Application of palladacycle complexes in C-C, C-N and C-P bonds formation reactions

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**NANYANG
TECHNOLOGICAL
UNIVERSITY**

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Bonds Formation Reactions**

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School of Physical and Mathematical Sciences

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Nomenclature

The Nomenclature used throughout the thesis conforms to the format adopted by Chemical Abstracts (Chemical Abstracts, 13th Collective Index, Index Guide, 1992-1996).

X-ray Structural Data

The X-ray structural analyses were kindly carried out by Dr. Li Yongxin at the Nanyang Technological University (Division of Chemistry and Biological Chemistry).

Abbreviations and Symbols

Ac	acetyl
acac	acetylacetone
AIBN	azobisisobutyronitrile
aq.	aqueous
Ar	aryl
BINAP	2,2'-Bis(diphenylphosphine)-1,1'-binaphthyl
BMS	Borane-dimethyl-sulfide
Bn	benzyl
Boc	<i>tert</i> -butoxycarbonyl
brs	broad singlet
BSA	N,O-Bis(trimethylsilyl) acetamide
Bu	butyl
Bz	benzoyl
calcd.	calculated
cat.	catalytic
Cbz	benzyloxycarbonyl
Conc.	Concentrated
d	doublet

D-A	Diels-Alder
DABCO	1,4-Diazabicyclo[2.2.2]octane
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
dd	doublets of doublet
ddd	doublets of doublets of doublet
dt	doublet of a triplet
de	diastereomeric excess
decomp.	Decomposed
deg	degree(s)
DMA	dimethylacetamide
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
DMPP	3,4-dimethyl-1-phenylphosphole
dppp	1,3-bis(diphenylphosphino)propane
dq	doublets of quartet
dt	doublets of triplet
<i>ee</i>	enantiomeric excess
EI	electron ionization
eq.	equivalent
<i>et. Al</i>	and others (Latin <i>alii</i>)
ESI	electrospray ionization
Et	ethyl
g	gram
h	hour
hex	hexyl
HPA	heteropoly acid
HPLC	high performance liquid chromatography

HRMS	high resolution mass spectroscopy
IAD	intramolecular aglycon delivery
IR	infrared
<i>i</i> Pr	isopropyl
<i>J</i>	coupling constants
M	concentration (mol/L)
M ⁺	parent ion peak (mass spectrum)
m	multiplet
<i>m</i>	meta
Me	methyl
min	minute
mp	melting point
MS	mass spectrum
M.S.	molecular sieves
Ms	methanesulfonyl
NAP	2-naphthylmethyl
NBA	<i>N</i> -bromoacetamide
NBS	<i>N</i> -bromosuccinimide
<i>n</i> Bu	<i>n</i> -butyl
NCS	<i>N</i> -chlorosuccinimide
NIS	<i>N</i> -iodosuccinimide
NMR	nuclear magnetic resonance
NOESY	nuclear overhauser enhancement spectroscopy
OTf	trifluoromethanesulfonate
<i>o</i>	ortho
<i>p</i>	para
Pd/C	palladium on carbon
Ph	phenyl
Phth	phthalate
ppm	parts per million

q	quartet
RAFT	reversible addition-chain transfer fragmentation
<i>R</i>	rectus (Latin: right absolute configuration)
Roesy	2D rotating frame Nuclear Overhauser Enhancement
rt	room temperature
s	singlet
<i>S</i>	sinister (Latin: left absolute configuration)
t	triplet
T	temperature (°C)
TBAI	tributylammonium iodide
TBAF	tetrabutylammonium fluoride
<i>t</i> Bu	<i>tert</i> -butyl
TES	triethylsilyl
TFA	trifluoroacetic acid
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
THP	tetrahydropyran
TLC	thin layer chromatography
TMS	trimethylsilyl
Tol	tolyl
Tr	triphenylmethyl
Ts	<i>p</i> -toluenesulfonyl
v	volume
δ	NMR chemical shift in ppm
Å	angstrom(s)
$[\alpha]_D$	specific rotation measure at sodium D line (589 nm)

Summary

This thesis describes the application of chiral NC-palladacycle in synthesis of chiral PN containing ligands via promoted formation of C-N and C-P bonds by asymmetric hydroamination and hydrophosphination reaction, respectively. An extended application in selective formation of C-N and C-C bonds via palladacycle-catalyzed allylic amination/ arylation of allylic alcohol is also explored in this thesis.

In chapter 1, a brief introduction of the development and application of NC-palladacycles is presented. In addition, we outline the historical development of chiral P,N containing ligands and their application in asymmetric catalysis.

As an excellent chiral auxiliary, orthopalladated [1-(dimethylamino)ethyl]naphthalene (*S*)-**33** have been proven as the most efficient promoter in asymmetric synthesis of chiral phosphorus ligands. In chapter 2, the prochiral diphenylphosphine maleate complex with chiral (*S*)-[1-(dimethylamino)ethyl]naphthalene as chiral auxiliary was synthesized via hydrophosphination reaction. Subsequently, an effective method for the synthesis of ester functionalized chiral bidentate P,N containing ligands via chiral organopalladium template promoted asymmetric hydroamination reaction has been demonstrated. The hydroamination reactions proceed with high regio- and stereo selectivities under mild conditions and provide an efficient way to simultaneously generated two stereogenic carbon centers. These optically pure bidentate P,N-ligands have been liberated from their dichloro Pd complexes and their absolute configurations have been confirmed by X-ray crystallography.

In chapter 3, amino functionalized vinylphosphines were synthesized via radical catalyzed hydrophosphination of alkynes. Relevant amino functionalized vinylphosphines palladium complexes were subsequently prepared via regio-coordination of formed vinylphosphines to the complex (*S*)-**33**. Optically pure chiral tridentate PPN containing ligands were synthesized via asymmetric hydrophosphination reaction of vinylphosphines palladium complexes under promotion and control of chiral palladium template with good stereoselectivity. Palladium-promoted asymmetric hydrophosphination of unactivated vinylphosphines establishes an efficient method to prepare amino functionalized carbon chiral PPN containing ligands which have been proven to play important role in asymmetric catalysis. These optically pure bidentate PPN ligands have been obtained via liberation of their dichloro complexes and their absolute configurations have been confirmed by X-ray crystallography.

In chapter 4, we describe the preparation of NC-palladacycle derivative **169** from the di- μ -chlorobis-{2-[(*N,N*-dimethylamino)methyl]phenyl-*C,N*} dipalladium dimer. Palladium complex **169** shows high reactivity in allylic amination. A “green” extended application of palladacycle complex **169** was explored in tandem allylic amination/ arylation of allylic alcohols which was studied to provide direct access to hitherto inaccessible 2-allylanilines and 4-allylanilines respectively in high yields with water being the only by-product and without any activator. We have also proposed a reaction pathway for this catalyzed tandem reaction protocol.

Chapter 1

General Introduction

1.1 Palladacycles

Based on Kleinman and Dubeck's ^[1] preliminary research of metallation reactions, Cope, ^[2] Siekman and Friedrich ^[3] expanded the analogous reaction and prepared the first isolated, well-characterized palladacycles **1** and **2** via palladation reactions of azobenzene and *N,N*-dimethylbenzylamines with PdCl₂ or Li₂PdCl₄ in 1965 and 1968, respectively. Since the first identified palladacycles were discovered, nitrogen-based NC-palladacycles compounds which are an important family of palladacycles have attracted much attention and represented a very interesting research topic in organic synthesis, homogeneous catalysis, design of new drugs, asymmetric synthesis, resolution of racemic ligands and in development of photo- and electroluminescent organic materials or even as nanoscale devices because of their unique physical and chemical properties. ^[4-7]

Figure 1.1

1.2 Synthesis of NC-palladacycles

Nitrogen-based NC-Palladacycles have been widely studied because of their unique

physical and chemical properties. Currently, various methods are available to prepare palladacycles and they are briefly summarized below.

1.2.1 C-H Bond Activation

Among the numerous synthetic methodologies available for the synthesis of NC-palladacycles, C-H activation reaction is perhaps the most commonly employed synthetic route to palladacycles. Both for practical significance in methodology and due to their application potential, reaction via heteroatom-mediated C-H bond activation with palladium to give palladacycles is great relevance. The intimate metal-mediated C-H activation was considered as the key step in this process, so the ability of coordinating donors (N atom) lone-pairs to bind to the metal center largely determined the control of activity of the metal center in order to accomplish the C-H bond activation. Most commonly, palladation agents including palladium acetate $\text{Pd}(\text{OAc})_2$ and tetrachloropalladated salts: Li_2PdCl_4 , Na_2PdCl_4 and K_2PdCl_4 have been employed for the preparation of NC-palladacycles. Palladation reactions are usually required to be performed with polar solvents such as methanol, ethanol, acetone, acetic acid as well as binary water-organic solvents. As shown in scheme 1.1, palladacycle **2** was prepared via C-H activation where the palladium sources are $\text{Pd}(\text{OAc})_2$ and Li_2PdCl_4 respectively. ^[2, 3, 8]

Scheme 1.1

1.2.2 Oxidative Addition

It is undoubted that C-H bond activation process has presented the most elegant ways to form palladacycles. However, the oxidative addition of organic halides also provides an important pathway to prepare palladacycles that can not be obtained via C-H bond activation. Due to their higher stability, good synthetic accessibility and better reactivity, aryl halides and alkyl halides were more commonly employed for the oxidative addition reaction to synthesize the palladacycle complexes although pseudo halides such as sulfonate, tosylates, acetates and carbonate also were efficient in this process. $\text{Pd}(\text{PPh}_3)_4$, $\text{Pd}(\text{dba})_2$, $\text{Pd}_2(\text{dba})_3$ are the most common $\text{Pd}(0)$ sources that were applied to the oxidative addition. Scheme 1.2 showed the method of oxidative addition that was initially introduced for the synthesis of palladacycles **3** by Dyke in 1983.^[9]

Scheme 1.2

1.2.3 Transmetalation

Another general and versatile method to prepare palladacycles is the transmetalation reaction. In this process, organolithium derivatives are the most widely used as transmetallating reagents due to their high reactivity. Aryl halides are more often employed in the reaction because organolithiums from an exchange of electrophilic organic halides and organolithium reagents such as BuLi , PhLi or MeLi have better

selectivity compared to direct metallation through H abstraction which gives more isomers. In 1994, van Koten and his coworkers published their research results on the synthesis of palladacycles **4** via transmetalation (Scheme 1.3).^[10]

Scheme 1.3

1.2.4 Nucleophile –Palladation

The other representative synthetic method to form palladacycles is nucleophile-palladation reactions of unsaturated organic substrates alkynes and alkenes bearing electron-donor heteroatoms. In this process, the nucleophile attacks the unsaturated bond which is coordinated to the metal center and nucleophilic addition at the unsaturated bond occurs. Dupont and his coworkers reported the synthesis of palladacycle **5** via the representative nucleophile-palladation (chloropalladation reactions) using propargyl amines as starting materials (Scheme 1.4).^[11]

Scheme 1.4

1.3 Achiral NC-Palladacycles

A characteristic feature of the NC-palladacycles is the thermostability, which makes it possible to perform the reactions at temperatures above 100 °C and need less reactive

substrate (e.g. non-activated aryl bromide). High turnover numbers of NC-palladacycles dimer as pre-catalysts lowers the catalyst loading in catalysis cycles. Their advantages in term of ease of handling, air stability, structural versatility, easy synthetic accessibility as well as their economy have made them attract continuing interest. Based on their multitudinous advantages of physical and chemical properties, NC-palladacycles were studied widely in the past decades and numerous building block of representative NC-palladacycles have been synthesized and employed to various areas. As part of a large class of palladacycles, NC-palladacycles have shown their excellent characteristic feature and reaction activity, and more and more building blocks of NC-palladacycles where N donors include azobenzenes (**1**),^[2,3] amines (**6**, **7**, **8**),^[3, 12] imines (**9**, **10**),^[13] oxazolines (**11**),^[14] pyrazole (**12**),^[15] pyridines (**13**, **14**, **15**),^[16] quinoline (**16**),^[17] amidines (**17**)^[18] and has been developed because of their structural versatility and easy synthetic accessibility. Although various palladacycles (**18**, **19**, **20**) with rings incorporating 3 to 11 members^[19, 20, 21] have been developed, the five- and six-membered ring palladacycles are still the most common. In comparison to the phosphorus-based and sulfur-based palladacycles, the nitrogen-based palladacycles are more easily obtained because the starting materials for NC-palladacycles are more readily available. Additionally, the nitrogen substrates are air stable and easily handled comparing to the substrates containing phosphorus which need to be prepared via tedious synthetic steps.

NC-Palladacycles have shown their versatile properties in various synthesis scenarios, and one of the most outstanding properties is their reactivity. This reactivity comes from the differing nature of Pd-C bond and Pd-N bond which binds to the palladium center. For the NC-palladacycles, the Pd-C bonds are highly reactive towards electrophilic reagents such as terminal alkenes, alkynes, allenes, acyls, and other small molecules such as carbon monoxide and isocyanides. It is a useful synthetic method for the generation of carbo- and heterocyclic organic compounds. Macrocyclic palladacycles were obtained by treatment of the palladacycles and various alkynes

because of intramolecular stabilization of the coordinated atom (Scheme 1.5). ^[21]

Scheme 1.5

New vinylated products were formed when NC-palladacycles reacted with terminal alkenes (Scheme 1.6). ^[22]

Scheme 1.6

Cationic N-heterobicycles were generated when palladacycles were treated with allenes (Scheme 1.7). ^[23]

Scheme 1.7

Ortho-halogenated compounds instead of *para*-halogenated compounds were selectively formed when NC-palladacycles reacted with halogens (Scheme 1.8). ^[24]

Scheme 1.8

Also, it is one of the important methods to prepare 2-acyl derivatives via treating NC-palladacycles with acyl halides (Scheme 1.9).^[12c]

Scheme 1.9

Carbo- organic compounds are easily prepared via treating the NC-palladacycles with carbon monoxide (Scheme 1.10).^[25]

Scheme 1.10

1.3.2 Application of NC-Palladacycles as Active Intermediates

C-H activation has become the most commonly employed synthetic route for synthesis of palladacycles. Because of atom economical reasons which have the advantage to avoid the insertion of the metal into a C-X (X = Cl, Br, I, etc.) bond, nitrogen-based palladacycles have emerged as active intermediates involving C-H activation or functionalization in catalytic transformation.

Significant synthetic achievements of C-H activations to direct C-C bond formation via nitrogen-mediated palladacycles have been reported. Various C-H activation via palladacycles to form C-C and C-heteroatom bond had attracted interest because of atom economical reasons and high regioselectivity. Various reactions involving C-C bond formation such as vinylations^[26], alkylations,^[27] arylations^[28], coupling

reaction^[29], and carbonylation^[30] have been successfully employed via formation of the active palladacycles (Scheme 1.11).

Scheme 1.11

1.3.3 Application of NC-Palladacycles as Precatalysts

Thermally and air stable nitrogen-based palladacycles have been widely employed to the homogeneous catalysis. In the past decades, NC-palladacycle have played very important role in C-C coupling reactions as efficient and versatile precatalysts.

1.3.3.1 Heck Reaction

Heck reaction has been one of the most powerful C-C bond formation methods and one of its benefits is outstanding *trans* selectivity.^[31] In palladium-catalyzed transformations, the Heck reaction has occupied a special place. Since discovery of the unique catalytic activity of a well-known dimeric complex $\text{Pd}_2(\text{P}(o\text{-Tol})_3)_2(i\text{-OAc})_2$ by Herrmann and Beller et al.^[32] Palladacycles have been

proven to be an family of efficient and versatile precatalysts for a wide range of useful and well known C-C coupling process such as Heck reactions. As a class of the most important palladacycles, nitrogen-based palladacycles have been widely employed in the Heck reaction and showed their special advantage in thermal stability, reactivity (Scheme 1.12).^[13d]

Scheme 1.12

1.3.3.2 Suzuki Coupling Reaction

Various modifications have been made for the reaction conditions since Suzuki coupling reaction was reported in 1979.^[33] Many of the recent development efforts on the cross-coupling reaction have focused on catalysts that facilitate the cross-coupling and expands its scope. Recently, much attention has also been focused on the use of organoboronic acids since they are convenient reagents, which are generally thermally stable and inert to water and oxygen, thus allow their handling without special precautions. In addition, both the boron containing reagents and byproducts of the Suzuki-Miyaura reaction display low toxicity. Base on these advantages, Suzuki coupling reaction have become one of powerful tools in C-C bond formation and is routinely used in fine chemicals research and development and pharmaceutical laboratories. Nitrogen-based NC-palladacycles have also been successfully employed to Suzuki coupling reaction with their characteristic feature of thermostability,

air-stability and high turnover numbers of catalyzed transformation. In 1999, Weissman and Milstein reported the first employment of NC-palladacycles in Suzuki coupling reaction and high reactivity and high yield were obtained (Scheme 1.13).^[34]

Scheme 1.13

1.3.3.3 Sonogashira Coupling Reaction

The conjugated acetylenic compounds are important intermediates and valuable building blocks in organic synthesis of natural products, pharmaceuticals and molecular organic materials. A variety of routes have been developed to prepare diarylacetylenes via C-C cross-coupling of terminal alkynes with aryl or vinyl halides or triflates. Among them, two important methods based on transition metal catalysis have been developed. The first method devised independently by Cassar and Heck involves a palladium complex to effect this reaction catalytically.^[35] The second method, developed by Sonogashira, Tahda and Hagihara, utilizes palladium catalyst, copper iodide cocatalyst and amine based to promote this reaction to give alkyl substituent under mild conditions.^[36] Along with the emergence of new techniques, numerous chemists focus on the study to find more efficient catalysts, mild reaction conditions, expanding the substrate scope of the reaction and understanding the mechanism of this process. The NC-palladacycles were introduced to the synthesis of substituent alkynes via C-C cross-coupling reactions based on their facile synthesis,

thermostability and air-stability. Among them, a representative NC-palladacycle was successfully employed to preparation for the substituent alkynes in good yield, in which no copper co-catalyst were needed (Scheme 1.14).^[37]

Scheme 1.14

1.3.3.4 Buchwald-Hartwig Cross-Coupling Reaction

Palladium-catalyzed synthesis of aryl amines from aryl halides or pseudohalides (for example triflates) and primary or secondary amines is a very powerful method for the formation of new C-N bonds and has been widely used in the preparation of organic compounds. The pioneering work employing palladacycles as a precatalyst in this reaction were discovered by Buchwald and Hartwig.^[38] Subsequently, nitrogen-based NC-palladacycles have been applied to this reaction of C-N bond formation and been proven to be efficient precatalysts (Scheme 1.15).^[39]

Scheme 1.15

1.3.3.5 Catalytic Aza-Claisen Rearrangement

Allylic amides and allylic amines are high useful synthetic intermediates which have

been widely applied in synthesis of natural products, various biologically active compounds and for many types of organic reactions. Aza-Claisen [3,3]-sigmatropic rearrangement have been proven to be an useful protocol to form allylic amides and allylic amines. Hitherto, considerable efforts have been devoted to developing new and effective catalysts for this rearrangement. NC-palladacycles, especially planar NC-palladacycles have been introduced to this reaction and have been proven to be a class of efficient catalysts to form corresponding allylic amines and allylic amides (Scheme 1.16). ^[40]

Scheme 1.16

1.4 Chiral NC-Palladacycles

Building blocks of NC-palladacycles have been developed because of their structural versatility and easy synthetic accessibility. Additionally, due to their easy synthesis and modular properties, these compounds have been functionalized to include chiral motifs in their structures. Palladacycles containing substituted benzylamine derivatives in which chirality is most often centered at the benzylic position are the first representative chiral NC-palladacycles. Various species containing N-centered chirality have also been used in stereoselective transformations and as chiral resolving agents.

1.4.1 Resolutions of Phosphines, Arsines and Nitrogen Ligands

Essentially, most palladacycles are considered as Lewis acids. This unique feature

makes them a particular class of outstanding resolving agents for mono- and bidentate ligands through the kinetics and thermodynamics procedure of ligand coordination. In 1971, the initial work of resolution of monodentate tertiary phosphine ligands via chiral NC-palladacycle **26** (Figure 1.3) was explored by Otsuka and his coworkers.^[41]^[42] Their work has made great contribution towards the synthesis of optical pure ligands through resolution. In the following decades, much effort has been devoted to the preparation of optically pure phosphine and arsine ligands via chiral palladacycles based on the achievement of Otsuka.

Based on their excellent ability in the resolution of mono- and bidentate ligands and their thermostability, air stability and facile synthesis, various chiral NC-palladacycles have been developed in the past decades. These chiral NC-palladacycles ((*S*)-**27** to (*S*)-**32**) containing chiral substituted benzylamines and are representative resolution reagents since palladacycle (*S*)-**26** was initially utilized in resolutions of racemic ligand (Figure 1.3).

Figure 1.3

The second important family of representative chiral NC-palladacycles is derivative of cyclometallated α - and β -naphthylethylamines **33-43** (Figure 1.4).

Figure 1.4

Chiral NC-palladacycles **44**, **45**, **46** (Figure 1.5) where chirality centers are concentrated on the planar- and centro-ferrocenyl moiety have also been investigated.

Figure 1.5

To date, NC-palladacycle complexes containing enantiomerically pure forms of orthometalated [1-(dimethylamino) ethyl] naphthalene are considered the most efficient resolving agents for certain types of heterobidentate phosphines.^[47] As shown in scheme 1.17^[58] and scheme 1.18^[59], the optically pure monodentate and bidentate ligands were obtained via the resolution using palladacycle **33** with the

[1-(dimethylamino) ethyl] naphthalene framework.

Scheme 1.17

Scheme 1.18

1.4.2 NC-palladacycles as Stoichiometric Reaction Promoter

Besides resolution, NC-palladacycles have been employed as an auxiliary on stoichiometric asymmetric catalysis. Chiral orthometalated NC-palladacycles have

been applied for stoichiometric asymmetric synthesis of various chiral phosphine ligands with phosphorus centers and chiral carbon backbones and arsines ligands via template controlled Diels-Alder cycloaddition, hydrophosphination, hydroamination and hydroarsination.

1.4.2.1 Diels-Alder Cycloaddition

The asymmetric Diels-Alder reaction is one of the most efficient and elegant methods for the construction of chiral six-membered rings. Enantiomerically pure monophosphines and diphosphines containing stereogenic phosphorus centers, carbon backbone stereogenic centers and selected functionalities have been considered as powerful auxiliaries for metal-based homogeneous asymmetric catalysis. Chiral NC-palladacycles complexes are very useful stoichiometric auxiliaries in asymmetric Diels-Alder reaction. A series of chiral monophosphines, diphosphines and phosphine heteroatom ligands have been synthesized via asymmetric Diels-Alder reaction under control of chiral NC-palladacycle containing ortho-palladated chiral amines auxiliaries.^[57a, 60] In scheme 1.19 and scheme 1.20, asymmetric Diels-Alder cycloaddition were studied under the promotion and control of chiral template in recent years.^[57a]

Scheme 1.19

Scheme 1.20

1.4.2.2 Hydrophosphination Reaction

Chiral mono- and bidentate phosphines play very important role in transition-metal promoted asymmetric reactions. Pioneering research had shown that phosphines with both P-chiral phosphorus and carbon backbone chirality have the capability to achieve high stereoselectivity in asymmetric catalysis. Our group has always focused on the asymmetric synthesis of various chiral phosphines ligands with chirality on carbon backbone and P-chirality under promotion and control of NC-palladacycles auxiliaries.

^[61] As shown in scheme 1.21, the representative chiral diphosphine ligand (*R*)-1,2-bis(diphenylphosphino)-1-phenylethane was synthesized via asymmetric hydrophosphination under the promotion of chiral NC-palladacycle template (Scheme 1.21). ^[62]

Scheme 1.21

Typical functionalized chiral phosphines ligands with chirality on P have also been synthesized via the chiral NC-palladacycle mediated asymmetric hydrophosphination reactions (Scheme 1.22). ^[63]

Scheme 1.22

It needs to be noted that the optically pure free diphosphines can be obtained by subsequent treatment with KCN.

1.4.2.3 Hydroarsination Reaction

Organoarsines have also been found to play important roles in many aspects of organic synthesis and homogenous catalysis. As ligands, arsines have shown their different advantages in transition-metal catalysis comparing with phosphines. Chiral arsines have been obtained via resolution of racemic or meso- arsines. Compared to resolution to obtain chiral arsines, the asymmetric synthesis via asymmetric addition

reaction between As-H moiety of an arsines and a C-C double bond is a more attractive method because of its economy reasons. NC-palladacycles with chiral amine auxiliaries have been proven to be efficient auxiliary reagents to promote this asymmetric hydroarsination (Scheme 1.23).^[64]

Scheme 1.23

1.4.2.4 Hydroamination Reaction

Except for asymmetric Diels-Alder cycloaddition, hydrophosphination, hydroarsination, NC-palladacycles with chiral amines auxiliaries have also been applied to the hydroamination to prepare P-chiral phosphorus donor and imine-based donor ligands. In 2001, Leung et.al have described the asymmetric hydroamination to prepare P-chiral ligands with phosphorus donor and imine donor under the control and promotion of chiral nitrogen-based NC-palladacycles containing naphthylamine auxiliaries (Scheme 1.24).^[65]

Scheme 1.24

1.4.3 Employment of NC-Palladacycles as Precatalyst

1.4.3.1 Asymmetric Allylic Amination

Transition metal-catalyzed transformation of allylic compounds via a π -allylmetal intermediate is one of the most powerful and useful methods for carbon-carbon and carbon-heteroatom (N, O, and S) bond formation. Palladium-catalyzed allylic amination is a well-established method for the synthesis of allyl amines. Asymmetric intramolecular allylic amination to prepare chiral allylic amines have also attracted much attention. Among them, planar NC-palladacycles have been found to be a class of efficient precatalysts for asymmetric allylic amination. Overman and Remarchuk have applied palladacycles **75** to the asymmetric intramolecular allylic amination and good activity and high ee have been obtained (Scheme 1.25).^[55a]

Scheme 1.25

1.4.3.2 Catalytic Allylic Rearrangement

Allylic amides and allylic amines have been widely employed as synthetic intermediates of natural products, biologically active compounds. Particularly, the resulting chiral allylic amines and their derivatives are valuable building blocks for the synthesis of important compounds classes such as unnatural amino acids. In 2003, Overman, Richards, and co-workers disclosed an additional breakthrough: the first highly enantioselective catalyst for the rearrangement of aza- [3,3] Sigmatropic trihaloacetimidates, using the planar chiral oxazoline-based NC-palladacycles.^[66]

Since then, more and more chemists have devoted their attention to the development of chiral NC-palladacycles and their application in asymmetric rearrangement reactions. To date, many NC-palladacycles, especially, planar NC-palladacycles such as **76** have been obtained and successfully employed for the asymmetric rearrangement reaction with high reactivity and high stereoselectivity (Scheme 1.26).^[56b]

Scheme 1.26

Asymmetric synthesis of *N*-substituted heterocycles with stereogenic centers at the α position of nitrogen atom has been widely investigated because these compounds have shown excellent biological and pharmacological activity. Aza-[3,3] Sigmatropic rearrangement has been considered as an efficient method to prepare this type of compounds. Among them, planar NC-palladacycles have been rapidly developed and they have been introduced to the investigation of aza-[3,3] Sigmatropic rearrangement. In 2010, Batey and his coworker used planar NC-palladacycles **77** as precatalysts to the asymmetric synthesis of *N*-substituted 2-pyridones via aza-[3,3] Sigmatropic rearrangement from 2-allyloxypyridines and both high reactivity and high selectivity were obtained (Scheme 1.27).^[67]

Scheme 1.27

1.4.3.3 Asymmetric Michael Addition Reaction

An important reaction for creating carbon-carbon bonds with enantioselectivity is catalytic asymmetric Michael addition reaction. Palladacycles have been proven to be an effective precatalyst in asymmetric Michael addition. Among those, direct conjugate additions of R-carbonyl-stabilized nucleophiles to activated olefins are very attractive for C-C bond constructions because of their atom economy and versatility of the activating functional groups. Peter and his coworkers applied the planar NC-palladacycle **78** in the asymmetric Michael addition reaction and both good stereoselectivity and reactivity were obtained (Scheme 1.28).^[68]

Scheme 1.28

1.4.3.4 Cyclopropanation

Due to their frequent occurrence in biologically active compounds and their use as valuable synthetic intermediates, cyclopropanes have attracted much attention in organic chemistry. Cyclopropanation reactions transition metal-catalyzed are important method to prepare this useful cyclopropanes. Cativiela and his coworkers

reported the synthesis of chiral cyclopropanes via asymmetric cyclopropanation reaction with NC-palladacycles **79** as the precatalysts in 1996 (Scheme 1.29).^[69]

Scheme 1.29

1.4.3.5 Asymmetric Hydrophosphination Reaction

Chiral mono- and bidentate phosphorus ligands are the most fundamental ligands in homogeneous catalysis. Asymmetric hydrophosphination of unsaturated C-C bond is a powerful tool to prepare chiral phosphine ligands with chiral carbon backbone. Transition metal mediated hydrophosphination of C-C double bond of α,β -unsaturated ketones have been reported to form chiral phosphines ligands.^[70] The NC-palladacycles derivatives **49** have been proven efficient template auxiliary in asymmetric stoichiometric catalyzed reactions. Very recently, our group has reported the catalyzed hydrophosphination Ph_2PH to the C-C double bond of α, β -unsaturated ketones (Scheme 1.30).^[71] In this process, good reactivity and high enantioselectivity have been obtained.

Scheme 1.30

1.5 Chiral P,N Containing Ligands

P,N-containing ligands, by virtue of the fact that they have soft phosphorus and hard

nitrogen donor atoms, can provide a hybrid environment in a catalytic scenario. P,N-containing ligands can furthermore stabilize intermediate oxidation states or geometries during a catalytic cycle in a transition-metal catalyzed reaction. In 1972, Hayashi and his coworkers reported the first representative chiral P,N-containing ligands (*S,R*)-PPFA (**80**) and (*R,S*)-PPFA (**81**)^[72] and successfully employed them to the asymmetric catalysis. Since then, much efforts have therefore been focused on the preparation and application of chiral P,N-containing ligands base on their characteristic features. To date, a variety of chiral P,N containing ligands have been developed and investigated in catalysis base on their extensive use in the coordination chemistry and catalysis arenas.

Figure 1.6

1.5.1 Chiral Bidentate P,N Containing Ligands

Clearly chiral bidentate P, N containing ligands have found extensive use in the coordination chemistry and catalysis arenas. As a result, the synthesis and application of such chiral derivatives are of great interest.

1.5.1.1 Chiral P,N-Ligands with Chirality Centering on the Chelate Ring of P-M-N

Chiral P,N containing ligands with the chirality centered on the chelate ring of P-M-N complexes have also been developed over the past decades. This family of chiral P, N-ligands has been proven to have good catalytic activity and stereoselectivity in

asymmetric catalysis. These type ligands have a distinct feature on molecular architecture, and this feature have the potential of transition of chirality information from the backbone of ligands on the chelating ring. The transfer of stereochemical information might be more efficient if the chirality was centered on the chelate ring of P-M-N.

A. Chiral P,N-Ligands without P-Heteroatom Bond

Chiral amino N donor, phosphine P donor ligands without P-heteroatom bond have been prepared using the amino acid and amino acid derivatives as the starting materials. As shown in **scheme 1.31**, Aderson and his coworkers reported the synthesis of chiral P,N-ligand **82** in five steps from the amino acid as the starting materials.^[73] Chiral P, N containing ligands **83**^[74] and **84**^[75] with two chiral carbon centers have been prepared from amino acid derivatives and tartaric acid respectively. Other important examples of these type chiral P,N-ligands **85** which contains the axially chiral BINAP framework were prepared.^[76]

Scheme 1.31

83^[74]

84^[75]

85^[76]

Figure 1.7

Chiral P,N-ligands containing schiff base imine N donor have received increasing attention due to their flexible coordination behavior associated with tunable steric and electronic properties.^[77, 78] Chiral imino phosphorus donor ligands **88** including planar ferrocenyl backbone have been synthesized.^[79]

86^[77]

87^[78]

88^[79]

Figure 1.8

Pyridine-based and phosphines-based ligands have become an important family of functionalized phosphines containing both P- and N- donor centers. Various pyridines containing cyclic-based nitrogen donor P, N containing ligands have been synthesized via different methods.^[80] Among them, our group had reported the synthesis of functionalized pyridine nitrogen donor P,N-ligands via metal complex promoted asymmetric hydrophosphination reaction under the control of chiral palladacycles containing chiral amines auxiliary (Scheme 1.32).^[61c]

Scheme 1.32

B. Chiral P,N-Ligands with P-O Bonds

Due to the nature of the donor atom, metals which coordinated to these ligands with P-O bonds should have a highly electronically dissymmetric environment. As inexpensive starting materials, chiral sugars have been used in the synthesis of these chiral P,N-ligands with P-O bonds because chiral sugars are readily available and easily modified. Diéguez and his coworkers took the advantage of chiral sugars D-(+)-xylose to prepare representative chiral P,N ligands with P-O bonds (Scheme 1.33)^[81] Additionally, P,N-ligands which have the cyclic backbone and the ferrocenyl sandwich structure architecture **91-96** (Figure 1.8) have been developed in the past decades.^[82, 83]

Scheme 1.33

Figure 1.8

C. Chiral P,N-Ligands with P-N Bonds

The family of chiral P,N-ligands with phosphine donor containing P-N bonds have received particular attention due to the different electronic properties transferred from the nitrogen center to the phosphorus center. These type ligands **97**, **98**, **99**, **100** (Figure 1.9) were synthesized by reaction between an amine and chlorodiphenylphosphine.^[84, 85]

Figure 1.9

1.5.1.2 Chiral P,N-Ligands with Chirality Centering outside the Chelate Ring of P-M-N

Various chiral P,N-ligands containing chirality centering out the chelate ring of P-M-N have also been prepared and play important roles in asymmetric metal-catalyzed reactions.

