Rational design of novel chiral organopalladium complexes : synthesis, optical resolution and stereochemical evaluation

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RATIONAL DESIGN OF NOVEL CHIRAL
ORGANOPALLADIUM COMPLEXES: SYNTHESIS, OPTICAL
RESOLUTION AND STEREOCHEMICAL EVALUATION

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SUMMARY

This thesis describes the design and synthesis of chiral organopalladium complexes and their applications in asymmetric reactions.

In Chapter 1, a brief introduction on organopalladium complexes, research development in our laboratory and the objectives of this project is presented.

Chapter 2 describes the preparation of a novel palladacycle by direct *ortho*-palladation of the ligand 1-(3,6-dimethylnaphthalen-1-yl)-*N,N*-dimethylethylamine. The structure and ring conformations of its triphenylphosphine derivative have been investigated by solid state X-ray structural analysis and solution 2D ^1H - ^1H ROESY NMR spectroscopy. The *ortho*-palladated ring is stereochemically rigid, with the five-membered ring conformation being locked by the repulsive interactions between the methyl group on the prochiral carbon and its neighboring naphthalene proton. The racemic cyclopalladated complex could be efficiently resolved *via* the formation of its (*S*)-prolinato derivatives and an efficient separation of the resulting diastereomeric complexes was achieved using a silica gel chromatography. The structures and absolute configurations of both the optically resolved palladium complexes were determined by X-ray crystallography. Both the (*R,R*) and (*S,S*)-di- μ -chloro dimeric palladium complexes could be obtained by treating the corresponding prolinato derivatives with 1 M hydrochloric acid. Despite the severe inter-chelate steric constraint within this new organopalladium complex, the bulky monodentate ligand 3,4-dimethyl-1-phenylphosphole (dmpp) was coordinated regiospecifically to the *ortho*-palladated amine unit *trans* to the NMe_2 group. Compared with its naphthylamine analogue, the new palladacycle showed a much higher stereoselectivity in the chiral template-promoted asymmetric Diels–Alder reaction between coordinated dmpp and *N,N*-dimethylacrylamide.

In Chapter 3, the novel chiral palladacycle containing *ortho*-palladated ($\pm$)-1-(3,6-dimethylnaphthalen-2-yl)-*N,N*-dimethylethylamine was synthesized. The structure and palladacycle ring conformations of its triphenylphosphine derivative have been investigated solid state by X-ray structural analysis and solution by 2D-ROESY NMR spectroscopy. Due to a designed intra-molecular steric interaction, the five-membered naphthylamine chelate can be locked into a fixed conformation, both in the solid state and in solution. The racemic cyclopalladated complex could be efficiently resolved *via* the formation of its (*S*)-prolinate and (*S*)-alaninato derivatives. With the new palladacycle used as the chiral template, the stereoselectivity of Diels–Alder cycloaddition between dmpp and ethyl vinyl ketone was found to be improved as compared with other earlier analogous complexes.

In Chapter 4, a novel five-membered dimeric phosphapalladacycle was prepared and a successful optical resolution of this palladacycle was achieved through the separation of its (*S*)-prolinate derivatives by fractional crystallization. Two phosphine ligands, triphenylphosphine (PPh₃) and 3,4-dimethyl-1-phenylphosphole (dmpp), were able to coordinate individually onto the dimeric palladium complex and thus the palladacycle coordination behavior was studied. The phosphapalladacycle conformational behavior was further studied by the 2D ¹H-¹H ROESY NMR of its acetylacetonate derivative which indicated that the α -methyl group was axially located and the palladacycle was conformationally rigid in solution. Furthermore, the Pd–C bond characters of the dimeric palladacycle and its dmpp derivative were also studied.

Chapter 5 describes synthesis of a novel amine ligand 1-(2,5-dimethyl phenyl)-*N,N*,2,2-tetramethylpropan-1-amine. The *ortho*-palladation reaction of this amine ligand proceeded readily to form the racemic dimeric complex, ($\pm$)-di- μ -chlorobis[1-[1-(dimethylamino)-2,2-

dimethylpropyl]-2,5-dimethyl-6-phenyl-*C,N*]dipalladium(II). The palladacycle structure and ring conformations of its triphenylphosphine derivative have been investigated both in the solid state and in solution. This racemic cyclopalladated complex could be efficiently resolved *via* the formation of its (*S*)-prolinato derivatives and an efficient separation of the resulting diastereomeric complexes was achieved by slow crystallization using different solvent systems. However, the novel palladacycle failed to exert good stereoselectivity in the Diels–Alder reaction. On the other hand, the preparation of a novel chiral *di*-ester-substituted diphosphine *via* the chiral palladacycle promoted asymmetric hydrophosphination reaction was demonstrated and this reaction between diphenylphosphine and diethyl acetylenedicarboxylate proceeded with excellent stereoselectivity.

Chapter 6 describes the synthesis of two novel prochiral amine ligands, 1-(2,4-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine and 1-(2,5-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine. Direct *ortho*-palladation of the sterically less-hindered 1-(2,4-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine using Pd(OAc)₂ and LiCl proceeded readily to form the dimeric chloro complex which was then converted to the corresponding triphenylphosphine derivative. The palladacycle structure and ring conformations of this mononuclear have been investigated. This new racemic cyclopalladated complex could be efficiently resolved *via* the formation of its (*L*)-phenylalanate derivatives and a successful separation of the resulting diastereomeric complexes was achieved by slow crystallization using different solvent systems. The other sterically hindered amine ligand, 1-(2,5-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine, could not be induced to form the dimeric palladium complex by using an array of palladium sources.

LIST OF NEW COMPOUNDS AND COMPLEXES

(±)-181

(±)-182

(±)-183

(±)-178

(±)-184

(*S_C*, *S_C*, *S_N*)-185

(*R_C*, *S_C*, *S_N*)-185

(*S*)-178

(*R*)-178

(*S*)-186

(*S_C*, *S_P*)-187

(R_C, S_C)-**239**

(S)-**228**

(R)-**228**

(R)-**240**

(S_C, S_P)-**241**

(S_C, R_P)-**241**

($\pm$)-**244**

($\pm$)-**245**

($\pm$)-**246**

($\pm$)-**242**

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NOMENCLATURE

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

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SOLUTION 2D ^1H - ^1H ROESY, NOESY AND COSY NMR SPECTROSCOPIC STUDIES

The solution 2D ^1H - ^1H ROESY, NOESY and COSY NMR Spectroscopic Studies were performed at Nanyang Technological University (Division of Chemistry and Biological Chemistry).

ABBREVIATIONS AND SYMBOLS

acac	acetylacetonate
Ar	Aryl group
<i>ax</i>	axial
br	broad
<i>c</i>	sample concentration for O.R.D analysis
<i>ca.</i>	Circa
calcd	calculated
CDCl ₃	chloroform-d ₁
CD ₂ Cl ₂	dichloromethane-d ₂
conc.	Concentrated
COSY	correlation spectroscopy
D	day(s) (for reaction time)
d	doublet (in NMR assignments)
dd	doublet of a doublet
<i>de</i>	diastereomeric excess
dec.	decomposed
dmpp	3,4-dimethyl-1-diphenylphosphole
dppe	1,2-bis(diphenylphosphino)ethane
dq	doublet of a quartet
ee	enantiomeric excess
eq	equatorial

Et	ethyl
g	gram(s)
h	hour(s)
HCl	hydrochloric acid
Hz	hertz
m	multiplet (in NMR assignments)
Me	methyl
mg	milligram(s)
min	minute(s)
mmol	millimole(s)
M.p.	melting point
MS	Mass Spectrometry
NMR	Nuclear Magnetic Resonance
NOE	Nuclear Overhauser Effect
<i>o</i>	<i>ortho</i>
<i>m</i>	meta
<i>p</i>	para
Ph	phenyl
³¹ P NMR	³¹ P{ ¹ H} NMR
ppm	parts per million
q	quartet
qn.	Quintet
<i>R</i>	rectus (Latin: right absolute configuration)

ROESY	2D rotating frame nuclear Overhauser enhancement
<i>S</i>	sinister (Latin: left absolute configuration)
<i>s</i>	singlet (in NMR assignments)
<i>t</i>	triplet (in NMR assignments)
<i>t</i>	tertiary
THF	tetrahydrofuran
Å	angstrom(s)
δ	NMR chemical shift in ppm
$[\alpha]_D$	specific optical rotation measures at D line (589 nm)

Chapter 1

1.1 Cyclopalladation

In the past decades, cyclopalladation reactions have been widely studied because they represent a facile method for the activation of a C–H bond in aromatic rings. In this reaction, a ligand undergoes an intramolecular palladation with the formation of a chelate ring containing a Pd–C bond which is stabilized by the additional coordination of a heteroatom from the same ligand to the palladium center (Scheme 1.1)

Scheme 1.1

Cyclopalladated complexes of a wide variety of ligands have been described. For example, the cyclopalladation of nitrogen-donor ligands has been extensively studied and has acquired great interest due to the range of applications of these palladacycles in many areas, for example, organic synthesis, homogeneous catalysis, the design of new drugs, asymmetric synthesis and resolution of racemic ligands.^[1]

1.2 Types of Palladacycles

Most of the cyclopalladated systems contain N, P, S, As or S- heteroatoms and the following discussion will mainly focus on the nitrogen-donor palladacycles. Specific examples will be given for the non-nitrogen palladium complexes.

1.2.1 Nitrogen-Donor Palladacycles

The cyclopalladation of nitrogen-donor ligands has been extensively studied ^[1] and as a field it has acquired great interest because of the applications of palladacycles in many areas. Depending on the nature of the ligands, these major N-donor palladacycles can be classified into different groups.

1.2.1.1 Amine Functionalized Ligands

In 1968, Cope and co-workers reported that an amine ligand *N,N*-dimethylbenzylamine **1** could react efficiently with a palladium salt (lithium tetrachloropalladate) and form the first benzylamine palladacycle complex di- μ -chlorobis(*N,N*-dimethylbenzylamine-*C,N*) dipalladium(II) **2** in 95 % yield (Scheme 1.2). They discovered and outlined three requirements that must be met by the ligand before such reactions can proceed: (i) the nitrogen must be a tertiary nitrogen center, (ii) the possibility of the formation of a planar five-membered ring containing the metal must be presented, and (iii) the metal must be able to displace a hydrogen ion from an aromatic carbon atom that can not be highly deactivated towards electrophilic attack. ^[2]

Scheme 1.2

In 1971, Otsuka and co-workers reported the first chiral benzylamine palladium (II) complex which was prepared from sodium tetrachloropalladate(II) and the chiral amine ligand (*S*)-*N,N*-dimethyl- α -methylbenzylamine **3** (Scheme 1.3). This chiral palladium complex (*S*)-**4** was applied in the kinetic resolution of a variety of tertiary phosphines by the bridge-splitting reactions.^[3]

Scheme 1.3

In 1977, Tani and co-workers treated sodium tetrachloropalladate with a 1:1 mixture of (+)-(*R*)-*N,N*-dimethyl- α -(2-naphthyl)ethylamine (*R*)-**5** and triethylamine and formed the chiral palladacycle complex (*R*)-**6** (Scheme 1.4).^[4a] The palladacycle was employed successfully in the kinetic resolution of several chiral diphosphines.

Scheme 1.4

In 1975, the preparation of the first naphthylethylamine palladium(II) complex **7** was reported by Julia and co-workers. They reported that the palladation of 1-dimethylaminomethylnaphthalene takes place only at the C₂ position of complex **7**. However formation of other two palladacycles **8** and **9** were observed when reactions of the 2-isomer was used with palladation occurring at the 1 and 3 position.^[4b]

In 1982, Wild and co-workers reported the synthesis of a widely used chiral palladium complex by using lithium tetrachloropalladate (II) and two equivalents of the chiral amine ligand (*R*)-*N,N*-dimethyl- α -naphthylethylamine (*R*)-**10** (Scheme 1.5).^[5] Over the past decades, the chiral palladacycle **11**, together with other similar chiral complexes, have been studied extensively due to a wide variety of interesting and novel applications in different areas^[1,7,8,9,174], which will be discussed in section 1.4.4.

Scheme 1.5

In 1997, Dunina and co-workers modified the structure of chiral palladium complex **11** and reported new palladacycles **12** and **13**. Both of them exhibit improved stereoselectivity in some applications, for example the optical resolution and

discrimination of chiral phosphines.^[6] Later, an *ortho*-palladated benzylamine analogue **14** bearing a phenyl substituent at the α -carbon stereocenter was also reported by this group.

In 2002, the optically active complex, *(S)*-**15**, was prepared and it was tested as a catalyst in the asymmetric Claisen rearrangement of an allylic amidate substrate.^[7,8] Soon after, chiral palladium complex *(S)*-**16** was reported.^[9] This complex was first obtained as a racemate by direct cyclopalladation of the free amine ligand using $[\text{Pd}(\text{NCMe})_4](\text{ClO}_4)_2$ as the palladium source, followed by a successful optical resolution through the separation of its proline derivative.

Since the early work of Cope and Friedrich on cyclopalladation of arylalkylamines, it had been generally accepted that the nitrogen should be tertiary and the primary amines inert towards cyclopalladation reactions.^[1] However, several exceptions to these rules were reported in the following twenty years and some primary amines can undergo cyclopalladation under appropriate reaction conditions.

In 1973, Lewis and co-workers reported the cyclopalladation of amine ligand **17** by using Cope's reaction conditions and an *ortho*-palladated complex **18** was formed (Scheme 1.6).^[10] It was postulated that the *ortho*-palladation process is promoted by the presence of sterically hindered substituents at the α -carbon.

Scheme 1.6

By changing the palladation agent, the *ortho*-palladation reaction of other primary amines were achieved. For example, in 1975, during the preparation of palladium complex **20**, $\text{Pd}(\text{acac})_2$ (acac = acetylacetonate) was used a palladation agent to *ortho*-palladate benzylamine (Scheme 1.7).^[11]

Scheme 1.7

In 1983, Avshu and co-workers reported that the amine compound $[\text{PdI}_2(\text{NH}_2\text{CH}_2\text{Ph})_2]$ **21** was treated with a silver(I) salt and an *ortho*-palladated complex **22** was isolated (Scheme 1.8).^[12]

Scheme 1.8

In 1993, Vicente and co-workers reported that the first optically active *ortho*-palladated primary amine derivative **24** could be prepared under similar reaction conditions (Scheme 1.9).^[13] The optically active complexes were obtained by using (*R*)- or (*S*)-**23** as starting materials.

Scheme 1.9

In the same year, Fuchita and co-workers for the first time used palladium acetate to form benzylamine *ortho*-palladacycle **26** which could be isolated in acceptable yield (Scheme 1.10).^[14,15]

Scheme 1.10

In 1995, Vicente reported the *ortho*-palladation of (*S*)-4-nitro- α -methylbenzylamine which was the first cyclopalladated complex containing a primary benzylamine with an electron-withdrawing substituent on the aromatic ring (Scheme 1.11).^[16]

Scheme 1.11

In 1997, Fuchita and co-workers also reported the palladation of (*R*)-2-phenylglycine methyl ester **29** using palladium acetate in acetone under reflux for 20 h to afford complex **30** (Scheme 1.12).^[17]

Scheme 1.12

Overall, the *ortho*-palladation method using palladium acetate has proven to be quite general. Moreover, it could be used in synthesizing six-membered palladacycles which is different from the three limits imposed by Cope's rule (Scheme 1.13).^[18] Sometimes it was hard to separate the acetato- or chloro-bridged dimers in pure forms, addition of a neutral ligand, for example triphenylphosphine, led to the formation of the monomeric species **33** which was easier to purify.

Scheme 1.13

In 2005, Vicente and co-workers reported the cyclopalladation of biologically active primary amines using $\text{Pd}(\text{OAc})_2$ as the palladation reagent which led to the formation of the six-membered ring palladacycles (**35**, **37**), respectively (Scheme 1.14).^[19]

Scheme 1.14

Two years later, the same group reported the *ortho*-palladation of (*S*)-phenylalanine methyl ester **38**. The cyclopalladated complex **39** thus formed can be further modified to synthesize functionalized derivative, **40** (Scheme 1.15).^[20]

Scheme 1.15

1.2.1.2 Ferrocenylmethylamines

In the past decades, ferrocenylmethylamine palladacycle analogues have been synthesized. Moreover, their reactions and applications have also been investigated. For

example, in 1979, Sokolov and co-workers reported that racemic *N,N*-dimethyl- α -ferrocenylethylamine **41** reacts readily with sodium tetrachloropalladate (II) using sodium acetate as base to afford the cyclopalladated complex **42** (Scheme 1.16). Palladacycle **42** also reacts with pyridine, sodium acetylacetonate, and amino acids to form corresponding monomeric complexes **43** and **44**. Synthesis of the optically active palladacycle **45** using a similar *ortho*-palladation method was also reported.^[21-24]

Scheme 1.16

In 1999, Bosque and co-workers reported the preparation of palladacycles (**46** and **47**) derived from primary ferrocenylamines containing a five- or six-membered ring (Scheme 1.17).^[25] The same year, Donde and co-workers reported a series of ferrocene derivatives such as complex **48** and **49**.^[26]

Scheme 1.17

1.2.1.3 Benzylideneamines

Benzylideneamine complexes containing a five-membered ring have also been reported in literature. In 1969, Molnar and co-workers reported the preparation of complex **51** from benzylideneaniline.^[27] Furthermore, this dimeric complex **51** reacts with triphenylphosphine, pyridine and thallium acetylacetonate to form the corresponding monomeric complexes **52**, **53** and **54** respectively.^[27] In 1975, Thompson and Heck reported the synthesis of palladacycle **55** from hydrazine derivatives.^[28]

Scheme 1.18

A chloro-bridged dimeric palladium complex **57** could be formed when ligand **56** was treated with palladation reagent lithium tetrachloropalladate(II) in the presence of sodium acetate in high yield. Similar to other dimeric palladium complexes, complex **57** can react with an array of ligands, for example, 4-methylpyridine, triphenylphosphine and 1-phenethylamine, forming the corresponding monomeric derivatives (Scheme 1.19).^[29, 30]

Scheme 1.19

In 1998, Benito and co-workers reported the synthesis of a chiral ferrocene palladacycle derivative (Scheme 1.20). It is worthy to note that the palladation takes place on the ferrocene ring rather than on the naphthalene ring despite the chiral ligand **59** containing both a ferrocenyl group and a naphthylethyl group.^[31]

Scheme 1.20

In 2008, Albert and co-workers reported the synthesis of palladacycle **62** using palladium acetate and described the formation of new palladacycles, some of them displaying hydrosolubility. Furthermore, cyclopalladated derivative **63** containing the palladated molecule as a dianionic bridging ligand has also been obtained (Scheme 1.21).^[32]

Scheme 1.21

1.2.1.4 Iminophosphoranes

Iminophosphoranes (phosphine imines) are compounds with a general structure of $\text{R}_3\text{P}=\text{NR}'$ (R, R' = alkyl, aryl, acyl, *etc.*). In 2005, Bielsa reported the *ortho*-palladated complexes (**65**) and (**67**) which were obtained by the reaction of palladium (II) acetate with the iminophosphoranes (**64**, **66**), respectively, in the presence of excess LiCl (Scheme 1.22).^[33]

Scheme 1.22

In 2008, Aguilar reported the synthesis and structure of an *ortho*-palladated complex derived from iminophosphorane **68**.^[34] The iminophosphorane $\text{Ph}_2\text{MeP}=\text{NPh}$ **68** reacts with palladium (II) acetate to give the *ortho*-palladated racemic mixture **69**, which was then reacted with $\text{Ti}(\text{acac})_3$ to give **70**.

In the same paper, the synthesis of the palladacycle **72** as a mixture of stereoisomeric isomers *via* the reaction of a phosphorus ylide compound using palladium (II) acetate was also reported (Scheme 1.23).

Scheme 1.23

1.2.1.5 Other Nitrogen Donor Complexes

Cyclopalladium complexes (**73-82**) could be formed from other nitrogen-donor ligands, for example pyridine, quinoline, and benzoquinoline, using different palladation reagents.^[35-46]

1.2.2 Phosphorus-Donor Complexes

Ortho-palladated phosphorus-donor ligands have recently attracted considerable attention due to the high activity they show as catalysts in C–C bond formation.^[47-62] *ortho*-palladation of tribenzylphosphine **83** gives a stable intermediate **84** which has a low reactivity towards cyclopalladation. By heating the intermediate in the presence of sodium acetate, chloro-bridged dimeric palladium complex **85** could be formed and isolated (Scheme 1.24).^[63]

Scheme 1.24

In 1978, Hyde and co-workers found that the methoxy group substitutions at C₃ and C₄ positions on the phenyl group could increase the reactivity of the benzylphosphines. Therefore cyclopalladation of 3,4-dimethoxybenzyl-diphenyl-phosphine **86** proceeded readily to form the chloro-bridged dimeric palladium **87** (Scheme 1.25).^[64]

Scheme 1.25

In 1999, Dunina and co-workers reported the preparation and characterization of the first optically active P-chiral phosphapalladacycle **88**.^[65] In 2003, Leung and co-workers reported the synthesis of an optically active palladium complex **89** by using a similar procedure.^[66]

In 1998, Shaw and co-workers demonstrated that the palladated naphthyl phosphine complexes **90** and **91** could be used as catalysts in the Heck reaction.^[67]

Three years later, Gibson and co-workers reported the preparation of *ortho*-palladated benzyl phosphine-containing complexes **92** which could be used in the Heck and Suzuki coupling of aryl bromides.^[68] Synthesis of *ortho*-palladated complexes of more π -acidic ligands such as triaryl phosphite and aryl phosphinites were further studied by the Bedford group. For example, they found that palladium complex **93** showed extremely high activity towards the coupling reactions of aryl bromides. Moreover they reported that palladium complex **94** can be used in the Suzuki and Stille couplings of aryl chlorides with excellent effects.^[69-74]

In 2003, the same group reported the *ortho*-palladation of a bulky phosphite ligand tri(2,4-di-*tert*-butylphenyl)phosphite and *ortho*-palladated complex **95** was found to be a good and active catalyst for the Suzuki coupling of aryl bromides with aryl boronic acids (Scheme 1.26).^[75]

Scheme 1.26

In 1997, Ohff and co-workers reported the synthesis of palladium complexes (**96** and **97**) and their application in the Heck coupling of aryl iodides.^[76] Later Shibasaki and co-

workers demonstrated the type of palladium complex **98** and found that complex **98a** shows even better activity. Furthermore, The *P,C,P*-bis(phosphinite) pincer complexes **98b** and **98c** were applied in the Suzuki coupling of aryl bromides and found to be very active, and can even be used to couple activated aryl chlorides. Morales-Morales and co-workers further reported the more electron rich analogue **98d** which was found to be an active catalyst for the Heck coupling of aryl chlorides.^[77,78]

In 2005, Leung and co-workers reported a novel phosphapalladacycle **100** derived from 1-(2',5'-dimethylphenyl)ethyldiphenylphosphine **99** in both the optically active and racemic forms (Scheme 1.27). The racemic phosphapalladacycle was subsequently obtained as the chloro-bridged dimer by the treatment of the phosphine with palladium (II) acetate followed by anion metathesis with lithium chloride.^[79]

Scheme 1.27

Two years later, they reported the *ortho*-palladation of the phosphine ligand (di-*tert*-butyl)(diphenylmethyl)phosphine **101** and studied the resulting palladacycle **102** characters: kinetic lability of the corresponding (+)-phosphapalladacyclic Pd–C bond and the reluctance of the phosphine to bind in a monodentate fashion. The same year, another

novel phosphapalladacycle **103** was prepared by direct cyclopalladation of the ligand (diphenylmethyl)diphenylphosphine. The corresponding μ -chloro five-membered phosphapalladacycle **103** was obtained by using $\text{Pd}(\text{OAc})_2$ followed by chloride ion metathesis. Optical resolution of racemic dimer **103** was employed by separation of its (*S*)-prolinato derivatives using fractional crystallization followed by treatment with dilute hydrochloric acid, yielding both enantiopure forms of the dimers **103**. The phosphapalladacycle **103** was noted to display different properties with respect to the analogous phosphapalladacycle **102** and thus the substituent effects on the stereoelectronic and chemical properties were studied. [80, 81]

1.2.3 Sulfur-Donor Complexes

Phosphorus- and nitrogen containing palladacycles are among the most active catalyst precursors to promote the Heck and Suzuki coupling reactions reported. In this aspect, some sulfur containing palladacycles are also catalyst precursors to promote such C–C bond forming reactions. One interesting aspect of this family of palladacycles is the creation of a stereogenic center at the sulfur atom during their formation (upon coordination to the metal center).

In 1981, Hiraki and co-workers synthesized the *ortho*-palladated complex **105** using palladium acetate as the palladation source followed by treating with excess LiCl

(Scheme 1.28). The corresponding mononuclear derivatives **106** and **107** could be formed when the dimeric complex **105** was treated with different ligands.^[80-84]

Scheme 1.28

In 1981, Sheldrich and co-workers reported the synthesis of acetate-bridged palladacycles **108** and **109** from dibenzyl sulfide or dibenzylsulfoxide by using palladium(II) acetate as the palladation reagent.^[85] It is worthy to note that in palladium complex **109** the dibenzylsulfoxide group is coordinated to the metal *via* the sulfur atom instead of the oxygen atom, according to the X-ray crystallographic study.

Sodium tetrachloropalladate(II) was also used as palladation reagent in the preparation of S-donor palladacycles, for example **111** (Scheme 1.29).^[86]

Scheme 1.29

Dupond and co-workers made great contributions to the development of S-donor palladacycles. For example, In 1989 they found that the treatment of PhCH_2SMe with palladium acetate in acetic acid at refluxing temperature and subsequent treatment with LiCl affords the chloride-bridged cyclopalladated complex **112**. This direct palladation method can also be successfully employed for the palladation of the naphthyl group in methyl 1-naphthyl sulfide. The palladium complex **113** was thus synthesized in good yields. Moreover when this method was applied to the palladation of 2-biphenyl methyl sulfide, it led to quantitative formation of a six-membered dimeric palladium complex **114**.^[87]

The ligand exchange in the presence of one equivalent of trifluoroacetic acid per palladium atom led to the formation of dimeric palladacycle **115** in high yield. The direct palladation at the C_2 position of ligand 1,3-bis(methylthiomethyl)benzene affords the monomeric complex **116** in which both sulfur atoms are coordinated to the palladium. Using a similar method, sulfur containing palladacycles **117**, **118** and **119** were synthesized.

In 2001, Dupont and co-workers reported non-racemic and configurationally stable sulfur-containing palladacycles (**120**, **121** and **122**). These complexes could be prepared from optically active ligands and applied in an asymmetric Heck reaction.^[88]

In 2007, Uehara reported a new water soluble sulfur-containing palladacycle, complex **124**. The cationic complex was prepared by the reaction of water insoluble dichloro palladacycle **123** with Ag₂SO₄ in water (Scheme 1.30).^[89]

Scheme 1.30

1.2.4 Arsenic-Donor Complexes

In our research group, the five-membered palladacycle **125** derived from the ligand, 1-(1'-naphthyl)ethyldiphenylarsine has been synthesized. The stereochemistry and coordination properties of the As-C ring were determined from the *O,O'*-acetylacetonate derivative by X-ray crystallography and 2D ^1H - ^1H ROESY NMR spectroscopy.^[66, 90]

1.2.5 Oxygen-Donor Palladacycles

There are few examples devoted to the synthesis of oxygen-donor palladacycles, for example **126** and **127**. They mainly consist of ligands in which the oxygen atom is part of an ether, alkoxy or carboxylate groups.^[91,92]

1.3 Synthesis Methodology of Palladacycles

There are several methods available for the generation of palladacycles (for example C-H activation, ligand exchange, oxidative addition and transmetalation).^[1,92-99]

1.3.1 Direct *ortho*-Palladation (C–H Activation)

The direct *ortho*-palladation reaction is the most popularly employed synthetic route to form the *ortho*-palladated complexes. It has generally been accepted, based on Cope's work, that *ortho*-palladation of organic ligands involves the electrophilic aromatic substitution with the Pd(II) center behaving as the electrophile. Common palladation agents include tetrachloropalladated salts, with a base (for example triethylamine and sodium acetate) or palladium acetate in acetate acid or benzene. Therefore, in the direct *ortho*-palladation an aromatic substitution reaction occurs and involves the interaction of an organic ligand with a metal salt, such as M_2PdCl_4 , $M_2PdCl_4/NaOAc$ and $Pd(OAc)_2$ ($M = Na$ or Li). Therefore, lithium and sodium tetrachloropalladate are the mildest metallation agents available. The system $M_2PdCl_4/NaOAc$ is usually more effective, where sodium acetate is acting as the base to facilitate the C–H bond cleavage. Palladation is usually performed in polar solvents such as methanol, ethanol, acetone, or acetic acid as well as in binary water-organic mixtures. Palladation occurs readily at ambient temperature, however, heating may be required in certain cases.

When treatment of the ligand with M_2PdCl_4 does not lead to cyclopalladated species (bi products of the type $[PdCl_2L_2]$ are often formed in this case), the palladacycles can often be obtained by treating the ligand with palladium acetate. The ability of palladium acetate as a palladation agent is not limited to aromatic fragments of a ligand. It allows one to obtain cyclopalladation complexes with aromatic, pseudo-aromatic and aliphatic ligands. Therefore palladium acetate was widely used in many direct *ortho*-palladation reactions.

1.3.2 Ligand Exchange

Generally, a soluble cyclopalladated binuclear chloro-bridged complex is able to react with an organic ligand possessing either an N or P donor center to form a new palladacycle. As illustrated in Scheme 1.32, the procedure involves a ligand exchange process occurring between the cyclopalladated complex and a ligand which is to be cyclopalladated. Therefore a new cyclopalladated complex was thus generated using this method.

Scheme 1.32

1.3.3 Transmetalation

The transmetalation reaction is a methodology for the generation of palladacycles in which organolithium or organomercurial reagents are the common used transmetalating agents. Therefore by treating the transmetalated reagents with the desired palladium salts the cyclometalated complexes can be formed. The metallated 1-methoxynaphthalene palladium complex **126** was prepared using this method (Scheme 1.33).^[1,91]

126

Scheme 1.33

1.3.4 Oxidative Addition

The oxidative addition of aryl halides and alkyl halides is also a useful method for the generation of various palladacycles which can not be obtained by direct C–H bond activation procedure. Alternatively, the synthesis of cyclopalladated complexes by oxidative addition to a Pd(0) source may be achieved by using organomercury complexes. Pd(dba)₂, Pd₂(dba)₃ (dba = dibenzylideneacetone) and Pd(PPh₃)₄ are the most commonly used palladium starting materials. As shown in scheme 1.34, preparation of chiral ferrocene derivative **128** involves interaction of organomercury complexes with zero-valent palladium complexes Pd(PPh₃)₄ and Pd(dba)_n.^[92, 100, 101]

Scheme 1.34

1.4 Applications of Palladacycles

Recently, a great deal of attention has been focused on the development of enantiomerically pure cyclopalladated complexes because these complexes play important roles in many aspects of synthetic stereochemistry. Many chiral cyclopalladated complexes have been reported and they could be used as resolving agents for chiral ligands, clear and reliable references for the NMR assignment of unknown absolute configurations, diamagnetic chiral shift reagents for the determination of optical purity of organic compounds and efficient chiral catalysts for asymmetric reactions.^[1]

1.4.1 Resolution of Phosphines and Arsines

Cyclopalladated complexes have been extensively employed for the resolution of enantiopure ligands. The resolution of enantiopure biaryl ligands remains an active area of research given the interest in probing steric and electronic effects in asymmetric catalysis.^[92] Chiral cyclopalladated complexes have been extensively employed for the resolution of ligands. For example, the *ortho*-palladated derivatives of optically active tertiary amines have been used as resolving agents for Lewis bases, noticeably by the group of Wild^[102-104] and our research group^[105-107]. The diastereomers generated by the cleavage of the chloro-bridged dipalladium dimers can usually be separated in high yield by fractional crystallization. This procedure is suited for large scale resolutions due to the high availability and stability of the resulting diastereomers. In addition, the configurational purities can easily be determined by NMR spectroscopy. Therefore a series of enantiomerically pure ligands (**129-133**) have been resolved by using this chiral palladacycle **11**.^[102-107]

In 1995, Dunina and co-workers reported the first example of the resolution of the chiral ligand **136**, by using the optically active secondary amine palladacycles (**134** and **135**) as chiral auxiliaries.^[108]

In 2006, Albert and co-workers reviewed the application of the primary amine cyclopalladacycles (**137-140**) for the resolution of chiral phosphines (**141-148**) and the general process for this kind of Lewis base resolution (Scheme 1.35).^[109]

Scheme 1.35

1.4.2 Optical Purity Determination

Chiral cyclopalladated complexes can be used to determine the enantiomeric excess of various species in solution in many applications that chiral ligands such as amino acids can be used to determine the *ee* value of chiral cyclopalladated complexes.^[92, 109] Chiral cyclopalladacycles have been used as chiral agents to determine the enantiomeric purity of 1,2-diamines, phosphines, arsines and amino acids. It has been demonstrated that NOE techniques^[110-113] or the NMR chemical shift regularities^[114-115] can be used to determine the absolute configurations of coordinated chiral diphosphines. When a chiral ligand is treated with the chiral dimeric palladacycles, the formation of a pair of diastereomers will result in the different ³¹P or ¹H NMR signals and thus the NMR spectrum provides a measure of the optical purity of the ligand. For example, in 2000 Albert and co-workers reported the synthesis of benzyisopropylphenylphosphine and its resolution by an optically active palladacycle. The assignment of the absolute configuration of the coordinated phosphine by mono- and bi-dimensional proton NMR spectra, using

homochiral palladacycle as a reference point was also described. The chemical shift of the ^1H proton can also be used to propose the absolute configuration of the phosphine. In the NMR spectrum of the (R_C, S_P)-diastereomer the signal of this proton is high field shifted (6.05 ppm) in relation to the signal of this proton in the (R_C, R_P)-diastereomer (6.48 ppm), as the consequence of the proximity of the phenyl group of the phosphine to the metallated ring (Scheme 1.36).^[116]

Scheme 1.36

1.4.3 Catalysis

Nitrogen-, phosphorus-, and sulfur-containing palladacycles are emerging as a new family of organometallic catalyst precursors. These thermally and air-stable complexes are easy to handle and their synthesis is often straightforward. The catalytic properties of cyclopalladated systems were thus investigated and successfully exploited in catalytic reactions.^[119]

1.4.3.1 Hydrogenations

The use of palladacycles as catalysts is relatively recent, with the first applications being reported in 1986 with the hydrogenation of $\text{C}=\text{C}$ bonds. Lewis, who had demonstrated that cyclopalladated complexes could show higher activities than their non-cyclopalladated analogues, reported an *ortho*-palladated triphenyl phosphite **152** which could effectively promote the hydrogenation of $\text{C}=\text{C}$ bonds (Scheme 1.37).^[117]

Scheme 1.37

1.4.3.2 Heck Coupling Reactions

In the past decades, organopalladium-catalyzed C–C bond formation has become one of the most important tools in the synthesis of organic molecules. Because of its synthetic potential for generating C–C bonds, the Heck coupling reaction has received increasing attention. This reaction is an important method for the preparation of the aryl-functionalized alkene in synthetic chemistry and the industry. This reaction involves the arylation of C=C double bonds is mediated by a variety of Pd (II) and Pd (0) systems (Scheme 1.38).^[118]

Scheme 1.38

In previous studies, some phosphorus-,^[67,69,76,77,78,120-125] nitrogen-,^[126-131] and sulfur-containing^[132-135] palladacycles (**153-160**) were used as the active catalyst precursors for the promotion of such reactions. Most of these complexes promoted the Heck coupling reaction of aryl iodides with acrylic esters.^[139]

1.4.3.3 Suzuki and Stille Cross-Coupling Reactions

The Suzuki cross-coupling reaction (involving cross-coupling of aryl halides with organoboron compounds)^[136] or Stille cross-coupling reaction (involving organotin compounds)^[137,138] is mediated by a few palladium catalyst precursors. Palladacycles are also rather efficient catalyst precursors for the coupling of aryl boronic acids and aryl halides under relatively mild reactions. Palladacycles promote the coupling of aryl iodides or bromides with aryl boronic acids at temperature above 80 °C, depending on the nature of the base and the solvent. For example, sulfur-containing palladacycles such as **160** (Scheme 1.39) can efficiently catalyze the homo-coupling of various aryl iodides and bromides in high yields (Scheme 1.39).^[139]

R = H, Me, COMe, OMe, NO₂, etc.; X = Br, I.

Scheme 1.39

In 2003, Bedford and co-workers reported the synthesis of palladacycle **95** from a bulky phosphite ligand tri(2,4-di-*tert*-butylphenyl)phosphite. Complex **95** is an excellent catalyst precursor, not only for the Suzuki coupling of aryl bromides with aryl or alkyl boronic acids, but also, when used in conjunction with PCy₃, for the Suzuki and Stille coupling of aryl chlorides (Scheme 1.40).^[75]

R = H, Me, COMe, OMe, NO₂, etc.

Scheme 1.40

1.4.3.4 Hydroarylation of Olefins

Cyclopalladated aminophosphine-based ligand systems are highly efficient catalysts for the hydroarylation of norbornenes. For example, in 2000 Brunel and co-workers reported the synthesis of new phosphapalladacycles (**161** and **162**) and their application in the hydroarylation of norbornene and norbornadiene (Scheme 1.41).^[140]

Scheme 1.41

1.4.3.5 Sonogashira Reaction

Palladacycles have proven to be useful and versatile catalytic precursors for C–C bond forming reactions, such as the Sonogashira reaction. In fact, the Sonogashira reaction of terminal alkynes with aryl or alkenyl halides provides a most straightforward and powerful method for the preparation of di-substituted alkynes has been mediated by phosphorus-,^[142] nitrogen-,^[127] and sulfur-containing palladacycles. Therefore, the palladium-catalyzed coupling of aryl iodides and bromides with terminal alkynes is a well-established method for the preparation of di-substituted alkynes. Generally CuI was usually as a co-catalyst in the palladium catalyst promoted reaction. However, palladacycle **153** can catalyze the reaction without a co-catalyst as shown in scheme 1.42.^[140]

Scheme 1.42

1.4.3.6 Amination of Aryl Halides

The synthesis of disubstituted anilines *via* palladium catalyzed amination of aryl halides by secondary amines was discovered by Buchwald and Hartwig independently in 1995.^[143,144] Palladacycles especially phosphapalladacycles were used to promote the amination of aryl halides leading to substituted anilines. For example, in 1997, Beller and co-workers reported the reactions of secondary amines with bromoarenes and activated chloroarenes. Palladacycle **153** was found to be effective for amination chemistry in the presence of NaO-*tert*-butyl or KO-*tert*-butyl as bases (Scheme 1.43).^[145]

Scheme 1.43

1.4.3.7 Hetero- and Carbo-Annulation Reactions

Precursors to the aporphine skeleton and related isoquinolines were formed by the catalytic heteroannulation of a tertiary amine with the internal alkynes with concomitant loss of methyl iodide, using palladacycle catalysts. In the preparation of *N*-methylbenzo[*d,e*]quinolines, *N*-methyldibenzo[*d,e,g*]quinolines, and 2,3-diphenylindenone, palladacycles were demonstrated to be effective catalyst precursors.^[146,147,119] For example, cyclopalladated complexes **163** and **164** were found to be efficient catalysts for this kind of reaction (Scheme 1.44)

Scheme 1.44

In 1999, phosphapalladacycle **153** was also reported in syntheses of 2,3-diphenylindenone from 2-bromobenzaldehyde and diphenylacetylene (Scheme 1.45).^[119]

Scheme 1.45

1.4.3.8 Telomerization of Dienes

Palladacycles are also effective and selective catalyst precursors for the telomerization of 1,3-dienes with alcohols and carbon dioxide. Nitrogen-donor palladacycles, such as those derived from amines, imines, and quinolines, promote the selective telomerization of 1,3-dienes with alcohols. For example, in 1996, Camargo and co-workers reported the synthesis of palladacycles (**165**, **166**) and their properties as catalyst precursors for the telomerization of 1,3-butadiene with methanol (Scheme 1.46).^[148]

Scheme 1.46

1.4.3.9 Aldol-Type Reactions

Palladacycles have also been employed as chiral Lewis acids for Aldol-type chemistry with reasonable success in terms of asymmetric induction. Cyclopalladated complexes containing (P,C,P) ligands have recently been utilized in asymmetric Aldol-type reactions. For example, the chiral palladacycle **167** was used as a catalyst in the

reaction between methyl isocyanoacetate and various aldehydes (Scheme 1.47).^[149-151]

Scheme 1.47

1.4.3.10 Cyclopropanation

Cyclopropanation reactions catalyzed by palladacycles have also been reported. For example in 1996, neutral acetylacetonate and amino acid chelated cyclopalladated complexes were reported in catalyzing cyclopropanation reactions.^[152,153]

Scheme 1.48

In 1997, palladacycle **169** was demonstrated to be an efficient catalyst for the cyclopropanation reaction in high yield (Scheme 1.49).^[153]

Scheme 1.49

1.4.3.11 Catalytic Allylic Rearrangement

Homochiral cyclopalladated complexes have been used as enantioselective catalysts, notably in allylic rearrangements.^[154,155] For example, chiral ferrocene derivative complex

45 was proved to be an effective catalyst, affording excellent enantioselectivities with good reaction rates and yields (Scheme 1.50).

Scheme 1.50

1.4.4 Asymmetric Synthesis

Chiral cyclopalladated complexes are very useful in asymmetric synthesis as stoichiometric templates. A series of organometallic reagents containing *ortho*-palladated chiral amine auxiliaries have been utilized as chiral templates to activate phospholes, vinylphosphines, and alkylphosphines toward asymmetric ligand transformations *via* cycloaddition and hydroamination reactions. By a systematic manipulation of the subtle stereoelectronic properties of the auxiliaries and the metal centers, the template properties could be modified and the origins of stereoselectivity revealed. The chiral templates are able to control the disposition of selected functionalities into designated locations on the transformed P-stereogenic mono- and diphosphine ligands.

The asymmetric Diels–Alder reaction is one of the most efficient and elegant methods for the construction of chiral six-membered rings. In the past twenty years, a study of the palladium(II) complex containing enantiomerically pure form of the *ortho*-metalated [1-(dimethylamino)ethyl]naphthalene **11** in promoted Diels–Alder reactions between 3,4-dimethylphenylphosphole (dmpp) and a wide range of dienophiles have been carried out. A series of optically pure norbornene-based P-chiral phosphines have been synthesized in this way.^[156-169] After activation with a chloride scavenger, reaction with

dmpp, and subsequent depalladation, the diphosphines are formed. Scheme 1.51 shows a typical *exo*-cycloaddition reaction between a dmpp complex and ethyl vinyl ketone. The complex (S_C, R_P)-**170** was found to be the sole product exhibiting excellent stereoselectivity in this reaction. The free phosphine ligand could be obtained by treatment of complex (S_C, R_P)-**170** with dppe. Many other chiral phosphines have been synthesized using similar methodology.

Scheme 1.51

When the chloro dmpp complex **171** was treated with the dienophile ethyl vinyl ketone, the reaction produced two comparable *endo*-cycloaddition products, (S_C, S_P)-**172** and (S_C, R_P)-**172** (Scheme 1.52). The major isomer (S_C, R_P)-**172** could be isolated from the reaction mixture by fractional crystallization, from which the free phosphine ligand could be liberated.^[160]

Scheme 1.52

Similarly, two *endo*-cycloadducts (S_C,S_P)-**173** and (S_C,R_P)-**173**, were formed when the complex (*S*)-**171** was treated with *N,N*-dimethylacrylamide (Scheme 1.53).^[165]

Scheme 1.53

As mentioned earlier, the two *endo*-diastereomers, for example, (S_C,R_P)-**173** and (S_C,S_P)-**173**, could usually be separated by fractional crystallization. In several instances however, the separation process was somewhat tedious and resulted in lower yields of a targeted enantiomer. In order to improve their stereoselectivity, two new *ortho*-palladated complexes (*S*)-**15** and (*S*)-**16** have been utilized as the chiral templates in these *endo*-cycloaddition reactions. The two new complexes exhibit the major stereoelectronic properties of the original naphthylamine template **11**. For example, the static λ organometallic ring conformation in both palladacycle (*S*)-**15** and (*S*)-**16** has been locked by a spacer. Furthermore, a second spacer is introduced on the aromatic carbon, which is adjacent to the Pd–C bond on each template complex. The second spacers were designed to project the stereochemistry of the chiral amine auxiliaries to their neighboring template sites.

The new chiral templates indeed generated the *endo*-cycloadducts with significantly higher stereoselectivities.^[7,9] For example, the reaction between complex (S)-174 and *N,N*-dimethylacrylamide generated a 1:6 mixture of the two expected diastereomers (*S_C*,*R_P*)- and (*S_C*,*S_P*)-175, respectively as compared to the 2:1 diastereomeric ratio when (S)-11 was used (Scheme 1.53), despite the fact that the synthesis was conducted at a lower temperature with a prolonged reaction time.

Scheme 1.53

Similarly, palladacycle (*R*)-11 produced equal quantities of the keto complexes (*S_C*,*R_P*)- and (*S_C*,*S_P*)-172 when the corresponding *endo*-cycloaddition was conducted at 70 °C. Under such conditions, the reaction between complex (*S_C*)-176 and ethyl vinyl ketone gave the diastereomeric complexes (*S_C*,*R_P*)- and (*S_C*,*S_P*)-177 in an improved ratio of 1:3.5 (Scheme 1.54).

Scheme 1.54

1.5 Aims of This Work

The above mentioned studies show that the chiral naphthylethylamine auxiliary exerts a weak stereochemical influence on the reaction site. In the transition state the dmpp group enjoys a certain degree of free rotation around the P–Pd bond and thus poor stereoselectivity was observed. It has been established that the coordination site *cis* to the N atom is controlled stereochemically by the two prochiral NMe groups. It is clear that by introducing a spacer on the aromatic carbon which is adjacent to the Pd–C bond on the template, this class of *ortho*-palladated complexes should induce better stereoselectivity in similar reactions. Taking into account the known fact of the practical uses of optically active palladacycles, this project aims to develop novel chiral *ortho*-palladated complexes. The development and stereochemical evaluation of each of these cyclopalladated complexes will be described in detail in the following chapters.

CHAPTER 2

CHIRAL *ORTHO*-PALLADATED 1-(3,6-DIMETHYLNAPHTHALEN-1-YL)-*N,N*-DIMETHYLETHANAMINE

2.1 Introduction

As discussed in chapter one, optically active palladacycles are widely used in many applications. In the past twenty years, we have been interested in the development of chiral *ortho*-palladated complexes of substituted benzyl- ((*S*)-**4**) and naphthylamine ((*S*)-**11**) for the purpose of synthesizing chiral phosphines. It has been proven that palladacycle (*S*)-**11** is superior over (*S*)-**4** in many asymmetric applications.^[174] Firstly, the five-membered organometallic ring in palladacycle (*S*)-**11** is kinetically and thermodynamically stable. Secondly, the intramolecular steric interaction between H8 and the methyl group at the stereogenic carbon center confines the methyl group in the axial position and hence locks the cyclopalladated ring into the non-interconvertable λ conformation both in solid and solution state. Due to this unique ring conformation, the chirality of the naphthylamine ring is transmitted efficiently *via* its prochiral N-methyl groups onto the neighboring coordination site. On the other hand, the stereochemistry of the five-membered organometallic ring in palladacycle (*S*)-**4** is not as well defined as palladacycle (*S*)-**11**, as the puckered benzylamine ring undergoes rapid transformation between the two nonequivalent δ and λ conformations in solution.

Therefore, we have chosen palladacycle (*S*)-**11** and its (*R*)-enantiomer as chiral templates for the asymmetric [4+2] *endo*-cycloaddition reaction between 3,4-dimethyl-1-phenylphosphole (dmpp) and a range of dienophiles.^[174] A series of functionalized P-chiral phosphines have been generated stereoselectively by using palladacycle **11** as the chiral reaction template. However, this naphthylamine auxiliary does not exhibit good selectivity in some dienophiles that we have screened in the asymmetric [4+2] *endo*-cycloaddition reactions mentioned above. For example, when the *N,N*-dimethylacrylamide was used as the dienophile, the two possible diastereomeric *endo*-cycloadducts were obtained as a 1:2 mixture (Scheme 1.53).^[165] This experiment shows that the chiral naphthylethylamine auxiliary **11** exerts a weak stereochemical influence on the reaction site. Evidently, in the transition state, the dmpp group experiences a certain degree of the free rotation around the P–Pd bond and thus the poor stereoselectivity was observed. It has been established that the coordination site *cis* to the N atom is controlled stereochemically by the two prochiral NMe groups. Accordingly, by the introduction of a spacer group on the aromatic carbon which is adjacent to the Pd–C bond on the template, this class of *ortho*-palladated complexes should induce better stereoselectivity in similar reactions.

2.2 Research Objectives

In order to improve the stereoselectivity, a novel chiral palladacycle (*S*)-**178** was designed and synthesized. The chiral complex (*S*)-**178** exhibits the same key stereochemical features of the chiral naphthylamine chelate ring in palladacycle (*S*)-**11**. The internal steric repulsion between and methyl substituent on the stereogenic carbon and its neighboring naphthalene proton H8 is expected to lock the five-membered organometallic ring conformation. Furthermore, a methyl group Me3 is introduced on the

aromatic ring which was designed to exert stereochemical influence on the neighboring reaction site. For comparison purposes, the application of this new chiral palladacycle in the analogous asymmetric *endo*-cycloaddition reaction was examined.

(S)-178

2.3 Results and Discussion

2.3.1 Synthesis of Racemic *ortho*-Palladated Complex ($\pm$)-178

The racemic form of the palladacycle was prepared according to Scheme 2.1. Based on the reported procedure, the ketone **180** was obtained using 2,7-dimethylnaphthalene **179**^[175] as starting material, in 17.3% yield.^[176] Reduction of ketone **180** by NaBH₄ gave racemic alcohol ($\pm$)-**181** in 92.8% yield. Conversion of compound ($\pm$)-**181** to the chloro species ($\pm$)-**182** was achieved by treatment with excess PCl₃ in dry dichloromethane. Reaction between compound ($\pm$)-**182** and aqueous dimethylamine afforded the target *N,N*-dimethylamine compound ($\pm$)-**183** in 89.1 % yield. Treatment of compound ($\pm$)-**183** with [Pd(MeCN)₄](ClO₄)₂ in the presence of triethylamine followed by the addition of aqueous 1M hydrochloric acid led to the chloro-bridged dimeric complex ($\pm$)-**178** in the form of a yellow powder, in 80.5 % isolated yield.^[9]

Scheme 2.1

2.3.2 Synthesis and Characterization of *ortho*-Palladated Complex (±)-184

2.3.2.1 Synthesis of Complex (±)-184

The dynamic *cis-trans* interconversion and the stereoisomeric properties of the dimeric complex (±)-178 posed difficulties in the assignment of its ^1H NMR signals. Thus the dimer was converted to its monomeric form complex (±)-184 by treatment with triphenylphosphine.^[7] Complex (±)-184 was prepared efficiently from the reaction between complex (±)-178 and triphenylphosphine *via* a standard $\mu\text{-Cl}$ bridge cleavage reaction in 90.0% yield. This mononuclear complex (±)-184 is more suitable for NMR spectroscopic studies of the organopalladium ring conformation on account of the improved spectral resolution of the signals with respect to that from its parent dimer which exists in solution as an equilibrium mixture of two regioisomers. Moreover, the simplicity of the ^1H NMR spectroscopic signals that are presented by the

triphenylphosphine ligand is another attractive feature. It possesses only protons from aromatic groups, and the absence of any aliphatic protons will therefore not contribute to the complexity at the aliphatic region of the ^1H NMR spectrum.^[177]

Scheme 2.2

2.3.2.2 Molecular Structure of Complex (±)-184

Yellow colored single crystals of complex (±)-**184** were formed by slow evaporation of a complex (±)-**184** solution (dichloromethane/hexane). The structure of complex (±)-**184** was reaffirmed crystallographically. The X-ray molecular structure and selected bond lengths and angles are presented in Figure 2.2 and Table 2.1, respectively. Complex (±)-**184** has a distorted square-planar geometry, with the five-membered ring in an envelope-like conformation. Analysis of the extent of the tetrahedral distortion on the central Pd atom reveals that it is located in a highly congested environment: as indicated by the large angle of 25.5° between the $\{\text{C}(1)\text{--Pd}(1)\text{--N}(1)\}$ and $\{\text{P}(1)\text{--Pd}(1)\text{--Cl}(1)\}$ planes (Figure 2.1).

Figure 2.1 Tetrahedral Distortion of Complex (±)-**184** at the Palladium(II) Centre

In the absence of a steric projecting group from the aromatic carbon, the steric repulsion between the PPh_3 ligand and the naphthylamine chelate in the PPh_3 derivative of complex (*S*)-**11** is relatively insignificant. Thus, the $\text{C}(1)\text{--Pd}(1)\text{--P}(1)$ bond angle is $94.01(11)^\circ$.^[6] In complex ($\pm$)-**184**, there is a strong steric repulsion between the triphenylphosphine ligand and the organometallic chelate, hence the bond angle $\text{C}(1)\text{--Pd}(1)\text{--P}(1)$ has been enlarged to $100.2(4)^\circ$. With these structural features, the $\text{Pd}\text{--P}$ bond would not be able to rotate freely, as all the possible rotational motions are blocked by the chloro ligand and the projecting methyl group. Therefore, among the three $\text{P}\text{--Ph}$ phenyl rings, the $\text{C}(29)\text{--C}(34)$ ring experiences the most intramolecular ligand–ligand repulsion. As a result, the bond angle $\text{Pd}(1)\text{--P}(1)\text{--C}(17)$ is enlarged to $119.6(5)^\circ$, which is larger than the two less affected $\text{Pd}(1)\text{--P}(1)\text{--C}(23)$ and $\text{Pd}(1)\text{--P}(1)\text{--C}(29)$ angles [$117.6(5)^\circ$ and $109.6(5)^\circ$].

Figure 2.2 Molecular structure of complex ($\pm$)-**184** with thermal ellipsoids at 50% probability. All hydrogen atoms are omitted for clarity.

Table 2.1 Selected bond lengths (Å) and angles (°) for complex (±)-**18**

Pd(1)–C(1)	2.017(2)	Pd(1)–N(1)	2.146(1)
Pd(1)–P(1)	2.259(4)	Pd(1)–Cl(1)	2.385(5)
P(1)–C(23)	1.836(2)	P(1)–C(17)	1.829(2)
P(1)–C(29)	1.819(2)	P(1)–Pd(1)–C (1)	100.2(4)
C(1)–Pd(1)–N(1)	79.6(6)	C(1)–Pd(1)–P(1)	101.7 (1)
N(1)–Pd(1)–P(1)	158.4(4)	C(1)–Pd(1)–Cl(1)	165.6(4)
N(1)–Pd(1)–Cl(1)	94.1(4)	P(1)–Pd(1)–Cl(1)	90.4(2)
C(29)–P(1)–Pd(1)	119.6(5)	C(17)–P(1)–Pd(1)	117.6(5)
C(23)–P(1)–Pd(1)	109.6(5)		

2.3.2.3 Solution Structure of Complex (±)-184

Despite the severe steric repulsion observed within complex (±)-**184**, the regiochemistry of this racemic complex remains unchanged in solution. In CDCl₃, the ³¹P NMR spectrum of complex (±)-**184** shows only a singlet resonance at δ 30.1, indicating the presence of a sole isomer in solution. The NMR study of the racemic adduct (±)-**184** has shown that in solution the five-membered palladacycle exists preferentially in the $\delta(R)$ or $\lambda(S)$ conformation with the α -methyl substituent in the axial position. This conclusion may be inferred from the ⁴J_{H,P} value of 6.4 Hz for the α -methine proton and is further confirmed by the results of 2D ¹H-¹H ROESY NMR measurements. The numbering of complex (±)-**184** is shown in Figure 2.3.

Figure 2.3 Numbering Scheme of Complex (±)-**184** for NMR Studies.

Figure 2.4 Newman projections of (S_C) palladacycle along the N-Me9 for ROESY-derived $\lambda(S)$ conformation for complex (S)-**184** (a), and that for the alternative $\delta(S)$ conformation (b).

Figure 2.4 shows the two possible conformations of complex ($\pm$)-**184**. When the α -Me group Me9 is axially located as in (a), the five-membered ring adopts a λ conformation. In such a case, Me9 is expected to show a strong interaction with NMe(eq) but not with NMe(ax) and the α -methine proton H9 will interact with both NMe groups. When the α -Me group Me9 is equatorially disposed as in (b), the conformation of the five membered ring changes to δ . This results in different correlations, that is, Me9 shows similar correlations with two NMe groups and the H9 interacts strongly with NMe(eq). The conformational behavior of the five-membered palladacycle was deduced from ROESY data obtained from the 2D ^1H - ^1H ROESY NMR spectrum of complex ($\pm$)-**184** (Figure 2.5).

The interaction between the α -methine H9 and methyl protons are the key interactions for the assignment of the conformational state of the palladacycle. These comprise the existence of ROESY correlations between H9 and the two NMe groups (C and D) and the interaction between H9 and Me9 (E). In addition, the α -methyl group Me9 interacts strongly with the equatorially disposed NMe group (B). The driving forces for Me9 to assume mainly the axial position, i.e. H9–H8 (F) and Me9–H8 (I) repulsive interactions, are prominently reflected. This set of ROESY interactions indicates that the five-membered ring is adopted in a fixed conformation ($\lambda(S)$, as depicted in Figure 2.4a)

Other expected ROESY interactions of H4–Me3 (J), NMe(ax)–NMe(eq) (A), Me6–H5 and Me6–H7 (G and H) are also observed. The above solution NMR spectroscopy investigations of complex ($\pm$)-**184** indicates that the α -methyl group Me9 is located in the axial position and the interaction between the Me9 and H8 can confine the five-membered organometallic ring conformation and the λ and δ conformations are adopted in the (*S*) and (*R*) enantiomers respectively.

Figure 2.5 2D ^1H - ^1H ROESY NMR Spectrum of Complex ($\pm$)-**184** in CDCl_3 . (refer to Figure 2.3 for the numbering scheme of complex ($\pm$)-**184**). Selected ROESY Interactions: (A) NMe(ax)–NMe(eq); (B) Me9–NMe(eq); (C) H9–NMe(eq); (D) H9–NMe(ax); (E) H9–Me9; (F) H8–H9; (G, H) Me6–H5, Me6–H7; (I) Me9–H8; (J) H4–Me3; (K) H5–H4.

2.3.3 Optical Resolution of Racemic Dimeric Complex ($\pm$)-**178**

In theory, in the presence of chiral amino acid salts as the chiral auxiliary ligands, a separation procedure by physical methods may be attempted on the diastereomeric mixture so as to obtain the chiral palladacycle in the optically active form.^[9, 49, 163] Here the optical resolution of racemic dimeric complex ($\pm$)-**178** was performed using (*S*)-prolinato as the auxiliary ligand (Scheme 2.3).

Scheme 2.3

By treatment of the racemic dimer ($\pm$)-**178** with two molar equivalents of sodium (*S*)-prolinate, the expected 1:1 mixture of diastereomeric adducts (*R_C*,*S_C*,*S_N*)-**185** and (*S_C*,*S_C*,*S_N*)-**185** was formed according to ¹H NMR spectroscopy. The initial attempted separation of the two diastereomers by fractional crystallization was unsuccessful as crystallization could not be induced despite the use of an array of solvent systems. Nevertheless, the neutral nature of these complexes has presented the alternate option of diastereomeric separation by column chromatography. Thus, the 1:1 diastereomeric mixture, complex (*R_C*,*S_C*,*S_N*)-**185** and (*S_C*,*S_C*,*S_N*)-**185**, was slowly eluted through a silica gel column with dichloromethane/acetone (V/V = 2/1) as mobile phase. The fractions were separated and checked by ¹H NMR spectroscopy for their optical purities. In this manner, both diastereomers were separated efficiently. Complex (*R_C*,*S_C*,*S_N*)-**185**, the diastereomer that eluted first, was crystallized from dichloromethane and hexane as light yellow prisms in an overall yield of 91.0% with [α]₃₆₅ +160 (*c* 0.5, methanol), > 99% *de* (according to the ¹H NMR spectrum). The second eluted diastereomer, complex

(S_C, S_C, S_N)-**185**, was initially isolated as a light yellow powder and then crystallized from dichloromethane and hexane in 88.0% yield with $[\alpha]_{365} +916$ (c 0.5, methanol), > 99% *de* (according to the ^1H NMR spectrum).

The absolute configurations and solid structures of both diastereomeric prolineate derivatives (S_C, S_C, S_N)-**185** and (R_C, S_C, S_N)-**185** were determined by X-ray single crystal diffraction investigation. Their solution structures were also studied by their 2D ^1H - ^1H ROESY NMR.

2.3.3.1 Molecular Structure of Diastereomer (R_C, S_C, S_N)-**185**

Light yellow colored single crystals of diastereomer (R_C, S_C, S_N)-**185** were formed from a dichloromethane and hexane solution. An X-ray diffraction study of complex (R_C, S_C, S_N)-**185** was performed (Figure 2.6).

Figure 2.6 Molecular structure of complex (R_C, S_C, S_N)-**185** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) and H(C20) are omitted for clarity.

Table 2.2 Selected bond lengths (Å) and angles (°) for complex (*R_C,S_C,S_N*)-**185**

Pd(1)–C(1)	2.030(6)	Pd(1)–O(1)	2.039(4)
Pd(1)–N(1)	2.047(5)	Pd(1)–N(2)	2.141(5)
N(1)–C(16)	1.477(8)	C(17)–N(2)	1.503(8)
C(21)–O(2)	1.221(9)	C(21)–O(1)	1.300(9)
C(1)–Pd(1)–N(1)	79.8(2)	C(1)–Pd(1)–N(2)	178.5(2)
N(1)–Pd(1)–O(1)	175.5(2)	N(2)–Pd(1)–O(1)	80.8(2)
C(1)–Pd(1)–O(1)	99.7(2)	N(1)–Pd(1)–N(2)	99.8(2)

The X-ray crystallographic study reveals the *R* absolute configuration of the α -carbon stereocenter and it is confirmed independently using (*S_C,S_N*)-proline as a reference point, and based on the anomalous X-ray scattering method. The α -methyl group Me14 occupies the axial position and the conformation of the five-membered palladacycle is δ . The tetrahedral distortion of the palladium coordination environment is minimal, with the angle between the {Pd(1)–C(1)–N(1)} and {Pd(1)–N(2)–O(1)} planes equal to 5.0°. This complex adopts a *cis*-(*N,N*) arrangement, as observed in similar proline complexes.^[9] The geometric parameters of the proline moiety of the diastereomer (*R_C,S_C,S_N*)-**185** are mainly in the range of the values typical for the other (*S*)-proline complexes of palladium(II) including those containing *ortho*-palladated ligands of the C,N-type. In the isomer (*R_C,S_C,S_N*)-**185**, the five-membered palladacycle has an envelope-like conformation with the distance 0.761 Å between N1 and the plane (C(13)–C(12)–C(1)–Pd(1)) and N1 lies below this plane.

2.3.3.2 Solution Structure of Complex (*R_C,S_C,S_N*)-**185**

Owing to the different arrangements of the coordinating atoms around the central palladium atom, there are two possible geometric isomers for each diastereomer, as shown in Figure 2.7. For reported (*S*)-proline palladium (II) complexes containing *ortho*-palladated ligands of the C,N-type, isomers of type II were always observed and

the two nitrogen atoms have a *trans* relationship. However in complex (R_C, S_C, S_N)-**185**, the two nitrogen atoms are *cis* related to each other (refer to Figure 2.6) in the solid state. This unusual arrangement may be partially due to requirements of the crystal lattice. In solution, on the other hand, molecules will enjoy more freedom and less restriction. Hence it is necessary to explore the behavior of the complex in solution by means of 2D ^1H - ^1H ROESY NMR study.

Figure 2.7 Two possible geometric isomers for each diastereomer of palladacycles.

In CDCl_3 , the 500 MHz ^1H NMR spectrum of complex (R_C, S_C, S_N)-**185** at room temperature shows a sole geometric isomer in solution which is indicated by the presence of one resonance observed for each chemically nonequivalent proton. The signal assignments are performed by a combination of ^1H NMR, 2D COSY NMR and 2D ^1H - ^1H ROESY NMR spectra. Figure 2.8 shows the numbering scheme for the NMR study and the 2D ^1H - ^1H ROESY NMR spectrum of complex (R_C, S_C, S_N)-**185** is presented.

Figure 2.8 Numbering Scheme of Complex (R_C, S_C, S_N)-**185** for NMR Studies

In the 2D ^1H - ^1H ROESY spectrum, strong ROESY interactions between H9 and NMe(eq) (NMe(ax), Me9) are clearly recorded (A, B and C). The α -methyl group Me9 interacts strongly with the equatorially disposed NMe group (F), however the interaction between Me9 and the axially disposed NMe group is not observed. The presence of this

set of ROESY interactions show that the five-membered palladacycle ring is locked in the δ conformation and hence the α -methyl group Me9 is axially disposed as illustrated in Figure 2.9. The absence of a Me9-NMe(ax) ROESY correlation definitely rules out a λ conformation in solution.

Figure 2.9 Two Possible Conformations of Complex (R_C, S_C, S_N) -185

It is interesting to note that interactions between Me3 and NH (H13) (D and E) are clearly recorded which indicate that in solution isomer (R_C, S_C, S_N) -185 retains a *trans*-(*N,N*) arrangement, which is different from its geometrical arrangement in the solid state. In addition, no ROESY interactions between both NMe groups and the proline ligand are observed in the spectrum, confirming the *trans*-(*N,N*) relationship in solution. Other expected ROESY interactions, for example H11–H11' (G); H12–H11 (H); H13–H13' (I); H9–H8 (J); Me3–H4 (K); Me6–H7 (L); Me6–H5 (M) are also observed.

Figure 2.10 2D ^1H - ^1H ROESY NMR Spectrum of Complex (S_C,S_C,S_N) -**185** in CDCl_3 . (refer to Figure 2.8 for the numbering scheme). Selected ROESY Interactions: (A) H9–NMe(ax); (B) H9–NMe(eq); (C) H10–Me9; (D) NH–Me3; (E) H13–Me3; (F) Me9–NMe(eq); (G) H11–H11'; (H) H12–H11; (I) H13–H13'; (J) H9–H8; (K) Me3–H4; (L) Me6–H7; (M) Me6–H5.

2.3.3.3 Molecular Structure of Diastereomer (S_C,S_C,S_N) -**185**

For the other diastereomer (S_C,S_C,S_N) -**185**, yellow colored crystals suitable for X-ray crystallography were obtained by slow evaporation of a solution of dichloromethane–hexane of complex (S_C,S_C,S_N) -**185**. There are two crystallographically distinguishable molecules in the asymmetric unit with the same stereochemistry but slightly different bond lengths and angles. For clarity, only one of them (molecule A) is depicted in Figure 2.11. Selected bond lengths and angles are listed in Table 2.3.

Figure 2.11 Molecular structure of complex (S_C, S_C, S_N)-**185** with thermal ellipsoids at 50% probability and hydrogen atoms except H(C13), H(N2) and H(C18) are omitted for clarity.

The *S* configuration of the α -carbon stereocenter in the palladacycle is confirmed independently using (S_C, S_N)-proline as a reference point and based on the anomalous X-ray scattering method with the Flack parameter of 0.036 (17). Unlike the *cis*-(N, N) arrangement in complex (R_C, S_C, S_N)-**185**, diastereomer (S_C, S_C, S_N)-**185** adopts a *trans*-(N, N) arrangement. The geometric parameters of the molecule are in the range of the values typical for the *ortho*-palladated derivatives of tertiary α -alkyl substituted amines previously studied. The tetrahedral distortion of the palladium coordination environment is moderate, with the angle between the {Pd(1)–C(1)–N(1)} and {Pd(1)–N(2)–O(1)} planes equal to 3.5°. The organopalladium five-membered ring has an envelope-like conformation and the distance between N(1) and the plane [Pd(1)–C(1)–C(12)–C(13)] is 0.699 Å. Due to the repulsive interaction between the protruding methyl group Me3 and the pyrrolidine, the angle of C(1)–Pd(1)–N(2) is enlarged to 104.6(1)° compared to the value of 99.9(1)° for a similar benzylamine derivative.^[9] This phenomenon can be rationally attributed to the presence of the methyl group Me3, which imposes repulsion to the adjacent pyrrolidine ring.

Table 2.3 Selected bond lengths (Å) and angles (°) for complex (S_C, S_C, S_N)-**185**.

Molecule A		Molecule B	
Pd(1)–C(1)	2.009(3)	Pd(2)–C(22)	2.002(3)
Pd(1)–N(1)	2.062(2)	Pd(2)–N(4)	2.061(3)
Pd(1)–N(2)	2.074(2)	Pd(2)–N(3)	2.062(3)
Pd(1)–O(1)	2.083(2)	Pd(2)–O(3)	2.083(2)
C(1)–Pd(1)–N(1)	81.8(1)	C(22)–Pd(2)–N(4)	102.3(1)
C(1)–Pd(1)–N(2)	104.6(1)	C(22)–Pd(2)–N(3)	80.7 (1)
N(1)–Pd(1)–N(2)	172.7(1)	N(4)–Pd(2)–N(3)	174.5(1)
C(1)–Pd(1)–O(1)	174.3(1)	C(22)–Pd(2)–O(3)	176.0(1)
N(1)–Pd(1)–O(1)	92.6(1)	N(4)–Pd(2)–O(3)	81.7(1)

2.3.3.4 Solution Structure of Complex (S_C, S_C, S_N)-185

Similar to diastereomer (R_C, S_C, S_N)-**185**, the solution behavior of complex (S_C, S_C, S_N)-**185**, especially its regiochemistry is of interest to us. In $CDCl_3$, isomer (S_C, S_C, S_N)-**185** shows the presence of the sole geometric isomer in solution as there is only one resonance observed for each chemically nonequivalent proton. Figure 2.12 shows the numbering scheme of complex (S_C, S_C, S_N)-**185** and the 2D 1H - 1H ROESY NMR spectrum was obtained at room temperature in $CDCl_3$ (Figure 2.14).

Figure 2.12 Numbering Scheme of Complex (S_C, S_C, S_N)-**185** for NMR Studies.

In this NMR spectrum, strong ROESY interactions between H9 and NMe(eq) (NMe(ax), Me9) are clearly recorded (A, B and C). The α -methyl group Me9 interacts strongly with the equatorially disposed NMe group (L), however the interaction between Me9 and the axially disposed NMe group is not observed. These interactions are consistent with the λ conformation shown in Figure 2.13. Therefore the ROESY

interaction shows that the five-membered palladacycle ring is locked in the λ conformation and hence the α -methyl group Me9 is axially disposed.

Figure 2.13 Two Possible Conformations of Complex (S_C, S_C, S_N) -**185**.

The ROESY correlations H9–H8 (O) and H8–Me9 (T) are reflective of the steric factors which are the main driving forces responsible for complex (S_C, S_C, S_N) -**185** adopting a λ conformation. The same ROESY experiment gives valuable information regarding the geometry of complex (S_C, S_C, S_N) -**185** and the palladacycle conformation. The newly introduced methyl group Me3 shows strong interactions with NH (H) and H13 (I) and these can be considered as an unambiguous support for the *trans*-(*N,N*)-geometry of prolinato adduct (S_C, S_C, S_N) -**185**. The absence of ROESY correlations between both NMe groups and the prolinato ligand in the spectrum, further confirms the *trans*-(*N,N*) relationship. Base on these data, further assignments of the other resonances of the prolinato ligand were performed using the routine spin–spin coupling technique. The signal assignment of the prolinato ligand is performed based on the interactions observed in the spectrum, for example, NH–H10 (E), NH–H13 (F), NH–H13' (G), H13–H12 (J), H13–H12' (K), H12'–H11(M) and H12'–H12(N). Some other expected ROESY signals within the protons of the naphthalene ring are also clearly recorded.

