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Asymmetric Synthesis of Functionalized Chiral Diphosphines via Organopalladium Promoted Hydrophosphination and Diels-Alder Reactions

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Abbreviations and Symbols

Ad	adamantyl
An	anisoyl
Ar	aryl
Bu	butyl
br	broad
ca.	about (Latin *circa*)
calcd	calculated
CAS	10-camphorsulfonic acid
conc.	concentrated
Cp	cyclopentadienyl
Cy	cyclohexyl
d	doublet, day(s)
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DBT	dibenzoyltartaric acid
dd	doublet of a doublet
ddd	doublet of a doublet of a doublet
dddd	doublet of a doublet of a doublet of a doublet
DPPE	1,2-*bis*(diphenylphosphino)ethane
dt	doublet of a triplet
de	diastereomeric excess
decomp.	Decomposed
deg	degree(s)

dm	decimeter
ee	enantiomeric excess
Et	ethyl
et. al.	and others (Latin *alii*)
g	gram(s)
h	hour(s)
Hz	hertz
i.e.	that is (Latin *id est*)
i	iso
J	coupling constant
LDA	lithium diisopropylamide
m	multiplet
Me	methyl
Men	menthyl
min	minute(s)
mp	melting point
Ms	methanesulfonyl
n	straight chain
NMR	Nuclear Magnetic Resonance
o	*ortho*
p	*para*
Pr	propyl
Ph	phenyl
^{31}P NMR	$^{31}P\{^{1}H\}$ NMR

ppm	parts per million
q	quartet
qn	quintet
R	*rectus* (Latin: right absolute configuration)
S	*sinister* (Latin: left absolute configuration)
s	singlet
s	secondary
t	triplet
t	tertiary
TBS	*t*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TMEDA	*N,N,N′,N′*-tetramethylethylenediamine
Ts	*p*-toluenesulfonyl
tol	tolyl
Å	angstrom(s)
δ	NMR chemical shift in ppm
$[\alpha]_D$	specific rotation measured at sodium D line (589 nm)

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Summary

This thesis describes the asymmetric synthesis of functionalized chiral diphosphines *via* enantiomeric organopalladium complex (*R*-**26**) promoted asymmetric hydrophosphination and Diels-Alder reactions. Introduction of functionalities on chiral diphosphines using organic transformations with palladium template as protection is also demonstrated.

In Chapter 1, a brief introduction on the synthesis and application of chiral diphosphines, research development in our research group and the aims of this project is presented.

In Chapter 2, the ester- and keto-functionalized allylic monophosphine palladium complexes containing the *ortho*-metalated (*R*)-(1-(dimethylamino)ethyl)naphthalene as the chiral auxiliary were synthesized *via* a versatile one-pot process. Subsequent asymmetric hydrophosphination of the coordinated allylic phosphine substrates generated the functionalized chiral 1,2-bis(diphenylphosphino)ethane products. The coordination properties and absolute configurations of the diphosphine ligands were established by single crystal X-ray crystallography. The optically pure 1,2-bis(diphenylphosphino)ethane ligands with ester and keto functionalities could be liberated in high yields from the corresponding dichloro palladium complexes by treatment with aqueous potassium cyanide.

In Chapter 3, an efficient synthesis of homoallylic monophosphine palladium substrates with ester- and keto-functionalities *via* the chemoselective hydrophosphination of acrolein and the subsequent Wittig reactions is described. The second-stage hydrophosphination of the monophosphine substrates gave the corresponding functionalized chiral 1,3-bis(diphenylphosphino)propane products with good yields and stereoselectivities. The naphthylamine auxiliary could be removed chemoselectively from the template products by treatment with concentrated hydrochloric acid. The dichloro complexes undergo ligand displacement with aqueous cyanide to generate the optically pure ester- and keto-

functionalized 1,3-diphosphine ligands. The second-stage hydrophosphination of acrolein in the presence of palladium template which yields stable chiral α-hydroxy 1,3-diphosphine complex is also presented.

In Chapter 4, a novel cyano-functionalized homoallylic 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 conducted, 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 performed by successive treatment of the hydrophosphination products with Dibal-H, which 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 from the corresponding dihalo palladium complexes by treatment with aqueous potassium cyanide.

In Chapter 5, the chiral organopalladium complex promoted asymmetric Diels-Alder reaction between 3,4-dimethyl-1-phenylphosphole (DMPP) and ester-functionalized allylic monophosphine precursors is demonstrated. The reactions proceeded with high chemo- and stereo-selectivities under mild conditions. The cycloaddition between *trans*-dienophile precursor (*trans*-*R*-**35a**) and DMPP afforded the functionalized P-chiral 1,3-diphosphine complexes as the major products. However, when the reaction was conducted in presence of triethylamine or by employment of the *cis*-dienophile (*cis*-*R*-**35a**) as reaction precursor, the

novel P-chiral 1,2-diphosphine products were chemoselectively generated *via* a double bond migration process. Subsequent ligand displacement of the dichloro palladium complexes with aqueous cyanide generated the corresponding functionalized P-chrial 1,2- and 1,3-diphosphine ligands with phosphanorbornene skeletons.

Chapter I

General Introduction

1.1 Significance of Chiral Diphosphines

Tertiary phosphine ligands are known to have the ability to act as both σ-donors and π-acceptors, which make their coordination bonds with metal ions stronger than their amine analogue. These ligands can stabilize a wide variety of transition metal ions in different oxidation states. Furthermore phosphine metal complexes exist in discrete molecular forms that can be dissolved in a wide range of organic solvents. These key features of phosphine ligands are essential to their role in homogeneous catalysis and significantly extend the scope of transition metal chemistry.[1] Meanwhile, the development of ^{31}P NMR techniques has provided useful and comprehensive tool for the characterization of the structures and chemical properties of phosphorus compounds, as well as mechanistic studies of their roles in catalytic processes. These features have greatly reinforced the application of phosphine ligand supported transition metal complexes.[2] In contrast to amines, interestingly, the pyramidal inversion barrier of tertiary phosphines is considerably higher, ranging from 30 to 38 kcal/mol.[3] This stereochemical stability has allowed for the preparation and separation of the stereogenic phosphorus products.

Enantiomerically pure organophosphorus compounds, particularly the chelating diphosphines, have played a critical role as chiral ligands in the development of transition metal catalyzed asymmetric reactions. The metal atoms involving diphosphine ligands

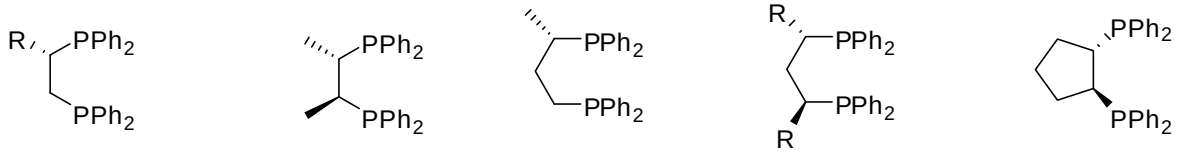
can normally give rise to rigid five- to seven-membered chelate rings, and adopt unique chiral chelating conformations. The novel coordination properties make the diphosphine complexes applicable under many harsh catalytic reaction conditions, and more importantly can afford consistently high optical yields for a wide range of organic substrates. Optically active diphosphine ligands can involve one or several sources of chirality. Besides the stereogenic phosphorus center, the chirality can also be located on their carbon side chain, or on both. As the substituents on the phosphorus atom and backbone can both be rationally designed, a large number of chiral diphosphine ligands have been synthesized and widely applied in various asymmetric organic reactions, such as hydrogenation, carbon-carbon bond and carbon-heteroatom bond formation, hydrocarboxylation, and hydroformylation reactions.[4,5]

1.1.1 Asymmetric Hydrogenation Reaction

Asymmetric hydrogenation, by employing the clean molecular hydrogen to reduce the prochiral C=C, C=O, and C=N double bonds, is probably one of the most simplest and powerful method to produce a myriad of chiral amino acid derivatives, chiral alcohols, and chiral amines, which are important building blocks for organic synthesis.[4,5] The pioneer work was presented in 1971 by Kagan,[6] who developed the first chiral diphosphine ligand, DIOP, derived from tartaric acid, for rhodium-catalized asymmetric hydrogenation reactions with high enantioselectivities. Knowles made his significant contribution by discover a P-chiral diphosphine, DIPAMP, in 1975.[7] Due to the high catalytic efficiency, the rhodium complexes incorporated DIPAMP were quickly employed in the industrial synthesis of $_{L}$-DOPA, a drug for the treatment of Parkinson's

disease. In 1980, Noyori reported the chiral atropisomeric diphosphine, BINAP, which opened up opportunities for high effective hydrogenations of a variety of substrates, especially when it is applied in the ruthenium complexes catalyzed asymmetric transformations.[8] Since these findings showed that chiral diphosphine ligands could provide superior enantioselectivities compared with that of chiral monophosphines, so far a good many novel chiral diphosphines have been developed as illustrated in Figure 1.1. PROPHOS,[9] CHIRAPHOS,[10] CHAIRPHOS,[11] BDPP,[11,12] DPCP,[13] PPCP,[14] NORPHOS,[15] BICP,[16] DUPHOS,[17] BPE,[17] and DIOP are classic diphosphines with chiralities on the backbones. Although the first P-stereogenic diphosphine DIPAMP has already been proven to be very efficient in asymmetric hydrogenation reactions, the gradual development of P-chiral diphosphine ligands including TANGPHOS[18] and BISP*[19] is partly due to the difficulties in ligand synthesis. The novel atropisomeric type ligands such as TolBINAP, BIPHEMP,[20] BIMOP,[21] H_8-BINAP,[22] BisbenzodioxanPhos,[23] and SEGPHOS[24,31] were developed based on modification of the electronic and steric properties of BINAP. FerroPHOS[25] and JOSIPHOS[26] are an important class of ferrocene-based diphosphines with planar chirality. SDP and its modified analogue were developed by Zhou[27] with chiral spirocyclic frameworks.

Figure 1.1



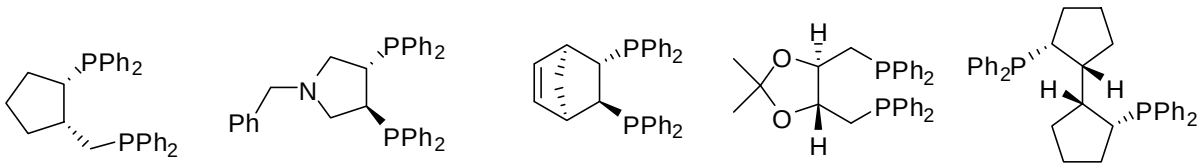
(*S*)-PROPHOS: R=Me
(*S*)-PHENPHOS: R=Ph

(*S,S*)-CHIRAPHOS

(*S*)-CHAIRPHOS

(*S,S*)-BDPP: R=Me
(*S,S*)-MOD-BDPP: R=Ph,Cy

(*S,S*)-DPCP



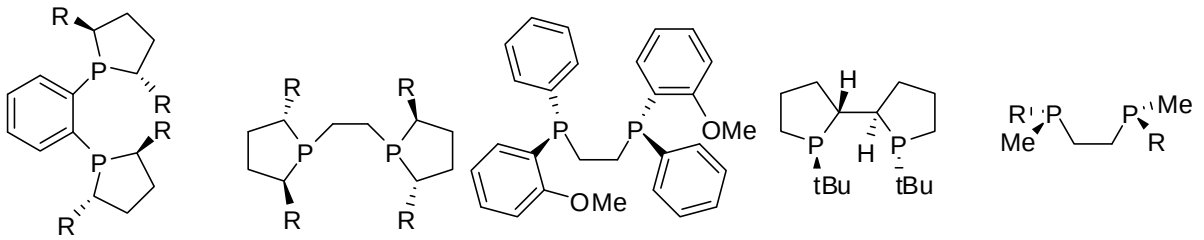
(*S,S*)-PPCP

(*S,S*)-PYRPHOS

(*S,S*)-NORPHOS

(*S,S*)-DIOP

(*R,R*)-BICP



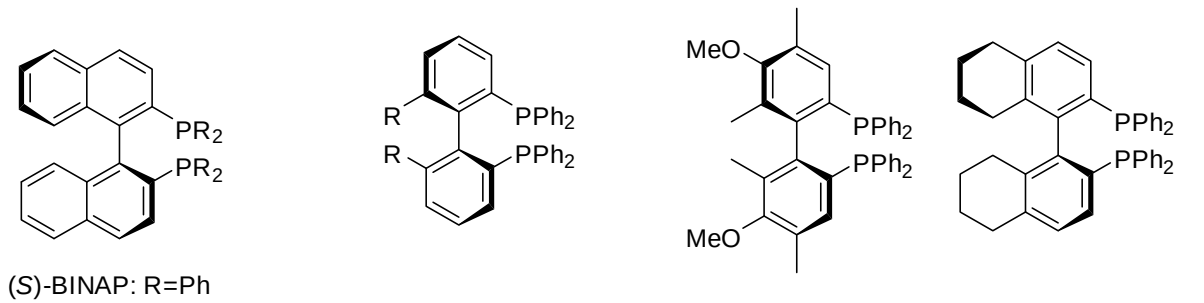
(*S,S*)-Me-DUPHOS
(*S,S*)-Et-DUPHOS
(*S,S*)-*i*-Pr-DUPHOS

(*S,S*)-Me-BPE
(*S,S*)-Et-BPE
(*S,S*)-*i*-Pr-BPE

(*S,S*)-DIPAMP

(1*S*,1*S*′)-TANGPHOS

(*S,S*)-*t*-Bu-BISP*
(*S,S*)-Ad-BISP*
(*S,S*)-Cy-BISP*

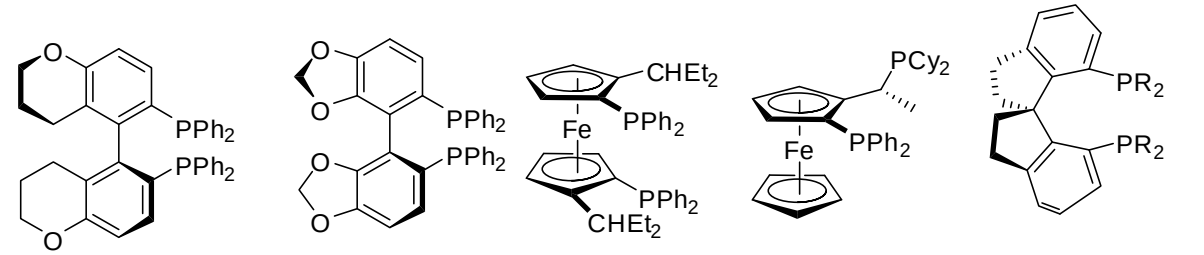


(*S*)-BINAP: R=Ph
(*S*)-TolBINAP: R= 4-MePh
(*S*)-XylBINAP: R= 3,5-$(Me)_2$Ph

(*S*)-BIPHEMP: R=Me
(*S*)-MeO-BIPHEP: R= OMe

(*S*)-BIMOP

(*S*)-H_8-BINAP



(*S*)-BisbenzodioxanPhos

(*S*)-SEGPHOS

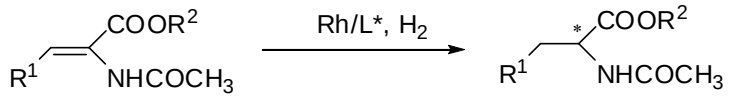
(*S,S*)-FerroPHOS

(*R,S*)-JOSIPHOS

(*S*)-SDP: R=Ph
(*S*)-Tol-SDP: R=4-MePh

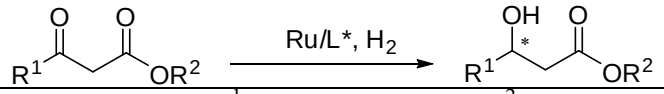
All theses well-designed chiral diphosphines are extensively employed in transition metal catalyzed asymmetric hydrogenation reactions with high enantioselectivities for a wide range of substrates. For example, the rhodium complexes catalyzed asymmetric hydrogenation of α-dehydroamino acid derivatives and the ruthenium catalyzed hydrogenation of β-keto esters as illustrated in Table 1.1 and Table 1.2, respectively.

Table 1.1 Rh-catalyzed Asymmetric Hydrogenation of α-Dehydroamino Acid Derivatives



L*	R^1	R^2	% *ee*
(*S*,*S*)-CHIRAPHOS[10a]	*i*-Pr	H	100
	Ph	H	99
(*R*,*R*)-DIPAMP[5a]	Ph	H	95
(*S*,*S*)-DUPHOS[17b]	H	Me	>99
	Ph	Me	>99
(*R*,*R*)-BICP[16a]	H	H	97.5
	p-OMePh	H	99
(1*S*,1*S*')-TANGPHOS[18]	Ph	H	>99
	Ph	Me	>99
(*S*,*S*)-BISP*[19]	Ph	Me	99.9
	Ph	H	98.4
(*S*,*S*)-FERROPHOS[25]	H	Me	97.5
	Ph	H	98.9

Table 1.2 Ru-catalyzed Asymmetric Hydrogenation of β-Keto Esters



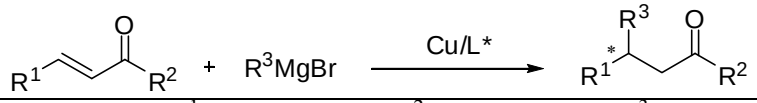
L*	R^1	R^2	% *ee*
(*R*)-BINAP[28]	Me	Me	>99
	Me	Et	99
	i-Pr	Me	>99
(*S*)-MeO-BIPHEP[29]	Me	Me	97
	Et	Me	99
(*R*,*R*)-BPE[30]	Me	*t*-Bu	99.4
	Cy	Me	99.1
(*S*)-SEGPHOS[31]	$ClCH_2$	Et	98.5
	$PhCH_2OCH_2$	Et	99.4
	Ph	Me	97.6
(*R*)- SYNPHOS[23,32]	Me	Me	98.1
	Me	Et	99.5
	i-Pr	Et	99

1.1.2 Asymmetric Conjugate 1,4-Addition: C-C Bond Formation

Besides the classic hydrogenation, chiral diphosphines have also been widely used as ligands in transition metal catalyzed asymmetric conjugated 1,4-addition reactions. The conjugate addition of organometallic reagents, including organozinc, organolithium, organomagnesium (Grignard reagents), to activated olefins is one of the most important methods for carbon-carbon bond formation reactions which affords *β*-substituted functionalized products.[33] Transition metal catalyzed enantioselective versions of these useful reactions have been studied extensively with addition of dialkylzinc to cyclic enones and chalcones. However, the asymmetric scenarios involving Grignard reagents pose many challenges, despite their ready availability from inexpensive starting materials. For example, it is not easy to get high enantiomeric excess (*ee*). Furthermore, the fast addition process can proceed as uncatalyzed addition of the highly reactive organomagnesium reagent to the carbonyl groups (1,2-addition).

In 2004, an excellent work was reported by Feringa, who employed the chiral diphosphine ligands in copper catalyzed asymmetric conjugated addition of organomagnesium reagents with high regio- and enantioselectivities.[34] The following series of studies reveal that the catalytic system was extremely efficient with a large number of substrates, such as *α*,*β*-unsaturated enones, esters, and thioesters, as shown in Table 1.3.[35]

Table 1.3 Copper-catalyzed Enantioselective Conjugate Addition of Grignard Reagents



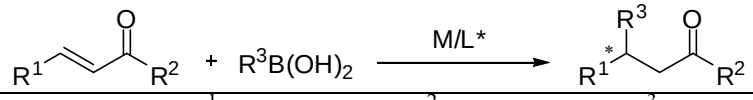
L*	R^1	R^2	R^3	% *ee*
(*R*,*S*)-JOSIPHOS[35c,d]	*n*-Bu	Me	Me	98
	n-Pr	Me	*n*-Bu	95
	Me	*n*-Bu	*n*-Pr	95
	2-thienyl	Me	Me	97
	Me	OMe	*i*-pent	96
	Me	OMe	*n*-Bu	95
	i-Pr	OMe	Et	99
	Ph	OMe	Et	98
(*S*)-TolBINAP[35e]	Ph	SMe	Me	94
	p-Cl-Ph	SEt	Me	99
	i-Pr	SEt	Me	99
	n-pent	SEt	*n*-Bu	94

Since the first report presented by Miyaura in 1997,[36] the arylboronic acids become a class of efficient nucleophiles in rhodium and palladium catalyzed 1,4-addition of electron deficient alkenes. The novel catalytic process has the following advantages over other conjugated addition reactions.[37] (1) The organoboronic acids are stable to moisture and oxygen, so the reaction could be conducted in protic media or even in aqueous solution. (2) In the absence of transition metal catalysis, the organoboronic acids are much less reactive toward enones than that of Grignard reagents, and no 1,2-addition will take place. (3) The addition reaction is catalyzed by transition metal complexes supported with phosphine ligands. Thus chiral diphosphine ligands can be employed for metal-catalyzed enantioselective versions which will further accumulate the application of the chiral phosphine ligands in the asymmetric catalytic reactions.

In 1998, Hayashi and Miyaura reported the first asymmetric 1,4-addition of aryl- and alkenylboronic acids to enones in the presence of BINAP-rhodium catalyst.[38] During the

past decade, the preceding contributions over this research area have successfully covered a wide variety of electron deficient olefins such as α,β-unsaturated ketones,[39] esters,[40] amides,[41] nitroalkenes,[42] phosphonates,[43] and sulfones compounds.[44] The addition reactions can be catalyzed by rhodium or palladium (Table 1.4) with chiral diphopshine ligands including BINAP, CHIRAPHOS, MeOBIPHEP with high enantioselectivities.

Table 1.4 Metal-catalyzed Asymmetric Conjugate Addition of Organoboronic Acid



M/L*	R^1	R^2	R^3	% *ee*
Rh/BINAP[38,40a]	*n*-Pr	OPr-*i*	Ph	94
	n-Pr	OBu-*t*	Ph	95
	i-Pr	Me	Ph	97
	n-pent	Me	Ph	92
	Me	$NHCH_2Ph$	Ph	93
Rh/Chiraphos[44]	*i*-pent	SO_2Py	*p*-F-Ph	87
	β-Naph	SO_2Py	*p*-F-Ph	92
	Ph	SO_2Py	Styryl	94
Pd/Chiraphos[39d,40c,41c]	Ph	4-AcPhO	4-MePh	97
	Ph	Me	3-ClPh	93
	Ph	*n*-Bu	3-MeOPh	99
	Ph	Ph	4-MePh	95
	Ph	$N(COPh)_2$	p-Tolyl	98

1.1.3 Other Reactions

Apart from hydrogenation and conjugated 1,4-addition reactions, due to their unique properties and high efficiency, optically pure diphosphines have also proven to be efficient and elegant ligands in a series of transition metal catalyzed asymmetric transformations such as Heck-type reaction,[45] cyclization,[46] cycloaddition (Scheme 1.1),[47] hydrocarbonylation,[48] hydroboration[49] and allylation reactions.[50]

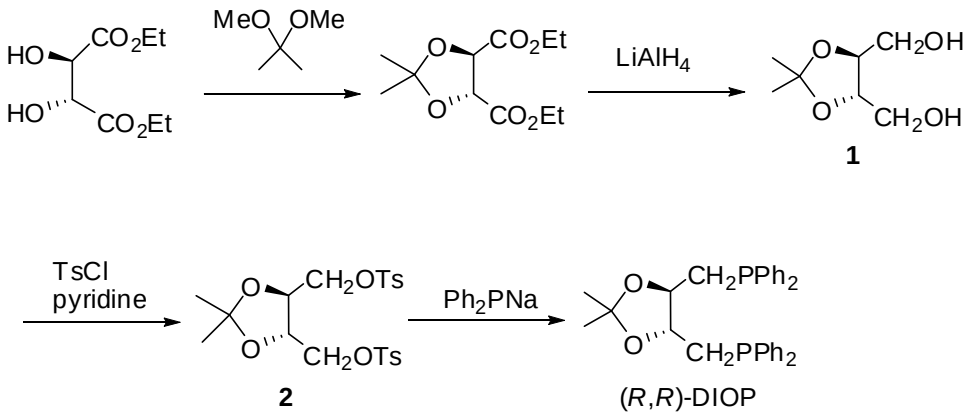
Scheme 1.1

1.2 Methods for Preparation of Chiral Diphosphines

Along with their widespread applications in transition metal catalyzed asymmetric reactions, a number of excellent reports have also documented the synthetic strategies of chiral diphosphines ligands, which can be generally divided into three categories.

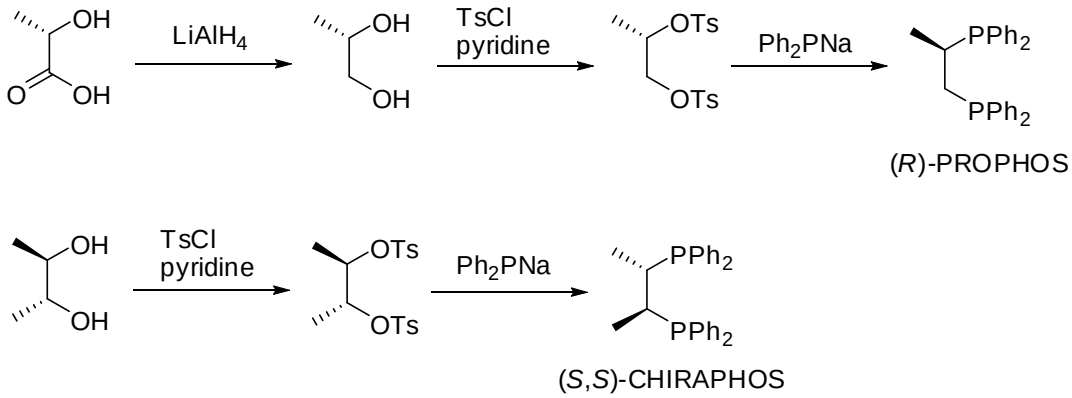
1.2.1 Transformation from Chiral Substrates

The stereospecific transformations of chiral organic substrates have been shown to provide a straightforward synthetic route to chrial diphosphine ligands, especially those with the chirality located on the side chains (chiral backbone). The most general synthetic approach for their preparation is based on the consecutive nucleophilic substitutions between phosphides and dimesylates, ditosylates or cyclic sulfates of optically active diols. The optically active diols used are usually generated from chiral natural compounds such as optically pure organic acids or derivatives (chiral pool).



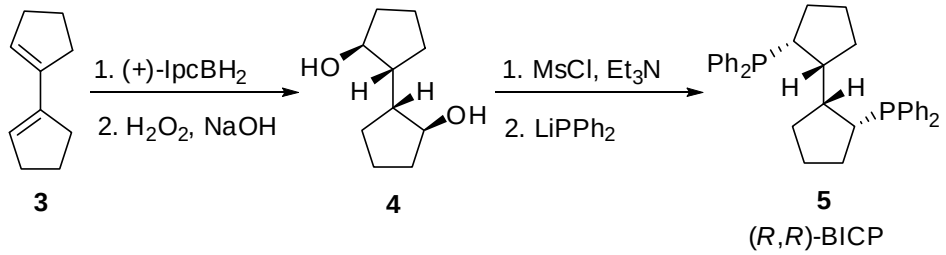
Scheme 1.2

The first chiral diphosphine ligand that was prepared by this method was Kagan's DIOP[6b] (Scheme 1.2). The synthesis started from (*R*,*R*)-diethyl tartrate, which was treated with lithium aluminum hydride after the protection by 2,2-dimethoxypropane to yield the diol **1**. Treatment of product **1** with tosyl chloride in pyridine gave rise to the ditosylate **2**, and the subsequent S_N2 type substitution with sodium diphenylphosphide afforded the novel chiral ligand. Bosnich's (*R*)-PROPHOS[9] and (*S*,*S*)-CHIRAPHOS[10a] can be prepared by following a similar synthetic pathway from (*S*)-lactic acid and (2*R*,3*R*)-butanediol (Scheme 1.3), respectively.



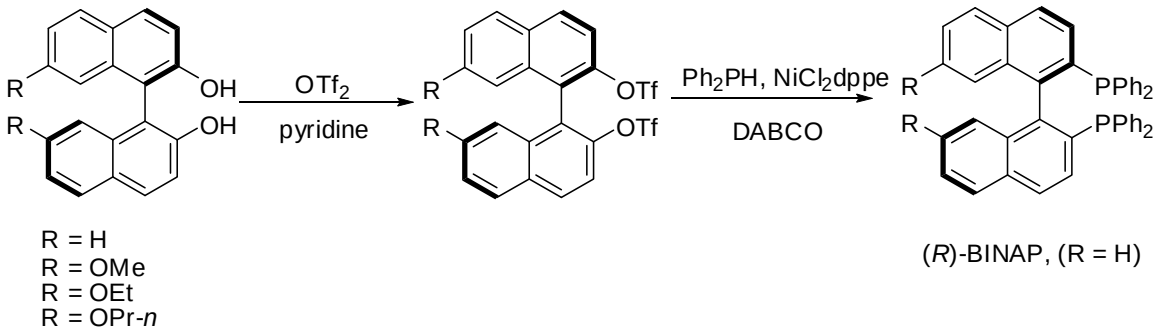
Scheme 1.3

The chiral diol precursors can also be synthesized by asymmetric reactions. For example, the synthesis of (*R*,*R*)-BICP (Scheme 1.4) by Zhang[16a] was from the prochiral diene **3**, asymmetric hydroboration of **3** using (+) $IpcBH_2$, followed by oxidation with H_2O_2 gave the optically active diol **4**. Upon conversion to the dimesylate, the subsequent nucleophilic substitution with lithium diphenylphosphide afforded the chiral diphosphine ligand.



Scheme 1.4

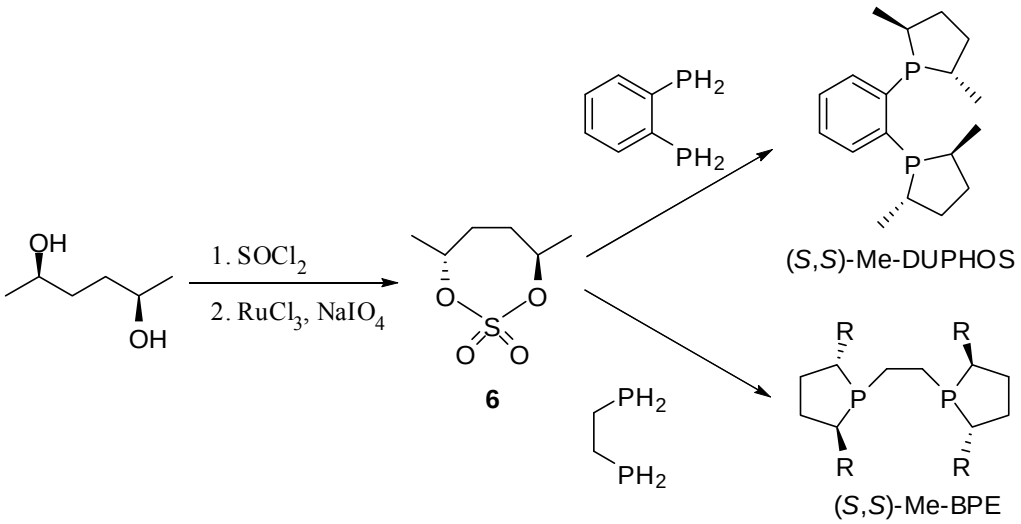
With the use of enantiomerically pure BINOL which can be obtained by resolution or asymmetric synthesis, the atropisomeric chiral diphosphine ligands can also be synthesized with the retention of chiral configuration. As shown in Scheme 1.5, treatment of the (*R*)-binaphthol with triflic anhydride and pyridine formed the chiral ditriflate, which was then reacted with diphenylphosphine in the presence of nickel catalyst and DABCO to give optically pure (*R*)-BINAP.[51] By using similar organic transformations, the modified derivatives such as 7,7′-dimethoxy, 7,7′-diethoxy, and 7,7′-dipropoxy-substituted BINAP were successfully prepared by Yuan and Gong (Scheme 1.5).[52]



Scheme 1.5

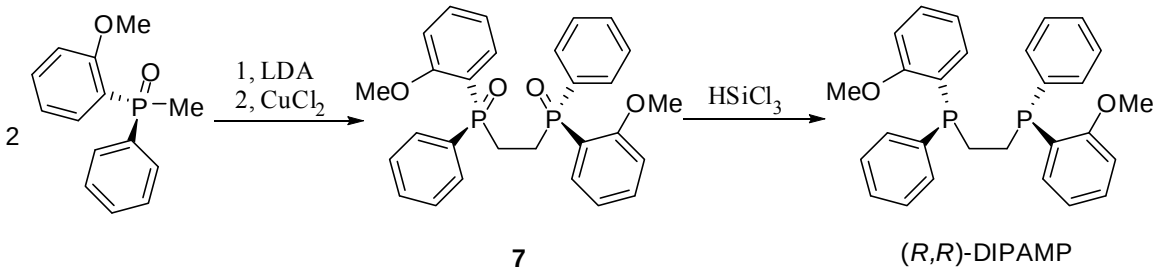
DUPHOS and BPE are of a kind of electron rich diphosphine ligands that can also be obtained by the general synthetic route, which involves a key intermediate of 1,4-diol cyclic sulfate **6** (Scheme 1.6).[17c] The stepwise substitution reaction with primary diphosphines such as 1,2-diphosphinobenzene and 1,2-diphosphinoethane afforded the

novel C-chiral cyclic diphosphines (*S*,*S*)-Me-DUPHOS and (*S*,*S*)-Me-BPE, respectively.



Scheme 1.6

The synthetic approach is also applicable for preparation of P-chiral diphoshine ligands, for example Knowles's DIPAMP.[7b] The key step of this transformation is the oxidative coupling of well resolved optically pure P-chiral monophosphine substrates after deprotonation with strong base to yield the chiral diphosphine oxide **7** (Scheme 1.7). The phosphine oxide precursor can be easily converted into (*R*,*R*)-DIPAMP by subsequent reduction with trichlorosilane.

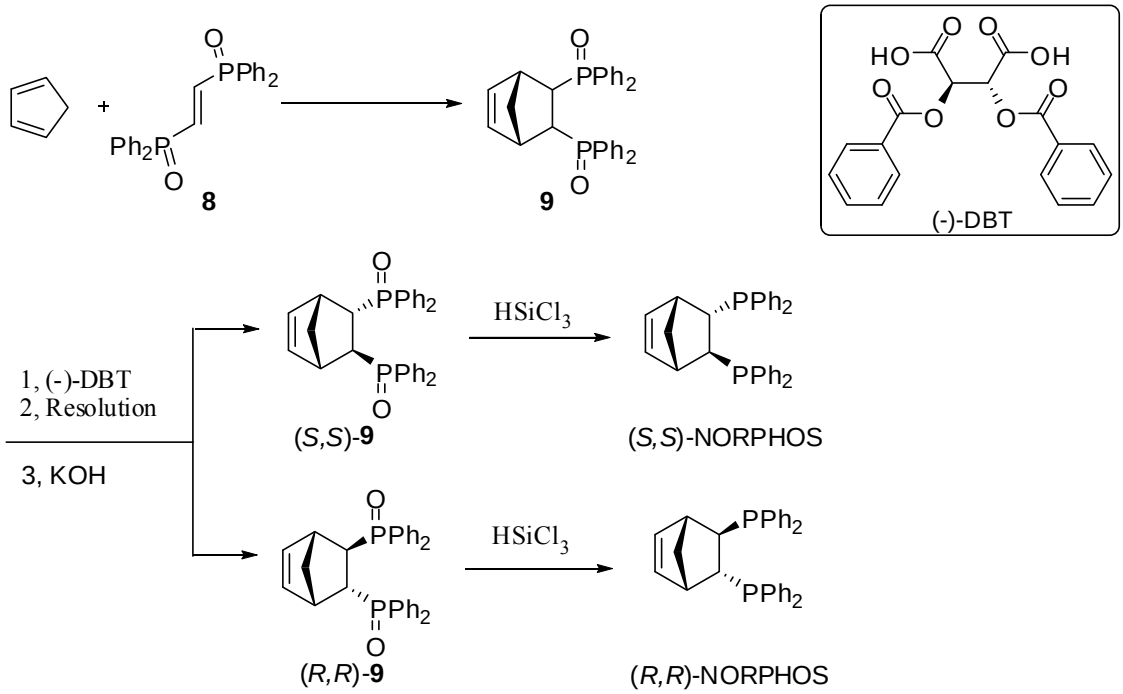


Scheme 1.7

1.2.2 Resolution

Another route to chiral diphosphines is the use of the classical resolution technique of

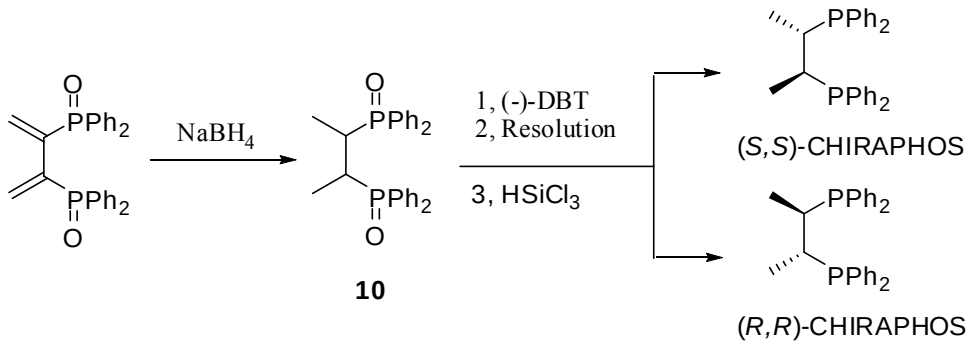
converting a pair of enantiomers into diastereomers by reaction with an optically active reagent. The diastereomers have different physical properties and thus can be separated by means of column chromatography or fractional crystallization. Optically pure organic acids such as (*R*,*R*)-dibenzoyltartaric acid ((–)-DBT) and (*S*)-(+)-10-camphorsulfonic acid ((+)-CAS), are a class of important resolving reagents especially for the weakly basic phosphine oxides. The well known C-chiral diphosphine NORPHOS was synthesized from the Diels-Alder reaction of cyclopentadiene and dienophile **8** (Scheme 1.8).[15b] Optical resolution of the racemic oxide version of NORPHOS **9** was achieved with the use of (*R*,*R*)-dibenzoyltartaric acid ((–)-DBT) followed by treatment with base. The reduction of resolved diphosphine oxide **9** with trichlorosilane afforded the enantiomerically pure (*R*,*R*)- and (*S*,*S*)-NORPHOS.



Scheme 1.8

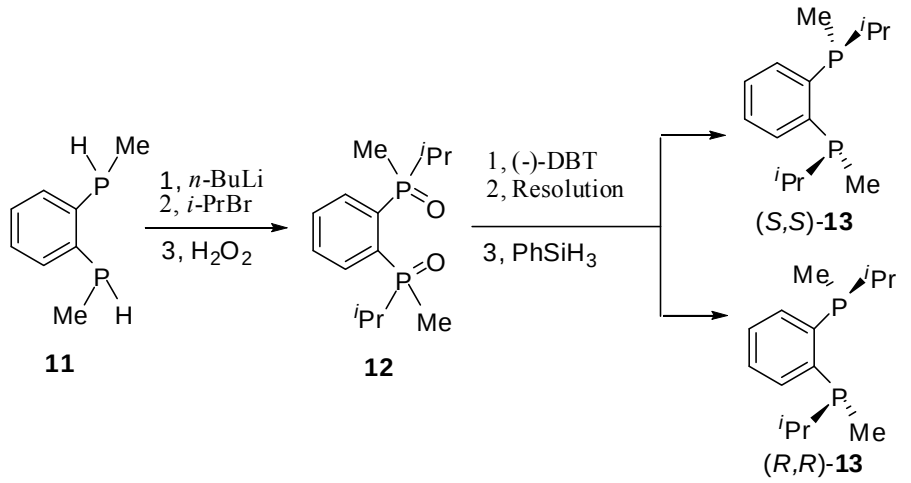
Another example of similar resolution process was reported by Matteoli for the preparation of CHIRAPHOS (Scheme 1.9).[53] The racemic oxide precursor **10** was

synthesized from 2,3-bis(diphenylphosphinyl)-1,3-butadiene by means of reduction with $NaBH_4$. The subsequent resolution by using (*R*,*R*)-dibenzoyltartaric acid ((–)-DBT) and reduction of separated phosphine oxide gave the optically pure novel C-chiral diphosphine ligand.



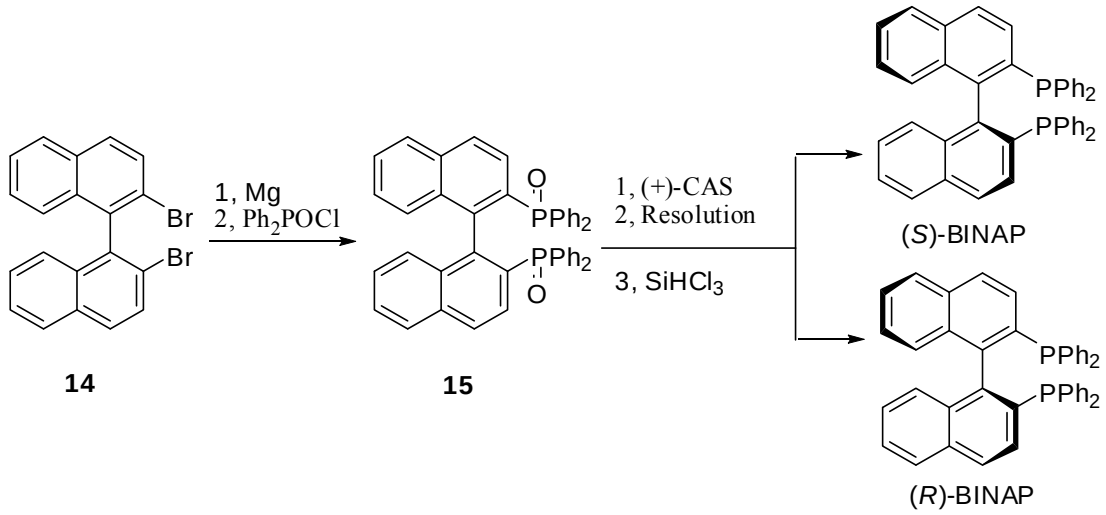
Scheme 1.9

Similarly, some P-chiral diphosphines can also be synthesized by means of resolution methodology. The racemic diphosphine oxide **12** was prepared starting from the secondary diphosphine **11** by successive organic transformations including deprotonation, nucleophilic substitution, and subsequent oxidation (Scheme 1.10).[54] The racemic oxide is resolved with (–)-DBT and subsequent reduction reaction gave the enantiopure P-chiral diphosphine ligand **13**.



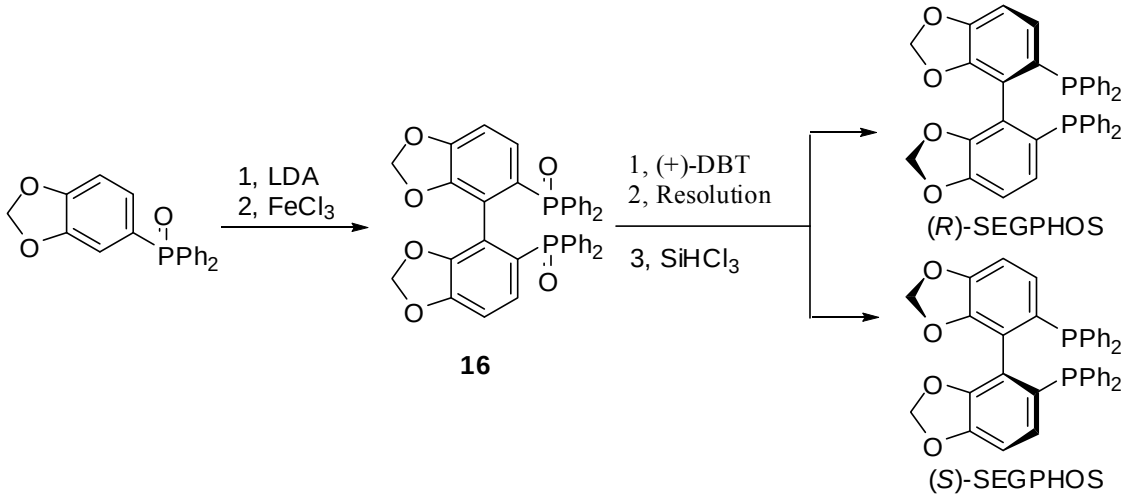
Scheme 1.10

Optical resolution is also an important method for the preparation of atropisomeric chiral diphosphines. The synthesis of BINAP by Noyori is a typical procedure for obtaining this kind of ligands (Scheme 1.11).[8b] In Noyori's process, condensation of Grignard reagent derived from dibromo precursor **14** with diphenylphosphinyl chloride afforded the racemic BINAP oxide **15**, which was resolved with (*S*)-(+)-10-camphorsulfonic acid ((+)-CAS) or (–)-DBT, followed by reduction to yield the novel chiral ligand in its optically pure form.



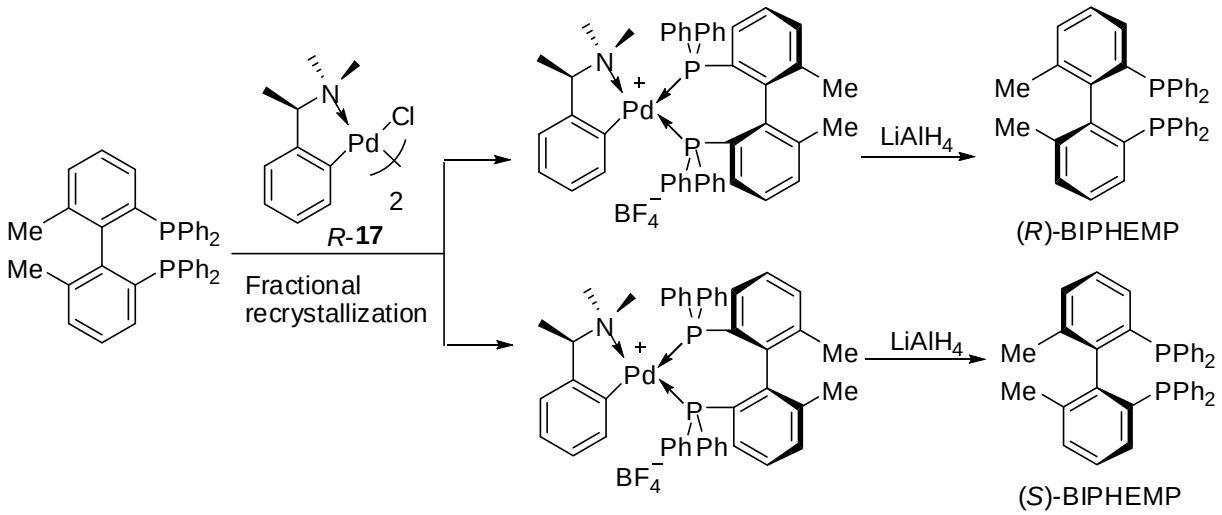
Scheme 1.11

The modified analogue of BINAP like (*S*)-SEGPHOS[24a] and (*S*)-BisbenzodioxanPhos[32,55] can be produced by similar resolution procedure as shown in Scheme 1.12, since there is no enantiopure atropisomeric biaryl synthon available in the natural chiral pool. The key step for preparation of these diphosphine ligands was the oxidative homo-coupling reaction to form the racemic diphosphine oxide precursor **16**.