A. Chiral P,N-Ligands without P-Heteroatom Bond

Chiral ligands without P-heteroatom bonds and chirality was centered outside the chelate ring are a family of common ligands. These ligands usually have the chiral centers near the nitrogen atom backbone because it is easier to introduce the chirality on the nitrogen fragment than to the phosphorus fragment. The diphenylphosphine are the most utilized as the P donor, the versatile N donor can be amino, imines, pyridines, oxazolines and so on. Synthesis of amino N donor, phosphine P donor ligands **101-105** (Figure 1.10) has been reported. [86-89]

Figure 1.10

The imine N donor phosphine P donor ligands **106-109** (Figure 1.11) have been developed. [90-92]

Figure 1.11

Pyridine-based ring donor phosphines P donor ligands **110-114** (Figure 1.12) have been synthesized. [93,94]

Figure 1.12

Representative chiral oxazoline-based **115**,^[95] amdozazine-based **116**^[96] and imidazoline-based **117**^[97] N donor phosphines P donor ligands (Figure 1.13) have also been synthesized and widely employed in asymmetric catalysis due to their easy accessibility. Representative chiral oxazoline-base P,N containing ligands **118** which contains planar ferrocenyl fragment also have been prepared.^[98]

Scheme 1.13

B. Chiral P,N-Ligands with P-O Bonds

Typical chiral P,N containing ligands with P-O bonds where the nitrogen-based donors are imine **119**,^[82] pyridine **120**,^[99] oxazoline **121**^[100] and imidazoline **122**^[97] (Figure 1.14) have been developed. These ligands have shown good reactivity and stereoselectivity in catalysis.

Figure 1.14

C. Chiral P,N-Ligands with P-N Bonds

P, N containing Ligands whose chirality is centered out of the P,N ring with P-N bonds **123**,^[85] **124**,^[101] and **125**^[102] (Figure 1.15) have been synthesized .

Figure 1.15

1.5.2 Chiral Tridentate P,N Containing Ligands

Since Shaw initially developed the initial PCP tridentate ligands,^[103] a considerable attention have been focused on hetero phosphorus tridentate ligands due to their particular electronic features. Compared to the simple diphosphine ligands, mixed donor tridentate ligands bearing soft and hard combination of donors in the same framework have additional advantages. Chiral mixed nitrogen-based and phosphorus-based tridentate ligands include these type of PNP, PPN and PNN pincers. Various nitrogen donor tridentate P,N containing ligands **126**,^[104] **127**^[105] and **128**^[106] (Figure 1.16) have been investigated.

Figure 1.16

1.5.3 Chiral Tetradentate P,N Containing Ligands

Since Rauchfuss prepared the first representative achiral tetradentate ligands with a

P2N2 donor set via condensation of *o*- Ph₂PC₆H₄CHO(2 equiv) with a diamine.^[107]

The tetradentate containing P,N ligands, particularly, chiral tritradentate P,N ligands with different amine backbone have attracted considerable interest. These ligands have two soft phosphorus atoms and two hard nitrogen atoms that restrict the coordination geometry around the metal centers. In particular, the introduction of chirality within their carbon backbone has made them useful in the asymmetric catalysis as efficient precursors. Among them, the most representative tetradentate P,N containing ligand with the chiral carbon backbone are the important class of ligands which were named as the Trost ligands. In the architecture of these chiral tetradentate ligands, the chirality is usually inherent to the nitrogen framework because the chiral fragments containing nitrogen are readily accessible. Representative amide-based **129** and **130**^[108], imino-based **131**^[109] and **132**^[110], imine-based **133**^[109], **134**^[111] and **135**^[110a, 112], and iminophosphorane-based **136**^[113] nitrogen donors, P, N tetradentate ligands (Figure 1.17) have been developed in the past decades.

Figure 1.17

1.5.4 Application of Chiral P,N-Ligands

Due to their unique properties, chiral P,N-ligands have been applied in various asymmetric catalysis.

1.5.4.1 Asymmetric Allylic Alkylation

Development of asymmetric metal-catalyzed reactions has played a significant role in allowing synthetic access to biologically important molecules. Allylic alkylation is one of the most powerful methods to form C-C, C-heteroatom bonds via π -allylmetal intermediate. Asymmetric alkylation of allylic alcohol and their derivatives have been well established to prepare various chiral allylic compounds (Scheme 1.34).^[78]

Scheme 1.34

1.5.4.2 Asymmetric Hydrogenation

Asymmetric hydrogenation is one of the most widely used, most reliable catalytic methods for the preparation of optically active compounds. Chiral alcohols are useful building blocks in organic synthesis and have been widely used in the fine chemicals industry. Therefore, the asymmetric synthesis of chiral alcohols from simple ketones has attracted much interest. In the synthesis via asymmetric hydrogenation, the chiral P, N containing ligands have played important role as precursor in homogeneous catalysis from the simple starting material ketones (Scheme 1.35). ^[114]

Scheme 1.35

Asymmetric hydrogenation have played dominant role in industrial asymmetric catalysis. To date, asymmetric hydrogenation of unsaturated carbon-carbon double bonds has been recognized as the one of the most practical methods for the optically pure compounds. Pfaltz and his coworkers have developed efficient chiral P,N containing ligands which were used to the asymmetric hydrogenation of olefins (Scheme 1.36). ^[83]

Scheme 1.36

1.5.4.3 Asymmetric Hydrosilylation

Due to the importance of optically pure alcohols in organic synthesis, in the past decades, the asymmetric hydrosilylation of prochiral ketones to chiral siloxanes, followed by hydrolysis to chiral alcohols, has been a well-studied system. Hydrosilylation is often preferred because its reaction conditions are milder in which higher stereoselectivity of products was obtained comparison to the normal asymmetric hydrogenation (Scheme 1.37). ^[115]

Scheme 1.37

1.5.4.4 Asymmetric Hydroamination

Asymmetric hydroamination of olefins is an efficient method to access chiral, nonracemic alkylamines. In the past decades, many efforts have been devoted to the research of finding suitable methods to develop asymmetric hydroamination. It is still a great challenge to developed asymmetric hydroaminaiton reaction with high yields and high stereoselectivity. As a family of important chiral coordinated ligands, chiral P, N containing ligands are playing an important role in asymmetric synthesis. Of

course, these types of P,N-ligands have been proven to be efficient precursor in asymmetric hydroamination reaction via transition metal catalysts. Among them, Trost-type chiral P, N containing ligands **129** have been used for palladium-catalyzed hydroamination of 1,3-dienes by Hartwig and his coworkers (Scheme 1.38).^[108b] In this process, good yields and high stereoselectivity have been obtained.

Scheme 1.38

1.5.4.5 Asymmetric Isomerization

Asymmetric isomerization is one of important ways to form chiral aldehydes. In 2010, Mazet and his coworkers have reported the asymmetric isomerization to get corresponding aldehyde from allylic alcohol (Scheme 1.39).^[116]

Scheme 1.39

1.5.3.6 Enantioselective Meerwein-Eschenmoser Claisen Rearrangement

The [3,3'] Sigmatropic rearrangements of allyl vinyl ethers (Claisen rearrangements) and their derivatives have enjoyed a long and rich history due to the utility of the

products. In 2008, Kozlowski reported the employment of chiral P, N-ligands to the Claisen rearrangements reaction and got the products with good yields and high enantioselectivity (Scheme 1.40).^[117]

Scheme 1.40

1.6 Aims of the Present Work

The above mentioned studies show that the nitrogen-based NC-palladacycles have become an important research topic due to their special physical and chemical feature. These characteristic features have made them versatile complexes in various areas, particularly in catalysis. It is clear that the chiral P,N containing ligands have played significant role in the synthesis of various optically pure organic chemicals which are used as biological, pharmaceutical compounds or important synthetic building blocks. In this present work, the potential utility of palladacycles in catalysis and the preparation of optically pure P,N containing ligands with simultaneous creation of two new stereogenic carbon centers will be investigated.

Chapter 2

Diastereoselective Synthesis of Functionalized P,N-Ligands Containing Two Stereogenic Carbon Centers via Sequential Hydrophosphination and Hydroamination Using Chiral Palladacycle

2.1 Introduction

Clearly, chiral bidentate P,N containing ligands have found quite extensive use in coordination chemistry and catalysis. As a result, the synthesis of such chiral derivatives is of potential interest. Heterobidentate P,N containing ligands, by virtue of the fact that they have soft phosphorus and hard nitrogen donor atoms, can provide a hybrid environment in a catalytic scenario. P,N containing ligands can furthermore stabilize intermediate oxidation states or geometries during a catalytic cycle in a transition-metal catalyzed reaction.^[80c, 118] Much efforts have therefore been focused on the preparation and application of achiral and chiral P,N containing ligands since Hayashi et. al. reported the first representative P,N containing ligands.^[72] In the past decades, chiral heterobidentate P,N containing ligands, which are one of most important P,N containing ligands, are being intensively investigated because they have played extremely important roles in catalysis. They have been successfully applied in various asymmetric catalysis scenarios such as allylic alkylation,^[73, 78, 108a, 119] hydrogenation,^[74a, 83, 114, 120] hydrosilylation,^[54, 115, 121] and hydroamination reactions^[122]. In view of the above mentioned, developments in the preparation and

application of a variety of P,N ligands has been rapid in recent years. From a more focused perspective it is evident that β -P,N containing ligands form an important category amongst P,N-type ligands and have shown significant catalytic activities.^[119-123] Currently, β -P,N containing ligands with one or two stereogenic carbon centers are still rare and their preparation mainly utilizes chiral amino acids and their derivatives which therefore limits their diversity.

The wide use of amines and their derivatives across many fields of chemistry has lead to considerable interest concerning the synthesis of C-N bonds.^[124] One of the most attractive routes for C-N bond formation is through the hydroamination of unsaturated C-C double and triple bonds by primary or secondary amines, with its 100% atom efficiency. The importance of amines and amine derivatives in the synthesis of pharmaceuticals and fine chemicals has stimulated considerable interest in catalytic olefin hydroamination as a route to nitrogen-containing molecules.^[124] Asymmetric hydroamination of olefins would be an efficient means to access chiral, nonracemic amines. Development of stereoselective catalysts for the formation of C-N bonds in an enantioselective fashion remains an unsolved challenge. Hitherto, reports on the catalytic asymmetric hydroamination of unsaturated carbon-carbon bonds with a high enantioselectivity are still rare.^[108b, 125, 126] However, no example of hydroamination was reported with simultaneous generation of two new chiral carbon centres from olefin with high stereoselectivity.

Phosphorus compounds are of great interesting compounds because of their pharmaceutical and biological activities that include anticancer, antiinflammatory,

cardiotonic, inotropic, antihypertensive, antimicrobial and antibacterial properties.^[127]

Phosphorus and nitrogen containing compounds with (2*R*_C,3*S*_C)-dimethyl-2-amino-3-phosphino succinate framework with two chiral carbon centers are not only chiral *P,N*-ligands which were potentially employed in catalysis, but also potential biological active drug. Complexes containing succinate fragment have been researched as anticancer and antitumor drugs.^[127a, 128]

Palladacycles have presented a very interesting research topic in organic synthesis, homogeneous catalysis since the first representative palladacycle was discovered by Cope and his coworker.^[2, 3] Chiral nitrogen-based NC-palladacycles of orthometalated [1-(dimethylamino)ethyl]naphthalene are considered the most efficient resolving reagents for certain types of heterobidentate phosphines and have been successfully employed in various areas of asymmetric synthesis such as Diels-Alder cycloaddition,^[47a, 60] hydrophosphination,^[61-63] hydroarsination^[64] and oxidative coupling reactions^[129]. However to the best of our knowledge, preparation of chiral *P,N* ligands with simultaneous generation of two stereogenic carbon centers via stepwise hydrophosphination and hydroamination reactions of prochiral functionalized substrates using chiral metal complexes has not been reported hitherto. Herein we described the first asymmetric synthesis of optically pure functionalized *P,N* containing ligands with (2*R*_C,3*S*_C)-dimethyl-2-amino-3-phosphino succinate fragment via stepwise hydrophosphination and hydroamination reactions leading to the simultaneous formation of two new stereogenic carbon centers with high stereoselectivity in good yields under mild conditions.

2.2 Results and Discussion

2.2.1 Preparation of Prochiral Diphenylphosphine Maleate Complex (S)-141 via Hydrophosphination Reaction

Scheme 2.1

Hydrophosphination reaction of unsaturated carbon-carbon triple bond is one of most important methods to form vinylphosphines. As illustrated in scheme 2.1, hydrophosphination of dimethyl acetylenedicarboxylate with diphenylphosphine promoted by the chiral NC-palladacycle ((S) -33) was carried out at -78°C for 4 h, followed by room temperature for 10 h to regioselectively form ((S) -141 in moderate yield. Prior to purification, the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum in CDCl_3 exhibited only one singlet signal at δ 41.7. After purification by running column chromatography, ((S) -141 was obtained in 57% yield. In this process, no oxide signal of diphenylphosphine and also no other phosphorus signals were observed. The regiospecific coordination on the metal center is due to the distinct electronic directing effects originating from the σ -donating nitrogen and the π -accepting aromatic carbon of the orthopalladated naphthylamine in which the incoming ligands with soft donors prefer to take up the coordination position trans to the NMe_2 moiety.^[47a, 65]

2.2.2 Asymmetric Hydroamination of Phosphine Functionalized Dimethyl acetylene Carboxylate with Alkyl Amines

Scheme 2.2

Our research group has previously reported the synthesis of imino-phosphine bidentate ligands containing P-chirality centers from ethynylphosphine and aniline via a hydroamination reaction promoted by a chiral metal template. However no new stereogenic carbon centers were created during the course of that reaction.^[65]

No reaction occurs between dimethyl 2-(diphenylphosphino) maleate and alkyl amines without catalyst or with PdCl₂ under mild conditions (at -40 °C or at room temperature). The chloro ligand in the monochloro complex **(S)-141** is thermodynamically and kinetically stable and it cannot be efficiently displaced by most incoming monodentate ligands, including phosphines and amines.^[44, 65, 130]

Therefore as expected, no reaction was observed between the chloro complex **(S)-141** and alkyl amines. Thus it was necessary to abstract the chloro ligand with silver perchlorate so as to facilitate the formation of one vacant coordination site prior to the introduction of the amine (Scheme 2.2). However the perchlorate species **(S)-142** was

not necessary to be isolated and was then used directly for subsequent hydroamination reactions. It needs to be noted that there is one prochiral double bond in (*S*)-**141**, and hence two new stereogenic carbon centers could potentially be created during this hydroamination reaction. Consequently, four diastereoisomers could be formed in principle during the course of the hydroamination. The intramolecular hydroamination reaction between the perchlorato complex (*S*)-**142** and dimethylamine as well as the one involving diethylamine proceeded smoothly at low temperature (−40 °C) for 12 h in dichloromethane and gave the desired corresponding hydroamination reaction products (*S_C, R_C, S_C*)-**143a** and (*S_C, R_C, S_C*)-**143b** with high stereoselectivity (up to 98%), as observed from the intensity of the ³¹P{¹H} NMR signals of the crude reaction products. A single ³¹P NMR signal was observed at δ 46.1 and 45.1 respectively in CDCl₃ (Table 2.1). However, no desired hydroamination products were observed when diisopropylamine was applied in this reaction. This maybe attribute to the steric bulky group on N atom which was blocked to coordinate to the metal center.

Table 2.1 Asymmetric hydroamination with alkyl amines^[a]

Entries	Amines	Products	³¹ P NMR/ δ	de(dr)/ % ^[b]
1	NMe ₂	(<i>S_C, R_C, S_C</i>)- 143a	46.1	99
2	NEt ₂	(<i>S_C, R_C, S_C</i>)- 143b	45.1	95
3	N(<i>i</i> -Pr) ₂	NR	--	--

[a] Reaction was performed at −40 °C for 12 h [b] Determined by ³¹P NMR

This is consistent with the hypothesis of reaction mechanism of the asymmetric hydroamination reaction which the amines firstly coordinate to the metal center and

subsequent intramolecular hydroamination reaction.

Hydroamination products (S_C, R_C, S_C)-**143a,b** were relatively stable in solid state and no change was found when they were kept at room temperature for one week. But when these two hydroamination products were kept in solution (DCM/Diethyl Ether or DCM/Hexane) at room temperature for 12 h several unidentified products were formed from decomposition. Therefore no suitable single crystals of (S_C, R_C, S_C)-**143a** or (S_C, R_C, S_C)-**143b** were obtained for single crystal X-ray diffraction studies. Running column chromatography using silica gel or alumina to purify the products also failed because the products decomposed while on the column. Hence the crude hydroamination products were treated directly with concentrated hydrochloric acid (Scheme 2.3) and the chiral auxiliary was thus chemoselectively removed to give the neutral dichloro complexes (R_C, S_C)-**147a** and (R_C, S_C)-**147b** respectively which were found to be stable in solution when compared to the original hydroamination products (S_C, R_C, S_C)-**143a,b**.

2.2.2.1 X-Ray Structure Analysis of Dichloro Complexes (R_C, S_C)-**147a** and (R_C, S_C)-**147b**

Scheme 2.3

Without further separation, the crude hydroamination products (S_C, R_C, S_C)-**143** were treated with concentrated HCl for 12 h to chemoselectively remove the chiral

auxiliary and neutral dichloro complexes (R_C , S_C)-**147** were obtained. In the process of removing the chiral auxiliary, the absolute configurations of the stereogenic carbon centers were retained (as seen from subsequent re-complexation studies, *vide infra*). After standard workup and purification by column chromatography, the neutral dichloro complexes (R_C , S_C)-**147a** and (R_C , S_C)-**147b** were subsequently grown crystal in dichloromethane and diethyl ether system at room temperature respectively. The absolute configuration of (R_C , S_C)-**147a** and (R_C , S_C)-**147b** was confirmed by X-ray crystallography (Figure 2.1 and Figure 2.2). Selected bond distances and angles are given in **Table 2.2** and **Table 2.3** respectively.

Figure 2.1 Molecular structure and absolute configuration of (R_C , S_C)-**147a**

Table 2.2 Selected bond lengths (Å) and angles (deg) of dichloro complex (R_C , S_C)-**147a**

Pd(1)-Cl(1)	2.381(1)	Pd(1)-Cl(2)	2.294(1)
Pd(1)-N(1)	2.133(2)	Pd(1)-P(1)	2.202(1)
C(1)-N(1)	1.486(3)	C(2)-N(1)	1.494(3)
C(4)-O(2)	1.328(3)	C(4)-O(1)	1.201(3)
C(5)-N(1)	1.518(3)	C(5)-C(6)	1.531(3)
C(6)-P(1)	1.849(2)	C(9)-P(1)	1.802(2)
N(1)-Pd(1)-P(1)	87.3(1)	N(1)-Pd(1)-Cl(2)	174.5(1)
P(1)-Pd(1)-Cl(2)	87.2(1)	N(1)-Pd(1)-Cl(1)	92.8(1)
P(1)-Pd(1)-Cl(1)	179.2 (1)	Cl(2)-Pd(1)-Cl(1)	92.7(1)
N(1)-C(5)-C(6)	110.8(2)	N(1)-C(5)-C(4)	112.3(2)
C(7)-C(6)-C(5)	110.3(2)	C(4)-C(5)-C(6)	111.2(2)
C(5)-C(6)-P(1)	105.9(2)	C(7)-C(6)-P(1)	113.0(2)
C(1)-N(1)-C(2)	109.7(2)	C(1)-N(1)-C(5)	111.4(2)
C(15)-P(1)-C(6)	105.3(1)	C(1)-N(1)-Pd(1)	107.1(2)
C(15)-P(1)-Pd(1)	113.2(1)	C(5)-N(1)-Pd(1)	111.0(1)
		C(6)-P(1)-Pd(1)	99.9(1)

Figure 2.2 Molecular structure and absolute configuration of (R_C , S_C)-**147b**

Table 2.3 Selected bond lengths (Å) and angles (deg) of dichloro complex (R_C , S_C)-**147b**

Pd(1)-N(1)	2.135(7)	Pd(1)-Cl(2)	2.277(1)
Pd(1)-P(1)	2.198(1)	C(2)-N(1)	1.522(8)
Pd(1)-Cl(1)	2.378(1)	N(1)-C(5)	1.529(7)
C(5)-C(8)	1.537(4)	C(5)-C(6)	1.532(4)
C(6)-O(1)	1.326(4)	C(6)-O(2)	1.197(4)
C(8)-P(1)	1.855(3)	C(11)-C(12)	1.380(5)
N(1)-Pd(1)-Cl(1)	93.8(2)	N(1)-Pd(1)-P(1)	89.0(2)
P(1)-Pd(1)-Cl(1)	177.3(1)	N(1)-Pd(1)-Cl(2)	172.9(2)
C(1)-C(2)-N(1)	114.5(6)	P(1)-Pd(1)-Cl(2)	86.2(1)
C(5)-N(1)-Pd(1)	108.6(4)	Cl(2)-Pd(1)-Cl(1)	91.1(1)
N(1)-C(5)-C(8)	116.7(3)	C(3)-N(1)-C(2)	105.6(6)
C(9)-C(8)-P(1)	110.9(2)	C(2)-N(1)-C(5)	111.8(5)
C(8)-P(1)-Pd(1)	102.0(1)	C(3)-N(1)-Pd(1)	106.1(4)
C(5)-C(8)-P(1)	105.3(2)	C(2)-N(1)-Pd(1)	112.1(4)
C(9)-C(8)-C(5)	114.2(2)	N(1)-C(5)-C(6)	114.0(3)
		C(6)-C(5)-C(8)	110.0(2)

The geometry at palladium center of (R_C , S_C)-**147a** is distorted square planar with angles of 87.3(1)° –92.7(1)° and 174.5(1)° –179.2(1)°. The absolute stereochemistry at the C(5) and C(6) stereogenic center are *R* and *S*, respectively. The five member P,N chelate ring adopt the conformation with both ester functional groups occupying the sterically favourable equatorial positions. Significant difference between the two Pd-Cl bond distances [2.381(1) and 2.294(1) Å], with the bond *trans*- to the phosphorus being noticeably enlarged from normal, reflects that the phosphorus has stronger electronic *trans*- effect than the nitrogen. The C(6)-P(1) [1.849(2) Å] and C(9)-P(1) [1.802(2) Å] distances are typical for C-P bonds. The C(5)-N(1) [1.518(3) Å] and C(5)-C(6) [1.531(3) Å] distances are typical for C-N and C-C bonds,

respectively. The C(4)-O(1) [1.201(3)) Å] and C(4)-O(2) [1.328(3) Å] distances are typical for C=O and C-O bonds, respectively.

The similar bond lengths and bond angles were observed for the (*R_C*, *S_C*)-**147b**.

2.2.2.2 Synthesis of the Optically Pure Free Ligands (*R_C*, *S_C*)-**148** via Liberation of Dichloro Complexes (*R_C*, *S_C*)-**147**

Scheme 2.4

Subsequently, the dichloro complexes (*R_C*, *S_C*)-**147a,b** were dissolved in DCM and treated with potassium cyanide at room temperature for 30 min to give the (*R_C*, *S_C*)-**148a,b**. After removal of the solvent, (*R_C*, *S_C*)-**148a** was obtained as pale yellow oil in 92%; [α]_D = −222° (*c* 0.5, DCM); ³¹P NMR spectrum of the free ligand in CDCl₃ exhibited at δ −8.1. Free ligand (*R_C*, *S_C*)-**148b** was obtained as pale yellow oil in 90%; [α]_D = −134° (*c* 0.5, DCM); ³¹P NMR spectrum exhibited in CDCl₃ at δ −8.7.

2.2.2.3 Reoordination of Free Optically Pure Ligands (*R_C*, *S_C*)-**148**

Scheme 2.5

In order to confirm the optical purity of these free ligands, the liberated optically pure free ligands were reoordinated to the chiral template (*S*)-**49** (Scheme 2.5). After these

free ligands recoordinated to the (*S*)-**49**, their signals of ^{31}P NMR spectrum were observed at 46.1 and 45.1 which are consistent with the asymmetric hydroamination products (S_C, R_C, S_C)-**143a** and (S_C, R_C, S_C)-**143b** respectively.

2.2.3 Asymmetric Hydroamination with Aryl Amines

Scheme 2.6

No reaction occurs between dimethyl 2-(diphenylphosphino) maleate and anilines without metal under heat. No stereoselectivity was observed for the reaction between dimethyl 2-(diphenylphosphino) maleate and anilines with PdCl_2 as catalyst. The asymmetric hydroamination reaction between primary aryl amines and the perchlorate complex (*S*)-**142** which was obtained via treatment of (*S*)-**141** with AgClO_4 were carried out smoothly at 60 °C for 12 h to selectively form the hydroamination products (S_C, S_N, R_C, S_C)-**149a-h** and (S_C, R_N, R_C, S_C)-**149'a-h** in high yields and good stereoselectivity (Scheme 2.6). These products (S_C, S_N, R_C, S_C)-**149a-h** and

(S_C, R_N, R_C, S_C)-**149'a-h** have the same configuration of carbon centers and their unique difference is the *N*-chirality centers which were formed because N atom coordinated to the metal centers and was locked. Various aryl amines which substituent are electron-donating or electron-withdrawing groups (Table 2.4, Entries 1-8) have no significant effect on the reactivity and stereoselectivity for this asymmetric hydroamination reaction. The positions of substituent groups on ortho-, meso- or para- also have no significant effect on the reactivity and stereoselectivity.

Table 2.4 Asymmetric hydroamination with aryl amines^[a]

Entries	Amines	Hydroamination Products	dr ^[b] /%	Yield ^[c] /%
1		(S_C, S_N, R_C, S_C)- 149a & (S_C, R_N, R_C, S_C)- 149'a	92	80
2		(S_C, S_N, R_C, S_C)- 149b & (S_C, R_N, R_C, S_C)- 149'b	91	83
3		(S_C, S_N, R_C, S_C)- 149c & (S_C, R_N, R_C, S_C)- 149'c	92	85
4		(S_C, S_N, R_C, S_C)- 149d & (S_C, R_N, R_C, S_C)- 149'd	90	85
5		(S_C, S_N, R_C, S_C)- 149e & (S_C, R_N, R_C, S_C)- 149'e	90	82
6		(S_C, S_N, R_C, S_C)- 149f & (S_C, R_N, R_C, S_C)- 149'f	85	80
7		(S_C, S_N, R_C, S_C)- 149g & (S_C, R_N, R_C, S_C)- 149'g	92	85
8		(S_C, S_N, R_C, S_C)- 149h & (S_C, R_N, R_C, S_C)- 149'h	90	87

[a] Unless otherwise indicated, all reactions were performed using substrate (0.15 mmol), amine (0.15 mmol) at 60 °C for 12h under argon; [b] Calculation depend on intensity of ^{31}P NMR; [c] Isolated yield of (S_C, S_N, R_C, S_C) -**149a-h** and (S_C, R_N, R_C, S_C) -**149'a-h**

For most asymmetric hydroamination products, these pairs of isomers (S_C, S_N, R_C, S_C) -**149a-h** and (S_C, R_N, R_C, S_C) -**149'a-h** containing *N*-Chirality centers coexist and no single isomer of them was separated. Luckily, (S_C, S_N, R_C, S_C) -**149g** can be isolated and its crystal also be obtained by crystallization in DCM/Ether system at room temperature. The absolute configuration of (S_C, S_N, R_C, S_C) -**149g** was confirmed by X-ray crystallography (Figure 2.3). Selected bond distance and angle are given in Table 2.5.

Figure 2.3 Molecular structure and absolute configuration of (S_C, S_N, R_C, S_C) -**149g**

Table 2.5 Selected bond lengths (Å) and angles (deg) of (*S_C*,*S_N*,*R_C*,*S_C*)-**149g**

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

2.2.3.1 Synthesis and X-Ray Structure Analysis of Complexes (S_N , R_C , S_C) -153a-h

and (R_N, R_C, S_C) –153'a-h

Scheme 2.7

For these pairs of isomers (S_C, S_N, R_C, S_C)-**149a-h** and (S_C, R_N, R_C, S_C)-**149'a-h** containing N -chirality centers, chemoselective removal of chiral auxiliary was carried out with treatment of concentrated HCl for 1 h. N -chirality center neutral dichloro complexes pairs of (S_N, R_C, S_C)-**153a-h** and (R_N, R_C, S_C)-**153'a-h** were obtained as co-products.

After standard workup and purification by column chromatography, pure mixture of (*S_N*,*R_C*,*S_C*)-**153a-h** and (*R_N*,*R_C*,*S_C*)-**153'a-h** were obtained as isomer pair. Co-crystals for the neutral dichloro complexes (*S_N*,*R_C*,*S_C*)-**153a-h** and (*R_N*,*R_C*,*S_C*)-**153'a-h** were obtained in dichloromethane and diethyl ether system at room temperature. Their absolute configuration was confirmed by X-ray crystallography (Figure 2.4 to Figure 2.7). For the neutral dichloro complexes (*S_N*,*R_C*,*S_C*)-**153a-h** and (*R_N*,*R_C*,*S_C*)-**153'a-h**, they appear as co-crystal in the same unit cell. Actually, it is not necessary to separated the co-product of (*S_N*,*R_C*,*S_C*)-**153a-h** and (*R_N*,*R_C*,*S_C*)-**153'a-h** because the same free ligands (*R_C*,*S_C*)-**154a-h** were obtained after liberation. The X-ray structural analysis of (*S_N*,*R_C*,*S_C*)-**153a-h** and (*R_N*,*R_C*,*S_C*)-**153'a-h** establishes unambiguously that the desired aminophosphine P,N bidentate chelate was formed regiospecifically and stereoselectively on the palladium center. Selected bond distances and angles are given in Table 2.6, Table2.7, Table2.8 and Table2.9.

