform (3 mL) at 60 °C for 16 h. [b] dr was determined by ^{31}P NMR. [c] Ratio was determined by ^{31}P NMR. [d] Isolated yield.

factor. The *N*-chirality would become insignificant once the *P*,*N*-bidentates are liberated from the palladium reaction promoter. Therefore, without further separation, *N*-chiral diastereomers of (*S*,*R*,*S*)-**10a–h** and (*S*,*R*,*S*)-**10′a–h** were treated with concentrated hydrochloric acid to remove the chiral naphthylamine auxiliary (Scheme 5).

The acid treatment generated the respective more crystalline *N*-chiral dichloro complexes (*R*,*S*)-**14a–h** and (*R*,*S*)-**14′a–h**. In all cases, the diastereomers co-crystallized together as a 1 : 1 mixture in the same unit cell. A pale yellow crystal containing the diastereomeric mixture (*R*,*S*)-**14f** and (*R*,*S*)-**14′f** was analyzed by X-ray crystallography (Fig. 3 and 4). The stereochemistry of complexes (*R*,*S*)-**14f** and (*R*,*S*)-**14′f** are similar and they differ only at the coordinated nitrogen stereogenic centers. The 5-membered *P*,*N*-chelates in both diastereomers adopted the same conformation with the ester functional groups occupying the sterically favorable equatorial positions. Accordingly N–C* and the P–C* centers adopt the *R* and *S* absolute configurations respectively. The N-aromatic rings in (*R*,*S*)-**14f** and (*R*,*S*)-**14′f** occupy the equatorial and axial positions, respectively. Selected bond distances and angles are given in Tables 5 and 6 respectively.

Liberation of chiral *P*,*N*-bidentates

Optically pure *P*,*N*-bidentates (*R*,*S*)-**9** and (*R*,*S*)-**15** could be liberated from the respective dichloro palladium complexes as air-sensitive oils by the treatment of their respective neutral complexes with aqueous potassium cyanide. The optical purities of these free ligands were established by the recomplexation of each of these ligands to the chiral reagent (*S*)-**1** and the equally accessible (*R*)-**1**. The ^{31}P NMR studies of the recomplexation products confirmed that these liberated ligands are enantiomerically pure.[22]

Conclusions

In conclusion, we have demonstrated a facile synthesis of diester functionalized chiral *P*,*N*-ligands *via* the stepwise hydrophosphination and hydroamination reaction with acetylenedicarboxylate. Both addition reactions were promoted by the same chiral organopalladium reagent in high regio- and stereo-selectivities under mild conditions. Further investigations on the catalytic potential of transition metal complexes generated from these chiral ligands and evaluation of their biological activity are currently in progress.

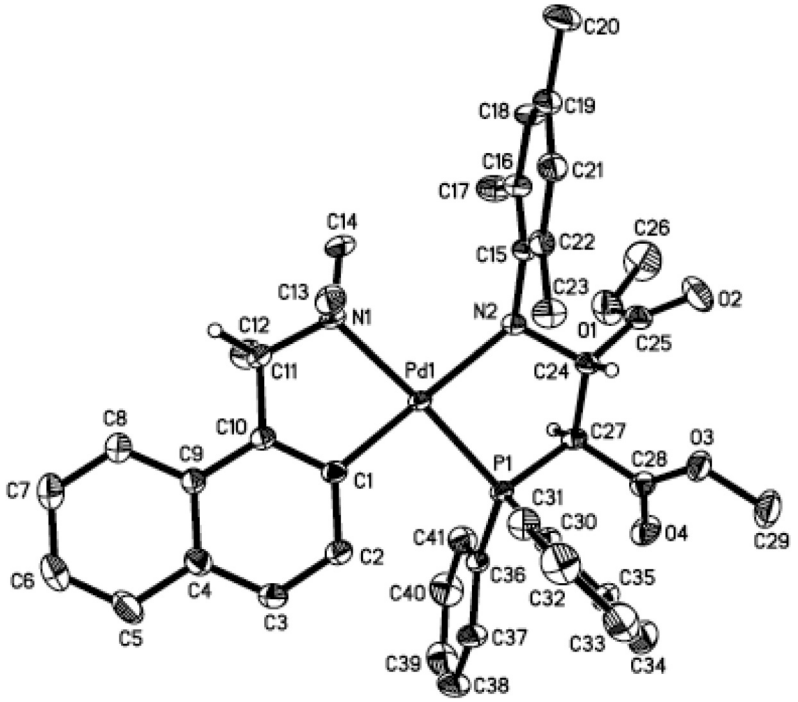


Fig. 2 Structure of (*S*,*R*,*S*)-**10g**.

Table 4 Selected bond lengths (Å) and angles (°) of (*S*,*R*,*S*)-**10g**

Pd(1)–C(1)	2.009(2)	Pd(1)–N(1)	2.149(2)
Pd(1)–P(1)	2.233(1)	Pd(1)–N(2)	2.264(2)
C(1)–C(10)	1.385(3)	C(11)–N(1)	1.510(3)
C(15)–N(2)	1.472(3)	C(24)–N(2)	1.501(3)
C(24)–C(27)	1.532(3)	C(24)–C(25)	1.538(3)
C(25)–O(2)	1.201(3)	C(25)–O(1)	1.332(4)
C(27)–P(1)	1.870(2)	C(30)–P(1)	1.818(2)
C(1)–Pd(1)–N(1)	80.9(1)	C(1)–Pd(1)–P(1)	94.9(1)
N(1)–Pd(1)–P(1)	175.7(1)	C(1)–Pd(1)–N(2)	178.7(1)
N(1)–Pd(1)–N(2)	99.9 (1)	P(1)–Pd(1)–N(2)	84.3(1)
C(28)–C(27)–P(1)	111.5(2)	C(10)–C(1)–Pd(1)	113.8(2)
C(11)–N(1)–Pd(1)	105.7(1)	C(24)–C(27)–P(1)	109.3(2)
C(15)–N(2)–Pd(1)	119.7(2)	C(24)–N(2)–Pd(1)	112.8 (2)
C(36)–P(1)–C(30)	106.5(1)	C(27)–P(1)–Pd(1)	102.3(1)

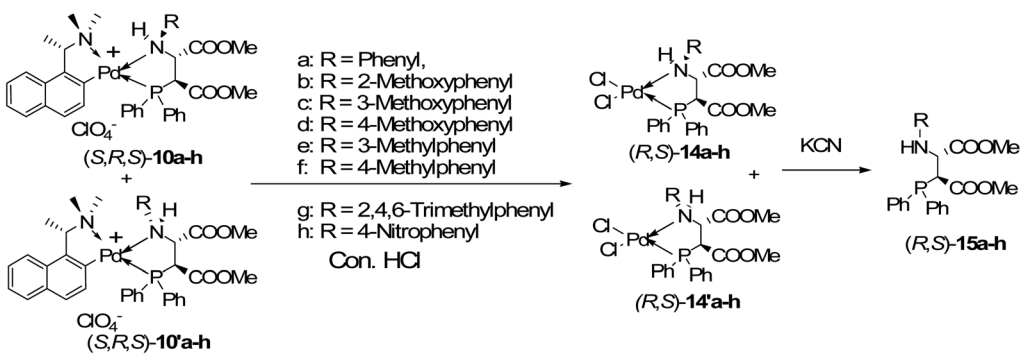
Experimental section

Reactions involving air-sensitive compounds were performed under an inert atmosphere of argon using standard Schlenk techniques. Solvents were dried and freshly distilled according to standard procedures and degassed prior to use when necessary. The ^{1}H and $^{31}P\{^{1}H\}$ NMR spectra were recorded at 25 °C on Bruker Avance 300, 400 and 500 spectrometers. Optical rotations were measured on the specified solution in a 0.1 dm cell at 20 °C with a Perkin-Elmer 341 polarimeter. Elemental analysis was performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at Nanyang Technological University. Melting points are uncorrected.