Scheme 1.12

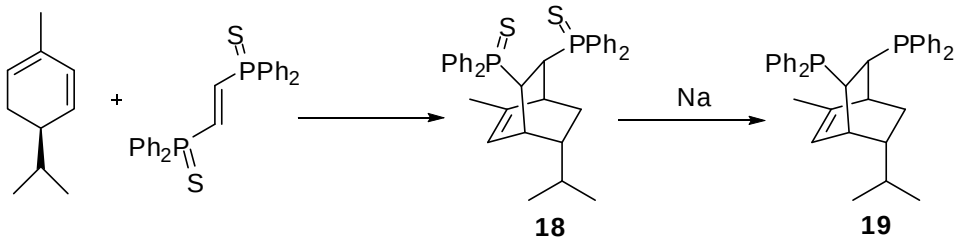
The organopalladium complex *R*-**17** containing (*R*)-(1-(dimethylamino)ethyl)-benzene as the chiral auxiliary is an alternative resolving reagent. The orthometallated amine complex is able to provide two coordination sites around the square planar palladium atom and thus can efficiently resolve diphosphine ligands, including the atropisomeric diphosphines like BINAP,[8a] BIPHEMP[56] (Scheme 1.13), MeO-BIPHEMP,[57] and some P-chiral diphosphines.[58]



Scheme 1.13

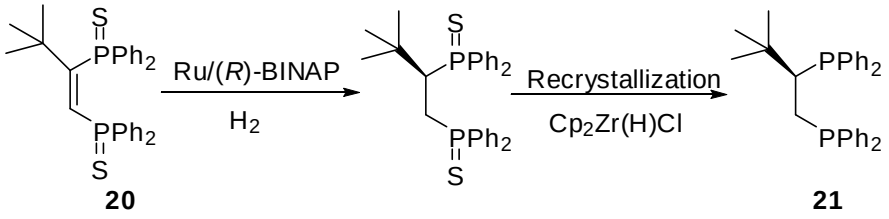
1.2.3 Asymmetric Synthesis

Asymmetric synthesis describes the preferential formation of one enantiomer or diastereomer as the sole or major product in a chemical reaction with the use of chiral starting materials, chiral auxiliaries, chiral catalysts, or application of asymmetric induction. Despite the successful preparation of various functionalized chiral monophosphines promoted by transition metal complexes[59] or more recently by organocatalysts,[60] the enantioselective synthesis of chiral diphosphine ligands remains relatively undeveloped. To date, only few examples on the asymmetric synthesis of C-chiral diphosphine have been reported in literature. Kagan developed a new chiral diphosphine ligand with novel C-chiral skeleton based on Diels-Alder reaction starting from (–)-α-phellandrene as diene (Scheme 1.14).[61] The reaction stereoselectively yielded the disulfide adduct **18** without any further resolution process, and the disulfide precursor can be converted to optically pure diphosphine **19** by treatment with sodium in toluene.



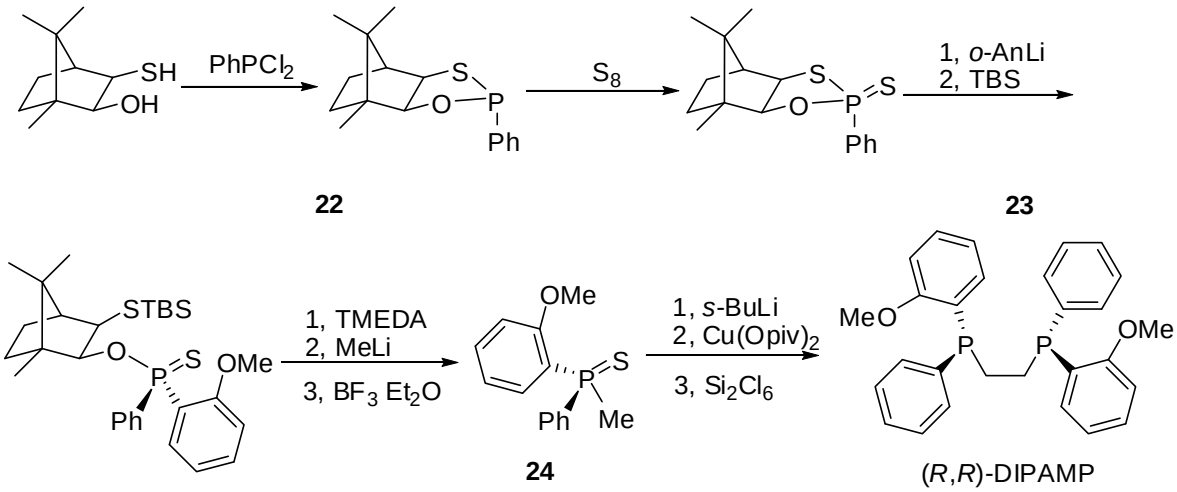
Scheme 1.14

In another example by Oshima[62] as shown in Scheme 1.15, a *tert*-butyl group functionalized 1,2-bis(diphenylphosphino)ethane **21** was synthesized by means of ruthenium catalyzed enantioselective hydrogenation of diphenylphosphorothioyl substituted prochiral olefin **20** and subsequent desulfurization reaction.



Scheme 1.15

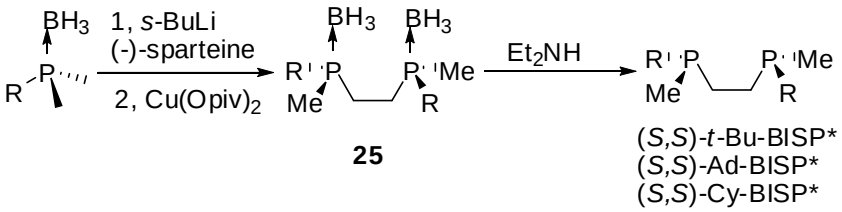
By employing of chiral auxiliary, the P-chiral diphosphine ligand can also be obtained without the need of resolution. A good example of such strategy is presented by Corey[63] for the synthesis of (*R*,*R*)-DIPAMP (Scheme 1.16). In this approach, the stereochemistry is controlled by a camphor derivative chiral auxiliary **22** containing both hydroxyl and thiol groups. The two heteroatoms attached to phosphorus in the thiophosphonate intermediate **23** can be displaced stereospecifically by nucleophilic aryl and alkyl groups to produce the P-chiral monophosphine sulfide **24**. Deprotonation and *in situ* oxidative coupling of **24**, followed by desulfurization afforded (*R*,*R*)-DIPAMP with excellent optical purity.



Scheme 1.16

Finally, Evans[64] disclosed an interesting process to the C_2-symmetric P-chiral

diphosphine BISP* that relied on enantioselective deprotonation of aryldimethylphosphine-boranes by using *s*-BuLi in the presence of (–)-sparteine. The resultant α-carbanion can undergo *in situ* oxidative coupling reaction and afforded the diphosphine precursors **25** with high overall enantioselectivity. Subsequent removal of the borane protecting group by treatment with diethylamine gave the corresponding chiral diphosphines in high yields.



25

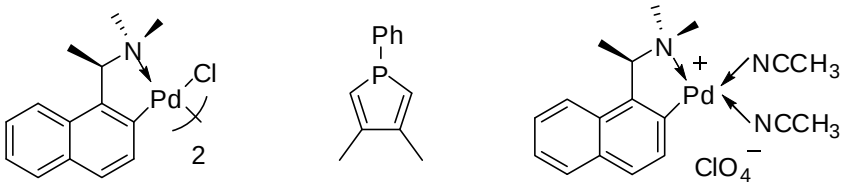
Scheme 1.17

1.3 Chiral Diphosphine Synthesis Using Chiral Organometallic Auxiliaries

During the last two decades, our group has successfully employed the organopalladium complex *R*-**26** containing the enantiomerically pure (1-(dimethylamino)ethyl)naphthalene as the chiral auxiliary for synthesis of a series of functionalized chiral diphosphines. A key stereochemical feature of the chiral naphthylamine complex *R*-**26** is that, due to the internal steric repulsion between the methyl substituent at the stereogenic carbon and its neighboring naphthylene proton, the five-membered chelate is locked into δ confirmation both in solid state and solution.[65] Thus the prochiral methyl groups on nitrogen atom are fixed into stereochemically non-equivalent pseudo-axial and pseudo-equatorial positions. Furthermore, the electronic difference of N-Pd coordination bond and C-Pd σ-bond around the square planar palladium atom can control the regioselectivity of incoming ligands. For example,

phosphorus atoms prefer to coordinate *trans* to the nitrogen moiety. Due to these special steric and electronic features, the organopalladium complex has been proven to be an efficient promoter for the synthesis of chiral 1,2-diphophine ligands by means of asymmetric Diels-Alder reactions[66] and hydrophosphination reactions[67] involving vinylic phosphine substrates.

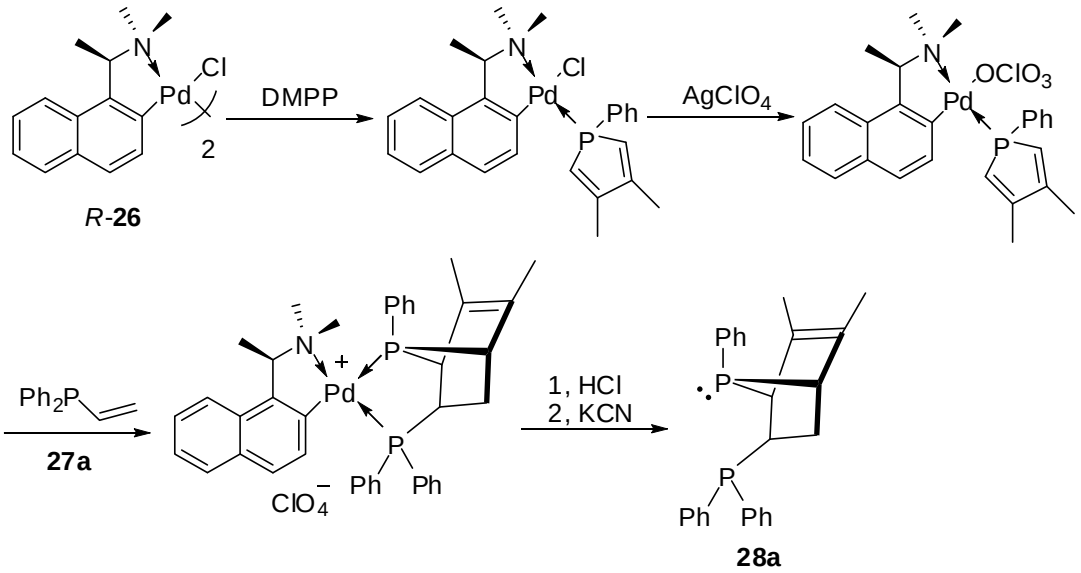
Figure 1.2



R-**26** DMPP *R*-**32**

1.3.1 Asymmetric Diels-Alder Reactions

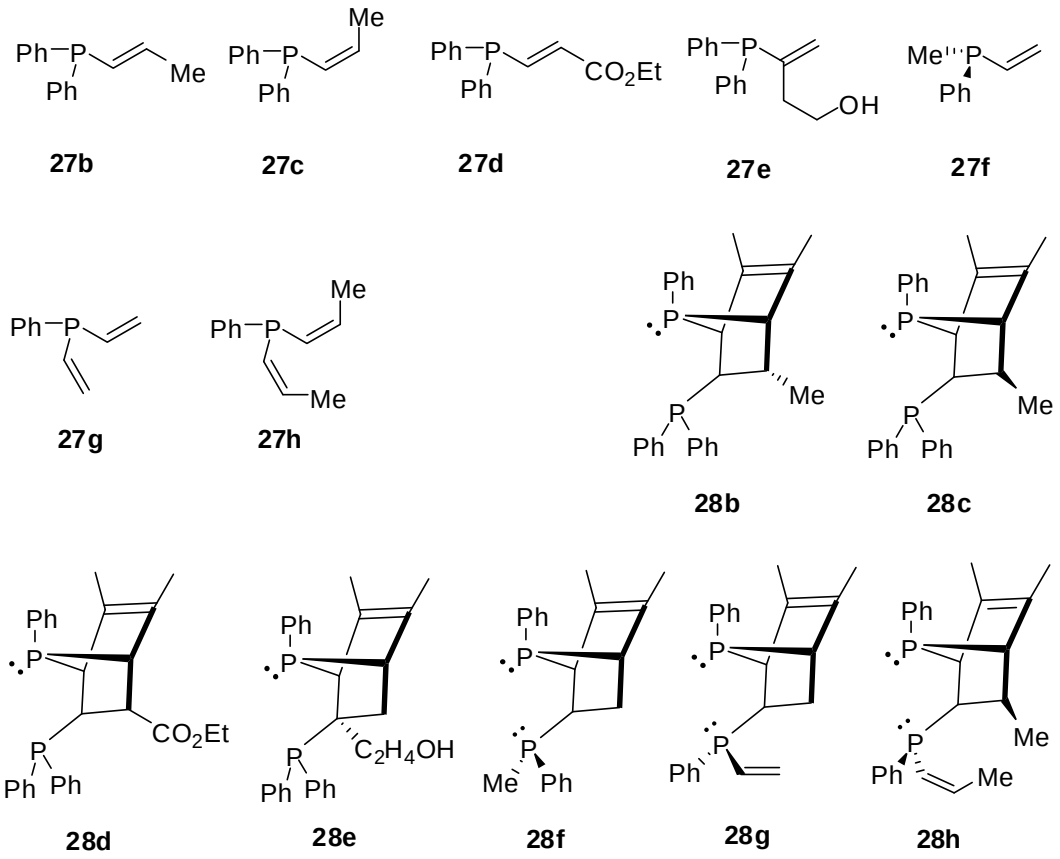
Asymmetric Diels-Alder reaction has been considered to be one of the most efficient and elegant methods for construction of chiral six-membered rings.[68] It is well known that the five-membered heterocycle, 3,4-dimethyl-1-phenylphosphole (DMPP)[69] (Figure 1.2) is a rather poor cyclic diene due to its aromaticity. The phosphole, upon coordination to palladium complex, is activated and thus capable of reacting with a variety of dienophiles, such as α,β-unsaturated ketone,[70] ester,[71] aldehyde,[72] amide,[73] thioester,[71] thioamide,[74] and sulfoxide compounds.[75] The asymmetric Diels-Alder reactions can proceed *via* controllable *exo*- and *endo*-pathways to afford a large group of functionalized P-chiral monophosphine ligands.



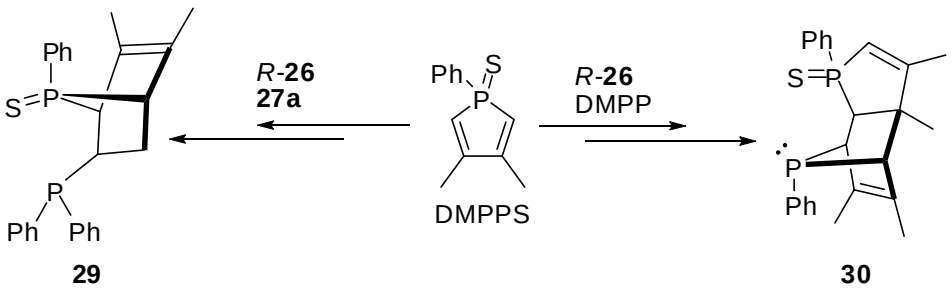
Scheme 1.18

In cases where vinyldiphenylphosphine is used as dienophile as shown in Scheme 1.18, the Diels-Alder reaction with DMPP stereoselectively gave a novel P-chiral diphosphine ligand **28a** with phosphanorbornene skeleton in high yield.[66b,c] By using this synthetic approach, a list of vinylic phosphine substrates including diphenylpropenylphosphine **27b**, **27c**,[66d] ester- and hydroxyl-functionalized vinylphosphines **27d**,[66e] **27e**,[66f] (*R*)- and (*S*)-methylphenylvinylphosphine **27f**,[66g,h] and the prochiral phenyldivinylphosphines **27g**,[66i] **27h**[66j] have been employed as dienophiles in our group (Figure 1.3). All the asymmetric cycloaddition reactions proceed exclusively *via exo*-pathways to form the corresponding chiral 1,2-diphosphine ligands **28b**-**28h** in high yields and stereoselectivities.

Figure 1.3



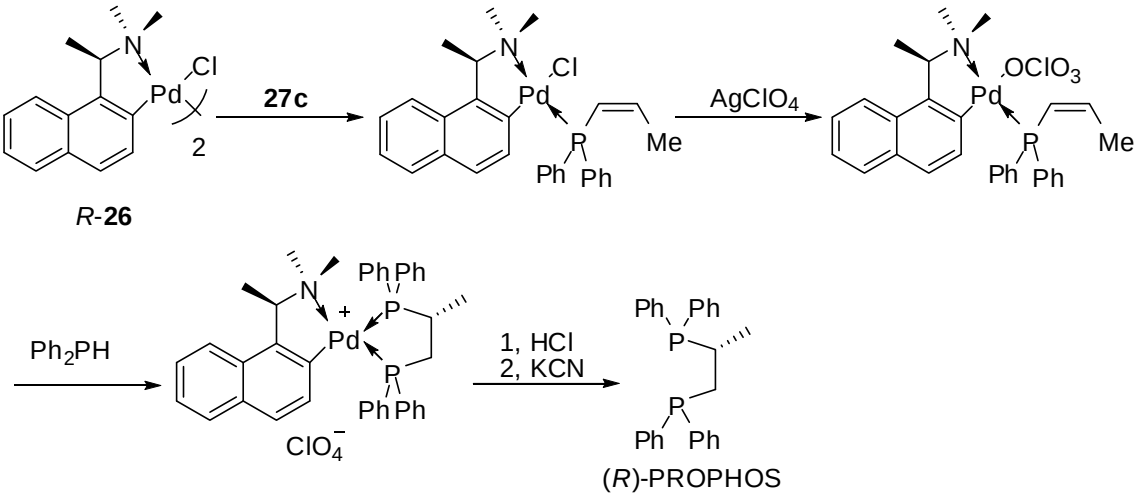
Interestingly, as illustrated in Scheme 1.19, 3,4-dimethyl-1-phenylphosphole sulfide (DMPPS) can act both as diene and dienophile in the organopalladium complex promoted asymmetric Diels-Alder reactions to afford the chiral diphosphine monosulfide ligands **29**[76] and **30**,[77] respectively.



Scheme 1.19

1.3.2 Asymmetric Hydrophosphination Reactions

The addition of secondary phosphines to carbon-carbon multiple bond, known as hydrophosphination, is the most valuable and convenient process for synthesis of functionalized tertiary phosphine ligands.[78] In general, when the phosphorus functionalized olefins were employed, the hydrophosphination reactions can produce a class of useful diphosphine ligands. Our initial study, as shown in Scheme 1.20, indicates that the chiral orthometallated amine complexes can also serve as efficient template for the asymmetric hydrophosphination reaction. In the absence of metal ion, diphenylphosphine shows no reactivity towards (Z)-diphenyl-1-propenylphosphine. However, upon activated by coordination to palladium complex, the hydrophosphination reaction proceeded smoothly with high regio- and stereoselectivity under mild conditions to generate the chiral 1,2-diphosphine (*R*)-PROPHOS.[67a]

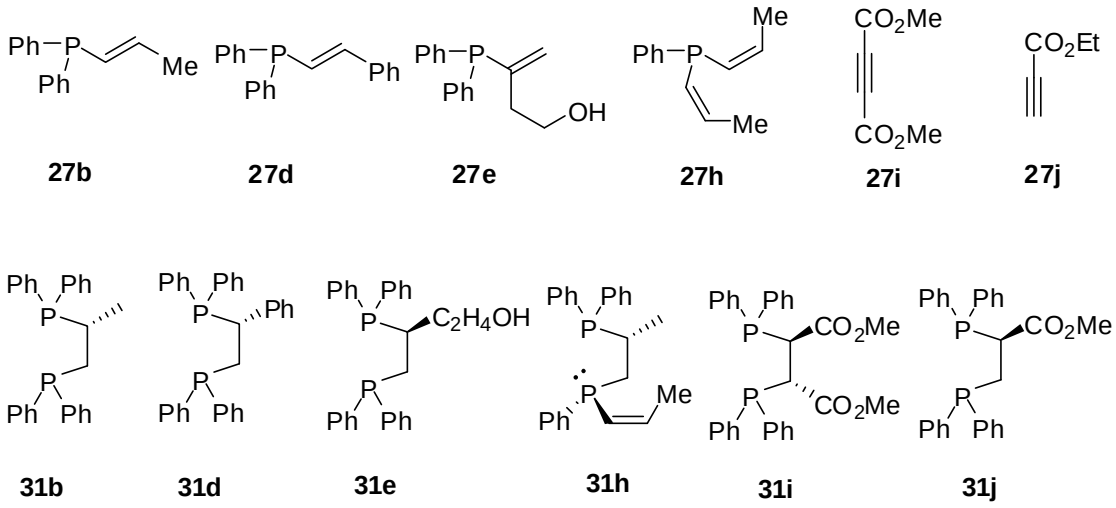


Scheme 1.20

Other vinylic phosphine like **27b**,[67a] **27d**,[67b] **27e**,[67c] and **27h**[67d] (Figure 1.4) have also proved to be reactive towards addition reactions with diphenylphosphine in the presence of the palladium complex *R*-**26** and yield a group of chiral 1,2-diphosphine ligands **31d-**

31h with high efficiency. It is noteworthy that the bis(acetonitrile) palladium complex *R*-**32** (Figure 1.2) derived for the palladium template *R*-**26**, can efficiently promote the hydrophosphination of activated alkynes such as dimethyl acetylenedicarboxylate **27i**[79a] and ethyl propiolate **27j**[79b] to form corresponding 1,2-diphosphine ligands **31i** and **31j** with high regio- and stereo-selectivities (Figure 1.4).

Figure 1.4



1.4 Aims of the Present Project

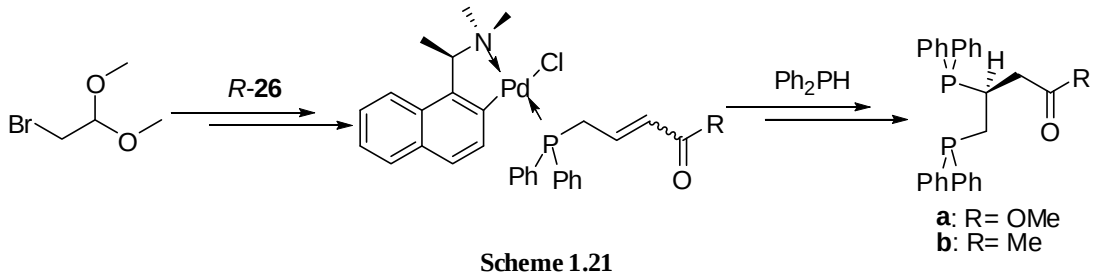
As aforementioned, the organopalladium complex (*R*-**26**) containing (1-(dimethylamino)ethyl)naphthalene as the chiral auxiliary has been successfully employed in our group for synthesis of a wide range of functionalized chiral diphosphines by means of asymmetric hydrophosphination and Diels-Alder reactions. However, the scope of reaction substrates and the products have been limited to selected vinylic phosphines and the synthesis of chiral 1,2-diphosphine ligands.

The current project aims at the development of new substrates including keto-, ester-, and cyano-substituted allylic and homoallylic monophosphines, and their subsequent

asymmetric hydrophosphination reactions to synthesize a new class of functionalized chiral 1,2- and 1,3-diphosphine ligands with high efficiency as shown in Scheme 1.21-1.24 (Chapter 2-4). Moreover, the asymmetric Diels-Alder reaction between DMPP and ester-substituted allylic phosphines has also been investigated. With appropriate controls, both P-chiral 1,2- and 1,3-diphosphines with the phosphanorbornene skeletons can be prepared with high yield, chemo- and stereoselectivities (Scheme 1.25, Chapter 5).

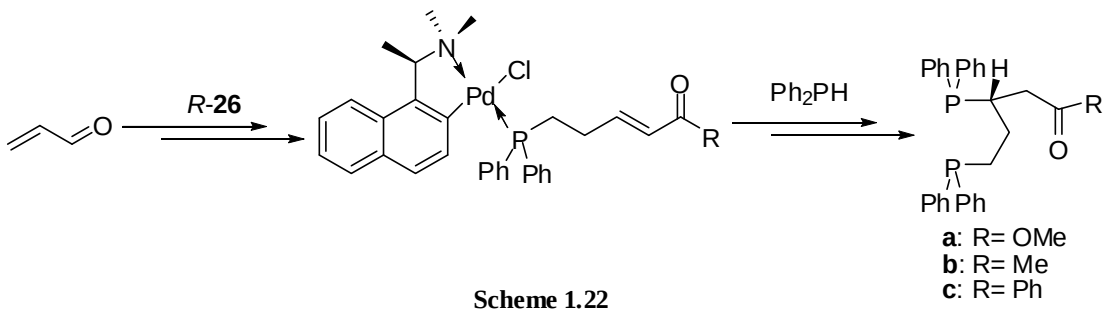
All research work reported in this thesis are parts of our ongoing efforts in the development of new chiral diphosphine ligands by employing the chiral cyclopalladated amine complex.

Chapter 2, Novel Synthesis of Functionalized 1,2-Diphosphines *via* Asymmetric Hydrophosphination of Coordinated Allylic Phosphines.

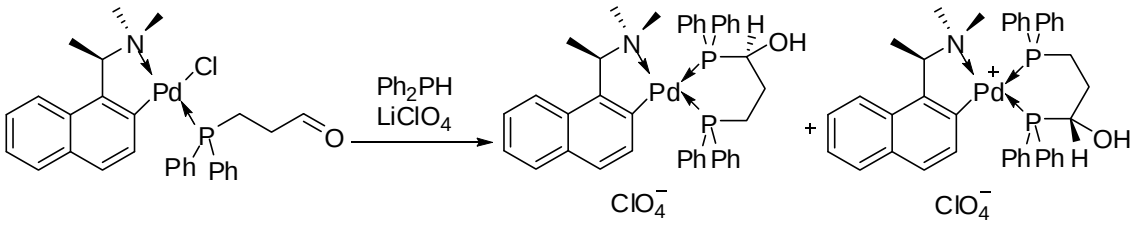


Scheme 1.21

Chapter 3, Asymmetric Synthesis of Functionalized 1,3-Diphosphines *via* Chiral Palladium Complex Promoted Hydrophosphination of Activated Olefins.

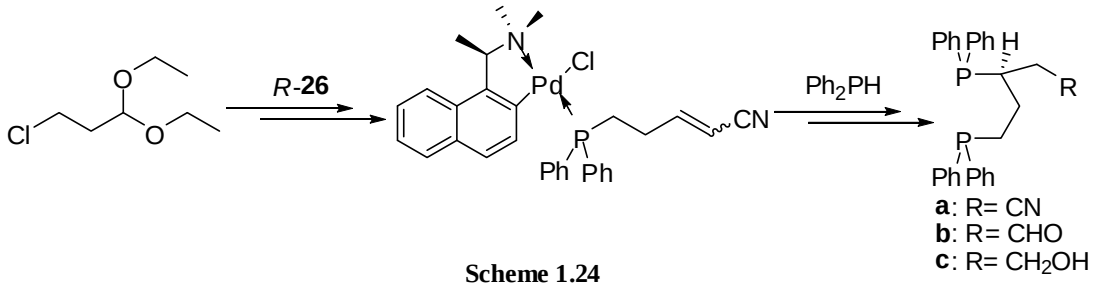


Scheme 1.22



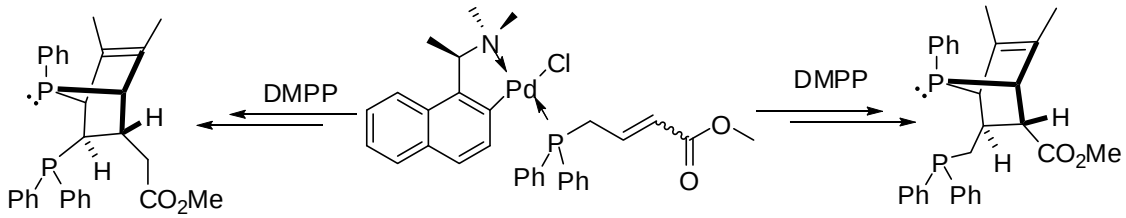
Scheme 1.23

Chapter 4, Palladium Template Promoted Asymmetric Synthesis of Novel 1,3-Diphosphines by Hydrophosphination and Functional Group Transformation Reactions.



Scheme 1.24

Chapter 5, Controllable Synthesis of P-Chiral 1,2- and 1,3-Diphosphines *via* Asymmetric Diels-Alder Reactions Involving Functionalized Allylic Phosphine as Dienophile.



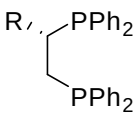
Scheme 1.25

Chapter II

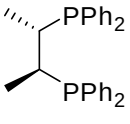
Novel Synthesis of Functionalized 1,2-Diphosphines *via* Asymmetric Hydrophosphination of Coordinated Allylic Phosphines

2.1 Introduction

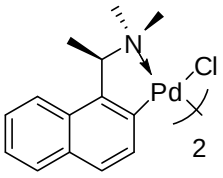
Chelating 1,2-bis(diphenylphosphino)ethanes bearing chirality on the carbon backbone, such as CHIRAPHOS and PROPHOS, have found widespread application as chiral bidentate ligands in transition metal catalyzed asymmetric reactions.[80] However, such chiral diphosphines are generally obtained by tedious optical resolution or derived from the chiral pool which may limit their structural diversity.[81] Therefore, the development of new methods or strategies for the synthesis of enantiomerically pure diphosphines is of significant importance.



(*S*)-PROPHOS: R=Me



(*S*,*S*)-CHIRAPHOS



R-**26**

In terms of atom economy and synthetic value, the addition of secondary phosphines to activated olefins such as *α*,*β*-unsaturated carbonyl derivatives, acrylonitriles, and nitroalkenes is an important process in organophosphorus chemistry,[78,82,83] since it allows the creation of a phosphorus-carbon bond and the introduction of various functional groups into the molecule in a single step. The process could be induced by thermal activation,[84] strong base,[85] radical initiators,[86] or organocatalysts.[60] In addition,

organometallic complexes can be efficient promoters as, by means of coordination, they can protect the phosphine species from oxidation during the addition reaction. Furthermore, when chiral auxillaries are employed, it also provides the protocol to synthesize chiral versions of the bidentate diphosphine ligands.[66,67]

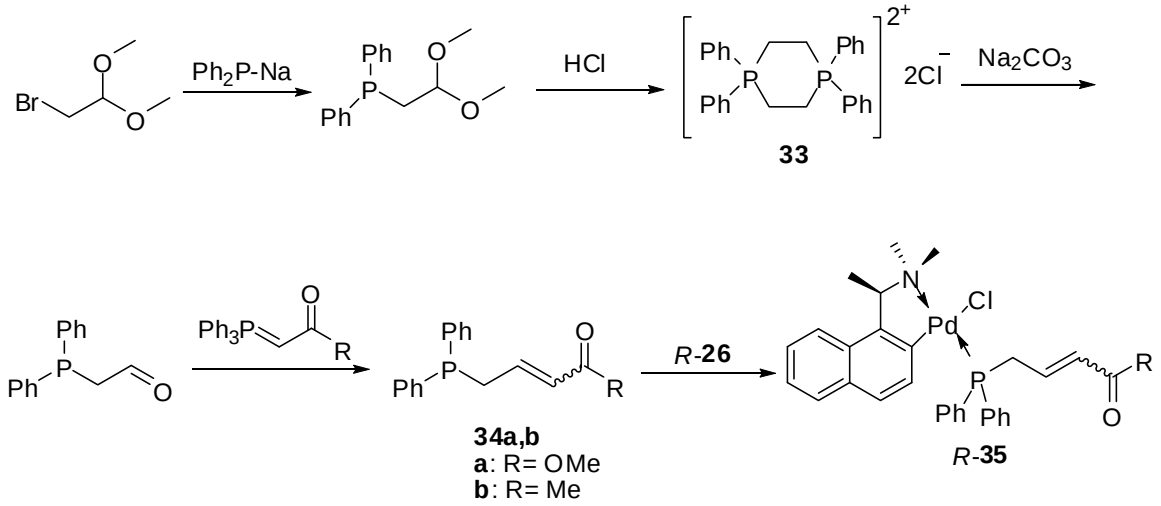
Over the past decade, our group has established that organopalladium complexes containing (*S*)- or (*R*)-(1-(dimethylamino)ethyl)-naphthalene as the chiral auxiliary (*R*-**26**) are good promoters for the synthesis of various chiral diphoshines by means of asymmetric Diels-Alder reactions[66] and hydrophosphination reactions[67] involving vinylic phosphine substrates. In pursuing our interests in the application of the palladium complex and development of facile strategies for synthesis of chiral diphosphine ligands, we herein report a simple and efficient synthesis of keto- and ester-functionalized chiral diphosphines. The synthesis involved the preparation of allylic phosphine substrates with ester- and keto-functionalities, and their subsequent Michael-type hydrophosphination reactions yielded the desired functionalized chiral diphosphine products with high yields and stereoselectivities.

2.2 Results and Discussion

We have recently reported the chiral palladium template promoted hydrophosphination of substituted vinylic phosphines with good stereoselectivities.[67] Consistent with the classic organic chemistry, when the vinylic groups bear electron withdrawing functionalities, they are more reactive toward Michael-type addition reactions than the unactivated carbon-carbon double bond. In principle, if the phosphorus atom is introduced into the activated olefins, for example at the allylic position, the

resultant substrates will be easily converted to functionalized bidentate phosphine ligands by means of Michael-type additions such as hydrophosphination, hydroamination, and hydrothiolation reactions. In contrast to vinylic phosphine substrates, interestingly, the literature reports on the preparation and reactions of allylic phosphine compounds are very rare.[87]

2.2.1 Synthesis of Ester- and Keto-Functionalized Allylic Phosphine Substrates



Scheme 2.1

Scheme 2.1 shows the preparation of the allylic monophosphine ligand methyl 4-(diphenylphosphino)but-2-enoate and its palladium complex. The diphosphonium salt **33**[88] was prepared from the substitution reaction of bromoacetaldehyde dimethyl acetal and sodium diphenylphosphide followed by hydrolysis with hydrochloric acid. Subsequent quenching with sodium carbonate and *in situ* reaction with methyl (triphenylphosphoranylidene)acetate at room temperature gave the allylic phosphine intermediate viz methyl 4-(diphenylphosphino)-but-2-enoate **34a**. The free phosphine ligand was not isolated and was allowed to coordinate to the palladium template *R*-**26** to

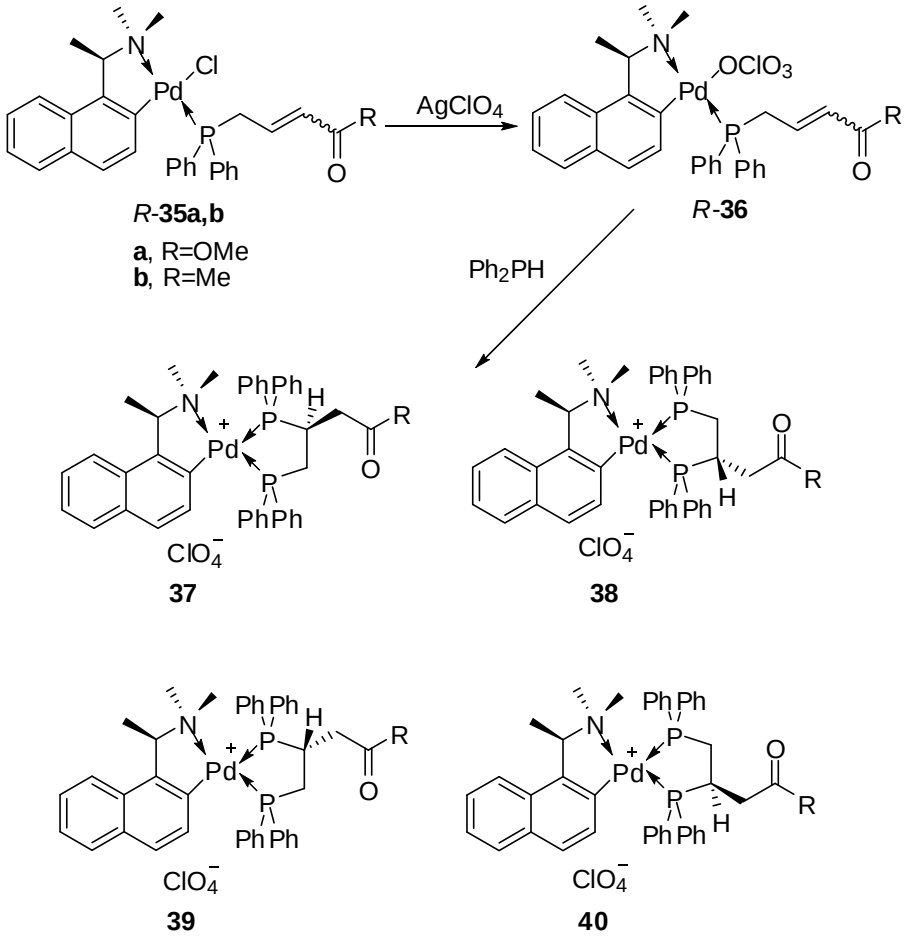
generate the monomeric complex *R*-**35a** as a mixture of the Z/E (1:3) isomers in 86% yield. It is noteworthy that this is the first instance of the preparation of an ester-functionalized allylic phosphine and its palladium complex.

The *cis*- and *trans*-isomeric products can be separated efficiently by column chromatography and thus provide an opportunity to characterize and test the two isomeric complexes for the subsequent hydrophosphination reaction. The ^{31}P NMR spectrum in $CDCl_3$ of the *cis*-*R*-**35a** isomer exhibited a singlet at δ 33.7, while the *trans*-*R*-**35a** isomer showed a singlet resonance at δ 33.2. The keto-functionalized allylic substrate 5-(diphenylphosphino)pent-3-en-2-one and its palladium complex *R*-**35b** were prepared according to a similar procedure by using 1-(triphenylphosphoranylidene)acetone for the Wittig reaction. It should be noted that the *trans* isomer, *trans*-*R*-**35b**, was obtained as the sole product. However this reaction needs to be conducted at an elevated temperature (60 ºC) due to the relatively inactive nature of the keto-substituted Wittig reagent. A sharp singlet signal at δ 33.4 was observed in the ^{31}P NMR spectrum of keto-functionalized allylic phosphine substrate.

2.2.2 Asymmetric Hydrophosphination of Coordinated Methyl 4-(Diphenylphosphino)-but-2-enoate (*R*-35a)

The asymmetric synthetic methodology adopted is illustrated in Scheme 2.2. The chloro ligand in complex *R*-**35a** is well known to be kinetically and thermodynamically stable.[66,67] Therefore, treatment of complex *R*-**35a** with aqueous silver perchlorate in dichloromethane gave the cationic perchlorate intermediate complex *R*-**36a** in essentially quantitative yield. In routine synthesis, however, this highly reactive species is not

isolated. Upon removal of the silver chloride, the dichloromethane solution of *R*-**36a** was subsequently treated with one equivalent of diphenylphosphine at −78 ºC to afford the desired hydrophosphination products. The addition process was monitored by ^{31}P NMR spectroscopy and was found to be complete within 1 hour. In theory, the hydrophosphination reaction may produce up to four diastereomers, i.e., **37a**, **38a**, **39a** and **40a**. Complexes **37a** and **38a** are regioisomers on the palladium atom which adopt the same *S* absolute configuration at the newly generated stereogenic carbon centers. Similarly, complexes **39a** and **40a** are regioisomers with *R* absolute configuration at the new stereogenic centers.



Scheme 2.2

Interestingly, when *cis*-*R*-**35a** was employed for the hydrophosphination, the reaction only yielded the two regioisomeric complexes **37a** and **38a** as an equilibrium mixture in solution. The ^{31}P NMR spectrum of the crude product in $CDCl_3$ exhibited two pairs of doublets at δ 30.3, 64.0 (J_{PP} = 35.3 Hz) and 44.9, 50.9 (J_{PP} = 33.5 Hz) with the intensity ratio of 1:9.5. Upon crystallization from dichloromethane-diethyl ether, the product **37a** was obtained as white prisms in 87% yield, $[\alpha]_D = -113.0°$ (*c* 0.9, CH_2Cl_2). The ^{31}P NMR spectrum of **37a** indicated a pair of doublets at δ 44.9, 50.9 (J_{PP} = 33.5 Hz). It clearly indicates that the product **38a** slowly converts into its regioisomeric complex **37a** during the crystallization process. Apparently, the addition process stereospecifically formed the *S* absolute configuration at the newly generated chiral carbon center.

The molecular structure and the absolute stereochemistry of complex **37a** were determined by single-crystal X-ray crystallographic analysis (Figure 2.1). Selected bond lengths and angle parameters are given in Table 2.1. The coordination around the palladium atom is distorted square planar. The P_1PdP_2 plane is rotated at an angle of 4.6° with respect to that of NPdC, and the angles around the palladium center are in the ranges of 81.0(1) – 98.6(1) and 175.0(1) – 177.9(1)°. The phosphorus atom that is adjacent to the ester substituent coordinates *trans* to the naphthalene carbon. The five-membered diphosphine chelate adopts the δ ring conformation with the ester functionality occupying the sterically favorable equatorial position. Both Pd-P bond length (2.343(1), 2.245(1) Å) and the bite angle (84.6(1)°) are comparable with the similar 1,2-diphosphine chelating palladium complexes previously reported.[67]

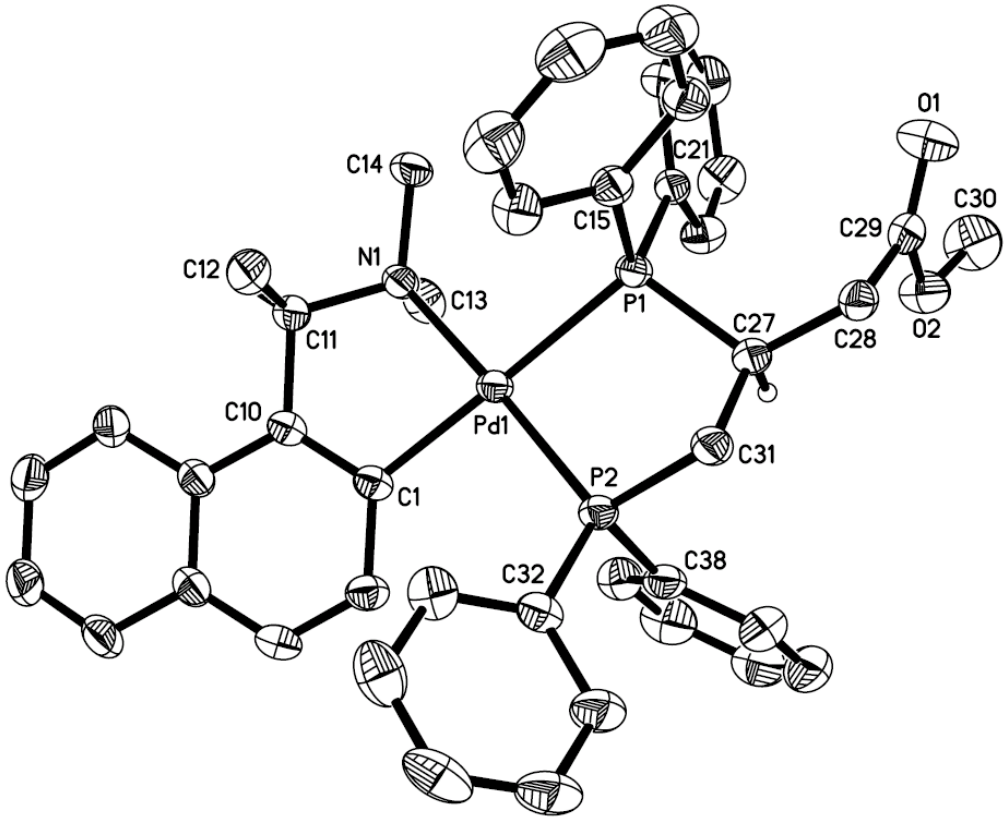
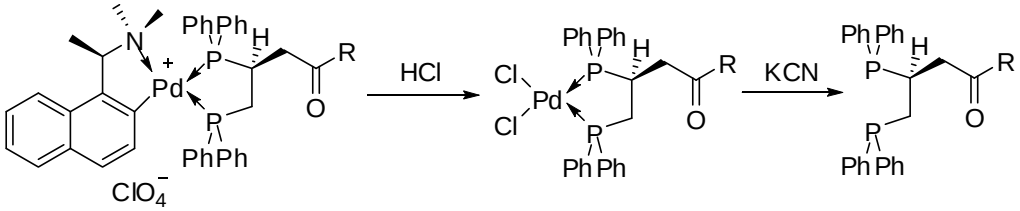


Figure 2.1. Molecular structure and absolute stereochemistry of complex **37a**

Table 2.1. Selected Bond Lengths (Å) and Angles (deg) of **37a**

Pd1–C1	2.055(2)	Pd1–N1	2.137(2)
Pd1–P1	2.343(1)	Pd1–P2	2.245(1)
C27–P1	1.852(2)	C27–C31	1.534(4)
C31–P2	1.830(3)	C27–C28	1.535(3)
C28–C29	1.502(4)	C29–O1	1.192(3)
C1–Pd1–N1	81.0(1)	C1–Pd1–P2	95.9(1)
N1–Pd1–P2	175.0(1)	C1–Pd1–P1	177.9(1)
N1–Pd1–P1	98.6(1)	P2–Pd1–P1	84.6(1)
C31–C27–P1	105.0(2)	C27–C31–P2	107.5(2)
C27–P1–Pd1	105.5(1)	C31–P2–Pd1	108.0(1)
C28–C27–P1	117.0(2)	C31–C27–C28	113.0(2)

For comparison of the stereoselectivity, the asymmetric hydrophosphination reaction was repeated using *trans*-*R*-**35a** as the precursor complex. Similarly the hydrophosphination may also generate the same four possible stereoisomeric products **37a**–**40a**. However, upon treatment of the perchlorate intermediate *trans*-*R*-**36a** with diphenylphosphine under similar reaction conditions, the ^{31}P NMR spectrum in $CDCl_3$ of the crude product exhibited three pairs of doublets at δ 44.9, 50.9 (J_{PP} = 33.5 Hz); 30.3, 64.0 (J_{PP} = 35.3 Hz), which indicated the formation of the regioisomers **37a** and **38a**, and a new pair of doublet signal at δ 45.7, 49.8 (J_{PP} = 31.3 Hz) with the intensity ratio of 12:1:1.2, respectively. The minor new signal showed that one of the regioisomers **39a** or **40a** was also formed during the addition reaction. Thus the absolute stereoselectivity at the newly formed chiral carbon center in the hydrophosphination of *trans*-*R*-**35a** is 10.8:1. The major product **37a** could be separated upon fractional recrystallization from acetonitrile-diethyl ether as white crystals in 70% yield. When an acetonitrile solution of **37a** was kept at room temperature for several day, a new pair of doublet phosphorus signals at δ 30.3, 64.0 (J_{PP} = 35.3 Hz) in the ^{31}P NMR spectrum appeared which indicated the formation of the regioisomeric complex **38a**.



