APPLICATION OF METALLACYCLES TOWARD ASYMMETRIC CYCLOADDITION AND HYDROPHOSPHINATION REACTIONS

NANYANG TECHNOLOGICAL UNIVERSITY

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ZHANG NA

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A thesis submitted to the Nanyang Technological University in fulfillment of the requirement for the degree of Doctor of Philosophy

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Table of Contents

Abbreviation and Symbols

An	anisoyl
Bn	benzyl
Bu	butyl
$CDCl_3$	chloroform-d1
CD_2Cl_2	dichloromethane-d2
$CHCl_3$	chloroform
CH_2Cl_2	dichloromethane
conc. HCl	concentrated hydrochloric acid
Cy	cyclohexyl
d	doublet
dd	doublet of doublets
ddd	doublet of doublets of doublets
decomp.	Decomposed
DMPP	3,4-dimethyl-1-phenylphosphole
ee	enantiomeric excess
equiv.	equivalent
Et	ethyl
et al.	and others
g	gram(s)
h	hour(s)

Hz	hertz
IR	infrared
J	coupling constant
KCN	potassium cyanide
m	multiplet
Me	methyl
mg	milligram
min	minute
mL	milliliter
Mp	melting point
NMR	Nuclear Magnetic Resonance
o	*ortho*
Pr	propyl
Ph	Phenyl
ppm	parts per million
q	quartet
R	*rectus* (Latin:absolute configuration)
RT	room temperature
S	*sinister* (Latin:absolute configuration)
s	singlet
t	tertiary
THF	tetrahydrofuran

°	degree of angles
Å	angstrom(s)
℃	degree Celsius
δ	NMR chemical shift in ppm
$[\alpha]_D$	specific rotation measured at sodium D line (589nm)

Summary

This thesis, consisting of three chapters, describes the application of the orthometalated [1-(dimethylamino)ethyl]naphthalene palladium(II) complex and its platinum analogue used as the chiral template to promote a range of asymmetric cycloaddition reactions and hydrophosphination reaction. This methodology provides the access to chiral P-S, P-As, P-N, and P-P bidentate ligands.

Firstly, in chapter 1, a brief introduction of chiral phosphines including their synthetic strategies and applications in asymmetric syntheses, the previous application of chiral metal template in the preparation of chiral phosphine ligands done by our research group and the aims of this project were presented.

In addition, chapter 2 covers the investigation of the chiral palladacycle containing orthometalated [1-(dimethylamino)ethyl]naphthalene and its platinum analogue as chiral auxiliary promoted asymmetric cycloaddition reactions to yield chiral P-S, P-As, and P-N bidentate ligands and the metal effect to these reactions. These reactions involved 3, 4-dimethyl-1-phenylphosphole (DMPP) and functionalized dienophiles such as divinyl sulfoxide, vinyl phenyl sulfoxide, (*E*)-methyl ester 3-(diphenylarsino)-acrylate, (*E*)-4-(diphenylarsino)-3-buten-2-one, (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone, (*E*)-1-methyl-3-pyridine-2-yl- 2-propenoate. The chiral palladium template and

platinum template showed different effect both on reactivity and selectivity of these reactions. In addition, when the same metal template was used as a chiral auxiliary, the reactivity and selectivity were totally different between *exo*-cycloaddition reactions and *endo*- cycloaddition reactions.

Last, chapter 3 describes the studies of a chiral palladacycle containing orthometalated [1-(dimethylamino)ethyl]naphthalene as the chiral auxiliary promoted asymmetric hydrophosphination reaction of 2-ethynyl-pyridine with diphenylphosphine. The hydrophosphination reaction involved C-P bonds formation and generated 1, 2-diphosphine ligand with one chiral center as the carbon backbone.

Chapter 1

General Introduction

1.1. Chiral Phosphines

1.1.1. Significance of Chiral Phosphines

Chirality plays a very important role in science and technology.[1] A wide range of significant physical, chemical, and biological functions arise from specific molecular recognition with chirality. In biology for instance, both enantiomers are desirable but have different therapeutic effect. But the preparation of chiral compounds is a challenging work. For a long time, chiral compounds were prepared only by biological or biochemical transformations. However, in the last two decades, enantioselective catalysis using metal complexes have been considered as an efficient method to synthesize chiral compounds.

Optically active phosphines have long been considered as very useful compounds for metal-based homogeneous asymmetric catalysis reactions.[2] Phosphine ligands with a lone pair of electrons can act as "soft" ligands to coordinate to "soft" metals, such as ruthenium, rhodium, palladium, iridium and platinum. The σ-donating and π-accepting properties provide chiral phosphines advantages in transition metal catalyzed asymmetric reactions. Meanwhile, the development of ^{31}P NMR spectroscopy technique provides an important method for the characterization of the compounds containing phosphorus functional group and the study of this catalytic mechanism. Hence, the design and synthesis of chiral phosphine ligands have been considered as a significant

part of the development of the catalytic asymmetric synthesis.

1.1.2 Synthesis of P-Chiral Phosphines

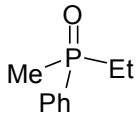
In general, P-chiral phosphines are much more difficult to synthesize than phosphines with side-chain chirality because free phosphines are very sensitive to the oxygen in the air. Hence, fewer methods for the synthesis of P-chiral phosphines have been reported than phosphines with side-chain chirality. P-chiral phosphines are usually protected as phosphine oxides, phosphine sulfides, phosphonium salts, phosphine-borane adducts and phosphine-metal complexes. Therefore, only selected examples of the synthesis of P-chiral phosphines will be mentioned here.

1.1.2.1 Resolution

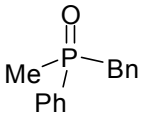
The classical resolution is converting the racemic mixture into a pair of diastereomers by reaction with an optically pure reagent. The original racemic mixture can not be separated directly, but the diastereomers could be separated by chromatography or fractional crystallization since the physical properties of the diastereomers are different. One of the most important methods for the preparation of P-chiral phosphines is therefore resolution.

The resolution of the weakly basic phosphine oxides could be achieved using optically active acids as resolving agents. For example, the first optically active organophosphorus compound ethylmethylphenylphosphine oxide **1** was obtained by the resolution using (+)-bromocamphorsulfonic acid as resolving

agent.[3] Benzylmethylphenylphosphine oxide **2** was similarly obtained by the resolution using camphorsulfonic acid.[4] Besides the direct resolution of the racemic mixture using acids, phosphine oxides such as **1** and **3** could also be resolved with optically active binaphthol, through the formation of hydrogen bonds.[5] The efficiency of the resolution depends on the steric effect at the phosphorus center.



1



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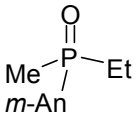
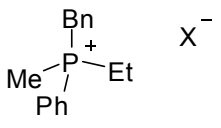
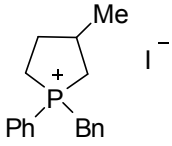


3

The exchange of the counterion is a useful method for the resolution of recemic P-chiral phosphonium salts, which use silver menthoxyacetates, silver or potassium hydrogen dibenzoyltartrates and silver camphorsulfonates as resolving agents. Phosphonium salts, **4-6,** are some of the examples that were resolved using this method.[6,7] Since the quaternary salts could convert stereospecifically to the desired phosphines, this method was one of the earliest and useful methods to prepare optically active P-chiral phosphines. In fact, the first optically active P-chiral phosphines were prepared by the electrolytic reduction using the resolved phosphonium salts as precursors.[7,8]



4a: R=Et
4b: R=*n*-Pr



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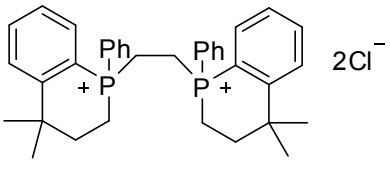
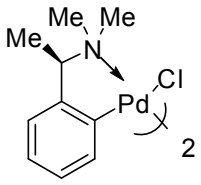


6

Using chiral metal complexes as resolving agents a pair of diastereomeric transition metal complexes could be formed, which could be separated by chromatography or fractional crystallization. After the decomplexation, the optically pure P-chiral phosphine ligands could be obtained.

N, N-dimethyl(α-methylbenzyl)amine chiral palladium (II) complex **7** and related complex **8** are very effective resolving agents for certain types of chiral phosphines.



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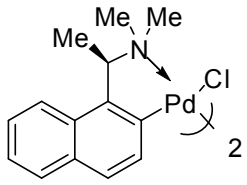
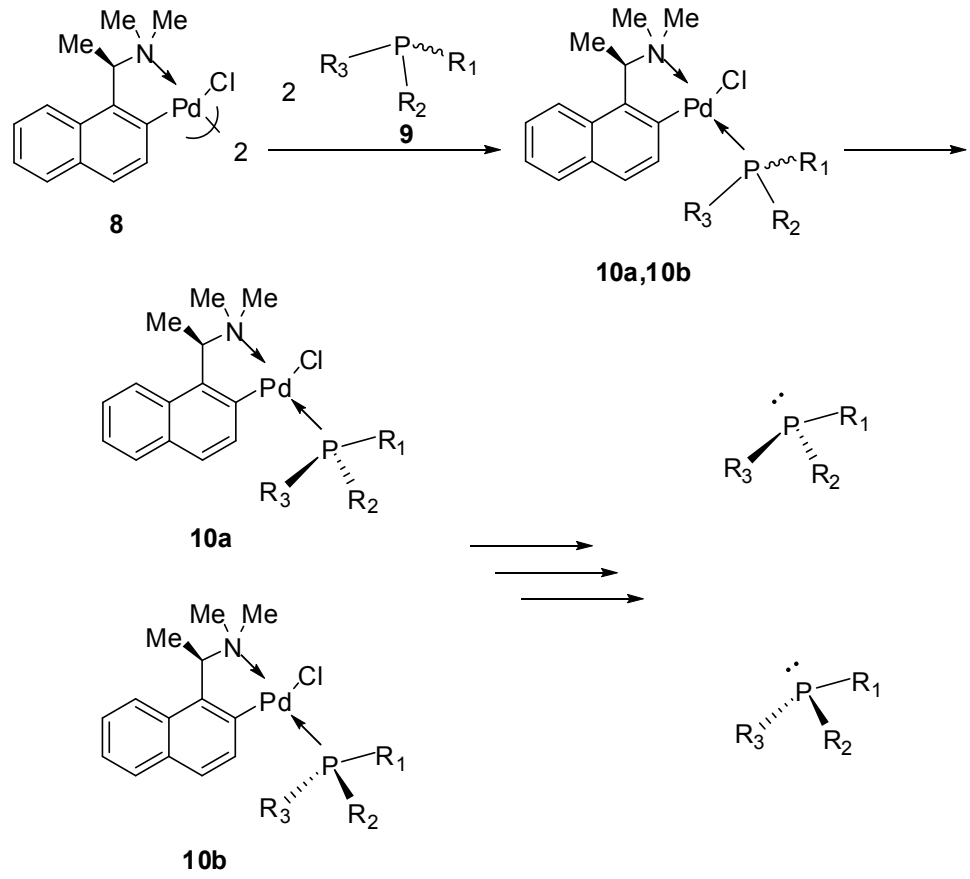
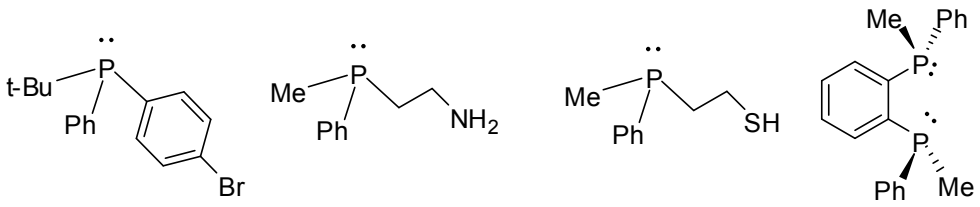


8

For example, the desired racemic P-chiral phosphines coordinate to the chiral palladium (II) complex **8** to give a pair of palladium complexes **10a** and **10b** in the ratio of 1:1. Due to the physical properties of the diastereomers **10a** and **10b** are different, they could be separated by column chromatography or fractional crystallization. After separation, the desired free phosphines could be liberated from the palladium by the treatment with DPPE or potassium cyanide. This method has been widely used to prepare monodentate and bidentate phosphines such as **11-14**. [9]

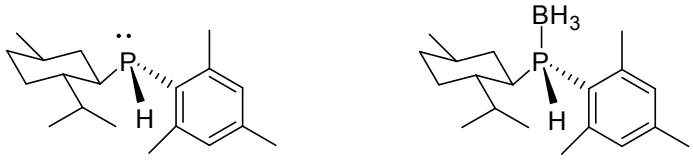


Scheme 1.1



11 **12** **13** **14**

In the presence of sodium acetylacetonate which acted as a proton scavenger, the first optically active free secondary phosphine **15** was obtained by fractional crystallization from a diastereomeric mixture.[10] However, after deboranation of the corresponding phosphine-borane complex **16** using diethylamine, optically active secondary phosphine **15** could also be obtained, with retention of configuration at the phosphorus center.



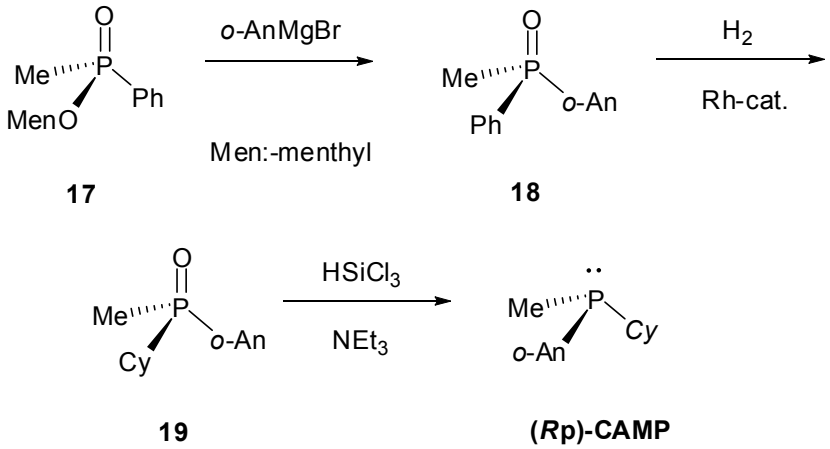
15 **16**

1.1.2.2 Asymmetric Synthesis

Another method to prepare P-chiral phosphins is asymmetric synthesis. The stereospecific nucleophilic displacement of P-chiral phosphinates by organometallic reagents is one of the most useful methods for the preparation of optically pure P-chiral phosphine oxides. This kind of nucleophilic displacement of P-chiral phosphinates using Grignard reagents or organolithium reagents could afford in high stereospecificity, with the inversion of configuration at phosphorus center and generate optically pure phosphine oxides. [11-13] However, the range of phosphine oxides which could be obtained is limited and the yield is quite variable. If the groups at phosphorus, oxygen and the organometallic reagents are different, the results of nucleophilic displacement would be variable.[12,13] Nevertheless, this method has been widely used for the synthesis of a range of optically pure P-chiral phosphine oxides which can subsequently yield the desired phosphine ligands.

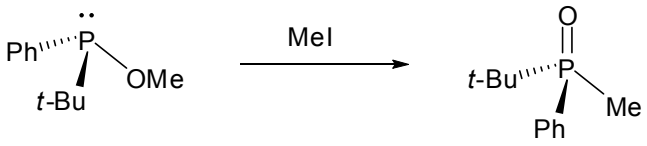
One such example is the synthesis of **CAMP** (Scheme 1.2). This preparation was the first reaction reported to synthesize P-chiral phosphine ligand which could give high stereoselectivity (90% ee) in Rh-catalyzed

asymmetric hydrogenation reaction of dehydroamino acid.[14,15] First, the menthoxy group of menthylphosphinate **17** could be replaced by *o*-anisylmagnesium bromide, with inversion of configuration to give **18**. After that, the hydrogenation reaction of compound **18** could occur and gave compound **19**. Compound **19** could be reduced to generate the free P-chiral phosphine **(*R*p)-CAMP**, with inversion of configuration at phosphorus.



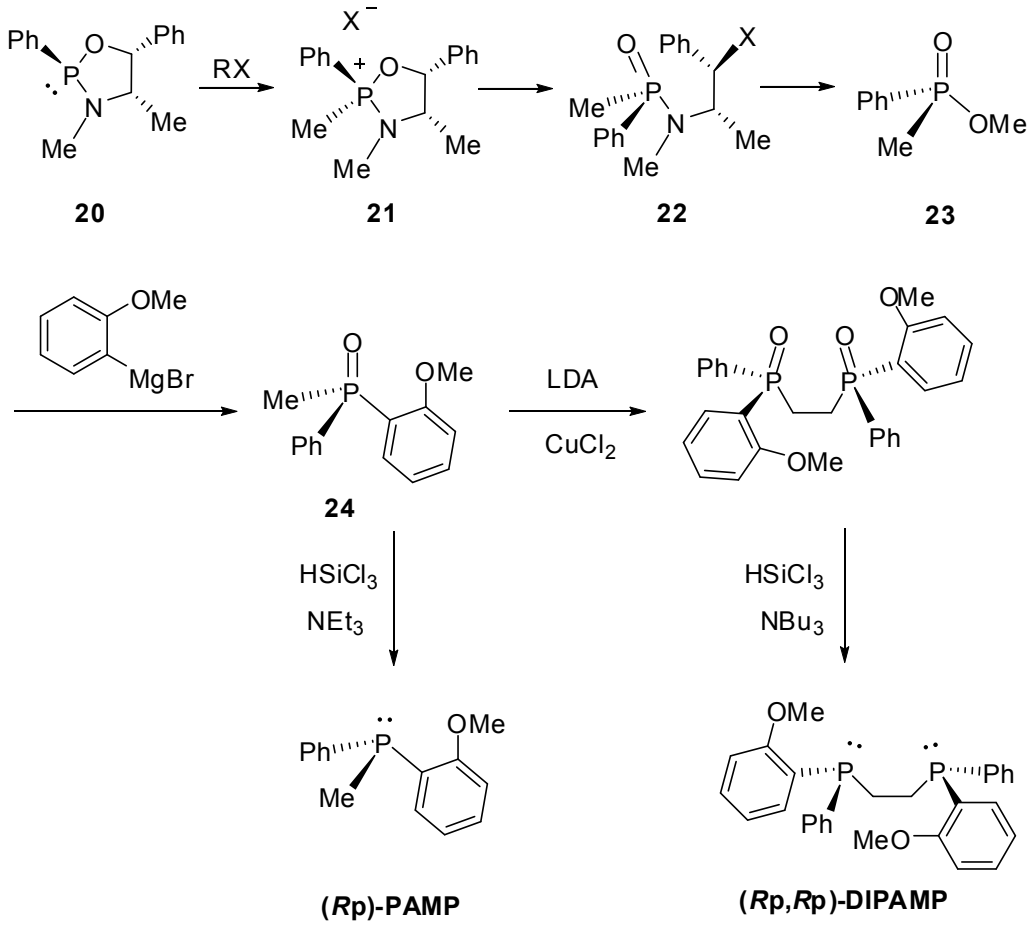
Scheme 1.2

Besides nucleophilic substitution, optically active P-chiral phosphinites could also undergo Michaelis-Arbusov reaction to generate phosphine oxides stereospecifically, with the retention of configuration at phosphorus (Scheme 1.3).[16]



Scheme 1.3

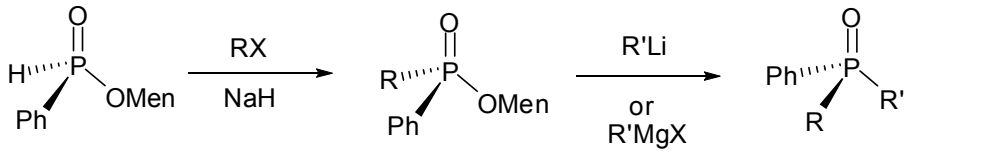
One of the examples of the use of (Michaelis-Arbusov)-Grignard reaction to prepare P-chiral phosphines is shown in Scheme 1.4.[17] Michaelis-Arbusov reaction between oxazaphospholidene **20** and alkyl halides could generate phosphinamide **22** with retention of configuration at phosphorus. Compound **21** is the major intermediate. Phosphinamide **22** could be purified by fractional crystallization or by column chromatography. The phosphinates **23** could be generated stereospecifically in up to > 96% ee, with inversion of configuration at phosphorus center, followed by the nucleophilic substitution of phosphinates with Grignard reagents. The nucleophilic substitution could generate optically active P-chiral phosphine oxides **24** in up to 95% ee. Free phosphine ligands



Scheme 1.4

(*R*p)-PAMP or **(*R*p,*R*p)-DIPAMP** could be obtained subsequently.

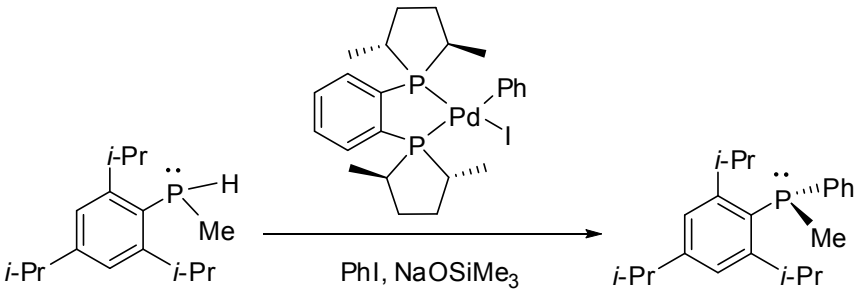
In the presence of base, optically active P-chiral H-phosphinates with alkyl halides could afford alkylation reaction, with retention of configuration at phosphorus centre.[18] The product of alkylation can be converted to useful phosphine oxides by nucleophilic displacement reaction with organometallic reagents, with inversion of configuration at phosphorus center (Scheme 1.5).



(*R*p)-25: R= Me, R'= *i*-Pr
(*S*p)-25: R= *i*-Pr, R'= Me

Scheme 1.5

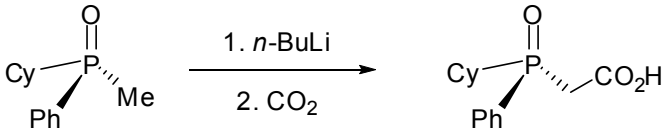
Transition metal catalyzed asymmetric phosphination reactions have also been used to synthesize optically pure P-chiral phosphines. For example, Pd-catalyzed asymmetric cross-coupling between a secondary phosphine and an aryl halide could generate P-chiral phosphines in up to 78% ee (Scheme 1.6).[19]



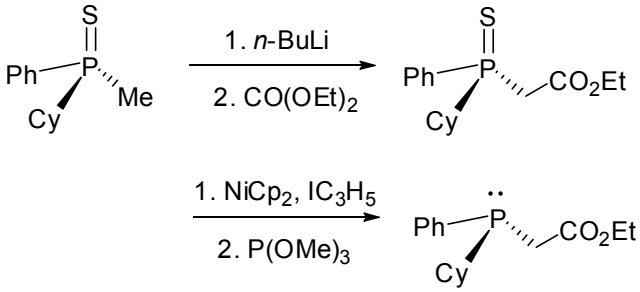
Scheme 1.6

1.1.2.3 Transformation External to the Stereogenic Phosphorus Center

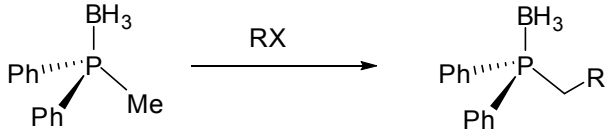
The protons on the α-carbons of P-chiral phosphine sulfides, phosphine oxides and phosphine-borane compounds are very easily deprotonated by strong bases, with retention of configuration at the neighbouring chiral phosphorus center. The deprotonated product can yield various reactions to prepare a range of functionalized P-chiral phosphines (Scheme 1.7-1.10).[12,20] The presence of β-dimethylamino substituent or an activating group can control the selectivity of deprotonation on the α-carbons (Scheme 1.10).



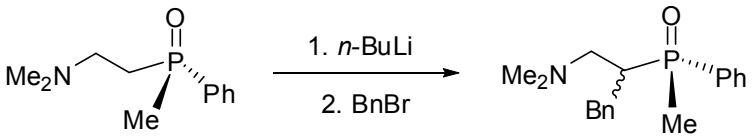
Scheme 1.7



Scheme 1.8

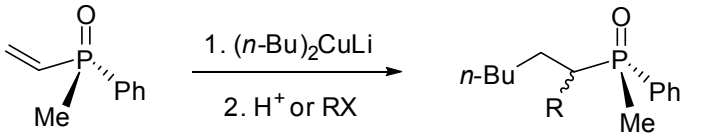


Scheme 1.9



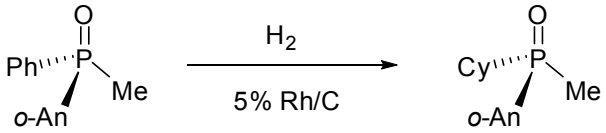
Scheme 1.10

P-chiral phosphines containing α,β-unsaturated groups are very useful to generate optically pure P-chiral phosphine derivatives. Michael addition (Scheme 1.11), hydrogenation (Scheme 1.12), [4+2] cycloaddition (Scheme 1.13) and Heck coupling (Scheme 1.14) are some of the reactions for this kind of phosphines to synthesize other P-chiral phosphines or precursors, with retention of configuration at chiral phosphorus center.[15,21]

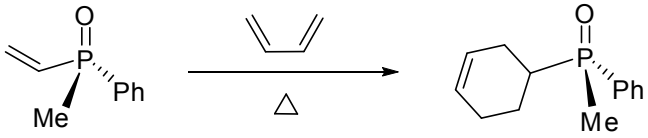


R=H, CH_2=$CHCH_2$

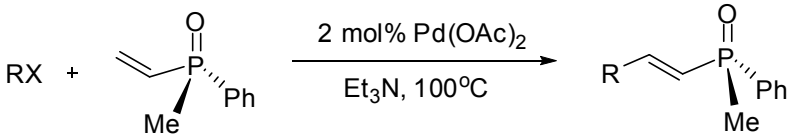
Scheme 1.11



Scheme 1.12



Scheme 1.13



R= Ph, *m*-BrC_6H_4, *o*-$OHCC_6H_4$, *o*-$HOCH_2C_6H_4$, 3-pyridyl, Me_3SiCH=CH

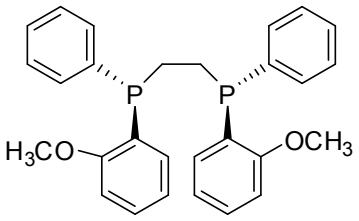
Scheme 1.14

1.1.3 Applications of Phosphines toward Asymmetric Syntheses

Optically pure P-chiral phosphines and diphosphines have long been considered as very useful compounds for metal-based homogeneous asymmetric catalysis.[2]

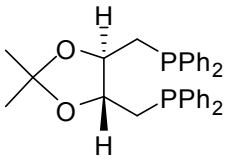
1.1.3.1 Asymmetric Hydrogenation Reaction

In the late 1960s, Horner and Knowles and co-workers discovered that Wilkinson's catalyst assisted by chiral monodentate phosphine ligands DIPAMP **26** could catalyze asymmetric hydrogenation reations.[22] In the early 1970s, Kagan and co-workers discovered that the bidentate ligand DIOP **27** could assist rhodium catalyst to catalyze asymmetric hydrogenation efficiently, in up to 82% ee.[23] Since then, transition metal assisted by chiral phosphine ligands have been developed extensively to catalyze asymmetric hydrogenation. Among thousands of reactions, only selected examples will be mentioned here.



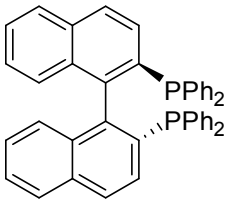
DIPAMP

26



DIOP

27

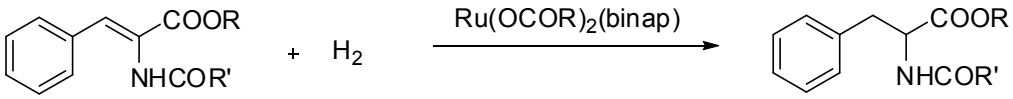


BINAP

28

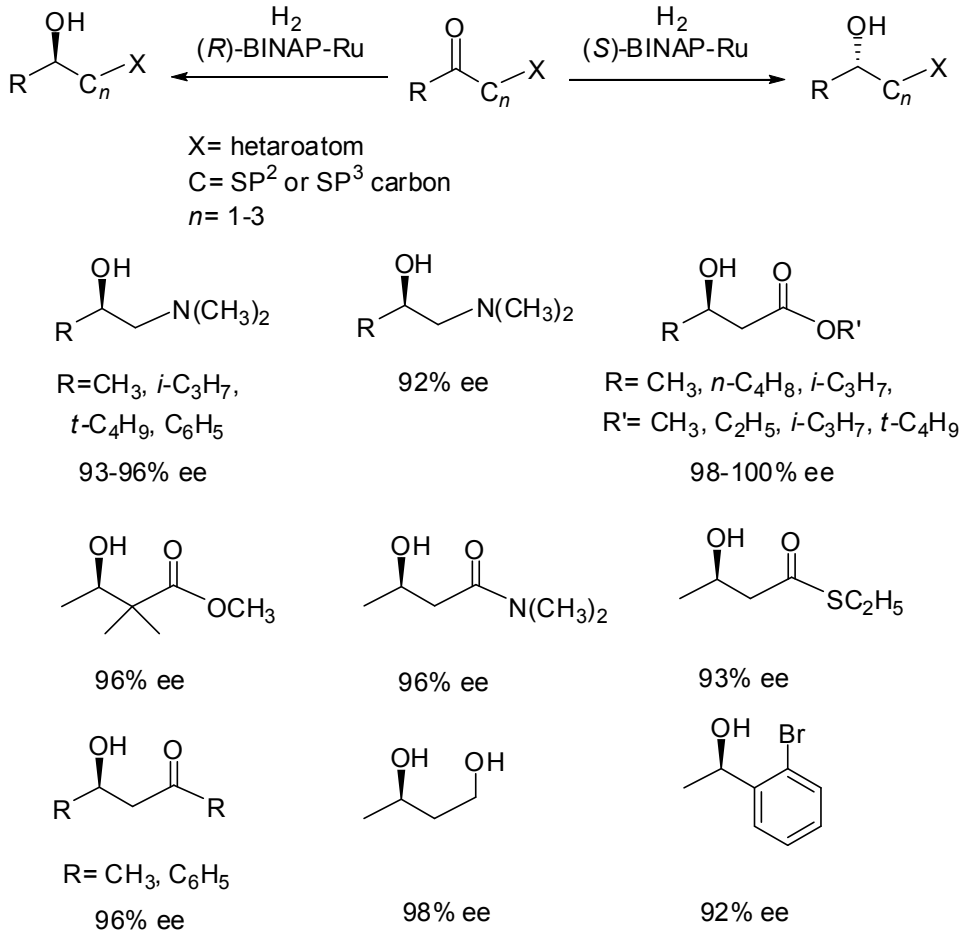
2,2'–bis(diarylphosphino)-1,1'-binaphthyl (BINAP **28**) is one of the most widely used ligands for asymmetric hydrogenation. For example, the

BINAP-Ru dicarboxlate complexes could catalyze asymmetric hydrogenation reaction of α,β- or β,γ-unsaturated compounds to generate optically pure saturated compounds (Scheme 1.15).[24]



Scheme 1.15

BINAP-Ru complexes could also catalyze asymmetric hydrogenation reaction of a wide range of functionalized ketones with good stereoselectivity.

