Extending the Phosphorus-donor Manifold from Symmetric to Unsymmetric in Pincer Metal Catalysts

Van een Symmetrische naar een Asymmetrische Fosfor-Donor Atoomset in Tang-Metaal Katalysatoren

(met een samenvatting in het Nederlands)

PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit Utrecht
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ingevolge het besluit van het college voor promoties
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door

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geboren op 26 september 1978 te Shanghai, China

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Prof. dr. R. J. M. Klein Gebbink

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For my wife Jin

Li, Jie

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Preface

Pincer metal complexes consist of a metal centre and a monoanionic, tridentate meridonal ECE-type ligand which is connected to the metal through one metal-carbon σ-bond and two metal-E coordination bonds.[1a, 1b] The ECE-pincer ligand framework contains several positions that are readily functionalized and by doing so offer a wealth of possibilities to modify and fine-tune the structural and electronic properties of the metal centre in ECE-pincer metal complexes (Chart 1). In the past decades, a large variety of pincer complexes with various donor atom containing groups, *e.g.* E = NR_2, SR, PR_2, SeR, OPR_2, $OP(OR)_2$, etc. have been synthesized.[1-4] Many ECE-type pincer metal complexes show remarkable catalytic performances in a number of catalytic reactions. With the aim to achieve enantioselective transformations, the development of chiral pincer metal complexes has been an integral part of pincer chemistry.[5-9] The development of ECE'-type (E≠E') pincer metal complexes is a relatively new aspect of pincer chemistry. In such ECE'-type pincer complexes, the combination and cooperation of two different types of donor atom groups, E and E', could lead to very interesting electronic and structural properties of the metal centers, which in turn could lead to improved catalytic performances.[10-13]

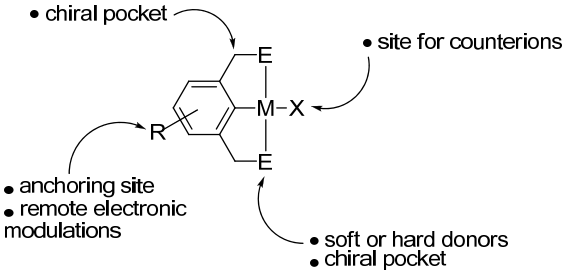

Chart 1. General structure of ECE-pincer metal complexes.

In this thesis, new methods to access novel chiral ECE-pincer metal complexes and ECE'-pincer metal complexes as well as the applications of these complexes in catalytic organic transformations are described and discussed.

In Chapter 1, an overview is provided of the synthesis and catalytic applications of asymmetrical ECE-pincer, ECE'-pincer, and planar-chiral ECE'-pincer metal complexes in which the pincer ligand contains at least one phosphorus E-donor. This chapter presents an up-to-date picture of the status and the new developments of the field of phosphorus pincer metal complexes.

Chapter 2 describes the P'CP'-pincer (P'=diphenylphosphinite) palladium complex-catalyzed allylation of protected aldimines with allyl(tributyl)stannane for the preparation of *N*-homoallylic sulfamides. In particular, the use of an easily removable protecting group, the *N,N*-dimethylsulfamoyl group, is described.

In Chapter 3, the synthesis of a series of mono- and bidentate phosphite pincer ligands derived from 2,2'-biphenol is described along with details on the preparation of their corresponding Pd complexes starting from different Pd precursors.

The synthesis of novel P-stereogenic pincer metal complexes derived from (*S*)-(−)-α,α-diphenyl-2-pyrrolidinemethanol and (*S*)-(+)-indolinemethanol is the subject of Chapter 4. The development of a novel P-chiral building block derived from (*S*)-(+)-indolinemethanol is reported, which is employed in a flexible and modular approach to the synthesis of new P-stereogenic pincer metal complexes.

In Chapter 5, the synthesis of a series of chiral bis-phosphite Pd and Pt complexes and *ortho*-metallated, *C,P*-chelate bonded monophosphite Pd and Pt complexes is reported. In this case, (*R*)-BINOL has been investigated as the enantiopure synthon for chiral arylphosphite pincer ligands.

Chapter 6 describes the synthesis of a series of PCN- and PCS-pincer ligands starting from isovanillin as the common precursor. The catalytic activities of the corresponding neutral ECE'-pincer palladium complexes in homoallylation reactions of aldehydes with allyl(tributyl)stannane were investigated. In addition, the analogous cationic palladium complexes were tested in the tandem catalytic reactions of aldehydes or sulfonimines with allyl chlorides and hexamethyldistannane to yield homoallylic alcohol and sulfonamide product.

Finally, Chapter 7 deals with the synthesis of a different series of PCN-pincer palladium and platinum complexes starting from 2-bromo-3-hydroxy-4-methoxybenzaldehyde. The relative Lewis acidity of the corresponding cationic PCN-pincer metal complexes was investigated along with their catalytic activity in the aza-Michael addition between morpholine and acrylonitrile.

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Chapter 1

Asymmetric PCP-Pincer and PCE-Pincer Metal Complexes: Synthesis and Applications

Abstract

The synthetic methods to access asymmetric PCP-pincer metal complexes and PCE-pincer metal complexes (including planar chiral complexes) transition metal complexes including palladium, platinum, rhodium, ruthenium, iridium, have been reviewed. Additionally, several applications of these pincer complexes in homogeneous and asymmetric catalysis have been summarized. This review shows the development of phosphine-based pincer metal complex chemistry in combination with recent achievements in, *e.g.* asymmetric catalysis by means of such complexes.

1.1 Introduction

Typical ECE-pincer metal complexes consist of a metal centre and a symmetric terdentate ECE-type ligand which is connected to the metal through one M−C σ-bond and two coordinative M−E bonds. In the past decades, ECE-pincer metal complexes have attracted much attention and a variety of structures with various donor atom containing groups, *e.g.* E = NR_2, SR, PR_2, SeR, OPR_2, $OP(OR)_2$, *etc*. have been synthesized and characterized.[1] Pincer transition metal complexes usually provide a unique balance of thermal stability and stability of the σ-M−C bond against oxidation and hydrolysis *vs.* catalytic activities in a variety of organic transformations. Through systematic ligand modifications and many different metal centers that can be included in pincer-type complexes, an enormous variety of different pincer metal complexes are accessible.[1-4] Among the greater part of the known pincer complexes of the NCN,[2] PCP,[3] and SCS[4] types, the development of P-donor containing symmetric PCP-pincer complexes has received enormous attention since Shaw's pioneering investigation.[5] The synthesis of symmetric PCP type complexes and their applications as catalysts or advanced materials have been intensively reviewed by different groups.[1d, 1e, 1f, 1g, 1i] Besides the well-developed symmetric PCP-pincer complexes, the development of asymmetric PCP- and of PCE-pincer complexes (E = N, P' (P ≠ P'), S, *etc*.) has recently become a very attractive and new aspect in the field of pincer chemistry. For instance, the rational design and development of asymmetric PCP-pincer complexes has blossomed over the last few years, because chiral pincer complexes can afford stereochemically and electronically tunable environments around active metal centers in order to control regio- and/or stereoselective catalysis.[7-9, 11-17, 29] Moreover, a lot of effort has been put in the development of PCE-pincer complexes, and it has been shown that their catalytic activities and reactivities can benefit from the combination and cooperativity of two different E-donors.[33, 35-41] A further, more recently reported development involves planar-chiral PCS- and PCN-pincer metal complexes that constitute yet another class of chiral pincer metal complexes.[42]

In this review, the synthesis of asymmetric PCP-pincer metal complexes and PCE-pincer metal complexes consisting of a phosphorus-donor containing meridional terdentate pincer ligand and a metal centre, which is connected to the aromatic or the heterocyclic skeleton through one carbon-metal σ-bond, are described in combination with their catalytic applications in homogeneous catalysis (Figure 1).

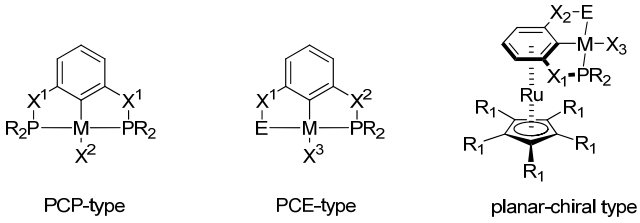


Figure 1. Main types of P-donor containg pincer metal complexes.

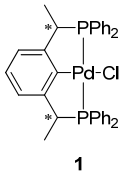
1.2 Synthesis of asymmetric PCP-pincer complexes

Generally, the asymmetric PCP-pincer complexes documented up to date can be mainly classified into two groups: 1) chiral, electron-enriched phosphine PCP type, which includes complexes bearing chirality at the benzylic carbon atoms and complexes bearing P-stereogenic phosphorus donor moieties; and 2) chiral, electron-deficient phosphite PCP-complexes bearing optically active diols as the chiral building blocks.

1.2.1 Asymmetric electron-enriched phosphine PCP-pincer complexes.

1.2.1.1 Chirality on the benzylic positions

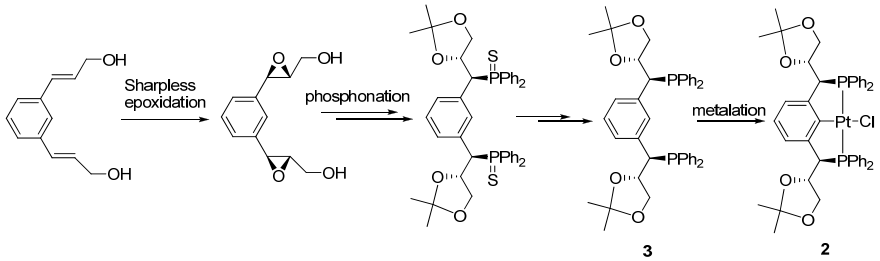
Venanzi *et al.* firstly reported the synthesis of a mixture of *rac*-**1** and *meso*-**1** (Figure 2) as the analogues of the asymmetric NCN-pincer complexes (Scheme 1).[6] The separation of *rac*-**1** and *meso*-**1** was achieved by fractional recrystallization in moderate yields (43% for *meso*-**1**; 38% for *rac*-**1**). However, the separation of the enantiomers of complex **1** was not successful by means of preparative chiral HPLC.[7] The problematic enantioselective formation of a chiral benzylic carbon centre in pincer ligands was later solved by the same group and the first asymmetric bisphosphine pincer platinum complex **2** was then reported.[8]



1

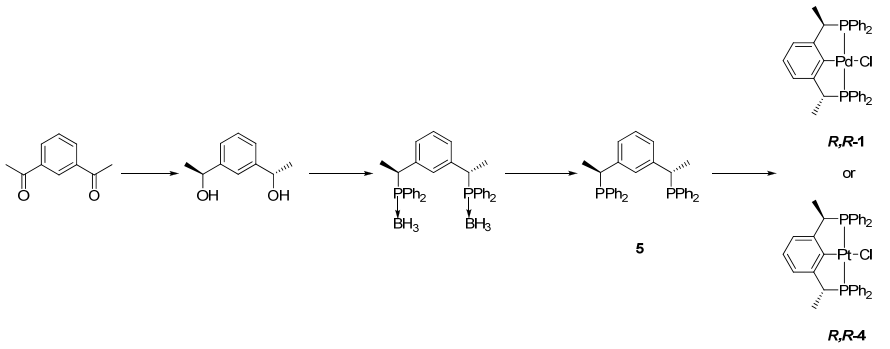
Figure 2. PCP-pincer Pd complex **1**.

As described in Scheme 1, the chiral pincer ligand **3** was obtained by Sharpless epoxidation through a tedious synthetic route. Platination of **3** was smoothly achieved by reacting $[Pt_2(\mu\text{-}Cl)_2(\eta^3\text{-}CH_2C(CH_3)\text{-}CH_2)_2]$ with ligand **3** under very mild conditions and the desired pincer Pt complex **2** was prepared in 91% isolated yield.



Scheme 1. Synthesis of pincer complex **2**.

Zhang *et al.* later developed a much more concise and straightforward synthetic route to prepare enantiopure *R,R*-**1** and its platinum analogue *R,R*-**4** in good yields (Scheme 2).[9] Compared to Venanzi's route, the chiral benzylic carbon centres in asymmetric pincer ligand **5** were formed by enantioselective reduction of 1,3-diacetylbenzene (>99% *ee* with *ca.* 5% meso) according to H.C. Brown's procedure.[10] Using BH_3 to protect the oxygen sensitive bisphosphine ligand gave ligand **5** in excellent isolated yield (91%) after facile phophine deprotecting. Metalation of **5** was also carried out *via* a C-H activation mode under very mild conditions with commonly used $[PdCl_2(PhCN)_2]$ and $[Pt_2(\mu\text{-}Cl)_2(\eta^3\text{-}CH_2C(CH_3)\text{-}CH_2)_2]$ as the metal precursors.

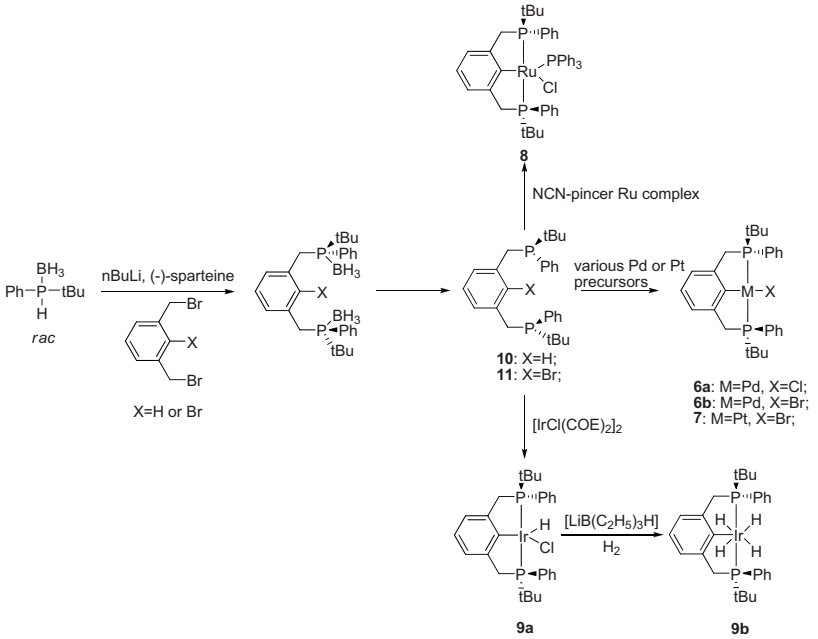


Scheme 2. Synthesis of *R,R*-**1** and *R,R*-**4**.

1.2.1.2 Chirality on the phosphorus donor moieties

Besides developing PCP-pincer complexes bearing the chiral information on the benzylic-C atoms, the development of complexes with the stereogenic centers at the P-donors is also of interest. Since the binding pocket of square-planar PCP-complexes is quite deep, phosphorus-bound substituents are in close proximity of a potential substrate and thus maybe expected to exert a large discriminatory effect on incoming substrates. The groups of Van Koten and Morales-Morales have independently prepared the C_2-symmetric pincer palladium, platinum, ruthenium, and iridium complexes **6** - **9** with sterically demanding P-substituents.[11, 12, 13]

As described in Scheme 3, the racemic monophosphorus compound *tert*-butyl(phenyl)phosphane-borane can be enantioselectively deprotonated by *n*-BuLi in the presence of (-)-sparteine in diethyl ether *via* a thermodynamic dynamic resolution process as reported by Livinghouse *et al*.[14] Reacting the resulting lithiophosphide with 1,3-bis(bromomethyl)benzene or 1,3-bis(bromomethyl)-2-bromobenzene afforded the borane protected P-chiral bisphosphine pincer ligands in good yields and excellent enantioselectivities.[11] In contrast, reacting the racemic monophosphorus compound methyl(phenyl)phosphane-borane in the same manner with 1,3-bis(bromomethyl)benzene merely afforded an equimolar mixture of diastereoisomers under the same reaction conditions. This is presumably the result of a difference in steric congestion between the lithium methyl-phosphide-sparteine complex and the *tert*-butyl-phosphide-sparteine complex.[11] Moreover, the proper choice of reaction solvent is also crucial for obtaining high enantioselectivity, since replacing diethyl ether by THF led to the complete loss of enantioselectivity. After removal of the borane groups, P-chiral bisphosphine pincer ligands **10** and **11** were further reacted with different metal precursors under appropriate conditions to yield the corresponding metal complexes.[6-9]



Scheme 3. Synthesis of P-chiral PCP-pincer complexes.

Van Koten reported that palladation of ligands **10** and **11** can be alternatively carried out by using a C-H activation mode in the presence of $[Pd(MeCN)_4(BF_4)_2]$ or an oxidative insertion mode in the presence of $[Pd_2(dba)_3]$. Complex **6a** and **6b** were obtained in low isolated yields

after recrystallization (15–19%). Morales-Morales *et al.* reacted ligand **10** with [$PdCl_2$(COD)] in refluxing toluene for 5 h and obtained complex **6a** in an excellent 98% isolated yield.[13] Pincer platinum complex **7** was similarly prepared by using an oxidative insertion mode in the presence of [Pt_2(*p*-tolyl)$_4$(μ-SEt_2)$_2$] in moderate yield (*i.e.*, 49%).[11]

Furthermore, P-chiral PCP-pincer Ru complex **8** can be synthesized in a reasonable yield (60%) through a transcyclometalation reaction (TCM) in which the NCN-pincer ruthenium complex [RuCl{2,6-(Me_2NCH_2)$_2$$C_6H_3$}($PPh_3$)] is used as metal source as documented by Van Koten *et al.* (Scheme 3).[12] This procedure benefits from a very facile purification, since the free NCN-pincer ligand 2,6-(Me_2NCH_2)$_2$$C_6H_4$ is the only by-product which is highly soluble in common apolar solvents.

The P-chiral PCP-pincer Ir complex **9a** was synthesized by Morales-Morales *et al.* in good yield (83%) by treating [Ir(μ-Cl)(COE)$_2$]$_2$ with two equivalents of ligand **10** at refluxing temperature in toluene for 24h (Scheme 3).[13] Further reacting complex **9a** with an excess of superhydride [$LiB(C_2H_5)_3H$] in a hydrogen atmosphere (1 bar) at room temperature afforded the tetrahydride complex **9b** in excellent isolated yield (98%).

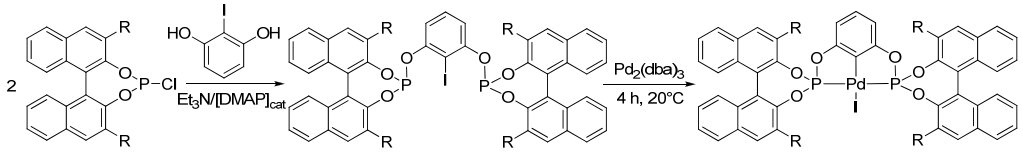
1.2.2 Asymmetric electron-deficient PCP-pincer phosphite or phosphoramidite complexes.

Although some examples of chiral biphosphine PCP-pincer complexes have been documented, the oxygen-sensitivity of phosphine donors and their tedious synthesis, as well as the poor flexibility of the chiral pockets rather restricts the development of these chiral pincer complexes and their applications in asymmetric catalysis. Besides employing chiral phosphines as the chiral building blocks, optically active diols have proven to be very suitable starting materials for the synthesis of enantiopure phosphites, phosphonites and phosphoramidites. Reacting optically active diols with PCl_3 results in the formation of the corresponding chiral phosphorochloridites, which can subsequently be combined with aryl-1,3-diols or aryl-1,3-diamines in the assistance of appropriate base to afford the corresponding chiral pincer ligands in good yields. Due to the air-resistance of electron-deficient phosphite and phosphoramidite P-donors, isolation and purification of the resulting chiral ligands is much more convenient in contrast to those of the chiral phosphine-based PCP-ligands.

1.2.2.1 BINOL-derived PCP-pincer palladium complexes.

Szabó *et al.* firstly reported the synthesis of a series of *γ*-functionalized 1,1'-bi-2-naphthol-based chiral PCP-pincer palladium complexes **12** - **17** (Scheme 4).[15, 16] The key chiral building

blocks **24** - **29** were prepared by reacting the corresponding γ-functionalized 1,1'-bi-2-naphthol with PCl_3. Without further purification, **24** - **29** were combined with 2-iodobenzene-1,3-diol in the presence of Et_3N and a catalytic amount of DMAP (*N,N*-dimethylpyridin-4-amine) to give the pre-ligands **18** - **23** in good yields. Electron-deficient chiral pincer complexes **12** - **17** were prepared in 18 - 89% isolated yields by oxidatively inserting zerovalent Pd species into the aryl-iodine bonds under very mild conditions (4 h, 20 ºC). According to the crystal structure of *R,R*-**12**, the authors claimed that the substitution of the γ-position on the BINOL moieties may change the steric congestion around the metal center and may increase the enantioselectivity of these pincer complex in catalysis.



R-**24**: R=H
R-**25**: R=Cl
S-**26**: R=Me
R-**27**: R=SMe
S-**27**: R=SMe
R-**28**: R=SEt
R-**29**: R=SPh

R,R-**18**: R=H
R,R-**19**: R=Cl
S,S-**20**: R=Me
R,R-**21**: R=SMe
S,S-**21**: R=SMe
R,R-**22**: R=SEt
R,R-**23**: R=SPh

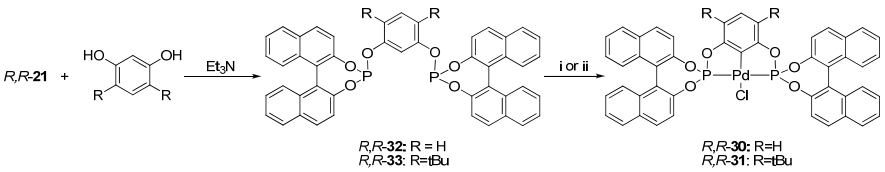
R,R-**12**: R=H
R,R-**13**: R=Cl
S,S-**14**: R=Me
R,R-**15**: R=SMe
S,S-**15**: R=SMe
R,R-**16**: R=SEt
R,R-**17**: R=SPh

Scheme 4. Synthesis of BINOL derived pincer complexes *via* an oxidative addition mode.

Bedford *et al*. independently reported the related BINOL-derived pincer ligands **32** and **33** and their palladation *via* a C-H activation mode (Scheme 5).[17] In contrast to the synthesis of chiral phosphite pincer complexes *via* an oxidative addition mode documented by Szabó *et al*. (*vide supra*), the synthesis of phosphite pincer complexes *via* a C-H activation mode at the 2-position of the parent phosphite ligands is not as facile as that of the phosphine or phosphinite PCP-pincer complexes.[18, 19]

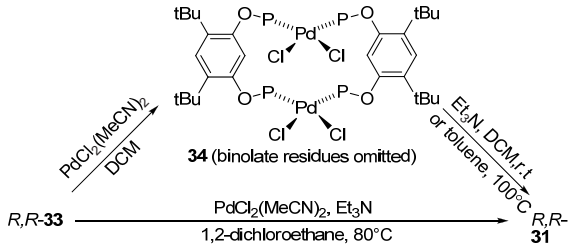
As described in Scheme 5, the thermal reaction of ligand **32** with $[PdCl_2(PhCN)_2]$ in a range of solvents for a short period (< 1 day) merely gave insoluble polymeric species rather than the desired monomeric pincer complex **30**. Upon extending the reaction time to 6 days at refluxing temperature in dichloroethane, the desired complex *R,R*-**30** was formed by eventual dissolution of the polymeric material. In contrast, the reaction rate can be dramatically increased by using microwave heating, and complex *R,R*-**30** can be obtained in good yield within 1 h. The authors furthermore reasoned that the introduction of two *t*Bu groups at the 4- and 6-positions of resorcinol could not only increase the rate of orthometallation, but also that these sterically demanding substituents could limit the rotation around the C-O and P-O bonds. Thus, this could prevent the formation of insoluble polymer species, would be prevented by means of the ligand adopting a bridging mode instead of the formation of oligomeric species. Indeed, heating ligand

33 and $[PdCl_2(MeCN)_2]$ in 1,2-dichloroethane at 80 ºC in the presence of Et_3N for 2 h led to the direct formation of complex *R,R*-**31** in reasonable yield (51%).



Scheme 5. Synthesis of BINOL derived pincer complexes *via* a C-H activation mode. Reaction conditions and reagents: i) For complex *R,R*-**30**: $[PdCl_2(PhCN)_2]$, 1,2-dichloroethane, refluxing 6 days or microwave 1 h; ii) For complex *R,R*-**31**: $[PdCl_2(MeCN)_2]$, 1,2-dichloroethane, Et_3N, 80 ºC, 2 h.

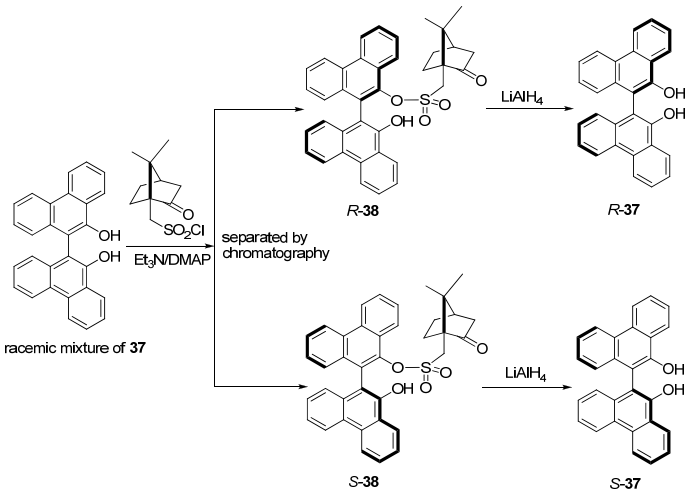
Actually, these authors have also reported the quantitative formation of the dimeric complex **34** by reacting ligand *R,R*-**33** with $[PdCl_2(MeCN)_2]$ in DCM at room temperature. Further treatment of complex **34** with Et_3N in DCM at room temperature or heating in toluene at 100 ºC smoothly afforded complex *R,R*-**31** in a comparable yield to directly converting *R,R*-**33** to *R,R*-**31**.



Scheme **6**. Synthesis of *R,R*-**31** through dimeric complex **34**.

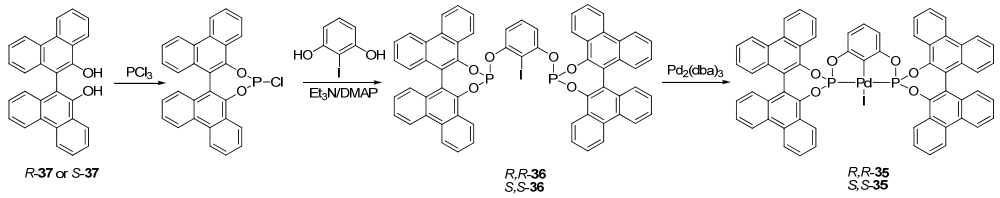
1.2.2.2 Biphenanthrol-derived PCP-pincer palladium complexes.

Besides the great variety of BINOL-derived pincer complexes, Szabó *et al.* described the synthesis of enantiopure biphenanthrol-derived pincer complexes *S,S*-**35** and *R,R*-**35** in moderate overall yields (*i.e.*, ≈30%).[16] As shown in Scheme 7, the literature procedures to access enantiopure biphenanthrol *R*-**37** and *S*-**37** were modified and improved. The racemic mixture of biphenanthrol **37** was reacted with (1*S*)-(+)-10-camphorsulfonyl chloride in the presence of Et_3N and a catalytic amount of DMAP to afford a mixture of diastereomeric monoesters *R*-**38** and *S*-**38**. These monoesters could easily be separated by column chromatography over silica gel in promising yields (*i.e.*, 43% for each diastereoisomers). The subsequent removal of the camphorsulfonyl groups was carried out by reducing the diastereoisomers with lithium aluminum hydride.



Scheme 7. Synthesis of the enantiomers of biphenanthrol.

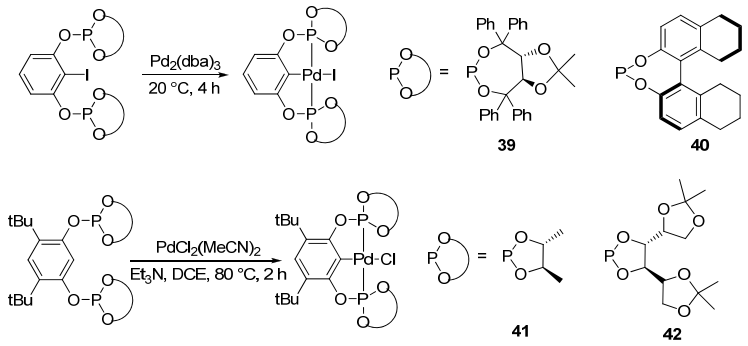
Afterwards, following the same synthetic approach as for the BINOL-derived pincer complexes, enantiopure biphenanthrol-derived pincer complexes *R,R*-**35** and *S,S*-**35** were prepared in promising yields (60%) by reacting the prepared enantiopure ligands *R*-**37** and *S*-**37** with $Pd_2(dba)_3$ (Scheme 8).



Scheme 8. Synthesis of biphenanthrol-derived pincer complexes.

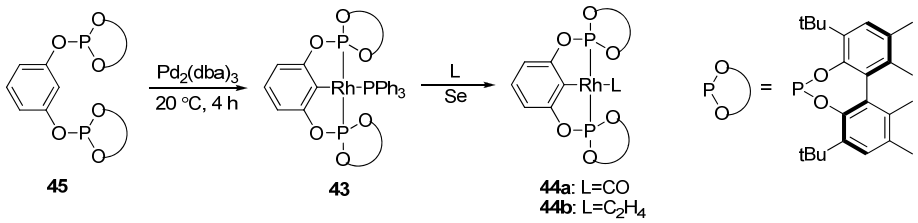
1.2.2.3 PCP-pincer complexes derived from other chiral diols.

Szabó's and Bedford's groups also reported several examples of chiral phosphite pincer Pd complexes bearing other chiral diols rather than BINOL and bisphenanthrol, such as TADDOL, *8H*-BINOL, (*2R*,*3R*)-(-)-2,3-butanediol and (D)-mannitoldiol, which were prepared in the same fashion as their corresponding analogues (complexes **39 - 42** in Scheme 9).[15, 17, 20]



Scheme 9. Synthesis of chiral phosphite Pd complexes **39 - 42**.

In 2007, Pizzano *et al*. reported the synthesis of the first phosphite PCP-pincer rhodium complex **43** in good isolated yield (*i.e.*, 85%) by reacting the pre-ligand **45** with $[RhCl(PPh_3)_3]$ at refluxing temperature in THF for 24 h and subsequently stirring the reaction mixture with Et_3N for another 24 h.[21] The co-ligand PPh_3 in complex **43** is labile and can be readily replaced by other ligands such as CO and C_2H_4. Complex **44a** can be rapidly formed by exposing complex **43** to an atmosphere of CO. The addition of Se to form $P(Se)Ph_3$ can afford the complex **44a** in quantitative yield. Complex **44b** bearing C_2H_4 as co-ligand can be prepared in the same fashion (Scheme 10).



Scheme 10. Synthesis of chiral phosphite PCP-pincer Rh complexes.

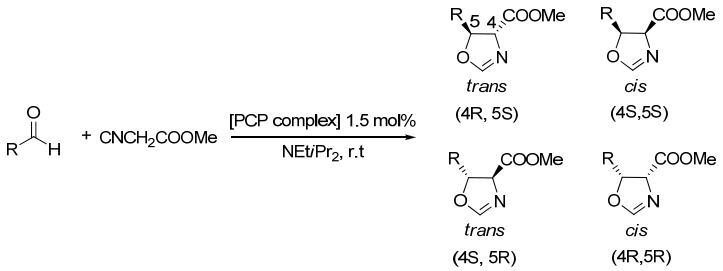
According to the crystal structure of complex **44b**, the authors claimed that the coordinated C_2H_4 moiety in complex **44b** displays an unusual *in-plane* (*ip*) conformation rather than an *upright* (*u*) conformation which has been almost exclusively observed for square-planar complexes.[21]

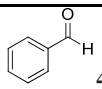
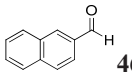
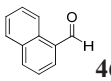
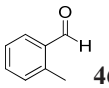
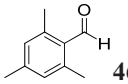
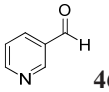
1.3 Applications of chiral PCP-pincer complexes in asymmetric catalysis.

1.3.1 Asymmetric condensation of aldehydes and isocyanoacetate

The aldol reaction of aldehydes and isocynaoacetates affording oxazoline derivatives is one of the important applications of pincer Pd complexes. The oxazolines obtained in these reactions can be hydrolyzed to non-natural α-aminoacids. The potential formation of enanotiopure α-aminoacids by this process has stimulated the development of asymmetric condensation reactions by using chiral pincer complexes.[7, 9, 22, 24] The use of chiral pincer complexes for this type of reaction was first reported by Venanzi *et al.* by using the triflate salt [Pt(CF_3SO_3)(PCP)] (**2a**) derived from complex **2** as the catalyst in the reaction of aldehydes with methyl α-isocyanoacetate into oxazolines.[8] The labile triflate anion affords a coordination site, which is available for the binding of the isocyanoacetate. A base is necessary to initialize the formation of the intermediate isocyano enolate, thus the authors employed NEt*i*Pr_2 as the base. Zhang *et al.* also examed the catalytic activities of the triflate salts [Pd(CF_3SO_3)(PCP)] (**1a**) and [Pt(CF_3SO_3)(PCP)] (**4a**) derived from complexes **1** and **4**, respectively, in the very same reactions. Pd complex **1a** was proven to be much more active than Pt complex **4a**, although their structures are quite smiliar.[9] In order to compare these works, the most representative results are summarized in Table 1. It was found that both complex **1a** and **2a** are active not only towards aromatic aldehydes but also towards hetereoatom-containing and aliphatic aldehydes (Table 1. entries 11-14). Interestingly, Venanzi *et al.* found that non-coordinative CH_2Cl_2 was the optimized solvent, whereas Zhang *et al.* claimed that coordinative THF was the optimized one for their catalytic system. Generally, complexes **1a** and **2a** can catalyze the formation of the desired oxazoline products in good to excellent isolated yields with the *trans*-isomers as the major products and with moderate to promising diastereoisomeric selectivities. Nevertheless, these two complexes showed very different enantioselectivities for each isomer. For example, when complex **2a** was used as the catalyst, *ee*'s for the *trans*-isomers are generally much higher than those of the *cis*-isomers (the only exception was found for aldehyde **46e**; Table 1. entry 10). In contrast, when complex **1a** was used as the catalyst, a completely opposite trend was observed, *i.e.* the *ee*'s of the *cis*-products are higher. This is most likely due to subtle differences in the structures of the chiral pockets of Pd-complex **1a** as compared to Pt-complex **2a**.

Table 1. Condensation of methyl α-isocyanoacetate and aldehydes.[a]



entry	aldehyde	catalyst	Yield [%][b]	*trans*/*cis* [%][c]	*ee trans* [%][d]	*ee cis* [%]
1[e]	 **46a**	**1a**	87	78/22	31	77
2		**2a**	96	70/30	65	3
3	 **46b**	**1a**	81	81/19	23	66
4		**2a**	95	69/31	52	6
5	 **46c**	**1a**	73	88/12	4	53
6		**2a**	94	87/13	54	8
7	 **46d**	**1a**	90	79/21	3	50
8		**2a**	96	85/15	61	9
9	 **46e**	**1a**	84	86/14	26	71
10[f]		**2a**	65	90/10	15	22
11	 **46f**	**1a**	80	71/29	16	61
12		**2a**	91	56/44	41	25
13	 **46g**	**1a**	97	72/28	11	74
14		**2a**	95	93/7	39	-

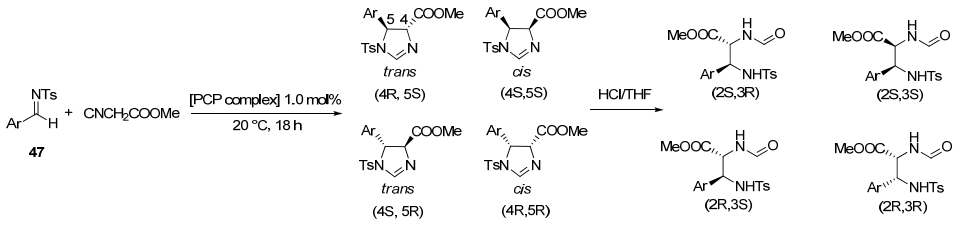
[a]: Conditions for the reactions catalyzed by complex **1a**: 0.11 mmol of aldehyde, 0.11 mmol of methyl α-isocyanoacetate, 1.0 mol% of pincer complex, 10 mol% of NEt*i*Pr$_2$, THF, 20 ºC, 20 h; Conditions for the reactions catalyzed by complex **2a**: 0.5 mmol of aldehyde, 0.5 mmol of methyl α-isocyanoacetate, 1.5 mol% of pincer complex, 12 mol% of NEt*i*Pr$_2$, CH_2Cl_2, 20 ºC, 4-18 h. [b] Isolated yield. [c] Diastereoisomeric ratio determined by ^{1}H NMR. [d] Enantiomeric excess. [e] Reaction was run at 0 ºC. [f] $ClCH_2CH_2Cl$, 50 ºC, 20 h.

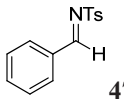
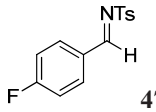
Van Koten *et al.* also investigated the catalytic activity of the tetrafluoroborate and triflate salts [**6a**(BF_4)] and [**6a**(TFA)] derived from Pd complex **6a** in the asymmetric aldol condensation of aldehyde and methyl α-isocyanoacetate.[11] The desired oxazoline product was obtained in excellent diastereoisomeric ratio (*trans*/*cis*=94/6～98/2). However, the *ee* value was never found to be higher than 11%. Variation of the catalyst loading ratio, aldehyde, solvent, and base did not appreciably affect the *ee*. It is striking that the enantioselectivity is not higher than that of the other PCP-pincer Pd/Pt complexes discussed above in which the ligand-based chirality is more distant from the active site of the catalyst.

1.3.2 Asymmetric condensation of sulfonimines and isocyanoacetate

Very recently, Szabó *et al.* reported the asymmetric condensation reaction of sulfonimines **47** and methyl α-isocyanoacetate as an analogue of the previously reported condensation of aldehydes and isocyanoacetates.[25] Generally, the desired 2-imidazoline derivatives were obtained in excellent isolated yields (98%). Interestingly, in this condensation, the addition of a base is not required. As these imidazolines easily hydrolyze during HPLC analysis, all the imidazoline products were directly converted into the corresponding α,β-diaminoacids and the *ee* was determined for these moisture-stable products. As shown in Table 2, the *ee* values were very dependent on the γ-substituents of the BINOL moieties of the pincer ligand. The best enantioselectivity, 86%, was obtained by using biphenanthrol-derived pincer complex *R,R*-**35**, although its diastereoselectivity is very poor (Table 2, entry 1). Most of the pincer complexes investigated in this reaction favored the selective formation of the *trans*-isomer. A strong solvent-effect was found for both the diastereo- and the enantioselectivity. It was found that the preferential formation of *trans*-isomer with a slight decrease of the enantioselectivity occurred when diglyme was used instead of THF as the solvent (Table 2, entry 4 *vs*. entry 5).

Table 2. Condesation of methyl α-isocyanoacetate and sulfonimines.[a]



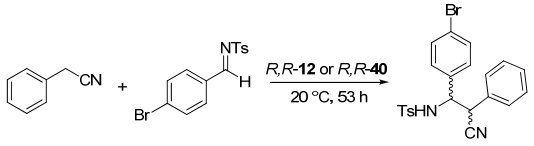
entry	sulfonimine	catalyst	Yield[b] [%]	*trans*/*cis* [%][c]	*ee trans* [%][d]	*ee cis* [%][d]
1		*R,R*-**35**	98	1:1	28	86
2[e]		*S,S*-**35**	98	4:1	75	25
3[f]		*S,S*-**35**	98	1:1	68	73
4	 **47a**	*S,S*-**35**	98	1:1	18	72
5[e]		*S,S*-**35**	98	2.5:1	62	20
6		*R,R*-**17**	98	4:1	64	37
7		*R,R*-**15**	98	2:1	46	10
8		*S,S*-**15**	98	2:1	12	44
9		*R,R*-**12**	98	4:1	46	14
10	 **47b**	*S,S*-**15**	98	2:1	7	35

[a] Reaction conditions: 0.2 mmol of **47a** or **47b**, 0.2 mmol of isocyanoacetate, 1 mol% of pincer complex, THF, 20 ºC and 18 h. [b] Isolated yield. [c] Diastereoisomeric ratio determined by ^{1}H NMR. [d] Enantiomeric excess. [e] Diglyme was used as solvent. [f] Dioxane was used as solvent.