Figure 2.14 2D ^1H - ^1H ROESY NMR Spectrum of Complex (S_C, S_C, S_N)-**185** in CDCl_3 . (refer to Figure 2.12 for the numbering scheme). Selected ROESY Interactions: (A) H9–NMe(eq); (B) H9–NMe(ax); (C) H10–H11; (D) H9–Me9; (E) NH–H10; (F) NH–H13; (G) NH–H13'; (H) NH–Me3; (I) H13–Me3; (J) H13–H12; (K) H13–H12'; (L) Me9–NMe(eq); (M) H12'–H11; (N) H12'–H12; (O) H9–H8; (P) H4–Me3; (Q) H5–Me3; (R) H7–Me6; (S) H5–Me6; (T) H8–Me9.

2.3.4 Synthesis of the Optically Active Palladacycle (*S*)-**178** and (*R*)-**178**

The optically active chloro bridging dimer (*S*)-**178** was obtained by mixing a dichloromethane solution of complex (S_C, S_C, S_N)-**185** with aqueous. 1M hydrochloric acid and was isolated as a yellow powder in 95.6% yield with $[\alpha]_D +120$ (c 0.5, dichloromethane) (Scheme 2.4). As is common with other dimeric α -arylalkylamine palladacycles, like (*S*)-**4** and (*S*)-**11**, the optically active dimer (*S*)-**178** exhibits two sets

of signals in its ^1H NMR spectrum in CDCl_3 at room temperature. Integration of the NMR signals reveals that the two isomers are present in a ratio of approximately 1:1. Therefore, both *cis* and *trans* isomers are observed in solution according to the ^1H NMR spectrum.

Scheme 2.4

In the solid state, the molecular structure of complex *(S)*-**178** was determined by X-ray crystallography (Figure 2.15) and yellow colored single crystals were obtained from a *(S)*-**178** solution of dichloromethane and hexane. The selected bond lengths and angles are listed in Table 2.4.

Figure 2.15 Molecular structure of complex *(S)*-**178** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) and H(C13A) are omitted for clarity.

Table 2.4 Selected bond lengths (Å) and angles (°) for complex (*S*)-**178**.

Pd(1)–C(1)	1.996(2)	Pd(1)–N(1)	2.075(2)
Pd(1)–Cl(1A)	2.355(6)	Pd(1)–Cl(1)	2.489(5)
Pd(1)–Pd(1A)	3.225(3)	Cl(1)–Pd(1A)	2.355(6)
C(1)–Pd(1)–N(1)	80.6(8)	C(1)–Pd(1)–Cl(1A)	98.7(6)
N(1)–Pd(1)–Cl(1A)	168.6(6)	C(1)–Pd(1)–Cl(1)	176.3(6)
N(1)–Pd(1)–Cl(1)	97.4(5)	Cl(1A)–Pd(1)–Cl(1)	83.9(2)
C(1)–Pd(1)–Pd(1A)	137.1(5)	N(1)–Pd(1)–Pd(1A)	123.9(6)
Cl(1A)–Pd(1)–Pd(1A)	50.1(1)	Cl(1)–Pd(1)–Pd(1A)	46.5 (1)
Pd(1A)–Cl(1)–Pd(1)	83.4 (2)	C(15)–N(1)–Pd(1)	111.2(2)
C(16)–N(1)–Pd(1)	113.8(2)	C(13)–N(1)–Pd(1)	104.4(1)

The X-ray crystallographic study confirms the expected *S* absolute configuration of the α -carbon stereocenter of the palladacycle. In line with most of the recorded X-ray structures of similar μ -chloro-bridged dimeric *ortho*-palladated amines or related dimers of C,N-type, complex (*S*)-**178** reveals the expected *trans*-relationship between two nitrogen and two carbon donor atoms. The coordination spheres of both the palladium centers are in a distorted square-planar geometry, with tetrahedral distortions of 10.4° and 11.0°. The angle between {Pd(1)–C(1)–C(10)–C(13)–N(1)} and {Pd(1)–Cl(1)–Pd(1A)–Cl(1A)} planes equal to 51.5°. The most interesting feature of complex (*S*)-**178** is that the central four-membered ring {Pd(1)–Cl(1)–Pd(1A)–Cl(1A)} is bent along the Cl(1)–Cl(1A) axis by 52.9°. This can be partially attributed to the repulsive interactions between the methyl groups (C(11), C(11A)) and the two bridged Cl atoms. The distances of C(11)–Cl(1) and C(11A)–Cl(1A) are both found to be 3.230 Å. These C–Cl bond distance are shorter than the sum of the van der Waals radii of the two atoms, 3.8 Å. Furthermore, the interaction between the NMe (C(16), C(16A)) and the bridged Cl atoms (Cl(1), C(1A)) also contribute to the large angle (the four-membered ring {Pd(1)–Cl(1)–

$\text{Pd(1A)-Cl(1A)}\}$ is bent along the Cl(1)-Cl(1A) axis by 52.9° since the distances of C(16)-Cl(1) and C(16A)-Cl(1A) were $3.285 \text{ \AA}$. The interactions mentioned above projected the naphthalene ring away from the chloro bridges and thus formed the butterfly-like dimeric complex (*S*)-**178**.

The enantiomeric palladacycle (*R*)-**178** could be prepared from complex (*R_C,S_C,S_N*)-**185** in a similar manner: $[\alpha]_{\text{D}} -118$ (*c* 0.5, dichloromethane) (Scheme 2.5).

Scheme 2.5

2.3.5 Regio-selective Formation of the dmpp Complex (*S*)-**186** and Its *endo*-Cycloaddition Reactions with *N,N*-dimethylacrylamide

In order to evaluate the efficiency of the new palladacycle (*S*)-**178** as a chiral template for intermolecular *endo*-cycloaddition reaction, the intermediate 3,4-dimethyl-1-phenylphosphole (dmpp) complex (*S*)-**186** was synthesized by the cleavage reaction of the dimeric complex (*S*)-**178** with two equivalents of dmpp. The reaction between complex (*S*)-**186** and *N,N*-dimethylacrylamide was subsequently investigated.

2.3.5.1 Formation and Isolation of Complex (*S*)-**186**

As shown in Scheme 2.6, the dichloro bridge in complex (*S*)-**178** could be split readily by the phosphine ligand dmpp at room temperature in 1 h, affording complex (*S*)-**186** as yellow powder in 89.7% yield, $[\alpha]_{\text{D}} +456$ (*c* 0.5 dichloromethane).

Scheme 2.6

2.3.5.2 Molecular Structure of dmpp Complex (S)-186

Light yellow colored single crystals of complex (S)-186 were obtained from a solution of chloroform and hexane. The structure of complex (S)-186 was determined by X-ray crystallography. Figure 2.16 presents the molecular structure and Table 2.5 tabulates selected inter-atomic distance and angles. According to Figure 2.16, the phosphole group is in the *trans* position of the amine nitrogen.

Figure 2.16 Molecular structure of complex (S)-186 with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) are omitted for clarity.

Table 2.5 Selected bond lengths (Å) and angles (°) for complex (*S*)-**186**.

Pd(1)–C(1)	2.018(2)	Pd(1)–N(1)	2.133(1)
Pd(1)–P(1)	2.244(3)	Pd(1)–Cl(1)	2.395(4)
C(1)–Pd(1)–N(1)	80.1(6)	C(1)–Pd(1)–P(1)	99.6(4)
N(1)–Pd(1)–P(1)	167.9(5)	C(1)–Pd(1)–Cl(1)	171.6(5)
N(1)–Pd(1)–Cl(1)	94.1(4)	P(1)–Pd(1)–Cl(1)	87.4(1)
C(12)–C(1)–Pd(1)	111.3(1)	C(2)–C(1)–Pd(1)	129.2(1)
C(17)–P(1)–Pd(1)	112.6(6)	C(22)–P(1)–Pd(1)	123.2(5)

Figure 2.17 Molecular structure of complex (*S*)-**186** (space filling diagram)

Complex (*S*)-**186** has a distorted square-planar coordination geometry with the tetrahedral distortion angle of 13.2°. The five-membered palladacycle has an envelope-like geometry with the N(1) atom 0.848 Å above the C(13)–C(12)–C(1)–Pd(1) mean plane. The distance between H(C3) and H(C22) is 2.181 Å. The angle C(22)–P(1)–Pd(1) [123.22(5)°] is significantly larger than those of C(17)–P(1)–Pd(1) [112.55(6)°] and C(23)–P(1)–Pd(1) [113.81(5)°]. One possible reason for this difference is the repulsive interactions between the coordinated dmpp group and the “spacer” methyl C(3) (Figure 2.17). As a result of this repulsion, the C(3) atom is not strictly coplanar with the phenyl ring C(1)–C(2)–C(4)–(5)–C(11)–C(12), but with a distance of 0.222 Å to the mean plane.

2.3.5.3 Solution Structure of the dmpp Complex (S)-186

The ^{31}P NMR spectrum of complex (S)-**186** in CDCl_3 shows only one singlet signal at δ 28.4 which indicates the formation of a sole isomer in solution. In the ^1H NMR spectrum, the long range P–H coupling constants of 3.4 and 6.5 Hz observed for resonance signals between NMe groups and the proton attached to the chiral center indicate that the dmpp group is coordinated *trans* to the nitrogen atom in solution. Figure 2.18 illustrates the numbering scheme for NMR assignment and Figure 2.19 shows the 2D ^1H - ^1H ROESY NMR.

Figure 2.18 Numbering Scheme of Complex (S)-**186** for NMR Studies.

Figure 2.19 2D ^1H - ^1H ROESY NMR Spectrum of Complex (S)-**186** in CDCl_3 . (refer to Figure 2.18 for the numbering scheme). Selected ROESY Interactions: (A) H9–NMe(eq); (B) H9–NMe(ax); (C) H9–Me9; (D) Me9–NMe(eq); (E) Me12–Me3; (F) Me9–Me6; (G) Me9–NMe(eq); (H) Me10–Me3; (I) Me10–Me6; (J) H9–H8; (K) Me6–H5; (L) Me9–H8; (M) Me6–H7; (N) Me3–H4.

In the 2D ^1H - ^1H ROESY NMR spectrum, the interactions about the five-membered (S)-palladacycle are clearly recorded. For example, Signals (A, B) show the interactions between α -methine proton H9 and NMe groups (NMe(eq) and NMe(ax)). Furthermore, signal C shows that the α -methine proton H9 also interacts with the α -methyl group Me9. The α -methyl group Me9 strongly interacts with NMe(eq) (D), but weakly with NMe(ax) (G). This set of ROESY signals shows that the ring is predominantly in λ conformation. The driving forces for such an arrangement, i.e. the H9–H8 (J) and Me9–H8 (L) repulsive interactions, are reflected in the spectrum. Signals of Me3–H12 (O), Me13–Me3 (E) and Me11–Me3 (H) show the interaction between Me3 and the phosphole and hence confirm the *trans*-*N,P* coordination geometry mentioned above. Some other ROESY signals, Me6–H5 (H7) (M and K), Me9–Me6 (F) and Me3–H4 (N) are also observed.

2.3.5.4 The Intermolecular *endo*-Cycloaddition Reaction Between Complex (S)-**186** and *N,N*-dimethylacrylamide

The intermolecular *endo*-cycloaddition reaction between complex (S)-**186** and *N,N*-dimethylacrylamide was carried out at room temperature in dichloromethane. The reaction was monitored by ^{31}P NMR spectroscopy and was found to be complete in 20 d. Prior to purification, the ^{31}P NMR spectrum of the crude reaction product in CDCl_3 exhibited two sharp singlets at δ 114.3 and 115.3 in a ratio of 1:5.9 indicating that two

diastereomeric products were formed in the *endo*-cycloaddition reaction.

The diastereomeric cycloadducts could be separated by column chromatography efficiently. The mixture was slowly eluted through a silica gel column with dichloromethane/ethyl acetate (V/V = 10:1) as the mobile phase. The two diastereomers were readily distinguished as two separated bands. The minor diastereomer (S_C, S_P)-**187** which eluted first, was isolated as a pale yellow powder in 11.9 % yield, $[\alpha]_D +120^\circ$, (c 0.5, dichloromethane). The other diastereomer, (S_C, R_P)-**187**, was isolated as a yellow powder in 69.5 % yield with $[\alpha]_D +60^\circ$ (c 0.5, dichloromethane) (Scheme 2.7). The known optically active phosphanorbornene (S_P)-**188**, δ 105.1 (^{31}P NMR), could be liberated efficiently by treatment of the major product (S_C, R_P)-**187** with 1,2-bis(diphenylphosphino)ethane (dppe) at room temperature^[160,165,168]. The apparent inversion of configuration that takes place at the phosphorus center when the functionalized phosphine is liberated from the reaction promoter is merely a consequence of the Cahn–Ingold–Prelog (CIP) sequence rules.^[178]

Scheme 2.7

Due to factors such as the potential air sensitivity of the noncoordinated phosphorus atoms, liberated phosphine ligand (*S_P*)-**188** was recomplexed to the optically active palladacycles, (*S*)-**11** and (*R*)-**11**, respectively. This recoordination process is also a means of verifying the optical purity of the liberated ligand. The reparation of the liberated ligand (*S_P*)-**188** to (*S*)-**11** and (*R*)-**11** was monitored by 121 MHz ³¹P NMR spectroscopy (CDCl₃), which exhibited singlet peaks at δ 123.7 and 121.7 respectively. The resonance signals at δ 123.7 and 121.7 are identical to the *endo*-cycloaddition reaction products, (*R_C*,*S_P*)-**173** and (*R_C*,*R_P*)-**173**, in the original *endo*-cycloaddition reaction promoted by (*R*)-**11** (Scheme 2.8).^[160,165,168] As expected, optically pure (*R_P*)-**188** was liberated from (*S_C*,*S_P*)-**187** in a similar manner.

Scheme 2.8

2.3.6 Conclusion

In this chapter, the synthesis of the novel palladacycle (*S*)-**178** was readily accomplished from 2,7-dimethylnaphthalene and was then resolved by the separation of the (*S*)-prolinate diastereomeric derivatives. When the naphthylamine auxiliary (*S*)-**11** was used as chiral template for the asymmetric *endo*-cycloaddition reaction between dmpp and *N,N*-dimethylacrylamide at room temperature, the cycloadducts were obtained in a ratio of 1:2. However, in this study, this ratio was improved to 1:5.9 in the presence of complex (*S*)-**178**. Clearly, the 1-(3,6-dimethylnaphthalen-1-yl)-*N,N*-dimethylethanamine palladium complex (*S*)-**178** exhibits a better stereoselectivity for this class of intermolecular cycloaddition reactions. Therefore, the introduction of a methyl group on the aromatic ring next to Pd–C bond indeed exerts a considerable influence on the selectivity in this asymmetric *endo*-cycloaddition reaction.

2.4 Experimental

Reactions involving air-sensitive compounds were performed under a positive pressure of purified nitrogen using standard Schlenk techniques. Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectroscopy were performed on Bruker Avance 300, 400 and 500 NMR spectrometers. The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a J value in Hz. Proton nuclear magnetic resonance spectra ^1H NMR are reported as δ in units of parts per million (ppm) downfield from SiMe_4 (δ 0.0). Carbon nuclear magnetic resonance spectra ^{13}C NMR are reported as δ in units of parts per million (ppm) relative to the signal of chloroform- d (δ 77.00, triplet). All the ^{31}P NMR spectra were recorded at 121 MHz on a Bruker Avance DPX300 NMR spectrometer. Unless stated otherwise, all NMR spectroscopic experiments were performed at room temperature (300 K). Chemical shifts (δ) are reported in ppm relative to TMS, and referenced to the chemical shifts of residual solvent resonances (^1H and ^{13}C NMR) or 85% H_3PO_4 (^{31}P NMR). Mass spectra were recorded on a Thermo Finnigan MAT 95 XP Mass Spectrometer with EI mode and Waters Q-ToF Premier Mass Spectrometer with ESI mode. Melting points were determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured on the specified solution in 0.1-dm cell at 20 °C with a Perkin-Elmer model 341 polarimeter. Elemental analyses were performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at the Nanyang Technological University of Singapore.

2.4.1 Synthesis of 1-(3,6-dimethylnaphthalen-1-yl)ethanone, **180**

A solution of 2,7-dimethylnaphthalene **179**, (7.30 g, 46.73 mmol) in nitromethane (100 mL) was added under stirring to a mixture of anhydrous AlCl_3 (7.33 g, 54.97 mmol) and

acetyl chloride (3.34 mL, 46.80 mmol) in nitromethane (20 mL). The resulting red solution was stirred at room temperature for 20 h and poured into a mixture of ice (50 g) and conc. hydrochloric acid (20 mL). After vigorous stirring for 30 min, the yellowish organic layer was separated, washed with H₂O and dried (MgSO₄). Removal the solvent gave a brown colored oil and the residue was thus passed through a silica gel column (diethyl ether/hexane = 1/40, V/V), compound **180** was separated as the minor product, colorless solid, 1.60 g (17.3 %), M.p. 78–80°C. (Compound 1-(3,6-dimethylnaphthalen-2-yl)ethanone was separated as the major product in 45.0% yield). Anal Calcd for C₁₄H₁₄O (198.26): C, 84.81; H, 7.12. Found: C, 84.98; H, 7.09. ¹H NMR (300 MHz, CDCl₃): δ = 2.49 (s, 3 H, CH₃), 2.53 (s, 3 H, CH₃), 2.72 (s, 3 H, COCH₃), 7.36 (dd, ³J_{H,H} = 8.8 Hz, ⁴J_{H,H} = 1.7 Hz, 1 H, aromatic proton), 7.53 (s, 1 H, aromatic proton), 7.65 (s, 1 H, aromatic proton), 7.69 (s, 1 H, aromatic proton), 8.60 (d, ³J_{H,H} = 8.8 Hz, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 21.52, 29.92, 125.64, 126.69, 126.76, 129.41, 130.16, 131.43, 133.85, 134.61, 135.18, 136.12, 201.94 ppm. HRMS (ESI, m/z (M + H))⁺ calcd for C₁₄H₁₅O 199.1123, found 199.1118.

2.4.2 Synthesis of 1-(3,6-dimethylnaphthalen-1-yl)ethanol, (±)-**181**

To 1.60 g (8.07 mmol) of compound **180** in ethanol (30 mL) was added a solution of NaBH₄ (0.60 g, 15.86 mmol) in the same solvent (20 mL). The mixture were stirred at room temperature for 24 h followed by treatment with dilute NaOH solution. The ethanol in the resulting solution was removed under vacuum and the aqueous phase was then extracted with dichloromethane. The organic layers were combined, washed with H₂O and dried with MgSO₄. Removal of the solvent gave the product (±)-**181** as a white solid, 1.50 g, 92.8%. Anal Calcd for C₁₄H₁₆O (200.28): C, 83.96; H, 8.05. Found: C, 83.71; H, 8.08. ¹H NMR (300 MHz, CDCl₃): δ = 1.65 (d, ³J_{H,H} = 6.4 Hz, 3 H, CHCH₃), 2.33 (s, 1

H, OH), 2.55 (s, 6 H, aryl-CH₃), 5.58 (q, $^3J_{\text{H,H}} = 6.4$ Hz, 1 H, CHCH₃), 7.30 (d, $^3J_{\text{H,H}} = 8.7$ Hz, $^4J_{\text{H,H}} = 1.6$ Hz, aromatic proton), 7.45 (s, 1 H, aromatic proton), 7.46 (s, 1 H, aromatic proton), 7.56 (s, 1 H, aromatic proton), 7.93 (d, $^3J_{\text{H,H}} = 8.7$ Hz, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 21.55, 21.83, 24.41, 67.07, 122.83, 123.38, 126.20, 126.73, 127.26, 127.38, 134.48, 135.12, 135.16, 141.10$ ppm. HRMS (ESI, m/z (M – OH)]⁺ calcd for C₁₄H₁₅ 183.1174, found 183.1166.

2.4.3 Synthesis of 1-(1-chloroethyl)-3,6-dimethylnaphthalene, (±)-**182**

A dichloromethane solution of compound (±)-**181** (1.50 g, 7.49 mmol) was dropped slowly into a solution of PCl₃ (4.50 g, 32.76 mmol) in the same solvent (30 mL). The mixture were stirred overnight at room temperature and quenched by addition of ice water at 0 °C. The organic layer was separated and washed with water and dried with MgSO₄. Removal of the solvent gave the product (±)-**182** as a colorless oil, 1.47 g (89.7%). ¹H NMR (300 MHz, CDCl₃): $\delta = 2.06$ (d, $^3J_{\text{H,H}} = 6.5$ Hz, 3 H, CHCH₃), 2.53 (s, 6 H, aryl-CH₃), 5.87 (q, $^3J_{\text{H,H}} = 6.5$ Hz, 1 H, CHCH₃), 7.36 (d, $^3J_{\text{H,H}} = 8.4$ Hz, 1 H, aromatic proton), 7.49 (s, 1 H, aromatic proton), 7.52 (s, 1 H, aromatic proton), 7.57 (s, 1 H, aromatic proton), 8.03 (d, $^3J_{\text{H,H}} = 8.4$ Hz, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 21.50, 21.75, 25.18, 54.80, 122.73, 125.01, 126.89, 127.33, 127.49, 127.83, 134.52, 134.87, 135.51, 137.29$ ppm. HRMS (EI, m/z (M – Cl)]⁺ calcd for C₁₄H₁₅ 183.1174, found 183.1175.

2.4.4 Synthesis of 1-(3,6-dimethylnaphthalen-1-yl)-N,N-dimethylethanamine, (±)-**183**

A 20 mL dichloromethane solution of compound (±)-**182** (1.47 g, 6.72 mmol) was added to a 10 mL dimethylamine (2M) and stirred vigorously for 48 h. The solvents were

removed under vacuum and the residue was then dissolved in dichloromethane which was washed with H₂O, dried with MgSO₄ and evaporated to dryness. The pure amine was obtained as a light yellow oil after passing through a silica gel column using ethyl acetate as the mobile phase, 1.36 g (89.1%). ¹H NMR (300 MHz, CDCl₃): δ = 1.50 (d, ³J_{H,H} = 6.6 Hz, 3 H, CHCH₃), 2.32 (s, 6 H, CH₃), 2.53 (s, 6 H, CH₃), 3.96 (q, ³J_{H,H} = 6.6 Hz, 1 H, CHCH₃), 7.30 (dd, ³J_{H,H} = 8.3 Hz, ⁴J_{H,H} = 1.6 Hz, 1 H, aromatic proton), 7.42 (s, 1 H, aromatic proton), 7.46 (s, 1 H, aromatic proton), 7.57 (s, 1 H, aromatic proton), 8.25 (d, ³J_{H,H} = 8.7 Hz, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 19.85, 21.53, 21.80, 43.85, 62.39, 123.45, 125.66, 125.71, 126.99, 127.19, 128.01, 134.65, 134.86, 135.09, 140.69 ppm. HRMS (ESI, m/z (M + H))⁺ calcd for C₁₆H₂₂N 228.1752, found 228.1746.

2.4.5 Synthesis of (±)-Di- μ -chlorobis[1-[1-(dimethylamino)ethyl]-3,6-dimethyl-2-naphthalenyl-C,N] dipalladium(II), (±)-178.

A mixture of *trans*-dichlorobis(acetonitrile)palladium(II) (1.56 g, 6.00 mmol) and silver perchlorate (2.48 g, 12.00 mmol) in acetonitrile (30 mL) was stirred in darkness at room temperature for 1 h. The precipitate (AgCl) was filtered off and the filtrate was added dropwise to a stirred mixture of 1-(3,6-dimethylnaphthalen-1-yl)-*N,N*-dimethylethanamine, (±)-**183** (1.36 g, 6.00 mmol) and triethylamine (0.60 g, 6.00 mmol) in dichloromethane (20 mL). The resulting mixture was stirred at room temperature for 24 h and filtered through Celite. The filtrate was evaporated and the residue was dissolved in dichloromethane (100 mL). Dilute hydrochloric acid (1 M, 50 mL) was then added to the solution and the mixture was vigorously stirred for 1 h. The organic layer was separated, washed with H₂O, and dried with MgSO₄. After removing the solvent, the residue was passed through a silica gel column using dichloromethane as mobile phase

yielding the yellow complex ($\pm$)-**178**, 1.78 g, (80.5%). M.p. 196–198°C (dec.), Anal Calcd for $C_{32}H_{40}Cl_2N_2Pd_2$ (736.42): C, 52.19; H, 5.47; N, 3.80. Found: C, 52.52; H, 5.34; N, 3.59. 1H NMR (300 MHz, $CDCl_3$): δ = 2.26–2.28 (m, 6 H, CH_3), 2.44 (b, 6 H, CH_3), 2.62–2.72 (m, 18 H, CH_3), 4.12–4.13 (m, 2 H, $CHCH_3$), 7.11–7.14 (m, 4 H, aromatic protons), 7.43 (m, 4 H, aromatic protons) ppm.

2.4.6 Synthesis of ($\pm$)-Chloro[1-[1-(dimethylamino)ethyl]-3,6-dimethyl-2-naphthalenyl-*C,N*](triphenylphosphine-*P*)palladium(II), ($\pm$)-**184**

A dichloromethane solution of complex ($\pm$)-**178** (0.18 g, 0.25 mmol) and triphenylphosphine (0.13 g, 0.50 mmol) was stirred for 30 min at room temperature and concentrated to ca 5 mL. The residue liquid was chromatographed on a silica gel column using dichloromethane as the eluent to give a light yellow powder which was recrystallized from dichloromethane/hexane as light yellow crystals ($\pm$)-**184**, 0.28 g (88.8%), M.p. 192–194 °C (dec.), Anal Calcd for $C_{34}H_{35}ClNPPd$ (630.50): C, 64.77; H, 5.60; N, 2.22. Found: C, 64.40; H, 5.42; N, 2.22. ^{31}P NMR (121 MHz, $CDCl_3$): δ = 30.1(s) ppm. 1H NMR (400 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, aryl- CH_3), 2.18 (d, $^3J_{H,H}$ = 6.4 Hz, 3 H, $CHCH_3$), 2.46 (s, 3 H, aryl- CH_3), 2.51 (s, 3 H, $NCH_{3(ax)}$), 2.92 (d, $^4J_{P,H}$ = 3.0 Hz, 3 H, $NCH_{3(eq)}$), 3.76 (qn, $^4J_{P,H}$ = $^3J_{H,H}$ = 6.4 Hz, 1 H, $CHCH_3$), 6.86 (s, 1 H, aromatic proton), 7.19–7.60 (m, 18 H, aromatic protons) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.39, 22.21, 26.82 (d, $J_{C,P}$ = 9.2 Hz), 49.03, 50.60 (d, $J_{C,P}$ = 2.7 Hz), 74.21 (d, $J_{C,P}$ = 3.0 Hz), 122.58, 124.95, 125.15, 126.79 (d, $J_{C,P}$ = 14.4 Hz), 126.83 (d, $J_{C,P}$ = 10.3 Hz), 130.14, 132.15, 133.19, 134.71 (b), 134.79 (b), 139.92 (d, $J_{C,P}$ = 2.3 Hz), 146.32, 156.63 ppm. HRMS (ESI, m/z ($M - Cl$)) $^+$ calcd for $C_{34}H_{35}NPPd$ 594.1542, found 594.1559.

2.4.7 Synthesis of (*R_C,S_C,S_N*)-Prolinato-[1-[1-(dimethylamino)ethyl]-3,6-dimethyl-2-naphthalenyl-*C,N*]palladium(II), (*R_C,S_C,S_N*)-185 and (*S_C,S_C,S_N*)-Prolinato-[1-[1-(dimethylamino)ethyl]-3,6-dimethyl-2-naphthalenyl-*C,N*]palladium(II), (*S_C,S_C,S_N*)-185.

To 1.47 g (2.00 mmol) of racemic dimer ($\pm$)-**178** was added a solution of (*S*)-sodium proline (0.55 g, 4.00 mmol) in methanol (30 mL). The mixture was stirred at room temperature for 1 h and the solvent was removed under reduced pressure. The solution of the residue in dichloromethane was washed with H₂O, and dried with MgSO₄. After removing the solvent, the 1:1 diastereomeric mixture was slowly eluted through a silica gel column (dichloromethane/acetone = 2:1, V/V as mobile phase) and the first eluted diastereomer (*R_C,S_C,S_N*)-**185** was crystallized slowly from dichloromethane and hexane as light yellowish crystals (0.81 g, 90.6%, based on half of the dimer used), > 99% *de* (according to the ¹H NMR spectrum), M.p. 190–192°C (dec.), [α]₄₃₆ +38, [α]₃₆₅ +160 (*c* 0.5, methanol). Anal Calcd for: C₂₁H₂₈N₂O₂Pd-dichloromethane (531.81): C, 49.69; H, 5.69; N, 5.27. Found: C, 49.85; H, 5.32; N, 5.39. ¹H NMR (500 MHz, CDCl₃): δ = 1.64–1.65 (m, 1 H, CH₂CH₂CH₂), 1.68–1.73 (m, 2 H, CH₂CH₂CH₂, COCHCH₂), 1.98 (d, ³J_{H,H} = 6.3 Hz, 3 H, CHCH₃), 2.30–2.32 (m, 1 H, COCHCH₂), 2.40 (s, 3 H, aryl-CH₃), 2.44 (s, 3 H, aryl-CH₃), 2.61 (s, 3 H, NCH_{3(ax)}), 2.64 (s, 3 H, NCH_{3(eq)}), 3.15–3.22 (m, 1 H, NHCH₂), 3.42–3.44 (m, 1 H, NHCH₂), 4.00–4.03 (m, 1 H, NH), 4.07–4.10 (m, 2 H, COCH, CHCH₃), 7.13–7.16 (m, 2 H, aromatic protons), 7.38 (s, 1 H, aromatic proton), 7.43 (d, ³J_{H,H} = 8.5 Hz, 1 H, aromatic proton) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 21.32, 22.93, 23.12, 25.26, 28.76, 29.13, 48.27, 51.05, 66.78, 72.86, 122.61, 124.47, 125.03, 126.77, 127.22, 131.95, 133.48, 139.75, 143.67, 148.36, 178.42 ppm. HRMS (ESI) (*m/z*): [*M* + H]⁺ calcd for C₂₁H₂₉N₂O₂Pd 447.1264, found 447.1274.

The second eluted diastereomer (*S_C,S_C,S_N*)-**185** was also crystallized slowly from

dichloromethane and hexane as yellowish crystals (0.79 g, 88.4%, based on half of the dimer used), > 99% *de* (according to the ^1H NMR spectrum), M.p. 190–192 °C (dec.), $[\alpha]_D^{25} +194$, $[\alpha]_{578}^{25} +206$, $[\alpha]_{546}^{25} +234$, $[\alpha]_{436}^{25} +446$, $[\alpha]_{365}^{25} +916$ (*c* 0.5, methanol). Anal Calcd for $\text{C}_{21}\text{H}_{28}\text{N}_2\text{O}_2\text{Pd}\cdot\text{H}_2\text{O}$ (464.89): C, 54.25; H, 6.50; N, 6.03. Found: C, 54.47; H, 7.04; N, 5.88. ^1H NMR (500 MHz, CDCl_3): δ = 1.61–1.73 (m, 1 H, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.01–2.04 (m, 1 H, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.07 (d, $^3J_{\text{H,H}} = 6.4$ Hz, 3 H, CHCH_3), 2.22–2.34 (m, 2 H, COCHCH_2), 2.44 (s, 3 H, aryl- CH_3), 2.58 (s, 3 H, aryl- CH_3), 2.64 (s, 3 H, $\text{NCH}_{3(\text{ax})}$), 2.78 (s, 3 H, $\text{NCH}_{3(\text{eq})}$), 3.10–3.24 (m, 2 H, NHCH_2), 4.09–4.10 (m, 1 H, COCH), 4.11 (q, $^3J_{\text{H,H}} = 6.5$ Hz, 1 H, CHCH_3), 4.38–4.42 (m, 1 H, NH), 7.16 (dd, $^3J_{\text{H,H}} = 8.7$ Hz, $^4J_{\text{H,H}} = 1.1$ Hz, 1 H, aromatic proton), 7.19 (s, 1 H, aromatic proton), 7.45 (s, 1 H, aromatic proton), 7.46 (d, $^3J_{\text{H,H}} = 8.3$ Hz, 1 H, aromatic proton) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 21.26, 23.20, 24.29, 25.29, 30.22, 48.01, 53.00, 53.29, 65.23, 73.01, 123.36, 124.88, 124.90, 126.72, 127.16, 131.70, 133.33, 139.40, 145.96, 147.69, 181.07 ppm. HRMS (ESI) (*m/z*): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{29}\text{N}_2\text{O}_2\text{Pd}$ 447.1264, found 447.1274.

2.4.8 Synthesis of (S)-Di- μ -chlorobis[1-[1-(dimethylamino)ethyl]-3,6-dimethyl-2-naphthalenyl-C,N]dipalladium(II), (S)-178

Dilute hydrochloric acid (20 mL, 1 M) was added to a dichloromethane solution (10 mL) of the diastereomer ($S_{\text{C}}, S_{\text{C}}, S_{\text{N}}$)-**185** (0.80 g, 1.79 mmol) and the resulting solution was vigorously stirred for 30 min at room temperature. The organic layer was separated and washed with H_2O , dried with MgSO_4 and the solvent was evaporated to dryness to afford complex (S)-**178** as a yellow power and crystallized by using dichloromethane and diethyl ether to yield yellow crystals, 0.63 g, 95.6%. M.p. 172–174 °C (dec.), $[\alpha]_D^{25} +120$, $[\alpha]_{578}^{25} +122$, $[\alpha]_{546}^{25} +120$, (*c* 0.5, dichloromethane). Anal Calcd for $\text{C}_{32}\text{H}_{40}\text{Cl}_2\text{N}_2\text{Pd}_2$ (736.42): C, 52.19; H, 5.47; N, 3.80. Found: C, 52.52; H, 5.34; N, 3.59. ^1H NMR (400

MHz, CD₂Cl₂): δ = 2.25–2.28 (m, 6 H), 2.46 (s, 6 H), 2.61–2.73 (m, 18 H), 4.12–4.18 (m, 2 H, CHCH₃), 7.11–7.13 (m, 2 H, aromatic protons), 7.17–7.19 (m, 2 H, aromatic protons), 7.47 (m, 4 H, aromatic protons) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 21.40, 23.30, 25.36, 25.60, 49.54, 50.25, 53.36, 53.84, 54.01, 74.58, 74.69, 122.61, 124.68, 124.91, 124.99, 126.79, 126.94, 132.14, 133.52, 141.09, 143.07, 143.19, 146.52 ppm.

The optically pure complex (*R*)-**178** was prepared from isomer (*R*_C,*S*_C,*S*_N)-**185** in a similar manner: [α]_D = –118, [α]₅₇₈ = –113, [α]₅₄₆ = –118, (*c* 0.4, dichloromethane).

2.4.9 Synthesis of (*S*)-Chloro[1-[1-(dimethylamino)ethyl]-3,6-dimethyl-2-naphthalenyl -*C,N*]{3',4'-dimethyl-1'-phenylphosphole-P}-palladium(II), (*S*)-**186**.

To a solution of complex (*S*)-**178** (0.37 g, 0.50 mmol) in dichloromethane (20 mL) was added a solution of 3,4-dimethyl-1-phenylphosphole (dmpp) (0.20 g, 1.06 mmol) in the same solvent (10 mL). The resulting light yellow solution was stirred at room temperature for 1 h and the solvent was removed under reduced pressure. The residue solid was chromatographed on a silica gel column (dichloromethane/ethyl acetate = 1:1 as the eluent) to give a pale yellow powder, which was recrystallized from chloroform/hexane as yellow prisms, 0.50 g, 89.7%, [α]_D +456, [α]₅₇₈ +484, [α]₅₄₆ +572, [α]₄₃₆ +1348, (*c* 0.5, dichloromethane), M.p. 188–190 °C (dec), Anal Calcd for C₂₈H₃₃CINPPd (556.37): C, 60.44; H, 5.98; N, 2.52. Found: C, 60.08; H, 6.40; N, 2.52. ³¹P NMR (121 MHz, CDCl₃): δ = 28.4 (s) ppm. ¹H NMR (500 MHz, CDCl₃): δ = 1.94 (d, ⁴*J*_{P,H} = 1.6 Hz, 3 H, C=CCH₃), 1.95 (d, ³*J*_{H,H} = 6.8 Hz, 3 H, CHCH₃), 2.02 (s, 3 H, C=CCH₃), 2.37 (s, 3 H, aryl-CH₃), 2.47 (s, 3 H, aryl-CH₃), 2.54 (d, ⁴*J*_{P,H} = 2.0 Hz, 3 H, NCH₃(ax)), 2.87 (d, ⁴*J*_{P,H} = 3.4 Hz, 3 H, NCH₃(eq)), 3.72 (qn, ³*J*_{H,H} = ⁴*J*_{P,H} = 6.5 Hz, 1 H, CH₃CH), 6.17 (d, ²*J*_{P,H} = 33.2 Hz, 1 H, C=CH), 6.81 (d, ²*J*_{P,H} = 32.1 Hz, 1 H, C=CH), 7.18 (dd, ³*J*_{H,H} = 8.6 Hz, ⁴*J*_{H,H} = 1.6 Hz, 1 H, aromatic proton), 7.24 (s, 1 H, aromatic

proton), 7.35–7.41 (m, 3 H, *p*-Ph, 2× *m*-Ph), 7.47 (s, 1 H, aromatic proton), 7.52 (d, $^3J_{\text{H,H}} = 8.6$ Hz, 1 H, aromatic proton), 7.88–7.92 (m, 2 H, 2× *o*-Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 17.13$ (d, $J_{\text{C,P}} = 12.7$ Hz), 17.71 (d, $J_{\text{C,P}} = 12.2$ Hz), 21.31, 22.69, 27.79 (d, $J_{\text{C,P}} = 9.7$ Hz), 48.39, 50.61 (d, $J_{\text{C,P}} = 2.7$ Hz), 73.37 (d, $J_{\text{C,P}} = 3.3$ Hz), 122.56, 124.04, 125.64 (d, $J_{\text{C,P}} = 49.2$ Hz), 125.74, 126.77 (d, $J_{\text{C,P}} = 21.4$ Hz), 127.59 (d, $J_{\text{C,P}} = 43.9$ Hz), 128.37 (d, $J_{\text{C,P}} = 10.8$ Hz), 129.30 (d, $J_{\text{C,P}} = 52$ Hz), 130.41 (d, $J_{\text{C,P}} = 2.5$ Hz), 131.89, 133.10, 133.22, 133.38, 141.00 (d, $J_{\text{C,P}} = 6.1$ Hz), 147.31 (d, $J_{\text{C,P}} = 1.3$ Hz), 148.05 (d, $J_{\text{C,P}} = 10.1$ Hz), 151.13, 153.57 (d, $J_{\text{C,P}} = 10.3$ Hz) ppm. HRMS (ESI) (m/z): $[\text{M} - \text{Cl}]^+$ calcd for $\text{C}_{28}\text{H}_{33}\text{NPPd}$ 520.1385, found 520.1398.

2.3.10 Asymmetric *endo*-Cycloaddition Reaction between complex (*S*)-**186** and *N,N*-Dimethylacrylamide. Synthesis and Isolation of complex ($S_{\text{C}},R_{\text{P}}$)-**187** and complex ($S_{\text{C}},S_{\text{P}}$)-**187**.

A solution of the chloro complex (*S*)-**186** (0.50 g, 0.9 mmol) in dichloromethane (10 mL) was stirred with *N,N*-dimethylacrylamide (0.30 g, 3.03 mmol) at room temperature for 20 day. Removal of solvent left a brownish oil. The ^{31}P NMR (CDCl_3) spectrum two singlets at δ 114.3 and 115.3 ppm of the crude product prior to purification indicated a 1:5.9 mixture of the diastereomeric cycloadducts. Both the diastereomeric products, ($S_{\text{C}},S_{\text{P}}$)-**187** and ($S_{\text{C}},R_{\text{P}}$)-**187**, were isolated on a silica gel column (ethyl acetate/dichloromethane = 1:10, V/V). The first eluted complex, the minor diastereomer ($S_{\text{C}},S_{\text{P}}$)-**187**, exhibited one ^{31}P NMR signal at δ 114.3 ppm, 0.07 g (11.9%), M.p. 181–183 °C (dec.), $[\alpha]_{\text{D}} +120$, $[\alpha]_{578} +124$, $[\alpha]_{546} +142$, $[\alpha]_{436} +164$, (*c* 0.5, dichloromethane). Anal Calcd for $\text{C}_{33}\text{H}_{42}\text{ClN}_2\text{OPPd}-\text{C}_4\text{H}_{10}\text{O}$ (729.67): C, 60.90; H, 7.18; N, 3.84. Found: C, 60.78; H, 7.52; N, 4.08. ^{31}P NMR (121 MHz, CDCl_3): $\delta = 114.3$ (s) ppm. ^1H NMR (400 MHz, CDCl_3): $\delta = 1.24$ (s, 3 H, $\text{C}=\text{CCH}_3$), 1.79 (s, 3 H, $\text{C}=\text{CCH}_3$), 1.94–2.05 (m, 2 H,

CH₂), 2.15 (d, $^3J_{\text{H,H}} = 6.4$ Hz, 3 H, CHCH₃), 2.28 (s, 3 H, aryl-CH₃), 2.46 (s, 3 H, aryl-CH₃), 2.50 (s, 3 H, NCH_{3(ax)}), 2.74 (br, 1 H, CH₂CHP), 2.86 (d, $^4J_{\text{P,H}} = 2.4$ Hz, 3 H, NCH_{3(eq)}), 2.89 (s, 3 H, NCH_{3(amide)}), 3.34 (s, 3 H, NCH_{3(amide)}), 3.67 (br, 1 H, CHCHP), 4.24 (qn, $^3J_{\text{H,H}} = ^4J_{\text{P,H}} = 6.2$ Hz, 1 H, CHCH₃), 4.58 (m, 1 H, COCH), 7.19 (d, $^3J_{\text{H,H}} = 8.5$ Hz, 1 H, aromatic proton), 7.24 (s, 1 H, aromatic proton), 7.39–7.41 (m, 3 H, *p*-Ph, 2 × *m*-Ph), 7.46 (s, 1 H, aromatic proton), 7.53 (d, $^3J_{\text{H,H}} = 8.6$ Hz, 1 H, aromatic proton), 7.98–8.02 (m, 2 H, 2 × *o*-Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.3 (d, $J_{\text{C,P}} = 3.4$ Hz), 14.9 (d, $J_{\text{C,P}} = 4.0$ Hz), 21.4, 22.4, 28.3, 35.9, 37.6, 41.0 (d, $J_{\text{C,P}} = 30.5$ Hz), 48.2 (d, $J_{\text{C,P}} = 38.3$ Hz), 48.6, 51.2 (d, $J_{\text{C,P}} = 3.3$ Hz), 54.8 (d, $J_{\text{C,P}} = 60.1$ Hz), 73.0 (d, $J_{\text{C,P}} = 3.9$ Hz), 122.8, 124.6, 125.7, 127.0 (d, $J_{\text{C,P}} = 35.4$ Hz), 127.9 (d, $J_{\text{C,P}} = 12.5$ Hz), 129.9 (d, $J_{\text{C,P}} = 2.8$ Hz), 130.2, 130.6, 131.0, 132.1, 133.7 (d, $J_{\text{C,P}} = 3.3$ Hz), 133.9, 134.5, 140.2 (d, $J_{\text{C,P}} = 8.1$ Hz), 147.2 (d, $J_{\text{C,P}} = 1.9$ Hz), 152.5, 171.8 (d, $J_{\text{C,P}} = 21.1$ Hz) ppm. HRMS (ESI) (*m/z*): [M – Cl]⁺ calcd for C₃₃H₄₂N₂OPPd 619.2070, found 619.2056. The second eluted complex, the major diastereomer (*S_C*,*R_P*)-**187**, 0.41 g (69.5%), M.p. 180–182 °C (dec.), [α]_D +60, [α]₅₇₈ +64, [α]₅₄₆ +66, (*c* 0.5, dichloromethane). Anal Calcd for C₃₃H₄₂ClN₂OPPd·C₄H₁₀O (729.67): C, 60.90; H, 7.18; N, 3.84. Found: C, 60.78; H, 7.52; N, 4.08. ³¹P NMR (121 MHz, CDCl₃): δ = 115.3 (s) ppm. ¹H NMR (500 MHz, CDCl₃): δ = 1.38 (s, 3 H, C=CCH₃), 1.56 (s, 3 H, C=CCH₃), 1.63 (s, 3 H, NCH_{3(amide)}), 2.10 (d, $^3J_{\text{H,H}} = 6.5$ Hz, 3 H, CHCH₃), 2.11–2.18 (m, 1 H, CH₂), 2.21 (m, 1 H, PCH), 2.34 (s, 3 H, aryl-CH₃), 2.40 (s, 3 H, aryl-CH₃), 2.43 (s, 3 H, NCH_{3(ax)}), 2.57 (s, 3 H, NCH_{3(amide)}), 2.80 (s, 3 H, NCH_{3(eq)}), 2.90–2.93 (m, 1 H, CH₂), 3.42 (br, 1 H, PCH), 3.53 (br, 1 H, COCH), 4.19 (qn, $^3J_{\text{H,H}} = ^4J_{\text{P,H}} = 6.1$ Hz, 1 H, CHCH₃), 7.14 (d, $^3J_{\text{H,H}} = 8.5$ Hz, 1 H, aromatic proton), 7.21 (s, 1 H, aromatic proton), 7.31–7.35 (m, 4 H, aromatic protons), 7.47 (d, $^3J_{\text{H,H}} = 8.6$ Hz, 1 H, aromatic proton), 7.94–7.98 (m, 2 H, 2 × *o*-Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 13.9 (d, $J_{\text{C,P}} = 3.0$ Hz), 15.7 (d, $J_{\text{C,P}} = 1.9$ Hz), 21.5, 22.3,

28.1 (d, $J_{C,P} = 9.4$ Hz), 29.3 (d, $J_{C,P} = 14.4$ Hz), 35.5 (d, $J_{C,P} = 22.7$ Hz), 39.9 (d, $J_{C,P} = 27.4$ Hz), 48.5, 50.9 (d, $J_{C,P} = 30.1$ Hz), 51.2 (d, $J_{C,P} = 1.9$ Hz), 52.1 (d, $J_{C,P} = 33.8$ Hz), 73.2 (d, $J_{C,P} = 2.6$ Hz), 122.6, 124.8, 125.8, 126.6, 127.5, 128.0 (d, $J_{C,P} = 9.0$ Hz), 129.3, 129.9 (d, $J_{C,P} = 1.4$ Hz), 130.7 (d, $J_{C,P} = 30.9$ Hz), 132.1, 133.6 (d, $J_{C,P} = 8.8$ Hz), 133.8, 134.5, 140.3 (d, $J_{C,P} = 6.1$ Hz), 147.6, 152.9, 171.7 (d, $J_{C,P} = 16.5$ Hz) ppm. HRMS (ESI) (m/z): $[M - Cl]^+$ calcd for $C_{33}H_{42}N_2OPPd$ 619.2070, found 619.2056.

2.3.11 Formation of Compound (*S_P*)-**188** and (*R_P*)-**188**.

A solution of complex (*S_C*,*R_P*)-**187** (0.065 g, 0.1 mmol) in dichloromethane (2 mL) was treated with a solution of 1,2-bis(diphenylphosphino)ethane (0.04 g, 0.1 mmol) in the same solvent (2 mL) for 3 h. The resulting yellowish mixture was passed through a column which was packed successively with silica gel (1 g) and florisil (10 g), with dichloromethane as the eluent to yield a colorless solution. Removal of solvent under reduced pressure gave (*S_P*)-**188** as an air-sensitive colorless oil, Yield 0.02 g (70%); $[\alpha]_D^{+5.9}$, (c 0.5, dichloromethane), ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 105.1$ (s) ppm. Compound (*R_P*)-**188** was liberated using the same method from complex (*S_C*,*S_P*)-**187**, $[\alpha]_D^{-1.0}$, (c 0.5, dichloromethane), ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 105.1$ (s) ppm. It is noteworthy that the phosphine ligands are air-sensitive and configurationally unstable. Therefore after the liberation, the liberated ligands must be re-complexed to selected metal ions within ca. 30 min. The configurational instabilities of (*S_P*)-**188** and (*R_P*)-**188** precluded the ligands from further purification and elemental characterization.^[166]

CHAPTER 3

CHIRAL *ORTHO*-PALLADATED 1-(3,6-DIMETHYL NAPHTHALEN-2-YL)-*N,N*-DIMETHYLETHANAMINE

3.1 Introduction

As discussed in chapter one, optically active organopalladium complex (*S*)-**11** and its derivatives have been used in the asymmetric syntheses of a series of functionalized mono- and diphosphines.^[156-172] The *endo*-cycloaddition reactions of the phosphole (dmpp) complex with a series of dienophiles promoted by palladacycle **11** have been extensively carried out. The *endo*-cycloadditions exclusively produce two stereoisomers, which can be postulated from two possible orientations of the dienophiles in the transition states. For example, when dmpp derivative (*S*)-**171** was treated with ethyl vinyl ketone at 70 °C, two *endo*-cycloaddition products were obtained as a 1:1 diastereomeric mixture of complexes (*S_C*,*S_P*)-**172** and (*S_C*,*R_P*)-**172** (Scheme 1.52).^[160] This experiment shows that the chiral naphthylethylamine auxiliary (*S*)-**11** exerts an insignificant influence on the reaction site. Evidently, in the transition state, the dmpp group experiences a certain degree of free rotation around the Pd–P bond thus rendering poor stereoselectivity.

Therefore in chapter two, a novel chiral palladacycle (*S*)-**178** was synthesized and applied in the *endo*-cycloaddition reaction and the stereoselectivity was significantly improved. Furthermore in our research group, another optically active palladacycle (*S*)-**16** was synthesized and promoted the same *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone. In this reaction two diastereomeric products were formed in a ratio of 3.5:1. These experiments demonstrate that the influence of the introduction of the methyl group next to the Pd–C bond on the stereoselectivity.^[7,9]

3.2 Research Objectives

In some synthesis, *endo*-cycloaddition reactions for example, the separation of the two *endo*-diastereomeric products were somewhat tedious and resulted in low yields of the target enantiomers due to the poor stereoselectivity. In order to improve the stereoselectivity and enrich the synthesis of different kinds of optically active palladacycles, we designed and synthesized a novel chiral complex (*S*)-**189**. We expect that complex (*S*)-**189** will retain all the desired stereoelectronic properties of the original naphthylamine template. It is essential for the five-membered organopalladium ring to be locked in a fixed conformation and here the interaction between Me2 and Me9 will lock the five-membered organopalladium ring in a fixed conformation. Furthermore, the aromatic hydrogen atom H5 is introduced adjacent to the Pd–C bond to exert an additional stereochemical influence on the coordination position *trans* to the N donor atom. The application of this new chiral template in asymmetric *endo*-cycloaddition reaction was thus examined.

(*S*)-**189**

3.3 Results and Discussion

3.3.1 Synthesis of Racemic *ortho*-Palladated Complex ($\pm$)-**189**

As illustrated in Scheme 3.1, the *di*-substituted naphthalene derivative **179**^[160] was acetylated with acetyl chloride in the presence of aluminum chloride giving the ketone **190** in 45.0 % yield. Reduction of compound **190** in ethanol by sodium borohydride produced the racemic alcohol ($\pm$)-**191** in 95.0 % yield, which was then converted to the

chloride ($\pm$)-**192** in 92.0 % yield by treatment with excess PCl_3 in dry dichloromethane. Reaction between the chloride ($\pm$)-**192** and aqueous dimethylamine afforded the target *N,N*-dimethylamine ($\pm$)-**193** as a pale yellow powder in 88.0 % yield. The molecular ion of compound ($\pm$)-**193** can be observed at $[\text{ESI}, m/z (\text{M} + \text{H})]^+ 228.1746$ by high resolution mass spectrometry. The *ortho*-palladation of amine compound ($\pm$)-**193** could be achieved in acetonitrile, using $[\text{Pd}(\text{MeCN})_4](\text{ClO}_4)_2$ as the palladium source in the presence of one molar amount of triethylamine. Treatment of the reaction mixture with dilute hydrochloric acid for 1 h gave the palladacycle ($\pm$)-**189** as yellow powder, in 85.0 % isolated yield.^[7,9] Furthermore, the racemic dimeric complex ($\pm$)-**189** could be also formed by using $\text{Pd}(\text{OAc})_2$ as palladation reagent in a similar yield.

Scheme 3.1

3.3.2 Synthesis and Characterization of Complex ($\pm$)-194

3.3.2.1 Formation of Complex ($\pm$)-194

One of the major challenges in the structural design of the auxiliary lies in the introduction of a sterically congestive environment around the template site that is adjacent to the protruding H atom. In order to establish a coordination site that is able to accommodate a bulky monodentate ligand in a regiospecific manner, complex ($\pm$)-189 was treated with triphenylphosphine. Furthermore, as discussed in chapter two, this kind of mononuclear triphenylphosphine complex is more suitable for NMR spectroscopic studies of the organopalladium ring conformation. Therefore this bulky phosphine ligand (triphenylphosphine) splits the chloro bridges of complex ($\pm$)-189 efficiently and generated the mononuclear complex ($\pm$)-194 as the sole product in 93.0% yield (Scheme 3.2).^[7]

Scheme 3.2

3.3.2.2 Crystal Structure of Complex ($\pm$)-194

The X-ray molecular structure and selected bond lengths and angles are presented in Figure 3.2 and Table 3.1, respectively. Light yellow colored single crystals were formed from a solution containing complex ($\pm$)-194 in dichloromethane and hexane. The structure of complex ($\pm$)-194 was reaffirmed crystallographically. From the X-ray study, complex ($\pm$)-194 adopts a distorted square-planar coordination geometry. The strong steric repulsion between the triphenylphosphine ligand and the organometallic chelate

results in the bond angle $C(1)-Pd(1)-P(1)$ being enlarged to $101.7(1)^\circ$. With these structural features, the Pd–P bond would not be able to rotate freely, as all the possible rotational motions are blocked by the chloro ligand and the projecting aromatic proton H3. Therefore, among the three P–Ph phenyl rings, the C(17)–C(22) ring experiences the most intramolecular ligand-ligand repulsion. As a result, the bond angle $Pd(1)-P(1)-C(17)$ is enlarged to $117.9(1)^\circ$, which is larger than the two less affected $Pd(1)-P(1)-C(23)$ and $Pd(1)-P(1)-C(29)$ angles [$111.5(1)^\circ$ and $115.5(1)^\circ$]. Most importantly, the ligand-ligand repulsive interactions in complex ($\pm$)-**194** also disturb the planarity of the conjugated rings. Thus, the central ring (C1,C2,C7,C8,C9,C10) and the adjacent projecting ring (C2–C7) do not lie within the same plane, with the dihedral angle between these two being 5.1° .

Figure 3.1 Molecular structure of complex ($\pm$)-**194** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) are omitted for clarity.

Table 3.1 Selected bond lengths (Å) and angles (°) for complex (±)-**194**.

Pd(1)–C(1)	2.048(3)	Pd(1)–N(1)	2.128(3)
Pd(1)–P(1)	2.273(1)	Pd(1)–Cl(1)	2.381(1)
P(1)–C(23)	1.823(4)	P(1)–C(17)	1.827(4)
P(1)–C(29)	1.841(4)	P(1)–Pd(1)–Cl(1)	87.9(1)
C(1)–Pd(1)–N(1)	80.0(1)	C(1)–Pd(1)–P(1)	101.7 (1)
N(1)–Pd(1)–P(1)	174.5(1)	C(1)–Pd(1)–Cl(1)	169.4(1)
N(1)–Pd(1)–Cl(1)	91.0(1)	C(23)–P(1)–Pd(1)	111.5(1)
C(17)–P(1)–Pd(1)	117.9(1)	C(29)–P(1)–Pd(1)	115.5(1)

3.3.2.3 Solution Structure of Complex (±)-194

In view of the severe steric repulsion observed within complex (±)-**194**, the regiochemistry of this complex remains unchanged in solution. In CDCl₃, the ³¹P NMR spectrum of the complex shows only one singlet resonance at 30.9 ppm, indicating the presence of a single species in solution. In the corresponding ¹H NMR spectrum, the two *N*-methyl groups show the characteristic P–H couplings (2.0 and 3.4 Hz). These ⁴*J*_(P,H) couplings confirm the *trans* relationship of the phosphorus atom and the nitrogen donor which could be observed and justified by the “transphobia”.^[179,180] Here, the complex does not undergo the possible ligand redistribution process in solution to form the other possible regio-isomer which would be sterically more favorable.

Figure 3.2 Numbering Scheme of Complex (±)-**194** for NMR Studies

As previously mentioned, the rigidity of the organopalladated five-membered ring in solution is crucial for chiral palladated α -arylalkylamines in their application as asymmetric catalysts and reaction templates. Therefore, the conformational behavior of complex ($\pm$)-**194** in solution was studied by a combination of ^1H and 2D ^1H - ^1H ROESY NMR spectroscopy experiments. The numbered structure and 2D ROESY NMR spectrum of complex ($\pm$)-**194** in CDCl_3 are shown in Figure 3.2 and Figure 3.3.

Figure 3.3 2D ^1H - ^1H ROESY NMR spectrum of Complex ($\pm$)-**194** in CDCl_3 (refer to Scheme 3.2 for the numbering scheme). Selected ROESY Interactions: (A) H9–NMe(eq); (B) H9–NMe(ax); (C) H9–Me2; (D) H9–Me9; (E) NMe(eq)–NMe(ax); (F) NMe(eq)–Me2; (G) NMe(eq)–Me9; (H) Me9–NMe(ax); (I) Me2–Me9; (J) H6–Me7; (K) H1–Me2; (L) H8–Me7.

The 2D NMR studies indicated that the five-membered organopalladium ring in complex ($\pm$)-**194** is stereochemically rigid. Strong ROESY signals (A, B) for the interactions between the α -methane proton H9 and the two NMe groups (NMe(eq) and NMe(ax)) are clearly recorded. On the other hand, the α -Me group Me9 interacts strongly with the equatorially disposed NMe group (G), but very weakly with the axially disposed one (H). The driving forces for Me9 to assume mainly the axial position, i.e. H9–Me2 (C) and Me9–Me2 (I) repulsive interactions, are prominently reflected. Other expected ROESY interactions of H9–Me9 (D), NMe(eq)–NMe(ax) (E) are also observed. This set of ROESY interactions indicates that the λ and δ conformations are adopted in the (*S*) and (*R*) enantiomers respectively and the Me9 group is located in the axial position. These spectroscopic results confirm that the five-membered palladacycle exists predominantly in the $\delta(R)$ or $\lambda(S)$ conformation in solution.

3.3.3 Optical Resolution of Racemic Dimeric Complex ($\pm$)-**189**

3.3.3.1 Formation of Complex **195** and Complex **196**

The optical resolution of the racemic complex ($\pm$)-**189** was performed using sodium (*S*)-prolinate and sodium (*S*)-alanate as resolving reagents, as shown in Scheme 3.3.^[9, 177] The racemic dimeric complex ($\pm$)-**189** was firstly treated with two molar equivalents of sodium (*S*)-prolinate and the formation of a 1:1 mixture of diastereomeric adducts, (*R*_C,*S*_C,*S*_N)- and (*S*_C,*S*_C,*S*_N)-**195**, was detected by means of ¹H NMR spectroscopy. A single crystallization from dichloromethane-diethyl ether afforded the less soluble diastereomer (*S*_C,*S*_C,*S*_N)-**195** in the form of pale-yellow flakes in 70.0% yield and > 99% *de* (according to the ¹H NMR spectrum) with [α]_D +331 (*c* 0.5, chloroform). However, the other diastereomeric complex (*R*_C,*S*_C,*S*_N)-**195** could not be separated by slow crystallization using an array of solvent systems. Therefore, the remaining mother liquor

was treated with dilute aqueous hydrochloric acid (1M) and the resulting enantiomerically enriched dimer **189** was then cleaved with another amino acid salt {sodium (*S*)-alaninate} forming a mixture of diastereomeric complex (*R_C,S_C*)-**196** and (*S_C,S_C*)-**196**. The less soluble diastereomer (*R_C,S_C*)-**196** was crystallized as pale yellow prisms from a mixture of chloroform and diethyl ether slowly in 75% yield, > 99% *de* (according to the ¹H NMR spectrum) with [α]_D –300 (*c* 0.5, chloroform).

The absolute configurations and solid state structures of both diastereomeric derivatives (*S_C,S_C,S_N*)-**195** and (*R_C,S_C*)-**196** were determined by an X-ray single crystal diffraction investigation. Their solution structures and regiochemistry were also studied by their 2D ¹H–¹H ROESY NMR studies.

Scheme 3.3

3.3.3.2 Molecular Structure of Diastereomer (S_C, S_C, S_N)-**195**

Light yellow colored single crystals of the diastereomer (S_C, S_C, S_N)-**195** were obtained by slow addition of diethyl ether to a dichloromethane solution. The X-ray diffraction study of diastereomer (S_C, S_C, S_N)-**195** was performed (Figure 3.4) and the selected bond lengths and angles are provided in Table 3.2.

Figure 3.4 Molecular structure of complex (S_C, S_C, S_N)-**195** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13), H(N2) and H(C18) are omitted for clarity.

The X-ray crystallographic study reveals the *S* absolute configuration of the α -carbon stereocenter. The α -methyl group occupies the axial position and the conformation of the five-membered palladacycle is λ . This complex adopts a *trans*-(*N,N*) arrangement, as observed in complex (S_C, S_C, S_N)-**185** and other similar prolinato complexes.^[9] Distortion of the square planar coordination geometry about the palladium center is minimal. The dihedral angle between the two coordination planes {Pd(1)–C(1)–N(1)} and {Pd(1)–N(2)–O(1)} is 10.2°. The bond lengths around the central Pd atom are

comparable to those reported for similar prolinato palladium(II) complexes.^[9, 92, 93, 98, 177] However, a slight widening of the angle, C(1)–Pd(1)–N(2) [102.2(6)°], is observed in comparison with an angle of 99.9(1)° recorded in the prolinato derivative of dimer (S)-**4**. This phenomenon can be attributed to the presence of the spacer group, which imposes a repulsive force onto the adjacent pyrrolidine ring. Consequently, the angle of N(1)–Pd(1)–O(1) is squeezed to 94.9(9)° compared to 98.0(9)° of complex (S)-**4**.^[177,181]

Table 3.2 Selected bond lengths (Å) and angles (°) for complex (S_C,S_C,S_N)-**195**.

Pd(1)–C(1)	2.000(2)	Pd(1)–O(1)	2.103(1)
Pd(1)–N(1)	2.074(2)	Pd(1)–N(2)	2.074(2)
N(1)–C(16)	1.485(3)	N(2)–C(21)	1.496(3)
O(1)–C(17)	1.278(3)	O(2)–C(17)	1.241(2)
C(1)–Pd(1)–N(1)	81.3(1)	C(1)–Pd(1)–N(2)	102.3(1)
N(1)–Pd(1)–O(1)	95.0(1)	N(2)–Pd(1)–O(1)	81.4(1)
C(1)–Pd(1)–O(1)	176.3(1)	N(1)–Pd(1)–N(2)	169.3(1)

3.3.3.3 Solution Structure of Complex (S_C,S_C,S_N)-**195**

Owing to the different arrangements of the coordinating atoms around the central palladium atom, there are two possible geometric isomers in the solution. Thus the solution structure of complex (S_C,S_C,S_N)-**195** is of interest to be investigated, especially its regiochemistry. In CDCl₃, isomer (S_C,S_C,S_N)-**195** shows the presence of the sole geometric isomer in solution as there is only one resonance observed for each chemically nonequivalent proton. Figure 3.5 shows the numbering scheme of complex (S_C,S_C,S_N)-**195**. The 2D ¹H-¹H ROESY NMR spectrum was obtained at room temperature in CDCl₃ (Figure 3.6).

Figure 3.5 Numbering Scheme of Complex (S_C, S_C, S_N)-**195** for NMR Studies

In this NMR spectrum, strong ROESY interactions between H9 and NMe(eq) (NMe(ax), Me2, Me9) were clearly recorded (interaction A-D). The most important information about the determination of the five-membered ring conformation are the interactions between the α -methyl group Me9 and the NMe groups. In the spectrum, Me9 interacted strongly with the equatorially disposed NMe group (E), however the interaction between Me9 and the axially disposed NMe group was not observed. This set of ROESY interactions shows that the five-membered palladacycle ring is locked in the λ conformation and hence the α -methyl group Me9 is axially disposed. The driving forces for such an arrangement Me2–Me9 (F) was also reflected in the spectrum. The newly introduced phenyl group shows strong interactions with the prolinato ring and the interaction (P) NH–H5 indicates that in solution, isomer (S_C, S_C, S_N)-**195** retains a *trans*-(*N,N*) arrangement, similar to its geometrical arrangement in the solid state. Furthermore, no ROESY interaction between both NMe groups and the prolinato ligand is observed in the spectrum, confirming the *trans*-(*N,N*) relationship of complex (S_C, S_C, S_N)-**195** in solution. The signal assignments of the prolinato ligand are performed on the interactions observed in the spectrum, for example, H12–H11 (G), H12'–H11 (H), H12–H12' (I), H10–H11 (J), H13–NH (K) and H10–NH (L). Some other expected ROESY signals within the protons of the naphthalene, H6–Me7 (M); H8–Me7 (N) and H1–Me2 (O), are also clearly recorded.

Figure 3.6 2D ^1H - ^1H ROESY NMR Spectrum of Complex (S_C, S_C, S_N)-**195** in CDCl_3 . (refer to Figure 3.5 for the numbering scheme of complex (S_C, S_C, S_N)-**195**). Selected ROESY Interactions: (A) H9–NMe(eq); (B) H9–NMe(ax); (C) H9–Me2; (D) H9–Me9; (E) Me9–NMe(eq); (F) Me9–Me2; (G) H12–H11; (H) H12'–H11; (I) H12'–H12; (J) H10–H11; (K) H13–NH; (L) NH–H10; (M, N) Me7–H6 (H8); (O) Me2–H1; (P) NH–H5; (#) dichloromethane.

3.3.3.4 Molecular Structure of Diastereomer (R_C, S_C)-**196**

The molecular structure and the absolute stereochemistry of diastereomer (R_C, S_C)-**196** was also investigated crystallographically. Interestingly, two regio-isomers, *trans*-(N, N)-(R_C, S_C)-**196** and *cis*-(N, N)-(R_C, S_C)-**196**, exist in the asymmetric unit in the solid state. The molecular structures and selected bond lengths and angles of both *trans*- and *cis*-**196** are presented in Figure 3.7 and Table 3.3 as well as Figure 3.8 and Tables 3.4 respectively. These crystallographic studies revealed the *R* absolute configuration of the carbon chiral center at C(13) or C(32).

For the isomer *trans*-(N, N)-(R_C, S_C)-**196**, the coordination geometry of the central palladium atom is in a slightly distorted square plane geometry. The dihedral angle between the two coordination planes {Pd(2)–C(20)–N(3)} and {Pd(2)–N(4)–O(3)} is 10.1°. The organopalladium five-membered ring adopts an envelope-like conformation with the N(3) atom occupying the peak of the envelope, which is 0.778 Å below the mean plane of C(32)–C(31)–C(20)–Pd(2).

Table 3.3 Selected bond lengths (Å) and angles (°) for complex *trans*-(N, N)-(R_C, S_C)-**196**

Pd(2)–C(20)	1.962(7)	Pd(2)–O(3)	2.149(5)
Pd(2)–N(4)	2.069(6)	Pd(2)–N(3)	2.073(5)
O(3)–C(36)	1.269(9)	N(3)–C(35)	1.477(1)
N(4)–C(37)	1.486(8)	C(20)–Pd(2)–N(4)	99.1(2)
C(20)–Pd(2)–N(3)	81.3(2)	N(4)–Pd(2)–N(3)	170.5(2)
C(20)–Pd(2)–O(3)	174.6(3)	N(4)–Pd(2)–O(3)	78.7(2)
N(3)–Pd(2)–O(3)	100.0(2)	C(36)–O(3)–Pd(2)	112.1(5)

Figure 3.7 Molecular structure of isomer *trans*-(*N,N*)-(*R_C*,*S_C*)-**196** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C32), H(N4) and H(C37) are omitted for clarity

For the other isomer, *cis*-(*N,N*)-(*R_C*,*S_C*)-**196**, the palladium atom is located in a distorted square planar coordination sphere as expected. The bond lengths and angles around Pd(1) are comparable to those of similar palladium(II) complexes ^[9, 92, 177] except the distance of Pd(1)–N(2) [2.112(5) Å], which is significantly longer than the reported value of 1.973–2.065 Å, and also longer than 2.069(6) Å of Pd(2)–N(4) in the isomer *trans*-(*N,N*)-(*R_C*,*S_C*)-**196**. Such a bond lengthening is an expected result of a large *trans* influence of the carbon donor atom of the palladacycle. The tetrahedral distortion of the palladium coordination environment is minimal with the dihedral angle between the two planes {Pd(1)–N(1)–C(1)} and {Pd(1)–N(2)–O(1)} being 3.1°.

Figure 3.8 Molecular structure of isomer *cis*-(*N,N*)-(*R_C*,*S_C*)-**196** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13), H(N2) and H(C17) are omitted for clarity.

Table 3.4 Selected bond lengths (Å) and angles (°) for complex (*cis-N,N*)-(*R_C*,*S_C*)-**196**

Pd(1)–C(1)	2.017(7)	Pd(1)–O(1)	2.043(5)
Pd(1)–N(1)	2.055(6)	Pd(1)–N(2)	2.112(5)
O(1)–C(19)	1.280(8)	O(2)–C(19)	1.225(8)
N(1)–C(13)	1.509(8)	N(2)–C(17)	1.454(9)
C(1)–Pd(1)–O(1)	101.0(2)	C(1)–Pd(1)–N(1)	81.4(3)
O(1)–Pd(1)–N(1)	176.4(2)	C(1)–Pd(1)–N(2)	177.9(3)
O(1)–Pd(1)–N(2)	79.8(2)	N(1)–Pd(1)–N(2)	97.7(2)

The observation that there are two regio-isomers in the asymmetric unit for complex (R_C, S_C) -**196** can be attributed to the less severe intramolecular ligand-ligand interaction. Compared to the prolinato ligand in complex (S_C, S_C, S_N) -**195** which possesses a pyrrolidine ring, the alanato ligand in complex **196** does not have such a bulky group. Consequently, less steric interactions exist between the alanato resolving unit and the amine auxiliary. The favorable steric environment in complex **196** allows the adoption of both the *trans* and *cis* isomers.

3.3.3.5 Solution Structure of Diastereomer (R_C, S_C) -**196**

Both *trans*- and *cis*-(*N,N*)- (R_C, S_C) -**196** were formed in the solid state, the solution structure of complex (R_C, S_C) -**196** is of interest and was further investigated, especially its regiochemistry and organopalladium ring conformation, by means of NMR studies. The 500 MHz ^1H NMR spectrum of complex (R_C, S_C) -**196** in CDCl_3 at room temperature shows only one resonance for each chemically nonequivalent proton, indicating the presence of the sole geometric isomer in solution. The signal assignments were performed by 2D ^1H - ^1H ROESY experiment. Figure 3.9 shows the numbering scheme of complex (R_C, S_C) -**196** and Figure 3.10 presents its 2D ^1H - ^1H ROESY spectrum.

Figure 3.9 Numbering Scheme of Complex (R_C, S_C) -**196** for NMR Studies

Figure 3.10 2D ^1H - ^1H ROESY NMR Spectrum of Complex (R_C, S_N)-**196** in CDCl_3 . (refer to Figure 3.9 for the numbering scheme). Selected ROESY Interactions: (A) H9–NMe(eq); (B) H9–NMe(ax); (C) H9–Me2; (D) H9–Me9; (E) Me9–NMe(eq); (F) Me10–NH; (G) Me10–H10; (H) NH'–NH(H10); (I) H5–NH; (J) H5–NH'; (K) H6–Me7; (L) H8–Me7; (M) Me2–H1.

In this spectrum, proton H9 borne on the stereogenic center shows strong ROESY interactions with NMe(eq), NMe(ax), Me2, Me9 (A–D). A strong interaction (E) Me9–NMe(eq), together with the absence of ROESY signals between Me9 and NMe(ax) shows that the five-membered organopalladium ring is locked into the δ conformation and hence the methyl group Me9 is axially disposed. The strong ROESY interactions (I) and (J) recording the interactions between H5 and NH_2 can be easily recognized, which indicates

that the *trans*-(*N,N*) arrangement exists exclusively in solution instead of both *trans*- and *cis*-(*N,N*) arrangement observed in the solid state. Furthermore, no ROESY interactions between the NMe groups and the alanato ligand are observed, confirming the *trans*-(*N,N*) relationship. Some other expected ROESY interactions, for example Me10–NH (F); Me10–H10 (G); NH'–NH (H10) (H); H6–Me7 (K); H8–Me7 (L); and Me2–H1 (M), are also clearly recorded. It is thus concluded that the regiochemistry of isomer (*R_C*,*S_C*)-**196** remains unchanged in solution.