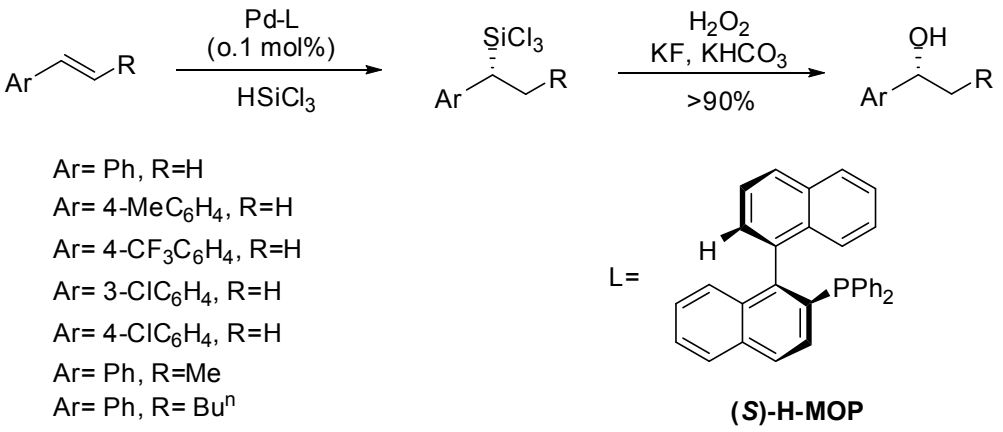


Scheme 1.16

The functional groups included dialkylamino, hydroxyl, alkoxyl, siloxyl, keto, alkoxycarbonyl, alkylthiocarbonyl *et al.*(Scheme 1.16).[25]

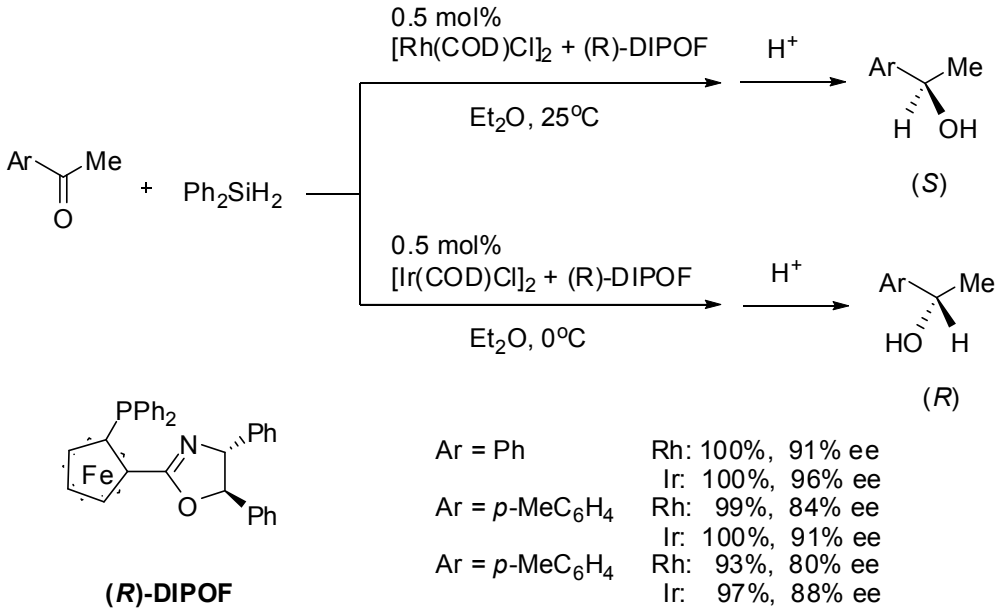
1.1.3.2 Asymmetric Hydrosilylation Reaction

Hydrosilylation reaction describes the addition reaction of Si-H bond across a π bond. Normally, the π bond is a C=C, C=O or C≡C bond. Hydrosilylation is one of the most important methods for forming Si-C bonds to synthesize organosilicon compounds. Chiral phosphines have been used widely in asymmetric hydrosilylation reaction. For instance, the monodentate phosphine ligand, (*S*)-2-diphenylphosphino-1,1'-binaphthyl (H-MOP), is a very effective ligand for the asymmetric hydrosilylation reaction of styrenes catalyzed by H-MOP-Pd complex. The selectivitity of the reaction is up to 96% ee (Scheme 1.17). [26]



Scheme 1.17

The chiral phosphine ligand oxazolylferrocene-phosphine (DIPOF) is a very effective ligand for Ir-catalyzed and Rh-catalyzed asymmetric hydrosilylation reaction of simple ketones. These reactions could generate alcohols in a high selectivity, up to 96% ee (Scheme 1.18). [27]

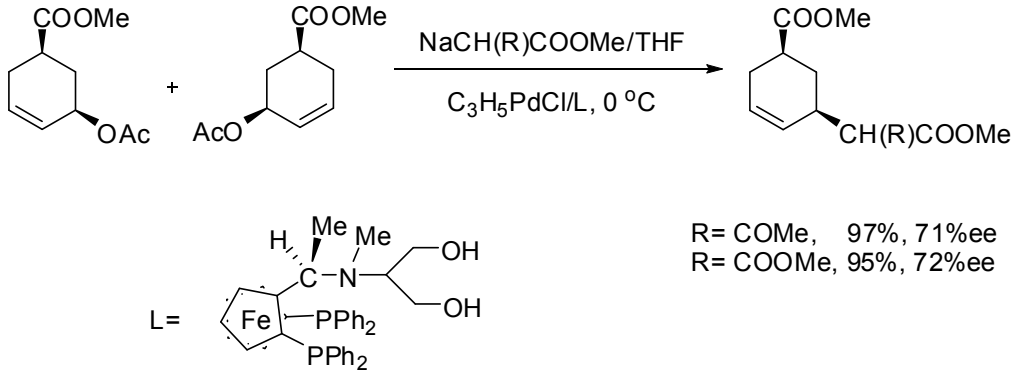


Scheme 1.18

1.1.3.3 Asymmetric Allylic Alkylation

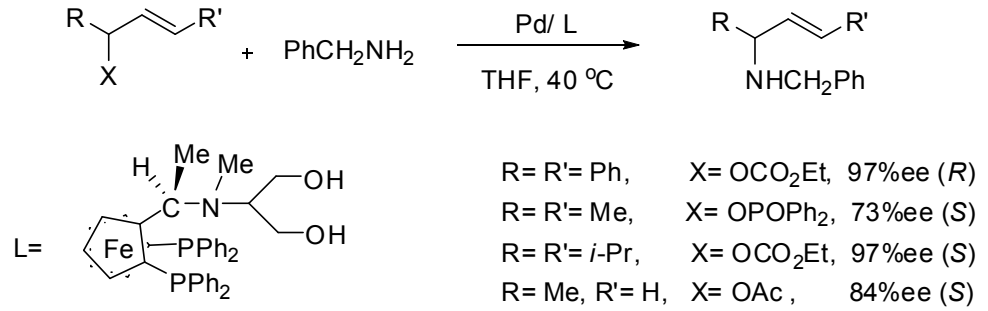
Asymmetric allylic alkylation is an effective route for the formation of new bond forming reaction.[28] Transition metal complexes assisted by optically active phosphine ligands have been wildly used as useful catalyst in asymmetric allylic alkylation reaction.[29] Chiral ferrocenylphosphines have been considered as very excellent ligands because chiral ferrocenylphosphines can modify the structure of the product by introduction of a desired functional group on the

side chain according to the demand of the reaction type. For instance, ferrocenylphosphine containing N-methyl-N-bis(hydroxymethyl)methylamino group can assist palladium catalyst to catalyze the allylic alkylation reaction of cyclic acetate in high stereoselectivity, over 70% ee (Scheme 1.19).[30]



Scheme 1.19

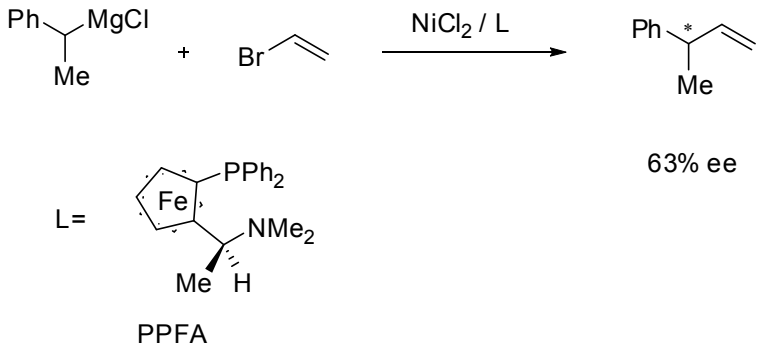
The ferrocenylphosphine ligand above could also assist palladium-catalyzed asymmetric allylic animation reation in high stereoseletivety (Scheme 1.20).[31] For example, the reaction between 1,3-diphenyl-2-propenyl ethyl carbonate and benzylamine catalyzed by palladium assisted by ferrocenylphosphine could obtain the product in 97% ee.



Scheme 1.20

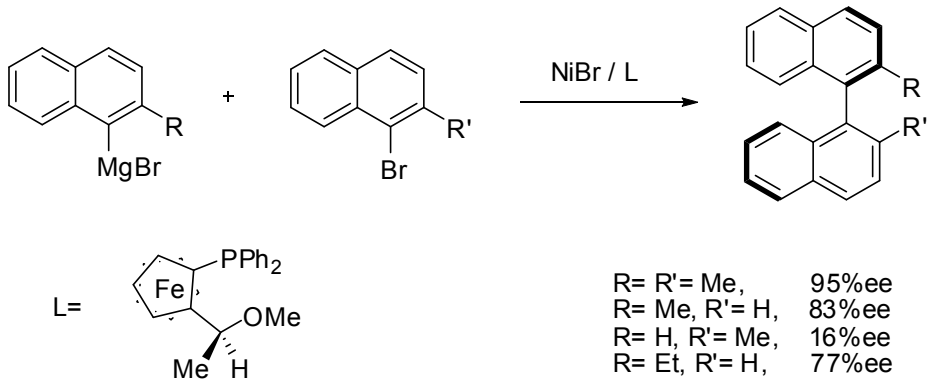
1.1.3.4 Asymmetric Grignard Cross-Coupling

In the 1970s, Kumada, Hayashi and co-workers reported that chiral [(aminoalkyl)ferrocenyl] phosphine ligand PPFA could assist the nickel-catalyzed asymmetric Grignard cross-coupling reaction between 1- phenyl-ethyl Grignard reagent and vinyl bromide stereoselectively (Scheme 1.21). [32]



Scheme 1.21

The similar ferrocenylphosphine ligand with methoxy group on the ferrocene side chain has been successfully used in the nickel-catalyzed asymmetric Grignard cross-coupling reaction to prepare optically active binaphthyls stereoselectively, up to 95% ee (Scheme 1.22).[33]

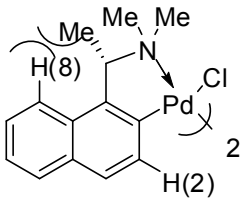


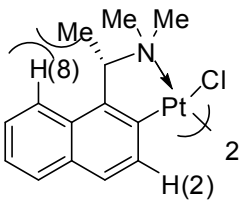
Scheme 1.22

1.2 The Two Important Chiral Metal Template Used in the Project

For many years, chiral cyclo-metalated-amine complexes have played very important roles in many aspects of chemistry.

For the past few years, Leung *et al.* has focused on the application of chiral cyclo-metalated complexes (for example, chiral cyclo-metalated-amine complexes) for chiral resolution and asymmetric synthesis. The most common chiral metal template reagents that were used are shown here (only one of the two equally available enantiomers is shown). The orthometalated [1-(dimethylamino)ethyl]naphthalene palladium(II) complexes were originally reported by Wild's group. The orthometalated [1-(dimethylamino)ethyl]naphthalene platinum(II) complexes were developed by Leung *et al.*.





The chiral palladium template is one of the most common chiral reagents used by Leung *et al.*. There is a key point of the stereochemistry of this chiral naphthyl-amine palladium complex. The five-membered ring containing palladium is locked because of the internal repulsion between the methyl group at the stereogenic chiral carbon and the neighbouring naphthylene proton

H(8).[9,34] This particular methyl substituent at the stereogenic carbon will be always in an axial position in this fixed five-membered ring. Therefore the two prochiral NMe_2 groups are fixed into non-convertible positions. These two fixed NMe_2 groups could control the stereochemistry of the incoming ligand which is cis to them. Apart from that, the naphthylene proton H(2) could fix the incoming ligand which is cis to the naphthylene ring due to the strict planarity of the naphthylene ring. Hence the two NMe_2 groups and the naphthylene proton H(2) of the chiral organometallic template could control the stereochemistry of the incoming groups from both side in asymmetric reations. In addition, the σ-donating nitrogen and the π-accepting naphthylene carbon of the organometallic ring can control the regioselectivity of the incoming ligands electronically. Soft ligands such as DMPP prefer to take up the position trans to the NMe_2 groups of the template.

Chiral palladium complexes and platinum complexes which are structurally similar but differ in the metal ions, have been shown to exhibit different reactivity.[35]

Leung and coworkers have previously reported that orthometalated [1-(dimethylamino)ethyl]naphthalene palladium(II) complexes and platinum(II) complexes can act as chiral templates which promote various reactions, namely [4+2] cycloaddition,[36,37] hydroamination,[38,39] hydrophosphination[40] and hydroarsination[41] reactions. These kinds of reactions could generate many useful P-chiral phosphines under mild reaction conditions.

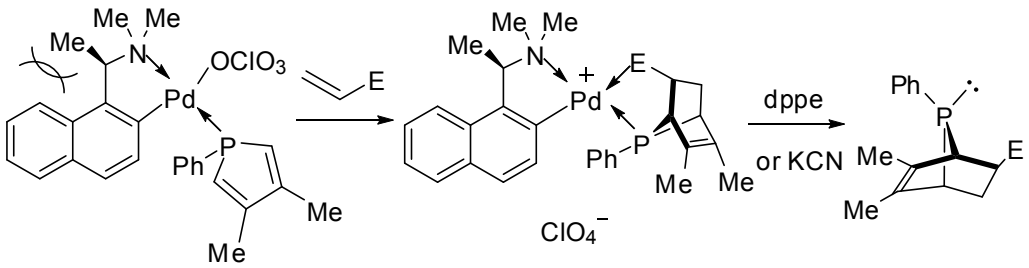
1.2.1 Asymmetric Diels-Alder Reaction

Leung and co-workers have already successfully applied the chiral *ortho*-metalated-amine palladium complexes to promote the asymmetric Diels –Alder reaction for the preparation of a lot of functionalized P-chiral mono- and diphosphines.[36,42]

One most used cyclic diene for the [4+2] cycloaddition reaction is the five-membered 3, 4-dimethyl-1-phenylphosphole (DMPP).[43] A key point in this synthetic approach is that DMPP itself is not a reactive cyclic diene. But the metal template could activate DMPP. When DMPP is coordinated onto a transition metal ion, it could become reactive.[44] This provides a unique opportunity to control the stereochemistry of the product. Leung *et al.* have chosen the palladium template and platinum template which had beed shown above to promote the cycloaddition reaction.

Generally, there are two different pathways (*exo*- and *endo*- cycloaddition pathways) that asymmetric Diels-Alder reactions can proceed via. When different metal templates were used, different pathways would be taken. DMPP coordinated onto the chiral palladium template. Then the chloro ligand of the metal template was abstracted with silver perchlorate to generate the palladium perchlorate complex **29**. This palladium perchlorate complex **29** underwent the intramolecular *exo*-cycloaddition pathway with a range of dienophiles. Since the perchlorate metal bond in complex **29** is weak and labile, it could be displaced by the electron-rich functionalized dienophile in the reaction. Both

DMPP and the dienophile are coordinated simultaneously onto the chiral metal template during the cycloaddition reaction. The *exo*-cycloadducts could be obtained and the stereoselectivity and regioselectivity is high. The softer donor atom prefers to take up the coordination position trans to the σ-donating NMe_2 group on the organometallic ring.



29

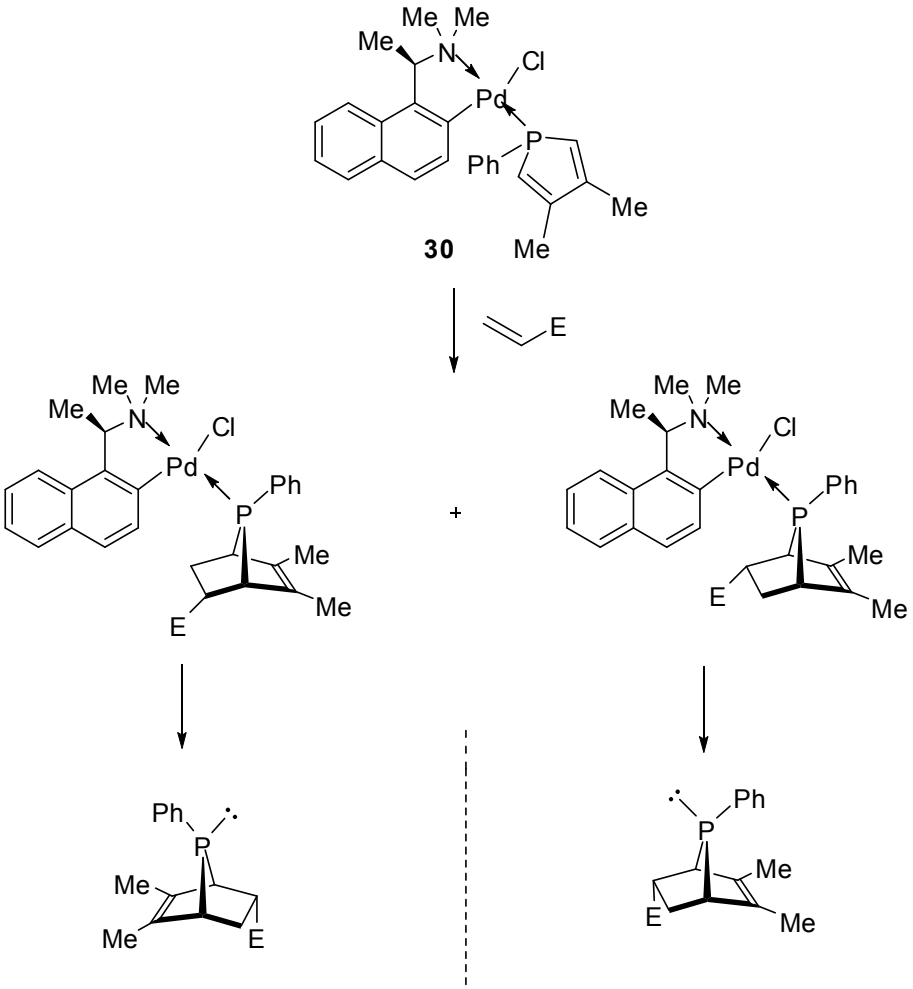
		temp °C	time	isolated yield%
a	E= -C(O)NMe_2	25	3 d	85
b	E= -C(O)Et	25	9 d	73
c	E= -C(O)OMe	75	14 d	48
d	E= -C(S)Et	75	15 h	15 (unstable)
e	E= -C(S)NMe_2	25	6 d	58
f	E= -SPh	75	17 d	65
g	E= -S(O)CH=CH_2	75	4 d	40
h	E= -2-pyridyl	75	20 d	60
i	E= -P(O)Ph_2	60	4d	30
j	E= -PPhMe	0	4h	85

Scheme 1.23

On the other hand, the Pd-Cl bond which is trans to the ortho-metalated aromatic carbon is well known to be a inert bond to ligand substitution reaction even with strong incoming ligands.[45,46] If the chloro ligand was not replaced by perchlorate ligand, the cycloaddition reactions between DMPP of the chloro palladium species **30** and a range of dienophiles proceed via the intermolecular

endo-pathway.

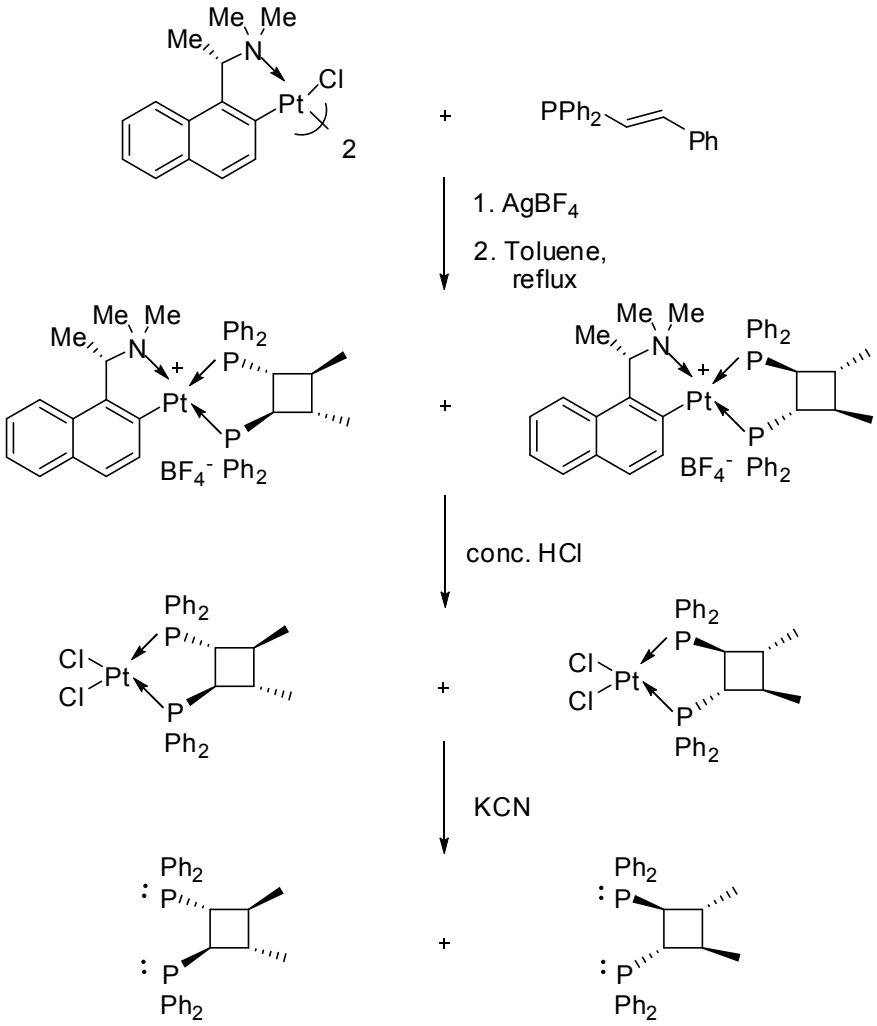
Thus dienophile can not coordinate onto the palladium template. Instead, the Diels-Alder reaction has to proceed via the intermolecular *endo*-pathway. The intermolecular *endo*-cycloaddition reaction is promoted and stereochemically controlled only by the chiral palladium template via the single and rotatable Pd-P bond. The effect of the chiral naphthylamine template is usually very weak. Hence the stereoselectivity of intermolecular *endo*-cycloaddition reaction is usually very poor. However, the functionalized P-chiral phosphines could be obtained after decomplexation from the templates.



Scheme 1.24

1.2.2 Asymmetric [2+2] Cycloaddition Reaction

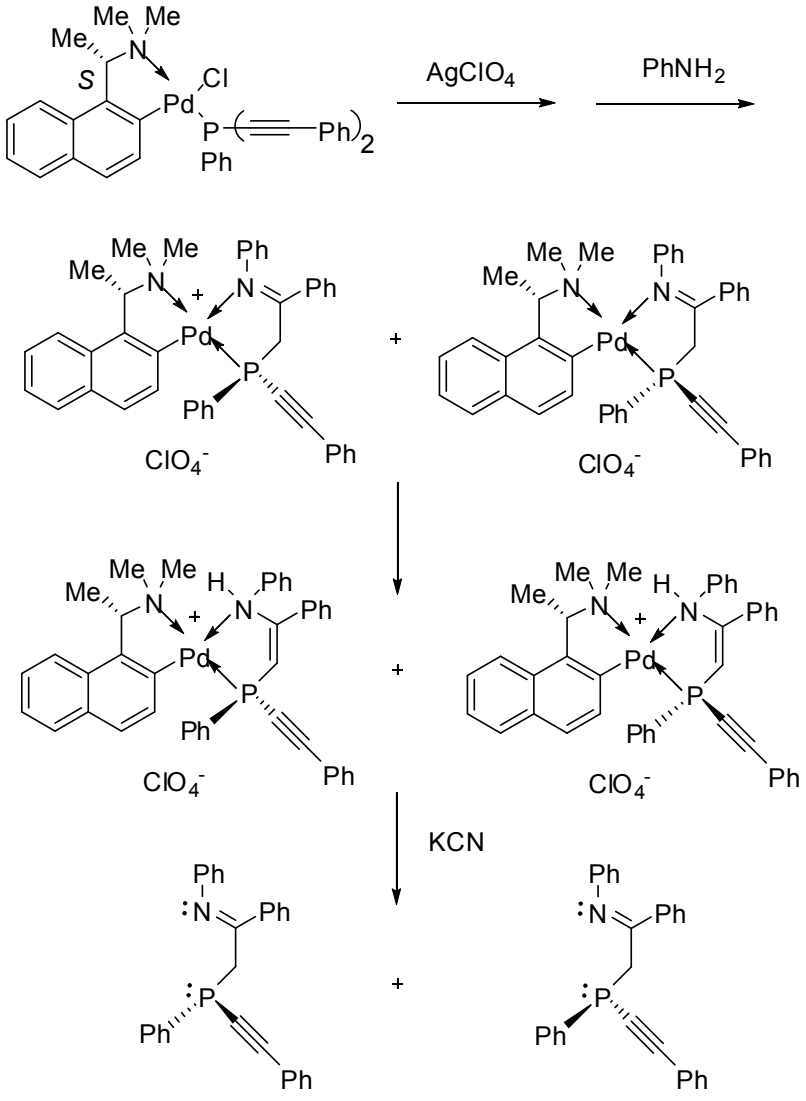
Our group had also proved that the platinum (II) template could promote asymmetric [2+2] cycloaddition reaction.[47] The stereoselectivity is very good, up to 6:1. Since the two cycloaddition products could not be separated by silica-gel column chromatograghy, the mixture of the two cycloadducts were treated with concentrated hydrochloric acid to remove the naphtlylamine auxiliary and generate the corresponding dichloro complexes. Free diphosphine ligands could be liberated by treatment the dichloro complexes with aqueous potassium cyanide.



Scheme 1.25

1.2.3 Asymmetric Hydroamination Reaction

Our group had also shown that the palladium (II) template could promote asymmetric hydroamination reaction between di(phenylethynyl) phenylphosphine and aniline.[39] Without the presence of the transition metal, the reaction between di(phenylethynyl) phenylphosphine and aniline won't occur. In the presence of the palladium template, two diastereomeric iminophosphine complexes could be obtained. Then both of these two complexes transformed into enamino complexes. Either iminophosphine complexes or

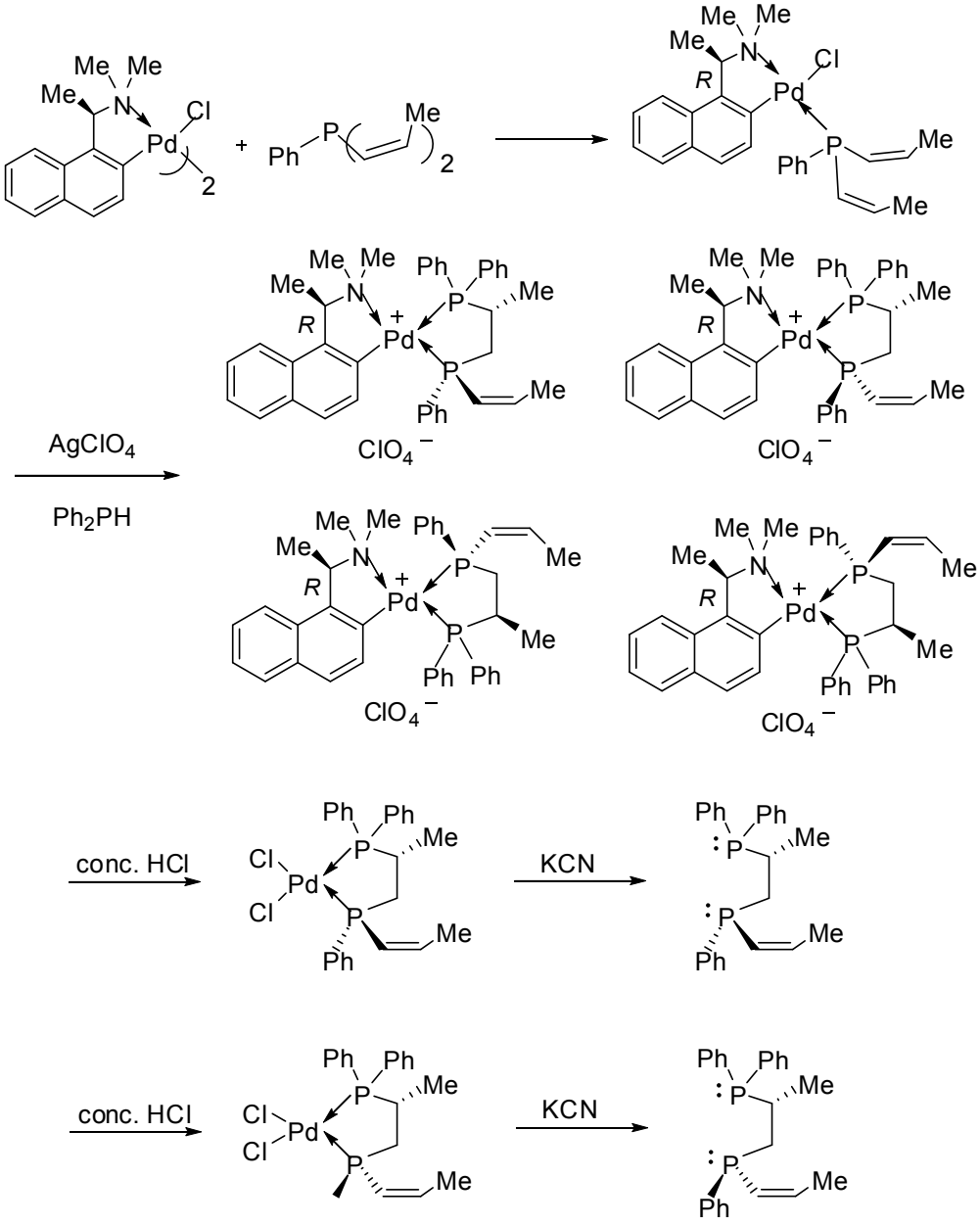


Scheme 1.26

enaminophosphine complexes were treated with aqueous potassium cyanide, the optically pure P-chiral P-N bidentate ligands would be obtained in quantitative yields.

1.2.4 Asymmetric Hydrophosphination Reaction

Our group had also proved that the palladium (II) template could promote

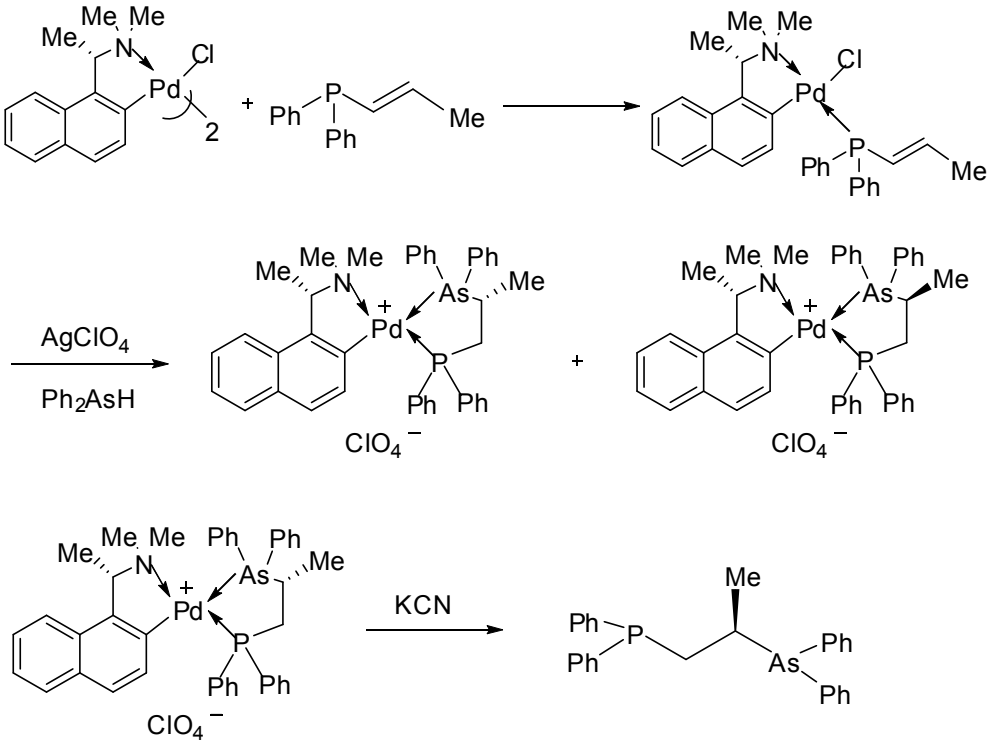


Scheme 1.27

asymmetric hydrophosphination reaction.[48] For example, in the absence of the transition metal ion, the reaction between diphenylphosphine and phenyldi[(*Z*)-prop-1-enyl]phosphine can not occur.[48] In the presence of the chiral palladium template, we could obtain two pairs of regioisomers. The treatment of these two pairs of regioisomers with concentrated hydrochloric acid could remove the naphtlylamine auxiliary and generate the corresponding dichloro complexes respectively. The dichloro complexes were treated with aqueous potassium cyanide, two kinds of optically pure P-chiral P-P bidentate ligands would be obtained in high yields.

1.2.5 Asymmetric Hydroarsination Reaction

The chiral palladium template had been proved to promote the asymmetric

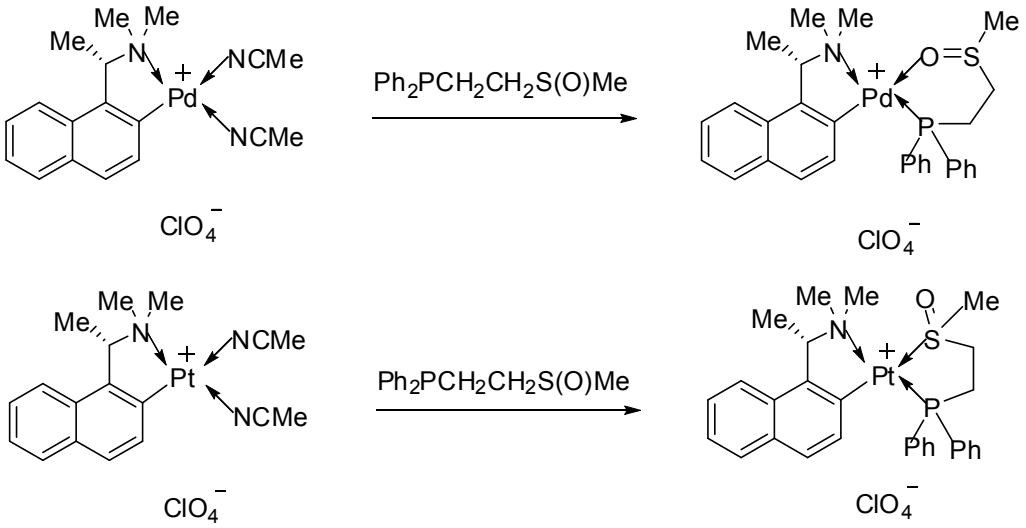


Scheme 1.28

hydroarsination for the preparation of asymmereic arsenic ligands by our group.[41] As shown in Scheme 1.28, the asymmetric hydroarsination reaction between diphenylarsine and diphenyl-1-propenyl-(*E*)-phosphine was promoted by the chiral palladium template to prepare bidentate P-As ligands. Two diastereomeric complexes could be obtained. Then the major product was treated with aqueous potassium cyanide, and the optically pure P-As bidentate ligands would be obtain in quantitive yields.

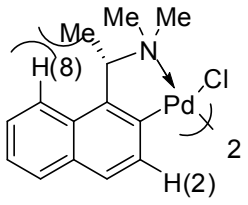
1.2.6 Resolution

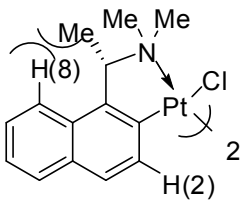
Polydentate ligands containing chiral sulfoxides functionalities show interesting bonding modes to transition metals.[49] For example, Leung *et al.* has also reported the optical resolution and the coordination properties of (±)-$Ph_2CH_2CH_2S(O)Me$. When palladium was used as the template metal, the sulfoxide oxygen coordinated to the metal.[50] On the other hand, when platinum was used as the template metal, the sulfoxide sulfur coordinated to the metal.[51]



Scheme 1.29

1.3 Aim of the Present Project





The chiral palladium template could promote various types of reactions as mentioned above. Meanwhile, the reactivity of the chiral platinum template is totally different from the the chiral palladium template. However, the study of the reaction promoted by the platinum template is fewer in comparison to the palladium template. So one of the objectives of this project is to study the metal effect of these two kinds of metal template by means of metal promoted Diels-Alder reaction and prepare a series of bidentate chiral ligands such as P-S, P-As, and P-N bidentate ligands. The other objective of this project is to prepare P-P diphosphine ligands by means of metal promoted hydrophosphination reaction.

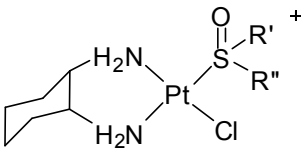
Chapter 2

Application of Metallacycles to Promote Asymmetric Cycloaddition Reactions

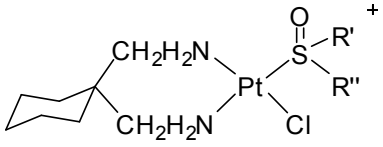
2.1 Introduction

The asymmetric [4+2] cycloaddition reaction is one of the most important methods to prepare compounds containing chiral six-membered rings. Leung *et al.* have been able to apply this reaction for the asymmetric synthesis of P-P, P-O and P-As optically pure chiral phosphine ligands.

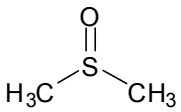
Since chiral sulfoxides play important roles in many aspects of chemistry and medicine, they have long been considered as useful auxiliaries. For example, chiral sulfoxide rhodium complexes have high selectivity in the homogeneous asymmetric hydrogenation reaction of prochiral ketones.[52] Some platinum drugs containing chiral sulfoxides groups have antitumor activities.[53] For instance, a serial of platinum complexes of formula shown below were the first well-defined antitumor platinum complexes containing sulfur ligands.

