**DEVELOPMENT OF PHOSPHAPALLADACYCLES
AS POTENTIAL CATALYSTS
FOR ASYMMETRIC SYNTHESIS**

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Abbreviations and Symbols

Ad	adamantyl
An	anisoyl
Ar	aryl
Bn	benzyl
Bu	butyl
<i>ca.</i>	about (Latin <i>circa</i>)
calcd	calculated
conc.	concentrated
Cp	cyclopentadienyl
CSA	10-camphorsulfonic acid
Cy	cyclohexyl
d	doublet, day(s)
dba	<i>trans,trans</i> -dibenzylideneacetone
DBTA	dibenzoyltartaric acid
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
dd	doublet of a doublet
ddd	doublet of a doublet of a doublet
de	diastereomeric excess
dec	decomposed
deg	degree(s)
dm	decimeter
DMPP	3,4-dimethyl-1-phenylphosphole
dppe	1,2-bis(diphenylphosphino)ethane

dr	diastereomeric ratio
ee	enantiomeric excess
eq	equatorial
equiv.	equivalent
Et	ethyl
<i>et. al.</i>	and others (Latin <i>alii</i>)
g	gram(s)
h	hour(s)
Hex	hexyl
Hz	hertz
<i>i.e.</i>	that is (Latin <i>id est</i>)
i	iso
IPA	isopropyl alcohol
<i>J</i>	coupling constant
m	multiplet
<i>m</i>	<i>meta</i>
Me	methyl
Men	menthyl
min	minute(s)
mp	melting point
MS(ESI)	Mass Spectrometry (Electrospray Ionization)
MS(FAB)	Mass Spectrometry (Fast Atom Bombardment)
<i>n</i>	straight chain
NMR	Nuclear Magnetic Resonance
NOE	Nuclear Overhauser Effect

<i>o</i>	<i>ortho</i>
<i>p</i>	<i>para</i>
Pr	propyl
Ph	phenyl
ppm	parts per million
q	quartet
qn	quintet
<i>R</i>	clockwise configuration of an absolute stereochemistry as defined by Cahn-Ingold-Prelog sequence rule (Latin <i>rectus</i>)
ROESY	2D rotating frame Nuclear Overhauser Enhancement
r.t.	room temperature
<i>S</i>	counter-clockwise configuration of an absolute stereochemistry as defined by Cahn-Ingold-Prelog sequence rule (Latin <i>sinister</i>)
s	singlet
<i>s</i>	secondary
t	triplet
<i>t</i>	tertiary
THF	tetrahydrofuran
tol	tolyl
Ts	tosyl
Å	angstrom(s)
δ	NMR chemical shift in ppm
$[\alpha]_D$	specific rotation measured at sodium D line (589 nm)

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Summary

This thesis describes the design and synthesis of chiral phosphapalladacycles and their applications in catalytic asymmetric reactions.

An introduction on the syntheses and applications of chiral phosphines and phosphapalladacycles, as well as the research development and the objective of this project were presented in Chapter 1.

Chapter 2 describes the synthesis of a 5-membered *ortho*-palladated complex derived from the chiral ligand 1-(2', 5'-diisopropylphenyl)ethyldiphenylphosphine. The phosphine was synthesized as a racemate by treating 1-chloro-1-(2', 5'-diisopropylphenyl)ethane with sodium diphenylphosphide. The ligand was optically resolved using the naphthylamine palladium template (R,R) -di- μ -chlorobis{1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}dipalladium(II), (*R*)-**4**. The diastereomeric products were separated by column chromatography and fractional crystallization. The naphthylamine auxiliary was removed chemoselectively by treatment with concentrated hydrochloric acid. *Ortho*-palladation of the coordinated ligand was accomplished by stirring with silver(II) hexafluorophosphate followed by lithium chloride to form an optically active chloro-bridged dimeric complex. Alternatively, the free phosphine was coordinated to an achiral benzylamine template di- μ -chlorobis{[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}dipalladium(II), **1** as the palladium source for *ortho*-palladation. The resulting racemic chloro-bridged dimeric complexes were resolved by conversion to their (*S*)-proline derivatives followed by fractional crystallization. The optically active chloro-bridged dimeric complex

was converted to its bis(acetonitrile) derivative for use as catalyst in promoting the asymmetric synthesis of P-stereogenic diarylphosphinites.

In Chapter 3, a phosphapalladacycle was prepared from a chiral phosphine ligand synthesized by catalytic asymmetric hydrophosphination reaction of a 1-naphthyl-based enone with diphenylphosphine. The template (*R*)-**4** was used to optically purify the phosphine ligand as well as providing a palladium source for *ortho*-palladation to form the palladacycle. Alternatively, **1** was used as the palladium source and the palladacycles could be optically purified by conversion to their (*S*)-proline derivatives followed by fractional crystallization. The hydrophosphination reaction of the 1-naphthyl-based enone was repeated with the racemic mixture of a chiral secondary phosphine *o*-anisylphenylphosphine. The resulting C*-P* phosphine ligand was coordinated to (*R*)-**4** for separation of stereoisomers and *ortho*-palladation, however the separation could not be done cleanly and *ortho*-palladation resulted in a racemic complex. The achiral **1** was used to coordinate to the free phosphine ligand and the diastereomeric pairs of the stereoisomers could then be separated by column chromatography. The major pair of enantiomers was *ortho*-palladated to form a racemic chloro-bridged dimeric complex, followed by conversion to their (*S*)-prolinate derivatives and separation by fractional crystallization to give an optically pure C*-P* palladacycle with a C chiral centre and a P chiral centre.

In Chapter 4, the syntheses of isoquinoline-based palladium complexes were attempted. The asymmetric hydrophosphination reactions of an isoquinoline-based enone with secondary phosphines could be promoted with stoichiometric or catalytic amount of the bis(acetonitrile) naphthylamine complex (*R*)-**5**. The stoichiometric reaction stereoselectively produced a P,N

bidentate ligand coordinated to the metal complex. The stereoisomers were separated by column chromatography and fractional crystallization. Attempts to chemoselectively remove the naphthylamine auxiliary by treatment with concentrated hydrochloric acid resulted in a dichloro complex which racemized when left standing in solution. The catalytic reaction produced the free P,N ligand which readily racemized in solution.

CHAPTER 1: INTRODUCTION

1.1 Chiral Phosphines

In the past decades, selective preparation of optically pure compounds has become the focus of organic synthesis. Asymmetric catalysis has been found to be an economical and efficient way to achieve this goal. Transition metal complexes containing chiral phosphine ligands are known to be effective catalysts in asymmetric hydrogenation reactions.¹ The importance of chiral phosphine ligands in these reactions has led to the design and synthesis of a huge number of ligands.²

The optical activity of a phosphine can be derived from a P-stereogenic centre, chirality in the side chain (centre, axial or planar chirality), or less commonly a combination of a P-chiral centre and side chain chirality. The most prominent P-stereogenic chiral phosphine is DIPAMP developed by Knowles et al. in 1975,³ which has found application in the asymmetric hydrogenation synthesis of L-DOPA used in treating Parkinson's Disease.⁴⁻⁵ An important chiral phosphine with axial chirality in the side chain is BINAP developed by Noyori in 1980,⁶⁻⁷ which was used in the asymmetric hydrogenation of various olefins and ketones as well as other asymmetric reactions.⁸ For their work on chirally catalyzed hydrogenation reactions, Knowles and Noyori were awarded the Nobel Prize in Chemistry in 2001.⁹ Other notable chiral phosphines include DIOP,¹⁰ DuPhos,¹¹ Chiraphos,¹² Josiphos,¹³ TangPhos,¹⁴ and DuanPhos¹⁵ (Figure 1.1).

Figure 1.1 Examples of chiral phosphines

1.1.1 Methods of Preparation of Chiral Phosphines

The importance of chiral phosphine ligands in asymmetric synthesis has led to various attempts at developing synthetic strategies to produce them efficiently. However, the lack of a natural pool of chirality, as well as the high chemical reactivity and configurational instability of the phosphorus stereocenters,¹⁶⁻¹⁷ makes the synthesis of this class of compounds a challenging process. There are two methods to prepare chiral phosphines: (1) chiral resolution and (2) asymmetric induction.

(1) Chiral resolution

The chiral resolution process is used to prepare an optically active compound from its racemic mixture. First, the compound is prepared in its racemic form from prochiral starting materials. A racemic mixture of a chiral compound contains equal amounts of its enantiomers. Enantiomers have identical chemical and physical properties, except for their ability to rotate plane-polarized light in equal amounts but in opposite directions, which make them difficult to separate. In the chiral resolution process, the enantiomers are

converted into a diastereomeric mixture through coordination with an optically pure resolving agent. Examples of resolving agents used are (*R,R*)-dibenzoyltartaric acid ((-)-DBTA) and (*S*)-(+)-10-camphorsulfonic acid ((+)-CSA). As diastereomers have different physical properties, the mixture can then be separated *via* column chromatography and fractional crystallization. After the separation is complete, the resolving agent is removed to give the desired optically pure product.

The synthesis of BINAP as reported by Noyori involves chiral resolution by either (+)-CSA or (-)-DBTA (Scheme 1.1).⁷

Scheme 1.1

(2) Asymmetric induction

Asymmetric induction refers to the preferential formation of one enantiomer or diastereomer in a chemical reaction by the influence of a chiral feature present in the substrate, reagent, catalyst or environment.¹⁸ There are three principle ways to introduce chirality in the product: (i) internal asymmetric induction, (ii) relayed asymmetric induction and (iii) external asymmetric induction.¹⁹

In internal asymmetric induction, the chiral centre of the chiral substrate is incorporated into the final product. For example, (*S,S*)-Chiraphos can be synthesized from (*2R,3R*)-2,3-butanediol through reaction with tosyl chloride and lithium diphenylphosphide (Scheme 1.2).¹²

Scheme 1.2

In relayed asymmetric induction, chirality is relayed through the use of a chiral auxiliary. The chiral auxiliary is introduced prior to the chirality generation step, and is removed after the new chiral centres are formed (Scheme 1.3).²⁰

Scheme 1.3

In external asymmetric induction, a chiral catalyst is used to control the stereoselectivity of the reaction in the transition state. As the catalyst is not consumed in the asymmetric catalytic process, only a small amount is needed in the reaction to give the product with high enantioselectivity (Scheme 1.4).²¹

Scheme 1.4

1.2 Palladacycles

Palladium compounds containing at least one metal-carbon bond intramolecularly stabilized by at least one donor atom, termed cyclopalladated compounds or palladacycles, are one of the most popular classes of organopalladium derivatives.²²

Palladacycles can be divided into two types: the anionic four-electron donor or CY type; and the anionic six-electron donor or YCY type, also known as the pincer type.²²

This thesis focuses on the discussion of the CY type of palladacycles.

In 1968, Cope reported the cyclopalladation of *N,N*-dimethylbenzylamine with a palladium salt, lithium tetrachloropalladate(II), to form a benzylamine palladacycle **1** (Scheme 1.5).²³

Scheme 1.5

In 1971, Otsuka reported the formation of a chiral benzylamine palladacycle (*S*)-**2** by the treatment of a chiral benzylamine with sodium tetrachloropalladate(II) (Scheme 1.6).²⁴ This chiral palladacycle (*S*)-**2** was used in the chiral resolution of various tertiary phosphines.

Scheme 1.6

In 1977, Tani reported a naphthalene-based chiral palladacycle (*S*)-**3** synthesized from the reaction between a chiral naphthylamine and sodium tetrachloropalladate(II) in the presence of triethylamine (Scheme 1.7).²⁵

Scheme 1.7

In 1982, Wild and co-workers reported a chiral naphthalene-based palladacycle (*R*)-**4** by treating a chiral naphthylamine with lithium tetrachloropalladate(II) (Scheme 1.8).²⁶

Scheme 1.8

Complex (*R*)-**4** was found to be more efficient in the chiral resolution process than the benzylamine analogue (*S*)-**2**. The interaction between the H(8) on the naphthyl ring with the methyl group on 5-membered palladacycle ring forces the methyl group to adopt the axial position, and locking the 5-membered ring in the δ position. On the other hand, the 5-membered ring on the benzylamine counterpart undergoes rapid transformation between the δ and λ conformations in solution, making it less effective in controlling stereoselectivity.²⁷

In 1992, Leung and co-workers reported the conversion of chloro-bridged (*R*)-**4** into its bis(acetonitrile) derivative (*R*)-**5** (Scheme 1.9), providing two active sites for the coordination of phosphines and other functional groups.²⁸

Scheme 1.9

Complex (*R*)-**5** was successfully used as a stoichiometric template to control the stereoselectivity of various reactions such as Diels–Alder, hydroamination, hydrophosphination and hydroarsination reactions.¹⁶ In 2010, the use of (*R*)-**5** was extended to catalyze asymmetric hydrophosphination reactions in a catalytic amount.²⁹

In 2003, Leung and co-workers reported the synthesis of a phosphine analogue of (*R*)-**4** via a multi-step approach, forming the complex (*R*)-**6**.³⁰ The

phosphapalladacycle (*R*)-**6** was converted to its bis(acetonitrile) complex (*R*)-**7** to be used in catalytic hydrophosphination reactions (Scheme 1.10).³¹

Scheme 1.10

Comparing (*R*)-**5** and (*R*)-**7**, (*R*)-**7** was found to be the better performing catalyst, as it offers a higher yield, higher stereoselectivity and faster reaction time (Scheme 1.11).³²

Scheme 1.11

The enhanced reactivity of (*R*)-**7** is due to the ability of the phosphorus in the palladacycle ring to accommodate extensive back-donation from the metal centre, making the activation of the diphenylphosphine and its nucleophilic attack on the *trans*-chalcone substrate more facile. The faster reaction time can be attributed to the classic features that *trans* P-Pd-P bonds are less stable than *trans* N-Pd-P bonds, thus resulting in faster product elimination in the catalytic cycle. In addition, the larger phenyl groups in (*R*)-**7**

phosphapalladacycles *via* asymmetric synthesis to simplify or eliminate the process of separating the enantiomers.

This thesis is divided into four chapters. Chapter 2 describes the synthesis of a new phosphapalladacycle *via* chiral resolution and its application in catalytic asymmetric synthesis. Chapter 3 deals with the preparation of a new naphthalene-based phosphapalladacycle *via* catalytic asymmetric synthesis of an enone, and the development of a C*-P* palladacycle using the same method. Chapter 4 investigates the formation of isoquinoline-based P-N bidentate ligands *via* asymmetric synthesis controlled by a palladacycle in both stoichiometric and catalytic amounts.

CHAPTER 2: CYCLOPALLADATION OF 1-[(2,5-DIISOPROPYLPHENYL)ETHYL]DIPHENYLPHOSPHINE

2.1 Introduction

The naphthylamine template (*R*)-**4** has been shown to be effective in controlling stereoselectivity of various reactions, including Diels-Alder reactions to form diphosphines.³⁴⁻³⁶

In addition to the steric effect by H(8) on the naphthyl ring, the regioselectivity in the Diels-Alders reaction is also influenced by the substituent on the C(3) position. The synthesis of a 3,6-dimethylnaphthylamine template and its use in Diels-Alder reactions showed a repulsion between the methyl group on C(3) and the phosphines that affected the selectivity of the reaction.³⁷

In this chapter, a 3,6-diisopropylbenzylphosphine template is designed to incorporate an isopropyl group in the C(3) position, another isopropyl group in the C(6) position to provide the steric effect to lock the palladacycle ring, as well as a diphenylphosphine group as phosphine-based templates have been showed to have a better stereoselectivity than amine-based templates. The new template is tested as a catalyst in hydrophosphination reaction as well as the asymmetric synthesis of P-chiral diarylphosphinites to study its effectiveness.

2.2 Research Objectives

The research objectives are to synthesize the phosphine analogue of the 3,6-dimethylnaphthylamine, and to attempt cyclopalladation of the phosphine to form a phosphapalladacycle. The properties of the phosphapalladacycle are then studied.

2.3 Results and Discussion

2.3.1 Synthesis of the racemic phosphine ligand **11**

The phosphine ligand was synthesized *via* a multistep approach. Aldehyde **8** was treated with methyl magnesium bromide to form a racemic alcohol ($\pm$)-**9**. The chlorination of ($\pm$)-**9** was done by adding phosphorus trichloride, resulting in ($\pm$)-**10**. The chloride underwent nucleophilic displacement by sodium diphenylphosphide to yield the racemic tertiary phosphine ($\pm$)-**11** (Scheme 2.1).

2.3.2 Optical resolution of **11** by coordination to (*R*)-**4**

The free phosphines were coordinated to (*R*)-**4** and separated by column chromatography and fractional crystallization (Scheme 2.2).

Both diastereomers (*R,R*)-**12** and (*R,S*)-**12** were successfully crystallized as yellow crystals. The less soluble (*R,S*)-**12** crystallized first as fine yellow needles and X-ray crystallography was performed to confirm the stereoconfiguration (Figure 2.1).

Figure 2.1 X-ray molecular structure of (*R,S*)-**12**

Table 2.1 Selected bond lengths (Å) and angles (°) of (*R,S*)-**12**

Pd(1)-C(1)	1.999(2)	Pd(1)-N(1)	2.1474(17)
Pd(1)-P(1)	2.2634(6)	Pd(1)-Cl(1)	2.4091(5)
C(11)-N(1)	1.511(3)	C(13)-N(1)	1.478(3)
C(14)-N(1)	1.488(3)	C(15)-P(1)	1.832(2)
C(21)-P(1)	1.824(2)	C(27)-P(1)	1.871(2)
C(27)-C(29)	1.510(3)	C(29)-C(30)	1.399(3)
C(1)-Pd(1)-N(1)	81.22(8)	C(1)-Pd(1)-P(1)	95.61(6)
N(1)-Pd(1)-P(1)	169.12(5)	C(1)-Pd(1)-Cl(1)	169.02(6)
N(1)-Pd(1)-Cl(1)	91.68(5)	P(1)-Pd(1)-Cl(1)	92.862(19)
C(15)-P(1)-Pd(1)	117.65(8)	C(21)-P(1)-Pd(1)	113.69(8)
C(27)-P(1)-Pd(1)	105.87(7)	C(29)-C(27)-P(1)	113.83(15)
C(30)-C(29)-C(27)	119.82(19)		

The X-ray crystallographic study showed that the chiral centre at C(27) adopts the *S* configuration.

2.3.3 Removal of naphthylamine auxiliary and *ortho*-palladation

The naphthylamine auxiliary was removed upon the addition of concentrated hydrochloric acid to (*R,S*)-**12** to give (*S,S*)-**13** (Scheme 2.3). The reaction proceeded in very high yield of 99%.

Scheme 2.3

Two methods were used to generate the *ortho*-palladation product. In the first method, (*S,S*)-**13** was heated to reflux in ethanol in the presence of sodium acetate trihydrate. (*S,S*)-**14** was formed in the yield of 32% (Scheme 2.4).

Scheme 2.4 Method 1

In the second method, (*S,S*)-**13** was stirred with silver(I) hexafluorophosphate, then followed by lithium chloride to form (*S,S*)-**14**, giving a yield of 35% (Scheme 2.5).

Scheme 2.5 Method 2

2.3.4 Coordination to **1** and cyclopalladation of **11**

An alternative approach was explored by using achiral benzylamine template **1** as palladium source (Scheme 2.6).

Scheme 2.6

The benzylamine auxiliary was removed by concentrated hydrochloric acid and *ortho*-palladation was carried out by refluxing with sodium acetate trihydrate in ethanol to form the racemic dimer **14** (Scheme 2.7).

Scheme 2.7

Optical resolution of the racemic dimer **14** was attempted by using potassium (S)-prolinate to form the diastereomers (*R,S_N*)-**16** and (*S,S_N*)-**16** (Scheme 2.8).

Scheme 2.8

Attempts to separate the diastereomers by crystallization using various solvents were unsuccessful.

2.3.5 Coordination of (*S,S*)-**14** with triphenylphosphine and dppe

The properties of (*S,S*)-**14** were studied by coordination to triphenylphosphine and 1,2-bis(diphenylphosphino)ethane (dppe).

Triphenylphosphine was added to (*S,S*)-**14** to give a mixture of *trans* and *cis* products (Scheme 2.9), however they could not be induced to crystallized.

Scheme 2.9

The bidentate ligand dppe was coordinated to (*S,S*)-**14** to form the monomer complex (*S*)-**18** (Scheme 2.10).

Scheme 2.10

Complex (*S*)-**18** was successfully crystallized from dichloromethane-hexane to give yellow crystals, and X-ray crystallographic study was performed (Figure 2.2).

Figure 2.2 X-ray molecular structure of (*S*)-**18**

Table 2.2 Selected bond lengths (Å) and angles (°) of (S)-18

Pd(1)-C(1)	2.082(4)	Pd(1)-P(1)	2.2738(12)
Pd(1)-P(3)	2.3130(12)	Pd(1)-P(2)	2.3473(12)
C(1)-C(12)	1.406(6)	C(12)-C(13)	1.527(6)
C(13)-P(1)	1.856(4)	C(15)-P(1)	1.822(4)
C(21)-P(1)	1.803(5)	C(39)-C(40)	1.531(6)
C(39)-P(2)	1.839(4)	C(40)-P(3)	1.828(5)
C(1)-Pd(1)-P(1)	76.24(13)	C(1)-Pd(1)-P(3)	97.32(13)
P(1)-Pd(1)-P(3)	156.70(4)	C(1)-Pd(1)-P(2)	168.31(13)
P(1)-Pd(1)-P(2)	108.15(4)	P(3)-Pd(1)-P(2)	82.68(4)
C(12)-C(1)-Pd(1)	119.4(3)	C(1)-C(12)-C(13)	116.1(4)
C(12)-C(13)-P(1)	102.7(3)	C(13)-P(1)-Pd(1)	98.96(15)
C(40)-C(39)-P(2)	109.3(3)	C(39)-C(40)-P(3)	108.2(3)
C(39)-P(2)-Pd(1)	109.52(15)	C(40)-P(3)-Pd(1)	108.30(15)

X-ray structure analysis of (S)-**18** showed that the stereogenic centre at C(13) adopts the *S* absolute configuration. The crystal structure obtained confirmed the formation of the cyclopalladated 5-membered ring structure. The geometry at the Pd centre is distorted square planar with angles of 76.24(13)-108.15(4)° and 156.70(4)-168.31(13)°. The C(14) methyl group is in the axial position, suggesting that steric repulsion with the isopropyl group on C(8) took place as expected.

2.3.6 Use of bis(acetonitrile) complex of (S,S)-**14** in promoting asymmetric reactions

The dichloro-bridge complex (S,S)-**14** can be converted to a bis(acetonitrile) complex (S)-**19** by treatment with a silver(I) salt in the presence of acetonitrile (Scheme 2.11).

Scheme 2.11

2.3.6.1 Asymmetric hydrophosphination reaction of *trans*-chalcone

The hydrophosphination reaction of *trans*-chalcone with diphenylphosphine was attempted using (S)-19 as the catalyst for comparison with (R)-5 and (R)-7 (Scheme 2.12).