Caution: Perchlorate salts of metal complexes are potentially explosive compounds and should be handled with care.

Preparation of monophosphine palladium (II) complex (*S*)-2

To a solution of (*S*)-**1** (1300 mg, 1.91 mmol) in dichloromethane (200 mL) at −78 °C was slowly added diphenylphosphine (711 mg, 3.82 mmol) in dichloromethane (5 mL), and the mixture was stirred at −78 °C for 1 h. Then, the dimethyl acetylenedicarboxylate (542 mg, 3.82 mmol) was added to the above



Scheme 5

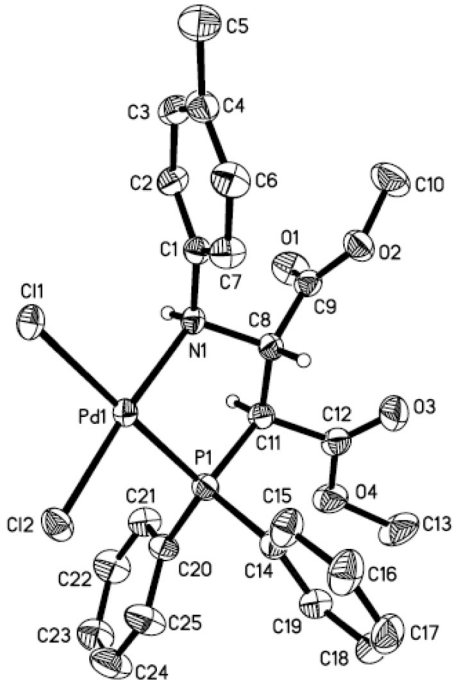


Fig. 3 Structure of (*R*,*S*)-**14f**.

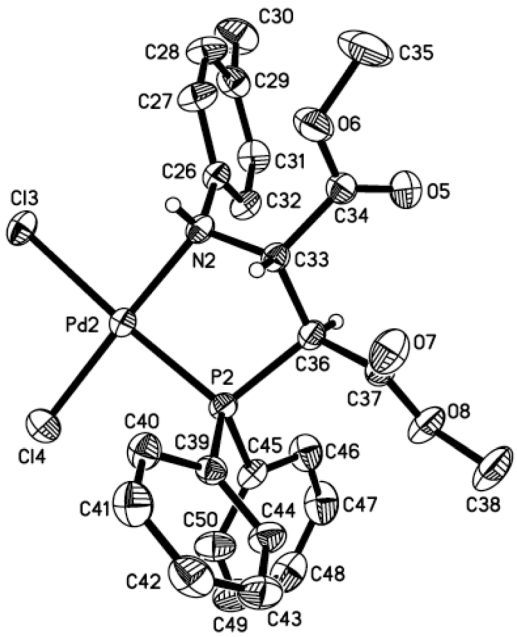


Fig. 4 Structure of (*R*,*S*)-**14′f**.

solution and the triethylamine (387 mg, 3.82 mmol) was added subsequently. The temperature was increased to room temperature nature after the mixture was stirred for 4 h at −78 °C and continued stirred for 10 h at room temperature. The reaction was monitored by ^{31}P NMR and the mixture was concentrate after reaction completed. The mixture was purified by column chromatography to give 1915 mg of (*S*)-**2** (75.0% yield). Yellow solid: mp 120–123 °C; $[\alpha]_D$ = +38° (*c* 0.5, CH_2Cl_2) at 20 °C. **^{31}P NMR**: (162 MHz, $CDCl_3$): δ 41.7; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 7.94–7.99 (m, 2H), 7.71–7.76 (m, 3H), 7.63–7.65 (m, 1H), 7.39–7.54 (m, 5H), 7.29–7.36 (m, 3H), 7.02 (d, J_{PH} = 8.6 Hz, 1H), 6.67–6.72 (m, 2H), 4.38 (m, 1H), 3.71 (s, 3H), 3.52 (s, 3H), 2.98 (d, J_{PH} = 3.6Hz, 3H), 2.76 (d, J_{HH} = 1.5 Hz, 3H), 2.06 (d, J_{HH} = 6.4 Hz, 3H); **^{13}C NMR**: (100 MHz, $CDCl_3$): δ 165.4 (d, J_{PC} = 7.3 Hz), 164.5 (d, J_{PC} = 17.6 Hz), 149.7, 149.2 (d, J_{PC} = 1.9 Hz), 142.4 (d, J_{PC} = 33.8 Hz), 136.2 (d, J_{PC} = 10.4 Hz), 135.8 (d, J_{PC} = 12.2 Hz), 135.6, 135.5, 135.3, 135.2, 131.4 (d, J_{PC} = 2.3 Hz), 131.3 (d, J_{PC} = 2.4 Hz), 131.2, 128.8, 128.68, 128.66, 128.5, 128.3, 128.2, 127.8 (d, J_{PC} = 110.0 Hz), 127.7 (d, J_{PC} = 11.2 Hz), 125.8, 124.8 (d, J_{PC} = 5.9 Hz), 124.2, 123.3, 73.3 (d, J_{PC} = 3.4 Hz), 52.4, 52.3, 51.3 (d, J_{PC} = 3.1 Hz), 48.7 (d, J_{PC} = 2.9 Hz), 23.7.

Table 5 Selected bond lengths (Å) and angles (°) of (*R*,*S*)-**14f**

Pd(1)–N(1)	2.100(2)	Pd(1)–P(1)	2.210(1)
Pd(1)–Cl(2)	2.297(1)	Pd(1)–Cl(1)	2.369(1)
C(1)–N(1)	1.447(3)	C(8)–N(1)	1.503(3)
C(8)–C(11)	1.530(3)	C(9)–O(2)	1.330(3)
C(9)–O(1)	1.208(3)	C(11)–P(1)	1.854(2)
C(20)–P(1)	1.807(3)	C(14)–P(1)	1.805(3)
N(1)–Pd(1)–P(1)	86.5(1)	N(1)–Pd(1)–Cl(2)	175.2(1)
P(1)–Pd(1)–Cl(2)	89.4(1)	N(1)–Pd(1)–Cl(1)	90.9(1)
P(1)–Pd(1)–Cl(1)	174.2(1)	Cl(2)–Pd(1)–Cl(1)	93.5(1)
N(1)–C(8)–C(11)	109.1(2)	C(8)–N(1)–Pd(1)	111.8(2)
C(11)–P(1)–Pd(1)	101.3(1)	C(8)–C(11)–P(1)	106.8(2)