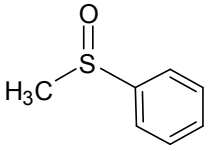


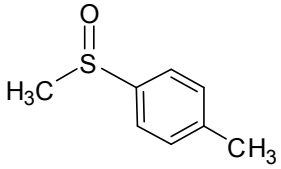
[PtCl(R'R"SO)(dach)]$^+$

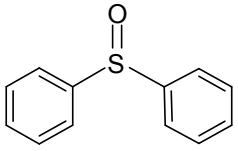


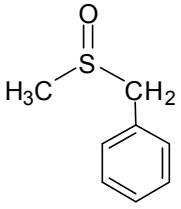
[PtCl(R'R"SO)(damch)]$^+$

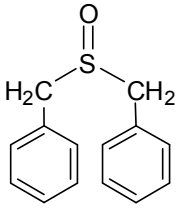








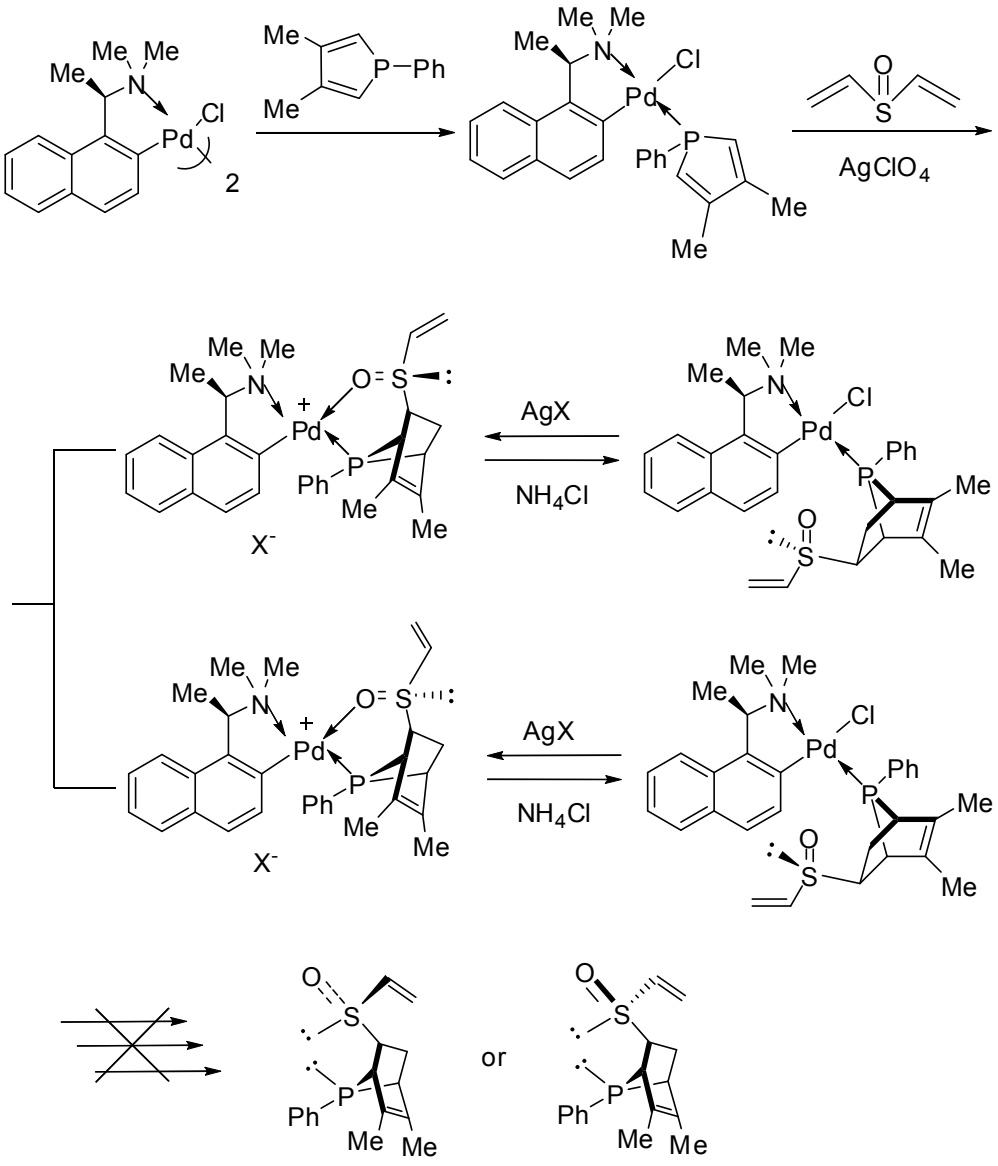




Polydentate ligands containing chiral sulfoxide functionalities show interesting bonding modes to transition metals.[49] For example, as shown in Scheme 1.29, our group has previously reported the optical resolution and the coordination properties of (±)-$Ph_2CH_2CH_2S(O)Me$. When palladium was used as the metal template, the sulfoxide oxygen coordinated to the metal.[50] On the other hand, when platinum was used as the metal template, the sulfoxide sulfur preferred to coordinate to the metal.[51]

Leung *et al.* have already reported asymmetric cycloaddition reaction between 3,4-dimethyl-1-phenylphosphole (DMPP) and divinyl sulfoxide promoted by a palladium complex (Scheme 2.1).[54] The Diels-Alder reaction between DMPP and divinyl sulfoxide promoted by the palladium complex was not efficient to prepare P-S or P-O ligands. Firstly, the ratio of the diastereomeric cycloadducts was 1:1. Secondly, when the crude cycloadducts were isolated through a silica-gel column, the unexpected chloro complexes were formed. Finally, the desired optically pure P ligand was not produced.

Leung *et al.* found that the metal played a considerable role on the selectivity and the stability of the formed cycloadduct.



Scheme 2.1

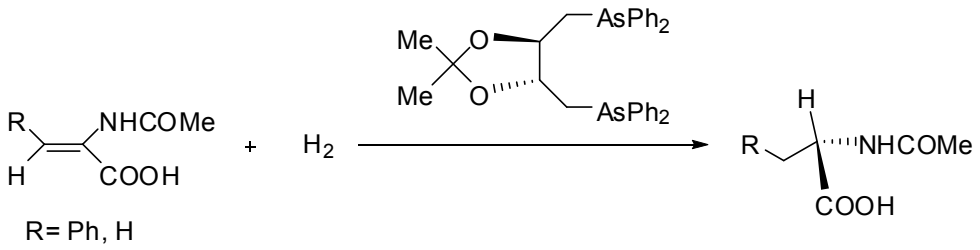
In order to synthesize chiral P-S bidentate ligands efficiently, asymmetric cycloaddition reactions which are promoted by the chiral metal template and the study on the metal effect of the two templates is discussed in chapter 2.2.1.

Arsenic is seated beneath phosphorus in the periodic table and there are five electrons in the outermost shell like phosphorus. However, arsenic has 18

electrons in the penultimate shell, which is different from phosphorus having eight electrons in the penultimate shell. The five 3d orbitals of arsenic were filled by ten electrons. The addition of ten positive charges to the nucleus frequently causes a general contraction of the electronic cloud, which increase in electronegativity of the elements. As ligands, both the lone pair electrons from the phosphine and arsenic could donate to the transition metal. In addition, phosphine could also accept electron density from the metal by back donation into the empty d orbitals.[55]

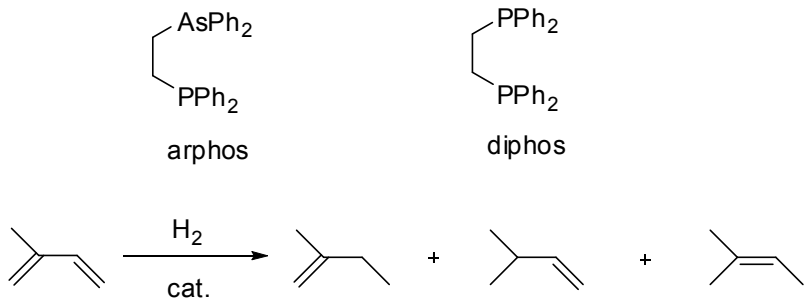
The thermal barrier to inversion of tertiary arsines is about 40 kcal mol^{-1} and more than that of tertiary phosphines which is about 30 kcal mol^{-1}.[9] This can provide an advantage to study the asymmetric synthesis of arsines.

A variety of optically active tertiary arsines are now available for application in inorganic and organic synthesis. Optically active arsines have been used for the asymmetric catalytic hydrogenation and hydrosilylation. For example, asymmetric hydrogenation of 2-acetamidocrylic acid using a rhodium catalyst containing an optically active arsine gave (*S*)-N-acetylalanine in good yield but poor stereoselectivity (Scheme 2.2). [68]



Scheme 2.2

Optically active heterobidentate ligands containing two or more chiral centers provide vast potential in asymmetric synthesis. However, in asymmetric catalysis, when compared to the chiral diphosphine ligands, the studies on the application of heterobidentate ligands were rare. The reason for this is their inefficiency in achieving high ee in most asymmetric reactions. The bidentate P-As ligands are relatively rare. However, P-As ligands have still been reported for some asymmetric catalysis reaction.[56] For example, in the hydrogenation of butadiene derivatives, arphos had shown that it could give better selectivity in comparison with diphos (Scheme 2.3).



$[Rh(NBD)(arphos)]^+PF_6^-$	3%	7%	90%
$[Rh(NBD)(diphos)]^+PF_6^-$	13%	18%	69%

Scheme 2.3

However, available methods to prepare P-As ligands are limited. Leung *et al.* have recently reported that the optically active P-As bidentate ligands could be synthesized via asymmetric cycloaddition reaction and asymmetric hydroarsination reaction which are promoted by chiral cyclometallated templates.[41,57]

In continuation of our exploration of chiral P-As bidentate ligands, a method of the synthesis of chiral P-As bidentate ligands via asymmetric cycloaddition reactions which are promoted by the chiral metal template and study on the metal effect of the two templates is discussed in chapter 2.2.2.

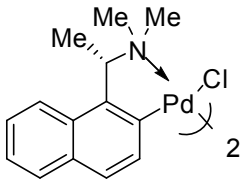
Pyridyl-substituted phosphines containing both P- and N-donor centers have long been considered as powerful auxiliaries for their important roles in many aspects of synthetic and inorganic chemistry.[58] Uncoordinated pyridylphosphines have been used as catalysts in the chlorination of alkyl alcohols[59] and in the Mitsunobu esterification reaction between a carboxylic acid and an alcohol.[60] Pyridylphosphines transition metal complexes have also been used as catalysts to catalyze a serial of carbonylation reaction, epoxidation reaction, and cycloaddition reactions.[61] In terms of coordination chemistry, pyridylphosphines possess a combination of hard (N) and soft donor (P) atoms, and therefore have many coordination features either as metal chelates via both their phosphorus and nitrogen donor atoms or as monodentate ligands via the phosphorus atoms only.[62,63] Thus, chiral pyridylphosphines transition metal complexes could provide unique reactivity in catalytic asymmetric reactions. Hence, chiral pyridylphosphines have been used very successfully in asymmetric catalytic reaction.

However, the studies about using optically active pyridylphosphines containing resolved tertiary phosphorus chiral centres were very rarely.[62]

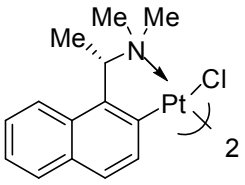
Perhaps, the reason was the difficulties of the optical resolution and asymmetric synthesis of P-chiral pyridylphosphines.

Leung and coworkers have already reported that the chiral orthometalated [1-(dimethylamino)ethyl]naphthalene palladium(II) **31** complexes and platinum(II) **32** complexes can act as chiral templates which promoted various reactions to synthesize a serials of P chiral ligands. Herein, an efficient method to prepare P-chiral pyridylphosphines by means of *exo* asymmetric cycloaddition reactions which are promoted by the chiral metal template and study on the metal effect of the two templates is presented here.

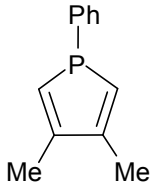
In continuation of our exploration of chiral P-N bidentate ligands, asymmetric cycloaddition reactions which are promoted by the chiral metal template and the study on the metal effect of the two templates are discussed in chapter 2.2.3.



31



32



DMPP

The key point of the approach is using a metal complex as chiral template. One of our synthetic methods is using 3, 4-dimethyl-1-phenylphosphole (DMPP) [43] as a cyclic diene for the asymmetric cycloaddition reaction. DMPP itself is not a reactive diene. But after DMPP is coordinated to a transition metal, it can become reactive towards cycloaddition reactions.

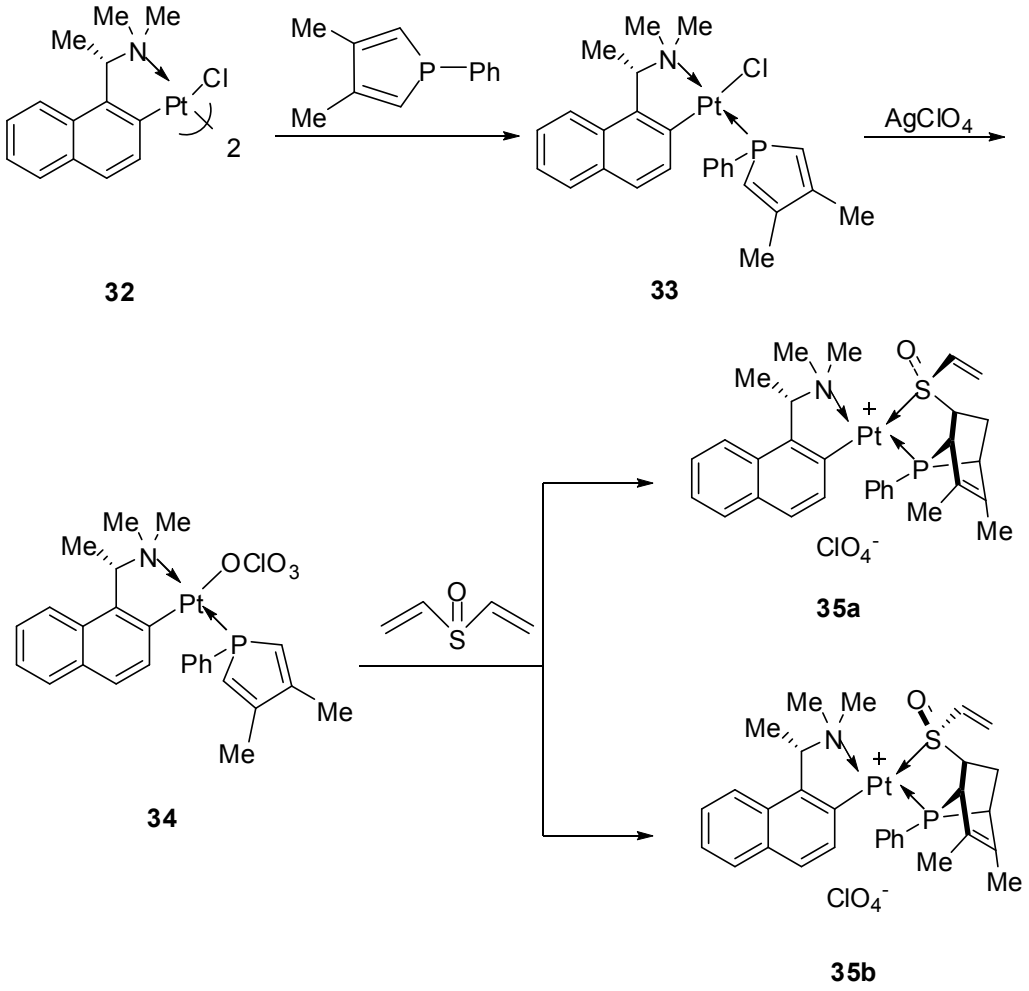
2.2 Results and Discussion

2.2.1 Metal Effect on Asymmetric Synthesis of P-S ligands

2.2.1.1 Asymmetric Cycloaddition Reaction between DMPP and Divinyl Sulfoxide

In the absence of a metal ion, no reaction was observed between divinyl sulfoxide and DMPP, because divinyl sulfoxide is not a chemically reactive dienophile and DMPP is not a reactive diene. Thus, the monodentate phosphole DMPP was coordinated to the dimeric chiral template **32** to give the monomeric neutral complex **33** as yellow prisms. It is important to note that the chloro ligand in the complex **33** is well-known to be kinetically and thermodynamically stable and is not readily displaced by other ligands.[45] The complex **33** was therefore treated with aqueous silver perchlorate in dichloromethane to provide a coordination site for the incoming sulfoxide, because $OClO_3^-$ was not a strong ligand and could be replaced by other incoming ligands easily. Since the yield of the perchlorate complex was almost 100%, the perchlorate platinum complex **34** was not isolated and the chlorobenzene solution containing the complex **34** was directly treated with divinyl sulfoxide at 100℃ for 5d to give a 5:1 mixture of diastereomeric complexes **35a** and **35b** (Scheme 2.4). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture in $CDCl_3$ exhibited two sharp singlets at δ 97.3 ($J_{Pt\text{-}P}$=3357 Hz) and δ 98.1 ($J_{Pt\text{-}P}$=3357 Hz). These low-field chemical shifts confirmed that the phosphorus of each complex are typical of bridgehead

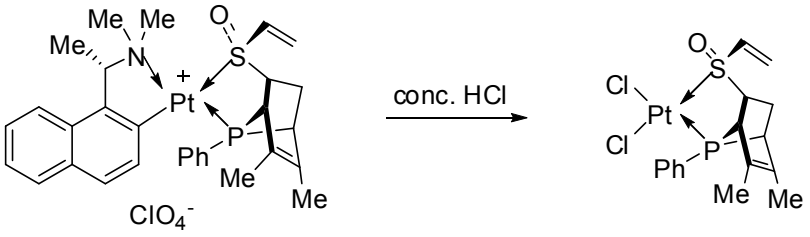
phosphorus found in phosphanorbornenes with the *exo-syn* stereochemistry.[64] The major product **35a** could be separated by silica-gel column chromatograghy as a yellow solid in 70% yield, $[\alpha]_D$ +69.7 (*c* 2.9, CH_2Cl_2).



Scheme 2.4

The chiral naphthylamine auxiliary on the major product **35a** could be removed by the treatment of the complex with concentrated hydrochloric acid for 20 min at room temperature (Scheme 2.5). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude mixture in $CDCl_3$ showed a singlet at δ 100.9 ($J_{Pt\text{-}P}$=3137 Hz). The dichloro platinum complex **36** was obtained by fractional crystallization from

dichloromethane- diethyl ether as white crystal in 94% yield, $[\alpha]_D$ +31.9 (*c* 6.9, CH_2Cl_2).



35a **36**

Scheme 2.5

The single crystal X-ray diffraction analysis established that the desired cycloadduct had formed via the *exo*-cycloaddition reaction. The cycloadduct in complex **36** was coordinated to the metal center as a bidentate ligand via the bridgehead phosphorus and sulfur of divinyl sulfoxide. The five new chiral centers have been generated with *S* absolute configuration at sulfur, *S* absolute configuration at phosphorus, *S*, *S* and *R* absolute configuration at C(10), C(5) and C(3) respectively. The geometry at platinum is slightly distorted square planar with angles at platinum in the range of 84.90(3)° -93.44(3)° and 175.40(3)° -178.17(3)° . The bond angle at the bridgehead phosphorus is 82.02(16)° . Selected bond lengths and angles are listed in Table 1.

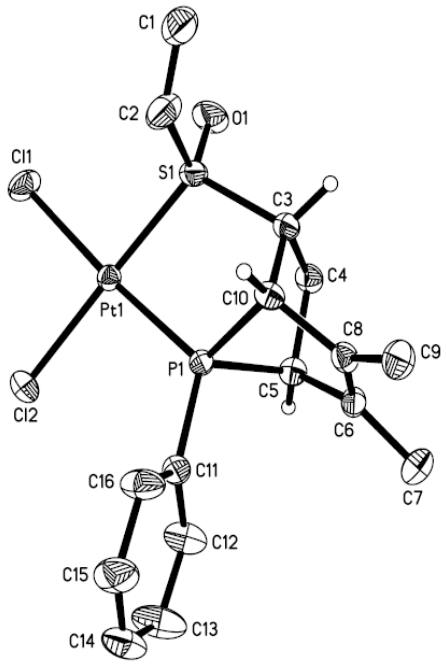
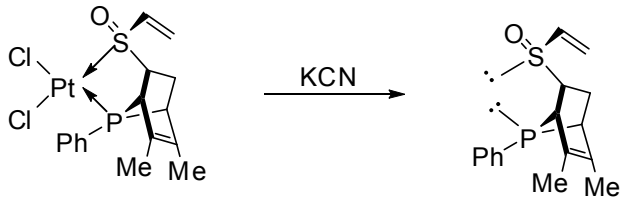


Figure 1. Molecular structure of complex **36**

Table 1. Selected bond lengths [Å] and angles [°] for **36**

Pt(1)-S(1)	2.2065(8)	Pt(1)-P(1)	2.2234(8)
Pt(1)-Cl(2)	2.3127(8)	Pt(1)-Cl(1)	2.3652(9)
C(5)-P(1)	1.840(3)	C(10)-P(1)	1.844(3)
O(1)-S(1)	1.463(3)		
S(1)-Pt(1)-P(1)	84.90(3)	S(1)-Pt(1)-Cl(2)	178.17(3)
P(1)-Pt(1)-Cl	93.44(3)	S(1)-Pt(1)-Cl(1)	91.08(3)
P(1)-Pt(1)-Cl(1)	175.40(3)	Cl(2)-Pt(1)-Cl(1)	90.61(3)
C(5)-P(1)-C(10)	82.02(16)		

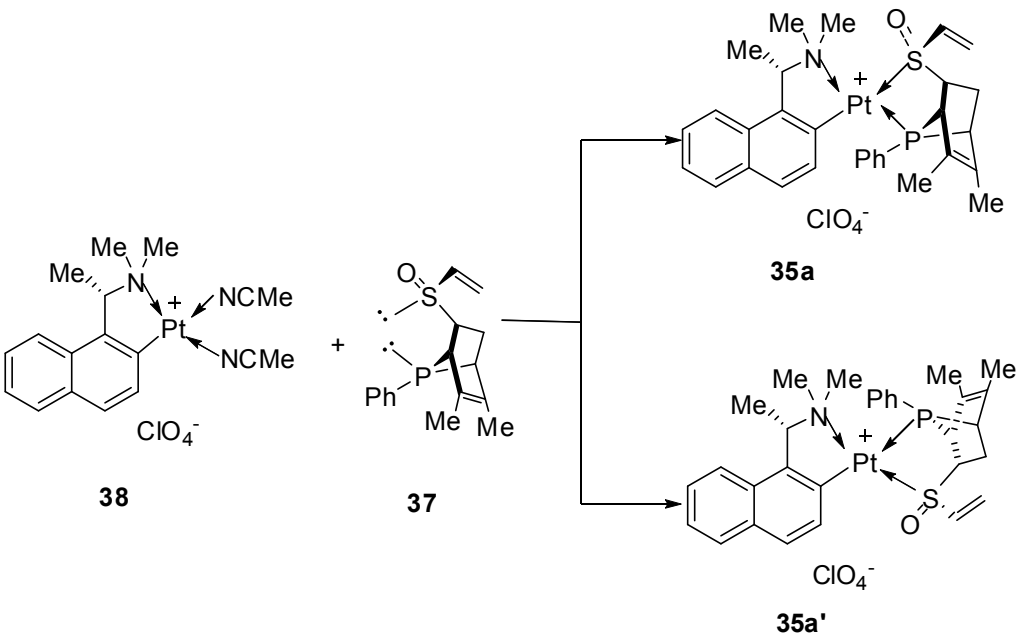
The newly generated P-S chiral bidentate ligand could be liberated efficiently from the dichloro platinum complex **36** by treatment with aqueous potassium cyanide (Scheme 2.6). The optically active ligand **37** was obtained as a white solid in quantitative yield, $[\alpha]_D$ +320.0 (*c* 1.0, CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum of the free ligand in $CDCl_3$ exhibited a singlet at δ 94.0. The five new chiral centers have been generated with *S* absolute configuration at sulfur, *S* absolute configuration at phosphorus, *S*, *S* and *R* absolute configuration at the three stereogenic carbon centers.



36 **37**

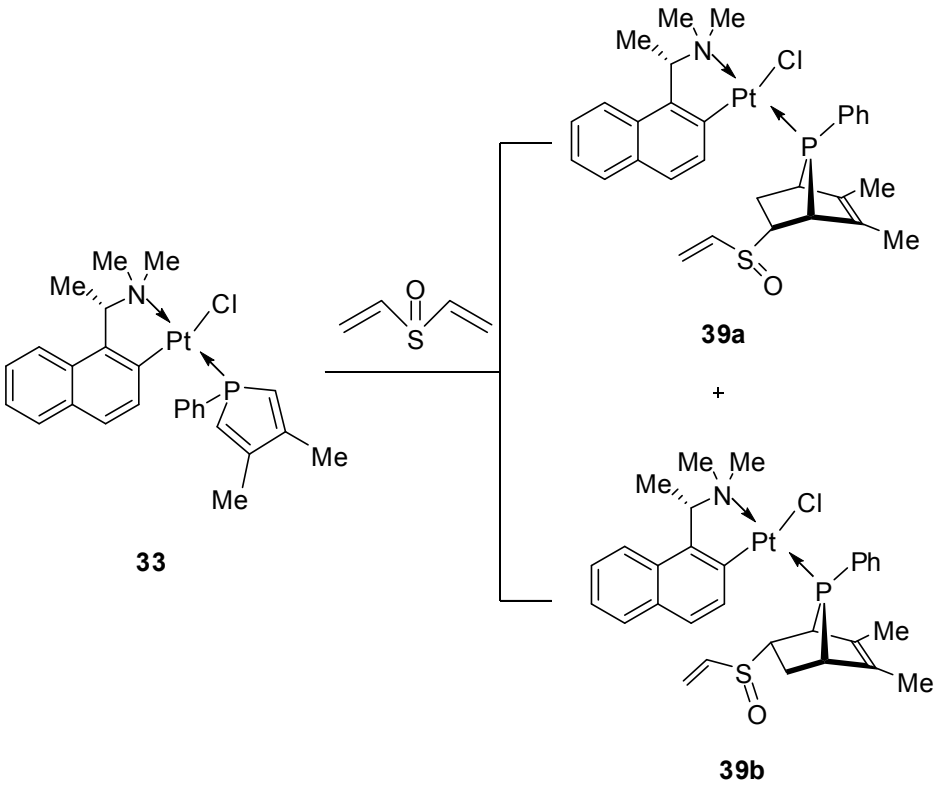
Scheme 2.6

Since the noncoordinated phosphorus and sulfur were not stable, the liberated ligand cannot be stored for a long duration. Therefore the liberated ligand **37** must be recoordinated to selected metal ions. In order to determine the optical purity of the liberated ligand, it was recoordinated to the bis-(acetonitrile) platinum complex **38** (Scheme 2.7). The 121 MHz $^{31}P\{^1H\}$ NMR spectra of the recomplexation products in $CDCl_3$ indeed exhibited two singlets at δ 98.1 ($J_{Pt\text{-}P}$=3282 Hz) and δ 127.7 ($J_{Pt\text{-}P}$=1577 Hz). The complex at δ 98.1 ($J_{Pt\text{-}P}$=3282 Hz) was identical to the original cycloaddition product **35a**. The complex **35a'** at δ 127.7 ($J_{Pt\text{-}P}$=1577 Hz) with a smaller coupling constant was the regioisomer of cycloaddition product **35a.**



Scheme 2.7

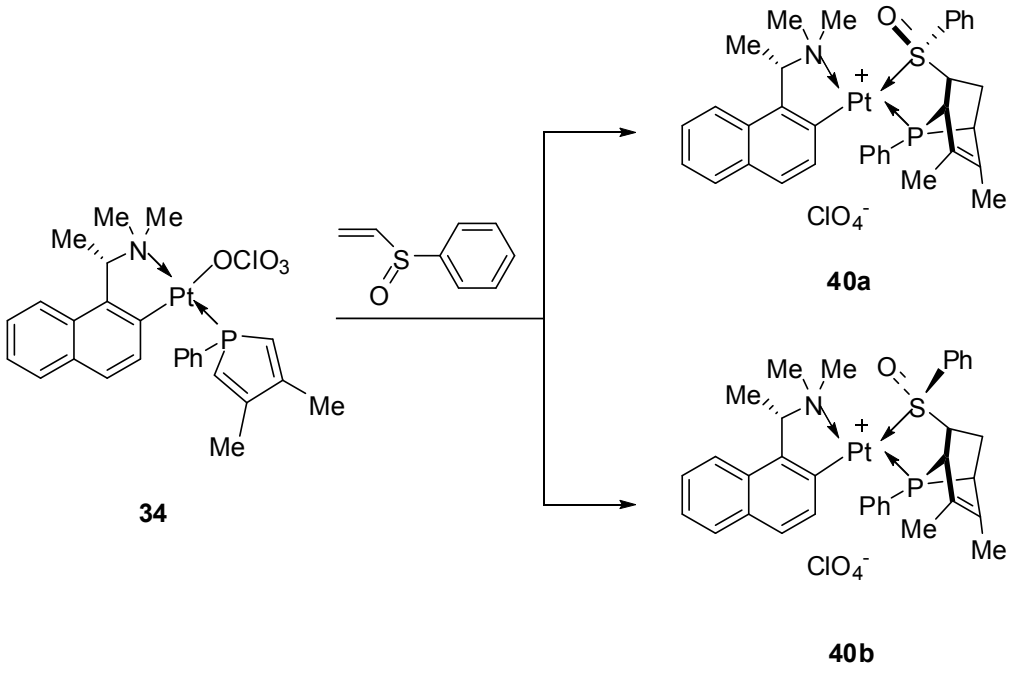
In order to compare the reactivity and selectivity of the reaction via the *exo*-pathway, the *endo*-pathway of the asymmetric cycloaddition reaction have also been attempted. Since the chloro ligand in the complex **33** is an inert ligand and DMPP have already taken the vacant coordination site of platinum, divinyl sulfoxide could not coordinate to the metal and could not be activated by the template metal. Although DMPP was activated by platinum, the reactivity between DMPP and divinyl sulfoxide was still not enough to provide the desired cycloadduct. The *endo* asymmetric cycloaddition reaction was carried out at 80℃. However, after one and a half months, the convertion of the *endo*-pathway was still below 5%, when monitored by ^{31}P NMR (Scheme 2.8).



Scheme 2.8

2.2.1.2 Asymmetric Cycloaddition Reaction between DMPP and Vinyl Phenyl Sulfoxide

By following the similar procedure as described for the cycloaddition reaction between DMPP and divinyl sulfoxide, the perchlorate platinum complex **34** was reacted with vinyl phenyl sulfoxide at 100℃ for 5 days to give a 9:1 mixture of diastereomeric complexes **40a** and **40b** (Scheme 2.9). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture in $CDCl_3$ exhibited two sharp singlets at δ 95.9 (($J_{Pt\text{-}P}$=3311 Hz) and 97.3 ($J_{Pt\text{-}P}$=3320 Hz). The major product **40a** could be separated by silica-gel column chromatograghy as a solid in 72% yield, $[\alpha]_D$ +105.4 (*c* 3.1, CH_2Cl_2).



Scheme 2.9

The minor product **40b** also could be obtained by fractional crystallization from dichloromethane-diethyl ether, $[\alpha]_D$ +137.7 (*c* 111.9, CH_2Cl_2). The single crystal X-ray diffraction analysis established that in the presence of the chiral amine auxiliary, DMPP with softer donor phosphorus took up the coordination position trans to the NMe_2 moiety and sulfur took up the coordination position cis to the NMe_2 group of the template. The cycloadduct in complex **40b** was coordinated to the metal center as a bidentate ligand via the bridgehead phosphorus and sulfur of vinyl phenyl sulfoxide. The five new chiral centers have been generated with *R* absolute configuration at sulfur, *R* absolute configuration at phosphorus, *R*, *R* and *S* absolute configuration at C(23), C(24) and C(21), respectively. The geometry at platinum is slightly distorted square planar with angles at platinum in the range of 79.80(3)° -100.26(16)° and

169.75(16)° -175.90(2)° . The bond angle at the bridgehead phosphorus is 81.40(2)° . Selected bond lengths and angles are listed in Table 2.

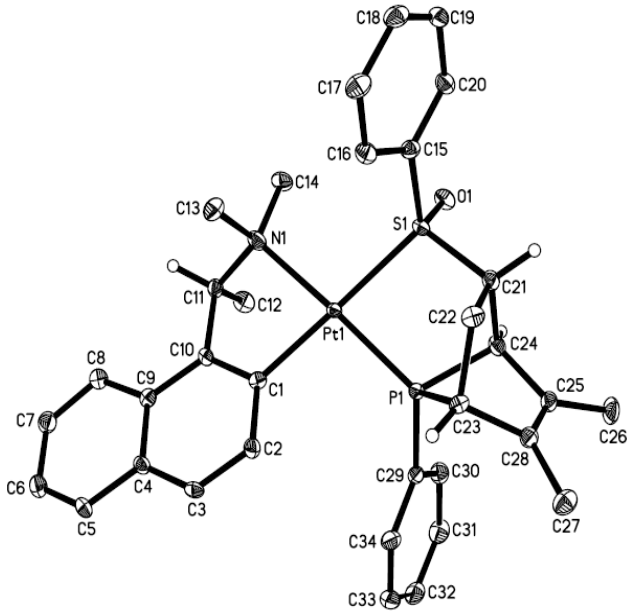
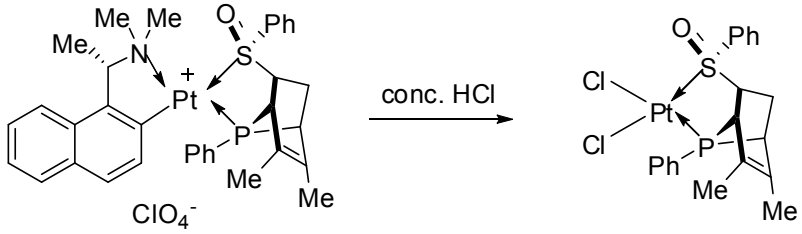


Figure 2. Molecular structure of complex **40b**

Table 2. Selected bond lengths [Å] and angles [°] for **40b**

Pt(1)-C(1)	2.015(7)	Pt(1)-N(1)	2.168(7)
Pt(1)-P(1)	2.2306(18)	Pt(1)-S(1)	2.3160(16)
C(23)-P(1)	1.841(5)	C(24)-P(1)	1.860(5)
O(1)-S(1)	1.475(4)		
C(1)-Pt(1)-N(1)	79.8(3)	C(1)-Pt(1)-P(1)	98.1(2)
N(1)-Pt(1)-P(1)	169.75(16)	C(1)-Pt(1)-S(1)	175.9(2)
N(1)-Pt(1)-S(1)	100.26(16)	P(1)-Pt(1)-S(1)	82.58(7)
C(23)-P(1)-C(24)	81.4(2)		

Upon removal of the chiral amine auxiliary of **40a** with concentrated hydrochloric acid at room temperature for 30 min, the optically pure dichloro platinum complex **41** was obtained as white crystal in 92% yield, $[\alpha]_D$ -145.6 (*c* 10.84, CH_2Cl_2) (Scheme 2.10). The $^{31}P\{^1H\}$ NMR spectrum of **41** in $CDCl_3$ showed a singlet at δ 100.6 (J_{Pt-P}=3128 Hz).



40a **41**

Scheme 2.10

The single crystal X-ray diffraction analysis established that the cycloadduct in complex **41** was coordinated to the metal center as a bidentate ligand via the bridgehead phosphorus and sulfur of phenyl vinyl sulfoxide. It also confirmed that the cycloadduct is an *exo*-cycloaddition product. The five new chiral centers have been generated with *S* absolute configuration at sulfur, *R* absolute configuration at phosphorus, *R*, *R* and *S* absolute configuration at C(8), C(13) and C(7), respectively. The geometry at platinum is slightly distorted square planar with angles at platinum in the range of 85.17(3)° -92.16(2)° and 173.37(2)° -176.42(3)° . The bond angle at the bridgehead phosphorus is 82.01(12)° . Selected bond lengths and angles are listed in Table

3.