Scheme 2.12

The reaction was found to be completed within 20 hours, indicated by formation of a new peak at δ -1.7 and the absence of the free diphenylphosphine peak in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum. The calculated yield from the spectrum is 95%. The complex (R)-4 was added to the free phosphine 21 to determine the ee of the reaction. The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (202 MHz, CDCl_3) showed two product peaks at δ 44.9 and 49.0 in the ratio of 1 : 1.34, giving an ee of 14.5%. This is very low compared to the 77% ee achieved by (R)-5²⁹ and the 98% ee achieved by (R)-7.³²

2.3.6.2 Asymmetric synthesis of P-chiral diarylphosphinites

Bis(acetonitrile) complex (S)-19 was also used in the asymmetric synthesis between racemic secondary phosphines and 2,5-

diphenylbenzoquinone for P-O bond formation. The resulting P-chiral diarylphosphinites can be functionalized by undergoing S_N2 reaction to generate various P-chiral phosphines derivatives.

2.3.6.2.1 (9-Phenanthryl)phenylphosphine with 2,5-diphenylbenzoquinone

Scheme 2.13

Table 2.3 Screening of reaction conditions for the formation of 24

Entry	Catalyst	Solvent	Temp (°C)	ee (%) ^a
1 ^b	Pd(OAc) ₂	CHCl ₃	r.t.	-
2	(<i>S</i>)- 7	CHCl ₃	-45	25
3	(<i>S</i>)- 7	DCM	-45	25
4	(<i>S</i>)- 7	DCM	-80	27
5	(<i>S</i>)- 7	THF	-80	-5
6	(<i>R</i>)- 7	CHCl ₃	-45	-25
7	(<i>S</i>)- 19	CHCl ₃	-45	2
8	(<i>S</i>)- 19	CHCl ₃	-60	-22

^a Determined by chiral HPLC analysis of **24**. IC column was used with eluant hexane:IPA = 98:2.

^b Reaction to produce racemic product for comparison purposes. Reaction completed in 2 hours at r.t.

The reaction between (9-phenanthryl)phenylphosphine with 2,5-diphenylbenzoquinone proceeded smoothly. (*S*)-**19** in entry 8, while requiring a lower temperature, produce similar selectivity with (*R*)/(*S*)-**7**.

The phosphinite sulfide **24** was crystallized as a racemic crystal and X-ray crystallography was performed (Figure 2.3).

Figure 2.3 X-ray molecular structure of *rac*-24

Table 2.4 Selected bond lengths (Å) and angles (°) of *rac*-24

C(1)-P(1)	1.8117(18)	C(15)-P(1)	1.8103(19)
O(1)-P(1)	1.6198(14)	P(1)-S(1)	1.9399(7)
C(21)-O(1)	1.408(2)	C(21)-C(22)	1.396(2)
C(22)-C(23)	1.392(3)	C(23)-C(24)	1.397(2)
C(24)-C(25)	1.400(3)	C(25)-C(26)	1.399(2)
C(21)-C(26)	1.386(2)	C(24)-O(2)	1.365(2)
C(22)-C(33)	1.488(2)	C(25)-C(27)	1.486(2)
O(1)-P(1)-C(15)	104.29(8)	O(1)-P(1)-C(1)	99.50(8)
C(15)-P(1)-C(1)	109.24(9)	O(1)-P(1)-S(1)	115.58(5)
C(15)-P(1)-S(1)	111.37(7)	C(1)-P(1)-S(1)	115.71(6)
C(21)-O(1)-P(1)	119.94(11)	C(26)-C(21)-C(22)	121.69(16)
C(26)-C(21)-O(1)	119.06(15)	C(22)-C(21)-O(1)	119.25(15)
O(2)-C(24)-C(23)	121.29(16)	O(2)-C(24)-C(25)	118.28(16)
C(23)-C(24)-C(25)	120.43(17)		

While the absolute stereoconfiguration was indeterminate, the crystal structure obtained confirmed the formation of the product with the presence of the P-O bond.

2.3.6.2.2 (1-Naphthyl)phenylphosphine with 2,5-diphenylbenzoquinone

Scheme 2.14

Table 2.5 Screening of reaction conditions for the formation of 27

Entry	Catalyst	Solvent	Temp (°C)	ee (%) ^a
1 ^b	Pd(OAc) ₂	CHCl ₃	r.t.	-
2	(<i>R</i>)- 7	CHCl ₃	-45	24 ^c
3	(<i>S</i>)- 7	CHCl ₃	-45	-13
4	(<i>S</i>)- 19	CHCl ₃	-45	25
5	(<i>S</i>)- 19	CHCl ₃	-60	27
6	(<i>S</i>)- 19	CHCl ₃	-80	31
7	(<i>S</i>)- 19	THF	-45	51

^a Determined by chiral HPLC analysis of **27**. AD-H column was used with eluant hexane:IPA = 95:5.

^b Reaction to produce racemic product for comparison purposes. Reaction completed in 2 hours at r.t.

^c Literature value³⁸

The reaction between (1-naphthyl)phenylphosphine with 2,5-diphenylbenzoquinone proceeded smoothly. The performance of (*S*)-**19** in entries 6 and 7 exceeds those of (*R*)/(*S*)-**7**.

2.4 Conclusion

1-[(2,5-Diisopropylphenyl)ethyl]diphenylphosphine was successfully synthesized as a racemate and optical resolution was done by using (*R*)-**4** as the

resolving agent. After the naphthylamine auxiliary was removed, *ortho*-palladation proceeded successfully to form the optically pure chloro-bridged dimer (*S,S*)-**14** with a cyclopalladated 5-membered ring. The structure of the cyclopalladated ring and the absolute configuration at the C chiral centre were confirmed by the X-ray crystal structure analysis of the dppe derivative (*S*)-**18**.

The phosphapalladacycles (*S,S*)-**14** was converted to its bis(acetonitrile) derivative (*S*)-**19** to be used as a catalyst in the asymmetric synthesis of P-chiral diarylphosphinites. The stereoselectivity of the new catalyst was found to be comparable to the catalyst (*S*)-**7**. The results could be further improved through the optimization of reaction conditions. The use of (*S*)-**19** as a catalyst in other reactions such as Diel-Alders reactions remains to be investigated.

2.5 Experimental

Reactions involving air-sensitive materials were performed under a positive pressure of nitrogen. NMR spectra were recorded on Bruker Avance 300, 400 and 500 spectrometers. ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR chemical shifts were referenced relative to SiMe_4 and H_3PO_4 respectively. Melting points were determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured on the specified solution in a 0.1 dm cell at 25°C with Atago AP-300 Automatic Polarimeter. Elemental Analyses and single crystal X-ray diffraction studies were performed by the Elemental Analysis Laboratory and X-ray Diffraction Laboratory, respectively, of the Division of Chemistry and Biological Chemistry at Nanyang Technological University. The starting materials, diphenylphosphine,³⁹ racemic 1-(2,5-diisopropylphenyl)ethanol,⁴⁰ **9**, di- μ -chlorobis{[(*N,N*-

dimethylamino)methyl]phenyl-*C,N*}dipalladium(II),²³ **1**, (*R,R*)-di- μ -chlorobis{1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}dipalladium(II),²⁶ (*R*)-**4**, racemic (1-naphthyl)phenylphosphine,^{38, 41} **25**, and bis(acetonitrile){(*R*)-1-[1-(diphenylphosphino)ethyl]naphthyl-*C,P*}palladium(II) perchlorate,³¹ (*R*)-**7**, were prepared according to literature procedures.

Racemic 1-chloro-1-(2,5-diisopropylphenyl)ethane, ($\pm$)-10. A dichloromethane solution (380 mL) of racemic 1-(2,5-diisopropylphenyl)ethanol, **9** (1.03 g, 5 mmol) was added very slowly dropwise to excess PCl_3 (5 mL) dissolved in the same solvent (250 mL) with vigorous stirring. The mixture was allowed to stir at r.t. for another 16 h. Water was then added to the mixture dropwise (to hydrolyse the excess PCl_3) with stirring. The organic phase was separated, further washed with water (3×100 mL), dried with anhydrous MgSO_4 and filtered. The dichloromethane was removed and the product was finally obtained as a colourless liquid upon distillation under reduced pressure, bp 62-64 °C, 0.3 mbar, 0.99 g (88%). ^1H NMR (400 MHz, CDCl_3) δ 1.24–1.32 (m, 12H, $\text{CH}(\text{CH}_3)_2$), 2.09 (d, $^3J_{\text{H-H}} = 6.8$ Hz, 3H, $\text{CH}(\text{CH}_3)\text{Cl}$), 2.91 (sep, $^3J_{\text{H-H}} = 6.9$ MHz, 1H, $\text{CH}(\text{CH}_3)_2$), 3.30 (sep, $^3J_{\text{H-H}} = 6.8$ MHz, 1H, $\text{CH}(\text{CH}_3)_2$), 5.59 (q, $^3J_{\text{H-H}} = 6.9$ MHz, 1H, $\text{CH}(\text{CH}_3)\text{Cl}$), 7.15 (dd, $^3J_{\text{H,H}} = 8.0$ Hz, $^4J_{\text{H,H}} = 1.6$ Hz, 1H, Ar- C_5H), 7.20 (d, $^3J_{\text{H,H}} = 8.0$ Hz, 1H, Ar- C_6H), 7.42 (d, $^4J_{\text{H,H}} = 1.2$ Hz, 1H, Ar- C_3H).

Racemic 1-(2,5-diisopropylphenyl)ethyldiphenylphosphine ($\pm$)-11. A dried THF solution (20 mL) of sodium diphenylphosphide, freshly prepared from sodium (0.15 g) and diphenylphosphine (0.75 g, 4.05 mmol), was added

dropwise to a solution of racemic 1-chloro-1-(2,5-diisopropylphenyl)ethane, **10** (0.91 g, 4.05 mmol) in dried THF (20 mL) with rapid stirring at r.t. White suspension obtained was evaporated until most of the THF has been removed. Fresh degassed water (40 mL) was added with stirring and the mixture was extracted with dichloromethane (3 × 40 mL). The combined organic extracts were dried by anhydrous MgSO₄, filtered and evaporated to give a colourless and air-sensitive liquid. The product was not isolated and directly used in further reactions.

Optical resolution of (±)-11. Isolation of chloro{(R)-1-[1-(N,N-dimethylamino)ethyl]naphthyl-C,N}[(R)-1-(2,5)-

diisopropylphenyl)ethyldiphenylphosphine]palladium(II), (R,R)-12 and chloro{(R)-1-[1-(N,N-dimethylamino)ethyl]naphthyl-C,N}[(S)-1-(2,5)-

diisopropylphenyl)ethyldiphenylphosphine]palladium(II), (R,S)-12. The racemic phosphine **11** was added with chiral template (R)-**4** (1.38 g, 2.03 mmol) in dichloromethane (5 mL). The resulting yellow solution was stirred for 30 min. The solvent was removed under reduced pressure to give a yellow solid; ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 45.8 (s) and δ 49.6 (s) in 1:1 ratio. The combined product was separated and purified by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant.

Chloro{(R)-1-[1-(N,N-dimethylamino)ethyl]naphthyl-C,N}[(S)-1-(2,5)-

diisopropylphenyl)ethyldiphenylphosphine]palladium(II), (R,S)-12. The product was recrystallized from dichloromethane-diethyl ether to give yellow crystals (1.26 g, 87%). mp 224-227 °C; ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 49.6 (s).

Chloro{(R)-1-[1-(N,N-dimethylamino)ethyl]naphthyl-C,N}[(R)-1-(2,5-diisopropylphenyl)ethyldiphenylphosphine]palladium(II), (R,R)-12. The product was recrystallized from dichloromethane-diethyl ether to give yellow crystals (1.23 g, 85%). mp 192-194 °C; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 45.8 (s).

(S,S)-Dichlorodi- μ -chlorobis[1-(2,5-diisopropylphenyl)ethyldiphenylphosphine]dipalladium(II), (S,S)-13. Conc. HCl (1 mL) was added to a solution of (R,S)-12 (0.40 g, 0.56 mmol) in dichloromethane (5 mL). The yellow solution turned orange upon adding the conc. HCl. The solution was stirred for an hour, and then quenched by water (50 mL). The organic phase was separated, further washed with water (2×50 mL), dried with anhydrous MgSO_4 and filtered. The solvent was removed under reduced pressure to give an orange solid (0.31 g, 99%). mp 169-172 °C; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 43.1 (s).

(S,S)-di- μ -chlorobis{1-[1-(diphenylphosphino)ethyl]-3,6-diisopropylphenyl-C,P}palladium(II), (S,S)-14. **Method 1:** (S,S)-13 (0.19 g, 0.17 mmol) was suspended in ethanol (25 mL) with sodium acetate trihydrate (0.7 g). The mixture was heated at reflux for 2 h, the solvent was then removed under reduced pressure. The crude product was redissolved in DCM, washed with water (50 mL $\times$ 2) and dried with anhydrous MgSO_4 . The product was purified by silica gel column chromatography to give a yellow solid (0.056 g, 32%). **Method 2:** (S,S)-13 (0.17 g, 0.16 mmol) was dissolved in dichloromethane (5 mL). AgPF_6 (0.16 g, 0.63 mmol, 4 equiv.) in water (1 mL) was added to the solution in darkness, and the solution was stirred for 2 h. The product mixture was washed with water (50 mL $\times$ 2) and dried with anhydrous MgSO_4 . The

organic extract was combined and the solvent was removed under reduced pressure. The product was redissolved in methanol (5 mL) and excess LiCl (0.3 g) was added. The solution was stirred overnight. The solvent was removed under reduced pressure. The product was redissolved in dichloromethane (5 mL), washed with water (50 mL x 2) and dried with anhydrous MgSO₄. The product was purified by silica gel column chromatography to give a yellow solid (0.056g, 35%). ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 57.3 (s).

Racemic chloro{[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}[1-(2,5-diisopropylphenyl)ethyldiphenylphosphine]palladium(II), (±)-15 The racemic phosphine **11** as prepared from **10** (0.91 g, 4.05 mmol) and sodium diphenylphosphide (4.05 mmol) was added with achiral template **1** (1.12 g, 2.03 mmol) in dichloromethane (5 mL). The resulting yellow solution was stirred for 30 min. The solvent was removed under reduced pressure to give a yellow solid. Recrystallization from dichloromethane-hexane gave orange crystals (1 g, 38%). NMR calculated conversion: 90%, calculated yield 43%; mp 139-142 °C; Anal. Calcd. for C₃₅H₄₃ClNPPd: C, 64.62; H, 6.66; N, 2.15. Found: C, 64.00; H, 6.68; N, 2.27. ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 51.0 (s).

Dichlorodi-μ-chlorobis[1-(2,5-diisopropylphenyl)ethyldiphenylphosphine]dipalladium(II), 13. Conc. HCl (1 mL) was added to a solution of **15** (0.52 g, 0.79 mmol) in dichloromethane (5 mL). The yellow solution turned orange upon adding the conc. HCl. The solution was stirred for an hour, and then quenched by water (50 mL). The organic phase was separated, further washed with water (2 × 50 mL), dried with anhydrous MgSO₄ and filtered. The solvent was removed under reduced

pressure to give an orange solid (0.43 g, 99%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 43.0 (s), 43.1 (s).

Di- μ -chlorobis{1-[1-(diphenylphosphino)ethyl]-3,6-diisopropylphenyl-*C,P*}dipalladium(II), 14.

Product **13** (0.43 g, 0.39 mmol) was suspended in ethanol (50 mL) with sodium acetate trihydrate (1.7 g). The mixture was heated at reflux for 2 h, the solvent was then removed under reduced pressure. The crude product was redissolved in DCM, washed with water (50 mL x 2) and dried with anhydrous MgSO_4 . The product was purified by silica gel column chromatography with hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant to give a yellow solid (0.19 g, 47%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 4 signals in ca. 3.5 : 1 : 1.2 : 5.1 ratio, δ 55.7 (s), 56.2 (s), 56.4 (s), 57.3 (s).

[(*S*)-Prolinato]{1-[1-(diphenylphosphino)ethyl]-3,6-diisopropylphenyl-*C,P*}palladium(II), 16.

The racemic complex **14** (0.18 g, 0.17 mmol) in dichloromethane (5 mL) was added to a solution of excess potassium (*S*)-prolinate generated from KOH (0.02 g) and (*S*)-proline (0.04 g) in methanol (5 mL). The combined solution was stirred for 2 h. The solvent was removed under reduced pressure, redissolved in dichloromethane, washed with water (50 mL x 2) and dried with anhydrous MgSO_4 . The dichloromethane was removed under reduced pressure to give a white solid. The products cannot be induced to crystallize despite the use of a variety of solvents. $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 4 signals in ca. 4.1 : 1.3 : 2.3 : 1 ratio, δ 55.2 (s), 54.6(s), 56.6(s), 60.4 (s).

Chloro{(S)-1-[1-(diphenylphosphino)ethyl]-3,6-diisopropylphenyl-C,P}(triphenylphosphine)palladium(II), (S)-17. Triphenylphosphine (0.08 g 0.31 mmol) was added to a solution of (S,S)-**14** (0.16 g, 0.155 mmol) in dichloromethane (5 mL). After stirring for 30 min, the solvent was removed under reduced pressure to give a yellow solid. The product cannot be induced to crystallize despite the use of a variety of solvents. $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 19.8 (d, $^2J_{\text{PP}} = 444.4$ Hz, coordinated PPh_3 ligand of *trans* geometric isomer), 49.3 (d, $^2J_{\text{PP}} = 444.4$ Hz, phosphapalladacycle *P* of *trans* geometric isomer).

[1,2-Bis(diphenylphosphino)ethane-*P,P'*]{(S)-1-[1-(diphenylphosphino)ethyl]-3,6-diisopropylphenyl-C,P}palladium(II) chloride, (S)-18. 1,2-Bis(diphenylphosphino)ethane (0.1 g, 0.25 mmol) was added to a solution of (S,S)-**14** (0.13 g, 0.13 mmol) in dichloromethane (5 mL). After stirring for 1 h, the solvent was removed under reduced pressure to give a yellow solid. The product was recrystallized from dichloromethane-hexane to give yellow crystals (0.053 g, 23%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 33.3 (dd, $^2J_{\text{P-P}(\text{trans})} = 358.0$ Hz, $^2J_{\text{P}(\text{trans})\text{-P}(\text{cis})} = 30.1$ Hz, coordinated dppe ligand *P trans* to phosphapalladacycle *P*), 40.4 (dd, $^2J_{\text{P}(\text{trans})\text{-P}(\text{cis})} = 30.1$ Hz, $^2J_{\text{P-P}(\text{cis})} = 15.7$ Hz, coordinated dppe ligand *P cis* to phosphapalladacycle *P*), 57.3 (dd, $^2J_{\text{P-P}(\text{trans})} = 358.0$ Hz, $^2J_{\text{P-P}(\text{cis})} = 15.7$ Hz, phosphapalladacycle *P*).

Bis(acetonitrile){(S)-1-[1-(diphenylphosphino)ethyl]-3,6-diisopropylphenyl-C,P}palladium(II) hexafluorophosphate, (S)-19. The dimeric complex (S,S)-**14** (0.11 g, 0.11 mmol) was dissolved in dichloromethane (5 mL) and acetonitrile (1 mL). A solution of silver(II) hexafluorophosphate (0.068 g, 0.27 mmol, 2.4 equiv.) in water (1 mL) was added. The mixture was stirred

vigorously for 2 h in darkness. The crude product was filtered through Celite, washed with water (50 mL x 2) and dried with anhydrous MgSO₄. The solvent was removed to give a yellow solid (0.077 g, 49%). mp 112-114 °C (dec); ³¹P{¹H} NMR (162 MHz, CDCl₃) δ 60.1 (s), -144.3 (septet, *J* = 712.1 Hz, PF₆⁻).

Asymmetric catalytic hydrophosphination of *trans*-chalcone, **20 with diphenylphosphine. Formation of 3-(diphenylphosphino)-1,3-diphenylpropan-1-one, **21**.** To a solution of diphenylphosphine (0.070 g, 0.37 mmol) in dichloromethane (5 mL), the catalyst (*S*)-**19** (0.013 g, 0.0187 mmol, 5 mol%) was added. The solution was stirred at r.t. for 5 min and then was cooled to -80 °C. Subsequently, **20** (0.086 g, 0.41 mmol, 1.1 equiv.) was added, followed by Et₃N (0.019 g, 0.0187 mmol, 0.5 equiv.) in DCM (1 mL) dropwise. The solution was subsequently stirred at -80 °C and the reaction was monitored by ³¹P{¹H} NMR. The reaction was found to be completed at 20 h. NMR calculated yield: 95%; ³¹P{¹H} NMR (202 MHz, CDCl₃) δ -1.7 (s).

Determination of ee of **21 by coordination to (*R*)-**4**.** The complex (*R*)-**4** (0.14 g, 0.205 mmol, 0.55 equiv.) in DCM (5 mL) was added to the free phosphine **21**. The solvent was removed to give a yellow solid. ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 44.9 (s), 49.0 (s) in 1 : 1.34 ratio, 14.5% ee.

(9-Phenanthryl)phenylphosphine, **22.** Mg turnings (0.7 g, 29 mmol, 1.5 equiv. of 9-phenanthryl bromide) and a few I₂ crystals were heated while stirring in dry THF (25 mL) until the mixture turned cloudy and slightly yellow. A solution of 9-phenanthryl bromide (5 g, 19 mmol) in dry THF (20 mL) was added dropwise into the mixture. The brown mixture was heated for 1 h and allowed to cool down to r.t. The resulting Grignard reagent was added dropwise

to a solution of dichlorophenylphosphine in dry THF at -78 °C over a period of 3 h, followed by an excess of LiAlH₄ at -78 °C, yielding a grey suspension. The mixture was allowed to warm up to r.t. and stirred for another 2 h. The reaction was quenched by a cautious addition of NH₄Cl in degassed water, followed by the removal of THF by distillation. The product was extracted with diethyl ether (3 x 50 mL) and the combined organic layers were dried with anhydrous MgSO₄. The diethyl ether was removed by distillation to give a white solid as product (5.2 g, 93%). ³¹P{¹H} NMR (202 MHz, CDCl₃) δ -48.0 (s).

[4-(2,5-Diphenylphenol)oxy](9-phenanthryl)phenylphosphine, 23. To a solution of (9-phenanthryl)phenylphosphine (0.098 g, 0.34 mmol) in degassed DCM (7 mL), the catalyst (*S*)-**7** (0.011 g, 0.017 mmol, 5 mol%) was added. The solution was stirred at r.t. for 2 min before it was cooled to -80 °C. 2,5-Diphenyl-1,4-benzoquinone (0.098 g, 0.38 mmol, 1.1 equiv.) was added, followed by dropwise addition of Et₃N (0.034 g, 0.34 mmol) in the solvent (0.5 mL). The solution was subsequently stirred for 12 h and the ³¹P{¹H} NMR spectrum was recorded. ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 111.0 (s).

