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Article

Novel Synthesis of Chiral 1,3-Diphosphines via Palladium Template Promoted Hydrophosphination and Functional Group Transformation Reactions

Mingjun Yuan, Sumod A. Pullarkat, Yongxin Li, Zhi-Yi Lee, and Pak-Hing Leung*

Division of Chemistry & Biological Chemistry, School of Physical & Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

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A novel cyano-functionalized monophosphine palladium substrate containing the *ortho*-metalated (*R*)-(1-(dimethylamino)ethyl)naphthalene as the chiral auxiliary was synthesized from 3-chloropropionaldehyde diethylacetal via a one-pot process. The asymmetric hydrophosphination reactions between diphenylphosphine and the *trans*- or *cis*-monophosphine substrates were carried out under mild conditions, which gave the corresponding cyano-substituted chiral 1,3-bis(diphenylphosphino)-propane palladium complexes with good yields and stereoselectivities. Subsequent functional group transformation reactions were conducted by successive treatment of the hydrophosphination products with Dibal-H and chemoselectively yielded the formyl- and hydroxyl-functionalized chiral 1,3-diphosphine complexes. The absolute configurations and coordination information of the novel 1,3-diphosphine complexes were analyzed by X-ray crystallography. The optically pure 1,3-bis-(diphenylphosphino)propane ligands with cyano, formyl, and hydroxyl functionalities could be liberated in high yields from the corresponding dihalo palladium complexes by treatment with aqueous potassium cyanide.

Introduction

The design and synthesis of new chiral phosphine ligands continues to be a research topic of great interest in modern organophosphorus chemistry, since the enantiomerically pure phosphines have established their position as highly effective ligands in transition metal catalyzed asymmetric reactions on both research laboratory and industrial scales.[1] It is conceivable that the presence of proper functional groups, for instance hydroxyl, amino, or ester, on these chiral phosphine frameworks can efficiently improve both reactivity and enantioselectivity in many reactions through the secondary interactions with the reacting substrates.[2] Over the past few years, our group has successfully prepared a series of functionalized chiral phosphine ligands by means of asymmetric hydrophosphination and Diels−Alder reactions, promoted by the organopalladium complexes containing (*R*)- or (*S*)-(1-(dimethylamino)ethyl)naphthalene as the chiral auxiliary.[3,4] In the course of these series of studies, the use of stoichiometric amounts of palladium complex as reaction promoter offers practical advantages. (1) By means of coordination, it can protect the phosphine species from oxidation or racemization especially when it comes to the synthesis of *P*-stereogenic phosphine ligands. (2) By tuning the chloro ligand that is *trans* to the naphthalene ring, it can alternatively provide one or two distinct coordination sites around the square-planar palladium center to selectively synthesize functionalized mono- or diphosphine ligands. (3) It can offer high stereoselectivity during the asymmetric process and can also serve as a resolving agent when there are more than one

*To whom correspondence should be addressed. E-mail: pakhing@ntu.edu.sg.

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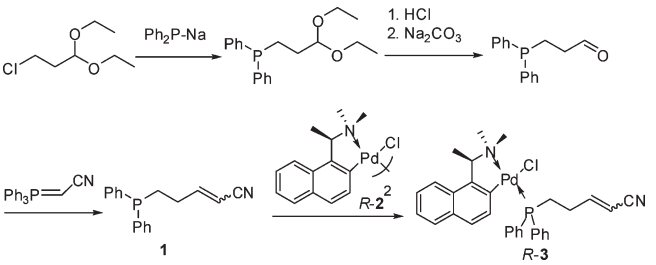
isomer produced, thus facilitating their easy separation and isolation. (4) We can *in situ* study the coordination properties and absolute stereochemistries of the chiral phosphine palladium complexes, which may give us some insights on how the metal complex interacts with substrates during the asymmetric transformations. And last, (5) the air-stable optically pure phosphine complexes could easily yield the free phosphine ligands by treatment with aqueous potassium cyanide.

Unlike the classical 1,2-diphosphines, 1,3-diphosphines can form six-membered chelates involving transition metals with interesting coordinated conformations[5] and have played an important role as ligands in a large family of homogeneous transition metal catalysis.[6] However, reports on the asymmetric synthesis of functionalized chiral 1,3-diphosphine ligands are relatively rare. This paper describes a facile synthesis of three novel chiral 1,3-bis(diphenylphosphino)propane ligands with cyano, formyl, and hydroxyl functionalities, via an organopalladium complex promoted hydrophosphination and subsequent *in situ* functional group transformation reactions. This current work is part of our efforts in the development of new chiral phosphines by employing chiral cyclopalladated amine complexes.

Scheme 1



Results and Discussion

From the perspective of atom economy, the addition of diphenylphosphine to α,β-unsaturated nitriles provides a direct route to a large family of useful functionalized phosphine ligands.[7] Furthermore, the cyano group is suitable for conversion to other functionalities such as acid, amide, amine, aldehyde, or alcohol by simple organic manipulations.[7h−j,8] In principle, if a phosphorus atom was introduced into the α,β-unsaturated nitrile substrates, the subsequent hydrophosphination and functional group transformation reactions will generate a class of novel diphosphines, for example, the chiral cyano-, formyl-, and hydroxyl-substituted 1,3-bis(diphenylphosphino)propane ligands.

The one-pot synthesis of cyano-functionalized monophosphine palladium complex *R*-**3** is illustrated in Scheme 1. The 3-chloropropionaldehyde diethylacetal reacted smoothly with sodium diphenylphosphide, and the resulting intermediate was hydrolyzed and subsequently treated with (triphenylphosphoranylidene)acetonitrile to afford 5-(diphenylphosphino)pent-2-enenitrile **1**. This new phosphine species was not isolated and was *in situ* coordinated to palladium template *R*-**2** to generate the monomeric phosphine complex *R*-**3** as a mixture of *Z*/*E* (1:1.8) isomers in 82% yield. The two products could be easily separated by column chromatography. The ^{31}P NMR spectrum in $CDCl_3$ of *trans*-*R*-**3** exhibited a sharp singlet at δ 34.6, while the *cis*-*R*-**3** isomer indicated a singlet resonance signal at δ 34.8. Both isomers can be easily recrystallized from ethyl acetate/hexanes as pale yellow prisms. The molecular structure and coordination property of *trans*-*R*-**3** were characterized by means of single-crystal diffraction analysis, as shown in Figure 1. Selected bond lengths and angles and other crystallographic data are listed in Tables 1 and 4, respectively. The geometry at the palladium atom is distorted square planar with angles at the metal center in the range 80.6(1)−97.0(1)° and 169.6(1)−169.9(1)°. The C17−C18 bond length is 1.295(5) Å, which exhibits clearly double-bond character. As expected, the monodentate phosphorus donor atom is located *trans* to the σ-donating nitrogen group of the chiral auxiliary.

