Design, syntheses and applications of chiral transition metal complexes bearing phosphorus-containing ligands

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**DESIGN, SYNTHESIS AND APPLICATIONS OF CHIRAL
TRANSITION METAL COMPLEXES BEARING PHOSPHORUS-
CONTAINING LIGANDS**

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Nomenclature

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

X-ray Structural Data

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

Abbreviations and Symbols

Ar	aryl group
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
BIPHEP	2,2'-Bis(diphenylphosphino)-1,1'-biphenyl
Bn	benzyl
Bp	boiling point
br	broad
calcd.	calculated
CDCl ₃	chloroform-d ₁
CHCl ₃	chloroform
conc.	concentrated
DCM	dichloromethane
dec.	decomposed
<i>de</i>	diastereomeric excess
DIOP	2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane
DIPAMP	1,2-bis((2-methoxyphenyl)phenylphosphino)ethane

dm	decimeter
d	doublet (NMR)
DMF	<i>N,N</i> -dimethylformamide
<i>ee</i>	enantiomeric excess
equiv.	equivalence
ESI-MS	electrospray ionization mass spectrometry
Et	ethyl
<i>et al.</i>	and others (Latin <i>et alii</i>)
g	gram(s)
h	hour(s)
Hz	hertz
<i>i.e.</i>	that is (Latin <i>id est</i>)
m	multiplet (NMR)
Me	methyl
min	minute(s)
mL	milliliter
mmol	millimole(s)
Mp	melting point
NMR	Nuclear Magnetic Resonance
Ph	phenyl
ppm	parts per million
Pr	propyl
<i>R</i>	rectus (Latin right absolute configuration)
rt	room temperature
<i>S</i>	sinister (Latin left absolute configuration)
s	singlet (NMR)

t	triplet (NMR)
T	temperature
THF	tetrahydrofuran
TMS	tetramethylsilane
TOF	turn over frequency
TON	turn over number
δ	NMR chemical shift in ppm
$^{\circ}$	degree of angles
Å	angstrom(s)
$^{\circ}\text{C}$	degree Celsius
$[\alpha]_{\text{D}}$	specific rotation measured at sodium D line (589 nm)

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Summary

This thesis is a compilation of research conducted over a period of four years, focusing mainly on the design, syntheses, purifications, characterizations and applications of optically active tertiary phosphine compounds and their transition metal complexes.

In Chapter 1, the different classification of chirality observed in phosphine compounds is reviewed, followed by a discussion on the classical and modern preparation techniques available for this class of important and valuable ligands. Subsequently, a brief overview of the recent developments in our research group is presented, covering the syntheses of chiral cyclometalated complexes, as well as their applications in asymmetric transformations such as Diels-Alder, hydroamination, hydroarsination and hydrophosphination reactions. The aims and objectives of the project are rationalized based on recent developments in these areas.

In Chapter 2, an asymmetric methodology involving a chiral PC-palladacycle-catalyzed hydrophosphination of specially designed substrates is used to prepare a series of optically pure diphosphine and aminophosphine compounds, thus eliminating the need for classical protection-deprotection and resolution protocols. The direct cyclometalation of the preligands affords the respective PCP- and PCN-pincer complexes, which is a class of industrially and synthetically important complexes. The electronic and steric effects of minor structural modifications to the pincer architecture are discussed. The determination of enantiomeric- and diastereomeric-excesses, the proposed catalytic cycle for the hydrophosphination reaction and the molecular structures of the pincer complexes are presented as well.

In Chapter 3, the formation of 8-membered “chair-like” $\text{Cu}_4\text{X}_4\text{L}_2$ (L = diphosphine ligand) and 12-membered “drum-like” $\text{Cu}_6\text{X}_6\text{L}_3$ copper clusters bearing chiral diphosphine ligands are explored. The X-ray crystallographic analyses of the

structures reveal unique features of their frameworks. The applicability of these chiral copper clusters in catalytic asymmetric hydroboration are examined.

In Chapter 4, the addition of diphenylphosphine to activated α,β - and $\alpha,\beta,\gamma,\delta$ -unsaturated substrates catalyzed by the chiral PC-palladacycle and PCP-Pd pincer complex is studied. An investigation is conducted to determine the origin of the stereo- and regio-selectivity control that is imparted by the two types of catalysts which operate *via* different mechanistic pathways. The catalysts result in the formation of different products (1,4- vs 1,6-addition) and the possible catalytic cycles involving either intra- or inter-molecular mechanisms are proposed.

In Chapter 5, the catalytic potentials of various chiral PCP- and PCN-transition metal pincer complexes are investigated in the asymmetric conjugate addition of diarylphosphines to $\alpha,\beta,\gamma,\delta$ -unsaturated substrates. The pincer complexes are screened to study the influence of the catalyst design in this reaction. An optimization of the reaction conditions affords the desired air-sensitive phosphines in quantitative yields with excellent enantioselectivities. An X-ray crystallographic analysis and a 2D ^1H - ^1H NOESY NMR study of the best performing pincer complex revealed the unique features contributing to the superior stereoselectivity of the P-C bond formation process.

Chapter 6 describes a variety of optically pure mono- and di-phosphine compounds that are prepared by catalytic hydrophosphination employing efficient catalysts developed previously. Subsequent functionalization of the phosphines affords potential unsymmetrical ECE' (E = neutral electron donors, E $\neq$ E') pincer ligand precursors which form novel C(sp^3)-hybridized pincer complexes. This deviates from the typical symmetrical aromatic C(sp^2)-hybridized counterparts.

Chapter 1 Introduction

1.1 Chirality

In 1848, Louis Pasteur discovered that a solution of ammonium sodium tartrate crystals could be separated microscopically into right- and left-hemihedral shaped crystals which rotated plane polarized light in the clockwise (dextrorotation, denoted *d*) and anticlockwise (levorotation, denoted *l*) direction respectively.^[1] This phenomenon was subsequently termed as “chirality” (from Greek word *kheir*, for hand) by Lord Kelvin (William Thomson) in 1884, defining “any geometric figure, or group of points, chiral, and say it has chirality, if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself”.^[2] Chirality would have remained much as a geometric concept for academic purposes if not for the astounding revelation that chiral molecules or compounds are present in various key aspects of life, in particular biochemistry.^[3] Many classes of molecules such as amino acids, carbohydrates, steroids, hormones, nucleic acids, enzymes, pheromones, *etc.* were found to be predominantly homochiral. For example, the occurrence rate of the amino acids with the absolute (*S*)-configuration in the proteome of all organisms in the Swiss-Prot database was experimentally determined to be ~99.9995%.^[4] Similarly, majority of the biological receptors, membranes and agents (such as pesticides, herbicides and drugs) possess chirality in order to effect suitable binding and biological responses. Indeed, extensive examples of chiral molecules having differing biological activities have conclusively established the biological significance of stereoisomers.^[5] In 1854, Louis Pasteur noted that the plant mold *Penicillium glaucum* metabolized (*R,R*)-tartaric acid but not the (*S,S*)-enantiomer, thus forming the principle of kinetic resolution. In another instance, the (*R*)-carbone stimulates the spearmint smell receptors but (*S*)-carbone triggers the caraway receptors. The anesthetic (*S*)-ropivacaine

Figure 1.1. Examples of chiral molecules and their enantiomers.

exhibits lower cardiotoxicity than its (*R*)-enantiomer.^[6] The highly controversial immunomodulatory drug thalidomide was reported to have caused thousands of birth defects when sold as a racemic mixture containing the teratogenic (*S*)-enantiomer.^[7] Since the enantiomers of a chiral molecule usually have entirely different effects on biological systems, it is extremely crucial to produce either of the enantiomers selectively. With the importance of chirality being recognized, it became a major concern in many areas such as the chemical and pharmaceutical industries.

1.1.1 Classification of Chirality

In principle, chirality may be classified into 4 main groups: 1) central, 2) axial, 3) planar and 4) helical chirality. Central chirality can be generally described as a stereogenic atom holding a set of ligands in a spatial arrangement which is not superposable on its mirror image. Axial chirality results from the non-planar arrangement of four groups in pairs about a chirality axis. Planar chirality refers to the arrangement of out-of-plane groups with respect to a chirality plane. Helicity is the chirality of a helical, propeller or screw-shaped molecular entity.^[8] Figure 2 shows some examples belonging to the different classification of chiral molecules and their respective stereodescriptors.

Figure 1.2. General classification of chirality in molecules.

Optically active molecules or compounds may often involve more than one type of chirality that functions in tandem to contribute to the overall success of asymmetric reactions. One notable example of such “privileged ligands” is the C_1 -symmetric ferrocene-based ligand Josiphos,^[9] which has been applied in asymmetric catalytic hydrogenation,^[9b,10] reduction (of activated alkenes),^[11] cross coupling,^[9b,12] Michael addition,^[13] nucleophilic ring opening,^[14] carbonylation,^[15] hydrophosphonation^[16] and amination^[17] reactions with spectacular results. Alongside a greater understanding of the impact on chirality, it is pertinent for this concept to be applied in many areas of chemistry.

1.2 Chiral Phosphines

Phosphines are undoubtedly one of the most important class of compounds in organophosphorus chemistry. Following the discovery of ^{31}P NMR spectroscopy in the 1950s and the historically first examples of monodentate chiral phosphines developed by Buthe^[18] and Sabacky^[19] simultaneously, the domain of phosphorus chemistry really began. This was further accelerated by the introduction of bidentate diphosphine ligands like DIOP in the 1970s.^[20] Since then, a plethora of phosphines with C-stereogenic centers (e.g. DIOP), P-stereogenic centers (e.g. DIPAMP), axial chirality (e.g. BIPHEP), planar chirality (e.g. PhanePhos) or a mixture of chiral elements (e.g. Josiphos), *etc.* were prepared and tested in various metal catalyzed reactions with remarkable success.^[10,21]

These marvellous results not only promoted phosphine compounds as a class of active and versatile ligands, but also fuelled the desire for even greater achievements in the field of phosphorus chemistry.

Figure 1.3. Structures and abbreviations for some examples of privileged chiral ligands.

After decades of intensive exploration, phosphines have firmly established themselves in pivotal and indispensable roles in many areas of science including pharmaceuticals, agrochemicals, transition metal catalysis and as organocatalysts.^[22] Especially in transition metal catalysis, phosphines have found applications in a non-exhaustive list of reactions such as hydrogenation of C=C and C=O bonds, hydrosilylation, allylation of aldehydes, allylic alkylation and substitution, alkoxy cyclization, hydrofunctionalization (hydroformylation, hydrovinylation, hydroarylation, hydrophosphonation, hydroboration, *etc.*), silaboration, amination, cross coupling (Suzuki, Heck, *etc.*), acylation, Baylis-Hillman, cycloaddition, cycloisomerization, cyclopropanation and many other reactions.^[22] The exceptional contribution of phosphines was recognized with the coveted Nobel Prize (Chemistry) being awarded to Knowles and Noyori in 2001 for their achievements in asymmetric hydrogenation with DIPAMP and BINAP. From the amalgamation of chiral phosphine ligands with transition metals, asymmetric catalysis is definitely one of the most powerful tool for the production of chiral compounds.^[22a-d] With increasing demand and pressure on the production of enantiopure pharmaceuticals, agrochemicals and other fine chemicals, the development of highly efficient and effective chiral phosphines is of paramount significance. Due to the astronomical amounts of literature available on

preparation of chiral phosphines, only selected or representative examples will be discussed in this chapter to illustrate the techniques or methods used for the synthesis of chiral phosphines and their derivatives. The term “phosphines” will be limited to compounds comprising of phosphorus atom(s) covalently bonded to carbon or hydrogen atoms only. All other phosphorus-heteroatom ligands (e.g. P-N, P-O, P-S) will be excluded from the discussion.

1.2.1 Preparation of Chiral Phosphines

In contrast to chiral amines which have low nitrogen inversion barriers of approximately 6-8 kcal/mol, phosphines have superior configuration stability at the stereogenic phosphorus center with pyramidal inversion barrier of 31-35 kcal/mol.^[23]

Figure 1.4. Inversion of a chiral amine.

Although the inversion of a P-stereogenic phosphine is immeasurably slow at room temperature, the inherent risk of racemization restricts the preparation of chiral phosphines at elevated temperatures. In addition, phosphines are generally sensitive to oxygen or oxidizing agents, which makes the handling of phosphines extremely cumbersome throughout the course of their syntheses. Consequently, chiral phosphines are often produced *via* their protected forms such as phosphine oxides, phosphine sulfides, phosphine boranes, phosphonium salts and phosphine metal complexes due to the ease of handling and storage of these configurationally stable phosphine derivatives. However, classical protection-deprotection methods involving such derivatives can adversely affect optical purity and yields.^[24] Furthermore, ordinary synthetic procedures usually afford the desired enantiomeric compounds as racemic mixtures of optical

isomers requiring laborious resolution techniques that are often detrimental to yield. For example, Noyori's BINAP was originally synthesized^[25] from BINOL **1a** via a multistep procedure involving high temperatures, a toxic mercury compound, a chiral Pd resolving agent (RA) and fractional recrystallization to produce both enantiopure (*R*)/(*S*)-BINAP with an overall yield of ~22%. The methodology would outrightly defy most, if not all, of the principles of green chemistry.

Scheme 1.1. First reported synthesis of enantiopure BINAP by diastereomeric complex formation.

Other separation and resolution techniques to obtain the optically active enantiomers from their racemates include crystallization (induced or otherwise), diastereomeric salt-, complex- or covalent compound-formation, kinetic resolution (with or without enzyme), distillation, supercritical fluid extraction, resolution with mixtures of RAs, substrate selective reaction, “half-equivalent”, enantioselective phase transfer and enantioselective chromatography.^[26] There have been numerous examples of such methods being employed in the preparation of chiral phosphines, but the preferred choice is through diastereomeric means, probably due to the weakly basic character of the phosphorus center, a wider availability of reagents and the simplicity of this method. The basic phosphorus atoms in the precursors have been exploited in the formation of

diastereomers with acidic RAs, optically active counteranions and chiral metal RAs, some of which are presented subsequently.

Figure 1.5. Examples of optically active A) RAs, B) silver RAs and C) metal RAs.

Figure 1.6. Examples of phosphine compounds resolved by diastereomeric means.

The resolution of phosphine precursors **8** and **9** was achieved by chiral CSA and MA respectively.^[27] Similarly, resolution can also rely on the presence of suitable

functional groups on the precursors, such as compound **10**, which involved formation of an ammonium salt with chiral BCSA (bromocamphorsulfonic acid).^[28] The formation of covalent diastereomers are commonly encountered in literature. Precursors **11** and **14** undergo chemical transformation reactions with enantiopure PEA to form amides,^[29] whereas compound **15** reacts with chiral camphanyl chloride to form an ester.^[30] Subsequent hydrolysis of the resolved compounds will afford the desired enantiomers. Phosphonium salts **12** and **13** were resolved by counterion exchange with optically active silver hydrogen dibenzoyltartrate and silver camphorsulfonate.^[31] This methodology facilitates the stereospecific conversion of the quaternary salts to the desired phosphines, or base-catalyzed hydrolysis and even Wittig reactions to afford the corresponding enantiopure phosphine oxides.^[32] In addition, the resolution of free phosphines can also be directly achieved with chiral metal RAs. The phosphines **16-19** were resolved with the metal complexes **2**, **6** and/or **7** with excellent enantio- or diastereo-meric purity.^[33] Subsequent decomplexation of the resolved metal-phosphine complexes gave the optically pure free phosphines.

Despite the commonly used technique of exploiting diastereomers for the purpose of resolution, advancement in modern technology has promoted the usage of other methods such as kinetic resolution and enantioselective chromatography.^[34] A notable example is the lipase-catalyzed kinetic resolution of ferrocenylethanol **20** to form Xyliphos **21**,^[35] an important analogue of Josiphos that is employed in the current largest scale application of asymmetric catalysis.

Scheme 1.2. Xyliphos synthesis through lipase-catalyzed kinetic resolution.

The kinetic resolution of P-stereogenic phosphine derivative **22** by means of the stereoselective 1,3-dipolar cycloadditions with chiral nitrones have also been reported, affording the unreacted (*R*)-**22** in up to 96% *ee*.^[36] Several other enzymatic systems have

Figure 1.7. Examples of phosphine precursors resolved by enzyme-catalyzed kinetic resolution.

also been reported for compounds **23** and **24** involving hydrolysis with pig liver esterase, cholesterol esterase or lipase from *Candida rugosa*.^[37] However it needs to be noted that in these examples; 1) the *ee* of the desired enantiomers fall within a range of 79-90%, the enzymes 2) selectively resolve only one of the enantiomers, 3) are highly sensitive to changes in the structures of the compounds, and 4) have narrow substrate scopes. In certain cases, minor structural changes between analogous compounds will render the enzymes ineffective due to high substrate specificities.^[38] The problematic recovery and strong pH dependency of some enzymes contribute to the list of drawbacks.^[39] Furthermore, the necessity for extensive screening of enzymes and condition optimizations make this method less attractive due to the laborious efforts required.

1.2.2 Chiral Auxiliaries for Preparation of Optically Active Phosphines

With the exponential increase in popularity and demand for chiral phosphines both scientifically and industrially, a simple and general protocol that permits easy access to optically pure phosphines is necessary. Over the last decade, the generation of phosphines involving chiral auxiliaries have seen significant progress.^[40] The commonly used auxiliaries include optically active secondary alcohols (e.g. (-)-menthol, *endo*-borneol),^[41] primary amines (e.g. (*S*)-PEA, esters of natural amino acids),^[42] amino acid derivatives

(e.g. SAMP, RAMP) and ephedrine.^[40a,43] Due to the enormous amount of examples available, only several representative protocols depicting the utilization of the chiral auxiliaries in the synthesis of enantiopure phosphines with: 1) P-stereogenic, 2) C-stereogenic centers, 3) axial and 4) planar chirality will be mentioned.

Scheme 1.3. Synthesis of a P-stereogenic phosphine with a chiral auxiliary.

At present, the reaction between chiral secondary alcohol and halophosphines^[40e-g,41a] is one of the most commonly used methods for the synthesis of menthyl phosphinite boranes such as intermediate (*S*)-**25**, which is a popular reagent due to the ease of preparation from PhPCl_2 . The Pd-catalyzed coupling of borane (*S*)-**25** with *o*-iodoanisole could either retain or invert the configuration at the phosphorus atom depending on the solvent used.^[40e,f,41c,d,44] Subsequent stepwise treatment of the intermediate with methyl lithium, *s*-BuLi, oxidative coupling with CuCl_2 , followed by deboration with diethylamine yielded (*R,R*)-DIPAMP.^[40e,f,41d]

Similarly, a synthetic protocol for the renowned C-stereogenic phosphine DIOP *via* optically pure (*R,R*)-tartaric acid has been reported.^[20,45] The five-steps synthetic method involving several organic transformation reactions such as nucleophilic substitution of the tosylate intermediate with sodium diphenylphosphide to produce the enantiopure DIOP.

Scheme 1.4. Synthesis of a C-stereogenic phosphine with a chiral auxiliary.

Such synthesis of C-stereogenic phosphines involving naturally occurring chiral compounds and their derivatives are common, even for phosphines bearing axial or planar chiralities. The optically pure MeO-NAPhePHOS is an atropisomeric phosphine with axial chirality that has been synthesized with a chiral auxiliary as depicted below.^[46] The aryl moieties are linked by a chiral tether to afford the biaryl **29**, which is subjected to a copper-catalyzed coupling to form compound **30**. Subsequent removal of the chiral auxiliary and introduction of the phosphine groups resulted in the formation of (*S*)-NAPhePHOS.

Scheme 1.5. Synthesis of an axial-stereogenic phosphine with a chiral auxiliary.

An optically active ferrocenyl-based Josiphos analogue (*R,S_p*)-**36** with planar chirality was prepared *via* a diastereoselective three-component reaction of ferrocene carbaldehyde **31**, TMS-ethyne and the chiral auxiliary (methoxymethyl)pyrrolidine (*S*)-**32**^[47] to give adduct (*S,R*)-**33** with excellent diastereoselectivity. After which, the

hydrolysis of the silyl group, hydrogenation of the $C\equiv C$ bond, substitution of the chiral auxiliary with Me_2NH gave amine (*R*)-**34** as a single enantiomer. The diastereoselective functionalization and substitution of amine (*R*)-**34** with R_2PCl and R'_2PH respectively followed by protection with borane formed intermediate (*R,S_p*)-**35**, which can be deprotected with an amine to give the Josiphos analogue (*R,S_p*)-**36**.

Scheme 1.6. Synthesis of Josiphos analogue with a chiral auxiliary.

In examining the synthesis of optically active phosphines with chiral auxiliaries, numerous successful examples have been reported in literature.^[48] However, several unfavorable points have been noted: 1) there is a high dependency on the chiral pool of auxiliaries, 2) stoichiometric amounts of chiral auxiliaries are needed, 3) the removal of the auxiliaries entail chemical transformations, which make their recycling impossible, 4) unwanted by-products may be produced from the process, 5) chiral auxiliaries do not necessary form one enantiomer exclusively in every scenario, 6) chiral auxiliaries are often expensive, and 7) often specific to the target compound (*i.e.* a slight change of substituents even in analogous compounds might render the auxiliaries ineffective in ensuring excellent stereoselectivities). In addition, from the viewpoint of Green Chemistry, the usage of chiral auxiliaries should be avoided as they contravene the main principles of sustainability. The analysis of the total life-cycle costs of chiral auxiliaries such as (-)-menthol has demonstrated that its production from natural sources and the

main synthetic routes consume large amounts of fossil fuel and results in the production of excessive carbon dioxide effluents.^[49] In response to these disadvantages, extensive research has been dedicated to the development of asymmetric catalytic methods to synthesize chiral phosphines.^[22i,50] By avoiding the use of chiral auxiliaries or RAs in their preparation, the productions and employabilities of chiral phosphines in synthetic scenarios will be greatly enhanced.

1.2.3 Catalytic Asymmetric Syntheses of Chiral Phosphines

Chiral phosphines are one of the most important group of ligands employed in homogeneous asymmetric catalytic reactions.^[22a-c,i] Most of these ligands are commonly prepared from the chiral pool of starting materials, such as amino acids, carbohydrates *etc.*, or in the presence of stoichiometric amounts of chiral auxiliaries. Surprisingly, methodologies involving asymmetric catalysis to prepare optically pure phosphines are sporadic possibly due to the stringent prerequisites relating to the chiral catalyst. The catalyst should be sufficiently active (high TON and TOF) and provide excellent enantioselectivities. P-chiral phosphines were the earliest class of chiral phosphines to be applied in asymmetric catalysis.^[18,51] The basis of the ligand design was to ensure that the stereogenic element(s) of the catalyst is situated close to the metal center so chiral information may be efficiently transmitted to the substrate or product in the course of the catalytic cycle. A multitude of P-chiral phosphines synthesized catalytically with homogeneous catalysts have been reported recently, such as the Pt[(*R,R*)-Me-DuPHOS](*trans*-stilbene) precursor (*R,R*)-**37**-catalyzed asymmetric hydrophosphination (AHP) of activated olefins^[52] (see Scheme 1.7) to produce P-chiral monophosphines in moderate to excellent selectivities (70-100%) with low enantiomeric excess ($ee \leq 22\%$). Even though the ee was poor, it demonstrated the applicability of asymmetric catalysis in the preparation of P-chiral phosphines.

Scheme 1.7. Pt-catalyzed AHP of activated olefins.

Subsequently, Glueck reported the Pd-catalyzed synthesis of PAMP-BH₃ (PAMP = phenylanisylmethylphosphine [PPhMe(*o*-An)]), an industrial importance phosphine (Scheme 1.8).^[53] Although the catalytic activity (TOF ca. 5 day⁻¹) and *ee* ($\leq 10\%$) were unappreciable, the amount of information gathered on the reaction mechanism paved the

Scheme 1.8. Pd-catalyzed asymmetric synthesis of PAMP-BH₃.

future direction for the catalytic synthesis of P-chiral phosphines. Since then, much progress have been achieved by the groups of Glueck^[54] and Helmchen.^[55] The former reported the Pd[(R,R)-Me-DuPHOS](Ph)(I)-catalyzed asymmetric cross-coupling reactions of racemic PHMeIs [Is = 2,4,6-(*i*-Pr)C₆H₂] with phenyl triflates or halides in the presence of NaOSiMe₃ to afford P-chiral phosphines with *ee* of up to 78%. The latter successfully applied the chiral bisphosphetane Et₂Et-FerroTANE as a ligand in the Pd-catalyzed P-C cross coupling reactions between racemic secondary phosphines and *ortho*-substituted aryl iodides to produce the respective phosphines with *ee* of up to 90%.

Contrary to the axiom that the stereogenic element(s) should be in close proximity to the metal center to achieve efficient relay of chiral information to the substrate or product during the catalytic cycle, Kagan in 1971,^[56] has demonstrated that DIOP, a C₂-symmetric diphosphine bearing C-stereogenic centers, is highly efficient as a chiral ligand

in several catalytic scenarios.^[10,20,21] Following which, the emergence of chiral phosphines with axial or planar chirality such as the BINAP^[25,57] or Josiphos^[9,10] ligand families have generated further interest in phosphines with C-stereogenic centers, axial or planar chiralities. Their widespread application in homogeneous catalysis^[10,21,22] have overshadowed the P-chiral counterparts mainly due to the ease of preparation as compared to the P-stereogenic phosphines. Several examples of phosphines bearing 1) C-stereogenic, 2) axial or 3) planar chiralities produced *via* asymmetric catalysis with excellent stereoselectivities are illustrated in Table 1.1 below.

Table 1.1. Chiral phosphines synthesized *via* asymmetric catalysis.

Type of Chirality	Examples	Structures	References
C-stereogenic	PROPHOS 42		[58]
	CHIRAPHOS 45		[59]
	DuPHOS 52		[60]
Axial	Phosphane 55		[61]
	Phosphane 59		[62]
	Phosphane 62		[63]
Planar	PHANEPHOS 64		[64]

Scheme 1.9. Asymmetric synthesis of (*R*)-PROPHOS **42**.

The C-chiral PROPHOS **42** was prepared by Bosnich and Fryzuk^[58] in the first “self-breeding” catalytic system involving ethyl 2-acetoxyacrylate **39**. The asymmetric hydrogenation of acrylate **39** by an (*R*)-PROPHOS modified Rh-catalyst gave the chiral compound **40** in 81% *ee*. Subsequent reduction with lithium aluminium hydride afforded the diol **41** in 80% *ee*. Conversion of the diol to ditosylate followed by a single recrystallization (from DCM/cyclohexane) improved the *ee* of the chiral ditosylate from 80% to 99%. Finally, nucleophilic substitution of the tosyl groups with LiPPh₂ gave the enantiomerically pure (*R*)-PROPHOS **42**. This synthetic methodology highlights the basis of “chirality breeding”, which in principle, means that infinite amounts of chiral PROPHOS can be generated with very small amounts of chiral PROPHOS.

Similarly, the preparation of C₂-symmetric CHIRAPHOS **45**^[59a] is dependent on optically pure enantiomers of 2,3-butanediol **44**, which are commonly synthesized catalytically *via* asymmetric hydrogenation of diacetyl **43**.^[59b-d] Besides hydrogenation, chiral diol **44** is also accessible by hydrosilylation,^[59e] or other specially designed substrate such as buta-1,3-diene-2,3-diylbis(diphenylphosphine oxide) **46**.^[59f] Table 1.2 provides examples of chiral diol **44** produced from asymmetric transformations of diacetyl **43**. After a single recrystallization, the optically pure diol **44** can be converted to enantiopure CHIRAPHOS **45** by sequential treatment with *p*-toluenesulfonyl chloride (TsCl) and LiPPh₂.

Scheme 1.10. Asymmetric synthesis of (*R,R*)-CHIRAPHOS **45**.

Table 1.2. Examples of asymmetric catalysis in the synthesis of diol **44**.

Entry	Chiral cat.	Reagents & Conditions	Yield (%)	<i>ee</i> (%)	<i>de</i> (%)	[ref]
1	RuBr ₂ [(<i>S</i>)-BINAP]	80 atm H ₂ , EtOH, 61 h, 30°C	100	100	48	59b
2	[NH ₂ Et ₂][{RuCl(<i>S</i>)-BINAP} ₂ (μ-Cl) ₃]	67 atm H ₂ , MeOH, 40 min, 60°C	86	>99.5	46	59c
3	BSDR ^[a]	Cat. NADH ^[b] , RT, 72 h, TEA-HCl buffer, cosubstrate	40	>98	>99	59d
4	{[(<i>R_c</i> , <i>R_c</i> , <i>S_p</i> , <i>S_p</i>)-EtTRAP]Rh(cod)}BF ₄ ^[c]	PhSiH ₂ , DME, 30 h, 0°C	69	95	80	59e

[a] BSDR = *Bacillus stearothermophilus* diacetyl reductase. [b] NADH = reduced nicotinamide adenine dinucleotide. [c] (*R_c*,*R_c*,*S_p*,*S_p*)-EtTRAP = (*S_p*,*S_p*)-2,2'-bis[(*R_c*)-1-(diethylphosphino)ethyl]-1,1'-biferrocene.

Scheme 1.11. Catalytic hydrogenation of buta-1,3-diene-2,3-diylbis(diphenylphosphine oxide) **46**.

The (*S*)-BINAP-Ru complex-catalyzed hydrogenation of phosphine oxide **46** produced the product (*S,S*)-**47** in 100% yield, 71% *ee* and 70% *de*. However, this strategy requires harsh conditions (100 atm H₂, 100°C), high catalyst loading (10 mol%) and has slow reactivity (310 h), which clearly exhibits its imperfections when employed in the synthesis of optically pure CHIRAPHOS **45** (Scheme 1.11).

Another example of a C-chiral phosphine synthesized catalytically is DuPHOS **52** (Scheme 1.12). The (*R*)-BINAP-Ru-catalyzed hydrogenation of β-keto ester **48**, followed by hydrolysis with KOH, formed acid (*R*)-**49**,^[59b] which is transformed into diol **50** by electrochemical Kolbe coupling.^[60a] Subsequently, the Ru-catalyzed formation of sulfate

51, and nucleophilic P-C bond formation with 1,2-diphosphenobenzene, gave the optically pure DuPHOS **52**.^[60b]

Scheme 1.12. Asymmetric synthesis of DuPHOS **52**.

In addition to C-stereogenic phosphines, axial- and planar-chiral building blocks have also been prepared by asymmetric catalysis, in which further P-C bond formation will yield the chiral phosphines. The enantioselective (*S*)-PhePhos-Pd complex-catalyzed cross coupling of triflate **53** with PhMgBr afforded compound **54** in high optical purity (Scheme 1.13). Another catalytic P-C cross coupling, followed by reduction, gave phosphine (*S*)-**55**.^[61] Similarly, the axial-chiral phosphine **59** was prepared sequentially by (*S*)-**57**-catalyzed Suzuki coupling, recrystallization of the intermediate biaryl **58** (to improve the optical purity), nucleophilic substitution of ethoxy groups with phenyl moieties and lastly, the reduction of the phosphine oxide will give the enantiopure (*R*)-**59** (Scheme 1.14).^[62]

Scheme 1.13. Asymmetric synthesis of axial-chiral phosphine **55**.

Scheme 1.14. Asymmetric synthesis of axial-chiral phosphine **59**.

Recently, a more spectacular strategy of accessing axial-chiral phosphines such as biaryl **62** involving enantioselective [2+2+2] cycloaddition catalyzed by chiral Rh^[63a] (Scheme 1.15) or Co^[63b] catalysts was reported. The Rh-catalyzed cycloaddition between 1,6-diynes and monoalkynes proceeded under mild conditions (RT, DCM, 1 h) to afford the corresponding chiral phosphines in quantitative yields with excellent enantioselectivities (91-98%). Likewise, the Co-catalyzed reaction between alkynes was conducted under mild conditions (visible light, 350-500 nm, 25-55°C, 12-48 h) to form the respective axial-chiral phosphines albeit with modest yields (24-80%) and enantioselectivities (56-83%). In some cases, a single recrystallization could improve the optical purities to >99%.

Scheme 1.15. Asymmetric synthesis of axial-chiral phosphine **62**.

A representative example of planar-chiral phosphines prepared in a catalytic manner is PHANEPHOS **64** (Scheme 1.16). The (S)-PHANEPHOS-Pd-catalyzed amination/kinetic resolution of dibromocyclophane **63** gave a mixture of amines and unreacted substrate (R)-**63** in 93% *ee*.^[64a] After a series of chemical transformations, dibromo (R)-**63** was successfully converted to the enantiopure (R)-PHANEPHOS **64**.^[64b]

Scheme 1.16. Kinetic resolution of dibromocyclophane **63** by catalytic amination.

The catalytic methodologies employed in the synthesis of P-, axial- and planar-chiral phosphines might seem to be less developed than their C-chiral counterparts. Nevertheless, efforts in the development of more effective and novel catalytic routes towards their formation are undoubtedly increasing, so one can expect to see interesting and new applications of chiral phosphorus ligands in the future. As the demand for chiral phosphines in areas such as pharmaceuticals and fine chemicals continues to increase, catalytic approaches for the preparation of chiral phosphines are highly valued due to the expected safety, economical and environmental benefits. The stereoselective energy- and atom-efficient catalytic processes reduce the amount of generated waste, hazards to human and environmental health, and cost of the reagents used. Ultimately, such “greener” synthetic methods will lead to an increase in the industrial importance of homogeneous catalysis, resulting in “greener” chemical production.

1.3 Recent Developments in Our Research Group

1.3.1 Chiral Cyclometalated Complexes

Chiral cyclometalated complexes, in particular the amine analogues, have contributed significantly to numerous aspects of synthetic chemistry. These organometallic complexes have established themselves as reliable references for the NMR spectroscopic assignment of compounds with unknown absolute configurations,^[65] resolving agents (RAs) in the preparation of chiral ligands,^[25,65a,66] chiral derivatizing

agents (CDAs) for determination of ee ^[67] and stoichiometric reaction promoters or chiral catalysts for asymmetric transformations.^[68] Of particular interest are the chiral cyclopalladated amine dimers **65** and **66**, the syntheses of which were reported by Otsuka and Wild respectively.

Figure 1.8. Cyclometalated amine complexes.

It was noted that the chiral palladacycle **66** is configurationally superior over the analogous benzylamine **65**,^[65c,70] as exemplified in several applications.^[70,71] The five-membered organometallic ring in complex (S)-**66** is both kinetically and thermodynamically stable. As a result of the intramolecular steric interaction between the methyl group at the stereogenic carbon with the proximal proton H(8), the methyl group invariably adopts the axial position and the prochiral NMe groups are fixed into the axial and equatorial positions (see Figure 1.9). Consequently, the cyclopalladated ring in complex (S)-**66** is locked into the non-interconvertible λ conformation in both solution and solid state.^[65b,66b] Hence the NMe groups and proton H(2) function as stereochemical directors of the organometallic ring in complex (S)-**66**. Electronically, the σ -donating nitrogen and the π -accepting naphthalene carbon of the five-membered organometallic

Figure 1.9. Structural representation of palladacycle (S)-**66**.

ring control the regioselectivity of the incoming substrates. On the contrary, the puckered ring of the analogous (*S*)-**65** is found to adopt both the δ and λ conformations in the solid state as well as in solution, indicating the absence of ring conformation lock.^[65b,66e,71,72]

Figure 1.10. Chiral cyclometalated complexes (only the (*S*)-enantiomers are shown).

In the past decade, the development and applications of chiral cyclometalated complexes in asymmetric synthesis and catalysis have been actively conducted in our research laboratory.^[70,91] To date, a wide range of chiral cyclometalated compounds have been prepared successfully by our group, comprising amine, phosphine and arsine substituents (see Figure 1.10). Although some of the complexes are structurally similar to one another, for example the benzylamine complexes **65**, **76**, **77**, **78**, **82** and **83**, it was found that minor alterations to the substituents have direct effects on the enantioselectivities obtained in certain intermolecular Diels-Alder reactions.^[82] In addition, changing the metal ion of a specific ligand (e.g. complexes **66** and **79**) have

exhibited differences in reactivities and stereoselectivities.^[92] As such, by systematically tuning and modifying the steric and electronic properties of the complexes, they will be applicable across a broad spectrum of asymmetric transformation reactions.

1.3.2 Asymmetric Diels-Alder Reaction

The Diels-Alder reaction is a concerted [4+2] cycloaddition occurring between a dienophile and a conjugated diene, to form a six-membered ring. We have investigated the application of chiral cyclometalated complexes **66**, **79** and their derivatives in this cycloaddition reaction. One of our main approaches in asymmetric Diels-Alder reaction involves the activation of a five-membered heterocycle (usually 3,4-dimethyl-1-phenylphosphole, DMPP^[93]), which only becomes reactive upon coordination to a transition metal ion.^[94] This provides a unique opportunity to control the stereochemistry of the reaction with the incorporation of an appropriate chiral auxiliary on the metal ion. In most of our asymmetric syntheses, the chiral palladacycle **66** or its monomeric derivatives were employed as the metal promoters. Depending on the species employed, the cycloaddition may proceed *via* an *exo* or *endo* pathway. Coordination of DMPP to the dimeric complex **66** formed the coordinated complex **87** (Scheme 1.17), which contains a Pd-Cl bond that is known to be inert towards ligand substitution even in the presence of strong coordinating ligands.^[95] This hinders the simultaneous coordination of DMPP and the dienophile to the metal center, thus the Diels-Alder reaction proceeds *via* an intermolecular *endo* pathway, affording adducts **91a** and **91b** upon liberation from the metal complexes. If complex **87** was subjected to chloride abstraction with a silver salt, subsequent addition of the dienophile would allow the reaction to undergo an intramolecular *exo* pathway *via* a cyclic transition state, ultimately yielding the products **92a** and **92b**. It is noted that through this elegant synthetic method, each of the adducts **91** and **92** comprises of four stereogenic centers.

Scheme 1.17. Schematic representation of *exo* and *endo* pathways.

The broad array of chiral phosphine and arsine mono-/bi-dentate ligands which were prepared in an efficient manner mainly by the chiral palladacycle **66** and its monomeric derivative are summarized in Figure 1.11. The unique stereochemical and electronic properties of the chiral metal templates (*vide supra*) have contributed significantly to the positive outcome of the asymmetric Diels-Alder reaction. This success motivated us to employ the chiral cyclometalated complexes (see Figure 1.12) in other asymmetric transformation reactions.

Figure 1.11. Products obtained from asymmetric Diels-Alder reaction.

1.3.3 Asymmetric Hydrofunctionalization (AHF) Reactions

Hydrofunctionalization of unsaturated organic compounds *via* direct addition of H-X to multiple bonds is an atom-economical process which does not produce waste. As the demand for complex molecular structures continues to increase, more emphasis is being placed on the development of novel synthetic methods that are “cleaner”. In carbon-heteroatom bond formation reactions, hydrofunctionalization processes are perhaps the solutions to green and sustainable chemistry. Asymmetric hydrofunctionalization (AHF) reactions are commonly employed in the preparation of biologically active pharmaceutical compounds and fine chemicals.^[99] Our contributions

towards the development of AHF involved the application of chiral metal complexes as either reaction promoters or catalysts.

1.3.4 Asymmetric Hydroamination (AHA) Reaction

The first example of a chiral palladium template-activated asymmetric hydroamination (AHA) reaction was performed with aniline and phenylbis(phenylethynyl)phosphine in the presence of dimer (*S*)-**66** (Scheme 1.18).^[100] The regioselective coordination of the phosphine at the position *trans* to the σ -donating nitrogen in complex (*S*)-**93** is attributed to the distinct electronic directing effects of the organometallic chelate ring. Subsequently, addition of aniline to the complex allowed the AHA reaction to proceed in an intramolecular manner, forming complex **94a** as the major isomer. On standing, complex **94a** undergoes imine-enamine tautomerization to form enamino **94b** quantitatively, which is the first reported instance of a dynamic imine-enamine tautomerism occurring within a bidentate metal chelate. The attempted liberation of the enantiopure phosphines from imino **94a** and enamino **94b** with aq. KCN only afforded the thermodynamically stable iminophosphine (*S*)-**95a**. Tautomerization of imino **95a** to enamino **95b** was not observed, which further indicates that the isomerization of complex **94a** to **94b** was triggered by the metal complexation. Regrettably, further investigations on synthetic applications of this novel chiral metal template-activated AHA reaction was to no avail.

Scheme 1.18. Chiral metal template activated AHA reaction.

1.3.5 Asymmetric Hydroarsination (AHS) Reaction

The performance of organoarsenic compounds have been found to be more superior than their phosphine counterparts in certain reactions such as Stille,^[101] Heck^[102] and Suzuki-Miyaura coupling reactions,^[103] hydroformylation,^[104] carbonylation^[105] and Wittig-type olefination of aldehydes.^[106] Presently, chiral amines are routinely synthesized *via* AHA reactions,^[99] but examples of chiral arsines prepared from AHS reactions are sporadic.^[107] As such, our group attempted the asymmetric synthesis of potentially powerful and stereospecific arsines involving As-H bond activation by chiral metal templates (see Scheme 1.19).

Scheme 1.19. AHS reactions conducted by our group.

The palladacycle *(S)/(R)*-**66** and the monomeric *(R)*-**99** were employed as metal promoters and stereochemical controllers in several AHS reactions.^[108] In each of the cases, the respective complexes *(S,R)*-**96**,^[108a] *(R,R)*-**100a**, *(R,S)*-**100b**^[108b] and *(R,R)*-**102**^[108c] were isolated as the major complexes. Liberation of the enantiopure As-P or As-N bidentate ligands was accomplished with aq. KCN. Investigations on the application and catalytic properties of transition metal complexes bearing these ligands are currently in progress.

1.3.6 Asymmetric Hydrophosphination (AHP) Reaction

In the field of organophosphorus chemistry, synthesis of new phosphine compounds *via* addition of P-H bonds to unsaturated substrates (*i.e.* asymmetric hydrophosphination) has immense significance towards achieving “greener” synthetic protocols. The direct synthesis of chiral phosphines has accorded considerable challenges

such as the instability of phosphines in air and lack of a natural chiral pool. AHP is therefore a potential solution towards most of the challenges faced by scientists working in the field of organophosphorus chemistry.

In the last decade, our group has reported numerous metal template-promoted AHP reactions with overwhelming success.^[91,109] Some of the results are illustrated below.^[109a,d,g,l,o] In the examples provided, the chiral metal templates (*S*)/(*R*)-**66** or (*S*)-**99** served as promoters to activate the unsaturated substrates towards AHP. The resulting diphosphines or aminophosphine formed five-membered chelate rings with the metal centers and the major products were isolated either by silica gel column chromatography or fractional crystallization. Subsequently, the optically pure P-N and P-P bidentate

Scheme 1.20. Examples of AHP reactions that generated one C- (**A**), two C- (**B**, **C**) and C,P- (**D**,**E**) stereogenic phosphines. (Note: In **D**, (*R,R,S*)-**113** and its (*R,R,R*)-isomer was formed in 1:1 ratio.) For clarity, the chiral naphthylamine auxiliaries on the metal complexes are denoted by C—N with the absolute configuration in parentheses.

as early as 1959, limitations such as poor selectivities, low efficiencies and uncontrolled reactions restrict the practicality of these methods. As a result, these impediments paved the way for the development of new methods, in particular metal-catalyzed HP.^[50a,109d,111]

Within the last decade, research on metal-catalyzed AHP has progressed dramatically and is considered as one of the most important tools to construct chiral organophosphorus compounds in a “greener” manner. In this area, our group has contributed significantly towards its development.^[112] In 2010, the palladacycle (*R*)-**99** was found to catalyze the AHP of α,β -unsaturated ketones to produce the corresponding chiral *tertiary* phosphines in excellent yields albeit with moderate *ee*'s.^[112a] However, this work was pivotal in aiding the further development and understanding of transition metal-catalyzed AHP.

Scheme 1.21. Palladacycle-catalyzed AHP of α,β -unsaturated ketones.^[112a]

After extensive screening of the chiral metal templates prepared previously (Figure 1.10) in the AHP of compound **117**, it was discovered that the phosphapalladacycle (*R*)-**119** (phosphorus analogue of (*R*)-**99**) was much more efficient as a catalyst than complex **99** in terms of both reactivity and stereoselectivity. Under identical reaction conditions (Scheme 1.21) but in the presence of catalyst (*R*)-**119**, adduct

Scheme 1.22. Formation of phosphapalladacycle catalyst (*R*)-**119**.

(*S*)-**118** was formed quantitatively in 92-99% *ee* within 2-40 h.^[112b] Subsequently, the palladacycle (*S*)/(*R*)-**119**-catalyzed AHP protocol was extended to a broad range of activated substrates, and in all cases, successfully afforded the corresponding chiral phosphine adducts.^[85,112] A series of phosphines containing one C-,^[112a,b,d,e,f,h-j] one P-,^[112g] two C-^[85,112c] and C,P-^[112b] stereogenic centers generated during the AHP are listed below. Of particular interest to us is the chiral diposphine **120**, as it belongs to a class of privileged ligand scaffold employed in transition-metal pincer complexes.

Figure 1.13. Chiral phosphines prepared by catalytic AHP.

Scheme 1.23. Synthesis of optically pure PCP-transition metal pincer complexes.

The direct synthesis of optically pure PCP transition metal pincer complexes **121a** and **122a** from phosphine (*S,S*)/(*R,R*)-**120a** was reported with excellent yields of up to

90%.^[112c,113] Recognizing the potential application of catalytic AHP in producing a wide spectrum of chiral pincer ligand precursors with high optical purities, this area deserves further explorations to assess the feasibility of this method.

1.4 Aims and Objectives of the Project

Although several of the chiral metal templates (Figure 1.10) prepared by our group have proven to be effective promoters or activators in asymmetric reactions such as Diels-Alder,^[81,89,96-98] hydroamination,^[100] hydroarsination^[108] and hydrophosphination,^[109] a major drawback lies in the stoichiometric usage of these valuable chiral metal complexes. Regardless of the potential application of the chiral products, the associated costs of their preparation deter such synthetic methods from being reproduced in larger scales. In order to bypass these impediments, it is essential to divert more attention towards the development of the chiral metallacycles as catalysts in asymmetric transformations.

With the discovery of the catalytic properties of palladacycle (*S*)/(*R*)-**119** in AHP,^[85,112b-k] a series of structurally related phosphines **B** (such as compound **120a**) may be catalytically generated. Studies on their employment as chiral ligands in transition metal pincer complexes **C** will be conducted in the area of homogeneous catalysis.

Scheme 1.24. Outline of project.

Figure 1.14. Schematic representation of pincer architecture.

In addition, systematic structural examination of these chiral pincer complexes **C** is expected to provide critical and crucial information on the following: (1) the electronic effects originating from the *para*-substituent Z, (2) the chiral functionalities R, (3) the steric effects of R, (4) the relationship between the neutral electron donors E and E', (5) the coordination chemistry of selected donor atoms, and (6) the choices of suitable transition metal ions for the formation of pincer complexes.

Figure 1.15. General architecture of a PCN-pincer complex.

Concurrently, the library of pincer complexes synthesized *via* catalytic AHP/cyclometalation will be expanded beyond the PCP-type to encompass unsymmetrical PCN-variants **D**. Furthermore, cheaper transition metals such as copper will be introduced as the metal center in the attempted formation of copper pincer complexes. Following which, the catalytic properties of selected pincer complexes will be investigated in several catalytic reactions.

Chapter 2 Chiral Phosphine Ligands in Transition Metal Complexes

2.1 General Introduction to Pincer Complexes

“Pincer chemistry” was introduced in the 1970s with the pioneering work of Shaw,^[114a] van Koten and Noltes^[114b] on PCP- and NCN-pincer complexes respectively. The general structure of the complexes comprises of a classical EYE architecture in which Y is often a carbon atom, and E is a neutral electron donor such as N, P or S. The neutral species with their spacers are commonly referred to as the side or pendant arms.

Figure 2.16. Schematic representation of pincer architecture.

Figure 2.17. Examples of pincer complexes.

The pincer complexes are classified based on the three atoms (EYE) coordinated to the metal center. For example, complex **123a** with phosphino ligands will be classified as a PCP complex, **123b** an NCN complex and the unsymmetrical **123c** will be known as a PCN complex. Due to the vast numbers of pincer complexes available in literature, the discussion henceforth will be focused on the most frequently employed d⁸-metal (such as Pd or Pt) complexes that are based on central aryl rings with symmetrical side arms. The conformationally rigid central aromatic ligating moiety with 2,6-benzylic links to the lateral coordination center generally promotes a stable meridional coordination environment, consequently imparting remarkable degree of thermal and chemical stability

to the complex. The well-defined metal-ligand framework accomplished by the tridentate ligand coupled with other desirable qualities of an ideal catalyst (such as low catalyst loading, high activity, high selectivity, high TON, broad reaction scope, stability towards air and moisture *etc.*), has guaranteed an optimistic future for the advancements of “pincer chemistry”. Over the past 40 years, a plethora of pincer complexes has been synthesized and studied in multifarious catalytic applications,^[115] ranging from cross coupling reactions such as Heck,^[116] Suzuki-Miyaura,^[117] Sonogashira,^[118] Hiyama,^[118c] Stille,^[119] and Negishi^[120] couplings to dehydrogenation,^[121] allylation of aldehydes and imines,^[122] borylation,^[122f,g,123] transfer hydrogenation,^[124] aldol^[125] and Michael^[125b,126] reactions.

The synthesis of pincer complexes is occasionally considered as a limiting factor for their application in catalysis.^[115f,127] Although some synthetic precursors are commercially available, the development of pincer complexes as catalysts inevitably requires a set of complexes with various substituents on the pendant arms or the central aryl ring (*para*-substituent Z). This will allow a comprehensive examination and systematic structural fine tuning of the complexes for specific catalytic transformations.

Several synthetic techniques of pincer complexes include: (1) oxidative addition of M(0) to a C-X bond, (2) C-H activation, (3) transmetalation, and (4) the “ligand introduction route”. Oxidative addition of M(0) such as Pd₂(dba)₃ to the C-X (X = Br or I) bond of the ligand is probably the simplest way of preparing pincer complexes. In Scheme 2.25, both pincer complexes **124c**^[128a] and **125c**^[128b] could be prepared efficiently from their respective amino **124b** and phosphinito **125b**. This strategy could also be extended to the synthesis of chiral pincer complexes with bulky side arms such as **126** and **127** by the oxidative addition of Pd(0) to the C-I bonds of the respective precursors.^[129]

Scheme 2.25. Synthesis of pincer complexes by oxidative addition.^[128]

Figure 2.18. Chiral pincer complexes prepared by oxidative addition.^[129]

The second method involving C-H activation is also commonly employed in the synthesis of pincer complexes. In general, the efficiency of C-H activation can be improved using metal salts with weakly coordinating ligands, such as $\text{Pd}(\text{BF}_4)_2(\text{MeCN})_4$ and $\text{Pd}(\text{TFA})_2$.^[128b,130] However, in the example provided below, the synthesis of chiral bisimine pincer **130** was successful *via* oxidative addition of $\text{Pd}(0)$ to bromide **128** but not through direct palladation of imine **129**.^[131] Evidently, C-H activation is more dependent on factors such as the bulkiness and electronic character of the side arms as compared to oxidative addition. Nevertheless, numerous pincer complexes such as **131c** and **132b** have

Scheme 2.26. Synthesis of pincer complex **130**.

been formed by C-H activation. The PCP-complex **131c** was prepared from phosphinite **131b** and $\text{Pd}(\text{TFA})_2$. The chiral PCP-pincer **132b** was synthesized analogously starting from resorcinol derivative **132a** and chiral chlorophosphonite **133**.^[132] An alternative way

Scheme 2.27. Synthesis of pincer complex by C-H activation.^[130b]

Scheme 2.28. Synthesis of chiral pincer complex by C-H activation.

Scheme 2.29. Synthesis of pincer complex by transcyclometalation (TCM).

of forming pincer complexes by C-H functionalization is through transcyclometalation (TCM),^[115b,133] described as the substitution of one cyclometalated ligand by another one without the formation of significant and detectable amounts of purely inorganic compounds (dissociated metal salts). An excellent source of palladium for TCM is palladacycle **134**,^[134] which when reacted with phosphinite **133b**, formed the PCP-complex **133c** efficiently (Scheme 2.29). The TCM route is usually employed when the pincer complexes are not easily accessible by other methods.

The third method of pincer complex synthesis is transmetalation, defined simply as the transfer of ligands from one metal to another. This process is often used in the preparation of NCN-pincer complexes due to the nature of the N donor atoms. The initial coordination of a NC(H)N ligand to the metal center is less favored than the corresponding PC(H)P ligand due to a relatively weaker $M \leftarrow N$ bond, which reduces the tendency for cyclometalation to occur.^[115b,127b] Hence it is necessary to activate the precursor to promote the formation of the pincer complex. In Scheme 2.30, the lithiation of bromide **135a** forms the aryllithium **135b** that facilitates the transmetalation process with either Pd(II) or Pt(II) to afford the complex **135c**.^[135] In a separate report, the chiral complex **136c** was prepared with organomercury **136b** and Pd(OAc)₂.^[136] It should be noted that transmetalation is not only restricted to the use of lithium and mercury intermediates but may be extended to other intermediates such as gold or tin compounds.

Scheme 2.30. Synthesis of pincer complex by transmetalation.^[135]

Scheme 2.31. Synthesis of chiral pincer complex by transmetalation.^[136]

Although transmetalation is a powerful strategy for the preparation of pincer complexes, several complications may arise. For instance, lithiation of aryl PC(H)P ligands predominantly yield the benzyllithium complexes instead of the aryllithium species. Even with the use of aryl halide precursors, the aryllithium complexes are generally unstable and susceptible to isomerization. Also, by virtue of transmetalation behaving like a

substitution reaction, the use of tin and mercury intermediates results in the formation of hazardous by-products. Despite having numerous drawbacks, transmetalation remains an important synthetic method for certain pincer complexes such as the NCN-Ru variants.^[137]

The methods presented above (oxidative addition, C-H activation and transmetalation) can be classified as “metal introduction routes” because the syntheses of the pincer proligands are done first before the final cyclometalation steps are performed. They provide easy access to pincer complexes, but are occasionally sensitive to the steric bulk of the substituents on the pendant arms. In addition, when confronted with the synthesis of more elaborate pincer frameworks, it might be advantageous to consider an alternative protocol involving prior introduction of the metal center followed by post-derivatization to yield the desired pincer complex. Uozumi and co-workers coined the strategy “ligand introduction route”, and demonstrated that a wide variety of PCP- and NCN-complexes can be prepared by this novel approach.^[138] A representative example of this methodology is the preparation of complex **137c**. The preformation of the Pd-C bond, followed by condensation of the aldehyde moieties on complex **137b** with prolinol derivative **138** created the final NCN-ligand framework.^[138a,b] In another report by Frech, a palladium tris(piperidino)phosphine complex **139a** (generated from PdCl₂(cod) and tris(piperidino)phosphine) was reacted with resorcinol or 1,3-diaminobenzene to construct the pincer complex **139b** (Scheme 2.33).^[139]

Scheme 2.32. Synthesis of chiral pincer complex by ligand introduction route.

Scheme 2.33. Synthesis of pincer complex by ligand introduction route.

The synthetic methodologies described above have demonstrated that most pincer complexes can be prepared in a straightforward manner. This might be one of the reasons for the explosive advancement and exploitation of pincer complexes in catalytic scenarios. As the demand and pressure on the production of enantiopure agrochemicals, pharmaceuticals and other fine chemicals continues to rise, the development of asymmetric catalysis based on chiral pincer complexes has to progress competitively. This suggests that the chiral catalysts should be amenable to rational design for the possibility of fine tuning the catalytic properties of the metal complexes. In the context of “pincer chemistry”, this may be achieved by systematic modifications of the: (1) *para*-substituent Z (Figure 2.16), (2) steric bulk of the pendant arms, and (3) substituents on E. However, a search of literature^[115f,h,140] for chiral PCP- and NCN-pincer complexes revealed four main categories of chiral auxiliaries incorporated into the framework, namely (1) oxazoline-,^[125b,126a,131a,141] (2) BINOL-,^[129,132] (3) TADDOL-,^[129a]

Figure 2.19. Examples of chiral moieties commonly found on pincer complexes.

and (4) pyrrolidine-derivatives (Figure 2.19).^[142] In general, most of the enantiopure oxazoline and pyrrolidine functionalities are derived from amino acids. The synthesis of 2-oxazoline rings often proceeds *via* the cyclization of optically pure 2-amino alcohols typically obtained from the reduction of chiral amino acids. The literature is dominated by four main processes: (1) the modified Appel reaction (between phosphonium salt and amino alcohol), (2) the cyclization of amino alcohol with acid chloride or (3) aldehyde, and (4) the Witte Seeliger reaction.^[143]

Scheme 2.34. Schematic representation of oxazoline synthesis.

The C_2 -symmetrical BINOL-derivatives are frequently prepared from enantiopure BINOL by a variety of methods such as: (1) the dilithiation of protected [1,1'-binaphthalene]-2,2'-diol followed by nucleophilic substitution and deprotection,^[144]

Scheme 2.35. General synthesis of BINOL-derivatives.

(2) the Suzuki cross coupling of 3,3'-dibromo-2,2'-bis(methoxymethoxy)-1,1'-binaphthalene with arylboronic acids,^[144b] and (3) the modified Mannich reaction with [1,1'-binaphthalene]-2,2'-diol.^[145]

The third category of chiral TADDOL-derivatives are most commonly synthesized from naturally occurring (*R,R*)-tartaric acid. After conversion to the tartrate, treatment with the appropriate aldehyde or ketone under acidic conditions will yield the corresponding TADDOL precursors. Alternatively, the tartrate may be reacted with the dimethyl acetal or ketal equivalents of the aldehyde or ketone in an acid-catalyzed transacetalization. Nucleophilic addition by aryl Grignard reagents will afford the desired TADDOL-derivatives.^[146]

Scheme 2.36. General synthesis of TADDOL-derivatives.

The last category of chiral functionalized-pyrrolidines are often derived from the natural amino acid (*S*)-proline. The nucleophilic substitution of the -OH group with an alkoxide will yield the desired prolineate esters. Due to the straightforward synthesis of prolineate esters, they have been employed as the chiral frameworks of several NCN-pincer complexes and studied in asymmetric reactions.^[142]

Scheme 2.37. General synthesis of prolineate esters.

In addition to the four categories of chiral auxiliaries mentioned above, pincer complexes have been known to possess other types of chiralities such as: (1) P- or S-

chirogenic moieties,^[147] (2) stereogenic centers at the benzylic positions of the ligand backbone,^[125a,c,133f,148] and (3) stereogenic centers on the *para*-substituent Z.^[125d,149]

Figure 2.20. Examples of chiral PCP- and NCN-complexes.

However, it needs to be noted that the synthesis of chiral pincer complexes bearing all the above types of chirality (including oxazoline-, BINOL-, TADDOL- and pyrrolidine-based chiral auxiliaries) have several major drawbacks. Firstly, the chiral auxiliaries are heavily dependent on the chiral pool of starting materials such as amino acids, BINOL and tartaric acid, thus limiting flexibility in modifications of the pincer architectures. Secondly, the preparation of chiral PCP ligand precursors often involves tedious synthetic protocols, protection-deprotection procedures or resolution steps.^[125c,148a,150] The protection-deprotection approach has been known to adversely impact optical purity and yield, and results in the unwanted conversion of desired functional groups.^[24] Lastly, the synthesis of pincer complexes with stereogenic centers on the neutral electron donor E (e.g. -PPh(*t*-Bu)) or on the benzylic carbons tends to be more challenging and time consuming. For instance, the preparation of complex **141b** requires a multi-step synthesis starting from PhPCl_2 . Sequential lithiation, treatment with

Scheme 2.38. Synthesis of P-stereogenic pincer complex.^[147a]

lithium aluminium hydride and protection with borane yielded the racemic compound **141a**. Further lithiation in the presence of (-)-sparteine, followed by addition of 1,3-bis(bromomethyl)benzene, deprotection with diethylamine and cyclometalation afforded the optically pure PCP-complex **141b**.^[147a] The major disadvantage of this method lies in the sensitivity of the lithium phenyl-phosphide-sparteine intermediate (*n*-BuLi and (-)-sparteine added to (±)-**141a**) towards solvents and steric congestion around the P atom. When the same lithium phosphide species was prepared in THF instead of Et₂O, the reaction was rendered completely non-stereoselective. In addition, the substitution of the bulky *t*-butyl group on (±)-**141a** with a Me moiety also resulted in the formation of the racemic lithium phosphide-sparteine intermediate. Therefore, the synthetic strategy applied in the preparation of chiral complex **141b** is not extendable to analogues of (±)-**141a**, which is a significant impediment towards the fine-tuning of the pincer complex **141b**.