[4-(2,5-Diphenylphenol)oxy](9-phenanthryl)phenylphosphine sulfide, 24. Excess sulfur was added to **23**. The solvent was removed and the crude product was purified by silica gel column chromatography to give a yellow solid (0.097 g, 49%). mp 184-186 °C; ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 80.0 (s). HPLC (Daicel Chiralpak IC), hexane/IPA = 98/2, flow 1.0 mL/min, 280 nm, *t*₁ = 36.9 min (minor), *t*₂ = 40.7 min (major) for 27% ee.

[4-(2,5-Diphenylphenol)oxy](1-naphthyl)phenylphosphine, 26. To a solution of (1-naphthyl)phenylphosphine (0.06 g, 0.26 mmol) in degassed solvent (7

mL), the catalyst (*S*)-**19** (0.009 g, 0.013 mmol, 5 mol%) was added. The solution was stirred at r.t. for 2 min before it was cooled to -45 °C. 2,5-Diphenyl-1,4-benzoquinone (0.073 g, 0.28 mmol, 1.1 equiv.) was added, followed by dropwise addition of Et₃N (0.026 g, 0.26 mmol) in the solvent (0.5 mL). The solution was subsequently stirred for 12 h and the ³¹P{¹H} NMR spectrum was recorded. ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 110.2 (s).

[4-(2,5-Diphenylphenol)oxy](1-naphthyl)phenylphosphine sulfide, 27.

Excess sulfur was added to **26**. The solvent was removed and the crude product was purified by silica gel column chromatography to give a yellow solid (0.085 g, 63%). ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 81.1 (s). HPLC (Daicel Chiralpak AD-H), hexane/IPA = 95/5, flow 1.0 mL/min, 280 nm, *t*₁ = 39.8 min (major), *t*₂ = 46.2 min (minor) for 51% ee.

CHAPTER 3: SYNTHESIS OF CP-PALLADACYCLES FROM CHIRAL PHOSPHINES VIA CATALYTIC ASYMMETRIC HYDROPHOSPHINATION REACTION

3.1 Introduction

Asymmetric hydrophosphination reaction controlled by a chiral template has been found to be an efficient way of generating a large class of chiral phosphines.

The multi-step approach to synthesize chiral phosphapalladacycles involves the synthesis of a racemic phosphine followed by a tedious optical resolution process.

In this chapter, a new method of synthesizing CP-palladacycles from catalytic asymmetric hydrophosphination reaction is explored. Through the optimization of reaction conditions, the chiral phosphines produced from the reaction can be directly cyclopalladated without the need of optical resolution. As 1-naphthyl-based palladacycles had been very effective in controlling stereoselectivity, a 1-naphthyl-based enone is used in the hydrophosphination reactions to synthesize 1-naphthyl-based palladacycles.

3.2 Research Objectives

The research objectives are to synthesize phosphapalladacycles from the phosphine products of catalytic asymmetric hydrophosphination reaction of 1-naphthyl based enones. The reaction conditions of hydrophosphination reaction are screened to optimize conditions for enantioenriched or enantiopure

phosphine products, reducing the complexities or eliminating the need to separate the enantiomers of the products.

The catalytic asymmetric hydrophosphination is extended to use a P-chiral secondary phosphine, *o*-anisylphenylphosphine, in place of diphenylphosphine, resulting in C*-P* phosphapalladacycles with two chiral centres at the carbon and phosphorus atoms.

3.3 Results and Discussion

3.3.1.1 Asymmetric catalytic hydrophosphination reaction with diphenylphosphine

Diphenylphosphine was dissolved in degassed dichloromethane and the catalyst (10-20 mol%) was added. The reaction was cooled to -80 °C and *E*-3-(1-naphthyl)-1-(4-chlorophenyl)-2-propen-1-one **28** was added. This was followed by the dropwise addition of the base triethylamine into the reaction mixture. The reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy (Scheme 3.1).

Scheme 3.1

Table 3.1 Screening of reaction conditions for the formation of 29

Entry	Catalyst	Cat mol %	Time (h)	Yield (%) ^a	Major isomer	ee (%)
1	(<i>R</i>)- 5	20	2	71	<i>S</i>	66
2	(<i>S</i>)- 7	10	26	83	<i>R</i>	70

^a Calculated from $^{31}\text{P}\{^1\text{H}\}$ NMR.

As shown in Table 3.1, the reaction was first carried out using the (*R*)-**5** catalyst with 20 mol % equivalent. The reaction was found to be completed within 2 hours. Monitoring by $^{31}\text{P}\{^1\text{H}\}$ NMR showed a single peak at δ 2.0.

The reaction was repeated using the (*S*)-**7** catalyst under the same reaction conditions but with only 10 mol % equivalent. The reaction took 26 hours to complete due to the low amount of catalyst used.

The reaction yield is calculated from the integration values of the various phosphorus peaks in the NMR spectra. It was found that the reaction catalyzed by (*S*)-**7** showed a higher yield at 83%.

3.3.1.2 Coordination to (*R*)-4** and cyclopalladation of **29****

From entry 1, the enantioenriched free phosphine **29** was coordinated to (*R*)-**4**, and the resulting complexes were separated by column chromatography and fractional crystallization (Scheme 3.2).

Scheme 3.2

Both diastereomers **(R,R)-30** and **(R,S)-30** were successfully crystallized as yellow crystals. The less soluble major product **(R,S)-30** crystallized first and X-ray crystallography was performed to confirm the stereoconfiguration (Figure 3.1).

Figure 3.1 X-ray molecular structure of (*R,S*)-30

Table 3.2 Selected bond lengths (Å) and angles (°) of (*R,S*)-30

Pd(1)-C(1)	1.999(3)	Pd(1)-N(1)	2.134(3)
Pd(1)-P(1)	2.2552(8)	Pd(1)-Cl(1)	2.4234(7)
C(11)-N(1)	1.511(4)	C(13)-N(1)	1.493(4)
C(14)-N(1)	1.490(4)	C(15)-P(1)	1.858(3)
C(34)-P(1)	1.837(3)	C(40)-P(1)	1.834(3)
C(15)-C(16)	1.526(8)	C(16)-C(17)	1.381(9)
C(15)-C(26)	1.532(4)	C(26)-C(27)	1.504(5)
C(27)-O(1)	1.214(4)	C(27)-C(28)	1.497(4)
C(1)-Pd(1)-N(1)	81.22(11)	C(1)-Pd(1)-P(1)	96.82(9)
N(1)-Pd(1)-P(1)	169.86(8)	C(1)-Pd(1)-Cl(1)	164.22(9)
N(1)-Pd(1)-Cl(1)	91.86(7)	P(1)-Pd(1)-Cl(1)	92.38(3)
C(40)-P(1)-Pd(1)	118.58(10)	C(34)-P(1)-Pd(1)	115.39(11)
C(15)-P(1)-Pd(1)	115.19(10)	C(16)-C(15)-P(1)	107.6(3)
C(17)-C(16)-C(15)	118.9(7)	C(16)-C(15)-C(26)	111.4(3)
C(27)-C(26)-C(15)	112.2(3)	O(1)-C(27)-C(28)	120.5(3)
O(1)-C(27)-C(26)	122.1(3)	C(28)-C(27)-C(26)	117.5(3)

The X-ray crystallographic study showed that the chiral centre at C(15) adopts the *S* configuration.

The naphthylamine auxiliary on (*R,S*)-**30** was removed by concentrated hydrochloric acid and the resulting complex (*S,S*)-**31** was refluxed in ethanol in the presence of sodium acetate trihydrate to give the *ortho*-palladated product (*S,S*)-**32** (Scheme 3.3).

Scheme 3.3

3.3.1.3 Coordination to **1** and cyclopalladation of **29**

Cyclopalladation of **29** generated from entry 1 was attempted by using the achiral benzylamine complex **1** in place of the naphthylamine complex (*R*)-**4** (Scheme 3.4).

Scheme 3.4

The resulting complex **33** was treated with concentrated hydrochloric acid to remove the benzylamine auxiliary, and then refluxed in ethanol in the presence of sodium acetate trihydrate to give the enantioenriched dimer **32** (Scheme 3.5).

Scheme 3.5

The *ortho*-palladated dimer product **32** was coordinated to (*S*)-proline to attempt separation of the enantiomers (Scheme 3.6).

Scheme 3.6

The major isomers (*Z*)/(*E*)-(*S*_C,*S*_N)-**34** were crystallized first to give white crystals, but the crystals were not suitable for X-ray crystallographic study. The stereoconfiguration of the crystallized product was corroborated by the coordination of (*S,S*)-**32** as synthesized in section 3.3.1.2 to (*S*)-proline and the ³¹P{¹H} NMR spectra were compared.

(*Z*)/(*E*)-(*S*_C,*S*_N)-**34** can be converted to the dichloro-bridged dimer (*S,S*)-**32** with the treatment of 1M hydrochloric acid to remove the (*S*)-proline auxiliary (Scheme 3.7).

Scheme 3.7

3.3.1.4 Coordination of (S,S)-32 with triphenylphosphine and dppe

The properties of (S,S)-32 were studied by coordination to triphenylphosphine and 1,2-bis(diphenylphosphino)ethane (dppe).

Triphenylphosphine was added to (S,S)-14 to give a mixture of *trans* and *cis* products (Scheme 3.8).

Scheme 3.8

The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum indicates the formation of a mixture of *cis* (δ 63.7 and 17.0) and *trans*-(P,P) (δ 53.2 and 25.6) isomers in the ratio of 1.4:1 in favour of the *cis* isomer. The peaks can be identified by their $^2J_{\text{P,P}}$ coupling constants. These were determined to be 26.7 Hz for *cis*-(S)-35 and 424.9 Hz for *trans*-(S)-35. (Figure 3.2)

Figure 3.2 $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of (*S*)-**35** (CDCl_3 , 202 MHz)

The bidentate ligand dppe was coordinated to (*S,S*)-**32** to form the monomer complex (*S*)-**36** (Scheme 3.9).

Scheme 3.9

Attempts to obtain crystals of (*S*)-**35** and (*S*)-**36** for X-ray crystallographic studies were unsuccessful.

3.3.2.1 Asymmetric catalytic hydrophosphination reaction with *o*-anisylphenylphosphine

The hydrophosphination reaction was extended to use *o*-anisylphenylphosphine in place of diphenylphosphine. The resulting free phosphine **37** has 2 chiral centres, giving 4 possible products (Scheme 3.10).

Scheme 3.10

Table 3.3 Screening of reaction conditions for the formation of **37**

Entry	Catalyst	Cat mol %	Solvent	Time (d)	Conversion (%) ^a	Yield (%) ^b
1	(<i>R</i>)- 5	15	CH ₂ Cl ₂	2	96	71
2	(<i>R</i>)- 5	15	CHCl ₃	2	97	81
3	(<i>R</i>)- 5	15	THF	1	99	68
4	(<i>R</i>)- 5	15	Acetone	2	99	76
5	(<i>S</i>)- 7	10	CH ₂ Cl ₂	4	93	79
6	(<i>S</i>)- 7	10	CHCl ₃	2.5	99	82
7	(<i>S</i>)- 7	10	THF	7	95	48
8	(<i>S</i>)- 7	10	Acetone	5	97	83

^{a,b} Calculated from ³¹P{¹H} NMR.

Compared to the hydrophosphination reaction of **28** with diphenylphosphine, the reaction with *o*-anisylphenylphosphine proceeded much more slowly, taking about 2 days to complete at room temperature.

3.3.2.2 Coordination to (*R*)-**4** and cyclopalladation of **37**

The free phosphines **37** were coordinated to (*R*)-**4** and the ³¹P NMR spectrum (202 MHz, CDCl₃) was recorded. However, instead of four peaks as

expected with 4 diastereomers, only two major peaks at δ 55.7 and δ 58.3 were observed in the NMR spectrum (Scheme 3.11).

Chemical shifts in $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CHCl_3): δ 55.7 = (*R*)-**38a**
 δ 58.3 = (*R*)-**38b**

Scheme 3.11

The compounds identified by the two NMR peaks (hereinafter referred to as (*R*)-**38a** for δ 55.7 and (*R*)-**38b** for δ 58.3 when coordinated with (*R*)-**4**) were separated by column chromatography. Attempts to recrystallize either compound were unsuccessful.

Ortho-palladation of the major product (*R*)-**38b** was attempted based on the method of synthesizing (*S*)-**6**. Firstly, the naphthylamine auxiliary was removed by concentrated hydrochloric acid, followed by refluxing the dimer product **39** with sodium acetate trihydrate in ethanol, giving the dimer product **40** (Scheme 3.12).

Scheme 3.12

Despite numerous attempts, **40** was unable to be induced to crystallized. Compound **40** was coordinated to triphenylphosphine to form compound **41** (Scheme 3.13).

Scheme 3.13

The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum indicated the formation of both *cis*- (δ 53.9 and 17.6) and *trans*-(R_C, R_P)-**14** (δ 49.5 and 25.5) in the ratio of 1:1.6 in favour of the *trans* isomer. $^2J_{\text{P,P}}$ coupling constants are 26.3 Hz for the *cis* isomer and 427.2 Hz for the *trans* isomer (Figure 3.3).

Figure 3.3 $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of **41** (CDCl_3 , 202 MHz)

Compound **41** was recrystallized from dichloromethane-hexane and X-ray crystallography was performed (Figure 3.4).

Figure 3.4 X-ray molecular structure of *cis-rac-41*

Table 3.4 Selected bond lengths (Å) and angles (°) of *cis-rac-41*

Pd(1)-C(1)	2.0654(12)	Pd(1)-P(1)	2.2058(4)
Pd(1)-Cl(1)	2.3705(4)	Pd(1)-P(2)	2.3876(4)
C(11)-P(1)	1.8594(12)	C(20)-P(1)	1.8202(12)
C(26)-P(1)	1.8146(12)	C(10)-C(11)	1.5041(16)
C(1)-C(10)	1.3894(16)	C(11)-C(12)	1.5401(16)
C(12)-C(13)	1.5196(17)	C(13)-O(1)	1.2225(16)
C(13)-C(14)	1.4895(18)	C(33)-P(2)	1.8229(12)
C(39)-P(2)	1.8147(13)	C(45)-P(2)	1.860(3)
C(1)-Pd(1)-P(1)	80.00(4)	C(1)-Pd(1)-Cl(1)	94.13(4)
P(1)-Pd(1)-Cl(1)	173.404(12)	C(1)-Pd(1)-P(2)	174.11(3)
P(1)-Pd(1)-P(2)	101.489(14)	Cl(1)-Pd(1)-P(2)	84.652(14)
C(10)-C(1)-Pd(1)	123.23(9)	C(1)-C(10)-C(11)	119.69(10)
C(10)-C(11)-P(1)	104.27(8)	C(11)-P(1)-Pd(1)	107.92(4)
C(10)-C(11)-C(12)	115.14(10)	C(12)-C(11)-P(1)	114.59(8)
C(13)-C(12)-C(11)	111.84(10)	O(1)-C(13)-C(14)	119.99(11)
O(1)-C(13)-C(12)	120.16(11)	C(14)-C(13)-C(12)	119.81(11)
C(39)-P(2)-Pd(1)	112.09(4)	C(33)-P(2)-Pd(1)	110.20(4)
C(45)-P(2)-Pd(1)	124.87(13)		

The crystal structure diagram showed the minor isomer *cis-rac-39*. The diagram also confirmed the formation of a 5-membered ring structure. However, the stereoconfiguration of the compound is indeterminate. No optical activity was observed when measured, suggesting that a racemic compound was obtained. Therefore, a different synthetic strategy had to be devised in order to obtain an optically active isomer.

3.3.2.3 Coordination to **1** and cyclopalladation of **37**

The free phosphines **37** from entry 2 were coordinated to achiral benzylamine dimer **1**, forming two distereomeric pairs of enantiomers. The two distereomeric pairs were separated by column chromatography (Scheme 3.14).

Scheme 3.14

The major product pair is $(R_C, R_P)\text{-42}$ and $(S_C, S_P)\text{-42}$, with $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) showing a single peak at δ 60.6.

The benzylamine auxiliary was removed from $(R_C, R_P)\text{-42}$ and $(S_C, S_P)\text{-42}$, and the resulting dimer mixture **39** was *ortho*-palladated by reflux with ethanol and sodium acetate trihydrate to form the dichloro-bridged dimer mixture **40** (Scheme 3.15).

Scheme 3.15

The racemic dimer was resolved by coordinating with (*S*)-proline and fractional crystallization (Scheme 3.16).

Scheme 3.16

The products $(Z)/(E)$ - (S_C, S_P, S_N) -**43** were successfully crystallized as white crystals and X-ray analysis was performed (Figure 3.5).

Figure 3.5 X-ray molecular structure of (Z) - (S_C, S_P, S_N) -**43**

Table 3.5 Selected bond lengths (Å) and angles (°) of (Z)-(S_C,S_P,S_N)-43

Pd(1)-C(1)	2.014(3)	Pd(1)-O(1)	2.0909(18)
Pd(1)-N(1)	2.110(2)	Pd(1)-P(1)	2.2108(7)
C(11)-P(1)	1.840(3)	C(25)-P(1)	1.810(3)
C(32)-P(1)	1.814(3)	C(1)-C(10)	1.387(3)
C(10)-C(11)	1.519(3)	C(11)-C(12)	1.551(4)
C(12)-C(13)	1.521(4)	C(13)-O(3)	1.216(4)
C(13)-C(14)	1.493(4)		
<hr/>			
C(1)-Pd(1)-O(1)	177.15(9)	C(1)-Pd(1)-N(1)	97.60(9)
O(1)-Pd(1)-N(1)	80.59(8)	C(1)-Pd(1)-P(1)	80.91(7)
O(1)-Pd(1)-P(1)	100.84(5)	N(1)-Pd(1)-P(1)	177.93(6)
C(10)-C(1)-Pd(1)	122.21(19)	C(1)-C(10)-C(11)	119.0(2)
C(10)-C(11)-P(1)	103.71(16)	C(11)-P(1)-Pd(1)	104.85(8)
C(10)-C(11)-C(12)	110.1(2)	C(12)-C(11)-P(1)	111.04(18)
C(13)-C(12)-C(11)	114.1(2)	O(3)-C(13)-C(14)	120.4(2)
O(3)-C(13)-C(12)	118.7(3)	C(14)-C(13)-C(12)	120.9(2)
N(1)-C(23)-C(24)	112.5(2)	O(1)-C(24)-C(23)	118.5(2)
C(23)-N(1)-Pd(1)	110.42(15)	C(24)-O(1)-Pd(1)	116.15(16)
C(24)-C(23)-C(22)	113.5(2)	N(1)-C(20)-C(21)	103.9(2)

The X-ray study gave the structure of (*E*)-(S_C,S_P,S_N)-**43**, which shows the *S* configuration at the C(11) chiral centre and *S* configuration at the P(1) chiral centre.

The dichloro-bridge dimer (S_C,S_P,S_{C'},S_{P'})-**40** can be obtained through the removal of the (S)-proline auxiliary by treating (Z)/(E)-(S_C,S_P,S_N)-**43** with 1M hydrochloric acid (Scheme 3.17).

Scheme 3.17

The other isomers (*Z*)/(*E*)-(*R_C*,*R_P*,*S_N*)-**43** were crystallized as very thin white crystals, but not suitable for X-ray analysis. Likewise, (*Z*)/(*E*)-(*R_C*,*R_P*,*S_N*)-**43** can be treated with 1M hydrochloric acid to give the dichloro-bridged dimer (*R_C*,*R_P*,*R_{C'}*,*R_{P'}*)-**40**.

3.3.2.4 Coordination of (*S_C*,*S_P*,*S_{C'}*,*S_{P'}*)-**40** with triphenylphosphine and dppe

(*S_C*,*S_P*,*S_{C'}*,*S_{P'}*)-**40** was coordinated with triphenylphosphine (Scheme 3.18) and dppe (Scheme 3.19) to form (*S_C*,*S_P*)-**41** and (*S_C*,*S_P*)-**44** respectively, however no crystal suitable for X-ray analysis was obtained.

Scheme 3.18

Scheme 3.19

3.4 Conclusion

The catalytic asymmetric hydrophosphination reaction of a 1-naphthyl-based enone, (*E*)-1-(4-chlorophenyl)-3-(1-naphthyl)prop-2-en-1-one, **28** with diphenylphosphine was successfully performed. The stereoselectivity of the

reaction could be improved by optimizing the reaction conditions. The enantioenriched free phosphine was coordinated to the (*R*)-**4** template for purification. The *ortho*-palladation of (*R,S*)-**30** proceeded to form the chloro-bridge dimer complex (*S,S*)-**32**, however efforts to obtain crystals suitable for X-ray analysis had been unsuccessful.

The synthetic method was extended to form a CP-palladacycle containing both a C chiral centre and a P chiral centre. The catalytic asymmetric hydrophosphination reaction of the 1-naphthyl-based enone **28** was repeated with a racemic secondary phosphine *o*-anisylphenylphosphine, which proceeded with 3:1 diastereoselectivity. Coordination to (*R*)-**4** failed to separate the stereoisomers properly, and the subsequent *ortho*-palladation resulted in a racemic product. An alternative method was used to resolve the issue. The achiral benzylamine template **1** was used to separate the two pairs of diastereomers, followed by *ortho*-palladation and optical resolution of the chloro-bridged dimer complex **40** by (*S*)-proline. The structure of the cyclopalladated ring and the absolute configuration at the chiral centres were confirmed by the X-ray crystal structure analysis of (*Z*)-(*S_C*,*S_P*,*S_N*)-**43**. The catalytic properties of the newly generated phosphapalladacycles remain to be studied.

3.5 Experimental

Reactions involving air-sensitive materials were performed under a positive pressure of nitrogen. NMR spectra were recorded on Bruker Avance 300, 400 and 500 spectrometers. ¹H and ³¹P{¹H} NMR chemical shifts were referenced relative to SiMe₄ and H₃PO₄ respectively. Melting points were

determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured on the specified solution in a 0.1 dm cell at 25°C with Atago AP-300 Automatic Polarimeter. Elemental Analyses and single crystal X-ray diffraction studies were performed by the Elemental Analysis Laboratory and X-ray Diffraction Laboratory, respectively, of the Division of Chemistry and Biological Chemistry at Nanyang Technological University. The starting materials, diphenylphosphine,³⁹ racemic *o*-anisylphenylphosphine,⁴² (R,R) -di- μ -chlorobis{1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}dipalladium(II),²⁶ **(*R*)-4**, bis(acetonitrile){(*R*)-1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}palladium(II) perchlorate,²⁸ **(*R*)-5** and bis(acetonitrile){(*S*)-1-[1-(diphenylphosphino)ethyl]naphthyl-*C,P*}palladium(II) perchlorate,³¹ **(*S*)-7** were prepared according to literature procedures.

(*E*)-1-(4-Chlorophenyl)-3-(1-naphthyl)prop-2-en-1-one, 28.

