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Synthesis, Optical Resolution and Stereochemical Properties of a Rationally Designed Chiral C-N Palladacycle

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ABSTRACT: A novel racemic tertiary amine, 1-(2,5-di-*iso*-propylphenyl)-*N,N*-dimethylethanamine, was synthesized from 2,5-di-*iso*-propylbenzaldehyde *via* a multistep approach in high overall yield. The *ortho*-palladation of this ligand was found to be sensitive to the reaction conditions and the palladating reagents employed. The metal complexation process could thus either generate a cyclopalladated complex in high yield or lead to an unexpected *N*-demethylated amine palladium(II) complex, or both. Both products have been isolated and characterized crystallographically in the solid state and spectroscopically in solution. The racemic cyclopalladated complex could be efficiently resolved *via* the formation of (*S*)-prolinato derivatives. The absolute stereochemistry of the resolved diastereomeric complexes were determined by single crystal X-ray crystallography in the solid state and by ^1H - ^1H Rotating Frame Overhauser Effect (ROESY) NMR spectroscopy in solution. An evaluation of the sterically-hindered resolved cyclopalladated units as chiral auxiliary was conducted in the *endo*-cycloaddition reaction between 3,4-dimethyl-1-phenylphosphole (DMPP) and ethyl vinyl ketone. The two expected phosphanorbornene adducts were generated with moderate stereoselectivity.

Introduction

Since the first reported cyclopalladated complex in 1965 by Cope and co-workers,¹ palladacycles have gained much attention due to their wide range of applications.² In particular, optically active palladacycles have found numerous practical uses as efficient resolving agents,^{2c,3} chiral derivatizing reagents,⁴ and in asymmetric reactions (both stoichiometric and catalytic).⁵⁻⁸ As such, these optically active complexes have been developed significantly over the past few decades.^{5b-f,9}

Our group is interested in the study of the chemistry of chiral palladacycles and their applications. The enantiomerically pure forms of the palladacycle **1** (Figure 1), and their derivatives, have been extensively used in our group. An inherent internal steric repulsion exists between the naphthylamine proton H(8) and the methyl substituent at the stereogenic center of **1** which confines the methyl group in the axial position. The five-membered cyclopalladated ring is thus locked in a particular skew chiral conformation resulting in a stereochemically rigid palladacycle in both solid state and in solution.¹⁰ This unique structural feature makes this class of palladacycles applicable in many asymmetric reactions such as cycloaddition,⁵ hydrophosphination⁶⁻⁷ and hydroarsination reactions.⁶

Although enantiomerically pure complex **1** and its derivatives usually show high efficiencies as chiral auxiliaries in many synthetic reactions, satisfactory stereoselectivity could not be achieved by these complexes in certain cases.^{5b} Therefore, palladacycles with structural modification on the aromatic framework were designed and synthesized.^{5b-5e} Introduction of spacer groups or additional aromatic rings into the framework, for instance in the case of complex **2** (Figure 1),^{5b} have indeed shown improvement in the stereoselectivity of cycloaddition reactions. In such a complex, one of the methyl substituents on the aromatic ring interacts with the methyl group at the stereogenic carbon center thus locking the organometallic five-membered ring into a fixed chiral conformation, both in solid state and in solution. Moreover, the introduction of another methyl group on the phenyl ring functions as a spacer which protrudes sterically towards the lower right corner of the square-planar complex. With these designed structural features, complex **2** has been showed to be a better chiral template in some Diels-Alder reactions, when compared to the original naphthylamine analogues.^{5b}

Figure 1. Chiral palladacycles (*S*)-**1**, (*S*)-**2** and (*S*)-**3**.

It should be noted that the introduction of sterically demanding groups on the aryl rings in complexes such as **1** and **2** may hinder the formation of the desired *ortho*-metallated complex as well as lower their reactivity in synthetic applications. Nonetheless, the success of the palladacycle **2** has prompted us to take up the challenge of exploring the impact and limitations of introducing bulky groups into the organometallic ligand system with the objective to improve on selectivity whilst maintaining the desired reactivity. The isopropyl spacer group was, therefore, selected and introduced onto the aromatic ring to give complex **3**. In this article, we report the preparation, resolution, comprehensive characterization and the novel organometallic chemistry of this highly sterically hindered palladacycle variant and its subsequent evaluation as a chiral template in a [4+2]-cycloaddition scenario.

Results and Discussion

Ligand and Complex Syntheses

Scheme 1. Synthesis of 1-(2,5-diisopropylphenyl)-*N,N*-dimethylethanamine (±)-7.

As illustrated in Scheme 1, the racemic amine ligand could be synthesized efficiently in three steps using 2,5-di-*iso*-propylbenzaldehyde **4** as the starting material. Treatment of the aldehyde with methylmagnesium bromide gave racemic alcohol (±)-**5** in 98% yield. Bromination of the alcohol with PBr₃ then provided the bromo product (±)-**6** in 99% yield. Finally, the reaction between (±)-**6** and aqueous dimethylamine afforded the desired racemic ligand (±)-**7** in 96% yield.

Scheme 2. *ortho*-Palladation of tertiary amine ligand (±)-7.

As aforementioned, the bulky *iso*-propyl groups in ligand (±)-**7** indeed rendered some complications in the *ortho*-palladation process (Scheme 2). Unlike the preparation of the analogous complexes **1** and **2**, the metal complexation process of ligand (±)-**7** was found to be highly sensitive to the reaction conditions employed. The optimal yield (78%) of complex (±)-**3** could be achieved by the treatment of the tertiary amine (±)-**7** in methanol with Li₂[PdCl₄] at room temperature in the presence of NaOAc. (Table 1). Interestingly, the yield dropped dramatically to 20% when the reaction was conducted under similar conditions but at a higher temperature (55 °C). Replacement of the palladating agent by PdCl₂(NCMe)₂ resulted in very low yields for the desired complex. Notably, the complexation was not observed when the ligand (±)-**7** was treated with Pd(NCMe)₄(ClO₄)₂ at ambient temperature with the amine recovered qualitatively *via* column chromatography. On the other hand, separate treatment of the ligand (±)-**7** with PdCl₂ or with Pd(OAc)₂ upon subsequent treatment with LiCl, gave a mixture of the desired product (±)-**3** and an unexpected product (±)-**8** that involved a novel C–N bond cleavage during the coordination process. The ratios of complexes (±)-**3** and (±)-**8** were found to be affected by the reaction temperature and the solvent employed.

Table 1. Optimization of conditions for palladation of tertiary amine (±)-7.

entry	conditions ^a				% yield ^b	
	palladating agent	solvent	base	T (°C)	(±)- 3	(±)- 8
1	PdCl ₂	MeOH	-	55	23	29
2	Pd(OAc) ₂ ^c	MeOH	-	55	16	2
3	Li ₂ (PdCl ₄)	MeOH	NaOAc	r.t.	78	0
4	Li ₂ (PdCl ₄)	MeOH	NaOAc	55	20	0
5	PdCl ₂ (NCMe) ₂	MeOH	-	55	19	0
6	Pd(NCMe) ₄ (ClO ₄) ₂	MeCN	-	r.t.	- ^d	- ^d
7	PdCl ₂	MeOH	-	80	10	23
8	PdCl ₂	Benzene	-	55	43	11
9	PdCl ₂	DMF	-	55	39	0

^a Unless otherwise specified, reaction employed 1 equivalent of palladating agent for 16 h. ^b Isolated yields following column chromatography. ^c Use of Pd(OAc)₂ as palladating agent yielded μ -acetato dimer instead of μ -chloro dimer. ^d No reaction.