The installation of stereogenic centers on the benzylic carbon is often tedious and inefficient. An example is the multi-step synthesis of chiral PCP-complex **142e** (Scheme 2.39).^[150] The compound **142a** was sequentially treated with sodium diphenylphosphide, octasulfur, *n*-BuLi and iodomethane to form the racemic sulfide intermediate **142c**. Fractional recrystallization afforded enantiopure (*R,R*)-**142c** in 38% isolated yield. Deprotection of the phosphine sulfide followed by cyclometalation generated the desired complex **142e**. This synthetic method is not only laborious, but also results in wastage

Scheme 2.39. Synthesis of chiral PCP-pincer complex.^[150]

due to the formation of *meso*-**142c** and the inability to separate (*S,S*)-**142c** from the mixture efficiently.

All the aforementioned limitations and difficulties associated with the preparation of optically pure pincer complexes directly hampers the progress in their application as catalysts in asymmetric transformations. In order to circumvent the traditional protocols of generating chiral phosphines *via* borane, sulfide or oxide intermediates, or to avoid the cumbersome resolution steps, we have been involved in the development of an efficient catalytic methodology for the enantioselective formation of P-C bonds.^[112] This attractive strategy is arguably the most economical and practical approach towards the synthesis of enantiopure phosphines. However, the profound affinity of phosphines toward most low valent late transition metals often causes *poisoning* of the catalysts. Nevertheless, numerous examples of transition-metal catalyzed P-H bond addition have been reported with pincer complexes^[113,151] and PC-palladacycles.^[85,112b-j] In one instance, a series of PC(H)P ligands were prepared catalytically in >99% *ee* and 86-98% *de* by our group (see Figure 1.13).^[112c] Exploiting the same catalytic methodology, we decided to prepare a series of chiral PCP-pincer complexes *via* one pot AHP/metalation reactions and investigate their applications in several catalytic scenarios.

2.2 Results and Discussion

2.2.1 Facile Syntheses of PCP-Transition Metal Complexes

The construction of benzylic PC(H)P ligands **147** and **148** started from commercially available dibromo derivatives **143** or substituted benzene-1,3-dicarboxyaldehyde **144** (Scheme 2.40). Typically, dibromo **143** was lithiated with

Scheme 2.40. Syntheses of various PCP-transition-metal pincer complexes. (Note: Absolute configurations are not indicated due to the use of both enantiomers of catalyst **119**.)

t-BuLi at -78°C and quenched with DMF to form aldehyde **144** in excellent yields. Subsequently, treatment of **144** with either substituted methyl ketone or dialkyl malonate *via* aldol or Knoevenagel condensation gave the corresponding substrates **145** and **146**. With the PCP ligand precursors in hand, the one pot AHP/metalation reactions were attempted with enantioimerically pure forms of catalyst **119** followed by direct C-H activation/cyclometalation of the air-sensitive diphosphine ligands **147** and **148** with palladium, platinum or nickel metals. The syntheses of the PCP-complexes **149** and **150** were accomplished with this method in excellent yields (70-91%), *ee* (>99%) and *de* (86-99%). A single recrystallization of the complexes is sufficient to afford the optically pure products. The *ee* and *de* of the phosphine ligands **147** and **148** were ascertained by $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy after coordination to the chiral derivatizing agent (*S*)/(*R*)-**66**.^[112c] A comprehensive explanation of the *ee/de* determination process will be provided in Section 2.2.3. The proposed mechanism for the (*R*)/(*S*)-**119**-catalyzed AHP will be examined in Section 2.2.4. In contrast to their free ligands, all the isolated pincer complexes were stable in air and moisture, both in the solid state and in solution. They were fully characterized by high-resolution mass spectroscopy (HR-MS), elemental analysis, ^1H , $^{31}\text{P}\{^1\text{H}\}$ and ^{13}C NMR spectroscopy. Single crystals of complexes **149b**, **d** and **150a-d** suitable for X-ray crystallographic analyses were obtained from either DCM/diethyl-ether or DCM/*n*-hexane. The complex **149a** could not be induced to form single crystals directly and was only characterized crystallographically upon conversion to the analogous iodo-complex **149a'**. The X-ray structures of pincer complexes **149b** and **150a** are shown below (the remaining structures can be found in the Appendix). Selected bond lengths and angles of the complexes are presented in Section 2.2.5 and will be discussed in greater detail subsequently.

There are multiple benefits of this synthetic approach. First, practically any dibromo or dicarboxaldehyde derivative may be used as building blocks (screening of

chemical catalogues revealed at least 200 suitable chemicals which are mostly inexpensive). Second, a variety of preligands **145** and **146** can be conveniently obtained *via* aldol or Knoevenagel condensation with an appropriate choice of substituted methyl ketones or malonates respectively. Third, the catalytic AHP of the substrates afforded the optically active PC(H)P ligands **147** and **148** in quantitative yields with excellent *ee* and *de*, thus avoiding the need for further resolution. Fourth, the one pot AHP/cyclometalation

Figure 2.21. Molecular structure of (*R,R*)-**149b**. Hydrogen atoms except H(C8) and H(C29) were omitted for clarity.

Figure 2.22. Molecular structure of (*R,R*)-**150a**. Hydrogen atoms except H(C7) and H(C25) were omitted for clarity.

reaction bypassed traditional protection-deprotection protocols to generate the corresponding chiral PCP-complexes **149** and **150** efficiently. Fifth, from the viewpoint of catalyst design, different transition metals (e.g. Pd, Pt, Ni, Rh, Ru *etc.*) may be selected for the metalation step. Lastly, as a result of the aforementioned benefits, this allows multifarious configurations of the generic pincer architecture which facilitates the systematic fine-tuning of the ligand scaffold especially for chemically and stereochemically demanding reactions. However, a limitation of this method is that the benzylic positions of the central aryl moiety must be sufficiently activated by electron-withdrawing groups for the catalytic AHP to ensue.

2.2.2 Facile Syntheses of PCN-Transition Metal Complexes

Motivated by the successful syntheses of the symmetrical PCP-complexes, we decided to attempt the construction of the more challenging unsymmetrical PCN-complexes using a similar methodology. A search of the Cambridge Crystallographic Database revealed the existence of about 370 benzylic PCP-, 260 benzylic NCN-, and a mere 4 benzylic PCN-pincers.^[152] The reports on preparation of chiral PCN complexes are limited and sporadic probably due to the difficulties associated with the ligand synthesis.^[151f,153] In addition, these hemilabile PCN-complexes^[154] are expected to be useful catalysts due to their unique reactivities.^[155] Employing a similar synthetic procedure as their PCP-counterparts, a mixture of 1-bromo-3-(bromomethyl)benzene

Scheme 2.41. Synthesis of chiral PCN-pincer complexes.

151a and diisopropylamine in toluene was refluxed to give quantitative yield of *N*-(3-bromobenzyl)-*N*-isopropylpropan-2-amine **151b**. The lithiation of **151b** followed by quenching with DMF gave aldehyde **151c** in 90% isolated yield. A mixture of aldehyde **151c** and Wittig reagent **152** in refluxing toluene produced the enone **151d**. To our surprise, the catalyst (*S*)-**119** was tolerant of the amine functionality on **151d** and proceeded to generate the chiral P-N ligand (*R*)-**151e** via catalytic AHP. The *ee* of ligand (*R*)-**151e** was determined to be >99% based on coordination to the chiral derivatizing agent (*R*)/(*S*)-**66** and $^{31}\text{P}\{^1\text{H}\}$ NMR techniques.^[112a-c] Direct metalation of the optically pure PC(H)N ligand afforded the PCN complex **153** in 81-90% isolated yields. Single crystals of complex **153a'** were obtained upon conversion of the chloro anion to a nitrate group by treating complex **153a** with AgNO_3 (1.5 equiv.) in DCM overnight. Selected bond lengths and angles are collated in Section 2.2.5. The X-ray structure of pincer complex **153a'** is depicted below.

Figure 2.23. Molecular structure of (*R*)-**153a'**. Hydrogen atoms except H(C48) were omitted for clarity.

The efficient synthesis of chiral PCN complexes **153a-b** offers a simple yet versatile approach to this class of unsymmetrical pincer complexes. Modifications of the ligand scaffold can be easily achieved by an appropriate choice of reagents throughout the

synthetic process, thereby allowing significant flexibility in design and fine-tuning. For example, the substitution of diisopropylamine with diphenylamine would result in a less basic and more sterically demanding N-donor. Similarly, with a wide variety of Wittig reagents available, it is evident that a series of analogous **151d** can be prepared easily.

2.2.3 Determination of *ee/de* of the Chiral Phosphine Ligands

For illustrative purposes, only the *ee/de* determination of PC(H)P ligand **147c** and PC(H)N ligand **151e** will be discussed. The *ee* and *de* of the remaining PC(H)P ligands were verified analogously and are summarized in Table 2.3.

Scheme 2.42. Coordination of PC(H)P ligand to chiral derivatizing agent (*R*)-**66**.

Theoretically, in a racemic mixture of diphosphine **147c**, four isomers coexist in equal ratios. Upon coordination to palladacycle (*R*)-**66**, four diastereomers will be formed with the configurations shown in Scheme 2.42. However, (*R,S,R,R*)-**154** and (*R,R,S,R*)-**154** are identical compounds and will be indistinguishable by $^{31}\text{P}\{^1\text{H}\}$ NMR, hence only three phosphorus peaks in the ratio of 1:2:1 ((*R,R,R,R*):(*R,S,R,R*)+(*R,R,S,R*):(*R,S,S,R*)) will be observed. The major isomer of the (*S*)-**119**-catalyzed AHP was determined to be (*R,R*)-**147c** based on X-ray crystallography.^[112c] After coordination to complex (*R*)-**66**, the $^{31}\text{P}\{^1\text{H}\}$ NMR spectra revealed one single peak at 43.1 ppm corresponding to (*R,R,R,R*)-**154**. In a separate experiment, the crude reaction mixture containing **147c** was

Figure 2.24. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of complex **154**.

$$ee (\%) = \frac{(R,R)\text{-}\mathbf{147c} - (S,S)\text{-}\mathbf{147c}}{(R,R)\text{-}\mathbf{147c} + (S,S)\text{-}\mathbf{147c}} = \frac{(R,R,R,R)\text{-}\mathbf{154} - (R,S,S,R)\text{-}\mathbf{154}}{(R,R,R,R)\text{-}\mathbf{154} + (R,S,S,R)\text{-}\mathbf{154}}$$

$$de (\%) = \frac{[(R,R)\text{-}\mathbf{147c} + (S,S)\text{-}\mathbf{147c}] - [(S,R)\text{-}\mathbf{147c} + (R,S)\text{-}\mathbf{147c}]}{[(R,R)\text{-}\mathbf{147c} + (S,S)\text{-}\mathbf{147c}] + [(S,R)\text{-}\mathbf{147c} + (R,S)\text{-}\mathbf{147c}]} \\ = \frac{[(R,R,R,R)\text{-}\mathbf{154} + (R,S,S,R)\text{-}\mathbf{154}] - [(R,S,R,R)\text{-}\mathbf{154} + (R,R,S,R)\text{-}\mathbf{154}]}{[(R,R,R,R)\text{-}\mathbf{154} + (R,S,S,R)\text{-}\mathbf{154}] + [(R,S,R,R)\text{-}\mathbf{154} + (R,R,S,R)\text{-}\mathbf{154}]}$$

Figure 2.25. Formulas for calculations of *ee* and *de*.

also reacted with (*S*)-**66** to form (*S,R,R,S*)-**154**, identified by the signal at 51.0 ppm. From the results of these experiments, ligand (*R,R*)-**147c** was computed to be formed in >99% *ee* and 99% *de*. The *de* was further confirmed by $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy after cyclopalladation to form the pincer complex **149c** ($^{31}\text{P}\{^1\text{H}\}$ of *rac*-**149c**: 45.0 ppm and $^{31}\text{P}\{^1\text{H}\}$ of *meso*-**149c**: 48.3 ppm). The *ee* obtained was verified by chiral High Performance Liquid Chromatography (HPLC, Diacel Chiralpak IC column, >99% *ee*) after separation of the oxidized *rac*-**147c** from the oxidized *meso*-**147c**. However, the use

of HPLC was not extended to the other phosphine ligands due to the laborious efforts required to separate the *rac*- and *meso*-isomers.

In the next example, the presence of only one stereogenic center on PC(H)N ligand **151e** indicates that a racemic mixture will contain equal proportions of both (*R*)- and (*S*)-**151e**. Coordination of the isomers to (*R*)-**66** will give a pair of diastereomeric complex **155** that can be differentiated by $^{31}\text{P}\{^1\text{H}\}$ NMR ((*R,R*)-**155**: 43.6 ppm and (*R,S*)-**155**: 49.2 ppm). Based on the results of two separate coordination experiments with (*R*)-

Scheme 2.43. Coordination of PC(H)N ligand to chiral derivatizing agent (*R*)-**66**.

Figure 2.26. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of complex **155**.

and (*S*)-**66**, only one signal was obtained in both cases, thus it was deduced that (*R*)-**151e** (absolute configuration was determined by X-ray crystallography; see Figure 2.23) was produced in >99% *ee* via (*S*)-**119**-catalyzed AHP reaction.

$$ee\ (\%) = \frac{(R)\text{-}\mathbf{151e} - (S)\text{-}\mathbf{151e}}{(R)\text{-}\mathbf{151e} + (S)\text{-}\mathbf{151e}} = \frac{(R,R)\text{-}\mathbf{155} - (R,S)\text{-}\mathbf{155}}{(R,R)\text{-}\mathbf{155} + (R,S)\text{-}\mathbf{155}}$$

Figure 2.27. Formula for calculation of *ee*.

All the associated *ee/de* of the PC(H)P and PC(H)N ligands **147**, **148** and **151e** (see Scheme 2.40) are presented below. It is gratifying to note that the catalytic AHP reaction was able to tolerate a range of functional groups to afford the chiral phosphine ligands in excellent *ee/de*. This will allow access to a broad spectrum of chiral pincer ligands in excellent *ee/de*. This will allow access to a broad spectrum of chiral pincer analogues with varying functionalities, thus enabling the tuning of the sterics, stereochemical and electronic properties of the complexes.

Table 2.3. Associated *ee/de* of PC(H)P and PC(H)N ligands.^[a]

Entry	R	Z	Ligand	<i>ee</i> (%)	<i>de</i> (%)
1	Ph	H	147a	>99	98
2	Ph	Me	147b	>99	94
3	Ph	OMe	147c	>99	99
4	Ph	F	147d	>99	99
5	2-furyl	H	147e	>99	94
6	2-pyridinyl	H	147f	>99	86
7	4'-ClC ₆ H ₄	H	147g	>99	96
8	Me	H	148a	>99	99
9	Bn	H	148b	>99	99
10	-	-	151e	>99	-

[a] *ee/de* determined by ³¹P{¹H} NMR upon coordination to chiral derivatizing agent (*R*)/(*S*)-**66**.

2.2.4 Proposed Mechanism for the Catalytic AHP Reaction

The (*R*)/(*S*)-**99**-catalyzed AHP of enone **117**^[112a] was reported in 2010 by our group. Following which, the phosphorus analogue (*R*)/(*S*)-**119** was found to outperform palladacycle **99** in terms of reactivity and stereoselectivity.^[112b] A brief comparison of the catalyst performance in the AHP of enones is presented in the table below. It should be reiterated that both five-membered organometallic rings in (*R*)-**99** and (*R*)-**119** are confined to the non-interconvertible δ conformation, with the prochiral NMe₂ or PPh₂ groups fixed in the axial and equatorial positions. As such, the excellent stereoselectivity observed (when palladacycle **119** was employed) is ascribed to the superior control offered by the two projecting P-phenyl groups. The sterically bulkier phenyl moieties are more efficient in relaying the stereogenic information onto coordination site A (see Figure 2.28) as opposed to the smaller N-methyl groups on (*R*)-**99**. The significantly

Figure 2.28. Structural representations of the chiral palladacycles.

Table 2.4. Brief comparison of catalyst performance.

cat.	<i>t</i> (h)	Yield ^[a] (%)	<i>ee</i> ^[b] (%)
(<i>R</i>)- 99	23-168	92-99	33-86
(<i>R</i>)- 119	2-40	98-99	92-99

[a] Range of isolated yields before recrystallization. [b] Range of *ee* before recrystallization.

to form the bis(diphenylphosphine) complex. Due to the strong *trans* effect, the PPh₂H *trans* to the naphthalene ring is labilized and dissociates easily, allowing the coordination of the substrate. Even though C=C bond coordination to Pd is possible,^[156] previous studies have suggested that the carbonyl oxygen is more likely to coordinate to Pd rather than the C=C moiety.^[112a] It has also been commonly observed that the position *trans* to the naphthalene ring on analogous palladium complexes prefers hard donors such as carbonyl O, amide O, sulfoxide O and perchlorato O atoms.^[157] Subsequently, the coordinated HPPH₂ is acidified by the Pd metal and deprotonation (by NEt₃) occurs to form the phosphido complex. An intramolecular 1,4-addition reaction ensues to generate an O-enolate intermediate which then undergoes protonation to afford the chiral tertiary phosphine.

In the catalytic double AHP of the substrates **145** and **146**, it is interesting to determine if the catalyst is affected by the monophosphine **145a'** that is formed. Under controlled reaction conditions, HPPH₂ and dienone **145a** were reacted in a 1:1 mole ratio catalyzed by (*S*)-**119**. The reaction progress was monitored by ³¹P{¹H} NMR and upon complete conversion of HPPH₂, the formation of both **145a'** (*ca.* 52%) and **147a** (*ca.* 24%) were observed instead of the exclusive generation of **145a'**. The unreacted **145a** (*ca.* 24%) in the crude reaction mixture was identified by ¹H NMR. This experiment suggests that the catalyst exhibits excellent substrate tolerance for activated olefins bearing tertiary phosphine moieties, allowing only the coordination of HPPH₂. The stability of the chiral C-P auxiliary on catalyst **119** towards displacement by free phosphines is a vital factor in the catalytic cycle, considering the fact that the phosphine

Scheme 2.45. Controlled catalytic AHP of dienone **145a**.

species involved are inherently labile on the Pd metal center.

It has been noted that symmetrical substrates with two equivalent reactive sites may present special opportunities or problems in asymmetric catalysis.^[158] Following the first P-H bond addition to substrates, the selectivity of the second AHP may either be the same (*rac* adduct) or different (*meso* adduct) depending on the nature of the catalyst and substrates. In the double AHP of **145** and **146**, it is pleasing to observe the excellent enantioselectivity of palladacycle **119** which allows the formation of the C₂-symmetrical diphosphines **147** and **148**.

2.2.5 Molecular Structures of PCP- and PCN-Pincer Complexes

In the earlier sections, the X-ray structures of pincer complexes **149a'**, **149b**, **d**, **150a-d** and **153a'** were successfully obtained. A detailed analysis of the collated data is essential to investigate the following: (1) the electronic effects originated from the *para*-substituent Z, (2) the steric effects contributed by the chiral functionalities R, and (3) the coordination chemistry of selected donor atoms. For simplicity, a general atom numbering scheme is adopted for the comparison of the key structural features. The selected bond lengths (Å), angles (°) and C₂ pincer twist parameters, θ (°) of the structures are presented in Table 2.5.

In general, all the complexes adopted distorted square planar geometries around the transition metal centers. Due to restrictions by the P-C(8)-C(2)-C(1)-C(6)-C(7)-E frameworks, the P→M←E angles are less than 180°, reflecting the steric strain imposed in pincers containing two-fused five-membered metallacycles.^[118c,153d,159] A literature review of 4-coordinate PCP systems turned up an average of 164.6°, which is slightly larger than the angles observed (160.7-162.2°) for complexes **149a'**, **b**, **d**, **150a-c** and **153a'**. It was established that in pincer complexes where steric demand is similar above and below the planes, decreases in P→M←E angles are attributed to bending towards the

Table 2.5. Selected bond lengths (Å), angles (°) and C₂ pincer twist parameters θ (°) of pincer complexes.

	149a'	149b	149d	150a	150b	150c	150d	153a'
M-X	2.671(1)	2.370(3)	2.382(1)	2.382(1)	2.368(1)	2.385(1)	2.208(1)	2.151(5)
M-C(1)	2.038(4)	2.040(10)	2.027(3)	2.017(2)	2.006(3)	2.007(6)	1.924(3)	1.954(6)
M-P	2.289(1)	2.273(3)	2.301(1)	2.287(1)	2.280(1)	2.272(2)	2.162(1)	2.236(2)
M-E	2.287(1)	2.310(3)	2.282(1)	2.302(1)	2.296(1)	2.282(2)	2.171(1)	2.198(5)
C(4)-Z	0.95	1.519(12)	1.365(3)	0.95	0.95	0.95	0.95	0.95
C(2)-C(8)	1.510(7)	1.521(16)	1.512(4)	1.517(3)	1.522(4)	1.534(9)	1.507(4)	1.511(8)
C(6)-C(7)	1.496(7)	1.510(16)	1.514(4)	1.511(2)	1.510(3)	1.525(9)	1.502(4)	1.498(9)
P-M-E	162.24(4)	161.30(11)	160.69(3)	161.05(2)	161.13(3)	162.03(6)	167.94(3)	161.82(14)
P-M-C(1)	81.05(17)	81.70(30)	80.44(9)	80.45(5)	80.55(8)	80.93(17)	83.90(9)	79.86(19)
P-M-X	98.86(3)	95.71(12)	102.44(3)	98.52(2)	99.13(3)	98.45(6)	84.04(9)	101.88(13)
E-M-C(1)	81.19(17)	79.80(30)	82.16(9)	80.69(5)	82.74(8)	81.16(17)	95.57(3)	82.20(20)
E-M-X	98.90(3)	102.88(12)	95.59(3)	100.43(2)	98.53(3)	99.52(6)	96.50(3)	96.26(18)
$\theta^{[a]}$	19.64	20.51	19.62	19.64	17.43	18.85	11.68	-

[a] The pincer twist parameters for the PCP complexes were determined from the corresponding cif files using Mercury 3.1 software.

central aryl moiety.^[160] The larger bond angle (167.9°) for pincer complex **150d** is due to the smaller covalent radii of Ni metal, resulting in the more effective enfolding of the metal center by the PC(H)P ligand. From the data obtained for complexes **149a'**, **b** and **d**, interestingly, the electronic properties arising from the *para*-substituent Z seems to affect the M-C bond. A strong electron withdrawing atom such as fluorine resulted in a noticeably shorter M-C(1) bond in complex **149d** [2.027(3) Å] than those in complexes **149a'** and **149b** [2.038(4) and 2.040(10) Å respectively]. However, the effects of Z are not pronounced in other neighboring bond lengths and angles.

A comparison of the structural features of complexes **149a'**, **b**, **d** and **150a-c** did not reveal any distinct trends with regards to the effects of the functionalities R at the chiral center. The sterically bulkier malonate moieties (on **150a-c**) did not have significant influence on the architecture of the complexes when compared to the smaller ketone groups (on **149a'**, **b** and **d**). In contrast, the sizes of the metal centers affect the structural features of the complexes significantly. The Ni(II) complex **150d** exhibited

shorter M→P bonds [2.162(1) and 2.171(1) Å] than the analogous Pd(II) [**150a**, 2.287(1) and 2.302(1) Å] and Pt(II) [**150c**, 2.272(2) and 2.282(2) Å] complexes. (For comparison, the metallic covalent radius of Ni, Pd and Pt are 1.24, 1.39 and 1.36 Å respectively.) Intriguingly, the Pt-C bond in **150c** [2.007(6) Å] is clearly shorter than the Pd-C bond in **150a** [2.017(2) Å] despite carbon being located further away from Pt in the periodic table and the two atoms having a larger difference in terms of electron density.

The Pd←P bond in the unsymmetrical pincer **153a'** [2.236(2) Å] is the shortest among all the Pd←P bonds [2.273(3)-2.310(3) Å] listed in the table. This might be due to the favorable electronic effect associated with P→Pd←N arrangement in which the σ -donating N atom is coordinated *trans* to a σ -donating/ π -accepting P atom.^[161] In the other Pd complexes, the competition between the two P donors in the P→Pd←P systems will weaken the Pd←P bonds due to competition for electrons from the same metal *d*-orbital.^[162] Detailed explanations of other possible factors affecting the P→M bond lengths have been discussed in several reports.^[163]

In meridional pincer coordination, the coplanarity of the ligating atoms is usually accompanied by a twist of the aryl backbone, which can be referred to as the C₂ pincer twist angle, θ .^[160] For four-coordinate pincer systems, CH₂-bridged pincers exhibit a large θ averaging 10.1° as compared to the NH-(4.2° average) and O-bridged (2.4° average) pincers.^[164] However, the twist distortion is energetically soft as evident by an average variation of 2° between crystallographically independent molecules.^[160] In the solid state structures of complexes **149a'**, **b**, **d** and **150a-c**, it was observed that the twist angles (17.4-20.5°) are larger than the average of 10.1° for analogous PCP pincers, even though the C(2)-C(8) and C(6)-C(7) bonds conform to the average value of 1.51 Å. The smaller twist angle of 11.7° for complex **150d** is a direct consequence of the smaller covalent radii of Ni metal, causing the PCP ligand to enfold the metal center with an associated

Figure 2.29. Diagrammatic representations of **(A)** a larger steric repulsion due to smaller θ , and **(B)** lower repulsion due to a larger θ .

minimization of θ . The enlarged θ values (of **149a'**, **b**, **d** and **150a-c**) may be related to the steric interactions between the substituents at the C-stereogenic centers and the P-phenyl groups. For a particular PCP system, a smaller $P \rightarrow M \leftarrow P$ angle accompanied by a large θ normally reflects a lower volume of the coordination sphere blocked by the ligand (measured by percent buried volume, $\%V_{\text{bur}}$ ^[165]). This indicates a more compact pincer conformation, which in turn restricts access of a reagent to the metal center. Consequently, these structural features influence the stereoselectivity and reactivity of the complexes in asymmetric catalysis.^[129a,132,166]

2.2.6 Preliminary Activity Test

Table 2.6. Preliminary catalytic screening for pincer complexes.

Entry	cat. ^[a]	<i>t</i> (h)	Yield ^[b] (%)	<i>ee</i> ^[c] (%)
1	(<i>R,R</i>)- 149a	1	90	11
2	(<i>R,R</i>)- 149h	4	95	3
3	(<i>R,R</i>)- 150a	5	96	43
4	(<i>R,R</i>)- 150d	48	76	0
5	(<i>R</i>)- 153a	9	88	3

[a] The catalysts were pre-treated with AgOAc (1.0 equiv.) in DCM for 1 h. [b] Isolated yield. [c] *ee* was determined by chiral HPLC.

The general chemical reactivities of selected chiral PCP- and PCN-complexes were briefly examined for a preliminary understanding of the differences in their electronic and chemical properties. The complexes **149a**, **h**, **150a**, **d** and **153a** were employed as catalysts in the AHP of chalcone with diphenylphosphine. The results of these tests were gratifying, with four out of five complexes displaying excellent reactivities to afford product **157** in 88-96% isolated yields without further optimization, albeit with low to moderate enantioselectivities. The Pd pincer **149a** is noticeably more reactive than its Pt analogue **149h** (entries 1, 2). Similarly, the heavily functionalized Pd complex **150a** is significantly more reactive than the Ni pincer **150d** (entries 3,4). Evidently, the choice of metal ion is a crucial factor in determining the chemical reactivity of the pincer complex. For this P-H addition reaction, palladium is a better choice of metal ion than both platinum and nickel. Comparing the Pd complexes **149a** and **150a**, the bulky ester functionalities on the pendant arms of **150a** improves the stereoselectivity greatly, forming the product in 43% *ee* although reactivity is slightly slower (entries 1, 3). Overall, the selected PCP Pd-pincers outperform the PCN Pd complex **153a** in terms of reactivities and stereoselectivities (entries 1, 3, 5). These preliminary tests revealed that the catalytic AHP reaction is indeed sensitive to minor alterations in the pincer architecture.

2.3 Conclusion

The methodology presented (*vide supra*) for the facile syntheses of the chiral PCP and PCN pincer complexes serves as a valuable and functional tool to prepare a series of pincer scaffolds. This synthetic pathway allows straightforward modifications of the *para*-substituent, functionalities and bulkiness of R, donor atoms, and the transition metal center. The use of palladacycle **119**-catalyzed AHP of the specially designed substrates circumvents the need for traditional protection-deprotection protocols or resolution steps

by affording the chiral ligands in quantitative yields with excellent *ee/de*. This permits the one-pot AHP/cyclometalation reactions to generate the respective pincer complexes efficiently. Consequently, this synthetic method grants access to a broad spectrum of pincer analogues with varying stereochemical and electronic properties, thus enabling the fine-tuning of the pincer ligands to best suit each specific transformation scenario.

In addition, the concept of *ee* and *de* determination of optically active phosphine ligands using the chiral derivatizing agent **66** was presented. Also, the proposed catalytic cycle involving chiral phosphapalladacycle **119** was revisited and discussed in detail to provide an in-depth understanding of the catalyst behavior. The structural properties of some complexes were examined on the basis of X-ray crystal analyses and comparisons were made to other PCP systems that have been reported in literature. Lastly, the general chemical reactivities of selected pincer complexes were investigated in the catalytic AHP of chalcone, which successfully demonstrated the significant differences in reactivities and stereoselectivities resulting from modifications to these pincer architectures.

The application of these pincer complexes as catalysts in asymmetric AHP reactions will be explored further. In the following chapter, the synthesis of chiral PCP copper pincer complexes was attempted with the diphosphine ligands prepared, but instead of forming the desired PCP copper(II) pincer complexes, a series of diphosphine copper(I) clusters were prepared from the one-pot AHP/metalation reactions.

2.4 Experimental Section

All reactions were carried out under a positive pressure of nitrogen using standard Schlenk technique. Solvents were purchased from their respective companies (DCM, THF, EtOH: Fisher, DEE, EA: Merck, toluene, *n*-hexane: Avantor, Acetone: Sigma-Aldrich) and used as supplied. Where necessary, solvents were degassed prior to use. A Low Temp Pairstirrer PSL-1800 was used for controlling low temperature reactions.

Column chromatography was done on Silica gel 60 (Merck). Melting points were measured using SRS Optimelt Automated Point System SRS MPA100. Optical rotation were measured with JASCO P-1030 Polarimeter in the specified solvent in a 0.1 dm cell at 22.0°C. NMR spectra were recorded on Bruker AV 300, AV 400 and AV 500 spectrometers. Chemical shifts were reported in ppm and referenced to an internal SiMe₄ standard (0 ppm) for ¹H NMR, chloroform-d (77.23 ppm) for ¹³C NMR, and an external 85% H₃PO₄ for ³¹P{¹H} NMR.

The palladacycle (*R*)/(*S*)-**119**^[112c] and Wittig reagent **152**^[167] were prepared according to literature methods. All other reactants and reagents were used as supplied.

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

General Procedure for Preparation of Mono-Substituted Isophthalaldehyde, 144a-d. *t*-BuLi (9.52 mL, 1.7M in pentane, 4.3 equiv.) was added dropwise to solution of **143** (3.76 mmol, 1.0 equiv.) in DEE (25 mL) at -78°C and stirred for 1h. DMF (9.40 mmol, 2.5 equiv.) was introduced into the mixture and allowed to react at RT overnight. The reaction was quenched with sat. NH₄Cl, extracted with EA (3 x 25 mL) and the combined organic layer was washed with water (1 x 25 mL), dried over MgSO₄, filtered and evaporated to dryness. The crude product **144** was purified by silica gel chromatography (3 DCM : 1 *n*-hexane) to afford the corresponding dicarboxaldehyde **144**.

144a White solid. Mp: 83-85°C. ¹H NMR (CDCl₃, 400 MHz): δ 10.12 (s, 2H, O=CH), 8.38 (t, ⁴*J* = 1.5 Hz, 1H, O=CHCCHCHC=O), 8.16 (dd, ⁴*J* = 1.6 Hz, ³*J* = 7.6 Hz, 2H, HCCHCH), 7.73 (t, ³*J* = 7.6 Hz, 1H, HCCHCH); ¹³C NMR (CDCl₃, 100 MHz): δ 191.2 (2C, O=CH), 137.2-130.1 (6C, Ar). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₈H₇O₂,

135.0446; found, 135.0444. Anal. Calcd for C₈H₆O₂: C, 71.64; H, 4.51. Found: C, 71.88; H, 4.71%.

144b White solid. Mp: 75-76°C. ¹H NMR (CDCl₃, 500 MHz): δ 10.03 (s, 2H, O=CH), 8.12 (s, 1H, Ar), 7.91 (s, 2H, Ar), 2.48 (s, 3H, ArCH₃); ¹³C NMR (CDCl₃, 125 MHz): δ 191.3 (2C, O=CH), 140.3-128.7 (6C, Ar), 21.1 (1C, CH₃). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₉H₉O₂, 149.0603; found, 149.0604. Anal. Calcd for C₉H₈O₂: C, 72.96; H, 5.44. Found: C, 72.83; H, 5.57%.

144c White solid. Mp: 90-91°C. ¹H NMR (CDCl₃, 500 MHz): δ 10.05 (s, 2H, O=CH), 7.96 (s, 1H, Ar), 7.65 (s, 2H, Ar), 3.93 (s, 3H, ArOCH₃); ¹³C NMR (CDCl₃, 125 MHz): δ 190.9 (2C, O=CH), 160.8-119.3 (6C, Ar), 25.9 (1C, OCH₃). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₉H₉O₃, 165.0552; found, 165.0551. Anal. Calcd for C₉H₈O₃: C, 65.85; H, 4.91. Found: C, 65.75; H, 5.27%.

144d White solid. Mp: 73-74°C. ¹H NMR (CDCl₃, 500 MHz): δ 10.08 (d, ⁵J_{HF} = 1.7 Hz, 2H, O=CH), 8.20 (d, ⁴J = 1.2 Hz, 1H, FCCHC(CHO)CH), 7.84 (dd, ³J_{HF} = 7.8 Hz, ⁴J = 1.2 Hz, 2H, FCCCH); ¹³C NMR (CDCl₃, 125 MHz): δ 189.6 (2C, O=CH), 139.1-120.8 (6C, Ar). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₈H₆FO₂, 153.0352; found, 153.0355. Anal. Calcd for C₈H₅FO₂: C, 63.16; H, 3.31. Found: C, 63.35; H, 3.57%.

General Procedure for Preparation of Dienones, 145a-g. NaOH (80 mL, 40% w/w in water) was added to substituted methyl ketone (29.9 mmol, 2.0 equiv.) in MeOH (120 mL) and cooled to RT. Aldehyde **144** (14.9 mmol, 1.0 equiv.) in MeOH (30 mL) was introduced to the mixture and stirred at RT for 20h followed by acidification with conc. HCl until pH = 3. The solid was filtered, redissolved in DCM, washed with sat. NaHCO₃ (1 x 50 mL), water (2 x 50 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was recrystallized from DCM/*n*-hexane.

145a Pale yellow solid. The data obtained is consistent with literature.^[168]

145b Pale yellow solid. Mp: 103-104°C. ¹H NMR (CDCl₃, 500 MHz): δ 8.04 (dd, ³J = 7.2, 4H, Ar), 7.80 (d, ³J = 15.7 Hz, 2H, ArHC=CH), 7.69 (s, 1H, Ar), 7.61-7.50 (m, 10H, Ar + ArHC=CH), 2.45 (s, 3H, ArCH₃); ¹³C NMR (CDCl₃, 125 MHz): δ 190.2 (2C, O=C), 144.0-122.7 (22C, Ar + ArCH=C), 21.3 (1C, ArCH₃). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₅H₂₁O₂, 353.1542; found, 353.1541. Anal. Calcd for C₂₅H₂₀O₂: C, 85.20; H, 5.72. Found: C, 85.29; H, 5.83%.

145c Pale yellow solid. Mp: 100-102°C. ¹H NMR (CDCl₃, 500 MHz): δ 8.03 (dd, ³J = 7.1 Hz, ⁴J = 1.3 Hz, 4H, Ar), 7.78 (d, ³J = 15.7 Hz, 2H, ArHC=CH), 7.63-7.57 (m, 2H, Ar), 7.54-7.50 (m, 7H, Ar), 7.23 (d, ³J = 15.7 Hz, 2H, ArHC=CH), 3.91 (s, 3H, OCH₃); ¹³C NMR (CDCl₃, 125 MHz): δ 190.3 (2C, O=C), 160.4-115.4 (22C, Ar + ArCH=C), 55.6 (1C, OCH₃). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₅H₂₁O₃, 369.1491; found, 369.1521. Anal. Calcd for C₂₅H₂₀O₃: C, 81.50; H, 5.47. Found: C, 81.65; H, 5.69%.

145d White solid. Mp: 111-112°C. ¹H NMR (CDCl₃, 500 MHz): δ 8.04 (dd, ³J = 7.2 Hz, ⁴J = 1.4 Hz, 4H, Ar), 7.78 (d, ³J = 15.7 Hz, 2H, ArHC=CH), 7.64-7.59 (m, 4H, Ar), 7.55-7.52 (m, 5H, Ar), 7.39 (d, ³J = 15.7 Hz, 2H, ArHC=CH); ¹³C NMR (CDCl₃, 100 MHz): δ 189.9 (2C, O=C), 142.4-124.1 (21C, Ar + ArCH=C), 116.1 (d, ¹J_{CF} = 22.0 Hz, 1C, Ar). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₄H₁₈FO₂, 357.1291; found, 357.1311. Anal. Calcd for C₂₄H₁₇FO₂: C, 80.88; H, 4.81. Found: C, 81.02; H, 4.73%.

145e Yellow solid. Mp: 103-104°C. ¹H NMR (CDCl₃, 400 MHz): δ 7.90 (d, ³J = 15.8 Hz, 2H, ArHC=CH), 7.89 (s, 1H, Ar), 7.70-7.68 (m, 4H, Ar), 7.50 (d, ³J = 15.9 Hz, 2H, ArHC=CH), 7.50-7.46 (m, 1H, Ar), 7.39 (d, ⁴J = 3.5 Hz, 2H, Ar), 6.62 (dd, ⁴J = 3.5, 1.6 Hz, 2H, Ar); ¹³C NMR (CDCl₃, 100 MHz): δ 177.9 (s, 2C, O=C), 153.7-112.8 (18C,

Ar + ArCH=C). HRMS (+ESI) m/z : (M + H)⁺ calcd for C₂₀H₁₅O₄, 319.0970; found, 319.0969. Anal. Calcd for C₂₀H₁₄O₄: C, 75.46; H, 4.43. Found: C, 75.62; H, 4.63%.

145f White solid. Mp: 100-101°C. ¹H NMR (CDCl₃, 400 MHz): δ 8.77 (d, ³J = 4.7 Hz, 2H, Ar), 8.36 (d, ³J = 16.0 Hz, 2H, ArHC=CH), 8.21 (d, ³J = 7.8 Hz, 2H, Ar), 8.05 (s, 1H, Ar), 7.97 (d, ³J = 16.1 Hz, 2H, ArHC=CH), 7.89 (td, ³J = 7.7 Hz, ⁴J = 1.7 Hz, 2H, Ar), 7.77 (dd, ³J = 7.7 Hz, ⁴J = 1.6 Hz, 2H, Ar), 7.52-7.48 (m, 3H, Ar); ¹³C NMR (CDCl₃, 100 MHz): δ 189.5 (2C, O=C), 154.3-122.0 (20C, Ar + ArCH=C). HRMS (+ESI) m/z : (M + H)⁺ calcd for C₂₂H₁₇N₂O₂, 341.1290; found, 341.1291. Anal. Calcd for C₂₂H₁₆N₂O₂: C, 77.63; H, 4.74; N, 8.23. Found: C, 77.82; H, 4.83; N, 8.25%.

145g White solid. The data obtained is consistent with literature.^[169]

General Procedure for Preparation of Compounds, 146a-b. Dicarboxaldehyde **144a** (7.45 mmol, 1.0 equiv.) and glacial AcOH (1.49 mmol, 0.2 equiv) were sequentially added to a mixture of dialkyl malonate (14.91 mmol, 2.0 equiv.) and piperidine (1.49 mmol, 0.2 equiv.) in *n*-heptane (5 mL). The mixture was refluxed at 140°C under Dean-Stark conditions for 24h and volatiles were removed under reduced pressure. Extraction was done with DCM (3 x 30 mL), the organic layer was washed with NaHCO₃ (10% w/w in water, 1 x 30 mL), water (3 x 30 mL), dried over MgSO₄, filtered and the solvent removed. The crude product was purified by silica gel chromatography (2 *n*-hexane : 1 EA) to afford compound **146**.

146a White solid. Mp: 113-114°C. ¹H NMR (CDCl₃, 500 MHz): δ 7.72 (s, 2H, ArCH=C), 7.44-7.41 (m, 4H, Ar), 3.85 (s, 6H, CO₂CH₃), 3.84 (s, 6H, CO₂CH₃); ¹³C NMR (CDCl₃, 125 MHz): δ 166.6 (2C, O=C), 164.2 (2C, O=C), 141.7-126.8 (10C, Ar + ArCH=C + ArCH=C), 52.9 (2C, CO₂CH₃), 52.8 (2C, CO₂CH₃). HRMS (+ESI) m/z : (M + H)⁺ calcd for C₁₈H₁₉O₈, 363.1080; found, 363.1081. Anal. Calcd for C₁₈H₁₈O₈: C, 59.67; H, 5.01. Found: C, 59.90; H, 4.93%.

146b White solid. Mp: 119-120°C. ^1H NMR (CDCl_3 , 400 MHz): δ 7.65 (s, 2H, $\text{ArCH}=\text{C}$), 7.37-7.34 (m, 10H, Ar), 7.30-7.23 (m, 13H, Ar), 7.07 (t, $^3J = 8.2$ Hz, 1H, Ar), 5.27 (s, 4H, $\text{CO}_2\text{CH}_2\text{Ph}$), 5.25 (s, 4H, $\text{CO}_2\text{CH}_2\text{Ph}$); ^{13}C NMR (CDCl_3 , 100 MHz): δ 166.0 (2C, $\text{O}=\text{C}$), 163.7 (2C, $\text{O}=\text{C}$), 142.1-127.0 (34C, Ar + $\text{ArCH}=\text{C}$ + $\text{ArCH}=\text{C}$), 67.9 (2C, $\text{CO}_2\text{CH}_2\text{Ph}$), 67.5 (2C, $\text{CO}_2\text{CH}_2\text{Ph}$). HRMS (+ESI) m/z : ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{42}\text{H}_{35}\text{O}_8$, 667.2332; found, 667.2333. Anal. Calcd for $\text{C}_{42}\text{H}_{34}\text{O}_8$: C, 75.66; H, 5.14. Found: C, 75.90; H, 5.33%.

General Procedure for Preparation of Pincer Complexes, **149a-k** and **150a-d**.

To a solution of Ph_2PH (1.22 mmol, 2.1 equiv.) in toluene (10 mL) was added catalyst (*R*)/(*S*)-**119**^[a] (0.061 mmol, 5 mol %) and stirred for 10 minutes before cooling to -80°C. The ligand precursor **145** or **146**^[b] (0.578 mmol, 1.0 equiv.) was added followed by the addition of NEt_3 (1.16 mmol, 2.0 equiv.) in toluene^[b] (1 mL) dropwise. The solution was stirred at -80°C and the completion of the reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR. Upon completion, the solution was allowed to reach room temperature. Volatiles were removed under reduced pressure to afford crude diphosphine **147** or **148**. $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (151 mg, 0.578 mmol, 1.0 equiv.) was added to a solution of ligand **147** or **148** in DCM (10 mL) and stirred overnight at room temperature. The solvent was removed and the crude product was purified *via* silica gel column chromatography (DCM or 19 DCM : 1 EA) to afford white solid of complex **149** or **150**.

[a] Catalyst (*R*)-**119** was used for the preparation of (*S,S*)-**149d**. Catalyst (*S*)-**119** was used for the preparation of all other pincer complexes (*R,R*)-**149a-c**, **e-k**, **150a-d**. The *ee* and *de* of ligands **147a-g** and **148a-b** were determined upon coordination to the chiral derivatizing agent **66** (*vide supra*).

[b] The catalytic AHP of substrates **146a-b** was done in DCM instead of toluene.

Note: For the metalation with $\text{PtCl}_2(\text{CH}_3\text{CN})_2$ to form complexes **149h-j** and **150c**, heating at 100°C in toluene for 4 h is necessary for product formation. For the syntheses of nickel pincers **149k** and **150d**, NiCl_2 in H_2O (1 mL) was added to a solution of the crude diphosphine in EtOH and heated at 60°C for 4 h. Subsequently, NEt_3 (1.0 equiv.) was added and the mixture was refluxed at 80°C for 1 h. The workup procedure is the same as above.

(*R,R*)-149a White solid. The data obtained is consistent with literature.^[113]

(*R,R*)-149b White solid. Recrystallized from DCM/*n*-hexane. $[\alpha]_{\text{D}} = -453$ (*c* 0.1, DCM). Mp: $144\text{--}145^\circ\text{C}$. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 45.2; ^1H NMR (CDCl_3 , 300 MHz): δ 8.03–7.98 (m, 4H, Ar), 7.94–7.90 (m, 4H, Ar), 7.42–7.36 (m, 12H, Ar), 7.32–7.31 (m, 6H, Ar), 7.16 (t, $^3J = 7.5$ Hz, 4H, Ar), 6.86 (s, 2H, Ar), 4.89–4.82 (m, 2H, PCHCH_2), 3.35–3.22 (m, 2H, PCHCHH), 3.10–2.99 (m, 2H, PCHCHH), 1.96 (s, 3H, ArCH_3); ^{13}C NMR (CDCl_3 , 100 MHz): δ 197.7 (t, $^3J_{\text{CP}} = 5.2$ Hz, 2C, COPh), 154.5–125.4 (42C, Ar), 47.6 (t, 2C, $^1J_{\text{CP}} = 14.8$ Hz, PCH), 44.9 (t, $^2J_{\text{PC}} = 4.3$ Hz, 2C, PCHCH_2), 31.6 (1C, ArCH_3). HRMS (+ESI) *m/z*: ($\text{M} - \text{Cl}$)⁺ calcd for $\text{C}_{49}\text{H}_{41}\text{O}_2\text{P}_2\text{Pd}$, 829.1617; found, 829.1636. Anal. Calcd for $\text{C}_{49}\text{H}_{41}\text{ClO}_2\text{P}_2\text{Pd}$: C, 67.98; H, 4.77. Found: C, 68.18; H, 4.99%.

(*R,R*)-149c White solid. $[\alpha]_{\text{D}} = -499$ (*c* 0.1, DCM). Mp: $150\text{--}151^\circ\text{C}$. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121 MHz): δ 45.0; ^1H NMR (CDCl_3 , 500 MHz): δ 8.03–8.02 (m, 4H, Ar), 7.89–7.88 (m, 4H, Ar), 7.41–7.38 (m, 12H, Ar), 7.33–7.32 (m, 6H, Ar), 7.19–7.17 (m, 4H, Ar), 6.67 (s, 2H, Ar), 4.89–4.85 (m, 2H, PCHCH_2), 3.51 (s, 3H, OCH_3), 3.35–3.29 (m, 2H, PCHCHH), 3.05–2.99 (m, 2H, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 197.5 (2C, COPh), 158.5 (1C, COCH_3), 152.7–110.7 (41C, Ar), 55.1 (1C, COCH_3), 47.9 (2C, PCH), 44.7 (2C, PCHCH_2). HRMS (+ESI) *m/z*: ($\text{M} - \text{Cl}$)⁺ calcd for $\text{C}_{49}\text{H}_{41}\text{O}_3\text{P}_2\text{Pd}$, 845.1566;

found, 845.1586. Anal. Calcd for $C_{49}H_{41}ClO_3P_2Pd$: C, 66.75; H, 4.69. Found: C, 67.08; H, 5.00%.

(*S,S*)-**149d** White solid. Recrystallized from DCM/*n*-hexane. $[\alpha]_D = +445$ (*c* 0.1, DCM). Mp: 225-227°C. $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ 44.2; 1H NMR ($CDCl_3$, 400 MHz): δ 8.05-8.00 (m, 4H, Ar), 7.89-7.85 (m, 4H, Ar), 7.44-7.38 (m, 12H, Ar), 7.34-7.32 (m, 6H, Ar), 7.22-7.18 (m, 4H, Ar), 6.86 (d, $^3J = 9.4$ Hz, 2H, Ar), 4.91-4.85 (m, 2H, *PCHCH*₂), 3.36-3.27 (m, 2H, *PCHCHH*), 3.08-3.02 (m, 2H, *PCHCHH*); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.1 (t, $^3J_{CP} = 5.5$ Hz, 2C, *COPh*), 162.8-111.8 (42C, Ar), 47.6 (t, $^2J_{CP} = 14.6$ Hz, 2C, *PCH*), 44.6 (2C, *PCHCH*₂). HRMS (+ESI) *m/z*: (*M* - Cl)⁺ calcd for $C_{48}H_{38}FO_2P_2Pd$, 833.1366; found, 833.1366. Anal. Calcd for $C_{48}H_{38}FCIO_2P_2Pd$: C, 66.29; H, 4.40. Found: C, 66.65; H, 4.55%.

(*R,R*)-**149e** White solid. $[\alpha]_D = -414$ (*c* 0.1, DCM). Mp: 162-164°C. $^{31}P\{^1H\}$ NMR ($CDCl_3$, 121 MHz): δ 45.0; 1H NMR ($CDCl_3$, 400 MHz): δ 8.06-8.04 (m, 4H, Ar), 7.86-7.84 (m, 4H, Ar), 7.41-7.38 (m, 12H, Ar), 7.30 (s, 2H, Ar), 6.98 (d, $^3J = 10.6$ Hz, 2H, Ar), 6.71 (t, $^3J = 7.7$ Hz, 1H, Ar), 6.21 (d, $^4J = 3.5$ Hz, 2H, Ar), 6.14-6.12 (m, 2H, Ar), 4.77-4.71 (m, 2H, *PCHCH*₂), 3.18-3.09 (m, 2H, *PCHCHH*), 2.82-2.74 (m, 2H, *PCHCHH*); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 186.4 (d, $^3J_{CP} = 6.5$ Hz, 2C, *C=O*), 152.3 (2C, *O-CC=O*), 151.1 (2C, *C-O-CC=O*), 146.9-112.2 (34C, Ar), 48.1 (d, $^3J_{CP} = 15.1$ Hz, 2C, *PCH*), 44.6 (2C, *PCHCH*₂). HRMS (+ESI) *m/z*: (*M* - Cl)⁺ calcd for $C_{44}H_{35}O_4P_2Pd$, 795.1045; found, 795.1055. Anal. Calcd for $C_{44}H_{35}ClO_4P_2Pd$: C, 63.55; H, 4.24. Found: C, 63.74; H, 4.52%.

(*R,R*)-**149f** White solid. $[\alpha]_D = -439$ (*c* 0.1, DCM). Mp: 176-178°C. $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 MHz): δ 45.2; 1H NMR ($CDCl_3$, 500 MHz): δ 8.42-8.41 (m, 2H, Ar), 7.96-7.94 (m, 8H, Ar), 7.65-7.64 (m, 4H, Ar), 7.39-7.38 (m, 6H, Ar), 7.33-7.32 (m, 2H, Ar), 7.22-7.21 (m, 6H, Ar), 7.07 (d, $^3J = 7.6$ Hz, 2H, Ar), 6.88 (t, $^3J = 7.5$ Hz, 1H, Ar), 4.96-

4.91 (m, 2H, PCHCH₂), 3.72-3.65 (m, 2H, PCHCHH), 3.53-3.45 (m, 2H, PCHCHH); ¹³C NMR (CDCl₃, 125 MHz): δ 198.6 (d, ³J_{CP} = 4.3 Hz, 2C, C=O), 167.8-121.5 (40C, Ar), 47.7 (d, ²J_{CP} = 7.3 Hz, 2C, PCH), 44.4 (2C, PCHCH₂). HRMS (+ESI) m/z: (M - Cl)⁺ calcd for C₄₆H₃₇N₂O₂P₂Pd, 817.1365; found, 8317.1365. Anal. Calcd for C₄₆H₃₇N₂ClO₂P₂Pd: C, 64.72; H, 4.37; N, 3.28. Found: C, 64.95; H, 4.59; N, 3.16%.

(*R,R*)-**149g** White solid. [α]_D = -416 (c 0.1, DCM). Mp: 173-175°C. ³¹P{¹H} NMR (CDCl₃, 202 MHz): δ 44.5; ¹H NMR (CDCl₃, 500 MHz): δ 8.01-7.97 (m, 4H, Ar), 7.88-7.85 (m, 4H, Ar), 7.43-7.38 (m, 6H, Ar), 7.33-7.31 (m, 6H, Ar), 7.24-7.21 (m, 4H, Ar), 7.07-7.04 (m, 4H, Ar), 6.99 (d, ³J = 7.6 Hz, 2H, Ar), 6.74 (t, ³J = 7.6 Hz, 1H, Ar), 4.85-4.81 (m, 2H, PCHCH₂), 3.29-3.22 (m, 2H, PCHCHH), 2.96-2.89 (m, 2H, PCHCHH); ¹³C NMR (CDCl₃, 125 MHz): δ 196.7 (t, ³J_{CP} = 5.4 Hz, 2C, C=O), 158.6-124.7 (42C, Ar), 48.1 (d, ²J_{CP} = 13.5 Hz, 2C, PCH), 44.7 (2C, PCHCH₂). HRMS (+ESI) m/z: (M - Cl)⁺ calcd for C₄₈H₃₇Cl₂O₂P₂Pd, 883.0681; found, 883.0686. Anal. Calcd for C₄₈H₃₇Cl₃O₂P₂Pd: C, 62.63; H, 4.05. Found: C, 62.88; H, 4.41%.

(*R,R*)-**149h** White solid. The data obtained is consistent with literature.^[112c]

(*R,R*)-**149i** Pale yellow solid. [α]_D = -471 (c 0.1, DCM). Mp: 178-180°C. ³¹P{¹H} NMR (CDCl₃, 202 MHz): δ 46.5 (¹J_{P-Pt} = 2936.2 Hz); ¹H NMR (CDCl₃, 500 MHz): δ 8.06-8.01 (m, 4H, Ar), 7.94-7.90 (m, 4H, Ar), 7.50-7.46 (m, 6H, Ar), 7.41-7.39 (m, 6H, Ar), 7.28-7.24 (m, 6H, Ar), 7.17 (t, ³J = 7.8 Hz, 4H, Ar), 6.81 (d, ³J = 9.4 Hz, 2H, Ar) 5.07-4.92 (m, 2H, PCHCH₂), 3.35-3.15 (m, 2H, PCHCHH), 3.13-3.09 (m, 2H, PCHCHH); ¹³C NMR (CDCl₃, 100 MHz): δ 197.2 (t, ³J_{CP} = 4.2 Hz, 2C, C=O), 152.8 (m, 1C, CF), 140.8-127.9 (39C, Ar), 111.5-111.1 (2C, CCF), 47.4 (t, ²J_{CP} = 18.4 Hz, 2C, PCH), 44.1 (2C, PCHCH₂). HRMS (+ESI) m/z: (M - Cl)⁺ calcd for C₄₈H₃₈FO₂P₂Pt, 922.1979; found, 922.1980. Anal. Calcd for C₄₈H₃₈ClFO₂P₂Pt: C, 60.16; H, 4.00. Found: C, 60.44; H, 4.32%.

(*R,R*)-**149j** Pale yellow solid. $[\alpha]_D = -463$ (c 0.1, DCM). Mp: 175-177°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 46.4 ($^1J_{\text{P-Pt}} = 2965.0$ Hz); ^1H NMR (CDCl_3 , 400 MHz): δ 8.06-8.02 (m, 4H, Ar), 7.96-7.91 (m, 4H, Ar), 7.48-7.44 (m, 6H, Ar), 7.38-7.35 (m, 6H, Ar), 7.25-7.21 (m, 6H, Ar), 7.14 (t, $^3J = 7.4$ Hz, 4H, Ar), 6.65 (s, 2H, Ar) 5.04-4.92 (m, 2H, PCHCH_2), 3.50 (s, 3H, $-\text{OCH}_3$), 3.26-3.13 (m, 2H, PCHCHH), 3.12-3.06 (m, 2H, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 197.5 (t, $^3J_{\text{CP}} = 4.2$ Hz, 2C, $\text{C}=\text{O}$), 158.0 (1C, COMe), 152.3-152.1 (2C, MeOCCHC), 136.6-127.7 (37C, Ar), 110.2-110.0 (2C, MeOCC), 55.1 (1C, OCH_3), 47.6 (t, $^2J_{\text{CP}} = 18.5$ Hz, 2C, PCH), 44.2 (2C, PCHCH_2). HRMS (+ESI) m/z : $(\text{M} - \text{Cl})^+$ calcd for $\text{C}_{49}\text{H}_{41}\text{O}_3\text{P}_2\text{Pt}$, 934.2179; found, 934.2178. Anal. Calcd for $\text{C}_{49}\text{H}_{41}\text{ClO}_3\text{P}_2\text{Pt}$: C, 60.65; H, 4.26. Found: C, 60.94; H, 4.61%.

(*R,R*)-**149k** Yellow solid. $[\alpha]_D = -431$ (c 0.1, DCM). Mp: 168-170°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 44.7; ^1H NMR (CDCl_3 , 400 MHz): δ 8.02-8.00 (m, 4H, Ar), 7.86-7.85 (m, 4H, Ar), 7.46-7.40 (m, 12H, Ar), 7.22-7.19 (m, 10H, Ar), 6.89-6.88 (m, 2H, Ar), 6.78-6.76 (m, 1H, Ar), 4.75-4.76 (m, 2H, PCHCH_2), 3.34-3.31 (m, 2H, PCHCHH), 3.15-3.10 (m, 2H, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 197.9 (2C, $\text{C}=\text{O}$), 154.4-123.9 (42C, Ar), 46.7 (d, $^2J_{\text{CP}} = 15.9$ Hz, 2C, PCH), 44.9 (2C, PCHCH_2). HRMS (+ESI) m/z : $(\text{M} - \text{Cl})^+$ calcd for $\text{C}_{48}\text{H}_{39}\text{NiO}_2\text{P}_2$, 767.1779; found, 767.1780. Anal. Calcd for $\text{C}_{48}\text{H}_{39}\text{ClNiO}_2\text{P}_2$: C, 71.71; H, 4.89. Found: C, 71.99; H, 5.11%.