Figure 2.4 Molecular structure and absolute configuration of (*S_N*,*R_C*,*S_C*)-**153a** and (*R_N*,*R_C*,*S_C*)-**153'a**

Table 2.6 Selected bond lengths (Å) and angles (deg) of dichloro complex
(S_N, R_C, S_C)-**153a** and (R_N, R_C, S_C)-**153'a**

Pd(1)-N(1)	2.103(4)	Pd(1)-P(1)	2.206(2)
Pd(1)-Cl(2)	2.281(1)	Pd(1)-Cl(1)	2.365(1)
C(1)-N(1)	1.464(6)	C(7)-N(1)	1.500(6)
C(7)-C(8)	1.504(6)	C(7)-C(10)	1.532(6)
C(8)-O(1)	1.320(16)	C(8)-O(2)	1.206(5)
C(9)-O(1)	1.446(18)	C(10)-C(11)	1.510(10)
C(10)-P(1)	1.873(5)	C(13)-P(1)	1.813(4)
C(19)-P(1)	1.812(4)		
N(1)-Pd(1)-P(1)	87.3(1)	N(1)-Pd(1)-Cl(2)	176.4(1)
P(1)-Pd(1)-Cl(2)	90.3(1)	N(1)-Pd(1)-Cl(1)	89.5(1)
P(1)-Pd(1)-Cl(1)	176.62(5)	Cl(2)-Pd(1)-Cl(1)	92.97(5)
N(1)-C(7)-C(8)	110.5(4)	N(1)-C(7)-C(10)	111.3(3)
C(8)-C(7)-C(10)	111.5(3)	C(11)-C(10)-C(7)	113.3(7)
C(11)-C(10)-P(1)	113.3(7)	C(7)-C(10)-P(1)	106.3(3)
C(1)-N(1)-C(7)	115.1(3)	C(1)-N(1)-Pd(1)	113.6(3)
C(7)-N(1)-Pd(1)	112.0(3)	C(25)-N(2)-C(31)	110.4(3)
C(25)-N(2)-Pd(2)	116.4(3)	C(19)-P(1)-C(13)	105.5(2)
C(19)-P(1)-C(10)	106.1(2)	C(13)-P(1)-C(10)	108.4(2)
C(19)-P(1)-Pd(1)	114.9(2)	C(13)-P(1)-Pd(1)	119.8(2)
C(10)-P(1)-Pd(1)	101.2(1)	C(37)-P(2)-C(43)	107.6(3)

Figure 2.5 Molecular structure and absolute configuration of (S_N, R_C, S_C)-**153b** and (R_N, R_C, S_C)-**153'b**

Table 2.7 Selected bond lengths (Å) and angles (deg) of dichloro complex (S_N, R_C, S_C)-**153b** and (R_N, R_C, S_C)-**153'b**

Pd(1)-N(1)	2.101(6)	Pd(1)-P(1)	2.212(2)
Pd(1)-Cl(2)	2.299(2)	Pd(1)-Cl(1)	2.369(2)
C(1)-O(1)	1.435(8)	C(2)-O(1)	1.373(8)
C(7)-N(1)	1.469(8)	C(8)-N(1)	1.494(8)
C(8)-C(9)	1.537(9)	C(8)-C(11)	1.544(8)
C(9)-O(2)	1.201(8)	C(9)-O(3)	1.301(14)
C(10)-O(3)	1.464(15)	C(11)-P(1)	1.854(6)
C(14)-P(1)	1.821(7)	C(20)-P(1)	1.810(6)
N(1)-Pd(1)-P(1)	85.9(2)	N(1)-Pd(1)-Cl(2)	175.5(2)
P(1)-Pd(1)-Cl(2)	89.6(1)	N(1)-Pd(1)-Cl(1)	92.3(2)
P(1)-Pd(1)-Cl(1)	175.4(1)	Cl(2)-Pd(1)-Cl(1)	92.2(1)
N(1)-C(8)-C(9)	110.0(5)	N(1)-C(8)-C(11)	108.6(5)
C(9)-C(8)-C(11)	113.7(5)	C(7)-N(1)-C(8)	110.3(5)
C(7)-N(1)-Pd(1)	116.9(4)	C(8)-N(1)-Pd(1)	113.6(4)
C(20)-P(1)-C(14)	109.0(3)	C(20)-P(1)-C(11)	107.3(3)
C(14)-P(1)-C(11)	107.9(3)	C(20)-P(1)-Pd(1)	116.7(2)
C(14)-P(1)-Pd(1)	114.3(2)	C(11)-P(1)-Pd(1)	100.9(2)

Figure 2.6 Molecular structure and absolute configuration of (S_N, R_C, S_C)-**153f** and (R_N, R_C, S_C)-**153'f**

Table 2.8 Selected bond lengths (Å) and angles (deg) of dichloro complex
(S_N, R_C, S_C)-**153f** and (R_N, R_C, S_C)-**153'f**

Pd(1)-N(1)	2.100(2)	Pd(1)-P(1)	2.210(1)
Pd(1)-Cl(2)	2.297(1)	Pd(1)-Cl(1)	2.369(1)
C(1)-N(1)	1.447(3)	C(8)-N(1)	1.503(3)
C(8)-C(11)	1.530(3)	C(8)-C(9)	1.531(3)
C(9)-O(1)	1.208(3)	C(9)-O(2)	1.330(3)
C(10)-O(2)	1.455(4)	C(11)-C(12)	1.507(4)
C(11)-P(1)	1.854(2)	C(14)-P(1)	1.805(3)
C(20)-P(1)	1.807(3)	C(26)-N(2)	1.458(3)
N(1)-Pd(1)-P(1)	86.5(1)	N(1)-Pd(1)-Cl(2)	175.2(1)
P(1)-Pd(1)-Cl(2)	89.4(1)	N(1)-Pd(1)-Cl(1)	90.9(1)
P(1)-Pd(1)-Cl(1)	174.2(1)	Cl(2)-Pd(1)-Cl(1)	93.5(1)
N(1)-C(8)-C(11)	109.1(2)	N(1)-C(8)-C(9)	108.6(2)
C(1)-N(1)-C(8)	111.6(2)	C(1)-N(1)-Pd(1)	115.6(2)
C(8)-N(1)-Pd(1)	111.8(2)	C(26)-N(2)-C(33)	116.5(2)
C(26)-N(2)-Pd(2)	112.8(1)	C(14)-P(1)-C(20)	107.8(1)
C(14)-P(1)-C(11)	106.3(1)	C(20)-P(1)-C(11)	108.7(1)
C(14)-P(1)-Pd(1)	114.9(1)	C(20)-P(1)-Pd(1)	117.1(1)
C(11)-P(1)-Pd(1)	101.3(1)	C(39)-P(2)-C(45)	105.3(1)
C(39)-P(2)-C(36)	106.0(1)	C(45)-P(2)-C(36)	108.8(1)
C(39)-P(2)-Pd(2)	115.2(1)	C(45)-P(2)-Pd(2)	118.9(1)
C(36)-P(2)-Pd(2)	101.9(1)

Figure 2.7 Molecular structure and absolute configuration of (S_N, R_C, S_C) -**153h** and (R_N, R_C, S_C) -**153'h**

Table 2.9 Selected bond lengths (Å) and angles (deg) of dichloro complex*(S_N,R_C,S_C)-153h* and *(R_N,R_C,S_C)-153'h*

Pd(1)-N(1)	2.101(9)	Pd(1)-P(1)	2.218(3)
Pd(1)-Cl(2)	2.276(3)	Pd(1)-Cl(1)	2.355(3)
C(4)-N(2)	1.495(14)	C(7)-N(1)	1.489(13)
C(7)-C(8)	1.534(14)	C(7)-C(10)	1.565(14)
C(8)-O(1)	1.181(16)	C(8)-O(2)	1.316(13)
C(9)-O(2)	1.466(18)	C(10)-P(1)	1.881(10)
C(13)-P(1)	1.813(9)	C(19)-P(1)	1.838(10)
N(2)-O(5)	1.217(17)	N(2)-O(6)	1.230(16)
N(1)-Pd(1)-P(1)	86.3(3)	N(1)-Pd(1)-Cl(2)	175.5(3)
P(1)-Pd(1)-Cl(2)	91.7(1)	N(1)-Pd(1)-Cl(1)	91.8(3)
P(1)-Pd(1)-Cl(1)	177.4(2)	Cl(2)-Pd(1)-Cl(1)	90.4(1)
C(2)-C(1)-N(1)	120.3(10)	C(6)-C(1)-N(1)	117.5(10)
N(1)-C(7)-C(8)	109.9(8)	N(1)-C(7)-C(10)	110.6(8)
C(8)-C(7)-C(10)	107.6(8)	C(11)-C(10)-C(7)	110.1(7)
C(11)-C(10)-P(1)	117.1(7)	C(7)-C(10)-P(1)	104.9(6)
C(1)-N(1)-C(7)	111.1(9)	C(1)-N(1)-Pd(1)	113.7(8)
C(7)-N(1)-Pd(1)	112.4(6)	O(5)-N(2)-O(6)	125.3(11)
O(5)-N(2)-C(4)	117.3(12)	O(6)-N(2)-C(4)	117.3(12)
C(13)-P(1)-C(19)	108.5(4)	C(13)-P(1)-C(10)	104.4(4)
C(19)-P(1)-C(10)	108.1(5)	C(13)-P(1)-Pd(1)	120.7(3)
C(19)-P(1)-Pd(1)	111.6(4)	C(10)-P(1)-Pd(1)	102.5(3)

2.2.3.2 Synthesis of Optically Pure Free Ligands (*R_C, S_C*)-154 via Liberation **Scheme 2.8**

For the isomer mixture of (*S_N*,*R_C*,*S_C*)-**153a-h** and (*R_N*,*R_C*,*S_C*)-**153'a-h** containing *N*-chirality centers, the same free ligands of optically pure (*R_C*,*S_C*)-**154a-h** were obtained after liberation in potassium cyanide because the N atom do not coordinate to metal center and *N*-chirality do not observed any more. After removal of solvent, optically pure free ligands (*R_C*,*S_C*)-**154a-h** were obtained and their signal of ³¹P NMR spectrum and optical rotation data were recorded in Table 2.10

Table 2.10 Data of free ligands of (*R_C*,*S_C*)-**154a-h**

Entry	Free ligands	³¹ P NMR /δ	[α] _D (c 0.5, DCM)	Yield%
1	(<i>R_C</i> , <i>S_C</i>)- 154a	-9.5	-112	92
2	(<i>R_C</i> , <i>S_C</i>)- 154b	-9.4	-102	93
3	(<i>R_C</i> , <i>S_C</i>)- 154c	-9.3	-92	93
4	(<i>R_C</i> , <i>S_C</i>)- 154d	-9.6	-94	92
5	(<i>R_C</i> , <i>S_C</i>)- 154e	-9.5	-82	90
6	(<i>R_C</i> , <i>S_C</i>)- 154f	-9.5	-88	91
7	(<i>R_C</i> , <i>S_C</i>)- 154g	-11.8	-46	93
8	(<i>R_C</i> , <i>S_C</i>)- 154h	-9.8	-84	89

2.2.3.3 Reoordination of Optically Pure Free Ligands (R_C, S_C)-**154a-h**

Scheme 2.9

In order to confirm the optical purity of these free ligands, the liberated optically pure free ligands (R_C, S_C)-**154a-h** were reoordinated to the chiral template (S)-**49**. After these free ligands were reoordinated to the (S)-**49**, relevant signal of ^{31}P NMR spectrum were observed which are consistent with the signals of asymmetric hydroamination products (S_C, S_N, R_C, S_C)-**149a-h** and (S_C, R_N, R_C, S_C)-**149'a-h** respectively.

2.2.4 Synthesis of Gold (I) Complexes

Scheme 2.10

Gold complexes have been one of most important potential catalysis and considered

as the candidates of anticancer and antitumor. When the fresh free ligands (R_C , S_C)-**148a** and (R_C , S_C)-**148b** were reacted with one equivalents chloro dimethylsulfide gold (I) respectively, gold complexes (R_C , S_C)-**155a** and (R_C , S_C)-**155b** were generated. The same results were observed even though two equivalents chloro dimethylsulfide gold (I) were employed because this N donor can not coordinate to the Gold centers as monodentate. However, these monodentate gold complexes (R_C , S_C)-**155a** and (R_C , S_C)-**155b** are not stable and very easy to undergo an elimination reaction to form **156** (Scheme 2.10).

Scheme 2.11

For aryl amino P,N containing ligands (R_C , S_C)-**154a-h**, only monodentate gold(I) complexes were obtained even though two equivalents chloro dimethylsulfide gold (I) were employed in this coordination reaction. Comparison to the monodentate gold (I) complexes of (R_C , S_C)-**155a** and (R_C , S_C)-**155b**, gold (I) complexes (R_C , S_C)-**157** are more stable and they can be analyzed by NMR and tested via optical rotation.

Table 2.11 Gold (I) complexes of (*R_C,S_C*)-**157a-h**^[a]

Entry	Products	³¹ P NMR /δ	[α] _D (c 0.5, DCM)	Yields ^[b] %
1	(<i>R_C,S_C</i>)- 157a	36.1	-40	97
2	(<i>R_C,S_C</i>)- 157b	36.0	-44	98
3	(<i>R_C,S_C</i>)- 157c	36.2	-38	90
4	(<i>R_C,S_C</i>)- 157d	36.2	-28	96
5	(<i>R_C,S_C</i>)- 157e	36.1	-26	95
6	(<i>R_C,S_C</i>)- 157f	36.2	-30	98
7	(<i>R_C,S_C</i>)- 157h	35.3	-68	91

[a] Unless otherwise indicated, all reactions were performed using free ligands (*R_C,S_C*)-**157** (0.1 mmol), chloro (dimethylsulfide) Gold(I) (0.1 mmol) at room temperature for 30 min under argon; [b] Isolated yield

2.3 Conclusion

From a mechanistic standpoint, it is proposed that the simultaneous coordination of phosphine functionalized dimethyl 2-(diphenylphosphino)maleate and amines on the chiral palladium template polarized the N-H bond and the C=C bonds concurrently. The more bulky amines diisopropylamine and 2, 6-diisopropylaniline were applied in this reaction and no desired products were observed, this maybe attribute to the steric effect so that they can not be coordinated to the metal center efficiently. This further provided the evidence supporting the mechanism. An intermediate involving the deprotonation of the highly reactive coordinated amido ligand could thus be generated. This nucleophilic amido moiety subsequently undergoes addition to the activated alkene and an intramolecular hydroamination reaction occurs. In conclusion, an

effective method for the synthesis of ester functionalized chiral β -P,N ligands via chiral organopalladium template promoted asymmetric hydroamination reaction has been demonstrated. The hydroamination reactions proceed with high regio- and stereo selectivities under mild conditions. Further investigations on the catalytic properties of transition metal complexes and biological activities involving the new β -P,N ligands are currently in progress.

2.4 Experimental Section

Reactions involving air-sensitive compounds were performed under an inert atmosphere of argon using standard Schlenk techniques. Solvents were dried and freshly distilled according to standard procedures and degassed prior to use when necessary. The ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR spectra were recorded at 25 °C on Bruker ACF 300 and 400 spectrometers. Optical rotations were measured on the specified solution in a 0.1 dm cell at 20 °C with a Perkin-Elmer 341 polarimeter. Elemental analysis was performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at the Nanyang Technological University. Melting points were measured using the SRS Optimelt automated melting point system, SRS MPA100.

The chiral palladium templates (*S*)-**33**^[47] and (*S*)-**49**^[58] were prepared as previously reported.

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

2.4.1 Preparation of (*S*)-Chloro{1-[(1-dimethylamino)ethyl]-2-naphthalenyl-C,N}

[(diphenylphosphino)maleate] Palladium (II), (S)-141

To the solution of (S)-**33** (1300 mg, 1.91 mmol) in dichloromethane (200 mL) at -78 °C was slowly added diphenylphosphine (711 mg, 3.82 mmol) in dichloromethane (5 mL), and the mixture was stirred at -78 °C for 1h. Then, the dimethyl acetylenedicarboxylate (543 mg, 3.82 mmol) was added to the above solution and the triethylamine (387 mg, 3.82 mmol) was added subsequently. After the mixture was stirred for 4 h at -78 °C, the temperature was allowed to increase to room temperature slowly and continued to stir for another 10h at the same temperature. The reaction was monitored by ^{31}P NMR and the mixture was concentrated after reaction completed. The crude product was purified by column chromatography to give 1500 mg of (S)-**141** as a yellow foam solid (58.8% yield).

Yellow foam: mp 120–123 °C; 58.8% yield; $[\alpha]_{\text{D}} = +38^{\circ}$ (c 0.5, CH_2Cl_2) at 20 °C; ^{31}P NMR (162 MHz, CDCl_3): δ 41.7; ^1H NMR (400 MHz, CDCl_3): δ 7.94–7.99 (m, 2H, Ar), 7.71–7.76 (m, 3H, Ar), 7.63–7.65 (m, 1H, Ar), 7.39–7.54 (m, 5H, Ar), 7.29–7.36 (m, 3H, Ar), 7.02 (d, $J_{\text{PH}} = 8.6$ Hz, 1H, $\text{PC}=\text{CH}$), 6.67–6.72 (m, 2H, Ar), 4.38 (m, 1H, MeCH), 3.71 (s, 3H, COOMe), 3.52 (s, 3H, COOMe), 2.98 (d, $J_{\text{PH}} = 3.6$ Hz, 3H, NMe), 2.76 (d, $J_{\text{HH}} = 1.5$ Hz, 3H, NMe), 2.06 (d, $J_{\text{HH}} = 6.4$ Hz, 3H, CHMe); ^{13}C NMR (100 MHz, CDCl_3): δ 165.4 (d, $J_{\text{PC}} = 7.3$ Hz), 164.5 (d, $J_{\text{PC}} = 17.6$ Hz), 149.7, 149.2 (d, $J_{\text{PC}} = 1.9$ Hz), 142.4 (d, $J_{\text{PC}} = 33.8$ Hz), 136.2 (d, $J_{\text{PC}} = 10.4$ Hz), 135.8 (d, $J_{\text{PC}} = 12.2$ Hz),

135.6, 135.5, 135.3, 135.2, 131.4 (d, $J_{\text{PC}} = 2.3$ Hz), 131.3 (d, $J_{\text{PC}} = 2.4$ Hz), 131.2, 128.8, 128.68, 128.66, 128.5, 128.3, 128.2, 127.8 (d, $J_{\text{PC}} = 110.0$ Hz), 127.7 (d, $J_{\text{PC}} = 11.2$ Hz), 125.8, 124.8 (d, $J_{\text{PC}} = 5.9$ Hz), 124.2, 123.3, 73.3 (d, $J_{\text{PC}} = 3.4$ Hz), 52.4, 52.3, 51.3 (d, $J_{\text{PC}} = 3.1$ Hz), 48.7 (d, $J_{\text{PC}} = 2.9$ Hz), 23.7

2.4.2 Asymmetric Hydroamination with Alkyl Amines

A solution of the monochloro complex of (*S*)-**141** (100 mg, 0.15 mmol) in dichloromethane (3 mL) was treated with silver perchlorate (68 mg, 0.30 mmol) in water (1 mL) for 30 min. The mixture was then filtered through Celite, washed with water, dried over MgSO_4 and the solvent was removed under reduced pressure. The resulting perchloro complex was dissolved in dichloromethane (3 mL) and cooled to -40 °C. The diethylamine (11 mg, 0.15 mmol) in DCM was added to the solution and the mixture was stirred for 16 h at -40 °C. Removal of the solvent gave the crude hydroamination product. The crude product was used to the next step directly in which chiral template auxiliary was removed without further purification.

{(*S_C*)-1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*}[(*2R_C*,*3S_C*)-dimethyl-2-(dimethylamino)-3-(diphenylphosphino)succinate-*N*²,*P*] palladium (II) Perchlorate, (*S_C*, *R_C*, *S_C*)-143a****

³¹P NMR (162 MHz, CDCl_3): δ 46.1; ¹H NMR (400 MHz, CDCl_3): δ 7.91–7.98 (m, 2H, Ar), 7.53–7.91 (m, 7H, Ar), 7.31–7.43 (m, 5H, Ar), 7.03 (d, $J_{\text{PH}} = 8.7$ Hz, 1H, Ar),

6.60–6.65 (m, 1H, Ar), 4.31– 4.45 (m, 2H, CHMe, NCH), 3.94– 4.01 (m, 1H, PCH), 3.78 (s, 3H, COOMe), 3.32 (s, 3H, COOMe), 3.21 (s, 3H, NMe), 3.00 (d, $J_{\text{PH}} = 3.6$ Hz, 3H, NMe), 2.75-2.83 (m, 6H, NMe₂), 1.87 (d, $J_{\text{HH}} = 6.6$ Hz, 3H, CHMe).

{(*S_C*)-1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*}[(*2R_C*,*3S_C*)-dimethyl-2-(diethylamino)-3-(diphenylphosphino)succinate-*N*²,*P*] palladium (II) Perchlorate, (*S_C*, *R_C*, *S_C*)-143b

³¹P NMR of (*S_C*, *R_C*, *S_C*)-143b was shown as followed: ³¹P NMR (400MHz, CDCl₃): δ 45.1

Preparation of Dichloro Complexes (*R_C*,*S_C*)-147

A solution of above crude hydroamination products (*S_C*,*R_C*,*S_C*)-143a,b in dichloromethane (10 mL) was treated with concentrated hydrochloric acid (10 mL) at room temperature for 24 h. The reaction mixture was then diluted with dichloromethane (20 mL), washed with water (3 × 10 mL) and dried over anhydrous MgSO₄. After removal of solvent and purification by column chromatography, the dichloro complexes were obtained as a yellow solid. These dichloro complexes were readily grown crystal from dichloromethane and diethyl ether to give the (*R_C*,*S_C*)-147a and (*R_C*,*S_C*)-147b as an yellow prism crystal respectively.

Dichloro[(*2R_C*,*3S_C*)-dimethyl-2-(dimethylamino)-3-(diphenylphosphino)succinate

-*N,P*] palladium (II), (*R_C*,*S_C*)-147a

(*R_C*,*S_C*)-147 a

$[\alpha]_D = +82^\circ$ (*c* 0.5, CH₂Cl₂); mp 190–191°C; Anal. Calcd for C₂₀H₂₄Cl₂NO₄PPd : C, 43.6; H, 4.4; N, 2.5; Found: C, 43.5; H, 4.4; N, 2.6; ³¹P NMR (202 MHz, CDCl₃): δ 42.3; ¹H NMR (500 MHz, CDCl₃): δ 7.91–8.01 (m, 4H, Ar), 7.62–7.66 (m, 2H, Ar), 7.51–7.56 (m, 4H, Ar), 4.57 (dd, *J*_{HH} = 13.2 Hz, *J*_{PH} = 8.1 Hz, 1H, *PCH*), 4.06 (dd, *J*_{HH} = 13.2 Hz, *J*_{PH} = 7.9 Hz, 1H, *NCH*), 3.79 (s, 3H, COOMe), 3.39 (s, 3H, COOMe), 3.36 (s, 3H, NMe), 2.94 (s, 3H, NMe); ¹³C NMR (125 MHz, CDCl₃): δ 165.6 (d, *J*_{PC} = 25.5 Hz), 165.2 (d, *J*_{PC} = 8.7 Hz), 135.2, 135.1, 133.6 (d, *J*_{PC} = 1.4 Hz), 133.5, 133.4, 132.7 (d, *J*_{PC} = 3.1 Hz), 129.3, 129.2, 129.0, 128.9, 124.8 (d, *J*_{PC} = 61.3 Hz), 123.4 (d, *J*_{PC} = 55.2 Hz), 74.5 (d, *J*_{PC} = 10.5 Hz), 53.4, 53.3, 52.9, 49.8 (d, *J*_{PC} = 17.7 Hz), 46.7

Dichloro[(2*R_C*,3*S_C*)-dimethyl-2-(diethylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*R_C*,*S_C*)-147b

(*R_C*,*S_C*)-147 b

$[\alpha]_D = +50^\circ$ (*c* 0.5, CH₂Cl₂); mp 170–171 °C; Anal. Calcd for C₂₂H₂₈Cl₂NO₄PPd: C, 45.7; H, 4.9; N, 2.4; Found: C, 45.5; H, 4.8; N, 2.2; ³¹P NMR (202 MHz, CDCl₃): δ 42.5; ¹H NMR (500 MHz, CDCl₃): δ 8.01–8.05 (m, 2H, Ar), 7.84–7.88 (m, 2H, Ar),

7.60–7.66 (m, 2H, Ar), 7.48–7.56 (m, 4H, Ar), 4.82 (dd, $J_{\text{HH}} = 13.3$ Hz, $J_{\text{PH}} = 9.1$ Hz, 1H, *PCH*), 4.50 (dd, $J_{\text{HH}} = 13.3$ Hz, $J_{\text{PH}} = 5.9$ Hz, 1H, *NCH*), 4.12–4.18 (m, 1H, *CH*₂*CH*₃), 3.81 (s, 3H, *COOMe*), 3.46–3.53 (m, 1H, *CH*₂*CH*₃), 3.39 (s, 3H, *COOMe*), 2.70–2.86 (m, 2H, *CH*₂*CH*₃), 1.92 (t, $J_{\text{HH}} = 6.9$ Hz, 3H, *CH*₂*CH*₃), 1.83 (t, $J_{\text{HH}} = 7.3$ Hz, 3H, *CH*₂*CH*₃); ¹³C NMR (125 MHz, CDCl₃): δ 166.3 (d, $J_{\text{PC}} = 25.0$ Hz), 165.9 (d, $J_{\text{PC}} = 8.4$ Hz), 134.9, 134.8, 133.7, 133.6, 133.3 (d, $J_{\text{PC}} = 2.8$ Hz), 132.6 (d, $J_{\text{PC}} = 2.9$ Hz), 129.10, 129.06, 129.01, 128.97, 125.5 (d, $J_{\text{PC}} = 60.7$ Hz), 124.1 (d, $J_{\text{PC}} = 56.2$ Hz), 68.8 (d, $J_{\text{PC}} = 10.3$ Hz), 56.7, 56.3, 53.3, 52.8, 51.9 (d, $J_{\text{PC}} = 17.6$ Hz), 15.8, 14.3.

Synthesis of Free Ligand (*R*_C, *S*_C)-148

A solution of the dichloro complex (*R*_C, *S*_C)-147a (165 mg, 0.3 mmol) in CH₂Cl₂ (10 mL) was treated with excess potassium cyanide (0.20 g, 3 mmol) in water (2 mL). The reaction mixture was stirred vigorously at room temperature for 10 min. The colorless organic layer was separated, washed with water (3 × 5 mL) and dried over anhydrous MgSO₄. Upon the removal of the solvent under reduced pressure, free ligand (*R*_C, *S*_C)-148a was obtained respectively as a pale yellow oil.

(2*R*_C, 3*S*_C)-dimethyl 2-(dimethylamino)-3-(diphenylphosphino)succinate, (*R*_C, *S*_C)-148a

Pale yellow oil: (103 mg, 92% yield); $[\alpha]_{\text{D}} = -222^\circ$ (*c* 0.5, DCM); ³¹P NMR (162

MHz, CDCl₃): δ -8.1; **¹H NMR** (400MHz, CDCl₃): δ 7.64–7.68 (m, 2H, Ar), 7.52–7.55 (m, 2H, Ar), 7.31–7.38 (m, 6H, Ar), 3.89 (dd, $J_{\text{HH}} = 12$ Hz, $J_{\text{PH}} = 2.4$ Hz, 1H, NCH), 3.81 (dd, $J_{\text{HH}} = 12$ Hz, $J_{\text{PH}} = 4.8$ Hz, 1H, PCH), 3.69 (s, 3H, COOMe), 3.06 (s, 3H, COOMe), 2.12 (s, 6H); **¹³C NMR** (100 MHz, CDCl₃): δ 171.4 (d, $J_{\text{PC}} = 9.1$ Hz), 171.1 (d, $J_{\text{PC}} = 25$ Hz), 136.2 (d, $J_{\text{PC}} = 15.3$ Hz), 135.1 (d, $J_{\text{PC}} = 18.4$ Hz), 134.8, 134.6, 133.7, 133.5, 129.2, 128.6, 128.2, 128.1, 128.0, 127.9, 67.8 (d, $J_{\text{PC}} = 19.6$ Hz), 51.2, 51.1, 46.4 (d, $J_{\text{PC}} = 22.2$ Hz), 41.8.

(2*R*_C, 3*S*_C)-dimethyl 2-(diethylamino)-3-(diphenylphosphino)succinate, (*R*_C,*S*_C)-148b

The same procedure was used to the synthesis of (*S*)-**148b**.

Pale yellow oil (108 mg, 90% yield) from dichloro complex (*R*_C,*S*_C)-**147b** (174 mg, 0.3 mmol); $[\alpha]_{\text{D}} = -134^\circ$ (c 0.5, DCM); **³¹P NMR** (162 MHz, CDCl₃): δ -8.7; **¹H NMR** (400MHz, CDCl₃): δ 7.71–7.75 (m, 2H, Ar), 7.39–7.50 (m, 5H, Ar), 7.29–7.31 (m, 3H, Ar), 4.12 (dd, $J_{\text{HH}} = 12$ Hz, $J_{\text{PH}} = 5.4$ Hz, 1H, PCH), 3.96 (d, $J_{\text{HH}} = 12$ Hz, 1H, NCH), 3.69 (s, 3H, COOMe), 3.02 (s, 3H, COOMe), 2.49–2.56 (m, 2H, CH₂CH₃), 2.31–2.40 (m, 2H, CH₂CH₃), 0.78 (t, $J_{\text{HH}} = 7.1$ Hz, 6H, CH₂CH₃); **¹³C NMR** (100 MHz, CDCl₃): δ 172.5 (d, $J_{\text{PC}} = 10.8$ Hz), 171.3 (d, $J_{\text{PC}} = 1.4$ Hz), 136.3 (d, $J_{\text{PC}} = 15.4$ Hz), 135.9 (d, $J_{\text{PC}} = 19.4$ Hz), 134.7, 134.5, 134.1, 133.8, 128.90, 128.88, 128.4,

128.3, 127.9, 127.8, 64.4 (d, $J_{\text{PC}} = 23.5$ Hz), 51.2, 50.1, 46.7 (d, $J_{\text{PC}} = 21.7$ Hz), 44.6, 12.9

2.4.3 Asymmetric Hydroamination with Alaryl Amines

A solution of the monochloro complex of (*S*)-**141** (100 mg, 0.15 mmol) in dichloromethane (3 mL) was treated with silver perchlorate (68 mg, 0.30 mmol) in water (1 mL) for 30 min. The mixture was then filtered through Celite washed with water, and dried over MgSO_4 and the solvent was removed under reduced pressure. The resulting perchloro complex was dissolved in chloroform and the anilines (10.4 mg, 0.15 mmol) in chloroform (1 mL) was added to above solution and the mixture was stirred for 16 h at 60 °C. Removal of the solvent gave the crude hydroamination products (S_C, S_N, R_C, S_C)-**149a** and (S_C, R_N, R_C, S_C)-**149'a** as mixture of two isomers (Table 2.12). Without further purification, the crude products were used to the next step directly in which chiral template auxiliary was removed.

Table 2.12 Data of hydroamination products (S_C, S_N, R_C, S_C)-**149** and (S_C, R_N, R_C, S_C)-**149'**

Entries	Amines	Products	^{31}P NMR/ δ	Ratio ^[a]
1		(S_C, S_N, R_C, S_C)- 149a , (S_C, R_N, R_C, S_C)- 149'a	49.6, 46.6	3.3/ 1
2		(S_C, S_N, R_C, S_C)- 149b , (S_C, R_N, R_C, S_C)- 149'b	49.3, 48.6	1/ 3.1
3		(S_C, S_N, R_C, S_C)- 149c , (S_C, R_N, R_C, S_C)- 149'c	50.1, 46.4	2.9/ 1

4		(S_C, S_N, R_C, S_C) - 149d , (S_C, R_N, R_C, S_C) - 149'd	49.7, 45.9	3.3/ 1
5		(S_C, S_N, R_C, S_C) - 149e , (S_C, R_N, R_C, S_C) - 149'e	50.3, 46.5	3.1/ 1
6		(S_C, S_N, R_C, S_C) - 149f , (S_C, R_N, R_C, S_C) - 149'f	49.5, 45.9	4/ 1
7		(S_C, S_N, R_C, S_C) - 149g , (S_C, R_N, R_C, S_C) - 149'g	54.9, 44.3	1/ 3.1
8		(S_C, S_N, R_C, S_C) - 149h , (S_C, R_N, R_C, S_C) - 149'h	48.0, 45.4	8/ 1

[a] Mixture ratio was determined by intensity of ^{31}P NMR

{ (S_C) -1-[(1-dimethylamino)ethyl]-2-naphthalenyl- C, N^1 }[$(2S_N, 2R_C, 3S_C)$ -dimethyl-2-(2,4,6-trimethylphenylamino)-3-(diphenylphosphino)succinate- N^2, P] Palladium

(II) Perchlorate, (S_C, S_N, R_C, S_C) -**149g**

Pale yellow prism crystal: mp 180-182 °C; 60% yield; $[\alpha]_D = +164^\circ$ (c 0.5, CH_2Cl_2);

Anal. Calcd for $\text{C}_{41}\text{H}_{46}\text{ClN}_2\text{O}_8\text{PPd}$: C, 56.8, H, 5.3; N, 3.2, Found: C, 54.9; H, 5.0; N,

3.4; ^{31}P NMR (162 MHz, CDCl_3): δ 44.3; ^1H NMR (400 MHz, CDCl_3): δ 8.05-8.15

(m, 4H, Ar), 7.77-7.81 (m, 1H, Ar), 7.66-7.70 (m, 2H, Ar), 7.58-7.61 (m, 2H, Ar),

7.29-7.40 (m, 5H, Ar), 7.05-7.07 (m, 1H, Ar), 6.89-6.92 (m, 3H, Ar), 6.30 (d, $J_{\text{HH}} =$

12.2 Hz, 1H, Ar), 5.13 (dd, $J_{\text{HH}} = 12.7$ Hz, $J_{\text{PH}} = 8.8$ Hz, 1H, *PCH*), 4.11-4.17 (m, 1H, *CH₃CH*), 3.94-4.03 (m, 1H, *NCH*), 3.53 (s, 3H, *COOMe*), 3.47 (s, 3H, *COOMe*), 3.19 (s, 3H, *CCH₃*), 2.56 (s, 3H, *NMe*), 2.33 (d, $J_{\text{PH}} = 3.7$ Hz, 3H, *NMe*), 2.27 (s, 6H, *CMe*), 1.91 (d, $J_{\text{HH}} = 6.4$ Hz, 3H, *CHMe*); ^{13}C NMR (100 MHz, CDCl_3): δ 168.1 (d, $J_{\text{PC}} = 19.2$ Hz), 167.3 (d, $J_{\text{PC}} = 9.0$ Hz), 149.3 (d, $J_{\text{PC}} = 2.7$ Hz), 144.1, 137.4, 136.9, 136.7, 136.6, 134.8, 134.7, 133.8 (d, $J_{\text{PC}} = 2.6$ Hz), 133.3, 133.1, 133.0, 131.5 (d, $J_{\text{PC}} = 3.8$ Hz), 131.4, 131.3, 130.7, 129.9, 129.6, 129.5, 129.0, 128.9, 128.7, 128.5, 126.3, 126.2, 125.94, 125.88, 125.7, 124.8, 123.3, 121.8 (d, $J_{\text{PC}} = 42.8$ Hz), 74.0 (d, $J_{\text{PC}} = 2.0$ Hz), 63.2 (d, $J_{\text{PC}} = 9.0$ Hz), 52.5, 52.4, 51.2 (d, $J_{\text{PC}} = 1.9$ Hz), 50.3, 50.2, 45.9, 23.8, 21.7, 20.7, 18.5.