The molecular structure of product (±)-**8** was confirmed by single crystal X-ray crystallography (Figure 2). The structural analyses of the complex confirmed that a C–N bond cleavage indeed occurred during the coordination process. Selected bond lengths and angles are provided in Table 2. The palladium center exhibits a typical square-planar coordination geometry with the bond angles of N(1)–Pd(1)–N(1A) and Cl(1)–Pd(1)–Cl(1A) both being 180.0°. The two nitrogen donor atoms are *trans* to each other with each of the nitrogen atoms bearing only one methyl substituent as a consequence of the C–N cleavage. The relative stereochemistry of asymmetric nitrogen and carbon atoms of complex (±)-**8** in solid state was (R_CS_N, R_CS_N)*. The ¹H NMR of complex (±)-**8** shows only one resonance observed for every chemically non-equivalent proton. The presence of the bulky *iso*-propyl groups on the aromatic ring have prevented the asymmetric nitrogen and carbon atoms to isomerize to other isomers as in the case of the unsubstituted aromatic ring.^{11a} It is noteworthy that such type of C–N bond cleavage is not usually observed in analogous naphthyl- and benzyl-amine ligands. Pfeffer *et al.* and Aresta *et al.* reported the Li₂PdCl₄-mediated dealkylation of *N,N*-dialkylanilines and 9-(diethylamino)naphthalene respectively.^{11b} The methanolysis or hydrolysis, by traces of water, of iminium ions produced *in situ* is the conceivable mechanism for this N-dealkylation. Interestingly, in our case, the use of Li₂PdCl₄ as palladium source afforded the dimeric complex (±)-**3** instead of the N-dealkylated complex (±)-**8**. It is notable that the chemoselectivity of cyclometallation will also be decreased when such C–N cleavage occurred. Such precedents of C–N bond cleavage during cycloplatination^{11c} and C–C bond cleavage during cyclopalladation of bulky benzylamines were known in literature.^{11d}

Figure 2. Molecular structure of complex (±)-8.

Table 2. Selected bond lengths (Å) and angles (°) for complex, (±)-8.

Pd(1)–N(1)	2.057(4)	Pd(1)–N(1A)	2.057(4)
Pd(1)–Cl(1)	2.302(1)	Pd(1)–Cl(1A)	2.302(1)
N(1)–C(13)	1.486(7)	N(1A)–C(13A)	1.486(7)
N(1)–C(15)	1.479(7)	N(1A)–C(15A)	1.479(7)
N(1)–Pd(1)–Cl(1)	93.0(1)	N(1)–Pd(1)–Cl(1A)	87.0(1)
Cl(1A)–Pd(1)–N(1A)	93.0(1)	N(1A)–Pd(1)–Cl(1)	87.0(1)
N(1)–Pd(1)–N(1A)	180.0(2)	Cl(1)–Pd(1)–Cl(1A)	180.0(4)
C(13)–N(1)–Pd(1)	115.9(3)	C(13A)–N(1A)–Pd(1)	115.9(3)
C(15)–N(1)–Pd(1)	112.6(3)	C(15A)–N(1A)–Pd(1)	112.6(3)
C(15)–N(1)–C(13)	112.1(4)	C(15A)–N(1A)–C(13A)	112.1(4)

The desired *ortho*-metallated complex (±)-3 obtained from the optimized reaction conditions (Table 1, entry 3) could be recrystallized efficiently as bright yellow needles. In the ¹H NMR spectrum, complex (±)-3 showed broad and poorly resolved resonance signals. The phenomenon can be attributed to the well-documented dynamic *syn-anti* interconversion of such dimeric complexes in solution (Figure 3).¹²

Figure 3. Dynamic *syn-anti* interconversion of the dimeric complex (±)-3.

In the solid state, structural investigations confirmed that no C–N bond cleavage occurred during the cyclopalladation reaction with each nitrogen atom bearing two methyl groups (Figure 4). Selected bond lengths and bond angles of complex are given in Table 3. In addition, the dimer exists in the crystal in its *transoid* configuration with the two chiral organometallic units adopting the same relative configurations. The palladium atoms, Pd(1) and Pd(1A), were found to adopt a distorted square-planar coordination geometry, the dihedral angles between the planes {Cl(1)–Pd(1)–Cl(1A)} and {N(1)–Pd(1)–C(1)}, and between the planes {Cl(1)–Pd(1A)–Cl(1A)} and {N(1A)–Pd(1A)–C(1A)} were both equal to 13.6°. As predicted, the *iso*-propyl substituents (C(8) and C(8A)) interacts with the methyl groups (C(14) and C(14A)) at the stereogenic center thus forcing the

methyl group to take up the axial position instead of the relatively more favorable equatorial position.

The four-membered ring bridged by the chlorine atoms to the palladium centers, Cl(1)–Pd(1)–Cl(1A)–Pd(1A), were found to be non-coplanar, with a bent angle of 27.8° about the Cl(1)–Cl(1A) axis. In addition, torsion angles for Cl(1)–Pd(1)–C(1)–C(2) and Cl(1A)–Pd(1A)–C(1A)–C(2A) were both calculated to be –45.0°. Such twisting of the rings was partly a consequence of the internal steric repulsions between the *iso*-propyl substituent and the bridged chlorine atoms.

Figure 4. Molecular structure of dimeric complex (±)-3.

Table 3. Selected bond lengths (Å) and angles (°) for complex, (±)-3.

Pd(1)–C(1)	1.993(2)	Pd(1A)–C(1A)	1.993(2)
Pd(1)–N(1)	2.071(2)	Pd(1A)–N(1A)	2.071(2)
Pd(1)–Cl(1)	2.347(4)	Pd(1A)–Cl(1A)	2.347(4)
Pd(1)–Cl(1A)	2.463(4)	Pd(1A)–Cl(1)	2.463(4)
C(1)–Pd(1)–N(1)	80.2(7)	C(1A)–Pd(1A)–N(1A)	80.2(7)
C(1)–Pd(1)–Cl(1)	98.8(5)	C(1A)–Pd(1A)–Cl(1A)	98.8(5)
N(1)–Pd(1)–Cl(1A)	97.9(4)	N(1A)–Pd(1A)–Cl(1)	97.9(4)
Cl(1)–Pd(1)–Cl(1A)	83.8(2)	Cl(1A)–Pd(1A)–Cl(1)	83.8(2)
C(1)–Pd(1)–Cl(1A)	176.3(5)	C(1A)–Pd(1A)–Cl(1)	176.3(5)
N(1)–Pd(1)–Cl(1)	167.2(5)	N(1A)–Pd(1A)–Cl(1A)	167.2(5)

Synthesis of Monomeric Complex (±)-9

In order to study the impact of the bulky *iso*-propyl groups on the coordination chemistry of the adjacent palladium coordination sites, the dimeric complex (±)-3 was converted to the corresponding monomeric neutral complex (±)-9 by addition of triphenylphosphine (Scheme 3).

Scheme 3. Conversion to monomeric complex (±)-9.