(*R,R*)-**150a** White solid. The data obtained is consistent with literature.^[151d]

(*R,R*)-**150b** White solid. Recrystallized from DCM/*n*-hexane. $[\alpha]_D = -424$ (c 0.1, DCM). Mp: 209-211°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 47.2; ^1H NMR (CDCl_3 , 400 MHz): δ 8.01-7.96 (m, 4H, Ar), 7.85-7.81 (m, 4H, Ar), 7.44-7.34 (m, 6H, Ar), 7.30-7.19 (m, 15H, Ar), 7.14 (dd, $^3J = 5.6, 7.7$ Hz, 6H, Ar), 7.03-7.01 (m, 4H, Ar), 6.80-6.78 (m, 4H, Ar), 4.94-4.90 (m, 2H, PCH), 4.71 (d, $^2J = 12.4$ Hz, 2H, $\text{CO}_2\text{CH}_2\text{Ph}$), 4.40 (d, $^2J = 12.5$ Hz, 2H, $\text{CO}_2\text{CH}_2\text{Ph}$), 4.36 (d, $^2J = 12.4$ Hz, 2H, $\text{CO}_2\text{CH}_2\text{Ph}$), 4.08 (d, $^2J = 12.4$ Hz,

2H, CO₂CH₂Ph) 3.86 (dd, ³*J* = 7.0, 15.2 Hz, 2H, PCHCH); ¹³C NMR (CDCl₃, 100 MHz): δ 166.6 (2C, CO₂Bn), 166.1 (t, ³*J*_{CP} = 5.5 Hz, 2C, CO₂Bn), 161.4-125.8 (54C, Ar), 66.9 (2C, CO₂CH₂Ph), 66.2 (2C, CO₂CH₂Ph), 56.1 (2C, PCHCH), 51.2 (t, ²*J*_{CP} = 13.0 Hz, 2C, PCH). HRMS (+ESI) *m/z*: (M - Cl)⁺ calcd for C₆₆H₅₅O₈P₂Pd, 1143.2407; found, 1143.2440. Anal. Calcd for C₆₆H₅₅ClO₈P₂Pd: C, 67.18; H, 4.70. Found: C, 67.48; H, 4.97%.

(*R,R*)-**150c** White solid. Recrystallized from DCM/*n*-hexane. [α]_D = -505 (*c* 0.1, DCM). Mp: 236-238°C. ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 50.1 (¹*J*_{P-Pt} = 3040.4 Hz); ¹H NMR (CDCl₃, 400 MHz): δ 8.01-7.96 (m, 4H, Ar), 7.87-7.84 (m, 4H, Ar), 7.49-7.40 (m, 12H, Ar), 7.06 (d, ³*J* = 7.5 Hz, 2H, Ar), 6.94 (t, ³*J* = 7.5 Hz, 1H, Ar), 4.96-4.80 (m, 2H, PCH), 3.89-3.83 (m, 2H, PCHCH), 3.18 (s, 6H, CO₂CH₃), 2.70 (s, 6H, CO₂CH₃); ¹³C NMR (CDCl₃, 100 MHz): δ 167.4 (t, ³*J*_{CP} = 6.1 Hz, 4C, CO₂CH₃), 149.6-125.0 (30C, Ar), 55.3 (2C, CO₂CH₃), 52.4 (2C, CO₂CH₃), 51.7 (2C, PCHCH), 51.3 (t, ²*J*_{CP} = 17.8 Hz, 2C, PCH). HRMS (+ESI) *m/z*: (M - Cl)⁺ calcd for C₄₂H₃₉O₈P₂Pt, 928.1768; found, 928.1777. Anal. Calcd for C₄₂H₃₉ClO₈P₂Pt: C, 52.32; H, 4.08. Found: C, 52.66; H, 4.45%.

(*R,R*)-**150d** Yellow solid. Recrystallized from DCM/*n*-hexane. [α]_D = -440 (*c* 0.1, DCM). Mp: 219-221°C. ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 46.5; ¹H NMR (CDCl₃, 400 MHz): δ 7.92-7.84 (m, 8H, Ar), 7.43-7.40 (m, 8H, Ar), 7.35 (t, ³*J* = 7.4 Hz, 4H, Ar), 6.95 (d, ³*J* = 7.3 Hz, 2H, Ar), 6.88 (t, ³*J* = 7.1 Hz, 1H, Ar), 4.66-4.61 (m, 2H, PCH), 3.97-3.91 (m, 2H, PCHCH), 3.20 (s, 6H, CO₂CH₃), 2.81 (s, 6H, CO₂CH₃); ¹³C NMR (CDCl₃, 100 MHz): δ 167.7 (2C, CO₂CH₃), 167.6 (2C, CO₂CH₃), 149.4-125.0 (30C, Ar), 56.5 (2C, CO₂CH₃), 52.5 (2C, CO₂CH₃), 52.0 (2C, PCHCH), 50.1 (t, ²*J*_{CP} = 15.1 Hz, 2C, PCH). HRMS (+ESI) *m/z*: (M - Cl)⁺ calcd for C₄₂H₃₉NiO₈P₂, 791.1474; found, 791.1477. Anal. Calcd for C₄₂H₃₉ClNiO₈P₂: C, 60.94; H, 4.75. Found: C, 61.15; H, 5.05%.

Synthesis of N-(3-bromobenzyl)-N-isopropylpropan-2-amine, **151b**.

Dibromide **151a** (0.495 g, 1.98 mmol, 1.0 equiv.) and diisopropylamine (1.39 mL, 9.91 mmol, 5.0 equiv.) in toluene (10 mL) was heated at 85°C for 1 wk. The volatiles were removed, the crude product was redissolved in DCM, washed with water (3 x 30 mL), dried over MgSO₄, filtered and the solvent was reduced to afford the pure amine **151b** as a yellow oil (0.525 g, 98%). ¹H NMR (CDCl₃, 500 MHz): δ 7.57 (s, 1H, Ar), 7.34-7.31 (m, 2H, Ar), 7.16 (t, ³J = 7.8 Hz, 1H, Ar), 3.63 (s, 2H, ArCH₂N), 3.04-3.02 (m, 2H, NCH(CH₃)₂), 1.04 (d, ³J = 6.7 Hz, 12H, NCH(CH₃)₂); ¹³C NMR (CDCl₃, 125 MHz): δ 146.1 (1C, Ar), 131.0-122.6 (5C, Ar), 48.8 (1C, ArCH₂N), 48.2 (2C, NCH(CH₃)₂), 21.0 (12C, NCH(CH₃)₂). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₁₃H₂₁BrN, 270.0857; found, 270.0857. Anal. Calcd for C₁₃H₂₀BrN: C, 57.78; H, 7.46; N, 5.18. Found: C, 57.86; H, 7.49; N, 5.11%.

Synthesis of 3-((diisopropylamino)methyl)benzaldehyde, 151c. *t*-BuLi (4.40 mmol, 1.7M in pentane, 2.0 equiv.) was added dropwise to a solution of amine **151b** (1.000 g, 3.70 mmol, 1.0 equiv.) in DEE (15 mL) at -78°C and stirred for 1h before DMF (0.408 mL, 5.55 mmol, 1.5 equiv.) was added. The mixture was allowed to stir at RT overnight and quenched with water. The solution was extracted with EA (3 x 50 mL), washed with water (1 x 50 mL), dried over MgSO₄, filtered and volatiles were removed. The crude product was purified *via* silica gel column chromatography to afford the aldehyde **151c** as a yellow solid (0.730 g, 90%). Mp: 63-64°C. ¹H NMR (CDCl₃, 500 MHz): δ 10.00 (d, ³J = 5.4 Hz, 1H, HC=O), 7.88 (s, 1H, CHOCCHCCH₂N), 7.70 (d, ³J = 7.0 Hz, 1H, Ar), 7.67 (d, ³J = 7.1 Hz, 1H, Ar), 7.43 (m, 1H, Ar), 3.70 (d, ⁴J = 4.2 Hz, 2H, ArCH₂N), 3.04-2.98 (m, 2H, NCH(CH₃)₂), 1.03 (d, ³J = 6.6 Hz, 6H, NCH(CH₃)₂), 1.02 (d, ³J = 6.6 Hz, 6H, NCH(CH₃)₂); ¹³C NMR (CDCl₃, 125 MHz): δ 192.1 (1C, HC=O), 144.5-127.7 (6C, Ar), 48.5 (1C, ArCH₂N), 48.0 (2C, NCH(CH₃)₂), 20.7 (4C, NCH(CH₃)₂). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₁₄H₂₂NO, 220.1701; found,

220.1703. Anal. Calcd for $C_{14}H_{21}NO$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.93; H, 9.78; N, 6.41%.

Synthesis of (E)-3-(3-((diisopropylamino)methyl)phenyl)-1-phenylprop-2-en-1-one, **151d.** A mixture of aldehyde **151c** (5 g, 22.80 mmol, 1.0 equiv.) and Wittig reagent **152** (17.35 g, 45.60 mmol, 2.0 equiv.) in toluene (150 mL) was refluxed for 1d. Upon cooling, the volatiles were removed and the crude mixture extracted with EA (3 x 60 mL). The organic layers were combined and washed with water (1 x 60 mL), dried over $MgSO_4$, filtered and evaporated to dryness. The crude product was purified *via* silica gel column chromatography (*n*-hexane) to afford enone **151d** as a yellow solid on standing (5.862 g, 80%). Mp: 96-97°C. 1H NMR ($CDCl_3$, 500 MHz): δ 8.02 (d, $^3J = 7.3$ Hz, 2H, Ar), 7.82 (d, $^3J = 15.8$ Hz, 1H, $ArCH=CH$), 7.66 (s, 1H, Ar), 7.60-7.44 (m, 6H, Ar + $ArCH=CH$), 7.35-7.32 (m, 1H, Ar), 3.68 (s, 2H, $ArCH_2N$), 3.03 (h, $^3J = 6.6$ Hz, 2H, $NCH(CH_3)_2$), 1.04 (d, $^3J = 6.6$ Hz, 6H, $NCH(CH_3)_2$), 1.03 (d, $^3J = 6.6$ Hz, 6H, $NCH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 190.7 (1C, $C=O$), 145.6-121.8 (14C, Ar + $ArCH=CH$ + $ArCH=CH$), 48.8 (1C, $ArCH_2N$), 48.0 (2C, $NCH(CH_3)_2$), 20.8 (4C, $NCH(CH_3)_2$). HRMS (+ESI) m/z : $(M + H)^+$ calcd for $C_{22}H_{28}NO$, 322.2171; found, 322.2173. Anal. Calcd for $C_{22}H_{27}NO$: C, 82.20; H, 8.47; N, 4.36. Found: C, 82.34; H, 8.58; N, 4.49%.

General Procedure for Preparation of PCN Pincers, (R)-153a-b. To a solution of Ph_2PH (0.636 mmol, 1.1 equiv.) in toluene (5 mL) was added catalyst (*S*)-**119** (0.029 mmol, 5 mol %) and stirred for 10 minutes before cooling to -80°C. The ligand precursor **151d** (0.578 mmol, 1.0 equiv.) was added followed by the addition of NEt_3 (0.578 mmol, 1.0 equiv.) in toluene (1 mL) dropwise. The solution was stirred at -80°C and the completion of the reaction was monitored by $^{31}P\{^1H\}$ NMR. Upon completion, the solution was allowed to reach room temperature. Volatiles were removed under reduced

pressure to afford crude phosphine which was immediately metalated with $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (0.578 mmol, 1.0 equiv.) in DCM (10 mL) and stirred overnight at room temperature. The solvent was removed and the crude product was purified *via* silica gel column chromatography (DCM or 19 DCM : 1 EA) to afford white solid of complex (*R*)-**153a**.

Note: The preparation of (*R*)-**153b** was done with $\text{PtCl}_2(\text{CH}_3\text{CN})_2$ in refluxing toluene and purified with silica gel column chromatography (19 DCM : 1 EA) to afford the white solid. The *ee* of the PCN ligand (*R*)-**151e** was determined upon coordination to the chiral derivatizing agent **66** (*vide supra*).

(*R*)-**153a**. Recrystallized from DCM/DEE after conversion of Cl to ONO_2 . $[\alpha]_{\text{D}} = -265$ (*c* 0.1, DCM). Mp: 189-191°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ 57.2; ^1H NMR (CDCl_3 , 500 MHz): δ 8.24-8.20 (m, 2H, Ar), 7.75 (dd, $^3J = 11.7$, 7.9 Hz, 2H, Ar), 7.53 (d, $^3J = 8.2$ Hz, 2H, Ar), 7.46-7.44 (m, 4H, Ar), 7.29 (t, $^3J = 7.8$ Hz, 2H, Ar), 7.20-7.13 (m, 3H, Ar), 6.92 (d, $^4J = 4.1$ Hz, 2H, Ar), 6.82 (t, $^4J = 4.5$ Hz, 1H, Ar), 5.06-5.01 (m, 1H, $\text{NCH}(\text{CH}_3)_2$), 4.32 (d, $^2J = 16.8$ Hz, 1H, ArCHHN), 3.99-3.96 (m, 1H, PCHCH_2), 3.85 (d, $^2J = 16.9$ Hz, 1H, ArCHHN), 3.40-3.36 (m, 1H, PCHCHH), 3.29-3.23 (m, 1H, PCHCHH), 3.15-3.06 (m, 1H, $\text{NCH}(\text{CH}_3)_2$), 1.77 (d, $^3J = 6.3$ Hz, 3H, NCHCH_3), 1.68 (d, $^3J = 6.4$ Hz, 3H, NCHCH_3), 1.40 (d, $^3J = 6.3$ Hz, 3H, NCHCH_3), 1.11 (d, $^3J = 6.5$ Hz, 3H, NCHCH_3); ^{13}C NMR (CDCl_3 , 125 MHz): δ 197.2 (1C, C=O), 158.6-119.4 (24C, Ar), 60.8 (1C, ArCH_2N), 59.1 (1C, ArCH_2NCH), 55.4 (1C, ArCH_2NCH), 48.3 (d, $^2J_{\text{CP}} = 35.2$ Hz, 1C, PCHCH_2), 44.5 (1C, PCH), 31.6 (1C, NCHCH_3), 23.0 (1C, NCHCH_3), 22.6 (1C, NCHCH_3), 14.2 (1C, NCHCH_3). HRMS (+ESI) m/z : $(\text{M} - \text{Cl})^+$ calcd for $\text{C}_{34}\text{H}_{37}\text{NOPPd}$, 612.1648; found, 612.1656. Anal. Calcd for $\text{C}_{34}\text{H}_{37}\text{ClNOPPd}$: C, 62.97; H, 5.75; N, 2.16. Found: C, 63.15; H, 5.96; N, 2.18%.

(*R*)-**153b**. $[\alpha]_D = -251$ (*c* 0.1, DCM). Mp: 233-235°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ 36.1 ($^1J_{\text{P-Pt}} = 4416.5$ Hz); ^1H NMR (CDCl_3 , 500 MHz): δ 8.32-8.28 (m, 2H, Ar), 7.75 (dd, $^3J = 12.0$, 7.3 Hz, 2H, Ar), 7.52-7.43 (m, 6H, Ar), 7.29-7.28 (m, 2H, Ar), 7.16-7.07 (m, 3H, Ar), 6.94-6.82 (m, 3H, Ar), 4.95-4.90 (m, 1H, $\text{NCH}(\text{CH}_3)_2$), 4.40 (d, $^2J = 16.4$ Hz, 1H, ArCHHN), 4.31-4.28 (m, 1H, PCHCH_2), 4.02 (d, $^2J = 16.4$ Hz, 1H, ArCHHN), 3.66-3.64 (m, 1H, PCHCHH), 3.32-3.25 (m, 1H, PCHCHH), 3.07-2.99 (m, 1H, $\text{NCH}(\text{CH}_3)_2$), 1.78 (d, $^3J = 6.4$ Hz, 3H, NCHCH_3), 1.73 (d, $^3J = 6.4$ Hz, 3H, NCHCH_3), 1.42 (d, $^3J = 6.4$ Hz, 3H, NCHCH_3), 1.18 (d, $^3J = 6.4$ Hz, 3H, NCHCH_3); ^{13}C NMR (CDCl_3 , 125 MHz): δ 197.4 (1C, $\text{C}=\text{O}$), 148.7-118.6 (24C, Ar), 61.0 (1C, ArCH_2N), 56.2 (2C, ArCH_2NCH), 47.9 (d, $^2J_{\text{CP}} = 56.7$ Hz, 1C, PCHCH_2), 44.2 (1C, PCH), 22.9 (1C, NCHCH_3), 22.5 (1C, NCHCH_3), 22.0 (1C, NCHCH_3), 14.2 (1C, NCHCH_3). HRMS (+ESI) m/z : ($\text{M} - \text{Cl}$) $^+$ calcd for $\text{C}_{34}\text{H}_{37}\text{NOPPt}$, 701.2261; found, 701.2289. Anal. Calcd for $\text{C}_{34}\text{H}_{37}\text{ClNOPPt}$: C, 55.40; H, 5.06; N, 1.90. Found: C, 55.75; H, 5.38; N, 2.18%.

General Procedure for Catalytic Addition of Diphenylphosphine to Chalcone.

A solution of catalyst (25 μmol , 5 mol %) and AgOAc (25 μmol , 5 mol %) in DCM (1 mL) was stirred for 1 h in the dark then filtered through a plug of silica gel. The volatiles were removed and the treated catalyst was added to a solution of diphenylphosphine (0.5 mmol, 1.0 equiv.) in DCM (1 mL). The mixture was stirred at RT followed by the subsequent addition of chalcone (0.5 mmol, 1.0 equiv.). Completion of the reaction was determined by the disappearance of the phosphorus signal attributed to diphenylphosphine (-40 ppm) in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum. Upon reaction completion, aq. H_2O_2 (0.1 mL, 30% v/v) was added and stirred for 30 mins. The volatiles were removed under reduced pressure and the crude product was directly loaded onto silica gel column (3 EA : 2 *n*-hexane) to afford the pure product **157**. The data obtained is consistent with literature.^[112b] The *ee* of the oxidized phosphine **157** was determined on a

Daicel Chiralpak IC column with *n*-hexane/2-propanol = 80/20, flow = 0.8 mL/min, wavelength = 240 nm. Retention times: 16.7 min, 24.0 min.

Chapter 3 Chiral Diphosphine Ligands in Copper Clusters

3.1 General Introduction to Copper Clusters

Of all the transition metals, copper is undoubtedly one of the cheapest and abundant metals that is extremely versatile from a coordination viewpoint, with its complexes freely accessing the coordination numbers of two to six.^[170] This characteristic, together with the coordinative lability of copper, have resulted in the extensive application of copper complexes across various fields such as homogeneous catalysis,^[171] organic synthesis,^[172] and the generation of metal-organic coordination complexes.^[173] Over the last few decades, copper clusters have attracted overwhelming attention due to their unusual yet interesting magnetic, structural and photophysical properties.^[174] For example, in 1998, Che discovered a copper(I) diphosphine cluster that is highly luminescent with a good quantum yield.^[175] Other reports include the applications of copper clusters in enzyme modelling,^[173a,174d,f] optics^[174i] and catalysis.^[176] The coordination driven self assembly processes often result in unique architectures^[177] such as helicates, tetrahedra and mesocates. It is noted that copper clusters predominantly involve polydentate ligands containing either nitrogen or oxygen donor atoms.^[178] Although phosphines have established themselves as valuable ligands in many areas of coordination chemistry,^[22] their involvement in copper clusters remains limited mainly due to the presence of bulky substituents and irregular shapes. This inevitably results in the unpredictable formation of complex geometries and reduces the probability of constructing well-defined structures.^[179] Copper clusters with cubane $\text{Cu}_4\text{X}_4\text{L}_4$ (X = halogen, L = ligand) and “drum-like” $\text{Cu}_6\text{X}_6\text{L}_6$ cores (see Figure 3.30) have been reported in the 1960s,^[180] but lack of applications and challenges faced in their syntheses^[181] led to the loss of interest. It was only until much later that the catalytic properties of copper clusters were recognized and attracted much attention.^[176b,d,182] Since then, copper

clusters bearing various phosphine moieties such as PR_3 ($\text{R} = \text{Et}, \text{NMe}_2, \text{Ph}, t\text{-Bu}$),^[183] $\text{PPh}_2\text{R}'$ ($\text{R}' = \text{Me}, \text{Cy}$)^[184] and diphosphine ligands^[174g,185] have been described in literature.

Figure 3.30. Structural representations of cubane Cu_4X_4 (**1**) and “drum-like” Cu_6X_6 (**2**) units (Ligands are omitted for clarity).

The synthesis of chiral phosphines *via* catalytic methods are extremely limited.^[50,85,109d,112,113,186] Their preparations often rely on the chiral pool of compounds or tedious synthetic processes involving protection-deprotection and resolution steps.^[50,186a,b,187] Furthermore, most phosphines are air-sensitive and therefore difficult to handle, which will indirectly affect the efficiencies of these stepwise protocols. Henceforth, it is essential to develop an effective methodology to provide access to optically pure phosphines. Their subsequent coordination to form copper clusters along with the abilities to control the architectures are of paramount importance in order to generate a viable molecular library for these types of unusual yet interesting compounds.

3.2 Results and Discussion

The successful syntheses of chiral PCP pincer complexes employing diphosphines **147** and **148** have enticed us to consider the direct addition of copper(I) and copper(II) ions to the same ligands. Herein, we report the one-pot syntheses of chiral 12-membered “drum-like” $\text{Cu}_6\text{X}_6\text{L}_3$ ($\text{L} = \text{diphosphine ligand}$) and 8-membered “chair-like” $\text{Cu}_4\text{X}_4\text{L}_2$ copper clusters bearing bridging diphosphine ligands with C-stereogenic centers. In order to demonstrate the versatility of the synthetic method, the same experimental procedures were repeated with a variety of diphosphine ligands. In each instance, the desired

products were obtained in 72-89% isolated yields. Several X-ray quality crystals of the clusters were obtained and studied in greater detail along with a preliminary examination to gauge the potential of the generated clusters in the asymmetric hydroboration (AHB) of α,β -unsaturated ketones.

3.2.1 Syntheses of Copper-Phosphine Clusters

The existence of polynuclear Cu(II) complexes^[188] in literature is relatively scarce as compared to their Cu(I) counterparts. To explore the formation of a Cu(II) complex with diphosphine **147a**, an ethanolic solution of CuCl₂ and **147a** in a 1:1 mole ratio was refluxed overnight. A ³¹P{¹H} NMR of the crude reaction mixture revealed that roughly 50% of **147a** was unreacted. Another equivalence of CuCl₂ was added to the mixture and after 10 h of further heating, **147a** was completely reacted. The ³¹P{¹H} NMR spectra of the mixture exhibited 3 signals at 44.4, 32.1 and -1.2 ppm in approximately 1:40:30 ratio. The purification of the crude mixture *via* silica gel column chromatography yielded three products, each corresponding to one phosphorus signal on ³¹P{¹H} NMR. Upon further investigation, it was established that the resonance signal at 32.1 ppm belonged to the oxidized derivative of **147a**. The identity of cluster **160a** (³¹P{¹H} NMR = -1.2 ppm) was elucidated by X-ray crystallographic studies upon recrystallization of the complex from

Scheme 3.46. Syntheses of Cu₄Cl₄L₂ (L = diphosphine ligand) and Cu₆Cl₆L₃ copper clusters.

DCM/*n*-hexane. The molecular structure of the tetra-coordinated Cu(I) cluster **160a** is depicted in Figures 3.31 and 3.32. Due to the extremely low isolated yield of product **159** ($^3\text{P}\{^1\text{H}\}$ NMR = 44.4 ppm), the synthesis was repeated on a larger scale with the racemic phosphine ($\pm$)-**147a**. Subsequently, an X-ray quality crystal of complex ($\pm$)-**159** was obtained and the molecular structure is shown in Figures 3.33 and 3.34. The selected bond lengths and angles of clusters **159** and **160a** will be presented in Section 3.2.2.

Figure 3.31. Molecular structure of complex **160a**. Hydrogen atoms except H(C13), H(C28), H(C61), H(C76), H(C109) and H(C124) were omitted for clarity.

Figure 3.32. Coordination sphere around the copper atoms in complex **160a**. The carbon backbones of the diphosphine ligands are omitted for clarity.

Figure 3.33. Molecular structure of complex **159**. All hydrogen atoms were omitted for clarity.

Figure 3.34. Coordination sphere around the copper atoms in complex **159**. The carbon backbones of the diphosphine ligands are omitted for clarity.

From the results above, we were intrigued by three aspects: (1) the copper centers of **159** and **160a** are in the +1 oxidation state, but the source of copper (CuCl_2) is in the +2 oxidation state, (2) the large proportion of oxidized phosphine **158a**, and (3) the self-assembly processes leading to the formation of clusters **159** and **160a**. In the 1990s, Corain observed the reduction of Cu(II) to Cu(I) ions in the presence of phosphine ligands.^[189] Following an extensive literature search, it was discovered that the reduction of CuCl_2 by carbonyl compounds^[190] was also plausible. Hence we postulated that the presence of an alternative source of reducing agent such as a carbonyl compound could replace the sacrificial role of the phosphine. To test our theory, the one-pot *in-situ*

reduction of CuCl_2 by acetone and coordination of diphosphine **147a** was attempted. The experiment was initially conducted with CuCl_2 and **147a** in a 2:1 mole ratio in acetone at room temperature, but no reaction was observed. After refluxing the mixture overnight, $^{31}\text{P}\{^1\text{H}\}$ NMR exhibited two peaks at 44.4 and -1.2 ppm in the ratio of 1:50. Notably, the oxidized phosphine **158a** ($^{31}\text{P}\{^1\text{H}\}$ NMR = 32.1 ppm) was absent. The clusters **159** and **160a** were isolated in 2% and 62% yield respectively. From the observations of the controlled experiment, it is evident that in the presence of acetone as the reducing agent, the reduction of Cu(II) to Cu(I) proceeded while the oxidation of phosphine **147a** was impeded. It should be noted that even though carbonyl functionalities are present on the phosphine ligands, we do not observed their participation in the reduction of Cu(II) to Cu(I) .

After confirming that the copper atoms are in the +1 oxidation state, it was apparent that CuCl can be used in place of CuCl_2 . Following the generation of the chiral

Scheme 3.47. Syntheses of diphosphine ligands and subsequent *in-situ* generation of $\text{Cu}_6\text{Cl}_6\text{L}_3$ clusters.

Table 3.7. Syntheses of copper(I) clusters.^[a]

Entry	145/146	147/148 ^[b]	160	Yield ^[c] (%)
1 ^[d]	145a	(<i>S,S</i>)- 147a	160a	72
2	145b	(<i>R,R</i>)- 147b	160b	72
3	145d	(<i>R,R</i>)- 147d	160c	77
4	145e	(<i>R,R</i>)- 147e	160d	89
5	146a	(<i>R,R</i>)- 148a	160e	85

[a] Conditions: 6 mol % (*S*)-**119**, solvent (**145a, b, d** toluene, **145e** THF, **146a**, DCM). [b] Absolute configurations were determined by X-ray crystallographic data of clusters **160a-e**; see Appendix. The *ee* and *de* of **145a, b, d, e** and **146a** were determined previously (see Table 2.3) [c] Isolated yield. [d] 6 mol % (*R*)-**119** was used instead.

diphosphines by catalytic AHP in >99% *ee* and >96% *de* (see Table 2.3), CuCl was directly added to the crude phosphines in acetone and refluxed overnight to afford the Cu₆Cl₆L₃ clusters **160a-e** exclusively. The formation of the clusters were confirmed by X-ray crystallographic analyses of single crystals obtained from solutions of DCM/*n*-hexane. The individual X-ray structures of clusters **160a-e** and their pertinent crystallographic data can be found in the Appendix.

Based on experimental observations in the formation of clusters **159** and **160a**, the following pathways were proposed for their syntheses. When CuCl₂ (2.0 equiv.) was added to diphosphine **147a** (1.0 equiv.), the generation of complex **159** proceeds *via* an initial coordination of the ligand to CuCl₂, then a sequential reduction of Cu(II) to Cu(I). As such, if CuCl₂ was replaced with CuCl, the formation of cluster **159** will be avoided. On the other hand, the synthesis of cluster **160a** involved the *in-situ* reduction of Cu(II) to Cu(I), followed by coordination of the ligand to the metal center. Hence, even if CuCl was used, the formation of complex **160a** will remain unaffected.

3.2.2 Molecular Structures of Copper-Phosphine Clusters

The large bite angles of the diphosphine ligands employed are the main factor contributing toward the formation of the cluster architectures. Each of the ligand framework wraps itself around the 8-membered “distorted-chair” conformation (cluster **159**) or the 12-membered “drum” core (clusters **160a-e**). The complexes crystallized in

the triclinic P1 (**159**), monoclinic C2 (**160a**), cubic P23 (**160b**) and trigonal R3 (**160c-e**) space groups. The selected bond lengths and angles of each individual cluster will be presented as an average summation of the values (see Table 3.8). The cif files of the complexes may be retrieved from the Cambridge Crystallographic Data Centre^[191] (CCDC) or from literature.^[192] The architecture of complex **159** consists of 4 Cu(I) centers and 4 bridging Cl ligands (see Figures 3.33 and 3.34). The Cu(1) and Cu(1A) atoms possess 18 electrons each whilst the Cu(2) and Cu(2A) have 16 electrons each. The

Table 3.8. Average bond lengths (Å) and angles (°) of the copper-phosphine clusters.^[a]

Complex	Avg. Cu←P (Å)	Range of Cu←P ^[b] (Å)	Avg. Cu-Cl (Å)	Range of Cu-Cl ^[b] (Å)	Avg. P→Cu-Cl (°)	Avg. Cl-Cu-Cl (°)
159	2.189	2.181(2)-2.198(2)	2.382	2.237(2)-2.534(2)	126.32	98.00
160a	2.206	2.202(2)-2.213(2)	2.414	2.345(2)-2.470(2)	118.50	98.89
160b	2.201	2.167(18)-2.234(11)	2.395	2.377(7)-2.413(7)	119.70	99.20
160c	2.199	2.189(15)-2.234(11)	2.405	2.345(4)-2.471(4)	118.69	99.03
160d	2.200	2.199(2)-2.201(2)	2.416	2.350(2)-2.456(2)	118.82	98.41
160e	2.195	2.194(2)-2.195(2)	2.409	2.342(2)-2.446(2)	119.24	97.90

[a] Average bond lengths and angles are calculated from the crystallographic data of the clusters. [b] Range of bond lengths are determined based on the shortest and longest bond lengths.

average P→Cu and Cu-Cl bond lengths (2.189 and 2.382 Å respectively) in the Cu₄Cl₄ framework of **159** are comparable to P→Cu (2.18 Å) and Cu-Cl (2.44 Å) bond lengths reported for other copper cubane complexes.^[193] It is noted that the Cu(I) atoms are not equally bridged by the Cl atoms, in particular, the Cu(1)-Cl(1) bond length is 2.378(2) Å and Cu(1)-Cl(2) is 2.534(2) Å. This could be attributed to the large bite angle of diphosphine **147a** which caused an elongation of the Cu(1)-Cl(2) and Cu(1A)-Cl(2A) bonds. The Cu(1) and Cu(1A) atoms exhibit distorted tetrahedral geometries whereas Cu(2) and Cu(2A) atoms adopt pseudotrigonal planar geometries with a torsion angle of 169.75°. The Cu...Cu distance measured 2.7911(10) Å, which is shorter than the sum of the van der Waals radii (2.80 Å) of Cu(I), indicating the presence of weak metal-metal interactions. The total cavity area within the 8-membered CuCl core of complex **159** is estimated to be 17 Å².

In each of the clusters **160a-e**, the 12-membered core comprises of two interconnecting Cu₃Cl₃ hexagonal faces with three diphosphine ligands extending

outwards from the core (see Figures 3.31 and 3.32). The diphosphine ligand is seen coordinating to Cu atom in the upper hexagonal face and another Cu atom in the lower face (e.g. P(1) attaches to Cu(1) in one face and P(2) to Cu(2) in the other face). Each of the six copper centers Cu(X) adopt a distorted tetrahedral geometry with the neighboring P(X), Cl(X), Cl(Y) and Cl(Z) atoms. The bridging Cl atoms connect the Cu atoms to form the “drum-like” core, ultimately resulting in the generation of a “paddle-wheel” structure for the overall molecular cluster. The C-stereogenic centers in the ligand backbone retain close proximity to the nearest Cu center, thus offering the possibility of stereogenic control on the adjacent metal reaction sites during asymmetric reactions.

In comparison to complex **159**, the solid state structures of clusters **160** revealed that they have slightly longer P→Cu and Cu-Cl bonds but smaller P→Cu-Cl bond angles. Based on examples of four-coordinate phosphine-based CuCl complexes obtained from the Cambridge Structural Database (CSD), the average Cu(I)←P and Cu(I)-Cl bond distances are 2.30 and 2.35 Å, indicating that the clusters **159** and **160** are in good agreement with other structurally stable tetra-coordinated copper(I) chloride complexes. Assuming that the Cu₆Cl₆ core is a right regular hexagonal prism, the cavity volumes of the clusters were determined to be 37 (**160a**), 36 (**160b**), 36 (**160c**), 38 (**160d**) and 37 Å³ (**160e**) respectively. The Cu⋯Cu distances averaged 3.19 (**160a**), 3.22 (**160b**), 3.26 (**160c**), 3.22 (**160d**) and 3.20 Å (**160e**),^[194] which are close to reported structures exhibiting near infrared (NIR) emissions due to Cu⋯Cu interactions,^[174j,n] suggesting the presence of weak cuprophilic interactions.

3.2.3 Spectroscopic and Spectrometric Analysis

To examine the persistence of the complexes in solution, ¹H, ¹³C, ³¹P{¹H} NMR spectroscopic analyses were performed. The ¹H NMR spectra^[195] of complexes **159** and **160a-d** show sharp and distinct peaks that can be assigned to their respective protons on

the diphosphine ligands. The ^{13}C NMR spectra^[196] of the same complexes reveal the highly symmetrical nature of these complexes due to the presence of only one set of signals arising from the diphosphine backbone. However, for cluster **160e**, the relatively broader ^1H and ^{13}C NMR signals^[197] might be attributed to dynamic motions of the flexible aliphatic chains on the ligand. The “chair-like” **159** exhibited a sharp distinct signal at 44.4 ppm,^[198] whereas the clusters **160a-e** displayed slightly broader $^{31}\text{P}\{^1\text{H}\}$ NMR peaks^[199] in the region of -1.2 to 2.4 ppm. The broadening of the signals might be a direct consequence of the relatively weak $\text{P}\rightarrow\text{Cu}$ bonds, thus resulting in dynamic behaviors.^[200] It is interesting to note that the $^{31}\text{P}\{^1\text{H}\}$ chemical shifts of the “drum-like” clusters **160a-e** are similar to their corresponding free diphosphine ligands. This suggests that the phosphorus centers are experiencing similar electronic environment before and after coordination to the Cu(I) ions. On the contrary, the $^{31}\text{P}\{^1\text{H}\}$ signal of complex **159** differs significantly from cluster **160a** even though the same diphosphine **147a** was used. A literature search revealed that a tetranuclear dipyrrolylmethane-based diphosphine Cu_4L_4 ^[201] has a $^{31}\text{P}\{^1\text{H}\}$ NMR signal at -6.2 ppm and the (1-(diphenylphosphino)butan-2-yl)oxy)diphenylphosphine) Cu_2I_2 ^[202] complex shows up at -23.0 ppm. In addition, the ^{31}P chemical shifts of di-, tetra- and octa-nuclear halide and hydride copper(I) complexes with diphosphines of different electronic structures and bite angles remain in a rather narrow range from -21.9 to -3.1 ppm.^[174c,g,200,201] A reasonable explanation for the unusual ^{31}P chemical shift of complex **159** could not be provided, but it is known that the value can vary depending on the metal, ions and coordination number. The persistence of the clusters in solution was further confirmed by high-resolution ESI-MS analysis which detected the presence of the complexes (as indicated by their solid state structures).

3.2.4 Attempted Syntheses of Other Copper(I) Complexes

An investigation on the possibilities of forming other cluster architectures was conducted by: (1) varying the mole ratio of the diphosphine ligand and Cu(I) source, and (2) using other Cu(I) compounds such as CuOTf, CuOAc, CuNO₃ and CuI. A recent report^[201] has demonstrated that a 1:1 ratio of a dipyrrolylmethane-based diphosphine ligand and CuI resulted in the formation of a tri-coordinate Cu(I) complex. When the mole ratio of CuI was doubled, a tetra-coordinate Cu(I) cluster was generated instead. However, our attempts at modifying the ligand to CuCl mole ratio (through 1:4, 1:10 and 1:20) in EtOH, MeOH, acetone or acetonitrile afforded the same Cu₆Cl₆L₃ clusters. The replacement of CuCl with CuOTf, CuOAc and CuNO₃ gave numerous products that could neither be isolated nor identified. The only positive outcome was from the reaction between stoichiometric amounts of phosphine **147a** and CuI in acetone at 65°C for 22 h. A major product^[203] (³¹P{¹H} NMR = -12.6 ppm) was isolated but repeated recrystallization attempts were unsuccessful. The positive mode high-resolution ESI-MS exhibited a fragmentation pattern analogous to that of complex **160a** with a [M+H]⁺ value of 3273.4280 (calculated [M+H]⁺ *m/z* 3273.4272), suggesting the probable formation of a Cu₆I₆L₃ cluster. Further examination did not yield any potential results.

3.2.5 Application of Copper Clusters in Catalytic Hydroboration

In the last decade, several reports on the application of Cu(I)-phosphine^[204] and Cu(I)-NHC^[205] complexes in hydroboration have emerged. The cavities within clusters **160a-e** could essentially control the stereoselectivity of the hydroboration reaction due to the close proximities of the adjacent C-stereogenic centers on the diphosphine backbones. The asymmetric hydroboration (AHB) of the α,β -unsaturated ketone **156** with bis(pinacolato)diboron was carried out efficiently in the presence of clusters **160a-e** as catalysts. The presence of moisture has undesirable effects on the AHB reaction, affecting

both reactivity and yield (Entries 1,2). In most cases, the product **161** was formed almost quantitatively but with low enantioselectivities. Efforts to improve the stereoselectivity by optimization of the reaction conditions were unsuccessful. Nevertheless, this forms the first reported instance of an AHB reaction catalyzed by copper clusters. This catalyst

Table 3.9. Catalytic hydroboration of chalone.^[a]

Entry	cat.	Solvent ^[b]	Base	<i>t</i> (h)	Yield ^[c] (%)	<i>ee</i> ^[d] (%)
1	160a	THF ^[e]	Cs ₂ CO ₃	24	70	9
2	160a	THF	Cs ₂ CO ₃	1	97	9
3	160a	DCM	Cs ₂ CO ₃	1	98	10
4	160a	Dioxane	Cs ₂ CO ₃	1	99	11
5	160a	Toluene	Cs ₂ CO ₃	1	99	11
6	160a	CHCl ₃	Cs ₂ CO ₃	4	95	3
7	160a	DMSO	Cs ₂ CO ₃	24	36	3
8	160a	MeOH	Cs ₂ CO ₃	1	97	3
9	160a	MeCN	Cs ₂ CO ₃	24	78	4
10	160a	MTBE	Cs ₂ CO ₃	1	96	12
11	160a	Benzene	Cs ₂ CO ₃	1	96	10
12	160a	DEE	Cs ₂ CO ₃	1	97	10
13	160a	EA	Cs ₂ CO ₃	2	96	14
14	160a	EA	K ₃ PO ₄	2	96	11
15	160a	EA	KOt-Bu	0.5	97	11
16	160a	EA	NaOAc	24	54	3
17	160a	EA	KOH	0.5	96	10
18	160a	EA	K ₂ CO ₃	24	82	9
19	160b	EA	Cs ₂ CO ₃	2	99	5
20	160c	EA	Cs ₂ CO ₃	2	99	8
21	160d	EA	Cs ₂ CO ₃	3	98	10
22	160e	EA	Cs ₂ CO ₃	2	99	9

[a] Conditions: cat. (1.0 μmol, 1 mol %), base (10.0 μmol, 10 mol %), B₂pin₂ (0.11 mmol, 1.1 equiv.), MeOH (0.20 mmol, 2.0 equiv.), enone **156** (0.10 mmol, 1.0 equiv.) and solvent (2 mL) at RT. [b] Solvents were dried according to standard literature methods. [c] Isolated yield. [d] *ee* was determined by chiral HPLC. [e] THF was used as supplied without drying.

system has also been employed in the asymmetric aldol reaction between methylisocyanoacetate and benzaldehyde to form oxazoline derivatives. With a catalyst loading of 0.5 mol % in THF at RT, the reaction proceeded to completion in 1 h. A pair of

diastereomeric products were formed in 56% *de* with negligible *ee* (<3%). Further optimization of the reaction conditions was unproductive.

3.3 Conclusion

A methodology was developed for the direct diastereoselective one-pot synthesis of optically pure 12-membered hexanuclear “drum-like” Cu(I)-phosphine complexes in up to 89% isolated yield. A separate pathway involving the substitution of CuCl with CuCl₂ resulted in the unusual formation of a 8-membered tetranuclear “chair-like” Cu(I) cluster, which exhibited stronger Cu...Cu interactions than its hexanuclear counterpart. All the complexes were characterized by ¹H, ¹³C and ³¹P{¹H} NMR spectroscopy as well as by single crystal X-ray diffraction analysis. The cavity of the generated clusters along with the presence of stereochemical directing centers on the phosphine backbone offer an opportunity to investigate potential cooperative catalysis as indicated by an exploratory study conducted on the AHB of α,β -unsaturated ketone with bis(pinacolato)diboron.

In the next chapter, the chiral PC-palladacycle **119** and PCP-pincer complex **149a** (see Scheme 2.40) will be examined in the catalytic asymmetric P-H addition of diphenylphosphine to α,β - and $\alpha,\beta,\gamma,\delta$ -unsaturated olefins.

3.4 Experimental Section

All reactions were carried out under a positive pressure of nitrogen using standard Schlenk technique. Solvents were purchased from their respective companies and used as supplied. Where necessary, solvents were degassed prior to use. A Low Temp Pairstirrer PSL-1800 was used for controlling low temperature reactions. Column chromatography was done on Silica gel 60 (Merck). Melting points were measured using SRS Optimelt Automated Point System SRS MPA100. Optical rotation were measured with JASCO P-1030 Polarimeter in the specified solvent in a 0.1 dm cell at 22.0°C. NMR spectra were

recorded on Bruker AV 300, AV 400 and AV 500 spectrometers. Chemical shifts were reported in ppm and referenced to an internal SiMe₄ standard (0 ppm) for ¹H NMR, chloroform-d (77.23 ppm) for ¹³C NMR, and an external 85% H₃PO₄ for ³¹P{¹H} NMR. All X-ray quality crystals were obtained *via* recrystallization from a dichloromethane solution layered with *n*-hexane.

THF, toluene and DEE were distilled from sodium benzophenone ketyl under nitrogen. DCM, MeCN and EA were distilled over CaH₂ under nitrogen and stored over 4A MS. MeOH was dried over 3A MS and distilled under nitrogen. Dioxane, CHCl₃, DMSO, MTBE and benzene were dried over 4A MS and distilled under nitrogen.

The palladacycle (*R*)/(*S*)-**119**,^[112c] substrates **145a**, **b**, **d**, **e** and **146a**^[206] were prepared according to literature methods. All other reactants and reagents were used as supplied.

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

Synthesis of Copper(I) Cluster, 159. To a solution of Ph₂PH (2.2 equiv.) in toluene (10 mL) was added catalyst (*R*)/(*S*)-**119** (6 mol %) and stirred for 10 minutes before cooling to -80°C. Diunsaturated alkene (1.0 equiv.) was added followed by NEt₃ (2.0 equiv.) in toluene (1 mL) dropwise. The solution was stirred at -80°C and the completion of the reaction was monitored by the disappearance of the phosphorus signal attributed to diphenylphosphine (-40 ppm) in the ³¹P{¹H} NMR spectrum. Upon completion, the solution was allowed to attain room temperature. Volatiles were removed under reduced pressure. The crude product was redissolved in acetone (10 mL) and CuCl₂ (2.0 equiv.) was added. The mixture was refluxed overnight and on cooling, concentrated to give the crude complex, which was purified *via* silica gel column chromatography (DCM or 9 DCM : 1 EA) to afford white solid of cluster **159**. 3% yield based on Cu

atoms. $[\alpha]_D = +39.5$ (*c* 0.1, DCM). Mp: 257-259°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ 44.4; ^1H NMR (CDCl_3 , 300 MHz): δ 8.04-8.02 (m, 4H, Ar), 7.92-7.89 (m, 4H, Ar), 7.41-7.33 (m, 19H, Ar), 7.16 (t, 4H, $^3J = 7.7$ Hz, 12.8 Hz, Ar), 7.05 (d, 2H, $^3J = 7.5$ Hz, Ar), 6.79 (t, 1H, $^3J = 7.3$ Hz, Ar), 4.91-4.90 (m, 2H, PCHCHH), 3.42-4.25 (m, 2H, PCHCHH), 3.07-2.96 (m, 2H, PCHCHH); ^{13}C NMR (CDCl_3 , 125 MHz): δ 198.0 (2C, C=O), 135.1-124.7 (42C, Ar), 48.0 (2C, PCHCH₂), 44.8 (2C, PCH). HRMS (ESI, m/z ($M + H$)⁺) calcd for $\text{C}_{96}\text{H}_{81}\text{O}_4\text{P}_4\text{Cu}_4\text{Cl}_4$ 1818.1023, found 1818.1033.

General Procedure for Preparation of Copper(I) Clusters, 160a-e. To a solution of Ph_2PH (2.2 equiv.) in toluene^[a] (10 mL) was added catalyst (*R*)/(*S*)-**119** (6 mol %) and stirred for 10 minutes before cooling to -80°C. Diunsaturated alkene (1.0 equiv.) was added followed by NEt_3 (2.0 equiv.) in toluene^[a] (1 mL) dropwise. The solution was stirred at -80°C and the completion of the reaction was monitored by the disappearance of the phosphorus signal attributed to diphenylphosphine (-40 ppm) in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum. Upon completion, the solution was allowed to attain room temperature. Volatiles were removed under reduced pressure. The crude product was redissolved in acetone (10 mL) and CuCl (2.0 equiv.) was added. The mixture was refluxed overnight and on cooling, concentrated to give the crude complex, which was purified *via* silica gel column chromatography (DCM or 9 DCM : 1 EA) to afford white solid of the clusters **160a-e**.

[a] The reaction involving substrates **145e** and **146a** was conducted in THF and DCM respectively.

160a The hydrophosphination step was completed in 8 h. (72% yield based on Cu atoms). $[\alpha]_D = -48.6$ (*c* 0.1, DCM). Mp: 206-208°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ -1.2; ^1H NMR (CDCl_3 , 500 MHz): δ 9.03 (brs, 1H, Ar), 8.19-8.17 (m, 4H, Ar), 8.02-8.00 (m, 4H, Ar), 7.67-7.36 (m, 16H, Ar), 6.94-6.76 (m, 9H, Ar), 4.73-4.69 (m, 2H,

PCHCHH), 4.59-4.54 (m, 2H, PCHCHH), 3.31 (dd, 2H, $J = 18.1$ Hz, 12.8 Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 197.8 (d, 2C, $^3J_{\text{PC}} = 14.9$ Hz, C=O), 140.1-128.0 (42C, Ar), 44.0 (d, 2C, $^2J_{\text{PC}} = 13.0$ Hz, PCHCH₂), 38.9 (d, 2C, $^1J_{\text{PC}} = 25.5$ Hz, PCH). HRMS (ESI, m/z ($\text{M} + \text{H}$)⁺) calcd for $\text{C}_{144}\text{H}_{121}\text{O}_6\text{P}_6\text{Cu}_6\text{Cl}_6$ 2727.1472, found 2727.1477. Elemental analysis calcd (%) for $\text{C}_{144}\text{H}_{121}\text{O}_6\text{P}_6\text{Cu}_6\text{Cl}_6$: C 63.44, H 4.44; found: C 63.48, H 4.49.

160b The hydrophosphination step was completed in 72 h. (72% yield based on Cu atoms). $[\alpha]_{\text{D}} = +44.5$ (c 0.1, DCM). Mp: 249-251°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ -1.0; ^1H NMR (CDCl_3 , 500 MHz): δ 9.00 (brs, 1H, Ar), 8.18-8.14 (m, 4H, Ar), 7.88-7.86 (m, 4H, Ar), 7.67-7.63 (m, 4H, Ar), 7.33-7.32 (m, 6H, Ar), 7.12-7.11 (m, 4H, Ar), 6.93-6.81 (m, 9H, Ar), 4.71-4.66 (m, 2H, PCHCHH), 4.46-4.41 (m, 2H, PCHCHH), 3.32 (dd, 2H, $J = 17.1$ Hz, 13.5 Hz, PCHCHH), 2.34 (s, 6H, $\text{C}_6\text{H}_4\text{CH}_3$); ^{13}C NMR (CDCl_3 , 125 MHz): δ 197.5 (2C, C=O), 143.6-128.0 (42C, Ar), 43.9 (2C, PCHCH₂), 38.8 (2C, PCH), 29.8 (1C, $\text{C}_6\text{H}_4\text{CH}_3$), 21.7 (1C, $\text{C}_6\text{H}_4\text{CH}_3$). HRMS (ESI, m/z ($\text{M} + \text{H}$)⁺) calcd for $\text{C}_{150}\text{H}_{133}\text{O}_6\text{P}_6\text{Cu}_6\text{Cl}_6$ 2811.2415, found 2811.2430.

160c The hydrophosphination step was completed in 45 h. (77% yield based on Cu atoms). $[\alpha]_{\text{D}} = +38.9$ (c 0.1, DCM). Mp: 226-228°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ -0.8; ^1H NMR (CDCl_3 , 500 MHz): δ 8.99 (brs, 1H, Ar), 8.15-8.11 (m, 4H, Ar), 7.99-7.95 (m, 4H, Ar), 7.68-7.64 (m, 4H, Ar), 7.38-7.33 (m, 6H, Ar), 6.97-6.85 (m, 13H, Ar), 4.68-4.63 (m, 2H, PCHCHH), 4.47-4.41 (m, 2H, PCHCHH), 3.30-3.24 (m, 2H, PCHCHH); ^{13}C NMR (CDCl_3 , 125 MHz): δ 196.3 (2C, C=O), 166.7 (1C, CF), 164.7 (1C, CF), 140.1-115.4 (40C, Ar), 43.6 (2C, PCHCH₂), 38.8 (2C, PCH). HRMS (ESI, m/z ($\text{M} + \text{H}$)⁺) calcd for $\text{C}_{144}\text{H}_{115}\text{O}_6\text{P}_6\text{F}_6\text{Cu}_6\text{Cl}_6$ 2835.0906, found 2835.0898.

160d The hydrophosphination step was completed in 36 h. (89% yield based on Cu atoms). $[\alpha]_{\text{D}} = +42.0$ (c 0.1, DCM). Mp: 266-268°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202

MHz): δ -0.6; ^1H NMR (CDCl_3 , 300 MHz): δ 9.02 (brs, 1H, Ar), 8.15-8.10 (m, 4H, Ar), 7.73-7.67 (m, 4H, Ar), 7.44-7.33 (m, 9H, Ar), 7.12-7.05 (m, 7H, Ar), 6.93-6.83 (m, 3H, Ar), 6.23 (brs, 2H, Ar), 4.63-4.55 (m, 2H, PCHCHH), 4.19-4.08 (m, 2H, PCHCHH), 3.12-3.03 (m, 2H, PCHCHH); ^{13}C NMR (CDCl_3 , 125 MHz): δ 186.3 (2C, C=O), 152.0 (2C, C(O)C-O), 146.8 (2C, O-CH=C), 139.7-128.2 (30C, Ar), 119.6 (2C, C(O)C=CH), 112.1 (2C, O-CH=CH), 43.0 (2C, PCHCH₂), 29.7 (2C, PCH). HRMS (ESI, m/z ($M + H$)⁺) calcd for $\text{C}_{132}\text{H}_{109}\text{O}_{12}\text{P}_6\text{Cu}_6\text{Cl}_6$ 2667.0222, found 2667.0217.

160e The hydrophosphination step was completed in 12 h. (85% yield based on Cu atoms). $[\alpha]_D = -19.5$ (c 0.1, DCM). Mp: 222-224°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 2.4; ^1H NMR (CDCl_3 , 300 MHz): δ 8.08-7.98 (m, 9H, Ar), 7.44-7.39 (m, 13H, Ar), 6.69-6.66 (m, 1H, Ar), 6.40 (brs, 1H, Ar), 4.71-4.64 (m, 2H, PCH), 4.49-4.45 (m, 2H, PCHCH), 3.04 (brs, 12H, CO_2CH_3); ^{13}C NMR (CDCl_3 , 100 MHz): δ 167.7 (4C, C=O), 137.9-127.6 (30C, Ar), 53.8 (2C, PCHCH), 52.3 (4C, CO_2CH_3), 44.1 (2C, PCH). HRMS (ESI, m/z ($M + H$)⁺) calcd for $\text{C}_{126}\text{H}_{121}\text{O}_{24}\text{P}_6\text{Cu}_6\text{Cl}_6$ 2799.0549, found 2799.0552.

General Procedure for Catalytic Hydroboration. Under a nitrogen atmosphere, Cu(I) cluster **160a-e** (2.7 mg, 1.0 μmol , 1 mol %), base (10 mol %) and B_2pin_2 (27.9 mg, 0.11 mmol, 1.1 equiv.) in solvent (2 mL) was stirred for 10 mins. Enone **156** (20.8 mg, 0.10 mmol, 1.0 equiv.) and MeOH (8.1 μL , 0.20 mmol, 2.0 equiv.) was added consecutively and stirred. The completion of the reaction was determined by TLC analysis and confirmed by ^1H NMR. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography to afford the desired product **161**. The data were consistent with the literature.^[205b] The *ee* was determined on a Daicel Chiralpak AD-H column with *n*-hexane/2-propanol = 97/3, flow = 0.9 mL/min, wavelength = 210 nm. Retention times: 8.7 min, 12.4 min.

Chapter 4 Metal Catalyzed P-H Bond Addition Reaction

4.1 General Introduction to P-H Bond Addition Reaction

Metal catalyzed asymmetric reactions are one of the most powerful tools for the production of chiral compounds^[22] that are frequently used in pharmaceutical, agrochemical, fine chemical or fragrance industries.^[22b,d] The intrinsic catalytic performance of late transition metals (e.g. Rh, Ru, Ir, Pd and Pt) are usually modified preferentially by trivalent P-ligands. Historical examples include P-stereogenic monophosphines developed independently by Sabacky^[19] and Buthe^[18] in 1968, and chelating diphosphines such as DIOP, DIPAMP and BINAP. Phosphorus compounds are important precursors for a variety of substances, and have found numerous applications such as in antitumor agents, antibiotics, organocatalytic and metal-catalyzed transformations.^[94a]

The construction of a C-P bond has been the subject of countless investigations, in particular, the most attractive strategy is the addition of a P-H bond to C-C/X (X = N, O, S) multiple bonds. In general, a C-P bond formation reaction can be classified into: (1) phosphanylation/phosphination (cross coupling of aryl halides with P-H reagents to form tertiary phosphines), (2) hydrophosponylation (addition of pentavalent phosphites across C-C/X (X = N, O, S) multiple bonds), (3) hydrophosphinylation (addition of pentavalent P-H reagents bearing aryl or alkyl substituents across C-C/X multiple bonds), and (4)

Scheme 4.48. Representative classification of P-H bond addition reactions.

hydrophosphination (addition of trivalent P-H species to unsaturated C-C/X bonds). The metal catalyzed addition of X-H (X = Si, CN, B, N, H *i.e.* hydrosilylation, hydrocyanation, hydroboration, hydroamination, hydrogenation, hydroformylation) bond to olefins has been discovered decades ago and is an important industrial process for several reactions. Intriguingly, hydrophosphination (HP) of alkenes are poorly explored and should be developed further. The first metal catalyzed HP of an alkene was reportedly achieved with PH_3 and acrylonitrile in the presence of platinum-tris(cyanoethyl)phosphine,^[111b] which yielded roughly equal amounts of primary, secondary and tertiary phosphines. It was noted that unlike other metal catalyzed HP of

Scheme 4.49. Pt(0)-catalyzed hydrophosphination of acrylonitrile.

alkenes, this reaction was not suppressed even with 50 equivalents of $\text{P}(\text{CH}_2\text{CH}_2\text{CN})_3$ present in solution. This observation was significant because product (phosphine) coordination has been a major concern in metal-catalyzed HP reactions. Phosphine compounds are powerful metal sequesters and form stable complexes with most transition metals, especially in their electron-rich lower oxidation states. Due to this profound affinity, excess phosphines can occupy all the available catalytic sites and are often considered as catalyst poisons. Therefore, it is rare for phosphines to be generated efficiently *via* metal-catalyzed HP reactions. Other examples of metal-catalyzed HP of alkenes include: (1) HP of acrylonitrile using Pt complexes of chelating diphosphine ligands,^[207] (2) HP of ethyl acrylate with PH_3 catalyzed by $[\text{Pt}\{\text{P}(\text{CH}_2\text{CH}_2\text{CO}_2\text{Et})_3\}_3]$,^[208] (3) Ni(0)-catalyzed HP of styrene,^[111c] and (4) Pd(II) and Ni(II) salts in the HP of vinyl ethers.^[209] Apart from late transition metals, early transition metals (e.g. $[\text{Cp}_2\text{Ti}(\text{PMe}_3)_2]$ ^[210] and $[\text{TiCl}_2\text{Cp}\{\eta^5\text{-C}_2\text{H}_4(\text{CH}_2)_2\text{PPh}_2\}]$ ^[211]), inexpensive metals (e.g.

$\text{Cu}(\text{OTf})_2$,^[212] Fe(II) and Fe(III) salts^[213], lanthanides of the type $\text{Cp}^* \text{LnE}(\text{SiMe}_3)$ ($\text{Cp}^* = \text{C}_5\text{Me}_5$; Ln = La, Sm, Y, Lu; E = CH, N)^[214] and alkaline earth metals (e.g. Ca(II) complexes^[215]) have also been reported to catalyze the HP of alkenes.

Despite achieving considerable success in catalytic HP of alkenes, the asymmetric variant of this reaction has proved to be more challenging. The sluggish development of chiral phosphines^[216] may be attributed to the difficulties faced in their syntheses which are traditionally prepared through resolution techniques or with stoichiometric amounts of chiral auxiliaries.^[32b,217] The metal catalyzed asymmetric hydrophosphination (AHP) offers an attractive strategy for the fabrication of optically pure phosphines in a single step, but has been relatively underdeveloped. The first metal catalyzed AHP to generate chiral phosphines was reported in 2000,^[52] employing Pt-(*R,R*)-MeDUPHOS (see Scheme 1.7) to afford P-stereogenic phosphines in *ee*'s of up to 22%. Improved protocols have resulted in slightly higher enantioselectivities of up to 56%.^[218] In addition, the seminal work of Togni involving the AHP of methacrylonitrile using dicationic $[\text{Ni}(\text{Pigiphos})(\text{THF})](\text{ClO}_4)_2$ as catalyst^[219] laid the foundation for installation of C-stereogenic centers *via* AHP. Since then, our group^[85,112b-j] (for a list of chiral phosphines produced catalytically; see Figure 1.13) and Duan^[113,151a,b,g,h,220] have extensively published in this area, conspicuously employing the chiral PC-palladacycle **119** and the optically pure PCP-Pd pincer complex **163** respectively. Other NCN-^[131b,221] and PCN-^[151f,153c] pincer complexes have also been reported to catalyze the AHP of olefins.

Scheme 4.50. Ni(II)-catalyzed AHP of methacrylonitrile.

Scheme 4.51. PCP-Pd pincer complex catalyzed AHP of various functional alkenes.

In Chapter 2, a wide range of chiral PCP-transition metal pincer complexes (see Scheme 2.40) was synthesized *via* a one-pot AHP/cyclometalation protocol.^[206] It should

be noted that the preparation of pincer complex **163** involves an enantiopure diol and extensive protection-deprotection steps,^[125c] ultimately affording the desired complex in a low overall yield of 32%. On the contrary, we are able to employ our synthetic methodology to produce a series of chiral PCP-pincer complexes in an efficient and catalytic manner utilizing readily accessible building blocks. As such, it is compelling to examine the impact of the architectural differences between the PC-palladacycle **119** and the PCP pincer complex **149a**.