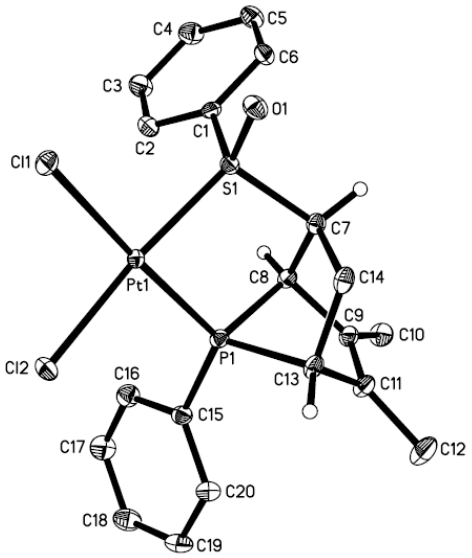
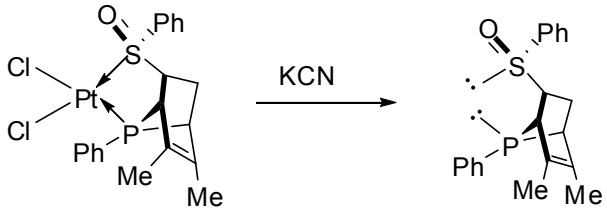


Figure 3. Molecular structure of complex **41**

Table 3. Selected bond lengths [Å] and angles [°] for **41**

Pt(1)-P(1)	2.2127(8)	Pt(1)-S(1)	2.2134(7)
Pt(1)-Cl(2)	2.3123(7)	Pt(1)-Cl(1)	2.3566(7)
C(8)-P(1)	1.848(3)	C(13)-P(1)	1.844(3)
O(1)-S(1)	1.467(2)		
P(1)-Pt(1)-S(1)	85.17(3)	P(1)-Pt(1)-Cl(2)	91.40(3)
S(1)-Pt(1)-Cl(2)	173.37(2)	P(1)-Pt(1)-Cl(1)	176.42(3)
S(1)-Pt(1)-Cl(1)	92.16(2)	Cl(2)-Pt(1)-Cl(1)	91.01(3)
C(13)-P(1)-C(8)	82.01(12)		

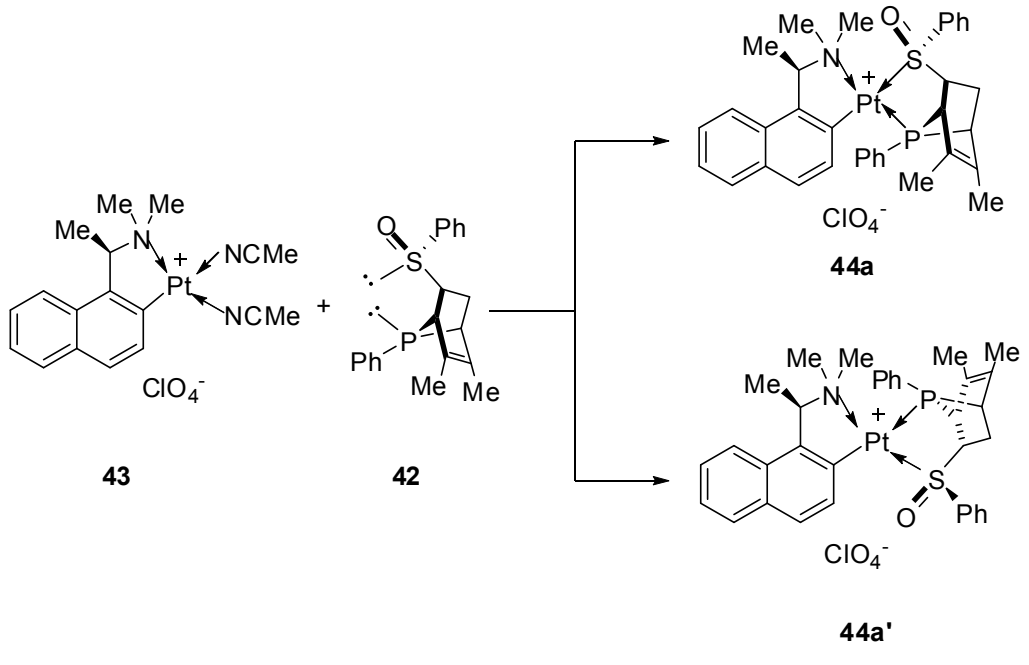
Treatment of a CH_2Cl_2 of complex **41** with aqueous potassium cyanide at room temperature for 20 min liberated the P-S chiral bidentate ligand (Scheme 2.11). The optically active ligand **42** was obtained as a white solid in quantitative yield, $[\alpha]_D$ +102.6 (*c* 7.6, CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum of the free ligand in $CDCl_3$ exhibited a singlet at δ 93.6. The five new chiral centers have been generated with *S* absolute configuration at sulfur, *R* absolute configuration at phosphorus, *R*, *R* and *S* absolute configuration at the three stereogenic carbon centers, respectively.



41 **42**

Scheme 2.11

In order to determine the optical purity of the liberated ligand, it was recoordinated to the bis-(acetonitrile) platinum complex **43** to give the recoordination product (Scheme 2.12). The 121 MHz $^{31}P\{^1H\}$ NMR of the recomplexation products in $CDCl_3$ indeed exhibited two singlets at δ 97.3 ($J_{Pt\text{-}P}$=3315 Hz) and δ 127.0 ($J_{Pt\text{-}P}$=1575 Hz). The complex **44a** at δ 97.3 ($J_{Pt\text{-}P}$=3315 Hz) was similar to the original cycloaddition product **40a**. The complex **44a'** at δ 127.7 ($J_{Pt\text{-}P}$=1575 Hz) was the regioisomer of cycloaddtion product **44a.**



Scheme 2.12

However, the new recoordination product **44a'** could be obtained by fractional crystallization from dichloromethane-diethyl ether. Interestingly, the single crystal X-ray diffraction analysis of complex **44a'** established that this time sulfur took up the coordination position trans to the NMe_2 moiety of the template and DMPP took up the position cis to the NMe_2 moiety. The five chiral centers have been generated with *S* absolute configuration at sulfur, *R* absolute configuration at phosphorus, *R*, *R* and *S* absolute configuration at C(21), C(26) and C(27), respectively. The geometry at platinum is slightly distorted square planar with angles at platinum in the range of 79.62(17)° - 102.60(11)° and 170.52(11)° - 172.81(13)° . The bond angle at the bridgehead phosphorus is 81.2(2)° . Selected bond lengths and angles are listed in Table 4.

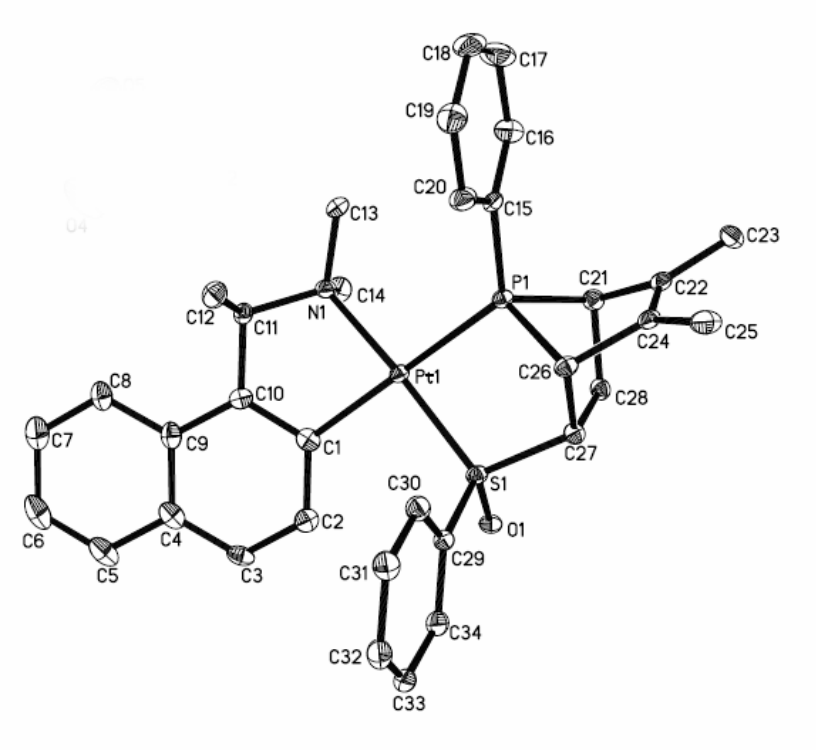


Figure 4. Molecular structure of complex **44a'**

Table 4. Selected bond lengths [Å] and angles [°] for **44a'**

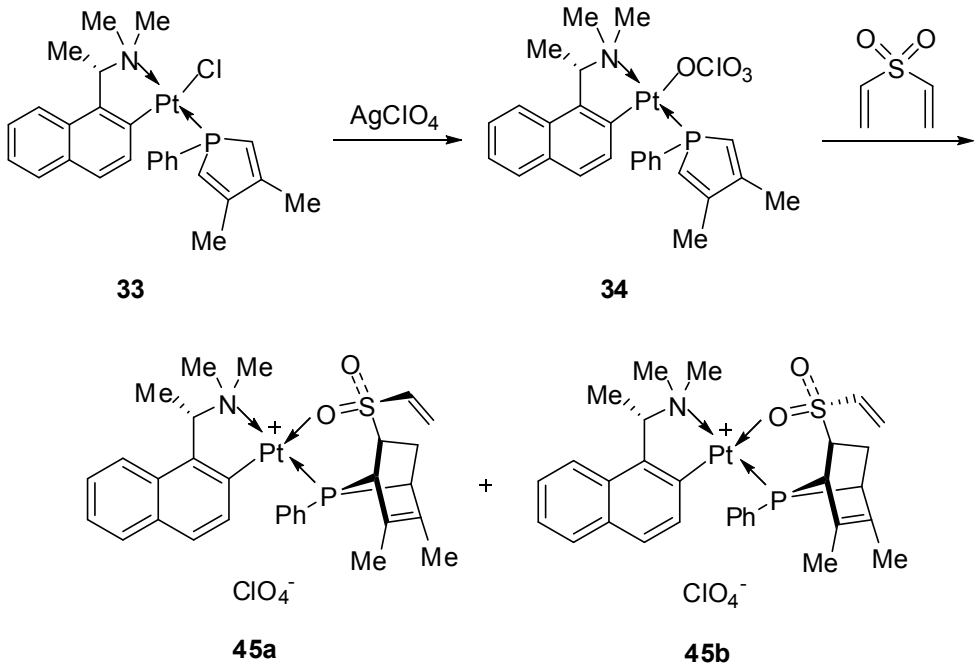
Pt(1)-C(1)	2.056(5)	Pt(1)-N(1)	2.105(4)
Pt(1)-P(1)	2.3344(12)	Pt(1)-S(1)	2.2070(11)
C(21)-P(1)	1.848(5)	C(26)-P(1)	1.848(4)
O(1)-S(1)	1.478(3)		
C(1)-Pt(1)-N(1)	79.62(17)	C(1)-Pt(1)-P(1)	172.81(13)
N(1)-Pt(1)-P(1)	102.60(11)	C(1)-Pt(1)-S(1)	94.76(14)
N(1)-Pt(1)-S(1)	170.52(11)	P(1)-Pt(1)-S(1)	83.92(4)
C(23)-P(1)-C(24)	81.2(2)		

The recoordination product **44a** was thermodynamically favourable complex and **44a'** was more kinetically favourable product. Therefore, complex **44a'** could convert to complex **44a** in solution. When a slolution of complex **44a'** in dichloromethane at room kept for 2 months, complex **44a'** could converted to complex **44a** slowly and the conversion was 20%.

2.2.1.3 Asymmetric cycloaddition reaction between DMPP and divinyl sulfone

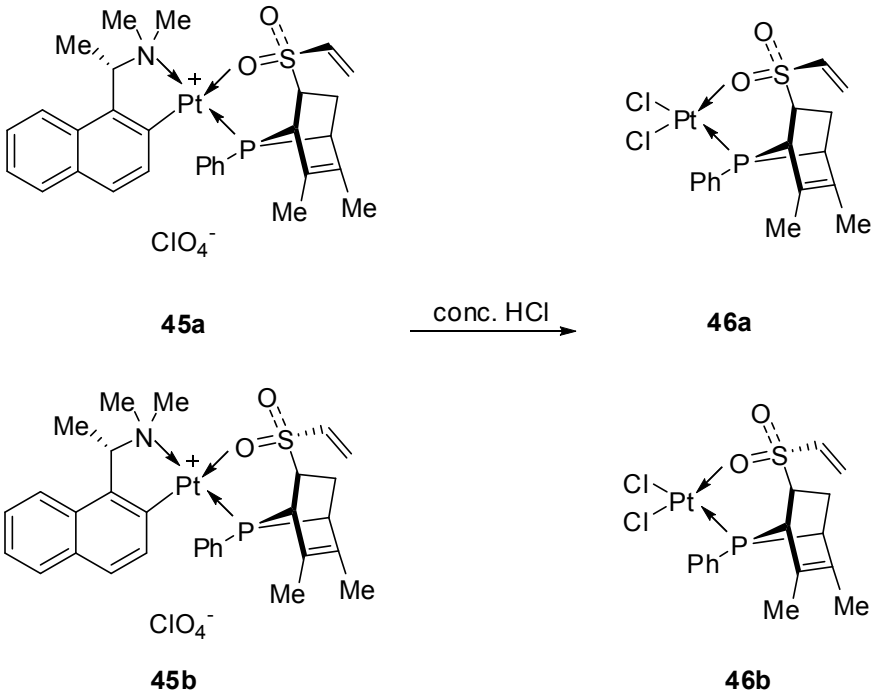
To study the effect of selectivity and reactivity of the distance between metal center and the incoming prochiral center, the asymmetric cycloaddition reaction between DMPP and divinyl sulfone which was promoted by the platinum template have also been attempted. Although the chemical structure of divinyl sulfone was quite similar to that of divinyl sulfoxide, the result was totally different as expected from the variation in electronic factors between the two.

The 1,2-dichloroethane solution containing the perchlorate platinum complex **34** was directly treated with divinyl sulfone at 100℃. 20 days later, the reaction was completed and gave a 1.5:1 mixture of diastereomeric complexes **45a** and **45b** (Scheme 2.13). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture in $CDCl_3$ exhibited two sharp singlets at δ 104.2 ($J_{Pt\text{-}P}$=3795 Hz) and δ 104.0 ($J_{Pt\text{-}P}$=3742 Hz).



Scheme 2.13

The chiral naphthylamine auxiliary on the two products **45a** and **45b** could be removed by the treatment of the complex with concentrated hydrochloric acid for 20 min at room temperature (Scheme 2.14). The $^{31}P\{^{1}H\}$ NMR spectrum of the dichloro platinum complexes in $CDCl_3$ showed two singlet at δ 89.2 ($J_{Pt\text{-}P}$=3488 Hz) and δ 88.1 ($J_{Pt\text{-}P}$=3609 Hz).



Scheme 2.14

Since there was no lone pair electron on sulfur of divinyl sulfone, it was the oxygen which coordinated to the platinum. The distance between platinum and vinyl group in divinyl sulfone was longer than that in divinyl sulfoxide. Therefore, the efficiency of activation was lower than the reaction between DMPP and divinyl sulfoxide. The reaction of DMPP and divinyl sulfone was quite slower and took 20 days to accomplish. But the reaction between DMPP and divinyl sulfoxide could finish in 5 days.

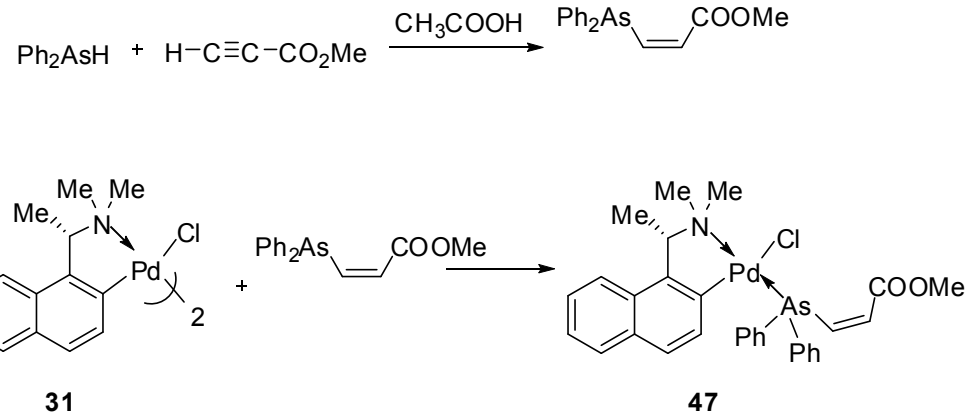
In addition, the impact on the selectivity of the metal template was weaker, because the prochiral sulfur center was farther away from the template metal. Since the distance of platinum and sulfur was too long, therefore the template could not lock the position of the incoming ligand efficiently. Comparing the ratio 5:1 of the cycloaddition reaction between DMPP and divinyl sulfoxide, the ratio of the reaction between DMPP and divinyl sulfone was only 1.5:1.

2.2.2 Metal Effect on Asymmetric Synthesis toward P-As ligands

2.2.2.1 The synthesis of chiral metal arsenic precursors

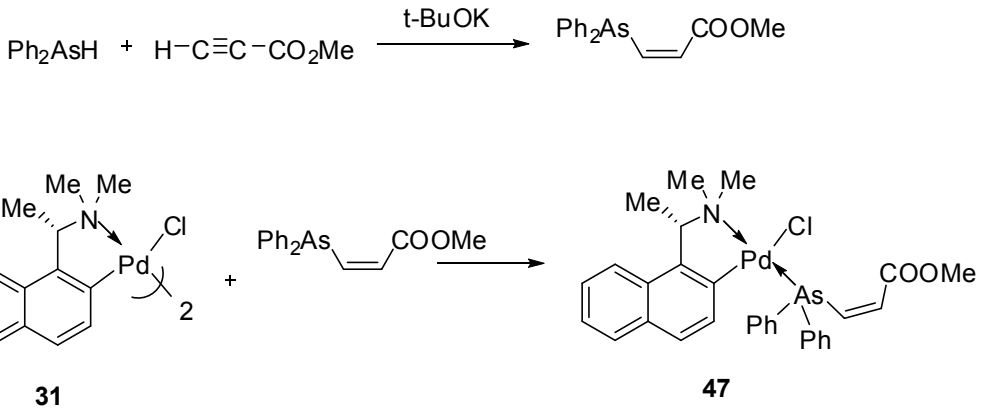
We attempted three methods to prepare the chiral metal arsenic precursors. All these three methods could be used to synthesize the precursors efficiently. For instance, for the preparation of chiral palladium arsenic precursor containing an ester group, we chose diphenylarsine and methyl propiolate as starting materials.

The first method was using acetic acid as catalyst in the first step to catalyze hydroarsination reaction between diphenylarsine and methyl propiolate. The mixture of diphenylarsine, methyl propiolate and acetic acid in tetrahydrofuran (THF) was allowed to react at room temperature for 3 days. Since the target product was an air-sensitive compound, the solution was worked up under a positive pressure of argon and subsequently was treated with a solution of chiral palladium template **31** in dichloromethane at room temperature and stirred overnight. Since arsenic could be stabilized after coordination to transition metal, the product could be purified by silica-gel column chromatograghy and fractional crystallization (Scheme 2.15).



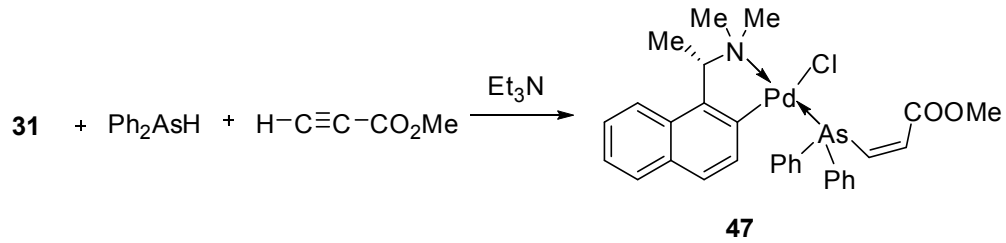
Scheme 2.15

The second method was very similar to the first one, and instead of acetic acid, the catalyst was potassium tert-butoxide (Scheme2.16).



Scheme 2.16

The third method was a one-pot reaction. The three compounds, diphenylarsine, methyl propiolate, and the chiral palladium template were dissolved in dichloromethane and reacted overnight. The product could be purified by silica-gel column chromatography (Scheme 2.17).



Scheme 2.17

Comparing these three methods, there was no significant change between the results, just the yield of the second method was a little higher than the other two methods. Therefore the second method was used to synthesize other chiral metal arsenic precursors.

The single crystal X-ray diffraction analysis of complex **47** established that in the presence of the chiral amine auxiliary, arsenic took up the coordination position trans to the NMe_2 moiety of the template. The geometry at platinum is slightly distorted square planar with angles at platinum in the range of 82.07(13)° -94.07(11)° and 164.71(11)° -173.65(9)° . Selected bond lengths and angles are listed in Table 5.

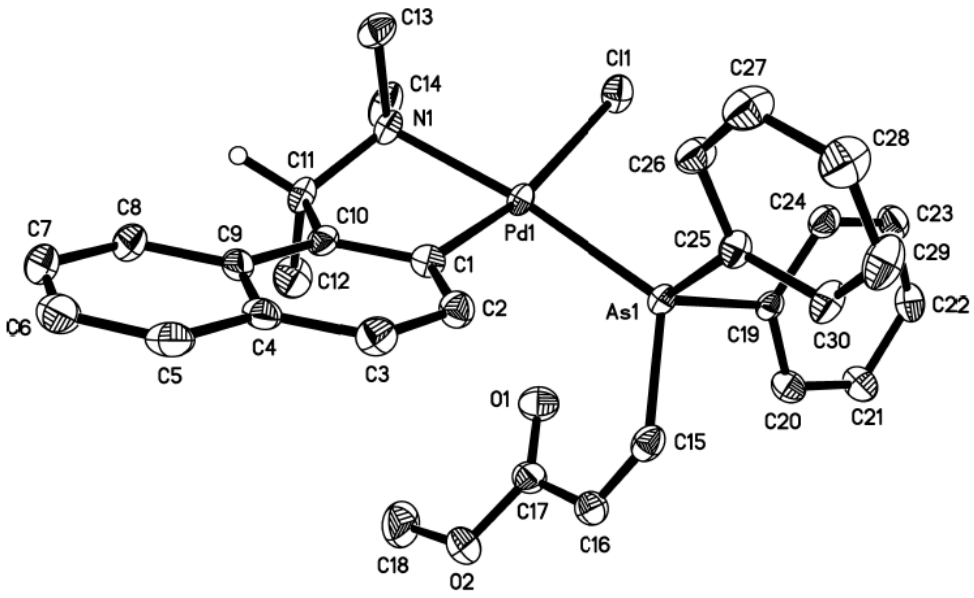


Figure 5. Molecular structure of complex **47**

Table 5. Selected bond lengths [Å] and angles [°] for **47**

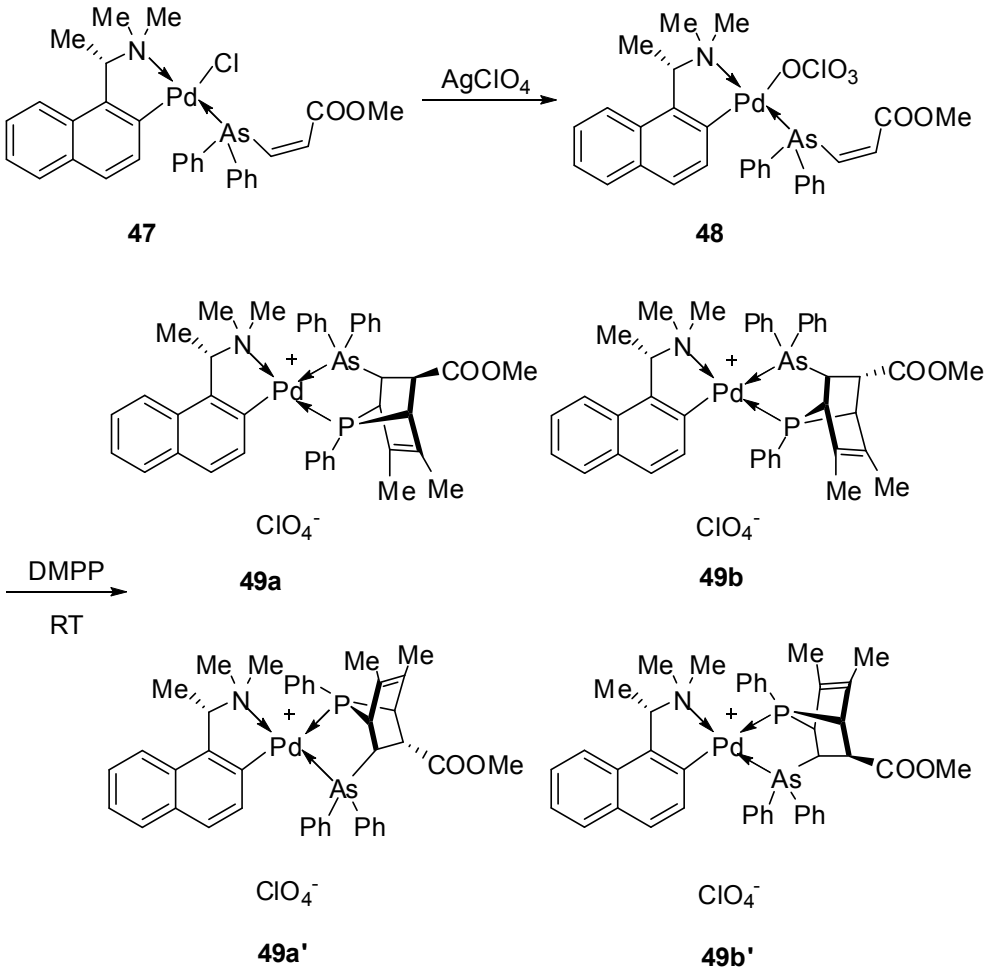
Pd(1)-C(1)	2.003(4)	Pd(1)-N(1)	2.117(3)
Pd(1)-As(1)	2.3666(4)	Pd(1)-Cl(1)	2.4032(10)
As(1)-C(15)	1.928(4)	As(1)-C(25)	1.938(3)
As(1)-C(19)	1.945(3)	C(15)-C(16)	1.326(6)
C(1)-Pd(1)-N(1)	82.07(13)	C(1)-Pd(1)-As(1)	94.07(11)
N(1)-Pd(1)-As(1)	173.65(9)	C(1)-Pd(1)-Cl(1)	164.71(11)
N(1)-Pd(1)-Cl(1)	93.04(9)	As(1)-Pd(1)-Cl(1)	91.95(3)

2.2.2.2 Asymmetric cycloaddition reaction between DMPP and methyl ester 3-(diphenylarsino)-acrylate promoted by chiral palladium template

As mentioned before, the palladium complex **47** was treated with silver perchlorate to replace the chloro ligand by perchlorate ligand. Then a solution of the perchlorate complex **48** in dichloromethane was treated with DMPP directly. The reaction temperature was found to have an impact on product selectivity.

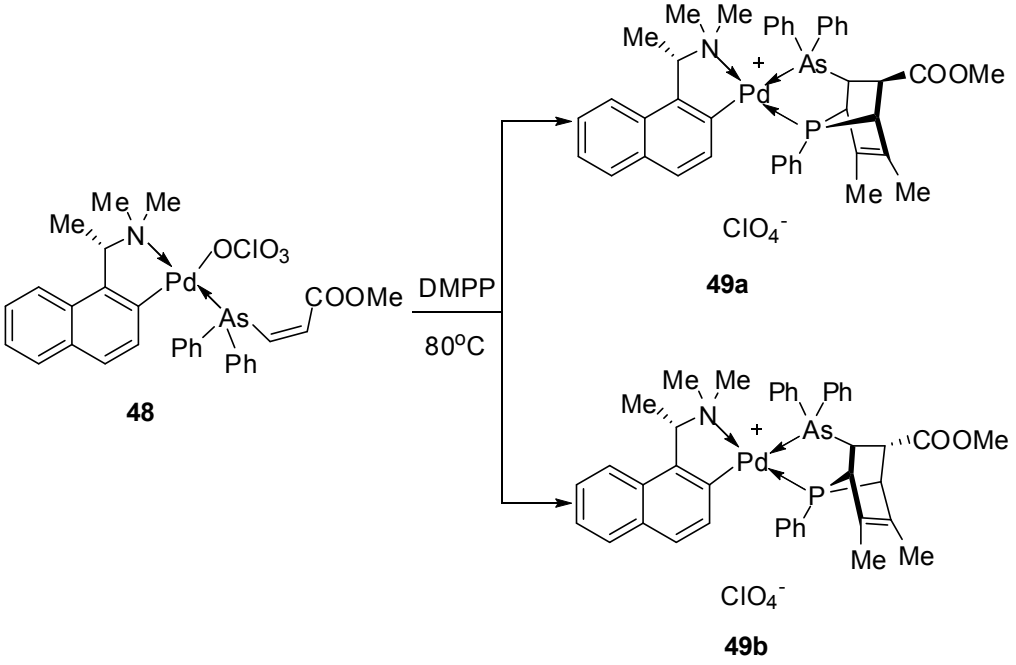
When the reaction was carried out at room temperature for 10 days, there were four products **49a**, **49a'**, **49b** and **49b'** as seen from $^{31}P\{^{1}H\}$ NMR, of which were two pairs of regioisomers (Scheme 2.18). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited four sharp singlets at δ 129.7, δ 127.2, δ 120.0 and δ 115.6, in the ratio of 1: 5.5: 2.4: 3.6. These low-field chemical shifts confirm that the phosphorus of each complex was the typical bridgehead phosphorus in phosphanorbornenes. In the chiral palladium arsenic precursor **47**, arsenic group took the trans position to the NMe_2 group of the chiral palladium template. Therefore, the cycloadducts **49a'** and **49b'** with arsenic taking up the coordination position trans to the NMe_2 group of the palladium template and phosphorus cis to NMe_2 group were more kinetically favourable than their regioisomers **49a** and **49b**. At the start of the reaction, the cycloadducts **49a'** and 4**9b'** with arsenic trans to NMe_2 were the major products. On the other hand, although both phosphorus and arsenic are soft atoms, phosphorus is softer than arsenic. Therefore, the softer donor

phosphorus preferred to take up the coordination position trans to the NMe_2 group. The cycloadducts **49a** and **49b** with phosphorus taking up the coordination position trans to the NMe_2 group and arsenic cis to NMe_2 group were more thermodynamically stable than their regioisomers **49a'** and 4**9b'**. Thus, during the reaction, the ratio of the four products would change and the more kinetically stable cycloadducts **49a'** and **49b'** converted to the more thermodynamically stable cylcoadduct **49a** and **49b**. Unfortunately, these four products could not be separated by silica-gel column chromatography or fractional crystallization.



Scheme 2.18

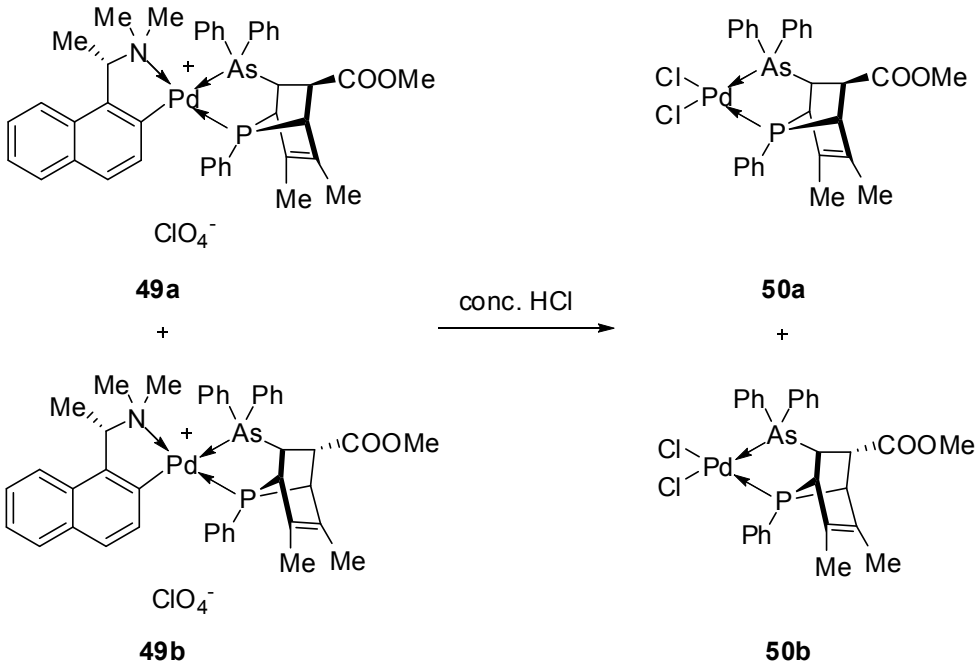
Therefore, when the reaction temperature was kept at 80℃ for 2 days, there were only two singlets exhibited in $^{31}P\{^{1}H\}$ NMR spectrum during monitoring (Scheme 2.19). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited two sharp singlets at δ 119.8 and δ115.4. Since the energy was enough to form the cycloadducts thermodynamically favourable **49a** and **49b** directly, no complex **49a'** or **49b'** was obtained in the whole reaction, which was monitored by ^{31}P NMR. In addition, the ratio of **49a** and **49b** was 1.7:1, which showed that this asymmetric cycloaddition reaction was not promoted efficiently by the palladium temeplate. Unfortunately, **49a** and **49b** could not be separated by silica-gel column chromatography or fractional crystallization. Thus, the mixture of products was used directly in the next step.



Scheme 2.19

Since the absolute configuration of all the chiral centers of the

regioisomers **49a** and **49a'** were the same, **49a** and **49a'** could generate the same dichloro complex **50a** after removing the chiral naphthylamine auxiliary. Meanwhile **49b** and **49b'** could generate the same dichloro complex **50b**. Therefore, the products **49a** and **49b** of the reaction done at 80℃ were used to generate dichloro complexes **50a** and **50b** by the treatment with concentrated hydrochloric acid at room temperature for 30 min (Scheme 2.20). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited only one sharp singlets at δ 128.5, which means the two dichloro complexes were regioisomers. Unfortunately, complexes **50a** and **50b** could not be separated by silica-gel column chromatography or fractional crystallization.



Scheme 2.20

The single crystal X-ray diffraction analysis established that the crystal was that of a racemic mixture. The cycloadducts in complexes **50a** and **50b** were coordinated to the metal center as a bidentate ligand via the bridgehead phosphorus and arsenic. The geometry at palladium is slightly distorted square planar with angles at palladium in the range of 82.12(4)° -93.86(3)° and 172.00(3)° -172.44(4)° . The bond angle at the bridgehead phosphorus is 80.9(2)° . Selected bond lengths and angles are listed in Table 6.