1.3.3 Asymmetric condensation of sulfonimines and benzyl nitriles

Szabó *et al.* also presented the first transition metal catalyzed cross coupling of benzyl nitriles and sulfonimines.[20] The reaction enjoys a very broad synthetic scope and proceeds with high diastereoselectivity, especially for the *ortho*-substituted sulfonimines. This reaction provides facile access to β-aminonitriles, which are highly valuable building blocks for synthesizing pharmaceuticals and fine chemicals.[20] The authors have also preliminarily investigated the asymmetric version of this reaction with chiral phosphite pincer complexes. As shown in Scheme 11, benzyl nitrile was reacted with *para*-functionalized tosylsulfonimine in the presence of 3-5 mol% of chiral pincer complexes *R,R*-**12** or *R,R*-**40** under mild conditions. It was found that *8H*-

BINOL derived *R,R*-**40** somehow showed higher stereoselectivity and catalytic activity than BINOL derived *R,R*-**12**. Up to 71% *ee* could be obtained without the use of base. When $NaHCO_3$ was used, the reaction became faster; however, the *ee* was slightly decreased by 7%.

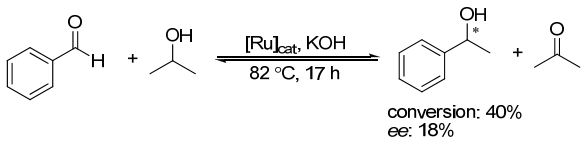


	yield	*dr.*	ee_{trans}	ee_{cis}
R,R-**12**	32%	1:1	4%	69%
R,R-**40**	99%	1.3:1	33%	71%

Scheme 11. Preliminary study of the asymmetric coupling of benzyl nitrile with a sulfonimine.

1.3.4 Asymmetric hydrogen transfer reaction of acetophenone

Van Koten and co-workers reported that NCN- and PCP-pincer Ru complexes are highly active catalysts in hydrogen transfer reductions of ketones. For example, PCP-pincer Ru complex $[Ru(OSO_2CF_3)\{C_6H_3(CH_2\text{-}PPh_2)_2\text{-}2,6\}(PPh_3)]$ can catalyze the reduction of cyclohexanone with a TOF up to 27 000 h^{-1}.[26] Accordingly, the P-chiral PCP-Ru complex **8** was tested as pre-catalyst in the asymmetric hydrogen transfer reactions of acetophenone (Scheme 12).[12] It was found that Ru complex **8** merely induced a modest chirality transfer (*ee* 18%) with low conversion (40%). Apparently, the chiral pocket of the catalyst precursors allows for transfer of dihydrogen to both faces of the substrate equally well. On the other hand, epimerization at the stereogenic P-centers under the reaction conditions could not be completely excluded. These preliminary results showed that P-chiral PCP-pincer Ru complex **8** is much less active in comparison with achiral PCP-pincer Ru complex $[RuCl\{C_6H_3(CH_2\text{-}PPh_2)_2\text{-}2,6\}(PPh_3)]$, which could be due to the bulky tBu substituents that could induce a considerable steric hindrance in contrast to phenyl groups of the non-chiral complex. Importantly, the observed chiral induction could be lost upon extending the reaction time since this hydrogen transfer reaction is reversible.

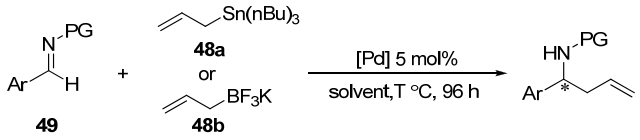


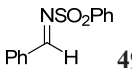
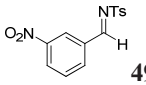
Scheme 12. Asymmetric hydrogen transfer reduction of acetophenone.

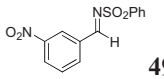
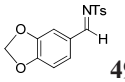
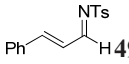
1.3.5 Asymmetric allylation reactions

Szabó *et al*. reported that pincer palladium complexes can catalyze the electrophilic allylic substitution of allylstannanes or trifluoro(allyl)borate with aldehyde and imine substrates. It was found that the catalytic activities of the pincer complexes is highly dependent on ligand effects.[27-29] In general, the electron-deficient pincer metal complexes with weakly coordinating counterions give a higher reactivity in these reactions. The key intermediate of the electrophilic substitution reaction, an η^1-allyl-coordinated pincer complex, was characterized by ^{1}H NMR spectroscopy. Density functional theory (DFT) modeling showed that the electrophilic attack can be accomplished with a low activation barrier at the γ-position of the η^1-allyl moiety.[27-29] In consideration of these features, the strategy for pincer Pd complex-catalyzed asymmetric allylation of imines or aldehydes are based on the application of electron-deficient chiral pincer complexes.

Table 3. Asymmetric allylation of sulfonimines in the presence of chiral pincer complexes.[a]



entry	allyl	imine	Cat.	Temp./time [ºC / h]	solvent	*ee* [%]	Yield [%][b]
1	**48a**		*R,R*-**12**	20/72	DMF	20	70
2	**48a**		*R,R*-**12a**	20/16	DMF	5	90
3	**48a**		*R,R*-**13**	20/72	DMF	34	65
4	**48a**		*R,R*-**14**	20/90	DMF	59	74
5	**48a**		**39**	20/72	DMF	5	60
6	**48a**	 **49a**	*R,R*-**15**	6/66	DMF	73	49
7	**48a**		*R,R*-**15**	20/94	DMSO	71	57
8	**48a**		*S,S*-**15**	20/94	DMSO	74	53
9	**48a**		*R,R*-**16**	20/94	DMSO	67	44
10	**48a**		*R,R*-**17**	20/94	DMF	48	70
11	**48b**		*R,R*-**15**	20/96	DMSO	60	66
12	**48b**		*S,S*-**15**	20/96	DMSO	54	68
15	**48a**	 **49b**	*S,S*-**15**	20/68	DMF	66	85

entry	allyl	imine	Cat.	Temp./time [ºC / h]	solvent	*ee* [%]	Yield [%][b]
16	**48a**	**49b**	*R,R*-**35**	20/94	DMF	85	71
17	**48a**	 **49**	*R,R*-**35**	20/68	DMF	82	78
18	**48a**	**49a**	*S,S*-**35**	20/91	DMF	83	28
19	**48a**	**49a**	*S,S*-**35**[c]	20/91	DMF	80	50
20	**48a**	 **49i**	*R,R*-**15**	20/116	DMF/THF (1:1)	48	55
21	**48a**	 **49j**	*S,S*-**15**	6/66	DMF	59	53

[a] Isolated yield. [b] 10 mol% catalyst was used.

As shown in Table 3, preliminary catalytic results indicated that the use of electron-deficient chiral pincer complexes (5 mol%) bearing bulky substituents gives a high catalytic activity in the allylation of **49a** with tributylallylstannane **48a** (Table 3, entries 1-5)[15] and the desired product was obtained in 60 - 90% isolated yields. It was found that the trifluoroacetate salt *R,R*-**12a** derived from *R,R*-**12** could significantly shorten the reaction time (Table 3, entry 1 *vs.* entry 2), although the stereoselectivity dramatically dropped to 5% (Table 3, entry 2). On the other hand, the substituents of the *γ*-position of the BINOL moiety considerably increased the stereoselectivity. For example, *γ*-Me and *γ*-Cl functionalized pincer complexes gave 59 and 34% *ee*, respectively, which are obviously higher than that of complex *R,R*-**12** (20%). TADDOL-based complex **39** showed a similar activity as BINOL-derived complexes, albeit that the enantioselectivity of this complex is very poor (Table 3, entry 5). In 2007, Szabó's group further reported a series of *γ*-SR (R=Me, Et, Ph) functionalized pincer complexes,[16] and the investigation of these complexes in the asymmetric allylation indicated that enantioselectivity can not be simply increased by replacing the thiomethyl group with more bulky substituents (Table 3, entries 6 – 10). Moreover, as the availability of *R*- and *S*-BINOL building blocks of complexes *R,R*-**15** and *S,S*-**15** is similar, the enantioselectivity of this reaction can be thoroughly controled by choosing the appropriate pincer complexes (Table 3, entries 7 and 8). Interestingly, potassium trifluoro(allyl)borate **48b** can readily react with sulfonimine **49a** to afford the allylic product in slightly higher yields, nevertheless, the enantioselectivity was somehow decreased (Table 3, entries 7 and 8 *vs* entries 11 and 12).

Besides BINOL-derived pincer complexes, these authors also investigated the catalytic activity and stereoselectivity of biphenanthrol-derived pincer complexes *R,R*-**35** and *S,S*-**35**, since the previous DFT calculations[29] suggested that substituents at the *δ*-position or simultaneous substitution of both the *γ*- and *δ*-positions of the BINOL system would improve the stereoselectivity. Actually, it was found that the enantioselectivity can be further increased up to 85% *ee* by using these complexes (Table 3, entries 16 -19). On the other hand, although these biphenanthrol-derived complexes can achieve higher stereoselectivities, their catalytic activities are inferior in comparison with BINOL-derived complexes. The product yield could be improved either by using 2-fold higher catalyst loading (10 mol%) or by employing activated sulfonimines such as **49b** and **49c** (Table 3, entry 15 – 19).

In 2006, Bedford *et al.* independently reported the asymmetric allylation of benzaldehyde and tributylallylstannane **48a** by employing complexes *R,R*-**30**, *R,R*-**31**, **41** and **42** as catalysts.[17] It was found that complex *R,R*-**31** can catalyze this allylation reaction to give 1-phenyl-but-3-en-1-ol in 78% conversion with 54.5% *ee*, when the reaction was carried out in THF at 0 ºC. Both the yield and *ee* can be improved to 80% and 62%, respectively, when CH_2Cl_2 was used as the solvent. Surprisingly, the structurally similar complex *R,R*-**30** merely gave 18% yield and 6% *ee* in this reaction, which showed that the ^{t}Bu groups on the resorcinol backbone play a significant role in allocating the binolate residues around the active metal centre. Complexes **41** and **42** were proven to be poorly active and gave no enantioselectivity in this allylation. It is worth pointing out that the non-orthometallated dimeric complex **34** is able to achieve 63% *ee*, which is as good as the complex **31**, but with a significantly lower conversion (23%).

1.3.6 Other reactions

In 2002, Morales-Morales *et al.* reported the application of P-chiral phosphine pincer Pd complex **6a** as a catalyst in the hydrosilylation of styrene, the allylic alkylation of PhCH(OAc)CH=CHPh and $CH_2(CO_2Me)_2$, along with Heck coupling reactions of phenyl triflate and 2,3-dihydrofuran. However, none of these reactions gave substantial *ee*'s.[13]

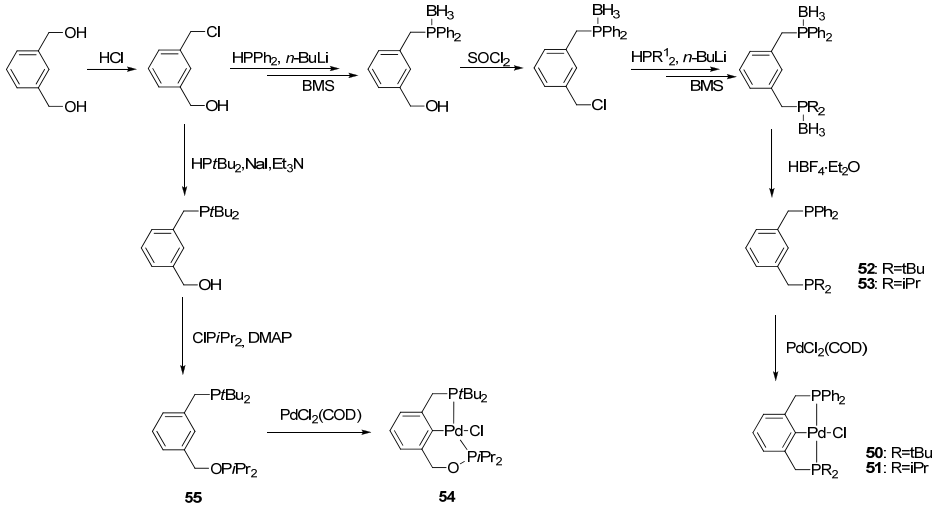
1.4. Synthesis of PCE-pincer (E = N, P', S) complexes and their applications in organic transformations

Whilst a few synthetic routes have been documented, the highly tunable and flexible synthesis of PCE-pincer complexes still remains a challenge and often is laborious and tedious. Therefore, many efforts have recently been taken by several independent research groups.

1.4.1 PCP'-pincer (P ≠ P') Pd complexes

1.4.1.1 1,3-benzenedimethanol as synthon

PCP'-type pincer Pd complexes (P ≠ P') were firstly documented by Jensen's group.[30, 31] As shown in Scheme 13, reacting 1,3-benzenedimethanol with concentrated HCl can selectively convert one of the two benzyl hydroxy groups into a benzyl chloride group in quantitative yield (100%). $SOCl_2$ can also be used for this conversion but the selectivity and yield are much lower (44%). Afterwards, the first phosphine substituent was regioselectively incorporated *via* the prepared benzyl chloride moiety, and the phosphine donor was subsequently protected with a borane group. The second benzyl hydroxy group was then converted into a benzyl chloride moiety by using $SOCl_2$ as the chlorination reagent. Afterwards, the second phosphine substituent was coupled with the aromatic backbone through an analogous manner as the first one. Removing the borane protecting group by $HBF_4 \cdot Et_2O$ led to phosphine pincer ligands **52** and **53** in good yields. Palladation of these pincer ligands was performed by heating the pincer ligands with $[PdCl_2(COD)]$ in toluene at refluxing temperature for 5 h, and the desired PCP'-pincer Pd complexes **50** and **51** were obtained in good yields (70 - 75%) after purification.



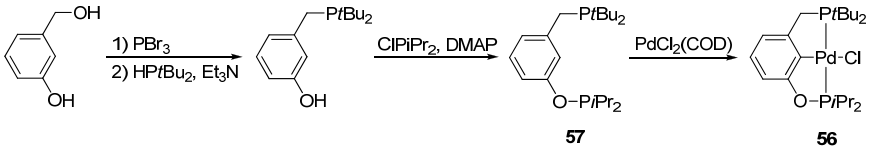
Scheme 13. Synthesis of PCP' pincer complexes starting from 1,3-benzenedimethanol.

On the other hand, the reaction of (3-(chloromethyl)phenyl)methanol with $HPtBu_2$ in acetone in the presence of NaI under reflux lead to the incorporation of the first phosphine substituent in good yield (89%) after the addition of Et_3N. Phosphinite chloride $ClPiPr_2$ was reacted with the remaining benzyl hydroxy group in the presence of DMAP to furnish the air and moisture sensitive pincer ligand **55**, which was subsequently reacted with $[PdCl_2(COD)]$ in toluene at refluxing temperature to afford PCP'-pincer complex **54** in 72% isolated yield. Remarkably,

complex **54** possesses one five-membered chelate ring and one six-membered chelate ring along the C−Pd σ-bond.

1.4.1.2 3-(hydroxylmethyl)phenol as synthon

Jensen *et al.* also reported on the synthesis of a PCP'-pincer complex with 3-(hydroxymethyl)phenol as the starting material. As shown in Scheme 14, PBr_3 was selectively reacted with the benzyl hydroxy group of 3-(hydroxymethyl)phenol to furnish a benzyl bromide group, which was further reacted with $HPtBu_2$ in the presence of Et_3N in order to introduce the first phosphine substituent. Afterwards, a phosphinite substituent was incorporated by reacting $ClPiPr_2$ with the aryl hydroxy group in the presence of DMAP, and the new PCP'-pincer ligand **57** was then obtained in 81% yield. Refluxing this ligand with $[PdCl_2(COD)]$ in toluene afforded complex **56** in 44% yield.



57 **56**

Scheme 14. Synthesis of PCP'-pincer palladium complex **56** starting from 3-(hydroxymethyl)phenol.

1.4.1.3 Catalytic application of complexes 50 and 51

Interestingly, the structurally related complexes **50** and **51** showed very different catalytic activities in the Heck reaction of aryl halides and styrene. Complex **51** (5 mol% loading) was inactive in the coupling of bromo- or chlorobezene and styrene, but afforded 80% conversion when iodobenzene was taken as the substrate. In contrast, complex **50** did not exhibit any detectable activity towards any of the halo-benzenes, even upon increasing the catalyst loading to 8 mol%. The bulky ^{t}Bu groups probably create significant steric congestion around the metal center, which could hamper its accessibility for substrates.

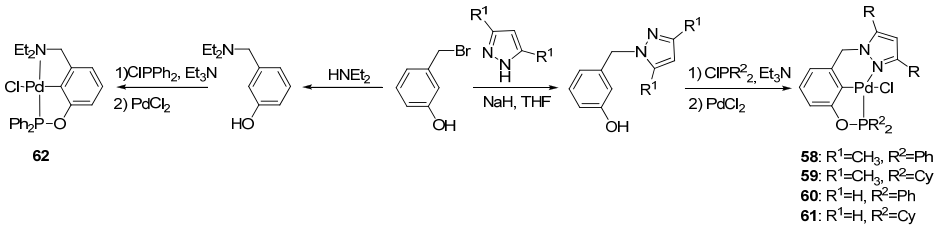
1.4.2 PCN-pincer metal complexes

1.4.2.1 PCN-pincer Pd complexes

1.4.2.1.1 3-(bromomethyl)phenol as synthon

In 2007, Song and co-workers reported on the efficient preparation of a series of PCN-pincer Pd complexes **58** - **62** starting from 3-(bromomethyl)phenol.[32] As shown in Scheme 15, the benzyl bromide moiety of 3-(bromomethyl)phenol can be readily reacted with an amine like

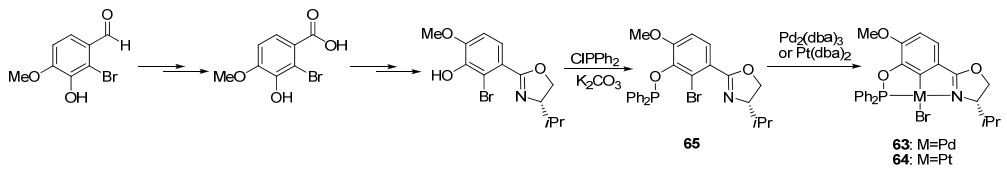
$HNEt_2$, pyrazole, or 3,5-dimethylpyrazole to afford the amine or pyrazolyl *m*-phenol derivatives. These were subsequently reacted with different phosphine chlorides in the presence of Et_3N in refluxing toluene to furnish the PCN-pincer ligands. Without purification, the crude ligands were refluxed in the presence of $PdCl_2$ to obtain a series of PCN-pincer Pd complexes **58-62** in 54 - 72% isolated yields after column chromatography over silica gel. It is worth pointing out that in complexes **58-61**, pyrazoyl moieties lead to the formation of six-membered chelate rings next to five-member rings including the C−Pd σ-bond. Thus, the Pd atoms in these complexes adopt a quite distorted-square-planar configuration.



Scheme 15. Synthesis of PCN-pincer complexes starting from 3-(bromomethyl)phenol.

1.4.2.1.2 Isovanillin as synthon

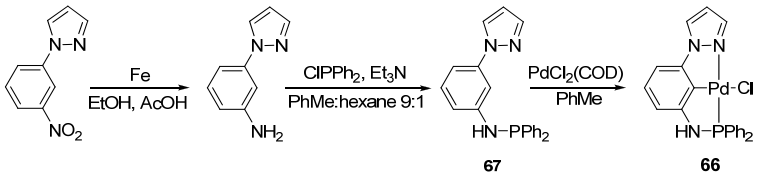
In 2006, Nishiyama *et al.* reported the PCN-pincer Pd and Pt complexes **63** and **64**, which were synthesized from commercially available isovanillin (Scheme 16). 2-bromoisovanillic acid was prepared by bromination and oxidation of isovanillin in 67% yield. The aryl hydroxyl group was protected prior to further organic transformations. An S-valinol derived chiral oxazolinyl N-donor functinality was incorporated through stepwise synthesis.[33] 3-acetoxy-2-bromo-isovanillic acid was reacted with thionyl chloride and subsequently with (S)-valinol in the presence of triethylamine. The oxazolinyl ring was formed *via* methanesulfonyl chloride-promoted cyclization. After removal of the acetyl protecting group, the diphenylphosphinite P-donor functionality was introduced to form the chiral PCN-pincer ligand **65** by reacting diphenylphosphine chloride with the aryl hydroxyl group in the presence of K_2CO_3. Oxidatively inserting zerovalent Pd or Pt species into the C−Br bond under very mild conditions (70 ºC, benzene, 2-5 h) smoothly afforded complexes **63** and **64** in 73% and 44% isolated yields, respectively.



Scheme 16. Synthesis of chiral PCN-pincer Pd and Pt complexes.

1.4.2.1.3 1-(3-nitrophenyl)-1H-pyrazole as synthon

In 2008, SanMartin *et al.* reported the synthesis of a novel PCN-pincer Pd complex starting from readily available 1-(3-nitrophenyl)pyrazole[34] *via* a rather short synthetic route (Scheme 17).[35, 36] First, the nitro group was reduced with Fe powder to give the amino functionality, which was further reacted with $ClPPh_2$ in the presence of Et_3N in a refluxing mixture of toluene and hexane. The resulting air-sensitive PCN-pincer ligand **67** was reacted with $[PdCl_2(COD)]$ in toluene at refluxing temperature for 4 h to afford the desired PCN-pincer palladium complex **66** in promising yield (64 %).



Scheme 17. Synthesis of PCN-pincer Pd complex **66**.

1.4.2.1.4 Catalytic application of complexes 58 – 62 and 66

The application of the PCN-pincer palladium complexes **58** – **62** were evaluated in Suzuki coupling reactions of phenylboronic acid with aryl halides, in particular for the more challenging aryl chlorides. As shown in Table 4, complexes **58** and **59** (1 mol%) achieved promising yields (about 75%) in the presence of K_2CO_3 for the coupling of 4-chloronitrobenzene and phenylboronic acid under very mild conditions in toluene (Table 4, entries 1-2). At elevated temperature (100 ºC) in DMF excellent yields (≧98%) were obtained with these substrates (Table 4, entries 3 and 4). Elevated temperatures probably stimulate the degradation of palladacycles Pd(II) to form the catalytically active Pd(0) species.[37] The less activated substrate 4-chlorotoluene gave only 56% product yield under the same reaction conditions, and doubling the reaction time merely improved the yield to 70% (Table 4, entries 5 and 6). Complex **62** showed an inferior performance (25%) under the same reaction conditions (Table 4, entry 7). Much higher yields were observed at 0.1 mol% catalyst loading for all of these PCN-pincer complexes when the more active bromotoluene was taken as the substrate, and complex **59** and **61** showed very similar and good catalytic activities (Table 4. entries 9 and 11).

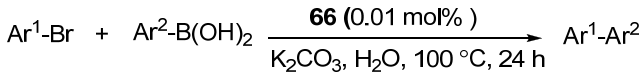
Table 4. Suzuki couplings of aryl chlorides with phenylboronic acid catalyzed by complexes **58-62**.[a]

entry	Catalyst (mol%)	Aryl halide	solvent	base	Time [h]	Temp. [ºC]	yield[b]
1	**58**(1)	4-chloronitrobenzene	toluene	K_2CO_3	24	40	73
2	**59**(1)	4-chloronitrobenzene	toluene	K_2CO_3	24	40	75
3	**58**(1)	4-chloronitrobenzene	DMF	K_3PO_4	24	100	98
4	**59**(1)	4-chloronitrobenzene	DMF	K_3PO_4	24	100	>99
5	**58**(1)	4-chlorotoluene	DMF	K_3PO_4	24	100	56
6	**58**(1)	4-chlorotoluene	DMF	K_3PO_4	48	100	70
7	**62**(1)	4-chlorotoluene	DMF	K_3PO_4	24	100	25
8	**58**(0.1)	4-bromotoluene	DMF	K_3PO_4	24	100	70
9	**59**(0.1)	4-bromotoluene	DMF	K_3PO_4	24	100	95
10	**60**(0.1)	4-bromotoluene	DMF	K_3PO_4	24	100	45
11	**61**(0.1)	4-bromotoluene	DMF	K_3PO_4	24	100	94
12	**62**(0.1)	4-bromotoluene	DMF	K_3PO_4	24	100	68

[a] Reaction conditions: aryl chloride (0.5 mmol), $PhB(OH)_2$ (0.6 mmol), catalyst, base (1.0 mmol), solvent (2 mL). [b] Isolated yields.

The catalytic activity of complex **66** was evaluated in Suzuki, Sonogashira, and Hiyama coupling reactions in neat water as a benign solvent. For the Hiyama coupling of 4-bromo-acetophenone with $PhSi(OMe)_3$, complex **66 (**2 mol%) achieved 80% isolated yield in refluxing water in the presence of NaOH within 3 h. In contrast, 4 mol% catalyst loading merely 57% isolated yield was achieved in *o*-xylene at 80 ºC for 4 h in the presence of nBu$_4$NF. For Sonogashira alkynylation reactions of various aryl iodides and phenylacetylene, complex **66** (2 mol%) showed moderate to promising yields (16 - 83%) for a wide range of functionalized aryl iodides at 50 ºC in water for 24 h in the presence of pyrrolidine. Investigations on the activity of complex **66** in Suzuki cross coupling reactions showed that this complex is quite insensitive to various bases, additives, and substrates, which definitely presented a clear advantage from a practical point of view. Substrate screening was carried out under optimized conditions and representative results are summarized in Table 5. Complex **66** furnished good to excellent yields in refluxing water in the presence of K_2CO_3, regardless of the electronic and steric features of the aryl bromides and aryl boronic acids that were tested.

Table 5. Complex **66** catalyzed Suzuki coupling reaction for the synthesis of biaryls.

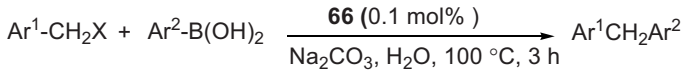


entry	Ar^1	Ar^2	Yield [%][a]
1	4-AcC_6H_4	4-$MeOC_6H_4$	>99
2	4-AcC_6H_4	Ph	>99
3	4-AcC_6H_4	4-FC_6H_4	92
4	4-AcC_6H_4	1-naphtyl	>99
5	3-$MeOC_6H_4$	4-$MeOC_6H_4$	>99
6	3-$MeOC_6H_4$	Ph	87
7	4-$MeOC_6H_4$	4-$MeOC_6H_4$	87
8	4-$NO_2C_6H_4$	Ph	>99
9	4-$NO_2C_6H_4$	4-$MeOC_6H_4$	>99

[a] Determined by ^1H NMR.

Very recently, SanMartin's group also reported complex **66** as a catalyst for Suzuki-Miyaura arylation of benzyl halides and other nonactived coupling partners.[36] Firstly, it was found that complex **66** afforded promising to good yields (38 - 90%) in the Suzuki coupling of 3-bromo-4-phenylbut-3-en-2-one and different arylboronic acids, such as $PhB(OH)_2$, 4-$MeOC_6H_4B(OH)_2$ and 1-naphtyl$B(OH)_2$ in refluxing water in the presence of Na_2CO_3 for 12 h. Encouraged by these results, the authors further investigated complex **66** in the Suzuki coupling of benzyl halides and arylboronic acids in neat water. As shown in Table 6, good yields were obtained with electronically dissimilar arylboronic acids (Table 6, entries 1 – 17). Even benzyl chloride afforded the desired coupling products in moderate yields (Table 6, entries 2, 4 and 6); nevertheless, higher pressures and a 20-fold higher catalyst loading were required. On the other hand, the reaction revealed to be vulnerable to steric effects, as the conversion was dramatically decreased to 22% (Table 6, entry 9) with 2,4,6-trimethylphenylboronic acid.

Table 6. Complex **66** catalyzed Suzuki coupling reaction for the synthesis of diarylmethanes.



entry	X	Ar^1	Ar^2	Yield[%][a]
1	Br	Ph	Ph	67
2[b]	Cl	Ph	Ph	35
3	Br	Ph	4-$OMeC_6H_4$	92
4[b]	Cl	Ph	4-$OMeC_6H_4$	51
5	Br	Ph	1-naphthyl	71
6[b]	Cl	Ph	1-naphthyl	42
7	Br	2-naphtyl	Ph	82
8	Br	2-naphtyl	4-$OMeC_6H_4$	82
9	Br	2-naphtyl	2,4,6-MeC_6H_2	22
10	Br	4-CNC_6H_4	Ph	61
11	Br	4-CNC_6H_4	4-$OMeC_6H_4$	94
12	Br	4-CNC_6H_4	1-naphthyl	84
13	Br	4-$CF_3C_6H_4$	Ph	82
14	Br	4-$CF_3C_6H_4$	4-$OMeC_6H_4$	86
15	Br	4-$CF_3C_6H_4$	1-naphthyl	99
16	Br	4-$CH_3C_6H_4$	Ph	73
17	Br	4-$CH_3C_6H_4$	4-$OMeC_6H_4$	59

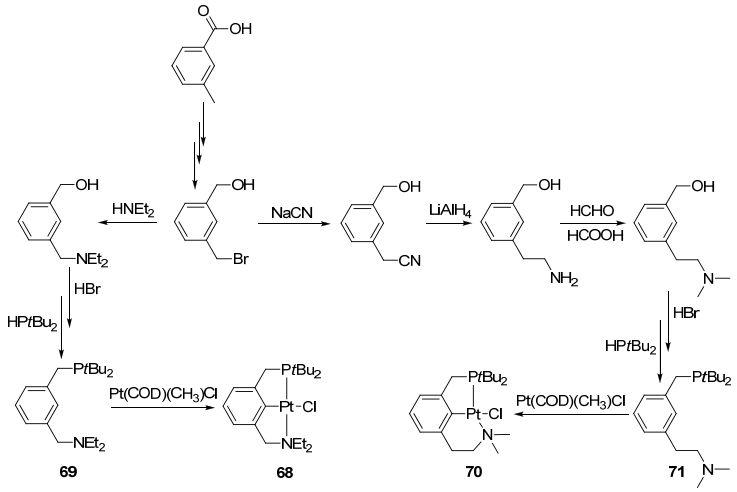
[a] Determined by ^1H NMR. [b] 2 mol% of **66** was used and the reactions were carried out in sealed tubes.

1.4.2.2 PCN- Pincer Pt and Rh complexes

1.4.2.2.1 3-(bromomethyl)benzyl alcohol as synthon

Milstein and co-workers independently reported on the development of two PCN-pincer Pt complexes **68** and **70**.[38, 39] PCN-pincer ligand **71** was prepared from 3-(bromomethyl)benzyl alcohol, which was stepwise synthesized by esterification, bromination, and reduction of 3-(methyl)benzoic acid (Scheme 18). The resulting 3-(bromomethyl)benzyl alcohol was treated with a slight excess of sodium cyanide to yield 3-(cyanomethyl)benzyl alcohol, which was subsequently reduced with $LiAlH_4$ to give 3-(aminoethyl)benzyl alcohol. This alcohol was methylated to give 3-(dimethylaminoethyl) benzyl alcohol, and which was reacted with an aqueous solution of HBr at room temperature to yield its HBr salt. Treatment of this salt with 2.4

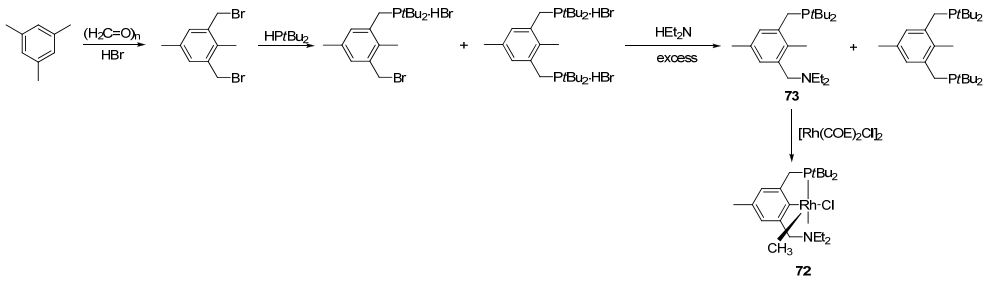
equivalents of tBu$_2$PH yielded ligand **71** in 63% yield. PCN-pincer ligand **69** was obtained in an analogous fashion, yet the *N,N'*-diethylamine donor functionality was incorporated by directly reacting an excess of HNEt$_2$ with 3-(bromomethyl)benzyl alcohol. Heating the resulting ligands **69** and **71** with [Pt(COD)CH$_3$Cl] in THF at refluxing temperature for 30 min efficiently afforded the desired PCN-pincer Pt complexes **68** and **70** in 90% and 87% isolated yields, respectively. Much like complexes **58-61** reported by Song *et al.* (vide supra), complex **70** possesses both a six-membered chelate ring and a five-membered chelate ring along the C-Pt σ-bond, while complex **68** comprises two five-member rings along the C-Pt σ-bond.



Scheme 18. Synthesis of PCN-pincer Pt complexes **68** and **70**.

1.4.2.2.2 1,3-bis(bromomethyl)-2,5-dimethylbenzene as synthon

In 1997, Milestein *et al.* reported on the synthesis of a new PCN-type of pincer ligand and the first PCN-pincer Rh complex.[40a] As shown in Scheme 19, PCN-pincer ligand **73** was prepared starting from bis(dibromomethyl)mesitylene, which was obtained by bromomethylation of mesitylene. Reacting the resulting dibromide adduct with 1.0 equiv of HPtBu$_2$ yielded a mixture of mono- and diphosphonium salts, which was further treated with a 10-fold excess of diethylamine. The separation of the resulting PCN-pincer ligand **73** and the diphosphine PCP-pincer ligand was achieved by column chromatography over a silica column. Heating ligand **73** with [Rh(COE)$_2$Cl]$_2$ (COE=cyclooctene) quantitatively furnished the PCN-pincer Rh complex **72** *via* a C–C activation mode after 5 h at room temperature or after 15 min at 45 °C (Scheme 19). Remarkably, the tetrafluoroborate salt of complex **72** exhibits a unique medium effect, *i.e.,* reversible coordination of the bulky counteranion or solvent stabilizes the metal center as a function of temperature.[40b]

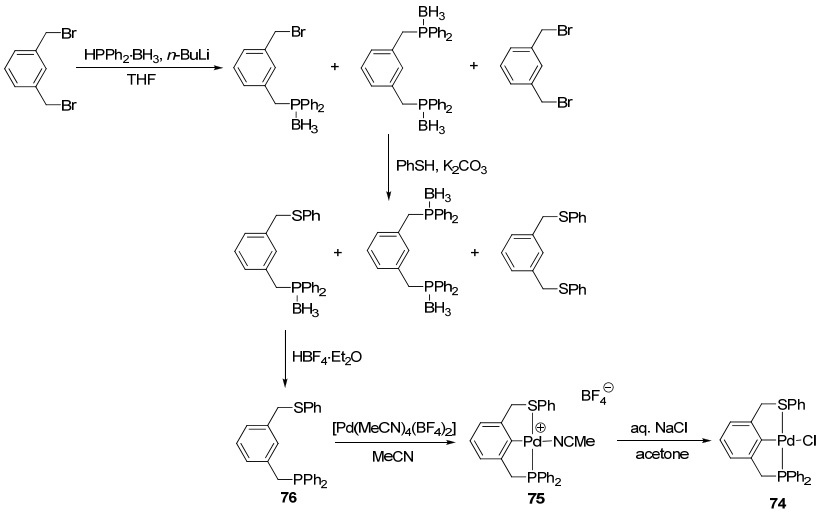


Scheme 19. Synthesis of PCN-pincer Rh complex **72**.

1.4.3 PCS-pincer complexes

1.4.3.1 α,α'-dibromo-m-xylene as synthon

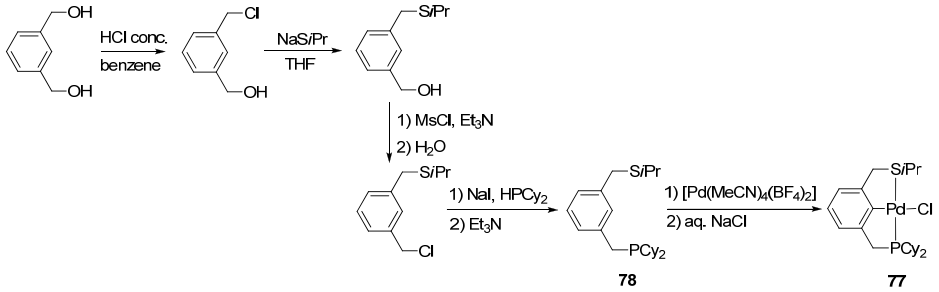
Recently, Klein Gebbink and co-workers developed a variety of PCS- and PCN-pincer complexes through a flexible and tunable synthetic approach. PCS-pincer Pd complexes **74** and **75** were synthesized in 70 - 95% yields starting from commercially available α,α'-dibromo-m-xylene.[41] Treatment of α,α'-dibromo-m-xylene with an equimolar amount of *in-situ* prepared $LiPPh_2 \cdot BH_3$ at low temperature (-78 ºC) in THF yielded a mixture containing monophosphine, diphosphine, and unreacted starting material. Without purification, the mixture was further reacted with PhSH in the presence of K_2CO_3 to convert all remaining benzylic bromide functonalities into thioethers. Thereafter, separation of borane-protected PCS-pincer ligand from the mixture was achieved in 51% isolated yield by using column chromatography over silica gel. After removing the borane group with $HBF_4 \cdot Et_2O$, the air-sensitive PCS-pincer ligand **76** was obtained in 74% yield (Scheme 20). Palladation of **76** was carried out in MeCN at room temperature in the presence of $[Pd(MeCN)_4(BF_4)_2]$, which gave the cationic PCS-pincer complex **75** in 70% isolated yield. The labile acetonitrile ligand could be easily replaced by Cl by stirring complex **75** in an acetone/water solution of excess NaCl to give complex **74** in quantitative yield.



Scheme 20. Synthesis of PCS-pincer Pd complexes **74** and **75**.

1.4.3.2 α,α'-dihydroxy-m-xylene as synthon

An improved procedure for the preparation of analogous PCS-pincer complexes was shortly reported by the same group.[42] By taking advantage of the selective monochlorination of 1,3-benzenedimethanol with concentrated HCl in benzene, the two different donor substituents can be introduced *via* stepwise transformations (Scheme 21). PCS-pincer ligand **78** was obtained in 45% overall yield based on 1,3-benzenedimethanol. Palladation of **78** was again carried out with $[Pd(MeCN)_4(BF_4)_2]$ to give complex **77** in 81% isolated yield.



Scheme 21. Synthesis of PCS-pincer complex **77**.

1.4.3.3 Catalytic application of complexes 74 and 75

The catalytic activity of complexes **74** and **75** in organic transformations were evaluated in the aldol condensation of isocyanoacetate and benzaldehyde along with a tandem catalytic transformation for the preparation of homoallylic products.[41] In the aldol condensation, PCS-complex **74** showed a higher reaction rate (TOF up to 75 h^{-1}) than the parent SCS-pincer complex

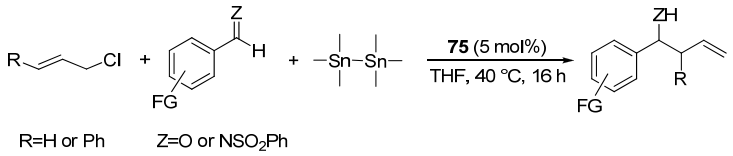
[PdCl{$C_6H_3(CH_2PPh_2)_2$}] and PCP-pincer complex [PdCl{$C_6H_3(CH_2SPh)_2$}], and gave a comparable diastereoisomeric product ratio as the SCS-pincer complex (*trans*:*cis* = 57:43). The catalytic results in this aldol condensation showed how the nature of the pincer ligand donor functionality can affect the reactivity of the corresponding metal complexes.

