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ARTICLE TYPE

# Development of a Novel Chiral Palladacycle and its Application in Asymmetric Hydrophosphination Reaction

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A novel amine ligand, 1-(2,5-dichlorophenyl)-*N*,*N*-dimethylethanamine, was synthesized from 1-(2,5-dichlorophenyl)ethanone *via* a three step synthetic route. Direct ortho-palladation of the amine ligand with $Pd(OAc)_2$ gave the racemic dimeric complex in high yield. This racemic palladacycle was efficiently resolved through the formation of its (*S*)-prolinato derivatives. The resulting diastereomeric complexes were separated efficiently by column chromatography. In solid state, the structure and absolute configuration of the two optically resolved palladium complexes were determined by single crystal X-ray crystallography. In solution, their absolute conformations were also investigated by the 2D $^1$H-$^1$H rotating frame nuclear overhauser enhancement (ROESY) NMR spectroscopy. Both (*R*,*R*) and (*S*,*S*)-di-$\mu$-chloro dimeric palladium complexes could be obtained chemoselectively by treating the corresponding prolinato derivatives with diluted hydrochloric acid. The amine auxiliary could be subsequently removed from the palladium center by treatment with concentrated hydrochloric acid. The enantiomerically pure palladacycle was used to promote the asymmetric hydrophosphination reaction between diphenylphosphine and dimethyl acetylenedicarboxylate. The $^{31}$P{$^1$H}NMR spectroscopy indicated that only one stereo-isomeric product was formed.

## Introduction

The development of enantiomerically pure diphosphines bearing chirality on the carbon backbone, such as chiraphos and prophos, have played important roles in transition metal catalyzed reactions. [1] Despite their vital roles, the preparations of these oxygen-sensitive, highly reactive and potentially unstable chiral ligands are tedious and remain a major challenge. They are generally prepared by direct addition of secondary phosphine to C–C multiple bonds with the assistance of thermal, [2] strong acids, [3] bases, [4] free radicals, [5] and metal catalyst. [6] Therefore, it is important to develop new methods for the synthesis of enantiomerically pure diphosphines. Over the past decades, our group has reported the use of chiral cyclometalated-amine complex (*S*)-**1** (Figure 1) as efficient chiral template for promoting hydrophosphination reactions. [7] The metal complexes generally show better selectivity in hydrophosphination reactions than other reaction promoters. Very recently, we have also shown that cyclopalladated complexes can be used as efficient catalysts for the synthesis of chiral monodentate phosphines. [8] Unfortunately, the catalytic method could not be applied directly to the synthesis of chelating diphosphine ligands due to the catalyst poisoning issues. In pursuit of our interest to further improve on the efficient synthesis of functionalized diphosphine ligands; herein we report the design and synthesis of a new palladacycle (*S*)-**2** (Figure 1) and its subsequent application as the chiral template in the asymmetric hydrophosphination reaction. The internal steric repulsion between one of the chloro groups and the methyl substituent on the stereogenic carbon in both (*S*)-**1** and (*S*)-**2** helps to lock the conformation of the organometallic five-membered ring while the introduction of the new chloro group in (*S*)-**2** adjacent to the reaction sphere on the Pd is expected to exert stereochemical influences on the reaction site.

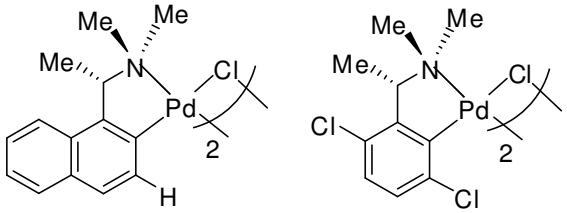
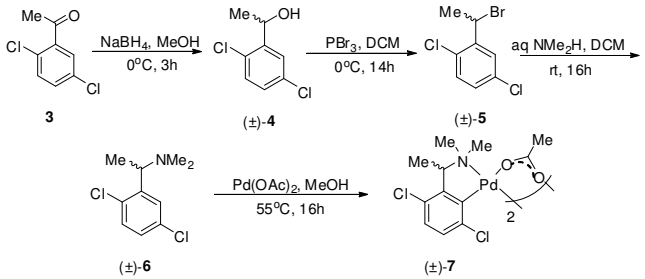



**Figure 1.** Chiral cyclometalated-amine complex (*S*)-**1** and (*S*)-**2**

## Results and Discussion

### Ligand and Complex Synthesis




**Scheme 1**. Synthesis of Racemic ortho-Palladated Complex (±)-**7**

As illustrated in Scheme 1, 1-(2,5-dichlorophenyl)ethanone **3** was converted into the target racemic ligand (±)-**6** *via* a three step synthetic route. The reduction of ketone **3** by $NaBH_4$ in MeOH gave the racemic alcohol, (±)-**4** in 99% yield. The racemic alcohol is then brominated using $PBr_3$, to afford (±)-**5** with a yield

of 91%. Finally the direct alkylamination of the alcohol with aqueous dimethylamine yielded the target *N*,*N*-dimethylamine ligand (±)-**6** in 92% yield. The *ortho*-metalation reaction was achieved by the treatment of the amine ligand (±)-**6** with $Pd(OAc)_2$ to form the dimeric palladated complex (±)-**7** in 95% yield.

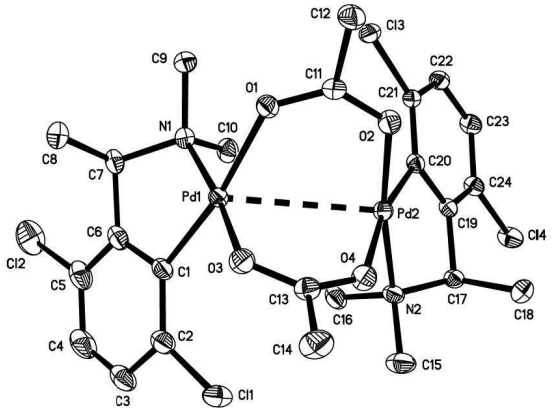
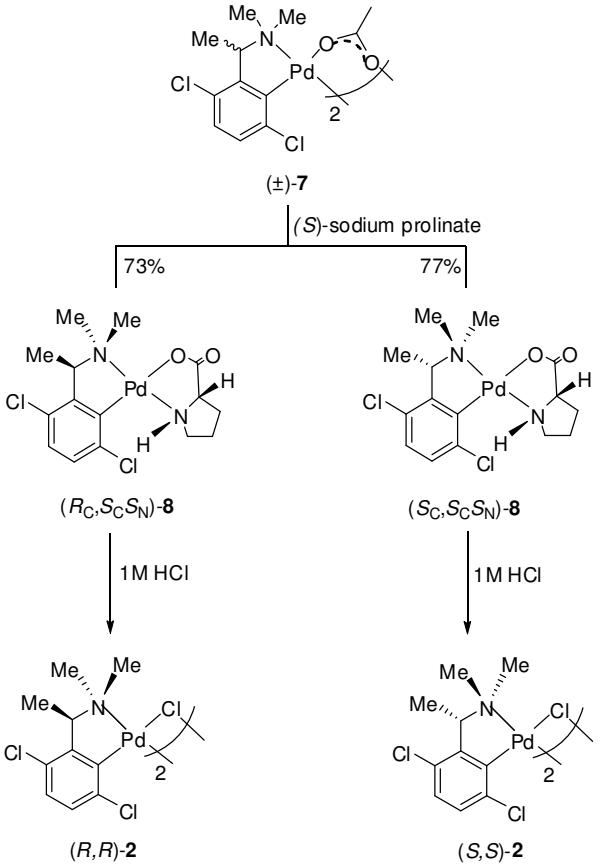