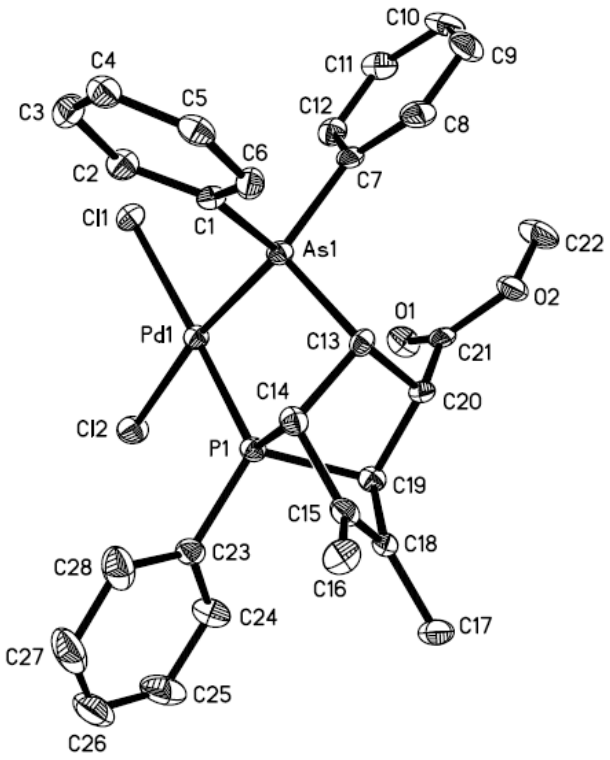


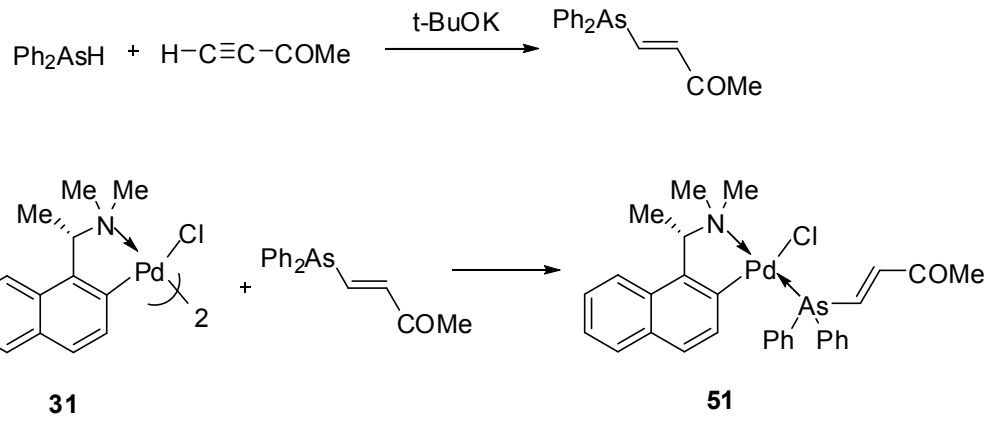
Figure 6. Molecular structure of complex **50**

Table 6. Selected bond lengths [Å] and angles [°] for **50**

Pd(1)-P(1)	2.2149(12)	Pd(1)-As(1)	2.3462(6)
Pd(1)-Cl(2)	2.3434(12)	Pd(1)-Cl(1)	2.3748(12)
C(19)-P(1)	1.855(5)	C(14)-P(1)	1.865(5)
As(1)-Pd(1)-P(1)	82.12(4)	As(1)-Pd(1)-Cl(2)	172.00(3)
P(1)-Pd(1)-Cl(2)	90.75(4)	As(1)-Pd(1)-Cl(1)	93.86(3)
P(1)-Pd(1)-Cl(1)	172.44(4)	Cl(2)-Pd(1)-Cl(1)	93.63(4)
C(19)-P(1)-C(14)	80.9(3)		

2.2.2.3 Asymmetric cycloaddition reaction between 4-(diphenylarsino)-3-buten-2-one and DMPP promoted by chiral palladium template

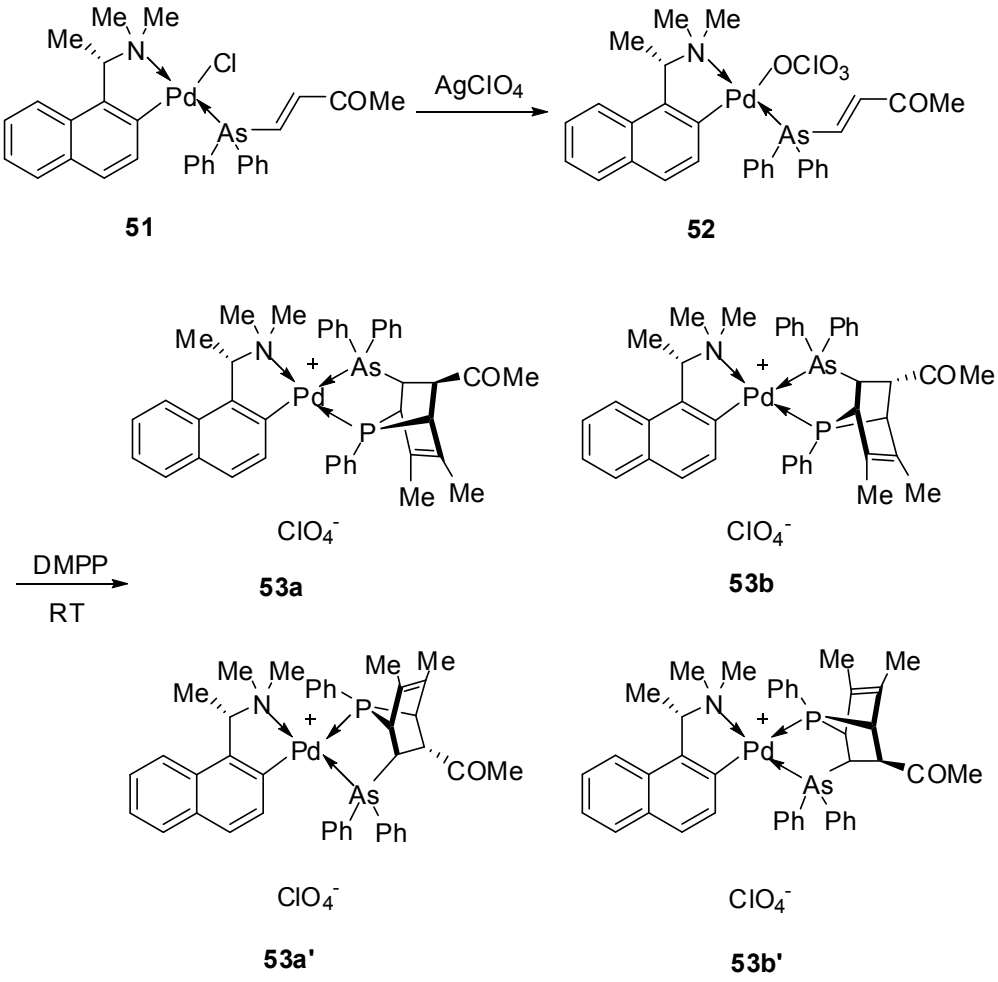
Following the similar procedure of the preparation of chiral palladium arsenic precursor **47**, the chiral palladium arsenic precursor **51** containing carbonyl group could be obtained efficiently (Scheme 2.21). Potassium tert-butoxide was used as catalyst to catalyze hydroarsination reaction between diphenylarsine and but-3-en-2-one. Since the target hydroarsination product was an air-sensitive compound, the solution was worked up under a positive pressure of argon and subsequently was treated with the dichloromethane solution of chiral palladium template **31** at room temperature and stirred overnight to generate chiral palladium complex **51**. The product **51** could be purified by silica-gel column chromatography and fractional crystallization subsequently.



Scheme 2.21

Similar to the reaction between complex **47** and DMPP, the reaction between complex **51** and DMPP provided different results at different reaction temperature. When the reaction was conducted at room temperature for 12 days, four products **53a**, **53a'**, **53b** and **53b'**could be obtained, which were two pairs of regioisomers (Scheme 2.22). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited four sharp singlets at δ 133.6, δ131.2, δ128.8 and δ 127.5, in the ratio of 3.4: 13.2: 33: 1. Complex **53a** and complex **53a'** were a pair of regioisomers. Meanwhile, complex **53b** and complex **53b'** were another pair of regioisomers. The cycloadducts **53a'** and **53b'** with arsenic taking up the coordination position trans to the NMe_2 group of the template and phosphorus cis to NMe_2 group were more kinetically favourable products. The cycloadducts **53a** and **53b** with phosphorus taking up the coordination position trans to the NMe_2 group and arsenic cis to NMe_2 group were more thermodynamically stable products. These four products could not be separated

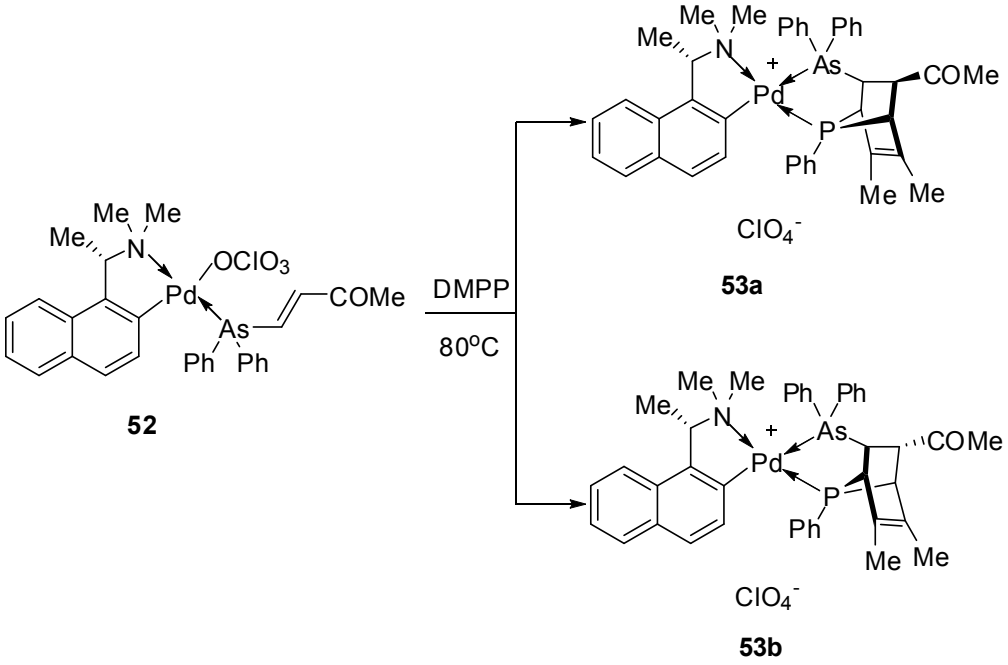
by silica-gel column chromatography or fractional crystallization.



Scheme 2.22

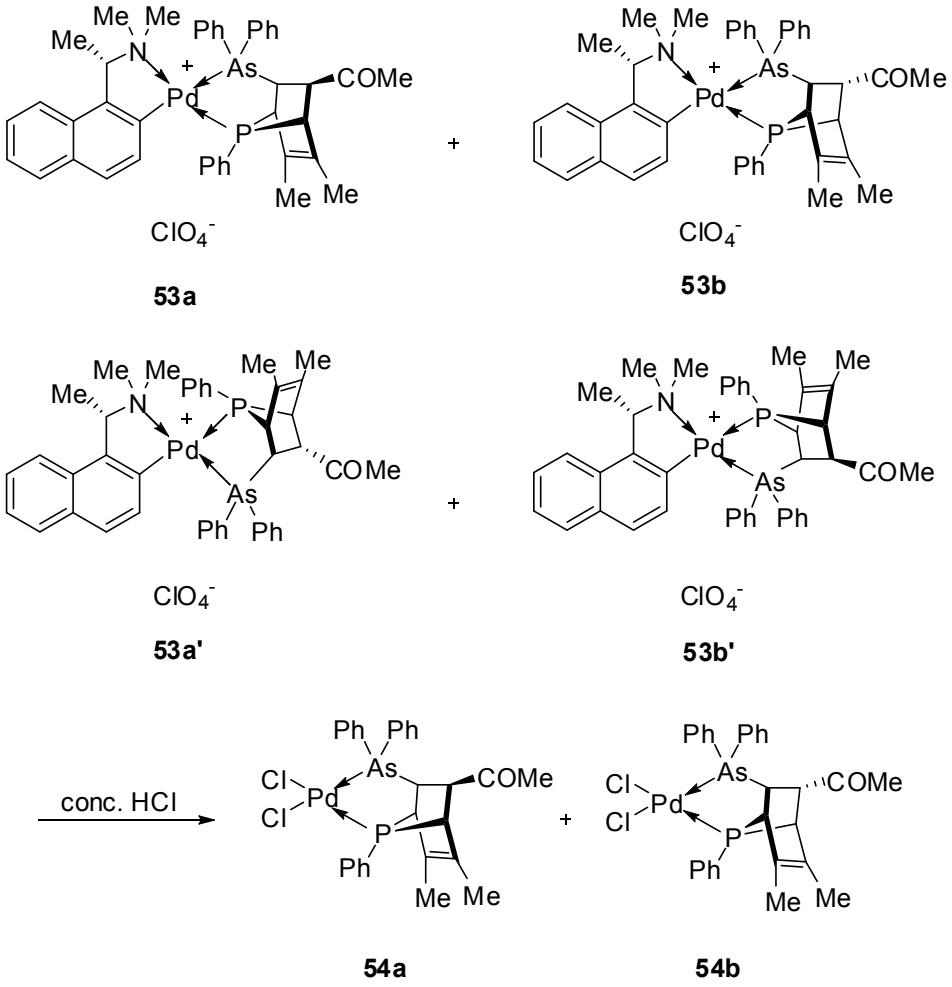
Therefore, when the reaction temperature was kept at 80℃ for 2 days, there were only two singlets exhibited in $^{31}P\{^{1}H\}$ NMR spectrum during monitoring (Scheme 2.23). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited two sharp singlets at δ128.8 and δ 127.5, in the ratio of 1.5:1. This showed that this asymmetric cycloaddition reaction was not promoted efficiently by the palladium temeplate. Unfortunately, **53a** and **54b** could not be separated by silica-gel column

chromatography or fractional crystallization.



Scheme 2.23

Since all the chiral centre of the regioisomer was in the same the absolute configuration, **53a** and **53a'** could generate the same dichloro complex **54a** by the treatment with concentrated hydrochloric acid to remove the chiral naphthylamine auxiliary. Meanwhile **53b** and **53b'** could generate the same dichloro complex **54b** by the treatment with concentrated hydrochloric acid. Therefore, the mixture of four cycloadducts **53a**, **53a**', **53b** and **53b'** was treated with concentrated hydrochloric acid at room temperature for 30 min to generate dichloro complex **54a** and **54b** (Scheme 2.24). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited two sharp singlets at δ 138.4 and δ 138.0, with the ratio of 1: 10.4.



Scheme 2.24

Dichloro palladium complexes **54a** could be obtained by fractional crystallization from dichloromethane-diethyl ether. The single crystal X-ray diffraction analysis established that the cycloadduct in complex **54a** was coordinated to the metal center as a bidentate ligand via the bridgehead phosphorus and arsenic. The five new chiral centers have been generated with *R* absolute configuration at phosphorus, *R*, *R*, *S* and *R* absolute configuration at C(17), C(22), C(13) and C(14) respectively. The geometry at palladium is slightly distorted square planar with angles at palladium in the range of 84.21(2)° - 94.95(3)° and 173.57(4)° -174.32(3)° . The bond angle at the bridgehead

phosphorus is 81.10(16)° . Selected bond lengths and angles are listed in Table 7.

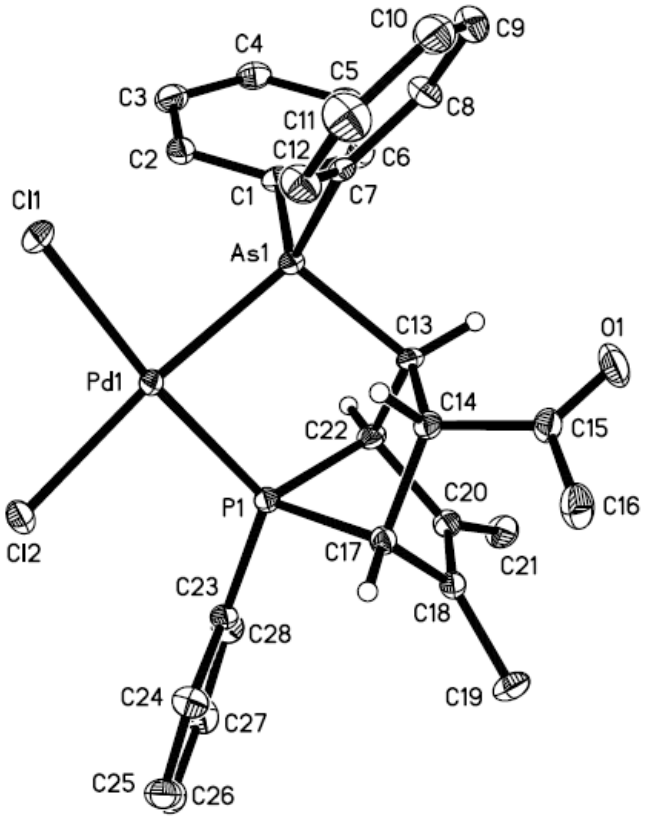


Figure 7. Molecular structure of complex **54a**

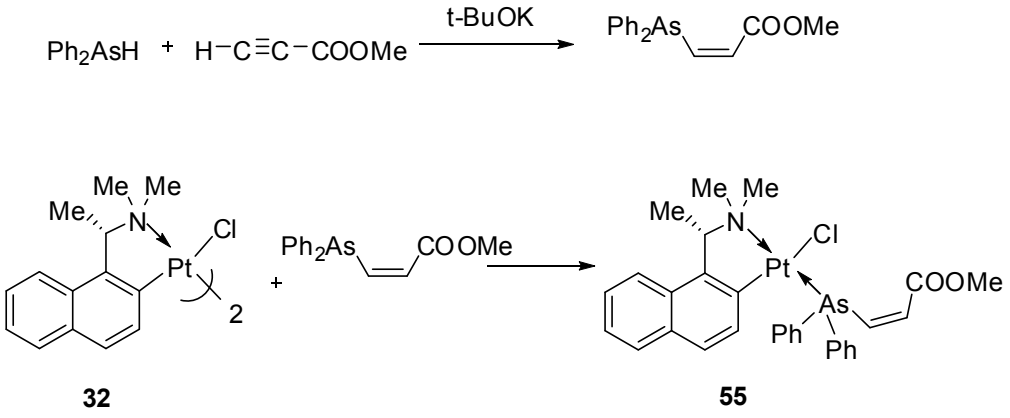
Table 7. Selected bond lengths [Å] and angles [°] for **54a**

Pd(1)-P(1)	2.2223(9)	Pd(1)-As(1)	2.3392(4)
Pd(1)-Cl(2)	2.3354(9)	Pd(1)-Cl(1)	2.3544(9)
C(17)-P(1)	1.857(3)	C(22)-P(1)	1.862(4)
As(1)-Pd(1)-P(1)	84.21(2)	As(1)-Pd(1)-Cl(2)	174.32(3)
P(1)-Pd(1)-Cl(2)	91.84(3)	As(1)-Pd(1)-Cl(1)	89.49(3)
P(1)-Pd(1)-Cl(1)	173.57(4)	Cl(2)-Pd(1)-Cl(1)	94.95(3)
C(17)-P(1)-C(22)	81.10(16)		

2.2.2.4 Asymmetric cycloaddition reaction between DMPP and methyl ester 3-(diphenylarsino)-acrylate promoted by chiral platinum template

In order to compare the different effect between chiral palladium template and its platinum analogue, chiral platinum template **32** was also used to promote these reactions.

The chiral platinum arsenic precursor **55** containing ester group could be synthesized following the procedure of the preparation of complex **47** (Scheme 2.25). Potassium tert-butoxide was used as catalyst to catalyze hydroarsination reaction between diphenylarsine and methyl propiolate. Then the arsine ligand was coordinated to the chiral platinum template **32** to give the desired chiral platinum arsenic precursor **55**.



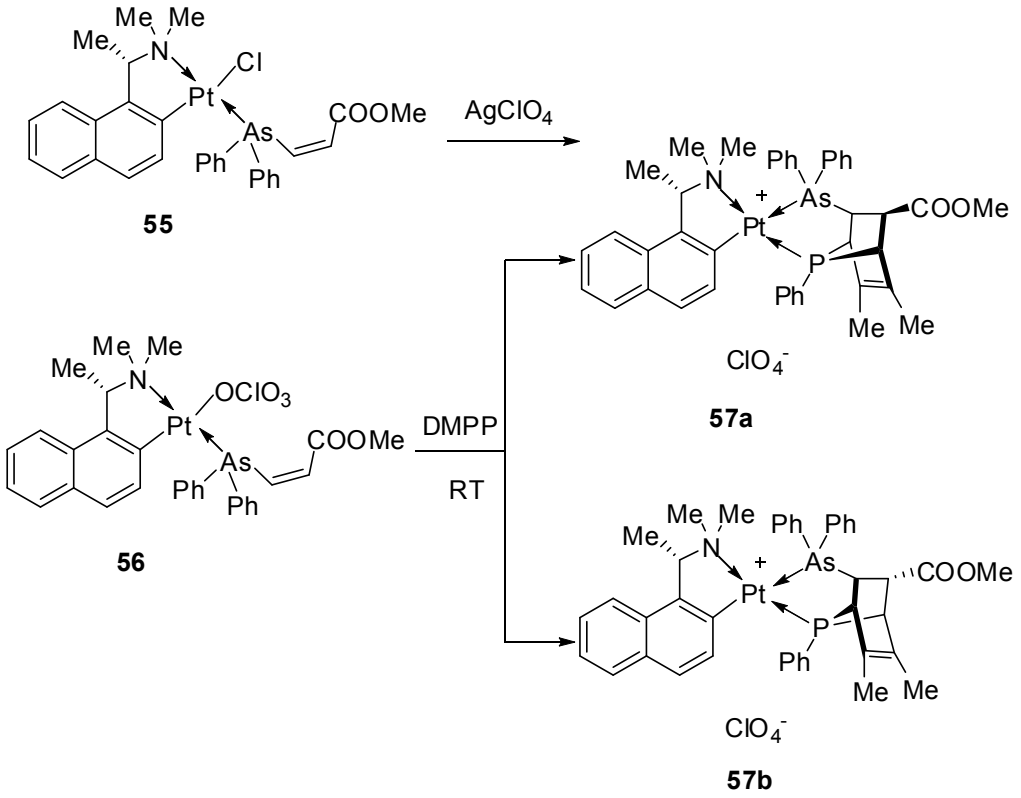
32 **55**

Scheme 2.25

As previously mentioned, it was necessary to replace the chloro ligand by perchlorate ligand in complex **55** with the treatement of aqueous silver perchlorate to provide a coordination site for the incoming ligands. Subsequently, the perchlorate complex **56** was treated with a solution of DMPP

in dichloromethane. The cycloaddition reaction promoted by chiral platinum template showed totally different result to the reaction promoted by chiral palladium template.

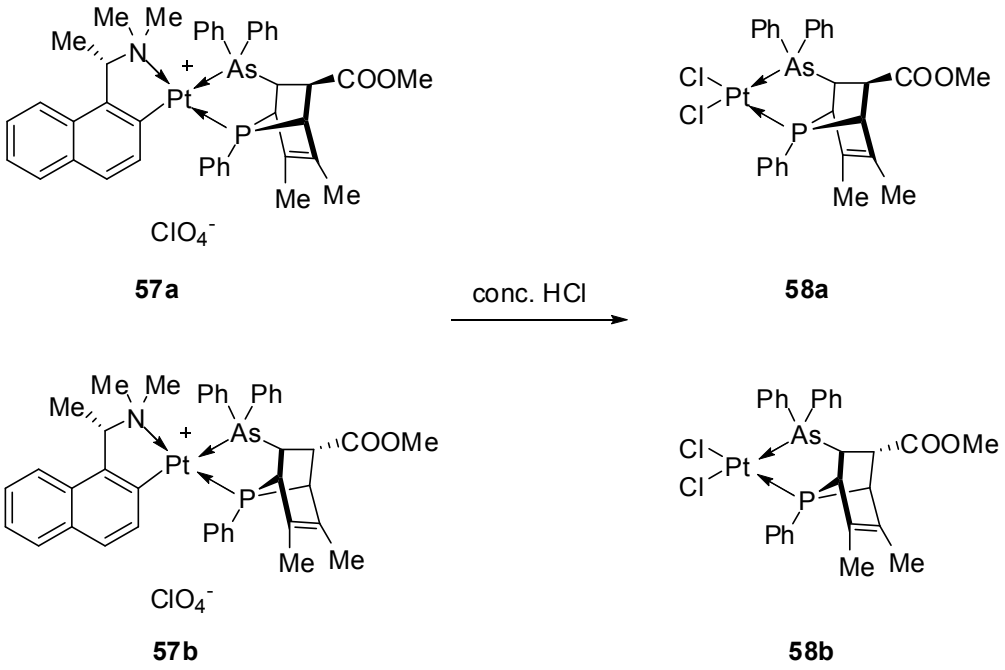
When the reaction was treated at room temperature for 25 days, there were only two products **57a** and **57b** could be obtained (Scheme 2.26). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited two sharp singlets at δ 91.8 and δ 91.0 (J_{Pt-P}=3400 Hz) in the ratio of 1:28 . The large coupling constant showed that in of these two products the softer phosphorus took up the trans coordination position to the NMe_2 group of the template and arsenic took up the cis coordination position to NMe_2 group. Unfortunately, although the selectivity of the cycloaddition reaction was



Scheme 2.26

appreciable, these two products could not be separated by silica-gel column chromatography or fractional crystallization.

The mixture of two cycloadducts **57a** and **57b** was treated with concentrated hydrochloric acid at room temperature for 30 min to remove the chiral naphthylamine auxiliary and generate dichloro complex **58a** and **59b** (Scheme 2.27). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited one sharp singlets at δ 98.8 ($J_{Pt\text{-}P}$=3235 Hz), which meaned that the two complexes were racemic mixture.



Scheme 2.27

Unfortunately, although the selectivity of the cycloaddition reaction was appreciable, the single crystal X-ray diffraction analysis established that the crystal of the dichloro platinum complex was obtained as a racemic mixture.

The cycloadduct was coordinated to the metal center as a bidentate ligand via the bridgehead phosphorus and arsenic. The geometry at platinum is slightly distorted square planar with angles at platinum in the range of 82.90(4)° - 94.65(3)° and 174.16(5)° -174.51(3)° . The bond angle at the bridgehead phosphorus is 81.00(2)° . Selected bond lengths and angles are listed in Table 8.

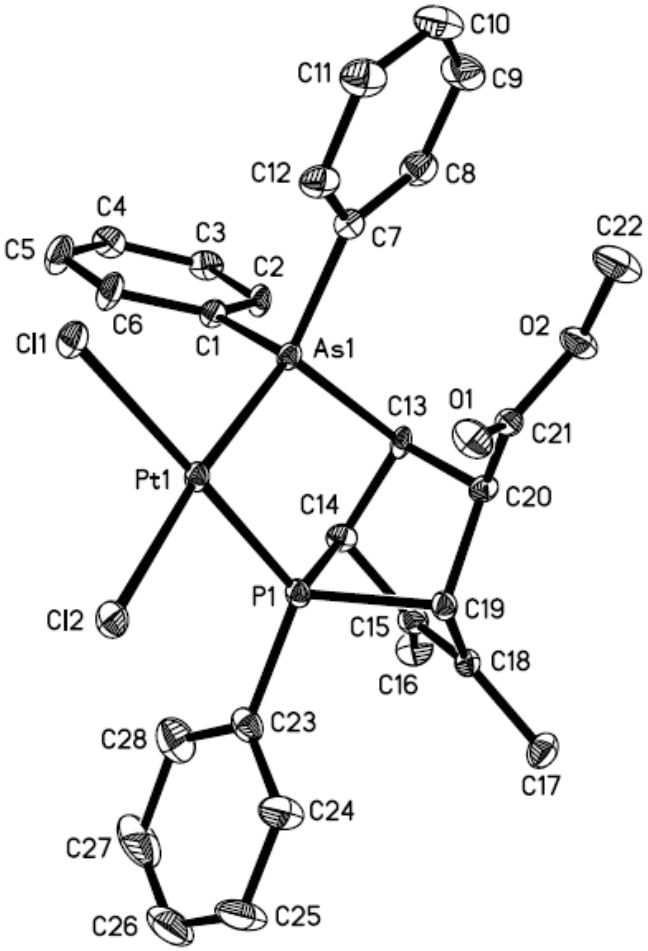
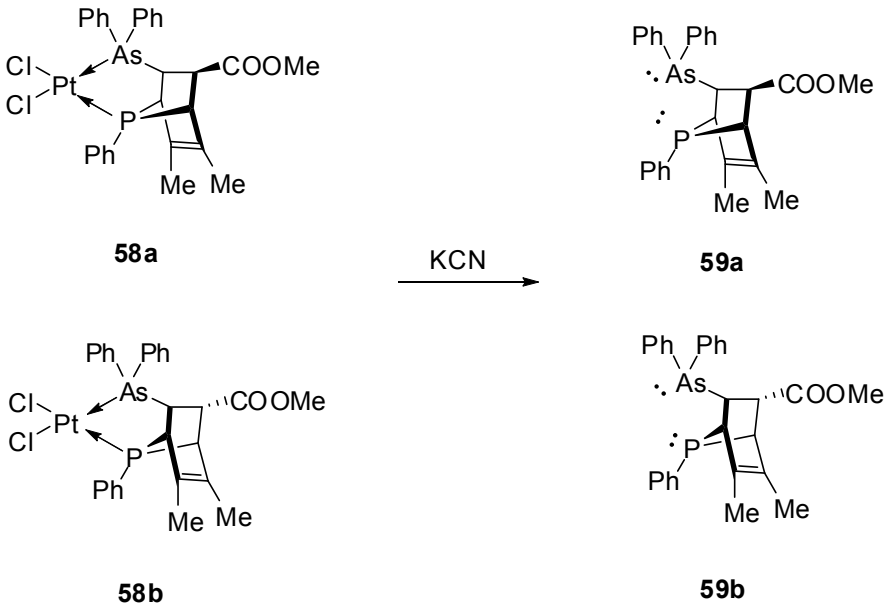


Figure 8. Molecular structure of complex **58**

Table 8. Selected bond lengths [Å] and angles [°] for **58**

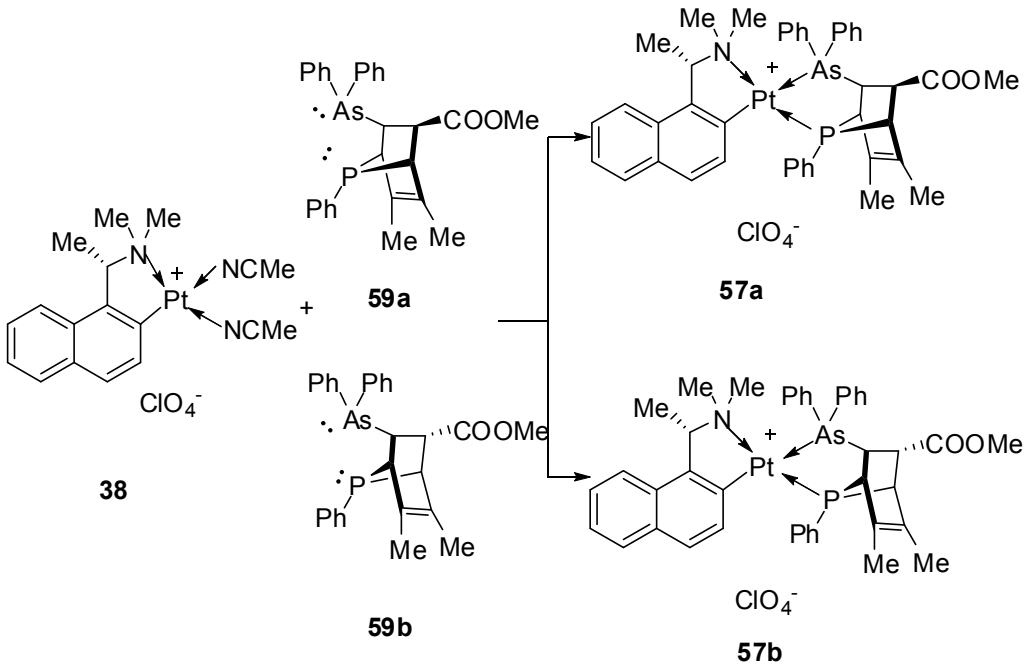
Pt(1)-P(1)	2.1986(13)	Pt(1)-As(1)	2.3340(5)
Pt(1)-Cl(2)	2.3399(13)	Pt(1)-Cl(1)	2.3712(12)
C(14)-P(1)	1.868(5)	C(19)-P(1)	1.840(5)
As(1)-Pt(1)-P(1)	82.90(4)	As(1)-Pt(1)-Cl(2)	174.51(3)
P(1)-Pt(1)-Cl(2)	92.14(5)	As(1)-Pt(1)-Cl(1)	94.65(3)
P(1)-Pt(1)-Cl(1)	174.16(5)	Cl(2)-Pt(1)-Cl(1)	90.51(4)
C(19)-P(1)-C(14)	81.00(2)		

The free P-As chiral bidentate ligand could be liberated efficiently from the dichloro platinum complex **58a** and **58b** by treatment with aqueous potassium cyanide (Scheme 2.28). The optically active ligand **59a** and **59b** was obtained as a white solid in quantitative yield, $[\alpha]_D$ +132.5 (*c* 1.4, CH_2Cl_2). The ^{31}P NMR spectrum of the free ligand in $CDCl_3$ exhibited a singlet at δ 87.3.



Scheme 2.28

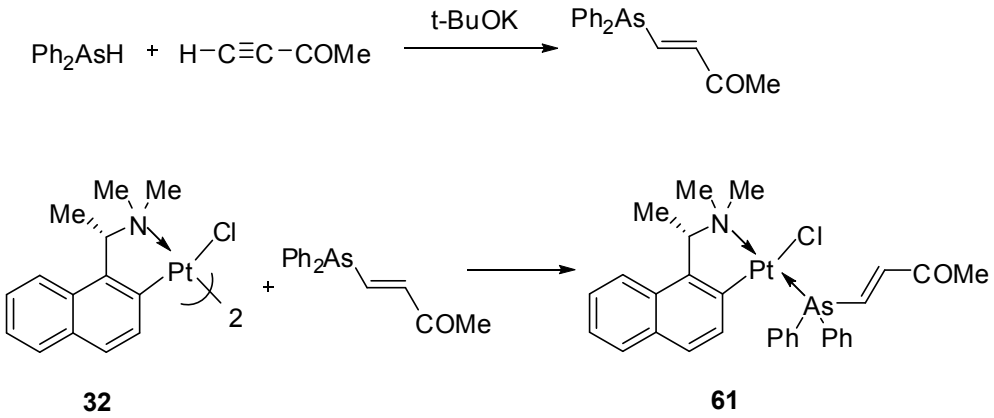
Since the noncoordinated phosphorus and arsenic were not stable, the liberated ligand cannot be stored for a long duration. Therefore the liberated ligand **59a** and **59b** must be recoordinated to selected metal ions. In order to determine the optical purity of the liberated ligand, it was recoordinated to the bis-(acetonitrile) platinum complex **38** (Scheme 2.29). The 121 MHz $^{31}P\{^{1}H\}$ NMR of the recomplexation products in $CDCl_3$ indeed exhibitedδ 91.8 and δ 91.0 ($J_{Pt\text{-}P}$=3400 Hz). The complex atδ 91.0 ($J_{Pt\text{-}P}$=3400 Hz) was identical to the original cycloaddition product **57a**.