Asymmetric Hydrophosphination of Cyano-Functionalized Monophosphine Palladium Complex *R*-3. The chloro ligand in *trans*-*R*-**3** and similar complexes that is *trans* to the *ortho*-metalated aromatic carbon is well known to be both kinetically and thermodynamically stable.[3] This terminal ligand, however, can be replaced efficiently by treatment of the complex with aqueous silver perchlorate to provide a vacant coordination site (Scheme 2). The highly reactive perchlorato complex *R*-**4** was not isolated and was subsequently reacted with one equivalent of diphenylphosphine in the

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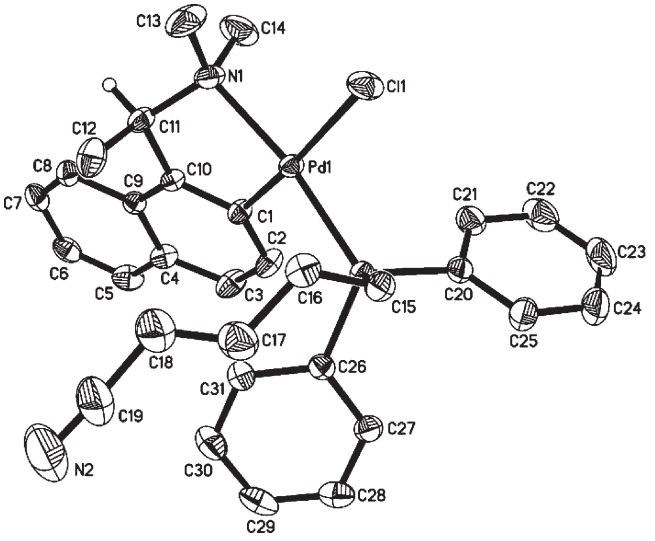


Figure 1. Molecular structure of complex *trans*-*R*-**3**.

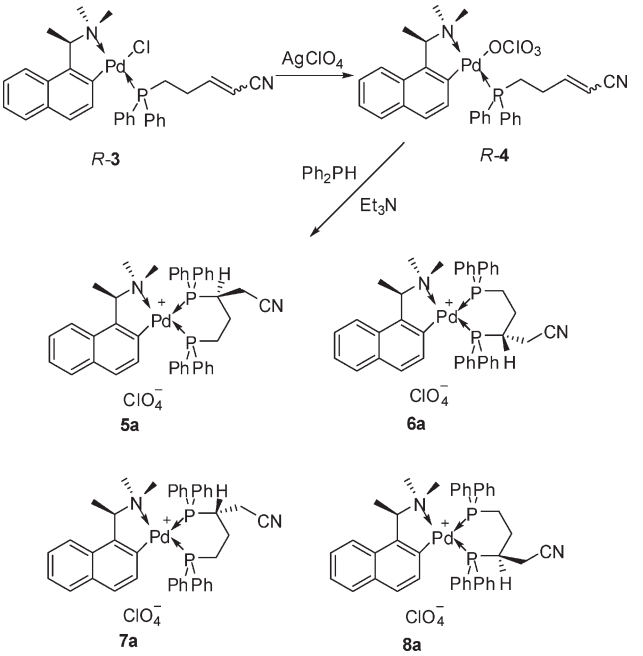
Table 1. Selected Bond Lengths (Å) and Angles (deg) of *trans*-*R*-3

Pd1−C1	2.000(2)	Pd1−N1	2.135(2)
Pd1−Cl1	2.389(1)	Pd1−P1	2.249(1)
P1−C15	1.843(2)	C15−C16	1.525(4)
C16−C17	1.486(4)	C17−C18	1.295(5)
C18−C19	1.441(5)	C19−N2	1.119(5)
C1−Pd1−N1	80.6(1)	C1−Pd1−P1	97.0(1)
P1−Pd1−Cl1	89.8(1)	N1−Pd1−Cl1	94.1(1)
N1−Pd1−P1	169.9(1)	C1−Pd1−Cl1	169.6(1)
P1−C15−C16	116.4(2)	C16−C17−C18	125.7(3)
C17−C18−C19	123.5(4)	C18−C19−N2	175.3(6)

presence of triethylamine as external base at −78 °C to yield the novel hydrophosphination products. The process was monitored by ^{31}P NMR spectroscopy and was found to be completed within 2 h. In $CDCl_3$, the 162 MHz ^{31}P NMR spectrum of the crude product exhibited the presence of three pairs of doublets at δ −10.2, 33.0 (J_{PP} = 55.7 Hz); −1.1, 35.3 (J_{PP} = 52.1 Hz); and 8.3, 27.1 (J_{PP} = 51.7 Hz) with the intensity ratio of 1:1.3:3.7, respectively. The signals indicated that three of the four possible isomeric products, i.e., **5a**, **6a**, **7a**, and **8a**, were generated during the hydrophosphination process, as shown in Scheme 2. It is noteworthy that complexes **5a** and **6a** are regioisomers that adopt the same *S* absolute configuration at the newly formed chiral carbon centers. Similarly, complexes **7a** and **8a** are regioisomers with *R* absolute configuration at the new stereogenic centers. Therefore the diastereomeric ratio was 1:5 for the overall process.

The two major regioisomers **5a** and **6a** can be efficiently separated as off-white solids by column chromatography in 70% yield.[9] The ^{31}P NMR spectrum ($CDCl_3$, 162 MHz) showed two pairs of doublets at δ −1.1, 35.3 (J_{PP} = 52.1 Hz) and 8.3, 27.1 (J_{PP} = 51.7 Hz). The chiral naphthylamine auxiliary on complexes **5a** and **6a** could be chemoselectively removed by treatment of the isomers with concentrated

Scheme 2



hydrochloric acid in the presence of NaI (Scheme 3).[10] Thus, the optically pure diiodo palladium complex **9a** was obtained as a red solid in 79% yield, $[\alpha]_D$ = −10.7 (*c* 1.3, CH_2Cl_2). The ^{31}P NMR spectrum (CD_2Cl_2, 162 MHz) of product **9a** exhibited a pair of doublets at δ 4.2, 8.8 (J_{PP} = 21.3 Hz). Unfortunately, efforts to crystallize the neutral complex **9a** from various solvent systems to get suitable crystals for X-ray crystallography were unsuccessful.[11]