**Figure 2.** Molecular Structure of Complex (±)-**7**

Complex (±)-**7** could be crystallized *via* slow evaporation of the dichloromethane (DCM)/hexane solution to give bright yellow single crystals. The solid state configuration was confirmed *via* single crystal X-ray crystallographic analysis, Figure 2. Complex (±)-**7** adopted distorted square planar coordination geometry around the palladium centers. The two arylamine units are located *trans* to each to other, adopting the "butterfly" geometry with the organometallic units linked by the bridging acetate ligands. The dihedral angles between the two palladium coordination planes at the Pd(1) and Pd(2) units are 9.8° and 12.6°, respectively. The acetate bridge and the palladium center form an eight-membered ring in boat-boat conformation with an interplanar angle between planes {O(1)–C(11)–O(2)} and {O(3)–C(13)–O(4)} of 84.3°. The average bond length of the four C–O bonds in the acetate bridge is 1.258 Å, which is consistent with the delocalized C–O bond length of 1.254 Å.[9] The Pd(1)–Pd(2) distance in the solid state is 3.161 Å.

### Optical Resolution of Dimeric Complex (±)-7

The optical resolution of racemic complex (±)-**7**, was performed using optically active sodium prolinate as the resolving agent (Scheme 2). The racemic dimer was treated with two molar equivalents of sodium (*S*)-prolinate to give a 1:1 mixture of the monomeric diastereomers, ($R_C$,$S_C$$S_N$)-**8** and ($S_C$,$S_C$$S_N$)-**8**. They were subsequently separated *via* column chromatography. The diastereomeric ratio of both fractions was verified with $^1$H NMR spectroscopy. The less polar diastereomer ($R_C$,$S_C$$S_N$)-**8** was eluted first with acetone/hexane (v/v: 1:1) and subsequently the more polar diastereomeric adduct ($S_C$,$S_C$$S_N$)-**8** was flushed out using acetone as mobile phase. The absolute configuration and the solid structure of both diastereomeric adducts ($R_C$,$S_C$$S_N$)-**8** and ($S_C$,$S_C$$S_N$)-**8** were confirmed by single crystal X-ray diffraction. Their structures in solution were also studied individually by the 2D $^1$H-$^1$H ROESY NMR spectroscopy.




**Scheme 2.** Optical Resolution of Dimeric Complex (±)-**7**

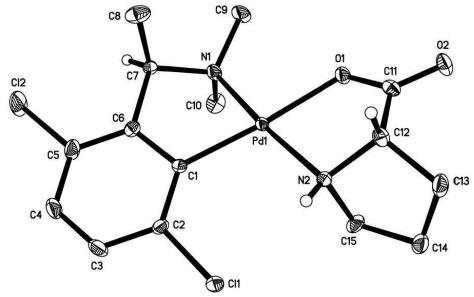



**Figure 3.** Molecular structure of complex ($R_C$,$S_C$$S_N$)-**8**

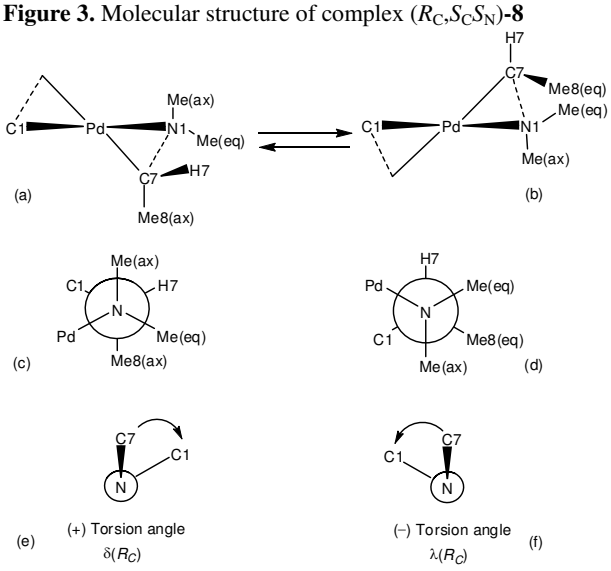


**Figure 4.** Chiral δ($R_C$) (**a**, **c, e**) and λ($R_C$) (**b**, **d, f**) conformations of the ($R_C$,$S_C$$S_N$)-**8** five-membered ring in projections to the plane orthogonal to the {C(1)–Pd(1)–N(1)} plane (**a**, **b**); in the Newman projections relative to N(1)–C(13) bond (**c**, **d**) and in the Newman projections relative to N(1)–Pd(1) bond (**e**, **f**).

Figure 3 shows the molecular structure and the absolute stereochemistry of the complex ($R_C$,$S_C$$S_N$)-**8**. The crystallographic study revealed the *R*-configuration at the α-carbon stereocenter within the five-membered organometallic ring. The secondary stereogenic nitrogen atom from the prolinato group is in the expected *S* absolute configuration. The distance between the chloro atom, Cl(2) and the proton, H(7) on the α-carbon stereocenter is 2.685 Å, which is smaller than the summation of the Van der Waals radii of the two atoms (2.95 Å). [10] This steric repulsion locked the five-membered organometallic ring. The torsion angle for C(1)–Pd(1)–N(1)–C(7) is +31.9°, showing that the C–methyl group occupies an axial position and the five-membered organometallic ring adopts the *δ* conformation (Figure 4). [11] The two coordinated nitrogen atoms are located *trans* to each other. The coordination geometry around the palladium center is distorted square planar. The dihedral angle between planes {N(1)–Pd(1)–C(1)} and {O(1)–Pd(1)–N(2)} is 4.7°.