The catalytic activity of PCS-pincer complex **75** was subsequently evaluated in a tandem catalytic reaction of allyl chlorides, hexamethyldistannane and aldehydes or aldimines.[41] Klein Gebbink and Szabó proposed a plausible catalytic cycle which includes C–Sn and C–C formation processes. The first catalytic process is the formation of allylstannane from allyl chloride and hexamethyldistannane (C–Sn formation). The second catalytic process involves two major steps: 1) the resulting allylstannane undergoes transmetalation with the pincer Pd-complex to form a $^1\eta$-allylpalladium intermediate; and 2) the electrophile (aldehyde or aldimine) attacks the γ-position of the $^1\eta$-allylpalladium moiety to furnish the desired homoallylic product (C–C formation).

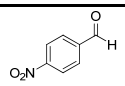
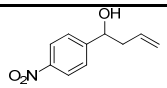
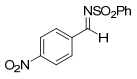
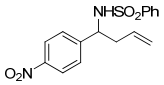
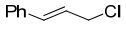
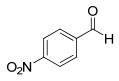
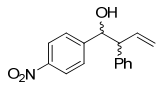
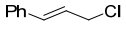
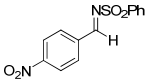
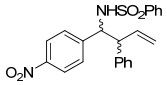
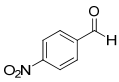
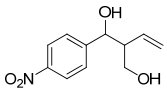
In this catalytic system, the PCS-complex **75** combines the attractive catalytic features of the symmetric SCS- and PCP-pincer complexes. Firstly, it showed a high catalytic activity in the stannylation reaction in which ECE-pincer Pd-complexes bearing electron-enriched heteroatom donors (*e.g.*, E = N, S or Se) show a high catalytic activity.[43] Secondly, it also showed a remarkable catalytic activity in the homoallylation of electrophiles, in which ECE-pincer Pd-complexes comprising electron-deficient heteroatom donors (*e.g.*, E = P) normally exhibit good catalytic activity.[15-17, 27, 28, 44]

In the tandem reaction, a catalytic amount of PCS-complex **75** (5 mol%) afforded very promising to good products yields (59 - 78%) under mild reaction conditions for both aldehyde and aldimine substrates (Table 7). Interestingly, when cinnamyl chloride was used, it was found that the *trans*-isomer was favored for the alcohol product and a completely opposite trend was observed for sulfonamine product (Table 7, entries 3 and 4). Remarkably, vinyloxirane was found to be an alternative allyl functionality source in the stannylation process in the presence of catalytic amount of LiOAc and H_2O. The coupling reaction of aldehyde with vinyloxirane leads to the formation of an unprotected homoallyl diol, which is a useful synthetic intermediate. It is worth pointing out that this reaction is the first example of a palladium-catalyzed coupling of a vinyloxirane with an aldehyde to afford homoallylic alcohols (Table 7, entry 5).

Table 7. Tandem catalytic reactions in the presence of complex **75**.



R=H or Ph Z=O or NSO_2Ph

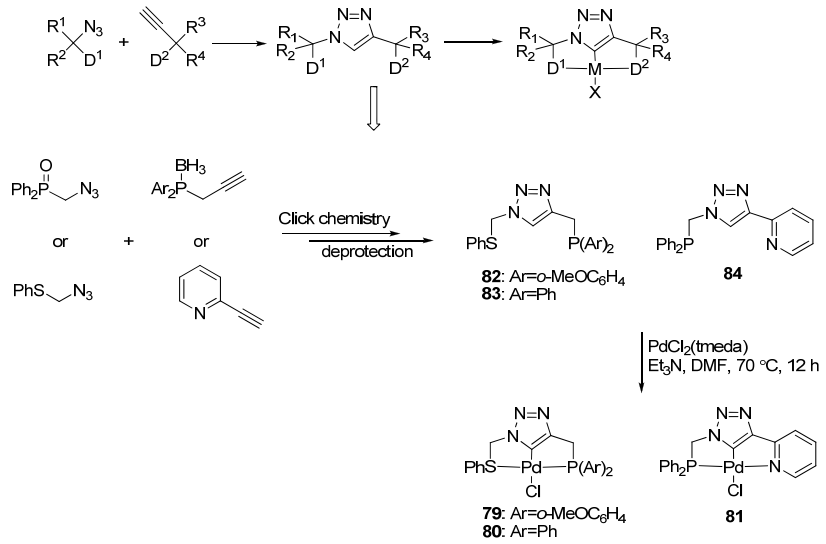
entry	allyl reagent	electrophile	product	Yield[%][a]	dr[b]
1				63	-
2				78	-
3				59	3:1
4				60	1:5
5				57	3:1

[a] Isolated yields. [b] Diastereoisomeric ratio: *trans*/*cis*.

1.4.4 Click-pincer complexes

1.4.4.1 Synthesis of click-pincer complexes

In 2008, Gandelman *et al.* developed an entirely different synthetic route to prepare a broad range of pincer ligands *via* so-called "click chemistry".[45] The authors conceived that using the Huisgen dipolar cycloaddition of azides and alkynes to yield triazoles could result in the selective and facile combination of two complementary monomeric donor functionalities D^1 and D^2 to form a pincer-type adduct D^1CD^2. This resulting molecular structure possesses a potential carbanion site between two donor functionalities, which is ready to form ECE-pincer type metal complexes (Scheme 22).



Scheme 22. Synthesis of PCN- and PCS-pincer complexes *via* "click-chemistry".

To this end, a number of azido- and alkynyl-based monomers were prepared and these compounds smoothly underwent Cu(I)-catalyzed [2+3] cycloaddition reactions under typical "click" conditions (CuSO4, Na ascorbate, THF/H_2O, 23 ºC, 24 h) to yield the three PCN- and PCS-pincer ligands **82-84** in good overall yields (up to 80%). Heating these pincer ligands with [$PdCl_2$(tmeda)] in DMF at 70 ºC for 24 h led to the formation of the anticipated PCN- and PCS-pincer Pd complexes **79-81**. This unprecedented approach benefits from several advantages. First, the employment of Sharpless "click" conditions allows for a broad functional group tolerance, high yields, and easy purification of the products. Secondly, this approach affords a flexible and straightforward synthetic route to access pincer ligands D_1CD_2, in which the donor functionalities can be easily varied by choosing different azido- or alkylnyl-based compunds. Moreover, the triazole unit in the backbone leads to the formation of an entirely new family of terdentate-ligand pincer complexes, which could be an interesting alternative to the traditional aryl-based framework.

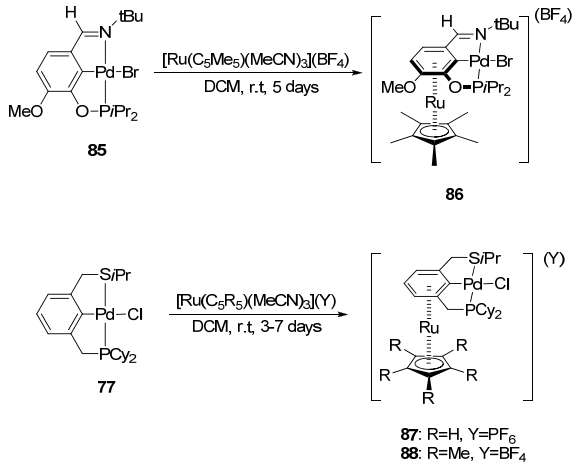
1.4.4.2 Catalytic application of complexes 79 – 81

The catalytic activities of the resulting pincer complexes were evaluated in the Heck reaction of methylacrylate with bromobenzene in DMF at 140 ºC in the presence of Na_2CO_3 for 48 h.[43] Complexes **79-81** showed high turnover numbers (TON) of 6900, 42 000, 125 000, respectively. This preliminary screening of the click-pincer reveals that the PCN-pincer complex **81** is more efficient for the Heck reaction with aryl bromides. Taking account of the TON, the substantially

lower activity of the PCS-pincer complexes **79** and **80** implies that the catalytic performance is highly dependent on the combination of different donor moieties.

1.5 Development of planar-chiral pincer complexes

Planar-chiral complexes rely on the ability of transition metals to bind the π electrons of dissymmetrically substituted five-[46] or six-membered aromatic rings[46a, 47]. In 2009, Klein Gebbink and co-workers firstly reported on the synthesis and attempt of chiral resolution of a series of planar-chiral PCE-pincer (E = N or S) metal complexes.[42] The authors employed the ECE'-pincer complexes **77** and **85** as the precursors; these possess two different donor functionalities exclusively carrying aliphatic substituents. At room temperature in dry DCM, complexes **77** and **85** were subjected to η^6-coordination by using 1.1 equivalent of $[Ru(C_5R_5)(MeCN)_3](BF_4)$ (R=H or Me). As η^6-coordination can take place from either side of the arene plane of the PCE-pincer complex, two enantiomers of the heterobimetallic η^6,η^1-complex were formed (Scheme 23).



Scheme 23. Synthesis of racemic planar-chiral pincer complexes.

In order to demonstrate the planar-chiral nature of complexes **87** and **88**, the achiral PF_6^- and BF_4^- counter-anions were exchanged for an enantiomerically pure chiral counter-anion, namely [Δ-TRISPHAT]$^-$.[48] [**87**][Δ-TRISPHAT] and [**88**][Δ-TRISPHAT] were obtained in 46% and 63% yield respectively *via* a two-fold anion exchange process. ^{31}P NMR spectra of [**87**][Δ-TRISPHAT] and [**88**][Δ-TRISPHAT] in $CDCl_2$ showed two well-resolved singlets in a 1:1 ratio for the coordinated P-ligand, whereas under the same conditions [**87**](Cl) and [**88**](Cl) gave one singlet. Remarkably, [**88**][Δ-TRISPHAT] crystallized as a single enantiomer of the cation [**88**]$^+$,

which is supposed to result from complementary **π-π** stacking between the [Δ-TRISPHAT]$^-$ counter-anion and the η^6,η^1-arene ring of the cation. This finding could lead to the chiral resolution of complexes [**86**]$^+$-[**88**]$^+$ on a larger scale.

1.6 Concluding remarks

In summary, we reviewed the synthesis of the P-donor containing asymmetric PCP-pincer metal complexes and PCE-pincer metal complexes reported up to date. In the earlier years, the synthesis of asymmetric PCP-pincer metal complexes often suffered from tedious synthesis and low yields, but more flexible and tunable synthetic strategies were recently developed by several research groups, which has made the synthesis of such complexes more straightforward and versatile. The applications of these pincer complexes as catalysts were reported for several organic transformations such as asymmetric aldol condensation, asymmetric transfer hydrogenation, asymmetric homoallylation, Heck reaction, Suzuki coupling, and tandem catalytic stannylation/allylation. In general, they showed very promising to good catalytic activities or stereoselectivities. It was found that, in several cases, PCE-pincer metal complexes bearing two different heteroatoms as donor functionalities presented better catalytic activities in comparison with the analogous PCP-pincer complexes bearing unique donor atoms. Furthermore, different combinations of heteroatoms can also lead to changes in catalytic activities, which implies that the selection of the proper combination of heteroatoms as donor functionalities could result in pincer-type catalysts that are more active or more selective than currnetly reported systems. This review also shows that in view of the rapid development of pincer metal chemistry over the last years, the synthesis and application of both asymmetric PCP-pincer as well as of PCE-pincer metal complexes is still in its infancy.

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Chapter 2

P'CP'-Pincer palladium complex catalyzed allylation of *N,N*-dimethylsulfamoyl-protected aldimines

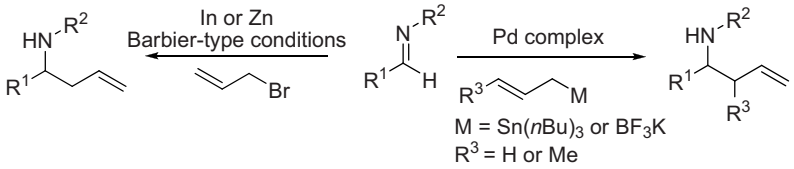
Abstract

The P'CP'-pincer palladium complex-catalyzed allylation of *N,N*-dimethylsulfamoyl-protected aldimines with allyl(tributyl)stannane is investigated for the preparation of *N*-homoallylic sulfamides. The desired *N,N*-dimethylsulfamoyl-protected products are obtained in moderate to high yields in DMF under very mild conditions and a high yielding and convenient deprotection of the *N,N*-dimethylsulfamoyl group is demonstrated.

2.1 Introduction

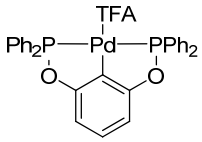
The development of novel methods to generate new carbon-carbon bonds is important for the preparation of compounds of interest from pharmaceutical, biological or advanced materials points of view, and belongs to the core of modern organic chemistry.[1] In particular, the allylation of imines has attracted increasing attention because of its importance for the preparation of nitrogen-containing compounds.[2, 3]

To date, numerous indium and zinc mediated allylic additions of imines under typical Barbier-type conditions have frequently been reported (Scheme 1).[4, 5] The synthesis often benefits from low toxicity, tolerance towards air and moisture and high yields.



Scheme 1. Allylation of aldimines.

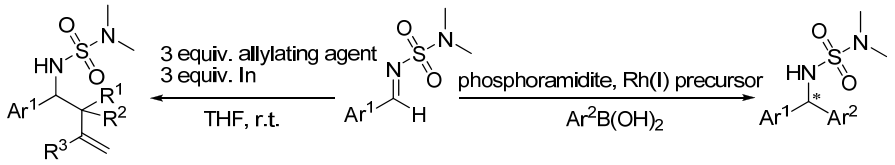
In addition, an alternative procedure involving a palladium-catalyzed reaction in which the η^1-allylpalladium intermediate generated reacts with electrophilic substrates (Scheme 1) has been reported.[6, 7] This reaction proceeds via a very different catalytic cycle compared to Babier-type metal-mediated allylations. First, allylstannanes or trifluoro(allyl)borates undergo a transmetalation reaction with the P'CP'-pincer palladium complex [**PdTFA(P'CP')**] (Figure 1).[8, 9] Subsequently, the resulting nucleophilic η^1-allylpalladium intermediate reacts with electrophilic aldehydes or aldimines to afford the corresponding allyl product. Szabo and co-workers reported the [**PdTFA(P'CP')**]-catalyzed allylation of tosylimines in the presence of allylstannane or trifluoro(allyl)borates showing high yields and a wide substrate scope.[6, 7] One drawback of this protocol is that removal of the tosyl protecting groups is not always straightforward, even under quite harsh conditions (*i.e.* liq. NH_3/Li or NH_3/Na), and suffers from limited functional group tolerance.[10, 11, 12] To overcome this problem and to improve the practicability of the allylation procedure, an easily removable protecting group is highly desirable. In this letter, the [**PdTFA(P'CP')**]-catalyzed allylation of *N,N*-dimethylsulfamoyl protected aldimines is described as an alternative.



[PdTFA(P'CP')]

Figure 1. [**PdTFA(P′CP′)**] complex.

Recently, Minnaard and co-workers presented the *N,N*-dimethylsulfamoyl group as an inexpensive and low-molecular-weight protecting/activating group for Rh(I)-catalyzed asymmetric arylation of aldimines and described an efficient method for its removal using a microwave assisted procedure.[13] Encouraged by these results, we extended this research to the Barbier-type allylation for the preparation of *N*-homoallylic sulfamides in high yields with different allyl bromides in THF as the optimal solvent (Scheme 2).[14] Interestingly, Minnaard found that even by simple conventional heating, the *N*-homoallylic sulfamides could be deprotected. So far, the latter procedure has been applied to only one substrate.



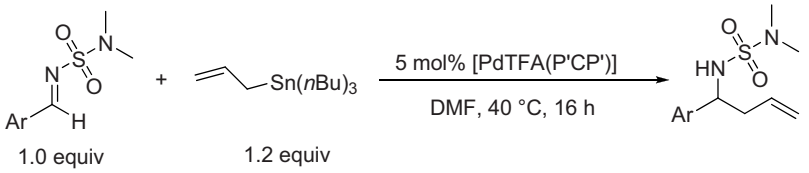
Ar^1 = Ph, R^1 = R^2 = R^3 = H, 90%
Ar^1 = Ph, R^1 = R^2 =H, R^3 = Me, 87%
Ar^1 = Ph, R^1 =Me, R^2 = R^3 = H, 89%
Ar^1 = Ph, R^1 = R^2 = Me, R^3 = H, 63%

Scheme 2. Applications of *N,N*-dimethylsulfamoyl-protected aldimines.

In the present study we demonstrate how the scope of this reaction can be extended by using the [**PdTFA(P'CP')**]-catalyzed allylation of a series of *N,N*-dimethylsulfamoyl-protected aldimines.

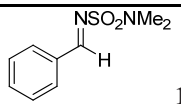
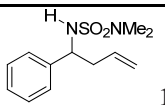
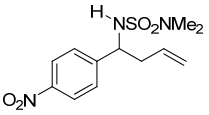
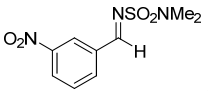
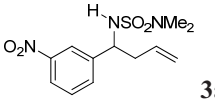
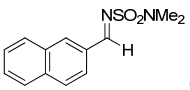
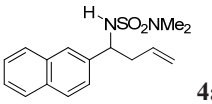
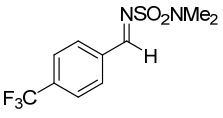
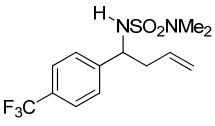
2.2 Results and discussion

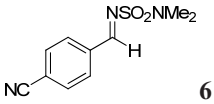
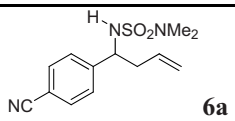
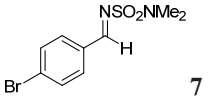
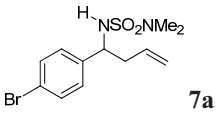
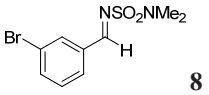
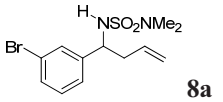
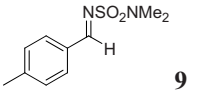
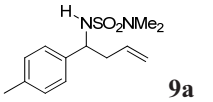
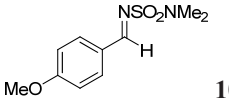
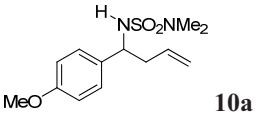
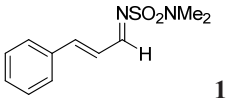
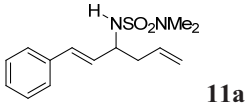
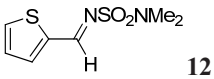
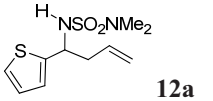
Using the typical reaction conditions reported by Szabo and co-workers,[7] 1 equiv of aldimine was reacted with 1.2 equiv of allylstannane in the presence of 5 mol% of [**PdTFA(P'CP')**] at 40 °C in DMF for 16 h (Scheme 3). After completion, the reaction mixture was quenched with saturated aqueous KF solution (1 mL) and the resulting mixture was stirred at room temperature (16 h) to remove toxic organic tin residues.[15] The products were extracted from the solution with ethyl acetate (3 x 2 mL) and were subjected to flash column chromatography to isolate analytically pure products.[16]



Scheme 3. Pincer complex catalyzed allylation of *N,N*-dimethylsulfamoyl-protected aldimines.

Table 1. [**PdTFA(P'CP')**]-catalyzed allylation of various aldimines with allyl(tributyl)stannane.

Entry	Substrate	Product	Yield (%)[a]
1	 **1**	 **1a**	81
2	 **2**	 **2a**	85
3	 **3**	 **3a**	93
4	 **4**	 **4a**	85
5	 **5**	 **5a**	80

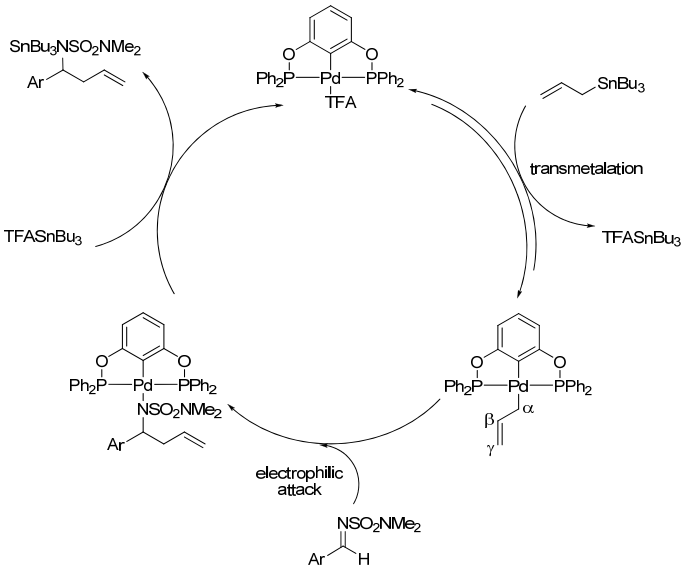
Entry	Substrate	Product	Yield (%)[a]
6	 **6**	 **6a**	80
7	 **7**	 **7a**	96
8	 **8**	 **8a**	80
9	 **9**	 **9a**	85
10	 **10**	 **10a**	60
11	 **11**	 **11a**	68
12	 **12**	 **12a**	70

[a] : Isolated yield (average of two runs). Reagents and conditions : 0.1 mmol of aldimine, 0.12 mmol of allyl(tributyl)stannane, 0.005 mmol of [**PdTFA(P'CP')**], 0.5 mL of DMF, 40 °C, 16 h.

These experiments show that *N,N*-dimethylsulfamoyl-protected aldimines can be allylated smoothly under mild conditions in moderate to excellent yields (data shown are those of the isolated, purified products) and show good functional group tolerance (Table 1). For benchmark substrate **1**, the corresponding homoallylic product **1a** was obtained in a good yield of 81%. Similarly, substrates **2**, **3**, **5** and **6** bearing various electron-withdrawing *para*-substituents were converted into the corresponding homoallylic products in 80-93% yield. The presence of weakly electron-donating functional groups in substrates **4** and **9** did not result in any loss of reactivity and both afforded the respective products **4a** and **9a** in 85% yield. In contrast, the yield was considerably lower for substrate **10** bearing the stronger electron-donating methoxy group. Remarkably, halogenated substrates **7** and **8** gave the desired products in good yields without loss

of the bromine atoms, that is, no products from palladium-catalyzed C-Br activation were observed. Undoubtedly, this is an attractive feature of this approach allowing further modification, that is, tandem reactions[17] *via* cross-coupling reactions using a different metal catalyst. Furthermore, successful transformation of the halogenated substrates strongly indicates that no Pd leaching from [**PdTFA(P'CP')**] occurs, for example, by decomposition, as otherwise, the formed active Pd(0) species could insert oxidatively into the C-Br bond affording undesired by-products. Moreover, cinnamylaldimine **11** and 2-thienylaldimine **12** were also converted into the corresponding homoallylic products (entries 11 and 12).

It is worth mentioning that the isolated yields obtained in this study are generally 10-15% lower than those of the tosyl-protected aldimines.[7] This is most likely due to the presence of the strongly electron-donating Me_2N group instead of the *p*-tolyl group which decreases the electrophilicity of corresponding aldimine. In particular, for the electron-enriched substrates (entries 10 and 11), both conversion and yield were lower in comparison with the corresponding tosyl-protected aldimines.

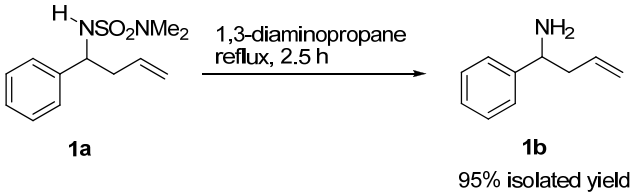


Scheme 4. Mechanism of [PdTFA(P'CP')]-catalyzed allylation of *N,N*-dimethylsulfamoyl-protected aldimines.

On the basis of the catalytic cycle proposed by Szabo and Yao[6, 9, 15], the [**PdTFA(P'CP')**]-catalyzed allylation of *N,N*-dimethylsulfamoyl aldimines can be depicted stepwise as shown in Scheme 4 : (1) Transmetalation of tri(*n*-butyl)allyltin with [**PdTFA(P'CP')**] and formation of an η^1-allyl-palladium complex ; (2) electrophilic attack on the γ-position of the η^1-allyl moiety by

the aldimine and formation of the Pd-coordinated homoallylic amide and (3) product exchange with the organotin salt and regeneration of the catalyst.

As a proof of concept, deprotection of *N*-homoallylic sulfamide **1a** was carried out in refluxing 1,3-diaminopropane by conventional heating in an oil bath (Scheme 5).[14] The conversion was monitored by TLC. The reaction was found to go to completion (95% yield) within 2.5 h. This result is in full agreement with previous reports[13, 14] and confirms the efficiency and reliability of this deprotection procedure.



Scheme 5. Removal of *N,N*-dimethylsulfamoyl protecting group.

2.3 Conclusion

In conclusion, [**PdTFA(P'CP')**] is shown to be an excellent homogeneous catalyst for the allylation of *N,N*-dimethylsulfamoyl-protected aldimines, affording the corresponding homoallylic products which are easily deprotected to homoallylic primary amines. The ease of deprotection and wide functional group tolerance of the C-C coupling reaction demonstrate the synthetic potential of this procedure.

2.4 Experimental section

General remarks: All reactions were performed under a dry N_2 atmosphere using standard Schlenk techniques. DMF was distilled over CaH_2 in convertional heating bath and was then stored under N_2 at –30°C. *N,N*-dimethylsulfamide was readily prepared from commercial dimethylsulfamoyl chloride and 30% aqueous ammonia.[1] All other reagents were purchased and used as received. ^{1}H-NMR (^{1}H 400.0 MHz) and ^{13}C-NMR (^{13}C 100.6 MHz) spectra were recorded at room temperature in $CDCl_3$ or d^6-acetone on a Varian INOVA spectrometer. Chemical shift values are reported in ppm (δ) relative to $(CH_3)_4Si$ (^{1}H and ^{13}C NMR). Flash chromatography was performed using ACROS silica gel , 0.06 – 0.200 mm, pore diameter ca. 6 nm. Elemental microanalyses were performed by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim a/d Ruhr, Germany.

Synthesis of *N,N*-dimethylsulfamide. According to the literature procedure,[2] 10 mL of dimethylsulfamoyl chloride was slowly added to 50 mL of 30% aqueous ammonia solution at 0℃ with vigorous stirring. The white suspension was stirred at room temperature for 2 h. Afterwards, water was evaporated off on a rotary evaporator to leave a white solid mixture, which was subsequently suspended in 150 mL of acetone. The white NH_4Cl salt was removed by filtration and the filter solution was concentrated to dryness. The resulting white solid was recrystallized from saturated aqueous NaCl solution to give a white crystalline solid, which was further dried in *vacuo* overnight. Yield: 75%. ^{1}H NMR (d^6-acetone, ppm) 2.70 (s, 6H, N*Me*$_2$), 5.90 (very br, 2H, N*H*$_2$). ^{13}C NMR (d^6-acetone, ppm) 37.9 (N*Me*$_2$) Anal. Calcd. for $C_2H_8N_2O_2S$: C, 19.35; H, 6.49; N, 22.56; Found : C, 19.40; H, 6.52; N, 22.50.

General Procedure for the synthesis of *N,N*-(dimethylsulfamoyl)arylaldimines (1-12): Substrates 1-12 were synthesized according to a literature procedure. 10 mmol of arylaldehyde and 1.27 g (10.3 mmol) of *N,N*-dimethylsulfamide were dissolved in 40 mL of toluene and water was azeotropically distilled off for 16 h using a Dean-Stark apparatus. Solvent was removed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 and filtered. After removing CH_2Cl_2 under reduced pressure, the crude products were recrystallized from isopropanol or hexanes.

1: ^{1}H NMR ($CDCl_3$, ppm) 2.89 (s, 6H, N*Me*$_2$), 7.51 (t, ^{3}J=8.0 Hz, 2H, Ar*H*), 7.63 (t, ^{3}J=9.2 Hz, 1H, Ar*H*), 7.93 (d, ^{3}J=7.6 Hz, 2H, Ar*H*), 8.90 (s, 1H aldimine *H*)

2: ^{1}H NMR ($CDCl_3$, ppm) 2.93 (s, 6H, N*Me*$_2$), 8.11 (d, ^{3}J=9.0 Hz, 2H, Ar*H*), 8.35 (d, ^{3}J=8.8 Hz, 2H, Ar*H*), 8.98 (s, 1H, aldimine *H*)

3: ^{1}H NMR ($CDCl_3$, ppm) 2.92 (s, 6H, N*Me*$_2$), 7.72 (t, ^{3}J=7.8 Hz, 1H Ar*H*), 8.23 (d, ^{3}J=7.7 Hz, 1H, Ar*H*), 8.45 (d, ^{3}J=8.0 Hz, 1H, Ar*H*), 8.80 (s, 1H, Ar*H*), 8.99 (s, 1H, aldimine *H*)

4: ^{1}H NMR ($CDCl_3$, ppm) 2.92 (s, 6H, N*Me*$_2$), 7.60 (m, 2H, Ar*H*), 7.90 (m, 3H, Ar*H*), 8.07 (d, ^{3}J=8.4 Hz, 2H, Ar*H*), 9.05, (s, 1H, aldimine *H*)

5: ^{1}H NMR ($CDCl_3$, ppm) 2.90 (s, 6H, N*Me*$_2$), 7.70 (d, ^{3}J=8.4 Hz, 2H, Ar*H*), 8.05 (d, ^{3}J=8.4 Hz, 2H, Ar*H*), 8.95 (s, 1H, aldimine *H*)

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[2] Huisman, M.; ten Have, R.; van Leusen, A. M. *Synth. Commun.* **1997**, *27*, 945–952.

6: ^{1}H NMR ($CDCl_3$, ppm) 2.91 (s, 6H, N*Me*$_2$), 7.80 (d, ^{3}J=8.0 Hz, 2H, Ar*H*), 8.04 (d, ^{3}J=8.0 Hz, 2H, Ar*H*), 8.93 (s, 1H, aldimine *H*)

7: ^{1}H NMR ($CDCl_3$, ppm) 2.88 (s, 6H, N*Me*$_2$), 7.66 (d, ^{3}J=8.0 Hz, 2H, Ar*H*), 7.79 (d, ^{3}J=8.0 Hz, 2H, Ar*H*), 8.85 (s, 1H, aldimine *H*)

8: ^{1}H NMR ($CDCl_3$, ppm) 2.89 (s, 6H, N*Me*$_2$), 7.38 (t, ^{3}J=8.0 Hz, 1H, Ar*H*), 7.73 (d, ^{3}J=8.0 Hz,1H, Ar*H*), 7.82 (d, ^{3}J=8.0 Hz, 1H, Ar*H*), 8.12 (s, 1H, Ar*H*), 8.84 (s, 1H, aldimine *H*)

9: ^{1}H NMR ($CDCl_3$, ppm) 2.45 (s, 3H, Ar*Me*), 2.85 (m, 6H, N*Me*$_2$), 7.30 (d, ^{3}J=8.1 Hz, 2H, Ar*H*), 7.81 (d, ^{3}J=8.1 Hz, 2H, Ar*H*), 8.85 (s, 1H, aldimine *H*)

10: ^{1}H NMR ($CDCl_3$, ppm) 2.86 (s, 6H, N*Me*$_2$), 3.90 (s, 3H, O*Me*), 7.00 (d, ^{3}J=8.8 Hz, 2H, Ar*H*), 7.89 (d, ^{3}J=8.8 Hz, 2H, Ar*H*), 8.81 (s, 1H, aldimine *H*)

11: ^{1}H NMR ($CDCl_3$, ppm) 2.85 (s, 6H, N*Me*$_2$), 6.98 (q, ^{3}J=9.2 Hz, 1H, ArC*H*=CH), 7.44 (d, ^{3}J=5.2 Hz, 3H, Ar*H*), 7.48 (s, 1H, ArCH=C*H*), 7.57 (m, 2H, Ar*H*), 8.64 (d, ^{3}J=9.2 Hz, 1H, aldimine *H*)

12: ^{1}H NMR ($CDCl_3$, ppm) 2.87 (s, 6H, N*Me*$_2$), 7.22 (m, 1H, thiophene *H*), 7.74 (m, 2H, thiophene *H*), 8.97 (s, 1H, aldimine *H*)

General Procedure for the palladium pincer-complex catalyzed allylation of *N,N*-(dimethylsulfamoyl)arylaldimines (1a-12a) : Corresponding aldimines **1-12** (0.1 mmol), allylstannane (0.12 mmol) and catalyst [**PdTFA(P'CP')**] (0.005 mmol) in DMF (0.5 mL) were stirred for 16 hours at 40°C. The reaction was then quenched by addition of 1 mL saturated aq. KF solution and was stirred overnight at room temperature, followed by extraction with EtOAc (3 x 2 mL). The combined organic layers were washed with brine once, then dried over $MgSO_4$ and concentrated in vacuum. The crude products were immediately subjected to silica gel chromatography using hexanes/EtOAc (7 : 3) as eluent.

1a: ^{1}H NMR ($CDCl_3$, ppm) 2.50-2.55 (m, 8H, N*Me*$_2$ + C*H*$_2$CH=CH$_2$), 4.41 (q, ^{3}J=6.8 Hz, 1H, C*H*=CH$_2$), 4.76 (d, ^{3}J=6 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.12 (m, 2H, CH=C*H*$_2$), 5.64 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7.25-7.37 (m, 5H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 37.7, 42.4, 57.7, 119.5, 126.9, 127.9, 128.8, 133.6, 141.9. Anal. Calcd. for $C_{12}H_{18}N_2O_2S$: C, 56.67; H, 7.13; N, 11.01; S, 12.61 Found : C, 56.43; H, 7.11; N, 11.05; S, 12.78.

2a: ^{1}H NMR ($CDCl_3$, ppm) 2.50-2.54 (m, 2H, C*H*$_2$CH=CH$_2$), 2.58-2.59 (m, 6H, N*Me*$_2$), 4.52 (q, ^{3}J=6.8 Hz, 1H, C*H*=CH$_2$), 5.01 (d, ^{3}J=6.4 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.13-5.18 (m, 2H, CH=C*H*$_2$), 5.60-5.70 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7.48 (d, ^{3}J=6.8 Hz , 2H, Ar*H*), 8.20 (d, ^{3}J=6.8 Hz, 2H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 37.9, 42.1, 57.1, 120.6, 124.0, 127.8, 132.5, 147.6, 149.4. Anal. Calcd. for $C_{12}H_{17}N_3O_4S$: C, 48.15; H, 5.72; N, 14.04; S, 10.71 Found : C, 48.23; H, 5.70; N, 14.11; S, 10.64.

3a: ^{1}H NMR ($CDCl_3$, ppm) 2.53-2.60 (m, 8H, N*Me*$_2$ + C*H*$_2$CH=CH$_2$), 4.54 (q, ^{3}J=6.0Hz, 1H, C*H*=CH$_2$), 4.81 (d, ^{3}J=5.2 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.17-5.21 (m, 2H, CH=C*H*$_2$), 5.63 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7.54 (t, ^{3}J=7.6 Hz, 1H, Ar*H*), 7.54 (d, ^{3}J=7.2 Hz, 1H, Ar*H*), 8.13 (d, ^{3}J=7.2 Hz, 1H, Ar*H*), 8.20 (s, 1H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 37. 8, 42.1, 57.0, 120.5, 121.8, 122.9, 129.8, 132.6, 133.2, 144.3, 148.6. Anal. Calcd. for $C_{12}H_{17}N_3O_4S$: C, 48.15; H, 5.72; N, 14.04; S, 10.71 Found : C, 48.11; H, 5.77; N, 14.40; S, 10.74.

4a: ^{1}H NMR ($CDCl_3$, ppm) 2.50 (m, 6H, N*Me*$_2$), 2.63 (t, ^{3}J=7.2 Hz, 2H, C*H*$_2$CH=CH$_2$), 4.61 (q, ^{3}J=6.4 Hz, 1H, C*H*=CH$_2$), 4.87 (d, ^{3}J=6.0 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.13-5.20 (m, 2H, CH=C*H*$_2$), 5.68-5.74 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7.43-7.51 (m, 3H, Ar*H*), 7.76 (s, 1H, Ar*H*), 7.83-7.87 (m, 3H, Ar*H*) ^{13}C NMR ($CDCl_3$, ppm) 37.7, 42.4, 57.8, 119.6, 124.7, 125.9, 126.3, 126.6, 127.9, 128.1, 128.7, 133.2,

133.4, 133.5, 139.3. Anal. Calcd. for $C_{16}H_{20}N_2O_2S$: C, 63.13; H, 6.62; N, 9.20; S, 10.53 Found : C, 63.31; H, 6.26; N, 9.25; S, 10.67.

5a: ^{1}H NMR ($CDCl_3$, ppm) 2.50-2.57 (m, 8H, N*Me*$_2$ + C*H*$_2$CH=CH$_2$), 4.46 (q, ^{3}J=6.8 Hz, 1H, C*H*=CH$_2$), 4.92 (d, ^{3}J=6.4 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.14-5.18 (m, 2H, CH=C*H*$_2$), 5.60-5.70 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7. 42 (d, ^{3}J=8.0 Hz, 2H, Ar*H*), 7.60 (d, ^{3}J=8.0 Hz, 2H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 37.8, 42.2, 57.2, 120.1, 125.7, 125.8, 129.9 (q, J=52Hz), 132.9, 146.1. Anal. Calcd. for $C_{13}H_{17}F_3N_2O_2S$: C, 48.44; H, 5.32; F, 17.68; N, 8.69; S, 9.95 Found : C, 48.40; H, 5.37; F, 17.78; N, 8.68; S, 9.99.

6a: ^{1}H NMR ($CDCl_3$, ppm) 2.47 (t, ^{3}J=7.6 Hz, 2H, C*H*$_2$CH=CH$_2$), 2.55-2.57 (m, 6H, N*Me*$_2$), 4.45 (q, ^{3}J=6.4 Hz, 1H, C*H*=CH$_2$), 5.05 (d, ^{3}J=6.0 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.11-5.16 (m, 2H, CH=C*H*$_2$), 5.59-5.65 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7.41 (d, ^{3}J=8.0 Hz, 2H, Ar*H*), 7.63 (d, ^{3}J=8.0 Hz, 2H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 37.8, 42.0, 57.4, 111.7, 118.8, 120.3, 127.8, 132.6, 147.5. Anal. Calcd. for $C_{13}H_{17}N_3O_2S$: C, 55.89; H, 6.13; N, 15.04; S, 11.48 Found : C, 55.98; H, 6.23; N, 15.00; S, 11.41.

7a: ^{1}H NMR ($CDCl_3$, ppm) 2.47 (t, ^{3}J=6.8 Hz, 2H, C*H*$_2$CH=CH$_2$), 2.54 (s, 6H, N*Me*$_2$), 4.35 (t, ^{3}J=6.4 Hz, 1H, C*H*=CH$_2$), 4.90 (d, ^{3}J=6.0 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.11-5.15 (m, 2H, CH=C*H*$_2$), 5.59-5.70 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7.17-7.20 (m, 2H, Ar*H*), 7.46 (d, ^{3}J=8.0 Hz, 2H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 32.6, 37.0, 52.0, 114.6, 123.5, 123.8, 126.7, 126.7, 135.9. Anal. Calcd. for $C_{12}H_{17}BrN_2O_2S$: C, 43.25; H, 5.14; Br, 23.98; N, 8.41; S, 9.62 Found : C, 43.35; H, 5.24; Br, 23.78; N, 8.56; S, 9.77.

8a: ^{1}H NMR ($CDCl_3$, ppm) 2.47-2.54 (m, 8H, N*Me*$_2$ + C*H*$_2$CH=CH$_2$), 4.35 (q, ^{3}J=6.4 Hz, 1H, C*H*=CH$_2$), 4.85 (d, ^{3}J=6.0 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.13 (s, 1H, CH=C*H*$_2$), 5.16 (m, 1H, CH=C*H*$_2$), 5.62-5.69 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7.17-7.26 (m, 2H, Ar*H*), 7.38 (m, 1H, Ar*H*), 7.40 (m, 1H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 37.7, 42.2, 57.1, 119.9, 122.8, 125.7, 130.0, 130.4, 131.0, 133.1, 144.4. Anal. Calcd. for $C_{12}H_{17}BrN_2O_2S$: C, 43.25; H, 5.14; Br, 23.98; N, 8.41; S, 9.62 Found : C, 43.45; H, 5.30; Br, 23.76; N, 8.59; S, 9.65.