Figure 4.35. Structure of PC-palladacycle and PCP-pincer complex.

Herein, we examine the catalytic abilities of both PC-cyclometalated and PCP-pincer type palladium complexes in the AHP of α,β - and $\alpha,\beta,\gamma,\delta$ -unsaturated malonate esters. From the mechanistic viewpoint, it is evident that these two types of catalysts operate *via* different pathways during the course of the HP reaction. In general, the phosphapalladacycle **119** allows the simultaneous but regiospecific coordination of both the substrate and the nucleophile to the two available reaction sites on the metal center, thus allowing an intramolecular P-C bond formation mechanism to be adopted.^[112b,c] On the other hand, the pincer catalysts operate by activating the P-H bonds through an initial P→Pd coordination, followed by the intermolecular P-C bond formation.^[113] Although this divergence in the mechanistic pathway may not have any significant impact on stereochemistry, especially for α,β -unsaturated substrates, from the regioselective standpoint, different HP products may be obtained when the substrates contain more than one chemically reactive positions, such as $\alpha,\beta,\gamma,\delta$ -diunsaturated compounds. In the case of these diunsaturated substrates, it was observed that the pincer catalyst typically generates

the 1,6-addition products^[151a,220c] (see Scheme 4.51). However, the formation of the same adduct by phosphapalladacycle **119** (via an intramolecular mechanism) would involve an

Figure 4.36. Diagrammatic representations of (A) favorable 6-membered transition state, and (B) unfavorable 8-membered transition state.

unfavorable 8-membered transition state since both reacting species need to be coordinated concurrently to the Pd center during the course of the catalytic cycle. Alternatively, the palladacycle **119** can operate through an intramolecular mechanism that involves a sterically favorable 6-membered transition state to form the 1,4-adduct.

4.2 Results and Discussion

4.2.1 Catalytic AHP of Alkylidenemalonate Esters

While complex **119** was previously used as the catalyst in numerous P-H bond addition reactions, the catalytic performance of the keto-functionalized PCP pincer **149a** is hitherto unknown especially in the context of the conjugate addition of HPPH₂ to an ester. The only previous report by Duan employing the PCP complex **163** for the AHP of an $\alpha,\beta,\gamma,\delta$ -unsaturated carboxylic ester resulted in zero yield.^[220c] Therefore, prior to the investigation of the more challenging $\alpha,\beta,\gamma,\delta$ -diunsaturated substrate, the general catalytic properties of the Pd(II) complexes **119** and **149a** were studied using simpler alkylidenemalonate esters wherein regioselectivity concerns do not exist. With these chemically well-defined substrates, identical 1,4-addition products are expected from the selected complexes, assuming that they are catalytically active. The results are summarized in Table 4.10.

Table 4.10. Catalytic AHP of alkylidenemalonate esters.^[a]

Entry	cat.	Product	Solvent	Base	T (°C)	Yield ^[b] (%)	ee ^[c] (%)
1	149a	179a	Toluene	-	RT	2	ND ^[d]
2	149a	179a	Toluene	NEt ₃	RT	50	1
3	149aa	179a	Toluene	-	RT	89	16
4	149ab	179a	Toluene	-	RT	0	-
5	149ab	179a	Toluene	NEt ₃	RT	71	5
6	149ac	179a	Toluene	-	RT	13	5
7	149aa	179a	MeCN	-	RT	93	3
8	149aa	179a	Acetone	-	RT	84	6
9	149aa	179a	DCM	-	RT	88	5
10	149aa	179a	DCM	-	-80	93	9
11	149aa	179a	Toluene	-	-80	93	44
12	(<i>S</i>)- 119	179a	DCM	NEt ₃	-80	93	67
13	(<i>S</i>)- 119	179a	Toluene	NEt ₃	-80	81	7
14	149aa	179b	Toluene	-	RT	78	1
15	149aa	179b	DCM	-	RT	76	3
16	149aa	179b	DCM	-	0	52	18
17	(<i>S</i>)- 119	179b	DCM	NEt ₃	-80	81	94
18	(<i>S</i>)- 119	179b	Toluene	NEt ₃	-80	70	27

[a] Conditions: cat. (25.0 μmol, 5 mol %), HPPPh₂ (0.6 mmol, 1.2 equiv.), substrate (0.5 mmol, 1.0 equiv.), base (0.5 mmol, 1.0 equiv.) and solvent (1 mL) at RT. [b] Isolated yield. [c] ee was determined by chiral HPLC. [d] ND = not determined.

Overall, it is evident that the cyclometalated catalyst (*S*)-**119** is more efficient than the best performing (*R,R*)-**149a** variant *viz.* (*R,R*)-**149aa** for the AHP of alkylidenemalonate esters. The addition of an external base (NEt₃) is required with catalyst (*S*)-**119** but not with (*R,R*)-**149aa** due to the presence of an internal base (AcO⁻). The base is necessitated by its role in generating the reactive phosphido species during the course of the catalytic cycle (see Scheme 2.44). From the evaluation of the pincer complexes in the AHP reaction, it was revealed that the neutral chloro complex **149a** is catalytically inactive (Entry 1). Even though the AHP proceeded with the addition of NEt₃, complex **149a** is unable to provide appreciable yield and ee (Entry 2). Hence, the chloride anion was replaced by better leaving moieties such as AcO⁻, TFA⁻ and I⁻.

Between pincer complexes **149aa** and **149ab**, the catalytic activity and stereoselectivity of **149aa** is significantly better than **149ab** (Entries 3-5). In the presence of **149ac**, low yield (13%) and *ee* (5%) were observed even after 24 h (Entry 6). This reactivity trend is attributed to the lability of the Pd-X bonds, in which the Pd-O bond is more labile than Pd-I followed by the Pd-Cl bond. An increasingly labile Pd-X bond will allow the coordination of HPPPh₂ to the metal center. However, the pK_a of trifluoroacetate is lower than that of an acetate anion, thus TFA⁻ is not sufficiently basic for the deprotonation of HPPPh₂ and the AHP is unable to proceed. An optimization of the reaction conditions for (*R,R*)-**149aa** was able to afford the products **179a** and **179b** in moderate to high yields with appreciable *ee*'s of 44% and 18% respectively (Entries 11, 16). The cyclopalladated catalyst (*S*)-**119** clearly performs better at low temperatures to afford the products in high yields with good *ee*'s of 67% and 94% (Entries 12, 17). Having established the catalytic activities of both PC- and PCP-type catalysts, we decided to evaluate their reactivity along with regio- and stereo-selectivity in the catalytic AHP of an $\alpha,\beta,\gamma,\delta$ -diunsaturated olefin.

4.2.2 Catalytic AHP of Diethyl-2-Cinnamylidenemalonate

When catalysts (*S*)-**119** and (*R,R*)-**149aa** were applied to the AHP of diethyl-2-cinnamylidenemalonate **180**, similar reactivity trends were observed. However, the two catalysts exhibited dramatically different regioselectivity preference for this reaction. At RT, the pincer (*R,R*)-**149aa** afforded the 1,6-adduct **181b** exclusively in 92% yield with moderate *ee* (Entry 2). When the same reaction was conducted at lower temperature (-80°C), the regioselectivity improved but a small amount (6%) of **181a** was generated (Entry 3). On the contrary, palladacycle (*S*)-**119** generated the enantiopure 1,4-adduct **181a** in 94% yield with >99% *ee* (Entry 8). At elevated temperatures, the AHP reaction catalyzed by (*S*)-**119** became progressively less stereo- and regio-selective (Entries 6, 7).

Table 4.11. Catalytic AHP of diethyl-2-cinnamylidenemalonate.^[a]

Entry	cat.	Solvent	Base	T (°C)	181a:181b ^[b]	Yield ^[c] (%)	ee ^[d] (%)
1	149aa	MTBE	-	RT	2:98	88	22
2	149aa	DCM	-	RT	0:100	92	38
3	149aa	DCM	-	-80	6:94	84	60
4	149aa	Toluene	-	RT	3:97	88	29
5	149aa	Toluene	-	-80	5:95	79	70
6	(<i>S</i>)- 119	DCM	NEt ₃	50	62:38	80	24(35) ^[e]
7	(<i>S</i>)- 119	DCM	NEt ₃	RT	97:3	77	55(<i>S</i>)
8	(<i>S</i>)- 119	DCM	NEt ₃	-80	100:0	94	>99(<i>S</i>) ^[f]
9	-	DCM	NEt ₃	50	100:0	<5 ^[g]	-
10	-	DCM	NaOAc	50	100:0	<5 ^[g]	-

[a] Conditions: cat. (25.0 μmol, 5 mol %), HPPPh₂ (0.6 mmol, 1.2 equiv.), substrate (0.5 mmol, 1.0 equiv.), base (0.5 mmol, 1.0 equiv.) and solvent (3 mL) at T. [b] Ratio of **181a**:**181b** was determined by integration of their respective ¹H NMR signals at 6.41 and 5.72 ppm. [c] Isolated yield. [d] ee was determined by chiral HPLC. [e] ee in parentheses belongs to the minor product. [f] Absolute configuration was determined by X-ray analysis. [g] Conversion was calculated based on ³¹P{¹H} NMR after 96 h. Only the 1,4-adduct **181a** was observed.

It needs to be highlighted that this is the only instance in literature wherein a 1,4-regioselectivity was observed in the conjugate P-H addition of HPPPh₂ to an ester in high yield and enantioselectivity of >99%. Only two cases have been reported and they involved an α,β,γ,δ-diunsaturated ketone (93% ee) and its *N*-pyrrole derivative (96% ee).^[220c] Notably, in the same report, the analogous pincer (*S,S*)-**163** catalyzed AHP of **180** gave the 1,6-adduct **181b** in 68% yield with a regioselectivity of 10:90 (**181a**:**181b**). In our case, pincer **149aa** formed the product **181b** in 88% yield with an improved regioselectivity of 3:97 (Entry 4). This difference in regioselectivity could be due to the increased steric bulk of the -CH₂C(O)Ph moieties (in **149aa**) as compared to the -CH₃ groups (in **163**).

4.2.3 Characterization of the Addition Products

For direct characterization of the phosphine adducts, they were converted into their corresponding oxides **181a** and **181b** after the completion of the AHP reaction was

verified with $^{31}\text{P}\{^1\text{H}\}$ NMR. The ^1H NMR of the crude reaction mixtures was essential in determining the ratio of **181a**:**181b**. By integration of a characteristic proton signal belonging to each of the adducts, in particular, a doublet of doublet centered at 6.41 ppm

Figure 4.37. Representative protons of the adducts.

represents H_a of **181a**, and a doublet of doublet of doublet located at 5.72 ppm signifies H_b of **181b**. The molecular structure and absolute stereochemistry of (*S*)-**181a** were established by X-ray crystallography (Figure 4.38). Due to the low enantioselectivity associated with the 1,6-addition reaction, adduct **181b** crystallized as a racemic mixture (Figure 4.39).

Figure 4.38. Molecular structure of (*S*)-**181a**. All hydrogen atoms except H(C9) were omitted for clarity.

Figure 4.39. Molecular structure of (±)-**181b**.

4.2.4 Mechanistic Considerations

In the absence of a catalyst, the reaction between HPPh_2 and diethyl-2-cinnamylidenemalonate **180** was extremely slow even at elevated temperature, affording only <5% of the products after 96 h (Table 4.11, entries 9, 10). Nevertheless, these two experiments have suggested that the β -position is more reactive (than the δ -position and the carbonyl C atom) towards the nucleophilic P species.

In theory, the PC-catalyst (*S*)-**119** may adopt either an inter- or intra-molecular reaction mechanism. Due to both electronic and steric factors, the intermolecular pathway would favor the formation of the 1,6-product. However, the exclusive generation of the 1,4-product **181a** (Table 4.11, entry 8) at low temperature indicates that the cyclometalated catalyst prefers to form a 6-membered transition state involving the simultaneous coordination of both HPPh_2 and the substrate (see Figure 4.36) during the course of the P-C bond formation. The nature of this intramolecular pathway allows palladacycle (*S*)-**119** to offer both high stereoselectivity and reactivity even at low temperatures. In line with the experimental observations, the synthesis of the 1,6-adduct **181b** via an intramolecular mechanism is sterically unfavorable as it requires a large 8-

membered transition state to be formed on the Pd center. Nonetheless, the presence of the minor product **181b** at higher temperatures (Table 4.11, entries 6, 7) can be attributed to the increasing competition between the intra- and inter-molecular pathways under harsher reaction conditions. The proposed catalytic cycle for the (*S*)-**119** catalyzed AHP of substrate **180** is depicted in Scheme 4.52. The labile acetonitrile ligands are displaced by HPPh₂ to produce species **A**. The strong *trans*-effect causes the dissociation of HPPh₂ *trans* to the naphthalene C and the vacant site is occupied by the substrate. The P-H bond of the coordinated HPPh₂ is acidified and addition of a base deprotonates the phosphine, generating a phosphido intermediate **C**. An intramolecular 1,4-addition ensues, followed by protonation to produce the chiral phosphine. Subsequently the product is released and the cycle is closed.

Scheme 4.52. Proposed catalytic cycle for (*S*)-**119**.

Figure 4.40. Stereochemical pathway for (*S*)-**119**.

The stereoselectivity for the 1,4-adduct (*S*)-**181a** can be explained by the proposed stereochemical pathway in Figure 4.40. The simultaneous coordination of substrate **180** and diphenylphosphine to the PC-catalyst (*S*)-**119** resulted in the favorable addition of the PPh₂-moiety to the *Si*-face of the substrate, resulting in the formation of the (*S*)-product. On the contrary, addition of the PPh₂-moiety to the *Re*-face of the substrate is sterically unfavorable.

In contrast to the PC-catalyst, the pincer complex **149aa** offers only one easily accessible vacant site, hence it is necessary for it to adopt an intermolecular mechanism. Technically, the pincer complex may either activate the olefin or the P-H bond of HPPH₂. To gain a better understanding of this aspect, a series of closely monitored NMR experiments were conducted. Based on the ¹H NMR spectrum (CDCl₃),^[222] the addition of substrate **180** to pincer complex (*R,R*)-**149aa** does not result in any visible chemical shifts in the proton signals of both the catalyst and substrate. Furthermore, the proton signal arising from the -OAc group on **149aa** remained unchanged at 1.98 ppm. This indicates that the -OAc moiety coordinated to the palladium center has not been displaced by the substrate. Similarly, the ³¹P{¹H} NMR (CDCl₃) studies showed that the original signal of complex **149aa** at 44.4 ppm remained unchanged when an excess of substrate **180** was added into the NMR sample. In a separate sample, two broad peaks at -10.2 and 49.9 ppm corresponding to the -PPh₂ moiety (from HPPH₂) and the PCP phosphines (from

[Pd(PCP)(PPh₂)] appeared after HPPH₂ (1.1 equiv.) was introduced to **149aa**. However, due to reasons such as the possibly small P-P cis coupling, no coupling of the phosphines on the [Pd(PCP)(PPh₂)] species were detected. Spontaneous changes of the pincer catalyst signal were also observed when other phosphines such as ClPPh₂ were used. With the subsequent addition of substrate **180** into the mixture, a signal at 4.8 ppm corresponding to the phosphinated product appeared. The observations were consistent with an analogous pincer catalyst reported by Duan.^[113]

With the NMR data collected, the mechanism of (*R,R*)-**149aa** catalyzed AHP was proposed. A *trans*-phosphination reaction generates a nucleophilic Pd-phosphido species and a subsequent external nucleophilic attack on the δ -position of substrate **180** yields a π -allyl intermediate. The cationic Pd-phosphine complex was then protonolyzed with acetic acid to regenerate the active catalyst and formed the 1,6-adduct. It was noted that the intermolecular 1,4-addition reaction involving the pincer catalyst would be sterically unfavorable, as illustrated in Figure 4.54.

Scheme 4.53. Proposed catalytic cycle for (*R,R*)-**149aa**.

Scheme 4.54. Steric effects associated with the pincer catalyst.

When the pincer catalyzed AHP was conducted at low temperature (Table 4.11, entries 3, 5), a small amount of the 1,4-adduct **181a** was formed. As discussed earlier, the formation of this minor product cannot be explained by the intermolecular pathway, especially at low temperature. From the organometallic chemistry standpoint, the two $P \rightarrow Pd$ bonds in the *trans* $P \rightarrow Pd \leftarrow P$ system are electronically unfavorable and kinetically

Scheme 4.55. Proposed alternative catalytic cycle of the pincer catalyst at low temperature.

labile^[162] because the two soft donors are competing for electrons from the same *d*-orbitals. It is plausible that one of the $P \rightarrow Pd$ bonds in complex **149aa** undergoes ligand dissociation in solution and generates the bidentate species **182**, which resembles the

structure of the PC-catalyst **119**. The kinetic species **182** is stabilized at low temperature and catalyzes the intramolecular 1,4-addition reaction, in a manner similar to (*S*)-**119**. A variable low temperature $^{31}\text{P}\{^1\text{H}\}$ NMR investigation of the pincer **149aa** was conducted.^[223] When subjected to lower temperatures of up to -80°C , the broadening of the phosphorus signal of **149aa** indicates the dynamic changes of the *trans* $\text{P}\rightarrow\text{Pd}\leftarrow\text{P}$ bonds. However the changes are so facile that the individual phosphorus signals (especially for the bidentate species **182**) could not be trapped even at -80°C . In order to ensure that the broadening of the peaks are not contributed by other factors such as poor shimming, reduced solubility or increased viscosity, an analogous PCN-Pd pincer complex was subjected to the same investigation.^[224] The favorable *trans* $\text{N}\rightarrow\text{Pd}\leftarrow\text{P}$ system exhibited no significant peak broadening, hence it is believed that the broadening of the phosphorus signal for complex **149aa** is due to the kinetic lability of the $\text{P}\rightarrow\text{Pd}$ bonds. Alternatively, a sterically unfavorable five-coordinate intermediate involving the coordination of the substrate *via* the carbonyl-O to the axial position of the square planar catalyst **149aa** at lower temperature might also be possible.

4.3 Conclusion

The growth of interest in the development of methodologies for 1,6-conjugate addition, especially those involving non-carbon nucleophiles, to $\alpha,\beta,\gamma,\delta$ -diunsaturated systems emphasizes the significance of this type of reaction. However its development is inhibited by limitations concerning the control of steric and electronic factors. In this chapter, it was conclusively demonstrated that the judicious choice of the ligand motif associated with the Pd catalysts offers significant control over reactivity and stereoselectivity in the conjugate addition of HPPH_2 to mono- and di-unsaturated malonate esters. The resulting chiral tertiary phosphines could be prepared with both PC- and PCP-type Pd catalysts in high yields. For the addition involving conjugated $\alpha,\beta,\gamma,\delta$ -

diunsaturated malonate ester, a novel regiodivergent method was revealed in an AHP protocol that allows the 1,4-adduct to be obtained exclusively with the PC-catalyst while the pincer catalyst produced only the 1,6-adduct. This catalyst-product specificity concept is critical for the development of future catalysts for targeted isomeric compounds and is hitherto not understood for this P-C bond formation process. The understanding of the difference in stereo- and regio-control imparted by the two classes of catalysts along with reactivity aspects will bear heavily on the design of catalysts involved in the advancement of AHP reactions.

In the following chapter, the catalytically generated chiral PCP- and PCN-transition metal pincer complexes (see Scheme 2.40) were systematically screened in the conjugate addition of diarylphosphines to $\alpha,\beta,\gamma,\delta$ -diunsaturated ketones. The important roles of the backbone architecture and metal ion were subsequently revealed in the methodical analysis of the results.

4.4 Experimental Section

All reactions were carried out under a positive pressure of nitrogen using standard Schlenk technique. NMR spectra were recorded on Bruker AV 300, AV 400 and AV 500 spectrometers. Chemical shifts were reported in ppm and referenced to an internal SiMe₄ standard (0 ppm) for ¹H NMR, chloroform-d (77.23 ppm) for ¹³C NMR, and an external 85% H₃PO₄ for ³¹P{¹H} NMR. DCM, toluene, THF, acetone, acetonitrile and MTBE were purchased from their respective companies and used as supplied. Solvents were degassed prior to use when necessary. A Low Temp Pairstirrer PSL-1800 was used for controlling low temperature reactions. Column chromatography was carried out with Silica gel 60 (Merck). Melting points were measured using SRS Optimelt Automated Point System SRS MPA100. Optical rotation were measured with JASCO P-1030 Polarimeter in the specified solvent in a 0.1 dm cell at 22.0°C.

The palladacycle (*S*)-**119**^[112c] and pincer complex (*R,R*)-**149a**^[206] was prepared according to literature methods. All other reactants and reagents were used as supplied.

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

Synthesis of PCP Pincer Complex (*R,R*)-149aa, ab or ac. To a solution of (*R,R*)-**149a** (100 mg, 0.120 mmol, 1.0 equiv.) in DCM (10 mL) was added AgOAc (29.4 mg, 0.177 mmol, 1.5 equiv.) or AgTFA (38.9 mg, 0.177 mmol, 1.5 equiv.) or KI (199.2mg, 1.20 mmol, 10.0 equiv.) and stirred vigorously overnight protected from light. The crude reaction mixture was passed through a short plug of silica gel, extracted into DCM (3 X 50 mL) and washed with water (2 X 50 mL). The organic layers were combined and dried over MgSO₄, filtered and evaporated to dryness to give white solid of (*R,R*)-**149aa, ab or ac**.

(*R,R*)-**149aa** (97.6 mg, 0.112 mmol, 95% yield). [α]_D = +380 (*c* 0.1, DCM). Mp: 138-140°C. ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 44.5; ¹H NMR (CDCl₃, 400 MHz): δ 8.04-8.00 (m, 4H, Ar), 7.86-7.81 (m, 4H, Ar), 7.40-7.35 (m, 18H, Ar), 7.16-7.12 (m, 4H, Ar), 6.97 (d, 2H, ³*J* = 7.52 Hz, Ar), 6.69 (t, 1H, ³*J* = 7.48 Hz, Ar), 4.79-4.73 (m, 2H, PCHCH₂), 3.58-3.49 (m, 2H, PCHCHH), 3.04 (ddd, 2H, ²*J* = 16.7 Hz, ³*J* = 10.2 Hz, 5.1 Hz, PCHCHH), 1.97 (s, 3H, OCOCH₃); ¹³C NMR (CDCl₃, 100 MHz): δ 198.0 (2C, C=O), 151.8 (1C, OCOCH₃), 136.8-124.5 (42C, Ar), 47.8 (t, 2C, ¹*J*_{PC} = 14.9 Hz, PCH), 44.8 (t, 2C, ²*J*_{PC} = 4.8 Hz, PCHCH₂). HRMS (+ESI) *m/z*: (M - OAc)⁺ calcd for C₄₈H₃₉O₂P₂Pd, 815.1460; found, 815.1476. Anal. Calcd for C₅₀H₄₂O₄P₂Pd: C, 68.61; H, 4.84. Found: C, 68.78; H, 4.97%.

(*R,R*)-**149ab** (102 mg, 0.108 mmol, 93% yield). [α]_D = +382 (*c* 0.1, DCM). Mp: 189-190°C (dec). ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 45.6; ¹H NMR (CDCl₃, 400 MHz): δ 8.00-7.96 (m, 4H, Ar), 7.75-7.71 (m, 4H, Ar), 7.42-7.32 (m, 18H, Ar), 7.19-7.16 (m,

4H, Ar), 7.03 (d, 2H, $^3J = 7.52$ Hz, Ar), 6.77 (t, 1H, $^3J = 7.44$ Hz, Ar), 4.85-4.80 (m, 2H, PCHCH₂), 3.53-3.44 (m, 2H, PCHCHH), 3.04 (ddd, 2H, $^2J = 16.3$ Hz, $^3J = 11.1$ Hz, 5.2 Hz, PCHCHH); ^{13}C NMR (CDCl₃, 100 MHz): δ 197.6 (2C, COPh), 151.9 (1C, OCOCF₃), 136.6-124.9 (43C, Ar and OCOCF₃), 47.2 (t, 2C, $^1J_{\text{PC}} = 15.0$ Hz, PCH), 44.8 (t, 2C, $^2J_{\text{PC}} = 4.6$ Hz, PCHCH₂). HRMS (+ESI) *m/z*: (M - TFA)⁺ calcd for C₄₈H₃₉O₂P₂Pd, 815.1460; found, 815.1474. Anal. Calcd for C₅₀H₃₉F₃O₃P₂Pd: C, 65.76; H, 4.30. Found: C, 65.91; H, 4.51%.

(*R,R*)-**149ac** (104 mg, 0.109 mmol, 90% yield). $[\alpha]_{\text{D}} = -566$ (*c* 0.1, DCM). Mp: 210-212°C (dec). $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl₃, 162 MHz): δ 47.9; ^1H NMR (CDCl₃, 400 MHz): δ 8.07-8.02 (m, 4H, Ar), 7.89-7.84 (m, 4H, Ar), 7.48-7.45 (m, 6H, Ar), 7.42-7.40 (m, 2H, Ar), 7.38-7.38 (m, 4H, Ar), 7.34-7.32 (m, 6H, Ar), 7.27-7.25 (m, 4H, Ar), 7.18-7.06 (m, 2H, Ar), 6.84 (t, 1H, $^3J = 7.60$ Hz, Ar), 5.01-4.98 (m, 2H, PCHCH₂), 3.27-3.21 (m, 2H, PCHCHH), 3.02 (m, 2H, PCHCHH); ^{13}C NMR (CDCl₃, 100 MHz): δ 197.6 (2C, COPh), 164.7-124.1 (42C, Ar), 49.1 (t, 2C, $^1J_{\text{PC}} = 14.9$ Hz, PCH), 44.9 (2C, PCHCH₂). HRMS (+ESI) *m/z*: (M - I)⁺ calcd for C₄₈H₃₉O₂P₂Pd, 815.1460; found, 815.1487. Anal. Calcd for C₄₈H₃₉IO₂P₂Pd: C, 61.13; H, 4.17. Found: C, 61.34; H, 4.30%.

General Procedure for Catalytic AHP without External Base. The catalyst (25 μmol , 5 mol %) was added to a solution of diphenylphosphine (0.6 mmol, 1.2 equiv.) in the stated solvent (1 mL) and brought to the desired temperature. The substrate (0.5 mmol, 1.0 equiv.) was subsequently added and stirred at the stated temperature. Completion of the reaction was determined by the disappearance of the phosphorus signal attributed to diphenylphosphine (-40 ppm) in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum. Upon completion of the reaction, aq. H₂O₂ (0.1 mL, 31% v/v) was added to form the respective product. The volatiles were removed under reduced pressure and the crude product was

directly loaded onto silica gel column (ethyl acetate : *n*-hexane = 2 : 1) to afford the pure product.

General Procedure for Catalytic AHP with External Base. The catalyst (25 μ mol, 5 mol %) was added to a solution of diphenylphosphine (0.5 mmol, 1.0 equiv.) in the stated solvent (0.5 mL) and brought to the desired temperature. The substrate (0.5 mmol, 1.0 equiv.) and NEt₃ (0.5 mmol, 1.0 equiv.) in the same solvent (0.5 mL) was consecutively added and stirred at the stated temperature. Completion of the reaction was determined by the disappearance of the phosphorus signal attributed to diphenylphosphine (-40 ppm) in the ³¹P{¹H} NMR spectrum. Upon completion of the reaction, aq. H₂O₂ (0.1 mL, 31% v/v) was added to form the respective product. The volatiles were removed under reduced pressure and the crude product was directly loaded onto silica gel column (ethyl acetate : *n*-hexane = 2 : 1) to afford the pure product.

179a White solid. The *ee* was determined on a Daicel Chiralpak AD column with *n*-hexane/2-propanol = 96.5/3.5, flow = 0.9 mL/min, wavelength = 220 nm. Retention times: 202.0 min (major product with catalyst (*S*)-**2**), 216.5 min (major product with catalyst (*R,R*)-**4b**). [α]_D = -32.1 (*c* 0.1, DCM). Mp: 108-110 °C. ³¹P{¹H} NMR (CDCl₃, 202 MHz): δ 34.2; ¹H NMR (CDCl₃, 500 MHz): δ 7.87-7.78 (m, 4H, Ar), 7.53-7.42 (m, 6H, Ar), 4.15 (q, 2H, ³*J* = 6.95 Hz, CO₂CH₂), 3.96-3.89 (m, 1H, MeCHCH), 3.84-3.75 (m, 2H, CO₂CH₂), 3.37-3.30 (m, 1H, (CO₂)₂CH), 1.27-1.23 (m, 6H, CH₃CHCH and CO₂CH₂CH₃), 1.12 (t, 3H, ³*J* = 7.10 Hz, CO₂CH₂CH₃); ¹³C NMR (CDCl₃, 125 MHz): δ 168.1 (1C, CO₂CH₂CH₃), 167.7 (1C, CO₂CH₂CH₃), 131.9-128.5 (10C, Ar), 61.8 (1C, CO₂CH₂CH₃), 61.6 (1C, CO₂CH₂CH₃), 50.6 (1C, (CO₂)₂CH), 32.7 (d, 1C, ¹*J*_{PC} = 70.8 Hz, PCH), 14.0 (1C, CO₂CH₂CH₃), 13.8 (1C, CO₂CH₂CH₃), 11.0 (1C, CH₃CHP). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₂₁H₂₆O₅P, 389.1519; found, 389.1522. Anal. Calcd for C₂₁H₂₅O₅P: C, 64.94; H, 6.49. Found: C, 65.09; H, 6.61%.

179b White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 87/13, flow = 1.0 mL/min, wavelength = 220 nm. Retention times: 93.5 min (major product with catalyst (*R,R*)-**4b**), 101.5 min (major product with catalyst (*S*)-**2**). $[\alpha]_{\text{D}} = +26.1$ (*c* 0.1, DCM). Mp: 134-137 °C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121 MHz): δ 30.8; ^1H NMR (CDCl_3 , 400 MHz): δ 7.96-7.91 (m, 2H, Ar), 7.52-7.46 (m, 5H, Ar), 7.35-7.31 (m, 1H, Ar), 7.25-7.19 (m, 4H, Ar), 7.09-7.08 (m, 3H, Ar), 4.56-4.42 (m, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 3.83-3.70 (m, 3H, PhCH and $\text{CO}_2\text{CH}_2\text{CH}_3$), 3.60-3.52 (m, 1H, $(\text{CO}_2)_2\text{CH}$), 1.07 (t, 3H, $^3J = 7.16$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 0.85 (t, 3H, $^3J = 7.12$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$); ^{13}C NMR (CDCl_3 , 125 MHz): δ 167.6 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 167.1 (d, 1C, $^2J_{\text{PC}} = 15.1$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 133.9-127.6 (15C, Ar), 62.0 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 61.7 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 52.7 (1C, $(\text{CO}_2)_2\text{CH}$), 46.4 (d, 1C, $^1J_{\text{PC}} = 64.3$ Hz, PCH), 13.9 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 13.7 (2C, $\text{CO}_2\text{CH}_2\text{CH}_3$). HRMS (+ESI) *m/z*: (*M* + *H*)⁺ calcd for $\text{C}_{26}\text{H}_{28}\text{O}_5\text{P}$, 451.1675; found, 451.1676. Anal. Calcd for $\text{C}_{26}\text{H}_{27}\text{O}_5\text{P}$: C, 69.32; H, 6.04. Found: C, 69.57; H, 6.31%.

181a White solid. The *ee* was determined on a Daicel Chiralpak AD column with *n*-hexane/2-propanol = 75/25, flow = 0.8 mL/min, wavelength = 230 nm. Retention times: 22.2 min, 28.2 min (major product with catalyst (*S*)-**2**). $[\alpha]_{\text{D}} = +50.7$ (*c* 0.1, DCM). Mp: 126-127 °C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ 30.4; ^1H NMR (CDCl_3 , 400 MHz): δ 7.90-7.79 (m, 4H, Ar), 7.52-7.45 (m, 6H, Ar), 7.26-7.15 (m, 5H, Ar), 6.41 (dd, 1H, $^3J = 15.9$ Hz, $^3J = 3.20$ Hz, PhCH=CH), 6.19-6.12 (m, 1H, PhCH=CH), 4.21-4.15 (m, 1H, $(\text{CO}_2)_2\text{CH}$), 4.13-3.99 (m, 4H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 3.98-3.88 (m, 1H, PCH), 1.15-1.10 (m, 6H, $\text{CO}_2\text{CH}_2\text{CH}_3$); ^{13}C NMR (CDCl_3 , 125 MHz): δ 167.6 (d, 1C, $^3J_{\text{PC}} = 10.8$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 167.3 (d, 1C, $^3J_{\text{PC}} = 10.8$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 136.4-121.5 (17C, Ar and C=C), 61.9 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 61.7 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 51.3 (1C, $(\text{CO}_2)_2\text{CH}$), 44.6 (d, 1C, $^1J_{\text{PC}} = 67.1$ Hz, PCH), 14.0 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 13.9 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$). HRMS (+ESI) *m/z*: (*M* + *H*)⁺ calcd for $\text{C}_{28}\text{H}_{30}\text{O}_5\text{P}$, 477.1832; found, 477.1830. Anal. Calcd for $\text{C}_{28}\text{H}_{29}\text{O}_5\text{P}$: C, 70.58; H, 6.13. Found: C, 70.77; H, 6.34%.

181b White solid. The *ee* was determined on a Daicel Chiralpak AD column with *n*-hexane/2-propanol = 75/25, flow = 0.8 mL/min, wavelength = 230 nm. Retention times: 23.7 min, 41.3 min. $[\alpha]_D = -8.4$ (*c* 0.1, DCM). Mp: 139-141 °C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ 33.6; ^1H NMR (CDCl_3 , 400 MHz): δ 7.86-7.81 (m, 2H, Ar), 7.53-7.47 (m, 5H, Ar), 7.37-7.35 (m, 2H, Ar), 7.30-7.24 (m, 3H, Ar), 7.20-7.17 (m, 3H, Ar), 6.14 (ddd, 1H, $^3J = 15.3$ Hz, 9.28 Hz, 6.64 Hz, PhCHPCH=CH), 5.72 (ddd, 1H, $^3J = 15.4$ Hz, 9.04 Hz, 3.80 Hz, PhCHPCH=CH), 4.29-4.24 (m, 1H, PhCHP), 4.10 (q, 2H, $^3J = 7.08$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 4.03-3.99 (m, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 3.93 (d, 1H, $^3J = 9.08$ Hz, $(\text{CO}_2)_2\text{CH}$), 1.19-1.14 (m, 6H, $\text{CO}_2\text{CH}_2\text{CH}_3$); ^{13}C NMR (CDCl_3 , 125 MHz): δ 167.7 (d, 1C, $^3J_{\text{PC}} = 3.14$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 167.5 (d, 1C, $^3J_{\text{PC}} = 2.86$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 135.3-126.7 (17C, Ar and C=C), 61.8 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 61.8 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 55.6 (1C, $(\text{CO}_2)_2\text{CH}$), 51.9 (d, 1C, $^1J_{\text{PC}} = 64.1$ Hz, PCH), 14.1 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$), 14.1 (1C, $\text{CO}_2\text{CH}_2\text{CH}_3$). HRMS (+ESI) *m/z*: (*M* + *H*)⁺ calcd for $\text{C}_{28}\text{H}_{30}\text{O}_5\text{P}$, 477.1832; found, 477.1835. Anal. Calcd for $\text{C}_{28}\text{H}_{29}\text{O}_5\text{P}$: C, 70.58; H, 6.13. Found: C, 70.73; H, 6.37%.

Chapter 5 Catalytic AHP of $\alpha,\beta,\gamma,\delta$ -Unsaturated Substrates

5.1 General Introduction to Conjugate Addition of $\alpha,\beta,\gamma,\delta$ -Unsaturated Substrates

The enantioselective formation of carbon-carbon bonds through conjugate addition (CA) is an attractive and practical strategy towards generating highly functionalized molecular synthons.^[225] Regrettably, the simultaneous control of stereo- and regio-selectivities is of major concern and remains a challenge in asymmetric CA, especially so in the case of activated linear $\alpha,\beta,\gamma,\delta$ -unsaturated substrates. Due to the presence of three potentially accessible electrophilic sites, the selective formation of 1,2-, 1,4- or 1,6-adducts becomes intrinsically difficult. Nevertheless, significant progress has

Scheme 5.56. Conjugate addition to electron deficient dienes.

been achieved by the groups of Hayashi,^[226] Feringa,^[227] Fillion^[228] and Alexakis^[229] in the regioselective construction of C-C bonds in a highly enantioselective manner. In comparison, the asymmetric formation of C-heteroatom bonds (e.g. C-Si, C-N, C-S and C-P bonds) involving linear $\alpha,\beta,\gamma,\delta$ -unsaturated compounds are relatively scarce in literature.^[230] In the case of C-P bond formation involving conjugated diunsaturated compounds, this is limited to just two reports.^[151d,220c] The well established roles of chiral phosphines in multiple areas of science such as pharmaceuticals, organocatalysis and transition metal catalysis^[22e,f,h,i,231] have generated compounding interest in the

asymmetric construction of C-P bonds *via* metal-catalyzed HP reactions with unsaturated olefins.^[50a,112,113,125a,151a,b,d-h,219] It should be iterated that this method is able to produce chiral tertiary phosphines in an economical, straightforward and practical manner. The two instances of chiral phosphines produced *via* regioselective CA employing PCP-pincer complexes catalyzed AHP protocol was reported by Duan^[220c] and our group.^[151d] The former focused on the addition of diarylphosphines to $\alpha,\beta,\gamma,\delta$ -unsaturated sulfonic esters which proceeded with 1,6-regioselectivity at -60°C. The latter involved the addition of HPPh₂ to an $\alpha,\beta,\gamma,\delta$ -diunsaturated malonate ester. Interestingly, a rational choice of either the PC-cyclometalated catalyst **119** or the PCP-pincer complex **149aa** could afford the 1,4- or 1,6-product respectively. This indicates the need to systematically investigate the role of catalyst design in this synthetically useful methodology.

Scheme 5.57. 1,6-regioselective addition of diarylphosphines reported by Duan.^[220c]

Scheme 5.58. Regioselective addition of diphenylphosphine reported by our group.^[151d]

Although both cases utilized chiral PCP pincer complexes, (*S,S*)-**163** was prepared from a chiral diol *via* the classical protection-deprotection methodology in low overall yields of 32%.^[125c] In our case, by leveraging on the newly developed synthetic protocol^[206] (see Schemes 2.40 and 2.41), we are able to prepare a series of chiral PCP- and PCN-pincer complexes in isolated yields of up to 75%. The new catalytic preparation of chiral pincer ligands grants flexibility in the facile incorporation of various functionalities on the backbones, and also allows the diversification from traditional pincer complexes whose synthesis rely heavily on the chiral pool of auxiliaries. To demonstrate the effects of different pincer architecture on catalytic activity and stereoselectivity, it is essential to conduct a systematic examination of the pincer complexes in a specific asymmetric catalytic scenario. We decided to apply the pincer complexes in the asymmetric CA of diarylphosphines to $\alpha,\beta,\gamma,\delta$ -diunsaturated substrates.

5.2 Results and Discussion

5.2.1 General Catalytic Investigation

Due to the wide array of potential pincer complexes that may be synthesized by the AHP/cyclometalation protocol, there is a need to narrow down the choices of catalyst for the targeted AHP reaction. The general catalytic properties of several PCP- and PCN-pincer complexes were investigated in the AHP of $\alpha,\beta,\gamma,\delta$ -diunsaturated enone **183a**. For the purpose of comparison, palladacycle (*S*)-**119** was included in the study due to its proven potential as an efficient catalyst in the AHP of activated olefins.^[112b-j] In conjunction with previous observations,^[151d] we believe that the acetate derivatives of the pincer complexes will serve as the most suitable form of active catalysts in this reaction. A preliminary catalytic screening of the cyclometalated complexes were conducted and the results are tabulated in Table 5.12.

Figure 5.41. Chiral cyclometalated complexes employed.

Table 5.12. Screening of catalysts in the AHP of enone **183a**.^[a]

Entry	cat.	<i>t</i> (h)	<i>ee</i> ^[b] (%)	Yield ^[c] (%)
1	(S) - 119 ^[d]	3	24	80
2	(R,R) - 149aa	3	5	80
3	(R,R) - 149ea	4	21	79
4	(R,R) - 149ha	24	2	73
5	(R,R) - 150aa	20	69	89
6	(R,R) - 150ba	24	68	87
7	(R,R) - 150ca	24	16	86
8	(R,R) - 150da	48	4	71
9	(R) - 153aa	24	10	85
10	(R) - 153ba	24	3	69

[a] Conditions: cat. (2.5 μmol, 5 mol %), HPh₂PPh₂ (0.06 mmol, 1.2 equiv.), enone **183a** (0.05 mmol, 1.0 equiv.) and DCM (3 mL) at RT. [b] *ee* was determined by chiral HPLC. [c] Isolated yield. [d] Addition of NEt₃ (1.2 equiv.) as an external base was necessary for the reaction to proceed.

The AHP reaction catalyzed by PC-palladacycle (S) -**119** (Entry 1) was encouraging in terms of yield and reactivity, but the *ee* achieved was substantially lower than the best performing pincer catalyst (R,R) -**150aa** or (R,R) -**150ba** (Entries 5, 6) at room temperature. As far as the pincer catalysts were concerned, a preliminary analysis of the collated data allowed three main inferences to be made: (1) palladium is a better metal ion than both platinum and nickel, (2) the PCN-pincer complexes were inferior to their

PCP counterparts in consideration of reactivities, *ee*'s and yields, and (3) the ester-functionalized Pd-pincer complexes **150aa** and **150ba** clearly outperforms the keto-functionalized **149aa**, **ea**, **ha**, **153aa** and **ba** in controlling the stereoselectivity of the reaction.

Comparing the same ligand backbone with different transition metals sheds light on the contrasting reactivity and stereoselectivity between Pd, Pt and Ni for this AHP reaction (Entries 2, 4, 5, 7-10). For example, the reactivities and *ee*'s of the ester-functionalized complexes **150aa** (Pd), **ca** (Pt) and **da** (Ni) decrease in the order Pd > Pt > Ni. Another point to note is that the modification of the terminal *R* groups in both the keto- and ester-functionalized complexes (Entries 2, 3, 5 and 6) had marginal impact on stereoselectivity and yields, possibly due to the remoteness of these groups from the metal centers. Overall, we were gratified to discover that in all cases, the 1,4-adduct **184a** was formed exclusively in excellent yields of up to 89%. In contrary to the previous study (see Scheme 5.58) in which the 1,6-product **181b** was formed in the presence of catalyst **149aa**, we believed that the reduced steric bulk of the ketone moiety on **183a** allowed the asymmetric CA to occur at the β -position of the diunsaturated substrate. In consideration of the optimum balance between reactivity, enantioselectivity and yield, the pincer complex (*R,R*)-**150aa** was shortlisted as the catalyst of choice for further optimization studies. The AHP reaction between HPPh₂ and diene **183a** catalyzed by complex **150aa** was subsequently screened in a variety of solvent and temperature to determine the optimal reaction conditions. The results are presented in Table 5.13.

We were delighted to find out that in majority of the cases, the AHP reaction afforded excellent *ee* and high yields under mild conditions, albeit with varying reaction durations. Acetone was selected as the solvent of choice due to the short reaction time, high *ee* and yield (Entry 9). The same reaction in acetone was conducted at 0°C and 99%

Table 5.13. Optimization of AHP reaction conditions with catalyst (*R,R*)-**150aa**.^[a]

Entry	Solvent	T (°C)	<i>t</i> (h)	<i>ee</i> ^[b] (%)	Yield ^[c] (%)
1	Toluene	RT	15	92	88
2	MTBE	RT	8	93	83
3	MeOH	RT	24	16	51 ^[d]
4	THF	RT	24	80	62 ^[d]
5	Benzene	RT	12	90	82
6	MeCN	RT	22	94	81
7	DEE	RT	4	92	81
8	EA	RT	4	91	76
9	Acetone	RT	5	97	84
10	Acetone	0	6	99	92
11 ^[e]	Acetone	RT	6	95	88

[a] Conditions: cat. (*R,R*)-**150aa** (2.5 μ mol, 5 mol %), HPPPh₂ (0.06 mmol, 1.2 equiv.), enone **183a** (0.05 mmol, 1.0 equiv.) and solvent (3 mL) at desired temperature. [b] *ee* was determined by chiral HPLC. [c] Isolated yield. [d] Incomplete conversion of HPPPh₂. [e] Catalyst (*R,R*)-**150ba** was used instead.

ee was achieved (Table 5.13, entry 10). In terms of both reactivity and *ee*, this surpassed a previously reported methyl-substituted PCP-pincer catalyzed AHP of substrate **183a** to form **184a** (in 93% *ee* and 93% yield at RT over 24 h).^[220c] The sterically bulkier benzyl-ester PCP complex **150ba** was also employed in the AHP reaction and the data obtained signifies that modification of the terminal functionalities has negligible effects on stereoselectivity (Table 5.13, entry 11).

With the optimal conditions established, a series of linear $\alpha,\beta,\gamma,\delta$ -diunsaturated enones were applied in the (*R,R*)-**150aa**-catalyzed AHP reaction. This is the first instance in literature wherein an AHP has been attempted on such a wide range of functionalized conjugated enones. The pincer complex (*R,R*)-**150aa** was found to exhibit excellent substrate tolerance, furnishing the 1,4-adducts **184a-q** exclusively in high *ee*'s (90-99%) and isolated yields of 78-92% (see Table 5.14). A broad spectrum of functional groups such as substituted aryls, heterocyclic rings and alkyl groups were screened. Notably present were electron-donating groups such as amino- and methoxy-moieties (Table 5.14, entries 15, 16) or electron-withdrawing groups such as nitro (Entries 3-5). In all these instances, the reactions proceeded smoothly to afford the desired products (4-6 h) without

Table 5.14. Substrate scope of AHP reaction.^[a]

Entry	R	R ¹	T (°C)	184	<i>ee</i> ^[b] (%)	Yield ^[c] (%)
1	Ph	4-PhC ₆ H ₄	RT	184b	90	81
2	Ph	4-PhC ₆ H ₄	0	184b	94	86
3	Ph	3-NO ₂ C ₆ H ₄	RT	184c	95	84
4 ^[d]	Ph	3-NO ₂ C ₆ H ₄	RT	184c	94	89
5	Ph	3-NO ₂ C ₆ H ₄	0	184c	>99	92
6	Ph	4-CF ₃ C ₆ H ₄	0	184d	>99	86
7	Ph	3,4-ClC ₆ H ₃	0	184e	>99	88
8	Ph	2-naphthyl	0	184f	>99	85
9	Ph	2-furyl	0	184g	99	78
10	Ph	4-pyrenyl	RT	184h	93	90
11 ^[d]	Ph	4-pyrenyl	RT	184h	96	89
12	Ph	4-pyrenyl	0	184h	97	86
13	Ph	4-BrC ₆ H ₄	0	184i	>99 (<i>S</i>) ^[e]	90
14	Ph	4-FC ₆ H ₄	0	184j	97	91
15	Ph	2-NH ₂ C ₆ H ₄	0	184k	98	82
16	Ph	4-OMeC ₆ H ₄	0	184l	>99	85
17	Ph	2,5-ClC ₆ H ₃	0	184m	96	88
18	Ph	2-pyridinyl	0	184n	>99	88
19	Ph	2-thionyl	0	184o	97	89
20	Et	Ph	0	184p	97	91
21 ^[f]	Ph	Ph	RT	184q	97	84

[a] Conditions: cat. (*R,R*)-**150aa** (2.5 μmol, 5 mol %), HPPPh₂ (0.06 mmol, 1.2 equiv.), enone **183** (0.05 mmol, 1.0 equiv.) and solvent (3 mL) at desired temperature. [b] *ee* was determined by chiral HPLC. [c] Isolated yield. [d] Catalyst (*R,R*)-**150ba** was used. [e] Absolute configuration was determined by X-ray analysis. [f] HP(*o*-tolyl)₂ (0.06 mmol, 1.2 equiv.) was used.

any noticeable changes in reactivities. The sterically bulkier di-*o*-tolylphosphine (Entry 21) was also successful in generating the 1,4-adduct **184q** in 97% *ee*. The single crystal of product (*S*)-**184i** was obtained from a solution of DCM/*n*-hexane. The molecular structure of (*S*)-**184i** is presented in Figure 5.42.

As aforementioned, Duan^[220c] had reported the regioselective addition of phosphines to $\alpha,\beta,\gamma,\delta$ -diunsaturated sulfonic esters to generate the 1,6-adducts selectively (see Scheme 5.57). Subsequently, we investigated the control of regioselectivity by an appropriate choice of palladium(II) catalyst for the AHP of an $\alpha,\beta,\gamma,\delta$ -diunsaturated malonate ester **180** (see Scheme 5.58). When the keto-based pincer (*R,R*)-**149aa** was

Figure 5.42. Molecular structure of product (*S*)-**184i**. Hydrogen atoms except H(C9) were omitted for clarity.

employed as the catalyst, 1,6-adducts were obtained regioselectively but with moderate *ee*'s (22-70%).^[151d] Encouraged by the excellent results gathered in the current study where 1,4-adducts were generated regioselectively with the ester-based complex (*R,R*)-**150aa**, we decided to examine the underlying factors which caused the dramatic regioselectivity reversal that was observed. A model reaction involving the AHP of diethyl-2-cinnamylidenemalonate **180** was set up as illustrated in Table 5.15, but this time utilizing both pincer complexes (*R,R*)-**149aa** and (*R,R*)-**150aa** for comparison. It was noted that in the AHP of $\alpha,\beta,\gamma,\delta$ -diunsaturated enone **183a**, the keto-functionalized (*R,R*)-**149aa** and the ester-functionalized (*R,R*)-**150aa** gave the 1,4-adduct **184a** with *ee*'s of 5% and 69% respectively. However, when both pincer complexes **149aa** and **150aa** were extended to the AHP of the bulkier substrate **180**, the corresponding 1,6-adduct **181b** was formed exclusively with *ee*'s of 37% and >99% respectively. Modifying the substrate bulk predictably resulted in the formation of **181b**, whereas the enone **183a** selectively formed the traditionally favored (in terms of activation towards nucleophilic attack) 1,4-adduct

Table 5.15. Catalytic AHP of substrate **180**.^[a]

Entry	cat.	<i>t</i> (h)	181a:181b ^[b]	<i>ee</i> ^[c] (%)	Yield ^[d] (%)
1	(<i>R,R</i>)- 149aa	2	0:100	38	92
2	(<i>R,R</i>)- 150aa	3	0:100	>99	93

[a] Conditions: cat. (2.5 μ mol, 5 mol %), HPPH₂ (0.06 mmol, 1.2 equiv.), substrate (0.05 mmol, 1.0 equiv.) and DCM (3 mL) at RT. [b] Ratio of **181a:181b** was determined by integration of their respective ¹H NMR signals at 6.41 and 5.72 ppm. [c] *ee* was determined by chiral HPLC. [d] Isolated yield.

184a. This is in agreement with our earlier explanation that the regioselectivity is controlled by the sterically unfavorable interaction between the pendant arms of the pincer complex and the bulky ester groups on substrate **180** during the course of the catalytic reaction (see Scheme 4.54). Furthermore, the analogous methyl-substituted pincer (*S,S*)-**163** afforded products **181a** and **181b** in a 1:9 ratio with 43% *ee*.^[220c] From the viewpoint of the PCP pincers, it was inferred that complex **163** experienced less steric interactions with substrate **180** compared to complexes **149aa** and **150aa**, which contributed to better regioselective control.

5.2.2 Enantioselectivity Control of Pincer Complex (*R,R*)-**150aa**

Notably, it was observed that complex (*R,R*)-**150aa** achieves higher enantio-discrimination than the analogous (*R,R*)-**149aa** with both substrates **180** and **183**. Under the same reaction conditions (DCM, RT), complex **149aa** gave an *ee* value of 5% for substrate **183a** (Table 5.12, entry 2) and 38% for substrate **180** (Table 5.15, entry 1), while complex **150aa** afforded 69% (enone **183a**, Table 5.12, entry 5) and >99% (substrate **180**, Table 5.15, entry 2) *ee*. To investigate the origin for the superior

stereochemical control exhibited by complex **(R,R)-150aa** as compared to **(R,R)-149aa**, their steric properties were first analyzed from the perspective of their characteristic twist angle, θ .^[165] For a particular pincer system, a larger θ with a smaller P→M←P angle will reflect a more compact conformation, which potentially limits the access of a reactant to the metal center in the direction *trans* to the M-C(aryl) bond axis.^[160] By comparing the single crystal X-ray structures^[206] (see Table 2.5) of the chloro-derivatives of both pincer complexes, it was revealed that their solid state structures have identical θ (19.64°) and similar P→Pd←P angles [**(R,R)-149aa** = 162.24(4)° and **(R,R)-150aa** = 161.05(2)°]. Bond lengths, angles and geometries of the atoms around the metal centers of the complexes are also comparable, therefore suggesting that the contrasting stereoselectivity of the pincer complexes might be directly related to the substituents on the C-stereogenic centers. A two dimensional ¹H-¹H Nuclear Overhauser Effect Spectroscopy (NOESY) experiment was conducted on complex **(R,R)-150a** (the chloro-derivative of **(R,R)-150aa**) and the spectrum is shown in Figure 5.43. It indicates a favorable disposition of the side arms (bearing the ester moieties) around the active site of the metal center, which is not observed for complex **(R,R)-149a** (the chloro-derivative of **(R,R)-149aa**). The assignments of the crucial proton NOE's are explained in detail according to the illustration in Figure 5.44.

The X-ray crystal structure of complex **(R,R)-150a** shows 2 five-membered rings each containing a C-stereogenic center. The bulky ester groups are located on the axial plane and H(1) are found at the equatorial position. This arrangement will avoid major steric repulsions between the ester groups and the adjacent central aryl ring as well as the -PPh₂ groups. The 2 phenyl substituents on each P atoms are non-equivalent. In this study, the ¹H-¹H NOESY NMR was used to investigate if the structural features of the pincer complex **150a** is retained in solution. It is particularly interesting to find out about:

Figure 5.43. ^1H - ^1H NOESY spectrum of complex (*R,R*)-**150a**.

Figure 5.44. Molecular structure of complex (*R,R*)-**150a**.

(1) the rotation of the $\text{CH}(\text{CO}_2\text{Me})_2$ groups along the $\text{C}(7)\text{-C}(8)$ and $\text{C}(25)\text{-C}(26)$ bond axes, and (2) the rigidity of the ring conformation in solution. As shown in Table 5.16, four of the ^1H NMR signals are unambiguously assigned to their respective protons. The X-ray structure suggests that it is likely for Me(1) to be located at $\text{C}(10)$ and $\text{C}(28)$. This assignment is supported by the ring-shielding effect, in which the protons on $\text{C}(10)$ and

Table 5.16. Assignment of H(1) to H(4).

δ (ppm)	multiplicity	Integration	Assignment
7.09	doublet	2	H(4)
6.94	triplet	1	H(3)
4.84-4.80	multiplet	2	H(1)
3.84	doublet of doublet	2	H(2)

C(28) will be shielded by the central aryl ring, resulting in an upfield shift.^[232] Therefore, the singlet at 2.68 ppm is assigned to Me(1) and the singlet at 3.18 ppm belongs to Me(2). Using the assignment determined as above, selected NOE signals have been summarized in Table 5.17 with some important observations noted (under remarks). From the crystal structure and model studies, the presence of signals A-E are as predicted. However, several interesting NOE interactions (signals F-I) were observed.

Table 5.17. Signals observed in 2D ^1H - ^1H NOESY of complex (*R,R*)-**150a**.

Signal	NOE	Remarks
A	H(1)-H(4)	-
B	H(1)-H(5)	-
C	H(1)-H(6)	-
D	H(5)-H(6)	-
E	H(1)-H(2)	-
F	H(2)-H(6)	No NOE signal for H(2)-H(5)
G	Me(1)-H(5)	No NOE signal for Me(1)-H(6)
H	Me(1)-H(4)	No NOE signal for Me(2)-H(4)
I	Me(2)-H(6)	No NOE signal for Me(2)-H(5)

Figure 5.45. Conformation of five-membered chelate ring in complex **150a**.

From the ^1H - ^1H NOESY data, a fixed δ conformation is observed for both chiral five-membered rings in solution. Accordingly, if the chelate ring undergoes rapid δ and λ conversion in solution, Me(2) would have NOE interactions with both H(5) and H(6). Furthermore, H(2) should also interact with both H(5) and H(6). But the absence of NOE

signals for Me(2)-H(5) and H(2)-H(5) indicate that the 5-membered rings are in the fixed δ conformation in solution. The model study revealed that the rotations of the CH(CO₂Me)₂ groups along the C(25)-C(26) and C(7)-C(8) bond axes are sterically hindered by the equatorial phenyl substituents on the P atoms. Indeed, the ¹H-¹H NOESY shows a long range NOE interaction between Me(1) and H(5) of the phenyl ring (signal G) (e.g. protons on C(28) with the *ortho*-protons on C(20) and C(24)), but not with H(6). In contrast, Me(2) has an NOE interaction with H(6) (signal I) but not with H(5). The absence of NOE interactions between H(4) and Me(2) seems to indicate the possibility of restricted rotation of the CH(CO₂Me)₂ groups on C(8) and C(26). If the chiral functionalities are rotatable along the C(25)-C(26) and C(7)-C(8) bond axes, both Me(1) and Me(2) should have NOE interactions with H(4), H(5) and H(6).

With all the information collated from the ¹H-¹H NOESY, X-ray crystal structure and model studies, it can be deduced that: (1) the CH(CO₂Me)₂ groups are indeed not freely rotatable along the C(25)-C(26) and C(7)-C(8) bond axes, and (2) the 5-membered rings adopt the fixed δ conformation both in solution and solid state. As a result, the fixed δ ring conformation together with restricted rotation of the bulkier ester groups in complex (*R,R*)-**150a** may exert more stereocontrol over the accessibility of the substrate to the active site, thereby translating into enantio-discrimination in the AHP of $\alpha,\beta,\gamma,\delta$ -diunsaturated substrates **180** and **183**.

5.3 Conclusion

A series of enantiopure PCP- and PCN-pincer complexes were screened in the asymmetric CA of diarylphosphine to linear $\alpha,\beta,\gamma,\delta$ -unsaturated enone **183**. The new methodology developed provides a substantial improvement in reactivity while allowing the AHP to be conducted on a wide range of conjugated enones with excellent functional group tolerance. The study provided key insights into the molecular structure required in

terms of metal ion and backbone functionalities for an efficient catalyst architecture. A straightforward preparation of synthetically useful chiral allylic phosphines was achieved in high yields (81-92%) with excellent enantioselectivities (94 to >99%) under mild reaction conditions catalyzed by pincer complex (*R,R*)-**150aa**. A comparative study subsequently revealed how the combination of substrate selection in conjunction with catalyst choice can provide excellent control on stereo- and regio-selectivity in this AHP reaction. The origin of the enhanced stereoselectivity exhibited by complex (*R,R*)-**150aa** was established.

In the following chapter, several novel mono- and di-metallic $\text{NC}_{\text{sp}}^3\text{X}$ ($\text{X} = \text{O}$ or S) pincer complexes were generated based on some of the chiral phosphines that were synthesized previously.