Synthesis of (*S_N*,*R_C*,*S_C*)-**153a-h** and (*R_N*,*R_C*,*S_C*)-**153'a-h**

A solution of above crude hydroamination product mixture of (*S_C*,*S_N*,*R_C*,*S_C*)-**149a-h** and (*S_C*,*R_N*,*R_C*,*S_C*)-**149'a-h** (0.2 mmol) in dichloromethane (5 mL) was treated with concentrated hydrochloric acid (5 mL) at room temperature for 2 h. The reaction mixture was then diluted with dichloromethane (20 mL), washed with water (3 $\times$ 5 mL) and dried over anhydrous MgSO_4 . Removal of solvent gave the yellow solid, which was readily grown crystal from dichloromethane and diethyl ether to give the pair (*S_N*,*R_C*,*S_C*)-**153a-h** and (*R_N*,*R_C*,*S_C*)-**153-153'a-h** as a yellow prism crystal.

Dichloro[(2*S_N*,2*R_C*,3*S_C*)-dimethyl-2-(phenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153a** and**

Dichloro[(2*R_N*,2*R_C*,3*S_C*)-dimethyl-2-(phenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*R_N*,*R_C*,*S_C*)-153'a

Yellow crystal: mp 202-204 °C (decomp); 94% yield; $[\alpha]_D = +144^\circ$ (*c* 0.5, CH₂Cl₂); Anal Calcd. for: C₂₄H₂₄Cl₂NO₄PPd : C, 48.1; H, 4.0; N, 2.3; Found: C, 48.2; H, 3.2; N, 2.5; ³¹P NMR (162 MHz, CDCl₃): δ₁ 50.9 and δ₂ 44.5 (δ₁/ δ₂ = 0.7/ 1); ¹H NMR (400 MHz, CDCl₃): δ 7.16-8.24(m, 25.5H, Ar), 5.38-5.44(m, 1H), 4.79-4.84(m, 1.7H), 4.05-4.22(m, 0.7H), 3.48(s, 2.1H, COOMe), 3.45(s, 3H, COOMe), 3.41(s, 2.1H, COOMe), 3.14(s, 3H, COOMe).

Dichloro[(2*S_N*,2*R_C*,3*S_C*)-dimethyl-2-(2-methoxyphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153b and Dichloro[(2*R_N*,2*R_C*,3*S_C*)-dimethyl-2-(2-methoxyphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*R_N*,*R_C*,*S_C*)-153'b

Yellow solid: mp 211-213 °C; 96% yield; $[\alpha]_D = +102^\circ$ (*c* 0.5, CH₂Cl₂); Anal. Calcd for C₂₅H₂₆Cl₂NO₅PPd: C, 47.8; H, 4.2; N, 2.2; Found: C, 46.8; H, 4.8; N, 2.2; ³¹P NMR (162 MHz, CD₂Cl₂): δ₁ 48.1 and δ₂ 46.2 (δ₁/ δ₂ = 1/ 0.8); ¹H NMR (400 MHz,

CD₂Cl₂) δ : 6.94-8.51 (m, 25.2H, Ar), 6.80-6.90 (brs, 1H, *NH*), 6.50-6.60 (brs, 0.8H, *NH*), 4.95-5.07 (m, 1.8H), 4.50-4.57 (m, 1H), 4.32-4.42 (m, 1H), 4.02 (s, 3H, *OMe*), 3.59 (s, 2.4H, *OMe*), 3.43 (s, 2.4H, *COOMe*), 3.41 (s, 3H, *COOMe*), 3.80 (s, 3H, *COOMe*), 3.20 (s, 2.4H, *COOMe*).

Dichloro[(2*S_N*,2*R_C*,3*S_C*)-dimethyl-2-(3-methoxyphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153c and Dichloro[(2*R_N*,2*R_C*,3*S_C*)-dimethyl-2-(3-methoxyphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*R_N*,*R_C*,*S_C*)-153'c

Yellow solid: mp 191-193 °C (decomp); 93% yield; $[\alpha]_D = +100^\circ$ (*c* 0.5, CH₂Cl₂);
 Anal. Calcd for C₂₅H₂₆Cl₂NO₅PPd: C, 47.8, H, 4.2; N, 2.2, Found: C, 46.2; H, 4.7; N, 2.4; ³¹P NMR (162 MHz, CDCl₃): δ_1 51.1 and δ_2 44.6 ($\delta_1/\delta_2 = 0.6/1$); ¹H NMR (400 MHz, CDCl₃): δ 6.71-8.70 (m, 22.4H, Ar), 5.45 (m, 1H), 4.85-4.95 (m, 0.6H), 4.75-4.82 (m, 1H), 4.02-4.12 (m, 0.6H), 3.67 (s, 1.8H, *OMe*), 3.56 (s, 1.8H, *COOMe*), 3.54 (s, 3H, *OMe*), 3.47 (s, 1.8H, *COOMe*), 3.31 (s, 3H, *COOMe*), 3.11 (s, 3H, *COOMe*).

Dichloro[(2*S_N*,2*R_C*,3*S_C*)-dimethyl-2-(4-methoxyphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153c

no)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153d and
Dichloro[(2*R_N*,2*R_C*,3*S_C*)-dimethyl-2-(4-methoxyphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*R_N*,*R_C*,*S_C*)-153'd

Yellow solid: mp182-184 °C (decomp); 96% yield; $[\alpha]_D = +126^\circ$ (*c* 0.5, CH₂Cl₂); Anal. Calcd for C₂₅H₂₆Cl₂NO₅PPd: C, 47.8, H, 4.2; N, 2.2, Found: C, 47.6; H, 3.5; N, 3.7; ³¹P NMR (162 MHz, CDCl₃): δ₁ 51.2 and δ₂ 44.3 (δ₁/ δ₂ = 0.7/ 1); ¹H NMR (400 MHz, CDCl₃): δ 6.57-8.56 (m, 23.8H, Ar), 5.32-5.40 (m, 1H), 4.68-4.74 (m, 1.7H), 3.90-4.01 (m, 0.7H), 3.75 (s, 2.1H, *OMe*), 3.67 (s, 3H, *OMe*), 3.43 (s, 2.1H, COOMe), 3.40 (s, 3H, COOMe), 3.33 (s, 2.1H, COOMe), 3.05 (s, 3H, COOMe).

Dichloro[(2*S_N*,2*R_C*,3*S_C*)-dimethyl-2-(3-methylphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153e and
Dichloro[(2*R_N*,2*R_C*,3*S_C*)-dimethyl-2-(3-methylphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*R_N*,*R_C*,*S_C*)-153'e

Yellow solid: mp 189-191 °C (decomp); 92% yield; $[\alpha]_D = +98^\circ$ (c 0.5, CH_2Cl_2); Anal.

Calcd for $\text{C}_{25}\text{H}_{26}\text{Cl}_2\text{NO}_4\text{PPd}$: C, 49.0; H, 4.3; N, 2.3; Found: C, 48.8; H, 5.0; N, 2.3;

^{31}P NMR (162 MHz, CDCl_3): δ_1 50.9 and δ_2 44.7 ($\delta_1/\delta_2 = 0.5/1$); ^1H NMR (400 MHz, CDCl_3): δ 6.98-8.67 (m, 21H, Ar), 5.45-5.53 (m, 1H), 4.82-4.90 (m, 0.5H), 4.70-4.81 (m, 1H), 4.05-4.12 (m, 0.5H), 3.52 (s, 1.5H, COOMe), 3.50 (s, 3H, COOMe), 3.42 (s, 1.5H, COOMe), 3.12 (s, 3H, COOMe), 2.30 (s, 1.5H, CMe), 2.06 (s, 3H, CMe).

Dichloro[(2*S_N*,2*R_C*,3*S_C*)-dimethyl-2-(4-methylphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153f and

Dichloro[(2*R_N*,2*R_C*,3*S_C*)-dimethyl-2-(4-methylphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*R_N*,*R_C*,*S_C*)-153'f

Yellow solid: mp 195-197 °C (decomp); 95% yield; $[\alpha]_D = +146^\circ$ (c 0.5, CH_2Cl_2);

Anal. Calcd for $\text{C}_{25}\text{H}_{26}\text{Cl}_2\text{NO}_4\text{PPd}$: C, 49.0; H, 4.3; N, 2.3; Found: C, 48.7; H, 4.9; N,

2.2; ^{31}P NMR (162 MHz, CDCl_3): δ_1 51.1 and δ_2 44.6 ($\delta_1/\delta_2 = 0.5/1$); ^1H NMR (400 MHz, CDCl_3): δ 6.95-8.64 (m, 21H, Ar), 5.35-5.42 (m, 1H), 4.75-4.86 (m, 1.5H), 4.04-4.12 (m, 0.5H), 3.51 (s, 1.5H, COOMe), 3.48 (s, 3H, COOMe), 3.40 (s, 1.5H, COOMe), 3.13 (s, 3H, COOMe), 2.38 (s, 1.5H, CMe), 2.26 (s, 3H, CMe).

Dichloro[(2*S_N*,2*R_C*,3*S_C*)-dimethyl-2-(2,4,6-trimethylphenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153g

(*S_N*,*R_C*,*S_C*)-153 g

Yellow solid: mp 174-176 °C (decomp); 91% yield; $[\alpha]_D = +70^\circ$ (*c* 0.5, DCM); ^{31}P NMR (202 MHz, CDCl_3): δ 46.3; ^1H NMR (500MHz, CDCl_3): δ 7.94–8.03 (m, 4H, Ar), 7.67–7.68 (m, 1H, Ar), 7.52–7.68 (m, 5H, Ar), 6.87 (s, 1H, Ar), 6.76 (s, 1H, Ar), 6.04 (brs, 1H, *NH*), 4.38–4.42 (m, 1H), 4.28-4.30 (m, 1H), 3.47 (s, 3H, *COOMe*), 3.42 (s, 3H, *COOMe*), 2.88 (s, 3H, *COOMe*), 2.36 (s, 3H, *COOMe*), 2.21 (s, 3H, *COOMe*).

Dichloro[(2*S_N*,2*R_C*,3*S_C*)-dimethyl-2-(4-nitrilephenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*S_N*,*R_C*,*S_C*)-153h and Dichloro[(2*R_N*,2*R_C*,3*S_C*)-dimethyl-2-(4-nitrilephenylamino)-3-(diphenylphosphino)succinate-*N,P*] palladium (II), (*R_N*,*R_C*,*S_C*)-153'h

(*S_N*,*R_C*,*S_C*)-153 h

(*R_N*,*R_C*,*S_C*)-153' h

Yellow solid: mp 171-173 °C (decomp); 93% yield; $[\alpha]_D = +96^\circ$ (c 0.5, CH₂Cl₂) ; Anal.

Calcd for C₂₄H₂₃Cl₂N₂O₆PPd: C, 44.8; H, 3.6; N, 4.4; Found: C, 44.2; H, 4.3; N, 4.3;

³¹P NMR (162 MHz, CDCl₃): δ ₁ 50.7 and δ ₂ 45.9 (δ ₁/ δ ₂=1/ 1.3); ¹H NMR (400 MHz, CDCl₃): δ 7.34-8.68 (m, 32.2H, Ar), 5.41-5.46 (m, 1H), 4.49-4.92 (m, 2.3H), 4.22-4.26 (m, 1.3H,), 3.52 (s, 3.9H, COOMe), 3.43 (s, 3.9H, COOMe), 3.41 (s, 3.0 H, COOMe), 3.18 (s, 3.0H, COOMe).

Synthesis of Optically Pure Free Ligands (*R_C*,*S_C*)-154a-h

A solution of the dichloro complex (0.2 mmol) in DCM (5 mL) was treated with excess potassium cyanide (65 mg, 1 mmol) in water (1 mL). The reaction mixture was stirred vigorously at room temperature for 10 min. The yellow organic layer became colorless and then the organic phase was transferred to the Schlenk tube by syringe under argon. The solvent was removed by flowing N₂ and vacuum to give the free ligands in 89-93% yields.

(2*R_C*, 3*S_C*)-dimethyl 2-(phenylamino)-3-(diphenylphosphino)succinate
(*R_C*,*S_C*)-154a

Pale yellow oil; 92% yield; $[\alpha]_D = -112^\circ$ (c 0.5, DCM); ³¹P NMR (162 MHz, CDCl₃):

δ -9.5; ¹H NMR (400MHz, CDCl₃): δ 7.63–7.68 (m, 2H, Ar), 7.45–7.49 (m, 2H, Ar),

7.40–7.42 (m, 3H, Ar), 7.29–7.33 (m, 3H, Ar), 7.10–7.13 (m, 2H, Ar), 6.74 (d, $J_{\text{HH}} = 7.3$ Hz, 1H, Ar), 6.46 (d, $J_{\text{HH}} = 7.8$ Hz, 1H, Ar), 4.49–4.55 (m, 1H, NCH), 4.19 (d, $J_{\text{HH}} = 9.6$ Hz, 1H, NH), 3.91 (dd, $J_{\text{PH}} = 7.3$, $J_{\text{HH}} = 0.6$ Hz, 1H, PCH), 3.70 (s, 3H, COOMe), 3.29 (s, 3H, COOMe); ^{13}C NMR (100 MHz, CDCl_3): δ 172.4 (d, $J_{\text{PC}} = 15.4$ Hz), 170.5 (d, $J_{\text{PC}} = 2.8$ Hz), 145.8, 135.6 (d, $J_{\text{PC}} = 15.4$ Hz), 134.9 (d, $J_{\text{PC}} = 17.0$ Hz), 134.0, 133.82, 133.80, 133.6, 129.44, 129.38, 129.2, 128.7, 128.6, 128.25, 128.17, 118.8, 113.9, 57.5 (d, $J_{\text{PC}} = 20.4$ Hz), 52.4, 51.7, 48.9 (d, $J_{\text{PC}} = 26.1$ Hz).

(2*R*_C, 3*S*_C)-dimethyl 2-(2-methoxyphenylamino)-3-(diphenylphosphino)

succinate, (*R*_C,*S*_C)-154b

Colorless oil; 93% yield; $[\alpha]_{\text{D}} = -102^{\circ}$ (c 0.5, DCM); ^{31}P NMR (202 MHz, CDCl_3): δ –9.4; ^1H NMR (500MHz, CDCl_3): δ 7.64–7.67 (m, 2H, Ar), 7.44–7.47 (m, 2H, Ar), 7.38–7.40 (m, 3H, Ar), 7.30–7.32 (m, 3H, Ar), 6.75–6.78 (m, 1H, MeOAr), 6.66–6.72 (m, 2H, MeOAr), 6.44–6.46 (m, 1H, MeOAr), 4.82 (d, $J_{\text{HH}} = 9.8$ Hz, 1H, NH), 4.52–4.57 (m, 1H, NCH), 3.97 (d, $J_{\text{PH}} = 13.3$ Hz, 1H, PCH), 3.69 (s, 3H, COOMe), 3.68 (s, 3H, OMe), 3.27 (s, 3H, COOMe); ^{13}C NMR (125 MHz, CDCl_3): δ 172.4 (d, $J_{\text{PC}} = 6.3$ Hz), 170.5 (d, $J_{\text{PC}} = 2.1$ Hz), 147.1, 135.8, 135.6 (d, $J_{\text{PC}} = 15.5$ Hz), 135.0 (d, $J_{\text{PC}} = 17.3$ Hz), 134.1, 134.0, 133.7, 133.5, 129.3, 129.2, 128.6, 128.5, 128.2, 128.1, 121.0, 117.8, 110.7, 109.9, 57.1 (d, $J_{\text{PC}} = 21.4$ Hz), 55.4, 52.4, 51.7, 48.7 (d, $J_{\text{PC}} = 26.3$ Hz).

(2*R*_C, 3*S*_C)-dimethyl 2-(3-methoxyphenylamino)-3-(diphenylphosphino)

succinate (*R*_C,*S*_C)-154c

Off white oil; 93% yield; $[\alpha]_{\text{D}} = -92^{\circ}$ (*c* 0.5, DCM); ³¹P NMR (202 MHz, CDCl₃): δ – 9.3; ¹H NMR (500MHz, CDCl₃): δ 7.64–7.67 (m, 2H, Ar), 7.45–7.48 (m, 2H, Ar), 7.29–7.41 (m, 6H, Ar), 7.01 (t, $J_{\text{HH}} = 8.0$ Hz, 1H, MeOAr), 6.30–6.31 (m, 1H, MeOAr), 6.04–6.06 (m, 2H, MeOAr), 4.48–4.53 (m, 1H, NCH), 4.21 (d, $J_{\text{HH}} = 9.6$ Hz, 1H, NH), 3.92 (d, $J_{\text{PH}} = 7.8$ Hz, 1H, PCH), 3.70 (s, 3H, COOMe), 3.70(s, 3H, OMe), 3.28 (s, 3H, COOMe); ¹³C NMR (125 MHz, CDCl₃): δ 172.4 (d, $J_{\text{PC}} = 5.5$ Hz), 170.5 (d, $J_{\text{PC}} = 3.2$ Hz), 160.7, 147.2, 135.6 (d, $J_{\text{PC}} = 15.9$ Hz), 134.9 (d, $J_{\text{PC}} = 17.2$ Hz), 134.0, 133.83, 133.81, 133.6, 130.0, 129.5, 129.4, 128.72, 128.66, 128.25, 128.19, 106.5, 104.4, 99.8, 57.5 (d, $J_{\text{PC}} = 20.9$ Hz), 55.0, 52.5, 51.8, 48.9 (d, $J_{\text{PC}} = 26.4$ Hz).

(2*R*_C, 3*S*_C)-dimethyl 2-(4-methoxyphenylamino)-3-(diphenylphosphino)

succinate (*R*_C,*S*_C)-154d

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

(2*R_C*, 3*S_C*)-dimethyl 2-(3-methylphenylamino)-3-(diphenylphosphino)succinate
(*R_C*, *S_C*)-154 e

Pale yellow oil; 90% yield; $[\alpha]_D = -82^\circ$ (*c* 0.5, DCM); ^{31}P NMR (202 MHz, CDCl_3): δ -9.5; ^1H NMR (500MHz, CDCl_3): δ 7.64–7.66 (m, 2H, Ar), 7.46–7.49 (m, 2H, Ar), 7.40–7.42 (m, 3H, Ar), 7.29–7.33 (m, 3H, Ar), 7.00 (t, $J_{\text{HH}} = 7.8$ Hz, 1H, MeAr), 6.56

(d, $J_{\text{HH}} = 7.5$ Hz, 1H, *MeAr*), 6.25–6.28 (m, 2H, *MeAr*), 4.48–4.52 (m, 1H, *NCH*), 4.16 (d, $J_{\text{HH}} = 9.7$ Hz, 1H, *NH*), 3.91 (dd, $J_{\text{PH}} = 7.6$, $J_{\text{HH}} = 0.8$ Hz, 1H, *PCH*), 3.71 (s, 3H, *COOMe*), 3.30 (s, 3H, *COOMe*), 2.21 (s, 3H, *CMe*); ^{13}C NMR (125 MHz, CDCl_3): δ 172.4 (d, $J_{\text{PC}} = 2.5$ Hz), 170.5 (d, $J_{\text{PC}} = 2.8$ Hz), 145.7, 139.0, 135.7 (d, $J_{\text{PC}} = 16.1$ Hz), 135.0 (d, $J_{\text{PC}} = 17.2$ Hz), 134.0, 133.8, 133.7, 129.4, 129.3, 129.1, 128.7, 128.6, 128.24, 128.18, 119.8, 114.5, 111.1, 57.5 (d, $J_{\text{PC}} = 20.6$ Hz), 52.4, 51.7, 48.9 (d, $J_{\text{PC}} = 26.3$ Hz), 21.5.

(2*R*_C, 3*S*_C)-dimethyl 2-(4-methylphenylamino)-3-(diphenylphosphino)succinate
(*R*_C,*S*_C)-154f

Off white oil; 91% yield; $[\alpha]_{\text{D}} = -88^\circ$ (*c* 0.5, DCM); ^{31}P NMR (202 MHz, CDCl_3): δ –9.5; ^1H NMR (500MHz, CDCl_3): δ 7.64–7.67 (m, 2H, *Ar*), 7.46–7.49 (m, 2H, *Ar*), 7.29–7.41 (m, 6H, *Ar*), 6.93 (d, $J_{\text{HH}} = 8.2$ Hz, 2H, *MeAr*), 6.39 (d, $J_{\text{HH}} = 8.2$ Hz, 2H, *MeAr*), 4.46–4.51 (m, 1H, *NCH*), 4.06 (d, $J_{\text{HH}} = 9.9$ Hz, 1H, *NH*), 3.90 (d, $J_{\text{PH}} = 7.9$ Hz, 1H, *PCH*), 3.69 (s, 3H, *COOMe*), 3.29 (s, 3H, *COOMe*), 2.22 (s, 3H, *CMe*); ^{13}C NMR (125 MHz, CDCl_3): δ 172.6 (d, $J_{\text{PC}} = 5.8$ Hz), 170.5 (d, $J_{\text{PC}} = 2.5$ Hz), 143.5, 135.7 (d, $J_{\text{PC}} = 15.7$ Hz), 135.1 (d, $J_{\text{PC}} = 17.2$ Hz), 134.0, 133.9, 133.8, 133.6, 129.7, 129.4, 129.3, 128.7, 128.6, 128.21, 128.16, 114.1, 58.0 (d, $J_{\text{PC}} = 20.3$ Hz), 52.4, 51.7,

48.9 (d, $J_{\text{PC}} = 26.1$ Hz), 20.4.

(2*R*_C,3*S*_C)-dimethyl 2-(2,4,6-trimethylphenylamino)-3-(diphenylphosphino)

Succinate, (*R*_C,*S*_C)-154g

(*R*_C,*S*_C)-154 g

Off white oil; 93% yield; $[\alpha]_{\text{D}} = -46^{\circ}$ (c 0.5, DCM); ^{31}P NMR (202 MHz, CDCl₃): δ -11.8; ^1H NMR (500MHz, CDCl₃): δ 7.63–7.65 (m, 2H, Ar), 7.43–7.46 (m, 2H, Ar), 7.37–7.39 (m, 3H, Ar), 7.29–7.33 (m, 3H, Ar), 6.72 (s, 2H, Me₃Ar), 4.28–4.32 (m, 1H, NHC), 3.85 (d, $J_{\text{PH}} = 6.7$ Hz, 1H, PCH), 3.66 (d, $J_{\text{HH}} = 12.8$ Hz, 1H, NH), 3.57 (s, 3H, COOMe), 3.28 (s, 3H, COOMe), 2.18 (s, 3H, CMe), 2.11 (s, 6H, CMe).

(2*R*_C, 3*S*_C)-dimethyl 2-(4-nitrilephenylamino)-3-(diphenylphosphino)succinate

(*R*_C,*S*_C)-154h

(*R*_C,*S*_C)-154 h

Yellow oil; 89% yield; $[\alpha]_{\text{D}} = -84^{\circ}$ (c 0.5, DCM); ^{31}P NMR (202 MHz, CDCl₃): δ -9.8; ^1H NMR (500MHz, CDCl₃): δ 8.01 (d, $J_{\text{HH}} = 9.1$ Hz, 2H, NO₂Ar), 7.61–7.64 (m, 2H, Ar), 7.44–7.47 (m, 5H, Ar), 7.30–7.35 (m, 3H, Ar), 6.36 (d, $J_{\text{HH}} = 9.1$ Hz, 2H,

NO₂Ar), 4.94 (d, $J_{\text{HH}} = 7.2$ Hz, 1H, *NH*), 4.58–4.62 (m, 1H, *NCH*), 3.92 (d, $J_{\text{PH}} = 7.5$ Hz, 1H, *PCH*), 3.74 (s, 3H, COOMe), 3.30 (s, 3H, COOMe); ¹³C NMR (125 MHz, CDCl₃): δ 171.0 (d, $J_{\text{PC}} = 5.1$ Hz), 170.2 (d, $J_{\text{PC}} = 3.0$ Hz), 151.0, 139.3, 134.8 (d, $J_{\text{PC}} = 15.5$ Hz), 133.9 (d, $J_{\text{PC}} = 7.1$ Hz), 133.8, 133.71, 133.66, 129.9, 129.7, 128.94, 128.88, 128.44, 128.38, 126.1, 112.1, 56.4 (d, $J_{\text{PC}} = 20.3$ Hz), 52.9, 52.0, 48.7 (d, $J_{\text{PC}} = 27.3$ Hz).

Preparation of Gold (I) complexes (*R_C*,*S_C*)-**155** and (*R_C*,*S_C*)-**156**

To a solution of chloro (dimethylsulfide) Gold (I) (30 mg, 0.1 mmol) in CDCl₃ (2 mL) was added the freshly prepared P, N-ligands (*R_C*,*S_C*)-**148a** (0.1 mmol) under argon, the mixture was stirred at room temperature for 10 min. Then the solution of (*R_C*,*S_C*)-**155a** in CDCl₃ was test by ³¹P NMR and ¹H NMR. The new ³¹P NMR signal was observed from the solution of (*R_C*,*S_C*)-**155a** after 20 min. After 2 days in solution, the ³¹P NMR signal of (*R_C*,*S_C*)-**155a** disappeared and new ³¹P NMR signal of **156a** was detected only.

Chloro[(2*R_C*, 3*S_C*)-dimethyl 2-(dimethylamino)-3-(diphenylphosphino)succinate]

Gold(I), (*R_C*,*S_C*)-**155a**

³¹P NMR (162 MHz, CDCl₃): δ 37.1; ¹H NMR (400MHz, CDCl₃): δ 7.80-8.00 (m, 4 H, Ar), 7.43-7.57 (m, 6H, Ar), 4.13-4.24 (m, 2H, *NCH*, *PCH*), 3.91 (s, 3H, COOMe), 3.15 (s, 3H, COOMe), 2.02 (s, 6H, NMe₂)

Chloro(diphenylphosphino maleate) Gold(I), **156a**

^{31}P NMR (162 MHz, CDCl_3): δ 34.4; ^1H NMR (400MHz, CDCl_3): δ 7.67-7.73 (m, 4 H, Ar), 7.57-7.59 (m, 2H, Ar), 7.50-7.54 (m, 4H, Ar), 6.38 (d, $J_{\text{PH}} = 16$ Hz, 1H), 3.79 (s, 3H, COOMe), 3.57 (s, 3H, COOMe).

Preparation of Gold (I) complexes (R_C, S_C)-**157**

To a solution of chloro (dimethylsulfide) Gold (I) (30 mg, 0.1 mmol) in DCM (2 mL) was added the freshly prepared P, N-ligands (R_C, S_C)-**154** (0.1 mmol) under argon, the mixture was stirred at room temperature for 30 min. Then the solvent was removed by vacuum to give the gold (I) complexes as pale yellow foam in 91-98% yield.

Chloro[($2R_C, 3S_C$)-dimethyl 2-(phenylamino)-3-(diphenylphosphino)succinate] Gold(I), (R_C, S_C)-**157a**

Off white solid: mp 72-74 °C; 97% yield; $[\alpha]_{\text{D}} = -40^\circ$ (c 0.5, DCM); ^{31}P NMR (202 MHz, CDCl_3): δ 36.1; ^1H NMR (500MHz, CDCl_3): δ 7.76-7.86 (m, 4H, Ar), 7.42-7.51 (m, 6H, Ar), 7.03-7.06 (m, 2H, Ar), 6.74 (t, $J_{\text{HH}} = 7.4$ Hz, 1H, Ar), 6.33 (d, $J_{\text{HH}} = 8.0$ Hz, 1H, Ar), 4.80-4.86 (m, 1H, NCH), 4.31-4.35 (m, 1H, PCH), 4.07 (d,

$J_{\text{HH}} = 10.8$ Hz, 1H, *NH*), 3.67 (s, 3H, *COOMe*), 3.37 (s, 3H, *COOMe*); ^{13}C NMR (125 MHz, CDCl_3): δ 171.1 (d, $J_{\text{PC}} = 9.5$ Hz), 167.7 (d, $J_{\text{PC}} = 3.2$ Hz), 144.2, 134.7, 134.5, 133.8, 133.7, 132.4 (d, $J_{\text{PC}} = 2.3$ Hz), 132.1 (d, $J_{\text{PC}} = 2.3$ Hz), 129.3, 129.2, 129.11, 129.08, 129.0, 127.6 (d, $J_{\text{PC}} = 60.3$ Hz), 126.5 (d, $J_{\text{PC}} = 60.0$ Hz), 119.8, 114.1, 57.8 (d, $J_{\text{PC}} = 4.6$ Hz), 52.9, 52.7, 48.9 (d, $J_{\text{PC}} = 32.4$ Hz).

Chloro[(2*R_C*,3*S_C*)-dimethyl 2-(2-methoxyphenylamino)-3-(diphenylphosphino)succinate] Gold(I), (*R_C*,*S_C*)-157b

Off white solid: mp 65-68 °C; 98% yield; $[\alpha]_{\text{D}} = -44^\circ$ (*c* 0.5, DCM); ^{31}P NMR (162 MHz, CDCl_3): δ 36.0; ^1H NMR (400MHz, CDCl_3): δ 7.75-7.87 (m, 4H, Ar), 7.39-7.48 (m, 6H, Ar), 6.65-6.72 (m, 2H, *MeOAr*), 6.60 (d, $J_{\text{HH}} = 7.6$ Hz, 1H, *MeOAr*), 6.34 (d, $J_{\text{HH}} = 7.4$ Hz, 1H, *MeOAr*), 4.84-4.89 (m, 1H, *NCH*), 4.70 (brs, 1H, *NH*), 4.39-4.44 (m, 1H, *PCH*), 3.66 (s, 3H, *COOMe*), 3.64 (s, 3H, *OMe*), 3.35 (s, 3H, *COOMe*); ^{13}C NMR (100 MHz, CDCl_3): δ 171.2 (d, $J_{\text{PC}} = 10.1$ Hz), 167.8 (d, $J_{\text{PC}} = 2.8$ Hz), 147.1, 134.8, 134.6, 134.0, 133.8, 133.6, 132.3 (d, $J_{\text{PC}} = 2.5$ Hz), 313.9 (d, $J_{\text{PC}} = 2.4$ Hz), 129.01, 129.00, 128.89, 128.88, 127.6 (d, $J_{\text{PC}} = 59.9$ Hz), 126.5 (d, $J_{\text{PC}} = 58.3$ Hz), 120.8, 118.8, 110.8, 109.8, 57.1 (d, $J_{\text{PC}} = 4.4$ Hz), 55.3, 52.8, 52.6, 48.7 (d, $J_{\text{PC}} = 32.5$ Hz).

Chloro[(2*R*_C,3*S*_C)-dimethyl 2-(3-methoxyphenylamino)-3-(diphenylphosphino)succinate] Gold(I), (*R*_C,*S*_C)-157c

Off white solid: mp 64-67 °C; 90% yield; $[\alpha]_{\text{D}} = -38^{\circ}$ (*c* 0.5, DCM); ^{31}P NMR (202 MHz, CDCl₃): δ 36.2; ^1H NMR (500MHz, CDCl₃): δ 7.42-7.85 (m, 10H, Ar), 6.95 (t, $J = 8.0$ Hz, 1H, MeOAr), 6.31 (dd, $J_{\text{HH}} = 8.0$ Hz, 2.0 Hz, 1H, MeOAr), 5.94 (dd, $J_{\text{HH}} = 8.0$ Hz, $J_{\text{HH}} = 2.0$ Hz, 1H, MeOAr), 5.88 (t, $J_{\text{HH}} = 2.0$ Hz, 1H, MeOAr), 4.79-4.84 (m, 1H, NCH), 4.32-4.36 (m, 1H, PCH), 4.08 (d, $J_{\text{HH}} = 15.5$ Hz, 1H, NH), 3.71 (s, 3H, COOMe), 3.68 (s, 3H, OMe), 3.37 (s, 3H, COOMe); ^{13}C NMR (125 MHz, CDCl₃): δ 171.0 (d, $J_{\text{PC}} = 8.1$ Hz), 167.7 (d, $J_{\text{PC}} = 2.0$ Hz), 160.6, 145.6, 134.6, 134.5, 133.8, 133.7, 132.4 (d, $J_{\text{PC}} = 2.5$ Hz), 132.1 (d, $J_{\text{PC}} = 2.5$ Hz), 130.1, 129.2, 129.11, 129.09, 129.0, 128.8, 127.6 (d, $J_{\text{PC}} = 60.1$ Hz), 126.6 (d, $J_{\text{PC}} = 71.0$ Hz), 106.5, 105.6, 100.2, 57.8 (d, $J_{\text{PC}} = 4.7$ Hz), 55.2, 52.9, 52.7, 48.7 (d, $J_{\text{PC}} = 19.5$ Hz).