9a: ^{1}H NMR ($CDCl_3$, ppm) 2.34 (s, 3H, ArC*H*$_3$), 2.50-2.54 (m, 8H, N*Me*$_2$ + C*H*$_2$CH=CH$_2$), 4.38 (q, ^{3}J=6.4 Hz, 1H, C*H*=CH$_2$), 4.63 (d, ^{3}J=6.0 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.11 (m, 2H, CH=C*H*$_2$), 5.64-5.71 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 7.14-7.20 (m, 4H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 21.3, 37.8, 42.5, 57.4, 119.4, 126.8, 129.4, 133.7, 137.6, 138.9. Anal. Calcd. for $C_{13}H_{20}N_2O_2S$: C, 58.18; H, 7.51; N, 10.44; S, 11.95 Found : C, 58.28; H, 7.41; N, 10.47; S, 11.75.

10a: ^{1}H NMR ($CDCl_3$, ppm) 2.50-2.53 (m, 8H, N*Me*$_2$ + C*H*$_2$CH=CH$_2$), 3.80 (s, 3H, ArO*Me*), 4.37 (q, ^{3}J=6.0 Hz, 1H, C*H*=CH$_2$), 4.52 (d, ^{3}J=5.6 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.12-5.17 (m, 2H, CH=C*H*$_2$), 5.63-5.70 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 6.86 (d, ^{3}J=6.4 Hz, 2H, Ar*H*), 7.20 (d, ^{3}J=6.4 Hz, 2H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 37.7, 42.5, 55.5, 57.1, 114.1, 119.5, 128.1, 133.7, 133. 9. Anal. Calcd. for $C_{13}H_{20}N_2O_3S$: C, 54.91; H, 7.09; N, 9.85; S, 11.28 Found : C, 54.71; H, 7.29; N, 9.87; S, 11.38.

11a: ^{1}H NMR ($CDCl_3$, ppm) 2.44-2.48 (m, 2H, C*H*$_2$CH=CH$_2$), 2.78 (s, 6H, N*Me*$_2$), 4.07-4.13 (m, 1H, C*H*=CH$_2$), 4.23 (d, ^{3}J=6.8 Hz, 1H, N*H*SO$_2$NMe$_2$), 5.18 (s, 1H, CH=C*H*$_2$), 5.22 (d, ^{3}J=6.8 Hz, 1H, CH=C*H*$_2$), 5.76-5.83 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 6.08 (q, 1H, ArCH=C*H*), 6.57 (d, ^{3}J=16.0 Hz, 1H, ArC*H*=CH), 7.20-7.40 (m, 5H, Ar*H*). ^{13}C NMR ($CDCl_3$, ppm) 31.1, 38.2, 40.6, 55.6, 119.7, 126.7, 128.1, 128.3, 128.6, 128.8, 129.5, 131.7, 136.5. Anal. Calcd. for $C_{14}H_{20}N_2O_2S$: C, 59.97; H, 7.19; N, 9.99; S, 11.44 Found : C, 59.77; H, 7.29; N, 9.97; S, 11.56.

12a: ^{1}H NMR ($CDCl_3$, ppm) 2.64-2.67 (m, 8H, N*Me*$_2$ + C*H*$_2$CH=CH$_2$), 4.62 (d, ^{3}J=6.8 Hz, 1H, C*H*=CH$_2$, N*H*SO$_2$NMe$_2$), 4.74 (q, ^{3}J=6.8 Hz, 1H, C*H*=CH$_2$), 5.16-5.23 (m ,2H, CH=C*H*$_2$), 5.68-5.78 (m, 1H, ArC*H*CH$_2$CH=CH$_2$), 6.94 (t, ^{3}J=3.2 Hz, 1H, thienyl*H*), 6.99 (d, ^{3}J=5.2 Hz ,1H, thienyl*H*), 7.22 (d,

^{3}J=5.2 Hz , 1H, thienyl*H*) ^{13}C NMR ($CDCl_3$, ppm) 39.9, 42.6, 53.5, 120.0, 124.8, 125.1, 127.0, 133.0, 145.7. Anal. Calcd. for $C_{10}H_{16}N_2O_2S_2$: C, 46.13; H, 6.19; N, 10.76; S, 24.63 Found : C, 46.33; H, 6.34; N, 10.67; S, 24.49.

The Procedure for deprotection of the *N,N*-dimethylsulfamoyl group: 0.20 mmol of aldamine **1a** in 2 mL of 1,3-diaminopropane was heated to 140 °C and refluxed for 2 hours under N_2. After cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and extracted with water (15 mL). Subsequent extraction of the water layer with CH_2Cl_2 (2 x 25 mL), drying of the combined organic layers with $MgSO_4$, and removal of the solvent under vacuum gave the product as a light yellow oil in 95% yield.

1b: ^{1}H NMR ($CDCl_3$, ppm) 1.56 (br s, 2H, NH_2), 2.36 (m, 1H, PhCH(NH_2)CH_2CHCH_2), 2.47 (m, 1H, PhCH(NH_2)CH_2CHCH_2), 3.99 (m, 1H, PhCH(NH_2)CH_2C*H*CH_2), 5.08 (m, 1H, PhCH(NH_2)CH_2CHCH_2), 5.12 (m, 1H, PhCH(NH_2)CH_2CHCH_2), 5.75 (m, 1H, PhC*H*(NH_2)CH_2CHCH_2), 7.23-7.34 (m, 5H, Ph*H*). ^{13}C NMR ($CDCl_3$, ppm) 44.4, 55.6, 117.8, 126.5, 127.2, 128.6, 135.7, 146.1.

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[16] General catalysis procedure : Aldimine **1-12** (0.1 mmol), allylstannane (0.12 mmol) and [PdTFA(P'CP')] (0.005 mmol) in DMF (0.5 mL) were stirred for 16 h at 40 °C. The reaction was then quenched by addition of 1 mL saturated aqueous KF solution and was stirred overnight at room temperature, followed by extraction with EtOAc (3 x 2 mL). The combined organic layers were washed with brine (1 x 5 mL), then dried over $MgSO_4$ and concentrated in vacuum. The crude products were immediately subject to silica gel column chromatography using hexanes/EtOAc (7 : 3) as eluent. ^{1}H and ^{13}C NMR spectral data of products **1a-12a** are available in the experimental section.

[17] Gagliardo, M.; Selander, N.; Mehendale, N. C.; van Koten, G.; Klein Gebbink, R. J. M.; Szabóm, K. J. *Chem. Eur. J.* **2008**, *14*, 4800-4809.

Chapter3

Novel Phosphite Palladium Complexes and their Application in C–P Cross Coupling Reactions

Abstract

A mono- and a 1,3-bis-phosphite arene ligand based on 2,2'-biphenol have been synthesized in order to study the synthesis of the corresponding palladium(II) complexes starting from different Pd precursors. Novel bis-phosphite palladium complex **1** $[PdCl_2(L)_2]$ (L = dibenzo[d,f][1,3,2]dioxaphosphepin, 6-phenoxy), *C,P*-chelate bonded monophosphite palladium complex **2** $[Pd(\kappa^2\text{-}L)(\mu\text{-}Cl)]_2$, and PCP-pincer palladium complex **3** have been prepared from these ligands in promising to excellent yields (50% - 95%). Additionally, complexes **1** and **3** have been characterized by X-ray crystal structure determinations. The application of 2,6-bisphosphite pincer palladium(II) complex **3** in C–P cross-coupling between diphenylphosphine borane and a wide range of aryl iodides substrates under very mild conditions is reported. Kinetic investigations indicate that pincer complex **3** merely acts as a precatalyst and that Pd nanoparticles are the actual catalytically active species.

3.1 Introduction

In the past decades, phosphine ligands,[1] as a major type of phosphorus donor ligands, have received much attention due to their excellent performance as ligands in transition metal catalyzed organic transformations.[2] The development of non-oxygen sensitive, electron-deficient phosphite ligands and their corresponding metallated complexes have become of increasing interest as supplements to phosphine ligands.[3] Phosphite ligands can be prepared from commercially available PCl_3 and a variety of different alcohols, which allows easy access to a great variety of ligands with various steric and electronic properties. For instance, Bedford *et al.* recently reported the synthesis of a series of triarylphosphite ligands $P(OAr)_3$ and their facile orthometallation with late transition metals, along with their remarkably catalytic activity in C-C bond formations.[4] Additionally, phosphite pincer complexes have been recently reported[4]. The excellent catalytic activities in Suzuki, Heck and allylation reactions[5] of these complexes stimulated the further development of phosphite-derived pincer complexes.

In this paper, 2,2'-biphenol was selected as an inexpensive and commercially available building block for the preparation of monodentate phosphite ligand **4** and bis(phosphite) pincer ligand **5** (Figure 1). The corresponding metal complexes **1** – **3** were obtained in promising to good yields by reacting ligands **4** and **5** with different metal precursors under various reaction conditions. Full details on the synthesis and structural characterization of these ligands and complexes are described here along with the catalytic properties of the complexes in C−P cross coupling reactions.

Transition metal catalyzed cross-coupling reactions are particularly important and powerful tools to realize chemical bond formations. In the past decades, vast examples of C-C, C-N, C-S and C-P cross coupling reactions have been developed by taking advantage of rationally designed ligands, appropriate transition metals and optimized reaction conditions.[6] Among the large number of documented ligands bearing a variety of diversified donors, phosphorus donor comprising ligands, especially, tertiary phosphine ligands, have held a core position in the domain of ligands design and catalysis.[7] Therefore, the development of new methodologies to easily access tertiary phosphines or their derivatives via direct P–C bond forming reactions became more and more desirable.[8] For instance, a versatile $Pd(OAc)_2$/1,1'-bis(diisopropylphosphino)ferrocene-catalyzed cross-coupling of secondary phosphines with aryl halides was developed by Buchwald and coworkers.[9] Zhao and coworkers reported an efficient copper-catalyzed approach for the P-arylation of primary and secondary organophosphorus compounds uses the commercially available and inexpensive proline and pipecolinic acid as ligands. This method provides an entry to arylphosphonates, arylphosphinates and arylphosphine

oxides.[10] To the best of our knowledge, pincer complexes have not been studied in C-P cross-coupling reactions for the preparation of tertiary phosphines, though, their remarkable catalytic performances in Heck[11], Suzuki[12] and Sonogashi[13] reactions have been carefully studied and well documented. In this paper, we report the first examples of the application of phosphite PCP-pincer complex in C-P cross-coupling reactions.

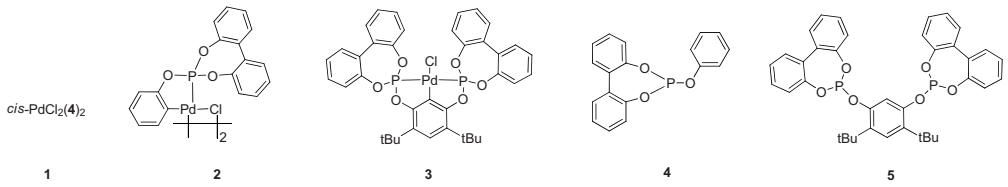
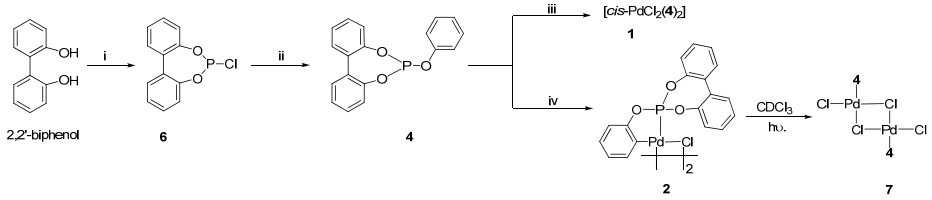


Figure 1. Entitled phosphite Pd complexes **1** – **3** and phosphite ligands **4** and **5**.

3.2 Results and discussion

3.2.1 Sythesis and characterization of phosphite Pd complexes 1 and 2.

In order to synthesize monodentate ligand **4**, 2,2'-biphenol was refluxed in freshly distilled PCl_3 for 2 h to yield phosphorochloridite **6** in quantitative yield (Scheme 1). Without isolation, **6** was subsequently reacted with phenol in the presence of triethylamine under refluxing temperature in toluene to afford the desired monodentate phosphite ligand **4** in good yield. Ligand **4** was reacted with different Pd(II) precursors under various conditions to give the corresponding phosphite Pd complexes **1** and **2**. For example, *cis*-$PdCl_2$(**4**)$_2$ (**1**) was obtained in excellent yield (95%) by reacting two equivalents of phosphite ligand **4** with 1.0 equivalent of $PdCl_2(MeCN)_2$ in dichloromethane at room temperature. Suitable colorless crystals of **1** were obtained by slow vapor diffusion of methanol into a dichloromethane solution of **1** at room temperature. The structure of complex **1** was determined by single crystal X-ray structure determination. As shown in Figure 2, complex **1** adopts a typical *cis*-configuration, in which two chloride ligands and two phoshite ligands both occupy mutual *cis*-positions (Cl-Pd-Cl angles of 92.54(3) and 91.92(3)°, and P-Pd-P angles of 95.36(3) and 95.74(3)°, respectively). As expected, when steric effects of the phosphite ligands do not override electronic effects, the weakly π-basic chloride ligands are preferentially positioned in the *trans*-positions with respect to the phosphite ligands by taking advantage of their strongly π-acidic feature.[4d, 4e, 14]



Scheme 1. Synthesis of phosphite Pd complexes **1** and **2**. Reaction conditions and reagents : i) PCl_3, reflux, 2 h, quantitative yield; ii) phenol, Et_3N, toluene, reflux, 2 h, 88%; iii) $PdCl_2(MeCN)_2$, DCM, r.t., 1 h, 95%; iv) $PdCl_2$, toluene, reflux, 16 h, 50%.

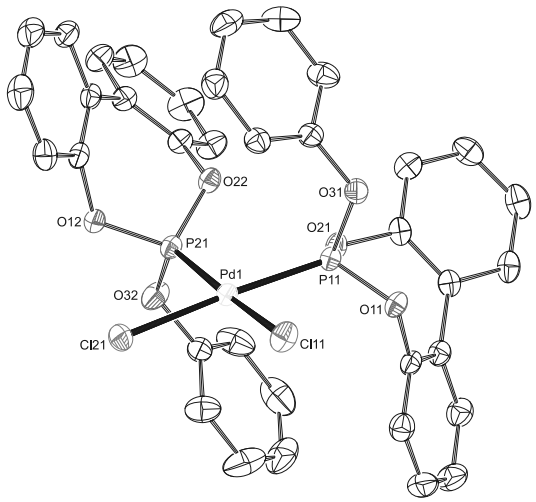


Figure 2. Displacement ellipsoid plot of **1** in the crystal (50% probability level). Hydrogen atoms have been omitted for clarity. Only one of two independent molecules is shown. Characteristic bond distances (Å) and bond angles (°) in **1** [second molecule in square brackets]: Pd1-Cl11=2.3388(7) [2.3246(7)], Pd1-Cl12=2.3298(7) [2.3303(7)], Pd1-P11=2.2105(7) [2.2154(7)], Pd1-P21=2.2207(7) [2.2115(7)], Cl11-Pd1-Cl21=92.54(3) [91.92(3)], P11-Pd1-P21=95.36(3) [95.74(3)].

Next to *cis*-bisphosphite Pd(II) complex **1**, orthopalladated complex **2** was prepared in good yield by refluxing ligand **4** in toluene overnight in the presence of a stoichiometric amount of $PdCl_2$ in accordance with the procedure published by Bedford *et al*.[4a, 4b] It is worth pointing out that other small size phosphite ligands, such as triphenylphosphite, do not yield orthometallated complexes under the same reaction conditions.[4d, 14] ^{13}C NMR analysis showed a signal at δ 150.1 ppm, which is very typical for the C_{ipso} of C-Pd σ-bonds in orthometallated complexes.[4, 5, 14] MALDI-TOF MS data confirmed the formation of a dimeric complex. ^{31}P NMR spectra in $CDCl_3$ at 25 °C showed complex **2** to be a mixture of *cis*- and *trans*-isomers, as was also reported

for other orthopalladated complexes.[4, 5, 14] Both ^{31}P and ^{1}H NMR spectra showed rather broad peaks at 25°C, which could be due to the facile interchange of *cis*- and *trans*-isomers and the conformational flexibility of the seven-member ring in the phosphite ligand at room temperature.[4d] The ratio of the two isomers in solution at room temperature was estimated as 1:15 (*cis*:*trans*) by comparing the ^{31}P NMR signals, which is rather high with respect to reported analogues.[4e, 14] This is presumably due to the small and rigid 2,2'-biphenol moiety that does not impose significant steric congestions in the *trans*-isomer.

Interestingly, upon standing of a solution of complex **2** in $CDCl_3$ for 10 days gradually showed the formation of dimer **7** which contains the non-orthometallated ligand. As shown in Figure 3, the C-Pd bonds in complex **2** have been split. It is well documented that palladacycles are sensitive to protonolysis by HCl in $CDCl_3$ solution in the presence of light in air.[4d]

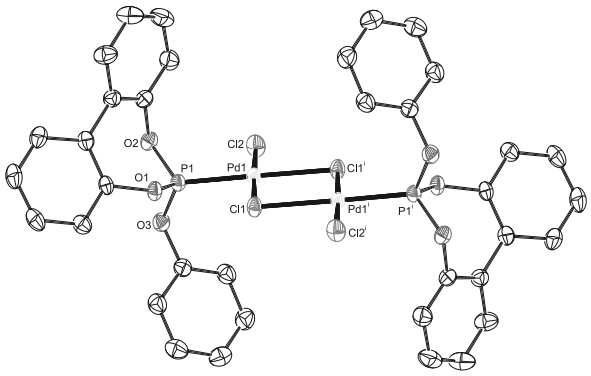
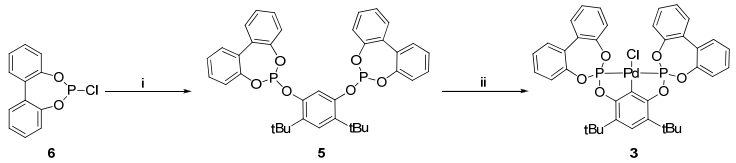


Figure 3. Displacement ellipsoid plot of **7** in the crystal (50% probability level). Hydrogen atoms and co-crystallized $CDCl_3$ have been omitted for clarity. Symmetry operation i: 1-x, 1-y, 1-z. Characteristic bond distances (Å) and bond angles (°) in **7**: Pd1-Cl1=2.3133(4), Pd1-Cl2=2.2749(4), Pd1-$Cl1^{i}$=2.3944(4), Pd1-P1=2.1783(4), P1-Pd1-Cl1=94.437(14), P1-Pd1-Cl2=87.353(15), Cl2-Pd1-$Cl1^{i}$=91.938(14).

3.2.2 Synthesis and characterization of phosphite pincer Pd complex 3.

In contrast to the relatively straightforward synthesis of phosphine and phosphinite PCP pincer ligands,[15] the metallation *via* direct C-H activation of phosphite pincer ligands in order to prepare phosphite PCP-pincer complexes is rather difficult.[5b] A small number of phosphite pincer Pd complexes have been prepared by the oxidative insertion of a zerovalent Pd precursor (e.g $Pd_2(dba)_3.CHCl_3$) into C-I or C-Br bonds.[5a, 5d] Recently, Bedford and co-workers found that the orthometallation *via* C-H activation of phosphite PCP-pincer ligands could be dramatically enhanced by using encumbered 4,6-di-*tert*-butylbenzene-1,3-diol as the key building block.[5b,16] As elaborated in Scheme 2, a novel pincer ligand **5** was prepared by following the same synthetic protocol as mentioned above. Reacting phosphorochloridite **2** with 4,6-di-*tert*-butylbenzene-1,3-

diol in the presence of Et_3N at 120 °C in toluene afforded pincer ligand **5** in high yield (88%). Reaction of ligand **5** with $PdCl_2(MeCN)_2$ in the presence of Et_3N in dichloroethane for 2 h at refluxing temperature smoothly yielded the desired pincer complex **3** in good yield (65%). It seems that the more hindered di-*tert*-butylresorcinol-based ligand **5** prevents the formation of polymers and/or decreases the degree of polymerization upon heating as documented for the BINOL-derived pincer ligand analogue.[5b]



Scheme 2. Synthesis of phosphite pincer complex **3**. Reaction conditions and reagents: i) 4,6-di-*tert*-butylbenzene-1,3-diol, Et_3N, toluene, reflux, 2 h, 88%; ii) $PdCl_2(MeCN)_2$, Et_3N, $ClCH_2CH_2Cl$, 80 °C , 2 h, 65%.

Colorless crystals of **3** were obtained by slow distillation of hexanes into a THF solution of **3** at room temperature. The structure of complex **3** in the solid state was determined by single crystal X-ray structure determination. As shown in Figure 4, the complex adopts a very typical *mer*-pincer configuration geometry. The palladium atom is located at the central position of a slightly distorted square-planar structure, with the chloride group occupying a *trans*-position to the *ipso*-carbon atom. The two phosphorus donors are mutually located in *trans*-positions, with P–Pd–P angles of 159.600(17) and 159.313(17)°.

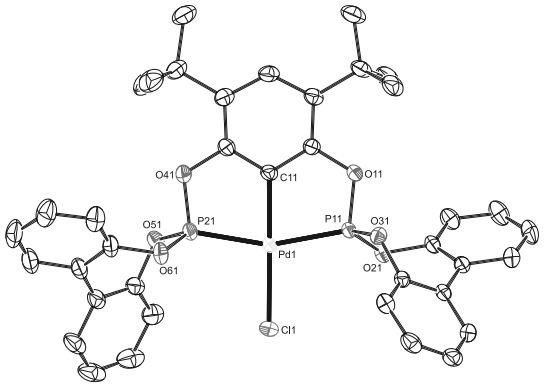
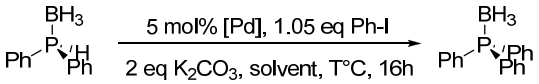


Figure 4. Displacement ellipsoid plot of **3** in the crystal (50% probability level). Hydrogen atoms and THF solvent molecules have been omitted for clarity. Only one of two independent molecules is shown. Characteristic bond distances (Å) and bond angles (°) in **3** [second molecule in square brackets]: Pd1-C11=2.0089(17) [2.0080(16)], Pd1-Cl1=2.3429(5) [2.3460(5)], Pd1-P11=2.2539(4) [2.2437(4)], Pd1-P21=2.2517(5) [2.2743(5)], C11-Pd1-Cl1=176.11(5) [176.90(5)], P11-Pd1-P21=159.600(17) [159.313(17)].

3.2.3 Bis-phosphite pincer palladium complex catalyzed C-P cross-coupling reactions. Recently, secondary phosphine-borane adducts have been widely used as versatile substrates to perform C-P cross coupling reactions due to their facile preparation, inertness towards oxygen and moisture, and good reactivities.[17] Thus, diphenylphosphine-borane was employed as model phosphine substrate and reaction optimization was carried out using a slight excess of Ph-I (1.05 equiv.) in the presence of 2 equiv. of K_2CO_3 as base and Pd-phosphite complexes **1**-**3** (5 mol%) as catalysts under various reaction conditions (Table 1).

Table 1. Pd-catalyzed C–P coupling between $Ph_2PH{\cdot}BH_3$ and phenyliodide; reaction optimization.[a]



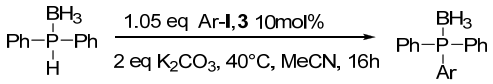
Entry	Cat.	Condition (T °C/Solvent)	Yield (%)[b]
1	**3**	40/Toluene	0
2	**3**	40/THF	10
3	**3**	40/MeCN	50
4[c]	**3**	40/MeCN	0
5	**2**	40/MeCN	40
6	**1**	40/MeCN	90
7	**3**	82/MeCN	44
8[d]	**3**	50/MeCN	70
9[e]	**3**	40/MeCN	> 95

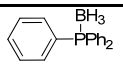
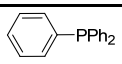
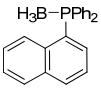
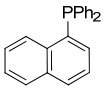
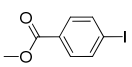
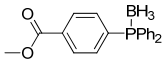
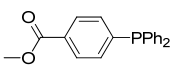
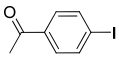
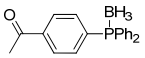
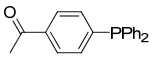
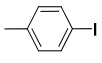
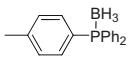
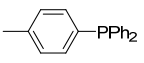
[a] Reaction conditions as follows unless otherwise stated: 0.105 mmol of Ph-I, 0.1 mmol of $Ph_2PH(BH_3)$, 5 mol% catalyst, 0.2 mmol of K_2CO_3, 1 mL of solvent, 16h, under N_2. [b] ^{31}P NMR yield with diethyl ethylphosphonate as internal standard. [c] In air. [d] 7.5 mol% [Pd] catalyst loading. [e] 10 mol% [Pd] catalyst loading.

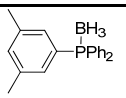
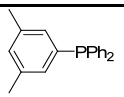
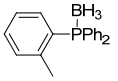
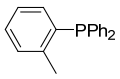
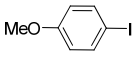
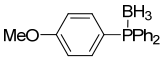
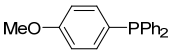
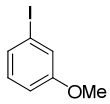
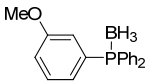
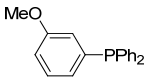
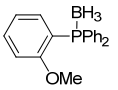
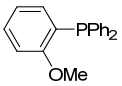
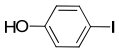
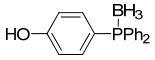
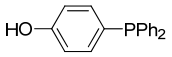
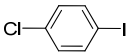
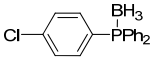
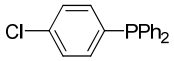
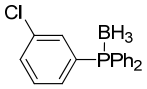
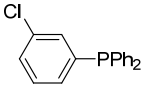
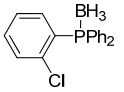
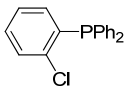
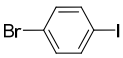
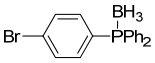
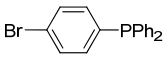
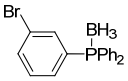
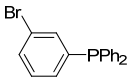
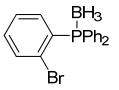
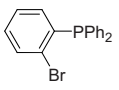
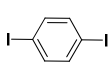
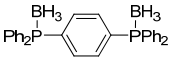
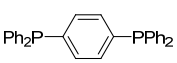
According to the experimental data showed in Table 1, the chemical yields of the product $PPh_3{\cdot}BH_3$ were higly solvent-depedent when using complex **3** as the catalyst. The reaction in MeCN at 40 °C proceeded with 50% chemcial yield, whereas the reaction in toluene did not furnish any conversion and the reaction merely gave a poor yield of 10% in THF (Table 1, entry

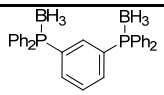
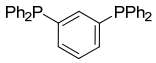
3 *vs* entries 1 and 2). Possibly, the reaction requires a polar and coordinating solvent to dissolve the inorganic base K_2CO_3. Interestingly, although both the diphenylphosphine-borane substrate and the triphenylphosphine-borane product are resistant towards oxidation and hydrolysis in air, the exclusion of air is crucial to afford conversion (Table 1, entry 4). Pd dimer complex **2** gave slightly lower yield in contrast to pincer complex **3** (Table 1, entry 3 *vs* entry 5), while complex **1** gave 90% yield (Table 1, entry 6), which is as good as the yield reported for *trans*-dichlorobis(triphenylphosphine)palladium.[17c,18] Elevated temperatures did not improve the yield when using **3**. Contrarily, it led to an increased formation of many unknow by-products (Table 1, entry 7). A remarkable improvement was achieved upon progressively increasing the loading of **3** (Table 1, entries 8 and 9). Eventually, complete conversion was obtained by using 10 mol% loading of **3** in MeCN at 40 °C in the presence of 2 equivalents of K_2CO_3. It is worth pointing out that when Ph-Br and MePhH(BH_3) were, respectively, tested as substrates under optimized conditions, neither of them gave any conversion and starting materials were fully recovered from the reaction mixtures. To illustrate the potential of the catalytic procedure, a substrate library of 19 different aryliodides was evaluated by using the optimized conditions (Table 2).

Table 2. Phosphite pincer complex **3** catalyzed C-P cross coupling reactions.[a]



Entry	Ar-I	Phosphine-borane	Yield (%)[b]	Phosphine	Yield (%)[c]	Ref.[d]
1			95		95	
2			74		95	[19]
3			98		87	[20]
4			96		91	[21]
5			95		83	[22]

Entry	Ar-I	Phosphine-borane	Yield (%)[b]	Phosphine	Yield (%)[c]	Ref.[d]
6			94		72	[23]
7			50		86	[23]
8			95		79	[24]
9			87		84	[25]
10			46		81	[26]
11			69		75	[27]
12			74		89	[28]
13			71		90	[29]
14			58		85	[30]
15			63		80	[31]
16			57		93	[32]
17			17		88	[33]
18[e]			95		95	[23]

Entry	Ar-I	Phosphine-borane	Yield (%)[b]	Phosphine	Yield (%)[b]	Ref.[d]
19[e]			95		95	[34]

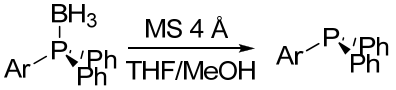
[a] Reaction conditions as follows unless otherwise stated: 0.105 mmol of Ar-I, 0.1 mmol of $Ph_2PH(BH_3)$, 0.01 mmol of **3**, 0.2 mmol of K_2CO_3, 1 mL of MeCN, 16 h, under N_2. [b] Isolated yields of tertiary phosphine-boranes. [c] Isolated yields of tertiary phosphines. [d] References are provided for the original synthesis of the reaction products. [e] 0.1 mmol of diiodobenzene, 0.21 mmol of $Ph_2PH(BH_3)$ and 0.021 mmol of **3** were used.

As shown in Table 2, complex **3** can smoothly catalyze C-P cross-couplings of diphenylphosphine-borane and a wide scope of aryl iodide substrates with promising to excellent isolated yields. The model substrate Ph-I gave 95% yield, whereas slightly electron-enriched and *ortho*-substituted 1-iodonaphthalene decreased the yield by 20% (Table 2**,** entries 1 and 2). As anticipated, substrates comprising electron-withdrawing methyl acetate and acetyl functional groups afforded excellent yields (Table 2, entries 3 and 4). Moreover, substrates functionalized with electron-donating methyl and methoxyl groups on either *meso* or *para* positions generally did not decrease the yields (Table 2, entries 5, 6, 8 and 9). Nevertheless, *ortho*-functionalized substrates gave significantly decreased yields of about 50% (Table 2, entries 7 and 10), which could be due to steric congestion effects. Noticeably, the *para* hydroxyl functionalized substrate gave much lower yield than the *para* methoxyl group functionalized substrate (Table 2, entry 8 *vs.* entry 11), presumably because the considerably acidic phenol moiety reacts with K_2CO_3 and the resulting potassium phenolate adduct is poorly soluble in MeCN.

Since we observed that bromobenzene is not active at all in this catalytic process (*vide supra*), substrates bearing either bromine or chlorine atoms were evaluated in catalysis. The resulting products bearing carbon-halogen bonds could be potentially valuable targets for further organic transformations through subsequent cross-coupling reactions. As shown in Table 2, chlorine functionalized substrates in most cases outperformed the corresponding bromine-functionalized ones under the same reactions conditions (Table 2, entries 12 and 13 *vs*. entries 15 and 16), while the yields of desired products were generally promising in both cases. Moreover, *meso*- and *para*-functionalized substrates also outperformed *ortho* functionalized ones as mentioned before (Table 2, entries 12 and 13 *vs*. entry 14 ; entries 15 and 16 *vs*. entry 17). Unfortunately, the yield was dramatically decreased to only 17% for 1-bromo-2-iodo-benzene. To our delight, besides monophosphine products, this method also works for the preparation of diphosphine products.

For example, reacting 2.1 equivalents of diphenylphosphine-borane adducts to 1.0 equivalent of 1,3- or 1,4-diiodobenzene under optimized conditions afforded the desired 1,3- or 1,4-phenylene-bis(diphenylphosphine-borane) products in excellent yields (Table 2, entries 18 and 19). Although it requires a relatively high catalyst loading (*i.e.*, 10 mol%), the present catalytic protocol can smoothly bring about the cross-coupling of diphenylphosphine-borane and aryliodides under very mild conditions in comparison with several other protocols that rely on bidentate phosphine ligands.[17c, 18]

According to reported procedures, the removal of BH_3 group can be easily accomplished by using strong acid[35] or strong base[36] under mild conditions. Recently, Hiyama *et al*. reported a novel benign deprotection method for phosphine-boranes under neutral conditions.[26] The procedure afford free phosphines in excellent yields by refluxing phosphine-borane adducts with activated molecular sieves (4 Å) in an ethereal solvent (THF/MeOH 7:3 (v/v)) for 96 h (Scheme 3). Accordingly, all the prepared phosphine-borane compounds were efficiently deprotected by using this procedure and all spectral data of the resulting free phosphines were fully identical to those reported in the literature (Table 2).



Scheme 3. Deprotection of tertiary phosphine-boranes.

3.2.4 Investigation into the nature of the catalytically active species.

To understand the mechanism of the reaction and to identify the catalytically active species, a reaction profile study along with poisoning tests were carried out. By means of ^{31}P NMR measurements, a reaction profile curve of the chemical yield of the product against time was obtained for the reaction of diphenylphosphine-borane and Ph-I (Figure 5).

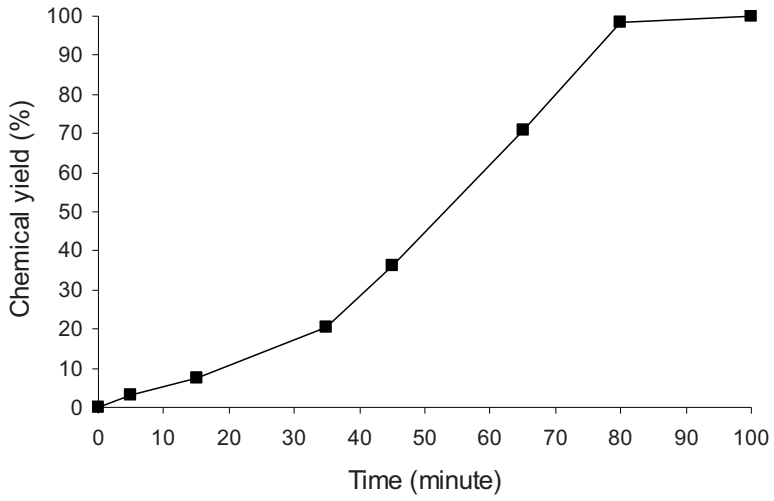


Figure 5. Reaction profile study of the C-P cross-coupling of $Ph_2PH(BH_3)$ and Ph-I using **3** as catalyst. (Reaction conditions: 1 mmol of $Ph_2PH(BH_3)$, 1.05 mmol of Ph-I, 2 mmol of K_2CO_3, 0.1 mmol of complex **3**, 4 ml of MeCN, 40°C, diethyl ethylphosphonate as internal standard.)

Figure 5 represents a S-shaped curve, which indicates that the reaction rate varied during the catalytic process and included an introduction period as well as an accelerating period. This observation strongly suggests that complex **3** might act as a precatalyst, which decomposes under the reaction conditions to form a catalytically active species. While Pd-black formation was not observed during the entire procedure, the development of a deeply orange color indicated the formation of Pd^0 clusters.

To confirm this assumption, a standard poisoning test was carried out. Crabtree[37a] and Whitesides[37b] independently reported that adding an excess of metallic mercury will lead to the amalgamation of the surface of heterogeneous metal particles thus poisoning them, whereas in most of the cases this will not affect homogeneous catalysts. To ensure sufficient time for the mercury droplets to capture Pd nanoparticles, the experiments were carried out 10 times more diluted than the previous profile study. As depicted in Figure 6, completely suppressed conversions were found after charging Hg at t = 0 or t = 2.5 h.

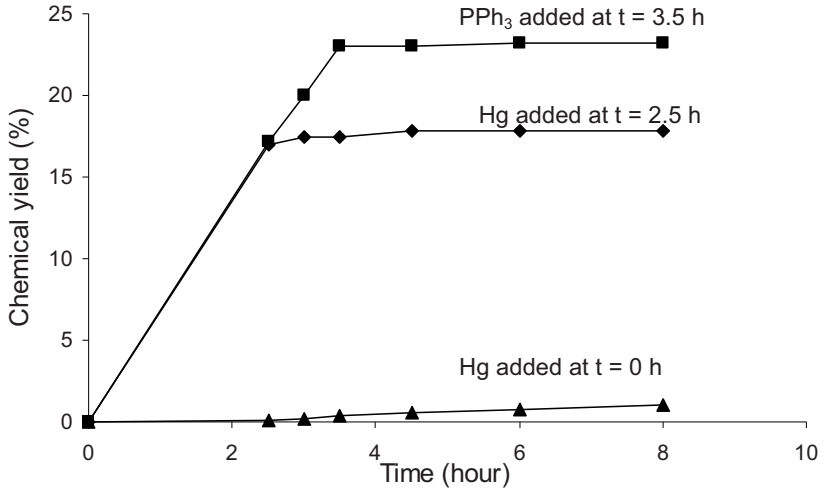
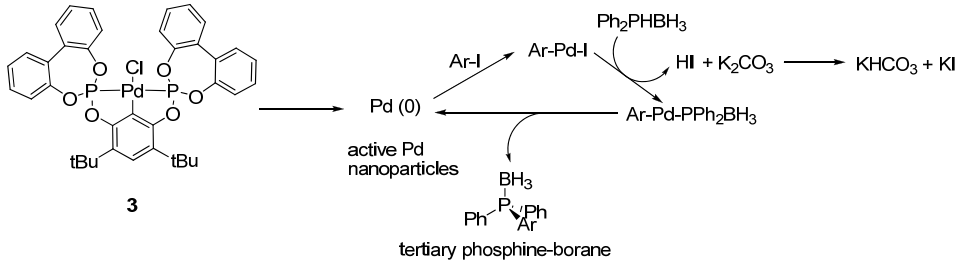


Figure 6. Poisoning tests with Hg and PPh_3 as the inhibitors. (Reaction conditions: 0.1 mmol of $Ph_2PH(BH_3)$, 0.105 mmol of Ph-I, 0.2 mmol of K_2CO_3, 0.01 mmol of complex **3**, 4 mL of MeCN, 40°C, diethyl ethylphosphonate as internal standard.)

Besides the use of mercury as a poison, the protocol described by Widegren and Finke[38] predicts that when catalytic activity can be completely terminated with <<1 equivalent of an external ligand, such as PPh_3, that it is highly suggestive of the presence of a heterogeneous catalyst. In the case of **3**, complete conversion was obtained when 0.05 equivalent of PPh_3 was added at t = 0 which does not agree with the reported poisoning protocol a heterogeneous catalyst. To understand this observation, complex **3** and 0.05 equivalent of PPh_3 were mixed in an NMR tube and the ^{31}P NMR spectrum of the resulting mixture was recorded at 40℃. A new single peak at 24.3 ppm was observed, which corresponds to the formation of *trans*-dichlorobis(triphenylphosphine)palladium, a highly active catalyst for C-P cross couplings was observed.[17c, 18] Nevertheless, completely suppressed catalytic activity was observed right after adding PPh_3 at t = 3.5 h (Figure 6), which is in accordance with a catalytic species of heterogeneous nature. Noticeably, PCP[15a] and SCS[12b, 39] pincer complexes have been reported to decompose upon heating (*e.g.* 160 °C) to form active Pd nanoparticles. Differently, in this study the active Pd species were formed at relatively low temperature (*i.e.* 40 °C).

According to these kinetic investigations, the present C–P cross coupling proces presumably proceeds via the pathway as following (Scheme 3)[40]: 1) Complex **3** decomposed under the reaction conditions to form catalytically active Pd^0 nanoparticles, which can be oxidized to Pd^{2+} after reacting to aryl iodides; 2) Ar-Pd-PPh_2BH_3 is formed and the generated HI is trapped by

K_2CO_3; 3) after reductive elimination, the desired product tertiary phosphine-borane forms and Pd^{2+} is reduced back to Pd^0.



Scheme 3. Proposed reaction mechanism for the C–P coupling process.