1-Naphthaldehyde (1.5 g, 1.3 mL, 9.6 mmol) and 4'-chloroacetophenone (1.48 g, 1.25 mL, 9.6 mmol) were dissolved in methanol (20 mL). Sodium hydroxide (0.038 g, 0.96 mmol) in water (10 mL) was added. The mixture was stirred and heated to reflux overnight. The solvent was removed under reduced pressure. The product mixture was redissolved in dichloromethane (10 mL), washed with water (50 mL x 2) and dried with anhydrous MgSO₄. The solvent was removed under reduced pressure and the product was purified by silica gel chromatography to give a yellow solid (2.23 g, 79%). mp 86-88 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.49-7.61 (m, 6H, aromatic), 7.89-7.95 (m, 3H, aromatic), 8.01-8.03 (m, 2H, aromatic), 8.25 (d, 1H, *J* = 8.3 Hz), 8.68 (d, 1H, *J* = 15.4 Hz).

[3-(4-Chlorophenyl)-1-(1-naphthyl)propan-3-onyl]diphenylphosphine, 29.

To a solution of diphenylphosphine (0.066 g, 0.35 mmol) in dichloromethane (5 mL), (*R*)-**5** (0.034 g, 0.07 mmol, 20 mol%) was added. The solution was stirred at r.t. for 5 min and then cooled to -80 °C. Subsequently, the enone **28** (0.103 g, 0.35 mmol) was added. Et₃N (0.035 g, 0.35 mmol) in DCM (1 mL) was added dropwise. The solution was subsequently stirred at -80 °C and the reaction was monitored by ³¹P{¹H} NMR. The reaction was found to be completed at 2 h. The product was not isolated and directly used in further reactions. NMR calculated yield: 71%; ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 2.0 (s).

Coordination of 29 to (R)-4. Separation of chloro{(R)-1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}{(R)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl]diphenylphosphine}palladium(II), (*R,R*)-30** and chloro{(R)-1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}{(*S*)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-**

onyl]diphenylphosphine}palladium(II), (*R,S*)-30**. (*R*)-**4** (0.12 g, 0.175 mmol, 0.5 equiv. of phosphine) in dichloromethane (5 mL) was added to free phosphine **29** and the mixture was stirred for 30 min. The solvent was removed under reduced pressure to give a yellow solid; ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 47.9 (s) and δ 50.9 (s) in 1 : 4.9 ratio. The combined product was separated and purified by silica gel column chromatography using hexanes/dichloromethane/acetone (3:1:0.2, v/v) as eluant to give a yellow solid.**

Chloro{(R)-1-[1-(N,N-dimethylamino)ethyl]naphthyl-C,N}{(R)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-

onyl]diphenylphosphine}palladium(II), (R,R)-30. The product was recrystallized from dichloromethane-diethyl ether as yellow crystals (0.030 g, 61%). mp 201-203 °C (dec); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 47.9 (s).

Chloro{(R)-1-[1-(N,N-dimethylamino)ethyl]naphthyl-C,N}{(S)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-

onyl]diphenylphosphine}palladium(II), (R,S)-30. The product was recrystallized from dichloromethane-diethyl ether as yellow crystals (0.16 g, 66%). mp 212-215 °C; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 50.9 (s).

Dichlorodi- μ -chlorobis{(S)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-

onyl]diphenylphosphine}dipalladium(II), (S,S)-31. Conc. HCl (1 mL) was added to a solution of (R,S)-30 (0.4 g, 0.49 mmol) in dichloromethane (5 mL). The yellow solution turned orange upon adding the conc. HCl. The solution was stirred for an hour, and then quenched by water (50 mL). The organic phase was separated, further washed with water (2×50 mL), dried with anhydrous MgSO_4 and filtered. The solvent was removed under reduced pressure to give an orange solid (0.32 g, 98%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 40.5 (s).

(S,S)-Di- μ -chlorobis{1-[3-(4-chlorophenyl)-1-(diphenylphosphino)propan-

3-onyl]naphthyl-C,P}dipalladium(II), (S,S)-32. Product (S,S)-31 (0.32 g, 0.24 mmol) was suspended in ethanol (50 mL) and sodium acetate trihydrate (1.8 g) was added. The mixture was heated to reflux for 2 h. After removing the solvent under reduced pressure, the crude product was dissolved in

dichloromethane (10 mL), washed with water (50 mL x 2) and dried with anhydrous MgSO_4 . The crude product was then purified by silica gel column chromatography using hexanes/dichloromethane/acetone (3:1:0.2, v/v) as eluant to give a yellow solid (0.18 g, 60%). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3) δ 64.0 (s), 64.2 (s).

Coordination of 29 to 1. Formation of chloro{[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl]diphenylphosphine}palladium(II), 33. The free phosphine **29** was prepared from diphenylphosphine (0.11 g, 0.59 mmol) and enone **28** (0.19 g, 0.65 mmol, 1.1 equiv.) in the presence of catalyst (*R*)-**5** (0.057 g, 0.12 mmol, 5 mol%) and Et_3N (0.043 g, 0.59 mmol) at -80°C . **1** (0.18 g, 0.32 mmol, 0.55 equiv.) in dichloromethane (5 mL) was added to free phosphine **29** and the mixture was stirred for 30 min. The solvent was removed under reduced pressure. The combined product was separated and purified by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant to give a yellow solid (0.35 g, 78%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 52.9 (s)

Dichlorodi- μ -chlorobis{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl]diphenylphosphine}dipalladium(II), 31. Conc. HCl (1 mL) was added to a solution of **33** (0.35 g, 0.46 mmol) in dichloromethane (5 mL). The yellow solution turned orange upon adding the conc. HCl. The solution was stirred for an hour, and then quenched by water (50 mL). The organic phase was separated, further washed with water (2×50 mL), dried with anhydrous MgSO_4 and filtered. The solvent was removed under reduced pressure to give an orange solid (0.32 g, 92%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 43.7 (s).

Di- μ -chlorobis{1-[3-(4-chlorophenyl)-1-(diphenylphosphino)propan-3-onyl]naphthyl-*C,P*}dipalladium(II), 32. Product **31** (0.32 g, 0.24 mmol) was dissolved in ethanol (10 mL) and sodium acetate trihydrate (0.95 g) was added. The mixture was heated to reflux for 2 h. After removing the solvent under reduced pressure, the crude product was dissolved in dichloromethane (10 mL), washed with water (50 mL x 2) and dried with anhydrous MgSO_4 . The crude product was then purified by silica gel column chromatography to give a yellow solid (0.13 g, 43%). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3) δ 63.9 (s), 64.0 (s), 64.2 (s), 64.3 (s).

[(*S*)-Prolinato]{1-[3-(4-chlorophenyl)-1-(diphenylphosphino)propan-3-onyl]naphthyl-*C,P*}palladium(II), 34. The complex **32** (0.13 g, 0.10 mmol) in dichloromethane (5 mL) was added to a solution of excess potassium (*S*)-prolinate (KOH and (*S*)-proline) in methanol (5 mL). The combined solution was stirred for 2 h. The solvent was removed under reduced pressure, redissolved in dichloromethane, washed with water (50 mL x 2) and dried with anhydrous MgSO_4 . The dichloromethane was removed under reduced pressure to give a white solid. $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 4 signals in ca. 4.9 : 1 : 1.8 : 8.2 ratio, δ 58.6 (s), 60.1 (s), 60.2 (s), 61.3 (s).

[(*S*)-Prolinato]{(*R*)-1-[3-(4-chlorophenyl)-1-(diphenylphosphino)propan-3-onyl]naphthyl-*C,P*}palladium(II), (*R*_C,*S*_N)-34. The product was crystallized from dichloromethane-diethyl ether as white crystals (0.020 g, 80%). mp 118-120 °C (dec); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 60.1 (s), 60.2 (s).

[(*S*)-Prolinato]{(*S*)-1-[3-(4-chlorophenyl)-1-(diphenylphosphino)propan-3-onyl]naphthyl-*C,P*}palladium(II), (*S*_C,*S*_N)-34. The product was crystallized

from dichloromethane-diethyl ether as white crystals (0.10 g, 83%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 58.6 (s), 61.2 (s).

Chloro{(S)-1-[3-(4-chlorophenyl)-1-(diphenylphosphino)propan-3-onyl]naphthyl-C,P}(triphenylphosphine)palladium(II), (S)-35.

Triphenylphosphine (0.027 g, 0.10 mmol, 2 equiv.) was added to (S,S)-32 (0.064 g, 0.05 mmol) in dichloromethane (5 mL) and stirred for 30 min. The solvent was removed under reduced pressure to give a yellow solid. The product cannot be induced to crystallize despite the use of a variety of solvents. $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 4 sets of signals in ca. 1.5 : 1 : 1 : 1.5 ratio, δ 17.0 (d, $^2J_{\text{PP}} = 26.3$ Hz, coordinated PPh_3 ligand of *cis* geometric isomer), 25.5 (d, $^2J_{\text{PP}} = 423.2$ Hz, coordinated PPh_3 ligand of *trans* geometric isomer), 53.1 (d, $^2J_{\text{PP}} = 423.2$ Hz, phosphapalladacycle *P* of *trans* geometric isomer), 63.6 (d, $^2J_{\text{PP}} = 26.3$ Hz, phosphapalladacycle *P* of *cis* geometric isomer).

[1,2-Bis(diphenylphosphino)ethane-P,P']{(S)-1-[3-(4-chlorophenyl)-1-(diphenylphosphino)propan-3-onyl]naphthyl-C,P}palladium(II)

perchlorate, (S)-36. Silver(II) perchlorate (0.1 g, 0.48 mmol, 3 equiv.) in water (1 mL) was added to (S,S)-32 (0.2 g, 0.16 mmol) in dichloromethane (5 mL) and stirred for 2 hours. The organic phase was washed with water (50 mL x 2) and dried with anhydrous MgSO_4 . 1,2-Bis(diphenylphosphino)ethane (0.125 g, 0.32 mmol, 2 equiv.) was added to the product and stirred for 30 min. The solvent was removed under reduced pressure to give a yellow solid. The product cannot be induced to crystallize despite the use of a variety of solvents. $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, CDCl_3) δ 41.1 (dd, $^2J_{\text{P}(\text{trans})-\text{P}(\text{cis})} = 28.0$ Hz, $^2J_{\text{P}-\text{P}(\text{cis})} = 24.1$ Hz, coordinated dppe ligand *P cis* to phosphapalladacycle P), 49.6 (dd, $^2J_{\text{P}-\text{P}(\text{trans})} = 343.5$ Hz, $^2J_{\text{P}(\text{trans})-\text{P}(\text{cis})} = 28.0$ Hz, coordinated dppe ligand *P trans* to

phosphapalladacycle P), 56.2 (dd, $^2J_{\text{P-P}(\text{trans})} = 343.5$ Hz, $^2J_{\text{P-P}(\text{cis})} = 24.1$ Hz, phosphapalladacycle P).

[3-(4-Chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-

methoxyphenyl)phenylphosphine, 37. To a solution of *o*-anisylphenylphosphine (0.12 g, 0.56 mmol) in chloroform (5 mL), (*R*)-**5** (0.041 g, 0.084 mmol, 15 mol%) was added. The solution was stirred at r.t. for 5 min and then was cooled to -80 °C. Subsequently, the enone **28** (0.18 g, 0.61 mmol, 1.1 equiv.) was added. Et₃N (0.57 g, 0.56 mmol) in chloroform (1 mL) was added dropwise. The solution was subsequently stirred at r.t. and the reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR. The reaction was found to be completed after 2 d. The product was not isolated and directly used in further reactions. NMR calculated conversion: 97%, calculated yield: 81%; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl₃) 2 overlapping signals at δ -8.8, (202 MHz, CD₂Cl₂) 2 overlapping signals at δ -6.4, (202 MHz, THF-*d*₈) 2 signals in ca. 1 : 1.6 ratio, δ -6.0 (s), -4.5 (s). (202 MHz, Acetone-*d*₆) 2 signals in ca. 1 : 2 ratio, δ -4.8 (s), -3.6 (s).

Chloro{(R)-1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}\{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-

methoxyphenyl)phenylphosphine}palladium(II), (R)-38. (*R*)-**4** (0.21 g, 0.31 mmol, 0.55 equiv. to phosphine) in dichloromethane (5 mL) was added to free phosphine **35** and the mixture was stirred for 30 min. The solvent was removed under reduced pressure to give a yellow solid; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl₃) δ 55.7 (s), 58.3 (s) in ca. 1.33 : 1 ratio. The product was separated by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant to give (*R*)-**38a** (0.20 g, 74%; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl₃) δ

55.7) and (*R*)-**38b** (0.16 g, 79%; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 58.3) as yellow solids.

Dichlorodi- μ -chlorobis{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), 39. Conc. HCl (1 mL) was added to a racemic mixture of (*R*)-**38b** (0.14 g, 0.17 mmol) in dichloromethane (5 mL). The yellow solution turned orange upon adding the conc. HCl. The solution was stirred for an hour, and then quenched by water (50 mL). The organic phase was separated, further washed with water (2×50 mL), dried with anhydrous MgSO_4 and filtered. The solvent was removed under reduced pressure to give an orange solid (0.11 g, 98%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 39.3 (s), 39.7 (s), 41.4 (s), 41.9 (s).

Di- μ -chlorobis{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), 40. Product **39** (0.11 g, 0.08 mmol) was dissolved in ethanol (10 mL) and sodium acetate trihydrate (0.33 g) was added. The mixture was heated to reflux for 2 h. After removing the solvent under reduced pressure, the crude product was dissolved in dichloromethane (10 mL), washed with water (50 mL $\times$ 2) and dried with anhydrous MgSO_4 . The crude product was then purified by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant to give a yellow solid (0.080 g, 77%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 57.1 (s), 57.6 (s).

Racemic chloro{1-[3-(4-chlorophenyl)-1-((2-methoxyphenyl)phenylphosphino)propan-3-onyl]naphthyl-

C,P}(triphenylphosphine)palladium(II), 41. The dimer **40** (0.074 g, 0.057 mmol) was dissolved in dichloromethane (5 mL). Triphenylphosphine (0.03 g, 0.11 mmol, 2 equiv.) was added and stirred for 30 min. The solvent was removed under pressure to give product as yellow solid. Recrystallization from dichloromethane-hexane gives racemic yellow crystals (0.090 g, 87%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 4 sets of signals in ca. 1 : 1.6 : 1.6 : 1 ratio, δ 17.6 (d, $^2J_{\text{PP}} = 26.3$ Hz, coordinated PPh_3 ligand of *cis* geometric isomer), 25.5 (d, $^2J_{\text{PP}} = 427.2$ Hz, coordinated PPh_3 ligand of *trans* geometric isomer), 49.5 (d, $^2J_{\text{PP}} = 427.2$ Hz, phosphapalladacycle *P* of *trans* geometric isomer), 53.9 (d, $^2J_{\text{PP}} = 26.3$ Hz, phosphapalladacycle *P* of *cis* geometric isomer).

Chloro{[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-

methoxyphenyl)phenylphosphine}palladium(II), 42. The free phosphine **37** was prepared from *o*-anisylphenylphosphine (0.155 g, 0.72 mmol) and enone **28** (0.23 g, 0.79 mmol, 1.1 equiv.) in the presence of catalyst (*R*)-**5** (0.052 g, 0.11 mmol, 15 mol%) and Et_3N (0.073 g, 0.72 mmol) at r.t. for 4 d. NMR calculated conversion: 99%, calculated yield: 78%. **1** (0.22 g, 0.39 mmol, 0.55 equiv.) in dichloromethane (5 mL) was added to free phosphine **37** and the mixture was stirred for 30 min. The solvent was removed under reduced pressure to give a yellow solid; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 2 signals in ca. 1 : 3 ratio, δ 44.8 (s), 60.6 (s). The combined product was purified by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant to give a yellow solid.

Racemic mixture of chloro{[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}{(*R_C*,*R_P*)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}palladium(II), (*R_C*,*R_P*)-42 and chloro{[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}{(*S_C*,*S_P*)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}palladium(II), (*S_C*,*S_P*)-42. Separation by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant gave a yellow solid (0.30 g, 71%). ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 60.6 (s), ³¹P{¹H} NMR (121 MHz, CDCl₃) δ 61.1 (s).

Racemic mixture of chloro{[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}{(*R_C*,*S_P*)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}palladium(II), (*R_C*,*S_P*)-42 and chloro{[(*N,N*-dimethylamino)methyl]phenyl-*C,N*}{(*S_C*,*R_P*)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}palladium(II), (*S_C*,*R_P*)-42. Separation by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant gave a yellow solid (0.052 g, 37%). ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 44.8 (s).

Racemic mixture of dichlorodi-μ-chlorobis{(*R_C*,*R_P*)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), (*R_C*,*R_P*,*R_{C'}*,*R_{P'}*)-39 and dichlorodi-μ-chlorobis{(*S_C*,*S_P*)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), (*S_C*,*S_P*,*S_{C'}*,*S_{P'}*)-39. Conc. HCl (1 mL) was added to a racemic mixture of (*R_C*,*R_P*)-42 and (*S_C*,*S_P*)-42 (0.30 g, 0.38 mmol) in dichloromethane (5 mL). The yellow solution

turned orange upon adding the conc. HCl. The solution was stirred for an hour, and then quenched by water (50 mL). The organic phase was separated, further washed with water (2×50 mL), dried with anhydrous MgSO_4 and filtered. The solvent was removed under reduced pressure to give an orange solid (0.26 g, 98%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 39.3 (s), 39.7 (s), 41.4 (s), 41.9 (s).

Racemic mixture of ($R_C, R_P, R_{C'}, R_{P'}$)-di- μ -chlorobis{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), ($R_C, R_P, R_{C'}, R_{P'}$)-40** and ($S_C, S_P, S_{C'}, S_{P'}$)-di- μ -chlorobis{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), ($S_C, S_P, S_{C'}, S_{P'}$)-**40**.** Racemic product mixture of ($R_C, R_P, R_{C'}, R_{P'}$)-**39** and ($S_C, S_P, S_{C'}, S_{P'}$)-**39** (0.26 g, 0.19 mmol) was dissolved in ethanol (10 mL) and sodium acetate trihydrate (0.73 g) was added. The mixture was heated to reflux for 2 h. After removing the solvent under reduced pressure, the crude product was dissolved in dichloromethane (10 mL), washed with water (50 mL $\times$ 2) and dried with anhydrous MgSO_4 . The crude product was then purified by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant to give a yellow solid (0.097 g, 40%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 57.1 (s), 57.6 (s).

Racemic mixture of dichlorodi- μ -chlorobis{(R_C, S_P)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), ($R_C, S_P, R_{C'}, S_{P'}$)-39 and dichlorodi- μ -chlorobis{(S_C, R_P)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), ($S_C, R_P, S_{C'}, R_{P'}$)-39. Conc. HCl (1 mL) was added to a racemic mixture of (R_C, S_P)-42 and (S_C, R_P)-42 (0.052 g, 0.066 mmol) in dichloromethane (5 mL). The yellow solution turned orange upon adding the conc. HCl. The solution was stirred for an hour, and then quenched by water (50 mL). The organic phase was separated, further washed with water (2 $\times$ 50 mL), dried with anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure to give an orange solid (0.043 g, 94%). $^{31}P\{^1H\}$ NMR (202 MHz, $CDCl_3$) δ 39.0 (s), 40.9 (s).

Racemic mixture of ($R_C, S_P, R_{C'}, S_{P'}$)-di- μ -chlorobis{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), ($R_C, S_P, R_{C'}, S_{P'}$)-40 and ($S_C, R_P, S_{C'}, R_{P'}$)-di- μ -chlorobis{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), ($S_C, R_P, S_{C'}, R_{P'}$)-40. Racemic product mixture of ($R_C, S_P, R_{C'}, S_{P'}$)-39 and ($S_C, R_P, S_{C'}, R_{P'}$)-39 (0.043 g, 0.031 mmol) was suspended in ethanol (10 mL) and sodium acetate trihydrate (0.12 g) was added. The mixture was heated to reflux for 2 h. After removing the solvent under reduced pressure, the crude product was dissolved in dichloromethane (10 mL), washed with water (50 mL $\times$ 2) and dried with anhydrous $MgSO_4$. The crude product was then purified by silica gel column chromatography using hexanes/dichloromethane/acetone (5:1:0.5, v/v) as eluant

to give a yellow solid (0.0054 g, 13%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 55.2 (s)

Optical resolution of $(R_C, R_P, R_{C'}, R_{P'})$ -40 and $(S_C, S_P, S_{C'}, S_{P'})$ -40. Isolation of $[(S)\text{-prolinato}]\{(R_C, R_P)\text{-1-[3-(4-chlorophenyl)-1-((2-methoxyphenyl)phenylphosphino)propan-3-onyl]naphthyl-*C,P*}\}$ palladium(II), (R_C, R_P, S_N) -43 and $[(S)\text{-prolinato}]\{(S_C, S_P)\text{-1-[3-(4-chlorophenyl)-1-((2-methoxyphenyl)phenylphosphino)propan-3-onyl]naphthyl-*C,P*}\}$ palladium(II), (S_C, S_P, S_N) -43. The racemic mixture of complexes $(R_C, R_P, R_{C'}, R_{P'})$ -40 and $(S_C, S_P, S_{C'}, S_{P'})$ -40 (0.093 g, 0.072 mmol) in dichloromethane (5 mL) was added to a solution of excess potassium (*S*)-prolinate (KOH and (*S*)-proline) in methanol (5 mL). The combined solution was stirred for 2 h. The solvent was removed under reduced pressure, redissolved in dichloromethane, washed with water (50 mL x 2) and dried with anhydrous MgSO_4 . The dichloromethane was removed under reduced pressure to give a white solid. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3) 4 signals in ca. 1.02 : 1.08 : 1 : 1.31 ratio, δ 53.4 (s), 54.1 (s), 54.4 (s), 55.1 (s).

$[(S)\text{-Prolinato}]\{(R_C, R_P)\text{-1-[3-(4-chlorophenyl)-1-((2-methoxyphenyl)phenylphosphino)propan-3-onyl]naphthyl-*C,P*}\}$ palladium(II), (R_C, R_P, S_N) -43. The product was recrystallized from dichloromethane-diethyl ether to give white crystals (0.046 g, 94%). mp 243-245 °C (dec); Anal. Calcd. for $\text{C}_{37}\text{H}_{33}\text{ClNO}_4\text{PPd}$: C, 61.00; H, 4.57; N, 1.92. Found: C, 60.39; H, 5.14; N, 2.47. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3) 54.1 (s), 54.4 (s).

[(S)-Prolinato]{(S_C,S_P)-1-[3-(4-chlorophenyl)-1-((2-methoxyphenyl)phenylphosphino)propan-3-onyl]naphthyl-C,P}palladium(II), (S_C,S_P,S_N)-43. The product was recrystallized from dichloromethane-diethyl ether to give white crystals (0.026 g, 47%). ³¹P{¹H} NMR (121 MHz, CDCl₃) 53.4 (s), 55.1 (s).