3.3.4 Synthesis of Optically Active Dimeric Complex **189**

3.3.4.1 Formation of Optically Active Dimeric Complex (*S*)-**189**

Treatment of complex (*S_C*,*S_C*,*S_N*)-**195** with dilute aq. hydrochloric acid gave the enantiomerically pure complex dimer (*S*)-**189** in the form of a yellow powder in 95% yield, [α]_D +476 (*c* 1.0, chloroform) (Scheme 3.4).

Scheme 3.4

Yellow colored single crystals were obtained from a dichloromethane-hexane solution of complex (*S*)-**189**. The solid-state structure of the dimeric complex (*S*)-**189** was determined by X-ray crystallography. There are four crystallographically distinguishable molecules in the asymmetric unit with the same stereochemistry but slightly different bond lengths and angles. For clarity, only one of them (molecule A) is depicted in Figure

3.11. Selected bond lengths and angles are listed in Table 3.5. The X-ray crystallographic study confirms the *S* absolute configuration of the α -carbon stereocenter of the palladacycle. The molecule has a *trans* relationship between the two nitrogen and the two carbon donor atoms. The bond lengths and angles around the palladium atoms are within the normal range and the coordination spheres of both the palladium centers are in a distorted square-planar geometry. The central four-membered ring {Pd(1)–Cl(1)–Pd(2)–Cl(2)} is bent along the Cl(1)–Cl(2) axis by 11.9°.

Figure 3.11 Molecular structure of complex (*S*)-**189** (Molecular A) with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) and H(C29) are omitted for clarity.

Table 3.5 Selected bond lengths (Å) and angles (°) for complex (*S*)-**189**

Molecule A		Molecule B	
Pd(1)–C(1)	1.99(2)	Pd(3)–C(33)	1.99(2)
Pd(1)–N(1)	2.069(2)	Pd(3)–N(3)	2.066(2)
Pd(1)–Cl(1)	2.348(6)	Pd(3)–Cl(3)	2.360(6)
Pd(1)–Cl(2)	2.458(6)	Pd(3)–Cl(4)	2.469(6)
Pd(2)–C(17)	1.99(2)	Pd(4)–C(49)	2.00(2)

Pd(2)–N(2)	2.077(2)	Pd(4)–N(4)	2.07(2)
Pd(2)–Cl(2)	2.351(6)	Pd(4)–Cl(4)	2.352(6)
Pd(2)–Cl(1)	2.470(6)	Pd(4)–Cl(3)	2.470(6)
C(1)–Pd(1)–N(1)	80.2(8)	C(33)–Pd(3)–N(3)	80.9(8)
C(1)–Pd(1)–Cl(1)	99.2(6)	C(33)–Pd(3)–Cl(3)	99.2(7)
N(1)–Pd(1)–Cl(1)	173.5(6)	N(3)–Pd(3)–Cl(3)	170.4(6)
C(1)–Pd(1)–Cl(2)	176.4(7)	C(33)–Pd(3)–Cl(4)	177.4(7)
Cl(1)–Pd(1)–Cl(2)	83.3(2)	Cl(3)–Pd(3)–Cl(4)	83.2(2)

Molecule C		Molecule D	
Pd(5)–C(65)	2.00(2)	Pd(7)–C(97)	2.00(2)
Pd(5)–N(5)	2.065(2)	Pd(7)–N(7)	2.08(2)
Pd(5)–Cl(5)	2.361(6)	Pd(7)–Cl(7)	2.446(6)
Pd(5)–Cl(6)	2.467(7)	Pd(7)–Cl(8)	2.335(6)
Pd(6)–C(81)	2.00(2)	Pd(8)–C(113)	2.00(2)
Pd(6)–N(6)	2.071(2)	Pd(8)–N(8)	2.079(2)
Pd(6)–Cl(6)	2.333(6)	Pd(8)–Cl(7)	2.347(6)
Pd(6)–Cl(5)	2.457(6)	Pd(8)–Cl(8)	2.445(6)
C(65)–Pd(5)–N(5)	80.8(9)	C(97)–Pd(7)–N(7)	81.0(9)
C(65)–Pd(5)–Cl(5)	100.9(6)	C(97)–Pd(7)–Cl(8)	98.5(7)
N(5)–Pd(5)–Cl(5)	172.0(6)	N(7)–Pd(7)–Cl(8)	175.1(6)
C(65)–Pd(5)–Cl(6)	175.9(6)	C(97)–Pd(7)–Cl(7)	176.1(7)

It is noteworthy that enantiomerically pure isomer (*R*)-**189** could be obtained from complex (*R*_C,*S*_C)-**196** with the same procedure, [α]_D – 471 (*c* 0.3, chloroform).

It has been discussed in chapter two that in solution the dimeric palladacycle (*S*)-**178** undergoes a facile regio-rearrangement to give an equilibrium mixture of both the *cis* and *trans* isomers. A similar dynamic equilibrium mixture was observed when complex (*S*)-**189** was dissolved in solution (CDCl₃). The ¹H NMR spectrum of complex (*S*)-**189** in CDCl₃ showed clearly two distinct pairs of *CMe* doublet resonances at δ 2.26 and 2.32 (³*J*_{H,H} = 6.3 Hz) in a ratio of ca. 1:1 for the two regio-isomers.

3.3.5 Regio-selective Formation of the dmpp Complex (S)-197 and Its *endo*-Cycloaddition Reactions with Ethyl Vinyl Ketone.

In order to evaluate the efficiency and stereoselectivity of the new palladacycle, the asymmetric *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone promoted by palladacycle (S)-189 was investigated.

3.3.5.1 Formation and Isolation of Complex (S)-197

The cycloaddition reaction involves the synthesis of the five-membered heterocycle dmpp coordinated complex (S)-197. Treatment of the dimeric palladacycle (S)-189 with two equivalents cyclic phosphole ligand dmpp formed the corresponding monomeric neutral complex (S)-197 in 88.9% yield, $[\alpha]_D +875$, $[\alpha]_{578} +920$, $[\alpha]_{546} +1090$, (*c* 0.5, chloroform) (Scheme 3.6).

Scheme 3.6

3.3.5.2 Molecular Structure of dmpp Complex (S)-197

Light yellow colored single crystals were obtained by slow evaporation of a dichloromethane and hexane solution of complex (S)-197. The structure of this complex was investigated by X-ray crystallography (Figure 3.12). Selected bond distances and angles are tabulated in Table 3.6.

Figure 3.12 Molecular structure of complex (*S*)-**197** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) are omitted for clarity.

Table 3.6 Selected bond lengths (Å) and angles (°) for complex (*S*)-**197**

Pd(1)–C(1)	2.035(3)	Pd(1)–P(1)	2.252(8)
Pd(1)–N(1)	2.132(3)	Pd(1)–Cl(1)	2.412(7)
N(1)–C(16)	1.487(4)	N(1)–C(13)	1.503(4)
P(1)–C(17)	1.799(3)	P(1)–C(20)	1.797(3)
C(1)–Pd(1)–N(1)	80.1(1)	C(1)–Pd(1)–P(1)	99.2(1)
N(1)–Pd(1)–P(1)	171.0(8)	C(1)–Pd(1)–Cl(1)	172.6(1)
N(1)–Pd(1)–Cl(1)	93.1(8)	P(1)–Pd(1)–Cl(1)	88.0(3)
C(16)–N(1)–Pd(1)	115.9(2)	C(13)–N(1)–Pd(1)	103.6(2)

The coordination geometry about the Pd center is distorted square planar with the phosphole coordinated *trans* to the amine nitrogen. The tetrahedral distortion of the palladium coordination environment is minimal with the dihedral angle between the two planes {Pd(1)–N(1)–C(1)} and {Pd(1)–P(1)–Cl(1)} being 9.5°. The bond lengths and

angles around Pd(1) atom are all comparable to those of other dmpp complexes of α -arylamine auxiliaries.^[7,9] Due to the fact that dmpp is smaller than triphenylphosphine, the angle C(1)–Pd(1)–P(1) [99.1(6)°] in complex (*S*)-**197** is significantly smaller than the corresponding angle [117.9(6)°] observed in complex ($\pm$)-**194**. Consistent with this observation, the dihedral angle between the phenyl ring and the projecting aromatic ring in complex (*S*)-**197** [4.9°] is also smaller than that observed in complex ($\pm$)-**194** [5.1°]. The bond angles around P(1) are significantly different. The angle C(20)–P(1)–Pd(1) [111.3(10)°] is significantly smaller than those of C(17)–P(1)–Pd(1) [122.7(1)°] and C(23)–P(1)–Pd(1) [117.6(1)°]. This difference can be attributed to the repulsive interactions between the coordinated dmpp group and the “spacer” H3 (Figure 3.12a). As expected, the five-membered palladacycle adopts the λ configuration, with the α -methyl group C(14) axially disposed.

Figure 3.12a Molecular structure of complex (*S*)-**197** (space filling diagram)

3.3.5.3 Solution Structure of the dmpp Complex (*S*)-197

In the ^{31}P NMR spectrum, the dmpp complex (*S*)-197 shows a sole peak which indicates that there is only one isomer in solution (CDCl_3). In order to study the solution structure of complex (*S*)-197, 2D ^1H - ^1H ROESY NMR was thus carried out. Figure 3.13 shows the numbering scheme of complex (*S*)-197 and Figure 3.14 indicates the 2D ^1H - ^1H ROESY NMR spectrum at room temperature in CDCl_3 .

Figure 3.13 Numbering Scheme of Complex (*S*)-197 for NMR Studies

Figure 3.14 2D ^1H - ^1H ROESY NMR Spectrum of Complex (S)-**197** in CDCl_3 . (refer to Figure 3.13 for the numbering scheme). Selected ROESY Interactions: (A) H9–NMe(eq); (B) H9–NMe(ax); (C) H9–Me2; (D) Me9–H9; (E) NMe(eq)–NMe(ax); (F) Me9–NMe(eq); (G) *o*-Ph–H5; (H) *o*-Ph-*m,p*-Ph; (I) H1–H8; (J) H5–H6; (K) H12–H5; (L) Me11–H10; (M) Me7–H6; (N) Me2–H1; (O) Me7–H8; (P) Me13–H12 (#) dichloromethane.

In the ROESY NMR spectrum, the interaction about the five-membered (S)-palladacycle are clearly recorded. Signals (A, B) show the interactions between α -methine proton H9 and NMe groups (NMe(eq) and NMe(ax)). Furthermore, signal D means that the α -methine proton H9 interacts with the α -methyl group Me9. A strong interaction (F) between Me9 and NMe(eq), together with the absence of the interaction between Me9 and NMe(ax), indicates that the five-membered ring is predominantly in λ conformation. Signal K shows the interaction between H5 and the phosphole proton H12 which confirms that complex (S)-**197** has the *trans*-N,P coordination geometry in solution, similar to its solid state. Some other ROESY signals, NMe(eq)–NMe(ax) (E); *o*-Ph–H5 (G); *o*-Ph-*m,p*-Ph (H); H1–H8 (I); H5–H6 (J); H12–H5 (K); Me11–H10 (L); Me7–H6 (M); Me2–H1 (N); Me7–H8 (O) and Me13–H12 (P) are also observed.

3.3.5.4 The Intermolecular *endo*-Cycloaddition Reaction Between Complex (S)-**197** and Ethyl Vinyl Ketone

When complex (S)-**197** was treated with excess ethyl vinyl ketone in chloroform at 50°C, the reaction was found to be completed in 2 d. The ^{31}P NMR spectrum of the crude reaction mixture in CDCl_3 exhibited two singlets at δ 121.1(major) and δ 120.9 (minor) in a ratio of 3.5:1, indicating that only two stereoisomeric cycloadducts, (S_C, S_P)- and (S_C, R_P)-**198**, were generated from the reaction. The products could not be crystallized

from a variety of solvents and were subsequently converted to the nitrate analogues, (*S_C*,*S_P*)- and (*S_C*,*R_P*)-**199**, by treatment with silver nitrate (Scheme 3.7). The ³¹P NMR spectrum of the resultant complex mixture showed two singlets, at δ 121.4 (major) and δ 120.4 (minor). The major isomer (*S_C*,*S_P*)-**199** crystallized readily from an ethyl acetate-diethyl ether solution in the form of yellow prisms with $[\alpha]_{\text{D}} +185$. The molecular structure and the absolute stereochemistry of this major product were determined by X-ray structural analysis (Figure 3.15). Selected bond distances and angles are given in Table 3.7.

Figure 3.15 Molecular structure of complex (*S_C*,*S_P*)-**199** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13), H(C17), H(C18) and H(C23) are omitted for clarity.

Scheme 3.7

Table 3.7 Selected bond lengths (Å) and angles (°) for complex (S_C,S_P)-199

Pd(1)–C(1)	2.009(5)	Pd(1)–N(1)	2.136(4)
Pd(1)–O(1)	2.180(4)	Pd(1)–P(1)	2.260(1)
C(1)–Pd(1)–N(1)	79.3(2)	C(1)–Pd(1)–O(1)	170.6(2)
N(1)–Pd(1)–O(1)	93.5(2)	C(1)–Pd(1)–P(1)	95.5(1)
N(1)–Pd(1)–P(1)	169.1(1)	O(1)–Pd(1)–P(1)	92.6(1)

Structural investigations reveals that the complex is complex (S_C, S_P)-**199**, where the *endo*-cycloadduct coordinates *trans* to the NMe_2 group as a typical monodentate ligand via its bridgehead P donor atom. The absolute configurations of the four newly generated stereogenic centers, P(1), C(17), C(18), and C(23), are *S*, *S*, *R*, and *S*, respectively, with the carbonyl group oriented in the *endo* position at C(18). Treatment of complex (S_C, S_P)-**199** with 1,2-bis(diphenylphosphino)ethane (dppe) gave the reported optically active ligand (R_P)-**200**.^[160] Conclusively, the P-chiral phosphanorbornene (R_P)-**200** was obtained as the major cycloaddition product when complex (*S*)-**189** was used as the chiral auxiliary.

3.3.6 Conclusions

In this chapter, A novel chiral palladacycle (*S*)-**189** was synthesized. The structure and palladacycle ring conformations of its triphenylphosphine derivative have been investigated solid state by X-ray structural analysis and solution by 2D-ROESY NMR spectroscopy. Due to a designed intra-molecular steric interaction, the five-membered naphthylamine chelate can be locked into a fixed conformation, both in the solid state and in solution. The racemic cyclopalladated complex ($\pm$)-**189** could be efficiently resolved via the formation of its (*S*)-prolinato and (*S*)-alaninato derivatives. When the more commonly used chiral reaction promoter (*S*)-**11** was employed for the analogous *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone under similar reaction conditions, the cycloadducts were obtained in the ratio of 1.3:1. With the new complex (*S*)-**189**, however, the increased ratio (3.5:1) indicates the stereoselectivity has been improved significantly. Thus, complex (*S*)-**189** exerts a greater selectivity for this class of intermolecular cycloaddition reaction.

3.4 Experimental

Reactions involving air-sensitive compounds were performed under a positive pressure of purified nitrogen using standard Schlenk techniques. Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectroscopy were performed on Bruker Avance 300, 400 and 500 NMR spectrometers. The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a J value in Hz. Proton nuclear magnetic resonance spectra ^1H NMR are reported as δ in units of parts per million (ppm) downfield from SiMe_4 (δ 0.0). Carbon nuclear magnetic resonance spectra ^{13}C NMR are reported as δ in units of parts per million (ppm) relative to the signal of chloroform- d (δ 77.00, triplet). All the ^{31}P NMR spectra were recorded at 121 MHz on a Bruker Avance DPX300 NMR spectrometer. Unless stated otherwise, all NMR spectroscopic experiments were performed at room temperature (300 K). Chemical shifts (δ) are reported in ppm relative to TMS, and referenced to the chemical shifts of residual solvent resonances (^1H and ^{13}C NMR) or 85% H_3PO_4 (^{31}P NMR). Mass spectra were recorded on a Thermo Finnigan MAT 95 XP Mass Spectrometer with EI mode and Waters Q-ToF Premier Mass Spectrometer with ESI mode. Melting points were determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured on the specified solution in 0.1-dm cell at 20 °C with a Perkin-Elmer model 341 polarimeter. Elemental analyses were performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at the Nanyang Technological University of Singapore.

3.4.1 Synthesis of 1-(3,6-dimethylnaphthalen-2-yl)ethanone, **190**

A solution of 2,7-dimethylnaphthalene **179** (7.30 g, 46.8 mmol) in nitromethane (100 mL) was added under stirring to a mixture of anhydrous AlCl_3 (7.33 g, 55 mmol) and acetyl chloride (3.34 mL, 46.8 mmol) in nitromethane (20 mL). The resultant red solution was stirred at room temperature for 20 h and poured into a mixture of ice (50 g) and conc. hydrochloric acid (20 mL). After vigorous stirring for 30 min, the yellowish organic layer was separated, washed with H_2O and dried (Na_2SO_4) and concentrated to dryness. The residue was passed through a silica gel column (diethyl ether/hexane = 1/40, V/V) and the solvent evaporated to give the product **190** as a colorless solid, 4.16 g (45.0%), M.p. 78–80 °C, Anal Calcd for $\text{C}_{14}\text{H}_{14}\text{O}$ (198.26): C, 84.81; H, 7.12. Found: C, 84.98; H, 7.09. ^1H NMR (300 MHz, CDCl_3): δ = 2.51 (s, 3 H, aryl- CH_3), 2.65 (s, 3 H, aryl- CH_3), 2.69 (s, 3 H, COCH_3), 7.30 (d, $^3J_{\text{H,H}}$ = 8.3 Hz, 1 H, aromatic proton), 7.52 (s, 1 H, aromatic proton), 7.54 (m, 1 H, aromatic proton), 7.76 (d, $^3J_{\text{H,H}}$ = 8.3 Hz, 1 H, aromatic proton), 8.20 (s, 1 H, aromatic proton) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 21.95, 22.08, 29.32, 125.96, 128.25, 128.42, 129.22, 129.42, 130.75, 134.81, 135.10, 135.28, 138.37, 201.24 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$)) $^+$ calcd for $\text{C}_{14}\text{H}_{15}\text{O}$ 199.1123, found 119.1118.

3.4.2 Synthesis of 1-(3,6-dimethylnaphthalen-2-yl)ethanol, ($\pm$)-**191**

To 1.0 g (5.05 mmol) of compound **190** in ethanol (20 mL) was added a solution of NaBH_4 (0.38 g, 10.1 mmol) in ethanol (20 mL). The mixture was stirred at room temperature for 24 h followed by treatment with dilute NaOH (3 %, 20 mL). The resulting solution was concentrated to 20 mL and extracted with dichloromethane. The organic layers were combined, washed with water and dried with Na_2SO_4 . Removal of the solvent gave the product ($\pm$)-**191** as a colorless oil 0.96 g, 95.0%. ^1H NMR (300 MHz, CDCl_3): δ = 1.34 (d, $^3J_{\text{H,H}}$ = 6.4 Hz, 3 H, aryl- CH_3), 2.26 (s, 3 H, aryl- CH_3), 2.36 (s, 3 H, aryl- CH_3),

2.61 (s, 1 H, OH), 4.94 (q, $^3J_{\text{H,H}} = 6.2$ Hz, 1 H, CHCH₃), 7.10 (d, $^3J_{\text{H,H}} = 8.3$ Hz, aromatic proton), 7.29 (s, 1 H, aromatic proton), 7.33 (s, 1 H, aromatic proton), 7.53 (d, $^3J_{\text{H,H}} = 8.3$ Hz, 1 H, aromatic proton), 7.71 (s, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 19.44, 21.83, 24.21, 67.03, 123.10, 125.91, 127.58, 127.66, 127.89, 130.57, 133.01, 133.07, 135.34, 142.00$ ppm. HRMS (ESI, m/z (M – OH)]⁺ calcd for C₁₄H₁₅ 183.1174, found 183.1166.

3.4.3 Synthesis of 2-(1-chloroethyl)-3,6-dimethylnaphthalene, (±)-**192**

A solution of compound (±)-**191** (1.0 g, 5.0 mmol) in dichloromethane (30 mL), was dropped slowly into a solution of PCl₃ (3.0 g, 22 mmol) in the same solvent (20 mL). The mixture was stirred overnight at room temperature followed by addition of ice water. The organic layer was separated, washed with water and dried with Na₂SO₄. Removal of the solvent gave the product (±)-**192** as a white waxy solid, 1.0 g (92.0%). ¹H NMR (300 MHz, CDCl₃): $\delta = 2.07$ (d, $^3J_{\text{H,H}} = 6.8$ Hz, 3 H, CHCH₃), 2.57 (s, 3 H, aryl-CH₃), 2.64 (s, 3 H, aryl-CH₃), 5.51 (q, $^3J_{\text{H,H}} = 6.8$ Hz, 1 H, CHCH₃), 7.33 (d, $^3J_{\text{H,H}} = 8.3$ Hz, 1 H, aromatic proton), 7.57 (s, 1 H, aromatic proton), 7.59 (s, 1 H, aromatic proton), 7.79 (d, $^3J_{\text{H,H}} = 8.3$ Hz, 1 H, aromatic proton), 8.01 (s, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 19.50, 21.88, 25.04, 55.55, 124.79, 125.92, 127.78, 127.90, 128.25, 130.38, 133.54, 133.67, 136.21, 138.20$ ppm. HRMS (EI, m/z (M – Cl)]⁺ calcd for C₁₄H₁₅ 183.1168, found 183.1175.

3.4.4 Synthesis of 1-(3,6-dimethylnaphthalen-2-yl)-N,N-dimethylethanamine, (±)-**193**

A solution of compound (±)-**192** (2.18 g, 10 mmol) in dichloromethane was stirred vigorously with an aqueous solution of dimethylamine (2 M) for 48 h. The solvents were removed and the residue in dichloromethane was washed with water, dried and evaporated

to dryness. The pure amine **193** was obtained as a pale oil after passing through a silica column using ethyl acetate as the eluent, 2.0 g (88.0 %). ^1H NMR (300 MHz, CDCl_3): δ = 1.34 (d, $^3J_{\text{H,H}}$ = 6.6 Hz, 3 H, CHCH_3), 2.22 (s, 6 H, NCH_3), 2.43 (s, 3 H, aryl- CH_3), 2.47 (s, 3 H, aryl- CH_3), 3.52 (q, $^3J_{\text{H,H}}$ = 6.5 Hz, 1 H, CHCH_3), 7.17 (d, $^3J_{\text{H,H}}$ = 8.3 Hz, 1 H, aromatic protons), 7.35 (s, 1 H, aromatic proton), 7.37 (s, 1 H, aromatic proton), 7.65 (d, $^3J_{\text{H,H}}$ = 8.3 Hz, 1 H, aromatic proton), 7.82 (s, 1 H, aromatic proton) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 19.23, 20.22, 21.81, 43.49, 61.75, 124.96, 125.83, 127.38, 127.53, 127.79, 130.71, 132.74, 134.51, 134.99, 141.33 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$)) $^+$ calcd for $\text{C}_{16}\text{H}_{22}\text{N}$ 228.1752, found 228.1746.

3.4.5 Synthesis of ($\pm$)-D- μ -chlorobis[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-C,N]dipalladium (II), ($\pm$)-**189**

A mixture of *trans*-dichlorobis(acetonitrile)palladium(II) (2.59 g, 10 mmol) and silver perchlorate (4.14 g, 20 mmol) in acetonitrile (30 mL) was stirred at room temperature for 1 h. The precipitate (AgCl) was filtered out and the filtrate was dropped under stirring into a mixture of *N,N*-dimethyl-1-(2,7-dimethylnaphthalen-5-yl)ethylamine ($\pm$)-**193** (2.28 g, 10 mmol) and triethylamine (1.01 g, 10 mmol) in dichloromethane (30 mL). The mixture was stirred at room temperature for 20 h and filtered through a Celite layer. The filtrate was evaporated and the residue was dissolved in dichloromethane (100 mL). Dilute hydrochloric acid (1M, 50 mL) was then added to the solution and the mixture was vigorously stirred for 1 h. The organic layer was separated, washed with H_2O , dried (Na_2SO_4) and concentrated to *ca.* 10 mL. Dilution of the solution with hexane precipitated the racemic dimer as yellow prisms ($\pm$)-**189**, 3.13 g, (85.0%). M.p. 150–152 °C (dec.), Anal Calcd for $\text{C}_{32}\text{H}_{40}\text{Cl}_2\text{N}_2\text{Pd}_2$ (736.42): C, 52.19; H, 5.47; N, 3.80. Found: C, 52.52; H, 5.34; N, 3.59. ^1H NMR (300 MHz, CDCl_3): δ = 2.19–2.28 (m, 6 H, CH_3), 2.26–2.42 (m,

12 H, CH_3), 2.55–2.66 (m, 12 H, CH_3), 3.56–3.70 (m, 2 H, CHCH_3), 6.89–7.30 (m, 6 H, aromatic protons), 8.33–8.61 (m, 2 H, aromatic protons) ppm.

3.4.6 Synthesis of (±)-Chloro[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-*C,N*](triphenylphosphine-*P*)palladium(II), (±)-194

To a solution of complex (±)-**189** (0.18 g, 0.25 mmol) in dichloromethane (10 mL) was added triphenylphosphine (0.13 g, 0.500 mmol) in the same solvent (10 mL). The resulting solution was stirred for 30 min at room temperature and concentrated to *ca.* 5 mL. Addition of hexane to the solution precipitated the product (±)-**194** as yellow fluffy crystals, 0.29 g (93.0%), M.p. 200–202 °C (dec.), Anal Calcd for $\text{C}_{34}\text{H}_{35}\text{ClNPPd}$ (630.45): C, 64.77; H, 5.60; N, 2.22. Found: C, 64.40; H, 5.42; N, 2.22. ^{31}P NMR (121 MHz, CDCl_3): δ = 30.9 (s) ppm. ^1H NMR (300 MHz, CDCl_3): δ = 2.11 (d, $^3J_{\text{H,H}}$ = 6.4 Hz, 3 H, CHCH_3), 2.17 (s, 3 H, aryl- CH_3), 2.38 (s, 3 H, aryl- CH_3), 2.50 (d, $^4J_{\text{P,H}}$ = 2.0 Hz, 3 H, NCH_3), 2.90 (d, $^4J_{\text{P,H}}$ = 3.4 Hz, 3 H, NCH_3), 3.76 (qn, $^4J_{\text{P,H}}$ = $^3J_{\text{H,H}}$ = 6.2 Hz, 1 H, CHCH_3), 6.36 (dd, $^4J_{\text{H,H}}$ = 1.3 Hz, $^3J_{\text{H,H}}$ = 8.5 Hz, 1 H, aromatic proton), 7.02–7.58 (m, 18 H, aromatic protons) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 20.90, 21.01, 21.14, 49.07, 50.75 (d, $J_{\text{C,P}}$ = 3.0 Hz), 74.99 (d, $J_{\text{C,P}}$ = 3.3 Hz), 124.55, 125.13, 125.31, 127.66 (d, $J_{\text{C,P}}$ = 14.7 Hz), 129.45, 129.87 (d, $J_{\text{C,P}}$ = 2.3 Hz), 131.69 (d, $J_{\text{C,P}}$ = 47.2 Hz), 132.12 (d, $J_{\text{C,P}}$ = 11.4 Hz), 133.13, 133.31, 133.53 (d, $J_{\text{C,P}}$ = 4.1 Hz), 134.80 (d, $J_{\text{C,P}}$ = 11.1 Hz), 147.86 (d, $J_{\text{C,P}}$ = 1.9 Hz), 156.53 ppm. HRMS (ESI, m/z ($\text{M} - \text{Cl}$)) $^+$ calcd for $\text{C}_{34}\text{H}_{35}\text{NPPd}$ 594.1542, found 594.1559.

3.4.7 Isolation of (S_C,S_C,S_N)-Prolinato-[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-*C,N*]palladium(II), (S_C,S_C,S_N)-195

To a suspension of the racemic dimer (±)-**189** (3.00 g, 4.07 mmol) in methanol (30 mL)

was added a solution of sodium proline (1.55 g, 11.3 mmol) in the same solvent (30 mL). The mixture was stirred at room temperature for 1 h and the solvent was removed under reduced pressure. A solution of the residue in dichloromethane (50 mL) was washed with H₂O, dried (Na₂SO₄) and diluted with diethyl ether. The less soluble diastereomer (*S*_C,*S*_C,*S*_N)-**195** crystallized slowly as slightly yellowish flakes (1.32 g, 73%, based on half of the dimer used), > 99% *de* (according to the ¹H NMR spectrum), M.p. 185–187 °C (dec.), [α]_D +331, [α]₅₇₈ +350, [α]₅₄₆ +407, [α]₄₃₆ +827, [α]₃₆₅ +1697 (*c* 0.5, chloroform). Anal Calcd for C₂₂H₃₀Cl₂N₂O₂Pd (531.78): C, 49.69; H, 5.69; N, 5.27. Found: C, 49.85; H, 5.32; N, 5.39. ¹H NMR (300 MHz, CDCl₃): δ = 1.55–1.64 (m, 1 H, CH), 1.92–2.03 (m, 1 H, CH), 2.07 (d, ³*J*_{H,H} = 6.2 Hz, 3 H, CHCH₃), 2.34–2.37 (overlapping m, 2 H, CH₂), 2.38 (s, 3 H, aryl-CH₃), 2.46 (s, 3 H, aryl-CH₃), 2.65 (s, 3 H, NCH₃), 2.77 (s, 3 H, NCH₃), 2.81–2.96 (m, 2 H, CH₂), 3.66–3.72 (m, 1 H, CH), 4.15 (q, ³*J*_{H,H} = 7.9 Hz, 1 H, CHCH₃), 4.50 (br, 1 H, NH), 7.18 (s, 1 H, aromatic proton), 7.20 (d, ³*J*_{H,H} = 8.5 Hz, 1 H, aromatic proton), 7.41 (s, 1 H, aromatic proton), 7.65 (d, ³*J*_{H,H} = 8.5 Hz, 1 H, aromatic proton) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 20.49, 21.31, 22.71, 25.24, 30.39, 48.17, 53.01, 53.25, 66.03, 74.04, 124.49, 126.69, 127.74, 129.46, 132.84, 134.01, 134.81, 147.93, 148.58, 181.25 ppm. HRMS (ESI) (*m/z*): [M + H]⁺ calcd for C₂₁H₂₉N₂O₂Pd 447.1264, found 447.1274.

3.4.7 Formation of (*R*_C,*S*_C)-Alanato-[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-*C,N*]palladium(II), (*R*_C,*S*_C)-**196**

The previously described (*R*)-isomer rich mother liquor of complex (*S*_C,*S*_C,*S*_N)-**195** was evaporated to dryness and treated with aqueous hydrochloric acid (1M, 30 mL) to reform a mixture of complex **189** (2.00 g, 2.71mmol). A solution of sodium alaninate (0.90 g, 8.13 mmol) in methanol was added to the mixture of complex ($\pm$)-**189** which was stirred

at room temperature for 1 h, and the solvent was removed under reduced pressure. A solution of the residue in chloroform (50 mL) was washed with H₂O, dried (Na₂SO₄) and diluted with diethyl ether. The less soluble diastereomer (*R*_C,*S*_C)-**196** crystallized slowly as slightly yellowish crystals (1.65 g, 75%, based on half of the dimer used), > 99% *de* (according to the ¹H NMR spectrum), M.p. 190–192 °C (dec.), [α]_D –300, [α]₅₇₈ –314, [α]₅₄₆ –364, [α]₄₃₆ –670, [α]₃₆₅ –1080, (*c* 0.5, chloroform). Anal Calcd for C₂₁H₃₀N₂O₃Pd (464.87): C, 54.25; H, 6.50; N, 6.03. Found: C, 54.47; H, 7.04; N, 5.88. ¹H NMR (300 MHz, CDCl₃): δ = 1.62 (d, ³*J*_{H,H} = 6.9 Hz, 3 H, CHCH₃), 2.01 (d, ³*J*_{H,H} = 6.3 Hz, 3 H, CHCH₃), 2.37 (s, 3 H, aryl-CH₃), 2.46 (s, 3 H, aryl-CH₃), 2.69 (s, 3 H, NCH_{3(ax)}), 2.75 (s, 3 H, NCH_{3(eq)}), 3.50 (br, 1 H, NH), 3.72–3.84 (m, 3 H, CHCH₃, NH), 7.17 (d, ³*J*_{H,H} = 8.5 Hz, 1 H, aromatic proton), 7.19 (s, 1 H, aromatic proton), 7.31 (d, ³*J*_{H,H} = 8.5 Hz, 1 H, aromatic proton), 7.43 (s, 1 H, aromatic proton) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 20.58, 21.09, 21.39, 22.67, 48.06, 53.19, 56.27, 74.14, 124.79, 127.06, 127.49, 129.92, 132.72, 134.22, 134.98, 145.32, 149.14, 179.31 ppm.

3.4.8 Synthesis of (*S*)-Di- μ -chlorobis[3-[1-(dimethylamino)ethyl]-2,7-dimethyl -4-naphthalenyl-*C,N*]dipalladium(II), (*S*)-**189**

A solution of the diastereomer (*S*_C,*S*_C,*S*_N)-**195** (1.25 g, 2.81 mmol) in dichloromethane (20 mL) was treated with aqueous hydrochloric acid (1 M, 30 mL). After vigorous stirring for 30 min, the organic layer was separated, washed with water, dried (Na₂SO₄), and concentrated to dryness yielding an amorphous yellow product (*S*)-**189**, 1.0 g (97.0%). M.p. 182–184 °C (dec.), [α]_D +476, [α]₅₇₈ +485, [α]₅₄₆ +562 (*c* 1.0, chloroform). Anal Calcd for C₃₂H₄₀Cl₂N₂Pd₂ (736.42): C, 52.19; H, 5.47; N, 3.80. Found: C, 52.52; H, 5.34; N, 3.59. ¹H NMR (300 MHz, CDCl₃): δ = 2.26 (d, ³*J*_{H,H} = 6.3 Hz, 3 H, CHCH₃), 2.32 (d, ³*J*_{H,H} = 6.3 Hz, 3 H, CHCH₃), 2.36–2.45 (m, 12 H), 2.63–2.76 (m, 12 H), 3.62–3.74 (m, 2

H, $CHCH_3$), 6.93–7.33 (m, 6 H, aromatic protons), 8.36–8.64 (m, 2 H, aromatic protons) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.24, 20.77, 21.35, 21.43, 22.87, 22.97, 49.47, 50.25, 53.74, 53.90, 75.45, 75.64, 125.32, 125.35, 125.53, 125.77, 125.92, 126.25, 128.82, 128.88, 130.43, 130.57, 132.80, 133.03, 134.20, 134.32, 144.20, 144.50, 147.23, 147.36 ppm.

The optically pure complex (*R*)-**189** was prepared from isomer (*R_C,S_C*)-**196** in a similar manner: $[\alpha]_D$ –471, $[\alpha]_{578}$ –503, $[\alpha]_{546}$ –564, $[\alpha]_{436}$ –587, $[\alpha]_{365}$ –1187, (*c* 0.3, chloroform).

3.4.9 Synthesis of (*S*)-Chloro[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-*C,N*]{3',4'-dimethyl-1'-phenylphosphole-*P*}-palladium(II), (*S*)-197**** To a solution of complex (*S*)-**189** (0.18 g, 0.25 mmol) in dichloromethane (10 mL) was added a solution of 3,4-dimethyl-1-phenylphosphole (dmpp) (0.10 g, 0.53 mmol) in the same solvent (5 mL). The resulting yellow solution was stirred at room temperature for 1 h and the solvent was removed under reduced pressure. The remaining solid was chromatographed on a silica gel column (dichloromethane/ethyl acetate = 1/1, V/V) to give a light yellow powder, which was recrystallized from dichloromethane/hexane as yellow colored crystals, 0.24 g, 88.9%, $[\alpha]_D$ +875°, $[\alpha]_{578}$ +920°, $[\alpha]_{546}$ +1090°, (*c* 0.5, chloroform), M.p. 190–192 °C (dec.), Anal Calcd for $C_{28}H_{33}ClNPPd$ (556.37): C, 60.44; H, 5.98; N, 2.52. Found: C, 60.08; H, 6.40; N, 2.52. ^{31}P NMR (121 MHz, $CDCl_3$): δ = 29.8 (s) ppm. 1H NMR (300 MHz, $CDCl_3$): δ = 1.82 (s, 3 H, $C=CCH_3$), 1.90 (d, $^3J_{H,H}$ = 6.4 Hz, 3 H, $CHCH_3$), 1.95 (s, 3 H, $C=CCH_3$), 2.40 (s, 6 H, aryl- CH_3), 2.54 (d, $^4J_{P,H}$ = 1.7 Hz, 3 H, $NCH_{3(ax)}$), 2.84 (d, $^4J_{P,H}$ = 3.4 Hz, 3 H, $NCH_{3(eq)}$), 3.72 (qn, $^3J_{H,H}$ = $^4J_{P,H}$ = 6.3 Hz, 1 H, CH_3CH), 5.61 (d, $^2J_{P,H}$ = 32.0 Hz, 1 H, $C=CH$), 6.75 (d, $^2J_{P,H}$ = 32.0 Hz, 1 H, $C=CH$), 6.76 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H, aromatic proton), 7.19 (s, 1 H, aromatic proton), 7.37 (s, 1 H, aromatic proton), 7.40–7.45 (m, 3 H, *p*-Ph, 2× *m*-Ph), 7.60 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H,

aromatic proton), 7.97–8.04 (m, 2 H, 2× *o*-Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.86 (d, $J_{\text{C,P}}$ = 12.6 Hz), 17.48 (d, $J_{\text{C,P}}$ = 12.2 Hz), 21.07, 22.45, 27.60, 48.15, 50.36, 73.14 (d, $J_{\text{C,P}}$ = 3.1 Hz), 122.39, 123.88, 125.19, 125.63 (d, $J_{\text{C,P}}$ = 10.1 Hz), 126.60 (d, $J_{\text{C,P}}$ = 10.1 Hz), 127.40 (d, $J_{\text{C,P}}$ = 43.7 Hz), 128.16 (d, $J_{\text{C,P}}$ = 10.8 Hz), 129.14 (d, $J_{\text{C,P}}$ = 52 Hz), 130.22, 131.71, 132.89, 133.01, 133.12, 140.73 (d, $J_{\text{C,P}}$ = 5.9 Hz), 147.13, 147.78 (d, $J_{\text{C,P}}$ = 10.0 Hz), 150.93, 153.36 (d, $J_{\text{C,P}}$ = 10.5 Hz) ppm. HRMS (ESI) (m/z): $[\text{M} - \text{Cl}]^+$ calcd for $\text{C}_{28}\text{H}_{33}\text{NPPd}$ 520.1385, found 520.1398.

3.4.10 Formation of complexes ($S_{\text{C}},R_{\text{P}}$)-**199** and ($S_{\text{C}},S_{\text{P}}$)-**199** and Isolation of complex ($S_{\text{C}},S_{\text{P}}$)-**199**

A mixture of the chloro complex (*S*)-**197** (0.56 g, 1.0 mmol) and ethyl vinyl ketone (0.50 g, 6.0 mmol) in chloroform (10 mL) was stirred at 50 °C for 2 days, passed through a layer of Celite and the solvent removed. The ^{31}P NMR (CDCl_3) spectrum of the crude product showed signals at δ 121.1, 120.9 in a ratio 3.5:1. This mixture in dichloromethane (5 mL) was stirred vigorously with excess AgNO_3 (0.50 g, 2.9 mmol) in water (5 mL) for 1 h in the dark. The precipitate (AgCl) was removed by filtration through a layer of Celite and the filtrate dried (MgSO_4) and the solvent removed. The crude product was chromatographed on a silica gel column using ethyl acetate / dichloromethane (1:10, V/V) as the eluent to give the diastereomeric mixture of ($S_{\text{C}},S_{\text{P}}$)- and ($S_{\text{C}},R_{\text{P}}$)-**199** as a yellow powder, which exhibited two ^{31}P NMR signals at δ 121.4 (major) and 120.4 (minor) in CDCl_3 . Recrystallization of the mixture from ethyl acetate/diethyl ether gave the major isomer ($S_{\text{C}},S_{\text{P}}$)-**199** as pale yellow prisms, 0.35 g, 52.0%, $[\alpha]_{\text{D}} +185$ (*c* 0.5, chloroform), M.p. 198–200 °C (dec.), Anal Calcd for $\text{C}_{33}\text{H}_{41}\text{N}_2\text{O}_4\text{PPd} \cdot \text{H}_2\text{O}$ (685.10): C, 57.85; H, 6.33; N, 4.09. Found: C, 57.64; H, 6.79; N, 4.10. ^{31}P NMR (121 MHz, CDCl_3): δ = 121.4 (s) ppm. ^1H NMR (300 MHz, CDCl_3): δ = 1.03 (t, $^3J_{\text{H,H}}$ = 7.3 Hz, 3 H, CH_2CH_3), 1.19 (s, 3 H, $\text{C}=\text{CCH}_3$), 1.25–1.32 (m, 1 H), 1.52 (s, 3 H, $\text{C}=\text{CCH}_3$), 1.58–1.74 (m, 1 H, *CH*), 2.15 (d,

$^3J_{\text{H,H}} = 6.4$ Hz, 3 H, CHCH_3), 2.41 (s, 3 H, aryl- CH_3), 2.50 (s, 3 H, aryl- CH_3), 2.52 (d, $^4J_{\text{P,H}} = 1.5$ Hz, 3 H, $\text{NCH}_{3(\text{ax})}$), 2.61–2.67 (m, 2 H, CH_2CH_3), 2.67–2.71 (m, 1 H, CH), 2.73 (d, $^4J_{\text{P,H}} = 3.3$ Hz, 3 H, $\text{NCH}_{3(\text{eq})}$), 3.49–3.50 (m, 1 H, CH), 3.77 (qn, $^3J_{\text{H,H}} = ^4J_{\text{P,H}} = 5.9$ Hz, 1 H, CHCH_3), 4.58 (m, 1 H, CH), 7.02 (d, $^3J_{\text{H,H}} = 8.5$ Hz, 1 H, aromatic proton), 7.23 (s, 1 H, aromatic proton), 7.40 (d, $^3J_{\text{H,H}} = 8.5$ Hz, 1 H, aromatic protons), 7.41 (s, 1 H, aromatic protons), 7.50–7.52 (m, 3 H, p -Ph, $2 \times m$ -Ph), 7.64–7.70 (m, 2 H, $2 \times o$ -Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): 7.77, 14.29, 15.01, 20.76, 21.46, 22.22, 25.39 (d, $J_{\text{C,P}} = 18.1$ Hz), 34.76, 45.08, 48.10 (d, $J_{\text{C,P}} = 31.6$ Hz), 50.64 (d, $J_{\text{C,P}} = 22.7$ Hz), 51.15, 52.74 (d, $J_{\text{C,P}} = 29.0$ Hz), 73.04, 125.66 (d, $J_{\text{C,P}} = 17.4$ Hz), 126.66, 128.58 (d, $J_{\text{C,P}} = 8.9$ Hz), 130.54 (d, $J_{\text{C,P}} = 50.7$ Hz), 130.34, 130.67, 131.29, 131.65 (d, $J_{\text{C,P}} = 12.3$ Hz), 132.45 (d, $J_{\text{C,P}} = 8.9$ Hz), 133.21, 134.77, 134.84, 134.90, 135.26, 146.33, 148.89, 209.34 (d, $J_{\text{C,P}} = 13.7$ Hz) ppm. HRMS (ESI) (m/z): $[\text{M} - \text{NO}_3]^+$ calcd for $\text{C}_{33}\text{H}_{41}\text{NOPPd}$ 604.1961, found 604.1959.

3.4.11 Formation of Compound (R_P)-200.

A solution of complex (S_C, S_P)-**199** (0.067 g, 0.1 mmol) in dichloromethane (2 mL) was treated with a solution of 1,2-bis(diphenylphosphino)ethane (0.04 g, 0.1 mmol) in the same solvent (2 mL) for 3 h. The resulting yellowish mixture was passed through a column which was packed successively with silica gel (1 g) and florisil (10 g), with dichloromethane as the eluent to yield a colorless solution. Removal of solvent under reduced pressure gave (R_P)-**200** as an air-sensitive colorless oil, Yield 0.02 g (73.5%); $[\alpha]_D -30$, (c 1, dichloromethane), ^{31}P NMR (121 MHz, CDCl_3): $\delta = 109$ (s) ppm. It is noteworthy that the phosphine ligand (R_P)-**200** is air-sensitive and configurationally unstable. Therefore after the liberation, the liberated ligand must be re-complexed to selected metal ions within ca. 30 min. The configurational instabilities of (R_P)-**200** precluded the ligands from further purification and elemental characterization.^[166]

CHAPTER 4

CHIRAL *ORTHO*-PALLADATED (1-(3,6-DIMETHYLNAPHTHALEN-2-YL)ETHYL)DIPHENYLPHOSPHINE

4.1 Introduction

In the past twenty years, the *ortho*-palladated dimethyl-[1-(α -naphthyl)ethyl]-amine [(*S*)-**11**] and its (*R*)-enantiomer have been chosen as the chiral auxiliaries in the majority of the asymmetric phosphine syntheses performed in our research group.^[156-170] For example, in the Diels–Alder reactions involving dmpp and an arrange of dienophiles, two *endo*-diastereomer products were formed and separated by fractional crystallization or by column chromatography. The lack of stereoselectivity was overcome by the introduction of a bulkier spacer group which was incorporated next to the Pd–C bond.^[7,9] As mentioned in chapter 3, a novel optically active palladacycle (*S*)-**189** has been developed and utilized as the chiral template in the *endo*-cycloaddition reaction. This palladacycle exhibited the major stereoelectronic properties of the *ortho*-palladated naphthylamine palladacycle (*S*)-**11** and is a promising new chiral promoter. Complex (*S*)-**189** has been found to be more efficient than complex (*S*)-**11** for the asymmetric [4 + 2] *endo*-cycloaddition involving ethyl vinyl ketone as the dienophile, such that a diastereoselectivity of up to 1:3.5 was obtained.

(S)-**11** (S)-**189**

The above complexes (*S*)-**11** and (*S*)-**189** are examples of cyclopalladated ligands of the N-donor type. They represent the most abundant type of palladacycles compared to other various heteroatom donors that are available. Phosphorus, being in the same group as nitrogen will therefore be able to be palladated, forming the organometallic intramolecular coordination compounds analogous to nitrogen ligands. However, because phosphorus differs from nitrogen in, for example, atomic radius, electronegativity, and in its ability to form bonds to metals using its vacant *d*-orbital for π -back bonding, the phosphorus compounds are therefore expected to exhibit significant differences in their synthesis reactions, reactivities and stabilities etc.^[66,79-84]

4.2 Research Objective

In line with our continued interests in expanding the structural diversities of this class of promising organopalladium complexes for the purpose of enhancing their efficiencies as promoters for various asymmetric transformations and taking into consideration the above demonstrated potential of the chiral palladacycle (*S*)-**189**, a structural modification of complex (*S*)-**189** could be made by the introduction of the phosphine-based palladacycle **201**. An addition to this rare class of P-donor palladacycles that have been prepared in the optically active forms. Furthermore, properties of this phosphapalladacycle, for example coordination features, conformational behavior and bond reactivity around the palladium center, are then studied.

4.3 Results and Discussions

4.3.1 Synthesis of the Racemic Phosphapalladacycle ($\pm$)-**201**

Many phosphapalladacycles have been synthesized in previous research as discussed in chapter one. There are several synthetic routes to optically active *P,C*-palladacycles: (i) direct cyclopalladation of optically active P-donor ligands,^[66,79] including cases where new chirality elements would appear in the resulting complex;^[181] (ii) resolution of racemic *P,C*-palladacycles using an optically active auxiliary ligand (usually (*S*)-proline)^[65,80,81] and (iii) asymmetric cyclopalladation of prochiral P-ligands *via trans* cyclopalladation (also known as the cyclopalladated ligand exchange reaction) using enantiopure cyclopalladated reagents.^[61] Preparation of the racemic dimeric palladacycle ($\pm$)-**201** is shown in Scheme 4.1. Synthesis of alkyl chloride ($\pm$)-**192** has been illustrated in chapter three. Treatment of complex ($\pm$)-**192** with sodium diphenylphosphide^[167] in THF afforded the air sensitive racemic phosphine ($\pm$)-**202** as a brown colored oil in 74.3 % yield at δ 5.0 in ³¹P NMR spectrum. The *ortho*-palladation of complex ($\pm$)-**202** was carried out by the treatment of the racemic phosphine with Pd(OAc)₂ in toluene, followed by the *in-situ* chloride metathesis with LiCl in methanol. Complex ($\pm$)-**201** was then isolated as yellow colored air-stable blocks, after column purification, in 79.2 % isolated yield.

Scheme 4.1

4.3.2 Solution Behavior of Phosphapalladacycle ($\pm$)-**201**

In the ^{31}P NMR spectrum at room temperature, the racemic dimeric phosphapalladacycle ($\pm$)-**201** appears as three signals; one singlet at δ 59.4 and two broad, overlapping singlets at δ 57.5, 57.9. However the peaks were resolved into four singlets at δ 58.3, 58.6, 58.9, 60.2 when the sample was cooled to 223 K. For comparative purposes, the variable temperature (VT) ^{31}P NMR spectra of complex ($\pm$)-**201** was performed and summarized in Figure 4.1 which indicated that the resolution of its NMR resonance signals is temperature-dependent. Such temperature dependence of the signals is therefore indicative of a facile exchange process occurring between the isomers in solution in equilibrium. These four peaks reflect the existence of the dimer as a mixture of six possible isomers in solution, which are the chiral *anti*-(*R,R*), *anti*-(*S,S*), *syn*-(*R,R*), *syn*-(*S,S*) as well as the achiral *anti*-(*R,S*), *syn*-(*R,S*) isomers, in which both isomers of the first two pairs are enantiomeric and can not be distinguished from each other by routine NMR spectroscopy.

Figure 4.1 (VT) ^{31}P NMR spectra of Complex ($\pm$)-**201**

4.3.3 Optical Resolution of the Dimeric Phosphapalladacycle ($\pm$)-**201**

4.3.3.1 Formation and Isolation of Proline Diastereomers (R_C, S_C, S_N)- and (S_C, S_C, S_N)-**203**

The optical resolution of the racemic complex ($\pm$)-**201** was performed using sodium (*S*)-proline as the resolving reagent, as shown in Scheme 4.2. After treating complex ($\pm$)-**201** with two equivalents of sodium (*S*)-proline, two pairs of geometric isomers were presented as four singlet peaks from the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (CDCl_3), at δ 53.3, 53.5, 56.6 and 57.4 in a relative ratio of 50:93:50:7.

Scheme 4.2

Slow evaporation of the toluene enriched solution of the diastereomeric mixtures afforded one diastereomer as the white blocks in 75.7 % yield. This less soluble diastereomer (R_C, S_C, S_N)-**203** was recrystallized as white prisms from chloroform-diethyl ether, $[\alpha]_D -32$, (c 0.5, dichloromethane). In the ^{31}P NMR spectrum (CDCl_3), two singlet peaks were observed at δ 53.7, 57.1 in a ratio of 1:1.

4.3.3.2 Molecular Structure of Complex *E*-(*R_C*,*S_C*,*S_N*)-**203**

Colorless single crystals of complex (*R_C*,*S_C*,*S_N*)-**203** were obtained from a chloroform-diethyl ether solution. There are two crystallographically distinguishable molecules in the asymmetric unit with the same stereochemistry but slightly different bond lengths and angles. For clarity, only one of them (molecule A) is depicted in Figure 4.2, the selected bond lengths and angles are provided in Table 4.1. The X-ray crystallographic study revealed the *R* absolute configuration of the α -carbon stereocenter on the basis of its Flack parameter of 0.01(3). In the solid state, the α -methyl group occupies the axial position. In complex (*R_C*,*S_C*,*S_N*)-**203**, the five-membered phosphapalladacycle has an envelope-like conformation and the distance between P(1) and the plane [Pd(1)–C(1)–C(12)–C(13)] is 1.100 Å. The tetrahedral distortion of the palladium coordination environment is minimal, with the angle between the {Pd(1)–C(1)–P(1)} and {Pd(1)–N(1)–O(1)} planes being 8.3°. The lengths of Pd–P and Pd–C bonds in the complex (*R_C*,*S_C*,*S_N*)-**203** are 2.203(2) and 2.025(5) Å, respectively. According to Figure 4.2, the diastereomer is presented as the (*E*) – geometrical isomer with the O,P-*trans* related, despite the presence of two geometrical isomers in solution with a ratio of 1:1, the geometric parameters of the proline moiety of the diastereomer (*R_C*,*S_C*,*S_N*)-**203** are mainly in the range of the values typical for the other (*S*)-proline complexes of palladium(II).^[81]

Table 4.1 Selected bond lengths (Å) and angles (°) for complex *E*-(*R_C*,*S_C*,*S_N*)-**203**.

Molecule A		Molecule B	
Pd(1)–C(1)	2.025(5)	Pd(2)–C(32)	2.048(4)
Pd(1)–O(1)	2.094(4)	Pd(2)–O(3)	2.082(4)
Pd(1)–N(1)	2.150(4)	Pd(2)–N(2)	2.139(4)
Pd(1)–P(1)	2.203(2)	Pd(2)–P(2)	2.215 (2)
C(1)–Pd(1)–O(1)	95.0(2)	C(32)–Pd(2)–O(3)	94.6(2)
C(1)–Pd(1)–N(1)	171.1(2)	C(32)–Pd(2)–N(2)	172.9 (2)

O(1)–Pd(1)–N(1)	78.4(1)	O(3)–Pd(2)–N(2)	79.9(1)
C(1)–Pd(1)–P(1)	75.8 (2)	C(32)–Pd(2)–P(2)	77.9(1)
O(1)–Pd(1)–P(1)	169.0(1)	O(3)–Pd(2)–P(2)	170.0(1)
N(1)–Pd(1)–P(1)	110.0(1)	N(2)–Pd(2)–P(2)	107.0(1)

Figure 4.2 Molecular structure of complex *E*-(*R*_C, *S*_C, *S*_N)-**203** with thermal ellipsoids at 50% probability and hydrogen atoms except H(C13), H(N1) and H(C30) are omitted for clarity.

Subsequent removal of the solvent from the mother liquor under vacuum led to the formation of light yellow colored solid. Slow addition of diethyl ether to the dichloromethane solution of the solid resulted in the precipitation of a mixture of both the (S_C, S_C, S_N)-**203** and (R_C, S_C, S_N)-**203** diastereomers as light yellow colored solid which were collected. After collecting the residue mother liquid and removing the solvent, diastereomer (S_C, S_C, S_N)-**203** was collected as a light yellow color solid in 52.1% yield. Two singlet peaks could be observed from the ^{31}P NMR spectrum (CDCl_3) at δ 53.5 57.4 in a ratio 6:1. Compared with complex (R_C, S_C, S_N)-**203**, diastereomer (S_C, S_C, S_N)-**203** has a better solubility in an array of solvents resulting in the failure to obtain X-ray quality crystals for the determination of the absolute configuration by X-ray crystallography. As demonstrated below, this problem can be solved by the cleavage of the chiral auxiliary proline ligand, leading to the formation of single crystals of the chiral dimer (S)-**201**.

4.3.4 Synthesis of the Optically Pure Dimeric Complex (S)-**201** and (R)-**201**

4.3.4.1 Formation of Complex (S)-**201** and (R)-**201**

The chiral chloro-bridged dimers, (R)-**201** and (S)-**201**, can be obtained for both of these diastereomeric complexes, (R_C, S_C, S_N)-**203** and (S_C, S_C, S_N)-**203**, respectively. Treatment of both diastereomers with dilute aqueous hydrochloric acid (1M) in a two-phase system led to the protonation and subsequent removal of the chiral auxiliary (S)-proline ligand (Scheme 4.3).

In common with the chloro-bridged dimeric complexes of other cyclopalladated ligands, the regio isomeric forms of the chiral dimer **201** underwent mutual interconversion in solution. For example at room temperature, the optically resolved complex (R)-**201** is presented as two singlets at δ 57.9, 59.4 in the ^{31}P NMR spectrum

(CDCl₃) which points to the existence of the dimer as a mixture of *anti*- and *syn*-regioisomers.

Scheme 4.3

4.3.4.2 Molecular Structure of Optically Active Dimeric Complex (S)-201

The unambiguous confirmation of the structure of phosphapalladacycle (*S_CS_CS_N*)-**203** was obtained from an X-ray diffraction study of optically active dimeric complex (*S*)-**201**. Treatment of complex (*S_CS_CS_N*)-**203** with aqueous 1M hydrochloric acid gave the enantiomerically pure complex (*S*)-**201** in the form of a yellow powder in 91.0% yield, [α]_D +470 (*c* 0.5, dichloromethane). The ³¹P NMR spectrum of complex (*S*)-**201** in CDCl₃ exhibited two singlets at δ 57.9, 59.4 indicating that the dimeric complex existed as an equilibrium mixture of the two possible *cis* and *trans* isomers. Single crystals were obtained from a dichloromethane and hexane solution of complex (*S*)-**201**. In the solid state, an X-ray diffraction study of complex (*S*)-**201** revealed that the complex was

crystallized as the chiral, *anti*-(*S*) isomer. The molecular structure is presented in Figure 4.3. The X-ray crystallographic study revealed the *S* absolute configuration of the α -carbon stereocenter and the α -methyl group occupying the axial position. Similar to most of the structurally characterized dimeric cyclopalladated complexes of the *C,P*- and *C,N*-type, dimer (*S*)-**201** reveals an *anti*-arrangement of the two phosphorus and two carbon donor atoms. Both palladium atoms in complex (*S*)-**201** are in a distorted square-planar coordination with a tetrahedral distortion of 9.2°. The complex consists of two crystallographically independent halves with minor differences in their structural parameters. The central four-membered ring {Pd(1)–Cl(1)–Pd(1A)–Cl(1A)} is bent along the Cl(1)–Cl(1A) axis by 52.8° compared to 11.9° observed in complex (*S*)-**189**. This phenomenon can be attributed to the introduction of the sterically demanding PPh₂ groups.

Figure 4.3 Molecular structure of complex (*S*)-**201** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) and H(C13A) are omitted for clarity.

Table 4.2 Selected bond lengths (Å) and angles (°) for complex (*S*)-**201**

Pd(1)–C(1)	2.043(6)	Pd(1)–P(1)	2.186(2)
Pd(1)–Cl(1)	2.437(2)	P(1)–C(15)	1.803(7)
P(1)–C(21)	1.815(9)	P(1)–C(13)	1.830(8)
C(1)–Pd(1)–P(1)	79.1(2)	C(1)–Pd(1)–Cl(1)	101.4(2)
P(1)–Pd(1)–Cl(1)	171.4(8)	C(15)–P(1)–C(21)	105.8(3)
C(15)–P(1)–C(13)	105.5(4)	C(21)–P(1)–C(13)	108.9(4)
C(15)–P(1)–Pd(1)	119.9(3)	C(21)–P(1)–Pd(1)	113.3(3)
C(13)–P(1)–Pd(1)	102.9(3)	C(12)–C(1)–Pd(1)	119.7(5)

4.3.4.3 Molecular Structure of Optically Active Dimeric Complex (*R*)-201****

The optically active dimeric complex (*R*)-**201** was formed using a similar method as mentioned above, $[\alpha]_D -476$ (c 0.5, dichloromethane). Single crystals of complex (*R*)-**201** were obtained from a chloroform-hexane solution. The molecular structure is presented in Figure 4.4, selected bond lengths and bond angles are provided in Table 4.3. The structure reveals an *anti* geometrical isomer, in which both phosphorus atoms are *trans* to each other. The *R* absolute configuration of the α -carbon stereocenter of the palladacycle was confirmed by X-ray crystallographic study. The bond lengths around the palladium atoms are comparable to the reported cyclopalladated complexes^[65, 79, 80, 81, 90, 181] and the coordination spheres of both the palladium centers are in a distorted square-planar geometry with the dihedral angle of 9.8° between the {P(1)–Pd(1)–C(1)} and {Cl(1)–Pd(1)–Cl(1A)} planes. The {C(21–26)} phenyl ring is axial while the {C(15–20)} phenyl ring is equatorial. The methyl substituents (Me14, Me14A) were noted to assume axial positions. The need to assume such a conformational state is most probably associated with the necessity to avoid an unfavorable steric repulsion between this methyl group and the spacer methyl Me11, when it is equatorially oriented. This can be supported by the close proximity of 2.6 Å between the equatorially disposed H(13) atom with the C(11) atom of the spacer methyl substituent. The closeness of these two atoms is significant

when comparing the above distance with the sum of the van der Waals radii of 3.0 Å for carbon and hydrogen.

Figure 4.4 Molecular structure of complex (*R*)-**201** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) and H(C13A) are omitted for clarity.

Table 4.3 Selected bond lengths (Å) and angles (°) for complex (*R*)-**201**

Pd(1)–C(1)	2.052(4)	Pd(1)–P(1)	2.195(1)
Pd(1)–Cl(1)	2.434(1)	P(1)–C(15)	1.812(4)
P(1)–C(21)	1.829(5)	P(1)–C(13)	1.843(4)
C(1)–Pd(1)–P(1)	79.1(1)	C(1)–Pd(1)–Cl(1)	101.2(1)
P(1)–Pd(1)–Cl(1)	171.3(4)	C(12)–C(1)–Pd(1)	119.1(3)
C(2)–C(1)–Pd(1)	122.2(3)	C(15)–P(1)–Pd(1)	119.2(1)
C(21)–P(1)–Pd(1)	112.9(2)	C(13)–P(1)–Pd(1)	102.5(1)

4.3.5 Coordination Behavior of the Phosphapalladacycle **201**

4.3.5.1 Synthesis of Triphenylphosphine Derivative (*R*)-**204**

In order to study the coordination features of the newly developed palladacycle, dimeric complex (*R*)-**201** was subjected to the adduct formation with two equivalents triphenylphosphine *via* the cleavage of the μ -dichloro bridge to yield complex (*R*)-**204**, $[\alpha]_D -270$ (*c* 0.5, dichloromethane) (Scheme 4.4).

Scheme 4.4

The phosphapalladacycle displays a very good level of regioselectivity with respect to the coordination of external ligands to the metal center. The triphenylphosphine adduct (*R*)-**204** exists in solution as the sole geometric isomer with the phosphine ligand located in the *trans* position with regard to the phosphorus atom of the palladacycle. This can be inferred from its ¹H NMR spectrum as only one set of signals are observed. Moreover in the ³¹P NMR spectrum, complex (*R*)-**204** shows only a pair of doublet signals at δ 50.2, 19.7 ($^2J_{\text{P-P}} = 442.5$ Hz), which also indicates the presence of the *trans* isomer in solution. This *trans* geometry can be identified from the ³¹P NMR spectrum through the consideration of the large $^2J_{\text{P-P}}$ coupling constants.

4.3.5.2 Molecular Structure of Triphenylphosphine Derivative (*R*)-**204**

Further evidence for this geometry was provided by its X-ray molecular structure. The yellow colored X-ray quality crystals of complex (*R*)-**204** were formed by slow evaporation of a dichloromethane-hexane solution. The X-ray molecular structure and selected bond lengths and angles are presented in Figure 4.5 and Table 4.4, respectively. The chiral nature of the phosphapalladacycle is obvious from the stereogenic α -C atom. Complex (*R*)-**204** has a distorted square-planar coordination geometry and the two phosphorus atoms are *trans* to each other. According to the X-ray structure, the α -methyl group, is located in the axial position. The central Pd atom is in a highly congested local environment as indicated by the large angle of 28.5° between the {P(1)–Pd(1)–C(1)} and {Cl(1)–Pd(1)–P(2)} planes, which is significantly larger than the dihedral angle of the triphenylphosphine derivative of palladacycle **189** (7.8°). The occurrence of such a large value can be induced by the steric repulsion between the naphthalene ring and the triphenylphosphine group.

Table 4.4 Selected bond lengths (Å) and angles ($^\circ$) for complex (*R*)-**204**.

Pd(1)–C(1)	2.024(3)	Pd(1)–P(1)	2.255(8)
Pd(1)–P(2)	2.368(8)	Pd(1)–Cl(1)	2.401(8)
C(13)–P(1)	1.843(3)	C(15)–P(1)	1.809(3)
C(1)–Pd(1)–Cl(1)	164.8(9)	C(1)–Pd(1)–P(1)	76.4(8)
C(1)–Pd(1)–P(2)	91.5(8)	P(1)–Pd(1)–P(2)	151.5(3)
P(1)–Pd(1)–Cl(1)	98.8(3)	P(2)–Pd(1)–Cl(1)	98.8(3)
C(12)–C(1)–Pd(1)	121.6(2)	C(2)–C(1)–Pd(1)	119.6(2)
C(15)–P(1)–Pd(1)	114.6(1)	C(21)–P(1)–Pd(1)	122.3(1)
C(13)–P(1)–Pd(1)	98.8(1)	C(39)–P(2)–Pd(1)	119.2(1)
C(33)–P(2)–Pd(1)	115.1(1)	C(27)–P(2)–Pd(1)	109.0(1)

Figure 4.5 Molecular structure of complex (*R*)-**204** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) are omitted for clarity.

4.3.5.3 Synthesis of dmpp Derivative (*R*)-**205**

Bulky ligand effects on the phosphapalladacycle coordination features were also studied using another electronically and sterically distinct phosphine ligand. The optically resolved phosphapalladacycle (*R*)-**201** was treated with another phosphine ligand, 3,4-dimethyl-1-phenylphosphole (dmpp) and the mononuclear adduct (*R*)-**205** was derived from the standard chloro bridge-splitting reaction, 87.0%, $[\alpha]_D -457$ (c 0.3, dichloromethane) (Scheme 4.5).

Scheme 4.5

In the ^{31}P NMR spectrum (CDCl_3), there were two pairs of doublets at δ 19.2 ($^2J_{\text{P,P}} = 26.0$ Hz), 20.6 ($^2J_{\text{P,P}} = 427.6$ Hz), 50.2 ($^2J_{\text{P,P}} = 427.6$ Hz), 60.2 ($^2J_{\text{P,P}} = 26.0$ Hz) in the ratio of 1:10:10:1. The NMR spectrum points to a mixture of *cis* and *trans* isomers, *trans*-P,P-(*R*)-205 and *cis*-P,P-(*R*)-205, as shown in Scheme 4.5. These two regioisomers are readily distinguished from each other by a consideration of the $^2J_{\text{P,P}}$ coupling constants. Hence the *trans*-P,P-(*R*)-205 isomer exists in solution as the major geometric isomer with the phosphine ligand located in the *trans* position with respect to the phosphorus atom of the phosphapalladacycle.

4.3.5.4 Molecular Structure of dmpp Derivative (*R*)-205

Yellow colored single crystals were obtained from a solution of chloroform and diethyl ether. The structure of this complex was investigated by X-ray crystallography (Figure 4.6). Selected bond distances and angles are tabulated in Table 4.5. The coordination geometry about the Pd(II) adopts a distorted square planar geometry with the phosphole *trans* coordinated to the P donor in the palladacycle. The angle of C(1)–Pd(1)–P(2) was 93.3° which was smaller than the angle observed in its amine analogue dmpp complex (99.2°). The bond angles around P(2) were slightly different to each other. The angle of C(32)–P(2)–Pd(1) was $111.2(2)^\circ$, which was significantly smaller than those of

C(27)–P(2)–Pd(1) ($118.8(2)^\circ$) and C(33)–P(2)–Pd(1) ($119.4(2)^\circ$). This can be reasonably attributed to the repulsive interactions between the coordinated dmpp group and the spacer phenyl ring at the C2 atom.

Figure 4.6 Molecular structure of complex (*R*)-**205** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13), H(N1) and H(C30) are omitted for clarity.

Table 4.5 Selected bond lengths (Å) and angles (°) for complex (*R*)-**205**.

Pd(1)–C(1)	2.041(7)	Pd(1)–P(1)	2.273(2)
Pd(1)–P(2)	2.345(2)	Pd(1)–Cl(1)	2.402(2)
C(13)–P(1)	1.840(7)	C(15)–P(1)	1.817(7)
C(21)–P(1)	1.806(8)	C(27)–P(2)	1.783(7)
C(32)–P(2)	1.803(8)	C(33)–P(2)	1.821(6)
C(1)–Pd(1)–P(1)	76.6(2)	C(1)–Pd(1)–P(2)	93.3(2)
P(1)–Pd(1)–P(2)	157.4(7)	C(1)–Pd(1)–Cl(1)	174.6(2)
P(1)–Pd(1)–Cl(1)	103.5(7)	P(2)–Pd(1)–Cl(1)	88.5(6)
C(12)–C(1)–Pd(1)	120.2(5)	C(2)–C(1)–Pd(1)	120.2(5)
C(27)–P(2)–Pd(1)	118.8(2)	C(32)–P(2)–Pd(1)	111.2(2)
C(33)–P(2)–Pd(1)	119.4(2)		

According to the above experiments, only one isomer *trans*-P,P-(*R*)-**204** was formed when the palladacycle (*R*)-**201** was coordinated to the bulky phosphine ligand triphenylphosphine. However, formation of both *trans* and *cis* isomers, *trans*-P,P-(*R*) and *cis*-P,P-(*R*)-**205**, were observed when complex (*R*)-**201** was coordinated with a less bulky phosphine ligand dmpp. The coordination difference can be explained with the different steric influence of the two phosphine ligands and the observation of the presence of only one regio-isomer in complex (*R*)-**204** can be attributed to the more severe intramolecular ligand-ligand interaction. Compared to the triphenylphosphine ligand, the dmpp ligand is less bulky. Consequently, less steric interactions exist between the dmpp ligand and the naphthyl group. Therefore the favorable steric environment in complex (*R*)-**205** allows the adoption of both the *trans*-P,P- and *cis*-P,P- isomers.

A stereoelectronic difference arising from a substitution of the *N,N*-dimethylamino group in the palladacycle **189** by a diphenylphosphino group in the newly developed phosphapalladacycle **201** has therefore been exemplified in these above simple reactions. The phosphapalladacycle contained two soft σ -donor/ π -acceptor groups with similar

trans influences in contrast to the N-donor type palladacycle **189**, which contains a hard σ -donating nitrogen atom and a soft carbon donor with π -accepting abilities. Therefore, the reaction of complex **201** with a soft donor such as phosphorus led to the formation of complexes with the *trans* geometry. Through the formation of both complex (*R*)-**204** and complex (*R*)-**205**, we can infer that the current palladacycle **201** will also display a comparative capability as palladacycle **189** in terms of its regioselective coordination with a phosphine ligand.

4.3.6 Conformational Behavior Study of Phosphapalladacycle **201**

4.3.6.1 Formation of Complex (*R*)-**206**

The study of the conformational behavior of the optically resolved phosphapalladacycle (*R*)-**201** was performed by a combination of ^1H NMR and 2D ^1H - ^1H ROESY NMR spectroscopy of its β -diketonate derivative (*R*)-**206**. Its preparation was achieved by treatment of the resolved dimer (*R*)-**201** with sodium acetylacetonate (Scheme 4.7).

Complex (*R*)-**206** is suitable for conformational behavior studies because of the following reasons. Firstly, in the ^1H NMR spectrum the dimeric complex (*R*)-**201** presents broad signals due to the dynamic *cis-trans* interconversion and the existence as mixtures of geometric *syn/anti* isomers in solution. Secondly, compared to the triphenylphosphine derivative (*R*)-**204**, complex (*R*)-**206** was more suitable for NMR spectroscopic studies of the organopalladium ring because there were fewer aromatic protons in the acetylacetonate mononuclear complex present. The absence of any aromatic protons within the acetylacetonate framework would therefore not contribute to the complexity at the aromatic region of the ^1H NMR spectrum. Most importantly, we can expect the phosphapalladacycle conformational behavior to be intrinsic, with no contributions by the

adjacent β -diketonate chelate because the chelated acetylacetonate ring is planar and nonchiral. This complex was obtained as a light yellow amorphous powder, with $[\alpha]_D -682$ (c 0.5, dichloromethane).