Treatment of a CH_2Cl_2 solution of product **9a** with aqueous potassium cyanide can conveniently liberate the enantiomerically pure cyano-functionalized 1,3-diphosphine ligand **10a** as a white solid in high yield, $[\alpha]_D$ = −28.5 (*c* 1.3, CH_2Cl_2). The ^{31}P NMR ($CDCl_3$, 162 MHz) spectrum of the free ligand showed two singlet signals at δ −17.5 (s), −8.3 (s). As illustrated in Scheme 4, in order to confirm the optical purity of the free phosphine ligand **10a** and the ^{31}P NMR assignment for the regioisomers, the liberated ligand was recoordinated to the bis(acetonitrile) complex *R*-**11**. The resultant recomplexation products in $CDCl_3$ indeed exhibited two pairs of phosphorus doublets at δ −1.1, 35.3 (J_{PP} = 52.1 Hz) and 8.3, 27.1 (J_{PP} = 51.7 Hz), which were identical with the two major products from the original hydrophosphination reaction and, therefore, indicated the formation of the regioisomers **5a** and **6a**. Furthermore, the recoordination of **10a** to the equally accessible bis(acetonitrile) complex *S*-**11** will generate the regioisomers **12a** and **13a**, which exhibited two distinct pairs of doublets at δ − 10.2, 33.0 (J_{PP} = 55.7 Hz) and 6.2, 26.6 (J_{PP} = 54.9 Hz). Note that the products **12a** and **13a** are the enantiomeric forms of **7a** and **8a**, respectively. Thus no resonance signals were observed at δ −1.1, 8.3, 27.1, and 35.3, and the free 1,3-diphosphine **10a** was hence confirmed to be optically pure.

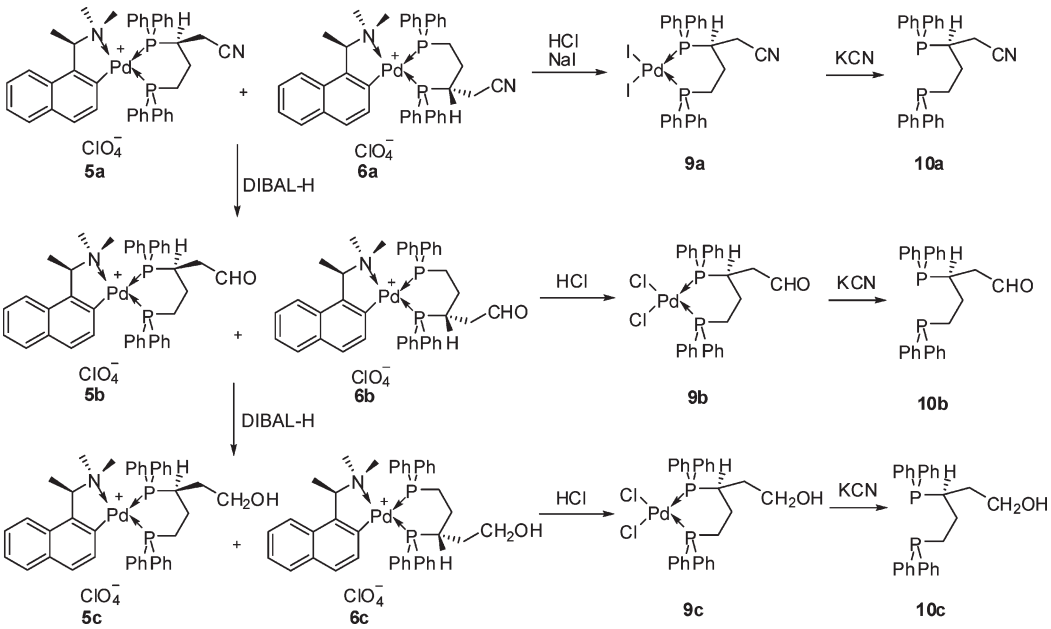
For comparison of the stereoselectivity, the *Z*-form monophosphine substrate *cis*-*R*-**3** was also employed for the same asymmetric hydrophosphination reaction. Under similar

(9) During the course of column chromatography, a pair of new doublet phosphorus signals at δ 6.2, 26.6 (J_{PP} = 54.9 Hz) appeared, which indicated the formation of one of the regioisomers **7a** or **8a**. So the ^{31}P NMR ($CDCl_3$, 162 MHz) signals of the regioisomers **7a** and **8a** were two pairs of doublets at δ −10.2, 33.0 (J_{PP} = 55.7 Hz); 6.2, 26.6 (J_{PP} = 54.9 Hz). However, the minor regioisomers **7a** and **8a** cannot be isolated at this stage.

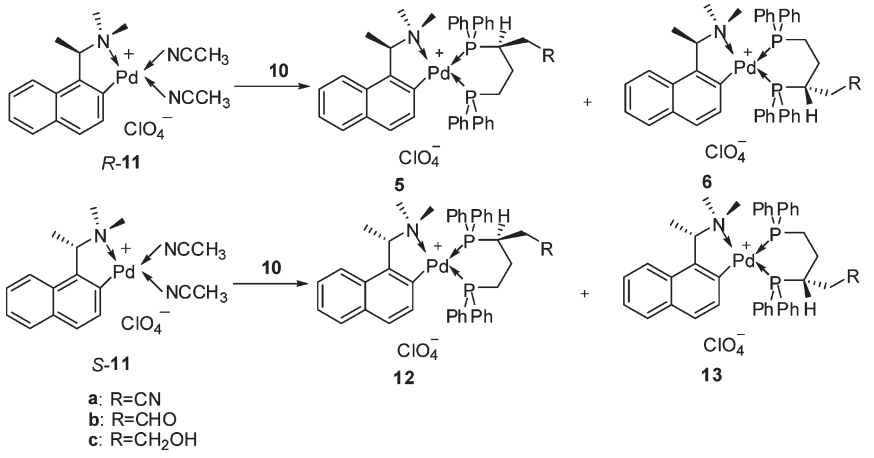
(10) Without addition of NaI, the reaction will yield the dichloro palladium complex. However, the solubility of the dichloro analogue of **10a** is too poor for characterization.

(11) The absolute configurations of the chiral diiodo palladium complex **9a** and the regioisomers **5a** and **6a** were revealed by the following functional group transformation reactions.