Scheme 2.3

As shown in Scheme 2.3, the chiral naphthylamine auxiliary on complex **37a** could be removed chemoselectively by the treatment with concentrated hydrochloric acid. The

neutral dichloro palladium complex **41a** was thus obtained as pale yellow prisms in quantitative yield. The molecular structure and coordination properties were studied by single-crystal X-ray diffraction analysis as shown in Figure 2.2. Selected bond and angle parameters are given in Table 2.2. As expected, the geometry around the Pd atom is square planar with slight tetrahedral distortion (4.9(1)°). Apparently, the absolute stereochemistry and the integrity of the ester-functional group remained unchanged during the acid treatment. The ^{31}P NMR spectrum of the dichloro product **41a** in CD_2Cl_2 exhibited a pair of doublets at δ 52.0, 70.6 (J_{PP} = 7.3 Hz).

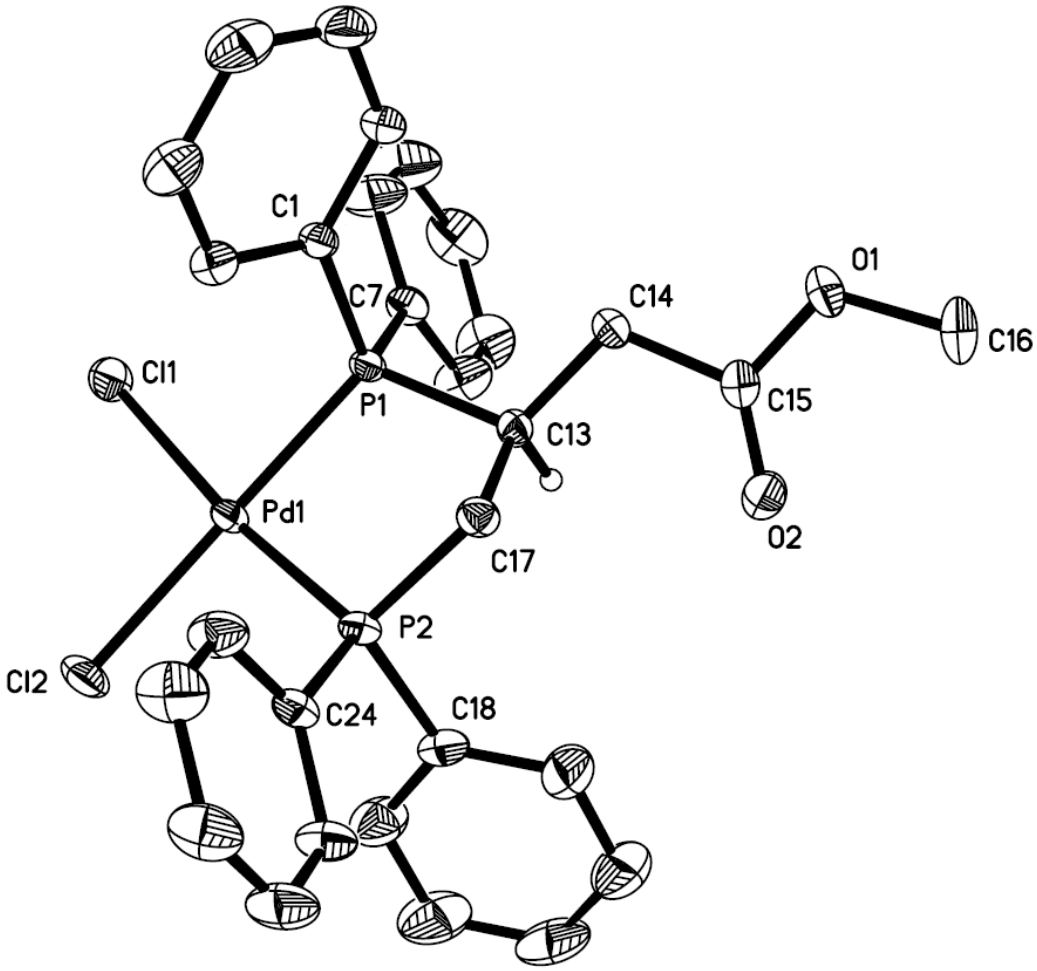
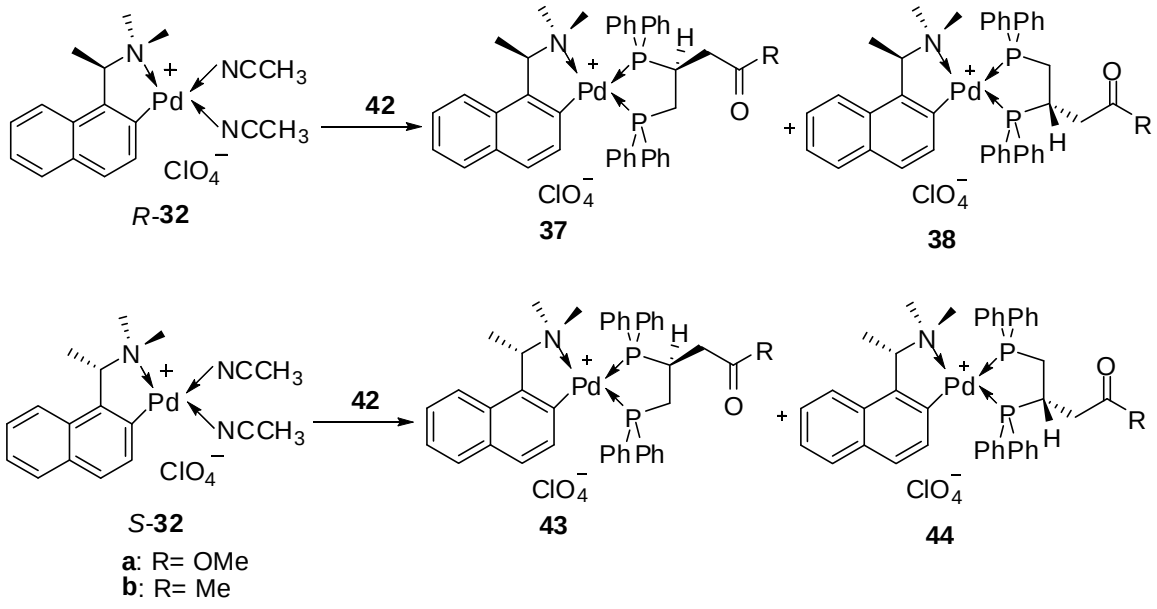


Figure 2.2. Molecular structure of complex **41a**

Table 2.2. Selected Bond Lengths (Å) and Angles (deg) of **41a**

Pd1–P1	2.232(1)	Pd1–P2	2.229(1)
C13–P1	1.858(2)	C13–C17	1.543(3)
C13–C14	1.522(3)	C17–P2	1.825(3)
P2–Pd1–P1	86.8(1)	Cl2–Pd1–Cl1	95.7(1)
P1–Pd1–Cl2	177.5(1)	P2–Pd1–Cl1	171.5(1)
P1–Pd1–Cl1	86.0(1)	P2–Pd1–Cl2	91.4(1)
C17–C13–P1	105.4(2)	C13–C17–P2	109.0(2)

The optically active ester-functionalized diphosphine ligand **42a** could be liberated from palladium complex **41a** by treatment of a dichloromethane solution of the complex with aqueous potassium cyanide as shown in Scheme 2.3. The liberated diphosphine ligand was thus obtained as a white solid in 86% yield, $[\alpha]_D = -50.7°$ (*c* 1.8, CH_2Cl_2). The ^{31}P NMR spectrum of the **42a** in $CDCl_3$ showed a pair of doublets at δ – 0.4, – 21.7 (J_{PP} = 29.2 Hz).



Scheme 2.4

In order to determine the optical purity of the liberated ligand and to establish the identity of the minor isomers that were generated in the original hydrophosphination

reactions, the free diphosphine **42a** was recoordinated to the bis(acetonitrile) complex *R*-**32** as illustrated in Scheme 2.4. The ^{31}P NMR spectrum of the recomplexation products in $CDCl_3$ indeed showed two pairs of doublet signals at δ 44.9, 50.9 (J_{PP} = 33.5 Hz); δ 30.3, 64.0 (J_{PP} = 35.3 Hz). These spectroscopic signals were identical to those recorded directly from the original hydrophosphination and thus confirmed that the two regioisomers **37a** and **38a** were formed from the recomplexation reaction. As a further test, the two regioisomers **43a** and **44a** were prepared from diphosphine ligand **42a** and the equally accessible enantiomeric complex *S*-**32**. The ^{31}P NMR spectrum of the crude products in $CDCl_3$ exhibited two different pairs of doublet phosphorus signals at δ 49.8, 45.7 (J_{PP} = 31.3 Hz); 74.6, 38.6 (J_{PP} = 24.5 Hz). Note that products **43a** and **44a** are the enantiomeric forms of **39a** and **40a** respectively. In the absence of any chiral deuterated solvent, the two pairs of enantiomers should reveal identical NMR signals. Thus the absence of resonances at δ 30.3, 44.9, 50.9, and 64.0 (^{31}P NMR signals of **37a** and **38a**) confirmed that liberated functionalized diphosphine ligand **42a** is optically pure.

2.2.3 Asymmetric Hydrophosphination of Coordinated 5-(Diphenylphosphino)-pent-3-en-2-one (*R*-35b)

A similar procedure was adopted for the hydrophosphination of the keto-functionalized precursor *R*-**35b**. As illustrated in Scheme 2.2, upon abstraction of the chloro ligand by treatment with silver salt, the reactive perchlorato complex *R*-**36b** was then reacted with one equivalent of diphenylphosphine at −78 ºC for 1 hour to give three of the four possible diastereomeric products **37b**–**40b**. Prior to purification, the ^{31}P NMR spectrum of the crude product in $CDCl_3$ indicated three pairs of doublets at δ 31.6, 65.9

(J_{PP} = 31.8 Hz); 45.7, 51.8 (J_{PP} = 33.3 Hz) and 46.4, 50.6 (J_{PP} = 30.9 Hz) with the intensity ratio of 1:15.6:1.8, respectively.

The two regioiosmers **37b** and **38b** could be isolated efficiently as an equilibrium mixture by column chromatography in 78% yield. The ^{31}P NMR spectrum exhibited two pairs of doublets at δ 31.6, 65.9 (J_{PP} = 31.8 Hz) and 45.7, 51.8 (J_{PP} = 33.3 Hz). Upon slow diffusion of diethyl ether into a dichloromethane solution of the isomeric mixture, the keto-substituted palladium complex **37b** was obtained as pale yellow prisms in 78% yield. Similarly, the isomer **38b** slowly converts into the regioisomeric product **37b** during the course of crystallization process. The ^{31}P NMR spectrum of crystallized **37b** indicated a pair of doublets at δ 45.7, 51.8 (J_{PP} = 33.3 Hz).

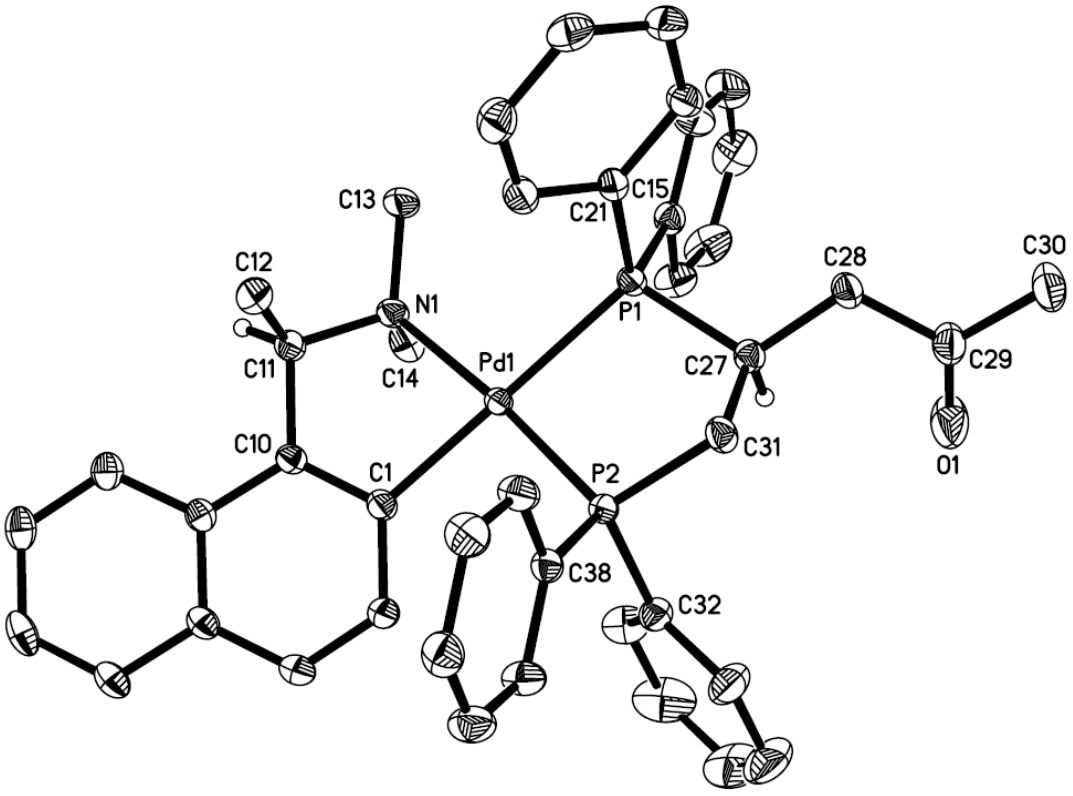


Figure 2.3. Molecular structure and absolute stereochemistry of complex **37b**

The single-crystal X-ray diffraction analysis unambiguously established its chelating properties and the absolute configuration (Figure 2.3). Selected bong lengths and bond angles are given in Table 2.3. The tetrahedral distortion around the palladium center (2.9°) is smaller than its counterpart in complex **37a**, resulting in a relative larger bite angle (85.1(1)°), and the angles around the metal center are in the ranges of of 80.5(1) – 99.8(1) and 174.4(1) – 178.4(1)°. The newly formed stereogenic center at C27 adopts the *S* absolute configuration with the keto functionality occupying the sterically favorable equatorial position.

Table 2.3. Selected Bond Lengths (Å) and Angles (deg) of **37b**

Pd1–C1	2.050(1)	Pd1–N1	2.135(1)
Pd1–P1	2.355(1)	Pd1–P2	2.247(1)
C27–P1	1.853(1)	C27–C31	1.534(2)
C31–P2	1.833(1)	C27–C28	1.528(2)
C28–C29	1.510(2)	C29–O1	1.210(2)
C1–Pd1–N1	80.5(1)	C1–Pd1–P2	94.6(1)
N1–Pd1–P2	174.4(1)	C1–Pd1–P1	178.4(1)
N1–Pd1–P1	99.8(1)	P2–Pd1–P1	85.1(1)
C31–C27–P1	106.8(1)	C27–C31–P2	110.4(1)
C27–P1–Pd1	105.5(1)	C31–P2–Pd1	109.0(1)
C28–C27–P1	115.1(1)	C31–C27–C28	112.5(1)

Treatment of complex **37b** with concentrated hydrochloric acid removed the chiral naphthylamine auxiliary and gave the enantiomerically pure keto-functionalized dichloro complex **41b** chemoselectively (Scheme 2.3). The ^{31}P NMR spectrum of the neutral dichloro complex in CD_2Cl_2 showed a pair of doublets at δ 53.6, 71.6 (J_{PP} = 7.1 Hz). Further treatment of **41b** with aqueous potassium cyanide liberated the optical pure keto-functionalized diphosphine ligand **42b** as a white solid in 92% yield, $[\alpha]_D$ = – 56.4° (*c* 1.5,

CH_2Cl_2). The ^{31}P NMR spectrum of the liberated diphosphine in $CDCl_3$ exhibited a pair of doublets at δ – 0.6, – 21.7 (J_{PP} = 34.1 Hz).

Similarly, the optical purity of the chiral diphosphine ligand **42b** was confirmed by recoordination of the ligand to *R*-**32** as illustrated in Scheme 2.4. The ^{31}P NMR spectrum of the recomplexation products undoubtedly gave a pair of doublets at δ 45.7, 51.8 (J_{PP} = 33.3 Hz) and 31.6, 65.9 (J_{PP} = 31.8 Hz), which indicated that the formation of the regioisomers **37b** and **38b**. Upon recoordination of the free ligand to equally accessible enantiomeric complex *S*-**32**, a pair of diasteromeric complexes **43b** and **44b** were formed. The ^{31}P NMR spectrum of the newly formed regioisomeric complexes indeed exhibited two distinct pairs of doublet signals at δ 46.4, 50.6 (J_{PP} = 30.9 Hz) and 38.9, 74.6 (J_{PP} = 24.0 Hz). It should be noted that complexes **43b** and **44b** are the enantiomeric forms of products **39b** and **40b**, respectively, and thus should have the same phosphorus signals in ^{31}P NMR spectrum. The recoordination reactions therefore confirmed that the liberated keto-functionalized diphosphine ligand **42b** is enantiomerically pure.

2.3 Mechanistic Considerations

As aforementioned in Chapter I, the five-membered chelate in complex *R*-**26** is locked into δ confirmation both in solid state and solution due to the internal steric repulsion between the methyl substituent at the stereogenic carbon and its neighboring naphthylene proton.[65] A key stereochemical feature of the orthometalated chiral naphthylamine complex is that the prochiral methyl groups on nitrogen atom are fixed into stereochemically non-equivalent axial and equatorial positions. From a mechanistic standpoint, the diphenylphosphine would kinetically coordinate on the vacant site that is

trans to the naphthalene carbon in the perchlorate intermediate complex *R*-**36** at –78 ºC. The P–H bond is relatively acidic upon coordination to palladium atom, and the phosphido complex could thus be generated by deprotonation with triethylamine. Therefore, the asymmetric intramolecular hydrophosphination will proceed by the Michael addition of the nucleophilic phosphido moiety to the activate double bond.

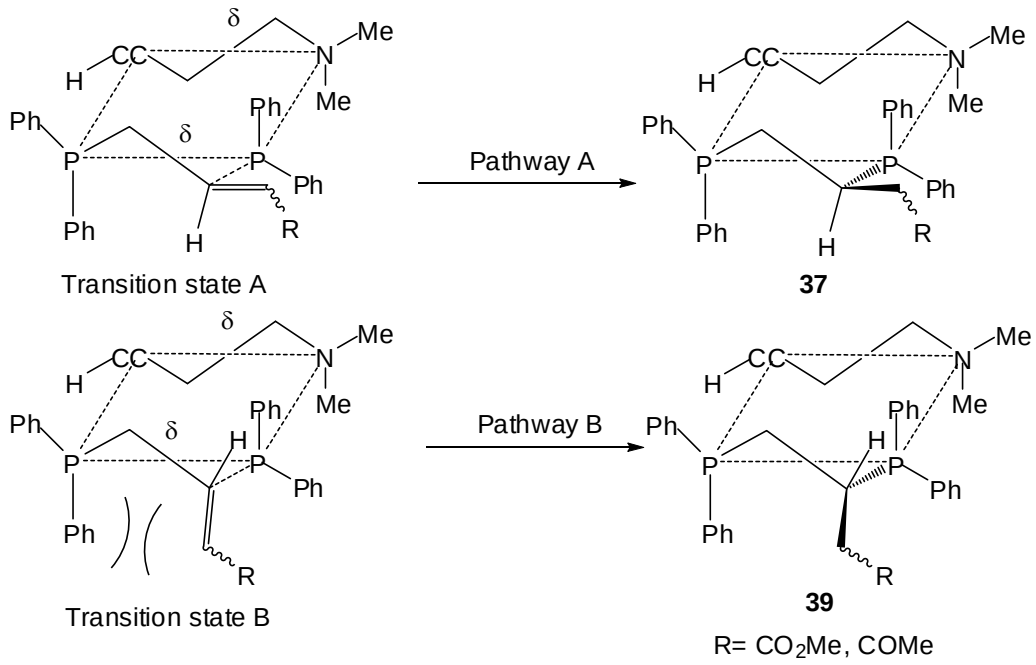


Figure 2.4. Two possible reaction pathways of hydrophosphination reaction

By correlation between a Dreiding model study and the X-ray crystallography data of the hydrophosphination product, transition states A and B are proposed as the two possible reaction pathways as illustrated in Figure 2.4. The five-membered diphosphine chelates in both transition states adopt the sterically favorable δ ring conformation with different orientations of the activated double bond. Within reaction pathway A, the hydrophosphination of the ester- and keto-functionalized allylic phosphine substrates *R*-**35** would generate complex **37** with the *S* absolute configuration at the newly formed chiral carbon center. In this transition state, the interchelate steric interactions between the

reacting phosphines and the chiral auxiliary are minimal. However, when it comes to reaction pathway B, due to the gauche interactions and steric repulsion between the double bond and one of phenyl groups on phosphorus atom, the formation of complex **39** in which the new stereogenic carbon centers adopt the *R* configuration is rather unfavorable. Furthermore, the exclusive formation of *S* configuration when *cis*-*R*-**35a** is employed for the hydrophosphination reaction indicates that the internal steric repulsion in the case of *cis*-*R*-**35a** is much stronger than that of *trans*-*R*-**35a**.

2.4 Conclusion

In summary, the ester- and keto-functionalized allylic monophosphine palladium complexes containing the ortho-metalated (*R*)-(1-(dimethylamino)ethyl)naphthalene as the chiral auxiliary were synthesized. The hydrophosphination reactions of the allylic substrates afforded the chiral 1,2-bis(diphenylphosphino)ethane ligands with ester and keto functionalities. When *cis*-*R*-**35a** was employed for the hydrophosphination, the addition process stereospecifically formed two regioisomeric complexes **37a** and **38a** with the *S* absolute configuration at the newly generated carbon center. When the hydrophosphination was performed by using the functionalized allylic substrates *trans*-*R*-**35a** and *trans*-*R*-**35b**, the reactions can also proceed with high regio and stereoselectivities under mild conditions. The major products in which the new stereogenic carbon centers adopt the *S* configuration can be separated by fractional crystallization or by column chromatography.

2.5 Experimental Section

All air-sensitive manipulations were performed under a positive pressure of argon using a standard Schlenk line. Solvents were dried and degassed prior to use when necessary. NMR spectra were recorded at 25 ºC on Bruker ACF 300 (^{1}H at 300 MHz, ^{13}C at 75 MHz and ^{31}P at 121.5 MHz) and 400 (^{1}H at 400 MHz and ^{13}C at 100 MHz) spectrometers. 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 ºC 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*-**26**,[89a,b] *R*-**32**, and *S*-**32**[89c] were prepared according to literature methods.

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

Preparation of Monophosphine Palladium Complex *R*-35a. Sodium diphenylphosphide generated from diphenylphosphine (0.5 g, 2.68 mmol) in THF (25 mL) solution was cooled to 0 ºC, bromoacetaldehyde dimethyl acetal (0.45 g, 2.68 mmol) in THF (5 mL) was added dropwisely over 10 min, the resulting mixture was stirred for 1h. 4 N HCl (10 mL) was added and stirred for 10 h at room temperature to yield the

intermediate diphosphonium salt **33**. Sodium carbonate solution was added slowly until the pH value of the solution was 9~10. The mixture was then extracted with ethyl acetate (3 × 20 mL). To the organic layer methyl (triphenylphosphoranylidene)-acetate (1.35 g, 4.03 mmol)) was added. After being stirred for 3 h at room temperature, palladium dimer *R*-**26** (0.87 g, 1.28 mmol) was added to the mixture and stirred for another 1 h. Upon removal of the solvent, the complex *R*-**35a** was isolated by chromatography on silica as a pale yellow powder (cis/trans = 1:3, 1.37 g, 86%).

trans-*R*-**35a** (1.02 g, 64.0%), $[\alpha]_D = -45.9°$ (*c* 1.7, CH_2Cl_2). Mp: 195.5–197 ºC. Anal. Calcd for $C_{31}H_{33}ClNO_2PPd$: C, 59.6; H, 5.3; N, 2.2. Found: C, 59.5; H, 5.5; N, 2.3. ^{31}P NMR ($CDCl_3$, 121 MHz): δ 33.2 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 2.04 (d, 3H, J_{HH} = 6.3 Hz, CH*Me*), 2.68 (s, 3H, N*Me*), 2.99 (d, 3H, J_{PH} = 3.4 Hz, N*Me*), 3.29 (ddd, 1H, J_{HH} = 9.0 Hz, J_{HH} = 12.5 Hz, J_{PH} = 14.0 Hz, PCH′*H*), 3.66 (s, 3H, CO_2*Me*), 3.88 (ddd, 1H, J_{HH} = 6.5 Hz, J_{HH} = 12.5 Hz, J_{PH} = 12.9 Hz, PC*H*′H), 4.33 (qn, 1H, $J_{HH} = J_{PH}$ = 6.2 Hz, C*H*CH_3), 5.63 (dd, 1H, J_{HH} = 15.7 Hz, J_{PH} = 4.6 Hz, C*H*CO_2Me), 6.62 (dd, 1H, J_{HH} = 8.5 Hz, J_{PH} = 6.3 Hz, Ar), 6.94 (d, 1H, J_{HH} = 8.5 Hz, Ar), 7.12-8.07 (m, 15H, Ar and CH_2C*H*). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.6 (s), 35.6 (d, J_{PC} = 29.5 Hz), 48.5 (s), 51.2 (d, J_{PC} = 3.0 Hz), 51.6 (s), 73.2 (d, J_{PC} = 3.2 Hz), 123.4 (s), 124.3 (s), 124.8 (d, J_{PC} = 8.3 Hz), 124.9 (d, J_{PC} = 8.8 Hz), 125.9 (s), 128.4 (d, J_{PC} = 10.5 Hz), 128.8 (s), 128.9 (s), 129.1 (d, J_{PC} = 10.5 Hz), 129.6 (d, J_{PC} = 44.3 Hz), 129.7 (d, J_{PC} = 44.8 Hz), 131.0 (d, J_{PC} = 2.4 Hz), 131.2 (s), 131.5 (d, J_{PC} = 2.4 Hz), 133.9 (d, J_{PC} = 10.8 Hz), 134.3 (d, J_{PC} = 11.8 Hz), 135.6 (d, J_{PC} = 12.1 Hz), 142.3 (d, J_{PC} = 4.5 Hz), 149.2 (d, J_{PC} = 2.1 Hz), 150.2 (s), 166.3 (d, J_{PC} = 2.8 Hz).

cis-*R*-**35a** (0.35 g, 22.0%), $[\alpha]_D$ = + 110.5° (*c* 1.5, CH_2Cl_2). Mp: 193–195 ºC. Anal. Calcd for $C_{31}H_{33}ClNO_2PPd$: C, 59.6; H, 5.3; N, 2.2. Found: C, 59.6; H, 5.4; N, 2.4. ^{31}P NMR ($CDCl_3$，121 MHz): δ 33.7 (s). ^1H NMR (CD_2Cl_2, 300 MHz): δ 2.03 (d, 3H, J_{HH} = 6.4 Hz, CH*Me*), 2.67 (d, 3H, J_{HH} = 1.6 Hz, N*Me*), 2.96 (d, 3H, J_{PH} = 3.5 Hz, N*Me*), 3.36 (s, CO_2*Me*), 4.02 (m, 1H, J_{HH} = 6.5 Hz, J_{HH} = 12.2 Hz, PCH′*H*), 4.30 (m, 1H, PC*H*′H), 4.36 (qn, 1H, J_{HH} = J_{PH} = 6.2 Hz, C*H*CH_3), 5.81 (dd, 1H, J_{HH} = 11.5 Hz, J_{PH} = 4.9 Hz, C*H*CO_2Me), 6.64 (dd, 1H, J_{HH} = 8.5 Hz, J_{PH} = 6.5 Hz, Ar), 6.84 (m, 1H, PCH_2C*H*), 6.90 (d, 1H, J_{HH} = 8.5 Hz, Ar), 7.16-8.17 (m, 14H, Ar). ^{13}C NMR (CD_2Cl_2, 75 MHz): δ 23.6 (s), 31.5 (d, J_{PC} = 31.3 Hz), 48.1 (d, J_{PC} = 2.6 Hz), 50.7 (s), 50.8 (d, J_{PC} = 3.1 Hz), 72.8 (d, J_{PC} = 3.3 Hz), 121.9 (d, J_{PC} = 11.5 Hz), 123.3 (s), 124.1 (s), 124.4 (d, J_{PC} = 5.7 Hz), 125.6 (s), 127.7 (d, J_{PC} = 10.6 Hz), 128.4 (s), 128.7 (s), 128.8 (d, J_{PC} = 10.5 Hz), 129.7 (d, J_{PC} = 44.7 Hz), 130.0 (d, J_{PC} = 45.3 Hz), 130.4 (d, J_{PC} = 2.5 Hz), 131.0 (s), 131.2 (d, J_{PC} = 2.4 Hz), 133.8 (d, J_{PC} = 11.1 Hz), 134.5 (d, J_{PC} = 12.1 Hz), 135.7 (d, J_{PC} = 12.1 Hz), 142.4 (d, J_{PC} = 2.8 Hz), 149.3 (d, J_{PC} = 2.1 Hz), 150.1 (s), 165.9 (d, J_{PC} = 3.5 Hz).

Preparation of Monophosphine Palladium Complex *R*-35b. A similar procedure as described for the synthesis of the intermediate diphosphonium salt **33**. Sodium carbonate solution was added slowly until the pH value of the solution was 9~10. The mixture was then extracted with ethyl acetate (3 × 20 mL). To the combined organic layer, 1-(triphenylphosphoranylidene)-acetone (1.28 g, 4.03 mmol) was added and stirred at 60 ºC for 24 h. The solution was cooled down to room temperature and palladium dimer *R*-**26** **(**0.64 g, 0.94 mmol**)** was added to the mixture. The resulting solution was stirred for 1 h. Upon removal of the solvent, the product *trans*-*R*-**35b** was isolated by chromatography on silica as a pale yellow powder (0.94 g, 82%, calculated on palladium dimer *R*-**26**). $[\alpha]_D$ =

– 22.0° (*c* 1.0, CH_2Cl_2). Mp: 196–198 ºC. Anal. Calcd for $C_{31}H_{33}ClNOPPd$: C, 61.2; H, 5.5; N, 2.3. Found: C, 61.1; H, 5.6; N, 2.5. ^{31}P NMR ($CDCl_3$，121 MHz): δ 33.4 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.04 (d, 3H, J_{HH} = 6.3 Hz, CH*Me*), 2.16 (s, 3H, CO*Me*), 2.70 (d, 3H, J_{PH} = 1.4 Hz, N*Me*), 2.99 (d, 3H, J_{PH} = 3.5 Hz, N*Me*), 3.26 (ddd, 1H, J_{HH} = 9.0 Hz, J_{HH} = 12.3 Hz, J_{PH} = 13.9 Hz, PCH′*H*), 3.94 (ddd, 1H, J_{HH} = 6.8 Hz, J_{HH} = 12.3 Hz, J_{PH} = 13.6 Hz, PC*H*′H), 4.35 (qn, 1H, J_{HH} = J_{PH} = 6.3 Hz, C*H*CH_3), 5.73 (dd, 1H, J_{HH} = 16.05 Hz, J_{PH} = 4.56 Hz, C*H*COMe), 6.64 (dd, 1H, J_{HH} = 8.6 Hz, J_{PH} = 8.5 Hz, Ar), 6.94 (d, 1H, J_{HH} = 8.6 Hz, Ar), 7.12 (m, 1H, J_{HH} = 16.05 Hz, J_{HH} = 6.8 Hz, CH_2C*H*), 7.22-8.09 (m, 14H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.7 (s), 26.9 (s), 36.2 (d, J_{PC} = 29.3 Hz), 48.5 (d, J_{PC} = 2.0 Hz), 51.3 (d, J_{PC} = 2.9 Hz), 73.1 (d, J_{PC} = 3.2 Hz), 123.4 (s), 124.4 (s), 125.0 (d, J_{PC} = 6.1 Hz), 125.9 (s), 128.4 (d, J_{PC} = 10.5 Hz), 128.8 (s), 128.9 (s), 129.2 (d, J_{PC} = 10.3 Hz), 129.5 (d, J_{PC} = 43.4 Hz), 129.6 (d, J_{PC} = 45.2 Hz), 131.1 (d, J_{PC} = 2.5 Hz), 131.3 (s), 131.6 (d, J_{PC} = 2.5 Hz), 133.9 (d, J_{PC} = 10.9 Hz), 134.3 (d, J_{PC} = 12.0 Hz), 134.7 (d, J_{PC} = 10.8 Hz), 135.6 (d, J_{PC} = 12.1 Hz), 141.7 (d, J_{PC} = 4.4 Hz), 149.2 (d, J_{PC} = 2.1 Hz), 149.9 (s), 198.0 (d, J_{PC} = 2.9 Hz).

Hydrophosphination of Monophosphine Substrate *R*-35a. The complex *cis*-*R*-**35a** (0.30 g, 0.48 mmol) in dichloromethane (15 mL) solution was treated with silver perchlorate (0.17 g, 0.75 mmol) in water (3 mL). The solution was stirred for 45 min at room temperature. Upon removal of AgCl precipitate, the organic layer was washed with H_2O (3 × 10 mL), dried over $MgSO_4$, concentrated and redissolved in dichloromethane (20 mL). The solution was allowed to cool down to – 78 ºC, after addition of 10% triethylamine, diphenylphosphine (0.09 g, 0.48 mmol) in dichloromethane (6 mL) was added slowly over 10 min. The mixture was stirred for 1 h, and then warmed to room

temperature. Upon removal of solvent, the crude product was purified by chromatography on silica to afford a mixture of regioisomers **37a** and **38a** (0.36 g, 87%). ^{31}P NMR ($CDCl_3$，121 MHz): 30.3 (d, J_{PP} = 35.3 Hz), 44.9 (d, J_{PP} = 33.5 Hz), δ 50.9 (d, J_{PP} = 33.5 Hz), δ 64.0 (d, J_{PP} = 35.3 Hz). Upon crystallization in dichloromethane-diethyl ether, product **37a** was isolated as white prisms (0.36 g, 87%). $[\alpha]_D$ = – 113.0° (*c* 0.9, CH_2Cl_2). Mp: 219–221 ºC. Anal. Calcd for $C_{43}H_{44}ClNO_6P_2Pd$: C, 59.1; H, 5.1; N, 1.6. Found: C, 59.0; H, 5.0; N, 1.8. ^{31}P NMR ($CDCl_3$，121 MHz): δ 44.9 (d, J_{PP} = 33.5 Hz), 50.9 (d, J_{PP} = 33.5 Hz). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.92 (m, 1H, C*H*H′CO_2Me), 1.94 (d, 3H, J_{HH} = 6.3 Hz, CH*Me*), 2.18 (m, 1H, J_{HH} = 10.5 Hz, J_{HH} = 14.5 Hz, PC*H*H′), 2.43 (s, 3H, N*Me*), 2.59 (m, 1H, PC*H*CH_2), 2.62 (m, 1H, CH*H*′CO_2Me), 2.63 (s, 3H, N*Me*), 3.12 (tdd, 1H, J_{HH} = 14.5 Hz, J_{PH} = 54.7 Hz, J_{PH} = 3.7 Hz, PCH*H*′), 3.49 (s, 3H, CO_2*Me*), 4.56 (qn, 1H, J_{HH} = J_{PH} = 6.0 Hz, C*H*CH_3), 6.93-8.29 (m, 26H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.2 (s), 34.0 (dd, J_{PC} = 17.9 Hz, J_{PC} = 4.8 Hz), 34.8 (dd, J_{PC} = 12.1 Hz, J_{PC} = 24.9 Hz), 35.7 (dd, J_{PC} = 20.7 Hz, J_{PC} = 36.7 Hz), 50.4 (s), 51.8 (s), 52.3 (s), 75.4 (s), 121.9 (d, J_{PC} = 31.8 Hz), 124.1 (s), 124.9 (d, J_{PC} = 48.8 Hz), 125.2 (s), 125.9 (dd, J_{PC} = 5.3 Hz, J_{PC} = 8.4 Hz), 125.9 (d, J_{PC} = 34.2 Hz), 126.4 (s), 127.6 (d, J_{PC} = 53.1 Hz), 128.6 (s), 129.0 (d, J_{PC} = 6.7 Hz), 129.5 (d, J_{PC} = 11.4 Hz), 130.2 (d, J_{PC} = 9.1 Hz), 130.3 (s), 130.4 (d, J_{PC} = 3.6 Hz), 131.9 (s), 132.0 (d, J_{PC} = 9.1 Hz), 132.0 (d, J_{PC} = 2.1 Hz), 132.9 (d, J_{PC} = 11.7 Hz), 133.7 (d, J_{PC} = 2.5 Hz), 133.9 (d, J_{PC} = 2.1 Hz), 135.4 (d, J_{PC} = 12.9 Hz), 135.8 (d, J_{PC} = 12.5 Hz), 136.2 (d, J_{PC} = 14.0 Hz), 150.8 (s), 156.1 (d, J_{PC} = 3.0 Hz), 157.6 (d, J_{PC} = 3.0 Hz), 170.9 (d, J_{PC} = 9.2 Hz).

By following the same procedure as described for the hydrophosphination of *trans*-*R*-**35a** (0.6 g, 0.96 mmol), product **37a** (0.58 g, 70%) could be isolated by repeated

fractional crystallization from acetonitrile-diethyl ether.

Hydrophosphination of Monophosphine Substrate *R*-35b. The same procedure was adopted for hydrophosphination reaction of *R*-**35b** (0.6 g, 0.98 mmol)**.** Product **37b** and **38b** could be separated efficiently as regioiosmers by column chromatography (0.66 g, 78%). ^{31}P NMR ($CDCl_3$，121 MHz): δ 31.6 (d, J_{PP} = 31.8 Hz), 45.7 (d, J_{PP} = 33.3 Hz), δ 51.8 (d, J_{PP} = 33.3 Hz), 65.9 (d, J_{PP} = 31.8 Hz). Upon slow diffusion of diethyl ether into the dichloromethane solution, **37b** can be crystallized out as pale yellow prisms (0.66 g, 78%). $[\alpha]_D$ = – 92.3° (*c* 1.3, CH_2Cl_2). Mp: 225–227 ºC. Anal. Calcd for $C_{43}H_{44}ClNO_5P_2Pd$: C, 60.2; H, 5.2; N, 1.6. Found: C, 60.1; H, 5.3; N, 1.8. ^{31}P NMR ($CDCl_3$，121 MHz): δ 45.7 (d, J_{PP} = 33.3 Hz), 51.8 (d, J_{PP} = 33.3 Hz). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.85 (m, 1H, PCH*H′*), 1.93 (d, 3H, J_{HH} = 6.1 Hz, CH*Me*), 2.03 (s, 3H, CO*Me*), 2.44 (s, 3H, N*Me*), 2.47 (m, 1H, C*H′*HCOMe), 2.61 (s, 3H, N*Me*), 2.68 (m, 1H, CH′*H*COMe), 2.70 (m, 1H, PC*H*CH_2), 3.05 (tdd, 1H, J_{HH} = 14.2 Hz, J_{PH} = 55.6 Hz, J_{PH} = 3.7 Hz, PC*H*H′), 4.54 (qn, 1H, J_{HH} = J_{PH} = 6.0 Hz, C*H*CH_3), 6.94-8.28 (m, 26H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.2 (s), 30.1 (s), 33.8 (dd, J_{PC} = 11.5 Hz, J_{PC} = 26.0 Hz), 35.2 (dd, J_{PC} = 20.8 Hz, J_{PC} = 36.5 Hz), 42.6 (dd, J_{PC} = 5.6 Hz, J_{PC} = 16.8 Hz), 50.4 (s), 51.8 (s), 75.4 (s), 122.4 (d, J_{PC} = 32.5 Hz), 124.0 (s), 125.1 (d, J_{PC} = 49.1 Hz), 125.2 (s), 125.9 (dd, J_{PC} = 6.0 Hz, J_{PC} = 7.3 Hz), 126.3 (d, J_{PC} = 34.4 Hz), 126.4 (s), 127.9 (d, J_{PC} = 52.7 Hz), 128.6 (s), 129.0 (d, J_{PC} = 6.9 Hz), 129.4 (d, J_{PC} = 11.5 Hz), 130.0 (d, J_{PC} = 11.1 Hz), 130.3 (d, J_{PC} = 9.5 Hz), 130.4 (d, J_{PC} = 10.5 Hz), 131.8 (d, J_{PC} = 10.1 Hz), 131.9 (s), 132.0 (d, J_{PC} = 2.0 Hz), 132.8 (d, J_{PC} = 11.6 Hz), 133.5 (d, J_{PC} = 2.4 Hz), 133.8 (d, J_{PC} = 1.6 Hz), 135.5 (d, J_{PC} = 12.9 Hz), 135.8 (d, J_{PC} = 12.3 Hz), 136.2 (d, J_{PC} = 13.9 Hz), 150.7 (s), 156.5 (d, J_{PC} = 2.8 Hz), 157.6 (d, J_{PC} = 2.8 Hz), 206.1 (d, J_{PC} = 7.6 Hz).

Removal of Chiral Auxiliary: Synthesis of Dichloro Complex 41. A solution of **37a** (0.3 g, 0.34 mmol) in dichloromethane (10 mL) was treated with concentrated hydrochloric acid (4 mL) for 5 h at room temperature. The mixture was then washed with water (3×20 mL), dried over $MgSO_4$, and subsenquently crystallized from dichloromethane-diethyl ether to give the ester-functionalized dichloro palladium complex **41a** as pale yellow prisms (0.21 g, 94%). $[\alpha]_D$ = + 46.4° (*c* 1.1, CH_2Cl_2). Mp: 250–253 ºC. Anal. Calcd for $C_{29}H_{28}Cl_2O_2P_2Pd$: C, 53.8; H, 4.4. Found: C, 54.1; H, 4.3. ^{31}P NMR (CD_2Cl_2，121 MHz): δ 52.0 (d, J_{PP} = 7.3 Hz), 70.6 (d, J_{PP} = 7.3 Hz). ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 2.05 (m, 1H, CH′*H*CO_2Me), 2.05 (m, 1H, PCH′*H*), 2.49 (m, 1H, J_{HH} = 3.2 Hz, J_{HH} = 17.0 Hz, C*H*′HCO$_2$Me), 2.86 (m, 1H, J_{HH} = 4.9 Hz, J_{HH} = 14.7 Hz, PC*H*′H), 3.15 (m, 1H, PC*H*CH_2), 3.45 (s, 3H, CO_2*Me*), 7.39-7.99 (m, 20H, Ar). ^{13}C NMR (CD_2Cl_2, 75 MHz): δ 32.8 (dd, J_{PC} = 16.8 Hz, J_{PC} = 35.3 Hz), 33.9 (d, J_{PC} = 18.6 Hz), 36.1 (dd, J_{PC} = 16.3 Hz, J_{PC} = 32.1 Hz), 52.2 (s), 124.5 (d, J_{PC} = 51.0 Hz), 125.9 (d, J_{PC} = 54.3 Hz), 126.7 (d, J_{PC} = 53.9 Hz), 128.9 (d, J_{PC} = 12.2 Hz), 129.1 (d, J_{PC} = 11.7 Hz), 129.1 (d, J_{PC} = 11.7 Hz), 129.2 (d, J_{PC} = 57.3 Hz), 129.3 (d, J_{PC} = 11.5 Hz), 132.1 (d, J_{PC} = 2.9 Hz), 132.3 (d, J_{PC} = 3.1 Hz), 132.4 (d, J_{PC} = 2.9 Hz), 133.0 (d, J_{PC} = 2.7 Hz), 133.2 (d, J_{PC} = 9.9 Hz), 133.4 (d, J_{PC} = 11.5 Hz), 133.7 (d, J_{PC} = 11.0 Hz), 136.1 (d, J_{PC} = 12.0 Hz), 170.8 (d, J_{PC} = 12.8 Hz).

By following the same procedure, the keto-functionalized dichloro complex **41b** (0.21 g, 89%) was prepared from **37b** (0.32 g, 0.37 mmol) after removal of the chiral auxiliary with concentrated HCl acid. Product **41b**, $[\alpha]_D$ = + 65.0° (*c* 1.0, CH_2Cl_2). Mp: 329–331 ºC (Decomp). Anal. Calcd for $C_{29}H_{28}Cl_2OP_2Pd$: C, 55.1; H, 4.5. Found: C, 54.9; H, 4.5. ^{31}P NMR (CD_2Cl_2, 121 MHz): δ 53.6 (d, J_{PP} = 7.1 Hz), 71.6 (d, J_{PP} = 7.1 Hz). ^{1}H NMR

(CD_2Cl_2, 300 MHz): δ 1.87 (s, 3H, CO*Me*), 2.04 (m, 1H, PCH′*H*), 2.28 (m, 1H, CH′*H*COMe), 2.60 (m, 1H, C*H*′HCOMe), 2.89 (m, 1H, PC*H*′H), 3.33 (m, 1H, PC*H*CH_2), 7.49-8.05 (m, 20H, Ar). ^{13}C NMR (CD_2Cl_2, 75 MHz): δ 29.4 (s), 32.3 (dd, J_{PC} = 16.3 Hz, J_{PC} = 35.1 Hz), 34.5 (dd, J_{PC} = 15.5 Hz, J_{PC} = 32.7 Hz), 42.5 (d, J_{PC} = 16.4 Hz), 124.9 (d, J_{PC} = 51.4 Hz), 125.8 (d, J_{PC} = 53.7 Hz), 126.8 (d, J_{PC} = 53.9 Hz), 128.7 (d, J_{PC} = 11.4 Hz), 128.8 (d, J_{PC} = 11.5 Hz), 128.9 (d, J_{PC} = 10.0 Hz), 129.0 (d, J_{PC} = 11.2 Hz), 129.2 (d, J_{PC} = 46.3 Hz), 131.9 (d, J_{PC} = 3.0 Hz), 132.0 (m, 4C), 132.7 (d, J_{PC} = 2.7 Hz), 133.1 (d, J_{PC} = 9.5 Hz), 133.3 (d, J_{PC} = 10.6 Hz), 133.3 (d, J_{PC} = 11.3 Hz), 135.7 (d, J_{PC} = 11.9 Hz), 204.3 (d, J_{PC} = 9.9 Hz).