(R_C,R_P,R_{C'},R_{P'})-Di-μ-chlorobis{[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), (R_C,R_P,R_{C'},R_{P'})-40. The resolved complex (R_C,R_P,S_N)-43 (0.046 g, 0.063 mmol) was dissolved in dichloromethane (5 mL). The solution was treated with 1M HCl (1 mL) and stirred for 1 h. The solution was washed with water (50 mL x 2) and dried with anhydrous MgSO₄. The solvent was removed under reduced pressure to give the produce as a yellow solid (0.040 g, 99%). ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 57.5 (s), 57.7 (s).

(S_C,S_P,S_{C'},S_{P'})-Di-μ-chlorobis{(S_C,S_P)-[3-(4-chlorophenyl)-1-(1-naphthyl)propan-3-onyl](2-methoxyphenyl)phenylphosphine}dipalladium(II), (S_C,S_P,S_{C'},S_{P'})-40. The resolved complex (S_C,S_P,S_N)-43 (0.026 g, 0.036 mmol) was dissolved in dichloromethane (5 mL). The solution was treated with 1M HCl (1 mL) and stirred for 1 h. The solution was washed with water (50 mL x 2) and dried with anhydrous MgSO₄. The solvent was removed under reduced pressure to give the produce as a yellow solid (0.023 g, 97%). [α]_D = +418° (c = 2.3, CH₂Cl₂); ³¹P{¹H} NMR (202 MHz, CDCl₃) δ 57.5 (s), 57.7 (s).

Chloro{(*S_C*,*S_P*)-1-[3-(4-chlorophenyl)-1-((2-

methoxyphenyl)phenylphosphino)propan-3-onyl]naphthyl-

***C,P*}(triphenylphosphine)palladium(II), (*S_C*,*S_P*)-41.** The dimer complex

(*S_C*,*S_P*,*S_{C'}*,*S_{P'}*)-43 (0.023 g, 0.017 mmol) was dissolved in dichloromethane (5 mL). Triphenylphosphine (0.0091 g, 0.0035 mmol, 2 equiv.) was added and stirred for 30 min. The solvent was removed under pressure to give product as yellow solid. The product cannot be induced to crystallize despite the use of a variety of solvents. $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 4 sets of signals in ca. 1 : 1.6 : 1.6 : 1 ratio, δ 17.6 (d, $^2J_{\text{PP}} = 27.0$ Hz, coordinated PPh_3 ligand of *cis* geometric isomer), 25.5 (d, $^2J_{\text{PP}} = 426.6$ Hz, coordinated PPh_3 ligand of *trans* geometric isomer), 49.5 (d, $^2J_{\text{PP}} = 426.6$ Hz, phosphapalladacycle *P* of *trans* geometric isomer), 54.0 (d, $^2J_{\text{PP}} = 27.0$ Hz, phosphapalladacycle *P* of *cis* geometric isomer).

[1,2-Bis(diphenylphosphino)ethane-*P,P'*]{(*S_C*,*S_P*)-1-[3-(4-chlorophenyl)-1-

((2-methoxyphenyl)phenylphosphino)propan-3-onyl]naphthyl-

***C,P*}(triphenylphosphine)palladium(II) chloride, (*S_C*,*S_P*)-44.** 1,2-Bis(diphenylphosphino)ethane

(0.0097 g, 0.024 mmol) was added to a solution of (*S_C*,*S_P*,*S_{C'}*,*S_{P'}*)-40 (0.016 g, 0.012 mmol) in dichloromethane (5 mL). After stirring for 2 h, the solvent was removed under reduced pressure to give a yellow solid. The product cannot be induced to crystallize despite the use of a variety of solvents. $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 42.2 (dd, $^2J_{\text{P}(\text{trans})-\text{P}(\text{cis})} = 28.3$ Hz, $^2J_{\text{P-P}(\text{cis})} = 22.7$ Hz, coordinated dppe ligand *P cis* to phosphapalladacycle P), 45.1 (dd, $^2J_{\text{P-P}(\text{trans})} = 351.2$ Hz, $^2J_{\text{P}(\text{trans})-\text{P}(\text{cis})} = 28.3$ Hz, coordinated dppe ligand *P trans* to phosphapalladacycle P), 51.8 (dd, $^2J_{\text{P-P}(\text{trans})} = 351.6$ Hz, $^2J_{\text{P-P}(\text{cis})} = 22.7$ Hz, phosphapalladacycle *P*).

CHAPTER 4: ASYMMETRIC SYNTHESIS OF ISOQUINOLINE-BASED CHIRAL P,N BIDENTATE LIGANDS

4.1 Introduction

P,N Bidentate ligands, consisting of a chelating P and N donor atoms, are an interesting class of ligands. This type of asymmetrical ligands possesses a combination of hard (N) and soft (P) donor atoms, and therefore have different features associated with each donor atom that provide unique reactivity to their metal complexes in catalytic asymmetric processes.⁴³⁻⁴⁴

Isoquinoline-based P,N ligands are usually in the form of atropisomeric axial chiral biaryl complexes such as QUINAP and its derivatives.⁴⁵⁻⁴⁶

Developing isoquinoline-based P,N ligands is of particular interest to this project because of the structural similarity of the isoquinoline ring and the naphthalene ring. In the naphthylamine and naphthylphosphine complexes discussed in the previous chapters, steric interaction between H(8) on the naphthyl ring and a substituent on the 5-member palladacycle ring locks the ring into a stable conformation, contributing to the effective controlling of stereoselectivity in asymmetric reactions. The same steric interaction is expected to be present in the analogous isoquinoline-based P,N ligands coordinated with a palladium metal centre in a 5-membered ring formation.

The combination of the H(8) steric factor and the electronic properties of P,N ligands in the proposed isoquinoline-based P,N palladium complexes may open up new possibilities for use in a wide range of reactions. The neutral

N in place of the anionic C will have an effect on the activity of the Pd metal centre. The formal charge on the Pd centre would be +2, and the increase in polarity may make it more useful in more polar solvents.

4.2 Research Objectives

The research objectives are to synthesize an isoquinoline-based palladium complex from the hydrophosphination product of 1-isoquinoline enones *via* the catalytic approach or the stoichiometric approach. Similar to Chapter 3, the diphenylphosphine can be replaced by a P-chiral secondary phosphine *o*-anisylphenylphosphine for the synthesis of a P,N ligand-based palladium complex with two chiral centres at the carbon and phosphorus atoms.

Leung and coworkers had previously reported the asymmetric hydrophosphination reaction of (*E*)-1-phenyl-3-pyridin-2-yl-2-propenone with diphenylphosphine, promoted by a stoichiometric amount of chiral bis(acetonitrile) complex (*R*)-**2**, in high regio- and stereoselectivities under mild conditions.⁴⁷ The same technique can be used in the asymmetric hydrophosphination reactions of the isoquinoline analogue (*E*)-3-isoquinoline-1-yl-1-phenyl-2-propenone, **45**, with secondary phosphines.

In addition to using a stoichiometric amount of complex (*R*)-**5**, the same reaction is also studied with a catalytic amount of (*R*)-**5**.

4.3 Results and Discussion

4.3.1.1 Asymmetric hydrophosphination with diphenylphosphine promoted by stoichiometric amount of Pd complex

The reaction between **45** and diphenylphosphine proceeded at room temperature in the presence of stoichiometric amount of the chiral template (*R*)-**5** (Scheme 4.1).

Scheme 4.1

The reaction was found to be completed in 2 hours. The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum showed two singlet peaks at δ 55.4 and δ 59.1 in 2.5:1 ratio, corresponding to the formation of two diastereomeric products. The absence of additional peaks also indicates the 100% regioselectivity of the reaction, where the diphenylphosphine coordinates exclusively *trans* to the NMe_2 . The high regioselectivity observed is consistent with what has been observed in other P,N heterobidentate ligands.⁴⁷⁻⁴⁸

The diastereomeric products can be separated by column chromatography and fractional crystallization. Pure (*R,R*)-**46** ($[\alpha]_{\text{D}} = -250^\circ$ ($c = 1$, CH_2Cl_2)) and (*R,S*)-**46** ($[\alpha]_{\text{D}} = +255^\circ$ ($c = 1$, CH_2Cl_2)) were obtained separately. The less soluble minor product (*R,S*)-**46** was crystallized first from dichloromethane-diethyl ether as white crystals. The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum showed a singlet peak at δ 59.1. The properties and absolute configuration of (*R,S*)-**46** were studied by single-crystal X-ray crystallography (Figure 4.1).

Figure 4.1 X-ray molecular structure of (*R,S*)-46

Table 4.1 Selected bond lengths (Å) and angles (°) of (*R,S*)-46

Pd(1)-C(1)	2.028(9)	Pd(1)-N(1)	2.156(7)
Pd(1)-N(2)	2.186(8)	Pd(1)-P(1)	2.228(2)
C(15)-N(2)	1.357(12)	C(23)-N(2)	1.345(12)
C(23)-C(24)	1.498(13)	C(24)-P(1)	1.837(9)
C(24)-C(25)	1.571(12)	C(25)-C(26)	1.523(12)
C(26)-O(1)	1.199(12)	C(26)-C(27)	1.478(15)
C(33)-P(1)	1.800(10)	C(39)-P(1)	1.825(10)
C(1)-Pd(1)-N(1)	79.3(4)	C(1)-Pd(1)-N(2)	167.5(3)
N(1)-Pd(1)-N(2)	103.8(3)	C(1)-Pd(1)-P(1)	98.6(3)
N(1)-Pd(1)-P(1)	170.4(2)	N(2)-Pd(1)-P(1)	80.2(2)
N(2)-C(23)-C(24)	116.3(8)	C(23)-C(24)-C(25)	110.9(7)
C(23)-C(24)-P(1)	109.2(6)	C(25)-C(24)-P(1)	111.8(7)
C(26)-C(25)-C(24)	110.9(7)	O(1)-C(26)-C(27)	122.0(9)
O(1)-C(26)-C(25)	121.8(10)	C(27)-C(26)-C(25)	116.2(8)
C(23)-N(2)-Pd(1)	119.6(6)	C(24)-P(1)-Pd(1)	100.7(3)

X-ray structure analysis showed that the newly-formed stereogenic centre at C(24) adopted the *S* absolute configuration. The crystal structure obtained confirmed the formation of the P,N-chelate 5-membered ring structure.

The geometry at the Pd centre is distorted square planar with angles of 79.3(4)-103.8(3)° and 167.5(3)-170.4(2)°. The CH₂COPh group at C(24) is in the axial position, suggesting that steric repulsion with the H on the C(21) in the isoquinoline ring forces it to adopt the usually less favourable position. The same phenomenon was found in naphthalene based palladacycles, where the steric repulsion between the methyl group at the stereogenic centre and the H(8) on the naphthalene ring forces the methyl group to adopt the axial position.^{27, 30} In contrast, the CH₂COPh group on the pyridine analogue adopts the usually favourable equatorial position in the absence of the steric repulsion.⁴⁷

The compound (*R,S*)-**46** was treated with concentrated hydrochloric acid to remove the naphthylamine auxiliary, giving the dichloro complex (*S*)-**47** (Scheme 4.2).

Scheme 4.2

The ³¹P{¹H} NMR spectrum showed a singlet peak at δ 51.9. After a few days, the dichloro complex was crystallized from dichloromethane-diethyl ether as yellow crystals and X-ray crystallographic study was performed (Figure 4.2).

Figure 4.2 X-ray molecular structure of *rac*-47

Table 4.2 Selected bond lengths (Å) and angles (°) of *rac*-47

Pd(1)-N(1)	2.067(7)	Pd(1)-P(1)	2.208(2)
Pd(1)-Cl(1)	2.295(2)	Pd(1)-Cl(2)	2.388(2)
C(1)-N(1)	1.390(11)	C(9)-N(1)	1.334(11)
C(9)-C(10)	1.529(12)	C(10)-P(1)	1.846(8)
C(10)-C(11)	1.562(12)	C(11)-C(12)	1.508(13)
C(12)-O(1)	1.216(10)	C(12)-C(13)	1.482(12)
C(19)-P(1)	1.826(9)	C(25)-P(1)	1.835(9)
N(1)-Pd(1)-P(1)	83.9(2)	N(1)-Pd(1)-Cl(1)	173.4(2)
P(1)-Pd(1)-Cl(1)	89.73(8)	N(1)-Pd(1)-Cl(2)	95.3(2)
P(1)-Pd(1)-Cl(2)	172.14(9)	Cl(1)-Pd(1)-Cl(2)	91.24(8)
N(1)-C(9)-C(10)	119.0(7)	C(9)-C(10)-C(11)	110.7(7)
C(9)-C(10)-P(1)	107.3(6)	C(11)-C(10)-P(1)	113.5(6)
C(12)-C(11)-C(10)	110.1(7)	O(1)-C(12)-C(13)	121.7(9)
O(1)-C(12)-C(11)	119.7(8)	C(13)-C(12)-C(11)	118.5(8)
C(9)-N(1)-Pd(1)	120.7(6)	C(10)-P(1)-Pd(1)	103.1(3)

X-ray crystallography of **47** revealed that racemization had occurred at the C(10) chiral centre. The racemization of an isoquinoline based P,N bidentate ligand was reported by Claridge *et al.*⁴⁹ The racemization even occurred when the ligand is coordinated to PdCl₂, but the rate was slower than the free ligand, showing the lability of the P,N chelate and ligand dissociation or partial dissociation from PdCl₂ before inversion.

4.3.1.2 Catalytic asymmetric hydrophosphination with diphenylphosphine promoted by catalytic amount of Pd complex

The hydrophosphination reaction between **45** and diphenylphosphine was repeated with catalytic amount of (*R*)-**5** (Scheme 4.3).

Scheme 4.3

Monitoring the reaction with ³¹P{¹H} NMR, a new singlet peak at δ 3.0 was found in the spectrum after 2 hours. The reaction was allowed to proceed for 3 days at -80°C until the reaction did not proceed any further. The reaction temperature was raised to room temperature and stirred for another 1 day, after which the diphenylphosphine was found to be completely consumed. The calculated yield from the NMR spectrum was 73%.

The free phosphine product was coordinated to (*R*)-**4** for the determination of ee (Scheme 4.4).

Scheme 4.4

The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum showed two singlet peaks at δ 53.0 and 54.8 in 1:1 ratio. This apparent lack of stereoselectivity was due to the racemization of the product as described earlier.

4.3.2.1 Asymmetric hydrophosphination with *o*-anisylphenylphosphine promoted by stoichiometric amount of Pd complex

The reaction was repeated with a P-chiral secondary phosphine, *o*-anisylphenylphosphine in place of diphenylphosphine. The reaction with stoichiometric amount of (R) -**5** proceeded at room temperature and completed in 3 days (Scheme 4.5).

Scheme 4.5

The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum exhibited 4 peaks corresponding to 4 stereoisomeric products at δ 46.4, 50.4, 55.6 and 58.4 in the ratio of 1 : 3.6 : 1.6 : 2.1. The major product at δ 50.4, (*R,R_C,R_P*)-**50** was isolated as white crystals from dichloromethane-diethyl ether and X-ray analysis was performed (Figure 4.3).

Figure 4.3 X-ray molecular structure of (*R,R_C,R_P*)-**50**

Table 4.3 Selected bond lengths (Å) and angles (°) of (*R,R_C,R_P*)-**50**

Pd(1)-C(1)	2.002(9)	Pd(1)-N(1)	2.140(8)
Pd(1)-N(2)	2.152(7)	Pd(1)-P(1)	2.226(2)
C(15)-N(2)	1.395(11)	C(23)-N(2)	1.348(11)
C(23)-C(24)	1.503(12)	C(24)-P(1)	1.886(9)
C(24)-C(25)	1.556(12)	C(25)-C(26)	1.499(11)
C(26)-O(1)	1.226(10)	C(26)-C(27)	1.501(12)
C(33)-P(1)	1.814(9)	C(39)-P(1)	1.793(9)
C(1)-Pd(1)-N(1)	80.7(3)	C(1)-Pd(1)-N(2)	173.6(3)
N(1)-Pd(1)-N(2)	102.4(3)	C(1)-Pd(1)-P(1)	98.9(3)
N(1)-Pd(1)-P(1)	172.9(2)	N(2)-Pd(1)-P(1)	78.7(2)
N(2)-C(23)-C(24)	115.0(8)	C(23)-C(24)-C(25)	111.3(7)
C(23)-C(24)-P(1)	104.1(6)	C(25)-C(24)-P(1)	117.8(6)
C(26)-C(25)-C(24)	112.6(7)	O(1)-C(26)-C(25)	121.8(8)
O(1)-C(26)-C(27)	120.1(8)	C(25)-C(26)-C(27)	118.1(7)
C(23)-N(2)-Pd(1)	120.9(6)	C(24)-P(1)-Pd(1)	98.8(3)

The product (*R,R_C,R_P*)-**50** was found to have adopted the *R* configuration at the C(24) chiral centre and *R* configuration at the P(1) chiral centre. The geometry at the Pd centre is distorted square planar with angles of 78.7(2)-102.4(3)° and 172.9(2)-173.6(3)°. Steric repulsion from the H on the C(21) in the isoquinoline ring forces the CH₂COPh group at C(24) to adopt the usually less favourable axial position.

The naphthylamine auxiliary was removed by treating with concentrated hydrochloric acid to give the dichloro complex (*R_C,R_P*)-**51** (Scheme 4.6). The ³¹P{¹H} NMR spectrum showed a singlet peak at δ 46.0.

Scheme 4.6

While no suitable crystals for X-ray analysis have been obtained, the compound was found to have diminished optical activity over a period of one week, suggesting racemization of the product. ³¹P{¹H} NMR of the solution after a few days showed another singlet peak at δ 54.4 in addition to the δ 46.0 peak, in the ratio of 1:1, suggesting the presence of two diastereomers in the product mixture as the result of racemization.

4.3.2.2 Catalytic asymmetric hydrophosphination with *o*-anisylphenylphosphine promoted by catalytic amount of Pd complex

The hydrophosphination reaction between enone **45** and *o*-anisylphenylphosphine was repeated with a catalytic amount of the chiral template (*R*)-**5** (Scheme 4.7).

Scheme 4.7

Monitoring the reaction with $^{31}\text{P}\{^1\text{H}\}$ NMR, two new single peaks appeared at δ -6.6 and -4.4 after 2 hours, corresponding to the formation of two pairs of diastereomeric products. The reaction was completed in 3 days. The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum showed the two free phosphine peaks δ -6.6 and -4.4 in 1 : 1.7 ratio, giving a dr of 37 : 63. The calculated yield from the NMR spectrum was 84%.

The free phosphine **52** was coordinated to (*R*)-**4** for further study and manipulation (Scheme 4.8).

Scheme 4.8

Interestingly, the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum showed four peaks corresponding to the four isomeric products at δ 46.4, 50.2, 55.3 and 56.4 in the ratio 1 : 3.8 : 10.2 : 0.25. This suggests the presence of an electron-donating group such as OMe may contribute to the stability of the ligand.

4.4 Conclusion

Isoquinoline-based P,N ligands with a C chiral centre, as well as a C*-P* ligand were successfully synthesized by the stoichiometric method. The predicted steric hindrance caused by H(8) was observed, with the PhOCH_2 group forced into the axial position on the 5-membered ring. The removal of the naphthylamine template to generate the P,N dichloro palladium complexes resulted in the racemization of the complexes. The synthesis of the P,N ligands by the catalytic method produced free phosphines which readily racemize in solution. The racemization of these P,N ligands make them unsuitable as catalysts in asymmetric synthesis. The cause of the racemization may be due to

a low barrier of inversion, which may be mitigated by the introduction of more π -donating functional groups to increase the barrier of inversion.

4.5 Experimental

Reactions involving air-sensitive materials were performed under a positive pressure of nitrogen. NMR spectra were recorded on Bruker Avance 300, 400 and 500 spectrometers. ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR chemical shifts were referenced relative to SiMe_4 and H_3PO_4 respectively. Melting points were determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured on the specified solution in a 0.1 dm cell at 25°C with Atago AP-300 Automatic Polarimeter. Elemental Analyses and single crystal X-ray diffraction studies were performed by the Elemental Analysis Laboratory and X-ray Diffraction Laboratory, respectively, of the Division of Chemistry and Biological Chemistry at Nanyang Technological University. The starting materials, diphenylphosphine,³⁹ racemic *o*-anisylphenylphosphine,⁴² 1-isoquinolinecarbaldehyde,⁵⁰ bis(acetonitrile){(*R*)-1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}palladium(II) perchlorate,²⁸ and (*R,R*)-di- μ -chlorobis{1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}dipalladium(II),²⁶ were prepared according to literature procedures.

(*E*)-3-Isoquinoline-1-yl-1-phenyl-2-propenone, 45.

1-isoquinolinecarbaldehyde (1.00 g, 6.4 mmol) and acetophenone (0.75 mL, 0.77 g, 6.4 mmol) were dissolved in ethanol (5 mL), and NaOH (0.25 g, 6.4 mmol) in water (2.5 mL) was added. The reaction mixture was stirred overnight at r.t., followed by the addition of water (50 mL). The ethanol was removed

under reduced pressure, and dichloromethane (50 mL x 3) was used to extract the product from the aqueous layer. The organic extracts were combined, dried with MgSO₄ and filtered. Removal of the solvent gave the crude product as a dark yellow solid. The product was purified by column chromatography with hexanes/dichloromethane (5:1, v/v) as eluant to give a yellow solid (1.08 g, 65%). mp 146-148 °C; ¹H NMR (500MHz, CDCl₃) δ 7.44-7.47 (m, 2H, aromatic), 7.52-7.61 (m, 4H, aromatic), 7.74 (d, 1H, *J* = 8.1 Hz, aromatic), 8.12 (d, 2H, *J* = 8.4 Hz, aromatic), 8.27 (d, 1H, *J* = 7.4 Hz, aromatic), 8.35 (d, 1H, *J* = 14.9 Hz, H_α), 8.55 (d, 1H, *J* = 5.5 Hz, aromatic), 8.61 (d, 1H, *J* = 14.9 Hz, H_β).

Synthesis of {(R)-1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}{(R)-1-[1-(diphenylphosphino)-3-phenylpropan-3-onyl]isoquinolyl-*N,P*}palladium(II) perchlorate, (*R,R*)-46** and {(R)-1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}{(S)-1-[1-(diphenylphosphino)-3-phenylpropan-3-onyl]isoquinolyl-*N,P*}palladium(II) perchlorate, (*R,S*)-**46**.** Bis(acetonitrile) complex (*R*)-**5** (0.55 g, 1.13 mmol) was added to a solution of diphenylphosphine (0.21g, 1.13 mmol, 1 equiv.) in dichloromethane (5 mL). Enone **45** (0.29 g, 1.13 mmol) was added, followed by Et₃N (0.11 g, 1.13 mmol) in DCM (1 mL) dropwise. The reaction was monitored by ³¹P{¹H} NMR and found to be completed overnight. The crude product was then purified by column chromatography. NMR calculated yield: 95%; ³¹P{¹H} NMR (202 MHz, CDCl₃) 2 signals in ca. 2.5 : 1 ratio, δ 54.8 (s), 58.5 (s). ³¹P{¹H} NMR (121 MHz, CDCl₃) 2 signals in ca. 2.5 : 1 ratio, δ 55.4 (s), 59.1 (s).