Scheme 2.29

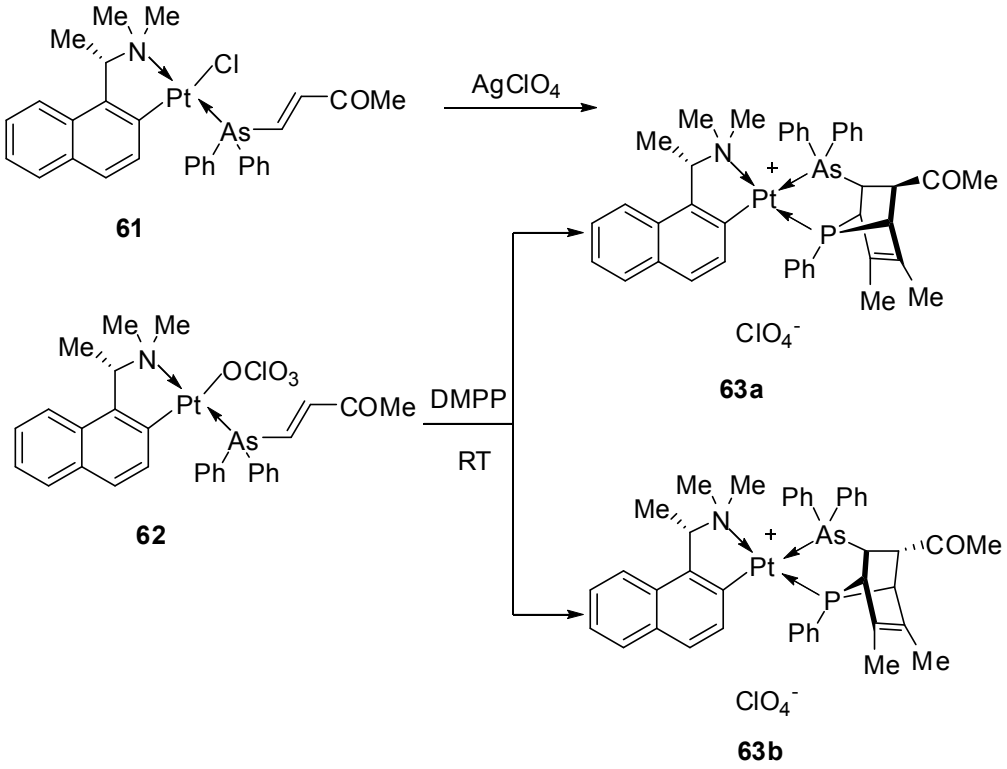
2.2.2.5 Asymmetric cycloaddition reaction between 4-(diphenylarsino)-3-buten-2-one and DMPP promoted by chiral platinum template

Following the similar procedure of the preparation of chiral palladium arsenic precursor **47**, the chiral platinum arsenic precursor **61** containing carbonyl group could be prepared efficiently (Scheme 2.30). Potassium tert-butoxide was used as catalyst to catalyze hydroarsination reaction between diphenylarsine and but-3-en-2-one. Subsequently, the arsine ligand was coordinated to the chiral platinum template **32** to give the desired chiral platinum arsenic precursor **61**. The product **61** could be purified by silica-gel column chromatograghy.



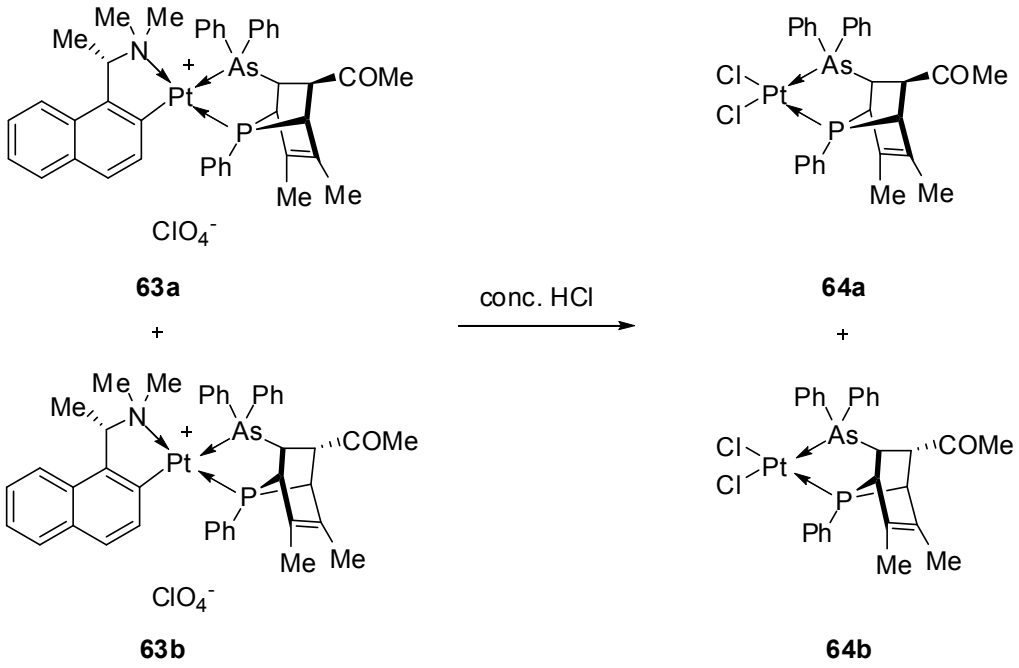
Scheme 2.30

Firstly, the platinum complex **61** was treated with aqueous silver perchlorate to give perchlorate complex **62.** The reaction between perchlorate complex **62** and DMPP was conducted at room temperature. Two chiral platinum complexes **63a** and **63b** could be obtained after 27 days (Scheme 2.31). Both of these two products **63a** and **63b** were with phosphorus taking up the coordination position trans to the NMe_2 group and arsenic cis to NMe_2 group of the chiral platinum template. The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture exhibited two sharp singlets at δ 107. 9 and δ 105.7 (J_{Pt-P}=3336 Hz), in the ratio of 1: 31.



Scheme 2.31

The chiral naphthylamine auxiliary on complexes **63a** and **63b** could be removed by the treatment of the complexes with concentrated hydrochloric acid for 30 min at room tempetature (Scheme 2.32). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture shows one sharp singlets at δ 108.0 ($J_{Pt\text{-}P}$=3242 Hz).



Scheme 2.32

Dichlro palladium complexes **64b** could be obtained by fractional crystallization from dichloromethane-diethyl ether. The single crystal X-ray diffraction analysis established that the cycloadduct in complex **64b** was coordinated to the metal center as a bidentate ligand via the bridgehead phosphorus and arsenic. The five new chiral centers have been generated with *S* absolute configuration at phosphorus, *S*, *S*, *S* and *R* absolute configuration at C(15), C(18), C(14) and C(13) respectively. The geometry at palladium is slightly distorted square planar with angles at palladium in the range of 84.77(5)° -92.85(7)° and 175.33(8)° -176.74(5)° . The bond angle at the bridgehead phosphorus is 81.2(3)° . Selected bond lengths and angles are listed in Table 9.

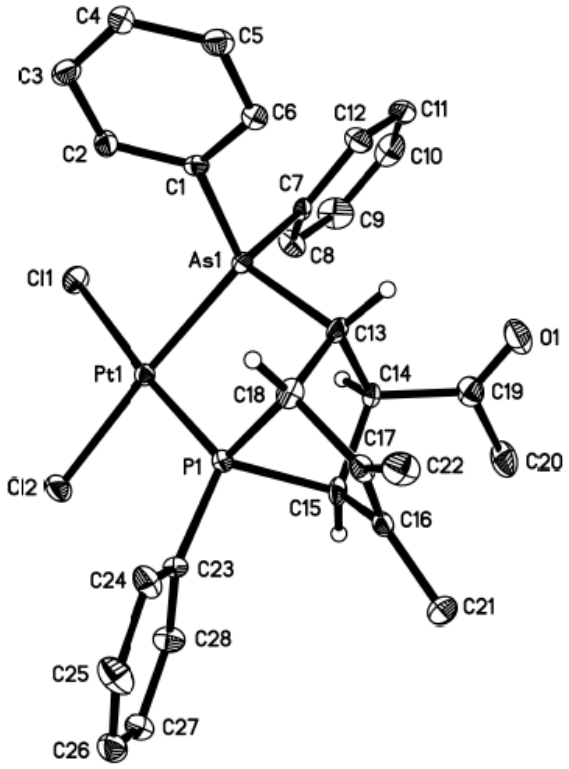
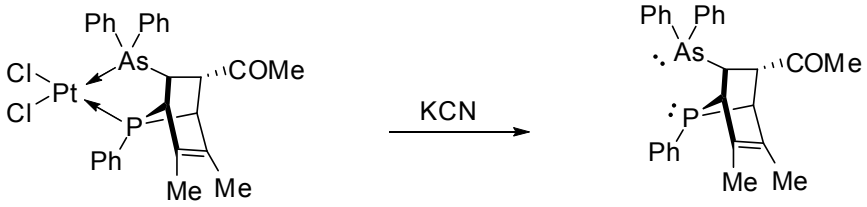


Figure 9. Molecular structure of complex **64b**

Table 9. Selected bond lengths [Å] and angles [°] for **64b**

Pt(1)-P(1)	2.2081(19)	Pt(1)-Cl(2)	2.336(2)
Pt(1)-As(1)	2.3369(8)	Pt(1)-Cl(1)	2.3563(18)
C(15)-P(1)	1.873(7)	C(18)-P(1)	1.852(8)
P(1)-Pt(1)-Cl(2)	92.85(7)	P(1)-Pt(1)-As(1)	84.77(5)
Cl(2)-Pt(1)-As(1)	176.74(5)	P(1)-Pt(1)-Cl(1)	175.33(8)
Cl(2)-Pt(1)-Cl(1)	91.81(7)	As(1)-Pt(1)-Cl(1)	90.58(5)
C(18)-P(1)-C(15)	81.2(3)		

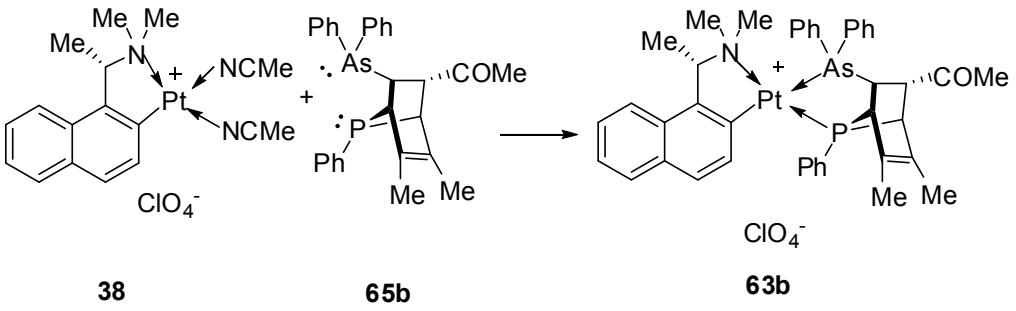
The free P-As chiral bidentate ligand could be liberated efficiently from the dichloro platinum complex **64b** by treatment with aqueous potassium cyanide at room temperature for 10min (Scheme 2.33). The optically active ligand **65b** was obtained as a white solid in quantitative yield, $[\alpha]_D$ +93.4 (*c* 1.0, CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum of the free ligand in $CDCl_3$ exhibited a singlet at δ 96.3. The five new chiral centers have been generated with *S* absolute configuration at phosphorus, *S*, *S*, *S* and *R* absolute configuration at the three stereogenic carbon centers, respectively.



64b **65b**

Scheme 2.33

The liberated ligand **65b** could recoordinate to bis-(acetonitrile) platinum complex **38**. The optical purity of the liberated ligand could be determined subsequently (Scheme 2.34). The 121 MHz $^{31}P\{^1H\}$ NMR of the recomplexation products in $CDCl_3$ indeed exhibited one singlets at δ 105.7 ($J_{Pt\text{-}P}$=3336 Hz). The complex atδ 105.7 ($J_{Pt\text{-}P}$=3336 Hz) was identical to the original cycloaddition product **63b**.



38 **65b** **63b**

Scheme 2.34

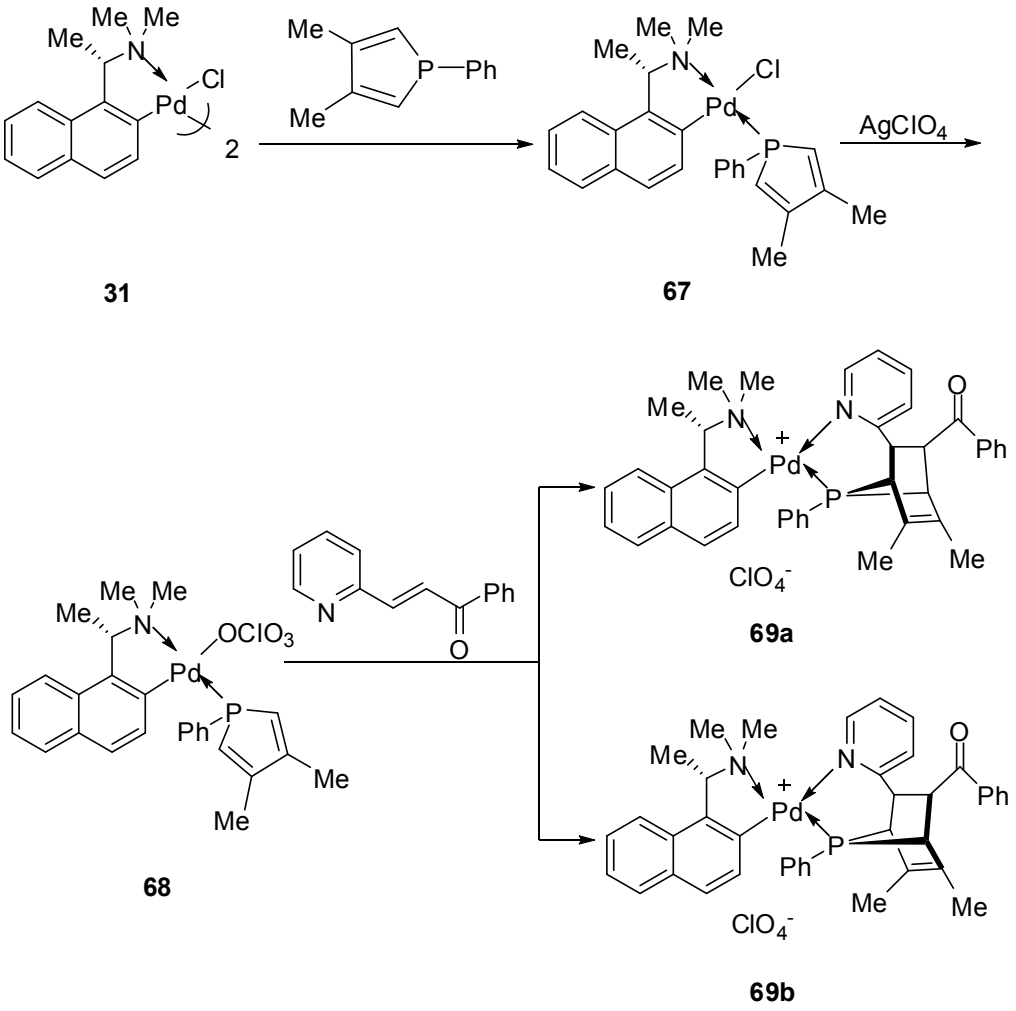
2.2.3 Metal Effect on Asymmetric Synthesis toward P-N Ligands

2.2.3.1 Asymmetric cycloaddition reaction between DMPP and (E)-1-phenyl-3-pyridin-2-yl-2-propenone promoted by chiral palladium template

In the absence of a metal ion, DMPP shows no reactivity with (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone. However, in the presence of chiral palladium template or chiral platinum template, the reaction could occur.

As illustrated in Scheme 2.35, DMPP was coordinated to the dimeric chiral template **31** to give the monomeric neutral complex **67** as yellow prisms. This coordination was conducted at room temperature for 1h and then the crude prodects were purified by silica-gel column. Subsequently, the terminal chloro ligand, which was both kinetically and thermodynamically stable and hindered the coordination of the incoming ligands, could be abstracted efficiently by treatment of the complex in dichloromethane with aqueous silver perchlorate. This process allowed DMPP and the incoming (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone to coordinated simultaneously onto the chiral palladium templated

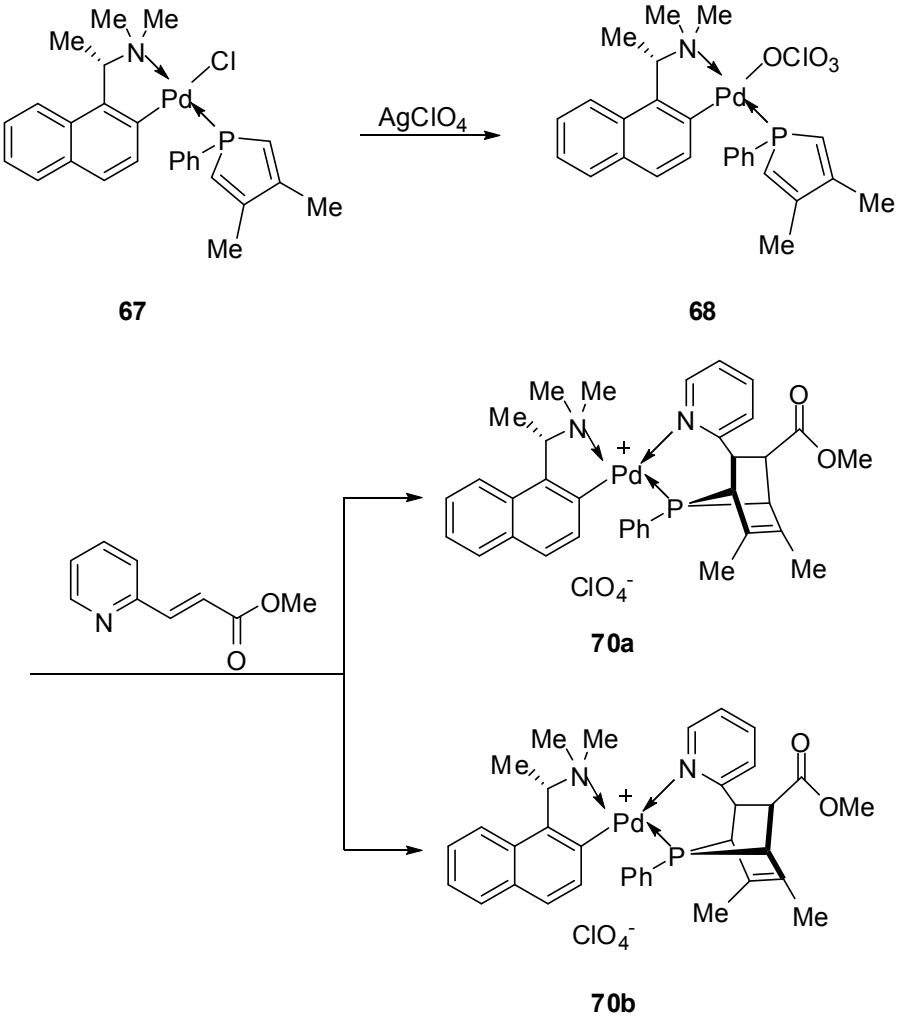
during the course of the intramolecular asymmetric cycloaddition reaction. The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture in $CDCl_3$ exhibited two sharp singlets at δ 115.4 and δ 116.2. However, the $^{31}P\{^{1}H\}$ NMR spectroscopic studies indicated that the conversion of the asymmetric cycloaddition reaction between DMPP and (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone was under 10% after 12 days at 80℃. This indicated that the cycloaddition reaction between DMPP and (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone could not be promoted efficiently by the chiral palladium template **31**.



Scheme 2.35

2.2.3.2 Asymmetric cycloaddition reaction between DMPP and (E)-1-methyl-3-pyridine-2-yl-2-propenoate promoted by chiral palladium template

The inert chloro ligand of the monomeric neutral complex **67** could be replaced by perchlorate ligand by treatment of the complex in dichloromethane with aqueous silver perchlorate (Scheme 2.36). The perchlorate palladium complex **68** was not isolate and the dichloromethane solution containing the perchlorate palladium complex **68** was directly treated with (*E*)-1-methyl-3-pyridine-2-yl-2- propenoate. The $^{31}P\{^{1}H\}$ NMR spectrum of



Scheme 2.36

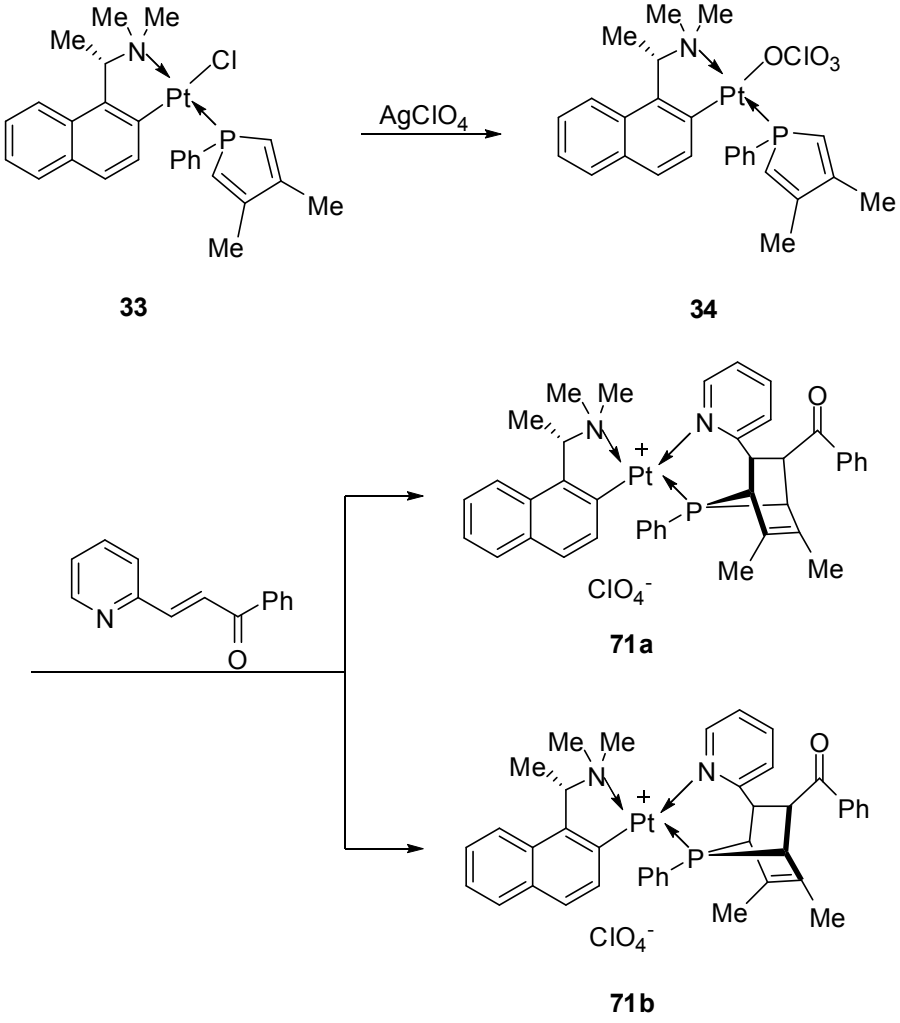
the crude cycloaddition reaction mixture in $CDCl_3$ exhibited two sharp singlets at δ 112.3 and δ 113.4. However, the $^{31}P\{^{1}H\}$ NMR spectroscopic studies indicated that the conversion of the asymmetric cycloaddition reaction between DMPP and (*E*)-1-methyl-3-pyridine-2-yl-2-propenoate was under 10% after 12 days at 80℃. This indicated that the cycloaddition reaction between DMPP and (*E*)-1-methyl-3-pyridine-2-yl-2-propenoate could not be promoted by the chiral palladium template **31** efficiently.

2.2.3.3 Asymmetric cycloaddition reaction between DMPP and (E)-1-phenyl-3-pyridin-2-yl-2-propenone promoted by chiral platinum template

As aforementioned, the asymmetric cycloaddition reaction between DMPP and (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone promoted by the chiral palladium template **31** could not produce the desired cycloadducts efficiently. However, we found that the metal ion had played a considerate role on this reaction, especially on the reactivity of the reaction. Palladium is more oxyphilic than platinum. When the reaction was promoted by palladium template, both nitrogen and oxygen could attach palladium. The competition of nitrogen and oxygen made the reaction messy and decreased the conversion rate. When the metal was changed from palladium to platinum, the yield was much higher.

As aforementioned, the chloro ligand in complex **33** which was both kinetically and thermodynamically stable could be replaced efficiently by the treatment of the complex in dichloromethane with aqueous silver perchlorate

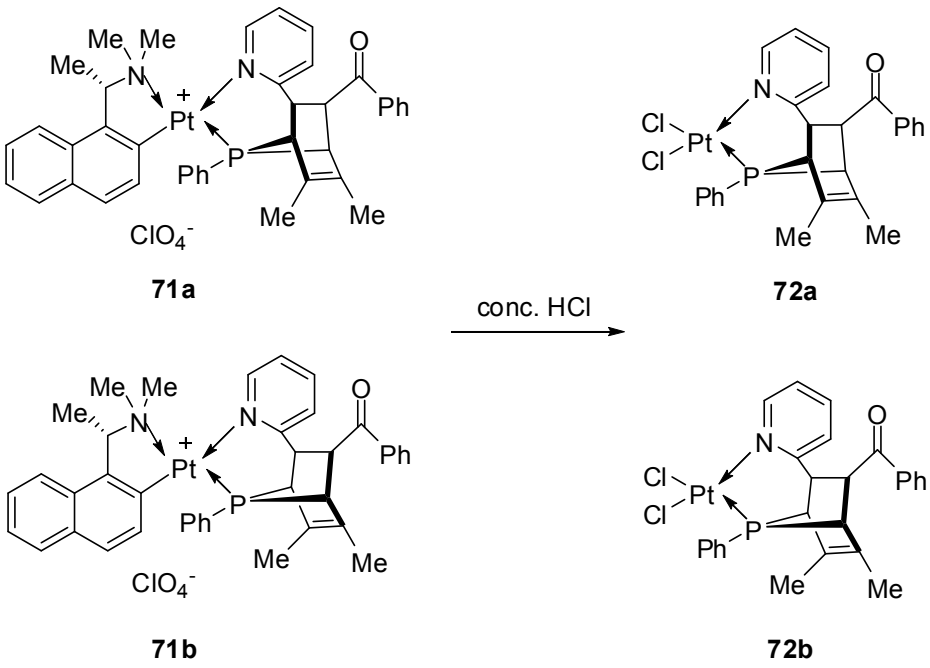
and provide a coordination site for the incoming (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone. The $^{31}P\{^{1}H\}$ NMR spectroscopic studies indicated that the asymmetric cycloaddition reaction between complex **34** was completed within 12 days at 80℃ (Scheme 2.37). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture in $CDCl_3$ exhibited two sharp singlets at δ 87.0 ($J_{Pt\text{-}P}$=3773 Hz) and δ 88.1, in the ratio of 12:1. This indicated that the reactivity and selectivity of asymmetric cycloaddition reaction promoted by chiral platinum template were much better than the reaction promoted by relative



Scheme 2.37

chiral palladium template.

The chiral naphthylamine auxiliary in complex **71a** and **71b** was subsequently removed chemoselectively by treatment the mixture with concentrated hydrochloric acid at room temperature for 1h (Scheme 2.38). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude mixture in $CDCl_3$ exhibited two sharp singlets at δ 80.0 (J_{Pt-P}=3411 Hz) and δ 80.4. The major product **72a** was isolated by fractional crystallization from dichloromethane-diethyl ether as white prisms in 78% yield, $[\alpha]_D$ +157.4 (*c* 1.41, CH_2Cl_2).



Scheme 2.38

The single crystal X-ray diffraction analysis established that the desired dichloro platinum complex **72a** had formed via the *exo*-cycloaddition reaction. The cycloadduct in complex **72a** was coordinated to the metal center as a

bidentate ligand via the bridgehead phosphorus and nitrogen of pyridine. The five new chiral centers have been generated with *S* absolute configuration at phosphorus, *S*, *S*, *S* and *S* absolute configuration at C(13), C(8), C(7) and C(6) respectively. The geometry at platinum is slightly distorted square planar with angles at platinum in the range of 86.58(11)° -91.9(3)° and 173.0(3)° - 176.61(11)° . The bond angle at the bridgehead phosphorus is 82.3(5)° . Selected bond lengths and angles are listed in Table 10.

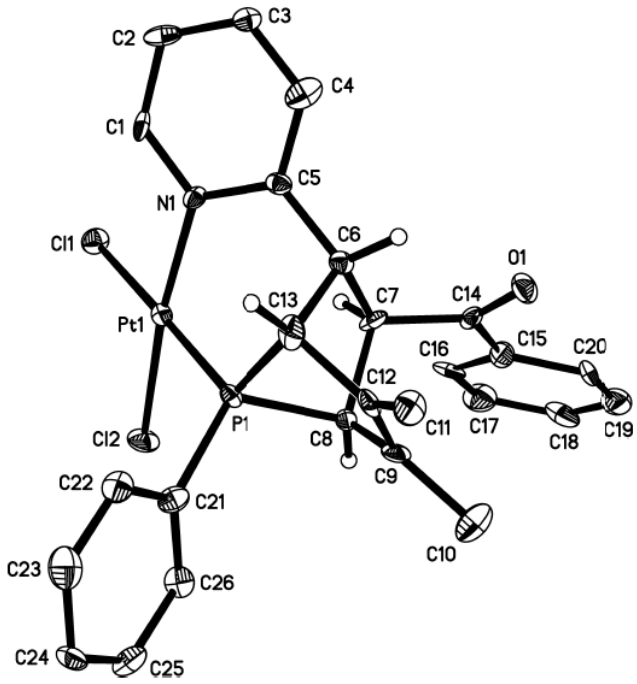


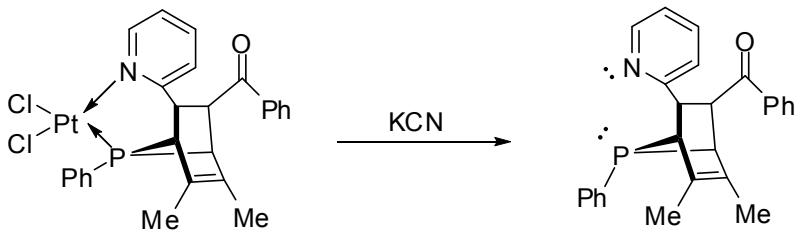
Figure 10. Molecular structure of complex **72a**

Table 10. Selected bond lengths [Å] and angles [°] for **72a**

Pt(1)-N(1)	2.038(9)	Pt(1)-P(1)	2.193(3)
Pt(1)-Cl(2)	2.312(3)	Pt(1)-Cl(1)	2.364(3)

C(8)-P(1)	1.841(10)	C(13)-P(1)	1.812(13)
N(1)-Pt(1)-P(1)	91.9(3)	N(1)-Pt(1)-Cl(2)	173.0(3)
P(1)-Pt(1)-Cl(2)	86.58(11)	N(1)-Pt(1)-Cl(1)	91.0(3)
P(1)-Pt(1)-Cl(1)	176.61(11)	Cl(2)-Pt(1)-Cl(1)	90.35(10)
C(13)-P(1)-C(8)	82.3(5)		

The optically active ligand **73** could be stereospecifically liberated from the dichloro complex **72a** by treatment with aqueous potassium cyanide at room temperature for 1h min (Scheme 2.39). The liberated bidentate ligand **73** was obtained as white solid in quantitative yield. The $^{31}P\{^{1}H\}$ NMR spectrum of the free ligand in $CDCl_3$ exhibited only one sharp singlet at δ 70.3, $[\alpha]_D$ +123.8 (*c* 1.26, CH_2Cl_2). The five new chiral centers have been generated with *S* absolute configuration at phosphorus, *S*, *S*, *S* and *S* absolute configuration at the three stereogenic carbon centers, respectively.

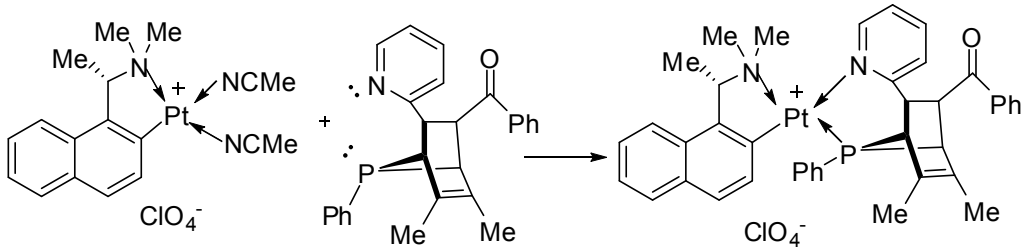


72a **73**

Scheme 2.39

Because of the potential air sensitivity of the noncoordinated phosphorus atoms, the liberated ligand **73** was not stored in its pure form. Therefore, the free ligand **73** must be recoordinated to selected metal ion

(Scheme 2.40). The recoordination process was also a mean of verifying the optical purity of the released ligand. The recoordination procedure was monitored by $^{31}P\{^{1}H\}$ NMR spectroscopy. In $CDCl_3$, the $^{31}P\{^{1}H\}$ NMR spectrum of the crude recoordination product showed only one singlet at δ 87.2 ($J_{Pt\text{-}P}$=3773 Hz), which confirmed that the liberated ligand **73** is optically pure.



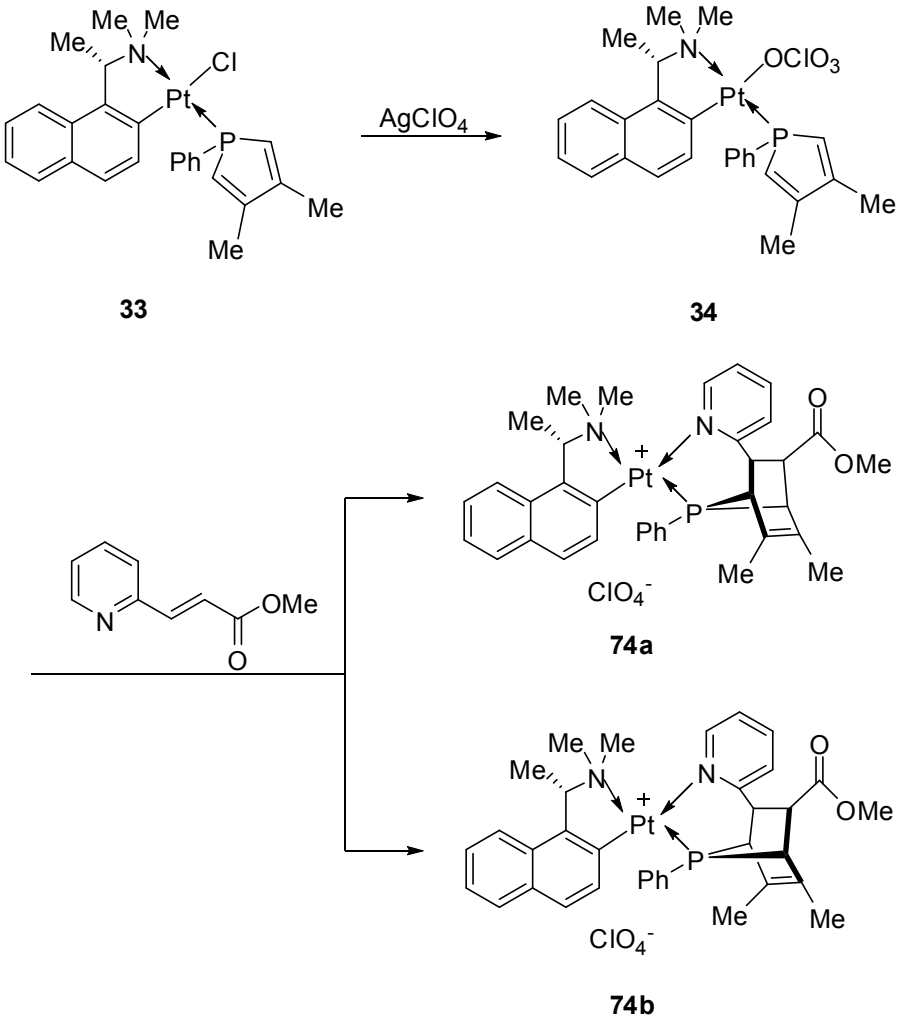
Scheme 2.40

2.2.3.4 Asymmetric cycloaddition reaction between DMPP and (E)-1-methyl-3-pyridine-2-yl-2-propenoate promoted by chiral platinum template

Chiral platinum template **32** could also be used to promote the asymmetric cycloaddition reaction between (*E*)-1-methyl-3-pyridine-2-yl-2-propenoate and DMPP efficiently.

