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Asymmetric Synthesis of Chiral Arsines and Phosphines and Their Stability Investigation

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2009

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My appreciation is also extended to Ee Ling from the NMR Lab and also to the staff of the Microanalytical Lab for their assistance.

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Summary

The organopalladium complex containing ortho-metalated (*S*)-[1-(dimethylamino)ethyl]naphthalene (+)-**2** as the chiral auxiliary has been successfully used as the chiral template to promote the asymmetric cycloaddition reactions between 3,4-dimethyl-1-phenylarsole (DMPA) and several kinds of vinylphosphines [diphenylvinylphosphine, (*Z*/*E*)-diphenyl-1-propenylphosphine, (*Z*/*E*)-diphenyl-1-styrylphosphine, phenyldivinylphosphine, diphenylvinylphosphine oxide, diphenylvinylphosphine sulfide], diphenylvinylarsine and ethyl vinyl ketone.

A diphenylphosphino-substituted asymmetrical heterobidentate arsanorbornene (As–P) ligand (–)-**46** was obtained stereoselectively *via* asymmetric cycloaddition reaction between DMPA and diphenylvinylphosphine. The chiral amine (benzylamine or naphthylamine) auxiliary could be removed chemoselectively from the template by treatment with concentrated hydrochloric acid to produce the neutral dichloro complex [(As–P)$PdCl_2$] (–)-**45**. In contrast to their reported P–P analogue, the arsenic donor in the dichloro complex could be eliminated stereospecifically under mild reaction conditions to generate the corresponding 1-(diphenylphosphino)-3,4-dimethyl-2,4-cyclohexadiene, which remained as a bidentate ligand at the $PdCl_2$ unit *via* phosphorus and the η^2-C_4–C_5 double bond [(+)-**48**]. The arsenic-elimination process was found to be influenced by the halo ligand in [(As–P)PdX_2] [X = Cl, Br or I]. A similar process was observed with the analogous dibromo complex, but the corresponding diiodo species did not show similar reactivity. It has been proven that the chiral template incorporating naphthylamine is more efficient than the benzylamine based analogue as evidenced by the drastic

improvement in stereoselectivity and reaction rate. However, when no chiral template was employed, *trans*-[$PdI_2(DMPA)_2$] reacted with *trans*-[PdI_2(diphenylvinylphosphine)$_2$] producing a structurally novel diiodo complex, as a result of an interesting selective cleavage of one As–C bond in the norbornene skeleton and subsequent rearrangements within the skeletal framework. Most of the novel As–Pd complexes have been characterized by X-ray crystallography.

Asymmetric cycloaddition reaction between DMPA and diphenylvinylarsine can be successfully promoted *via* using complex (+)**-2** as the reaction promoter to afford the optically pure diarsine ligand (–)**-61**. However, the corresponding diiodo complex (–)**-60** is less stable, and consequently all the As–C bonds in the As–As bidentate arsanorbornene skeleton cleaved to give an unexpected bimetallic complex [μ–I_2\{μ–(As–O–As)$_2$\}Pd_2I_2], **62**.

Asymmetric [4+2] Diels–Alder reactions between DMPA and (*Z*/*E*)-diphenyl-1-propenylphosphine using (+)**-2** as reaction promoter also generate enantiomerically pure As–P bidentate ligands *endo*-(–)-**68a** [(*1R,4R,5S,6S,7S*)-5-(diphenylphosphino)-2,3,6-trimethyl-7-phenyl-7-arsabicyclio[2.2.1]hept-2-ene] and *exo*-(–)-**68b** [(*1R,4R,5S,6R,7S*)-5-(diphenylphosphino)-2,3,6-trimethyl-7-phenyl-7-arsabicyclio[2.2.1]hept-2-ene] as expected. Both reactions could produce one arsenic and four new carbon chiral centers in a single step and the stereoselectivity was high (33:1). The terminal methyl group in the propenyl moiety has a considerable effect on the rate of the cycloaddition reactions. When no methyl group was present ie a vinyl moiety, the corresponding Diels–Alder reaction needed only 40 min; however, when the (*Z*/*E*)-methyl group is introduced, the reactions needed 2 to 3 weeks to complete. Upon comparison with the similar dichloro

complex (+)-**48**, an arsenic elimination was also observed in the corresponding [Cl_2Pd(As–P)] complexes [*endo*-(+)-**66a** and *exo*-(–)-**66b**]. However, the reaction is totally different when the methyl group was replaced by a Ph moiety, the asymmetric Diels–Alder reactions between DMPA and both (*Z*/*E*)-diphenyl-1-styrylphosphines produced the same *endo*-cycloadduct (–)-**72**. The enantioselectivity is 15:1. The reaction temperature has a considerable effect on the reaction rate of (*E*)-diphenyl-1-styrylphosphine but little effect on that of (*Z*)-substituted ligand.

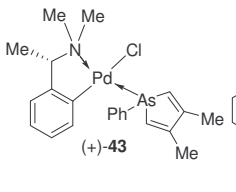
The intermolecular reaction between DMPA and ethyl vinyl ketone using (+)-**2** as reaction promoter resulted in the formation of a pair of diastereomers in *syn-endo* stereochemistry [(S_c,S_{As})-**76** and (S_c,R_{As})-**76**] in the ratio of 2:1. On the other hand, the intramolecular reaction between DMPA and ethyl vinyl ketone using the corresponding perchlorate complex of (+)-**2** as reaction promoter showed high stereoselectivity to produce only one isomer (S_c,R_{As})-**78**. Unlike the analogous phosphine palladium complexes, all three resulting arsine palladium complexes [(S_c,S_{As})-**76**, (S_c,R_{As})-**76** and (S_c,R_{As})-**78**] are not stable in solution and their corresponding free ketoarsine ligands decompose to give different retro Diels–Alder reaction products depending on the reaction conditions. Under inert atmosphere and in the air, the elimination products, 1-(3,4-dimethyl-2,4-cyclohexadienyl)-1-propanone and 1-(3,4-dimethylphenyl)-1-propanone, were produced respectively.

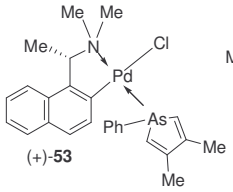
A chiral heterobidentate As–P ligand containing both As and P–stereogenic centers was obtained stereoselectively *via* a facile metal template promoted cycloaddition reaction between DMPA and phenyldivinylphosphine. Similarly, an arsenic elimination process was observed in their dichloro and dibromo palladium complex whereas the

diiodo species did not show such reactivity. However, the corresponding η^2-diiodo complex could be obtained from the η^2-dibromo complex by treatment with sodium iodide.

The asymmetric Diels–Alder reaction between DMPA and diphenylvinylphosphine oxide showed high stereoselectivity with only one isomer being formed. The rate of this reaction using the chiral palladium promoter is much faster than that of the platinum. But the resulting dichloro palladium complex was very unstable which could not yield the desired As–P=O hemilabile ligand. It decomposed rapidly to the retro Diels–Alder reaction product (3,4-dimethyl-2,4-cyclohexadienyl)diphenylphosphine oxide (–)-**90**. However, the corresponding dichloro platinum complex (+)-**94** is stable and the desired optically pure As–P=O ligand (–)-**95** could be liberated from the platinum complex by the treatment with potassium cyanide. The cycloaddition reaction between DMPA and diphenylvinylphosphine sulfide, however, exhibited low selectivity and the diastereomeric mixture **97** (1:2) cannot be separated *via* column chromatography or fractional crystallization. Attempted separation of the enantiomers *via* the corresponding dihalogen complexes was also unsuccessful. When the chiral metal promoter was changed from palladium to platinum, the reaction selectivity is similar, but the major isomer (S_c,R_{As})-**102** and dichloro complex (–)-**103** could be separated *via* fractional crystallization and column chromatography. Alternatively they could be firstly converted into the corresponding iodide complexes (S_c,R_{As})-**105** and (–)-**104**, the two resulting iodide complexes could then be separated by means of column chromatography. The optically pure As–P=S ligand (+)-**106** can be liberated by treatment of (–)-**104** with potassium cyanide.

List of New Complexes


(+)-**43**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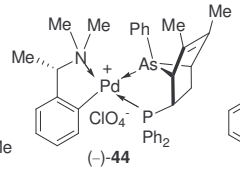
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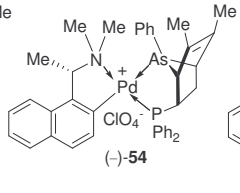
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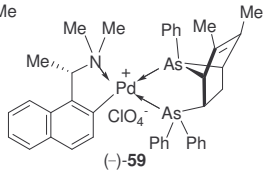
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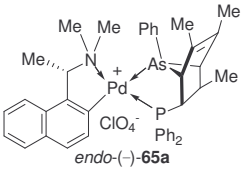
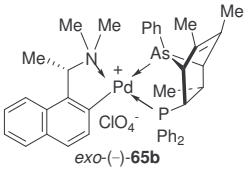

endo-(–)-**65a**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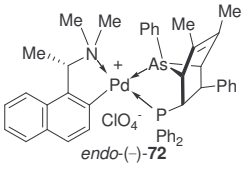
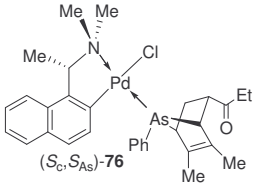
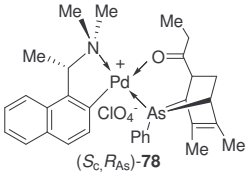
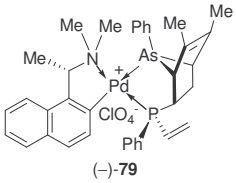

endo-(–)-**72**


(S_c,S_{As})-**76**


(S_c,R_{As})-**78**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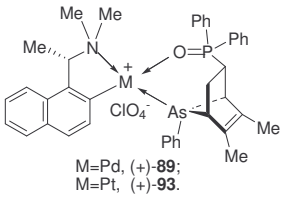
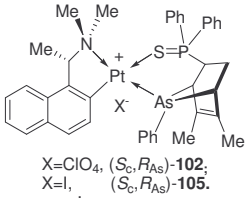
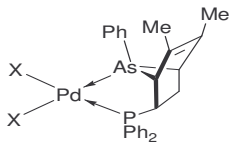
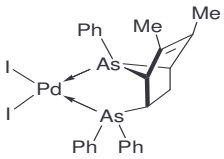

M=Pd, (+)-**89**;
M=Pt, (+)-**93**.


X=ClO_4, (S_c,R_{As})-**102**;
X=I, (S_c,R_{As})-**105.**


X=Cl, (–)-**45**;
X=Br, (–)-**50**;
X=I, (–)-**52**.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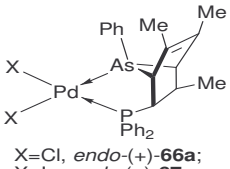
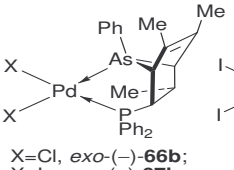
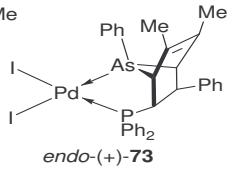

X=Cl, *endo*-(+)-**66a**;
X=I, *endo*-(+)-**67a**.


X=Cl, *exo*-(–)-**66b**;
X=I, *exo*-(–)-**67b**.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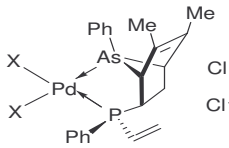
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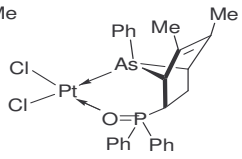
X=Br, (–)-**83**;
X=I, (–)-**85**.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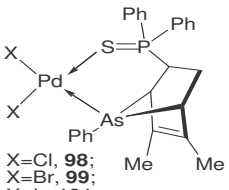
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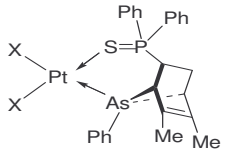
X=Br, **99**;
X=I, **101**.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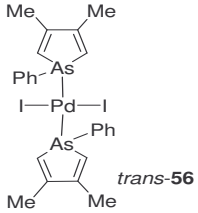
X=I, (–)-**104**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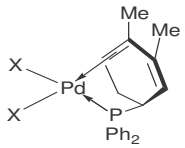
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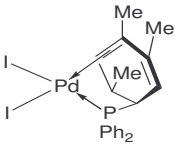
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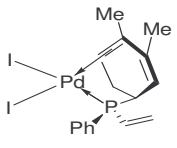
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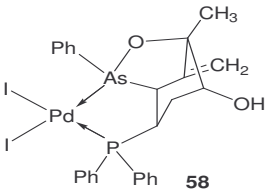
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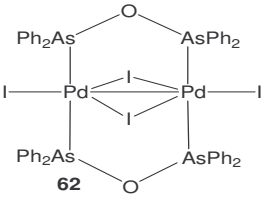
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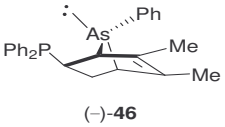
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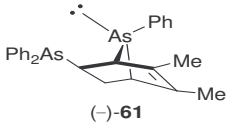
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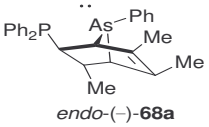
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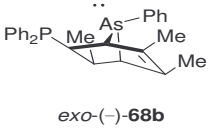
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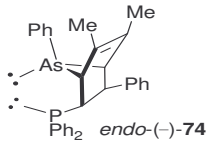
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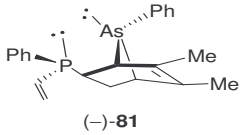
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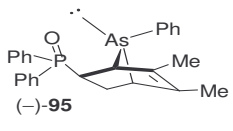
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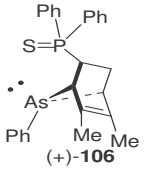
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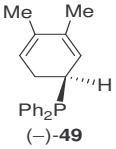
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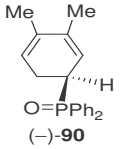
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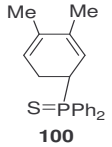
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Nomenclature

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

X-ray Structural Data

The single crystal X-ray analyses were kindly performed by Dr. Li Yongxin and Professor Mok Kum Fun at the Nanyang Technological University (Division of Chemistry and Biological Chemistry). Full structural data (listings of crystal and refinement data, bond distances and angles and thermal parameters) are available from Prof. Leung Pak-Hing upon request.

Abbreviations and Symbols

br	broad
c	sample concentration for O.R.D analysis
$CDCl_3$	chloroform-d_1
CD_2Cl_2	dichloromethane-d_2
$CHCl_3$	chloroform
CH_2Cl_2	dichloromethane
conc. HCl	concentrated hydrochloric acid
d	doublet

dd	doublet of doublet
ddd	doublet of doublet of doublet
decomp.	decomposed
DMPA	3,4-dimethyl-1-phenylarsole
DMPP	3,4-dimethyl-1-phenylphosphole
DMPPS	3,4-dimethyl-1-phenylphosphole sulfide
ee	enantiomeric excess
equiv.	equivalent
Et	ethyl
et al.	and others
g	gram(s)
h	hour(s)
Hz	hertz
IR	infrared
KCN	potassium cyanide
KBr	potassium bromide
m	multiplet
Me	methyl
mg	milligram
min	minute
mL	milliliter
Mp	melting point
NaI	sodium iodide

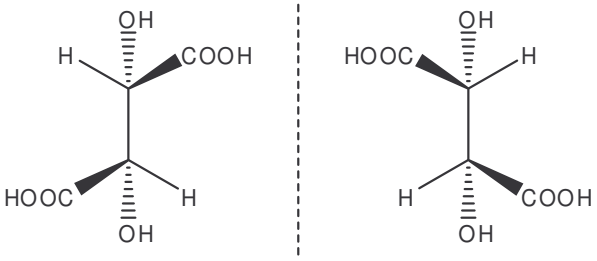
NMR	Nuclear Magnetic Resonance
Ph	phenyl
ppm	parts per million
q	quartet
qn	quintet
R	*rectus* (Latin: absolute configuration)
rt	room temperature
S	*sinister*(Latin: absolute configuration)
s	singlet
t	tertiary
THF	tetrahydrofuran
vs	versus
°	degree of angles
Å	angstrom(s)
ºC	degree Celsius
$^{n}J_{AB}$	n-bond coupling constant between nuclei A and B
δ	NMR chemical shift in ppm
$[\alpha]_D$	specific rotation measured at sodium D line (589nm)

CHAPTER 1

General Introduction

1.1 The Phenomenon of Chirality

In chemistry, the term chirality is used to describe a molecule that is non-superimposable on its mirror image. The chiral molecule and its mirror image are called enantiomers. Since chiral compounds exhibit optical activity, enantiomers are also called optical isomers. So far human hands are perhaps the most wildly recognized example of chirality: the right hand is a non-superimposable mirror image of the left hand; no matter how the two hands are changed, it is not possible for all the major features of both hands to superimpose.

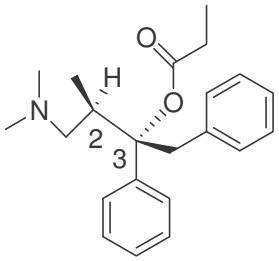


Enantiomers of tartaric acid

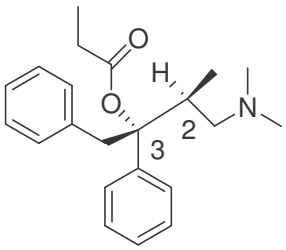
The discovery of chirality could be dated back to the 18th century. In 1815, Frenchman Jean-Baptiste Biot was the first person to discover the unique optical properties of mica.[1,2] Later in 1848, Louis Pasteur observed that the crystals of sodium

ammonium double salt of racemic tartaric acid came in two dissymmetric forms which were mirror images of one another,[3] and he successfully separated these two different forms of the compound by hand: solution of one form rotated polarized light clockwise, while the other form rotated it counterclockwise, and an equal mixture of the two had no polarizing effect on the light. So he correctly deduced that the molecule was dissymmetric.

Chiral compounds widely distributed in nature and play a critical role in the metabolism of all living organisms. They have a wide variety of successful applications in many fields such as pharmaceuticals, insecticides, herbicides and biological systems. In some cases, both enantiomers have a desirable, but different therapeutic effect. For example, dextropropoxyphene is an analgesic agent while levopropoxyphene is devoid of any analgesic properties but is an effective antitussive agent.[4]



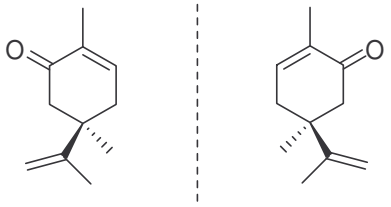
(*2R*, *3S*)-(+)-Dextropropoxyphene



(*2S*, *3R*)-(–)-Levopropoxyphene

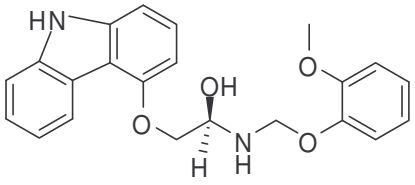
Sometimes the two enantiomers will have different effects as they interact differently with the chiral compounds. For instance, (*R*)-(–)-carvone is the aroma of spearmint, while its mirror image, (*S*)-(+)-carvone is the aroma of caraway.[5] The fact that the two enantiomers smell differently proves that olfactory receptors must contain

different chiral groups, allowing them to react more strongly to one enantiomer than to the other.

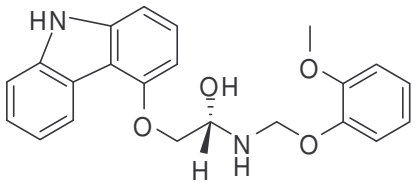


Enantiomers of carvone

In most cases, one isomer is effective but the other has lesser or no effect. For example, (*R*)-carvedilol that interacts with adrenoceptors is 100 times more powerful as a beta receptor than its (*S*)-isomer.[6]

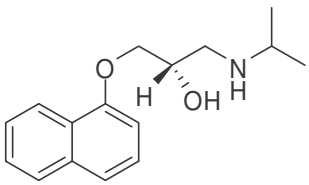


(*R*)-Carvedilol

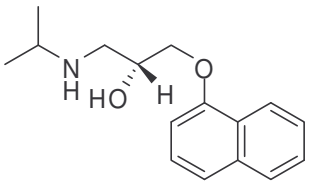


(*S*)-Carvedilol

Another example, (–)-propranolol is a good adrenoceptor antagonist, whereas (+)-propranolol is not.[7]

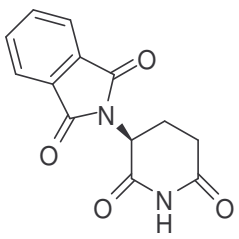


(–)-Propranolol

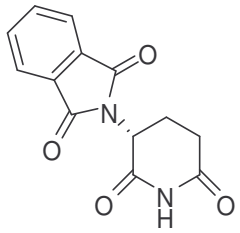


(+)-Propranolol

The most dramatic case is that one of the enantiomers is a very useful drug, but the other induces serious undesirable side effects or may even be causing death. There are many examples in this field. An example of this is thalidomide.[8-10] It normally exists in the racemic form, namely, it contains both right and left handed isomers in equal amounts. (*R*)-Enantiomer is an effective sedative, however, (*S*)-enantiomer is highly teratogenic which causes fetal abnormalities. It should be noted that the enantiomers can be interconverted in living organisms. That is, if a human is given (*S*)-thalidomide or (*R*)-thalidomide, both isomers can exist in the serum. Hence, administering only one enantiomer will not preclude the teratogenic effect in humans.

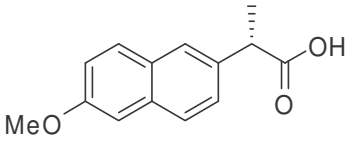


(*S*)-Thalidomide

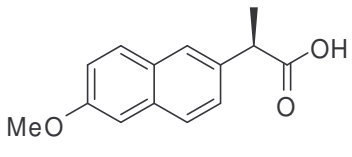


(*R*)-Thalidomide

In the case of naproxen, one enantiomer [(*S*)-naproxen] can be used to reduce arthritic pain, but the other enantiomer [(*R*)-naproxen] causes liver poisoning with no analgesic effect.[11]

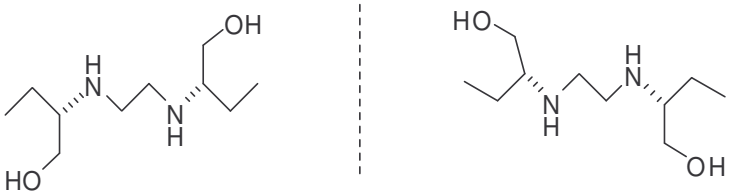


(*S*)-Naproxen



(*R*)-Naproxen

Another example is ethambutol. The (*S*, *S*)-ethambutol can be used to treat tuberculosis, whereas its (*R*, *R*)-enantiomer causes blindness.



(*S*, *S*)-Ethambutol (*R*, *R*)-Ethambutol

Thus, it is very important to produce highly pure chiral drugs because their enantiomers may have potential side effects or even high fatality. Therefore one of the most interesting areas of research for synthetic chemists is to prepare optically pure compounds in a selective manner, rather than a mixture of enantiomers.

1.2 Basic Synthetic Strategies for the Preparatin of Chiral Compounds

In the preparation of enantiomerically pure compounds, various well established methods have been developed. They will be briefly discussed in this section.

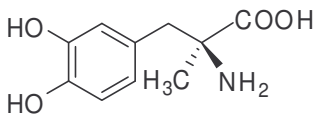
1.2.1 Chiral Pool Synthesis

The chiral pool approach makes use of the cheap, readily available enantiomerically pure natural products, such as sugars, amino acids, carbohydrates, lactic acid and their derivatives.[12] These starting materials can be converted to the desired

products through chemical processes with the retention or inversion of configuration or chirality. This strategy is especially useful if the desired molecule has a great resemblance to inexpensive enantiopure natural products. If not, a long, tortuous preparation process involving many steps with attendant losses in yield may be required. The reactions from chiral pool produce the least side-products, however, there is evident limitation due to the limited diversity of the chiral pool.

1.2.2 Resolution

Resolution is a process for the separation of racemic compounds into their enantiomers. It is an important method in the production of optically active drugs. Louis Pasteur was the first to demonstrate a resolution when he discovered the concept of optical activity by the manual separation of each optical isomer of tartaric acid crystals in 1849.[3] Now it is considered the classical method of obtaining chiral compounds. It can be divided into three categories: direct preferential crystallization, crystallization of diastereomeric compounds and kinetic resolution.



α-Methyl-L-dopa

The first method is widely applied in industrial applications, for example, the preparation of α-methyl-L-dopa.[13] But it is only technically possible for conglomerates,

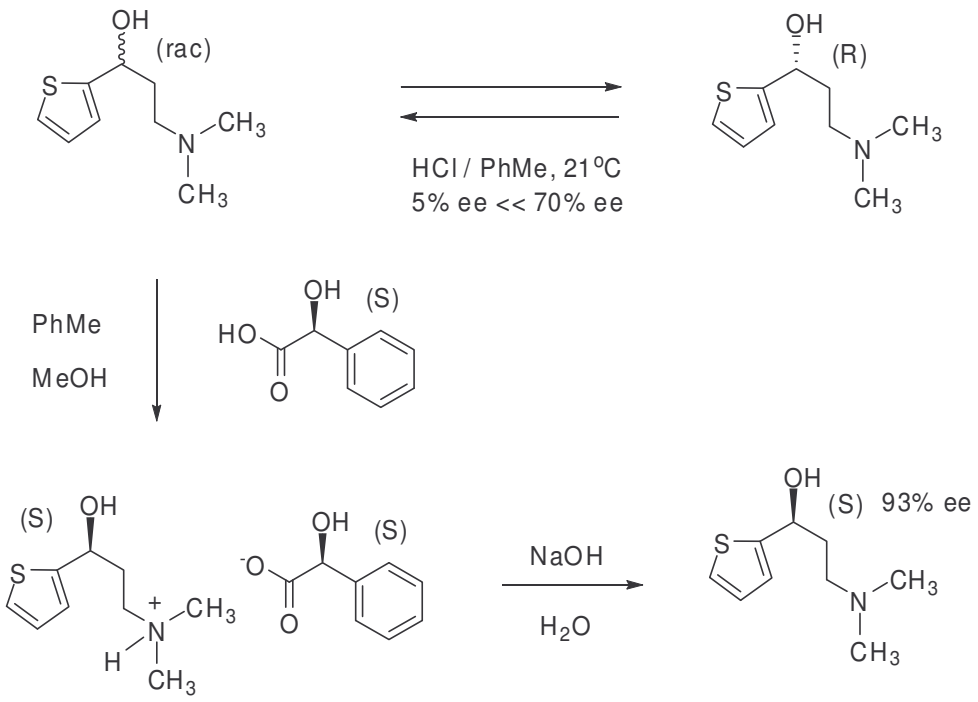
normally the mixture of two enantiomers. The success of preferential crystallization depends on the fact that for a conglomerate, the enantiomer is less soluble than the racemic mixture.

The second was introduced by Louis Pasteur in 1853 by resolving racemic tartaric acid with optically pure (+)-cinchotoxine.[14,15] This procedure relies on the fact that diastereomers, which are different from enantiomers, have different physical properties. The racemic substrate which is to be resolved is derived from optically pure reagents and the resultant diastereomeric compound is isolated, usually *via* crystallization or chromatography. Finally the desired enantiomer is regenerated from the corresonding diastereomers by chemical manipulation.

Another method of resolution, known as the kinetic resolution, was first observed by Marckwald and McKenzie in 1899 during the esterification reaction of racemic mandelic acid with optically pure (–)-menthol to produce a pair of diastereomeric esters.[16,17] It includes the selective reaction of one enantiomer of the racemic mixture with another chiral reagent due to the different reaction rates. Due to the asymmetry of the active site of the chiral compounds, one enantiomer is more favorable than the other and hence reacts faster. In a perfect case, one enantiomer is completely converted to the product whereas the other remains unchanged.

One modern-day method of chiral resolution is used in the organic synthesis of the drug Duloxetine (Scheme 1.1).[18] In one of its steps, the racemic alcohol is dissolved in a mixed solution of toluene and methanol. Then, chiral (*S*)-mandelic acid is added into the above mixture. The (*S*)-enantiomer of the alcohol generates an insoluble diastereomeric salt with the mandelic acid and can be isolated from the solution *via* filtration. Simple

deprotonation with NaOH liberates free (*S*)-alcohol. On the other hand, the (*R*)-alcohol remains in the solution unchanged and is recycled back to the racemic mixture *via* epimerization with HCl in toluene.



Scheme 1.1

Nevertheless, one disadvantage of chiral resolution of racemates is that the maximum obtainable yield of each enantiomer is not more than 50%. In practice, repeated recrystallizations are often necessary to ensure total purity, and hence the yields are quite low.

1.2.3 Asymmetric Synthesis

The solution for the aforementioned problem is asymmetric synthesis. Asymmetric synthesis can be defined as a reaction where an achiral unit is converted by a reactant into a chiral unit, so that the stereoisomeric products could be formed in unequal amounts. The excess of one enantiomer over the other is commonly expressed in percentage as enantiomeric excess (ee).

Asymmetric synthesis is a kinetic phenomenon. Usually, only one chiral reagent is needed. The interaction of two reactants causes different diastereomeric transition states. The difference in transition state energy controls the degree of selectivity, and the lower energy pathway will provide the major enantiomer no matter what its thermodynamic feature.

The chiral auxiliary affecting the asymmetric synthesis can be used either catalytically or stoichiometrically and they may be chemical or enzymatic. Among the various techniques employed, enantioselective catalysis using chiral metal complexes should be one of the most flexible and common methods for such synthesis. The discovery by Wilkinson and coworkers that chlorotris(triphenylphosphine)rhodium [$RhCl(PPh_3)_3$] can be used as an efficient hydrogenation catalyst for unhindered olefins, sparked a considerable interest in asymmetric catalysis.[19-30] The idea of displacing the triphenylphosphine in Wilkinson's catalyst with a chiral phosphine has produced lots of powerful homogeneous catalysts which allow the synthesis of chiral compounds in high enantiomeric purity. The stereospecificity of the reaction is affected by the choice of the metal and ligand with suitable substituents capable of directing the course of the reaction by electronic and/or steric factors.

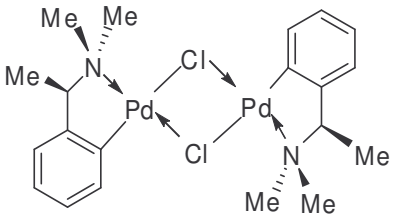
1.3 Preparation of Chiral Arsines

Compared with the extensive work with phosphines, relatively few syntheses of chiral arsines have been reported hitherto.[31-37] The reason for this is perhaps due to their toxicity and their instability resulting in difficulty in the synthesis and characterization. Since the resolution of a simple ammonium salt of the type $[NR^1R^2R^3\ R^4]^+$ in 1899, the question of optical activity in arsonium and phosphonium ions of the type $[ER^1R^2R^3\ R^4]^+$ became paramount.[38-41] Not until 1962 was the first simple arsonium ion resolved and converted into stable optically active tertiary arsines of the type $AsR^1R^2R^3$ after following similar work on phosphonium ions and phosphines in 1959.[42] Due to improvements in instrumental techniques, especially X-ray crystallography and NMR spectroscopy etc, the field has now developed rapidly and they can be used to determine directly the absolute configurations of the enantiomers and to investigate the stereochemistry, stability and properties of organic and inorganic arsenic derivatives. A brief introduction on the development of bidentate and multidentate chiral arsine complexes is given in the following section.

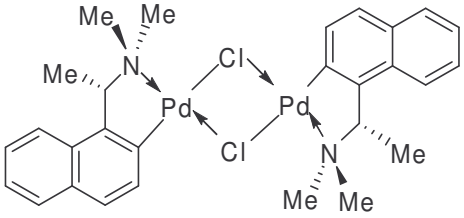
1.3.1 Bidentate Chiral Arsines

In view of the potential usefulness of optically active bidentate arsines as ligands in coordination chemistry and asymmetric catalysis, versatile synthetic methods of these compounds are essential for the development of this field.

1.3.1.1 Asymmetric As–S Bidentate Chiral Arsines



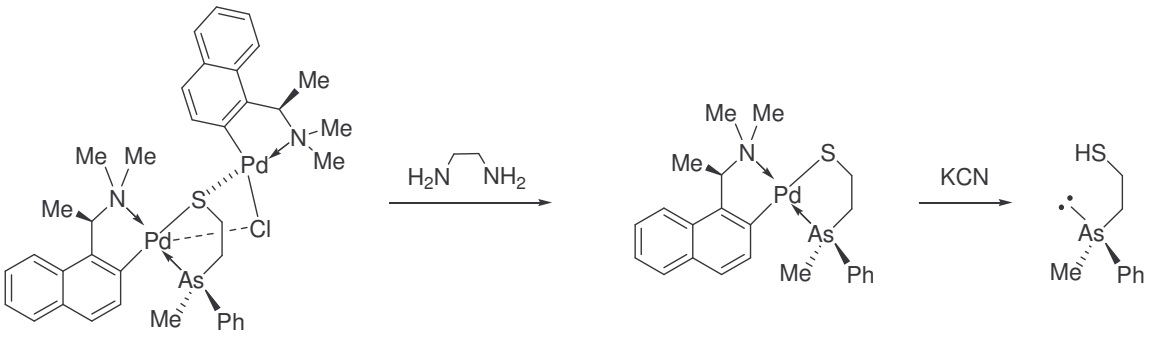
(*R*)-(–)-**1**



(*S*)-(+)-**2**

Resolution of racemic arsines by complexation with chiral transition metal complexes is a useful and reliable method. The dimeric complexes (+/–)-**1** and (+/–)-**2** were found to be particularly effective as resolving agents for chiral bidentates.[43-45] In 1986, Wild *et al.* reported that the asymmetric chelating compound, (±)-(2-mercaptoethyl)methylphenylarsine **3**, could be resolved into its optical antipodes by the fractional crystallization of unusual μ-thiolato diastereomers **4**, which was obtained from 2 equivalent of (*R*)-**2**, 1 equivalent of each of **3** and triethylamine (Scheme 1.2).[46] The single crystal and molecular structure of (R,R,S_{As},S_s)-**4** was determined. Treatment of the pure diastereomer with 1,2-diaminoethane removed one of the resolving units and afforded the monomeric (R,S_{As})-**5** from which the optically active (*R*)-**3** with $[\alpha]_D$ –16.7° (CH_2Cl_2) was liberated by treatment with KCN. It could be distilled without racemization. The optical purity of the bidentate arsine compound was confirmed by preparing the kinetically labile nickel complex of the deprotonated ligand, which showed no evidence of the thermodynamically stable meso diastereomer in the ^{1}H NMR spectrum in $CDCl_3$.[47] The (*S*)-enantiomer of the ligand was obtained in a state of 72% optical purity from the residual mixture of the epimeric complexes and was subsequently brought

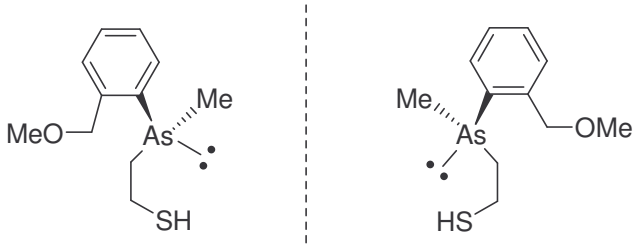
to purity by fractional crystallization. However, the analogous light-sensitive 2-mercaptoethylphosphine required alkylation before it could be displaced from the metal.[48,49]



(R, R, S_{As}, S_S)-**4** (R, S_{As})-**5** (R)-**3**

Scheme 1.2

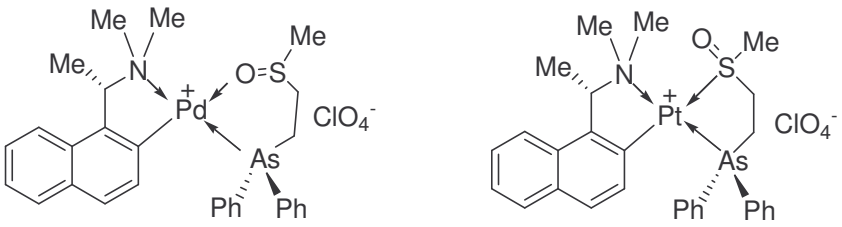
By following a similar procedure, the enantiomers of the corresponding (±)-(2-mercaptoethyl)[2-(methoxymethyl)phenyl] methylarsine **6** were obtained.[50,51]



(±)-**6**

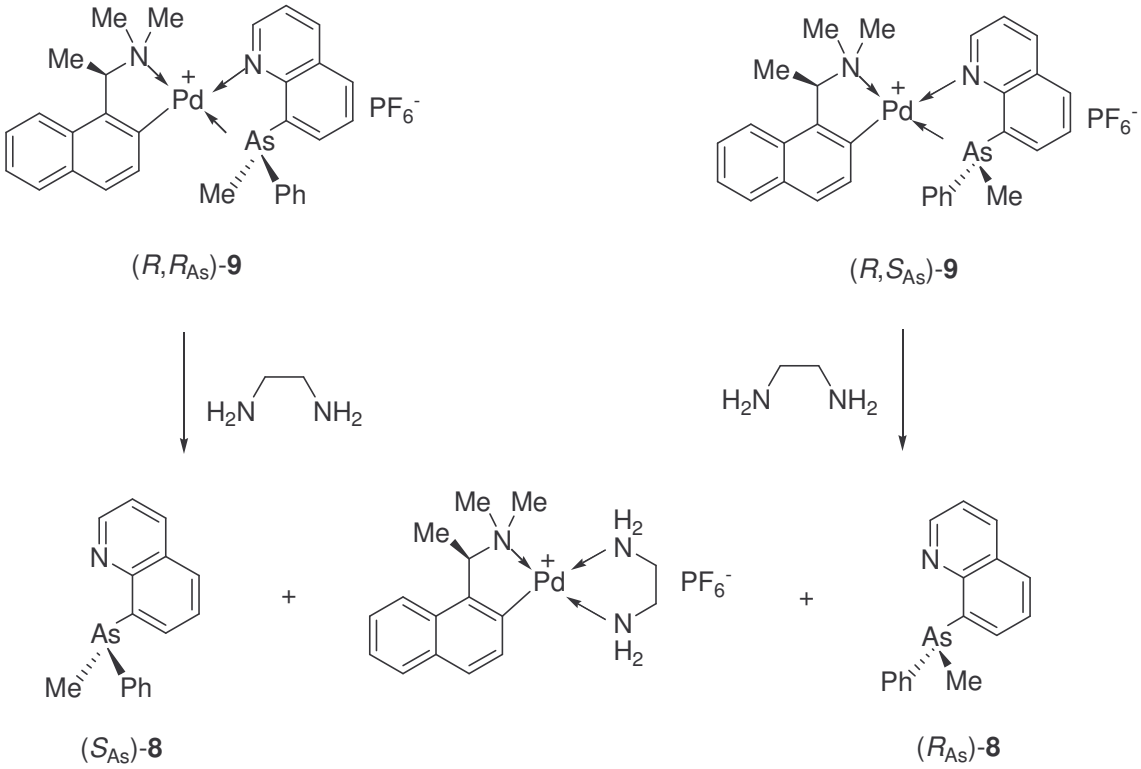
Another optical resolution of the asymmetric chelating agent (±)-[(2-methylsulfinyl)ethyl]diphenylarsine **7** has been achieved *via* the same method.[52-54] In contrast to the palladium(II) complex that coordinates to the metal *via* arsenic and oxygen, the As–O chelation is not observed in the presence of platinum(II) complexes

although there will be less severe ligand-ligand interactions if the As–(S)O ligands form six-membered chelate rings in these square-planar systems. The crystal structure of the arsenic complex shows that the ligand is coordinated to platinum(II) in both diastereomers exclusively as a bidentate chelate *via* arsenic and sulfur atoms.



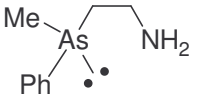
1.3.1.2 Asymmetric As–N Bidentate Chiral Arsines

(a) Metal Complexation



Scheme 1.3

Several As–N heterobidentate ligands have been resolved with the use of palladium resolving agent (*R*/*S*)-**2**.[45,55,56] Methylphenyl(8-quinolyl)arsine **8** was resolved by the fractional crystallization of a pair of internally diastereomeric palladium complexes (R,R_{As})- and (R,S_{As})-**9** which contained the chiral resolving agent and an optically pure As–N ligand.[45] These ligands were readily liberated from the palladium complex by 1, 2-diaminoethane (Scheme 1.3). The chiral amine complex was converted back into the chloro-bridged resolving agent (*R*)-**2** with HCl.



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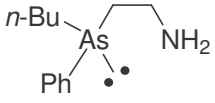

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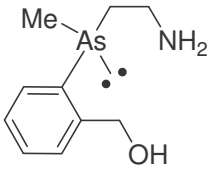

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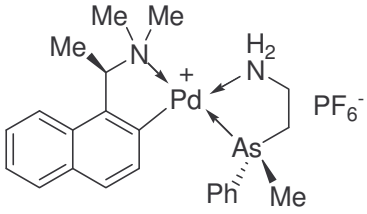
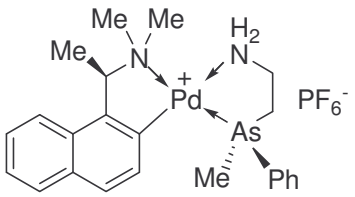
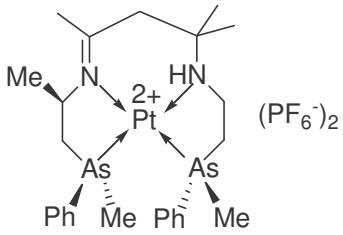


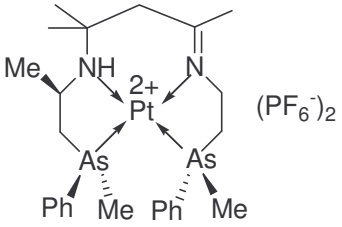
(*R*, R_{As})-**13**



(*R*, S_{As})-**13**



14a



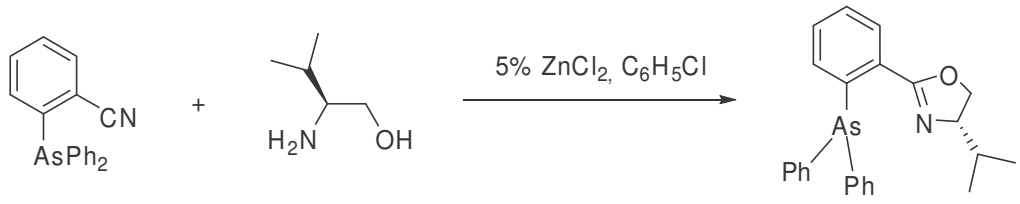
14b

The asymmetric bidentate ligand 1-amino-2-(methylphenylarsino)ethane **10** has been resolved *via* the separation of the diastereomers (R,R_{As})- and (R,S_{As})-**13**.[55] A mixture

of the epimers **14a** and **14b** was obtained in high yield when the complex (+)-*cis*-[Pt((*R*)-**10**)$_2$](PF$_6$)$_2$ was stirred for 16 h in acetone at 25 ºC in the presence of a trace amount of (*S*)-**10**. In 1985, Fujita *et al.* also reported the resolutions of compound **10** and the similar n-butyl analogue **11**, but neither arsine was isolated.[56] The highly functionalized arsine **12** was resolved with the same method.[57]

(b) Synthesis from Chiral Pool

The tertiary (*o*-cyanophenyl)diphenylarsine was reacted with (*S*)-2-amino-3-methyl-1-butanol in the presence of $ZnCl_2$ catalyst in chlorobenzene to generate a new optically active arsine-oxazoline ligand in 54% yield (Scheme 1.4).[58] The palladium complex of this ligand can catalyze the copolymerization of CO and olefin, but with low conversions.[59]

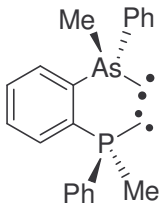


Scheme 1.4

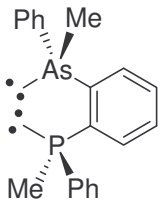
1.3.1.3 Asymmetric As–P Bidentate Chiral Arsines

(a) Metal Complexation

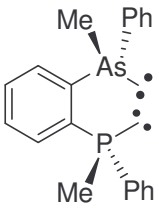
The resolution of the (R_{As}*,R_P*) and (R_{As}*,S_P*) diastereomers of the asymmetric As–P heterobidentate 1-(methylphenylarsino)-2-(methylphenylphosphino)benzene **15** has been achieved *via* the method of metal complexation.[60,61] The (R_{As}*,R_P*)-(±) form of the above ligand was resolved *via* the separation of the diastereomers [*R*,(R_{As},R_P)]-(–)- and [*R*,(S_{As},S_P)]-(+)-**16** and the (R_{As}*,S_P*)-(±) form *via* the separation of [*R*,(R_{As},S_P)]- (+)- and [*R*,(S_{As},R_P)]-(–)-**17**. When heated at 140 ºC for 2 h, (R_{As}*,R_P*)-(±)- and (R_{As}*,S_P*)-(±)-**15** epimerized at phosphorus, however, epimerization at arsenic was not effected by the usual racemizing conditions for tertiary arsines (methanolic HCl); indeed, optically active salts protonated at phosphorus were isolated.



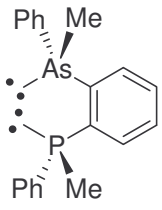
(R_{As},R_P)-(+)-**15**



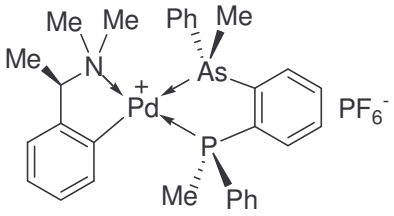
(S_{As},S_P)-(–)-**15**



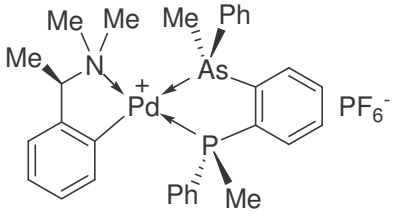
(R_{As},S_P)-(+)-**15**



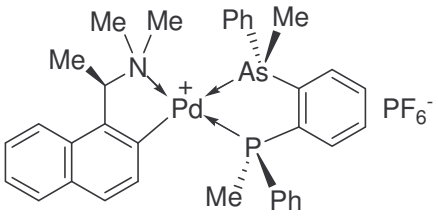
(S_{As},R_P)-(–)-**15**



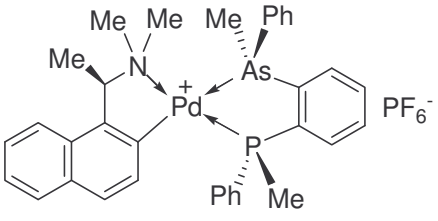
[*R*,(R_{As},R_P)]-(–)-**16**



[*R*,(S_{As},S_P)]-(+)-**16**

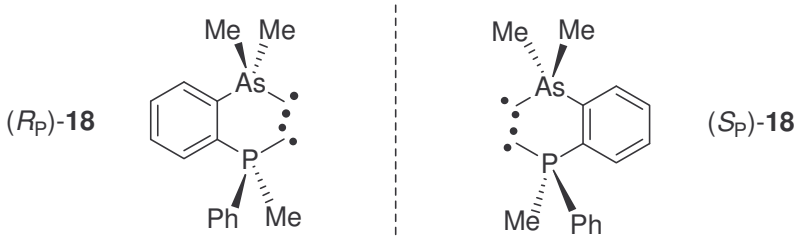


[*R*,(R_{As},S_P)]-(+)-**17**



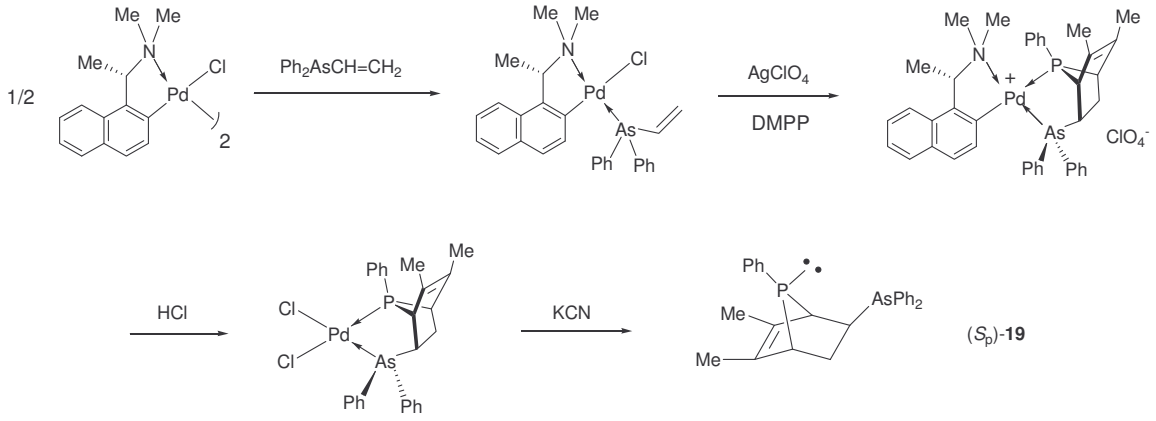
[*R*,(S_{As},R_P)]-(–)-**17**

Another similar As–P bidentate (±)-1-(dimethylarsino)-2-(methylphenylphosphino)benzene **18** was synthesized by the reaction of sodium dimethylarsenide with (±)-1-chloro-2-(methylphenylphosphino)benzene in THF. Its resolution has been achieved by the same method of metal complexation.[62]



(b) Asymmetric Diels–Alder Reactions

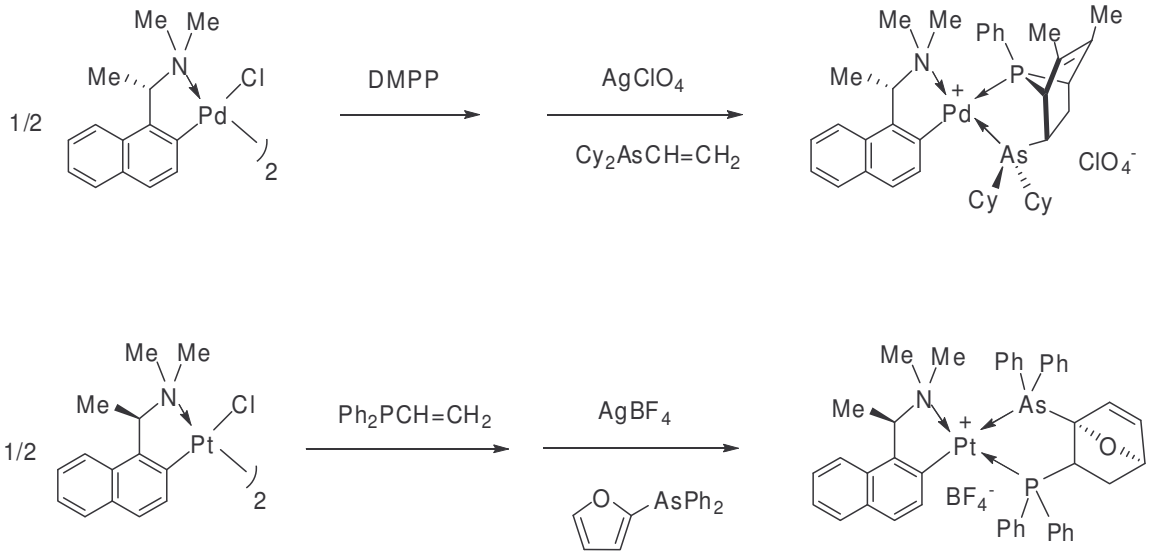
The first asymmetric synthesis of As–P heterobidentate was reported by Leung *et al.* in 1996.[63] The enantiomerically pure rigid bidentate ligand (–)-{5-(diphenylarsino)-2,3-dimethyl-7-phenyl-7-phosphabicyclo[2.2.1]}hept-2-ene **19** was prepared *via*



Scheme 1.5

asymmetric [4 + 2] cycloaddition between diphenylvinylarsine and 3,4-dimethyl-1-phenylphosphole (DMPP) using the chiral organopalladium(II) complex (*S*)-**2** as the reaction promoter (Scheme 1.5). The absolute configurations of the four newly generated chiral centers have been confirmed by a single crystal X-ray analysis.

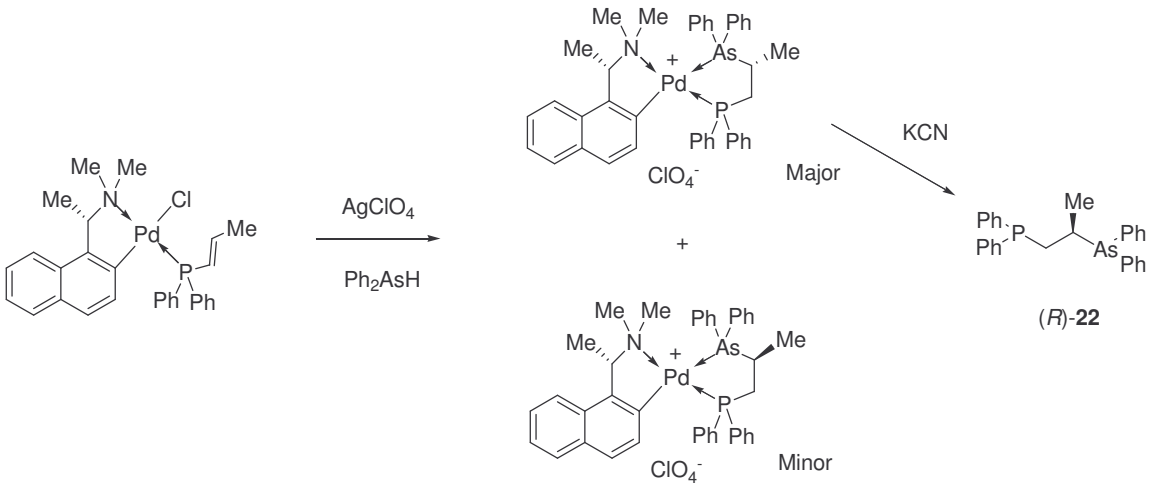
Two analogous As–P bidentate ligands 5-(dicyclohexylarsino)-2,3-dimethyl-7-phenyl-7-phosphabicyclo[2.2.1]hept-2-ene **20** and 4-(diphenylarsino)-5-(diphenylphosphino)-7-oxabicyclo[2.2.1]hept-2-ene (+)-**21** have been achieved by intramolecular [4 + 2] Diels–Alder reactions between dicyclohexylvinylarsine and 3,4-dimethyl-1-phenylphosphole or between diphenylvinylphosphine and 2-furyldiphenylarsine respectively with the similar chiral reaction promoters (Scheme 1.6).[64]



Scheme 1.6

(c) Asymmetric Hydroarsination

Quite recently, Leung *et al*. reported another method to synthesize the enantiomerically pure As–P hetero-bidentate ligands.[65] The asymmetric optically pure bidentate (*R*)-(+)-1-(diphenylphosphino)-2-(diphenylarsino)propane (*R*)-**22** has been prepared stereoselectively by the novel asymmetric hydroarsination reaction between (*E*)-diphenyl-1-propenylphosphine and diphenylarsine using the same reaction promoter (*S*)-**2** (Scheme 1.7).

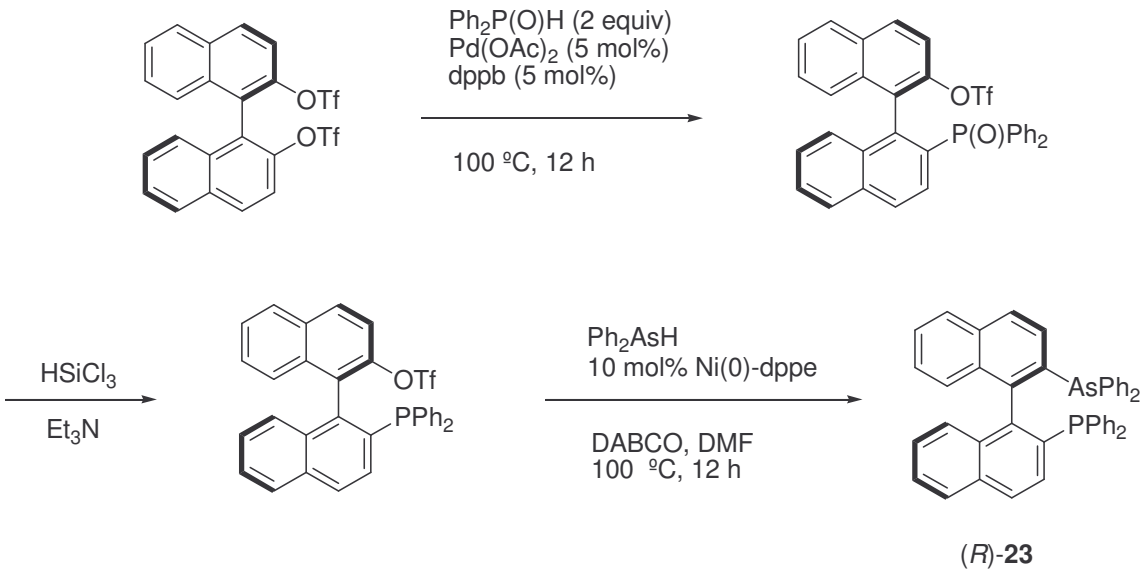


Scheme 1.7

(d) Synthesis from Chiral Pool

Since the discovery of BINAP by Noyori in 1980, this ligand as asymmetric catalyst has been successfully applied in the scientific and economic field. In 1998, Shibasaki *et al*. reported the synthesis of an analogous chiral 2-diphenylarsino-2'-diphenylphosphino-1,1'-binaphthyl (BINAPAs) (*R*)-**23** and it was found to be an

effective ligand in an asymmetric Heck reaction using an aryl triflate (Scheme 1.8).[66]



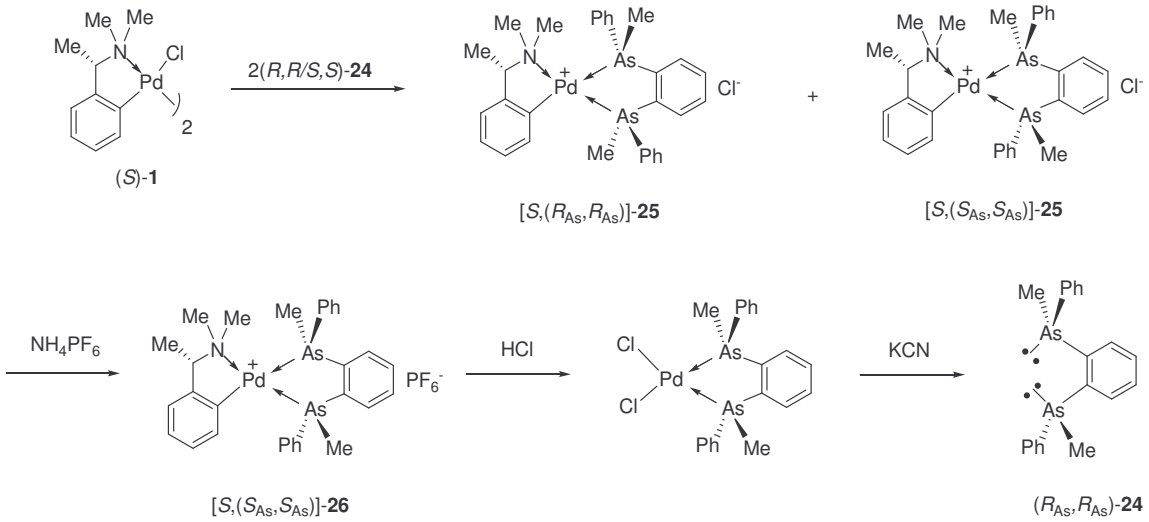
Scheme 1.8

1.3.1.4 Chiral Diarsines

(a) Metal Complexation

The chelating bis(tertiary arsine) 1,2-phenylenebis(methylphenylarsine) **24** has been prepared in 80% yield from sodium methylphenylarsenide and1,2-dichlorobenzene in THF.[67] Recrystallization of the equimolar mixture of (R_{As}*,R_{As}*) and (R_{As}*,S_{As}*) diastereomers of **24** from diethyl ether-methanol produced the (R_{As}*,R_{As}*) diastereomer as air-stable needles; the more soluble (R_{As}*,S_{As}*) diastereomer was recoverd *via* its sparingly soluble nickel(II) chloride derivative. The bridge-splitting reaction between (*R,R,/S,S*)-**24** and (*S*)-**1** in methanol gave a solution of the chloride salts [*S*,(R_{As},R_{As})]- and

[*S*,(S_{As},S_{As})]-**25** which when treated with 1 equiv. NH_4PF_6, yielded the less soluble [*S*,(S_{As},S_{As})]-**26**. Compound (R_{As},R_{As})-**24** was cleanly liberated from [*S*,(S_{As},S_{As})]-**26** in a dichloromethane-water mixture (Scheme 1.9). The corresponding optically active (S_{As},S_{As})-**24** was obtained by a similar procedure involving (*R*)-**1**.

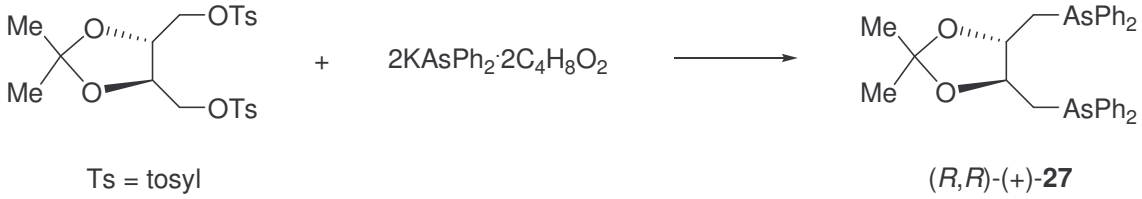


Scheme 1.9

(b) Synthesis from Chiral Pool

The arsenic analogue of Diop, (+)- and (–)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylarsino)butane **27**, was synthesised by the reaction of commercially available (+)- and (–)-1,4-ditosyl-2,3-*O*-isopropylidene-threitol with potassium diphenylarsenide dioxanate in a mixture of THF and dioxane (Scheme 1.10).[68,69] These compounds are air-stable solids. The ligands produce similar optical yields to Diop in the asymmetric hydrosilylation of ketones, however, lower optical yields for the asymmetric

hydrogenation of α-acetamidocinnamic acid.

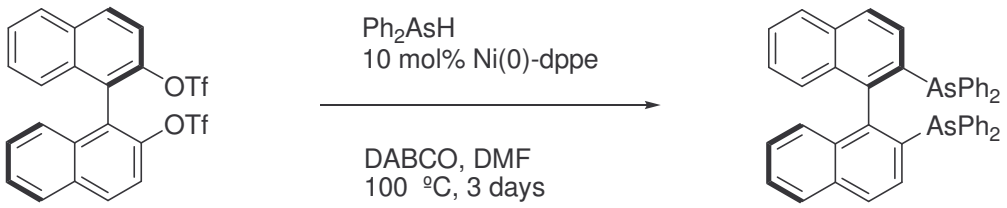


Ts = tosyl

(*R*,*R*)-(+)-**27**

Scheme 1.10

The arsine analogue of BINAP, 2,2'-bis(diphenylarsino)-1,1'-binaphthyl (BINAs) (*R*)-**28** was prepared by means of heating a mixture of the chiral ditriflate of binaphthol, diphenylarsine and 1,4-diazabicyclo[2.2.2]octane (DABCO) with 10 mol% bis(1,5-cyclooctadiene)nickel and 11 mol% bis(diphenylphosphino)ethane in DMF at 100 ºC for 3 days in 34% isolated yield and found to be effective in an intramolecular asymmetric Heck reaction using alkenyl iodide (Scheme 1.11).[70]



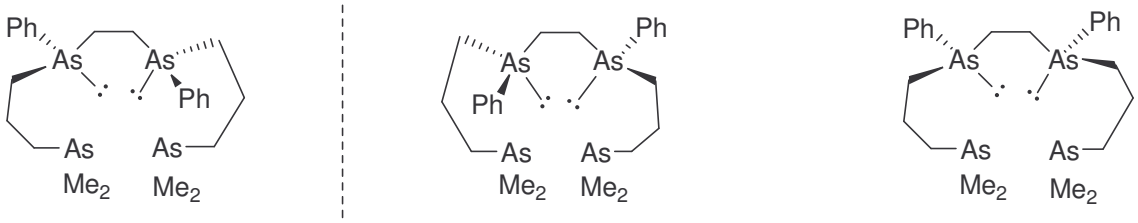
(*R*)-**28**

Scheme 1.11

1.3.2 Multidentate Chiral Arsines

1.3.2.1 As–As Multidentate Chiral Arsines

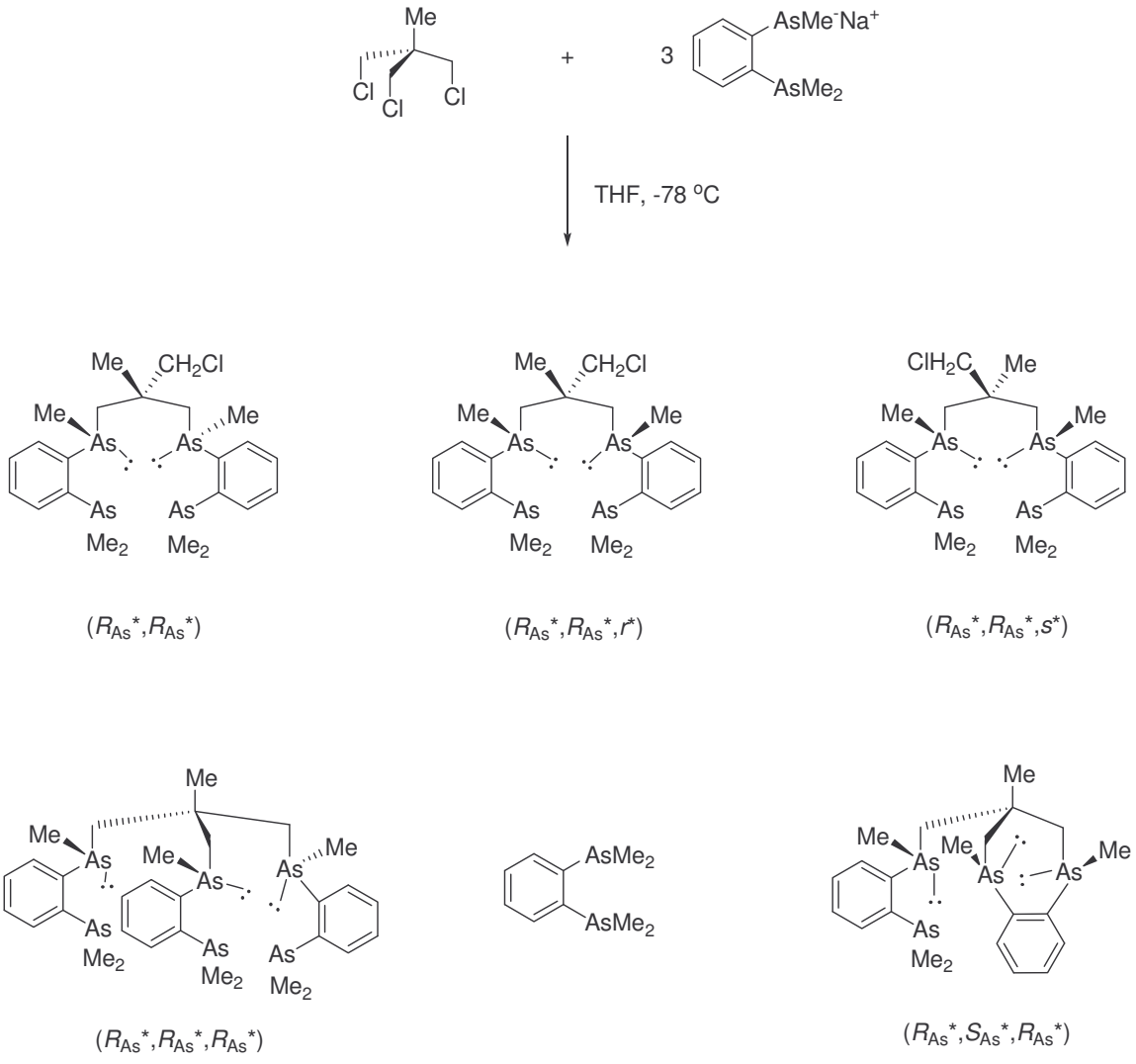
The quadridentate tetra(tertiary arsine) ligand **29** has been separated into (R_{As}*,R_{As}*) and (R_{As}*,S_{As}*) diastereomers *via* fractional crystallization of dichlorocobalt(II) complexes.[57] The complex [$CoCl_2$(**29**)]Cl was obtained in *ca* 80% yield from the reaction of ligand with cobalt(II) chloride in methanolic HCl in air which consisted *ca* 60% of the blue *cis*-[$CoCl_2${(R_{As}*,R_{As}*)-**29**}]Cl, (R_{As}*,R_{As}*)-**30**, and *ca* 40% of the green *trans*-[$CoCl_2${(R_{As}*,S_{As}*)-**29**}]Cl, (R_{As}*,S_{As}*)-**30**. Liberation of the two forms of the complex with cyanide afforded the pure (R_{As}*,R_{As}*) and (R_{As}*,S_{As}*) diastereomers of **29**. The reaction between the complex (R_{As}*,R_{As}*)-**30** and (–)-dibenzoylhydrogentartrate afforded the corresponding pair of diastereomeric *cis*-*α*-complexes that were separated and individually converted into the perchlorate salts, from which the respective enantiomers of (R_{As}*,R_{As}*)-**29** were displaced with KCN.