Liberation of the Chiral Diphosphine Ligand 42. A solution of complex **41a** (0.15 g, 0.23 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 ester-functionalized chiral diphosphine ligand **42a** was obtained as white solid upon removal of solvent under reduced pressure (0.094 g, 86%). $[\alpha]_D$ = – 50.7° (*c* 1.8, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 121 MHz) δ – 0.4 (d, J_{PP} = 29.2 Hz), – 21.7 (d, J_{PP} = 29.2 Hz). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.00 (m, 1H, J_{HH} = 10.9 Hz, J_{HH} = 13.6 Hz, CH′*H*CO_2Me), 2.26 (m, 1H, J_{HH} = 3.5 Hz, J_{HH} = 13.6 Hz, C*H*′HCO_2Me), 2.63 (m, 2H, J_{HH} = 6.2 Hz, J_{HH} = 17.4 Hz, PC*H*$_2$), 2.84 (m, 1H, PC*H*CH_2), 3.53 (s, 3H, CO_2*Me*), 7.22-7.40 (m, 20H, Ar).

Similarly the keto-functionalized diphosphine ligand **42b** (0.08 g, 92%) was liberated from **41b** (0.12 g, 0.19 mmol) as a white solid. $[\alpha]_D$ = – 56.4° (*c* 1.5, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 121 MHz) δ – 0.6 (d, J_{PP} = 34.1 Hz), – 21.7 (d, J_{PP} = 34.1 Hz). ^{1}H NMR ($CDCl_3$,

300 MHz): δ 1.90 (s, 3H, CO*Me*), 1.96 (m, 1H, J_{HH} = 12.3 Hz, CH′*H*COMe), 2.29 (m, 1H, J_{HH} = 13.4 Hz, C*H*′HCOMe), 2.59 (m, 1H, J_{HH} = 4.9 Hz, J_{HH} = 18.0 Hz, PCH′*H*), 2.77 (m, 1H, J_{HH} = 6.4 Hz, J_{HH} = 18.0 Hz, PC*H*′H), 3.06 (m, 1H, PC*H*CH_2), 7.22-7.39 (m, 20H, Ar).

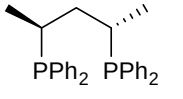
Crystal Structure Determinations of Complexes 37a, 41a, and 37b. X-ray crystallographic data for all three complexes are given in the Appendices. Crystal data were collected on a Bruker X8 CCD diffractometer with Mo Kα radiation (graphite monochromator). SADABS absorption corrections were applied. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were introduced at calculated positions and refined with a riding model. The absolute configurations of all chiral complexes were determined unambiguously by using the Flack parameter. We thank Dr Li Yongxin for undertaking the X-ray analysis.

Chapter III

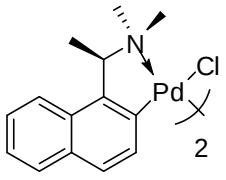
Asymmetric Synthesis of Functionalized 1,3-Diphosphines *via* Chiral Palladium Complex Promoted Hydrophosphination of Activated Olefins

3.1 Introduction

Enantiomerically pure diphosphines containing the 1,3-bis(diphenylphosphino)-propane backbones have long been proven to be powerful bidentate ligands in transition metal catalyzed asymmetric reactions.[12,90,91] For example, Mikami has reported the enantioselective spiro cyclization of 1,6-enynes catalyzed by rhodium-(*S*,*S*)-skewphos complex with up to 90% *ee*.[92] Compared with classical 1,2-diphosphines, the 1,3-diphosphines can form six-membered metallacycles involving transition metals with new catalytic activity and interesting ring conformations.[93] However, literature reviews show that such chiral diphosphine ligands are generally synthesized by tedious resolution or derived from chiral pools which may limit their structure diversity.[91] To our best knowledge, there has been no report on the asymmetric synthesis of functionalized chiral 1,3-bis(diphenylphosphino)propane ligands.



(S,S)-skewphos



R-**26**

As part of our efforts to develop efficient methods for synthesis of new chiral phosphine ligands, we have successfully employed an easily accessible orthopalladated

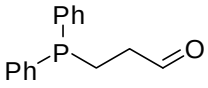
chiral naphthylamine complex *R*-**26** for asymmetric hydrophosphination reactions. Over the past few years, a series of chiral 1,2-diphosphine ligands including (*S*)-Prophos and (*S*)-Phenphos, have been synthesized *via* asymmetric addition of diphenylphosphine to various vinylphosphine substrates (Figure 1.4, Chapter I).[67,79] In general, when the carbon-carbon double bonds are connected to electronic withdrawing groups, they are more reactive towards hydrophosphination reactions. For example, in Chapter II, we have demonstrated that the addition of secondary phosphine to activated allylic phosphine substrates can be finished within 1 h at −78 ºC and generated functionalized 1,2-diphosphines. This addition reaction process is much faster than that of the inactivated scenarios such as diphenyl-1-propenylphosphine, which has proven to be a slow addition reaction.[67a]

Continuing our interests in the development of new kind of chiral diphosphine ligands and further application of the chiral organopalladium complex in asymmetric transformations, in this chapter, we describe a facile strategy to synthesize three homoallylic monophosphine palladium complexes with ester- and keto-functionalities from acrolein, and their second-stage hydrophosphination reactions under mild conditions that afford the corresponding novel chiral 1,3-diphosphine ligands. Furthermore, a chiral α-hydroxy 1,3-diphosphine palladium complex is also obtained by means of a successive two-stage hydrophosphination of acrolein.

3.2 Results and Discussion

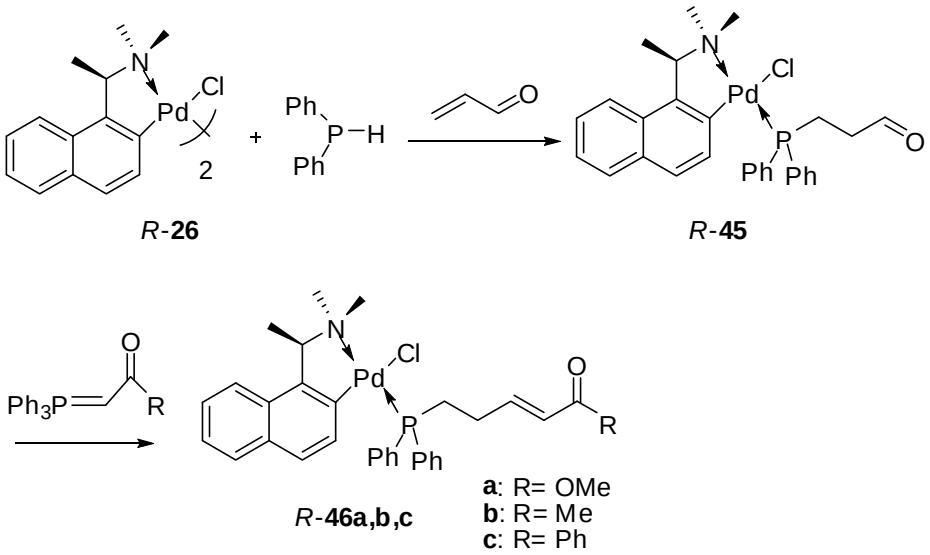
Substituted *α,β*-unsaturated aldehydes, like cinnamaldehyde, have been known to be reactive towards diphenylphosphine and its analogues, wherein the addition reactions can

occur either at the activated olefin or at the carbonyl group.[94] However, acrolein was found to be inert towards diphenylphosphine when the addition reaction was performed in a series of solvent systems, even in the presence of external bases such as sodium hydroxide, triethylamine, DBU, and potassium *ter*-butoxide. Literature reports reveal that previous synthesis of the free monophosphine ligand 3-(diphenylphosphino)propanal involves tedious organic manipulations from 3-chloropropanol or chloro-substituted dimethylacetal with the protection of borane.[95]



3-(diphenylphosphino)propanal

3.2.1 Synthesis of Ester- and Keto-Functionalized Monophosphine Precursors



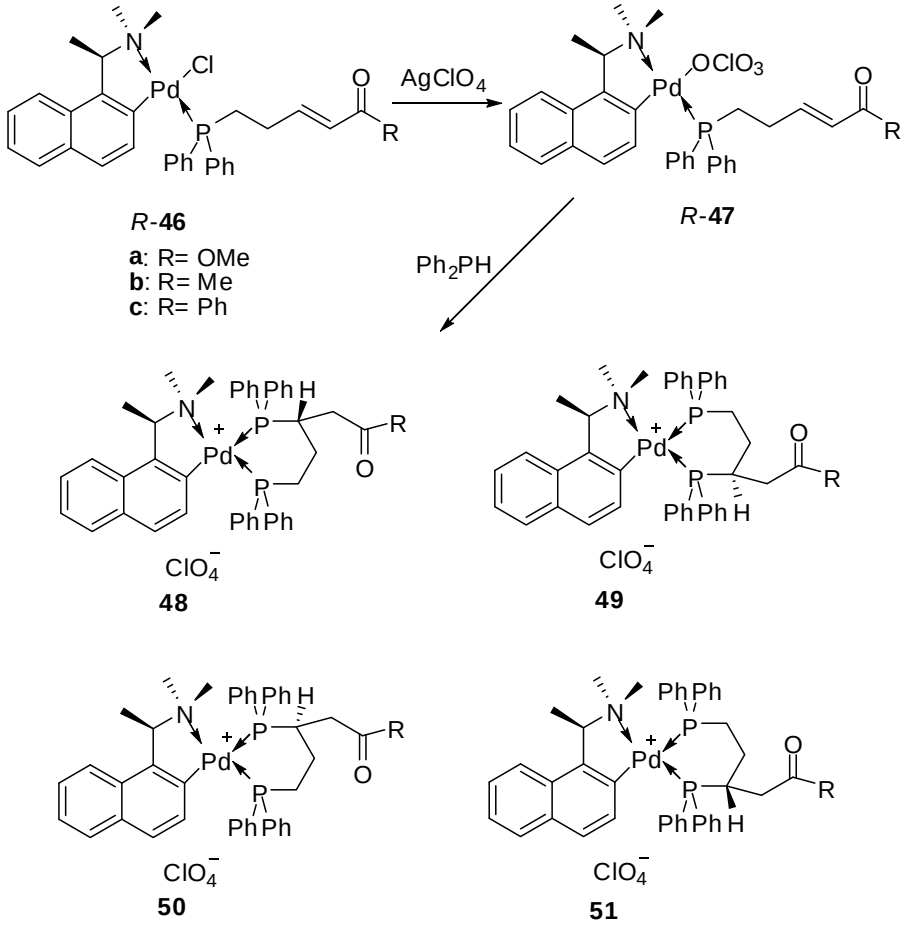
Scheme 3.1

Interestingly, when the orthopalladated chiral naphthylamine complex *R*-**26** was employed as reaction promoter, the Michael-type hydrophosphination reaction of acrolein proceeded chemoselectively to produce the 3-(diphenylphosphino)propanal palladium complex *R*-**45** with the carbonyl group intact (Scheme 3.1). The addition process was

monitored by ^{31}P NMR spectroscopy, and was found to be complete within 30 min at 0 ºC in acetonitrile to afford the product *R*-**45** as a white solid in 87% yield. The ^{31}P NMR spectrum in $CDCl_3$ of *R*-**45** exhibited a sharp singlet signal at δ 35.6.

As illustrated in Scheme 3.1, in situ reaction of product *R*-**45** with methyl (triphenylphosphoranylidene)acetate in chloroform at room temperature for 2 h generated the ester-functionalized homoallylic phosphine palladium complex *R*-**46a** in 85% yield, with a singlet resonance at δ 35.0 in the ^{31}P NMR spectrum. The keto-functionalized product *R*-**46b** could also be obtained by using 1-(triphenylphosphoranylidene)-acetone for the Wittig reaction in 81% yield. However this reaction needs to be performed at an elevated temperature (50 ºC) for 24 h due to the relatively inactive nature of the employed Wittig reagent. The ^{31}P NMR spectrum in $CDCl_3$ of *R*-**46b** showed a singlet signal at δ 35.2. Similarly, *R*-**46c** was isolated as a pale yellow powder in 79% yield after the reaction of *R*-**45** with (phenacylidene)triphenylphosphorane in chloroform at 50 ºC for 36 h and a sharp singlet phosphorus signal at δ 35.1 was observed in the ^{31}P NMR spectrum. It should be noted that all the three homoallylic monophosphine substrates were isolated only as *trans* isomers.

3.2.2 Asymmetric Hydrophosphination of Ester-Functionalized Homoallylic Phosphine Palladium Complex *R*-46a



Scheme 3.2

As shown in Scheme 3.2, the phosphorus atom in complex *R*-**46a** coordinated *trans* to the NMe_2 group. Treatment of the monomeric phosphine complex with silver perchlorate can remove the chloro ligand and yielded the intermediate cationic perchlorate species *R*-**47a** in essentially quantitative yield. This highly reactive species was not isolated, and a CH_3CN/CH_2Cl_2 (1:2) solution of *R*-**47a** was treated directly with a stoichiometric amount of diphenylphosphine and triethylamine as external base at – 78 ºC for the second-stage hydrophosphination reaction. The process was monitored by ^{31}P NMR spectroscopy and was found to be completed within 2 h. Prior to purification, the ^{31}P NMR spectrum of the

crude product in $CDCl_3$ exhibited four pairs of doublets at δ – 6.1, 38.8 (J_{PP} = 55.3 Hz); 0.9, 36.2 (J_{PP} = 51.9 Hz); 8.6, 28.6 (J_{PP} = 55.3 Hz) and 10.1, 28.5 (J_{PP} = 51.7 Hz) with the intensity ratio of 15:1:9:5, respectively. The signals indicated that all the four possible isomeric products i.e., **48a**, **49a, 50a**, and **51a** were formed in the hydrophosphination reaction (Scheme 3.2). It should be noted that complexes **48a** and **49a** are regioisomers which adopt the same *R* absolute configuration at the newly formed chiral carbon centers. Similarly, complexes **50a** and **51a** are regioisomers with *S* absolute configuration at the new stereogenic centers. Apart from electronic effect, the chelate stabilization of 6-membered ring as compared to the 7-membered analog also contributes to the regioselectivity seen in the hydrophosphination process.

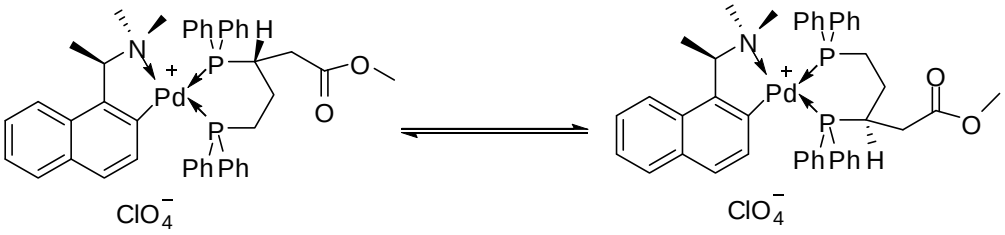
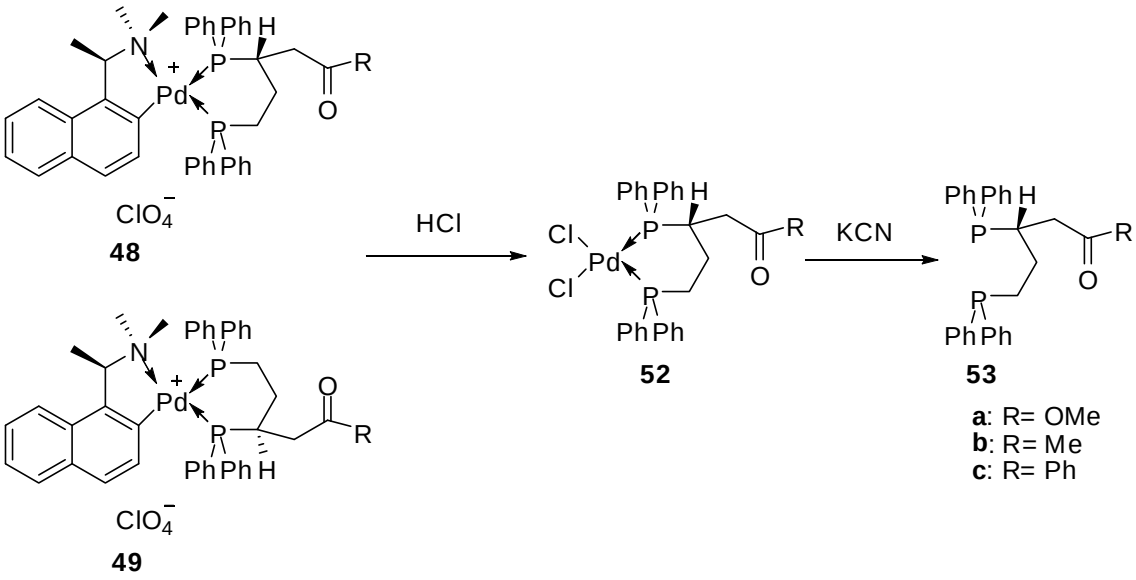


Figure 3.1. Interconversion of regioisomers **48a** and **49a**

The two major products **48a** and **49a** could be isolated efficiently as an equilibrium mixture by column chromatography in 66% yield. The ^{31}P NMR spectrum in $CDCl_3$ ndicated two pairs of doublets at δ – 6.1, 38.8 (J_{PP} = 55.3 Hz) and 8.6, 28.6 (J_{PP} = 55.3 Hz). It is interesting to find that the interconversion between the two regioisomers **48a** and **49a** is very fast especially in a coordinating solvent such as acetonitrile, when compared with the similar 1,2-diphosphine palladium complexes (Figure 3.1). The equilibrium can be attained within 2 h at room temperature. Unfortunately, attempts to

crystallize the isomeric complex mixtures for X-ray crystallography from various solvent systems were unsuccessful.



Scheme 3.3

The chiral amine auxiliary on complexes **48a** and **49a**, however, could be chemoselectively removed from the palladium template by treatment with concentrated hydrochloric acid (Scheme 3.3). The resultant enantiomerically pure dichloro complex **52a** was obtained as pale yellow prisms in 88% isolated yield upon crystallization from dichloromethane and diethyl ether, $[\alpha]_D = -17.5$ (*c* 1.7, CH_2Cl_2). The ^{31}P NMR in $CDCl_3$ of the neutral dichloro product **52a** showed a pair of doublets at δ 15.5, 21.9 (J_{PP} = 13.0 Hz).

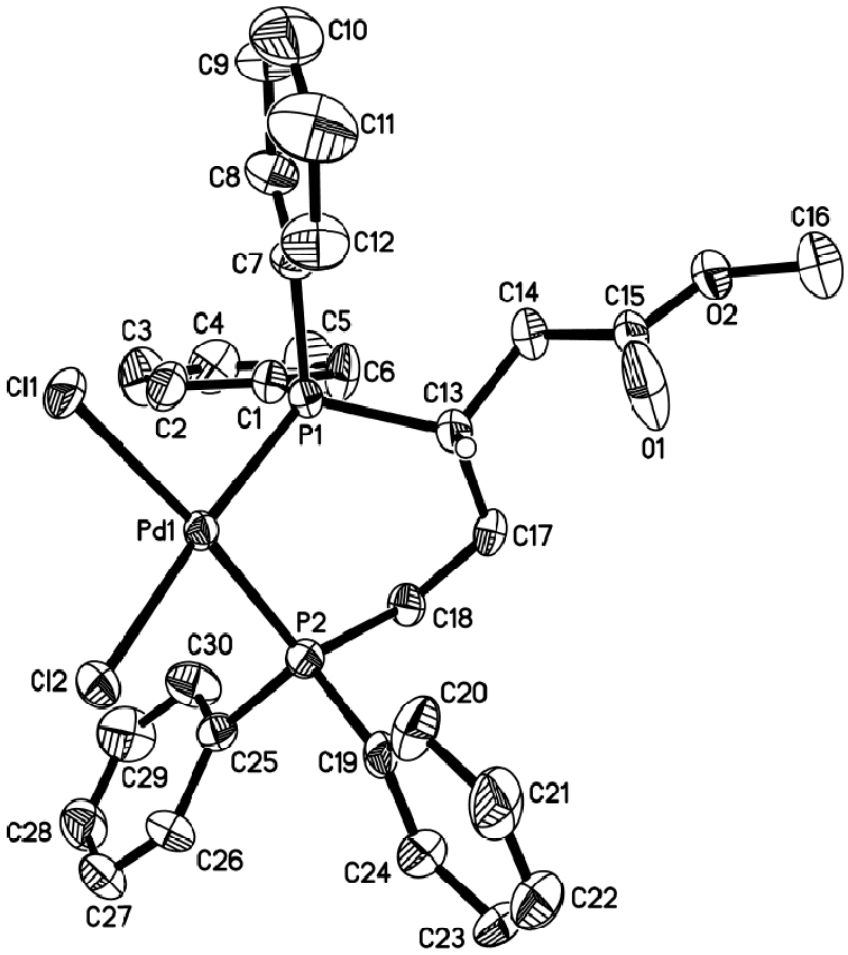


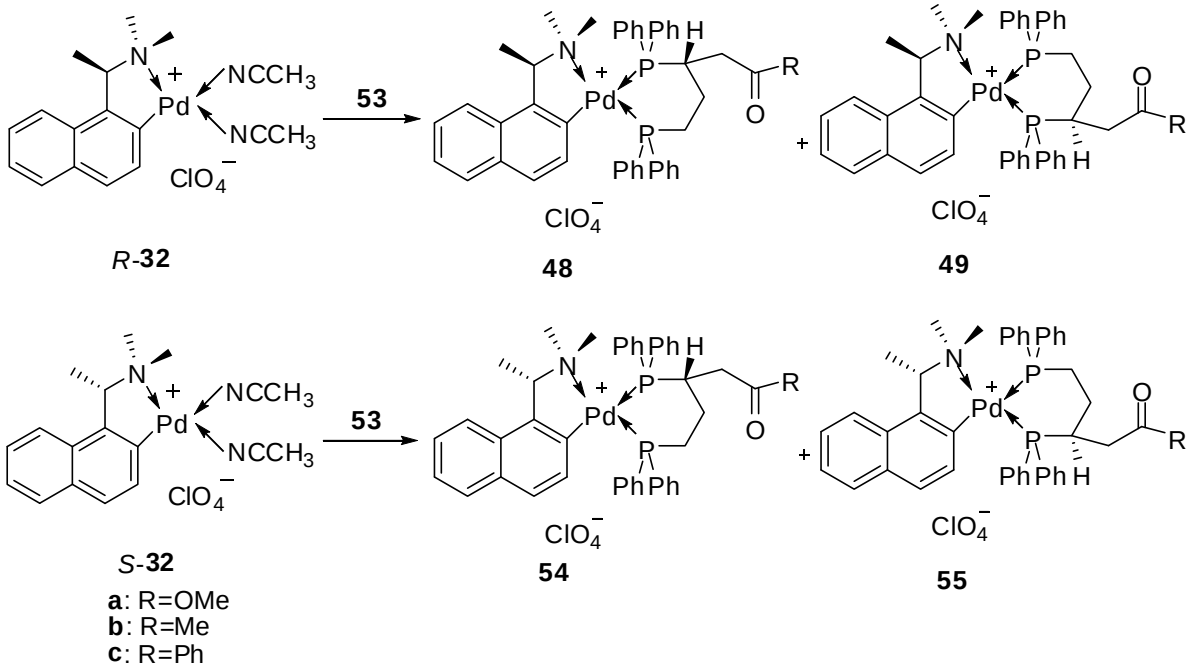
Figure 3.2. Molecular structure and absolute stereochemistry of complex **52a**

Table 3.1. Selected Bond Lengths (Å) and Angles (deg) of **52a**

Pd1–P1	2.258(2)	Pd1–P2	2.249(3)
Pd1–Cl1	2.367(3)	Pd1–Cl2	2.366(3)
C13–P1	1.866(9)	C13–C17	1.514(14)
C17–C18	1.521(14)	C18–P2	1.818(9)
C13–C14	1.533(10)	C13–C17–C18	119.3(8)
P2–Pd1–P1	90.2(1)	Cl2–Pd1–Cl1	91.8(1)
P1–Pd1–Cl2	175.3(1)	P2–Pd1–Cl1	171.1(1)
P1–Pd1–Cl1	91.3(1)	P2–Pd1–Cl2	87.3(1)
C17–C13–P1	116.2(7)	C17–C18–P2	114.2(7)

The chelating properties and the absolute stereochemistry of the coordinated ester-substituted 1,3-diphosphine palladium complex **52a** were studied by single-crystal X-ray crystallography. There are two crystallographically distinguishable molecules in the asymmetric unit with similar bond lengths, angles, and the same *R* absolute configuration at the newly formed chiral carbon center. Figure 3.2 shows the ORTEP drawing of molecule 1, and the selected bond lengths and angles are listed in Table 3.1. The Pd atom adopts the expected distorted square planar coordination geometry. The PdP_2 plane is rotated at an angle of 9.5(2)° with respect to that of $PdCl_2$, while the angles around the palladium center are in the ranges 87.3(1) – 91.8(1) and 171.1(1) – 175.3(1)°. Both the Pd–P bond (2.258(2), 2.249(3) Å) and the P–Pd–P bite angle (90.2(1)°) are larger than in the case of 1,2-diphosphine metallacycles previously reported.[67,79] The six-membered chelate ring in **52a** has a novel boat conformation with the ester functionality occupying the sterically favorable equatorial position. The phenyl rings on the phosphorus atom P1 that is adjacent to the ester substituent are of axial (ipso atom C1) and equatorial (ipso atom C7) disposition, respectively, while the other two phenyl rings on P2 adopt bisectional orientations.

As illustrated in Scheme 3.3, the optically pure ester-functionalized 1,3-diphosphine ligand **53a** could be liberated stereospecifically from **52a** by treatment of the dichloro complex with aqueous potassium cyanide. The liberated chiral diphosphine was obtained as a white solid in 95% yield, $[\alpha]_D$ = + 19.0 (*c* 1.0, CH_2Cl_2). The ^{31}P NMR spectrum in $CDCl_3$ of **53a** exhibited a pair of singlet at δ – 15.3 and – 6.4.



Scheme 3.4

In order to determine the optical purity of the chiral 1,3-diphosphine **53a**, the liberated ligand was recoordinated to the bis(acetonitrile) complex *R*-**32 (**Scheme 3.4**)**. The ^{31}P NMR of the recomplexation products in $CDCl_3$ indeed exhibited two pair of doublets at δ – 6.1, 38.8 (J_{PP} = 55.3 Hz) and 8.6, 28.6 (J_{PP} = 55.3 Hz). These signals are identical with the two major products from the original hydrophosphination reaction, which indicated the formation of the regioisomers **48a** and **49a**. In a further check, the recoordination of the free ligand **53a** to equally accessible enantiomeric complex *S*-**32** generated the regioisomers **54a** and **55a** with two clearly different pairs of doublet phosphorus signals at δ 0.9, 36.2 (J_{PP} = 51.9 Hz) and 10.1, 28.5 (J_{PP} = 51.7 Hz). Note that products **54a** and **55a** are the enantiomeric forms of **50a** and **51a** respectively. The two pairs of enantiomers exhibited the same ^{31}P NMR signals as expected. Importantly, no resonances were observed at δ – 6.1, 38.8, 8.6 and 28.6, thus confirming that the liberated ester-functionalized 1,3-diphosphine ligand **53a** was optically pure.

3.2.3 Asymmetric Hydrophosphination of Keto-Functionalized Monophosphine Substrates *R*-46b and *R*-46c

Similarly, the abstraction of the chloro ligand in complex *R*-**46b** with silver perchlorate gave the reactive perchlorato intermediate *R*-**47b** in high yield (Scheme 3.2). Unfortunately, when the second-stage hydrophosphination reaction was performed by treatment with diphenylphosphine and triethylamine as external base at – 78 ºC, the addition process resulted in very poor stereoselectivity at the newly formed chiral carbon center compared with the ester-substituted annlogue *R*-**46a**. However, the stereoselectivity could be dramatically improved when the perchlorato complex *R*-**47b** was subsequently reacted with 1 equivalent of diphenylphosphine in acetonitrile at 0 ºC for 2 h. The ^{31}P NMR spectrum of the crude product in $CDCl_3$ indicated four pairs of doublets at δ – 6.7, 36.7 (J_{PP} = 55.7 Hz); 1.0, 38.8 (J_{PP} = 51.8 Hz); 8.8, 27.2 (J_{PP} = 56.3 Hz) and 10.9, 28.5 (J_{PP} = 52.0 Hz) with the intensity ratio of 17.5:1:11.2:3.1, which indicated that all the four possible isomeric products **48b**–**51b** were formed during the hydrophosphination process.

The two major regioisomers **48b** and **49b** was subsequently isolated efficiently by column chromatography in 75% yield with two pairs of doublets at δ – 6.7, 36.7 (J_{PP} = 55.7 Hz); and 8.8, 27.2 (J_{PP} = 56.3 Hz) in the ^{31}P NMR spectrum. Upon removal of the chiral amine auxiliary of complexes **48b** and **49b** by treatment with concentrated hydrochloric acid, the optically pure dichloro product **52b** was crystallized as pale yellow prisms in 85% yield from dichloromethane and diethyl ether, $[\alpha]_D$ = – 20.4 (*c* 0.9, CH_2Cl_2). The ^{31}P NMR spectrum showed a pair of doublet signals at δ 16.3, 22.5 (J_{PP} =

12.7 Hz).

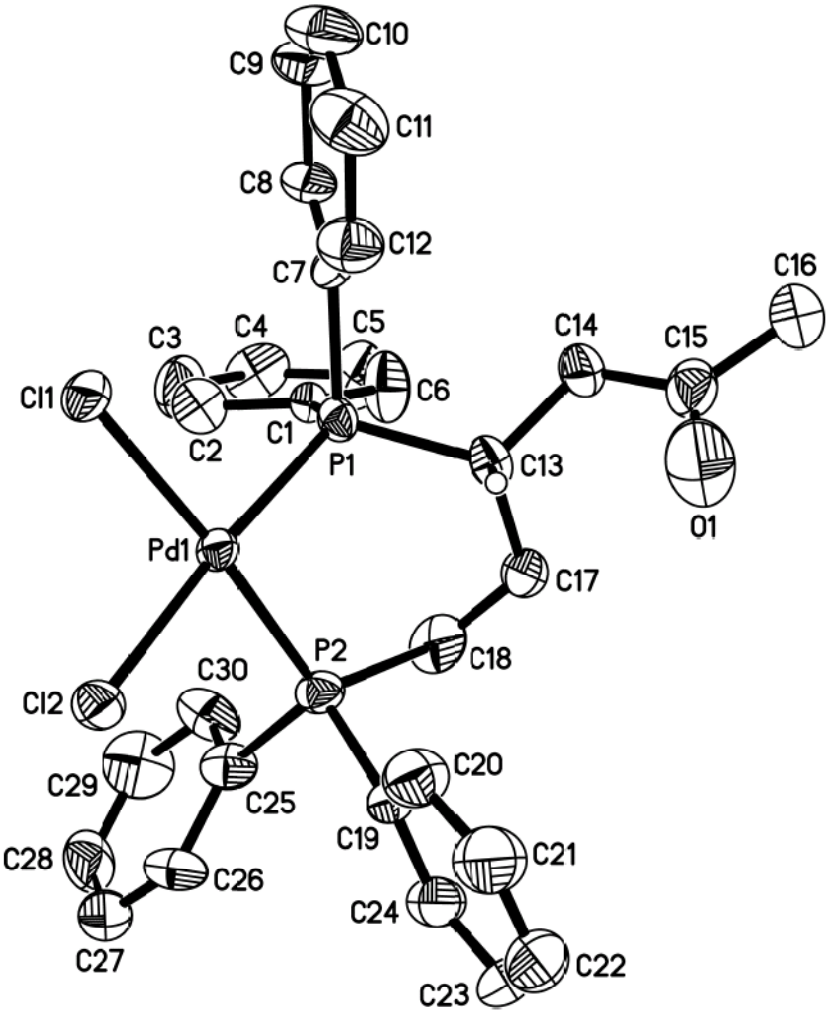


Figure 3.3. Molecular structure and absolute stereochemistry of complex **52b**

The single-crystal X-ray crystallographic analysis clearly established the coordination mode and the absolute stereochemistry of keto-functionalized 1,3-diphosphine palladium complex **52b** (Figure 3.3). The newly formed chiral carbon center at C13 is *R* configuration. And the novel six-membered metallacycle adopts boat conformation with the keto-substituent occupying the sterically favorable equatorial position. Both bond lengths and angles are comparable with the analogous ester complex **52a** as showed in Table 3.2.

Table 3.2. Selected Bond Lengths (Å) and Angles (deg) of **52b**

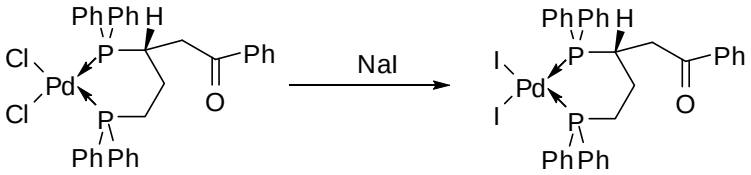
Pd1–P1	2.245(2)	Pd1–P2	2.246(3)
Pd1–Cl1	2.353(2)	Pd1–Cl2	2.370(2)
C13–P1	1.869(8)	C13–C17	1.552(12)
C17–C18	1.487(14)	C18–P2	1.861(8)
P2–Pd1–P1	90.1(1)	Cl2–Pd1–Cl1	92.4(1)
P1–Pd1–Cl2	175.1(1)	P2–Pd1–Cl1	172.0(1)
P1–Pd1–Cl1	91.4(1)	P2–Pd1–Cl2	86.5(1)
C17–C13–P1	114.3(6)	C17–C18–P2	114.2(6)
C13–P1–Pd1	113.0(3)	C18–P2–Pd1	115.7(3)

Treatment of a CH_2Cl_2 solution of **52b** with aqueous potassium cyanide liberated the optical pure keto-functionalized 1,3-diphosphine ligand **53b** as a white solid in 92% yield, with $[\alpha]_{436}$ = + 30.8 (*c* 0.9, CH_2Cl_2). The ^{31}P NMR spectrum of the free diphosphine exhibited two singlets at δ – 15.8 and – 6.6. The optical purity of **53b** was confirmed by subsequent recoordination process (Scheme 3.4). The recomplexation products involving the bis(acetonitrile) complex *R*-**32** showed two pairs of doublets at δ – 6.7, 36.7 (J_{PP} = 55.7 Hz); and 8.8, 27.2 (J_{PP} = 56.3 Hz), which indicated the formation of the regioisomers **48b** and **49b**. Upon recoodination of the free ligand **53b** to complex *S*-**32**, a pair of regioisomers **54b** and **55b** were formed. The ^{31}P NMR of products **54b** and **55b** exhibited two distinct pairs of doublet phosphorus peaks at δ 1.0, 38.8 (J_{PP} = 51.8 Hz); and 10.9, 28.5 (J_{PP} = 52.0 Hz), which were identical with two minor products i.e. **50b** and **51b** from the original hydrophosphination reaction. The liberated keto-functionalized 1,3-diphosphine **53b** reaction was therefore confirmed to be enantiomerically pure.

The same procedure was used for the hydrophosphination of monophosphine substrate *R*-**46c**. The ^{31}P NMR spectrum of the crude product in $CDCl_3$ showed four pairs of

doublets at δ – 6.3, 37.8 (J_{PP} = 56.9 Hz); 0.4, 38.6 (J_{PP} = 51.9 Hz); 8.6, 26.9 (J_{PP} = 56.3 Hz) and 10.6, 27.8 (J_{PP} = 53.0 Hz) with the intensity ratio of 12:1:7:3.5, respectively. The two major regioisomers **48c** and **49c**, with two pairs of doublet signals at δ – 6.3, 37.8 (J_{PP} = 56.9 Hz) and 8.6, 26.9 (J_{PP} = 56.3 Hz), could be isolated efficiently by column chromatography in 70% yield.

As shown in Scheme 3.3, the regioisomers **48c** and **49c** were subsequently converted to the dichloro complex **52c**, which showed a pair of doublets at δ 15.8, 22.4 (J_{PP} = 13.8 Hz). The product **52c** was failed to give suitable crystals for X-ray crystallographic analysis from any solvent system. However, the dichloro complex **52c** can be converted to its diiodo analogue **56** by treatment with sodium iodide (Scheme 3.5). The diiodo palladium product was isolated as red prisms in 85% yield upon crystallization from dichloromethane and diethyl ether, $[\alpha]_D$ = + 43.0 (*c* 0.8, CH_2Cl_2).



52c **56**

Scheme 3.5

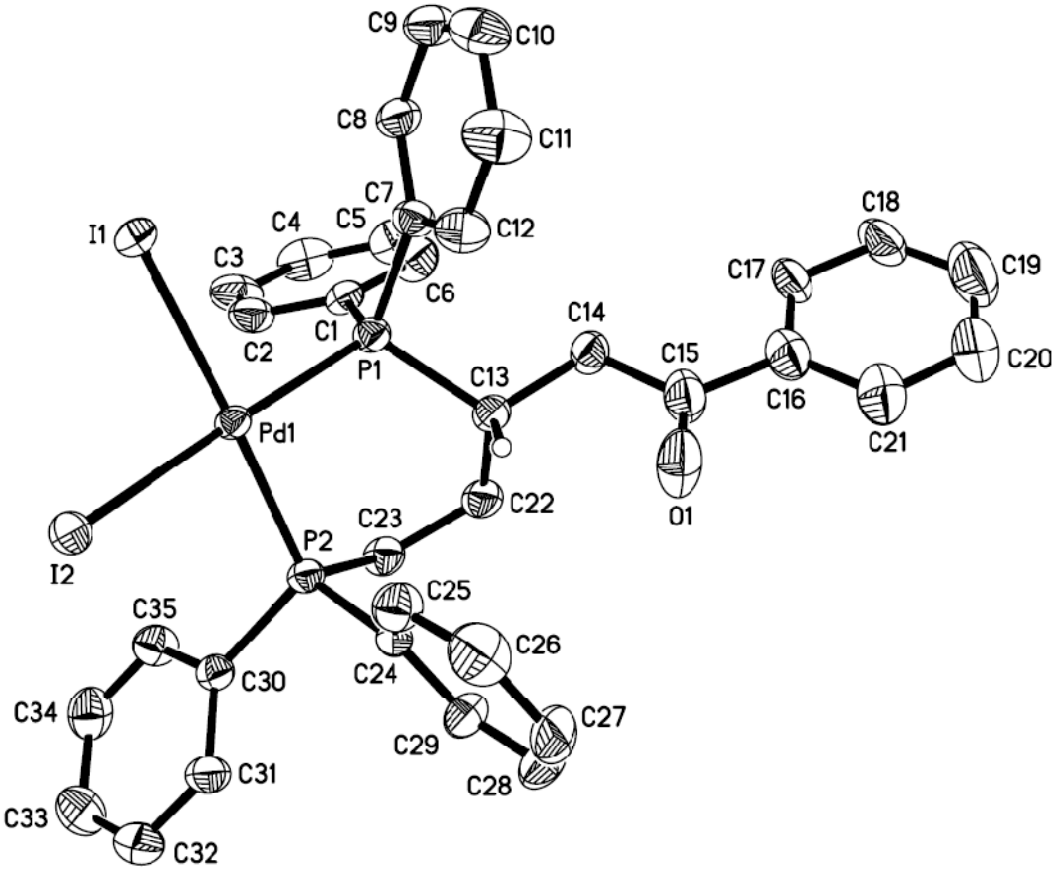


Figure 3.4. Molecular structure of complex **56**

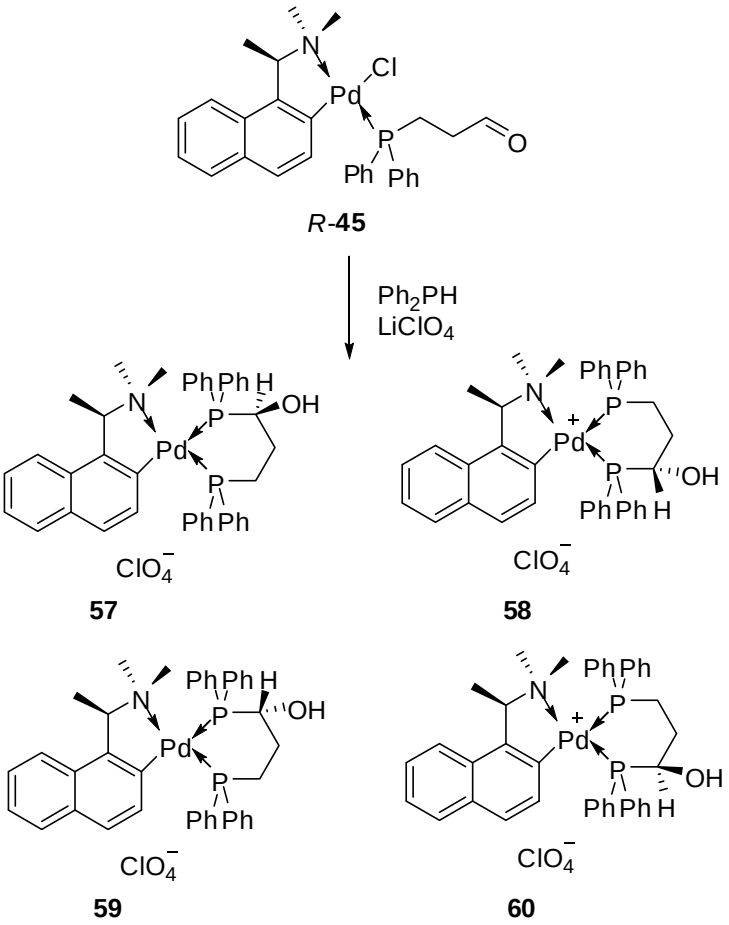
The molecular structure of complex **56** was confirmed by X-ray crystallography (Figure 3.4). Selected bond and angle parameters are given in Table 3.3. There is only one molecule in the asymmetric unit with the keto-substituent slightly disordered. The absolute configuration at the newly formed chiral carbon center is *R* expectedly. The six-membered diphosphine chelate adopts a λ-skew conformation while the keto-substituent is of equatorial disposition. The tetrahedral distortion around the square-planar palladium atom center (4.6(1)°) is much smaller than in the case of the dichloro complexes **52a** and **52b**. Interestingly, the phenyl groups on the two phosphorus atoms were fixed into a chiral array with alternating axial and equatorial positions.

Table 3.3. Selected Bond Lengths (Å) and Angles (deg) of **56**

Pd1–P1	2.280(1)	Pd1–P2	2.264(1)
Pd1–I1	2.647(1)	Pd1–I2	2.629(1)
C13–P1	1.856(4)	C13–C22	1.524(6)
C22–C23	1.523(6)	C23–P2	1.827(4)
P2–Pd1–P1	90.5(1)	I2–Pd1–I1	90.0(1)
P1–Pd1–I2	176.4(1)	P2–Pd1–I1	176.8(1)
P1–Pd1–I1	90.7(1)	P2–Pd1–I2	88.8(1)
C22–C13–P1	113.0(3)	C22–C23–P2	116.2(3)
C13–P1–Pd1	112.3(1)	C23–P2–Pd1	112.0(1)

The chiral 1,3-diphosphine ligand **53c** was liberated from complexes **52c** or **56** in 95% yield, $[\alpha]_D$ = + 11.4 (*c* 0.7, CH_2Cl_2). The ^{31}P NMR spectrum of the free ligand in $CDCl_3$ exhibited a pair of singlets at δ – 15.7 and – 6.4. It is noteworthy that the recomplexation products of the free phosphine ligand **53c** with *S*-**32** showed two pairs of doublets at δ 0.4, 38.6 (J_{PP} = 51.9 Hz) and 10.6, 27.8 (J_{PP} = 53.0 Hz), which confirmed that liberated keto-functionalized chiral 1,3-diphosphine **53c** was optically pure.

3.2.4 Asymmetric Hydrophosphination of 3-(Diphenylphosphino)-Propanal Palladium Complex *R*-45



Scheme 3.6

Unlike the ester- and keto-functionalized monophosphine substrates *R*-**46**, the perchlorato analogue of *R*-**45** generated from abstraction of the chloro ligand with silver perchlorate is quite unstable. However, as shown is Scheme 3.6, the second-stage hydrophosphination of acrolein can occur at the carbonyl group by treatment of *R*-**45** with one equivalent of diphenylphosphine in the presence of $LiClO_4$. The reaction was performed in acetonitrile for 2 h to afford the hydroxyl-functionalized 1,3-phosphine products **57**, **58**, **59** and **60**. The ^{31}P NMR spectrum of the crude reaction mixture exhibited four pairs of doublets at δ – 5.1, 30.1 (J_{PP} = 56.7 Hz); 0.0, 39.3 (J_{PP} = 53.0 Hz);

5.3, 25.8 (J_{PP} = 54.1 Hz) and 13.1, 26.0 (J_{PP} = 52.5 Hz) with the intensity ratio of 1:4.1:1:6.6, respectively.

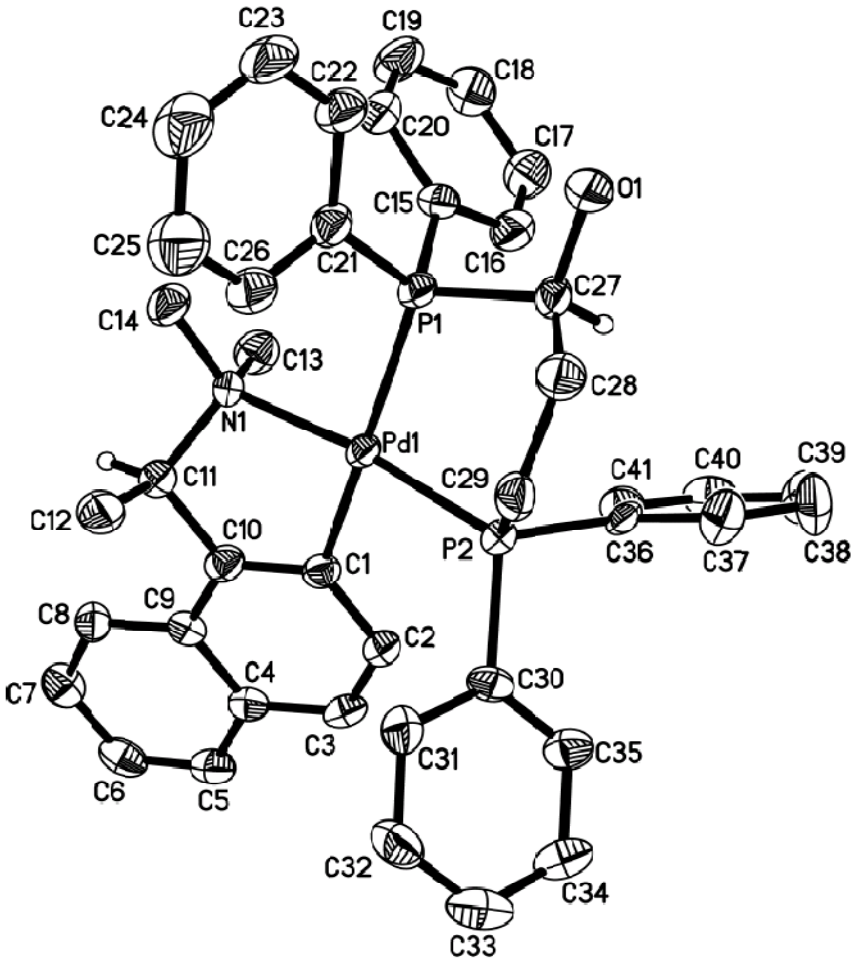


Figure 3.5. Molecular structure of complex **57**

The major regioiosmers **57** and **58** could be isolated as an equilibrium mixture by column chromatography in 42% yield. The ^{31}P NMR spectrum exhibited two pairs of doublets at δ 0.0, 39.3 (J_{PP} = 53.0 Hz) and 13.1, 26.0 (J_{PP} = 52.5 Hz). Upon slow diffusion of diethyl ether into the dichloromethane solution of the isomeric mixture, the product **57** was obtained as pale yellow prisms in 40% yield with a pair of doublets at δ 13.1, 26.0 (J_{PP} = 52.5 Hz), $[\alpha]_D = -90.7°$ (*c* 0.8, CH_2Cl_2). The molecular structure was analyzed by means of single-crystal X-ray diffraction analysis (Figure 3.5). Selected bond lengths and

angles are provided in Table 3.4. The six-membered chelating diphosphine ring has a skew conformation of δ helicity, with the hydroxyl group occupying the sterically favorable equatorial position. The newly formed stereogenic carbon center at C27 is in the *R* absolute configuration.