The monomeric complex (±)-9 could be isolated as yellow prisms from dichloromethane-hexane. The coordination chemistry of the complex was confirmed by X-ray structural analysis. Interestingly, four crystallographically unique molecules were found in the unit cell with

each differing only slightly in bond lengths and bond angles. For clarity, only one of these molecules is depicted in Figure 5. The coordination geometry at palladium is distorted square-planar and the chiral five-membered ring adopts an envelope-like conformation in the solid state. More importantly, complex ($\pm$)-**9** adopts the highly unfavourable *trans* N–Pd–P geometry in which the bulky *iso*-propyl spacer and the PPh₃ ligand were located at the adjacent positions of the square-planar complex. The *trans* effect (transphobia) for the C–Pd–P geometry is larger than that of the N–Pd–P geometry resulting in a greater degree of destabilisation for the C–Pd–P geometry. Clearly, the strong electronic directing effects must be the dominating influence, even in such sterically demanding complexation scenarios.^{9a,13} As a consequence of these strong steric repulsions, the palladium center exhibits a large dihedral angles of 21.8° between the planes {P(1)–Pd(1)–Cl(1)} and {N(1)–Pd(1)–C(1)}.

Figure 5. Molecular structure of monomeric complex ($\pm$)-**9**.

Resolution of Complex ($\pm$)-**3**

The resolution of racemic dimeric complex ($\pm$)-**3** was performed using sodium (*S*)-prolinate as the resolving agent (Scheme 4) to give a 1:1 mixture of diastereomers (*R_C,S_C,S_N*)-**10** and (*S_C,S_C,S_N*)-**10**. The diastereomeric adducts were then separated *via* column chromatography. The diastereomeric ratio of both fractions were verified by ¹H NMR spectroscopy. The less polar diastereomer (*R_C,S_C,S_N*)-**10** was eluted out first with acetone/dichloromethane (V/V = 1:1) and subsequently recrystallized to give pale yellow plate-like crystals. The more polar diastereomer (*S_C,S_C,S_N*)-**10** was obtained as colourless needles. The absolute configurations and the solid state structure of both diastereomeric adducts, (*R_C,S_C,S_N*)-**10** and (*S_C,S_C,S_N*)-**10**, were confirmed by single crystal X-ray diffraction investigations.

Scheme 4. Resolution of dimeric complex ($\pm$)-**3**.

Figure 6. Molecular structure of diastereomer (*R_C,S_C,S_N*)-**10**.

The molecular structure of the complex (*R_C,S_C,S_N*)-**10** is shown in Figure 6. The absolute configuration of the stereogenic carbon center within the organometallic ring is *R*. The torsion angle for C(1)–Pd(1)–N(1)–C(13) is +40.9°. The methyl group at the chiral center occupies the expected axial position and the absolute conformation of the five-membered ring is δ (Figure 7).¹⁴ The secondary stereogenic nitrogen atom from the prolinate group is in *S* absolute configuration.

Figure 7. Chiral $\delta(R_C)$ (a, c, e) and $\lambda(R_C)$ (b, d, f) conformations of the $(R_C,ScSn)$ -10 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 the $N(1)-C(13)$ bond (c, d) and in the Newman projections relative the $N(1)-Pd(1)$ bond (e, f).

The palladium center adopts a slightly distorted square planar coordination geometry with tetrahedral distortion of 2.8° . The organometallic five-membered ring is in an envelope conformation wherein $N(1)$ is $0.803 \text{ \AA}$ below the mean plane formed by $C(1)-C(12)-C(13)-Pd(1)$. The two coordinated nitrogen groups are in unusual *cis*-(N,N)-geometry.^{Sb,Se} This phenomenon can be attributed to the steric interaction between the protruding *iso*-propyl spacer adjacent to the $Pd-C$ bond and the nitrogen of the prolinato group which forces the complex to adopt the sterically more favourable *cis*-(N,N)-geometry and the requirement of the crystal lattice. The angle between the mean plane of the organometallic five-membered ring $C(1)-C(12)-C(13)-N(1)-Pd(1)$ and the mean plane formed from $O(1)-C(17)-C(18)-N(2)-Pd(1)$ of the prolinato ligand is 13.1° . The bond length of $Pd(1)-N(2)$ is $2.140 \text{ \AA}$ (Table 4) and is comparable to reported values of the *cis*-(N,N)-geometry.^{Sb,Se} On the other hand, the distance is much longer than the reported value of $2.037-2.083 \text{ \AA}$ for the *trans*-(N,N)-geometry.^{Sc,14a} The bond lengthening is an expected result of the *trans* influence caused by the aryl-carbon and the repulsion between the $C(15)$ on the NMe and the $C(21)$ of the prolinato moiety.

Table 4. Selected bond lengths ($\text{\AA}$) and angles ($^\circ$) for complex, $(R_C,ScSn)$ -10

$Pd(1)-C(1)$	2.014(2)	$Pd(1)-O(1)$	2.046(2)
$Pd(1)-N(1)$	2.053(2)	$Pd(1)-N(2)$	2.140(2)
$C(17)-O(1)$	1.283(3)	$C(17)-O(2)$	1.235(3)
$C(1)-Pd(1)-O(1)$	99.6 (9)	$C(1)-Pd(1)-N(1)$	80.5(9)
$O(1)-Pd(1)-N(1)$	177.4(8)	$C(1)-Pd(1)-N(2)$	178.5(10)
$O(1)-Pd(1)-N(2)$	80.5(8)	$N(1)-Pd(1)-N(2)$	99.3(9)

Figure 8. Molecular structure of diastereomer $(S_C,ScSn)$ -10.

Similarly, X-ray crystallographic studies on diastereomer $(S_C,ScSn)$ -10 were performed and five crystallographically unique molecules were observed in the asymmetric unit cell. These molecules adopt the same stereochemistry, only differing slightly in bond lengths and bond angles. For clarity, only one of these molecules is shown in Figure 8. The crystallographic study showed that the absolute stereochemistry at the stereogenic carbon within the organometallic ring is *S*. Similarly, the secondary stereogenic nitrogen atom in the prolinato moiety also adopted the *S* absolute configuration. The torsion angle for $C(1)-Pd(1)-N(1)-C(13)$ is -43.5° with the skewed five-membered ring locked in λ conformation (Figure 9).¹⁴ The coordination geometry at palladium is distorted square-planar. The dihedral angles between the planes $\{N(1)-Pd(1)-C(1)\}$ and $\{O(1)-Pd(1)-N(2)\}$ is 5.5° . The two coordinated nitrogen groups adopt the *trans*-(N,N) arrangement.

Figure 9. Chiral $\delta(S_C)$ (a, c, e) and $\lambda(S_C)$ (b, d, f) conformations of the $(S_C,ScSn)$ -10 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 the $N(1)-C(13)$ bond (c, d) and in the Newman projections relative the $N(1)-Pd(1)$ bond (e, f).

The above structural analyses revealed that (R_C, S_{CS_N})-**10** and (S_C, S_{CS_N})-**10**, adopted the *cis*- and *trans*-(N, N) coordination geometries, respectively, in the solid state. However, due to the aforementioned dynamic ligand redistribution processes in solution, the *cis*- and *trans*-(N, N) arrangements may interconvert. Hence, the properties of the complexes in solution were examined through the ^1H NMR and 2D ^1H - ^1H ROESY NMR experiments. The numbering scheme of diastereomers (R_C, S_{CS_N})-**10** and (S_C, S_{CS_N})-**10** used in the NMR experiments are shown in Figure 10 and Figure 11 respectively.