Table 6 Selected bond lengths (Å) and angles (°) of (*R*,*S*)-**14′f**

Pd(2)–N(2)	2.087(2)	Pd(2)–P(2)	2.203(1)
Pd(2)–Cl(4)	2.284(1)	Pd(2)–Cl(3)	2.371(1)
C(26)–N(2)	1.458(3)	C(33)–N(2)	1.512(3)
C(33)–C(36)	1.521(3)	C(34)–O(5)	1.194(3)
C(34)–O(6)	1.324(3)	C(36)–P(2)	1.876(3)
C(39)–P(2)	1.812(2)	C(45)–P(2)	1.812(2)
N(2)–Pd(2)–P(2)	87.3(1)	N(2)–Pd(2)–Cl(4)	177.2(1)
P(2)–Pd(2)–Cl(4)	90.4(1)	N(2)–Pd(2)–Cl(3)	89.3(1)
P(2)–Pd(2)–Cl(3)	176.5(1)	Cl(4)–Pd(2)–Cl(3)	93.1(1)
N(2)–C(33)–C(36)	112.3(2)	C(33)–N(2)–Pd(2)	112.7(1)
C(36)–P(2)–Pd(2)	101.9(1)	C(33)–C(36)–P(2)	106.5(2)

Synthesis of (*S*,*R*,*S*)-4a,b by asymmetric hydroamination reaction

A solution of the monochloro complex of (*S*)-**2** (0.15 mmol) in dichloromethane (3 mL) was treated with silver perchlorate (0.30 mmol) in water (1 mL) for 30 min. The mixture was then filtered through Celite, washed with water, and dried over $MgSO_4$ and the solvent was removed under reduced pressure. The resulting perchloro complex (*S*)-**3** was dissolved in dichloromethane (5 mL) and cooled to −40 °C. Dimethylamine (0.15 mmol) in THF was added to the solution and the mixture was stirred for another 12 h at −40 °C. After removal of solvent, crude hydroamination products were obtained as pale yellow foaming solid. Without further purification, the crude products were applied to the next step directly, in which chiral template auxiliary was removed chemoselectively.

Table 7 Crystallographic data for complexes (*R*,*S*)-**8a**, (*S*,*R*,*S*)-**10g**, (*R*,*S*)-**14f** and (*R*,*S*)-**14′f**

	(*R*,*S*)-**8a**	(*S*,*R*,*S*)-**10g**	(*R*,*S*)-**14f** and (*R*,*S*)-**14′f**
Formula	$C_{20}H_{24}Cl_2NO_4PPd$	$C_{42}H_{48}Cl_3N_2O_8PPd$	$C_{25}H_{26}Cl_2NO_4PPd$
fw	550.67	952.54	612.74
Space group	*P*2(1)2(1)2(1)	*P*2(1)	*P*2(1)
Cryst syst	Orthorhombic	Monoclinic	Monoclinic
a (Å)	10.8879(2)	11.2143(4)	10.5919(14)
b (Å)	12.1286(3)	17.4999(6)	20.528(3)
c (Å)	17.4097(4)	11.5906(4)	12.6956(16)
α (°)	90	90	90
β (°)	90	111.861(2)	109.676(8)
γ (°)	90	90	90
V (Å^3)	2299.04(9)	2111.07(13)	2599.2(6)
Z	4	2	4
T (K)	173(2)	173(2)	173(2)
D_{calcd} (g cm^{-3})	1.591	1.499	1.566
λ (Å)	0.71073	0.71073	0.71073
μ (mm^{-1})	1.134	0.722	1.013
F (000)	1112	980	1240
Flack param	−0.049(19)	−0.019(15)	−0.018(12)
R_1 (obs data)[a]	0.0359	0.0415	0.0287
wR_2 (obs data)[b]	0.0534	0.0918	0.0701

[a] $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR_2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}$, $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$.

Palladium complex (*S*,*R*,*S*)-4a. **^{31}P NMR** (162 MHz, $CDCl_3$): *δ* 46.1.

Palladium complex (*S*,*R*,*S*)-4b. **^{31}P NMR** (162 MHz, $CDCl_3$): *δ* 45.1.

Synthesis of (*S*,*R*,*S*)-8a,b

A solution of above crude hydroamination products (*S*,*R*,*S*)-**4a,b** in dichloromethane (5 mL) was treated with concentrated hydrochloric acid (5 mL) at room temperature for 24 h. The reaction mixture was then diluted with dichloromethane (20 mL), washed with water (3 × 5 mL) and dried over anhydrous $MgSO_4$. Removal of solvent gave the yellow solid, which was readily grown crystal from dichloromethane and diethyl ether to give the (*R*,*S*)-**8a** and (*R*,*S*)-**8b** respectively.

(*R*,*S*)-8a. Yellow prism crystal: mp 190–191 °C; $[\alpha]_D$ = +82° (*c* 0.5, CH_2Cl_2). Anal. Calcd for $C_{20}H_{24}Cl_2NO_4PPd$: C, 43.6; H, 4.4; N, 2.5; Found: C, 43.5; H, 4.4; N, 2.6; **^{31}P NMR** (202 MHz, $CDCl_3$): *δ* 42.3; **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 7.91–8.01 (m, 4H), 7.62–7.66 (m, 2H), 7.51–7.56 (m, 4H), 4.57 (dd, J_{HH} = 13.2 Hz, J_{PH} = 8.1 Hz, 1H), 4.06 (dd, J_{HH} = 13.2 Hz, J_{PH} = 7.9 Hz, 1H), 3.79 (s, 3H), 3.39 (s, 3H), 3.36 (s, 3H), 2.94 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* 165.6 (d, J_{PC} = 25.5 Hz), 165.2 (d, J_{PC} = 8.7 Hz), 135.2, 135.1, 133.6 (d, J_{PC} = 1.4 Hz), 133.5, 133.4, 132.7 (d, J_{PC} = 3.1 Hz), 129.3, 129.2, 129.0, 128.9, 124.8 (d, J_{PC} = 61.3 Hz), 123.4 (d, J_{PC} = 55.2 Hz), 74.5 (d, J_{PC} = 10.5 Hz), 53.4, 53.3, 52.9, 49.8 (d, J_{PC} = 17.7 Hz), 46.7.

(*R*,*S*)-8b. Yellow prism crystal: mp 170–171 °C; $[\alpha]_D$ = +50° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{22}H_{28}Cl_2NO_4PPd$: C, 45.7, H, 4.9; N, 2.4, Found: C, 45.5; H, 4.8; N, 2.2.; **^{31}P NMR** (202 MHz, $CDCl_3$): *δ* 42.5; **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.01–8.05 (m, 2H), 7.84–7.88 (m, 2H), 7.60–7.66 (m, 2H), 7.48–7.56 (m, 4H), 4.82 (dd, J_{HH} = 13.2 Hz, J_{PH} = 9.1 Hz, 1H), 4.50 (dd, J_{HH} = 13.2 Hz, J_{PH} = 9.1 Hz, 1H), 4.12–4.18 (m, 1H), 3.81 (s, 3H), 3.39–3.50 (m, 1H), 2.73–2.84 (m, 2H), 1.92 (t, J_{HH} = 6.9 Hz, 3H), 1.83 (t, J_{HH} = 7.3 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* 166.3 (d, J_{PC} = 25.0 Hz), 165.9 (d, J_{PC} = 8.4 Hz), 134.9, 134.8, 133.7, 133.6, 133.3 (d, J_{PC} = 2.8 Hz), 132.6 (d, J_{PC} = 2.9 Hz), 129.10, 129.06, 129.01, 128.97, 125.5 (d, J_{PC} = 60.7 Hz), 124.1 (d, J_{PC} = 56.2 Hz), 68.8 (d, J_{PC} = 10.3 Hz), 56.7, 56.3, 53.3, 52.8, 51.9 (d, J_{PC} = 17.6 Hz), 15.8, 14.3.