3.3 Conclusion

In summary, we have developed a series of novel phosphite palladium complexes **1**-**3** by using a straightforward synthetic route. Complexes **1** and **3** were characterized by X-ray crystal structure determinations. The application of phosphite PCP-pincer complex **3** in C-P cross-coupling reactions was optimized with Ph-I and $Ph_2PhH(BH_3)$ as model substrates and complete conversion was obtained by using 10 mol% loading of pincer complex **3** in MeCN at 40 °C in the presence of 2 equivalents of K_2CO_3. Following the optimized procedure, a series of tertiary phosphine-borane compounds were synthesized in promising to excellent yields with a very wide functional group tolerence and under very mild conditions. The reaction profile and poisonning studies with metallic mercury and PPh_3 indicated the involvement of heterogeneous Pd^0 species as the actual catalyst. Pincer complex **3**, therefore, merely acts as a precatalyst which decomposes to generate catalytically active Pd nanoparticles that are able to carry out C−P coupling reactions at very mild conditions.

3.4 Experimental section

General remarks: All reactions were performed under a dry N_2 atmosphere using standard Schlenk techniques. CH_2Cl_2, $ClCH_2CH_2Cl$, MeCN, and Et_3N were distilled over CaH_2 in a conventional heating bath before use. Toluene was freshly distilled over Na sand prior to use. PCl_3 was freshly distilled and stored under N_2 before use. All other reagents were purchased and used as received. ^{1}H-NMR (^{1}H 400.0 MHz), ^{13}C-NMR (^{13}C 100.6 MHz) and ^{31}P-NMR (161.9 MHz) spectra were recorded at room temperature in $CDCl_3$ on a Varian 400 MHz INOVA spectrometer. Chemical shift values are reported in ppm (δ) relative to $(CH_3)_4Si$ (^{1}H and ^{13}C NMR) or a capillary containing 85% H_3PO_4 in D_2O, (^{31}P{^{1}H} NMR). Flash chromatography was performed using ACROS silica gel , 0.06-0.200 mm, pore diameter ca. 6 nm. MS measurements were carried out on an Applied Biosystems Voyager DE-STR MALDI-TOF MS. Elemental microanalyses were performed by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim a/d Ruhr, Germany.

General Procedure for the Preparation of Phosphite ligands. 2,2'-biphenol (2 mmol, 0.3730 g) was azeotropically dried over toluene in vacuum three times and was suspended in freshly distilled PCl_3 (5 mL) at room temperature. The resulting mixture was heated at refluxing temperature for 2 h with vigorously stirring. During this procedure, HCl gas evolved and was trapped by a saturated aqueous NaOH solution. After cooling, the remaining PCl_3 was removed under reduced pressure and the trace amounts of PCl_3 were further azeotropically evaporated with dry toluene (3 x 5 mL). The resulting colorless oily product was directly used in the next step without purification. The oily product was redissolved in toluene (25 mL) and was added to a solution of azeotropically dried aryl alcohol (2 mmol of phenol; 1 mmol of resorcinol or 2,4-*tert*-butylbenzene-1,3-diol) in toluene (10 mL) at 0 °C (ice bath). To this mixture, a solution of Et_3N (0.31 mL, 2.2 mmol) in toluene (5 mL) was added dropwise over 5 min. The reaction mixture was then heated to 110 °C for 2 h under N_2. After cooling, the resulting white suspension mixture was filtered over a short plug of silica gel and the filter cake was washed with toluene (3 x 10 mL). The combined toluene layers were conentrated to dryness and a white solid was obtained. The analytic sample was obtained after further purification via flash chromatography with EtOAC/hexanes (1:1, v/v).

Ligand 4: 0.5430 g, 1.76 mmol; Yield: 88%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.54 (d, $^3J_{H\text{-}H}$ =1.5 Hz, 1 H, BIPOL*H,* biphenyl-H2), 7.52 (d, $^3J_{H\text{-}H}$=1.5 Hz, 1 H, BIPOL*H*， biphenyl-H3), 7.42–7.31 (m, 4 H, BIPOL*H,* biphenyl-H4, 4′ and H5, 5′ + 2 H, Ar*H*), 7.26–7.17 (m, 2 H, BIPOL*H*, biphenyl-H2′ and H3′ + 3H, Ph*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 131.7, 130.5, 129.9, 129.8, 128.4, 127.1, 126.2, 125.3, 121.7, 120.4. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 145.0 (s). Anal.Calcd for C, 70.13; H, 4.25; P, 10.05; found : C, 70.10; H, 4.27; P, 10.07;

Ligand 5: 0.5730 g, 0.88 mmol; Yield: 88%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.52(m, 4H, BIPOL*H,* biphenyl-H2, 2′), 7.26-7.42(m, 12H, BIPOL*H,* biphenyl- H3, 3′, H4, 4′ and H5, 5′), 7.13 (s, 1H, Ar*H*), 7.04-7.07 (m, 1H, Ar*H*), 1.42 (s, 12H, *tBu*), 1.40 (s, 6H, *tBu*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 135.4, 131.6, 129.9, 129.3, 127.2, 125.7, 122.4, 121.9, 121.7, 117.0, 35.0, 30.4. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 145.0 (s). Anal.Calcd for C, 70.15; H, 5.58; P, 9.52; found : C, 70.17; H, 5.63; P, 9.49;

Complex 1: A mixture of $[PdCl_2(NCMe)_2]$ (0.1 mmol, 0.0263 g) and ligand **4** (0.2 mmol, 0.062 g) in 10 mL dichloromethane was stirred at room temperature for 1 h. The reaction mixture was then concentrated

under reduced pressure and a white solid was precipitated from the solution by the addition of hexanes. The solid was collected by centrifugation and further washed with 2 x 10 mL hexanes. The product was obtained as a fine white powder (0.0755 g, 0.095 mmol). Yield: 95%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.49-7.60 (m, 8H, BIPOL*H,* biphenyl-H2, 2′, H3, 3′), 7.40-7.45 (m, 8H, BIPOL*H,* biphenyl-H4, 4′, H5, 5′), 7.10 (d, $^{3}J_{H\text{-}H}$=7.2 Hz, 6H, Ph*H*), 6.84-6.92 (m, 4H, Ph*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 149.3, 148.0, 130.5, 130.3, 129.6, 129.3, 127.2, 126.5, 122.6, 121.6. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 111.7 (s). Anal.Calcd for $C_{36}H_{26}Cl_2O_6P_2Pd$: C, 54.47; H, 3.30; P, 7.80; Pd, 13.41; found : C, 54.49; H, 3.37; P, 7.86; Pd, 13.45;

Complex 2: A mixture of ligand **4** (0.1 mmol) and $PdCl_2$ (0.0180g, 0.1 mmol) in 5 mL of toluene was heated at 110 °C for overnight under N_2. After cooling, the reaction mixture was filtered over a pad of Celite, all volatiles were removed under vacuum, and the residue crystallized from CH_2Cl_2/MeOH (1:9, v/v) to afford an orange solid (0.0450 g, 0.05 mmol). Yield: 50%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.55 (br d, $^{3}J_{H\text{-}H}$=8 Hz, 4H, Ph*H*), 7.35-7.50 (very br m, 16H, BIPOL*H*), 7.21-7.28 (very br s, 4H, Ph*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 150.1, 148.0 (d, *J*=12 Hz), 131.8, 130.4, 129.1, 129.0, 127.5, 127.2, 126.8, 122.6, 121.5 (d, *J*=4.5 Hz), 116.4. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 80.1 (br s) minor isomer, 81.4 (br s) major isomer. Anal.Calcd for $C_{36}H_{24}Cl_2O_6P_2Pd_2$: C, 48.14; H, 2.69; P, 6.90; Pd, 23.69 found : C, 48.22; H, 2.79; P, 6.88; Pd, 23.65

Complex 3: A mixture of the ligand **5** (0.0650 g, 0.1 mmol) and $[PdCl_2(NCMe)_2]$ (0.0264 g, 0.1 mmol) in 2 mL of 1,2-dichloroethane was treated with NEt_3 (14 µL, 0.10 mmol) and then heated at 80 °C for 2h. After cooling, the reaction mixture was filtered over a pad of Celite, all volatiles were removed under vacuum and the residue crystallised from CH_2Cl_2/pentane to afford a slightly orange solid (0.0515 g, 0.065 mmol). Yield: 65%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.55(d, $^{3}J_{H\text{-}H}$=7.6 Hz, 4H, BIPOL*H,* biphenyl-H2, 2′), 7.35-7.43 (m, 12H, BIPOL*H,* biphenyl-H3, 3′, H4, 4′ and H5, 5′), 7.22 (s, 1H, Ar*H*), 1.34 (s, 18H, *tBu*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 152.6, 148.2, 137.1, 135.8, 132.6, 130.2 (d, *J*=23 Hz), 129.5, 127.1, 125.6, 122.6, 35.0, 30.0. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 146.2 (s). MS (MALDI-TOF): m/z calcd for $C_{38}H_{35}O_6P_2Pd$: 756.05 $[M\text{-}Cl]^+$; found: 756.04; Anal.Calcd for $C_{38}H_{35}ClO_6P_2Pd$: C, 57.66; H, 4.46; P, 7.83; Pd, 13.45; found : C, 57.71; H, 4.48; P, 7.79; Pd, 13.42;

General procedure of synthesis of tertiary phosphine-boranes: To a flame dried Schlenk tube, $Ph_2PH(BH_3)$ (20.0 mg, 0.1 mmol), aryliodide (0.105 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), complex **3** (7.9 mg, 0.01 mmol), and MeCN (1 mL) were added. This resulting mixture was warmed to 40 °C for 16 h under N_2. After cooling, water (2 mL) was added and the mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were concentrated on a rotary evaporator and the residue was subjected to flash chromoatography (EtOAc/hexanes 3:7 (v/v)) to obtain the entitled tertiary phosphine-boranes as white solids. The spectral data of these compounds were identical to those reported in the literature (see Table 2, references).

General procedure of deprotection of tertiary phosphine-boranes: According to reported procedure,[24] to a Schlenk tube equipped with condenser were added activated molecular sieves (250 mg, 4Å), phosphine-boranes (0.05 mmol), THF (3.5 mL) and MeOH (1.5 mL). The reaction mixture was then refluxed for 96 h under N_2. After cooling, the reaction mixture was filtered through a pad of Celite and the filter cake was washed with THF (3 x 5 mL). All volatiles were removed on a rotary evaporator and the resultant waxy product was recrystallized from MeOH/EtOAc at - 30°C to yield analytically pure

samples as white solids. The spectral data of these compounds were identical to those reported in the literature (see Table 2, references).

Procedure of reaction profile study: A flame dried schlenk tube equipped with a condenser was charged with $Ph_2PH(BH_3)$ (1 mmol), Ph-I (1.05 mmol), K_2CO_3 (2 mmol), complex **3** (0.1 mmol) and MeCN (4 mL). This reaction mixture was then warmed to 40 °C with vigorous stirring. Small aliquot (50 μL) was taken at alloted time and diluted in EtOAc (1 mL). The resulting organic mixture was washed with water (1 mL) and the aqueous layer was extracted with EtOAc (3 x 1 mL). The combined organic layers were dried over $MgSO_4$. Removal of all the volatiles under reduced pressure gave an oily orange mixure, which was redissovled in $CDCl_3$ and transfered into an NMR tube. Diethyl ethylphosphonate (10 μL) was added to the sample as an internal standard.

Procedure of poisoning tests: A flame dried Schlenk tube equipped with a condenser was charged with Ph_2PHBH_3 (0.1 mmol), Ph-I (0.105 mmol), K_2CO_3 (0.2 mmol), complex **3** (0.01 mmol) and MeCN (4 mL). This reaction mixture was warmed to 40°C with vigorous stirring. Metallic mercury (300 equivalents) or PPh_3 (0.05 equivalent) were added to the reaction mixture at alloted time. Small aliquot (50 μL) was taken at alloted time and diluted in EtOAc (1 mL). The resulting organic mixture was washed with water (1 mL) and the aqueous layer was extracted with EtOAc (3 x 1 mL). The combined organic layers were dried over $MgSO_4$. Removal of all the volatiles under reduced pressure gave an oily orange mixure, which was redissovled in $CDCl_3$ and transfered into an NMR tube. Diethyl ethylphosphonate (10 μL) was added to the sample as an internal standard.

X-ray crystal structure determinations: X-ray reflections were measured with Mo-K_α radiation (λ = 0.71073 Å) on a Nonius KappaCCD diffractometer with rotating anode at a temperature of 150 K up to a resolution of $(\sin\theta/\lambda)_{max}$ = 0.65 $Å^{-1}$. Integration of the intensities was performed with EvalCCD[41] and absorption correction with SADABS[42]. The structures were solved with Direct Methods (program SHELXS-97[43] for complexes **1** and **3**; program SIR-97[44] for complexes **2a**). Refinement was performed with SHELXL-97[43] against F^2 of all reflections. Non hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were located in difference Fourier maps (complexes **1** and **2a**) or introduced in calculated positions (complex **3**) and refined with a riding model. Geometry calculations and checking for higher symmetry was performed with the PLATON program[45]. Further details are given in Table 1.

Complex 1: With the matrix (1,0,-2/-1,0,0/0,1,0) the triclinic cell parameters can be transformed into a *pseudo*-monoclinic C-centered cell. The *a*-axis of the triclinic cell then becomes the *b*-axis of the pseudo-monoclinic cell. The two independent molecules in the triclinic cell are related by an approximate twofold rotation roughly about the *a*-axis. The reflection intensities only support a triclinic symmetry and there is no indication for twinning.

Complex 3: Besides the ordered THF molecule, the crystal structure contains a large void (852.4 $Å^3$ / unit cell), filled with disordered THF solvent molecules. Their contribution to the structure factors was secured by back-Fourier transformation using the SQUEEZE routine of the program PLATON[45], resulting in 60 electrons / unit cell.

Table 3. Selected crystallographic data for complexes **1, 2a,** and **3**.

	1	**2a**	**3**
formula	$C_{36}H_{26}Cl_2O_6P_2Pd$	$C_{36}H_{26}Cl_4O_6P_2Pd_2 \cdot 2(CHCl_3)$	$C_{38}H_{35}ClO_6P_2Pd \cdot 0.5(C_4H_8O)$ + disordered solvent
FW	793.81	1209.84	827.50[a]
crystal colour	colourless	yellow	colourless
crystal size [mm^3]	0.54x0.36x0.36	0.51x0.30x0.08	0.30x0.30x0.30
crystal system	triclinic	triclinic	triclinic
space group	$P\bar{1}$ (no. 2)	$P\bar{1}$ (no. 2)	$P\bar{1}$ (no. 2)
a [Å]	12.2961(2)	9.50019(17)	14.6466(10)
b [Å]	14.6736(3)	10.13286(18)	16.1015(7)
c [Å]	19.8556(4)	12.2159(2)	20.4137(12)
α [°]	71.927(1)	80.303(1)	99.657(2)
β [°]	72.144(1)	73.343(1)	94.758(2)
γ [°]	88.825(1)	85.570(1)	112.789(2)
V [$Å^3$]	3230.65(10)	1109.99(3)	4317.2(4)
Z	4	1	4
D_x [g/cm^3]	1.632	1.810	1.273[a]
refl. meas./unique	55800 / 14758	26489 / 5077	123398 / 19826
μ [mm^{-1}]	0.887	1.529	0.607[a]
abs. corr.	multi-scan	multi-scan	multi-scan
abs. corr. range	0.49-0.73	0.72-0.89	0.61-0.83
param./restraints	847 / 0	262 / 0	922 / 0
R1/wR2 [$I>2\sigma(I)$]	0.0333 / 0.0835	0.0187 / 0.0470	0.0245 / 0.0705
R1/wR2 [all refl.]	0.0444 / 0.0876	0.0208 / 0.0481	0.0326 / 0.0736
S	1.170	1.039	1.063
res. density [$e/Å^3$]	-1.18 / 0.62	-0.32 / 0.64	-0.41 / 0.54

[a] Derived parameters do not contain the contribution of the disordered solvent.

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Chapter 4

Chiral Amino Alcohol Derived Bis-Phosphoramidite Pincer Metal Complexes and Their Applications in Asymmetric Allylation of Aldimines

Abstract

Novel P-stereogenic bisphosphoramidite pincer metal complexes **1** and **2** derived from (*S*)-(−)-α,α-diphenyl-2-pyrrolidinemethanol and (*S*)-(+)-indolinemethanol, respectively, were synthesized in reasonable yields (*i.e.* 55%-62%) by using a flexible, modular synthetic approach and were characterized by X-ray crystal structure determination. Reacting (*S*)-(+)-indolinemethanol with PCl_3 leads to the formation of a novel P-chiral building block, which exhibits good thermal stability of its stereochemical features. This enabled the design and development of new P-chiral bisphosphoramidite pincer arene ligands and their corresponding metal complexes. The molecular structure of the new indolinemethanol-derived phosphoramidite pincer metal complex screens quadrants I and III, which is in contrast to the previously reported *L*-proline derived P-chiral ligands that screen quadrants II and IV. The bisphosphoramidite pincer palladium complexes **1** and **2** are active catalysts for asymmetric homoallylation of sulfonimines, where low (*ee* 33%) or no enantioselectivity was observed for reactions catalysed by **2** and **1**, respectively. Preliminary catalytic results revealed that enantiomeric excess values varied by using differently functionalized sulfonimines, suggesting that both electronic properties and steric congestions of sulfonimines do affect the transition state of the electrophilic attack of the $^{1}\eta$-allyl Pd intermediate in the allylation.

4.1 Introduction

In the past decades, the chemistry of pincer metal complexes, especially their application as homogeneous catalysts, sensors or switches, has attracted considerable attention due to their unique reactivities and structural properties.[1] The synthesis of chiral pincer metal complexes and their applications in asymmetric catalysis have more recently been reported. Some representative frameworks of these complexes documented up to date are summarized in Figure 1. Various groups independently developed a series of NCN-bisoxazolinyl-phenyl pincer metal complexes bearing as the metal, *e.g.*, rhodium, ruthenium, palladium or platinum, and explored their catalytic properties in, for example asymmetric allylation, asymmetric hydrosilylation, and asymmetric hydrogen transfer reactions. (Figure 1, type A).[2] The heterocyclic oxazoline skeleton supplies a tunable and rigid chiral pocket to the metal coordination sphere of bisoxazolinyl-phenyl pincer metal complexes, including chiral centres at the 4- and 5-positions by using various β-amino alcohols. Besides the well-developed chiral NCN-pincer metal complexes, the development of chiral PCP-pincer metal complexes has recently attracted much attention. Zhang and co-workers reported a practical synthesis of chiral PCP-pincer metal complexes bearing stereogenic benzylic methylene centres by using Corey's chiral reduction of 1,3-diacetylbenzene (Figure 1, type B).[3] Alternatively, Van Koten and co-workers developed the first example of a PCP-pincer palladium complex bearing P-stereogenic *tert*-butylphenylphosphine moieties by using a (-)-sparteine assisted asymmetric lithiation step[4a] and subsequently reported its analogous ruthenium pincer metal complexes (Figure 1, type C).[4b] Szabó and Bedford independently reported a series of easily accessible and tunable 1,1'-bi-2-naphthol- and biphenanthrol based chiral PCP-pincer palladium complexes and demonstrated their application in the asymmetric homoallylation of benzaldehyde and sulfonimines with *ee's* up to 85% (Figure 1, type D).[5, 6] The synthesis of chiral phosphite pincer metal complexes benefits from the structual diversity of easily available chiral diols and an efficient modular synthesis. Accordingly, chiral phosphite or bis(diamidophosphinite)pincer metal complexes derived from chiral diols or chiral diamines have been reported by several groups.[5-7] In contrast to the extensive use of chiral diols, especially members of the BINOL-family, little is known about the use of other chiral building blocks.

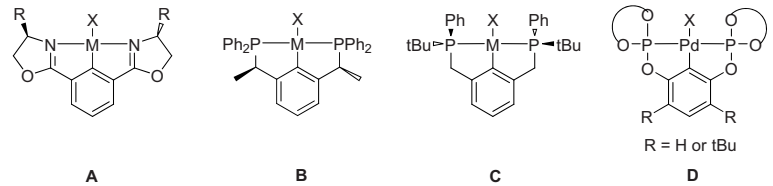


Figure 1. Representative framework of chiral pincer metal complexes.

Inspiring results have recently been reported for the successful use of *L*-proline and chiral amino alcohols derivatives which has expanded the library of new P-chiral ligands and their corresponding metal complexes. The possibility to shape the molecular environment of the phosphorus atom(s) provides an excellent opportunity for the facile construction of tunable chiral pockets at the metal centre from which catalysts could emerge with improved regio- and stereoselectivity.[8, 9] There are two major synthetic routes for accessing L-proline derived P-chiral ligands (Figure 2), and both we have explored for the synthesis of new P-chiral pincer ligands and metal complexes.

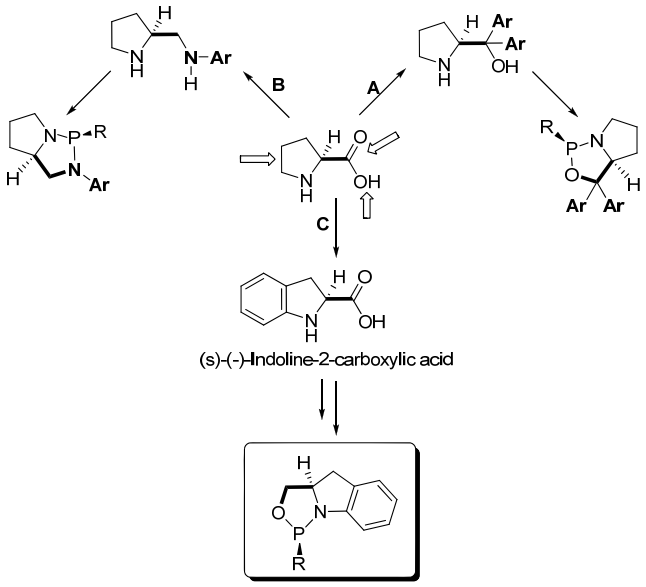
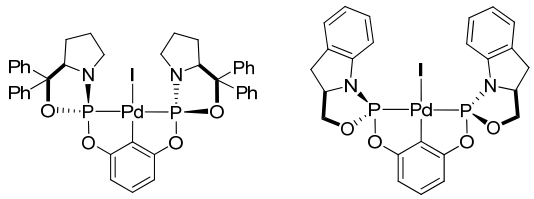


Figure 2. *L*-Proline derived P-chiral building blocks.

Starting from *L*-proline, the carboxylic acid group can be converted to arrive at functionalized amino alcohols bearing bulky functional groups (*e.g.*, aryl groups) with the corresponding Grignard reagents (Figure 2, route A).[10] The resulting compounds can be used to prepare P-chiral bisphosphoramidite arene ligands through further organic transformations. Actually, this protocol has led to the efficient synthesis of a novel P-chiral pincer palladium complex **1** (*vide infra*). Alternatively, the carboxylic acid group can be converted to arrive at functionalized chiral secondary amines bearing bulky functional groups (*e.g.*, aryl groups) through stepwise organic transformations (Figure 2, route B).[11] In this case, the chiral pockets are supposed to be improved by taking advantage of a closer proximity of bulky substituents with respect to the phosphorus donor. In an attempt to apply this protocol to synthesize corresponding pincer palladium

complexes, however, we were not able to obtained analytically pure samples, because their isolation was hampered by the high moisture sensitivity of the N-P-N manifold of the bis(diamidophosphinite)pincer ligand.

In order to expand the library of P-chiral building blocks, new starting materials can be of key interest. So far, much less effort has been put into the modification of the cyclic pyrrolidine moiety of proline. To this end we have explored the use of (*S*)-2-hydroxymethylindoline (Figure 2, route C), which can be easily prepared by reducing commercially available (*S*)-indoline-2-carboxylic acid with $BH_3 \cdot Me_2S$,[12] as a new starting material to access a novel P-chiral building block and its corresponding P-chiral pincer palladium complex **2** (*vide infra*).



1 **2**

Figure 3. P-chiral pincer palladium complexes **1** and **2**.

In this paper, we report on the development of a novel P-chiral building block derived from (*S*)-2-hydroxymethylindoline and the synthesis of two amino alcohol-derived, chiral bis(phosphoramidite) pincer palladium complexes **1** and **2** *via* a modular synthetic approach (Figure 3). The potential of stereocontrol of the novel P-chiral pincer metal complexes has been tested by using **1** and **2** as catalysts in asymmetric allylation reactions.

4.2 Results and discussion

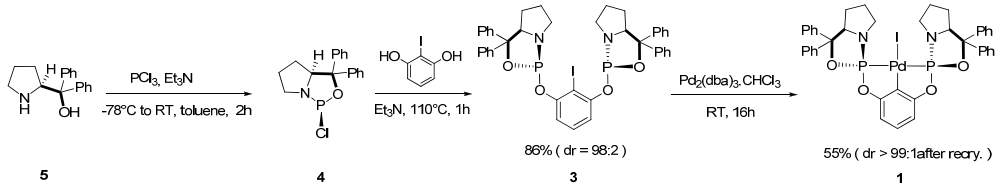
4.2.1 Synthesis of Chiral Pincer Palladium Complex 1

Complex **1** was prepared *via* a straightforward synthetic route by using optically active (*S*)-(-)-2-[diphenyl(hydroxylmethyl)]pyrrolidine **5** as starting material. This synthetic route is very suitable for a modular approach allowing the synthesis of a small library of P-chiral ligands starting from *L*-proline derivatives (Scheme 1). Optically active amino alcohol **5** was phosphonated by using PCl_3 in the presence of triethylamine to afford the corresponding phosphorochloridate adduct **4**, which was subsequently coupled with 2-iodoresorcinol in toluene at 110 °C to yield pincer arene ligand **3** in good yield. The diastereomeric ratio (*dr*) of a sample of crude **3** in solution after filtration was roughly estimated as 98:2 by comparing the integral

values of the large singlet at 141.1 ppm and a tiny singlet at 138.7 ppm in ^{31}P NMR, which were assigned to the two phosphoramidite diastereoisomers. The fact that **3** was obtained with high *dr* while being prepared at 110 °C indicated that epimerization on the P-stereogenic phoshorus donors was not taking place, which proved that the epimerization energy barrier at the P-centers is high enough for the retention of their stereochemistry under most practical conditions.[13]

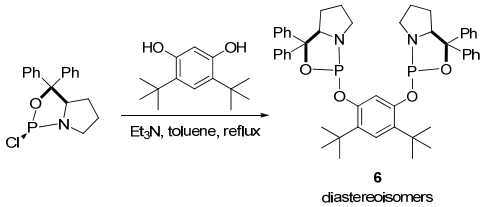
Ligand **3** was directly used in the next step after filtering over a short plug of Celite to remove any [$HNEt_3$]Cl salt. Palladation of pincer arene ligand **3,** with complete retention of the stereospecificity, was achieved *via* an oxidative addition reaction of **3** with a zerovalent Pd species (*i.e.*, $Pd_2(dba)_3.CHCl_3$) under mild conditions (20 °C, 16 h). Warming the reaction mixture to 80 °C can shorten the reaction time to 4 h without loss of any stereospecificity. However, under these conditions a substantial amount of side products was formed. In contrast to the partial racemization of the functionalized BINOL or biphenanthrol moieties upon warming to 60 °C as was reported by Szabó *et al*.,[5b] the present P-stereogenic pincer arene ligand is superior to commonly used building blocks having axial chirality in terms of retention of configuration of the stereocentres.

The pincer palladium complex **1** was obtained in reasonable yield (55%) and with excellent diastereoselectivity (*dr* > 99:1) after fractional crystallization from concentrated CH_2Cl_2 solution by the addition of hexanes. The complex can also be purified by flash chromatography, although this does require the use of pre-dried silica gel and eluent to prevent hydrolysis of the complex.



Scheme 1. Synthesis of pincer palladium complex **1**.

Bedford and co-workers developed an alternative approach to prepare diol-derived pincer metal complexes involving C-H activation by using sterically encumbered 2,4-di-*tert*-butylbenzene-1,3-diol as backbone.[6] In an attempt to use this particular approach for the diastereoselective synthesis of P-chiral pincer arene ligand **6**, we found instead that it led to a complete loss of stereospecificity on phosphorus (Scheme 2). Two sharp singlets of equal intensity at 145.3 ppm and 147.6 ppm were found in ^{31}P NMR spectra of ligand **6**.



Scheme 2. Synthesis of the racemic pincer arene ligand **6**.

4.2.2 X-ray Crystal Structure of 1·(Et_2O)

The detailed structure of pincer palladium complex **1** in the solid state was established by X-ray crystal structure determination (Figures 4 and 5). Compound **1**·(Et_2O) crystallizes in the non-centrosymmetric space group $P2_1$ and its enantiopurity was confirmed by the Flack *x* parameter (see Experimental Section). The molecular geometry of the complex consists of a P-chiral meridonal-tridentate ligand and contains a direct σ-carbon–metal bond to the palladium metal centre. The Pd-P (2.2628(8) and 2.2609(8) Å) and Pd-C (1.981(3) Å) bond lengths are very close to the corresponding bond lengths in the previously reported 1,1'-bi-2-naphthol pincer palladium complex (Table 1).[5a] The bond angle P-Pd-P (160.24(3)°) derivates from 180° due to the steric strain in the five-membered chelate rings. The ligand has the expected pseudo-equatorial orientation of the exocyclic substituents at the phosphorus atoms (*i.e.*, (*S*)-configuration at the P-stereocentres) and has two pairs of bulky diphenyl groups independently situated in quadrants II and IV, respectively (Figure 5). The phospholidine ring at P2 has an envelope conformation, while the other phospholidine and pyrrolidine cycles are best described as twisted conformations. The P-N-C (at N1 and N2) and C-C-C (at C10 and C27) angles are 120.5(2)/121.7(2)° and 118.3(3)/119.7(3)°, respectively.

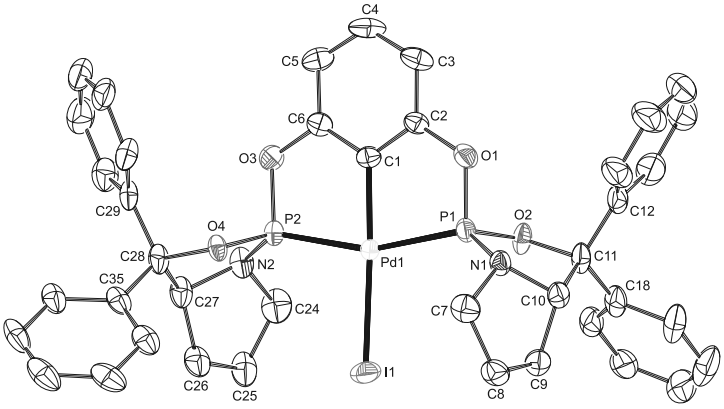


Figure 4. Displacement ellipsoid plot of complex **1**·(Et_2O) (50% probability level). Hydrogen atoms and the non-coordinated Et_2O molecule are omitted for clarity.

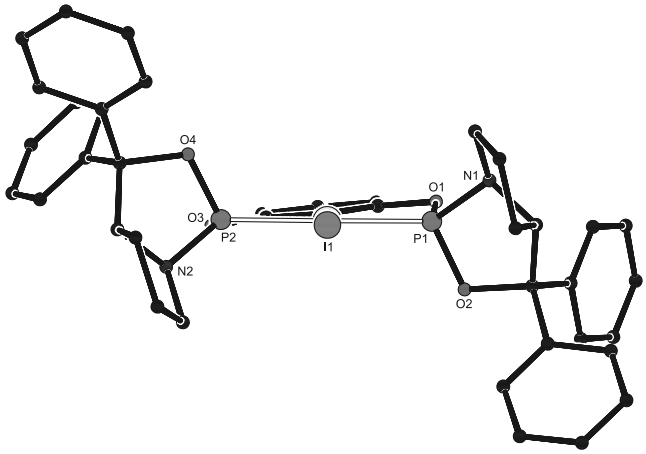
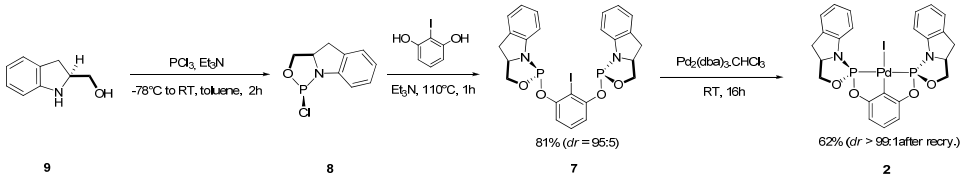


Figure 5. Molecular plot of **1**·(Et_2O) in the crystal, viewed along the I1-Pd1 bond. Hydrogen atoms and the Et_2O molecule are omitted for clarity.

4.2.3 Synthesis of Chiral Pincer Palladium Complex 2

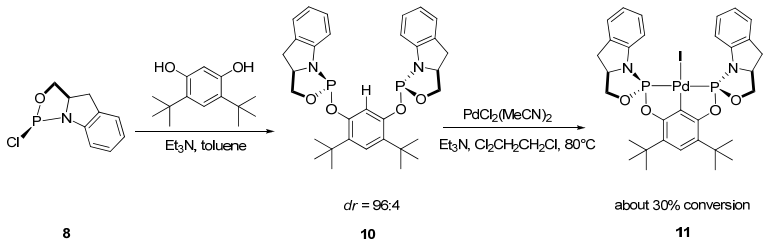
Following a similar synthesis route as reported for **1**, (*S*)-(+)-indolinemethanol **9** was reacted with PCl_3 in the presence of triethylamine to form the corresponding phosphorochloridate **8** at low temperature (Scheme 3). Without isolation and purification, **8** was subsequently reacted with 2-iodoresorcinol at 110 °C to yield pincer arene ligand **7** in good yield and acceptable purity after a simple filtration. The diastereomeric ratio of crude **7** in solution after filtration was roughly estimated at 95:5 by comparing the integral values of the large singlet at 142.3 ppm and a tiny singlet at 139.4 ppm in ^{31}P NMR. Palladation of the resulting pincer aryl iodide ligand **7** was smoothly achieved through oxidative addition with [$Pd_2(dba)_3$·$CHCl_3$] under mild conditions (20 °C, 16h). Complex **2** was obtained in promising yield (62%) with excellent diastereoselectivity (*dr* > 99:1) after fractional recrystallization from CH_2Cl_2/hexanes.



Scheme 3. Synthesis of pincer palladium complex **2**.

Besides the synthetic method mentioned above, also the alternative synthetic approach following Bedford's protocol was investigated in this case. In contrast to the unsuccessful synthesis of pincer arene ligand **6**, pincer arene ligand **10** was obtained in good yield (85%) with excellent diastereoselectivity (*dr* = 96:4 estimated by ^{31}P NMR; Scheme 4). Subsequent

metalation of modified pincer ligand **10** through a C-H activation reaction with $PdCl_2(MeCN)_2$ occurred very sluggishly but yielded some of the desired pincer metal complex **11**. Maximum conversion to **11** as estimated by ^{31}P NMR was merely about 30%. From the crude reaction mixture no analytically pure sample of complex **11** could be isolated.



Scheme 4. Synthesis of pincer palladium complex **11**.

4.2.4 X-ray Crystal Structure of **2**·(Et_2O).

We succeeded in growing single crystals of **2** and an X-ray crystal structure determination was carried out (Figures 6 and 7). Complex **2**·(Et_2O) crystallizes enantiomerically pure in the non-centrosymmetric space group P1 with two independent molecules in the unit cell. These molecules are related by an approximate, non-crystallographic twofold rotation axis roughly about the crystallographic *c*-axis, which is probably the reason for the observed formation of twinned crystals (see Experimental Section). Much like complex **1**, complex **2** possesses the typical structural features of ECE-pincer metal complexes. The Pd-P (2.2574(14)-2.2701(14) Å) and Pd-C (1.981(5) and 1.988(5) Å) bond lengths and P-Pd-P bond angles (161.11(6) and 159.87(5) °) are very close to the corresponding bond lengths and bond angle for complex **1** (Table 2), and the adopted slightly distorted square-planar geometries. The molecular structure found in the solid state confirms that the new P-chiral ligand has two P-stereogenic phosporus atoms (*i.e.*, (*S*)-configuration at both P-stereocentres). One phospholidine ring within the unit cell has a twisted conformation and three phospholidine rings are best described with an envelope conformation. The pyrrolidine rings are essentially flat. The C-C-C angles at C8*x* and C17*x* are 116.0(6)-118.2(5)°, which is comparable to the corresponding angles in complex **1** (118.3(3)/119.7(3)°), but the P-N-C angles of 123.0(4)-129.8(4)° are significantly larger than in complex **1** (120.5(2)/121.7(2)°). Interestingly, the two phenyl moieties are independently situated in quadrants I and III, respectively (Figure 7), which is exactly opposite to complex **1** (Figure 5).

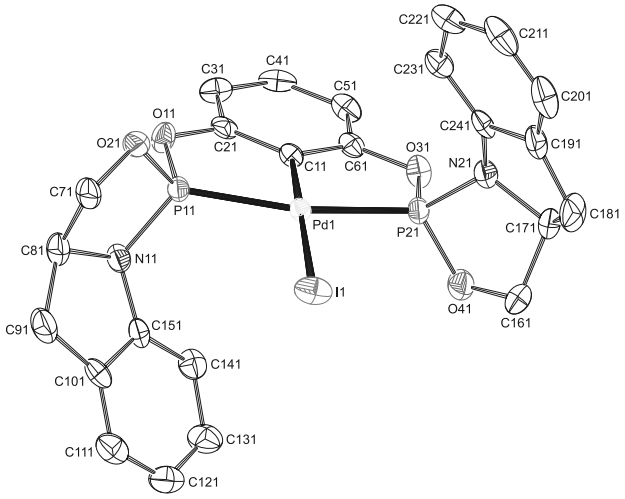


Figure 6. Displacement ellipsoid plot of complex **2**·(Et_2O) in the crystal (50% probability level). Only one of two independent molecules is shown. Hydrogen atoms and non-coordinated Et_2O molecules are omitted for clarity.

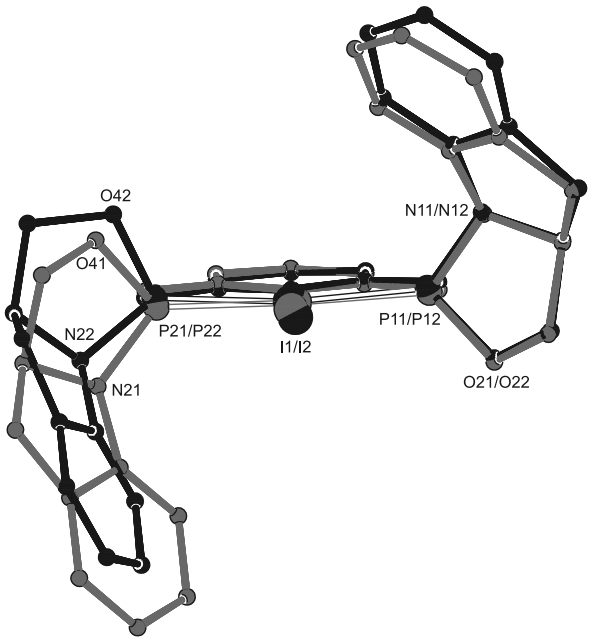


Figure 7. Quaternion fit of the two independent residues in the crystal structure of **2**·(Et_2O). Only the metal coordination plane and the coordinated phenyl ring were used for the fit. The first residue is drawn in red, the second residue in black. Hydrogen atoms and Et_2O molecules are omitted for clarity.

Table 1. Selected bond lengths [Å], angles and torsion angles [°] in **1**·(Et_2O).

Pd1-I1	2.6254(3)	Pd1-C1	1.981(3)
Pd1-P1	2.2628(8)	Pd1-P2	2.2609(8)
P1-N1	1.651(3)	P2-N2	1.646(3)
P1-O1	1.627(2)	P2-O3	1.630(2)
P1-O2	1.598(2)	P2-O4	1.594(2)
P1-Pd1-P2	160.24(3)	C1-Pd1-I1	176.97(9)
C1-Pd1-P1	79.58(9)	C1-Pd1-P2	80.68(9)
O1-P1-O2	105.02(13)	O3-P2-O4	105.64(12)
O1-P1-N1	103.90(13)	O3-P2-N2	103.80(14)
O2-P1-N1	97.15(12)	O4-P2-N2	96.77(12)
P1-N1-C7	120.5(2)	P2-N2-C24	121.7(2)
P1-N1-C10	109.5(2)	P2-N2-C27	110.3(2)
C7-N1-C10	106.8(2)	C24-N2-C27	107.8(3)
C9-C10-C11	118.3(3)	C26-C27-C28	119.7(3)
Pd1-P1-O1-C2	-15.1(2)	Pd1-P2-O3-C6	-11.8(2)

Table 2. Selected bond lengths [Å], angles and torsion angles [°] for the two independent molecules (x = 1, 2) in **2**·(Et_2O).