Figure 10. Numbering scheme of complex (R_C, S_{CS_N})-**10**.

Figure 11. Numbering scheme of complex (S_C, S_{CS_N})-**10**.

Figure 12 showed the expanded 2D ^1H - ^1H ROESY NMR spectrum of complex (R_C, S_{CS_N})-**10**. The interaction between H10/H11 of the prolinato group and NMe(*eq*), represented by signal A, depicts that the two nitrogen groups are *cis* to each other in solution as observed in the solid state investigations. The presence of NOE signals between Me8 and the equatorially disposed NMe group (B) and the interactions of H7 with NMe(*ax*), NMe(*eq*) and Me8 (E, F and G respectively) shows that the methyl group (Me8) at the stereogenic center is axially positioned and the five-membered organometallic ring is locked in δ conformation in solution (Figure 7).¹⁴ The distance between the Me8 carbon, C(14) and the NMe(*eq*) carbon, C(15) is 2.876 Å, and is smaller than the summation of the Van der Waals radii of 3.40 Å¹⁵ and is indicative of the steric repulsion between them. These signals were consistent with the assignment shown in the solid state investigations wherein the organometallic ring is adopting exclusively the δ conformation. The inter-ligand and intra-ligand interactions of the CH (iso-propyl) group with the NH of the prolinato group and H7 were represented by NOE signals C and D, respectively.

Figure 12. Expanded 2D ^1H - ^1H ROESY NMR spectrum of the complex (R_C, S_{CS_N})-**10** in CDCl_3 .

Similarly, Figure 13 shows the expanded 2D ^1H - ^1H ROESY NMR spectrum of the diastereomeric complex (S_C, S_{CS_N})-**10**. The presence of interaction of Me8 with NMe(*eq*) represented by NOE signal A and the interactions of H7 with the Hb, NMe(*eq*), NMe(*ax*) and Me8 (correspond to NOE signals D to G) indicated that the five-membered organometallic ring is locked in λ conformation and the Me8 take up the axial position in solution (Figure 9).¹⁴ The distance between the Me8 carbon, C(14) and the NMe(*eq*) carbon, C(15) and the distance between the H7 proton H(13) and the Hb proton H(9) is 2.925 Å and 2.072 Å respectively. Both are smaller than the summation of the corresponding Van der Waals radii of 3.40 Å and 2.40 Å.¹⁵ The NOE signals in solution matches the interactions of the complex in solid state investigations. The presence of inter-ligand interaction between Ha and NH is denoted as C which indicates that the two nitrogen groups are *trans* to each other. This is further supported by solid state investigations where the distance between the Ha proton H(3) and the NH proton N(2) is 1.962 Å.¹⁵

Figure 13. Expanded 2D ^1H - ^1H ROESY NMR spectrum of the complex ($S_C,S_C\text{Sn}$)-**10** in CDCl_3 .

The enantiopure dimeric complex (*S*)-**3** was prepared by treating the diastereomer ($S_C,S_C\text{Sn}$)-**10** with 1 M aqueous hydrochloric acid and was obtained in 90% yield as yellow solid (Scheme 4). Similarly, the enantiomer (*R*)-**3** could also be liberated from ($R_C,S_C\text{Sn}$)-**10** by acid treatment. Unfortunately, the enantiomerically pure dimeric complex (*S*)-**3** could not be induced to crystallize despite numerous solvent systems being employed. The optically pure dimers were used directly for subsequent reactions.

Application of Complex (*S*)-**3** as Chiral Auxiliary for the [4+2] *endo*-Cycloaddition Reaction between DMPP and Ethyl Vinyl Ketone

The detailed structural analysis of *ortho*-metallated complexes had unambiguously revealed that the *iso*-propyl moiety projected a significant steric impact on the neighboring coordination sites. Although the formation of the triphenylphosphine complex ($\pm$)-**9** had confirmed that the dominating electronic directing forces originating from the organometallic ring allowed the coordination of the bulky monodentate phosphine ligand onto this sterically congested position, we were uncertain if the *ortho*-metallated unit will perform as a suitable template in sterically demanding asymmetric reaction scenarios. In order to assess its efficiency in such scenarios, (*S*)-**3** was used as a chiral auxiliary for the asymmetric [4+2] *endo*-cycloaddition reaction between 3,4-dimethyl-1-phenylphosphole (DMPP) and ethyl vinyl ketone.^{5h}

Scheme 5. Synthesis of DMPP-coordinated complex (*S*)-**11**.

It has been well established that DMPP can be activated as a cyclic diene *via* metal complexation.^{5h} The DMPP-coordinated complex (*S*)-**11** (Scheme 5) was prepared by cleavage of the optically pure dimeric complex (*S*)-**3** with two molar equivalents of DMPP. In the solid state, X-ray structural analysis of (*S*)-**11** confirmed that, like complex **9**, the ligand was coordinated in the position *trans* to the amine moiety (Figure 14). The torsion angle for $\text{C}(1)\text{-Pd}(1)\text{-N}(1)\text{-C}(13)$ is -39.3° showing that the the organometallic five-membered ring is locked in λ conformation and the methyl group on the stereogenic carbon is axially positioned.¹⁴

Figure 14. Molecular structure of complex (*S*)-**11**.

Figure 15. Numbering scheme of DMPP-coordinated complex (*S*)-**11**.

Figure 16. Expanded 2D ^1H - ^1H ROESY NMR spectrum of the complex (*S*)-**11** in CD_3CN .

The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of (S)-**11** in d_3 -acetonitrile exhibited only one sharp singlet at δ 28.9 indicating that only one structural isomer was present in solution. A ^1H - ^1H ROESY NMR experiment was subsequently conducted to confirm that only the *trans* N-Pd-P species exists in solution. The numbering scheme of the DMPP complex (S)-**11** and the corresponding ^1H - ^1H ROESY NMR spectrum are given in Figure 15 and Figure 16, respectively. The $^4J_{\text{HP}}$ values of 6.4 Hz falls within the values (5.4-6.5 Hz) for equatorially position proton on the stereogenic carbon.^{14b} The presence of strong interactions between Me8 with NMe(*eq*) was noted as signal A in the spectrum and the distance between these two carbons is 2.878 Å, which is smaller than the summation of the van der Waals radii of 3.40 Å. ROESY correlations C to F correspond to the interactions of H7 with Hb, NMe(*eq*), NMe(*ax*) and Me8 respectively. These signals were consistent with the solid state structural assignment in which Me8 occupies an axial position and the five-membered organometallic ring was locked into the λ conformation in solution.¹⁴ The NOE signal B represents the interaction of both NMe groups on the amine moiety. The absence of any interactions between the phosphole and the NMe groups indicate that they are not located next to each other. The ROSEY NMR study, thus, revealed that complex (S)-**11** does not undergo the *cis-trans* isomerization in solution.

Scheme 6. [4+2] *endo*-Cycloaddition reactions between DMPP-complex (S)-**11** and ethyl vinyl ketone.