Synthesis of (*R*,*S*)-9a,b

A solution of the dichloro complex (*R*,*S*)-**8a** (165 mg, 0.3 mmol) in CH_2Cl_2 (10 mL) was treated with excess potassium cyanide (195 mg, 3 mmol) in water (2 mL). The reaction mixture was stirred vigorously at room temperature for 10 min. The colorless organic layer was separated, washed with water (3 × 5 mL) and dried over anhydrous $MgSO_4$. Upon the removal of the solvent under reduced pressure, free ligands (*R*,*S*)-**9a** was obtained as a pale yellow oil.

(*R*,*S*)-9a. Pale yellow oil: (103 mg, 92%); $[\alpha]_D$ = −222° (*c* 0.5, CH_2Cl_2); **^{31}P NMR** (162 MHz, $CDCl_3$): *δ* −8.1; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 7.64–7.68 (m, 2H), 7.52–7.55 (m, 2H), 7.31–7.38 (m, 6H), 3.89 (dd, J_{HH} = 12 Hz, J_{PH} = 2.4 Hz, 1H), 3.81 (dd, J_{HH} = 12 Hz, J_{PH} = 4.8 Hz, 1H), 3.69 (s, 3H), 3.06 (s, 3H), 2.12 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 171.4 (d, J_{PC} = 9.1 Hz), 171.1 (d, J_{PC} = 25 Hz), 136.2 (d, J_{PC} = 15.3 Hz), 135.1 (d, J_{PC} = 18.4 Hz), 134.8, 134.6, 133.7, 133.5, 129.2, 128.6, 128.2, 128.1, 128.0, 127.9, 67.8 (d, J_{PC} = 19.6 Hz), 51.2, 51.1, 46.4 (d, J_{PC} = 22.2 Hz), 41.8.

(*R*,*S*)-9b. Pale yellow oil (108 mg, 90%) from dichloro complex (*R*,*S*)-**8b** (174 mg, 0.3 mmol); $[\alpha]_D$ = −134° (*c* 0.5, CH_2Cl_2); **^{31}P NMR** (162 MHz, $CDCl_3$): *δ* −8.7; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 7.71–7.75 (m, 2H), 7.39–7.50 (m, 5H), 7.29–7.31 (m, 3H), 4.12 (dd, J_{HH} = 12 Hz, J_{PH} = 5.4 Hz, 1H),

3.96 (d, J_{HH} = 12 Hz, 1H), 3.69 (s, 3H), 3.02 (s, 3H), 2.49–2.56 (m, 2H), 2.31–2.40 (m, 2H), 0.78 (*t*, J_{HH} = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.5 (d, J_{PC} = 10.8 Hz), 171.3 (d, J_{PC} = 1.4 Hz), 136.3 (d, J_{PC} = 15.4 Hz), 135.9 (d, J_{PC} = 19.4 Hz), 134.7, 134.5, 134.1, 133.8, 128.90, 128.88, 128.4, 128.3, 127.9, 127.8, 64.4 (d, J_{PC} = 23.5 Hz), 51.2, 50.1, 46.7 (d, J_{PC} = 21.7 Hz), 44.6, 12.9.

Synthesis of (*S*,*R*,*S*)-10a–h and (*S*,*R*,*S*)-10′a–h by asymmetric hydroamination reaction

A solution of the monochloro complex of (*S*)-**2** (100 mg, 0.15 mmol) in dichloromethane (3 mL) was treated with silver perchlorate (68 mg, 0.30 mmol) in water (1 mL) for 30 min. The mixture was then filtered through Celite, washed with water, and dried over $MgSO_4$ and the solvent was removed under reduced pressure. The resulting perchloro complex (*S*)-**3** was dissolved in chloroform (3 mL). Amine (0.15 mmol) was added to the solution and the mixture was stirred for another 16 h at 60 °C. After removal of solvent, crude hydroamination product was obtained as pale yellow foam. The crude product was separated by column chromatography give the (*S*,*R*,*S*)-**10a–h** and (*S*,*R*,*S*)-**10′a–h** as a pair *N*-chiral isomers. Without separation of this pair of isomers, they were applied to the next step directly, in which chiral template auxiliary was removed chemoselectively.

(*S*,*R*,*S*)-10g. Pale yellow prism crystal: mp 180–182 °C; 60% yield; $[\alpha]_D$ = +164° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{41}H_{46}ClN_2O_8PPd$: C, 56.8; H, 5.3; N, 3.2, Found: C, 54.9; H, 5.0; N, 3.4; **^{31}P NMR** (162 MHz, $CDCl_3$): δ 42.5; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05–8.15 (m, 4H), 7.77–7.81 (m, 1H), 7.66–7.70 (m, 2H), 7.58–7.61 (m, 2H), 7.29–7.40 (m, 5H), 7.05–7.07 (m, 1H), 6.89–6.92 (m, 3H), 6.30 (d, J_{HH} = 12.2 Hz), 5.13 (dd, J_{HH} = 12.7 Hz, J_{PH} = 8.8 Hz, 1H), 4.11–4.17 (m, 1H), 3.94–4.03 (m, 1H), 3.53 (s, 3H), 3.47 (s, 3H), 3.19 (s, 3H), 2.56 (s, 3H), 2.33 (d, J_{PH} = 3.7 Hz, 3H), 2.27 (s, 6H), 1.91 (d, J_{HH} = 6.4 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 168.1 (d, J_{PC} = 19.2 Hz), 167.3 (d, J_{PC} = 9.0 Hz), 149.3 (d, J_{PC} = 2.7 Hz), 144.1, 137.4, 136.9, 136.7, 136.6, 134.8, 134.7, 133.8 (d, J_{PC} = 2.6 Hz), 133.3, 133.1, 133.0, 131.5 (d, J_{PC} = 3.8 Hz), 131.4, 131.3, 130.7, 129.9, 129.6, 129.5, 129.0, 128.9, 128.7, 128.5, 126.3, 126.2, 125.94, 125.88, 125.7, 124.8, 123.3, 121.8 (d, J_{PC} = 42.8 Hz), 74.0 (d, J_{PC} = 2.0 Hz), 63.2 (d, J_{PC} = 9.0 Hz), 52.5, 52.4, 51.2 (d, J_{PC} = 1.9 Hz), 50.3, 50.2, 45.9, 23.8, 21.7, 20.7, 18.5.