Scheme 3



Scheme 4



reaction conditions, the addition process could be completed within 2 h. Interestingly, the ^{31}P NMR ($CDCl_3$, 162 MHz) spectrum of the crude product obtained from this addition process indicated the same three pairs of doublets at δ −10.2, 33.0 (J_{PP} = 55.7 Hz); −1.1, 35.3 (J_{PP} = 52.1 Hz); and 8.3, 27.1 (J_{PP} = 51.7 Hz), however, with the distinct intensity ratio of 1:1.5:5.3, respectively. Apparently, the selectivity at the newly formed chiral carbon center slightly improved from 1:5 (for *trans*-*R*-**3**) to 1:6.8 (for *cis*-*R*-**3**).

Functional Group Transformations: Synthesis of Formyl- and Hydroxyl-Substituted 1,3-Diphosphine Products. As aforementioned, the cyano group could be converted to other functionalities, for example, acid, amide, amine, aldehyde, or alcohol by simple functional group transformations.[7h−j,8] Thus, upon treatment of the CH_2Cl_2 solution of regioisomers **5a** and **6a** with DIBAL-H at −78 °C for 2 h, the ^{31}P NMR spectrum in $CDCl_3$ of the reduction products showed two new pairs of doublet signals at δ −0.1, 37.2 (J_{PP} = 52.3 Hz) and 9.9, 27.7 (J_{PP} = 52.7 Hz), which indicated the formation of the formyl-functionalized regioisomers **5b** and **6b** (Scheme 3). The chiral naphthylamine auxiliary in **5b** and **6b** was removed by stirring a CH_2Cl_2 solution of the regioisomers with concentrated hydrochloric acid at room temperature. The optically pure dichloro complex **9b** was subsequently crystallized from dichloromethane and diethyl ether as yellowish prisms in 68% yield, $[\alpha]_D$ = +24.4 (*c* 0.9, CH_2Cl_2). The ^{31}P NMR spectrum of this neutral dichloro complex **9b** in CD_2Cl_2 exhibited a pair of doublets at δ 15.3, 21.8 (J_{PP} = 12.5 Hz).

The single-crystal X-ray crystallographic analysis unambiguously established its absolute configuration and the functionality transformation. There are two crystallographically independent molecules in the asymmetric unit with the backbone slightly disordered. Both molecules have similar bond lengths and angles and the identical *S* absolute configuration at the newly formed chiral carbon center. Figure 2 shows the ORTEP drawing of molecule 1; selected bond and angle parameters are given in Table 2. The coordinated geometry around the Pd atom is square planar with slight tetrahedral distortion (9.6°), while the angles around the palladium center are in the ranges 87.0(5)−93.2(5)° and 171.4(1)−173.9(5)°. The P−Pd−P bite angle (93.2(5)°) is clearly larger than in the case of 1,2-diphosphine chelates previously reported.[3] The six-membered chelate in complex

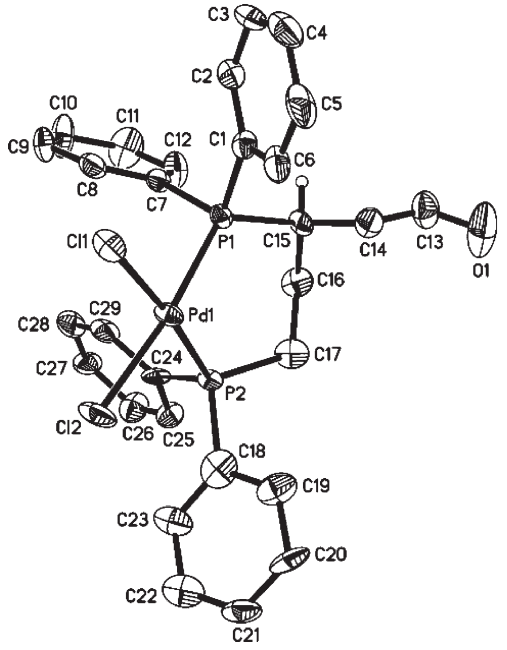


Figure 2. Molecular structure and absolute stereochemistry of complex **9b**.

Table 2. Selected Bond Lengths (Å) and Angles (deg) of 9b

Pd1−P1	2.270(3)	Pd1−Cl1	2.343(2)
Pd1−P2	2.264(8)	Pd1−Cl2	2.344(3)
C15−P1	1.862(9)	C15−C16	1.553(17)
C17−P2	1.807(16)	C13−O1	1.177(12)
P2−Pd1−P1	93.2(5)	Cl2−Pd1−Cl1	88.4(1)
P1−Pd1−Cl2	171.4(1)	P2−Pd1−Cl1	173.9(5)
P1−Pd1−Cl1	90.8(1)	P2−Pd1−Cl2	87.0(5)

9b adopts a twist-chair conformation with the formyl group occupying the sterically favorable equatorial position.

The optically active 1,3-diphosphine **10b** could be liberated by treatment of the **9b** with aqueous potassium cyanide as a white solid in 86% yield, $[\alpha]_D = -22.6$ (*c* 1.7, CH_2Cl_2). The ^{31}P NMR spectrum of the liberated diphosphine ligand in $CDCl_3$ showed two singlets at δ −16.4 and −6.8. The optical purity of **10b** was also confirmed by recoordination of the chiral ligand to the bis(acetonitrile) complex *R*-**11** (Scheme 4). The ^{31}P NMR spectrum of the recomplexation products gave two pairs of doublets at δ −0.1, 37.2 (J_{PP} = 52.3 Hz) and 9.9, 27.7 (J_{PP} = 52.7 Hz), which were apparently due to the formation of the original regioisomers **5b** and **6b**. However, the recomplexation products involving *S*-**11** generated two new regioisomers, **12b** and **13b**, with two pairs of different doublets at δ −8.0, 36.6 (J_{PP} = 54.9 Hz) and 7.7, 26.9 (J_{PP} = 55.8 Hz). Thus, the recoordination process therefore confirmed that the liberated formyl-substituted 1,3-diphosphine was enantiomerically pure, and the chirality remained unaffected throughout the reduction reaction.