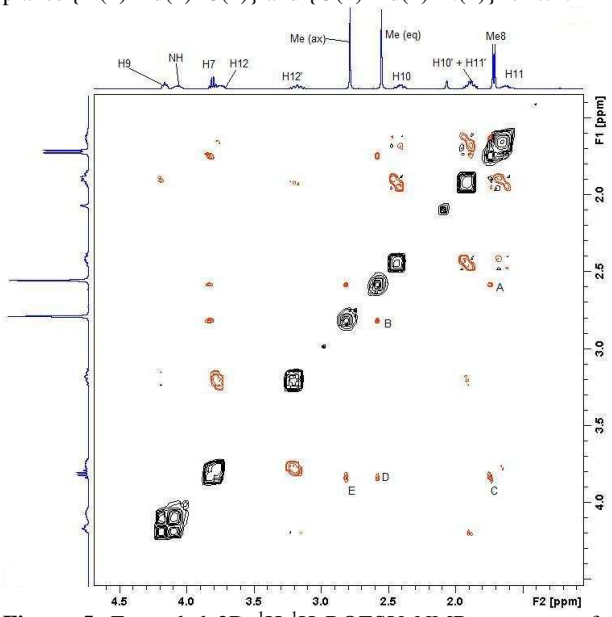



**Figure 5.** Expanded 2D $^1$H-$^1$H ROESY NMR spectrum of the complex ($R_C$,$S_C$$S_N$)-**8** in $CDCl_3$

The chiral five-membered organometallic ring of the less polar diastereomer ($R_C$,$S_C$$S_N$)-**8** , adopts the same static *δ* conformation in solution as revealed by a $^1$H-$^1$H ROESY NMR study in $CDCl_3$ (Figure 5).[12]

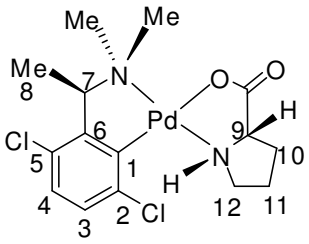



**Figure 6.** Numbering scheme of complex ($R_C$,$S_C$$S_N$)-**8**

Figure 6 shows the detailed numbering scheme of the diastereomer ($R_C$,$S_C$$S_N$)-**8** used in the ROESY NMR assignments. All the expected intra-molecular $^1$H-$^1$H interaction signals were observed in the 400 MHz NMR spectrum. A key feature observed in Figure 5 is the signal (A) due to the strong interaction between Me8 and the equatorially disposed NMe group. This observation comply with the crystallographic findings where the distance between the Me8 carbon, C(8) and the NMe(*eq*) carbon, C(9) (2.825 Å) is smaller than the summation of the Van der Waals radii of 3.40 Å. [10] ROESY correlations C to E correspond to the interactions of H7 with the Me8, NMe(eq) and NMe(ax) respectively. These clearly indicated that the Me8 is axially positioned and the five-membered organometallic ring is locked into the single static *δ* conformation in solution, Figure 4. [11] Furthermore, intra-ligand interactions of the prolinato ligand were also observed. This observation is consistent with the solid state investigation in which the two nitrogen groups adopt the *trans*-(*N*,*N*)-geometry.

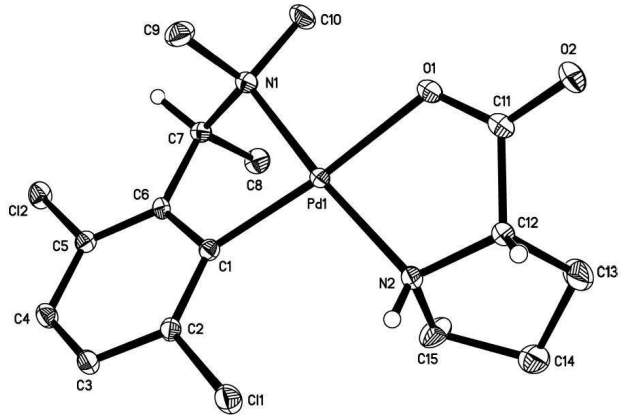



**Figure 7.** Molecular structure of complex ($S_C$,$S_C$$S_N$)-**8**

The X-ray molecular structure of the more polar diastereomeric complex ($S_C$,$S_C$$S_N$)-**8** is depicted in Figure 7. The X-ray crystallographic study revealed that the stereogenic α-carbon of the arylamine chelate and the secondary nitrogen atom from the prolinato ligand both adopt the *S* absolute configuration. The organometallic five-membered ring is locked into the *λ* configuration with torsion angle of -36.7° for C(1)–Pd(1)–N(1)–C(7). [11] The coordination geometry of the palladium center is distorted square-planar and the tetrahedral distortion between the triangular planes {N(1)–Pd(1)–C(1)} and {O(1)–Pd(1)–N(2)} is 9.7°. The two coordinated nitrogen donors are *trans* to each other.