(*R*,R**)-**29** (*R*,S**)-**29**

Another example involved the reaction of 1,1,1-tri(chloromethyl)ethane with *ca* three equivalents of sodium or lithium (2-dimethylarsinophenyl)methylarsenide in THF to give several products including the tetra(tertiary arsine) (R_{As}*,R_{As}*)-, (R_{As}*,S_{As}*,*r**)-

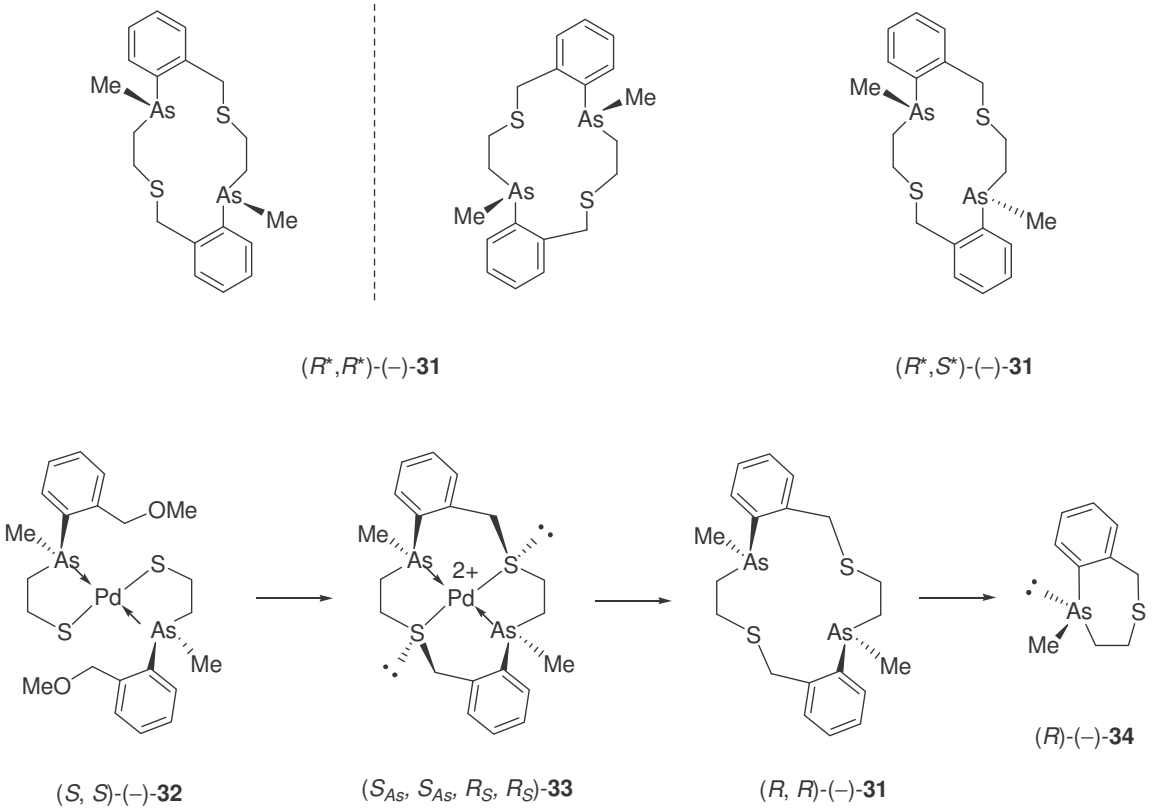
and (R_{As}*,S_{As}*,*s**)-1-(chloromethyl)-1,1-bis{[(2-dimethylarsinophenyl)methylarsino] methyl}ethane and the hexa(tertiary arsine) (R_{As}*,R_{As}*,R_{As}*)-1,1,1-tris{[(2-dimethylarsinophenyl)methylarsino]methyl}ethane (Scheme 1.12).[71] The latter was the first example of a chiral hexa(tertiary arsine) ligand. The products from the reaction were separated by the means of complexation to cobalt(III).



Scheme 1.12 Only one enantiomer of each chiral compound is shown.

1.3.2.2 As–S Multidentate Chiral Arsines

The air-stable enantiomers of (R_{As}*,R_{As}*)-**31** were obtained by treatment of $CHCl_3$ solution of the respective enantiomers of the palladium(II) complex of deprotonated **6**, (S_{As},S_{As})-(–)- and (R_{As},R_{As})-(+)-**32**, with boron tribromide and subsequent replacement of the optically pure forms of the *trans*-As_2S_2 ligand from the intermediate complexes with KCN.[50] The reaction of the thermodynamically preferred *trans* diastereomer of the precursor complex (S_{As},S_{As})-(–)-**32** produced stereoselectively the most stable one amongst six diastereomers of the product complex, that is (S_{As},S_{As},R_S,R_S)-**33**. The

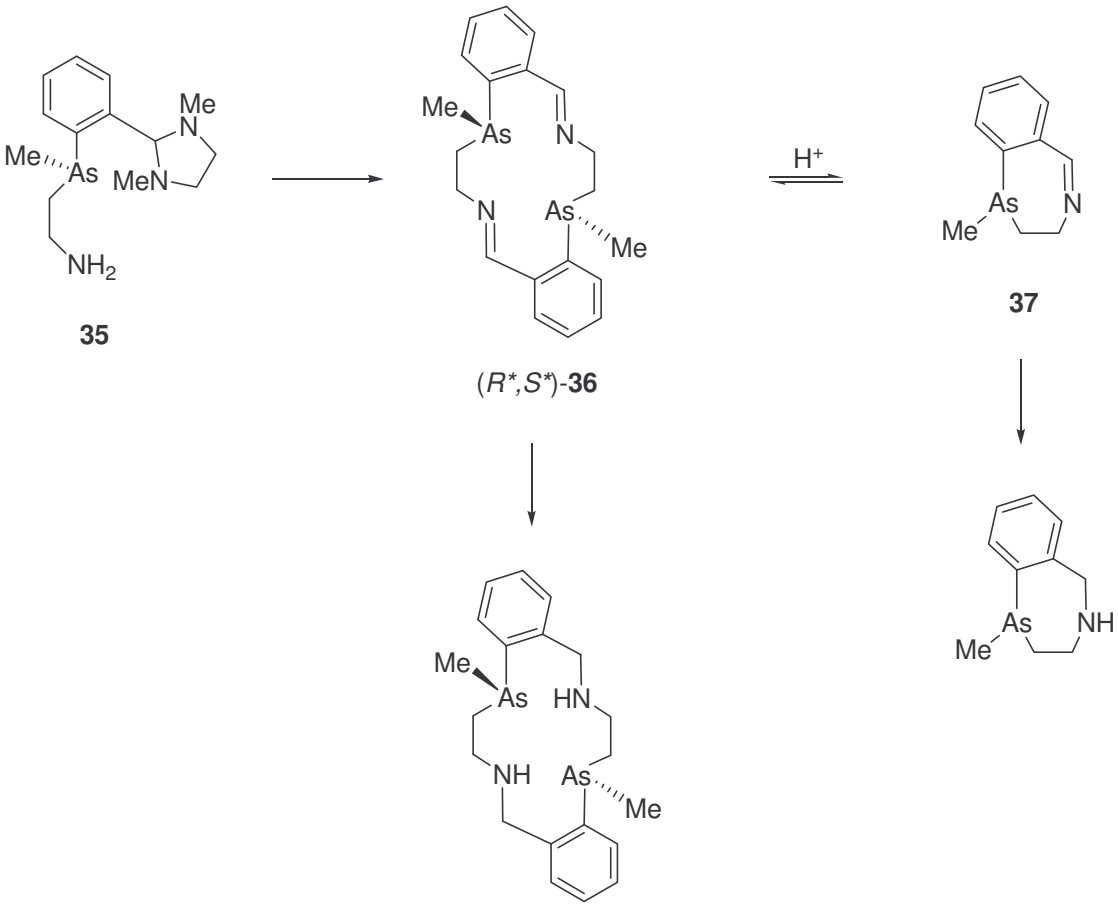


Scheme 1.13

cyclization proceeded in 79% yield to produce 66% (R_{As},R_{As})-(–)-**31** and 13% (*R*)-(–)-**34** (Scheme 1.13). However, (R_{As}*,S_{As}*)-**31** was quantitatively transformed into (R_{As}^{*},R_{As}^{*},S_{S}^{*},S_{S}^{*})-**31** after half an hour of heating in dimethyl sulfoxide when it was coordinated to palladium.

1.3.2.3 As–N Multidentate Chiral Arsines

In 1988, Wild *et al*. reported the preparation of the pure diastereomers and enantiomers of *trans*-As_2N_2 macrocycles.[72] In a dramatic demonstration of stereospecificity, (±)-**35** was heated at 80 ºC *in vacuo* and yielded diastereomerically pure (R_{As}*,S_{As}*)-**36** in high yield (Scheme 1.14). The diimine rearranged quantitatively into a 7-membered ring (±)-**37** in the solution of $CHCl_3$; (R_{As}*,S_{As}*)-**36** was recovered when the solvent was removed. Thus, (R_{As}*,R_{As}*)-**36** could not be isolated and the preparation of (R_{As}*,S_{As}*)-**36** from (±)-**35** is totally stereospecific. The individual enantiomers of (R_{As}*,R_{As}*)-**36**, namely (R_{As},R_{As})- and (S_{As},S_{As})-**36**, however, could be prepared by asymmetric synthesis and each individual enantiomer was optically active. Under acidic conditions, the reaction of (R_{As}*,S_{As}*)-**36** with (*R*)-**2** produced a diastereomerically pure palladium complex containing (R_{As},R_{As})-**36** after a work-up, involving treatment of the reaction mixture with ammonium hexaflurophosphate. Chiral (R_{As},R_{As})-**36** could be liberated from the palladium complex. Reduction of (R_{As}*,S_{As}*)- and (R_{As},R_{As})-**36** with lithium aluminium hydride gave the corresponding diamines.

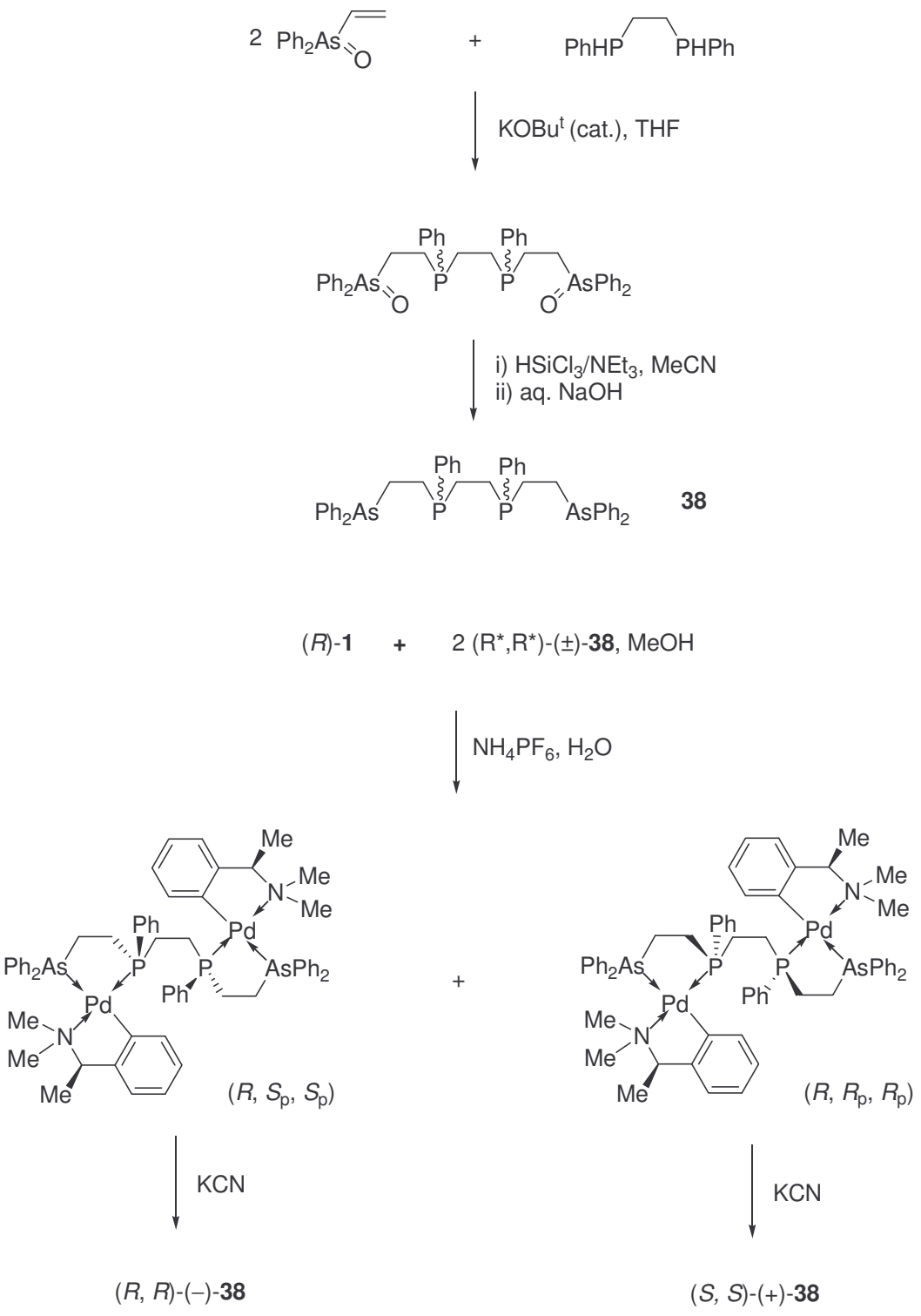


Scheme 1.14

1.3.2.4 As–P Multidentate Chiral Arsines

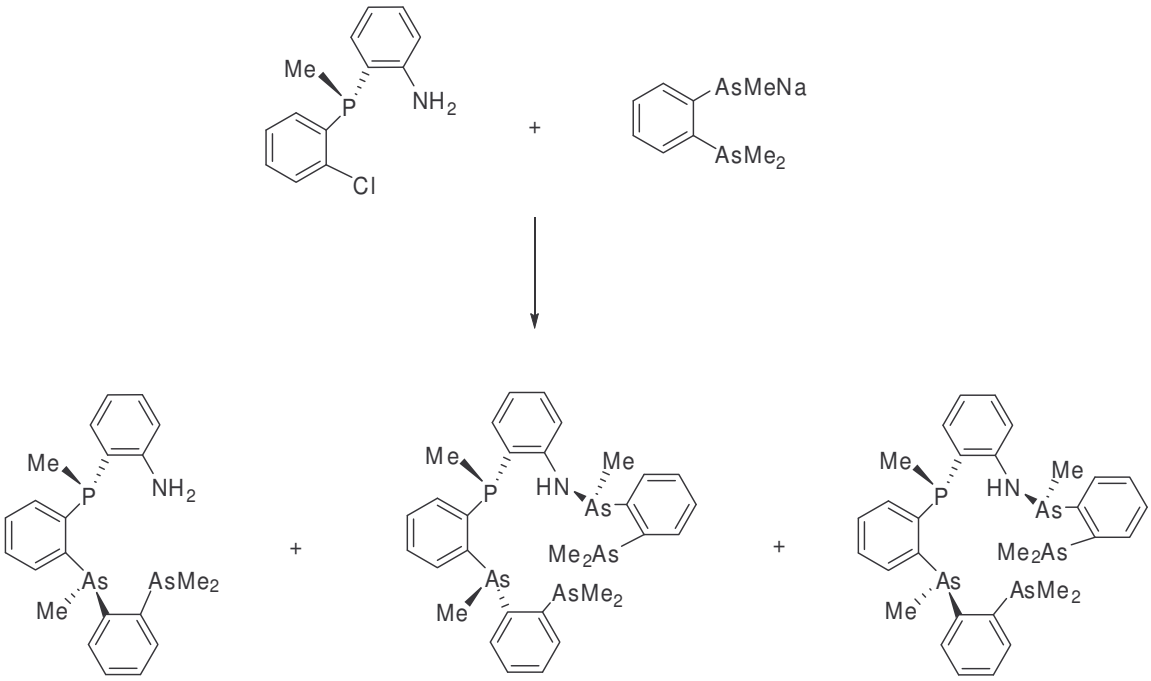
The reaction of diphenylvinylarsine oxide with 1,2-bis(phenylphosphino)ethane in the presence of ^{t}BuOK produced the *anti*-Markovnikov product (*R**, *R**)-(±)/(*R**, *S**)-1,1,4,7,10,10-hexaphenyl-1,10-diarsa-4,7-diphosphadecane dioxide-1*AsO*, 10*AsO*. The quadridentate As_2P_2 ligand (*R**, *R**)-(±)/(*R**, *S**)-**38** was obtained in 84% overall yield after reduction with $HSiCl_3/NEt_3$ in boiling acetonitrile (Scheme 1.15).[73] The corresponding (*R**, *R**)-(±) form of the multidentate ligand has been resolved *via* metal complexation with (*R*)-**1** before the separation of the diastereomers by fractional

crystallization.



Scheme 1.15

Some chiral As–P–N multidentate ligands were obtained *via* stereoselective synthesis (Scheme 1.16). The structure of these ligands was characterized by the X-ray structure analysis of the corresponding cobalt(III) complexes.[74]



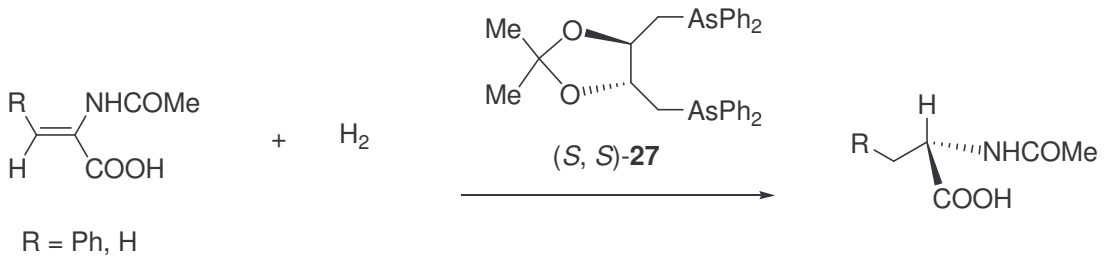
Scheme 1.16

1.3 Application of Chiral Arsines in Asymmetric Syntheses

Despite the uncertain beginning, a variety of optically active tertiary arsines is now available for application in inorganic and organic synthesis. Tertiary arsines are powerful ligand for metals over a range of oxidation states, a feature that makes them particularly suitable for the design of stereochemical investigations and for use in asymmetric syntheses.

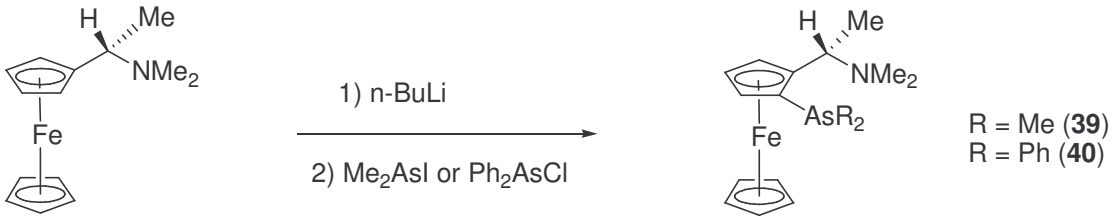
1.3.1 Hydrogenation

There are several examples on the application of chiral arsine complexes in catalytic hydrogenation. The rhodium(I) complex containing (*S*, *S*)-**27** catalyzed asymmetric hydrogenation of *Z*-α-acetamidocinnamic acid in methanol has afforded (*S*)-(+)-*N*-acetylphenylalanine in up to 39% ee when excess of triethylamine was present.[68,69] With the same catalyst hydrogenation of 2-acetamidocrylic acid afforded (*S*)-(–)-*N*-acetylalanine in good yield but low stereoselectivity. The arsine gave the amino acid of opposite configuration to that obtained with the similar phosphine (Scheme 1.17).



Scheme 1.17

However, the ferrocenyl arsine complexes **39** and **40** obtained from ferrocenyl-amine treated with *n*-BuLi and iododimethylarsine or diphenylchloroarsine did not catalyze the hydrogenation reactions when they were mixed with $[RhCl(COD)]_2$ (COD = cyclooctadiene) (Scheme 1.18).[75]

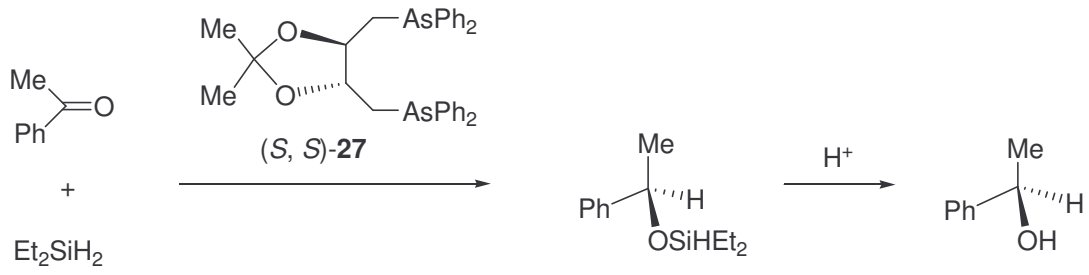


Scheme 1.18

Improved work has been carried out on the As-chiral bidentate **24** and phosphorus analogue in rhodium(I) complexes for the catalytic asymmetric hydrogenation of a series of prochiral *Z*-substituted enamide esters and acids in ethanol.[76] The stereoselectivity of the reaction was remarkably dependent upon the nature of the *β*-substituent on the enamide-olefin bond as well as the presence of triethylamine, however, it was found that the arsine-catalyst has out-performed the corresponding phosphine catalyst for several substrates. For example, the arsine-catalyst produced (*S*)-(+)-*N*-benzoylvaline in 89% e.e. from *α*-benzamide-*β,β*-dimethylacrylic acid in the presence of triethylamine, however, the phosphine-catalyst failed to effect the reduction. Furthermore, the optical yield for the valine derivative was much higher than that obtained with the use of any chelating phosphine.

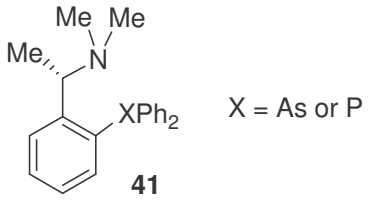
1.3.2 Hydrosilylation

The ligand **27** was also utilized in the catalytic hydrosilylation of ketones. The preparation of (*R*)-(+)-1-phenylethanol from acetophenone and diethylsilane catalyzed by (*S*, *S*)-**27** was the most effective (Scheme 1.19).[68,69]



Scheme 1.19

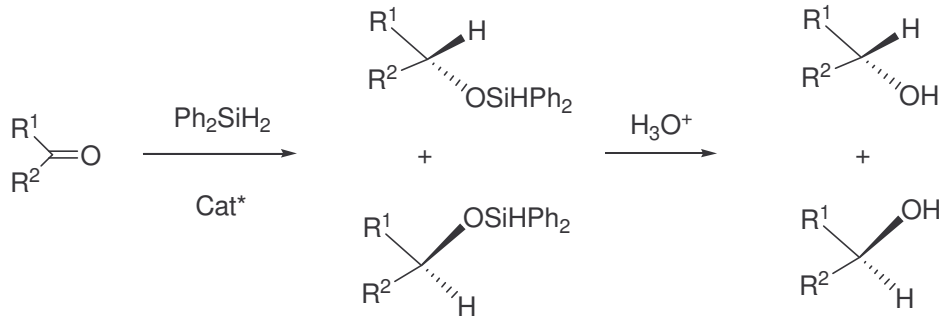
The rhodium(I) complexes containing ligands **41** have been used for the asymmetric hydrosilylation of a series of prochiral ketones.[77] Although the maximum ee of 72% was obtained using the phosphine catalyst, the arsine catalyst gave no induction. An explanation for this phenomenon is proposed on the basis of the results of X-ray crystal structure analysis.



X = As or P

41

Another application of the ligand **24** is the catalytic asymmetric hydrosilylation of acetophenone and *t*-butylmethyl ketone by the corresponding rhodium(I) complex (Scheme 1.20).[78]

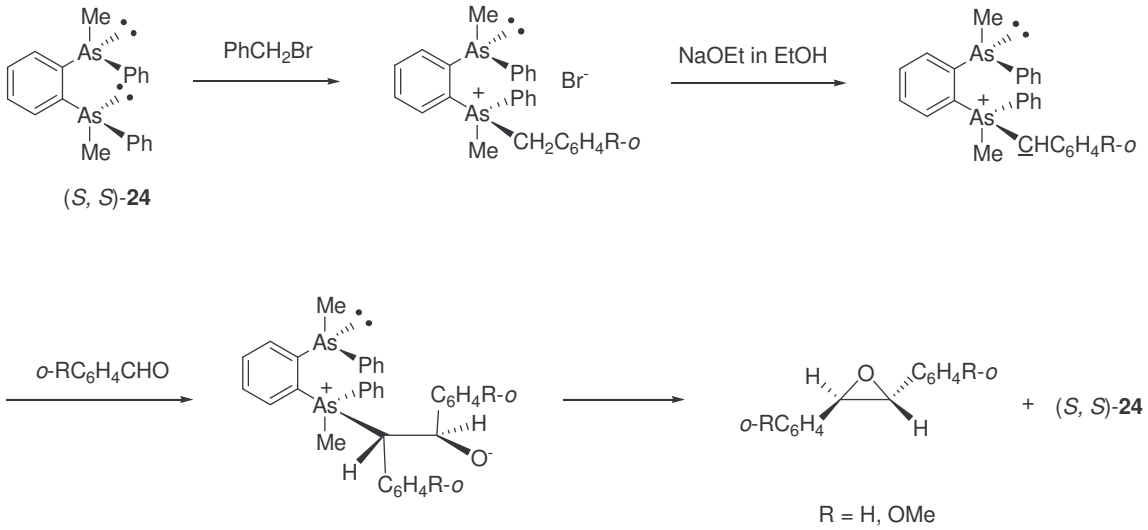


R^1 = Me, R^2 = Ph, *t*-Bu, o-$MeOC_6H_4$

Scheme 1.20

1.3.3 Benzylidene Transfer

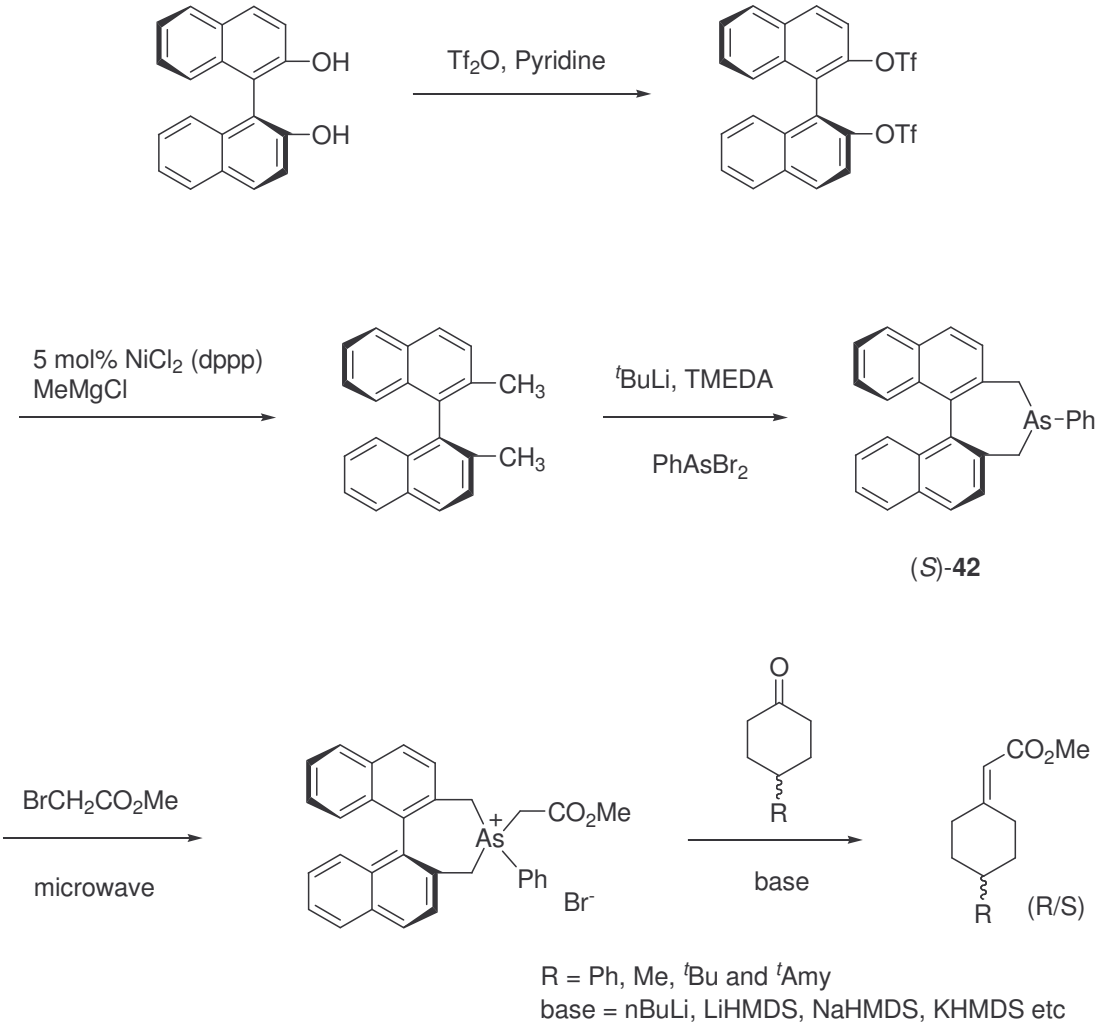
The reaction between chiral arsonium ylides containing the benzylidene group and aromatic aldehydes gave trans-2,3-diaryloxiranes with optical purities of up to 41% (Scheme1.21).[79] The factors affecting asymmetric induction included the nature of the substituents on the ylide, the substrate and the reaction conditions.



Scheme 1.21

1.3.4 Witting reaction

A C_2-symmetric chiral arsine **42** was prepared from the starting material (*S*)-(–)-1,1′-bi-2-naphthol in three steps (Scheme 1.22).[80] It could be used in the enantioselective olefination of 4-substituted cyclohexanones *via* a stabilized ylide formed *in situ* from the corresponding arsonium salt. Enantioselectivity up to 40% was achieved using this approach. Interestingly when the counter cation of the base was changed from lithium to potassium a reversal in the stereochemistry of the product was observed.



Scheme 1.22

1.4 Aim of the Present Project

The extensive literature on phosphorus chemistry, for example, there are many reports about phosphole metal complexes, but relatively few reports on related arsole metal complexes. So the objective of this project is to prepare a series of chiral arsine ligands by means of asymmetric Diels–Alder reaction and compare the similarities and differences between the corresponding arsenic and phosphorus compounds in terms of their reactivities and stereoselectivities. The complexes **1** and **2** are selected as the promoters for the Diels–Alder reactions between 3,4-dimethyl-1-phenylarsole and the various dienophiles such as diphenylvinylphosphine, diphenylvinylarsine, phenyldivinylphosphine and so on. We will investigate the template, steric and metal effects for these reactions in detail.

The work also assumes importance due to the differences observed especially in terms of the lack of stability of the As–C bonds in the norbornene skeleton.

CHAPTER 2

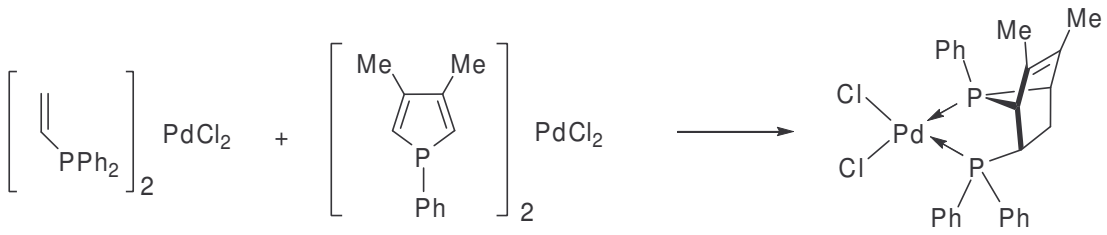
Asymmetric Syntheses of As–P and As–As Bidentate Ligands with Chirality on Arsenic Centre

2.1 Introduction

In general, the chemistry of five-membered heterocyclic rings is dramatically affected by the presence of heteroatoms. For instance, the pyrrole rings rarely react in the cycloaddition reaction,[81] but we have previously reported that the analogous phospholes are much more reactive toward various types of dienophiles in the metal-promoted [4 + 2] cycloaddition reactions.[82] In view of the general importance of the heterocycles and the fact that the diversity of heterocyclic chemistry is often unpredictable by the classic periodicity trends, the relatively unexplored arsole system as a building block deserved attention.[83] The pronounced difference in electronic as well as in steric properties between the coordination atoms is vital in many important applications of these ligands including as active catalysts.[84]

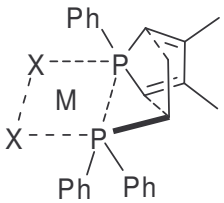
As part of our studies on asymmetric ligand transformation reactions, a series of organometallic reagents containing an orthometalated chiral amine auxiliary have been efficiently utilized as chiral templates to activate cyclic and noncyclic phosphines in cycloaddition, hydroamination, hydrophosphination, and most recently, hydroarsination reactions. In 1985 Nelson *et al*. reported the synthesis of 5-(diphenylphosphino)-2,3-dimethyl-7-phenyl-7-phosphabicyclo[2.2.1]-hept-2-ene ligand. Its racemic form was

initially prepared diastereoselectively from the Diels–Alder reaction between $Pd(Ph_2PCH{=}CH_2)_2X_2$ and $Pd(DMPP)_2X_2$ (X = Cl, Br, I) (Scheme 2.1).[85] The X-ray



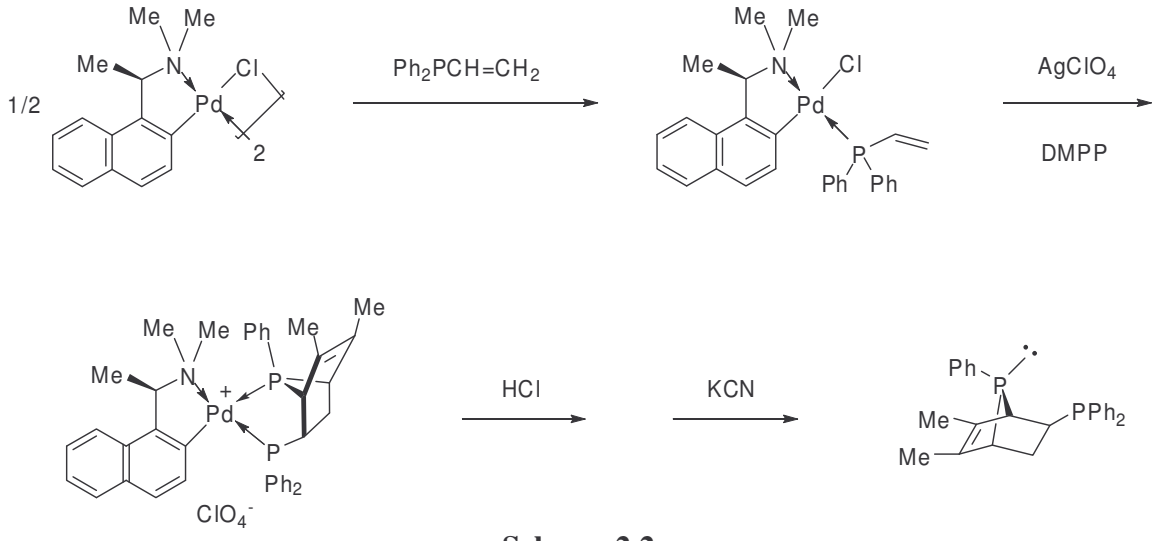
Scheme 2.1

crystal structural investigation of the dichloro complex confirmed that it exists as a racemic mixture. However no account of attempted resolution of the ligand had been reported. This intramolecular [4+2] Diels–Alder cycloaddition reaction does not occur in the absence of the metal ion. No reaction was observed when DMPP and diphenylvinylphosphine were placed in a sealed tube and heated at 60 ºC for 1 month. It was suggested that the coordination of the phosphole to the palladium centre polarizes the ring, increasing the electron density at the α-carbon and decreasing the electron density at the β-carbon. Likewise, coordination of the diphenylvinylphosphine to palladium polarizes the vinyl group in a similar manner. The substrates, thus activated undergo intramolecular [4+2] cycloaddition in mutually *cis* positions of the square planar mixed ligand complex *via* a transition state schematically represented below. The metal provides both electronic activation and molecular direction for a highly organised transition state.



The same cycloaddition has also been observed to take place within the coordination sphere of Pt(II), Ru(II), Mo(II), Fe(II), Ni(II) and Rh(I).[85-90] In principle it is possible to resolve the bidentate diphosphine ligand into its optical antipodes using established methods such as formation of a pair of diastereomeric phosphonium salts or by means of metal complexation. However, the resolution is expected to be tedious and inefficient. In this case, it is further hampered by the thermodynamic instability of the uncoordinated phosphorus stereogenic centre at the bridgehead position.

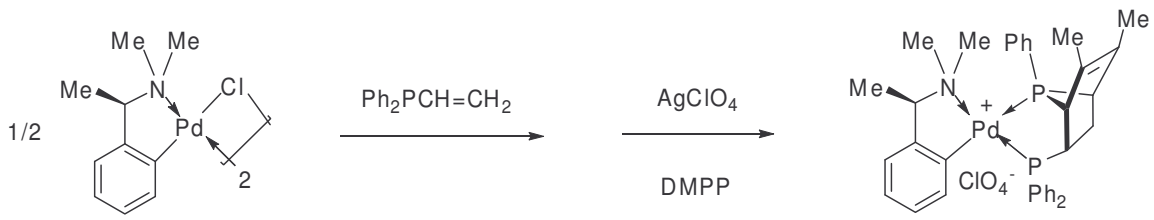
In 1994, the corresponding enantiomerically pure diphosphine ligand was successfully synthesized in our group. The dichloro-bridged palladium complex (+/–)-**2** is capable of promoting the asymmetric Diels–Alder reaction between DMPP and diphenylvinylphosphine (Scheme 2.2).[91] Both enantiomeric forms of the corresponding rigid P-chiral diphosphine were obtained enantiospecifically as air-sensitive oils in high yields by using the appropriate forms of the naphthylamine auxiliary (*R* or *S*). Unfortunately, the absolute configurations of these new diphosphines were not assigned



Scheme 2.2

due to the difficulty of producing single crystals suitable for X-ray structural analysis of the intermediate palladium template complexes that contain the chiral naphthylamine auxiliary and the diphosphine ligand. Although these complexes are chemically stable and can be readily crystallized from most solvent system, these crystals generally grow as hollow tubes and suffer from problems of rapid desolvation.

Then in 1996 a simple ^{1}H ROESY NMR experiment was established to assign the absolute stereochemistry of these template complexes in solution.[92] This NMR technique utilized the unique stereochemical features of the ortho-metallated 1-[1-(dimethylamino)ethyl]naphthalene palladium unit as the internal reference. According to the solution NMR study, when the *R*-naphthylamine auxiliary was used, the resulting diphosphine ligand was assigned the *R* absolute configuration at the bridged-head phosphorus stereogenic centre. In order to consolidate the above highly convenient and relatively new NMR assignment, in 1997 the more economical analogous palladium complex (–)-**1** was used as the chiral promoter for the same reaction (Scheme 2.3).[93] In contrast to its naphthylamine analogue, the resulting perchlorate complex was crystallized from acetone-diethyl ether as highly stable clear prisms which were suitable for the conventional absolute stereochemical determination *via* single-crystal X-ray analysis. The subsequent X-ray analysis fully supported the stereochemical assignments derived from the ^{1}H ROESY NMR experiments.



Scheme 2.3

Compared to phospholes, however, the stereoselectivity and reactivity of cyclic arsines in these reactions have been much less studied. In order to enrich this heterobidentate chemistry, we have decided to explore the chemistry of arsoles. In this chapter we will report the palladium-promoted cycloaddition reaction of 3,4-dimethyl-1-phenylarsole (DMPA) with diphenylvinylphosphine and diphenylvinylarsine, the stability of the resulting novel arsanorbornene and the template effects on the reaction between DMPA and diphenylvinylphosphine. Some chiral phosphine-olefin complexes and other novel palladium complexes were unexpectedly obtained in this work.

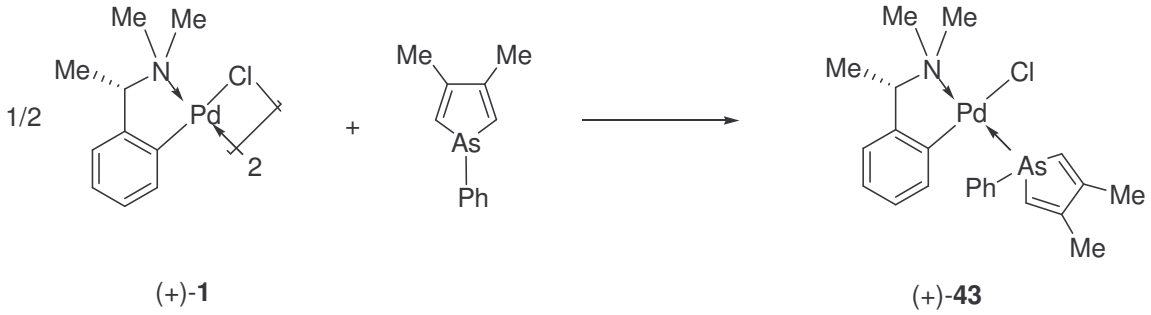
2.2 Results and Discussion

2.2.1 Asymmetric Cycloaddition Reaction between DMPA and Diphenylvinylphosphine Promoted by the Benzylamine Template

2.2.1.1 Preparation and Characterization of the Monomeric Palladium(II) Complex (+)-43

Compared to its phosphorus analogue (DMPP), reports on the reactivity of uncoordinated arsoles including DMPA are rare. Interestingly, the As–heterocycles become reactive when they are coordinated onto a transition-metal ion.[94] As illustrated in Scheme 2.4, DMPA was coordinated regiospecifically to (+)-**1** to give the monomeric neutral complex (+)-**43** as yellow prisms. The X-ray structural analysis of (+)-**43** (Figure 2.1) reveals a marked bond ordering within the planar arsole ring in which the C(11)–C(12) and C(13)–C(14) bonds exhibit significant double-bond character [1.320(7) and 1.335(7) Å, respectively, Table 2.1]. The two As–C bonds [1.910(4) and 1.914(4) Å]

within the arsole ring are significantly shorter than the As–Ph bond [1.939(3) Å].



(+)-**1** (+)-**43**

Scheme 2.4

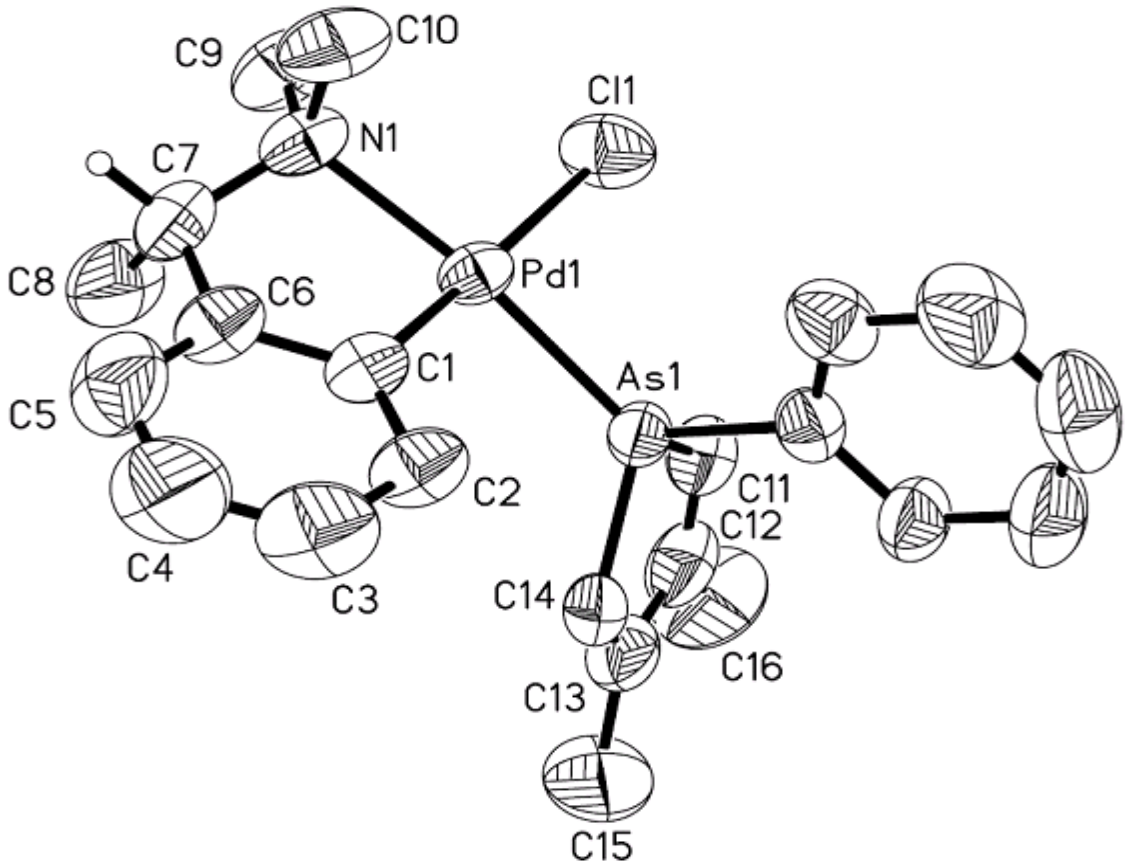


Figure 2.1 Molecular structure of complex (+)-**43**

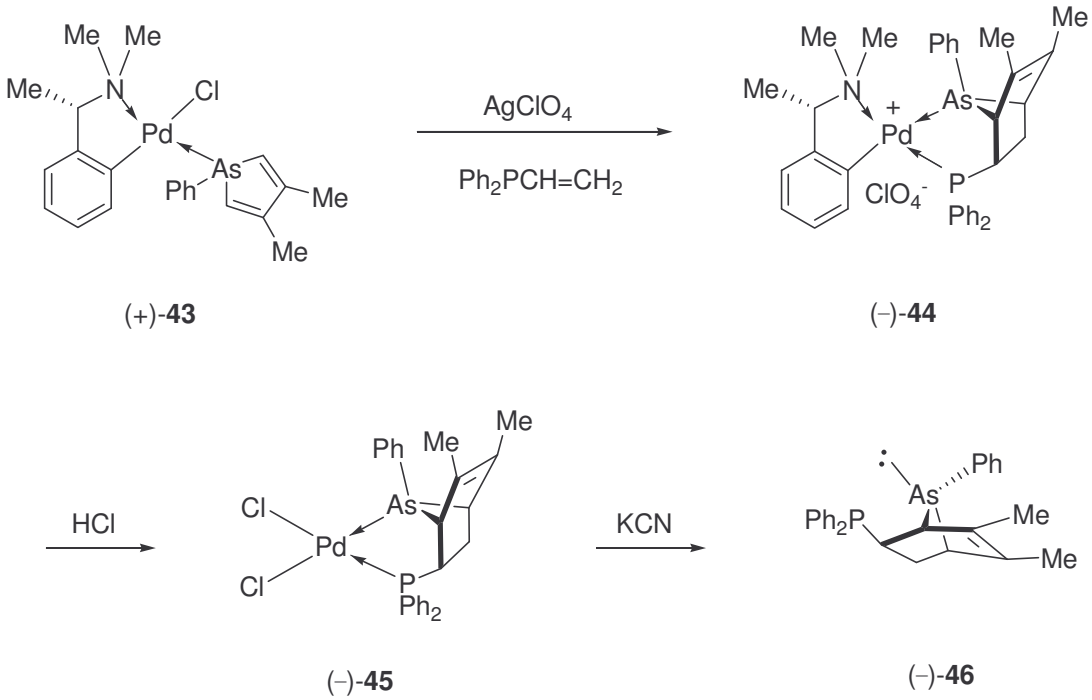
Table 2.1 Selected bond lengths (Å) and angles (°) for (+)-**43**

Pd(1)–C(1)	1.982(3)	Pd(1)–N(1)	2.141(3)
Pd(1)–As(1)	2.343(1)	Pd(1)–Cl(1)	2.424 (1)
As(1)–C(11)	1.910(4)	As(1)–C(14)	1.914(4)
As(1)–C(17)	1.939(3)	C(11)–C(12)	1.320(7)
C(12)–C(13)	1.496(8)	C(13)–C(14)	1.335(7)
C(12)–C(16)	1.518(8)	C(13)–C(15)	1.484(7)
C(1)–Pd(1)–N(1)	81.0 (1)	C(1)–Pd(1)–As(1)	93.9(1)
N(1)–Pd(1)–As(1)	172.9 (1)	C(1)–Pd(1)–Cl(1)	172.8 (1)
N(1)–Pd(1)–Cl(1)	97.4(1)	As(1)–Pd(1)–Cl(1)	88.3(1)
C(11)–As(1)–C(14)	86.9(2)	C(11)–As(1)–C(17)	105.0(2)
C(14)–As(1)–C(17)	103.7(2)	C(11)–As(1)–Pd(1)	118.5(1)
C(14)–As(1)–Pd(1)	123.6(1)	C(17)–As(1)–Pd(1)	114.8(1)
C(12)–C(11)–As(1)	111.0(4)	C(11)–C(12)–C(13)	116.2(4)
C(11)–C(12)–C(16)	123.0(6)	C(13)–C(12)–C(16)	120.7(6)
C(14)–C(13)–C(15)	124.0(6)	C(14)–C(13)–C(12)	114.3(4)
C(15)–C(13)–C(12)	121.7(5)	C(13)–C(14)–As(1)	111.4(4)

Interestingly, the C(11)–As(1)–C(14) bond angle [86.9(2)°] is dramatically smaller than the other four bond angles [111.0(4)–116.2(4)°] within the arsole ring. It is noteworthy that (+)-**43** is the first complex containing the DMPA ligand that has been characterized by X-ray crystallography.

2.2.1.2 Asymmetric Cycloaddition Reaction between DMPA and Diphenylvinylphosphine

The chloro ligand in (+)-**43** and indeed in similar orthometalated amine complexes is well-known to be both kinetically and thermodynamically stable.[95] This terminal ligand, however, can be abstracted efficiently by treatment of the complex in dichloromethane with aqueous silver salts (Scheme 2.5). This process allowed DMPA and diphenylvinylphosphine, the incoming dienophile, to coordinate simultaneously onto the chiral palladium template during the course of the intramolecular cycloaddition reaction. The $^{31}P\{^{1}H\}$ NMR spectroscopic studies indicated that the cycloaddition reaction was completed within 3 h and a 3.2:1 diastereomeric mixture was produced at



(+)-**43** (–)-**44**

(–)-**45** (–)-**46**

Scheme 2.5

room temperature. The $^{31}P\{^{1}H\}$ NMR spectrum of the crude product in $CDCl_3$ showed a strong singlet at δ 50.1 and a weaker singlet at δ 49.8. The major arsanorbornene complex (–)-**44** was crystallized as colorless prisms from chloroform-diethyl ether in 60% yield, $[\alpha]_D$ –71.9° (*c* 0.6, CH_2Cl_2). As shown in Figure 2.2, the structural analysis of (–)-**44** revealed that, in addition to the cycloaddition reaction, a ligand redistribution process was also involved in the formation of (–)-**44**. Because of the distinct electronic-directing effects originating from the σ-donating nitrogen and the π-accepting aromatic carbon of the orthometalated benzylamine ring, it has been well-established that the position trans

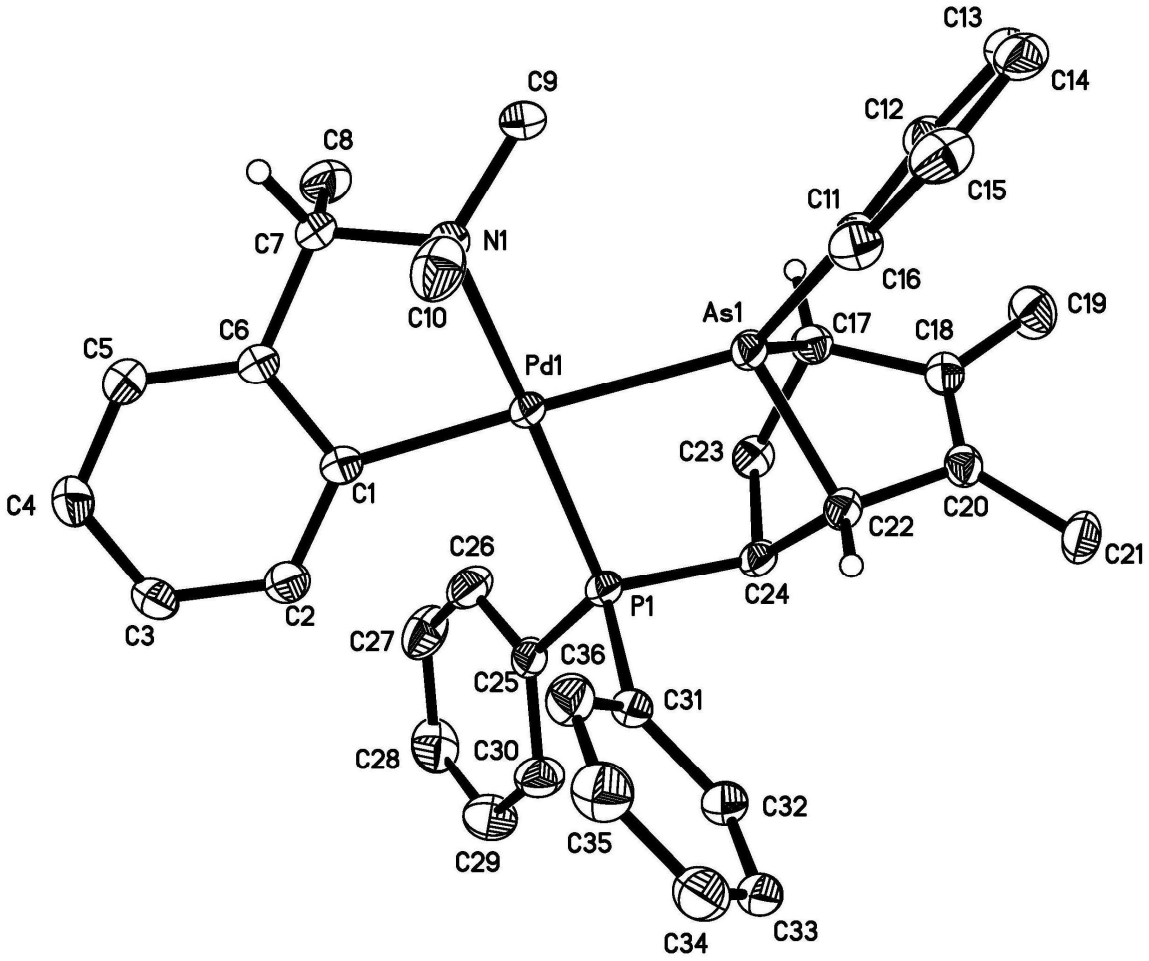
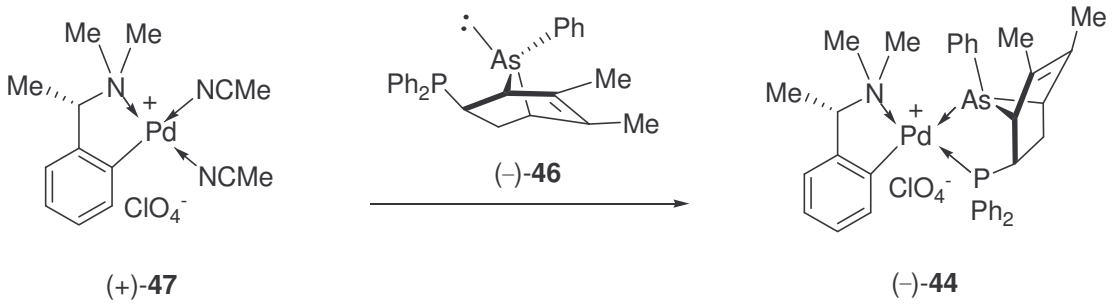


Figure 2.2 Molecular structure of complex (–)-**44**

Table 2.2 Selected bond lengths (Å) and angles (°) for (–)**-44**

Pd(1)–C(1)	2.051(2)	Pd(1)–N(1)	2.146(2)
Pd(1)–As(1)	2.447(1)	Pd(1)–P(1)	2.261(1)
P(1)–C(24)	1.849(2)	As(1)–C(11)	1.925(2)
As(1)–C(17)	1.978(2)	As(1)–C(22)	1.980(2)
C(17)–C(18)	1.522(3)	C(17)–C(23)	1.557(3)
C(18)–C(20)	1.334(3)	C(18)–C(19)	1.501(3)
C(20)–C(21)	1.492(3)	C(20)–C(22)	1.507(3)
C(22)–C(24)	1.558(3)	C(23)–C(24)	1.567(3)
C(1)–Pd(1)–N(1)	81.8(1)	C(1)–Pd(1)–P(1)	96.8(1)
N(1)–Pd(1)–P(1)	172.8(1)	C(1)–Pd(1)–As(1)	178.7(1)
N(1)–Pd(1)–As(1)	99.5(1)	P(1)–Pd(1)–As(1)	81.9(2)
C(17)–As(1)–C(22)	76.7(1)	C(11)–As(1)–Pd(1)	129.1(1)
C(17)–As(1)–Pd(1)	116.8(1)	C(22)–As(1)–Pd(1)	105.7(1)
C(18)–C(17)–C(23)	106.2(2)	C(18)–C(17)–As(1)	101.5(1)
C(23)–C(17)–As(1)	99.6(2)	C(20)–C(18)–C(19)	128.7(2)
C(20)–C(18)–C(17)	111.6(2)	C(19)–C(18)–C(17)	119.5(2)
C(18)–C(20)–C(21)	129.6(2)	C(18)–C(20)–C(22)	111.8(2)
C(21)–C(20)–C(22)	118.5(2)	C(20)–C(22)–C(24)	110.2(2)
C(20)–C(22)–As(1)	103.0(2)	C(24)–C(22)–As(1)	95.9(1)
C(17)–C(23)–C(24)	107.0(2)	C(22)–C(24)–C(23)	105.7(2)
C(22)–C(24)–P(1)	107.8(2)	C(23)–C(24)–P(1)	111.1(1)

to the NMe_2 group invariably takes up the softest donor atom available.[45] Therefore, the phosphorus donor in the arsanorbornene ligand is a stronger π acceptor than the arsenic atom.[63] The four new chiral centers have been generated with *R* absolute stereochemistry at As(1) and *R*, *R* and *S* stereochemistry at C(17), C(22) and C(24), respectively. Similar to its phosphorus analogue,[93] a noticeable feature of the arsanorbornene skeleton is a marked contraction in the C(17)–As(1)–C(22) bridgehead angle to 76.7 (1)° that accompanies a significant lengthening of these two As–C bonds [1.978(2) and 1.980(2) Å; Table 2.2] (compared with those observed in complex (+)-**43**). The chiral amine auxiliary on complex (–)-**44** could be removed chemoselectively by the treatment of the complex with concentrated hydrochloric acid. The neutral dichloro complex (–)-**45** (Figure 2.3) was thus obtained as stable yellow prisms in 60% yield, $[\alpha]_D$ –40.0° (*c* 0.6, CH_2Cl_2). The structural analysis of the dichloro complex reaffirmed that the arsanorbornene skeleton remained unchanged after the acid treatment. Selected bond lengths and angles are listed in Table 2.3. Treatment of a dichloromethane solution of (–)-**45** with aqueous potassium cyanide gave the optically active free ligand (–)-**46** as a white solid in quantitative yield, $[\alpha]_D$ –70.4° (*c* 0.9, CH_2Cl_2). In $CDCl_3$, the $^{31}P\{^1H\}$ NMR spectrum of (–)-**46** exhibited a singlet at δ –11.1. The optical purity of As–P bidentate ligand (–)-**46** was confirmed by the quantitative preparation of (–)-**44** from the liberated ligand (–)-**46** and bis(acetonitrile)[(*S*)-[(1-(dimethylamino)ethyl)phenyl)palladium(II) perchlorate, (+)-**47**[96] (Scheme 2.6): the $^{31}P\{^1H\}$ NMR spectrum of the crude product in $CDCl_3$ exhibited only the singlet signal of (–)-**44** at δ 50.1.