Chloro[(2*R*_C,3*S*_C)-dimethyl 2-(4-methoxyphenylamino)-3-(diphenylphosphino)succinate] Gold(I) (*R*_C,*S*_C)-157d

Off white solid: mp 76-78 °C; 96% yield; $[\alpha]_D = -28^\circ$ (*c* 0.5, DCM); ^{31}P NMR (202 MHz, CDCl_3): δ 36.2; ^1H NMR (500MHz, CDCl_3): δ 7.77-7.85 (m, 4H, Ar), 7.49-7.52 (m, 2H, Ar), 7.43-7.46 (m, 3H, Ar), 6.64 (d, $J_{\text{HH}} = 8.9$ Hz, 2H, MeOAr), 6.36 (d, $J_{\text{HH}} = 8.9$ Hz, 2H, MeOAr), 4.69-4.72 (m, 1H, NCH), 4.26-4.30 (m, 1H, PCH), 3.71 (s, 3H, COOMe), 3.66 (s, 3H, OMe), 3.36 (s, 3H, COOMe); ^{13}C NMR (125 MHz, CDCl_3): δ 171.4 (d, $J_{\text{PC}} = 9.9$ Hz), 167.7 (d, $J_{\text{PC}} = 2.6$ Hz), 153.9, 138.1, 134.7, 134.6, 133.7, 133.6, 132.4 (d, $J_{\text{PC}} = 2.4$ Hz), 132.1 (d, $J_{\text{PC}} = 2.4$ Hz), 129.2, 129.11, 129.10, 129.0, 128.0 (d, $J_{\text{PC}} = 60.6$ Hz), 126.7 (d, $J_{\text{PC}} = 58.6$ Hz), 116.4, 114.7, 59.3 (d, $J_{\text{PC}} = 4.2$ Hz), 55.6, 52.8, 52.7, 49.0 (d, $J_{\text{PC}} = 33.1$ Hz).

Chloro[(2*R_C*,3*S_C*)-dimethyl 2-(3-methylphenylamino)-3-(diphenylphosphino) succinate] Gold(I), (*R_C*,*S_C*)-157e

Pale yellow solid: mp 61-63 °C; 95% yield; $[\alpha]_D = -26^\circ$ (*c* 0.5, DCM); ^{31}P NMR (162 MHz, CDCl_3): δ 36.1; ^1H NMR (400MHz, CDCl_3): δ 7.75-7.88 (m, 4H, Ar),

7.41-7.54 (m, 6H, Ar), 6.94 (t, $J_{\text{HH}} = 7.6$ Hz, 1H, MeAr), 6.56 (d, $J_{\text{HH}} = 7.4$ Hz, 1H, MeAr), 6.13-6.17 (m, 2H, MeAr), 4.78-4.85 (m, 1H, NCH), 4.32 (dd, $J_{\text{HH}} = 11.2$ Hz, $J_{\text{HH}} = 9.3$ Hz, 1H, PCH), 4.00 (d, $J_{\text{HH}} = 10.8$ Hz, 1H, NH), 3.67 (s, 3H, COOMe), 3.37 (s, 3H, COOMe), 2.18 (s, 3H, CMe); ^{13}C NMR (100 MHz, CDCl_3): δ 171.1 (d, $J_{\text{PC}} = 9.7$ Hz), 167.7 (d, $J_{\text{PC}} = 2.2$ Hz), 144.2, 139.1, 134.7, 134.5, 133.8, 133.6, 132.4 (d, $J_{\text{PC}} = 2.6$ Hz), 132.1 (d, $J_{\text{PC}} = 2.5$ Hz), 129.8, 210 Hz), 129.2, 129.1, 129.0, 127.7 (d, $J_{\text{PC}} = 60.0$ Hz), 126.6 (d, $J_{\text{PC}} = 58.4$ Hz), 120.7, 115.0, 111.3, 57.8 (d, $J_{\text{PC}} = 4.7$ Hz), 52.9, 52.7, 48.9 (d, $J_{\text{PC}} = 32.1$ Hz), 21.4.

Chloro[(2*R*_C,3*S*_C)-dimethyl 2-(4-methylphenylamino)-3-(diphenylphosphino) succinate] Gold(I), (*R*_C,*S*_C)-157f

Pale yellow solid: mp 70-73 °C; 98% yield; $[\alpha]_{\text{D}} = -30^\circ$ (c 0.5, DCM); ^{31}P NMR (202 MHz, CDCl_3): δ 36.2; ^1H NMR (500MHz, CDCl_3): δ 7.76-7.87 (m, 4H, Ar), 7.42-7.52 (m, 6H, Ar), 6.87 (d, $J_{\text{HH}} = 8.2$ Hz, 2H, MeAr), 6.28 (d, $J_{\text{HH}} = 8.2$ Hz, 2H, MeAr), 4.75-4.80 (m, 1H, NCH), 4.27-4.32 (m, 1H, PCH), 3.66 (s, 3H, COOMe), 3.37 (s, 3H, COOMe), 2.20(s, 3H, CMe); ^{13}C NMR (125 MHz, CDCl_3): δ 171.2 (d, $J_{\text{PC}} = 9.5$ Hz), 167.7 (d, $J_{\text{PC}} = 2.4$ Hz), 141.8, 134.6, 134.5, 133.8, 133.6, 132.4 (d, $J_{\text{PC}} = 2.4$ Hz), 132.1 (d, $J_{\text{PC}} = 2.6$ Hz), 129.8, 129.3, 129.2, 129.10, 129.09, 129.0, 127.9

(d, $J_{\text{PC}} = 60.1$ Hz), 126.7 (d, $J_{\text{PC}} = 58.4$ Hz), 114.6, 58.3 (d, $J_{\text{PC}} = 4.5$ Hz), 52.8, 52.7, 48.9 (d, $J_{\text{PC}} = 32.4$ Hz), 20.4.

Chloro[(2*R_C*,3*S_C*)-dimethyl 2-(4-nitrophenylamino)-3-(diphenylphosphino)succinate] Gold(I), (*R_C*,*S_C*)-157h

Yellow solid: mp 90-93 °C; 91% yield; $[\alpha]_{\text{D}} = -68^{\circ}$ (*c* 0.5, DCM); ^{31}P NMR (162 MHz, CDCl_3): δ 35.3; ^1H NMR (400MHz, CDCl_3): δ 7.93 (d, $J_{\text{HH}} = 9.1$ Hz, 2H, NO_2Ar), 7.75-7.89 (m, 4H, Ar), 7.50-7.54 (m, 2H, Ar), 7.43-7.46 (m, 4H, Ar), 6.33 (d, $J_{\text{HH}} = 9.1$ Hz, 2H, NO_2Ar), 5.07 (d, $J_{\text{HH}} = 10.3$ Hz, 1H, *NH*), 4.90-4.97 (m, 1H, *NCH*), 4.42-4.47 (m, 1H, *PCH*), 3.69 (s, 3H, *COOMe*), 3.35 (s, 3H, *COOMe*); ^{13}C NMR (100 MHz, CDCl_3): δ 169.9 (d, $J_{\text{PC}} = 9.9$ Hz), 167.5 (d, $J_{\text{PC}} = 3.1$ Hz), 149.9, 140.0, 134.9, 134.7, 133.9, 133.7, 132.9 (d, $J_{\text{PC}} = 2.1$ Hz), 132.5 (d, $J_{\text{PC}} = 2.6$ Hz), 129.4, 129.3, 129.2, 126.9 (d, $J_{\text{PC}} = 59.0$ Hz), 126.0, 125.5 (d, $J_{\text{PC}} = 69.3$ Hz), 112.4, 56.6 (d, $J_{\text{PC}} = 5.2$ Hz), 53.3, 52.8, 48.7 (d, $J_{\text{PC}} = 30.7$ Hz).

Chapter 3

Asymmetric Synthesis of Chiral PPN-Ligands by Hydrophosphination via Chiral Palladacycle Template

3.1 Introduction

Chiral phosphines attract increasing interest as ligands in transition metal complexes mediated stereoselective synthesis and catalysis.^[131] Optically pure diphosphines containing selected functionalities have long been considered as powerful auxiliaries in transition metal mediated homogenous asymmetric catalysis.^[132] Compared to monodentate ligands with comparable donor groups, a properly designed polydentate ligands can simultaneously provide more control on the coordination number, stereochemistry, and magnetic properties of the resulting complex, and increased basicity (or nucleophilicity) at the metal, and higher optical yields in catalytic asymmetric synthesis.^[103-113, 133] Incorporation of other group donor atoms to form a "mixed" phosphine readily facilitates controlled variation of the steric and electronic properties of the ligands. The addition of secondary phosphines to carbon–carbon multiple bonds is generally considered as a straightforward and efficient organic synthetic process for the optically pure heterophosphines ligangs.^[61-63, 70, 71, 134] Despite their important roles in many aspects of science, the synthesis of these reactive and potentially unstable chiral ligands remains a major challenge. Our group has always being focused on the synthesis of functionalized optically pure

diphosphines via asymmetric hydrophosphination reaction promoted by chiral templates containing chiral (1-(dimethylamino)ethyl)-naphthalenes framework. [61-63, 71] Herein, we describe the synthesis of chiral PPN ligands containing amino functionalized groups via asymmetric hydrophosphination reaction under control of chiral NC-palladacycle template. Amino functionalized diphosphine ligands with chirality centered on the carbon backbone were prepared using a novel two-stage asymmetric synthetic methodology from the corresponding terminal imino.

3.2 Results and Discussion

3.2.1 Preparation of Intermediate Vinylphosphines via Free Radical Addition of Alkynes and Subsequent Coordination

α , β -Unsaturated phosphorus compounds are useful building blocks in organic synthesis and they were often prepared by substitution reaction of halophosphines and or lithium phosphonium. [134a, 135] The cross-coupling reaction of alkenyl halides and triflates with dialkyl phosphate and diphenylphosphine has also been explored by using metal complexes under basic conditions. [136] In addition, hydrophosphination of alkynes has been investigated as an efficient method to prepare α , β -unsaturated phosphorus compounds. [134a, 135a, 137] Hydrophosphination reaction of alkynes is one of the most important ways to prepare these kinds of α , β -unsaturated phosphorus containing building blocks. Hydrophosphination reactions were explored under different conditions such as basic conditions, [138] radical conditions, [139] neutral conditions [140] and metal-catalyzed. [141]

The first radical addition of phosphine to alkynes was described as early as 1961. [139d]

It thus appeared of interest to study the reactions between diphenylphosphine and various alkynes and allenes in order to obtain detailed information on the regio- and stereo-chemistry of such reactions, and thus on the suitability of the reactions for the preparation of vinylphosphines. Hydrophosphination of 1-alkynes bearing a tertiary N group β -position to the triple bond were carried out under radical conditions.^[139] Hydrophosphination reaction was conducted with alkynes and diphenylphosphine in the presence of AIBN initiator under refluxing for 7 days to give the mixture of *trans*- and *cis*- vinylphosphine selectively. In this process, β -adducts which the diphenylphosphine group was added to the terminal α -positions were exclusively obtained under radical-catalyzed condition (Table 3.1). In this case, hydrophosphination of 1-alkynes under radical conditions predominantly gave the *Z*-isomer (*Z*)-**158** as major products and *E*-product (*E*)-**159** as minor products. The ratio of *Z/E* isomers was observed as 6/1, 7/1, 2.6/1 and 1.3/1 respectively under radical conditions when the R groups are Me₂NCH₂, Et₂NCH₂, BnMeNCH₂ and 2-Pyridine respectively (Table 3.1). Amino functionalized 1-alkynes reacted with two equivalents of diphenylphosphine under refluxing to afford the diphosphine products in the presence of catalytic amounts AIBN in THF.

Entry	R	Reaction conditions	Consumption ^[b] (%)	Z/ E ratio ^[c]
1	Me ₂ NCH ₂	5% AIBN, 7d	100	6/ 1
2	Et ₂ NCH ₂	5% AIBN, 7d	100	7/ 1
3	BnMeNCH ₂	5% AIBN, 8d	100	2.6/ 1
4	2-Pyridine	5% AIBN, 10d	100	1.3/ 1

[a] Unless other noted, reaction was performed under refluxing in THF. [b] Determined by ³¹P NMR. [c] Determined by ³¹P NMR

Without further isolation, these selectively forming vinylphosphines were subsequently coordinated to the chiral palladacycle templates (*S*)-**33** and regioselectively gave the intermediate complexes (*S*)-**160** and (*S*)-**161** as a configuration mixture. This regioselective coordination to metal center trans- to the amino NMe₂ group based on the N σ donor trans-effect. As air stable complexes, these intermediates mixture were isolated by column chromatography to give the single isomer (*S*)-**160a-d** and single isomer (*S*)-**160a-b** respectively. In this process, the ratio of *E/Z* isomer retains and consists with the ratio of vinylphosphines.

Table 3.2 Coordination reaction^[a]

Entry	R	Ratio of <i>E</i> / <i>Z</i> ^[b]	Yields ^[c] / (%)
1	Me ₂ NCH ₂	1/ 6	70
2	Et ₂ NCH ₂	1/ 7	65
3	BnMeNCH ₂	1/ 2.6	60
4	2-Pyridine	1/1.3	50

[a] Unless other noted, reaction was performed under refluxing in THF. [b] Ratio was determined by intensity of ³¹P NMR [c] Isolated yields of (S)-160 and (S)-161

3.2.2 Asymmetric Hydrophosphination

A series of chiral functionalized diphosphine ligands have been previously reported via promotion of the chiral palladacycle templates. In the absence of base such as triethylamine, no reaction was observed between diphenylphosphines and the functionalized vinylphosphine in our previously reported hydrophosphination

reactions.^[61-63] No reaction occurs between 3-(diphenylphosphino) prop-2-en-1-amine and Ph₂PH without template or metal such as PdCl₂. No stereoselectivity was observed for the reaction between 3-(diphenylphosphino) prop-2-en-1-amine and Ph₂PH when PdCl₂ was used as catalyst. The complex (*S*)-**160** was carried out in DCM with AgClO₄ to withdraw the Cl ligand, so that provided a vacancy for the incoming Ph₂PH to coordinate on the metal center. Subsequently, stoichiometric Ph₂PH was added to the solution of intermediates (*S*)-**162** at -78 °C under argon and the hydrophosphination reaction was smoothly promoted to selectively give the hydrophosphination products (*S*)-**163**, (*S*)-**164** and (*S*)-**165** in a ratio of 5:1:3 and 11:1:5 respectively when R group is Me₂NCH₂ and Et₂NCH₂, which indicated that only three diastereoisomers were generated. Herein, (*S*)-**163** and (*S*)-**165** are a pair of regioisomers that have the same chirality carbon center. Usually, additional bases were required to promote this hydrophosphination reaction in precious reports. However, in this process, no extra bases such as NEt₃ were required because the tertiary N group of intermediates can play the role as base. Usually, the chiral tridentate P,N containing ligands were prepared with starting chiral substrates. However, for our preparation of chiral PPN ligands via this asymmetric hydrophosphination reaction, a new stereogenic carbon center was created instead of introduction from chiral substrates. Without promotion of the chiral template, no reaction was observed between the vinylphosphine and diphenylphosphine. Herein, the chiral template plays the role not only as catalyst but also as controller of auxiliary. In this process, diphenylphosphine was firstly coordinated to the palladium center. In

this stage, the regioselective isomers that the diphenylphosphines trans to the nitrogen or cis to NMe₂ nitrogen donor should be formed respectively. Subsequently, an intramolecular hydrophosphination reaction occurred.

Scheme 3.1

When the single isomer (*S*)-**163a** or (*S*)-**165a** was kept in solution at room temperature for over 3 days, an equilibrium mixtures of regioisomers (*S*)-**163a** and (*S*)-**165a** were formed as shown in scheme 3.2. This information and recomplexation of free ligand (*S*)-**168** provide the evidence that (*S*)-**163a** and (*S*)-**165a** are regioisomers.

Scheme 3.2

3.2.3 Synthesis of Dichloro complexes (S_C) -167

These isolated hydrophosphination products (S_C, S_C) -163 and (S_C, S_C) -165 appear as pairs of regioisomers in solution. After chiral template of these isomers was chemoselectively removed, the same dichloro complexes were obtained because no regioisomers existed any more for the generated dichloro complexes. These hydrophosphination products were treated with Con. HCl in DCM for 3 h (Scheme 3.3), and the desired solution was neutralized by weak base NaHCO_3 . Here, it is needed to note that strong base such as sodium hydroxide can not be utilized because the product will become unidentified products under the action of strong base. So, weak base such as sodium carbonate or sodium dicarbonate was applied to neutralize these hydrochloride salts. After neutralization, the crude products were concentrated and purified by running column chromatography to give the optically pure dichloro complexes (S_C) -167. The signal of ^{31}P NMR spectrum was recorded at δ 67.5, 53.6 (d, $J_{\text{PP}} = 5.2$ Hz) for (S_C) -167a and the ^{31}P NMR spectrum signal of (S_C) -167b exhibited at δ 64.6, 50.1 (d, $J_{\text{PP}} = 5.9$ Hz). These complexes were grown crystal under the DCM/

Diether system and gave the pale yellow prism crystal (*S_C*)-**167**.

Scheme 3.3

The absolute configuration of (*S_C*)-**167b** was confirmed by X-ray crystallography (Figure 3.1). Selected bond distance and angle are given in Table 3.3. The geometry at palladium center of (*S_C*)-**167b** is distorted square planar with angles of 85.4(1)°–93.6(1)° and 174.6(1)°–176.2(1)°. No significant difference between the two Pd–Cl bond distances [2.235(1) and 2.249(1) Å] was observed, with both the bond *trans*- to the phosphorus. The C(1)–P(1) [1.821(6) Å] and C(14)–P(2) [1.852(3) Å] distances are typical for C–P bonds. The C(16)–N(1) [1.464(4) Å] and C(13)–C(14) [1.509(4) Å] distances are typical for C–N and C–C bonds respectively.

Figure 3.1 Structure and absolute configuration of complex (*S_C*)-**167b**

Table 3.3 Selected bond lengths (Å) and Angles (deg) of (*S_C*)-**167b**

C(1)-P(1)	1.821(6)	Pd(1)-P(2)	2.235(1)
Pd(1)-P(1)	2.240(1)	Pd(1)-Cl(2)	2.351(1)
Pd(1)-Cl(1)	2.363(1)	C(7)-P(1)	1.806(3)
C(13)-P(1)	1.850(3)	C(13)-C(14)	1.509(4)
C(15)-N(1)	1.461(4)	C(16)-N(1)	1.464(4)
C(14)-P(2)	1.852(3)	C(17)-N(1)	1.458(4)
P(2)-Pd(1)-P(1)	85.4(1)	P(2)-Pd(1)-Cl(2)	89.5(1)
P(1)-Pd(1)-Cl(2)	174.6(1)	P(2)-Pd(1)-Cl(1)	176.2(1)
P(1)-Pd(1)-Cl(1)	91.4(1)	Cl(2)-Pd(1)-Cl(1)	93.6(1)
C(14)-C(13)-P(1)	110.2(2)	C(13)-C(14)-P(2)	106.3(2)
C(7)-P(1)-C(1)	105.8(3)	C(13)-P(1)-Pd(1)	108.6(1)

3.2.4 Synthesis of Optically Pure PPN Free Ligands by Liberation

The free optically pure PPN ligands (*S_C*)-**168** were released from the dichloro complexes (*S_C*)-**167** which were treated with aqueous potassium cyanide at room temperature for 30 min (Scheme 3.4). The liberated free PPN ligand (*S_C*)-**168a** was obtained as a colorless oil in 90% yield, $[\alpha]_D = +10^\circ$ (*c* 0.5, DCM). Its ^{31}P NMR spectrum in CDCl_3 exhibited a pair doublets at δ -3.9, -19.6 (d, $J_{\text{PP}} = 31.0$ Hz). For the (*S_C*)-**168b**, it was obtained as an colorless oil in 88%, $[\alpha]_{365\text{nm}} = -20^\circ$ (*c* 0.5, DCM) and signal of ^{31}P NMR spectrum in CDCl_3 was recorded at δ -3.4, -19.6 (d, $J_{\text{PP}} = 30.6$ Hz).

Scheme 3.4

3.2.5 Recomplexation of Optically Pure Free PPN Ligands

Scheme 3.5

In order to confirm the optical purity of these free ligands, the liberated optically pure free ligands were recomplexed to the chiral template **(S)-49** (Scheme 3.5). After free ligand **(S_C)-168a** was recomplexed to the **(S)-49**, two pairs of doublet signal of ³¹P NMR spectrum at δ 72.9, 39.2 (d, *J* = 24.0 Hz) and δ 49.3, 43.1 (d, *J* = 30.3 Hz) with equal relative intensities were observed. These signals are identical to those asymmetric hydrophosphination products of regioisomers **(S_C,S_C)-163a** and **(S_C,S_C)-165a** respectively.

For the optically pure free ligand **(S_C)-168b**, ³¹P NMR signals of the recoordination complexes exhibited at δ 70.0, 37.7 (d, *J* = 25.6 Hz) and δ 47.1, 40.1 (d, *J* = 32.2 Hz) whose ratio is 1:1. These signals of ³¹P NMR spectrum are consistent with the asymmetric hydrophosphination products of regioisomers **(S_C,S_C)-163b** and **(S_C,S_C)-165b** respectively.

3.3 Conclusion

Optically pure chiral PPN containing ligands have been synthesized via asymmetric hydrophosphination reaction of vinylphosphines under promotion and control of

chiral palladium template with good stereoselectivity. Palladium-catalyzed asymmetric hydrophosphination of unactivated vinylphosphines provides an efficient method to prepare amino functionalized carbon chiral PPN containing ligands which have been proven to play important role in asymmetric catalysis.

3.4 Experimental Section

Reactions involving air-sensitive compounds were performed under an inert atmosphere of argon using standard Schlenk techniques. Solvents were dried and freshly distilled according to standard procedures and degassed prior to use when necessary. The ^1H and ^{31}P $\{^1\text{H}\}$ NMR spectra were recorded at 25 °C on Bruker ACF 300 and 400 spectrometers. Optical rotations were measured on the specified solution in a 0.1 dm cell at 20 °C with a Perkin-Elmer 341 polarimeter. Elemental analysis was performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at the Nanyang Technological University. Melting points were measured using the SRS Optimelt automated melting point system, SRS MPA100.

The chiral palladium templates (S)-**33**^[47] and (S)-**49**^[58] were prepared as previously reported.

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

Preparation of Complex (S_C)-160 and (S_C)-161

To a solution of 1-alkyne (2.9 mmol), diphenylphosphine (2.6 mmol) in THF (8 mL) was added AIBN (5 mmol %) under argon, the mixture was heated to 80 °C and refluxed at the same temperature for 7 days. The reaction mixture was monitored by

^{31}P NMR and cooled to room temperature after the diphenylphosphine was consumed completely. Without further treatment, the above cool solution was added to a solution of dimer (*S*)-**33** (877 mg, 2.6 mmol) in CH_2Cl_2 (150 mL), and the reaction mixture was continued to stir at room temperature for 1 h. After the coordination reaction completed, the reaction mixture was concentrated under vacuum rotary evaporator to give the crude residue. After purification by column chromatography, the products (*S_C*)-**160** and (*S_C*)-**161** were obtained respectively.

(*S_C*)-Chloro{1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*}[((*Z*)-*N,N*-dimethyl-3-(diphenylphosphino)prop-2-en-1-amine] palladium (II), (*S_C*)-160a****

(*S_C*)-160a****

Pale yellow foam: mp 73-76 °C; 60% yield; $[\alpha]_{\text{D}} = +16^\circ$ (*c* 0.5, DCM). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3): δ 16.38; ^1H NMR (500MHz, CDCl_3): δ 7.70-7.71 (m, 5H, Ar), 7.61 (d, $J_{\text{HH}} = 7.9$ Hz, 1H, Ar), 7.25-7.38 (m, 8H, Ar), 7.01 (d, $J_{\text{HH}} = 8.3$ Hz, 1H, Ar), 6.72-6.83 (m, 2H, Ar, *PCH=CH*), 6.52-6.56 (m, 1H, *PCH=CH*), 4.36 (m, 1H, *MeCH*), 3.76-3.93 (m, 2H, CH_2NMe_2), 2.96 (s, 3H, *NMe*), 2.74 (s, 3H, *NMe*), 2.13 (s, 6H, NMe_2), 2.05 (d, $J_{\text{HH}} = 5.1$ Hz, 3H, *CHMe*); ^{13}C NMR (125 MHz, CDCl_3): δ 150.0, 148.8 (d, $J_{\text{PC}} = 4.0$ Hz), 148.7 (d, $J_{\text{PC}} = 1.2$ Hz), 135.4 (d, $J_{\text{PC}} = 12.5$ Hz), 134.0, 133.9, 133.7, 133.6, 132.9 (d, $J_{\text{PC}} = 52.5$ Hz), 132.0 (d, $J_{\text{PC}} = 50.8$ Hz), 131.0, 130.2, 129.9 (d, $J_{\text{PC}} = 1.7$ Hz), 128.6, 128.4, 128.1, 128.02, 127.99, 127.90, 125.5, 124.5 (d, $J_{\text{PC}} =$

5.7 Hz), 123.9, 123.1, 122.7 (d, $J_{\text{PC}} = 45.8$ Hz), 72.8 (d, $J_{\text{PC}} = 3.9$ Hz), 60.1 (d, $J_{\text{PC}} = 12.6$ Hz), 51.5 (d, $J_{\text{PC}} = 2.4$ Hz), 48.3, 45.4, 23.5.

(*S_C*)-Chloro{1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*}[((*Z*)-*N,N*-diethyl-3-(diphenylphosphino)prop-2-en-1-amine] palladium (II), (*S_C*)-160b

(*S_C*)-160b

Pale yellow foam: mp 67-69 °C; 56% yield; $[\alpha]_{\text{D}} = +10^{\circ}$ (*c* 0.5, DCM); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3): δ 16.19; ^1H NMR (500MHz, CDCl_3): δ 7.69-7.75 (m, 5H, Ar), 7.63-7.65 (m, 1H, Ar), 7.27-7.42 (m, 8H, Ar), 7.03 (d, $J_{\text{HH}} = 8.6$ Hz, 1H, Ar), 6.77-6.89 (m, 2H, Ar, $\text{PCH}=\text{CH}$), 6.50-6.54 (m, 1H, $\text{PCH}=\text{CH}$), 4.34-4.39 (m, 1H, MeCH), 3.92-3.97 (m, 1H, CH_2NMe_2), 3.81-3.85 (m, 1H, CH_2NEt_2), 2.97 (d, $J_{\text{PH}} = 3.5$ Hz, 3H, *NMe*), 2.73 (d, $J_{\text{PH}} = 1.1$ Hz, 3H, *NMe*), 2.42 (q, $J_{\text{HH}} = 7.1$ Hz, 4H, CH_2CH_3), 2.07 (d, $J_{\text{HH}} = 6.4$ Hz, 3H, CH_2CH_3), 0.89 (t, $J_{\text{HH}} = 7.1$ Hz, 6H, CH_2CH_3); ^{13}C NMR (125 MHz, CDCl_3): δ 150.1, 148.8 (d, $J_{\text{PC}} = 2.3$ Hz), 135.5 (d, $J_{\text{PC}} = 12.4$ Hz), 134.2, 134.1, 133.84, 133.75, 132.6 (dd, $J_{\text{PC}} = 116.7$ Hz, 52.6 Hz), 131.2, 130.3 (d, $J_{\text{PC}} = 1.9$ Hz), 130.0 (d, $J_{\text{PC}} = 3.0$ Hz), 128.7, 128.6, 128.25, 128.16, 128.1, 128.0, 125.6, 124.6 (d, $J_{\text{PC}} = 5.7$ Hz), 124.0, 123.2, 122.1 (d, $J_{\text{PC}} = 45.3$ Hz), 73.0 (d, $J_{\text{PC}} = 2.8$ Hz), 55.0 (d, $J_{\text{PC}} = 12.6$ Hz), 51.4 (d, $J_{\text{PC}} = 2.3$ Hz), 48.40, 47.37, 23.6, 11.8

(*S_C*)-Chloro{1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*}[((*Z*)-*N*-benzyl-*N*-me

thyl-3-(diphenylphosphino)prop-2-en-1-amine] palladium (II), (*S_C*)-160c

(*S_C*)-160c

Yellow foam: mp 76-78 °C; 43% yield; $[\alpha]_D = +28^\circ$ (*c* 0.5, DCM); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3): δ 16.6; ^1H NMR (500MHz, CDCl_3): δ 7.74-7.80 (m, 5H, Ar), 7.66 (d, $J_{\text{HH}} = 7.9$ Hz, 1H, Ar), 7.13-7.45 (m, 13H, Ar), 7.06 (d, $J_{\text{HH}} = 7.9$ Hz, 1H, Ar), 6.80-6.92 (m, 2H, Ar, $\text{PCH}=\text{CH}$), 6.57-6.61 (m, 1H, $\text{PCH}=\text{CH}$), 4.39-4.41 (m, 1H, MeCH), 3.87-3.98 (m, 2H, CH_2Bn), 3.26-3.38 (m, 2H, CH_2NMe_2), 3.01 (s, 3H, *NMe*), 2.77(s, 3H, *NMe*), 2.10-2.11 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 150.1, 149.30, 149.26, 148.74, 138.65, 135.5 (d, $J_{\text{PC}} = 12.5$ Hz), 134.1, 134.0, 133.9, 133.8, 132.87 (d, $J_{\text{PC}} = 52.0$ Hz), 132.14 (d, $J_{\text{PC}} = 50.8$ Hz), 131.1, 130.2, 130.0, 128.7, 128.6, 128.5, 128.14, 128.10, 128.06, 127.99, 126.8, 125.6, 124.6 (d, $J_{\text{PC}} = 5.8$ Hz), 123.9, 123.1, 122.89 (d, $J_{\text{PC}} = 45.6$ Hz), 72.9, 61.9, 58.5 (d, $J_{\text{PC}} = 12.5$ Hz), 51.5, 48.4, 42.3, 23.6.

(*S_C*)-Chloro{1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*}[2-((*Z*)-2-(diphenylphosphino)vinyl)pyridine] palladium (II), (*S_C*)-160d

(*S_C*)-160d

Brown yellow foam: mp 141-144 °C; 28% yield; $[\alpha]_D = +254^\circ$ (*c* 0.5, DCM); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3): δ 24.6; ^1H NMR (500MHz, CDCl_3): δ 8.93 (d, $J_{\text{HH}} = 4.0$

Hz, 1H, Ar), 7.57-7.83 (m, 8H, Ar), 7.27-7.45 (m, 8H, Ar), 7.16-7.19 (m, 2H, Ar), 6.92 (d, $J_{\text{HH}} = 8.5$ Hz, 1H, Ar), 6.70 (dd, $J_{\text{PH}} = 12.3$ Hz, $J_{\text{PH}} = 7.9$ Hz, 1H, PCH=CH), 6.59-6.62 (m, 1H, PCH=CH), 4.24-4.29 (m, 1H, MeCH), 2.76 (s, 3H, NMe), 2.49 (d, $J_{\text{PH}} = 2.1$ Hz, 3H, NMe), 1.91 (d, $J_{\text{HH}} = 6.2$ Hz, 3H, CHMe); ^{13}C NMR (125 MHz, CDCl_3): δ 151.3 (d, $J_{\text{PC}} = 7.3$ Hz), 150.8, 148.5, 147.9, 143.8, 139.2, 136.0, 135.9, 134.1, 134.0, 133.1, 133.0, 131.6, 131.1, 130.9, 129.0, 128.9, 128.54, 128.51, 128.42, 128.39, 127.0, 126.7, 125.7, 125.0 (d, $J_{\text{PC}} = 8.9$ Hz), 124.3, 122.8, 73.1 (d, $J_{\text{PC}} = 2.7$ Hz), 51.5, 47.6, 23.7.

(*S*_C)-Chloro{1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*}[*(E)*-*N,N*-dimethyl-3-(diphenylphosphino)prop-2-en-1-amine] palladium (II), (*S*_C)-161a

(*S*_C)-161a

Pale yellow foam: mp 102-105 °C; 10% yield; $[\alpha]_{\text{D}} = +70^\circ$ (*c* 0.5, DCM); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3): δ 31.25; ^1H NMR (500 MHz, CDCl_3): δ 7.90-7.94 (m, 2H, Ar), 7.69-7.71 (m, 1H, Ar), 7.54-7.60 (m, 3H, Ar), 7.25-7.48 (m, 8H, Ar), 6.84-6.92 (m, 2H, Ar), 6.63-6.66 (m, 1H, PCH=CH), 5.88-5.97 (m, 1H, PCH=CH), 4.33-4.36 (m, 1H, MeCH), 3.03-3.13 (m, 2H, CH_2NMe_2), 2.96 (s, 3H, NMe), 2.74 (s, 3H, NMe), 2.17 (s, 6H, NMe_2), 2.02 (d, $J_{\text{HH}} = 6.0$ Hz, 3H, CHMe); ^{13}C NMR (125 MHz, CDCl_3): δ 149.7, 149.2 (d, $J_{\text{PC}} = 2.2$ Hz), 145.8, 136.1 (d, $J_{\text{PC}} = 10.7$ Hz), 135.0, 134.9, 134.4, 134.3, 131.0, 130.9 (d, $J_{\text{PC}} = 2.3$ Hz), 130.6 (d, $J_{\text{PC}} = 2.4$ Hz), 129.8 (d, $J_{\text{PC}} = 5.6$ Hz), 129.5 (d, $J_{\text{PC}} = 6.1$ Hz), 128.7, 128.65, 128.56, 128.3, 128.2, 126.6, 126.2, 125.6,

124.3 (d, $J_{\text{PC}} = 5.8$ Hz), 124.0, 123.2, 72.8 (d, $J_{\text{PC}} = 2.9$ Hz), 62.7 (d, $J_{\text{PC}} = 15.6$ Hz), 51.1 (d, $J_{\text{PC}} = 2.6$ Hz), 48.2, 45.3, 23.7.