The cycloaddition reaction between complex (S)-**11** and ethyl vinyl ketone was conducted in chloroform at 50 °C (Scheme 6). The reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy and was found to be complete in five days. The spectrum of the crude reaction mixture displayed two new sharp singlets at δ 118.2 and 119.4 with intensity ratio of 1:4.4. The high field $^{31}\text{P}\{^1\text{H}\}$ NMR signals are consistent with the formation of the two stereoisomeric endo-cycloadducts.⁵ No other signals could be detected in the 161 MHz spectrum. We have previously conducted the same endo-cycloaddition reaction between DMPP and ethyl vinyl ketone under similar conditions using complexes (S)-**1**^{5a} and (S)-**2**^{5b} as chiral auxiliaries. When (S)-**1** was used as the chiral template at 70 °C, the reaction was completed within 16 h to give a 1:1 mixture of the two *endo*-adducts.^{5a} On the other hand, when (S)-**2** was used at 50 °C, the reaction was completed in 27 h generating a 1:3.5 diastereomeric mixture.^{5b} A comparison between the three chiral inducers for the same cycloaddition reaction clearly revealed that a suitable spacer attached to the *meta*-position of the *ortho*-palladated ligand indeed projects its stereochemical influence more efficiently toward the neighbouring coordination and reaction site. However, these spacer groups also impose steric hindrances that would slow down the desired reaction. To balance off the aforementioned reactivity-stereoselectivity effects, it appeared that the *iso*-propyl substituent or its sterically equivalent counterparts may be the largest substituents that could be employed as spacers in this family of cyclopalladated reagents.

We are currently exploring other applications of complex **3**. Furthermore, the mechanistic details of the unexpected C-N bond cleavage observed during the metal complexation process is also currently being investigated in-depth.

Experimental

General Considerations

Reactions involving air-sensitive compounds were performed under positive pressure of purified nitrogen by using standard Schlenk techniques. 2,5-Disopropylbenzaldehyde (**4**) was prepared according to procedures as reported in literature.¹⁶ Proton nuclear magnetic resonance (^1H NMR), carbon nuclear magnetic resonance (^{13}C NMR) and phosphorus nuclear magnetic resonance ($^{31}\text{P}\{^1\text{H}\}$ NMR) spectroscopy were performed on a Bruker Avance III 400 Spectrometer (^1H at 400 MHz, ^{13}C at 100 MHz, $^{31}\text{P}\{^1\text{H}\}$ at 161 MHz). Multiplicities were given as: s (singlet); brs (broad singlet); d (doublet); t (triplet); q (quartet); qn (quintet); sep (septet); dd (doublets of doublet); m (multiplet). 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 quoted as δ in units of parts per million (ppm) and referenced to chemical shift of the residual solvent of *d*-chloroform (^1H at δ 7.26 and ^{13}C at δ 77.00), unless otherwise stated. All NMR experiments were conducted at 300 K. Mass spectra were recorded on a Thermo Finnigan Trace GC Ultra instrument with EI mode. 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 Atago automatic polarimeter (AP-300). Elemental analysis were obtained using Perkin-Elmer's 2400 Series II CHNS.

1-(2,5-diisopropylphenyl)ethanol, (±)-**5**

A colourless solution of methylmagnesium bromide (3 M, 7.9 mL, 23.70 mmol) in dry THF (10 mL) was added dropwise to a stirring solution of **4** (2.25 g, 11.82 mmol) dissolved in the same solvent (10 mL) at 0 °C. The reaction mixture was stirred at room temperature for 16 h. The pale yellow mixture was poured into a mixture of ice water (20 mL) and concentrated HCl (1 mL) and left to stir for 5 min. The resulting mixture was then extracted with dichloromethane (3 x 50 mL), dried with MgSO_4 , filtered and evaporated to dryness. The crude product was purified *via* column chromatography using hexane/dichloromethane (*v/v* = 1:1) as eluent affording colourless oil. Yield: 2.39 g (98%); ^1H NMR (400 MHz, CDCl_3): δ = 1.24 (d, $^3J_{\text{H,H}}$ = 7.2 Hz, 6H, $\text{CH}(\text{CH}_3)_2$), 1.26 (d, $^3J_{\text{H,H}}$ = 6.8 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 1.49 (d, $^3J_{\text{H,H}}$ = 6.4 Hz, 3H, CHCH_3), 1.86 (brs, 1H, OH), 2.89 (sep, $^3J_{\text{H,H}}$ = 6.9 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 3.19 (sep, $^3J_{\text{H,H}}$ = 6.8 Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 5.25 (q, $^3J_{\text{H,H}}$ = 6.4 Hz, 1H, CHCH_3), 7.12 (dd, $^3J_{\text{H,H}}$ = 8.0 Hz, $^4J_{\text{H,H}}$ = 2.0 Hz, 1H, Ar-C₄H), 7.20 (d, $^3J_{\text{H,H}}$ = 8.0 Hz, 1H, Ar-C₃H), 7.38 (d, $^4J_{\text{H,H}}$ = 2.0 Hz, 1H, Ar-C₆H); ^{13}C NMR (100 MHz, CDCl_3): δ = 23.96, 24.01, 24.41, 25.02, 27.82, 33.82, 66.30, 122.81, 125.53, 142.12, 142.52, 142.47; HRMS (ESI, *m/z* (*M*+Na))⁺ calcd. for $\text{C}_{14}\text{H}_{22}\text{O}$ 229.1568, found 229.1559. Note: The isolated compound is highly hygroscopic and not suitable for elemental analysis.

2-(1-bromoethyl)-1,4-diisopropylbenzene, (±)-**6**

A solution of PBr_3 (1.3 mL, 13.9 mmol) dissolved in the dichloromethane (10 mL) was added drop wise to a solution of racemic alcohol (±)-**5** (2.39 g, 11.6 mmol) in dry dichloromethane (10 mL) at 0 °C. The mixture was left to stir at room temperature for 3 h. The excess PBr_3 was quenched by drop wise addition of H_2O (10 mL). The mixture was then extracted with dichloromethane (3 x 10 mL),

dried with MgSO_4 , filtered and evaporated to dryness, affording a colourless solution. Yield: 3.08 g (99%); ^1H NMR (400 MHz, CDCl_3): δ = 1.24–1.32 (m, 12H, $\text{CH}(\text{CH}_3)_2$), 2.09 (d, $^3J_{\text{H-H}} = 6.8$ Hz, 3H, $\text{CH}(\text{CH}_3)\text{Br}$), 2.91 (sep, $^3J_{\text{H-H}} = 6.9$ MHz, 1H, $\text{CH}(\text{CH}_3)_2$), 3.30 (sep, $^3J_{\text{H-H}} = 6.8$ MHz, 1H, $\text{CH}(\text{CH}_3)_2$), 5.59 (q, $^3J_{\text{H-H}} = 6.9$ MHz, 1H, $\text{CH}(\text{CH}_3)\text{Br}$), 7.15 (dd, $^3J_{\text{H-H}} = 8.0$ Hz, $^4J_{\text{H-H}} = 1.6$ Hz, 1H, Ar–C₅H), 7.20 (d, $^3J_{\text{H-H}} = 8.0$ Hz, 1H, Ar–C₆H), 7.42 (d, $^4J_{\text{H-H}} = 1.2$ Hz, 1H, Ar–C₃H); ^{13}C NMR (100 MHz, CDCl_3): δ = 23.27, 23.90, 23.94, 26.72, 28.13, 33.73, 45.77, 124.62, 125.50, 126.57, 139.34, 142.91, 146.53; HRMS (ESI, m/z (M+H))⁺ calcd. for $\text{C}_{16}\text{H}_{28}\text{N}$ 234.2222, found 234.2220. Note: The isolated compound must be converted to the amine immediately as it decomposes and not suitable for elemental analysis.