(+)-**47** (–)-**44**

Scheme 2.6

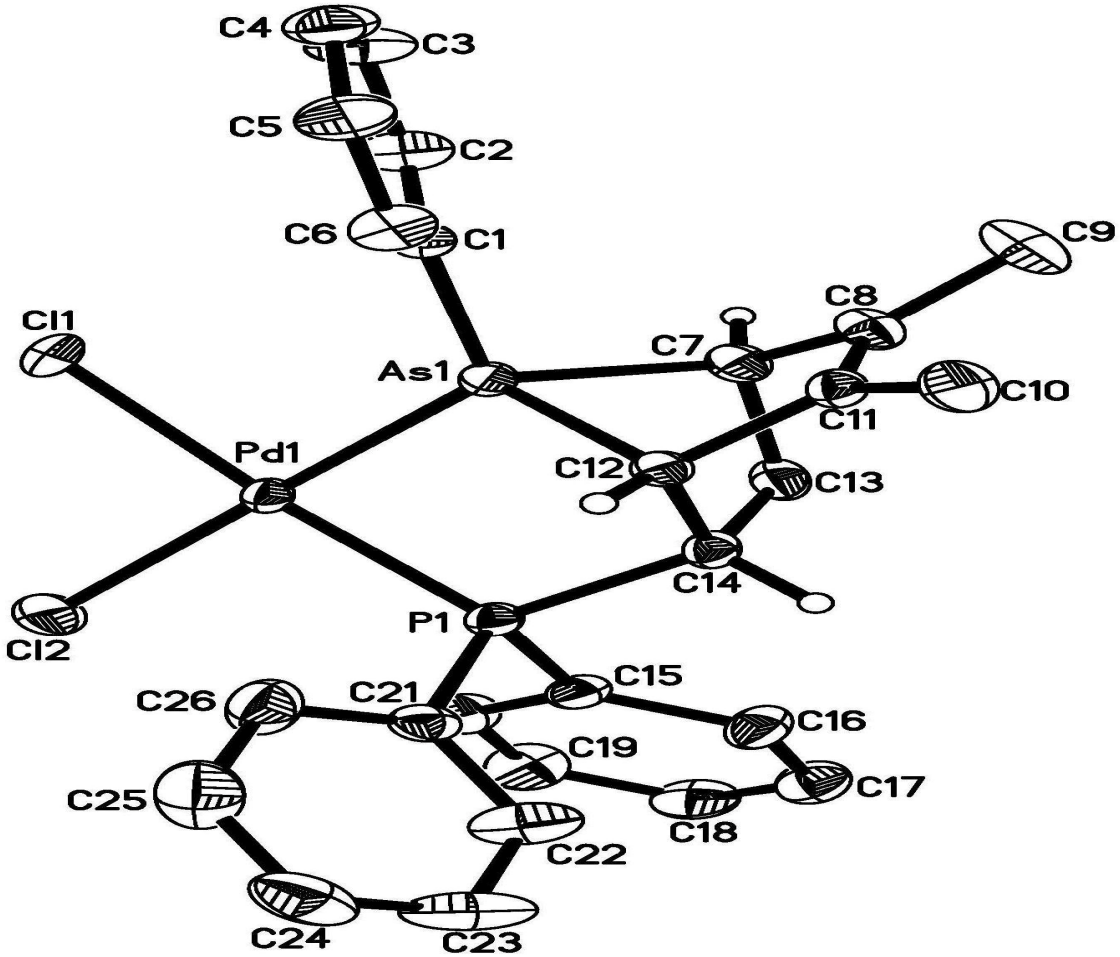
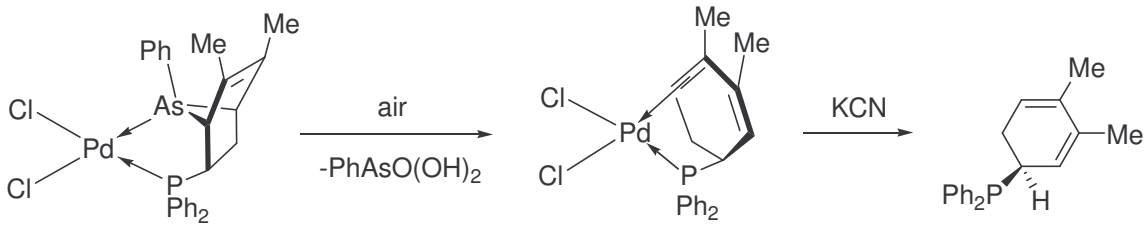


Figure 2.3 Molecular structure of dichloro complex (–)**-45**

Table 2.3 Selected bond lengths (Å) and angles (°) for (–)**-45**

Pd(1)–Cl(1)	2.345(1)	Pd(1)–Cl(2)	2.353(1)
Pd(1)–As(1)	2.325(1)	Pd(1)–P(1)	2.260(1)
As(1)–C(1)	1.922(3)	As(1)–C(7)	1.980(3)
As(1)–C(12)	1.961(3)	P(1)–C(14)	1.843(3)
C(7)–C(8)	1.513(5)	C(7)–C(13)	1.545(5)
C(8)–C(11)	1.342(5)	C(8)–C(9)	1.490(5)
C(10)–C(11)	1.498(5)	C(11)–C(12)	1.522(4)
C(12)–C(14)	1.552(4)	C(13)–C(14)	1.565(4)
P(1)–Pd(1)–As(1)	83.6(1)	Cl(1)–Pd(1)–P(1)	170.8(1)
As(1)–Pd(1)–Cl(1)	88.6(1)	P(1)–Pd(1)–Cl(2)	94.8(1)
As(1)–Pd(1)–Cl(2)	174.7(1)	Cl(1)–Pd(1)–Cl(2)	92.6(1)
C(12)–As(1)–C(7)	77.5(1)	C(1)–As(1)–Pd(1)	124.2(1)
C(12)–As(1)–Pd(1)	106.1(1)	C(7)–As(1)–Pd(1)	120.1(1)
C(8)–C(7)–C(13)	107.3(3)	C(8)–C(7)–As(1)	100.5(2)
C(13)–C(7)–As(1)	99.4(2)	C(11)–C(8)–C(9)	128.3(3)
C(11)–C(8)–C(7)	111.6(3)	C(9)–C(8)–C(7)	119.9(3)
C(8)–C(11)–C(10)	127.8(3)	C(8)–C(11)–C(12)	111.8(3)
C(10)–C(11)–C(12)	120.4(3)	C(11)–C(12)–C(14)	110.7(3)
C(11)–C(12)–As(1)	101.8(2)	C(14)–C(12)–As(1)	95.3(2)
C(7)–C(13)–C(14)	106.8(3)	C(12)–C(14)–C(13)	106.5(3)
C(12)–C(14)–P(1)	109.9(2)	C(13)–C(14)–P(1)	107.8(2)

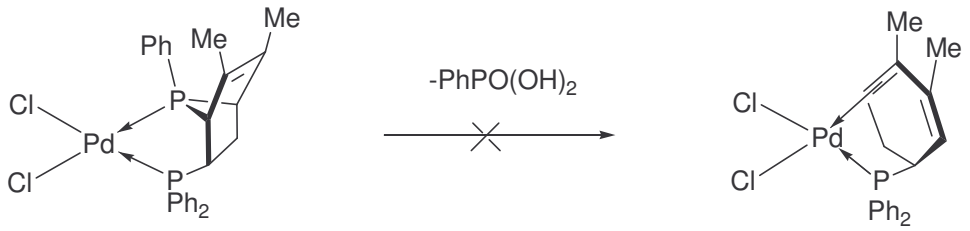


(–)-**45** (+)-**48** (–)-**49**

Scheme 2.7

When DMPA and DMPP are treated separately with coordinated diphenylvinylphosphine, they both show similar reactivity and stereoselectivity towards the cycloaddition reaction using the same chiral template.[93] However, the resulting arsanorbornene cycloadduct appeared to be less stable than the corresponding phosphanorbornene. As illustrated in Scheme 2.7, when a $CDCl_3$ solution of the yellow dichloro complex (–)-**45** was allowed to stand for 3 weeks, an interesting stereospecific arsenic elimination occurred to give the red retrodiene complex (+)-**48** (Figure 2.4), $[\alpha]_D$ +395.6° (*c* 0.2, CH_2Cl_2) and phenylarsonic acid. Phenylarsonic acid was subsequently crystallized in quantitative yield and the structure confirmed by X-ray crystallography. It is interesting to note that the rate of this elimination reaction is affected by the solvent employed. For example, the elimination reaction was found to be completed in 3 weeks in $CDCl_3$ but only 1 week was needed in dichloromethane. Compared with the $^{31}P\{^1H\}$ NMR chemical shift (δ 33.6) of the dichloro complex (–)-**45**, the retrodiene complex (+)-**48** showed an unusually high $^{31}P\{^1H\}$ NMR chemical shift (δ 139.2). The single-crystal X-ray diffraction studies of (+)-**48** revealed the absence of arsine in the palladium complex. One of the double bonds of the six-membered ring coordinated onto the palladium metal center in a η^2 mode. The *S* absolute stereochemistry at C(3) remained

unchanged, thus reaffirming that the P–C and C–C bonds were not involved in the mechanism of the elimination reaction (Table 2.3). Furthermore, it is interesting to note that, under similar or even drastic reaction conditions, the phosphanorbornene analogue of complex (–)-**45** is stable and a similar phenomenon is not observed (Scheme 2.8).[91]



Scheme 2.8

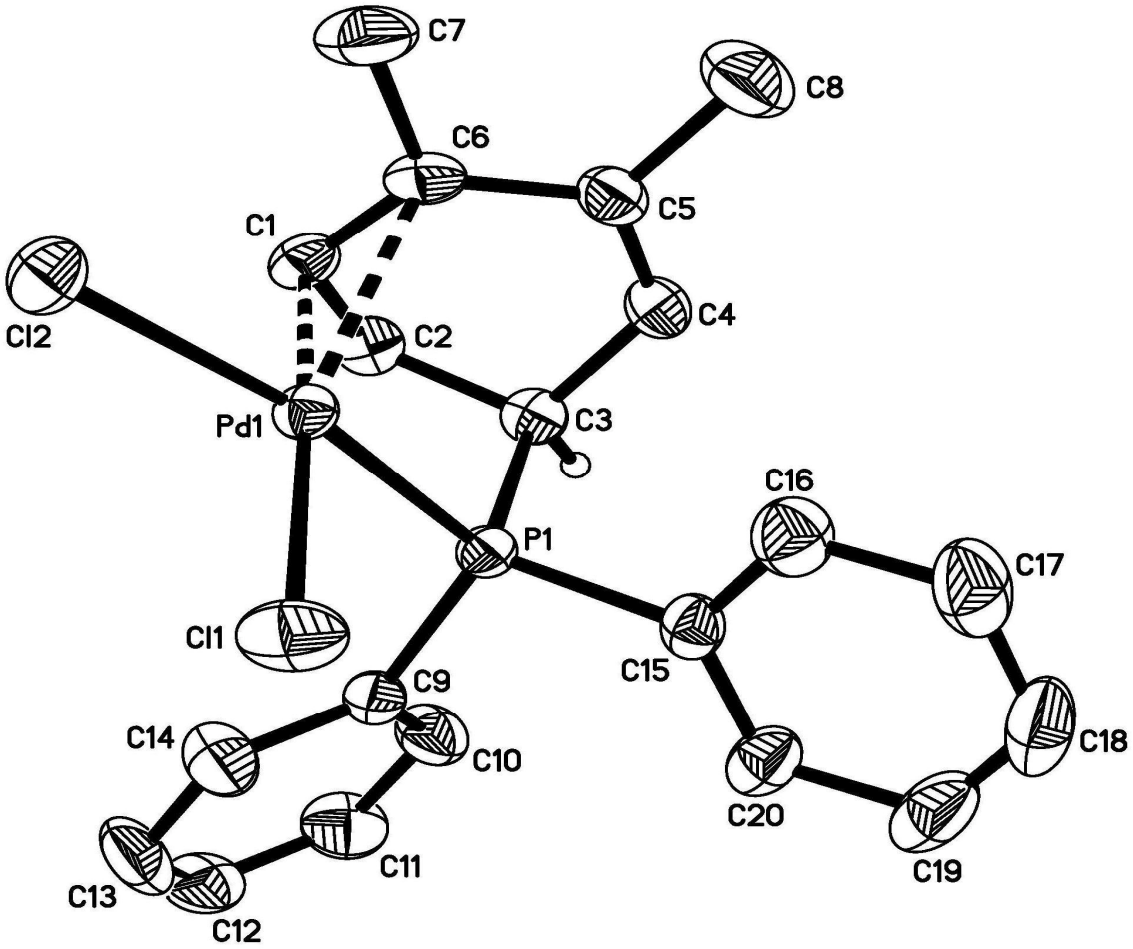


Figure 2.4 Molecular structure of dichloro complex (+)-**48**

Table 2.4 Selected bond lengths (Å) and angles (°) for (+)**-48**

Pd(1)–Cl(1)	2.316(1)	Pd(1)–Cl(2)	2.370(1)
Pd(1)–P(1)	2.226(1)	Pd(1)–C(1)	2.190(3)
Pd(1)–C(6)	2.409(3)	P(1)–C(3)	1.862(3)
C(1)–C(6)	1.399(4)	C(1)–C(2)	1.506(3)
C(2)–C(3)	1.515(3)	C(3)–C(4)	1.485(3)
C(4)–C(5)	1.326(4)	C(5)–C(6)	1.476(4)
C(5)–C(8)	1.512(4)	C(6)–C(7)	1.493(3)
C(1)–Pd(1)–P(1)	84.6 (1)	C(1)–Pd(1)–Cl(1)	167.5(1)
P(1)–Pd(1)–Cl(1)	87.4(1)	C(1)–Pd(1)–Cl(2)	94.7 (1)
P(1)–Pd(1)–Cl(2)	169.2(1)	Cl(1)–Pd(1)–Cl(2)	91.3(1)
C(1)–Pd(1)–C(6)	35.0(1)	P(1)–Pd(1)–C(6)	91.2(1)
Cl(1)–Pd(1)–C(6)	155.2(1)	Cl(2)–Pd(1)–C(6)	94.5(1)
C(6)–C(1)–C(2)	117.9(2)	C(6)–C(1)–Pd(1)	81.1(2)
C(2)–C(1)–Pd(1)	109.8(2)	C(1)–C(2)–C(3)	108.9(2)
C(4)–C(3)–C(2)	111.1(2)	C(4)–C(3)–P(1)	107.1(2)
C(2)–C(3)–P(1)	103.8(2)	C(5)–C(4)–C(3)	120.8(2)
C(4)–C(5)–C(6)	119.3(2)	C(4)–C(5)–C(8)	121.3(3)
C(6)–C(5)–C(8)	119.4(2)	C(1)–C(6)–C(5)	119.8(2)
C(1)–C(6)–C(7)	120.3(2)	C(5)–C(6)–C(7)	118.0(2)
C(1)–C(6)–Pd(1)	63.9(2)	C(5)–C(6)–Pd(1)	111.3(2)
C(7)–C(6)–Pd(1)	107.0(2)		

It is noteworthy that the η^2 bond in (+)-**48** (Table 2.4) is chemically inert under normal conditions both in the solid state and in solution. However, the optically pure phosphine ligand (–)-**49** could be liberated from the dichloro complex (+)-**48** by treatment with aqueous potassium cyanide. The phosphine ligand (–)-**49**, $[\alpha]_D$ –10.4° (*c* 0.6, CH_2Cl_2) was obtained as an air-sensitive white solid. The $^{31}P\{^1H\}$ NMR spectrum of (–)-**49** in $CDCl_3$ showed a singlet resonance at δ –11.2. It should be noted that attempts to reprepare the dichloro complex (+)-**48** from the liberated ligand (–)-**49** and $PdCl_2(NCMe)_2$ and indeed many other palladium(II) starting materials were unsuccessful. These observations reveal that, although the dichloro complex (+)-**48** is thermodynamically stable, the formation of the P–η^2 chelate on Pd is a kinetically challenging process. It is noteworthy that a synthetic process that involves free ligands and metal ions is not always the most efficient approach to prepare this class of potentially important complexes.

2.2.1.3 Arsenic–Elimination Reaction

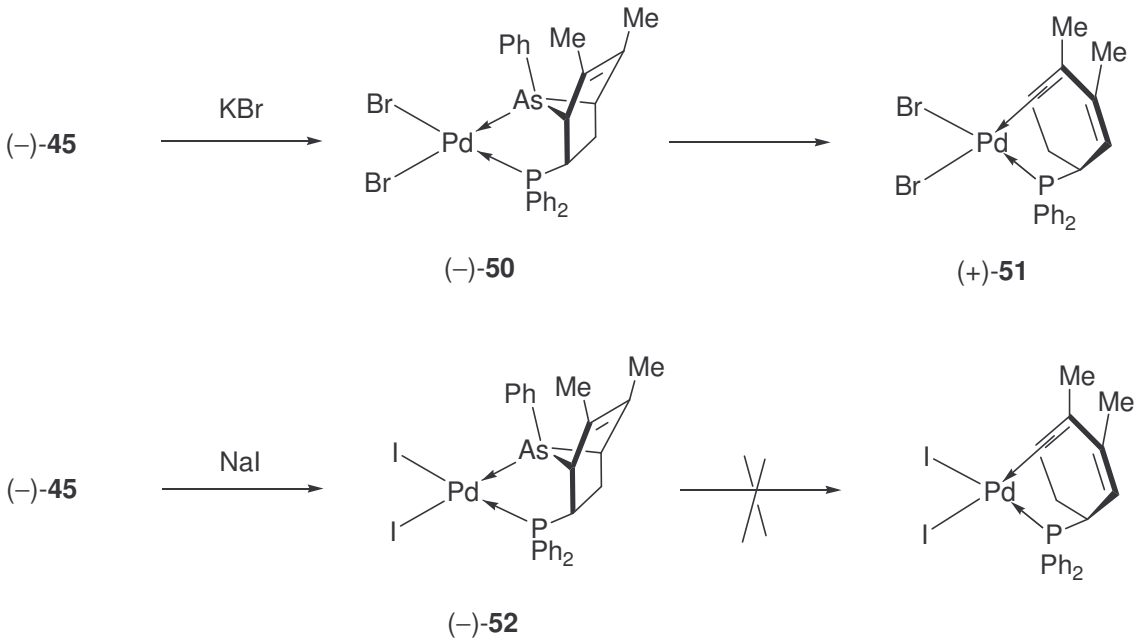
Recently, chiral phosphine-olefin hybrid ligands have received considerable attention in asymmetric catalysis. These ligands display unusual phosphorus and η^2 bonding, with the olefin performing the unconventional role of a "spectator" ligand that stays on the metal during catalysis and influences the metal's catalytic property. However, only a small number of chiral phosphine-olefin hybrid palladium complexes have been reported.[97] These palladium complexes showed high catalytic activity in asymmetric reactions. For example, the phenanthrene-based phosphinepalladium

dibenzylideneacetone (dba) complex was successfully used in the Suzuki cross-coupling reaction to form sterically hindered tetra-ortho-substituted biaryls in high yields.[97c]

Accordingly the reactivity of the hybrid chiral phosphine-olefin palladium complex (+)-**48** has been investigated in this work.

In contrast to the arsenic-elimination reaction observed in [(As–P)$PdCl_2$] [(–)-**45**], the analogous diphosphinepalladium complex [(P–P)$PdCl_2$] cannot be converted to the η^2-complex (+)-**48** under similar or even more drastic reaction conditions (Scheme 2.8).[91] Such an observation is perhaps not surprising because P–C bonds are generally more stable than their As–C counterparts. On the other hand, it is interesting to note that no arsenic-elimination reaction was observed when the complex (–)-**44** containing the same arsanorbornene (As–P) ligand was used. Indeed, complex (–)-**44** is stable, both in the solid state and in solution. Apparently, the other ligands in complexes (–)-**44** and (–)-**45** must play a vital role in stabilising the chelating arsanorbornene (As–P) ligand and the breaking of the two As–C bonds in the elimination process.

In order to gain further insight into this novel arsenic-elimination process, complex (–)-**45** was converted to its analogous halo-derivatives [(As–P)$PdBr_2$] [(–)-**50**] and [(As–P)PdI_2] [(–)-**52**] (Figure 2.5, Table 2.5) by treatment of the dichloro complex with potassium bromide and sodium iodide, respectively (Scheme 2.9). The dibromo complex (–)-**50** was isolated as yellow needles in 70% yield, $[\alpha]_D$ –51.7° (*c* 0.6, CH_2Cl_2). The diiodo complex (–)-**52** was obtained as red prisms in 62% yield, $[\alpha]_D$ –55.0° (*c* 0.6, CH_2Cl_2). Similar to their dichloro derivative, the dibromo and diiodo complexes are stable in the solid state. In $CDCl_3$, however, the $^{31}P\{^1H\}$ NMR spectroscopic studies



Scheme 2.9

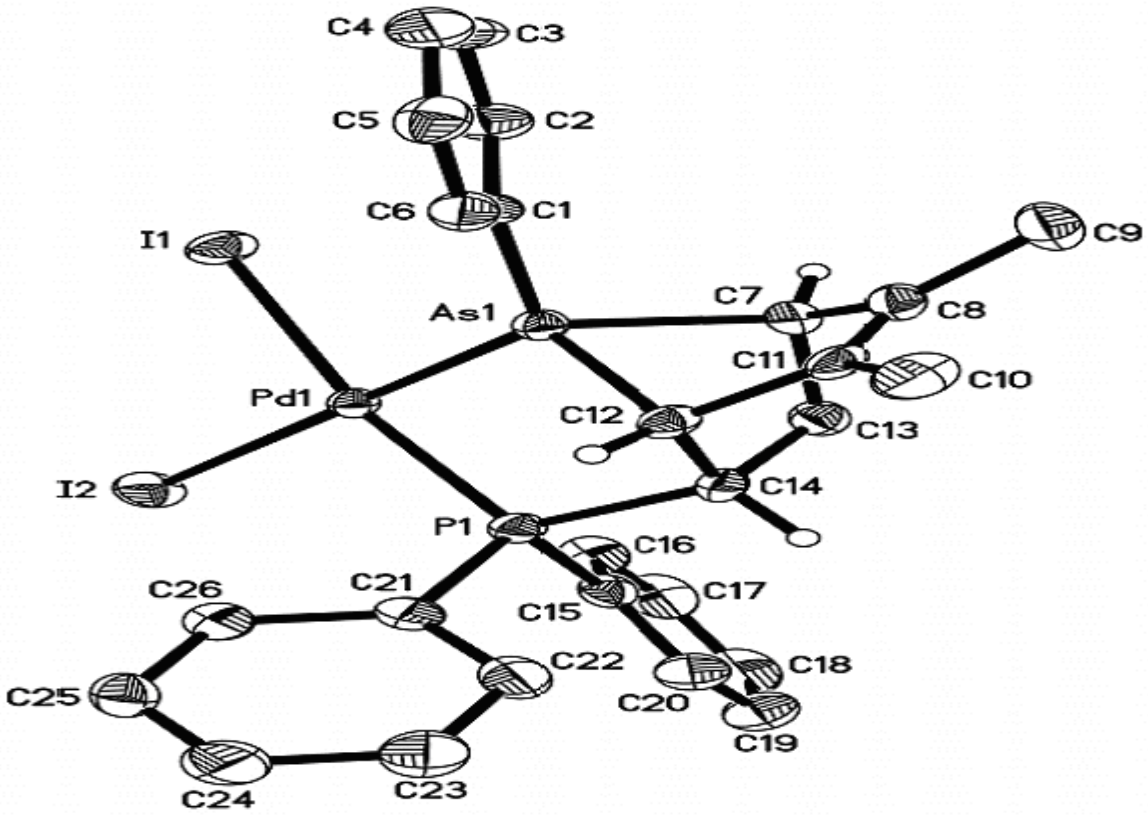


Figure 2.5 Molecular structure of diiodo complex (–)**-52**

Table 2.5 Selected bond lengths (Å) and angles (°) for (–)**-52**

Pd(1)–I(1)	2.630(1)	Pd(1)–I(2)	2.660(1)
Pd(1)–As(1)	2.354(1)	Pd(1)–P(1)	2.278(1)
As(1)–C(1)	1.931(5)	As(1)–C(7)	1.982(5)
As(1)–C(12)	1.989(4)	P(1)–C(14)	1.846(5)
C(7)–C(8)	1.520(7)	C(7)–C(13)	1.542(7)
C(8)–C(11)	1.333(7)	C(8)–C(9)	1.502(7)
C(10)–C(11)	1.514(7)	C(11)–C(12)	1.509(6)
C(12)–C(14)	1.560(7)	C(13)–C(14)	1.571(7)
P(1)–Pd(1)–As(1)	82.8(1)	I(1)–Pd(1)–P(1)	169.7(1)
As(1)–Pd(1)–I(1)	88.3(2)	P(1)–Pd(1)–I(2)	96.0(1)
As(1)–Pd(1)–I(2)	176.3(1)	I(1)–Pd(1)–I(2)	93.2(1)
C(7)–As(1)–C(12)	76.9(2)	C(1)–As(1)–Pd(1)	129.3(1)
C(7)–As(1)–Pd(1)	114.5(2)	C(12)–As(1)–Pd(1)	108.4(1)
C(8)–C(7)–C(13)	108.3(4)	C(8)–C(7)–As(1)	99.4(3)
C(13)–C(7)–As(1)	99.9(3)	C(11)–C(8)–C(9)	128.9(5)
C(11)–C(8)–C(7)	111.5(4)	C(9)–C(8)–C(7)	119.6(5)
C(8)–C(11)–C(12)	112.5(4)	C(8)–C(11)–C(10)	128.4(5)
C(12)–C(11)–C(10)	119.1(5)	C(11)–C(12)–C(14)	112.4(4)
C(11)–C(12)–As(1)	100.6(3)	C(14)–C(12)–As(1)	95.2(3)
C(7)–C(13)–C(14)	107.4(4)	C(12)–C(14)–C(13)	105.6(4)
C(12)–C(14)–P(1)	109.3(3)	C(13)–C(14)–P(1)	109.1(3)

showed that the dibromo complex (–)-**50** was converted quantitatively to the retrodiene η^2-dibromo complex (+)-**51** (Figure 2.6, Table 2.6) within 25 days with the temperature maintained at 23 ºC. Thus, the arsanorbornene ligand in both the dichloro complex (–)-**45** and the dibromo complex (–)-**50** exhibited similar stability and reactivity. Interestingly, and to our surprise, the arsenic-elimination reaction did not occur when the diiodo complex (–)-**52** was dissolved in solution. At higher temperature, however, (–)-**52** decomposed rapidly. A comparison of the solid-state structures of the complex (–)-**44**, the dichloro complex (–)-**45** and the diiodo complex (–)-**52** revealed that the structural features of

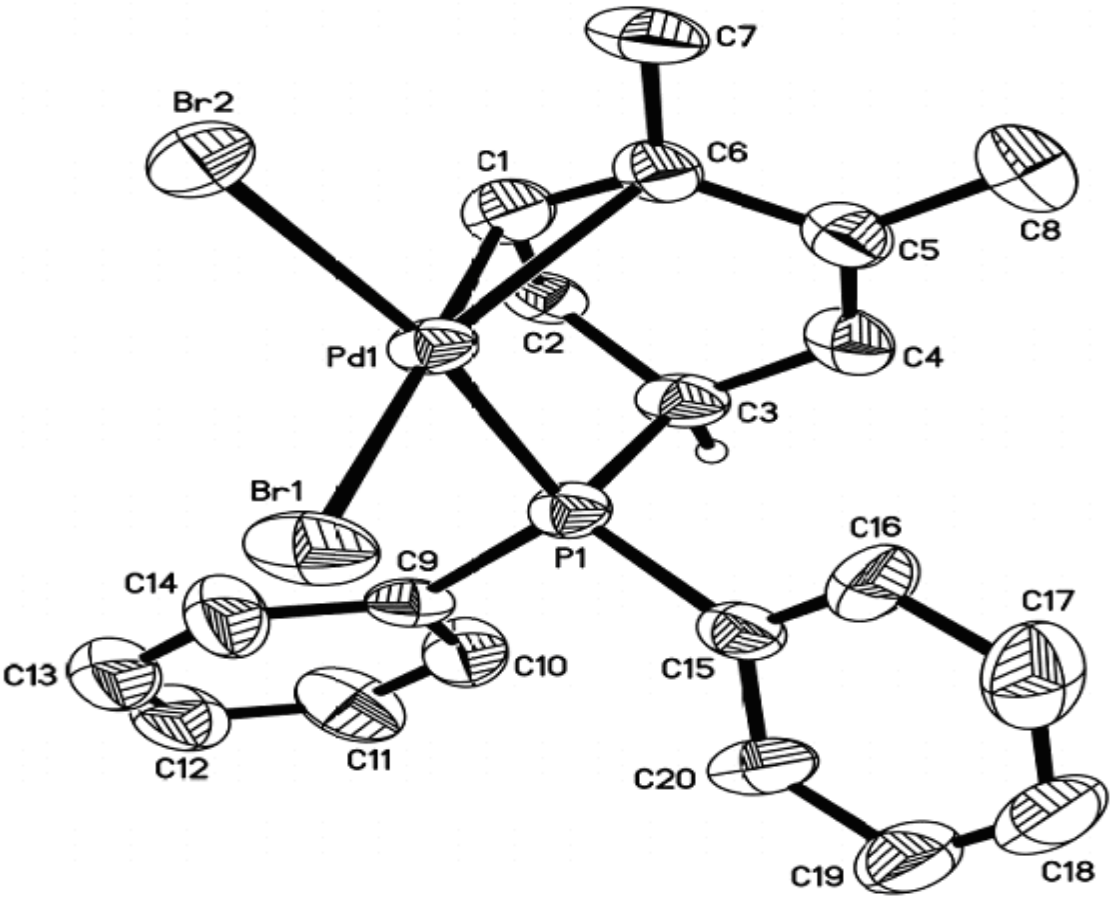


Figure 2.6 Molecular structure of dibromo complex (+)**-51**

Table 2.6 Selected bond lengths (Å) and angles (°) for (**+**)-**51**

Pd(1)–C(1)	2.168(10)	Pd(1)–P(1)	2.235(2)
Pd(1)–Br(1)	2.436(1)	Pd(1)–C(6)	2.446(9)
Pd(1)–Br(2)	2.496(1)	P(1)–C(3)	1.872(10)
C(1)–C(6)	1.362(15)	C(1)–C(2)	1.553(14)
C(2)–C(3)	1.515(13)	C(3)–C(4)	1.481(15)
C(4)–C(5)	1.329(16)	C(5)–C(6)	1.489(15)
C(5)–C(8)	1.493(15)	C(6)–C(7)	1.514(14)
C(1)–Pd(1)–P(1)	85.0(3)	C(1)–Pd(1)–Br(1)	168.5(3)
P(1)–Pd(1)–Br(1)	87.4(1)	C(1)–Pd(1)–C(6)	33.7(4)
P(1)–Pd(1)–C(6)	91.1(2)	Br(1)–Pd(1)–C(6)	155.4(3)
C(1)–Pd(1)–Br(2)	94.6(3)	P(1)–Pd(1)–Br(2)	168.5(1)
Br(1)–Pd(1)–Br(2)	91.2(1)	C(6)–Pd(1)–Br(2)	94.9(2)
C(3)–P(1)–Pd(1)	100.7(3)	C(6)–C(1)–Pd(1)	84.4(7)
C(6)–C(1)–C(2)	118.5(9)	C(3)–C(2)–C(1)	106.2(8)
C(4)–C(3)–C(2)	111.7(9)	C(4)–C(3)–P(1)	107.4(8)
C(2)–C(3)–P(1)	104.5(7)	C(5)–C(4)–C(3)	122.2(10)
C(4)–C(5)–C(6)	117.3(10)	C(4)–C(5)–C(8)	123.1(12)
C(6)–C(5)–C(8)	119.5(11)	C(1)–C(6)–C(5)	121.1(10)
C(1)–C(6)–C(7)	120.1(10)	C(5)–C(6)–C(7)	117.8(9)
C(1)–C(6)–Pd(1)	61.9(6)	C(5)–C(6)–Pd(1)	110.8(7)
C(7)–C(6)–Pd(1)	106.3(7)		

the chiral arsanorbornene (As–P) bidentate in all three complexes are similar; they all suffer from severe intrachelate steric constraints. The torsional strain within these five-membered chelate rings can be observed from the noticeable distortion of the As–C–C angles [95.8(2), 95.3(2) and 95.2(3)° for (–)-**44**, (–)-**45** and (–)-**52**, respectively]. All of these angles are seriously distorted from the ideal tetrahedral angle of 109° for tertiary carbon centers. Interestingly, the Pd–As bond distance [2.325(1) Å] in the reactive dichloro complex (–)-**45** is the shortest among the three complexes [2.447(1) and 2.354(1) Å in (–)-**44** and (–)-**52**, respectively]. This structural feature indicates that the Pd–As bond in the dichloro complex is more chemically inert under normal conditions than its counterparts in the other two complexes. It is noteworthy that the observed relative stabilities of the Pd–As bonds are consistent with the trend that is derived from the classical electronic trans effects:[98] among the three trans X–Pd–As donors, chloride exhibits the weakest effect on the stability of the Pd–As bond. Furthermore, the structural investigation revealed that, within the five-membered chelate rings, the As–C bond distance in the dichloro complex (–)-**45** [1.961(3) Å] is the shortest when compared with those in complexes (–)-**44** and (–)-**52** [1.980(2) and 1.989(4) Å in (–)-**44** and (–)-**52**, respectively]. Thus, the structural analysis indicated that the stronger As–Pd coordination effect associated with the dichloro complex is able to transmit to the As–C bond, thus affecting its chemical stability and reactivity. Apparently, the arsenic-elimination reaction from the arsanorbornene (As–P) ligand is therefore controlled by the strength of the As–Pd bonds. In view of the difficulty observed in the subsequent recoordination of the η^2 ligand to palladium(II), we believe that, during the arsenic-elimination reaction, the breaking of the two As–C bonds and the formation of the η^2-Pd coordination must have

occurred concertedly.

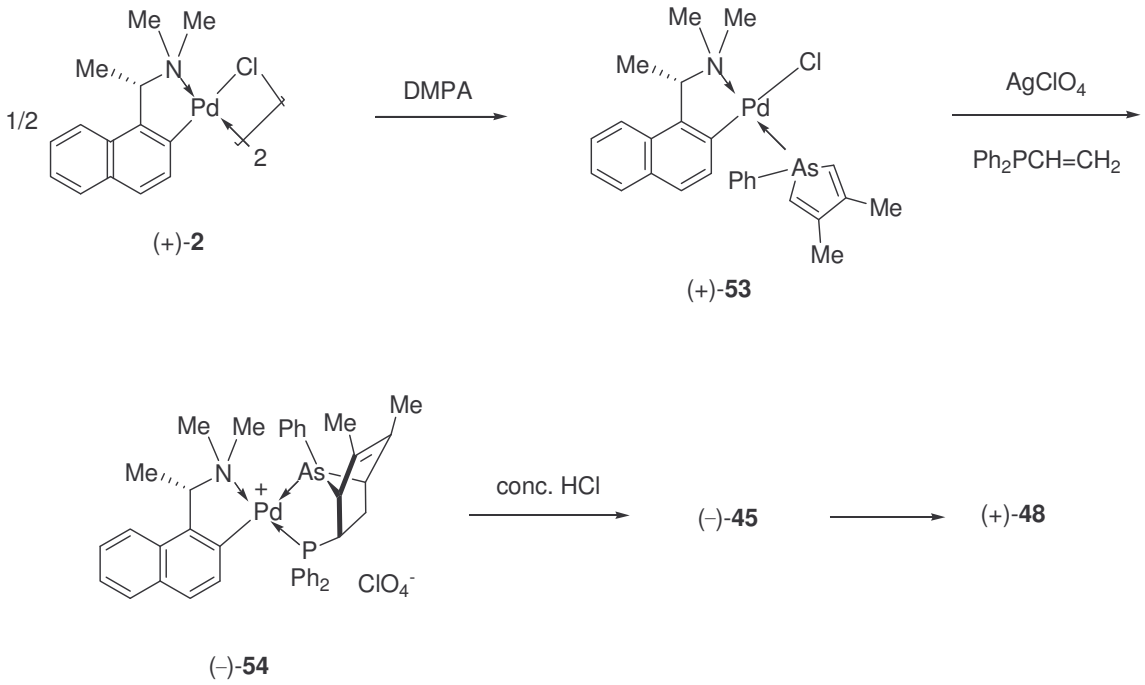
2.2.2 Template Effects on Cycloaddition Reaction between DMPA and Diphenylvinylphosphine

In order to further understand the intricacies of the stereoselectivity and stability factors influencing the As–C bonds in such systems, we undertook a synthesis of the cycloadduct where the reaction was allowed to proceed under the assistance and influence of the corresponding naphthylamine auxiliary as well as in the absence of any chiral auxiliary. It was observed that the stereoselectivity of the Diels–Alder reaction between DMPA and diphenylvinylphosphine was vastly improved using the organopalladium complex (+)**-2** as the chiral template in comparison with the above mentioned cycloaddition. More interestingly, the *trans*-[$PdI_2(DMPA)_2$] reacted with *trans*-[$PdI_2(DPVP)_2$] (DPVP = diphenylvinylphosphine) to give an unexcepted coupled product. Furthermore a different mode of arsenic elimination reaction was observed from the novel coupled product (See Scheme 2.12).

2.2.2.1 Asymmetric Cycloaddition Reaction between DMPA and Diphenylvinylphosphine Promoted by the Naphthylamine Template

DMPA was coordinated regiospecifically to (+)**-2** to give monomeric neutral complex (+)**-53** as stable yellow prisms in 64% isolated yield, $[\alpha]_D$ +259.1° (*c* 0.6, CH_2Cl_2) (Scheme 2.10). The molecular structure of (+)**-53** was confirmed by X-ray

crystallography (Figure 2.7). Selected bond lengths and angles are listed in Table 2.7. As observed in other analogous arsine complexes, the arsenic atom in DMPA is *trans* to the NMe_2 group by virtue of the hard soft donor preference exhibited by the chiral amine based auxiliary.[63]



Scheme 2.10

Treatment of complex (+)**-53** with silver perchlorate yielded the intermediate perchlorate complex in essentially quantitative yield. This highly reactive species was not isolated and upon subsequent removal of AgCl and excess silver perchlorate, the dichloromethane solution of the complex was treated directly with a stoichiometric amount of diphenylvinylphosphine. This cycloaddition reaction was monitored by $^{31}P\{^{1}H\}$ NMR spectroscopy and was found to be completed within 40 min at room temperature. Prior to purification, the $^{31}P\{^{1}H\}$ NMR spectrum of the crude Diels–Alder

reaction in $CDCl_3$ exhibited only two singlets at δ 50.2 and 48.6 in the ratio 19:1, thus indicating that only two stereochemically distinct cycloadducts were formed with high stereoselectivity being exercised. Compared to the same reaction conducted using benzylamine auxiliary as chiral template, the selectivity improved roughly six fold (from 3.2:1 to 19:1) and the reaction time reduced significantly from 3 hours to 40 minutes. The reason is that the naphthylamine auxiliary is superior to the benzylamine analogue in certain asymmetric synthesis scenarios due to the unique stereochemistry associated with the rigid *ortho*-metalated naphthylamine ring.[31] For example, there is an internal steric

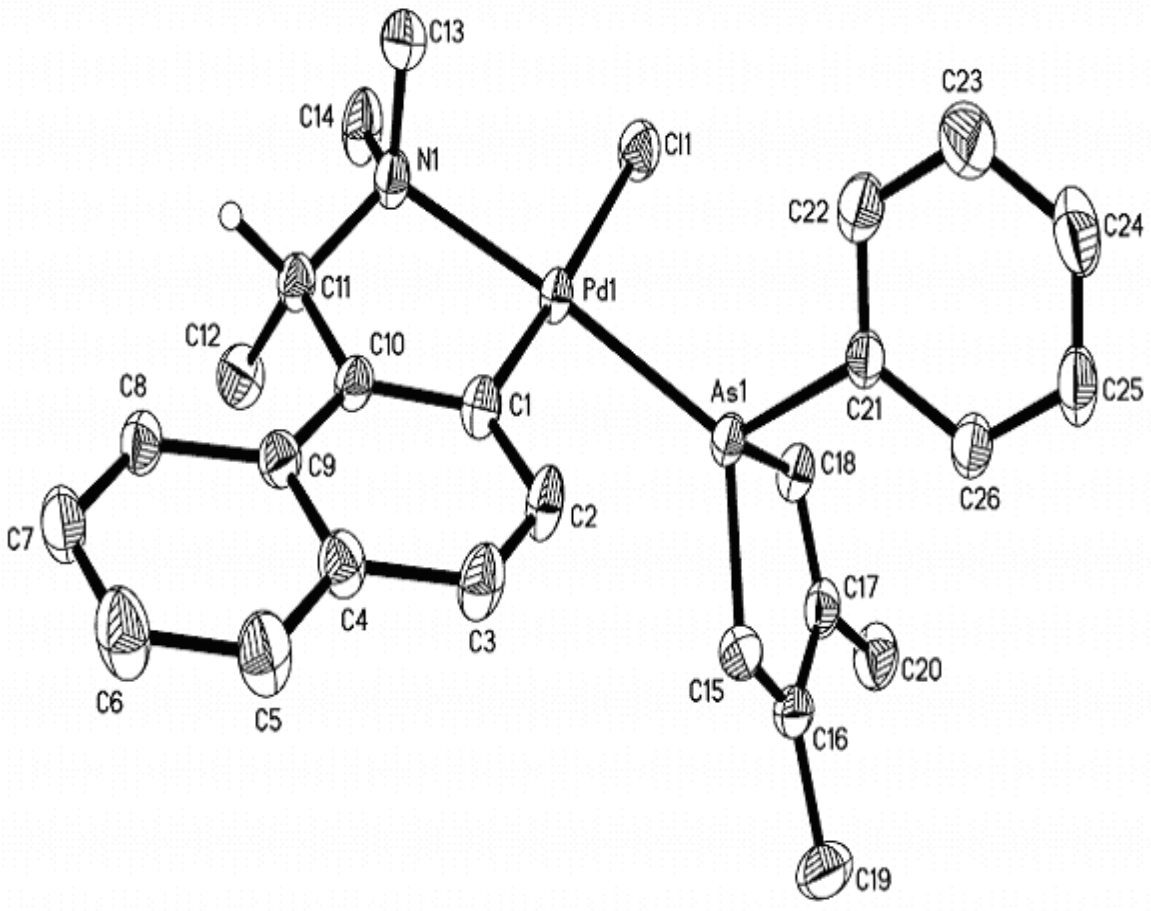


Figure 2.7 Molecular structure of complex (+)**-53**

Table 2.7 Selected bond lengths (Å) and angles (°) for (**+**)-**53**

Pd(1)–C(1)	1.987(2)	Pd(1)–N(1)	2.128(2)
Pd(1)–As(1)	2.359(1)	Pd(1)–Cl(1)	2.410(1)
As(1)–C(18)	1.906(2)	As(1)–C(15)	1.921(2)
As(1)–C(21)	1.946(2)	C(15)–C(16)	1.337(3)
C(16)–C(17)	1.497(4)	C(16)–C(19)	1.501(4)
C(17)–C(18)	1.338(3)	C(17)–C(20)	1.503(3)
C(1)–Pd(1)–N(1)	81.1(1)	C(1)–Pd(1)–As(1)	95.4(1)
N(1)–Pd(1)–As(1)	175.8(1)	C(1)–Pd(1)–Cl(1)	173.6(1)
N(1)–Pd(1)–Cl(1)	96.53(6)	As(1)–Pd(1)–Cl(1)	87.2(1)
C(18)–As(1)–C(15)	87.4(1)	C(18)–As(1)–C(21)	101.3(1)
C(15)–As(1)–C(21)	102.3(1)	C(18)–As(1)–Pd(1)	121.5(1)
C(15)–As(1)–Pd(1)	125.6(1)	C(21)–As(1)–Pd(1)	113.67(7)
C(16)–C(15)–As(1)	110.6(2)	C(15)–C(16)–C(17)	115.6(2)
C(15)–C(16)–C(19)	123.3(3)	C(17)–C(16)–C(19)	121.0(2)
C(18)–C(17)–C(16)	115.1(2)	C(18)–C(17)–C(20)	123.1(3)
C(16)–C(17)–C(20)	121.7(2)	C(17)–C(18)–As(1)	111.3(2)

repulsion between the methyl substituent on the stereogenic carbon and its neighboring naphthylene proton in complex (+)-**2**. The crystallographic determinations and rotating overhauser effect (ROESY) NMR investigations confirmed that the organometallic ring is locked into the static λ conformation, both in the solid state and in solution.[92] Thus the

prochiral NMe groups are fixed into the non-equivalent axial and equatorial positions. These NMe groups control the stereochemistry of the neighboring coordination sites. On the other hand, the stereochemistry of the five-membered organometallic ring in the corresponding benzylamine complex cannot be well defined, as the puckered benzylamine ring undergoes rapid transformation between the two non-equivalent δ and λ conformations in solution.

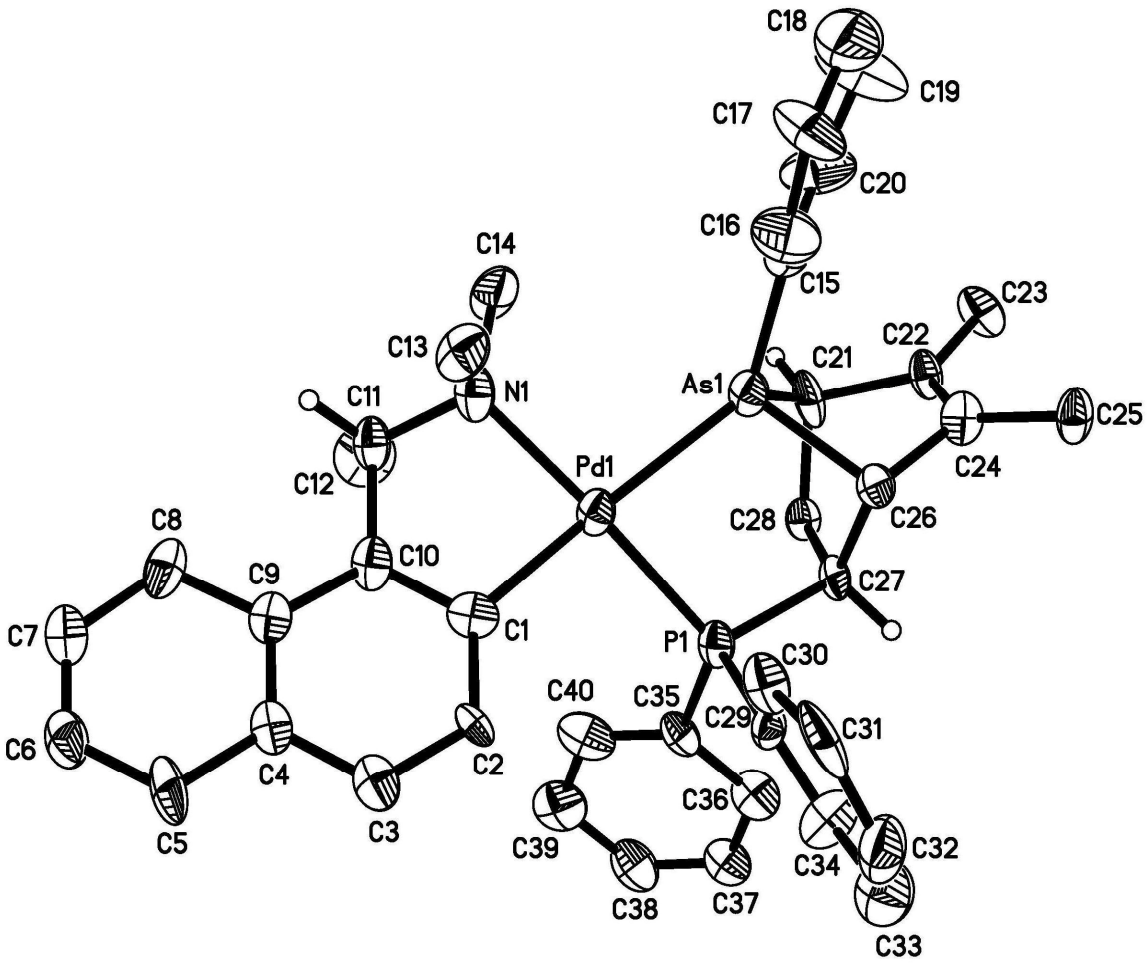


Figure 2.8 Molecular structure of complex (–)-**54**

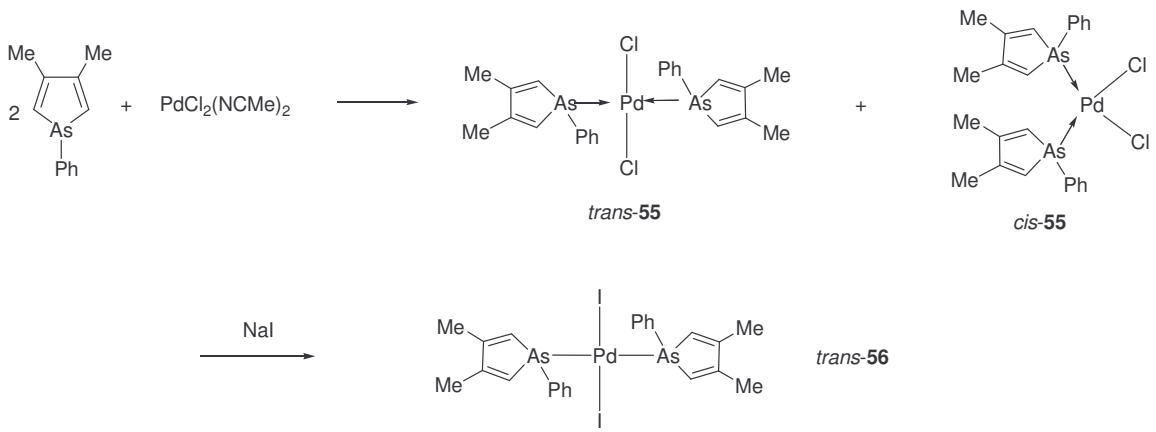
Table 2.8 Selected bond lengths (Å) and angles (°) for (–)-**54**

Pd(1)–C(1)	2.024(14)	Pd(1)–N(1)	2.095(13)
Pd(1)–As(1)	2.443(2)	Pd(1)–P(1)	2.264(4)
As(1)–C(15)	1.896(16)	As(1)–C(21)	1.984(13)
As(1)–C(26)	1.968(14)	P(1)–C(27)	1.872(11)
C(21)–C(28)	1.57(2)	C(21)–C(22)	1.579(19)
C(22)–C(24)	1.277(18)	C(22)–C(23)	1.470(17)
C(24)–C(25)	1.491(19)	C(24)–C(26)	1.548(19)
C(26)–C(27)	1.590(18)	C(27)–C(28)	1.540(17)
C(1)–Pd(1)–N(1)	82.3(5)	C(1)–Pd(1)–P(1)	95.7(4)
N(1)–Pd(1)–P(1)	174.0(3)	C(1)–Pd(1)–As(1)	173.7(4)
N(1)–Pd(1)–As(1)	99.4(3)	P(1)–Pd(1)–As(1)	83.2(1)
C(26)–As(1)–C(21)	77.5(6)	C(26)–As(1)–Pd(1)	104.6(4)
C(21)–As(1)–Pd(1)	119.0(4)	C(27)–P(1)–Pd(1)	107.7(4)
C(28)–C(21)–C(22)	105.3(12)	C(28)–C(21)–As(1)	97.4(8)
C(22)–C(21)–As(1)	101.2(9)	C(24)–C(22)–C(23)	127.8(13)
C(24)–C(22)–C(21)	112.0(12)	C(23)–C(22)–C(21)	120.2(11)
C(22)–C(24)–C(25)	129.0(14)	C(22)–C(24)–C(26)	113.0(13)
C(25)–C(24)–C(26)	118.0(12)	C(24)–C(26)–C(27)	110.0(10)
C(24)–C(26)–As(1)	102.2(9)	C(27)–C(26)–As(1)	96.0(9)
C(28)–C(27)–C(26)	105.0(10)	C(28)–C(27)–P(1)	110.3(9)
C(26)–C(27)–P(1)	107.5(7)	C(27)–C(28)–C(21)	109.1(10)

The major diastereomer (–)**-54** was obtained as pale yellow needles from dichloromethane-diethyl ether in 73% isolated yield, $[\alpha]_D = -33.0°$ (*c* 0.6, CH_2Cl_2). The molecular structure and absolute confirmation of complex (–)**-54** have been resolved by X-ray crystallography (Figure 2.8). Selected bond lengths and angles are listed in Table 2.8. It is structurally the same as the one obtained by utilizing the analogous benzyl complex, the arsenic is *trans* to the aromatic carbon and the phosphorus is *trans* to nitrogen as expected from the hard soft preference exerted by the template in such systems. Four new chiral centers have been generated with *R* absolute stereochemistry at As(1) and *R*, *R* and *S* stereochemistry at C(21), C(26) and C(27). The complex (–)**-54** is stable in solution and the naphthylamine auxiliary could be removed chemoselectively from (–)**-54** by treatment with concentrated hydrochloric acid to generate the dichloro complex (–)**-45** at room temperature. The same phenomenon as in the Scheme 2.7 was observed with the two As–C bridgehead bonds in (–)**-45** easily collapsing to give the new η^2–P palladium complex (+)**-48**.

2.2.2.2 Diels–Alder Reaction between DMPA and Diphenylvinylphosphine without Template

DMPA was coordinated to the $[PdCl_2(NCMe)_2]$, resulting in the *cis* and *trans* (monitored by its crude ^{1}H NMR spectrum) isomeric mixture of the dichloro complex **55** with the two DMPA ligands coordinated to the Pd center (Scheme 2.11). The crystals of pure *trans* dichloro complex **55** could be obtained *via* repeated recrystallization from dichloromethane-diethyl ether. The molecular structure of *trans* dichloro complex **55**



Scheme 2.11

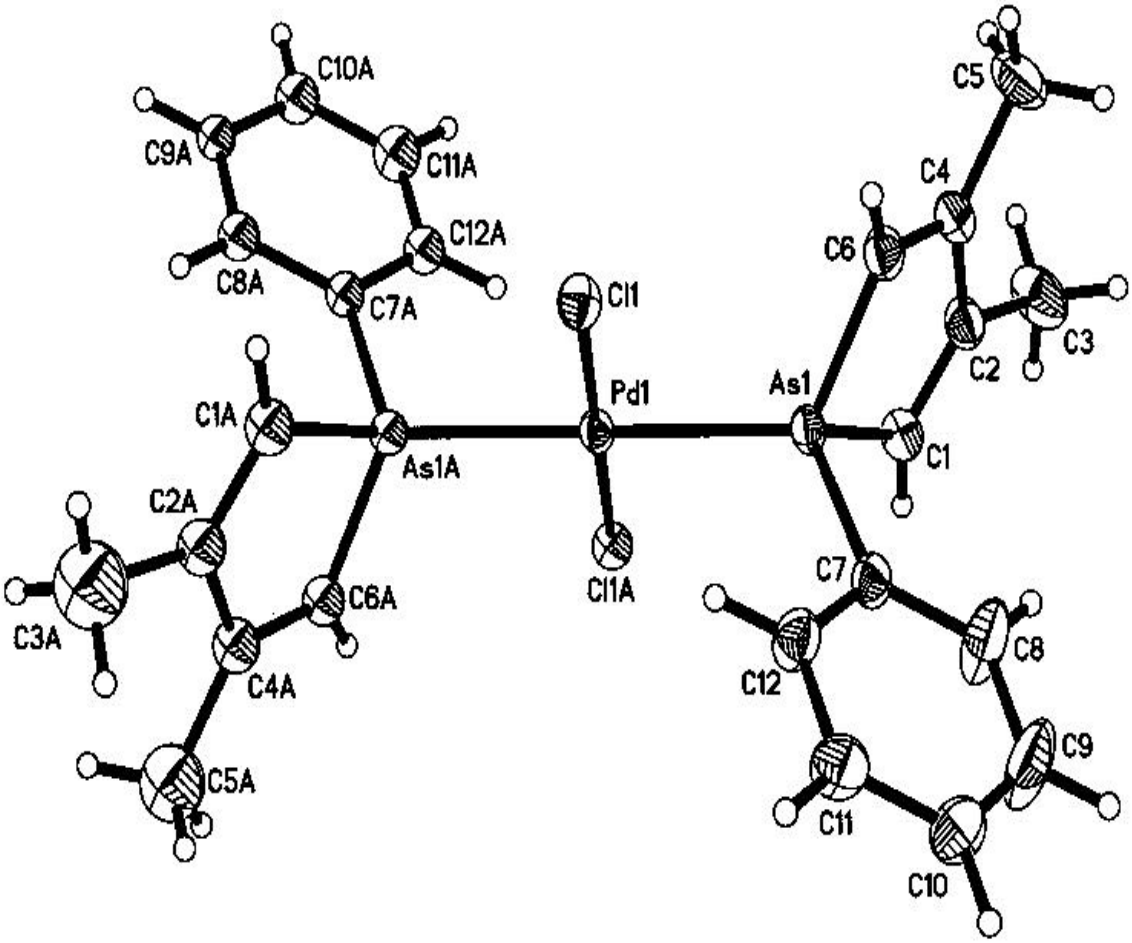


Figure 2.9 Molecular structure of complex *trans*-**55**

Table 2.9 Selected bond lengths (Å) and angles (°) for complex *trans*-**55**

Pd(1)–Cl(1)	2.333(1)	Pd(1)–Cl(1)#1	2.333(1)
Pd(1)–As(1)	2.407 (1)	Pd(1)–As(1)#1	2.407 (1)
As(1)–C(1)	1.913(3)	As(1)–C(6)	1.912(3)
C(1)–C(2)	1.341(4)	C(2)–C(4)	1.501(4)
C(4)–C(6)	1.337(4)		
Cl(1)#1–Pd(1)–Cl(1)	180.0(1)	Cl(1)#1–Pd(1)–As(1)	91.1(1)
Cl(1)–Pd(1)–As(1)	88.9 (1)	Cl(1)#1–Pd(1)–As(1)#1	88.9 (1)
Cl(1)–Pd(1)–As(1)#1	91.1(1)	As(1)–Pd(1)–As(1)#1	180.0(1)
C(6)–As(1)–C(1)	88.3(1)	C(2)–C(1)–As(1)	110.0(2)
C(1)–C(2)–C(4)	115.7(3)	C(6)–C(4)–C(2)	115.8(2)
C(4)–C(6)–As(1)	110.0(2)		

(Figure 2.9) has been confirmed by X-ray crystallography. Selected bond lengths and angles are listed in Table 2.9. The geometry at palladium is a parallelogram with bond angles at metal center ranging between 88.9(1) to 91.1(1) and 180.0(1)°. In fact, the mixture of *trans* and *cis* dichloro complexes of **55** need not be separated because when the complex **55** was subsequently converted to the analogous diiodo complex **56** in high yield (97%) by treatment with sodium iodide at room temperature, only the *trans* isomer was obtained. This can be confirmed by the single-crystal X-ray analysis of complex **56** in which the arsenic is *trans* to each other (Figure 2.10). Selected bond lengths and angles are listed in Table 2.10.

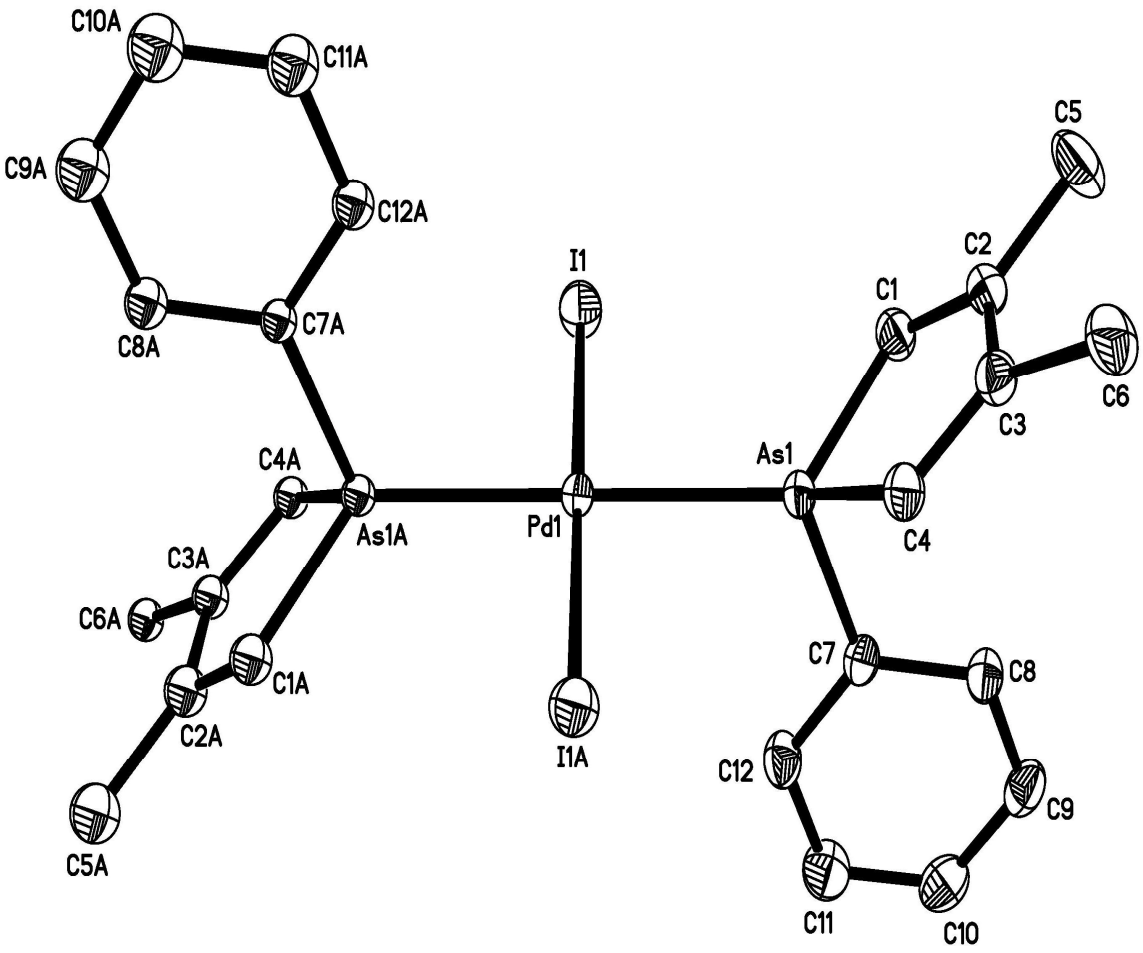


Figure 2.10 Molecular structure of complex **56**

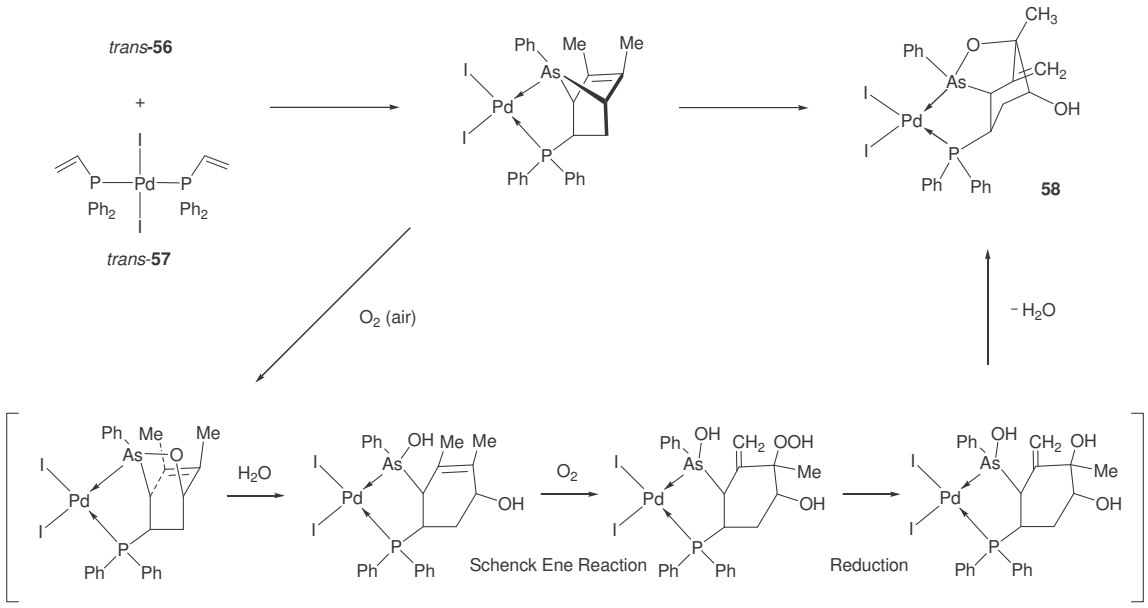
Table 2.10 Selected bond lengths (Å) and angles (°) for complex **56**

Pd(1)–I(1)	2.600(1)	Pd(1)–I(1)#1	2.600(1)
Pd(1)–As(1)	2.394(1)	Pd(1)–As(1)#1	2.394(1)
As(1)–C(1)	1.911(2)	As(1)–C(4)	1.916(2)
C(1)–C(2)	1.341(3)	C(2)–C(3)	1.497(3)
C(3)–C(4)	1.340(3)		

I(1)–Pd(1)–I(1)#1	180.0(1)	I(1)#1–Pd(1)–As(1)	87.7(1)
I(1)–Pd(1)–As(1)	92.3(1)	I(1)#1–Pd(1)–As(1)#1	92.3(1)
I(1)–Pd(1)–As(1)#1	87.7(1)	As(1)–Pd(1)–As(1)#1	180.0(1)
C(1)–As(1)–C(4)	88.0(1)	C(2)–C(1)–As(1)	110.5(1)
C(1)–C(2)–C(3)	115.4(2)	C(4)–C(3)–C(2)	115.9(2)
C(3)–C(4)–As(1)	110.1(2)		

The diiodo complex **56** was then allowed to react with *trans*-[$PdI_2(DPVP)_2$] **57** at room temperature (Scheme 2.12). The Diels–Alder reaction was monitored by $^{31}P\{^1H\}$ NMR spectroscopy. Analysis of the crude reaction mixture indicated the formation of several products amongst which complex **58** was subsequently isolated by recrystallization. However, attempts to isolate other products were not successful. The molecular structure of complex **58** was confirmed by X-ray crystallography and indicated the formation of an unusual ligand system that may have resulted from a novel rearrangement of the norbornene skeletal system of **52** (Figure 2.11). Selected bond lengths and angles are listed in Table 2.11. Upon further detailed analysis of the $^{31}P\{^1H\}$ NMR spectral data of the reaction it was seen that when the two *trans* diiodo complexes, **56** and **57**, were mixed together, a new peak at δ 13.0 appeared immediately which can be attributed to the *trans* or *cis* intermediate [$PdI_2(DMPA)(DPVP)$][85b]. After 1 day, the Diels–Alder reaction product was found to be formed as observed from the $^{31}P\{^1H\}$ signal at δ 37.7 which is identical to the value obtained for the enantiomerically pure version of the cycloadduct (–)-**52**. Cyclic phosphine oxides with contracted internal C–P–C angles have been found to undergo oxygen insertion into a C–P bond.[99] The same

phenomenon may occur in the cycloadduct resulting in oxygen being inserted into the As–C bond of the complex and thereafter, due to the inherent instability of such compounds, it undergoes hydrolysis[99a]. Subsequently a Schenck Ene reaction[100] caused the double bond migration to a methyl group.[101] Finally, the reduction of the peroxide[102] gave the alcohol intermediate which eliminated a molecule of water to yield the complex **58**. Taking into consideration the low yield and numerous unidentified side products obtained along with the fact that the presence of phenylarsonic acid in similar reactions has been discussed earlier, the possibility of the acid acting as a reductant in this reaction could not be ruled out.



Scheme 2.12

The diiodo complex **58** is very different from the η^2-P palladium complexes formed as a result of As–C bridgehead bond collapse, only one As–C bond broke in this case, and meanwhile one new five-membered ring containing As–O and the seven-membered ring

containing hydroxyl group were generated during the course of the reaction. To our knowledge this is the first instance of such unique bridgehead collapse coupled with rearrangement observed in cyclic arsenic systems. We are currently in the process of fine-tuning the conditions in order to improve the yield of the reaction which will allow us to do a more thorough investigation of the mechanism involved as well as pave the way for potential application of the ligand system in various catalytic scenarios.