(*S_C*)-Chloro{1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*}[(*E*)-*N,N*-diethyl-3-(diphenylphosphino)prop-2-en-1-amine] palladium (II), (*S_C*)-161b

(*S_C*)-161b

Pale yellow foam: mp 84-87 °C; 8% yield; $[\alpha]_{\text{D}} = +48^{\circ}$ (c 0.5, DCM). $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, CDCl_3): δ 31.4; ^1H NMR (400MHz, CDCl_3): δ ; 7.84-7.89 (m, 2H, Ar), 7.70 (d, $J = 8.4$ Hz, 1H, Ar); 7.58-7.63 (m, 3H, Ar), 7.28-7.50 (m, 8H, Ar), 6.93 (d, $J_{\text{HH}} = 12.6$ Hz, 1H), 6.79-6.88 (m, 1H, Ar), 6.65 (dd, $J_{\text{PH}} = 8.5$, $J_{\text{PH}} = 6.0$ Hz, 1H, $\text{PCH}=\text{CH}$), 6.00-6.10 (m, 1H, $\text{PCH}=\text{CH}$), 4.31-4.36 (m, 1H, MeCH), 3.20-3.32 (m, 2H, CH_2NEt_2), 2.96 (d, $J_{\text{HH}} = 3.2$ Hz, 3H, NMe), 2.73 (s, 3H, NMe), 2.37-2.46 (m, 4H, CH_2CH_3), 2.03 (d, $J_{\text{HH}} = 6.3$ Hz, 3H, MeCH), 0.93 (t, $J_{\text{HH}} = 7.2$ Hz, 6H, CH_2CH_3); ^{13}C NMR (100 MHz, CDCl_3): δ 149.8, 149.2 (d, $J_{\text{PC}} = 3.3$ Hz), 136.1 (d, $J_{\text{PC}} = 19.6$ Hz), 134.8, 134.7, 134.4, 134.3, 131.0, 130.80, 130.78, 130.58, 130.56, 130.3 (d, $J_{\text{PC}} = 41.7$ Hz), 129.8 (d, $J_{\text{PC}} = 40.0$ Hz), 128.7, 128.6, 128.4, 128.3, 128.2, 125.6, 124.3 (d, $J_{\text{PC}} = 9.4$ Hz), 124.0, 123.2, 72.8 (d, $J_{\text{PC}} = 3.1$ Hz), 56.5 (d, $J_{\text{PC}} = 15.9$ Hz), 51.1 (d, $J_{\text{PC}} = 2.8$ Hz), 48.2, 47.0, 23.7, 11.7.

Asymmetric hydrophosphination

Complex (*S_C*)-**160** (1.64 mmol) in dichloromethane (5 mL) and aqueous silver perchlorate (740 mg, 3.28 mmol) were stirred vigorously at room temperature for 1 h. The reaction mixture was filtered through Celite (to remove silver chloride), washed with water, and dried over anhydrous magnesium sulfate. The solution was concentrate and re-dissolved in dichloromethane (50 mL). The mixture was then degassed and cooled down to -78 °C, subsequently, diphenylphosphine (305 mg, 1.64 mmol) was added the cooling solution under argon. The reaction mixture was stirred at -78 °C for 10 h and then allowed to increase to room temperature gradually. After concentration, crude products were obtained and then the crude products were purified by running column chromatography (Hexane/DCM/ Acetone: from 5/ 4/ 4 to 3/ 4/ 8).

{(*S_C*)-1-[(1-dimethylamino)ethyl]-2-naphthalenyl-*C,N*¹}[(*S_C*)-*N,N*-dimethyl-2,3-bis(diphenylphosphino)propan-1-amine -*P, P*] palladium (II) Perchlorate, (*S_C*, *S_C*)-163a** or (*S_C*,*S_C*)-**165a****

Pale yellow solid: mp 173-176 °C; [α]_D = +100° (*c* 0.5, DCM); ³¹P{¹H} NMR (162 MHz, CDCl₃): δ 72.9, 39.2 (d, *J*_{PP} = 24.0 Hz); ¹H NMR (400MHz, CDCl₃): δ 8.40-8.46 (m, 1H, Ar), 7.93-7.98 (m, 2H, Ar), 7.75-7.82 (m, 6H, Ar), 7.67-7.68 (m, 3H, Ar), 7.60-7.62 (m, 1H, Ar), 7.34-7.51 (m, 9H, Ar), 7.23-7.27 (m, 1H, Ar), 7.00 (m,

1H, Ar), 6.76-6.81 (m, 1H, Ar), 4.58-4.61 (m, 1H, MeCH), 3.10-3.30 (m, 2H, CH₂NMe₂), 2.71 (s, 3H, NMe), 2.48 (s, 3H, NMe), 2.11 (d, $J_{\text{HH}} = 6.2$ Hz, 3H, CHMe), 1.99-2.07 (m, 2H, PCH₂), 1.68-1.73 (m, 1H, PCH), 1.57 (s, 6H, NMe₂); ¹³C NMR (100 MHz, CDCl₃): δ 158.6 (d, $J_{\text{PC}} = 3.0$ Hz), 157.4 (d, $J_{\text{PC}} = 3.0$ Hz), 150.3 (d, $J_{\text{PC}} = 1.5$ Hz), 136.5 (dd, $J_{\text{PC}} = 11.5$ Hz, 3.0 Hz), 135.8, 135.7, 135.0, 134.9, 134.3, 134.2, 133.3 (d, $J_{\text{PC}} = 2.2$ Hz), 132.6 (d, $J_{\text{PC}} = 2.1$ Hz), 132.3 (d, $J_{\text{PC}} = 2.7$ Hz), 132.2, 132.0, 131.8, 131.6 (d, $J_{\text{PC}} = 2.0$ Hz), 130.2, 130.1, 129.9, 129.82, 129.76, 129.7, 129.11 (d, $J_{\text{PC}} = 48.2$ Hz), 128.5, 128.3 (d, $J_{\text{PC}} = 35.5$ Hz), 126.3, 125.6 (d, $J_{\text{PC}} = 48.1$ Hz), 125.5 (dd, $J_{\text{PC}} = 7.5$ Hz, 5.3 Hz), 125.2, 125.0 (d, $J_{\text{PC}} = 47.7$ Hz), 75.3, 57.3, 52.3 (d, $J_{\text{PC}} = 2.2$ Hz), 50.8 (d, $J_{\text{PC}} = 3.0$ Hz), 44.4, 41.3 (dd, $J_{\text{PC}} = 35.0$ Hz, 17.3 Hz), 31.1 (dd, $J_{\text{PC}} = 27.7$ Hz, 11.6 Hz), 29.2, 25.7.

Preparation of Dichloro Complexes via Chemoselective Removal of Chiral Template

To a solution of (*S_C*, *S_C*)-**163** and (*S_C*, *S_C*)-**165** (0.2 mmol) in DCM (10 mL) was added concentrated hydrochloric acid (10 mL). The reaction mixture was stirred vigorously at room temperature for 3 h. The reaction mixture was neutralized by NaHCO₃ to neutral (PH = 7.0), extracted with DCM, washed with water, and dried over anhydrous magnesium sulfate. The crude product was purified by column chromatography (DCM/ EA = 1:20) to give the pure desired product (*S_C*)-**167**.

Dichloro[(*S_C*)-*N,N*-dimethyl-2,3-bis(diphenylphosphino)propan-1-amine]

palladium (II), (*S_C*)-**167a**

(*S_C*)-167a

Pale yellow prism: mp 231-234 °C (Decomp.); 93% yield; $[\alpha]_D = +86^\circ$ (*c* 0.5, DCM);

$^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, CDCl_3): δ 67.5, 53.6 (d, $J_{\text{PP}} = 5.2$ Hz); ^1H NMR (400MHz, CDCl_3): δ 7.81-7.96 (m, 8H, Ar), 7.43-7.60 (m, 12H, Ar), 2.73-2.97 (m, 2H, PCH_2), 2.43-2.57 (m, 1H, PCH), 1.98-2.14 (m, 2H, CH_2NMe_2), 1.89 (s, 6H, NMe_2); ^{13}C NMR (100 MHz, CDCl_3): δ 135.9, 135.8, 133.7, 133.63, 133.62, 133.5, 133.1, 133.0, 132.6 (d, $J_{\text{PC}} = 2.5$ Hz), 132.1 (d, $J_{\text{PC}} = 2.6$ Hz), 132.0 (d, $J_{\text{PC}} = 2.9$ Hz), 131.9 (d, $J_{\text{PC}} = 2.9$ Hz), 129.2, 129.1, 129.0, 128.89 (d, $J_{\text{PC}} = 45.8$ Hz), 128.88, 128.83, 128.76, 128.71, 128.1 (d, $J_{\text{PC}} = 53.6$ Hz), 126.7 (d, $J_{\text{PC}} = 53.2$ Hz), 124.8 (d, $J_{\text{PC}} = 51.1$ Hz), 58.4 (d, $J_{\text{PC}} = 15.5$ Hz), 45.0, 38.3 (dd, $J_{\text{PC}} = 31.8$ Hz, 14.4 Hz), 31.8 (dd, $J_{\text{PC}} = 24.9$ Hz, 15.8 Hz).

Dichloro[(*S_C*)-*N,N*-diethyl-2,3-bis(diphenylphosphino)propan-1-amine]

palladium (II), (*S_C*)-167b

(*S_C*)-167b

Pale yellow prism: mp 228-230 °C; 90% yield; $[\alpha]_D = +52^\circ$ (*c* 0.5, DCM); $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, CDCl_3): δ 64.6, 50.1 (d, $J_{\text{PP}} = 5.9$ Hz); ^1H NMR (400MHz, CDCl_3): δ 7.98-8.03 (m, 4H, Ar), 7.81-7.86 (m, 2H, Ar), 7.70-7.75 (m, 2H, Ar), 7.44-7.63 (m, 12H, Ar), 2.77-3.11 (m, 2H, PCH_2), 2.12-2.45 (m, 7H), 0.76 (t, $J_{\text{HH}} = 7.8$ Hz, 6H,

CH_2CH_3); ^{13}C NMR (100 MHz, CDCl_3): δ 136.2, 136.1, 133.9, 133.8, 133.4, 133.3, 132.9, 132.8, 132.7 (d, $J_{\text{PC}} = 2.4$ Hz), 132.3 (d, $J_{\text{PC}} = 2.5$ Hz), 131.9 (d, $J_{\text{PC}} = 2.8$ Hz), 131.8 (d, $J_{\text{PC}} = 2.9$ Hz), 129.4 (d, $J_{\text{PC}} = 56.2$ Hz), 129.3, 129.2, 129.0, 128.92, 128.90, 128.87, 128.81, 128.75, 127.4 (d, $J_{\text{PC}} = 52.9$ Hz), 126.8 (d, $J_{\text{PC}} = 54.0$ Hz), 124.5 (d, $J_{\text{PC}} = 51.0$ Hz), 53.1 (d, $J_{\text{PC}} = 18.3$ Hz), 46.4, 39.0 (dd, $J_{\text{PC}} = 30.8$ Hz, 14.1 Hz), 31.9 (dd, $J_{\text{PC}} = 35.7$ Hz, 16.3 Hz), 11.4.

Preparation of Optically Pure Free PPN Ligands

Dichloro complex (*S_C*)-**167** (0.1 mmol) was dissolved in DCM (5 mL), and the potassium cyanide (0.2 g) aqueous solution was added to the above solution under argon. Then, the mixture was stirred vigorously at room temperature for 1 h. The organic phase was transferred to a Schlenk tube and the solvent was removed under vacuum to get the optically pure free ligands (*S_C*)-**168**.

(*S_C*)-*N,N*-dimethyl-2,3-bis(diphenylphosphino)propan-1-amine, (*S_C*)-**168a**

(*S_C*)-**168a**

Colorless oil; 90% yields; $[\alpha]_{\text{D}} = +10^\circ$ (*c* 0.5, DCM). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3): δ -3.9 –19.6 (d, $J_{\text{PP}} = 31.0$ Hz); ^1H NMR (500 MHz, CDCl_3): δ 7.28-7.46 (m, 20H, Ar), 2.48-2.58 (m, 2H, PCH_2 , PCH), 2.25-2.34 (m, 2H, PCH_2 , CH_2NMe_2), 2.14 (s, 6H, NMe_2), 2.05-2.11 (m, 1H, CH_2NMe_2); ^{13}C NMR (125 MHz, CDCl_3): δ 139.3

(d, $J_{\text{PC}} = 10.8$ Hz), 139.2 (d, $J_{\text{PC}} = 10.5$ Hz), 136.7 (d, $J_{\text{PC}} = 16.0$ Hz), 136.0 (d, $J_{\text{PC}} = 16.8$ Hz), 134.2, 134.0, 133.6, 133.5, 133.4, 133.2, 132.6, 132.4, 128.71, 128.66, 128.34, 128.29, 128.26, 128.23, 128.21, 128.17, 128.15, 61.1 (d, $J_{\text{PC}} = 12.9, 8.0$ Hz), 45.8, 31.7 (d, $J_{\text{PC}} = 15.4, 10.7$ Hz), 29.4 (d, $J_{\text{PC}} = 16.3, 8.4$ Hz).

(*S*)-*N,N*-diethyl-2,3-bis(diphenylphosphino)propan-1-amine, (*S_C*)-168b

(*S_C*)-168b

Colorless oil; 88% yields; $[\alpha]_{365\text{nm}} = -20^\circ$ (c 0.5, DCM, 365nm). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3): δ -3.4, -19.6 (d, $J_{\text{PP}} = 30.6$ Hz); ^1H NMR (500MHz, CDCl_3): δ 7.22-7.41 (m, 20H, Ar), 2.63-2.71 (m, 1H, PCH_2), 2.37-2.52 (m, 6H), 2.14-2.19 (m, 2H, CH_2NMe_2), 0.86 (t, $J_{\text{HH}} = 7.1$ Hz, 6H, CH_2CH_3); ^{13}C NMR (125 MHz, CDCl_3): δ 139.5 (d, $J_{\text{PC}} = 8.9$ Hz), 139.3 (d, $J_{\text{PC}} = 8.5$ Hz), 136.9 (d, $J_{\text{PC}} = 16.1$ Hz), 136.5 (d, $J_{\text{PC}} = 16.4$ Hz), 134.1, 133.9, 133.6, 133.51, 133.47, 133.35, 132.7, 132.6, 128.5, 128.32, 128.26, 128.24, 128.19, 128.11, 129.06, 55.3 (dd, $J_{\text{PC}} = 13.2$ Hz, 8.0 Hz), 46.4, 32.0 (dd, $J_{\text{PC}} = 15.3$ Hz, 11.3 Hz), 29.4 (dd, $J_{\text{PC}} = 15.4$ Hz, 9.3 Hz), 11.0.

Chapter 4

Study on Palladacycle-Catalyzed Allylic Amination and Tandem Allylic Amination/ Arylation of Allylic Alcohols

4.1 Introduction

Transition metal-catalyzed transformation of allylic compounds via a π -allylmetal intermediate is one of the most powerful and useful methods for carbon-carbon and carbon-heteroatom (N, O, and S) bond formation.^[142] Palladium-catalyzed allylic amination is a well-established method for the synthesis of allyl amines. During the past three decades, a variety of allylic alcohol derivatives, in particular, allylic halides, carboxylates, and carbonates have been employed in allylic amination reaction because of the poor leaving-group ability of the hydroxyl group.^[143] A “green” direct catalytic substitution of allylic alcohols with the inherent dual advantages of avoiding the formation of stoichiometric amounts of unwanted chemical waste (in synthesis of activated substrates and during amination) as well as the formation of water as the sole co-product has recently attracted much attention from both an environmental and economical point of view.^[144] However, due to the poor leaving ability of the hydroxyl moiety, direct substitutions of allylic alcohols typically require high temperatures^[145], neat conditions,^[146] or considerable amounts of activators such as As_2O_3 ,^[147] B_2O_3 ,^[148] SnCl_2 ,^[149] PPh_3 -DEAD,^[150] $\text{Ti}(\text{O-}i\text{-Pr})_4$,^[151] BPh_3 ,^[152] $\text{BF}_3 \cdot \text{Et}_2\text{O}$,^[153] CO_2 ,^[154] BEt_3 ,^[155] or $1\text{-AdCO}_2\text{H}$ ^[156]. One of the targets for such

synthesis is 2-allylanilines and 4-allylanilines which are simple building blocks that occupy an important place in organic synthesis and can provide a significant amplification of molecular complexity. To date, there are several reports on transition metal-catalyzed allylic amination of allylic alcohols or allylic alcohol derivatives with arylamines leading to the predominant generation of the C-N bond formation products *N*-allylanilines.^[142, 144d, 152b, 157] Conversion of the *N*-allylanilines themselves into 2-allylanilines is attractive since the products obtained are starting materials for the preparation of bicyclic nitrogen containing heterocycles through the cyclization of the nitrogen onto the double bond.^[158] However thermal, protic acid promoted and charge accelerated rearrangements reported to date all have drawbacks of harsh reaction conditions, low yield or limited substrate scope.^[159] A few recent reports have also appeared of microwave assisted and heteropoly acid (HPA) catalyzed processes but these have demonstrated limited substrate scope or low yields.^[160] A one pot procedure which combines the efficient allylic amination of allylic alcohols and the subsequent allylation of the products under mild conditions to provide direct access to 2-allylanilines and 4-allylanilines with good regioselectivity and high yield is therefore an attractive synthetic methodology. This attractive synthetic methodology will avoid the formation of unwanted chemical waste in multistep synthesis and is atom economical. However, there are no reports on the use of arylamines for metal-catalyzed tandem allylic amination/ allylation to give 2-allylanilines and 4-allylanilines directly from allylic alcohols^[161] even though arylamines are one of the most attractive nitrogen sources from a cost and atom-economy point of view.

Nitrogen-based NC-palladacycles and their derivatives have been widely employed in homogeneous catalysis as catalysts or precatalysts. As part of a preliminary study we initially evaluated the catalytic potential of a simple palladacycle complex **169** (Figure 4.1) easily derived from $\{[\text{Pd}[\text{Me}_2\text{NCH}_2\text{C}_6\text{H}_4]](\mu\text{-Cl})\}$ **2**^[2, 3] towards the one-pot tandem allylic amination/ allylation of allylic alcohols to afford direct access to 2-allylanilines and 4-allylanilines. Catalyst **169** takes advantage of the fact that the starting material, benzylamine, is significantly cheaper and the established synthetic protocol available is straightforward and efficient.

Figure 4.1 Structure of Palladacycle **169**

4.2 Results and Discussion

4.2.1 Preparation of Palladacycle **169**

Scheme 4.1

Nitrogen-based NC-Palladacycles have been proven to be a class of efficient catalysts or precatalysts in homogeneous catalysis and have been widely applied in various catalyzed reactions due to their unique characters on thermostability, air-stability, easy

synthesis and high reactivity. Palladacycle derivative **169** is a readily accessible complex which was obtained via treatment of amino-based NC-palladacycle **2** with AgOTf in a high yield (Scheme 4.1). As mentioned in chapter 1, complex **2** is an easy access palladacycle dimer via the C-H activation reaction using *N,N*-dimethyl benzylamine as starting material and Li₂PdCl₄ or Pd(OAc)₂ as palladium sources.^[2, 3] In general, increased catalytic activity of the late transition metal complexes is observed with bulkier and less coordinating anions, for example, TfO⁻ > Tfa⁻ (Pd-catalysts),^[162] Ts⁻ ≈ TfO⁻, ClO₄⁻ ≈ BF₄⁻ ≈ Tfa⁻ ≈ PF₆⁻ ≈ NO₃⁻, Bz⁻ > Ac⁻ (Ag and Pd catalysts).^[163]

4.2.2 Allylic Amination of Allylic Alcohol

Scheme 4.2

Usually, allylic amination was conducted with allylic alcohol derivatives such as allylic halides, carboxylates and carbonates because the leaving-group ability of the hydroxyl group is poor. For the inert leaving ability of allylic alcohol, allylic amination reaction usually needs hard conditions or extra activator. Herein, an allylic amination of allylic alcohol and various amides have been carried out in DCE at 70 °C for 12 h without any additional activator (Scheme 4.2). Palladacycle **169** can provide high reactivity in allylic amination of allylic alcohol. As shown in Table 4.1, high yields were exclusively obtained for various amides including TsNH₂, BocNH₂, CbzNH₂, benzamide, acetamide and urea.

Table 4.1 Allylic amination of allylic alcohol **170a** and various amides^[a]

Entries	Amides 171	Products 172	Yield ^[b] [%]
1			95
2			97
3			94
4			98
5			97
6			91

[a] Unless otherwise indicated, all reactions were performed at 70 °C using substrate **170a** (0.5 mmol), amide **171** (0.75 mmol) Catalyst **169** (5 mol%) in 1,2-dichloromethane (5 mL) for 12h. [b] Isolated yield.

4.2.3 Synthesis of 2-Allylanilines and 4-Allylanilines via Tandem Allylic Amination/ Arylation Reaction

With the achiral NC-palladacycle catalyst **169** in hand, we proceeded to further evaluate the suitability of substituted aryl amines as an inexpensive, commercially available starting material for the palladium-catalyzed tandem allylic amination/ arylation of allylic alcohols to afford direct access to 2-allylanilines and

4-allylanilines without the need for an activator and under mild conditions (Table 4.1). Initially, we evaluated the solvent effects using 1, 3-diphenyl-2-propen-1-ol (**170a**) and *p*-toluidine (**173a**) as representative substrates at 70 °C. To analyze the solvent effects, reactions assisted by palladacycle **169** (5 mol %) in various solvents were investigated for a period of 12 h. These studies revealed that the non-coordinating solvent DCE provided the best results (Table 4.2, entry 1) with all starting materials being converted to **175aa** and **176aa** (91: 9). However, DMF, Toluene and dioxane showed no reactivity (Table 4.2, entries 2, 3 and 4) and when acetonitrile was used as solvent only 20% of the starting material was converted to **174aa** after 12 h (Table 4.2, entry 5). Upon exploring the possibility of a lower reaction temperature it was observed that only 50% starting material was converted to **174aa** and **175aa** (4:1) at 60 °C or 50 °C in 12 h (Table 4.2, entries 8 and 9), while only 20% starting material was converted to **174aa** and trace amount of **175aa** at 40 °C (Table 4.2, entry 7). Moreover, no products were formed when the reaction was conducted at room temperature (Table 4.2, entry 6). We then proceeded to optimize the reaction time in DCE. Initially, **174aa** was observed as the major product and **175aa** was observed as minor product after 3h (Table 4.2, entry 10). Subsequently **174aa**/ **175aa** were observed as the major products and little amount of **176aa** was found after 6 h (Table 4.2, entry 11). When the reaction time was prolonged to 24 h, **174aa** disappeared completely and **175aa** and **176aa** (89:11) were observed as the major products and the ratio of disubstituted product **176aa** was found to increase slightly (Table 4.2, entry 12). During the evaluation of different ratios of allylic alcohol to arylamine, more

diallylated product **176aa** was observed when the ratio was 1:1 (Table 4.2, entry 16) while less **176aa** was found when the ratio was decreased to 1:1.5 or 1:2 (Table 4.2, entry 17). No significant difference was found when the ratio of allylic alcohol to aniline was in the range 1:1.5, 1:2 and 1:3. Therefore the impact of ratio of allylic alcohol to amine on product selectivity became consistent after the ratio reached 1:1.5. As expected, the reaction resulted only in the formation of disubstituted products **176aa** when allylic alcohol to amine ratio was increased to 2:1 because the formed mono-substituted product is more reactive than the substrate.^[164] Lower catalyst loading led to longer reaction times (Table 4.2, entries 13, 14 and 15).

Table 4.2 Optimization of reaction conditions for palladium-catalyzed tandem allylic amination /arylation reaction ^[a]

170a	173a		174aa	175aa	176aa
Entry	Solvent	T. [°C]	Time [h]	Yield ^[b] [%]	Product ratio ^[c]
1	DCE	70	12	94	0:91:9
2	Toluene	70	12	--	--
3	Dioxane	70	12	--	--
4	DMF	70	12	--	--

5	CH ₃ CN	70	12	16	100:0:0
6	DCE	30	12	--	--
7	DCE	40	12	17	100:0:0
8	DCE	50	12	45	80:20:0
9	DCE	60	12	50	70:30:0
10	DCE	70	3	60	68:30:2
11	DCE	70	6	85	15:80:5
12	DCE	70	24	94	0:89:11
13 ^[e]	DCE	70	12	60	0:92:8
14 ^[e]	DCE	70	24	87	0:90:10
15 ^[f]	DCE	70	12	40	35:65:trace
16 ^[g]	DCE	70	12	93	0:85:15
17 ^[h]	DCE	70	12	94	0:92:8

[a] Unless otherwise indicated, all reactions were performed using substrate **170a** (0.2 mmol), amine **173a** (0.3 mmol) Catalyst **169** (5 mol%). [b] Isolated yield of **174aa+175aa+176aa**. [c] Product ratio of **174aa+175aa+176aa**. [d] Catalyst **169** (5 mol%). [e] Catalyst **169** (2 mol%). [f] Catalyst **169** (1 mol%). [g] **170a** (0.2 mmol), **173a** (0.2 mmol). [h] **170a** (0.2 mmol), **173a** (0.4 mmol)

With the optimum conditions established, we proceeded to screen various

commercially available arylamines. In all cases, good to high yields were achieved employing the previously optimized conditions. The electronic character of the arylamines seems to greatly influence the selectivity, while the reactivity towards allylic amination seems relatively unaffected. As shown in Table 4.3 and Table 4.4, electron-donating groups at the ortho or para position of anilines enhanced both reactivity and selectivity towards the *C*-allylated products (Table 4.3, entries 1-4, Table 4.4, entries 1 and 2), while the presence of a strongly electron-withdrawing group such as nitro or carboxylate favored the *N*-allylated products (Table 4.3, entries 15, 16 and 17) and no *C*-allylated product was observed in such instances. This trend however seems to be disrupted when a very strong electron withdrawing groups like trifluoromethyl (Table 4.3, entries 8) is involved. This observation can be attributed to the fact that the lone pair of amino groups in this aniline substrates are not able to interact with the Pd center as compared to aniline substrates with weaker electron withdrawing groups. The trend reversal also occurs in the presence of a potentially coordinated group such as cyano (Table 4.3, entry 9) which competes with the amino group for coordination on the palladium. When halogens (F, Cl, Br) were introduced (with their electron donation ability by conjugation and electron withdrawing potential by induction) at the ortho or para position of aniline, the *C*-allylation products were preferred (Table 4.3, entries 5, 6 and 7, Table 4.4, entries 3, 4 and 5). When one of the ortho positions of the monosubstituted arylamines were occupied, the para substituted products were preferentially obtained instead of the ortho substituted products in good yields. Obviously, in these cases the selectivity between

ortho and para substitution is dictated by steric hindrance (Table 4.4, entries 1-7). In all instances the corresponding diallylation products in which both ortho and para positions were allylated were obtained as the minor products. For para mono-substituted arylamines, monoallylation products in which allylation occurred at the ortho position was observed as the major products (Table 4.3, entries 1-9), and the diallylation products in which substitution occurred simultaneously at both the ortho positions were the minor ones. To avoid such an undesired diallylation, 2, 4- and 2, 6-disubstituted arylamines were also screened as reactants. As expected, the results showed that only the corresponding monoallylation products were formed and higher yields were obtained when 2,4-disubstituted and 2,6-disubstituted arylamines were employed (Table 4.3, entries 10-14, Table 4.4, entries 8-12).

Table 4.3 Palladium-catalyzed tandem allylic amination/ arylation^[a]

Entries	Anilines	174 Yield ^[b] [%]	175 Yield ^[b] [%]
1	173a	--	85
2	173b	--	86
3	173c	--	89

4		173d			75
5		173e			85
6		173f	--		88
7		173g	--		70
8		173h	--		83
9		173i	--		90
10		173j	--		95
11		173k	--		93
12		173l			90
13		173m			88
14		173n			86
15		173o		--	
16		173p		--

[a] Unless otherwise indicated, all reactions were performed at 70 °C using substrate (0.5 mmol), amine (0.75 mmol) Catalyst **169** (5 mol%) in DCE for 12 h. [b] Isolated yield.

Various aromatic amines were thus employed to react with the allylic substrate **170a** ($R = \text{Ph}$) in the presence of catalyst (5 mol %) at 70 °C in 1,2-dichloroethene (Scheme 1), providing the *C*-allylation products in good yields (75–94%) (Table 4.3 and Table 4.4). Reactions involving relatively less activated allylic alcohol substrates **170b**, **170d** and **170f** needs higher temperature (90 °C) in order to obtain good yields. Excellent regioselectivities were observed when substituted anilines were employed in the tandem one-pot allylic amination/ arylation of other allylic alcohols **170b–f** (Table 4.5) with **175** or **180** being formed as the major products. This reaction favors the less sterically hindered products.

Table 4.4 Palladium-catalyzed tandem allylic amination/ arylation ^[a]

Entries	Anilines 177	Products 178	Yield ^[b] [%]
---------	---------------------	---------------------	--------------------------

1	177a		81
2	177b		80
3	177c		85
4	177d		86
5	177e		83
6	177f		90
7	177g		87
8	177h		92
9	177i		94
10	177j		92
11	177k		90

[a] Unless otherwise indicated, all reactions were performed at 70 °C using substrate (0.5 mmol), amine (0.75 mmol) Catalyst **169** (5 mol%) in DCE for 12 h. [b] Isolated yield.

Table 4.5 Palladacycle-catalyzed tandem allylic amination/ arylation reaction of various alcohols^[a]

Entry	Alcohols 170	Anilines	Yield ^[b] of 175 [%]	Yield ^[b] of 180 [%]
1 ^[c]	170b	173a	80	
2 ^[c]	170b	173b	75	
3 ^[c]	170b	173j	92	
4	170c	173j		75
5	170d	173j		78

[a] Unless otherwise indicated, all reactions were performed at 70 °C using allylic alcohol **170** (0.5 mmol), amine **173** (0.75 mmol) Catalyst **169** (5 mol%) in 1,2-dichloroethane (3 mL) for 12h. [b] Isolated yield. [c] Reactions were performed at 90 °C. [d] For 24 h

4.2.4 Proposed Reaction Pathway of Tandem Allylic Amination/ Arylation Reaction

To obtain some insights into the reaction mechanism, a closely monitored experiment was conducted with **170a** in the presence of **169** (5 mol%) at 70 °C for 1 h. The results indicated the gradual formation of *N*-allylated product **174aj** along with the formation of an intermediate **181a** at the early stage of the reaction. The intermediate **181a** was isolated and characterized as di(1,3-diphenyl-2-propenyl) ether. Separately, we also confirmed the subsequent transformation of isolated **181a** into **174aj/ 175aj** (1:1) in 3 h and to exclusively **175aj** in 12h in the presence of **169** (5 mol%). Also, the gradual formation **174aj** had been separated and characterized by spectrum. We also isolated

174aj and reaction of **174aj** with 2,4-dimethylaniline (**173 j**) was carried out to give **175aj** under the optimized conditions. These results revealed that the formation of **174aj** may proceed via two pathways as shown in Scheme 4.4: namely, a direct allylic amination with **170a** and an allylation via the intermediate **181a**. The allylic amination product **174aj** then underwent further arylation reaction to give the desired product **175aj**.

Scheme 4.4

There are three proposed ways to give the **175aj** from **174aj**: Aza-Claisen rearrangement, Hofmann-Martius rearrangement and allylic arylation reaction (Scheme 4.5).

Scheme 4.5

In order to clear the reaction mechanism, we also conducted several monitored experiments to provide the evidence.

Under the optimum reaction conditions, control experiment was conducted that compound **182** underwent a Hofmann-Maritius rearrangement and no rearrangement product was obtained even though higher temperature or longer time (Scheme 4.6).

Scheme 4.6

We used **174bj** to conduct the control experiment, and **175bj** was obtained as the major product. Additionally, mixture of **175bj** and **175bk** was observed when **174bj** reacted with equivalent aniline **173k** under previously optimum reaction conditions (Scheme 4.7).

Scheme 4.7

These evidences demonstrated that the reaction proposed to undergo allylic arylation in the conversion from **174bj** to **175bj** instead of Aza-Claisen rearrangement reaction

and Hofmann-Maritius.

4.3 Conclusion

In summary, we prepared the NC-palladacycle derivative **169** from the di- μ -chlorobis-{2-[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}dipalladium dimer and **169** showed its high reactivity in allylic amination. Extended application of palladacycle complex **169** was explored in tandem allylic amination/ arylation of allylic alcohols which was studied to provide direct access to hitherto inaccessible 2-allylanilines and 4-allylanilines respectively in high yields with water being the only by-product and without any activator. We have also proposed a reaction pathway for this catalyzed tandem reaction protocol.