Table 3.4. Selected Bond Lengths (Å) and Angles (deg) of **57**

Pd1–C1	2.048(5)	Pd1–N1	2.161(4)
Pd1–P1	2.377(1)	Pd1–P2	2.255(1)
C27–P1	1.845(5)	C27–C28	1.529(8)
C28–C29	1.548(8)	C29–P2	1.831(5)
N1–C11	1.518(6)	C10–C11	1.518(7)
C1–Pd1–N1	80.4(2)	C1–Pd1–P2	94.8(1)
N1–Pd1–P2	173.1(1)	C1–Pd1–P1	172.2(2)
N1–Pd1–P1	96.1(1)	P2–Pd1–P1	89.3(1)
C28–C27–P1	113.1(4)	C27–C28–C29	116.7(5)
C28–C29–P2	118.7(4)	P1–C27–O1	109.8(3)
C27–P1–Pd1	113.6(2)	C29–P2–Pd1	109.4(2)

The addition of a secondary phosphine to an aldehyde is usually more complex, as the process proved to be reversible. Furthermore, the corresponding adducts are prone to undergo isomerization to form phosphine oxides.[96] Interestingly, the chiral hydroxyl group in coordinated 1,3-diphosphine palladium complexes with the chiral naphthylamine auxiliary is quite stable. The dichloromethane solution of the complex **57** can be kept for 15 d without any racemization of the chiral carbon center. However, the subsequent liberation of the α-hydroxyl functionalized 1,3-phosphine ligand from complex **57** was unsuccessful due to its unstable nature.

3.3 Conclusion

We have demonstrated an efficient synthesis of homoallylic monophosphine palladium substrates with ester- and keto-functionalities *via* the chemoselective hydrophosphination of acrolein and the subsequent Wittig reactions in a one-pot process. The second-stage hydrophosphination of the monophosphine substrates gives the corresponding functionalized chiral 1,3-bis(diphenylphosphino)propane ligands with good yields, regio- and stereoselectivities under mild conditions. In addition, the successive double hydrophosphination of acrolein yields a chiral α-hydroxy 1,3-diphosphine palladium complex. Upon coordination to palladium atom, the newly formed chiral center in the novel hydroxyl-functionalized 1,3-diphosphine palladium complex is rather stable, and can be kept for days in solution without any racemization of the chiral carbon center.

3.4 Experimental Section

Reactions involving air-sensitive compounds were performed under a positive pressure of argon using standard Schlenk line. NMR spectra were recorded at 25 ºC on Bruker ACF 300 (^{1}H at 300 MHz, ^{13}C at 75 MHz and ^{31}P at 121.5 MHz), 400 (^{1}H at 400 MHz, ^{13}C at 100 MHz and ^{31}P at 162 MHz) and 500 (^{1}H at 500 MHz and ^{31}P at 202 MHz) spectrometers. Chemical shifts (δ) are reported in ppm. Proton and carbon chemical shifts are relative to the residual solvent peaks. Coupling constants are reported in Hz. Optical rotations were measured on the specified solution in a 0.1 dm cell at 20 ºC 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*-**26**, [89a,b] *R*-**32**, and *S*-**32**[89c] were prepared according to literature methods.

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

Preparation of 3-(Diphenylphosphino)-Propanal Palladium Complex *R*-45. A mixture of diphenylphosphine (0.70 g, 3.76 mmol) and palladium complex *R*-**26** (1.22 g, 1.78 mmol) in acetonitrile (60 mL) was stirred at room temperature until all of *R*-**26** had dissolved (ca. 1 h). The solution was cooled to 0 ºC, and fresh distilled acrolein (0.32 g, 5.71 mmol) was added in one portion. The solution was stirred at 0 ºC for 30 min. The solvent was then removed via rotary evaporation; the resultant white solid was washed with hexanes/diethyl ether (2:1, 100 mL), and dissolved into ethyl acetate/diethyl ether (1:1, 150 mL), filtered to remove the insoluble impurity. The filtrate was collected; upon removal of the solvent, the product *R*-**45** was obtained as a white solid (1.82 g, 87%). Note: *R*-**45** was not stable for flash column chromatography on silica. $[\alpha]_{436} = +94.0°$ (*c* 0.8, CH_2Cl_2). Mp: 126–128 ºC. Anal. Calcd for $C_{29}H_{31}ClNOPPd$: C, 59.8; H, 5.4; N, 2.4. Found: C, 59.5; H, 5.6; N, 2.5. ^{31}P NMR ($CDCl_3$，121 MHz): δ 35.6 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.06 (d, 3H, J_{HH} = 6.3 Hz, CH*Me*), 2.47 (m, 2H, CH_2CHO), 2.70 (d, 3H, J_{PH} = 1.3 Hz, N*Me*), 2.99 (d, 3H, J_{PH} = 3.4 Hz, N*Me*), 3.07-3.29 (m, 1H, PCH_2), 4.37 (qn, 1H, $J_{HH} = J_{PH}$ = 6.2 Hz, C*H*CH_3), 6.64-8.12 (m, 16H, Ar). 9.68 (br, C*H*O). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.7 (d, J_{PC} = 35.6 Hz), 23.8 (s), 39.7 (d, J_{PC} = 3.6 Hz), 48.3 (s), 51.1

(d, J_{PC} = 2.9 Hz), 72.8 (d, J_{PC} = 3.2 Hz), 123.2 (s), 124.2 (s), 124.7 (d, J_{PC} = 5.7 Hz), 125.7 (s), 128.4 (d, 2C, J_{PC} = 10.4 Hz), 128.7 (s), 128.8 (s), 128.9 (d, 2C, J_{PC} = 10.3 Hz), 129.5 (d, J_{PC} = 45.0 Hz), 130.3 (d, J_{PC} = 44.8 Hz), 130.9 (d, J_{PC} = 2.4 Hz), 131.1 (d, J_{PC} = 2.4 Hz), 131.1 (s), 133.8 (d, 2C, J_{PC} = 11.6 Hz), 134.1 (d, 2C, J_{PC} = 11.4 Hz), 135.4 (d, J_{PC} = 12.2 Hz), 149.1 (d, J_{PC} = 1.2 Hz), 149.2 (s), 200.4 (d, J_{PC} = 16.6 Hz).

Preparation of Homoallylic Monophosphine Palladium Complex *R*-46a. *R*-**45** was synthesized as described previously from diphenylphosphine (0.70 g, 3.76 mmol) and *R*-**26** (1.22 g, 1.78 mmol). Upon removal of the organic solvent under reduced pressure, the resulting white silod was redissolved into chloroform (50 mL), and to the solution methyl (triphenylphosphoranylidene) acetate (1.88 g, 5.62 mmol) was added. The mixture was stirred for 2 h at room temperature and concentrated. Complex *R*-**46a** was isolated by column chromatography on silica (EtOAc/Hexanes = 1:2) as a pale yellow solid (*E*/*Z*>10, 1.94 g, 85%). *R*-**46a** (*trans* isomer), $[\alpha]_D$ = –11.9° (*c* 1.4, CH_2Cl_2). Mp: 120–122 ºC. Anal. Calcd for $C_{32}H_{35}ClNO_2PPd$: C, 60.2; H, 5.5; N, 2.2. Found: C, 60.5; H, 5.6; N, 2.1. ^{31}P NMR ($CDCl_3$, 121 MHz): δ 35.0 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 2.05 (d, 3H, J_{HH} = 6.2 Hz, CH*Me*), 2.26 (m, 2H, PCH_2CH_2), 2.67 (s, 3H, N*Me*), 2.86 (m, 1H, PCH′*H*), 2.97 (d, 3H, J_{PH} = 3.0 Hz, N*Me*), 3.05 (m, 1H, PC*H*′H), 3.64 (s, 3H, CO_2Me), 4.34 (qn, 1H, $J_{HH} = J_{PH}$ = 6.1 Hz, C*H*CH_3), 5.73 (d, 1H, J_{HH} = 15.7 Hz, C*H*CO_2Me), 6.66-8.10 (m, 17H, Ar and CH_2CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.7 (s), 27.9 (d, J_{PC} = 3.6 Hz), 29.5 (d, J_{PC} = 32.6 Hz), 48.3 (s), 51.1 (d, J_{PC} = 2.8 Hz), 51.4 (s), 72.8 (d, J_{PC} = 3.1 Hz), 121.2 (s), 123.2 (s), 124.1 (s), 124.7 (d, J_{PC} = 5.7 Hz), 125.8 (s), 128.4 (d, 2C, J_{PC} = 10.3 Hz), 128.7 (s), 128.8 (s), 128.9 (d, 2C, J_{PC} = 11.2 Hz), 129.7 (d, J_{PC} = 44.6 Hz), 130.6 (d, J_{PC} = 45.6 Hz), 130.8 (d, J_{PC} = 2.3 Hz), 131.0 (d, J_{PC} = 2.5 Hz), 131.1 (s), 133.8 (d, 2C, J_{PC} = 11.5

Hz), 134.2 (d, 2C, J_{PC} = 11.3 Hz), 135.5 (d, J_{PC} = 12.0 Hz), 148.3 (d, J_{PC} = 16.8 Hz), 149.2 (d, J_{PC} = 2.1 Hz), 149.4 (s), 166.8 (s).

Preparation of Homoallylic Monophosphine Palladium Complexes *R*-46b and *R*-46c. The similar procedure was adopted to synthesize palladium complex *R*-**46b** from *R*-**26** (1.22 g, 1.78 mmol). After dissolving *R*-**45** into chloroform (50 mL), 1-(triphenylphosphoranylidene)-acetone (1.72 g, 5.38 mmol) was added and stirred at 50 ºC for 24 h. Upon removal of the solvent, the product *R*-**46b** was isolated by column chromatography on silica (EtOAc/Hexanes = 1:2) as a pale yellow powder (1.80 g, 81%). $[\alpha]_D$ = – 5.7° (*c* 1.1, CH_2Cl_2). Mp: 121–123 ºC. Anal. Calcd for $C_{32}H_{35}ClNOPPd$: C, 61.7; H, 5.7; N, 2.2. Found: C, 61.5; H, 5.9; N, 2.0. ^{31}P NMR ($CDCl_3$, 121 MHz): δ 35.2 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.06 (d, 3H, J_{HH} = 6.3 Hz, CH*Me*), 2.16 (s, 3H, CO*Me*), 2.26 (m, 2H, PCH_2CH_2), 2.69 (d, 3H, J_{PH} = 1.5 Hz, N*Me*), 2.89 (m, 1H, PCH′*H*), 2.98 (d, 3H, J_{PH} = 3.4 Hz, N*Me*), 3.09 (m, 1H, PC*H*′H), 4.36 (qn, 1H, J_{HH} = J_{PH} = 6.1 Hz, C*H*CH_3), 5.93 (d, 1H, J_{HH} = 16.0 Hz, C*H*COMe), 6.65-8.12 (m, 17H, Ar and CH_2CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.8 (s), 26.7 (s), 28.3 (d, J_{PC} = 3.5 Hz), 29.6 (d, J_{PC} = 32.6 Hz), 48.3 (s), 51.1 (d, J_{PC} = 2.8 Hz), 72.8 (d, J_{PC} = 3.2 Hz), 123.2 (s), 124.2 (s), 124.7 (d, J_{PC} = 5.7 Hz), 125.8 (s), 128.4 (d, 2C, J_{PC} = 10.3 Hz), 128.7 (s), 128.8 (s), 128.9 (d, 2C, J_{PC} = 10.3 Hz), 129.6 (d, J_{PC} = 44.7 Hz), 130.6 (d, J_{PC} = 44.4 Hz), 130.9 (d, J_{PC} = 2.2 Hz), 131.0 (d, J_{PC} = 2.2 Hz), 131.1 (s), 131.4 (s), 133.7 (d, 2C, J_{PC} = 11.5 Hz), 134.2 (d, 2C, J_{PC} = 11.4 Hz), 135.5 (d, J_{PC} = 12.2 Hz), 147.4 (d, J_{PC} = 16.4 Hz), 149.1 (d, J_{PC} = 2.0 Hz), 149.3 (s), 198.6 (s).

The same procedure was used to prepare product *R*-**46c** from *R*-**26** (1.22 g, 1.78 mmol).

A chloroform solution (50 mL) of *R*-**45** and (phenacylidene)triphenylphosphorane (2.05 g, 5.38 mmol) was heated at 50 ºC for 36 h. Upon removal of the solvent, the product *R*-**46c** was isolated by column chromatography on silica (EtOAc/Hexanes = 1:2) as a pale yellow powder (1.93 g, 79%). $[\alpha]_D = -20.9°$ (*c* 1.0, CH_2Cl_2). Mp: 116–119 ºC. Anal. Calcd for $C_{37}H_{37}ClNOPPd$: C, 64.9; H, 5.4; N, 2.0. Found: C, 64.7; H, 5.5; N, 1.9. ^{31}P NMR ($CDCl_3$, 121 MHz): δ 35.1 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 2.07 (d, 3H, J_{HH} = 6.3 Hz, CH*Me*), 2.35 (m, 2H, PCH_2CH_2), 2.69 (d, 3H, J_{PH} = 1.4 Hz, N*Me*), 2.98 (d, 3H, J_{PH} = 3.4 Hz, N*Me*), 2.91-2.91 (m, 2H, PCH_2), 4.36 (qn, 1H, $J_{HH} = J_{PH}$ = 6.1 Hz, $CHCH_3$), 6.68-8.11 (m, 23H, Ar and CH=CHCOPh). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.7 (s), 28.4 (d, J_{PC} = 3.7 Hz), 29.6 (d, J_{PC} = 32.3 Hz), 48.3 (d, J_{PC} = 2.0 Hz), 51.1 (d, J_{PC} = 2.9 Hz), 72.9 (d, J_{PC} = 3.2 Hz), 123.2 (s), 124.1 (s), 124.7 (d, J_{PC} = 5.8 Hz), 125.7 (s), 126.3 (s), 128.4 (d, 2C, J_{PC} = 10.0 Hz), 128.5 (s, 2C), 128.6 (s, 2C), 128.7 (s), 128.8 (s), 128.9 (d, 2C, J_{PC} = 10.4 Hz), 129.7 (d, J_{PC} = 44.7 Hz), 130.7 (d, J_{PC} = 44.5 Hz), 130.9 (d, J_{PC} = 2.3 Hz), 131.0 (d, J_{PC} = 2.4 Hz), 131.1 (s), 132.6 (s), 133.8 (d, 2C, J_{PC} = 11.5 Hz), 134.2 (d, 2C, J_{PC} = 11.3 Hz), 135.5 (d, J_{PC} = 12.0 Hz), 137.8 (s), 148.3 (d, J_{PC} = 17.0 Hz), 149.2 (d, J_{PC} = 2.1 Hz), 149.4 (s), 190.8 (s).

Hydrophosphination of Monophosphine Substrate *R*-46a. A solution of *R*-**46a** (1.0 g, 1.57 mmol) in dichloromethane (40 mL) was treated with $AgClO_4 \cdot H_2O$ (0.53 g, 2.4 mmol) in water (3 mL). The mixture was stirred for 1 h at room temperature. The organic layer, after the removal of AgCl precipitate, was washed with H_2O (3 × 20 mL), dried over $MgSO_4$, concentrated and redissolved in dichloromethane/acetonitrile (1:1, 40 mL). The solution was allowed to cool down to –78 ºC, and treated with diphenylphosphine (0.30 g, 1.57 mmol) in dichloromethane (6 mL), followed by triethylamine (0.16 g, 1.57

mmol). The mixture was stirred for 2 h, and then 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 a mixture of regioisomers **48a** and **49a** as pale yellow solid (0.92 g, 66%). ^{31}P NMR ($CDCl_3$，121 MHz): δ –6.1 (d, J_{PP} = 55.3 Hz), 8.6 (d, J_{PP} = 55.3 Hz), 28.6 (d, J_{PP} = 55.3 Hz), 38.8 (d, J_{PP} = 55.3 Hz).

Hydrophosphination of Monophosphine Substrates *R*-46b and *R*-46c. *R*-**46b** (1.0 g, 1.61 mmol), upon abstraction of the chloro ligand with silver perchlorate, was dissolved in acetonitrile (20 mL) and cooled down to 0 ºC. The solution was subsequently treated with diphenylphosphine (0.30 g, 1.57 mmol) and stirred for 2 h. The regioisomers **48b** and **49b** could be isolated by column chromatography (CH_2Cl_2/Acetone/Hexanes = 2:1:3) as pale yellow powder (1.05 g, 75%) upon removal of solvent. ^{31}P NMR ($CDCl_3$，121 MHz): δ – 6.7 (d, J_{PP} = 55.7 Hz), 8.8 (d, J_{PP} = 56.3 Hz), 27.2 (d, J_{PP} = 56.3 Hz), 36.7 (J_{PP} = 55.7 Hz).

By following the same procedure as described for the hydrophsophination of *R*-**46c** (1.0 g, 1.46 mmol), the regioisomers **48c** and **49c** could be isolated by column chromatography (CH_2Cl_2/Acetone/Hexanes = 2:1:3) as pale yellow powder (0.95 g, 70%). ^{31}P NMR ($CDCl_3$，121 MHz): δ – 6.3 (d, J_{PP} = 56.9 Hz), 8.6 (d, J_{PP} = 56.3 Hz), 26.9 (d, J_{PP} = 56.3 Hz), 37.8 (J_{PP} = 56.9 Hz).

Preparation of the Dichloro Palladium Complexes 52a, 52b and 52c. A solution of regioisomers **48a** and **49a** (0.8 g, 0.90 mmol) in dichloromethane (15 mL) was treated with concentrated hydrochloric acid (8 mL) for 5 h at room temperature. The mixture was then washed with water (3×20 mL), dried over $MgSO_4$, and subsequently crystallized

from CH_2Cl_2-Et_2O to give the dichloro complex **52a** as pale yellow prisms (0.52 g, 88%). $[\alpha]_D$ = – 17.5° (*c* 1.7, CH_2Cl_2). Mp: 275–277 ºC (decomp.). Anal. Calcd for $C_{30}H_{30}Cl_2O_2P_2Pd$: C, 54.4; H, 4.6. Found: C, 54.8; H, 4.4. ^{31}P NMR ($CDCl_3$, 121 MHz): δ 15.5 (d, J_{PP} = 13.0 Hz), 21.9 (d, J_{PP} = 13.0 Hz). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.93-2.13 (m, 2H, PCH_2CH_2), 2.22 (m, 1H, J_{HH} = 10.6 Hz, J_{HH} = 16.6 Hz, C*H*′HCO$_2$Me), 2.43-2.53 (m, 3H, CH′*H*CO$_2$Me and P*CH*$_2$), 2.96 (m, 1H, P*CH*CH$_2$), 3.56 (s, 3H, CO$_2$*Me*), 7.36-7.87 (m, 20H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.8 (dd, J_{PC} = 8.0 Hz, J_{PC} = 31.1 Hz), 24.9 (d, J_{PC} = 4.1 Hz), 29.2 (dd, J_{PC} = 10.6 Hz, J_{PC} = 29.3 Hz), 35.3 (s), 52.3 (s), 126.3 (d, J_{PC} = 54.2 Hz), 126.8 (d, J_{PC} = 55.5 Hz), 128.4 (d, 2C, J_{PC} = 11.4 Hz), 128.6 (d, 2C, J_{PC} = 11.5 Hz), 128.7 (d, J_{PC} = 56.8 Hz), 128.9 (d, 4C, J_{PC} = 11.2 Hz), 130.1 (d, J_{PC} = 59.0 Hz), 131.3 (d, J_{PC} = 2.9 Hz), 131.6 (d, J_{PC} = 2.6 Hz), 131.7 (d, J_{PC} = 3.1 Hz), 131.9 (d, J_{PC} = 2.7 Hz), 133.3 (d, 2C, J_{PC} = 10.2 Hz), 133.7 (d, 2C, J_{PC} = 9.6 Hz), 133.8 (d, 2C, J_{PC} = 10.9 Hz), 135.3 (d, 2C, J_{PC} = 10.9 Hz), 171.1 (d, J_{PC} = 12.8 Hz).

The same procedure was used to prepare dichloro complexes **52b** and **52c**. **52b** (0.38 g, 85%) from regioisomers **48b** and **49b** (0.6 g, 0.69 mmol). $[\alpha]_D$ = – 20.4° (*c* 0.9, CH_2Cl_2). Mp: 285–287 ºC (decomp.). Anal. Calcd for $C_{30}H_{30}Cl_2OP_2Pd$: C, 55.8; H, 4.7. Found: C, 55.9; H, 4.5. ^{31}P NMR ($CDCl_3$，121 MHz): δ 16.3 (d, J_{PP} = 12.7 Hz), 22.5 (d, J_{PP} = 12.7 Hz). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.90 (s, 3H, CO*Me*), 1.91-2.06 (m, 2H, PCH_2CH_2), 2.34 (m, 1H, J_{HH} = 9.4 Hz, J_{HH} = 18.3 Hz, C*H*′HCOMe), 2.47 (m, 2H, P*CH*$_2$), 2.54 (m, 1H, CH′*H*COMe), 3.08 (m, 1H, P*CH*CH$_2$), 7.35-7.84 (m, 20H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.3 (dd, J_{PC} = 8.1 Hz, J_{PC} = 31.4 Hz), 25.4 (d, J_{PC} = 4.0 Hz), 27.6 (dd, J_{PC} = 11.0 Hz, J_{PC} = 29.8 Hz), 30.1 (s), 44.5 (d, J_{PC} = 1.9 Hz), 126.6 (d, J_{PC} = 54.0 Hz), 127.2 (d, J_{PC} = 55.6 Hz), 128.4 (d, 2C, J_{PC} = 11.4 Hz), 128.7 (d, 2C, J_{PC} = 11.5 Hz), 128.8

(d, 2C, J_{PC} = 10.9 Hz), 128.9 (d, 2C, J_{PC} = 11.4 Hz), 129.1 (d, J_{PC} = 57.3 Hz), 129.9 (d, J_{PC} = 58.4 Hz), 131.3 (d, J_{PC} = 2.8 Hz), 131.5 (d, J_{PC} = 2.8 Hz), 131.6 (d, J_{PC} = 2.7 Hz), 131.9 (d, J_{PC} = 2.7 Hz), 133.4 (d, 2C, J_{PC} = 10.3 Hz), 133.5 (d, 2C, J_{PC} = 9.3 Hz), 133.8 (d, 2C, J_{PC} = 10.8 Hz), 135.4 (d, 2C, J_{PC} = 10.6 Hz), 204.5 (d, J_{PC} = 8.8 Hz).

52c (0.39 g, 87%) from regioisomers **48c** and **49c** (0.6 g, 0.64 mmol). $[\alpha]_D$ = +12.6 (*c* 1.0, CH_2Cl_2). Mp: 160–163 ºC. Anal. Calcd for $C_{35}H_{32}Cl_2OP_2Pd$: C, 59.4; H, 4.6. Found: C, 59.7; H, 4.4. ^{31}P NMR ($CDCl_3$， 162 MHz): δ 15.8 (d, J_{PP} = 13.8 Hz), 22.4 (d, J_{PP} = 13.8 Hz). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.07 (br, 2H, PCH_2CH_2), 2.53 (br, 2H, CH_2COPh), 2.90 (m, 1H, J_{HH} = 10.0 Hz, J_{HH} = 17.4 Hz, PCH′H), 3.01 (dd, 1H, J_{PH} = 8.8 Hz, J_{HH} = 17.4 Hz, PCH′H), 3.26 (br, 1H, $PCHCH_2$), 7.36-7.91 (m, 25H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.2 (dd, J_{PC} = 8.0 Hz, J_{PC} = 31.2 Hz), 25.3 (d, J_{PC} = 4.2 Hz), 27.8 (dd, J_{PC} = 10.9 Hz, J_{PC} = 29.8 Hz), 39.5 (s), 126.8 (d, J_{PC} = 54.3 Hz), 127.0 (d, J_{PC} = 55.0 Hz), 127.9 (s, 2C), 128.4 (d, 2C, J_{PC} = 11.4 Hz), 128.7 (d, 2C, J_{PC} = 11.5 Hz), 128.8 (s, 2C), 128.9 (d, 2C, J_{PC} = 11.3 Hz), 128.9 (d, 2C, J_{PC} = 11.0 Hz), 129.2 (d, J_{PC} = 55.0 Hz), 130.0 (d, J_{PC} = 58.4 Hz), 131.3 (d, J_{PC} = 2.8 Hz), 131.6 (d, 2C, J_{PC} = 2.7 Hz), 131.9 (d, J_{PC} = 2.7 Hz), 133.5 (d, 2C, J_{PC} = 10.2 Hz), 133.6 (d, 2C, J_{PC} = 9.3 Hz), 133.7 (d, 2C, J_{PC} = 10.7 Hz), 133.9 (s), 135.4 (d, 2C, J_{PC} = 10.6 Hz), 135.8 (s), 196.1 (d, J_{PC} = 10.0 Hz).

Preparation of the Keto-Fuctionalized Diiodo Palladium Complexes 56. The solution of **52c** (0.15 g, 0.21 mmol) in dichloromethane (8 mL) was mixed with sodium iodide (0.13 g, 0.87 mmol) in water (3 mL) and stirred vigorously for 1 h. The mixture was washed with water (3×20 mL), and concentrated. Upon on purification by chromatography on silica, the diiodide product **56** was isolated as red prisms by slow

diffusion of diethyl ether into the dichloromethane solution (0.16 g, 85%). $[\alpha]_D$ = +43.0 (*c* 0.8, CH_2Cl_2). Mp: 280–282 ºC (decomp.). Anal. Calcd for $C_{35}H_{32}I_2OP_2Pd$: C, 47.2; H, 3.6. Found: C, 47.5; H, 3.5. ^{31}P NMR ($CDCl_3$，162 MHz): δ 6.8 (d, J_{PP} = 22.4 Hz), 11.4 (d, J_{PP} = 22.4 Hz). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.89-2.15 (m, 2H, PCH_2CH_2), 2.53-2.62 (m, 1H, CH*H*′COPh), 2.66-2.74 (m, 1H, C*H*H′COPh), 2.77-2.85 (ddd, 1H, J_{HH} = 10.3 Hz, J_{HH} = 17.3 Hz, PC*H*′H), 2.96-3.02 (dd, 1H, J_{PH} = 8.3 Hz, J_{HH} = 17.2 Hz, PCH′*H*), 3.18-3.25 (m, 1H, PC*H*CH_2), 7.34-8.02 (m, 25H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.4 (d, J_{PC} = 4.4 Hz), 26.0 (dd, J_{PC} = 9.3 Hz, J_{PC} = 27.2 Hz), 27.9 (dd, J_{PC} = 13.9 Hz, J_{PC} = 24.8 Hz), 40.6 (d, J_{PC} = 3.6 Hz), 127.8 (s, 2C), 128.4 (d, 4C, J_{PC} = 11.0 Hz), 128.6 (d, 2C, J_{PC} = 10.7 Hz), 128.7 (d, J_{PC} = 50.1 Hz), 128.8 (s, 2C), 128.9 (d, 2C, J_{PC} = 11.0 Hz), 129.4 (d, J_{PC} = 52.6 Hz), 130.5 (d, J_{PC} = 52.0 Hz), 131.0 (d, J_{PC} = 2.6 Hz), 131.3 (d, J_{PC} = 2.7 Hz), 131.7 (d, J_{PC} = 2.4 Hz), 131.8 (d, J_{PC} = 2.4 Hz), 133.2 (d, 2C, J_{PC} = 9.6 Hz), 133.3 (d, 2C, J_{PC} = 10.4 Hz), 133.4 (d, J_{PC} = 56.4 Hz), 133.8 (s), 134.1 (d, 2C, J_{PC} = 10.8 Hz), 135.8 (s), 135.9 (d, 2C, J_{PC} = 10.3 Hz), 196.4 (d, J_{PC} = 9.1 Hz).

Liberation of Functionalized 1,3-Diphosphine Ligand 53a, 53b and 53c. A solution of complex **52a** (0.3 g, 0.45 mmol) in dichloromethane (10 mL) was stirred vigorously with aqueous KCN (1.0 g, 15.4 mmol) for 30 min. The organic layer was separated, washed with water (3×15 mL), and dried with $MgSO_4$. The 1,3-diphosphine ligand **53a** was obtained as white solid upon removal of solvent under reduced pressure (0.21 g, 95%). $[\alpha]_D$ = +19.0 (*c* 1.0, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 121 MHz): δ –15.3 (s), –6.4 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.51 (m, 2H, PCH_2CH_2), 2.09-2.19 (m, 3H, CH_2CO_2Me and PC*H*′H), 2.35 (m, 1H, J_{HH} = 6.8 Hz, J_{HH} = 13.8 Hz, PCH′*H*), 2.88 (br, 1H, PC*H*CH_2), 3.47 (s, 3H, CO_2*Me*), 7.19-7.40 (m, 20H, Ar).

Similarly the keto-functionalized 1,3-diphosphine ligand **53b** (0.20 g, 92%) was achieved from **52b** (0.3 g, 0.46 mmol) as a white solid. $[\alpha]_D$ = + 30.8° (*c* 0.9, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 202 MHz): δ – 15.8 (s), – 6.6 (s). ^1H NMR ($CDCl_3$, 500 MHz): δ 1.48 (m, 1H, $PCH_2CH'H$), 1.57 (m, 1H, $PCH_2CH'H$), 1.95 (s, 3H, CO*Me*), 2.14 (t, 2H, $J_{HH} = J_{PH}$ = 8.4 Hz, CH_2COMe), 2.36 (m, 1H, J_{PH} = 8.6 Hz, J_{HH} = 17.6 Hz, $PCH'H$), 2.45 (m, 1H, J_{HH} = 17.6 Hz, $PCH'H$), 3.10 (br, 1H, $PCHCH_2$), 7.26-7.44 (m, 20H, Ar).

53c (0.21 g, 95%) was prepared from **52c** (0.3 g, 0.42 mmol) as a white solid. $[\alpha]_D$ = + 11.4° (*c* 0.7, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 202 MHz): δ – 15.7 (s), – 6.4 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ 1.64 (m, 2H, PCH_2CH_2), 2.02 (t, 2H, $J_{HH} = J_{PH}$ = 8.5 Hz, CH_2COPh), 2.99 (m, 2H, PCH_2), 3.34 (br, 1H, $PCHCH_2$), 7.25-7.80 (m, 25H, Ar).

Hydrophosphination of Monophosphine palladium Complex *R*-45. A solution of *R*-**45** (1.0 g, 1.72 mmol) in acetonitrile (25 mL) was treated with diphenylphosphine (0.32 g, 1.72 mmol), followed by $LiClO_4 \cdot 3H_2O$ (0.68 g, 4.30 mmol) and triethylamine (0.17 g, 1.72 mmol). The mixture was stirred for 2 h at room temperature and the solvent was removed under reduced pressure. Redissolved the residue in dichloromethane, washed with H_2O (3 × 15 mL), dried over $MgSO_4$, concentrated and purified by column chromatography on silica ($CH_2Cl_2/(C_2H_5)_2O$ = 10:1) to afford a mixture of regioisomers **57** and **58** as pale yellow solid (0.60 g, 42%). ^{31}P NMR ($CDCl_3$，202 MHz): δ 0.0 (d, J_{PP} = 53.0 Hz), 13.1 (d, J_{PP} = 52.5 Hz), 26.0 (d, J_{PP} = 52.5 Hz). 39.3 (d, J_{PP} = 53.0 Hz). Upon crystallization in dichloromethane-diethyl ether, product **57** was isolated as pale yellow prisms (0.57 g, 40%). $[\alpha]_D$ = – 90.7° (*c* 0.8, CH_2Cl_2). Mp: 178–180 ºC. Anal. Calcd for $C_{41}H_{42}ClNO_5P_2Pd$: C, 59.1; H, 5.1; N, 1.7. Found: C, 59.4; H, 5.0; N, 1.8. ^{31}P NMR

($CDCl_3$, 202 MHz): δ 13.1 (d, J_{PP} = 52.5 Hz), 26.0 (d, J_{PP} = 52.5 Hz). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.76-1.89 (m, 1H, $PCH_2CH'H$), 2.06 (d, 3H, J_{HH} = 6.2 Hz, CH*Me*), 2.16-2.28 (m, 1H, $PCH_2CH'H$), 2.22 (s, 3H, N*Me*), 2.44-2.55 (m, 2H, PCH_2), 2.48 (s, 3H, N*Me*), 3.47 (b, 1H, J_{HH} = 4.6 Hz, O*H*), 4.34 (qn, 1H, $J_{HH} = J_{PH}$ = 6.0 Hz, $CHCH_3$), 4.73 (m, 1H, PC*H*OH), 6.98-8.27 (m, 26H, Ar).

Crystal Structure Determinations of Complexes 52a, 52b, 56, and 57. X-ray crystallographic data for all four complexes are given in the Appendices. Crystal data were collected on a Bruker X8 CCD diffractometer with Mo Kα radiation (graphite monochromator). SADABS absorption corrections were applied. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were introduced at calculated positions and refined with a riding model. The absolute configurations of all chiral complexes were determined unambiguously by using the Flack parameter. We thank Dr Li Yongxin for undertaking the X-ray analysis.

Chapter IV

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

4.1 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.[4,5] It is conceivable that the presence of proper functional groups, for instance hydroxyl, amino, or ester on chiral phosphine frameworks can efficiently improve both reactivity and enantioselectivity in many reactions through the secondary interactions with the reacting substrates.[97] Over the past few years, our group has successfully prepared a series of functionalized chiral phosphine ligands by means of asymmetric hydrophosphination[67,79] and Diels-Alder reactions,[66] promoted by the organopalladium complexes containing (*R*)- or (*S*)-(1-(dimethylamino)ethyl)- naphthalene as the chiral auxiliaries. During the course of these series of studies, the use of stoichiometric amount of palladium complex as reaction promoter offers practical advantages. (1) By means of coordination, it can protect the air-sensitive 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 carbon, it can alternatively provide one or two distinct coordination sites around the square planar palladium center

to selectively synthesize functionalized mono- or bidentate phosphine 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 isomers 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 lastly, (5) the air stable optically pure phosphine complexes could easily yield the free phosphine ligands by treatment with aqueous potassium cyanide.

In Chapter II and Chapter III, we have demonstrated the asymmetric synthesis of novel keto- and ester-functionalized chiral 1,2- and 1,3-diphosphines by chiral palladium template assisted asymmetric hydrophosphination of activated olefins. In pursuing the interest in the synthesis of new chiral diphosphines with selected functionalities, this chapter reports a preparation of cyano-functionalized 1,3-diphosphine ligand, by means of chiral metal template promoted asymmetric hydrophosphination reaction of a cyano-substituted homoallylic monophosphine precursor. As the cyano group has been shown to be easily derivatized with versatility and selectivity, the cyano-functionalized 1,3-diphosphine palladium complex is subsequently subjected to organic transformation reactions, which afford the novel formyl- and hydroxyl-functionalized 1,3-bis(diphenylphosphino)propane ligands.

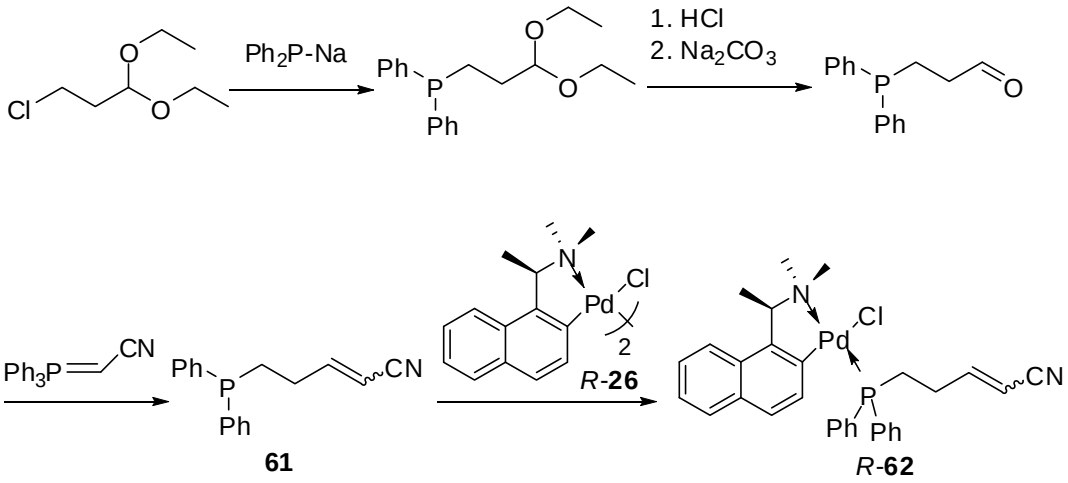
4.2 Results and Discussion

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.[78b,c,98] Furthermore, the cyano group is suitable for conversion to other functionalities such as acid, amide, amine, aldehyde, or alcohol by simple organic manipulations.[98f-h,99] In general, 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 functionalized diphosphines, for example, the chiral cyano-, formyl- and hydroxyl-substituted 1,3-bis(diphenylphosphino)propane ligands.

4.2.1 Synthesis of Cyano-Functionalized Homoallylic Monophosphine Palladium complex *R*-62

The synthesis of cyano-functionalized monophosphine palladium complex *R*-**62** is illustrated in Scheme 4.1. 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 **61**. This new phosphine species was not isolated and was *in situ* coordinated to palladium template *R*-**26** to generate the monomeric phosphine complex *R*-**62** as a mixture of the 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 the *trans*-*R*-**62** exhibited a sharp singlet at δ 34.6 while the *cis*-*R*-**62** isomer indicated a single resonance at δ 34.8.



Scheme 4.1

Both isomers can be easily recrystallized from ethyl acetate and hexanes as pale yellow prisms. The molecular structure and coordination property of *trans*-*R*-**62** were characterized by means of single-crystal diffraction analysis, and the ORTEP drawing of complex *trans*-*R*-**62** is shown in Figure 4.1. Selected bond length and angle parameters are populated in Table 4.1. As expected, the phosphorus moiety coordinated specifically *trans* to the σ–donating nitrogen group of the chiral auxiliary. The geometry at the palladium atom is distorted square planar. The angles around the metal center are in the range of 80.6(1)–97.0(1) and 169.6(1)–169.9(1)°. The PPdCl plane is rotated at an angle of 13.4° with respect to that of CPdN which is apparently larger than in the case of the diphosphine palladium complexes **37a** (4.6°) and **37b** (2.9°) reported in Chapter 2. The C17–C18 bond length is 1.295(5) which clearly exhibits the double bond characteristic.

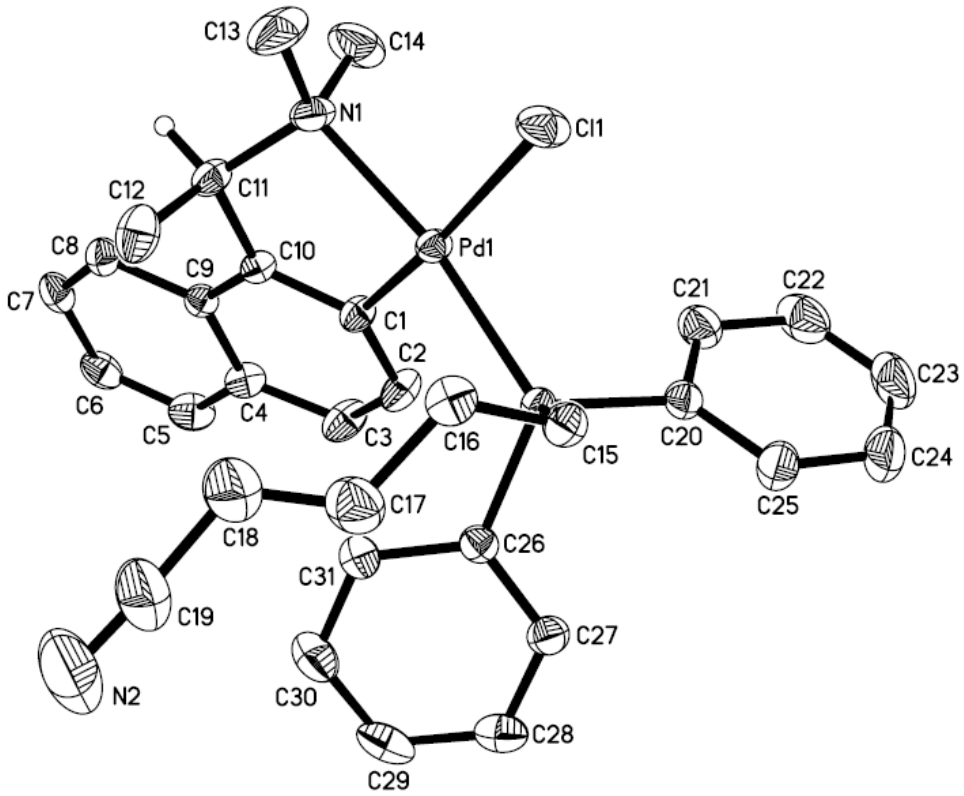
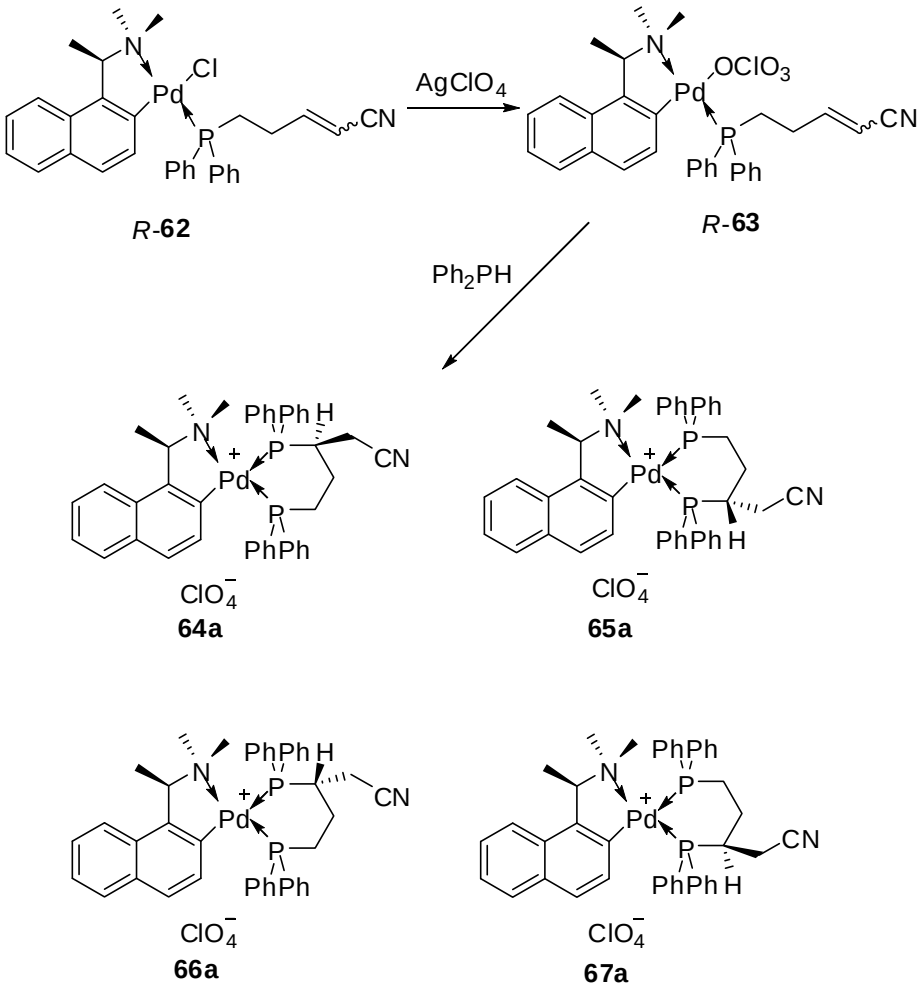


Figure 4.1. Molecular structure of complex *trans*-*R*-**62**

Table 4.1. Selected Bond Lengths (Å) and Angles (deg) of *trans*-*R*-**62**

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)
C11–N1	1.508(3)	C11–C10	1.509(3)
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)
C11–N1–Pd1	104.7(1)	N1–C11–C10	106.2(2)

4.2.2 Asymmetric Hydrophosphination of Cyano-Functionalized Monophosphine Palladium Complex *R*-62

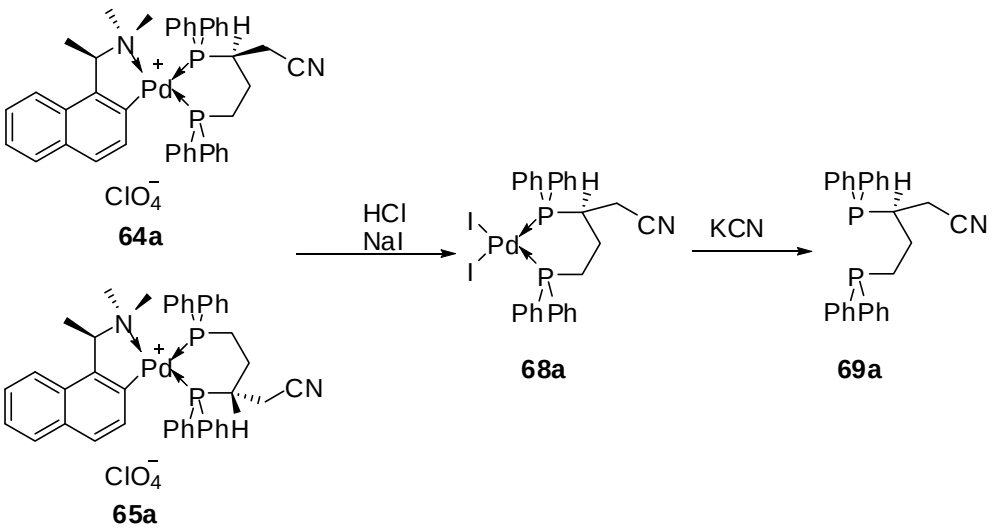


Scheme 4.2

In the absence of metal ion, diphenylphosphine shows no reactivity towards the free phosphine substrate **61** under ambient conditions. As illustrated in Scheme 4.2, treatment of the complex *trans*-*R*-**62** with silver perchlorate can abstract the chloro ligand which is known to be both kinetically and thermodynamically stable, and thus provides a vacant coordination site for any incoming phosphorous donor atoms.[67,79] The resultant reactive perchlorato complex *R*-**63** was not isolated and subsequently reacted with one equivalent of diphenylphosphine in dichloromethane at −78 ºC 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 ^{31}P NMR spectrum of the crude product exhibited 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., **64a**, **65a, 66a**, and **67a** were generated during the hydrophosphination process (Scheme 4.2). Our previous studies on a series of regioisomeric diphosphine palladium complex containing (*R*)- or (*S*)-naphthylamine as the chiral auxiliary have revealed that the ^{31}P NMR spectrum of a pair of regioisomers such as **64a** and **65a** have the following characteristics. (1) The ^{31}P NMR signals of one regioisomer for instance **64a** will be between or flanking those of another regioisomer **65a**, and more importantly, (2) the two regioisomers should always have similar phosphorus coupling constants in the ^{31}P NMR spectrum.