Continuous treatment of the regioisomers **5b** and **6b** with DIBAL-H could chemoselectively yield the novel hydroxyl-functionalized regioisomers **5c** and **6c** (Scheme 3). The reduction process could be finished within 2 h at −78 °C, and the ^{31}P NMR spectrum exhibited two pairs of doublets at δ −0.8, 37.1 (J_{PP} = 53.3 Hz) and 11.3, 28.5 (J_{PP} = 52.8 Hz). *In situ* removal of the chiral amine auxiliary of **5c** and **6c** with concentrated hydrochloric acid yielded the optically pure dichloro complex **9c** as pale yellow cubic crystals from dichloromethane and diethyl ether in 72% yield, $[\alpha]_D = +31.1$ (*c* 1.0, CH_2Cl_2). The dichloro product **9c** showed a pair of doublets at δ 15.6, 23.5 (d, J_{PP} = 14.5 Hz). The molecular structure was studied by X-ray crystallography (Figure 3). Selected bond lengths and angles are listed in Table 3. As expected, the palladium atom adopted a square-planar geometry but with a smaller tetrahedral distortion (2.8°), while the angles

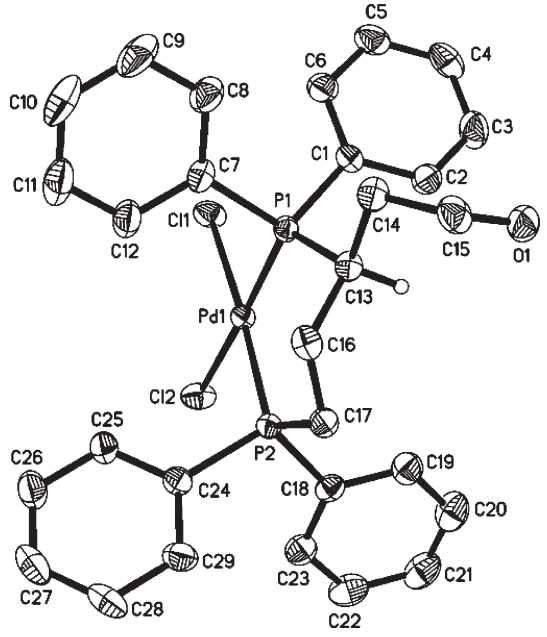


Figure 3. Molecular structure and absolute stereochemistry of complex **9c**.

Table 3. Selected Bond Lengths (Å) and Angles (deg) of 9c

Pd1−P1	2.247(1)	Pd1−Cl1	2.341(1)
Pd1−P2	2.245(1)	Pd1−Cl2	2.373(1)
C13−P1	1.838(3)	C13−C16	1.539(4)
C17−P2	1.832(3)	C15−O1	1.423(4)
P2−Pd1−P1	96.5(1)	Cl2−Pd1−Cl1	90.6(1)
P1−Pd1−Cl2	176.7(1)	P2−Pd1−Cl1	176.2(1)
P1−Pd1−Cl1	86.2(1)	P2−Pd1−Cl2	86.7(1)

Table 4. Crystallographic Data for Complexes *trans*-*R*-3, 9b, and 9c

	trans-*R*-**3**	**9b**	**9c**
formula	$C_{31}H_{32}ClN_2PPd$	$C_{29}H_{28}Cl_2OP_2Pd$	$C_{29}H_{30}Cl_2OP_2Pd\cdot 2CH_2Cl_2$
fw	605.41	631.75	803.62
space group	*P*2(1) 2(1) 2(1)	*P*2(1)	*P*2(1)
cryst syst	orthorhombic	monoclinic	monoclinic
a/Å	11.752(1)	10.865(1)	9.171(1)
b/Å	13.481(1)	15.416(1)	15.718(1)
c/Å	18.026(1)	16.302(1)	12.203(1)
α/deg	90	90	90
β/deg	90	100.2(1)	97.8(1)
γ/deg	90	90	90
V/Å^3	2855.8(1)	2687.0(2)	1742.9(1)
Z	4	4	2
T/K	173(2)	103(2)	173(2)
D_{calcd}/g cm^{-3}	1.408	1.562	1.531
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	0.821	1.030	1.108
F(000)	1240	1280	812
Flack param	−0.005(18)	0.06(5)	−0.003(18)
R1 (obsd data)[a]	0.0323	0.0583	0.0362
wR2 (obs data)[b]	0.0728	0.1471	0.0819

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$, $w^{-1} = \sigma^2(F_o)^2 + (aP)^2 + bP$.

around palladium are in the ranges 86.2(1)−96.5(1)° and 176.2(1)−176.7(1)°. The configuration at the chiral carbon center is the *S* form, and the hydroxyl substituent has an equatorial orientation.

Further treatment of **9c** with aqueous potassium cyanide can liberate the chiral hydroxyl-functionalized 1,3-diphosphine ligand **10c** in nearly quantitative yield, $[\alpha]_D = -38.5$ (*c* 0.5, CH_2Cl_2). The ^{31}P NMR spectrum of **10c** in $CDCl_3$ exhibited a pair of singlets at δ −16.3 and −6.6. The optical purity of the free ligand was confirmed by similar recoordination reactions (Scheme 4). It is noteworthy that the recoordination products of **10c** with *S*-**11** revealed two distinct pairs of doublets at δ −7.8, 38.2 (J_{PP} = 55.9 Hz) and 9.0, 27.1 (J_{PP} = 55.8 Hz) in the ^{31}P NMR spectrum.

In summary, we have presented a facile synthesis of three novel 1,3-bis(diphenylphosphino)propane ligands with cyano, formyl, and hydroxyl functionalities, by means of organo-palladium complex promoted hydrophosphination and subsequent functional group transformation reactions. The reactions proceeded with good yields and stereoselectivities. Investigations on other organic transformations of the cyano group to synthesize new chiral 1,3-diphosphine ligands and the screening of transition metal complexes containing these optically active diphosphines for catalytic reactions are currently in progress.

Experimental Section

All air-sensitive reactions were performed under a positive pressure of argon using a standard Schlenk line. Solvents were dried according to standard procedures and degassed prior to use when necessary. NMR spectra were recorded at 25 °C on a Bruker ACF 400 (^1H at 400 MHz, ^{13}C at 100 MHz, and ^{31}P at 162 MHz) spectrometer. Chemical shifts (δ) are reported in parts per million. Proton and carbon chemical shifts are relative to the residual solvent peaks. Coupling constants are reported in hertz. Optical rotations were measured on the specified solution in a 0.1 dm cell at 20 °C with a Perkin-Elmer 341 polarimeter. Elemental analyses were performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at Nanyang Technological University. Melting points were measured using the SRS Optimelt Automated Melting Point System, SRS MPA100.

The chiral palladium templates *R*-**2**,[12a,b] *R*-**11**, and *S*-**11**[12c] and the Wittig reagent (triphenylphosphoranylidene)acetonitrile[13] were prepared according to literature methods. 3-Chloropropionaldehyde diethylacetal is commercially available (CAS: 35573-93-4) and was used as received.