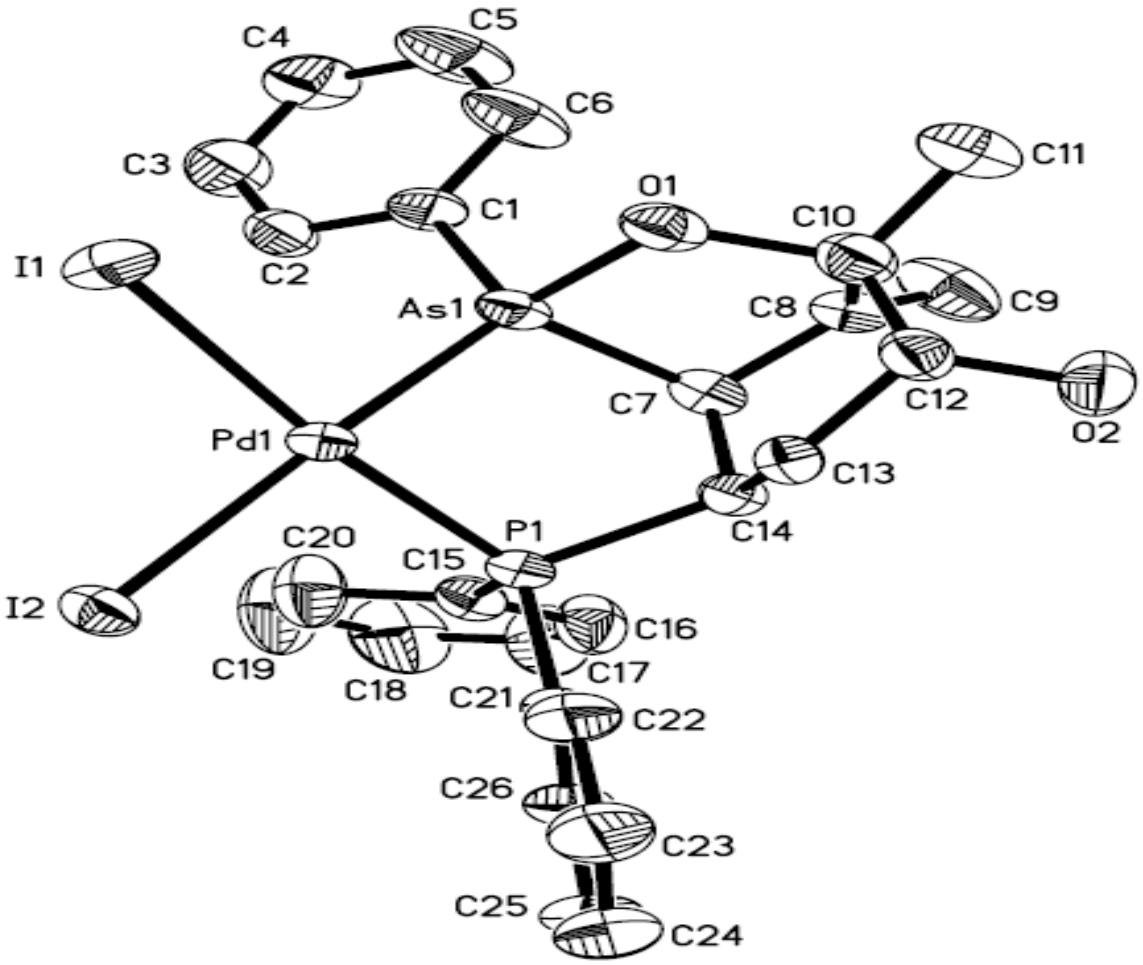


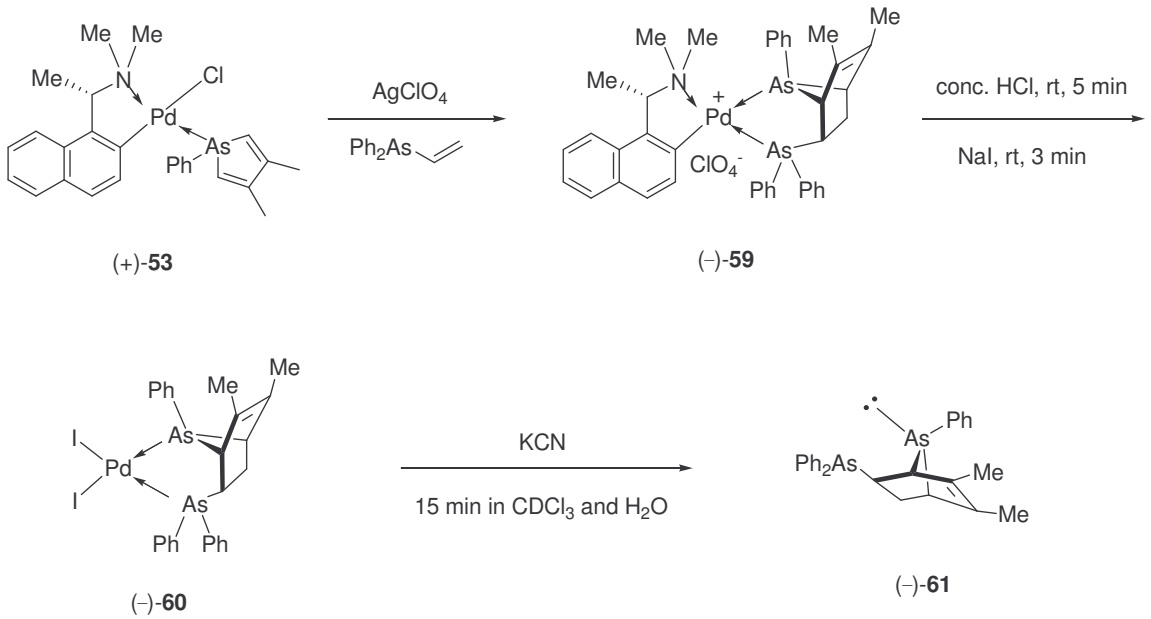
Figure 2.11 Molecular structure of complex **58**

Table 2.11 Selected bond lengths (Å) and angles (°) for complex **58**

Pd(1)–P(1)	2.276(1)	Pd(1)–As(1)	2.345(1)
Pd(1)–I(2)	2.620(1)	Pd(1)–I(1)	2.649(1)
As(1)–O(1)	1.786(4)	As(1)–C(7)	1.976(6)
C(7)–C(8)	1.490(7)	C(7)–C(14)	1.537(7)
C(8)–C(9)	1.304(9)	C(8)–C(10)	1.509(8)
C(10)–C(11)	1.516(8)	C(10)–O(1)	1.531(7)
C(10)–C(12)	1.549(8)	C(12)–O(2)	1.416(7)
C(12)–C(13)	1.525(7)	C(13)–C(14)	1.553(7)
P(1)–Pd(1)–As(1)	83.7(1)	P(1)–Pd(1)–I(2)	91.8(1)
As(1)–Pd(1)–I(2)	173.4(1)	P(1)–Pd(1)–I(1)	172.7(1)
As(1)–Pd(1)–I(1)	89.2(1)	I(2)–Pd(1)–I(1)	95.4(1)
O(1)–As(1)–C(7)	89.6(2)	C(8)–C(7)–C(14)	112.9(5)
C(9)–C(8)–C(7)	125.9(6)	C(9)–C(8)–C(10)	126.8(6)
C(7)–C(8)–C(10)	107.3(5)	C(8)–C(10)–O(1)	106.9(5)
C(8)–C(10)–C(12)	108.5(5)	O(1)–C(10)–C(12)	106.5(4)
O(2)–C(12)–C(13)	113.0(5)	O(2)–C(12)–C(10)	107.1(5)
C(13)–C(12)–C(10)	111.2(4)	C(12)–C(13)–C(14)	116.3(4)
C(7)–C(14)–C(13)	111.7(4)		

2.2.3 Asymmetric Cycloaddition Reaction between DMPA and Diphenylvinylarsine

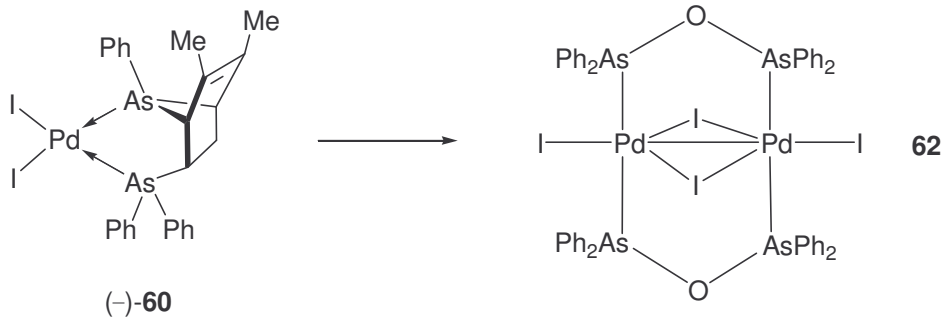
The cycloaddition reaction between (+)**-53** and diphenylvinylarsine was completed in 5 days at room temperature and resulted in the formation of two diastereomers in the ratio of 6:1 (Scheme 2.13). The major isomer (–)**-59** was isolated by column chromatography in 75% yield, $[\alpha]_D$ –91.8° (*c* 0.5, CH_2Cl_2, 436 nm), and was then recrystallized from chloroform–diethyl ether in the form of pale yellow needles. The chiral amine auxiliary on complex (–)**-59** can be removed from the template complex chemoselectively using concentrated hydrochloric acid for 5 min at room temperature. The resulting dichloro complex is unstable for isolation by column chromatography and fractional recrystallization. Hence it was further converted to the analogous diiodo complex (–)**-60** by treatment with sodium iodide for 3 min at room temperature. The diiodo complex (–)**-60** was readily isolated by column chromatography in 70% yield, $[\alpha]_D$ –78.6° (*c* 0.14, CH_2Cl_2).



(+)-**53** (–)-**59** (–)-**60** (–)-**61**

Scheme 2.13

Owing to the configurational instability of the uncoordinated As–As bidentate ligand, the liberation process must be carried out under strictly inert atmospheric condition. A mixture of (–)-**60** and excess potassium cyanide in $CDCl_3$ and H_2O was vigorously shaken for 15 min at room temperature to liberate the optically active homobidentate ligand (–)-**61** as air-sensitive solid in 85% yield, $[\alpha]_D$ = –81.7° (*c* 6.16, $CDCl_3$). During the recrystallization of complex (–)-**60**, deep red crystals were obtained. From the X-ray structural analysis of this complex, however, it was evident that it is not the original diiodo complex (–)-**60**, on the contrary an unexpected complex **62** (Scheme 2.14, Figure 2.12) was obtained. Selected bond lengths and angles are listed in Table 2.12. All the As–C bonds in the As–As bidentate arsanorbornene skeleton have undergone cleavage. This is contrast to the analogous dichloro and dibromo complexes (–)-**45** and (–)-**50**, in which cases, only the bridged head arsenic atom was eliminated and the phosphorus atom was retained. The coordination about each Pd atom is a distorted octahedron. Analysis of the X-ray data showed that the two diphenylarsine ligands occupy the axial positions, whereas the terminal iodo ligand, two bridging iodo ligands and a formal Pd–Pd bond can be considered to occupy the equatorial positions.



(–)-**60**

Scheme 2.14

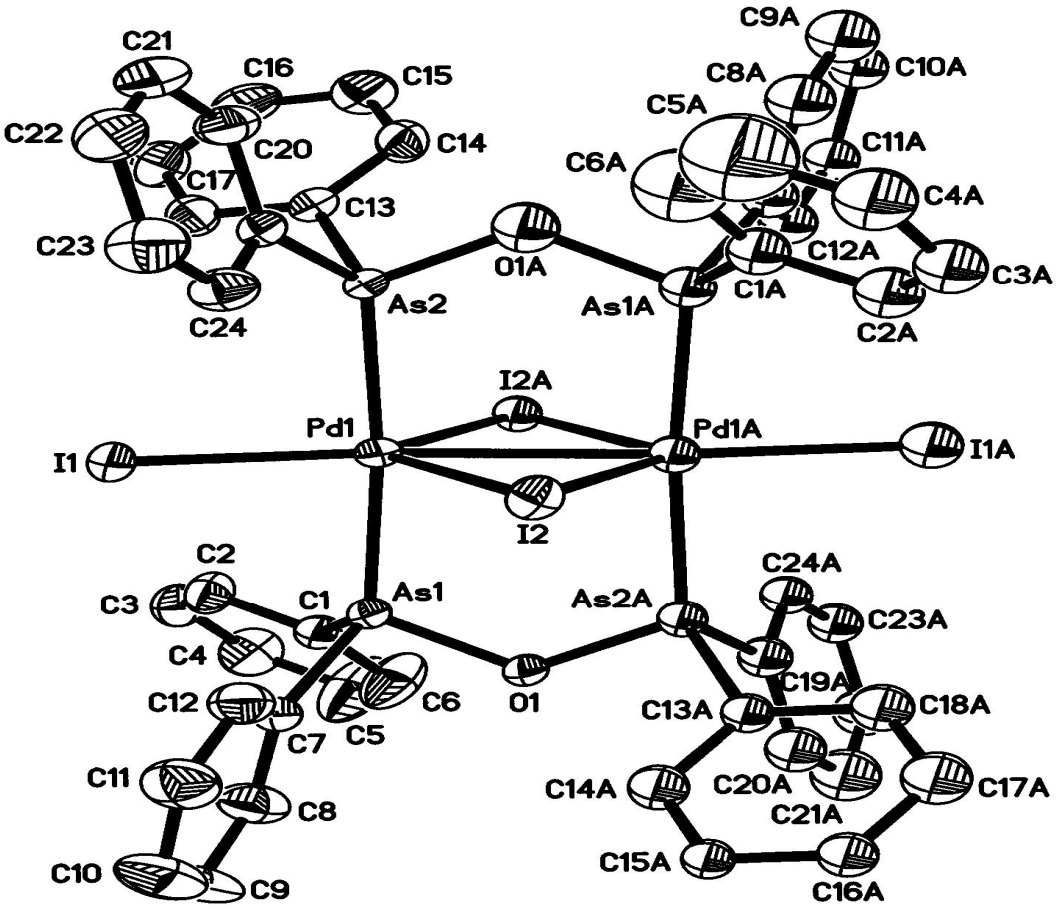


Figure 2.12 Molecular structure of complex **62**

Table 2.12 Selected bond lengths (Å) and angles (°) for **62**

Pd(1)–As(1)	2.379(1)	Pd(1)–As(2)	2.379(1)
Pd(1)–I(1)	2.665(1)	Pd(1)–I(2)#1	2.743(1)
Pd(1)–I(2)	2.954(1)	Pd(1)–Pd(1)#1	2.966(1)
As(1)–O(1)	1.785(2)	As(1)–C(7)	1.931(3)
As(1)–C(1)	1.934(4)	As(2)–O(1)#1	1.783(2)
As(2)–C(19)	1.931(3)	As(2)–C(13)	1.938(3)

I(2)–Pd(1)#1	2.7431(3)	O(1)–As(2)#1	1.783(2)
As(1)–Pd(1)–As(2)	173.8(1)	As(1)–Pd(1)–I(1)	87.8(1)
As(2)–Pd(1)–I(1)	88.0(1)	As(1)–Pd(1)–I(2)#1	89.5(1)
As(2)–Pd(1)–I(2)#1	89.9(1)	I(1)–Pd(1)–I(2)#1	131.8(1)
As(1)–Pd(1)–I(2)	93.4(1)	As(2)–Pd(1)–I(2)	92.4(1)
I(1)–Pd(1)–I(2)	110.8(1)	I(2)#1–Pd(1)–I(2)	117.4(1)
As(1)–Pd(1)–Pd(1)#1	92.9(1)	As(2)–Pd(1)–Pd(1)#1	92.3(1)
I(1)–Pd(1)–Pd(1)#1	166.0(1)	I(2)#1–Pd(1)–Pd(1)#1	62.2(1)
I(2)–Pd(1)–Pd(1)#1	55.2(1)	O(1)–As(1)–C(7)	96.5(1)
O(1)–As(1)–C(1)	98.6(1)	C(7)–As(1)–C(1)	105.2(1)
O(1)–As(1)–Pd(1)	113.9(1)	C(7)–As(1)–Pd(1)	121.4(1)
C(1)–As(1)–Pd(1)	117.2(1)	O(1)#1–As(2)–C(19)	97.1(1)
O(1)#1–As(2)–C(13)	99.0(1)	C(19)–As(2)–C(13)	103.8(1)
O(1)#1–As(2)–Pd(1)	114.4(1)	C(19)–As(2)–Pd(1)	121.3(1)
C(13)–As(2)–Pd(1)	117.3(1)		

2.3 Conclusions

The organopalladium complex (+)-**1** has been successfully used as the chiral template to promote the asymmetric cycloaddition reaction between DMPA and diphenylvinylphosphine. A diphenylphosphino-substituted asymmetrical heterobidentate arsanorbornene (As–P) ligand (–)-**46** was obtained stereoselectively. In contrast to their

reported P–P analogue, the arsenic donor in the dichloro complex (–)-**45** could be eliminated stereospecifically under mild reaction conditions to generate the corresponding 1-(diphenylphosphino)-3,4-dimethyl-2,4-cyclohexadiene, which remained as a bidentate ligand at the $PdCl_2$ unit *via* phosphorus and the η^2-C_4–C_5 double bond. The arsenic-elimination process was found to be influenced by the halo ligand in [(As–P)PdX_2]. A similar process was observed with the analogous dibromo complex (–)-**50**, but the corresponding diiodo species (–)-**52** did not show similar reactivity.

The property of the metal template was found to have a considerable effect on the above reaction. The naphthyl complex (+)-**2** is more effective than the benzyl analogue (+)-**1**. The reaction selectivity was improved from 3.2:1 to 19:1. However, when no chiral auxiliary was employed, *trans*-PdI_2(DMPA)$_2$ reacted with *trans*-PdI_2(diphenylvinylphosphine)$_2$ producing a structural novel diiodo complex **58**, as a result of an interesting selective cleavage of one As–C bond in the norbornene skeleton and subsequent rearrangements within the skeletal framework.

The asymmetric cycloaddition reaction between DMPA and diphenylvinylarsine also could be successfully promoted *via* using complex (+)-**2** as the reaction promoter in the ratio of 6:1 to afford the optically pure diarsine ligand (–)-**61**. The corresponding diiodo complex (–)-**60** is unstable, and consequently all the As–C bonds in the As–As bidentate arsanorbornene skeleton cleaved to give an unexpected dimetal complex **62**.

2.4 Experimental Section

General: Reactions involving air-sensitive compounds were performed under an inert atmosphere of argon or nitrogen using standard Schlenk techniques. Solvents were dried and freshly distilled according to standard procedure and degassed prior to use when necessary. The ^{1}H, $^{31}P\{^{1}H\}$ and ^{13}C NMR spectra were recorded at 25 ºC on Bruker Avance 300, 400 and 500 spectrometers. Optical rotations were measured on the specified solution in a 0.1 dm cell at 20 ºC with a Perkin-Elmer 341 polarimeter. Elemental analysis was performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at Nanyang Technological University. Melting points were determined on OptiMelt SRS MAP-100 and were uncorrected.

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

(+)-**1**,[43] (+)-**2**,[45] DMPA,[103,104] diphenylvinylphosphine[105] and diphenylvinylarsine[52] were prepared following the literature procedures.

Preparation of Complex (+)-43

A mixture of DMPA (1.50 g, 6.46 mmol) and (+)-**1** (1.87 g, 3.22 mmol) in dichloromethane (70 mL) was stirred at room temperature for 2 h. The solvent was removed from the reaction mixture, and the complex (+)**-43** was isolated by column chromatography on a silica column with dichloromethane-*n*-hexane to give a yellow powder, which was recrystallized from chloroform-*n*-hexane in the form of bright-yellow prisms (2.53 g, 75%). $[\alpha]_D$ = +60.4° (*c* 0.6, CH_2Cl_2). Mp: 110–111 ºC. Anal. Calcd for

$C_{22}H_{27}AsClNPd$: C, 50.6; H, 5.2; N, 2.7. Found: C, 50.8; H, 5.4; N, 2.8. ^{1}H NMR ($CDCl_3$, δ): 1.64 (d, $^{3}J_{HH}$ = 6.5 Hz, 3H, CH*CH₃*), 2.09 (s, 6H, =C*CH₃*), 2.76 (s, 3H, N*CH₃*), 2.93 (s, 3H, N*CH₃*), 3.88 (q, $^{3}J_{HH}$ = 6.5 Hz, 1H, *CH*CH_3), 6.77–7.79 (m, 11H, aromatics).

Cycloaddition Reaction: Preparation of Complex (–)-44

A solution of (+)-**43** (0.91 g, 1.74 mmol) in dichloromethane (50 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (1.0 g) in H_2O (1 mL). The organic layer, after the removal of AgCl, was then washed with H_2O (3 × 50 mL), dried ($MgSO_4$), and subsequently treated with diphenylvinylphosphine (0.37 g, 1.74 mmol) at room temperature for 3 h. Removal of the solvent gave (–)-**44** as a thick oil, which was then recrystallized from chloroform-diethyl ether to give the complex as colorless prisms (0.77 g, 60%). $[\alpha]_D$ = –71.9° (*c* 0.6, CH_2Cl_2). Mp: 164–165 ºC. Anal. Calcd for $C_{36.5}H_{40.5}AsCl_{2.5}NO_4PPd$: C, 51.1; H, 4.8; N, 1.6. Found: C, 50.9; H, 4.6; N, 1.7. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, δ): 50.1. ^{1}H NMR ($CDCl_3$, δ): 1.40 (s, 3H, =C*CH₃*), 1.60 (d, $^{5}J_{PH}$ = 1.0 Hz, 3H, =C*CH₃*), 1.86 (d, $^{3}J_{HH}$ = 6.4 Hz, 3H, CH*CH₃*), 1.95 (m, 1H, CH*CH₂*), 2.56 (dd, $^{2}J_{HH}$ = 13.9, $^{3}J_{PH}$ = 24.3 Hz, 1H, CH*CH₂*), 2.74 (d, $^{4}J_{PH}$ = 1.5 Hz, 3H, N*CH₃*), 2.80 (s, 3H, N*CH₃*), 2.82 (s, 1H, As*CH*), 3.10 (t, $^{3}J_{HH}$ = 9.0 Hz, 1H, *CH*CH_2), 3.64 (qn, $^{3}J_{HH}$ = $^{4}J_{PH}$ = 6.0 Hz, 1H, *CH*CH_3), 3.82 (s, 1H, As*CH*), 6.46–8.19 (m, 19H, aromatics).

Removal of Chiral Auxiliary: Synthesis of Dichloro Complex (–)-45

The complex (–)-**44** (0.18 g, 0.16 mmol) was dissolved in dichloromethane (60 mL) and treated with excess concentrated HCl (4 mL) at room temperature for 0.5 h. The mixture was then washed with H_2O (3 × 50 mL), dried ($MgSO_4$), and subsequently

recrystallized from chloroform-diethyl ether as pale-yellow crystals (–)-**45** (0.06 g, 60%). $[\alpha]_D$ = –40.0° (*c* 0.6, CH_2Cl_2). Mp: 162–163 °C. Anal. Calcd for $C_{26.5}H_{26.5}AsCl_{3.5}PPd$: C, 43.8; H, 3.7. Found: C, 43.6; H, 3.9. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 33.6. ^1H NMR ($CDCl_3$, δ): 1.61 (s, 3H, =C*CH*$_3$), 1.65 (d, $^5J_{PH}$ = 0.8 Hz, 3H, =C*CH*$_3$), 1.94 (ddd, $^3J_{HH}$ = 10.0, $^2J_{HH}$ = 13.2, $^3J_{HH}$ = 19.3 Hz, 1H, CH*CH*$_2$), 2.60 (dd, $^2J_{HH}$ = 12.8, $^3J_{PH}$ = 23.8 Hz, 1H, CH*CH*$_2$), 3.04 (dt, $^3J_{HH}$ = 6.7, $^2J_{PH}$ = 2.0 Hz, 1H, *CH*CH$_2$), 3.16 (s, 1H, As*CH*), 3.49 (d, $^3J_{HH}$ = 3.0 Hz, 1H, As*CH*), 7.38–8.26 (m, 15H, aromatics).

Liberation of the As–P Ligand (–)-46

A solution of (–)-**45** (0.13 g, 0.21 mmol) in dichloromethane (20 mL) was stirred vigorously with a saturated aqueous solution of KCN (1.0 g) for 3 min. The organic layer was separated, then washed with H_2O (3 × 20 mL), and dried ($MgSO_4$). Upon removal of the solvent, the free ligand (–)-**46** was obtained as an air-sensitive white solid (0.08 g, 86%). $[\alpha]_D$ = –70.4° (*c* 0.9, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): –11.1.

Arsenic-Elimination Reaction: Isolation of Complex (+)-48

The complex (–)-**45** (0.12 g, 0.19 mmol) was dissolved in dichloromethane and allowed to stand at room temperature for 1 week; red crystals of (+)-**48** were obtained (0.03 g, 34%). $[\alpha]_D$ = +395.6° (*c* 0.2, CH_2Cl_2). Mp: 149–150 °C. Anal. Calcd for $C_{20}H_{21}Cl_2PPd$: C, 51.1; H, 4.5. Found: C, 51.0; H, 4.6. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 139.2. ^1H NMR ($CDCl_3$, δ): 1.91 (d, $^5J_{PH}$ = 5.6 Hz, 3H, =C*CH*$_3$), 2.17 (s, 2H, CH*CH*$_2$), 2.50 (s, 3H, =C*CH*$_3$), 3.29 (t, $^3J_{HH}$ = 5.5 Hz, 1H, P*CH*), 5.81 (d, $^3J_{HH}$ = 4.8 Hz, 1H, =*CH*), 6.04 (s, 1H, =*CH*), 7.45–8.02 (m, 10H, aromatics).

Liberation of Monodentate Phosphine Ligand (–)-49

A solution of (+)-**48** (0.02 g, 0.04 mmol) in dichloromethane (20 mL) was stirred vigorously with a saturated aqueous solution of KCN (1.0 g) for 3 min. The organic layer was separated, washed with H_2O (3 × 20 mL), and dried ($MgSO_4$). Upon removal of the solvent, the free ligand (–)-**49** was obtained as an air-sensitive white solid (0.01 g, 86%). $[\alpha]_D$ = –10.4° (*c* 0.6, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): –11.2. ^1H NMR ($CDCl_3$, δ): 1.25 (s, 3H, =C*CH*$_3$), 1.74 (d, 3H, $^5J_{PH}$ = 1.3 Hz, =C*CH*$_3$), 2.03–2.17 (m, 2H, CH*CH*$_2$), 3.11 (m, 1H, P*CH*), 5.36 (d, $^3J_{PH}$ = 5.7 Hz, 1H, =*CH*), 5.45 (s, 1H, =*CH*), 7.31–7.52 (m, 10H, aromatics).

Preparation of the Dibromo Complex (–)-50

The solution of (–)-**45** (0.10 g, 0.16 mmol) in dichloromethane (50 mL) was added to potassium bromide (0.20 g) in acetone (50 mL) and water (10 mL) and stirred vigorously for 10 min. The solvents were removed and the residue was extracted with dichloromethane and water and dried with $MgSO_4$. Removal of the solvent gave (–)-**50** as a solid, which was then recrystallized from chloroform-diethyl ether to give the product as yellow needle crystals (0.08 g, 70%). $[\alpha]_D$ = –51.7° (*c* 0.6, CH_2Cl_2). Mp: 161–162 ºC. Anal. Calcd for $C_{26}H_{26}AsBr_2PPd$: C, 44.0; H, 3.7. Found: C, 43.8; H, 3.8. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 35.8. ^1H NMR ($CDCl_3$, δ): 1.57 (s, 3H, =C*CH*$_3$), 1.64 (s, 3H, =C*CH*$_3$), 1.96 (ddd, $^3J_{HH}$ = 9.9, $^2J_{HH}$ = 13.1, $^3J_{HH}$ = 19.6 Hz, 1H, CH*CH*$_2$), 2.65 (dd, $^2J_{HH}$ = 13.0, $^3J_{PH}$ = 25.9 Hz,1H, CH*CH*$_2$), 3.04 (dt, $^3J_{HH}$ = 4.5, $^2J_{PH}$ = 2.2 Hz, 1H, *CH*CH$_2$), 3.13 (s, 1H, As*CH*), 3.50 (d, $^3J_{HH}$ = 3.2 Hz, 1H, As*CH*), 7.38–8.27 (m, 15H, aromatics).

Preparation of the Elimination Product (+)-51

A solution of complex (–)-**50** (0.05 g, 0.07 mmol) was dissolved in dichloromethane and allowed to stand at room temperature for several days. Red crystals of (+)-**51** were obtained (0.02 g, 57%). $[\alpha]_D$ = +495.0° (*c* 0.2, CH_2Cl_2). Mp: 185–186 ºC. Anal. Calcd for $C_{20}H_{21}Br_2PPd$: C, 43.0; H 3.79. Found: C, 42.7; H, 3.88. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 141.8. ^1H NMR (CD_2Cl_2, δ): 1.87 (d, $^5J_{PH}$ = 6.2 Hz, 3H, =C*CH*$_3$), 2.12 (s, 2H, CH*CH*$_2$), 2.51 (s, 3H, =C*CH*$_3$), 3.29 (t, $^3J_{HH}$ = 8.0 Hz, 1H, P*CH*), 5.82 (d, $^3J_{HH}$ = 7.4 Hz, 1H, =*CH*), 6.21 (s, 1H, =*CH*), 7.46–7.97 (m, 10H, aromatics).

Preparation of the Diiodo Complex (–)-52

The solution of (–)-**45** (0.10 g, 0.16 mmol) in dichloromethane (80 mL) was mixed with sodium iodide (0.20 g) in acetone (80 mL) and stirred vigorously for 10 min. The solvents were removed, and the residue was extracted with dichloromethane. Removal of the solvent gave (–)-**52** as a solid, which was then recrystallized from chloroform-diethyl ether to give the product as red microcrystals (0.08 g, 62%). $[\alpha]_D$ = –55.0° (*c* 0.6, CH_2Cl_2). Mp: 144–145 ºC. Anal. Calcd for $C_{26}H_{26}AsI_2PPd$: C, 38.8; H, 3.3. Found: C, 38.5; H, 3.3. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 37.7. ^1H NMR ($CDCl_3$, δ): 1.50 (s, 3H, =C*CH*$_3$), 1.63 (s, 3H, =C*CH*$_3$), 2.00 (ddd, $^3J_{HH}$ = 9.5, $^2J_{HH}$ = 13.7, $^3J_{HH}$ = 20.8 Hz, 1H, CH*CH*$_2$), 2.70 (dd, $^2J_{HH}$ = 12.9, $^3J_{PH}$ = 24.8 Hz, 1H, CH*CH*$_2$), 2.86 (dt, $^3J_{HH}$ = 8.2, $^2J_{PH}$ = 2.2 Hz, 1H, *CH*CH_2), 3.04 (d, $^3J_{HH}$ = 1.8 Hz, 1H, As*CH*), 3.52 (d, $^3J_{HH}$ = 3.0 Hz, 1H, As*CH*), 7.39–8.24 (m, 15H, aromatics).

Preparation of Complex (+)-53

A mixture of DMPA (1.15 g, 4.95 mmol) and (+)-**2** (1.68 g, 2.47 mmol) in dichloromethane (80 mL) was stirred at room temperature for 2 h. The solvent was removed from the reaction mixture, and the complex (+)**-53** was isolated by column chromatography on a silica column with dichloromethane–*n*-hexane to give a yellow solid, which was recrystallized from chloroform–*n*-hexane in the form of bright yellow prisms (1.81 g, 64%). $[\alpha]_D$ = +259.1° (*c* 0.6, CH_2Cl_2). Mp: 168–169 ºC. Anal. Calcd for $C_{26}H_{29}AsClNPd$: C, 54.6; H, 5.1; N, 2.5. Found: C, 54.5; H, 4.9; N, 2.6. ^{1}H NMR ($CDCl_3$, δ): 1.92 (d, $^3J_{HH}$ = 6.4 Hz, 3H, CH*CH*$_3$), 2.08 (s, 3H, =C*CH*$_3$), 2.11 (s, 3H, CH*CH*$_3$), 2.88 (s, 3H, N*CH*$_3$), 2.95 (s, 3H, N*CH*$_3$), 4.35 (q, $^3J_{HH}$ = 6.4 Hz, 1H, *CH*CH_3), 6.69 (s, 1H, As*CH*), 6.97 (s, 1H, As*CH*), 7.18–7.82 (m, 11H, aromatics).

Cycloaddition Reaction: Preparation of Complex (–)-54

A solution of (+)-**53** (0.59 g, 1.03 mmol) in dichloromethane (50 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (0.36 g) in H_2O (1 mL). The organic layer, after the removal of AgCl, was then washed with H_2O (3 × 50 mL), dried ($MgSO_4$), and subsequently treated with diphenylvinylphosphine (0.22 g, 1.03 mmol) at room temperature for 40 min. Removal of the solvent gave (–)-**54** as a yellow solid, which was then recrystallized from dichloromethane-diethyl ether to give the complex as pale yellow needle crystals (0.66 g, 73%). $[\alpha]_D$ = –33.0° (*c* 0.6, CH_2Cl_2). Mp: 161–162 ºC. Anal. Calcd for $C_{40.33}H_{42.66}AsCl_{1.66}NO_4PPd$: C, 55.3; H, 4.9; N, 1.6. Found: C, 55.7; H, 5.0; N, 1.7. ^{31}P{^{1}H} NMR ($CDCl_3$, δ): 50.2. ^{1}H NMR ($CDCl_3$, δ): 1.41 (s, 3H, =C*CH*$_3$), 1.61 (s, 3H, =C*CH*$_3$), 1.92 (m, 1H, CH*CH*$_2$), 2.03 (d, $^3J_{HH}$ = 6.1 Hz, 3H, CH*CH*$_3$), 2.52 (dd, $^3J_{PH}$ = 24.5, $^2J_{HH}$ =13.6 Hz, 1H, CH*CH*$_2$), 2.79 (s, 3H, N*CH*$_3$), 2.84 (s, 1H, As*CH*),

2.93 (d, $^4J_{PH}$ = 3.1 Hz, 3H, N*CH*$_3$), 3.15 (t, $^3J_{HH}$ = 9.0 Hz, 1H, *CH*CH$_2$), 3.81 (s, 1H, As*CH*), 4.46 (qn, $^3J_{HH}$ = $^4J_{PH}$= 5.9 Hz, 1H, *CH*CH$_3$), 6.68–8.26 (m, 21H, aromatics).

Preparation of the Dichloro Complex 55

The complex $PdCl_2(NCMe)_2$ (0.11 g, 0.43 mmol) and the ligand DMPA (0.20 g, 0.86 mmol) in dichloromethane (60 mL) were stirred at room temperature overnight. The solvent was removed and the residue was crystallized with chloroform-diethyl ether to give the product (*tran* and *cis* mixture) as yellow crystals (0.45 g, 82%), which was further recrystallized with dichloromethane-diethyl ether to produce pure *tran* isomer **55**. Mp: 177–178 ºC. Anal. Calcd for $C_{24}H_{26}As_2Cl_2Pd$: C, 44.9; H, 4.1. Found: C, 44.4; H, 4.4. ^{1}H NMR ($CDCl_3$, δ): 2.04 (s, 6H, *CH*$_3$), 6.60 (s, 2H, =*CH*), 7.33–7.62 (m, 5H, aromatics).

Preparation of the *trans*-Diiodo Complex 56

The solution of $[PdCl_2(DMPA)_2]$ (*tran* and *cis* mixture) (0.45 g, 0.70 mmol) in dichloromethane (50 mL) was added to sodium iodide (0.5 g) in acetone (50 mL) and was stirred vigorously for 10 min. The solvent was removed and the residue was extracted with dichloromethane, Removal of solvent gave **56** as a solid, which was then recrystallized from dichloromethane-diethyl ether to give the product as red crystals (0.56 g, 97%). Mp: 192–193 ºC. Anal. Calcd for $C_{24}H_{26}As_2I_2Pd$: C, 35.0; H, 3.2. Found: C, 34.8; H, 3.1. ^{1}H NMR ($CDCl_3$, δ): 2.11 (s, 6H, *CH*$_3$), 7.03 (s, 2H, =*CH*), 7.33–7.72 (m, 5H, aromatics).

Preparation of the Diiodo Complex 58

The complexes *trans*-[$PdI_2(DMPA)_2$] (0.45 g, 0.55 mmol) and [$PdI_2(DPVP)_2$] (0.43 g, 0.55 mmol) in dichloromethane (90 mL) were stirred at 30 ºC for 5 days. The solvent was removed and the residue was recrystallized with dichloromethane–diethyl ether from –78 ºC to room temperature to produce brown crystals **58** (0.05 g, 5%). Mp: 180–181 ºC. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 79.0. ^1H NMR (CD_2Cl_2, δ): 1.64 (s, 3H, C*CH*$_3$), 2.04 (s, 1H, O*CH*), 2.74 (m, 1H, CH*CH*$_2$), 3.02 (d, $^4J_{HH}$ = 3.4 Hz, 1H, As*CH*), 3.26 (m, 1H, CH*CH*$_2$), 3.92 (d, $^2J_{PH}$ = 2.6 Hz, 1H, P*CH*), 5.00 (s, 1H, =*CH*$_2$), 5.13 (d, $^4J_{HH}$ = 4.2 Hz, 1H, =*CH*$_2$), 7.00–8.19 (m, 15H, aromatics). ^{13}C NMR (CD_2Cl_2 δ): 20.1, 30.5, 38.6, 38.9, 73.1, 73.2, 86.6, 113.9, 125.2, 128.1, 128.2, 128.7, 129.8, 129.9, 130.3, 132.1, 132.4, 132.9, 134.1, 134.2, 135.0, 135.1, 136.6. EI MS: m/z 837.3, $[M]^+$.

Cycloaddition Reaction: Preparation of Complex (–)-59

A solution of (+)-**53** (0.63 g, 1.10 mmol) in dichloromethane (30 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (0.40 g) in H_2O (1 mL). The organic layer, after the removal of AgCl, was then washed with H_2O (3 × 50 mL), dried ($MgSO_4$), and subsequently treated with diphenylvinylarsine (0.28 g, 1.10 mmol) for 5 days at room temperature. The solvent was removed from the reaction mixture, and the complex (–)-**59** was isolated by column chromatography on a silica column with dichloromethane–diethyl ether to give a pale yellow solid, which was recrystallized from chloroform–diethyl ether in the form of needles (0.74 g, 75%). [α] = –91.8° (*c* 0.5, CH_2Cl_2, 436nm). Mp: 152–153 ºC. Anal. Calcd for $C_{40}H_{42}As_2ClNO_4PPd$: C, 53.8; H, 4.7; N, 1.6. Found: C, 53.6; H, 4.9; N, 1.6. ^1H NMR ($CDCl_3$, δ): 1.41 (s, 3H, =C*CH*$_3$), 1.60 (s,

3H, =C*CH*$_3$), 2.03 (d, $^3J_{HH}$ = 6.2 Hz, 3H, CH*CH*$_3$), 2.08 (d, $^2J_{HH}$ =14.0 Hz, 1H, CH*CH*$_2$), 2.51 (d, $^2J_{HH}$ =14.0 Hz, 1H, CH*CH*$_2$), 2.80 (s, 3H, N*CH*$_3$), 2.90 (s, 3H, N*CH*$_3$), 2.95 (s, 1H, As*CH*), 3.21 (d, $^3J_{HH}$ = 9.2 Hz, 1H, *CH*CH$_2$), 3.80 (s, 1H, As*CH*), 4.44 (q, $^3J_{HH}$ = 6.2 Hz, 1H, *CH*CH$_3$), 6.87–8.04 (m, 21H, aromatics). ^{13}C NMR ($CDCl_3$, δ): 14.1, 14.9, 25.3, 32.0, 35.3, 52.3, 52.7, 53.2, 54.9, 75.5, 123.9, 125.2, 125.7, 126.4, 127.6, 128.7, 128.9, 129.2, 129.3, 129.7, 130.2, 130.5, 130.6, 131.0, 131.6, 131.9, 132.1, 132.8, 133.0, 133.2, 133.4, 133.6, 133.9, 136.1, 136.8, 136.9, 151.9 152.2.

Removal of Chiral Auxiliary: Preparation of Complex (–)-60

The complex (–)-**59** (0.29 g, 0.32 mmol) was dissolved in dichloromethane (50 mL) and treated with excess concentrated hydrochloric acid (2 mL) at room temperature for 5 min. The mixture was then washed with H_2O (3 × 50 mL). Sodium iodide (0.1 g) in water (50 mL) was added and stirred vigorously for 3 min. The organic layer was washed with H_2O (3 × 50 mL) and dried ($MgSO_4$). The solvent was removed and the complex (–)-**60** was isolated by column chromatography on a silica column with dichloromethane (0.19 g, 70%). $[\alpha]_D$ = –78.6° (*c* 0.1, CH_2Cl_2). Mp: 85–86 ºC. Anal. Calcd for $C_{26}H_{26}As_2I_2Pd$: C, 36.8; H, 3.1. Found: C, 36.9; H, 3.0. ^{1}H NMR ($CDCl_3$, δ): 1.48 (s, 3H, =C*CH*$_3$), 1.57 (s, 3H, =C*CH*$_3$), 2.05 (dd, $^3J_{HH}$ = 9.5, $^2J_{HH}$ = 13.6 Hz, 1H, CH*CH*$_2$), 2.55 (d, $^2J_{HH}$ = 13.0 Hz, 1H, CH*CH*$_2$), 2.96 (dt, $^3J_{HH}$ = 2.1, $^3J_{HH}$ = 9.4 Hz, 1H, *CH*CH$_2$), 3.07 (d, $^3J_{HH}$ = 2.1 Hz, 1H, As*CH*), 3.52 (d, $^3J_{HH}$ = 2.6 Hz, 1H, As*CH*), 7.37–8.02 (m, 15H, aromatics). ^{13}C NMR ($CDCl_3$, δ): 14.3, 15.7, 30.5, 31.4, 52.2, 56.3, 128.6, 129.1, 129.8, 129.9, 130.0, 130.9, 131.0, 131.1, 131.3, 131.6, 133.3, 133.7, 134.3, 135.8.

Liberation of Diarsine Ligand (–)-61

A solution of (–)-**60** (0.10 g, 0.12 mmol) and potassium cyanide (1.0 g) in $CDCl_3$ (0.6 mL) and H_2O (0.1 mL) was shaken vigorously for 15 min. The organic layer was separated, washed with H_2O (3 × 0.5 mL), and dried ($MgSO_4$). Upon removal of the solvent, the free ligand (–)-**61** was obtained as an air-sensitive solid (0.05 g, 85%). $[\alpha]_D$ = –81.7° (*c* 6.2, $CDCl_3$). ^{1}H NMR ($CDCl_3$, δ): 1.43 (s, 3H, *CH*$_3$), 1.48 (d, 3H, *CH*$_3$), 2.02 (dt, $^3J_{HH}$ = 1.8, $^3J_{HH}$ = 11.4 Hz, 1H, Ph_2AsCH), 2.42 (ddd, $^3J_{HH}$ = 2.3, $^2J_{HH}$ = 4.4, $^3J_{HH}$ = 13.3 Hz, 1H, $CHCH_2$), 2.65 (s, 1H, PhAs*CH*), 2.79 (dd, 1H, $^2J_{HH}$ = 4.7, $^3J_{HH}$ = 8.9 Hz, $CHCH_2$), 2.93 (s, 1H, PhAs*CH*), 7.23–7.60 (m, 15H, aromatics).

Preparation of Complex 62

The complex (–)-**60** (0.09 g, 0.11 mmol) was dissolved in dichloromethane–diethyl ether and allowed to stand for several days at room temperature; deep red crystals of **62** were obtained (0.02 g, 22%). Mp: 174–175 ºC. Anal. Calcd for $C_{48}H_{40}As_4I_4O_2Pd_2$: C, 34.5; H, 2.4. Found: C, 34.2; H, 2.6. ^{1}H NMR (CD_2Cl_2, δ): 7.34–7.79 (m, 5H, aromatics).

CHAPTER 3

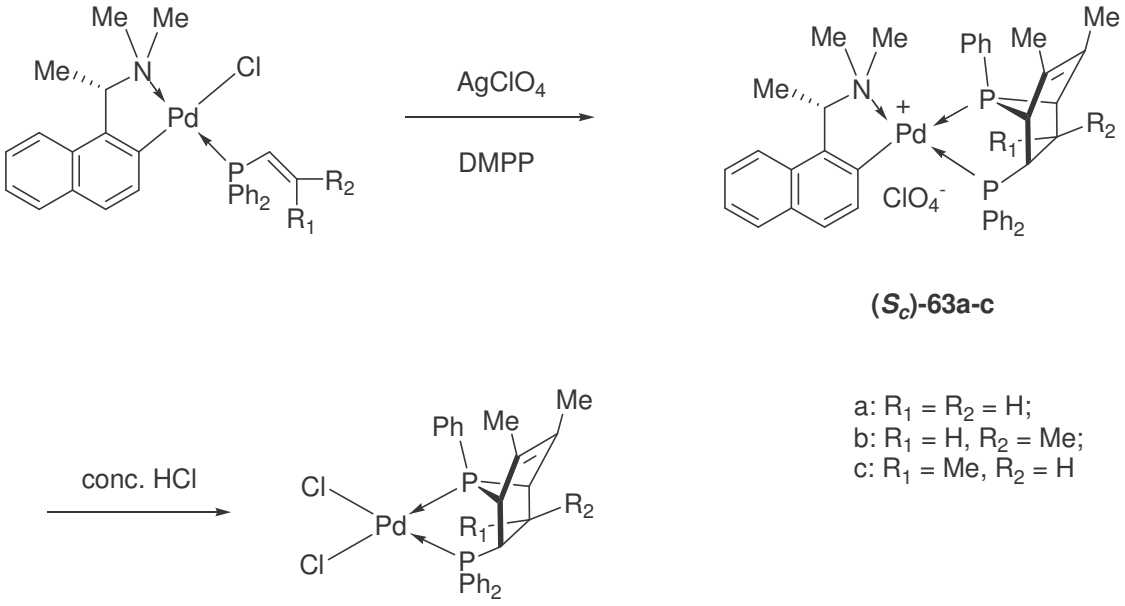
Steric Effects on Asymmetric Cycloaddition Reactions between DMPA and (*Z*/*E*)-Diphenyl-1-propenylphosphine / Diphenyl-1-styrylphosphine

3.1 Introduction

In studies concerning the stereochemistry of chelating arsine and phosphine ligands with resolved chiral donor atoms, several types of As–As,[67] As–P,[60-62] As–S[46,47,50-54] and As–N[45,55,56] bidentate ligands have been resolved by the Wild group *via* the metal complexation technique. For example, in 1979, they reported that the dissymmetric chelating agent (*RR*,*SS*)-*ortho*-phenylenebis(methylphenylarsine) could be resolved into its enantiomers by fractionally crystallizing the internally diastereoisomeric palladium complexes containing the ditertiary arsine and optically active *ortho*-metallated dimethyl(α-methylbenzyl)amine.[67b] When monodentates or other resolving agents are involved, however, the resolution process could become rather tedious and inefficient. Furthermore, separation of diastereomers is a prerequisite when the target ligand contains more than one stereogenic centre. For instance, in the case for the ligand 1-(methylphenylarsino)-2-(methylphenylphosphino)bezene, it required the somewhat difficult separation of the (R_{As}*,R_P*) and (S_{As}*,S_P*) diastereomers prior to the individual resolution of the two pairs of racemic diastereoisomers.[60] Therefore the development of a more efficient asymmetric synthesis to these arsenic–based bidentate ligand system deserves attention.

The asymmetric Diels–Alder reaction is one of the best known reactions with high efficiency for the construction of chiral six-membered rings. The ability of this reaction, in which the formation of two carbon–carbon bonds lead to the creation of up to four stereogenic centres in a single step from the achiral dienes and dienophiles, makes it one of the most fascinating and elegant methods in asymmetric organic synthesis. Its usefulness has been illustrated by strategic application to the synthesis of important chiral natural products such as antibiotics and prostaglandins. Recently our group have successfully utilized this powerful synthetic tool for the enantiospecific synthesis of a series of bidentate phosphines.[82] One of the examples of As–P hetero-bidentate ligand is that convenient access to the eanatiomerically pure rigid bidentate ligand (–)-[5-(diphenylarsino)-2,3-dimethyl-7-phenyl-7(*S*)-phosphabicyclo[2.2.1]hept-2-ene is established *via* an asymmetric [4+2] cyccloaddition between DMPP and diphenylvinylarsine using the chiral organopalladium(II) complex containing ortho-metalated dimethyl[1-(2-naphthyl)ethyl]amine as the reaction promoter.[63]

It is observed that the Diels–Alder cycloaddition is sensitive to steric factors, with sterically bulky substituents on either the diene or dienophile generally suppressing the reaction. For example, in 1997, it was reported that in the asymmetric Diels–Alder reaction between DMPP and (*Z/E*)-methyl-substituted diphenylvinylphosphines under similar reaction conditions, the methyl substituent had a considerable effect on the selectivity and reaction rate (Scheme 3.1).[95] The ratio of isomers obtained for (S_c)-**63a-c** is 7:1, 9:1 and 1:0, respectively. But the reaction time observed for reaction (S_c)-**63a-c** are 2, 3 and 50 h, respectively.



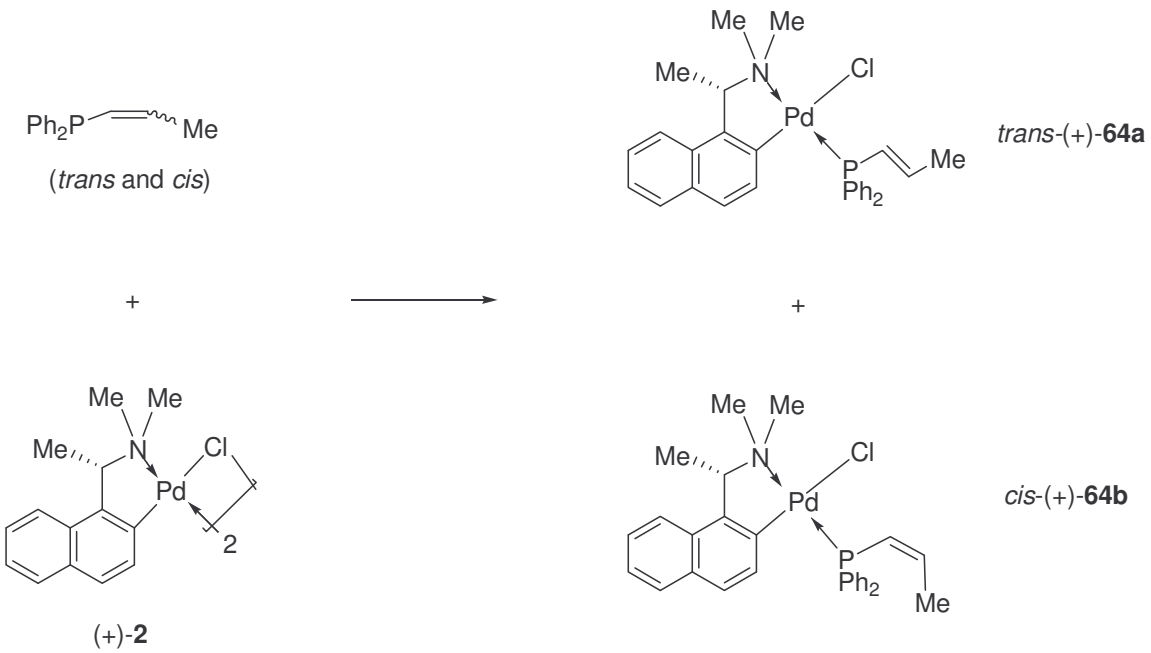
Scheme 3.1

As mentioned earlier, compared to the relatively stable phosphole chemistry, less attention has been concentrated on the arsole chemistry due to their inherent instability. This introduced much difficulty in the synthesis and characterization of the arsine compounds and precluded the large scale investigation of the arsine compounds. In this chapter, we will investigate the steric effect associated with the methyl and phenyl group in (*Z*/*E*)-diphenyl-1-propenylphosphine or (*Z*/*E*)-diphenyl-1-styrylphosphine for the preparation of three new enatiomerically pure As–P heterobidentate ligands *via* Diels–Alder reactions.

3.2 Results and Discussion

3.2.1 Separation of *trans*-(+)-64a and *cis*-(+)-64b and X-ray Crystal Structural Characterization of *trans*-(+)-64a

Due to the difficulty and inconvenience involved in the separation of the mixed free ligands, (*Z*/*E*)-diphenyl-1-propenylphosphine, which need to be performed under strictly dry, oxygen-free atmosphere, a simple alternative route was designed for the separation. A mixture of vinylic phosphine ligands readily splits the chloro bridges in the chiral dimeric complex (+)-**2** regioselectively to give the monomeric neutral complexes *trans*-(+)-**64a** and *cis*-(+)-**64b** at room temperature (Scheme 3.2), subsequently the mixed *trans*-(+)-**64a** and *cis*-(+)-**64b** complexes can be readily separated by column chromatography with dichloromethane-diethyl ether as eluting solvent.



Scheme 3.2

In order to confirm their structural features, a crystal suitable for X-ray structural analysis was obtained. From the X-ray structural analysis of complex *trans*-(+)-**64a**, it was revealed that the "soft" phosphine ligand is indeed coordinated *trans* to the NMe_2

group due to the unique electronic directing effects originating from the strong π-accepting aromatic carbon and the σ-donating nitrogen donor of the organopalladium unit. The methyl substituent of the phosphine is *trans* to PPh_2 group (Figure 3.1). Selected bond lengths and angles are listed in Table 3.1.

The geometry at palladium is distorted square planar with bond angles at metal centre ranging between 81.1(3) to 94.9(3) and 173.6(3) to 175.0(2)°. The Pd(1)–P(1), Pd(1)–N(1) and Pd(1)–Cl(1) bond distances [2.246(3), 2.117(8) and 2.382(3) Å, respectively] in complex *trans*-(+)-**64a** are all slightly shorter than that of analogous

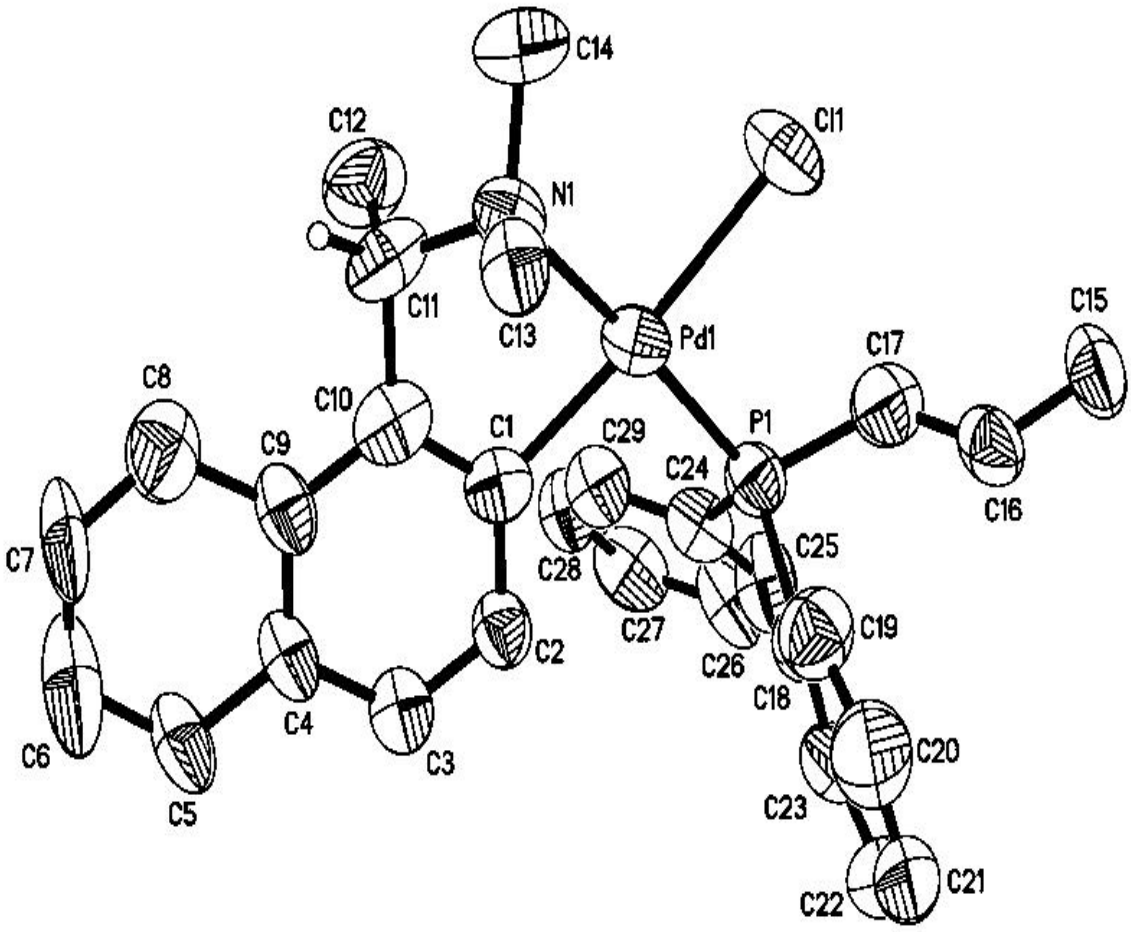


Figure 3.1 Molecular structure of complex *trans*-(+)-**64a**

Table 3.1 Selected bond lengths (Å) and angles (°) for *trans*-(**+**)-**64a**

Pd(1)–C(1)	2.056(10)	Pd(1)–N(1)	2.117(8)
Pd(1)–P(1)	2.246(3)	Pd(1)–Cl(1)	2.382(3)
P(1)–C(17)	1.777(13)	P(1)–C(18)	1.832(10)
P(1)–C(24)	1.850(10)	C(15)–C(16)	1.512(14)
C(16)–C(17)	1.309(15)		
C(1)–Pd(1)–N(1)	81.1(3)	C(1)–Pd(1)–P(1)	94.9(3)
N(1)–Pd(1)–P(1)	175.0(2)	C(1)–Pd(1)–Cl(1)	173.6(3)
N(1)–Pd(1)–Cl(1)	92.6(2)	P(1)–Pd(1)–Cl(1)	91.4(1)
C(17)–P(1)–C(18)	101.3(5)	C(17)–P(1)–C(24)	101.8(5)
C(18)–P(1)–C(24)	110.2(5)	C(17)–P(1)–Pd(1)	115.8(4)
C(18)–P(1)–Pd(1)	111.6(3)	C(24)–P(1)–Pd(1)	114.8(4)
C(17)–C(16)–C(15)	124.0(11)	C(16)–C(17)–P(1)	128.6(10)

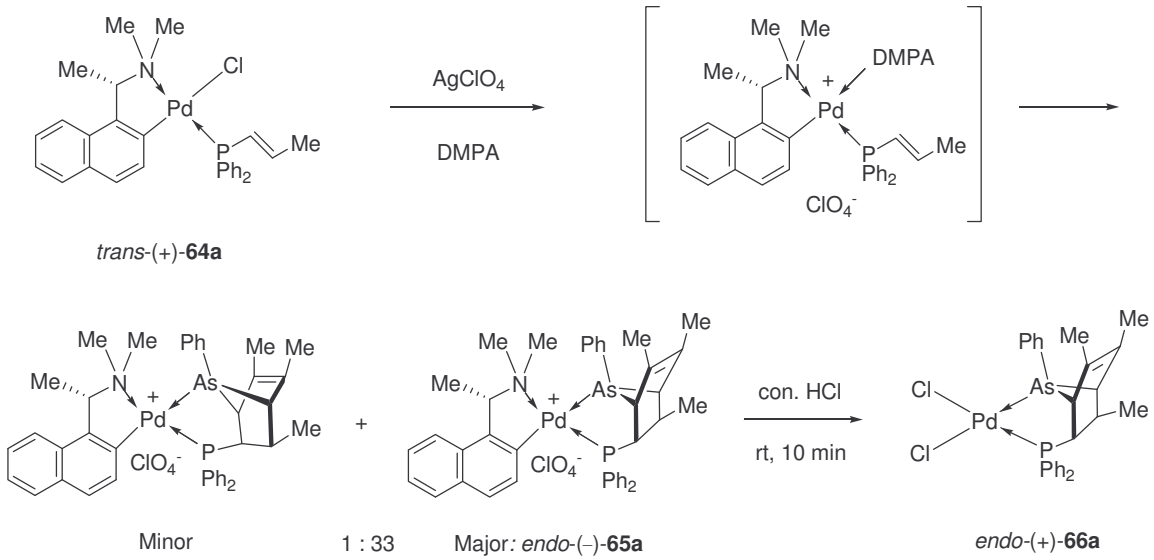
benzylamine complex [2.248(2), 2.154(7) and 2.409(2) Å, respectively]. However, the Pd(1)–C(1) bond distance [2.056(10) Å] in complex *trans*-(+)-**64a** is 0.045 Å longer than that of the corresponding benzylamine complex [2.006(8) Å].[106]

3.2.2 Asymmetric Cycloaddition Reactions between DMPA and (*Z*/*E*)-Diphenyl-1-propenylphosphine

3.2.2.1 Asymmetric Cycloaddition Reactions between DMPA and (*Z*/*E*)-Diphenyl-1-propenylphosphine

(*a*) Asymmetric Cycloaddition Reaction between DMPA and *trans*-(+)-64a

The subsequent asymmetric Diels–Alder reaction between the optically pure complex *trans*-(+)-**64a** and DMPA in dichloromethane proceeded to completion in two weeks at room temperature after the chloro ligand was replaced with the more labile perchlorate. Finally, two isomers were observed in the ratio of 33:1 as indicated by the $^{31}P\{^{1}H\}$ NMR spectrum in $CDCl_3$ (Scheme 3.3).



trans-(+)-**64a**

Minor

Major: *endo*-(–)-**65a**

endo-(+)-**66a**

Scheme 3.3

In the initial stages of this cycloaddition reaction, no desired Diels–Alder reaction product was evident from the crude $^{31}P\{^{1}H\}$ NMR spectrum. However, there was a broad singlet at δ 28.5 ppm and two sets of doublets at δ 27.7 and 6.6 ppm. The latter two doublets had identical coupling constants (J_{pp} = 95.9 Hz). Based on this observation we believe that after the chloro ligand in the complex (+)-**64a** was displaced by perchlorate

upon treatment with $AgClO_4$, another coordination site was thus vacated on the Pd. The incoming diene (DMPA) therefore can coordinate onto the palladium centre. The broad singlet at δ 28.5 ppm may be due to this intermediate complex, which consisted of both the (*E*)-diphenyl-1-propenylphosphine and DMPA coordinated simultaneously onto the palladium metal centre. Subsequently due to the fact that the (*E*)-diphenyl-1-propenylphosphine is a stronger coordinating ligand than DMPA, and the Pd–O bond in the perchlorate complex is very labile, the (*E*)-diphenyl-1-propenylphosphine ligand replaced the DMPA ligand *trans* to the aromatic carbon and the two phosphine ligands jointly coordinated to the palladium centre. This explained why there are two sets of doublets observed in the crude $^{31}P\{^{1}H\}$ NMR spectrum. This is a competitive equilibrium process as during the prolonged reaction time, the intensity of these two set of doublets declined, while the intensity of the desired cycloadduct *endo*-(–)-**65a** at δ 49.7 ppm increased. Eventually the doublets disappeared completely from the crude $^{31}P\{^{1}H\}$ NMR spectrum.

Upon completion of the reaction, the major isomer *endo*-(–)-**65a** can be isolated by column chromatography in 45% yield, $[\alpha]_D$ –65.0° (*c* 0.6, CH_2Cl_2), and was subsequently recrystallized from chloroform-diethyl ether as pale yellow needles. The complex *endo*-(–)-**65a** has similar $^{31}P\{^{1}H\}$ NMR chemical shift (δ 49.7) for the 5-phosphino phosphorus as compared to the analogous diphosphine complex (δ 50.7),[95] and in its ^{1}H NMR spectrum the proton resonance (*CH*CH_3, δ 4.52) near the chiral carbon in naphthylamine auxiliary is a quintet, not a quartet which is indication of the As coordinated *trans* to NMe_2 group. All this information indicated that as expected, in solution the phosphorus in the major isomer *endo*-(–)-**65a** is *trans* to the NMe_2 group of the chiral naphthylamine

auxiliary and the bridgehead arsenic is *trans* to the carbon of the chiral naphthylamine auxiliary. In contrast, the two diasteoreomeric products obtained from the diphosphine complex have significantly different $^{31}P\{^{1}H\}$ NMR chemical shifts with a magnitude greater than 20 ppm for the 5-phosphino phosphorus (δ 50.7 and 26.8, respectively), the minor isomer in this cycloaddition showed relatively close $^{31}P\{^{1}H\}$ NMR chemical shifts (δ 49.7 and 46.5, respectively). So unlike the two isomers of the corresponding diphosphine complex which are related as regio-isomers, these two isomers obtained from the reaction between (*E*)-diphenyl-1-propenylphosphine and DMPA should be diastereomers based on the deduction from the corresponding analogous diphosphine complexes.[95]

The chiral naphthylamine auxiliary in complex *endo*-(–)-**65a** can be removed from the palladium template chemoselectively by treatment with concentrated hydrochloric acid in dichloromethane for 10 min at room temperature. The chiral auxiliary can be recovered quantitatively from the mother liquor after treatment with base. The neutral dichloro complex *endo*-(+)-**66a** was obtained as pale yellow crystals in 85% yield, $[\alpha]_D$ +32.6° (*c* 0.5, CH_2Cl_2).

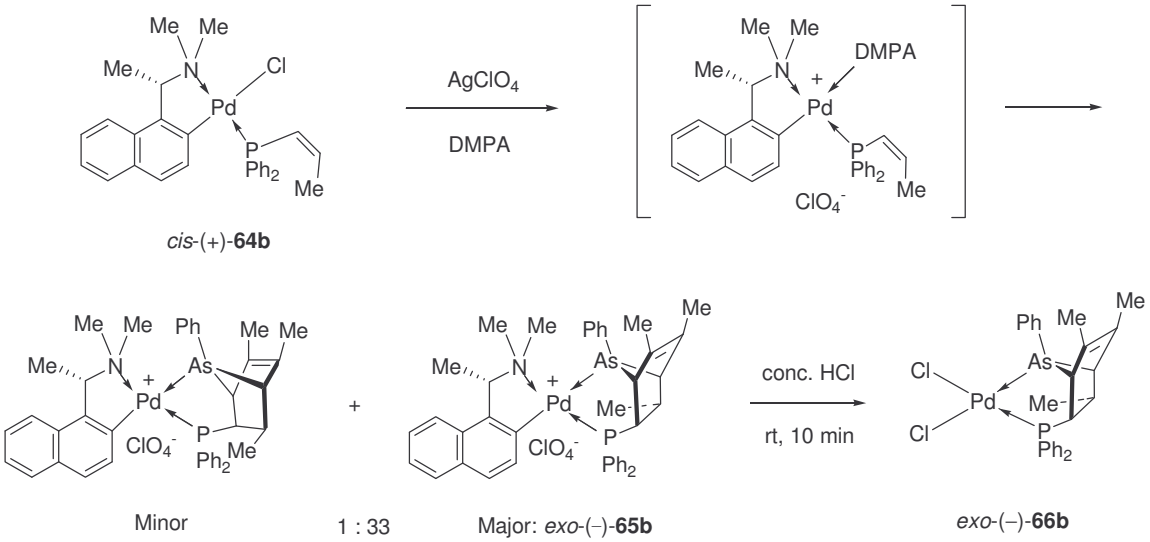
(*b*) Asymmetric Cycloaddition Reaction between DMPA and *cis*-(+)-64b

Similar to the above procedure, the chloro ligand in the optically pure complex *cis*-(+)-**64b** can be abstracted efficiently by treatment of the complex in dichloromethane with aqueous silver perchlorate ($AgClO_4$). The resulting perchlorate complex allowed the (*Z*)-diphenyl-1-propenylphosphine and DMPA, the incoming diene, to coordinate

simultaneously onto the palladium centre during the intramolecular cycloaddition reaction (Scheme 3.4). Similarly, at the beginning of the cycloaddition reaction, no desired Diels–Alder reaction product appeared from the crude $^{31}P\{^{1}H\}$ NMR spectrum, there is a broad singlet at δ 15.1 ppm and two sets of doublets at δ 13.7 and –4.3 ppm. The coupling constants of latter two doublets are identical. As the (*Z*)-diphenyl-1-propenylphosphine is the only phosphine ligand present in the cycloaddition reaction mixture, it appeared that the cycloaddition reaction proceeded *via* a stepwise manner. First, after the chloro ligand in *cis*-(+)-**64b** was replaced by perchlorate, the incoming diene (DMPA) coordinated onto the palladium centre *via* another vacated coordination site, the broad singlet at δ 15.1 ppm may be the intermediate complex, which is the (*Z*)-diphenyl-1-propenylphosphine and DMPA coordinated simultaneously onto the metal centre. Like its *E*-form analogue, the (*Z*)-diphenyl-1-propenylphosphine is also a stronger coordinated ligand than DMPA and therefore the (*Z*)-diphenyl-1-propenylphosphine ligand replaced the DMPA ligand *trans* to the aromatic carbon. Two *Z*-form phosphine ligands then simultaneously coordinated onto the palladium centre. Hence, there are two sets of doublets in the crude $^{31}P\{^{1}H\}$ NMR spectrum (J_{pp} = 94.6 Hz). Due to the fact that it is a competitive equilibrium process, the intensity of these two set of doublets diminished throughout the course of the reaction, while the intensity of the signals for the desired cycloadduct *exo*-(–)-**65b** at δ 42.2 ppm increased. After 3 weeks at room temperature, the intermediate doublets disappeared completely from the crude $^{31}P\{^{1}H\}$ NMR spectrum.

There are two isomers produced from the reaction between (*Z*)-diphenyl-1-propenylphosphine and DMPA, the ratio of the two diastereomer indicated high

selectivity (33:1). However, compared to the sole isomer obtained from the corresponding analogous diphosphine complex reaction, the selectivity in the current work is slightly lower. This is contrary to the corresponding *E*-form phosphine ligand where the selectivity with DMPA is much higher than that with DMPP (33:1 *vs* 9:1).[107]



Scheme 3.4

The major isomer *exo*-(–)-**65b** can be isolated by column chromatography in 43% yield, $[\alpha]_D$ –43.3° (*c* 0.3, CH_2Cl_2), which was subsequently recrystallized from chloroform-diethyl ether as pale yellow needles. The major isomer *exo*-(–)-**65b** has similar $^{31}P\{^1H\}$ NMR chemical shift (δ 42.2) for the 5-phosphino phosphorus compared to the diphosphine complex (δ 43.7),[95] and like *endo*-(–)-**65a**, in its proton NMR spectrum the proton resonance (*CH*CH_3, δ 4.51) near the chiral carbon in naphthylamine auxiliary is a quintet, not a quartet. All this information indicated that, in solution the phosphorus in *exo*-(–)-**65b** is *trans* to the NMe_2 group of the chiral naphthylamine auxiliary and the bridgehead arsenic is *trans* to the carbon of the chiral naphthylamine

auxiliary. Similar to *endo*-(–)-**65a** and its minor isomer, the major isomer *exo*-(–)-**65b** and its minor isomer have very small separation in $^{31}P\{^{1}H\}$ NMR chemical shifts with a magnitude of only 1 ppm for the 5-phosphino phosphorus (δ 42.2 and 43.2, respectively). Hence, similar to *endo*-(–)-**65a** and its minor isomer, the two isomers obtained from the reaction between (*Z*)-diphenyl-1-propenylphosphine and DMPA should be diastereomers which is different from the two isomers of the analogous diphosphine complex which are related as regio-isomers.