5.4 Experimental Section

All reactions were carried out under a positive pressure of nitrogen using standard Schlenk technique. Solvents were purchased from their respective companies and used as supplied. Where necessary, solvents were degassed prior to use. A Low Temp Pairstirrer PSL-1800 was used for controlling low temperature reactions. Column chromatography was done on Silica gel 60 (Merck). Melting points were measured using SRS Optimelt Automated Point System SRS MPA100. Optical rotation were measured with JASCO P-1030 Polarimeter in the specified solvent in a 0.1 dm cell at 21.0°C. NMR spectra were recorded on Bruker AV 300, AV 400 and AV 500 spectrometers. Chemical shifts were reported in ppm and referenced to an internal SiMe_4 standard (0 ppm) for ^1H NMR, chloroform-*d* (77.23 ppm) for ^{13}C NMR, and an external 85% H_3PO_4 for $^{31}\text{P}\{^1\text{H}\}$ NMR. HPLC analysis was done with Agilent Technologies 1200 Series HPLC machine.

The palladacycle (*S*)-**119**,^[112c] (*R,R*)-**149aa**, **ea**, **ha**, (*R,R*)-**150aa**, **ba**, **ca**, **da**, (*R*)-**153aa** and **ba**^[206] were prepared according to literature methods. All other reactants and reagents were used as supplied.

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

Scheme 5.59. Preparation of Wittig Reagents.

General Procedure for Preparation of Wittig Reagents, A-F. Aryl-substituted 2-bromoethanone (5.00 mmol, 1.0 equiv.) and PPh₃ (1.44 g, 5.50 mmol, 1.1 equiv.) were refluxed in THF (10 mL) for 4 h. Upon cooling, volatiles were removed, the solids redissolved in DCM and extracted with aq. NaOH (20% w/w in H₂O, 1 x 20 mL), washed with water (1 x 20 mL), dried over MgSO₄, filtered and evaporated to dryness. The crude product was purified by silica gel chromatography (2 EA : 1 *n*-hexane) to afford the pure product.

A White solid (95% yield). The data is consistent with literature.^[167]

B Pale yellow powder (89% yield). Mp: 215-217°C (dec). ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 16.7; ¹H NMR (CDCl₃, 400 MHz): δ 8.06-8.04 (m, 2H, Ar), 7.77-7.41 (m, 21H, Ar), 7.35-7.31 (m, 1H, Ar), 4.49 (brs, 1H, P=CH); ¹³C NMR (CDCl₃, 100 MHz): δ 184.1 (d, 1C, ²J_{PC} = 3.2 Hz, C=O), 141.8 (1C, Ar), 140.8 (1C, Ar), 140.1-140.0 (1C, Ar), 133.1-126.3 (27C, Ar), 50.8 (d, 1C, ¹J_{PC} = 111.4 Hz, P=CH). HRMS (+ESI) m/z: (M +

H)⁺ calcd for C₃₂H₂₆OP, 457.1721; found, 457.1721. Anal. Calcd for C₃₂H₂₅OP: C, 84.19; H, 5.52. Found: C, 84.42; H, 5.63%.

C Bright yellow solid (99% yield). Mp: 200-202°C (dec). ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 16.9; ¹H NMR (CDCl₃, 400 MHz): δ 8.78-8.78 (m, 1H, Ar), 8.30-8.28 (m, 1H, Ar), 8.19-8.17 (m, 1H, Ar), 7.74-7.64 (m, 6H, Ar), 7.60-7.56 (m, 3H, Ar), 7.53-7.42 (m, 7H, Ar), 4.50 (d, 1H, ²J_{PH} = 22.7 Hz, P=CH); ¹³C NMR (CDCl₃, 100 MHz): δ 180.8 (d, 1C, ²J_{PC} = 3.6 Hz, C=O), 147.6 (1C, CNO₂), 142.8-142.7 (1C, Ar), 132.7-121.4 (22C, Ar), 52.0 (d, 1C, ²J_{PC} = 110.9 Hz, P=CH). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₆H₂₁NO₃P, 426.1259; found, 426.1260. Anal. Calcd for C₂₆H₂₀NO₃P: C, 73.41; H, 4.74; N, 3.29. Found: C, 73.55; H, 4.88; N, 3.33%.

D Pale yellow solid (82% yield). Mp: 199-201°C (dec). ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 16.7; ¹H NMR (CDCl₃, 400 MHz): δ 8.05 (d, 2H, ³J_{HH} = 8.1 Hz, Ar), 7.74-7.69 (m, 6H, Ar), 7.61-7.56 (m, 5H, Ar), 7.51-7.47 (m, 6H, Ar), 7.51-7.47 (m, 6H, Ar), 4.46 (d, 1H, ²J_{PH} = 23.4 Hz, P=CH) ¹³C NMR (CDCl₃, 100 MHz): δ 183.1 (1C, C=O), 144.8-144.6 (1C, Ar), 133.2-123.0 (24C, Ar), 52.3 (d, 1C, ¹J_{PC} = 110.0 Hz, P=C). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₇H₂₃F₃OP, 451.1439; found, 451.1440. Anal. Calcd for C₂₇H₂₂F₃OP: C, 72.00; H, 4.92. Found: C, 71.91; H, 4.91%.

E White powder (97% yield). Mp: 177-179°C (dec). ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 16.8; ¹H NMR (CDCl₃, 400 MHz): δ 8.05 (d, 1H, ⁴J_{HH} = 1.9 Hz, Ar), 7.77 (dd, 1H, ³J_{HH} = 8.3 Hz, ⁴J_{HH} = 1.9 Hz, Ar), 7.72-7.64 (m, 6H, Ar), 7.60-7.46 (m, 9H, Ar), 7.39 (d, 1H, ³J_{HH} = 8.3 Hz, Ar), 4.37 (d, 1H, ²J_{PH} = 23.2 Hz, P=CH); ¹³C NMR (CDCl₃, 100 MHz): δ 181.7 (1C, C=O), 141.5-141.4 (1C, Ar), 153.2-126.0 (22C, Ar), 51.9 (d, 1C, ¹J_{PC} = 111.5 Hz, P=C). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₆H₂₀Cl₂OP, 449.0629; found, 446.0631. Anal. Calcd for C₂₆H₁₉Cl₂OP: C, 69.50; H, 4.26. Found: C, 69.74; H, 4.42%.

F Yellow flakes (98% yield). Mp: 165-167°C (dec). $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 15.0; ^1H NMR (CDCl_3 , 400 MHz): 9.01 (d, 2H, $^3J_{\text{HH}} = 9.2$ Hz, Ar), 8.39 (d, 1H, $^3J_{\text{HH}} = 8.0$ Hz Ar), 8.16-8.12 (m, 3H, Ar), 8.08-8.04 (m, 3H, Ar), 7.99-7.95 (m, 1H, Ar), 7.89-7.83 (m, 6H, Ar), 7.69-7.66 (m, 2H, Ar), 7.63-7.58 (m, 2H, Ar), 7.55-7.51 (m, 7H, Ar), 7.49-7.45 (m, 2H, Ar), 4.38 (d, 1H, $^2J_{\text{PH}} = 26.0$ Hz, $\text{P}=\text{CH}$); ^{13}C NMR (CDCl_3 , 100 MHz): δ 189.2 (d, 1C, $^2J_{\text{PC}} = 3.12$ Hz, $\text{C}=\text{O}$), 139.8-139.6 (1C, Ar), 133.3-124.2 (33C, Ar), 56.7 (d, 1C, $^1J_{\text{PC}} = 105.7$ Hz, $\text{P}=\text{C}$). HRMS (+ESI) m/z : ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{36}\text{H}_{26}\text{OP}$, 505.1721; found, 505.1720. Anal. Calcd for $\text{C}_{36}\text{H}_{25}\text{OP}$: C, 85.70; H, 4.99. Found: C, 85.91; H, 4.91%.

General Procedure for Preparation of Substrates by Wittig Reaction, 183b, c, d, e, h and p. A solution of aldehyde (7.57 mmol, 1.0 equiv.) and Wittig reagent (8.32 mmol, 1.0 equiv.) in toluene (30 mL) was refluxed for 24 h. The mixture was cooled and extracted with EA (3 x 40 mL), washed with H_2O (1 x 40 mL), dried over MgSO_4 , filtered and evaporated to dryness. The crude product was purified by silica gel chromatography (2 *n*-hexane : 1 DCM) to afford the pure product.

183b Yellow solid (83% yield). Mp: 159-162°C. ^1H NMR (CDCl_3 , 400 MHz): δ 8.08-8.06 (m, 2H, Ar), 7.73-7.71 (m, 2H, Ar), 7.67-7.64 (m, 3H, Ar), 7.53-7.46 (m, 4H, Ar + $\text{C}(\text{O})\text{CH}=\text{CH}$), 7.43-7.33 (m, 3H, Ar + $\text{PhHC}=\text{CH}$), 7.39 (d, 1H, $^3J_{\text{HH}} = 15.5$ Hz, $\text{C}(\text{O})\text{HC}=\text{CH}$), 7.15 (d, 1H, $^3J_{\text{HH}} = 14.9$ Hz, $\text{PhHC}=\text{CH}$), 7.06-7.04 (m, 2H, Ar); ^{13}C NMR (CDCl_3 , 100 MHz): δ 189.8 (1C, $\text{C}=\text{O}$), 145.4 (1C, Ar), 144.8 (1C, $\text{HC}=\text{CHC}(\text{O})$), 142.0 (1C, $\text{PhHC}=\text{CH}$), 140.0-125.4 (19C, Ar + $\text{HC}=\text{CHC}(\text{O})$ + $\text{PhHC}=\text{CH}$). HRMS (+ESI) m/z : ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{23}\text{H}_{19}\text{O}$, 311.1436; found, 311.1439. Anal. Calcd for $\text{C}_{23}\text{H}_{18}\text{O}$: C, 89.00; H, 5.85. Found: C, 88.91; H, 5.67%.

183c Yellow solid (87% yield). Mp: 129-131°C. ^1H NMR (CDCl_3 , 400 MHz): δ 8.79-8.78 (m, 1H, Ar), 8.43-8.40 (m, 1H, Ar), 8.32-8.29 (m, 1H, Ar), 7.71-7.65 (m, 1H,

C(O)HC=CH), 7.69 (d, 1H, $^3J_{\text{HH}} = 15.6$ Hz, C(O)HC=CH), 7.53-7.51 (m, 2H, Ar), 7.41-7.35 (m, 3H, Ar), 7.10 (d, 1H, $^3J_{\text{HH}} = 15.1$ Hz, PhHC=CH), 7.08-7.06 (m, 2H, Ar) ; ^{13}C NMR (CDCl_3 , 100 MHz): δ 187.8 (1C, C=O), 148.4 (1C, CNO₂), 146.6 (1C, HC=CHC(O)), 143.5 (1C, PhHC=CH), 139.5 (1C, C(O)=C(Ar)), 139.5-123.2 (12C, Ar + HC=CHC(O) + PhHC=CH). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₁₇H₁₄NO₃, 280.0947; found, 280.0949. Anal. Calcd for C₁₇H₁₃NO₃: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.19; H, 4.76; N, 5.00%.

183d Yellow solid (99% yield). Mp: 125-127°C. ^1H NMR (CDCl_3 , 400 MHz): δ 8.06 (d, 2H, $^3J_{\text{HH}} = 8.2$ Hz, Ar), 7.75 (d, 2H, $^3J_{\text{HH}} = 8.3$ Hz, Ar), 7.66-7.59 (m, 1H, Ar), 7.53-7.50 (m, 2H Ar), 7.41-7.32 (m, 3H, Ar), 7.09- 7.03 (m, 3H, Ar); ^{13}C NMR (CDCl_3 , 100 MHz): δ 189.4 (1C, C=O), 146.0 (1C, HC=CHC(O)), 142.9 (1C, PhHC=CH), 141.1-135.9 (2C, Ar), 133.5 (q, 1C, $^1J_{\text{CF}} = 32.5$ Hz, CF₃), 129.5-122.4 (12C, Ar + HC=CHC(O) + PhHC=CH). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₁₈H₁₄F₃O, 303.0997; found, 303.1000. Anal. Calcd for C₁₈H₁₃F₃O: C, 71.52; H, 4.33. Found: C, 71.71; H, 4.55%.

183e Yellow solid (85% yield). Mp: 121-123°C. ^1H NMR (CDCl_3 , 400 MHz): δ 8.06 (d, 1H, $^4J_{\text{HH}} = 2.0$ Hz, Ar), 7.80 (dd, 1H, $^3J_{\text{HH}} = 8.3$ Hz, $^4J_{\text{HH}} = 2.0$ Hz, Ar), 7.63 (ddd, 1H, $^3J_{\text{HH}} = 14.9$ Hz, $^3J_{\text{HH}} = 8.9$ Hz, $^4J_{\text{HH}} = 1.4$ Hz, C(O)CH=CH), 7.57 (d, 1H, $^3J_{\text{HH}} = 8.3$ Hz, Ar), 7.52-7.50 (m, 2H, Ar), 7.41-7.34 (m, 3H, Ar + PhCH=CH + C(O)CH=CH), 7.05-6.99 (m, 3H, Ar + PhCH=CH) ; ^{13}C NMR (CDCl_3 , 100 MHz): δ 187.8 (1C, C=O), 146.0 (1C, HC=CHC(O)), 143.0 (1C, PhHC=CH), 137.8-127.4 (12C, Ar), 126.6 (1C, HC=CHC(O)), 124.2 (1C, PhHC=CH). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₁₇H₁₃Cl₂O, 303.0343; found, 303.0344. Anal. Calcd for C₁₇H₁₂Cl₂O: C, 67.35; H, 3.99. Found: C, 67.51; H, 4.21%.

183h Yellow solid (78% yield). Mp: 120-123°C. ^1H NMR (CDCl_3 , 400 MHz): δ 8.60 (d, 1H, $^3J_{\text{HH}} = 9.3$ Hz, Ar), 8.25-8.20 (m, 4H, Ar), 8.18-8.15 (m, 2H, Ar), 8.10-8.03

(m, 2H, Ar), 7.48-7.46 (m, 2H, Ar), 7.43 (dd, 1H, $^3J_{\text{HH}} = 15.3$ Hz, $^3J_{\text{HH}} = 4.4$ Hz, C(O)CH=CH), 7.38-7.30 (m, 3H, Ar), 7.05 (dd, 1H, $^3J_{\text{HH}} = 15.5$ Hz, $^3J_{\text{HH}} = 10.9$ Hz, PhHC=CH), 7.01 (d, 1H, $^3J_{\text{HH}} = 15.2$ Hz, C(O)HC=CH), 6.90 (d, 1H, $^3J_{\text{HH}} = 15.5$ Hz, PhHC=CH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 195.9 (1C, C=O), 146.0 (1C, HC=CHC(O)), 142.1 (1C, PhHC=CH), 136.0-124.1 (24C, Ar + HC=CHC(O) + PhHC=CH). HRMS (+ESI) m/z : (M + H) $^+$ calcd for $\text{C}_{27}\text{H}_{19}\text{O}$, 359.1436; found, 359.1436. Anal. Calcd for $\text{C}_{27}\text{H}_{18}\text{O}$: C, 90.47; H, 5.06. Found: C, 90.70; H, 5.11%.

183p Yellow oil (75% yield). The data is consistent with literature.^[233]

General Procedure for Preparation of Substrates by Aldol Condensation, 183a, f, g, i-o. To a solution of NaOH (55.0 mmol, 1.2 equiv.) in H_2O (20 mL) and aromatic ketone (45.8 mmol, 1.0 equiv.) in ethanol (12 mL) at 0°C was gradually added aromatic aldehyde (45.8 mmol, 1.0 equiv.). The mixture was allowed to warm to room temperature and stirred for 4 h, after which the precipitate of the product was collected by suction filtration on a Buchner funnel and washed repeatedly with cold water. The residue was redissolved in DCM and extracted, washed with H_2O (1 x 40 mL), dried over MgSO_4 , filtered and evaporated to dryness. The crude product was purified by silica gel chromatography (2 *n*-hexane : 1 DCM) to afford the pure enone.

183a Pale yellow solid (85% yield). The data is consistent with literature.^[234]

183f Yellow solid (88% yield). The data is consistent with literature.^[235]

183g Yellow solid (85% yield). The data is consistent with literature.^[236]

183i Yellow solid (82% yield). The data is consistent with literature.^[237]

183j Yellow solid (85% yield). The data is consistent with literature.^[238]

183k Yellow solid (69% yield). Mp: 114-116°C. ¹H NMR (CDCl₃, 300 MHz): δ 7.77 (d, 1H, ³J_{HH} = 8.2 Hz, Ar), 7.52 (dd, 1H, ³J_{HH} = 14.7 Hz, ³J_{HH} = 10.1 Hz, C(O)CH=CH), 7.46 (d, 1H, ³J_{HH} = 7.2 Hz, Ar), 7.36-7.22 (m, 4H Ar), 7.15 (d, 1H, ³J_{HH} = 14.8 Hz, C(O)CH=CH), 7.02-6.90 (m, 2H, Ar + PhCH=CH), 6.68-6.64 (m, 2H, Ar + PhCH=CH), 6.33 (brs, 2H, NH₂); ¹³C NMR (CDCl₃, 100 MHz): δ 191.8 (1C, C=O), 151.1 (1C, CNH₂), 143.2 (1C, HC=CHC(O)), 140.8 (1C, PhCH=CH), 136.5-131.0 (3C, Ar), 129.1 (1C, HC=CHC(O)), 128.9-127.3 (4C, Ar), 126.7 (1C, PhHC=CH), 119.2-115.9 (4C, Ar). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₁₇H₁₆NO, 250.1232; found, 250.1236. Anal. Calcd for C₁₇H₁₅NO: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.91; H, 6.31; N, 5.69%.

183l Yellow solid (87% yield). The data is consistent with literature.^[238]

183m Yellow solid (81% yield). ¹³C NMR (CDCl₃, 100 MHz): δ 192.4 (1C, C=O), 147.3 (1C, HC=CHC(O)), 143.3 (1C, PhCH=CH), 140.6-129.3 (10C, Ar), 129.1 (1C, HC=CHC(O)), 127.7 (2C, Ar), 126.6 (1C, PhHC=CH). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₁₇H₁₃Cl₂O, 303.0343; found, 303.0346. Anal. Calcd for C₁₇H₁₂Cl₂O: C, 67.35; H, 3.99. Found: C, 67.51; H, 4.21%. The remaining data is consistent with literature.^[239]

183n Yellow solid (89% yield). The data is consistent with literature.^[240]

183o Yellow solid (83% yield). The data is consistent with literature.^[241]

General Procedure for Catalytic Hydrophosphination Reaction. The catalyst (2.5 μmol, 5 mol %) was added to a solution of diarylphosphine (0.06 mmol, 1.2 equiv.) in the stated solvent (3 mL) and brought to the desired temperature. The substrate (0.05 mmol, 1.0 equiv.) was subsequently added and stirred at the stated temperature. Completion of the reaction was determined by the disappearance of the phosphorus signal

attributed to diphenylphosphine (-40 ppm) or di(*o*-tolyl)phosphine (-60 ppm) in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum. Upon completion of the reaction, aq. H_2O_2 (0.1 mL, 31% v/v) was added to form the respective product. The volatiles were removed under reduced pressure and the crude product was directly loaded onto silica gel column (ethyl acetate : *n*-hexane = 3: 2) to afford the pure product.

184a White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 80/20, flow = 1.0 mL/min, wavelength = 254 nm. Retention times: 15.6 min (major), 18.8 min (minor). $[\alpha]_{\text{D}} = -79.7$ (*c* 0.1, DCM). Mp: 188-190°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ 34.2; ^1H NMR (CDCl_3 , 300 MHz): δ 7.95-7.88 (m, 4H, Ar), 7.85-7.78 (m, 2H, Ar), 7.55-7.38 (m, 9H, Ar), 7.23-7.12 (m, 5H, Ar), 6.41 (dd, 1H, $^4J_{\text{HP}} = 4.2$ Hz, $^3J_{\text{HH}} = 15.9$ Hz, PhCH=CH), 6.12 (ddd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^3J_{\text{HP}} = 9.1$ Hz, $^3J_{\text{HH}} = 6.4$ Hz, PhCH=CH), 4.22-4.11 (m, 1H, PCH), 3.67 (ddd, 1H, $^2J_{\text{HH}} = 17.7$ Hz, $^3J_{\text{HP}} = 10.2$ Hz, $^3J_{\text{HH}} = 4.5$ Hz, PCHCHH), 3.29 (ddd, 1H, $^2J_{\text{HH}} = 17.7$ Hz, $^3J_{\text{HP}} = 11.4$ Hz, $^3J_{\text{HH}} = 2.4$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 196.9 (d, 1C, $^3J_{\text{PC}} = 13.1$ Hz, C=O), 136.8-123.5 (26C, Ar + HC=CH), 39.1 (d, 1C, $^2J_{\text{PC}} = 70.1$ Hz, PCHCH₂), 33.5 (d, 1C, $^1J_{\text{PC}} = 739.5$ Hz, PCH). HRMS (+ESI) *m/z*: (*M* + *H*)⁺ calcd for $\text{C}_{29}\text{H}_{26}\text{O}_2\text{P}$, 437.1670; found, 437.1676. Anal. Calcd for $\text{C}_{29}\text{H}_{25}\text{O}_2\text{P}$: C, 79.80; H, 5.77. Found: C, 79.89; H, 5.97%.

184b Yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 75/25, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 14.8 min (major), 17.8 min (minor). $[\alpha]_{\text{D}} = -77.9$ (*c* 0.1, DCM). Mp: 197-200°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 34.3; ^1H NMR (CDCl_3 , 400 MHz): δ 7.99-7.91 (m, 4H, Ar), 7.82 (ddd, 2H, $^3J_{\text{HH}} = 9.8$ Hz, $^3J_{\text{HH}} = 7.8$ Hz, $^4J_{\text{HH}} = 1.3$ Hz, Ar), 7.65-7.58 (m, 4H, Ar), 7.53-7.37 (m, 9H, Ar), 7.23-7.14 (m, 5H, Ar), 6.43 (dd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^4J_{\text{HP}} = 4.2$ Hz, PhCH=CH), 6.15 (ddd, 1H, $^3J_{\text{HH}} = 15.6$ Hz, $^3J_{\text{HP}} = 9.1$ Hz, $^3J_{\text{HH}} = 6.4$ Hz,

PhCH=CH), 4.23-4.16 (m, 1H, PCH), 3.71 (ddd, 1H, $^2J_{\text{HH}} = 17.6$ Hz, $^3J_{\text{HP}} = 10.2$ Hz, $^3J_{\text{HH}} = 4.5$ Hz, PCHCHH), 3.32 (ddd, 1H, $^2J_{\text{HH}} = 17.6$ Hz, $^3J_{\text{HP}} = 11.4$ Hz, $^3J_{\text{HH}} = 2.4$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 196.5 (d, 1C, $^3J_{\text{PC}} = 13.0$ Hz, C=O), 146.3-123.5 (32C, Ar + HC=CH), 39.2 (d, 1C, $^2J_{\text{PC}} = 69.9$ Hz, PCHCH₂), 33.6 (d, 1C, $^1J_{\text{PC}} = 742.0$ Hz, PCH). HRMS (+ESI) m/z : (M + H)⁺ calcd for C₃₅H₃₀O₂P, 513.1983; found, 513.1985. Anal. Calcd for C₃₅H₂₉O₂P: C, 82.01; H, 5.70. Found: C, 82.44; H, 5.87%.

184c Yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 75/25, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 38.6 min (major), 73.6 min (minor). $[\alpha]_{\text{D}} = -75.6$ (*c* 0.1, DCM). Mp: 141-143°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 33.7; ^1H NMR (CDCl_3 , 400 MHz): δ 8.69 (t, 1H, $^4J_{\text{HH}} = 1.9$ Hz, Ar), 8.36 (ddd, 1H, $^3J_{\text{HH}} = 8.2$ Hz, $^4J_{\text{HH}} = 2.2$ Hz, $^4J_{\text{HH}} = 1.0$ Hz, Ar), 8.20 (dt, 1H, $^3J_{\text{HH}} = 7.8$ Hz, $^4J_{\text{HH}} = 1.2$ Hz, Ar), 7.91 (ddd, 2H, $^3J_{\text{HH}} = 10.9$ Hz, $^3J_{\text{HH}} = 7.5$ Hz, $^4J_{\text{HH}} = 1.5$ Hz, Ar), 7.81 (ddd, 2H, $^3J_{\text{HH}} = 11.1$ Hz, $^3J_{\text{HH}} = 7.8$ Hz, $^4J_{\text{HH}} = 1.3$ Hz, Ar), 7.61 (t, 1H, $^3J_{\text{HH}} = 8.0$ Hz, Ar), 7.52-7.41 (m, 6H, Ar), 7.23-7.14 (m, 5H, Ar), 6.43 (dd, 1H, $^3J_{\text{HH}} = 15.8$ Hz, $^4J_{\text{HP}} = 4.1$ Hz, PhCH=CH), 6.12 (ddd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^3J_{\text{HP}} = 9.2$ Hz, $^3J_{\text{HH}} = 6.3$ Hz, PhCH=CH), 4.20-4.12 (m, 1H, PCH), 3.65 (ddd, 1H, $^2J_{\text{HH}} = 17.7$ Hz, $^3J_{\text{HP}} = 9.8$ Hz, $^3J_{\text{HH}} = 5.4$ Hz, PCHCHH), 3.38 (ddd, 1H, $^2J_{\text{HH}} = 17.7$ Hz, $^3J_{\text{HP}} = 11.2$ Hz, $^3J_{\text{HH}} = 2.8$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 195.0 (d, 1C, $^3J_{\text{PC}} = 12.9$ Hz, C=O), 148.6 (1C, CNO₂), 137.9-123.1 (25C, Ar + HC=CH), 39.3 (d, 1C, $^2J_{\text{PC}} = 69.5$ Hz, PCHCH₂), 33.8 (d, 1C, $^1J_{\text{PC}} = 785.9$ Hz, PCH). HRMS (+ESI) m/z : (M + H)⁺ calcd for C₂₉H₂₅NO₄P, 482.1521; found, 482.1521. Anal. Calcd for C₂₉H₂₄NO₄P: C, 72.34; H, 5.02; N, 2.91. Found: C, 72.44; H, 5.47; N, 3.01%.

184d Yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 75/25, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 7.5 min (major), 9.7 min (minor). $[\alpha]_{\text{D}} = -69.2$ (*c* 0.1, DCM). Mp: 146-148°C. $^{31}\text{P}\{^1\text{H}\}$

NMR (CDCl₃, 162 MHz): δ 33.9; ¹H NMR (CDCl₃, 400 MHz): 7.88 (d, 2H, ³J_{HH} = 8.2 Hz, Ar), 7.93-7.87 (m, 2H, Ar), 7.84-7.77 (m, 2H, Ar), 7.68 (d, 2H, ³J_{HH} = 8.2 Hz, Ar), 7.52-7.43 (m, 6H, Ar), 7.22-7.14 (m, 5H, Ar), 6.41 (dd, 1H, ³J_{HH} = 15.9 Hz, ⁴J_{HP} = 4.1 Hz, PhCH=CH), 6.10 (ddd, 1H, ³J_{HH} = 15.7 Hz, ³J_{HP} = 9.2 Hz, ³J_{HH} = 6.4 Hz, PhCH=CH), 4.18-4.09 (m, 1H, PCH), 3.65 (ddd, 1H, ²J_{HH} = 17.7 Hz, ³J_{HP} = 10.0 Hz, ³J_{HH} = 5.0 Hz, PCHCHH), 3.35 (ddd, 1H, ²J_{HH} = 17.7 Hz, ³J_{HP} = 11.2 Hz, ³J_{HH} = 2.6 Hz, PCHCHH); ¹³C NMR (CDCl₃, 100 MHz): δ 196.2 (d, 1C, ³J_{PC} = 13.1 Hz, C=O), 139.3-123.2 (27C, Ar + HC=CH), 39.3 (d, 1C, ²J_{PC} = 69.6 Hz, PCHCH₂), 33.8 (d, 1C, ¹J_{PC} = 779.5 Hz, PCH). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₃₀H₂₅F₃O₂P, 504.1466; found, 504.1465. Anal. Calcd for C₃₀H₂₄F₃O₂P: C, 71.42; H, 4.80. Found: C, 71.67; H, 5.11%.

184e Yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 75/25, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 10.6 min (major), 15.7 min (minor). [α]_D = -81.8 (*c* 0.1, DCM). Mp: 139-142°C. ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 34.0; ¹H NMR (CDCl₃, 300 MHz): δ 7.96 (d, 1H, ⁴J_{HH} = 1.89 Hz, Ar), 7.93-7.86 (m, 2H, Ar), 7.83-7.76 (m, 2H, Ar), 7.71 (dd, 1H, ³J_{HH} = 8.34 Hz, ⁴J_{HH} = 1.98 Hz, Ar), 7.52-7.43 (m, 7H, Ar), 7.22-7.14 (m, 5H, Ar), 6.40 (dd, 1H, ³J_{HH} = 15.9 Hz, ⁴J_{HP} = 4.1 Hz, PhCH=CH), 6.09 (ddd, 1H, ³J_{HH} = 15.8 Hz, ³J_{HP} = 9.2 Hz, ³J_{HH} = 6.4 Hz, PhCH=CH), 4.15-4.06 (m, 1H, PCH), 3.56 (ddd, 1H, ²J_{HH} = 17.7 Hz, ³J_{HP} = 9.9 Hz, ³J_{HH} = 5.0 Hz, PCHCHH), 3.27 (ddd, 1H, ²J_{HH} = 17.7 Hz, ³J_{HP} = 11.2 Hz, ³J_{HH} = 2.6 Hz, PCHCHH); ¹³C NMR (CDCl₃, 100 MHz): δ 194.9 (d, 1C, ³J_{PC} = 13.1 Hz, C=O), 138.2-123.1 (26C, Ar + HC=CH), 39.3 (d, 1C, ²J_{PC} = 69.5 Hz, PCHCH₂), 33.6 (d, 1C, ¹J_{PC} = 751.0 Hz, PCH). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₉H₂₄Cl₂O₂P, 505.0891; found, 505.0893. Anal. Calcd for C₂₉H₂₃Cl₂O₂P: C, 68.92; H, 4.59. Found: C, 69.09; H, 4.88%.

184f White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 90/10, flow = 1.0 mL/min, wavelength = 270 nm. Retention times:

39.1 min (major), 54.8 min (minor). $[\alpha]_D = -106.4$ (*c* 0.1, DCM). Mp: 182-185°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ 34.6; ^1H NMR (CDCl_3 , 300 MHz): δ 8.45 (brs, 1H, Ar), 7.98-7.92 (m, 4H, Ar), 7.87-7.80 (m, 4H, Ar), 7.61-7.41 (m, 8H, Ar), 7.19-7.14 (m, 5H, Ar), 6.45 (dd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^4J_{\text{HP}} = 4.1$ Hz, PhCH=CH), 6.17 (ddd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^3J_{\text{HP}} = 9.0$ Hz, $^3J_{\text{HH}} = 6.4$ Hz, PhCH=CH), 4.27-4.18 (m, 1H, PCH), 3.85 (ddd, 1H, $^2J_{\text{HH}} = 17.5$ Hz, $^3J_{\text{HP}} = 10.2$ Hz, $^3J_{\text{HH}} = 4.5$ Hz, PCHCHH), 3.41 (ddd, 1H, $^2J_{\text{HH}} = 17.5$ Hz, $^3J_{\text{HP}} = 11.4$ Hz, $^3J_{\text{HH}} = 2.4$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 196.8 (d, 1C, $^3J_{\text{PC}} = 13.0$ Hz, C=O), 136.8-123.4 (32C, Ar + HC=CH), 39.2 (d, 1C, $^2J_{\text{PC}} = 69.7$ Hz, PCHCH₂), 33.6 (d, 1C, $^1J_{\text{PC}} = 738.3$ Hz, PCH). HRMS (+ESI) *m/z*: (*M* + *H*)⁺ calcd for C₃₃H₂₈O₂P, 487.1827; found, 487.1826. Anal. Calcd for C₃₃H₂₇O₂P: C, 81.46; H, 5.59. Found: C, 81.54; H, 5.76%.

184g White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 85/15, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 34.9 min (major), 44.0 min (minor). $[\alpha]_D = -86.2$ (*c* 0.1, DCM). Mp: 152-154°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 34.3; ^1H NMR (CDCl_3 , 400 MHz): δ 7.93-7.75 (m, 4H, Ar), 7.52-7.40 (m, 7H, Ar), 7.19-7.12 (m, 6H, Ar), 6.48-6.46 (m, 1H, Ar), 6.39 (dd, 1H, $^3J_{\text{HH}} = 15.7$ Hz, $^4J_{\text{HP}} = 3.9$ Hz, PhCH=CH), 6.10 (ddd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^3J_{\text{HP}} = 9.2$ Hz, $^3J_{\text{HH}} = 6.3$ Hz, PhCH=CH), 4.13-4.04 (m, 1H, PCH), 3.51 (ddd, 1H, $^2J_{\text{HH}} = 17.0$ Hz, $^3J_{\text{HP}} = 10.6$ Hz, $^3J_{\text{HH}} = 5.1$ Hz, PCHCHH), 3.08 (ddd, 1H, $^2J_{\text{HH}} = 17.0$ Hz, $^3J_{\text{HP}} = 11.0$ Hz, $^3J_{\text{HH}} = 2.6$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 186.0 (d, 1C, $^3J_{\text{PC}} = 13.8$ Hz, C=O), 152.5 (1C, C(O)CO), 147.0 (1C, C(O)COCH), 139.5-112.5 (32C, Ar + HC=CH), 39.1 (d, 1C, $^2J_{\text{PC}} = 69.9$ Hz, PCHCH₂), 33.3 (d, 1C, $^1J_{\text{PC}} = 743.7$ Hz, PCH). HRMS (+ESI) *m/z*: (*M* + *H*)⁺ calcd for C₂₇H₂₄O₃P, 427.1463; found, 427.1465. Anal. Calcd for C₂₇H₂₃O₃P: C, 76.04; H, 5.44. Found: C, 76.23; H, 5.55%.

184h Yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 85/15, flow = 1.0 mL/min, wavelength = 240 nm. Retention times: 51.3 min (major), 59.3 min (minor). $[\alpha]_D = -110.9$ (*c* 0.1, DCM). Mp: 214-217°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 33.8; ^1H NMR (CDCl_3 , 300 MHz): δ 8.72 (d, 1H, $^3J_{\text{HH}} = 9.4$ Hz, Ar), 8.25-7.94 (m, 10H, Ar), 7.87-7.81 (m, 2H, Ar), 7.55-7.44 (m, 6H, Ar), 7.19-7.12 (m, 5H, Ar), 6.44 (dd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^4J_{\text{HP}} = 4.1$ Hz, PhCH=CH), 6.20 (ddd, 1H, $^3J_{\text{HH}} = 15.7$ Hz, $^3J_{\text{HP}} = 9.2$ Hz, $^3J_{\text{HH}} = 6.3$ Hz, PhCH=CH), 4.32-4.22 (m, 1H, PCH), 3.80 (ddd, 1H, $^2J_{\text{HH}} = 17.7$ Hz, $^3J_{\text{HP}} = 10.5$ Hz, $^3J_{\text{HH}} = 5.7$ Hz, PCHCHH), 3.64 (ddd, 1H, $^2J_{\text{HH}} = 16.9$ Hz, $^3J_{\text{HP}} = 10.7$ Hz, $^3J_{\text{HH}} = 3.0$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 201.5 (d, 1C, $^3J_{\text{PC}} = 13.3$ Hz, C=O), 136.8-123.6 (36C, Ar + HC=CH), 40.4 (d, 1C, $^2J_{\text{PC}} = 69.5$ Hz, PCHCH₂), 35.4 (d, 1C, $^1J_{\text{PC}} = 1100.4$ Hz, PCH). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₃₉H₃₀O₂P, 561.1983; found, 561.1982. Anal. Calcd for C₃₉H₂₉O₂P: C, 83.55; H, 5.21. Found: C, 83.74; H, 5.39%.

184i White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 88/12, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 18.4 min (major), 24.2 min (minor). $[\alpha]_D = -74.9$ (*c* 0.1, DCM). Mp: 187-190°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 202 MHz): δ 34.0; ^1H NMR (CDCl_3 , 300 MHz): δ 7.93-7.73 (m, 6H, Ar), 7.57-7.43 (m, 8H, Ar), 7.21-7.13 (m, 5H, Ar), 6.40 (dd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^4J_{\text{HP}} = 4.1$ Hz, PhCH=CH), 6.10 (ddd, 1H, $^3J_{\text{HH}} = 15.8$ Hz, $^3J_{\text{HP}} = 9.2$ Hz, $^3J_{\text{HH}} = 6.5$ Hz, PhCH=CH), 3.64-3.53 (m, 1H, PCH), 3.59 (ddd, 1H, $^2J_{\text{HH}} = 17.6$ Hz, $^3J_{\text{HP}} = 10.1$ Hz, $^3J_{\text{HH}} = 4.8$ Hz, PCHCHH), 3.27 (ddd, 1H, $^2J_{\text{HH}} = 17.6$ Hz, $^3J_{\text{HP}} = 11.3$ Hz, $^3J_{\text{HH}} = 2.6$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 196.0 (d, 1C, $^3J_{\text{PC}} = 13.1$ Hz, C=O), 136.7-123.3 (26C, Ar + HC=CH), 39.2 (d, 1C, $^2J_{\text{PC}} = 69.6$ Hz, PCHCH₂), 33.6 (d, 1C, $^1J_{\text{PC}} = 737.5$ Hz, PCH). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₂₉H₂₅BrO₂P, 515.0776; found, 515.0777. Anal. Calcd for C₂₉H₂₄BrO₂P: C, 67.58; H, 4.69. Found: C, 67.74; H, 4.86%.

184j White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 88/12, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 18.3 min (major), 26.1 min (minor). $[\alpha]_D = -77.8$ (*c* 0.1, DCM). Mp: 186-189°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 34.1; ^1H NMR (CDCl_3 , 300 MHz): δ 7.95-7.87 (m, 4H, Ar), 7.80 (ddd, 2H, $^3J_{\text{HH}} = 11.0$ Hz, $^3J_{\text{HH}} = 7.6$ Hz, $^4J_{\text{HH}} = 1.3$ Hz, Ar), 7.53-7.40 (m, 6H, Ar), 7.24-7.05 (m, 7H, Ar), 6.41 (dd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^4J_{\text{HP}} = 4.2$ Hz, PhCH=CH), 6.11 (ddd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^3J_{\text{HP}} = 9.1$ Hz, $^3J_{\text{HH}} = 6.3$ Hz, PhCH=CH), 4.19-4.09 (m, 1H, PCH), 3.61 (ddd, 1H, $^2J_{\text{HH}} = 17.6$ Hz, $^3J_{\text{HP}} = 10.1$ Hz, $^3J_{\text{HH}} = 4.7$ Hz, PCHCHH), 3.27 (ddd, 1H, $^2J_{\text{HH}} = 17.4$ Hz, $^3J_{\text{HP}} = 11.1$ Hz, $^3J_{\text{HH}} = 2.4$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 195.4 (d, 1C, $^3J_{\text{PC}} = 13.1$ Hz, C=O), 167.4 (1C, CF), 164.8-115.8 (25C, Ar + HC=CH), 39.2 (d, 1C, $^2J_{\text{PC}} = 69.8$ Hz, PCHCH₂), 33.6 (d, 1C, $^1J_{\text{PC}} = 730.9$ Hz, PCH). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₂₉H₂₅FO₂P, 455.1576; found, 455.1576. Anal. Calcd for C₂₉H₂₄FO₂P: C, 76.64; H, 5.32. Found: C, 76.88; H, 5.63%.

184k Yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 85/15, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 43.4 min (minor), 49.4 min (major). $[\alpha]_D = -73.2$ (*c* 0.1, DCM). Mp: 170-172°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121 MHz): δ 35.2; ^1H NMR (CDCl_3 , 300 MHz): δ 7.94-7.87 (m, 2H, Ar), 7.84-7.77 (m, 2H, Ar), 7.71-7.68 (m, 2H, Ar), 7.52-7.42 (m, 6H, Ar), 7.20-7.13 (m, 5H, Ar), 6.63-6.58 (m, 2H, Ar), 6.37 (dd, 1H, $^3J_{\text{HH}} = 8.0$ Hz, $^4J_{\text{HP}} = 2.1$ Hz, PhCH=CH), 6.17-6.06 (m, 3H, PhCH=CH + NH₂), 4.19-4.09 (m, 1H, PCH), 3.64 (ddd, 1H, $^2J_{\text{HH}} = 17.3$ Hz, $^3J_{\text{HP}} = 10.4$ Hz, $^3J_{\text{HH}} = 4.3$ Hz, PCHCHH), 3.26 (ddd, 1H, $^2J_{\text{HH}} = 17.3$ Hz, $^3J_{\text{HP}} = 11.7$ Hz, $^3J_{\text{HH}} = 2.3$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 198.6 (d, 1C, $^3J_{\text{PC}} = 13.3$ Hz, C=O), 150.6 (s, 1C, C-N), 135.4-116.1 (25C, Ar + HC=CH), 39.3 (d, 1C, $^2J_{\text{PC}} = 69.7$ Hz, PCHCH₂), 33.7 (d, 1C, $^1J_{\text{PC}} = 755.5$ Hz, PCH). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₂₉H₂₇NO₂P, 452.1779; found, 452.1781. Anal. Calcd for C₂₉H₂₆NO₂P: C, 77.15; H, 5.80; N, 3.10. Found: C, 77.36; H, 5.97; N, 3.19%.

184l Pale yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 88/12, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 45.2 min (major), 56.1 min (minor). $[\alpha]_D = -75.0$ (*c* 0.1, DCM). Mp: 160-163°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 34.5; ^1H NMR (CDCl_3 , 400 MHz): δ 7.93-7.86 (m, 4H, Ar), 7.82-7.77 (m, 2H, Ar), 7.69-7.64 (m, 1H, Ar), 7.55-7.39 (m, 5H, Ar), 7.21-7.13 (m, 5H, Ar), 6.89-6.85 (m, 2H, Ar), 6.39 (dd, 1H, $^3J_{\text{HH}} = 15.9$ Hz, $^4J_{\text{HP}} = 4.2$ Hz, PhCH=CH), 6.12 (ddd, 1H, $^3J_{\text{HH}} = 15.7$ Hz, $^3J_{\text{HP}} = 9.1$ Hz, $^3J_{\text{HH}} = 6.4$ Hz, PhCH=CH), 4.20-4.12 (m, 1H, PCH), 3.83 (s, 3H, OCH₃), 3.62 (ddd, 1H, $^2J_{\text{HH}} = 17.4$ Hz, $^3J_{\text{HP}} = 10.2$ Hz, $^3J_{\text{HH}} = 4.4$ Hz, PCHCHH), 3.21 (ddd, 1H, $^2J_{\text{HH}} = 17.4$ Hz, $^3J_{\text{HP}} = 11.6$ Hz, $^3J_{\text{HH}} = 2.4$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 195.4 (d, 1C, $^3J_{\text{PC}} = 12.9$ Hz, C=O), 163.9 (1C, C-OCH₃), 136.9-123.6 (23C, Ar + HC=CH), 114.0 (2C, CHC-OCH₃), 55.7 (1C, OCH₃), 39.2 (d, 1C, $^2J_{\text{PC}} = 70.2$ Hz, PCHCH₂), 33.4 (d, 1C, $^1J_{\text{PC}} = 692.8$ Hz, PCH). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₃₀H₂₈O₃P, 467.1776; found, 467.1775. Anal. Calcd for C₃₀H₂₇O₃P: C, 77.24; H, 5.83. Found: C, 77.29; H, 5.97%.

184m Pale yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 88/12, flow = 1.0 mL/min, wavelength = 270 nm. Retention times: 26.4 min (major), 32.2 min (minor). $[\alpha]_D = -105.4$ (*c* 0.1, DCM). Mp: 132-135°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 33.3; ^1H NMR (CDCl_3 , 300 MHz): δ 7.93-7.86 (m, 2H, Ar), 7.82-7.75 (m, 2H, Ar), 7.52-7.42 (m, 6H, Ar), 7.29-7.15 (m, 8H, Ar), 6.40 (dd, 1H, $^3J_{\text{HH}} = 7.94$ Hz, $^4J_{\text{HP}} = 2.05$ Hz, PhCH=CH), 6.09 (ddd, 1H, $^3J_{\text{HH}} = 15.6$ Hz, $^3J_{\text{HP}} = 9.4$ Hz, $^3J_{\text{HH}} = 6.3$ Hz, PhCH=CH), 4.11-4.00 (m, 1H, PCH), 3.50 (ddd, 1H, $^2J_{\text{HH}} = 17.7$ Hz, $^3J_{\text{HP}} = 9.9$ Hz, $^3J_{\text{HH}} = 6.1$ Hz, PCHCHH), 3.33 (ddd, 1H, $^2J_{\text{HH}} = 17.7$ Hz, $^3J_{\text{HP}} = 10.7$ Hz, $^3J_{\text{HH}} = 3.3$ Hz, PCHCHH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 199.0 (d, 1C, $^3J_{\text{PC}} = 13.5$ Hz, C=O), 140.1-123.0 (26C, Ar + HC=CH), 39.9 (d, 1C, $^2J_{\text{PC}} = 69.1$ Hz, PCHCH₂), 35.7 (d, 1C, $^1J_{\text{PC}} = 1171.3$ Hz, PCH). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₂₉H₂₄Cl₂O₂P,

505.0891; found, 505.0891. Anal. Calcd for C₂₉H₂₃Cl₂O₂P: C, 68.92; H, 4.59. Found: C, 69.14; H, 4.87%.

184n White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 82/18, flow = 1.0 mL/min, wavelength = 254 nm. Retention times: 51.6 min (major), 57.8 min (minor). [α]_D = -90.4 (*c* 0.1, DCM). Mp: 155-157°C. ³¹P{¹H} NMR (CDCl₃, 121 MHz): δ 34.2; ¹H NMR (CDCl₃, 300 MHz): δ 8.65-8.63 (m, 1H, Ar), 7.97-7.90 (m, 3H, Ar), 7.85-7.73 (m, 3H, Ar), 7.52-7.40 (m, 7H, Ar), 7.22-7.12 (m, 5H, Ar), 6.35 (dd, 1H, ³J_{HH} = 15.9 Hz, ⁴J_{HP} = 4.3 Hz, PhCH=CH), 6.12 (ddd, 1H, ³J_{HH} = 15.9 Hz, ³J_{HP} = 8.7 Hz, ³J_{HH} = 5.9 Hz, PhCH=CH), 4.21-4.11 (m, 1H, PCH), 4.03 (ddd, 1H, ²J_{HH} = 17.5 Hz, ³J_{HP} = 10.6 Hz, ³J_{HH} = 4.9 Hz, PCHCHH), 3.46 (ddd, 1H, ²J_{HH} = 17.3 Hz, ³J_{HP} = 10.7 Hz, ³J_{HH} = 2.2 Hz, PCHCHH); ¹³C NMR (CDCl₃, 100 MHz): δ 199.1 (d, 1C, ³J_{PC} = 13.6 Hz, C=O), 153.1 (1C, NCC=O), 149.2 (1C, NCCH), 137.0-122.1 (23C, Ar + HC=CH), 39.8 (d, 1C, ²J_{PC} = 69.6 Hz, PCHCH₂), 33.2 (d, 1C, ¹J_{PC} = 669.3 Hz, PCH). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₂₈H₂₅NO₂P, 438.1623; found, 438.1623. Anal. Calcd for C₂₈H₂₄NO₂P: C, 76.87; H, 5.53; N, 3.20. Found: C, 76.99; H, 5.67; N, 3.28%.

184o Pale yellow solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 85/15, flow = 1.0 mL/min, wavelength = 254 nm. Retention times: 19.6 min (major), 24.7 min (minor). [α]_D = -95.5 (*c* 0.1, DCM). Mp: 143-145°C. ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 34.0; ¹H NMR (CDCl₃, 500 MHz): δ 7.93-7.90 (m, 2H, Ar), 7.81-7.78 (m, 2H, Ar), 7.70 (d, 1H, ⁴J_{HH} = 3.70 Hz, Ar), 7.60 (d, 1H, ⁴J_{HH} = 4.90 Hz, Ar), 7.52-7.40 (m, 6H, Ar), 7.21-7.14 (m, 5H, Ar), 7.08-7.06 (m, 1H, Ar), 6.41 (dd, 1H, ³J_{HH} = 15.9 Hz, ⁴J_{HP} = 4.10 Hz, PhCH=CH), 6.14 (ddd, 1H, ³J_{HH} = 15.9 Hz, ³J_{HP} = 9.2 Hz, ³J_{HH} = 6.4 Hz, PhCH=CH), 4.15-4.10 (m, 1H, PCH), 3.60 (ddd, 1H, ²J_{HH} = 17.1 Hz, ³J_{HP} = 10.4 Hz, ³J_{HH} = 4.6 Hz, PCHCHH), 3.20 (ddd, 1H, ²J_{HH} = 17.1 Hz, ³J_{HP} = 11.2 Hz, ³J_{HH} = 2.4 Hz, PCHCHH); ¹³C NMR (CDCl₃, 100 MHz): δ 189.7 (d, 1C, ³J_{PC} = 13.7

Hz, C=O), 143.9 (1C, SCC=O), 136.6-123.0 (23C, Ar + HC=CH), 39.3 (d, 1C, $^2J_{PC}$ = 69.9 Hz, PCHCH₂), 33.7 (d, 1C, $^1J_{PC}$ = 800.0 Hz, PCH). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₇H₂₄O₂PS, 443.1235; found, 443.1237. Anal. Calcd for C₂₇H₂₃O₂PS: C, 73.28; H, 5.24. Found: C, 73.34; H, 5.40%.

184p White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 90/10, flow = 1.0 mL/min, wavelength = 230 nm. Retention times: 28.6 min (major), 32.5 min (minor). [α]_D = -69.2 (c 0.1, DCM). Mp: 126-129°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl₃, 162 MHz): δ 34.7; ^1H NMR (CDCl₃, 400 MHz): δ 7.90-7.84 (m, 4H, Ar), 7.82-7.76 (m, 2H, Ar), 7.55-7.40 (m, 9H, Ar), 5.51-5.45 (m, 1H, PCHCH=CH), 5.38-5.31 (m, 1H, PCHCH=CH), 3.96-3.89 (m, 1H, PCH), 3.56 (ddd, 1H, $^2J_{HH}$ = 17.4 Hz, $^3J_{HP}$ = 10.3 Hz, $^3J_{HH}$ = 4.4 Hz, PCHCHH), 3.12 (ddd, 1H, $^2J_{HH}$ = 17.4 Hz, $^3J_{HP}$ = 11.5 Hz, $^3J_{HH}$ = 2.4 Hz, PCHCHH); ^{13}C NMR (CDCl₃, 100 MHz): δ 197.4 (d, 1C, $^3J_{PC}$ = 13.5 Hz, C=O), 139.0-122.1 (20C, Ar + HC=CH), 38.7 (d, 1C, $^2J_{PC}$ = 70.8 Hz, PCHCH₂), 33.5 (d, 1C, $^1J_{PC}$ = 711.7 Hz, PCH), 25.9 (1C, CH₃CH₂), 13.4 (d, 1C, $^5J_{PC}$ = 2.9 Hz, CH₃CH₂). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₂₅H₂₆O₂P, 389.1670; found, 389.1671. Anal. Calcd for C₂₅H₂₅O₂P: C, 77.30; H, 6.49. Found: C, 77.44; H, 6.57%.

184q White solid. The *ee* was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol = 95/5, flow = 1.0 mL/min, wavelength = 254 nm. Retention times: 34.4 min (major), 42.1 min (minor). [α]_D = -82.6 (c 0.1, DCM). Mp: 114-116°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl₃, 162 MHz): δ 37.8; ^1H NMR (CDCl₃, 400 MHz): δ 7.95 (dd, 2H, $^4J_{HH}$ = 1.4 Hz, $^3J_{HH}$ = 8.5 Hz, Ar), 7.83-7.78 (m, 2H, Ar), 7.53 (tt, 1H, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.4 Hz, Ar), 7.44-7.29 (m, 5H, Ar), 7.25-7.09 (m, 8H, Ar), 6.49 (dd, 1H, $^4J_{HP}$ = 3.9 Hz, $^3J_{HH}$ = 15.9 Hz, PhCH=CH), 6.21 (ddd, 1H, $^3J_{HH}$ = 15.9 Hz, $^3J_{HP}$ = 9.2 Hz, $^3J_{HH}$ = 6.9 Hz, PhCH=CH), 4.43-4.36 (m, 1H, PCH), 3.81 (ddd, 1H, $^2J_{HH}$ = 18.0 Hz, $^3J_{HP}$ = 9.9 Hz, $^3J_{HH}$ = 4.0 Hz, PCHCHH), 3.46 (ddd, 1H, $^2J_{HH}$ = 18.0 Hz, $^3J_{HP}$ = 11.2 Hz, $^3J_{HH}$ = 2.2 Hz,

PCHCHH), 2.39 (s, 3H, CH₃), 2.36 (s, 3H, CH₃); ¹³C NMR (CDCl₃, 100 MHz): δ 197.1 (d, 1C, ³J_{PC} = 12.0 Hz, C=O), 142.8 (d, 1C, ²J_{PC} = 8.0 Hz, C-CH₃), 142.2 (d, 1C, ²J_{PC} = 8.0 Hz, C-CH₃), 136.9-124.3 (24C, Ar + HC=CH), 37.7 (d, 1C, ²J_{PC} = 71.0 Hz, PCHCH₂), 25.7 (d, 1C, ¹J_{PC} = 833.0 Hz, PCH), 22.1 (d, 1C, ³J_{PC} = 4.0 Hz, Ar-CH₃), 21.4 (d, 1C, ³J_{PC} = 4.0 Hz, Ar-CH₃). HRMS (+ESI) m/z: (M + H)⁺ calcd for C₃₁H₃₀O₂P, 465.1983; found, 465.1986. Anal. Calcd for C₃₁H₂₉O₂P: C, 80.15; H, 6.29. Found: C, 80.24; H, 6.37%.

181b White solid. The *ee* was determined on a Daicel Chiralpak AD-H column with *n*-hexane/2-propanol = 75/25, flow = 0.8 mL/min, wavelength = 210 nm. Retention times: 23.7 min (minor), 41.3 min (major). The data is consistent with literature.^[151d]

Chapter 6 Unsymmetrical C(sp^3)-Metalated Pincer Complexes

6.1 General Introduction to C(sp^3)-Hybridized Pincer Complexes

Transition metal pincer complexes represent a class of powerful and synthetically useful complexes having vast applications in many areas such as material science, organic synthesis, catalysis, organometallic, bioinorganic and supramolecular chemistry.^[115b,c,f,242] The ECE η^3 -mer coordination mode of the C(sp^2)-metal bond reinforced by two neutral electron donating groups (Figure 6.46, left) gives rise to the thermodynamically favorable five-membered bicyclic C-M bond-sharing system^[243] that boasts exceptional thermal stability.^[244] Furthermore, the coordinating groups and ligand scaffold can be tailored to control the reactivity of the C-M bond by modification of the steric environment and electronic properties of the metal center.^[245]

Figure 6.46. Schematic representation of pincer complexes.

Since the appearance of pincer complexes in the 1970s,^[114] specially crafted pincer complexes have been prepared to address various applications. The most popular ECE pincer ligands rely heavily on aromatic moieties (Figure 6.46, left) possibly due to the availability of synthetic methods for their facile installation. The C(sp^2)-M bond in such complexes is essentially coplanar to the [2,6-(ECH₂)₂C₆H₃] system, which enhances communication between the metal *d*-orbital and the π -orbitals of the aromatic backbone.^[246] Furthermore, the high sensitivity of the aryl rings towards the electronic nature of the *para*-substituents makes the C(sp^2)-metalated pincer complexes as ideal candidates for studies pertaining to structural activity relationships.

On the contrary, the chemistry and practical applications of the $C(sp^3)$ -metalated pincer complexes (Figure 6.46, right) are underdeveloped. The main debilitating factor is the difficulties involved in the structural modification of the framework, which prevents the fine-tuning of their properties. However, certain singular properties attributed to $C(sp^3)$ -metalated pincer complexes are worthy to be investigated in detail. Unlike the averagely planar five-membered bicyclic rings present in aromatic $C(sp^2)$ -pincer complexes, a distinguishing aspect of $C(sp^3)$ -metalated complexes is the three-dimensional environment around the metal center. This three-dimensional structural feature of $C(sp^3)$ -based complexes might contribute significantly towards their application as stereoselective catalysts. In addition, it is generally accepted that a better σ -donation exerted by the anionic $C(sp^3)$ ligand increases electron density at the metal center, which might vary the reactivity of the $C(sp^3)$ -metalated complexes as compared to the aromatic analogues. For the purpose of illustration, a series of iridium, nickel, palladium and platinum $C(sp^3)$ -pincer complexes **185a-d** were reported with 1,5-bis(di-*tert*-butylphosphino)pentane and appropriate metal sources.^[247] The comparative IR studies

Figure 6.47. Aliphatic $C(sp^3)$ -metalated pincer complexes.

confirmed the expected *trans* influence of the sp^3 -metalated carbon. The $\nu(M-Cl)$ vibrations in complexes **185a-d** were revealed to be 10-30 cm^{-1} lower than the analogous aromatic $C(sp^2)$ -pincer complexes, indicating a more electron-rich character of the metal center as well as a more reactive $C(sp^3)$ -M bond.^[114a] In a separate report, the high reactivity of the $C(sp^3)$ -based pincer complex **186** was demonstrated experimentally.^[248] The complex **186** oxidatively adds across the N-H bond of ammonia to generate the Ir(III)

Scheme 6.60. N-H activation in ammonia.

amido hydride **187**. Remarkably, the aromatic $\text{C}(\text{sp}^2)$ -based pincer analogues failed to form the corresponding oxidized Ir(III) product. This result clearly shows that the stronger donating ability of the aliphatic backbone enhances electron density at the Ir(I) center needed to achieve activation of the otherwise inert ammonia. In another study by the same group, the N-H activation of 1-aminopiperidine by the aliphatic pincer complex **186** and its aromatic analogue **189** were found to react in a similar fashion, but resulted in the formation of products with different stability.^[249] The hydrido-iridium hydrazido complex **188** was stable at room temperature, but complex **190** underwent a second N-H bond cleavage to generate the aminonitrene complex **191**. Structural characterization of complex **188** suggests the presence of N-Ir π -stabilizing interaction which can rationalize the relative stability of sp^3 -complex **188** over the sp^2 -analogue **190**.

Scheme 6.61. N-H activation in hydrazine.

Another unique feature of $\text{C}(\text{sp}^3)$ -based pincer complexes is the tendency of the aliphatic ligands to undergo reversible α - or β -hydride elimination (see Scheme 6.62). The

Scheme 6.62. Reversible α - or β -hydride elimination of aliphatic $C(sp^3)$ -metalated complexes.

α - or β -hydride elimination of complexes **185a**, **193a** and **194a** resulted in the formation of isomeric carbene **192a**,^[247a] olefin chelate complexes **193b**^[250] and **194b**^[251] respectively, which is another evidence demonstrating the high reactivity of the $C(sp^3)$ -M bond. This coordination flexibility observed in aliphatic pincer complexes was utilized in the development of efficient catalyst for H/D exchange at vinyl groups under mild reaction conditions (Scheme 6.63). The Ir(III) complex **187**-catalyzed deuteration of both internal and terminal double bonds exhibited excellent functional group tolerance with absolute regio- and chemo-selectivity.^[252] Under the same conditions, aromatic pincer complexes were found to be practically inactive, hence it was proposed that the mechanism involves the methine position of the backbone.

Scheme 6.63. Catalytic H/D exchange.

In terms of catalytic relevance, $C(sp^3)$ -metalated pincer complexes have also achieved notable success in other reactions such as Mizoroki-Heck olefination,^[253] hydroamination,^[254] Kumada,^[255] Suzuki-Miyaura^[117e,256] and Negishi coupling reactions.^[257] However, the development of $C(sp^3)$ -based pincer complexes is slow and literature reports are dominated almost exclusively by $PC(sp^3)P$ -type complexes.^[114a,258]

Figure 6.48. $C(sp^3)$ -based pincer preligands.