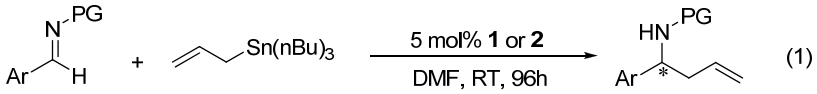
	x=1	*x*=2		*x*=1	*x*=2
Pd*x*-I*x*	2.6442(5)	2.6468(5)	Pd*x*-C1*x*	1.981(5)	1.988(5)
Pd*x*-P1*x*	2.2640(14)	2.2574(14)	Pd*x*-P2*x*	2.2616(15)	2.2701(14)
P1*x*-N1*x*	1.657(5)	1.665(5)	P2*x*-N2*x*	1.657(5)	1.673(5)
P1*x*-O1*x*	1.632(4)	1.636(4)	P2*x*-O3*x*	1.632(4)	1.632(4)
P1*x*-O2*x*	1.596(5)	1.614(4)	P2*x*-O4*x*	1.596(5)	1.595(5)
P1*x*-Pd*x*-P2*x*	161.11(6)	159.87(5)	C1*x*-Pd*x*-I*x*	176.02(16)	178.86(15)
C1*x*-Pd*x*-P1*x*	80.64(16)	80.54(15)	C1*x*-Pd*x*-P2*x*	80.48(16)	80.06(16)
O1*x*-P1*x*-O2*x*	100.7(2)	100.1(2)	O3*x*-P2*x*-O4*x*	101.0(2)	104.4(2)
O1*x*-P1*x*-N1*x*	106.9(2)	107.0(2)	O3*x*-P2*x*-N2*x*	107.0(2)	103.5(2)

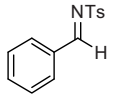
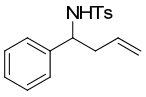
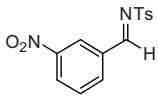
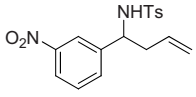
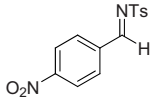
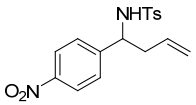
	x=1	*x*=2		*x*=1	*x*=2
O2*x*-P1*x*-N1*x*	96.2(2)	95.1(2)	O4*x*-P2*x*-N2*x*	95.0(2)	97.2(2)
P1*x*-N1*x*-C8*x*	111.4(4)	111.9(4)	P2*x*-N2*x*-C17*x*	113.4(4)	110.3(4)
P1*x*-N1*x*-C15*x*	123.9(4)	128.5(4)	P2*x*-N2*x*-C24*x*	129.8(4)	123.0(4)
C8*x*-N1*x*-C15*x*	108.9(5)	110.7(4)	C17*x*-N2*x*-C24*x*	109.1(5)	107.3(4)
C7*x*-C8*x*-C9*x*	116.0(6)	116.7(6)	C16*x*-C17*x*-C18*x*	117.5(6)	118.2(5)
Pd*x*-P1*x*-O1*x*-C2*x*	7.6(4)	4.6(4)	Pd*x*-P2*x*-O3*x*-C6*x*	3.4(4)	-8.6(4)

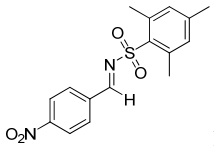
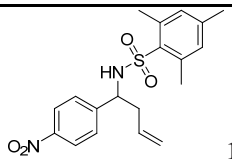
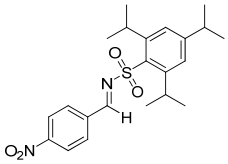
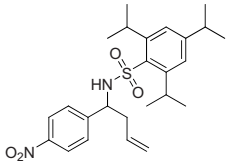
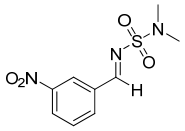
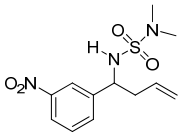
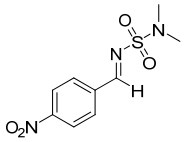
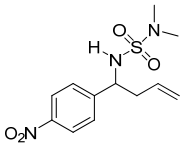
4.2.5 Catalytic Asymmetric Allylation.

Since electron-deficient ECE-pincer palladium complexes are known to be efficient catalysts in the (asymmetric) homoallylation of aldehydes and aldimines,[5, 6, 14] we embarked on testing the stereocontrolling potential of the two novel complexes **1** and **2**. These tests were carried out for the reaction of allyltributyltin with sulfonimines, *i.e.* with protected aryl aldimines, at room temperature in dry DMF without additives (Table 2, reaction 1).

Table 3. Asymmetric homoallylation of sulfonimines catalyzed by P-chiral pincer metal complexes **1** and **2**.



Entry	Substrate	Catalyst	Product	Yield (%)[b]	*e.e* (%)[c,d]
1	 **12**	**1**	 **12a**	60	0
2	**12**	**2**	**12a**	65	11
3	 **13**	**2**	 **13a**	75	20
4	 **14**	**2**	 **14a**	81	12

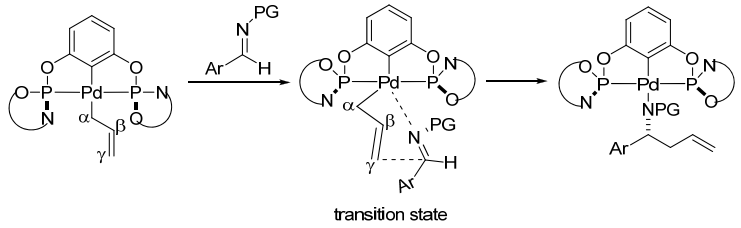
Entry	Substrate	Catalyst	Product	Yield (%)[b]	e.e (%)[c,d]
5	 **15**	**2**	 **15a**	75	14.5
6	 **16**	**2**	 **16a**	78	29
7	 **17**	**2**	 **17a**	70	28
8	 **18**	**2**	 **18a**	78	33

[a] Reaction conditions: 0.15 mmol of sulfonimine, 0.18 mmol of allyltributyltin, 5 mol% of pincer Pd complex, 1 mL of DMF, room termperature, 96 h. [b] Isolated yields. [c] Detected by chiral HPLC. [d] The absolute configurations of the allylic products have not been assigned.

The data in Table 3 show that both **1** and **2** are active catalysts in the homoallylation reaction of various aldimines bearing *N*-sulfonyl protecting groups. The allyl products were obtained in 60-81% yield, which is consistent with previous reports.[5]

Although both **1** and **2** afforded the desired allylic product **12a** in similar yields (about 60%), they exhibited very different stereoselectivities for the same substrate. For substrate **12**, complex **1** gave no *ee* whereas complex **2** gave moderate *ee*'s of 11% (Table 3, entries 1 and 2). The molecular geometries of **1** and **2** in the solid state, see Figures 5 and 7, respectively, show that in the case of complex **1**, the bulky diphenyl moieties are not oriented towards the metal centre. Differently, for complex **2**, the two P-ring skeletons form a more defined chiral pocket where the catalytic conversion takes place. This is reflected by the observation that no stereoselctivity has been obtained for the reaction with benchmark substrate **12** catalysed by **1**, whereas in the case of **2** the product was formed at least with moderate *ee*'s. Moreover, in the latter case the nature of the substituents in both the aldimine aryl ring and the *N*-sulfonyl group did have an effect on the *ee*-levels.

Mechanistic studies of ECE-pincer Pd catalysed homoallylation reactions by Szabó *et al*.,[14] showed that 1) the crucial Pd η^1-allyl moiety formed upon transmetallation of the allylstannane undergoes an electrophilic attack by an aldimine and 2) the enantioselectivity of the product is predominantly determined by the geometry of the transition state involved in this step, see Scheme 5. Accordingly, we assumed that both the geometries and electronic properties of aryl and the protecting groups could have strong influences on yield and enantioselectivity.



Scheme 5. Reaction pathway for the pincer Pd-catalyzed allylation of aldimines.

Substrates **13** and **14** bearing electron-withdrawing nitro groups on *meta* and *para* positions were tested under the same conditions with complex **2** and the corresponding allylic products were obtained in reasonable 75% and 81% yields, respectively. It seemed the yields were improved due to the enhanced electrophilicity of the sulfonimines. Interestingly, for product **13a**, the *ee* was improved to 20%, whereas it did not improve for product **14a** (Table 3, entries 3 and 4). Besides varying the substitution pattern on the aldimine phenyl ring, different protecting groups were also attempted to reveal their influences on the *ee* values. It was found that larger protecting groups resulted in better enantioselectivities, which could be explained by an enhanced recognition by the rigid chiral pockets due to the steric bulk of the protecting groups. For instance, the *ee* was slightly impoved to 14.5% for 2-mesitylenesulfonimine **15** as substrate and was further improved to 29% for 2,4,6-triisopropylbenzenesulfonimine **16** as substrate (Table 3, entries 5 and 6).

Recently, we reported on the use of the *N,N*-dimethylsulfamoyl group as a new low molecular weight and easily removable protecting/activating group for ECE-pincer metal complex catalyzed allylation reactions with a wide range of functional group tolerance.[15] Remarkably, application of this protecting group increased the *ee* of the products to 28% and 33% for substrates **17** and **18**, respectively (Table 3, entries 7 and 8), which are better than the reaults obtained with the arylsulfonimine protecting groups (Table 3, entries 5 and 6). Apparently, it is not only the size of the protecting groups but in particular their electronic properties that can somehow influence enantioselectivity, as the smaller sized *N,N*-dimethysulfamoyl protecting groups resulted in higher *ee*'s than the considerably larger triisopropylbenzenesulfonyl protecting group.

Unfortunately, although P-chiral pincer metal complexes showed comparable activities to BINOL- and biphenanthrol-based chiral pincer metal complexes,[5] the enantioselectivities were overall rather moderate. As shown in Scheme 5, electrophilic attack of aldimines takes place at the γ position of an η^1-allyl Pd moiety and this position is rather far away from the Pd centre. Plausibly, good stereocontrolling requires relatively bulkier substituents such as BINOL or biphenanthrol to afford deeper chiral pockets.

4.3 Conclusion

In this paper, we have reported the preparation of two novel P-chiral pincer palladium complexes **1** and **2** by using optically active amino alcohols as starting materials *via* template synthesis. A novel P-chiral building block derived from (*S*)-(+)-indolinemethanol was reported, which offers a nice perspective for employing this building block in further P-chiral ligand design. Through X-ray diffraction analysis, it was found that the new indoline-derived P-chiral building block provides an opposite steric congestion with respect to previously reported *L*-proline derived P-chiral ligands. This opens the possibility of making use of opposite steric congestion through appropriate modifications on various positions of the *L*-proline skeleton.

The novel P-chiral pincer metal complexes were shown to be active catalysts for the homoallylation of aldimines, with complex **2** outperforming complex **1** in terms of product enantioselectivity, which is possibly due to its more defined chiral pocket. It has also been found that both the geometries and the electronic properties of the aryl and the protecting groups on the aldimine substrates have a strong influence on both the product yield and enantioselectivity. It seemed that good stereocontrolling requires relatively bulkier ligand substituents in order to form a deeper chiral pocket. To further improve enantioselectivities and yields in these reactions, the synthesis of novel P-chiral pincer metal complexes bearing well-tailored bulkier substituents is currently ongoing in our lab.

4.4 Experimental Section

General remarks: All reactions were performed under a dry N_2 atmosphere by using standard Schlenk techniques. DMF and Et_3N were distilled over CaH_2 in a conventional heating bath and were then stored under N_2 at – 30 °C on molecular sieves. Toluene was freshly dried over sodium. PCl_3 was freshly distilled and stored under N_2 prior to use. (*S*)-(+)-indolinemethanol was prepared as previously reported.[12] Substrates **15**, **16**, **17**, and **18** were synthesized according to reported procedures.[16] All other reagents were purchased from ACROS Organics and Sigma-Aldrich Chemical Co. Inc, and used as received. ^{1}H-NMR (400.0 MHz), ^{13}C-NMR (100.6 MHz) and ^{31}P-NMR (161.9 MHz) spectra were recorded at room temperature in $CDCl_3$ on a Varian 400 MHz INOVA spectrometer. Chemical shift values are reported in ppm (δ) relative to $(CH_3)_4Si$ (^{1}H and ^{13}C NMR) or a capillary containing 85% H_3PO_4 in D_2O (^{31}P{^{1}H} NMR). Optical rotations were recorded on a Perkin-Elemer 241 polarimeter at 20 °C. Flash chromatography was performed using ACROS silica gel, 0.06 – 0.200 mm, pore diameter ca. 6 nm. Elemental microanalyses were performed by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim a/d Ruhr, Germany. MS measurements were carried out on an Applied Biosystems Voyager DE-STR MALDI-TOF MS. Enantiomeric excess values (*ee*) were measured by means of chiral-phase HPLC (Daicel Chiracel AD or AS-H) at the Department of Organic and Molecular Inorganic Chemistry, University of Groningen, Groningen, The Netherlands.

General Procedure for Synthesis of P-chiral Pincer metal complexes 1 and 2 (*S*)-(−)-α,α-diphenyl-2-pyrrolidinemethanol (0.507 g, 2 mmol) or (*S*)-(+)-indolinemethanol (0.300 g, 2 mmol) was azeotropically dried with dry toluene (3 x 2 mL) and was suspended in dry toluene (15 mL) at –78 °C. In a separated flame-dried schlenk flask, PCl_3 (2 mmol, 175 μL) and Et_3N (4 mmol, 553 μL) were diluted in dry toluene (10 mL) and this solution was added dropwise to the –78 °C precooled solution of amino alcohol with vigorously stirring. After addition, the cooling bath was removed and the reaction mixture was allowed to slowly warm to ambient temperature, at which it was stirred for an additional 2 h. Afterwards, a solution of azeotropically predried iodoresorcinol (1 mmol, 0.236 g) and Et_3N (2.2 mmol, 304 μL) in toluene (5 mL) was slowly added to the reaction mixture, which was then heated to 110 °C for 1 h. After cooling, a white salt was rapidly filtered off over a short plug of Celite and the filtre cake was washed with toluene (2 x 5 mL). The combined toluene fractions were concentrated under reduced pressure and were thoroughly dried in vacuum to yield an off-white solid. ^{31}P NMR spectra indicated that the purity of crude products was higher than 90%, so that they were directly used in the next step without further purification. Thereafter, the off-white solid was redissolved in toluene (20 mL) and this solution was added to $Pd_2(dba)_3.CHCl_3$ (0.9 mmol, 0.932 g) in toluene (10 mL). The reaction mixture was stirred at ambient temperature overnight in the absence of light. The crude reaction mixture was then concentrated under reduced pressure and the entitled complex was purified by repeating precipitation out of a small amount of CH_2Cl_2 by the addition of hexanes. Alternatively, the complex was directly subjected to chromatography by using predried silica gel and eluent (EtOAc/hexanes 3:7 (v/v)).

Spectral Data for crude product of compound 3: Yield: quantitative (0.805 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.40 (m, 2H, C*H*$_2$), 1.53 (m, 4H, C*H*$_2$), 1.71 (m, 2H, C*H*$_2$), 2.85 (apparent t, *J*=8.4 Hz, 2H, NC*H*$_2$), 3.15 (m, 2H, NC*H*$_2$), 4.11 (m, 2H, NC*H*), 6.18 (d, *J*=6.8 Hz, 2H, Ar*H*), 6.85 (t, *J*=7.2 Hz, 1H, Ar*H*), 7.20 (t, *J*=7.8 Hz, 4H, Ph*H*), 7.22-7.38 (m, 8H, Ph*H*), 7.43 (d, *J*=6.4 Hz, 4H, Ph*H*), 7.55 (d, *J*=7.2

Hz, 4H, Ph*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 24.8, 30.73, 47.9 (t, *J*=9.0 Hz), 69.8, 94.5 (t, *J*=4.0 Hz), 105.8 (t, *J*=9.6 Hz), 125.5, 126.3, 127.8, 128.5, 128.9, 129.0, 129.2, 129.4, 129.7, 133.5, 139.4 (t, *J*=4.0 Hz), 143.9, 146.5. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 141.1 (s).

Spectral Data for Complex 1: **1** was obtained as a slightly yellow solid (0.497 g, 0.55 mmol). Yield: 55%. The single crystals were grown by slow diffusion of diethyl ether into a solution of CH_2Cl_2. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.44 (m, 2H, CH_2), 1.79 (m, 4H, CH_2), 2.18 (m, 2H, CH_2), 3.33 (apparent t, *J*=9.2Hz, 2H, NCH_2), 4.26 (m, 2H, NCH_2), 4.79 (m, 2H, NC*H*), 6.26 (d, *J*=7.6 Hz, 2H, Ar*H*), 6.93 (t, J=8.0 Hz, 1H, Ar*H*), 7.26 (t, *J*=8 Hz, 4H, Ph*H*), 7.32-7.40 (m, 8H, Ph*H*), 7.47 (d, *J*=7.2 Hz, 4H, Ph*H*), 7.61 (d, *J*=6.8 Hz, 4H, Ph*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 25.8, 30.7, 48.0 (t, *J*=9.6 Hz), 71.0, 94.4 (t, *J*=3.3 Hz), 106.8 (t, *J*=9.5 Hz), 126.5, 127.3, 127.8, 128.1, 128.3, 128.4, 128.6, 128.7, 129.7, 141.4 (t, *J*=3.7 Hz), 143.7, 157.1 (t, *J*=11 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 160.3 (s). $[\alpha]_D^{20}$ -83, (C=0.1, $CHCl_3$); MS (MALDI-TOF): m/z calcd for $C_{40}H_{37}N_2O_4P_2Pd$: 777.13 $[M\text{-}I]^+$; found: 777.11; Anal.Calcd for $C_{40}H_{37}IN_2O_4P_2Pd$: C, 53.09; H, 4.12; N, 3.10; P, 6.84; found : C, 53.12; H, 4.16; N, 3.07; P, 6.82;

Spectral Data for crude product of compound 7: Yield: quantitative (0.601 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 3.10 (d, *J*=7.2 Hz, 1H, CH_2), 3.14 (d, *J*=7.0 Hz, 1H, CH_2), 3.18 (d, *J*=8.4 Hz, 1H, CH_2), 3.26 (d, *J*=8.8 Hz, 1H, CH_2), 3.65 (m, 4H, OCH_2), 4.30 (apparent t, *J*=8.8 Hz, 2H, NC*H*), 6.70 (d, *J*=7.6 Hz, 2H, Ph*H*), 6.78 (d, *J*=7.0 Hz, 2H, Ph*H*), 6.88 (t, *J*=7.7 Hz, 2H, Ph*H*), 7.15 (d, *J*=7.2 Hz, 2H, Ar*H*), 7.18 (t, *J*=7.8 Hz, 2H, Ph*H*), 7.24-7.28 (m, 1H, Ar*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl^3$, 100.6Hz): δ 34.2, 62.1, 74.5, 105.8 (t, *J*=8 Hz), 112.4, 114.5, 121.7, 123.4, 125.4, 127.9, 130.1, 132.5, 141.7 (t, *J*=6.0 Hz), 148.9. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 142.3 (s).

Spectral Data for Complex 2: **2** was obtained as an off-white solid (0.431 g, 0.62 mmol). Yield: 62%. The single crystals were grown by slow diffusion of hexanes into a solution of diethyl ether. ^{1}H NMR ($CDCl_3$, 400MHz): δ 3.09 (d, *J*=6.8 Hz, 1H, CH_2), 3.13 (d, *J*=7.6 Hz, 1H, CH_2), 3.26 (d, *J*=9.2 Hz, 1H, CH_2), 3.30 (d, *J*=8.4 Hz, 1H, CH_2), 4.34 (t, *J*=8.4 Hz, 2H, NC*H*), 4.83-4.95 (m, 4H, OCH_2), 6.77 (d, *J*=8 Hz, 2H, Ph*H*), 6.88 (d, *J*=7.6 Hz, 2H, Ph*H*), 6.94 (t, *J*=7.6 Hz, 2H, Ph*H*), 7.07 (d, *J*=7.6 Hz, 2H, Ar*H*), 7.12 (t, *J*=8 Hz, 2H, Ph*H*), 7.22-7.25 (m, 1H, Ar*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl^3$, 100.6Hz): δ 34.0, 62.5, 75.6, 107.6 (t, *J*=10 Hz), 114.5, 123.7, 125.6, 128.0, 130.5, 132.0, 142.4 (t, *J*=6.64 Hz), 156.9 (t, *J*=10.8 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 150.2 (s). $[\alpha]_D^{20}$ -470, (C = 0.1, $CHCl_3$); MS (MALDI-TOF): m/z calcd for $C_{24}H_{21}N_2O_4P_2Pd$: 569.00 $[M\text{-}I]^+$; found: 569.03; Anal.Calcd for $C_{24}H_{21}IN_2O_4P_2Pd$: C, 41.37; H, 3.04; N, 4.02; P, 8.89; found : C, 41.41; H, 3.01; N, 3.98; P, 8.93;

General Procedure for P-Chiral Palladium Pincer metal complex-Catalyzed Allylation of Aldimines. Allyltributylstannane (56 μL, 0.18 mmol) was added to a mixture of sulfonimine (0.15 mmol), pincer Pd complex **1** or **2** (0.0075 mmol) and dry DMF (1 mL). The reaction mixture was then stirred for 96 h at room temperature and was quenched by the addition of a saturated aqueous KF solution (1 mL). The resulting mixture was vigirously stirred at room temperature for another 24 h. The crude product was extracted with EtOAc (3 x 2 mL) and the combined organic layers were dried over $MgSO_4$. Analytically pure allylic product was obtained by purification on a silica gel column (hexanes/EtOAc, 7:3 (v/v)). The enantiomeric excess was determined by chiral-phase HPLC (Daicel Chiracel OD-H or AS-H columns).

N1-[1-(4-Nitrophenyl)-3-butenyl]-2,4,6-trimethyl-1-benzenesulfonamide 15a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.21 (s, 3H, *Me*), 2.43 (t, *J*=6.8 Hz, 2H, CH_2CH=CH_2), 2.48 (s, 6H, *Me*), 4.40 (q, *J*=7.2 Hz, 1H,

C*H*=CH_2), 5.08-5.12 (apparent t, 2H, CH=CH_2), 5.30 (br s, 1H, N*H*), 5.47-5.54 (m, 1H, ArC*H*(NH)), 6.78 (s, 2H, mesitylene*H*), 7.22 (d, *J*=8 Hz, 2H, Ar*H*), 7.94 (d, *J*=8 Hz, 2H, Ar*H*). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 21.1, 23.2, 42.0, 56.7, 120.8, 123.6, 127.7, 132.0, 132.4, 133.9, 139.1, 143.0, 147.3, 148.1. Anal. Calcd. for $C_{19}H_{22}N_2O_4S$: C, 60.94; H, 5.92; N, 7.48; S, 8.56 Found : C, 60.99; H, 5.88; N, 7.45; S, 8.51. The enantiomeric excess of **15a** was determined by chiral-phase HPLC (Daicel Chiracel AD, hexane/iPrOH 9:1 (v/v), flow rate 1.0 mL/min): major enantiomer t_r=13.4 min, minor enantiomer t_r=11.0 min.

N1-[1-(4-Nitrophenyl)-3-butenyl]-2,4,6-triisopropyl-1-benzenesulfonamide 16a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.13 (d, *J*=6.8 Hz, 7H, *i*Pr*H*), 1.21-1.24 (m, 14H, *i*Pr*H*), 2.45-2.52 (m, 2H, CH_2CH=CH_2), 4.60 (q, *J*=5.2 Hz, 1H, C*H*=CH_2), 4.99 (d, *J*=4.4 Hz, 1H, N*H*), 5.10-5.16 (apparent t, 2H, CH=CH_2), 5.21-5.60 (m, 1H, ArC*H*(NH)), 7.06 (s, 2H, (*i*Pr)$_3$Ar*H*), 7.27 (d, *J*=8.4 Hz, 2H, Ar*H*), 8.00 (d, *J*=8.4 Hz, 2H, Ar*H*). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 9.3, 13.9, 23.8, 25.0, 27.5, 29.3, 30.0, 34.4, 42.2, 56.5, 120.7, 123.7 (d, *J*=19 Hz), 127.9, 132.4, 133.2, 147.4, 148.4, 150.2, 153.5. Anal. Calcd. for $C_{25}H_{34}N_2O_4S$: C, 65.47; H, 7.47; N, 6.11; S, 6.99 Found : C, 65.51; H, 7.55; N, 6.13; S, 7.01. The enantiomeric excess of **16a** was determined by chiral-phase HPLC (Daicel Chiracel AD, hexane/iPrOH 9:1 (v/v), flow rate 1.0 mL/min): major enantiomer t_r=9.0 min, minor enantiomer t_r=7.1 min.

N1-[1-(3-Nitrophenyl)-3-butenyl]-*N,N'*-dimethylsulfamoylamide 17a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.53-2.60 (m, 8H, NMe_2 + CH_2CH=CH_2), 4.54 (q, *J*=6.0 Hz, 1H, C*H*=CH_2), 4.81 (d, *J*=5.2 Hz, 1H, N*H*), 5.17-5.21 (m, 2H, CH=CH_2), 5.63 (m, 1H, ArC*H*(NH)), 7.54 (t, *J*=7.6 Hz, 1H, Ar*H*), 7.54 (d, *J* =7.2 Hz, 1H, Ar*H*), 8.13 (d, *J*=7.2 Hz, 1H, Ar*H*), 8.20 (s, 1H, Ar*H*). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 37.8, 42.1, 57.0, 120.5, 121.8, 122.9, 129.8, 132.6, 133.2, 144.3, 148.6. Anal. Calcd. for $C_{12}H_{17}N_3O_4S$: C, 48.15; H, 5.72; N, 14.04; O, 21.38; S, 10.71 Found : C, 48.11; H, 5.77; N, 14.40; S, 10.74. The enantiomeric excess of **17a** was determined by chiral-phase HPLC (Daicel Chiracel AS-H, hexane/iPrOH 9:1 (v/v), flow rate 1.0 mL/min): major enantiomer t_r = 23.1 min, minor enantiomer t_r = 26.0 min.

N1-[1-(4-Nitrophenyl)-3-butenyl]-*N,N'*-dimethylsulfamoylamide 18a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.50-2.54 (m, 2H, CH_2CH=CH_2), 2.58-2.59 (m, 6H, NMe_2), 4.52 (q, *J*=6.8 Hz, 1H, C*H*=CH_2), 5.01 (d, *J*=6.4 Hz, 1H, N*H*), 5.13-5.18 (m, 2H, CH=CH_2), 5.60-5.70 (m, 1H, ArC*H*(NH)), 7.48 (d, *J*=6.8 Hz , 2H, Ar*H*), 8.20 (d, *J*=6.8 Hz, 2H, Ar*H*). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 37.9, 42.1, 57.1, 120.6, 124.0, 127.8, 132.5, 147.6, 149.4. Anal. Calcd. for $C_{12}H_{17}N_3O_4S$: C, 48.15; H, 5.72; N, 14.04; O, 21.38; S, 10.71 Found : C, 48.23; H, 5.70; N, 14.11; S, 10.64. The enantiomeric excess of **18a** was determined by chiral-phase HPLC (Daicel Chiracel AS-H, hexane/iPrOH 9:1 (v/v), flow rate 1.0 mL/min): major enantiomer t_r=25.3 min, minor enantiomer t_r=30.1 min.

X-ray Crystal Structure Determinations. X-ray reflections were measured with Mo-K_α radiation (λ = 0.71073 Å) on a Nonius KappaCCD diffractometer with rotating anode at a temperature of 150 K up to a resolution of $(\sin\theta/\lambda)_{max}$ = 0.65 Å^{-1}. Integration of the reflections was performed with EvalCCD[17]. The structures were solved with automated Patterson methods (program DIRDIF-99[18] for **2**·(Et_2O)) or Direct Methods (SHELXS-97[19] for **1**·(Et_2O)). Refinement was performed with SHELXL-97[19] against F^2 of all reflections. Non hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were introduced in calculated positions and refined with a riding model. Geometry calculations and checking for higher symmetry was performed with the PLATON[20] program. In **1**·(Et_2O) the diethylether solvent molecule was refined with a partial occupancy of 0.85. The crystal of **2**·(Et_2O) was non-merohedrally twinned with a twofold rotation about *hkl* (001) as twin operation. This twin law was taken

into account during intensity integration and the HKLF5 structure refinement.[21] The twin fraction refined to 0.5361(6). Further details about the crystal structure determinations are given in Table 4.

Table 4. Selected crystallographic data for complexes **1**·(Et_2O) and **2**·(Et_2O).

	1·(Et_2O)	**2**·(Et_2O)
formula	$C_{40}H_{37}IN_2O_4P_2Pd \cdot 0.85(C_4H_{10}O)$	$C_{24}H_{21}IN_2O_4P_2Pd \cdot C_4H_{10}O$
Fw	967.96	770.79
crystal colour	colourless	colourless
crystal size [mm^3]	0.39x0.21x0.12	0.63x0.39x0.09
crystal system	monoclinic	triclinic
space group	$P2_1$ (no. 4)	P1 (no. 1)
a [Å]	13.5613(5)	10.3714(3)
b [Å]	9.5680(2)	11.8544(2)
c [Å]	17.5560(9)	13.0540(3)
α [°]	90	89.198(1)
β [°]	108.878(2)	84.462(2)
γ [°]	90	68.804(1)
V [$Å^3$]	2155.43(14)	1489.01(6)
Z	2	2
D_x [g/cm^3]	1.491	1.719
refl. meas./unique	40685 / 9826	18348 / 11751
μ [mm^{-1}]	1.265	1.807
abs. corr.	multi-scan	multi-scan
abs. corr. range	0.42-0.86	0.41-0.85
param./restraints	498 / 4	708 / 3
R1/wR2 [I>2σ(I)]	0.0293 / 0.0577	0.0298 / 0.0768
R1/wR2 [all refl.]	0.0428 / 0.0618	0.0319 / 0.0786
Flack x parameter [505]	-0.027(12)	0.007(15)
S	1.035	1.102
res. density [$e/Å^3$]	-0.90 / 0.71	-0.98 / 1.05

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Chapter 5

Chiral *Ortho*-palladated and -platinated Arylphosphite Complexes

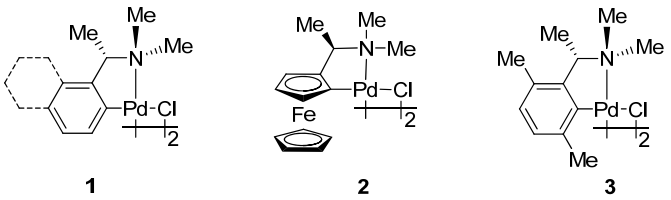
Abstract

A series of chiral bis-phosphite complexes **8** – **11** $[MCl_2(L)_2]$ (M=Pd or Pt) and *ortho*-metallated, *C,P*-chelate bonded monophosphite complexes **12** – **14** $[M(\kappa^2\text{-}L)(\mu\text{-}Cl)]_2$ have been prepared by reacting enantiopure (*R*)-BINOL-derived arylphosphite ligands L with readily accessible palladium or platinum precursors under appropriate conditions. The reactivity of complexes **12** − **14** containing the chiral *C,P*-bidentate bonded arylphosphite ligands towards various monodentate and bidentate ligands was studied. It was found that the *ortho*-palladated complexes **12** and **13** do not cleanly react with triphenylphosphine in dichloromethane, whereas *ortho*-platinated complex **14** smoothly reacts with typical monodentate or bidentate ligands such as pyridine, triphenylphosphine, tricyclohexylphosphine, triphenylphosphite and [1,2-bis(diphenylphosphino)ethane] to generate the corresponding monomeric chiral *ortho*-platinated complexes **18** – **23** in good to excellent yields. Besides the full characterization of all novel complexes by NMR techniques and mass spectroscopy as well as elemental analysis, the structures of complexes **10**, **18**, **19** and **23** in the solid state (X-ray crystal structure determination) were established. The purpose and potential of employing the *ortho*-platinated complex **14** either as a resolution reagent or as a chiral NMR shift reagent were studied. Both enantiomers of racemic α-methylbenzylamine could be resolved with promising yields.

5.1 Introduction

Chiral *C,E*-cyclopalladated (E = *e.g.* N-, P-donor atom containing group) complexes have been widely used in many areas of synthetic stereochemistry due to their insensitivity towards air and moisture, tunable structural features and recyclability.[1] These complexes find a versatile use as efficient resolving agents,[2] sensitive diamagnetic shift reagents,[3] reliable stereochemical references[4] and active catalysts in stereoselective organic transformations.[5] Among these complexes, the synthesis and applications of dimeric halogen bridged chiral *C,N*-cyclopalladated complexes have been intensively studied, see Figure 1 for examples.

N,N-dimethyl-1-phenylethanamine and its derivatives are quite often used as amine ligands due to their easy accessibility (*e.g.* complex **1**, Figure 1). Planar-chiral *C,N*-cyclopalladated complexes bearing metallocene moieties have also been documented (*e.g.* complex **2**, Figure 1).[6] Generally, both enantiomers of these *C,N*-cyclopalladated complexes can be obtained by resolving a pair of diastereoisomers, which can be prepared by reacting dimeric *C,N*-cyclopalladated racemates with another chiral auxiliary such as (*S*)-sodium prolinate.[7] The chiral informaton in the five membered *C,N*-chelate ring is most efficiently transferred to the coordination site *cis* with respect to the N atom, since this position is stereochemically controlled by the two NMe_2 methyl groups.[8] However, the external donors would prefer to occupy the position *trans* with respect to the N-donor atom according to the antisymbiosis effect.[9] Van Koten *et al.* firstly found that introduction of a group, *e.g.* Me or non-coordinating CH_2NMe_2 group, *ortho* to the cyclometallated Ar-M bond could induce a unique and unprecedented intramolecular rearrangement in the corresponding Ir and Rh complexes,[10] which implied that stereochemical control of *C,N*-chelated chiral ligands might be affected by this approach. In 2003, Leung *et al.* independently described that by introduction of an *ortho*-substituent, *i.e.,* a methyl group next to the Ar-Pd bond as in **3** (Figure 1), the steric control of the coordination site *trans* with respect to the N-donor atom can be enhanced as the aryl ring is a part of the chiral backbone of the *C,N*-chelated amine ligands.[7]



1 **2** **3**

Figure 1. Representative examples of chiral *C,N*-cyclopalladated complexes.

Inspired by Leung's work, we have designed and synthesized a series of chiral *ortho*-palladated and -platinated arylphosphite complexes. The resulting metallates containing two *C,P*-chelate

monophosphite ligands would provide a phosphorus donor atom steering the incoming ligand to occupy the desired *cis*-position next to the chiral moieties. As depicted in Figure 2, chiral phosphite ligands can be easily prepared by coupling phenol or its derivatives with various chiral diol phosphorochloridates and the P-donor atom in these ligands is the intimate part of the chiral group. The resulting arylphosphite ligands are able to react with metal precursors under appropriate conditions to afford the entitled chiral *C,P*-cyclometallated complexes in which the arylphosphite ligand acts as a *C,P*-bidentate coordinating ligand. The chiral pockets in such complexes could in principle be fine-tuned by applying different chiral diols, such as optically active BINOL. Particularly, both enantiomers of the *C,P*-cyclometallated complexes are easily accessible without tedious resolution by using commercially available enantiopure chiral alcohols.

Recently, during the preparation of this paper, Dunina *et al.* independently reported the preparation of (*S*)-BINOL-derived *C,P*-cyclopalladated complex **13** in a very similar manner as well as the reactions of this complex with PPh_3 or (*R*)-valinate.[11]

In this paper, we report on the preparation, reactivities and application of chiral *C,P*-cyclometallated arylphosphite complexes derived from (*R*)-BINOL. In contrast to the *C,N*-cyclopalladated complexes derived from chiral amine ligands, it has been found that the present *C,P*-cyclometallated arylphosphite complexes react with a monodentate ligand D to selectively form the *cis*-substituted product with respect to the P-donor atom of the *C,P*-chelate bonded arylphosphite moiety, *i.e.*, at the position closest to the chiral pocket.

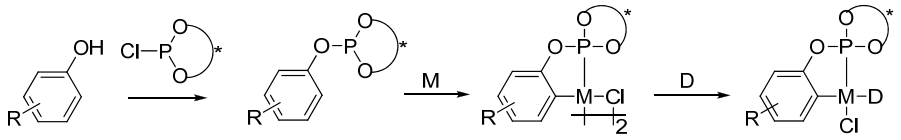
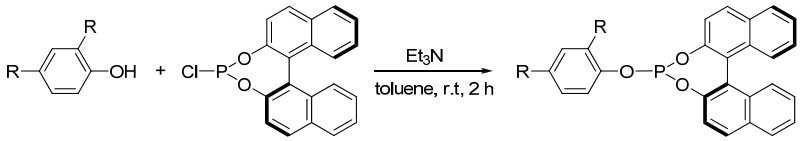


Figure 2. Synthesis of chiral *C,P*-cyclometallated complexes.

5.2 Results and discussion

5.2.1 Synthesis of monomeric bis-phosphite complexes

As shown in Scheme 1, (*R*)-(+)-1,1'-bi-(2-naphthol) (BINOL) derived monophosphite ligands **6** and **7** were easily prepared according to a reported procedure.[12]

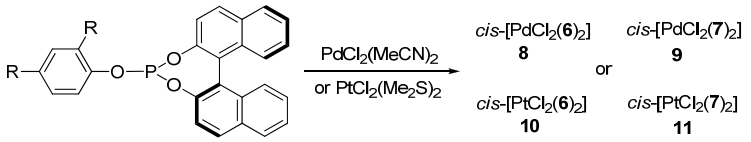


4 R = H
5 R = *tert*-butyl

6 R = H
7 R = *tert*-butyl

Scheme 1. Synthesis of monophosphite ligands **6** and **7**.

Subsequently, as elaborated in Scheme 2, the reaction of either $[PdCl_2(MeCN)_2]$ or $[PtCl_2(Me_2S)_2]$ with two equivalents of the respective monophosphite ligands **6** or **7** gave the corresponding bis-phosphite complexes $[MCl_2(L)_2]$ (M = Pd or Pt; L = **6** or **7**) **8** − **11** in good to excellent yields (*i.e.,* 65-91% isolated yields).



6 R = H
7 R = *tert*-butyl

Scheme 2. Synthesis of complexes $[MCl_2(L)_2]$ (M = Pd or Pt; L = **6** or **7**).

^{31}P NMR spectra of complexes **8** – **11** nicely showed a single unique signal, which indicates that only one of the possible isomers was isolated. Interestingly, ^{31}P NMR spectra of complexes **8** and **10** derived from ligand **6** showed a sharp peak, whereas those of complexes **9** and **11** derived from ligand **7** showed a fairly broad peak. This indicates that an increased steric interference of the sterically bulky *tert*-butyl groups in the phosphite ligand **7** induces intermolecular ligand exchange between coordinated and dissociated ligands. The *cis*-configuration of platinum complexes **10** and **11** was assigned by comparing their Pt-P coupling constants with those of reported complexes. Complexes **10** and **11** possess a rather large Pt-P coupling constant, *i.e.*, $J_{Pt\text{-}P}$ are 5764 and 5805 Hz for **10** and **11**, respectively, which, however fully agrees with the Pt-P coupling constant reported for *cis*-$[PtCl_2(P(OPh)_3)_2]$ (*i.e.*, $J_{Pt\text{-}P}$=5805 Hz).[13] The *cis-P,P'*-configuration of **10** in the solid state was confirmed by X-ray crystal structure determination (Figure 3). In the asymmetric unit of the crystal structure there are 1.5 independent molecules, meaning that one molecule is located on a general position and has C_1 symmetry while the other molecule is located on an exact, crystallographic twofold axis. The determination of the Flack x parameter proves that the crystal is enantiomerically pure. The characteristic Pd-Cl stretches in the IR spectra of complexes **8** and **9** (*i.e.*, ν(Pd-Cl): 218 and 335 cm^{-1} for **8**; ν(Pd-Cl): 212 and 340 cm^{-1} for **9**) indicate the presence of a *cis*-$PdCl_2$ complex.[14] Accordingly, this confirms that

the *cis*-configuration found for the structure of the bis-phosphite palladium complexes in the solid state is retained in solution. It is obvious, that the π-acidic phosphite ligands in complexes **8** - **11** would preferentially be *trans* to the π-basic chlorides.