The chiral naphthylamine auxiliary in *exo*-(–)-**65b** can be removed from the palladium template chemoselectively by treatment with concentrated hydrochloric acid in dichloromethane for 10 min at room temperature. The neutral dichloro complex *exo*-(–)-**66b** was obtained as pale yellow crystals in 79% yield, $[\alpha]_D = -90.9°$ (*c* 0.1, CH_2Cl_2).

(*c*) X-ray Structural Analysis of *exo*-(–)-66b

In order to confirm the formation of arsanorbornene skeleton and its absolute configuration, a crystal of *exo*-(–)-**66b** suitable for X-ray structural analysis was obtained (Figure 3.2). From the X-ray structural analysis, as expected, the arsanorbornene is indeed formed with the desired retention of chirality at the As(1), C(7), C(12) and C(13) centre (*R*, *R*, *R* and *S*, respectively) which is similar to the diphosphine complex; however, the absolute configuration of the newly created chiral centre at C(14) is *R* which is in contrast to the analogous dichloro diphosphine complex.[95] The methyl substituent of the vinyl group has a *syn* relationship with PPh_2 group. Selected bond lengths and angles are listed in Table 3.2.

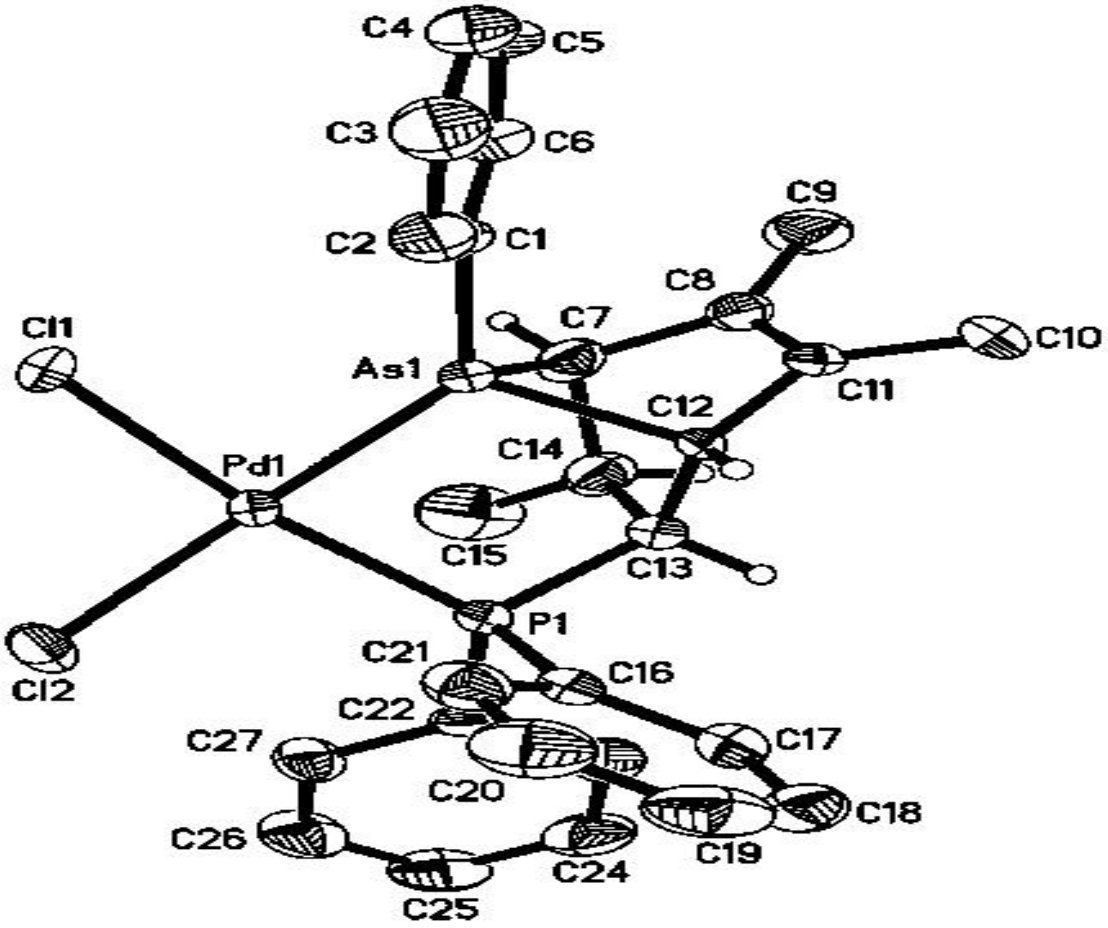


Figure 3.2 Molecular structure of dichloro complex *exo*-(–)-**66b**

The geometry at palladium metal centre is distorted square planar with bond angles at palladium in the range of 82.9(1)–96.6(1) and 169.5(1)–173.0(1)°. The two Pd–Cl bonds in the similar diphosphine complex are, within statistical significance, the same [2.360(4) and 2.364(4) Å],[95] however, the Pd–Cl(2) bond *trans* to As in dichloro complex *exo*-(–)-**66b** is much longer than that of *trans* to P [2.368(1) and 2.337(1) Å] which suggested the arsine ligand has a stronger *trans* effect than that of phosphine ligand. The Pd–As and Pd–P bond distances [2.324(1) and 2.259(1) Å] in *exo*-(–)-**66b** are the same as those in the similar complex (–)-**45** [2.325(1) and 2.260(1) Å], respectively. The C(12)–

Table 3.2 Selected bond lengths (Å) and angles (°) for *exo*-(–)-**66b**

Pd(1)–P(1)	2.259(1)	Pd(1)–As(1)	2.324(1)
Pd(1)–Cl(1)	2.337(1)	Pd(1)–Cl(2)	2.368(1)
As(1)–C(7)	1.989(4)	As(1)–C(12)	1.982(4)
P(1)–C(13)	1.841(4)	C(7)–C(14)	1.563(6)
C(7)–C(8)	1.522(6)	C(8)–C(9)	1.505(6)
C(8)–C(11)	1.335(6)	C(10)–C(11)	1.496(6)
C(11)–C(12)	1.508(5)	C(12)–C(13)	1.555(5)
C(13)–C(14)	1.599(6)	C(14)–C(15)	1.476(6)
P(1)–Pd(1)–As(1)	82.9(1)	P(1)–Pd(1)–Cl(1)	169.5(1)
As(1)–Pd(1)–Cl(1)	87.3(1)	P(1)–Pd(1)–Cl(2)	96.6(1)
As(1)–Pd(1)–Cl(2)	173.0(1)	Cl(1)–Pd(1)–Cl(2)	93.6(1)
C(1)–As(1)–C(12)	109.1(2)	C(1)–As(1)–C(7)	111.9(2)
C(12)–As(1)–C(7)	76.9(2)	C(1)–As(1)–Pd(1)	122.9(1)
C(12)–As(1)–Pd(1)	108.2(1)	C(7)–As(1)–Pd(1)	117.6(1)
C(8)–C(7)–C(14)	108.2(3)	C(8)–C(7)–As(1)	100.1(3)
C(14)–C(7)–As(1)	100.1(3)	C(11)–C(8)–C(7)	111.2(4)
C(8)–C(11)–C(12)	112.7(4)	C(11)–C(12)–C(13)	112.6(3)
C(11)–C(12)–As(1)	101.6(3)	C(13)–C(12)–As(1)	94.2(2)
C(12)–C(13)–C(14)	106.4(3)	C(12)–C(13)–P(1)	108.2(3)
C(14)–C(13)–P(1)	112.1(3)	C(15)–C(14)–C(7)	112.2(4)
C(15)–C(14)–C(13)	122.2(4)	C(7)–C(14)–C(13)	105.2(3)

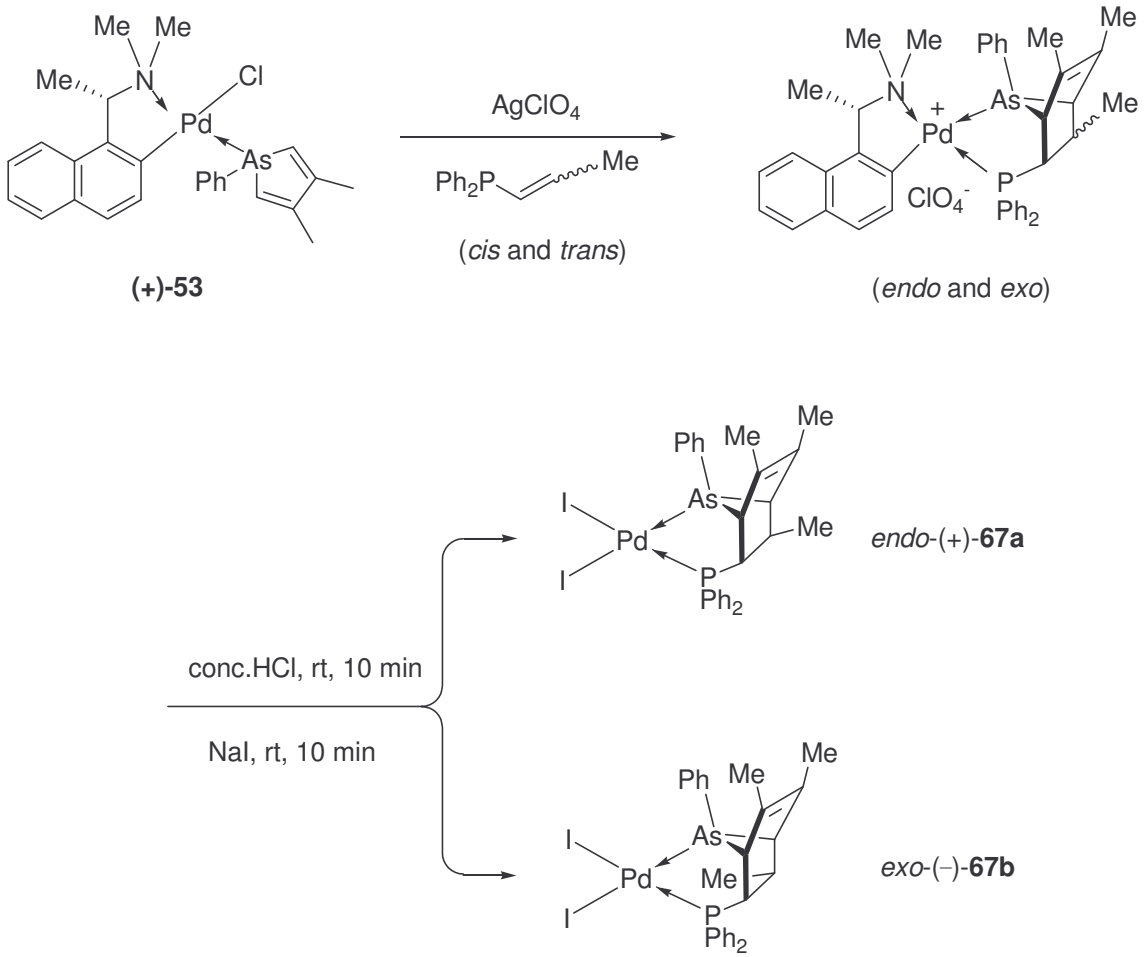
As(1)–C(7) bond angle within the arsanorbornene skeleton [76.9(2)°] is equivalent to the similar arsine complexes (–)-**44** and (–)-**45** [76.7(1) and 77.5(1)°]. However, the associated As–C bonds in *exo*-(–)-**66b** are similar [As(1)–C(7) for 1.989(4) Å and As(1)–C(12) for 1.982(4) Å] which, in turn, are similar to the complex (–)-**44** [1.978(2) and 1.980(2) Å] and different from the complex (–)-**45** [1.961(3) and 1.980(3) Å].

Similar to its phosphorus analogue, the generation of the *R* stereochemistry at C(14), with retention of a *syn* geometry for C(15) and P(1), resulted in an axial positioning of the methyl group C(15) relative to the six-membered chelate ring. Hence, the slow rate of Diels–Alder reaction for this isomer is possibly due to the combination of the sterically hindered relationship between this axial methyl group and the methyl group on the chiral centre of the (*S*)-naphthylamine auxiliary which lies on the same side of the coordination plane.

3.2.2.2 One–Pot Syntheses and Separation of Diiodo Complexes *endo*-(+)-67a and *exo*-(–)-67b

In addition to the above method, there is a more efficient "one–pot" route to separate and prepare the *exo*- and *endo*-arsanorbornene ligands. The chloro ligand in complex (+)-**53** was replaced with perchlorate by treatment with $AgClO_4$, the resulting perchlorate complex was then reacted with the mixture of (*Z*/*E*)-diphenyl-1-propenylphosphine ligands (Scheme 3.5). The cycloaddition reactions were found to be completed in 3 days at 40 ºC as indicated by their $^{31}P\{^{1}H\}$ NMR spectra in $CDCl_3$. The ratio of diastereomers is the same (33:1) as observed in the previous pathway. The

cycloadduct mixtures were then treated with concentrated hydrochloric acid for 10 min at room temperature. The resultant mixed dichloro complexes, however, cannot be separated into their enantiopure counterpart *via* recrysallization or column chromatography. Therefore sodium iodide was added to the crude mixed dichloro complexes for another 10 min. The diiodo complexes *endo*-(+)-**67a** and *exo*-(–)-**67b** obtained were readily separated. First the *exo*-(–)-**67b** recrystallized from the crude products with dichloromethane–diethyl ether as red microcrystals in 64% yield, $[\alpha]_D$ – 149.5° (*c* 0.2, CH_2Cl_2). Then the mother liquid was further purified by column



Scheme 3.5

chromatography on a silica column with dichloromethane to give *endo*-(+)-**67a** as a solid, which was subsequently recrystallized from chloroform-diethyl ether-*n*-hexane in the form of red crystals. It was obtained in 61% yield, $[\alpha]_D$ +106.3° (*c* 0.2, CH_2Cl_2).

The molecular structure and the absolute stereochemistry of the diiodo complex *endo*-(+)-**67a** were determined by single crystal X-ray structure analysis (Figure 3.3). Selected bond lengths and angles are listed in Table 3.3. The study of *endo*-(+)-**67a** revealed that the absolute configuration has been retained from the template complex. As expected, the arsanorbornene skeleton is formed. The absolute configurations at the

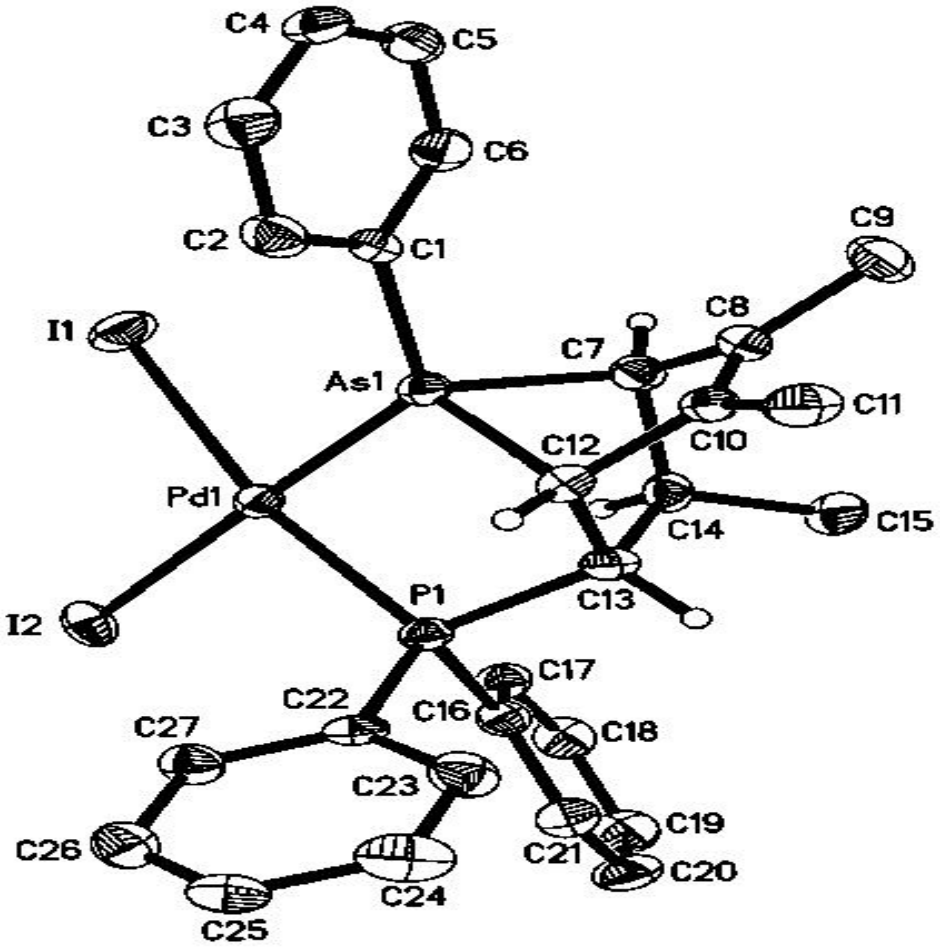


Figure 3.3 Molecular structure of diiodo complex *endo*-(+)-**67a**

Table 3.3 Selected bond lengths (Å) and angles (°) for *endo*-(**+**)-**67a**

Pd(1)–P(1)	2.288(1)	Pd(1)–As(1)	2.353(1)
Pd(1)–I(1)	2.636(1)	Pd(1)–I(2)	2.647(1)
As(1)–C(12)	1.985(5)	As(1)–C(7)	1.968(6)
P(1)–C(13)	1.857(5)	C(7)–C(14)	1.572(8)
C(7)–C(8)	1.517(7)	C(8)–C(9)	1.512(8)
C(8)–C(10)	1.340(8)	C(10)–C(11)	1.502(7)
C(10)–C(12)	1.504(7)	C(12)–C(13)	1.551(7)
C(13)–C(14)	1.578(8)	C(14)–C(15)	1.528(8)
P(1)–Pd(1)–As(1)	83.4(1)	P(1)–Pd(1)–I(1)	168.8(1)
As(1)–Pd(1)–I(1)	87.4(1)	P(1)–Pd(1)–I(2)	95.0(1)
As(1)–Pd(1)–I(2)	178.2(1)	I(2)–Pd(1)–I(1)	94.4(1)
C(1)–As(1)–C(12)	110.1(2)	C(1)–As(1)–C(7)	106.0(2)
C(12)–As(1)–C(7)	77.0(2)	C(1)–As(1)–Pd(1)	129.5(2)
C(12)–As(1)–Pd(1)	108.2(2)	C(7)–As(1)–Pd(1)	113.8(2)
C(8)–C(7)–C(14)	108.0(4)	C(8)–C(7)–As(1)	100.8(4)
C(14)–C(7)–As(1)	99.0(4)	C(10)–C(8)–C(7)	112.4(5)
C(8)–C(10)–C(12)	111.2(5)	C(10)–C(12)–C(13)	112.0(4)
C(10)–C(12)–As(1)	101.8(3)	C(13)–C(12)–As(1)	95.5(3)
C(12)–C(13)–C(14)	106.9(4)	C(12)–C(13)–P(1)	109.3(4)
C(14)–C(13)–P(1)	107.5(3)	C(15)–C(14)–C(7)	113.1(5)
C(15)–C(14)–C(13)	112.6(4)	C(7)–C(14)–C(13)	105.7(4)

As(1), C(7), C(12) and C(13) centres are *R*, *R*, *R* and *S*, respectively, which is same as the dichloro complex *exo*-(–)-**66b**. However, the absolute configuration of another newly created chiral centre at C(14) is *S*, which is in contrast to the dichloro complex *exo*-(–)-**66b**. Contrary to that of *exo*-(–)-**66b**, the methyl substituent of the vinyl group in complex *endo*-(+)**-67a** has an *anti* relationship with PPh_2 group.

The geometry at palladium metal centre is distorted square planar with bond angles at palladium in the range of 83.4(1)–95.0(1) and 168.8(1)–178.2(1)°. The two Pd–Cl bond distances [2.368(1) and 2.337(1) Å] in the dichloro complex *exo*-(–)-**66b** are significantly different. However, the two Pd–I bond distances in *endo*-(+)**-67a** are almost equal [2.636(1) and 2.647(1) Å]. The Pd–As and Pd–P bond distances [2.324(1) and 2.259(1) Å] in *exo*-(–)-**66b** are similar to that of the dichloro complex (–)-**45** [2.325(1) and 2.260(1) Å], respectively, but the Pd–As and Pd–P bond distances [2.353(1) and 2.288(1) Å] in *endo*-(+)**-67a** [and (–)-**52**] are much longer than the above two analogues. The C(7)–As(1)–C(12) bond angle within the arsanorbornene skeleton [77.0(2)°] is acute and equivalent to *exo*-(–)-**66b** [76.9(2)°], however, the associated As–C bonds [As(1)–C(7) for 1.968(6) Å and As(1)–C(12) for 1.985(5)Å] in *endo*-(+)**-67a** are different from that of *exo*-(–)-**66b** which are the same [As(1)–C(7) for 1.989(4) Å and As(1)–C(12) for 1.982(4) Å]. Similar to its phosphorus analogue, the generation of the *S* stereochemistry at C(14), with retention of a *anti* geometry for C(15) and P(1), resulted in an axial positioning of the methyl group C(15) relative to the six-membered chelate ring. Hence, compared to the large steric effect in *exo*-(–)-**66b**, the slow rate of Diels–Alder reaction for the complex *endo*-(+)**-67a** is possibly due to the combination of the less sterically hindered relationship between this axial methyl group and the methyl group on the chiral

centre of the (*S*)-naphthylamine auxiliary.

Similar to *exo*-(–)-**66b** and *endo*-(+)-**67a**, the arsanorbornene skeleton in *exo*-(–)-**67b** (Figure 3.4) is also formed with the desired retention of chirality at the As(1), C(7), C(12) and C(13) centres (*R*, *R*, *R* and *S*, respectively). However, in contrast to *endo*-(+)-**67a**, the absolute configuration of the new created chiral centre at C(14) is *R*. Similar to the dichloro complex *exo*-(–)-**66b**, the methyl substituent of the vinyl group has a *syn* relationship with PPh_2 group which is contrary to *endo*-(+)-**67a**. Selected bond lengths and angles are listed in Table 3.4.

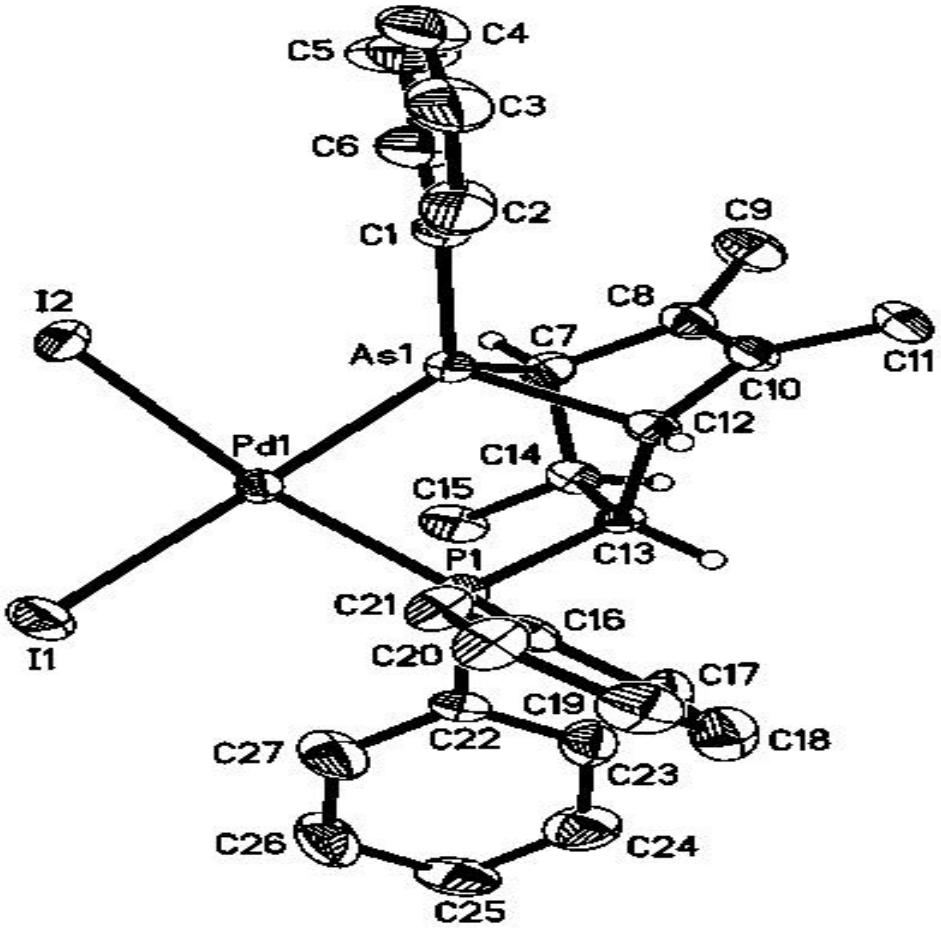


Figure 3.4 Molecular structure of diiodo complex *exo*-(–)-**67b**

Table 3.4 Selected bond lengths (Å) and angles (°) for *exo*-(–)-**67b**

Pd(1)–P(1)	2.299(2)	Pd(1)–As(1)	2.346(1)
Pd(1)–I(1)	2.649(1)	Pd(1)–I(2)	2.640(1)
As(1)–C(12)	1.997(7)	As(1)–C(7)	1.997(7)
P(1)–C(13)	1.871(7)	C(7)–C(14)	1.545(10)
C(7)–C(8)	1.488(10)	C(8)–C(9)	1.520(11)
C(8)–C(10)	1.355(10)	C(10)–C(11)	1.500(11)
C(10)–C(12)	1.497(10)	C(12)–C(13)	1.548(8)
C(13)–C(14)	1.594(9)	C(14)–C(15)	1.526(10)
P(1)–Pd(1)–As(1)	82.2(1)	P(1)–Pd(1)–I(2)	168.1(1)
As(1)–Pd(1)–I(2)	87.5(1)	P(1)–Pd(1)–I(1)	98.7(1)
As(1)–Pd(1)–I(1)	170.9(1)	I(2)–Pd(1)–I(1)	92.5(1)
C(1)–As(1)–C(12)	110.5(3)	C(1)–As(1)–C(7)	110.7(3)
C(12)–As(1)–C(7)	76.1(3)	C(1)–As(1)–Pd(1)	123.8(2)
C(12)–As(1)–Pd(1)	109.2(2)	C(7)–As(1)–Pd(1)	116.2(2)
C(8)–C(7)–C(14)	109.6(6)	C(8)–C(7)–As(1)	99.7(5)
C(14)–C(7)–As(1)	100.1(4)	C(10)–C(8)–C(7)	111.8(6)
C(8)–C(10)–C(12)	111.7(6)	C(10)–C(12)–C(13)	113.7(5)
C(10)–C(12)–As(1)	100.8(5)	C(13)–C(12)–As(1)	94.8(4)
C(12)–C(13)–C(14)	105.9(5)	C(12)–C(13)–P(1)	107.8(4)
C(14)–C(13)–P(1)	111.7(4)	C(15)–C(14)–C(7)	112.4(6)
C(15)–C(14)–C(13)	119.0(6)	C(7)–C(14)–C(13)	106.0(5)

The geometry at the palladium metal centre is distorted square planar with bond angles at palladium in the range of 82.2(1)–98.7(1) and 168.1(1)–170.9(1)°. The two Pd–I bonds [2.640(1) and 2.649(1) Å] in *exo*-(–)-**67b** are the similar to *endo*-(+)-**67a** [2.636(1) and 2.647(1) Å]. The Pd–P bond distance [2.299(2) Å] in *exo*-(–)-**67b** is slightly longer than that of *endo*-(+)-**67a** [2.288(1) Å], however, the Pd–As bond distance [2.346(1) Å] in *exo*-(–)-**67b** is slightly shorter than that of *endo*-(+)-**67a** [2.353(1) Å]. The C(7)–As(1)–C(12) bond angle within the arsanorbornene skeleton [76.1(3)°] is very acute and smaller than the similar diiodo complex *endo*-(+)-**67a** [77.0(2)°]. The associated As–C bonds in *exo*-(–)-**67b** are the same [1.997(7) Å], whereas the bridgehead As–C bond lengths are different in *endo*-(+)-**67a**.

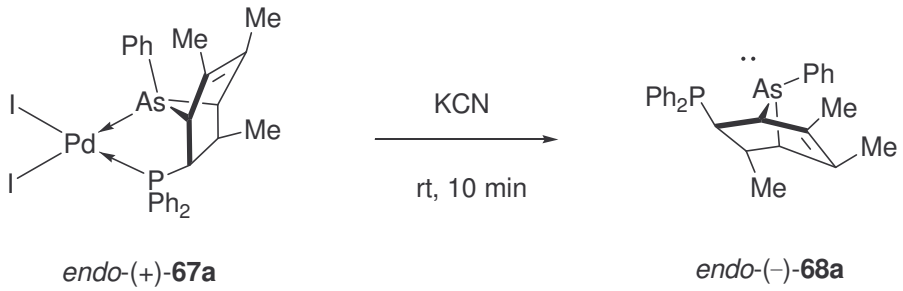
Similar to the dichloro complex *exo*-(–)-**66b** and the analogous diphosphine complex,[95] the generation of the *R* stereochemistry at C(14) in *exo*-(–)-**67b**, with retention of a *syn* geometry for C(15) and P(1), resulted in an axial positioning of the methyl group C(15) relative to the six-membered chelate ring. Hence, the slow rate of Diels–Alder reaction for complex *exo*-(–)-**67b** is possibly due to the same reason: that is a combination of the sterically hindered relationship between this axial methyl group and the methyl group on the chiral centre of the (*S*)-naphthylamine auxiliary which lies on the same side of the coordination plane.

3.2.2.3 Preparation of the As–P Bidentate Ligands *endo*-(–)-68a and *exo*-(–)-68b

(*a*) Liberation of Optically Pure *endo*-(–)-68a

The enantiomerically pure As–P bidentate ligand *endo*-(–)-**68a** was liberated from

endo-(+)-**67a** by the treatment of a dichloromethane solution of the complex with aqueous potassium cyanide for 10 min at room temperature (Scheme 3.6). The liberated ligand was obtained as an air sensitive white solid in 86% yield, $[\alpha]_D$ –80.0° (*c* 0.8, CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum of the ligand in $CDCl_3$ exhibited a singlet at δ –11.3 ppm. It is noteworthy that the apparent inversion of configuration that takes place at the bridgehead arsenic stereogenic centre (*R* to *S*) when the As–P bidentate ligand is liberated from the metal is merely a consequence of the Cahn-Ingold-Prelog (CIP) sequence rule.

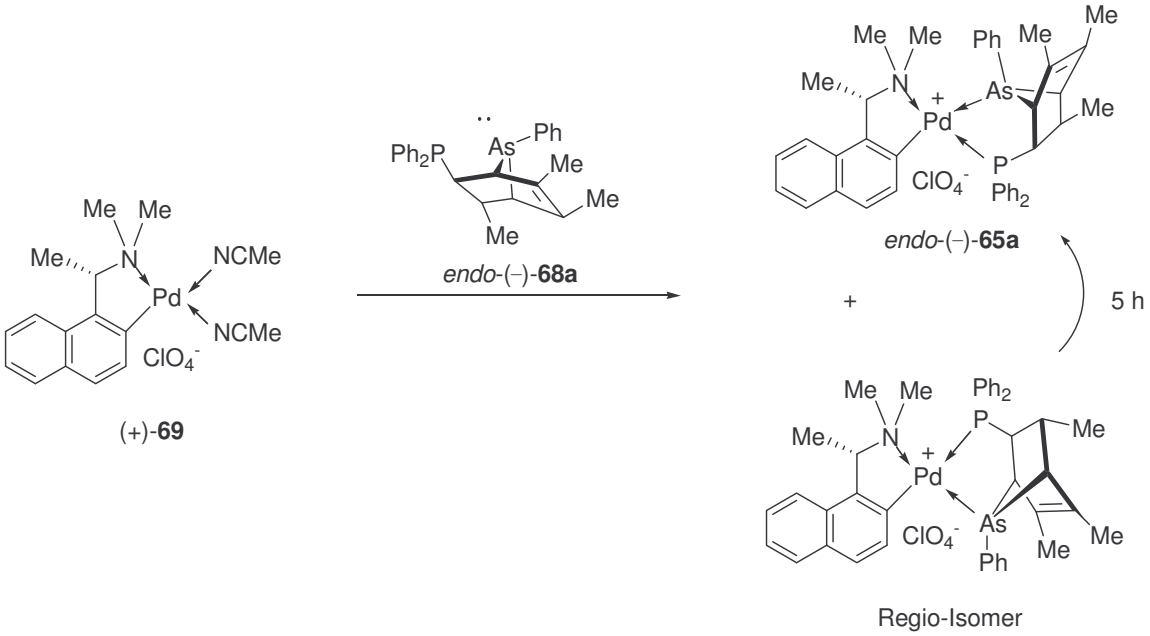


endo-(+)-**67a** *endo*-(–)-**68a**

Scheme 3.6

The optically active ligand *endo*-(–)-**68a** could not be stored because of its inherent instability. Therefore it is necessary to re-coordinate the liberated ligand to metal centres immediately upon liberation. Accordingly the liberated ligand was re-coordinated to the bis(acetonitrile) complex (+)-**69** (Scheme 3.7). The re-coordination process was monitored by $^{31}P\{^1H\}$ NMR spectroscopy which reflected the presence of two isomeric complexes in the 1:1 ratio. One signal at δ 49.2 ppm was identical to that recorded for the crude Diels–Alder reaction. Another (δ 26.3 ppm) was not recorded in the spectrum of the original cycloaddition reaction. According to the deductions made from the

phosphorus analogues,[107] the new signal at δ 26.3 ppm should be the regio-isomer of *endo*-(–)-**65a** in which As is *trans* to NMe_2 group and P is *cis* to NMe_2 group. However this unfavored isomer was completely converted to the favorable product *endo*-(–)-**65a**. Accordingly, the signal at δ 26.3 ppm totally disappeared from the initial 1:1 mixture and exhibited only the signal at δ 49.2 ppm after 5 hours. No other $^{31}P\{^{1}H\}$ NMR signal could be detected at this stage, thus confirming that the liberated *endo*-(–)-**68a** is optically pure.

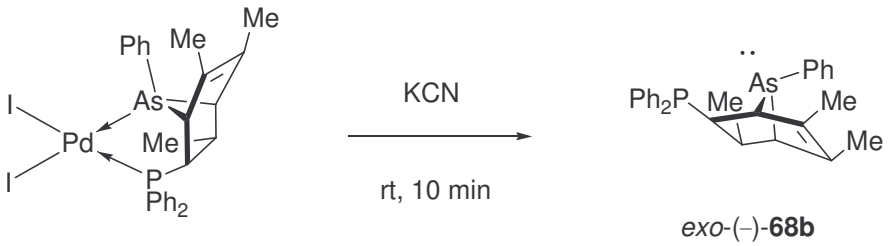


Scheme 3.7

(*b*) Liberation of Optically Pure *exo*-(–)-68b

Similar to the liberated ligand *endo*-(–)-**68a**, the optically pure *exo*-(–)-**68b** was also obtained from *exo*-(–)-**67b** by the treatment of the diiodo complex *exo*-(–)-**67b** with

aqueous potassium cyanide for 10 min at room temperature (Scheme 3.8). The liberated ligand was obtained as an air-sensitive white solid in 82% yield, $[\alpha]_D$ –40.0° (*c* 0.1, CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum in $CDCl_3$ exhibited a singlet at δ –9.0.

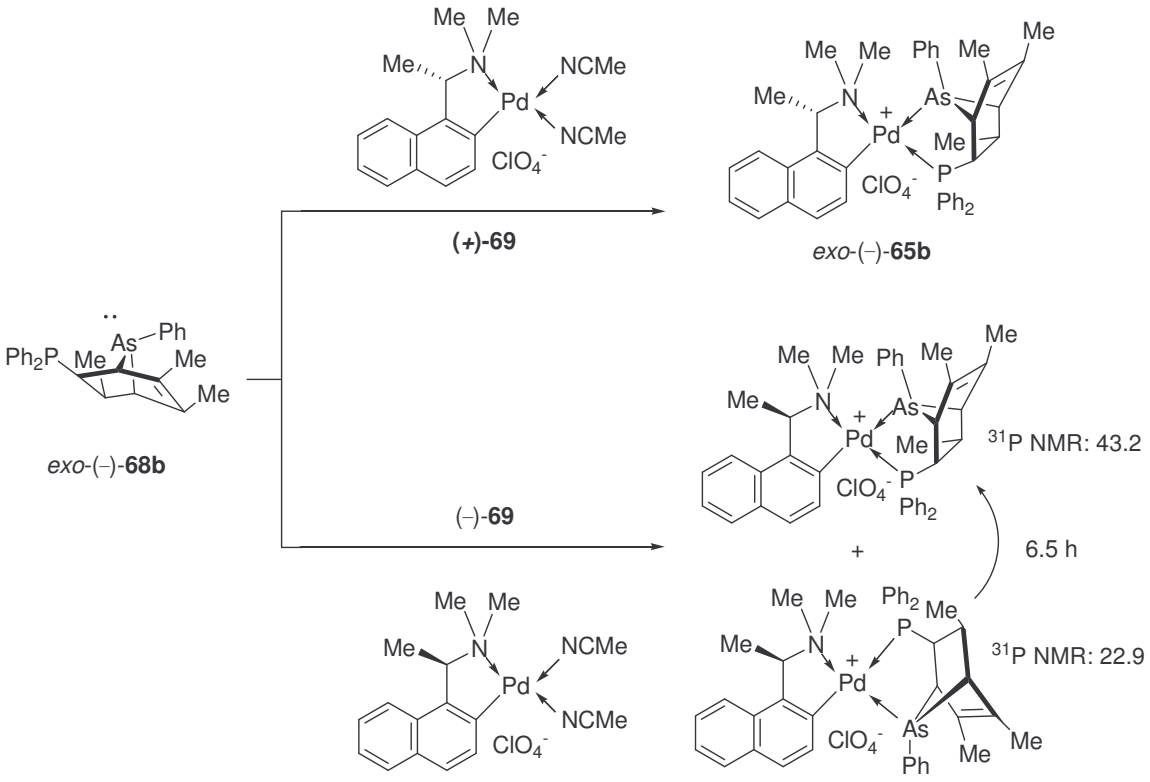


exo-(–)-**67b** *exo*-(–)-**68b**

Scheme 3.8

Due to its instability, the optically active ligand *exo*-(–)-**68b** was not isolated and stored. It is therefore necessary to re-coordinate the free ligand to the selected metal ions immediately upon liberation. For instance, the liberated ligand was re-complexed to the bis(acetonitrile) complex (+)-**69** (Scheme 3.9). The re-coordination process was monitored by $^{31}P\{^1H\}$ NMR spectroscopy. Unlike the recomplexation of free ligand *endo*-(–)-**68a**, the $^{31}P\{^1H\}$ NMR spectrum of the crude product showed only one signal at δ 42.2 ppm. This $^{31}P\{^1H\}$ NMR signal is identical to that recorded for the major diastereomer *exo*-(–)-**65b** generated from the original cycloaddition reaction. No other $^{31}P\{^1H\}$ NMR signal could be detected, thus confirming that the liberated *exo*-(–)-**68b** is optically pure. In a further check, however, the liberated ligand was re-complexed to the bis(acetonitrile) complex (–)-**69**. Two isomeric complexes were formed in almost equal amounts. One signal at δ 43.2 ppm was identical to that recorded for the minor product of the original Diels–Alder reaction (Scheme 3.4) and therefore it was assigned to the

enantiomer of the minor product. Another signal was recorded at δ 22.9 ppm and was assigned to the regio-isomer of the enantiomer. Similarly, this unfavored regio-isomer (δ 22.9 ppm) was completely converted to the favorable isomer (δ 43.2 ppm) in 6.5 hours.



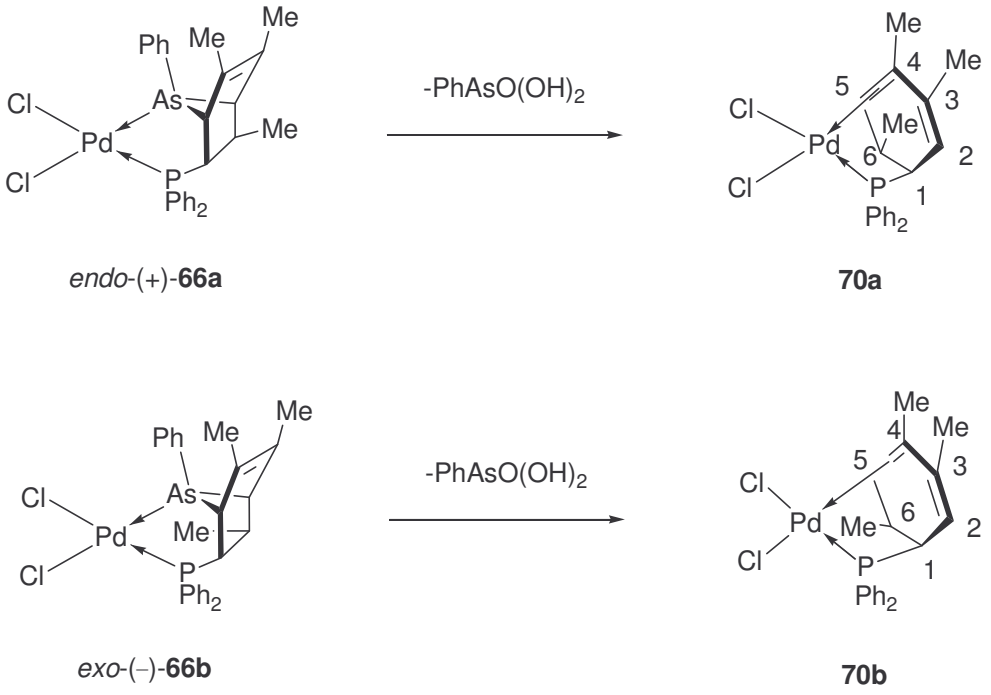
Scheme 3.9

3.2.3 Arsenic–Elimination Reaction

Apart from the evaluation of the stereo-inductive effects of complex (+)-**2**, one of the key objectives of this project is to compare the difference between phosphole and arsole chemistry. As mentioned in chapter 2, when DMPA and DMPP were treated

separately with diphenylvinylphosphine, they both showed similar reactivity and stereoselectivity toward the cycloaddition reaction using the same chiral template. However, the resulting arsanorbornene cycloadduct appeared to be less stable than the corresponding phosphanorbornene. Following this pattern, the arsenic elimination reaction was observed in the dichloro complexes *endo*-(+)-**66a** and *exo*-(–)-**66b**. When *endo*-(+)-**66a** was kept for 1 day in $CDCl_3$, a new peak at δ 130.5 ppm was observed in the $^{31}P\{^{1}H\}$ NMR spectrum (Scheme 3.10). After 7 days, the original ^{31}P NMR signal at δ 32.2 for the dichloro complex *endo*-(+)-**66a** completely disappeared and only the new signal at δ 130.5 was recorded. No other signal was detected in the $^{31}P\{^{1}H\}$ NMR spectrum. The new peak at δ 130.5 may be due to the corresponding arsenic elimination cycloadduct **70a**. This can be further proved by its ^{1}H NMR spectrum. The proton spectrum of complex **70a** is very similar to the similar complex (+)-**48** reported in Chapter 2. There are two characteristic double bond signals in the ^{1}H NMR spectrum of **70a**, one is a singlet peak at δ 5.83 ppm (H_5) and another is a doublet peak at δ 5.67 ppm (H_2, J = 6.5 Hz).

Some colorless crystals were obtained and it was confirmed *via* its NMR spectrum and X-ray crystal structure that it was another side product, phenylarsonic acid. This indirectly proved that arsenic–elimination of *endo*-(+)-**66a** had indeed occured. Unfortunately, complex **70a** can not be obtained in pure form *via* fractional crystallization and was decomposed during the column chromatography on a silica column.



Scheme 3.10

Similarly, the phenomenon was also observed in the case of the complex *exo*-(–)-**66b**. In the $^{31}P\{^{1}H\}$ NMR spectrum, its chemical shift changed from δ 20.2 to 140.7 ppm within 10 days in $CDCl_3$ at room temperature. There are two characteristic double bond signals [singlet at δ 5.86 ppm (H_5) and doublet at δ 5.78 ppm (H_2, J = 6.7 Hz)] in its ^{1}H NMR spectrum. Unfortunately, the complex **70b** also can not be isolated *via* fractional crystallization and column chromatography due to its instability.

However, when **70a** was converted to the corresponding diiodo complex (+)-**71a**, the resulting diiodo complex (+)-**71a** could be isolated *via* column chromatography and was further recrystallized with dichloromethane–diethyl ether to give deep red crystals, $[\alpha]_D$ +195.0° (*c* 0.2, CH_2Cl_2) (Scheme 3.11). In its $^{31}P\{^{1}H\}$ NMR spectrum, there is only one signal at δ 130.3 ppm which is very similar to the dichloro complex **70a**.

70a **(+)-71a**

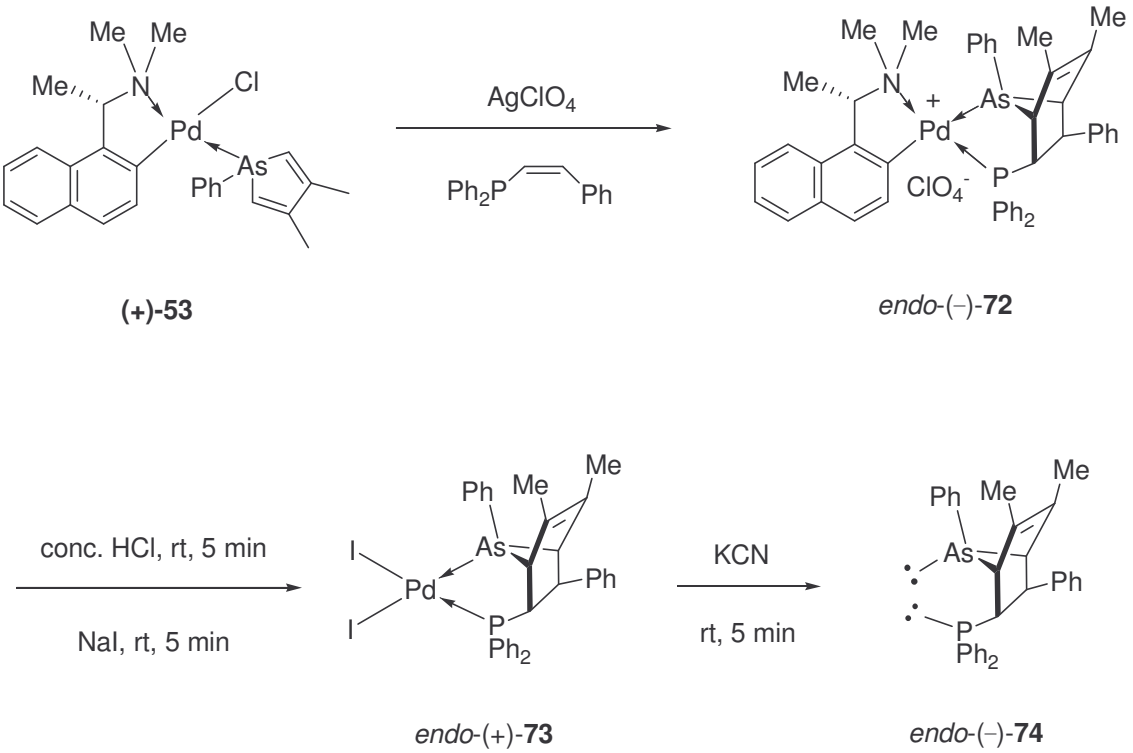
Scheme 3.11

3.2.4 Asymmetric Cycloaddition Reactions between DMPA and (*Z*/*E*)-Diphenyl-1-styrylphosphine

3.2.4.1 Asymmetric Cycloaddition Reaction between DMPA and (*Z*)-Diphenyl-1-styrylphosphine

In order to provide further evidence as to whether the steric interactions between the axial methyl substituent and the methyl group on the chiral centre of the (*S*)-naphthylamine auxiliary are the determining factors for the selectivity and the rate of the reaction, a more bulky phenyl group was introduced onto the terminal position of the diphenylvinylphosphine. The asymmetric Diels–Alder reaction between complex (+)-**53** and (*Z*)-diphenyl-1-styrylphosphine was completed in 41h at 40 ºC to give the major product as colourless crystals in 70% isolated yield, $[\alpha]_D$ –98.6° (*c* 0.7, CH_2Cl_2) (Scheme 3.12). It should be noted that, prior to purification, the $^{31}P\{^1H\}$ NMR spectrum of the crude Diels–Alder reaction product in $CDCl_3$ exhibits only two sharp singlets at δ 51.0 and 49.0 ppm in the ratio of 15:1. No other $^{31}P\{^1H\}$ NMR signals can be detected. However, when this reaction was performed at room temperature there were many unknown peaks other than those for the cycloadducts recorded in the crude $^{31}P\{^1H\}$ NMR

spectrum. Furthermore, the reaction required longer time to complete.



Scheme 3.12

The X-ray analysis of the major product *endo*-(–)-**72** (Figure 3.5) confirmed that, as in the similar complex (–)-**54** and in other analogous complexes, in addition to the cycloaddition reaction, a ligand redistribution process occurred during the formation of *endo*-(–)-**72**. The arsenic donor is located in the position *trans* to the aromatic naphthylene carbon in *endo*-(–)-**72**. Most surprisingly the *endo*-occupancy of the phenyl group at the terminal position of (*Z*)-diphenyl-1-styrylphosphine is not consistent with its *Z*-geometrical relationship with the PPh_2 group in the dienophile precursor. This geometrical rearrangement was not observed in the analogous reactions between *Z*-methyl substituted diphenylvinylphosphine and DMPA or DMPP.

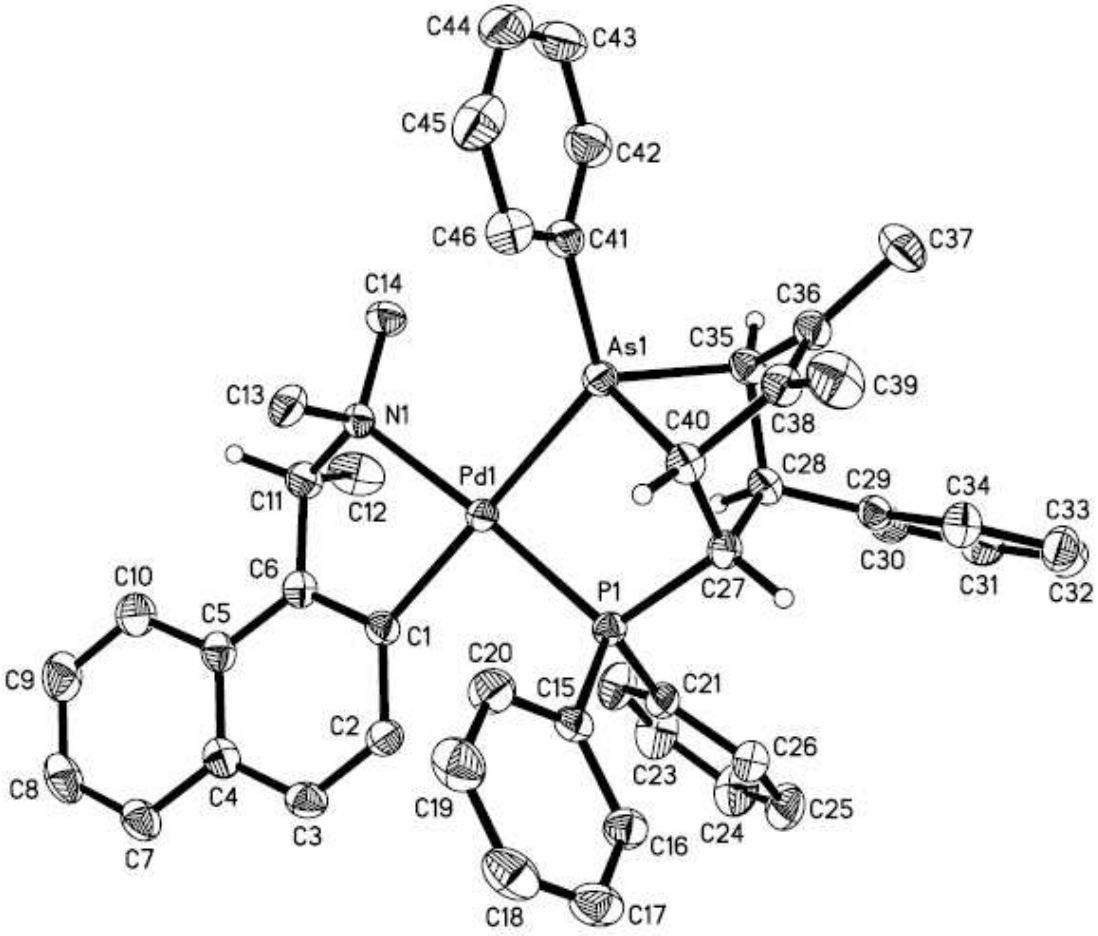


Figure 3.5 Molecular structure of complex *endo*-(–)-**72**

Table 3.5 Selected bond lengths (Å) and angles (°) for *endo*-(–)-**72**

Pd(1)–C(1)	2.042(2)	Pd(1)–N(1)	2.114(2)
Pd(1)–P(1)	2.299(2)	Pd(1)–As(1)	2.346(1)
As(1)–C(35)	1.986(2)	As(1)–C(40)	1.978(2)
As(1)–C(41)	1.930(2)	C(27)–P(1)	1.844(2)
C(27)–C(28)	1.571(3)	C(28)–C(35)	1.569(3)

C(35)–C(36)	1.517(3)	C(36)–C(38)	1.341(3)
C(38)–C(40)	1.509(3)	C(27)–C(40)	1.564(3)
C(1)–Pd(1)–N(1)	81.6(1)	C(1)–Pd(1)–P(1)	94.6(1)
N(1)–Pd(1)–P(1)	175.9(1)	C(1)–Pd(1)–As(1)	172.2(1)
N(1)–Pd(1)–As(1)	99.9(1)	P(1)–Pd(1)–As(1)	83.6(1)
C(41)–As(1)–C(40)	106.5(1)	C(41)–As(1)–C(35)	106.2(1)
C(40)–As(1)–C(35)	76.6(1)	C(41)–As(1)–Pd(1)	129.2(1)
C(40)–As(1)–Pd(1)	101.2(1)	C(35)–As(1)–Pd(1)	121.4(1)
C(40)–C(27)–C(28)	107.5(2)	C(35)–C(28)–C(27)	105.4(2)
C(36)–C(35)–C(28)	110.3(2)	C(36)–C(35)–As(1)	101.9(1)
C(28)–C(35)–As(1)	97.2(1)	C(38)–C(36)–C(35)	111.3(2)
C(36)–C(38)–C(40)	112.0(2)	C(38)–C(40)–C(27)	109.5(2)
C(38)–C(40)–As(1)	103.0(1)	C(27)–C(40)–As(1)	95.6(1)

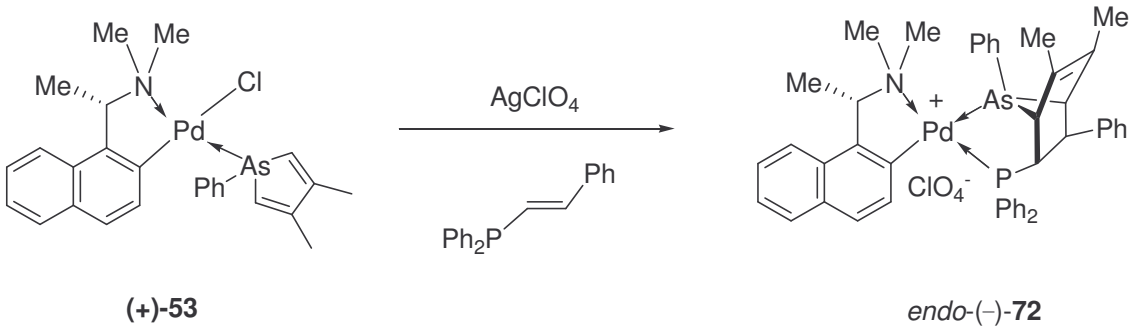
Despite the above geometrical changes the X-ray structural analysis revealed that the arsanorbornene is indeed formed and five new chiral centres at the As(1), C(27), C(28), C(35) and C(40) centre are *R*, *S*, *S, R* and *R*, respectively. The phenyl substituent on the original vinyl group has an *anti* relationship with the PPh_2 group. Selected bond lengths and angles are listed in Table 3.5. The geometry at the palladium metal centre is a distorted square planar with bond angles at palladium in the range of 81.6(1)–99.9(1) and 172.2(1)–175.9(1)°. The C(40)–As(1)–C(35) bond angle within the arsanorbornene skeleton [76.6(1)°] is equivalent to those found in similar complexes (–)-**44** [76.7(1)°].

The chiral amine auxiliary on *endo*-(–)-**72** could be removed subsequently from the template complex chemoselectively using concentrated hydrochloric acid at room temperature. Due to the difficulty in isolation of the resultant dichloro complex, it was converted into the corresponding diiodo complex *endo*-(+)-**73**. The *endo*-(+)-**73** was readily isolated by column chromatography on a silica column with dichloromethane as eluting solvent. The *endo*-(+)-**73** was obtained as yellow solid in high yield (94%), $[\alpha]_D$ +7.1° (*c* 0.4, CH_2Cl_2). Similar to its dichloro analogue, the diiodo complex *endo*-(+)-**73** was unstable in solution and decomposed after being kept for 2 days in $CDCl_3$.

Treatment of a dichloromethane solution of *endo*-(+)-**73** with aqueous potassium cyanide liberated the optically active bidentate ligand *endo*-(–)-**74** as a solid in 87% yield, $[\alpha]_D$ –240.0° (*c* 0.3, CH_2Cl_2). Significantly, the $^{31}P\{^1H\}$ NMR spectrum of *endo*-(–)-**74** in $CDCl_3$ exhibits a sharp singlet at δ –7.3. This liberation required only 5 min to complete when it was stirred at room temperature.

3.2.4.2 Asymmetric Cycloaddition Reaction between DMPA and (*E*)-Diphenyl-1-styrylphosphine

The asymmetric Diels–Alder reaction between complex (+)-**53** and (*E*)-diphenyl-1-styrylphosphine was completed in 45 h at room temperature. At 40 ºC the reaction could be accelerated to be completed within 34 h. As desired, the reaction gave the cycloadduct *endo*-(–)-**72** in the ratio of 15:1 and the similar yield (75%) (Scheme 3.13). At room temperature, as indicated by the $^{31}P\{^1H\}$ NMR spectrum, the reaction proceeded with high selectivity.



(+)-53 *endo*-(–)-**72**

Scheme 3.13

From the above experiments, the *exo*-oriented methyl group in complex *exo*-(–)-**68** is found to be stable. However, the analogous complex could not be formed when the methyl group was replaced by a phenyl moiety. We believe that the conversion of the Ph group from the *exo* to the *endo* position in Scheme 3.12 was due to the steric hinderance between the terminal phenyl group on the (*Z*)-diphenyl-1-styrylphosphine and the methyl group on the chiral center of the (*S*)-naphthylamine auxiliary (which lies on the same side of the palladium coordination plane). Furthermore, the phenyl group is sterically bigger than the methyl group which results in another huge repulsion between the terminal phenyl group and one neighboring phenyl group on the PPh_2. This intra ligand repulsion forces the terminal phenyl group from the *exo*-position to *endo*-position during the course of Diels–Alder reaction when both diene and dienophile are simultaneously coordinated on the palladium.

3.3 Conclusions

Experimentally the naphthyl palladium complex (+)-**2** has showed an outstanding chiral inductive effect. Through its prochiral NMe_2 group, it exerts absolute

enantiocontrol over the asymmetric [4+2] Diels–Alder reactions between DMPA and (*Z*/*E*)-diphenyl-1-propenylphosphine to generate enantiomerically pure As–P bidentate ligands *endo*-(–)-**68a** and *exo*-(–)-**68b**. Both reactions produced one arsenic and four new carbon chiral centers in a single step with high stereoselectivity (33:1). The methyl group of the propenylphosphine has a considerable effect on the rate of the cycloaddition reactions. In the absence of the methyl group, the corresponding Diels–Alder reaction needed only 40 min to complete. When the methyl group is introduced, however, the reactions needed 2 to 3 weeks to complete.

Upon comparison with the similar dichloro complex (+)-**48**, the arsenic centers in the dichloro complexes *endo*-(+)-**66a** and *exo*-(–)-**66b** are eliminated stereospecifically under mild reaction conditions to generate the corresponding retrodiene palladium complexes **70a** and **70b**. Unfortunately these complexes could not be isolated *via* fractional crystallization or column chromatography. The complex **70a** was further converted into its corresponding diiodo complex (+)-**71a** which could be isolated in enantiomerically pure form. The methyl group of the propenylphosphine also has considerable effect on the rate of the arsenic elimination reaction. The arsenic elimination reactions of complexes *endo*-(+)-**66a** and *exo*-(–)-**66b** are faster than that of dichloro complex (–)-**45** (7, 10 and 21days in $CDCl_3$, respectively).

Importantly the asymmetric Diels–Alder reactions between DMPA and (*Z*/*E*)-diphenyl-1-styrylphosphine produced the same *endo*-cycloadduct *endo*-(–)-**72**, with the same selectivity of 15:1. Furthermore the reaction temperature has a significant effect on the reaction rate with the (*E*)-diphenyl-1-styrylphosphine dienophile but little effect on the reaction rate with the (*Z*)-diphenyl-1-styrylphosphine.

3.4 Experimental Section

General: Similar to that described in section 2.4. (*Z*/*E*)-Diphenyl-1-propenylphosphine,[108] (*Z*/*E*)-diphenyl-1-styrylphosphine,[109] and (+/–)-**69**[110] were prepared following the literature procedures.

Cycloaddition Reaction: Preparation of Complex *endo*-(–)-65a

A solution of *trans*-(+)-**64a** (0.39 g, 0.69 mmol) in dichloromethane (60 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (1.0 g) in water (1 mL). The organic layer, after the removal of AgCl, was then washed with water (3 × 60 mL), dried ($MgSO_4$), and subsequently treated with DMPA (0.16 g, 0.69 mmol) for 2 weeks at room temperature. Removal of the solvent gave *endo*-(–)-**65a** as a solid, which was then recrystallized from chloroform–diethyl ether to give the complex as pale yellow needles (0.27 g, 45%). $[\alpha]_D$ = –65.0° (*c* 0.6, CH_2Cl_2). Mp: 172–173 °C. Anal. Calcd for $C_{41}H_{44}AsClNO_4PPd$: C, 57.1; H, 5.1; N, 1.6. Found: C, 57.2; H, 5.4; N, 1.7. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 49.7. ^1H NMR (CD_2Cl_2, δ): 0.75 (d, $^3J_{HH}$ = 6.8 Hz, 3H, PCC*CH*$_3$), 1.47 (s, 3H, =C*CH*$_3$), 1.69 (d, $^5J_{PH}$ = 1.0 Hz, 3H, =C*CH*$_3$), 2.02 (d, $^3J_{HH}$ = 6.3 Hz, 3H, CH*CH*$_3$), 2.63 (dt, $^3J_{HH}$ = 2.3, $^2J_{PH}$ = 8.9 Hz, 1H, P*CH*), 2.79 (s, 1H, As*CH*), 2.82 (d, $^4J_{PH}$ = 1.5 Hz, 3H, N*CH*$_3$), 2.87 (d, $^4J_{PH}$ = 3.8 Hz, 3H, N*CH*$_3$), 3.07 (m, 1H, PCH*CH*), 3.46 (d, $^3J_{HH}$ = 2.4 Hz, 1H, As*CH*), 4.52 (qn, $^3J_{HH}$ = $^4J_{PH}$ = 6.3 Hz, 1H, *CH*CH_3), 6.71–8.28 (m, 21H, aromatics).

Cycloaddition Reaction: Preparation of Complex *exo*-(–)-65b

The cycloaddition reaction was performed similarly from *cis*-(+)-**64b** (0.17 g, 0.30

mmol) and DMPA (0.07 g, 0.30 mmol) for 3 weeks at room temperature. The major product *exo*-(–)-**65b** was recrystallized from chloroform–diethyl ether to give the complex as pale yellow needles (0.11 g, 43%). $[\alpha]_D$ = –43.3° (*c* 0.3, CH_2Cl_2). Mp: 195–196 ºC. Anal. Calcd for $C_{41}H_{44}AsClNO_4PPd$: C, 57.1; H, 5.1; N, 1.6. Found: C, 56.9; H, 5.3; N, 1.7. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 42.2. ^1H NMR (CD_2Cl_2, δ): 1.39 (d, $^3J_{HH}$ = 2.3 Hz, 3H, PCC*CH*$_3$), 1.41 (s, 3H, =C*CH*$_3$), 1.70 (s, 3H, =C*CH*$_3$), 2.04 (d, $^3J_{HH}$ = 6.2 Hz, 3H, CH*CH*$_3$), 2.56 (m, 1H, PCH*CH*), 2.75 (s, 1H, As*CH*), 2.76 (s, 3H, N*CH*$_3$), 2.88 (d, $^4J_{PH}$ = 3.7 Hz, 3H, N*CH*$_3$), 3.10 (s, 1H, As*CH*), 3.43 (dt, $^3J_{HH}$ = 2.0, $^2J_{PH}$ = 9.6 Hz, 1H, P*CH*), 4.51 (qn, $^3J_{HH}$ = $^4J_{PH}$ = 6.2 Hz, 1H, *CH*CH_3), 6.83–8.34 (m, 21H, aromatics).

Removal of Chiral Auxiliary: Synthesis of Complex *endo*-(+)-66a

The complex *endo*-(–)-**65a** (0.45 g, 0.52 mmol) was dissolved in dichloromethane (60 mL) and treated with excess concentrated hydrochloric acid (3 mL) for 10 min at room temperature. The mixture was then washed with water (3 × 60 mL), dried ($MgSO_4$), and subsequently recrystallized from chloroform–diethyl ether as pale-yellow crystals *endo*-(+)-**66a** (0.28 g, 85%). $[\alpha]_D$ = +32.6° (*c* 0.5, CH_2Cl_2). Mp: 131–133 ºC. Anal. Calcd for $C_{27}H_{28}AsCl_2PPd$: C, 51.0; H, 4.4. Found: C, 50.7; H, 4.5. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 32.2. ^1H NMR ($CDCl_3$, δ): 0.68 (d, $^3J_{HH}$ = 6.8 Hz, 3H, PCC*CH*$_3$), 1.57 (s, 3H, =C*CH*$_3$), 1.66 (s, 3H, =C*CH*$_3$), 2.47 (d, $^2J_{PH}$ = 6.5 Hz, 1H, P*CH*), 3.04 (m, 1H, PCH*CH*), 3.16 (s, 1H, As*CH*), 3.49 (d, $^3J_{HH}$ = 2.4 Hz, 1H, As*CH*), 7.37–8.30 (m, 15H, aromatics).

Removal of Chiral Auxiliary: Synthesis of Complex *exo*-(–)-66b

The chiral auxiliary was removed similarly from the complex *exo*-(–)-**65b** (0.06 g,

0.07 mmol) using concentrated hydrochloric acid (3 mL). The complex *exo*-(–)-**66b** was recrystallized from dichloromethane–diethyl ether as yellow crystals (0.04 g, 79%). $[\alpha]_D$ = –90.9° (*c* 0.1, CH_2Cl_2). Mp: 139–140 ºC. Anal. Calcd for $C_{27}H_{28}AsCl_2PPd{\cdot}CH_2Cl_2$: C, 46.7; H, 4.2. Found: C, 46.7; H, 4.5. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 20.5. ^1H NMR (CD_2Cl_2, δ): 1.50 (s, 3H, =C*CH*$_3$), 1.56 (d, $^3J_{HH}$ = 7.4 Hz, 3H, PCC*CH*$_3$), 1.63 (d, $^5J_{PH}$ = 1.0 Hz, 3H, =C*CH*$_3$), 2.57 (m, 1H, PCH*CH*), 2.96 (s, 1H, As*CH*), 3.08 (s, 1H, As*CH*), 3.36 (dt, $^3J_{HH}$ = 2.4, $^2J_{PH}$ = 7.6 Hz, 1H, P*CH*), 7.43–8.41 (m, 15H, aromatics).