Scheme 4.7

4.3.6.2 Solution Structure and Conformational Behavior of Chiral Phosphapalladacycle (*R*)-206

The five-membered organopalladium ring conformation in solution is provided by the 2D ^1H - ^1H ROESY NMR spectroscopic study of the β -diketonate derivative (*R*)-206. Figure 4.7 shows the numbering Scheme of complex (*R*)-206 and Figure 4.8 shows its 2D ^1H - ^1H ROESY NMR spectrum.

Figure 4.7a Numbering Scheme of Complex (*R*)-206

Figure 4.8 Expanded 2D ^1H - ^1H ROESY NMR Spectrum of Complex (*R*)-**206** in CDCl_3 . (refer to Figure 4.7a for the numbering scheme). Selected ROESY Interactions: (A) H9–eq.*o*-PPh; (B) H9–eq.*m*-PPh, (C) H9–ax.*o*-PPh; (D) Me9–eq.*o*-PPh; (E) acac.Me–H5, (F) acac.Me–eq.*o*-PPh, (G) Me7–H8, (H) Me7–H6, (I) Me2–H1.

The NMR study of complex (*R*)-**206** shows that in solution the five-membered palladacycle exists preferentially in the $\delta(R)$ conformation with the α -Me substituent Me9 strictly in the axial position. The α -methine H9 exhibits characteristic ROESY interactions with the *o*-PPh₂ protons that are the key indications to the conformational state of the phosphapalladacycle. Strong ROESY signals (interaction A, C) from the interactions between the α -methine proton H9 and both sets of diastereotopic *o*-PPh

protons are clearly recorded. Moreover, ROESY interactions between the α -methyl substituent Me9 with only one set of the *ortho*-PPh protons (interaction D) are observed. Other expected ROESY interactions of α -CH-*eq.m*-PPh (B), *acac*.Me-H5 (E), *acac*.Me-*eq.o*-PPh (F), Me7-H8 (G), Me7-H6 (H), and Me2-H1 (I) are also observed. The *o*-PPh protons interact with both the α -methine and methyl protons and must therefore belong to the equatorially oriented phenyl ring on the phosphorus atom. The other PPh ring must hence be axially oriented. Therefore, these specific ROESY interactions between the α -methyl and only one set of *o*-PPh protons indicates that the α -methyl group is located strictly in the axial position and the interaction between the α -methyl group Me9 and Me2 can effectively confine the five-membered organometallic ring conformation and therefore δ conformation is adopted in the (*R*) enantiomer. (Figure 4.7b)

Figure 4.7b Two Possible Conformations of Complex (*R*)-**206**

As shown in Scheme 4.8, a previously reported phosphapalladacycle ($\pm$)-**103** generated a mixture of *trans*-P,P-($\pm$)-**207** and *cis*-P,P-($\pm$)-**207** isomers in a ratio of 1.1:1 when coordinated with ligand triphenylphosphine.^[81]

Scheme 4.8

It is obvious that the current palladacycle (*R*)-**201** displays a good regioselectivity which gave the isomer *trans*-**P,P-(R)-204** exclusively. This coordination difference can probably be explained by the rigidity of the palladacycle ring. According to the 2D ^1H - ^1H ROESY NMR spectrum of the β -diketonate derivative ($\pm$)-**207**, the interaction between the aromatic proton H5 and α -Ph can not efficiently confine the phosphapalladacycle in one conformation.^[81] The lack of conformational rigidity of the PPh_2 based phosphapalladacycle resulted in the low possibility of the ring to adopt either one of the two conformational states. The free rotation of the two P-phenyl groups (PPh_2) made the site *cis* to the P (PPh_2) less sterically hindered, hence the *cis*-**P,P-(±)-207** isomer was observed. In contrast, the current PPh_2 based phosphapalladacycle (*R*)-**201** has proven to be conformationally rigid. The conformational rigidity evoked a strictly conformational behavior with one P-Ph equatorially located and the other one axially located, therefore inducing more steric repulsion to the position *cis* to the P (PPh_2). Therefore palladacycle (*R*)-**201** gave only one isomer *trans*-**P,P-(R)-204** exclusively.

4.3.7 Coordination Chemistry of the Phosphapalladacycle

4.3.7.1 Stability and Behavior of the Dimeric Phosphapalladacycle ($\pm$)-**201** in Acidic Media

In previous research devoted to the chemistry of palladacycles, much has been investigated about the stability and therefore the Pd–C bond reactivity. In particular, this

bond is known to be reactive toward various nucleophiles. For example, Louie and Hartwig have established that Pd^0 complexes are indeed formed in Stille reactions or cross-coupling reactions.^[183] Recently, d'Orlye and Jutand studied a Pd^0 complex formation in situ from a *P,C*-palladacycle by the Pd-C bond cleavage.^[184] Therefore, one of the other main interests of cyclopalladated complexes is based on the exploitation of the reactivity of this bond as a means of functionalizing the metalated chelate so that a plethora of organic molecules could be derived thereafter. For the palladacycles **89**^[66] reported in 2003 and **100** reported in 2005^[79] that we have developed, the Pd-C bonds of such systems were found to be unstable in the presence of concentrated hydrochloric acid, so that the addition of one drop of the latter to the NMR samples of the CDCl_3 solutions of their chloro-bridged dimers at room temperature was sufficient to bring about the immediate rupture of these Pd-C bonds. In these cases, the palladacycles could not survive and were dechelated instantaneously to the $\eta^1\text{-P}$ monodentate dimers *via* Pd-C bond cleavage.

The Pd-C bond of complex **102** was noted to be only kinetically unstable and the phosphapalladacycle ring opens and closes reversibly by Pd-C bond cleavage in refluxing acetone containing concentrated HCl .^[80] This effect was attributed to the thermodynamic stability imparted to the palladacycle by the steric influence of the bulky *t*-Bu substituents. Furthermore, in order to study the substituent effect, complex **103** was treated with drops concentrated HCl . For example in the presence of a few drops of concentrated HCl in a CDCl_3 solution of the chloro dimer **103** led to a permanent ring opening of the

phosphapalladacycle by cleavage of the Pd–C bond.^[81]

The current phosphapalladacycle **201** has shown to be stable in dilute acid media. This conclusion was drawn during the process of the regenerating the optically resolved palladacycle (*S*)-**201** and (*R*)-**201** from the prolinated diastereomers (*R*_C,*S*_C,*S*_N)-**203** and (*S*_C,*S*_C,*S*_N)-**203** in which the latter was treated with aqueous 1M hydrochloric acid. However as discussed above, the Pd–C bond of the phosphapalladacycle exhibits a limited stability in strong acid condition. In the presence of conc. hydrochloric acid, the racemic *ortho*-palladated complex (±)-**201** underwent an immediate de-chelation *via* the Pd–C bond rupture leading to the ring opened product of the phosphapalladacycle (±)-**208**. The transformation was instantaneous, as observed from the color change from yellow to orange-red. The fact of the Pd–C bond permanent cleavage was affirmed by the separation of the binuclear product (±)-**208** by column purification, δ 43.9 in ³¹P NMR spectrum.

Scheme 4.9

4.3.7.2 Molecular Structure of Complex (±)-208

The structural evidence of the binuclear complex (±)-**208** was provided by its X-ray study (Figure 4.9). It is clear from the structure that the phosphine ligand is attached to the palladium center with the absence of the *ortho* Pd–C bond. Like the *ortho*-palladated structure in Figure 4.9, the complex reveals a dimeric structure composed of two half

units. The overall binuclear complex has an *anti* structure by the occupation of the two phosphorus atoms at diagonally opposite ends.

Figure 4.9 Molecular structure of complex (±)-**208** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C13) and H(C13A) are omitted for clarity.

Table 4.6 Selected bond lengths (Å) and angles (°) for complex (±)-**208**

Pd(1)–P(1)	2.243(1)	Pd(1)–Cl(1)	2.276(1)
Pd(1)–Cl(2)	2.324(1)	Pd(1)–Cl(2)#1	2.436(1)
P(1)–Pd(1)–Cl(1)	90.1(5)	P(1)–Pd(1)–Cl(2)	93.6(5)
Cl(1)–Pd(1)–Cl(2)	174.8(5)	P(1)–Pd(1)–Cl(2)#1	178.2(5)
Cl(1)–Pd(1)–Cl(2)#1	190.7(5)	Cl(2)–Pd(1)–Cl(2)#1	85.5(5)
Pd(1)–Cl(2)–Pd(1)#1	94.5(4)	C(15)–P(1)–Pd(1)	110.5(2)
C(21)–P(1)–Pd(1)	111.4(2)	C(13)–P(1)–Pd(1)	114.8(2)

4.3.7.3 Stability and Behavior of the dmpp Derivative (±)-**205** in Acidic Media

The Pd–C bond stability of the dmpp derivative (±)-**205** was also examined. In common with the *ortho*-palladated dimeric complex (±)-**201**, the Pd–C bond in complex (±)-**205** also exhibits a limited stability. Addition of a drop of conc. hydrochloric acid to an NMR sample of complex (±)-**205** led to the immediate rupture of the phosphapalladacycle ring evidenced by an immediate color change from light yellow to red yellow. Complex (±)-**209** was isolated in 88.2% yield by column purification, δ 27.0 (s), 37.8 (s) in ^{31}P NMR spectrum (CDCl_3) (Scheme 4.10).

Scheme 4.10

4.3.7.4 Molecular Structure of Complex (±)-**209**

Complex (±)-**209** was isolated by silica gel column purification by using dichloromethane and acetone (V/V = 1/1). Yellow colored X-ray quality single crystals were obtained from a dichloromethane and hexane solution of complex (±)-**209**. X-ray diffraction study of complex (±)-**209** was performed (Figure 4.10). The selected bond lengths and angles are provided in Table 4.7. It is clear from the structure that the dmpp phosphine ligand is *cis* to the P atom in the phosphapalladacycle and a dichloro product was formed by the absence of the *ortho* Pd–C bond. The Pd center experienced a tetrahedral distortion and the dihedral angle between the {P(1)–Pd(1)–Cl(1)} and {P(2)–Pd(1)–Cl(2)} planes was 13.6° which was smaller than the angle (21.4°) between {P(1)–Pd(1)–C(1)} and {P(2)–Pd(1)–Cl(1)} in the *ortho*-palladated complex **205**.

Figure 4.10 Molecular structure of complex (±)-**209** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C25) are omitted for clarity.

Table 4.7 Selected bond lengths (Å) and angles (°) for complex (±)-**209**

C(3)–P(1)	1.815(2)	C(7)–P(1)	1.791(2)
C(12)–P(1)	1.796(2)	C(13)–P(2)	1.816(2)
C(19)–P(2)	1.823(2)	C(25)–P(2)	1.870(2)
Cl(1)–Pd(1)	2.343(4)	Cl(2)–Pd(1)	2.347(5)
P(1)–Pd(1)	2.256(5)	P(2)–Pd(1)	2.275(4)
C(13)–P(2)–Pd(1)	110.9(6)	C(19)–P(2)–Pd(1)	112.4(6)
C(25)–P(2)–Pd(1)	112.2(6)	P(1)–Pd(1)–P(2)	94.8(2)
P(1)–Pd(1)–Cl(1)	84.6 (2)	P(2)–Pd(1)–Cl(1)	175.3(2)
P(1)–Pd(1)–Cl(2)	166.1(2)	P(2)–Pd(1)–Cl(2)	91.6(2)
Cl(1)–Pd(1)–Cl(2)	90.0 (2)		

For the current phosphapalladacycle, formation of the monodentate η^1 state is more favorable than its *ortho*-palladated state and the reversible opening and closing ring by Pd–C bond cleavage can not be observed under the strongly acidic condition. Therefore, the Pd–C bond in this phosphapalladacycle is unstable under strong acid condition.

4.3.7.5 Thermal Stability of Complex ($\pm$)-**205**

As mentioned above, the current phosphapalladacycle derivative ($\pm$)-**205** reveals the limitations in the Pd–C bond reactivity under acid condition. It is also necessary to study the bond thermal stability, for example Pd–C and Pd–P bonds. At first, an acetone solution of the complex ($\pm$)-**205** was kept at room temperature and the ^{31}P NMR spectroscopy revealed no chemical transformation after 12 h. To determine if the phosphapalladacycle ($\pm$)-**205** was able to withstand an even harsher reaction condition, the same complex was subsequently treated at 50 °C for 12 h and a Pd–P (dmpp) bond rupture was observed. According to the ^{31}P NMR in CDCl_3 , racemic dimeric complex ($\pm$)-**201** and compound **210** were formed and isolated by column purification (Scheme 4.11). According to the ^1H NMR and ^{31}P NMR spectra, compound **210**, δ 54.6 (d, $^3J_{\text{P,P}} = 39.5$ Hz), 74.7 (d, $^3J_{\text{P,P}} = 39.5$ Hz), was found to be a cycloaddition product of two molecules of oxidised dmpp.^[186,187] Based on the above experiments, the Pd–P (dmpp) bond was found to be unstable at 50 °C and a bond cleavage was observed.

Scheme 4.11

4.3.8 Attempt for Asymmetric Diels–Alder Reaction

In chapter 3, the dmpp derivative (*S*)-**197** reacted with excess ethyl vinyl ketone and led to the formation of two *endo* cycloadducts according to the ^{31}P NMR spectrum. In order to evaluate the reactivity and stereoselectivity of phosphapalladacycle (*R*)-**205**, the PPh_2 analogue of complex (*S*)-**197**, was applied in the catalyst-promoted *endo* Diels–

Alder reactions. At room temperature complex (*R*)-**205** was treated with excess ethyl vinyl ketone, the ^{31}P NMR spectrum showed that no cycloadduct formation even after 7 days. However when the reaction temperature was increased to 35 °C for 4 days, the dmpp complex (*R*)-**205** was found to be fragment affording complex (*R*)-**201** and compound **210**, with no formation of chiral cycloaddition products based on the ^{31}P NMR spectrum. Clearly, the attempt to perform an asymmetric *endo* Diels–Alder reaction promoted by phosphapalladacycle (*R*)-**201** has been a failure. On account of the above observation, the lack of reactivity at room temperature and instability of the Pd–P (dmpp) bond at higher temperature could perhaps explain the phenomenon observed.

4.3.9 Conclusions

In this chapter, a novel phosphapalladacycle **201** was prepared and a successful optical resolution of this palladacycle was achieved through the separation of its (*S*)-prolinate derivatives by fractional crystallization. Two phosphine ligands, triphenylphosphine and 3,4-dimethyl-1-phenylphosphole, were able to coordinate individually onto the dimeric palladium complex and thus the palladacycle coordination behavior was studied. The phosphapalladacycle conformational behavior was further studied by the 2D ^1H - ^1H ROESY NMR of its acetylacetonate derivative which indicated that the α -methyl group was axially located and the palladacycle was conformationally rigid in solution. Furthermore, the Pd–C bond characters of the dimeric palladacycle and its dmpp derivative were also studied. At last, dmpp complex **205**, was applied in the *endo* Diels–Alder reactions with ethyl vinyl ketone. The reaction has been a failure which could perhaps be explained by the lack of reactivity at room temperature and instability of the Pd–P (dmpp) bond at higher temperature.

4.4 Experimental

Reactions involving air-sensitive compounds were performed under a positive pressure of purified nitrogen using standard Schlenk techniques. Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectroscopy were performed on Bruker Avance 300, 400 and 500 NMR spectrometers. The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a J value in Hz. Proton nuclear magnetic resonance spectra ^1H NMR are reported as δ in units of parts per million (ppm) downfield from SiMe_4 (δ 0.0). Carbon nuclear magnetic resonance spectra ^{13}C NMR are reported as δ in units of parts per million (ppm) relative to the signal of chloroform- d (δ 77.00, triplet). All the ^{31}P NMR spectra were recorded at 121 MHz on a Bruker Advance DPX300 NMR spectrometer. Unless stated otherwise, all NMR spectroscopic experiments were performed at room temperature (300 K). Chemical shifts (δ) are reported in ppm relative to TMS, and referenced to the chemical shifts of residual solvent resonances (^1H and ^{13}C NMR) or 85% H_3PO_4 (^{31}P NMR). Mass spectra were recorded on a Thermo Finnigan MAT 95 XP Mass Spectrometer with EI mode and Waters Q-ToF Premier Mass Spectrometer with ESI mode. Melting points were determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured on the specified solution in 0.1-dm cell at 20 °C with a Perkin-Elmer model 341 polarimeter. Elemental analyses were performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at the Nanyang Technological University of Singapore.

4.4.1 Synthesis of (1-(3,6-dimethylnaphthalen-2-yl)ethyl)diphenylphosphine, ($\pm$)-202

A solution of sodium diphenylphosphide in THF was prepared from diphenylphosphine (8.00 g, 44.0 mmol) and sodium (1.00 g, 43.5 mmol). The phosphide solution was added

slowly into a stirring solution of 2-(1-chloroethyl)-3,6-dimethylnaphthalene, ($\pm$)-**192** (8.80 g, 40.4 mmol) in the same solvent (20 mL). The addition of the sodium diphenylphosphide was carried out over a period of 0.5 h. After stirring for overnight, the solvent was removed by distillation under N_2 and the residue was treated with deoxygenated H_2O (50 mL). The product was then extracted into diethyl ether, dried ($MgSO_4$) and evaporated to dryness, affording a light yellow liquid ($\pm$)-**202** (11.0 g, 74.3%). 1H NMR (300 MHz, $CDCl_3$): δ = 1.44 (dd, 3 H, $^3J_{H,H}$ = 7.0 Hz, $^3J_{P,H}$ = 14.0 Hz, $CHCH_3$), 2.19 (s, 3 H, aryl- CH_3), 2.51 (s, 3 H, aryl- CH_3), 3.91–3.95 (m, 1 H, CH_3CH), 6.94–7.97 (m, 15 H, aromatic protons) ppm. ^{31}P NMR (121 MHz, $CDCl_3$): δ = 5.0 (s) ppm.

4.4.2 Synthesis of ($\pm$)- μ -chlorobis[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-*C,N*]dipalladium (II), ($\pm$)-**201**

The fresh synthesized racemic phosphine ($\pm$)-**202** (11.0 g, 29.9 mmol) and palladium(II) acetate (6.70 g, 30.0 mmol) were suspended in degassed toluene (100 mL). The mixture was stirred at 50 °C for 10 h to give a deep red-wine like solution. The solvents were evaporated from the mixture to give a yellow-orange oil. The crude mixture was then dissolved in acetone (15 mL) and a solution of lithium chloride (3.78 g, 90.0 mmol) in acetone/ methanol (V/V = 1:3) was added, and the mixture was then stirred for 4 h. The black-green mixture was evaporated to dryness, and suspended in dichloromethane. The suspension was then washed with H_2O and the organic layer was combined, dried with $MgSO_4$. After removing the solvent, the residue was purified on a silica gel column using dichloromethane from which the racemic dichloro dimeric complex ($\pm$)-**201** eluted as a yellowish fraction, 12.1 g (79.2%), M.p. 210–212 °C (dec.), Anal Calcd for $C_{52}H_{48}Cl_2P_2Pd_2$ (1018.54); C, 61.31; H, 4.75; Found: C, 61.45; H, 4.92. 1H NMR (300 MHz, $CDCl_3$): δ = 1.76–1.91 (m, 6 H, $CHCH_3$), 2.35–2.41 (m, 6 H, aryl- CH_3), 2.47–2.57

(m, 6 H, aryl-CH₃), 4.02–4.07 (m, 2 H, CHCH₃), 7.07–7.52 (m, 22 H, aromatic protons), 7.93 (br, 4 H, aromatic protons), 8.94 (br, 1 H, aromatic proton), 8.96 (d, 1 H, ³J_{H,H} = 8.7 Hz, aromatic proton) ppm. ³¹P NMR (121 MHz, CDCl₃, 298 K): δ = 57.5 (br s) 57.9 (br s), 59.4 (s) ppm; δ (223 K) = 58.0 (s), 58.4 (s), 58.6 (s), 60.1 (s) ppm.

4.4.3 Optical Resolution of Racemic Dimeric Complex ($\pm$)-**201**

A methanol solution (20 mL) of sodium (*S*)-prolinate (2.30 g, 20.0 mmol) was added to ($\pm$)-**201** (10.2 g, 10.0 mmol) dissolved in the same solution and the mixture was stirred vigorously at room temperature overnight. The resulting light yellow suspension was evaporated to dryness, washed with H₂O (10 mL), and was extracted with dichloromethane. The combined organic extracts were dried with MgSO₄. After removing the solvent, a light yellow color solid, 11.1 g, 94.5%. ³¹P NMR (121 MHz, CDCl₃, 25 °C): four sets of signals in 50.0, 93.0, 50.0, 7.0 relative intensities at δ = 53.3 (s), 53.5 (s), 56.6 (s), 57.4 (s) ppm.

4.4.3.1 Isolation of (*R*_C,*S*_C,*S*_N)-[Prolinato-*N,O*]{[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-*C,N*]palladium(II)}, (*R*_C,*S*_C,*S*_N)-**203**

A dichloromethane solution (15 mL) of the diastereomeric mixture of (*R*_C,*S*_C,*S*_N)-**203** and (*S*_C,*S*_C,*S*_N)-**203** (11.1 g, 18.9 mmol) was diluted with toluene of the same volume, and the light yellow solution was concentrated in vacuum. The resulting solution was mainly enriched in toluene as the solvent was left to stand at room temperature, from which got a white solid (*R*_C,*S*_C,*S*_N)-**203** isomer, 4.20 g (75.7 %), [α]_D –32, [α]₅₇₈ –48, [α]₅₄₆ –48, [α]₄₃₆ –96, (*c* 0.5, dichloromethane), M.p. 218–220 °C (dec), Anal Calcd for C₃₁H₃₂NO₂PPd·0.1dichloromethane (595.52); C, 62.62; H, 5.44; N, 2.35. Found: C, 62.48; H, 5.09; N, 2.72. ¹H NMR (300 MHz, CDCl₃) two sets of signals in 1: 1 ratio, δ = 1.43–1.55

(overlapping m, 2 H), 1.70–1.75 (overlapping m, 4 H), 1.80 (dd, 3 H, $^3J_{\text{H,H}} = 6.9$ Hz, $^3J_{\text{P,H}} = 19.1$ Hz, CHCH₃), 1.97–2.08 (overlapping m, 2 H), 2.14 (dd, 3 H, $^3J_{\text{H,H}} = 6.8$ Hz, $^3J_{\text{P,H}} = 18.8$ Hz, CHCH₃), 2.26–2.35 (m, 1 H), 2.37 (s, 3 H, aryl-CH₃), 2.39 (s, 3 H, aryl-CH₃), 2.46 (s, 3 H, aryl-CH₃), 2.51 (s, 3 H, aryl-CH₃), 2.82–2.94 (m, 1 H), 3.11–3.17 (overlapping m, 2 H), 3.38–3.50 (m, 1 H), 3.62–3.64 (m, 1 H), 4.05–4.22 (overlapping m, 4 H), 7.16–7.74 (m, 22 H, aromatic protons), 7.97–8.04 (m, 2 H, aromatic protons), 8.21 (d, 2 H, $^3J_{\text{H,H}} = 8.4$ Hz, aromatic protons), 8.59 (d, 2 H, $^3J_{\text{H,H}} = 8.6$ Hz, aromatic protons) ppm. ³¹P NMR (121 MHz, CDCl₃): two signals with relative intensities of 1:1, δ 53.3(s), 56.6(s). HRMS (ESI) (m/z): [M + H]⁺ calcd for C₃₁H₃₃NO₂PPd 588.1284, found 588.1385.

4.4.3.2 Isolation of Complex (S_C,S_C,S_N)-[Prolinato-*N,O*] [3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-*C,N*]palladium(II), (S_C,S_C,S_N)-**203**

Removal of the above remaining mother liquor, a light yellow color waxy solid was obtained. Slow addition of diethyl ether to its dichloromethane solution afforded a mixture of both (S_C,S_C,S_N)-**203** and (R_C,S_C,S_N)-**203** as light yellow blocks base on the ³¹P NMR. After gathering the mother liquid and removed the solvent, the other diastereomer (S_C,S_C,S_N)-**203** was obtained as yellow colored solid 2.89 g, 52.1%. [α]_D +193, [α]₅₇₈ +196, [α]₅₄₆ +235 (c 0.8, dichloromethane), M.p. 225–227 °C (dec). Anal Calcd for C₃₁H₃₂NO₂PPd-0.1dichloromethane (595.52); C, 62.62; H, 5.44; N, 2.35. Found: C, 62.48; H, 5.09; N, 2.72. ¹H NMR (500 MHz, CDCl₃, only the ¹H NMR of the major isomer was presented), δ = 1.51–1.55 (m, 1 H, NHCH₂), 1.71 (dd, 3 H, $^3J_{\text{H,H}} = 6.9$ Hz, $^3J_{\text{P,H}} = 19.1$ Hz, CHCH₃), 1.87–1.91 (m, 1 H, NHCH₂), 2.31–2.41 (m, 2 H, COCHCH₂), 2.46 (s, 3 H, aryl-CH₃), 2.54 (s, 3 H, aryl-CH₃), 2.61–2.67 (m, 1 H, NHCH₂CH₂), 2.80–2.84 (m, 1 H, NHCH₂CH₂), 3.88–3.90 (m, 1 H, NH), 4.01–4.09 (m, 1 H, CH₃CH), 4.16–4.22 (m, 1 H, COCH₃), 7.08–7.12 (m, 2 H, aromatic protons), 7.17–7.22 (m, 2 H, aromatic protons),

7.22–7.26 (m, 2 H, aromatic protons), 7.42 (s, 1 H, aromatic proton), 7.50–7.53 (m, 4 H, aromatic protons), 8.00–8.04 (m, 2 H, aromatic protons), 8.12 (d, 1 H, $^3J_{\text{H,H}} = 8.4$ Hz, aromatic proton) ppm. ^{31}P NMR (121 MHz, CDCl_3): $\delta = 53.5$ (s), 57.4 (s) ppm in 6:1 intensities. HRMS (ESI) (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{31}\text{H}_{33}\text{NO}_2\text{PPd}$ 588.1284, found 588.1385.

4.4.4 Synthesis of (*R,R*)-di-*μ*-chlorobis[3-[1-(dimethylamino)ethyl]- 2,7-dimethyl-4-naphthalenyl-*C,N*]dipalladium (II), (*R*)-201.

A diluted hydrochloric acid (10 mL, 1 M) solution was added to a dichloromethane (20 mL) of complex (*R_C*,*S_C*,*S_N*)-**203** (1.17 g, 2.0 mmol) and the two-phase mixtures were vigorously stirred for 15 min at room temperature. The organic layer was separated, washed with H_2O , dried with MgSO_4 and evaporated to dryness under vacuum to afford the optically active dimer (*R*)-**201** as a yellow color solid, 0.92 g, 90.4%. M.p. 209–211 °C (dec), $[\alpha]_{\text{D}} -476$, $[\alpha]_{578} -478$, $[\alpha]_{546} -596$, $[\alpha]_{436} -1764$, (*c* 0.5, dichloromethane), Anal Calcd for $\text{C}_{52}\text{H}_{48}\text{Cl}_2\text{P}_2\text{Pd}_2$ (1018.54); C, 61.31; H, 4.75; Found: C, 61.45; H, 4.92. ^1H NMR (500 MHz, CDCl_3) $\delta = 1.54$ – 1.89 (m, 6 H, CHCH_3), 2.31 – 2.39 (m, 6 H, aryl- CH_3), 2.51 – 2.56 (m, 6 H, aryl- CH_3), 4.00 – 4.05 (m, 2 H, CH_3CH), 7.04 – 7.50 (m, 22 H, aromatic protons), 7.90 – 7.92 (m, 4 H, aromatic protons), 8.93 – 8.95 (m, 2 H, aromatic protons). ^{31}P NMR (121 MHz, CDCl_3): $\delta = 57.9$ (s), 59.4(s) ppm.

4.4.5 Synthesis of (*S,S*)-di-*μ*-chlorobis[3-[1-(dimethylamino)ethyl]- 2,7-dimethyl-4-naphthalenyl-*C,N*]dipalladium (II), (*S*)-201

The other isomer (*S*)-**201** was obtained as a yellow powder in the similar manner mentioned above, 0.93 g, 91.3%. M.p. 208–210 °C (dec), $[\alpha]_{\text{D}} +470$, $[\alpha]_{578} +482$, $[\alpha]_{546} +600$, $[\alpha]_{436} +1727$, (*c* 0.5, dichloromethane), Anal Calcd for $\text{C}_{52}\text{H}_{48}\text{Cl}_2\text{P}_2\text{Pd}_2$ (1018.54);

C, 61.31; H, 4.75; Found: C, 61.45; H, 4.92. ^1H NMR (300 MHz, CDCl_3) δ = 1.77–1.82 (m, 6 H, CHCH_3), 2.37 (m, 6 H, aryl- CH_3), 2.54 (m, 6 H, aryl- CH_3), 3.97–4.14 (m, 2 H, CH_3CH), 7.05–7.53 (m, 22 H, aromatic protons), 7.88–7.94 (m, 4 H, aromatic protons), 8.93–8.95 (m, 2 H, aromatic protons) ppm. ^{31}P NMR (121 MHz, CDCl_3): δ = 57.9 (s), 59.4 (s) ppm.

4.4.6 Synthesis of (*R*)-chloro{[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl- C^2, P] (triphenylphosphine)palladium(II), (*R*)-204

A dichloromethane solution of complex (*R*)-**201** (0.25 g, 0.25 mmol) and triphenylphosphine (0.13 g, 0.50 mmol) was stirred for overnight at room temperature and concentrated to ca 5 mL. The residue liquid was chromatographed on a silica gel column using dichloromethane as the eluent to give a yellow powder which was recrystallized from dichloromethane/hexane as yellow crystals, (*R*)-**204**, 0.36 g (93.0%), M.p. 140–142 °C, Anal Calcd for $\text{C}_{44}\text{H}_{39}\text{ClP}_2\text{Pd}$ -dichloromethane (856.53): C, 63.10; H, 4.82. Found: C, 63.18; H, 4.87. ^{31}P NMR (121 MHz, CDCl_3): δ = 50.2 (d, $^2J_{\text{P,P}} = 442.5$ Hz), 19.7 (d, $^2J_{\text{P,P}} = 442.5$ Hz) ppm. ^1H NMR (500 MHz, CDCl_3): δ = 1.56 (dd, 3 H, $^3J_{\text{H,H}} = 7.0$ Hz, $^3J_{\text{P,H}} = 18.4$ Hz, CHCH_3), 2.19 (s, 3 H, aryl- CH_3), 2.50 (s, 3 H, aryl- CH_3), 3.98–4.03 (m, 1 H, CH_3CH), 6.56 (d, $^3J_{\text{H,H}} = 8.5$ Hz, 1 H, aromatic proton), 6.93 (s, 1 H, aromatic proton), 6.98 (s, 1 H, aromatic proton), 7.11–7.51 (m, 23 H, aromatic protons), 8.04–8.08 (m, 2 H, aromatic protons), 8.24 (d, $^3J_{\text{H,H}} = 8.4$ Hz, 1 H, aromatic proton) ppm. HRMS (ESI, m/z ($\text{M} - \text{Cl} - \text{triphenylphosphine}$) $^+$) calcd for $\text{C}_{26}\text{H}_{24}\text{PPd}$ 473.0650, found 473.0653.

4.4.7 Synthesis of (*R*)-Chloro{[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl- C^2, P]-3',4'-dimethyl-1'-phenylphospholepalladium(II), (*R*)-205

To a solution of complex (*R*)-**201** (0.51 g, 0.50 mmol) in deoxygenated dichloromethane (20 mL) was added a solution of 3,4-dimethyl-1-phenylphosphole (dmpp) (0.20 g, 1.06 mmol) in the same solvent (10 mL). The resulting yellow solution was stirred at room temperature for overnight and the solvent was removed under reduced pressure, 0.60 g, 87.0%. The residue solid was recrystallized from chloroform/diethyl ether as yellow prisms. M.p. 205–207 °C (dec), $[\alpha]_{\text{D}}$ –457, $[\alpha]_{578}$ –460, $[\alpha]_{546}$ –570, $[\alpha]_{436}$ –1447, (*c* 0.3, dichloromethane), Anal Calcd for $\text{C}_{38}\text{H}_{37}\text{ClP}_2\text{Pd}$ (696.11); C, 65.43; H, 5.35. Found: C, 65.60; H, 4.79. Only the ¹H NMR of the *trans*-(*P,P*) isomer was presented. ¹H NMR (500 MHz, CDCl_3): δ = 1.56 (dd, 3 H, $^3J_{\text{H,H}}$ = 6.9 Hz, $^3J_{\text{P,H}}$ = 18.3 Hz, CHCH_3), 1.83 (s, 3 H, $\text{C}=\text{CCH}_3$), 1.88 (s, 3 H, $\text{C}=\text{CCH}_3$), 2.37 (s, 3 H, aryl- CH_3), 2.48 (s, 3 H, aryl- CH_3), 3.98–4.04 (m, 1 H, CH_3CH), 5.76 (d, $^2J_{\text{P,H}}$ = 32.3 Hz, 1 H, $\text{C}=\text{CH}$), 6.23 (d, $^2J_{\text{P,H}}$ = 32.6 Hz, 1 H, $\text{C}=\text{CH}$), 6.76 (dd, 1 H, $^4J_{\text{H,H}}$ = 1.5 Hz, $^3J_{\text{H,H}}$ = 8.5 Hz, aromatic proton), 7.06–7.84 (m, 18 H, aromatic protons) ppm. ³¹P NMR (121 MHz, CDCl_3 , 25°C): four sets of doublets at δ 19.2 (d, $J_{\text{P,P}}$ = 25.8 Hz), 20.6 (d, $J_{\text{P,P}}$ = 427.5 Hz), 60.2 (d, $J_{\text{P,P}}$ = 26.0 Hz), 50.2 (d, $J_{\text{P,P}}$ = 427.5 Hz) with relative intensities of 1:10:10:1. HRMS (ESI) (*m/z*): $[\text{M} - \text{Cl}]^+$ calcd for $\text{C}_{38}\text{H}_{37}\text{P}_2\text{Pd}$ 661.1405, found 661.1404.

4.4.8 Synthesis of (*R*)-(Acetylacetonato-*O,O'*){[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl-*C*²,*P*]}palladium(II), (*R*)-**206**

Sodium acetylacetonate monohydrate (27.0 mg, 0.196 mmol) was added to an acetone suspension (5 mL) of complex (*R*)-**201** (0.10 g, 0.098 mmol) and the mixture was stirred vigorously for 2 h at room temperature. After removing the solvent under vacuum, the pale yellow solid was purified by column using dichloromethane as mobile phase. The product was crystallized as pale yellow needles from dichloromethane and diethyl ether, 0.10 g, 89.0%. M.p. 215–217 °C (dec), $[\alpha]_{\text{D}}$ –682, $[\alpha]_{578}$ –658, $[\alpha]_{546}$ –830, $[\alpha]_{436}$ –1976,

(*c* 0.5, dichloromethane), Anal Calcd for C₃₁H₃₃O₂PPd (574.98); C, 64.75; H, 5.78. Found: C, 64.53; H, 5.46. ¹H NMR (500 MHz, CDCl₃): δ = 1.76 (dd, 3 H, ³J_{H,H} = 7.0 Hz, ³J_{P,H} = 19.2 Hz, CHCH₃), 2.03 (s, 3 H, acac-CH₃), 2.06 (s, 3 H, acac-CH₃), 2.46 (s, 3 H, aryl-CH₃), 2.51 (s, 3 H, aryl-CH₃), 4.02–4.08 (m, 1 H, CHCH₃), 5.52 (s, 1 H, acac-CH), 7.12 (dd, 1 H, ³J_{H,H} = 8.7 Hz, ⁴J_{H,H} = 1.7 Hz, aromatic proton), 7.15–7.19 (m, 2 H, ax. *m*-PPh), 7.22–7.25 (m, 2 H, aromatic protons), 7.36 (s, 1 H, aromatic proton), 7.41–7.45 (m, 2 H, ax. *o*-PPh), 7.47–7.51 (m, 2 H, eq. *m*-PPh), 7.53–7.56 (m, 1 H, eq. *p*-PPh), 8.00–8.03 (m, 2 H, eq. *o*-PPh), 8.54 (d, 1 H, ³J_{H,H} = 8.6 Hz, aromatic proton) ppm. ³¹P NMR (201 MHz, CDCl₃, 25 °C): δ = 53.1(s) ppm. HRMS (ESI) (*m/z*): [M – acac]⁺ calcd for C₂₆H₂₄PPd 473.0650, found 473.0663.

4.4.9 Synthesis of (±)-sym-Dichlorodi-μ-chlorobis{[3-[1-(dimethylamino)ethyl]- 2,7-dimethyl-4-naphthalenyl-C²,P }dipalladium(II), (±)-208

To a dichloromethane solution (5 mL) of the racemic dimeric complex (±)-**201** (0.10 g, 0.098 mmol) was added 0.1 mL conc. hydrochloric acid. The mixture was stirred vigorously for 1 h at room temperature and washed H₂O. The red color organic layer was separated and dried with MgSO₄. Removal of the solvent, the product was obtained as red color powder and the crystals from dichloromethane/diethyl ether, 0.08 g, 76.0%. M.p. 187–189 °C (dec), Anal Calcd for C₅₂H₅₀Cl₄P₂Pd₂ (1088.02); C, 57.22; H, 4.62. Found: C, 57.74; H, 4.98. ¹H NMR (500 MHz, CDCl₃): δ = 1.99 (br, 6 H, aryl-CH₃), 2.09 (dd, 6 H, ³J_{H,H} = 7.0 Hz, ³J_{P,H} = 19.4 Hz, CHCH₃), 2.46 (br, 6 H, aryl-CH₃), 4.84 (br, 2 H, CHCH₃), 6.69 (s, 2 H, aromatic protons), 7.15 (s, 4 H, aromatic protons), 7.29–7.31 (m, 4 H, aromatic protons), 7.39–7.51 (m, 8 H, aromatic protons), 7.58–7.62 (m, 8 H, aromatic protons), 7.76–7.81 (m, 4 H, aromatic protons) ppm. ³¹P NMR (121 MHz, CDCl₃): δ =

43.9 (s) ppm. HRMS (ESI) (m/z): $[0.5M - Cl]^+$ calcd for $C_{26}H_{25}ClPPd$ 509.0417, found 509.0408.

4.4.10 Synthesis of ($\pm$)-sym-Dichlorodi{[3-[1-(dimethylamino)ethyl]-2,7-dimethyl-4-naphthalenyl- C^2,P]-3',4'-dimethyl-1'-phenylphospholepalladium(II), ($\pm$)-209

A complex ($\pm$)-**205** (0.10 g, 0.14 mmol) acetone solution (5 mL) of was added 0.1 mL conc. hydrochloric acid. The mixture was stirred vigorously for 1 h at room temperature and then washed with H_2O . The yellow color organic layer was separated and dried with $MgSO_4$. After removing the solvent, the crude product was purified by chromatography on a silica gel column using dichloromethane and acetone ($V/V = 1/1$) as the eluent. Removal of the solvents, yellow color solid was obtained 0.09 g, 88.2%. The yellow color crystals were formed from dichloromethane/hexane. M.p. 238–240 °C (dec), Anal Calcd for $C_{38}H_{38}Cl_2P_2Pd$ -dichloromethane (816.04); C, 57.20; H, 4.92. Found: C, 57.74; H, 4.98. 1H NMR (500 MHz, $CDCl_3$): δ = 1.43 (s, 3 H, CH_3), 1.76 (s, 3 H, CH_3), 1.78 (s, 3 H, CH_3), 1.83 (dd, 3 H, $^3J_{H,H} = 7.1$ Hz, $^3J_{H,P} = 20.0$ Hz, $CHCH_3$), 2.49 (s, 3 H, CH_3), 4.94 (d, $^2J_{H,P} = 32.2$ Hz, $C=CH$), 5.32–5.38 (m, 1 H, $PCHCH_3$), 6.47 (s, 1 H, aromatic proton), 6.61 (d, $^2J_{H,P} = 31.7$ Hz, $C=CH$), 7.01–7.68 (m, 19 H, aromatic protons). ^{31}P NMR (121 MHz, $CDCl_3$): δ = 27.0 (s), 37.8 (s) ppm. HRMS (ESI) (m/z): $[M - Cl]^+$ calcd for $C_{38}H_{38}P_2PdCl$ 697.1172, found 697.1231.

4.4.11 Formation and Isolation of 4,7-Phosphinidene-1H-phosphindole, 210

A complex ($\pm$)-**205** (0.10 g, 0.14 mmol) acetone solution (5 mL) of was heated to 50 °C for 12 h. After removal the solvent, the crude product was purified by chromatography on a silica gel column using dichloromethane as the eluent and racemic dimeric complex ($\pm$)-**201** was isolated, 0.05 g, (according to 1H and ^{31}P NMR spectrum). Compound **210** was

then separated by using a polar solvent (dichloromethane/methanol = 1/1, V/V), 0.02 g, white color powder, ^1H NMR (300 MHz, CDCl_3): δ = 1.54 (s, 3 H, CH_3), 1.82 (s, 3 H, CH_3), 1.85 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 2.97 (dd, 1 H, $^3J_{\text{H,H}} = 6.4$ Hz, $^4J_{\text{H,H}} = 1.9$ Hz, CH), 3.15–3.16 (m, 1 H, CH), 3.42–3.43 (m, 1 H, CH), 5.87 (dd, $^4J_{\text{H,H}} = 3.6$ Hz, $^2J_{\text{H,P}} = 23.0$ Hz, $\text{C}=\text{CH}$), 7.39–7.60 (m, 10 H, aromatic protons) ppm. ^{31}P NMR (121 MHz, CDCl_3): δ = 54.6 (d, $J_{\text{P,P}} = 39.5$ Hz), 74.7 (d, $J_{\text{P,P}} = 39.5$ Hz) ppm. HRMS (ESI) (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{27}\text{P}_2\text{O}_2$ 409.1486, found 409.1461.

Crystal Structure Determination of Complex ($R_{\text{C}}, S_{\text{C}}, S_{\text{N}}$)-203, (S)-201, (R)-201, (R)-204, (R)-205, ($\pm$)-208 and ($\pm$)-209. Diffraction data were collected on a Bruker X8 CCD diffractometer with Mo- $\text{K}\alpha$ radiation (graphite monochromator). SADABS absorption corrections were applied. All non-hydrogen atoms were refined anisotropically while hydrogen atoms were introduced at calculated positions and refined riding on their carrier atoms. The absolute configurations of the chiral complexes were determined unambiguously using the Flack parameter. For Crystal Structure Determination of Complex ($\pm$)-208, apart from the three diethyl ether, three water and three dichloromethane molecules, the unit cell also contains 6 dichloromethane molecules which have been treated as a diffuse contribution to the overall scattering without specific atom positions by SQUEEZE/PLATON.

CHAPTER 5

CHIRAL *ORTHO*-PALLADATED 1-(2,5-DIMETHYL PHENYL)-
N,N,2,2-TETRAETHYLPROPAN-1-AMINE

5.1 Introduction

As discussed in the earlier chapters, in the asymmetric *endo* cycloaddition reactions with dienophiles, dmpp derivatives (*S*)-**176** and (*S*)-**186** have demonstrated their superiority over the *ortho*-palladated naphthylethylamine dmpp complex (*S*)-**171**. The different behaviors of the dmpp complexes could be partially attributed to the different distance between the α -methyl group attached to the chiral center and the dmpp heterocycle in the complexes. For example, the introduction of the methyl group Me₃ results in the dmpp group in complex (*S*)-**186** closer to the α -methyl group. Therefore the methyl group introduced next to the Pd–C bond is believed to play an important role in the improvement of stereoselectivity by blocking the approach of the dienophile to the reaction site from one side.

(S)-**171** (S)-**176** (S)-**186**

5.2 Research Objective

Based on the discussion above, the methyl group on the α -carbon is replaced with a *tert*-butyl group, giving rise to a novel complex, (*S*)-**211**. Three major differences are presented by palladacycle (*S*)-**211** as compared to (*S*)-**11**: firstly, the interaction between the aromatic methyl group Me₅ and the *tert*-butyl group would lock the five-membered

palladacycle in one conformation more effectively in solution and hence the *tert*-butyl will be strictly axially located. Secondly, the methyl group Me₂ was introduced on the aromatic ring *ortho* to the Pd–C bond; through this introduction the stereochemistry of the coordination site *trans* to the N donor atom would be controlled more efficiently. Third and foremost, the selectivity of *endo*-cycloaddition reaction is expected to be further improved as the bulky *tert*-butyl group may completely block attack from one direction. Therefore, a novel palladacycle (S)-**211** was prepared and its application in *endo*-cycloaddition reaction is hereby examined.

5.3 Results and Discussion

5.3.1 Synthesis of *ortho*-Palladated Complex (±)-**211**

Preparation of the novel organopalladacycle is illustrated in Scheme 5.1. The first step involved a reaction between *p*-xylene **212** and isobutyryl chloride in the presence of aluminum(III) chloride, which afforded ketone compound **213** in 93.0% yield. Further treatment of compound **213** with iodomethane in sodium hydride, led to the alkylation of the ketone side-chain to form compound **214**.^[188] Reduction of this ketone through sodium borohydride in ethanol resulted in racemate (±)-**215** in 87.5% yield. The alcohol was then converted into the azide compound (±)-**216** in the presence of sodium azide and trifluoroacetic acid, with a yield of 95.1%.^[189] The azide compound was reduced to form compound (±)-**217** in 85.4% yield using lithium aluminum hydride in dry THF. Compound (±)-**218** was synthesized as a yellow oil in 84.0% yield tertiary amines *via* treatment of compound (±)-**217** with formaldehyde and formic acid. The molecular ion

peak of complex ($\pm$)-**218** can be observed at [ESI, m/z ($M + H$)]⁺ 220.2059 by high resolution mass spectrum. The *N,N*-dimethyl amine ($\pm$)-**218** was *ortho*-palladated to give the racemic dimeric complex ($\pm$)-**211** in 67.9% yield *via* $\text{Li}_2[\text{PdCl}_4]/\text{NaOAc}$ as the palladation reagents. However, failure of the amine ($\pm$)-**218** to undergo cyclopalladation was observed when $\text{Pd}(\text{OAc})_2$ or $\text{Pd}(\text{NCMe})_4(\text{ClO}_4)_2/\text{Et}_3\text{N}$ were employed as palladation reagents.

Scheme 5.1

5.3.2 Synthesis and Characterization of *ortho*-Palladated Complex ($\pm$)-219

5.3.2.1 Synthesis of Complex ($\pm$)-219

The racemic μ -chloro dimer ($\pm$)-**211** exists as a dynamic mixture of two regioisomers interconverting in solution. This ‘fluxional’ behavior rendered difficulties in the characterization and confirmation of the palladacycle, which resulted in cluttered ^1H and ^{13}C NMR spectra. For example, the multiplet resonance exhibited at δ 1.64–1.69 in the ^1H

NMR spectrum, indicative of the *tert*-butyl group, suggests the presence of preferential arrangements in solution due to the variation in peak intensities. Several attempts were made to crystallize the dimeric complex out fractionally in a series of solvent systems. However none of the above attempts resulted in the formation of crystals that were suitable for single X-ray crystallography. Thus the racemic dimer ($\pm$)-**211** was converted to its mononuclear phosphine derivative ($\pm$)-**219** by the treatment with triphenylphosphine. Reaction of complex ($\pm$)-**211** with two molar equivalents of triphenylphosphine in dichloromethane gave a bright yellow solid which was slowly crystallized in dichloromethane/hexane in 91.0% yield (Scheme 5.2). Through the formation of this phosphine derivative ($\pm$)-**219**, a thorough examination of the chemical properties and structural characterization in both the solid state and in solution became possible.

Scheme 5.2

5.3.2.2 Molecular Structure of Complex ($\pm$)-**219**

In the solid state, the structure of complex ($\pm$)-**219** was reaffirmed crystallographically. The single crystal X-ray molecular structure and selected bond lengths and angles are presented in Figure 2 and Table 1, respectively. In complex ($\pm$)-**219**, the PPh_3 group is located *trans* to the nitrogen donor and the palladium center has a distorted square-planar coordination geometry. Analysis of the extent of the tetrahedral distortion on the central Pd atom reveals that it is located in a highly congested environment: the dihedral angle between the $\{\text{N}(1)\text{-Pd}(1)\text{-C}(1)\}$ and $\{\text{Cl}(1)\text{-Pd}(1)\text{-P}(1)\}$ planes have a large value of 19.5° . The torsion angle of $\text{P}(1)\text{-Pd}(1)\text{-C}(1)\text{-C}(2)$ is 52.0° ,

such a twisting can be partially attributed to the repulsive interaction between the methyl spacer C3 and the phenyl group (C(22)–C(27)). The five-membered palladacycle, in this case, adopts a single conformation and the *tert*-butyl substituent attached to the α -carbon stereocenter, remains axially located. The distance between C(10) and C(15) was found to be 3.060 Å which is less than 3.4 Å, the sum of the Van der Waals radii of the two atoms. This implies that the bulky *tert*-butyl group must be projected away from C(15) to relieve steric repulsion in the crowded local environment which is the main driving force for this group to assume the axial position. Thus the ring conformation is effectively locked. Furthermore, the distance between C(15) and Cl(1) was found to be 3.190 Å, which is also smaller than the Van der Waals radii of the two atoms, being 3.5 Å. This is also indicative of a highly crowded localized environment hence explaining the stereochemical influence exhibited by the organopalladium complex as well as the regioselectivity observed.

Figure 5.1 Molecular Structure of Complex (±)-**219** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C9) are omitted for clarity.

Table 5.1 Selected bond lengths (Å) and angles (°) for complex (±)-**219**

Pd(1)–C(1)	2.014(2)	Pd(1)–N(1)	2.145(2)
Pd(1)–P(1)	2.275(5)	Pd(1)–Cl(1)	2.392(5)
C(1)–Pd(1)–N(1)	79.06(6)	C(1)–Pd(1)–P(1)	101.8(5)
N(1)–Pd(1)–P(1)	166.0(5)	C(1)–Pd(1)–Cl(1)	164.3(6)
N(1)–Pd(1)–Cl(1)	92.3(4)	P(1)–Pd(1)–Cl(1)	89.8(2)
C(2)–C(1)–Pd(1)	127.1(1)	C(8)–C(1)–Pd(1)	112.6(1)

Figure 5.1a Molecular Structure of Complex (±)-**219** (space filling diagram)

5.3.2.3 Solution Structure of Complex (±)-**219**

In solution, the NMR spectroscopic characterization of this racemic palladacycle was achieved by a combination of ^1H NMR and 2D ^1H - ^1H ROESY NMR. In CDCl_3 , the ^{31}P NMR spectrum of complex (±)-**219** shows only a singlet resonance at δ 30.0 indicating the presence of a sole isomer in solution. Hence in comparison with the dimeric complex (±)-**211**, mononuclear complex (±)-**219** is more suitable for NMR spectroscopic studies. In the ^1H NMR spectrum, the two NMe groups show the characteristic P–H couplings (1.5 and 3.4 Hz). These $J_{\text{P,H}}$ couplings confirm the *trans* relationship of the phosphorus atom and the nitrogen donor. Given the aromatic nature of the protons in

triphenylphosphine, it was also possible to clearly analyze the five-membered ring conformation in solution through 2D ^1H - ^1H ROESY NMR spectroscopy. The NMR study of the racemic adduct ($\pm$)-**219** has shown that in solution the five-membered palladacycle exists in the $\delta(R)$ or $\lambda(S)$ conformation with the *tert*-butyl substituent in the axial position. This conclusion can be inferred from the coupling constant $^4J_{\text{PH}}$ of 5.2 Hz for the α -*tert*-butyl proton and further confirmed by the 2D ^1H - ^1H ROESY NMR (Figure 5.3). Figure 5.2 shows the numbering scheme of complex ($\pm$)-**219** for the NMR study.

Figure 5.2 Numbering Scheme of Complex ($\pm$)-**219** for NMR Studies

Figure 5.3 2D ^1H - ^1H ROESY NMR Spectrum of complex ($\pm$)-**219** in CDCl_3 . (refer to Figure 5.2 for the numbering scheme of ($\pm$)-**219**). Selected ROESY Interactions: (A) NMe(eq)-H7; (B) NMe(ax)-H7; (C) H7-Me5; (D) H7-*tert*-butyl; (E) NMe(eq)-NMe(ax); (F) NMe(eq)-*tert*-butyl; (G) Me5-*tert*-butyl; (H) Me5-H4; (I) triphenylphosphine-*tert*-butyl; (J) Me2-H3.

In the NMR spectrum, the key ROESY interaction is F, demonstrating that the *tert*-butyl group exhibits a strong interaction with NMe(eq), and lack of interaction with (*tert*-butyl-NMe(ax)). This set of interactions confirm that the methyl groups of the nitrogen are fully fixed in position and that the ring is locked in either the (*S*) λ or (*R*) δ conformation. Furthermore, the driving forces for the *tert*-butyl group to assume the axial position can also be attributed to the repulsive interactions, (C) Me5-H7 and (G) Me5-*tert*-butyl. Other expected ROESY interactions of NMe(eq)-NMe(ax) (E), *tert*-butyl-H7 (D), Me5-H4 (H) and Me2-H3 (J) are also observed. Interestingly, the interaction between *tert*-butyl and triphenylphosphine (I) is also observed which indicates that through the introduction of the bulky *tert*-butyl group, a steric effect will be experienced when the reaction site *trans* to the nitrogen donor is coordinated to a bulky group (for example triphenylphosphine here) (Figure 5.1a).

5.3.3 Optical Resolution of Racemic Dimer ($\pm$)-**211**

5.3.3.1 Formation of Diastereomeric Complexes (R_C, S_C, S_N)-**220** and (S_C, S_C, S_N)-**220**

The optical resolution of racemic dimeric complex ($\pm$)-**211** was achieved *via* the formation and separation of a pair of diastereomeric (*S*)-prolinate derivatives (Scheme 5.3). By treating the racemic dimer with two molar equivalents of sodium (*S*)-prolinate, the expected 1:1 mixture of diastereomeric adducts (R_C, S_C, S_N)-**220** and (S_C, S_C, S_N)-**220** were formed and confirmed by the ^1H NMR spectroscopy.

Scheme 5.3

Successful resolution was achieved by fractional crystallization in dichloromethane/diethyl ether affording the less soluble diastereomer (S_C,S_C,S_N)-220 in the form of yellow prisms with $[\alpha]_D +246$, $[\alpha]_{578} +256$, $[\alpha]_{546} +292$, $[\alpha]_{436} +562$, $[\alpha]_{365} +890$ (*c* 0.5, dichloromethane), > 99% *de* (according to the ¹H NMR spectrum). The diastereomerically enriched mother liquor allowed the isolation of the remaining (R_C,S_C,S_N)-220 diastereomer from chloroform/diethyl ether as pale yellow feather-like crystals with $[\alpha]_D -32$, $[\alpha]_{578} -36$, $[\alpha]_{546} -26$, $[\alpha]_{436} +22$, $[\alpha]_{365} +346$ (*c* 0.5, dichloromethane), > 99% *de* (according to the ¹H NMR spectrum). The absolute configurations and solid structures of both diastereomeric proline derivatives (S_C,S_C,S_N)-220 and (R_C,S_C,S_N)-220 were determined by a single crystal X-ray diffraction investigation. Their solution structures were also studied by their 2D ¹H-¹H ROESY NMR spectra.

5.3.3.2 Molecular Structure of Diastereomer (R_C,S_C,S_N)-220

The X-ray diffraction study of the diastereomer (R_C,S_C,S_N)-220 was carried out and there are three crystallographically distinguishable molecules in the unit cell with the same stereochemistry but with slightly different bond lengths and angles. For clarity, only one of them (molecule A) is depicted in Figure 5.4. The selected bond lengths and angles are provided in Table 5.2. The X-ray crystallographic study reveals the *R* absolute configuration of the *tert*-butyl stereocenter. The *tert*-butyl group occupies the expected axial position and the conformation of the five-membered palladacycle is δ . In accordance

with the previously reported (*S*)-prolinate complexes, the secondary stereogenic nitrogen atom from the N,O-chelate is noted to adopt the (*S*) configuration. The coordination geometry of the central palladium atom is in a slightly distorted square plane. The dihedral angle between the planes {N(1)–C(1)–Pd(1)} and {O(1)–N(2)–Pd(1)} is 6.7°. Worthy to note, the two coordinated nitrogen atoms are *trans* related, which is in contrast to the *cis* (*N,N*)- relationship for its α -methyl analogue reported before.⁹ This phenomenon can be attributed to the severe intramolecular ligand-ligand steric interaction arising from the presence of the bulky *tert*-butyl group as compared to its α -methyl analogue. Consequently, less steric interactions exist between the *tert*-butyl group and the prolinate ligand when the complex (*R_C*,*S_C*,*S_N*)-**220** adopts the more favorable *trans*-*N,N* isomer.

Figure 5.4 Molecular Structure of Complex (*R_C*,*S_C*,*S_N*)-**220** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C9), H(N2) and H(C17) are omitted for clarity.

Table 5.2 Selected bond lengths (Å) and angles (°) for complex (*R_C*,*S_C*,*S_N*)-**220**

Molecule A		Molecule B		Molecule C	
Pd(1)–C(1)	2.018(5)	Pd(2)–C(21)	2.009(6)	Pd(3)–C(41)	2.007(6)
Pd(1)–N(1)	2.062(5)	Pd(2)–N(3)	2.067(5)	Pd(3)–N(6)	2.072(5)
Pd(1)–N(2)	2.083(4)	Pd(2)–N(4)	2.071(5)	Pd(3)–N(5)	2.079(5)
Pd(1)–O(1)	2.136(4)	Pd(2)–O(3)	2.130(4)	Pd(3)–O(5)	2.112(4)
C(1)–Pd(1)–N(1)	80.4(2)	C(21)–Pd(2)–N(3)	81.0(2)	C(41)–Pd(3)–N(6)	105.7(2)
C(1)–Pd(1)–N(2)	106.1(2)	C(21)–Pd(2)–N(4)	105.5(2)	C(41)–Pd(3)–N(5)	81.8(2)
N(1)–Pd(1)–N(2)	173.3(2)	N(3)–Pd(2)–N(4)	173.4(2)	N(6)–Pd(3)–N(5)	171.6(2)
C(1)–Pd(1)–O(1)	174.6(2)	C(21)–Pd(2)–O(3)	173.9(2)	C(41)–Pd(3)–O(5)	174.4(2)
N(1)–Pd(1)–O(1)	95.2(2)	N(3)–Pd(2)–O(3)	95.0(2)	N(6)–Pd(3)–O(5)	79.2(2)
N(2)–Pd(1)–O(1)	78.3 (2)	N(4)–Pd(2)–O(3)	78.4(2)	N(5)–Pd(3)–O(5)	93.2(2)

5.3.3.3 Solution Structure of Complex (*R_C*,*S_C*,*S_N*)-220****

The solution structure and signal assignments of diastereomer (*R_C*,*S_C*,*S_N*)-**220** were established on the basis of the ¹H NMR and 2D ¹H-¹H ROESY NMR experiments. In CDCl₃, the 500 MHz ¹H NMR spectrum of complex (*R_C*,*S_C*,*S_N*)-**185** at room temperature shows a sole geometric isomer in solution since there is only one resonance observed for each chemically nonequivalent proton. Figure 5.5 shows the numbering scheme for the NMR study and the 2D ¹H-¹H ROESY NMR spectrum of complex (*R_C*,*S_C*,*S_N*)-**220** is presented in Figure 5.6.

Figure 5.5 Numbering Scheme of Complex (*R_C*,*S_C*,*S_N*)-**220** for NMR Assignment

Figure 5.6 Expanded 2D ^1H - ^1H ROESY NMR Spectrum of Complex (R_C, S_C, S_N) -**220** in CDCl_3 . (refer to Figure 5.5 for the numbering scheme). Selected ROESY Interactions: (A) $\text{NMe}(\text{eq})$ - $\text{H}7$; (B) $\text{NMe}(\text{ax})$ - $\text{H}7$; (C) NH - $\text{Me}2$; (D) $\text{H}7$ - $\text{Me}5$; (E) *tert*-butyl- $\text{H}7$; (F) $\text{NMe}(\text{eq})$ - $\text{NMe}(\text{ax})$; (G) $\text{NMe}(\text{eq})$ -*tert*-butyl; (H) $\text{H}10$ - $\text{H}10'$; (I) $\text{H}10$ - $\text{H}11'$; (J) $\text{Me}5$ -*tert*-butyl; (K) $\text{H}11$ - $\text{H}11'$; (L) $\text{H}8$ - $\text{H}9$.

In this NMR spectrum, strong ROESY interactions between $\text{H}7$ and $\text{NMe}(\text{eq})$ ($\text{NMe}(\text{ax})$, $\text{Me}5$, *tert*-butyl) are clearly recorded (A, B, D, E). The α -*tert*-butyl group interacts strongly with the equatorially disposed NMe group (G), however the interaction between the *tert*-butyl group and the axially disposed NMe group is not observed. This set of ROESY interactions shows that the five-membered palladacycle ring is locked in the δ conformation and hence the *tert*-butyl group is strictly axially disposed. Interactions between $\text{Me}2$ and NH (C) indicates that in solution isomer (R_C, S_C, S_N) -**220** retains a *trans*-

(*N,N*) arrangement, same as observed in the solid state. Furthermore, no ROESY correlation between both NMe groups and the prolinato ligand is observed in the spectrum, confirming the *trans*-(*N,N*) relationship. Other expected ROESY interactions, for example NMe(eq)–NMe(ax) (F); H10–H10' (H); H10–H11' (I); Me5–*tert*-butyl (J); H11–H11' (K) and H8–H9 (L) are also observed

5.3.3.4 Molecular Structure of Diastereomer (*S_C*,*S_C*,*S_N*)-220

For the other diastereomer (*S_C*,*S_C*,*S_N*)-220, yellow colored crystals suitable were obtained from diethyl ether/dichloromethane. There are two crystallographically unique molecules in the asymmetric unit cell with the same stereochemistry but slightly different bond lengths and angles and therefore only one of them (molecule A) is depicted in Figure 5.7. The (*S*) configuration of the α -carbon stereocenter of palladacycle is confirmed independently using (*S_C*,*S_N*)-prolinate as a reference point and based on the anomalous X-ray scattering method with the Flack parameter 0.01(3). The geometric parameters of the molecule are in the range of the values typical for the *ortho*-palladated derivatives of tertiary α -alkyl substituted benzylamines previously studied. The tetrahedral distortion of palladium coordination environment is moderate, with the angle between the {N(1)–Pd(1)–C(1)} and {Cl(1)–Pd(1)–P(1)} planes equal to 6.7°. Consistent with its α -methyl counterpart, the two nitrogen atoms in each molecule are *trans* related.^[9]

Figure 5.7 Molecular structure of complex (S_C,S_C,S_N)-**220** with Thermal ellipsoids at 50% probability. Hydrogen atoms except H(C9), H(N2) and H(C17) are omitted for clarity.

Table 5.3 Selected bond lengths (Å) and angles (°) for complex (S_C,S_C,S_N)-**220**

Molecule A		Molecule B	
Pd(1)–C(1)	2.022(7)	Pd(2)–C(21)	2.016(7)
Pd(1)–N(1)	2.030(1)	Pd(2)–N(3)	2.044(1)
Pd(1)–N(2)	2.065(1)	Pd(2)–N(4)	2.090(1)
Pd(1)–O(1)	2.128(6)	Pd(2)–O(3)	2.116(5)
C(1)–Pd(1)–N(1)	81.2(4)	C(21)–Pd(2)–N(3)	80.6(3)
C(1)–Pd(1)–N(2)	103.1(3)	C(21)–Pd(2)–N(4)	102.0(3)
N(1)–Pd(1)–N(2)	173.4(3)	N(3)–Pd(2)–N(4)	173.5(3)
C(1)–Pd(1)–O(1)	174.6(3)	C(21)–Pd(2)–O(3)	175.8(3)
N(1)–Pd(1)–O(1)	94.0(3)	N(3)–Pd(2)–O(3)	95.9(3)
N(2)–Pd(1)–O(1)	81.5(3)	N(4)–Pd(2)–O(3)	81.7(3)

5.3.3.5 Solution Structure of Complex (S_C, S_C, S_N)-**220**

The solution structure and signal assignments for diastereomer (S_C, S_C, S_N)-**220** were established on the basis of the ^1H NMR and 2D ^1H - ^1H ROESY NMR experiments. Similar to diastereomer (R_C, S_C, S_N)-**220**, the 500 MHz ^1H NMR spectrum of isomer (S_C, S_C, S_N)-**220** at room temperature (CDCl_3) also shows a sole geometric isomer in solution. Figure 5.8 shows the numbering scheme for the NMR study and the 2D ^1H - ^1H ROESY NMR spectrum of (S_C, S_C, S_N)-**220** is presented in Figure 5.9.

Figure 5.8 Numbering Scheme of Complex (S_C, S_C, S_N)-**220** for NMR Studies

In this NMR spectrum, strong ROESY interactions between H7 and NMe(eq) (NMe(ax), Me5, *tert*-butyl) are clearly recorded (A, B, C, D). The α -*tert*-butyl group interacts strongly with the equatorially disposed NMe group (F), however the interaction between the *tert*-butyl group and the axially disposed NMe group is not observed. This ROESY interaction shows that the five-membered palladacycle ring is locked in the λ conformation and hence the *tert*-butyl group is axially disposed. Steric factors are the main driving force for such an arrangement, and it is evident from the interaction (G) between Me5 and *tert*-butyl from the spectrum. The same ROESY experiment gives valuable information regarding the geometry of complex (S_C, S_C, S_N)-**220** and the palladacycle conformation. The newly introduced methyl group Me2 shows strong interaction with NH (E) may be considered as unambiguous support for the *trans*-(N, N)-geometry of proline adduct (S_C, S_C, S_N)-**220**. Furthermore, no ROESY correlation between both NMe groups and the proline ligand is observed in the spectrum, confirming the *trans*-(N, N) relationship. Starting from these data, further assignments of

the other resonances of the proline ligand are performed using the routine spin–spin coupling technique. In addition the other expected signals are also observed in the spectrum, for example H11–H11' (H) and NMe(ax)–NMe(eq) (I).

Figure 5.9 Expanded 2D ^1H - ^1H ROESY NMR Spectrum of (S_C,S_C,S_N)-**220** in CDCl_3 . (refer to Figure 5.8 for the numbering scheme). Selected ROESY Interactions: (A) NMe(eq)–H7; (B) NMe(ax)–H7; (C) H7–Me5; (D) *tert*-butyl–H7; (E) NH–Me2; (F) NMe(eq)–*tert*-butyl; (G) Me5–*tert*-butyl; (H) H11–H11'; (I) NMe(ax)–NMe(eq).

5.3.4 Synthesis of the Palladacycle in the Optically Active Form

5.3.4.1 Formation of Optically Active Palladacycle (*R*)-**211** and (*S*)-**211**

A standard protonation of the auxiliary amino ligand, (R_C,S_C,S_N)-**220**, by 1 M aq.

hydrochloric acid under two-phase conditions readily led to the enantiomerically pure palladium complex dimer (*R*)-**211** in 94.0% isolated yield, $[\alpha]_D -208$, $[\alpha]_{578} -214$, $[\alpha]_{546} -224$, (*c* 0.5, dichloromethane) (Scheme 5.4).

Scheme 5.4

Similarly the other proline derivative, (*S_C*, *S_C*, *S_N*)-**220**, was converted to its respective dichloro dimer (*S*)-**211** in a similar manner, using dilute aq. hydrochloric acid in 94.0% yield, $[\alpha]_D +210$, $[\alpha]_{578} +216$, $[\alpha]_{546} +228$, (*c* 0.5, dichloromethane) (Scheme 5.5).

Scheme 5.5

5.3.4.2 Formation of Optically Active Palladacycle (*R*)-221

Unfortunately, the optically active dimeric palladium complexes, (*R*)-**211** and (*S*)-**211** could not be crystallized even after using an array of solvent systems. Thus, a conversion of this dimeric (*R*)-**211** to its perchlorate salt derivative (*R*)-**221** by treatment with excess silver perchlorate monohydrate in acetonitrile was performed, $[\alpha]_D -124$, $[\alpha]_{578} -128$, $[\alpha]_{546} -148$, (*c* 0.5, dichloromethane) (Scheme 5.6), to solve this problem.

Scheme 5.6

5.3.4.3 Molecular Structure of Complex (R)-221

X-ray quality single crystals of complex (R)-**221** were obtained as yellow colored crystals from a dichloromethane/hexane mixture which allowed the determination of the absolute configuration of the chiral palladacycle by crystal diffractometry. Its molecular structure is presented in Figure 5.10 while selected bond lengths and angles are given in Table 5.4. X-ray investigations of complex (R)-**221** reveals that the *tert*-butyl group at the *R* chiral center is located in the axial position. The geometry at palladium is distorted square planar with one molecule of H₂O and one molecule of CH₃CN coordinated *cis* and *trans* to the NMe₂, respectively. The dihedral angle between the planes {N(1)–C(1)–Pd(1)} and {O(1)–N(2)–Pd(1)} is 5.7°.

Table 5.4 Selected bond lengths (Å) and angles (°) for complex (R)-**221**

Pd(1)–C(1)	1.989(2)	Pd(1)–N(2)	2.015(2)
Pd(1)–N(1)	2.052(1)	Pd(1)–O(1)	2.207(2)
C(1)–Pd(1)–N(2)	100.2(7)	C(1)–Pd(1)–N(1)	81.7(6)
N(2)–Pd(1)–N(1)	176.1 (6)	C(1)–Pd(1)–O(1)	173.3(7)
N(2)–Pd(1)–O(1)	85.3(6)	N(1)–Pd(1)–O(1)	93.1(6)
C(2)–C(1)–Pd(1)	127.5(1)	C(8)–C(1)–Pd(1)	112.2(1)

Figure 5.10 Molecular structure of complex (*R*)-**221** with thermal ellipsoids at 50% Probability. Hydrogen atoms except H(C9) and H(O1) are omitted for clarity.

5.3.5 Regio-Selective Formation of the dmpp Complex (*S*)-**222** and Its *endo*-Cycloaddition Reaction with Ethyl Vinyl Ketone

In order to evaluate the efficiency of the new palladacycle (*S*)-**211** as a chiral template for intermolecular *endo* cycloaddition reaction, the intermediate dmpp complex (*S*)-**222** was synthesized. This was achieved through the cleavage of the chloro bridge of the dimeric complex (*S*)-**221** with dmpp. The reactions between (*S*)-**222** and ethyl vinyl ketone was subsequently investigated.

5.3.5.1 Formation and Isolation of Complex (*S*)-**222**

As shown in Scheme 5.7, the dichloro bridge in complex (*S*)-**211** could be readily cleared by addition of the phosphine ligand dmpp at room temperature in 1 h, affording complex (*S*)-**222** as a yellow powder in 95.0% yield, $[\alpha]_D +408$ (c 0.5 dichloromethane).

Scheme 5.7

5.3.5.2 Solution Structure of the dmpp Complex (S)-222

The ^{31}P NMR spectrum in CDCl_3 gave only one singlet at δ 27.7 which indicates the presence of a sole isomer in solution. In the ^1H NMR spectrum, the P-H coupling constant value (5.0 Hz) observed for the resonance signal of the proton attached to the α -carbon, means that the phosphole is *trans* to the nitrogen atom in solution. Unfortunately, complex (S)-222 could not be crystallized because of its excellent solubility in a variety of solvents and therefore the X-ray structure could not be obtained for analysis. Therefore the solution structure of complex (S)-222 was studied by a combination of its ^1H NMR spectrum and 2D ^1H - ^1H ROESY NMR spectrum (Figure 5.12). Figure 5.11 shows the numbering scheme of complex (S)-222.

Figure 5.11 Numbering Scheme of Complex (S)-222

In the NMR spectrum, strong ROESY correlations (A, B, C, D) show the interactions between H7 and NMe(eq) (NMe(ax), Me5, *tert*-butyl). The interaction between α -*tert*-butyl group and NMe(eq) (F), together with the absence of the interaction between the *tert*-butyl group and NMe(ax) indicates that the five-membered palladacycle ring is strictly locked in the λ conformation and the *tert*-butyl group is axially located.