1-(2,5-diisopropylphenyl)-N,N-dimethylethanamine, (±)-7

A solution of aqueous dimethylamine (40 wt. %, 19.3 mL, 17.1 mmol) was added to a solution of bromo compound (±)-6 (3.08 g, 11.4 mmol) in dichloromethane (20 mL). The mixture was then left to stir at room temperature for 16 h. The organic layer was separated and the aqueous layer was extracted further with dichloromethane (2 x 25 mL). The clear organic solution was then washed with brine (50 mL), dried with MgSO_4 , filtered and evaporated to dryness. The crude product was purified *via* column chromatography using dichloromethane/ethyl acetate (v/v = 2:1) as eluent affording colorless oil. Yield: 2.62 g (98%); ^1H NMR (400 MHz, CDCl_3): δ = 1.22 (d, $^3J_{\text{H-H}} = 6.8$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$), 1.24 (d, $^3J_{\text{H-H}} = 6.8$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$), 1.32 (d, $^3J_{\text{H-H}} = 6.4$ Hz, 3H, CHCH_3), 2.22 (s, 6H, NCH_3), 2.88 (sep, $^3J_{\text{H-H}} = 6.9$ Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 3.34 (sep, $^3J_{\text{H-H}} = 6.9$ Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 3.47 (q, $^3J_{\text{H-H}} = 6.5$ Hz, 1H, CHCH_3), 7.07 (dd, $^3J_{\text{H-H}} = 8.0$ Hz, $^4J_{\text{H-H}} = 2.0$ Hz, 1H, Ar–C₄H), 7.18 (d, $^3J_{\text{H-H}} = 8.0$ Hz, 1H, Ar–C₃H), 7.31 (d, $^4J_{\text{H-H}} = 2.0$ Hz, 1H, Ar–C₆H); ^{13}C NMR (100 MHz, CDCl_3): δ = 21.85, 24.24, 24.26, 24.27, 24.29, 27.86, 33.94, 44.32, 61.44, 124.51, 125.13, 125.16, 142.04, 143.33, 146.36; HRMS (ESI, m/z (M+H))⁺ calcd. for $\text{C}_{16}\text{H}_{28}\text{N}$ 234.2222, found 234.2220. Note: The isolated compound is highly hygroscopic and not suitable for elemental analysis.

General procedure for palladation of tertiary amine ligand (±)-7

A solution of (±)-7 (0.10 g, 0.43 mmol) in the preferred solvent (3 mL) was added to a stirring mixture of palladating agent (0.43 mmol, 1.0 equivalent) in the presence of base (0.43 mmol, 1.0 equivalent) if required in the same solvent (3 mL). The reaction mixture was then stirred at the desired temperature for 16 h. The mixture was filtered through a plug of Celite® and concentrated. The crude product was then washed with H_2O , dried with MgSO_4 , filtered and evaporated to dryness. The crude product was purified *via* column chromatography. Complexes (±)-8 and palladacycle (±)-3 was eluted out using hexane/dichloromethane (V/V = 1:1) and dichloromethane as mobile phase respectively.

(±)-trans-dichlorobis[1-(2,5-diisopropylphenyl)-N-methylethanamine]palladium(II), (±)-8

The complex (±)-8 was obtained from PdCl_2 as palladating agent in methanol at 55 °C. Recrystallized from a solution of dichloromethane/diethyl ether to give bright yellow prisms. Yield: 38.3 mg (29%); m.p. 193–196 °C; ^1H NMR (400 MHz, CDCl_3): δ = 1.17–1.27 (m, 12H, $\text{CH}(\text{CH}_3)_2$), 2.09 (d, $^3J_{\text{H-H}} = 6.7$ Hz, 3H, CHCH_3), 2.34 (d, $^3J_{\text{H-H}} = 6.0$ Hz, 3H, NHCH_3), 2.89 (sep, $^3J_{\text{H-H}} = 6.6$ MHz, 1H,

$\text{CH}(\text{CH}_3)_2$), 3.17 (sep, $^3J_{\text{H-H}} = 6.8$ MHz, 1H, $\text{CH}(\text{CH}_3)_2$), 3.45 (brs, 1H, NHCH_3), 4.51 (q, 1H, CHCH_3), 6.90 (s, 1H, Ar–C₆H), 7.14 (dd, $^3J_{\text{H-H}} = 8.2$ Hz, $^4J_{\text{H-H}} = 1.6$ Hz, 1H, Ar–C₄H), 7.22 (d, $^3J_{\text{H-H}} = 8.2$ Hz, 1H, Ar–C₃H); ^{13}C NMR (100 MHz, CDCl_3): δ = 23.36, 23.89, 24.06, 24.62, 25.02, 28.03, 33.75, 38.17, 56.04, 121.85, 125.81, 125.96, 136.91, 144.40, 147.33; HRMS (ESI, m/z (M–Cl))⁺ calcd. for $\text{C}_{30}\text{H}_{50}\text{N}_2\text{ClPd}$ 581.2701, found 581.2690. Anal. Calcd for $\text{C}_{30}\text{H}_{50}\text{Cl}_2\text{N}_2\text{Pd}$: C, 58.49, H, 8.18, N, 4.55. Found: C, 58.30, H, 8.39, N, 4.64.

(±)-Di-μ-chlorobis{2-[1'-(dimethylamino)ethyl]-3,6-diisopropylphenyl-C,N}dipalladium(II)), (±)-3

The complex (±)-3 was obtained from the reaction of $\text{Li}_2[\text{PdCl}_4]$ with tertiary amine (±)-7 dissolved in methanol in the presence of NaOAc at room temperature. Recrystallized from a solution of dichloromethane/diethyl ether to give needle-like bright yellow crystals. Yield: 125.0 mg (78%); m.p. 189–190 °C (dec.); ^1H NMR (400 MHz, CDCl_3): δ = 1.12–1.25 (m, 12H, $\text{CH}(\text{CH}_3)_2$), 2.28–2.29 (m, 3H, CHCH_3), 2.59–2.62 (m, 6H, NCH_3), 2.78 (sep, $^3J_{\text{H-H}} = 6.8$ Hz, 1H, $\text{CH}(\text{CH}_3)_2$), 3.61 (m, 1H, $\text{CH}(\text{CH}_3)_2$), 3.86 (m, 1H, CHCH_3), 6.76–6.87 (m, 2H, aromatic); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 23.39, 24.34, 25.04, 26.84, 31.22, 33.92, 50.71, 75.28, 122.24, 140.56, 149.56, 149.12, 151.03; HRMS (ESI, m/z (M–Cl))⁺ calcd. for $\text{C}_{32}\text{H}_{52}\text{N}_2\text{Cl}_2\text{Pd}_2$ 713.1893, found 713.1901. Anal. Calcd for $\text{C}_{32}\text{H}_{52}\text{Cl}_2\text{N}_2\text{Pd}_2$: C, 51.35, H, 7.00, N, 3.74. Found: C, 51.53, H, 6.71, N, 3.80.