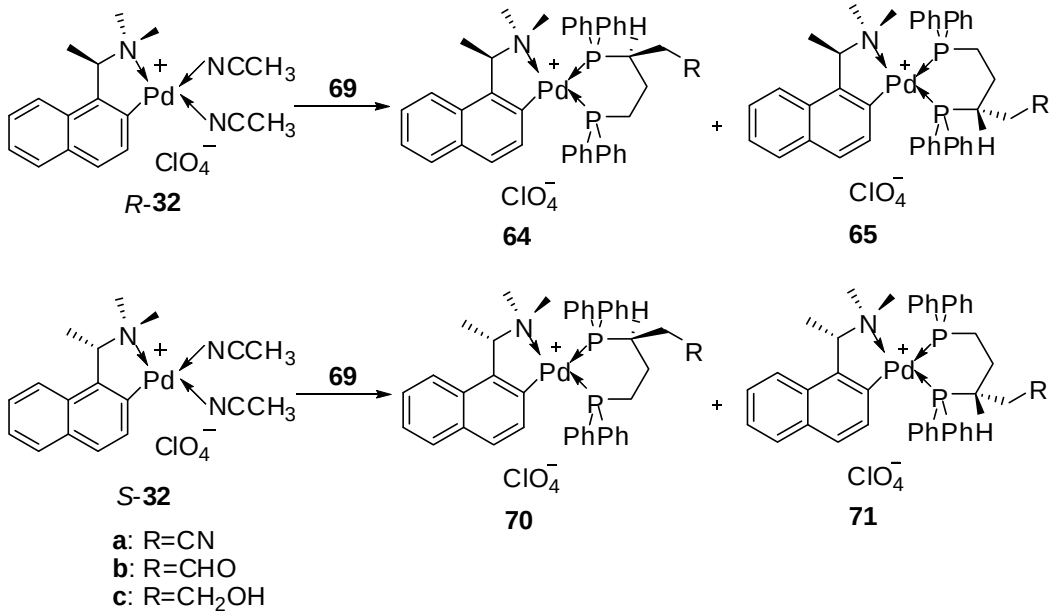
The two major regioisomers **64a** and **65a**, which adopt the same *S* absolute configuration at the newly formed chiral carbon centers, can be efficiently separated as off-white solids by column chromatography in 70% yield. The ^{31}P NMR spectrum showed two pairs of doublets at δ – 1.1, 35.3 (J_{PP} = 52.1 Hz) and 8.3, 27.1 (J_{PP} = 51.7 Hz). It is noteworthy that, during the course of column chromatography, a pair of new doublet signals at δ 6.2, 26.6 (J_{PP} = 54.9 Hz) appeared. This new pair of doublets along with the signals at δ – 10.2, 33.0 (J_{PP} = 55.7 Hz) are due to the minor regioisomers **66a** and **67a**. The ^{31}P NMR spectrum assignment was confirmed by means of the subsequent liberation of recoordination process.



Scheme 4.3

It has been well established that the chiral naphthylamine auxiliary on similar complexes **64a** and **65a** could be chemoselectively removed by treatment with concentrated hydrochloric acid to form the neutral dichloro palladium complex.[67,79] However, the dichloro analogue of the cyano-functionalized complex **68a** exhibited rather poor solubility. Thus, as illustrated in Scheme 4.3, treatment of the regioisomers **64a** and **65a** with concentrated hydrochloric acid in the presence of NaI gave the optically pure diiodo palladium complex **68a** as a red solid in 79% yield, $[\alpha]_D = -10.7°$ (*c* 1.3, CD_2Cl_2). The diiodo product **68a** has a good solubility in dichloromethane and exhibited a pair of doublets at δ 4.2, 8.8 (J_{PP} = 21.3 Hz) in the ^{31}P NMR spectrum. Unfortunately, efforts to crystallize the diiodo complex **68a** from various solvent systems to get suitable crystals for X-ray crystallography were unsuccessful.

Treatment of a CH_2Cl_2 solution of product **68a** with aqueous potassium cyanide can conveniently liberate the enantiomerically pure cyano-functionalized 1,3-diphosphine ligand **69a** as a white solid in high yield, $[\alpha]_D = -28.5$ (*c* 1.3, CH_2Cl_2). The ^{31}P NMR spectrum in $CDCl_3$ of the free ligand showed two singlet signals at δ – 17.5 (s), – 8.3 (s).



Scheme 4.4

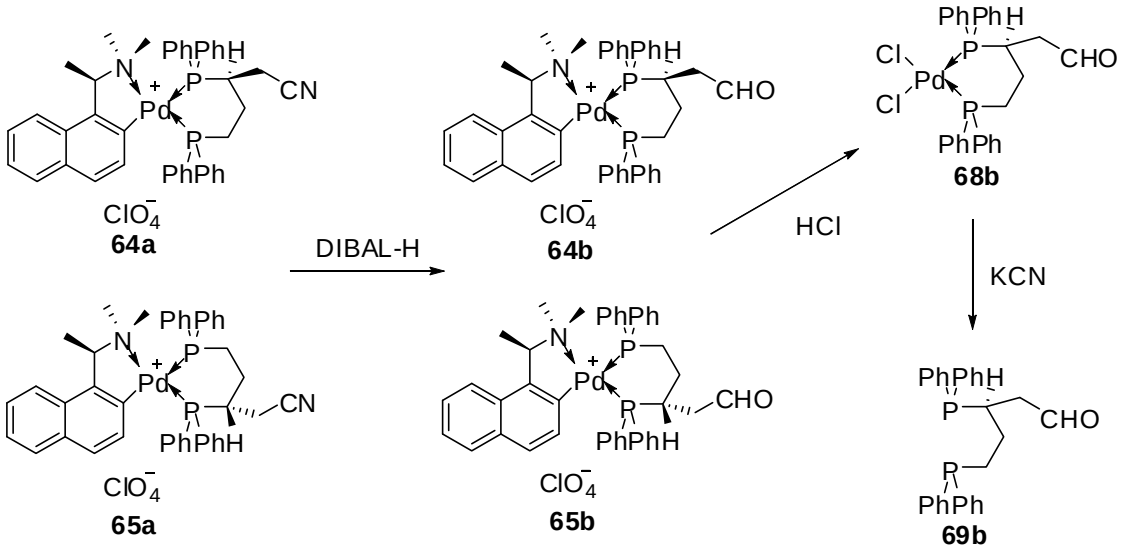
As illustrated in Scheme 4.4, in order to confirm the optical purity of the free diphosphine ligand **69a** and the ^{31}P NMR assignment for the regioisomers, the liberated ligand was recoordinated to the bis(acetonitrile) complex *R*-**32**. The resultant recomplexation products in $CDCl_3$ indeed exhibited two pair 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 ^{31}P NMR signals of two major products from the original hydrophosphination reaction, and therefore indicated the formation of the regioisomers **64a** and **65a**. Furthermore, the recoordination of **69a** to the equally accessible bis(acetonitrile) complex *S*-**32** will generate the regioisomers **70a** and **71a**, 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 **70a** and **71a** are the enantiomeric forms of **66a** and **67a**, respectively. Thus no signals were observed at δ – 1.1, 8.3, 27.1 and 35.3, and the free 1,3-diphosphine **69a** was hence confirmed to be optically pure.

For comparison of the stereoselectivity, the *Z*-form monophosphine substrate *cis*-*R*-**62**

was employed for the same asymmetric hydrophosphination reaction. Upon abstraction of the terminal chloro ligand with silver perchlorate, the reactive perchlorato complex *cis*-*R*-**63** reacted with one equivalent of diphenylphosphine at −78 ºC. The addition process could be completed within 2 h. Interestingly, the 162 MHz ^{31}P NMR spectrum in $CDCl_3$ of the crude product mixture 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 different 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*-**62**) to 1:6.8 (for *cis*-*R*-**62**) which may due to stronger internal steric repulsion in the case of the *cis*-*R*-**62** as we have discussed in Chapter II.

4.2.3 Functional Group Transformations: Synthesis of Formyl- and Hydroxyl-Substituted 1,3-Diphosphine Products

As aforementioned, the cyano group could be easily converted to other functionalities, for example amine, aldehyde, or alcohol by simple organic manipulations for instance reduction reactions.[98f-h,99] However, organic transformations involving the chiral diphosphine ligands on chiral Pd(II) complexes are not common due to its instability towards reductive reagents. For example, the reductive decomplexation occurred when the diphosphine palladium complexes containing (*R*)-(1-(dimethylamino)ethyl)-benzene as the chiral auxiliary were treated with $LiAlH_4$.[8a,20a]



Scheme 4.5

Interestingly, upon treatment of the dichloromethane solution of regioisomers **64a** and **65a** with DIBAL–H at – 78 ºC 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 **64b** and **65b** as shown in Scheme 4.5. The chiral naphthylamine auxiliary in the products **64b** and **65b** was removed by stirring a dichloromethane solution of the regioisomers with concentrated hydrochloric acid at room temperature. The optically pure dichloro complex **68b** 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 **68b** in CD_2Cl_2 exhibited a pair of doublets at δ 15.3, 21.8 (J_{PP} = 12.5 Hz).

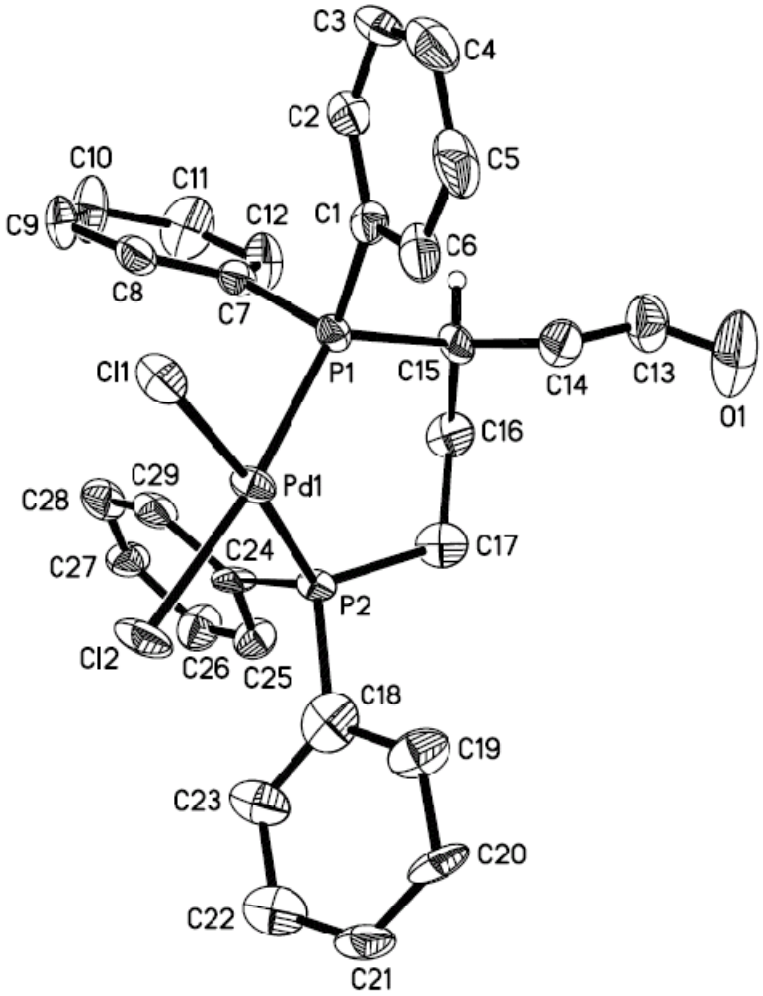


Figure 4.2. Molecular structure and absolute stereochemistry of complex **68b**

The single-crystal X-ray crystallographic analysis unambiguously established its absolute configuration and confirmed 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 4.2 shows the ORTEP drawing of molecule 1, the selected bond and angle parameters are provided in Table 4.2. The coordination 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)°)

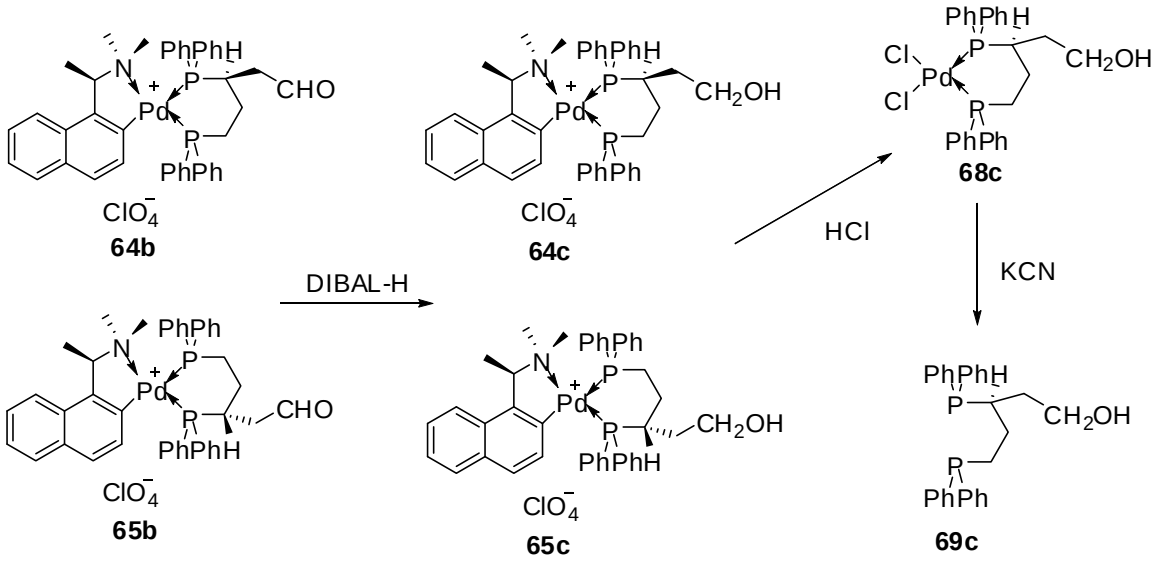
is clearly larger than in the case of 1,2-diphosphine chelates previously reported.[67,79] The six-membered chelate in complex **68b** adopts a twist-chair conformation with the formyl group occupying the sterically favorable equatorial position.

Table 4.2. Selected Bond Lengths (Å) and Angles (deg) of **68b**

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)
C16–C17	1.533(18)	C14–C15	1.521(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)
C17–P2–Pd1	114.2(18)	Pd1–P1–C15	121.2(3)

As illustrated in Scheme 4.5, the optically active formyl-functionalized 1,3-diphosphine **69b** could be liberated by treatment of **68b** 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 **69b** was also confirmed by recoordination of the free ligand to the bis(acetonitrile) complex *R*-**32** (Scheme 4.4). 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 **64b** and **65b**. However, the recomplexation products involving *S*-**32** generated two new regioisomers **70b** and **71b** with two pairs of different doublets at δ – 8.0, 36.6 (J_{PP} = 54.9 Hz), 7.7, 26.9 (J_{PP} = 55.8 Hz). Thus, the recoordination process confirmed that the liberated formyl-substituted 1,3-diphosphine was enantiomerically

pure, and the chirality remained unaffected throughout the reduction reaction.



Scheme 4.6

As illustrated in Scheme 4.6, continuous treatment of the regioisomers **64b** and **65b** with DIBAL-H could chemoselectively yield the novel hydroxyl-functionalized regioisomers **64c** and **65c**. The reduction process could be finished within 2 h at –78 ºC, 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 **64c** and **65c** by treatment with concentrated hydrochloric acid yield the optically pure dichloro complex **68c** as pale yellow cubic crystals upon crystallization from dichloromethane and diethyl ether in 72% yield, $[\alpha]_D$ = + 31.1° (*c* 1.0, CH_2Cl_2). The dichloro product **68c** showed a pair of doublets at δ 15.6, 23.5 (d, J_{PP} = 14.5 Hz). The molecular structure is determined by X-ray crystallography and there is only one molecule in the asymmetric unit as shown in Figure 4.3. Selected bond lengths and angles are listed in Table 4.3. As expected, the palladium atom adopted square planar geometry but with a smaller tetrahedral distortion (2.8°), while the angles around palladium are in ranges of 86.2(1) –

96.5(1) and 176.2(1) – 176.7(1)°. The configuration at the chiral carbon center is the expected *S* form and the hydroxyl substituent is of equatorial orientation.

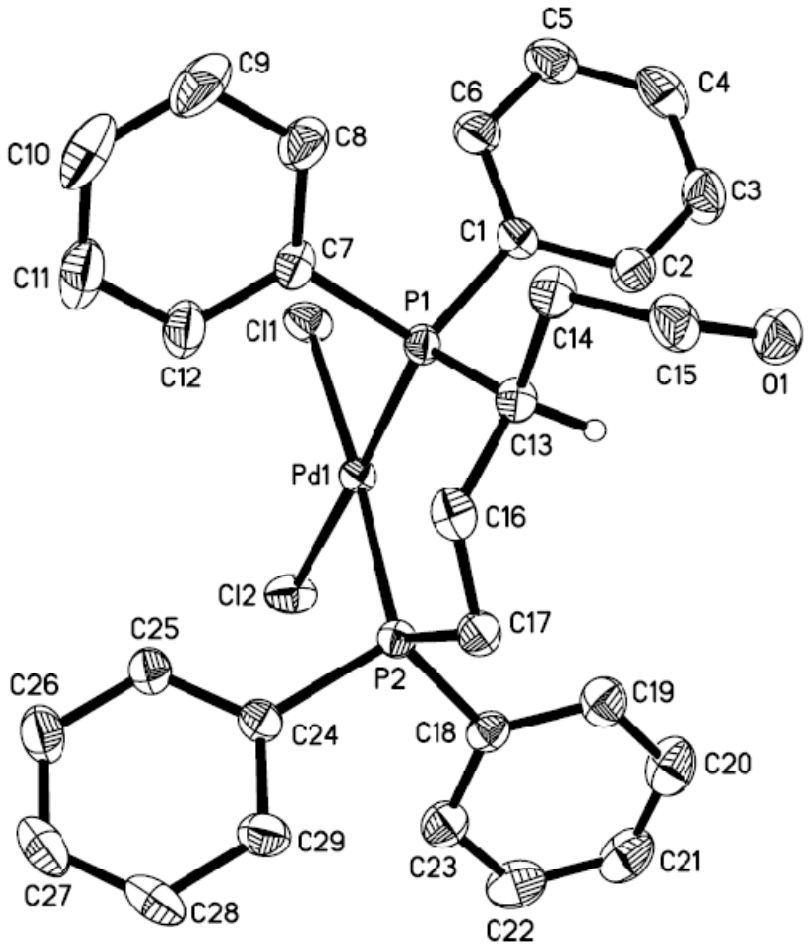


Figure 4.3. Molecular structure and absolute stereochemistry of complex **68c**

Table 4.3. Selected Bond Lengths (Å) and Angles (deg) of **68c**

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)	C16–C17	1.538(4)
C13–C14	1.537(4)	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)
Pd1–P1–C13	117.2(1)	Pd1–P2–C17	119.9(1)

Similarly, further treatment of **68c** with aqueous potassium cyanide can liberate the chiral hydroxyl-functionalized 1,3-diphosphine ligand **69c** in nearly quantitative yield, $[\alpha]_D = -38.5°$ (*c* 0.5, CH_2Cl_2) (Scheme 4.6). The ^{31}P NMR spectrum of **69c** in $CDCl_3$ exhibited a pair of singlets at δ – 16.3 and – 6.6. The enantiomeric purity of the free diphosphine **69c** was approved by the subsequent recoordination process. When the liberated phosphine ligand **69c** was recoordinated to the bis(acetonitrile) complex *R*-**32** (Scheme 4.4), 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) were observed in the ^{31}P NMR spectrum, while the recoordination products involving *S*-**32** revealed two different pairs of doublet signals at δ –7.8, 38.2 (J_{PP} = 55.9 Hz) and 9.0, 27.1 (J_{PP} = 55.8 Hz).

4.3 Conclusion

In summary, we have presented a facile synthesis of a novel 1,3-bis(diphenylphosphino)propane ligand with cyano-functionality by means of organo-palladium complex promoted hydrophosphination of cyano-functionalized homoallylic monophosphine substrate with good yield and stereoselectivity. Subsequent organic transformations can chemoselectively yield the formyl- and hydroxyl-functionalized chiral phosphine metal complexes and the free ligands by treatment with DIBAL-H. The controllable reduction reactions proceeded in high yield without any protection and deprotection steps, which were usually involved in the synthesis of functionalized chiral phosphine ligands.

4.4 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 ºC on Bruker ACF 400 (^{1}H 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 ºC 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*-**26**, [89a,b] *R*-**32**, and *S*-**32**[89c] were prepared according to literature methods.

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

Preparation of Homoallylic Monophosphine Palladium Complex *R*-62. Sodium diphenylphosphide solution prepared from diphenylphosphine (0.80 g, 4.30 mmol) in THF (20 mL) was cooled to 0 ºC, 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 1h at room temperature, and 4 N HCl (15 mL) was added and stirred for 5 h.

The solution was adjusted to pH=10 with sodium carbonate. The mixture was extracted with ethyl acetate (3 × 20 mL). To the combined organic phases, (triphenylphosphoranylidene)acetonitrile (1.94 g, 6.44 mmol)) was added. The mixture was stirred for 2 h at room temperature, and palladium dimer *R*-**26** (1.46. g, 2.15 mmol) was added, and stirred for another 1 h. Upon removal of the solvent, the complex *R*-**62** 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*-**62** (1.37 g, 53%), $[\alpha]_D$ = – 19.3° (*c* 1.1, CH_2Cl_2). Mp: 123–125 ºC. 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). ^{1}H 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*-**62** (0.76 g, 29%), $[\alpha]_{436}$ = +128.6° (*c* 1.0, CH_2Cl_2). Mp: 205–207 ºC. 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). ^{1}H 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 *trans*-*R*-62 and Synthesis of the Diiodo Palladium Complex 68a. A mixture of *trans*-*R*-**62** (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 down to –78 ºC, 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 a mixture of regioisomers **64a** and **65a** as 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 **64a** and **65a** (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 **68a** as red solid (0.26 g, 79%). $[\alpha]_D$ = – 10.7° (*c* 1.3, CH_2Cl_2). Mp: 330–333 ºC (decomp.). 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). ^{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*-**62**.

Preparation of the Formyl-Functionalized Complexes 64b, 65b, and the Dichloro Palladium Complexes 68b. A solution of regioisomers **64a** and **65a** (0.5 g, 0.58 mmol) in dichloromethane (20 mL) was cooled to –78 ºC under argon. DIBAL-H (1 M in heptane, 1.8 mL, 1.8 mmol) was added and stirred for 2h at the same temperature. The

mixture was quenched with water (2 mL), warmed to 0 ºC, 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 **64b** and **65b** 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 **64b** and **65b** was not isolated, and a solution of **64b** and **65b** 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 **68b** was isolated as pale yellow prisms (0.25 g, 68%). $[\alpha]_D$ = + 24.4° (*c* 0.9, CH_2Cl_2). Mp: 281–283 ºC (decomp.). 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, PC*H*H′), 2.53 (m, 2H, CH_2CHO), 2.64 (ddd, 1H, PCH*H*′), 3.10 (m, 1H, PC*H*CH_2), 7.42-7.87 (m, 20H, Ar), 9.42 (d, 1H, J_{PH} = 2.3 Hz, C*H*O). ^{13}C NMR (CD_2Cl_2, 100 MHz): δ 25.0 (d, J_{PC} = 3.7 Hz), 35.1 (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 64c, 65c, and the Dichloro Palladium Complexes 68c. A solution of regioisomers **64b** and **65b** (generated from **64a** and **65a**, 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 ºC for 2h. The mixture was quenched with water (2 mL), warmed to 0 ºC, and 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 **64c** and **65c** 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). A solution of **64c** and **65c** in dichloromethane (10 mL) was treated with concentrated hydrochloric acid (5 mL) for 3 h at room temperature. The resultant 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). The dichloro product **68c** was isolated 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 ºC (decomp.). 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, C*H*H′CH_2OH), 1.62 (br, 1H, CH_2O*H*), 1.70 (m, 1H, CH*H*′CH_2OH), 1.96 (m, 1H, PCH_2C*H*H′), 2.17 (m, 1H, PCH_2CH*H*′), 2.50 (m, 2H, PC*H*$_2$), 2.62 (m, 1H, P*C*HCH_2), 3.47 (br, 2H, C*H*$_2$OH), 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 Functionalized chiral 1,3-Diphosphine Ligands 69a, 69b, and 69c. A solution of **68a** (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 **69a** was obtained as 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 **69b** (0.093 g, 86%) was achieved from **68b** (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 **69c** (0.10 g, 95%) was prepared from **68c** (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).

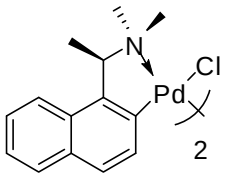
Crystal Structure Determinations of Complexes *tran*-*R*-62, 69b, and 69c. X-ray crystallographic data for all three complexes are given in the Appendices. Crystal data were collected on a Bruker X8 CCD diffractometer with Mo Kα radiation (graphite monochromator). SADABS absorption corrections were applied. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were introduced at calculated positions and refined with a riding model. The absolute configurations of all chiral complexes were determined unambiguously by using the Flack parameter. We thank Dr Li Yongxin for undertaking the X-ray analysis.

Chapter V

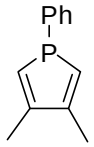
Controllable Synthesis of P-Chiral 1,2- and 1,3-Diphosphines *via* Asymmetric Diels-Alder Reactions Involving Functionalized Allylic Phosphine as Dienophile

5.1 Introduction

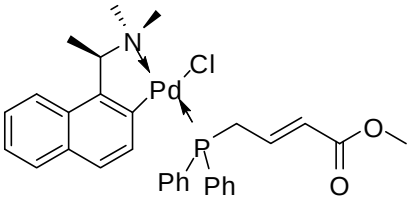
Optically pure P-chiral diphosphines are a class of powerful auxiliaries in homogeneous asymmetric catalysis,[5h,18,19] since the novel P-stereogenic diphosphine DIPAMP[7] developed by Knowles exhibits exceptional activity and high enantioselectivity in asymmetric hydrogenation of *a*-(acylamino)acrylic acids. The chiral features of P-chirogenic ligands lie that they can provide the primary chirality induction by direct coordination onto the catalytic metal atoms, and simultaneously, a secondary control is operated by the conformation of the chelate backbone or selected functionalities. It is noteworthy that, due to the aromaticity of the five-membered heterocycle ring, 3,4-dimethyl-1-phenylphosphole (DMPP), is a rather poor cyclic diene for the classic Diels-Alder reaction. For example, DMPP shows no reaction activity towards diphenylvinylphosphine upon heating at 60 ºC for one month.[101] However, the heterocyclic diene could be activated by means of coordination onto transition metals including tungsten,[102] molybdenum,[102a,103] nickel,[104] rhodium,[105] ruthenium,[106] palladium,[101,107] and platinum.[101] This feature provides an unique opportunity for controlling the stereochemistry of the Diels-Alder reaction by employing any appropriate chiral auxiliary onto the activating metal ion.



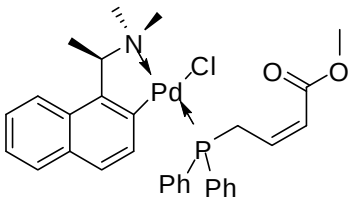
R-**26**



DMPP



trans-R-**35a**



cis-R-**35a**

Over the past decade, our group has successfully established that the organopalladium complex *R*-**26** containing (*R*)-(1-(dimethylamino)ethyl)-naphthalene as the chiral auxiliary is an efficient promoter for asymmetric Diels-Alder reactions of DMPP and selected dienophiles.[66] In this series of P-chirogenic phosphines synthesis, the *exo*- and *endo*-cycloaddition pathways can be effectively controlled by manipulating the number of coordination sites on the chiral palladium template for intra- and inter-molecular cycloaddition reactions. By this approach, various functionalities can be conveniently introduced into the P-chiral phosphanorbornene frameworks which subsequently form an efficient class of anti-cancer agents when they are coordinated to gold(I) ion.[108]

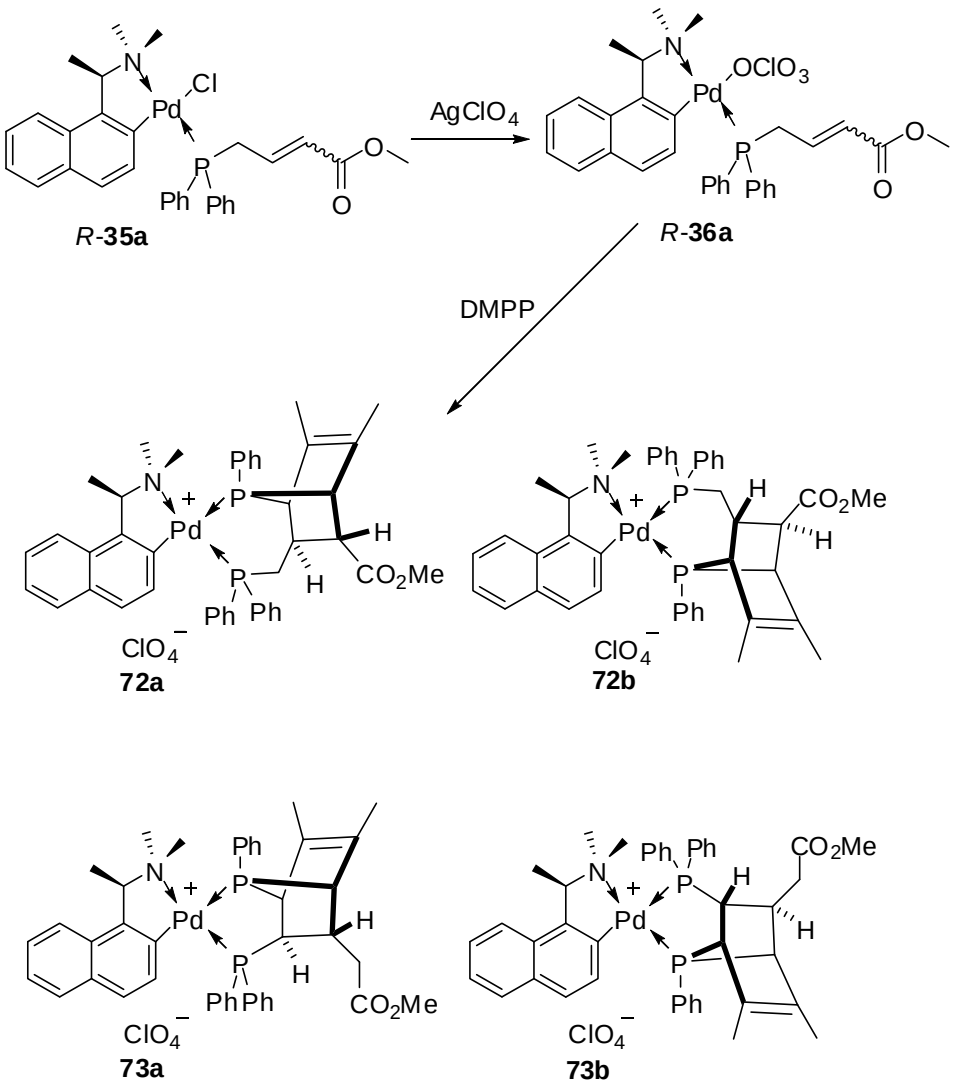
In particular, when the vinylic phosphine substrates including vinyldiphenylphosphine, propenyldiphenylphosphine, ester- and hydroxyl-functionalized vinyldiphenylphosphines, methylphenylvinylphosphine, and divinylphenylphosphines were used as dienophiles (Figure 1.3, Chapter I), a class of novel P-chiral 1,2-diphosphine ligands were generated with high yields and stereoselectivities.[66b-j] To our best knowledge, however, there are no literature reports on the analogous asymmetric cycloaddition reactions involving allylic phosphines, perhaps due to the difference in their chemical reactivity in these metal

template induced reaction scenarios. In Chapter II, we have reported a facile one-pot preparation of ester-substituted allylic phosphine substrate *R*-**35a**, and found it to be a good substrate towards Michael-type hydrophosphination reactions to synthesize ester-functionalized chiral 1,2-bis(diphenylphosphino)ethane with high regio- and stereoselectivities. Continuing our interests of the further exploration of the useful monophosphine substrate, in this chapter, we present the first asymmetric Diels-Alder reactions between the allylic moiety *R*-**35a** and DMPP. With appropriate controls, both of the 1,2- and 1,3-diphosphino exo-cycloadducts could be obtained efficiently with high chemo- and stereoselectivities.

5.2 Results and Discussion

5.2.1 Asymmetric Diels-Alder Reaction of Allylic Monophosphine Substrate *R*-35a and DMPP

The asymmetric synthetic methodology adopted is illustrated in Scheme 5.1. Upon abstraction of the chloro ligand in complex *trans*-*R*-**35a** with silver perchlorate,[66,67] the resultant perchlorato complex *trans*-*R*-**36a** was reacted with one equivalent of DMPP in dichloroethane. The reaction was monitored by ^{31}P NMR spectroscopy and was found to be complete in 30 days at room temperature without any additives (Table 5.1, entry 1). Prior to purification, the ^{31}P NMR spectrum of the crude product in $CDCl_3$ exhibited four pairs of doublets at δ – 2.3, 106.5 (J_{PP} = 57.0 Hz); 24.0, 95.3 (J_{PP} = 57.0 Hz); 27.1, 127.8 (J_{PP} = 39.0 Hz) and 52.7, 126.0 (J_{PP} = 40.1 Hz) with the intensity ratio of 19:13:3.5:1, respectively.



Scheme 5.1

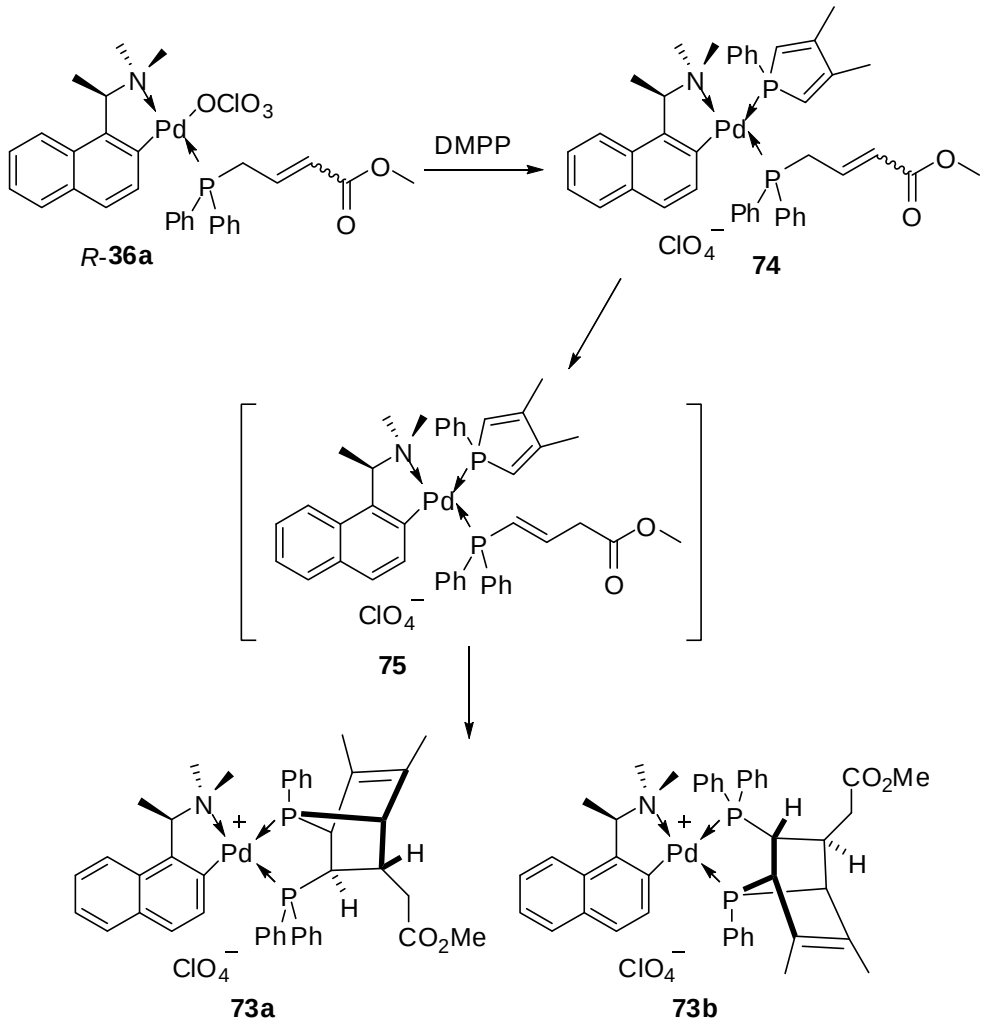
The two major pairs of phosphorus signals at δ – 2.3, 106.5 (J_{PP} = 57.0 Hz) and 24.0, 95.3 (J_{PP} = 57.0 Hz) indicated the formation of the 1,3-diphosphine regioisomers **72a** and **72b** as an equilibrium mixture (72%), which adopt the same absolute configurations at the newly generated stereogenic carbon and phosphorus centers with the nonequivalent phosphorus atoms coordinated in different regio-arrangements in the chelating six-membered ring. The minor pairs of doublets with phosphorus NMR signals at 27.1, 127.8, (J_{PP} = 39.0 Hz) and 52.7, 126.0 (J_{PP} = 40.1) have the similar coupling constants, which are apparently smaller than that of the major regioisomers **72a** and **72b**. The phosphorus NMR signals, however, indicated that a pair of 1,2-diphosphine complexes **73a** and **73b**

were generated from the cycloaddition reaction in 9% yield. Similarly, complexes **73a** and **73b** are regioisomers with the same absolute configuration at the new stereogenic chiral centers in the five-membered chelating ring. It should be noted that all the products were produced exclusively via the *exo*-cycloaddition reaction pathway.

Table 5.1. Asymmetric Diels-Alder Reaction of *R*-**35a** and DMPP

entry	*R*-**35a**	temperature	additive (equiv.)	time	% yield	
					72	**73**
1	*trans*-*R*-**35a**	r.t	none	30 d	72	9
2		40 ºC	none	9 d	59	20
3		60 ºC	none	4 d	33	42
4		r.t	$(CH_3CH_2)_3N$/0.2	3 d	0	84
5		40 ºC	$(CH_3CH_2)_3N$/0.2	20 h	0	80
6		r.t	CH_3COOH/0.1	4 d	0	48
7		40 ºC	CH_3COOH/0.1	2 d	0	40
8	*cis*-*R*-**35a**	r.t	none	12 d	0	83
9		40 ºC	$(CH_3CH_2)_3N$/0.2	20 h	0	79

Interestingly, when the asymmetric cycloaddition was repeated by using *cis*-*R*-**35a** as the dienophile (Table 5.1, entry 8), the reaction proceeded significantly faster than in the case of *trans*-*R*-**35a** and could be complete within 12 days. The ^{31}P NMR spectrum of the reaction products in $CDCl_3$ indicated only two pairs of doublets at δ 27.1, 127.8 (J_{PP} = 39.0 Hz) and 52.7, 126.0 (J_{PP} = 40.1 Hz) with the intensity ratio of 2.8:1. Thus, the asymmetric Diels-Alder reaction involving *cis*-*R*-**35a** chemoselectively afforded the five-membered chelating regioisomers 1,2-diphosphine **73a** and **73b** in 83% yield.



Scheme 5.2

We have previously reported that the organopalladium template promoted asymmetric Diels-Alder reactions between coordinated vinylic phosphines with DMPP could be completed within several hours under similar conditions. Consistent with the classic organic chemistry, the reactivity of the coordinated allylic dienophile in *R*-**35a** is significantly lower than was observed in its vinylic counterparts. It is important to note that, when the perchlorate complex *R*-**36a** was treated with one equivalent of DMPP, the diene and the dienophile would simultaneously coordinate onto the chiral palladium template to form the intermediate complex **74** for the subsequent intramolecular Diels-Alder reaction (Scheme 5.2). When *trans*-*R*-**35a** was employed, the intermediate **74**

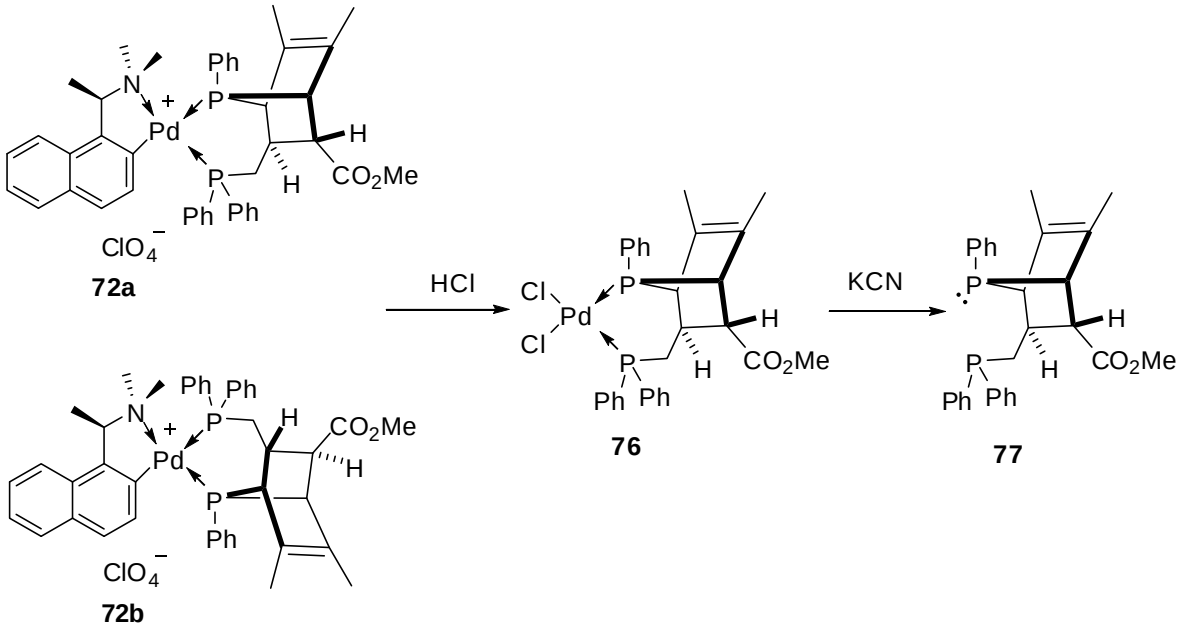
showed two pairs of doublets at δ 14.5, 29.6 (J_{PP} = 36.6 Hz) and 15.3, 33.3 (J_{PP} = 39.6 Hz) in ^{31}P NMR spectrum in CD_2Cl_2 due to its regioisomeric interconvertion.

From a mechanistic standpoint, the formation of the unexpected five-membered chelate 1,2-diphosphine products **73a** and **73b** from the allylic intermediate **74** necessarily involved the vinylic intermediate complex **75**, *via* a double bond migration mechanism.[109] As to the case of *cis*-*R*-**35a**, the cycloaddition reaction between *cis*-*R*-**35a** and DMPP is sterically unfavorable, thus even if the expected 1,3-diphosphine cycloadducts could be generated, the Diels-Alder reaction would be rather slow. On the other hand, the relatively slow (12 d), but exclusive, formation of the 1,2-diphosphine complexes **73a**,**b** is an indication of the slowness of the double bond migration process, as the reaction of vinylic intermediate with DMPP was known to be complete within several hours. Comparatively, the double bond migration process involving *trans*-*R*-**35a** to the vinylic intermediate occurs even at a much slower rate as, after 30 d, only *ca* 12.5% of the migrated 1,2-diphosphine template complexes **73a**,**b** were obtained from the cycloaddition reaction. Clearly, the allylic dienophile of the intermediate complex **74** is more thermodynamically stable compared to the vinylic analogue **75 (**the latter is however more reactive toward the Diels-Alder reaction). Thus the cycloaddition reaction of *trans*-*R*-**35a** and DMPP will proceed slowly to generate the 1,3-diphosphine complexes **72a**,**b** as the major products.

It is noteworthy that the double bond migration in the perchlorato allylic phosphine complex **74** to form the reactive vinylic intermediate **75** could be accelerated by temperature (Table 5.1, entries 2 and 3). When the asymmetric cycloaddition of *trans*-*R*-**35a** with DMPP was conducted at 60 ºC, the process was found to be finished within 4 day

to yield **73a**,**b** in 42% yield, with the decrease of 1,3-diphosphine products **72a**,**b** (33%). Importantly, in the presence of triethylamine, the reaction proceeded remarkably fast and could be complete within 20 h at 40 ºC to chemoselectively furnish the corresponding 1,2-diphosphine cycloadducts in 80% yield (Table 5.1, entries 5). Similar result was achieved when *cis*-*R*-**35a** was employed for the asymmetric Diels-Alder reaction in the presence of triethylamine (entry 9). The acetic acid can also accelerate the migration process to selectively afford complexes **73a**,**b**, however, with somewhat low yield (entries 6 and 7). This may be due to the decreased stability of the palladium template towards acid species.

5.2.2 Synthesis of the Dichloro Palladium Complex 76, Liberation, and Recoordination



Scheme 5.3

As illustrated in Scheme 5.3, treatment of the regioisomeric complexes **72a** and **72b** (from entry 1, Table 5.1) with concentrated hydrochloric acid removed the naphthylamine auxiliary chemoselectively. The resultant neutral dichloro complex **76** was thus obtained

as pale yellow prisms upon crystallization from chloroform-diethyl ether in 68% overall yield, $[\alpha]_D = -107.1°$ (*c* 0.8, CH_2Cl_2). The ^{31}P NMR spectrum of product **76** in CD_2Cl_2 exhibited a pair of doublets at δ 16.5, 99.2 (J_{PP} = 19.8 Hz). The chelating property and the absolute stereochemistry of the novel 1,3-diphosphine dichloro palladium complex **76** were established by X-ray crystallographic analysis (Figure 5.1). Selected bond lengths and angles are given in Table 5.2.