Interactions (G) Me5-*tert*-butyl and (F) NMe(ax)–NMe(eq) are also reflected in the spectrum. This ROESY experiment gives valuable information regarding the geometry of complex (S)-**222** and the palladacycle conformation. The interaction (H) between H10 and Me2 may be considered as an unambiguous support for the *trans*-(*N,P*)-geometry of prolinato adduct (S)-**222**. In addition, no ROESY correlation between both NMe groups and the prolinato ligand is observed in the spectrum which confirms the *trans*-(*N,P*) relationship. Some other expected ROESY correlations, H10–Me11 (I); H3–Me2 (J); H4–Me5 (K) and H8–Me9 (L), are recorded.

Figure 5.12 2D ^1H - ^1H ROESY NMR Spectrum of complex (S)-**222** in CDCl_3 . (refer to Figure 5.11 for the numbering scheme). Selected ROESY Interactions: (A) NMe(eq)-H7; (B) NMe(ax)-H7; (C) H7-Me5; (D) *tert*-butyl-H7; (E) NMe(ax)-NMe(eq); (F) NMe(eq)-*tert*-butyl; (G) Me5-*tert*-butyl; (H) H10-Me2; (I) H10-Me11; (J) H3-Me2; (K) H4-Me5; (L) H8-Me9; (#) CDCl_3 ; (*) dichloromethane.

5.3.5.3 The Intermolecular *endo*-Cycloaddition Reaction Between (S)-**222** and Ethyl Vinyl Ketone

Complex (S)-**222** was treated with excess ethyl vinyl ketone in dichloromethane and stirred at room temperature. After 7 days no new peaks were observed according to the ^{31}P NMR spectrum, indicating that no reaction had occurred. Even after the temperature was raised to 50 °C in chloroform, no reaction occurred. When the reaction mixture was further heated to 70 °C in dichloroethane, the peak of complex (S)-**222** disappeared and two sharp singlets at δ 130.7 and 131.0 ppm in a 1:1 diastereomeric ratio were observed after 6 days. However, the solution also appeared to darken, indicating the possible decomposition of Pd(II) to Pd(0) and/or the formation of PdO. Clearly the auxiliary did not exert the desired stereochemical influence as we had expected (Scheme 5.8).

Scheme 5.8

It should be noted that, as mentioned in early chapters, the dmpp derivative (S)-**176**, methyl analogue of (S)-**211**, gave the cycloadducts in the ratio of 1:3.5 at 50 °C when it was treated with ethyl vinyl ketone. However in this instance, the dmpp complex (S)-**222**

formed the cycloadducts in the ratio of 1:1 at 70 °C with partial palladium decomposition observed. In addition, another reaction was attempted in order to support these observations using *N,N*-dimethylacrylamide. However even after 10 days at 70 °C in dichloroethane no reaction took place according to the ^{31}P NMR spectrum

Disappointingly, not only does the chiral auxiliary not exhibit good selectivity in these reactions, reactions did not proceed well at all. Comparing the structures of complex (*S*)-**176** and complex (*S*)-**222**, the only difference is the substituent (Me for (*S*)-**176** and *tert*-butyl for (*S*)-**222**) at the α -carbon center. However the slight difference in structure results in big differences in both stereoselectivity and reactivity as discussed above. It appears that the steric interaction manifested by the axially disposed *tert*-butyl with the dmpp heavily reduces the reactivity of the complex. As shown in Scheme 5.9, the *endo* product is always formed as a result of the stabilizing bonding interaction in the transition state between the carbonyl group on the dienophile and the back of the diene (Scheme 5.9).

Scheme 5.9

From a mechanistic view point, the discriminative formation of the two diastereomers are governed by the reaction transition states I and II shown in Figure 5.13. As illustrated in the dmpp complexes, for example complex (*S*)-**186** and (*S*)-**197**, the phenyl ring of the coordinated dmpp moiety is oriented towards the space above the five-membered heterocycle and thus restricts the approach of the dienophile to the *re*-face of the α -carbons of dmpp. Therefore, the *si*-face of the α -carbons of dmpp is attacked

preferentially. In the complex (*S*)-**222**, however, the *si*-face is very close to the bulky *tert*-butyl which could prevent the dienophile approaching from this angle. The only way for the dienophile to attack the heterocycle is to approach from the spatially crowded *re*-face, leading to the poor reactivity observed (Figure 5.13).

Figure 5.13 Two Possible Transition States of the *endo*-Cycloaddition Reaction

5.3.6 Chiral Palladium Template (*R*)-**211** promoted Asymmetric Hydrophosphination Reaction between Diphenylphosphine and Diethyl Acetylenedicarboxylate

5.3.6.1 Introduction

In terms of synthetic value and atom economy, the addition of P–H bonds to saturated compounds is an important reaction in organophosphorus chemistry. Addition of the P–H bonds to the carbon-carbon unsaturated compounds can proceed *via* thermal, acidic, basic, or free radical pathways. However, the use of transition metal complexes for such addition reactions often offers vast improvement in rate, selectivity and stereocontrol. Moreover, many functional groups can be incorporated into the substrates without special protection as relatively mild reaction conditions are usually required in these metal activated addition reactions. Therefore recently the optically active *ortho*-palladated naphthalene complex **11** has been applied in asymmetric hydrophosphination reaction in our research group.^[190-192]

Functionalities play a significant role in classical organic chemistry, as in certain cases they can determine the fundamental physical and chemical properties of the organic molecules that they are attached to.^[193] Therefore by introducing different particular functional groups into enantiomerically pure phosphine ligands, their reactivity as efficient catalysts in asymmetric synthesis may be enhanced. Indeed, optically active phosphine ligands containing selected functionalities have been extensively used in asymmetric organic synthesis, biochemistry and chemotherapy.^[169,194]

However in some previous synthesis, the hydrophosphination reactions promoted by **11** exhibit poor stereoselectivity, forming mixtures and resulting in low yields of the target enantiomers due to the tedious separation process by either slow crystallization and/or column chromatography.^[190-192] In order to study the asymmetric synthesis of chiral diphosphines *via* the addition of P–H bonds to unsaturated carbon–carbon bonds, we applied these chiral cyclopalladated-amine complexes in the synthesis of diphosphines by means of asymmetric hydrophosphination reactions.^[192]

5.3.6.2 Research Objective

Despite the poor stereoselectivity in the *endo*-cycloaddition reactions, this new chiral palladacycle template could have greater success in promoting asymmetric hydrophosphination reactions. In pursuit of our interest in the design of new chiral palladacycles and subsequent improvements of the stereoselectivity in asymmetric reactions (for example hydrophosphination reaction here), the novel palladacycle **211** was applied in asymmetric hydrophosphination reaction. As discussed earlier, the interaction between the aromatic methyl group Me5 and the *tert*-butyl group locks the five-membered palladacycle in a fixed conformation in solution and the *tert*-butyl is axially located. Secondly, methyl group Me2 is introduced on the aromatic ring next to the Pd–C

bond; through this introduction the stereochemistry of the coordination site *trans* to the N donor atom is controlled more efficiently. Most importantly, the strictly axially located *tert*-butyl group on the prochiral carbon enhances the interaction between it and the NMe groups and this interactions would have a stronger steric effect on the reaction site *cis* to the N donor atom. In order to evaluate the above structure and hypothesis, a hydrophosphination reaction between diphenylphosphine and diethyl acetylenedicarboxylate promoted by the chiral palladium complex derivative (*R*)-**221** was hereby examined.

5.3.6.3 Asymmetric Hydrophosphination Reaction between Diphenylphosphine and Diethyl Acetylenedicarboxylate promoted Chiral Palladium Complex Derivative (*R*)-**221**

In order to evaluate the stereoselectivity of the new palladacycle, the asymmetric hydrophosphination reaction between diphenylphosphine and diethyl acetylenedicarboxylate promoted by palladacycle (*R*)-**211** was investigated.

As illustrated in Scheme 5.10, two equivalents of diphenylphosphine was allowed to coordinate to complex (*R*)-**221** in dichloromethane yielding complex (*R*)-**224**, ^{31}P NMR spectrum of which showed a pair of doublets at δ -14.8 and 2.0 ($J_{\text{P,P}} = 42.6$ Hz). The hydrophosphination reaction between diphenylphosphine and diethyl acetylenedicarboxylate was carried out at -78 °C in the presence of 20% equivalent of NEt_3 in dichloromethane. The reaction was monitored by ^{31}P NMR spectroscopy and was found to be complete in 12 h. The ^{31}P NMR spectrum of the reaction mixture in CDCl_3 exhibited only one pair of doublets and the resonances were observed at δ 30.2 and 39.5 ($J_{\text{P,P}} = 40.5$ Hz). This indicated that only one isomer was generated in the hydrophosphination reaction. Theoretically there should be four possible isomers formed

in this reaction, adopting the (*R,R,S*), (*R,RR*), (*R,SR*) and (*R,SS*) configurations. However in both the (*R,R,S*) and (*R,SR*) diastereomers, one of the ester substituents must occupy the sterically unfavorable axial position, regardless of the conformation adopted by the five-membered ring. On the other hand, in both the (*R,RR*) and (*R,SS*) diastereomers, the ester substituents can occupy the sterically favorable equatorial position. Therefore, a logical hypothesis that the sole product obtained in the asymmetric hydrophosphination reaction is either isomer (*R,RR*)-**225** or isomer (*R,SS*)-**225**.

Scheme 5.10

However, the cationic product could not be crystallized from a series of solvent systems. Hence a dichloromethane solution of this complex was subsequently treated with concentrated HCl to remove the amine auxiliary chemoselectively giving the dichloro complex (*S,S*)-**226** which was confirmed by X-ray study.

5.3.6.4 Molecular Structure of Complex (*S,S*)-**226**

In CDCl₃, the dichloro palladium complex (*S,S*)-**226** exhibited a sharp singlet at δ 57.7 when monitored by ³¹P NMR spectroscopy. Slow crystallization of the dichloro complex (*S,S*)-**226** using dichloromethane and diethyl ether resulted in the formation of yellow colored crystals suitable for single-crystal X-ray diffraction analysis, 0.10 g, 70.0%, [α]₄₃₆ –138 (*c* 0.5, dichloromethane). The molecular structure and the absolute stereochemistry of complex (*S,S*)-**226** was determined by X-ray crystallography. There are two crystallographically distinguished molecules in the asymmetric unit with the same stereochemistry and only one of them is depicted in Figure 5.14. Selected bond distances and angles are given in Table 5.5. The absolute stereochemistry at C29 and C29A were established to be *S* and both the ester substituents on the chiral carbon centers were in the equatorial position. Thus, the asymmetric hydrophosphination reaction demonstrated that only one isomer (*R,SS*)-**225** was generated in presence of our new chiral palladacycle (*R*)-**211**.

Table 5.5 Selected bond lengths (Å) and angles (°) for complex (*S,S*)-**226**

Molecular A		Molecular B	
Pd(1)–P(1)A	2.233(6)	Pd(2)–P(2)	2.229(6)
Pd(1)–P(1)	2.233(6)	Pd(2)–P(2)A	2.229(6)
Pd(1)–Cl(1)	2.355(6)	Pd(2)–Cl(2)A	2.348(7)
Pd(1)–Cl(1)A	2.355(6)	Pd(2)–Cl(2)	2.348(7)
P(1)A–Pd(1)–P(1)	87.4(3)	P(2)–Pd(2)–P(2)A	87.9(3)
P(1)A–Pd(1)–Cl(1)	173.6(2)	P(2)–Pd(2)–Cl(2)A	176.3(2)

P(1)–Pd(1)–Cl(1)	89.0(2)	P(2)A–Pd(2)–Cl(2)A	88.9(2)
P(1)A–Pd(1)–Cl(1)A	89.0(2)	P(2)–Pd(2)–Cl(2)	88.9(2)
P(1)–Pd(1)–Cl(1)A	173.6(2)	P(2)A–Pd(2)–Cl(2)	176.3(3)
Cl(1)–Pd(1)–Cl(1)A	95.1(3)	Cl(2)A–Pd(2)–Cl(2)	94.5(3)

Figure 5.14 Molecular structure of complex (*S,S*)-**226** with thermal ellipsoids at 50% Probability. Hydrogen atoms except H(C29) and H(C29A) are omitted for clarity.

It needs to be noted that the optically active diphosphine ligand (*S,S*)-**227** could be stereospecifically liberated from (*S,S*)-**226** by treating the dichloro complex with aqueous potassium cyanide, liberating complex (*S,S*)-**227** as an air-sensitive ligand in 95.0% yield, $[\alpha]_{\text{D}} +300$ (*c* 0.5, dichloromethane). In CDCl_3 , only a sharp singlet was observed at $\delta -6.4$.

The optical purity of compound (*S,S*)-**227** was confirmed by the quantitative reparation of isomer (*R,SS*)-**225** from the liberated ligand and complex (*R*)-**221** (Scheme 5.11). In CDCl₃, the crude product ³¹P NMR spectrum exhibited only a pair of doublet signals at δ 39.5 ($J_{\text{P,P}} = 40.5$ Hz) and 30.2 ($J_{\text{P,P}} = 40.5$ Hz). These signals are identical to those recorded for the sole diastereomer (*R,SS*)-**225**, which was generated directly from the asymmetric hydrophosphination reaction. As a further test of the optical purity of the liberated ligand, the liberated free ligand (*S,S*)-**227** was recoordinated to the equally accessible isomer (*S*)-**221**. The ³¹P NMR spectrum of the crude product in CDCl₃ exhibited only a pair of doublets at δ 45.0 ($J_{\text{P,P}} = 43.0$ Hz) and 34.6 ($J_{\text{P,P}} = 43.0$ Hz). The chemical shift of these signals were different from the signals for the sole product that was generated from the previous mentioned hydrophosphination reaction. Hence, it could be confirmed that the liberated diphosphine (*S,S*)-**227** is optically pure and in the asymmetric hydrophosphination reaction, only one isomer (*R,SS*)-**225** was generated in presence of our new chiral palladacycle (*R*)-**211**.

Scheme 5.11

Worthy to note, when the widely used naphthylethylamine auxiliary (*R*)-**11** was employed for the analogous asymmetric hydrophosphination reaction between diphenylphosphine and diethyl acetylenedicarboxylate under the same reaction condition, two sets of doublets were observed in the ^{31}P NMR spectrum at δ 56.4 (d, $J_{\text{P,P}} = 37.0$ Hz), 54.8 (d, $J_{\text{P,P}} = 39.0$ Hz), 35.6 (d, $J_{\text{P,P}} = 37.0$ Hz), 35.2 (d, $J_{\text{P,P}} = 39.0$ Hz) in a ratio of 1:7:1:7. The above experiments indicate that two isomers were formed in a 1:7 ratio in the asymmetric hydrophosphination reaction between diphenylphosphine and diethyl acetylenedicarboxylate promoted by the chiral palladacycle (*R*)-**11**. Therefore compared to palladacycle (*R*)-**11**, palladacycle (*R*)-**211** exhibits excellent selectivity (>99 %) in this asymmetric hydrophosphination reaction.

5.3.6.5 Mechanistic Considerations

Considering in this case that the first step is coordination of the phosphine ligands onto the metal, we believe that this is followed by the activation of the P–H bonds by the metal. Upon coordination of secondary phosphines to palladium, the P–H proton is relatively acidic and can undergo proton exchange with the solvents.^[190-192] In the presence of a base, a nucleophilic phosphido complex can be generated which subsequently undergoes nucleophilic addition to the alkyne to give the product(s).

Using the formation of complex (*R,SS*)-**225** as the example, Scheme 5.12 describes pathways A and B, illustrating a steric explanation for the generation of the sole isomer (*R,SS*)-**225**. Usually, four stereomeric products are expected from a system with two chiral centers. Only two have been depicted here as the others would produce isomers with the substituted ester functions axially disposed, which is particularly unfavorable and have been found not to form.

Scheme 5.12 Transition states and reaction pathways A and B for the hydrophosphination reaction between (*R*)-**221** and diethyl acetylenedicarboxylate.

Pathway A describes the five-membered ring in the product being formed in a λ conformation *via* transition state A. This is sterically unfavorable given the eclipsing shown between both of the methyl groups bound to the nitrogen atom with the phenyl groups bound to the phosphorus atom. In contradiction, transition state B is in the δ conformation with minimal steric clashing. As a result this is the major isomer in these hydrophosphination reactions. In this chapter, the novel organopalladium complex only produces the sole isomer (*R,SS*)-**225**, which is because of the extreme projection of the α -*tert*-butyl into the NMe groups. This increases the severity of the steric clashing in transition state B to such an extent that pathway A does not occur.

5.3.7 Conclusion

In this chapter, a novel palladacycle **211** was readily designed from 1,4-dimethylbenzene which was then resolved through the separation of the (*S*)-proline diastereomeric derivatives. It was found that the five-membered *ortho*-palladium ring exists in one conformation, either the (*S*) λ or the (*R*) δ , as a result of extreme steric hindrance from the aromatic methyl group and the bulky *tert*-butyl group. This was found to be the case in both the solid state proven by X-ray structural analysis and solution state proven by 2D ^1H - ^1H ROESY NMR spectroscopy. The preparation of a novel chiral diester-substituted diphosphine *via* the chiral palladacycle (*R*)-**211** promoted asymmetric hydrophosphination reaction was demonstrated and this hydrophosphination reaction between diphenylphosphine and diethyl acetylenedicarboxylate proceeded with excellent stereoselectivity (>99 %).

It was also demonstrated that as a result of the *tert*-butyl group and the protruding methyl group on the aromatic ring, the novel μ -chloride palladacycle failed to exert good stereoselectivity in *endo*-cycloaddition reaction and the temperature had to be raised to 70 °C, at which point the palladium complex slowly decomposes, in order for it to proceed at all. Hence, in comparison to other organometallic chiral auxiliaries used for this *endo*-cycloaddition reaction, it is not as effective.

5.4 Experimental

Reactions involving air-sensitive compounds were performed under a positive pressure of purified nitrogen using standard Schlenk techniques. Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectroscopy were performed on Bruker Avance 300, 400 and 500 NMR spectrometers. The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported

as a J value in Hz. Proton nuclear magnetic resonance spectra ^1H NMR are reported as δ in units of parts per million (ppm) downfield from SiMe_4 (δ 0.0). Carbon nuclear magnetic resonance spectra ^{13}C NMR are reported as δ in units of parts per million (ppm) relative to the signal of chloroform- d (δ 77.00, triplet). All the ^{31}P NMR spectra were recorded at 121 MHz on a Bruker Advance DPX300 NMR spectrometer. Unless stated otherwise, all NMR spectroscopic experiments were performed at room temperature (300 K). Chemical shifts (δ) are reported in ppm relative to TMS, and referenced to the chemical shifts of residual solvent resonances (^1H and ^{13}C NMR) or 85% H_3PO_4 (^{31}P NMR). Mass spectra were recorded on a Thermo Finnigan MAT 95 XP Mass Spectrometer with EI mode and Waters Q-ToF Premier Mass Spectrometer with ESI mode. Melting points were determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured on the specified solution in 0.1-dm cell at 20 °C with a Perkin-Elmer model 341 polarimeter. Elemental analyses were performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at the Nanyang Technological University of Singapore.

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

5.4.1 Synthesis of 1-Isobutyryl-2,5-dimethylbenzene, **213**

A isobutyryl chloride (5.3 mL, 50 mmol) dichloromethane solution was added to a suspension of anhydrous AlCl_3 (7.34 g, 55 mmol) in the same solvent (30 mL). A solution of *p*-xylene **212** (5.30 g, 50 mmol) was then added dropwise to the mixture. The orange mixture was allowed to stir at room temperature for 3 h which was then poured into a mixture of ice water and conc. hydrochloric acid (40 mL) and stirred for 10 min. The mixture was extracted with dichloromethane. The organic layers were combined, washed

with H₂O and dried (MgSO₄). Removal of solvent gave the product **213** as yellow oil, 8.18 g, (93.0%). ¹H NMR (400 MHz, CDCl₃): δ = 1.16 (d, ³J_{H,H} = 6.8 Hz, 6 H, CHCH₃), 2.35 (s, 3 H, aryl-CH₃), 2.37 (s, 3 H, aryl-CH₃), 3.30–3.37 (m, ³J_{H,H} = 6.8 Hz, 1 H, CHCH₃), 7.10–7.15 (m, 2 H, aromatic protons), 7.29 (s, 1 H, aromatic proton) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 18.55, 20.21, 20.95, 38.77, 127.91, 131.26, 131.47, 134.17, 135.00, 138.68, 209.53 ppm. HRMS (EI, m/z) calcd for C₁₂H₁₆O 176.1196, found 176.1191.

5.4.2 Synthesis of 1-(2,5-dimethylphenyl)-2,2-dimethylpropan-1-one, **214**

A solution of compound **213** (16.6 g, 94.4 mmol) in dry THF (100 mL) was added dropwise to 60 % NaH (4.32 g, 108 mmol) solution in the same solvent under nitrogen and the pale yellow solution was refluxed for 1 h. The orange-brown solution was cooled to room temperature and CH₃I (15 mL, 188 mmol) was added dropwise. The mixture was heated at 50 °C for 1 h then cooled to 0 °C. Ice water was added to quench the excess NaH and the organic phase was extracted using diethyl ether, washed with H₂O and dried (MgSO₄). Removal of the solvent gave the product **214** as yellow oil, 13.9 g (77.9%). ¹H NMR (400 MHz, CDCl₃): δ = 1.25 (s, 9 H, CCH₃), 2.18 (s, 3 H, aryl-CH₃), 2.31 (s, 3 H, aryl-CH₃), 6.92 (s, 1 H, aromatic proton), 7.04–7.09 (m, 2 H, aromatic protons) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 19.33, 21.10, 27.25, 45.04, 124.94, 129.25, 130.58, 134.33, 140.99, 215.19 ppm. HRMS (ESI, m/z (M + H))⁺ calcd for C₁₃H₁₉O 191.1436, found 191.1437.

5.4.3 Synthesis of 1-(2,5-dimethylphenyl)-2,2-dimethylpropan-1-ol, (±)-**215**

A suspension of compound **214** (13.9 g, 73.5 mmol) in ethanol (100 mL) was treated with NaBH₄ (5.56 g, 147 mol) in the same solvent and allowed to stir overnight at room

temperature followed by treatment with dilute NaOH solution. The resulting clear solution was concentrated under vacuum and extracted with dichloromethane. The organic layers were combined, washed with H₂O and dried (MgSO₄). Removal of the solvent gave the product (±)-**215** as yellow oil, 12.3 g (87.5%). ¹H NMR (500 MHz, CDCl₃): δ = 0.97 (s, 9 H, CCH₃), 1.72 (s, 1 H, OH), 2.31 (s, 3 H, aryl-CH₃), 2.33 (s, 3 H, aryl-CH₃), 4.75 (d, ³J_{H,H} = 3.5 Hz, 1 H, CH), 6.98 (d, ³J_{H,H} = 7.5 Hz, 1 H, aromatic proton), 7.02 (d, ³J_{H,H} = 7.7 Hz, 1 H, aromatic proton), 7.29 (s, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 20.00, 21.28, 26.13, 36.89, 76.75, 127.81, 128.16, 130.14, 132.67, 134.77, 140.67 ppm. HRMS (ESI, m/z (M + H))⁺ calcd for C₁₃H₂₁O 192.1592, found 192.1603.

5.4.4 Synthesis of 2-(1-azido-2,2-dimethylpropyl)-1,4-dimethylbenzene, (±)-216 A mixture of compound (±)-**215** (5.80 g, 30 mmol) and sodium azide (3.00 g, 45 mmol) in chloroform (30 mL) were cooled below 0 °C. A solution of trifluoroacetic acid (18 mL) in chloroform (15 mL) was added slowly. The mixture was left to stir overnight at ambient temperature and a dilute NaOH solution was added till pH = 7. The organic layer was separated, washed with H₂O and dried (MgSO₄). Removal of solvent gave the product (±)-**216** yellow oil, 6.23 g (95.1%). ¹H NMR (300 MHz, CDCl₃): δ = 1.03 (s, 9 H, CCH₃), 2.40 (s, 3 H, aryl-CH₃), 2.41 (s, 3 H, aryl-CH₃), 4.70 (s, 1 H, CH), 7.05–7.13 (m, 2 H, aromatic protons), 7.22 (s, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 20.08, 21.26, 26.57, 37.01, 71.20, 128.41, 128.91, 130.42, 133.22, 135.09, 136.00 ppm. HRMS (EI, m/z (M – N₃)) calcd for C₁₃H₁₉ 175.1481, found 175.1477.

5.4.5 Synthesis of 1-(2,5-dimethylphenyl)-2,2-dimethylpropan-1-amine, (±)-217

A solution of compound (±)-**216** (5.30 g, 24.4 mmol) in dry THF (50 mL) was added

dropwise to a stirred solution of LAH (1.82 g, 48.0 mmol) in the same solvent (100 mL) at 0 °C. The reaction was then heated to reflux for 3 h and then cooled to 0 °C. The excess LAH was quenched by consecutive addition of cold ethyl acetate and ice water. The granular precipitate was removed by filtration under vacuum and the filtrate was dried (MgSO₄). Removal of solvent gave the amine product (±)-**217** light yellow oil, 3.98 g (85.4%). ¹H NMR (300 MHz, CDCl₃): δ = 1.01 (s, 9 H, CCH₃), 1.51 (br, 2 H, NH), 2.37 (s, 6 H, aryl-CH₃), 4.09 (s, 1 H, CH), 6.99 (dd, ⁴J_{H,H} = 1.6 Hz, ³J_{H,H} = 7.7 Hz, 1 H, aromatic proton), 7.05 (d, ³J_{H,H} = 7.7 Hz, 1 H, aromatic proton), 7.31 (s, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 20.26, 21.30, 26.64, 36.30, 58.60, 127.13, 128.08, 130.08, 132.86, 134.63, 142.30 ppm. HRMS (ESI, m/z (M + H))⁺ calcd for C₁₃H₂₂N 192.1752, found 192.1750.

5.4.6 1-(2,5-dimethylphenyl)-N,N,2,2-tetramethylpropan-1-amine, (±)-**218**

A solution of compound (±)-**217** (13.2 g, 69.1 mmol) in formic acid (24 mL) was treated with formaldehyde (35 mL) at 0 °C. The reaction mixture was heated to 100 °C for 6 h and was then cooled to room temperature. Concentrated hydrochloric acid (10 mL) was added and stirred for 15 min. After removal of solvent under vacuum, the sticky residual oil was treated with NaOH solution to pH = 14 and the liberated amine was extracted with dichloromethane. The organic layers were combined and dried (MgSO₄). After removing the solvent, the product (±)-**218** was obtained as yellow oil, 12.7 g (84.0%). ¹H NMR (300 MHz, CDCl₃): δ = 1.06 (s, 9 H, CCH₃), 2.30 (s, 6 H, NCH₃), 2.34 (s, 3 H, aryl-CH₃), 2.35 (s, 3 H, aryl-CH₃), 3.56 (s, 1 H, CH), 6.98 (dd, ⁴J_{H,H} = 1.3 Hz, ³J_{H,H} = 7.7 Hz, 1 H, aromatic proton), 7.07 (d, ³J_{H,H} = 7.7 Hz, 1 H, aromatic proton), 7.25 (s, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 21.00, 21.45, 29.18, 36.18, 45.44, 71.68, 126.92, 129.37, 130.25, 134.07, 134.26, 137.94 ppm. HRMS (ESI, m/z (M + H))⁺ calcd for C₁₅H₂₆N 220.2065, found 220.2059.

5.4.7 ($\pm$)-Di- μ -chlorobis[1-[1-(dimethylamino)-2,2-dimethylpropyl]-2,5-dimethyl- 6-phenyl-*C,N*]dipalladium(II), ($\pm$)-**211**

A mixture of palladium(II) chloride (10.3 g, 58.7 mmol) and lithium chloride (9.24 g, 220 mmol) in methanol (100 mL) was stirred at room temperature for 3 h. Sodium acetate trihydrate (8.02 g, 59.0 mmol) was then dissolved in the solution followed by addition of compound ($\pm$)-**211** (12.7 g, 58.0 mmol). The resulting mixture was stirred at room temperature for 5 h and filtered through Celite. The filtrate was evaporated under vacuum and the brown residue was dissolved in dichloromethane. The resulting solution was washed with H₂O, dried (MgSO₄) and evaporated. The crude product was purified by chromatography on a silica gel column using dichloromethane and hexane (V/V = 1/1) as the eluent (14.17 g, 67.9%). M.p. 129–130 °C (dec.), Anal Calcd for C₃₀H₄₈Cl₂N₂Pd₂ (720.46): C, 50.01; H, 6.72; N, 3.89. Found: C, 50.05; H, 6.72; N, 3.26. ¹H NMR (300 MHz, CDCl₃): δ = 1.64–1.69 (m, 18 H, CCH₃), 2.24 (s, 6 H), 2.51–2.57 (m, 12 H), 2.70–2.78 (m, 6 H), 3.48–3.50 (m, 2 H, CH), 6.58–6.66 (m, 4 H, aromatic protons) ppm.

5.4.8 Synthesis of ($\pm$)-Chloro[1-[1-(dimethylamino)-2,2-dimethylpropyl]-2,5-dimethyl- 6-phenyl-*C,N*] (triphenylphosphine-*P*)palladium(II), ($\pm$)-**219**

A dichloromethane solution of complex ($\pm$)-**211** (0.184 g, 0.250 mmol) and triphenylphosphine (0.131 g, 0.500 mmol) was stirred for 1 h at r.t. and concentrated to ca 5 mL. The residue liquid was chromatographed on a silica gel column using dichloromethane as the eluent to give a light yellow powder which was recrystallized from dichloromethane/hexane as light yellow crystals, ($\pm$)-**219**, 0.28 g (91.0%), M.p. 170–172 °C (dec.), Anal Calcd for C₃₃H₃₉ClNPPd (621.15): C, 63.67; H, 6.31; N, 2.25. Found: C, 63.95; H, 6.31; N, 2.53. ³¹P NMR (121 MHz, CDCl₃): δ = 30.0 (s) ppm. ¹H NMR (500 MHz, CDCl₃): δ = 1.46 (s, 9 H, CCH₃), 1.71 (s, 3 H, aryl-CH₃), 2.30 (s, 3 H,

aryl-CH₃), 2.37 (s, $^4J_{\text{P,H}} = 1.5$ Hz, 3 H, NCH₃), 2.90 (d, $^4J_{\text{P,H}} = 3.4$ Hz, 3 H, NCH₃), 3.60 (d, $^4J_{\text{P,H}} = 5.2$ Hz, 1 H, CCH), 6.41 (dd, $^3J_{\text{H,H}} = 7.6$ Hz, $^5J_{\text{P,H}} = 1.4$ Hz, 1 H, aromatic proton), 6.64 (d, $^3J_{\text{H,H}} = 7.6$ Hz, 1 H, aromatic proton), 7.20–8.00 (m, 15 H, aromatic protons) ppm. ¹³C NMR (125 MHz, CDCl₃): $\delta = 23.46$, 27.75 (d, $J_{\text{C,P}} = 10.8$ Hz), 31.68, 36.22, 51.29 (d, $J_{\text{C,P}} = 1.4$ Hz), 53.56 (d, $J_{\text{C,P}} = 2.76$ Hz), 88.38 (d, $J_{\text{C,P}} = 2.5$ Hz), 126.97, 127.76 (br.), 130.11 (br.), 131.11, 134.12 (br.), 136.52 (br.), 139.78 (d, $J_{\text{C,P}} = 5.3$ Hz), 149.92 (d, $J_{\text{C,P}} = 1.3$ Hz), 158.70 (d, $J_{\text{C,P}} = 3.8$ Hz) ppm. HRMS (ESI, m/z (M – Cl)]⁺ calcd for C₃₃H₃₉NPPd 586.1855, found 586.1874.

5.4.9 Synthesis and Separation of (*S*_C,*S*_C,*S*_N)-Prolinato-[1-[1-(dimethylamino)- 2,2-dimethylpropyl]-2,5-dimethyl-6-phenyl-*C,N*]palladium(II), (*S*_C,*S*_C,*S*_N)-220

A methanol solution of sodium (*S*)-prolinate (0.83 g, 6 mmol) was added to a suspension of the racemic dimer (±)-**211** (2.18 g, 3 mmol) in the same solvent (30 mL). The mixture was stirred at room temperature for 1 h and the solvent was removed under pressure. The residue was then dissolved in dichloromethane, washed with H₂O and dried (MgSO₄). Removal of solvent gave light yellow solid which was dissolved in minima dichloromethane. By slowly addition of diethyl ether, the less soluble diastereomer (*S*_C,*S*_C,*S*_N)-**220** was crystallized as yellow needle-like crystals, 1.01 g, 77.0%. M.p. 185–187 °C (dec.), [α]_D +246, [α]₅₇₈ +256, [α]₅₄₆ +292, [α]₄₃₆ +562, [α]₃₆₅ +890 (*c* 0.5, dichloromethane). Anal Calcd for C₂₀H₃₂N₂O₂Pd (438.15): C, 54.73; H, 7.35; N, 6.38. Found: C, 54.75; H, 7.79; N, 6.42. ¹H NMR (500 MHz, CD₂Cl₂): $\delta = 1.51$ (s, 9 H, CCH₃), 1.63–1.73 (m, 1 H, CHCH₂), 1.96–2.04 (m, 1 H, CHCH₂), 2.13–2.24 (m, 2 H, CH₂CH₂CH₂), 2.29 (s, 3 H, aryl-CH₃), 2.38 (s, 3 H, aryl-CH₃), 2.56 (s, 3 H, NCH_{3(ax)}), 2.82 (s, 3 H, NCH_{3(eq)}), 3.19–3.31 (m, 2 H, NHCH, NHCH₂), 3.56 (s, 1 H, CCH), 4.02–4.07 (m, 1 H, NHCH₂), 4.20 (br, 1 H, NH), 6.67–6.72 (m, 2 H, aromatic protons) ppm. ¹³C NMR (100

MHz, CDCl_3): δ = 22.79, 23.78, 25.03, 29.75, 30.09, 35.80, 50.70, 53.26, 55.12, 64.92, 85.97, 126.00, 127.42, 131.05, 137.96, 147.14, 149.51, 180.17 ppm. HRMS (ESI) (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{33}\text{N}_2\text{O}_2\text{Pd}$ 439.1577, found 439.1581.

5.4.10 Separation of (R_C, S_C, S_N) -Prolinato-[1-[1-(dimethylamino)-2,2-dimethylpropyl]-2,5-dimethyl-6-phenyl- C,N]palladium(II), (R_C, S_C, S_N) -**220**

Above the mother liquor of complex (S_C, S_C, S_N) -**220** were evaporated to dryness and the residue was dissolved in minima chloroform. The less soluble diastereomer, (R_C, S_C, S_N) -**220**, was crystallized by slow addition of diethyl ether as pale yellow feather-like crystals, 0.98 g, 75.0%. M.p. 182–184 °C (dec.), $[\alpha]_D -32$, $[\alpha]_{578} -36$, $[\alpha]_{546} -26$, $[\alpha]_{436} +22$, $[\alpha]_{365} +346$ (c 0.5, dichloromethane). Anal Calcd for $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_2\text{Pd}$ (438.15): C, 54.73; H, 7.35; N, 6.38. Found: C, 54.75; H, 7.79; N, 6.42. ^1H NMR (500 MHz, CDCl_3): δ = 1.47 (s, 9 H, CCH_3), 1.70–1.87 (m, 3 H, $\text{CH}_2\text{CH}_2\text{CH}_2, \text{NHCH}_2$), 2.27 (s, 3 H, aryl- CH_3), 2.34 (s, 3 H, aryl- CH_3), 2.39–2.43 (m, 1 H, CHCH_2), 2.64 (s, 3 H, $\text{NCH}_{3(\text{ax})}$), 2.74 (s, 3 H, $\text{NCH}_{3(\text{eq})}$), 3.16–3.23 (m, 1 H, CHCH_2), 3.52–3.53 (m, 1 H, NHCH_2), 3.55 (s, 1 H, CCH), 3.80 (br, 1 H, NH), 4.14–4.17 (t, 1 H, COCH), 6.67–6.71 (m, 2 H, aromatic protons) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 23.02, 24.43, 28.90, 30.33, 36.23, 50.84, 51.01, 55.69, 67.22, 77.32, 86.06, 126.46, 127.15, 131.31, 138.02, 145.63, 150.03, 177.80 ppm. HRMS (ESI) (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{33}\text{N}_2\text{O}_2\text{Pd}$ 439.1577, found 439.1581.

5.4.11 Synthesis of (S) -Di- μ -chlorobis[1-[1-(dimethylamino)-2,2-dimethylpropyl]-2,5-dimethyl-6-phenyl- C,N]dipalladium(II), (S) -**211**

A solution of the diastereomer (S_C, S_C, S_N) -**220** (1.01 g, 2.30 mmol) in dichloromethane (15 mL) was treated with aqueous hydrochloric acid (1 M, 20 mL). After vigorous stirring for 45 min, the organic layer was separated, washed with H_2O and dried (MgSO_4).

Removal of solvent and purification by column using dichloromethane as eluent gave the product as light yellow solid, 0.78 g, 94.0%. $[\alpha]_{\text{D}} +210$, $[\alpha]_{578} +216$, $[\alpha]_{546} +228$, (c 0.5, dichloromethane). Anal Calcd for $\text{C}_{30}\text{H}_{48}\text{Cl}_2\text{N}_2\text{Pd}_2$ (718.13): C, 50.01; H, 6.72; N, 3.89. Found: C, 50.26; H, 6.25; N, 4.16. ^1H NMR (400 MHz, CD_2Cl_2): δ = 1.65–1.67 (m, 18 H, CCH_3), 2.22–2.23 (m, 6 H), 2.50–2.56 (m, 12 H), 2.71–2.73 (m, 6 H), 3.47–3.49 (m, 2 H, CHCH_3), 6.56–6.64 (m, 4 H, aromatic protons) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 23.00, 24.75, 25.27, 30.76, 36.34, 36.43, 52.25, 52.56, 53.35, 55.91, 56.12, 87.78, 126.43, 126.55, 127.75, 128.03, 130.33, 130.39, 139.67, 139.81, 144.10, 144.34, 148.44, 148.49 ppm.

The optically pure (*R*)-**211** was prepared from isomer ($R_{\text{C}}, S_{\text{C}}, S_{\text{N}}$)-**220** in a similar manner: $[\alpha]_{\text{D}} -208$, $[\alpha]_{578} -214$, $[\alpha]_{546} -224$, (c 0.5, dichloromethane).

5.4.12 Synthesis of (*R*)-[1-[1-(dimethylamino)-2,2-dimethylpropyl]-2,5-dimethyl-6-phenyl-*C,N*] palladium(II) perchlorate, (*R*)-**221**

The chiral palladium complex (*R*)-**211** (1.10 g, 1.53 mmol) was dissolved in CH_3CN (20 mL) and $\text{AgClO}_4 \cdot \text{H}_2\text{O}$ (1.38 g, 6.11 mmol), The mixture was stirred vigorously in dark at room temperature for 1 h. The mixture was filtered through the Celite (to remove AgCl) and the filtrate was concentrated under vacuum. The resulting residue was dissolved in dichloromethane, washed with H_2O and dried (MgSO_4). Removal of solvent gave complex (*R*)-**221** (1.28 g, 87.0%) as yellow powder and light yellow crystals were formed by slow evaporation of a (*R*)-**221** dichloromethane/hexane solution. M.p. 128–130 °C (dec); $[\alpha]_{\text{D}} -124$, $[\alpha]_{578} -128$, $[\alpha]_{546} -148$ (c 0.5, dichloromethane). Anal. Calcd for $\text{C}_{17}\text{H}_{29}\text{ClN}_2\text{O}_5\text{Pd}$ (482.08): C, 42.25; H, 6.05; N, 5.80. Found: C, 42.52; H, 5.93; N, 6.13. ^1H NMR (400 MHz, CD_2Cl_2): δ = 1.54 (s, 9 H, CCH_3), 2.27 (s, 3 H, aryl- CH_3), 2.39 (s, 6 H, aryl- CH_3 , NCCCH_3), 2.61 (s, 3 H, $\text{NCH}_{3(\text{ax})}$), 2.77 (s, 3 H, $\text{NCH}_{3(\text{eq})}$), 3.06 (br, 2 H, OH_2),

3.53 (s, 1 H, CCH), 6.78–6.89 (m, 2 H, aromatic protons) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 3.42, 22.88, 24.95, 30.28, 36.34, 50.72, 55.84, 87.41, 122.27, 127.57, 128.17, 131.56, 137.82, 140.99, 148.42 ppm. HRMS (ESI) (m/z): $[\text{M} - \text{ClO}_4]^+$ calcd for $\text{C}_{17}\text{H}_{29}\text{N}_2\text{OPd}$ 383.1315, found 383.1322.

5.4.13 Synthesis of (S)-chloride[1-[1-(dimethylamino)-2,2-dimethylpropyl]-2,5-dimethyl-6-phenyl-C,N][(3,4-dimethyl-1-phenylphosphole)-P]palladium(II), (S)-222

Under a nitrogen atmosphere, 3,4-dimethyl-1-phenylphosphole dmpp (29.0 mg, 0.16 mmol) was added to a stirred solution of complex (S)-**211** (56.0 mg, 0.08 mmol) in DCM (10 mL). This reaction was allowed to stir for 2 h at room temperature before the solvent was removed and the yellow solid was dried under vacuum to give compound (S)-**222** (81.0 mg, 95.0%). $[\alpha]_{\text{D}} +424$, $[\alpha]_{578} +444$, $[\alpha]_{546} +516$, $[\alpha]_{436} +886$ (c 0.5, dichloromethane). Anal. Calcd for $\text{C}_{27}\text{H}_{37}\text{ClNPPd}$ (547.14): C, 59.13; H, 6.80; N, 2.55. Found: C, 59.16; H, 7.14; N, 2.67. ^{31}P NMR (121 MHz, CDCl_3) δ = 27.7 (s) ppm. ^1H NMR (500 MHz, CDCl_3): δ = 1.27 (s, 9 H, CCH_3), 2.00 (s, 3 H, $\text{C}=\text{CCH}_3$), 2.03 (s, 3 H, $\text{C}=\text{CCH}_3$), 2.20 (s, 3 H, aryl- CH_3), 2.27 (s, 3 H, aryl- CH_3), 2.40 (s, 3 H, $\text{NCH}_{3(\text{ax})}$), 2.93 (d, 3 H, $^4J_{\text{P,H}} = 3.2$ Hz, $\text{NCH}_{3(\text{eq})}$), 3.53 (d, 1 H, $^4J_{\text{P,H}} = 5.0$ Hz, CCH), 6.27 (d, 1 H, $^2J_{\text{P,H}} = 33.0$ Hz, $\text{C}=\text{CCH}$), 6.68–6.74 (m, 2 H, aromatic protons), 6.84 (d, 1 H, $^2J_{\text{P,H}} = 31.5$ Hz, $\text{C}=\text{CCH}$), 7.33–7.34 (m, 3 H, aromatic protons), 7.86–7.90 (m, 2 H, aromatic protons) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 16.86 (d, $J_{\text{P,C}} = 12.6$ Hz), 17.50 (d, $J_{\text{P,C}} = 12.1$ Hz), 23.18, 28.05 (d, $J_{\text{P,C}} = 12.0$ Hz), 30.32, 35.82, 51.00, 52.98, 53.26, 87.28 (d, $J_{\text{P,C}} = 2.5$ Hz), 125.59, 125.97, 126.52, 127.18, 127.55, 128.28 (d, $J_{\text{P,C}} = 10.8$ Hz), 130.24, 130.50, 131.89, 133.08 (d, $J_{\text{P,C}} = 12.0$ Hz), 139.67 (d, $J_{\text{P,C}} = 6.0$ Hz), 147.21 (d, $J_{\text{P,C}} = 9.7$ Hz), 150.05, 153.33, 153.67 (d, $J_{\text{P,C}} = 10.5$ Hz) ppm. HRMS (ESI) (m/z): $[\text{M} - \text{Cl}]^+$ calcd for $\text{C}_{27}\text{H}_{37}\text{NPPd}$ 512.1698, found 512.1683.

5.4.14 Asymmetric *endo*-Cycloaddition Reaction between Complex (S)-222 and Ethyl Vinyl Ketone. Formation of Complex (S_C,R_P)-223 and Complex (S_C,S_P)-223.

A dichloroethane (10 mL) solution of complex (S)-222 (0.55 g, 1 mmol) was stirred with excess ethyl vinyl ketone (0.42 g, 5 mmol) at 70 °C, the peak of complex (S)-222 disappeared and two sharp singlets at δ 130.7 and 131.0 ppm in ³¹P NMR were observed in a 1:1 diastereomeric ratio after 6 days. The solution also appeared to darken, indicating the possible decomposition of Pd(II) to Pd(0) and/or the formation of PdO. However complex (S_C,R_P)-223 and (S_C,S_P)-223 could not be separated by column purification. Furthermore, both the products could not be separated by slow crystallization using a series of solvent systems because of the 1:1 diastereomeric ratio.

5.4.15 Synthesis of (S,S)-dichloro-[diethyl-1,2-bis-(diphenylphosphino)-ethane dicarboxylate]palladium (II), (S,S)-226

Complex (R)-221 (0.10 g, 0.20 mmol) and diphenylphosphine (74.0 mg, 0.40 mmol) in dichloromethane were stirred under nitrogen at room temperature for 1 h. A solution of diethyl acetylenedicarboxylate (34.0 mg, 0.20 mmol) and triethylamine (4 mg, 0.04 mmol) in dichloromethane (5 mL) were added dropwise to the reaction above and stirred at –78 °C overnight. After removal the solvent, a yellow color solid (R,SS)-225 was obtained. $[\alpha]_D -22$, $[\alpha]_{578} -24$, $[\alpha]_{546} -26$, $[\alpha]_{436} -26$ (*c* 0.5, dichloromethane). ³¹P NMR (121 MHz, CDCl₃) δ 39.5 (d, $J_{PP} = 40.5$ Hz), 30.2 (d, $J_{PP} = 40.5$ Hz) ppm. ¹H NMR (500 MHz, CDCl₃) δ = 0.78 (t, 3 H, ³ $J_{H,H} = 7.1$ Hz, COOCH₂CH₃), 0.82 (t, 3 H, ³ $J_{H,H} = 7.1$ Hz, COOCH₂CH₃), 1.41 (s, 9 H, *tert*-butyl), 1.86 (s, 3 H, CH₃), 2.25 (s, 3 H, CH₃), 2.28 (s, 3 H, CH₃), 2.73 (s, 3 H, CH₃), 3.49–3.55 (m, 1 H, PCH), 3.60–3.66 (m, 1 H, PCH), 3.69 (d, 1 H, ⁴ $J_{PH} = 6.2$ Hz, *tert*-butylCH), 3.73–3.86 (m, 4 H, COOCH₂CH₃), 6.51–6.53 (m, 1 H, aromatic proton), 6.68 (d, 1 H, ³ $J_{H,H} = 7.7$ Hz, aromatic proton), 7.18–8.20 (m, 20 H,

aromatic protons) ppm. HRMS (ESI) (m/z): $[M - ClO_4]^+$ calcd for complex (*R,S,S*)-**225** $C_{47}H_{56}NO_4P_2Pd$ 866.2719, found 866.2711.

Concentrated hydrochloric acid (10 mL) was then added and stirred vigorously overnight. The reaction mixture was washed with water, dried ($MgSO_4$) and subsequently crystallized from dichloromethane and diethyl ether giving complex (*S,S*)-**226** as yellow crystals (0.11 g, 74.0%). M.p. 251–253 °C (dec); $[\alpha]_{436} -138$ (c 0.5, dichloromethane); Anal. Calcd for $C_{32}H_{32}Cl_2O_4P_2Pd$ -dichloromethane (801.97): C, 49.25; H, 4.26;. Found: C, 49.60; H, 4.10; N, 2.67. ^{31}P NMR (121 MHz CD_2Cl_2) $\delta = 57.7$ (s, 2P, P_1 and P_2) ppm. 1H NMR (300 MHz $CDCl_3$) $\delta = 0.91$ (t, 6 H, $^3J_{H,H} = 7.1$ Hz, $COOCH_2CH_3$), 3.80–3.93 (m, 4 H, $COOCH_2CH_3$), 4.18 (d, 2 H, $^2J_{P,H} = 5.9$ Hz, $PCHCOOEt$), 7.53–7.94 (m, 20 H, aromatic protons). ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = 13.28, 48.82$ (m), 62.34, 123.62 (d, $J_{P,C} = 2.0$ Hz), 124.16 (d, $J_{P,C} = 2.0$ Hz), 125.74 (d, $J_{P,C} = 1.5$ Hz), 126.33 (d, $J_{P,C} = 1.7$ Hz), 128.55 (m), 129.28 (m), 132.42, 133.45 (m), 135.78, 165.88 (d, $J_{P,C} = 9.3$ Hz), 165.83 (d, $J_{P,C} = 9.3$ Hz), 166.18 (d, $J_{P,C} = 9.2$ Hz) ppm.

5.4.16 Liberation of (*S,S*)-diethyl-1,2-bis-(diphenylphosphino)-ethanedicarboxylate, Formation of Compound (*S, S*)-**227**

A solution of complex (*S, S*)-**226** (20.0 mg) in dichloromethane (20 mL) was stirred vigorously with a saturated aqueous solution of KCN (0.50 g) for 1 h. The colorless organic layer was separated, washed with H_2O (3×20 mL), and dried ($MgSO_4$). Upon the removal of solvent, a white solid was obtained: 14 mg (95.0% yield); $[\alpha]_D + 280$ (c 0.5, dichloromethane). ^{31}P NMR (300 MHz, $CDCl_3$) $\delta = -6.4$ (s, 2P, P_1 and P_2) ppm; 1H NMR (300 MHz, $CDCl_3$) $\delta = 0.85$ (t, 6 H, $^3J_{H,H} = 7.1$ Hz, $COOCH_2CH_3$), 3.41–3.58 (m, 4 H, $COOCH_2CH_3$), 3.88 (t, 2 H, $^2J_{P,H} = 4.1$ Hz, $PCHCOOEt$), 7.23–7.86 (m, 20 H, aromatic protons) ppm.

Crystal Structure Determination

Diffraction data were collected on a Bruker X8 CCD diffractometer with Mo-K α radiation (graphite monochromator). SADABS absorption corrections were applied. All non-hydrogen atoms were refined anisotropically while hydrogen atoms were introduced at calculated positions and refined riding on their carrier atoms. The absolute configurations of the chiral complexes were determined unambiguously using the Flack parameter.

CHAPTER 6

1-(2,4-DI-*TERT*-BUTYLPHENYL)-*N,N*-DIMETHYLETHANAMINE
AND 1-(2,5-DI-*TERT*-BUTYLPHENYL)-*N,N*-
DIMETHYLETHANAMINE

6.1 Introduction

In palladium complex (S)-**11** and its monomeric derivatives, the methyl group on the chiral center is exclusively in the axial position due to the interactions between H8 and the α -methyl group. If a group is introduced next to the Pd–C bond, the coordination site *trans* to the nitrogen donor would be stereochemically controlled. Based on these arguments, we designed and synthesized optically active palladacycles (S)-**178** and (S)-**189** which can act as a stereochemical controller on the position *trans* to nitrogen donor and therefore will exhibit better stereoselectivity in the *endo*-cycloaddition reaction between their dmpp derivatives and dienophiles (as shown in chapter 2 and 3). Furthermore when the α -methyl group was replaced by a bulky *tert*-butyl group as in complex (S)-**211**, the organopalladium ring's conformation will be strictly fixed, with the *tert*-butyl group occupying the axial position exclusively. However complex (S)-**211** shows poor stereoselectivity for the chiral template promoted *endo*-cycloaddition reactions between dmpp and dienophiles as described in chapter 5.

6.2 Research Objective

It is of interest to synthesise a novel chiral palladacycle (*S*)-**228**. The chiral complex (*S*)-**228** exhibits the key stereochemical features of the chiral naphthylamine chelate ring in palladacycle (*S*)-**11**. The internal steric repulsion between the methyl substituent on the stereogenic carbon and its neighboring *tert*-butyl group is expected to lock the five-membered organometallic ring conformation both in solution and in the solid state. Furthermore, the other *tert*-butyl group is introduced in position 3 of the aromatic ring instead of position 2. In order to determine the influence of the introduced 3-position *tert*-butyl group on the neighboring reaction site, this new chiral palladacycle (*S*)-**228** was applied in the analogous asymmetric *endo*-cycloaddition reaction.

6.3 Results and Discussion

6.3.1 Synthesis of Racemic Amine Ligand (±)-**234**

Preparation of the racemic dimethyl amine compound (±)-**234** is shown in Scheme 6.1. In the presence of aluminum chloride, 1,4-di-*tert*-butylbenzene **229** was acetylated with acetyl chloride in dichloromethane to give a rearranged ketone product **230** as a colorless oil in 30.6 % yield.^[195] Reduction of compound **230** at 50 °C by sodium borohydride gave the racemic alcohol (±)-**231** in 82.7% yield. The alcohol (±)-**231** was then converted to amide (±)-**232** in 88.3% yield *via* the Ritter reaction.^[196,197] The amide (±)-**232** was then heated to 100 °C with a strong base to give the amine (±)-**233** as a light yellow colored oil in 93.1% yield. Compound (±)-**233** was subsequently converted to the

racemic dimethyl amine ($\pm$)-**234** upon acidic hydrolysis in a yield of 85.7%. A molecular ion peak of compound ($\pm$)-**234** at $[m/z (M + H)]^+ 262.2533$ was observed in the high resolution mass spectrum.

Scheme 6.1

6.3.2 Preparation and Isolation of Compound 230

Preparation of ketone compound **230** is shown in Scheme 6.2. Friedel–Crafts acetylation reaction of *p*-di-*tert*-butylbenzene **229** with acetyl chloride was done in dry dichloromethane at 0 °C. The ketone products were separated by silica gel column chromatography (diethyl ether/hexane = 1/10, V/V), giving 1-(2,4-di-*tert*-butylphenyl)ethanone **230**, 1-(3,5-di-*tert*-butylphenyl)ethanone **235** and 1-(4-*tert*-butylphenyl)ethanone **236**.

Scheme 6.2

The three ketone compounds (**230**, **235** and **236**) produced, was not surprising as *p*-di-*tert*-butylbenzene undergoes rapid isomerisation in the presence of aluminum chloride^[198]. The abnormal behavior of *p*-di-*tert*-butylbenzene toward Friedel-Crafts acetylation was first noted by Koch and then by Hennion.^[199] In addition to *p*-*tert*-butylacetophenone (**236**) identified by these workers, Nightingale and co-worker^[200] reported a second ketone and subsequent analysis identified it to be a di-*tert*-butylacetophenone. The structure of this ketone was later established by Beets and van Essen^[201] as 2,4-di-*tert*-butylacetophenone (**230**). Here, the Friedel-Crafts acetylation reaction was repeated under similar conditions using dry dichloromethane as the solvent and the reaction gave the same three substituted ketone compounds (**230**, **235** and **236**) and compound **237** could not be formed.

6.3.3 *ortho*-Palladation Studies of Amine Ligand (±)-**234**

As discussed in chapter one, there are three main methods normally used in direct *ortho*-palladation. Therefore the *ortho*-palladation studies of amine ligand (±)-**234** were performed using methods shown in Scheme 6.3-6.5. Three Pd(II) sources, [Pd(NCMe)₄](ClO₄)₂, Li[PdCl₄] and Pd(OAc)₂, were used. All these synthetic methods

resulted in the formation of palladium dimeric complex ($\pm$)-**228**.

The first *ortho*-palladation method used for the synthesis of compound ($\pm$)-**228** involved treatment of the racemic tertiary amine ($\pm$)-**234** with $[\text{Pd}(\text{NCMe})_4](\text{ClO}_4)_2$ in methanol with one equimolar of triethylamine at room temperature for 20 h followed by anion exchange with 1 M hydrochloric acid forming the racemic dimeric palladium complex. The dimeric complex was isolated using silica gel column chromatography with dichloromethane as the eluent giving complex ($\pm$)-**228** in 66.7% yield (Scheme 6.3).

Scheme 6.3

The second *ortho*-palladation generating dimeric palladium complex ($\pm$)-**228** was achieved by treating compound ($\pm$)-**234** with $\text{Li}_2[\text{PdCl}_4]/\text{NEt}_3$ in methanol at room temperature for 5 h and subsequent isolation by silica gel column chromatography with dichloromethane as the eluent. The *ortho*-palladated dimeric complex ($\pm$)-**228** was then obtained in 56.0% isolated yield (Scheme 6.4).

Scheme 6.4

The last *ortho*-palladation method employed involved the treatment of compound ($\pm$)-**234** with $\text{Pd}(\text{OAc})_2$ in methanol at 50 °C for 2 h followed by anion exchange with lithium chloride resulting in the racemic dimeric palladium complex ($\pm$)-**228** which was also purified by column chromatography with 63.0% yield (Scheme 6.5).

Scheme 6.5

The successfully *ortho*-palladation of racemic amine ($\pm$)-**234** by using three commonly used method shows that the *tert*-butyl group at the 3 position on the phenyl ring has a smaller steric influence on the formation of the Pd–C bond and hence the *ortho*-palladation product ($\pm$)-**228** can be obtained *via* all the three commonly used methods.

6.3.4 Molecular Structure of Racemic Dimeric Palladacycle ($\pm$)-**228**

Yellow colored single crystals of complex ($\pm$)-**228** were formed by slow addition of diethyl ether to a complex ($\pm$)-**228** dichloromethane solution. The molecular structure of complex ($\pm$)-**228** was determined by X-ray crystallography (Figure 6.1). The coordination spheres of both palladium centers are of distorted square planar geometry. The bond lengths around the central Pd atom are comparable to the reported dimeric cyclopalladated arylamines.^[6, 7, 9, 96] The dihedral angle between the planes N(1)–C(1)–Pd(1) and Cl(1)–Pd(1)–Cl(1A) is 2.3°. The two organometallic rings in ($\pm$)-**228** are orientated in the *trans* geometry with *C*₂ symmetry. The bridging Pd–(μ -Cl)₂–Pd unit in complex ($\pm$)-**228** is planar, which indicated that the repulsive interactions

between the *tert*-butyl group and the two Cl atoms are minimal. The distances of C(7)–Cl(1A) and C(7A)–Cl(1) were found to be 5.399 Å. The large distance indicates that the *tert*-butyl group (position 3) will most probably exert a small or even insignificant steric influence at the coordination site.

Figure 6.1 Molecular structure of complex (±)-**228** with thermal ellipsoids at 50% probability. All hydrogen atoms are omitted for clarity.

Table 6.1 Selected bond lengths (Å) and angles (°) for complex (±)-**228**

Pd(1)–C(1)	1.979(1)	Pd(1)–N(1)	2.070(1)
Pd(1)–Cl(1)	2.476(3)	Pd(1)–Cl(1A)	2.339(4)
Cl(1)–Pd(1A)	2.339(4)	N(1)–C(15)	1.511(2)
C(1)–Pd(1)–N(1)	80.2(5)	C(1)–Pd(1)–Cl(1A)	96.3(4)
N(1)–Pd(1)–Cl(1A)	176.1(3)	C(1)–Pd(1)–Cl(1)	177.7(4)
N(1)–Pd(1)–Cl(1)	98.3(3)	Cl(1A)–Pd(1)–Cl(1)	85.2(1)
Pd(1)#–Cl(1)–Pd(1)	94.8(1)		

6.3.5 Synthesis and Characterization of Complex (±)-238

6.3.5.1 Synthesis of Complex (±)-238

In solution, the dimeric complex (±)-228 exists as mixtures of geometric *syn/anti* isomers. The dynamic *cis-trans* interconversion renders difficulties in characterization of its ^1H NMR signals and spectral confirmation of the palladacycle formation. In an attempt to study the behavior of the five membered organometallic ring conformation, dimeric palladacycle (±)-228 is converted to its mononuclear triphenylphosphine derivative (±)-238 by a standard $\mu\text{-Cl}$ bridge cleavage reaction in 93.0% yield (Scheme 6.6).

Scheme 6.6

6.3.5.2 Molecular Structure of Complex (±)-238

Light yellow colored crystals can be formed from a dichloromethane/hexane solution and the structure of complex (±)-238 was reaffirmed crystallographically. There are two crystallographically unique molecules in the asymmetric unit with slightly different bond lengths and angles. For clarity, only one of them (molecule A) is depicted in Figure 6.2. The selected bond lengths and angles are presented in Table 6.2.

Figure 6.2 Molecular structure of complex (±)-**238** with thermal ellipsoids at 50% probability. All hydrogen atoms are omitted for clarity.

Table 6.2 Selected bond lengths (Å) and angles (°) for complex (±)-**238**.

Molecule A		Molecule B	
Pd(1)–C(1)	2.003(4)	Pd(2)–C(37)	2.026(4)
Pd(1)–N(1)	2.126(3)	Pd(2)–N(2)	2.141(3)
Pd(1)–P(1)	2.258(1)	Pd(2)–P(2)	2.255(1)
Pd(1)–Cl(1)	2.389(1)	Pd(2)–Cl(2)	2.407(1)
C(1)–Pd(1)–N(1)	80.6(1)	C(37)–Pd(2)–N(2)	80.1(1)
C(1)–Pd(1)–P(1)	96.7(1)	C(37)–Pd(2)–P(2)	95.7(1)
N(1)–Pd(1)–P(1)	173.4(9)	N(2)–Pd(2)–P(2)	173.6(9)
C(25)–P(1)–Pd(1)	113.4(1)	C(67)–P(2)–Pd(2)	112.7(1)
C(31)–P(1)–Pd(1)	115.3(1)	C(61)–P(2)–Pd(2)	116.1(1)
C(19)–P(1)–Pd(1)	118.2(1)	C(55)–P(2)–Pd(2)	117.4(1)

Complex ($\pm$)-**238** has a distorted square-planar coordination geometry. In comparison with other triphenylphosphine derivatives, ($\pm$)-**184** and ($\pm$)-**194**, discussed in chapter 2 and chapter 3, there is a weaker steric repulsion between the triphenylphosphine ligand and the organometallic chelate in complex ($\pm$)-**238**. This steric factor is manifested in the C(1)–Pd(1)–P(1) angles [100.2(4)° for complex ($\pm$)-**184** and 101.7(1)° for complex ($\pm$)-**194**] of the two complexes. In the absence of a steric projecting group from the aromatic carbon, the steric repulsion between the triphenylphosphine ligand and the phenyl ring chelate in complex ($\pm$)-**238** is relatively insignificant. Thus, the C(1)–Pd(1)–P(1) bond angle in complex ($\pm$)-**238** (96.7(1)°) is close to the ideal square planar geometry. In addition, because of the absence of such a ligand-ligand repulsion in complex ($\pm$)-**238**, the three Pd–P–C bond angles in complex ($\pm$)-**238** are within the normal range of 113.4(1)–118.2(1)° (Table 6.2). However in complex ($\pm$)-**184** and complex ($\pm$)-**194**, the bond angle Pd–P–C bond angle range is enlarged to [109.6(5)°–119.6(5)°] and [111.5(1)°–117.9(1)°], respectively (Table 2.1 and Table 3.1).

6.3.5.3 Solution Structure of Complex ($\pm$)-**238**

In CDCl₃, the ³¹P NMR spectrum of complex ($\pm$)-**238** shows only a singlet resonance at δ 41.8, indicating the presence of a sole isomer in solution. In the ¹H NMR spectrum, the two N-methyl groups show the characteristic P–H couplings (1.6 and 3.3 Hz). These $J_{\text{P-H}}$ couplings confirm the *trans* relationship of the phosphorus atom and the nitrogen donor. The ¹H NMR study of the racemic adduct ($\pm$)-**238** has shown that the five-membered palladacycle exists preferentially in the $\delta(R)$ or $\lambda(S)$ conformation with the α -Me substituent in the axial position. This conclusion can be inferred from the coupling constant ⁴ $J_{\text{P-H}}$ of 5.9 Hz for the proton H7 and confirmed by the 2D ¹H-¹H ROESY NMR (Figure 6.4). Figure 6.3 shows the numbering scheme of complex ($\pm$)-**238**.

Figure 6.3 Numbering Scheme of Complex (±)-**238** for NMR Studies.

Figure 6.4 2D ^1H - ^1H ROESY NMR Spectrum of Complex (±)-**238** in CDCl_3 . (refer to Figure 6.3 for the numbering scheme of complex (±)-**238**). Selected ROESY Interactions: (A) H7–NMe(eq); (B) H7–NMe(ax); (C) Me7–H7; (D) *tert*-butyl5–H7; (E) NMe(eq)–NMe(ax); (F) Me7–NMe(eq); (G) *tert*-butyl5–NMe(ax); (H) *tert*-butyl5–Me7; (I) *tert*-butyl5–H4; (J) *tert*-butyl3–H4; (K) *tert*-butyl3–H2; (L) H2–triphenylphosphine.

In the spectrum, strong ROESY signals (A, B) from the interactions between the α -Me proton H7 and the two NMe groups were clearly recorded. Moreover, the α -Me substituent Me7 interacts strongly with the equatorially disposed NMe group (F), but very weakly with the axially disposed one. This set of ROESY interactions indicates that the α -methyl group Me7 is in the axial position. Furthermore, the driving forces for α -methyl group Me7 to mainly assume the axial position can also be attributed to the repulsive interactions, i.e. *tert*-butyl5–H7 (D) and Me7–*tert*-butyl5 (H). The strong ROESY interaction (L) (triphenylphosphine–H2) indicates the *trans*-(*N,N*)-arrangement in solution, similar to its solid state. Furthermore, no ROESY correlation between the NMe groups and the triphenylphosphine ligand is observed, confirming the *trans*-(*N,N*)-relationship. Other expected ROESY interactions of Me7–H7 (C), NMe(eq)–NMe(ax) (E), *tert*-butyl5–NMe(ax) (G), *tert*-butyl5–H4 (I), *tert*-butyl3–H4 (J) and *tert*-butyl3–H2 (K) were also observed. The above NMR spectroscopic investigations of complex ($\pm$)-**238** in solution indicate that the α -Me group Me7 is located in the axial position and the interaction between Me7 and *tert*-butyl5 can effectively confine the five-membered organometallic ring conformation, the λ and δ conformations are adopted in the (*S*) and (*R*) enantiomers respectively.

6.3.4 Optical Resolution of Racemic Dimeric Palladacycle ($\pm$)-**228** and Isolation of the Diastereomeric Isomers (*S_C*,*S_C*)-**239** and (*R_C*,*S_C*)-**239**

6.3.4.1 Formation of Diastereomeric Isomers (*S_C*,*S_C*)-**239** and (*R_C*,*S_C*)-**239**

Normally, the optical resolution of racemic dimeric palladacycles can be achieved *via* the formation and separation of a pair of diastereomeric amino acid derivatives. After trying a series of amino acids, sodium (*L*)-phenylalanate was found to be the resolution reagent of choice for the current palladacycle ($\pm$)-**228** (Scheme 6.7). By treating the

racemic dimer ($\pm$)-**228** with two molar equivalents of sodium (*L*)-phenylalanate, the expected 1:1 mixture of diastereomeric adducts (*R_C,S_C*)-**239** and (*S_C,S_C*)-**239** were formed according to the ^1H NMR spectrum. Successful separation was achieved by using a dichloromethane/diethyl ether solution and the less soluble diastereomer (*S_C,S_C*)-**239** crystallized out selectively, $[\alpha]_{\text{D}} +48$ (*c* 0.5, dichloromethane), $> 99\%$ *de* (according to the ^1H NMR spectrum). After removing the solvent in the diastereomerically (*R*) enriched mother liquor, the residue allowed the isolation of the remaining diastereomer (*R_C,S_C*)-**239** from a chloroform/hexane solution as white crystals with $[\alpha]_{\text{D}} -46$ (*c* 0.5, dichloromethane), $> 99\%$ *de* (according to the ^1H NMR spectrum). The absolute configurations and solid structures of both diastereomeric derivatives, complexes (*R_C,S_C*)-**239** and (*S_C,S_C*)-**239**, can be determined by X-ray single crystal diffraction investigation. Their solution structures were also studied by their 2D ^1H - ^1H ROESY NMR spectra.

Scheme 6.7

6.3.4.2 Molecular Structure of Diastereomer (*S_C,S_C*)-**239**

For diastereomer (*S_C,S_C*)-**239**, white colored single crystals suitable for X-ray crystallography can be obtained by the slow diffusion of diethyl ether into a dichloromethane solution. There are two crystallographically unique molecules in the asymmetric unit with the same stereochemistry but slightly different bond lengths and angles. Only one of them (molecule A) is depicted in Figure 6.5 and Table 6.3. The X-ray crystallographic study reveals that the palladacycle is *S*, with the α -Me group in the axial

position. All the bond lengths and angles at the central palladium atoms are all within the normal ranges. This complex adopts a *trans*-(*N,N*) arrangement and the tetrahedral distortion of palladium coordination environment is minimal, with the angle between the {Pd(1)–C(1)–N(1)} and {Pd(1)–N(2)–O(1)} planes equal to 3.4°.

Figure 6.5 Molecular Structure of Complex (*S_C*,*S_C*)-**239** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C15) and H(C20) are omitted for clarity.

Table 6.3 Selected bond lengths (Å) and angles (°) for complex (*S_C*,*S_C*)-**239**

Molecule A		Molecule B	
Pd(1)–C(1)	1.977(3)	Pd(2)–C(28)	1.967(3)
Pd(1)–N(2)	2.049(3)	Pd(2)–N(4)	2.037(3)
Pd(1)–N(1)	2.075(3)	Pd(2)–N(3)	2.066(3)
Pd(1)–O(1)	2.142(3)	Pd(2)–O(3)	2.153(2)
C(1)–Pd(1)–N(2)	98.3(1)	C(28)–Pd(2)–N(4)	97.6(1)
C(1)–Pd(1)–N(1)	81.4(1)	C(28)–Pd(2)–N(3)	80.8(1)
N(2)–Pd(1)–N(1)	178.2(1)	N(4)–Pd(2)–N(3)	177.3(1)
C(1)–Pd(1)–O(1)	176.3(1)	C(28)–Pd(2)–O(3)	176.9(1)
N(2)–Pd(1)–O(1)	79.0(1)	N(4)–Pd(2)–O(3)	79.3(1)

6.3.4.3 Solution Structure of Diastereomer (S_C, S_C)-**239**

In order to study the regiochemistry and the organopalladium ring conformation in solution, a NMR study of complex (S_C, S_C)-**239** was carried out. In the 500 MHz NMR spectrum of complex (S_C, S_C)-**239** in $CDCl_3$ at room temperature, there is only one resonance for each chemically nonequivalent proton which indicates the presence of a sole geometric isomer in solution. The signal assignment were performed by 2D 1H - 1H ROESY NMR experiment. Figure 6.6 shows the numbering scheme of complex (S_C, S_C)-**239** and Figure 6.7 shows its 2D 1H - 1H ROESY NMR spectrum.

Figure 6.6 Numbering Scheme of Complex (S_C, S_C)-**239** for NMR Studies.

In the ROESY NMR spectrum, strong ROESY interactions between H7 and NMe(eq) (NMe(ax), Me7) are clearly recorded (A, B and C). The α -methyl group Me7 interacts strongly with the equatorially disposed NMe group (E), however the interaction between Me7 and the axially disposed NMe group is not observed. This set of ROESY interactions showed that the five-membered palladacycle ring is locked in the λ conformation and hence the α -methyl group Me7 is axially disposed. The driving force of such an arrangement can be attributed to the desire of the Me7 group to occupy the axial position exclusively in order to minimize unfavorable steric repulsions within the molecule. This is evident from the ROESY correlation Me7-*tert*-Butyl5 (F) that is clearly recorded in the spectrum. In addition, an interaction between NH' and H2 (M) is clearly recorded which indicates that in solution, isomer (S_C, S_C)-**239** retains a *trans*-(N, N) arrangement, the same as its geometrical arrangement in the solid state. Furthermore, no ROESY correlation

between both NMe groups and the phenylalanate ligand is observed in the spectrum, further confirming the *trans*-(*N,N*) relationship. The signal assignments are based on the interactions observed in the spectrum, for example, *tert*-butyl5–NMe (ax) (G), H8–NH (H), H9–H8 (I), H9'–H8 (J, K), NH–NH' (L), *tert*-butyl3–H2 (N), NH'–Ph (O), *tert*-butyl5–H4 (P), *tert*-butyl3–H4(Q), H8–Ph (R), H9–Ph (S) and H9'–Ph (T).