Due to the unusual reactivities and structural features of the $C(sp^3)$ -metalated pincer complexes, the advancement of this class of complexes, especially the chiral, unsymmetrical $EC(sp^3)E'$ -based ($E \neq E'$) complexes, may open new avenues in many research areas where their aromatic counterparts are in use.

6.2 Results and Discussion

Herein, the phosphapalladacycle (*S*)-**119** and pincer complex (*R,R*)-**150aa** were exploited in the catalytic AHP of selected substrates to generate a series of air-sensitive phosphine ligands. Upon oxidation or sulfurization of the phosphine compounds, potential $NC(sp^3)X$ -type ($X = O, S$) pincer preligands were produced and subsequent cyclometalation of these preligands afforded novel unsymmetrical $NC(sp^3)X$ -based pincer complexes. It is worthy to note that these complexes are optically active and contain either two or four C-stereogenic centers.

6.2.1 Syntheses of NC(sp^3)X-Bimetallic Pincer Complexes

Scheme 6.64. Synthesis of $\text{PC}(sp^2)\text{P}$ - and $\text{NC}(sp^3)\text{X}$ -pincer complexes.

The optically pure diphosphine **(R,R)-147f** was prepared *via* complex **(S)-119**-catalyzed AHP of dienone **145f** (see Scheme 2.40). The *ee* and *de* of phosphine **147f** was determined to be >99 and 86% respectively (see Table 2.3). It should be reiterated that the direct cyclopalladation of the air-sensitive phosphine afforded the $\text{PC}(sp^2)\text{P}$ pincer complex **(R,R)-149f** in 80% isolated yield. However, if the same ligand was treated with either aqueous H_2O_2 or S_8 prior to cyclopalladation, the quantitative formation of the novel bimetallic $\text{NC}(sp^3)\text{X}$ pincer complexes **(S,S,S,S)-195a-b** was observed instead. Generation of the six-membered bicyclopalladated $\text{XC}(sp^2)\text{X}$ pincer complex was not detected in the reaction mixture. The absolute configuration of the chiral centers was determined from the X-ray quality crystal of complex **195b** obtained from a solution of DCM/*n*-hexane. The molecular structure of complex **195b** is presented in Figure 6.49. During the formation of complexes **195a-b**, the apparent inversion of configuration at the stereogenic centers is merely the consequence of the Cahn-Ingold-Prelog sequence rules.^[259] The stereochemistry of the two newly generated $\text{C}(sp^3)$ stereogenic centers are controlled by the existing chiral centers produced during the catalytic AHP process. The ^1H , ^{13}C and $^{31}\text{P}\{^1\text{H}\}$ NMR analysis conducted on the crude reaction mixture of the

cyclopalladation step revealed only the existence of a single diastereomer of complex **195a** or **195b**.

Figure 6.49. Molecular structure of (*S,S,S,S*)-**195b**. Hydrogen atoms except H(C1), H(C8), H(C27) and H(C28) were omitted for clarity.

A similar synthetic methodology for complex **195a/b** was extended to the formation of the analogous bimetallic NC(*sp*³)X pincer complexes **197a-b** and **199a-b**. In both cases, the syntheses of the specially designed substrates **196b** and **198c** were materialized in high overall yields. The catalytic AHP of dienones **196b** and **198c** afforded the corresponding diphosphines in >99% *ee*'s and 99% *de*'s as determined by ³¹P{¹H} NMR spectroscopy after coordination of the crude diphosphines to the chiral derivatizing agent (*S*)/(*R*)-**66** (see Section 2.2.3). Stepwise oxidation or sulfurization of the air-sensitive phosphines followed by addition of PdCl₂(NCMe)₂ produced the respective NC(*sp*³)X complexes **197a-b** and **199a-b** quantitatively.

Scheme 6.65. Synthesis of NC(*sp*³)X-pincer complexes **197a-b**.

Scheme 6.66. Synthesis of NC(*sp*³)X-pincer complexes **199a-b**.

6.2.2 Syntheses of NC(*sp*³)X-Monometallic Pincer Complexes

The synthesis of the simpler monometallic NC(*sp*³)X analogue **201** was done in a similar fashion as the bimetallic pincer complexes. The aldol condensation of 2-acetylpyridine **200a** with benzaldehyde gave the enone **200b**, which was subjected to catalytic AHP with phosphapalladacycle (*S*)-**119** to form phosphine (*R*)-**200c** in >99% *ee* after a single recrystallization.^[112b] Treatment of the phosphine with aqueous H₂O₂ or S₈ followed by cyclopalladation afforded the corresponding pincer complexes **201a-b**. Recrystallization from DCM/*n*-hexane gave yellow crystals of complex **201b** that are

suitable for X-ray crystallographic analysis. Figure 6.50 shows the molecular structure of complex **201b**.

Scheme 6.67. Synthesis of NC(*sp*³)X-pincer complexes **201a-b**.

Figure 6.50. Molecular structure of (*S,S*)-**201b**. Hydrogen atoms except H(C1) and H(C8) were omitted for clarity.

In order to establish the effects of minor structural changes in the NC(*sp*³)X complexes, the monometallic analogues **203a/b** were prepared by catalytic AHP of $\alpha,\beta,\gamma,\delta$ -diunsaturated olefin **202b** in the presence of 5 mol % of PCP pincer catalyst (*R,R*)-**150aa**, followed by oxidation/sulfurization of the enantiomerically pure phosphine **202c** and sequential addition of PdCl₂(NCMe)₂. The *ee* of phosphine **202c** obtained *via* catalytic AHP was determined to be >99% (see Table 5.14). The X-ray quality crystal of

complex **203b** was obtained from a solution of DCM/EtOH and the molecular structure is depicted in Figure 6.51.

Scheme 6.68. Synthesis of $\text{NC}(sp^3)\text{X}$ -pincer complexes **203a-b**.

Figure 6.51. Molecular structure of (R,R) -**203b**. Hydrogen atoms except H(C1) and H(C8) were omitted for clarity.

6.2.3 Molecular Structures of $\text{NC}(sp^3)\text{X}$ Pincer Complexes

Selected bond lengths and angles of the complexes **195b**, **201b** and **203b** are presented in Table 6.18. All the three complexes adopted slightly distorted square planar

Table 6.18. Selected bond lengths (Å) and angles (°) of pincer complexes.

	(<i>S,S,S,S</i>)- 195b	(<i>S,S</i>)- 201b	(<i>R,R</i>)- 203b
Pd←N	2.047(4)	2.052(4)	2.051(3)
Pd←S	2.292(1)	2.298(1)	2.288(1)
Pd←Cl	2.382(1)	2.396(1)	2.390(1)
Pd←C(2)	2.061(4)	2.045(4)	2.049(4)
C(2)–Pd←S	91.50(13)	90.89(15)	91.97(11)
C(2)–Pd←N	81.50(17)	82.21(19)	81.84(14)
C(2)–Pd←Cl	170.94(12)	174.72(15)	174.66(12)
Cl–Pd←S	92.66(4)	92.94(5)	91.43(3)
Cl–Pd←N	95.58(11)	94.04(13)	95.24(10)
N→Pd←S	168.56(11)	172.93(13)	170.95(10)
H–C(2)–C(1) ^[a]	106.12	107.93	104.66
H–C(2)–C(3) ^[a]	106.07	107.97	104.74
H–C(2)–Pd ^[a]	106.08	107.95	104.67
Pd–C(2)–C(1) ^[a]	102.18	101.36	103.34
Pd–C(2)–C(3) ^[a]	120.78	117.98	122.81
C(1)–C(2)–C(3) ^[a]	114.55	113.14	114.89

[a] The angles (°) were determined from the corresponding cif files using Mercury 3.1 software.

geometries around the Pd centers. The expected tetrahedral geometry around the C(sp^3)-palladated C(2) atoms was observed with a slight deviation in the Pd–C(2)–C(3) and C(1)–C(2)–C(3) angles. Due to the absence of analogous NC(sp^3)S pincer complexes in literature, no suitable comparison with regards to the selected bond lengths and angles can be made. Instead, a comparison was made to the related NC(sp^2)S-Pd pincer complexes^[260] to establish several noticeable features in the NC(sp^3)X-complexes. The Pd←S and Pd←Cl bond lengths of complexes **195b**, **201b** and **203b** are in close agreement to the range of reported values [Pd←S: 2.281(1)–2.359(1) Å and Pd←Cl: 2.386(1)–2.389(1) Å]. The Pd←N bond lengths for the C(sp^3)-metalated complexes are slightly shorter than literature values of 2.062(4)–2.140(2) Å while the Pd–C(2) bond lengths observed are longer than the range of 1.908(2)–1.974(5) Å. The longer Pd–C(2) bonds could be the direct consequence of the weaker electron delocalization effect of the NC(sp^3)S backbone.

6.3 Future Work

Due to the ongoing work that is currently in progress while this thesis is being written, it is regretted that a satisfactory closure to this chapter could not be achieved. However, it has been demonstrated that the syntheses of these optically pure $\text{NC}(sp^3)\text{X}$ ($\text{X} = \text{O}, \text{S}$) pincer complexes can be accomplished conveniently, and it is definitely worthwhile to divert more attention to this relatively underdeveloped class of pincer complexes. In the next phase of our studies, the catalytic potential of the $\text{NC}(sp^3)\text{X}$ complexes will be evaluated in several asymmetric transformations such as hydroamination and hydrophosphination. In the long term, we hope to explore the idea of a “self-breeding” catalytic system to generate a limitless supply of these valuable complexes.

6.4 Conclusion

Employing the PC-palladacycle (*S*)-**119** and the PCP-pincer complex (*R,R*)-**150aa** as catalysts in asymmetric hydrophosphination, a series of $\text{NC}(sp^3)\text{X}$ ($\text{X} = \text{O}, \text{S}$) pincer preligands were produced in excellent yields and stereoselectivities. The cyclopalladation of the preligands were successful in forming the corresponding novel mono-/bi-metallic pincer complexes. The presence of a likely hemilabile $\text{NC}(sp^3)\text{X}$ preligand in a complex may result in dramatic rate enhancements in catalytic reactions or considerably influence the reactivity of incoming substrates and promote transformations that would not otherwise occur.^[154a,261] The unsymmetrical pincer complexes could benefit from the advantages of varied donors and provide unique reactivities arising from the singular structural features of the $\text{NC}(sp^3)\text{X}$ frameworks. Although “pincer chemistry” has progressed tremendously over the years, the full potential of unsymmetrical $\text{NC}(sp^3)\text{X}$ -pincer complexes has yet to be fully appreciated due to the challenges associated with their preparation. Careful and systematic studies of these pincer complexes will help to

design new analogues that are oriented towards a given property. Furthermore, development of new reactions catalyzed by the unsymmetrical $EC(sp^3)E'$ ($E \neq E'$) species would be of great significance.

6.5 Experimental Section

All reactions were carried out under a positive pressure of nitrogen using standard Schlenk technique. NMR spectra were recorded on Bruker AV 300, AV 400 and AV 500 spectrometers. Chemical shifts were reported in ppm and referenced to an internal $SiMe_4$ standard (0 ppm) for 1H NMR, chloroform- d (77.23 ppm) for ^{13}C NMR, and an external 85% H_3PO_4 for $^{31}P\{^1H\}$ NMR. DCM, toluene and acetone were purchased from their respective companies and used as supplied. Solvents were degassed prior to use when necessary. A Low Temp Pairstirrer PSL-1800 was used for controlling low temperature reactions. Column chromatography was carried out with Silica gel 60 (Merck). Melting points were measured using SRS Optimelt Automated Point System SRS MPA100. Optical rotation were measured with JASCO P-1030 Polarimeter in the specified solvent in a 0.1 dm cell at 22.0°C.

The palladacycles (*S*)-**119**,^[112c] (*R,R*)-**150aa**,^[151d,206] compounds **196b**^[262] and **200b**^[263] were prepared according to literature methods. All other reactants and reagents were used as supplied.

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

General procedure for Preparation of Diphosphine Oxide/Sulfide. To a solution of Ph_2PH (0.44 mmol, 2.2 equiv.) in toluene (15 mL) was added catalyst (*S*)-**119** (0.035 mmol, 8 mol %) and stirred for 10 minutes before cooling to -80°C. The substrate **145f**, **196b** or **198c** (0.20 mmol, 1.0 equiv.) was added followed by the addition of NEt_3

(0.40 mmol, 2.0 equiv.) in toluene (1 mL) dropwise. The solution was stirred at -80°C and the completion of the reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR. Upon completion, the solution was allowed to room temperature. Aq. H_2O_2 (31% w/w, 0.1 mL) or S_8 (25.0 μmol , 0.125 equiv.) was added and stirred for 30 min. The crude product was purified by silica gel column chromatography to afford the corresponding pure diphosphine oxide or sulfide.

Preligand for (*S,S,S,S*)-**195a** White solid (0.14 g, 0.18 mmol, 85% yield). Purified by silica gel column chromatography (100 EA : 1 MeOH to 10 EA : 1 MeOH). Mp: 122-124°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 33.6; ^1H NMR (CDCl_3 , 300 MHz): δ 8.62-8.61 (m, 2H, Ar), 7.97-7.90 (m, 4H, Ar), 7.66-7.62 (m, 4H, Ar), 7.48-7.35 (m, 13H, Ar), 7.21-7.11 (m, 8H, Ar), 6.91 (t, 1H, $^3J = 7.65$ Hz, Ar), 4.39-4.32 (m, 2H, PCHCH_2), 4.16-4.05 (m, 2H, PCHCH_2), 3.54 (ddd, 2H, $^2J_{\text{PH}} = 18.2$ Hz, $^3J = 11.3, 3.1$ Hz, O=CCH_2); ^{13}C NMR (CDCl_3 , 100 MHz): δ 198.0 (d, 2C, $^3J_{\text{PC}} = 13.0$ Hz, C=O), 152.9 (2C, Ar), 149.1 (2C, Ar), 136.7-121.7 (36C, Ar), 41.3 (d, 2C, $^1J_{\text{PC}} = 68.4$ Hz, PCH), 38.7 (2C, O=CCH_2). HRMS (+ESI) m/z : ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{46}\text{H}_{39}\text{N}_2\text{O}_4\text{P}_2$, 745.2385; found, 745.2386. Anal. Calcd for $\text{C}_{46}\text{H}_{38}\text{N}_2\text{O}_4\text{P}_2$: C, 74.18; H, 5.14; N, 3.76. Found: C, 74.25; H, 5.19; N, 3.81 %.

Preligand for (*S,S,S,S*)-**195b** White solid (0.14 g, 0.19 mmol, 88% yield). Purified by silica gel column chromatography (DCM to 20 DCM : 1 EA). Mp: 121-123°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 50.9; ^1H NMR (CDCl_3 , 400 MHz): δ 8.66-8.65 (m, 2H, Ar), 8.15-8.09 (m, 4H, Ar), 7.66-7.63 (m, 4H, Ar), 7.49-7.36 (m, 13H, Ar), 7.21-7.12 (m, 6H, Ar), 7.06-7.04 (m, 2H, Ar), 6.72 (t, 1H, $^3J = 7.7$ Hz, Ar), 4.72 (td, 2C, $^2J_{\text{PH}} = 10.2$ Hz, $^3J = 2.6$ Hz, PCHCH_2), 4.37 (ddd, 2H, $^3J_{\text{PH}} = 18.6$ Hz, $^2J = 10.5$ Hz, $^3J = 6.4$ Hz, O=CCH_2), 3.45 (ddd, 2H, $^2J = 18.6$ Hz, $^3J_{\text{PH}} = 12.0$ Hz, $^3J = 2.7$ Hz, O=CCH_2); ^{13}C NMR (CDCl_3 , 100 MHz): δ 197.8 (d, 2C, $^3J_{\text{PC}} = 14.9$ Hz, C=O), 152.4 (2C, Ar), 148.7 (2C, Ar), 136.7-121.2 (36C, Ar), 41.2 (d, 2C, $^1J_{\text{PC}} = 52.7$ Hz, PCH), 39.1 (2C, O=CCH_2). HRMS

(+ESI) m/z : $(M + H)^+$ calcd for $C_{46}H_{39}N_2O_2P_2S_2$, 777.1928; found, 777.1932. Anal. Calcd for $C_{46}H_{38}N_2O_2P_2S_2$: C, 71.12; H, 4.93; N, 3.61. Found: C, 71.18; H, 5.03; N, 3.66 %.

Preligand for (*S,S,S,S*)-**197a** White solid (0.13 g, 0.18 mmol, 90% yield). Purified by silica gel column chromatography (EA to 10 EA : 1MeOH). Mp: 200-202°C (dec.). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ 33.5; 1H NMR ($CDCl_3$, 400 MHz): δ 8.58 (d, 2H, $^3J = 4.2$ Hz, Ar), 7.90-7.86 (m, 4H, Ar), 7.75-7.64 (m, 4H, Ar), 7.49-7.43 (m, 6H, Ar), 7.38-7.30 (m, 8H, Ar), 7.17-7.13 (m, 4H, Ar), 7.08 (s, 4H, Ar), 4.35-4.27 (m, 2H, $PCHCH_2$), 4.26-4.20 (m, 2H, $O=CCH_2$), 3.53-3.45 (m, 2H, $O=CCH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.5 (d, 2C, $^3J_{PC} = 12.9$ Hz, $C=O$), 152.7 (2C, Ar), 149.0 (2C, Ar), 136.6-121.6 (36C, Ar), 41.1 (d, 2C, $^1J_{PC} = 68.7$ Hz, PCH), 38.2 (2C, $O=CCH_2$). HRMS (+ESI) m/z : $(M + H)^+$ calcd for $C_{46}H_{39}N_2O_4P_2$, 745.2385; found, 745.2387. Anal. Calcd for $C_{46}H_{38}N_2O_4P_2$: C, 74.18; H, 5.14; N, 3.76. Found: C, 74.18; H, 5.17; N, 3.79 %.

Preligand for (*S,S,S,S*)-**197b** White solid (0.16 g, 0.18 mmol, 88% yield). Purified by silica gel column chromatography (2 *n*-hexane : 1 DCM). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ 51.3; 1H NMR ($CDCl_3$, 400 MHz): δ 8.62 (d, 2H, $^3J = 4.7$ Hz, Ar), 8.14-8.09 (m, 4H, Ar), 7.77 (d, 2H, $^3J = 7.8$ Hz, Ar), 7.69 (td, 2H, $^3J = 7.6$ Hz, $^4J = 1.6$ Hz, Ar), 7.50-7.49 (m, 5H, Ar), 7.40-7.33 (m, 7H, Ar), 7.24-7.20 (m, 4H, Ar), 6.94 (s, 4H, Ar), 4.68 (td, 2H, $^2J_{PH} = 10.5$ Hz, $^3J = 2.4$ Hz, $PCHCH_2$), 4.41 (ddd, 2H, $^2J = 18.5$ Hz, $^3J_{PH} = 10.8$ Hz, $^3J = 5.7$ Hz, $O=CCH_2$), 3.38 (ddd, 2H, $^2J = 18.5$ Hz, $^3J_{PH} = 11.9$ Hz, $^3J = 2.4$ Hz, $O=CCH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.8 (d, 2C, $^3J_{PC} = 15.1$ Hz, $C=O$), 152.9 (2C, Ar), 149.2 (2C, Ar), 136.8-121.8 (36C, Ar), 42.1 (d, 2C, $^1J_{PC} = 52.9$ Hz, PCH), 38.6 (2C, $O=CCH_2$). HRMS (+ESI) m/z : $(M + H)^+$ calcd for $C_{46}H_{39}N_2O_2P_2S_2$, 777.1928; found, 777.1929. Anal. Calcd for $C_{46}H_{38}N_2O_2P_2S_2$: C, 71.12; H, 4.93; N, 3.61. Found: C, 71.19; H, 4.99; N, 3.65 %.

Synthesis of Compound 198b. To a solution of 6,6'-dibromo-2,2'-bipyridine (3.50 g, 11.1 mmol, 1.0 equiv.) in THF (250 mL) at -80°C was added 2.5 M *n*-BuLi in DEE (9.36 mL, 23.4 mmol, 2.1 equiv.) and stirred for 1 h. *N,N*-dimethylacetamide (2.28 mL, 24.5 mmol, 2.2 equiv.) in DEE (50 mL) was added dropwise and the purple solution stirred for 2h. The mixture was raised to -10°C, hydrolyzed with 6 N HCl (20 mL), concentrated under reduced pressure and neutralized with dilute aq. NaOH. The organic layer was extracted with DCM (3 X 50 mL), washed with H₂O (2 X 50 mL), dried over MgSO₄, filtered and the solvent evaporated. The crude product was recrystallized from EtOH twice to afford pure yellow solid of **198b**. (1.87 g, 7.80 mmol, 70% yield). Mp: 175-177°C. ¹H NMR (CDCl₃, 300 MHz): δ 8.72 (d, 2H, ³*J* = 7.6 Hz, O=CCNCCH), 8.09 (d, 2H, ³*J* = 7.6 Hz, O=CCCH), 8.00 (t, 2H, ³*J* = 7.7 Hz, O=CCCHCH), 2.84 (s, 6H, CH₃); ¹³C NMR (CDCl₃, 100 MHz): δ 200.2 (2C, C=O), 154.8 (2C, O=CCNC), 153.2 (2C, O=CCN), 138.1 (2C, O=CCCHC), 124.5 (2C, O=CCNCCH), 122.0 (2C, O=CCCH₂), 25.9 (2C, CH₃). HRMS (+ESI) *m/z*: (M + H)⁺ calcd for C₁₄H₁₃N₂O₂, 241.0977; found, 241.0975. Anal. Calcd for C₁₄H₁₂N₂O₂: C, 69.99; H, 5.03; N, 11.66. Found: C, 70.05; H, 5.10; N, 11.80 %.

Synthesis of Compound 198c. A mixture of 1,1'-([2,2'-bipyridine]-6,6'-diyl)diethanone (1.00 g, 4.16 mmol, 1.0 equiv.), benzaldehyde (0.93 mL, 9.16 mmol, 2.2 equiv.) and KOH (10 % w/v in MeOH, 20 mL) was refluxed overnight. The pure product was crystallized from the reaction mixture. (1.30 g, 3.12 mmol, 75% yield). Mp: 251-252°C. ¹H NMR (CDCl₃, 400 MHz): δ 8.82 (d, 2H, ³*J* = 7.7 Hz, O=CCNCCH), 8.46 (d, 2H, ³*J* = 16.0 Hz, PhCH=CH), 8.29 (d, 2H, ³*J* = 7.6 Hz, O=CCCH), 8.12 (t, 2H, ³*J* = 7.8 Hz, O=CCCHCH), 8.02 (d, 2H, ³*J* = 16.1 Hz, PhCH=CH), 7.78-7.77 (m, 4H, Ar), 7.48-7.46 (m, 6H, Ar); ¹³C NMR (CDCl₃, 75 MHz): δ 189.5 (2C, C=O), 154.9 (2C, O=CCNC), 154.0 (2C, O=CCN), 145.1 (2C, PhCH=CH), 138.4 (2C, O=CCCHCH), 135.5 (2C, Ph), 130.9 (2C, O=CCNCCH), 129.2 (4C, Ph), 129.0 (4C, Ph), 124.5 (2C, Ph), 123.5 (2C,

PhCH=CH), 121.1 (2C, O=CCCH). HRMS (+ESI) m/z : (M + H)⁺ calcd for C₂₈H₂₁N₂O₂, 417.1603; found, 417.1605. Anal. Calcd for C₂₈H₂₀N₂O₂: C, 80.75; H, 4.84; N, 6.73. Found: C, 80.80; H, 4.90; N, 6.80 %.

Synthesis of NC(*sp*³)X preligand for complexes (*S,S*)-201a-b**.** To a solution of Ph₂PH (0.22 mmol, 1.1 equiv.) in toluene (15 mL) was added catalyst (*S*)-**119** (0.009 mmol, 4 mol %) and stirred for 10 minutes before cooling to -80°C. The enone **200b** (0.20 mmol, 1.0 equiv.) was added followed by the addition of NEt₃ (0.20 mmol, 1.0 equiv.) in toluene (1 mL) dropwise. The solution was stirred at -80°C and the completion of the reaction was monitored by ³¹P{¹H} NMR. Upon completion, the solution was allowed to room temperature. Aq. H₂O₂ (31% w/w, 0.1 mL) or S₈ (25.0 μmol, 0.125 equiv.) was added and stirred for 30 min. The crude product was purified by silica gel column chromatography to afford the pure phosphine oxide/sulfide.

Preligand for (*S,S*)-**201a** White solid (77.3 mg, 0.19 mmol, 94% yield). Purified by silica gel column chromatography (EA). Mp: 218-219°C. ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 33.6; ¹H NMR (CDCl₃, 400 MHz): δ 8.62-8.61 (m, 1H, Ar), 8.02-7.97 (m, 2H, Ar), 7.83-7.81 (m, 1H, Ar), 7.71 (td, 1H, ³*J* = 7.7 Hz, ⁴*J* = 1.7 Hz, Ar), 7.51-7.46 (m, 5H, Ar), 7.41-7.36 (m, 2H, Ar), 7.35-7.31 (m, 2H, Ar), 7.27-7.23 (m, 2H, Ar), 7.14-7.08 (m, 3H, Ar), 4.48-4.41 (m, 1H, PCHCH₂), 4.39-4.34 (m, 1H, O=CCH₂), 3.58 (ddd, 1H, ²*J* = 17.5 Hz, ³*J*_{PH} = 9.9 Hz, ³*J* = 1.4 Hz, O=CCH₂); ¹³C NMR (CDCl₃, 125 MHz): δ 199.0 (d, 1C, ³*J*_{PC} = 12.9 Hz, C=O), 153.0 (1C, Ar), 149.1 (2C, Ar), 136.8-121.9 (20C, Ar), 41.8 (d, 1C, ¹*J*_{PC} = 68.2 Hz, PCH), 38.4 (1C, O=CCH₂). HRMS (+ESI) m/z : (M + H)⁺ calcd for C₂₆H₂₃NO₂P, 412.1466; found, 412.1466. Anal. Calcd for C₂₆H₂₂NO₂P: C, 75.90; H, 5.39; N, 3.40. Found: C, 75.95; H, 5.37; N, 3.46 %.

Preligand for (*S,S*)-**201b** Pale yellow solid (75.2 mg, 0.18 mmol, 88% yield). Purified by silica gel column chromatography (1 *n*-hexane : 1 DCM to 1 *n*-hexane : 10

DCM). Mp: 94-96°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 51.5; ^1H NMR (CDCl_3 , 400 MHz): δ 8.63-8.61 (m, 1H, Ar), 8.23-8.18 (m, 2H, Ar), 7.80 (d, 1H, $^3J = 7.8$ Hz, Ar), 7.68 (td, 1H, $^3J = 7.7$ Hz, $^4J = 1.7$ Hz, Ar), 7.54-7.49 (m, 5H, Ar), 7.39-7.35 (m, 1H, Ar), 7.33-7.25 (m, 3H, Ar), 7.23-7.19 (m, 2H, Ar), 7.08-7.05 (m, 3H, Ar), 4.87 (td, 1H, $^2J_{\text{PH}} = 10.6$ Hz, $^3J = 2.6$ Hz, PCHCH_2), 4.51 (ddd, 1H, $^2J = 18.2$ Hz, $^3J_{\text{PH}} = 10.9$ Hz, $^3J = 6.2$ Hz, O=CCH_2), 3.51 (ddd, 1H, $^2J = 18.4$ Hz, $^3J_{\text{PH}} = 11.6$ Hz, $^3J = 2.7$ Hz, O=CCH_2); ^{13}C NMR (CDCl_3 , 100 MHz): δ 198.8 (d, 1C, $^3J_{\text{PC}} = 15.1$ Hz, C=O), 152.9 (1C, Ar), 149.2 (1C, Ar), 136.8-121.8 (21C, Ar), 42.1 (d, 1C, $^1J_{\text{PC}} = 52.9$ Hz, PCH), 38.6 (1C, O=CCH_2). HRMS (+ESI) m/z : $(\text{M} + \text{H})^+$ calcd for $\text{C}_{26}\text{H}_{23}\text{NOPS}$, 428.1238; found, 428.1236. Anal. Calcd for $\text{C}_{26}\text{H}_{22}\text{NOPS}$: C, 73.05; H, 5.19; N, 3.28. Found: C, 73.08; H, 5.19; N, 3.33 %.

Synthesis of Compound 202b. To a solution of NaOH (55.0 mmol, 1.2 equiv.) in H_2O (20 mL) and aromatic ketone (45.8 mmol, 1.0 equiv.) in ethanol (12 mL) at 0°C was gradually added aromatic aldehyde (45.8 mmol, 1.0 equiv.). The mixture was allowed to warm to room temperature and stirred for 4 h, after which the precipitate of the product was collected by suction filtration on a Buchner funnel and washed repeatedly with cold water. The residue was redissolved in DCM and extracted, washed with H_2O (1 x 40 mL), dried over MgSO_4 , filtered and evaporated to dryness. The crude product was purified by silica gel chromatography (2 *n*-hexane : 1 DCM) to afford the pure yellow solid of enone **202b** (89% yield). The data is consistent with literature.^[264]

Synthesis of $\text{NC}(\text{sp}^3)\text{X}$ preligand for complexes (*R,R*)-203a-b. To a solution of Ph_2PH (0.22 mmol, 1.1 equiv.) in acetone (15 mL) was added catalyst (*R,R*)-**150aa** (0.011 mmol, 5 mol %) and stirred for 10 minutes before cooling to 0°C. The enone **202b** (0.20 mmol, 1.0 equiv.) was added. The solution was stirred at 0°C and the completion of the reaction was monitored by $^{31}\text{P}\{^1\text{H}\}$ NMR. Upon completion, the solution was allowed to room temperature. Aq. H_2O_2 (31% w/w, 0.1 mL) or S_8 (25.0 μmol , 0.125 equiv.) was

added and stirred for 30 min. The crude product was purified by silica gel column chromatography to afford the pure preligand.

Preligand for (*R,R*)-**203a** White solid (75.2 mg, 0.17 mmol, 86% yield). Purified by silica gel column chromatography (4 EA : 1 *n*-hexane). $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 33.8; ^1H NMR (CDCl_3 , 400 MHz): δ 8.65 (d, 1H, $^3J = 4.2$ Hz, Ar), 7.96-7.92 (m, 3H, Ar), 7.84-7.74 (m, 3H, Ar), 7.50-7.41 (m, 7H, Ar), 7.22-7.13 (m, 5H, Ar), 6.35 (dd, 1H, $^3J = 16.0$ Hz, $^4J_{\text{PH}} = 4.3$ Hz, $\text{PhCH}=\text{CH}$), 6.12 (ddd, 1H, $^3J = 15.9$ Hz, $^3J_{\text{PH}} = 8.8$ Hz, $^3J = 5.9$ Hz, $\text{PhCH}=\text{CH}$), 4.19-4.13 (m, 1H, PCHCH_2), 4.03 (ddd, 1H, $^2J = 17.6$ Hz, $^3J_{\text{PH}} = 10.7$, $^3J = 5.2$ Hz, $\text{O}=\text{CCH}_2$), 3.47 (ddd, 1H, $^2J = 17.4$ Hz, $^3J_{\text{PH}} = 10.9$ Hz, $^3J = 2.4$ Hz, $\text{O}=\text{CCH}_2$); HRMS (+ESI) m/z : $(\text{M} + \text{H})^+$ calcd for $\text{C}_{28}\text{H}_{25}\text{NO}_2\text{P}$, 438.1623; found, 438.1625. Anal. Calcd for $\text{C}_{28}\text{H}_{24}\text{NO}_2\text{P}$: C, 76.87; H, 5.53; N, 3.20. Found: C, 76.89; H, 5.49; N, 3.22 %.

Preligand for (*R,R*)-**203b** Pale yellow solid (81.6 mg, 0.18 mmol, 90% yield). Purified by silica gel column chromatography (1 *n*-hexane : 1 DCM to 1 *n*-hexane : 2 DCM). $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 49.6; ^1H NMR (CDCl_3 , 400 MHz): δ 8.66 (d, 1H, $^3J = 4.2$ Hz, Ar), 8.13-8.07 (m, 2H, Ar), 7.93-7.89 (m, 3H, Ar), 7.78-7.74 (m, 1H, Ar), 7.50-7.38 (m, 7H, Ar), 7.21-7.12 (m, 5H, Ar), 6.29 (dd, 1H, $^3J = 15.9$ Hz, $^4J_{\text{PH}} = 4.6$ Hz, $\text{PhCH}=\text{CH}$), 6.16 (ddd, 1H, $^3J = 15.8$ Hz, $^3J_{\text{PH}} = 8.7$ Hz, $^3J = 6.5$ Hz, $\text{PhCH}=\text{CH}$), 4.50-4.42 (m, 1H, PCHCH_2), 4.11 (ddd, 1H, $^2J = 17.7$ Hz, $^3J_{\text{PH}} = 10.5$, $^3J = 5.6$ Hz, $\text{O}=\text{CCH}_2$), 3.35 (ddd, 1H, $^2J = 17.6$ Hz, $^3J_{\text{PH}} = 12.5$ Hz, $^3J = 2.3$ Hz, $\text{O}=\text{CCH}_2$); ^{13}C NMR (CDCl_3 , 100 MHz): δ 198.9 (d, 1C, $^3J_{\text{PC}} = 15.1$ Hz, $\text{C}=\text{O}$), 152.9 (1C, Ar), 149.1 (1C, Ar), 136.9-122.0 (23C, Ar + $\text{C}=\text{C}$), 40.5 (d, 1C, $^1J_{\text{PC}} = 54.9$ Hz, PCH), 37.5 (1C, $\text{O}=\text{CCH}_2$). HRMS (+ESI) m/z : $(\text{M} + \text{H})^+$ calcd for $\text{C}_{28}\text{H}_{25}\text{NOPS}$, 454.1394; found, 454.1396. Anal. Calcd for $\text{C}_{28}\text{H}_{24}\text{NOPS}$: C, 74.15; H, 5.33; N, 3.09. Found: C, 74.18; H, 5.47; N, 3.13 %.

General Preparation of NC(*sp*³)X pincer complexes, (*S,S,S,S*)-195a-b**, **197a-b** and **199a-b**.** A mixture of the NC(*sp*³)X preligand (0.50 mmol, 1.0 equiv.) and PdCl₂(NCMe)₂ (259.4 mg, 1.00 mmol, 2.0 equiv.) in DCM (50 mL) was stirred for 12 h at RT. On removal of the solvent, the residue was purified by silica gel column chromatography to afford the pure pincer complex.

Note: The data for all bimetallic NC(*sp*³)X complexes except (*S,S,S,S*)-**195b** were not obtained prior to the completion of the thesis.

(*S,S,S,S*)-**195b** Yellow solid (0.46 g, 0.44 mmol, 88% yield). Purified by silica gel column chromatography (1 EA : 1 DCM). ³¹P{¹H} NMR (CDCl₃, 162 MHz): δ 65.7; ¹H NMR (CDCl₃, 500 MHz): δ 9.20 (d, 2H, ³*J* = 5.5 Hz, Ar), 7.97-7.89 (m, 6H, Ar), 7.68-7.65 (m, 4H, Ar), 7.60-7.56 (m, 4H, Ar), 7.53-7.49 (m, 4H, Ar), 7.35-7.38 (m, 4H, Ar), 7.28-7.22 (m, 4H, Ar), 6.85 (s, 4H, Ar), 5.08 (dd, 2H, ²*J*_{PH} = 13.0 Hz, ³*J* = 8.5 Hz, PCH), 4.83 (dd, 2H, ³*J* = 8.4 Hz, ³*J*_{PH} = 7.0 Hz, PdCH); ¹³C NMR (CDCl₃, 75 MHz): δ 193.8 (t, 2C, ³*J*_{PC} = 7.0 Hz, C=O), 155.9 (2C, Ar), 149.3 (2C, Ar), 139.6-122.6 (36C, Ar), 55.3 (2C, O=CCH), 38.6 (d, 2C, ¹*J*_{PC} = 60.4 Hz, PCH). HRMS (+ESI) *m/z*: (M - Cl)⁺ calcd for C₄₆H₃₆ClN₂O₂P₂Pd₂S₂, 1020.9452; found, 1020.9455. Anal. Calcd for C₄₆H₃₆Cl₂N₂O₂P₂Pd₂S₂: C, 52.19; H, 3.43; N, 2.65. Found: C, 52.25; H, 3.48; N, 2.72 %.

General Preparation of NC(*sp*³)X pincer complexes, (*S,S*)-201a-b** and (*R,R*)-**203a-b**.** A mixture of the NC(*sp*³)X preligand (0.47 mmol, 1.0 equiv.) and PdCl₂(NCMe)₂ (0.12 g, 0.47 mmol, 1.0 equiv.) in DCM (50 mL) was stirred for 12 h at RT. On removal of the solvent, the residue was purified by silica gel column chromatography to afford the corresponding complex.

Note: The data for the monometallic NC(*sp*³)S complex (*R,R*)-**203b** were not obtained prior to the completion of the thesis.

(*S,S*)-**201a** White solid (251.4 mg, 0.46 mmol, 97% yield). Purified by silica gel column chromatography (2 DCM: 1 EA). Mp: 176-178°C. $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 73.2; ^1H NMR (CDCl_3 , 400 MHz): δ 9.10 (d, 1H, $^3J = 5.0$ Hz, Ar), 7.92-7.84 (m, 3H, Ar), 7.62-7.54 (m, 7H, Ar), 7.44-7.40 (m, 3H, Ar), 7.19-7.16 (m, 3H, Ar), 7.00-6.97 (m, 2H, Ar), 5.20 (dd, 1H, $^3J = 9.5$ Hz, $^3J_{\text{PH}} = 4.2$ Hz, PdCH), 4.91 (dd, 1H, $^2J_{\text{PH}} = 16.3$ Hz, $^3J = 9.6$ Hz, PCH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 192.7 (d, 1C, $^3J_{\text{PC}} = 13.5$ Hz, C=O), 157.2 (1C, Ar), 151.2 (1C, Ar), 139.6-122.6 (21C, Ar), 55.8 (1C, PdCH), 48.6 (d, 1C, $^1J_{\text{PC}} = 72.1$ Hz, PCH). HRMS (+ESI) m/z : (M - Cl) $^+$ calcd for $\text{C}_{26}\text{H}_{21}\text{NO}_2\text{PPd}$, 516.0345; found, 516.0345. Anal. Calcd for $\text{C}_{26}\text{H}_{21}\text{ClNO}_2\text{PPd}$: C, 56.54; H, 3.83; N, 2.54. Found: C, 56.70; H, 3.75; N, 2.56 %.

(*S,S*)-**201b** Yellow solid (245.4 mg, 0.43 mmol, 92% yield). Purified by silica gel column chromatography (1 DCM : 1 EA). Mp: 236-238°C (dec.). $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 66.4; ^1H NMR (CDCl_3 , 400 MHz): δ 9.20 (d, 1H, $^3J = 5.2$ Hz, Ar), 7.97-7.91 (m, 3H, Ar), 7.67-7.62 (m, 2H, Ar), 7.58-7.47 (m, 6H, Ar), 7.39-7.34 (m, 2H, Ar), 7.21-7.13 (m, 3H, Ar), 7.03-7.01 (m, 2H, Ar), 5.18 (ddd, 1H, $^2J_{\text{PH}} = 13.8$ Hz, $^3J = 8.6$ Hz, PCH), 4.96 (dd, 1H, $^3J = 8.4$ Hz, $^3J_{\text{PH}} = 6.9$ Hz, PdCH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 193.7 (d, 1C, $^3J_{\text{PC}} = 14.5$ Hz, C=O), 156.1-122.6 (23C, Ar), 55.4 (1C, PdCH), 52.6 (d, 1C, $^1J_{\text{PC}} = 59.2$ Hz, PCH). HRMS (+ESI) m/z : (M - Cl) $^+$ calcd for $\text{C}_{26}\text{H}_{21}\text{NOPPdS}$, 532.0116; found, 532.0115. Anal. Calcd for $\text{C}_{26}\text{H}_{21}\text{ClNOPPdS}$: C, 54.94; H, 3.72; N, 2.46. Found: C, 54.98; H, 3.75; N, 2.46 %.

(*R,R*)-**203a** White solid (273.4 mg, 0.46 mmol, 98% yield). Purified by silica gel column chromatography (10 DCM : 1 EA to 8 DCM : 1 EA). Mp: 170-171°C (dec.). $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 162 MHz): δ 74.9; ^1H NMR (CDCl_3 , 400 MHz): δ 9.07 (d, 1H, $^3J = 5.1$ Hz, Ar), 8.12-8.08 (m, 2H, Ar), 7.95 (td, 1H, $^3J = 7.7$ Hz, $^4J = 1.4$ Hz, Ar), 7.86-7.81 (m, 2H, Ar), 7.70-7.58 (m, 5H, Ar), 7.51 (td, 2H, $^3J = 7.6$ Hz, $^4J = 3.3$ Hz, Ar), 7.45-

7.42 (m, 1H, Ar), 7.30-7.20 (m, 5H, Ar), 6.59 (dd, 1H, $^3J = 15.8$ Hz, $^3J = 4.5$ Hz, PhCH=CH), 5.85 (ddd, 1H, $^3J = 15.8$, 5.6 Hz, $^3J_{\text{PH}} = 8.5$ Hz, PhCH=CH), 4.76 (dd, 1H, $^3J_{\text{PH}} = 10.4$ Hz, $^3J = 2.1$ Hz, PdCH), 4.71-4.62 (m, 1H, PCH); ^{13}C NMR (CDCl_3 , 100 MHz): δ 193.0 (d, 1C, $^3J_{\text{PC}} = 15.5$ Hz, C=O), 157.4 (1C, Ar), 151.5 (1C, Ar), 139.6-121.6 (23C, Ar + C=C), 55.6 (1C, PdCH), 46.3 (d, 1C, $^1J_{\text{PC}} = 75.6$ Hz, PCH). HRMS (+ESI) m/z : (M - Cl) $^+$ calcd for $\text{C}_{28}\text{H}_{23}\text{NOPPdS}$, 558.0273; found, 558.0275. Anal. Calcd for $\text{C}_{28}\text{H}_{23}\text{ClNOPPdS}$: C, 56.58; H, 3.90; N, 2.36. Found: C, 56.66; H, 4.00; N, 2.46 %.

References

- [1] L. Pasteur, *Ann. Chim. Phys.* **1848**, *III*, 442.
- [2] Lord Kelvin *Baltimore Lectures (1884) on Molecular Dynamics and the Wave Theory of Light*; Clay and Sons: London, **1904**, 449.
- [3] a) L. Stryer, *Biochemistry*, 4th ed., W. H. Freeman and Co.; New York, **1995**. b) J. S. Siegel, *Chirality* **1998**, *10*, 24.
- [4] G. A. Khoury, R. C. Baliban, C. A. Floudas, *Sci. Rep.* **2011**, DOI: 10.1038/srep00090.
- [5] R. Crossley, *Chirality and the Biological Activity of Drugs*; CRC Press: Boca Ratan Florida, **1995**.
- [6] R. H. deJong, *Local Anesthetics*; Mosby: St. Louis, MO, **1994**.
- [7] T. Eriksson, S. Bjorkman, B. Roth, P. Hoglund, *J. Pharm. Pharmacology* **2000**, *52*, 807.
- [8] PAC, **1996**, *68*, 2193.
- [9] a) A. Togni, *Angew. Chem., Int. Ed.* **1996**, *35*, 1475. b) H.-U. Blaser, W. Brieden, B. Pugin, F. Spindler, M. Studer, A. Togni, *Top. Catal.* **2002**, *19*, 3, and the references therein.
- [10] H. U. Blaser, F. Spindler, M. Thommen, *Handbook of Homogeneous Hydrogenation*, (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim, **2007**, 1279.
- [11] a) C. Czekelius, E. M. Carreira, *Angew., Chem. Int. Ed.* **2003**, *42*, 4793. b) C. Czekelius, E. M. Carreira, *Org. Lett.* **2004**, *6*, 4575. c) B. H. Lipshutz, J. M. Servesko, *Angew. Chem., Int. Ed.* **2003**, *42*, 4789. d) B. H. Lipshutz, J. M.

- Servesko, B. R. Taft, *J. Am. Chem. Soc.* **2004**, *126*, 8352. e) D. Lee, D. Kim, J. Yun, *Angew., Chem. Int. Ed.* **2006**, *45*, 2785.
- [12] a) M. E. P. Lormann, M. Nieger, S. Bräse, *J. Organomet. Chem.* **2006**, *691*, 2159. b) M. A. Fernandez-Rodriguez, Q. Shen, J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 2180. c) M. E. Limmert, A. H. Roy, J. F. Hartwig, *J. Org. Chem.* **2005**, *70*, 9364.
- [13] a) F. Lopez, S. R. Harutyunyan, A. Meetsma, A. J. Minnaard, B. L. Feringa, *Angew. Chem., Int. Ed.* **2005**, *44*, 2752. b) R. Des Mazery, M. Pullez, F. Lopez, S. R. Harutyunyan, A. J. Minnaard, B. L. Feringa, *J. Am. Chem. Soc.* **2005**, *127*, 9966. c) G. P. Howell, S. P. Fletcher, K. Geurts, B. ter Horst, B. L. Feringa, *J. Am. Chem. Soc.* **2006**, *128*, 14977. d) M. Pucheault, S. Darses, J.-P. Genêt, *Eur. J. Org. Chem.* **2002**, 3552.
- [14] a) M. Lautens, K. Fagnou, S. Hiebert, *Acc. Chem. Res.* **2003**, *36*, 48. b) M. Lautens, K. Fagnou, *Proc. N. Y. Acad. Sci.* **2004**, *101*, 5455. c) E. A. Bercot, T. Rovis, *J. Am. Chem. Soc.* **2004**, *126*, 10248.
- [15] a) C. Goddard, A. Ruiz, C. Claver, *Helv. Chim. Acta.* **2006**, *89*, 161. b) C. Cai, N. R. Rivera, J. Balsells, R. R. Sidler, J. C. McWilliam, C. S. Shultz, Y. Sun, *Org. Lett.* **2006**, *8*, 5161.
- [16] G. Xu, L.-B. Han, *Org. Lett.* **2006**, *8*, 2099.
- [17] Q. Shen, J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 10028.
- [18] L. Horner, H. Siegel, H. Buthe, *Angew. Chem., Int. Ed.* **1968**, *7*, 942.
- [19] W. S. Knowles, M. J. Sabacky, *J. Chem. Soc. Chem. Commun.* **1968**, 1445.
- [20] H. B. Kagan, T.-P. Dang, *J. Am. Chem. Soc.* **1972**, *94*, 6429.

- [21] *Handbook of Enantioselective Catalysis: With Transition Metal Compounds* (Eds.: H. Brunner, W. Zettlmeier), Wiley-VCH, Weinheim, **1993**.
- [22] a) *Asymmetric Catalysis in Organic Synthesis* (Ed.: R. Noyori), Wiley, New York, **1994**. b) *Comprehensive Asymmetric Catalysis, Vol. I-III* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**. c) *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), Wiley, New York, **2000**. d) *Asymmetric Catalysis on Industrial Scale* (Eds.: H.-U. Blaser, S. Schmidt), Wiley-VCH, Weinheim, **2004**. e) *A Guide to Organophosphorus Chemistry* (Ed.: L. D. Quin), Wiley-Interscience, New York, **2000**. f) D. Sinou, *Adv. Synth. Catal.* **2002**, 334, 221. g) D. Dwars, G. Oehme, *Adv. Synth. Catal.* **2002**, 334, 239. h) J. L. Methot, W. R. Roush, *Adv. Synth. Catal.* **2004**, 346, 1035. i) *Phosphorus Ligands in Asymmetric Catalysis, Vol. I-III* (Ed.: A. Börner), Wiley-VCH, Weinheim, **2008**.
- [23] C. Kölmel, C. Ochsenfeld, R. Ahlrichs, *Theor. Chim. Acta.* **1991**, 82, 271.
- [24] a) C. A. Busacca, R. Raja, N. Grinberg, N. Haddad, P. James-Jones, H. Lee, J. C. Lorenz, A. Saha, C. H. Sennanayake, *J. Org. Chem.* **2008**, 73, 1524. b) V. T. Trepohl, S. Mori, K. Itami, M. Oestreich, *Org. Lett.* **2009**, 11, 1091. c) H. Ohmiya, H. Yorimitsu, K. Oshima, *Angew. Chem., Int. Ed.* **2005**, 44, 2368. d) C. A. Busacca, E. Farber, J. DeYoung, S. Campbell, N. C. Gonnella, N. Grinberg, N. Haddad, H. Lee, S. Ma, D. Reeves, S. Shen, C. H. Sennanayake, *J. Org. Chem.* **2009**, 74, 5594. e) M. Stankevič, K. M. Pietrusiewicz, *Synthesis* **2005**, 1279.
- [25] A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi, R. Noyori, *J. Am. Chem. Soc.* **1980**, 102, 7932.
- [26] V. Ujj, T. Szuhánszki, J. Schindler, M. Czugler, E. Fogassy, Gy. Keglevich, *Hung. J. Ind. Chem.* **2008**, 36, 131, and refs [5, 8-19] therein.

- [27] a) J. Meisenheimer, L. Lichtenstadt, *Chem. Ber.* **1911**, *44*, 356. b) P. Drabowicz, P. Łyżwa, J. Omelańczuk, K. M. Pietrusiewicz, M. Mikołajczyk, *Tetrahedron: Asymmetry* **1999**, *10*, 2757.
- [28] G. Ostrogovich, F. Kerek, *Angew. Chem.* **1971**, *13*, 496.
- [29] a) W. C. Davies, F. G. Mann, *J. Chem. Soc.* **1944**, 276. b) I. G. M. Campbell, J. K. Way, *J. Chem. Soc.* **1961**, 2133.
- [30] R. Bodalski, T. Janecki, Z. Galdecki, M. Glowka, *Phosphorus, Sulfur* **1982**, *14*, 15.
- [31] a) K. F. Kumli, W. E. McEwen, C. A. VanderWerf, *J. Am. Chem. Soc.* **1959**, *81*, 248. b) K. L. Marsi, H. Tuinstra, *J. Org. Chem.* **1975**, *40*, 1843.
- [32] a) T. Imamoto, in *Handbook of Organophosphorus Chemistry* (Ed.: R. Engel), CRC Press: Boca Ratan Florida, **1992**, 1. b) K. M. Pietrusiewicz, M. Zablocka, *Chem. Rev.* **1994**, *94*, 1375. c) G. S. Quin, *A Guide to Organophosphorus Chemistry* (Ed.: L. D. Quin), Wiley-Interscience, New York, **2000**, 272.
- [33] a) V. V. Dunina, L. G. Kuz'mina, M. Y. Rubina, Y. K. Grishin, Y. A. Veits, E. I. Kazakova, *Tetrahedron: Asymmetry* **1999**, *10*, 1483. b) S. B. Wild, *Coord. Chem. Rev.* **1997**, *166*, 291, and the references therein.
- [34] a) W. H. Pirkle, T. C. Pochapsky, *Adv. Chromatogr.* **1987**, *27*, 73. b) A. Brandi, S. Cicchi, F. Gasparrini, F. Maggio, C. Villani, M. Koprowski, K. M. Pietrusiewicz, *Tetrahedron: Asymmetry* **1995**, *6*, 2017. c) F. Gasparrini, D. Misiti, C. Villani, *Chirality* **1992**, *4*, 447. d) W. H. Pirkle, T. C. Pochapsky, *Chem. Rev.* **1989**, *89*, 347. e) A. Tambute, P. Gareil, M. Caude, R. Rosset, *J. Chromatogr.* **1986**, *363*, 81. f) P. Pescher, M. Caude, R. Rosset, A. Tambute, *J. Chromatogr.* **1986**, *371*, 159. g) G. Fuchs, L. Doguet, D. Barth, M. Perrut, *J. Chromatogr.* **1992**, *623*, 329.
- [35] a) H.-U. Blaser, H. P. Buser, K. Coers, R. Hanreich, H.-P. Jalett, E. Jelsh, B. Pugin, H.-D. Schneider, F. Spindler, A. Wegmann, *Chimia* **1999**, *53*, 275. b) A. Wickli, E.

- Schmidt, J. R. Bourne, in *Biocatalysis in Non-Conventional Media* (Ed.: J. Tramper), Elsevier, Amsterdam, **1992**, 577. c) H.-U. Blaser, *Adv. Synth. Catal.* **2002**, *334*, 17.
- [36] A. Brandi, S. Cicchi, A. Goti, M. Koprowski, K. M. Pietrusiewicz, *J. Org. Chem.* **1994**, *59*, 1315.
- [37] a) P. Kielbasiński, R. Żurawiński, K. M. Pietrusiewicz, M. Zablocka, M. Mikolajczyk, *Tetrahedron Lett.* **1994**, *35*, 7081. b) A. N. Serreqi, R. J. Kazlauskas, *J. Org. Chem.* **1994**, *59*, 7609.
- [38] E. Fogassy, M. Nógrádi, D. Kozma, G. Egri, E. Pálovics, V. Kiss, *Org. Biomol. Chem.* **2006**, *4*, 3011.
- [39] S. J. Faulconbridge, K. E. Holt, L. G. Sevillano, P. D. Lock, N. Tiffin, S. Winter, *Tetrahedron Lett.* **2000**, *41*, 2679.
- [40] a) S. Jugé, *Phosphorus, Sulfur* **2008**, *183*, 233. b) J. M. Brunel, B. Faure, M. Maffei, *Coord. Chem. Rev.* **1998**, *178-180*, 665. c) E. Rudzińska, Ł. Łukasz Berlicki, P. Kafarski, M. Lämmerhofer, A. Mucha, *Tetrahedron: Asymmetry* **2009**, *20*, 2709. d) P. Majewska, P. Kafarski, B. Lejczak, *Tetrahedron: Asymmetry* **2006**, *17*, 2870. e) P. Guga, A. Okruszek, J. Stec, in *Topics in Current Chemistry* (Ed.: J. P. Majoral), Springer, Berlin, Heidelberg, **2002**, 220, 169. f) K. V. L. Crépy, T. Imamoto, in *Topics in Current Chemistry* (Ed.: J. P. Majoral), Springer, Berlin, Heidelberg, **2003**, 229, 1. g) O. I. Kolodiazhnyi, in *Advances in Asymmetric Synthesis* (Ed.: A. Hassner), JAI Press, Stamford, **1998**, *3*, 273.
- [41] a) O. Korpium, R. A. Lewis, J. Chickos, K. Mislow, *J. Am. Chem. Soc.* **1968**, *90*, 4842. b) Y.-M. Li, F.-Y. Kwong, W.-Y. Yu, A. S. C. Chan, *Coord. Chem. Rev.* **2007**, *251*, 2119. c) T. Oshiki, T. Imamoto, *J. Am. Chem. Soc.* **1992**, *114*, 3975. d)

- B. D. Vineyard, W. S. Knowles, M. J. Sabacky, G. L. Bachman, D. J. Weinkauff, *J. Am. Chem. Soc.* **1977**, 99, 5946. e) G. Hoge, *J. Am. Chem. Soc.* **2003**, 125, 10219.
- [42] a) O. I. Kolodiazhnyi, E. V. Gryshkun, N. V. Andrushko, M. Freytag, P. G. Jones, R. Schmutzler, *Tetrahedron: Asymmetry* **2003**, 14, 181. b) E. V. Gryshkun, N. V. Andrushko, O. I. Kolodiazhnyi, *Phosphorus, Sulfur* **2004**, 179, 1027. c) N. V. Andrushko, O. I. Kolodiazhnyi, *Phosphorus, Sulfur* **2002**, 177, 2109.
- [43] a) S. Jugé, J. P. Genêt, *Tetrahedron Lett.* **1989**, 30, 2783. b) S. Jugé, M. Stephan, J. A. Laffitte, J. P. Genêt, *Tetrahedron Lett.* **1990**, 31, 6357.
- [44] A. Bader, M. Pabel, A. C. Willis, S. B. Wild, *Inorg. Chem.* **1996**, 35, 3874.
- [45] T. P. Dang, H. B. Kagan, *J. Chem. Soc., Chem. Commun.* **1971**, 481.
- [46] G. Michaud, M. Bulliard, L. Ricard, J.-P. Genêt, A. Marinetti, *Chem. Eur. J.* **2002**, 8, 3327.
- [47] S. Yasuike, C. C. Kofink, R. J. Kloetzing, N. Gommermann, K. Tappe, A. Gavryushin, P. Knochel, *Tetrahedron: Asymmetry* **2005**, 16, 3385.
- [48] a) *Key Chiral Auxiliary Application, 2nd ed.* (Ed.: G. Roos), Academic Press, Elsevier Science, **2014**. b) F. Glorius, Y. Gnass, *Synthesis* **2006**, 12, 1899. c) D. A. Evans, G. Helmchen, M. Rüping, in *Asymmetric Synthesis –The Essentials* (Eds.: M. Christmass, S. Bräse), Wiley-VCH, Weinheim, **2007**, 3.
- [49] *The Chemistry of Fragrances: From Perfumer to Consumer* (Ed.: C. S. Sell), Royal Society of Chemistry, Great Britain, **2006**.
- [50] a) D. S. Glueck, *Chem. Eur. J.* **2008**, 14, 7108. b) O. I. Kolodiazhnyi, V. P. Kukhar, A. O. Kolodiazhna, *Tetrahedron: Asymmetry* **2014**, 25, 865.

- [51] a) L. Horner, H. Büthe, H. Siegel, *Tetrahedron Lett.* **1968**, 4023. b) W. S. Knowles, M. J. Sabacky, B. D. Vineyard, *J. Chem. Soc., Chem. Commun.* **1972**, 10.
- [52] I. Kovacic, D. K. Wicht, N. S. Grewal, D. S. Glueck, C. D. Incarvito, I. A. Guzei, A. L. Rheingold, *Organometallics* **2000**, *19*, 950.
- [53] J. R. Moncarz, T. J. Bruncker, J. C. Jewett, M. Orchowski, D. S. Glueck, R. D. Sommer, K.-C. Lam, C. D. Incarvito, T. E. Concolino, C. Ceccarelli, L. N. Zakharov, A. L. Rheingold, *Organometallics* **2003**, *22*, 3205.
- [54] J. R. Moncarz, N. F. Lritcheva, D. S. Glueck, *J. Am. Chem. Soc.* **2006**, *128*, 2788.
- [55] C. Korff, G. Helmchen, *Chem. Commun.* **2004**, 530.
- [56] T. P. Dang, H. B. Kagan, *J. Chem. Soc., Chem. Commun.* **1971**, 481.
- [57] A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi, R. Noyori, *J. Am. Chem. Soc.* **1980**, *102*, 7932.
- [58] M. D. Fryzuk, B. Bosnich, *J. Am. Chem. Soc.* **1978**, *100*, 5491.
- [59] a) M. D. Fryzuk, B. Bosnich, *J. Am. Chem. Soc.* **1977**, *99*, 6262. b) M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.* **1988**, *110*, 629. c) Q. Fan, C. Yeung, A. S. C. Chan, *Tetrahedron: Asymmetry* **1997**, *8*, 4041. d) O. Bortolini, G. Fantin, M. Fogagnolo, P. P. Giovanni, A. Guerrini, A. Medici, *J. Org. Chem.* **1997**, *62*, 1854. e) R. Kuwano, M. Sawamura, J. Shirai, M. Takahashi, Y. Ito, *Tetrahedron Lett.* **1995**, 5239. f) V. Beghetto, U. Matteoli, A. Scrivanti, *Chem. Commun.* **2000**, 155.
- [60] a) M. J. Burk, J. E. Feaster, R. L. Harlow, *Organometallics* **1990**, *9*, 2653. b) M. J. Burk, J. E. Feaster, W. A. Nugent, R. L. Harlow, *J. Am. Chem. Soc.* **1993**, *115*, 10125.