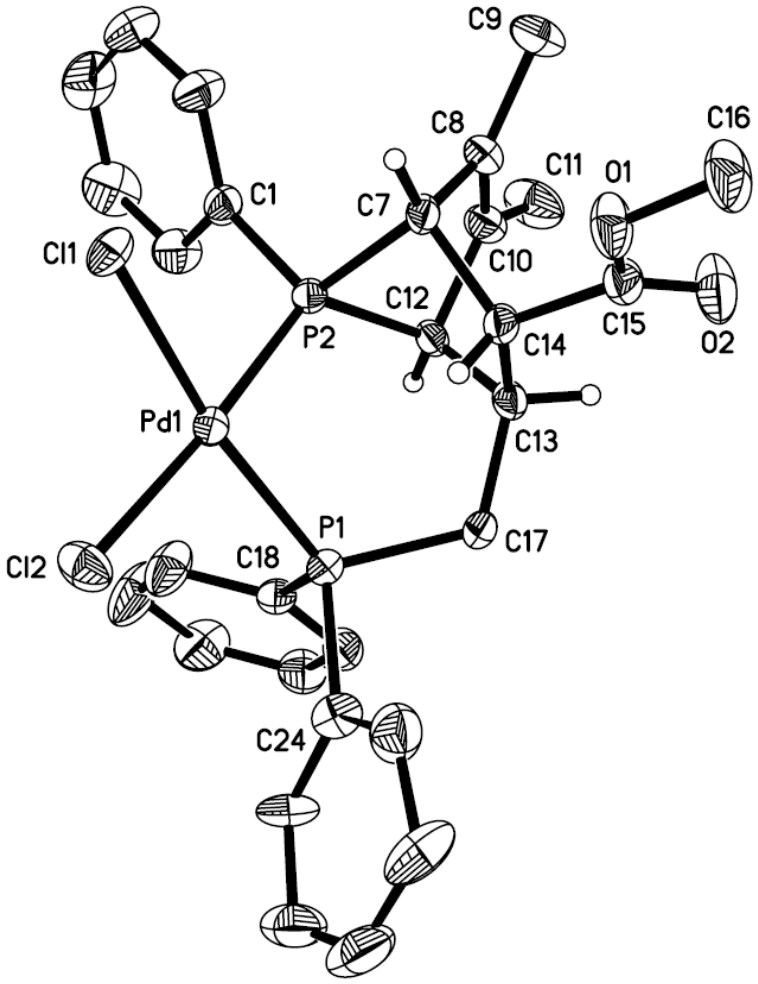


Figure 5.1. Molecular structure and absolute stereochemistry of complex **76**

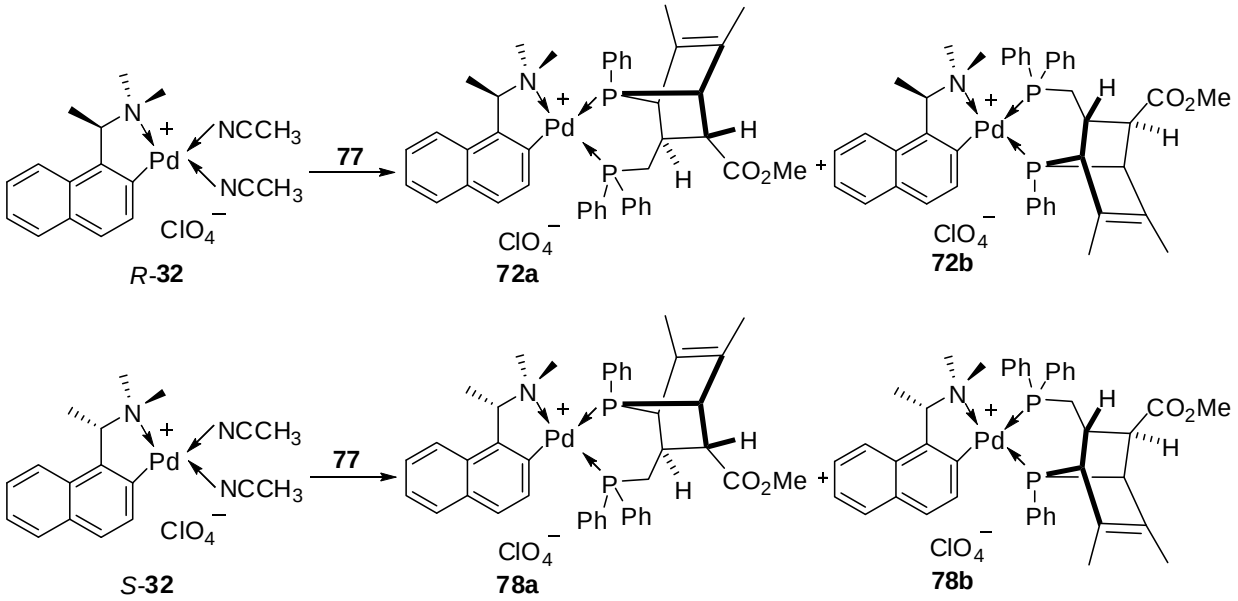
Table 5.2. Selected Bond Lengths (Å) and Angles (deg) of **76**

Pd1–P1	2.242(1)	Pd1–Cl1	2.358(1)
Pd1–P2	2.224(1)	Pd1–Cl2	2.346(1)
C17–P1	1.838(4)	C17–C13	1.544(5)
C13–C12	1.560(5)	C13–C14	1.571(5)
C7–C14	1.566(5)	C8–C10	1.338(6)
C12–P2	1.843(4)	C7–P2	1.832(4)
P2–Pd1–P1	89.4(1)	P1–Pd1–Cl2	93.5(1)
Cl2–Pd1–Cl1	93.7(1)	P1–Pd1–Cl1	171.7(1)
P2–Pd1–Cl1	83.6(1)	P2–Pd1–Cl2	175.4(1)
C7–P2–C12	82.3(2)	Pd1–P2–C12	121.8(1)
P2–C12–C13	99.9(2)	C12–C13–C17	114.0(3)
C13–C17–P1	117.0(2)	C17–P1–Pd1	114.5(1)

The X-ray structural analysis revealed that the 1,3-diphosphine cycloadduct was clearly formed *via* the exo-cycloaddition pathway. The geometry at palladium atom is square planar with slight tetrahedral distortion (5.6(1)°). The angles around palladium center are in ranges of 83.6(1) – 93.7(1) and 171.7(1) – 175.4(1)°. The P2–Pd1–P1 bite angle (89.4(1)°) is apparently larger than in the case of P-chiral 1,2-diphosphine metallacycles previously reported.[66b-j] The bridge head angle (C7–P2–C12) is 82.3(2)° which is a characteristic feature of the novel phosphanorbornene skeleton. The absolute configurations of the newly formed five chiral centers at P2, C7, C12, C13, C14 are *S*, *S*, *R*, *S*, *S*, respectively.

The subsequent liberation of the ester-functionalized novel 1,3-diphosphine from **76** can be achieved by the treatment of the dichloro palladium complex with aqueous cyanide (Scheme 5.3). The optically pure diphospohine ligand **77** was thus obtained as an air-sensitive white solid in high yield, $[\alpha]_D = -18.1°$ (*c* 0.9, CH_2Cl_2). The ^{31}P NMR

spectrum of the free ligand **77** in $CDCl_3$ exhibited two singlets at δ – 18.6 and 104.6. It is noteworthy that the apparent inversion of configuration that takes place at the bridgehead phosphorus stereogenic center during the liberation process is merely a consequence of the Cahn-Ingold-Prelog (CIP) rules.[110]

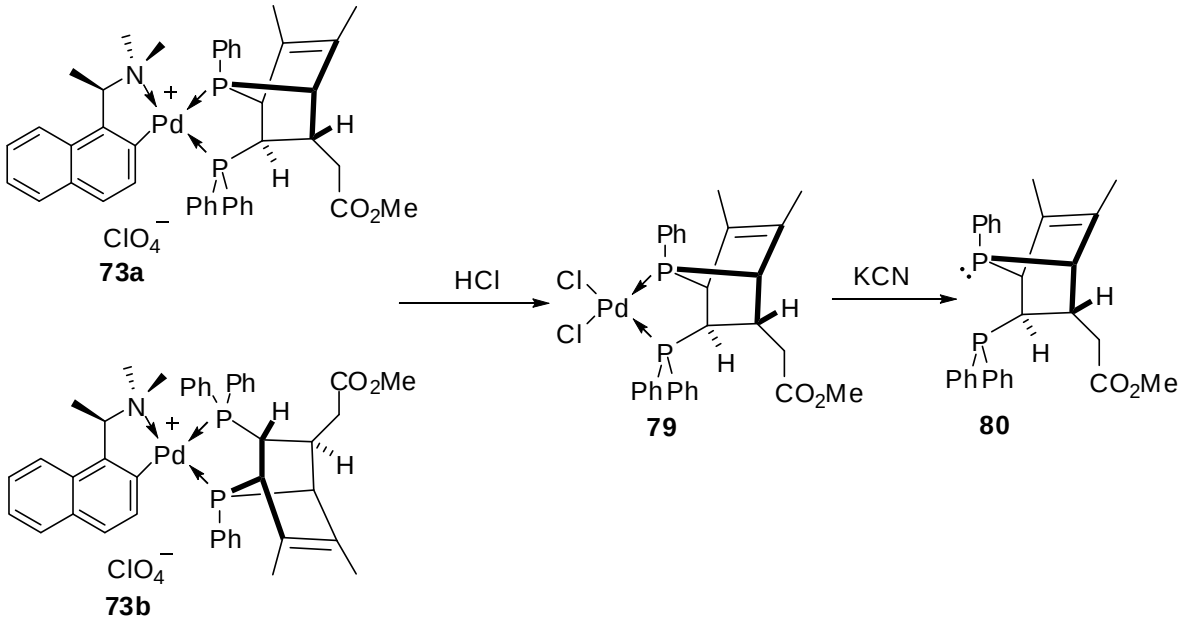


Scheme 5.4

Owing to high air sensitivity and configurational instability of the uncoordinated bridgehead phosphorus stereogenic center, the liberated phosphine ligand **77** was therefore re-complexed to palladium atom. The recoordiantion process is also a means of verifying the optical purity of the reseased ligand as shown in Scheme 5.4. The ^{31}P NMR spectrum of recomplexation products involving the bis(acetonitrile) complex *R*-**32** gave two pairs of doublets at δ – 2.3, 106.5 (J_{PP} = 57.0 Hz) and 24.0, 95.3 (J_{PP} = 57.0 Hz) which indicated the formation of the original regioisomers **72a** and **72b**. As a further test of the optical purity, the free ligand **77** was recoordinated to the equally accessible bis(acetonitrile) complex *S*-**32** which will generate a new pair of

regioisomers **78a** and **78b**. The ^{31}P NMR spectrum of the recomplexation products in $CDCl_3$ showed two different pairs of doublet signals at δ – 0.1, 106.8 (J_{PP} = 57.0 Hz) and 17.4, 94.7 (J_{PP} = 57.0 Hz) in the ratio of 1.2:1. More importantly, no doublet ^{31}P NMR peaks were detected at δ – 2.3, 106.5, 24.0, and 95.3, and thus reaffirming that the liberated ester-functionalized novel 1,3-diphosphine ligand **77** was enantiomerically pure.

5.2.3 Synthesis of the Dichloro Palladium Complex 79, Liberation, and Recoordination



Scheme 5.5

The chiral naphthylamine auxiliary of 1,2-diphosphine regioisomeric complexes **73a** and **73b** (from entries 4, or 8, Table 5.1) could be chemoselectively removed by the reaction with concentrated hydrochloric acid (Scheme 5.5). Upon crystallization from dichloromethane-diethyl ether, the neutral dichloro palladium complex **79** was easily

obtained as pale yellow prisms in 81% yield, $[\alpha]_D = -60.7°$ (*c* 0.6, CH_2Cl_2). The ^{31}P NMR spectrum of complex **79** in CD_2Cl_2 exhibited a pair of doublets at δ 34.2, 133.4 (J_{PP} = 5.2 Hz). The single-crystal X-ray diffraction analysis of the yellow prisms unambiguously confirmed its molecular structure and the absolute configurations as depicted in Figure 5.2. Selected bond and angle parameters are populated in Table 5.3.

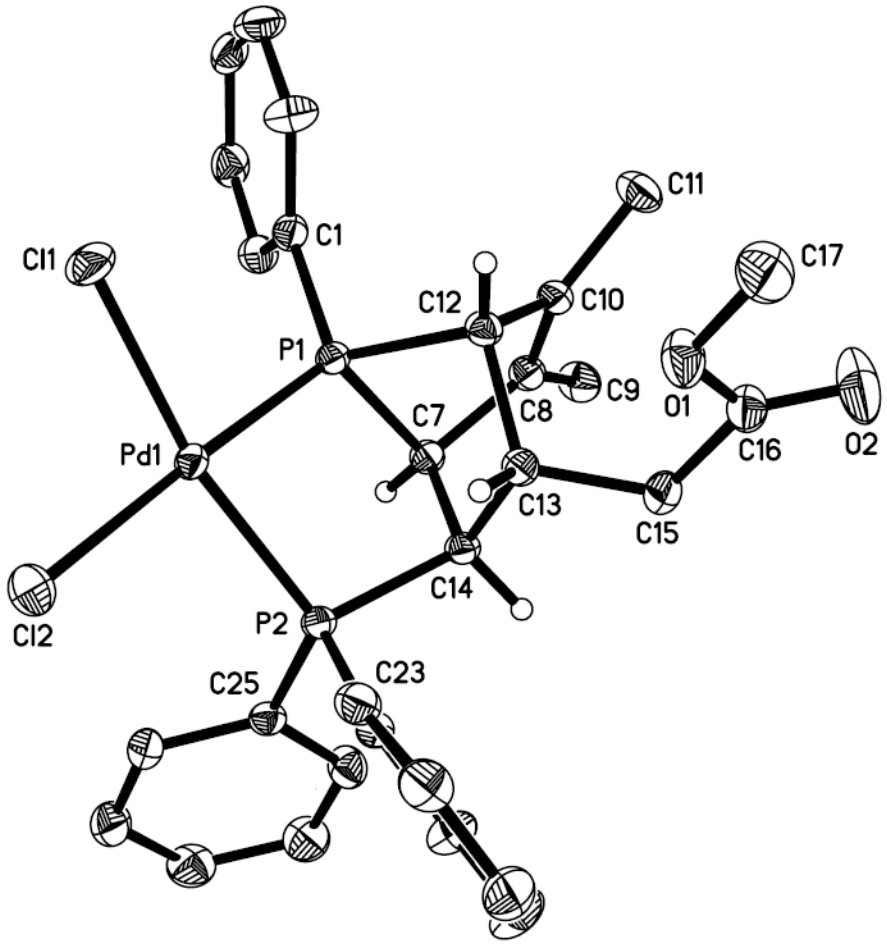


Figure 5.2. Molecular structure of dichloro palladium complex **79**

The sturctural analysis of **79** confirmed that 1,2-dphisphine complexes with phosphanorbornene frameworks were formed during the asymmetric Diels-Alder reaction *via* double bond migration. The coordination at Pd atom adopts expected distorted square planar (7.1(1)°) with angles around palladium center are in the ranges of 82.5(1) – 94.8(1)

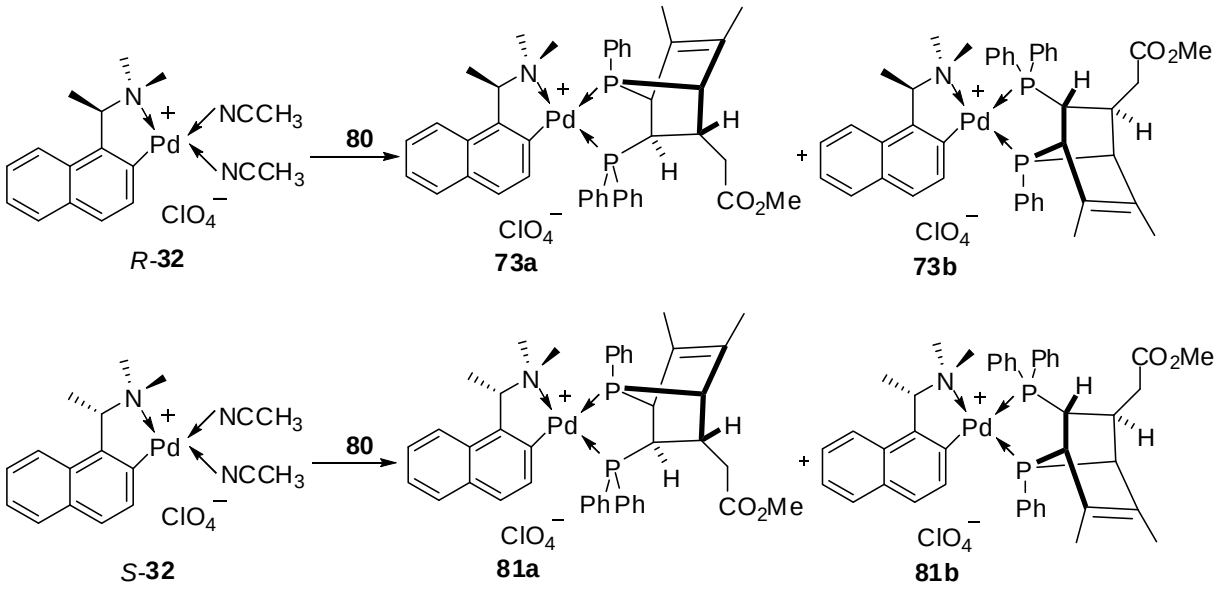
and 169.0(1) – 176.7(1)°. Both of bite angle (P1–Pd1–P2: 82.5(1)°) and the bridge head angle (C7–P1–C12: 81.7(2)°) are comparable with similar P-chiral diphosphine palladium complexes previously reported.[66b-j] The absolute configurations of five new stereogenic centers at P1, C7, C12, C13, C14 are *S*, *S*, *S*, *S*, *R*, respectively. Similar to its 1,3-diphosphine analogue **77**, the chiral 1,2-diphosphine **80** could be liberated from dichloro palladium complex **79** by treatment with aqueous potassium cyanide as a white solid in 91% yield, $[\alpha]_D$ = + 124.3° (*c* 1.1, CH_2Cl_2) (Scheme 5.5). The liberated ligand exhibited a pair of doublets at δ – 7.5, 104.7 (J_{PP} = 68.0 Hz) in the ^{31}P NMR spectrum in $CDCl_3$.

Table 5.3. Selected Bond Lengths (Å) and Angles (deg) of **79**

Pd1–P1	2.213(1)	Pd1–Cl1	2.368(1)
Pd1–P2	2.249(1)	Pd1–Cl2	2.354(1)
C7–P1	1.846(2)	C12–P1	1.853(2)
C7–C14	1.552(3)	C12–C13	1.574(3)
C13–C14	1.575(3)	C13–C15	1.527(3)
C14–P2	1.847(2)	C8–C10	1.343(3)
P2–Pd1–P1	82.5(1)	Cl2–Pd1–Cl1	93.9(1)
P1–Pd1–Cl1	88.9(1)	P2–Pd1–Cl2	94.8(1)
P1–Pd1–Cl2	176.7(1)	P2–Pd1–Cl1	169.0(1)
Pd1–P1–C7	113.0(1)	P1–C7–C14	95.4(1)
C7–C14–P2	107.9(1)	C14–P2–Pd1	104.7(1)
C7–P1–C12	81.7(1)	C13–C14–P2	108.1(1)

As illustrated in Scheme 5.6, the optical purity of the P-chiral 1,2-diphosphine **80** was confirmed by means of recoordination of the free ligand to the bis(acetonitrile) complex *R*-**32**. The ^{31}P NMR spectrum of the recomplexation products exhibited two pairs of doublets at δ 27.1, 127.8 (J_{PP} = 39.0 Hz) and 52.7, 126.0 (J_{PP} = 40.1 Hz), which were apparently due to the formation of the regioiosmers **73a** and **73b**. Further recoordination

of **80** to complex *S*-**32** furnished a pair of new regioisomers **81a** and **81b** with two distinct pairs of phosphorus signals at δ 31.5, 130.6 (J_{PP} = 39.4 Hz) and 50.9, 129.3 (J_{PP} = 39.6 Hz) in the ^{31}P NMR spectrum, and the functionalized P-chiral 1,2-diphosphine ligand **80** was therefore confirmed to be enantiomerically pure.



Scheme 5.6

5.3 Conclusion

In conclusion, the chiral organopalladium complex promoted asymmetric Diels-Alder reaction between 3,4-dimethyl-1-phenylphosphole (DMPP) and ester-functionalized allylic monophosphine precursors has been demonstrated. The reactions proceeded with high chemo- and stereo-selectivities under mild conditions. The cycloaddition between *trans*-dienophile *trans*-*R*-**35a** with DMPP afforded the functionalized P-chiral 1,3-diphosphine complexes as the major products. However, when the reaction was conducted in presence of triethylamine or by employment of the *cis*-dienophile *cis*-*R*-**35a**

as reaction precursor, the novel P-chiral 1,2-diphosphine products were chemoselectively generated *via* a double bond migration process.

5.4 Experimental Section

All air-sensitive manipulations were performed under a positive pressure of argon using a standard Schlenk line. Solvents were dried and degassed prior to use when necessary. NMR spectra were recorded at 25 ºC on a Bruker ACF 300 (^{1}H at 300 MHz, ^{13}C at 75 MHz and ^{31}P at 121.5 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 ºC 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*-**26**, [89a,b] *R*-**32**, and *S*-**32**[89c] were prepared according to literature methods. Allylic monophosphine substrates *trans*-*R*-**35a** and *cis*-*R*-**35a** were prepared by the methods described in Chapter II.

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

Diels-Alder Reaction of Allylic Monophosphine Substrate *trans*-*R*-35a and DMPP to Synthesize the Dichloro Palladium Complex 76. A solution of *trans*-*R*-**35** (0.60 g,

0.96 mmol) in dichloromethane (20 mL) was treated with silver perchlorate (0.43 g, 1.92 mmol) in water (5 mL). The mixture was stirred for 30 min at room temperature. After the removal of AgCl precipitate, the organic layer was washed with H_2O (3 × 15 mL), and dried over $MgSO_4$. The perchlorato intermediate was subsequently treated with DMPP (0.18 g, 0.96 mmol) in dichloroethane and the resultant mixture was stirred for 30 days at room temperature. Upon removal the solvent, the crude product was purified by chromatography on silica (CH_2Cl_2/Acetone/Hexanes = 2:1:2) to afford two pairs of regioisomers **72a,b** and **73a,b** as pale yellow solid in the ratio of 7:1 (0.68 g, 81%). ^{31}P NMR ($CDCl_3$, 121 MHz), **72a,b**: δ – 2.3, 106.5 (J_{PP} = 57.0 Hz); 24.0, 95.3 (J_{PP} = 57.0 Hz), **73a,b**: δ 27.1, 127.8 (J_{PP} = 39.0 Hz); 52.7, 126.0 (J_{PP} = 40.1 Hz).

The two pairs of regioisomers **72a,b** and **73a,b** were not isolated, and a solution of **72a,b** and **73a,b** in dichloromethane (8 mL) was treated with concentrated hydrochloric acid (5 mL) at room temperature for 4 h. The organic layer was separated, washed with water (3×20 mL), dried over $MgSO_4$. Chromatography on silica with CH_2Cl_2/Acetone/Hexanes = 2:1:3 can separate the dichloro palladium complex **76** (0.43 g, 68%) and **79** (0.06 g, 9%) efficiently. The 1,3-diphosphine palladium complex **76** could be crystallized from chloroform-diethyl ether as pale yellow prisms. $[\alpha]_D$ = – 107.1° (*c* 0.8, CH_2Cl_2). Mp: 268–270 ºC. Anal. Calcd for $C_{29}H_{30}Cl_2O_2P_2Pd$: C, 53.6; H, 4.6. Found: C, 53.3; H, 4.8. ^{31}P NMR (CD_2Cl_2, 121 MHz): δ 16.5 (d, J_{PP} = 19.8 Hz), 99.2 (d, J_{PP} = 19.8 Hz). ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 1.29 (s, 3H, C=C*Me*), 1.58 (s, 3H, C=C*Me*), 2.28 (br, s, 1H, PC*H*), 3.00 (m, 1H, J_{HH} = 8.0 Hz, PC*H*′H), 3.02 (d, 1H, J_{PH} = 6.7 Hz, PC*H*), 3.40 (m, 1H, PCH′*H*), 3.77 (s, 3H, CO_2*Me*), 4.02 (q, 1H, J_{PH} = J_{HH} =2.2 Hz, C*H*CO_2Me), 4.55 (br, 1H, PCH_2C*H*), 7.23–8.22 (m, 15H, Ar). ^{13}C NMR (CD_2Cl_2): δ 14.0 (d, J_{PC} = 1.7 Hz),

14.7 (d, J_{PC} = 3.0 Hz), 33.6 (dd, J_{PC} = 3.1 Hz, J_{PC} = 32.7 Hz), 38.3 (d, J_{PC} = 19.7 Hz), 46.6 (dd, J_{PC} = 17.6 Hz, J_{PC} = 30.5 Hz), 51.4 (d, J_{PC} = 27.1 Hz), 52.3 (d, J_{PC} = 37.9 Hz), 52.4 (s), 125.9 (d, J_{PC} = 53.4 Hz), 128.1 (d, J_{PC} = 5.1 Hz), 128.2 (d, J_{PC} = 4.1 Hz), 128.7 (dd, J_{PC} = 2.7 Hz, J_{PC} = 52.7 Hz), 129.9 (d, J_{PC} = 11.3 Hz), 130.2 (d, J_{PC} = 58.7 Hz), 130.8 (d, J_{PC} = 3.2 Hz), 131.3 (d, J_{PC} = 2.8 Hz), 132.3 (s), 132.4 (d, J_{PC} = 1.6 Hz), 132.6 (s), 133.2 (d, J_{PC} = 2.6 Hz), 135.1 (d, J_{PC} = 12.6 Hz), 136.4 (br s), 171.8 (d, J_{PC} = 21.2 Hz).

Diels-Alder Reaction of Allylic Monophosphine Substrate *cis*-*R*-35a and DMPP to Synthesize the Dichloro Palladium Complex 79. By following the similar procedure, *cis*-*R*-**35** (0.30 g, 0.48 mmol), after the removal of the chloro ligand by treatment with silver perchlorate (0.20 g, 0.88 mmol), was treated with one equivalent of DMPP (0.09 g, 0.48 mmol) in dichloroethane. The solution was stirred at room temperature for 12 days. Upon removal of solvent, the crude was purified by chromatography on silica (CH_2Cl_2/Acetone/Hexanes = 2:1:3) to afforded the regioisomers **73a** and **73b** as pale yellow solid (0.35 g, 83%). ^{31}P NMR ($CDCl_3$, 121 MHz): δ 27.1, 127.8 (J_{PP} = 39.0 Hz); 52.7, 126.0 (J_{PP} = 40.1 Hz).

An alternative method for the synthesis of regioisomers **73a** and **73b** is that treatment the perchlorato intermediates *trans*-*R*-**36a** and *cis*-*R*-**36a** with one equivalent of DMPP and 0.2 equivalent of triethylamine for the asymmetric Diels-Alder reactions.

The regioisomers **73a** and **73b** 0.35 g, 0.40 mmol) thus obtained were dissolved in dicloromethane (8 mL) and treated with concentrated hydrochloric acid (4 mL) at room temperature for 4 h. The mixture was washed with water (3×20 mL), dried over $MgSO_4$. Upon crystallized from dichloromethane-diethyl ether, the dichloro complex **79** was

isolated as pale yellow prisms (0.25 g, 81%). $[\alpha]_D = -60.7°$ (*c* 0.6, CH_2Cl_2). Mp: 281–283 ºC. Anal. Calcd for $C_{29}H_{30}Cl_2O_2P_2Pd$: C, 53.6; H, 4.6. Found: C, 53.4; H, 4.9. ^{31}P NMR (CD_2Cl_2, 121 MHz): δ 34.2 (d, J_{PP} = 5.2 Hz), 133.4 (d, J_{PP} = 5.2 Hz). ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 1.59 (s, 3H, C=C*Me*), 1.60 (s, 3H, C=C*Me*), 1.91 (dd, 1H, J_{HH} = 5.7 Hz, J_{HH} = 15.3 Hz, CHCH′*H*), 2.15 (dd, 1H, J_{HH} = 9.8 Hz, J_{HH} = 15.3 Hz, CHC*H*′H), 2.69 (dd, 1H, J_{PH} = 7.3 Hz, J_{PH} = 50.3 Hz, PPh_2C*H*), 3.17 (br m, 1H, PC*H*), 3.30 (br m, 1H, C*H*CH_2), 3.47 (s, 3H, CO_2*Me*), 3.60 (br, 1H, PC*H*), 7.40–8.30 (m, 15H, Ar). ^{13}C NMR (CD_2Cl_2): δ 14.8 (br s), 15.7 (d, J_{PC} = 3.3 Hz), 37.4 (t, $J_{PC} = J_{PC}$ = 34.6 Hz), 37.5 (t, $J_{PC} = J_{PC}$ = 8.0 Hz), 39.8 (dd, J_{PC} = 7.3 Hz, J_{PC} = 21.7 Hz), 51.4 (d, J_{PC} = 30.0 Hz), 51.8 (s), 55.4 (dd, J_{PC} = 16.0 Hz, J_{PC} = 34.3 Hz), 124.9 (d, J_{PC} = 48.6 Hz), 125.7 (d, J_{PC} = 47.2 Hz), 126.4 (d, J_{PC} = 53.2 Hz), 128.3 (d, J_{PC} = 11.2 Hz), 128.7 (d, J_{PC} = 11.4 Hz), 129.6 (d, J_{PC} = 10.8 Hz), 131.7 (d, J_{PC} = 2.8 Hz), 132.2 (d, J_{PC} = 2.7 Hz), 132.3 (dd, J_{PC} = 2.0 Hz, J_{PC} = 19.6 Hz), 132.5 (s), 132.6 (d, J_{PC} = 6.8 Hz), 134.0 (d, J_{PC} = 10.6 Hz), 134.8 (d, J_{PC} = 2.1 Hz), 134.9 (d, J_{PC} = 10.7 Hz), 170.4 (s).

Liberation of the Functionalized Novel Diphosphine Ligand 77 and 80. A solution of dichloro complex **76** (0.15 g, 0.23 mmol) in dichloromethane (6 mL) was stirred vigorously with aqueous KCN (0.8 g, 12.3 mmol) for 30 min. The organic layer was separated, and washed with water (3×10 mL). The ester-functionalized 1,3-diphosphine ligand **5** was obtained as white solid upon removal of solvent under reduced pressure (0.10 g, 92%). $[\alpha]_D = -18.1°$ (*c* 0.9, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 121 MHz): δ –18.6 (s), 104.6 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.40 (s, 3H, C=C*Me*), 1.42 (s, 3H, C=C*Me*), 2.41 (m, 1H, PCH_2C*H*), 2.60 (m, 1H, J_{HH} = 8.6 Hz, J_{HH} = 13.5 Hz, PC*H*′H), 2.74 (m, 1H, J_{HH} = 6.8 Hz, J_{HH} = 13.5 Hz, PCH′*H*), 2.78 (m, 1H, PC*H*), 3.12 (dt, 1H, J_{HH} = 2.2 Hz, J_{PH}

= 11.0 Hz, PC*H*), 3.34 (m, 1H, J_{HH} = 2.4 Hz, J_{HH} =5.0 Hz, C*H*CO_2Me), 3.60 ((s, 3H, CO_2*Me*), 7.12–7.54 (m, 15H, Ar).

By using the same procedure, the ester-functionalized P-chiral 1,2-diphosphine ligand **80** (0.07 g, 91%) was liberated from dichloro palladium complex **79** (0.11 g, 0.17 mmol) as a white solid. $[\alpha]_D$ = + 124.3° (*c* 1.1, CH_2Cl_2). ^{31}P NMR ($CDCl_3$, 121 MHz): δ – 7.5 (d, J_{PP} = 68.0 Hz), 104.7 (d, J_{PP} = 68.0 Hz). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.20 (m, 1H, J_{HH} = 3.4 Hz, CHCH′*H*), 1.46 (s, 3H, C=C*Me*), 1.56 (s, 3H, C=C*Me*), 1.66 (dd, 1H, J_{HH} = 12.3 Hz, J_{HH} = 14.9 Hz, CHC*H*′H), 2.03 (dt, 1H, J_{PH} = J_{HH} = 5.2 Hz, J_{PH} = 18.7 Hz, PPh_2C*H*), 2.58 (br d, 1H, J_{PH} = 10.9 Hz, PC*H*), 2.87 (br d, 1H, J_{PH} = 11.0 Hz, PC*H*), 3.12 (m, 1H, C*H*CH_2), 3.51 (s, 3H, CO_2*Me*), 7.05–7.60 (m, 15H, Ar).

Crystal Structure Determinations of Complexes 76 and 79. X-ray crystallographic data for the two complexes are given in the Appendices. Crystal data were collected at Nanyang Technological University using a Bruker X8 CCD diffractometer with Mo Kα radiation (graphite monochromator). SA-DABS absorption corrections were applied. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were introduced at calculated positions and refined as riding on their carrier atoms. The absolute configurations of all chiral complexes were determined unambiguously by using the Flack parameter. We thank Dr Li Yongxin for undertaking the X-ray analysis.

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Appendix

X-ray Crystallographic Data

The X-ray structural analyses were kindly performed by Dr. Yongxin Li at Division of Chemistry & Biological Chemistry, Nanyang Technological University. Complete tables of crystal data, data collection, solution and refinement, final positional parameters, bond distances and angles, thermal parameters of non-hydrogen atoms and calculated hydrogen parameters are available from Professor Leung Pak Hing upon request.

$R1 = \sum||F_o| - |F_c|| / \sum|F_o|$

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

Table A1. Crystal Data and Structure Refinement for complex **37a**.

Empirical formula	$C_{43}H_{44}ClNO_6P_2Pd$	
Formula weight	874.58	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.6190(2) Å	a= 90°.
	b = 21.2446(5) Å	b= 90°.
	c = 21.6007(5) Å	g = 90°.
Volume	3955.24(16) $Å^3$	
Z	4	
Density (calculated)	1.469 Mg/m^3	
Absorption coefficient	0.667 mm^{-1}	
F(000)	1800	
Crystal size	0.30 x 0.10 x 0.06 mm^3	
Theta range for data collection	2.99 to 31.14°.	
Index ranges	-11<=h<=12, -30<=k<=30, -31<=l<=31	
Reflections collected	70832	
Independent reflections	12569 [R(int) = 0.0468]	
Completeness to theta = 31.14°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9611 and 0.8250	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12569 / 18 / 491	
Goodness-of-fit on F^2	1.036	
Final R indices [I>2sigma(I)]	R1 = 0.0350, wR2 = 0.0751	
R indices (all data)	R1 = 0.0497, wR2 = 0.0830	
Absolute structure parameter	-0.037(16)	
Largest diff. peak and hole	1.035 and -0.754 $e.Å^{-3}$	

Table A2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **37a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	5794(1)	8322(1)	2118(1)	22(1)
C(1)	6188(3)	8772(1)	1291(1)	24(1)
C(2)	5719(4)	8606(1)	682(1)	29(1)
C(3)	6019(3)	8985(1)	187(1)	30(1)
C(4)	6849(3)	9549(1)	259(1)	28(1)
C(5)	7190(4)	9943(1)	-254(1)	41(1)
C(6)	8082(5)	10465(2)	-184(1)	52(1)
C(7)	8661(5)	10631(1)	402(1)	48(1)
C(8)	8322(4)	10275(1)	912(1)	35(1)
C(9)	7405(3)	9720(1)	858(1)	26(1)
C(10)	7022(3)	9324(1)	1369(1)	25(1)
C(11)	7434(3)	9518(1)	2020(1)	29(1)
C(12)	6157(4)	9937(1)	2275(1)	42(1)
C(13)	9097(4)	8615(1)	2230(1)	35(1)
C(14)	7766(4)	9106(1)	3066(1)	37(1)
C(15)	3996(3)	8302(1)	3556(1)	26(1)
C(16)	3312(4)	8836(1)	3297(1)	35(1)
C(17)	2266(4)	9193(2)	3646(2)	46(1)
C(18)	1891(4)	9016(2)	4236(2)	49(1)
C(19)	2566(4)	8490(2)	4498(2)	41(1)
C(20)	3619(4)	8130(1)	4163(1)	32(1)
C(21)	6947(3)	7610(1)	3537(1)	24(1)
C(22)	7317(3)	7887(1)	4102(1)	28(1)
C(23)	8695(4)	7746(1)	4397(1)	35(1)
C(24)	9697(4)	7313(2)	4137(2)	40(1)
C(25)	9326(4)	7026(1)	3583(2)	40(1)
C(26)	7966(3)	7180(1)	3278(1)	32(1)
C(27)	4226(3)	7108(1)	2887(1)	25(1)
C(28)	3558(3)	6734(1)	3433(1)	27(1)
C(29)	4759(3)	6425(1)	3836(1)	29(1)
C(30)	6782(5)	5668(2)	3843(2)	53(1)
C(31)	2988(3)	7306(1)	2415(1)	28(1)

C(32)	2460(3)	7956(1)	1256(1)	28(1)
C(33)	1478(4)	7554(2)	931(1)	41(1)
C(34)	323(4)	7803(2)	563(2)	47(1)
C(35)	124(4)	8444(2)	513(1)	46(1)
C(36)	1087(4)	8840(2)	831(2)	45(1)
C(37)	2254(4)	8600(2)	1203(2)	36(1)
C(38)	4910(4)	6979(1)	1385(1)	30(1)
C(39)	4193(5)	6389(1)	1366(1)	42(1)
C(40)	4996(5)	5881(2)	1125(2)	50(1)
C(41)	6473(5)	5947(2)	900(2)	51(1)
C(42)	7175(4)	6525(2)	917(2)	48(1)
C(43)	6419(4)	7041(1)	1162(1)	36(1)
Cl(1)	189(1)	856(1)	2852(1)	49(1)
N(1)	7632(3)	8932(1)	2401(1)	26(1)
O(1)	4904(3)	6505(1)	4379(1)	46(1)
O(2)	5638(3)	6029(1)	3508(1)	37(1)
O(3)	665(8)	1474(3)	2950(2)	202(4)
O(4)	-254(4)	594(2)	3411(1)	81(1)
O(5)	1299(7)	495(4)	2621(2)	237(5)
O(6)	-990(4)	888(1)	2408(1)	74(1)
P(1)	5291(1)	7841(1)	3073(1)	21(1)
P(2)	3995(1)	7654(1)	1753(1)	24(1)

Table A3. Crystal Data and Structure Refinement for complex **41a**.

Empirical formula	$C_{29}H_{28}Cl_2O_2P_2Pd \cdot CH_2Cl_2$	
Formula weight	732.68	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.6992(3) Å	a= 90°.
	b = 15.1810(5) Å	b= 103.7840(10)°.
	c = 10.9048(3) Å	g = 90°.
Volume	1559.42(8) $Å^3$	
Z	2	
Density (calculated)	1.560 Mg/m^3	
Absorption coefficient	1.067 mm^{-1}	
F(000)	740	
Crystal size	0.30 x 0.30 x 0.10 mm^3	
Theta range for data collection	1.92 to 29.99°.	
Index ranges	-7<=h<=13, -21<=k<=21, -15<=l<=15	
Reflections collected	27444	
Independent reflections	8974 [R(int) = 0.0223]	
Completeness to theta = 29.99°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9008 and 0.7402	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8974 / 1 / 352	
Goodness-of-fit on F^2	1.075	
Final R indices [I>2sigma(I)]	R1 = 0.0265, wR2 = 0.0693	
R indices (all data)	R1 = 0.0285, wR2 = 0.0750	
Absolute structure parameter	-0.014(16)	
Largest diff. peak and hole	0.966 and -0.912 $e.Å^{-3}$	

Table A4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **41a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	11152(1)	5484(1)	8765(1)	16(1)
C(1)	8044(3)	6479(2)	8537(2)	18(1)
C(2)	8973(3)	7175(2)	8940(2)	23(1)
C(3)	8455(4)	7996(2)	9162(3)	32(1)
C(4)	7007(4)	8121(2)	9001(3)	37(1)
C(5)	6077(3)	7429(2)	8613(3)	36(1)
C(6)	6582(3)	6602(2)	8376(2)	25(1)
C(7)	7912(3)	4521(2)	8650(3)	21(1)
C(8)	7107(4)	4584(2)	9547(3)	37(1)
C(9)	6525(5)	3831(2)	9931(4)	52(1)
C(10)	6756(4)	3015(2)	9472(4)	44(1)
C(11)	7599(4)	2942(2)	8619(3)	42(1)
C(12)	8165(4)	3693(2)	8202(3)	35(1)
C(13)	8299(2)	5399(2)	6384(2)	17(1)
C(14)	6748(2)	5608(2)	5793(2)	22(1)
C(15)	6355(2)	5453(2)	4380(2)	23(1)
C(16)	4428(3)	5434(4)	2588(3)	56(1)
C(17)	9341(3)	6026(2)	5950(2)	20(1)
C(18)	11677(3)	4811(2)	5891(2)	24(1)
C(19)	10988(4)	4633(2)	4656(3)	41(1)
C(20)	11524(5)	3999(3)	3978(4)	49(1)
C(21)	12740(5)	3542(2)	4528(4)	48(1)
C(22)	13419(5)	3724(3)	5744(4)	53(1)
C(23)	12885(4)	4347(2)	6441(3)	40(1)
C(24)	12170(3)	6655(2)	6409(2)	21(1)
C(25)	11987(3)	7467(2)	6937(3)	30(1)
C(26)	12620(4)	8210(2)	6587(3)	37(1)
C(27)	13467(4)	8144(2)	5732(3)	37(1)
C(28)	13693(4)	7337(2)	5230(3)	36(1)
C(29)	13036(3)	6583(2)	5567(3)	29(1)
C(30)	8429(8)	6704(4)	2107(4)	98(2)
Cl(1)	10829(1)	5345(1)	10834(1)	27(1)

Cl(2)	13640(1)	5575(1)	9368(1)	32(1)
Cl(3)	6875(2)	7167(1)	1963(2)	101(1)
Cl(4)	9807(2)	7265(2)	3350(2)	131(1)
O(1)	4976(2)	5570(2)	3938(2)	43(1)
O(2)	7159(2)	5244(1)	3751(2)	30(1)
P(1)	8788(1)	5449(1)	8137(1)	16(1)
P(2)	11154(1)	5725(1)	6749(1)	18(1)

Table A5. Crystal Data and Structure Refinement for complex **37b**.

Empirical formula	$C_{43}H_{44}ClNO_5P_2Pd$	
Formula weight	858.58	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 11.9138(3) Å	a= 90°.
	b = 15.8503(4) Å	b= 90°.
	c = 21.0527(5) Å	g = 90°.
Volume	3975.54(17) $Å^3$	
Z	4	
Density (calculated)	1.434 Mg/m^3	
Absorption coefficient	0.660 mm^{-1}	
F(000)	1768	
Crystal size	0.30 x 0.28 x 0.09 mm^3	
Theta range for data collection	2.75 to 34.41°.	
Index ranges	-18<=h<=18, -25<=k<=24, -33<=l<=33	
Reflections collected	57653	
Independent reflections	16635 [R(int) = 0.0371]	
Completeness to theta = 34.41°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9430 and 0.8265	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	16635 / 70 / 510	
Goodness-of-fit on F^2	1.015	
Final R indices [I>2sigma(I)]	R1 = 0.0302, wR2 = 0.0644	
R indices (all data)	R1 = 0.0388, wR2 = 0.0681	
Absolute structure parameter	-0.018(12)	
Largest diff. peak and hole	0.559 and -0.456 $e.Å^{-3}$	

Table A6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **37b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	7460(1)	4875(1)	10063(1)	15(1)
C(1)	8933(1)	5080(1)	9574(1)	18(1)
C(2)	9202(1)	4893(1)	8933(1)	22(1)
C(3)	10217(1)	5104(1)	8676(1)	24(1)
C(4)	11035(1)	5536(1)	9037(1)	20(1)
C(5)	12050(2)	5823(1)	8764(1)	24(1)
C(6)	12816(2)	6262(1)	9114(1)	27(1)
C(7)	12627(2)	6403(1)	9762(1)	25(1)
C(8)	11652(1)	6124(1)	10048(1)	22(1)
C(9)	10813(1)	5700(1)	9692(1)	18(1)
C(10)	9748(1)	5459(1)	9944(1)	17(1)
C(11)	9447(1)	5676(1)	10623(1)	21(1)
C(12)	9027(2)	6582(1)	10647(1)	28(1)
C(13)	8084(2)	5336(1)	11459(1)	26(1)
C(14)	9117(2)	4223(1)	10959(1)	27(1)
C(15)	5691(2)	3917(1)	11261(1)	20(1)
C(16)	6221(2)	3147(1)	11135(1)	29(1)
C(17)	6153(2)	2487(1)	11567(1)	37(1)
C(18)	5560(2)	2590(1)	12125(1)	40(1)
C(19)	5068(2)	3354(1)	12267(1)	36(1)
C(20)	5139(2)	4026(1)	11838(1)	28(1)
C(21)	5157(1)	5679(1)	10865(1)	18(1)
C(22)	4135(2)	5769(1)	11187(1)	21(1)
C(23)	3722(2)	6560(1)	11340(1)	25(1)
C(24)	4319(2)	7279(1)	11171(1)	27(1)
C(25)	5326(2)	7200(1)	10854(1)	28(1)
C(26)	5739(2)	6410(1)	10701(1)	23(1)
C(27)	4773(1)	4224(1)	10029(1)	18(1)
C(28)	3550(1)	4183(1)	10246(1)	22(1)
C(29)	2861(2)	3502(1)	9931(1)	28(1)
C(30)	1625(2)	3552(1)	10057(1)	32(1)
C(31)	4919(1)	4729(1)	9413(1)	20(1)

C(32)	6593(2)	3818(1)	8711(1)	21(1)
C(33)	5910(2)	3687(1)	8178(1)	33(1)
C(34)	6042(2)	2960(2)	7819(1)	46(1)
C(35)	6847(3)	2376(1)	7984(1)	52(1)
C(36)	7526(3)	2507(1)	8507(1)	48(1)
C(37)	7400(2)	3228(1)	8875(1)	30(1)
C(38)	6492(1)	5663(1)	8653(1)	18(1)
C(39)	6952(2)	5612(1)	8046(1)	24(1)
C(40)	7038(2)	6330(1)	7669(1)	28(1)
C(41)	6658(2)	7097(1)	7888(1)	26(1)
C(42)	6204(2)	7154(1)	8491(1)	26(1)
C(43)	6131(2)	6446(1)	8875(1)	23(1)
Cl(1)	6604(1)	9838(1)	7831(1)	29(1)
Cl(1A)	6622(5)	9732(3)	7641(3)	35(1)
N(1)	8574(1)	5056(1)	10845(1)	19(1)
O(1)	3286(1)	2944(1)	9621(1)	55(1)
O(2)	7629(2)	9580(3)	7533(1)	63(1)
O(3)	6852(2)	10299(2)	8400(1)	52(1)
O(2A)	7094(12)	9180(6)	7208(6)	80(4)
O(3A)	7469(9)	10273(5)	7884(6)	79(5)
O(4)	5997(2)	9122(1)	8031(1)	55(1)
O(5)	5912(2)	10323(1)	7395(1)	56(1)
P(1)	5761(1)	4680(1)	10616(1)	16(1)
P(2)	6402(1)	4763(1)	9183(1)	16(1)

Table A7. Crystal Data and Structure Refinement for complex **52a**.