Figure 6.7 2D ^1H - ^1H ROESY NMR Spectrum of Complex (S_C,S_C)-**239** in CDCl_3 . (refer to Figure 6.6 for the numbering scheme of complex (S_C,S_C)-**239**). Selected ROESY Interactions: (A) H7–NMe(eq); (B) H7–NMe(ax); (C) Me7–H7; (D) *tert*-butyl5–H7; (E) Me7–NMe(eq); (F) Me7–*tert*-butyl5; (G) *tert*-butyl5–NMe(ax); (H) H8–NH; (I) H9–H8; (J, K) H9'–H8; (L) NH–NH'; (M) NH'–H2; (N) *tert*-butyl3–H2; (O) NH'–Ph; (P) *tert*-butyl5–H4; (Q) *tert*-butyl3–H4; (R) H8–Ph; (S) H9–Ph; (T) H9'–Ph.

6.3.4.4 Molecular Structure of Diastereomer (R_C, S_C)-**239**

Colorless single crystals were obtained from a (R_C, S_C)-**239** chloroform/hexane solution. The X-ray diffraction study of diastereomer (R_C, S_C)-**239** was carried out and there are two crystallographically unique molecules in one asymmetric unit with the same stereochemistry but with slightly different bond lengths and angles. For clarity, only one of them (molecule A) is depicted in Figure 6.8. The selected bond lengths and angles are provided in Table 6.4. The X-ray crystallographic study further reveals the *R* absolute configuration of the α -Me stereocenter. The methyl group occupies the expected axial position and the conformation of the five-membered palladacycle is δ . The coordination geometry of the central palladium atom is in a slightly distorted square plane. The dihedral angle between the planes N(1)–C(1)–Pd(1) and O(1)–N(2)–Pd(1) is 4.0°. Worthy to note, the two coordinated nitrogen atoms are *trans* related. This phenomenon can be attributed to the severe intramolecular ligand-ligand interaction arising from the presence of the phenyl ring group in the *L*-phenylalanate. Consequently, less steric interactions exist between the NMe group and the phenylalanate ligand when complex (R_C, S_C)-**239** adopts the favorable *trans*-*N,N* isomer in the solid state.

Table 6.4 Selected bond lengths (Å) and angles (°) for complex (R_C, S_N)-**239**

Molecule A		Molecule B	
Pd(1)–C(1)	1.969(4)	Pd(2)–C(28)	1.985(4)
Pd(1)–N(1)	2.062(4)	Pd(2)–N(3)	2.046(4)
Pd(1)–N(2)	2.067(3)	Pd(2)–N(4)	2.065(3)
C(1)–Pd(1)–N(1)	80.9(2)	C(28)–Pd(2)–N(3)	80.7(2)
C(1)–Pd(1)–N(2)	99.9(2)	C(28)–Pd(2)–N(4)	102.6 (2)
N(1)–Pd(1)–N(2)	177.9(2)	N(3)–Pd(2)–N(4)	176.5(2)
C(1)–Pd(1)–O(1)	175.9(2)	C(28)–Pd(2)–O(3)	176.0(2)
N(1)–Pd(1)–O(1)	100.4(1)	N(3)–Pd(2)–O(3)	98.1(1)
N(2)–Pd(1)–O(1)	78.7(1)	N(4)–Pd(2)–O(3)	78.5(1)

Figure 6.8 Molecular structure of complex (R_C,S_C)-**239** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C15) and H(C20) are omitted for clarity.

6.3.4.5 Solution Structure of Diastereomer (R_C,S_C)-**239**

Similar to diastereomer (S_C,S_C)-**239**, the solution structure of complex (R_C,S_C)-**239** is of interest, especially its regiochemistry and organopalladium conformation. In the 500 MHz NMR spectrum in $CDCl_3$ at room temperature, complex (R_C,S_C)-**239** shows only one resonance for each chemically nonequivalent proton which indicates the presence of a sole geometric isomer in solution. The signal assignment was performed by 2D 1H - 1H ROESY NMR experiment. Figure 6.9 shows the numbering scheme of complex (R_C,S_C)-**239** and Figure 6.10 shows its 2D 1H - 1H ROESY NMR spectrum.

Figure 6.9 Numbering Scheme of Complex (R_C, S_C)-**239** for NMR Studies

Figure 6.10 2D ^1H - ^1H ROESY NMR Spectrum of Complex (R_C, S_C)-**239** in CDCl_3 . (refer to Figure 6.9 for the numbering scheme of complex (R_C, S_C)-**239**). Selected ROESY Interactions: (A) H7–NMe(eq); (B) H7–NMe(ax); (C) NH–NH'; (D) Me7–H7; (E) *tert*-butyl5–H7; (F) Me7–NMe(eq); (G) *tert*-butyl5–NMe(ax); (H) Me7–*tert*-butyl5; (I) H9–H9'; (J) H8–H9; (K) H9'–H8; (L) H9'–Ph; (M) NH'–H2; (N) *tert*-butyl3–H2; (O) *tert*-butyl5–H4; (P) *tert*-butyl3–H4.

In the 2D ^1H - ^1H ROESY NMR spectrum, the proton attached to the stereogenic center H7 interacts strongly with NMe(eq), NMe(ax), Me7, *tert*-butyl5 (A, B, D and E) respectively. The ROESY correlation (F) [Me7–NMe(eq)] together with the absence of a ROESY signal between Me7 and NMe(ax) shows that the five-membered organopalladium ring is locked in the δ conformation and hence the methyl group Me7 is axially located. Moreover, the strong ROESY interaction (M) (NH'–H2) indicates that complex (R_C, S_C)-**239** adopts the *trans*-(*N,N*) arrangement in solution, the same as in the solid state. No ROESY correlation between the NMe groups and the phenylalanate ligand was observed, confirming the *trans*-(*N,N*) relationship. Some other expected ROESY interactions, for example (C) NH–NH', *tert*-butyl5–NMe(ax) (G), Me7–*tert*-butyl5 (H), H9–H9' (I), H8–H9 (J), H9'–H8 (K), H9'–Ph (L), *tert*-butyl3–H2 (N), *tert*-butyl5–H4 (O) and *tert*-butyl3–H4 (P) are clearly recorded.

6.3.5 Synthesis of the Optically Active Palladacycle (*S*)-**228** and (*R*)-**228**

6.3.5.1 Synthesis of Palladacycle (*S*)-**228**

The optically pure dichloro dimer (*S*)-**228** was obtained by mixing complex (S_C, S_C)-**239** in dichloromethane with 1 M aqueous hydrochloric acid and was isolated as a yellow powder in 96% yield with $[\alpha]_D +140$ (*c* 0.5, dichloromethane) (Scheme 6.8).

Scheme 6.8

6.3.5.2 Molecular Structure of Palladacycle (*S*)-228

Single crystals were obtained from a dichloromethane/hexane solution of complex (*S*)-228. The structure of the chiral dimeric complex (*S*)-228 was determined by X-ray crystallography (Figure 6.11) and the selected bond lengths and angles are listed in Table 6.5. The X-ray crystallographic study confirmed the expected *S* absolute configuration of the α -carbon stereocenter of the palladacycle. In line with most of the recorded X-ray data of similar μ -chloro-bridged dimeric *ortho*-palladated amines or related dimers of *C,N*-type, the two organometallic rings in (*S*)-228 are orientated in the *trans* geometry with *C*₂ symmetry. The coordination spheres of both the palladium centers are in a distorted square-planar geometry, with tetrahedral distortions of 2.4° and 3.5°. The central four-membered ring {Pd(1)–Cl(1)–Pd(2)–Cl(2)} is bent along the Cl(1)–Cl(1A) axis by 25.9°.

Figure 6.11 Molecular structure of complex (*S*)-228 with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C15) and H(C33) are omitted for clarity.

Table 6.5 Selected bond lengths (Å) and angles (°) for complex (*S*)-**228**

Pd(1)–C(1)	1.982(3)	Pd(1)–N(1)	2.078(2)
Pd(1)–Cl(2)	2.339(7)	Pd(1)–Cl(1)	2.484(7)
Pd(2)–C(19)	1.990(2)	Pd(2)–N(2)	2.068(2)
Pd(2)–Cl(1)	2.362(7)	Pd(2)–Cl(2)	2.471(7)
C(1)–Pd(1)–N(1)	80.7(1)	C(1)–Pd(1)–Cl(2)	96.0(8)
N(1)–Pd(1)–Cl(2)	176.3(7)	C(1)–Pd(1)–Cl(1)	178.2(9)
N(1)–Pd(1)–Cl(1)	98.4(7)	Cl(2)–Pd(1)–Cl(1)	85.0(2)
C(19)–Pd(2)–N(2)	81.4(1)	C(19)–Pd(2)–Cl(1)	97.0(8)
N(2)–Pd(2)–Cl(1)	178.3(6)	C(19)–Pd(2)–Cl(2)	176.2(7)
N(2)–Pd(2)–Cl(2)	96.9(6)	Cl(1)–Pd(2)–Cl(2)	84.8(2)

6.3.5.3 Synthesis of Chiral Palladacycle (*R*)-228

The optically active dichloro palladium complex (*R*)-**228** is obtained in a similar manner to syntheses of complex (*S*)-**228**: $[\alpha]_{\text{D}} -142$ (*c* 0.5, dichloromethane).

Scheme 6.9**6.3.5.4 Molecular Structure of Palladacycle (*R*)-228**

X-ray quality crystals of complex (*R*)-**228** were obtained as yellow crystals from dichloromethane/hexane which allowed the determination of the absolute configuration of the chiral palladacycle by single crystal X-ray diffractometry. The molecular structure and its numbering scheme are presented in Figure 6.12 while selected bond lengths and angles are given in Table 6.6. The (*R*) absolute configuration of the optically palladacycle was confirmed from the Flack parameter of $-0.02(3)$. The X-ray analysis of complex (*R*)-**228**

reveals that the *tert*-butyl group at the carbon center is located in the axial position and

The bond lengths and angles around the central Pd atom are comparable to the reported arylamine cyclopalladated dimeric complexes.^[6, 7, 9, 96]

Figure 6.12 Molecular structure of complex (*R*)-**228** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C15) and H(C33) are omitted for clarity.

Table 6.6 Selected bond lengths (Å) and angles (°) for complex (*R*)-**228**

Pd(1)–C(1)	1.978(3)	Pd(1)–N(1)	2.076(3)
Pd(1)–Cl(2)	2.466(9)	Pd(1)–Cl(1)	2.357(9)
Pd(2)–C(19)	1.980(4)	Pd(2)–N(2)	2.068(3)
Pd(2)–Cl(1)	2.481(9)	Pd(2)–Cl(2)	2.335(9)
C(1)–Pd(1)–N(1)	81.6(1)	C(1)–Pd(1)–Cl(2)	176.3(1)
N(1)–Pd(1)–Cl(2)	96.9(9)	C(1)–Pd(1)–Cl(1)	178.1(9)
N(1)–Pd(1)–Cl(1)	178.1(9)	Cl(2)–Pd(1)–Cl(1)	84.8(3)
C(19)–Pd(2)–N(2)	80.7(1)	C(19)–Pd(2)–Cl(2)	95.8(1)
N(2)–Pd(2)–Cl(2)	176.4(1)	C(19)–Pd(2)–Cl(1)	178.4(1)
N(2)–Pd(2)–Cl(1)	98.6(1)	Cl(2)–Pd(2)–Cl(1)	85.0(3)

6.3.6 Asymmetric *endo*-Cycloaddition Reaction between the dmpp Complex and *N,N*-Dimethylacrylamide

6.3.6.1 Formation of dmpp Complex **(R)-240**

The dmpp complex (**(R)-240**) was synthesized by treating complex (**(R)-228**) with two equivalents of dmpp at room temperature for 1 h in 91.0% yield, $[\alpha]_{\text{D}} -350$ (c 0.5, dichloromethane) (Scheme 6.10).

Scheme 6.10

6.3.6.2 Molecular Structure of Complex (**(R)-240**)

Light yellow colored single crystals were obtained from a chloroform/hexane solution of complex (**(R)-240**). The solid structure of this complex was determined by X-ray crystallography. Figure 6.13 presents the molecular structure and Table 6.7 tabulates selected inter-atomic distance and angles. According to the X-ray structure of complex (**(R)-240**), the phosphole group is in the *trans* position of the amine atom. Complex (**(R)-240**) has a distorted square-planar coordination geometry with the tetrahedral distortion angle of 13.2° . As expected, the five-membered palladacycle has an envelope-like geometry with the N(1) atom $0.743 \text{ \AA}$ above the C(15)–C(14)–C(1)–Pd(1) mean plane. Like the triphenylphosphine derivative ($\pm$)-**238**, in complex (**(R)-240**), the bond angles around P(1) are also within the normal range ($114.1(2)^\circ$, $115.8(2)^\circ$ and $119.1(2)^\circ$) (Table 6.7).

Figure 6.13 Molecular structure of complex (*R*)-**240** with thermal ellipsoids at 50% probability. Hydrogen atoms except H(C15) are omitted for clarity.

Table 6.7 Selected bond lengths (Å) and angles (°) for complex (*R*)-**240**

Pd(1)–C(1)	2.025(5)	Pd(1)–N(1)	2.142(4)
Pd(1)–P(1)	2.2397(1)	Pd(1)–Cl(1)	2.400(1)
P(1)–C(24)	1.785(5)	P(1)–C(19)	1.803(5)
P(1)–C(25)	1.824(5)	C(1)–Pd(1)–N(1)	81.1(2)
C(1)–Pd(1)–P(1)	95.2(1)	N(1)–Pd(1)–P(1)	171.4(1)
C(1)–Pd(1)–Cl(1)	170.7(1)	N(1)–Pd(1)–Cl(1)	94.7(1)
P(1)–Pd(1)–Cl(1)	90.1(5)	C(17)–N(1)–Pd(1)	110.0(3)
C(18)–N(1)–Pd(1)	114.7(3)	C(15)–N(1)–Pd(1)	103.3(3)
C(24)–P(1)–Pd(1)	119.1(2)	C(19)–P(1)–Pd(1)	114.1(2)
C(25)–P(1)–Pd(1)	115.8(2)

Figure 6.13a Molecular structure of complex (*R*)-**240** (space filling diagram)

6.3.6.3 Solution Structure of the dmpp Complex (*R*)-**240**

Similar to the analogous triphenylphosphine complex **238**, the ^{31}P NMR spectrum of the dmpp complex (*R*)-**240** in CDCl_3 shows only one singlet resonance at δ 35.0. The corresponding ^1H NMR spectrum showed the $^4J_{\text{P,H}}$ coupling in the two nonequivalent NMe signals to be 1.8 and 3.3 Hz, respectively. These NMR signals confirmed that the regio stereochemistry of the dmpp complex is retained in solution. The signal assignment is performed by 2D ^1H - ^1H ROESY NMR experiment. Figure 6.14 shows the numbering scheme of complex (*R*)-**240** and Figure 6.15 shows the 2D ^1H - ^1H ROESY NMR spectrum.

Figure 6.14 Numbering Scheme of Complex (*R*)-**240** for NMR Studies.

In the 2D ^1H - ^1H ROESY NMR spectrum, the interactions about the five-membered (*S*)-palladacycle are clearly recorded. For example, signals (A, B) show the interactions between α -methine proton H7 and NMe groups (NMe(eq) and NMe(ax)). Furthermore, signal (C, D) show that H7 also interacts with the α -methyl group Me7 and *tert*-butyl5. The α -methyl group Me7 interacts strongly with NMe(eq) (E), but very weakly with NMe(ax). All these signals show that the ring is fixed in δ conformation. The driving force for such an arrangement, Me7-*tert*-butyl5 (G), is reflected in the spectrum. In the spectrum, the interaction (N) between H10 and H2 is clearly recorded, together with the absence of interactions between dmpp group and NMe groups, all these indicate that the dmpp ligand is coordinated to palladium center *trans* to the nitrogen donor, as observed in the solid state. Some other expected ROESY signals, for example NMe(eq)-NMe(ax) (H); H8-Me9, H10-Me11 (I, J); H4-*tert*-butyl5 (K) and H4-*tert*-butyl3 (M) are observed. Furthermore, In the 2D ^1H - ^1H ROESY NMR spectrum no interactions between *tert*-butyl3 and dmpp group were recorded which shows that the *tert*-butyl3 has a limited interaction with the dmpp group (Figure 6.13a)

Figure 6.15 2D ^1H - ^1H ROESY NMR Spectrum of Complex (*R*)-**240** in CDCl_3 . (refer to Figure 6.14 for the numbering scheme of complex (*R*)-**240**). Selected ROESY Interactions: (A) H7–NMe(eq); (B) H7–NMe(ax); (C) H7–Me7; (D) H7–*tert*-butyl5; (E) Me7–NMe(eq); (F) *tert*-butyl5–NMe(ax); (G) *tert*-butyl5–Me7; (H) NMe(eq)–NMe(ax); (I, J) H8–Me9, H10–Me11; (K) H4–*tert*-butyl5; (L) H2–*tert*-butyl3; (M) H4–*tert*-butyl3; (N) H10–H2.

6.3.6.4 The Intermolecular *endo*-Cycloaddition Reaction Between Complex (*S*)-**240** and *N,N*-dimethylacrylamide

In order to study the efficiency of the new optically active palladacycle, the dmpp

complex (*S*)-**240** is subjected to the asymmetric *endo*-cycloaddition reaction with *N,N*-dimethylacrylamide (Scheme 6.11).

Scheme 6.11

Compared to the naphthylethylamine palladated complex (*S*)-**11**, the palladacycle (*S*)-**228** exhibits poor reactivity in this inter-molecular cycloaddition reaction. When the dmpp complex (*S*)-**240** is treated with excess *N,N*-dimethylacrylamide in chloroform at room temperature for 7 d, no new signals are observed based on the ^{31}P NMR spectrum. After heating up to 50°C for 15 d, the completion of the reaction is indicated by the ^{31}P NMR spectrum. Prior to purification, the ^{31}P NMR spectrum of the crude reaction mixture in CDCl_3 revealed two new sharp singlets at δ 122.9 (minor) and 125.0 (major) in a ratio of 1:2.3. As no other ^{31}P NMR signals were detected, it is affirmed that only two isomers, (*S_C, S_P*)-**241** and (*S_C, R_P*)-**241** were generated from the reaction and the starting material has been converted. The diastereomeric cycloadducts can be separated by column chromatography efficiently. The mixture was eluted slowly through a silica gel column with dichloromethane/ethyl acetate (10:1, V/V) as the mobile phase. The two

diastereomers can be readily distinguished as two well-separated bands. The major diastereomer (S_C, S_P)-**241** eluted first and was isolated as a pale yellow powder in 63.5% yield. The other diastereomer, (S_C, R_P)-**241**, was isolated as a yellow powder in 27.3% yield (Scheme 6.11). Similar to those reported in chapter 2, the known optically active ligands (S_P)-**188** and (R_P)-**188**, δ 105.1 (^{31}P NMR), could be liberated efficiently from the enantiomerically pure complex (S_C, R_P)-**241** and (S_C, R_P)-**241** respectively by treatment of these products with dppe at room temperature.^[149] The apparent inversion of configuration that takes place at the phosphorus center when the functionalized phosphine is liberated from the reaction promoter is merely a consequence of the Cahn–Ingold–Prelog (CIP) sequence rules.^[178]

A novel palladacycle (S)-**228** has been synthesized from *p*-di-*tert*-butylbenzene and was then resolved by the separation of the (*L*)-phenylalanate diastereomeric derivatives. The intermolecular *endo*-cycloaddition reaction between dmpp and *N,N*-dimethylacrylamide promoted by the new chiral palladacycle was examined and resulted the formation of a 1:2.3 diastereomeric mixture. Therefore, the bulky *tert*-butyl group on the C_3 position on the aromatic ring indeed does not exert a significant influence on the selectivity in this asymmetric cycloaddition reaction.

6.4 Attempts to the Cyclopalladation of Amine ($\pm$)-**242**

By synthesizing the optically active palladacycle (S)-**228**, we have experimentally proven that the introduction of a bulky *tert*-butyl group on the C_3 position of the phenyl ring indeed does not exert an obvious influence on the selectivity in the asymmetric cycloaddition reaction. Introduction of the protruding group next to the Pd–C bond definitely attributed to an improvement of stereoselectivity for this kind of *endo*-cycloaddition reactions. In order to extend our research scope and to seek a better chiral

auxiliary, we designed and synthesized a racemic amine ligand ($\pm$)-**242**. Compare to amine ligand ($\pm$)-**234**, the amine has a bulky *tert*-butyl group which, upon coordinating to a palladium (II) ion, could exert a larger influence on the coordination site *trans* to the nitrogen atom.

6.4.1 Synthesis of Racemic Amine Ligand ($\pm$)-**242**

As discussed in the earlier part of this chapter (6.3.2), the ketone complex **237** could not be formed using the normal Friedel-Crafts acetylation reaction. Therefore the amine ligand ($\pm$)-**242** has to be prepared from an alternative synthetic route, as illustrated in Scheme 6.12. The starting material 1,4-di-*tert*-butylbenzene **229**, was halogenated with bromine in the presence of trimethyl phosphate to give compound **243** in 94.9% yield. Both trimethyl phosphate and triethyl phosphate can be used for the halogenation reaction, but reaction using trimethyl phosphate as solvent gave a higher yield. Compound **243** reacted with magnesium in dry THF to form the desired Grignard reagent, followed by addition of acetaldehyde, which led to the formation of the alcohol compound ($\pm$)-**244** in 95.1% yield. The racemic alcohol ($\pm$)-**244** reacted with acetonitrile *via* Ritter reaction in strong acidic condition (acetic acid and sulfuric acid) to form the amide compound ($\pm$)-**245** in 75.0% yield. The amide ($\pm$)-**245** was reduced to the primary amine ($\pm$)-**246** in 76.0% yield. The primary amine ($\pm$)-**246** was heated with formaldehyde and formic acid at 100 °C for 6 h after which a tertiary amine complex ($\pm$)-**242** was formed in a 78.0% yield (Scheme 6.12).

Scheme 6.12

6.4.2 Attempt to the Cyclopalladation of amine (±)-242

The biggest challenge in *ortho*-palladation of amine (±)-**242** was to find a suitable Pd source and base to activate the *ortho* C–H bond as there is a bulky *tert*-butyl group at β -position which posed a steric hindrance. Thus a series of Pd(II) salts such as $\text{Pd}(\text{OAc})_2$, $\text{Li}[\text{PdCl}_4]$ and $[\text{Pd}(\text{NCMe})_4](\text{ClO}_4)_2$ and bases such as triethylamine, Na_2CO_3 , NaOAc and *tert*-butoxide were used. Unfortunately *ortho*-palladated complex (±)-**247** could not be formed (Scheme 6.13).

Scheme 6.13

6.4.3 Conclusions

In this chapter, two novel amine ligands, 1-(2,4-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine and 1-(2,5-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine were synthesized. Direct *ortho*-palladation of the sterically less-hindered 1-(2,4-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine using Pd(OAc)₂ and LiCl proceeded readily to form the dimeric chloro complex which was then converted to the corresponding triphenylphosphine derivative. The palladacycle structure and ring conformations of this mononuclear have been investigated. This new racemic cyclopalladated complex could be efficiently resolved *via* the formation of its (*L*)-phenylalanate derivatives and a successful separation of the resulting diastereomeric complexes was achieved by slow crystallization using different solvent systems. The intermolecular *endo*-cycloaddition reaction between dmpp and *N,N*-dimethylacrylamide promoted by the new chiral palladacycle was examined and resulted the formation of a 1:2.3 diastereomeric mixture. Therefore, the bulky *tert*-butyl group on the C₃ position on the aromatic ring indeed does not exert a significant influence on the selectivity in this asymmetric cycloaddition reaction. The other sterically hindered amine ligand, 1-(2,5-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine (±)-**242**, could not be induced to form the dimeric palladium complex by using an array of palladium sources. The bulky *tert*-butyl group protruding uncompromisingly into the space near the donor atoms (N and C) could be the main obstacle for the dimeric complex formation.

6.5 Experimental

Reactions involving air-sensitive compounds were performed under a positive pressure of purified nitrogen using standard Schlenk techniques. Proton nuclear magnetic resonance (¹H NMR) and carbon nuclear magnetic resonance (¹³C NMR) spectroscopy

were performed on Bruker Avance 300, 400 and 500 NMR spectrometers. The number of protons (n) for a given resonance is indicated by nH . Coupling constants are reported as a J value in Hz. Proton nuclear magnetic resonance spectra 1H NMR is reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0). Carbon nuclear magnetic resonance spectra ^{13}C NMR is reported as δ in units of parts per million (ppm) relative to the signal of chloroform- d (δ 77.00, triplet). All the ^{31}P NMR spectra were recorded at 121 MHz on a Bruker Avance DPX300 NMR spectrometer. Unless stated otherwise, all NMR spectroscopic experiments were performed at room temperature (300 K). Chemical shifts (δ) are reported in ppm relative to TMS, and referenced to the chemical shifts of residual solvent resonances (1H and ^{13}C NMR) or 85% H_3PO_4 (^{31}P NMR). Mass spectra were recorded on a Thermo Finnigan MAT 95 XP Mass Spectrometer with EI mode and Waters Q-ToF Premier Mass Spectrometer with ESI mode. Melting points were determined on SRS-Optimelt MPA-100 apparatus and were uncorrected. Optical rotations were measured on the specified solution in 0.1-dm cell at 20 °C with a Perkin-Elmer model 341 polarimeter. Elemental analyses were performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at the Nanyang Technological University of Singapore.

6.5.1 Synthesis of 1-(2,4-di-*tert*-butylphenyl)ethanone, **230**

A mixture of 1,4-di-*tert*-butylbenzene **229** (7.90 g, 41.6 mmol) and acetyl chloride (3.20 g, 2.86 mL, 40.8 mmol) in 100 mL of dichloromethane was added to the suspension of $AlCl_3$ (5.90 g, 44.2 mmol) in 150 mL of the same solvent at 0 °C. The mixture was stirred for 3 h at 40 °C, poured into cold conc. hydrochloric acid and extracted with dichloromethane. The organic layer was washed with H_2O and dried with $MgSO_4$. After removing the solvent, the crude mixture was separated by silica gel column

chromatography (diethyl ether/hexane = 1:10) to give compound **230** as a colorless oil, 2.90 g, 30.1%. ^1H NMR (300 MHz, CDCl_3): δ = 1.36 (s, 9 H, CCH_3), 1.42 (s, 9 H, CCH_3), 2.61 (s, 3 H, COCH_3), 7.13 (d, $^3J_{\text{H,H}} = 6.0$ Hz, 1 H, aromatic proton), 7.27 (dd, $^3J_{\text{H,H}} = 6.0$ Hz, $^4J_{\text{H,H}} = 1.4$ Hz, 1 H, aromatic proton), 7.55 (d, 1 H, $^4J_{\text{H,H}} = 1.4$ Hz, 1 H, aromatic proton) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 31.29, 31.91, 32.44, 34.90, 36.19, 122.13, 124.28, 125.91, 139.40, 146.58, 151.96, 207.98 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$)) $^+$ calcd for $\text{C}_{16}\text{H}_{25}\text{O}$ 233.1905, found 233.1893.

The other two isomers, 1-(3,5-di-*tert*-butylphenyl)ethanone **235** and 1-(4-*tert*-butylphenyl)ethanone **236** were also isolated.

1-(3,5-di-*tert*-butylphenyl)ethanone **235**, colorless oil, ^1H NMR (300 MHz, CDCl_3): δ = 1.36 (s, 18 H, CCH_3), 2.61 (s, 3 H, COCH_3), 7.64–7.65 (m, 1 H, aromatic proton), 7.81 (s, 2 H, aromatic protons) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 26.80, 31.13, 35.98, 122.53, 128.3, 136.89, 151.22, 198.91 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$)) $^+$ calcd for $\text{C}_{16}\text{H}_{25}\text{O}$ 233.1905, found 233.1896.

1-(4-*tert*-butylphenyl)ethanone **236**, colorless oil, ^1H NMR (300 MHz, CDCl_3): δ = 1.34 (s, 9 H, CCH_3), 2.58 (s, 3 H, COCH_3), 7.45–7.48 (m, 2 H, aromatic protons), 7.88–7.91 (d, 2 H, aromatic protons) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 26.52, 31.09, 35.09, 125.50, 128.30, 134.63, 156.79, 197.77 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$)) $^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{O}$ 177.1279, found 177.1280.

6.5.2 Synthesis of 1-(2,4-di-*tert*-butylphenyl)ethanol, ($\pm$)-**231**

A methanol solution of NaBH_4 (0.95 g, 25.0 mmol) was added to 2.90 g (12.5 mmol) compound **230** in the same solvent (30 mL). The mixture was stirred at 60 °C for 2 days followed by treatment with dilute NaOH (3 %, 40 mL). The resulting solution was concentrated to 40 mL and extracted with dichloromethane. The organic layers were

combined, washed with H₂O and dried with MgSO₄. Removal of the solvent gave the product (±)-**231** as a light yellow waxy solid, 2.42 g, 82.7%. M.p. 87–88 °C. ¹H NMR (300 MHz, CDCl₃): δ = 1.38 (s, 9 H, CCH₃), 1.50 (s, 9 H, CCH₃), 1.56 (d, ³J_{H,H} = 4.7 Hz, 3 H, CHCH₃), 2.09 (s, 1 H, OH), 5.65 (q, ³J_{H,H} = 4.7 Hz, 1 H, CHCH₃), 7.36 (dd, ³J_{H,H} = 6.2 Hz, ⁴J_{H,H} = 1.5 Hz, 1 H, aromatic proton), 7.44 (d, ⁴J_{H,H} = 1.5 Hz, 1 H, aromatic proton), 7.60 (d, ³J_{H,H} = 6.2 Hz, 1 H, aromatic proton). ¹³C NMR (75 MHz, CDCl₃): δ = 24.92, 31.47, 32.33, 34.77, 35.77, 66.17, 122.59, 123.57, 127.40, 141.82, 145.60, 149.74 ppm. HRMS (ESI, m/z (M – OH)]⁺ calcd for C₁₆H₂₅ 217.1956, found 217.1951.

6.5.3 Synthesis of N-(1-(2,4-di-*tert*-butylphenyl)ethyl)acetamide, (±)-**232**

The alcohol (±)-**231** (2.42 g, 10.3 mmol) was led into a solution of 2 mL acetonitrile in 5 mL glacial acetic acid containing 1 mL concentrated sulfuric while the temperature was maintained at room temperature. The reaction was then kept loosely and allowed to stand overnight. The mixture was poured into H₂O, neutralized with NaOH solution (pH = 7) and extracted with dichloromethane. The combined organic layers were dried with MgSO₄. Removal of the solvent gave the product (±)-**232** as a white solid, 2.51 g (88.3%). M.p. 161–162 °C. ¹H NMR (300 MHz, CDCl₃): δ = 1.33 (s, 9 H, CCH₃), 1.44 (s, 9 H, CCH₃), 1.52 (d, ³J_{H,H} = 6.3 Hz, 3 H, CHCH₃), 1.94 (s, 3 H, COCH₃), 5.65 (s, 1 H, NH), 5.67 (q, ³J_{H,H} = 6.8 Hz, 1 H, CHCH₃), 7.28 (s, 2 H, aromatic protons), 7.43 (s, 1 H, aromatic proton). ¹³C NMR (75 MHz, CDCl₃): δ = 22.81, 23.50, 31.35, 31.75, 34.72, 34.74, 46.14, 123.37, 123.48, 126.74, 139.08, 146.53, 149.8, 168.72 ppm. HRMS (ESI, m/z (M + H)]⁺ calcd for C₁₈H₃₀NO 276.2327, found 276.2318.

6.5.4 Synthesis of 1-(2,4-di-*tert*-butylphenyl)ethanamine, (±)-**233**

A 25 mL Claisen base (8.80 g KOH was dissolved in 6 mL H₂O which was diluted to 25

ml by methanol) was added to compound ($\pm$)-**232** (2.51 g, 9.13 mmol) and the mixture was heated to 125 °C for 2 d. The solvent was removed under vacuum and the residue was dissolved in dichloromethane. The solution was washed with H₂O and dried (MgSO₄). Removal of the solvent gave the product ($\pm$)-**233** as light yellow oil, 1.98 g (93.1%). ¹H NMR (300 MHz, CDCl₃): δ = 1.24 (s, 9 H, CCH₃), 1.33 (d, ³J_{H,H} = 6.5 Hz, 3 H, CHCH₃), 1.37 (s, 9 H, CCH₃), 1.55 (s, 2 H, NH), 4.72 (q, ³J_{H,H} = 6.5 Hz, 1 H, CHCH₃), 7.19 (dd, ³J_{H,H} = 8.2 Hz, ⁴J_{H,H} = 2.0 Hz, 1 H, aromatic proton), 7.28 (d, ⁴J_{H,H} = 2.0 Hz, 1 H, aromatic proton), 7.37 (d, ⁴J_{H,H} = 8.2 Hz, 1 H, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 25.42, 31.46, 32.16, 34.67, 35.73, 46.44, 122.61, 123.40, 126.88, 143.97, 145.36, 148.71 ppm. HRMS (ESI, m/z (M + H)⁺) calcd for C₁₆H₂₈N 234.2222, found 234.2230.

6.5.5 Synthesis of 1-(2,4-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine, ($\pm$)-**234**

The amine compound ($\pm$)-**233** (1.98 g, 8.50 mmol) was dissolved in 12.5 ml of formic acid at 0 °C, followed by addition of formaldehyde solution. The resulting solution was heated to 100 °C for 6 h. After being cooled to room temperature, the mixture was added 10 ml conc. hydrochloric acid. After removal of the solvent under vacuum, the residual oil was treated with conc. NaOH solution till pH = 14 and the liberated amine was extracted into dichloromethane. The organic layers were dried (MgSO₄) and removed under vacuum. The crude product was chromatographed on a silica gel column using ethyl acetate as the eluent gave compound ($\pm$)-**234** as a light yellow liquid, 1.91 g (86.1%). ¹H NMR (300 MHz, CDCl₃): δ = 1.32 (s, 9 H, CCH₃), 1.34 (d, ³J_{H,H} = 6.4 Hz, 3 H, CHCH₃), 1.45 (s, 9 H, CCH₃), 2.26 (s, 6 H, NCH₃), 3.86 (q, ³J_{H,H} = 6.3 Hz, 1 H, CHCH₃), 7.21 (dd, ³J_{H,H} = 8.2 Hz, ⁴J_{H,H} = 2.0 Hz, 1 H, aromatic proton), 7.35 (d, ⁴J_{H,H} = 2.0 Hz, 1 H, aromatic proton), 7.58 (d, ³J_{H,H} = 8.2 Hz, 1 H, aromatic proton) ppm. ¹³C NMR (100

MHz, CDCl₃): δ = 23.37, 31.47, 32.30, 34.60, 36.02, 44.34, 61.56, 122.63, 123.17, 127.93, 142.03, 145.35, 148.43 ppm. HRMS (ESI, m/z (M + H)⁺ calcd for C₁₈H₃₂N 262.2535, found 262.2533.

6.5.6 Synthesis of (±)-Di- μ -chlorobis[1-[1-(dimethylamino)ethyl]-3,5-di-*tert*-butyl- 6-phenyl-*C,N*]dipalladium(II), (±)-228

Method A: A mixture of *trans*-dichlorobis(acetonitrile)palladium(II) (0.29 g, 1.14 mmol) and silver perchlorate (0.47 g, 2.29 mmol) in acetonitrile (15 mL) was stirred at room temperature for 1 h. The precipitate (AgCl) was filtered out and the filtrate was added into a mixture of compound (±)-**234** (0.30 g, 1.14 mmol) and triethylamine (0.11 g, 1.14 mmol) in dichloromethane (15 mL). The mixture was allowed to stir at room temperature for 20 h before filtering through Celite. The filtrate was evaporated and the residue was dissolved in dichloromethane. Dilute hydrochloric acid (1 M, 20 mL) was added to the solution and the mixture was stirred vigorously for 1 h. The organic layer was separated, washed with H₂O and dried over MgSO₄. Removal of solvent gave the crude product which was purified using a silica gel column with dichloromethane as the eluent. Removal of solvent obtained the product (±)-**228** as yellow solid, 0.32 g, 66.7%. M.p. 210–212 °C. Anal Calcd for C₃₆H₆₀Cl₂N₂Pd₂ (802.22): C, 53.47; H, 7.52; N, 3.48. Found: C, 53.55; H, 7.55; N, 3.67. ¹H NMR (300 MHz, CDCl₃): δ = 1.29–1.35 (m, 36 H, CCH₃), 1.96–2.00 (m, 6 H, CHCH₃), 2.71–2.84 (m, 12 H, NCH₃), 3.92 (q, ³J_{H,H} = 5.0 Hz, 2 H, CHCH₃), 7.03–7.19 (m, 4 H, aromatic protons) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 26.26, 31.14, 31.55, 34.6, 35.41, 48.88, 49.36, 119.67, 119.72, 128.36, 128.60, 143.12, 146.73, 146.89, 147.21 ppm.

Method **B**: A mixture of palladium(II) chloride (0.20 g, 1.14 mmol) and lithium chloride (1.18 g, 4.29 mmol) in methanol (15 mL) was stirred at room temperature for 3 h. Amine ($\pm$)-**234** (0.3 g, 1.14 mmol) in triethylamine (0.11 g, 1.14 mmol) was added to the reaction and stirred for 5 h before filtering through Celite. The filtrate was evaporated and the residue was dissolved in dichloromethane. The organic layer was separated, washed with H₂O and dried over MgSO₄. Removal of solvent gave the crude product which was then purified using a silica gel column with dichloromethane as the eluent. Removal of solvent gave the product ($\pm$)-**228** as yellow solid, 0.27 g, 56.0%.

Method **C**: A mixture of compound ($\pm$)-**234** (0.44 g, 1.7 mmol) and palladium acetate (0.38 g, 1.14 mmol) in methanol (15 mL) was stirred at 50 °C for 1.5 h. The reaction was cooled to room temperature and excess amount of lithium chloride (0.21 g, 5.15 mmol) was added to the reaction and stirred at room temperature for 1 h before filtering through Celite. The filtrate was evaporated and the residue was dissolved in dichloromethane. The organic layer was separated, washed with H₂O and dried over MgSO₄. Removal of solvent formed the crude product which was purified using a silica gel column with dichloromethane as the eluent. Removal of solvent gave the purified product ($\pm$)-**228** as yellow solid, 0.45 g, 63.0%.

6.5.7 Synthesis of ($\pm$)-Chloro[1-[1-(dimethylamino)ethyl]-3,5-di-*tert*-butyl- 6-phenyl-*C,N*](triphenylphosphine-*P*)palladium(II), ($\pm$)-**238**

A dichloromethane (10 mL) solution of complex ($\pm$)-**228** (0.20 g, 0.25 mmol) was treated with triphenylphosphine (0.13 g, 0.50 mmol) in the same solvent (10 mL). The resulting solution was stirred for 1 h at room temperature. After removing the solvent, the residue

solid was chromatographed on a silica gel column (dichloromethane/ethyl acetate = 4/1) as the eluent to give a pale yellow powder complex ($\pm$)-**238**, which was recrystallized from a solution of dichloromethane and hexane as yellow crystals, 0.29 g (88.0%). M.p. 213–215 °C (dec.), Anal Calcd for $C_{36}H_{45}ClNPPd$ (664.60): C, 65.06; H, 6.82; N, 2.11. Found: C, 65.31; H, 6.88; N, 2.34. ^{31}P NMR (121 MHz, $CDCl_3$): δ = 41.8 (s) ppm. 1H NMR (500 MHz, $CDCl_3$): δ = 0.72 (s, 9 H, CCH_3), 1.41 (s, 9 H, CCH_3), 2.09 (d, $^3J_{H,H}$ = 5.9 Hz, 3 H, $CHCH_3$), 2.72 (d, $^4J_{P,H}$ = 1.6 Hz, 3 H, $NCH_{3(ax)}$), 2.95 (d, $^4J_{P,H}$ = 3.3 Hz, 3 H, $NCH_{3(eq)}$), 4.19 (qn, $^4J_{P,H}$ = $^3J_{H,H}$ = 5.9 Hz, 1 H, $CHCH_3$), 6.48 (dd, $^4J_{P,H}$ = 8.0 Hz, $^4J_{H,H}$ = 1.4 Hz, 1 H, aromatic proton), 6.92 (d, $^4J_{H,H}$ = 1.4 Hz, 1 H, aromatic proton), 7.33–7.41 (m, 9 H, aromatic protons), 7.74–7.79 (m, 6 H, aromatic protons) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.07, 30.72, 31.76, 34.01, 35.46, 48.56, 50.44 (d, $J_{C,P}$ = 2.4 Hz), 72.41 (d, $J_{C,P}$ = 2.8 Hz), 118.62, 127.74 (d, $J_{C,P}$ = 10.4 Hz), 129.96 (d, $J_{C,P}$ = 2.0 Hz), 131.80 (d, $J_{C,P}$ = 47.5 Hz), 134.64, 134.85 (d, $J_{C,P}$ = 10.4 Hz), 142.51, 146.03 (d, $J_{C,P}$ = 5.9 Hz), 148.51 (d, $J_{C,P}$ = 1.8 Hz), 152.87 ppm. HRMS (ESI, m/z ($M - Cl$)) $^+$ calcd for $C_{36}H_{45}NOPd$ 628.2324, found 628.2333.

6.5.8 Synthesis and Isolation of (S_C,S_N)-Prolinato-[1-[1-(dimethyl amino)ethyl]-3,5-di-*tert*-butyl-6-phenyl- C,N]palladium(II), (S_C,S_C)-239** and (R_C,S_N)-Prolinato-[1-[1-(dimethylamino)ethyl]-3,5-di-*tert*-butyl-6-phenyl- C,N]palladium(II), (R_C,S_C)-**239****

To a suspension of the racemic dimer ($\pm$)-**228** (4.00 g, 5 mmol) in methanol (30 mL) was added a solution of sodium (*L*)-phenylalanate (2.06 g, 11 mmol) in the same solvent (30 mL). The mixture was stirred at room temperature for 1 h and the solvent was removed under reduced pressure. The solution of the residue in dichloromethane (50 mL) was washed with H_2O , dried ($MgSO_4$) and diluted with diethyl ether. The less soluble diastereomer (S_C,R_C)-**239** crystallized slowly as white flakes (2.04 g, 77.0%, based on half

of the dimer used), > 99% *de* (according to the ^1H NMR spectrum), M.p. 190–192 °C (dec.), $[\alpha]_{\text{D}} +48$, $[\alpha]_{578} +28$, $[\alpha]_{546} +36$, $[\alpha]_{436} +60^\circ$, $[\alpha]_{365} +66$ (*c* 0.5, dichloromethane). Anal Calcd for $\text{C}_{27}\text{H}_{40}\text{N}_2\text{O}_2\text{Pd}$ (530.21): C, 61.07; H, 7.59; N, 5.28. Found: C, 60.68; H, 8.13; N, 5.26. ^1H NMR (400 MHz, CDCl_3): δ = 1.21 (s, 9 H, CCH_3), 1.35 (s, 9 H, CCH_3), 1.90 (d, $^3J_{\text{H,H}} = 5.7$ Hz, 3 H, CHCH_3), 2.39 (s, 1 H, *NH*), 2.54 (s, 1 H, *NH*), 2.70 (s, 3 H, $\text{NMe}_{(\text{ax})}$), 2.78 (s, 3 H, $\text{NMe}_{(\text{eq})}$), 3.39–3.57 (m, 2 H, Ar-CH_2), 3.77–3.81 (m, 1 H, *CH*), 3.98 (q, $^3J_{\text{H,H}} = 5.8$ Hz, 1 H, CHCH_3), 6.31 (s, 1 H, aromatic proton), 7.05 (s, 1 H, aromatic proton), 7.26 (m, 5 H, aromatic protons) ppm. ^{13}C NMR (125 MHz, CDCl_3): δ = 26.15, 31.42, 31.78, 34.53, 35.56, 40.56, 47.74, 52.90, 61.01, 72.75, 119.53, 126.62, 126.21, 129.06, 129.17, 136.95, 143.44, 146.23, 147.03, 148.35, 179.88 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$) $^+$) calcd for $\text{C}_{27}\text{H}_{41}\text{N}_2\text{O}_2\text{Pd}$ 531.2203, found 531.2195.

After removing the solvent of the *R* diastereomer rich mother liquor, the light yellow residue was dissolved in minimum chloroform. Slow addition of hexane resulted in the precipitation of the other diastereomer, (*R*_C,*S*_C)-**239**, in the form of white flakes (1.78 g, 67.0%, based on half of the dimer used), > 99% *de* (according to the ^1H NMR spectrum), M.p. 195–197 °C (dec.), $[\alpha]_{\text{D}} -46$, $[\alpha]_{578} -48$, $[\alpha]_{546} -52$, $[\alpha]_{436} -72$, (*c* 0.5, dichloromethane). Anal Calcd for $\text{C}_{27}\text{H}_{40}\text{N}_2\text{O}_2\text{Pd}$ (530.21): C, 61.07; H, 7.59; N, 5.28. Found: C, 60.68; H, 8.13; N, 5.26. ^1H NMR (500 MHz, CDCl_3): δ = 1.19 (s, 9 H, CCH_3), 1.32 (s, 9 H, CCH_3), 1.88 (d, $^3J_{\text{H,H}} = 6.0$ Hz, 3 H, CHCH_3), 2.52–2.53 (m, 1 H, *NH*), 2.66 (s, 3 H, $\text{NCH}_3_{(\text{ax})}$), 2.74 (s, 3 H, $\text{NCH}_3_{(\text{eq})}$), 3.34–3.54 (m, 2 H, CHCH_2), 3.74–3.77 (m, 1 H, *NH*), 3.93–3.95 (m, 2 H, CHCH_3 , COCH), 6.29 (s, 1 H, aromatic proton), 7.02 (s, 1 H, aromatic proton), 7.23–7.26 (m, 5 H, aromatic protons) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 25.80, 31.17, 31.49, 34.23, 35.22, 40.21, 47.42, 52.53, 60.65, 72.34, 119.02, 126.68, 126.76, 128.65, 128.97, 136.73, 142.96, 146.14, 146.65, 148.03, 179.92 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$) $^+$) calcd for $\text{C}_{27}\text{H}_{41}\text{N}_2\text{O}_2\text{Pd}$ 531.2203, found 531.2195.

6.5.9 Synthesis of (*S*)-Di- μ -chlorobis[1-[1-(dimethylamino)ethyl]-3,5-di-*tert*-butyl-6-phenyl-*C,N*]dipalladium(II), (*S*)-228

A dilute hydrochloric acid aqueous solution (1 M, 30 mL) was added to a dichloromethane solution diastereomer (S_C, S_C)-**239** (2.04 g, 3.85 mmol). After vigorous stirring for 1 h, the organic layer was separated, washed with H₂O and dried (MgSO₄). Removal of the solvent, yellow solid was formed which was then recrystallized from dichloromethane/hexane as yellow crystals, 1.50 g (97.0%). M.p. 127–129 °C, $[\alpha]_D +140$, $[\alpha]_{578} +146$, $[\alpha]_{546} +164$, $[\alpha]_{436} +302$ (*c* 0.5, dichloromethane). ¹H NMR (400 MHz, CDCl₃): δ = 1.27 (s, 18 H, CCH₃), 1.32 (s, 18 H, CCH₃), 1.97 (d, ³*J*_{H,H} = 5.8 Hz, 6 H, CHCH₃), 2.69–2.82 (m, 12 H, NCH₃), 3.90 (q, ³*J*_{H,H} = 5.6 Hz, 2 H, CHCH₃), 7.01–7.17 (m, 4 H, aromatic protons) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 26.37, 31.34, 31.44, 31.82, 34.80, 35.48, 48.90, 49.52, 53.36, 53.51, 53.72, 73.75, 73.85, 76.68, 119.62, 128.10, 128.42, 128.83, 128.90, 142.83, 146.54, 146.67, 146.87, 146.95 ppm.

The optically pure complex (*R*)-**228** was prepared from complex (R_C, S_C)-**239** in a similar manner: $[\alpha]_D -142$, $[\alpha]_{578} -152$, $[\alpha]_{546} -168$, $[\alpha]_{436} -312$, (*c* 0.5, dichloromethane).

6.5.10 Synthesis of Chloro[*(R)*-1-(1-(dimethylamino)ethyl)-3,5-di-*tert*-butyl- 6-phenyl -*C,N*][3,4-dimethyl-1-phenylphosphole]palladium(II), (*R*)-240

A solution of complex (*R*)-**228** (0.20 g, 0.25 mmol) in dichloromethane (10 mL) was added to a solution of 3,4-dimethyl-1-phenylphosphole (dmpp) (0.10 g, 0.53 mmol) in the same solvent (5 mL). The resulting yellow solution was stirred at room temperature for 1 h and the solvent was removed under reduced pressure. The residue solid was chromatographed on a silica gel column (dichloromethane/ethyl acetate = 1:1, V/V) as the eluent to give a pale yellow powder complex (*R*)-**240**, 0.27 (91.0%). M.p. 196–108 °C, $[\alpha]_D -350$, $[\alpha]_{578} -370$, $[\alpha]_{546} -424$, $[\alpha]_{436} -860$ (*c* 0.5, dichloromethane). ³¹P NMR (121

MHz, CDCl₃): δ = 37.5 (s) ppm. ¹H NMR (300 MHz, CDCl₃): δ = 1.05 (s, 9 H, CCH₃), 1.38 (s, 9 H, CCH₃), 1.87 (d, ³J_{H,H} = 6.0 Hz, 3 H, CHCH₃), 2.10 (s, 3 H, C=CCH₃), 2.10 (s, 3 H, C=CCH₃), 2.68 (d, ⁴J_{P,H} = 1.8 Hz, 3 H, NCH₃(_{ax})), 2.88 (d, ⁴J_{P,H} = 3.3 Hz, 3 H, NCH₃(_{eq})), 4.11 (qn, ³J_{H,H} = 6.0 Hz, 1 H, CH₃CH), 6.45 (d, ²J_{P,H} = 32.5 Hz, 1 H, C=CH), 6.83 (dd, ³J_{H,H} = 7.5 Hz, ⁵J_{P,H} = 1.7 Hz, 1 H, aromatic proton), 6.90 (d, ²J_{P,H} = 32.5 Hz, 1 H, C=CH), 7.04 (s, 1 H, aromatic proton), 7.28–7.41 (m, 3 H, *p*-Ph, 2× *m*-Ph), 7.87–7.94 (m, 2 H, 2× *o*-Ph) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 17.69 (d, *J*_{C,P} = 6.4 Hz), 17.81 (d, *J*_{C,P} = 6.3 Hz), 26.20, 31.22, 31.88, 34.55, 35.75, 48.07, 50.63 (d, *J*_{C,P} = 2.5 Hz), 72.48 (d, *J*_{C,P} = 2.9 Hz), 119.23, 124.67 (d, *J*_{C,P} = 49.6 Hz), 127.29 (d, *J*_{C,P} = 45.3 Hz), 128.06 (d, *J*_{C,P} = 50.9 Hz), 128.50 (d, *J*_{C,P} = 10.8 Hz), 130.64 (d, *J*_{C,P} = 2.2 Hz), 133.25 (d, *J*_{C,P} = 14.6 Hz), 133.74 (d, *J*_{C,P} = 12.8 Hz), 143.76, 147.10 (d, *J*_{C,P} = 5.8 Hz), 149.12 (d, *J*_{C,P} = 2.2 Hz), 149.90 (d, *J*_{C,P} = 9.9 Hz), 151.25, 153.63 (d, *J*_{C,P} = 11.0 Hz) ppm. HRMS (ESI) (*m/z*): [M – Cl]⁺ calcd for C₃₀H₄₃NPPd 554.2168, found 554.2156.

6.5.11 Asymmetric *endo*-Cycloaddition Reaction between (*S*)-**240** and *N,N*-Dimethyl acrylamide. Synthesis and Isolation of Complex (*S*_C,*R*_P)-**241** and (*S*_C,*S*_P)-**241**

A solution of the chloro complex (*S*)-**240** (0.59 g, 1.0 mmol) in chloroform (10 mL) was stirred with *N,N*-dimethylacrylamide (0.30 g, 3.0 mmol) at 50 °C for 15 d. Removal of solvent left a brownish oil. The ³¹P NMR (CDCl₃) spectrum of the crude product prior to purification indicated a 1:2.3 mixture of the diastereomeric cycloadducts at δ 122.9 and 125.0 ppm. Both the diastereomeric products, (*S*_C,*S*_P)-**241** and (*S*_C,*R*_P)-**241**, were isolated on a silica gel column (ethyl acetate/dichloromethane = 1:10, V/V). The first eluted complex, the major diastereomer (*S*_C,*S*_P)-**241**, exhibited one ³¹P NMR signals at δ 125.0 ppm, 0.44 g (63.5%), M.p. 193–195 °C (dec.), [α]_D +154, [α]₅₇₈ +154, [α]₅₄₆ +156, [α]₄₃₆ +130, (*c* 0.5, dichloromethane). Anal Calcd for C₃₅H₅₂ClN₂OPPd- 0.5C₆H₁₄ (731.31): C,

62.29; H, 8.12; N, 3.82. Found: C, 62.21; H, 7.67; N, 3.94. ^{31}P NMR (121 MHz, CDCl_3): $\delta = 122.9$ (s) ppm. ^1H NMR (400 MHz, CDCl_3): $\delta = 1.21$ (s, 9 H, CCH_3), 1.30 (s, 3 H, $\text{C}=\text{CCH}_3$), 1.34 (s, 9 H, CCH_3), 1.83 (s, 3 H, $\text{C}=\text{CCH}_3$), 1.92 (d, $^3J_{\text{H,H}} = 5.9$ Hz, 3 H, CHCH_3), 2.22–2.35 (m, 1 H, CH), 2.41–2.44 (m, 1 H), 2.48 (s, 3 H, NCH_3), 2.83 (s, 3 H, NCH_3), 2.91 (s, 3 H), 3.10 (br, 1 H), 3.37 (s, 3H), 3.65 (br, 1 H), 4.08 (qn, $^3J_{\text{H,H}} = ^4J_{\text{P,H}} = 7.3$ Hz, 1 H, CHCH_3), 4.50–4.51 (m, 1H), 6.71 (d, $^3J_{\text{H,H}} = 8.0$ Hz, 1 H, aromatic proton), 7.03 (s, 1 H, aromatic proton), 7.40–7.45 (m, 3 H, p -Ph, $2 \times m$ -Ph), 7.88–7.92 (m, 2 H, $2 \times o$ -Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 14.33$ (d, $J_{\text{C,P}} = 2.6$ Hz), 15.07 (d, $J_{\text{C,P}} = 2.7$ Hz), 26.04, 27.96 (d, $J_{\text{C,P}} = 19.1$ Hz), 31.56, 31.88, 34.91, 35.83, 37.76, 40.98 (d, $J_{\text{C,P}} = 22.9$ Hz), 47.12 (d, $J_{\text{C,P}} = 31.5$ Hz), 48.04, 50.51, 52.75 (d, $J_{\text{C,P}} = 33.7$ Hz), 71.69 (d, $J_{\text{C,P}} = 2.4$ Hz), 119.56, 128.08, 129.17, 129.94, 130.26, 131.82, 133.60, 134.52, 143.52, 147.34, 148.70, 152.10, 171.9 ppm. HRMS (ESI) (m/z): $[\text{M} - \text{Cl}]^+$ calcd for $\text{C}_{35}\text{H}_{52}\text{N}_2\text{OPd}$ 653.2852, found 653.2844.

The second eluted complex, the minor diastereomer ($S_{\text{C}}, R_{\text{P}}$)-**241**, 0.19 g (27.3%), M.p. 195–197 °C (dec.), $[\alpha]_{\text{D}} +88$, $[\alpha]_{578} +90$, $[\alpha]_{546} +82$, $[\alpha]_{436} +98$ (c 0.5, dichloromethane). Anal Calcd for $\text{C}_{35}\text{H}_{52}\text{ClN}_2\text{OPd} \cdot 0.5\text{C}_6\text{H}_{14}$ (731.31): C, 62.29; H, 8.12; N, 3.82. Found: C, 62.15; H, 7.62; N, 4.00. ^{31}P NMR (121 MHz, CDCl_3): $\delta = 125.0$ (s) ppm.

^1H NMR (400 MHz, CDCl_3): $\delta = 1.23$ (s, 9 H, CCH_3), 1.31 (s, 9 H, CCH_3), 1.46 (s, 3 H, $\text{C}=\text{CCH}_3$), 1.63 (s, 3 H, $\text{C}=\text{CCH}_3$), 1.90 (d, $^3J_{\text{H,H}} = 4.8$ Hz, 3 H, CHCH_3), 2.10–2.21 (m, 1 H, CH), 2.41 (s, 3 H), 2.45 (s, 3 H), 2.78 (s, 3 H, NCH_3), 2.79 (s, 3 H, NCH_3), 2.99 (t, 1 H), 3.17 (br, 1 H), 3.45 (br, 1 H), 3.94 (br, 1 H), 4.03 (m, 1 H), 4.06 (qn, $^3J_{\text{H,H}} = ^4J_{\text{P,H}} = 7.1$ Hz, 1 H, CHCH_3), 6.86 (d, $^3J_{\text{H,H}} = 7.3$ Hz, 1 H, aromatic proton), 7.00 (s, 1 H, aromatic proton), 7.37 (br, 3 H, p -Ph, $2 \times m$ -Ph), 7.83 (br, 2 H, $2 \times o$ -Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 13.88$ (d, $J_{\text{C,P}} = 2.5$ Hz), 14.04, 15.73 (d, $^3J_{\text{C,P}} = 1.9$ Hz), 20.89, 25.81, 31.51, 31.88, 34.77, 35.65 (d, $J_{\text{C,P}} = 2.5$ Hz), 36.11, 39.90 (d, $J_{\text{C,P}} = 29.3$ Hz), 47.82, 50.22 (d,

$J_{C,P} = 33.0$ Hz), 60.20, 71.57 (d, $^3J_{C,P} = 2.4$ Hz), 119.53, 128.08 (d, $^2J_{C,P} = 8.9$ Hz), 130.09 (d, $J_{C,P} = 18.9$ Hz), 131.58 (d, $J_{C,P} = 14.6$ Hz), 132.80 (d, $J_{C,P} = 9.3$ Hz), 135.43, 143.89, 147.22 (d, $J_{C,P} = 5.5$ Hz), 148.61, 152.67, 170.93, 172.00 (d, $J_{C,P} = 17$ Hz) ppm. HRMS (ESI) (m/z): $[M - Cl]^+$ calcd for $C_{35}H_{52}N_2OPPd$ 653.2852, found 653.2844.

6.5.12 Formation of Compound (*S_P*)-**188** and (*R_P*)-**188**.

A solution of complex (*S_C,R_P*)-**241** (0.069 g, 0.1 mmol) in dichloromethane (2 mL) was treated with a solution of 1,2-bis(diphenylphosphino)ethane (0.04 g, 0.1 mmol) in the same solvent (2 mL) for 3 h. The resulting yellowish mixture was passed through a column which was packed successively with silica gel (1 g) and florisil (10 g), with dichloromethane as the eluent to yield a colorless solution. Removal of solvent under reduced pressure gave (*S_P*)-**188** as an air-sensitive colorless oil, Yield 0.022 g (76.6%); $[\alpha]_D +5.9$, (c 0.5, dichloromethane), ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 105.1$ (s) ppm. Compound (*R_P*)-**188** was liberated using the same method from complex (*S_C,S_P*)-**142**, $[\alpha]_D -1.0$, (c 0.5, dichloromethane), ^{31}P NMR (121 MHz, $CDCl_3$): $\delta = 105.1$ (s) ppm. Compound (*R_P*)-**188** and (*S_P*)-**188** are air-sensitive and configurationally unstable. Therefore after the liberation, the liberated ligands must be re-complexed to selected metal ions within ca. 30 min. The configurational instabilities of (*S_P*)-**188** and (*R_P*)-**188** precluded the ligands from further purification and elemental characterization.^[166]

6.5.13 Synthesis of 2-bromo-1,4-di-*tert*-butylbenzene, **243**

A solution of bromine (6 mL) in trimethylphosphate (20 mL) was added to the 1,4-di-*tert*-butylbenzene **229** (15.0 g, 78.9 mmol) in the same solvent (100 mL). The solution was heated to 100 °C overnight protected from moisture and light. After cooling to room temperature, the solution was diluted with H_2O and extracted with hexane. The organic

layer was washed with H₂O and dried (MgSO₄). Removal of the solvent gave the product **243** as light yellow oil, 20.2 g (94.9%). ¹H NMR (500 MHz, CDCl₃): δ = 1.32 (s, 9 H, CCH₃), 1.52 (s, 9 H, CCH₃), 7.27 (dd, 1 H, ⁴J_{H,H} = 3.2 Hz, ³J_{H,H} = 8.3 Hz, aromatic proton), 7.38 (d, 1 H, ³J_{H,H} = 8.3 Hz, aromatic proton), 7.60 (d, 1 H, ⁴J_{H,H} = 2.1 Hz, aromatic proton) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 29.85, 31.19, 34.11, 36.15, 122.60, 124.14, 127.54, 132.78, 144.50, 150.40 ppm. HRMS (EI, m/z) calcd for C₁₄H₂₁Br 268.0821, found 268.0820.

6.5.14 Synthesis of 1-(2,5-di-*tert*-butylphenyl)ethanol, (±)-**244**

A THF solution of compound **243** (2 mL) was added to a mixture of magnesium and one piece of iodine in the same solvent. After the mixture turned pale, a compound **243** THF solution was added dropwise and the suspension was heated to gentle reflux for 2 h. The mixture was cooled to 0 °C followed by the addition of the acetaldehyde (10 mL) dropwise. The solution was heated up to 85 °C for 1 h and was poured into a cold hydrochloric acid aqueous solution. The mixture was extracted with dichloromethane (50 ml × 3). The organic layers were combined and dried (MgSO₄). After removing the solvent, the product (±)-**244** was obtained as yellow oil. 16.7 g (95.1%) ¹H NMR (300 MHz, CDCl₃): δ = 1.35 (s, 9 H, CCH₃), 1.44 (s, 9 H, CCH₃), 1.55 (d, ³J_{H,H} = 6.3 Hz, 3 H, CHCH₃), 1.81 (br, 1 H, OH), 6.65 (q, ³J_{H,H} = 6.3 Hz, 3 H, CH₃CH), 7.23 (dd, 1 H, ⁴J_{H,H} = 2.3 Hz, ³J_{H,H} = 8.4 Hz, aromatic proton), 7.29 (d, 1 H, ³J_{H,H} = 8.4 Hz, aromatic proton), 7.68 (d, 1 H, ⁴J_{H,H} = 2.2 Hz, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 25.05, 31.32, 32.26, 34.37, 35.05, 66.49, 124.22, 124.48, 125.34, 143.14, 144.31, 149.14 ppm. HRMS (EI, m/z) calcd for C₁₆H₂₆O 234.1978, found 234.1979.

6.5.15 Synthesis of N-(1-(2,5-di-*tert*-butylphenyl)ethyl)acetamide, (±)-244

The amide (±)-**244** was synthesized as a light yellow solid using the same method as synthesis of compound (±)-**232** demonstrated in **6.5.3**, 14.7 g (75.0%), M.p. 169–171 °C.

^1H NMR (400 MHz, CDCl_3): δ = 1.35 (s, 9 H, CCH_3), 1.42 (s, 9 H, CCH_3), 1.53 (d, $^3J_{\text{HH}}$ = 6.4 Hz, 3 H, CHCH_3), 1.96 (s, 3 H, COCH_3), 5.73 (q, $^3J_{\text{H,H}}$ = 6.6 Hz, 1 H, CH_3CH), 5.87 (d, $^3J_{\text{H,H}}$ = 6.3 Hz, 1 H, NH), 7.23 (dd, 1 H, $^4J_{\text{H,H}}$ = 2.3 Hz, $^3J_{\text{H,H}}$ = 8.4 Hz, aromatic proton), 7.33 (d, 1 H, $^3J_{\text{H,H}}$ = 8.4 Hz, aromatic proton), 7.38 (d, 1 H, $^4J_{\text{H,H}}$ = 1.2 Hz, aromatic proton) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 22.89, 23.46, 31.34, 31.79, 34.37, 35.10, 46.58, 123.87, 124.87, 126.10, 141.59, 144.11, 149.29, 169.11 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$)) $^+$ calcd for $\text{C}_{18}\text{H}_{30}\text{NO}$ 276.2327, found 276.2321.

6.5.16 Synthesis of 1-(2,5-di-*tert*-butylphenyl)ethanamine, (±)-246

The amide (±)-**246** was synthesized as brown oil using the Ritter reaction similar as the synthesis of compound (±)-**233** demonstrated in **6.5.4**, 9.46 g (76.0 %) ^1H NMR (300 MHz, CDCl_3): δ = 1.35 (s, 9 H, CCH_3), 1.45 (s, 9 H, CCH_3), 1.43 (d, $^3J_{\text{H,H}}$ = 6.4 Hz, 3 H, CHCH_3), 1.66 (br, 2 H, NH_2), 4.85 (q, $^3J_{\text{H,H}}$ = 6.5 Hz, 3 H, CH_3CH), 7.19 (dd, 1 H, $^4J_{\text{H,H}}$ = 2.3 Hz, $^3J_{\text{H,H}}$ = 8.4 Hz, aromatic proton), 7.29 (d, 1 H, $^3J_{\text{H,H}}$ = 8.4 Hz, aromatic proton), 7.58 (d, 1 H, $^4J_{\text{H,H}}$ = 2.2 Hz, aromatic proton) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 25.60, 31.35, 32.15, 34.36, 35.05, 46.75, 123.27, 124.12, 125.31, 142.99, 146.51, 148.92 ppm. HRMS (ESI, m/z ($\text{M} + \text{H}$)) $^+$ calcd for $\text{C}_{16}\text{H}_{28}\text{N}$ 234.2222, found 234.2231.

6.5.17 1-(2,5-di-*tert*-butylphenyl)-*N,N*-dimethylethanamine, (±)-242

The dimethyl amine (±)-**242** was synthesized as a brown color solid using similar method as the synthesis of compound (±)-**234**, 8.26 g (78.0 %). M.p. 71–73 °C. ^1H NMR (300 MHz, CDCl_3): δ = 1.34 (s, 9 H, CCH_3), 1.36 (d, 3 H, $^3J_{\text{H,H}}$ = 6.3 Hz, CHCH_3), 1.45 (s, 9

H, CCH₃), 2.29 (s, 6 H, NCH₃), 3.90 (q, ³J_{H,H} = 6.2 Hz, 1 H, CH₃CH), 7.17 (dd, 1 H, ⁴J_{H,H} = 2.4 Hz, ³J_{H,H} = 8.4 Hz, aromatic proton), 7.29 (d, 1 H, ³J_{H,H} = 8.4 Hz, aromatic proton), 7.58 (d, 1 H, ⁴J_{H,H} = 2.3 Hz, aromatic proton) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 23.72, 31.35, 32.33, 34.29, 35.37, 44.37, 61.99, 122.74, 125.37, 125.80, 143.10, 144.81, 148.86 ppm. HRMS (ESI, m/z (M + H))⁺ calcd for C₁₈H₃₂N 262.2535, found 262.2530.

Crystal Structure Determination

Diffraction data were collected on a Bruker X8 CCD diffractometer with Mo-Kα radiation (graphite monochromator). SADABS absorption corrections were applied. All non-hydrogen atoms were refined anisotropically while hydrogen atoms were introduced at calculated positions and refined riding on their carrier atoms. The absolute configurations of the chiral complexes were determined unambiguously using the Flack parameter.

CHAPTER 7

CONCLUSIONS

Cyclopalladated complexes has been extensively studied and has acquired great interest due to the range of applications of these palladacycles in many areas, for example, organic synthesis, homogeneous catalysis, asymmetric synthesis and resolution of racemic ligands.^[1,99,102] For example, *ortho*-palladated dimethyl-[1-(α -naphthyl)ethyl]-amine complex **11**^[5] has been used as the chiral auxiliary in some phosphine syntheses *via* asymmetric Diels-Alder reaction.^[174]

(S)-**11**

Recently, we have been able to apply this synthetic methodology for the asymmetric synthesis of functionalized mono- and diphosphines.^[156-169, 174] One of our approaches involves the activation of the five-membered heterocycle 3,4-dimethyl-1-phenylphosphole (dmpp) as a cyclic diene for the cycloaddition reaction.. A unique stereochemical feature of the chiral naphthylamine chelate ring in complex (S)-**11** is that there is an internal steric repulsion between the methyl substituent on the stereogenic carbon and its neighboring naphthylene proton. The crystallographic determinations and rotating Overhauser effect (ROESY) NMR investigations confirmed that the organometallic ring is locked into the static λ conformation, both in the solid state and in solution. Thus the prochiral NMe groups are fixed into the nonequivalent axial and

equatorial positions. These NMe groups control the stereochemistry of the neighboring coordination sites. Electronically, the σ -donating nitrogen and the π -accepting naphthylene carbon of the organopalladium ring control the regioselectivity of the incoming ligands: dmpp and other ligands with soft donors prefer to take up the coordination position *trans* to the NMe₂ moiety, for example, formation of dmpp complex (S)-**171**.

(S)-**171**

Stereochemically, the *endo*-cycloaddition reaction is controlled by the chiral template **11** via only a single and rotatable P–Pd bond. Thus this intermolecular process does not show high stereoselectivity and produces a pair of diastereomeric *endo*-cycloadducts. In several instances the separation process was somewhat tedious and resulted in lower yields of a targeted enantiomer. In the transition state the dmpp group enjoys a certain degree of free rotation around the P–Pd bond and thus poor stereoselectivity was observed. It has been established that the coordination site *cis* to the N atom is controlled stereochemically by the two prochiral NMe groups. It is clear that by introducing a spacer on the aromatic carbon which is adjacent to the Pd–C bond on the template, this class of *ortho*-palladated complexes should induce better stereoselectivity in similar reactions.

In pursuit of our interest in the design of new chiral palladacycles and subsequent improvements of the stereoselectivity in asymmetric *endo*-cycloaddition reactions, in

chapter 2 and 3 new *ortho*-palladated complexes (*S*)-**178** and (*S*)-**189** have been synthesized and utilized as the chiral templates in these *endo*-cycloaddition reactions.

The two new complexes exhibit the major stereoelectronic properties of the original naphthylamine template **11**. For example, the static λ organometallic ring conformation in both palladacycle (*S*)-**178** and (*S*)-**189** has been locked. Furthermore, a second spacer {Me for (*S*)-**178** and phenyl ring for (*S*)-**189**} is introduced on the aromatic carbon, which is adjacent to the Pd–C bond on each template complex. The second spacers were designed to project the stereochemistry of the chiral amine auxiliaries to their neighboring template sites.

When the naphthylamine auxiliary (*S*)-**11** was used as chiral template for the asymmetric *endo*-cycloaddition reaction between dmpp and *N,N*-dimethylacrylamide at room temperature, the cycloadducts were obtained in a ratio of 1:2.^[174] However, in chapter 2, this ratio was improved to 1:5.9 in the presence of complex (*S*)-**178** (Table 7.1).

Table 7.1 *endo*-cycloaddition reaction between dmpp and *N,N*-dimethylacrylamide promoted by (*S*)-**11** and (*S*)-**178**

Reaction Conditions	(<i>S</i>)- 11	(<i>S</i>)- 178
<i>endo</i> -cycloaddition reaction between dmpp and <i>N,N</i> -dimethylacrylamide (room temperature)	1:2	1:5.9

When the naphthylamine auxiliary (*S*)-**11** was employed for the analogous *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone, the cycloadducts were obtained in the ratio of 1.3:1. In chapter 3, with complex (*S*)-**189**, the increased ratio (3.5:1) under similar reaction conditions, indicates the stereoselectivity has been improved significantly (Table 7.2).

Table 7.2 *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone promoted by (*S*)-**11** and (*S*)-**189**

Reaction Conditions	(<i>S</i>)- 11	(<i>S</i>)- 189
<i>endo</i> -cycloaddition reaction between dmpp and ethyl vinyl ketone (50°C)	1:1.3	1:3.5

In chapter 4, in line with our continued interests in expanding the structural diversities of this class of promising organopalladium complexes for the purpose of enhancing their efficiencies as promoters for various asymmetric transformations, a structural modification of complex (*S*)-**189** could be made by the introduction of the phosphine-based palladacycle **201**. Properties of this phosphapalladacycle, for example coordination features, conformational behavior and bond reactivity around the palladium center, were then studied. Furthermore, complex (*S*)-**201** was applied in asymmetric *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone (Table 7.3).