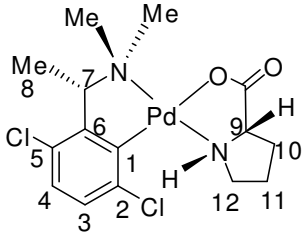



**Figure 8.** Numbering scheme of complex ($S_C$,$S_C$$S_N$)-**8**

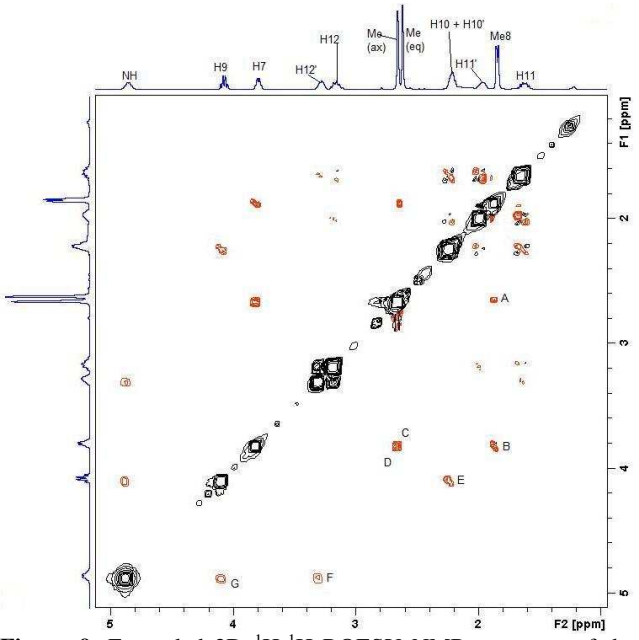



**Figure 9.** Expanded 2D $^{1}$H-$^{1}$H ROESY NMR spectrum of the complex ($S_C$,$S_C S_N$)-**8** in $CDCl_3$

The organometallic ring conformation of the more polar isomer in solution was confirmed *via* the $^{1}$H-$^{1}$H ROESY NMR. The numbering scheme of the diastereomer ($S_C$,$S_C S_N$)-**8** and the $^{1}$H-$^{1}$H ROESY NMR spectrum are shown in Figure 8 and Figure 9 respectively. Strong NOE signals between the Me8 and NMe(eq) denoted as A, and interactions between H7 with Me8, NMe(eq) and NMe(ax) are clearly recorded as signals B, C, D respectively and illustrate that the Me8 occupies an axial position.[11,12] These signals, in conjunction with the confirmed *S* configuration at its chiral carbon center, leads to the conclusion that the five-membered organometallic ring adopts the $\lambda$ conformation, as observed in the solid state investigation where the distance between the Me8 carbon, C(8) and the NMe(*eq*) carbon, C(10) is (2.889 Å) is smaller than the summation of the Van der Waals radii. [10] Similarly the interactions within the prolinate fragments are also clearly observed: signals E, F and G correspond to the interactions of H9 with both H10 and H10'; NH–H12' and NH–H9 respectively indicated that the nitrogen donors retained the *trans*-(*N*,*N*)-geometry in solution.

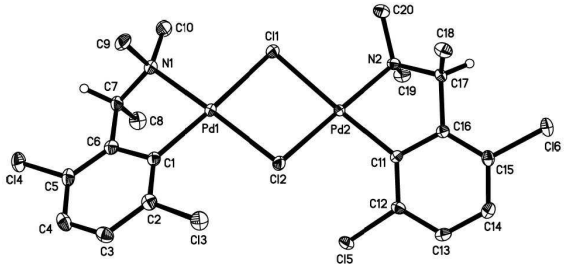
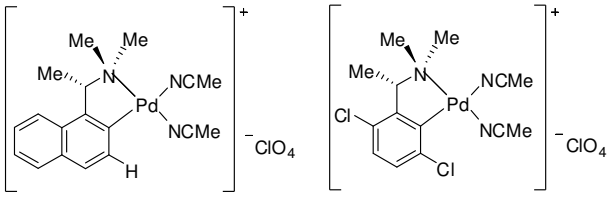



**Figure 10.** Molecular structure of complex (*S,S*)-**2**

The prolinato resolving agents could be removed chemoselectively from the resolved diastereomeric complexes by the treatment of individual complex with diluted (1 M) hydrochloric acid. Accordingly, both dimeric complexes (*R*)-**2** and (*S*)-**2** could be obtained efficiently in high yields from ($R_C$,$S_C S_N$)- and ($S_C$,$S_C S_N$)-**8**, respectively. A yellow single crystal of complex (*S*)-**2** suitable for X-ray crystallography was obtained from the corresponding dichloromethane/hexane solution. The structural study confirms that, as desired, the C–N organometallic ring remains unchanged during the acid treatment (Figure 10). The coordination geometry at both palladium centers is slightly distorted square planar. The dihedral angles about the palladium planes on Pd(I) and Pd(II) is 6.6° and 6.3°, respectively. Similar to that observed in the analogous complex ($S_C$,$S_C S_N$)-**8**, both five-member rings adopt the $\lambda$ conformation with torsion angles for C(1)–Pd(1)–N(1)–C(7) and C(11)–Pd(2)–N(2)–C(17) are -38.6° and -38.8°, respectively. [11] The bridging chloro ligands and the palladium centers formed a four-member ring that is bent 8.6° along the Cl(1)–Cl(2) axis. In contrast to the racemic acetate-bridged dimeric complex **7**, the two nitrogen donors in (*S*)-**2** adopted the *cis*-(*N*,*N*)-geometry.

**Chiral Palladacycle Promoted Asymmetric Hydrophosphination Reaction**




(*S*)-**9** (*S*)-**10**

**Figure 11.** Monomeric bis-acetonitrile complex (S)-9 and (S)-10

We have been interested in the application of chiral organopalladium complex in stoichiometric and catalytic asymmetric transformations. The stable bridging chloro ligands in the chiral dimeric complex (*S*)-**1** can be replaced by the weakly coordinating acetonitrile ligands.[7a] The monomeric bis-acetonitrile species (*S*)-**9** (Figure 11) thus offers two readily available and electronically distinct coordination sites to promote addition reactions, such as cycloaddition[13] and hydrophosphination reactions.[7,8] When (*S*)-**9** was used as a chiral template for the asymmetric hydrophosphination between diphenylphosphine and dimethyl acetylenedicarboxylate, a 6:1 diastereomeric product mixture was obtained.[7a] Although the reaction appeared to be diastereoselective, unfortunately, the separation of two diastereomers was found to be very difficult. In order to search for a better metal template for this particular reaction, the new complex (*S*)-**2** with a chloro group substituted on the aromatic framework adjacent to the Pd–C bond was evaluated.

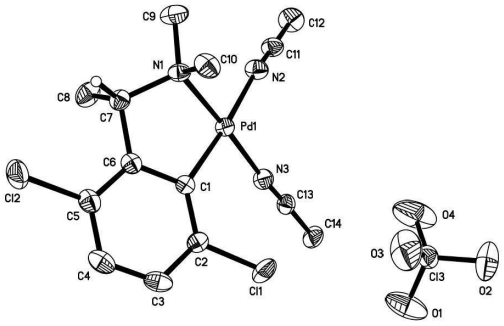
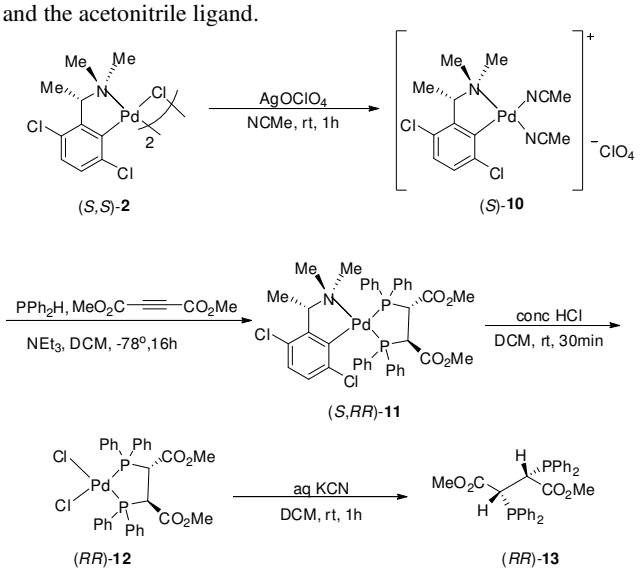



**Figure 12.** Molecular structure of complex (*S*)-**10**

According to the earlier reported procedures, the dimeric complex (*S*)-**2** was first treated with silver perchlorate in acetonitrile to generate the cationic complex (*S*)-**10**. In the absence of other stronger ligands, the kinetically labile bis-acetonitrile complex can be crystallized as stable pale yellow needles from dichloromethane-hexane solution. The coordination chemistry of (*S*)-**10** is confirmed by X-ray crystallography (Figure 12). The organometallic five membered ring adopted the $\lambda(S_C)$ configuration with torsion angle at C(1)–Pd(1)–N(1)–C(7) of 72.8°. [11] The coordination geometry of the palladium center is distorted square planar with the dihedral angle of 5.3° between the two {N(1)–Pd(1)–C(1)} and {N(3)–Pd(1)–N(2)} trigonal planes. The distance between the Cl(1) and the N(3) of the acetonitrile ligand is 3.032 Å which is smaller than the sum of van der Waals radii table of contents (3.30 Å), [10] showing the significant steric interaction between the protruding chloro group and the acetonitrile ligand.