Synthesis of the Diiodo Complexes *endo*-(+)-67a and *exo*-(–)-67b

A solution of (+)-**53** (0.50 g, 0.88 mmol) in dichloromethane (80 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (1.0 g) in water (1 mL). The organic layer, after the removal of AgCl, was then washed with water (3 × 80 mL), dried ($MgSO_4$), and subsequently treated with (*Z*/*E*)-diphenyl-1-propenylphosphine (0.20 g, 0.88 mmol) for 3 days at 40 ºC. The mixture was treated with excess concentrated hydrochloric acid (2 mL) for 10 min at room temperature. The solution was then washed with water (3 × 80 mL). The solution of crude dichloro complexes were mixed with sodium iodide (0.5 g) in water (80 mL) and stirred vigorously for 10 min. The colour of solution changed from yellow to red. The solvents were removed, and the residue was extracted with dichloromethane. Removal of the solvent gave the product as a solid, which was then recrystallized from dichloromethane–diethyl ether to give *exo*-(–)-**67b** as red microcrystals (0.23 g, 64%). $[\alpha]_D$ = –149.5° (*c* 0.2, CH_2Cl_2). Mp: 130–131 ºC. Anal. Calcd for $C_{27}H_{28}AsI_2PPd$: C, 39.6; H, 3.5. Found: C, 39.2; H, 3.5. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 28.1. ^1H NMR (CD_2Cl_2, δ): 1.40 (s, 3H, =C*CH*$_3$), 1.62 (s, 3H, =C*CH*$_3$), 1.64

(s, 3H, PCC*CH*$_3$), 2.56 (m, 1H, PCH*CH*), 2.77 (s, 1H, As*CH*), 3.10 (s, 1H, As*CH*), 3.13 (dd, $^3J_{HH}$ = 2.5, $^2J_{PH}$ = 8.4 Hz, 1H, P*CH*), 7.43–8.41 (m, 15H, aromatics).

The remainder was purified by column chromatography on a silica column with dichloromethane to give *endo*-(+)-**67a** as a solid, which was recrystallized from chloroform–diethyl ether–*n*-hexane in the form of red crystals (0.22 g, 61%). $[\alpha]_D$ = +106.3° (*c* 0.2, CH_2Cl_2). Mp: 144–145 ºC. Anal. Calcd for $C_{27}H_{28}AsI_2PPd$: C, 39.6; H, 3.5. Found: C, 39.5; H, 3.5. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 35.4. ^1H NMR ($CDCl_3$, δ): 0.66 (d, $^3J_{HH}$ = 6.8 Hz, 3H, PCC*CH*$_3$), 1.57 (s, 3H, =C*CH*$_3$), 1.64 (s, 3H, =C*CH*$_3$), 2.31 (dt, $^3J_{HH}$ = 2.2, $^2J_{PH}$ = 7.0 Hz, 1H, P*CH*), 3.08 (s, 1H, As*CH*), 3.14 (m, 1H, PCH*CH*), 3.41 (d, $^3J_{HH}$ = 2.8 Hz, 1H, As*CH*), 7.38–8.31 (m, 15H, aromatics).

Liberation of the As–P Ligand *endo*-(–)-68a

A solution of *endo*-(+)-**67a** (0.23 g, 0.28 mmol) in dichloromethane (20 mL) was stirred vigorously with a saturated aqueous solution of potassium cyanide (1.0 g) for 10 min. The organic layer was separated, then washed with water (3 × 20 mL), and dried ($MgSO_4$). Upon removal of the solvent, the free ligand *endo*-(–)-**68a** was obtained as an air-sensitive white solid (0.11 g, 86%). $[\alpha]_D$ = –80.0° (*c* 0.8, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): –11.3.

Liberation of the As–P Ligand *exo*-(–)-68b

The liberated free ligand *exo*-(–)-**68b** was liberated similarly from *exo*-(–)-**67b** (0.13 g, 0.24 mmol) by treatment with excess potassium cyanide (0.09 g, 82%). $[\alpha]_D$ = –40.0° (*c* 0.1, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): –9.0.

Arsenic–Elimination Reaction: Isolation of Complex (+)-71a

The complex *endo*-(+)-**66a** (0.010 g, 0.014 mmol) was allowed to stand in $CDCl_3$ for 7 days at room temperature, then treated with excess sodium iodide (0.01g), washed with water and dried ($MgSO_4$). The solvent was removed to give the product as solid which was recrystallized from dichloromethane–diethyl ether. Deep red crystals of (+)-**71a** were obtained (4 mg, 43%). $[\alpha]_D$ = +195.0° (*c* 0.2, CH_2Cl_2). Mp: 268–269 ºC. Anal. Calcd for $C_{21}H_{23}I_2PPd$: C, 37.8; H, 3.5. Found: C, 37.5; H, 3.6. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 130.3. ^1H NMR ($CDCl_3$, δ): 0.96 (d, $^3J_{HH}$ = 6.6 Hz, 3H, CH*CH*$_3$), 1.92 (d, $^5J_{PH}$ = 6.7 Hz, 3H, =C*CH*$_3$), 2.47 (s, 3H, =C*CH*$_3$), 2.95 (m, 1H, *CH*CH_3), 3.28 (m, 1H, P*CH*), 5.66 (br s, 1H, =*CH*), 5.83 (s, 1H, =*CH*), 7.44–8.05 (m, 10H, aromatics).

Cycloaddition Reaction: Preparation of Complex *endo*-(–)-72

A solution of (+)-**53** (0.85 g, 1.49 mmol) in dichloromethane (80 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (0.6 g) in water (1 mL). The organic layer, after the removal of AgCl, was then washed with water (3 × 50 mL), dried ($MgSO_4$), and subsequently treated with (*Z*)-diphenyl-1-styrylphosphine (0.43 g, 1.49 mmol) for 41 h at 40 ºC. Removal of the solvent gave *endo*-(–)-**72** as a solid, which was then recrystallized from dichloromethane to give the complex as colourless crystals (0.97 g, 70%). $[\alpha]_D$ = –98.6° (*c* 0.7, CH_2Cl_2). Mp: 176–177 ºC. Anal. Calcd for $C_{46}H_{46}AsClNO_4PPd$: C, 59.8; H, 5.0; N, 1.5. Found: C, 59.9; H, 5.1; N, 1.6. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 51.0. ^1H NMR (CD_2Cl_2, δ): 1.12 (d, $^4J_{HH}$ = 0.8 Hz, 3H, =C*CH*$_3$), 1.57 (s, 3H, =C*CH*$_3$), 2.08 (d, $^3J_{HH}$ = 6.3 Hz, 3H, CH*CH*$_3$), 2.84 (d, $^4J_{PH}$ = 1.2 Hz, 3H, N*CH*$_3$), 2.94 (d, $^4J_{PH}$ = 3.8 Hz, 3H, N*CH*$_3$), 3.08 (s, 1H, As*CH*), 3.49 (dt, $^3J_{HH}$ = 2.6, $^2J_{PH}$ = 9.5 Hz,

1H, P*CH*), 3.75 (d, $^{3}J_{HH}$ = 2.1 Hz, 1H, As*CH*), 4.09 (dt, $^{3}J_{HH}$ = 3.0, $^{3}J_{PH}$ = 28.0 Hz, 1H, Ph*CH*), 4.54 (qn, $^{3}J_{HH}$ = $^{4}J_{PH}$ = 6.2 Hz, 1H, *CH*CH_3), 6.70–8.24 (m, 26H, aromatics).

Removal of Chiral Auxiliary: Synthesis of Diiodo Complex *endo*-(+)-73

The complex *endo*-(–)-**72** (0.37 g, 0.40 mmol) was dissolved in dichloromethane (50 mL) and treated with excess concentrated hydrochloric acid (3 mL) for 5 min at room temperature. The solution was then washed with water (3 × 50 mL). The solution of crude dichloro complex was mixed with sodium iodide (0.5 g) in water (50 mL) and stirred vigorously for 5 min. The solution was washed with water (3 × 50 mL), dried ($MgSO_4$). Removal of the solvent gave *endo*-(+)-**73** as a solid, which was then isolated by column chromatography on a silica column with dichloromethane–diethyl ether (0.33 g, 94%). $[\alpha]_D$ = +7.1° (*c* 0.4, CH_2Cl_2). Mp: 143–144 ºC. Anal. Calcd for $C_{32}H_{30}AsI_2PPd$: C, 43.6; H, 3.4. Found: C, 43.3; H, 3.5. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, δ): 40.4. ^{1}H NMR ($CDCl_3$, δ): 1.10 (d, $^{4}J_{HH}$ = 1.0 Hz, 3H, =C*CH*$_3$), 1.64 (s, 3H, =C*CH*$_3$), 3.11 (d, $^{3}J_{HH}$ = 1.3 Hz, 1H, As*CH*), 3.22 (dt, $^{3}J_{HH}$ = 2.5, $^{2}J_{PH}$ = 7.6 Hz, 1H, P*CH*), 3.63 (d, $^{3}J_{HH}$ = 2.8 Hz, 1H, As*CH*), 4.30 (dt, $^{3}J_{HH}$ = 2.8, $^{3}J_{PH}$ = 25.0 Hz, 1H, Ph*CH*), 6.81–8.22 (m, 20H, aromatics).

Liberation of the As–P Ligand *endo*-(–)-74

A solution of *endo*-(+)-**73** (0.10 g, 0.11 mmol) in dichloromethane (20 mL) was stirred vigorously with a saturated aqueous solution of KCN (1.0 g) for 5 min. The organic layer was separated, then washed with water (3 × 20 mL), and dried ($MgSO_4$). Upon removal of the solvent, the free ligand *endo*-(–)-**74** was obtained as an air-sensitive solid (0.05 g, 87%). $[\alpha]_D$ = –240.0° (*c* 0.3, CH_2Cl_2). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, δ): –7.3.

CHAPTER 4

Asymmetric Syntheses of As–Chiral Ketoarsine Palladium Complexes

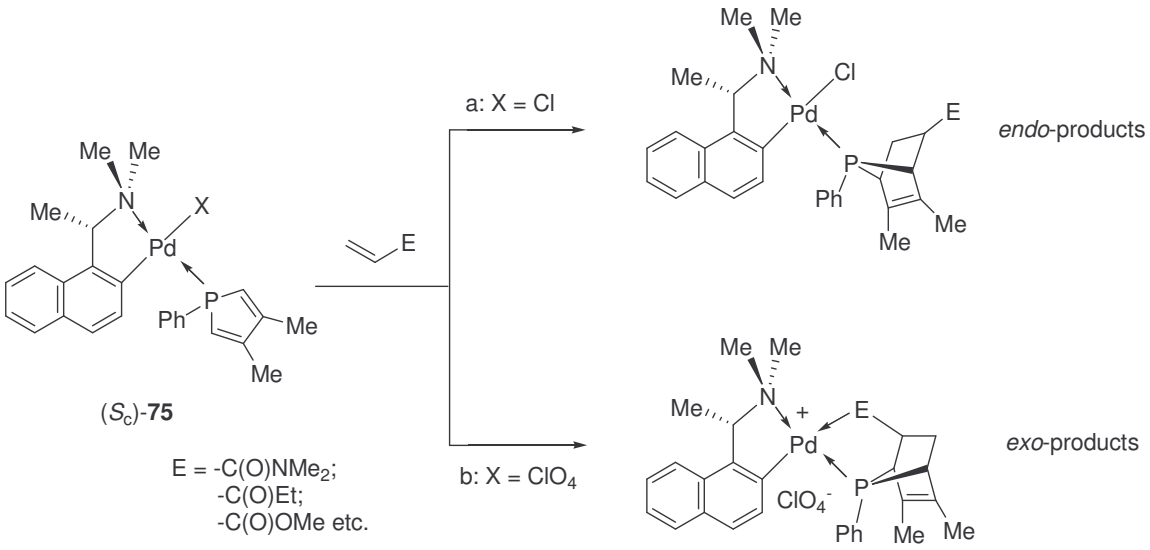
4.1 Introduction

In many reactions catalyzed by transition metals, tertiary phosphines are very useful ligands which increase the selectivity of the desired product.[111] When these substitutionally inert phosphorus ligands contain the substitutionally labile oxygen donor atom, they form interesting P–O heterobidentates. These P–O ligands are also of considerable importance in the development of homogeneous catalysts.[112] The P–O chelating ligands provide tertiary phosphorus atoms, which are responsible for a close contact to the metal centre, and also oxygen donors such as ketone, ether or alcohols that form weak metal-oxygen bonds which may be cleaved reversibly. As a result of this "opening and closing mechanism"[113] empty coordination sites are made available when needed in the course of the catalytic cycles without permanent separation of the oxygen donors from the complex fragment. Hence these hemilabile P–O ligands have been shown to be useful for various catalytic transformations.[114] For example, they exhibit an unusual selectivity enhancing effect in the nickel-catalyzed oligomerization and polymerization of ethene and in the carbonylation and hydrocarbonylation of methanol. Moreover, they have also been used in the stereoselective hydrogenations, hydrosilylations and hydroformylations.[115]

Ketophosphine is a common type amongst these P–O ligands which is capable of

undergoing conversion to enolate moiety upon deprotonation.[116] The coordination chemistry of certain achiral ketophosphine ligands on various metals has been well studied, however, the reports about chiral ketophosphine is relative few.[117]

In a recent communication we briefly described the asymmetric synthesis of a series of functionalized monophosphines containing stereogenic phosphorus centers *via* cycloaddition reactions.[82] Particularly by a systematic manipulation of the subtle stereoelectronic properties of auxiliaries and metal centers, the chiral templates are able to control the disposition of selected functionalities into designated locations such as *exo* or *endo* positions of the phosphanorbornene skeleton (Scheme 4.1). In the *endo*-cycloaddition pathway, the kinetically stable chloro ligand in (S_c)-**75a** (X = Cl) remains coordinated to the neutral template throughout the course of the intermolecular cycloaddition reaction and hence the reacting dienophile cannot be involved in any form of metal complexation. In the *exo*-cycloaddition pathway, however, the kinetically labile perchlorate ligand on the palladium complex (S_c)-**75b** (X = ClO_4) can be displaced by

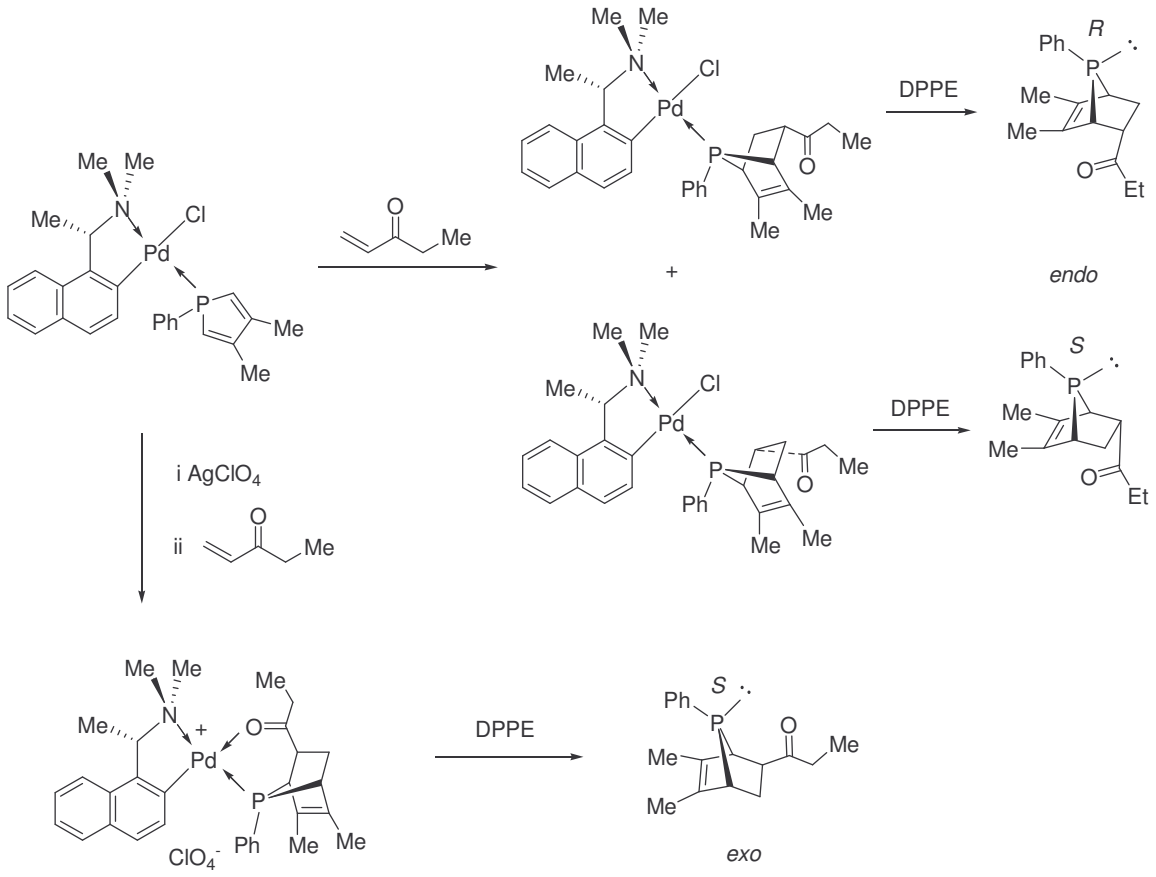


(S_c)-**75**

E = -C(O)NMe$_2$;
-C(O)Et;
-C(O)OMe etc.

Scheme 4.1

the incoming dienophile to form a cationic intermediate in which the diene and dienophile are coordinated simultaneously onto the chiral template during the course of cycloaddition reaction. For instance, an asymmetric Diels–Alder reaction between DMPP and ethyl vinyl ketone promoted by the chiral organopalladium complex (+)-**2** gives the corresponding ketophosphine ligands in which the keto group can be stereospecifically located in the *endo*- and *exo*-positions of the phosphanorbornene skeleton (Scheme 4.2).[118]



Scheme 4.2

Although several functionalized monophosphines have been synthesized by means

of this method, no corresponding arsenic analogue has been reported hitherto. At this point, we intend to prepare the corresponding ketoarsine compounds by the analogous route and thus to study the stereoselectivity and stability factors associated with such systems. In this chapter, we describe an efficient approach to different stereoisomeric forms of the As-chiral palladium complexes *via* an unusual *exo-endo* stereochemically controlled asymmetric Diels–Alder reaction between DMPA and ethyl vinyl ketone.

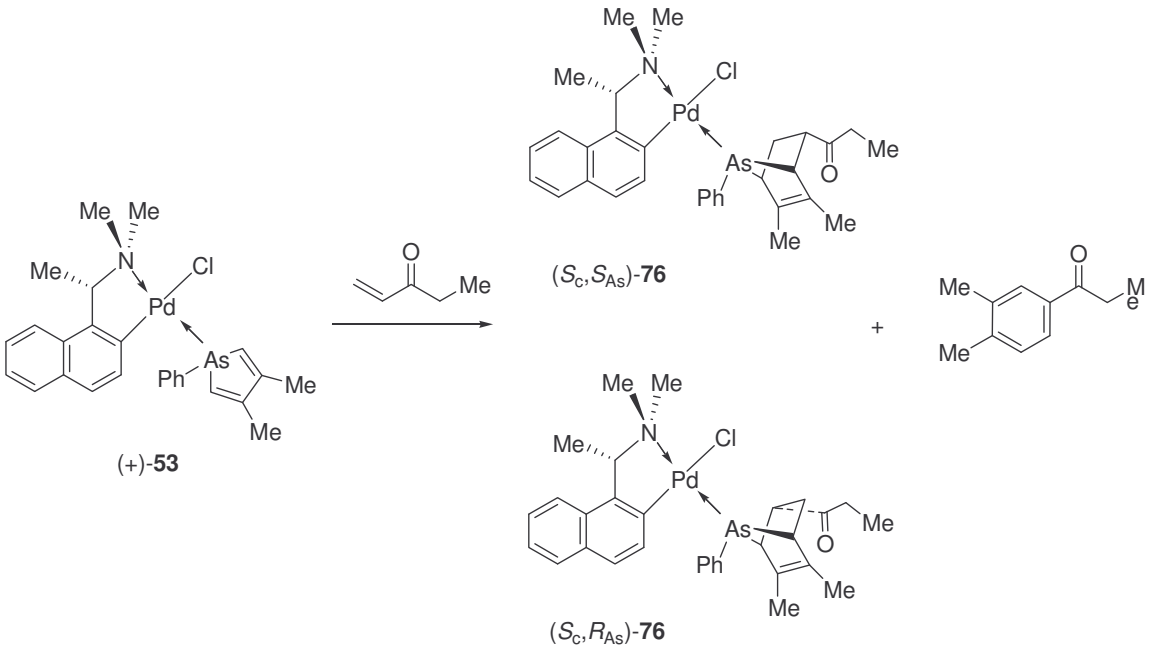
4.2 Results and Discussion

4.2.1 Formation and Isolation of the *Endo*-Cycloadduct (S_c,S_{As})-76

Uncoordinated DMPP shows no reaction with ethyl vinyl ketone despite strong reaction conditions being employed. The coordination of the phosphole ligand to the chiral reaction template, however, activates the cyclic diene towards [4+2] Diels–Alder reaction.[44] Upon direct treatment of the neutral chloride complex (+)-**53** with ethyl vinyl ketone in dichloromethane for 1 month at room temperature, a 2:1 diastereomeric mixture of the two *endo*-cycloaddition products (S_c,S_{As})-**76** and (S_c,R_{As})-**76** were obtained as indicated by the ^{1}H NMR spectrum (Scheme 4.3).

The major isomer (S_c,S_{As})-**76** could subsequently be recrystallized from dichloromethane–diethyl ether as pale yellow crystals, $[\alpha]_D$ +129.3° (*c* 0.6, CH_2Cl_2). The chemical shifts (δ 3.16 and 3.85) of As*CH* as single bonds in (S_c,S_{As})-**76** were different from the corresponding signals as double bond in complex (+)-**53** (δ 6.69 and 6.97). Meanwhile the ^{13}C NMR analysis revealed a characteristic carbonyl signal at δ 209.8 ppm. This observation was consistent with the stretching mode of normal ketone

function, and hence indicated that the *endo*-cycloaddition product was indeed formed in this diastereoselective intermolecular reaction.



Scheme 4.3

During the isolation of the crude cycloadducts or when the pure complex (S_c,S_{As})-**76** was kept in solution for several weeks, a side product 1-(3, 4-dimethylphenyl)-1-propanone was obtained. Therefore, it was deduced that although initially the cycloadducts (S_c,S_{As})-**76** and (S_c,R_{As})-**76** were formed, due to their instability, the arsenic–elimination reaction subsequently occurred. Accordingly the cycloaddition products decomposed to give the elimination product as the minor product.

4.2.2 X-ray Structural Analysis of Complex (S_c,S_{As})-76

The X-ray analysis of the major isomer (S_c,S_{As})-**76** reveals that the cycloaddition reaction between the coordinated DMPA and ethyl vinyl ketone has resulted in the formation of the *syn-endo* cycloadduct (Figure 4.1). The ketoarsine ligand coordinated in a monodentate fashion *via* the bridgehead arsenic to the palladium centre, while the free ketone moiety occupied the *endo* position at C(27). The absolute configurations of the four new chiral centres at As(1), C(21), C(26) and C(27) are *S*, *S*, *R* and *R*, respectively.

The geometry at the palladium coordination sphere is distorted square planar. The bond angles at palladium are in the range of 80.6(2)–96.7(2) and 176.5(2)–177.3(1)^o (Table 4.1). The C(26)–As(1)–C(21) bond angle of 76.4(2)^o is typical for acute

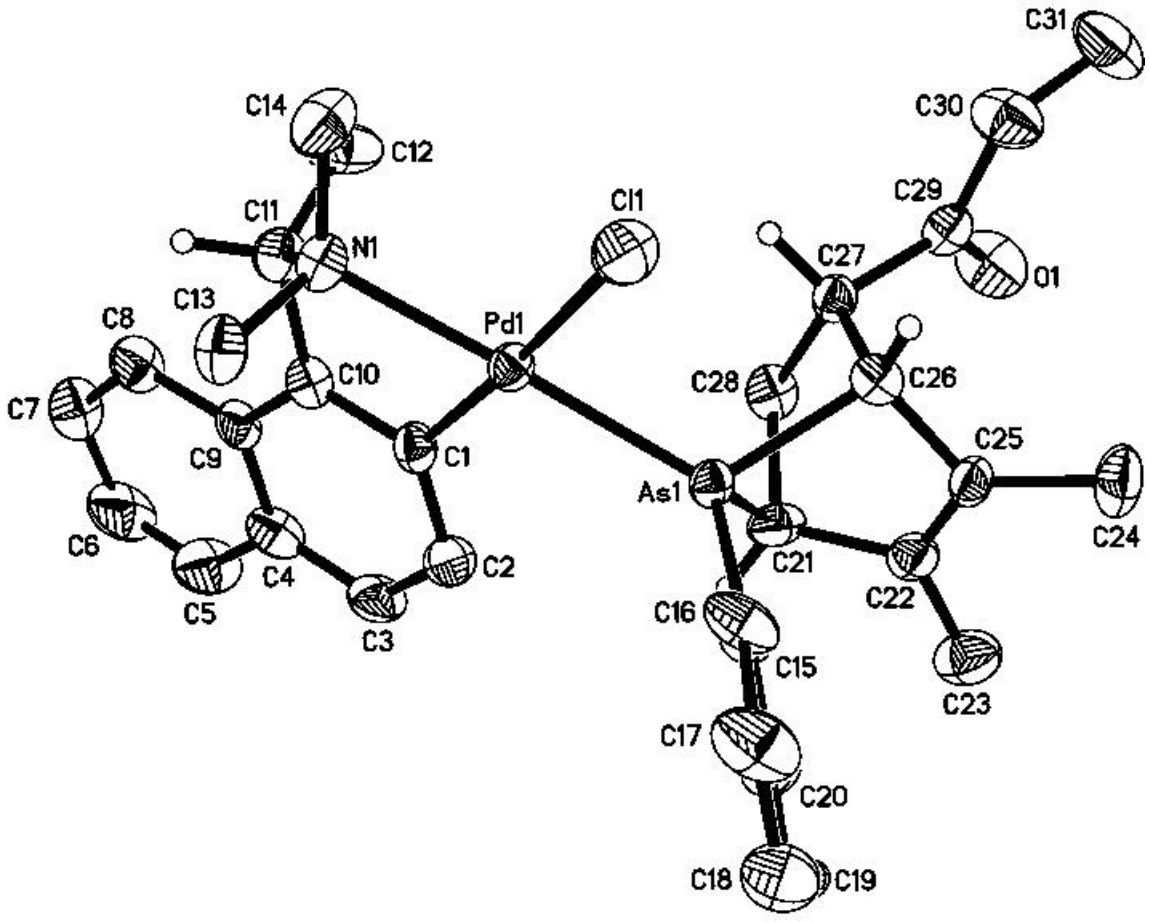


Figure 4.1 Molecular structure and absolute stereochemistry of complex (S_c,S_{As})-**76**

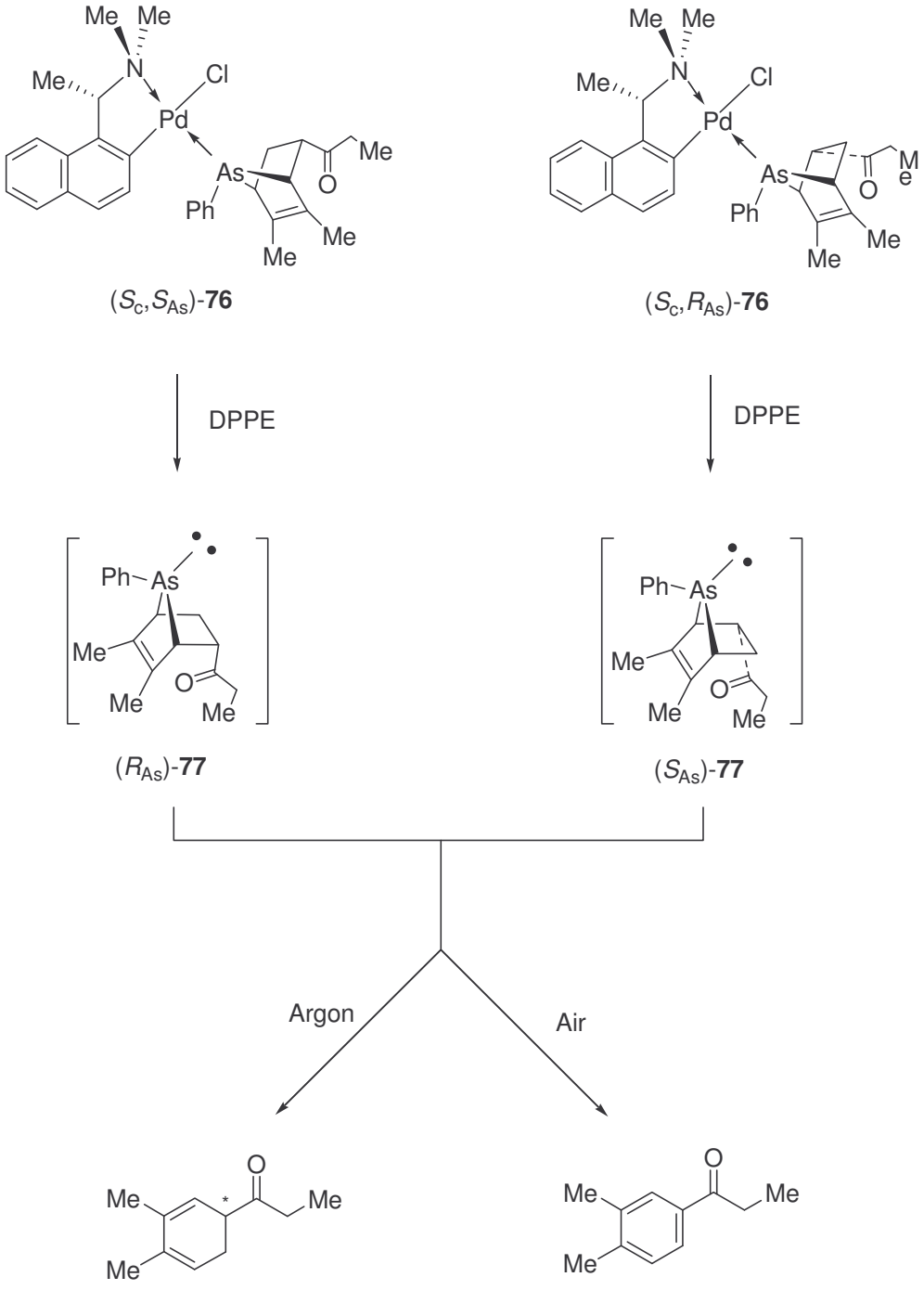
Table 4.1 Selected bond lengths (Å) and angles (°) for (S_c,S_{As})-**76**

Pd(1)–C(1)	2.006(5)	Pd(1)–N(1)	2.134(4)
Pd(1)–As(1)	2.343(1)	Pd(1)–Cl(1)	2.407(1)
As(1)–C(21)	2.005(6)	As(1)–C(26)	1.974(5)
C(21)–C(28)	1.568(8)	C(21)–C(22)	1.482(8)
C(22)–C(23)	1.497(8)	C(22)–C(25)	1.338(8)
C(24)–C(25)	1.500(8)	C(25)–C(26)	1.506(8)
C(26)–C(27)	1.571(7)	C(27)–C(28)	1.570(8)
C(27)–C(29)	1.507(8)	C(29)–C(30)	1.486(9)
C(29)–O(1)	1.230(7)	C(30)–C(31)	1.500(1)
C(1)–Pd(1)–N(1)	80.6(2)	C(1)–Pd(1)–As(1)	96.7(2)
N(1)–Pd(1)–As(1)	177.3(1)	C(1)–Pd(1)–Cl(1)	176.5(2)
N(1)–Pd(1)–Cl(1)	96.0(1)	As(1)–Pd(1)–Cl(1)	86.7(1)
C(26)–As(1)–C(21)	76.4(2)	C(28)–C(21)–As(1)	98.6(4)
C(22)–C(21)–C(28)	107.2(5)	C(22)–C(21)–As(1)	102.2(4)
C(25)–C(22)–C(21)	112.0(5)	C(22)–C(25)–C(26)	112.1(5)
C(25)–C(26)–C(27)	106.8(4)	C(25)–C(26)–As(1)	101.7(3)
C(27)–C(26)–As(1)	99.3(3)	C(28)–C(27)–C(26)	106.6(4)
C(29)–C(27)–C(28)	113.1(4)	C(29)–C(27)–C(26)	111.1(4)
C(21)–C(28)–C(27)	106.4(4)	O(1)–C(29)–C(27)	122.6(6)
O(1)–C(29)–C(30)	120.0(6)	C(30)–C(29)–C(27)	117.3(5)
C(29)–C(30)–C(31)	116.5(6)		

arsanorbornene skeletons. It is similar to the above analogous arsine complexes, and quite smaller than that of analogous phosphanorbornene [81.0(1)°].[118] The highly strained six-membered ring showed the double bond character between C(22)–C(25) and the *syn* geometry at arsenic. The Pd(1)–C(1), Pd(1)–N(1) and Pd(1)–Cl(1) bond distances [2.006(5), 2.134(4) and 2.407(1) Å, respectively] in complex (S_c,S_{As})-**76** are all slightly shorter than that of analogous phosphine complex [2.014(2), 2.151(1) and 2.411(1) Å, respectively].[118] However, the Pd(1)–As(1) bond distance [2.343(1) Å] is 0.1 Å longer than that of the corresponding Pd(1)–P(1) bond distance [2.241(0) Å]. The C=O bond distance of 1.230(7) Å, is within the normal range for carbonyl functions.

4.2.3 Arsenic–Elimination Reactions

Treatment of (S_c,S_{As})-**76** with 1,2-bis(diphenylphosphino)ethane (DPPE) in dichloromethane liberated the optically pure ketoarsine (R_{As})-**77** from the chiral metal template (Scheme 4.4), but unlike its analogous ketophosphine, the resulting ketoarsine ligand is very unstable and subsequently decomposed to produce some unidentified products. The reaction conditions have effects on the formation of the final product. For example, under argon condition, the optically pure complex (S_c,S_{As})-**76** was treated with DPPE for 10 min at room temperature, then the liberated product was purified by subjecting the resulting mixture to a column of florisil to trap all the metal complexes. The intermediate free arsine ligand instantly decomposed to give 1-(3,4-dimethyl-2,4-cyclohexadienyl)-1-propanone, $[\alpha]_D$ –20.0° (*c* 0.4, CH_2Cl_2), and other side products which could not be identified. However, in air condition, the intermediate



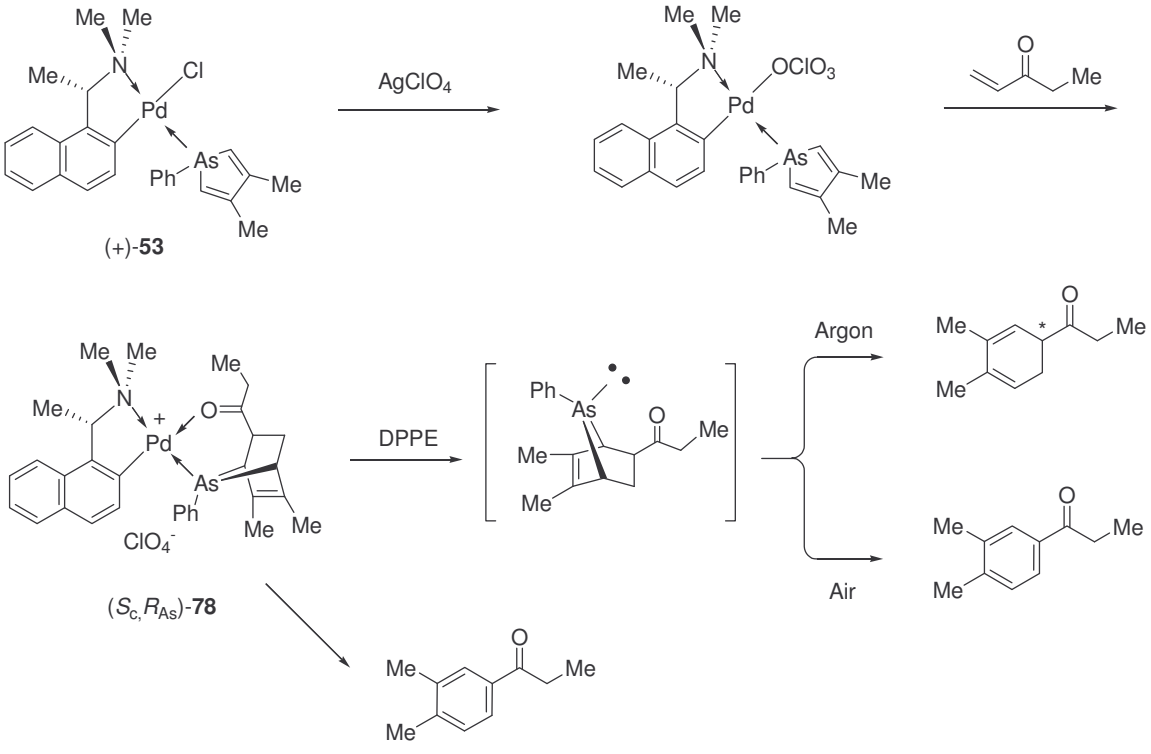
Scheme 4.4

ketoarsine decomposed to give another arsenic–elimination reaction product, 1-(3,4-dimethylphenyl)-1-propanone, which can be further purified by silica column to give the

pure compound. The ^{1}H NMR and ^{13}C NMR spectra are consistent with this inferred compound. The outcome of the above mentioned liberation reaction is in contrast to analogous ketophosphine. The same phenomenon was observed with (S_c,R_{As})-**76**.

4.2.4 Formation and Isolation of the *Exo*-Cycloadduct (S_c,R_{As})-78

Prior to the Diels–Alder reaction, the chloride complex (+)-**53** was treated with silver perchlorate to give the perchlorate intermediate complex. It was then reacted with excess ethyl vinyl ketone in dichloromethane at room temperature. In this step, both DMPA and the dienophile, ethyl vinyl ketone, were activated after coordination onto the palladium centre. This intramolecular reaction was found to be complete in 1 month and produce only one isomer (Scheme 4.5).



Scheme 4.5

The crude product was purified by column chromatography in 20% yield, $[\alpha]_D$ +126.5° (*c* 0.7, CH_2Cl_2). The formation of the by-product, 1-(3,4-dimethylphenyl)-1-propanone, was responsible for the low yield. During the isolation of (+)-**78**, this side product was obtained in 35% yield. So similar to the *endo*-cycloadduct (S_c,S_{As})-**76**, the *exo*-cycloaddition reaction product (S_c,R_{As})-**78** is also unstable in solution and decomposes to give the arsenic–elimination reaction product.

Similar to the *endo*-cycloadduct (S_c,S_{As})-**76**, the optically pure complex (S_c,R_{As})-**78** was also treated with DPPE for 10 min at room temperature to liberate the *exo*-ketoarsine ligand. Due to its high instability, however, it decomposed to give the arsenic–elimination reaction products, 1-(3,4-dimethyl-2,4-cyclohexadienyl)-1-propanone and 1-(3,4-dimethylphenyl)-1-propanone, under argon and air reaction conditions, respectively.

4.3 Conclusions

The dimeric organopalladium complex (S_c)-**2** as an efficient asymmetric inducer in promoting Diels–Alder reaction between DMPA and ethyl vinyl ketone to form enantiomerically pure functionalized monoarsine has been amply demonstrated.

The intermolecular reaction between the chloride complex (+)-**53** and ethyl vinyl ketone resulted in the formation of a pair of diastereomers in *syn-endo* stereochemistry [(S_c,S_{As})-**76** and (S_c,R_{As})-**76** in the ratio of 2:1]. On the other hand, the intramolecular reaction between the corresponding perchlorate complex and ethyl vinyl ketone showed high stereoselectivity to produce only one isomer (S_c,R_{As})-**78**.

Finally, unlike the analogous phosphine palladium complexes, all three resulting

arsine palladium complexes [(S_c,S_{As})-**76**, (S_c,R_{As})-**76** and (S_c,R_{As})-**78**] are not stable in solution and their corresponding free ketoarsine ligands decompose readily to give different arsenic–elimination reaction products depending on the reaction conditions employed [1-(3,4-dimethyl-2,4-cyclohexadienyl)-1-propanone and 1-(3,4-dimethylphenyl)-1-propanone, under argon and air reaction conditions, respectively].

4.4 Experimental Section

General: Similar to that described in section 2.4.

Endo-Cycloaddition Reaction: Isolation of (S_c,S_{As})-76 and (S_c,R_{As})-76

A mixture of complex (+)-**53** (0.78 g, 1.36 mmol) and excess ethyl vinyl ketone (0.35 g, 4.16 mmol) in dichloromethane (50 mL) were stirred for 1 month at room temperature. The solvent was removed under reduced pressure. The residue was purified by column chromatography on a silica column with dichloromethane–diethyl ether to give the diastereomeric neutral complexes (S_c,S_{As})-**76** and (S_c,R_{As})-**76** in 30 and 16% yield, respectively. Complex (S_c,S_{As})-**76** could be recrystallized from dichloromethane–diethyl ether as pale yellow crystals. $[\alpha]_D$ = +129.3° (*c* 0.6, CH_2Cl_2). Mp: 117–118 ºC. Anal. Calcd for $C_{35}H_{47}AsClNO_2Pd$: C, 57.5; H, 6.5; N, 1.9. Found: C, 57.2; H, 6.8; N, 2.0. ^{1}H NMR ($CDCl_3$, δ): 1.06 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_2CH_3), 1.40 (d, $^5J_{HH}$ = 0.8 Hz, 3H, =CCH_3), 1.74 (d, $^5J_{HH}$ = 1.0 Hz, 3H, =CCH_3), 1.92 (d, $^3J_{HH}$ = 6.3, 3H, CHCH_3), 2.15 (m, 1H, CHCH_2), 2.30 (m, 1H, CHCH_2), 2.62 (q, $^3J_{HH}$ = 7.4 Hz, 2H, CH_2CH$_3$), 2.71 (s, 3H, NCH_3), 2.91 (s, 3H, NCH_3), 3.16 (s, 1H, AsC*H*), 3.85 (d, $^3J_{HH}$ = 1.7 Hz, 1H, AsC*H*), 4.30 (q, $^3J_{HH}$ = 6.3, 1H, C*H*CH$_3$), 4.40 (m, 1H, CH_2C*H*), 7.00–7.83 (m, 11H, aromatics). ^{13}C NMR ($CDCl_3$, δ): 7.9, 15.0, 15.8, 23.9, 26.5, 34.8, 48.0, 49.5, 50.6, 51.8, 53.6, 72.8, 123.1, 124.2, 125.8, 126.0, 128.8, 129.0, 130.3, 131.3, 132.0, 132.2, 133.4, 134.8, 136.0, 146.5, 149.4, 209.8.

Exo-Cycloaddition Reaction: Isolation of (+)-78

A solution of (+)-**53** (0.82 g, 1.43 mmol) in dichloromethane (60 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (0.50 g) in water (1 mL). The

organic layer, after the removal of AgCl then washed with water (3 × 60 mL), dried ($MgSO_4$) and subsequently treated with excessive ethyl vinyl ketone (0.53 g, 6.30 mmol) for 1 month at room temperature. The solvent was removed from the reaction mixture and complex (+)-**78** was isolated by column chromatography on a silica column with dichloromethane–diethyl ether to give a yellow solid (0.21 g, 20%). $[\alpha]_D$ = +126.5° (*c* 0.7, CH_2Cl_2). Mp: 111–112 ºC. Anal. Calcd for $C_{31}H_{37}AsClNO_5Pd$: C, 51.7; H, 5.2; N 1.9. Found: C, 51.5; H, 5.0; N, 2.0. ^{1}H NMR (CD_2Cl_2, δ): 0.45 (t, $^3J_{HH}$ = 7.0 Hz, 3H, CH_2CH_3), 1.47 (s, 3H, =CCH_3), 1.77 (s, 3H, =CCH_3), 1.80 (d, $^3J_{HH}$ = 6.4, 3H, $CHCH_3$), 1.92 (dt, $^3J_{HH}$ = 2.0, $^3J_{HH}$ = 11.7 Hz, 1H, $CHCH_2$), 2.19 (m, 1H, $CHCH_2$), 2.30 (m, 1H, $CHCH_2$), 2.67 (s, 3H, NCH_3), 2.70 (q, $^3J_{HH}$ = 5.4, 1H, CH_2CH_3), 2.79 (s, 3H, NCH_3), 3.33 (dq, $^3J_{HH}$ = 5.4, $^2J_{HH}$ = 7.7 Hz, 1H, CH_2CH_3), 3.52 (s, 1H, AsC*H*), 3.61 (s, 1H, AsC*H*), 4.23 (q, $^3J_{HH}$ = 6.4, 1H, $CHCH_3$), 7.00–7.83 (m, 11H, aromatics). ^{13}C NMR (CD_2Cl_2, δ): 7.1, 14.5, 14.6, 22.8, 27.3, 34.0, 47.7, 49.4, 50.6, 51.9, 53.3, 72.9, 123.3, 123.9, 125.2, 125.7, 128.5, 128.6, 129.1, 129.7, 131.3, 133.3, 133.6, 135.3, 136.5, 137.7, 146.5, 149.7, 207.7.

CHAPTER 5

Asymmetric Synthesis of a Chiral Heterobidentate As–P Ligand Containing both As and P–Stereogenic Centres

5.1 Introduction

Optically active heterobidentate ligands bearing two or more stereogenic centers offer enormous potential as chiral auxiliaries in asymmetric synthesis. Their utility in such scenarios is attributed mainly to their ability to exercise stereoelectronic control over the reactions of coordinated substrates. Although many reports on such compounds containing two dissimilar asymmetric donor atoms have been reported for achiral and non-chiral phosphine based ligands (mainly involving P and N/O/S),[119] review of the literature reveals that very few studies involving development of a heterobidentate As*–P* ligand system has been reported so far. It is also noteworthy that the sole report on such a ligand system utilized a method that involved multi-step separation and resolution of the antipodes by the method of metal complexation. For example, the well known optical resolution of 1-(methylphenylarsino)-2-(methylphenylphosphino)benzene required the somewhat difficult separation of the (*R**,*R**) and (*R**,*S**) diastereoisomers prior to the individual resolution of the two racemic diasteoreoisomers.[60]

As part of our efforts to develop a more efficient procedure for achieving asymmetric ligand transformation reactions such as cycloaddition, hydroamination, hydrophosphination and hydroarsination, we have successfully employed an easily

accessible orthometallated chiral amine auxiliary as a chiral template to achieve all the above goals with a wide variety of substrates.[65,120] We have also utilized this chiral template for the generation of the As–P*[63a] as well as As*–P (chapter 2) systems wherein the chirality resides on either the phosphorus or arsenic centre as well as the carbon backbone. Interesting results including new insights into the influence of *trans* ligand in a novel arsine elimination process observed during the course of that study prompted us to attempt the challenging task of simultaneous generation of P and As chiral centers in an asymmetric manner thus providing a pathway for the development of a new class of compounds containing both As and P chiral centers associated with various functionalities. To our knowledge, no asymmetric synthesis involving the enantioselective generation of both As and P chiral centers has been reported in literature.

In this chapter, we report an efficient synthesis of a chiral heterobidentate As*–P* ligand *via* metal template promoted cycloaddition reaction between DMPA and phenyldivinylphosphine. The norbornene based ligand system thus obtained is also useful for the study of the intricacies of the stability factors with respect to the As–C bond cleavage observed in our earlier studies.

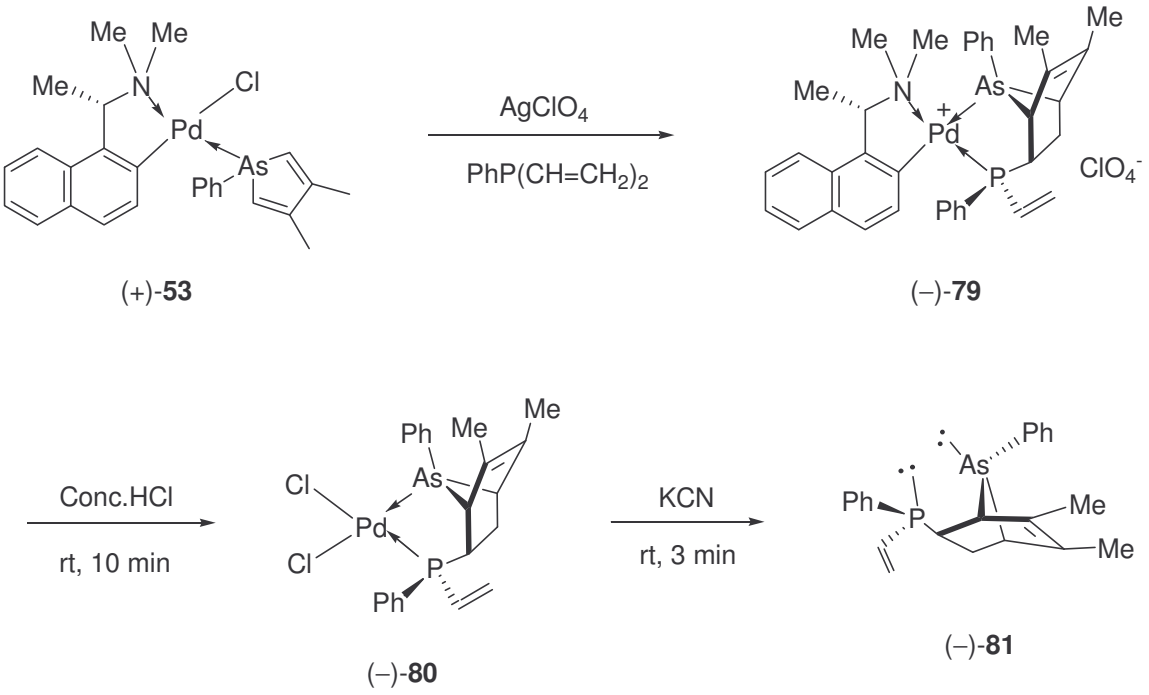
5.2 Results and Discussion

5.2.1 Asymmetric Cycloaddition Reaction between DMPA and Phenyldivinylphosphine

In contrast to those reported for their phosphorus analogues,[82,121] cycloaddition reactions involving cyclic arsines are relatively rare in literature.[122] The few reports

involving attempted cycloaddition reactions of uncoordinated arsoles generally utilized high temperature and produced a mixture of products with resultant low yield.[94,123] We had mentioned an alternative approach wherein the coordinated arsole can be activated to undergo asymmetric Diels–Alder reactions in the presence of a metal template. The metal template served the dual role of reaction promoter as well as chiral auxiliary during the course of the cycloaddition reaction. Considering the efficacy of that procedure, we decided to utilize the same methodology for the simultaneous generation of phosphorus and arsenic chiral centers in this novel [4+2] cycloaddition reaction between DMPA and phenyldivinylphosphine.

Treatment of the chloro complex (+)**-53** with silver perchlorate yielded the intermediate cationic perchlorate species in essentially quantitative yield.[124] This highly reactive species was not isolated and was treated directly with a stoichiometric amount of phenyldivinylphosphine (Scheme 5.1). The Diels–Alder reaction was found to be completed in an hour at room temperature. Prior to purification, the $^{31}P\{^{1}H\}$ NMR spectrum of the crude Diels–Alder reaction product in $CDCl_3$ exhibited two singlets at δ 49.0 and 48.6 in the ratio 1:3 respectively. The major diasteoreomer (–)**-79** could be separated by column chromatography as yellow solid in 56% yield, $[\alpha]_D$ –40.0° (*c* 0.6, CH_2Cl_2). Attempts to crystallize the complex as single crystals suitable for X-ray crystallographic studies were unsuccessful. The chiral amine auxiliary on (–)**-79** could however be removed from the metal complex chemoselectively and efficiently using concentrated hydrochloric acid. The resultant neutral dichloro complex (–)**-80** was thus obtained as pale yellow needles in 72% yield, $[\alpha]_D$ –146.7° (*c* 0.6, CH_2Cl_2).



Scheme 5.1

The X–ray structural analysis of (–)**-80** confirmed that the desired cycloadduct was formed with the norbornene skeletal framework coordinated to the Pd center through both As and P donors. The study also confirmed that the absolute configurations of the five new chiral centers formed at As(1), P(1), C(7), C(12) and C(14) are *R*, *S*, *R*, *R* and *S,* respectively (Figure 5.1). Selected bond lengths and angles are listed in Table 5.1. In complex (–)**-80** the geometry at Pd is slightly distorted square-planar with angles at Pd in the ranges 82.7(1)–95.8(1) and 171.6(1)–174.8(1)°, the smallest of these former bond angles being associated with the bite of the novel As–P ligand. The Pd–As [2.320(1) Å] and Pd–P [2.246(1) Å] distances are unexceptional. The two Pd–Cl distances are similar [2.366(1) and 2.360(1) Å].

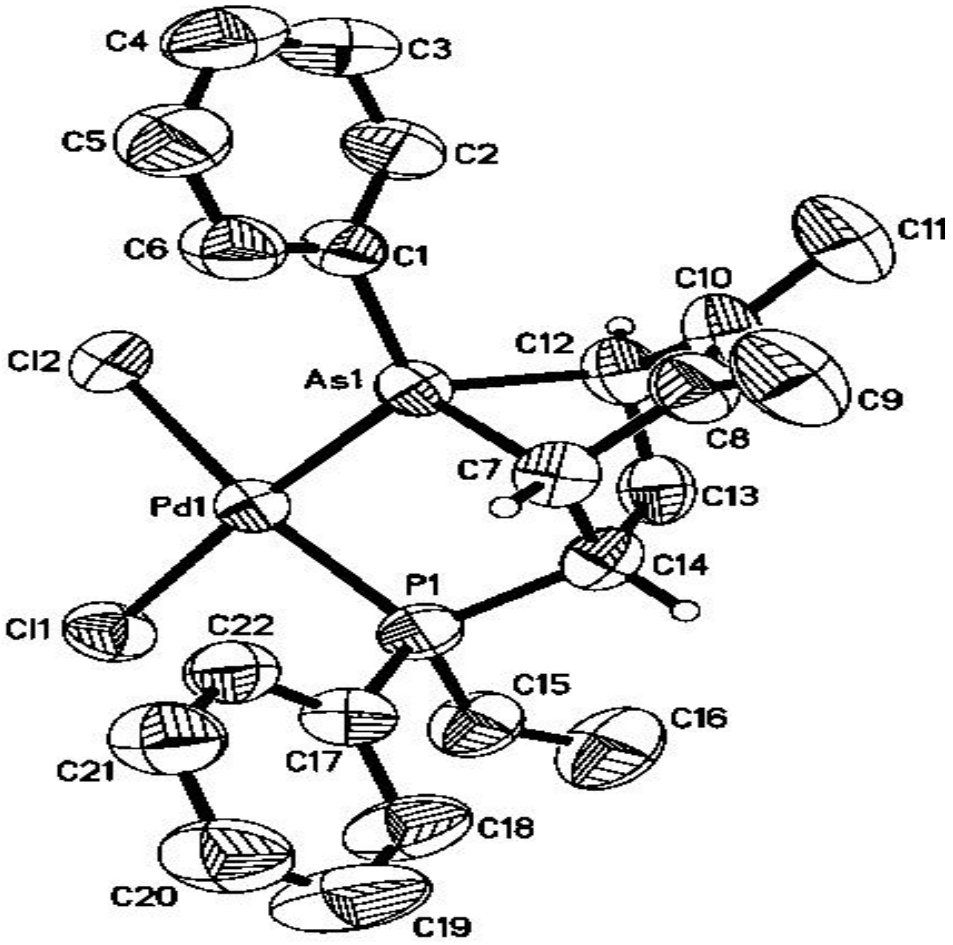


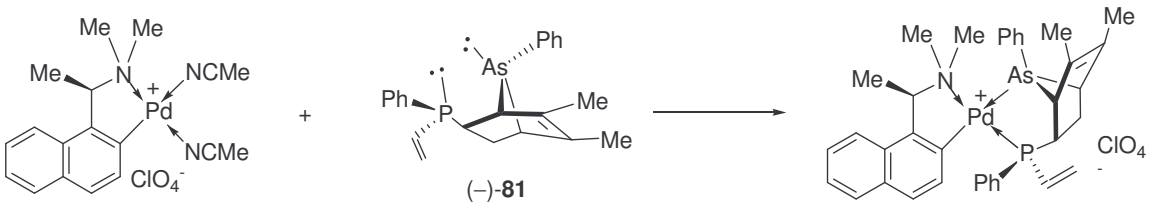
Figure 5.1 Molecular structure of dichloro complex (–)-**80**

Treatment of the dichloro complex (–)**-80** with aqueous potassium cyanide liberated the optically pure heterobidentate arsanorbornene ligand (–)**-81** as a white solid in 91% yield, $[\alpha]_D$ –40.8° (*c* 1.3, CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum of this liberated chiral free ligand in $CDCl_3$ exhibited a sharp singlet at δ –13.3. Owing to the configurational instability of the uncoordinated bridgehead arsenic stereogenic center, the liberated ligand was re-coordinated immediately to other selected metal ions. When (–)**-81** was coordinated to the enantiomeric bis(acetonitrile)[(*R*)-1-[1- (dimethylamino)ethyl]-2-naphthalenyl-*C*,*N*] palladium(II) perchlorate (Scheme 5.2), the $^{31}P\{^1H\}$ NMR

Table 5.1 Selected bond lengths (Å) and angles (°) for (–)-**80**

Pd(1)–Cl(1)	2.366(1)	Pd(1)–Cl(2)	2.360(1)
Pd(1)–As(1)	2.320(1)	Pd(1)–P(1)	2.246(1)
As(1)–C(12)	1.971(4)	As(1)–C(7)	1.974(4)
P(1)–C(15)	1.801(5)	P(1)–C(14)	1.853(5)
C(7)–C(8)	1.521(6)	C(7)–C(14)	1.556(6)
C(8)–C(10)	1.336(6)	C(10)–C(12)	1.514(6)
C(12)–C(13)	1.548(7)	C(13)–C(14)	1.554(6)
C(15)–C(16)	1.289(8)		
P(1)–Pd(1)–As(1)	82.7(1)	P(1)–Pd(1)–Cl(2)	171.6(1)
As(1)–Pd(1)–Cl(2)	89.4(3)	P(1)–Pd(1)–Cl(1)	92.1(1)
As(1)–Pd(1)–Cl(1)	174.8(1)	Cl(2)–Pd(1)–Cl(1)	95.8(1)
C(1)–As(1)–C(12)	110.4(2)	C(1)–As(1)–C(7)	111.5(2)
C(12)–As(1)–C(7)	77.4(2)	C(1)–As(1)–Pd(1)	124.1(1)
C(12)–As(1)–Pd(1)	115.0(1)	C(7)–As(1)–Pd(1)	108.9(1)
C(14)–P(1)–Pd(1)	107.1(1)	C(15)–P(1)–C(14)	107.5(2)
C(8)–C(7)–C(14)	111.9(3)	C(8)–C(7)–As(1)	100.9(3)
C(14)–C(7)–As(1)	94.9(2)	C(10)–C(8)–C(7)	111.7(4)
C(8)–C(10)–C(12)	112.0(4)	C(10)–C(12)–C(13)	107.4(4)
C(10)–C(12)–As(1)	100.6(3)	C(13)–C(12)–As(1)	98.9(3)
C(12)–C(13)–C(14)	107.6(3)	C(13)–C(14)–C(7)	106.2(3)

spectrum of the crude product exhibited only one singlet at δ 46.5, which is attributed to the diastereomer that was not formed in the original cycloaddition reaction. The signal due to the original major isomer was not detected thus confirming the optical purity of the isolated ligand.

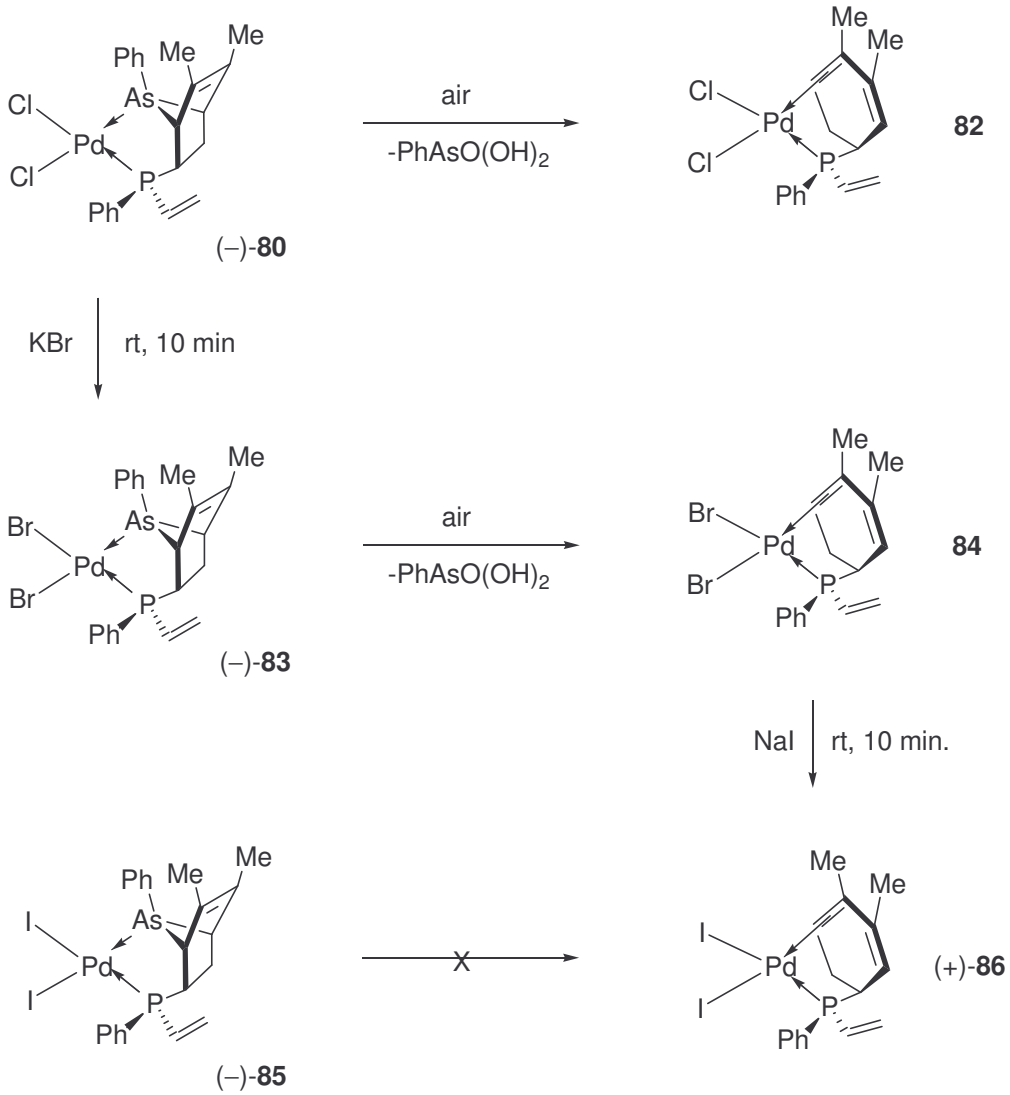


Scheme 5.2

5.2.2 Arsenic–Elimination Reaction

As mentioned in previous chapters, we had observed an interesting arsenic elimination process with the similar heterobidentate arsanorbornene (As–P) palladium complexes obtained from the cycloaddition reaction between DMPA and diphenylvinylphosphine. The nature of the *trans* ligand in these complexes appeared to affect the rate of the elimination process. These eliminations had led to the generation of an interesting 1-(diphenylphosphino)-3,4-dimethyl-2,4-cyclohexadiene ligand which coordinated to Pd *via* its phosphorus donor and the η^2-C-C bond. The present reaction allowed an opportunity to study the various factors affecting this process in further detail as well as the opportunity to develop such ligand systems further with introduction of additional chirality on the phosphine donor atoms. Previous work (chapter 2) has given some indication that a concerted mechanism exists wherein two As–C bonds in the

norbornene bridgehead system breaks along with the formation of the η^2-Pd coordination during the course of such elimination reactions.



Scheme 5.3

Unlike in the case of our previous work, the complex (–)-**80** was found to convert with difficulty into the possible analogous retrodiene complex **82** (Scheme 5.3). From the analysis of the $^{31}P\{^1H\}$ NMR spectrum of (–)-**80** in $CDCl_3$, we found that its $^{31}P\{^1H\}$

NMR value shifted from δ 34.0 to 135.9 over a period of 17 days at room temperature indicating the formation of complex **82**. Further evidence for the formation of the complex was obtained from the ^{1}H NMR spectrum in which we observed the two new double bond hydrogen signals of the retrodiene complex at δ 5.6 (doublet) and 6.0 (singlet), respectively. Another proof was obtained by the isolation of phenylarsonic acid from the reaction system which confirmed that the arsenic elimination process has indeed occurred.