Table 7.3 *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone promoted by (S)-**201**

Reaction Conditions	(S)- 201
<i>endo</i> -cycloaddition reaction between dmpp and ethyl vinyl ketone (room temperature)	No reaction,
<i>endo</i> -cycloaddition reaction between dmpp and ethyl vinyl ketone (35°C)	No reaction, Pd–P (dmpp) bond cleavage observed,

On account of the above observation, the lack of reactivity at room temperature and instability of the Pd–P (dmpp) bond at higher temperature could perhaps explain the phenomenon observed.

In chapter 5, in order to study the steric effect of the introduction of a bulky *tert*-butyl group connected to the chiral carbon, a novel palladacycle (S)-**211** was prepared and its application in *endo*-cycloaddition reaction was examined (Table 7.4)

(S)-**211****Table 7.4** *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone promoted by (S)-**11** and (S)-**211**

Reaction Conditions	(S)- 11	(S)- 211
<i>endo</i> -cycloaddition reaction between dmpp and ethyl vinyl ketone (room temperature)	1:2.5,	No reaction
<i>endo</i> -cycloaddition reaction between dmpp and ethyl vinyl ketone (70°C)	1:1	1:1 with palladium decomposition
<i>endo</i> -cycloaddition reaction between dmpp and <i>N,N</i> -dimethylacrylamide (70°C)	1:2	No reaction

It was demonstrated that as a result of the *tert*-butyl group and the protruding methyl group on the aromatic ring, the novel palladacycle (S)-**211** failed to exert good reactivity in *endo*-cycloaddition reaction between dmpp and ethyl vinyl ketone and the temperature

had to be raised to 70 °C, at which point the palladium complex slowly decomposes, in order for it to proceed at all. Hence, in comparison to other organometallic chiral auxiliaries {for example complex (*S*)-**178** and (*S*)-**189**} used for this *endo*-cycloaddition reaction, it is not as effective.

In chapter 6, in order to determine the influence of the introduced 3-position *tert*-butyl group on the neighboring reaction site, a new chiral palladacycle (*S*)-**228** was synthesized. The intermolecular *endo*-cycloaddition reaction between dmpp and *N,N*-dimethylacrylamide promoted by the new chiral palladacycle was examined and resulted the formation of a 1:2.3 diastereomeric mixture. Therefore, the bulky *tert*-butyl group on the C₃ position on the aromatic ring indeed shows a limited influence on the selectivity in this asymmetric cycloaddition reaction (Table 7.5).

(*S*)-**228**

Table 7.5 *endo*-cycloaddition reaction between dmpp and *N,N*-dimethylacrylamide promoted by (*S*)-**11** and (*S*)-**228**

Reaction Conditions	(<i>S</i>)- 11	(<i>S</i>)- 228
<i>endo</i> -cycloaddition reaction between dmpp and <i>N,N</i> -dimethylacrylamide (room temperature)	1:1.3	No reaction
<i>endo</i> -cycloaddition reaction between dmpp and <i>N,N</i> -dimethylacrylamide (50°C)	1:1	1:2.3

Overall, in this thesis, five novel chiral *ortho*-palladated complexes have been synthesized and their stereochemical evaluations in asymmetric *endo*-cycloaddition reactions were performed.

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APPENDICES

Publications

1. Ding, Yi; Zhang, Yi; Li, Yongxin; Pullarkat, Sumod A.; Leung, Pak-Hing. Synthesis of a Novel Chiral Organopalladium Complex and Its Application in Asymmetric Hydrophosphination Reaction. (*submitted for publication*).
2. Ding, Yi; Chiang, Minyi; Pullarkat, Sumod A.; Li, Yongxin; Leung, Pak-Hing, Synthesis, Coordination Characteristics, Conformational Behavior and Bond Reactivity Studies of a Novel Chiral Phosphapalladacycle Complex. *Organometallics*, **2009**, 28, 4358-4370.
3. Ding, Yi; Li, Yongxin; Pullarkat, Sumod A.; Yap, See Leng; Leung, Pak-Hing. Rational design of a novel chiral palladacycle: synthesis, optical resolution, and stereochemical evaluation. *European Journal of Inorganic Chemistry* **2009**, 2, 267-276.
4. Ding, Yi; Li, Yongxin; Zhang, Yi; Pullarkat, Sumod A.; Leung, Pak-Hing. Design, synthesis, and stereochemical evaluation of a novel chiral amine-palladacycle. *European Journal of Inorganic Chemistry* **2008**, 11, 1880-1891.
5. Zhang, Yi; Tang, Lulu; Ding, Yi; Chua, Jia-Hui; Li, Yongxin; Yuan, Mingjun; Leung, Pak-Hing. Base controlled (1,1)- and (1,2)-hydrophosphination of functionalized alkynes. *Tetrahedron Letters* **2008**, 11, 1762-1767.
6. Pullarkat, Sumod A.; Yi, Ding; Li, Yongxin; Tan, Geok-Kheng; Leung, Pak-Hing. A Novel Approach toward Asymmetric Synthesis of Alcohol Functionalized C-Chiral Diphosphines via Two-Stage Hydrophosphination of Terminal Alkynols. *Inorganic Chemistry* **2006**, 18, 7455-7463.
7. Huang, Yinhua; Pullarkat, Sumod A.; Yuan, Mingjun; Ding, Yi; Li, Yongxin; Leung, Pak-Hing. Palladium Template Promoted Asymmetric Synthesis of 1,2-Diphosphines by Hydrophosphination of Functionalized Allenes, *Organometallics*, **2009**, om-2009-00829t, accepted for publication.

Table A 1-1 Crystallographic Data for Complex ($\pm$)-**184**

Empirical formula	C ₃₄ H ₃₅ ClNPPd
Formula weight	630.45
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	a = 15.0712(6) Å $\alpha = 90^\circ$. b = 12.1873(4) Å $\beta = 96.437(2)^\circ$. c = 16.3450(6) Å $\gamma = 90^\circ$.
Volume	2983.28(19) Å ³
Z	4
Density (calculated)	1.404 Mg/m ³
Absorption coefficient	0.788 mm ⁻¹
F(000)	1296
Crystal size	0.10 x 0.10 x 0.10 mm ³
Theta range for data collection	2.09 to 30.54°.
Index ranges	-19 ≤ h ≤ 21, -14 ≤ k ≤ 17, -23 ≤ l ≤ 23
Reflections collected	37678
Independent reflections	9106 [R(int) = 0.0225]
Completeness to theta = 30.54°	99.7 %
Absorption correction	None
Max. and min. transmission	0.9253 and 0.9253
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	9106 / 0 / 348
Goodness-of-fit on F ²	1.044
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0269, wR2 = 0.0659
R indices (all data) ^{a,b}	R1 = 0.0358, wR2 = 0.0719
Largest diff. peak and hole	0.983 and -0.454 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 1-2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for ($\pm$)-**184**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Cl(1)	-839(1)	7607(1)	3215(1)	34(1)
N(1)	1164(1)	6466(1)	3241(1)	31(1)
P(1)	-771(1)	7427(1)	1211(1)	20(1)
C(1)	1389(1)	7219(1)	1746(1)	22(1)
C(2)	1693(1)	8015(1)	1199(1)	24(1)
C(3)	2533(1)	7909(2)	949(1)	31(1)
C(4)	3112(1)	7036(2)	1209(1)	33(1)
C(5)	3967(1)	6930(2)	930(2)	46(1)
C(6)	4523(1)	6073(2)	1177(2)	56(1)
C(7)	4228(1)	5279(2)	1709(1)	52(1)
C(8)	3413(1)	5360(2)	2001(1)	40(1)
C(9)	2829(1)	6258(2)	1771(1)	30(1)
C(10)	1977(1)	6403(1)	2054(1)	26(1)
C(11)	1164(1)	9020(1)	919(1)	29(1)
C(12)	5440(2)	5968(3)	888(2)	90(1)
C(13)	1688(1)	5712(2)	2740(1)	32(1)
C(14)	1152(2)	4717(2)	2404(1)	46(1)
C(15)	1784(1)	7257(2)	3705(1)	39(1)
C(16)	707(2)	5842(2)	3847(1)	50(1)
C(17)	-1567(1)	8561(1)	1213(1)	26(1)
C(18)	-1258(1)	9614(2)	1383(2)	46(1)
C(19)	-1849(2)	10496(2)	1336(2)	57(1)
C(20)	-2743(2)	10332(2)	1138(1)	49(1)
C(21)	-3061(1)	9290(2)	995(1)	49(1)
C(22)	-2479(1)	8398(2)	1028(1)	38(1)
C(23)	-1486(1)	6203(1)	1126(1)	22(1)
C(24)	-1673(1)	5616(1)	1814(1)	28(1)
C(25)	-2247(1)	4718(2)	1727(1)	33(1)
C(26)	-2638(1)	4401(2)	957(1)	32(1)
C(27)	-2459(1)	4985(2)	272(1)	32(1)
C(28)	-1885(1)	5875(1)	349(1)	28(1)
C(29)	-424(1)	7450(1)	181(1)	21(1)
C(30)	-764(1)	8188(1)	-424(1)	27(1)
C(31)	-516(1)	8122(2)	-1213(1)	34(1)
C(32)	76(1)	7321(2)	-1405(1)	35(1)

Table A 2-1 Crystallographic Data for Complex (S_C, S_C, S_N)-**185**.

Empirical formula	$C_{21}H_{29}N_2O_{2.50}Pd$
Formula weight	455.86
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	$a = 11.7939(4)$ Å $\alpha = 90^\circ$. $b = 10.4704(4)$ Å $\beta = 101.108(2)^\circ$. $c = 16.8695(6)$ Å $\gamma = 90^\circ$.
Volume	2044.13(13) Å ³
Z	4
Density (calculated)	1.481 Mg/m ³
Absorption coefficient	0.928 mm ⁻¹
F(000)	940
Crystal size	0.30 x 0.24 x 0.24 mm ³
Theta range for data collection	1.23 to 35.00°.
Index ranges	-19 ≤ h ≤ 18, -16 ≤ k ≤ 16, -26 ≤ l ≤ 27
Reflections collected	46594
Independent reflections	16927 [R(int) = 0.0345]
Completeness to theta = 35.00°	96.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8081 and 0.7683
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	16927 / 181 / 544
Goodness-of-fit on F ²	1.105
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0343, wR2 = 0.0797
R indices (all data) ^{a,b}	R1 = 0.0454, wR2 = 0.1030
Absolute structure parameter	-0.036(17)
Largest diff. peak and hole	0.824 and -1.009 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 2-2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (S_C, S_C, S_N)-**185**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

–	x	y	z	U(eq)
Pd(1)	8341(1)	2229(1)	3147(1)	22(1)
Pd(2)	6224(1)	3288(1)	6867(1)	26(1)
C(1)	6878(3)	2601(3)	2353(2)	23(1)
C(2)	5713(2)	2202(3)	2351(2)	26(1)
C(3)	5402(3)	1330(4)	2987(2)	41(1)
C(4)	4826(3)	2604(3)	1749(2)	26(1)
C(5)	5008(2)	3433(3)	1122(2)	23(1)
C(6)	4096(3)	3846(3)	516(2)	28(1)
C(7)	4267(3)	4691(3)	-67(2)	31(1)
C(8)	3286(3)	5144(4)	-714(2)	48(1)
C(9)	5393(3)	5153(3)	-50(2)	34(1)
C(10)	6304(3)	4754(3)	515(2)	33(1)
C(11)	6155(3)	3872(3)	1126(2)	24(1)
C(12)	7069(2)	3427(3)	1747(2)	23(1)
C(13)	8310(3)	3822(3)	1762(2)	27(1)
C(14)	8881(3)	2894(3)	1264(2)	37(1)
C(15)	8495(4)	5005(3)	3016(2)	41(1)
C(16)	10163(3)	3960(4)	2739(3)	42(1)
C(17)	9984(3)	1109(3)	4448(2)	30(1)
C(18)	8888(3)	346(3)	4458(2)	31(1)
C(19)	9107(12)	-1096(7)	4497(7)	45(2)
C(20)	8387(6)	-1736(5)	3777(3)	41(2)
C(19A)	9160(30)	-1048(14)	4660(12)	54(5)
C(20A)	9011(16)	-1443(14)	3784(9)	60(4)
C(21)	8132(4)	-619(3)	3193(2)	40(1)
C(22)	7771(3)	3042(3)	7586(2)	26(1)
C(23)	8769(3)	3838(3)	7696(2)	29(1)
C(24)	8768(3)	5091(4)	7253(2)	39(1)
C(25)	9729(3)	3515(3)	8253(2)	30(1)
C(26)	9771(3)	2424(3)	8754(2)	28(1)
C(27)	10733(3)	2147(3)	9374(2)	30(1)
C(28)	10730(3)	1173(3)	9913(2)	32(1)
C(29)	11691(3)	963(4)	10623(2)	42(1)
C(30)	9741(3)	365(3)	9797(2)	36(1)
C(31)	8818(3)	587(3)	9202(2)	35(1)

Appendices

C(32)	8768(3)	1643(3)	8670(2)	28(1)
C(33)	7794(3)	1973(3)	8080(2)	27(1)
C(34)	6691(3)	1213(3)	7976(2)	33(1)
C(35)	6689(3)	170(4)	7351(3)	44(1)
C(36)	5646(3)	2950(4)	8474(2)	43(1)
C(37)	4602(3)	1527(4)	7476(3)	46(1)
C(38)	4469(3)	4182(4)	5551(2)	37(1)
C(39)	5584(3)	4652(4)	5339(2)	42(1)
C(40)	5777(8)	3832(10)	4559(4)	50(2)
C(41)	6749(7)	2882(9)	4890(5)	55(2)
C(42)	7527(7)	3613(12)	5538(7)	43(2)
C(40A)	5645(10)	4616(17)	4481(5)	69(3)
C(41A)	6857(7)	4108(10)	4528(5)	55(2)
C(42A)	7171(9)	3434(12)	5342(6)	42(2)
N(1)	8884(2)	3852(2)	2636(2)	28(1)
N(2)	8013(2)	526(2)	3689(2)	26(1)
N(3)	5736(2)	2167(3)	7749(2)	33(1)
N(4)	6643(2)	4279(3)	5908(2)	30(1)
O(1)	9938(2)	1979(2)	3911(1)	31(1)
O(2)	10836(2)	868(3)	4951(2)	49(1)
O(3)	4568(2)	3464(3)	6175(2)	38(1)
O(4)	3547(3)	4491(4)	5138(2)	60(1)
O(5)	7353(3)	7142(4)	5870(4)	101(2)

Table A 3-1 Crystallographic Data for Complex (R_C, S_C, S_N)-**185**.

Empirical formula	$C_{21}H_{28}N_2O_2Pd$
Formula weight	446.85
Temperature	223(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	$a = 9.7485(2)$ Å $\alpha = 90^\circ$. $b = 11.5735(2)$ Å $\beta = 115.2040(10)^\circ$. $c = 9.9185(2)$ Å $\gamma = 90^\circ$.
Volume	1012.51(3) Å ³
Z	2
Density (calculated)	1.466 Mg/m ³
Absorption coefficient	0.933 mm ⁻¹
F(000)	460
Crystal size	0.16 x 0.14 x 0.08 mm ³
Theta range for data collection	2.27 to 29.00°.
Index ranges	-13 ≤ h ≤ 13, -15 ≤ k ≤ 15, -13 ≤ l ≤ 13
Reflections collected	10044
Independent reflections	5052 [R(int) = 0.0436]
Completeness to theta = 29.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9291 and 0.8651
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5052 / 45 / 243
Goodness-of-fit on F ²	1.096
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0492, wR2 = 0.1326
R indices (all data) ^{a,b}	R1 = 0.0552, wR2 = 0.1397
Absolute structure parameter	0.09(6)
Largest diff. peak and hole	1.586 and -0.669 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 3-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (R_C, S_C, S_N)-**185**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	2922(1)	2502(1)	2238(1)	30(1)
C(1)	5136(7)	2971(5)	3042(7)	34(1)
C(2)	5802(8)	3916(6)	2621(7)	40(1)
C(3)	4857(10)	4657(7)	1317(8)	53(2)
C(4)	7315(9)	4125(7)	3400(8)	48(2)
C(5)	8283(7)	3407(6)	4594(8)	43(2)
C(6)	9859(8)	3648(8)	5437(9)	56(2)
C(7)	10755(9)	2950(9)	6584(10)	63(2)
C(8)	12399(10)	3212(12)	7518(13)	89(4)
C(9)	10134(8)	1973(8)	6931(8)	59(2)
C(10)	8623(7)	1690(8)	6156(8)	49(2)
C(11)	7651(6)	2408(9)	4959(6)	40(1)
C(12)	6040(6)	2243(5)	4137(6)	38(2)
C(13)	5292(7)	1208(6)	4497(7)	40(1)
C(14)	4812(10)	1532(8)	5721(8)	55(2)
C(15)	2959(8)	68(5)	3324(8)	43(1)
C(16)	4429(8)	392(6)	1991(8)	45(2)
C(17)	-205(7)	1745(6)	2318(8)	42(1)
C(18)	-1855(8)	1874(6)	1276(9)	46(2)
C(19)	-1910(8)	2876(7)	274(9)	53(2)
C(20)	-304(7)	2923(6)	327(7)	38(1)
C(21)	468(9)	4081(6)	800(7)	44(1)
N(1)	3942(5)	949(4)	3055(5)	33(1)
N(2)	592(6)	1988(4)	1343(5)	30(1)
O(1)	1928(5)	4080(4)	1591(5)	42(1)
O(2)	-277(7)	4967(5)	398(6)	57(1)

Table A 4-1 Crystallographic Data for Complex (S)-**178**

Empirical formula	C ₃₂ H ₄₀ Cl ₂ N ₂ Pd ₂
Formula weight	736.36
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2
Unit cell dimensions	a = 12.2080(4) Å α = 90°. b = 18.1509(6) Å β = 90°. c = 7.0581(2) Å γ = 90°.
Volume	1563.98(9) Å ³
Z	2
Density (calculated)	1.564 Mg/m ³
Absorption coefficient	1.344 mm ⁻¹
F(000)	744
Crystal size	0.15 x 0.10 x 0.10 mm ³
Theta range for data collection	2.01 to 34.26°.
Index ranges	-18<=h<=19, -28<=k<=28, -10<=l<=11
Reflections collected	44011
Independent reflections	6473 [R(int) = 0.0364]
Completeness to theta = 34.26°	99.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8773 and 0.8239
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	6473 / 0 / 177
Goodness-of-fit on F ²	1.031
Final R indices [I>2sigma(I)] ^{a,b}	R1 = 0.0274, wR2 = 0.0579
R indices (all data) ^{a,b}	R1 = 0.0375, wR2 = 0.0617
Absolute structure parameter	-0.03(2)
Largest diff. peak and hole	1.103 and -0.422 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 4-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (S)-**178**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	8684(1)	9922(1)	9486(1)	33(1)
Cl(1)	9966(1)	10892(1)	10625(1)	45(1)
N(1)	7644(2)	10605(1)	7962(3)	46(1)
C(1)	7579(2)	9180(1)	8651(3)	34(1)
C(2)	7268(2)	8512(1)	9592(3)	38(1)
C(3)	6478(2)	8075(1)	8751(3)	45(1)
C(4)	5992(2)	8252(1)	7009(3)	44(1)
C(5)	5239(2)	7756(2)	6115(4)	57(1)
C(6)	4755(2)	7931(2)	4425(4)	63(1)
C(7)	5005(2)	8608(2)	3578(4)	66(1)
C(8)	5724(2)	9104(2)	4389(4)	56(1)
C(9)	6245(2)	8930(1)	6139(3)	42(1)
C(10)	7031(2)	9398(1)	7033(3)	37(1)
C(11)	7753(2)	8263(1)	11438(4)	47(1)
C(12)	3968(3)	7402(2)	3468(6)	94(1)
C(13)	7313(2)	10151(1)	6271(3)	47(1)
C(14)	8223(3)	10108(2)	4781(4)	70(1)
C(15)	6650(2)	10791(2)	9073(5)	75(1)
C(16)	8164(3)	11313(1)	7343(5)	78(1)

Table A 5-1 Crystallographic Data for Complex (S)-**186**

Empirical formula	C ₂₉ H ₃₄ Cl ₄ NPPd
Formula weight	675.74
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 10.9885(3) Å α = 90°. b = 7.5360(2) Å β = 90.7000(10)°. c = 18.3493(4) Å γ = 90°.
Volume	1519.38(7) Å ³
Z	2
Density (calculated)	1.477 Mg/m ³
Absorption coefficient	1.034 mm ⁻¹
F(000)	688
Crystal size	0.30 x 0.25 x 0.10 mm ³
Theta range for data collection	1.11 to 36.45°.
Index ranges	-18 ≤ h ≤ 18, -11 ≤ k ≤ 11, -29 ≤ l ≤ 30
Reflections collected	32458
Independent reflections	12187 [R(int) = 0.0266]
Completeness to theta = 36.45°	97.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9036 and 0.7467
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	12187 / 1 / 332
Goodness-of-fit on F ²	1.026
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0268, wR2 = 0.0580
R indices (all data) ^{a,b}	R1 = 0.0317, wR2 = 0.0607
Absolute structure parameter	-0.013(12)
Largest diff. peak and hole	0.629 and -0.645 e.Å ⁻³

$$a \text{ R1} = \sum ||\text{Fo}| - |\text{Fc}|| / \sum |\text{Fo}|.$$

$$b \text{ wR2} = \sqrt{\{\sum [w(\text{Fo}^2 - \text{Fc}^2)^2] / \sum [w(\text{Fo}^2)^2]\}}, w^{-1} = \sigma^2(\text{Fo}^2) + (aP)_2 + bP.$$

Table A 5-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (*S*)-**186**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

–	x	y	z	U(eq)
Pd(1)	8963(1)	8769(1)	2729(1)	18(1)
C(1)	7781(1)	7632(2)	3420(1)	19(1)
C(2)	7045(2)	6091(2)	3318(1)	21(1)
C(3)	7064(2)	4991(2)	2632(1)	29(1)
C(4)	6370(2)	5471(2)	3893(1)	23(1)
C(5)	6401(2)	6267(2)	4588(1)	21(1)
C(6)	5723(2)	5562(2)	5179(1)	25(1)
C(7)	5786(2)	6295(2)	5865(1)	25(1)
C(8)	5103(2)	5521(3)	6496(1)	33(1)
C(9)	6525(2)	7811(2)	5969(1)	24(1)
C(10)	7194(2)	8524(2)	5416(1)	24(1)
C(11)	7172(1)	7752(2)	4707(1)	20(1)
C(12)	7878(1)	8367(2)	4113(1)	19(1)
C(13)	8840(2)	9775(2)	4222(1)	26(1)
C(14)	8335(2)	11610(3)	4050(1)	39(1)
C(15)	10466(2)	7611(4)	4016(1)	43(1)
C(16)	10820(2)	10649(4)	3729(1)	54(1)
C(17)	7803(2)	10940(2)	1273(1)	22(1)
C(18)	6658(2)	11517(2)	1165(1)	23(1)
C(19)	6303(2)	13224(3)	798(1)	33(1)
C(20)	5718(2)	10272(2)	1438(1)	24(1)
C(21)	4390(2)	10731(3)	1384(1)	41(1)
C(22)	6173(1)	8776(3)	1721(1)	22(1)
C(23)	8313(1)	7271(2)	1012(1)	18(1)
C(24)	7891(2)	7410(2)	292(1)	22(1)
C(25)	8346(2)	6280(3)	-238(1)	25(1)
C(26)	9212(2)	5011(3)	-57(1)	29(1)
C(27)	9622(2)	4857(3)	658(1)	28(1)
C(28)	9181(2)	5995(2)	1190(1)	22(1)
C(29)	2387(2)	6044(3)	1982(1)	34(1)
Cl(1)	10593(1)	9890(1)	2006(1)	27(1)
Cl(2)	1734(1)	3973(1)	2166(1)	42(1)
Cl(3)	3088(1)	6008(1)	1125(1)	60(1)
Cl(4)	3453(1)	6621(1)	2667(1)	55(1)
N(1)	9882(1)	9257(2)	3740(1)	29(1)

Table A 6-1 Crystal data and structure refinement for Complex (±)-194

Empirical formula	C ₃₄ H ₃₅ ClNPPd
Formula weight	630.45
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 11.0844(8) Å α = 90°. b = 8.2465(6) Å β = 104.626(4)°. c = 16.3569(12) Å γ = 90°.
Volume	1446.69(18) Å ³
Z	2
Density (calculated)	1.447 Mg/m ³
Absorption coefficient	0.813 mm ⁻¹
F(000)	648
Crystal size	0.20 x 0.20 x 0.10 mm ³
Theta range for data collection	1.90 to 30.65°.
Index ranges	-15 ≤ h ≤ 15, -11 ≤ k ≤ 11, -23 ≤ l ≤ 23
Reflections collected	34548
Independent reflections	8850 [R(int) = 0.1050]
Completeness to theta = 30.65°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9231 and 0.8543
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	8850 / 1 / 348
Goodness-of-fit on F ²	1.120
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0431, wR2 = 0.1052
R indices (all data) ^{a,b}	R1 = 0.0530, wR2 = 0.1118
Absolute structure parameter	-0.01(3)
Largest diff. peak and hole	2.480 and -1.405 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 6-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for ($\pm$)-**194**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	6981(1)	5844(1)	1567(1)	20(1)
Cl(1)	4818(1)	6177(1)	1478(1)	28(1)
N(1)	6784(3)	7075(4)	397(2)	22(1)
P(1)	7109(1)	4316(1)	2742(1)	21(1)
C(1)	8810(3)	5955(6)	1524(2)	21(1)
C(2)	9945(3)	6066(4)	2178(2)	21(1)
C(3)	10004(3)	6131(4)	3052(2)	25(1)
C(4)	11113(4)	6272(5)	3661(3)	31(1)
C(5)	12256(4)	6423(5)	3434(3)	29(1)
C(6)	12233(3)	6378(5)	2598(3)	28(1)
C(7)	11107(3)	6195(4)	1957(2)	24(1)
C(8)	11136(3)	6200(4)	1099(2)	27(1)
C(9)	10059(3)	6210(4)	469(2)	26(1)
C(10)	8905(3)	6114(4)	690(2)	22(1)
C(11)	13463(4)	6649(6)	4109(3)	39(1)
C(12)	10106(4)	6347(6)	-446(3)	36(1)
C(13)	7696(3)	6218(4)	7(2)	24(1)
C(14)	7261(4)	4524(6)	-304(3)	35(1)
C(15)	7151(4)	8797(5)	564(3)	31(1)
C(16)	5522(4)	7083(6)	-209(3)	31(1)
C(17)	8447(3)	2964(5)	3083(2)	25(1)
C(18)	8989(4)	2576(5)	3928(3)	31(1)
C(19)	9934(4)	1429(7)	4127(3)	41(1)
C(20)	10335(4)	633(7)	3500(3)	41(1)
C(21)	9816(4)	1023(7)	2669(3)	41(1)
C(22)	8886(4)	2193(6)	2457(3)	34(1)
C(23)	7034(3)	5569(4)	3646(2)	23(1)
C(24)	6751(4)	4924(5)	4368(2)	29(1)
C(25)	6693(4)	5932(9)	5035(2)	35(1)
C(26)	6926(5)	7562(6)	4999(3)	41(1)
C(27)	7181(5)	8226(6)	4293(3)	40(1)
C(28)	7239(4)	7242(5)	3619(3)	29(1)
C(29)	5821(3)	2876(4)	2683(2)	23(1)
C(30)	5938(4)	1228(5)	2519(2)	32(1)
C(31)	4952(4)	179(6)	2472(3)	38(1)

Table A 7-1 Crystal data and structure refinement for Complex (S_C, S_C, S_N)-195

Empirical formula	$C_{22}H_{30}Cl_2N_2O_2Pd$
Formula weight	531.78
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 8.9397(4)$ Å $\square \alpha = 90^\circ$. $b = 11.3292(5)$ Å $\square \beta = 90^\circ$. $c = 23.2746(10)$ Å $\square \gamma = 90^\circ$.
Volume	$2357.24(18)$ Å ³
Z	4
Density (calculated)	1.498 Mg/m ³
Absorption coefficient	1.034 mm ⁻¹
F(000)	1088
Crystal size	0.30 x 0.30 x 0.20 mm ³
Theta range for data collection	1.75 to 30.67°.
Index ranges	-12 ≤ h ≤ 12, -16 ≤ k ≤ 16, -33 ≤ l ≤ 33
Reflections collected	65559
Independent reflections	7195 [R(int) = 0.0243]
Completeness to theta = 30.67°	98.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8199 and 0.7468
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	7195 / 0 / 271
Goodness-of-fit on F ²	1.162
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0202, wR2 = 0.0582
R indices (all data) ^{a,b}	R1 = 0.0212, wR2 = 0.0624
Absolute structure parameter	-0.003(19)
Largest diff. peak and hole	0.545 and -0.857 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 7-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (S_C, S_C, S_N)-**195**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	417(1)	6206(1)	1092(1)	19(1)
N(1)	-1504(2)	5663(2)	1515(1)	26(1)
N(2)	2335(2)	6434(2)	603(1)	21(1)
O(1)	-578(2)	6249(2)	273(1)	30(1)
O(2)	-155(2)	6801(2)	-631(1)	38(1)
C(1)	1237(2)	6130(2)	1891(1)	18(1)
C(2)	2471(2)	6746(2)	2144(1)	18(1)
C(3)	3320(2)	7628(2)	1852(1)	20(1)
C(4)	4468(2)	8222(2)	2118(1)	24(1)
C(5)	4881(2)	7980(2)	2694(1)	25(1)
C(6)	4071(2)	7140(2)	2985(1)	25(1)
C(7)	2855(2)	6519(2)	2730(1)	21(1)
C(8)	1976(2)	5726(2)	3058(1)	25(1)
C(9)	734(2)	5189(2)	2830(1)	24(1)
C(10)	389(2)	5390(2)	2241(1)	20(1)
C(11)	-251(3)	4414(2)	3198(1)	37(1)
C(12)	6138(3)	8641(3)	2973(1)	38(1)
C(13)	-930(2)	4794(2)	1956(1)	23(1)
C(14)	-438(3)	3628(2)	1682(1)	34(1)
C(15)	-2296(3)	6633(3)	1819(1)	41(1)
C(16)	-2600(3)	5108(3)	1120(1)	44(1)
C(17)	277(3)	6584(2)	-135(1)	26(1)
C(18)	1941(2)	6732(2)	-7(1)	26(1)
C(19)	2929(3)	5981(3)	-394(1)	51(1)
C(20)	4059(3)	5388(3)	6(1)	38(1)
C(21)	3212(3)	5311(3)	570(1)	43(1)
C(22)	8435(5)	4130(3)	9395(2)	76(1)
Cl(1)	6894(2)	3305(1)	9194(1)	98(1)
Cl(2)	9857(2)	3285(1)	9699(1)	115(1)

Table A 8-1 Crystal data and structure refinement for complex (R_C, S_C)-196

Empirical formula	$C_{21}H_{30}N_2O_3Pd$
Formula weight	464.87
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2
Unit cell dimensions	$a = 26.346(3)$ Å $\alpha = 90^\circ$. $b = 9.8051(13)$ Å $\beta = 112.293(6)^\circ$. $c = 18.340(3)$ Å $\gamma = 90^\circ$.
Volume	$4383.5(10)$ Å ³
Z	8
Density (calculated)	1.409 Mg/m ³
Absorption coefficient	0.868 mm ⁻¹
F(000)	1920
Crystal size	0.30 x 0.15 x 0.02 mm ³
Theta range for data collection	1.20 to 26.41° .
Index ranges	$-32 \leq h \leq 32$, $-12 \leq k \leq 10$, $-22 \leq l \leq 22$
Reflections collected	18930
Independent reflections	7644 [R(int) = 0.0452]
Completeness to $\theta = 26.41^\circ$	97.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9828 and 0.7807
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7644 / 1 / 497
Goodness-of-fit on F^2	1.159
Final R indices [$I > 2\sigma(I)$] ^{a,b}	$R1 = 0.0366$, $wR2 = 0.0895$
R indices (all data) ^{a,b}	$R1 = 0.0496$, $wR2 = 0.1182$
Absolute structure parameter	-0.01(4)
Largest diff. peak and hole	0.854 and -0.899 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 8-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (R_C, S_C) -**196**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	2575(1)	1073(1)	3387(1)	28(1)
Pd(2)	10205(1)	2913(1)	4105(1)	32(1)
O(1)	2238(2)	-154(6)	3984(3)	38(1)
O(2)	2331(2)	-873(6)	5176(3)	47(1)
O(3)	10673(2)	4439(6)	4926(3)	38(1)
O(4)	10757(2)	6683(6)	5029(4)	50(2)
O(5)	616(3)	4351(9)	9009(4)	72(2)
O(6)	759(4)	5195(10)	7985(4)	104(3)
N(1)	2913(2)	2406(6)	2832(3)	32(1)
N(2)	3082(2)	1564(6)	4559(3)	31(1)
N(3)	10772(2)	1336(6)	4395(4)	37(2)
N(4)	9710(2)	4609(6)	3706(3)	32(1)
C(1)	2079(2)	676(8)	2262(4)	37(2)
C(2)	1746(2)	-503(9)	1945(4)	39(2)
C(3)	1722(2)	-1633(8)	2406(4)	35(2)
C(4)	1397(3)	-2720(8)	2082(4)	38(2)
C(5)	1060(3)	-2794(9)	1271(4)	41(2)
C(6)	688(3)	-3997(12)	937(5)	58(2)
C(7)	1075(3)	-1720(10)	816(5)	52(2)
C(8)	1413(2)	-562(9)	1116(4)	40(2)
C(9)	1445(3)	540(10)	631(4)	47(2)
C(10)	1778(3)	1648(9)	918(5)	47(2)
C(11)	1805(4)	2803(13)	380(5)	70(3)
C(12)	2086(3)	1697(7)	1738(4)	33(2)
C(13)	2440(2)	2912(9)	2117(4)	37(2)
C(14)	2098(3)	3953(9)	2351(5)	49(2)
C(15)	3295(3)	1641(9)	2550(5)	44(2)
C(16)	3225(3)	3527(8)	3338(4)	42(2)
C(17)	3055(3)	459(8)	5072(4)	38(2)
C(18)	3217(3)	889(12)	5930(4)	59(3)
C(19)	2496(3)	-248(7)	4730(4)	31(2)
C(20)	9793(2)	1616(7)	3278(4)	32(2)
C(21)	9205(2)	1577(7)	2807(4)	27(1)
C(22)	8822(2)	2395(8)	2986(4)	35(2)
C(23)	8275(2)	2420(8)	2486(4)	38(2)

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C(24)	8081(3)	1660(8)	1777(4)	36(2)
C(25)	7491(3)	1771(10)	1213(5)	50(2)
C(26)	8441(3)	805(8)	1623(4)	39(2)
C(27)	9008(3)	739(7)	2132(4)	33(2)
C(28)	9370(3)	-168(9)	1951(5)	42(2)
C(29)	9922(3)	-204(8)	2436(5)	40(2)
C(30)	10295(4)	-1201(10)	2232(6)	63(3)
C(31)	10124(2)	692(7)	3080(4)	35(2)
C(32)	10738(3)	800(9)	3605(5)	43(2)
C(33)	11027(3)	1686(10)	3205(5)	57(2)
C(34)	11341(3)	1787(10)	4883(6)	57(2)
C(35)	10631(3)	229(8)	4830(5)	41(2)
C(36)	10540(3)	5637(8)	4662(5)	36(2)
C(37)	10098(2)	5767(7)	3831(4)	32(2)
C(38)	9821(3)	7141(8)	3662(5)	47(2)
C(39)	1306(5)	6065(17)	9251(6)	98(4)
C(40)	873(4)	5154(11)	8684(6)	62(3)
C(41)	209(4)	3415(13)	8512(6)	79(3)
C(42)	-1(5)	2548(15)	9009(7)	91(4)

Table A 9-1 Crystal data and structure refinement for complex (S)-189

Empirical formula	C ₃₃ H ₄₂ Cl ₄ N ₂ Pd ₂
Formula weight	821.29
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 15.6457(4) Å α = 90°. b = 24.4883(7) Å β = 107.005(2)°. c = 19.2722(6) Å γ = 90°.
Volume	7061.1(3) Å ³
Z	8
Density (calculated)	1.545 Mg/m ³
Absorption coefficient	1.346 mm ⁻¹
F(000)	3312
Crystal size	0.25 x 0.25 x 0.15 mm ³
Theta range for data collection	1.10 to 26.00°.
Index ranges	-19 ≤ h ≤ 19, -30 ≤ k ≤ 30, -23 ≤ l ≤ 23
Reflections collected	73675
Independent reflections	26001 [R(int) = 0.0393]
Completeness to theta = 26.00°	96.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8236 and 0.7296
Refinement method	Full-matrix-block least-squares on F ²
Data / restraints / parameters	26001 / 52 / 1511
Goodness-of-fit on F ²	1.025
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0329, wR2 = 0.0772
R indices (all data) ^{a,b}	R1 = 0.0394, wR2 = 0.0821
Absolute structure parameter	-0.03(7)
Largest diff. peak and hole	0.957 and -0.879 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 9-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (S)-**189**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	6151(1)	6856(1)	2122(1)	29(1)
Pd(2)	6960(1)	5674(1)	3210(1)	30(1)
Pd(3)	1291(1)	675(1)	9954(1)	28(1)
Pd(4)	-50(1)	-257(1)	8637(1)	29(1)
Cl(1)	6229(4)	5913(2)	1928(3)	32(1)
Cl(2)	6650(5)	6591(3)	3408(3)	44(2)
Cl(3)	-195(4)	354(2)	9617(3)	38(1)
Cl(4)	1470(4)	-21(2)	9081(3)	38(1)
N(1)	6229(13)	7692(8)	2286(11)	35(4)
N(2)	7343(13)	4885(8)	3038(11)	36(5)
N(3)	2516(13)	1050(8)	10110(11)	34(4)
N(4)	-1400(13)	-357(9)	8109(12)	39(5)
C(1)	5803(14)	7110(9)	1093(12)	28(5)
C(2)	5264(14)	6835(9)	459(12)	29(5)
C(3)	4776(15)	6352(9)	467(14)	35(5)
C(4)	4297(17)	6104(10)	-156(15)	42(6)
C(5)	4254(18)	6327(11)	-848(15)	46(6)
C(6)	3750(30)	6016(19)	-1530(20)	92(9)
C(7)	4678(17)	6806(11)	-870(14)	41(6)
C(8)	5182(16)	7077(9)	-239(14)	36(5)
C(9)	5603(17)	7590(10)	-275(14)	40(6)
C(10)	6075(16)	7861(10)	337(14)	37(5)
C(11)	6480(20)	8417(11)	267(17)	57(8)
C(12)	6163(15)	7621(9)	1028(13)	33(5)
C(13)	6648(16)	7904(9)	1722(15)	38(6)
C(14)	7659(16)	7787(10)	1942(16)	43(6)
C(15)	5320(18)	7935(11)	2152(16)	46(6)
C(16)	6770(20)	7862(12)	3032(15)	49(7)
C(17)	7677(16)	5480(9)	4217(14)	35(5)
C(18)	7613(14)	5698(10)	4894(12)	32(5)
C(19)	6909(17)	6031(10)	4960(13)	38(6)
C(20)	6888(18)	6237(10)	5612(14)	41(6)
C(21)	7570(19)	6120(10)	6254(14)	41(6)
C(22)	7510(30)	6370(13)	6959(15)	62(9)
C(23)	8253(17)	5781(10)	6217(14)	39(6)

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C(24)	8283(15)	5548(9)	5547(13)	34(5)
C(25)	8949(16)	5167(10)	5509(15)	40(6)
C(26)	8963(16)	4929(10)	4883(15)	40(6)
C(27)	9640(19)	4497(12)	4892(18)	56(8)
C(28)	8320(15)	5092(10)	4230(14)	35(5)
C(29)	8307(16)	4854(10)	3501(15)	40(6)
C(30)	8934(19)	5169(11)	3167(16)	47(7)
C(31)	7260(19)	4764(11)	2265(15)	48(7)
C(32)	6809(18)	4466(11)	3298(17)	50(7)
C(33)	1206(15)	1234(9)	10679(12)	30(5)
C(34)	639(15)	1226(10)	11146(12)	33(5)
C(35)	149(16)	768(12)	11252(13)	43(6)
C(36)	-430(20)	792(15)	11679(15)	58(8)
C(37)	-550(20)	1286(17)	12007(16)	67(9)
C(38)	-1230(30)	1320(20)	12430(20)	92(9)
C(39)	-53(19)	1733(15)	11951(15)	58(9)
C(40)	568(16)	1712(11)	11537(13)	39(6)
C(41)	1133(19)	2163(12)	11523(14)	48(7)
C(42)	1757(17)	2145(10)	11146(14)	40(6)
C(43)	2390(20)	2619(12)	11190(19)	61(8)
C(44)	1772(16)	1675(9)	10710(13)	33(5)
C(45)	2358(18)	1650(10)	10211(14)	40(6)
C(46)	1910(20)	1936(12)	9497(16)	56(8)
C(47)	2889(19)	952(11)	9497(17)	49(7)
C(48)	3190(17)	850(11)	10792(16)	47(7)
C(49)	34(16)	-761(9)	7845(12)	30(5)
C(50)	732(15)	-1132(9)	7855(13)	29(5)
C(51)	1453(16)	-1254(9)	8476(13)	33(5)
C(52)	2106(17)	-1621(10)	8447(14)	38(6)
C(53)	2102(18)	-1895(10)	7810(15)	42(6)
C(54)	2840(20)	-2297(13)	7810(18)	61(8)
C(55)	1403(19)	-1796(10)	7193(14)	41(6)
C(56)	704(16)	-1424(9)	7205(13)	32(5)
C(57)	-25(18)	-1343(11)	6586(15)	45(6)
C(58)	-744(18)	-1005(11)	6584(15)	44(6)
C(59)	-1520(20)	-949(17)	5909(18)	71(10)
C(60)	-708(16)	-728(10)	7238(14)	37(6)
C(61)	-1458(17)	-368(10)	7307(14)	41(6)
C(62)	-1340(20)	214(13)	7035(18)	63(9)
C(63)	-1752(17)	-888(11)	8289(15)	44(6)
C(64)	-1957(18)	83(13)	8286(18)	57(8)
Pd(5)	9912(1)	3559(1)	6523(1)	32(1)
Pd(6)	9528(1)	2596(1)	5083(1)	31(1)
Pd(7)	6419(1)	1542(1)	6971(1)	28(1)

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Pd(8)	7303(1)	2258(1)	8633(1)	27(1)
Cl(5)	10758(4)	3160(3)	5821(4)	46(2)
Cl(6)	8649(4)	3146(3)	5589(4)	55(2)
Cl(7)	6790(4)	2478(2)	7395(3)	37(1)
Cl(8)	6788(5)	1341(2)	8208(3)	38(1)
N(5)	9172(13)	3801(8)	7197(11)	35(5)
N(6)	10325(13)	2036(8)	4757(12)	36(5)
N(7)	6205(14)	1706(9)	5874(11)	37(5)
N(8)	7900(13)	2050(7)	9712(10)	30(4)
C(65)	10873(14)	3931(8)	7293(13)	29(5)
C(66)	11700(14)	4158(8)	7234(13)	29(5)
C(67)	11953(15)	4186(9)	6594(14)	32(5)
C(68)	12767(16)	4392(10)	6583(14)	37(6)
C(69)	13393(16)	4586(9)	7219(16)	40(6)
C(70)	14287(18)	4799(13)	7192(19)	59(8)
C(71)	13158(16)	4579(10)	7838(15)	38(6)
C(72)	12317(16)	4376(9)	7874(13)	33(5)
C(73)	12082(18)	4394(10)	8531(14)	39(6)
C(74)	11274(17)	4204(10)	8573(14)	39(6)
C(75)	11040(20)	4238(15)	9292(17)	62(8)
C(76)	10675(15)	3975(9)	7949(13)	32(5)
C(77)	9796(16)	3738(10)	7958(14)	39(6)
C(78)	9890(20)	3151(12)	8203(17)	53(7)
C(79)	8905(18)	4386(11)	7071(15)	45(6)
C(80)	8337(17)	3491(13)	7095(16)	52(7)
C(81)	8570(16)	2101(9)	4498(13)	31(5)
C(82)	7639(14)	2215(9)	4155(12)	30(5)
C(83)	7236(17)	2738(10)	4101(14)	39(6)
C(84)	6341(17)	2810(11)	3769(15)	43(6)
C(85)	5771(18)	2376(12)	3472(15)	48(7)
C(86)	4790(20)	2459(17)	3100(30)	90(14)
C(87)	6147(17)	1868(12)	3497(14)	43(6)
C(88)	7078(15)	1773(10)	3819(13)	35(5)
C(89)	7442(18)	1249(11)	3820(15)	43(6)
C(90)	8326(17)	1139(10)	4107(16)	43(6)
C(91)	8680(20)	572(12)	4110(20)	77(11)
C(92)	8901(15)	1585(10)	4447(14)	36(5)
C(93)	9887(16)	1495(10)	4797(15)	42(6)
C(94)	10060(20)	1298(14)	5570(20)	73(11)
C(95)	11276(16)	2035(11)	5206(18)	49(7)
C(96)	10334(18)	2140(10)	3997(15)	44(6)
C(97)	6174(14)	784(9)	6584(12)	28(5)
C(98)	5897(14)	320(9)	6916(12)	28(5)
C(99)	5583(14)	349(10)	7535(13)	32(5)

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C(100)	5418(16)	-111(10)	7875(14)	37(6)
C(101)	5534(16)	-640(10)	7611(15)	41(6)
C(102)	5380(20)	-1149(12)	8014(18)	59(8)
C(103)	5770(16)	-675(10)	6990(15)	39(6)
C(104)	5942(14)	-208(10)	6613(13)	34(5)
C(105)	6169(17)	-255(11)	5956(14)	43(6)
C(106)	6341(19)	197(12)	5601(15)	48(7)
C(107)	6520(30)	129(15)	4870(19)	76(11)
C(108)	6366(15)	723(11)	5928(12)	38(5)
C(109)	6626(17)	1229(11)	5601(14)	41(6)
C(110)	7637(17)	1285(12)	5789(14)	45(6)
C(111)	5232(18)	1717(13)	5491(16)	53(7)
C(112)	6578(19)	2236(11)	5730(14)	46(6)
C(113)	7820(14)	2984(8)	9013(12)	26(5)
C(114)	7546(14)	3511(9)	8729(12)	27(5)
C(115)	6766(15)	3630(9)	8151(13)	34(5)
C(116)	6583(17)	4139(10)	7862(15)	40(6)
C(117)	7163(18)	4579(10)	8117(14)	39(6)
C(118)	6990(20)	5122(11)	7727(17)	54(7)
C(119)	7888(17)	4494(9)	8700(15)	38(6)
C(120)	8113(15)	3971(9)	9029(12)	30(5)
C(121)	8880(15)	3891(9)	9623(13)	33(5)
C(122)	9103(15)	3387(9)	9927(12)	31(5)
C(123)	9930(16)	3318(11)	10564(14)	41(6)
C(124)	8548(14)	2928(9)	9613(12)	28(5)
C(125)	8783(15)	2358(9)	9904(13)	32(5)
C(126)	9454(17)	2097(10)	9571(15)	42(6)
C(127)	7354(17)	2246(10)	10177(13)	39(6)
C(128)	8045(18)	1455(10)	9845(14)	41(6)
C(129)	6220(40)	4609(19)	5130(40)	140(30)
C(130)	3360(50)	2940(40)	5050(30)	400(140)
C(131)	6290(20)	4225(14)	9810(20)	68(10)
C(132)	10040(40)	1290(20)	7960(40)	180(30)
CI(9)	6640(30)	4010(10)	5120(13)	262(18)
CI(10)	5830(19)	4771(13)	5840(10)	220(12)
CI(11)	2780(30)	2792(13)	4080(30)	430(40)
CI(12)	4310(40)	3277(16)	5280(40)	520(60)
CI(13)	5859(6)	3566(4)	9842(6)	75(2)
CI(14)	5476(8)	4726(5)	9797(11)	131(6)
CI(15)	9085(16)	1678(11)	7626(11)	202(11)
CI(16)	10848(19)	1591(12)	7567(13)	229(13)

Table A 10-1 Crystal data and structure refinement for complex (S)-**197**

Empirical formula	C ₂₈ H ₃₃ ClNPPd
Formula weight	556.37
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 11.7694(7) Å α = 90°. b = 8.3483(5) Å β = 98.838(4)°. c = 13.2810(8) Å γ = 90°.
Volume	1289.42(13) Å ³
Z	2
Density (calculated)	1.433 Mg/m ³
Absorption coefficient	0.901 mm ⁻¹
F(000)	572
Crystal size	0.35 x 0.10 x 0.06 mm ³
Theta range for data collection	1.55 to 30.53°.
Index ranges	-16 ≤ h ≤ 16, -11 ≤ k ≤ 11, -18 ≤ l ≤ 18
Reflections collected	32983
Independent reflections	7786 [R(int) = 0.0386]
Completeness to theta = 30.53°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9479 and 0.7433
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	7786 / 1 / 296
Goodness-of-fit on F ²	1.114
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0307, wR2 = 0.0688
R indices (all data) ^{a,b}	R1 = 0.0387, wR2 = 0.0827
Absolute structure parameter	-0.02(2)
Largest diff. peak and hole	1.160 and -0.611 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 10-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (S)-**197**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	3026(1)	5630(1)	8355(1)	21(1)
Cl(1)	5029(1)	5446(1)	8160(1)	29(1)
N(1)	3295(2)	4463(3)	9799(2)	29(1)
P(1)	2762(1)	7221(1)	6969(1)	22(1)
C(1)	1378(2)	5539(5)	8642(2)	22(1)
C(2)	322(2)	5474(5)	7941(2)	22(1)
C(3)	252(2)	5383(4)	6871(2)	25(1)
C(4)	-775(3)	5309(4)	6230(2)	29(1)
C(5)	-1829(3)	5320(4)	6616(3)	33(1)
C(6)	-1800(3)	5372(5)	7642(3)	34(1)
C(7)	-740(2)	5425(5)	8334(2)	26(1)
C(8)	-720(3)	5359(4)	9403(2)	33(1)
C(9)	275(3)	5322(4)	10070(2)	33(1)
C(10)	1334(3)	5401(4)	9676(2)	28(1)
C(11)	-2963(3)	5224(5)	5902(3)	46(1)
C(12)	246(3)	5177(6)	11204(3)	49(1)
C(13)	2475(3)	5301(4)	10385(2)	32(1)
C(14)	2875(4)	6976(5)	10741(3)	47(1)
C(15)	2971(3)	2738(4)	9667(3)	37(1)
C(16)	4489(3)	4518(5)	10362(3)	39(1)
C(17)	1690(3)	8774(4)	6787(2)	28(1)
C(18)	2197(3)	10222(4)	6800(2)	30(1)
C(19)	3477(3)	10164(3)	6923(2)	28(1)
C(20)	3901(3)	8662(4)	7006(2)	26(1)
C(21)	1582(4)	11800(5)	6686(3)	43(1)
C(22)	4185(4)	11656(4)	6930(3)	42(1)
C(23)	2745(3)	6271(4)	5721(2)	25(1)
C(24)	3712(3)	5399(5)	5561(2)	31(1)
C(25)	3748(4)	4670(5)	4618(3)	44(1)
C(26)	2831(4)	4810(6)	3848(3)	53(1)
C(27)	1872(3)	5678(9)	3998(2)	53(1)
C(28)	1823(3)	6413(5)	4931(3)	38(1)

Table A 11-1 Crystal data and structure refinement for complex (S_C, S_P)-199

Empirical formula	$C_{33}H_{41}N_2O_4PPd$
Formula weight	667.05
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 11.0169(3)$ Å $\alpha = 90^\circ$. $b = 14.3105(4)$ Å $\beta = 90^\circ$. $c = 20.2012(5)$ Å $\gamma = 90^\circ$.
Volume	$3184.87(15)$ Å ³
Z	4
Density (calculated)	1.391 Mg/m ³
Absorption coefficient	0.671 mm ⁻¹
F(000)	1384
Crystal size	0.10 x 0.10 x 0.04 mm ³
Theta range for data collection	1.74 to 30.58° .
Index ranges	$-15 \leq h \leq 15$, $-20 \leq k \leq 20$, $-28 \leq l \leq 28$
Reflections collected	47669
Independent reflections	9732 [R(int) = 0.0922]
Completeness to $\theta = 30.58^\circ$	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9736 and 0.9359
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9732 / 0 / 378
Goodness-of-fit on F^2	0.989
Final R indices [$I > 2\sigma(I)$] ^{a,b}	$R1 = 0.0443$, $wR2 = 0.0898$
R indices (all data) ^{a,b}	$R1 = 0.1238$, $wR2 = 0.1245$
Absolute structure parameter	0.01(3)
Largest diff. peak and hole	0.569 and -1.386 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 11-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (S_C, S_P)-**199**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	7203(1)	5828(1)	8010(1)	40(1)
N(1)	8769(4)	4950(3)	8058(2)	54(1)
O(1)	7790(4)	6504(3)	7097(2)	72(1)
P(1)	5658(1)	6847(1)	8152(1)	38(1)
C(1)	6770(4)	5012(3)	8784(2)	39(1)
C(2)	5599(4)	4702(3)	8986(2)	37(1)
C(3)	4519(4)	4821(3)	8600(2)	43(1)
C(4)	3426(4)	4473(4)	8806(3)	50(1)
C(5)	3303(4)	4003(4)	9417(2)	45(1)
C(6)	2068(5)	3670(4)	9633(3)	65(2)
C(7)	4325(4)	3884(3)	9795(2)	46(1)
C(8)	5493(4)	4191(4)	9595(2)	40(1)
C(9)	6533(4)	3987(4)	9957(2)	47(1)
C(10)	7673(4)	4183(4)	9724(2)	50(1)
C(11)	8776(5)	3866(5)	10104(3)	72(2)
C(12)	7767(5)	4703(3)	9112(2)	44(1)
C(13)	9004(5)	4870(4)	8788(3)	55(2)
C(14)	9615(5)	5747(5)	9059(3)	77(2)
C(15)	8471(6)	4002(4)	7793(3)	68(2)
C(16)	9871(5)	5269(5)	7702(3)	79(2)
C(17)	6174(4)	8060(3)	8296(2)	45(1)
C(18)	6917(5)	7887(4)	8943(2)	49(1)
C(19)	7287(6)	8816(4)	9254(3)	67(2)
C(20)	8296(6)	9354(5)	8929(3)	81(2)
C(21)	9541(6)	8996(7)	9134(4)	107(3)
C(22)	6081(5)	7266(4)	9382(2)	49(1)
C(23)	4947(5)	7060(4)	8962(2)	44(1)
C(24)	4314(5)	7995(4)	8852(2)	50(1)
C(25)	3115(6)	8208(5)	9178(3)	79(2)
C(26)	4998(5)	8547(4)	8477(2)	49(1)
C(27)	4764(6)	9552(4)	8286(3)	67(2)
C(28)	4510(4)	6882(3)	7509(2)	37(1)
C(29)	4854(4)	7125(3)	6870(2)	44(1)
C(30)	4016(5)	7159(4)	6364(3)	55(1)
C(31)	2830(6)	6956(4)	6488(3)	61(1)

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C(32)	2462(4)	6726(4)	7119(3)	60(2)
C(33)	3301(5)	6688(4)	7633(3)	50(1)
N(2)	8587(5)	7122(5)	7106(3)	82(2)
O(2)	9133(5)	7314(5)	6597(3)	128(2)
O(3)	8844(5)	7486(4)	7648(3)	109(2)

Table A 12-1 Crystal data and structure refinement for Complex *E*-(*R*_C,*S*_C,*S*_N)-**203**

Empirical formula	C _{31.50} H ₃₃ ClNO ₂ PPd
Formula weight	630.41
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 11.0151(3) Å α = 90°. b = 13.9586(4) Å β = 90°. c = 37.1293(12) Å γ = 90°.
Volume	5708.8(3) Å ³
Z	8
Density (calculated)	1.467 Mg/m ³
Absorption coefficient	0.829 mm ⁻¹
F(000)	2584
Crystal size	0.28 x 0.10 x 0.08 mm ³
Theta range for data collection	1.10 to 29.00°.
Index ranges	-14 ≤ h ≤ 15, -19 ≤ k ≤ 19, -50 ≤ l ≤ 50
Reflections collected	62466
Independent reflections	15144 [R(int) = 0.0388]
Completeness to theta = 29.00°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9366 and 0.8011
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	15144 / 84 / 688
Goodness-of-fit on F ²	1.148
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0498, wR2 = 0.1295
R indices (all data) ^{a,b}	R1 = 0.0565, wR2 = 0.1391
Absolute structure parameter	0.01(3)
Largest diff. peak and hole	1.614 and -1.542 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 12-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for *E*-(R_C, S_C, S_N)-**203**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Pd(1)	1412(1)	6996(1)	1079(1)	26(1)
Pd(2)	5974(1)	124(1)	1012(1)	22(1)
N(1)	205(4)	8151(3)	943(1)	28(1)
N(2)	5286(4)	-566(3)	540(1)	25(1)
O(1)	2607(3)	7979(3)	843(1)	33(1)
O(2)	2712(4)	9271(3)	503(1)	45(1)
O(3)	7238(4)	-975(3)	957(1)	33(1)
O(4)	7823(4)	-2193(3)	616(1)	40(1)
P(1)	442(1)	5913(1)	1401(1)	27(1)
P(2)	4908(1)	1455(1)	1087(1)	23(1)
C(1)	2726(5)	6068(3)	1233(1)	28(1)
C(2)	3754(4)	5856(3)	1008(1)	28(1)
C(3)	3849(5)	6155(3)	641(1)	30(1)
C(4)	4844(5)	5954(4)	437(2)	34(1)
C(5)	5856(6)	5448(4)	587(2)	36(1)
C(6)	6998(6)	5324(5)	369(2)	50(2)
C(7)	5765(5)	5114(4)	935(2)	35(1)
C(8)	4721(5)	5294(3)	1150(1)	30(1)
C(9)	4649(5)	4939(4)	1507(2)	33(1)
C(10)	3648(5)	5111(4)	1721(1)	35(1)
C(11)	3609(7)	4742(5)	2102(2)	52(2)
C(12)	2667(5)	5672(4)	1576(1)	29(1)
C(13)	1510(5)	5822(4)	1781(1)	32(1)
C(14)	1493(6)	6732(4)	2012(2)	40(1)
C(15)	380(5)	4706(3)	1205(1)	28(1)
C(16)	837(7)	3914(4)	1379(2)	48(2)
C(17)	762(8)	3015(5)	1217(2)	60(2)
C(18)	235(6)	2930(5)	874(2)	49(2)
C(19)	-224(7)	3726(5)	703(2)	49(2)
C(20)	-159(6)	4613(4)	868(2)	37(1)
C(21)	-1070(5)	6119(3)	1574(1)	31(1)
C(22)	-1447(6)	5761(4)	1904(2)	40(1)
C(23)	-2624(6)	5914(5)	2027(2)	46(2)
C(24)	-3432(6)	6430(4)	1825(2)	45(1)
C(25)	-3083(6)	6783(4)	1492(2)	46(1)

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C(26)	-1926(5)	6630(4)	1367(2)	36(1)
C(27)	150(6)	8910(4)	1232(2)	38(1)
C(28)	-23(5)	9863(4)	1039(2)	43(1)
C(29)	170(6)	9660(4)	641(2)	39(1)
C(30)	746(5)	8661(4)	634(1)	28(1)
C(31)	2130(5)	8650(3)	660(1)	27(1)
C(32)	6842(4)	754(3)	1438(1)	21(1)
C(33)	7487(4)	216(3)	1703(1)	23(1)
C(34)	7358(5)	-784(3)	1754(1)	27(1)
C(35)	8019(5)	-1271(4)	2011(1)	30(1)
C(36)	8865(4)	-810(3)	2232(1)	27(1)
C(37)	9621(6)	-1360(4)	2499(2)	39(1)
C(38)	8988(4)	168(3)	2196(1)	27(1)
C(39)	8305(4)	703(3)	1940(1)	26(1)
C(40)	8388(5)	1715(3)	1922(1)	31(1)
C(41)	7702(5)	2240(3)	1691(1)	31(1)
C(42)	7754(6)	3329(4)	1694(2)	42(1)
C(43)	6912(4)	1753(3)	1445(1)	24(1)
C(44)	6155(4)	2303(3)	1174(1)	26(1)
C(45)	6859(6)	2521(4)	828(2)	38(1)
C(46)	3893(5)	1457(4)	1477(2)	33(1)
C(47)	4010(9)	2091(6)	1763(2)	76(3)
C(48)	3140(10)	2067(7)	2042(3)	85(3)
C(49)	2200(7)	1436(6)	2038(2)	54(2)
C(50)	2127(8)	813(7)	1767(2)	70(2)
C(51)	2919(8)	851(6)	1480(2)	66(2)
C(52)	3973(4)	2020(3)	740(1)	27(1)
C(53)	3876(6)	3021(4)	732(2)	46(1)
C(54)	3186(7)	3467(4)	470(2)	59(2)
C(55)	2584(7)	2922(5)	213(2)	51(2)
C(56)	2609(6)	1942(5)	232(2)	47(2)
C(57)	3323(5)	1488(4)	489(2)	35(1)
C(58)	5519(6)	-60(4)	189(1)	41(1)
C(59)	6326(9)	-699(7)	-28(2)	74(3)
C(60)	5959(8)	-1708(5)	100(2)	62(2)
C(61)	5848(6)	-1542(3)	508(1)	33(1)
C(62)	7058(5)	-1586(3)	702(1)	29(1)
C(63)	4430(30)	8960(20)	2005(4)	352(18)
CI(1)	3658(11)	8548(10)	2396(3)	402(9)
CI(2)	3996(5)	8406(4)	1583(2)	181(2)

Table A 13-1 Crystal data and structure refinement for Complex (S)-201

Empirical formula	C ₅₂ H ₄₈ Cl ₂ P ₂ Pd ₂
Formula weight	1018.54
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2
Unit cell dimensions	a = 21.9239(10) Å α = 90°. b = 6.8683(3) Å β = 94.667(2)°. c = 15.0574(7) Å γ = 90°.
Volume	2259.82(18) Å ³
Z	2
Density (calculated)	1.497 Mg/m ³
Absorption coefficient	1.020 mm ⁻¹
F(000)	1032
Crystal size	0.30 x 0.15 x 0.02 mm ³
Theta range for data collection	1.36 to 27.00°.
Index ranges	-27 ≤ h ≤ 28, -8 ≤ k ≤ 8, -19 ≤ l ≤ 18
Reflections collected	11375
Independent reflections	4588 [R(int) = 0.0466]
Completeness to theta = 27.00°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9799 and 0.7495
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4588 / 1 / 265
Goodness-of-fit on F ²	1.067
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0500, wR2 = 0.1393
R indices (all data) ^{a,b}	R1 = 0.0633, wR2 = 0.1575
Absolute structure parameter	0.08(6)
Largest diff. peak and hole	1.996 and -1.165 e.Å ⁻³

^a $R1 = \sum ||F_o| - |F_c|| / \sum |F_o|$.