{(R)-1-[1-(N,N-Dimethylamino)ethyl]naphthyl-C,N}{(R)-1-[1-(diphenylphosphino)-3-phenylpropan-3-onyl]isoquinolyl-N,P}palladium(II) perchlorate, (R,R)-46. Recrystallization from dichloromethane-diethyl ether gives the product as white crystals (0.45 g, 68%). mp 207-210 °C (dec); $[\alpha]_D = -250^\circ$ ($c = 1$, CH₂Cl₂); $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl₃) δ 55.4 (s).

{(R)-1-[1-(N,N-Dimethylamino)ethyl]naphthyl-C,N}{(S)-1-[1-(diphenylphosphino)-3-phenylpropan-3-onyl]isoquinolyl-N,P}palladium(II) perchlorate, (R,S)-46. Recrystallization from ethyl acetate-diethyl ether gives the product as white crystals (0.21 g, 75%). mp 217-219 °C (dec); $[\alpha]_D = +255^\circ$ ($c = 1$, CH₂Cl₂); $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl₃) δ 59.1 (s).

Dichloro{1-[1-(diphenylphosphino)-3-phenylpropan-3-onyl]isoquinolyl-N,P}palladium(II), 47. Conc. HCl (1 mL) was added to (R,R)-46 (0.022 g, 0.026 mmol) in dichloromethane (5 mL) and stirred for 2 h. The reaction was quenched with water (50 mL). The organic layer was extracted, washed with water (50 mL x 2) and dried with anhydrous MgSO₄. The product was recrystallized from dichloromethane-diethyl ether to give yellow crystals (0.016 g, 97%). mp 236-238 °C (dec); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl₃) δ 51.9 (s).

[1-(1-Isoquinolyl)-3-phenylpropan-3-onyl]diphenylphosphine, 48. To a solution of diphenylphosphine (0.055 g, 0.29 mmol) in dichloromethane (5 mL), (R)-5 (0.029 g, 0.058 mmol, 20 mol%) was added. The solution was stirred at r.t. for 5 min and then was cooled to -80 °C. Subsequently, the enone 45 (0.078 g, 0.3 mmol) was added. Et₃N (0.03 g, 0.29 mmol) in dichloromethane (1 mL) was added dropwise. The solution was subsequently stirred at -80 °C and the reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR. The reaction was found to be

completed at 3 d. The product was not isolated and directly used in further reactions. NMR calculated yield: 73%; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) δ 3.0 (s).

Coordination of 48 to (R)-4. Formation of chloro{(R)-1-[1-(N,N-dimethylamino)ethyl]naphthyl-C,N}{(R)-[1-(1-isoquinolyl)-3-phenylpropan-3-onyl]diphenylphosphine}palladium(II), (R,R)-49, and chloro{(R)-1-[1-(N,N-dimethylamino)ethyl]naphthyl-C,N}{(S)-[1-(1-isoquinolyl)-3-phenylpropan-3-onyl]diphenylphosphine}palladium(II), (R,S)-49. (R)-4 (0.1 g, 0.145 mmol, 0.5 equiv.) in dichloromethane (5 mL) was added to **48** and stirred for 30 min. The solvent was removed under reduced pressure to give a yellow solid. $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 2 signals in 1 : 1 ratio, δ 53.0 (s), 54.8 (s); $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3) 2 signals in 1 : 1 ratio, δ 53.5 (s), 55.4 (s).

Synthesis of $\{(R)-1-[1-(N,N\text{-dimethylamino})ethyl]naphthyl-C,N\}\{(R_C,R_P)-1-[1-((2\text{-methoxyphenyl})phenylphosphino)-3\text{-phenylpropan-3-onyl}]isoquinolyl-N,P\}$ palladium(II) perchlorate, $(R,R_C,R_P)\text{-50}$, $\{(R)-1-[1-(N,N\text{-dimethylamino})ethyl]naphthyl-C,N\}\{(S_C,S_P)-1-[1-((2\text{-methoxyphenyl})phenylphosphino)-3\text{-phenylpropan-3-onyl}]isoquinolyl-N,P\}$ palladium(II) perchlorate, $(R,S_C,S_P)\text{-50}$, $\{(R)-1-[1-(N,N\text{-dimethylamino})ethyl]naphthyl-C,N\}\{(R_C,S_P)-1-[1-((2\text{-methoxyphenyl})phenylphosphino)-3\text{-phenylpropan-3-onyl}]isoquinolyl-N,P\}$ palladium(II) perchlorate, $(R,R_C,S_P)\text{-50}$ and $\{(R)-1-[1-(N,N\text{-dimethylamino})ethyl]naphthyl-C,N\}\{(S_C,R_P)-1-[1-((2\text{-methoxyphenyl})phenylphosphino)-3\text{-phenylpropan-3-onyl}]isoquinolyl-N,P\}$ palladium(II) perchlorate, $(R,S_C,R_P)\text{-50}$. Bis(acetonitrile) complex $(R)\text{-5}$ (0.082 g, 0.31 mmol) was added to a solution of *o*-anisylphenylphosphine (0.068 g, 0.31 mmol, 1 equiv.) in dichloromethane (5 mL). Enone **45** (0.15 g, 0.31 mmol) was added, followed by Et₃N (0.032 g, 0.31 mmol) in DCM (1 mL) dropwise. The reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR and found to be completed in 3 d. The crude product was then purified by column chromatography. NMR calculated yield: 93%; $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, CDCl₃) 4 signals in ca. 1 : 3.6 : 1.6 : 2.1 ratio, δ 46.4 (s), 50.4 (s), 55.6 (s), 58.4 (s).

$\{(R)-1-[1-(N,N\text{-Dimethylamino})ethyl]naphthyl-C,N\}\{(R_C,R_P)-1-[1-((2\text{-methoxyphenyl})phenylphosphino)-3\text{-phenylpropan-3-onyl}]isoquinolyl-N,P\}$ palladium(II) perchlorate, $(R,R_C,R_P)\text{-50}$. Recrystallization from dichloromethane-diethyl ether gives the product as white crystals (0.104 g,

88%). mp 197-200 °C (dec); $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, CDCl_3) δ 50.4 (s), (202 MHz, CDCl_3) δ 50.1 (s).

Dichloro{1-[1-((2-methoxyphenyl)phenylphosphino)-3-phenylpropan-3-onyl]isoquinolyl-*N,P*}palladium(II), **51.** Conc. HCl (1 mL) was added to (*R,R_C,R_P*)-**50** (0.018 g, 0.02 mmol) in dichloromethane (5 mL) and stirred for 2 h. The reaction was quenched with water (50 mL). The organic layer was extracted, washed with water (50 mL x 2) and dried with anhydrous MgSO_4 . The product was purified by column chromatography to give a yellow solid (0.013 g, 95%). $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3), δ 46.0 (s).

[1-(1-Isoquinolyl)-3-phenylpropan-3-onyl](2-methoxyphenyl)phenylphosphine, **52.** To a solution of *o*-anisylphenylphosphine (0.066 g, 0.31 mmol) in dichloromethane (5 mL), (*R*)-**5** (0.022 g, 0.046 mmol, 15 mol%) was added. The solution was stirred at r.t. for 5 min. Enone **45** (0.088 g, 0.34 mmol) was added. Et_3N (0.031 g, 0.31 mmol) in dichloromethane (1 mL) was added dropwise. The solution was subsequently stirred at r.t. and the reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR. The reaction was found to be completed in 24 h. The product was not isolated and directly used in further reactions. NMR calculated yield: 84%; $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 2 signals in ca. 1 : 1.7 ratio, δ -6.6 (s), -4.4 (s).

Chloro{(*R*)-1-[1-(*N,N*-dimethylamino)ethyl]naphthyl-*C,N*}{[1-(1-isoquinolyl)-3-phenylpropan-3-onyl](2-methoxyphenyl)phenylphosphine}palladium(II), (*R*)-53**.** (*R*)-**4** (0.105 g, 0.155 mmol, 0.5 equiv.) in dichloromethane (5 mL) was added to **50** and stirred for 30 min. The solvent was removed under reduced pressure to give a yellow

solid. $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, CDCl_3) 4 signals in ca. 1 : 3.8 : 10.2 : 0.25
ratio, δ 46.4 (s), 50.2 (s), 55.3 (s), 56.4 (s).

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Appendices

Table A1-1 Crystal data and structure refinement for (R,S)-12

Chemical formula	C ₄₀ H ₄₇ ClNPPd		
Formula weight	714.60		
Temperature	103(2) K		
Wavelength	0.71073 Å		
Crystal size	0.340 x 0.400 x 0.420 mm		
Crystal habit	yellow block		
Crystal system	orthorhombic		
Space group	P 21 21 21		
Unit cell dimensions	a = 9.8837(4) Å	α = 90°	
	b = 18.2439(8) Å	β = 90°	
	c = 19.3437(8) Å	γ = 90°	
Volume	3488.0(3) Å ³		
Z	4		
Density (calculated)	1.361 g/cm ³		
Absorption coefficient	0.683 mm ⁻¹		
F(000)	1488		
Theta range for data collection	2.34 to 32.03°		
Reflections collected	81864		
Coverage of independent reflections	99.9%		
Absorption correction	multi-scan		
Max. and min. transmission	0.8010 and 0.7620		
Refinement method	Full-matrix least-squares on F ²		
Refinement program	SHELXL-2013 (Sheldrick, 2013)		
Function minimized	Σ w(F _o ² - F _c ²) ²		
Data / restraints / parameters	12139 / 0 / 405		
Goodness-of-fit on F ²	1.081		
Δ/σ _{max}	0.002		
Final R indices	11409 data; I>2σ(I)	R1 = 0.0256, wR2 = 0.0584	
	all data	R1 = 0.0295, wR2 = 0.0602	
Weighting scheme	w=1/[σ ² (F _o ²)+(0.0279P) ² +0.5978P] where P=(F _o ² +2F _c ²)/3		
Absolute structure parameter	-0.0(0)		
Largest diff. peak and hole	0.388 and -0.610 eÅ ⁻³		
R.M.S. deviation from mean	0.083 eÅ ⁻³		

Table A1-2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$) for (R,S)-12. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Pd1	0.62296(2)	0.31668(2)	0.14131(2)	0.00810(4)
C1	0.6299(2)	0.21014(11)	0.11750(10)	0.0099(4)
C2	0.7356(2)	0.15962(12)	0.13271(11)	0.0113(4)
C3	0.7311(2)	0.08892(12)	0.10868(12)	0.0124(4)
C4	0.6229(3)	0.06461(11)	0.06602(11)	0.0116(4)
C5	0.6176(3)	0.99143(11)	0.04136(12)	0.0152(4)
C6	0.5114(3)	0.96848(13)	0.00067(13)	0.0178(5)
C7	0.4091(2)	0.01790(13)	0.98141(12)	0.0166(5)
C8	0.4132(2)	0.08911(12)	0.00405(12)	0.0134(4)
C9	0.5187(2)	0.11491(12)	0.04762(11)	0.0103(4)
C10	0.5246(2)	0.18806(13)	0.07473(11)	0.0102(4)
C11	0.4147(2)	0.24378(12)	0.06107(12)	0.0104(4)
C12	0.3109(3)	0.24331(13)	0.11967(13)	0.0137(5)
C13	0.5581(2)	0.32018(14)	0.98899(11)	0.0152(4)
C14	0.3847(3)	0.37795(12)	0.05594(12)	0.0147(4)
C15	0.7332(2)	0.21641(11)	0.28566(11)	0.0113(4)
C16	0.6078(2)	0.18114(13)	0.29086(11)	0.0154(4)
C17	0.5973(3)	0.11332(13)	0.32351(13)	0.0191(5)
C18	0.7121(3)	0.07950(13)	0.34984(14)	0.0216(5)
C19	0.8370(3)	0.11272(14)	0.34261(13)	0.0206(5)
C20	0.8485(2)	0.18130(13)	0.31072(11)	0.0154(4)
C21	0.9110(2)	0.33703(11)	0.23837(12)	0.0101(4)
C22	0.9537(2)	0.36791(12)	0.17559(12)	0.0125(4)
C23	0.0808(3)	0.40001(13)	0.16952(14)	0.0169(5)
C24	0.1678(2)	0.40129(14)	0.22568(13)	0.0171(5)
C25	0.1279(3)	0.37018(12)	0.28813(12)	0.0163(4)
C26	0.0005(2)	0.33907(12)	0.29490(12)	0.0126(4)
C27	0.6516(2)	0.37083(11)	0.30382(11)	0.0098(4)
C28	0.5051(2)	0.34809(14)	0.32013(13)	0.0165(5)
C29	0.7356(2)	0.38884(11)	0.36676(11)	0.0103(4)
C30	0.7397(2)	0.33986(12)	0.42238(12)	0.0128(4)
C31	0.8213(3)	0.35167(13)	0.47998(12)	0.0156(5)
C32	0.8243(3)	0.29929(13)	0.54169(13)	0.0198(5)
C33	0.7358(4)	0.32755(18)	0.59994(15)	0.0373(8)
C34	0.7867(4)	0.22069(16)	0.52278(17)	0.0416(9)
C35	0.8997(3)	0.41514(13)	0.48124(13)	0.0178(5)
C36	0.8958(3)	0.46483(13)	0.42644(12)	0.0162(5)
C37	0.8147(2)	0.45309(12)	0.36840(12)	0.0120(4)
C38	0.8090(2)	0.50808(12)	0.30891(12)	0.0125(4)

	x/a	y/b	z/c	U(eq)
C39	0.6766(3)	0.55190(13)	0.31184(14)	0.0179(5)
C40	0.9297(3)	0.56040(14)	0.30612(14)	0.0216(5)
Cl1	0.62258(6)	0.44860(3)	0.14677(3)	0.01572(10)
N1	0.48496(18)	0.31709(11)	0.05556(9)	0.0100(3)
P1	0.73583(6)	0.30586(3)	0.24260(3)	0.00821(10)

Table A2-1 Crystal data and structure refinement for (S)-18

Chemical formula	$C_{52}H_{57}ClO_{1.50}P_3Pd$	
Formula weight	940.73	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.120 x 0.180 x 0.320 mm	
Crystal habit	colorless block	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	$a = 10.7690(6)$ Å	$\alpha = 90^\circ$
	$b = 11.1444(6)$ Å	$\beta = 104.6581(19)^\circ$
	$c = 20.4571(11)$ Å	$\gamma = 90^\circ$
Volume	$2375.2(2)$ Å ³	
Z	2	
Density (calculated)	1.315 g/cm ³	
Absorption coefficient	0.585 mm ⁻¹	
F(000)	978	
Theta range for data collection	3.04 to 31.05°	
Index ranges	-15 ≤ h ≤ 15, -16 ≤ k ≤ 16, -29 ≤ l ≤ 25	
Reflections collected	46805	
Independent reflections	15170 [R(int) = 0.0801]	
Coverage of independent reflections	99.8%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9330 and 0.8350	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2013 (Sheldrick, 2013)	
Function minimized	$\sum w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	15170 / 218 / 600	
Goodness-of-fit on F²	0.992	
$\Delta/\sigma_{\max}$	0.001	
Final R indices	11870 data; I > 2σ(I) R1 = 0.0503, wR2 = 0.0768	
	all data R1 = 0.0764, wR2 = 0.0865	
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0235P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	
Absolute structure parameter	-0.0(0)	
Largest diff. peak and hole	0.624 and -0.764 eÅ ⁻³	
R.M.S. deviation from mean	0.104 eÅ ⁻³	

Table A2-2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$) for (S)-18. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Pd1	0.82197(3)	0.38148(3)	0.24951(2)	0.01181(7)
C1	0.7490(4)	0.3331(4)	0.1488(2)	0.0162(10)
C2	0.6164(4)	0.3362(4)	0.1180(2)	0.0174(10)
C3	0.5243(4)	0.3971(5)	0.1523(2)	0.0186(10)
C4	0.5172(5)	0.5309(4)	0.1314(2)	0.0228(11)
C5	0.3883(4)	0.3454(4)	0.1364(2)	0.0237(11)
C6	0.5751(5)	0.2935(4)	0.0515(2)	0.0219(11)
C7	0.6598(5)	0.2521(4)	0.0168(2)	0.0238(11)
C8	0.7917(5)	0.2598(4)	0.0433(2)	0.0188(10)
C9	0.8821(5)	0.2214(4)	0.0011(2)	0.0203(10)
C10	0.8665(5)	0.3006(5)	0.9381(3)	0.0318(13)
C11	0.8637(5)	0.0895(4)	0.9816(3)	0.0309(13)
C12	0.8343(4)	0.3051(4)	0.1091(2)	0.0148(9)
C13	0.9745(4)	0.3396(4)	0.1388(2)	0.0155(9)
C14	0.0559(5)	0.2351(4)	0.1743(2)	0.0218(11)
C15	0.8975(4)	0.5957(4)	0.1451(2)	0.0161(10)
C16	0.8984(4)	0.7056(4)	0.1778(2)	0.0197(10)
C17	0.8388(5)	0.8055(4)	0.1428(3)	0.0268(12)
C18	0.7789(5)	0.7960(5)	0.0745(3)	0.0302(13)
C19	0.7781(5)	0.6879(5)	0.0418(3)	0.0290(12)
C20	0.8362(5)	0.5872(4)	0.0761(2)	0.0212(11)
C21	0.1243(4)	0.5034(4)	0.2404(2)	0.0136(9)
C22	0.1910(4)	0.6000(4)	0.2215(2)	0.0179(10)
C23	0.3181(5)	0.6199(4)	0.2544(3)	0.0234(11)
C24	0.3822(5)	0.5419(4)	0.3043(2)	0.0212(11)
C25	0.3184(4)	0.4452(4)	0.3236(2)	0.0185(10)
C26	0.1906(4)	0.4275(4)	0.2916(2)	0.0161(10)
C27	0.7602(4)	0.5885(4)	0.3540(2)	0.0159(10)
C28	0.7145(4)	0.6447(4)	0.2918(2)	0.0177(10)
C29	0.6334(5)	0.7435(4)	0.2856(3)	0.0232(11)
C30	0.5941(5)	0.7831(4)	0.3411(3)	0.0276(12)
C31	0.6364(5)	0.7271(4)	0.4027(3)	0.0318(13)
C32	0.7213(5)	0.6308(4)	0.4099(3)	0.0257(12)
C33	0.0227(5)	0.5104(4)	0.4056(2)	0.0198(10)
C34	0.0656(5)	0.6208(4)	0.3878(3)	0.0267(12)
C35	0.1899(5)	0.6599(5)	0.4183(3)	0.0323(14)
C36	0.2711(5)	0.5907(5)	0.4659(3)	0.0339(14)
C37	0.2292(5)	0.4815(6)	0.4829(3)	0.0483(18)
C38	0.1058(5)	0.4410(5)	0.4531(3)	0.0368(15)
C39	0.8089(4)	0.3535(4)	0.4147(2)	0.0202(11)
C40	0.6903(5)	0.2872(4)	0.3733(2)	0.0212(11)

	x/a	y/b	z/c	U(eq)
C41	0.5878(15)	0.1404(18)	0.2550(9)	0.016(3)
C42	0.5915(16)	0.0800(18)	0.1965(9)	0.023(3)
C43	0.4880(16)	0.0093(13)	0.1629(8)	0.025(3)
C44	0.3827(13)	0.0016(13)	0.1902(11)	0.030(3)
C45	0.3771(13)	0.0601(15)	0.2481(11)	0.031(3)
C46	0.4817(15)	0.1313(18)	0.2811(10)	0.022(2)
C41A	0.599(3)	0.138(3)	0.2451(17)	0.024(6)
C42A	0.615(3)	0.084(3)	0.1865(17)	0.023(5)
C43A	0.518(3)	0.013(2)	0.1475(15)	0.034(5)
C44A	0.404(2)	0.9958(19)	0.1670(18)	0.035(6)
C45A	0.388(2)	0.050(2)	0.2256(18)	0.034(5)
C46A	0.485(3)	0.121(3)	0.2646(16)	0.032(6)
C47	0.8533(4)	0.1199(4)	0.3303(2)	0.0191(10)
C48	0.9821(5)	0.1541(4)	0.3462(3)	0.0259(12)
C49	0.0783(5)	0.0760(5)	0.3788(3)	0.0305(13)
C50	0.0448(5)	0.9609(5)	0.3940(3)	0.0344(14)
C51	0.9178(5)	0.9258(5)	0.3775(3)	0.0376(15)
C52	0.8229(5)	0.0042(4)	0.3463(3)	0.0301(13)
Cl1	0.41408(12)	0.18761(11)	0.43586(6)	0.0272(3)
O1	0.627(2)	0.408(2)	0.5288(14)	0.024(4)
O1A	0.602(3)	0.3991(19)	0.5057(19)	0.055(5)
O2	0.6606(12)	0.4325(10)	0.6380(7)	0.024(4)
O3	0.8855(14)	0.3990(16)	0.7437(7)	0.039(5)
P1	0.96202(11)	0.46542(10)	0.19622(6)	0.0128(2)
P2	0.86581(12)	0.45922(10)	0.35962(6)	0.0142(2)
P3	0.72705(12)	0.22938(10)	0.29671(6)	0.0162(3)

Table A3-1 Crystal data and structure refinement for 24

Chemical formula	C ₃₈ H ₂₇ O ₂ PS	
Formula weight	578.62 g/mol	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal size	0.400 x 0.410 x 0.420 mm	
Crystal habit	colorless block	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 11.2623(4) Å	α = 91.346(3)°
	b = 11.3502(5) Å	β = 111.966(2)°
	c = 12.3959(5) Å	γ = 104.270(2)°
Volume	1412.34(10) Å ³	
Z	2	
Density (calculated)	1.361 g/cm ³	
Absorption coefficient	0.207 mm ⁻¹	
F(000)	604	
Theta range for data collection	3.03 to 31.11°	
Index ranges	-16 ≤ h ≤ 16, -16 ≤ k ≤ 16, -17 ≤ l ≤ 17	
Reflections collected	44486	
Independent reflections	9054 [R(int) = 0.0736]	
Coverage of independent reflections	99.7%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9220 and 0.9180	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)	
Function minimized	Σ w(F _o ² - F _c ²) ²	
Data / restraints / parameters	9054 / 0 / 380	
Goodness-of-fit on F²	1.022	
Final R indices	6104 data; I > 2σ(I)	R1 = 0.0524, wR2 = 0.1205
	all data	R1 = 0.0925, wR2 = 0.1456
Weighting scheme	w = 1/[σ ² (F _o ²) + (0.0614P) ² + 0.8455P] where P = (F _o ² + 2F _c ²)/3	
Largest diff. peak and hole	0.633 and -0.434 eÅ ⁻³	
R.M.S. deviation from mean	0.075 eÅ ⁻³	