Synthesis of (*R*,*S*)-14a–h and (*R*,*S*)-14′a–h

A solution of above crude hydroamination product mixture of (*S*,*R*,*S*)-**10a–h** and (*S*,*R*,*S*)-**10′a–h** in dichloromethane (5 mL) was treated with concentrated hydrochloric acid (5 mL) at room temperature for 2 h. The reaction mixture was then diluted with dichloromethane (20 mL), washed with water (3 × 5 mL) and dried over anhydrous $MgSO_4$. Removal of solvent gave the yellow solid, which was readily crystallized from dichloromethane and diethyl ether to give the pair (*R*,*S*)-**14a–h** and (*R*,*S*)-**14′a–h** as a yellow prism co-crystal.

(*R*,*S*)-14a and (*R*,*S*)-14′a. Yellow solid: mp 202–204 °C (decomp); 94% yield; $[\alpha]_D$ = +144° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{24}H_{24}Cl_2NO_4PPd$: C, 48.1; H, 4.0; N, 2.3; Found: C, 48.2; H, 3.2; N, 2.5; **^{31}P NMR** (162 MHz, $CDCl_3$): δ_1 50.9 and δ_2 44.5 (δ_1/δ_2 = 0.7/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.16–8.24 (m, 25.5H), 5.38–5.44 (m, 1H), 4.79–4.84 (m, 1.7H), 4.05–4.22 (m, 0.7H), 3.48 (s, 2.1H), 3.45 (s, 3H), 3.41 (s, 2.1H), 3.14 (s, 3H).

(*R*,*S*)-14b and (*R*,*S*)-14′b. Yellow solid: mp 211–213 °C (decomp); 96% yield; $[\alpha]_D$ = +102° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{25}H_{26}Cl_2NO_5PPd$: C, 47.8; H, 4.2; N, 2.2; Found: C, 46.8; H, 4.8; N, 2.2; **^{31}P NMR** (162 MHz, CD_2Cl_2): δ_1 48.1 and δ_2 46.2 (δ_1/δ_2 = 1/0.8); **^{1}H NMR** (400 MHz, CD_2Cl_2): δ 6.94–8.51 (m, 25.2H), 6.80–6.90 (brs, 1H), 6.50–6.60 (brs, 0.8H), 4.95–5.07 (m, 1.8H), 4.50–4.57 (m, 1H), 4.32–4.42 (m, 1H), 4.02 (s, 3H), 3.59 (s, 2.4H), 3.43 (s, 2.4H), 3.41 (s, 3H), 3.80 (s, 3H), 3.20 (s, 2.4H).

(*R*,*S*)-14c and (*R*,*S*)-14′c. Yellow solid: 191–193 °C (decomp); 93% yield; $[\alpha]_D$ = +100° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{25}H_{26}Cl_2NO_5PPd$: C, 47.8; H, 4.2; N, 2.2; Found: C, 46.2; H, 4.7; N, 2.4; **^{31}P NMR** (162 MHz, $CDCl_3$): δ_1 51.1 and δ_2 44.6 (δ_1/δ_2 = 0.6/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.71–8.70 (m, 22.4H), 5.45 (m, 1H), 4.85–4.95 (m, 0.6H), 4.75–4.82 (m, 1H), 4.02–4.12 (m, 0.6H), 3.67 (s, 1.8H), 3.56 (s, 1.8H), 3.54 (s, 3H), 3.47 (s, 1.8H), 3.31 (s, 3H), 3.11 (s, 3H).

(*R*,*S*)-14d and (*R*,*S*)-14′d. Yellow solid 182–184 °C (decomp); 96% yield; $[\alpha]_D$ = +126° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{25}H_{26}Cl_2NO_5PPd$: C, 47.8; H, 4.2; N, 2.2; Found: C, 47.6; H, 3.5; N, 3.7; **^{31}PNMR** (162 MHz, $CDCl_3$): δ_1 51.2 and δ_2 44.3 (δ_1/δ_2 = 0.7/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.57–8.56 (m, 23.8H), 5.32–5.40 (m, 1H), 4.68–4.74 (m, 1.7H), 3.90–4.01 (m, 0.7H), 3.75 (s, 2.1H), 3.67 (s, 3H), 3.43 (s, 2.1H), 3.40 (s, 3H), 3.33 (s, 2.1H), 3.05 (s, 3H).

(*R*,*S*)-14e and (*R*,*S*)-14′e. Yellow solid: mp 189–191 °C (decomp); 92% yield; $[\alpha]_D$ = +98° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{25}H_{26}Cl_2NO_4PPd$: C, 49.0; H, 4.3; N, 2.3; Found: C, 48.8; H, 5.0; N, 2.3; **^{31}P NMR** (162 MHz, $CDCl_3$): δ_1 50.9 and δ_2 44.7 (δ_1/δ_2 = 0.5/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.98–8.67 (m, 21H), 5.45–5.53 (m, 1H), 4.82–4.90 (m, 0.5H), 4.70–4.81 (m, 1H), 4.05–4.12 (m, 0.5H), 3.52 (s, 1.5H), 3.50 (s, 3H), 3.42 (s, 1.5H), 3.12 (s, 3H), 2.30 (s, 1.5H), 2.06 (s, 3H).

(*R*,*S*)-14f and (*R*,*S*)-14′f. Yellow solid: 195–197 °C (decomp); 95% yield; $[\alpha]_D$ = +146° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{25}H_{26}Cl_2NO_4PPd$: C, 49.0; H, 4.3; N, 2.3; Found: C, 48.7; H, 4.9; N, 2.2; **^{31}P NMR** (162 MHz, $CDCl_3$): δ_1 51.1 and δ_2 44.6 (δ_1/δ_2 = 0.5/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.95–8.64 (m, 21H), 5.35–5.42 (m, 1H), 4.75–4.86 (m, 1.5H), 4.04–4.12 (m, 0.5H), 3.51 (s, 1.5H), 3.48 (s, 3H), 3.40 (s, 1.5H), 3.13 (s, 3H), 2.38 (s, 1.5H), 2.26 (s, 3H).

(*R*,*S*)-14g. Yellow solid: mp 174–176 °C (decomp); 91% yield; $[\alpha]_D$ = +70° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{27}H_{30}Cl_2NO_4PPd$: C, 50.6; H, 4.7; N, 2.2; Found: C, 48.8; H, 4.3; N, 2.8; **^{31}P NMR** (202 MHz, $CDCl_3$): δ 46.3; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.94–8.03 (m, 4H), 7.67–7.68 (m, 1H), 7.52–7.68 (m, 5H), 6.87 (s, 1H), 6.76 (s, 1H), 6.04 (brs, 1H), 4.38–4.42 (m, 1H), 4.28–4.30 (m, 1H), 3.47 (s, 3H), 3.42 (s, 3H), 2.88 (s, 3H), 2.36 (s, 3H), 2.21 (s, 3H).

(*R*,*S*)-14h and (*R*,*S*)-14′h. Yellow solid: mp 171–173 °C (decomp); 93% yield; $[\alpha]_D$ = +96° (*c* 0.5, CH_2Cl_2); Anal. Calcd for $C_{24}H_{23}Cl_2N_2O_6PPd$: C, 44.8; H, 3.6; N, 4.4; Found: C, 44.2; H, 4.3; N, 4.3; **^{31}P NMR** (162 MHz, $CDCl_3$): δ_1 50.7 and δ_2 45.9 (δ_1/δ_2 = 1/1.3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.34–8.68 (m, 32.2H), 5.41–5.46 (m, 1H), 4.49–4.92 (m, 2.3H), 4.22–4.26 (m, 1.3H), 3.52 (s, 3.9H), 3.43 (s, 3.9H), 3.41 (s, 3.0 H), 3.18 (s, 3.0H).