^b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 13-2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for (*S*)-**201**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	5061(1)	10005(1)	8933(1)	23(1)
Cl(1)	4258(1)	11179(3)	9827(1)	34(1)
P(1)	5767(1)	8541(3)	8236(1)	26(1)
C(1)	4561(3)	9078(11)	7808(4)	25(1)
C(2)	4037(3)	10135(17)	7427(4)	28(1)
C(3)	3850(3)	12011(13)	7736(5)	34(2)
C(4)	3378(4)	13011(16)	7306(5)	45(2)
C(5)	3036(4)	12204(19)	6540(5)	51(3)
C(6)	2513(5)	13390(20)	6080(7)	72(4)
C(7)	3212(4)	10447(17)	6244(5)	49(3)
C(8)	3711(3)	9404(13)	6649(5)	37(2)
C(9)	3900(4)	7644(17)	6278(5)	48(2)
C(10)	4410(4)	6682(14)	6582(5)	39(2)
C(11)	4609(5)	4910(20)	6140(6)	58(3)
C(12)	4752(3)	7430(12)	7352(5)	30(2)
C(13)	5354(3)	6485(12)	7698(6)	35(2)
C(14)	5277(4)	4786(17)	8339(7)	51(2)
C(15)	6422(3)	7490(12)	8862(5)	32(2)
C(16)	6355(4)	6844(13)	9738(6)	44(2)
C(17)	6831(5)	5837(17)	10207(7)	59(3)
C(18)	7376(4)	5506(14)	9806(7)	55(3)
C(19)	7443(4)	6147(16)	8949(7)	49(2)
C(20)	6959(4)	7104(15)	8505(6)	42(2)
C(21)	6073(3)	10040(17)	7384(4)	31(1)
C(22)	6488(4)	11478(15)	7626(6)	48(2)
C(23)	6710(6)	12701(17)	7012(8)	63(3)
C(24)	6480(6)	12631(19)	6145(8)	71(4)
C(25)	6067(5)	11210(20)	5870(8)	67(3)
C(26)	5861(4)	9920(20)	6496(5)	47(2)

Table A 14-1 Crystal data and structure refinement for Complex (R)-201

Empirical formula	C ₅₂ H ₄₈ Cl ₂ P ₂ Pd ₂
Formula weight	1018.54
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2
Unit cell dimensions	a = 21.8837(11) Å α = 90°. b = 6.7962(4) Å β = 94.418(3)°. c = 15.0892(8) Å γ = 90°.
Volume	2237.5(2) Å ³
Z	2
Density (calculated)	1.512 Mg/m ³
Absorption coefficient	1.030 mm ⁻¹
F(000)	1032
Crystal size	0.26 x 0.25 x 0.04 mm ³
Theta range for data collection	2.22 to 30.53°.
Index ranges	-31 ≤ h ≤ 30, -9 ≤ k ≤ 6, -21 ≤ l ≤ 21
Reflections collected	14929
Independent reflections	6006 [R(int) = 0.0255]
Completeness to theta = 30.53°	98.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9600 and 0.7755
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	6006 / 7 / 265
Goodness-of-fit on F ²	1.256
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0292, wR2 = 0.0817
R indices (all data) ^{a,b}	R1 = 0.0311, wR2 = 0.0833
Absolute structure parameter	-0.01(3)
Largest diff. peak and hole	1.432 and -1.313 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 14-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (*R*)-**201**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	5067(1)	7052(1)	8931(1)	15(1)
Cl(1)	4256(1)	5904(2)	9821(1)	23(1)
P(1)	5780(1)	8520(2)	8226(1)	16(1)
C(1)	4569(2)	7958(6)	7796(2)	18(1)
C(2)	4048(1)	6884(9)	7419(2)	19(1)
C(3)	3854(2)	5024(7)	7733(3)	23(1)
C(4)	3379(2)	3983(8)	7305(3)	27(1)
C(5)	3048(2)	4755(8)	6537(3)	29(1)
C(6)	2532(2)	3557(10)	6072(3)	46(2)
C(7)	3218(2)	6534(8)	6227(3)	31(1)
C(8)	3718(2)	7628(7)	6632(3)	24(1)
C(9)	3909(2)	9382(8)	6239(3)	27(1)
C(10)	4427(2)	10384(7)	6569(3)	24(1)
C(11)	4631(2)	12218(11)	6113(3)	33(1)
C(12)	4761(2)	9605(6)	7350(2)	19(1)
C(13)	5361(2)	10595(7)	7678(3)	23(1)
C(14)	5285(2)	12284(9)	8324(3)	30(1)
C(15)	6434(2)	9592(6)	8860(3)	19(1)
C(16)	6362(2)	10302(7)	9718(3)	26(1)
C(17)	6835(2)	11324(8)	10177(3)	34(1)
C(18)	7387(2)	11644(7)	9792(3)	32(1)
C(19)	7459(2)	10969(7)	8943(3)	29(1)
C(20)	6985(2)	9946(7)	8476(3)	22(1)
C(21)	6084(1)	6964(10)	7374(2)	22(1)
C(22)	6512(2)	5528(7)	7635(3)	27(1)
C(23)	6720(3)	4238(8)	7006(4)	39(1)
C(24)	6498(3)	4360(8)	6124(3)	39(1)
C(25)	6074(2)	5814(9)	5857(3)	37(1)
C(26)	5864(2)	7090(12)	6478(2)	29(1)

Table A 15-1 Crystal data and structure refinement for Complex (R)-204

Empirical formula	C ₄₅ H ₄₁ Cl ₃ P ₂ Pd
Formula weight	856.47
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 10.6099(3) Å α = 90°. b = 17.1231(4) Å β = 90°. c = 22.2070(5) Å γ = 90°.
Volume	4034.44(17) Å ³
Z	4
Density (calculated)	1.410 Mg/m ³
Absorption coefficient	0.769 mm ⁻¹
F(000)	1752
Crystal size	0.36 x 0.30 x 0.28 mm ³
Theta range for data collection	1.50 to 30.19°.
Index ranges	-14 ≤ h ≤ 14, -24 ≤ k ≤ 23, -27 ≤ l ≤ 31
Reflections collected	35803
Independent reflections	11912 [R(int) = 0.0430]
Completeness to theta = 30.19°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8135 and 0.7692
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	11912 / 0 / 463
Goodness-of-fit on F ²	1.090
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0360, wR2 = 0.0809
R indices (all data) ^{a,b}	R1 = 0.0509, wR2 = 0.1006
Absolute structure parameter	-0.01(2)
Largest diff. peak and hole	0.736 and -0.771 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 15-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (*R*)-**204** U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	2725(1)	4900(1)	-14(1)	21(1)
C(1)	2170(3)	5928(2)	349(1)	22(1)
C(2)	1036(3)	5962(2)	690(1)	23(1)
C(3)	173(3)	5330(2)	722(2)	30(1)
C(4)	-913(3)	5384(2)	1052(2)	37(1)
C(5)	-1198(3)	6063(2)	1387(2)	34(1)
C(6)	-2391(4)	6085(3)	1766(2)	57(1)
C(7)	-393(3)	6680(2)	1351(1)	32(1)
C(8)	725(3)	6664(2)	999(1)	25(1)
C(9)	1507(3)	7326(2)	922(1)	26(1)
C(10)	2508(3)	7327(2)	529(1)	24(1)
C(11)	3233(3)	8064(2)	399(2)	31(1)
C(12)	2822(3)	6611(2)	242(1)	22(1)
C(13)	3878(3)	6557(2)	-220(1)	23(1)
C(14)	5136(3)	6318(2)	59(2)	29(1)
C(15)	1951(3)	6171(2)	-1148(1)	25(1)
C(16)	1650(3)	6970(2)	-1182(2)	34(1)
C(17)	593(4)	7208(3)	-1497(2)	46(1)
C(18)	-153(4)	6673(3)	-1776(2)	45(1)
C(19)	144(4)	5873(3)	-1754(2)	45(1)
C(20)	1194(4)	5636(2)	-1438(2)	37(1)
C(21)	4496(3)	5607(2)	-1269(1)	26(1)
C(22)	4599(3)	6068(2)	-1784(1)	27(1)
C(23)	5636(4)	5996(2)	-2164(1)	36(1)
C(24)	6556(3)	5443(3)	-2033(2)	42(1)
C(25)	6446(4)	4971(3)	-1535(2)	46(1)
C(26)	5425(3)	5050(2)	-1152(1)	38(1)
C(27)	4587(3)	3976(2)	1033(1)	27(1)
C(28)	5239(3)	3721(2)	528(2)	35(1)
C(29)	6435(4)	3404(3)	578(2)	50(1)
C(30)	6990(4)	3322(3)	1136(2)	49(1)
C(31)	6352(4)	3583(3)	1643(2)	54(1)
C(32)	5168(4)	3914(3)	1596(2)	45(1)
C(33)	2789(3)	5012(2)	1586(1)	26(1)
C(34)	1754(3)	4987(2)	1973(1)	30(1)

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C(35)	1610(4)	5548(2)	2423(2)	38(1)
C(36)	2479(4)	6124(2)	2490(2)	46(1)
C(37)	3490(4)	6172(2)	2104(2)	45(1)
C(38)	3653(4)	5615(2)	1655(2)	37(1)
C(39)	2011(3)	3484(2)	1153(1)	26(1)
C(40)	1141(3)	3208(2)	737(2)	31(1)
C(41)	375(4)	2578(2)	870(2)	42(1)
C(42)	467(4)	2210(2)	1421(2)	43(1)
C(43)	1344(4)	2469(2)	1834(2)	49(1)
C(44)	2119(4)	3108(2)	1710(2)	39(1)
C(45)	9620(6)	3333(3)	8993(3)	88(2)
CI(1)	2909(1)	3737(1)	-612(1)	33(1)
CI(2)	9385(2)	3603(1)	8248(1)	87(1)
CI(3)	8964(2)	4005(1)	9486(1)	110(1)
P(1)	3261(1)	5786(1)	-720(1)	21(1)
P(2)	2964(1)	4333(1)	952(1)	22(1)

Table A 16-1 Crystal data and structure refinement for Complex (R)-205

Empirical formula	C ₃₈ H ₃₇ ClP ₂ Pd
Formula weight	697.47
Temperature	223(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 12.4956(4) Å α = 90°. b = 15.5587(4) Å β = 90°. c = 17.5950(5) Å γ = 90°.
Volume	3420.74(17) Å ³
Z	4
Density (calculated)	1.354 Mg/m ³
Absorption coefficient	0.739 mm ⁻¹
F(000)	1432
Crystal size	0.30 x 0.24 x 0.24 mm ³
Theta range for data collection	2.09 to 28.00°.
Index ranges	-14 ≤ h ≤ 16, -19 ≤ k ≤ 20, -23 ≤ l ≤ 23
Reflections collected	24091
Independent reflections	8114 [R(int) = 0.0375]
Completeness to theta = 28.00°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8426 and 0.8088
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	8114 / 0 / 384
Goodness-of-fit on F ²	1.153
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0545, wR2 = 0.1059
R indices (all data) ^{a,b}	R1 = 0.0794, wR2 = 0.1343
Absolute structure parameter	-0.03(4)
Largest diff. peak and hole	1.492 and -1.594 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 16-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (*R*)-**205**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

–	x	y	z	U(eq)
Pd(1)	3418(1)	5635(1)	8040(1)	45(1)
C(1)	2911(5)	6795(4)	8444(4)	46(2)
C(2)	1787(5)	6954(4)	8562(4)	45(1)
C(3)	972(5)	6394(4)	8308(4)	50(2)
C(4)	-88(5)	6562(5)	8454(4)	56(2)
C(5)	-423(6)	7316(5)	8833(4)	57(2)
C(6)	-1577(7)	7461(6)	8986(5)	81(2)
C(7)	365(6)	7883(5)	9044(4)	57(2)
C(8)	1466(6)	7735(4)	8905(3)	48(1)
C(9)	2267(6)	8337(5)	9128(4)	57(2)
C(10)	3320(6)	8214(4)	8976(4)	54(2)
C(11)	4154(7)	8866(5)	9222(5)	76(3)
C(12)	3633(6)	7424(4)	8606(3)	49(2)
C(13)	4786(6)	7276(5)	8349(4)	53(2)
C(14)	5470(7)	6825(6)	8940(5)	79(3)
C(15)	4117(5)	7255(4)	6740(3)	43(1)
C(16)	3932(6)	8122(5)	6794(4)	58(2)
C(17)	3576(7)	8590(5)	6181(4)	65(2)
C(18)	3366(7)	8191(5)	5508(4)	63(2)
C(19)	3534(9)	7332(5)	5440(4)	77(3)
C(20)	3911(8)	6865(5)	6048(4)	69(2)
C(21)	5914(6)	6254(5)	7222(4)	53(2)
C(22)	6631(6)	6850(5)	6909(5)	67(2)
C(23)	7672(6)	6613(6)	6733(5)	75(2)
C(24)	8013(5)	5795(6)	6879(5)	73(2)
C(25)	7344(6)	5209(6)	7191(6)	80(3)
C(26)	6301(5)	5430(5)	7357(5)	65(2)
C(27)	2452(6)	5337(4)	9928(4)	55(2)
C(28)	3060(6)	4908(5)	10431(4)	58(2)
C(29)	3223(9)	5139(6)	11246(4)	87(3)
C(30)	4260(8)	3557(7)	10602(6)	92(3)
C(31)	3590(6)	4138(5)	10110(4)	61(2)
C(32)	3404(6)	4026(4)	9377(4)	56(2)
C(33)	1274(5)	4352(4)	8811(4)	47(1)
C(34)	405(6)	4443(5)	9295(5)	66(2)

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C(35)	-559(7)	4061(6)	9118(6)	82(3)
C(36)	-675(6)	3577(6)	8477(5)	74(2)
C(37)	175(7)	3483(5)	8002(5)	75(2)
C(38)	1159(6)	3867(5)	8156(5)	64(2)
Cl(1)	3898(1)	4289(1)	7466(1)	63(1)
P(1)	4589(1)	6582(1)	7514(1)	47(1)
P(2)	2555(1)	4865(1)	9007(1)	45(1)

Table A 17-1 Crystal data and structure refinement for Complex ($\pm$)-**208**

Identification code	leung403p
Empirical formula	C _{58.67} H ₆₈ Cl _{9.33} O ₃ P ₂ Pd ₂
Formula weight	1426.74
Temperature	173(2) K
Wavelength	0.71073 $\approx$
Crystal system	Trigonal
Space group	P-3
Unit cell dimensions	a = 25.8527(14) Å $\alpha = 90^\circ$. b = 25.8527(14) Å $\beta = 90^\circ$. c = 9.6397(13) Å $\gamma = 120^\circ$.
Volume	5579.6(9) Å ³
Z	3
Density (calculated)	1.274 Mg/m ³
Absorption coefficient	0.897 mm ⁻¹
F(000)	2174
Crystal size	0.32 x 0.08 x 0.06 mm ³
Theta range for data collection	0.91 to 29.98°.
Index ranges	-35 $\leq$ h $\leq$ 36, -36 $\leq$ k $\leq$ 36, -12 $\leq$ l $\leq$ 13
Reflections collected	61143
Independent reflections	10832 [R(int) = 0.1034]
Completeness to theta = 29.98°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9481 and 0.7623
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	10832 / 81 / 345
Goodness-of-fit on F ²	1.061
Final R indices [I > 2 σ (I)] ^{a,b}	R1 = 0.0807, wR2 = 0.2404
R indices (all data) ^{a,b}	R1 = 0.1156, wR2 = 0.2754
Largest diff. peak and hole	2.497 and -1.143 e. Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 17-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for ($\pm$)-**208**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	5097(1)	697(1)	10457(1)	29(1)
C(1)	4858(3)	2746(3)	11906(6)	52(2)
C(2)	4880(2)	2824(2)	10350(5)	33(1)
C(3)	4700(3)	3199(2)	9744(6)	39(1)
C(4)	4726(2)	3301(2)	8337(5)	31(1)
C(5)	4554(3)	3696(2)	7708(6)	39(1)
C(6)	4596(3)	3804(2)	6323(6)	42(1)
C(7)	4412(4)	4222(3)	5682(7)	64(2)
C(8)	4788(3)	3494(3)	5469(6)	48(1)
C(9)	4967(3)	3115(2)	6023(6)	42(1)
C(10)	4939(2)	3008(2)	7441(5)	31(1)
C(11)	5123(2)	2631(2)	8073(6)	34(1)
C(12)	5093(2)	2529(2)	9431(5)	31(1)
C(13)	5304(2)	2124(2)	10051(5)	33(1)
C(14)	5938(2)	2302(2)	9543(6)	42(1)
C(15)	4086(2)	1140(3)	10585(6)	42(1)
C(16)	3772(3)	1446(3)	10350(9)	67(2)
C(17)	3258(3)	1308(4)	11125(10)	85(3)
C(18)	3063(4)	871(5)	12113(11)	98(3)
C(19)	3339(4)	553(5)	12331(9)	89(3)
C(20)	3850(3)	696(3)	11559(7)	55(2)
C(21)	4648(2)	1250(2)	7867(5)	33(1)
C(22)	4153(3)	1210(3)	7244(7)	49(1)
C(23)	4121(4)	1247(3)	5811(7)	61(2)
C(24)	4596(4)	1319(3)	5029(6)	59(2)
C(25)	5098(4)	1344(3)	5630(7)	59(2)
C(26)	5114(3)	1297(2)	7035(6)	43(1)
C(27)	6667	3333	4379(12)	118(6)
C(28)	1622(19)	1217(13)	150(40)	320(20)
C(29)	1939(16)	1906(14)	510(40)	259(13)
C(30)	2923(12)	2709(9)	1430(30)	180(9)
C(31)	3369(10)	2909(10)	2600(30)	157(10)
Cl(1)	5565(1)	1316(1)	12282(1)	42(1)
Cl(2)	4586(1)	-6(1)	8736(1)	37(1)

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Cl(3)	6667	3333	6148(5)	139(2)
Cl(4)	6192(3)	2667(2)	3727(6)	83(2)
O(1)	2433(10)	2068(9)	1550(20)	189(8)
O(2)	2062(6)	8848(6)	3062(18)	261(8)
P(1)	4775(1)	1311(1)	9723(1)	28(1)

Table A 18-1 Crystal data and structure refinement for Complex ($\pm$)-**209**

Empirical formula	$C_{39}H_{40}Cl_4P_2Pd$
Formula weight	818.85
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	$a = 10.5008(3)$ Å $\alpha = 75.362(2)^\circ$ $b = 13.3740(5)$ Å $\beta = 77.898(2)^\circ$ $c = 14.0042(5)$ Å $\gamma = 78.338(2)^\circ$
Volume	1837.32(11) Å ³
Z	2
Density (calculated)	1.480 Mg/m ³
Absorption coefficient	0.911 mm ⁻¹
F(000)	836
Crystal size	0.25 x 0.25 x 0.10 mm ³
Theta range for data collection	1.52 to 30.62°
Index ranges	-15 ≤ h ≤ 15, -19 ≤ k ≤ 19, -20 ≤ l ≤ 20
Reflections collected	46506
Independent reflections	11280 [R(int) = 0.0304]
Completeness to theta = 30.62°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9144 and 0.8043
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	11280 / 0 / 439
Goodness-of-fit on F ²	1.146
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0266, wR2 = 0.0770
R indices (all data) ^{a,b}	R1 = 0.0347, wR2 = 0.0942
Largest diff. peak and hole	0.514 and -0.663 e.Å ⁻³

^a $R1 = \sum ||F_o| - |F_c|| / \sum |F_o|$.

^b $wR2 = \sqrt{\{ \sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2] \}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 18-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for ($\pm$)-**209**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	13296(2)	9737(2)	413(2)	38(1)
C(2)	12564(2)	9045(2)	281(2)	32(1)
C(3)	12219(2)	8223(1)	1069(1)	23(1)
C(4)	12627(2)	8096(2)	1982(1)	27(1)
C(5)	13343(2)	8808(2)	2113(2)	32(1)
C(6)	13672(2)	9620(2)	1337(2)	35(1)
C(7)	12073(2)	6813(2)	-195(1)	26(1)
C(8)	11366(2)	7146(2)	-938(1)	27(1)
C(9)	11692(2)	6776(2)	-1897(2)	41(1)
C(10)	10168(2)	7918(2)	-724(1)	28(1)
C(11)	9239(2)	8340(2)	-1461(2)	47(1)
C(12)	9998(2)	8140(2)	183(1)	25(1)
C(13)	7711(2)	6490(1)	1471(1)	20(1)
C(14)	8479(2)	6014(1)	714(1)	25(1)
C(15)	7914(2)	5872(2)	-45(2)	32(1)
C(16)	6580(2)	6201(2)	-58(2)	33(1)
C(17)	5808(2)	6676(2)	685(2)	31(1)
C(18)	6364(2)	6818(2)	1447(1)	25(1)
C(19)	8256(2)	8022(1)	2471(1)	21(1)
C(20)	7133(2)	8722(2)	2219(1)	28(1)
C(21)	6953(2)	9746(2)	2326(2)	36(1)
C(22)	7884(3)	10088(2)	2680(2)	41(1)
C(23)	9001(2)	9405(2)	2931(2)	40(1)
C(24)	9183(2)	8377(2)	2834(1)	29(1)
C(25)	7711(2)	6010(1)	3687(1)	22(1)
C(26)	8430(2)	6134(2)	4494(1)	30(1)
C(27)	6233(2)	6358(1)	3896(1)	21(1)
C(28)	5336(2)	5745(1)	3767(1)	22(1)
C(29)	4005(2)	6048(1)	4029(1)	24(1)
C(30)	3477(2)	6951(1)	4417(1)	23(1)
C(31)	4363(2)	7576(1)	4517(1)	24(1)
C(32)	5728(2)	7255(1)	4254(1)	23(1)
C(33)	5798(2)	4770(2)	3358(1)	26(1)
C(34)	2100(2)	7239(2)	4720(1)	28(1)

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C(35)	1607(2)	8118(2)	5094(1)	31(1)
C(36)	2498(2)	8760(2)	5152(2)	33(1)
C(37)	3830(2)	8500(2)	4884(1)	30(1)
C(38)	153(2)	8387(2)	5459(2)	39(1)
C(39)	6277(3)	7407(2)	6943(3)	64(1)
Cl(1)	13007(1)	5397(1)	1913(1)	29(1)
Cl(2)	10366(1)	4344(1)	3143(1)	31(1)
Cl(3)	6678(5)	8616(5)	6285(8)	71(1)
Cl(4)	4823(4)	7450(4)	7785(5)	52(1)
Cl(3A)	6794(12)	8687(8)	6560(17)	67(2)
Cl(4A)	4936(15)	7562(14)	7911(14)	69(3)
P(1)	11246(1)	7341(1)	868(1)	21(1)
P(2)	8545(1)	6643(1)	2425(1)	18(1)
Pd(1)	10729(1)	5986(1)	2133(1)	18(1)

Table A 19-1 Crystal data and structure refinement for Complex ($\pm$)-**219**

Empirical formula	$C_{33}H_{39}ClNPPd$
Formula weight	622.47
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 10.6581(3)$ Å $\square \alpha = 90^\circ$. $b = 15.7791(5)$ Å $\square \beta = 90^\circ$. $c = 17.6760(5)$ Å $\square \gamma = 90^\circ$.
Volume	$2972.67(15)$ Å ³
Z	4
Density (calculated)	1.391 Mg/m ³
Absorption coefficient	0.790 mm^{-1}
F(000)	1288
Crystal size	0.30 x 0.30 x 0.29 mm ³
Theta range for data collection	2.83 to 25.05°.
Index ranges	$-12 \leq h \leq 12$, $-17 \leq k \leq 17$, $-21 \leq l \leq 21$
Reflections collected	22946
Independent reflections	5032 [R(int) = 0.0237]
Completeness to theta = 25.05°	96.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8033 and 0.7975
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5032 / 0 / 341
Goodness-of-fit on F ²	1.068
Final R indices [I > 2sigma(I)] ^{a,b}	R1 = 0.0165, wR2 = 0.0418
R indices (all data) ^{a,b}	R1 = 0.0171, wR2 = 0.0421
Absolute structure parameter	0.044(14)
Largest diff. peak and hole	0.340 and -0.228 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 19-2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for ($\pm$)-**219**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Pd(1)	9461(1)	4536(1)	2732(1)	19(1)
C(1)	11310(2)	4481(1)	2963(1)	19(1)
C(2)	11877(2)	4138(1)	3611(1)	21(1)
C(3)	11139(2)	3929(2)	4312(1)	27(1)
C(4)	13164(2)	3964(1)	3599(1)	25(1)
C(5)	13881(2)	4107(1)	2967(1)	25(1)
C(6)	13358(2)	4414(1)	2307(1)	26(1)
C(7)	14195(2)	4505(2)	1625(1)	42(1)
C(8)	12066(2)	4604(1)	2309(1)	22(1)
C(9)	11376(2)	4826(2)	1588(1)	29(1)
C(10)	11186(2)	5798(2)	1448(1)	36(1)
C(11)	12422(3)	6257(2)	1641(2)	54(1)
C(12)	10948(3)	5984(2)	601(1)	52(1)
C(13)	10164(2)	6216(2)	1918(1)	38(1)
C(14)	10589(2)	3367(2)	1594(1)	38(1)
C(15)	9337(2)	4404(2)	987(1)	40(1)
C(16)	7302(2)	5772(1)	3545(1)	23(1)
C(17)	7488(2)	6496(2)	3116(1)	31(1)
C(18)	6491(2)	6978(2)	2865(1)	37(1)
C(19)	5284(2)	6743(2)	3045(1)	38(1)
C(20)	5085(2)	6028(2)	3478(2)	40(1)
C(21)	6088(2)	5546(2)	3736(1)	29(1)
C(22)	8155(2)	4418(1)	4536(1)	23(1)
C(23)	7454(2)	3722(2)	4309(1)	30(1)
C(24)	7066(2)	3126(2)	4833(1)	37(1)
C(25)	7391(2)	3214(2)	5591(1)	36(1)
C(26)	8092(2)	3898(2)	5816(1)	34(1)
C(27)	8467(2)	4502(2)	5297(1)	27(1)
C(28)	9587(2)	5964(1)	4304(1)	23(1)
C(29)	9009(2)	6447(2)	4860(1)	27(1)
C(30)	9673(2)	7051(2)	5257(1)	34(1)
C(31)	10922(2)	7192(2)	5099(1)	36(1)
C(32)	11496(2)	6730(2)	4539(1)	37(1)
C(33)	10844(2)	6114(2)	4140(1)	28(1)
Cl(1)	7370(1)	4216(1)	2333(1)	36(1)

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N(1)	10212(2)	4275(1)	1631(1)	28(1)
P(1)	8689(1)	5147(1)	3801(1)	19(1)

Table A 20-1 Crystallographic Data for Complex (R_C, S_C, S_N)-220

Empirical formula	$C_{21}H_{33}Cl_3N_2O_2Pd$
Formula weight	558.24
Temperature	223(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 10.3779(3)$ Å $\alpha = 90^\circ$. $b = 20.8123(8)$ Å $\beta = 90^\circ$. $c = 34.2018(12)$ Å $\gamma = 90^\circ$.
Volume	7387.2(4) Å ³
Z	12
Density (calculated)	1.506 Mg/m ³
Absorption coefficient	1.098 mm ⁻¹
F(000)	3432
Crystal size	0.30 x 0.14 x 0.08 mm ³
Theta range for data collection	1.15 to 26.37°.
Index ranges	-12 ≤ h ≤ 12, -24 ≤ k ≤ 25, -42 ≤ l ≤ 42
Reflections collected	41688
Independent reflections	14995 [R(int) = 0.0493]
Completeness to theta = 26.37°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9173 and 0.7341
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	14995 / 15 / 830
Goodness-of-fit on F ²	1.031
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0467, wR2 = 0.1079
R indices (all data) ^{a,b}	R1 = 0.0630, wR2 = 0.1214
Absolute structure parameter	0.04(3)
Largest diff. peak and hole	1.146 and -1.001 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 20-2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (R_C, S_C, S_N)-**220** U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	3538(1)	3674(1)	636(1)	24(1)
Pd(2)	1495(1)	6234(1)	2396(1)	26(1)
Pd(3)	6369(1)	8441(1)	1065(1)	26(1)
C(1)	2380(5)	3778(3)	1106(2)	24(1)
C(2)	1026(5)	3787(3)	1121(2)	28(1)
C(3)	188(6)	3669(3)	777(2)	38(2)
C(4)	438(6)	3961(4)	1475(2)	40(2)
C(5)	1139(6)	4139(4)	1801(2)	43(2)
C(6)	2481(6)	4139(3)	1790(2)	38(2)
C(7)	3199(7)	4402(4)	2143(2)	53(2)
C(8)	3090(5)	3917(3)	1451(2)	25(1)
C(9)	4544(5)	3868(3)	1413(2)	29(1)
C(10)	5077(7)	3175(4)	1515(2)	42(2)
C(11)	4517(9)	2970(4)	1911(2)	59(2)
C(12)	6573(8)	3195(5)	1569(3)	83(3)
C(13)	4680(8)	2655(4)	1215(2)	54(2)
C(14)	6165(7)	4084(5)	879(2)	63(3)
C(15)	4467(8)	4840(3)	1021(2)	56(2)
C(16)	4677(5)	3082(3)	-45(2)	28(1)
C(17)	3358(5)	2748(3)	9(2)	26(1)
C(18)	2701(6)	2566(3)	-374(2)	38(2)
C(19)	1710(7)	3096(4)	-438(2)	46(2)
C(20)	1922(6)	3581(3)	-111(2)	38(2)
C(21)	2657(6)	6148(3)	2862(2)	26(1)
C(22)	4021(5)	6105(3)	2885(2)	31(1)
C(23)	4874(6)	6182(4)	2532(2)	40(2)
C(24)	4591(6)	5987(3)	3244(2)	41(2)
C(25)	3871(6)	5857(3)	3575(2)	42(2)
C(26)	2544(6)	5860(3)	3563(2)	36(2)
C(27)	1801(7)	5622(4)	3923(2)	53(2)
C(28)	1940(6)	6058(3)	3216(2)	29(1)
C(29)	495(6)	6115(3)	3177(2)	28(1)
C(30)	-22(6)	6827(3)	3252(2)	37(2)
C(31)	572(8)	7064(4)	3642(2)	54(2)
C(32)	-1495(8)	6843(4)	3328(2)	64(2)

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C(33)	347(7)	7312(3)	2938(2)	43(2)
C(34)	461(8)	5124(3)	2815(2)	52(2)
C(35)	-1149(6)	5873(4)	2653(2)	49(2)
C(36)	406(6)	6838(3)	1711(2)	32(1)
C(37)	1765(6)	7098(3)	1743(2)	31(1)
C(38)	2407(8)	7186(4)	1341(2)	49(2)
C(39)	3350(30)	6630(11)	1301(6)	61(7)
C(39A)	2900(30)	6510(9)	1259(4)	48(7)
C(40)	3093(7)	6198(4)	1657(2)	47(2)
C(41)	7554(6)	8706(3)	630(2)	30(1)
C(42)	8913(6)	8750(3)	627(2)	35(2)
C(43)	9798(6)	8467(4)	929(2)	55(2)
C(44)	9505(7)	9100(4)	327(2)	59(2)
C(45)	8828(7)	9405(4)	48(2)	64(2)
C(46)	7469(7)	9333(4)	19(2)	46(2)
C(47)	6726(9)	9684(4)	-299(2)	69(3)
C(48)	6882(6)	8957(3)	308(2)	34(2)
C(49)	5473(5)	8782(3)	283(2)	27(1)
C(50)	5197(7)	8110(3)	84(2)	41(2)
C(51)	6091(9)	8070(4)	-291(2)	65(3)
C(52)	3818(8)	8062(5)	-72(2)	74(3)
C(53)	5554(8)	7522(3)	334(2)	50(2)
C(54)	3656(7)	8635(4)	763(2)	48(2)
C(55)	5030(8)	9557(3)	798(2)	54(2)
C(56)	5375(6)	7841(3)	1768(2)	31(1)
C(57)	6755(6)	7612(3)	1741(2)	30(1)
C(58)	7450(6)	7554(4)	2131(2)	48(2)
C(59)	8314(8)	8129(4)	2156(2)	59(2)
C(60)	7948(6)	8547(3)	1808(2)	40(2)
C(61)	2266(8)	933(5)	411(2)	63(2)
C(62)	7957(8)	5908(4)	1291(2)	62(2)
C(63)	2958(8)	8933(4)	2081(2)	56(2)
N(1)	4795(5)	4133(3)	1011(2)	36(1)
N(2)	2458(4)	3181(2)	220(1)	23(1)
N(3)	199(5)	5832(3)	2784(2)	31(1)
N(4)	2615(5)	6649(3)	1963(1)	31(1)
N(5)	5000(5)	8843(3)	695(2)	36(1)
N(6)	7549(5)	8074(3)	1500(2)	28(1)
CI(1)	1409(3)	374(2)	671(1)	145(2)
CI(2)	3047(4)	585(2)	20(1)	170(2)
CI(3)	3423(3)	1280(1)	716(1)	101(1)
CI(4)	6834(2)	6196(1)	955(1)	82(1)
CI(5)	8975(3)	5364(2)	1068(1)	124(1)
CI(6)	7136(3)	5550(2)	1683(1)	121(1)

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Cl(7)	1949(3)	9036(2)	1693(1)	114(1)
Cl(8)	1963(4)	8807(2)	2487(1)	153(2)
Cl(9)	3993(4)	9540(2)	2149(2)	158(2)
O(1)	4910(4)	3553(2)	177(1)	36(1)
O(2)	5430(4)	2871(2)	-300(1)	37(1)
O(3)	118(4)	6373(2)	1942(1)	37(1)
O(4)	-336(4)	7078(2)	1470(1)	40(1)
O(5)	4999(4)	8234(2)	1504(1)	38(1)
O(6)	4660(4)	7653(2)	2039(1)	38(1)

Table A 21-1 Crystal data and structure refinement for complex (S_C, S_C, S_N)-220

Empirical formula	$C_{20}H_{32}N_2O_2Pd$
Formula weight	438.88
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	$a = 13.3928(6)$ Å $\square \alpha = 90^\circ$. $b = 10.6090(4)$ Å $\square \beta = 107.854(2)^\circ$. $c = 15.0850(6)$ Å $\square \gamma = 90^\circ$.
Volume	$2040.12(14)$ Å ³
Z	4
Density (calculated)	1.429 Mg/m ³
Absorption coefficient	0.924 mm ⁻¹
F(000)	912
Crystal size	$0.25 \times 0.20 \times 0.20$ mm ³
Theta range for data collection	1.42 to 30.59° .
Index ranges	$-19 \leq h \leq 18$, $-14 \leq k \leq 15$, $-21 \leq l \leq 21$
Reflections collected	36451
Independent reflections	11046 [R(int) = 0.0364]
Completeness to theta = 30.59°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8367 and 0.8018
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	11046 / 162 / 504
Goodness-of-fit on F ²	1.133
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0366, wR2 = 0.1023
R indices (all data) ^{a,b}	R1 = 0.0425, wR2 = 0.1168
Absolute structure parameter	0.01(3)
Largest diff. peak and hole	1.669 and -1.053 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 21-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (S_C, S_C, S_N)-**220** U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

–	x	y	z	U(eq)
Pd(1)	2580(1)	3726(1)	2483(1)	28(1)
Pd(2)	6638(1)	6356(1)	3921(1)	32(1)
C(1)	1031(3)	4006(4)	2085(3)	33(1)
C(2)	273(4)	3235(5)	2300(3)	38(1)
C(3)	507(4)	2047(6)	2849(4)	48(1)
C(4)	-775(4)	3638(7)	2023(4)	50(1)
C(5)	-1053(4)	4819(7)	1624(4)	60(2)
C(6)	-297(5)	5628(6)	1458(4)	50(1)
C(7)	-615(6)	6977(8)	1154(5)	74(2)
C(8)	729(4)	5162(5)	1649(3)	38(1)
C(9)	1597(4)	5969(4)	1507(3)	34(1)
C(10)	1787(4)	5778(5)	534(3)	39(1)
C(11)	717(4)	5793(7)	-232(3)	59(2)
C(12)	2428(5)	6889(5)	302(4)	54(1)
C(13)	2302(4)	4531(5)	431(3)	43(1)
C(14)	2302(5)	6270(5)	3187(3)	51(1)
C(15)	3543(4)	6227(5)	2357(4)	48(1)
C(16)	4592(4)	2442(4)	2933(3)	37(1)
C(17)	3800(4)	1388(5)	2612(3)	43(1)
C(18)	3846(8)	643(14)	1767(8)	65(3)
C(19)	2827(7)	1064(9)	1041(6)	50(2)
C(18A)	3734(16)	1185(19)	1570(11)	59(4)
C(19A)	2718(12)	470(30)	1138(17)	69(5)
C(20)	2042(4)	1133(6)	1600(3)	48(1)
C(21)	6464(3)	6883(4)	2601(3)	32(1)
C(22)	6036(3)	6240(5)	1769(3)	38(1)
C(23)	5754(4)	4844(6)	1710(3)	50(1)
C(24)	5833(4)	6899(6)	921(3)	49(1)
C(25)	6010(4)	8150(7)	897(3)	54(1)
C(26)	6457(4)	8841(6)	1712(3)	45(1)
C(27)	6582(5)	10256(6)	1640(4)	60(2)
C(28)	6716(3)	8188(5)	2549(3)	36(1)
C(29)	7203(4)	8820(5)	3485(3)	44(1)
C(30)	8433(4)	8715(6)	3855(4)	62(2)
C(31)	8832(6)	9161(7)	3039(6)	79(1)

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C(32)	8951(6)	9582(7)	4690(6)	79(1)
C(33)	8862(6)	7394(7)	4106(6)	79(1)
C(34)	5492(5)	8735(6)	3747(4)	58(2)
C(35)	6992(7)	8670(6)	5086(3)	75(2)
C(36)	7123(4)	4805(5)	5580(3)	43(1)
C(37)	6960(4)	3863(4)	4799(3)	38(1)
C(38)	7739(8)	2770(8)	4907(6)	46(2)
C(39)	8121(6)	2825(7)	4049(5)	43(2)
C(40)	7930(7)	4212(8)	3752(7)	40(2)
C(38A)	8055(14)	3220(20)	5026(17)	70(7)
C(39A)	8579(11)	3902(16)	4389(10)	65(5)
C(40A)	7608(12)	3866(14)	3488(9)	31(3)
N(1)	2529(3)	5680(6)	2366(3)	36(1)
N(2)	2691(3)	1779(5)	2470(2)	32(1)
N(3)	6595(4)	8262(5)	4096(3)	47(1)
N(4)	6846(4)	4452(5)	3875(2)	36(1)
O(1)	4228(2)	3564(3)	2947(2)	40(1)
O(2)	5530(3)	2174(4)	3153(3)	59(1)
O(3)	6895(3)	5953(3)	5340(2)	49(1)
O(4)	7435(5)	4449(4)	6389(2)	75(2)

Table A 22-1 Crystal data and structure refinement for Complex (R)-221

Empirical formula	C ₁₇ H ₂₉ ClN ₂ O ₅ Pd
Formula weight	483.27
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 8.4659(2) Å α = 90°. b = 10.7872(3) Å β = 90°. c = 22.7291(6) Å γ = 90°.
Volume	2075.70(9) Å ³
Z	4
Density (calculated)	1.546 Mg/m ³
Absorption coefficient	1.051 mm ⁻¹
F(000)	992
Crystal size	0.30 x 0.30 x 0.29 mm ³
Theta range for data collection	3.00 to 31.12°.
Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 15, -32 ≤ l ≤ 33
Reflections collected	26428
Independent reflections	6674 [R(int) = 0.0264]
Completeness to theta = 31.12°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7503 and 0.7434
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	6674 / 1 / 249
Goodness-of-fit on F ²	1.052
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0208, wR2 = 0.0508
R indices (all data) ^{a,b}	R1 = 0.0224, wR2 = 0.0515
Absolute structure parameter	0.001(16)
Largest diff. peak and hole	0.302 and -0.436 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 22-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for Complex (*R*)-**221**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	-866(1)	8877(1)	1648(1)	22(1)
C(1)	736(2)	8187(1)	1098(1)	20(1)
C(2)	970(2)	6941(2)	947(1)	26(1)
C(3)	-65(3)	5885(2)	1147(1)	41(1)
C(4)	2282(2)	6650(2)	602(1)	29(1)
C(5)	3386(2)	7527(2)	443(1)	30(1)
C(6)	3221(2)	8757(2)	615(1)	25(1)
C(7)	4560(2)	9642(2)	502(1)	37(1)
C(8)	1833(2)	9089(2)	914(1)	21(1)
C(9)	1459(2)	10411(2)	1085(1)	20(1)
C(10)	428(2)	11103(2)	613(1)	25(1)
C(11)	484(3)	12527(2)	694(1)	36(1)
C(12)	-1305(2)	10690(2)	588(1)	31(1)
C(13)	1133(3)	10846(2)	2(1)	41(1)
C(14)	2058(2)	9892(2)	2107(1)	31(1)
C(15)	132(2)	11456(2)	1945(1)	30(1)
C(16)	-3647(2)	6960(2)	1606(1)	30(1)
C(17)	-4985(2)	6127(2)	1655(1)	42(1)
Cl(1)	5421(1)	2762(1)	1762(1)	30(1)
N(1)	763(2)	10282(1)	1701(1)	22(1)
N(2)	-2571(2)	7583(1)	1575(1)	31(1)
O(1)	-2406(2)	9717(1)	2322(1)	40(1)
O(2)	4992(2)	3193(2)	2338(1)	53(1)
O(3)	4188(2)	3045(2)	1358(1)	63(1)
O(4)	5643(2)	1438(1)	1782(1)	53(1)
O(5)	6841(2)	3357(2)	1589(1)	53(1)

Table A 23-1 Crystal data and structure refinement for Complex (S,S)-**226**.

Empirical formula	C ₃₃ H ₃₄ Cl ₄ O ₄ P ₂ Pd
Formula weight	804.74
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2
Unit cell dimensions	a = 16.0113(4) Å α = 90°. b = 14.8142(4) Å β = 115.7270(10)°. c = 16.6228(5) Å γ = 90°.
Volume	3551.99(17) Å ³
Z	4
Density (calculated)	1.505 Mg/m ³
Absorption coefficient	0.949 mm ⁻¹
F(000)	1632
Crystal size	0.35 x 0.30 x 0.25 mm ³
Theta range for data collection	2.55 to 30.60°.
Index ranges	-22 ≤ h ≤ 22, -21 ≤ k ≤ 21, -23 ≤ l ≤ 23
Reflections collected	40227
Independent reflections	10886 [R(int) = 0.0248]
Completeness to theta = 30.60°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7974 and 0.7325
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	10886 / 69 / 421
Goodness-of-fit on F ²	1.034
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0280, wR2 = 0.0661
R indices (all data) ^{a,b}	R1 = 0.0314, wR2 = 0.0681
Absolute structure parameter	-0.009(13)
Largest diff. peak and hole	1.244 and -1.202 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 23-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for Complex (S,S)-**226**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	5000	7089(1)	10000	21(1)
Pd(2)	10000	4252(1)	5000	21(1)
C(1)	6927(2)	5800(2)	10989(1)	28(1)
C(2)	6953(2)	6209(2)	11758(2)	35(1)
C(3)	7714(2)	6063(2)	12577(2)	51(1)
C(4)	8437(2)	5535(3)	12633(2)	60(1)
C(5)	8411(2)	5123(2)	11880(2)	60(1)
C(6)	7651(2)	5250(2)	11048(2)	42(1)
C(7)	6349(2)	6105(2)	9088(1)	24(1)
C(8)	5818(2)	5822(2)	8213(1)	28(1)
C(9)	6166(2)	5901(2)	7584(2)	31(1)
C(10)	7023(2)	6279(2)	7808(2)	35(1)
C(11)	7545(2)	6588(2)	8671(2)	47(1)
C(12)	7212(2)	6495(2)	9311(2)	38(1)
C(13)	5231(1)	4943(1)	9683(1)	21(1)
C(14)	5778(1)	4086(1)	9765(1)	23(1)
C(15)	6374(10)	3127(7)	9014(9)	38(2)
C(16)	6311(10)	3077(10)	8087(7)	57(2)
C(15A)	6320(30)	3148(18)	8880(30)	34(5)
C(16A)	6540(30)	3290(30)	8102(19)	48(6)
C(17)	8918(2)	3298(2)	6153(1)	28(1)
C(18)	8108(2)	3698(2)	6077(2)	46(1)
C(19)	7984(3)	3897(3)	6839(2)	66(1)
C(20)	8671(3)	3699(3)	7664(2)	62(1)
C(21)	9475(3)	3312(2)	7748(2)	61(1)
C(22)	9622(2)	3114(2)	6996(2)	43(1)
C(23)	8030(1)	2994(1)	4219(1)	22(1)
C(24)	7381(2)	2371(2)	4224(2)	29(1)
C(25)	6578(2)	2211(2)	3449(2)	35(1)
C(26)	6416(2)	2681(2)	2673(2)	38(1)
C(27)	7048(2)	3303(2)	2667(2)	38(1)
C(28)	7859(2)	3468(2)	3436(1)	30(1)
C(29)	9774(1)	2093(1)	5319(1)	23(1)
C(30)	9179(2)	1256(2)	5181(2)	26(1)
C(31)	8502(2)	280(2)	5860(2)	42(1)

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C(32)	9108(2)	-531(2)	6082(2)	46(1)
C(33)	5000	2344(4)	5000	181(6)
C(34)	5000	264(4)	10000	143(5)
Cl(1)	6115(1)	8162(1)	10071(1)	31(1)
Cl(2)	9004(1)	5328(1)	5156(1)	36(1)
Cl(3)	5928(1)	2851(1)	5742(1)	109(1)
Cl(4)	5086(1)	866(1)	9167(1)	107(1)
O(1)	6117(1)	3635(1)	10432(1)	36(1)
O(2)	5820(1)	3915(1)	9000(1)	29(1)
O(3)	8892(1)	812(1)	4509(1)	34(1)
O(4)	9028(1)	1098(1)	5894(1)	30(1)
P(1)	5932(1)	5999(1)	9934(1)	21(1)
P(2)	9130(1)	3168(1)	5181(1)	21(1)

Table A 24-1 Crystal data and structure refinement for Complex ($\pm$)-**228**

Empirical formula	$C_{36}H_{60}Cl_2N_2Pd_2$
Formula weight	804.56
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	$a = 6.2898(3)$ Å $\alpha = 90^\circ$. $b = 17.6495(8)$ Å $\beta = 96.624(2)^\circ$. $c = 16.8637(8)$ Å $\gamma = 90^\circ$.
Volume	$1859.57(15)$ Å ³
Z	2
Density (calculated)	1.437 Mg/m ³
Absorption coefficient	1.136 mm ⁻¹
F(000)	832
Crystal size	0.20 x 0.15 x 0.15 mm ³
Theta range for data collection	1.68 to 30.58°.
Index ranges	$-8 \leq h \leq 9$, $-25 \leq k \leq 25$, $-24 \leq l \leq 24$
Reflections collected	49279
Independent reflections	5670 [R(int) = 0.0231]
Completeness to theta = 30.58°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8480 and 0.8046
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5670 / 0 / 199
Goodness-of-fit on F ²	1.236
Final R indices [I > 2sigma(I)] ^{a,b}	R1 = 0.0172, wR2 = 0.0505
R indices (all data) ^{a,b}	R1 = 0.0210, wR2 = 0.0620
Largest diff. peak and hole	0.584 and -0.839 e.Å ⁻³

^a $R1 = \sum ||F_o| - |F_c|| / \sum |F_o|$.

^b $wR2 = \sqrt{\{ \sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2] \}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 24-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for ($\pm$)-**228**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Pd(1)	4100(1)	5813(1)	4441(1)	16(1)
Cl(1)	3040(1)	4474(1)	4593(1)	26(1)
N(1)	1698(2)	6122(1)	3557(1)	18(1)
C(1)	4937(2)	6876(1)	4272(1)	16(1)
C(2)	6229(2)	7304(1)	4828(1)	18(1)
C(3)	6706(2)	8055(1)	4660(1)	18(1)
C(4)	5789(2)	8364(1)	3938(1)	20(1)
C(5)	4447(2)	7963(1)	3365(1)	17(1)
C(6)	4064(2)	7194(1)	3539(1)	16(1)
C(7)	8174(2)	8547(1)	5239(1)	23(1)
C(8)	9112(4)	8108(1)	5975(1)	43(1)
C(9)	6897(4)	9220(1)	5513(1)	40(1)
C(10)	10036(3)	8855(1)	4824(1)	39(1)
C(11)	3448(2)	8376(1)	2599(1)	21(1)
C(12)	997(3)	8424(1)	2581(1)	28(1)
C(13)	4045(3)	7993(1)	1841(1)	28(1)
C(14)	4262(3)	9197(1)	2565(1)	32(1)
C(15)	2794(2)	6625(1)	3004(1)	17(1)
C(16)	4273(3)	6153(1)	2539(1)	25(1)
C(19)	26(2)	6565(1)	3912(1)	26(1)
C(20)	605(3)	5472(1)	3125(1)	28(1)

Table A 25-1 Crystal data and structure refinement for Complex ($\pm$)-**238**

Empirical formula	$C_{36}H_{45}ClNPPd$
Formula weight	664.55
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	$a = 14.3640(4)$ Å $\alpha = 90^\circ$. $b = 17.7484(5)$ Å $\beta = 99.147(2)^\circ$. $c = 25.5539(8)$ Å $\gamma = 90^\circ$.
Volume	$6431.8(3)$ Å ³
Z	8
Density (calculated)	1.373 Mg/m ³
Absorption coefficient	0.735 mm ⁻¹
F(000)	2768
Crystal size	$0.30 \times 0.14 \times 0.12$ mm ³
Theta range for data collection	1.40 to 25.00° .
Index ranges	$-17 \leq h \leq 16$, $-21 \leq k \leq 21$, $-30 \leq l \leq 30$
Reflections collected	74885
Independent reflections	11311 [$R(\text{int}) = 0.0579$]
Completeness to $\theta = 25.00^\circ$	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9170 and 0.8096
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11311 / 0 / 739
Goodness-of-fit on F^2	1.124
Final R indices [$I > 2\sigma(I)$] ^{a,b}	$R1 = 0.0419$, $wR2 = 0.1134$
R indices (all data) ^{a,b}	$R1 = 0.0658$, $wR2 = 0.1418$
Largest diff. peak and hole	2.780 and -1.202 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 25-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for Complex ($\pm$)-**238**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Pd(1)	197(1)	6499(1)	7677(1)	15(1)
Pd(2)	2178(1)	8562(1)	4841(1)	17(1)
C(1)	730(3)	7351(2)	8144(2)	18(1)
C(2)	801(3)	8102(2)	7977(2)	17(1)
C(3)	1313(3)	8635(2)	8301(2)	20(1)
C(4)	1420(3)	9456(2)	8131(2)	28(1)
C(5)	863(4)	9625(3)	7586(2)	53(2)
C(6)	1125(4)	9988(2)	8543(2)	48(1)
C(7)	2463(4)	9600(3)	8094(2)	45(1)
C(8)	1766(3)	8397(2)	8800(2)	22(1)
C(9)	1728(3)	7663(2)	8988(1)	17(1)
C(10)	2311(3)	7470(2)	9538(2)	22(1)
C(11)	2705(3)	8177(3)	9837(2)	34(1)
C(12)	1707(3)	7074(2)	9904(2)	31(1)
C(13)	3159(3)	6977(3)	9465(2)	32(1)
C(14)	1198(3)	7137(2)	8648(1)	16(1)
C(15)	1060(3)	6309(2)	8774(1)	17(1)
C(16)	100(3)	6194(2)	8951(2)	25(1)
C(17)	2087(3)	5889(3)	8158(2)	29(1)
C(18)	818(3)	5080(2)	8318(2)	30(1)
C(19)	-1427(3)	7991(2)	7408(2)	19(1)
C(20)	-1869(3)	8571(2)	7096(2)	23(1)
C(21)	-2435(3)	9081(2)	7311(2)	27(1)
C(22)	-2575(3)	9009(2)	7833(2)	29(1)
C(23)	-2131(3)	8437(2)	8146(2)	28(1)
C(24)	-1550(3)	7935(2)	7937(2)	23(1)
C(25)	-412(3)	7521(2)	6539(2)	19(1)
C(26)	-324(3)	6981(2)	6151(2)	26(1)
C(27)	65(3)	7180(3)	5713(2)	33(1)
C(28)	385(3)	7899(3)	5655(2)	35(1)
C(29)	307(3)	8435(3)	6036(2)	35(1)
C(30)	-93(3)	8250(2)	6479(2)	25(1)
C(31)	-1948(3)	6694(2)	6852(2)	19(1)
C(32)	-2292(3)	6119(2)	7141(2)	22(1)
C(33)	-3180(3)	5824(2)	6968(2)	27(1)

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C(34)	-3712(3)	6081(2)	6510(2)	29(1)
C(35)	-3372(3)	6650(3)	6218(2)	29(1)
C(36)	-2488(3)	6956(2)	6391(2)	22(1)
C(37)	1678(3)	7666(2)	4391(1)	17(1)
C(38)	1687(3)	6925(2)	4571(2)	19(1)
C(39)	1259(3)	6353(2)	4250(2)	18(1)
C(40)	1312(3)	5519(2)	4426(2)	22(1)
C(41)	1735(3)	5438(2)	5010(2)	32(1)
C(42)	316(3)	5185(3)	4340(2)	34(1)
C(43)	1928(3)	5078(2)	4091(2)	33(1)
C(44)	782(3)	6547(2)	3749(2)	22(1)
C(45)	718(3)	7286(2)	3556(2)	20(1)
C(46)	100(3)	7436(2)	3008(2)	23(1)
C(47)	-252(3)	6701(3)	2724(2)	34(1)
C(48)	640(3)	7862(3)	2628(2)	33(1)
C(49)	-790(3)	7883(3)	3082(2)	37(1)
C(50)	1194(3)	7851(2)	3887(2)	19(1)
C(51)	1260(3)	8683(2)	3748(2)	21(1)
C(52)	2194(3)	8836(2)	3551(2)	31(1)
C(53)	236(3)	9070(2)	4374(2)	28(1)
C(54)	1401(3)	9934(2)	4170(2)	31(1)
C(55)	3846(3)	7117(2)	5109(2)	19(1)
C(56)	4307(3)	6546(2)	5423(2)	24(1)
C(57)	4844(3)	6017(2)	5202(2)	31(1)
C(58)	4958(3)	6077(2)	4675(2)	31(1)
C(59)	4513(3)	6647(2)	4365(2)	29(1)
C(60)	3949(3)	7160(2)	4578(2)	22(1)
C(61)	4344(3)	8424(2)	5662(2)	18(1)
C(62)	4872(3)	8223(2)	6140(2)	23(1)
C(63)	5733(3)	8550(2)	6306(2)	29(1)
C(64)	6086(3)	9078(2)	5992(2)	30(1)
C(65)	5575(3)	9277(2)	5511(2)	27(1)
C(66)	4695(3)	8958(2)	5344(2)	21(1)
C(67)	2834(3)	7581(2)	5987(2)	18(1)
C(68)	2748(3)	8126(2)	6377(2)	26(1)
C(69)	2355(3)	7933(3)	6815(2)	33(1)
C(70)	2042(3)	7214(3)	6878(2)	34(1)
C(71)	2110(3)	6684(3)	6499(2)	34(1)
C(72)	2518(3)	6860(2)	6055(2)	25(1)
CI(1)	-96(1)	5431(1)	7105(1)	33(1)
CI(2)	2475(1)	9674(1)	5382(1)	38(1)
N(1)	1101(2)	5880(2)	8263(1)	18(1)
N(2)	1199(2)	9122(2)	4248(1)	19(1)
P(1)	-860(1)	7189(1)	7127(1)	16(1)

Table A 26-1 Crystal data and structure refinement for Complex (S_C, S_C)-**239**.

Empirical formula	$C_{27}H_{40}N_2O_2Pd$
Formula weight	531.01
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 11.0034(5)$ Å $\alpha = 90^\circ$. $b = 16.0783(7)$ Å $\beta = 90^\circ$. $c = 31.4925(13)$ Å $\gamma = 90^\circ$.
Volume	$5571.5(4)$ Å ³
Z	8
Density (calculated)	1.266 Mg/m ³
Absorption coefficient	0.689 mm ⁻¹
F(000)	2224
Crystal size	$0.19 \times 0.19 \times 0.16$ mm ³
Theta range for data collection	1.96 to 26.00° .
Index ranges	$-13 \leq h \leq 13$, $-19 \leq k \leq 19$, $-38 \leq l \leq 38$
Reflections collected	62825
Independent reflections	10959 [R(int) = 0.0470]
Completeness to $\theta = 26.00^\circ$	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8977 and 0.8802
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10959 / 93 / 656
Goodness-of-fit on F^2	1.036
Final R indices [$I > 2\sigma(I)$] ^{a,b}	$R1 = 0.0304$, $wR2 = 0.0680$
R indices (all data) ^{a,b}	$R1 = 0.0380$, $wR2 = 0.0722$
Absolute structure parameter	-0.03(2)
Largest diff. peak and hole	0.784 and -0.486 e.Å ⁻³

$$^a R1 = \sum ||F_o| - |F_c|| / \sum |F_o|.$$

$$^b wR2 = \sqrt{\{\sum [w(F_o2 - F_c2)^2] / \sum [w(F_o2)^2]\}}, w^{-1} = \sigma^2(F_o2) + (aP)^2 + bP.$$

Table A 26-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (S_C, S_C)-**239**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	308(1)	2103(1)	3824(1)	29(1)
Pd(2)	2217(1)	-683(1)	186(1)	31(1)
N(1)	-1566(2)	2053(2)	3757(1)	34(1)
N(2)	2163(2)	2164(2)	3872(1)	30(1)
N(3)	4094(3)	-645(2)	190(1)	43(1)
N(4)	367(3)	-660(2)	185(1)	34(1)
O(1)	527(2)	3247(2)	4165(1)	52(1)
O(2)	1966(3)	4161(2)	4341(2)	105(2)
O(3)	1840(2)	-1380(2)	-382(1)	47(1)
O(4)	309(3)	-1641(2)	-829(1)	71(1)
C(1)	186(3)	1015(2)	3535(1)	28(1)
C(2)	1097(3)	417(2)	3543(1)	29(1)
C(3)	907(3)	-370(2)	3367(1)	32(1)
C(4)	-245(3)	-543(2)	3202(1)	34(1)
C(5)	-1202(3)	37(2)	3195(1)	30(1)
C(6)	-957(3)	834(2)	3355(1)	30(1)
C(7)	1916(3)	-1028(2)	3381(1)	43(1)
C(8)	3006(12)	-646(11)	3134(6)	87(5)
C(9)	1598(12)	-1803(7)	3139(5)	79(6)
C(10)	2330(15)	-1202(11)	3815(4)	104(7)
C(8A)	3157(16)	-645(18)	3369(11)	164(18)
C(9A)	1823(16)	-1684(11)	3037(6)	78(8)
C(10A)	1700(20)	-1503(16)	3809(5)	154(14)
C(11)	-2466(3)	-255(2)	3030(1)	42(1)
C(12)	-2452(4)	-1171(3)	2882(2)	63(1)
C(13)	-3386(4)	-222(3)	3399(2)	56(1)
C(14)	-2909(4)	263(3)	2657(1)	58(1)
C(15)	-1779(3)	1600(2)	3345(1)	34(1)
C(16)	-1425(3)	2140(3)	2964(1)	43(1)
C(17)	-2127(3)	1565(3)	4110(1)	41(1)
C(18)	-2131(4)	2887(2)	3759(1)	48(1)
C(19)	1624(4)	3527(3)	4154(2)	60(1)
C(20)	2518(3)	3057(2)	3877(1)	38(1)
C(21)	2490(3)	3420(2)	3428(1)	46(1)
C(22)	3465(3)	3082(2)	3148(1)	36(1)

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C(23)	4583(4)	3493(3)	3114(1)	45(1)
C(24)	5491(4)	3178(3)	2851(1)	50(1)
C(25)	5314(4)	2447(3)	2635(1)	56(1)
C(26)	4226(4)	2029(3)	2672(1)	55(1)
C(27)	3299(4)	2352(3)	2925(1)	43(1)
C(28)	2467(3)	-34(2)	709(1)	31(1)
C(29)	1614(3)	42(2)	1030(1)	34(1)
C(30)	1873(3)	494(2)	1399(1)	39(1)
C(31)	3005(4)	859(2)	1431(1)	46(1)
C(32)	3908(3)	805(2)	1113(1)	44(1)
C(33)	3622(3)	339(2)	749(1)	36(1)
C(34)	907(4)	559(3)	1755(1)	49(1)
C(35)	-270(6)	922(4)	1568(2)	98(2)
C(36)	587(5)	-318(3)	1913(2)	76(2)
C(37)	1321(6)	1073(5)	2125(2)	132(3)
C(38)	5126(4)	1263(3)	1199(1)	57(1)
C(39)	5298(10)	1940(6)	807(3)	81(3)
C(40)	6143(8)	694(7)	1196(4)	80(3)
C(41)	5117(11)	1800(9)	1585(3)	104(6)
C(39A)	4831(11)	2157(6)	1276(6)	88(6)
C(40A)	6264(9)	1105(9)	931(4)	67(4)
C(41A)	5677(9)	946(7)	1663(3)	52(3)
C(42)	4413(4)	200(3)	357(1)	46(1)
C(43)	4099(5)	858(3)	12(2)	74(2)
C(44)	4620(4)	-1281(3)	487(2)	60(1)
C(45)	4622(4)	-798(3)	-239(1)	60(1)
C(46)	731(3)	-1296(3)	-513(1)	47(1)
C(47)	-56(3)	-690(3)	-264(1)	42(1)
C(48)	88(4)	171(3)	-469(1)	53(1)
C(49)	-609(4)	856(3)	-245(1)	54(1)
C(50)	-1811(5)	1032(4)	-344(2)	75(2)
C(51)	-2459(5)	1653(4)	-134(2)	92(2)
C(52)	-1910(6)	2091(4)	183(2)	92(2)
C(53)	-708(6)	1930(3)	294(2)	88(2)
C(54)	-62(5)	1325(3)	80(2)	70(1)

Table A 27-1 Crystal data and structure refinement for complex (R_C, S_C)-239

Empirical formula	$C_{27.50}H_{41}ClN_2O_2Pd$
Formula weight	573.47
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	$a = 10.0675(3)$ Å $\alpha = 90^\circ$. $b = 28.1679(10)$ Å $\beta = 102.200(2)^\circ$. $c = 10.2842(4)$ Å $\gamma = 90^\circ$.
Volume	$2850.53(17)$ Å ³
Z	4
Density (calculated)	1.336 Mg/m ³
Absorption coefficient	0.770 mm ⁻¹
F(000)	1196
Crystal size	0.30 x 0.30 x 0.25 mm ³
Theta range for data collection	2.03 to 30.55° .
Index ranges	$-14 \leq h \leq 14$, $-40 \leq k \leq 40$, $-14 \leq l \leq 14$
Reflections collected	34174
Independent reflections	16866 [R(int) = 0.0424]
Completeness to $\theta = 30.55^\circ$	98.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8309 and 0.8020
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	16866 / 2 / 604
Goodness-of-fit on F^2	1.029
Final R indices [$I > 2\sigma(I)$] ^{a,b}	R1 = 0.0505, wR2 = 0.1160
R indices (all data) ^{a,b}	R1 = 0.0598, wR2 = 0.1226
Absolute structure parameter	-0.02(2)
Largest diff. peak and hole	1.670 and -1.639 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 27-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (R_C, S_C) -**239**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	6383(1)	440(1)	7474(1)	23(1)
Pd(2)	4880(1)	9312(1)	8941(1)	23(1)
C(1)	4921(4)	847(1)	6490(4)	20(1)
C(2)	3947(4)	1064(1)	7054(4)	21(1)
C(3)	2906(4)	1335(1)	6274(4)	20(1)
C(4)	1858(4)	1602(2)	6890(5)	28(1)
C(5)	1794(9)	1428(3)	8267(9)	78(1)
C(6)	2264(9)	2124(3)	7001(9)	78(1)
C(7)	443(9)	1564(3)	6017(8)	78(1)
C(8)	2886(4)	1364(1)	4916(4)	22(1)
C(9)	3829(4)	1142(1)	4280(4)	22(1)
C(10)	3616(5)	1178(2)	2751(4)	28(1)
C(11)	2394(6)	1495(2)	2157(5)	44(1)
C(12)	3300(7)	680(2)	2118(5)	44(1)
C(13)	4850(6)	1388(2)	2309(5)	44(1)
C(14)	4873(4)	883(1)	5099(4)	21(1)
C(15)	6075(4)	633(2)	4695(4)	29(1)
C(16)	7311(5)	961(2)	4917(6)	43(1)
C(17)	5246(6)	-150(2)	5137(5)	40(1)
C(18)	7677(6)	-29(2)	5502(5)	50(2)
C(19)	8654(4)	256(2)	9632(4)	29(1)
C(20)	7924(4)	694(2)	10074(4)	27(1)
C(21)	8617(5)	1151(2)	9749(5)	34(1)
C(22)	8014(5)	1594(2)	10251(5)	34(1)
C(23)	8309(6)	1717(2)	11601(6)	44(1)
C(24)	7742(7)	2114(3)	12042(7)	55(2)
C(25)	6856(8)	2400(2)	11177(8)	60(2)
C(26)	6528(8)	2281(2)	9839(7)	60(2)
C(27)	7099(7)	1883(2)	9383(6)	51(2)
C(28)	4035(4)	8828(1)	7619(4)	21(1)
C(29)	4686(4)	8577(2)	6784(4)	22(1)
C(30)	3958(4)	8261(2)	5825(4)	25(1)
C(31)	4700(5)	7977(2)	4925(6)	42(1)
C(32)	3852(8)	7607(3)	4114(10)	89(3)
C(33)	5819(8)	7673(3)	5856(7)	62(2)

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C(34)	5448(10)	8300(3)	4151(8)	77(2)
C(35)	2561(4)	8223(2)	5732(4)	25(1)
C(36)	1847(4)	8469(1)	6550(4)	20(1)
C(37)	293(4)	8420(2)	6297(4)	26(1)
C(38)	-389(6)	8887(2)	5746(7)	47(1)
C(39)	-201(5)	8255(2)	7546(6)	45(1)
C(40)	-266(5)	8032(2)	5241(6)	41(1)
C(41)	2619(4)	8769(1)	7536(4)	21(1)
C(42)	2104(5)	9039(2)	8597(5)	34(1)
C(43)	2358(6)	8763(3)	9891(5)	53(2)
C(44)	2674(7)	9769(3)	9947(8)	68(2)
C(45)	2427(7)	9799(2)	7526(8)	68(2)
C(46)	6834(5)	9658(2)	11196(4)	28(1)
C(47)	7517(4)	9222(2)	10689(4)	27(1)
C(48)	7272(5)	8781(2)	11504(4)	32(1)
C(49)	7874(5)	8338(2)	11027(5)	33(1)
C(50)	9284(6)	8250(2)	11382(5)	39(1)
C(51)	9827(6)	7852(2)	10860(7)	51(2)
C(52)	9004(8)	7550(2)	10025(6)	51(2)
C(53)	7656(8)	7634(2)	9650(6)	52(2)
C(54)	7088(6)	8026(2)	10155(5)	39(1)
C(55)	9394(6)	4815(2)	6750(6)	45(1)
CI(1)	8978(2)	5287(1)	5592(2)	60(1)
CI(2)	8144(2)	4368(1)	6487(2)	61(1)
N(1)	6358(4)	204(1)	5572(4)	31(1)
N(2)	6480(3)	687(1)	9385(3)	22(1)
N(3)	2883(4)	9499(2)	8739(5)	39(1)
N(4)	6921(3)	9147(1)	9247(3)	22(1)
O(1)	8055(3)	43(1)	8565(3)	29(1)
O(2)	9773(4)	151(2)	10310(4)	49(1)
O(3)	5731(3)	9803(1)	10460(3)	27(1)

Table A 28-1 Crystal data and structure refinement for Complex (S)-**228**.

Empirical formula	$C_{36}H_{60}Cl_2N_2Pd_2 \cdot 2\text{chloroform}$	
Formula weight	1043.30	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	$a = 11.7630(4)$ Å	$\alpha = 90^\circ$.
	$b = 14.9516(5)$ Å	$\beta = 90^\circ$.
	$c = 27.1508(9)$ Å	$\gamma = 90^\circ$.
Volume	$4775.2(3)$ Å ³	
Z	4	
Density (calculated)	1.451 Mg/m ³	
Absorption coefficient	1.228 mm^{-1}	
F(000)	2128	
Crystal size	0.20 x 0.08 x 0.06 mm ³	
Theta range for data collection	1.50 to 30.54° .	
Index ranges	$-16 \leq h \leq 15$, $-21 \leq k \leq 21$, $-38 \leq l \leq 38$	
Reflections collected	54645	
Independent reflections	14331 [R(int) = 0.0446]	
Completeness to $\theta = 30.54^\circ$	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9300 and 0.7913	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	14331 / 0 / 500	
Goodness-of-fit on F ²	1.014	
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0326, wR2 = 0.0618	
R indices (all data) ^{a,b}	R1 = 0.0480, wR2 = 0.0680	
Absolute structure parameter	-0.012(18)	
Largest diff. peak and hole	0.458 and -0.423 e.Å ⁻³	

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 28-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for (*S*)-**228**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	3254(1)	7992(1)	8410(1)	28(1)
Pd(2)	2452(1)	6959(1)	9501(1)	25(1)
N(1)	3992(3)	7643(2)	7742(1)	37(1)
N(2)	1232(2)	7179(1)	10037(1)	31(1)
Cl(1)	3838(1)	6661(1)	8894(1)	30(1)
Cl(2)	2428(1)	8480(1)	9146(1)	36(1)
C(1)	2760(2)	9029(2)	8008(1)	29(1)
C(2)	2415(3)	9844(2)	8207(1)	29(1)
C(3)	2114(3)	10555(2)	7903(1)	31(1)
C(4)	1714(3)	11448(2)	8113(1)	34(1)
C(5)	1604(8)	11397(5)	8683(2)	50(2)
C(6)	2599(8)	12134(5)	7980(4)	68(3)
C(7)	551(7)	11640(5)	7910(3)	53(2)
C(5A)	2633(9)	11856(4)	8453(3)	74(3)
C(6A)	1507(8)	12203(4)	7715(3)	55(3)
C(7A)	564(9)	11324(5)	8374(4)	76(4)
C(8)	2237(3)	10436(2)	7395(1)	33(1)
C(9)	2612(3)	9641(2)	7179(1)	31(1)
C(10)	2820(3)	9611(2)	6612(1)	40(1)
C(11)	2431(4)	10487(2)	6360(1)	60(1)
C(12)	4099(3)	9531(3)	6521(1)	51(1)
C(13)	2184(4)	8851(3)	6359(1)	58(1)
C(14)	2852(3)	8917(2)	7498(1)	29(1)
C(15)	3167(3)	7967(2)	7352(1)	36(1)
C(16)	2103(3)	7386(2)	7340(1)	53(1)
C(17)	5081(3)	8132(3)	7681(1)	47(1)
C(18)	4225(4)	6671(2)	7691(1)	59(1)
C(19)	2506(3)	5770(2)	9830(1)	26(1)
C(20)	3384(3)	5160(2)	9773(1)	28(1)
C(21)	3401(3)	4366(2)	10049(1)	31(1)
C(22)	4331(3)	3670(2)	9962(1)	41(1)
C(23)	4293(4)	2892(2)	10337(1)	62(1)
C(24)	4149(4)	3265(2)	9441(1)	56(1)
C(25)	5512(3)	4110(3)	9989(1)	52(1)
C(26)	2536(3)	4240(2)	10392(1)	32(1)

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C(27)	1632(3)	4840(2)	10467(1)	32(1)
C(28)	748(3)	4640(2)	10875(1)	40(1)
C(29)	1010(4)	3760(2)	11150(1)	53(1)
C(30)	767(4)	5379(2)	11272(1)	51(1)
C(31)	-458(3)	4547(3)	10663(2)	53(1)
C(32)	1608(3)	5604(2)	10160(1)	27(1)
C(33)	660(3)	6291(2)	10125(1)	32(1)
C(34)	-137(3)	6060(2)	9691(1)	43(1)
C(35)	1797(3)	7460(2)	10505(1)	37(1)
C(36)	391(3)	7883(2)	9900(1)	41(1)
C(37)	1827(4)	4934(2)	8594(1)	47(1)
C(38)	242(4)	3728(2)	6552(1)	49(1)
CI(3)	1128(1)	4089(1)	8929(1)	65(1)
CI(4)	2881(1)	4492(1)	8214(1)	73(1)
CI(5)	860(1)	5550(1)	8245(1)	91(1)
CI(6)	655(1)	4121(1)	7129(1)	87(1)
CI(7)	636(1)	2601(1)	6476(1)	85(1)
CI(8)	852(1)	4369(1)	6079(1)	62(1)

Table A 29-1 Crystal data and structure refinement for complex (R)-228.

Empirical formula	C ₃₈ H ₆₂ Cl ₈ N ₂ Pd ₂
Formula weight	1043.30
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 11.7373(4) Å α = 90°. b = 14.9208(5) Å β = 90°. c = 27.0882(8) Å γ = 90°.
Volume	4744.0(3) Å ³
Z	4
Density (calculated)	1.461 Mg/m ³
Absorption coefficient	1.236 mm ⁻¹
F(000)	2128
Crystal size	0.20 x 0.15 x 0.15 mm ³
Theta range for data collection	1.89 to 30.50°.
Index ranges	-16 ≤ h ≤ 16, -8 ≤ k ≤ 21, -38 ≤ l ≤ 37
Reflections collected	37950
Independent reflections	14438 [R(int) = 0.0403]
Completeness to theta = 30.50°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8363 and 0.7901
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	14438 / 89 / 500
Goodness-of-fit on F ²	1.044
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0392, wR2 = 0.0981
R indices (all data) ^{a,b}	R1 = 0.0500, wR2 = 0.1063
Absolute structure parameter	-0.02(3)
Largest diff. peak and hole	0.963 and -0.517 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 29-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for complex (*R*)-**228**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	2460(1)	1962(1)	498(1)	23(1)
Pd(2)	3259(1)	2996(1)	1590(1)	26(1)
N(1)	1225(3)	2180(2)	-37(1)	29(1)
N(2)	3977(4)	2646(2)	2260(1)	36(1)
C(1)	2517(3)	776(2)	173(1)	25(1)
C(2)	3391(3)	163(2)	227(1)	26(1)
C(3)	3420(3)	-630(2)	-49(1)	27(1)
C(4)	4329(4)	-1336(3)	38(2)	39(1)
C(5)	5506(4)	-893(4)	11(2)	50(1)
C(6)	4152(6)	-1727(3)	559(2)	54(1)
C(7)	4302(5)	-2097(4)	-338(2)	59(2)
C(8)	2523(4)	-758(2)	-390(1)	32(1)
C(9)	1638(4)	-165(2)	-463(1)	30(1)
C(10)	758(4)	-354(3)	-872(2)	39(1)
C(11)	-456(4)	-455(4)	-657(2)	52(1)
C(12)	1016(5)	-1241(3)	-1151(2)	53(1)
C(13)	790(6)	379(3)	-1267(2)	54(1)
C(14)	1616(3)	601(2)	-160(1)	26(1)
C(15)	665(3)	1292(3)	-122(2)	29(1)
C(16)	-133(4)	1066(3)	306(2)	40(1)
C(17)	412(4)	2885(3)	98(2)	38(1)
C(18)	1806(4)	2463(3)	-502(2)	34(1)
C(19)	2765(3)	4038(3)	1989(1)	27(1)
C(20)	2420(4)	4851(2)	1791(1)	28(1)
C(21)	2119(3)	5558(3)	2098(2)	31(1)
C(22)	1732(4)	6453(3)	1884(2)	33(1)
C(23)	2619(10)	6845(6)	1534(4)	76(4)
C(24)	583(8)	6342(6)	1623(5)	63(3)
C(25)	1530(9)	7193(5)	2287(3)	44(2)
C(23A)	1600(8)	6398(6)	1316(3)	40(2)
C(24A)	569(7)	6678(7)	2086(4)	52(3)
C(25A)	2590(11)	7158(6)	2011(4)	79(4)
C(26)	2225(3)	5433(3)	2608(2)	31(1)
C(27)	2597(4)	4641(3)	2822(1)	30(1)

Appendices

C(28)	2807(4)	4612(3)	3390(2)	40(1)
C(29)	2429(7)	5485(4)	3642(2)	63(2)
C(30)	2175(5)	3856(4)	3645(2)	53(1)
C(31)	4094(5)	4537(4)	3483(2)	50(1)
C(32)	2843(3)	3918(3)	2505(1)	27(1)
C(33)	3161(4)	2967(3)	2647(1)	34(1)
C(34)	2122(5)	2390(3)	2658(2)	51(1)
C(35)	4219(6)	1674(3)	2313(2)	53(1)
C(36)	5066(4)	3125(4)	2319(2)	42(1)
C(37)	9763(5)	3733(3)	1548(2)	49(1)
C(38)	1836(5)	-66(3)	1404(2)	46(1)
CI(1)	3847(1)	1664(1)	1105(1)	28(1)
CI(2)	2436(1)	3483(1)	853(1)	33(1)
CI(3)	9155(1)	4370(1)	1077(1)	60(1)
CI(4)	9374(2)	2601(1)	1475(1)	83(1)
CI(5)	9357(2)	4124(1)	2128(1)	83(1)
CI(6)	1141(1)	-908(1)	1074(1)	63(1)
CI(7)	2895(1)	-508(1)	1786(1)	70(1)
CI(8)	866(2)	549(1)	1757(1)	89(1)

Table A 30-1 Crystal data and structure refinement for complex (*R*)-**240**

Empirical formula	C ₃₀ H ₄₃ ClNPPd
Formula weight	590.47
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 9.3173(4) Å α = 90°. b = 11.2089(4) Å β = 90°. c = 28.0220(11) Å γ = 90°.
Volume	2926.5(2) Å ³
Z	4
Density (calculated)	1.340 Mg/m ³
Absorption coefficient	0.798 mm ⁻¹
F(000)	1232
Crystal size	0.25 x 0.24 x 0.22 mm ³
Theta range for data collection	1.45 to 30.59°.
Index ranges	-13 ≤ h ≤ 13, -7 ≤ k ≤ 16, -39 ≤ l ≤ 37
Reflections collected	28326
Independent reflections	8755 [R(int) = 0.0454]
Completeness to theta = 30.59°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8440 and 0.8254
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	8755 / 0 / 318
Goodness-of-fit on F ²	1.136
Final R indices [I > 2σ(I)] ^{a,b}	R1 = 0.0496, wR2 = 0.1177
R indices (all data) ^{a,b}	R1 = 0.0573, wR2 = 0.1283
Absolute structure parameter	0.02(4)
Largest diff. peak and hole	1.896 and -1.034 e.Å ⁻³

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

b $wR2 = \sqrt{\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o^2) + (aP)_2 + bP$.

Table A 30-2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement

parameters ($\text{\AA}^2 \times 10^3$) for (*R*)-**240**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

–	x	y	z	U(eq)
Pd(1)	6379(1)	1278(1)	8878(1)	26(1)
Cl(1)	6217(2)	-855(1)	8937(1)	46(1)
N(1)	5100(4)	1610(3)	9499(1)	26(1)
P(1)	7476(1)	1102(1)	8170(1)	27(1)
C(1)	6679(4)	3062(4)	8932(2)	28(1)
C(2)	7830(4)	3677(5)	8740(1)	28(1)
C(3)	8024(4)	4885(4)	8837(2)	26(1)
C(4)	9220(5)	5639(4)	8608(2)	30(1)
C(5)	10161(6)	4915(6)	8267(3)	52(2)
C(6)	8547(7)	6654(5)	8319(2)	48(1)
C(7)	10174(8)	6172(9)	8995(2)	76(2)
C(8)	7091(5)	5425(5)	9161(2)	30(1)
C(9)	5954(5)	4825(4)	9385(2)	26(1)
C(10)	5037(6)	5527(4)	9756(2)	34(1)
C(11)	5659(9)	6768(6)	9855(3)	68(2)
C(12)	3516(7)	5709(5)	9558(2)	50(1)
C(13)	4960(6)	4892(5)	10242(2)	38(1)
C(14)	5721(4)	3624(4)	9254(1)	23(1)
C(15)	4477(5)	2831(4)	9406(2)	27(1)
C(16)	3324(5)	2791(5)	9019(2)	33(1)
C(17)	6024(5)	1644(5)	9929(2)	38(1)
C(18)	3964(5)	713(5)	9589(2)	37(1)
C(19)	6771(5)	-76(4)	7800(2)	29(1)
C(20)	6238(5)	364(4)	7398(2)	31(1)
C(21)	5480(7)	-354(6)	7023(2)	47(1)
C(22)	5866(7)	2304(5)	6917(2)	44(1)
C(23)	6424(6)	1672(4)	7348(2)	29(1)
C(24)	7117(5)	2179(5)	7716(2)	31(1)
C(25)	9411(5)	858(4)	8191(2)	30(1)
C(26)	9935(6)	-94(5)	8455(2)	40(1)
C(27)	11389(7)	-317(5)	8473(2)	50(1)
C(28)	12348(6)	401(6)	8237(2)	47(1)
C(29)	11844(5)	1363(6)	7971(2)	42(1)
C(30)	10391(5)	1604(5)	7947(2)	35(1)