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

Preparation of Monophosphine Palladium Complex *R*-3. A sodium diphenylphosphide solution prepared from diphenylphosphine (0.80 g, 4.30 mmol) in THF (20 mL) was cooled to 0 °C, and 3-chloropropionaldehyde diethylacetal (0.86 g, 5.16 mmol) in THF (5 mL) was added dropwisely over 5 min. The resulting mixture was stirred for 1 h at room temperature, 4 N HCl (15 mL) was added, and the solution was stirred for 5 h. The pH of the solution was adjusted with sodium carbonate to 10. The mixture was extracted with ethyl acetate (3 × 20 mL). To the combined organic phases was added (triphenylphosphoranylidene)acetonitrile (1.94 g, 6.44 mmol). The mixture was stirred for 2 h at room temperature, palladium dimer *R*-**2** (1.46. g, 2.15 mmol) was added, and the solution was stirred for another 1 h. Upon removal of the solvent, the complex *R*-**3** was isolated by chromatography on silica (EtOAc/hexanes, 1:2.5) as a pale yellow powder (*cis*/*trans* = 1:1.8, 2.13 g, 82%). *trans*-*R*-**3** (1.37 g, 53%): $[\alpha]_D = -19.3$ (*c* 1.1, CH_2Cl_2). Mp: 123−125 °C. Anal. Calcd for $C_{31}H_{32}ClN_2PPd$: C, 61.5; H, 5.3; N, 4.6. Found: C, 61.3; H, 5.4; N, 4.8. ^{31}P NMR ($CDCl_3$, 162 MHz): δ 34.6 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ 2.05 (d, 3H, J_{HH} = 6.3 Hz, CH*Me*), 2.13−2.27 (m, 2H, PCH_2CH_2), 2.70 (s, 3H, N*Me*), 2.88 (m, 1H, PCH′*H*), 2.98 (d, 3H, J_{PH} = 3.2 Hz, N*Me*), 3.07 (m, 1H, PC*H*′H), 4.36 (qn, 1H, $J_{HH} = J_{PH}$ = 6.1 Hz, C*H*CH_3), 5.27 (d, 1H, J_{HH} = 16.2 Hz, C*H*CN), 6.64−8.11 (m, 17H, Ar and CH_2CH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 23.8 (s), 29.0 (d, J_{PC} = 4.0 Hz), 29.4 (d, J_{PC} = 32.7 Hz), 48.4 (d, J_{PC} = 1.8 Hz), 51.2 (d, J_{PC} = 2.8 Hz), 72.9 (d, J_{PC} = 3.1 Hz), 100.3 (s), 117.3 (s), 123.3 (s), 124.2 (s), 124.8 (d, J_{PC} = 5.8 Hz), 125.8 (s), 128.4 (s), 128.6 (d, 2C, J_{PC} = 11.0 Hz), 128.8 (s), 129.0 (d, 2C, J_{PC} = 10.2 Hz), 129.1 (d, J_{PC} = 44.7 Hz), 130.2 (d, J_{PC} = 44.3 Hz), 131.0 (d, J_{PC} = 2.2 Hz), 131.2 (d, J_{PC} = 2.2 Hz), 131.2 (s), 133.7 (d, 2C, J_{PC} = 11.7 Hz), 134.2 (d, 2C, J_{PC} = 11.4 Hz), 135.4 (d, J_{PC} = 12.3 Hz), 149.0 (s), 149.2 (d, J_{PC} = 2.0 Hz), 154.8 (d, J_{PC} = 16.6 Hz).

cis-*R*-**3** (0.76 g, 29%): $[\alpha]_{436} = +128.6$ (*c* 1.0, CH_2Cl_2). Mp: 205−207 °C. Anal. Calcd for $C_{31}H_{32}ClN_2PPd$: C, 61.5; H, 5.3; N, 4.6. Found: C, 61.4; H, 5.2; N, 4.9. ^{31}P NMR ($CDCl_3$, 162 MHz): δ 34.8 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ 2.06 (d, 3H, J_{HH} = 6.3 Hz, CH*Me*), 2.28 (m, 1H, $PCH_2CH'H$), 2.49 (m, 1H, $PCH_2CH'H$), 2.70 (s, 3H, N*Me*), 2.98 (m, 1H, PCH′*H*), 2.98 (d, 3H, J_{PH} = 3.3 Hz, N*Me*), 3.12 (m, 1H, PC*H*′H), 4.36 (qn, 1H, $J_{HH} = J_{PH}$ = 6.2 Hz, C*H*CH_3), 5.21 (d, 1H, J_{HH} = 10.9 Hz, C*H*CN), 6.59−8.12 (m, 17H, Ar and CH_2CH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 23.8 (s), 27.8 (d, J_{PC} = 3.7 Hz), 29.6 (d, J_{PC} = 32.4 Hz), 48.3 (d, J_{PC} = 1.9 Hz), 51.1 (d, J_{PC} = 2.8 Hz), 72.9 (d, J_{PC} = 3.0 Hz), 99.5 (s), 115.6 (s), 123.3 (s), 124.2 (s), 124.7 (d, J_{PC} = 5.8 Hz), 125.7 (s), 128.5 (d, 2C, J_{PC} = 10.3 Hz), 128.6 (s), 128.8 (s), 128.9 (d, J_{PC} = 45.0 Hz), 129.0 (d, 2C, J_{PC} = 10.2 Hz), 130.3 (d, J_{PC} = 44.3 Hz), 131.0 (d, J_{PC} = 2.5 Hz), 131.1 (d, J_{PC} = 2.5 Hz), 131.2 (s), 133.7 (d, 2C, J_{PC} = 11.6 Hz), 134.2 (d, 2C, J_{PC} = 11.5 Hz), 135.5 (d, J_{PC} = 12.3 Hz), 149.1 (s), 149.2 (d, J_{PC} = 2.0 Hz), 154.3 (d, J_{PC} = 16.3 Hz).

Hydrophosphination of Complex *R*-3 and Synthesis of the Diiodo Complex 9a. A mixture of *trans*-*R*-**3** (1.0 g, 1.65 mmol) in dichloromethane (30 mL) and $AgClO_4 \cdot H_2O$ (0.56 g, 2.48 mmol) in water (5 mL) was stirred vigorously for 1 h at room temperature. The organic layer, upon the removal of AgCl precipitate, was washed with H_2O (3 × 20 mL), concentrated, and redissolved in dichloromethane (20 mL). The solution was allowed to cool to −78 °C and treated with diphenylphosphine (0.31 g, 1.65 mmol) in dichloromethane (6 mL), followed by triethylamine (0.25 g, 2.48 mmol). The mixture was stirred for 2 h and warmed to room temperature. Upon removal of solvent, the crude product was purified by chromatography on silica (CH_2Cl_2/acetone/hexanes, 2:1:3) to afford an equilibrium mixture of regioisomers **5a** and **6a** as an off-white solid (0.99 g, 70%). ^{31}P NMR ($CDCl_3$, 162 MHz): δ −1.1 (J_{PP} = 52.1 Hz), 8.3 (J_{PP} = 51.7 Hz), 27.1 (J_{PP} = 51.7 Hz), 35.3 (J_{PP} = 52.1 Hz).