4.4 Experimental Section

4.4.1 Synthesis of NC-Palladacycle Complex 169

To a solution of di- μ -chlorobis-{2-[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}dipalladium **2**^[2, 3] (1.1 g, 2 mmol) in acetonitrile (20 mL) was added silver trifluoromethanesulfate (2.1 g, 8 mmol), and the mixture was stirred at room temperature in darkness for 30 min. Silver chloride formed was filtered off through Celite, washed with water, and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure to give a green yellow oil **169** (1.7 g, 90% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.12-7.15 (m, 1H, Ar), 6.96-7.00 (m, 3H, Ar), 3.97 (s, 2H, CH₂NMe₂), 2.82 (s, 6H, NMe₂), 2.43 (s, 3H, NCMe), 2.18 (s, 3H, NCMe); ¹³C NMR (125 MHz, CDCl₃): δ 148.0, 136.4, 132.7,

126.4, 125.8, 122.7, 121.5, 119.7 (q, $J_{\text{FC}} = 381.3$ Hz), 119.0, 72.8, 52.3, 3.4, 2.1

4.4.2 Synthesis of *N*-allylamines **172** via Palladacycle-Catalyzed Allylic Amination

To a solution of **170a** (105 mg, 0.5 mmol) and amides **171** (0.75 mmol) in DCE (3 mL), was added 5 mol% catalyst **169** under argon, and the mixture was heated to 70 °C and stirred at the same temperature for 12h. After the starting material **170a** converted completely (monitored by TLC), the reaction mixture was concentrated to give the crude products. The crude products were purification by column chromatography to give the *N*-allylamides **172** in 91-98% yields.

(*E*)-1,3-diphenyl-*N*-tosylprop-2-en-1-amine (**172a**)

Pale yellow solid: mp 129-131 °C; 95% isolated yield; $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.66 (d, $J_{\text{HH}} = 8.2$ Hz, 2H, Ar), 7.13-7.24 (m, 12H, Ar), 6.35 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.08 (dd, $J = 15.9, 6.4$ Hz, 1H, $\text{CH}=\text{CHCH}$), 5.10-5.14 (m, 1H, $\text{CH}=\text{CHCH}$), 5.03 (brs, 1H, NH), 2.33 (s, 3H, Me); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 143.7, 140.1, 138.2, 136.5, 132.5, 129.8, 129.1, 128.9, 128.6, 128.3, 127.7, 127.5, 126.9, 60.2, 21.8.

N-((*E*)-1,3-diphenylallyl)benzamide (**172b**)

White solid: mp 157-159 °C; 97% isolated yield. **¹H NMR** (400 MHz, CDCl₃): δ 7.82-7.84 (m, 2H, Ar), 7.23-7.53 (m, 13H, Ar), 6.60-6.64 (m, 2H, CH=CHCH, *NH*), 6.45 (dd, *J*_{HH} = 15.8, 6.1 Hz, 1H, CH=CHCH), 6.02-6.05 (m, 1H, CH=CHCH); **¹³C NMR** (100 MHz, CDCl₃): δ 166.5, 140.9, 136.4, 134.4, 131.8, 131.6, 128.9, 128.8, 128.59, 128.55, 127.81, 127.77, 127.2, 127.0, 126.6, 55.2; **HRMS (ESI)**: Calcd for 314.1545; C₂₂H₂₀NO (*M*⁺+H), found 314.1553

***N*-((*E*)-1,3-diphenylallyl)acetamide (172c)**

Pale white solid: mp 128-129 °C; 94% isolated yield; **¹H NMR** (400 MHz, CDCl₃): δ 7.23-7.37 (m, 10H, Ar), 6.52 (d, *J*_{HH} = 15.9 Hz, 1H, CH=CHCH), 6.33 (dd, *J*_{HH} = 15.9, 6.0 Hz, 1H, CH=CHCH), 6.06 (d, *J*_{HH} = 15.9 Hz, 1H, *NH*), 5.79-5.82 (m, 1H, CH=CHCH), 2.04 (s, 3H, COMe); **¹³C NMR** (100 MHz, CDCl₃): δ 169.1, 140.9, 136.4, 131.4, 128.9, 128.8, 128.5, 127.8, 127.7, 127.2, 126.5, 54.8, 23.4; **HRMS (ESI)**: Calcd for 252.1388; C₁₇H₁₈NO (*M*⁺+H), found 252.1390

1-((*E*)-1,3-diphenylallyl)urea (172d)

Pale white solid: mp 185-187 °C; 91% isolated yield; **¹H NMR** (400 MHz, CDCl₃): δ

7.20-7.29 (m, 10H, Ar), 6.42-6.52 (m, 1H, $CH=CHCH$), 6.22-6.29 (m, 1H, $CH=CHCH$), 5.50-5.52 (m, 1H, NH), 5.11 (t, $J_{HH} = 6.8$ Hz, 1H, $CH=CHCH$); ^{13}C **NMR** (100 MHz, $CDCl_3$): δ 156.7, 136.4, 131.1, 131.0, 129.8, 128.9, 128.8, 128.52, 128.50, 127.73, 127.68, 127.05, 127.01, 126.6, 56.4; **HRMS (ESI)**: Calcd for 253.1341; $C_{16}H_{17}N_2O$ ($M^+ + H$), found 253.1342

***tert*-butyl (*E*)-1,3-diphenylallylcarbamate (172e)**

White solid: mp 117-118 °C; 97% isolated yield; 1H **NMR** (400 MHz, $CDCl_3$): δ 7.24-7.39 (m, 10H, Ar), 6.55 (d, $J_{HH} = 15.9$ Hz, 1H, $CH=CHCH$), 6.33 (dd, $J_{HH} = 15.9$, 6.0 Hz, 1H, $CH=CHCH$), 5.47 (m, 1H, $CH=CHCH$), 4.99 (brs, 1H, CMe_3), 1.47 (s, 9H); ^{13}C **NMR** (100 MHz, $CDCl_3$): δ 155.0, 141.4, 136.6, 131.0, 129.6, 128.7, 127.7, 127.5, 127.0, 126.5, 79.8, 56.4, 28.4; **HRMS (ESI)**: Calcd for 310.1807; $C_{20}H_{24}NO_2$ ($M^+ + H$), found 310.1802

Benzyl (*E*)-1,3-diphenylallylcarbamate (172f)

White solid: mp 112-113 °C; 98% isolated yield; 1H **NMR** (400 MHz, $CDCl_3$): δ 7.24-7.39 (m, 15H, Ar), 6.56 (d, $J_{HH} = 15.9$ Hz, 1H, $CH=CHCH$), 6.34 (dd, $J_{HH} = 15.9$, 6.0 Hz, 1H, $CH=CHCH$), 5.54 (m, 1H, $CH=CHCH$), 5.23 (brs, 1H, NH), 5.11-5.18 (m, 2H, $COOCH_2Ph$); ^{13}C **NMR** (100 MHz, $CDCl_3$): δ 155.5, 140.9, 136.40, 136.37, 131.3, 129.1, 128.8, 128.54, 128.50, 128.4, 128.1, 127.8, 127.7, 127.0, 126.6, 67.0,

56.9; **HRMS (ESI)**: Calcd for 344.1651; C₂₃H₂₂NO₂ (M⁺+H), found 344.1656

4.4.3 Synthesis of 2-Allylanilines and 4-Allylanilines

A typical procedure for tandem allylic amination/ arylation of allylic alcohols and anilines

To a 25 ml sealed tube were successively added allylic alcohols **170** (0.5 mmol), aniline **173** (0.75 mmol), Cat. **169** (0.025 mmol) and 1,2-dichloroethene (3 mL). The resultant reaction mixture was stirred at 70 °C for 12 h. On completion, the reaction mixture was concentrated under reduced pressure and the resultant residue was directly purified by flash column chromatography on silica gel (EtOAc/*n*-hexane: 1/50→1/15) to give 2-allylanilines and 4-allylanilines in 70-95% yields.

4-methyl-2-((*E*)-1,3-diphenylallyl)benzenamine (**175aa**)

Pale yellow oil; 84% isolated yield; ¹H NMR (400 MHz, CDCl₃): δ 7.19-7.43 (m, 10H, Ar), 6.90-6.92 (m, 2H, NH₂Ar), 6.68 (dd, *J*_{HH} = 15.9 , 7.0 Hz, 1H, CH=CHCH), 6.60 (d, *J*_{HH} = 8.2 Hz, 1H, NH₂Ar), 6.28 (d, *J*_{HH} = 15.9 Hz, 1H, CH=CHCH), 4.87 (d, *J* = 7.0 Hz, 1H, CH=CHCH), 3.40 (brs, 2H, NH₂), 2.23 (s, 3H, Me); ¹³C NMR (100 MHz, CDCl₃): δ 141.9, 141.7, 137.2, 131.6, 131.4, 129.7, 128.8, 128.7, 128.5, 128.2, 128.09, 128.05, 127.3, 126.7, 126.3, 116.6, 49.6, 20.7; **HRMS (ESI)**: Calcd for C₂₂H₂₂N (M⁺+H): 300.1752, found 300.1754.

4-methoxy-2-((*E*)-1,3-diphenylallyl)benzenamine (**175ab**)

Pale yellow oil; 86% isolated yield; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.20-7.38 (m, 10H, Ar), 6.64-6.72 (m, 4H), 6.30(d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.91 (d, $J_{\text{HH}} = 6.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.76 (s, 3H, OMe), 3.31 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 153.0, 141.7, 137.9, 137.1, 131.7, 131.2, 130.1, 128.8, 128.7, 128.5, 127.4, 126.8, 126.4, 117.5, 115.9, 112.3, 55.7, 49.6; **HRMS (ESI)**: Calcd for $\text{C}_{22}\text{H}_{22}\text{NO}$ (M^++H): 316.1701, found 316.1705

4-phenoxy-2-((E)-1,3-diphenylallyl)benzenamine (175ac)

Pale yellow oil; 89% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.19-7.34 (m, 12H, Ar), 6.99 (t, $J = 7.4$ Hz, 1H, Ar), 6.89-6.93 (m, 3H, Ar), 6.79 (dd, $J_{\text{HH}} = 8.5$, 2.6 Hz, 1H, Ar), 6.66 (d, $J_{\text{HH}} = 8.5$ Hz, 1H, Ar), 6.62 (dd, $J_{\text{HH}} = 15.9$, 7.0 Hz, 1H, $\text{CH}=\text{CHCH}$), 6.30 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.88 (d, $J_{\text{HH}} = 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.46 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 158.8, 148.6, 141.3, 140.5, 136.9, 131.8, 130.9, 129.9, 129.5, 128.8, 128.7, 128.5, 127.5, 127.0, 126.4, 122.0, 121.3, 119.2, 117.4, 117.1, 49.6; **HRMS (ESI)**: Calcd for $\text{C}_{27}\text{H}_{24}\text{NO}$ (M^++H): 378.1858, found 378.1863

4-hydroxy-2-((E)-1,3-diphenylallyl)benzenamine (175ad)

Brown yellow oil; 75% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.22-7.36(m, 10H, Ar), 6.56-6.64 (m, 4H, Ar), 6.26(d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.88 (d, $J_{\text{HH}} = 6.9$ Hz, 1H, $\text{CH}=\text{CHCH}$); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 148.9, 141.5, 137.2, 137.0, 131.6, 131.1, 130.3, 128.9, 128.7, 128.5, 127.4, 126.8, 126.3, 118.0, 116.4, 114.4, 49.3; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{20}\text{NO}$ ($\text{M}^+ + \text{H}$): 302.1545, found 302.1546

4-fluoro-2-((*E*)-1,3-diphenylallyl)benzenamine (175ae)

Pale yellow oil; 85% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.22-7.37 (m, 10H, Ar), 6.79-6.82 (m, 2H), 6.58-6.63 (m, 2H), 6.28 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.86 (d, $J_{\text{HH}} = 6.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.41 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 156.6 (d, $J_{\text{FC}} = 235.9$ Hz), 141.1, 140.2, 136.8, 132.0, 130.6, 129.9 (d, $J_{\text{FC}} = 6.2$ Hz), 128.83, 128.78, 128.6, 127.6, 127.0, 126.4, 117.2 (d, $J_{\text{FC}} = 7.8$ Hz), 115.8 (d, $J_{\text{FC}} = 23.2$ Hz), 113.9 (d, $J_{\text{FC}} = 22.2$ Hz), 49.4; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{19}\text{FN}$ ($\text{M}^+ + \text{H}$): 304.1502, found 304.1490

4-chloro-2-((*E*)-1,3-diphenylallyl)benzenamine (175af)

Pale yellow oil; 88% isolated yield; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.24-7.43 (m, 10H, Ar), 7.16 (d, $J_{\text{HH}} = 1.8$ Hz, 1H, NH_2Ar), 6.97 (dd, $J_{\text{HH}} = 10.0, 1.8$ Hz, 1H, NH_2Ar), 6.75 (d, $J_{\text{HH}} = 10.0$ Hz, 1H, NH_2Ar), 6.65 (dd, $J_{\text{HH}} = 15.8, 7.5$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.37 (d, $J_{\text{HH}} = 15.8$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.82 (d, $J_{\text{HH}} = 7.5$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.01 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 143.4, 141.3, 137.2, 134.5, 132.5, 131.4, 129.3, 128.6, 128.5, 127.9, 127.3, 126.5, 126.3, 119.3, 115.9, 53.1; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{19}\text{ClN}$ ($\text{M}^+ + \text{H}$): 320.1206, found 320.1200

4-bromo-2-((E)-1,3-diphenylallyl)benzenamine (175ag)

Pale yellow oil; 70% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.18-7.38 (m, 12H, Ar), 6.61 (dd, $J_{\text{HH}} = 15.9, 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.57 (d, $J_{\text{HH}} = 8.2$ Hz, 1H, NH_2Ar), 6.28 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.83 (d, $J_{\text{HH}} = 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.55 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 143.4, 140.9, 136.8, 132.1, 131.7, 130.39, 130.36, 130.2, 128.9, 128.7, 128.6, 127.6, 127.1, 126.4, 118.0, 110.8, 49.5; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{19}\text{BrN}$ ($\text{M}^+ + \text{H}$): 364.0701, found 364.0695

4-(trifluoromethyl)-2-((E)-1,3-diphenylallyl)benzenamine (175ah)

Pale yellow oil; 83% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.24-7.40 (m, 12H, Ar), 6.71 (d, $J_{\text{HH}} = 8.0$ Hz, 1H, NH_2Ar), 6.66 (dd, $J_{\text{HH}} = 15.9, 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.33 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.87 (d, $J_{\text{HH}} = 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.85 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 147.3, 140.7, 136.8, 132.3, 130.0, 129.0, 128.62, 128.59, 127.7, 127.4, 127.2, 126.4, 126.3 (q, $J_{\text{FC}} = 3.7$ Hz), 125.0 (q, $J_{\text{FC}} = 3.7$ Hz), 124.8 (q, $J_{\text{FC}} = 270.4$ Hz), 120.4 (q, $J_{\text{FC}} = 32.5$ Hz), 115.7, 49.7; **HRMS (ESI)**: Calcd for $\text{C}_{22}\text{H}_{19}\text{F}_3\text{N}$ ($\text{M}^+ + \text{H}$): 354.1470, found 354.1476.

4-amino-3-((*E*)-1,3-diphenylallyl)benzonitrile (175ai)

Pale yellow oil; 90% isolated yield; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.17-7.37 (m, 12H, Ar), 6.67 (d, $J_{\text{HH}} = 8.5$ Hz, 1H, NH_2Ar), 6.56 (dd, $J_{\text{HH}} = 15.8, 7.4$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.31 (d, $J_{\text{HH}} = 15.8$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.76 (d, $J_{\text{HH}} = 7.4$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.33 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 148.2, 142.8, 136.9, 134.6, 133.4, 131.8, 128.64, 128.54, 128.47, 127.5, 126.7, 126.3, 117.6, 115.5, 96.0, 52.8; **HRMS (ESI)**: Calcd for $\text{C}_{22}\text{H}_{19}\text{N}_2$ ($\text{M}^+ + \text{H}$): 311.1548, found 311.1547.

2,4-dimethyl-6-((*E*)-1,3-diphenylallyl)benzenamine (175aj)

Pale yellow oil; 95% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.23-7.42 (m,

10H, Ar), 6.88 (s, 1H, NH_2Ar), 6.84 (s, 1H, NH_2Ar), 6.72 (dd, $J_{\text{HH}} = 15.9, 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.31 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.91 (d, $J_{\text{HH}} = 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.45 (brs, 2H, NH_2), 2.26 (s, 3H, CMe), 2.17 (s, 3H, CMe); ^{13}C NMR (125 MHz, CDCl_3): δ 142.0, 139.9, 137.2, 131.8, 131.3, 129.7, 128.8, 128.7, 128.5, 127.7, 127.5, 127.3, 127.2, 126.7, 126.3, 122.9, 49.8, 20.6, 17.7; **HRMS (ESI)**: Calcd for $\text{C}_{23}\text{H}_{24}\text{N}$ ($\text{M}^+ + \text{H}$): 314.1909, found 314.1920.

2,4-dimethoxy-6-((*E*)-1,3-diphenylallyl)benzenamine (175ak)

Pale yellow oil; 93% isolated yield; ^1H NMR (500 MHz, CDCl_3): δ 7.20-7.38 (m, 10H, Ar), 6.66 (dd, $J_{\text{HH}} = 15.9, 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.43 (s, 1H, NH_2Ar), 6.32 (s, 1H, NH_2Ar), 6.30 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.96 (d, $J_{\text{HH}} = 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.83 (s, 3H, OMe), 3.71 (s, 3H, OMe), 3.46 (brs, 2H, NH_2); ^{13}C NMR (125 MHz, CDCl_3): δ 152.5, 148.6, 141.7, 137.1, 131.5, 131.2, 129.3, 128.8, 128.6, 128.5, 127.6, 127.3, 126.7, 126.3, 105.6, 97.1, 55.7(2C), 49.5; **HRMS (ESI)**: Calcd for $\text{C}_{23}\text{H}_{24}\text{NO}_2$ ($\text{M}^+ + \text{H}$): 346.1807, found 346.1801

2,4-difluoro-6-((*E*)-1,3-diphenylallyl)benzenamine (175al)

Pale yellow oil; 90% isolated yield; ^1H NMR (500 MHz, CDCl_3): δ 7.24-7.39 (m,

10H, Ar), 6.76 (m, 1H, NH_2Ar), 6.67 (d, $J_{\text{HH}} = 9.6$ Hz, 1H, NH_2Ar), 6.61 (dd, $J_{\text{HH}} = 15.9, 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.30 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.93 (d, $J_{\text{HH}} = 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.46 (brs, 2H, NH_2); ^{13}C NMR (125 MHz, CDCl_3): δ 155.0 (dd, $J_{\text{FC}} = 238.3, 12.2$ Hz), 151.6 (dd, $J_{\text{FC}} = 240.6, 12.3$ Hz), 140.6, 136.7, 132.3, 131.5 (q, $J_{\text{FC}} = 3.9$ Hz), 129.9, 128.9, 128.8 (d, $J_{\text{FC}} = 2.9$ Hz), 128.7, 128.6, 127.7, 127.2, 126.4, 111.1 (dd, $J_{\text{FC}} = 22.9, 3.0$ Hz), 101.9 (dd, $J_{\text{FC}} = 26.5, 24.0$ Hz), 49.2; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{18}\text{F}_2\text{N}$ ($\text{M}^+ + \text{H}$): 322.1407, found 322.1407

2,4-dichloro-6-((*E*)-1,3-diphenylallyl)benzenamine (175am)

Colorless oil; 88% isolated yield; ^1H NMR (500 MHz, CDCl_3): δ 7.24-7.40 (m, 11H, Ar), 7.01 (d, $J_{\text{HH}} = 2.5$ Hz, 1H, Ar), 6.61 (dd, $J_{\text{HH}} = 15.9, 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.31 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.86 (d, $J_{\text{HH}} = 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.02 (brs, 2H, NH_2); ^{13}C NMR (125 MHz, CDCl_3): δ 140.3, 139.7, 136.6, 132.5, 130.4, 129.7, 129.0, 128.7, 128.6, 127.8, 127.7, 127.4, 127.3, 126.4, 122.7, 120.6, 50.0; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{18}\text{Cl}_2\text{N}$ ($\text{M}^+ + \text{H}$): 354.0816, found 354.0808

2,4-dibromo-6-((*E*)-1,3-diphenylallyl)benzenamine (175an)

Pale yellow oil; 86% isolated yield; ^1H NMR (500 MHz, CDCl_3): δ 7.53 (d, $J_{\text{HH}} = 1.9$

Hz, 1H, Ar), 7.22-7.39 (m, 10H, Ar), 7.15 (d, $J_{\text{HH}} = 1.8$ Hz, 1H, Ar), 6.58 (dd, $J_{\text{HH}} = 15.9, 7.0$ Hz, 1H, CH=CHCH), 6.29 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, CH=CHCH), 4.84 (d, $J_{\text{HH}} = 7.0$ Hz, 1H, CH=CHCH), 4.07 (brs, 2H, NH_2); ^{13}C NMR (125 MHz, CDCl_3): δ 141.2, 140.2, 136.6, 132.9, 132.5, 131.1, 130.7, 129.7, 129.1, 128.7, 128.6, 127.8, 127.4, 126.5, 111.1, 109.9, 50.3; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{18}\text{Br}_2\text{N}$ ($\text{M}^+ + \text{H}$): 443.9786, found 443.9789

4-nitro-*N*-((*E*)-1,3-diphenylallyl)benzenamine (174ao)

Yellow foam solid: mp 136-138 °C; 96% isolated yield; ^1H NMR (400 MHz, CDCl_3): δ 8.06 (d, $J_{\text{HH}} = 9.0$ Hz, 2H, NO_2Ar), 7.26-7.41 (m, 10H, Ar), 6.61 (d, $J_{\text{HH}} = 15.8$ Hz, 1H, CH=CHCH), 6.59 (d, $J_{\text{HH}} = 9.0$ Hz, 2H, NO_2Ar), 6.39 (dd, $J_{\text{HH}} = 15.8, 6.1$ Hz, 1H, CH=CHCH), 5.20-5.23 (m, 1H), 4.94 (d, $J_{\text{HH}} = 5.1$ Hz, 1H, NH); ^{13}C NMR (100 MHz, CDCl_3): δ 152.1, 140.3, 138.6, 136.0, 132.3, 129.1, 128.7, 128.6, 128.2, 128.1, 127.1, 126.6, 126.2, 112.1, 60.0;

4-((*E*)-1,3-diphenylallylamino)benzoic acid (174ap)

Pale yellow solid: mp 83-85 °C; 95% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.91 (d, $J_{\text{HH}} = 12.3$ Hz, 2H, NHAr), 7.24-7.43 (m, 10H, Ar), 6.60-6.63 (m, 3H), 6.39 (dd, $J_{\text{HH}} = 15.8, 6.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 5.20 (d, $J_{\text{HH}} = 6.0$ Hz, 1H, $\text{CH}=\text{CHCH}$); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 172.1, 151.4, 141.0, 136.3, 132.2, 131.8, 129.4, 129.0, 128.6, 127.91, 127.89, 127.2, 126.6, 117.9, 112.4, 59.9; **HRMS (ESI)**: Calcd for $\text{C}_{22}\text{H}_{20}\text{NO}_2$ ($\text{M}^+ + \text{H}$): 330.1494, found 330.1502

Methyl 4-((*E*)-1,3-diphenylallylamino)benzoate (174aq)

Pale yellow oil; 85% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.80 (d, $J = 8.4$ Hz, 2H, NHAr), 7.20-7.38 (m, 10H, Ar), 6.55-6.58 (m, 3H), 6.34 (dd, $J_{\text{HH}} = 15.8, 6.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 5.13 (m, 1H, NH), 4.54 (d, $J_{\text{HH}} = 6.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.79 (s, 3H, COOMe); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 167.2, 150.8, 141.1, 136.3, 131.7, 131.4, 129.5, 128.9, 128.6, 127.9, 127.8, 127.1, 126.5, 118.8, 112.4, 59.9, 51.5; **HRMS (ESI)**: Calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_2$ ($\text{M}^+ + \text{H}$): 344.1651, found 344.1641

4-methyl-2-((*E*)-4-phenylbut-3-en-2-yl)benzenamine (175ba)

Pale yellow oil; 80% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.19-7.37 (m, 5H,

Ar), 6.98 (s, 1H, NH_2Ar), 6.89 (dd, $J_{\text{HH}} = 8.0, 1.2$ Hz, 1H, NH_2Ar), 6.62 (d, $J_{\text{HH}} = 8.0$ Hz, 1H, NH_2Ar), 6.45 (d, $J_{\text{HH}} = 16.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.34 (dd, $J_{\text{HH}} = 16.0, 2.4$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.63-3.68 (m, 1H, $\text{CH}=\text{CHCH}$), 3.60 (brs, 2H, NH_2), 2.28 (s, 3H, CMe), 1.49 (d, $J_{\text{HH}} = 7.0$ Hz, 3H, CHMe); ^{13}C NMR (125 MHz, CDCl_3): δ 141.8, 137.3, 134.2, 129.3, 129.0, 128.5, 128.2, 127.73, 127.69, 127.2, 126.2, 116.5, 37.5, 20.7, 19.3; **HRMS (ESI)**: Calcd for $\text{C}_{17}\text{H}_{20}\text{N}$ ($\text{M}^+\text{+H}$): 238.1596, found 238.1591

4-methoxyl-2-((*E*)-4-phenylbut-3-en-2-yl)benzenamine (175bb)

Pale yellow oil; 75% isolated yield; ^1H NMR (500 MHz, CDCl_3): δ 7.35 (d, $J_{\text{HH}} = 7.4$ Hz, 2H, Ar), 7.29 (t, $J_{\text{HH}} = 7.4$ Hz, 2H, Ar), 7.21 (t, $J_{\text{HH}} = 7.4$ Hz, 1H, Ar), 6.79 (d, $J_{\text{HH}} = 0.8$ Hz, 1H, NH_2Ar), 6.64-6.69 (m, 2H, NH_2Ar), 6.43 (d, $J_{\text{HH}} = 16.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.31 (dd, $J_{\text{HH}} = 16.0, 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.77 (s, 3H, OMe), 3.65-3.68 (m, 1H, CHMe), 3.47 (brs, 2H, NH_2), 1.49 (d, $J_{\text{HH}} = 7.0$ Hz, 3H, CHMe); ^{13}C NMR (125 MHz, CDCl_3): δ 153.2, 137.9, 137.1, 133.8, 131.1, 129.1, 128.5, 127.2, 126.2, 117.3, 113.6, 111.9, 55.7, 37.6, 19.3; **HRMS (ESI)**: Calcd for $\text{C}_{17}\text{H}_{20}\text{NO}$ ($\text{M}^+\text{+H}$): 254.1545, found 254.1554

2,4-dimethyl-2-((*E*)-4-phenylbut-3-en-2-yl)benzenamine (175bj)

Pale yellow oil; 92% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.37 (d, $J = 7.6$ Hz, 2H, Ar), 7.28-7.32 (m, 2H, Ar), 7.22 (t, $J_{\text{HH}} = 7.3$ Hz, 1H, Ar), 6.88 (s, 1H, NH_2Ar), 6.84 (s, 1H, NH_2Ar), 6.47 (d, $J_{\text{HH}} = 16.1$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.35 (dd, $J_{\text{HH}} = 16.1, 7.0$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.64-3.69 (m, 1H, CHMe), 3.61 (brs, 2H, NH_2), 2.27 (s, 3H, CMe), 2.18 (s, 3H, CMe), 1.51 (d, $J_{\text{HH}} = 7.0$ Hz, 3H, CHMe); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 139.9, 137.3, 134.3, 129.3, 128.9, 128.6, 128.5, 127.4, 127.2, 126.2, 125.5, 122.8, 37.7, 20.6, 19.4, 17.8; **HRMS (ESI)**: Calcd for $\text{C}_{18}\text{H}_{22}\text{N}$ ($\text{M}^+\text{+H}$): 252.1752, found 252.1750

4-methyl-2,6-bis((*E*)-1,3-diphenylallyl)benzenamine (176aa)

Pale yellow foam solid: mp 87-89 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.18-7.36 (m, 20H, Ar), 6.89 (s, 1H, NH_2Ar), 6.85 (s, 1H, NH_2Ar), 6.66 (dd, $J_{\text{HH}} = 16.0, 6.9$ Hz, 2H, $\text{CH}=\text{CHCH}$), 6.19-6.27 (m, 2H, $\text{CH}=\text{CHCH}$), 4.83-4.88 (m, 2H, $\text{CH}=\text{CHCH}$), 3.40 (brs, 2H, NH_2), 2.22 (d, $J_{\text{HH}} = 5.4$ Hz, 3H, Me); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 141.86, 141.84, 139.74, 139.65, 137.2, 131.7, 131.6, 131.4, 131.3, 128.8, 128.7, 128.6, 128.49, 128.46, 128.4, 127.32, 127.30, 127.28, 127.2, 126.8, 126.7, 126.4, 126.3, 49.7, 20.93, 20.91; **HRMS (ESI)**: Calcd for $\text{C}_{37}\text{H}_{34}\text{N}$ ($\text{M}^+\text{+H}$): 492.2691, found 492.2711

4-methoxy-2,6-bis((*E*)-1,3-diphenylallyl)benzenamine (176ab)

Pale yellow oil; **¹H NMR** (500 MHz, CDCl₃): δ 7.21-7.35 (m, 20 H, Ar), 6.62-6.68 (m, 4H), 6.20-6.28 (m, 2H), 4.88-4.92 (m, 2H, CH=CHCH), 3.65 (d, *J*_{HH} = 8.8 Hz, 3H, OMe), 3.29 (brs, 2H, NH₂); **¹³C NMR** (125 MHz, CDCl₃): δ 152.3, 141.63, 141.60, 137.1, 136.0, 135.9, 131.71, 131.66, 131.3, 131.1, 130.1, 130.0, 128.8, 128.72, 128.67, 128.5, 127.41, 127.39, 126.89, 126.85, 126.36, 126.35, 113.7, 113.6, 55.55, 55.51, 49.8; **HRMS (ESI)**: Calcd for C₃₇H₃₄NO (M⁺+H): 508.2640, found 508.2645

2-methyl-4-((*E*)-1,3-diphenylallyl)benzenamine (178aa)

Pale yellow oil; 81% isolated yield; **¹H NMR** (400 MHz, CDCl₃): δ 7.21-7.41 (m, 10H, Ar), 6.95 (s, 1H, NH₂Ar), 6.93 (d, *J*_{HH} = 8.5 Hz, 1H, NH₂Ar), 6.68 (dd, *J*_{HH} = 15.9, 7.5 Hz, 1H, CH=CHCH), 6.65 (d, *J*_{HH} = 8.5 Hz, 1H, NH₂Ar), 6.36 (d, *J*_{HH} = 15.9 Hz, 1H, CH=CHCH), 4.81 (d, *J* = 7.5 Hz, 1H, CH=CHCH), 3.51 (brs, 2H, NH₂), 2.16 (s, 3H, Me); **¹³C NMR** (100 MHz, CDCl₃): δ 144.2, 143.0, 137.5, 133.6, 133.3, 130.8, 130.7, 128.6, 128.4, 128.3, 127.10, 127.06, 126.3, 126.2, 122.4, 115.1, 53.5, 17.4; **HRMS (ESI)**: Calcd for C₂₂H₂₂N (M⁺+H): 300.1752, found 300.1754

2-methoxy-4-((*E*)-1,3-diphenylallyl)benzenamine (178ab)

Pale yellow oil; 80% isolated yield; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.18-7.37 (m, 10H, Ar), 6.62-6.68 (m, 4H), 6.32 (d, $J_{\text{HH}} = 15.8$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.80 (d, $J_{\text{HH}} = 7.4$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.77 (s, 3H, OMe), 3.72 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 147.3, 144.0, 137.4, 134.5, 133.7, 133.1, 130.9, 128.6, 128.5, 128.4, 127.2, 126.3, 121.0, 114.8, 111.0, 55.4, 53.8; **HRMS (ESI)**: Calcd for $\text{C}_{22}\text{H}_{22}\text{NO}$ ($\text{M}^+ + \text{H}$): 316.1701, found 316.1705

2-fluoro-4-((*E*)-1,3-diphenylallyl)benzenamine (178ac)

Pale yellow oil; 85% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.25-7.40 (m, 10H, Ar), 6.91 (dd, $J_{\text{HH}} = 12.2, 1.6$ Hz, 1H, NH_2Ar), 6.86 (dd, $J_{\text{HH}} = 8.1, 1.6$ Hz, 1H, NH_2Ar), 6.74-6.78 (m, 1H, NH_2Ar), 6.66 (dd, $J_{\text{HH}} = 15.8, 7.5$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.38 (d, $J_{\text{HH}} = 15.8$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.83 (d, $J_{\text{HH}} = 7.5$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.68 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 151.6 (d, $J_{\text{FC}} = 238.9$ Hz), 143.5, 137.2, 134.4 (d, $J_{\text{FC}} = 5.5$ Hz), 132.7 (d, $J_{\text{FC}} = 12.8$ Hz), 132.5, 131.3, 128.53, 128.49, 128.48, 127.3, 126.5, 126.3, 124.4 (d, $J_{\text{FC}} = 3.1$ Hz), 116.8 (d, $J_{\text{FC}} = 3.6$ Hz), 115.4 (d, $J_{\text{FC}} = 19.1$ Hz), 53.2; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{19}\text{FN}$ ($\text{M}^+ + \text{H}$): 304.1502, found