(±)-chloro{2-[1'-(dimethylamino)ethyl]-3,6-diisopropylphenyl-C,N}(triphenylphosphine-P)palladium(II), (±)-9

Triphenylphosphine (0.35 g, 1.33 mmol) was added to a solution of racemic dimer (±)-3 (0.50 g, 0.67 mmol) dissolved in dichloromethane (10 mL). The mixture was left to stir for 1 h at room temperature. The reaction mixture was then evaporated to dryness to afford complex (±)-9. Recrystallized from a solution of dichloromethane/hexane to give bright yellow crystals. Yield: 0.20 g (95%); m.p. 178–181 °C; ^1H NMR (400 MHz, CDCl_3): δ = 0.22 (d, $^3J_{\text{H-H}} = 6.8$ Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.16 (d, $^3J_{\text{H-H}} = 6.8$ Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 1.25–1.28 (m, 6H, $\text{CH}(\text{CH}_3)_2$), 2.08 (d, $^3J_{\text{H-H}} = 6.4$ Hz, 3H, CHCH_3), 2.43 (d, $^4J_{\text{P-H}} = 2.0$ Hz, 3H, $\text{NCH}_3(\text{ax})$), 2.48–2.53 (m, 1H, $\text{CH}(\text{CH}_3)_2$), 2.81 (d, $^4J_{\text{P-H}} = 3.6$ Hz, 3H, $\text{NCH}_3(\text{eq})$), 2.84–2.90 (m, 1H, $\text{CH}(\text{CH}_3)_2$), 3.73 (qn, $^3J_{\text{H-H}} = ^4J_{\text{P-H}} = 6.4$ Hz, 1H, CHCH_3), 6.39–7.64 (m, 17H, aromatic); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 19.72, 22.50, 23.38, 24.61, 29.25, 30.44, 33.84 (d, $J_{\text{C-P}} = 11.8$ Hz), 49.09, 50.47, 74.31 (d, $J_{\text{C-P}} = 3.1$ Hz), 121.08–158.70 (13C, aromatic); $^{31}\text{P}\{^1\text{H}\}$ NMR (161 MHz, CDCl_3): δ 30.7 (s); HRMS (ESI, m/z (M–Cl))⁺ calcd. for $\text{C}_{34}\text{H}_{41}\text{N}_2\text{PPd}$ 600.2011, found 600.1981. Anal. Calcd for $\text{C}_{34}\text{H}_{41}\text{ClN}_2\text{PPd}$: C, 64.15, H, 6.49, N, 2.20. Found: C, 64.52, H, 6.34, N, 2.22.

($R_C\text{ScSc}_N$)-{2-[1'-(dimethylamino)ethyl]-3,6-diisopropylphenyl-C,N}(prolinato-N,O)palladium(II)), ($R_C\text{ScSc}_N$)-10

A solution of sodium (S)-proline (0.65 g, 4.74 mmol) in methanol (20 mL) was added to a solution of racemic dimer, (±)-3 (1.79 g, 2.39 mmol) dissolved in the same solvent (20 mL). The mixture was stirred for 1 h. The solvent was subsequently removed under reduced pressure before being dissolved in dichloromethane. The solution was then washed with water (3 x 100 mL), dried with MgSO_4 , filtered and evaporated to dryness. The ($R_C\text{ScSc}_N$)-10 adduct was separated *via*

column chromatography using dichloromethane/acetone (v/v: 1:1). The complex was recrystallized from a solution of dichloromethane and diethyl ether to give yellow plate-like single crystals. Yield: 0.44 g (82%) (based on half equivalent of dimer used); m.p. 200–201 °C (dec.); [α] $^{23.4}_D$ = +43.4° (c 0.02, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 1.13–1.29 (m, 12H, CH(CH₃)₂), 1.67–1.96 (m, 3H, CH₂CH₂CH₂ and COCHCH₂), 2.03 (d, ³J_{H,H} = 6.4 Hz, 3H, CHCH₃), 2.52–2.58 (m, 1H, COCHCH₂), 2.59 (s, 3H, NCH₃(eq)), 2.63 (s, 3H, NCH₃(ax)), 2.79 (sep, ³J_{H,H} = 6.7 Hz, 2H, CH(CH₃)₂), 3.20–3.36 (m, 3H, NHCH₂ and NH), 3.63 (q, ³J_{H,H} = 6.4 Hz, 1H, CHCH₃), 4.20 (m, 1H, COCHCH₂), 6.85 (d, ³J_{H,H} = 8.0 Hz, 1H, Ar–C₄H), 6.92 (d, ³J_{H,H} = 8.0 Hz, 1H, Ar–C₅H); ¹³C NMR (100 MHz, CDCl₃): δ = 22.78, 23.17, 23.65, 23.78, 24.84, 26.24, 28.84, 30.40, 33.73, 48.51, 50.92, 53.33, 66.98, 73.14, 121.73, 122.48, 140.40, 144.06, 149.44, 150.09, 177.89; HRMS (ESI, m/z (M+H))⁺ calcd for C₂₁H₃₅N₂O₂Pd 453.1733, found 453.1742. Anal. Calcd for C₂₁H₃₄ClN₂O₂Pd·0.05CH₂Cl₂: C, 55.30, H, 7.52, N, 6.13. Found: C, 55.20, H, 7.48, N, 5.94.

(S_C,S_CN)-{2-[1'-(dimethylamino)ethyl]-3,6-diisopropylphenyl-C,N}-{prolinato-N,O}palladium(II)), (S_C,S_CN)-**10**

The other diastereomer (S_C,S_CN)-**10** was obtained by using methanol as mobile phase. The complex was recrystallized from a solution of dichloromethane and hexane to give colorless needles single crystals. Yield: 0.43 g (80%); [α] $^{23.4}_D$ = +196.9° (c 0.02, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 1.13–1.33 (m, 12H, CH(CH₃)₂), 1.60–2.05 (m, 2H, CH₂CH₂CH₂), 2.07 (d, ³J_{H,H} = 6.4 Hz, 3H, CHCH₃), 2.17–2.39 (m, 2H, COCHCH₂), 2.55 (s, 3H, NCH₃(ax)), 2.67 (s, 3H, NCH₃(eq)), 2.72 (sep, ³J_{H,H} = 6.8 Hz, 1H, CH(CH₃)₂), 2.81 (sep, ³J_{H,H} = 6.8 Hz, 1H, CH(CH₃)₂), 3.10–3.25 (m, 2H, NHCH₂), 2.51–2.53 (m, 1H, NH), 3.63 (q, ³J_{H,H} = 6.2 Hz, 1H, CHCH₃), 4.06 (m, 1H, COCHCH₂), 6.84 (d, ³J_{H,H} = 8.0 Hz, 1H, Ar–C₄H), 6.91 (d, ³J_{H,H} = 8.4 Hz, 1H, Ar–C₅H); ¹³C NMR (100 MHz, CDCl₃): δ = 22.75, 23.07, 23.93, 24.89, 25.09, 26.34, 29.77, 30.45, 34.28, 48.30, 52.92, 53.43, 65.41, 73.22, 121.34, 122.79, 140.05, 145.60, 149.40, 149.89, 179.84. Anal. Calcd for C₂₁H₃₄ClN₂O₂Pd·0.10CH₂Cl₂: C, 54.92, H, 7.47, N, 6.07. Found: C, 55.05, H, 7.49, N, 5.95.