Synthesis of (*R*,*S*)-15a–h

A CH_2Cl_2 solution of the dichloro complex (*R*,*S*)-**14a–h** and (*R*,*S*)-**14′a–h** (0.2 mmol) was treated with excess potassium cyanide (195 mg, 3 mmol) in water (1 mL). The reaction mixture was stirred vigorously at room temperature for 10 min. The yellow organic layer became colorless and then the organic phase was transferred to the Schlenk tube by syringe under argon. The solvent was removed by flowing N_2 and vacuum to give the free ligands (*R*,*S*)-**15a–h**.

(*R*,*S*)-15a. Pale yellow oil, 94% yield; $[\alpha]_D$ = −112° (*c* 0.5, CH_2Cl_2). **^{31}P NMR** (162 MHz, $CDCl_3$): δ −9.5; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.63–7.68 (m, 2H), 7.45–7.49 (m, 2H), 7.40–7.42 (m, 3H), 7.29–7.33 (m, 3H), 7.10–7.13 (m, 2H), 6.74 (d, J_{HH} = 7.3 Hz, 1H), 6.46 (d, J_{HH} = 7.8 Hz, 1H), 4.49–4.55 (m, 1H), 4.19 (d, J_{HH} = 9.6 Hz, 1H), 3.91 (dd, J_{PH} = 7.3 Hz, J_{HH} = 0.6 Hz, 1H), 3.70 (s, 3H), 3.29 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.4 (d, J_{PC} = 15.4 Hz), 170.5 (d, J_{PC} = 2.8 Hz), 145.8, 135.6 (d, J_{PC} = 15.4 Hz), 134.9 (d, J_{PC} = 17.0 Hz), 134.0, 133.82, 133.80, 133.6, 129.44, 129.38, 129.2, 128.7, 128.6, 128.25, 128.17, 118.8, 113.9, 57.5 (d, J_{PC} = 20.4 Hz), 52.4, 51.7, 48.9 (d, J_{PC} = 26.1 Hz).

(*R*,*S*)-15b. Colorless oil; 93% yields; $[\alpha]_D$ = −102° (*c* 0.5, CH_2Cl_2). **^{31}P NMR** (202 MHz, $CDCl_3$): δ −9.1; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.64–7.67 (m, 2H), 7.44–7.47 (m, 2H), 7.38–7.40 (m, 3H), 7.30–7.32 (m, 3H), 6.75–6.78 (m, 1H), 6.66–6.72 (m, 2H), 6.44–6.46 (m, 1H), 4.82 (d, J_{HH} = 9.8 Hz, 1H, *NH*), 4.52–4.57 (m, 1H), 3.97 (d, J_{PH} = 13.3 Hz, 1H), 3.69 (s, 3H), 3.68 (s, 3H), 3.27 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 172.4 (d, J_{PC} = 6.3 Hz), 170.5 (d, J_{PC} = 2.1 Hz), 147.1, 135.8, 135.6 (d, J_{PC} = 15.5 Hz), 135.0 (d, J_{PC} = 17.3 Hz), 134.1, 134.0, 133.7, 133.5, 129.3, 129.2, 128.6, 128.5, 128.2, 128.1, 121.0, 117.8, 110.7, 109.9, 57.1 (d, J_{PC} = 21.4 Hz), 55.4, 52.4, 51.7, 48.7 (d, J_{PC} = 26.3 Hz).

(*R*,*S*)-15c. Off white oil; 93% yields; $[\alpha]_D$ = −92° (*c* 0.5, CH_2Cl_2). **^{31}P NMR** (202 MHz, $CDCl_3$): δ −9.3; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.64–7.67 (m, 2H), 7.45–7.48 (m, 2H), 7.29–7.41 (m, 6H), 7.01 (t, J_{HH} = 8.0 Hz, 1H), 6.30–6.31 (m, 1H), 6.04–6.06 (m, 2H), 4.48–4.53 (m, 1H), 4.21 (d, J_{HH} = 9.6 Hz, 1H, *NH*), 3.92 (d, J_{PH} = 7.8 Hz, 1H), 3.70 (s, 3H), 3.70 (s, 3H), 3.28 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 172.4 (d, J_{PC} = 5.5 Hz), 170.5 (d, J_{PC} = 3.2 Hz), 160.7, 147.2, 135.6 (d, J_{PC} = 15.9 Hz), 134.9 (d, J_{PC} = 17.2 Hz), 134.0, 133.83, 133.81, 133.6, 130.0, 129.5, 129.4, 128.72, 128.66, 128.25, 128.19, 106.5, 104.4, 99.8, 57.5 (d, J_{PC} = 20.9 Hz), 55.0, 52.5, 51.8, 48.9 (d, J_{PC} = 26.4 Hz).

(*R*,*S*)-15d. Off white oil; 92% yields; $[\alpha]_D$ = −94° (*c* 0.5, CH_2Cl_2); **^{31}P NMR** (202 MHz, $CDCl_3$): δ −9.6; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.62–7.66 (m, 2H), 7.45–7.48 (m, 2H), 7.39–7.40 (m, 3H), 7.29–7.34 (m, 3H), 6.70 (d, J_{HH} = 8.9 Hz, 1H), 6.46 (d, J_{HH} = 8.9 Hz, 1H), 4.40–4.45 (m, 1H), 3.91 (d, *J* = 10.1 Hz, 1H, *NH*), 3.88 (d, *J* = 8.2 Hz, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.28 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 172.7 (d, J_{PC} = 6.0 Hz), 170.5 (d, J_{PC} = 2.5 Hz), 153.2, 139.9, 135.8 (d, J_{PC} = 15.5 Hz), 135.1 (d, J_{PC} = 16.9 Hz), 134.1, 133.9, 133.7, 133.5, 129.3, 128.63, 128.58, 128.22, 128.16, 115.9, 114.7, 58.9 (d, J_{PC} = 20.1 Hz), 55.6, 52.4, 51.7, 48.9 (d, J_{PC} = 25.8 Hz).

(*R*,*S*)-15e. Pale yellow oil; 95% yields; $[\alpha]_D$ = −82° (*c* 0.5, CH_2Cl_2). **^{31}P NMR** (202 MHz, $CDCl_3$): δ −9.5; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.64–7.66 (m, 2H), 7.46–7.49 (m, 2H), 7.40–7.42 (m, 3H), 7.29–7.33 (m, 3H), 7.00 (t, J_{HH} = 7.8 Hz, 1H), 6.56 (d, J_{HH} = 7.5 Hz, 1H), 6.25–6.28 (m, 2H), 4.48–4.52 (m, 1H), 4.16 (d, J_{HH} = 9.7 Hz, 1H, *NH*), 3.91 (dd, J_{PH} = 7.6, J_{HH} = 0.8 Hz, 1H), 3.71 (s, 3H), 3.30 (s, 3H), 2.21 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 172.4 (d, *J* = 2.5 Hz), 170.5 (d, J_{PC} = 2.8 Hz), 145.7, 139.0, 135.7 (d, J_{PC} = 16.1 Hz), 135.0 (d, J_{PC} = 17.2 Hz), 134.0, 133.8, 133.7, 129.4, 129.3, 129.1, 128.7, 128.6, 128.24, 128.18, 119.8, 114.5, 111.1, 57.5 (d, J_{PC} = 20.6 Hz), 52.4, 51.7, 48.9 (d, J_{PC} = 26.3 Hz), 21.5.