- [61] T. Hayashi, S. Niizuma, T. Kamikawa, N. Suzuki, Y. Uozumi, *J. Am. Chem. Soc.* **1995**, *117*, 9101.
- [62] J. Yin, S. L. Buchwald, *J. Am. Chem. Soc.* **2000**, *122*, 12051.
- [63] a) G. Nishida, K. Noguchi, M. Hirano, K. Tanaka, *Angew. Chem., Int. Ed.* **2007**, *46*, 3951. b) B. Heller, A. Gutnov, C. Fischer, H.-J. Drexler, A. Spannenberg, D. Redkin, C. Sundermann, B. Sundermann, *Chem. Eur. J.* **2007**, *13*, 1117.
- [64] a) K. Rossen, P. J. Pye, A. Maliakal, R. P. Volante, *J. Org. Chem.* **1997**, *62*, 6462. b) P. J. Pye, K. Rossen, R. A. Reamer, N. N. Tsou, R. P. Volante, P. J. Reider, *J. Am. Chem. Soc.* **1997**, *119*, 6207.
- [65] a) V.V. Dunina, L. G. Kuz'mina, M. Y. Rubina, Y. K. Grishin, Y. A. Veits, E. I. Kazakova, *Tetrahedron: Asymmetry* **1999**, *10*, 1483. b) J. L. Bookham, W. McFarlane, *J. Chem. Soc., Chem. Commun.* **1993**, 1352. c) B. H. Aw, S. Selvaratnam, P. H. Leung, N. H. Rees, W. McFarlane, *Tetrahedron: Asymmetry* **1996**, *7*, 1753.
- [66] a) V. V. Dunina, E. B. Golovan, *Tetrahedron: Asymmetry* **1995**, *6*, 2747. b) S. B. Wild, *Coord. Chem. Rev.* **1997**, *166*, 291 and refs. therein. c) A. Miyashita, H. Takaya, T. Souchi, R. Noyori, *Tetrahedron* **1984**, *40*, 1245. d) R. Schmid, J. Foricher, M. Cereghetti, P. Schönholzer, *Helv. Chim. Acta* **1991**, *74*, 370. e) N. W. Alcock, J. M. Brown, D. I. Hulmes, *Tetrahedron: Asymmetry* **1993**, *4*, 743. f) H. Doucet, J. M. Brown, *Tetrahedron: Asymmetry* **1997**, *8*, 3775. g) F. Bienewald, L. Richard, F. Mercier, F. Mathey, *Tetrahedron: Asymmetry* **1999**, *10*, 4701.
- [67] a) A. Miyashita, H. Karino, J. Shinamura, T. Chiba, K. Nagano, H. Nohira, H. Takaya, *Chem. Lett.* **1989**, 1849. b) E. P. Kyba, S. P. Rines, *J. Org. Chem.* **1982**, *47*, 4800. c) S. Y. M. Chooi, P. H. Leung, C. C. Lim, K. F. Mok, G. H. Quek, K. Y.

- Sim, M. K. Tan, *Tetrahedron: Asymmetry* **1992**, 3, 529. d) V. V. Dunina, L. G. Kuz'mina, M. Y. Kazakova, Y. K. Grishin, Y. A. Veits, E. I. Kazakova, *Tetrahedron: Asymmetry* **1997**, 8, 2537. e) A. Böhm, D. Seebach, *Helv. Chim. Acta* **2000**, 83, 3262.
- [68] a) T. K. Hollis, L. E. Overman, *J. Organomet. Chem.* **1999**, 576, 290 and refs. therein. b) P. H. Leung, K. H. Ng, Y. Li, A. J. P. White, D. J. Williams, *J. Chem. Soc., Chem. Commun.* **1999**, 2435. c) N. Gül, J. H. Nelson, *Tetrahedron* **2000**, 56, 71. d) N. Gül, J. H. Nelson, *Organometallics* **2000**, 19, 91. e) P. A. Guggers, A. C. Willis, S. B. Wild, G. A. Heath, R. D. Webster, J. H. Nelson, *J. Organomet. Chem.* **2002**, 643-644, 136. f) R. Navarro, E. P. Urriolabeitia, C. Cativiela, M. D. Diaz-de-Villegas, M. P. López, E. Alonso, *J. Mol. Catal. A* **1996**, 105, 111. g) J. Dupont, C. S. Consorti, J. Spencer, *Chem. Rev.* **2005**, 105, 2527 and refs. therein. h) I. Omae, *Coord. Chem. Rev.* **2004**, 248, 995 and refs. therein. i) K. Takenaka, Y. Uozumi, *Org. Lett.* **2004**, 6, 1833.
- [69] a) S. Otsuka, A. Nakamura, T. Kano, K. Tani, *J. Am. Chem. Soc.* **1971**, 93, 4301. b) D. G. Allen, G. M. McLaughlin, G. B. Robertson, W. L. Steffen, G. Salem, S. B. Wild, *Inorg. Chem.* **1982**, 21, 1007.
- [70] P.-H. Leung, *Acc. Chem. Res.* **2004**, 37, 169.
- [71] a) S. Y. M. Chooi, T. S. A. Hor, P.-H. Leung, K. F. Mok, *Inorg. Chem.* **1992**, 31, 1494. b) S. Y. M. Chooi, M. K. Tan, P.-H. Leung, *Inorg. Chem.* **1994**, 33, 3096.
- [72] N. W. Alcock, D. I. Hulmes, J. M. Brown, *J. Chem. Soc., Chem. Commun.* **1995**, 395.
- [73] J. K.-P. Ng, G.-K. Tan, J. J. Vittal, P.-H. Leung, *Inorg. Chem.* **2003**, 42, 7674.

- [74] Y.-X. Jia, B.-B. Li, Y. Li, S. A. Pullarkat, K. Xu, H. Hirao, P.-H. Leung, *Organometallics* **2014**, *33*, 6053.
- [75] J. K.-P. Ng, Y. Li, G.-K. Tan, L.-L. Koh, J. J. Vittal, P.-H. Leung, *Inorg. Chem.* **2005**, *44*, 9874.
- [76] J. K.-P. Ng, S. Chen, Y. Li, G.-K. Tan, L.-L. Koh, P.-H. Leung, *Inorg. Chem.* **2007**, *46*, 5100.
- [77] J. K.-P. Ng, S. Chen, G.-K. Tan, P.-H. Leung, *Eur. J. Inorg. Chem.* **2007**, 3124.
- [78] Y. Ding, Y. Li, Y. Zhang, S. A. Pullarkat, P.-H. Leung, *Eur. J. Inorg. Chem.* **2008**, 1880.
- [79] Y. Ding, M. Chiang, S. A. Pullarkat, Y. Li, P.-H. Leung, *Organometallics* **2009**, *28*, 4358.
- [80] Y. Ding, Y. Li, S. A. Pullarkat, S. L. Yap, P.-H. Leung, *Eur. J. Inorg. Chem.* **2009**, 267.
- [81] Y. Li, S. Selvaratnam, J. J. Vittal, P. H. Leung, *Inorg. Chem.* **2003**, *42*, 3229.
- [82] Y. Li, *Ph. D. Dissertation: Design, Synthesis and Application of Chiral Ortho-Palladated 1-Arylalkylamine Complexes*; National University of Singapore, **2002**.
- [83] Y. Ding, Y. Zhang, Y. Li, S. A. Pullarkat, P. Andrews, P.-H. Leung, *Eur. J. Inorg. Chem.* **2010**, 4427.
- [84] S. Y. M. Chooi, J. D. Ranford, P. H. Leung, K. F. Mok, *Tetrahedron: Asymmetry* **1994**, *5*, 1805.
- [85] Y. Huang, S. A. Pullarkat, S. Teong, R. J. Chew, Y. Li, P.-H. Leung, *Organometallics* **2012**, *31*, 4871.

- [86] Y. Huang, R. J. Chew, S. A. Pullarkat, Y. Li, P.-H. Leung, *J. Org. Chem.* **2012**, *77*, 6849.
- [87] J. S. L. Yap, H. J. Chen, Y. Li, S. A. Pullarkat, P.-H. Leung, *Organometallics* **2014**, *33*, 930.
- [88] J. S. L. Yap, B. B. Li, J. Wong, Y. Li, S. A. Pullarkat, P.-H. Leung, *Dalton Trans.* **2014**, *43*, 5777.
- [89] Y. Li, K. H. Ng, S. Selvaratnam, G. K. Tan, J. J. Vittal, P. H. Leung, *Organometallics* **2003**, *22*, 834.
- [90] K. Gan, A. Sadeer, C. Xu, Y. Li, S. A. Pullarkat, *Organometallics* **2014**, *33*, 5074.
- [91] S. A. Pullarkat, P.-H. Leung, *Top. Organomet. Chem.* **2013**, *43*, 145 and refs. therein.
- [92] G. He, Y. Qin, K. F. Mok, P. H. Leung, *Chem. Commun.* **2000**, 167.
- [93] A. Breque, F. Mathey, *Synthesis* **1981**, 983.
- [94] a) *Phosphorus: The Carbon Copy* (Eds.: K. B. Dillion, F. Mathey), John Wiley & Sons, New York, **1998**. b) M. S. Holt, J. H. Nelson, P. Savignac, N. W. Alcock, *J. Am. Chem. Soc.* **1985**, *107*, 6396. c) W. L. Wilson, J. A. Rahn, N. W. Alcock, J. Fischer, J. H. Frederick, J. H. Nelson, *Inorg. Chem.* **1994**, *33*, 109.
- [95] a) V. V. Dunina, E. B. Golovan, N. S. Gulyukina, A. V. Buyevich, *Tetrahedron: Asymmetry* **1995**, *6*, 2731. b) B. H. Aw, T. S. A. Hor, S. Selvaratnam, K. F. Mok, A. J. P. White, D. J. Williams, N. H. Rees, W. McFarlane, P. H. Leung, *Inorg. Chem.* **1997**, *36*, 2138.
- [96] a) Y. Qin, H. Lang, J. J. Vittal, G.-K. Tan, S. Selvaratnam, A. J. P. White, D. J. Williams, P.-H. Leung, *Organometallics* **2003**, *22*, 3944. b) S.-K. Loh, G.-K. Tan, L. L. Koh, S. Selvaratnam, P.-H. Leung, *J. Organomet. Chem.* **2005**, *690*, 4933. c)

T.-W. Teo, S. Selvaratnam, J. J. Vittal, P.-H. Leung, *Inorg. Chim. Acta* **2003**, 352, 213.

[97] a) M. Ma, S. A. Pullarkat, Y. Li, P.-H. Leung, *Inorg. Chem.* **2007**, 46, 9488. b) M. Ma, S. A. Pullarkat, K. Chen, Y. Li, P.-H. Leung, *J. Organomet. Chem.* **2009**, 694, 1929. c) M. Ma, S. A. Pullarkat, Y. Li, P.-H. Leung, *J. Organomet. Chem.* **2008**, 693, 3289. d) M. Ma, S. A. Pullarkat, M. Yuan, N. Zhang, Y. Li, P.-H. Leung, *Organometallics* **2009**, 28, 4886. e) M. Ma, S. A. Pullarkat, Y. Li, P.-H. Leung, *Eur. J. Inorg. Chem.* **2010**, 1865. f) M. Ma, R. Lu, S. A. Pullarkat, W. Deng, P.-H. Leung, *Dalton Trans.* **2010**, 39, 5453. g) W. Yao, M. Ma, W. Wang, J. Cheng, L. Xu, S. A. Pullarkat, P.-H. Leung, *Tetrahedron: Asymmetry* **2014**, 25, 1100. h) M. Ma, Z. Yu, L. Zhu, S. A. Pullarkat, P.-H. Leung, *J. Organomet. Chem.* **2014**, 756, 34.

[98] a) W.-C. Yeo, J. J. Vittal, A. J. P. White, D. J. Williams, P.-H. Leung, *Organometallics* **2001**, 20, 2167. b) Y. Qin, S. Selvaratnam, J. J. Vittal, P.-H. Leung, *Organometallics* **2002**, 21, 5301. c) S. A. Pullarkat, K.-W. Tan, M. Ma, G.-K. Tan, L. L. Koh, J. J. Vittal, P.-H. Leung, *J. Organomet. Chem.* **2006**, 691, 3083. d) S. A. Pullarkat, Y. L. Cheow, Y. Li, P.-H. Leung, *Eur. J. Inorg. Chem.* **2009**, 2375. e) M. Yuan, S. A. Pullarkat, C. H. Yeong, Y. Li, D. Krishnan, P.-H. Leung, *Dalton Trans.* **2009**, 3668. f) F. Liu, S. A. Pullarkat, K.-W. Tan, Y. Li, P.-H. Leung, *Organometallics* **2009**, 28, 6254. g) F. Liu, S. A. Pullarkat, K.-W. Tan, Y. Li, P.-H. Leung, *Inorg. Chem.* **2009**, 48, 11394. h) W.-C. Yeo, J. J. Vittal, L. L. Koh, G.-K. Tan, P.-H. Leung, *Organometallics* **2004**, 23, 3474. i) K.-W. Tan, F. Liu, Y. Li, G.-K. Tan, P.-H. Leung, *J. Organomet. Chem.* **2006**, 691, 4753. j) W.-C. Yeo, S. Chen, G.-K. Tan, P.-H. Leung, *J. Organomet. Chem.* **2007**, 692, 2539.

- [99] *Hydrofunctionalization* (Eds.: V. P. Ananikov, M. Tanaka), Springer-Verlag, Berlin, **2013**.
- [100] X. Liu, K. F. Mok, P.-H. Leung, *Organometallics* **2001**, *20*, 3918.
- [101] a) V. K. Farina, B. Krishnan, *J. Am. Chem. Soc.* **1991**, *113*, 9585. b) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem., Int. Ed.* **2005**, *44*, 4442. c) K. C. Y. Lau, P. Chiu, *Tetrahedron Lett.* **2007**, *48*, 1813.
- [102] R. A. Baber, S. Collard, M. Hooper, A. G. Orpen, P. G. Pringle, M. J. Wilkinson, R. L. Wingad, *Dalton Trans.* **2005**, 1491.
- [103] a) C. R. Johnson, M. P. Braun, *J. Am. Chem. Soc.* **1993**, *115*, 11014. b) R. B. Bedford, C. S. J. Cazin, S. J. Coles, T. Gelbrich, M. B. Hursthouse, V. J. M. Scordia, *Dalton Trans.* **2003**, 3350.
- [104] L. A. van der Veen, P. K. Keeven, P. C. Kamer, P. W. N. M. van Leeuwen, *Chem. Commun.* **2000**, 333.
- [105] S. Ceccarelli, U. Piarulli, C. Gennari, *J. Org. Chem.* **2000**, *65*, 6254.
- [106] P. Cao, C.-Y. Li, Y.-B. Kang, Z. Xie, X.-L. Sun, Y. Tang, *J. Org. Chem.* **2007**, *72*, 6628.
- [107] For an example of As-H addition to unsaturated carbon-carbon bonds, see: R. B. King, P. N. Kapoor, *J. Am. Chem. Soc.* **1971**, *93*, 4158.
- [108] a) M. L. Bungabong, K. W. Tan, Y. Li, S. V. Selvaratnam, K. G. Dongol, P.-H. Leung, *Inorg. Chem.* **2007**, *46*, 4733. b) F. Liu, S. A. Pullarkat, Y. Li, S. Chen, P.-H. Leung, *Eur. J. Inorg. Chem.* **2009**, 4134. c) Y. L. Cheow, S. A. Pullarkat, Y. Li, P.-H. Leung, *J. Organomet. Chem.* **2012**, *696*, 4215.
- [109] For transition metal-promoted AHP reactions, see: a) W.-C. Yeo, S.-Y. Tee, H.-B. Tan, G.-K. Tan, L. L. Koh, P.-H. Leung, *Inorg. Chem.* **2004**, *43*, 8102. b) W.-C.

Yeo, L. Tang, B. Yan, S.-Y. Tee, L. L. Koh, G.-K. Tan, P.-H. Leung, *Organometallics* **2005**, *24*, 5581. c) S. A. Pullarkat, D. Yi, Y. Li, G.-K. Tan, P.-H. Leung, *Inorg. Chem.* **2006**, *45*, 7455. d) L. Tang, Y. Zhang, L. Ding, Y. Li, K.-F. Mok, W.-C. Yeo, P.-H. Leung, *Tetrahedron Lett.* **2007**, *48*, 33. e) Y. Zhang, L. Tang, Y. Ding, J.-H. Chua, Y. Li, M. Yuan, P.-H. Leung, *Tetrahedron Lett.* **2008**, *49*, 1762. f) M. Yuan, S. A. Pullarkat, M. Ma, Y. Zhang, Y. Huang, Y. Li, A. Goel, P.-H. Leung, *Organometallics* **2009**, *28*, 780. g) Y. Zhang, S. A. Pullarkat, Y. Li, P.-H. Leung, *Inorg. Chem.* **2009**, *48*, 5535. h) F. Liu, S. A. Pullarkat, Y. Li, S. Chen, M. Yuan, Z. Y. Lee, P.-H. Leung, *Organometallics* **2009**, *28*, 3941. i) Y. Zhang, L. Tang, S. A. Pullarkat, F. Liu, Y. Li, P.-H. Leung, *J. Organomet. Chem.* **2009**, *694*, 3500. j) M. Yuan, N. Zhang, S. A. Pullarkat, Y. Li, F. Liu, P.-T. Pham, P.-H. Leung, *Inorg. Chem.* **2010**, *49*, 989. k) Y. Huang, S. A. Pullarkat, M. Yuan, Y. Ding, Y. Li, P.-H. Leung, *Organometallics* **2010**, *29*, 536. l) S. Chen, J. K.-P. Ng, S. A. Pullarkat, F. Liu, Y. Li, P.-H. Leung, *Organometallics* **2010**, *29*, 3374. m) M. Yuan, S. A. Pullarkat, Y. Li, Z.-Y. Lee, P.-H. Leung, *Organometallics* **2010**, *29*, 3582. n) M. Yuan, S. A. Pullarkat, Y. Li, P.-H. Leung, *J. Organomet. Chem.* **2011**, *696*, 905. o) K. Chen, S. A. Pullarkat, M. Ma, Y. Li, P.-H. Leung, *Dalton Trans.* **2012**, *41*, 5391.

[110] a) S. Chikkali, D. Gudat, *Eur. J. Inorg. Chem.* **2006**, 3005. b) *The Chemistry of Organo-Phosphorus Compounds, Vol. 1* (Ed.: F. R. Hartley), Wiley, New York, **1992**. c) M. M. Rauhut, I. Hechenbleikner, H. A. Currier, R. C. Scjaefer, V. P. Wystrach, *J. Am. Chem. Soc.* **1959**, *81*, 1103. d) H. O. Berger, H. Noeth, *J. Organomet. Chem.* **1983**, *250*, 33.

[111] a) D. S. Glueck, *Synlett* **2007**, *17*, 2627. b) P. G. Pringle, M. B. Smith, *J. Chem. Soc., Chem. Commun.* **1990**, 1701. c) M. O. Shulyupin, M. A. Kazankova, I. P.

Beletskaya, *Org. Lett.* **2002**, *4*, 761. d) D. S. Glueck, *Dalton Trans.* **2008**, 5276. e) D. S. Glueck, *Coord. Chem. Rev.* **2008**, *252*, 2171.

[112] For transition metal-catalyzed AHP reactions, see: a) Y. Huang, S. A. Pullarkat, Y. Li, P.-H. Leung, *Chem. Commun.* **2010**, *46*, 6950. b) Y. Huang, S. A. Pullarkat, Y. Li, P.-H. Leung, *Inorg. Chem.* **2012**, *51*, 2533. c) Y. Huang, R. J. Chew, Y. Li, S. A. Pullarkat, P.-H. Leung, *Org. Lett.* **2011**, *13*, 5862. d) C. Xu, G. J. H. Kennard, F. Hennesdorf, Y. Li, S. A. Pullarkat, P.-H. Leung, *Organometallics* **2012**, *31*, 3022. e) Y. Huang, R. J. Chew, S. A. Pullarkat, Y. Li, P.-H. Leung, *J. Org. Chem.* **2012**, *77*, 6849. f) R. J. Chew, Y. Huang, Y. Li, S. A. Pullarkat, P.-H. Leung, *Adv. Synth. Catal.* **2013**, *355*, 1403. g) Y. Huang, Y. Li, P.-H. Leung, T. Hayashi, *J. Am. Chem. Soc.* **2014**, *136*, 4865. h) R. J. Chew, Y. Lu, Y.-X. Jia, B.-B. Li, E. H. Y. Wong, R. Goh, Y. Li, Y. Huang, S. A. Pullarkat, P.-H. Leung, *Chem. Eur. J.* **2014**, *20*, 14514. i) R. J. Chew, K. Y. Teo, Y. Huang, B.-B. Li, Y. Li, S. A. Pullarkat, P.-H. Leung, *Chem. Commun.* **2014**, *50*, 8768. j) R. J. Chew, X.-R. Li, Y. Li, S. A. Pullarkat, P.-H. Leung, *Chem. Eur. J.* **2015**, *21*, 4800.

[113] J.-J. Feng, X.-F. Chen, M. Shi, W.-L. Duan, *J. Am. Chem. Soc.* **2010**, *132*, 5562.

[114] a) C. J. Moulton, B. L. Shaw, *J. Chem. Soc., Dalton Trans.* **1976**, 1020. b) G. van Koten, K. J. Timmer, G. Noltes, A. L. Spek, *J. Chem. Soc., Chem Commun.* **1978**, 250.

[115] For selected reviews, see: a) M. H. P. Rietveld, D. M. Grove, G. van Koten, *New J. Chem.* **1997**, *21*, 751. b) M. Albrecht, G. van Koten, *Angew. Chem., Int. Ed.* **2001**, *40*, 3750. c) M. E. van der Boom, D. Milstein, *Chem. Rev.* **2003**, *103*, 1759. d) D. Morales-Morales, *Mini-Rev. Org. Chem.* **2008**, *5*, 141. e) N. Selander, K. J. Szabó, *Dalton Trans.* **2009**, 6267. f) N. Selander, K. J. Szabó, *Chem. Rev.* **2011**, *111*, 2048. g) *Phosphorus(III) Ligands in Homogeneous Catalysis: Design and*

Synthesis, (Eds.: P. C. J. Kamer, P. W. N. M. van Leeuwen), Wiley-VCH: Weinheim, Germany, **2012**. h) *Organometallic Pincer Chemistry, Topics in Organometallic Chemistry*, (Eds.: G. van Koten, D. Milstein), Springer-Verlag, Berlin, Heidelberg, **2013**. i) D. Morales-Morales, R. E. Cramer, C. M. Jensen, *J. Organomet. Chem.* **2002**, 654, 44. j) S. Medici, M. Gagliardo, S. B. Williams, P. A. Chase, S. Gladiali, M. Lutz, A. L. Spek, G. P. M. van Klink, G. van Koten, *Helv. Chim. Acta*, **2005**, 88, 694.

[116] For selected examples, see: a) M. Ohff, A. Ohff, M. E. van der Boom, D. Milstein, *J. Am. Chem. Soc.* **1997**, 119, 11687. b) M. Beller, A. Zapf, *Synlett* **1998**, 792. c) D. Morales-Morales, R. Redón, C. Yung, C. M. Jensen, *Chem. Commun.* **2000**, 1619. d) F. Miyazaki, K. Yamaguchi, M. Shibasaki, *Tetrahedron Lett.* **1999**, 40, 7379. e) V. Leigh, W. Ghattas, H. Mueller-Bunz, M. Albrecht, *J. Organomet. Chem.* **2014**, 771, 33.

[117] For selected examples, see: a) B. Inés, R. SanMartin, M. J. Moure, E. Domínguez, *Adv. Synth. Catal.* **2009**, 351, 2124. b) J. L. Bolliger, O. Blacque, C. M. Frech, *Angew. Chem., Int. Ed.* **2007**, 46, 6514. c) M. A. Solano-Prado, F. Estudiante-Negrete, D. Morales-Morales, *Polyhedron* **2010**, 29, 592. d) J. Kjellgren, J. Aydin, O. A. Wallner, I. V. Saltanova, K. J. Szabó, *Chem. Eur. J.* **2005**, 11, 5260. e) D. Olsson, O. F. Wendt, *J. Organomet. Chem.* **2009**, 694, 3112. f) L.-Y. Wu, X.-Q. Hao, Y.-X. Xu, M.-Q. Jia, Y.-N. Wang, J.-F. Gong, M.-P. Song, *Organometallics* **2009**, 28, 3369.

[118] For selected examples, see: a) J. L. Bolliger, C. M. Frech, *Adv. Synth. Catal.* **2009**, 351, 891. b) S. Gu, W. Chen, *Organometallics* **2009**, 28, 909. c) B. Inés, R. SanMartin, F. Churruca, E. Domínguez, M. K. Urtiaga, M. I. Arriortua, *Organometallics* **2008**, 27, 2833. d) B.-S. Zhang, C. Wang, J.-F. Gong, *J.*

- Organomet. Chem.* **2009**, 694, 2555. e) F. Churrua, R. SanMartin, I. Tellitu, E. Domínguez, *Synlett* **2005**, 3116.
- [119] D. Olsson, P. Nilsson, M. El Masnaouy, O. F. Wendt, *Dalton Trans.* **2005**, 1924.
- [120] For selected examples, see: a) J. Liu, H. Wang, H. Zhang, X. Wu, H. Zhang, Y. Deng, Z. Yang, A. Lei, *Chem. Eur. J.* **2009**, 15, 4437. b) H. Wang, J. Liu, Y. Deng, T. Min, G. Yu, X. Wu, Z. Yang, A. Lei, *Chem. Eur. J.* **2009**, 15, 1499.
- [121] For selected examples, see: a) M. Gupta, C. Hagen, R. J. Flesher, W. C. Kaska, C. M. Jensen, *Chem. Commun.* **1996**, 2083. b) K. Wang, M. E. Goldman, T. J. Emge, A. S. Goldman, *J. Organomet. Chem.* **1996**, 518, 55. c) W. Xu, G. P. Rosini, M. Gupta, C. M. Jensen, W. C. Kaska, K. Krogh-Jespersen, A. S. Goldman, *Chem. Commun.* **1997**, 2273. d) X. Jia, L. Zhang, C. Qin, X. Leng, Z. Huang, *Chem. Commun.* **2014**, 50, 11056.
- [122] For selected examples, see: a) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, 93, 2207. b) R. Bloch, *Chem. Rev.* **1998**, 98, 1407. c) S. E. Denmark, J. Fu, *Chem. Rev.* **2003**, 103, 2763. d) H. Nakamura, H. Iwama, Y. Yamamoto, *J. Am. Chem. Soc.* **1996**, 118, 6641. e) R. A. Fernandes, A. Stimac, Y. Yamamoto, *J. Am. Chem. Soc.* **2003**, 125, 14133. f) N. Solin, O. A. Wallner, K. J. Szabó, *Org. Lett.* **2005**, 7, 689. g) O. A. Wallner, K. J. Szabó, *Chem. Eur. J.* **2006**, 12, 6976. h) O. Piechaczyk, T. Cantat, N. Mézailles, P. Le Floch, *J. Org. Chem.* **2007**, 72, 4228.
- [123] For selected examples, see: a) S. Sebelius, V. J. Olsson, K. J. Szabó, *J. Am. Chem. Soc.* **2005**, 127, 10478. b) V. J. Olsson, S. Sebelius, N. Selander, K. J. Szabó, *J. Am. Chem. Soc.* **2006**, 128, 4588. c) N. Selander, B. Willy, K. J. Szabó, *Angew. Chem., Int. Ed.* **2010**, 49, 4051.
- [124] a) P. Dani, T. Karlen, R. A. Gossage, S. Gladiali, G. van Koten, *Angew. Chem., Int. Ed.* **2000**, 39, 743. b) D. F. Brayton, P. R. Beaumont, E. Y. Fukushima, H. T. Sartain, D. Morales-Morales, C. M. Jensen, *Organometallics* **2014**, 33, 5198.

- [125] For selected examples, see: a) F. Gorla, A. Togni, L. M. Venanzi, A. Albinati, F. Lianza, *Organometallics* **1994**, *13*, 1607. b) M. A. Stark, C. J. Richards, *Tetrahedron Lett.* **1997**, *38*, 5881. c) J. M. Longmire, X. Zhang, M. Shang, *Organometallics* **1998**, *17*, 4374. d) R. Giménez, T. Swager, *J. Mol. Catal. A: Chem.* **2001**, *166*, 265. e) M. S. Yoon, R. Ramesh, J. Kim, D. Ryu, K. H. Ahn, *J. Organomet. Chem.* **2006**, *691*, 5927. f) S. Gosiewska, S. M. Herreras, M. Lutz, A. L. Spek, R. W. A. Havenith, G. P. M. van Klink, G. van Koten, R. J. M. Klein Gebbink, *Organometallics* **2008**, *27*, 2549.
- [126] a) M. A. Stark, G. Jones, C. J. Richards, *Organometallics* **2000**, *19*, 1282. b) K. Mitsudo, T. Imura, T. Yamaguchi, H. Tanaka, *Tetrahedron Lett.* **2008**, *49*, 7287.
- [127] a) G. van Koten, *Top. Organomet. Chem.* **2013**, *40*, 1. b) P. Steenwinkel, R. A. Gossage, G. van Koten, *Chem. Eur. J.* **1998**, *4*, 759.
- [128] a) P. L. Alsters, P. J. Baesjou, M. D. Janssen, H. Kooijman, A. Sicherer-Roetman, A. L. Spek, G. van Koten, *Organometallics* **1992**, *11*, 4124. b) J. Aydin, K. S. Kumar, L. Eriksson, K. J. Szabó, *Adv. Synth. Catal.* **2007**, *349*, 2585.
- [129] a) O. A. Wallner, V. J. Olsson, L. Eriksson, K. J. Szabó, *Inorg. Chim. Acta* **2006**, *359*, 1767. b) J. Aydin, K. S. Kumar, M. J. Sayah, O. A. Wallner, K. J. Szabó, *J. Org. Chem.* **2007**, *72*, 4689. c) J. Aydin, C. S. Conrad, K. J. Szabó, *Org. Lett.* **2008**, *10*, 5175.
- [130] For examples, see: a) W. J. Sommer, K. Yu, J. S. Sears, Y. Ji, X. Zheng, R. J. Davis, C. D. Sherrill, C. W. Jones, M. Weck, *Organometallics* **2005**, *24*, 4351. b) R. B. Bedford, S. M. Draper, P. N. Scully, S. L. Welch, *New J. Chem.* **2000**, *24*, 745. c) M. Gagliardo, N. Selander, N. C. Mehendale, G. van Koten, R. J. M. Klein Gebbink, K. J. Szabó, *Chem. Eur. J.* **2008**, *14*, 4800.
- [131] a) J. S. Fossey, C. J. Richards, in *The Chemistry of Pincer Compounds* (Eds.: D. Morales-Morales, C. M. Jensen), Elsevier: Amsterdam, **2007**, 45. b) J. S. Fossey,

- C. J. Richards, *Organometallics* **2002**, *21*, 5259. c) J. S. Fossey, C. J. Richards, *Tetrahedron Lett.* **2003**, *44*, 8773.
- [132] R. A. Baber, R. B. Bedford, M. Betham, M. E. Blake, S. J. Coles, M. F. Haddow, M. B. Hursthouse, A. G. Orpen, L. T. Pilarski, P. G. Pringle, R. L. Wingad, *Chem. Commun.* **2006**, 3880.
- [133] For selected examples, see: a) M. Albrecht, P. Dani, M. Lutz, A. L. Spek, G. van Koten, *J. Am. Chem. Soc.* **2000**, *122*, 11822. b) A. D. Ryabov, A. K. Yatsimirsky, *Inorg. Chem.* **1984**, *23*, 789. c) A. D. Ryabov, *Inorg. Chem.* **1987**, *26*, 1252. d) M. Hejda, L. Dostal, R. Jambor, A. Ruzicka, R. Jirasko, J. Holecek, *Eur. J. Inorg. Chem.* **2012**, 2578. e) P. A. Shaw, J. M. Phillips, C. P. Newman, G. J. Clarkson, J. P. Rourke, *Chem. Commun.* **2015**, DOI: 10.1039/C5CC02355F. f) P. Dani, M. Albrecht, G. P. M. van Klink, G. van Koten, *Organometallics* **2000**, *19*, 4468.
- [134] A. C. Cope, E. C. Friedrich, *J. Am. Chem. Soc.* **1968**, *90*, 909.
- [135] D. M. Grove, G. van Koten, J. N. Louwen, J. G. Noltes, A. L. Spek, H. J. C. Ubbels, *J. Am. Chem. Soc.* **1982**, *104*, 1982.
- [136] B. Soro, S. Stoccoro, G. Minghetti, A. Zucca, M. A. Cinellu, M. Manassero, S. Gladiali, *Inorg. Chim. Acta* **2006**, *359*, 1879.
- [137] J.-P. Sutter, S. L. James, P. Steenwinkel, T. Karlen, D. M. Grove, N. Veldman, W. J. J. Smeets, A. L. Spek, G. van Koten, *Organometallics* **1996**, *15*, 941.
- [138] For selected examples, see: a) K. Takenaka, Y. Uozumi, *Org. Lett.* **2004**, *6*, 1833. b) K. Takenaka, M. Minakawa, Y. Uozumi, *J. Am. Chem. Soc.* **2005**, *127*, 12273. c) T. Kimura, Y. Uozumi, *Organometallics* **2006**, *25*, 4883. d) T. Kimura, Y. Uozumi, *Organometallics* **2008**, *27*, 5159.
- [139] J. L. Bolliger, O. Blacque, C. M. Frech, *Angew. Chem., Int. Ed.* **2007**, *46*, 6514.
- [140] a) *The Chemistry of Pincer Compounds* (Eds.: D. Morales-Morales, C. M. Jensen), Elsevier: Amsterdam, **2007**. b) H. Nishiyama, *Chem. Soc. Rev.* **2007**, *36*, 1133.

- [141] For selected examples, see: a) J. S. Fossey, C. J. Richards, *J. Organomet. Chem.* **2004**, 689, 3056. b) J. Ito, T. Shiomi, H. Nishiyama, *Adv. Synth. Catal.* **2006**, 348, 1235. c) Y. Motoyama, N. Makihara, Y. Mikami, K. Aoki, H. Nishiyama, *Chem. Lett.* **1997**, 26, 951. d) Y. Motoyama, H. Kawakami, K. Shimozono, K. Aoki, H. Nishiyama, *Organometallics* **2002**, 21, 3408. e) S. E. Denmark, R. A. Stavenger, A.-M. Faucher, J. P. Edwards, *J. Org. Chem.* **1997**, 62, 3375. f) Y. Motoyama, Y. Mikami, H. Kawakami, K. Aoki, H. Nishiyama, *Organometallics* **1999**, 18, 3584. g) J. S. Fossey, G. Jones, M. Motevalli, H. V. Nguyen, C. J. Richards, M. A. Stark, H. V. Taylor, *Tetrahedron: Asymmetry* **2004**, 15, 2067. h) Y. Tsuchiya, Y. Kanazawa, T. Shiomi, K. Kobayashi, H. Nishiyama, *Synlett* **2004**, 2493. i) Y. Kanazawa, Y. Tsuchiya, K. Kobayashi, T. Shiomi, J. Itoh, M. Kikuchi, Y. Yamamoto, H. Nishiyama, *Chem. Eur. J.* **2006**, 12, 63. j) Y. Motoyama, H. Narusawa, H. Nishiyama, *Chem. Commun.* **1999**, 131. k) Y. Motoyama, M. Okano, H. Narusawa, N. Makihara, K. Aoki, H. Nishiyama, *Organometallics* **2001**, 20, 1580. l) Y. Motoyama, Y. Koga, K. Kobayashi, K. Aoki, H. Nishiyama, *Chem. Eur. J.* **2002**, 8, 2968. m) A. Weissberg, M. Portnoy, *Chem. Commun.* **2003**, 1538. n) M. Gerisch, J. R. Krumper, R. G. Bergman, T. D. Tilley, *J. Am. Chem. Soc.* **2001**, 123, 5818. o) M. Gerisch, J. R. Krumper, R. G. Bergman, T. D. Tilley, *Organometallics* **2003**, 22, 47.
- [142] For selected examples, see: a) S. Gosiewska, M. Huis in't Veld, J. J. M. de Pater, P. C. A. Bruijninx, M. Lutz, A. L. Spek, G. van Koten, R. J. M. Klein Gebbink, *Tetrahedron: Asymmetry* **2006**, 17, 674. b) L. A. van de Kuil, Y. S. J. Veldhuizen, D. M. Grove, J. W. Zwikker, L. W. Jenneskens, W. Drenth, W. J. J. Smeets, A. L. Spek, G. van Koten, *Recl. Trav. Chim. Pays-Bas.* **1994**, 113, 267.
- [143] For selected examples, see: a) T. G. Gant, A. I. Meyers, *Tetrahedron* **1994**, 50, 2297. b) M. N. Holerca, V. Percec, *Eur. J. Org. Chem.* **2000**, 2257. c) D. A. Evans,

- G. S. Peterson, J. S. Johnson, D. M. Barnes, K. R. Campos, K. A. Woerpel, *J. Org. Chem.* **1998**, *63*, 4541. d) H. Vorbrüggen, K. Krolikiewicz, *Tetrahedron* **1993**, *49*, 9353. e) K. Schwekendiek, F. Glorius, *Synthesis* **2006**, 2996. f) S. Sayama, *Synlett* **2006**, 1479. g) S. Takahashi, H. Togo, *Synthesis* **2009**, 2329. h) M. Ishihara, H. Togo, *Tetrahedron* **2007**, *63*, 1474. i) H. Witte, W. Seeliger, *Angew. Chem., Int. Ed.* **1972**, *11*, 287. j) H. Witte, W. Seeliger, *Liebigs Ann. Chem.* **1974**, 996. k) C. Bolm, K. Weickhardt, M. Zehnder, T. Ranff, *Chem. Ber.* **1991**, *124*, 1173.
- [144] a) C. Börner, M. R. Dennis, E. Sinn, S. Woodward, *Eur. J. Org. Chem.* **2001**, 2435. b) P. J. Cox, W. Wang, V. Snieckus, *Tetrahedron Lett.* **1992**, *33*, 2253.
- [145] D. J. Cram, R. C. Helgeson, S. C. Peacock, L. J. Kaplan, L. A. Domeier, P. Moreau, K. Koga, J. M. Mayer, Y. Chao, M. G. Siegel, D. H. Hoffman, G. D. Y. Sogah, *J. Org. Chem.* **1978**, *43*, 1930.
- [146] a) D. Seebach, A. K. Beck, A. Heckel, *Angew. Chem., Int. Ed.* **2001**, *40*, 92. b) D. Seebach, A. K. Beck, R. Imwinkelried, S. Roggo, A. Wonnacott, *Helv. Chim. Acta* **1987**, *70*, 954. c) A. K. Beck, B. Bastani, D. A. Plattner, W. Petter, D. Seebach, H. Braunschweiger, P. Gysi, L. La Vecchia, *Chimia* **1991**, *45*, 238. d) A. K. Beck, P. Gysi, L. La Vecchia, D. Seebach, *Org. Synth.* **1999**, *76*, 12. e) D. Seebach, R. Dahinden, R. E. Marti, A. K. Beck, D. A. Plattner, F. N. M. Kühnle, *J. Org. Chem.* **1995**, *60*, 1788.
- [147] a) B. S. Williams, P. Dani, M. Lutz, A. L. Spek, G. van Koten, *Helv. Chim. Acta* **2001**, *84*, 3519. b) D. R. Evans, M. Huang, W. M. Seganish, J. C. Fettingier, T. L. Williams, *Organometallics* **2002**, *21*, 893.
- [148] a) J. M. Longmire, X. Zhang, *Tetrahedron Lett.* **1997**, *38*, 1725. b) J. G. Donkervoot, J. L. Vicario, J. T. B. H. Jastrzebski, W. J. J. Smeets, A. L. Spek, G. van Koten, *J. Organomet. Chem.* **1998**, *551*, 1. c) M. Albrecht, B. M. Kocks, A. L. Spek, G. van Koten, *J. Organomet. Chem.* **2001**, *624*, 271. d) E. Diez-Barra, J.

- Guerra, I. Lopez-Solera, S. Merino, J. Rodrigues-Lopez, P. Sanchez-Verdu, J. Tejada, *Organometallics* **2003**, 22, 541.
- [149] a) M. Albrecht, G. Rodríguez, J. Schoenmaker, G. van Koten, *Org. Lett.* **2000**, 2, 3461. b) G. Guillena, G. Rodriguez, G. van Koten, *Tetrahedron Lett.* **2002**, 43, 3895.
- [150] F. Gorla, L. M. Venanzi, A. Albinati, *Organometallics* **1994**, 13, 43.
- [151] a) J. Huang, M.-X. Zhao, W.-L. Duan, *Tetrahedron Lett.* **2014**, 55, 629. b) J. Lu, J. Ye, W.-L. Duan, *Org. Lett.* **2013**, 15, 5016. c) B. Ding, Z. Zhang, Y. Xu, Y. Liu, M. Sugiya, T. Imamoto, W. Zhang, *Org. Lett.* **2013**, 15, 5476. d) X.-Y. Yang, J. H. Gan, Y. Li, S. A. Pullarkat, P.-H. Leung, *Dalton Trans.* **2015**, 44, 1258. e) X.-Q. Hao, Y.-W. Zhao, J.-J. Yang, J.-L. Niu, J.-F. Gong, M.-P. Song, *Organometallics* **2014**, 33, 1801. f) M.-J. Yang, Y.-J. Liu, J.-F. Gong, M.-P. Song, *Organometallics* **2011**, 30, 3793. g) D. Du, Z.-Q. Lin, J.-Z. Lu, C. Li, W.-L. Duan, *Asian J. Org. Chem.* **2013**, 2, 392. h) J.-J. Feng, M. Huang, Z.-Q. Lin, W.-L. Duan, *Adv. Synth. Catal.* **2012**, 354, 3122.
- [152] Cambridge Crystallographic Data Base, www.ccdc.cam.ac.uk.
- [153] a) Y. Motoyama, K. Shimozono, H. Nishiyama, *Inorg. Chim. Acta* **2006**, 359, 1725. b) S. Bonnet, J. Li, M. A. Siegler, L. S. von Chrzanowski, A. L. Spek, G. van Koten, R. J. M. Klein Gebbink, *Chem. Eur. J.* **2009**, 15, 3340. c) J.-L. Niu, Q.-T. Chen, X.-Q. Hao, Q.-X. Zhao, J.-F. Gong, M.-P. Song, *Organometallics* **2010**, 29, 2148. d) B. S. Zhang, W. Wang, D.-D. Shao, X.-Q. Hao, J.-F. Gong, M.-P. Song, *Organometallics* **2010**, 29, 2579. e) B.-S. Zhang, C. Wang, J.-F. Gong, M.-P. Song, *J. Organomet. Chem.* **2009**, 694, 2555. f) X.-Q. Hao, J.-J. Huang, T. Wang, J. Lv, J.-F. Gong, M.-P. Song, *J. Org. Chem.* **2014**, 79, 9512.

- [154] a) C. S. Slone, D. A. Weinberger, C. A. Mirkin, *Prog. Inorg. Chem.* **1999**, *48*, 233.
 b) A. Fleckhaus, A. H. Mousa, N. S. Lawal, N. K. Kazemifar, O. F. Wendt, *Organometallics* **2015**, DOI: 10.1021/om501231k.
- [155] a) I. Moreno, R. SanMartin, B. Ines, M. T. Herrero, E. Domínguez, *Curr. Org. Chem.* **2009**, *13*, 878. b) E. Poverenov, I. Efremenko, A. I. Frenkel, Y. Ben-David, L. J. W. Shimon, G. Leitun, L. Konstantinovski, J. M. L. Martin, D. Milstein, *Nature* **2008**, *455*, 1093. c) E. Poverenov, M. Gandelman, L. J. W. Shimon, H. Rozenberg, Y. Ben-David, D. Milstein, *Chem. Eur. J.* **2004**, *10*, 4673. d) J.-F. Gong, Y.-H. Zhang, M.-P. Song, C. Xu, *Organometallics* **2007**, *26*, 6487.
- [156] a) T. Nishikata, Y. Yamamoto, I. D. Gridnev, N. Miyaura, *Organometallics* **2005**, *24*, 5025. b) T. Nishikata, Y. Yamamoto, N. Miyaura, *Organometallics* **2004**, *23*, 4317.
- [157] a) S. Y. M. Chooi, S. Y. Siah, P.-H. Leung, K. F. Mok, *Inorg. Chem.* **1993**, *32*, 4812. b) S. Y. Siah, P.-H. Leung, K. F. Mok, M. G. B. Drew, *Tetrahedron: Asymmetry* **1996**, *7*, 357. c) P.-H. Leung, G. H. Quek, H. Lang, A. M. Liu, K. F. Mok, A. J. P. White, D. J. Williams, N. H. Rees, W. McFarlane, *J. Chem. Soc., Dalton Trans.* **1998**, *27*, 1639. d) P.-H. Leung, S. Y. Siah, A. J. P. White, D. J. Williams, *J. Chem. Soc., Dalton Trans.* **1998**, *27*, 893. e) P.-H. Leung, S. K. Loh, K. F. Mok, A. J. P. White, D. J. Williams, *J. Chem. Soc., Chem. Commun.* **1996**, *42*, 591. f) P.-H. Leung, G. He, H. Lang, A. Liu, S. K. Loh, S. Selvaratnam, K. F. Mok, A. J. P. White, D. J. Williams, *Tetrahedron* **2000**, *56*, 7. g) P.-H. Leung, S. K. Loh, J. J. Vittal, A. J. P. White, D. J. Williams, *J. Chem. Soc., Chem. Commun.* **1997**, *43*, 1987. h) P.-H. Leung, H. F. Lang, A. J. P. White, D. J. Williams, *Tetrahedron: Asymmetry* **1998**, *9*, 2961. i) S. K. Loh, K. F. Mok, P.-H. Leung, A. J. P. White, D. J. Williams, *Tetrahedron: Asymmetry* **1996**, *7*, 45.

- [158] a) T. W. Chapp, A. J. Schoenfeld, D. S. Glueck, *Organometallics* **2010**, 29, 2465.
 b) T. W. Chapp, D. S. Glueck, J. A. Golen, C. E. Moore, A. L. Rheingold, *Organometallics* **2010**, 29, 378.
- [159] J. Li, M. Siegler, M. Lutz, A. L. Spek, R. J. M. Klein Gebbink, G. van Koten, *Adv. Synth. Catal.* **2010**, 352, 2474.
- [160] D. M. Roddick, *Top. Organomet. Chem.* **2013**, 40, 49.
- [161] a) M. M. Rahman, H.-Y. Liu, K. Eriks, A. Prock, W. P. Giering, *Organometallics* **1989**, 8, 1. b) J. Ansell, M. Wills, *Chem. Soc. Rev.* **2002**, 31, 259.
- [162] P. H. Leung, J. W. L. Martin, S. B. Wild, *Inorg. Chem.* **1986**, 25, 3396.
- [163] a) J. Vicente, A. Arcas, D. Bautista, M. C. R. de Arellano, *J. Organomet. Chem.* **2002**, 663, 164. b) J. Vicente, A. Arcas, D. Bautista, *Organometallics* **1997**, 16, 2127.
- [164] M. Rubio, A. Suarez, R. D. Del, A. Galindo, E. Alvarez, A. Pizzano, *Organometallics* **2009**, 28, 547.
- [165] a) A. Poater, B. Cosenza, A. Correa, S. Giudice, F. Ragone, V. Scarano, L. Cavallo, *Eur. J. Inorg. Chem.* **2009**, 1759. b) H. Clavier, S. P. Nolan, *Chem. Commun.* **2010**, 46, 841.
- [166] J. Aydin, A. Ryden, K. J. Szabó, *Tetrahedron: Asymmetry* **2008**, 19, 1867.
- [167] D. Belmessieri, L. C. Morrill, C. Simal, A. M. Z. Slawin, A. D. Smith, *J. Am. Chem. Soc.* **2011**, 133, 2714.
- [168] D. C. Pinto, A. M. Silva, J. A. Cavaleiro, J. Elguero, *Eur. J. Org. Chem.* **2003**, 747.
- [169] H. Parvenn, F. Hayat, S. Mukhtar, A. Salahuddin, A. Khan, F. Islam, A. Azam, *Eur. J. Med. Chem.* **2011**, 46, 4669.
- [170] a) C. E. Holloway, M. Melnik, *Rev. Inorg. Chem.* **1995**, 15, 147. b) M. Melnik, M. Kabešová, Ľ. Macášková, C. E. Holloway, *J. Coord. Chem.* **1998**, 45, 31. c) M. Dunaj-Jurčo, G. Ondrejovič, M. Melnik, J. Garaj, *Coord. Chem. Rev.* **1988**, 83, 1.

- [171] For examples, see: a) R. P. Rucker, A. M. Whittaker, H. Dang, G. Lalic, *J. Am. Chem. Soc.* **2012**, *134*, 6571. b) N. Rodríguez, L. J. Goossen, *Chem. Soc. Rev.* **2011**, *40*, 5030.
- [172] For examples, see: a) F. Ullmann, *Ber. Dtsch. Chem. Ges.* **1904**, *37*, 853. b) P. E. Fanta, *Chem. Rev.* **1964**, *64*, 613. c) E. Sperotto, G. P. M. van Klink, G. van Koten, J. G. de Vries, *Dalton Trans.* **2010**, *39*, 10338.
- [173] For examples, see: a) R. P. Houser, J. V. G. Young, W. B. Tolman, *J. Am. Chem. Soc.* **1996**, *118*, 2101. b) X. Xue, X.-S. Wang, R.-G. Xiong, X.-Z. You, B. F. Abraham, C.-M. Che, H.-X. Ju, *Angew. Chem., Int. Ed.* **2002**, *41*, 2944. c) M. R. Churchill, S. A. Bezman, J. A. Osborn, J. Wormald, *Inorg. Chem.* **1972**, *11*, 1819. d) X. Wang, P. Liu, H. Lin, C. Xu, J. Zhang, G. Liu, *Inorg. Chem. Commun.* **2013**, *30*, 79.
- [174] a) J. A. Bertrand, *Inorg. Chem.* **1967**, *6*, 495. b) J. A. Bertrand, J. A. Kelley, *J. Am. Chem. Soc.* **1966**, *88*, 4746. c) T. H. Lemmen, K. Folting, J. C. Huffman, K. G. Caulton, *J. Am. Chem. Soc.* **1985**, *107*, 7774. d) A. Presta, M. J. Stillman, *Chirality* **1994**, *6*, 521. e) H. Oshio, Y. Saito, T. Ito, *Angew. Chem.* **1997**, *109*, 2789. f) M. C. Mimmi, M. Gullotti, L. Santagostini, G. Battaini, E. Monzani, R. Pagliarin, G. Zoppellaro, L. Casella, *Dalton Trans.* **2004**, 2192. g) W.-F. Fu, X. Gan, C.-M. Che, Q.-Y. Cao, Z.-Y. Zhou, N. N.-Y. Zhu, *Chem. Eur. J.* **2004**, *10*, 2228. h) T. Kawamoto, M. Nishiwaki, M. Nishijima, K. Nozaki, A. Igashira-Kamiyama, T. Konno, *Chem. Eur. J.* **2008**, *14*, 9842. i) S. Thakurta, P. Roy, R. J. Butcher, M. S. El Fallah, J. Tercero, E. Garribba, S. Mitra, *Eur. J. Inorg. Chem.* **2009**, 4385. j) C. Yue, C. Yan, R. Feng, M. Wu, L. Chen, F. Jiang, G. Hong, *Inorg. Chem.* **2009**, *48*, 2873. k) S. Perruchas, X. F. Le Goff, S. Maron, I. Maurin, F. Guillen, A. Garcia, T. Gacoin, J.-P. Boilot, *J. Am. Chem. Soc.* **2010**, *132*, 10967. l) Z. W. Liu, M. F. Qayyum, C. Wu, M. T. Whited, P. I. Djurovich, K. O. Hodgson, B. Hedman, E. I.

- Solomon, M. E. Thompson, *J. Am. Chem. Soc.* **2011**, *133*, 3700. m) S. Perruchas, C. Tard, X. F. Le Goff, A. Fargues, A. Garcia, S. Kahlal, J.-Y. Saillard, T. Gacoin, J.-P. Boilot, *Inorg. Chem.* **2011**, *50*, 10682. n) X.-C. Shan, F.-L. Jiang, D.-Q. Yuan, M.-Y. Wu, S.-Q. Zhang, M.-C. Hong, *Dalton Trans.* **2012**, *41*, 9411. o) C. M. Wyss, B. K. Tate, J. Bacsá, T. G. Gray, J. P. Sadighi, *Angew. Chem., Int. Ed.* **2013**, *52*, 12920.
- [175] W.-H. Chan, Z.-Z. Zhang, T. C. W. Mak, C.-M. Che, *J. Organomet. Chem.* **1998**, *556*, 169.
- [176] For selected examples, see: a) C. Mukherjee, T. Weyhermüller, E. Bothe, E. Rentschler, P. Chaudhuri, *Inorg. Chem.* **2007**, *46*, 9895. b) G. Tan, Y. Yang, C. Chu, H. Zhu, H. W. Roesky, *J. Am. Chem. Soc.* **2010**, *132*, 12231. c) M. V. Kirillova, Y. N. Kozlov, L. S. Shul'pina, O. Y. Lyakin, A. M. Kirillov, E. P. Talsi, A. J. L. Pombeiro, G. B. Shul'pin, *J. Catal.* **2009**, *268*, 26. d) H.-X. Li, W. Zhao, H.-Y. Li, Z.-L. Xu, W.-X. Wang, J.-P. Lang, *Chem. Commun.* **2013**, *49*, 4259.
- [177] For examples, see: a) S. H. Lim, Y. Su, S. M. Cohen, *Angew. Chem., Int. Ed.* **2012**, *51*, 5106. b) A. Lapprand, M. Dutartre, N. Khiri, E. Levert, D. Fortin, Y. Rousselin, A. Soldera, S. Jugé, P. D. Harvey, *Inorg. Chem.* **2013**, *52*, 7958. c) X.-C. Shan, F.-L. Jiang, D.-Q. Yuan, H.-B. Zhang, M.-Y. Wu, L. Chen, J. Wei, S.-Q. Zhang, J. Pan, M.-C. Hong, *Chem. Sci.* **2013**, *4*, 1484. d) S. H. Lim, S. M. Cohen, *Inorg. Chem.* **2013**, *52*, 7862. e) L. Bergmann, J. Friedrichs, M. Mydlak, T. Baumann, M. Nieger, S. Bräse, *Chem. Commun.* **2013**, *49*, 6501.
- [178] R. Chakrabarty, P. S. Mukherjee, P. J. Stang, *Chem. Rev.* **2011**, *111*, 6810 and refs. therein.
- [179] S. L. James, *Chem. Soc. Rev.* **2009**, *38*, 1744.
- [180] J. A. Bertrand, J. A. Kelley, C. E. Kirkwood, *J. Chem. Soc., Chem. Commun.* **1968**, 1329.

- [181] S. Sculfort, P. Braunstein, *Chem. Soc. Rev.* **2011**, 40, 2741.
- [182] M. Dey, C. P. Rao, P. K. Saarenketo, K. Rissanen, *Inorg. Chem. Commun.* **2002**, 5, 380.
- [183] a) M. R. Churchill, K. L. Kalra, *Inorg. Chem.* **1974**, 13, 1899. b) J. C. Dyason, P. C. Healy, L. M. Engelhardt, C. Pakawatchai, V. A. Patrick, C. L. Raston, A. H. White, *J. Chem. Soc., Dalton Trans.* **1985**, 831. c) T. M. Arkhireeva, B. M. Bulychev, A. I. Sizov, T. A. Sokolova, V. K. Belsky, G. L. Soloveichik, *Inorg. Chim. Acta* **1990**, 169, 109. d) I. Medina, J. T. Mague, M. J. Fink, *Acta Crystallogr.* **2005**, 61, 1550.
- [184] a) M. R. Churchill, F. J. Rotella, *Inorg. Chem.* **1977**, 16, 3267. b) Z. S. Seddigi, G. M. G. Hossain, A. Banu, *Acta Crystallogr.* **2007**, 63, 756.
- [185] a) M. Semmelmann, D. Fenske, J. F. Corrigan, *J. Chem. Soc., Dalton Trans.* **1998**, 2541. b) B.-J. Liaw, T. S. Lobana, Y.-W. Lin, J.-C. Wang, C. W. Liu, *Inorg. Chem.* **2005**, 44, 9921. c) C. B. Khadka, B. K. Najafabadi, M. Hesari, M. S. Workentin, J. F. Corrigan, *Inorg. Chem.* **2013**, 52, 6798.
- [186] a) I. Wauters, W. Debrouwer, C. V. Stevens, *Beilstein J. Org. Chem.* **2014**, 10, 1064. b) O. I. Kolodiaznyi, *Tetrahedron: Asymmetry* **2012**, 23, 1. c) V. Koshti, S. Gaikwad, S. H. Chikkali, *Coord. Chem. Rev.* **2014**, 265, 52.
- [187] S. Lühr, J. Holz, A. Börner, *ChemCatChem* **2011**, 3, 1708.
- [188] a) T. S. M. Abedin, L. K. Thompson, D. O. Miller, E. Krupicka, *Chem. Commun.* **2003**, 708. b) Y. L. Bai, V. Tangoulis, R. B. Huang, L. S. Zheng, J. Tao, *Chem. Eur. J.* **2009**, 15, 2377. c) J. A. Sheikh, H. S. Jena, A. Adhikary, S. Khatua, S. Konar, *Inorg. Chem.* **2013**, 52, 9717.
- [189] a) F. Tisato, F. Vallotto, G. Pilloni, F. Refosco, C. Corvaja, B. Corain, *J. Chem. Soc., Chem. Commun.* **1994**, 2397. b) G. Pilloni, G. Bandoli, F. Tisato, B. Corain, *Chem. Commun.* **1996**, 433. c) F. Tisato, G. Pilloni, F. Refosco, G. Bandoli, C. Corvaja, B. Corain, *Inorg. Chim. Acta* **1998**, 275, 401.

- [190] a) J. K. Kochi, *J. Am. Chem. Soc.* **1955**, 77, 5274. b) J. C. Barnes, D. N. Hume, *Inorg. Chem.* **1963**, 2, 444. c) C. E. Castro, E. J. Gaughan, D. C. Owsley, *J. Org. Chem.* **1965**, 30, 587.
- [191] CCDC-1003027 (**159**), -1003022 (**160a**), -1003024 (**160b**), -1003023 (**160c**), -1003025 (**160d**) and -1003026 (**160e**) contains the supplementary crystallographic data. These data can be obtained from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.
- [192] X.-Y. Yang, Y. Li, S. A. Pullarkat, *Inorg. Chem.* **2014**, 53, 10232.
- [193] A. Vega, J.-Y. Saillard, *Inorg. Chem.* **2004**, 43, 4012.
- [194] The Cu...Cu distances were determined from the respective cif files of the clusters using Mercury 3.1 software.
- [195] See Appendix for a sample of ^1H NMR spectrum of cluster **160a** (Figure A.1).
- [196] See Appendix for a sample of ^{13}C NMR spectrum of cluster **160a** (Figure A.2).
- [197] See Appendix for ^1H and ^{13}C NMR spectra of cluster **160e** (Figures A.3 and A.4).
- [198] See Appendix for $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of cluster **159** (Figure A.5).
- [199] See Appendix for a sample of $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of cluster **160a** (Figure A.6).
- [200] S. Gischig, A. Togni, *Organometallics* **2005**, 24, 203.
- [201] S. Kumar, G. Mani, D. Dutta, S. Mishra, *Inorg. Chem.* **2014**, 53, 700.
- [202] A. Bayler, A. Schier, H. Schmidbaur, *Inorg. Chem.* **1998**, 37, 4353.
- [203] See Appendix for ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of major product (Figures A.7 and A.8).
- [204] a) J.-E. Lee, J. Yun, *Angew. Chem., Int. Ed.* **2008**, 47, 145. b) S. Sole, E. Fernández, *Chem. Asian, J.* **2009**, 4, 1790. c) S. Sole, A. Tatla, J. A. Mata, A. Whiting, H.