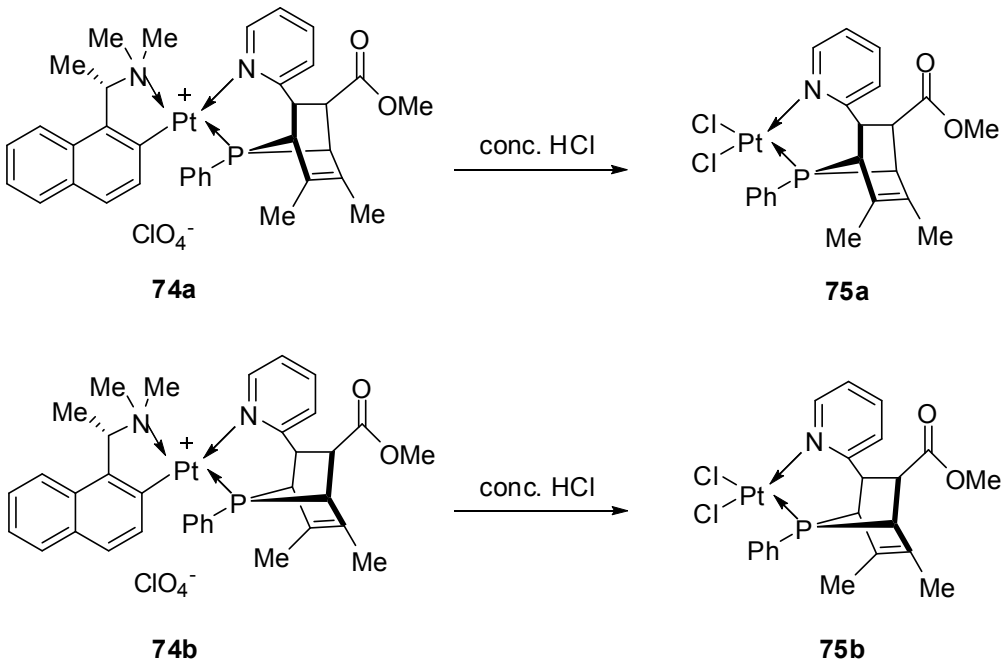
Aqueous silver perchlorate salt was added to the solution of the platinum complex **32** in dichloromethane to abstract the stable chloro ligand and provide a coordination site for the incoming ligand. The cycloaddtion reaction was monitored by $^{31}P\{^{1}H\}$ NMR spectroscopy. The $^{31}P\{^{1}H\}$ NMR

spectroscopic studies indicated that the asymmetric cycloaddition reaction between (*E*)-1-methyl-3-pyridine-2-yl-2-propenoate and DMPP was completed within 13 days at 80℃ and the crude cycloaddition reaction mixture in $CDCl_3$ exhibited two sharp singlets at δ 89.4 and δ 87.0 (J_{Pt-P}=3776 Hz), in the ratio of 1:12 (Scheme 2.41). This indicated that the reactivity and selectivity of asymmetric cycloaddition reaction between (*E*)-1-methyl-3-pyridine-2-yl-2-propenoate and DMPP promoted by chiral platinum template were much better than that of the reaction promoted by relative chiral palladium template.



Scheme 2.41

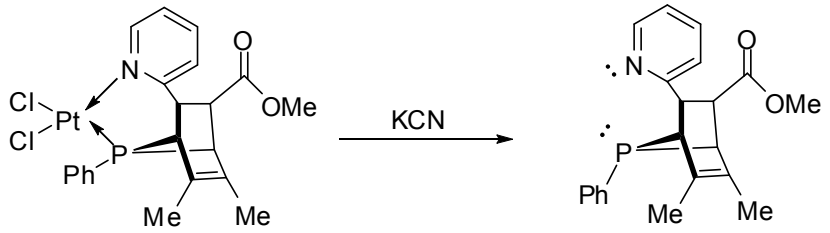
Chiral platinum complexes **74a** and **74b** were treated with concentrated hydrochloric acid at room temperature for 1h to remove the chiral naphthylamine auxiliary and generate dichloro platinum complex **75a** and **75b** (Scheme 2.42). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction mixture in $CDCl_3$ exhibited two sharp singlets at δ 78.4 (J_{Pt-P}=3397 Hz) and δ 79.1. The major product **75a** was isolated by fractional crystallization from dichloromethane-diethyl ether as white prisms in 81% yield, $[\alpha]_D$ +56.6 (*c* 0.53, CH_2Cl_2).



Scheme 2.42

The dichloro complex **75a** or **75b** could be treated with aqueous potassium cyanide to generate the optically pure P-N bidentate ligand **76** efficeintly. The liberation could be completed for 1h at room temperature (Scheme 2.43). The

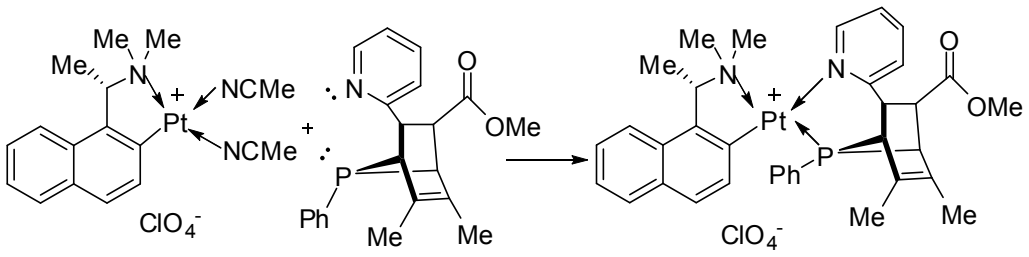
$^{31}P\{^{1}H\}$ NMR spectrum of the free ligand in $CDCl_3$ exhibited only one sharp singlets at δ 72.5. The liberated bidentate ligand **76** was obtained as white solid in quantitative yield.



75a **76**

Scheme 2.43

Subsequently, the liberated ligand **76** could recoordinate back to the chiral platinum template **38** and be stabilized (Scheme 2.44). The $^{31}P\{^{1}H\}$ NMR spectrum of the crude recoordination product showed only one singlet at δ 87.0 ($J_{Pt\text{-}P}$=3776 Hz) in $CDCl_3$. This meaned that the liberated ligand **76** is optically pure compound.



38 **76** **74a**

Scheme 2.44

2.3 Conclusion

Both the organopalladium complex **31** and organoplatinum complex **32** has been successfully used as the chiral template to promote the asymmetric cycloaddition reaction to synthesize P-S, P-As and P-N chiral bidantate ligands. However, the organopalladium complex **31** could not promote the reactions efficiently. On the other hand, organoplatinum complex **32** could promote the asymmetric cycloaddtion reaction efficiently, with good selectivity.

2.4 Experimental section

All air-sensitive compounds were manipulating using Schlenk line under a positive pressure of argon. All NMR spectra were recorded at 25℃ on Bruker ACF 300, 400 and 500 MHz spectrometers. Chemical shift are reported in parts per million. Optical rotations were measured on the specified solution in a 0.1 dm cell at 25℃ with a Perkin-Elmer model 341 polarimeter. Elemental analyses were performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at Nanyang Technological University. All melting points were measured using the SRS Optimelt Automated Melting Point System, SRS MPA 100.

Caution! *All perchlorate salts should be handled with care as potentially explosive compounds.*

The chiral platinum complex **32**,[51] bis-(acetonitrile) platinum complex

43,[51] DMPP,[43] diphenylarsine,[65] (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone[66] and (*E*)-1-methyl-3-pyridine-2-yl-2-propenoate[67] were prepared according to the literature.

Cycloaddition reaction between platinum complex 34 and divinyl sulfoxide.

A solution of complex **33** (1.00g, 1.62mmol) in dichloromethane (30mL) was treated with aqueous silver perchlorate (0.72g, 3.24mmol) in water (5mL) and stirred for 1h at room temperature. The resulting mixture was filtered off using Celite to remove the white precipitate, silver chloride. The organic layer was washed with water (50mL×3), and then dried over magnesium sulfate. The solvent was removed, and then the yellow solid was treated the solution of divinyl sulfoxide (0.165g, 1.62mmol) in chlorobenzene. The mixture was stirred for 5d at 100℃. Upon removal the solvent, the crude product was purified by silica-gel column chromatograghy (CH_2Cl_2: diethyl ether = 5:1) to obtain the major product **35a** as a yellow solid (0.89g, 70%). m.p. > 205℃ (decomp.) $[\alpha]_D$ +69.7 (*c* 2.9, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 1.56 (s, 3H, C=CMe), 1.87 (d, 3H, $3J_{HH}$=6.2 Hz, CHMe), 1.96-2.16 (m, 1H, $CH_{exo}C_{endo}$) ,2.01 (s, 3H, C=CMe), 2.79 (s, 3H, NMe), 3.22 (d, 1H, $^3J_{HH}$=14.1 Hz, $CH_{exo}H_{endo}$) , 3.35 (s, 3H, NMe), 3.52 (s, 1H, PCH), 3.74 (s, 1H, PCH), 3.82 (ddd, 1H, $^3J_{HH}$=7.56 Hz, $^3J_{HH}$=7.96 Hz, $^3J_{PH}$=32.46 Hz, SCH), 4.79 (qnt, 1H, CHMe), 6.58 (d,1H, $^3J_{HH}$=9.48 Hz, Z-SC=CH), 6.66 (d,1H, $^3J_{HH}$=16 Hz, E-SC=CH), 6.80-7.84 (m, 12H, aromatics + SCH=C). ^{31}P { ^{1}H } NMR

($CDCl_3$): δ 98.1 (s, 1P, $J_{Pt\text{-}P}$=3324 Hz).

By following the same procedure as described for the cycloaddition reaction of platinum complex **34** and vinyl phenyl sulfoxide (0.31g, 2mmol), the major product **40a** could be separated by silica-gel column chromatograghy as a yellow solid in (0.89g, 72%), m.p. > 212℃ (decomp.) $[\alpha]_D$ +105.4 (*c* 3.1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 1.37 (s, 3H, C=CMe), 1.92 (d, 3H, $3J_{HH}$=5.8 Hz, CHMe), 2.00 (s, 3H, C=CMe), 2.09-2.17 (m, 1H, $CH_{exo}C_{endo}$) , 2,68 (s, 1H, PCH), 2.83 (s, 3H, NMe), 3.18 (s, 3H, NMe), 3.32 (d, 1H, $^3J_{HH}$=14.7 Hz, $CH_{exo}H_{endo}$) , 3.78(s, 1H, PCH), 3.90 (ddd, 1H, $^3J_{HH}$=7.40 Hz, $^3J_{HH}$=7.55 Hz, $^3J_{PH}$=13.20 Hz, SCH), 4.82 (qnt, 1H, CHMe), 6.82-8.33 (m, 16H, aromatics). ^{31}P { ^{1}H } NMR ($CDCl_3$): δ 97.3 (s, 1P, $J_{Pt\text{-}P}$=3308 Hz). The minor product **40b** could be obtained by fractional crystallization from dichloromethane-diethyl ether, m.p. > 215℃ (decomp.) $[\alpha]_D$ +137.7 (*c* 111.9, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 1.53 (s, 3H, C=CMe), 1.71- 1.85(m, 1H, $CH_{exo}C_{endo}$), 1.75 (s, 3H, C=CMe),1.98 (d, 3H, $3J_{HH}$=6.27 Hz, CHMe), 2.70(d, 1H, $^3J_{HH}$=12.51 Hz, $CH_{exo}H_{endo}$), 2.72 (s, 3H, NMe), 3.09 (s, 3H, NMe),3.77 (s, 1H, PCH) , 3.96(s, 1H, PCH), 3.77 (ddd, 1H, $^3J_{HH}$=8.94 Hz, $^3J_{HH}$=8.94 Hz, $^3J_{PH}$=32.13 Hz, SCH), 4.82 (qnt, 1H, CHMe), 6.87-8.30 (m, 16H, aromatics). ^{31}P { ^{1}H } NMR ($CDCl_3$): δ 95.9 (s, 1P, $J_{Pt\text{-}P}$=3417 Hz).

Preparation of the dichloro platinum complexes 36 and 41.

A solution of **35a** (0.24g, 0.3mmol) was treated with concentrated hydrochloric

acid (5mL) for 30 min at room temperature. The resulting mixture was washed with water (30mL ×3) and then dried over magnesium sulfate. The crude product were crystallized from dichloromethane-diethyl ether to give the pure dichloro platinum complex **36** as white crystals (0.16g, 94%), m.p. > 300℃ (decomp.) $[\alpha]_D$ +31.9 (*c* 6.9, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ 1.54 (s, 3H, C=CMe), 1.73 (s, 3H, C=CMe),1.88-2.05 (m, 1H, $CH_{exo}C_{endo}$) , 2.95 (s, 1H, PCH) , 3.19 (d, 1H, $CH_{exo}C_{endo}$), 3.55 (s, 1H, PCH), 3.70 (ddd, 1H, $^3J_{HH}$=7.23 Hz, $^3J_{HH}$=8.13 Hz, $^3J_{PH}$=49.88 Hz, SCH), 6.40 (d, 1H, SCH=C). 6.84-6.98 (m,2H, Z-SC=CH + E-SC=CH), 7.7.50-7.64 (m, 5H, aromatics), $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 100.9 (s, 1P, J_{Pt-P}=3137 Hz). Anal. Calcd for $C_{16}H_{19}Cl_2OPPtS$: C, 34.5; H, 3.4; S, 5.8. Found: C, 34.4; H, 3.5; S, 5.6

The same procedure was used to prepare the dichloro platinum complex **41**. The optically pure dichloro platinum complex **41** was obtainted as white crystal (0.15g, 92%). m.p. > 300℃ (decomp.) $[\alpha]_D$ -145.6 (*c* 10.84, CH_2Cl_2), ^1H NMR ($CDCl_3$): δ 1.38 (s, 3H, C=CMe), 1.72 (s, 3H, C=CMe),19.8-2.14 (m, 1H, $CH_{exo}C_{endo}$) , 2.52 (s, 1H, PCH) , 3.31 (d, 1H, $CH_{exo}C_{endo}$), 3.61 (s, 1H, PCH), 3.79 (ddd, 1H, $^3J_{HH}$=7.35 Hz, $^3J_{HH}$=7.95 Hz, $^3J_{PH}$=15.27 Hz, SCH), 7.56-8.37 (m, 10H, aromatics), $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 100.6 (s, 1P, J_{Pt-P}=3128 Hz). Anal. Calcd for $C_{20}H_{21}Cl_2OPPtS$: C, 39.6; H, 3.5; S, 5.3. Found: C, 39.4; H, 3.6; S, 5.1

Liberation of S-P chiral bidentate ligands 37 and 42.

The dichloro platinum complex **36** (0.1g) was dissolved in dichloromethane (10mL) and then treated with aqueous potassium cyanide (0.19g) in water (15mL). The solution was stirred for 20 min at room temperature. After the two layers were settled, the organic layer was separated, washed with water (20mL ×3) and then dried over magnesium sulfate. After removal of the solvent, the chiral ligand **37** was obtained as a white solid. $[\alpha]_D$ +320.0 (*c* 1.0, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 94.0

The same procedure was used to prepare **42**. The chiral ligand **42** was obtained as white solid. $[\alpha]_D$ +102.6 (*c* 7.6, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 93.6.

Recoordination of S-P chiral bidentate ligands 37 and 42.

Upon liberation of S-P chiral bidentate ligand **37**, a solution of compound **37** in dichloromethane was directly added into the sulotion of complex **38** in dichloromethane which was excess to generate the recoordination products **35a** and **35a'**.

The same procedure was used to recoordinate chiral ligand **42** to complex **43** and gave complexes **44a** and **44a'**.

Cycloaddition reaction between platinum complex 34 and divinyl sulfone.

A solution of complex **33** (0.306 g, 0.5 mmol) in dichloromethane (30 mL) was treated with aqueous silver perchlorate (excess) in water (5 mL) and stirred

for 1h at room temperature. The resulting mixture was filtered off using Celite to remove the white precipitate, silver chloride. The organic layer was washed with water (50 mL×3), and then dried over magnesium sulfate. The solvent was removed, and then the yellow solid was treated the solution of divinyl sulfone (0.059 g, 1.0 mmol) in chlorobenzene. The mixture was stirred for 20d at 100℃.

Preparation of the dichloro platinum complexes 46a and 46b.

A solution of the mixture of **45a** and **45b** (0.074 g, 0.1 mmol) was treated with concentrated hydrochloric acid (5 mL) for 20 min at room temperature. The resulting mixture was washed with water (30mL ×3) and then dried over magnesium sulfate. The pure product 45a or 45b cannot be isolated.

Preparation of chiral palladium arsenic precursors 47 and 51

0.35 g of methyl propiolate (4.15 mmol) was dissolved in tetrahydrofuran (THF) and added to 0.80 g of diphenylarsine (3.46 mmol) under ice bath condition. 0.05 g of potassium tert-butoxide (0.42 mmol) was then added to the solution and left to stir for 3 days at room temperature. The solution was subsequently washed with deionised water (3 × 50 mL), ethyl acetate (3 × 50 mL) and dried over $MgSO_4$, producing methyl ester 3-(diphenylarsino)-acrylate. 1.17 g of **31** (1.72 mmol) was dissolved in dichloromethane and added to methyl ester 3-(diphenylarsino)-acrylate and left to stir overnight at room

temperature, forming **47**. Upon removal the solvent, the crude product was purified by silica-gel column chromatography and fractional crystallization from dichloromethane-diethyl ether as a yellow solid (1.55 g, 68%), ^{1}H NMR ($CDCl_3$): δ 2.10 (d, 3H, J_{HH}=4.8 Hz, CHMe), 2.75 (s, 3H, NMe), 2.95 (s, 3H, NMe), 3.56 (s, 3H, COOMe), 4.31 (qnt, 1H, CHMe), 6.71 (d,1H, J_{HH}=11.4 Hz, CH=CH), 6.85-7.80 (m, 17H, aromatics + CH=CH).

Complexes **51** could be synthesized by following the same procedure as described above. In stead of methyl propiolate, but-3-yn-2-one was used as starting material. The crude product was purified by silica-gel column chromatography and fractional crystallization from dichloromethane-diethyl ether as yellow solid (1.79 g, 69%), ^{1}H NMR ($CDCl_3$): δ 2.13 (d, 3H, J_{HH}=5.2 Hz, CHMe), 2.73 (s, 3H, NMe), 2.43 (s, 3H, COMe), 2.89 (s, 3H, NMe), 4.34 (qnt, 1H, CHMe), 6.75 (d,1H, J_{HH}=16.4 Hz, CH=CH), 6.88-7.85 (m, 17H, aromatics + CH=CH).

Preparation of the dichloro palladium complexes 50 and 54a

A solution of complex **47** (0.40 g, 0.61 mmol) in dichloromethane (30 mL) was treated with aqueous silver perchlorate (0.31 g, 1.50 mmol) in water (5 mL) and stirred for 1h at room temperature. The organic layer, after removal of AgCl then washed with water (50 mL×3), dried over magnesium sulfate to give complex **48**. Complex **48** in 1,2-dichloroethane (10 mL) was treated DMPP (0.10 g, 0.53 mmol). The mixture was stirred for 2d at 80℃ to give the mixture

of complexes **49a** and **49b**. Since **49a** and **49b** could not be separated by silica-gel column chromatography or fractional crystallization. Thus, the mixture of products was used directly in the next step. A solution of **49a** and **49b** was treated with concentrated hydrochloric acid (5 mL) for 30 min at room temperature. The resulting mixture was washed with water (30 mL ×3) and then dried over magnesium sulfate. The crude product crystallized from dichloromethane-diethyl ether to give the dichloro palladium complex **50a** and **50b** as white crystals (0.22 g, 58%), m.p. 189-192°C. ^{1}H NMR (CD_2Cl_2): δ 1.43 (s, 3H, C=CMe), 1.52 (s, 3H, C=CMe), 2.17 (s, 1H, PCH) , 3.02 (d, 1H, J_{HH}=4.3Hz, PCHC*H*As), 3.48 (s, 1H, PCH), 3.60 (s, 3H, COOMe), 3.84 (d, 1H, J_{HH}=4.1 Hz, PCHC*H*CO), 7.43-8.19 (m, 15H, aromatics),. ^{31}P { ^{1}H } NMR (CD_2Cl_2): δ 128.5.

The same procedure was used to prepare dichloro palladium complex **54a**. The optically pure dichloro palladium complex **54a** was obtainted as white crystal (0.32 g, 60%). ^{1}H NMR (CD_2Cl_2): δ 1.43 (s, 3H, C=CMe), 1.49 (s, 3H, C=CMe), 2.10 (s, 3H, COMe), 3.02 (s, 1H, PCH) , 3.75 (s, 1H, PCH), 3.75 (d, 1H, J_{HH}=4.5Hz, PCHC*H*As), 4.08 (d, 1H, J_{HH}=4.0 Hz, PCHC*H*CO), 7.43-8.09 (m, 15H, aromatics), ^{31}P { ^{1}H } NMR (CD_2Cl_2): δ 138.0.

Preparation of chiral platinum arsenic precursors 55 and 61

The chiral platinum arsenic precursor **55** and **61** were synthesized by by following the same procedure as described for the preparation of complex **47**

and conplex **51**.

Chiral platinum arsenic precursor **55** was obtainted as yellow crystals (80%). ^{1}H NMR ($CDCl_3$): δ 1.87 (d, 3H, J_{HH}=6.15 Hz, CHMe), 2.85 (s, 3H, NMe), 2.90 (s, 3H, NMe), 3.47 (s, 3H, COOMe), 4.51 (qnt, 1H, CHMe), 6.72 (d,1H, J_{HH}=11.8 Hz, CH=CH), 7.20 (d,1H, J_{HH}=11.8 Hz, CH=CH), 6.93-7.86 (m, 16H, aromatics).

Chiral platinum arsenic precursor **61** was obtainted as yellow crystals (76%). ^{1}H NMR ($CDCl_3$): δ 1.94 (d, 3H, J_{HH}=6.15 Hz, CHMe), 2.35 (s, 3H, COMe), 2.95 (s, 3H, NMe), 3.18 (s, 3H, NMe), 4.56 (qnt, 1H, CHMe), 6.12 (d,1H, J_{HH}=17.5 Hz, CH=CH), 6.77-7.94 (m, 16H, aromatics), 8.08 (d,1H, J_{HH}=11.8 Hz, CH=CH).

Preparation of the dichloro platinum complexes 58 and 64b

The dichloro platinum complex **58** and **64b** were synthesized by following the same procedure as described for the preparation of complex **50** and **54a**.

The crude product crystallized from dichloromethane-diethyl ether to give the dichloro platinum complexes **58** as white crystals (0.45g, 85%). ^{1}H NMR (CD_2Cl_2): δ 1.45 (s, 3H, C=CMe), 1.67 (s, 3H, C=CMe), 2.74 (s, 1H, PCH) , 2.96 (dd, 1H, J_{HH}=4.1Hz, J_{HH}=16.9Hz, PCHC*H*As), 3.07 (s, 3H, COOMe),3.54 (s, 1H, PCH), 4.61 (d, 1H, J_{HH}=4.1 Hz, PCHC*H*CO), 7.38-8.14 (m, 15H, aromatics), ^{31}P { ^{1}H } NMR (CD_2Cl_2): δ 98.8 (J_{Pt-P}=3235 Hz). Anal. Calcd for $C_{28}H_{28}AsCl_2O_2PPt$: C, 43.77; H, 3.67. Found: C, 43.95; H, 3.59

The crude product crystallized from dichloromethane-diethyl ether to give the dichloro platinum complex **64b** as white crystals (0.40g, 87%). ^{1}H NMR (CD_2Cl_2): δ 1.53 (s, 3H, C=CMe), 1.96 (s, 3H, C=CMe), 2.17 (s, 3H, COMe), 2.85 (s, 1H, PCH) , 3.59 (s, 1H, PCH), 3.63 (d, 1H, J_{HH}=4.1Hz, PCHC*H*As), 3.79 (d, 1H, J_{HH}=3.1 Hz, PCHC*H*CO), 7.44-8.08 (m, 15H, aromatics),. ^{31}P { ^{1}H } NMR (CD_2Cl_2): δ 108.0 (J_{Pt-P}=3242 Hz). Anal. Calcd for $C_{28}H_{28}AsCl_2OPPt$: C, 44.70; H, 3.75. Found: C, 44.83; H, 3.86

Liberation of S-P chiral bidentate ligands 58 and 64b

The dichloro platinum complexes **58a** and **58b** (0.1 g) were dissolved in dichloromethane (10 mL) and then treated with aqueous potassium cyanide (0.1 g) in water (5 mL). The solution was stirred for 10 min at room temperature. After the two layers were settled, the organic layer was separated, washed with water (20 mL ×3) and then dried over magnesium sulfate. After removal of the solvent, the chiral ligand **59** was obtained as a white solid. $[\alpha]_D$ +132.5 (*c* 1.4, CH_2Cl_2). ^{31}P { ^{1}H } NMR ($CDCl_3$): δ 87.3

The same procedure was used to prepare **65**. The chiral ligand **65** was obtained as a white solid. $[\alpha]_D$ +93.4 (*c* 1.0, CH_2Cl_2).. ^{31}P { ^{1}H } NMR ($CDCl_3$): δ 96.3

Preparation of the dichloro platinum complexes 69a and 69b

A solution of complex **67** (0.10 g, 0.19 mmol) in dichloromethane (30mL) was treated with aqueous silver perchlorate (excess) in water (5mL) and stirred for 1h at room temperature. The resulting mixture was filtered off using Celite to remove the white precipitate, silver chloride. The organic layer was washed with water (50mL×3), and then dried over magnesium sulfate. The solvent was removed, and then the yellow solid was treated (E)-1- phenyl-3-pyridin-2-yl-2-propenone (0.165g, 1.62mmol). The mixture was stirred for 12d at 80℃, the conversion rate was under 10%.

Preparation of the dichloro platinum complexes 72a and 75a

A solution of **33** (0.53 g, 0.09 mmol) in dichloromethane (30 mL) was treated with aqueous silver perchlorate (0.04 g, 0.18 mmol) in water (5 mL) and stirred for 1h at room temperature. The organic layer, after removal of AgCl was washed with water (50 mL×3), and dried over magnesium sulfate to give complex **34**. Complex **34** in 1,2-dichloroethane (10 mL) was treated with (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone (0.02 g, 0.09 mmol). The mixture was stirred for 12d at 80℃ to give the mixture of complexes **71a** and **71b**. Since **71a** and **71b** could not be separated by silica-gel column chromatography or fractional crystallization. The mixture of products was used directly in the next step. A solution of **71a** and **71b** was treated with concentrated hydrochloric acid (5 mL) for 30 min at room temperature. The resulting mixture was washed with water (30 mL ×3) and then dried over magnesium sulfate. The crude product

crystallized from dichloromethane-diethyl ether to give the dichloro platinum complex **72a** as white crystals (84%). $[\alpha]_D$ +157.4 (*c* 1.41, CH_2Cl_2). ^1H NMR (CD_2Cl_2): δ 1.41 (s, 3H, C=CMe), 1.56 (s, 3H, C=CMe), 2.71 (s, 1H, PCH) , 4.01 (s, 1H, PCH), 4.24 (d, 1H, J_{HH}=4.1 Hz, PCHC*H*CO), 6.13 (d, 1H, J_{HH}=3.1 Hz, PCHC*H*CN), 7.35-8.11 (m, 13H, aromatics), 9.89 (d, 1H, J_{HH}=5.9 Hz, NC*H*). $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 77.3 (s, 1P, J_{Pt-P}=3421 Hz). ^{13}C NMR (CD_2Cl_2): 14.0, 14.7, 29.7, 46.0, 47.4, 52.6, 123.1, 123.5, 124.7, 128.1, 128.2, 128.3, 128.7, 129.2, 130.0, 131.3, 131.5, 132.6, 132.7, 133.1, 133.9, 135.3, 139.4, 156.3, 162.1, 195.3. Anal. Calcd for $C_{26}H_{24}Cl_2NOPPt$: C, 47.07; H, 3.65. Found: C, 45.93; H, 3.55

The same procedure was used to prepare dichloro platinum complex **75a**. The optically pure dichloro platinum complex **75a** was obtainted as white crystals (92%). $[\alpha]_D$ +56.6 (*c* 0.53, CH_2Cl_2). ^1H NMR (CD_2Cl_2): δ 1.54 (s, 3H, C=CMe), 1.72 (s, 3H, C=CMe), 2.61 (s, 1H, PCH) , 3.77 (s, 1H, OMe),3.78 (dd, 1H, J_{HH}=4.1 Hz, J_{HH}=26.6 Hz,PCHC*H*CO), 4.06 (s, 1H, PCH), 5.96 (m, 1H, PCHC*H*CN), 7.30-7.92 (m, 8H, aromatics), 9.93 (d, 1H, J_{HH}=5.9 Hz, NC*H*). $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 78.7 (s, 1P, J_{Pt-P}=3415 Hz).

Liberation of S-P chiral bidentate ligand 73a and 76

The dichloro platinum complexes **72a** (0.1 g) were dissolved in dichloromethane (10 mL) and then treated with aqueous potassium cyanide (0.1 g) in water (5 mL). The solution was stirred for 1h at room temperature. After

the two layers were settled, the organic layer was separated, washed with water (20 mL ×3) and then dried over magnesium sulfate. After removal of the solvent, the chiral ligand **73** was obtained as white solid, $[\alpha]_D$ +123.8 (*c* 1.26, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 70.3

The same procedure was used to prepare **76**. The chiral ligand **76** was obtained as a white solid, $[\alpha]_D$ +87.8 (*c* 1.74, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 72.5 .

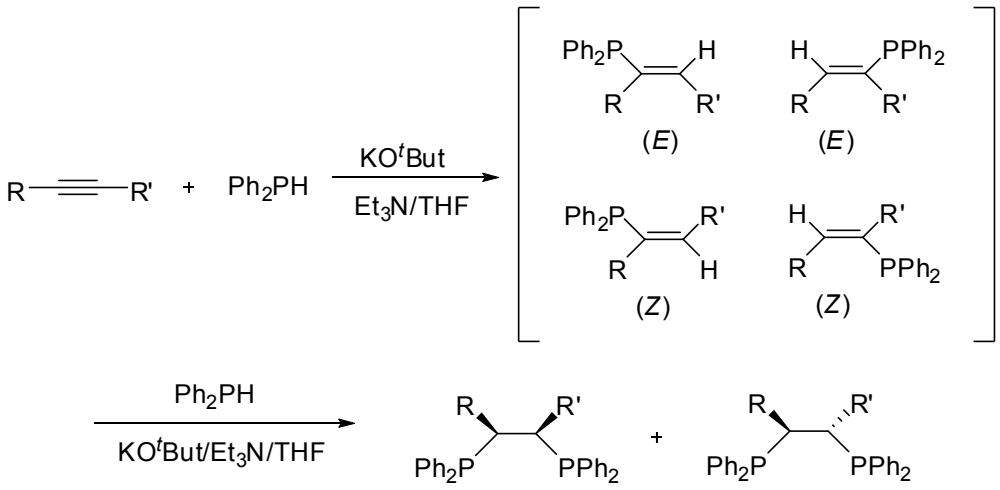
Chapter 3

Palladacycle-Promoted Asymmetric Hydrophosphination Reaction to Synthesize Diphosphine Ligand

3.1 Introduction

Chiral tertiary diphosphines were well known as important ligands for transition metal catalyzed asymmetric transformations in organic and organometallic chemistry.[68] Since 1,2-diphosphines bearing chirality on the carbon backbone, such as CHIRAPHOS and PROPHOS, have strong bonding ability with metal and stereocontrol for asymmetric transformation reaction, this type of chiral diphosphines have long been considered as powerful auxiliaries.[68]

Among the various approaches to the asymmetric synthesis of functionalized optically active phosphines, the asymmetric synthesis of chiral diphosphines via the addition of phosphorus-hydrogen bonds to carbon-carbon bonds of unsaturated compounds is an important method.[69,70] The addition of secondary phosphines to carbon-carbon multiple bonds, namely hydrophosphination reaction, is one of the most valuable and convenient methods to synthesize functionalized tertiary phosphine ligands.[71] In general, when the phosphorus functionalized olefins were employed, the hydrophosphination reactions could yield a range of useful phosphine ligands. With free phosphines, addition of the phosphorus-hydrogen moiety onto carbon-carbon multiple bonds requires strong bases,[72] Brønsted acids,[73] radical initiators,[74] or transition metal catalysis.[70,75] One example of base catalyzed hydrophosphination reaction was shown in Scheme 3.1.

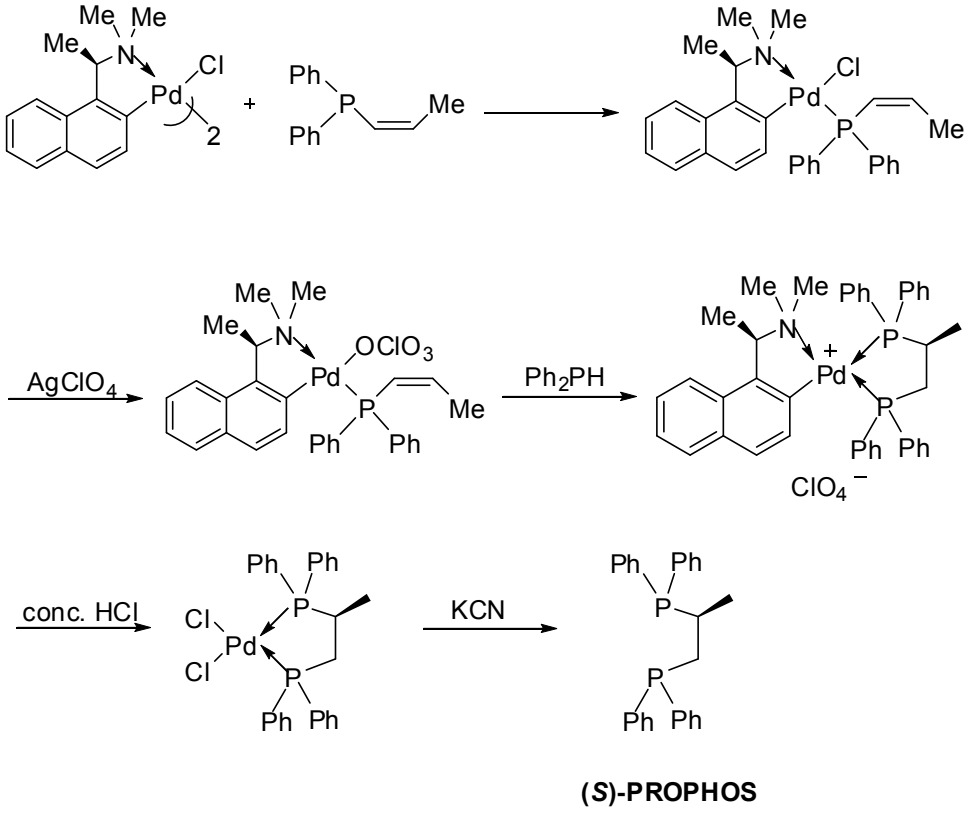


stereochem.	R	R'	*stereochem.*
meso	2-pyridyl	2-pyridyl	*rac*
meso	3-pyridyl	3-pyridyl	*rac*

Scheme 3.1

So far, a lot of examples of transition metal catalyzed addition of P-H bonds to carbon-carbon multiple bonds using palladium, platinum, nickel, and rhodium complexes have been reported.[76] Besides these catalytic processes, there were also some examples of hydrophosphination reactions which are promoted by transition metal complexes.[77,78] However, compared to the catalytic hydrophosphination reactions, metal complex activated asymmetric hydrophosphination reactions of carbon-carbon multiple bonds were relatively rare.[78,79] Transition metal promoted asymmetric hydrophosphination reaction which can control the stereoselectivity of the reaction is an efficient method to synthesize chiral diphosphines.