(*R*,*S*)-15f. Off white oil; 91% yields; $[\alpha]_D$ = −88° (*c* 0.5, CH_2Cl_2). **^{31}P NMR** (202 MHz, $CDCl_3$): δ −9.5; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.64–7.67 (m, 2H), 7.46–7.49 (m, 2H), 7.29–7.41 (m, 6H), 6.93 (d, J_{HH} = 8.2 Hz, 2H), 6.39 (d, J_{HH} = 8.2 Hz, 2H), 4.46–4.51 (m, 1H), 4.06 (d, J_{HH} = 9.9 Hz, 1H), 3.90 (d, J_{HH} = 7.9 Hz, 1H), 3.69 (s, 3H), 3.29 (s, 3H), 2.22 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 172.6 (d, J_{PC} = 5.8 Hz), 170.5 (d, J_{PC} = 2.5 Hz), 143.5, 135.7 (d, J_{PC} = 15.7 Hz), 135.1 (d, J_{PC} = 17.2 Hz), 134.0, 133.9, 133.8, 133.6, 129.7, 129.4, 129.3, 128.7, 128.6, 128.21, 128.16, 114.1, 58.0 (d, J_{PC} = 20.3 Hz), 52.4, 51.7, 48.9 (d, J_{PC} = 26.1 Hz), 20.4.

(*R*,*S*)-15g. Off white oil; 93% yields; $[\alpha]_D$ = −46° (*c* 0.5, CH_2Cl_2). **^{31}P NMR** (202 MHz, $CDCl_3$): δ −11.8; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.63–7.65 (m, 2H), 7.43–7.46 (m, 2H), 7.37–7.39 (m, 3H), 7.29–7.33 (m, 3H), 6.72 (s, 2H), 4.28–4.32 (m, 1H), 3.85 (d, J_{PH} = 6.7 Hz, 1H), 3.66 (d, J_{HH} = 12.8 Hz, 1H), 3.57 (s, 3H), 3.28 (s, 3H), 2.18 (s, 3H), 2.11 (s, 6H).

(*R*,*S*)-15h. Yellow oil; 96% yields; $[\alpha]_D$ = −84° (*c* 0.5, CH_2Cl_2). **^{31}P NMR** (202 MHz, $CDCl_3$): δ −9.8; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.01 (d, *J* = 9.1 Hz, 2H), 7.61–7.64 (m, 2H), 7.44–7.47 (m, 5H), 7.30–7.35 (m, 3H), 6.36 (d, J_{HH} = 9.1 Hz, 2H), 4.94 (d, J_{HH} = 7.2 Hz, 1H, *NH*), 4.58–4.62 (m, 1H), 3.92 (d, J_{PH} = 7.5 Hz, 1H), 3.74 (s, 3H), 3.30 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 171.0 (d, J_{PC} = 5.1 Hz), 170.2 (d, J_{PC} = 3.0 Hz), 151.0, 139.3, 134.8 (d, J_{PC} = 15.5 Hz), 133.9 (d, J_{PC} = 7.1 Hz), 133.8, 133.71, 133.66, 129.9, 129.7, 128.94, 128.88, 128.44, 128.38, 126.1, 112.1, 56.4 (d, J_{PC} = 20.3 Hz), 52.9, 52.0, 48.7 (d, J_{PC} = 27.3 Hz).

Acknowledgements

We thank Nanyang Technological University for support of this research and for Ph.D. scholarships to K. C.

References

1 (*a*) P. Espinet and K. Soulantica, *Coord. Chem. Rev.*, 1999, **193–195**, 499; (*b*) P. J. Guiry and C. P. Saunders, *Adv. Synth. Catal.*, 2004, **346**, 497; (*c*) L. C. Liang, *Coord. Chem. Rev.*, 2006, **250**, 1152; (*d*) I. D. Kostas, *Curr. Org. Synth.*, 2008, **5**, 227; (*e*) S. Maggini, *Coord. Chem. Rev.*, 2009, **253**, 1793.

2 (*a*) J. C. Anderson, R. J. Cubbon and J. D. Harling, *Tetrahedron: Asymmetry*, 2001, **12**, 923; (*b*) T. Mino, Y. Tanaka, Y. Hattori, T. Yabusaki, H. Saotome, M. Sakamoto and T. Fujita, *J. Org. Chem.*, 2006, **71**, 7346; (*c*) R. J. Detz, S. A. Heras, R. de Gelder, P. W. N. M. van Leeuwen, H. Hiemstra, J. N. H. Reek and J. H. van Maarseveen, *Org. Lett.*, 2006, **8**, 3227; (*d*) S. Fukuzawa, M. Yamamoto, M. Hosaka and S. Kikuchi, *Eur. J. Org. Chem.*, 2007, 5540; (*e*) T. Mino, K. Wakui, S. Oishi, Y. Hattori, M. Sakamoto and T. Fujita, *Tetrahedron: Asymmetry*, 2008, **19**, 2711; (*f*) F. Leca, F. Fernández, G. Muller, C. Lescop, R. Réau and M. Gómez, *Eur. J. Org. Chem.*, 2009, 5583.

3 (*a*) B. M. Trost and M. L. Crawley, *Chem. Rev.*, 2003, **103**, 2921; (*b*) K. H. Kim, C.-K. Jeong, D.-H. Kim and D.-C. Ha, *Tetrahedron: Asymmetry*, 2006, **17**, 1688; (*c*) J. D. Huang, X. P. Hu, S. B. Yu, J. Deng, D. Y. Wang, Z. C. Duan and Z. Zheng, *J. Mol. Catal. A: Chem.*, 2007, **270**, 127.

4 (*a*) R. Guo, A. J. Lough, R. H. Morris and D. Song, *Organometallics*, 2004, **23**, 5524; (*b*) L. Dahlenburg and R. Götz, *Eur. J. Inorg. Chem.*, 2004, 888; (*c*) K. Abdur-Rashid, R. Guo, A. J. Lough, R. H. Morris and D. Song, *Adv. Synth. Catal.*, 2005, **347**, 571; (*d*) R. Guo, R. H. Morris and D. Song, *J. Am. Chem. Soc.*, 2005, **127**, 516; (*e*) M. Ito, A. Sakaguchi, C. Kobayashi and T. Ikariya, *J. Am. Chem. Soc.*, 2007, **129**, 290; (*f*) R. Puchta, L. Dahlenburg and T. Clark, *Chem.–Eur. J.*, 2008, **14**, 8898; (*g*) L. Dahlenburg and C. Kühnlein, *Inorg. Chim. Acta*, 2008, **361**, 2785; (*h*) W. Jia, X. Chen, R. Guo, C. Sui-Seng, D. Amoroso, A. J. Lough and K. Abdur-Rashid, *Dalton Trans.*, 2009, 8301; (*i*) K. E. Thiesen, K. Maitra, M. M. Olmstead and S. Attar, *Organometallics*, 2010, **29**, 6334.