**Scheme 3.** Hydrophosphination Reaction of Diphenylphosphine and Dimethyl Acetylenedicarboxylate Promoted by Complex (*S*)-**10**

As shown in Scheme 3, the cationic complex (*S*)-**10** was used as the chiral template for the addition reaction between dimethyl acetylenedicarboxylate and two molar equivalent of diphenylphosphine in presence of a base, $NEt_3$ in DCM at -78°C for 24 h. The 202 MHz $^{31}P\{^1H\}$ NMR spectrum of the crude reaction product in $CDCl_3$ exhibited only one pair of doublets at $\delta$ 34.8 and 45.2 ppm with $J_{PP}$ = 39.7 Hz. No other diphosphine signals could be detected in the $^{31}P\{^1H\}$ NMR spectrum. The $^{31}P$ NMR study therefore indicated that only one stereoisomeric complex, i.e. product complex **11**, was generated in this reaction. Attempts to crystallize this product in wide range of solvent systems, however, were not successful. The chiral amine auxiliary was subsequently removed from the template complex **11** by the treatment with concentrated hydrochloric acid to give the dichloro palladium complex (*RR*)-**12**. Prior to crystallization, the $^{31}P\{^1H\}$ NMR spectrum of (*RR*)-**12** in $CDCl_3$ shows a single sharp singlet at $\delta$ 58.0 The neutral diphosphine complex was subsequently crystallized from dichloromethane-diethyl ether as yellow blocks in 54 % yield. The molecular structure and the absolute stereochemistry of (*RR*)-**12** has been confirmed by X-ray crystallography and was found to be identical to that reported in our earlier report.[7a] Accordingly, the absolute stereochemistry of the non-crystalline cationic template complex **11** was (*S*,*RR*). The functionalized diphosphine ligand (*RR*)-**13** can be liberated from (*RR*)-**12** by the treatment of the neutral complex with aqueous potassium cyanide (Scheme 3) and this provides an avenue for subsequent coordination to other metal centers.

## Conclusions

Herein we have described the efficient synthesis and optical resolution of the novel palladacycles (*S*)-**2** and (*S*)-**10** derived from 1-(2,5-dichlorophenyl)ethanone. When compared with their well established napthylamine analogues, the newly synthesized *ortho*-palladated dichloro-substituted benzyl amine based auxiliary showed a significantly higher stereoselectivity in the hydrophosphination reaction involving diphenylphosphine and dimethyl acetylenedicarboxylate, thus providing a much more facile access to enantiopure functionalized diphosphines. We believe that the higher selectivity is a consequence of the stereoelectronic effect arising from the protruding chloro-substituent on the auxiliary. We are currently exploring the application of complexes **2** and **10** in other catalytic applications.

## Experimental Section

**General Consideration**: Reactions involving air-sensitive compounds were performed under positive pressure of purified nitrogen by using standard Schlenk techniques. Proton nuclear magnetic resonance ($^1H$ NMR) and carbon nuclear magnetic resonance ($^{13}C$ NMR) spectroscopy were performed on a Bruker Avance III 400 Spectrometer ($^1H$ at 400 MHz, $^{13}C$ at 100 MHz). The phosphorus nuclear magnetic resonance ($^{31}P\{^1H\}$ NMR) spectroscopy was performed on a Bruker Avance 300, 500 and a Bruker Avance III 400 NMR Spectrometer. Multiplicities were given as: s (singlet); br s (broad singlet); d (doublet); t (triplet); q (quartet); qn (quintet); dd (doublets of doublet); m (multiplets) and etc. The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a *J* value in Hz. Chemical shifts are reported as $\delta$ in units of parts per million (ppm) downfield from tetramethylsilane ($\delta$ 0.0) and referenced to the chemical shifts of residual resonances of the respective deutero-solvent, chloroform-*d* ($^1H$ at $\delta$ 7.26, singlet and $^{13}C$ NMR $\delta$ 77.00, triplet), unless otherwise stated. Phase-sensitive $^1H$ –$^1H$ ROESY spectra were obtained with a Bruker Avance III 400 spectrometer and were acquired into a 2048 x 256 matrix with a 200-msec spin lock time and a spin lock field strength of 16.72 dB and then transformed into 1024 x 1024 points by using a sine-bell weighting function in both dimensions. All NMR spectroscopic experiments were performed at room temperature (300 K). Mass spectra were recorded on a JEOL AccuTOF-DART HRMS. Melting points were determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured using a 0.1-dm cell at 589 nm with a Perkin-Elmer polarimeter (model 341) at 20 °C or Atago automatic polarimeter model (AP-300).

**1-(2,5-dichlorophenyl)ethanol, (±)-4:** A solution of $NaBH_4$ (3.15 g, 83.3 mmol) in MeOH (100 ml) was added dropwise into

1-(2,5-dichlorophenyl)ethanone **3** (8.00 ml, 10.5g, 55.5 mmol) in the same solvent (MeOH) at 0°C. The mixture was stirred rapidly at 0°C for 3 hours. Then a solution of 6 wt% NaOH (20 ml) was added and was stirred for an hour. The resulting mixture was concentrated *via* reduced pressure. Followed by, extraction with DCM (3 x 100 mL). The organic layers were combined over anhydrous $MgSO_4$ and removal of solvent under reduced pressure yielded a white solid (10.5 g, 99 %). M.p. 59-61 °C. $^1$H NMR (400 MHz): $\delta$ = 1.48 (d, $^3J_{H,H}$ = 6.0 Hz, 3H, CHC*H*3), 2.03 (d, $^4J_{H,H}$ = 3.2 Hz 1H, O*H*), 5.23 (m, $^3J_{H,H}$ = 6.4 Hz, $^4J_{H,H}$ = 3.6 Hz 1H, C*H*CH$_3$), 7.17 (dd, $^3J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 2.4 Hz, 1H, aromatic proton), 7.25 (d, $^3J_{H,H}$ = 8.4 Hz, 1H, aromatic proton), 7.60(d, $^3J_{H,H}$ = 2.8 Hz, 1H, aromatic proton). $^{13}$C NMR (100 MHz): $\delta$ = 23.74, 67.04, 126.94, 128.60, 129.88, 130.73, 133.48, 145.09. HRMS (m/z (M − OH)]$^+$ calcd for $C_8H_7Cl_2$ 172.9925, found 172.9926.