The dichloro complex (–)-**80** was treated with potassium bromide for 10 min at room temperature and the analogous dibromo complex (–)**-83** was obtained as yellow solid in 90% yield, $[\alpha]_D$ –146.7° (*c* 0.6, CH_2Cl_2). The $^{31}P\{^{1}H\}$ NMR spectrum exhibited only one signal at δ 35.0 indicating the absence of any side reaction. This complex was subsequently recrystallized with chloroform-diethyl ether to give the product as yellow needles. The molecular structure of (–)**-83** was confirmed by X-ray crystallography (Figure 5.2). Selected bond lengths and angles are listed in Table 5.2. Unfortunately, the arsenic elimination product arising from complex (–)-**83**, *viz.* complex **84**, could not be isolated by fractional crystallization or by column chromatography using a wide range of solvent systems. Finally, the dichloro complex (–)**-80** was converted into the analogous diiodo derivative (–)**-85** by treatment of the dichloro complex with sodium iodide. The diiodo complex was isolated as yellow solid in 95% yield, $[\alpha]_D$ –97.8° (*c* 0.5, CH_2Cl_2). Similar to the reported analogous diphenylphosphino-substituted asymmetrical heterobidentate arsanorbornene complex [(As–P)PdI_2], (–)-**52**, the arsenic elimination reaction in this case did not occur when the diiodo complex (–)**-85** was dissolved in solution. On the contrary the complex decomposed rapidly in solution. But interestingly,

the retrodiene diiodo complex (+)-**86** was subsequently obtained *via* an alternate pathway. This involved treatment of complex **84** with sodium iodide for 10 min. at room temperature. The complex (+)-**86** thus obtained was isolated by column chromatography in 55% yield, $[\alpha]_D$ +756.7° (*c* 0.3, CH_2Cl_2). It is noteworthy that the rate of arsenic elimination reaction in (–)-**80** apparently decelerates relative to the analogous complex obtained *via* cycloaddition between diphenylvinylphosphine and DMPA, (–)-**45**, in our earlier studies. The reason can be attributed to the fact that the two As–C bonds [1.971(4) and 1.974(4) Å] within the arsanorbornene of (–)-**80** are significantly more symmetrical

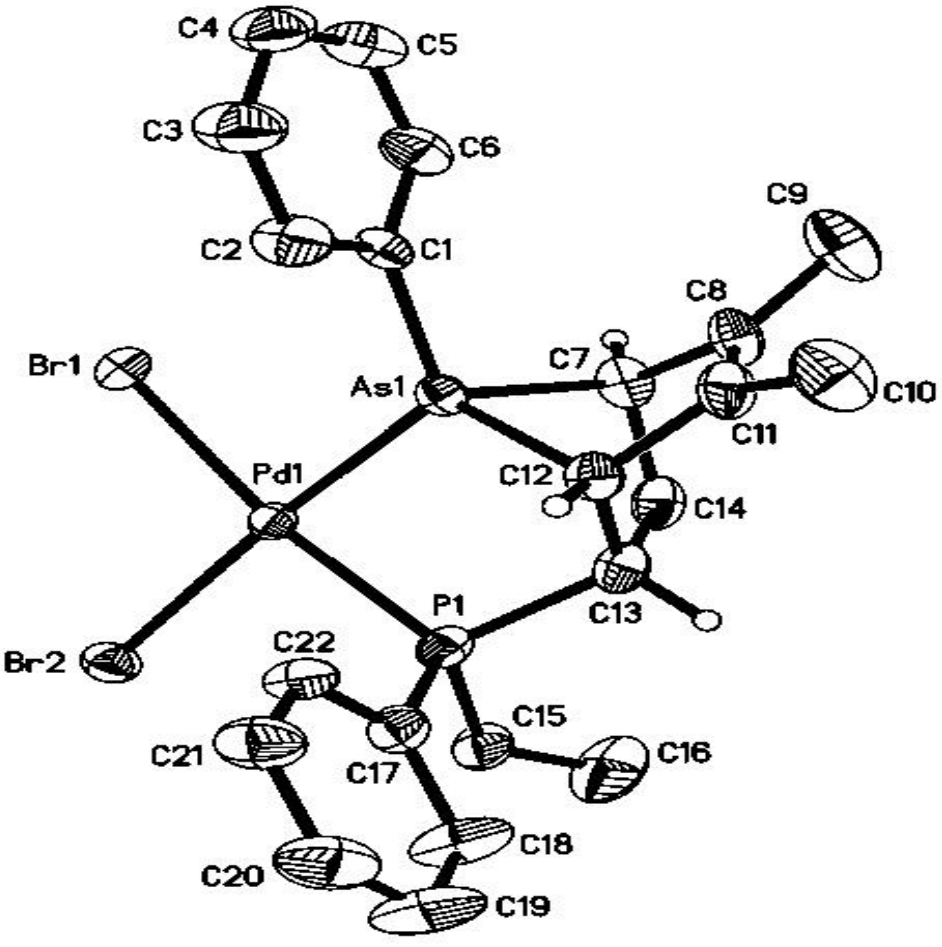


Figure 5.2 Molecular structure of dibromo complex (–)-**83**

Table 5.2 Selected bond lengths (Å) and angles (°) for (–)-**83**

Pd(1)–Br(1)	2.481(1)	Pd(1)–Br(2)	2.492(1)
Pd(1)–As(1)	2.328(1)	Pd(1)–P(1)	2.256(1)
As(1)–C(12)	1.973(4)	As(1)–C(7)	1.982(5)
P(1)–C(15)	1.797(5)	P(1)–C(13)	1.853(5)
C(7)–C(8)	1.528(6)	C(7)–C(14)	1.540(7)
C(8)–C(11)	1.338(8)	C(11)–C(12)	1.513(7)
C(12)–C(13)	1.556(7)	C(13)–C(14)	1.577(8)
C(15)–C(16)	1.307(8)		
P(1)–Pd(1)–As(1)	82.8(1)	P(1)–Pd(1)–Br(1)	171.2(1)
As(1)–Pd(1)–Br(1)	89.1(1)	P(1)–Pd(1)–Br(2)	92.8(1)
As(1)–Pd(1)–Br(2)	175.4(1)	Br(1)–Pd(1)–Br(2)	95.4(1)
C(1)–As(1)–C(12)	112.2(2)	C(1)–As(1)–C(7)	110.8(2)
C(12)–As(1)–C(7)	77.5(2)	C(1)–As(1)–Pd(1)	123.3(1)
C(12)–As(1)–Pd(1)	108.8(1)	C(7)–As(1)–Pd(1)	115.0(1)
C(13)–P(1)–Pd(1)	106.6(2)	C(15)–P(1)–C(13)	107.5(2)
C(8)–C(7)–C(14)	107.4(4)	C(8)–C(7)–As(1)	99.7(3)
C(14)–C(7)–As(1)	99.4(3)	C(11)–C(8)–C(7)	112.1(5)
C(8)–C(11)–C(12)	111.7(4)	C(11)–C(12)–C(13)	111.7(4)
C(11)–C(12)–As(1)	101.8(3)	C(13)–C(12)–As(1)	94.8(3)
C(12)–C(13)–C(14)	106.0(4)	C(7)–C(14)–C(13)	107.1(4)

than that of the analogue [1.961(3) and 1.980(3) Å]. The deviance between the two As–C bond distances in the latter (0.019 Å) is much bigger than that of the former (0.003 Å), thus resulting in an enhanced configurational instability in the analogue compared to that of (–)**-80**.

5.3 Conclusions

In conclusion, we have synthesized a new chiral heterobidentate As–P ligand containing both As and P–stereogenic centers *via* a facile metal template promoted cycloaddition reaction. This has provided us with an avenue for the synthesis of a new class of heterobidentate ligand system which can incorporate various functionalities. We have also obtained a better understanding of the arsenic elimination process occurring in such systems leading to the formation of the novel chiral phosphine–olefin ligand. It needs to be noted that such chiral phosphine–olefin systems themselves are assuming importance as "spectator" ligands in catalysis.[97]

5.4 Experimental Section

General: Similar to that described in section 2.4. Phenyldivinylphosphine[105] was prepared following the literature procedures.

Cycloaddition Reaction: Preparation of Complex (–)-79

A solution of (+)-**53** (0.67 g, 1.17 mmol) in dichloromethane (60 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (0.39 g) in water (1 mL). The organic layer, after the removal of AgCl then washed with water (3 × 60 mL), dried ($MgSO_4$) and subsequently treated with phenyldivinylphosphine (0.19 g, 1.17 mmol) at room temperature for 1h. The solvent was removed from the reaction mixture and the complex (–)-**79** was isolated by column chromatography on a silica column with dichloromethane-diethyl ether, to give a yellow solid (0.52 g, 56%). $[\alpha]_D$ = –40.0° (*c* 0.6, CH_2Cl_2). Mp: 166–167 ºC. Anal. Calcd for $C_{36}H_{40}AsClNO_4PPd$: C, 54.2; H, 5.0; N, 1.8. Found: C, 53.8; H, 5.2; N, 1.8. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 48.6. ^1H NMR ($CDCl_3$, δ): 1.33 (s, 3H, =C*CH*$_3$), 1.64 (s, 3H, =C*CH*$_3$), 1.95 (d, $^3J_{HH}$ = 6.1 Hz, 3H, CH*CH*$_3$), 2.14 (ddd, $^3J_{HH}$ = 20.3, $^2J_{HH}$ = 9.8 Hz, $^3J_{HH}$ = 3.7 Hz, 1H, CH*CH*$_2$), 2.61 (s, 1H, As*CH*), 2.68 (m, 1H, CH*CH*$_2$), 2.75 (s, 3H, N*CH*$_3$), 2.85 (m, 1H, P*CH*), 2.89 (d, $^4J_{PH}$ = 2.6 Hz, 3H, N*CH*$_3$), 3.77 (s, 1H, As*CH*), 4.42 (qn, $^3J_{HH}$ = $^4J_{PH}$= 5.9 Hz, 1H, *CH*CH$_3$), 6.15 (dd, $^3J_{PH}$ = 21.9, $^3J_{HH}$ = 4.2 Hz, 1H, =*CH*$_2$), 6.24 (dd, $^3J_{PH}$ = 34.7, $^3J_{HH}$ = 11.9 Hz,1H, =*CH*$_2$), 6.72 (ddd, $^2J_{PH}$ = 16.4, $^3J_{HH}$ = 12.0, $^3J_{HH}$ = 4.4 Hz, 1H, =*CH*), 6.80–8.15 (m, 16H, aromatics).

Removal of Chiral Auxiliary: Synthesis of Dichloro Complex (–)-80

The complex (–)-**79** (0.21 g, 0.26 mmol) was dissolved in dichloromethane (60

mL) and treated with excess concentrated hydrochloric acid (2 mL) at room temperature for 10 min. The mixture was then washed with water (3 × 60 mL), dried ($MgSO_4$), and subsequently recrystallized from chloroform-diethyl ether as pale yellow needle crystals (–)-**80** (0.13 g, 72%). $[\alpha]_D$ = –146.7° (*c* 0.6, CH_2Cl_2). Mp: 191–192 ºC. Anal. Calcd for $C_{23}H_{25}AsCl_5PPd$: C, 40.0; H, 3.7. Found: C, 39.9; H, 3.6. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 34.0. ^1H NMR ($CDCl_3$, δ): 1.56 (s, 3H, =C*CH*$_3$), 1.67 (d, $^5J_{PH}$ = 0.9 Hz, 3H, =C*CH*$_3$), 2.12 (ddd, $^3J_{HH}$ = 21.6, $^2J_{HH}$ = 10.2 Hz, $^3J_{HH}$ = 3.1 Hz, 1H, CH*CH*$_2$), 2.68 (m, 1H, CH*CH*$_2$), 2.78 (m, 1H, P*CH*), 2.86 (s, 1H, As*CH*), 3.54 (d, $^3J_{HH}$ = 3.0 Hz, 1H, As*CH*), 6.22 (dd, $^3J_{PH}$ = 20.9, $^3J_{HH}$ = 18.4 Hz, 1H, =*CH*$_2$), 6.33 (dd, $^3J_{PH}$ = 31.4, $^3J_{HH}$ = 12.4 Hz,1H, =*CH*$_2$), 6.83 (ddd, $^2J_{PH}$ = 23.0, $^3J_{HH}$ = 18.3, $^3J_{HH}$ = 12.4 Hz, 1H, =*CH*), 7.39–8.11 (m, 10H, aromatics).

Liberation of the As–P Ligand (–)-81

A solution of (–)-**80** (0.10 g, 0.14 mmol) in dichloromethane (20 mL) was stirred vigorously with a saturated aqueous solution of potassium cyanide (1.0 g) for 3 min. The organic layer was separated, then washed with water (3 × 20 mL) and dried ($MgSO_4$). Upon removal of the solvent, the free ligand (–)-**81** was obtained as an air-sensitive white solid (0.05 g, 91%). $[\alpha]_D$ = –40.8° (*c* 1.3, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): –13.3.

Preparation of the Dibromo Complex (–)-83

The solution of (–)-**80** (0.07 g, 0.10 mmol) in dichloromethane (50 mL) was added to potassium bromide (0.05 g) in acetone (50 mL) and water (10 mL) and stirred vigorously for 10 min. The organic solvents were removed and the residue was extracted

with dichloromethane and water, dried with $MgSO_4$, Removal of solvent gave (–)-**83** as a solid, which was then recrystallized from chloroform–diethyl ether to give the product as yellow needle crystals (0.07 g, 90%). $[\alpha]_D$ = –146.7° (*c* 0.6, CH_2Cl_2). Mp: 188–189 ºC. Anal. Calcd for $C_{23}H_{25}AsBr_2Cl_3PPd$: C, 35.4; H, 3.2. Found: C, 35.9; H, 3.4. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 35.0. ^1H NMR (CD_2Cl_2, δ): 1.47 (s, 3H, =C*CH*$_3$), 1.65 (d, $^5J_{PH}$ = 1.0 Hz, 3H, =C*CH*$_3$), 2.15 (ddd, $^3J_{HH}$ = 22.3, $^2J_{HH}$ = 10.6 Hz, $^3J_{HH}$ = 3.3 Hz, 1H, CH*CH*$_2$), 2.68 (m, 1H, CH*CH*$_2$), 2.76 (m, 1H, P*CH*), 2.87 (s, 1H, As*CH*), 3.59 (d, $^3J_{HH}$ = 3.2 Hz, 1H, As*CH*), 6.17 (dd, $^3J_{PH}$ = 20.4, $^3J_{HH}$ = 18.5 Hz, 1H, =*CH*$_2$), 6.33 (dd, $^3J_{PH}$ = 42.3, $^3J_{HH}$ = 12.4 Hz,1H, =*CH*$_2$), 6.92 (ddd, $^2J_{PH}$ = 23.8, $^3J_{HH}$ = 18.5, $^3J_{HH}$ = 12.4 Hz, 1H, =*CH*), 7.45–8.06 (m, 10H, aromatics).

Synthesis of the Diiodo Complex (–)-85

The solution of (–)-**80** (0.05 g, 0.07 mmol) in dichloromethane (30 mL) was mixed with sodium iodide (0.1 g) in acetone (30 mL) and stirred vigorously for 10 min. The solvents were removed and the residue was extracted with dichloromethane. The solvent was removed from the reaction mixture and the complex (–)**-85** was isolated by column chromatography on a silica column with dichloromethane to give a yellow solid (0.05 g, 95%). $[\alpha]_D$ = –97.8° (*c* 0.5, CH_2Cl_2). Mp: 178–179 ºC. Anal. Calcd for $C_{22}H_{24}AsI_2PPd$: C, 35.0; H, 3.2. Found: C, 34.6; H, 3.0. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 34.8. ^1H NMR ($CDCl_3$, δ): 1.45 (s, 3H, =C*CH*$_3$), 1.65 (d, $^5J_{PH}$ = 0.8 Hz, 3H, =C*CH*$_3$), 2.12 (ddd, $^3J_{HH}$ = 21.6, $^2J_{HH}$ = 9.6 Hz, $^3J_{HH}$ = 3.4 Hz, 1H, CH*CH*$_2$), 2.61 (m, 1H, P*CH*), 2.78 (m, 1H, CH*CH*$_2$), 2.75 (d, $^3J_{PH}$ = 1.9 Hz, 1H, As*CH*), 3.54 (d, $^3J_{HH}$ = 2.9 Hz, 1H, As*CH*), 6.06 (dd, $^3J_{PH}$ = 19.0, $^3J_{HH}$ = 18.8 Hz, 1H, =*CH*$_2$), 6.24 (dd, $^3J_{PH}$ = 40.7, $^3J_{HH}$ = 12.4 Hz,1H, =*CH*$_2$), 7.05 (ddd,

$^{2}J_{PH}$ = 24.3, $^{3}J_{HH}$ = 18.4, $^{3}J_{HH}$ = 12.4 Hz, 1H, =*CH*), 7.40–8.01 (m, 10H, aromatics).

Arsenic–Elimination Reaction: Isolation of Complex (+)-86

The complex (–)-**83** (0.01 g, 0.013 mmol) was dissolved in dichloromethane (40 mL) and allowed to stir at room temperature for 8 days. Then sodium iodide (0.05 g) in acetone (40 mL) was added and stirred vigorously for 10 min. The solvents were removed and the residue was extracted with dichloromethane. The complex (+)-**86** was isolated by column chromatography on a silica column with dichloromethane to give a solid (4 mg, 52%). $[\alpha]_D$ = +756.7° (*c* 0.3, CH_2Cl_2). Mp: 126–127 ºC. Anal. Calcd for $C_{16}H_{19}I_2PPd$: C, 31.9; H, 3.2. Found: C, 32.0; H, 3.3. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, δ): 130.9. ^{1}H NMR ($CDCl_3$, δ): 1.84 (s, 3H, =C*CH*$_3$), 2.26 (m, 2H, CH*CH*$_2$), 2.51 (s, 3H, =C*CH*$_3$), 2.97 (s, 1H, P*CH*), 5.56 (d, $^{3}J_{HH}$ = 6.6 Hz, 1H, =*CH*), 6.18 (m, 1H, =*CH*), 6.30 (m, 2H, =*CH*$_2$), 6.69 (m, 1H, =*CH*), 7.40–7.69 (m, 5H, aromatics).

CHAPTER 6

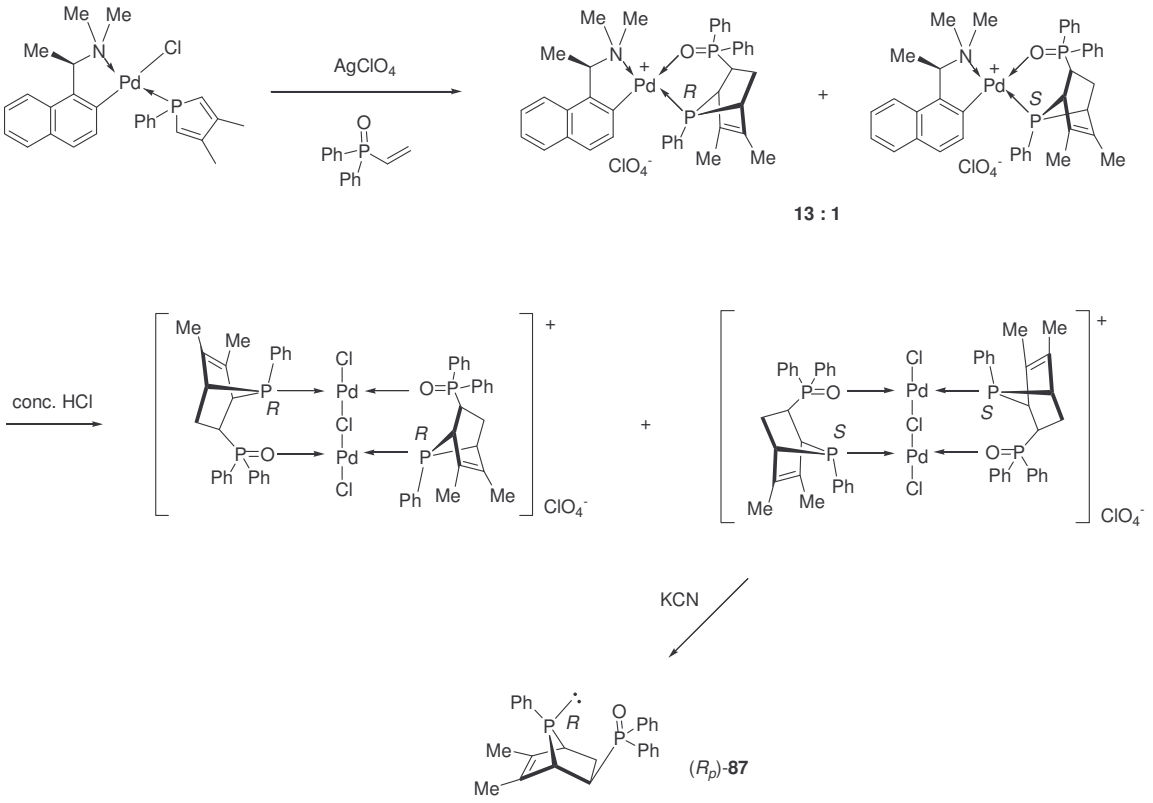
Metal Effects on Asymmetric Syntheses of As–P=O and As–P=S Hemilabile Ligands

6.1 Introduction

It is well known that enantiomerically pure phosphines such as BINAP are very important chiral auxiliaries in asymmetric catalysis.[125-127] Similarly, their corresponding oxides and sulfides also are very useful for asymmetric syntheses and catalysis.[128] For instance, due to the presence of both the soft (P) and hard (O) Lewis base centers on one molecule, the hemilabile ligand[112b,114b,129] bis(phosphine) monoxide can stabilize a lot of transition metals in various oxidation state; at the same time, its weak chelation with metals can easily generate reactive, coordinatively unsaturated species which provides low activation energy paths to various transformations at the metal center. A number of bis(phosphine) monoxides have shown widespread applications in the field of catalysis such as carbonylation of alcohols, hydroformylation of olefins, etc.[112a] In a quiet recent example Charette *et al.* found the chiral Me-DuPHOS monoxide to be very effective ligand in the enantioselective copper-catalyzed addition of dialkylzinc to *N*-phosphinoylimines mostly in more than 90% yield and 90% *ee*. The resulting chiral amines are very important synthons for the preparation of chiral drugs.[130]

There are two general synthetic routes for the preparation of bis(phosphine) monoxides. One involves two phosphorus units coming together to form a molecule. The other approach is based on selective oxidation of one phosphorus atom in readily

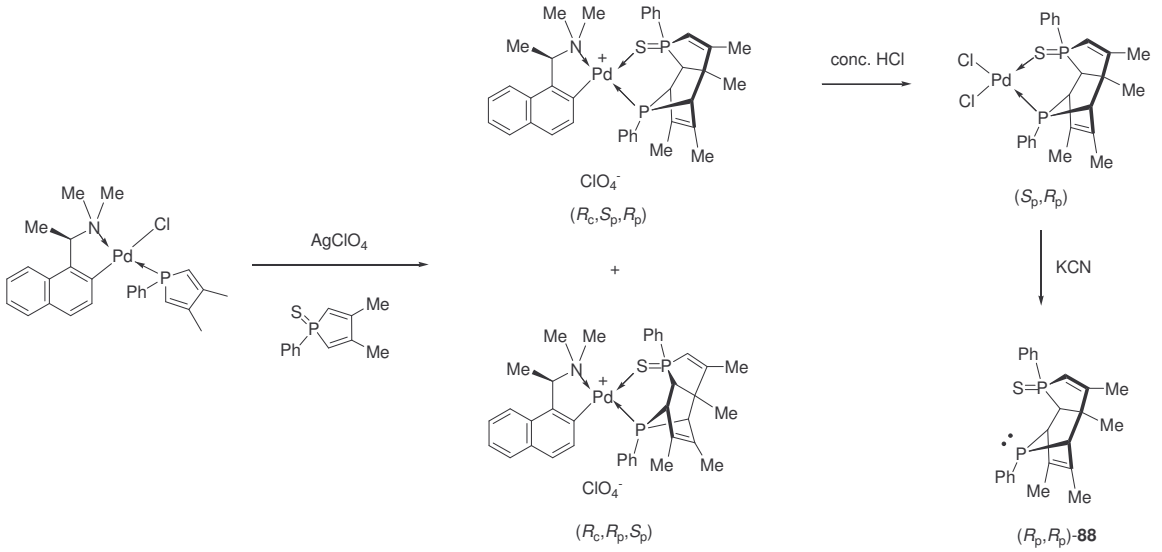
available bidentate tertiary organic phosphines.[112a] Recently, our group has reported a simple and efficient approach for the preparation of an optically pure bis(phosphine) monoxide from an organopalladium complex promoted asymmetric Diels–Alder reaction between DMPP and diphenylvinylphosphine oxide. The resulting P-chiral phosphanorbornene was obtained as a P–P=O bidentate ligand chelate on the palladium center. The (R_p)-**87** could be liberated from the dichloro palladium complex as highly air-sensitive oil by treated with aqueous potassium cyanide (Scheme 6.1).[131]



Scheme 6.1

Our group also reported the synthesis of P–P=S bidentate ligand (R_p,R_p)-**88** wherein the ligand chelated through P and S atoms. The asymmetric [4+2] Diels–Alder reaction

involving DMPP as the cyclic diene and its P-sulfide analogue DMPP=S (3,4-dimethyl-1-phenylphosphine sulfide) as the dienophile was carried out by utilizing the palladium template complex containing *ortho*-metalated (*R*)-(1-(dimethylamino)ethyl)naphthalene as the chiral auxiliary (Scheme 6.2). The reaction proceeded regiospecifically and stereoselectively giving corresponding phosphanorbornene P–P=S ligand as the major product.[120a]



Scheme 6.2

Compared to the phosphorus based hemilabile ligands, especially bis(phosphine) mono-oxide or sulfide bidentate ligands, the arsenic based hemilabile ligands are rare.[112b] To our knowledge, no asymmetric synthesis of the enantiomerically pure As–P=O and As–P=S hetero-bidentate ligands have been reported hitherto. So we sought to utilize the above mentioned synthetic strategy for P–P=O ligand on the syntheses of As–P=O and As–P=S hetero-bidentate ligands. In this chapter, we report the preparation of optically pure As(III)–P=O(V) and As(III)–P=S (V) hetero-bidentate ligands by means of

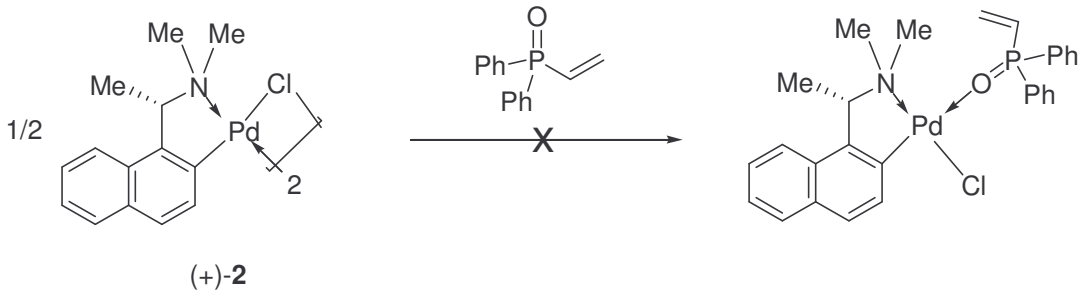
asymmetric cycloaddition reaction between DMPA and diphenylvinylphosphine oxide and sulfide.

6.2 Results and Discussion

6.2.1 Asymmetric Cycloaddition Reaction between DMPA and Diphenylvinylphosphine Oxide

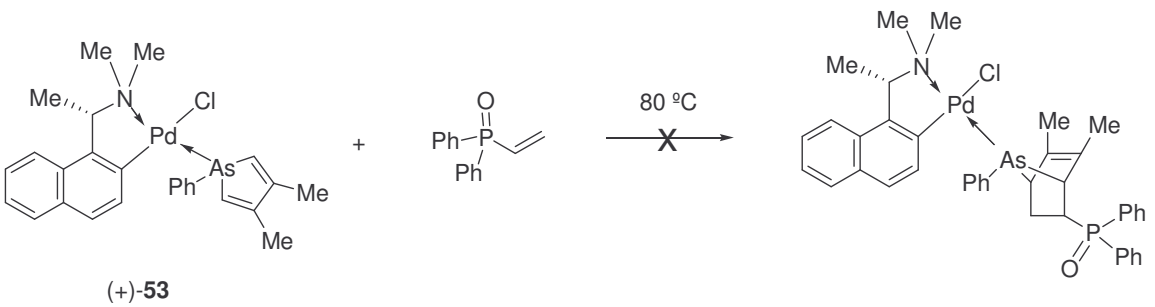
6.2.1.1 Asymmetric Cycloaddition between DMPA and Diphenylvinylphosphine Oxide Promoted by Palladium Complex

Due to the weak coordinative ability, diphenylvinylphosphine oxide could not split the chloro bridge of dimeric palladium complex (+)-**2** (Scheme 6.3).



Scheme 6.3

Therefore, the coordinated cyclic diene complex (+)-**53** was used as the starting material. Interestingly diphenylvinylphosphine oxide is not a chemically reactive dienophile in this reaction because no reaction was observed when the neutral complex (+)-**53** was directly treated with diphenylvinylphosphine oxide, despite strong reaction conditions (80 ºC) being employed (Scheme 6.4).

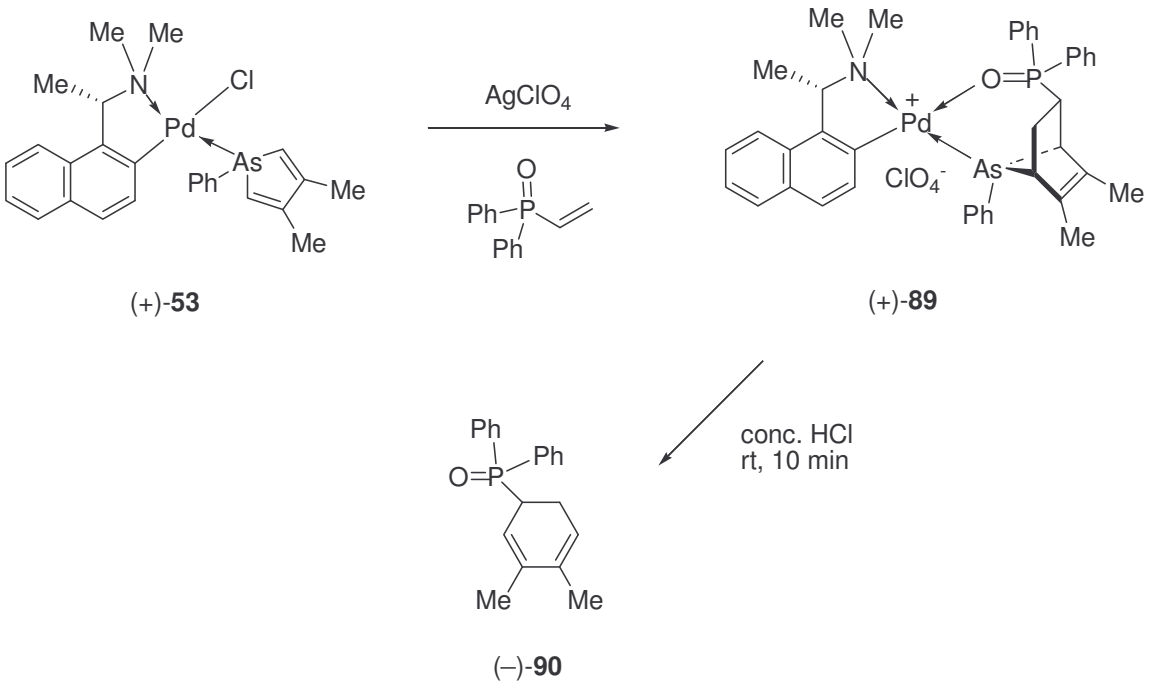


Scheme 6.4

However, when the complex (+)-**53** was treated with aqueous silver perchlorate in dichloromethane, the resultant perchlorate complex is chemically reactive toward diphenylvinylphosphine oxide. Temperature is an important factor in this Diels–Alder reaction. For example, the reaction took 3 months to complete at room temperature. However, when it was carried out at higher temperature 60 ºC, it was completed in 6 days. The $^{31}P\{^{1}H\}$ NMR spectrum of the crude cycloaddition reaction in $CDCl_3$ exhibited only one singlet at δ 49.5 (Scheme 6.5). The cycloadduct (+)-**89** was isolated by column chromatography on a silica column with dichloromethane-diethyl ether to give a pale yellow solid in 76% yield, $[\alpha]_D$ +83.8° (*c* 0.8, CH_2Cl_2). Attempts to obtain crystals suitable for single-crystal X-ray determination were not successful.

In order to confirm the absolute configuration of the generated cycloadduct, we sought to get the corresponding dichloro complex. When the complex (+)-**89** was treated with concentrated hydrochloric acid for 10 min at room temperature, the $^{31}P\{^{1}H\}$ NMR spectrum of the crude mixture in $CDCl_3$ exhibited one singlet at δ 34.0. The compound was isolated by column chromatography on a silica column with dichloromethane-acetone in 67% yield, $[\alpha]_D$ –72.3° (*c* 0.1, CH_2Cl_2). However, from its ^{1}H and ^{13}C NMR spectra and other methods of characterisation, it was evident that it was not the desired

dichloro complex, and was in fact the arsenic–elimination reaction product, (3,4-dimethyl-2,4-cyclohexadienyl) diphenylphosphine oxide (–)-**90**. The possible reason is that first the naphthylamine was removed chemoselectively to give the dichloro complex. Due to the fact that the resulting dichloro complex is unstable, an arsenic elimination occurred and the resultant intermediate (with η^2 and oxygen coordinated on Pd similar to (+)-**48** discussed earlier) dissociated to produce the organic compound (–)-**90** and other unidentified side products.



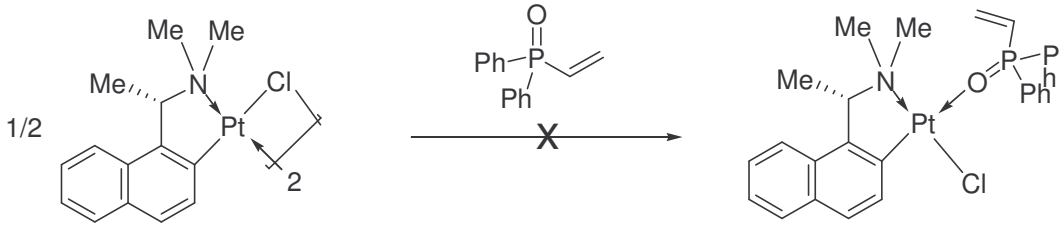
(+)-**53** (+)-**89** (–)-**90**

Scheme 6.5

6.2.1.2 Metal Ion Effect: Asymmetric Cycloaddition between DMPA and Diphenylvinylphosphine Oxide Promoted by Platinum Complex

As aforementioned, the Diels–Alder reaction between DMPA and

diphenylvinylphosphine oxide promoted by the palladium complex did not produce the desired enantiomerically pure As–P=O ligand. However we found that the metal ion has a considerate effect on this reaction, especially on the stability of the product complex. When the metal was changed from palladium to platinum, the same coordination properties were observed, that is, the diphenylvinylphosphine oxide cannot split the chloro bridges in the chiral dimeric platinum complex (+)-**91** to give the corresponding monomeric neutral platinum complex (Scheme 6.6).



(+)-**91**

Scheme 6.6

However, DMPA is a powerful ligand which readily splits the chloro bridges of the platinum complex (+)-**91** regiospecifically to give the neutral complex (+)-**92** in 54% yield, $[\alpha]_D$ +140.0° (*c* 0.6, CH_2Cl_2) (Scheme 6.7). The chloro complex was recrystallized with chloroform–*n*-hexane–diethyl ether to give yellow crystals. The molecular structure and absolute configuration of (+)-**92** were determined by the single-crystal X-ray structural analysis (Figure 6.1). As in the palladium complex (+)-**53**, the bridgehead arsenic in (+)-**92** is *trans* to NMe_2 group. The geometry at the platinum in (+)-**92** is the distorted square planar with angles at platinum in the range of 80.6(1)–96.9(1) and 173.8(1)–177.1(1)°. Selected bond lengths and angles are listed in Table 6.1. The bond

angle at the bridgehead arsenic [C(21)–As(1)–C(26), 87.5(2)°] is almost the same as that of the palladium complex (+)-**53** [87.4(1)°].

(+)-**91** (+)-**92**

Scheme 6.7

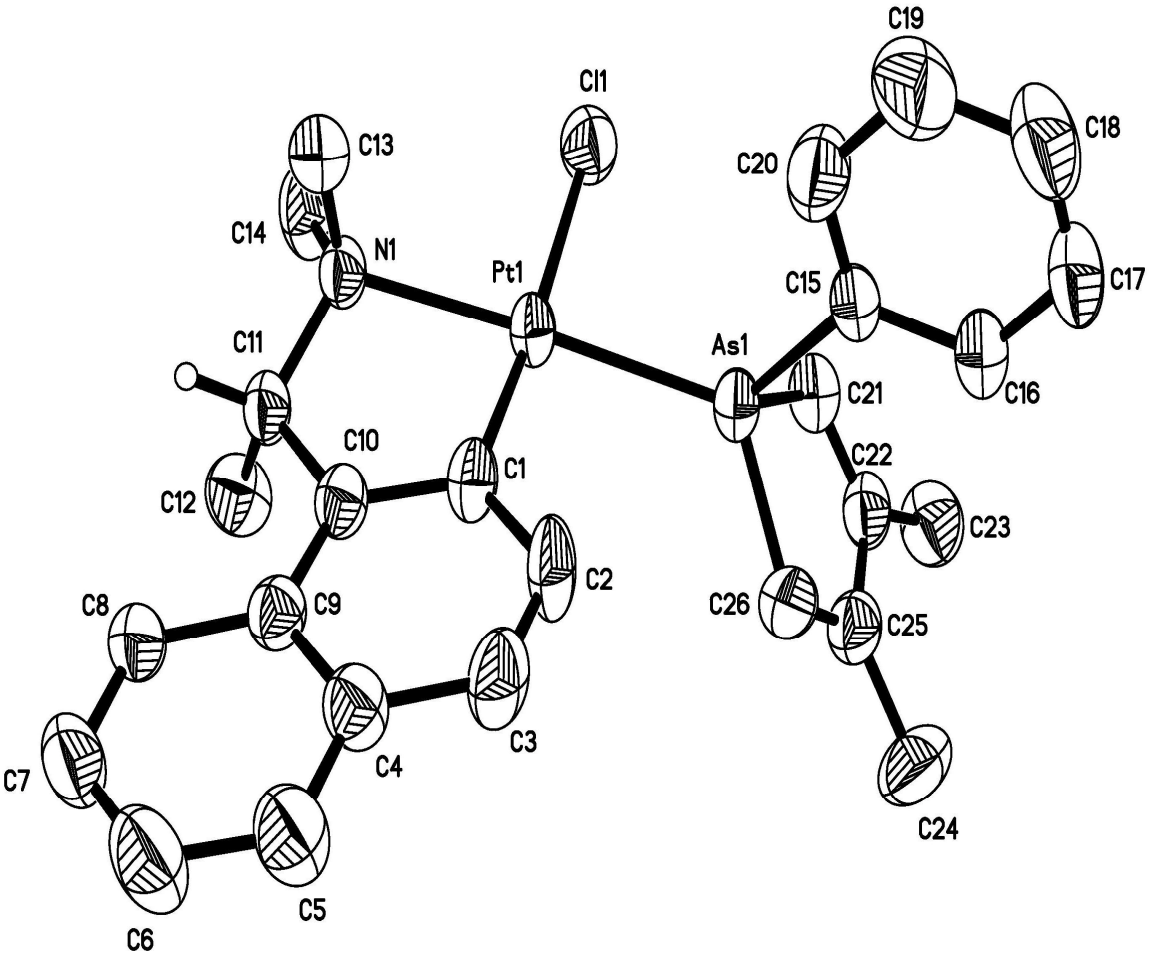


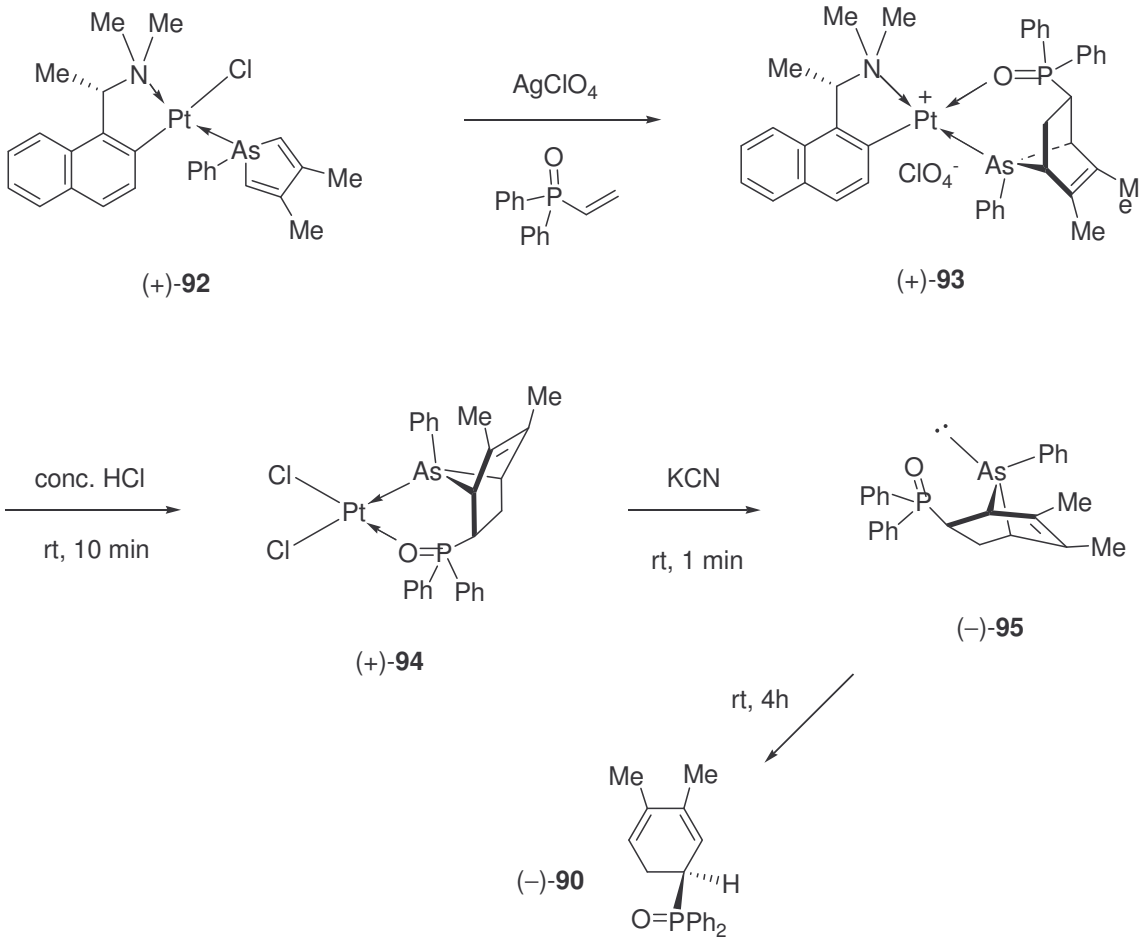
Figure 6.1 Molecular structure of complex (+)-**92**

Table 6.1 Selected bond lengths (Å) and angles (°) for (+)-**92**

Pt(1)–C(1)	1.995(3)	Pt(1)–N(1)	2.134(3)
Pt(1)–As(1)	2.342(1)	Pt(1)–Cl(1)	2.411(1)
As(1)–C(15)	1.949(4)	As(1)–C(26)	1.915(4)
As(1)–C(21)	1.912(4)	C(21)–C(22)	1.345(6)
C(22)–C(25)	1.484(7)	C(22)–C(23)	1.505(6)
C(24)–C(25)	1.514(6)	C(25)–C(26)	1.338(6)
C(1)–Pt(1)–N(1)	80.6(1)	C(1)–Pt(1)–As(1)	96.9(1)
N(1)–Pt(1)–As(1)	177.1(1)	C(1)–Pt(1)–Cl(1)	173.8(1)
N(1)–Pt(1)–Cl(1)	95.4(1)	As(1)–Pt(1)–Cl(1)	87.2(1)
C(21)–As(1)–C(26)	87.5(2)	C(21)–As(1)–C(15)	102.3(2)
C(26)–As(1)–C(15)	103.3(2)	C(21)–As(1)–Pt(1)	121.1(1)
C(26)–As(1)–Pt(1)	124.1(1)	C(15)–As(1)–Pt(1)	114.0(1)
C(22)–C(21)–As(1)	110.6(3)	C(21)–C(22)–C(25)	115.4(4)
C(21)–C(22)–C(23)	122.2(4)	C(25)–C(22)–C(23)	122.3(4)
C(26)–C(25)–C(22)	115.9(4)	C(26)–C(25)–C(24)	122.9(4)
C(22)–C(25)–C(24)	121.1(4)	C(25)–C(26)–As(1)	110.5(3)

The chloro ligand in (+)-**92** and similar complexes is well-known to be both kinetically and thermodynamically stable.[95] This terminal ligand, however, can be replaced efficiently by treatment of the complex in dichloromethane with aqueous silver perchlorate. So the incoming dienophile, diphenylvinylphosphine oxide, can coordinate

jointly to the platinum centre during the intramolecular reaction. The $^{31}P\{^{1}H\}$ NMR spectroscopic studies indicates that the cycloaddition reaction was completed within one month at 60 ºC which is slower than that of palladium complex (+)-**89**. Only one stereoisomer with a singlet $^{31}P\{^{1}H\}$ NMR signal at δ 51.3 was produced (Scheme 6.8). The complex (+)-**93** was isolated by column chromatography on a silica column with dichloromethane–diethyl ether as a solid in 68% yield, $[\alpha]_D$ +67.2° (*c* 0.6, CH_2Cl_2).



Scheme 6.8

The chiral naphthylamine auxiliary on (+)-**93** could be removed chemoselectively

by the treatment of the complex with concentrated hydrochloric acid for 10 min at room temperature. The $^{31}P\{^{1}H\}$ NMR spectrum of the crude mixture showed a singlet at δ 57.0. The dichloro platinum complex (+)-**94** was obtained as yellow crystals in 86% yield, $[\alpha]_D$ +122.2° (*c* 0.1, CH_2Cl_2). The X-ray structural analysis confirmed that the desired cycloadduct had formed *via* the *exo*-cycloaddition reaction (Figure 6.2). The complex (+)-**94** coordinated to the platinum centre as a bidentate ligand *via* the bridgehead arsenic and the oxygen atom of diphenylvinylphosphine oxide. The complex (+)-**94** is a monomer which is different from the similar bridge dimeric phosphorus

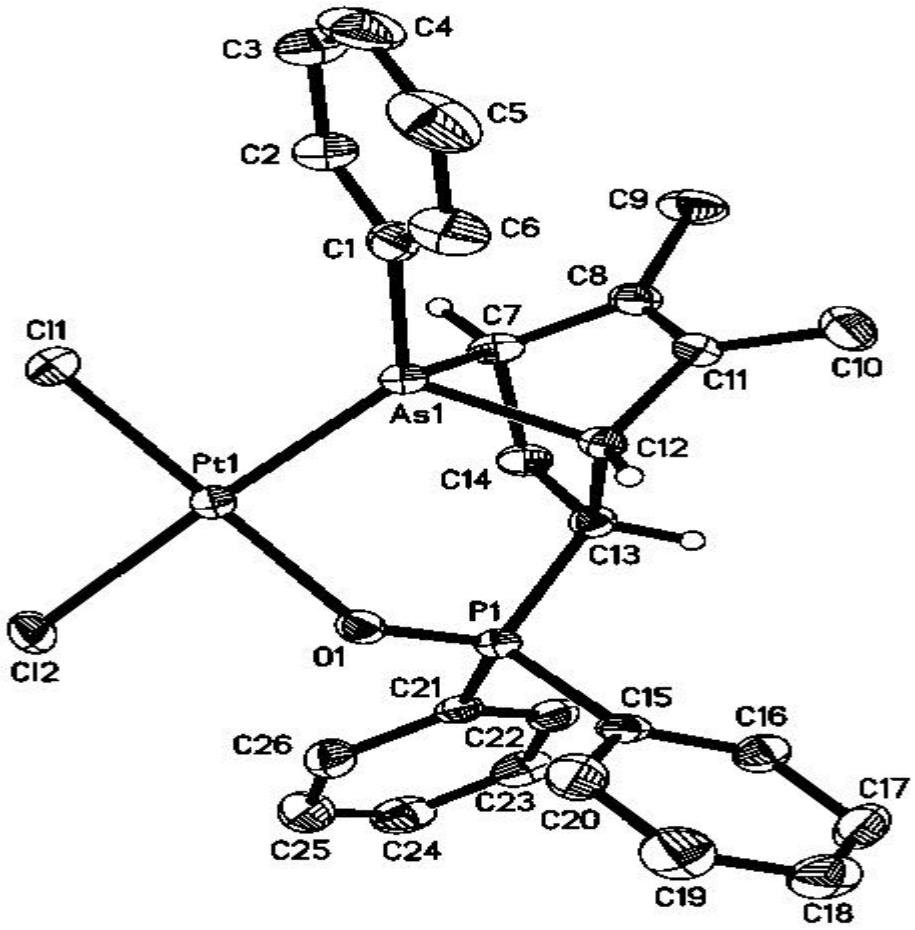


Figure 6.2 Molecular structure of complex (+)-**94**

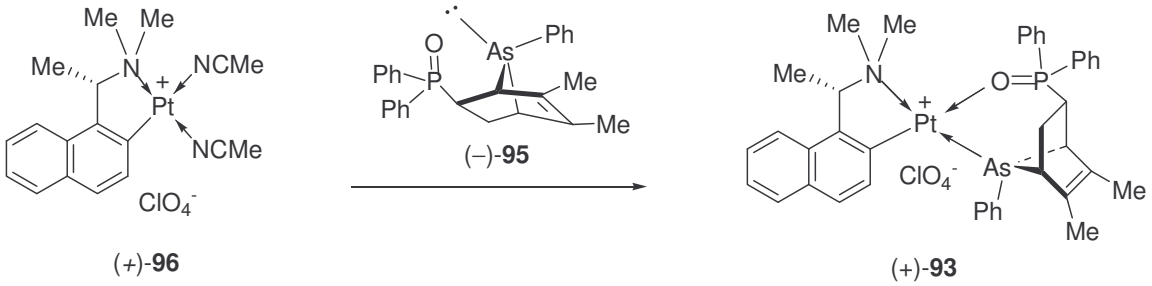
Table 6.2 Selected bond lengths (Å) and angles (°) for (+)-**94**

Pt(1)–O(1)	2.070(3)	Pt(1)–Cl(1)	2.276(1)
Pt(1)–As(1)	2.320(1)	Pt(1)–Cl(2)	2.344(1)
As(1)–C(7)	1.974(3)	As(1)–C(12)	1.978(3)
C(13)–P(1)	1.819(3)	O(1)–P(1)	1.508(3)
C(7)–C(14)	1.559(5)	C(7)–C(8)	1.517(5)
C(8)–C(11)	1.346(5)	C(11)–C(12)	1.510(4)
C(12)–C(13)	1.565(4)	C(13)–C(14)	1.573(5)
O(1)–Pt(1)–Cl(1)	176.8(1)	O(1)–Pt(1)–As(1)	89.5(1)
Cl(1)–Pt(1)–As(1)	90.0 (3)	O(1)–Pt(1)–Cl(2)	88.1 (1)
Cl(1)–Pt(1)–Cl(2)	92.5(1)	As(1)–Pt(1)–Cl(2)	176.1(1)
C(7)–As(1)–C(12)	77.1(1)	P(1)–O(1)–Pt(1)	125.0(2)
O(1)–P(1)–C(13)	113.6(2)	C(8)–C(7)–C(14)	108.7(3)
C(8)–C(7)–As(1)	100.9(2)	C(14)–C(7)–As(1)	99.2(2)
C(11)–C(8)–C(7)	111.3(3)	C(8)–C(11)–C(12)	112.0(3)
C(11)–C(12)–C(13)	107.7(3)	C(11)–C(12)–As(1)	101.0(2)
C(13)–C(12)–As(1)	99.4(2)	C(12)–C(13)–C(14)	106.5(2)
C(12)–C(13)–P(1)	110.6(2)	C(14)–C(13)–P(1)	114.9(2)
C(7)–C(14)–C(13)	106.6(3)		

analogue.[131] The geometry at the platinum centre is distorted square planar with angles at platinum in the range of 88.1(1)–92.5(1) and 176.1(1)–176.8(1)°. Selected bond lengths

and angles are listed in Table 6.2. Compared to the above unstable dichloro palladium complex, the dichloro platinum complex (+)-**94** is very stable which maybe attributable to the greater strength of the Pt–O [2.070(3) Å] bond compared with that of Pd–O [2.124(5) and 2.138(5) Å].[112b,131]

The optically active ligand (–)-**95** could be stereospecifically liberated from the dichloro complex (+)-**94** by treatment with aqueous potassium cyanide in one min at room temperature. The compound (–)-**95** was obtained as a white solid in 89% yield, $[\alpha]_D$ –18.6° (*c* 0.7, CH_2Cl_2). The $^{31}P\{^1H\}$ NMR spectrum of the liberated ligand in $CDCl_3$ exhibited a singlet at δ 30.9. Owing to the instability of the non-coordinated bridgehead arsenic, the liberated ligand cannot be stored for long, otherwise it will decompose to the arsenic–elimination product (–)-**90**. This process was monitored by its $^{31}P\{^1H\}$ NMR spectrum and found that it completely changed from δ 30.9 to 34.0 [(–)-**95** to (–)-**90**] in 4 hours. Hence, the liberated ligand (–)-**95** must be re-coordinated to selected metal ions. Furthermore, in order to determined the optical purity of (–)-**95**, it was re-coordinated to the bis(acetonitrile) complex (+)-**96** (Scheme 6.9). The $^{31}P\{^1H\}$ NMR spectrum of the crude re-coordinated product showed a singlet at δ 51.3 which is identical with that recorded from the original cycloaddition reaction. No other $^{31}P\{^1H\}$ signals could be detected, thus confirming that the liberated ligand is optically pure.

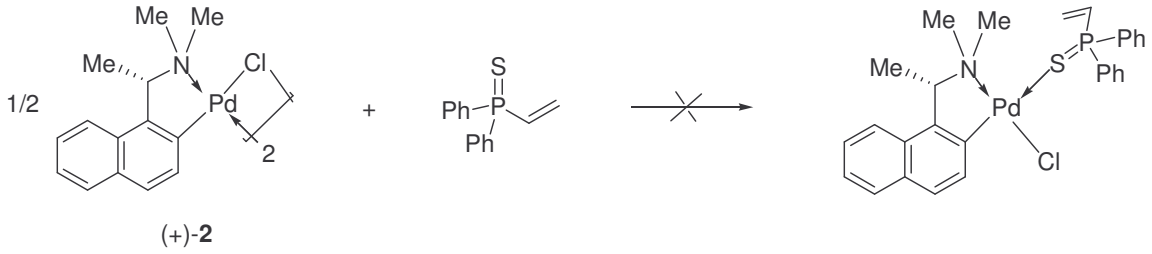


Scheme 6.9

6.2.2 Asymmetric Diels–Alder Reaction between DMPA and Diphenylvinylphosphine Sulfide

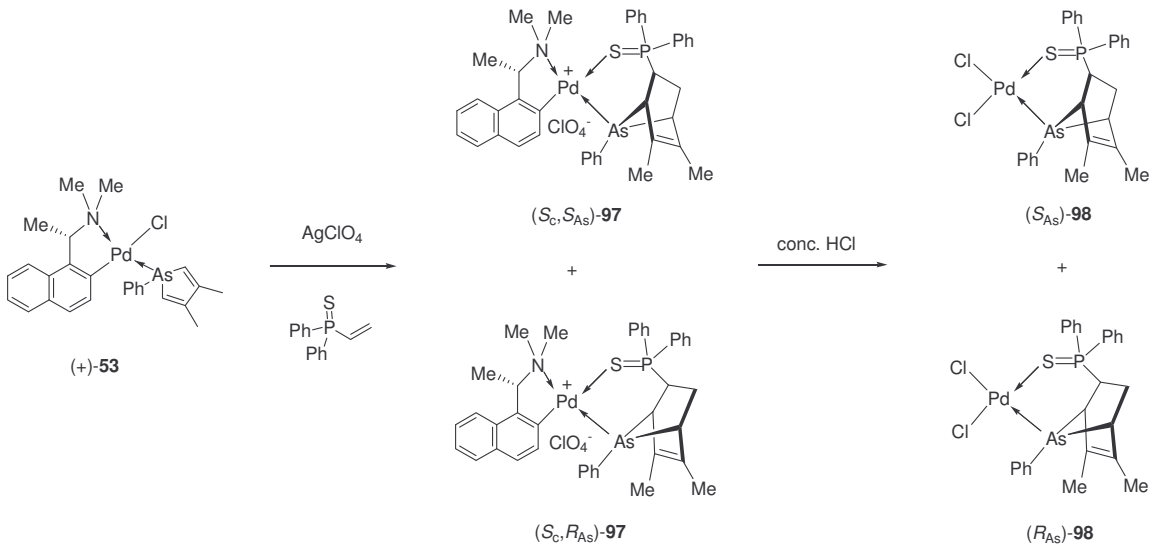
6.2.2.1 Asymmetric Diels–Alder Reaction between DMPA and Diphenylvinylphosphine Sulfide Promoted by Palladium Complex

Similar to diphenylvinylphosphine oxide, diphenylvinylphosphine sulfide could not split the chloro bridges in the complex (+)-**2** (Scheme 6.10).



Scheme 6.10

After the complex (+)-**53** was treated with aqueous silver perchlorate in dichloromethane, the resulting perchlorate complex could be used directly for subsequent reaction with diphenylvinylphosphine sulfide without isolation. The reaction was monitored by $^{31}P\{^{1}H\}$ NMR spectroscopy. When the reaction mixture was stirred for 13 days at 40 ºC, the $^{31}P\{^{1}H\}$ NMR spectrum of the crude reaction mixture in $CDCl_3$ exhibited two singlets at δ 50.2 and 51.5 in the ratio of 1:2 (Scheme 6.11). Attempts to isolate the two diastereomers (S_c,S_{As})- and (S_c,R_{As})-**97** *via* column chromatography or fractional crystallization, however, were not successful.



Scheme 6.11

In order to confirm the identity of the two diastereomers, the chiral naphthylamine auxiliary in the diastereomeric mixture was removed chemoselectively from (S_c,S_{As})- and (S_c,R_{As})-**97** by stirring a dichloromethane solution of the mixture with concentrated hydrochloric acid for 10 min at room temperature. The $^{31}P\{^{1}H\}$ NMR spectrum of the crude dichloro complex **98** in $CDCl_3$ showed one singlet at δ 50.7. Brown yellow crystals suitable for single crystal X-ray diffraction analysis were obtained from acetonitrile in 70% yield.

However, the X-ray structural analysis of dichloro complex **98** reveals the presence of both enantiomers in the unit cell. The molecular structure of dichloro complex **98** is shown in Figure 6.3 and is taken as the representative molecule in order to study the coordination aspects for the cycloadducts which were formed as racemic mixture. Selected bond lengths and angles are listed in Table 6.3.

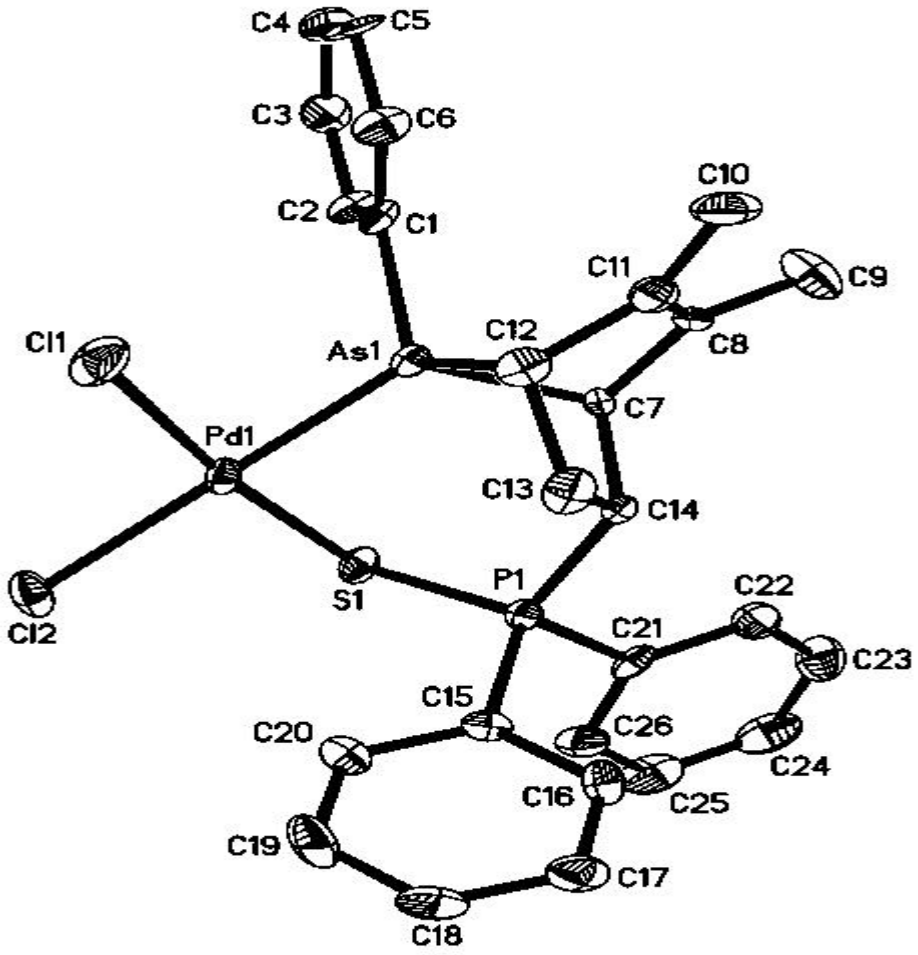


Figure 6.3 Molecular structure of dichloro complex **98**

Table 6.3 Selected bond lengths (Å) and angles (°) for **98**

Pd(1)–S(1)	2.301(2)	Pd(1)–As(1)	2.305(1)
Pd(1)–Cl(1)	2.323(2)	Pd(1)–Cl(2)	2.389(2)
As(1)–C(7)	1.976(7)	As(1)–C(12)	1.961(8)
P(1)–S(1)	2.012(3)	P(1)–C(14)	1.842(7)
C(7)–C(14)	1.562(10)	C(7)–C(8)	1.511(10)
C(8)–C(11)	1.332(12)	C(8)–C(9)	1.501(11)

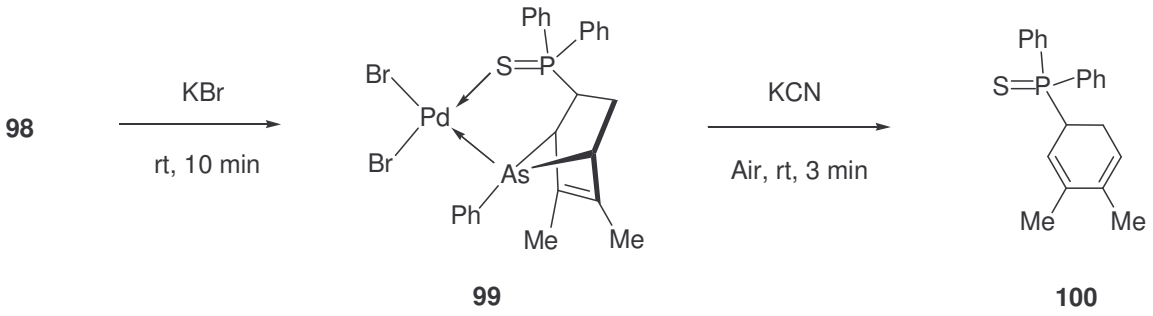
C(10)–C(11)	1.499(11)	C(11)–C(12)	1.514(11)
C(12)–C(13)	1.540(11)	C(13)–C(14)	1.564(11)
S(1)–Pd(1)–As(1)	89.0(1)	S(1)–Pd(1)–Cl(1)	172.6(1)
As(1)–Pd(1)–Cl(1)	83.7(1)	S(1)–Pd(1)–Cl(2)	91.4(1)
As(1)–Pd(1)–Cl(2)	179.4(1)	Cl(1)–Pd(1)–Cl(2)	95.9(1)
C(1)–As(1)–C(12)	112.2(3)	C(1)–As(1)–C(7)	107.9(3)
C(12)–As(1)–C(7)	77.1(3)	C(1)–As(1)–Pd(1)	116.2(2)
C(12)–As(1)–Pd(1)	117.1(2)	C(7)–As(1)–Pd(1)	120.2(2)
C(14)–P(1)–S(1)	114.2(3)	P(1)–S(1)–Pd(1)	103.9(1)
C(8)–C(7)–As(1)	100.5(5)	C(14)–C(7)–As(1)	99.1(4)
C(8)–C(7)–C(14)	107.3(6)	C(11)–C(8)–C(7)	112.2(7)
C(8)–C(11)–C(12)	111.4(7)	C(13)–C(12)–As(1)	99.3(5)
C(11)–C(12)–C(13)	109.8(7)	C(11)–C(12)–As(1)	100.2(5)
C(12)–C(13)–C(14)	106.8(6)	C(13)–C(14)–P(1)	113.9(5)
C(7)–C(14)–C(13)	106.6(6)	C(7)–C(14)–P(1)	111.1(5)

The cycloadduct coordinated to the palladium centre as bidentate ligand *via* arsenic and sulphur donor atoms. It also confirmed that the desired cycloadduct had formed *via* the *exo*-cycloaddition reaction. The geometry at the palladium is the distorted square planar with angles at palladium in the range of 83.7(1)–95.9(1) and 172.6(1)–179.4(1)°. The bond angle at the bridgehead arsenic [C(12)–As(1)–C(7), 77.1(3)°] is much smaller than that of the similar P–P=S palladium complex [81.47(15)°] formed between DMPP

and diphenylvinylphosphine sulfide[132] which is indicative of higher strain. The bond length of P(1)–C(14) [1.842(7) Å] is longer than that observed for the corresponding diphosphine sulfide [1.826(3) Å]. The bond lengths of Pd(1)–S(1) and P(1)–S(1) [2.301(2) and 2.012(3) Å, respectively] are similar to the corresponding diphosphine sulfide [2.299(9) and 2.012(1) Å, respectively].

6.2.2.2 Arsenic–Elimination Reactions

The dichloro complex **98** was treated with potassium bromide for 10 min at room temperature and the dibromo complex **99** was obtained as yellow solid in 96% yield (Scheme 6.12). The $^{31}P\{^{1}H\}$ NMR spectrum exhibited only one singlet at δ 51.4 indicating the absence of any side reaction. Complex **99** was subsequently recrystallized



Scheme 6.12

with dichloromethane–acetonitrile to give the product as orange yellow crystals. The molecular structure of **99** was confirmed by X-ray crystallography (Figure 6.4). The structural analysis of dibromo complex **99** reveals the presence of both enantiomers in unit cell which is similar to the analogous dichloro complex **98**. Selected bond lengths

and angles are listed in Table 6.4. The geometry at the palladium in **99** is the distorted square planar with angles at palladium in the range of 83.1(1)–95.4(1) and 172.5(1)–178.4(1)°. The bond angle at the bridgehead arsenic [C(12)–As(1)–C(7), 77.3(1)°] is very close to that of the similar dichloro complex **98** [77.1(3)°].