- Gulyás, E. Fernández, *Chem. Eur. J.* **2011**, *17*, 14248. d) H. R. Kim, J. Yun, *Chem. Commun.* **2011**, *47*, 2943. e) W. Yuan, S. Ma, *Org. Biomol. Chem.* **2012**, *10*, 7266.
- [205] a) J.-L. Zhang, L.-A. Chen, R.-B. Xu, C.-F. Wang, Y.-P. Ruan, A. E. Wang, P.-Q. Huang, *Tetrahedron: Asymmetry* **2013**, *24*, 492. b) L. Zhao, Y. Ma, F. He, W. Duan, J. Chen, C. Song, *J. Org. Chem.* **2013**, *78*, 1677.
- [206] X.-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, P.-H. Leung, *Organometallics* **2015**, *34*, 1582.
- [207] D. K. Wicht, I. V. Kourkine, I. Kovacik, D. S. Glueck, *Organometallics* **1999**, *18*, 5381.
- [208] E. Costa, P. G. Pringle, K. Worboys, *Chem. Commun.* **1998**, 49.
- [209] M. A. Kazankova, M. O. Shulyupin, I. P. Beletskaya, *Synlett* **2003**, *14*, 2155.
- [210] A. Perrier, V. Comte, C. Moise, P. L. Gendre, *Chem. Eur. J.* **2010**, *16*, 64.
- [211] A. Perrier, V. Comte, C. Moise, P. Richard, P. L. Gendre, *Eur. J. Org. Chem.* **2010**, 1562.
- [212] A. Leyva-Perez, J. A. Vidal-Moya, J. R. Cabrero-Antonino, S. A. Al-Deyab, S. I. Al-Resayes, A. Corma, *J. Organomet. Chem.* **2011**, *696*, 362.
- [213] L. Routaboul, F. Toulgoat, J. Gatignol, J. F. Lohier, B. Norah, O. Delacroix, C. Alayrac, M. Taillefer, A. C. Gaumont, *Chem. Eur. J.* **2013**, *19*, 8760.
- [214] a) M. R. Douglass, C. L. Stern, T. J. Marks, *J. Am. Chem. Soc.* **2001**, *123*, 10221. b) A. M. Kawaoka, M. R. Douglass, T. J. Marks, *Organometallics* **2003**, *22*, 4630.
- [215] a) M. R. Crimmin, A. G. M. Barrett, M. S. Hill, P. B. Hitchcock, P. A. Procopiu, *Organometallics* **2007**, *26*, 2953. b) T. M. A. Al-Shboul, H. Goerls, M. Westerhausen, *Inorg. Chem. Commun.* **2008**, *11*, 1419. c) B. Liu, T. Roisnel, J. F. Carpentier, Y. Sarazin, *Chem. Eur. J.* **2013**, *19*, 13445. d) H. Hu, C. Cui, *Organometallics* **2012**, *31*, 1208.
- [216] A. Grabulosa, J. Granell, G. Muller, *Coord. Chem. Rev.* **2007**, *251*, 25.

- [217] W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029.
- [218] C. Scriban, I. Kovacic, D. S. Glueck, *Organometallics* **2005**, *24*, 4871.
- [219] a) A. D. Sadow, I. Haller, A. Togni, *J. Am. Chem. Soc.* **2004**, *126*, 14704. b) A. D. Sadow, A. Togni, *J. Am. Chem. Soc.* **2005**, *127*, 17012.
- [220] a) D. Du, W.-L. Duan, *Chem. Commun.* **2011**, *47*, 11101. b) Y.-R. Chen, W.-L. Duan, *Org. Lett.* **2011**, *13*, 5824. c) J. Lu, J. Ye, W.-L. Duan, *Chem. Commun.* **2014**, *50*, 698.
- [221] a) J. S. Fossey, C. J. Richards, *Organometallics* **2004**, *23*, 367. b) X.-Q. Hao, Y.-N. Wang, J.-R. Liu, K.-L. Wang, J.-F. Gong, M.-P. Song, *J. Organomet. Chem.* **2010**, *695*, 82. c) K. Takenaka, M. Minakawa, Y. Uozumi, *J. Am. Chem. Soc.* **2005**, *127*, 12273. d) J. S. Fossey, M. L. Russell, K. M. Abdul Malik, C. J. Richards, *J. Organomet. Chem.* **2007**, *692*, 4843.
- [222] See Appendix for ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR studies of complex **149aa** (Figures A.9 and A.10).
- [223] See Appendix for variable low temperature $^{31}\text{P}\{^1\text{H}\}$ NMR study of complex **149aa** (Figure A.11).
- [224] See Appendix for variable low temperature $^{31}\text{P}\{^1\text{H}\}$ NMR study of PCN-Pd pincer complex (Figure A.12).
- [225] a) M. R. Britten-Kelly, B. J. Willis, D. H. R. Barton, *J. Org. Chem.* **1981**, *46*, 5027. b) K. C. Majumdar, U. Das, *J. Org. Chem.* **1998**, *63*, 9997. c) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901.
- [226] a) T. Hayashi, S. Yamamoto, N. Tokunaga, *Angew. Chem., Int., Ed.* **2005**, *44*, 4224. b) T. Nishimura, Y. Yauhara, T. Sawano, T. Hayashi, *J. Am. Chem. Soc.* **2010**, *132*, 7872. c) T. Nishimura, H. Makino, M. Nagaosa, T. Hayashi, *J. Am. Chem. Soc.* **2010**, *132*, 12865.

- [227] T. den Hartog, S. R. Harutyunyan, D. Font, A. J. Minnaard, B. L. Feringa, *Angew. Chem., Int. Ed.* **2008**, *47*, 398.
- [228] E. Fillion, A. Wilsily, E.-T. Liao, *Tetrahedron: Asymmetry* **2006**, *17*, 2957.
- [229] a) H. Hénon, M. Mauduit, A. Alexakis, *Angew. Chem., Int. Ed.* **2008**, *47*, 9122. b) M. Tissot, D. Müller, S. Belot, A. Alexakis, *Org. Lett.* **2010**, *12*, 2770. c) J. Wencel-Delord, A. Alexakis, C. Crévisy, M. Mauduit, *Org. Lett.* **2010**, *12*, 4335.
- [230] For selected examples, see: a) N. Yamagiwa, S. Matsunaga, M. Shibasaki, *J. Am. Chem. Soc.* **2003**, *125*, 16178. b) K. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2010**, *132*, 2898. c) X. Tian, Y. Liu, P. Melchiorre, *Angew. Chem., Int. Ed.* **2012**, *51*, 6439.
- [231] a) P. B. Dias, M. E. Minas de Piedade, J. A. Martinho Simões, *Coord. Chem. Rev.* **1994**, *135*, 737. b) G. Erre, S. Enthaler, K. Junge, S. Gladiali, M. Beller, *Coord. Chem. Rev.* **2008**, *252*, 471. c) D. K. Dutta, B. Deb, *Coord. Chem. Rev.* **2011**, *255*, 1686.
- [232] Y.-H. Lai, *J. Am. Chem. Soc.* **1985**, *107*, 6678.
- [233] S.-H. Lin, G.-H. Lee, S.-M. Peng, R.-S. Liu, *Organometallics* **1993**, *12*, 2591.
- [234] Z. Ma, F. Xie, H. Yu, Y. Zhang, X. Wu, W. Zhang, *Chem. Commun.* **2013**, *49*, 5292.
- [235] J. V. Allen, S. Bergeron, M. J. Griyths, S. Mukherjee, S. M. Roberts, N. M. Williamson, L. E. Wu, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 3171.
- [236] A. Armstrong, R. D. C. Pullin, C. R. Jenner, J. N. Scutt, *J. Org. Chem.* **2010**, *75*, 3499.
- [237] C. G. Oliva, A. M. S. Silva, D. I. S. P. Resende, F. A. A. Paz, J. A. S. Cavaleiro, *Eur. J. Org. Chem.* **2010**, 3449.
- [238] D. C. G. A. Pinto, A. M. S. Silva, A. Lévai, J. A. S. Cavaleiro, T. Patonay, J. Elguero, *Eur. J. Org. Chem.* **2000**, 2593.

- [239] H. Jin, L. Xiang, F. Wen, K. Tao, Q. Liu, T. Hou, *Ultrason. Sonochem.* **2008**, *15*, 681.
- [240] N. Molleti, N. K. Rana, V. K. Singh, *Org. Lett.* **2012**, *14*, 4322.
- [241] Z. Li, J. Yin, T. Li, G. Wen, X. Shen, J. Yang, *Tetrahedron* **2014**, *70*, 5619.
- [242] a) H. A. Mayer, W. C. Kaska, *Chem. Rev.* **1994**, *94*, 1239. b) C. Limberg, *Angew. Chem., Int. Ed.* **2009**, *48*, 2270. c) C. M. Jensen, *Chem. Commun.* **1999**, 2443. d) J. Choi, A. H. R. MacArthur, M. Brookhart, A. S. Goldman, *Chem. Rev.* **2011**, *111*, 1761. e) C. Gunanathan, D. Milstein, *Acc. Chem. Res.* **2011**, *44*, 588. f) M. Q. Slagt, D. A. P. van Zwieten, A. J. C. M. Moerkerk, R. J. M. Klein Gebbink, G. van Koten, *Coord. Chem. Rev.* **2004**, *248*, 2275. g) H. Lang, R. Packheiser, B. Walfort, *Organometallics* **2006**, *25*, 1836. h) B. Wieczorek, H. P. Dijkstra, M. R. Egmond, R. J. M. Klein Gebbink, G. van Koten, *J. Organomet. Chem.* **2009**, *694*, 812. i) G. Guillena, C. A. Kruithof, M. A. Casado, M. R. Egmond, G. van Koten, *J. Organomet. Chem.* **2003**, *668*, 3. j) S.-E. Stiriba, M. Q. Slagt, H. Kautz, R. J. M. Klein Gebbink, R. Thomann, H. Frey, G. van Koten, *Chem. Eur. J.* **2004**, *10*, 1267. k) W. W. Gerhardt, A. J. Zuccherro, J. N. Wilson, C. R. South, U. H. F. Bunz, M. Weck, *Chem. Commun.* **2006**, *20*, 2141. l) Y. Chen, K. Li, W. Lu, S. S.-Y. Chui, C.-W. Ma, C.-M. Che, *Angew. Chem., Int. Ed.* **2009**, *48*, 9909. m) B. M. J. M. Suijkerbuijk, D. J. Schamhart, H. Kooijman, A. L. Spek, G. van Koten, R. J. M. Klein Gebbink, *Dalton Trans.* **2010**, *39*, 6198.
- [243] a) B. L. Shaw, *J. Am. Chem. Soc.* **1975**, *97*, 3856. b) J. Dehand, M. Pfeffer, *Coord. Chem. Rev.* **1976**, *18*, 327.
- [244] G. R. Newkome, W. E. Puckett, V. K. Gupta, G. E. Kiefer, *Chem. Rev.* **1986**, *86*, 451.

- [245] a) I. Moreno, R. SanMartin, B. Ines, F. Churruca, E. Domínguez, *Inorg. Chim. Acta* **2010**, 363, 1903. b) G. van Koten, *Pure Appl. Chem.* **1989**, 61, 1681. c) D. Benito-Garagorri, K. Kirchner, *Acc. Chem. Res.* **2008**, 41, 201.
- [246] a) L. A. van de Kuil, H. Luitjes, D. M. Grove, J. W. Zwikker, J. G. M. van der Linden, A. M. Roelofsen, L. W. Jenneskens, W. Drenth, G. van Koten, *Organometallics* **1994**, 13, 468. b) H. A. Y. Mohammad, J. C. Grimm, K. Eichele, H.-G. Mack, B. Speiser, F. Novak, M. G. Quintanilla, W. C. Kaska, H. A. Mayer, *Organometallics* **2002**, 21, 5775. c) J. F. Riehl, Y. Jean, O. Eisenstein, M. Pelissier, *Organometallics* **1992**, 11, 729.
- [247] a) H. D. Empsall, E. M. Hyde, R. Markham, W. S. McDonald, M. C. Norton, B. L. Shaw, B. Weeks, *J. Chem. Soc., Chem. Commun.* **1977**, 589. b) A. Castonguay, C. Sui-Seng, D. Zargarian, A. L. Beauchamp, *Organometallics* **2006**, 25, 602. c) N. A. Al-Salem, H. D. Empsall, R. Markham, B. L. Shaw, B. Weeks, *J. Chem. Soc., Dalton Trans.* **1979**, 1972.
- [248] J. Zhao, A. S. Goldman, J. F. Hartwig, *Science* **2005**, 307, 1080.
- [249] Z. Huang, J. Zhou, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, 132, 11458.
- [250] D. G. Gusev, A. J. Lough, *Organometallics* **2002**, 21, 5091.
- [251] A. Vigalok, H.-B. Kraatz, L. Konstantinovsky, D. Milstein, *Chem. Eur. J.* **1997**, 3, 253.
- [252] J. Zhou, J. F. Hartwig, *Angew. Chem., Int. Ed.* **2008**, 47, 5783.
- [253] a) P. Nilsson, O. F. Wendt, *J. Organomet. Chem.* **2005**, 690, 4197. b) S. Sjoevall, O. F. Wendt, C. Andersson, *J. Chem. Soc., Dalton Trans.* **2002**, 1396.
- [254] A. Castonguay, D. M. Spasyuk, N. Madern, A. L. Beauchamp, D. Zargarian, *Organometallics* **2009**, 28, 2134.
- [255] A. Castonguay, A. L. Beauchamp, D. Zargarian, *Organometallics* **2008**, 27, 5723.
- [256] R. Gerber, O. Blacque, C. M. Frech, *ChemCatChem* **2009**, 1, 393.

- [257] R. Gerber, O. Blacque, C. M. Frech, *Dalton Trans.* **2011**, 40, 8996.
- [258] a) H. A. Mayer, R. Fawzi, M. Steimann, *Chem. Ber.* **1993**, 126, 1341. b) R. Gerber, T. Fox, C. M. Frech, *Chem. Eur. J.* **2010**, 16, 6771. c) S. Nemeh, R. J. Flesher, K. Gierling, C. Maichle-Moessmer, H. A. Mayer, W. C. Kaska, *Organometallics* **1998**, 17, 2003. d) M. Gozin, A. Weisman, Y. Ben-David, D. Milstein, *Nature* **1993**, 364, 699. e) W. Weng, S. Parkin, O. V. Ozerov, *Organometallics* **2006**, 25, 5345. f) S. V. Hoskins, C. E. F. Richard, W. R. Roper, *J. Chem. Soc., Chem. Commun.* **1984**, 1000. g) M. Ciclosi, J. Lloret, F. Estevan, P. Lahuerta, M. Sanau, J. Perez-Prieto, *Angew. Chem., Int. Ed.* **2006**, 45, 6741. h) A. A. Koridze, A. V. Polezhaev, S. V. Safronov, A. M. Sheloumov, F. M. Dolgushin, M. G. Ezernitskaya, B. V. Lokshin, P. V. Petrovskii, A. S. Peregudov, *Organometallics* **2010**, 29, 4360. i) C. Azerraf, D. Gelman, *Chem. Eur. J.* **2008**, 14, 10364.
- [259] R. S. Cahn, C. K. Ingold, V. Prelog, *Angew. Chem., Int. Ed.* **1966**, 5, 385.
- [260] a) C. S. Consorti, G. Ebeling, F. R. Flores, F. Rominger, J. Dupont, *Adv. Synth. Catal.* **2004**, 346, 617. b) S. S. Racharlawar, A. Kumar, N. Mirzadeh, S. K. Bhargava, J. Wagler, P. R. Likhar, *J. Organomet. Chem.* **2014**, 772-773, 182.
- [261] P. Braunstein, F. Naud, *Angew. Chem., Int. Ed.* **2001**, 40, 680.
- [262] M. Higuchi, Y. Otsuka, R. Shomura, D. G. Kurth, *Thin Solid Films* **2008**, 516, 2416.
- [263] P. K. Singh, V. K. Singh, *Org. Lett.* **2008**, 10, 4121.
- [264] N. Molleti, N. K. Rana, V. K. Singh, *Org. Lett.* **2012**, 14, 4322.

Appendix

Crystallographic Data for Complex 149a'

Table A.1. Crystal data and structure refinement for **149a'**.

Chemical formula	C ₅₆ H ₅₉ IO ₄ P ₂ Pd
Formula weight	1091.27
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal size	0.160 x 0.180 x 0.420 mm
Crystal habit	colorless block
Crystal system	hexagonal
Space group	P 65
Unit cell dimensions	a = 13.4441(2) Å α = 90° b = 13.4441(2) Å β = 90° c = 49.8415(10) Å γ = 120°
Volume	7801.6(3) Å ³
Z	6
Density (calculated)	1.394 g/cm ³
Absorption coefficient	1.055 mm ⁻¹
F(000)	3336
Theta range for data collection	3.06 to 26.38°
Index ranges	-16 ≤ h ≤ 16, -16 ≤ k ≤ 16, -60 ≤ l ≤ 47
Reflections collected	45660
Independent reflections	9461 [R(int) = 0.0333]
Coverage of independent reflections	96.4%
Absorption correction	multi-scan
Max. and min. transmission	0.8490 and 0.6660
Refinement method	Full-matrix least-squares on F ²

Refinement program	SHELXL-2013 (Sheldrick, 2013)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	9461 / 411 / 673
Goodness-of-fit on F^2	1.070
$\Delta/\sigma_{\max}$	0.001
	9141
Final R indices	data; R1 = 0.0259, wR2 = 0.0547 I>2 σ (I)
	all data R1 = 0.0274, wR2 = 0.0553
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0199P)^2+4.0172P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	0.0(0)
Largest diff. peak and hole	0.316 and -0.388 e $\text{\AA}^{-3}$
R.M.S. deviation from mean	0.063 e $\text{\AA}^{-3}$

Crystallographic Data for Complex 149b

Table A.2. Crystal data and structure refinement for **149b**.

Chemical formula	$C_{55}H_{55}ClO_2P_2Pd$	
Formula weight	951.78	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.040 x 0.120 x 0.240 mm	
Crystal habit	yellow block	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	$a = 9.4806(5)$ Å	$\alpha = 90^\circ$
	$b = 14.6862(8)$ Å	$\beta = 90^\circ$
	$c = 34.3657(15)$ Å	$\gamma = 90^\circ$
Volume	$4784.9(4)$ Å ³	
Z	4	
Density (calculated)	1.321 g/cm ³	
Absorption coefficient	0.551 mm ⁻¹	
F(000)	1976	
Theta range for data collection	1.82 to 25.70°	
Index ranges	-10 ≤ h ≤ 11, -15 ≤ k ≤ 17, -41 ≤ l ≤ 41	
Reflections collected	40241	
Independent reflections	9058 [R(int) = 0.1294]	
Coverage of independent reflections	99.5%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9780 and 0.8790	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2013 (Sheldrick, 2013)	
Function minimized	$\sum w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	9058 / 1567 / 825	

Goodness-of-fit on F^2	1.025
	6007
Final R indices	data; $R1 = 0.0764$, $wR2 = 0.1700$ $I > 2\sigma(I)$
	all data $R1 = 0.1211$, $wR2 = 0.1906$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0982P)^2 + 0.7069P]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.0(0)
Extinction coefficient	0.0176(15)
Largest diff. peak and hole	0.898 and -0.544 eÅ ⁻³
R.M.S. deviation from mean	0.114 eÅ ⁻³

Crystallographic Data for Complex 149d

Table A.3. Crystal data and structure refinement for **149d**.

Empirical formula	C ₄₈ H ₃₈ Cl F O ₂ P ₂ Pd	
Formula weight	869.57	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 17.9347(17) Å	a = 90°.
	b = 9.6113(8) Å	b = 91.492(4)°.
	c = 23.039(2) Å	g = 90°.
Volume	3970.1(6) Å ³	
Z	4	
Density (calculated)	1.455 Mg/m ³	
Absorption coefficient	0.660 mm ⁻¹	
F(000)	1776	
Crystal size	0.40 x 0.12 x 0.10 mm ³	
Theta range for data collection	1.14 to 30.72°.	
Index ranges	-25 ≤ h ≤ 25, -9 ≤ k ≤ 13, -32 ≤ l ≤ 32	
Reflections collected	74964	
Independent reflections	21675 [R(int) = 0.0469]	
Completeness to theta = 30.72°	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9369 and 0.7782	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	21675 / 1 / 991	
Goodness-of-fit on F²	1.032	
Final R indices [I > 2σ(I)]	R1 = 0.0366, wR2 = 0.0736	

R indices (all data)	R1 = 0.0488, wR2 = 0.0802
Absolute structure parameter	-0.038(12)
Largest diff. peak and hole	1.063 and -0.964 e.Å ⁻³

Crystallographic Data for Complex **149h**

Note: The X-ray structure of **149h** was not included in the discussion under Section 2.2.5 as it was obtained after the completion of the thesis.

Table A.4. Crystal data and structure refinement for **149h**.

Chemical formula	$C_{49.50}H_{42}Cl_4O_2P_2Pt$	
Formula weight	1067.66 g/mol	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.240 x 0.280 x 0.420 mm	
Crystal habit	yellow block	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	$a = 11.1031(3)$ Å	$\alpha = 90^\circ$
	$b = 15.7879(4)$ Å	$\beta = 90^\circ$
	$c = 49.6831(14)$ Å	$\gamma = 90^\circ$
Volume	$8709.2(4)$ Å ³	
Z	8	
Density (calculated)	1.629 g/cm ³	
Absorption coefficient	3.582 mm ⁻¹	
F(000)	4248	
Theta range for data collection	5.34 to 31.14°	
Index ranges	-15 ≤ h ≤ 16, -22 ≤ k ≤ 22, -67 ≤ l ≤ 72	
Reflections collected	63981	
Independent reflections	27724 [R(int) = 0.0526]	
Coverage of independent reflections	98.7%	

Absorption correction	multi-scan
Max. and min. transmission	0.4800 and 0.3150
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2014/6 (Sheldrick, 2014)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	27724 / 150 / 1082
Goodness-of-fit on F^2	1.098
$\Delta/\sigma_{\max}$	0.002
Final R indices	24098 data; $I > 2\sigma(I)$ $R1 = 0.0581$, $wR2 = 0.1178$ all data $R1 = 0.0692$, $wR2 = 0.1215$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0258P)^2 + 25.5467P]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.0(0)
Largest diff. peak and hole	2.359 and -2.936 $\text{e}\text{\AA}^{-3}$
R.M.S. deviation from mean	0.363 $\text{e}\text{\AA}^{-3}$

Atom	U ¹¹	U ²²	U ³³	U ¹²	U ¹³	U ²³
C1	0.025	0.025	0.025	0.000	0.000	0.000
C2	0.025	0.025	0.025	0.000	0.000	0.000
C3	0.025	0.025	0.025	0.000	0.000	0.000
C4	0.025	0.025	0.025	0.000	0.000	0.000
C5	0.025	0.025	0.025	0.000	0.000	0.000
C6	0.025	0.025	0.025	0.000	0.000	0.000
C7	0.025	0.025	0.025	0.000	0.000	0.000
C8	0.025	0.025	0.025	0.000	0.000	0.000
C9	0.025	0.025	0.025	0.000	0.000	0.000
C10	0.025	0.025	0.025	0.000	0.000	0.000
C11	0.025	0.025	0.025	0.000	0.000	0.000
C12	0.025	0.025	0.025	0.000	0.000	0.000
C13	0.025	0.025	0.025	0.000	0.000	0.000
C14	0.025	0.025	0.025	0.000	0.000	0.000
C15	0.025	0.025	0.025	0.000	0.000	0.000
C16	0.025	0.025	0.025	0.000	0.000	0.000
C17	0.025	0.025	0.025	0.000	0.000	0.000
C18	0.025	0.025	0.025	0.000	0.000	0.000
C19	0.025	0.025	0.025	0.000	0.000	0.000
C20	0.025	0.025	0.025	0.000	0.000	0.000
C21	0.025	0.025	0.025	0.000	0.000	0.000
C22	0.025	0.025	0.025	0.000	0.000	0.000
C23	0.025	0.025	0.025	0.000	0.000	0.000
C24	0.025	0.025	0.025	0.000	0.000	0.000
C25	0.025	0.025	0.025	0.000	0.000	0.000
C26	0.025	0.025	0.025	0.000	0.000	0.000
C27	0.025	0.025	0.025	0.000	0.000	0.000
C28	0.025	0.025	0.025	0.000	0.000	0.000
C29	0.025	0.025	0.025	0.000	0.000	0.000
C30	0.025	0.025	0.025	0.000	0.000	0.000
C31	0.025	0.025	0.025	0.000	0.000	0.000
C32	0.025	0.025	0.025	0.000	0.000	0.000
C33	0.025	0.025	0.025	0.000	0.000	0.000
C34	0.025	0.025	0.025	0.000	0.000	0.000
C35	0.025	0.025	0.025	0.000	0.000	0.000
C36	0.025	0.025	0.025	0.000	0.000	0.000
C37	0.025	0.025	0.025	0.000	0.000	0.000
C38	0.025	0.025	0.025	0.000	0.000	0.000
C39	0.025	0.025	0.025	0.000	0.000	0.000
C40	0.025	0.025	0.025	0.000	0.000	0.000
C41	0.025	0.025	0.025	0.000	0.000	0.000
C42	0.025	0.025	0.025	0.000	0.000	0.000
N1	0.025	0.025	0.025	0.000	0.000	0.000
N2	0.025	0.025	0.025	0.000	0.000	0.000
O1	0.025	0.025	0.025	0.000	0.000	0.000
O2	0.025	0.025	0.025	0.000	0.000	0.000
O3	0.025	0.025	0.025	0.000	0.000	0.000
O4	0.025	0.025	0.025	0.000	0.000

Chemical formula	C ₄₃ H ₄₁ Cl ₃ O ₈ P ₂ Pd		
Formula weight	960.45		
Temperature	173(2) K		
Wavelength	0.71073 Å		
Crystal size	0.320 x 0.400 x 0.400 mm		
Crystal habit	colorless block		
Crystal system	orthorhombic		
Space group	P 21 21 21		
Unit cell dimensions	a = 10.4536(4) Å	α = 90°	
	b = 17.2754(6) Å	β = 90°	
	c = 24.4730(9) Å	γ = 90°	
Volume	4419.6(3) Å ³		
Z	4		
Density (calculated)	1.443 g/cm ³		
Absorption coefficient	0.724 mm ⁻¹		
F(000)	1960		
Theta range for data collection	1.44 to 37.57°		
Index ranges	-17<=h<=11, -24<=k<=29, -41<=l<=41		
Reflections collected	63361		
Independent reflections	23124 [R(int) = 0.0479]		
Coverage of independent reflections	99.8%		
Absorption correction	multi-scan		
Max. and min. transmission	0.8015 and 0.7607		
Structure solution technique	direct methods		
Structure solution program	SHELXS-97 (Sheldrick, 2008)		
Refinement method	Full-matrix least-squares on F ²		

Refinement program	SHELXL-97 (Sheldrick, 2008)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	23124 / 85 / 547
Goodness-of-fit on F^2	1.013
$\Delta/\sigma_{\max}$	0.003
	18774
Final R indices	data; R1 = 0.0415, wR2 = 0.0776 I>2 σ (I)
	all data R1 = 0.0605, wR2 = 0.0880
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0373P)^2+0.0000P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	-0.0(0)
Largest diff. peak and hole	0.617 and -0.634 e $\text{\AA}^{-3}$
R.M.S. deviation from mean	0.101 e $\text{\AA}^{-3}$

Crystallographic Data for Complex **150b**

Table A.6. Crystal data and structure refinement for **150b**.

Chemical formula	$C_{66}H_{56}ClO_{8.50}P_2Pd$	
Formula weight	1188.89	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.220 x 0.320 x 0.400 mm	
Crystal habit	colorless block	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	$a = 10.0983(3)$ Å	$\alpha = 90^\circ$
	$b = 19.6982(5)$ Å	$\beta = 103.6885(12)^\circ$
	$c = 14.5659(4)$ Å	$\gamma = 90^\circ$
Volume	$2815.13(14)$ Å ³	
Z	2	
Density (calculated)	1.403 g/cm ³	
Absorption coefficient	0.492 mm ⁻¹	
F(000)	1226	
Theta range for data collection	2.52 to 33.31°	
Index ranges	-15 ≤ h ≤ 15, -30 ≤ k ≤ 30, -21 ≤ l ≤ 22	
Reflections collected	51057	
Independent reflections	21436 [R(int) = 0.0445]	
Coverage of independent reflections	99.5%	
Absorption correction	multi-scan	
Max. and min. transmission	0.8990 and 0.8270	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2013 (Sheldrick, 2013)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	

Data / restraints / parameters	21436 / 1 / 712
Goodness-of-fit on F^2	1.015
$\Delta/\sigma_{\max}$	0.002
	18882
Final R indices	data; R1 = 0.0399, wR2 = 0.0748 I>2 σ (I)
	all data R1 = 0.0501, wR2 = 0.0797
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0275P)^2+0.2805P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	-0.0(0)
Largest diff. peak and hole	1.115 and -0.895 eÅ ⁻³
R.M.S. deviation from mean	0.080 eÅ ⁻³

Crystallographic Data for Complex **150c**

Table A.7. Crystal data and structure refinement for **150c**.

Chemical formula	$\text{C}_{43}\text{H}_{41}\text{Cl}_3\text{O}_8\text{P}_2\text{Pt}$	
Formula weight	1049.14	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.180 x 0.200 x 0.400 mm	
Crystal habit	colorless block	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	$a = 10.4318(10)$ Å	$\alpha = 90^\circ$
	$b = 17.092(2)$ Å	$\beta = 90^\circ$
	$c = 24.423(3)$ Å	$\gamma = 90^\circ$
Volume	$4354.6(8)$ Å ³	
Z	4	
Density (calculated)	1.600 g/cm ³	
Absorption coefficient	3.530 mm ⁻¹	
F(000)	2088	
Theta range for data collection	2.77 to 31.13°	
Index ranges	-15 ≤ h ≤ 15, -24 ≤ k ≤ 24, -35 ≤ l ≤ 33	
Reflections collected	80607	
Independent reflections	13941 [R(int) = 0.1304]	
Coverage of independent reflections	99.5%	
Absorption correction	multi-scan	
Max. and min. transmission	0.5690 and 0.3320	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2013 (Sheldrick, 2013)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	

Data / restraints / parameters	13941 / 218 / 556
Goodness-of-fit on F^2	0.974
$\Delta/\sigma_{\max}$	0.002
	11589
Final R indices	data; R1 = 0.0437, wR2 = 0.0735 I>2 σ (I)
	all data R1 = 0.0614, wR2 = 0.0792
Weighting scheme	$w=1/[\sigma^2(F_o^2)]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	0.0(0)
Largest diff. peak and hole	0.992 and -1.597 eÅ ⁻³
R.M.S. deviation from mean	0.167 eÅ ⁻³

Crystallographic Data for Complex **150d**

Table A.8. Crystal data and structure refinement for **150d**.

Chemical formula	$C_{42}H_{39}ClNiO_8P_2$	
Formula weight	827.83 g/mol	
Temperature	133(2) K	
Wavelength	0.71073 Å	
Crystal size	0.100 x 0.140 x 0.220 mm	
Crystal habit	yellow block	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	$a = 10.4056(4)$ Å	$\alpha = 90^\circ$
	$b = 10.8470(5)$ Å	$\beta = 90^\circ$
	$c = 35.2683(14)$ Å	$\gamma = 90^\circ$
Volume	$3980.7(3)$ Å ³	
Z	4	
Density (calculated)	1.381 g/cm ³	
Absorption coefficient	0.687 mm ⁻¹	
F(000)	1720	
Theta range for data collection	2.56 to 29.66°	
Index ranges	-14 ≤ h ≤ 14, -15 ≤ k ≤ 8, -49 ≤ l ≤ 49	
Reflections collected	43828	
Independent reflections	11217 [R(int) = 0.0677]	
Coverage of independent reflections	99.7%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9340 and 0.8640	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2014 (Sheldrick, 2014)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	11217 / 0 / 491	
Goodness-of-fit on F²	1.016	
Final R indices	9167	R1 = 0.0408, wR2 = 0.0744

	data; $I > 2\sigma(I)$
	all data $R1 = 0.0595$, $wR2 = 0.0819$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0289P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.0(0)
Largest diff. peak and hole	0.462 and -0.430 eÅ ⁻³
R.M.S. deviation from mean	0.071 eÅ ⁻³

Crystallographic Data for Complex 153a'

Table A.9. Crystal data and structure refinement for **153a'**.

Chemical formula	$C_{34}H_{37}N_2O_4PPd$	
Formula weight	675.03	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.020 x 0.120 x 0.400 mm	
Crystal habit	colorless needle	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	$a = 9.3721(8)$ Å	$\alpha = 90^\circ$
	$b = 16.0243(14)$ Å	$\beta = 92.120(3)^\circ$
	$c = 20.1099(18)$ Å	$\gamma = 90^\circ$
Volume	$3018.1(5)$ Å ³	
Z	4	
Density (calculated)	1.486 g/cm ³	
Absorption coefficient	0.709 mm ⁻¹	
F(000)	1392	
Theta range for data collection	1.63 to 30.98°	
Index ranges	$-12 \leq h \leq 13$, $-23 \leq k \leq 22$, $-29 \leq l \leq 29$	
Reflections collected	43793	
Independent reflections	18958 [R(int) = 0.0864]	
Coverage of independent reflections	99.5%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9859 and 0.7645	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick, 2008)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-97 (Sheldrick, 2008)	
Function minimized	$\sum w(F_o^2 - F_c^2)^2$	

Data / restraints / parameters	18958 / 1 / 765
Goodness-of-fit on F^2	1.042
$\Delta/\sigma_{\max}$	0.001
Final R indices	14503 data; $I > 2\sigma(I)$ $R1 = 0.0618$, $wR2 = 0.1349$ all data $R1 = 0.0911$, $wR2 = 0.1719$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0796P)^2 + 0.0000P]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.0(0)
Largest diff. peak and hole	0.924 and -1.838 $e\text{\AA}^{-3}$
R.M.S. deviation from mean	0.259 $e\text{\AA}^{-3}$

Crystallographic Data for Complex 159

Table A.10. Crystal data and structure refinement for **159**.

Empirical formula	C ₉₆ H ₈₀ Cl ₄ Cu ₄ O ₄ P ₄	
Formula weight	1817.44	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 12.6496(9) Å	a = 64.969(3)°.
	b = 13.5286(9) Å	b = 80.065(4)°.
	c = 14.9416(10) Å	g = 62.687(4)°.
Volume	2057.8(2) Å ³	
Z	1	
Density (calculated)	1.467 Mg/m ³	
Absorption coefficient	1.281 mm ⁻¹	
F(000)	932	
Crystal size	0.24 x 0.10 x 0.08 mm ³	
Theta range for data collection	1.50 to 25.07°.	
Index ranges	-15 ≤ h ≤ 15, -16 ≤ k ≤ 16, -17 ≤ l ≤ 17	
Reflections collected	31644	
Independent reflections	7233 [R(int) = 0.0540]	
Completeness to theta = 25.07°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9045 and 0.7486	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	7233 / 0 / 505	
Goodness-of-fit on F²	1.111	

Final R indices [I>2sigma(I)]	R1 = 0.0583, wR2 = 0.1620
R indices (all data)	R1 = 0.0846, wR2 = 0.1949
Largest diff. peak and hole	2.903 and -1.073 e.Å ⁻³

Crystallographic Data for Complex 160a

160

Table A.11. Crystal data and structure refinement for **160a**.

Empirical formula	C150 H132 Cl18 Cu6 O6 P6	
Formula weight	3235.72	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 29.8580(18) Å b = 17.4887(10) Å c = 28.7963(17) Å	a = 90°. b = 105.650(2)°. g = 90°.
Volume	14479.3(15) Å ³	
Z	4	
Density (calculated)	1.484 Mg/m ³	
Absorption coefficient	1.319 mm ⁻¹	
F(000)	6600	
Crystal size	0.40 x 0.30 x 0.08 mm ³	
Theta range for data collection	1.64 to 30.59°.	
Index ranges	-40 ≤ h ≤ 42, -25 ≤ k ≤ 16, -41 ≤ l ≤ 34	
Reflections collected	78054	
Independent reflections	37663 [R(int) = 0.0739]	
Completeness to theta = 30.59°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9018 and 0.6205	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	37663 / 140 / 1713	
Goodness-of-fit on F²	0.991	
Final R indices [I > 2σ(I)]	R1 = 0.0672, wR2 = 0.1511	

R indices (all data)	R1 = 0.1405, wR2 = 0.1983
Absolute structure parameter	-0.005(11)
Largest diff. peak and hole	2.497 and -1.244 e.Å ⁻³

Crystallographic Data for Complex 160b

Table A.12. Crystal data and structure refinement for **160b**.

Chemical formula	$C_{150}H_{132}Cl_6Cu_6O_6P_6$	
Formula weight	2810.31	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.200 x 0.240 x 0.260 mm	
Crystal habit	colorless block	
Crystal system	cubic	
Space group	P 2 3	
Unit cell dimensions	$a = 24.3499(19)$ Å	$\alpha = 90^\circ$
	$b = 24.3499(19)$ Å	$\beta = 90^\circ$
	$c = 24.3499(19)$ Å	$\gamma = 90^\circ$
Volume	$14437.(3)$ Å ³	
Z	4	
Density (calculated)	1.293 g/cm ³	
Absorption coefficient	1.097 mm ⁻¹	
F(000)	5784	
Theta range for data collection	1.18 to 25.37°	
Index ranges	$-29 \leq h \leq 6, -16 \leq k \leq 29, -29 \leq l \leq 21$	
Reflections collected	33072	
Independent reflections	8840 [R(int) = 0.0788]	
Coverage of independent reflections	99.7%	
Absorption correction	multi-scan	

Max. and min. transmission	0.8100 and 0.7630
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2013 (Sheldrick, 2013)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	8840 / 2970 / 842
Goodness-of-fit on F^2	1.313
$\Delta/\sigma_{\max}$	0.001
Final R indices	4823 data; $I > 2\sigma(I)$ R1 = 0.1173, wR2 = 0.3159
	all data R1 = 0.2083, wR2 = 0.3854
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.2000P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.0(0)
Largest diff. peak and hole	1.094 and -1.032 $e\text{\AA}^{-3}$
R.M.S. deviation from mean	0.198 $e\text{\AA}^{-3}$

ORTEP diagram of the crystal structure of compound 160. The structure is shown with thermal ellipsoids at the 50% probability level. A simplified diagram of the repeating unit is shown to the right, labeled 160.

Chemical formula	C _{144.62} H _{115.25} Cl _{7.25} Cu ₆ F ₆ O ₆ P ₆
Formula weight	2887.18
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal size	0.340 x 0.380 x 0.400 mm
Crystal habit	colorless block
Crystal system	trigonal
Space group	R 3
Unit cell dimensions	a = 33.8786(6) Å α = 90° b = 33.8786(6) Å β = 90° c = 42.7681(9) Å γ = 120°
Volume	42511.0(18) Å ³
Z	12
Density (calculated)	1.353 g/cm ³
Absorption coefficient	1.149 mm ⁻¹
F(000)	17667
Theta range for data collection	1.47 to 26.44°
Index ranges	-40 ≤ h ≤ 41, -42 ≤ k ≤ 42, -53 ≤ l ≤ 53
Reflections collected	95011
Independent reflections	38828 [R(int) = 0.0676]
Coverage of independent reflections	99.7%
Absorption correction	multi-scan
Max. and min. transmission	0.6960 and 0.6570
Refinement method	Full-matrix least-squares on F ²

Refinement program	SHELXL-2013 (Sheldrick, 2013)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	38828 / 14440 / 3501
Goodness-of-fit on F^2	1.031
$\Delta/\sigma_{\max}$	0.002
Final R indices	24942 data; $I > 2\sigma(I)$ R1 = 0.0720, wR2 = 0.1907 all data R1 = 0.1256, wR2 = 0.2329
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.1437P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.1(0)
Largest diff. peak and hole	0.943 and -1.270 eÅ ⁻³
R.M.S. deviation from mean	0.216 eÅ ⁻³

Crystallographic Data for Complex 160d

Table A.14. Crystal data and structure refinement for **160d**.

Chemical formula	$C_{140}H_{128.79}Cl_{16}Cu_6O_{15}P_6$
Formula weight	3185.47
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal size	0.300 x 0.380 x 0.400 mm
Crystal system	trigonal
Space group	R 3
Unit cell dimensions	$a = 17.3752(10)$ Å $\alpha = 90^\circ$ $b = 17.3752(10)$ Å $\beta = 90^\circ$ $c = 40.085(2)$ Å $\gamma = 120^\circ$
Volume	$10480.3(14)$ Å ³
Z	3
Density (calculated)	1.514 g/cm ³
Absorption coefficient	1.333 mm ⁻¹
F(000)	4874
Theta range for data collection	2.80 to 31.00°
Index ranges	-24 ≤ h ≤ 23, -21 ≤ k ≤ 25, -58 ≤ l ≤ 58
Reflections collected	45537
Independent reflections	14843 [R(int) = 0.0684]
Max. and min. transmission	0.6910 and 0.6180
Refinement method	Full-matrix least-squares on F ²
Refinement program	SHELXL-2013 (Sheldrick, 2013)
Function minimized	$\sum w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	14843 / 687 / 722

Goodness-of-fit on F^2	1.007	
$\Delta/\sigma_{\max}$	0.003	
Final R indices	9863 data; $I > 2\sigma(I)$	R1 = 0.0686, wR2 = 0.1828
	all data	R1 = 0.1080, wR2 = 0.2106
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.1211P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	
Absolute structure parameter	0.0(0)	
Largest diff. peak and hole	1.287 and -0.992 eÅ ⁻³	
R.M.S. deviation from mean	0.121 eÅ ⁻³	

Crystallographic Data for Complex 160e

Table A.15. Crystal data and structure refinement for **160e**.

Chemical formula	$\text{C}_{142}\text{H}_{152}\text{Cl}_{38}\text{Cu}_6\text{O}_{24}\text{P}_6$	
Formula weight	4156.80	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal size	0.180 x 0.220 x 0.300 mm	
Crystal habit	colorless block	
Crystal system	trigonal	
Space group	R 3	
Unit cell dimensions	$a = 29.118(3)$ Å	$\alpha = 90^\circ$
	$b = 29.118(3)$ Å	$\beta = 90^\circ$
	$c = 16.8751(14)$ Å	$\gamma = 120^\circ$
Volume	$12390.8(18)$ Å ³	
Z	3	
Density (calculated)	1.671 g/cm ³	
Absorption coefficient	1.497 mm ⁻¹	
F(000)	6318	
Theta range for data collection	1.40 to 29.68°	
Index ranges	-40 ≤ h ≤ 40, -40 ≤ k ≤ 40, -22 ≤ l ≤ 23	
Reflections collected	77824	
Independent reflections	15493 [R(int) = 0.1246]	
Coverage of independent reflections	99.7%	
Absorption correction	multi-scan	
Max. and min. transmission	0.7744 and 0.6623	
Structure solution technique	direct methods	

Structure solution program	SHELXS-97 (Sheldrick, 2008)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-97 (Sheldrick, 2008)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	15493 / 2470 / 836
Goodness-of-fit on F^2	0.951
$\Delta/\sigma_{\max}$	0.001
Final R indices	8256 data; $I > 2\sigma(I)$ $R1 = 0.0826$, $wR2 = 0.2082$ all data $R1 = 0.1317$, $wR2 = 0.2272$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.1236P)^2 + 0.0000P]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.1(0)
Largest diff. peak and hole	0.645 and -1.841 $e\text{\AA}^{-3}$
R.M.S. deviation from mean	0.169 $e\text{\AA}^{-3}$

¹H and ¹³C NMR Spectra of Cluster 160a

Figure A.1. ¹H NMR spectrum of cluster 160a.

Figure A.2. ¹³C NMR spectrum of cluster 160a.

¹H and ¹³C NMR Spectra of Cluster 160e

Figure A.3. ¹H NMR spectrum of cluster 160e.

Figure A.4. ¹³C NMR spectrum of cluster 160e.

$^{31}\text{P}\{^1\text{H}\}$ NMR Spectra of Clusters 159 and 160a

Figure A.5. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of cluster **159**.

Figure A.6. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of cluster **160a**.

^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR Spectra of Major Product

Figure A.7. ^1H NMR spectrum of major product.

Figure A.8. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of major product.

Crystallographic Data for Complex 181a

Table A.16. Crystal data and structure refinement for **181a**.

Chemical formula	C ₂₈ H ₂₉ O ₅ P	
Formula weight	476.48	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.080 x 0.100 x 0.420 mm	
Crystal habit	colorless needle	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 10.751(2) Å	α = 90°
	b = 5.8887(8) Å	β = 103.361(9)°
	c = 19.552(3) Å	γ = 90°
Volume	1204.3(3) Å ³	
Z	2	
Density (calculated)	1.314 g/cm ³	
Absorption coefficient	0.152 mm ⁻¹	
F(000)	504	
Theta range for data collection	3.21 to 31.22°	
Index ranges	-15 ≤ h ≤ 15, -8 ≤ k ≤ 8, -28 ≤ l ≤ 26	
Reflections collected	20068	
Independent reflections	7734 [R(int) = 0.0856]	
Coverage of independent reflections	99.2%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9880 and 0.9390	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2013 (Sheldrick, 2013)	
Function minimized	Σ w(F _o ² - F _c ²) ²	

Data / restraints / parameters	7734 / 1 / 309
Goodness-of-fit on F^2	0.990
Final R indices	5156 data; $I > 2\sigma(I)$ $R1 = 0.0648$, $wR2 = 0.1045$ all data $R1 = 0.1106$, $wR2 = 0.1236$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0327P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.1(1)
Largest diff. peak and hole	0.480 and -0.477 $e\text{\AA}^{-3}$
R.M.S. deviation from mean	0.076 $e\text{\AA}^{-3}$

Crystallographic Data for Complex 181b

Table A.17. Crystal data and structure refinement for **181b**.

Chemical formula	C ₂₈ H ₂₉ O ₅ P	
Formula weight	476.48	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.200 x 0.400 x 0.420 mm	
Crystal habit	colorless block	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 5.6363(4) Å	α = 103.051(6)°
	b = 12.4972(11) Å	β = 96.273(5)°
	c = 18.9559(17) Å	γ = 102.019(5)°
Volume	1254.98(18) Å ³	
Z	2	
Density (calculated)	1.261 g/cm ³	
Absorption coefficient	0.145 mm ⁻¹	
F(000)	504	
Theta range for data collection	3.15 to 31.21°	
Index ranges	-8 ≤ h ≤ 8, -18 ≤ k ≤ 18, -27 ≤ l ≤ 27	
Reflections collected	38041	
Independent reflections	8090 [R(int) = 0.0705]	
Coverage of independent reflections	99.2%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9710 and 0.9410	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2013 (Sheldrick, 2013)	
Function minimized	Σ w(F _o ² - F _c ²) ²	
Data / restraints / parameters	8090 / 925 / 489	
Goodness-of-fit on F²	1.043	

Final R indices	5837 data; $I > 2\sigma(I)$	$R1 = 0.0502$, $wR2 = 0.1138$
	all data	$R1 = 0.0775$, $wR2 = 0.1272$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0580P)^2 + 0.1067P]$ where $P = (F_o^2 + 2F_c^2)/3$	
Largest diff. peak and hole	0.375 and -0.364 eÅ ⁻³	
R.M.S. deviation from mean	0.062 eÅ ⁻³	

¹H and ³¹P{¹H} NMR Studies of Complex 149aa

Figure A.9. ^1H NMR studies of complex **149aa**.

Figure A.10. $^{31}\text{P}\{^1\text{H}\}$ NMR studies of complex **149aa**.

Variable Low Temperature $^{31}\text{P}\{^1\text{H}\}$ NMR Study of Complex 149aa

Figure A.11. Variable low temperature $^{31}\text{P}\{^1\text{H}\}$ NMR of **149aa**.

Variable Low Temperature $^{31}\text{P}\{^1\text{H}\}$ NMR study of PCN-Pd Pincer Complex

Figure A.12. Variable low temperature $^{31}\text{P}\{^1\text{H}\}$ NMR of PCN-Pd pincer complex.

Crystallographic Data for Complex 184i

Table A.18. Crystal data and structure refinement for **184i**.

Chemical formula	$C_{29}H_{24}BrO_2P$	
Formula weight	515.36 g/mol	
Temperature	133(2) K	
Wavelength	0.71073 Å	
Crystal size	0.100 x 0.140 x 0.420 mm	
Crystal habit	colorless prism	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	$a = 5.6283(3)$ Å	$\alpha = 90^\circ$
	$b = 17.6395(11)$ Å	$\beta = 90^\circ$
	$c = 23.9438(16)$ Å	$\gamma = 90^\circ$
Volume	$2377.1(3)$ Å ³	
Z	4	
Density (calculated)	1.440 g/cm ³	
Absorption coefficient	1.821 mm ⁻¹	
F(000)	1056	
Theta range for data collection	2.80 to 31.09°	
Index ranges	-7 ≤ h ≤ 8, -25 ≤ k ≤ 25, -25 ≤ l ≤ 34	
Reflections collected	17706	
Independent reflections	7608 [R(int) = 0.1103]	
Coverage of independent reflections	99.6%	
Absorption correction	multi-scan	
Max. and min. transmission	0.8390 and 0.5150	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2014 (Sheldrick, 2014)	
Function minimized	$\sum w(F_o^2 - F_c^2)^2$	

Data / restraints / parameters	7608 / 0 / 298	
Goodness-of-fit on F^2	0.899	
$\Delta/\sigma_{\max}$	0.001	
Final R indices	4687 data; $I > 2\sigma(I)$	R1 = 0.0591, wR2 = 0.1089
	all data	R1 = 0.1141, wR2 = 0.1302
Weighting scheme	$w = 1/[\sigma^2(F_o^2)]$ where $P = (F_o^2 + 2F_c^2)/3$	
Absolute structure parameter	0.0(0)	
Largest diff. peak and hole	0.438 and -0.463 $e\text{\AA}^{-3}$	
R.M.S. deviation from mean	0.095 $e\text{\AA}^{-3}$	

Crystallographic Data for Complex 195b

Table A.19. Crystal data and structure refinement for **195b**.

Chemical formula	$C_{24.50}H_{21}Cl_4NOPPdS$	
Formula weight	656.65 g/mol	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.120 x 0.300 x 0.420 mm	
Crystal habit	yellow block	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	$a = 9.4797(8)$ Å	$\alpha = 90^\circ$
	$b = 28.175(2)$ Å	$\beta = 104.9626(15)^\circ$
	$c = 10.1153(9)$ Å	$\gamma = 90^\circ$
Volume	$2610.1(4)$ Å ³	
Z	4	
Density (calculated)	1.671 g/cm ³	
Absorption coefficient	1.281 mm ⁻¹	
F(000)	1312	
Theta range for data collection	2.08 to 31.07°	
Index ranges	$-13 \leq h \leq 11$, $-40 \leq k \leq 40$, $-14 \leq l \leq 14$	
Reflections collected	25467	
Independent reflections	15305 [R(int) = 0.0343]	
Coverage of independent reflections	97.2%	
Absorption correction	multi-scan	
Max. and min. transmission	0.8610 and 0.6150	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2014/6 (Sheldrick, 2014)	
Function minimized	$\sum w(F_o^2 - F_c^2)^2$	

Data / restraints / parameters	15305 / 1 / 604
Goodness-of-fit on F^2	1.042
$\Delta/\sigma_{\max}$	0.001
Final R indices	14485 data; $I > 2\sigma(I)$ $R1 = 0.0359$, $wR2 = 0.0770$ all data $R1 = 0.0386$, $wR2 = 0.0784$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0246P)^2 + 0.7498P]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	-0.0(0)
Largest diff. peak and hole	0.970 and -0.712 $e\text{\AA}^{-3}$
R.M.S. deviation from mean	0.107 $e\text{\AA}^{-3}$

Crystallographic Data for Complex 201b

Table A.20. Crystal data and structure refinement for **201b**.

Chemical formula	$C_{27}H_{23}Cl_3NOPPdS$	
Formula weight	653.24 g/mol	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.100 x 0.120 x 0.420 mm	
Crystal habit	yellow block	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	$a = 9.7127(5)$ Å	$\alpha = 90^\circ$
	$b = 11.5076(6)$ Å	$\beta = 105.963(4)^\circ$
	$c = 12.7323(6)$ Å	$\gamma = 90^\circ$
Volume	$1368.21(12)$ Å ³	
Z	2	
Density (calculated)	1.586 g/cm ³	
Absorption coefficient	1.127 mm ⁻¹	
F(000)	656	
Theta range for data collection	3.44 to 35.13°	
Index ranges	$-15 \leq h \leq 15$, $-18 \leq k \leq 18$, $-19 \leq l \leq 20$	
Reflections collected	37087	
Independent reflections	12103 [R(int) = 0.0884]	
Coverage of independent reflections	99.5%	
Absorption correction	multi-scan	
Max. and min. transmission	0.8960 and 0.6490	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2014/6 (Sheldrick, 2014)	
Function minimized	$\sum w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	12103 / 1 / 316	

Goodness-of-fit on F^2	0.988	
$\Delta/\sigma_{\max}$	0.001	
Final R indices	9028 data; $I > 2\sigma(I)$	R1 = 0.0543, wR2 = 0.0968
	all data	R1 = 0.0840, wR2 = 0.1103
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0362P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	
Absolute structure parameter	0.0(0)	
Largest diff. peak and hole	0.960 and -1.311	$\text{e}\text{\AA}^{-3}$
R.M.S. deviation from mean	0.154	$\text{e}\text{\AA}^{-3}$

Crystallographic Data for Complex 202b

Table A.21. Crystal data and structure refinement for **202b**.

Chemical formula	C ₂₈ H ₂₃ ClNOPPdS	
Formula weight	594.35 g/mol	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.400 x 0.410 x 0.420 mm	
Crystal habit	yellow block	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 8.3737(3) Å	α = 90°
	b = 12.3461(4) Å	β = 90°
	c = 23.8575(7) Å	γ = 90°
Volume	2466.45(14) Å ³	
Z	4	
Density (calculated)	1.601 g/cm ³	
Absorption coefficient	1.033 mm ⁻¹	
F(000)	1200	
Theta range for data collection	2.94 to 37.90°	
Index ranges	-14 ≤ h ≤ 14, -21 ≤ k ≤ 14, -40 ≤ l ≤ 40	
Reflections collected	13283	
Independent reflections	12637 [R(int) = 0.0992]	
Coverage of independent reflections	99.5%	
Absorption correction	multi-scan	
Max. and min. transmission	0.8960 and 0.6490	
Refinement method	Full-matrix least-squares on F ²	
Refinement program	SHELXL-2014/6 (Sheldrick, 2014)	
Function minimized	Σ w(F _o ² - F _c ²) ²	

Data / restraints / parameters	13283 / 1 / 419
Goodness-of-fit on F^2	1.250
$\Delta/\sigma_{\max}$	0.001
Final R indices	12637 data; $I > 2\sigma(I)$ $R1 = 0.0555$, $wR2 = 0.0992$ all data $R1 = 0.0520$, $wR2 = 0.1002$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0362P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.048(11)
Largest diff. peak and hole	1.144 and -2.716 eÅ ⁻³

Publications

- 1) K.-W. Tan, X.-Y. Yang, Y. Li, Y. Huang, S. A. Pullarkat, P.-H. Leung, *Reactivity of Cycloplatinated Amine Complexes: Intramolecular C–C Bond Formation, C–H Activation, and PPh₂ Migration in Coordinated Alkynylphosphines*; *Organometallics* **2012**, *31*, 8407.
- 2) J. S. L. Yap, Y. Ding, X.-Y. Yang, J. Wong, Y. Li, S. A. Pullarkat, P.-H. Leung, *Mechanistic Insights into the Pd^{II}-Catalyzed Chemoselective N-Demethylation vs. Cyclometalation Reactivity Pathways in 1-Aryl-N,N-dimethylethanamines*; *Eur. J. Inorg. Chem.* **2014**, 5046.
- 3) X.-Y. Yang, Y. Li, S. A. Pullarkat, *A One-Pot Diastereoselective Self Assembly of C-Stereogenic Copper(I) Diphosphine Clusters*; *Inorg. Chem.* **2014**, *53*, 10232.
- 4) X.-Y. Yang, J. H. Gan, Y. Li, S. A. Pullarkat, P.-H. Leung, *Palladium Catalyzed Asymmetric Hydrophosphination of α,β - and $\alpha,\beta,\gamma,\delta$ -Unsaturated Malonate Esters-Efficient Control of Reactivity, Stereo- and Regio-selectivity*; *Dalton Trans.* **2015**, *44*, 1258.
- 5) X.-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, P.-H. Leung, *Versatile Syntheses of Optically Pure PCE Pincer Ligands: Facile Modifications of The Pendant Arms and Ligand Backbones*; *Organometallics* **2015**, *34*, 1582.
- 6) X.-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, P.-H. Leung, *Asymmetric 1,4-Conjugate Addition of Diarylphosphines to $\alpha,\beta,\gamma,\delta$ -Unsaturated Ketones Catalyzed by Transition-Metal Pincer Complexes*; *Organometallics* **2015**, *34*, 5196.

- 7) Y.-X. Jia, X.-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, K. Xu, H. Hirao, P.-H. Leung, *Computational and Carbon-13 NMR Studies of Pt-C Bonds in P-C-P Pincer Complexes*; *Dalton Trans.* **2016**, Advance Article (DOI: 10.1039/c5dt02049b).
- 8) X.-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, P.-H. Leung, *An Efficient One-Pot Catalytic “Self-Breeding” of Chiral Unsymmetrical C(sp³)-Hybridized Pincer Complexes*; submitted for publication.
- 9) X.-Y. Yang, S. A. Pullarkat, P. H. Leung, *The Asymmetric Synthesis of Chiral PCP Transition Metal Pincer Complexes*; *The International Kasetsart University Science and Technology Annual Research Symposium*, 28-29 March, **2013**, Bangkok, Thailand.
- 10) X.-Y. Yang, J. H. Gan, Y. Li, S. A. Pullarkat, P.-H. Leung, *Control of Regioselectivity via Rational Selection of Catalyst in the Enantioselective Addition of Diphenylphosphine to Malonate Esters*; *20th International Conference on Phosphorus Chemistry*, 28 June-2 July, **2014**, Dublin, Ireland.
- 11) X.-Y. Yang, S. A. Pullarkat, P.-H. Leung, *Palladium-Catalyzed Regio- and Enantioselective P-H Bond Addition to Alkylidenemalonate Esters*; *41st International Conference on Coordination Chemistry*, 21-25 July, **2014**, Singapore.
- 12) X.-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, P.-H. Leung, *The Versatile Syntheses of Optically Pure ECE' Pincer Complexes*; *249th American Chemical Society National Meeting & Exposition*, 22-26 March, **2015**, Colorado, United States of America.
- 13) W. Tay, X.-Y. Yang, Y. Li, S. A. Pullarkat, P.-H. Leung, *Chiral Pincer Complexes: A Study on the Influence of Catalyst Design in an Asymmetric P-H Bond Addition Reaction*; *249th American Chemical Society National Meeting & Exposition*, 22-26 March, **2015**, Colorado, United States of America.