Table A3-2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$) for 24. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C1	0.23312(17)	0.81756(17)	0.20380(16)	0.0167(3)
C2	0.33691(17)	0.93055(17)	0.22288(16)	0.0169(3)
C3	0.34746(19)	0.03829(17)	0.28871(17)	0.0197(4)
C4	0.4465(2)	0.14397(19)	0.30468(18)	0.0242(4)
C5	0.5389(2)	0.1462(2)	0.2545(2)	0.0298(5)
C6	0.5328(2)	0.0431(2)	0.1916(2)	0.0292(5)
C7	0.43306(19)	0.93275(19)	0.17377(17)	0.0209(4)
C8	0.42887(19)	0.82279(19)	0.10831(17)	0.0215(4)
C9	0.5250(2)	0.8170(2)	0.0625(2)	0.0339(5)
C10	0.5148(2)	0.7123(2)	0.9982(2)	0.0370(5)
C11	0.4090(2)	0.6083(2)	0.9766(2)	0.0331(5)
C12	0.3168(2)	0.6097(2)	0.0236(2)	0.0299(5)
C13	0.32491(19)	0.71626(19)	0.08967(17)	0.0219(4)
C14	0.22896(19)	0.71636(18)	0.13960(18)	0.0218(4)
C15	0.01869(18)	0.91058(17)	0.22452(19)	0.0211(4)
C16	0.0042(2)	0.9886(2)	0.3044(2)	0.0318(5)
C17	0.9237(2)	0.0675(2)	0.2631(3)	0.0450(7)
C18	0.8599(2)	0.0690(2)	0.1440(3)	0.0458(7)
C19	0.8729(2)	0.9908(3)	0.0660(3)	0.0419(6)
C20	0.9527(2)	0.9119(2)	0.1055(2)	0.0307(5)
C21	0.93359(17)	0.60085(16)	0.25871(15)	0.0155(3)
C22	0.95024(17)	0.48670(16)	0.28943(15)	0.0159(3)
C23	0.87373(19)	0.42540(17)	0.34757(16)	0.0185(4)
C24	0.78257(18)	0.47342(16)	0.37248(16)	0.0177(3)
C25	0.76203(17)	0.58517(16)	0.33597(16)	0.0166(3)
C26	0.83948(17)	0.64733(16)	0.27823(16)	0.0170(3)
C27	0.66952(18)	0.64368(17)	0.36168(16)	0.0180(3)
C28	0.5454(2)	0.5760(2)	0.35655(19)	0.0262(4)
C29	0.4625(2)	0.6345(2)	0.3824(2)	0.0315(5)
C30	0.5022(2)	0.7598(2)	0.41277(18)	0.0285(5)
C31	0.6236(2)	0.8283(2)	0.41747(18)	0.0270(4)
C32	0.7078(2)	0.77062(19)	0.39254(17)	0.0224(4)
C33	0.03929(18)	0.42739(16)	0.25846(16)	0.0173(3)
C34	0.12544(19)	0.37394(18)	0.34064(17)	0.0220(4)
C35	0.2046(2)	0.3147(2)	0.31007(19)	0.0276(4)
C36	0.1963(2)	0.3062(2)	0.1956(2)	0.0286(5)
C37	0.1095(2)	0.3577(2)	0.11244(19)	0.0269(4)
C38	0.0323(2)	0.41843(18)	0.14385(17)	0.0227(4)
O1	0.01486(12)	0.67103(12)	0.20717(11)	0.0176(3)

	x/a	y/b	z/c	U(eq)
O2	0.71184(15)	0.41361(13)	0.43304(14)	0.0254(3)
P1	0.11632(5)	0.80281(4)	0.27436(4)	0.01615(11)
S1	0.19294(5)	0.81594(5)	0.44422(4)	0.02355(12)

Table A4-1 Crystal data and structure refinement for (R,S)-30

Empirical formula	C ₄₇ H ₄₄ C ₁₆ N O P Pd	
Formula weight	988.9	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 9.9217(3) Å	α = 90°
	b = 17.8163(7) Å	β = 90°
	c = 24.6478(9) Å	γ = 90°
Volume	4356.9(3) Å ³	
Z	4	
Density (calculated)	1.508 Mg/m ³	
Absorption coefficient	0.868 mm ⁻¹	
F(000)	2016	
Crystal size	0.40 x 0.32 x 0.22 mm ³	
Theta range for data collection	1.41 to 31.10°	
Index ranges	-13 ≤ h ≤ 14, -20 ≤ k ≤ 25, -35 ≤ l ≤ 35	
Reflections collected	45943	
Independent reflections	13860 [R(int) = 0.0557]	
Completeness to theta = 31.10°	99.2%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8319 and 0.7227	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	13860 / 620 / 608	
Goodness-of-fit on F²	1.099	
Final R indices [I > 2σ(I)]	R1 = 0.0396, wR2 = 0.0894	
R indices (all data)	R1 = 0.0538, wR2 = 0.1135	
Absolute structure parameter	-0.03(2)	
Largest diff. peak and hole	0.743 and -0.816 e.Å ⁻³	

Table A4-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for (R,S)-30. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Pd(1)	4200(1)	9985(1)	3317(1)	10(1)
C(1)	5242(3)	10442(2)	3927(1)	12(1)
C(2)	4827(3)	10488(2)	4480(1)	12(1)
C(3)	5501(3)	10923(2)	4847(1)	14(1)
C(4)	6654(3)	11348(2)	4689(1)	14(1)
C(5)	7381(3)	11784(2)	5066(1)	19(1)
C(6)	8471(3)	12194(2)	4914(1)	21(1)
C(7)	8883(3)	12192(2)	4364(1)	19(1)
C(8)	8211(3)	11772(2)	3988(1)	16(1)
C(9)	7066(3)	11330(2)	4132(1)	12(1)
C(10)	6345(3)	10867(2)	3762(1)	13(1)
C(11)	6749(3)	10800(2)	3173(1)	12(1)
C(12)	7699(3)	10133(2)	3095(1)	19(1)
C(13)	5709(3)	10466(2)	2290(1)	19(1)
C(14)	4797(3)	11475(2)	2828(1)	19(1)
C(15)	3084(3)	8145(2)	3464(1)	13(1)
C(16)	4514(8)	7900(5)	3319(4)	13(2)
C(17)	5227(10)	8311(8)	2940(5)	16(2)
C(18)	6534(12)	8127(8)	2787(6)	20(2)
C(19)	7149(11)	7528(9)	3028(6)	20(2)
C(20)	6466(10)	7078(8)	3418(5)	16(2)
C(21)	7047(12)	6421(7)	3634(6)	21(2)
C(22)	6392(13)	5984(6)	4013(5)	20(2)
C(23)	5108(14)	6194(8)	4188(5)	21(2)
C(24)	4489(15)	6824(10)	3975(8)	19(2)
C(25)	5130(12)	7270(9)	3576(7)	16(2)
C(16A)	4509(10)	7829(7)	3365(5)	14(3)
C(17A)	5326(12)	8187(10)	2985(7)	17(3)
C(18A)	6665(13)	7986(10)	2894(8)	17(3)
C(19A)	7152(14)	7363(10)	3157(8)	20(3)
C(20A)	6350(14)	6937(9)	3521(8)	19(2)
C(21A)	6831(16)	6273(10)	3772(8)	24(3)
C(22A)	6070(20)	5886(10)	4142(9)	33(3)
C(23A)	4790(20)	6136(10)	4273(9)	27(3)
C(24A)	4280(20)	6774(12)	4027(10)	18(2)
C(25A)	5009(15)	7189(10)	3640(9)	13(2)
C(26)	2150(3)	8110(2)	2970(1)	13(1)
C(27)	1426(3)	7370(2)	2928(1)	15(1)
C(28)	471(3)	7268(2)	2464(1)	12(1)
C(29)	-68(3)	6556(2)	2377(1)	14(1)
C(30)	-985(3)	6431(2)	1961(1)	16(1)
C(31)	-1367(3)	7033(2)	1642(1)	15(1)

	x	y	z	U(eq)
C(32)	-872(3)	7750(2)	1727(1)	17(1)
C(33)	73(3)	7864(2)	2136(1)	15(1)
C(34)	1469(3)	9272(2)	4026(1)	13(1)
C(35)	432(3)	8751(2)	4004(1)	16(1)
C(36)	-851(3)	8938(2)	4183(1)	18(1)
C(37)	-1095(3)	9633(2)	4402(1)	20(1)
C(38)	-67(3)	10154(2)	4434(1)	20(1)
C(39)	1210(3)	9977(2)	4235(1)	15(1)
C(40)	4044(3)	8735(2)	4422(1)	12(1)
C(41)	3323(3)	8420(2)	4848(1)	15(1)
C(42)	3974(3)	8108(2)	5287(1)	20(1)
C(43)	5380(3)	8107(2)	5305(1)	20(1)
C(44)	6108(3)	8420(2)	4886(1)	19(1)
C(45)	5454(3)	8732(2)	4443(1)	14(1)
C(46)	8718(5)	10225(3)	1114(2)	43(1)
C(51)	6842(5)	3771(3)	3749(2)	44(1)
Cl(1)	2714(1)	9781(1)	2550(1)	17(1)
Cl(2)	-2496(1)	6881(1)	1112(1)	20(1)
Cl(3)	6866(2)	3947(1)	4444(1)	64(1)
Cl(4)	5427(2)	3260(1)	3547(1)	73(1)
Cl(5)	10049(1)	9928(1)	1542(1)	48(1)
Cl(6)	7348(1)	9589(1)	1144(1)	47(1)
N(1)	5450(2)	10723(2)	2858(1)	12(1)
O(1)	1573(3)	6877(2)	3263(1)	28(1)
P(1)	3201(1)	9072(1)	3806(1)	11(1)

Table A5-1 Crystal data and structure refinement for *cis-rac-41*

Chemical formula	C _{50.50} H ₄₁ Cl ₃ O ₂ P ₂ Pd
Formula weight	954.52
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal size	0.260 x 0.400 x 0.420 mm
Crystal habit	colorless block
Crystal system	triclinic
Space group	P -1
Unit cell dimensions	a = 13.2656(11) Å α = 99.718(2)° b = 13.8080(13) Å β = 116.4120(10)° c = 14.7389(13) Å γ = 106.6050(10)°
Volume	2175.0(3) Å ³
Z	2
Density (calculated)	1.457 g/cm ³
Absorption coefficient	0.725 mm ⁻¹
F(000)	974
Theta range for data collection	7.31 to 45.46°
Index ranges	-26 ≤ h ≤ 26, -27 ≤ k ≤ 27, -29 ≤ l ≤ 29
Reflections collected	123380
Independent reflections	36304 [R(int) = 0.0796]
Coverage of independent reflections	98.8%
Absorption correction	multi-scan
Max. and min. transmission	0.8339 and 0.7505
Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick, 2008)
Refinement method	Full-matrix least-squares on F ²
Refinement program	SHELXL-97 (Sheldrick, 2008)
Function minimized	Σ w(F _o ² - F _c ²) ²
Data / restraints / parameters	36304 / 205 / 573
Goodness-of-fit on F²	1.002
Δ/σ_{max}	0.003
Final R indices	24361 data; I > 2σ(I) R1 = 0.0484, wR2 = 0.0937 all data R1 = 0.0897, wR2 = 0.1112
Weighting scheme	w = 1/[σ ² (F _o ²) + (0.0390P) ² + 0.3957P] where P = (F _o ² + 2F _c ²)/3
Largest diff. peak and hole	1.296 and -1.413 eÅ ⁻³
R.M.S. deviation from mean	0.139 eÅ ⁻³

Table A5-2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$) for *cis-rac-41*. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Pd1	0.973166(8)	0.552962(7)	0.735587(7)	0.01032(2)
C1	0.06084(11)	0.44961(10)	0.74985(9)	0.01179(17)
C2	0.99010(11)	0.33733(10)	0.71907(10)	0.01394(19)
C3	0.04325(12)	0.26536(10)	0.73050(11)	0.0154(2)
C4	0.17201(11)	0.29941(10)	0.77581(10)	0.01331(19)
C5	0.22889(13)	0.22598(11)	0.79178(12)	0.0178(2)
C6	0.35417(13)	0.26130(11)	0.83894(12)	0.0179(2)
C7	0.42786(12)	0.37113(11)	0.87132(10)	0.0148(2)
C8	0.37527(11)	0.44391(10)	0.85665(10)	0.01240(18)
C9	0.24559(11)	0.41072(10)	0.80830(9)	0.01134(17)
C10	0.18720(10)	0.48436(9)	0.79351(9)	0.01017(16)
C11	0.26612(10)	0.60233(9)	0.83090(9)	0.01052(17)
C12	0.32005(11)	0.63456(10)	0.76166(10)	0.01212(18)
C13	0.43134(11)	0.74214(10)	0.82314(10)	0.01280(18)
C14	0.47870(11)	0.79911(10)	0.76376(10)	0.01380(19)
C15	0.42980(13)	0.75553(12)	0.65325(11)	0.0195(2)
C16	0.47856(15)	0.81213(14)	0.60242(13)	0.0245(3)
C17	0.57672(15)	0.91167(14)	0.66285(14)	0.0243(3)
C18	0.62766(15)	0.95661(13)	0.77314(13)	0.0239(3)
C19	0.57828(13)	0.90002(11)	0.82284(12)	0.0194(2)
C20	0.21863(11)	0.70711(10)	0.98368(10)	0.01232(18)
C21	0.34354(12)	0.76097(11)	0.06503(10)	0.0161(2)
C22	0.37895(14)	0.77893(13)	0.17260(11)	0.0219(3)
C23	0.29080(16)	0.74383(14)	0.20029(12)	0.0235(3)
C24	0.16710(15)	0.69087(13)	0.12057(12)	0.0218(3)
C25	0.13108(13)	0.67193(12)	0.01248(11)	0.0164(2)
C26	0.21075(11)	0.79175(10)	0.81017(10)	0.01195(18)
C27	0.28838(13)	0.89338(11)	0.88931(11)	0.0165(2)
C28	0.32457(16)	0.98358(12)	0.86264(13)	0.0241(3)
C29	0.28217(17)	0.97196(12)	0.75508(14)	0.0251(3)
C30	0.20371(15)	0.87248(12)	0.67422(12)	0.0197(2)
C31	0.16732(11)	0.78252(10)	0.70126(10)	0.01366(19)
C32	0.05863(14)	0.66531(14)	0.51710(11)	0.0218(3)
C33	0.79132(11)	0.64181(10)	0.80846(10)	0.01267(18)
C34	0.74833(12)	0.71444(11)	0.84037(11)	0.0152(2)
C35	0.70083(12)	0.69926(12)	0.90637(11)	0.0167(2)
C36	0.69609(12)	0.61170(12)	0.94148(11)	0.0176(2)
C37	0.73758(13)	0.53867(12)	0.90962(12)	0.0190(2)
C38	0.78456(12)	0.55347(11)	0.84297(11)	0.0156(2)

	x/a	y/b	z/c	U(eq)
C39	0.74706(11)	0.64226(10)	0.59520(10)	0.01352(19)
C40	0.62796(12)	0.63090(13)	0.56488(12)	0.0193(2)
C41	0.54421(14)	0.61709(15)	0.45903(13)	0.0252(3)
C42	0.58003(15)	0.61674(15)	0.38400(12)	0.0251(3)
C43	0.69855(16)	0.62819(16)	0.41371(12)	0.0272(3)
C44	0.78127(13)	0.63904(14)	0.51850(11)	0.0222(3)
C45	0.9398(4)	0.8161(3)	0.7847(4)	0.0143(8)
C46	0.8959(6)	0.8770(3)	0.7234(3)	0.0215(7)
C47	0.9464(7)	0.9885(3)	0.7698(4)	0.0274(9)
C48	0.0408(5)	0.0390(3)	0.8775(4)	0.0249(8)
C49	0.0847(4)	0.9780(4)	0.9388(4)	0.0213(8)
C50	0.0342(5)	0.8666(4)	0.8924(5)	0.0158(7)
C45A	0.9455(6)	0.8127(4)	0.7911(6)	0.0132(10)
C46A	0.9250(11)	0.8749(5)	0.7252(4)	0.0251(15)
C47A	0.9808(13)	0.9865(5)	0.7707(6)	0.0349(19)
C48A	0.0573(9)	0.0360(5)	0.8820(6)	0.0314(16)
C49A	0.0778(7)	0.9739(7)	0.9479(4)	0.0198(11)
C50A	0.0219(8)	0.8622(6)	0.9024(6)	0.0140(9)
C51	0.9267(5)	0.9101(4)	0.4934(4)	0.0399(9)
Cl3	0.79936(12)	0.93821(11)	0.47810(9)	0.0460(3)
Cl4	0.03742(14)	0.01560(13)	0.49351(12)	0.0564(3)
Cl1	0.77339(3)	0.41399(3)	0.61464(3)	0.01776(6)
Cl2	0.63812(5)	0.98239(5)	0.59987(4)	0.04185(12)
O1	0.48434(9)	0.78026(9)	0.92141(8)	0.01841(18)
O2	0.09044(9)	0.68147(8)	0.62684(8)	0.01671(17)
P1	0.16705(3)	0.67021(3)	0.84092(2)	0.00961(5)
P2	0.86611(3)	0.66639(3)	0.73153(3)	0.01135(5)

Table A6-1 Crystal data and structure refinement for (Z)-(S_C,S_P,S_N)-43

Chemical formula	C ₃₉ H ₃₇ Cl ₅ NO ₄ PPd		
Formula weight	898.32		
Temperature	103(2) K		
Wavelength	0.71073 Å		
Crystal size	0.340 x 0.340 x 0.360 mm		
Crystal habit	colorless block		
Crystal system	monoclinic		
Space group	P 1 21 1		
Unit cell dimensions	a = 13.5433(9) Å	α = 90°	
	b = 8.3171(6) Å	β = 97.313(3)°	
	c = 16.8968(15) Å	γ = 90°	
Volume	1887.8(2) Å ³		
Z	2		
Density (calculated)	1.580 g/cm ³		
Absorption coefficient	0.930 mm ⁻¹		
F(000)	912		
Theta range for data collection	1.21 to 31.33°		
Index ranges	-19<=h<=19, -12<=k<=12, -24<=l<=24		
Reflections collected	40922		
Independent reflections	12169 [R(int) = 0.0417]		
Coverage of independent reflections	98.7%		
Absorption correction	multi-scan		
Max. and min. transmission	0.7427 and 0.7306		
Structure solution technique	direct methods		
Structure solution program	SHELXS-97 (Sheldrick, 2008)		
Refinement method	Full-matrix least-squares on F ²		
Refinement program	SHELXL-97 (Sheldrick, 2008)		
Function minimized	Σ w(F _o ² - F _c ²) ²		
Data / restraints / parameters	12169 / 1 / 465		
Goodness-of-fit on F ²	1.082		
Δ/σ _{max}	0.004		
Final R indices	11139 data; I>2σ(I)	R1 = 0.0295, wR2 = 0.0704	
	all data	R1 = 0.0363, wR2 = 0.0883	
Weighting scheme	w=1/[σ ² (F _o ²)+(0.0480P) ² +0.0000P] where P=(F _o ² +2F _c ²)/3		
Absolute structure parameter	-0.0(0)		
Largest diff. peak and hole	0.713 and -0.571 eÅ ⁻³		
R.M.S. deviation from mean	0.142 eÅ ⁻³		

Table A6-2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$) for (Z)-(S_C,S_P,S_N)-43. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Pd1	0.624046(12)	0.59533(2)	0.660888(9)	0.01101(4)
C1	0.70904(18)	0.7926(3)	0.65521(15)	0.0128(5)
C2	0.72886(19)	0.8520(3)	0.58001(15)	0.0155(5)
C3	0.7904(2)	0.9800(3)	0.57367(15)	0.0163(5)
C4	0.83587(19)	0.0618(3)	0.64189(15)	0.0137(5)
C5	0.90315(19)	0.1901(3)	0.63635(16)	0.0161(5)
C6	0.9481(2)	0.2663(3)	0.70347(17)	0.0175(5)
C7	0.9273(2)	0.2157(3)	0.77887(17)	0.0185(5)
C8	0.86254(17)	0.0925(4)	0.78665(14)	0.0168(4)
C9	0.81533(19)	0.0097(3)	0.71836(15)	0.0136(5)
C10	0.75111(18)	0.8735(3)	0.72301(15)	0.0124(4)
C11	0.73336(18)	0.8104(3)	0.80438(15)	0.0135(5)
C12	0.82270(19)	0.7058(3)	0.84046(15)	0.0160(5)
C13	0.84392(19)	0.7141(4)	0.93096(16)	0.0177(5)
C14	0.86311(19)	0.5649(3)	0.97964(15)	0.0172(6)
C15	0.8883(2)	0.5819(4)	0.06212(15)	0.0219(5)
C16	0.9049(2)	0.4477(4)	0.11071(17)	0.0230(6)
C17	0.8959(2)	0.2974(4)	0.07651(17)	0.0194(5)
C18	0.8719(2)	0.2756(4)	0.99515(17)	0.0221(6)
C19	0.8551(2)	0.4100(4)	0.94712(17)	0.0191(6)
C20	0.72261(19)	0.4432(3)	0.52603(17)	0.0171(5)
C21	0.6928(2)	0.3357(3)	0.45426(17)	0.0192(5)
C22	0.5992(2)	0.2554(3)	0.47711(17)	0.0188(5)
C23	0.54930(18)	0.3894(3)	0.52156(15)	0.0123(4)
C24	0.50392(18)	0.3290(3)	0.59374(15)	0.0129(5)
C25	0.61513(18)	0.5494(3)	0.86477(15)	0.0140(5)
C26	0.61667(17)	0.6053(4)	0.94394(14)	0.0161(4)
C27	0.6450(2)	0.8287(4)	0.03372(17)	0.0256(6)
C28	0.6148(2)	0.4962(4)	0.00628(16)	0.0205(6)
C29	0.6126(2)	0.3329(4)	0.99012(17)	0.0220(6)
C30	0.6111(2)	0.2752(4)	0.91299(17)	0.0212(5)
C31	0.6122(2)	0.3841(3)	0.85061(16)	0.0177(5)
C32	0.51121(19)	0.8157(3)	0.78373(15)	0.0140(5)
C33	0.5132(2)	0.9803(3)	0.76686(16)	0.0190(5)
C34	0.4258(2)	0.0701(3)	0.76290(16)	0.0211(6)
C35	0.3371(2)	0.9969(4)	0.77469(17)	0.0210(6)
C36	0.3347(2)	0.8330(4)	0.78970(17)	0.0211(6)
C37	0.42104(19)	0.7435(3)	0.79466(16)	0.0180(5)
C38	0.2595(3)	0.3865(4)	0.6599(2)	0.0294(7)

	x/a	y/b	z/c	U(eq)
C39	0.9912(2)	0.7098(4)	0.6437(2)	0.0294(7)
Cl1	0.91413(5)	0.12722(8)	0.13674(4)	0.02599(16)
Cl2	0.23769(7)	0.41210(11)	0.75982(5)	0.03652(19)
Cl3	0.17939(6)	0.24040(10)	0.61094(5)	0.03109(17)
Cl4	0.00299(6)	0.58539(13)	0.56109(5)	0.03563(17)
Cl5	0.08220(7)	0.86156(11)	0.65530(6)	0.0388(2)
N1	0.62725(16)	0.5150(3)	0.54278(13)	0.0110(4)
O1	0.53152(14)	0.3942(2)	0.66158(11)	0.0165(4)
O2	0.43967(14)	0.2224(2)	0.58357(11)	0.0181(4)
O3	0.84717(16)	0.8452(3)	0.96307(12)	0.0216(4)
O4	0.62196(15)	0.7672(2)	0.95359(11)	0.0210(4)
P1	0.61979(5)	0.68842(8)	0.78296(4)	0.01220(12)