The dichloro complex **98** is very stable in solid state, but it decomposes completely after 17 days in NMR tube ($CDCl_3$). However, the dibromo complex **99** is stable both in solid state and in solution. These can be proven by its $^{31}P\{^{1}H\}$ NMR spectra in CD_2Cl_2 where the chemical shift do not change even after the sample was kept in solution for

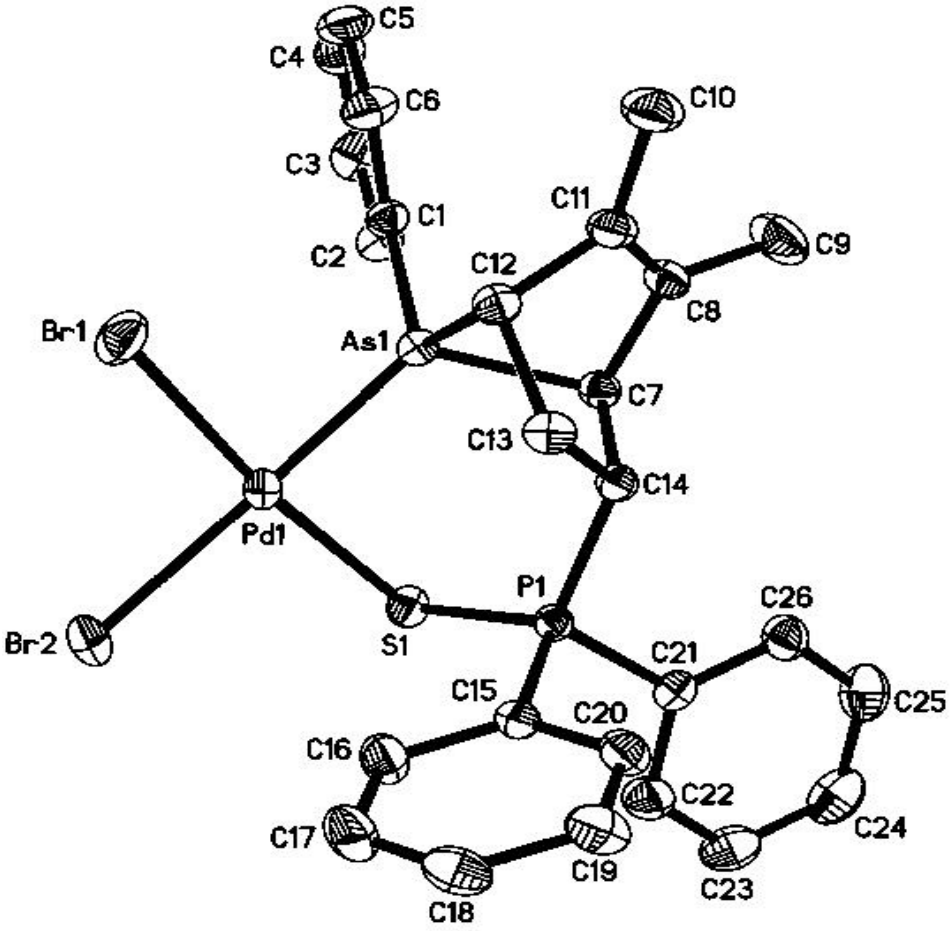


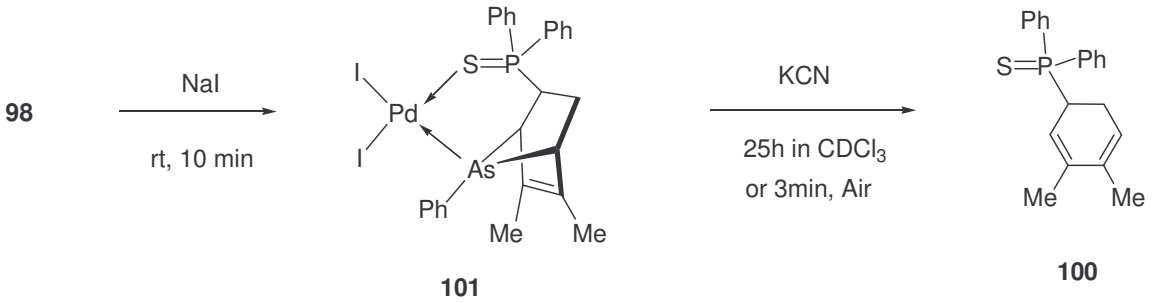
Figure 6.4 Molecular structure of dibromo complex **99**

Table 6.4 Selected bond lengths (Å) and angles (°) for **99**

Pd(1)–S(1)	2.312(1)	Pd(1)–As(1)	2.315(1)
Pd(1)–Br(1)	2.441(1)	Pd(1)–Br(2)	2.510(1)
As(1)–C(1)	1.919(2)	As(1)–C(12)	1.969(2)
As(1)–C(7)	1.986(2)	P(1)–C(14)	1.832(2)
P(1)–S(1)	2.020(1)	C(7)–C(8)	1.517(3)
C(7)–C(14)	1.552(2)	C(8)–C(11)	1.343(3)
C(11)–C(12)	1.511(3)	C(12)–C(13)	1.555(3)
C(13)–C(14)	1.567(3)		
S(1)–Pd(1)–As(1)	89.4(1)	S(1)–Pd(1)–Br(1)	172.5(1)
As(1)–Pd(1)–Br(1)	83.1(1)	S(1)–Pd(1)–Br(2)	92.1(1)
As(1)–Pd(1)–Br(2)	178.4(1)	Br(1)–Pd(1)–Br(2)	95.4(1)
C(1)–As(1)–C(12)	112.9(1)	C(1)–As(1)–C(7)	107.3(1)
C(12)–As(1)–C(7)	77.3(1)	C(1)–As(1)–Pd(1)	116.9(1)
C(12)–As(1)–Pd(1)	116.4(1)	C(7)–As(1)–Pd(1)	119.6(1)
C(14)–P(1)–S(1)	114.3(1)	P(1)–S(1)–Pd(1)	103.7(1)
C(14)–C(7)–As(1)	99.1(1)	C(8)–C(7)–C(14)	108.2(2)
C(8)–C(7)–As(1)	100.1(1)	C(11)–C(8)–C(7)	112.1(2)
C(8)–C(11)–C(12)	111.6(2)	C(13)–C(12)–As(1)	98.5(1)
C(11)–C(12)–C(13)	109.3(2)	C(11)–C(12)–As(1)	100.5(1)
C(12)–C(13)–C(14)	107.2(2)	C(13)–C(14)–P(1)	114.8(1)
C(7)–C(14)–C(13)	106.6(2)	C(7)–C(14)–P(1)	111.5(1)

more than two months. But when the dibromo complex **99** was treated with potassium cyanide under air condition for 3 min at room temperature, the color of solution rapidly changed from red to colorless. The uncoordinated ligand is very unstable and the arsenic–elimination reaction instantly occurred to give new compound **100**. The organic compound **100** could be isolated and purified by column chromatography on a silica column with dichloromethane–*n*-hexane. It is also not stable and changed to numerous unknown compounds after being kept for one week even in the solid state.

The similar diiodo complex **101** was obtained by treatment of dichloro complex **98** with sodium iodide for 10 min at room temperature in 93% yield (Scheme 6.13). It was recrystallized from dichloromethane–acetonitrile as deep red crystals. The molecular structure of **101** was confirmed by X-ray crystallography (Figure 6.5). Selected bond lengths and angles are listed in Table 6.5. The geometry at the palladium in **101** is the distorted square planar with angles at palladium in the range of 87.2(1)–93.7(1) and 174.6(1)–175.0(1)°. The bond angle at the bridgehead arsenic [C(12)–As(1)–C(7), 76.9(2)°] in the diiodo complex **101** is the most smallest amongst the similar dihalogen complex **98**, **99** and **101**.



Scheme 6.13

The $^{31}P\{^{1}H\}$ NMR studies indicated that the diiodo complex **101** is stable in dichloromethane at 40 ºC. However it decomposed in solution after being kept for 3 days at higher temperature (80 ºC). Further treatment of diiodo complex **101** with aqueous potassium cyanide liberated the free ligand. The configuration of free ligand is unstable at room temperature and converted into compound **100** after 25 h in $CDCl_3$. Furthermore when it was exposed to air condition, the arsenic–elimination reaction occurs rapidly.

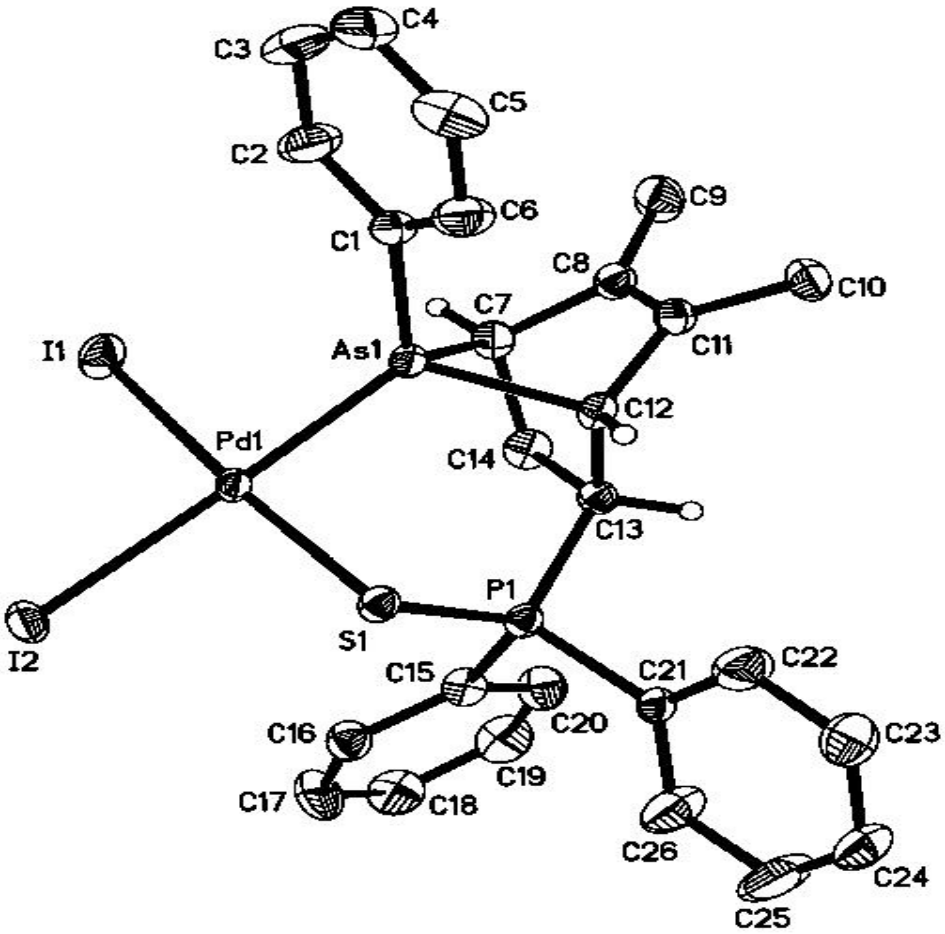


Figure 6.5 Molecular structure of diiodo complex **101**

Table 6.5 Selected bond lengths (Å) and angles (°) for **101**

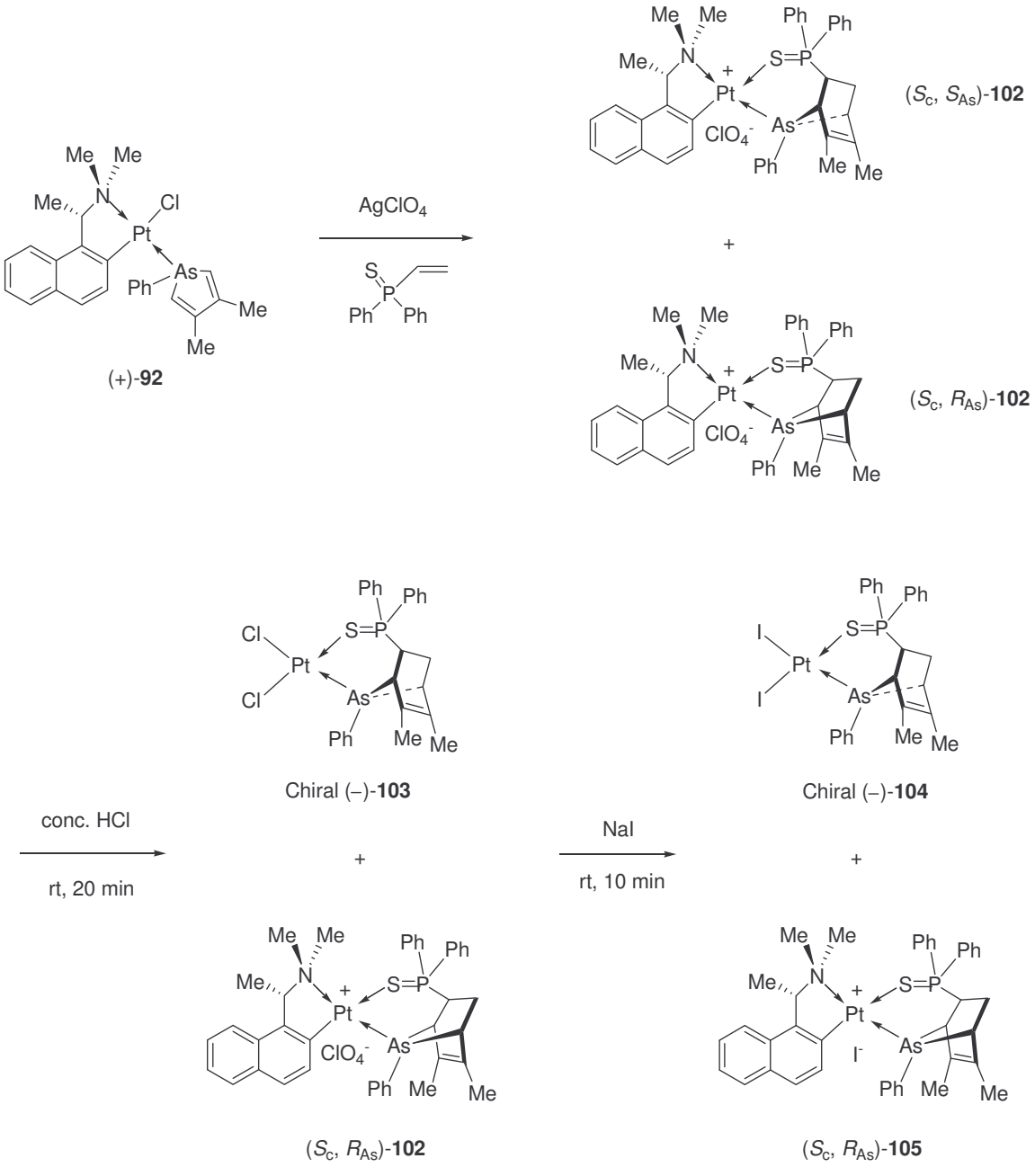
Pd(1)–S(1)	2.332(1)	Pd(1)–As(1)	2.342(1)
Pd(1)–I(1)	2.601(1)	Pd(1)–I(2)	2.652(1)
As(1)–C(1)	1.930(4)	As(1)–C(7)	1.972(4)
As(1)–C(12)	1.979(3)	P(1)–C(13)	1.842(4)
P(1)–S(1)	2.017(1)	C(7)–C(8)	1.511(5)
C(7)–C(14)	1.539(6)	C(8)–C(11)	1.345(5)
C(11)–C(12)	1.525(5)	C(12)–C(13)	1.558(5)
C(13)–C(14)	1.574(5)		
S(1)–Pd(1)–As(1)	88.5(1)	S(1)–Pd(1)–I(1)	174.6(1)
As(1)–Pd(1)–I(1)	87.2(1)	S(1)–Pd(1)–I(2)	90.8(1)
As(1)–Pd(1)–I(2)	175.0(1)	I(1)–Pd(1)–I(2)	93.7(1)
C(1)–As(1)–C(7)	113.5(2)	C(1)–As(1)–C(12)	104.5(2)
C(7)–As(1)–C(12)	76.9(2)	C(1)–As(1)–Pd(1)	118.2(1)
C(7)–As(1)–Pd(1)	118.1(1)	C(12)–As(1)–Pd(1)	117.9(1)
P(1)–S(1)–Pd(1)	101.3(1)	C(13)–P(1)–S(1)	113.4(1)
C(14)–C(7)–As(1)	98.2(2)	C(8)–C(7)–C(14)	109.4(3)
C(8)–C(7)–As(1)	101.5(3)	C(11)–C(8)–C(7)	111.8(3)
C(8)–C(11)–C(12)	111.2(3)	C(13)–C(12)–As(1)	99.3(2)
C(11)–C(12)–C(13)	108.6(3)	C(11)–C(12)–As(1)	100.8(2)
C(14)–C(13)–P(1)	115.4(3)	C(12)–C(13)–C(14)	105.7(3)
C(12)–C(13)–P(1)	111.1(2)	C(7)–C(14)–C(13)	107.4(3)

6.2.2.3 Metal Ion Effect: Asymmetric Diels–Alder Reaction between DMPA and Diphenylvinylphosphine Sulfide Promoted by Platinum Complex

Similar to the analogous palladium complex, upon the removal of the chloro ligand in (+)-**92** with silver perchlorate, the resulting perchlorate complex was treated with diphenylvinylphosphine sulfide for 5 days at room temperature (Scheme 6.14). Two diastereomers (S_c,S_{As})-**102** and (S_c,R_{As})-**102** were obtained in the ratio of 1:2 [as indicated by two singlet at δ 49.6 and 47.7 ppm respectively, in the $^{31}P\{^{1}H\}$ NMR spectrum]. Unfortunately these diastereomeric products could not be separated by column chromatography or fractional crystallization. However, when they were treated with concentrated hydrochloric acid for 20 min at room temperature, the minor isomer (S_c,S_{As})-**102** was converted into the corresponding dichloro platinum complex (–)-**103**, while the major isomer (S_c,R_{As})-**102** remained unchanged. The mixture was recrystallized with dichloromethane–diethyl ether to produce the yellow crystals of the optically pure (–)-**103** in 83% yield, $[\alpha]_D$ –57.7° (*c* 0.3, CH_2Cl_2). The unreacted (S_c,R_{As})-**102** was readily isolated from the mother liquid by column chromatography. Due to the fact that the dichloro complex (–)-**103** crystallized very slowly (several weeks). It was more efficient to treat the resultant mixture with sodium iodide for 10 min at room temperature. The resulting diiodo complex (–)-**104** and (S_c,R_{As})-**105** was separated relatively faster *via* column chromatography.

The X-ray analysis of dichloro complex (–)-**103** indeed showed it was the chiral dichloro complex (Figure 6.6). Selected bond lengths and angles are listed in Table 6.6. The geometry at the platinum in (–)-**103** is the distorted square planar with angles at

platinum in the range of 88.2(1)–92.2(1) and 176.0(1)–176.4(1)°. The cycloadduct coordinated to the platinum centre as bidentate ligand *via* arsenic and sulphur donor atoms.



Scheme 6.14

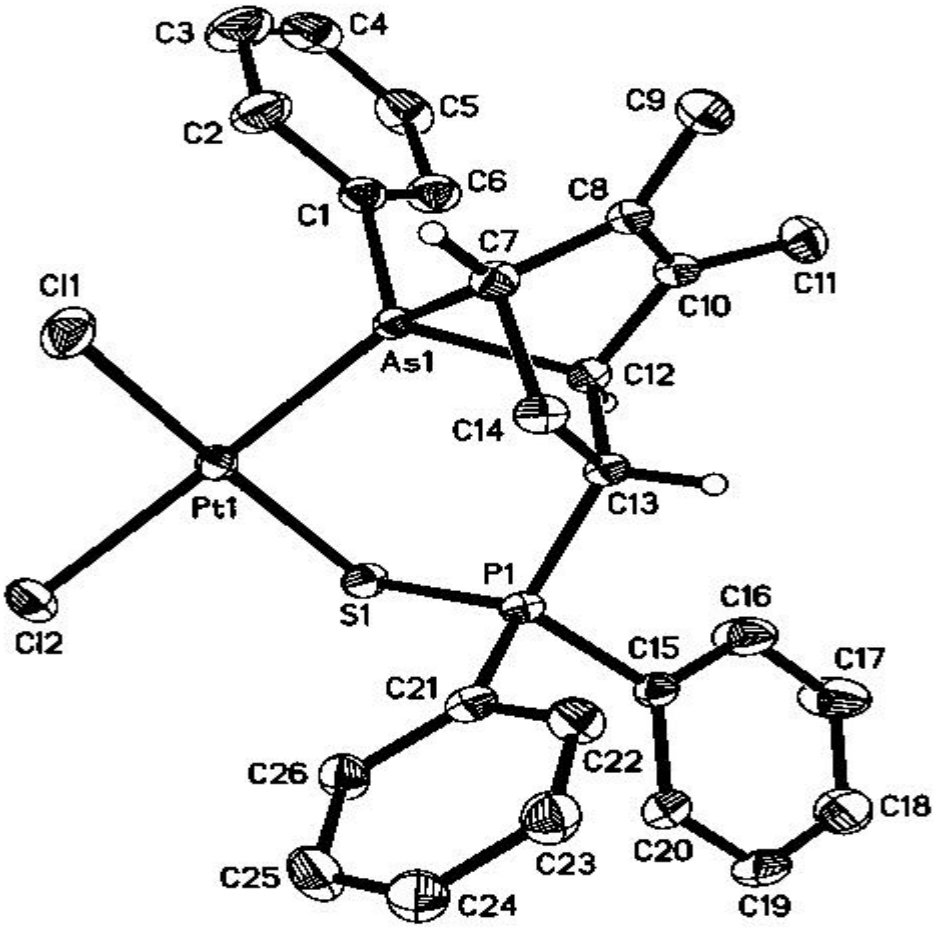


Figure 6.6 Molecular structure of dichloro complex (–)-**103**

Table 6.6 Selected bond lengths (Å) and angles (°) for (–)-**103**

Pt(1)–S(1)	2.301(1)	Pt(1)–As(1)	2.312(1)
Pt(1)–Cl(1)	2.329(1)	Pt(1)–Cl(2)	2.355(1)
As(1)–C(7)	1.967(3)	As(1)–C(12)	1.968(3)
C(13)–P(1)	1.839(3)	P(1)–S(1)	2.021(1)
C(7)–C(8)	1.496(5)	C(8)–C(10)	1.348(5)
C(10)–C(12)	1.512(5)	C(12)–C(13)	1.562(5)

C(13)–C(14)	1.574(5)	C(7)–C(14)	1.557(5)
S(1)–Pt(1)–As(1)	89.4(1)	S(1)–Pt(1)–Cl(1)	176.4(1)
As(1)–Pt(1)–Cl(1)	88.2(1)	S(1)–Pt(1)–Cl(2)	90.4(1)
As(1)–Pt(1)–Cl(2)	176.0(1)	Cl(1)–Pt(1)–Cl(2)	92.2(1)
C(7)–As(1)–C(12)	77.8(1)	C(8)–C(7)–C(14)	108.0(3)
C(8)–C(7)–As(1)	102.5(2)	C(14)–C(7)–As(1)	97.1(2)
C(10)–C(8)–C(7)	111.9(3)	C(8)–C(10)–C(12)	111.9(3)
C(10)–C(12)–C(13)	106.8(3)	C(10)–C(12)–As(1)	101.5(2)
C(13)–C(12)–As(1)	98.4(2)	C(12)–C(13)–C(14)	106.4(3)
C(12)–C(13)–P(1)	111.5(2)	C(14)–C(13)–P(1)	114.3(2)
C(7)–C(14)–C(13)	107.0(3)	C(13)–P(1)–S(1)	113.1(1)
P(1)–S(1)–Pt(1)	99.3(1)		

As expected, the structural analysis of (S_c,R_{As})-**105** revealed that the perchlorate was replaced by an iodide (Figure 6.7). Selected bond lengths and angles are listed in Table 6.7. The geometry at the platinum in (S_c,R_{As})-**105** is the distorted square planar with angles at platinum in the range of 80.0(2)–93.8(2) and 172.6(2)–173.4(1)°. The cycloadduct coordinated to the platinum centre as bidentate ligand *via* arsenic and sulphur donor atoms. As expected, the sulphur is *trans* to carbon and arsenic is *trans* to nitrogen.

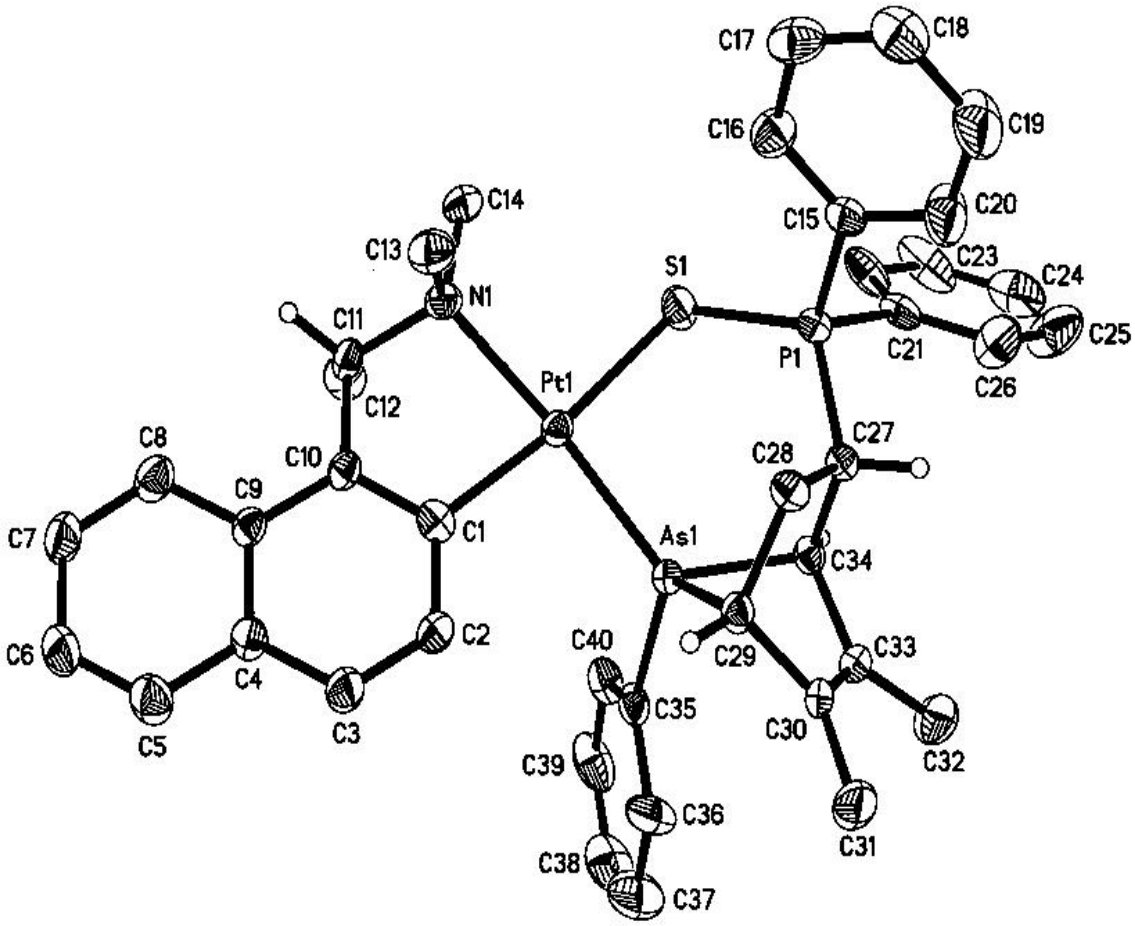


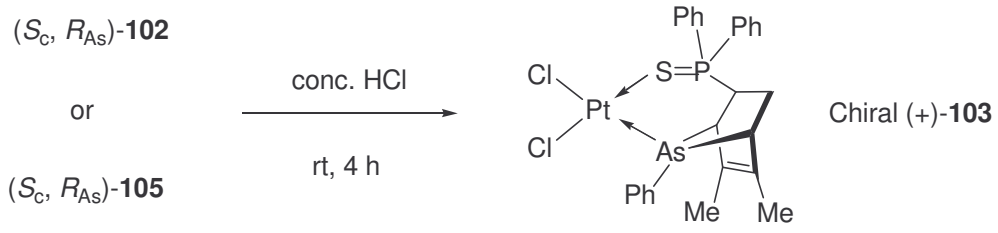
Figure 6.7 Molecular structure of complex (S_c,R_{As})-**105**

Table 6.7 Selected bond lengths (Å) and angles (°) for (S_c,R_{As})-**105**

Pt(1)–C(1)	2.024(7)	Pt(1)–N(1)	2.136(5)
Pt(1)–As(1)	2.321(1)	Pt(1)–S(1)	2.406(2)
As(1)–C(29)	1.964(6)	As(1)–C(34)	1.980(6)
C(27)–P(1)	1.813(6)	P(1)–S(1)	2.005(2)
C(27)–C(28)	1.567(8)	C(28)–C(29)	1.556(8)
C(29)–C(30)	1.514(9)	C(30)–C(33)	1.342(9)

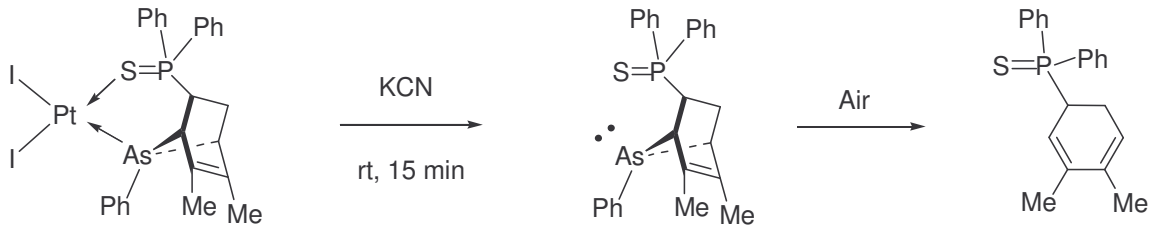
C(33)–C(34)	1.515(9)	C(27)–C(34)	1.554(7)
C(1)–Pt(1)–N(1)	80.0(2)	C(1)–Pt(1)–As(1)	93.8(2)
N(1)–Pt(1)–As(1)	173.4(1)	C(1)–Pt(1)–S(1)	172.6(2)
N(1)–Pt(1)–S(1)	93.7(1)	As(1)–Pt(1)–S(1)	92.6(1)
C(29)–As(1)–C(34)	77.1(3)	C(34)–C(27)–C(28)	106.7(4)
C(34)–C(27)–P(1)	111.1(4)	C(28)–C(27)–P(1)	115.7(4)
C(29)–C(28)–C(27)	106.4(4)	C(30)–C(29)–C(28)	108.8(5)
C(30)–C(29)–As(1)	101.8(4)	C(28)–C(29)–As(1)	98.3(4)
C(33)–C(30)–C(29)	111.2(5)	C(30)–C(33)–C(34)	112.1(5)
C(33)–C(34)–C(27)	105.9(5)	C(33)–C(34)–As(1)	100.5(4)
C(27)–C(34)–As(1)	100.6(4)	C(27)–P(1)–S(1)	116.2(2)
P(1)–S(1)–Pt(1)	111.7(1)		

The enantiomer of (–)-**103**, dichloro complex (+)-**103**, could be obtained by treatment of optically active (S_c,R_{As})-**102** or (S_c,R_{As})-**105** with concentrated hydrochloric acid for 4 hours at room temperature (Scheme 6.15).



Scheme 6.15

Further treatment of enantiomerically pure diiodo complex (–)-**104** with aqueous potassium cyanide liberated the desired optically pure As–P=S ligand (+)-**106** in 87% yield, $[\alpha]_D$ +44.3° (*c* 0.43, CH_2Cl_2). The liberated ligand was very unstable and readily produced the optically active (+)-**100**, $[\alpha]_D$ +60.7° (*c* 0.40, CH_2Cl_2) (Scheme 6.16).



Chiral (–)-**104** (+)-**106** (+)-**100**

Scheme 6.16

6.3 Conclusions

The asymmetric Diels–Alder reaction between DMPA and diphenylvinylphosphine oxide showed high stereoselectivity with only one isomer being formed. The rate of this reaction using the chiral palladium promoter is much faster than that of the platinum (6 days *vs* 30 days at 60 ºC). The resulting dichloro palladium complex was rather unstable which could not generate the desired As–P=O hemilabile ligand. It decomposed rapidly to give the elimination product (3,4-dimethyl-2,4-cyclohexadienyl)diphenylphosphine oxide (–)-**90**. In contrast the corresponding dichloro platinum complex (+)-**94** is stable and, upon treatment with KCN, the desired optically pure As–P=O ligand (–)-**95** could be liberated.

The cycloaddition reaction between DMPA and diphenylvinylphosphine sulfide was promoted by the chiral palladium complex (+)-**2**, however, the reaction exhibited low selectivity and the diastereomeric mixture **97** (1:2) could not be separated *via* column chromatography or fractional crystallization. The corresponding dihalogen complexes were isolated in the racemic forms. The arsenic–elimination reaction was observed when the dibromo or diiodo complex (**99** and **101**) was treated with potassium cyanide to give (3,4-dimethyl-2,4-cyclohexadienyl)diphenylphosphine sulfide **100**. When the chiral metal promoter was changed from palladium to platinum, the reaction selectivity is similar. However the major isomer (S_c,R_{As})-**102** and dichloro complex (–)-**103** could be separated *via* fractional crystallization and column chromatography. Alternatively they could be converted into the corresponding iodide complexes (S_c,R_{As})-**105** and (–)-**104**. The two iodide complexes were readily separated by means of column chromatography. The optically pure As–P=S ligand (+)-**106** could be liberated by treatment of (–)-**104** with potassium cyanide.

6.4 Experimental Section

General: Similar to that described in section 2.4. Diphenylvinylphosphine oxide,[133] diphenylvinylphosphine sulfide,[134] (+)-**91**[54] and (+)-**96**[54] were prepared following the literature procedures.

Cycloaddition Reaction: Preparation of Complex (+)-89

A solution of (+)-**53** (0.73 g, 1.27 mmol) in dichloromethane (50 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (1.0 g) in water (1 mL). The organic layer, after the removal of AgCl, was then washed with water (3 × 50 mL), dried ($MgSO_4$), and subsequently treated with diphenylvinylphosphine oxide (0.29 g, 1.27 mmol) for 6 days at 60 ºC. The solvent was removed from the reaction mixture, and the complex (+)-**89** was isolated by column chromatography on a silica column with dichloromethane-diethyl ether to give a pale yellow solid (0.83 g, 76%). $[\alpha]_D$ = +83.8° (*c* 0.8, CH_2Cl_2). Mp: 172–173 ºC. Anal. Calcd for $C_{40}H_{42}AsClNO_5PPd$: C, 55.6; H, 4.9; N, 1.6. Found: C, 55.2; H, 5.3; N, 1.7. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 49.5. ^1H NMR ($CDCl_3$, δ): 1.51 (s, 3H, =C*CH*$_3$), 1.94 (s, 3H, =C*CH*$_3$), 2.03 (d, $^3J_{HH}$ = 6.3 Hz, 3H, CH*CH*$_3$), 2.54 (m, 1H, CH*CH*$_2$), 2.86 (s, 3H, N*CH*$_3$), 2.94 (d, $^3J_{HH}$ = 5.1 Hz, 1H, As*CH*), 2.99 (m, 1H, CH*CH*$_2$), 3.06 (s, 3H, N*CH*$_3$), 3.65 (dd, $^3J_{HH}$ = 5.0, $^3J_{HH}$ = 10.7 Hz, 1H, P*CH*), 3.76 (s, 1H, As*CH*), 4.43 (q, $^3J_{HH}$ = 6.3 Hz, 1H, *CH*CH_3), 6.61–7.97 (m, 21H, aromatics).

Removal of Chiral Auxiliary: Synthesis of (–)-90

The complex (+)-**89** (0.25 g, 0.29 mmol) was dissolved in dichloromethane (60 mL) and treated with excess concentrated hydrochloric acid (2 mL) for 10 min at room

temperature. The solution was then washed with water (3 × 60 mL) and dried ($MgSO_4$). The solvent was removed from the reaction mixture and the complex (–)-**90** was isolated by column chromatography on a silica column with dichloromethane–acetone (0.06 g, 67%). $[\alpha]_D$ = –72.3° (*c* 0.1, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 34.0. ^1H NMR ($CDCl_3$, δ): 1.57 (s, 3H, =C*CH*$_3$), 1.72 (s, 3H, =C*CH*$_3$), 2.27 (m, 1H, P*CH*), 2.60 (m, 1H, CH*CH*$_2$), 3.30 (m, 1H, CH*CH*$_2$), 5.39 (s, 2H, =*CH*), 7.42–7.82 (m, 10H, aromatics). ^{13}C NMR ($CDCl_3$, δ): 19.1, 19.92, 19.94, 20.0, 20.1, 34.6, 35.6, 115.7, 115.8, 120.5, 120.7, 128.1, 128.3, 128.34, 128.5, 128.6, 130.5, 131.1, 131.3, 131.6, 131.62, 131.7, 131.8, 131.9, 132.0, 132.2, 133.1, 133.7, 133.74, 137.6, 137.7. EI MS: m/z 309.0, $[M]^+$.

Preparation of Complex (+)-92

A mixture of DMPA (1.39 g, 5.99 mmol) and complex (+)-**91** (2.56 g, 2.99 mmol) in dichloromethane (100 mL) was stirred for 2 h at room temperature. The solvent was removed from the reaction mixture and the complex (+)**-92** was isolated by column chromatography on a silica column with dichloromethane–diethyl ether to give a yellow powder, which was recrystallized from chloroform–*n*-hexane–diethyl ether in the form of yellow crystals (2.14 g, 54%). $[\alpha]_D$ = +140.0° (*c* 0.6, CH_2Cl_2). Mp: 205–206 ºC. Anal. Calcd for $C_{26}H_{29}AsClNPt$: C, 47.3; H, 4.4; N, 2.1. Found: C, 47.0; H, 4.5; N, 2.2. ^1H NMR ($CDCl_3$, δ): 1.84 (d, $^3J_{HH}$ = 6.2 Hz, 3H, CH*CH*$_3$), 2.08 (s, 3H, =C*CH*$_3$), 2.12 (s, 3H, =C*CH*$_3$), 3.00 (s, 3H, N*CH*$_3$), 3.14 (s, 3H, N*CH*$_3$), 4.55 (q, $^3J_{HH}$ = 6.2 Hz, 1H, *CH*CH_3), 6.74 (s, 1H, As*CH*), 7.01 (s, 1H, As*CH*), 7.29–7.81 (m, 11H, aromatics).

Cycloaddition Reaction: Preparation of Complex (+)-93

A solution of (+)-**92** (0.38 g, 0.57 mmol) in dichloromethane (50 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (1.0 g) in water (1 mL). The organic layer, after the removal of AgCl, was then washed with water (3 × 50 mL), dried ($MgSO_4$), and subsequently treated with diphenylvinylphosphine oxide (0.13 g, 0.57 mmol) for 1 month at 60 ºC. The solvent was removed from the reaction mixture and the complex (+)-**93** was isolated by column chromatography on a silica column with dichloromethane–diethyl ether to give a white solid (0.37 g, 68%). $[\alpha]_D$ = +67.2° (*c* 0.6, CH_2Cl_2). Mp: 182–183 ºC. Anal. Calcd for $C_{40}H_{42}AsClNO_5PPt$: C, 50.4; H, 4.4; N, 1.5. Found: C, 50.0; H, 4.7; N, 1.4. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 51.3. ^1H NMR ($CDCl_3$, δ): 1.50 (s, 3H, CH*CH*$_3$), 1.97 (s, 6H, =C*CH*$_3$), 2.39 (m, 1H, CH*CH*$_2$), 2.90 (s, 3H, N*CH*$_3$), 2.94 (d, $^3J_{HH}$ = 5.2 Hz, 1H, As*CH*), 3.05 (m, 1H, CH*CH*$_2$), 3.25 (s, 3H, N*CH*$_3$), 3.59 (dd, $^3J_{HH}$ = 5.1, $^3J_{HH}$ = 10.7 Hz, 1H, P*CH*), 3.77 (s, 1H, As*CH*), 4.70 (q, $^3J_{HH}$ = 6.3 Hz, 1H, *CH*CH$_3$), 6.63–7.98 (m, 21H, aromatics).

Removal of Chiral Auxiliary: Synthesis of Dichloro Complex (+)-94

The complex (+)-**93** (0.08 g, 0.08 mmol) was dissolved in dichloromethane (60 mL) and treated with excess concentrated hydrochloric acid (2 mL) for 10 min at room temperature. The mixture was then washed with water (3 × 50 mL), dried ($MgSO_4$), and subsequently recrystallized from dichloromethane–diethyl ether as yellow crystals (+)-**94** (0.05 g, 86%). $[\alpha]_D$ = +122.2° (*c* 0.1, CH_2Cl_2). Mp: 144–145 ºC. Anal. Calcd for $C_{26}H_{26}AsCl_2OPPt$: C, 43.0; H, 3.6. Found: C, 42.6; H, 3.7. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 57.0. ^1H NMR (CD_2Cl_2, δ): 1.47 (s, 3H, =C*CH*$_3$), 1.66 (s, 3H, =C*CH*$_3$), 2.03 (m, 1H, CH*CH*$_2$), 2.97 (dd, $^3J_{HH}$ = 4.5, $^3J_{HH}$ = 10.4 Hz, 1H, P*CH*), 3.06 (d, $^3J_{HH}$ = 4.5 Hz, 1H,

As*CH*), 3.37 (m, 1H, CH*CH*$_2$), 3.62 (s, 1H, As*CH*), 7.38–8.08 (m, 15H, aromatics).

Liberation of the As–P=O Ligand (–)-95

A solution of (+)-**94** (0.16 g, 0.22 mmol) in dichloromethane (20 mL) was stirred vigorously with a saturated aqueous solution of potassium cyanide (1.0 g) for 1 min. The organic layer was separated, then washed with water (3 × 20 mL), and dried ($MgSO_4$). Upon removal of the solvent, the free ligand (–)-**95** was obtained as an air-sensitive white solid (0.09 g, 89%). $[\alpha]_D = -18.6°$ (*c* 0.7, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 30.9.

Preparation of Dichloro Complex 98

A solution of (+)-**53** (0.47 g, 0.82 mmol) in dichloromethane (50 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (1.0 g) in water (1 mL). The organic layer, after the removal of AgCl, was then washed with water (3 × 50 mL), dried ($MgSO_4$), and subsequently treated with diphenylvinylphosphine sulfide (0.20 g, 0.82 mmol) for 13 days at 40 ºC. The crude diastereomeric mixture was treated with excess concentrated hydrochloric acid (2 mL) for 10 min at room temperature. The mixture was then washed with water (3 × 50 mL), dried ($MgSO_4$) and subsequently recrystallized from acetonitrile to give **98** as brown yellow crystals (0.40 g, 70%). Mp: 126–127 ºC. Anal. Calcd for $C_{28}H_{29}AsCl_2NPPdS$: C, 48.4; H, 4.2; N, 2.0; S, 4.6. Found: C, 48.0; H, 3.9; N, 1.7; S, 4.5. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 51.3. ^1H NMR (CD_2Cl_2, δ): 1.63 (s, 3H, =C*CH*$_3$), 1.64 (s, 3H, =C*CH*$_3$), 2.15 (dd, $^3J_{HH}$ = 10.6, $^2J_{PH}$ = 25.4 Hz, 1H, P*CH*), 2.95 (m, 1H, CH*CH*$_2$), 3.40 (d, $^3J_{HH}$ = 5.0 Hz, 1H, As*CH*), 3.45 (m, 1H, CH*CH*$_2$), 3.55 (s, 1H, As*CH*), 7.42–8.29 (m, 15H, aromatics).

Preparation of the Dibromo Complex 99

The solution of **98** (0.07 g, 0.10 mmol) in dichloromethane (50 mL) was added with excessive potassium bromide (0.20 g) in acetone (50 mL) and water (10 mL) and stirred vigorously for 10 min at room temperature. The solvents were removed and the residue was extracted with dichloromethane and water and the organic layer was dried with $MgSO_4$. Removal of the solvent gave **99** as a solid, which was then recrystallized from dichloromethane–acetonitrile to give the product as orange yellow crystals (0.075 g, 96%). Mp: 131–132 ºC. Anal. Calcd for $C_{28}H_{29}AsBr_2NPPdS$: C, 42.9; H, 3.7; N, 1.8; S, 4.1. Found: C, 42.7; H, 3.4; N, 1.7; S, 4.3. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 51.4. ^1H NMR (CD_2Cl_2, δ): 1.59 (s, 3H, =C*CH*$_3$), 1.67 (s, 3H, =C*CH*$_3$), 2.12 (dd, $^3J_{HH}$ = 11.0, $^2J_{PH}$ = 25.8 Hz, 1H, P*CH*), 2.85 (m, 1H, CH*CH*$_2$), 3.39 (d, $^3J_{HH}$ = 4.8 Hz, 1H, As*CH*), 3.41 (m, 1H, CH*CH*$_2$), 3.55 (s, 1H, As*CH*), 7.43–8.28 (m, 15H, aromatics).

Preparation of Compound 100

The dibromo complex **99** (0.16 g, 0.22 mmol) in dichloromethane (30 mL) was treated with potassium cyanide (0.2 g) in water (30 mL) for 3 min at room temperature in air. The colour of solution was change from red to colourless. The organic layer was washed with water (3 × 30 mL), dried ($MgSO_4$) and the solvent was removed. The residue was purified by column chromatography with dichloromethane to give compound **100** as a white solid (0.06 g, 84%). Mp: 94–95 ºC. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 49.0. ^1H NMR ($CDCl_3$, δ): 1.54 (s, 3H, =C*CH*$_3$), 1.70 (s, 3H, =C*CH*$_3$), 2.15 (m, 1H, P*CH*), 2.78 (dd, $^3J_{HH}$ = 16.2, $^3J_{PH}$ = 32.3 Hz, 1H, CH*CH*$_2$), 3.58 (dd, $^3J_{HH}$ = 10.0, $^3J_{PH}$ = 15.2 Hz, 1H, CH*CH*$_2$), 5.37 (s, 1H, =*CH*), 5.39 (s, 1H, =*CH*), 7.42–7.95 (m, 10H, aromatics). ^{13}C NMR

($CDCl_3$, δ): 19.0 (*CH*$_3$), 19.9 (d, $^4J_{PC}$ = 7.3 Hz, *CH*$_3$), 22.6 (d, $^2J_{PC}$ = 6.7 Hz, *CH*$_2$), 37.1 (d, $^1J_{PC}$ = 220.7 Hz, P*CH*), 116.1 (d, $^3J_{PC}$ = 20.4 Hz, =*CH*), 120.6 (d, $^2J_{PC}$ = 53.7 Hz, =*CH*), 128.0, 128.1, 128.4, 128.6, 129.9, 130.9, 131.1, 131.19, 131.2, 131.3, 131.4, 131.9, 132.3, 132.4, 132.9 (aromatics), 133.4 (d, $^4J_{PC}$ = 14.8 Hz, =*C*CH_3), 137.8 (d, $^3J_{PC}$ = 47.5 Hz, =*C*CH_3). EI MS: m/z 325.1, $[M]^+$.

Synthesis of the Diiodo Complex 101

The solution of **98** (0.34 g, 0.49 mmol) in dichloromethane (60 mL) was mixed with excessive sodium iodide (0.4 g) in acetone (60 mL) and stirred vigorously for 10 min at room temperature. The solvents were removed and the residue was extracted with dichloromethane. Removal of the solvent gave **101** as a solid, which was then recrystallized from dichloromethane–acetonitrile to give the product as deep red microcrystals (0.38 g, 93%). Mp: 156–157 ºC. Anal. Calcd for $C_{26}H_{26}AsI_2PPdS$: C, 37.3; H, 3.1, S, 3.8. Found: C, 37.0; H, 2.8; S, 3.8. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 51.7. ^1H NMR (CD_2Cl_2, δ): 1.55 (s, 3H, =C*CH*$_3$), 1.70 (s, 3H, =C*CH*$_3$), 2.08 (dd, $^3J_{HH}$ = 10.6, $^2J_{PH}$ = 25.4 Hz, 1H, P*CH*), 2.67 (m, 1H, CH*CH*$_2$), 3.33 (d, $^3J_{HH}$ = 5.5 Hz, 1H, As*CH*), 3.40 (m, 1H, CH*CH*$_2$), 3.52 (s, 1H, As*CH*), 7.42–8.26 (m, 15H, aromatics).

Preparation of Complexes (S_c,R_{As})-102, (–)-103, (–)-104 and (S_c,R_{As})-105

A solution of (+)-**92** (0.26 g, 0.39 mmol) in dichloromethane (30 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (0.15 g) in water (1 mL). The organic layer, after the removal of AgCl, was then washed with water (3 × 30 mL), dried ($MgSO_4$), and subsequently treated with diphenylvinylphosphine sulfide (0.10 g, 0.39

mmol) for 5 days at room temperature. The crude diastereomeric mixture was treated with excess concentrated hydrochloric acid (2 mL) for 20 min at room temperature.

Method A: The mixture was then washed with water (3 × 30 mL), dried ($MgSO_4$), and subsequently recrystallized from dichloromethane–diethyl ether to give (–)-**103** as pale yellow crystals (0.08 g, 83%). $[\alpha]_D$ = –57.7° (*c* 0.3, CH_2Cl_2). Mp: >300 ºC. Anal. Calcd for $C_{26}H_{26}AsCl_2PPtS$: C, 42.1; H, 3.5; S, 4.3. Found: C, 42.2; H, 3.9; S, 4.1. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 43.9 (s, 1P, J_{PtP} =147 Hz). ^1H NMR (CD_2Cl_2, δ): 1.46 (s, 3H, =C*CH*$_3$), 1.59 (s, 3H, =C*CH*$_3$), 1.92 (dd, $^3J_{HH}$ = 1.5, $^3J_{HH}$ = 12.2 Hz, 1H, CH*CH*$_2$), 2.94 (m, 1H, P*CH*), 3.16 (d, $^3J_{HH}$ = 10.6 Hz, 1H, CH*CH*$_2$), 3.38 (s, 1H, As*CH*), 3.42 (d, $^3J_{HH}$ = 5.2 Hz, 1H, As*CH*), 7.32–8.18 (m, 15H, aromatics).

The solvents from the remainder solution was removed and the residue was isolated by column chromatography with dichloromethane–diethyl ether to give (S_c,R_{As})-**102** as a yellow solid (0.18 g, 71%), $[\alpha]_D$ = +196.4° (*c* 0.3, CH_2Cl_2). Mp: 160–161 ºC. Anal. Calcd for $C_{40}H_{42}AsClNO_4PPtS$: C, 49.6; H, 4.4; N, 1.5; S, 3.3. Found: C, 49.4; H, 4.6; N, 1.4; S, 3.4. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 47.7 (s, 1P, J_{PtP} =63 Hz). ^1H NMR ($CDCl_3$, δ): 1.61 (s, 3H, =C*CH*$_3$), 1.86 (d, $^3J_{HH}$ = 6.2 Hz, 3H, CH*CH*$_3$), 2.00 (s, 3H, =C*CH*$_3$), 2.63 (m, 1H, CH*CH*$_2$), 2.71 (s, 3H, N*CH*$_3$), 2.84 (m, 1H, CH*CH*$_2$), 3.20 (d, $^3J_{HH}$ = 6.5 Hz, 1H, As*CH*), 3.37 (s, 3H, N*CH*$_3$), 3.70 (s, 1H, As*CH*), 3.86 (broad s, 1H, P*CH*), 4.65 (q, $^3J_{HH}$ = 6.2 Hz, 1H, *CH*CH_3), 6.61–7.97 (m, 21H, aromatics).

Method B: The mixture was then washed with water (3 × 30 mL), excess NaI (0.2 g) in acetone (20 mL) was added and stirred for 10 min at room temperature. The solvents were removed and the diiodo complex (–)-**104** and (S_c,R_{As})-**105** was easily isolated by column chromatography with dichloromethane–diethyl ether. The complex (–)-**104** was

recrystallized with dichloromethane–diethyl ether to produce yellow crystals (0.09 g, 75%). $[\alpha]_D$ = –48.8° (*c* 0.1, CH_2Cl_2). Mp: 186–187 ºC. Anal. Calcd for $C_{26}H_{26}AsI_2PPtS$: C, 33.8; H, 2.8; S, 3.5. Found: C, 34.0; H, 2.9; S, 3.3. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, δ): 44.4 (s, 1P, J_{PtP} =132 Hz). ^1H NMR (CD_2Cl_2, δ): 1.57 (d, $^5J_{HH}$ = 0.8 Hz, 3H, =C*CH*$_3$), 1.75 (s, 3H, =C*CH*$_3$), 1.97 (dt, $^3J_{HH}$ = 11.9, $^2J_{PH}$ = 12.1 Hz, 1H, P*CH*), 2.83 (m, 1H, CH*CH*$_2$), 3.28 (m, 1H, CH*CH*$_2$), 3.46 (s, 1H, As*CH*), 3.47 (d, $^3J_{HH}$ = 5.2 Hz, 1H, As*CH*), 7.42–8.27 (m, 15H, aromatics). Complex (S_c,R_{As})-**105** was recrystallized with dichloromethane–diethyl ether to produce yellow crystals (0.19 g, 73%). $[\alpha]_D$ = +171.4° (*c* 0.35, CH_2Cl_2). Mp: 180–181 ºC. Anal. Calcd for $C_{40}H_{42}AsINPPtS$: C, 48.2; H, 4.3; N, 1.4; S, 3.2. Found: C, 48.4; H, 4.1; N, 1.2; S, 3.4. $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 47.2. ^1H NMR ($CDCl_3$, δ): 1.65 (s, 3H, =C*CH*$_3$), 1.87 (d, $^3J_{HH}$ = 6.1 Hz, 3H, CH*CH*$_3$), 2.04 (s, 3H, =C*CH*$_3$), 2.73 (s, 3H, N*CH*$_3$), 2.78 (m, 1H, CH*CH*$_2$), 2.89 (q, $^3J_{HH}$ = $^2J_{PH}$ = 11.5 Hz, 1H, P*CH*), 3.19 (d, $^3J_{PH}$ = 6.4 Hz, 1H, As*CH*), 3.39 (s, 3H, N*CH*$_3$), 3.70 (s, 1H, As*CH*), 4.60 (broad s, 1H, CH*CH*$_2$), 4.68 (q, $^3J_{HH}$ = 6.2 Hz, 1H, *CH*CH$_3$), 7.10–8.41 (m, 21H, aromatics).

Removal of Chiral Auxiliary: Synthesis of Dichloro Complex (+)-103

The optical pure (S_c,R_{As})-**102** (0.14 g, 0.14 mmol) [or (S_c,R_{As})-**105**] was dissolved in dichloromethane (30 mL) and treated with excess concentrated hydrochloric acid (2 mL) for 4 h at room temperature. The solution was washed with water (3 × 30 mL) and dried ($MgSO_4$). The solvent was removed and the residue was subsequently recrystallized from dichloromethane–diethyl ether to give (+)-**103** as yellow crystals (0.09 g, 84%). $[\alpha]_D$ = +80.5° (*c* 0.2, CH_2Cl_2). Other data were the same to complex (–)-**103.**

Liberation of the As–P=S Ligand (+)-106

A solution of (–)-**104** (0.06 g, 0.06 mmol) in dichloromethane (10 mL) was stirred vigorously with a saturated aqueous solution of potassium cyanide (1.0 g) for 15 min. The organic layer was separated, then washed with water (3 × 10 mL), and dried ($MgSO_4$). Upon removal of the solvent, the free ligand (+)**-106** was obtained as an air-sensitive solid (0.025 g, 87%). $[\alpha]_D$ = +44.3° (*c* 0.43, CH_2Cl_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ): 48.0.

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List of Publications and Manuscripts

1. **Novel Stereochemistry, Reactivity and Stability of an Arsenic Heterocycle in a Metal-Promoted Asymmetric Cycloaddition Reaction**

   Mengtao Ma, Sumod A. Pullarkat, Yongxin Li and Pak-Hing Leung

   Inorg. Chem. **2007**, *46*, 9488–9494

2. **Asymmetric Synthesis of a Chiral Hetero-bidentate As–P Ligand Containing both As and P–Stereogenic Centres**

   Mengtao Ma, Sumod A. Pullarkat, Yongxin Li and Pak-Hing Leung

   J. Organomet. Chem. **2008**, *693*, 3289–3294

3. **Metal Effects on the Asymmetric Cycloaddition Reaction between 3,4-Dimethyl-1-phenylarsole and Diphenylvinylphosphine Oxide**

   Mengtao Ma, Sumod A. Pullarkat, Mingjun Yuan, Na Zhang, Yongxin Li and Pak-Hing Leung

   Organometallics **2009**, *28*, 4886–4889

4. **Template Effects on the Asymmetric Cycloaddition Reaction between 3,4-Dimethyl-1-phenylarsole and Diphenylvinylphosphine and Their Arsenic Elimination Reaction**

   Mengtao Ma, Sumod A. Pullarkat, Ke Chen, Yongxin Li and Pak-Hing Leung

   J. Organomet. Chem. **2009**, *694*, 1929–1933

5. **Asymmetric Synthesis of a P–Chiral Heteroditopic P–P=S Ligand *via* Chiral Metal Template Promoted Cycloaddition between 3,4-Dimethyl-1-phenylphosphole and Its Sulfonated Analog**

   Sumod A. Pullarkat, Kien-Wee Tan, Mengtao Ma, Geok-Kheng Tan, Lip Lin Koh, Jagadese J. Vittal and Pak-Hing Leung

   J. Organomet. Chem. **2006**, *691*, 3083–3088

6. **Asymmetric Synthesis of Functionalized 1,2-Diphosphine *via* the Chemoselective Hydrophosphination of Coordinated Allylic Phosphines**

   Mingjun Yuan, Sumod A. Pullarkat, Mengtao Ma, Yi Zhang, Yinhua Huang, Yongxin Li, Akash Goel and Pak-Hing Leung

   Organometallics **2009**, *28*, 780–786

7. **Steric Effects on Control of Endo/Exo-Selectivity in Asymmetric Cycloaddition Reaction and their Mechanistic Investigation**

   Mengtao Ma, Ruifeng Lu, Sumod A. Pullarkat, Yongxin Li, Weiqiao Deng and Pak-Hing Leung (submitted)

Appendices

Table A1 Crystallographic data for complexes (+)**-43**, (–)**-44** and (–)**-45**

	(+)**-43**	(–)**-44**	(–)**-45**
formula	$C_{23}H_{28}AsCl_4NPd$	$C_{36.5}H_{40.5}AsCl_{2.5}NO_4PPd$	$C_{27}H_{27}AsCl_5PPd$
fw	641.58	858.11	741.03
space group	$P3_1$	$P1$	$P2_12_12_1$
crystal system	Trigonal	Triclinic	Orthorhombic
a/Å	10.1936(3)	9.9874(3)	8.6453(3)
b/Å	10.1936(3)	10.4103(3)	14.7344(6)
c/Å	22.6287(8)	18.6414(7)	22.8349(9)
α/°	90	93.513(2)	90
β/°	90	103.462(2)	90
γ/°	120	100.6610(10)	90
V/Å^3	2036.32(11)	1841.32(10)	2908.78(19)
Z	3	2	4
T/K	296(2)	173(2)	173(2)
D_{calcd}/g cm^{-3}	1.570	1.548	1.692
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	2.297	1.660	2.298
F(000)	960	870	1472
R1 (obs data)[a]	0.0321	0.0253	0.0296
wR2 (obs data)[b]	0.0857	0.0623	0.0613
Flack param	0.017(7)	0.003(3)	–0.001(8)

Table A2 Crystallographic data for complexes (+)**-48**, (**+**)-**51** and (–)**-52**

	(+)**-48**	(**+**)-**51**	(–)**-52**
formula	$C_{20}H_{21}Cl_2PPd$	$C_{20}H_{21}Br_2PPd$	$C_{26}H_{26}AsI_2PPd$
fw	469.64	558.56	804.56
space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
crystal system	Orthorhombic	Orthorhombic	Orthorhombic
a/Å	7.6291(3)	7.8162(4)	9.3153(3)
b/Å	14.2545(5)	14.3662(6)	17.0471(7)
c/Å	17.1460(6)	17.5008(8)	17.1125(7)
α/°	90	90	90
β/°	90	90	90
γ/°	90	90	90
V/Å^3	1864.61(12)	1965.15(16)	2717.45(18)
Z	4	4	4
T/K	298(2)	298(2)	273(2)
D_{calcd}/g cm^{-3}	1.673	1.888	1.967
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	1.366	5.091	4.234
F(000)	944	1088	1528
R1 (obs data)[a]	0.0279	0.0610	0.0261
wR2 (obs data)[b]	0.0511	0.1394	0.0714
Flack param	0.00(2)	0.11(2)	0.022(12)

Table A3 Crystallographic data for complexes (+)-**53**, (–)-**54** and **62**

	(+)-**53**	(–)-**54**	**62**
formula	$C_{26}H_{29}AsClNPd$	$C_{40.33}H_{42.67}AsCl_{1.67}NO_4PPd$	$C_{48}H_{40}As_4I_4O_2Pd_2$
fw	572.27	876.79	1668.88
space group	$P2_12_12_1$	$C2$	P-1
crystal system	Orthorhombic	Monoclinic	Triclinic
a/Å	9.0856(2)	30.3585(16)	10.0982(3)
b/Å	11.1569(3)	17.5355(7)	10.6280(3)
c/Å	23.3671(6)	25.7191(8)	12.4365(4)
α/°	90	90	100.939(2)
β/°	90	90.066(5)	100.910(2)
γ/°	90	90	97.918(2)
V/Å^3	2368.66(10)	13691.6(10)	1265.74(7)
Z	4	12	1
T/K	173(2)	173(2)	223(2)
D_{calcd}/g cm^{-3}	1.605	1.276	2.189
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	2.296	1.294	5.780
F(000)	1152	5352	780
R1 (obs data)[a]	0.0195	0.0864	0.0254
wR2 (obs data)[b]	0.0438	0.2032	0.0616
Flack param	0.006(6)	0.007(17)	–

Table A4 Crystallographic data for complexes **55**, **56** and **58**

	55	**56**	**58**
formula	$C_{24}H_{26}As_2Cl_2Pd$	$C_{24}H_{26}As_2I_2Pd$	$C_{26.5}H_{27}AsClI_2O_2PPd$
fw	641.59	824.49	878.52
space group	*C*2/c	*C*2/c	*P*-1
crystal system	Monoclinic	Monoclinic	Triclinic
a/Å	9.9807(6)	17.0458(9)	9.9521(3)
b/Å	14.9247(9)	7.5236(3)	11.7499(4)
c/Å	16.5276(13)	20.0657(8)	14.3409(5)
α/°	90	90	108.790(2)
β/°	100.005(2)	95.381(3)	91.610(2)
γ/°	90	90	111.672(2)
V/Å^3	2424.5(3)	2562.0(2)	1454.62(8)
Z	4	4	2
T/K	173(2)	173(2)	173(2)
D_{calcd}/g cm^{-3}	1.758	2.138	2.006
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	3.704	5.707	4.058
F (000)	1264	1552	837
R1 (obs data)[a]	0.0298	0.0179	0.0459
wR2 (obs data)[b]	0.0778	0.0428	0.1041
GOF on F^2	1.020	1.135	1.038

Table A5 Crystallographic data for complexes *trans*-(+)-**64a**, *exo*-(–)-**56b** and *endo*-(+)-**67a**

	trans-(+)-**64a**	*exo*-(–)-**66b**	*endo*-(+)-**67a**
formula	$C_{29}H_{31}ClNPPd$	$C_{28}H_{30}AsCl_4PPd$	$C_{27}H_{28}AsI_2PPd$
fw	566.37	720.61	818.58
space group	$P2_12_12_1$	$P1$	$P2_12_12_1$
crystal system	Orthorhombic	Triclinic	Orthorhombic
a/Å	13.0949(8)	8.5524(3)	10.3021(4)
b/Å	13.3829(7)	10.8891(4)	14.7810(7)
c/Å	15.0270(8)	15.9999(5)	18.3942(8)
α/°	90	99.245(2)	90
β/°	90	93.378(2)	90
γ/°	90	91.177(2)	90
V/Å^3	2633.4(3)	1467.45(9)	2801.0(2)
Z	4	2	4
T/K	173(2)	173(2)	173(2)
D_{calcd}/g cm^{-3}	1.429	1.631	1.941
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	0.884	2.186	4.110
F(000)	1160	720	1560
R1 (obs data)[a]	0.0568	0.0372	0.0363
wR2 (obs data)[b]	0.1258	0.0746	0.0917
Flack param	–0.02(7)	0.026(6)	0.027(14)

Table A6 Crystallographic data for complexes *exo*-(–)-**67b**, *endo*-(–)-**72** and (S_c,S_{As})-**76**

	exo-(–)-**67b**	*endo*-(–)-**72**	(S_c,S_{As})-**76**
formula	$C_{27}H_{28}AsI_2PPd$	$C_{49}H_{52}AsCl_7NO_4PPd$	$C_{35}H_{47}AsClNO_2Pd$
fw	818.58	1179.36	730.51
space group	*P*1	$P2_12_12_1$	$P2_12_12_1$
crystal system	Triclinic	Orthorhombic	Orthorhombic
a/Å	9.0804(5)	12.6237(3)	11.8491(4)
b/Å	9.1106(9)	17.1807(4)	13.7371(4)
c/Å	9.3713(5)	23.4194(5)	21.0572(7)
α/°	100.727(4)	90	90
β/°	110.589(3)	90	90
γ/°	98.244(4)	90	90
V/Å^3	694.44(9)	5079.3(2)	3427.53(19)
Z	1	4	4
T/K	173(2)	173(2)	223(2)
D_{calcd}/g cm^{-3}	1.957	1.542	1.416
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	4.144	1.455	1.608
F(000)	390	2392	1504
R1 (obs data)[a]	0.0416	0.0278	0.0522
wR2 (obs data)[b]	0.1011	0.0678	0.1399
Flack param	0.022(15)	0.002(5)	0.043(14)

Table A7 Crystallographic data for complexes (–)-**80**, (–)-**83** and (+)-**92**

	(–)-**80**	(–)-**83**	(+)-**92**
formula	$C_{23}H_{25}AsCl_5PPd$	$C_{23}H_{25}AsBr_2Cl_3PPd$	$C_{26}H_{29}AsClNPt$
fw	690.97	779.89	660.96
space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
crystal system	Orthorhombic	Orthorhombic	Orthorhombic
a/Å	10.1493(3)	10.2852(3)	9.2070(3)
b/Å	15.0866(4)	14.9894(5)	11.1969(4)
c/Å	17.9988(5)	18.0683(5)	23.6013(8)
α/°	90	90	90
β/°	90	90	90
γ/°	90	90	90
V/Å^3	2755.95(13)	2785.57(15)	2433.05(14)
Z	4	4	4
T/K	296(2)	173(2)	298(2)
D_{calcd}/g cm^{-3}	1.665	1.860	1.804
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	2.418	5.070	7.239
F(000)	1368	1512	1280
R1 (obs data)[a]	0.0351	0.0374	0.0195
wR2 (obs data)[b]	0.0846	0.0828	0.0463
Flack param	–0.002(10)	0.016(8)	–0.005(6)

Table A8 Crystallographic data for complexes (+)-**94**, **98** and **99**

	(+)-**94**	**168**	**99**
formula	$C_{27}H_{28}AsCl_4OPPt$	$C_{28}H_{29}AsCl_2NPPdS$	$C_{28}H_{29}AsBr_2NPPdS$
fw	811.27	694.77	783.69
space group	*P*1	$P2_1/n$	$P2_1/n$
crystal system	Triclinic	Monoclinic	Monoclinic
a/Å	8.9256(8)	12.5118(9)	12.4925(5)
b/Å	9.1485(4)	18.4493(14)	18.7724(8)
c/Å	10.0788(4)	13.1877(9)	13.3221(6)
α/°	113.854(2)	90	90
β/°	100.832(3)	110.221(4)	109.532(2)
γ/°	95.984(3)	90	90
V/Å^3	724.24(8)	2856.5(4)	2944.4(2)
Z	1	4	4
T/K	173(2)	173(2)	173(2)
D_{calcd}/g cm^{-3}	1.860	1.616	1.768
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	6.421	2.134	4.603
F(000)	392	1392	1536
R1 (obs data)[a]	0.0163	0.0619	0.0238
wR2 (obs data)[b]	0.0382	0.1546	0.0505
Flack param	–0.003(3)	-	-

Table A9 Crystallographic data for complexes **101**, (–)-**103** and (S_c,R_{As})-**105**

	101	(–)-**103**	(S_c,R_{As})-**105**
formula	$C_{26}H_{26}AsI_2PPdS$	$C_{26}H_{26}AsCl_2PPtS$	$C_{40}H_{42}AsINPPtS$
fw	836.62	742.41	996.69
space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
crystal system	Orthorhombic	Orthorhombic	Orthorhombic
a/Å	9.6620(4)	9.4457(2)	13.4708(3)
b/Å	12.8878(6)	12.4631(3)	16.2313(4)
c/Å	22.2332(8)	21.4517(5)	17.7194(4)
V/Å^3	2768.5(2)	2525.35(10)	3874.32(16)
Z	4	4	4
T/K	173(2)	173(2)	173(2)
D_{calcd}/g cm^{-3}	2.007	1.953	1.709
λ/Å	0.71073	0.71073	0.71073
μ/mm^{-1}	4.233	7.228	5.389
F(000)	1592	1432	1936
R1 (obs data)[a]	0.0270	0.0232	0.0305
wR2 (obs data)[b]	0.0569	0.0454	0.0706
Flack param	-	–0.001(4)	–0.003(6)

[a] $R1 = \sum||F_o| - |F_c|| / \sum|F_o|$;

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