**2-(1-bromoethyl)-1,4-dichlorobenzene, (±)-5:** A solution of $PBr_3$ (40.0 ml, 112 g, 413 mmol) in DCM (75ml) was added dropwise to the alcohol, (±)-**4** (19.7 g, 103 mmol) dissolved in DCM (150 ml). The mixture was stirred at 0 °C for 14 h, followed by the addition of water. The organic layer was separated and washed with water (3 x 200 ml). The organic layers were combined, dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure yielded (±)-**5** as colourless oil, Yield: 23.7 g (91 %). $^1$H NMR (400 MHz): $\delta$ = 2.00 (d, $^3J_{H,H}$ = 7.2 Hz, 3H, CHC*H*$_3$), 5.53 (q, $^3J_{H,H}$ = 6.9 Hz, 1H, C*H*CH$_3$), 7.17 (dd, $^3J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 2.4 Hz, 1H, aromatic proton), 7.27 (d, $^3J_{H,H}$ = 8.4 Hz, 1H, aromatic proton), 7.60 (d, $^3J_{H,H}$ = 2.4 Hz, 1H, aromatic proton). $^{13}$C NMR (100 MHz): $\delta$ = 25.85, 43.36, 128.44, 129.60, 130.97, 131.01, 133.46, 142.093. HRMS (m/z (M − Br)]$^+$ calcd for $C_8H_7Cl_2$ 172.9925, found 172.9925.

**1-(2,5-dichlorophenyl)-N,N-dimethylethanamine,** (±)-**6:** An aqueous solution of 40 wt.% dimethylamine (375 ml) was added to a solution of 2-(1-bromoethyl)-1,4-dichlorobenzene, (±)-**5** (23.7 g, 93.5mmol) in DCM (200 ml) and stirred vigorously for 16h at room temperature, after which, the solvents were removed. The residue was dissolved in DCM and washed with water (3 x 200 ml). The organic layer was dried over anhydrous $MgSO_4$. Removal of solvent under reduced pressure yielded colorless oil. Yield: 18.7 g (92 %) $^1$H NMR (400 MHz): $\delta$ = 1.28 (d, $^3J_{H,H}$ = 6.4 Hz, 3H, CHC*H*$_3$), 2.23 (s, 6H, N(C*H*3)$_2$), 3.70 (q, $^3J_{H,H}$ = 6.7 Hz, 1H, C*H*CH$_3$), 7.12 (dd, $^3J_{H,H}$ = 8.6 Hz, $^3J_{H,H}$ = 2.6 Hz, 1H, aromatic proton), 7.27 (d, $^3J_{H,H}$ = 8.4 Hz, 1H, aromatic proton), 7.56 (d, $^3J_{H,H}$ = 2.4 Hz, 1H, aromatic proton). $^{13}$C NMR (100 MHz): $\delta$ = 20.15, 43.45, 61.41, 127.76, 128.34, 130.45, 131.29, 133.02, 144.42. HRMS (m/z (M + H)]$^+$ calcd for $C_{10}H_{14}Cl_2N$ 218.0503, found 218.0511.

**(±)-Di-$\mu$-acetatobis-{6-(1'-dimethylaminoethyl)-2,5-dichlorophenyl-C,N}dipalladium(II),** (±)-**7:** The palladium agent, $Pd(OAc)_2$ (2.13 g, 9.48 mmol) was added to a solution of amine (±)-**6** (2.06, 9.44 mmol), in MeOH (50 ml). The mixture was heated to 55 °C and stirred for 16h. The mixture was filtered through Celite® and concentrated *via* reduced pressure. The residue was dissolved in DCM, followed by washing with water (3 x 50 ml), dried over anhydrous $MgSO_4$ and concentrated to give bright yellow solids. Yield: 3.44 g (95 %). M.p. 172-174 °C. $^1$H NMR (400 MHz): $\delta$ =1.95(s, 3H, C*H*$_3$COO-), 2.04 (d, $^3J_{H,H}$ = 6.3 Hz, 3H, CHC*H*$_3$), 2.60 (s, 3H, NC*H*$_3$ (eq)), 2.87 (s, 3H, NC*H*$_3$ (ax)), 3.79 (q, $^3J_{H,H}$ = 6.3 Hz, 1H, C*H*CH$_3$), 6.81 (d, $^3J_{H,H}$ = 8.4 Hz, 1H, aromatic proton), 6.88 (d, $^3J_{H,H}$ = 8.4 Hz, 1H, aromatic proton). $^{13}$C NMR (100 MHz): $\delta$ = 22.23, 24.39, 48.32, 54.30, 76.43, 125.47, 126.54, 129.40, 138.63, 139.21, 152.56, 181.78. HRMS (m/z (M - OAc)]$^+$ calcd for $C_{22}H_{27}Cl_4N_2O_2Pd_2$ 706.8880, found 706.8905.