Table A7-1 Crystal data and structure refinement for (R,S)-46

Chemical formula	C ₄₄ H ₄₀ ClN ₂ O ₅ PPd	
Formula weight	849.60	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal size	0.120 x 0.300 x 0.400 mm	
Crystal habit	colorless block	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 10.5693(17) Å	$\alpha = 90^\circ$
	b = 14.901(2) Å	$\beta = 109.764(4)^\circ$
	c = 12.849(2) Å	$\gamma = 90^\circ$
Volume	1904.4(5) Å ³	
Z	2	
Density (calculated)	1.482 g/cm ³	
Absorption coefficient	0.649 mm ⁻¹	
F(000)	872	
Theta range for data collection	1.68 to 27.61°	
Index ranges	-12 ≤ h ≤ 13, -19 ≤ k ≤ 19, -16 ≤ l ≤ 16	
Reflections collected	21590	
Independent reflections	8813 [R(int) = 0.0620]	
Coverage of independent reflections	99.8%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9262 and 0.7813	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick, 2008)	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-97 (Sheldrick, 2008)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	8813 / 283 / 536	
Goodness-of-fit on F²	1.126	
$\Delta/\sigma_{\max}$	0.001	
Final R indices	6883 data; I > 2σ(I)	R1 = 0.0773, wR2 = 0.1996
	all data	R1 = 0.1087, wR2 = 0.2333
Weighting scheme	w = 1/[σ ² (F _o ²) + (0.1107P) ² + 9.9362P] where P = (F _o ² + 2F _c ²)/3	
Absolute structure parameter	-0.0(1)	
Largest diff. peak and hole	2.907 and -2.216 eÅ ⁻³	
R.M.S. deviation from mean	0.255 eÅ ⁻³	

Table A7-2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$) for (R,S)-46. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Pd1	0.36306(7)	0.62928(4)	0.77418(5)	0.02166(18)
C1	0.1731(9)	0.6785(6)	0.7144(8)	0.0229(19)
C2	0.0552(10)	0.6474(7)	0.7330(9)	0.030(2)
C3	0.9403(11)	0.6944(8)	0.6974(9)	0.035(3)
C4	0.9318(10)	0.7783(8)	0.6428(8)	0.029(2)
C5	0.8140(12)	0.8321(8)	0.6108(10)	0.035(2)
C6	0.8123(11)	0.9160(8)	0.5643(9)	0.036(2)
C7	0.9269(12)	0.9476(7)	0.5453(9)	0.033(2)
C8	0.0408(10)	0.8970(7)	0.5733(9)	0.029(2)
C9	0.0501(10)	0.8102(6)	0.6241(7)	0.0214(19)
C10	0.1680(10)	0.7567(6)	0.6567(7)	0.024(2)
C11	0.2937(10)	0.7894(6)	0.6376(7)	0.0204(19)
C12	0.3725(12)	0.8558(6)	0.7257(9)	0.033(2)
C13	0.5062(11)	0.7330(7)	0.6252(9)	0.030(2)
C14	0.3056(13)	0.6530(7)	0.5316(7)	0.037(3)
C15	0.6753(11)	0.6558(6)	0.8773(8)	0.027(2)
C16	0.8063(10)	0.6397(8)	0.9389(8)	0.030(2)
C17	0.8415(10)	0.5586(7)	0.0013(8)	0.028(2)
C18	0.9712(11)	0.5383(8)	0.0687(8)	0.031(2)
C19	0.9986(12)	0.4612(10)	0.1285(10)	0.043(3)
C20	0.8941(12)	0.3983(8)	0.1157(9)	0.033(2)
C21	0.7668(12)	0.4167(7)	0.0509(9)	0.034(2)
C22	0.7360(10)	0.4987(6)	0.9903(7)	0.023(2)
C23	0.6028(10)	0.5226(6)	0.9290(7)	0.0212(19)
C24	0.4870(10)	0.4624(5)	0.9231(7)	0.0184(18)
C25	0.4698(10)	0.3869(6)	0.8341(8)	0.0223(19)
C26	0.4166(11)	0.3008(6)	0.8682(9)	0.029(2)
C27	0.3577(11)	0.2345(6)	0.7795(8)	0.025(2)
C28	0.3665(10)	0.2392(6)	0.6751(8)	0.025(2)
C29	0.3108(14)	0.1743(6)	0.5959(9)	0.038(3)
C30	0.2338(14)	0.1064(6)	0.6180(10)	0.039(3)
C31	0.2191(14)	0.1024(7)	0.7200(11)	0.041(3)
C32	0.2808(13)	0.1640(7)	0.8022(10)	0.037(3)
C33	0.1989(10)	0.4502(6)	0.8528(8)	0.0212(19)
C34	0.1440(11)	0.4200(7)	0.7409(8)	0.034(2)
C35	0.0462(14)	0.3562(9)	0.7087(10)	0.047(3)
C36	0.9956(12)	0.3208(8)	0.7856(10)	0.042(3)
C37	0.0405(13)	0.3491(9)	0.8926(11)	0.043(3)
C38	0.1426(10)	0.4131(7)	0.9274(9)	0.027(2)

	x/a	y/b	z/c	U(eq)
C39	0.3342(11)	0.5778(6)	0.0253(8)	0.025(2)
C40	0.3844(11)	0.5303(8)	0.1257(8)	0.030(2)
C41	0.3795(13)	0.5711(8)	0.2227(9)	0.038(2)
C42	0.3318(12)	0.6503(6)	0.2197(8)	0.032(2)
C43	0.2786(11)	0.6996(7)	0.1216(9)	0.031(2)
C44	0.2818(11)	0.6630(7)	0.0267(10)	0.029(2)
N1	0.3745(8)	0.7085(5)	0.6372(6)	0.0175(15)
N2	0.5729(8)	0.5977(5)	0.8673(6)	0.0207(16)
O1	0.4278(9)	0.2860(5)	0.9626(6)	0.0393(19)
Cl1	0.6263(8)	0.4468(5)	0.5942(6)	0.0361(14)
O2	0.6327(18)	0.3544(9)	0.6306(13)	0.056(4)
O3	0.606(2)	0.5067(11)	0.6682(14)	0.087(5)
O4	0.5240(14)	0.4526(9)	0.4833(11)	0.065(4)
O5	0.7472(13)	0.4689(10)	0.5764(13)	0.069(4)
Cl1A	0.631(3)	0.4506(18)	0.613(2)	0.038(5)
O2A	0.667(5)	0.361(2)	0.656(4)	0.044(8)
O3A	0.511(4)	0.480(3)	0.620(3)	0.046(7)
O4A	0.644(5)	0.457(3)	0.504(3)	0.059(7)
O5A	0.729(4)	0.514(3)	0.672(4)	0.064(8)
P1	0.3340(3)	0.53048(15)	0.89424(19)	0.0196(5)

Table A8-1 Crystal data and structure refinement for *rac*-47

Chemical formula	$C_{31}H_{26.50}Cl_2NO_{1.25}PPd$	
Formula weight	641.30	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.020 x 0.120 x 0.200 mm	
Crystal habit	yellow plate	
Crystal system	monoclinic	
Space group	P 1 2 ₁ /n 1	
Unit cell dimensions	$a = 10.7255(10)$ Å	$\alpha = 90^\circ$
	$b = 40.711(4)$ Å	$\beta = 110.519(3)^\circ$
	$c = 13.3492(13)$ Å	$\gamma = 90^\circ$
Volume	$5459.1(9)$ Å ³	
Z	8	
Density (calculated)	1.561 g/cm ³	
Absorption coefficient	0.961 mm ⁻¹	
F(000)	2596	
Theta range for data collection	1.70 to 30.48°	
Index ranges	$-13 \leq h \leq 14$, $-50 \leq k \leq 53$, $-17 \leq l \leq 18$	
Reflections collected	41271	
Independent reflections	12959 [R(int) = 0.1027]	
Coverage of independent reflections	78.0%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9810 and 0.8310	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick, 2008)	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-97 (Sheldrick, 2008)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	12959 / 34 / 697	
Goodness-of-fit on F²	1.047	
$\Delta/\sigma_{\max}$	0.001	
Final R indices	6844 data; $I > 2\sigma(I)$	R1 = 0.0852, wR2 = 0.1855
	all data	R1 = 0.1742, wR2 = 0.2440
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.1141P)^2 + 0.0000P]$ where $P = (F_o^2 + 2F_c^2)/3$	
Extinction coefficient	0.0124(6)	
Largest diff. peak and hole	1.184 and -1.780 eÅ ⁻³	
R.M.S. deviation from mean	0.348 eÅ ⁻³	

Table A8-2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$) for *rac*-47. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Pd1	0.65907(7)	0.184285(16)	0.84419(5)	0.0226(2)
Pd2	0.73905(7)	0.100677(16)	0.68387(5)	0.0208(2)
C1	0.8962(8)	0.2156(2)	0.8120(7)	0.029(2)
C2	0.9630(9)	0.2387(2)	0.7762(7)	0.028(2)
C3	0.8960(9)	0.2613(2)	0.6990(7)	0.026(2)
C4	0.9614(11)	0.2873(2)	0.6680(8)	0.037(3)
C5	0.8913(12)	0.3093(3)	0.5954(9)	0.048(3)
C6	0.7512(12)	0.3069(3)	0.5468(9)	0.047(3)
C7	0.6869(10)	0.2816(2)	0.5757(8)	0.034(2)
C8	0.7570(10)	0.2591(2)	0.6528(7)	0.028(2)
C9	0.6907(8)	0.2328(2)	0.6878(6)	0.0201(19)
C10	0.5411(9)	0.2272(2)	0.6326(7)	0.024(2)
C11	0.5127(8)	0.2065(2)	0.5285(6)	0.024(2)
C12	0.3682(10)	0.2095(2)	0.4587(7)	0.027(2)
C13	0.3070(9)	0.1827(2)	0.3819(7)	0.027(2)
C14	0.1701(9)	0.1844(2)	0.3250(7)	0.030(2)
C15	0.1060(10)	0.1595(2)	0.2548(8)	0.040(3)
C16	0.1813(11)	0.1330(3)	0.2437(8)	0.046(3)
C17	0.3132(11)	0.1312(3)	0.2980(8)	0.042(3)
C18	0.3795(10)	0.1560(2)	0.3682(7)	0.034(2)
C19	0.3349(9)	0.1823(2)	0.6630(7)	0.024(2)
C20	0.3550(10)	0.1518(2)	0.6251(7)	0.030(2)
C21	0.2497(10)	0.1314(2)	0.5729(7)	0.031(2)
C22	0.1229(9)	0.1415(2)	0.5604(7)	0.030(2)
C23	0.1023(10)	0.1718(2)	0.5993(7)	0.032(2)
C24	0.2081(8)	0.1922(2)	0.6496(7)	0.024(2)
C25	0.4161(8)	0.2431(2)	0.7849(7)	0.023(2)
C26	0.4330(10)	0.2431(2)	0.8933(8)	0.032(2)
C27	0.3880(10)	0.2701(2)	0.9345(8)	0.034(2)
C28	0.3320(10)	0.2964(2)	0.8720(8)	0.036(2)
C29	0.3166(9)	0.2959(2)	0.7651(8)	0.032(2)
C30	0.3563(8)	0.2697(2)	0.7211(7)	0.029(2)
C31	0.0156(9)	0.1244(2)	0.7897(7)	0.025(2)
C32	0.1462(8)	0.1236(2)	0.8573(7)	0.0220(19)
C33	0.1860(9)	0.1021(2)	0.9457(7)	0.023(2)
C34	0.3208(10)	0.0993(2)	0.0155(7)	0.031(2)
C35	0.3537(9)	0.0775(2)	0.0972(7)	0.027(2)
C36	0.2563(9)	0.0578(2)	0.1161(7)	0.024(2)
C37	0.1257(9)	0.0601(2)	0.0505(7)	0.023(2)
C38	0.0877(8)	0.0818(2)	0.9621(6)	0.0196(19)
C39	0.9556(9)	0.0838(2)	0.8891(7)	0.023(2)

	x/a	y/b	z/c	U(eq)
C40	0.8472(8)	0.0638(2)	0.9069(6)	0.0214(19)
C41	0.7953(9)	0.0822(2)	0.9867(6)	0.024(2)
C42	0.7849(9)	0.0598(2)	0.0737(7)	0.026(2)
C43	0.7399(8)	0.0749(2)	0.1583(7)	0.0213(19)
C44	0.7380(10)	0.0547(2)	0.2443(7)	0.035(2)
C45	0.6996(9)	0.0682(3)	0.3262(7)	0.037(3)
C46	0.6658(10)	0.1012(3)	0.3254(8)	0.037(2)
C47	0.6667(9)	0.1207(2)	0.2403(7)	0.032(2)
C48	0.7045(9)	0.1081(2)	0.1574(7)	0.028(2)
C49	0.5632(9)	0.0501(2)	0.7989(7)	0.024(2)
C50	0.5513(10)	0.0218(2)	0.8512(7)	0.032(2)
C51	0.4314(10)	0.0160(2)	0.8692(7)	0.034(2)
C52	0.3282(10)	0.0378(2)	0.8368(7)	0.036(2)
C53	0.3429(10)	0.0664(2)	0.7846(8)	0.037(2)
C54	0.4587(9)	0.0727(2)	0.7661(7)	0.027(2)
C55	0.7553(8)	0.0190(2)	0.7259(6)	0.0214(19)
C56	0.6524(9)	0.0032(2)	0.6451(7)	0.030(2)
C57	0.6743(11)	0.9743(2)	0.6008(8)	0.040(3)
C58	0.8018(11)	0.9615(3)	0.6376(7)	0.039(3)
C59	0.9058(9)	0.9769(2)	0.7149(7)	0.029(2)
C60	0.8820(9)	0.0062(2)	0.7589(7)	0.029(2)
O3	0.983(2)	0.0061(3)	0.4843(13)	0.044(4)
C61	0.984(3)	0.0573(5)	0.573(2)	0.054(7)
C62	0.063(2)	0.0276(5)	0.5698(15)	0.043(5)
C63	0.047(2)	0.9749(5)	0.4830(18)	0.052(5)
C64	0.958(3)	0.9535(6)	0.398(2)	0.055(7)
Cl1	0.5272(2)	0.15328(5)	0.91082(18)	0.0306(6)
Cl2	0.8557(2)	0.16515(6)	0.98147(19)	0.0334(6)
Cl3	0.7672(2)	0.14699(5)	0.58532(17)	0.0252(5)
Cl4	0.5442(2)	0.08774(5)	0.54986(17)	0.0276(5)
N1	0.7581(7)	0.21360(17)	0.7699(5)	0.0228(17)
N2	0.9214(7)	0.10388(17)	0.8042(5)	0.0206(16)
O1	0.3061(6)	0.23400(15)	0.4641(5)	0.0300(15)
O2	0.8115(6)	0.03044(14)	0.0757(5)	0.0311(15)
P1	0.4794(2)	0.20794(6)	0.73135(18)	0.0226(5)
P2	0.7162(2)	0.05771(5)	0.77583(18)	0.0214(5)

Table A9-1 Crystal data and structure refinement for (R,R_C,R_P)-50

Chemical formula	C ₄₆ H ₄₄ Cl ₃ N ₂ O ₆ PPd	
Formula weight	964.55	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal size	0.040 x 0.100 x 0.400 mm	
Crystal habit	colorless plate	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 10.451(4) Å	α = 90°
	b = 13.846(6) Å	β = 90°
	c = 30.951(12) Å	γ = 90°
Volume	4479.(3) Å ³	
Z	4	
Density (calculated)	1.430 g/cm ³	
Absorption coefficient	0.678 mm ⁻¹	
F(000)	1976	
Theta range for data collection	1.61 to 26.37°	
Index ranges	-12 ≤ h ≤ 8, -17 ≤ k ≤ 17, -33 ≤ l ≤ 38	
Reflections collected	18164	
Independent reflections	9054 [R(int) = 0.0793]	
Coverage of independent reflections	99.4%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9734 and 0.7731	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick, 2008)	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-97 (Sheldrick, 2008)	
Function minimized	Σ w(F _o ² - F _c ²) ²	
Data / restraints / parameters	9054 / 177 / 593	
Goodness-of-fit on F²	0.996	
Δ/σ_{max}	0.001	
Final R indices	5709 data; I > 2σ(I)	R1 = 0.0732, wR2 = 0.1582
	all data	R1 = 0.1248, wR2 = 0.1958
Weighting scheme	w = 1/[σ ² (F _o ²) + (0.0953P) ² + 0.0000P] where P = (F _o ² + 2F _c ²)/3	
Absolute structure parameter	-0.0(1)	
Extinction coefficient	0.0162(9)	
Largest diff. peak and hole	0.849 and -1.269 eÅ ⁻³	
R.M.S. deviation from mean	0.196 eÅ ⁻³	

Table A9-2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2$) for (*R,R_C,R_P*)-50. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
Pd1	0.13563(6)	0.54603(4)	0.86848(2)	0.0314(2)
C1	0.2687(9)	0.6148(6)	0.9034(3)	0.031(2)
C2	0.2640(9)	0.6356(6)	0.9488(3)	0.036(2)
C3	0.3481(9)	0.6955(6)	0.9682(3)	0.037(2)
C4	0.4481(9)	0.7397(6)	0.9450(3)	0.031(2)
C5	0.5359(9)	0.8025(6)	0.9637(3)	0.036(2)
C6	0.6357(10)	0.8411(6)	0.9409(3)	0.0323(19)
C7	0.6468(9)	0.8215(6)	0.8972(3)	0.039(2)
C8	0.5620(8)	0.7603(6)	0.8766(3)	0.033(2)
C9	0.4577(8)	0.7184(6)	0.8999(3)	0.028(2)
C10	0.3650(9)	0.6578(6)	0.8802(3)	0.032(2)
C11	0.3634(10)	0.6370(6)	0.8312(3)	0.036(2)
C12	0.4379(10)	0.5444(8)	0.8213(3)	0.051(3)
C13	0.1692(10)	0.7307(6)	0.8182(3)	0.047(3)
C14	0.2087(11)	0.5884(8)	0.7732(3)	0.050(3)
C15	0.9037(10)	0.5287(7)	0.8052(3)	0.042(2)
C16	0.7972(10)	0.4939(7)	0.7875(3)	0.043(3)
C17	0.7512(10)	0.4020(7)	0.7991(3)	0.037(2)
C18	0.6389(11)	0.3604(7)	0.7822(3)	0.041(2)
C19	0.5970(9)	0.2719(7)	0.7952(3)	0.042(3)
C20	0.6650(9)	0.2222(7)	0.8262(3)	0.042(3)
C21	0.7716(9)	0.2590(7)	0.8443(3)	0.035(2)
C22	0.8189(8)	0.3494(6)	0.8313(3)	0.030(2)
C23	0.9322(9)	0.3926(6)	0.8483(3)	0.031(2)
C24	0.0110(9)	0.3428(6)	0.8823(3)	0.033(2)
C25	0.1155(9)	0.2774(6)	0.8616(3)	0.032(2)
C26	0.1603(9)	0.1994(6)	0.8916(3)	0.031(2)
C27	0.2582(9)	0.1291(6)	0.8751(3)	0.035(2)
C28	0.3038(9)	0.1333(7)	0.8327(3)	0.037(2)
C29	0.3897(9)	0.0664(6)	0.8187(3)	0.040(2)
C30	0.4306(10)	0.9937(7)	0.8458(4)	0.048(3)
C31	0.3870(11)	0.9874(7)	0.8875(4)	0.057(3)
C32	0.2989(10)	0.0530(8)	0.9020(3)	0.052(3)
C33	0.9122(8)	0.4775(5)	0.9418(3)	0.028(2)
C34	0.8383(9)	0.4112(6)	0.9646(3)	0.036(2)
C35	0.7175(9)	0.4337(8)	0.9801(3)	0.043(3)
C36	0.6679(11)	0.5263(8)	0.9723(4)	0.058(3)
C37	0.7419(10)	0.5937(8)	0.9504(4)	0.054(3)
C38	0.8620(10)	0.5693(6)	0.9356(3)	0.040(2)

	x/a	y/b	z/c	U(eq)
C39	0.1618(9)	0.4053(6)	0.9635(3)	0.035(2)
C40	0.1235(9)	0.4198(6)	0.0067(3)	0.035(2)
C41	0.2060(9)	0.4002(7)	0.0414(3)	0.044(3)
C42	0.3262(10)	0.3690(7)	0.0338(3)	0.044(3)
C43	0.3694(10)	0.3540(6)	0.9912(3)	0.039(2)
C44	0.2895(9)	0.3729(6)	0.9560(3)	0.037(2)
C45	0.4513(10)	0.3356(8)	0.9014(4)	0.063(4)
C46	0.996(3)	0.4401(15)	0.6375(6)	0.109(5)
Cl2	0.9970(15)	0.3920(11)	0.5862(4)	0.186(5)
Cl3	0.0808(6)	0.5418(4)	0.6532(3)	0.109(3)
C46A	0.980(9)	0.430(4)	0.6528(12)	0.099(8)
Cl2A	0.017(3)	0.525(2)	0.6852(9)	0.159(9)
Cl3A	0.000(2)	0.4082(15)	0.5991(8)	0.080(5)
Cl1	0.2522(3)	0.3001(2)	0.73386(9)	0.0556(7)
O3	0.3355(8)	0.2182(5)	0.7311(2)	0.059(2)
O4	0.254(2)	0.3624(13)	0.6998(5)	0.114(7)
O5	0.1242(12)	0.2622(11)	0.7427(6)	0.094(6)
O6	0.2849(14)	0.3469(9)	0.7749(3)	0.053(4)
O4A	0.1570(18)	0.2859(14)	0.7008(7)	0.086(7)
O5A	0.197(3)	0.3313(16)	0.7724(5)	0.090(7)
O6A	0.325(2)	0.3812(9)	0.7158(6)	0.068(7)
N1	0.2210(7)	0.6311(5)	0.8185(2)	0.0365(19)
N2	0.9771(7)	0.4793(5)	0.8356(2)	0.0342(18)
O1	0.1184(6)	0.1916(4)	0.9284(2)	0.0390(15)
O2	0.3213(6)	0.3615(5)	0.9136(2)	0.0393(16)
P1	0.0654(2)	0.44389(16)	0.91873(7)	0.0297(5)