Concentrated hydrochloric acid (8 mL) and NaI (0.25 g, 1.64 mmol) were added to a solution of regioisomers **5a** and **6a** (0.35 g, 0.41 mmol) in dichloromethane (15 mL). The mixture was stirred vigorously at room temperature for 12 h, washed with water (3 × 20 mL), concentrated, and subsequently purified by chromatography on silica (CH_2Cl_2/acetone/hexanes, 2:1:3) to afford the diiodo complex **9a** as a red solid (0.26 g, 79%): $[\alpha]_D = -10.7$ (*c* 1.3, CH_2Cl_2). Mp: 330−333 °C (dec). Anal. Calcd for $C_{29}H_{27}I_2NP_2Pd$: C, 42.9; H, 3.4. Found: C, 42.7; H, 3.6. ^{31}P NMR (CD_2Cl_2, 162 MHz): δ 4.2 (d, J_{PP} = 21.3 Hz), 8.8 (d, J_{PP} = 21.3 Hz).

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^{1}H NMR (CD_2Cl_2, 400 MHz): δ 2.05 (m, 1H, PCH_2CHH'), 2.25−2.48 (m, 3H, PCH_2CHH' and CH_2CN), 2.54−2.70 (m, 3H, $PCHCH_2$ and PCH_2), 7.46−7.92 (m, 20H, Ar). ^{13}C NMR (CD_2Cl_2, 100 MHz): δ 20.5 (s), 24.1 (d, J_{PC} = 3.3 Hz), 24.7 (dd, J_{PC} = 10.7 Hz, J_{PC} = 27.6 Hz), 30.1 (dd, J_{PC} = 13.4 Hz, J_{PC} = 21.7 Hz), 116.8 (d, J_{PC} = 12.8 Hz), 127.1 (d, J_{PC} = 49.8 Hz), 128.4 (d, 2C, J_{PC} = 11.4 Hz), 128.5 (d, J_{PC} = 53.9 Hz), 128.7 (d, 2C, J_{PC} = 11.1 Hz), 128.9 (d, 2C, J_{PC} = 11.0 Hz), 129.0 (d, 2C, J_{PC} = 11.1 Hz), 129.3 (d, J_{PC} = 52.5 Hz), 131.2 (d, J_{PC} = 2.7 Hz), 131.8 (d, J_{PC} = 2.7 Hz), 132.0 (d, J_{PC} = 2.6 Hz), 132.3 (d, J_{PC} = 2.4 Hz), 133.1 (d, 2C, J_{PC} = 9.8 Hz), 133.2 (d, J_{PC} = 58.0 Hz), 133.4 (d, 2C, J_{PC} = 9.4 Hz), 134.2 (d, 2C, J_{PC} = 10.7 Hz), 135.6 (d, 2C, J_{PC} = 11.0 Hz).

The same procedure was used for the hydrophosphination of *cis-R*-**3**.

Preparation of the Formyl-Functionalized Complexes 5b and 6b and the Dichloro Palladium Complex 9b. A solution of regioisomers **5a** and **6a** (0.5 g, 0.58 mmol) in dichloromethane (20 mL) was cooled to −78 °C under argon. DIBAL-H (1 M in heptane, 1.8 mL, 1.8 mmol) was added, and the solution was stirred for 2 h at the same temperature. The mixture was quenched with water (2 mL), warmed to 0 °C, and then treated with H_2SO_4 acid (0.5 M, 20 mL). The organic phase was separated, washed with H_2O (3 × 20 mL), and concentrated to give the regioisomers **5b** and **6b** as a pale yellow solid. ^{31}P NMR ($CDCl_3$, 162 MHz): δ −0.1, 37.2 (J_{PP} = 52.3 Hz); 9.9, 27.7 (J_{PP} = 52.7 Hz).

The crude regioisomers **5b** and **6b** were not isolated, and a solution of **5b** and **6b** in dichloromethane (10 mL) was subsequently treated with concentrated hydrochloric acid (5 mL) for 3 h at room temperature. The mixture was then washed with water (3 × 20 mL), concentrated, and purified by column chromatography on silica (CH_2Cl_2/acetone/hexanes, 3:1:1). Upon crystallization in dichloromethane/diethyl ether, product **9b** was isolated as pale yellow prisms (0.25 g, 68%): $[\alpha]_D$ = +24.4 (*c* 0.9, CH_2Cl_2). Mp: 281−283 °C (dec). Anal. Calcd for $C_{29}H_{28}Cl_2OP_2Pd$: C, 55.1; H, 4.5. Found: C, 54.9; H, 4.7. ^{31}P NMR (CD_2Cl_2, 162 MHz): δ 15.3 (d, J_{PP} = 12.5 Hz), 21.8 (d, J_{PP} = 12.5 Hz). ^{1}H NMR (CD_2Cl_2, 400 MHz): δ 1.86−2.10 (m, 2H, PCH_2CH_2), 2.46 (m, 1H, J_{HH} = 9.8 Hz, J_{HH} = 18.7 Hz, $PCHH'$), 2.53 (m, 2H, CH_2CHO), 2.64 (ddd, 1H, $PCHH'$), 3.10 (m, 1H, $PCHCH_2$), 7.42−7.87 (m, 20H, Ar), 9.42 (d, 1H, J_{PH} = 2.3 Hz, CHO). ^{13}C NMR (CD_2Cl_2, 100 MHz): δ 25.0 (d, J_{PC} = 3.7 Hz), 25.1 (dd, J_{PC} = 8.0 Hz, J_{PC} = 31.5 Hz), 26.8 (dd, J_{PC} = 10.8 Hz, J_{PC} = 29.7 Hz), 44.8 (d, J_{PC} = 2.2 Hz), 126.2 (d, J_{PC} = 53.8 Hz), 127.2 (d, J_{PC} = 56.2 Hz), 128.5 (d, 2C, J_{PC} = 10.9 Hz), 128.6 (d, 2C, J_{PC} = 11.0 Hz), 128.8 (d, 2C, J_{PC} = 11.0 Hz), 128.85 (d, 2C, J_{PC} = 11.3 Hz), 128.9 (d, J_{PC} = 57.1 Hz), 129.9 (d, J_{PC} = 58.7 Hz), 131.4 (d, J_{PC} = 2.8 Hz), 131.6 (d, J_{PC} = 2.9 Hz), 131.7 (d, J_{PC} = 2.8 Hz), 132.0 (d, J_{PC} = 2.8 Hz), 133.3 (d, 2C, J_{PC} = 10.2 Hz), 133.4 (d, 2C, J_{PC} = 9.8 Hz), 133.7 (d, 2C, J_{PC} = 10.7 Hz), 135.3 (d, 2C, J_{PC} = 10.8 Hz), 197.6 (d, J_{PC} = 9.7 Hz).