**($R_C$,$S_C$$S_N$)-{6-(1'-dimethylaminoethyl)-2,5-dichlorophenyl-C,N}(prolinato-N,O)palladium(II), ($R_C$,$S_C$$S_N$)-8:** The racemic dimer, (±)-**7** (13.18 g, 17.2 mmol) was dissolved in MeOH (100 mL). Then a solution of sodium prolinate (4.97 g, 36.3 mmol) in the same solvent was added. The mixture was stirred for 1 h, and the solvent was removed under reduced pressure. The residue was dissolved in DCM and washed with water (3 x 100 mL). The organic layer was dried over anhydrous $MgSO_4$. The ($R_C$,$S_C$$S_N$)-**8** adduct was separated by flash column chromatography over silica (acetone:hexane, v/v: 1:1). The ($R_C$,$S_C$$S_N$)-**8** was crystallized from a ethyl acetate/diethyl ether solution, yielding pale yellow flakes. Yield: 5.52 g M.p. 174-177 °C (dec). (73%) $[\alpha]^{23.2}$ +28.5$^o$ (*c* 0.03, DCM). $^1$H NMR (400 MHz): $\delta$ =1.62−1.67 (m, 1H, CH$_2$C*H*$_2$CH$_2$), 1.71 (d, $^3J_{H,H}$ = 6.4 Hz, 3H, CHC*H*$_3$), 1.84−1.94 (m, 2H, CH$_2$C*H*$_2$CH$_2$, COCHC*H*$_2$), 2.38−2.45 (m, 1H, COCHC*H*$_2$), 2.55 (s, 3H, NC*H*$_3$ (eq)), 2.78 (s, 3H, NC*H*$_3$ (ax)), 3.18−3.23 (m, 1H, NHC*H*$_2$), 3.72−3.77 (m, 1H, NHC*H*$_2$), 3.81 (q, $^3J_{H,H}$ = 6.4 Hz, 1H, C*H*CH$_3$), 4.05−4.08 (m, 1H, N*H*), 4.14−4.18 (m, 1H, COC*H*CH$_2$), 6.84 (d, $^3J_{H,H}$ = 8.4 Hz, 1H, aromatic protons) 6.90 (d, $^3J_{H,H}$ = 8.4 Hz, 1H, aromatic protons). $^{13}$C NMR (100 MHz): $\delta$ =22.00, 23.13, 28.79, 47.91, 51.33, 53.47, 66.27, 74.70, 126.37, 126.75, 128.50, 140.04, 143.12, 153.38, 179.19. HRMS (m/z (M + H)]$^+$ calcd for $C_{15}H_{21}Cl_2N_2O_2Pd$ 439.0019, found 439.0020.

**($S_C$,$S_C$$S_N$)-{6-(1'-dimethylaminoethyl)-2,5-dichlorophenyl-C,N}(prolinato-N,O)palladium(II), ($S_C$,$S_C$$S_N$)-8:** The other diastereomeric adduct, ($S_C$,$S_C$$S_N$)-**8** was separated using acetone as mobile phase and was crystallized from acetone/heptane solution, afford pale yellow needle-like crystal. Yield: 5.80 g (77%). $[\alpha]^{22.8}$ +306.4$^o$ (*c* 0.02, DCM). $^1$H NMR (400 MHz): $\delta$ =1.60−1.67 (m, 1H, CH$_2$C*H*$_2$CH$_2$), 1.84 (d, $^3J_{H,H}$ = 6.4 Hz, 3H, CHC*H*$_3$), 1.96−1.98 (m, 1H, CH$_2$C*H*$_2$CH$_2$,), 2.17−2.23 (m, 2H, COCHC*H*$_2$), 2.61 (s, 1H, NCH$_3$ (eq)), 2.65 (s, 1H, NCH$_3$ (ax)), 3.11−3.19 (m, 1H, NHC*H*$_2$), 3.24−3.31 (m, 1H, NHC*H*$_2$), 3.78 (q, $^3J_{H,H}$ = 6.4 Hz, 1H, C*H*CH$_3$), 4.04−4.09 (q, 1H, COC*H*CH$_2$), 4.85−4.87 (m, 1H, N*H*), 6.83 (d, $^3J_{H,H}$ = 8.8 Hz, 1H, aromatic protons), 6.89 (d, $^3J_{H,H}$ = 8.4 Hz, 1H, aromatic protons). $^{13}$C NMR (100 MHz): $\delta$ = 22.05, 25.60, 30.20, 47.78, 52.98, 53.09, 64.91, 74.93, 126.46, 126.51, 128.59, 140.14, 144.61, 152.79, 181.10. HRMS (m/z (M + H)]$^+$ calcd for $C_{15}H_{21}Cl_2N_2O_2Pd$ 439.0019, found 439.0020.

**(*S*,*S*)-Di-$\mu$-chlorobis{6-(1'-dimethylaminoethyl)-2,5-dichlorophenyl-C,N}dipalladium(II), (*S*,*S*)-2:** Hydrochloric acid (1 M, 20 ml) was added into the solution of ($S_C$,$S_C$$S_N$)-**8** (2.51g, 5.74 mmol) complex in DCM (40 ml) and stirred at room temperature. After vigorous stirring for 30 min, the organic layer

was separated, washed with water, dried over $MgSO_4$ and followed by removal of solvent under vacuum to give the dimeric complex (*S*)-**2**. Yield: 1.83 g (89%). M.p. 170-173°C (dec). $[\alpha]_D$ +345 (*c* 0.01, DCM) $^1$H NMR (400 MHz): $\delta$ = 2.07–2.11 (m, 6H, CHC$H_3$), 2.49 (d, 6H, NC$H_3$ (eq)), 2.68 (6, 6H, NC$H_3$(ax)), 3.73–3.76 (m, 2H, C*H*CH$_3$), 6.78–6.87 (m, 4H, aromatic protons) ppm. $^{13}$C NMR (100 MHz): $\delta$ = 21.78, 49.13, 50.10, 53.82, 54.10, 76.75, 76.82, 124.78, 124.94, 126.32, 126.38, 129.14, 129.27, 139.27, 139.41, 140.02, 140.18, 150.72, 150.87 ppm. HRMS (m/z (M – Cl)]$^+$ calcd for $C_{20}H_{24}Cl_5N_2Pd_2$ 678.8433, found 678.8452.

**(*S*)-Bis(acetonitrile-N){6-(1'-dimethylaminoethyl)-2,5-dichlorophenyl-C,N}palladium(II) perchlorate, (*S*)-10:** A suspension of silver perchlorate (0.18 g, 0.87 mmol) in acetonitrile was added into the optically pure (*S*)-**2** (0.28 g, 0.38 mmol) dissolved in acetonitrile and the mixture was stirred vigorously in the dark at room temperature for 1 h. The resulting solution was filtered and the filtrate was washed with water once. The organic layer was dried over anhydrous $MgSO_4$ and concentrated to give pale yellow solids. The pale yellow solids were crystallized from DCM/hexane yielding pale yellow crystals. Yield: 0.28 g (71 %). M.p. 198-201 °C (dec). $[\alpha]^{21.9}$ = +151.4 (c = 0.02, DCM). $^1$H NMR (400 MHz): $\delta$ = 1.75 (s, 3H, N≡CC$H_3$), 1.98 (d, $^3J_{H,H}$ = 6.4 Hz, 3H, CHC$H_3$), 2.35 (s, 3H, N≡CC$H_3$), 2.62 (s, 3H, NC$H_3$ (eq)), 2.76 (s, 3H, NC$H_3$ (ax)), 3.83 (q, $^3J_{H,H}$ = 6.4 Hz, 1H, C*H*CH$_3$), 6.90 (d, $^3J_{H,H}$ = 8.5 Hz, 1H, aromatic proton), 6.98 (d, $^3J_{H,H}$ = 8.5 Hz, 1H, aromatic proton) ppm. $^{13}$C NMR (100 MHz): $\delta$ = 2.20, 3.21, 21.81, 50.05, 53.88, 77.00, 118.57, 125.48, 127.50, 129.01, 137.84, 139.39, 151.35 ppm. HRMS (m/z (M – $ClO_4$)]$^+$ calcd for $C_{14}H_{18}Cl_2N_3Pd$ 405.9878, found 405.9915.