Over the past few years, our group has already established that the (*S*)- or (*R*)- orthometalated [1-(dimethylamino)ethyl]naphthalene palladium complexes could be used as efficient promoters for the synthesis of various chiral diphosphines by means of asymmetric hydrophosphination reaction involving a serial of vinylic phosphine substrates. The chiral palladium complex promoted hydrophosphination reaction could yield the chiral 1,2-diphosphine (*S*)-PROPHOS with high stereoselectivity under mild reaction condition (Scheme 3.2).[80]



Scheme 3.2

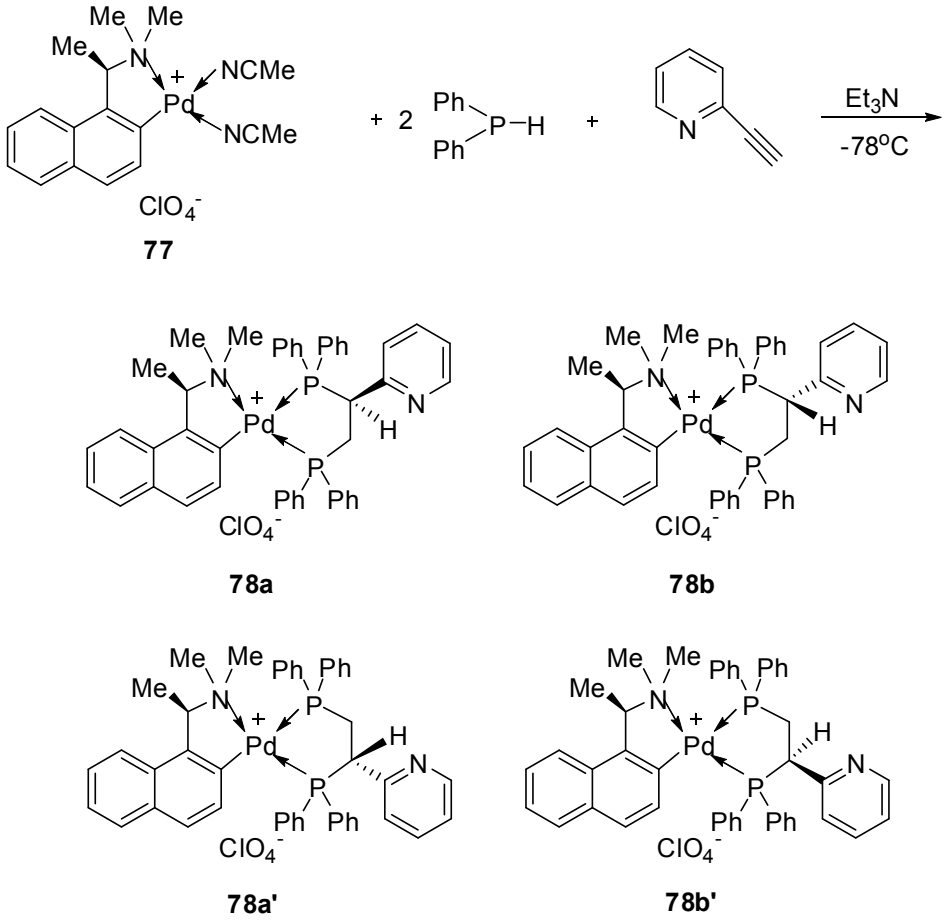
In pursing our interests in the application of the palladium complex and development of the method for synthesis of chiral phosphine ligands, in this chapter the preparation of a functionalized diphosphine via a simple chiral palladium template-promoted asymmetric hydrophosphination reaction was presented.

3.2 Results and Discussion

In the absence of the palladium template, diphenylphosphine showed no reactivity with 2-ethynyl-pyridine under ambient condition. However, as illustrated in Scheme 3.3, in the presence of chiral complex **77**, the reaction proceeded smoothly under mild condition.

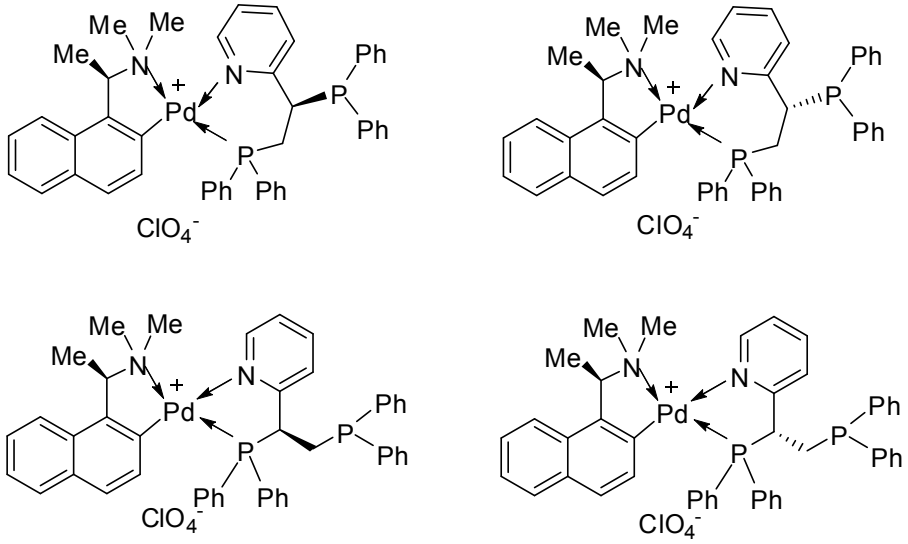
In the presence of the chiral bis-(acetonitrile) palladium complex **77** and triethylamine, treatment of 2-ethynyl-pyridine with diphenylphosphine in dichloromethane at -78℃ yielded the corresponding hydrophosphination products **78a**, **78a'**, **78b, and 78b'** (Scheme 3.3). Prior to purification, the $^{31}P\{^{1}H\}$ NMR spectrum of the crude hydrophosphination reaction mixture in $CDCl_3$ exhibited four pairs of doublets at δ 73.8, 66.2 (J_{P-P}=18.15Hz), δ 51.6, 48.9 (J_{P-P}=30.25Hz), δ 51.5, 47.5 (J_{P-P}=30.25Hz), and δ 39.4, 37.3 (J_{P-P}=18.15Hz), with the relative intensities of 1:19.4:2.4:1.3. This means although four products were yielded, the amount of the major product was much more than the other three products and the selectivity was good.

The amount of triethylamine which was added into the reaction mixture had an impact on the selectivity of the hydrophosphination reaction. 0.4 equiv of triethylamine was found to be the appropriate amount, because with more or less triethylamine the regioselectivity and stereoselectivity decreased. Unfortunately, pure hydrophosphination product **78a**, **78a'**, **78b**, **and 78b'** could not be separated by silica-gel column chromatography or fractional crystallization. Thus, the mixture of products was used directly in the next step.



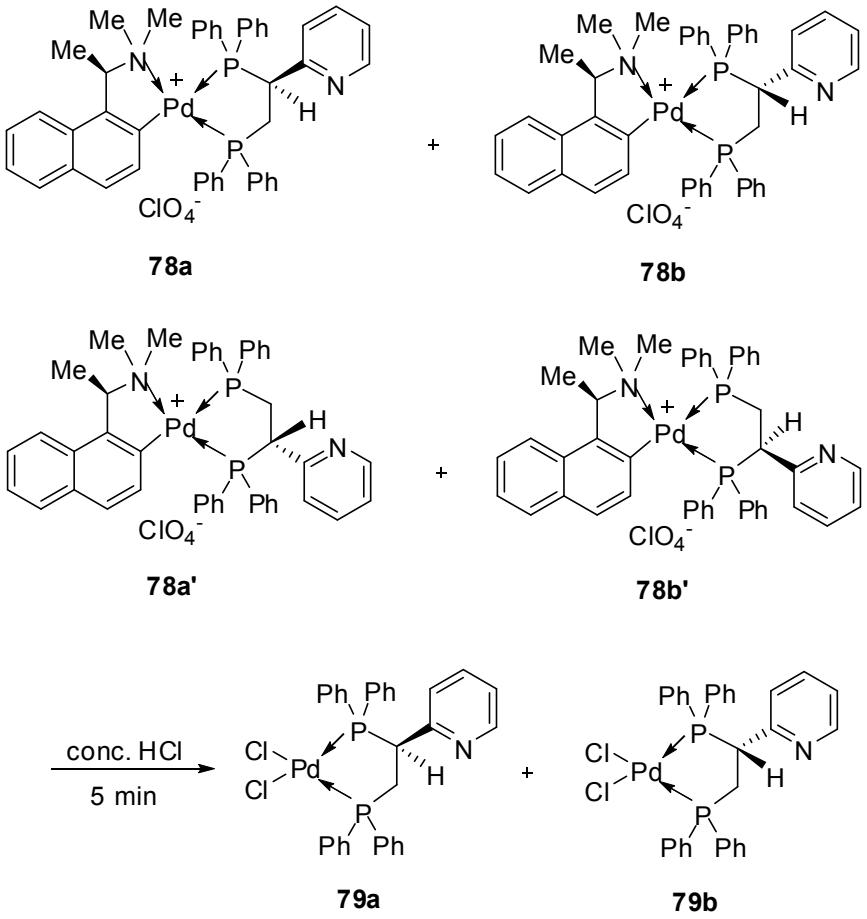
Scheme 3.3

The products **78a**, **78a'**, **78b**, **and 78b'** aforementioned were proposed products. There were also many complexes that could be formed in the hydrophosphination reaction, which were with P-N bidentate ligands coordinated to the palladium center. Since phosphorus is softer than nitrogen, phosphorus was easier to coordinate to palladium center. Therefore, the possibility of structure of the products above was higher than what shown below.



A solution of **78a**, **78a'**, **78b**, **and 78b'** in dichloromethane was treated with concentrated hydrochloric acid for 5 min at room tempetature to remove the chiral naphthylamine auxiliary on complexes **78a**, **78a'**, **78b**, **and 78b'** chemoselectively and gave the neutral dichloro complex **79a** (Scheme 3.4). Dichloro palladium complex **79a** could be obtained by fractional crystallization from dichloromethane-diethyl ether as white prisms $[\alpha]_D$ -95.24 (*c* 1.47,

CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum of the isolated complex in CD_2Cl_2 showed a pair of doublets at δ 76.2, 48.7 ($J_{P\text{-}P}$=6.6Hz).



Scheme 3.4

The single crystal X-ray diffraction analysis established that complex **79a** was coordinated to the metal center as a diphosphine bidentate ligand and the stereogenic center at carbon was with *S* configuration. The geometry at palladium is slightly distorted square planar with angles at palladium in the range of 86.244(17)° - 92.375(17)° and 173.889(19)° - 174.508(19)° . Selected bond lengths and angles are listed in Table 11.

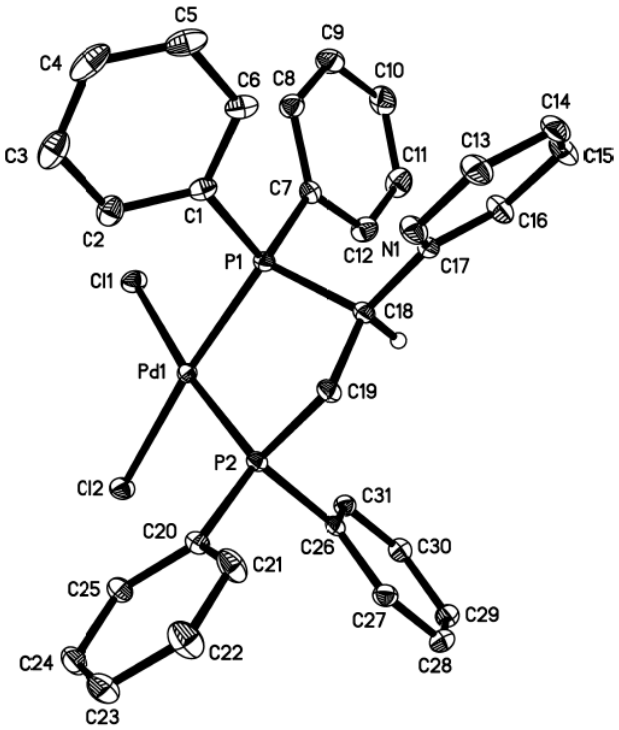
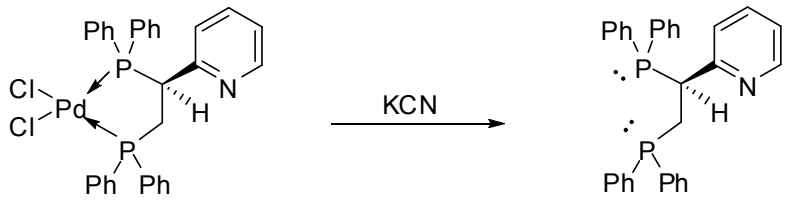


Figure 11. Molecular structure of complex **79a**

Table 11. Selected bond lengths [Å] and angles [°] for **79a**

Pd(1)-P(1)	2.2465(5)	Pd(1)-P(2)	2.2481(5)
Pd(1)-Cl(1)	2.3421(5)	Pd(1)-Cl(2)	2.3669(5)
C(1)-P(1)	1.8108(15)	C(7)-P(1)	1.8131(15)
C(17)-C(18)	1.502(2)	C(18)-C(19)	1.527(2)
C(18)-P(1)	1.8677(16)	C(20)-P(2)	1.8128(14)
C(26)-P(2)	1.8164(15)		
P(1)-Pd(1)-P(2)	86.244(17)	P(1)-Pd(1)-Cl(1)	89.115(18)
P(2)-Pd(1)-Cl(1)	173.889(19)	P(1)-Pd(1)-Cl(2)	174.508(19)
P(2)-Pd(1)-Cl(2)	92.375(17)	Cl(1)-Pd(1)-Cl(2)	91.873(16)
C(17)-C(18)-C(19)	113.04(12)	C(17)-C(18)-P(1)	116.05(11)
C(19)-C(18)-P(1)	106.59(10)	C(18)-C(19)-P(2)	108.61(10)
C(18)-P(1)-Pd(1)	105.57(5)	C(19)-P(2)-Pd(1)	108.35(5)

The free P-P chiral bidentate ligand could be liberated efficiently from the dichloro palladium complex **79a** by treatment with aqueous potassium cyanide at room temperature for 10 min (Scheme 3.5). The optically active ligand **80** was obtained as a white solid in quantitative yield, $[\alpha]_D$ -57.9 (*c* 0.95, CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum of the free ligand in $CDCl_3$ exhibited a pair of doublet at δ 3.0, -20.5 (J_{pp}=20Hz). The stereogenic center at carbon was with *S* configuration.

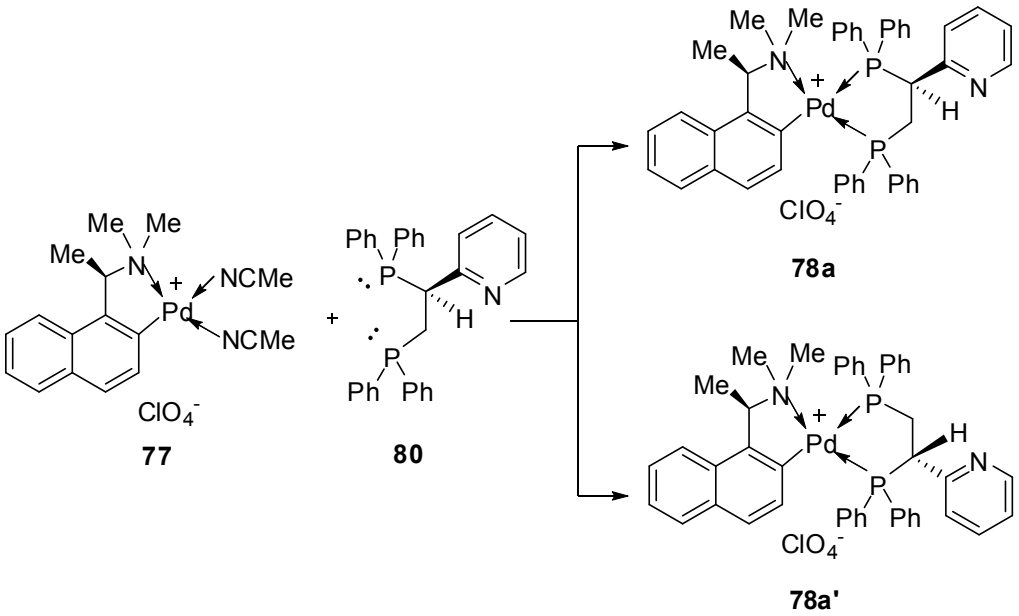


79a **80**

Scheme 3.5

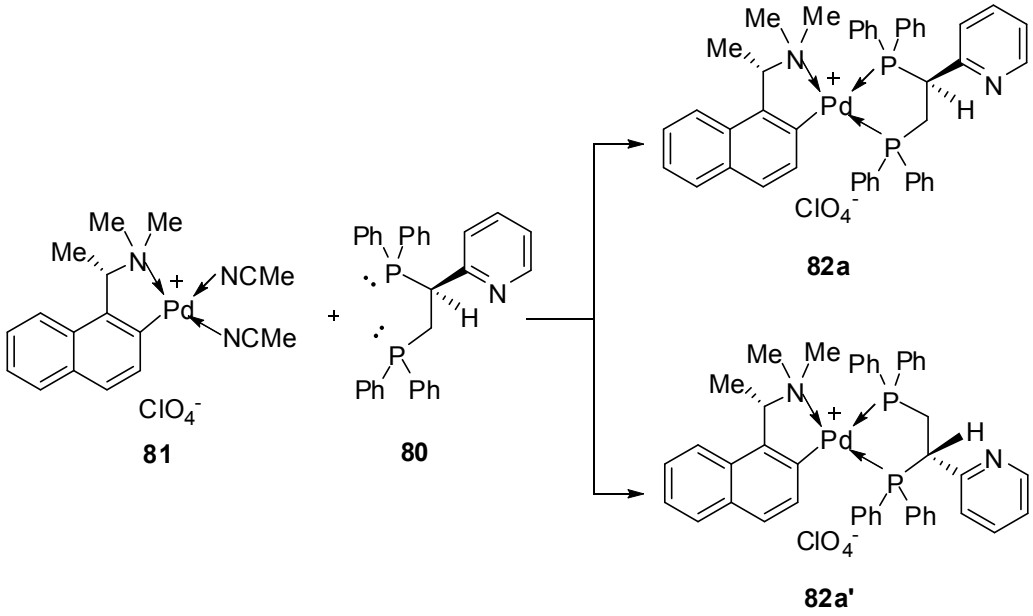
In order to determine the optical purity of the liberated ligand and to stabilize the the noncoordinated phosphorus of the free ligand **80**, the liberated ligand **80** must be recoordinated to the bis-(acetonitrile) palladium complex **77** as illustrated in Scheme 3.6. The recoordination could also establish the identity of the minor isomers which were generated in the original hydrophosphination reaction. The 121 MHz $^{31}P\{^1H\}$ NMR of the recomplexation products in $CDCl_3$ indeed exhibited a pair of doublet at δ73.8, 66.2 ($J_{P\text{-}P}$=18.15Hz) and δ 51.6, 48.9 ($J_{P\text{-}P}$=30.25Hz). The resonance signals at δ 51.6, 48.9 ($J_{P\text{-}P}$=30.25Hz) were the identical to those observed for the major product **78a** in the original

hydrophosphination reaction. The resonance signals atδ 73.8, 66.2 ($J_{P\text{-}P}$=18.15Hz) matched the signals detected in the original hydrophosphination reaction and were assigned to the regioisomeric product of complex **78a**, that is, **78a'**.



Scheme 3.6

As a further confirmation of the optical purity of the liberated ligand **80,** the recoordination reaction with the equally accessible enantiomerically pure complex **81** gave two pairs of doublets at δ 73.6, 66.2 ($J_{P\text{-}P}$=22.5Hz) and δ 51.6, 47.7 ($J_{P\text{-}P}$=33.9Hz). These signals confirmed that a pair of regioisomers **82a** and **82a'** were generated. Therefore, the recoordination reaction confirmed that the liberated diphosphine ligand was optically pure.



Scheme 3.7

3.3 Conclusion

The palladacycle complex **77** has been successfully used as the chiral template to promote the hydrophosphination reaction between 2-ethynyl-pyridine and diphenylphosphine. Chiral P-P bidentate ligands were obtained stereoselectively when the reactions were promoted by platinum complex **77**.

3.4 Experimental Section

General: the same as the Chapter 2.1.3.

Preparation of the dichloro palladium complex 79

A solution of chiral bis-(acetonitrile) palladium complex **77** (63.3 mg, 0.13

mmol) and diphenylphosphine (48.5 mg, 0.26 mmol) in dichloromethane (5 mL) was cooled to -78℃ with stirring. 2-ethynyl-pyridine (13.7 mg, 0.13 mmol) in dichloromethane (1 mL) was added subsequently, followed by adding triethylamine (10.4 mg, 0.10 mmol) in dichloromethane (1 mL). The reaction mixture was allowed to stir for X days at -78℃ and then warm to room temperature. Although the products could not be totally separated by silica-gel column chromatography, it was better to purify the products before the next step.

A solution of **78a** and **78b** was treated with concentrated hydrochloric acid (5 mL) for 5 min at room temperature. The resulting mixture was wash with water (30 mL ×3) and then dried over magnesium sulfate. The crude product crystallized from dichloromethane-diethyl ether to give the dichloro platinum complex **79a** as white crystals (51%). $[\alpha]_D$ -95.24 (*c* 1.47, CH_2Cl_2). ^1H NMR (CD_2Cl_2): δ 2.96 (m, 1H, PCH*H*), 3.25 (m, 1H, PC*H*H), 4.16 (m, 1H, PC*H*CH_2), 6.54-8.15 (m, 24H, aromatics). $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 76.2, 48.7 ($J_{P\text{-}P}$=6.6Hz). ^{13}C NMR (CD_2Cl_2): δ 33.8, 48.3, 123.1, 123.5, 126.8, 127.2, 127.5, 128.0, 128.3, 128.4, 128.6, 128.7, 128.8, 128.9, 129.5, 129.5, 131.8, 132.0, 132.0, 132.7, 132.7, 133.0, 133.1, 133.2, 134.5, 134.6, 136.3, 136.4, 136.6, 148.8, 153.1. Anal. Calcd for $C_{31}H_{27}Cl_2NP_2Pd$: C, 57.03; H, 4.17. Found: C, 56.94; H, 4.05

Liberation of chiral bidentate ligand 80

The dichloro platinum complexes **79a** (0.1 g) were dissolved in dichloromethane (10 mL) and then treated with aqueous potassium cyanide (0.10 g) in water (15 mL). The solution was stirred for 10 min at room temperature. After the two layers were settled, the organic layer was separated, washed with water (20mL ×3) and then dried over magnesium sulfate. After removal of the solvent, the chiral ligand **80** was obtained as a white solid, $[\alpha]_D$ -57.9 (*c* 0.95, CH_2Cl_2). $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 3.0, -20.5 (J_{pp}=20Hz)

Overall conclusion

P-S, P-As, P-N and N-P-P optically active ligands were synthesized through asymmetric cycloaddition and hydrophosphination Reactions promoted by platinum and palladium complexes and the metal effect was discussed. In the future, the application of these chiral ligands toward asymmetric catalytic reaction should be investigated systematically.

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Appendices

Table 1. Crystal data and structure refinement for 36.

Empirical formula	C16 H19 Cl2 O P Pt S
Formula weight	556.33
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 9.4029(4) Å a= 90°. b = 11.0824(5) Å b= 91.226(3)°. c = 17.4783(8) Å g = 90°.
Volume	1820.94(14) $Å^3$
Z	4
Density (calculated)	2.029 Mg/m^3
Absorption coefficient	8.199 mm^{-1}
F(000)	1064
Crystal size	0.38 x 0.14 x 0.10 mm^3
Theta range for data collection	2.84 to 33.25°.
Index ranges	-14<=h<=14, -17<=k<=15, -26<=l<=26
Reflections collected	36061
Independent reflections	12262 [R(int) = 0.0302]
Completeness to theta = 33.25°	98.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.4944 and 0.1467
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12262 / 1 / 401
Goodness-of-fit on F^2	1.016
Final R indices [I>2sigma(I)]	R1 = 0.0199, wR2 = 0.0482
R indices (all data)	R1 = 0.0221, wR2 = 0.0488
Absolute structure parameter	0.012(3)
Largest diff. peak and hole	1.353 and -1.071 $e.Å^{-3}$

Table 2. Crystal data and structure refinement for 40b.

Empirical formula	C40 H42 Cl2 N O5 P Pt S
Formula weight	945.77
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P1
Unit cell dimensions	a = 10.1288(2) Å a= 109.3020(10)° b = 10.6698(2) Å b= 98.4130(10)° c = 10.8789(3) Å g =117.4910(10)°
Volume	919.46(4) $Å^3$
Z	1
Density (calculated)	1.708 Mg/m^3
Absorption coefficient	4.107 mm^{-1}
F(000)	472
Crystal size	0.40 x 0.40 x 0.28 mm^3
Theta range for data collection	2.12 to 29.00°.
Index ranges -14<=l<=14	-13<=h<=13, -14<=k<=14,
Reflections collected	15313
Independent reflections	7968 [R(int) = 0.0255]
Completeness to theta = 29.00°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.3926 and 0.2904
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7968 / 3 / 465
Goodness-of-fit on F^2	0.995
Final R indices [I>2sigma(I)]	R1 = 0.0176, wR2 = 0.0439
R indices (all data)	R1 = 0.0179, wR2 = 0.0614
Absolute structure parameter	0.003(4)
Largest diff. peak and hole	0.529 and -1.965 $e.Å^{-3}$

Table 3. Crystal data and structure refinement for 41.

Empirical formula	C21 H23 Cl4 O P Pt S	
Formula weight	691.31	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 10.2265(5) Å	a= 90°.
	b = 14.4513(7) Å	b= 90°.
	c = 16.0003(7) Å	g = 90°.
Volume	2364.62(19) $Å^3$	
Z	4	
Density (calculated)	1.942 Mg/m^3	
Absorption coefficient	6.554 mm^{-1}	
F(000)	1336	
Crystal size	0.40 x 0.10 x 0.06 mm^3	
Theta range for data collection	1.90 to 33.38°.	
Index ranges	-15<=h<=13, -22<=k<=22,	
-24<=l<=24		
Reflections collected	38770	
Independent reflections	9139 [R(int) = 0.0277]	
Completeness to theta = 33.38°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.6945 and 0.1791	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9139 / 0 / 264	
Goodness-of-fit on F^2	1.087	
Final R indices [I>2sigma(I)]	R1 = 0.0160, wR2 = 0.0428	
R indices (all data)	R1 = 0.0186, wR2 = 0.0570	
Absolute structure parameter	0.007(4)	
Largest diff. peak and hole	1.209 and -0.989 $e.Å^{-3}$	

Table 4. Crystal data and structure refinement for 44a'.

Empirical formula	C34 H37 Cl N O5 P Pt S	
Formula weight	833.22	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 9.9305(2) Å	a= 90°.
	b = 14.6373(3) Å	b= 90°.
	c = 22.0322(5) Å	g = 90°.
Volume	3202.51(12) $Å^3$	
Z	4	
Density (calculated)	1.728 Mg/m^3	
Absorption coefficient	4.623 mm^{-1}	
F(000)	1656	
Crystal size	0.40 x 0.18 x 0.10 mm^3	
Theta range for data collection	1.67 to 28.28°.	
Index ranges	-6<=h<=13, -19<=k<=19,	
-29<=l<=29		
Reflections collected	37433	
Independent reflections	7903 [R(int) = 0.0433]	
Completeness to theta = 28.28°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.6549 and 0.2592	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7903 / 0 / 402	
Goodness-of-fit on F^2	1.116	
Final R indices [I>2sigma(I)]	R1 = 0.0216, wR2 = 0.0500	
R indices (all data)	R1 = 0.0265, wR2 = 0.0709	
Absolute structure parameter	-0.014(5)	
Largest diff. peak and hole	1.087 and -0.946 $e.Å^{-3}$	

Table 5. Crystal data and structure refinement for 47.

Empirical formula	C30 H31 As Cl N O2 Pd	
Formula weight	654.33	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 10.9955(4) Å	a= 90°.
	b = 15.7212(6) Å	b= 90°.
	c = 16.2711(6) Å	g = 90°.
Volume	2812.66(18) $Å^3$	
Z	4	
Density (calculated)	1.545 Mg/m^3	
Absorption coefficient	1.949 mm^{-1}	
F(000)	1320	
Crystal size	0.32 x 0.30 x 0.21 mm^3	
Theta range for data collection	1.80 to 31.01°.	
Index ranges	-15<=h<=11, -18<=k<=22,	
-21<=l<=23		
Reflections collected	16266	
Independent reflections	8863 [R(int) = 0.0413]	
Completeness to theta = 31.01°	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.6850 and 0.5743	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8863 / 0 / 329	
Goodness-of-fit on F^2	0.986	
Final R indices [I>2sigma(I)]	R1 = 0.0367, wR2 = 0.0787	
R indices (all data)	R1 = 0.0484, wR2 = 0.0961	
Absolute structure parameter	0.013(10)	
Largest diff. peak and hole	0.539 and -0.762 $e.Å^{-3}$	

Table 6. Crystal data and structure refinement for 50.

Empirical formula	C28 H28 As Cl2 O2 P Pd
Formula weight	679.69
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	a = 8.5655(4) Å a= 90°. b = 18.2134(9) Å b= 111.584(2)° c = 18.2029(8) Å g = 90°.
Volume	2640.6(2) $Å^3$
Z	4
Density (calculated)	1.710 Mg/m^3
Absorption coefficient	2.234 mm^{-1}
F(000)	1360
Crystal size	0.18 x 0.10 x 0.08 mm^3
Theta range for data collection	2.24 to 25.60°.
Index ranges -17<=l<=21	-10<=h<=9, -22<=k<=22,
Reflections collected	27419
Independent reflections	4861 [R(int) = 0.0544]
Completeness to theta = 25.60°	97.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8415 and 0.6892
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4861 / 0 / 319
Goodness-of-fit on F^2	1.192
Final R indices [I>2sigma(I)]	R1 = 0.0318, wR2 = 0.0899
R indices (all data)	R1 = 0.0481, wR2 = 0.1064
Largest diff. peak and hole	0.679 and -0.797 $e.Å^{-3}$

Table7. Crystal data and structure refinement for 54a.

Empirical formula	C28 H28 As Cl2 O P Pd
Formula weight	663.69
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 10.1868(3) Å a= 90°. b = 9.2953(2) Å b= 102.6180(10)° c = 14.1254(4) Å g = 90°.
Volume	1305.22(6) $Å^3$
Z	2
Density (calculated)	1.689 Mg/m^3
Absorption coefficient	2.255 mm^{-1}
F(000)	664
Crystal size	0.40 x 0.10 x 0.08 mm^3
Theta range for data collection	2.05 to 31.15°.
Index ranges	-14<=h<=14, -12<=k<=13, -20<=l<=20
Reflections collected	22819
Independent reflections	7439 [R(int) = 0.0368]
Completeness to theta = 31.15°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8402 and 0.4657
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7439 / 1 / 310
Goodness-of-fit on F^2	1.091
Final R indices [I>2sigma(I)]	R1 = 0.0287, wR2 = 0.0666
R indices (all data)	R1 = 0.0332, wR2 = 0.0837
Absolute structure parameter	0.018(7)
Largest diff. peak and hole	0.625 and -0.828 $e.Å^{-3}$

Table 8. Crystal data and structure refinement for 58.

Empirical formula	C28 H28 As Cl2 O2 P Pt
Formula weight	768.38
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	a = 8.5582(3) Å a= 90°. b = 18.2142(6) Å b= 95.7430(10)° c = 17.0520(5) Å g = 90°.
Volume	2644.74(15) $Å^3$
Z	4
Density (calculated)	1.930 Mg/m^3
Absorption coefficient	6.835 mm^{-1}
F(000)	1488
Crystal size	0.14 x 0.12 x 0.10 mm^3
Theta range for data collection	2.24 to 29.71°.
Index ranges	-11<=h<=11, -24<=k<=25, -23<=l<=15
Reflections collected	26797
Independent reflections	7411 [R(int) = 0.0477]
Completeness to theta = 29.71°	99.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.5481 and 0.4479
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7411 / 0 / 319
Goodness-of-fit on F^2	1.128
Final R indices [I>2sigma(I)]	R1 = 0.0393, wR2 = 0.1033
R indices (all data)	R1 = 0.0517, wR2 = 0.1120
Largest diff. peak and hole	3.621 and -2.583 $e.Å^{-3}$

Table 9. Crystal data and structure refinement for 64b.

Empirical formula	C28 H28 As Cl2 O P Pt
Formula weight	752.38
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 10.1976(5) Å a= 90°. b = 9.3796(4) Å b= 102.096(2)°. c = 14.0573(5) Å g = 90°.
Volume	1314.72(10) $Å^3$
Z	2
Density (calculated)	1.901 Mg/m^3
Absorption coefficient	6.870 mm^{-1}
F(000)	728
Crystal size	0.10 x 0.10 x 0.08 mm^3
Theta range for data collection	1.48 to 31.00°.
Index ranges	-14<=h<=14, -13<=k<=12, -17<=l<=20
Reflections collected	16586
Independent reflections	7912 [R(int) = 0.0493]
Completeness to theta = 31.00°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.6095 and 0.5466
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7912 / 1 / 310
Goodness-of-fit on F^2	1.008
Final R indices [I>2sigma(I)]	R1 = 0.0398, wR2 = 0.0819
R indices (all data)	R1 = 0.0470, wR2 = 0.1064
Absolute structure parameter	-0.003(9)
Largest diff. peak and hole	1.678 and -1.265 $e.Å^{-3}$

Table 10. Crystal data and structure refinement for 72a.

Empirical formula	C26 H24 Cl2 N O P Pt
Formula weight	663.42
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 8.8284(5) Å a= 90°. b = 30.3313(14) Åb= 103.242(3)°. c = 9.1117(5) Å g = 90°.
Volume	2375.0(2) $Å^3$
Z	4
Density (calculated)	1.855 Mg/m^3
Absorption coefficient	6.220 mm^{-1}
F(000)	1288
Crystal size	0.22 x 0.08 x 0.06 mm^3
Theta range for data collection	2.37 to 37.36°.
Index ranges -14<=l<=14	-14<=h<=14, -46<=k<=47,
Reflections collected	16197
Independent reflections	16197 [R(int) = 0.0000]
Completeness to theta = 25.00°	97.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7066 and 0.3415
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	16197 / 22 / 583
Goodness-of-fit on F^2	0.989
Final R indices [I>2sigma(I)]	R1 = 0.0631, wR2 = 0.1317
R indices (all data)	R1 = 0.0999, wR2 = 0.1494
Absolute structure parameter	0.024(9)
Largest diff. peak and hole	5.670 and -5.428 $e.Å^{-3}$

Table 11. Crystal data and structure refinement for 79a.

Empirical formula	C31 H27 Cl2 N P2 Pd
Formula weight	652.78
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P1
Unit cell dimensions	a = 8.3033(2) Å a= 66.3410(10)° b = 9.5925(3) Å b= 85.5250(10)° c = 9.8331(3) Å g = 74.7500(10)°
Volume	691.78(3) $Å^3$
Z	1
Density (calculated)	1.567 Mg/m^3
Absorption coefficient	1.002 mm^{-1}
F(000)	330
Crystal size	0.30 x 0.26 x 0.24 mm^3
Theta range for data collection	2.40 to 36.52°.
Index ranges -16<=l<=16	-13<=h<=13, -14<=k<=16,
Reflections collected	22295
Independent reflections	11899 [R(int) = 0.0262]
Completeness to theta = 27.00°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7950 and 0.7532
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11899 / 3 / 334
Goodness-of-fit on F^2	1.016
Final R indices [I>2sigma(I)]	R1 = 0.0245, wR2 = 0.0540
R indices (all data)	R1 = 0.0252, wR2 = 0.0544
Absolute structure parameter	0.001(9)
Largest diff. peak and hole	0.652 and -0.539 $e.Å^{-3}$