Preparation of the Hydroxyl-Functionalized Complexes 5c and 6c and the Dichloro Palladium Complex 9c. A solution of regioisomers **5b** and **6b** (generated from **5a** and **6a**, 0.5 g, 0.58 mmol) in dichloromethane (20 mL) was treated with DIBAL-H (1 M in heptane, 1.8 mL, 1.8 mmol) at −78 °C for 2 h. The mixture was quenched with water (2 mL) and warmed to 0 °C, followed by treatment with H_2SO_4 acid (0.5 M, 20 mL). The organic phase was separated, washed with H_2O (3 × 20 mL), and concentrated to give the regioisomers **5c** and **6c** as a crude pale yellow solid. ^{31}P NMR ($CDCl_3$, 162 MHz): δ −0.8, 37.1 (J_{PP} = 53.3 Hz); 11.3, 28.5 (J_{PP} = 52.8 Hz). By following the same procedure to remove the chiral amine auxiliary as described in the synthesis of **9b**, **9c** was generated from the crude regioisomers **5c** and **6c** as pale yellow prisms upon crystallization from dichloromethane/diethyl ether (0.27 g, 72%): $[\alpha]_D$ = +31.1 (*c* 1.0, CH_2Cl_2). Mp: 271−273 °C (dec). Anal. Calcd for $C_{29}H_{30}Cl_2OP_2Pd$: C, 55.0; H, 4.8. Found: C, 54.8; H, 4.9. ^{31}P NMR (CD_2Cl_2, 162 MHz): δ 15.6 (d, J_{PP} = 14.5 Hz), 23.5 (d, J_{PP} = 14.5 Hz). ^{1}H NMR (CD_2Cl_2, 400 MHz): δ 1.37 (m, 1H, $CHH'CH_2OH$), 1.62 (br, 1H, CH_2OH), 1.70 (m, 1H, CHH'-CH_2OH), 1.96 (m, 1H, PCH_2CHH'), 2.17 (m, 1H, PCH_2CHH'), 2.50 (m, 2H, PCH_2), 2.62 (m, 1H, $PCHCH_2$), 3.47 (br, 2H, CH_2OH), 7.40−7.84 (m, 20H, Ar). ^{13}C NMR (CD_2Cl_2, 100 MHz): δ 23.4 (d, J_{PC} = 3.5 Hz), 24.8 (dd, J_{PC} = 7.9 Hz, J_{PC} = 31.6 Hz), 29.2 (dd, J_{PC} = 9.8 Hz, J_{PC} = 29.9 Hz), 32.5 (d, J_{PC} = 2.8 Hz), 59.0 (d, J_{PC} = 10.2 Hz), 126.7 (d, J_{PC} = 53.7 Hz), 127.7 (d, J_{PC} = 55.7 Hz), 128.2 (d, 2C, J_{PC} = 11.1 Hz), 128.5 (d, 4C, J_{PC} = 10.7 Hz), 128.8 (d, 2C, J_{PC} = 10.4 Hz), 129.0 (d, J_{PC} = 56.5 Hz), 130.2 (d, J_{PC} = 58.7 Hz), 131.2 (d, J_{PC} = 2.7 Hz), 131.3 (d, J_{PC} = 2.9 Hz), 131.5 (d, J_{PC} = 2.7 Hz), 131.6 (d, J_{PC} = 2.7 Hz), 133.3 (d, 2C, J_{PC} = 10.3 Hz), 133.7 (d, 4C, J_{PC} = 10.9 Hz), 135.4 (d, 2C, J_{PC} = 10.5 Hz).

Liberation of the 1,3-Diphosphine Ligands 10a, 10b, and 10c. A solution of **9a** (0.15 g, 0.18 mmol) in dichloromethane (10 mL) was stirred vigorously with aqueous KCN (0.5 g, 7.68 mmol) for 30 min. The organic layer was separated, washed with water (3 × 12 mL), and dried with $MgSO_4$. The diphosphine ligand **10a** was obtained as a white solid upon removal of solvent under reduced pressure (0.077 g, 93%): $[\alpha]_D$ = −28.5 (*c* 1.3, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 162 MHz): δ −17.5 (s), −8.3 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.77 (m, 2H, PCH_2CH_2), 2.18 (m, 2H, PCH_2), 2.32 (m, 1H, $CHH'CN$), 2.53 (m, 1H, J_{HH} = 4.2 Hz, J_{HH} = 17.2 Hz, $CHH'CN$), 2.71 (br, 1H, $PCHCH_2$), 7.28−7.43 (m, 20H, Ar).

Similarly the formyl-functionalized 1,3-diphosphine ligand **10b** (0.093 g, 86%) was obtained from **9b** (0.15 g, 0.24 mmol) as a white solid: $[\alpha]_D$ = −22.6 (*c* 1.7, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 162 MHz): δ −16.4 (s), −6.8 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.60 (m, 2H, PCH_2CH_2), 2.15 (m, 2H, PCH_2), 2.45 (m, 2H, CH_2CHO), 3.06 (br, 1H, $PCHCH_2$), 7.27−7.45 (m, 20H, Ar), 9.61 (br, 1H, CH_2CHO).

The hydroxyl-functionalized 1,3-diphosphine **10c** (0.10 g, 95%) was prepared from **9c** (0.15 g, 0.24 mmol) as a white solid: $[\alpha]_D$ = −38.5 (*c* 0.5, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 162 MHz): δ −16.3 (s), −6.6 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.37 (br, 1H, CH_2OH), 1.58 (m, 3H, $CHH'CH_2OH$ and PCH_2CH_2), 1.73 (m, 1H, $CHH'CH_2OH$), 2.16 (m, 2H, PCH_2), 2.57 (br, 1H, $PCHCH_2$), 3.59 (m, 2H, CH_2OH), 7.26−7.47 (m, 20H, Ar).

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Supporting Information Available: Crystallographic data in CIF format for complexes *trans-R*-**3**, **9b**, and **9c**. This material is available free of charge via the Internet at http://pubs.acs.org.