304.1510

2-chloro-4-((*E*)-1,3-diphenylallyl)benzenamine (178ad)

Pale yellow oil; 86% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.27-7.42 (m, 10H, Ar), 7.16 (d, $J_{\text{HH}} = 2.0$ Hz, 1H, NH_2Ar), 6.97 (dd, $J_{\text{HH}} = 7.2, 2.0$ Hz, 1H, NH_2Ar), 6.75 (d, $J_{\text{HH}} = 7.2$ Hz, 1H, NH_2Ar), 6.65 (dd, $J_{\text{HH}} = 15.9, 7.4$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.37 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.81 (d, $J_{\text{HH}} = 7.4$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.01 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 143.4, 141.3, 137.2, 134.5, 132.4, 131.3, 129.3, 128.54, 128.49, 127.9, 127.3, 126.5, 126.3, 119.3, 115.9, 53.1; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{19}\text{ClN}$ ($\text{M}^+ + \text{H}$): 320.1206, found 320.1214

2-bromo-4-((*E*)-1,3-diphenylallyl)benzenamine (178ae)

Pale yellow oil; 82% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.18-7.37 (m, 11H, Ar), 6.95 (dd, $J_{\text{HH}} = 8.2, 1.9$ Hz, 1H, NH_2Ar), 6.69 (d, $J_{\text{HH}} = 8.2$ Hz, 1H, NH_2Ar), 6.59 (dd, $J_{\text{HH}} = 15.9, 7.5$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.31 (d, $J_{\text{HH}} = 15.9$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.75 (d, $J_{\text{HH}} = 7.5$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.98 (brs, 2H, NH_2); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 143.4, 142.4, 137.2, 134.8, 132.40, 132.35, 131.3, 128.6,

128.52, 128.49, 127.3, 126.5, 126.3, 115.8, 109.4, 53.0; **HRMS (ESI)**: Calcd for $C_{21}H_{19}BrN$ ($M^+ + H$): 364.0701, found 364.0695

2- (trifluoromethyl) -4-((E)-1,3-diphenylallyl)benzenamine (178af)

Pale yellow oil; 90% isolated yield; 1H NMR (500 MHz, $CDCl_3$): δ 7.24-7.41 (m, 11H, Ar), 7.18 (d, $J_{HH} = 7.9$ Hz, 1H, NH_2Ar), 6.71 (d, $J_{HH} = 8.2$ Hz, 1H, NH_2Ar), 6.64 (dd, $J_{HH} = 15.3, 7.2$ Hz, 1H, $CH=CHCH$), 6.36 (d, $J_{HH} = 15.3$ Hz, 1H, $CH=CHCH$), 4.83 (d, $J_{HH} = 7.2$ Hz, 1H, $CH=CHCH$), 4.12 (brs, 2H, NH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.2, 142.9, 137.1, 133.1, 132.9, 132.3, 131.5, 128.54, 128.52, 128.50, 127.4, 126.6, 126.4, 126.3, 124.9 (d, $J_{FC} = 272.4$ Hz), 117.4, 113.7 (q, $J_{FC} = 30.0$ Hz), 53.1; **HRMS (ESI)**: Calcd for $C_{22}H_{19}F_3N$ ($M^+ + H$): 354.1470, found 354.1474

2-amino-5-((E)-1,3-diphenylallyl)benzonitrile (178ag)

Colorless oil; 85% isolated yield; 1H NMR (500 MHz, $CDCl_3$): δ 7.20-7.40 (m, 12H, Ar), 6.70 (d, $J_{HH} = 8.5$ Hz, 1H, NH_2Ar), 6.59 (dd, $J_{HH} = 15.8, 7.2$ Hz, 1H, $CH=CHCH$), 6.34 (d, $J_{HH} = 15.8$ Hz, 1H, $CH=CHCH$), 4.79 (d, $J_{HH} = 7.2$ Hz, 1H, $CH=CHCH$), 4.36 (brs, 2H, NH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.2, 142.7,

136.9, 134.6, 133.4, 131.7, 128.6, 128.52, 128.45, 127.5, 126.7, 126.3, 117.6, 115.4, 95.9, 52.8; **HRMS (ESI)**: Calcd for C₂₂H₁₉N₂ (M⁺+H): 311.1548, found 311.1545

2,6-dimethyl-4-((*E*)-1,3-diphenylallyl)benzenamine (178ah)

Pale yellow oil; 92% isolated yield; ¹H NMR (500 MHz, CDCl₃): δ 7.22-7.40 (m, 10H, Ar), 6.84 (s, 2H, NH₂Ar), 6.68 (dd, *J*_{HH} = 15.8, 7.2 Hz, 1H, CH=CHCH), 6.35 (d, *J*_{HH} = 15.8 Hz, 1H, CH=CHCH), 4.77 (d, *J*_{HH} = 7.2 Hz, 1H, CH=CHCH), 3.52 (brs, 2H, NH₂), 2.17 (s, 6H, Me); ¹³C NMR (125 MHz, CDCl₃): δ 144.3, 141.1, 137.5, 133.4, 132.9, 130.7, 128.6, 128.43, 128.39, 128.3, 127.1, 126.3, 126.1, 121.8, 53.5, 17.7; **HRMS (ESI)**: Calcd for C₂₃H₂₄N (M⁺+H): 314.1909, found 314.1914

2,6-dimethoxy-4-((*E*)-1,3-diphenylallyl)benzenamine (178ai)

Pale yellow oil; 94% isolated yield; ¹H NMR (500 MHz, CDCl₃): δ 7.18-7.38 (m, 10H, Ar), 6.65 (dd, *J*_{HH} = 15.8, 7.4 Hz, 1H, CH=CHCH), 6.40 (s, 2H, NH₂Ar), 6.33 (d, *J*_{HH} = 15.8 Hz, 1H, CH=CHCH), 4.81 (d, *J*_{HH} = 7.4 Hz, 1H, CH=CHCH), 3.77 (s, 6H, OMe); ¹³C NMR (125 MHz, CDCl₃): δ 147.4, 143.9, 137.4, 133.0, 132.4, 131.0, 128.6, 128.5, 128.3, 127.2, 126.3, 123.7, 104.7, 55.8, 54.1; **HRMS (ESI)**: Calcd for

C₂₃H₂₄NO₂ (M⁺+H): 346.1807, found 346.1808

2,6-difluoro-4-((E)-1,3-diphenylallyl)benzenamine (178aj)

Pale yellow oil; 92% isolated yield; ¹H NMR (500 MHz, CDCl₃): δ 7.23-7.40 (m, 10H, Ar), 6.74 (d, *J*_{FH} = 6.2 Hz, 2H, NH₂Ar), 6.59 (dd, *J*_{HH} = 15.9, 7.5 Hz, 1H, CH=CHCH), 6.36 (d, *J*_{HH} = 15.9 Hz, 1H, CH=CHCH), 4.78 (d, *J*_{HH} = 7.5 Hz, 1H, CH=CHCH), 3.66 (brs, 2H, NH₂); ¹³C NMR (125 MHz, CDCl₃): δ 151.9 (dd, *J*_{FC} = 240.5, 8.2 Hz), 142.8, 137.0, 133.0 (t, *J*_{FC} = 7.3 Hz), 131.74, 131.72, 128.59, 128.53, 128.49, 127.5, 126.7, 126.3, 122.1 (t, *J*_{FC} = 16.8 Hz), 111.1 (dd, *J*_{FC} = 15.9, 6.7 Hz), 53.1; HRMS (ESI): Calcd for C₂₁H₁₈F₂N (M⁺+H): 322.1407, found 322.1401

2,6-dichloro-4-((E)-1,3-diphenylallyl)benzenamine (178ak)

Pale yellow solid: mp 95-97 °C; 90% isolated yield; ¹H NMR (500 MHz, CDCl₃): δ 7.26-7.40 (m, 10H, Ar), 7.23 (s, 2H, NH₂Ar), 6.58 (dd, *J*_{HH} = 15.9, 7.0 Hz, 1H, CH=CHCH), 6.35 (d, *J*_{HH} = 15.9 Hz, 1H, CH=CHCH), 4.76 (d, *J*_{HH} = 7.0 Hz, 1H, CH=CHCH), 4.38 (brs, 2H, NH₂); ¹³C NMR (125 MHz, CDCl₃): δ 142.8, 138.5, 137.0, 133.9, 131.8, 131.7, 128.6, 128.54, 128.50, 127.9, 127.5, 126.7, 126.3, 119.6,

52.9; **HRMS (ESI)**: Calcd for $C_{21}H_{18}Cl_2N$ ($M^+ + H$): 354.0816, found 354.0823

2,6-dibromo-4-((E)-1,3-diphenylallyl)benzenamine (178al)

Pale yellow solid: mp 93-94 °C; 88% isolated yield; 1H NMR (500 MHz, $CDCl_3$): δ 7.39 (d, $J_{HH} = 7.4$ Hz, 2H, Ar), 7.31-7.36 (m, 4H, Ar), 7.22-7.28 (m, 6H, Ar), 6.58 (dd, $J_{HH} = 15.8, 7.5$ Hz, 1H, $CH=CHCH$), 6.35 (d, $J_{HH} = 15.8$ Hz, 1H, $CH=CHCH$), 4.76 (d, $J_{HH} = 7.5$ Hz, 1H, $CH=CHCH$), 4.94 (brs, 2H, NH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.7, 140.4, 136.9, 135.1, 131.8, 131.7, 128.6, 128.54, 128.48, 127.5, 126.7, 126.4, 108.9, 52.7; **HRMS (ESI)**: Calcd for $C_{21}H_{18}Br_2N$ ($M^+ + H$): 443.9786, found 443.9782

4-methyl-N-((E)-1,3-diphenylallyl)benzenamine (174aa)

Pale yellow oil; 1H NMR (500 MHz, $CDCl_3$): δ 7.22-7.45 (m, 10H), 6.97 (d, $J = 8.2$ Hz, 2H), 6.63 (d, $J = 15.8$ Hz, 1H), 6.57 (d, $J = 8.2$ Hz, 2H), 6.41 (dd, $J_1 = 15.8$ Hz, $J_2 = 6.2$ Hz, 1H), 5.06 (d, $J = 6.2$ Hz, 1H), 4.01 (brs, 1H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.0, 142.2, 136.7, 131.0, 130.9, 129.6, 128.8, 128.5, 127.6, 127.4, 127.2, 126.9, 126.5, 113.7, 61.0, 20.4; **HRMS (ESI)**: Calcd for $C_{22}H_{22}N$ ($M^+ + H$): 300.1752, found 300.1745

2,4-dimethyl-N-((E)-1,3-diphenylallyl)benzenamine (174aj)

Pale yellow oil; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.25-7.50 (m, 10H, Ar), 6.96 (s, 1H, NH_2Ar), 6.88 (d, $J_{\text{HH}} = 8.1$ Hz, 1H, NH_2Ar), 6.67 (d, $J = 15.8$ Hz, 1H, $\text{CH}=\text{CHCH}$), 6.53 (d, $J_{\text{HH}} = 8.1$ Hz, 1H, NH_2Ar), 6.48 (dd, $J_{\text{HH}} = 15.8, 6.2$ Hz, 1H, $\text{CH}=\text{CHCH}$), 5.15 (d, $J_{\text{HH}} = 6.2$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.88 (brs, 1H, NH_2), 2.26 (s, 3H, *Me*), 2.24 (s, 3H, *Me*); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 142.8, 142.3, 136.7, 131.1, 131.0, 130.9, 128.8, 128.5, 127.6, 127.4, 127.2, 127.1, 126.4, 122.2, 111.5, 60.8, 20.3, 17.6; **HRMS** (**ESI**): Calcd for $\text{C}_{23}\text{H}_{24}\text{N}$ ($\text{M}^+ + \text{H}$): 314.1909, found 314.1915

2,4-dimethyl-N-((E)-4-phenylbut-3-en-2-yl)benzenamine (174bj)

Colorless oil; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.36 (d, $J_{\text{HH}} = 8.0$ Hz, 2H, Ar), 7.29 (d, $J_{\text{HH}} = 8.0$ Hz, 2H, Ar), 7.21 (d, $J_{\text{HH}} = 8.0$ Hz, 1H, Ar), 6.88-6.90 (m, 2H), 6.55-6.61 (m, 2H), 6.25 (dd, $J_{\text{HH}} = 16.0$ Hz, 4.0 Hz, 1H, $\text{CH}=\text{CHCH}$), 4.13-4.19 (m, 1H, CHMe), 3.42 (brs, 1H, NH), 2.22 (s, 3H, *CMe*), 2.17 (s, 3H, *CMe*), 1.44 (d, $J_{\text{HH}} = 8.0$ Hz, 3H, CHMe); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 143.0, 137.1, 133.6, 131.0, 129.1, 128.5, 127.29, 127.27, 126.3, 126.0, 121.9, 111.2, 51.0, 22.3, 20.3, 17.6; **HRMS** (**ESI**):

Calcd for C₁₈H₂₂N (M⁺+H): 252.1752, found 252.1749

(1*E*)-3-((*E*)-1,3-diphenylallyloxy)-1,3-diphenylprop-1-ene (181a)

Colorless oil; ¹H NMR (500 MHz, CDCl₃): δ 7.22-7.43 (m, 20H, Ar), 6.64 (dd, *J*_{HH} = 15.5, 3.8 Hz, 2H, CH=CHCH), 6.32-6.39 (m, 2H, CH=CHCH), 5.12-5.17 (m, 2H, CH=CHCH); ¹³C NMR (125 MHz, CDCl₃): δ 141.23, 141.15, 136.6, 131.6, 131.4, 130.5, 130.3, 128.53, 128.51, 127.71 (2C), 127.66, 127.1, 126.62, 126.61, 79.2, 79.1; HRMS (ESI): Calcd for C₃₀H₂₇O (M⁺+H): 403.2062, found 403.2065

1-((1*E*)-3-((*E*)-4-phenylbut-3-en-2-yloxy)but-1-enyl)benzene (181b)

Colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 7.24-7.45 (m, 10H, Ar), 6.55 (d, *J*_{HH} = 16.0 Hz, 1H, CH=CHCH), 6.52 (d, *J*_{HH} = 8.0 Hz, 1H, CH=CHCH), 6.21 (dd, *J*_{HH} = 16.0 Hz, 8.0 Hz, 1H, CH=CHCH), 6.14 (dd, *J*_{HH} = 16.0 Hz, 8.0 Hz, 1H, CH=CHCH), 4.18-4.27 (m, 2H, CH=CHCH), 1.38 (d, *J*_{HH} = 8.0 Hz, 3H, CHMe), 1.35 (d, *J*_{HH} = 8.0 Hz, 3H, CHMe); ¹³C NMR (100 MHz, CDCl₃): δ 136.9, 136.7, 132.5, 132.1, 131.0, 130.2, 128.6, 128.5, 127.6, 127.4, 126.5, 126.4, 73.4, 73.2, 22.28, 22.25; HRMS (ESI): Calcd for C₂₀H₂₃O (M⁺+H): 279.1749, found 279.1753

2,4-dimethyl-6-((*E*)-4,4-dimethyl-1-phenylpent-2-enyl)benzenamine (180cj)

Yellow oil; 75% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.30-7.33 (m, 2H, Ar), 7.20-7.24 (m, 3H, Ar), 6.84 (s, 1H, NH_2Ar), 6.71 (s, 1H, NH_2Ar), 5.80 (dd, $J_{\text{HH}} = 15.7$, 7.4 Hz, 1H, $\text{CH}=\text{CHCH}$), 5.47 (d, $J_{\text{HH}} = 15.7$ Hz, 1H, $\text{CH}=\text{CHCH}$), 4.67 (d, $J_{\text{HH}} = 7.4$ Hz, 1H, $\text{CH}=\text{CHCH}$), 3.43 (brs, 2H, NH_2), 2.22 (s, 3H, *Me*), 2.15 (s, 3H, *Me*), 1.05 (s, 9H, CMe_3); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 143.4, 143.0, 139.9, 129.3, 128.7, 128.5, 128.4, 127.5, 126.9, 126.3, 126.2, 122.6, 49.5, 33.1, 29.7, 20.7, 17.7; **HRMS (ESI)**: Calcd for $\text{C}_{21}\text{H}_{28}\text{N}$ ($\text{M}^+ + \text{H}$): 294.2222, found 294.2230

2,4-dimethyl-6-(3-phenylcyclohex-2-enyl)benzenamine (180dj)

Pale yellow oil; 78% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.47-7.49 (m, 2H, Ar), 7.34-7.37 (m, 2H, Ar), 7.27-7.28 (m, 1H, Ar), 6.82 (s, 2H), 6.21 (s, 1H, $\text{C}=\text{CH}$), 3.61-3.64 (m, 3H), 2.51-2.57 (m, 2H), 2.23 (s, 3H, *Me*), 2.18 (s, 3H), 1.97-2.05 (m, 2H), 1.77-1.82 (m, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 142.0, 139.6, 138.0, 129.4, 129.3, 128.3, 127.63, 127.60, 127.2, 126.9, 125.1, 122.8, 39.0, 28.1, 27.3, 21.9, 20.5, 17.8; **HRMS (ESI)**: Calcd for $\text{C}_{20}\text{H}_{24}\text{N}$ ($\text{M}^+ + \text{H}$): 278.1909, found 278.1915

2,4-dimethyl-6-(3-methylcyclohex-2-enyl)benzenamine (180ej)

Colorless oil; 75% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 6.80 (s, 1H, Ar), 6.78 (s, 1H, Ar), 5.46 (s, 1H, $\text{C}=\text{CH}$), 3.62 (brs, 2H, NH_2), 3.38 (m, 1H, $\text{C}=\text{CHCH}$), 2.24 (s, 3H, *Me*), 2.17 (s, 3H, *Me*), 1.89-2.16 (m, 3H), 1.79-1.83 (m, 1H), 1.77 (s, 3H, *Me*), 1.61-1.69 (m, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 139.6, 135.9, 129.9, 129.0, 127.4, 127.0, 124.3, 122.7, 38.6, 29.9, 28.2, 24.0, 21.8, 20.5, 17.8; **HRMS (ESI)**: Calcd for $\text{C}_{15}\text{H}_{22}\text{N}$ ($\text{M}^+ + \text{H}$): 216.1752, found 216.1758

2-cinnamyl-4,6-dimethylbenzenamine(180fj)

Light brown oil; 72% isolated yield; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.36-7.38 (m, 2H, Ar), 7.28-7.32 (m, 2H, Ar), 7.20-7.23 (m, 1H, Ar), 6.84 (s, 1H, NH_2Ar), 6.83 (s, 1H, NH_2Ar), 6.49 (d, $J_{\text{HH}} = 15.9$ Hz, 1H), 6.32-6.39 (m, 1H, $\text{CH}=\text{CHCH}_2$), 3.57 (brs, 2H, NH_2), 3.47 (d, $J_{\text{HH}} = 6.1$ Hz, 2H, $\text{CH}=\text{CHCH}_2$), 2.25 (s, 3H, *Me*), 2.18 (s, 3H, *Me*); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 140.4, 137.2, 131.1, 129.6, 128.53, 128.50, 128.1, 127.4, 127.2, 126.1, 123.7, 122.6, 35.9, 20.4, 17.6; **HRMS (ESI)**: Calcd for $\text{C}_{17}\text{H}_{20}\text{N}$ ($\text{M}^+ + \text{H}$): 238.1596, found 238.1605

2,4-dimethyl-6-((*E*)-pent-3-en-2-yl)benzenamine (175jj)

Pale brown oil; 70% isolated yield; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 6.85 (s, 1H, Ar), 6.84 (s, 1H, Ar), 5.51-5.62 (m, 2H), 3.61 (brs, 2H, NH_2), 3.43-3.49 (m, 1H), 2.28 (s, 3H, *Me*), 2.20 (s, 3H, *Me*), 1.73 (d, $J_{\text{HH}} = 5.7$ Hz, 3H, $\text{CH}=\text{CHMe}$), 1.41 (d, $J_{\text{HH}} = 7.0$ Hz, 3H, $\text{CH}=\text{CHCHMe}$); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 139.8, 135.3, 129.3, 129.0, 127.2, 125.2, 124.1, 122.5, 37.3, 20.6, 19.6, 17.8, 17.7; **HRMS (ESI)**: Calcd for $\text{C}_{13}\text{H}_{20}\text{N}$ ($\text{M}^+ + \text{H}$): 190.1596, found 190.1603

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Publications

1. **Ke Chen**, Yongxin Li, Sumod A. Pullarkat*, Pak-Hing Leung*, “Palladacycle catalyzed tandem allylic amination/ allylation protocol for one pot synthesis of 2-allylanilines from allylic alcohols” *Advanced synthesis and catalysis*, **2012**, 354, 83-87.
2. **Ke Chen**, Sumod A. Pullarkat, Mengtao Ma, Yongxin Li, Pak-Hing Leung*, “Chiral cyclopalladated complex promoted asymmetric synthesis of diester-substituted *P,N*-ligands via stepwise hydrophosphination and hydroamination reactions” *Dalton transactions*, Accepted.
3. **Ke Chen**, Sumod A. Pullarkat*, Pak-Hing Leung*, “Palladacycle catalyzed tandem Heck reaction/ aza-Michael addition for one pot synthesis of isoindoline.” Manuscript in preparation
4. Mengtao Ma, Sumod A. Pullarkat, **Ke Chen**, Yongxin Li, Pak-Hing Leung*, “Template effects on the asymmetric cycloaddition reaction between 3,4-dimethyl-1-phenylarsole and diphenylvinylphosphine and their arsenic elimination reaction” *Journal of Organometallic Chemistry*, **2009**, 694, 1929–1933
5. **Ke Chen**, Sumod A. Pullarkat, Mengtao Ma, Yongxin Li, Pak-Hing Leung*, “Diastereoselective synthesis of *P,N* ligands via a chiral naphthylamine palladium (II) complex controlled asymmetric hydroamination reactions” *241st ACS National Meeting & Exposition*, **2011**, Anaheim, CA, USA.

6. **Ke Chen**, Sumod A. Pullarkat, Mengtao Ma, Yongxin Li, Pak-Hing Leung*,
“Asymmetric synthesis of P,N ligands by sequential hydrophosphination and
hydroamination reactions promoted by a chiral naphthylamine palladium (II)
complex” *6th Asian-European Symposium on metal mediated efficient reactions*,
2010, NTU, Singapore.

Appendix

Table A1. Crystal data and structure refinement for (*R_C*, *S_C*)-147a

Identification code	leung381	
Empirical formula	C ₂₀ H ₂₄ Cl ₂ N O ₄ P Pd	
Formula weight	550.67	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 10.8879(2) Å	a = 90°.
	b = 12.1286(3) Å	b = 90°.
	c = 17.4097(4) Å	g = 90°.
Volume	2299.04(9) Å ³	
Z	4	
Density (calculated)	1.591 Mg/m ³	
Absorption coefficient	1.134 mm ⁻¹	
F(000)	1112	
Crystal size	0.34 x 0.28 x 0.16 mm ³	
Theta range for data collection	2.05 to 31.58°.	
Index ranges	-11 ≤ h ≤ 16, -17 ≤ k ≤ 17, -25 ≤ l ≤ 25	
Reflections collected	28298	
Independent reflections	7490 [R(int) = 0.0473]	
Completeness to theta = 31.58°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8393 and 0.6990	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	7490 / 0 / 266	
Goodness-of-fit on F ²	1.045	
Final R indices [I > 2σ(I)]	R1 = 0.0359, wR2 = 0.0534	
R indices (all data)	R1 = 0.0474, wR2 = 0.0578	
Absolute structure parameter	-0.049(19)	
Largest diff. peak and hole	0.442 and -0.704 e.Å ⁻³	

Table A2. Crystal data and structure refinement for (*R_C*, *S_C*)-147b

Identification code	leung402
Empirical formula	C ₂₂ H ₂₈ Cl ₂ N O ₄ P Pd
Formula weight	578.72
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 8.0168(3) Å a = 90°. b = 17.2994(7) Å b = 91.136(2)°. c = 8.7571(4) Å g = 90°.
Volume	1214.25(9) Å ³
Z	2
Density (calculated)	1.583 Mg/m ³
Absorption coefficient	1.078 mm ⁻¹
F(000)	588
Crystal size	0.34 x 0.32 x 0.16 mm ³
Theta range for data collection	2.33 to 28.00°.
Index ranges	-9<= <i>h</i> <=10, -22<= <i>k</i> <=22, -11<= <i>l</i> <=11
Reflections collected	20791
Independent reflections	5764 [R(int) = 0.0388]
Completeness to theta = 28.00°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8464 and 0.7107
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5764 / 9 / 332
Goodness-of-fit on F ²	1.157
Final R indices [I>2sigma(I)]	R1 = 0.0235, wR2 = 0.0459
R indices (all data)	R1 = 0.0281, wR2 = 0.0575
Absolute structure parameter	0.00(2)
Largest diff. peak and hole	0.420 and -1.227 e.Å ⁻³

Table A3. Crystal data and structure refinement for (*S_C*,*S_N*,*R_C*,*S_C*)-149g

Identification code	leung344
Empirical formula	C ₄₂ H ₄₈ Cl ₃ N ₂ O ₈ P Pd
Formula weight	952.54
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 11.2143(4) Å a = 90°. b = 17.4999(6) Å b = 111.861(2)°. c = 11.5906(4) Å g = 90°.
Volume	2111.07(13) Å ³
Z	2
Density (calculated)	1.499 Mg/m ³
Absorption coefficient	0.722 mm ⁻¹
F(000)	980
Crystal size	0.34 x 0.30 x 0.26 mm ³
Theta range for data collection	1.89 to 36.86°.
Index ranges	-18 ≤ h ≤ 18, -29 ≤ k ≤ 29, -8 ≤ l ≤ 19
Reflections collected	50086
Independent reflections	20717 [R(int) = 0.0377]
Completeness to theta = 36.86°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8346 and 0.7915
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	20717 / 4 / 525
Goodness-of-fit on F ²	1.084
Final R indices [I > 2σ(I)]	R1 = 0.0415, wR2 = 0.0918
R indices (all data)	R1 = 0.0584, wR2 = 0.1122
Absolute structure parameter	-0.019(15)
Largest diff. peak and hole	1.569 and -1.050 e.Å ⁻³

Table A4. Crystal data and structure refinement for (*S_N*,*R_C*,*S_C*)-153a and (*R_N*,*R_C*,*S_C*)-153'a

Identification code	leung343	
Empirical formula	C ₂₄ H ₂₄ Cl ₂ N O ₄ P Pd	
Formula weight	598.71	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.4898(3) Å	a = 90°.
	b = 20.3883(6) Å	b = 109.719(2)°.
	c = 12.5453(3) Å	g = 90°.
Volume	2525.71(12) Å ³	
Z	4	
Density (calculated)	1.575 Mg/m ³	
Absorption coefficient	1.040 mm ⁻¹	
F(000)	1208	
Crystal size	0.32 x 0.20 x 0.12 mm ³	
Theta range for data collection	1.72 to 31.09°.	
Index ranges	-15 ≤ h ≤ 15, -29 ≤ k ≤ 29, -18 ≤ l ≤ 18	
Reflections collected	48882	
Independent reflections	16079 [R(int) = 0.0360]	
Completeness to theta = 31.09°	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8854 and 0.7320	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	16079 / 118 / 661	
Goodness-of-fit on F ²	1.081	
Final R indices [I > 2σ(I)]	R1 = 0.0430, wR2 = 0.1087	
R indices (all data)	R1 = 0.0588, wR2 = 0.1294	
Absolute structure parameter	-0.03(2)	
Largest diff. peak and hole	1.162 and -0.961 e.Å ⁻³	

Table A5. Crystal data and structure refinement for (*S_N*,*R_C*,*S_C*)-153b and (*R_N*,*R_C*,*S_C*)-153'b

Identification code	leuung404	
Empirical formula	C ₂₆ H ₂₈ Cl ₄ N O ₅ P Pd	
Formula weight	713.66	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.8765(11) Å	a = 90°.
	b = 13.4241(15) Å	b = 90.417(3)°.
	c = 20.538(2) Å	g = 90°.
Volume	2998.6(6) Å ³	
Z	4	
Density (calculated)	1.581 Mg/m ³	
Absorption coefficient	1.065 mm ⁻¹	
F(000)	1440	
Crystal size	0.32 x 0.26 x 0.18 mm ³	
Theta range for data collection	0.99 to 26.42°.	
Index ranges	-13 ≤ h ≤ 13, -16 ≤ k ≤ 16, -25 ≤ l ≤ 25	
Reflections collected	25277	
Independent reflections	11534 [R(int) = 0.0282]	
Completeness to theta = 26.42°	98.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8315 and 0.7269	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	11534 / 98 / 745	
Goodness-of-fit on F ²	1.121	
Final R indices [I > 2σ(I)]	R1 = 0.0397, wR2 = 0.1111	
R indices (all data)	R1 = 0.0524, wR2 = 0.1390	
Absolute structure parameter	-0.01(3)	
Largest diff. peak and hole	1.377 and -1.143 e.Å ⁻³	

Table A6. Crystal data and structure refinement for (*S_N*,*R_C*,*S_C*)-153f and (*R_N*,*R_C*,*S_C*)-153'f

Identification code	leung475	
Empirical formula	C ₂₅ H ₂₆ Cl ₂ N O ₄ P Pd	
Formula weight	612.74	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.5919(14) Å	a = 90°.
	b = 20.528(3) Å	b = 109.676(8)°.
	c = 12.6956(16) Å	g = 90°.
Volume	2599.2(6) Å ³	
Z	4	
Density (calculated)	1.566 Mg/m ³	
Absorption coefficient	1.013 mm ⁻¹	
F(000)	1240	
Crystal size	0.30 x 0.20 x 0.18 mm ³	
Theta range for data collection	1.70 to 33.30°.	
Index ranges	-15 ≤ h ≤ 16, -31 ≤ k ≤ 31, -18 ≤ l ≤ 19	
Reflections collected	65855	
Independent reflections	19720 [R(int) = 0.0396]	
Completeness to theta = 33.30°	98.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8387 and 0.7510	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	19720 / 4 / 625	
Goodness-of-fit on F ²	1.088	
Final R indices [I > 2σ(I)]	R1 = 0.0287, wR2 = 0.0701	
R indices (all data)	R1 = 0.0377, wR2 = 0.0811	
Absolute structure parameter	-0.018(12)	
Largest diff. peak and hole	0.704 and -0.941 e.Å ⁻³	

Table A7. Crystal data and structure refinement for (*S_N*,*R_C*,*S_C*)-153h and (*R_N*,*R_C*,*S_C*)-153'h

Identification code	leung418	
Empirical formula	C ₂₄ H ₂₃ Cl ₂ N ₂ O ₆ P Pd	
Formula weight	643.71	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 10.5470(4) Å	a = 89.535(2)°.
	b = 10.7713(4) Å	b = 68.438(2)°.
	c = 12.6698(5) Å	g = 79.481(2)°.
Volume	1313.39(9) Å ³	
Z	2	
Density (calculated)	1.628 Mg/m ³	
Absorption coefficient	1.013 mm ⁻¹	
F(000)	648	
Crystal size	0.34 x 0.24 x 0.14 mm ³	
Theta range for data collection	1.73 to 31.12°.	
Index ranges	-15 ≤ h ≤ 15, -15 ≤ k ≤ 15, -18 ≤ l ≤ 18	
Reflections collected	33262	
Independent reflections	15790 [R(int) = 0.0717]	
Completeness to theta = 31.12°	98.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8712 and 0.7246	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	15790 / 3 / 653	
Goodness-of-fit on F ²	1.089	
Final R indices [I > 2σ(I)]	R1 = 0.0746, wR2 = 0.2045	
R indices (all data)	R1 = 0.1098, wR2 = 0.2743	
Absolute structure parameter	0.11(4)	
Largest diff. peak and hole	1.474 and -3.993 e.Å ⁻³	

Table A8. Crystal data and structure refinement for (S)-167

Identification code	leung593	
Empirical formula	C ₃₁ H ₃₅ Cl ₂ N P ₂ Pd	
Formula weight	660.84	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 7.9454(3) Å	a = 90°.
	b = 16.7036(6) Å	b = 97.215(2)°.
	c = 11.3518(4) Å	g = 90°.
Volume	1494.65(9) Å ³	
Z	2	
Density (calculated)	1.468 Mg/m ³	
Absorption coefficient	0.928 mm ⁻¹	
F(000)	676	
Crystal size	0.40 x 0.40 x 0.18 mm ³	
Theta range for data collection	1.81 to 32.63°.	
Index ranges	-10 ≤ h ≤ 11, -21 ≤ k ≤ 25, -17 ≤ l ≤ 17	
Reflections collected	29980	
Independent reflections	9784 [R(int) = 0.0373]	
Completeness to theta = 32.63°	98.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8508 and 0.7079	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	9784 / 180 / 391	
Goodness-of-fit on F ²	1.055	
Final R indices [I > 2σ(I)]	R1 = 0.0362, wR2 = 0.0747	
R indices (all data)	R1 = 0.0428, wR2 = 0.0828	
Absolute structure parameter	0.003(19)	
Largest diff. peak and hole	0.779 and -0.829 e.Å ⁻³	