(S,S)-Di- μ -chlorobis{2-[1'-(dimethylamino)ethyl]-3,6-diisopropylphenyl-C,N}dipalladium(II)), (S,S)-**3**

The complex (S_C,S_CN)-**10** (0.41 g, 0.93 mmol) dissolved in dichloromethane (10 mL) was treated with 1 M HCl (5 mL) and left to stir at room temperature for 30 min. The organic layer was then separated, washed with water (2 x 10 mL), dried with MgSO₄, filtered and evaporated to dryness to afford the dimeric complex (S)-**3**. Yield: 0.31 g (90%); [α] $^{23.8}_D$ = +180.7° (c 0.02, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 1.14–1.25 (m, 12H, CH(CH₃)₂), 2.28 (d, ³J_{H,H} = 6.0 Hz, 3H, CHCH₃), 2.59–2.62 (m, 6H, NCH₃), 2.78 (sep, ³J_{H,H} = 6.8 Hz, 1H, CH(CH₃)₂), 3.61 (m, 1H, CH(CH₃)₂), 3.60–3.85 (m, 2H, CHCH₃ and CH(CH₃)₂), 6.76–6.87 (m, 2H, aromatic); ¹³C NMR (100 MHz, CDCl₃): δ = 22.96, 23.88, 24.81, 26.64, 30.67, 50.18, 74.61, 121.64, 123.62, 123.76, 139.90, 150.36 ppm. HRMS (ESI, m/z (M–Cl))⁺ calcd. for C₃₂H₅₂N₂ClP₂ 713.1893, found 713.1901. Anal. Calcd for C₃₂H₅₂Cl₂N₂Pd₂: C, 51.35, H, 7.00, N, 3.74. Found: C, 51.52, H, 7.11, N, 3.77.

(S)-{2-[1'-(dimethylamino)ethyl]-3,6-diisopropylphenyl-C,N}{3,4-dimethyl-1-phenylphosphole-P}palladium(II)), (S)-**11**

A solution of the dimeric complex (S)-**3** (1.0 g, 1.3 mmol) dissolved in degassed dichloromethane (5 mL) was added to a mixture of 3,4-

dimethyl-1-phenylphosphole (DMPP) (0.49 g, 2.6 mmol) in the same solvent (5 mL). The mixture was subsequently stirred for 30 min at room temperature. The reaction mixture was then evaporated to dryness and purified *via* column chromatography using dichloromethane as eluent affording yellow solids. The complex was recrystallized from a solution of dichloromethane and hexane to give yellow needles single crystals. Yield: 1.35 g (90 %); m.p. 158–161 °C (dec); [α] $^{23.4}_D$ = +431.5° (c 0.01, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 0.96–1.24 (m, 12H, CH(CH₃)₂), 1.87 (d, ³J_{H,H} = 6.4 Hz, 3H, CH(CH₃), 1.98 (s, 3H, C=CCH₃), 2.01 (s, 3H, C=CCH₃), 2.43 (d, ⁴J_{P,H} = 2.0 Hz, 3H, NCH₃(ax)), 2.71 (sep, ³J_{H,H} = 6.4 Hz, 1H, CH(CH₃)₂), 2.67 (d, ⁴J_{P,H} = 3.6 Hz, 3H, NCH₃(eq)), 2.83 (sep, ³J_{H,H} = 6.8 Hz, 1H, CH(CH₃)₂), 3.67 (qn, ³J_{H,H} = ⁴J_{H,P} = 6.4 Hz, 1H, CH(CH₃), 6.06 (d, ²J_{P,H} = 32.4 Hz, 1H, C=CCH), 6.76 (d, ²J_{P,H} = 31.6 Hz, 1H, C=CCH), 6.81 (d, ³J_{H,H} = 8.0 Hz, 1H, Ar–C₄H), 6.87 (d, ³J_{H,H} = 8.0 Hz, 1H, Ar–C₅H), 7.29–7.84 (m, 5H, PPh); ¹³C NMR (100 MHz, CDCl₃): δ = 17.26 (d, J_{C,P} = 20.2 Hz), 17.76 (d, J_{C,P} = 19.7 Hz), 20.75, 22.53, 22.83, 23.08, 28.55, 30.42, 37.79 (d, J_{C,P} = 20.1 Hz), 48.62, 50.54 (d, J_{C,P} = 4.6 Hz), 73.44 (d, J_{C,P} = 5.3 Hz), 121.16–152.91 (22C, aromatic); ³¹P{¹H} NMR (161 MHz, CDCl₃): δ = 28.4 (s); HRMS (ESI, m/z (M–Cl))⁺ calcd. for C₂₈H₃₉NPPd 526.1855, found 526.1874. Anal. Calcd for C₂₈H₃₉NPPd·0.1CH₂Cl₂: C, 59.11, H, 6.92, N, 2.45. Found: C, 59.35, H, 6.58, N, 2.59.

Asymmetric [4+2] endo-Cycloaddition Reactions between Complex (S)-**11** and Ethyl Vinyl Ketone

A mixture of the DMPP-coordinated complex (S)-**11** (83.8 mg, 0.15 mmol) and ethyl vinyl ketone (0.1 mL, 1.00 mmol) in chloroform (3 mL) was left to stir at 50 °C and was monitored by ³¹P{¹H} NMR spectroscopy. After 5 days, two new peaks with a diastereomeric ratio of 4.4:1 were observed. The reaction mixture was then filtered through a plug of Celite® and evaporated to dryness. The major product was eluted *via* column chromatography using dichloromethane as the eluent affording yellow oil. Yield: 6.8 mg (7.4%); ¹H NMR (400 MHz, CDCl₃): δ = 0.69–0.76 (m, 3H, COCH₂CH₃), 1.16–1.42 (m, 12H, CH(CH₃)₂), 1.55 (s, 3H, C=CCH₃), 1.60 (s, 3H, C=CCH₃), 1.91–2.06 (m, 3H, COCH₂CH₃ and CH₂CHCO), 2.08 (d, ³J_{H,H} = 6.4 Hz, 3H, CHCH₃), 2.41 (s, 3H), 2.71 (sep, ³J_{H,H} = 6.4 Hz, 1H, CH(CH₃)₂), 2.41 (d, ⁴J_{P,H} = 1.6 Hz, 3H, NCH₃(ax)), 2.64 (sep, ³J_{H,H} = 6.4 Hz, 1H, CH(CH₃)₂), 2.76 (d, ⁴J_{P,H} = 3.2 Hz, 3H, NCH₃(eq)), 2.82–2.90 (m, 1H, CH(CH₃)₂), 3.73 (qn, ³J_{H,H} = 6.4 Hz, 1H, CH(CH₃), 6.87–7.92 (m, 5H, PPh) ppm. ³¹P{¹H} NMR (161 MHz, CDCl₃): δ = 119.4 (s) (other unknown by-products peaks at δ 21.2 (s) and 67.4 (d)) were also observed).

Supporting Information available:

¹H, ¹³C, ³¹P{¹H}, 2D ¹H–¹H, ROSEY Spectrums and single crystal X-ray crystallographic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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