5 (*a*) S. Bell, B. Wüstenberg, S. Kaiser, F. Menges, T. Netscher and A. Pfaltz, *Science (Washington, D. C.)*, 2006, **311**, 642; (*b*) J. Mazuela, P. O. Norrby, P. G. Andersson, O. Pàmies and M. Dièguez, *J. Am. Chem. Soc.*, 2011, **133**, 13634; (*c*) A. Franzke and A. Pfaltz, *Chem.–Eur. J.*, 2011, **17**, 4131.

6 (*a*) J. W. Faller and K. J. Chase, *Organometallics*, 1994, **13**, 989; (*b*) B. Tao and G. C. Fu, *Angew. Chem., Int. Ed.*, 2002, **41**, 3892; (*c*) M. Stradiotto, J. Cipot and R. McDonald, *J. Am. Chem. Soc.*, 2003, **125**, 5618; (*d*) M. A. Rankin, D. F. MacLean, G. Schatte, R. McDonald and M. Stradiotto, *J. Am. Chem. Soc.*, 2007, **129**, 15855; (*e*) J. Cipot, R. McDonald, M. J. Ferguson, G. Schatte and M. Stradiotto, *Organometallics*, 2007, **26**, 594; (*f*) D. Wechsler, G. Schatte and M. Stradiotto, *J. Organomet. Chem.*, 2009, **694**, 1943; (*g*) D. Wechsler and M. Stradiotto, *Can. J. Chem.*, 2009, **87**, 72.

7 R.-Y. Lai, K. Surekha, A. Hayashi, F. Ozawa, Y.-H. Liu, S.-M. Peng and S.-T. Liu, *Organometallics*, 2007, **26**, 1062.

8 (*a*) A. R. Shaffer and J. A. R. Schmidt, *Organometallics*, 2008, **27**, 1259; (*b*) S. R. Beeren, S. L. Dabb and B. A. Messerle, *J. Organomet. Chem.*, 2009, **694**, 309; (*c*) G. Kuchenbeiser, A. R. Shaffer, N. C. Zingales, J. F. Beck, A. R. Joseph and J. A. R. Schmidt, *J. Organomet. Chem.*, 2010, **695**, 179.

9 (*a*) T. Hayashi, M. Fukushima, M. Konishi and M. Kumada, *Tetrahedron Lett.*, 1980, **21**, 79; (*b*) T. Hayashi, M. Konishi, M. Fukushima, K. Kanehira, T. Hioki and M. Kumada, *J. Org. Chem.*, 1983, **48**, 2195; (*c*) S. Pellet-Rostaing, C. Saluzzo, R. T. Halle, J. Breuzard, L. Vial, F. L. Guyaderb and M. Lemaire, *Tetrahedron: Asymmetry*, 2001, **12**, 1983.

10 (*a*) F. Speiser and P. Braunstein, *Organometallics*, 2004, **23**, 2613; (*b*) F. Speiser and P. Braunstein, *Organometallics*, 2004, **23**, 2625; (*c*) F. Speiser and P. Braunstein, *Organometallics*, 2004, **23**, 2633; (*d*) F. Speiser, P. Braunstein and A. Saussine, *Acc. Chem. Res.*, 2005, **38**, 784; (*e*) R. J. Lundgren, M. A. Rankin, R. Robert McDonald and M. Mark Stradiotto, *Organometallics*, 2008, **27**, 254; (*f*) P. W. Dyer, J. Fawcett and M. J. Hanton, *Organometallics*, 2008, **27**, 5082; (*g*) M. M. Mogorosi, T. Mahamo, J. R. Moss, S. F. Mapolie, J. C. Slootweg, K. Lammertsma and G. S. Smith, *J. Organomet. Chem.*, 2011, **696**, 3585.

11 (*a*) J. Andrieu, P. Richard, J.-M. Camus and R. Poli, *Inorg. Chem.*, 2002, **41**, 3876; (*b*) C. Wetzel, P. C. Kunz, I. Thiel and B. Spingler, *Inorg. Chem.*, 2011, **50**, 7863.

12 (*a*) J. H. Griffin and R. M. Kellogg, *J. Org. Chem.*, 1985, **50**, 3261; (*b*) B. K. Vriesema and R. M. Kellogg, *Tetrahedron Lett.*, 1986, **27**, 2049; (*c*) G. A. Cross and R. M. Kellogg, *J. Chem. Soc., Chem. Commun.*, 1987, 1746; (*d*) G. Cross, B. K. Vriesema, G. Boven and R. M. Kellogg, *J. Organomet. Chem.*, 1989, **370**, 357; (*e*) J. C. Anderson, R. J. Cubbon and J. D. Harling, *Tetrahedron: Asymmetry*, 1999, **10**, 2829.

13 F. Liu, S. A. Pullarkat, Y. Li, S. Chen, M. Yuan, Z. Y. Lee and P. H. Leung, *Organometallics*, 2009, **28**, 3941.

14 (*a*) P. Rönnholm, M. Södergren and G. Hilmersson, *Org. Lett.*, 2007, **9**, 3781; (*b*) R. Guo, S. Lu, X. Chen, C. W. Tsang, W. Jia, C. Sui-Seng, D. Amoroso and K. Abdur-Rashid, *J. Org. Chem.*, 2010, **75**, 937.

15 A. Kondoh, H. Yorimitsu and K. Oshima, *Org. Lett.*, 2008, **10**, 3093.

16 X. Fu, Z. Jiang and C.-H. Tan, *Chem. Commun.*, 2007, 5058.

17 P. H. Leung, S. H. Chan and Y. S. Song, Gold Complexes. *PCT Int. Appl*, WO 0177121 A1, 2001.

18 P. H. Leung, *Acc. Chem. Res.*, 2004, **37**, 169.

19 X. Liu, K. F. Mok and P. H. Leung, *Organometallics*, 2001, **20**, 3918.

20 (*a*) P. G. Kerr, P. H. Leung and S. B. Wild, *J. Am. Chem. Soc.*, 1987, **109**, 4321; (*b*) V. V. Dunina, E. B. Golovan, N. S. Gulyukina and A. V. Buyevich, *Tetrahedron: Asymmetry*, 1995, **6**, 2731; (*c*) D. C. R. Hockless, P. A. Gugger, P. H. Leung, R. C. Mayadunne, M. Pabel and S. B. Wild, *Tetrahedron*, 1997, **53**, 4083; (*d*) G. He, S. K. Loh, J. J. Vittal, K. F. Mok and P. H. Leung, *Organometallics*, 1998, **17**, 3931.

21 S. K. Loh, K. F. Mok, P. H. Leung, A. J. P. White and D. J. Williams, *Tetrahedron: Asymmetry*, 1996, **7**, 45.

22 S. Y. M. Chooi, P. H. leung, C. C. Lim, K. F. Mok, G. H. Quek, K. Y. Sim and M. K. Tan, *Tetrahedron: Asymmetry*, 1992, **3**, 529.