Empirical formula	$C_{30}H_{30}Cl_2O_2P_2Pd$	
Formula weight	661.78	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 8.6202(3) Å	a= 96.552(2)°.
	b = 10.7327(4) Å	b= 99.248(2)°.
	c = 16.3388(6) Å	g = 106.096(2)°.
Volume	1413.29(9) $Å^3$	
Z	2	
Density (calculated)	1.555 Mg/m^3	
Absorption coefficient	0.986 mm^{-1}	
F(000)	672	
Crystal size	0.26 x 0.24 x 0.04 mm^3	
Theta range for data collection	2.00 to 30.60°.	
Index ranges	-12<=h<=12, -15<=k<=15, -22<=l<=23	
Reflections collected	31857	
Independent reflections	14208 [R(int) = 0.0352]	
Completeness to theta = 30.60°	97.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9616 and 0.7837	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	14208 / 3 / 667	
Goodness-of-fit on F^2	1.148	
Final R indices [I>2sigma(I)]	R1 = 0.0467, wR2 = 0.1372	
R indices (all data)	R1 = 0.0590, wR2 = 0.1534	
Absolute structure parameter	0.00(4)	
Largest diff. peak and hole	1.391 and -1.474 $e.Å^{-3}$	

Table A8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **52a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	4071(1)	8534(1)	5543(1)	22(1)
Pd(2)	5525(1)	6648(1)	-28(1)	23(1)
C(1)	6313(10)	6577(9)	6216(5)	22(2)
C(2)	5528(13)	6526(11)	6891(7)	39(2)
C(3)	6322(16)	6251(13)	7648(6)	47(3)
C(4)	7805(15)	6064(13)	7714(7)	45(3)
C(5)	8594(18)	6138(16)	7059(8)	54(3)
C(6)	7845(13)	6401(12)	6290(7)	39(2)
C(7)	3868(12)	5400(10)	4691(6)	29(2)
C(8)	3882(15)	4237(11)	4981(7)	38(2)
C(9)	2799(19)	3037(13)	4490(9)	54(3)
C(10)	1830(20)	3044(17)	3768(10)	70(4)
C(11)	1880(19)	4223(17)	3486(9)	73(4)
C(12)	2875(15)	5410(13)	3940(7)	49(3)
C(13)	6708(13)	7477(9)	4535(6)	31(2)
C(14)	7179(8)	6353(7)	4073(4)	31(1)
C(15)	7318(13)	6523(10)	3202(6)	33(2)
C(16)	8449(17)	5872(11)	2044(7)	63(3)
C(17)	8178(13)	8684(11)	4875(7)	35(2)
C(18)	8291(11)	9491(10)	5722(7)	32(2)
C(19)	6698(12)	11266(10)	5082(7)	32(2)
C(20)	5759(16)	10960(14)	4291(8)	47(3)
C(21)	6080(20)	11827(16)	3706(8)	59(4)
C(22)	7340(20)	12959(14)	3925(9)	58(3)
C(23)	8274(19)	13303(12)	4707(10)	58(4)
C(24)	7989(15)	12474(12)	5308(8)	45(3)
C(25)	6935(12)	10931(9)	6869(6)	30(2)
C(26)	6587(15)	12099(11)	7084(8)	41(3)
C(27)	6817(16)	12644(12)	7915(8)	45(3)
C(28)	7434(16)	12052(13)	8553(7)	45(3)
C(29)	7757(19)	10927(15)	8351(8)	52(3)
C(30)	7518(16)	10326(12)	7504(7)	47(3)

C(31)	3359(11)	8584(9)	-738(6)	25(2)
C(32)	4181(15)	8623(13)	-1410(6)	45(3)
C(33)	3511(15)	8885(14)	-2179(7)	47(3)
C(34)	1992(14)	9106(12)	-2292(7)	40(2)
C(35)	1174(17)	9068(17)	-1627(9)	58(3)
C(36)	1871(16)	8841(14)	-857(7)	50(3)
C(37)	5812(12)	9810(10)	775(6)	28(2)
C(38)	5708(16)	11000(11)	541(7)	40(2)
C(39)	6785(18)	12172(12)	957(9)	52(3)
C(40)	7944(19)	12181(13)	1653(9)	63(4)
C(41)	8124(17)	11039(15)	1903(9)	64(3)
C(42)	7028(15)	9864(12)	1455(7)	46(2)
C(43)	2789(12)	7941(10)	887(6)	32(2)
C(44)	3500(11)	8246(9)	1828(4)	49(2)
C(45)	2225(17)	8602(15)	2342(8)	57(4)
C(46)	1308(13)	8744(15)	3573(6)	74(4)
C(47)	1452(15)	6557(12)	655(7)	40(3)
C(48)	1272(12)	5742(10)	-217(7)	32(2)
C(49)	2798(14)	3885(10)	393(7)	36(2)
C(50)	3820(17)	4226(12)	1192(7)	45(3)
C(51)	3632(18)	3353(16)	1754(10)	60(4)
C(52)	2440(20)	2154(16)	1503(10)	66(4)
C(53)	1400(20)	1809(13)	712(10)	70(4)
C(54)	1567(18)	2701(12)	158(9)	52(3)
C(55)	2582(13)	4305(10)	-1378(6)	31(2)
C(56)	2949(15)	3151(12)	-1579(7)	41(2)
C(57)	2658(17)	2557(13)	-2425(8)	46(3)
C(58)	2165(16)	3210(14)	-3043(8)	50(3)
C(59)	1789(17)	4377(14)	-2861(8)	44(3)
C(60)	2013(15)	4905(12)	-2029(6)	39(2)
Cl(1)	1536(3)	6925(3)	5509(2)	37(1)
Cl(2)	2887(4)	10260(3)	5742(2)	35(1)
Cl(3)	6660(4)	4896(3)	-251(2)	35(1)
Cl(4)	8083(4)	8177(3)	-26(2)	47(1)
O(1)	6699(10)	7210(8)	2791(4)	69(2)
O(2)	8177(8)	5816(5)	2863(3)	46(1)
O(3)	1294(15)	9207(9)	2071(6)	104(3)
O(4)	2347(9)	8245(8)	3053(4)	67(2)
P(1)	5285(3)	6963(3)	5266(2)	21(1)
P(2)	6532(3)	10090(3)	5792(2)	26(1)

P(3)	3032(3)	5133(3)	-291(2)	27(1)
P(4)	4372(3)	8244(3)	237(2)	23(1)

Table A9. Crystal Data and Structure Refinement for complex **52b**.

Empirical formula	$C_{30}H_{30}Cl_2OP_2Pd$	
Formula weight	645.78	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 8.5973(10) Å	a= 97.704(5)°.
	b = 10.8849(12) Å	b= 99.824(5)°.
	c = 16.260(2) Å	g = 107.217(5)°.
Volume	1404.3(3) $Å^3$	
Z	2	
Density (calculated)	1.527 Mg/m^3	
Absorption coefficient	0.987 mm^{-1}	
F(000)	656	
Crystal size	0.20 x 0.18 x 0.08 mm^3	
Theta range for data collection	1.30 to 27.00°.	
Index ranges	-10<=h<=10, -13<=k<=12, -20<=l<=20	
Reflections collected	35186	
Independent reflections	9991 [R(int) = 0.0408]	
Completeness to theta = 27.00°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9252 and 0.8270	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9991 / 31 / 651	
Goodness-of-fit on F^2	1.101	
Final R indices [I>2sigma(I)]	R1 = 0.0302, wR2 = 0.0791	
R indices (all data)	R1 = 0.0363, wR2 = 0.0916	
Absolute structure parameter	0.06(3)	
Largest diff. peak and hole	0.717 and -0.966 $e.Å^{-3}$	

Table A10. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **52b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	655(1)	3891(1)	9086(1)	24(1)
Pd(2)	2293(1)	2333(1)	3613(1)	25(1)
C(1)	3049(9)	2112(8)	9792(5)	32(2)
C(2)	2318(11)	2125(9)	10496(5)	41(2)
C(3)	3084(12)	1812(11)	11221(6)	57(3)
C(4)	4566(11)	1570(10)	11298(6)	51(2)
C(5)	5316(11)	1640(11)	10616(6)	56(2)
C(6)	4546(11)	1872(11)	9857(6)	49(2)
C(7)	579(9)	746(8)	8272(5)	29(2)
C(8)	620(11)	-305(8)	8636(5)	41(2)
C(9)	-475(15)	-1577(10)	8164(8)	63(3)
C(10)	-1491(13)	-1716(10)	7418(7)	58(3)
C(11)	-1470(12)	-615(10)	7078(6)	60(3)
C(12)	-471(11)	637(9)	7511(6)	46(2)
C(13)	3313(9)	2925(7)	8078(5)	33(2)
C(14)	3831(7)	1892(5)	7590(3)	38(1)
C(15)	4119(11)	2166(9)	6729(5)	45(2)
C(16)	4971(11)	1354(7)	6272(5)	72(2)
C(17)	4841(11)	4180(9)	8457(7)	52(3)
C(18)	4968(9)	4993(10)	9293(6)	46(2)
C(19)	3267(11)	6696(8)	8654(6)	37(2)
C(20)	2192(13)	6359(10)	7862(6)	48(2)
C(21)	2454(17)	7178(11)	7288(7)	67(3)
C(22)	3786(16)	8291(12)	7491(7)	64(3)
C(23)	4834(15)	8655(10)	8270(7)	69(3)
C(24)	4608(10)	7854(8)	8860(6)	44(2)
C(25)	3578(10)	6409(8)	10457(5)	35(2)
C(26)	3254(12)	7572(8)	10666(6)	44(2)
C(27)	3500(13)	8178(10)	11503(7)	52(2)
C(28)	4108(13)	7641(12)	12149(7)	63(3)

C(29)	4469(14)	6495(13)	11971(7)	67(3)
C(30)	4196(13)	5857(10)	11109(6)	52(3)
C(31)	17(9)	4110(8)	2831(4)	28(2)
C(32)	789(11)	4146(10)	2174(5)	42(2)
C(33)	97(11)	4358(10)	1384(5)	44(2)
C(34)	-1366(12)	4585(11)	1288(6)	53(2)
C(35)	-2135(14)	4631(15)	1945(7)	79(4)
C(36)	-1520(12)	4351(11)	2718(6)	50(2)
C(37)	2446(10)	5466(8)	4362(5)	30(2)
C(38)	2332(12)	6631(9)	4088(6)	45(2)
C(39)	3400(14)	7827(9)	4470(6)	50(2)
C(40)	4619(14)	7947(11)	5165(7)	65(3)
C(41)	4760(11)	6869(10)	5484(6)	53(2)
C(42)	3689(11)	5644(9)	5091(5)	38(2)
C(43)	-587(9)	3485(8)	4479(5)	31(2)
C(44)	241(7)	3872(6)	5442(3)	47(1)
C(45)	-997(13)	3715(9)	6029(6)	52(2)
C(46)	-2214(11)	4441(7)	5952(6)	75(2)
C(47)	-1823(11)	2068(10)	4263(6)	43(2)
C(48)	-1981(10)	1252(8)	3372(5)	35(2)
C(49)	-388(11)	-466(9)	3986(5)	36(2)
C(50)	665(12)	-157(10)	4776(6)	49(2)
C(51)	412(14)	-1032(13)	5338(7)	68(3)
C(52)	-837(16)	-2211(12)	5091(8)	73(3)
C(53)	-1895(15)	-2540(10)	4309(7)	62(3)
C(54)	-1686(13)	-1662(9)	3742(6)	59(3)
C(55)	-613(10)	-131(8)	2212(5)	33(2)
C(56)	-277(12)	-1280(10)	2014(6)	46(2)
C(57)	-610(13)	-1897(11)	1165(7)	58(3)
C(58)	-1173(11)	-1332(10)	523(6)	48(2)
C(59)	-1441(13)	-166(10)	727(6)	48(2)
C(60)	-1187(12)	420(9)	1550(6)	44(2)
Cl(1)	-1876(3)	2225(2)	9004(2)	45(1)
Cl(2)	-576(3)	5560(2)	9279(2)	40(1)
Cl(3)	4891(3)	3924(2)	3684(2)	46(1)
Cl(4)	3484(3)	656(2)	3400(2)	42(1)
O(1)	3709(10)	3023(8)	6415(4)	76(2)
O(2)	-946(11)	3034(10)	6543(5)	108(3)
P(1)	1943(3)	2408(2)	8832(1)	25(1)
P(2)	3112(3)	5516(2)	9362(2)	31(1)

P(3)	1033(3)	3860(2)	3839(1)	25(1)
P(4)	-184(3)	736(2)	3306(2)	28(1)

Table A11. Crystal Data and Structure Refinement for complex **56**.

Empirical formula	$C_{35}H_{32}I_2OP_2Pd \cdot CH_2Cl_2$	
Formula weight	975.67	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 9.8011(3) Å	a= 90°.
	b = 13.3212(4) Å	b= 90°.
	c = 29.5362(9) Å	g = 90°.
Volume	3856.3(2) $Å^3$	
Z	4	
Density (calculated)	1.681 Mg/m^3	
Absorption coefficient	2.330 mm^{-1}	
F(000)	1896	
Crystal size	0.40 x 0.10 x 0.08 mm^3	
Theta range for data collection	1.68 to 31.20°.	
Index ranges	-14<=h<=14, -19<=k<=19, -42<=l<=42	
Reflections collected	77120	
Independent reflections	12424 [R(int) = 0.0325]	
Completeness to theta = 31.20°	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8355 and 0.4559	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12424 / 423 / 470	
Goodness-of-fit on F^2	1.176	
Final R indices [I>2sigma(I)]	R1 = 0.0316, wR2 = 0.0849	
R indices (all data)	R1 = 0.0385, wR2 = 0.0964	
Absolute structure parameter	-0.018(16)	
Largest diff. peak and hole	1.220 and -1.349 $e.Å^{-3}$	

Table A12. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **56**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	-445(1)	1498(1)	1625(1)	21(1)
C(1)	2612(4)	1391(3)	2178(1)	26(1)
C(2)	1951(5)	2078(3)	2459(1)	34(1)
C(3)	2676(6)	2542(4)	2812(2)	44(1)
C(4)	4009(6)	2349(4)	2877(2)	44(1)
C(5)	4697(5)	1667(4)	2602(2)	43(1)
C(6)	3995(4)	1188(4)	2255(2)	36(1)
C(7)	1703(4)	-503(3)	1768(1)	27(1)
C(8)	2063(5)	-977(3)	2169(2)	34(1)
C(9)	2005(5)	-2022(4)	2200(2)	42(1)
C(10)	1602(6)	-2580(4)	1838(2)	46(1)
C(11)	1239(7)	-2109(4)	1436(2)	51(1)
C(12)	1279(5)	-1081(3)	1400(2)	37(1)
C(13)	2757(4)	1037(3)	1193(1)	28(1)
C(14)	4021(4)	361(4)	1161(1)	32(1)
C(15)	4328(17)	44(12)	684(4)	47(3)
C(16)	5692(18)	-466(17)	599(6)	46(3)
C(17)	6610(20)	-660(20)	942(6)	40(3)
C(18)	7806(18)	-1174(15)	860(6)	54(3)
C(19)	8080(17)	-1514(16)	429(6)	72(4)
C(20)	7185(17)	-1322(16)	80(5)	72(4)
C(21)	6043(17)	-745(17)	164(5)	67(4)
O(1)	3482(18)	158(19)	379(6)	59(5)
C(15A)	4440(20)	82(15)	688(4)	40(4)
C(16A)	5650(30)	-610(30)	631(9)	50(4)
C(17A)	6610(40)	-770(30)	964(9)	50(5)
C(18A)	7720(30)	-1390(20)	893(8)	58(5)
C(19A)	7870(20)	-1848(19)	480(8)	67(4)
C(20A)	6910(20)	-1720(20)	144(7)	72(4)
C(21A)	5810(20)	-1103(18)	223(8)	58(4)
O(1A)	3800(20)	380(20)	358(8)	50(4)
C(22)	3165(4)	2128(3)	1118(2)	33(1)

C(23)	2133(4)	2953(3)	1220(1)	30(1)
C(24)	274(4)	2198(3)	543(1)	26(1)
C(25)	-469(5)	1354(3)	433(2)	37(1)
C(26)	-427(7)	979(4)	-9(2)	54(1)
C(27)	346(7)	1463(6)	-338(2)	61(2)
C(28)	1070(6)	2312(5)	-225(2)	50(1)
C(29)	1044(5)	2676(4)	211(2)	40(1)
C(30)	-444(4)	3872(3)	1144(1)	25(1)
C(31)	-1105(5)	4294(3)	772(1)	33(1)
C(32)	-1667(6)	5240(4)	808(2)	45(1)
C(33)	-1578(6)	5775(4)	1208(2)	48(1)
C(34)	-917(5)	5360(4)	1576(2)	43(1)
C(35)	-349(5)	4416(3)	1544(1)	34(1)
C(36)	5348(9)	4788(6)	1599(3)	75(2)
Cl(1)	4484(3)	4165(2)	2019(1)	92(1)
Cl(2)	4299(4)	5478(3)	1238(1)	134(1)
I(1)	-1396(1)	245(1)	2244(1)	33(1)
I(2)	-2927(1)	2177(1)	1483(1)	31(1)
P(1)	1695(1)	853(1)	1707(1)	23(1)
P(2)	343(1)	2641(1)	1121(1)	22(1)

Table A13. Crystal Data and Structure Refinement for complex **57**.

Empirical formula	$C_{41}H_{42}ClNO_5P_2Pd \cdot 2CH_2Cl_2$	
Formula weight	1002.40	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.6961(4) Å	a= 90°.
	b = 10.1443(4) Å	b= 91.964(2)°.
	c = 22.3638(9) Å	g = 90°.
Volume	2198.41(15) $Å^3$	
Z	2	
Density (calculated)	1.514 Mg/m^3	
Absorption coefficient	0.844 mm^{-1}	
F(000)	1024	
Crystal size	0.30 x 0.20 x 0.15 mm^3	
Theta range for data collection	0.91 to 25.99°.	
Index ranges	-11<=h<=11, -12<=k<=12, -27<=l<=27	
Reflections collected	74786	
Independent reflections	8641 [R(int) = 0.0539]	
Completeness to theta = 25.99°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8839 and 0.7859	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8641 / 1 / 519	
Goodness-of-fit on F^2	1.155	
Final R indices [I>2sigma(I)]	R1 = 0.0465, wR2 = 0.0931	
R indices (all data)	R1 = 0.0499, wR2 = 0.0959	
Absolute structure parameter	0.07(3)	
Largest diff. peak and hole	0.773 and -1.503 $e.Å^{-3}$	

Table A14. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **57**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	8252(1)	5916(1)	2546(1)	23(1)
Cl(1)	2005(3)	7904(2)	4531(1)	91(1)
Cl(2)	1793(2)	8191(2)	3242(1)	57(1)
Cl(3)	9257(4)	1817(3)	519(1)	115(1)
Cl(4)	7939(3)	108(2)	-347(1)	105(1)
Cl(5)	4248(2)	2290(1)	1943(1)	38(1)
P(1)	7662(1)	7181(1)	1680(1)	27(1)
P(2)	6485(1)	6857(1)	3018(1)	24(1)
O(1)	6221(5)	9290(4)	1300(2)	48(1)
O(2)	4811(7)	3425(6)	2225(3)	85(2)
O(3)	5213(6)	1762(5)	1538(2)	75(2)
O(4)	3037(6)	2644(6)	1602(3)	83(2)
O(5)	3894(6)	1305(5)	2366(2)	79(2)
N(1)	9881(4)	4798(4)	2148(2)	26(1)
C(1)	9018(5)	4948(5)	3289(2)	24(1)
C(2)	8947(6)	5298(5)	3903(2)	30(1)
C(3)	9650(5)	4608(5)	4348(2)	30(1)
C(4)	10473(5)	3507(5)	4212(2)	29(1)
C(5)	11171(6)	2762(6)	4666(2)	36(1)
C(6)	11970(6)	1708(6)	4527(2)	37(1)
C(7)	12131(5)	1350(5)	3930(2)	36(1)
C(8)	11453(5)	2053(5)	3481(2)	32(1)
C(9)	10605(5)	3142(5)	3600(2)	25(1)
C(10)	9852(5)	3883(5)	3153(2)	27(1)
C(11)	9923(5)	3515(5)	2497(2)	28(1)
C(12)	8716(7)	2601(6)	2324(2)	41(1)
C(13)	11226(5)	5482(6)	2246(2)	38(1)
C(14)	9745(6)	4481(6)	1501(2)	37(1)
C(15)	9192(6)	8121(5)	1495(2)	32(1)
C(16)	9688(6)	8998(6)	1923(2)	37(1)
C(17)	10908(7)	9703(6)	1838(3)	45(2)
C(18)	11634(6)	9525(6)	1325(3)	43(1)

C(19)	11147(6)	8636(6)	901(3)	45(2)
C(20)	9936(6)	7940(6)	979(2)	38(1)
C(21)	6966(6)	6353(5)	1015(2)	30(1)
C(22)	6934(6)	6937(6)	448(2)	39(1)
C(23)	6362(7)	6262(6)	-40(2)	48(2)
C(24)	5828(7)	5012(7)	30(3)	53(2)
C(25)	5813(7)	4460(7)	592(3)	54(2)
C(26)	6393(6)	5113(6)	1082(3)	37(1)
C(27)	6381(6)	8484(5)	1813(2)	31(1)
C(28)	4976(6)	7942(6)	1984(2)	37(1)
C(29)	4973(6)	6942(5)	2506(2)	33(1)
C(30)	5738(4)	5993(7)	3649(2)	26(1)
C(31)	5236(6)	4712(6)	3561(3)	40(1)
C(32)	4572(7)	4075(6)	4021(3)	51(2)
C(33)	4432(6)	4692(7)	4568(3)	49(2)
C(34)	4962(5)	5945(9)	4661(2)	40(1)
C(35)	5580(5)	6589(6)	4200(2)	34(1)
C(36)	6819(5)	8496(5)	3312(2)	24(1)
C(37)	5791(6)	9446(6)	3332(3)	41(1)
C(38)	6081(6)	10694(6)	3561(3)	48(2)
C(39)	7388(6)	10974(8)	3798(2)	48(1)
C(40)	8406(6)	10051(6)	3781(3)	42(1)
C(41)	8142(6)	8819(5)	3534(2)	32(1)
C(42)	2048(7)	7119(7)	3834(3)	54(2)
C(43)	7775(12)	983(12)	306(4)	127(5)

Table A15. Crystal Data and Structure Refinement for complex *trans-R*-**62**.

Empirical formula	$C_{31}H_{32}ClN_2PPd$	
Formula weight	605.41	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 11.7521(3) Å	a= 90°.
	b = 13.4810(3) Å	b= 90°.
	c = 18.0259(4) Å	g = 90°.
Volume	2855.84(12) $Å^3$	
Z	4	
Density (calculated)	1.408 Mg/m^3	
Absorption coefficient	0.821 mm^{-1}	
F(000)	1240	
Crystal size	0.40 x 0.40 x 0.22 mm^3	
Theta range for data collection	1.89 to 34.14°.	
Index ranges	-17<=h<=18, -21<=k<=20, -24<=l<=28	
Reflections collected	50106	
Independent reflections	11615 [R(int) = 0.0376]	
Completeness to theta = 34.14°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8400 and 0.7347	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	11615 / 0 / 328	
Goodness-of-fit on F^2	1.113	
Final R indices [I>2sigma(I)]	R1 = 0.0323, wR2 = 0.0728	
R indices (all data)	R1 = 0.0445, wR2 = 0.0953	
Absolute structure parameter	-0.005(18)	
Largest diff. peak and hole	0.781 and -0.939 $e.Å^{-3}$	

Table A16. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex *trans*-*R*-**62**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	2088(1)	6155(1)	8966(1)	18(1)
C(1)	2962(2)	5046(2)	9434(1)	20(1)
C(2)	2623(2)	4043(2)	9510(2)	27(1)
C(3)	3296(2)	3367(2)	9865(2)	29(1)
C(4)	4352(2)	3645(2)	10181(1)	23(1)
C(5)	5074(2)	2953(2)	10533(2)	29(1)
C(6)	6072(2)	3252(2)	10857(1)	28(1)
C(7)	6381(2)	4257(2)	10850(1)	26(1)
C(8)	5711(2)	4944(2)	10509(1)	23(1)
C(9)	4671(2)	4663(2)	10156(1)	19(1)
C(10)	3954(2)	5346(2)	9777(1)	19(1)
C(11)	4268(2)	6428(2)	9704(1)	23(1)
C(12)	4954(2)	6574(2)	8991(2)	34(1)
C(13)	3362(3)	8042(2)	9454(2)	47(1)
C(14)	2686(3)	7015(3)	10446(2)	45(1)
C(15)	1032(2)	5958(2)	7218(1)	24(1)
C(16)	2037(2)	6590(2)	6966(1)	28(1)
C(17)	2986(3)	6019(2)	6628(2)	40(1)
C(18)	4059(3)	6166(3)	6746(2)	53(1)
C(19)	4947(3)	5596(3)	6397(3)	66(1)
C(20)	-218(2)	4889(2)	8317(1)	22(1)
C(21)	-525(2)	4885(2)	9064(2)	31(1)
C(22)	-1632(3)	4640(2)	9274(2)	42(1)
C(23)	-2423(3)	4407(2)	8736(2)	49(1)
C(24)	-2133(3)	4412(2)	8000(2)	42(1)
C(25)	-1033(2)	4649(2)	7785(2)	32(1)
C(26)	1943(2)	4111(2)	7782(1)	21(1)
C(27)	1350(2)	3291(2)	7517(1)	25(1)
C(28)	1919(3)	2434(2)	7311(1)	31(1)
C(29)	3094(3)	2394(2)	7357(2)	37(1)
C(30)	3696(3)	3218(2)	7593(2)	40(1)
C(31)	3134(2)	4068(2)	7809(2)	31(1)

Cl(1)	938(1)	7546(1)	8634(1)	32(1)
N(1)	3161(2)	6994(2)	9687(1)	26(1)
N(2)	5671(3)	5148(3)	6172(3)	96(2)
P(1)	1231(1)	5247(1)	8082(1)	18(1)

Table A17. Crystal Data and Structure Refinement for complex **68b**.

Empirical formula	$C_{29}H_{28}Cl_2OP_2Pd$	
Formula weight	631.75	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.8650(5) Å	a= 90°.
	b = 15.4156(8) Å	b= 100.227(3)°.
	c = 16.3015(8) Å	g = 90°.
Volume	2687.0(2) $Å^3$	
Z	4	
Density (calculated)	1.562 Mg/m^3	
Absorption coefficient	1.030 mm^{-1}	
F(000)	1280	
Crystal size	0.24 x 0.12 x 0.02 mm^3	
Theta range for data collection	1.83 to 26.41°.	
Index ranges	-13<=h<=13, -19<=k<=19, -20<=l<=20	
Reflections collected	28574	
Independent reflections	10405 [R(int) = 0.0617]	
Completeness to theta = 26.41°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9797 and 0.7901	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10405 / 1216 / 899	
Goodness-of-fit on F^2	1.096	
Final R indices [I>2sigma(I)]	R1 = 0.0583, wR2 = 0.1471	
R indices (all data)	R1 = 0.0861, wR2 = 0.1690	
Absolute structure parameter	0.06(5)	
Largest diff. peak and hole	1.199 and -1.471 $e.Å^{-3}$	

Table A18. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **68b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(53)	3072(18)	6910(12)	9589(10)	31(3)
C(54)	3728(19)	7374(14)	9071(11)	32(4)
C(55)	4670(20)	7968(13)	9403(12)	31(4)
C(56)	4904(19)	8115(13)	10244(12)	31(4)
C(57)	4190(30)	7733(18)	10761(12)	30(4)
C(58)	3290(20)	7114(16)	10416(10)	24(3)
C(53A)	2940(30)	6973(17)	9631(16)	29(5)
C(54A)	3430(30)	7560(20)	9120(20)	36(5)
C(55A)	4300(40)	8190(20)	9470(20)	35(5)
C(56A)	4660(40)	8240(20)	10320(20)	34(5)
C(57A)	4230(50)	7650(30)	10840(20)	29(5)
C(58A)	3330(50)	7040(30)	10470(15)	23(5)
C(47)	2440(12)	5331(8)	8525(7)	43(3)
C(48)	3707(14)	5301(10)	8494(10)	45(4)
C(49)	4091(16)	4667(9)	7990(9)	40(4)
C(50)	3219(16)	4085(10)	7590(9)	43(4)
C(51)	1958(17)	4126(11)	7608(10)	53(4)
C(52)	1566(17)	4778(10)	8081(10)	51(4)
C(47A)	2700(20)	5352(15)	8650(13)	43(5)
C(48A)	3980(20)	5440(20)	8700(30)	42(5)
C(49A)	4590(40)	4810(30)	8320(30)	43(6)
C(50A)	3870(50)	4170(30)	7860(30)	44(6)
C(51A)	2600(50)	4060(20)	7830(30)	48(5)
C(52A)	2000(40)	4680(20)	8230(30)	51(6)
C(18)	2380(20)	7723(15)	6346(16)	42(7)
C(19)	3220(30)	8213(14)	6922(13)	44(6)
C(20)	2820(30)	8865(14)	7420(12)	40(6)
C(21)	1550(30)	9022(17)	7341(16)	42(6)
C(22)	680(30)	8554(15)	6768(19)	46(6)
C(23)	1100(20)	7910(15)	6277(19)	40(6)
C(18A)	2750(20)	7838(15)	6515(15)	25(5)
C(19A)	3680(20)	8381(15)	6959(13)	28(5)

C(20A)	3400(20)	9073(15)	7450(13)	31(5)
C(21A)	2180(20)	9196(14)	7570(13)	28(5)
C(22A)	1220(20)	8676(12)	7121(15)	27(5)
C(23A)	1490(20)	7998(13)	6613(15)	24(5)
P(2)	3055(17)	6954(12)	5732(8)	19(3)
C(24)	1810(20)	6186(18)	5323(14)	26(6)
C(25)	1100(20)	5801(16)	5854(15)	31(6)
C(26)	230(20)	5181(16)	5536(16)	40(6)
C(27)	80(20)	4924(19)	4713(15)	37(6)
C(28)	780(20)	5310(19)	4174(15)	37(6)
C(29)	1630(30)	5952(19)	4486(14)	33(6)
P(2A)	3287(19)	7059(13)	5837(9)	32(4)
C(24A)	2000(20)	6287(18)	5548(15)	32(6)
C(25A)	1440(20)	5881(16)	6144(16)	33(5)
C(26A)	490(20)	5296(15)	5882(17)	37(6)
C(27A)	110(20)	5107(16)	5044(18)	34(6)
C(28A)	690(20)	5494(19)	4440(16)	42(6)
C(29A)	1590(30)	6120(20)	4707(17)	43(7)
C(16)	4850(70)	5600(40)	6100(60)	36(3)
C(17)	4150(40)	6330(30)	6460(30)	34(5)
C(16A)	4810(80)	5640(40)	6080(60)	36(3)
C(17A)	4370(40)	6400(30)	6550(30)	32(5)
Pd(1)	3907(1)	7605(1)	4720(1)	23(1)
Pd(2)	1074(1)	5509(1)	10209(1)	25(1)
C(1)	6762(9)	6847(7)	4330(5)	25(2)
C(2)	7269(10)	6354(8)	3777(6)	34(3)
C(3)	8353(10)	6576(10)	3545(7)	45(3)
C(4)	8953(10)	7323(9)	3850(7)	44(3)
C(5)	8443(9)	7837(10)	4418(7)	47(3)
C(6)	7305(9)	7597(9)	4642(6)	38(2)
C(7)	4518(8)	5742(7)	3912(5)	24(2)
C(8)	4030(9)	6055(8)	3127(6)	30(2)
C(9)	3338(9)	5510(9)	2541(6)	36(2)
C(10)	3187(10)	4660(9)	2722(6)	49(3)
C(11)	3703(12)	4324(8)	3495(7)	51(3)
C(12)	4380(10)	4867(8)	4110(7)	40(3)
C(13)	7624(9)	5565(8)	6789(6)	45(3)
C(14)	7023(8)	6249(6)	6189(5)	34(2)
C(15)	5902(8)	5854(6)	5618(5)	27(2)
C(30)	264(8)	7338(7)	10908(6)	25(2)

C(31)	836(9)	7091(8)	11717(6)	33(3)
C(32)	1393(9)	7631(10)	12284(6)	46(3)
C(33)	1490(12)	8516(9)	12076(9)	57(4)
C(34)	932(13)	8787(9)	11316(9)	62(4)
C(35)	327(10)	8229(7)	10723(8)	41(3)
C(36)	-1797(9)	6185(7)	10537(6)	27(2)
C(37)	-2224(9)	6600(9)	11186(7)	39(3)
C(38)	-3352(10)	6341(10)	11421(8)	50(3)
C(39)	-4056(10)	5677(12)	10984(9)	66(5)
C(40)	-3647(12)	5276(10)	10363(10)	71(5)
C(41)	-2523(10)	5495(9)	10122(7)	45(3)
O(2)	-3584(15)	7544(10)	7787(7)	43(4)
C(42)	-3197(14)	7160(11)	8421(9)	35(4)
C(43)	-2233(14)	7524(15)	9162(11)	38(5)
O(2A)	-2940(20)	7454(17)	7770(11)	64(6)
C(42A)	-2989(15)	7849(13)	8411(8)	33(4)
C(43A)	-1967(19)	7738(15)	9212(11)	32(5)
C(44)	-1024(10)	6985(8)	9156(6)	40(3)
C(45)	-31(9)	7396(9)	8693(6)	46(3)
C(46)	769(9)	6721(9)	8378(6)	42(3)
Cl(1)	4572(2)	8299(2)	3597(2)	32(1)
Cl(2)	2271(3)	8613(2)	4610(2)	40(1)
Cl(3)	2894(3)	4651(2)	10390(2)	40(1)
Cl(4)	309(2)	4750(2)	11260(2)	32(1)
O(1)	8161(9)	5677(8)	7474(5)	81(3)
P(1)	5299(2)	6515(2)	4677(1)	21(1)
P(3)	-408(2)	6521(2)	10182(2)	24(1)
P(4)	1860(3)	6158(2)	9176(2)	30(1)

Table A19. Crystal Data and Structure Refinement for complex **68c**.

Empirical formula	$C_{29}H_{30}Cl_2OP_2Pd \cdot 2CH_2Cl_2$	
Formula weight	803.62	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.1714(3) Å	a= 90°.
	b = 15.7179(6) Å	b= 97.793(2)°.
	c = 12.2030(4) Å	g = 90°.
Volume	1742.88(10) $Å^3$	
Z	2	
Density (calculated)	1.531 Mg/m^3	
Absorption coefficient	1.108 mm^{-1}	
F(000)	812	
Crystal size	0.38 x 0.38 x 0.22 mm^3	
Theta range for data collection	1.68 to 33.18°.	
Index ranges	-14<=h<=14, -24<=k<=24, -18<=l<=18	
Reflections collected	47270	
Independent reflections	13254 [R(int) = 0.0478]	
Completeness to theta = 33.18°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7926 and 0.6781	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	13254 / 1 / 371	
Goodness-of-fit on F^2	1.087	
Final R indices [I>2sigma(I)]	R1 = 0.0362, wR2 = 0.0819	
R indices (all data)	R1 = 0.0488, wR2 = 0.1012	
Absolute structure parameter	-0.003(18)	
Largest diff. peak and hole	0.874 and -0.839 $e.Å^{-3}$	

Table A20. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **68c**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	9556(1)	350(1)	1175(1)	19(1)
C(1)	8619(3)	305(2)	-1593(2)	24(1)
C(2)	9708(4)	753(2)	-2048(3)	30(1)
C(3)	10218(4)	470(3)	-2993(3)	39(1)
C(4)	9654(4)	-268(2)	-3505(3)	38(1)
C(5)	8596(4)	-728(2)	-3056(3)	37(1)
C(6)	8089(4)	-453(2)	-2096(3)	31(1)
C(7)	6164(3)	316(2)	-240(2)	25(1)
C(8)	5131(4)	157(2)	-1167(3)	36(1)
C(9)	3693(4)	-63(3)	-1041(4)	48(1)
C(10)	3287(4)	-122(3)	-1(4)	51(1)
C(11)	4281(4)	35(3)	914(4)	46(1)
C(12)	5725(4)	247(2)	813(3)	34(1)
C(13)	7731(3)	1853(2)	-626(2)	21(1)
C(14)	6549(3)	2010(2)	-1624(3)	27(1)
C(15)	6675(4)	2880(2)	-2128(3)	32(1)
C(16)	7423(3)	2338(2)	414(2)	25(1)
C(17)	8844(3)	2561(2)	1180(2)	24(1)
C(18)	11641(3)	1986(2)	2220(3)	25(1)
C(19)	12334(4)	2242(2)	1325(3)	32(1)
C(20)	13799(4)	2492(3)	1492(3)	41(1)
C(21)	14579(4)	2479(3)	2536(4)	43(1)
C(22)	13909(4)	2221(2)	3434(3)	41(1)
C(23)	12437(4)	1967(2)	3283(3)	31(1)
C(24)	8955(3)	1673(2)	3239(2)	24(1)
C(25)	8273(3)	946(2)	3601(3)	29(1)
C(26)	7617(4)	994(3)	4575(3)	39(1)
C(27)	7658(4)	1732(3)	5165(3)	41(1)
C(28)	8337(4)	2453(3)	4816(3)	38(1)
C(29)	8978(4)	2418(2)	3849(3)	31(1)
C(30)	1494(5)	3019(3)	7083(3)	51(1)
C(31)	6205(6)	5149(4)	4992(5)	77(2)

Cl(1)	9352(1)	-1043(1)	492(1)	31(1)
Cl(2)	11171(1)	-114(1)	2745(1)	31(1)
Cl(3)	2428(2)	3433(1)	6035(1)	86(1)
Cl(4)	2600(1)	2349(1)	7983(1)	52(1)
Cl(5)	5397(2)	4223(1)	4454(2)	106(1)
Cl(6)	6096(1)	5973(1)	4032(1)	60(1)
O(1)	8042(3)	2919(2)	-2556(2)	35(1)
P(1)	8002(1)	712(1)	-338(1)	19(1)
P(2)	9731(1)	1652(1)	1939(1)	20(1)

Table A21. Crystal Data and Structure Refinement for complex **76**.

Empirical formula	$C_{29}H_{30}Cl_2O_2P_2Pd \cdot C_2H_5OH$	
Formula weight	695.84	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 9.9121(3) Å	a= 90°.
	b = 15.1031(4) Å	b= 90°.
	c = 22.4411(6) Å	g = 90°.
Volume	3359.51(16) $Å^3$	
Z	4	
Density (calculated)	1.376 Mg/m^3	
Absorption coefficient	0.835 mm^{-1}	
F(000)	1424	
Crystal size	0.30 x 0.10 x 0.08 mm^3	
Theta range for data collection	2.62 to 30.58°.	
Index ranges	-13<=h<=14, -21<=k<=21, -32<=l<=32	
Reflections collected	75867	
Independent reflections	10294 [R(int) = 0.0396]	
Completeness to theta = 30.58°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9362 and 0.7878	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10294 / 349 / 440	
Goodness-of-fit on F^2	1.173	
Final R indices [I>2sigma(I)]	R1 = 0.0418, wR2 = 0.1163	
R indices (all data)	R1 = 0.0484, wR2 = 0.1237	
Absolute structure parameter	-0.02(3)	
Largest diff. peak and hole	1.458 and -0.810 $e.Å^{-3}$	

Table A22. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **76**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	-610(1)	2205(1)	1974(1)	18(1)
C(1)	-1058(4)	977(3)	716(2)	24(1)
C(2)	-951(5)	1359(3)	148(2)	33(1)
C(3)	-1897(6)	1162(4)	-282(2)	40(1)
C(4)	-2978(6)	607(4)	-154(2)	46(1)
C(5)	-3106(6)	249(4)	411(2)	44(1)
C(6)	-2148(5)	431(3)	845(2)	33(1)
C(7)	1803(4)	1503(2)	1022(2)	21(1)
C(8)	2148(4)	678(3)	669(2)	27(1)
C(9)	3023(6)	739(4)	122(2)	44(1)
C(10)	1661(4)	-49(3)	936(2)	27(1)
C(11)	1790(7)	-989(3)	757(3)	45(1)
C(12)	955(4)	196(2)	1522(2)	21(1)
C(13)	2072(4)	570(2)	1941(2)	22(1)
C(14)	2568(4)	1446(3)	1630(2)	22(1)
C(15)	4079(4)	1482(3)	1526(2)	28(1)
C(16)	5840(5)	2451(4)	1227(3)	44(1)
C(17)	1599(4)	706(3)	2590(2)	24(1)
C(18)	-1301(4)	403(3)	2775(2)	25(1)
C(19)	-2591(5)	561(4)	2552(2)	41(1)
C(20)	-3600(6)	-79(5)	2633(3)	57(2)
C(21)	-3321(6)	-849(4)	2938(2)	45(1)
C(22)	-2056(5)	-1011(3)	3153(2)	36(1)
C(23)	-1036(4)	-391(3)	3075(2)	30(1)
C(24)	150(30)	1620(17)	3465(6)	27(3)
C(25)	1250(20)	2161(16)	3586(9)	43(4)
C(26)	1530(20)	2394(17)	4164(7)	52(4)
C(27)	570(20)	2229(19)	4609(7)	50(4)
C(28)	-570(30)	1718(15)	4480(9)	45(4)
C(29)	-770(30)	1390(30)	3909(9)	38(4)
C(24A)	230(16)	1779(10)	3432(4)	29(3)
C(25A)	1169(13)	2443(8)	3492(5)	35(2)

C(26A)	1502(11)	2771(10)	4046(5)	49(3)
C(27A)	968(18)	2409(10)	4551(5)	57(3)
C(28A)	-8(18)	1750(10)	4500(6)	52(3)
C(29A)	-394(18)	1442(14)	3938(6)	44(3)
O(3)	5531(10)	6628(7)	1557(5)	77(3)
C(30)	6058(14)	5396(10)	1022(6)	70(4)
C(31)	5080(17)	6219(13)	1079(6)	104(6)
O(3A)	5155(12)	7289(11)	2131(6)	111(5)
C(30A)	4924(12)	8388(8)	1403(6)	51(3)
C(31A)	4611(13)	7408(10)	1547(7)	72(4)
Cl(1)	-944(1)	3118(1)	1135(1)	27(1)
Cl(2)	-1533(1)	3239(1)	2640(1)	33(1)
O(1)	4422(3)	2284(2)	1340(2)	37(1)
O(2)	4859(4)	885(3)	1580(2)	48(1)
P(1)	-34(1)	1257(1)	2700(1)	20(1)
P(2)	115(1)	1234(1)	1301(1)	18(1)

Table A23. Crystal Data and Structure Refinement for complex **79**.

Empirical formula	$C_{29}H_{30}Cl_2O_2P_2Pd$	
Formula weight	649.77	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.8932(2) Å	a= 90°.
	b = 15.1804(3) Å	b= 90°.
	c = 20.1229(4) Å	g = 90°.
Volume	2716.64(10) $Å^3$	
Z	4	
Density (calculated)	1.589 Mg/m^3	
Absorption coefficient	1.024 mm^{-1}	
F(000)	1320	
Crystal size	0.30 x 0.20 x 0.04 mm^3	
Theta range for data collection	1.68 to 31.96°.	
Index ranges	-13<=h<=13, -22<=k<=22, -29<=l<=29	
Reflections collected	43231	
Independent reflections	9379 [R(int) = 0.0314]	
Completeness to theta = 31.96°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9602 and 0.7487	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9379 / 0 / 328	
Goodness-of-fit on F^2	1.141	
Final R indices [I>2sigma(I)]	R1 = 0.0220, wR2 = 0.0515	
R indices (all data)	R1 = 0.0259, wR2 = 0.0633	
Absolute structure parameter	-0.007(14)	
Largest diff. peak and hole	0.431 and -0.446 $e.Å^{-3}$	

Table A24. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for complex **79**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	3812(1)	-436(1)	1782(1)	16(1)
C(1)	4092(2)	-974(1)	96(1)	18(1)
C(2)	3023(2)	-580(2)	-310(1)	27(1)
C(3)	2439(3)	-1046(2)	-846(1)	29(1)
C(4)	2918(2)	-1899(2)	-972(1)	26(1)
C(5)	3988(3)	-2288(1)	-569(1)	26(1)
C(6)	4567(2)	-1833(1)	-29(1)	22(1)
C(7)	6924(2)	-584(1)	815(1)	16(1)
C(8)	7393(2)	-227(1)	133(1)	18(1)
C(9)	8654(2)	-644(1)	-240(1)	24(1)
C(10)	6549(2)	471(1)	-37(1)	17(1)
C(11)	6492(3)	972(1)	-674(1)	26(1)
C(12)	5520(2)	729(1)	530(1)	16(1)
C(13)	6533(2)	975(1)	1144(1)	17(1)
C(14)	7246(2)	80(1)	1384(1)	16(1)
C(15)	7793(2)	1630(1)	996(1)	21(1)
C(16)	7373(2)	2485(1)	676(1)	23(1)
C(17)	5506(3)	3563(2)	560(1)	37(1)
C(18)	6615(2)	581(1)	2714(1)	18(1)
C(19)	8091(2)	662(1)	2947(1)	26(1)
C(20)	8492(3)	1392(2)	3320(1)	33(1)
C(21)	7451(3)	2048(2)	3459(1)	30(1)
C(22)	5981(3)	1964(1)	3236(1)	27(1)
C(23)	5556(2)	1226(1)	2867(1)	21(1)
C(25)	7119(2)	-1268(1)	2446(1)	17(1)
C(26)	8662(2)	-1421(1)	2351(1)	23(1)
C(27)	9334(3)	-2149(2)	2642(1)	29(1)
C(28)	8500(3)	-2730(2)	3023(1)	30(1)
C(29)	6991(3)	-2575(1)	3127(1)	29(1)
C(30)	6285(2)	-1852(1)	2840(1)	23(1)
Cl(1)	1428(1)	-390(1)	1259(1)	33(1)
Cl(2)	2798(1)	-540(1)	2860(1)	34(1)

O(1)	5975(2)	2726(1)	824(1)	28(1)
O(2)	8201(2)	2905(1)	328(1)	45(1)
P(1)	4878(1)	-381(1)	789(1)	15(1)
P(2)	6205(1)	-291(1)	2127(1)	15(1)