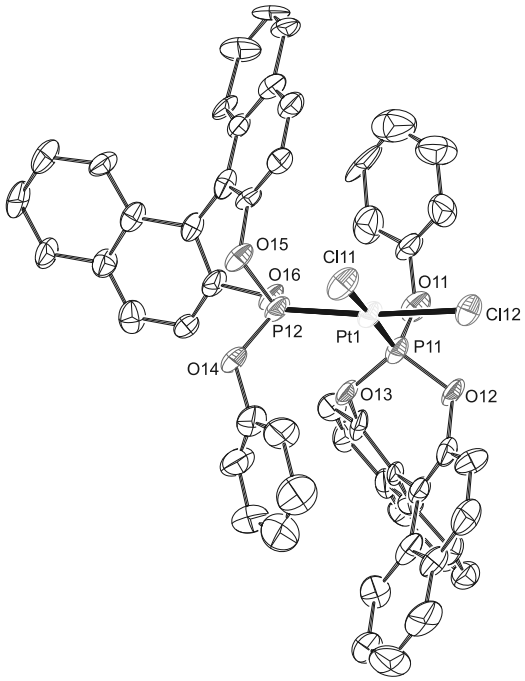
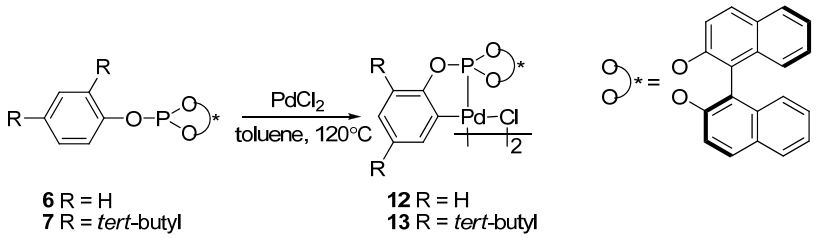


Figure 3. Displacement ellipsoid plot of **10** in the crystal (50% probability level). Hydrogen atoms and disordered solvent molecules have been omitted for clarity. Only the molecule with C_1 symmetry is shown. Characteristic bond distances (Å) and bond angles (°) in **10** Pt1-Cl11 2.342(3), Pt1-Cl12 2.328(3), Pt1-P11 2.185(2), Pt1-P12 2.188(3), Cl11-Pt1-Cl12 90.11(10), P11-Pt1-P12 93.31(10).

5.2.2 Synthesis of chiral *C,P*-cyclometallated complexes

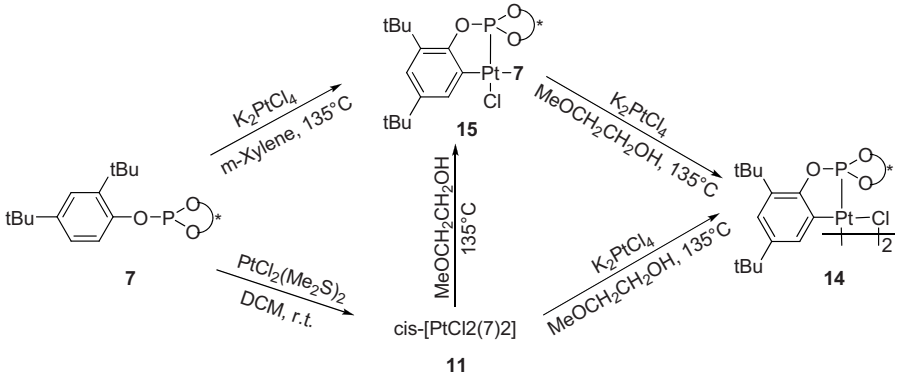
Following the reaction conditions reported by Bedford *et* al,[14, 15] reacting monophosphite ligands **6** and **7** with stoichiometric amounts of $PdCl_2$ in toluene at refluxing temperature overnight afforded the desired *C,P*-cyclopalladated complexes **12** and **13** in 65 and 55% isolated yields, respectively (Scheme 3). The structures of the resulting complexes were confirmed by NMR techniques and mass spectrometry as well as elemental analysis. ^{31}P NMR spectra of complexes **12** and **13** both showed two peaks at 25°C, which implies that these complexes are formed as a mixture of the *cis*- and *trans*-isomers as previously documented for the other *C,P*-cyclopalladated triarylphosphite complexes.[13,14,15] Remarkably, ^{31}P NMR as well as ^{1}H NMR spectra displayed rather broad peaks at 25°C, which could be due to a facile interchange of *cis*- and *trans*-isomers at room temperature.



Scheme 3. Synthesis of chiral *C,P*-cyclopalladated complexes **12** and **13**.

In contrast to the straightforward synthesis of *C,P*-cyclopalladated complexes **12** and **13**, the synthesis of *C,P*-cycloplatinated analogues was more challenging. Refluxing stoichiometric amounts of ligands **6** or **7** and K_2PtCl_4 in toluene or in higher boiling *m*-xylene or 2-methoxyethanol did not give any of the desired products. In the latter case, amorphous Pt^0 black was formed. Pregosin *et al.* independently reported that refluxing *cis*-$[PtCl_2(P(OPh)_3)_2]$ and 1.1 equivalent of $PtCl_2$ in xylene leads to the formation of $[Pt(\mu\text{-}Cl)(P(OPh)_2(OC_6H_4))]_2$ in 84% isolated yield.[13] Following this procedure, *cis*-$[PtCl_2(\mathbf{6})_2]$ (**10**) and 1.2 equivalent of K_2PtCl_4 were refluxed in m-xylene or methoxyethanol for 3.5 h. Nevertheless, no *ortho*-metallation occurred. On the other hand, refluxing *cis*-$[PtCl_2(\mathbf{7})_2]$ (**11**) and 1.2 equivalent of K_2PtCl_4 in methoxyethanol did yield the desired *C,P*-cycloplatinated complex **14** in 55% (isolated) yield (*See* Experimental Section, the synthesis of complex **14**, Method A). The structure of this complex was confirmed by NMR techniques and mass spectroscopy as well as elemental analysis. The ^{31}P NMR spectrum showed a singlet with platinum satellites at 102.9 ppm ($J_{Pt\text{-}P}$ =7858 Hz) corresponding to the *trans*-isomer and a second singlet at 103.2 ppm ($J_{Pt\text{-}P}$ =8127 Hz) corresponding to the *cis*-isomer. It is found that these $J_{Pt\text{-}P}$ values and the quotient of them (*i.e.*, q=1.034) are slightly larger than those of reported analogues $[Pt(\mu\text{-}Cl)(P(OPh)_2(OC_6H_4))]_2$ (*i.e.*, $J_{Pt\text{-}P}$ =7760 Hz and $J_{Pt\text{-}P}$ =7860 Hz; q=1.013)[13] and $[Pt(\mu\text{-}Cl)(P(OC_6H_3\text{-}2,4\text{-}tBu_2)_2(OC_6H_2\text{-}2,4\text{-}tBu_2))]_2$ (*i.e.*, $J_{Pt\text{-}P}$=7750 Hz and $J_{Pt\text{-}P}$=7875 Hz; q=1.016).[16] Interestingly, only heating complex **11** in methoxyethanol at refluxing temperature smoothly yielded *ortho*-platinated adduct **15** in quantitative yield (*See* Experimental Section, the synthesis of complex **15**, Method A). This complex comprises both an *ortho*-platinated ligand **7** and a non-*ortho*-platinated one. The P-P coupling constant of complex **15** (*i.e.*, $J_{P\text{-}P}$=27 Hz) implies that the non-*ortho*-platinated ligand is located *cis* to the *ortho*-platinated one,[13] which is in accordance with the analogous complex $[Pt(\mu\text{-}Cl)(P(OC_6H_3\text{-}2,4\text{-}tBu_2)_2(OC_6H_2\text{-}2,4\text{-}tBu_2))]_2$.[16] Moreover, complex **15** could be converted into the *C,P*-cycloplatinated complex **14** by refluxing it in methoxyethanol in the presence of 1.2 equivalent of K_2PtCl_4. To our delight, treatment of ligand **7** with 0.5 equivalent of K_2PtCl_4 in refluxing m-xylene smoothly resulted in

the formation of complex **15** in excellent yield (*See* Experimental Section, the synthesis of complex **15**, Method B). Accordingly, complex **14** was alternatively prepared in comparable yield (*i.e.*, 50%) by using a one-pot procedure that includes two steps (*See* Experimental Section, the synthesis of complex **14**, Method B): 1) heating ligand **7** and 0.5 equivalent of K_2PtCl_4 in *m*-xylene followed by, 2) using *in situ* formed complex **15**, adding another 0.6 equivalent of K_2PtCl_4 and refluxing in methoxyethanol. The portion-wise addition of platinum precursor dramatically and positively affected the yield, since adding 1.1 equivalent of K_2PtCl_4 in one portion at the beginning of the procedure merely gave complex **14** in 25% (isolated) yield (*See* Experimental Section, the synthesis of complex **14**, Method C). The integrated synthetic route for the preparation of chiral *C,P*-cycloplatinated complex **14** is elaborated in Scheme 4. It is worth pointing out that the sterically encumbered *tert*-butyl groups in phosphite ligand **7** play a pivotal role in both *ortho*-platinated reactions. For instance, refluxing complex **10** in methoxyethanol did not result in an *ortho*-platinated reaction. Moreover, treating ligand **6** with 0.5 equivalent of K_2PtCl_4 at refluxing temperature in *m*-xylene for 48 h merely afforded bis-phosphite complex **10** instead of an *ortho*-platinated product. As a result, we have been able to prepare the chiral *C,P*-cyclopalladated complexes **12** and **13**, and the chiral *C,P*-cycloplatinated complex **14**, whereas the synthesis of the analogous Pt complex starting from ligand **6** or complex **10** still remains a challenge.

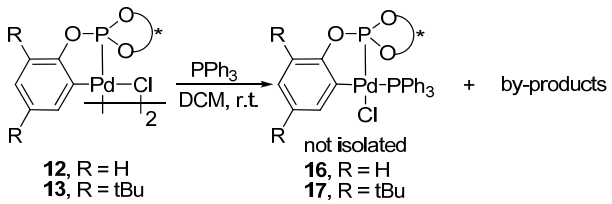


Scheme 4. Synthesis of *ortho*-platinated dimeric complex **14**.

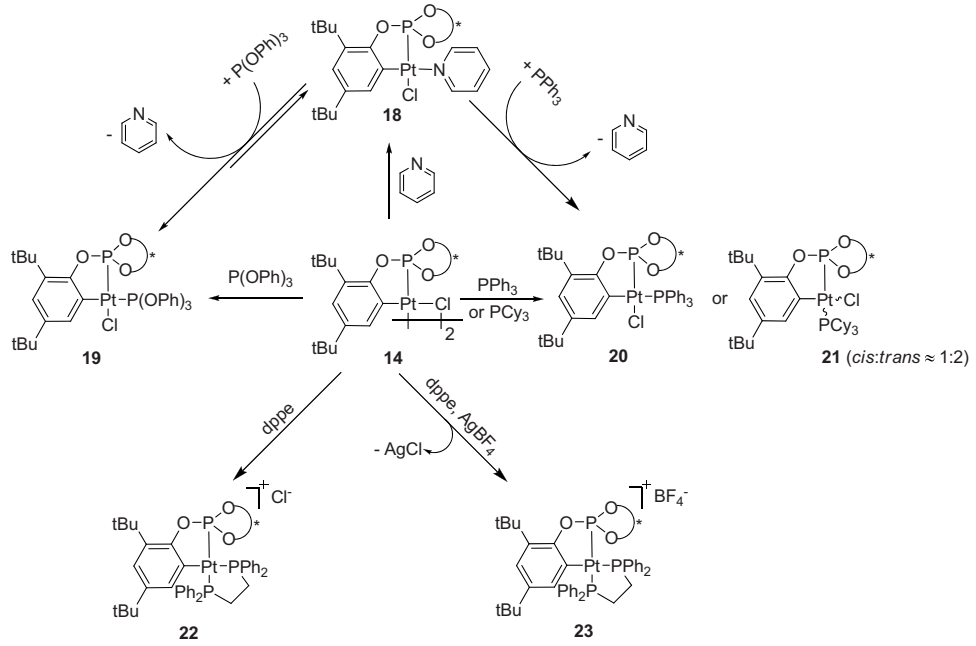
5.2.3 Synthesis and reactivities of chiral *C,P*-cyclometallated complexes 12 - 14

A distinctly different reactivity behavior of chiral *C,P*-cyclometallated complexes **12** - **14** towards monodentate and bidentate ligands bearing phosphorus or nitrogen donors was observed. Palladium complexes **12** and **13** reacted with triphenylphosphine under mild conditions (*i.e.*, dichloromethane, room temperature, 2 h) and formed the expected *ortho*-palladated complexes.

The configurations of these triphenylphosphine adducts were confirmed and assigned according to the indicative P-P coupling constants (Scheme 5). For example, the ^{31}P NMR spectra of the reaction mixture of complex **12** and triphenylphosphine clearly showed a pair of doublets at δ=18.70 ppm and at δ=150.90 ppm with the coupling constant $J_{P\text{-}P}$ = 45 Hz, which implies that the phosphine P-donor atom coordinates *cis* with respect to the BINOL-phosphite P-donor atoms.[13] The isolation of products **16** and **17** was, however frustrated by low chemical yields and the presence of considerable amounts of unknown by-products. Eventually, no analytically pure samples could be obtained. This is in contrast to the highly selective preparation of **17** when toluene was employed as the solvent as recently has been reported by Dunina *et al*.[11]



Scheme 5. Reactivity of chiral *C,P*-cyclopalladated complexes **12** and **13**.



Scheme 6. Reactivities of *C,P*-cycloplatinated complex **14**.

In contrast with these poor results for the *C,P*-cyclopalladated chemistry, the chiral *C,P*-cycloplatinated complex **14** smoothly reacted with various monodentate ligands, such as pyridine, triphenylphosphite, triphenylphosphine and tricyclohexylphosphine, to quantitatively generate the corresponding *ortho*-platinated complexes **18** – **21**.

Although the ^{31}P NMR spectra of **18** nicely showed a singlet at 109.8 ppm with platinum satellites ($J_{Pt\text{-}P}$ =7194 Hz), the assignment of the absolute configuration of **18** only based on NMR-data was problematic since no reference compounds were at hand. This problem was solved after we had succeeded in growing suitable single crystals of this complex. As is shown by the X-ray structure in Figure 4, complex **18** adopts a slightly distorted square-planar geometry in which the two P- and N-donors are in a *cis*-arrangement as confirmed by the P-Pt-N angles of 99.09(8) and 96.71(8)° for the two independent metal complexes in the crystals.

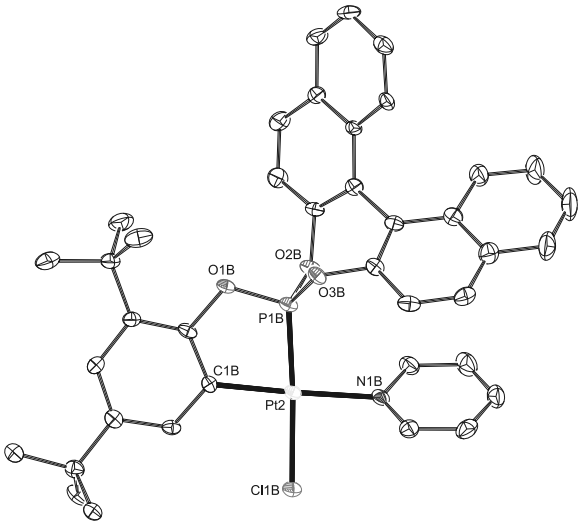


Figure 4. Displacement ellipsoid plot of **18** in the crystal (50% probability level). Ordered and disordered solvent molecules and hydrogen atoms have been omitted for clarity. Only one of two independent metal complexes is shown. Characteristic bond distances (Å) and bond angles (°) in **18** Pt2-C1B 2.028(3), Pt2-Cl1B 2.3463(8), Pt2-P1B 2.1296(9), Pt2-N1B 2.122(3), C1B-Pt2-P1B 80.78(9), P1B-Pt2-N1B 96.71(8), Cl1B-Pt2-N1B 86.48(8), Cl1B-Pt2-C1B 96.03(9).

The assignment of the configuration at the platinum centres of complexes **19** – **21** was established by indicative ^{31}P NMR P-P coupling constant of the two phosphorus donors. For instance, both complexes **19** and **20** exclusively adopt a *cis*-configuration as indicated by their P-P coupling constants of $^{2}J_{P\text{-}P}$ = 29 and 22 Hz, respectively.[13] This means that strong electron-withdrawing or moderately electron-donating ligands would preferentially locate at the *cis*-position with respect to the BINOL-phosphite moiety. The solid state structure of **19** was

obtained by single crystal X-ray structure determination. As shown in Figure 5, **19** adopts a slightly distorted square-planar geometry and a *cis*-arrangement of the two P donors with a P1-Pt1-P2 angle of 100.65(5)°.

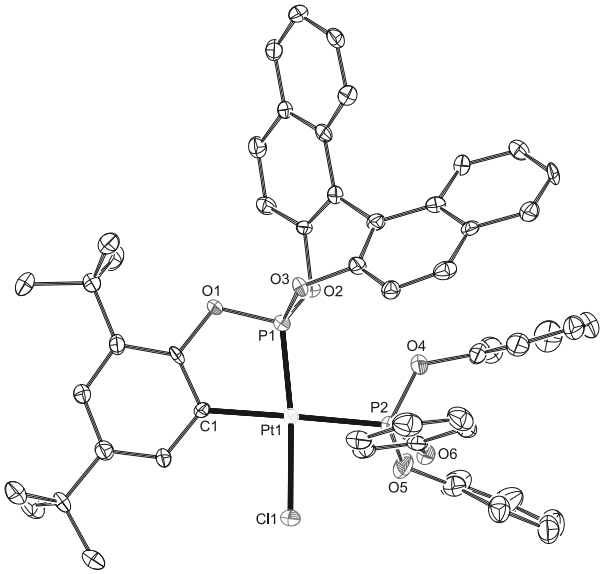


Figure 5. Displacement ellipsoid plot of **19** in the crystal (50% probability level). Hydrogen atoms and disordered solvent molecules have been omitted for clarity. Characteristic bond distances (Å) and bond angles (°) in **19** Pt1-C1 2.052(5), Pt1-Cl1 2.3542(13), Pt1-P1 2.1592(13), Pt1-P2 2.2696(14), C1-Pt1-P1 80.43(15), C1-Pt1-P2 175.09(16), P1-Pt1-P2 100.65(5), P1-Pt1-Cl1 173.15(5).

Interestingly, reaction of **14** with two equivalents of PCy_3 afforded the *ortho*-platinated complex **21** as a mixture of *cis*- and *trans*-isomers in which the *trans*-isomer was present in excess (*i.e., cis* : *trans* ≈ 1 : 2). It is worth pointing out that the *ortho*-platinated complex [PtCl{κ^2-*P,C*-P(OC_6H_2-2,4-*t*Bu_2)(OC_6H_3-2,4-*t*Bu_2)$_2$}(PCy_3)] bearing bulky triarylphosphite ligand was prepared under similar conditions as a mixture of *cis*- and *trans*-isomers in which, however, the *cis*-isomer was present in excess.[15] It is likely that, not only the strong *trans*-effect of the considerably electron-donating PCy_3 ligand partially overrides the strong π-acceptance of the BINOL-phosphite ligand and leads to the formation of both *cis*- and *trans*-isomers, but that also the steric bulkiness of PCy_3 favors the *trans*-substitution due to the stereochemical control of the rigid BINOL-phosphite chiral pocket.

Complex **14** also underwent clean and high-yielding reactions with the chelating bidentate phosphine ligand [1,2-bis(diphenylphosphino)ethane] (dppe) to generate the cationic complexes **22** and **23** bearing Cl^- or BF_4^- as counter anions, respectively. The solid state structure of

complex **23** was determined by single crystal X-ray structure determination. As shown in Figure 6, **23** adopts a slightly distorted square-planar structure with the two phosphine P-donor atoms respectively occupying *cis*- and *trans*-positions with respect to the P-donor atom of the BINOL-phosphite ligand. It is worth pointing out that the configuration of the BINOL moieties (*i.e.*, *R* configuration) in complexes **18**, **19** and **23** was completely retained during the reactions according to the X-ray diffraction analysis. This implies that the BINOL moieties in both their parent *C,P*-cycloplatinated complex **14** and the BINOL-derived ligand **7** are enantiopure as well.

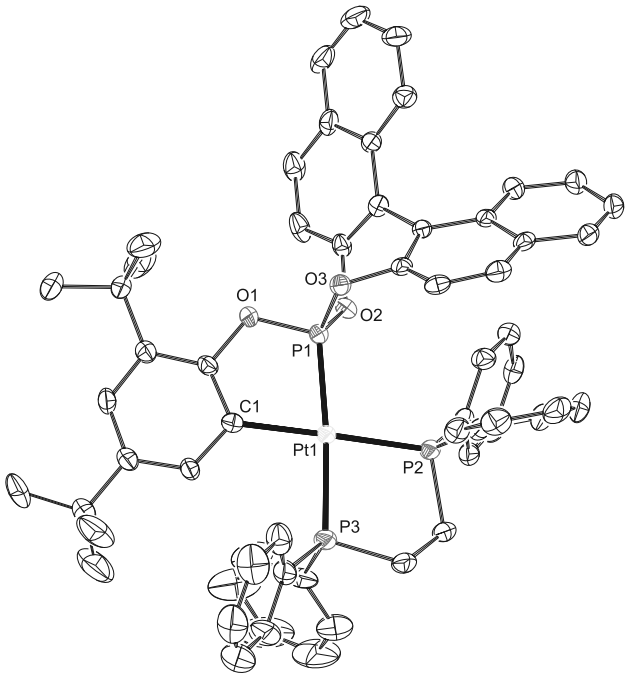


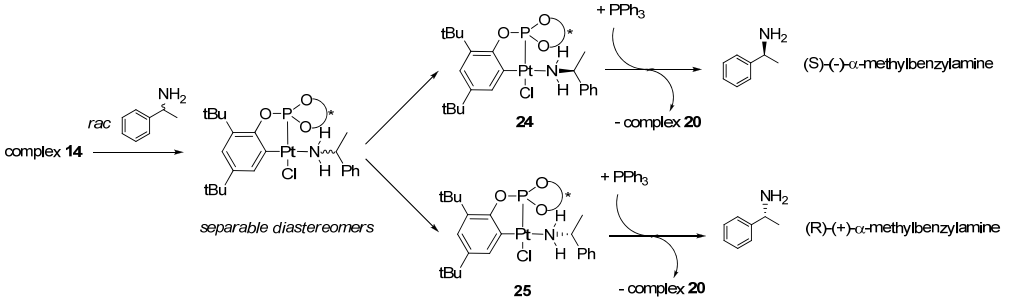
Figure 6. Displacement ellipsoid plot of **23** in the crystal (50% probability level). Disordered THF solvent molecules, hydrogen atoms and BF_4^- anion have been omitted for clarity. Only one orientation of the disordered tBu group is shown. Characteristic bond distances (Å) and bond angles (°) in **23** Pt1-C1 2.089(3), Pt1-P1 2.2292(9), Pt1-P2 2.3342(9), Pt1-P3 2.3260(9), C1-Pt1-P2 176.19(9), P1-Pt1-P3 175.10(3), P2-Pt1-P3 83.37(3).

In order to investigate the reactivities of complexes **18** – **20**, ligand exchange and interconversion studies were carried out as depicted in Scheme 6. It was found that the pyridine moiety in **18** can be smoothly and stoichiometrically replaced by triphenylphosphine at room temperature in dichloromethane. Under the same reaction conditions, a stoichiometric amount of triphenylphosphite replaces most of the pyridine moiety and leaves about 15% complex **18** unreacted. Further increasing the loading of triphenylphosphite to one equivalent in excess still did not complete the reaction. These experiments show that, for *ortho*-platinated complexes, the

platinum metal center favors triphenylphosphine, triphenylphosphite and pyridine coordination in a descending order.

5.2.4 Applications of *C,P*-cycloplatinated complex 14.

Finally, the properties of the present chiral *C,P*-cycloplatinated phosphite complex, **14** as a resolving reagent for separating both enanotiomers of a racemic mixture of a primary amine was evaluated. As described in Scheme 7, a mixture of two diastereomers was generated by reacting **14** with two equivalents of (*rac*)-α-methylbenzylamine in dichloromethane at room temperature. The ^{31}P NMR spectrum of this crude reaction mixture nicely showed two distinctly separated singlets with platinum satellites, one at 110.9 ppm (J_{Pt-P} = 7285 Hz) and a second at 112.7 ppm (J_{Pt-P} = 7281 Hz). These ^{31}P NMR data confirmed that a mixture of two diastereoisomers is present which have the respective amine enantiomer located at the *cis*-position with respect to the chiral phosphite ligands (*cf.* the $^{2}J_{Pt-P}$ values with those of **18)**. Fractional recrystallization of the samples did not properly resolve the two diastereomers. However, easy separation of the two diastereoisomers was accomplished by employing flash chromatography over silica gel (pore diameter *ca.* 4 nm).



Scheme 7. Resolution of (*rac*)-α-methylbenzylamine.

After separation, the respective diastereoisomers **24** and **25** were reacted with stoichiometric amounts of triphenylphosphine, which smoothly released the resolved *R*- and *S*-enantiomers, respectively. These were isolated in promising yields (*i.e.*, 66% for *R*-(+)-α-methylbenzylamine and 77% for *S*-(-)-α-methylbenzylamine, respectively). The excellent enantiopurities were confirmed by comparing their optical rotation to that of authentic samples.

By taking advantage of the orientation of the α-methylbenzylamine enantiomeric ligand in the cycloplatinated-BINOL-phosphite chiral pocket, the chemical shifts of characteristic protons of the N-coordinated *α*-methylbenzylamine moieties are clearly distinguishable. For instance, the ^{1}H NMR spectrum showed a doublet at δ = 0.85 ppm ($^{3}J_{H-H}$ = 6.8 Hz) for its α-methyl group of **24**

while this resonance appears at δ = 1.44 ppm ($^3J_{H-H}$ = 8.0 Hz) for the same group of in **25**. Similarly, the ^{1}H NMR spectra showed a multiplet at δ = 3.65 ppm for the benzylic proton of **24**, and a multiplet at δ=3.25 ppm for the same proton of **25**. These results provide a proof of principle for the effectiveness of this type of chiral *C,P*-cycloplatinated phosphite complexes, as both chiral shift reagents for the determination of enantiomeric ratios of chiral amine products by NMR techniques and for the easy separation in the pure enantiomers by employing flash chromatography over silica gel.

5.3 Conclusion

A series of chiral bis-phosphite complexes and *ortho*-metallated, *C,P*-chelate bonded chiral phosphite complexes have been synthesized by using enantiopure (*R*)-BINOL-derived chiral phosphite ligands and readily accessible palladium or platinum precursors.[c] Remarkably, both the bulkiness of BINOL-derived phosphite ligands and the metal species play important roles in the formation of *C,P*-cyclometallated complexes. *C,P*-cycloplatinated complex **14** can react with typical monodentate or bidentate ligands such as pyridine, triphenylphosphine, tricyclohexylphosphine, triphenylphosphite and dppe to generate the corresponding monomeric chiral orthoplatinated complexes **18** – **23** in good to excellent yields. Ligand-exchange and interconversion studies of *ortho*-platinated complexes **18** – **20** suggest that *ortho*-platinated complexes favor triphenylphosphine, triphenylphosphite and pyridine coordination in a descending order, which indicates the bulky BINOL moiety perturbs the expected order of interaction with external donors. Eventually, complex **14** was successfully employed either as a resolution reagent or as a chiral NMR shift reagent.

[c] *C,P*-cyclometallated complexes have been reported as robust catalysts for 1,4-additions of arylboronic acids and arylsiloxanes to enones,[17] 1,2-additions and 1,4 additions of arylboronic acids to aldehydes, aldimines, α,β-unsaturated ketones and α-ketoesters[18] and allylation of aldehydes.[19] Our work in preparing the chiral *C,P*-cyclopalladated and –platinated complexes **12** – **14** could pave a route to access the asymmetric catalytic version of these reactions.

5.4 Experimental Section

General remarks: All reactions were performed under a dry N_2 atmosphere using standard Schlenk techniques unless otherwise stated. Et_3N was distilled over CaH_2 and was then stored under N_2 at – 30°C with molecular sieves. Toluene was freshly dried over sodium. PCl_3 was freshly distilled and stored under N_2 prior to use. (*R*)-1,1'-binaphthyl-2,2'-diyl chlorophosphite and (*R*)-1,1'-binaphthane-2,2'-diyl phenyl phosphite **6** were prepared according to a literature procedure.[20] All other reagents were purchased from ACROS Organics and Sigma-Aldrich Chemical Co. Inc, and used as received. ^{1}H-NMR (400.0 MHz), ^{13}C-NMR (100.6 MHz), ^{31}P-NMR (121.5 MHz or 161.9 MHz) and ^{19}F-NMR (376.3 MHz) spectra were recorded at room temperature in $CDCl_3$ on a Varian spectrometer at 300 MHz or 400 MHz. Chemical shift values are reported in ppm (δ) relative to $(CH_3)_4Si$ (^{1}H and ^{13}C NMR) or a capillary containing 85% H_3PO_4 in D_2O ($^{31}P\{^1H\}$ NMR). Optical rotations were recorded on a Perkin-Elmer 241 polarimeter at 20 °C. Flash chromatography was performed using ACROS silica gel, 0.06 – 0.200 mm, pore diameter *ca.* 4 or 6 nm. MS measurements were carried out on an Applied Biosystems Voyager DE-STR MALDI-TOF MS. Elemental microanalyses were performed by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim a/d Ruhr, Germany.

Compound 7: 2,4-Di-tert-butylphenol (1.050 g, 5 mmol) was azeotropically dried over toluene (3 x 5 mL) and redissolved in toluene (25 mL). To this solution was dropwise added another solution of (*R*)-1,1'-binaphthyl-2,2'-diyl chlorophosphite (1.760 g, 5 mmol) in toluene (10 mL) at 0 ºC and the resulting white suspension was stirred at room temperature for an additional 2 h. After removing the white salt by filtration, the solution was concentrated and the resultant oily crude product was subjected to flash chromatography with EtOAc/hexanes (1:9) as eluent. The desired phosphite ligand was obtained as a white solid after drying in vacuum. Yield: 2.21 g, 85%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.35 (s, 9H, *tBu*), 1,41 (s, 9H, *tBu*), 7.18-7.22 (m, 2H, Ar*H*), 7.24-7.31 (m, 4H, BINOL*H*), 7.42-7.52 (m, 4H, BINOL*H*), 7.60 (d, *J*=8 Hz, 1H, Ar*H*), 7.90-8.02 (m, 4H, BINOL*H*). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6Hz): δ 30.3, 31.8, 34.8, 35.2, 119.6 (d, *J*=15 Hz), 122.1 (d, *J*=14 Hz), 123.2, 124.7, 125.3 (d, *J*=26 Hz), 126.5 (d, *J*=21 Hz), 127.3 (d, *J*=10 Hz), 128.6 (d, *J*=7 Hz), 129.3, 130.0, 130.7, 131.7 (d, *J*=44 Hz), 133.0 (d, *J*=33 Hz), 139.7, 146.7, 147.4, 148.3 (d, *J*=5 Hz), 148.7 (d, *J*=9 Hz) . $^{31}P\{^1H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 146.1 (s). MS (MALDI-TOF): m/z calcd for $C_{34}H_{34}O_3P$: 521.60 $[M+H]^+$; found: 521.50; Anal.Calcd for C, 78.44; H, 6.39; P, 5.95; found: C, 78.50; H, 6.31; P, 5.93;

General procedure of synthesis of complexes 8 – 11. Phosphite ligand **6** or **7** (0.5 mmol) and $[PdCl_2(MeCN)_2]$ or $[PtCl_2(Me_2S)_2]$ (0.25 mmol) were dissolved in dichloromethane (5 mL) and stirred at room temperature for 2 h. The solution was concentrated on a rotary evaporate until about 1 mL and the product was precipitated from this solution by the addition of hexanes. Off-white or slightly yellow solids were collected by centrifugation and were dried in vacuum.

Complex 8: The product was obtained as a slightly yellow solid. Yield : 0.230 g, 91%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 5.81 (t, *J*=7.6 Hz, 2H, Ar*H*), 6.30 (t, *J*=7.6 Hz, 4H, Ar*H*), 7.03 (d, *J*=8.4 Hz, 4H, Ar*H*), 7.33-7.38 (m, 2H, BINOL*H*), 7.39-7.46 (m, 6H, BINOL*H*), 7.52 (t, *J*=7.6 Hz, 2H, BINOL*H*), 7.60-7.66 (m, 4H, BINOL*H*), 7.98 (t, *J*=9.2 Hz, 4H, BINOL*H*), 8.10 (q, *J*=8.8 Hz, 6H, BINOL*H*). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6Hz): δ 119.9, 121.3, 122.1, 122.6, 122.9, 125.7, 126.4, 126.6, 126.8, 127.5, 127.6,

128.7, 129.2, 131.5 (d, *J*=5 Hz), 132.1, 132.5, 132.7, 146.4 (t, *J*=3Hz), 147.0 (t, *J*=5.4Hz), 148.9. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 115.5 (s). MS (MALDI-TOF): m/z calcd for $C_{52}H_{34}Cl_1O_6P_2Pd$: 958.63 $[M\text{-}Cl]^+$; found: 958.71; and calcd for $C_{52}H_{34}O_6P_2Pd$: 923.20 $[M\text{-}2Cl]^+$; found: 923.42; Anal.Calcd for C, 62.83; H, 3.45; P, 6.23; Pd, 10.71; found: C, 62.79; H, 3.41; P, 6.22; Pd, 10.69.

Complex 9: The product was obtained as an off-white solid. Yield: 0.232 g, 76%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.82 (s, 18H, *tBu*), 1.13 (s, 18H, *tBu*), 6.26 (apparent br d, 2H, Ar*H*), 6.97 (d, *J*=8.4 Hz, 2H, Ar*H*), 7.06 (s, 2H, Ar*H*), 7.17 (apparent br d, 2H, BINOL*H*), 7.25-7.40 (m, 8H, BINOL*H*), 7.45 (t, *J*=8 Hz, 2H, BINOL*H*), 7.56 (t, *J*=8 Hz, 2H, BINOL*H*), 7.67 (apparent d, 2H, BINOL*H*), 7.83 (d, *J*=8 Hz, 2H, BINOL*H*), 7.90-8.10 (m br, 6H, BINOL*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 29.9, 31.6, 34.7, 119.3, 120.2, 122.6 (t, *J*=9.6 Hz), 123.7, 124.6, 126.3 (d, *J*=5.3 Hz), 127.0 (d, *J*=15.8 Hz), 127.3, 128.5, 129.1, 130.8, 131.7, 131.9, 132.4 (d, *J*=5.4 Hz), 132.6, 138.4, 164.7, 147.6, 148.1 (t, *J*=5 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 104.9 (very br s). MS (MALDI-TOF): m/z calcd for $C_{68}H_{66}Cl_1O_6P_2Pd$: 1183.10 $[M\text{-}Cl]^+$; found: 1183.00; and calcd for $C_{68}H_{66}O_6P_2Pd$: 1147.62 $[M\text{-}2Cl]^+$; found: 1147.70; Anal.Calcd for C, 67.03; H, 5.46; P, 5.08; Pd, 8.73; found: 66.95; H, 5.49; P, 5.11; Pd, 8.71.

Complex 10: The product was obtained as a white solid and single crystals were grown by slow diffusion of CH_2Cl_2/hexanes. Yield: 0.2385 g, 88%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 5.94 (t, *J*=7.6 Hz, 2H, Ar*H*), 6.28 (t, *J*=7.6 Hz, 4H, Ar*H*), 6.94 (d, *J*=8 Hz, 4H, Ar*H*), 7.32-7.38 (m, 2H, BINOL*H*), 7.40-7.48 (m, 6H, BINOL*H*), 7.53 (t, *J*=6.8 Hz, 2H, BINOL*H*), 7.60-7.66 (m, 4H, BINOL*H*), 7.96 (q, *J*=8 Hz, 4H, BINOL*H*), 8.04-8.12 (m, 6H, BINOL*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 120.0, 121.0, 122.2, 122.6, 122.9, 125.5, 126.3, 126.4, 126.6, 126.8, 127.0, 127.3, 127.6, 128.8, 129.1, 132.6 (t, *J*=12 Hz), 146.5, 146.7 (t, *J*=5.7 Hz), 149.3. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 90.1 (s with sat., $J_{Pt\text{-}P}$=5764 Hz). MS (MALDI-TOF): m/z calcd for $C_{52}H_{34}Cl_1O_6P_2Pt$: 1047.30 $[M\text{-}Cl]^+$; found: 1047.25; and calcd for $C_{52}H_{34}O_6P_2Pt$: 1011.85 $[M\text{-}2Cl]^+$; found: 1011.93; Anal.Calcd for C, 57.68; H, 3.17; P, 5.72; Pt, 18.02; found: C, 57.73; H, 3.24; P, 5.71; Pt, 17.99.

Complex 11: The product was obtained as an off-white solid. Yield: 0.2124 g, 65%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.86 (s, 18H, *tBu*), 1.18 (s, 18H, *tBu*), 6.34 (very br s, 2H, Ar*H*), 6.81 (d, *J*=8.8 Hz, 2H, Ar*H*), 7.11 (s, 2H, Ar*H*), 7.22-7.64 (very br m, 18H, BINOL*H*), 7.81 (d, *J*=8 Hz, 2H, BINOL*H*), 7.9-8.10 (very br m, 4H, BINOL*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 29.9, 31.6, 34.7, 119.4, 120.2, 122.4, 122.8, 124.5, 126.2 (d, *J*=9 Hz), 126.9 (d, *J*=9 Hz), 127.2, 128.5, 129.0, 130.8, 131.6, 131.8, 132.4, 132.7, 138.4, 146.7, 147.4, 147.9 (d, *J*=8 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 80.7 (very br s with sat., $J_{Pt\text{-}P}$=5808 Hz). MS (MALDI-TOF): m/z calcd for $C_{68}H_{66}Cl_1O_6P_2Pt$: 1271.73 $[M\text{-}Cl]^+$; found: 1271.72; and calcd for $C_{68}H_{66}O_6P_2Pt$: 1236.28 $[M\text{-}2Cl]^+$; found: 1236.45; Anal.Calcd for C, 62.48; H, 5.09; P, 4.74; Pt, 14.92; found: C, 62.45; H, 5.13; P, 4.79; Pt, 14.87.

General procedure of synthesis of complexes 12 and 13. Ligand **6** (0.4084 g, 1 mmol) or ligand **7** (0.5210 g, 1 mmol) and $PdCl_2$ (0.1775 g, 1 mmol) were suspended in toluene (5 mL) and the reaction mixture was refluxed under N_2 at 120 ºC overnight. After cooling, the mixture was filtered over a short pad of Celite and the filter cake was washed with toluene (3 x 10 mL). The collected filtrate was concentrated on a rotavapor until about 2 mL and the product was precipitated by the addition of MeOH (30 mL). The slight yellow-brown solids were collected by centrifugation and dried in vacuum.

Complex 12: Yield: 0.3020 g, 55%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 6.68 (very br s, 2H, Ar*H*), 6.96 (very br s, 2H, Ar*H*), 7.18 (br m, 4H, Ar*H*), 7.28-7.58 (br m, 16H, BINOL*H*), 7.78 (br s, 2H, BINOL*H*), 8.00 (apparent q, br, *J*=8.8 Hz, 6H, BINOL*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 112.1 (d, *J*=8 Hz),

121.0, 122.0, 122.3, 124.7, 125.2, 127.1, 128.0, 128.4, 128.5, 131.3, 131.8, 132.6, 132.8, 133.0, 136.8, 138.5, 147.2, 148.6 (d, *J*=4 Hz), 156.2 (m). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 140.2 (major isomer, br s), 141.0 (minor isomer, br s). MS (MALDI-TOF): m/z calcd for $C_{52}H_{32}Cl_1O_6P_2Pd$: 1063.05 $[M\text{-}Cl]^+$; found: 1063.45; Anal.Calcd for C, 56.86; H, 2.94; P, 5.64; Pd, 19.38; found: C, 56.81; H, 2.99; P, 5.61; Pd, 19.35.