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

**(*RR*)-Dichloro{dimethyl-1,2-bis(diphenylphosphino)ethane-dicarboxylate-P,P}palladium(II), (*RR*)-12:** A solution of diphenylphosphine (114.5 mg, 0.62 mmol) dissolved in degassed DCM (5 ml) was added to the complex (*S*)-**10** (149.0 mg, 0.31 mmol) with dimethyl acetylenedicarboxylate (43.4 mg, 0.31 mmol) dissolved in degassed DCM (5 ml) under positive pressure of nitrogen. The solution was cooled to -78 $^o$C, followed by addition of $NEt_3$ (62.2 mg, 0.62 mmol). The reaction mixture was allowed to stir at -78 $^o$C for 24 hours and gradually warmed to room temperature. The crude product, (*S,RR*)-**11** was purified using column chromatography with DCM/acetone (V/V = 1: 0.02) as the eluent. Concentrated hydrochloric acid (1 ml) was added dropwised to a solution of (*S,RR*)-**11** (165 mg, 0.18 mmol) in DCM (20 ml), the mixture was stirred vigorously at room temperature for 30 min. The resulting mixture was washed with $H_2O$ (5 x 50 ml), the organic layer obtained was dried with $MgSO_4$, filter and concentrated under vacuum to give (*RR*)-**12** as yellow solid (reported complex in literature). [6a] Yield: 54% (0.11 g) $^{31}$P{$^1$H} NMR (121 MHz, $CDCl_3$): $\delta$ 58.0 ppm. $[\alpha]_{436}$ = +140.0$^o$ (*c* = 0.1, $CHCl_3$)

**Crystal Structure Determination**: Crystal data and a summary of the crystallographic analyses are given in the supporting document. CCDC-971801 [for (±)-**7**], -971802 [for ($R_C$,$S_C$$S_N$)-**8**], -971803 [for ($S_C$,$S_C$$S_N$)-**8**], -971804 [for (*S,S*)-**2**], and -971805 [for (*S*)-**10**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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## References

[1] (a) M. Sawamura, Y. Ito, *Chem. Rev.*, **1992**, *92*, 857; (b) S. Gladiali, E. Alberico, *Phosphorus Ligands in Asymmetric Catalysis; Synthesis and Applications*, A. Boerner ed., Wiley-VCH, **2008**, p. 73; (c) S. Luhr, J. Holz, A. Borner, *ChemCatChem*, **2011**, 1708.

[2] (a) F. G. Mann, I. T. Millar, *J. Chem. Soc.*, **1952**, 4453; (b) M. A. Weiner, G. Pasternack, *J. Org. Chem.*, **1969**, *34*, 1130.

[3] (a) M. C. Hoff, P. Hill, *J. Org. Chem.*, **1959**, *24*, 356; (b) B. D. Dombek, *J. Org. Chem.*, **1978**, *43*, 3408.

[4] M. M. Rauhut, I. Hechenbleikner, H. A. Currier, F. C. Schaefer, V. P. Wystrach, *J. Am. Chem. Soc.*, **1959**, *81*,1103.

[5] Rauhut, M. M.; Currier, H. A.; Semsel, A. M.; Wystrach, V. P. *J. Org. Chem.*, **1961**, *26*, 5138.

[6] For example: (a) Shulyupin, M. O.; Kazankova, M. A.; Beletskaya, I. P. *Org. Lett.* **2002**, *4*, 761. (b) Kondoh, A.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2007**, *129*, 4099. (c) Sadow, A. D.; Haller, I.; Fadini, L.; Togni, A. *J. Am. Chem. Soc.* **2004**, *126*, 1470. (d) Behrle, A. C.; Schmidt, J. A. R. *Organometallics* **2013**, *32*, 1141. (e) Rosenberg, L. *ACS Catal.* **2013**, *3*, 2845. (f) Kawaguchia, S.-i.; Ogawa, A. *Synlett.* **2013**; *24*, 2199.

[7] (a) L. Tang, Y. Zhang, D. Luo, Y. Li, K. F. Mok, W. C. Yeo, P.-H. Leung, *Tetrahedron Lett*., **2007**, *48*, 33; (f) Y. Zhang, S. A. Pullarkat, Y. Li, P.-H. Leung, *Inorg. Chem*., **2009**, *48*, 5535 and references cited therein; (c) K. Chen, S. A. Pullarkat, M. Ma, Y. Li, P.-H. Leung, *Dalton Trans*., **2012**, *41*, 539; (d) S. A. Pullarkat, P.-H. Leung, *Chiral Metal Complex Promoted Asymmetric Hydrophosphinations*, In Topics in Organometallic Chemistry: Hydrofunctionalization, Tanaka M. Ed., Springer, New York, **2012**, pp. 145. (e) Ding, Y.; Zhang, Y.; Li, Y.; Pullarkat, S. A.; Andrews, P.; Leung, P.-H. *Eur. J. Inorg. Chem.* **2010**, 4427.

[8] (a) Y. Huang, Y.; S. A. Pullarkat, Y. Li, P.-H. Leung, *Inorg. Chem*., 2012, *51*, 2533; (b) R. J. Chew, Y. Huang, Y. Li, S. A. Pullarkat, P.-H. Leung, *Adv. Synth. Catal.*, **2013**, *355*, 1403 and references cited therein.

[9] F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, **1987**, S1.

[10] A. Bondi, *J. Phys. Chem.*, **1964**, *68*, 441–451.

[11] V. V. Dunina, *Curr. Org. Chem.*, **2011**, *15*, 3415.

[12] For example: (a) B.-H. Aw, S. Selvaratnam, P.-H. Leung, *Tetrahedron: Asymmetry*, **1996**, *7*, 1753; (b) Y. Ding, Y. Li, S.A. Pullarkat, S. L. Yap, P.-H. Leung, *Eur. J. Inorg. Chem.,* **2009**, 267; (c) D. Krishnan, S. A. Pullarkat, M. Wu, Y. Li, P.-H. Leung,

*Chem. Eur. J.*, **2013**, *19*, 5468.
[13] P.-H. Leung, *Acc. Chem. Res.,* **2004**, *37*, 169–177.

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# Table of Contents

A novel chiral palladacycle promoted the asymmetric hydrophosphination reaction between diphenylphosphine and dimethyl acetylenedicarboxylate, affording only one stereo-isomeric product.