Complex 13: Yield: 0.3310 g, 50%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.13 (br s, 12H, *t*Bu), 1.21 (br s, 24H, *t*Bu), 7.10-7.17 (br apparent d, 4H, Ar*H*), 7.32-7.54 (very br m, 14H, BINOL*H*), 7.81-8.10 (very br m, 10H, BINOL*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 30.0, 31.9, 35.1, 120.9, 121.5, 121.7, 126.5, 126.9, 127.1, 127.5, 128.1, 128.8, 130.3, 130.6, 130.8, 131.1, 131.5, 132.1, 132.5, 132.6, 133.0, 133.9, 134.5, 134.7, 137.0, 139.3, 146.0, 147.2, 147.3, 151.5 (d, *J*=5 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 139.4 (major isomer, br s), 141.7 (minor isomer, br s). MS (MALDI-TOF): m/z calcd for $C_{68}H_{64}Cl_1O_6P_2Pd_2$: 1287.48 $[M\text{-}Cl]^+$; found: 1287.25; Anal.Calcd for C, 61.74; H, 4.88; P, 4.68; Pd, 16.09; found: C, 61.79; H, 4.81; P, 4.73; Pd, 16.11.

Synthesis of complex 14. Method **A**: Complex **11** (0.6430 g, 0.5 mmol) and K_2PtCl_4 (0.2500 g, 0.6 mmol) were suspended in 2-methoxyethanol (5 mL) and the mixture was refluxed under N_2 at 135 ºC for 3.5 h. After cooling, the black mixture was filtered over a short pad of Celite and the filter cake was washed with dichloromethane (3 x 5 mL). The combined filtrates were concentrated in vacuum until about 1 mL and a white solid was precipitated by the addition of MeOH (≈ 40 mL). The product was then collected by filtration and further washed with cold MeOH (2 x 5 mL). Finally, the fine white powder was thoroughly dried in vacuum. Yield: 0.4160 g, 55%.

Method **B**: ligand **7** (0.5210 g, 1 mmol) and K_2PtCl_4 (0.2080 g, 0.5 mmol) were suspended in *m*-xylene (5 mL) and the mixture was refluxed under N_2 at 135 ºC overnight. After cooling, *m*-xylene was removed under vacuum to leave an off-white solid mixture. To this mixture was added another K_2PtCl_4 (0.2500 g, 0.6 mmol) and 2-methoxyethanol (5 mL), after which the suspension was refluxed under N_2 at 135 ℃ for 3.5 h. After cooling, the black mixture was filtered over a short pad of Celite and the filter cake was washed with dichloromethane (3 x 5 mL). The combined filtrates were concentrated in vacuum until about 1 mL and a white solid was precipitated by the addition of MeOH (≈ 40 mL). The product was then collected by filtration and further washed with cold MeOH (2 x 5 mL). Finally, the fine white powder was thoroughly dried in vacuum. Yield: 0.3780 g, 50%.

Method **C**: Ligand **7** (0.5210 g, 1 mmol) and K_2PtCl_4 (0.4155 g, 1 mmol) were suspended in *m*-xylene (5 mL) and the mixture was refluxed under N_2 at 135 ºC overnight. After cooling, *m*-xylene was removed under vacuum to leave a pink solid mixture. To this mixture was added 2-methoxyethanol (5 mL) and the suspension was refluxed under N_2 at 135 ºC for 5 h. After cooling, the black mixture was filtered over a short pad of Celite and the filter cake was washed with dichloromethane (3 x 5 mL). The combined filtrates were concentrated in vacuum until about 1 mL and a white solid was precipitated by the addition of MeOH (≈ 40 mL). The product was then collected by filtration and further washed with cold MeOH (2 x 5 mL). Finally, the fine white powder was thoroughly dried in vacuum. Yield: 0.1880 g, 25%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.11 (s, 18H, *tBu*), 1.22 (s, 18H, *tBu*), 6.91 (s, 2H, Ar*H*), 7.06 (s, 2H, Ar*H*), 7.30-7.36 (m, 4H, BINOL*H*), 7.40-7.45 (m, 6H, BINOL*H*), 7.52-7.56 (m, 4H, BINOL*H*), 7.81 (d, *J*=8.8 Hz, 2H, BINOL*H*), 7.95-8.10 (m, 6H, BINOL*H*), 8.04-8.10 (m, 2H, BINOL*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 30.1, 31.9, 35.0 d, *J*=5 Hz), 120.5 (d, *J*=10 Hz), 121.2, 122.1, 122.2, 122.4, 126.6, 127.3 (d, *J*=26 Hz), 127.9, 128.9 (d, *J*=20 Hz), 131.1, 131.3, 132.0, 132.2, 132.5 (d, *J*=5 Hz), 133.3 (d, *J*=17 Hz), 145.2, 146.1

(d, *J*=6.6 Hz), 146.9 (d, *J*=14 Hz), 153.6 (d, *J*=17 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 102.9 (major isomer, s with sat., $J_{Pt\text{-}P}$=7858 Hz), 103.2 (monor isomer, s with sat., $J_{Pt\text{-}P}$=8127 Hz). MS (MALDI-TOF): m/z calcd for $C_{68}H_{64}Cl_1O_6P_2Pt_2$: 1464.79 $[M\text{-}Cl]^+$; found: 1464.58; Anal.Calcd for C, 54.44; H, 4.30; P, 4.13; Pt, 26.01; found: C, 54.41; H, 4.24; P, 4.17; Pt, 25.99.

Synthesis of complex 15. Method **A**: Complex **11** (0.065 g, 0.05 mmol) was dissolved in $MeOCH_2CH_2OH$ (1 mL) and this reaction mixture was heated at 135 ºC overnight under N_2. After cooling, the resulting mixture was concentrated in vacuum and an off-white solid was precipitated by the addition of hexanes. The solid was collected by filtration and was completely dried in vacuum. The product was obtained as an off-white solid. Yield: 0.075 g, 58%. Method **B**: Ligand **7** (0.053 g, 0.1 mmol) and K_2PtCl_4 (0.021 g, 0.05 mmol) were suspended in m-xylene (2 mL) and this reaction mixture was heated at 135 ºC overnight under N_2. After cooling, the resulting mixture was concentrated in vacuum and an off-white solid was precipitated by the addition of hexanes. The solid was collected by filtration and was completely dried in vacuum. The product was obtained as an off-white solid. Yield: 0.070 g, 54%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.29 (s, 12H, *tBu*), 1.37 (s, 24H, *tBu*), 5.82 (d, *J*=8.8 Hz, 1H, Ar*H*), 6.10 (d, *J*=9.2 Hz, 1H, Ar*H*), 6.57 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.64 (d, *J*=8.8 Hz, 1H, Ar*H*), 6.71 (t, *J*=6.8 Hz, 1H, BINOL*H*), 6.78 (t, *J*=6.8 Hz, 1H, BINOL*H*), 6.94 (d, *J*=8.4 Hz, 1H, BINOL*H*), 7.04-7.10 (m, 6H, BINOL*H*), 7.18 (s, 1H, BINOL*H*), 7.24-7.38 (m, 4H, BINOL*H*), 7.46 (t, *J*=12 Hz, 2H, BINOL*H*), 7.58 (d, *J*=8 Hz, 1H, BINOL*H*), 7.78 (q, *J*=8 Hz, 2H, BINOL*H*), 7.86 (d, *J*=8 Hz, 1H, BINOL*H*), 7.95 (d, *J*=8Hz, 1H, BINOL*H*), 8.07 (d, *J*=10 Hz, 2H, BINOL*H*), 8.37 (apparent dt, $J_{C\text{-}H}$=10.8 Hz and $J_{Pt\text{-}H}$=22 Hz, 1H, Ar*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 30.2 (d, *J*=32 Hz), 31.9 (d, *J*=18 Hz), 34.8, 35.0, 35.2, 35.5, 119.2 (d, *J*=10 Hz), 119.5, 119.9, 120.7, 121.0, 121.4, 121.8, 123.5, 124.8, 125.2, 125.5, 125.7, 126.0, 126.2, 126.3 (d, *J*=6 Hz), 127.1 (d, *J*=6 Hz), 128.1, 12.5, 129.4, 130.3 (d, *J*=24 Hz), 130.9 (apparent t, *J*=18 Hz), 131.4 (d, *J*=11 Hz), 131.8, 132.1, 132.3, 132.6 (d, *J*=8 Hz), 146.1 (d, *J*=5 Hz), 146.9, 147.5 (d, *J*=8 Hz), 148.6 (d, *J*=5 Hz), 155.1 (d, *J*=17 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 121.4 Hz): δ 123.20 (d with sat., $J_{P\text{-}P}$=27 Hz and $J_{Pt\text{-}P}$=6478 Hz), 134.6 (d with sat., $J_{P\text{-}P}$=27 Hz and $J_{Pt\text{-}P}$=3167 Hz). MS (MALDI-TOF): m/z calcd for $C_{69}H_{68}O_6P_2Pt$: 1250.30 $[M\text{-}Cl]^+$; found: 1250.47; Anal.Calcd for C, 64.46; H, 5.33; P, 4.82; Pt, 15.17; found: C, 64.38; H, 5.29; P, 4.78; Pt, 15.20.

General procedure of synthesis of complexes 18 – 21. Pt dimer complex **14** (0.0750 g, 0.05 mmol) and pyridine, triphenylphosphine, tricyclohexylphosphine or triphenylphosphite (0.1 mmol) were dissolved in dichloromethane and the reaction mixture was stirred at room temperature for 1 h. The resulting mixture was then concentrated on rotavapor until about 1 mL and products were precipitated from this solution by the addition of hexanes (≈10 mL). The precipitate was collected by centrifuge and was further quickly washed with cold hexanes (2 x 5 mL). Finally, the desired products were thoroughly dried in vacuum.

Complex 18: The product was obtained as a white solid and the single crystals were grown by slow diffusion of CH_2Cl_2/hexanes. Yield: 0.064 g, 77%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.30 (s, 9H, *tBu*), 1.39 (s, 9H, *tBu*), 6.61 (t, *J*=6.4 Hz, 2H, Ar*H*), 7.15-7.39 (m, 8H, BINOL*H*), 7.42-7.58 (m, 3H, Py*H*), 7.68 (apparent d, *J*=8.8 Hz, 1H, BINOL*H*), 8.00 (d, *J*=8.8 Hz, 1H, BINOL*H*), 8.06 (apparent d, *J*=8.8 Hz, 1H, BINOL*H*), 8.37 (apparent t, *J*=24 Hz, 1H, BINOL*H*), 8.50 (d, *J*=6 Hz, 2H, Py*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 30.1, 32.1, 35.1 (d, *J*=10 Hz), 119.6 (d, *J*=10.8 Hz), 120.8 (d, *J*=21.6 Hz), 122.1 (t, *J*=53 Hz),

124.9, 126.1 (d, *J*=8 Hz), 127.1, 128.3, 128.5, 128.9, 130.9, 131.5, 131.7, 131.9, 132.2, 132.4, 132.8, 137.2, 145.7, 147.1 (d, *J*=14 Hz), 152.0, 155.9 (d, *J*=18 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 109.8 (s with sat., $J_{Pt\text{-}P}$=7194 Hz). MS (MALDI-TOF): m/z calcd for $C_{39}H_{37}NO_3PPt$: 793.77 $[M\text{-}Cl]^+$; found: 793.59; Anal.Calcd for C, 56.49; H, 4.50; N, 1.69; P, 3.74; Pt, 23.53; found: C, 56.51; H, 4.47; N, 1.67; P, 3.75; Pt, 23.51.

Complex 19: The product was obtained as a white solid and its single crystals were obtained by slow evaporation of $CDCl_3$ solution in NMR tube at room temperature. Yield: 0.085 g, 80%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.15 (s, 9H, *tBu*), 1.37 (s, 9H, *tBu*), 6.95-7.00 (m, 6H, OPh*H*), 7.03-7.07 (m, 3H, OPh*H*), 7.10-7.17 (m, 7H, Ar*H* + OPh*H*), 7.20-7.38 (m, 6H, BINOL*H*), 7.55 (d, *J*=8 Hz, 2H, BINOL*H*), 7.59 (d, *J*=8 Hz, 2H, BINOL*H*), 8.06 (d, *J*=8.4 Hz, 2H, BINOL*H*), 8.35-8.46 (br apparent dt, 1H, Ar*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 30.1, 32.0, 35.0, 35.5, 121.8, 122.3, 123.7, 125.5, 125.7, 125.8, 126.2, 126.8, 126.9, 127.0, 127.6, 128.5, 128.8, 129.0, 129.3, 129.6, 129.7, 130.1, 130.3, 132.2, 132.4, 132.5, 132.9, 139.4 (d, *J*=9 Hz), 141.1 (d, *J*=9 Hz), 145.3 (d, *J*=9 Hz), 147.6 (d, *J*=9 Hz), 147.8 (d, *J*=9 Hz), 150.6 (d, *J*=7.4 Hz), 155.2 (d, *J*=21 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 116.1 (d with sat., $J_{P\text{-}P}$=29 Hz and $J_{Pt\text{-}P}$=3207 Hz), 125.1 (d with sat., $J_{P\text{-}P}$=29 Hz and $J_{Pt\text{-}P}$=6222 Hz). MS (MALDI-TOF): m/z calcd for $C_{52}H_{47}O_6P_2Pt$: 1024.95 $[M\text{-}Cl]^+$; found: 1025.05; Anal.Calcd for C, 58.90; H, 4.47; P, 5.84; Pt, 18.40; found: C, 58.85; H, 4.41; P, 5.90; Pt, 18.39.

Complex 20: The product was as an off-white solid. Yield: 0.069 g, 68%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.10 (s, 9H, *tBu*), 1.38 (s, 9H, *tBu*), 6.98-7.06 (m, 6H, PPh*H*), 7.08-7.12 (m, 3H, PPh*H*), 7.14-7.20 (m, 2H, BINOL*H*), 7.21-7.28 (m, 2H, BINOL*H*), 7.28-7.34 (m, 2H, BINOL*H*), 7.36-7.42 (m, 7H, Ar*H* + PPh*H*), 7.46-7.52 (m, 3H, BINOL*H*), 7.80 (d, *J*=8 Hz, 1H, BINOL*H*), 7.95 (t, *J*=8.8 Hz, 2H, BINOL*H*), 8.57 (apparent dt, $J_{C\text{-}H}$= 6 Hz, $J_{Pt\text{-}H}$=45 Hz, 1H, Ar*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 30.0, 32.1, 34.9, 35.5, 121.5 (d, J=32 Hz), 121.7, 122.2, 122.9, 125.9 (d, *J*=12.5 Hz), 126.6 (d, *J*=19.5 Hz), 127.5, 127.8 (d, *J*=10 Hz), 128.0, 128.5 (d, *J*=18 Hz), 130.2, 130.5, 130.8, 131.1, 131.9, 132.2, 132.8, 133.9 (d, *J*=10 Hz), 134.9 (d, *J*=5 Hz), 138.7 (d, *J*=10 Hz), 139.7, (d, *J*=10 Hz), 145.2 (d, *J*=9 Hz), 146.6 (d, *J*=9 Hz), 147.1 (d, *J*=14 Hz), 153.7 (d, *J*=18 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 23.1 (d with sat., $J_{P\text{-}P}$=22 Hz and $J_{Pt\text{-}P}$=1868 Hz), 123.0 (d with sat., $J_{P\text{-}P}$=22 Hz and $J_{Pt\text{-}P}$=6756 Hz). MS (MALDI-TOF): m/z calcd for $C_{52}H_{47}O_3P_2Pt$: 976.96 $[M\text{-}Cl]^+$; found: 977.10; Anal.Calcd for C, 61.69; H, 4.68; P, 6.12; Pt, 19.27; found: C, 61.64; H, 4.73; P, 6.15; Pt, 19.25.

Complex 21: *Only cis-product was isolated in analytical purity*. The *cis*-product was obtained as an white solid. Yield: 0.0186 g, 18% (based on Pt). ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.51 (br s, 3H, Cy*H*), 0.80-1.18 (br m, 14H, Cy*H* + *tBu*), 1.19-1.40 (br m, 17H, Cy*H* + *tBu*), 1.40-1.58 (br s, 6H, Cy*H*), 1.60-1.80 (br m, 5H, Cy*H*), 1.81-1.97 (br m, 4H, Cy*H*), 2.00-2.18 (br s, 2H, Cy*H*), 7.09 (s, 1H, Ar*H*), 7.22-7.34 (m, 3H, BINOL*H*), 7.35-7.38 (m, 1H, BINOL*H*), 7.42-7.56 (m, 4H, BINOL*H*), 7.90-8.01 (m, 3H, BINOL*H*), 8.03 (d, *J*=8.8 Hz, 1H, BINOL*H*), 8.51 (apparent dt, $J_{C\text{-}H}$= 5.2 Hz, $J_{Pt\text{-}H}$=44 Hz, 1H, Ar*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 26.5, 27.1 (d, *J*=8.6 Hz), 27.6 (d, *J*=8.6 Hz), 29.7, 30.0, 30.7, 30.9, 31.2, 31.7, 32.1, 34.7, 35.2, 35.5, 35.9 (m), 120.2, 120.8, 121.6, 122.0, 122.4, 123.5, 124.6, 126.0, 126.9 (d, *J*=12 Hz), 127.2, 127.6, 128.6 (d, *J*=26.6 Hz), 130.2, 131.2, 132.5, 133.2, 139.8, 140.1 (d, *J*=10 Hz), 145.0 (d, *J*=5 Hz), 147.1, 147.7 (d, *J*=10 Hz), 148.0 (d, *J*=13 Hz), 153.7 (d, *J*=15 Hz). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 29.1 (d with sat., $J_{P\text{-}P}$=20.8 Hz and $J_{Pt\text{-}P}$=928 Hz), 126.5 (d with sat., $J_{P\text{-}P}$=20.8 Hz and $J_{Pt\text{-}P}$=3500 Hz). MS (MALDI-TOF): m/z calcd for $C_{52}H_{65}O_3P_2Pt$: 955.10 $[M\text{-}Cl]^+$; found: 955.25; Anal.Calcd for C, 60.60; H, 6.36; P, 6.01; Pt, 18.93; found: C, 60.49; H, 6.28; P, 6.07; Pt, 18.85.

General procedure of synthesis of complex 22 and 23. Pt dimer complex **14** (0.0750 g, 0.05 mmol) and dppe (0.040 g, 0.1 mmol) (In the case of complex **23**, $AgBF_4$ (0.020 g, 0.1 mmol) was also added.) were dissolved in dichloromethane and the reaction mixture was stirred at room temperature for 1 h. AgCl salt was firstly removed by filtration and the filter cake was washed with dichloromethane (3 x 5 mL). The combined filtrates were concentrated on a rotavapor until about 1 mL and product was precipitated from this solution by the addition of hexanes (≈10 mL). The precipitate was collected by centrifuge and was further quickly washed with cold hexanes (2 x 5 mL). Finally, the desired products were thoroughly dried in vacuum.

Complex 22: The product was obtained as white fine powder. Yield: 0.086 g, 75%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.75 (s, 9H, *tBu*), 1.10 (s, 9H, *tBu*), 2.02 (br s, 1H, PCH_2), 2.30 (br s, 1H, PCH_2), 3.00 (br m, 1H, PCH_2), 3.49 (very br d, 1H, PCH_2), 6.37-6.41 (m, 2H, PPh*H*), 6.51-6.56 (m, 2H, PPh*H*), 6.76 (t, *J*=7.6 Hz, 1H, Ar*H*), 6.89 (d, *J*=8 Hz, 1H, PPh*H*), 7.08-7.14 (m, 3H, BINOL*H*), 7.22-7.34 (m, 4H, BINOL*H*), 7.48 (t, *J*=8 Hz, 1H, BINOL*H*), 7.50-7.61 (m, 10H, PPh*H*), 7.68 (t, *J*=8 Hz, 1H, Ar*H*), 7.78-7.98 (m, 7H, BINOL*H* + PPh*H*), 8.19 (q, *J*=8 Hz, 2H, BINOL*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 30.1, 31.3, 34.5, 35.4, 120.8, 121.8 (d, *J*=56 Hz), 124.2, 126.2 (d, *J*=19 Hz), 127.0-127.2 (m), 128.01, 128.8 (d, *J*=13 Hz), 128.8, 129.78 (d, *J*=11 Hz), 130.12 (t, *J*=12 Hz), 130.5, 131.0-131.8 (m), 131.9, 132.5 (d, *J*=49 Hz), 133.9 (d, *J*=9 Hz), 135.2 (d, *J*=9 Hz), 135.8 (d, *J*=9 Hz), 138.5 (d, *J*=11 Hz), 145.9 (d, *J*=8 Hz), 146.4, 146.7, 146.8, 155.3 (d, *J*=21.6 Hz). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 43.8 (dd with sat., $J_{Pt\text{-}P}$=1506 Hz, $J_{P\text{-}P}$=8 Hz, $J_{P\text{-}P}$=23 Hz), 55.0 (dd with sat., $J_{Pt\text{-}P}$=2804 Hz, $J_{P\text{-}P}$=8.6 Hz, $J_{P\text{-}P}$=528 Hz), 151.3 (dd with sat., $J_{Pt\text{-}P}$=4528 Hz, $J_{P\text{-}P}$=23.8 Hz, $J_{P\text{-}P}$=528 Hz). MS (MALDI-TOF): m/z calcd for $C_{60}H_{56}O_3P_3Pt$: 1113.09 $[M\text{-}Cl]^+$; found: 1113.25; Anal.Calcd for C, 62.74; H, 4.91; P, 8.09; Pt, 16.98; found: C, 62.70; H, 4.99; P, 8.14; Pt, 16.93.

Complex 23: The product was obtained as white fine powder and the single crystals were grown by slow diffusion of THF/hexanes. Yield: 0.094 g, 78%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.75 (s, 9H, *tBu*), 1.10 (s, 9H, *tBu*), 1.96 (br s, 1H, PCH_2), 2.27 (br s, 1H, PCH_2), 2.86 (br d, 1H, PCH_2), 3.16 (br d, 1H, PCH_2), 6.42-6.44 (apparent t, 2H, PPh*H*), 6.65 (t, *J*=5.4 Hz, 2H, PPh*H*), 6.78 (t, *J*=4 Hz, 1H, Ar*H*), 6.91 (d, *J*=8.8 Hz, 1H, PPh*H*), 7.10-7.16 (m, 3H, BINOL*H*), 7.24-7.28 (m, 2H, BINOL*H*), 7.48-7.68 (m, 12H, BINOL*H* + PPh*H*), 7.79-7.89 (m, 5H, PPh*H*), 7.94-8.05 (m, 4H, BINOL*H*), 8.15 (q, *J*=8 Hz, 2H, BINOL*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 30.1, 31.3, 34.5, 35.4, 120.8, 121.4, 121.5, 123.8, 124.2, 124.4, 126.5 (d, *J*=8.6 Hz), 127.1, 127.3, 127.5, 127.8, 128.4 (d, *J*=11 Hz), 128.9, 129.9 (d, *J*=11 Hz), 130.2 (q, *J*=8 Hz), 130.6, 131.2, 131.4, 131.9, 132.2, 132.7, 132.9, 133.3, 133.7, 133.8, 134.8 (d, *J*=10 Hz), 135.1 (d, *J*=10 Hz), 138.5 (d, *J*=11 Hz), 145.9 (d, *J*=8 Hz), 146.4, 146.7 (d, *J*=13 Hz), 155.3 (d, *J*=21.6 Hz). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 44.0 (dd with sat., $J_{Pt\text{-}P}$=1563 Hz, $J_{P\text{-}P}$=8.4 Hz, $J_{P\text{-}P}$=23.8 Hz), 55.0 (dd with sat., $J_{Pt\text{-}P}$=2810 Hz, $J_{P\text{-}P}$=9 Hz, $J_{P\text{-}P}$=528.8 Hz), 151.3 (dd with sat., $J_{Pt\text{-}P}$=4536 Hz, $J_{P\text{-}P}$=24.3 Hz, $J_{P\text{-}P}$=521.8 Hz). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -154.0 (s). MS (MALDI-TOF): m/z calcd for $C_{60}H_{56}O_3P_3Pt$: 1164.44 $[M\text{-}Cl]^+$; found: 1164.29; Anal.Calcd for C, 60.06; H, 4.70; P, 7.74; Pt, 16.26; found: C, 60.10; H, 4.64; P, 7.79; Pt, 16.24.

Resolution of diastereomers 24 and 25. Pt dimer complex **14** (0.1500 g, 0.1 mmol) and racemic α-methylbenzylamine (25.8 μL, 0.2 mmol) were dissolved in dichloromethane and the reaction mixture was stirred at room temperature for 1 h. The mixture was then concentrated on a rotavapor and was subjected to flash chromatography (ACROS silica gel , 0.06 – 0.200 mm, pore diameter ca. 4 nm;

diameter of column ≈ 18 mm; length of column ≈ 270 mm; positive pressure (N_2) at the top of column ≈ 1025 mbar) with EtOAc/hexanes (1:9) as eluent. Complex **24**, R_f = 0.60. Complex **25**, R_f = 0.35.

Complex 24: The product was obtained as a white solid. Yield: 0.1290 g, 74%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.85 (d, *J*=6.8 Hz, 3H, *Me*), 1.30 (s, 9H, *tBu*), 1.38 (s, 9H, *tBu*), 2.20 (br t, *J*=10 Hz, 1H, N*H*), 3.38 (br d, *J*=11.6 Hz, 1H, N*H*), 3.65 (br m, 1H, PhC*H*(NH_2)Me), 6.44 (d, *J*=7.6 Hz, 2H, Ph*H*), 7.07 (t, *J*=7.2 Hz, 1H, BINOL*H*), 7.12 (d, *J*=7.2 Hz, 1H, BINOL*H*), 7.16 (s, 1H, Ar*H*), 7.28-7.42 (m, 2H, BINOL*H*), 7.44-7.58 (m, 3H, Ph*H*), 7.60 (d, *J*=8.4 Hz, 1H, BINOL*H*), 7.66 (t, *J*=7.2 Hz, 1H, BINOL*H*), 7.78 (d, *J*=8.8 Hz, 1H, BINOL*H*), 7.88 (d, *J*=8.8 Hz, 2H, BINOL*H*), 8.00 (q, *J*=10 Hz, 2H, BINOL*H*), 8.08 (d, *J*=8.8 Hz, 1H, BINOL*H*), 8.32 (t, *J*=27 Hz, 1H, ArH). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 30.1, 32.1, 35.1 (d, *J*=11 Hz), 53.7, 55.4, 120.6, 121.2, 121.3, 122.0, 122.1 (d, *J*=11 Hz), 124.4, 125.7, 126.2, 126.9 (d, *J*=12.8 Hz), 127.3 (d, *J*=6.6 Hz), 128.0 (d, *J*=4 Hz), 128.9, 129.0, 129.3, 131.8 (d, *J*=17.5 Hz), 131.0 (d, *J*=10 Hz), 132.4, 132.5, 132.7, 132.9, 143.4, 145.5, 145.7 (d, *J*=6 Hz), 147.4 (d, *J*=14.6 Hz), 155.6 (d, *J*=18 Hz). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 110.9 (s with sat., J_{Pt-P}=7285 Hz). MS (MALDI-TOF): m/z calcd for $C_{42}H_{43}NO_3PPt$: 835.85 $[M-Cl]^+$; found: 835.91; Anal.Calcd for C, 57.90; H, 4.97; N, 1.61; P, 3.55; Pt, 22.39; found: C, 57.85; H, 4.99; N, 1.59; P, 3.49; Pt, 22.35.

Complex 25: The product was obtained as an off-white foam. Yield: 0.1551 g, 89%. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.28 (s, 9H, *tBu*), 1.39 (s, 9H, *tBu*), 1.44 (d, *J*=8 Hz, 3H, *Me*), 2.44 (br d, *J*=8.8 Hz, 1H, N*H*), 3.25 (br m, 1H, PhC*H*(NH_2)Me), 3.72 (br t, *J*=11.2 Hz, 1H, N*H*), 6.04 (d, *J*=7.6 Hz, 2H, PPh*H*), 6.84 (t, *J*=7.6 Hz, 2H, BINOL*H*), 7.00 (t, *J*=7.2 Hz, 1H, BINOL*H*), 7.17 (s, 1H, Ar*H*), 7.32-7.41 (m, 3H, PPh*H*), 7.51 (q, *J*=8.8 Hz, 2H, BINOL*H*), 7.61 (q, *J*=8 Hz, 2H, BINOL*H*), 7.72 (q, *J*=9.2 Hz, 2H, BINOL*H*), 7.81 (d, *J*=8 Hz, 1H, BINOL*H*), 8.02 (d, *J*=8 Hz, 1H, BINOL*H*), 8.08 (d, *J*=8.8 Hz, 1H, BINOL*H*), 8.31 (t, *J*=27 Hz, 1H, Ar*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 30.1, 32.1, 35.1 (d, *J*=13 Hz), 53.7, 56.6, 120.5, 120.8, 121.6 (d, *J*=2.5 Hz), 122.1, 122.4, 122.5, 124.0, 125.2, 126.2, 126.7, 127.3, 127.5, 127.8 (d, *J*=3.7 Hz), 128.9, 129.0, 129.3, 129.4, 131.5, 131.9, 132.0, 132.4, 132.6, 132.8. 143.6, 145.6, 147.4 (d, *J*=14 Hz), 155.5 (d, *J*=18 Hz). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 112.7 (s with sat., J_{Pt-P}=7281 Hz). MS (MALDI-TOF): m/z calcd for $C_{42}H_{43}NO_3PPt$: 835.85 $[M-Cl]^+$; found: 835.78; Anal.Calcd for C, 57.90; H, 4.97; N, 1.61; P, 3.55; Pt, 22.39; found: C, 57.83; H, 5.01; N, 1.57; P, 3.57; Pt, 22.37.

Release enantiopure (*R*)- or (*S*)-α-methylbenzylamine. To a solution of complex **24** or **25** (0.088 g, 0.1 mmol) in dichloromethane (2 mL) was added triphenylphosphine (0.0263 g, 0.1 mmol) in one portion at room temperature. The reaction mixture was stirred for 1 h and was *immediately* subjected to flash chromatography (ACROS silica gel, 0.06 – 0.200 mm, pore diameter ca. 6 nm; diameter of column≈18 mm; length of column≈270 mm; positive pressure (N_2) at the top of column≈1025 mbar) with MeOH/EtOAc/Et_3N (95/4/1) as eluent. The fractions were concentrated and dried on a rotary evaporator *without warming*. This procedure was repeated 3 times in the same scale until collected sufficient sample for measuring optical rotation. (*Caution: The amine products should be stored under N_2 at -30 ℃.*) Both enantiomers were obtained as a very slightly yellow oil. For (*R*)-(+)-α-methylbenzylamine, yield: 0.024 g, 66%, $[\alpha]_D^{20}$=+3.504 (C=0.1, $CHCl_3$); For (*S*)-(-)-α-methylbenzylamine, yield: 0.0250 g, 70%, $[\alpha]_D^{20}$=-3.508 (C=0.1, $CHCl_3$). Optical rotation of authentic samples: for (*R*)-(+)-α-methylbenzylamine: $[\alpha]_D^{20}$=+35.100 (C=1, $CHCl_3$); for (*R*)-(+)-α-methylbenzylamine: $[\alpha]_D^{20}$=-35.110 (C=1, $CHCl_3$).

X-ray crystal structure determinations. X-ray reflections were measured with Mo-K_α radiation (λ = 0.71073 Å) on a Nonius KappaCCD diffractometer with rotating anode. The structures were solved with automated Patterson methods (program DIRDIF-08,[21] compounds **18**, **19**, and **23**) or Direct Methods (program SHELXS-97,[22] compound **10**). Refinement was performed with SHELXL-97[22] against F^2 of all reflections. Non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were introduced in calculated positions and refined with a riding model. Geometry calculations and checking for higher symmetry was performed with the PLATON program.[23] Further details are given in Table **1**.

10: The crystal was cracked into two fragments. Only the intensities of the major fragment were used. The crystal structure contains very large solvent accessible voids (2852 $Å^3$ / unit cell, corresponding to 32%) filled with severely disordered solvent molecules. Their contribution to the structure factors was taken into account using back-Fourier transformation with the SQUEEZE routine of the program PLATON,[23] resulting in 388 electrons / unit cell. In the refinement of the structure strong restraints were used for all carbon atoms to approximate isotropic behaviour. The determination of the Flack x parameter proves that the crystal is enantiomerically pure.[24]

18: The crystal structure contains large solvent accessible voids (920 $Å^3$ / unit cell, corresponding to 12%) filled with severely disordered solvent molecules. Their contribution to the structure factors was taken into account using back-Fourier transformation with the SQUEEZE routine of the program PLATON,[23] resulting in 162 electrons / unit cell. In the refinement of the structure rigid-bond restraints for the displacement parameters, distance restraints were used for one disordered tBu group and the acetone solvent molecule. The latter was also restrained to be planar.

19: The crystal structure contains large solvent accessible voids (860 $Å^3$ / unit cell, corresponding to 17%) filled with severely disordered solvent molecules. Their contribution to the structure factors was taken into account using back-Fourier transformation with the SQUEEZE routine of the program PLATON,[23] resulting in 308 electrons / unit cell. In the refinement of the structure rigid-bond restraints for the displacement parameters were used for carbon atoms C28-C30.

23: The crystal structure contains large solvent accessible voids (602 $Å^3$ / unit cell, corresponding to 20%) filled with severely disordered THF solvent molecules. Their contribution to the structure factors was taken into account using back-Fourier transformation with the SQUEEZE routine of the program PLATON,[23] resulting in 151 electrons / unit cell. In the refinement of the structure distance and angle restraints were used for one disordered tBu group and the displacement parameters of this group were restrained to approximate isotropic behaviour.

Table 1: Details of the X-ray crystal structure determinations.

	10	**19**	**18**	**23**
formula	$C_{52}H_{34}Cl_2O_6P_2Pt$ + disordered solvent	$C_{52}H_{47}ClO_2P_2Pt$ + disordered solvent	$2(C_{39}H_{37}ClNO_3PPt) \cdot C_3H_6O$ + disordered solvent	$[C_{60}H_{56}O_3P_3Pt](BF_4)$ + disordered solvent
fw	1082.72[a]	1060.38[a]	1716.49[a]	1199.86[a]
crystal colour	colourless	colourless	colourless	colourless
crystal size [mm^3]	0.42x0.12x0.06	0.20x0.12x0.08	0.36x0.10x0.10	0.36x0.33x0.06
Temp. [K]	150	110	110	150
crystal system	orthorhombic	orthorhombic	orthorhombic	monoclinic
space group	$P2_12_12$ (no. 18)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_1$ (no. 4)
a [Å]	34.9820(12)	12.0861(1)	13.3733(7)	14.8486(2)
b [Å]	23.9547(10)	15.9892(1)	19.7636(10)	10.0752(3)
c [Å]	10.4698(6)	26.1500(3)	29.3397(6)	20.7515(6)
β [°]	-	-	-	99.713(1)
V [$Å^3$]	8773.6(7)	5053.41(8)	7754.6(6)	3059.99(14)
Z	6	4	4	2
D_x [g/cm^3]	1.230[a]	1.394[a]	1.470[a]	1.302[a]
$(\sin\theta/\lambda)_{max}$ [$Å^{-1}$]	0.55	0.65	0.65	0.65
refl. meas./unique	43951 / 11886	70304 / 11614	98527 / 17801	50993 / 14031
μ [mm^{-1}]	2.584[a]	2.938[a]	3.767[a]	2.423[a]
abs. corr.	multi-scan	multi-scan	analytical	multi-scan
abs. corr. range	0.17-0.86	0.55-0.85	0.43-0.79	0.36-0.87
param./restraints	852 / 468	565 / 12	910 / 146	686 / 82
Flack x parameter[23]	-0.032(7)	0.000(5)	-0.020(3)	-0.054(3)
R1/wR2 [I>2σ(I)]	0.0513 / 0.1355	0.0402 / 0.0866	0.0253 / 0.0451	0.0252 / 0.0585
R1/wR2 [all refl.]	0.0646 / 0.1423	0.0495 / 0.0893	0.0319 / 0.0466	0.0318 / 0.0605
S	1.077	1.084	1.054	1.061
res. density [$e/Å^3$]	-2.26 / 1.28	-1.00 / 3.60	-0.68 / 0.57	-0.90 / 0.88

[a] Derived parameters do not contain the contribution of the disordered solvent.

5.5 Reference

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Chapter 6

PCN- and PCS-Pincer Palladium Complexes as Tandem Catalysts in Homoallylation Reactions

Abstract

Novel PCN- and PCS-pincer palladium complexes [PdCl{C_6H_2-($OPPh_2$)-2-(OMe)-3-CH_2NMe_2)-6)}] **1**, [PdBr{C_6H_2-($OPPh_2$)-2-(OMe)-3-(HC=NPh)-6)}] **2**, [PdBr{C_6H_2-($OPPh_2$)-2-(OMe)-3-(CH_2SPh)-6)}] **3** and [PdCl{C_6H_2-($OPPh_2$)-2-(OMe)-3-(CH_2SPh)-6)}] **4** have been synthesized (55 - 95% yield) by using a flexible and straightforward synthetic route starting from isovanillin as the common precursor. The structures of complexes **1**, **2** and **4** in the solid state were determined using X-ray diffraction and showed a typical pincer-type geometry. The catalytic activities of **1**-**3** in the homoallylation reactions of aldehydes and allyl(tributyl)stannane as well as of their corresponding cationic complexes **1a**-**3a** in the tandem reaction of aldehydes or sulfonimines with allyl chlorides and hexamethyldistannane were investigated. It was found that the catalytic activities are very dependent on the combination of the E-donor moieties in the pincer ligand. Generally, PCS-pincer complex **3** and its cationic complex **3a** outperform PCN-pincer complexes **1** and **2** as well as their cationic complexes **1a** and **2a** in both the homoallylation and tandem reaction. PCS-pincer palladium complexes **3** and **3a** seem to benefit in a positive sense from the combination and cooperativity of a π-accepting phosphorus donor and a σ-donating sulfur donor.

6.1 Introduction

In the past decades, ECE-pincer metal complexes have attracted much attention and a variety of structures with various donor atom containing groups, *e.g.* E = NR_2, SR, PR_2, SeR, OPR_2, $OP(OR)_2$ have been synthesized. [1a, 1b, 1c] A common characteristic of some of these complexes is their robustness, *i.e.* thermal stability and stability of the σ-M-C bond against oxidation and hydrolysis. In addition, a range of ECE-pincer metal complexes show remarkable performances as catalysts in C−C cross coupling, transfer hydrogenation, Michael addition, aldol condensation, homoallylation, and a number of other reactions.[1]

The greater part of the known ECE-pincer metal complexes have identical *ortho*-substituents along the C_{ipso}–metal bond, *i.e* these are of the NCN,[2] PCP,[3] or SCS[4] types. Recently, ECE'-type (E ≠ E') pincer complexes, *i.e*. pincer ligands in which the *ortho*-substituents are different, have become a new aspect of pincer chemistry.[5-7] As elaborated in Figure 1, some examples of PCN- and PCS-pincer palladium complexes and their applications in C−C cross coupling reactions,[5] aldol condensations and tandem catalysis[6] have been independently reported by different groups. The PCN-pincer Pd complexes **A** and **B** are able to catalyze the Suzuki-Miyaura arylation of benzyl halides and other nonactived coupling partners,[5b, 5c] while the PCS-pincer complex [Pd{$C_6H_3(CH_2PPh_2)$-2-(CH_2SPh)-6}(MeCN)](BF_4) **C** is an excellent catalyst in the stannylation/homoallylation tandem reaction of allyl chloride, hexamethylditin and aldehydes or aryl sulfonimines (Scheme 1).[6] It is worthy to note that several pincer palladium complexes have been reported as active catalysts for only one of the two reactions that are part of this tandem reaction.[6,8–10] For example, the corresponding PCP-pincer palladium complex [Pd{$C_6H_3(CH_2PPh_2)_2$-2,6}(MeCN)](BF_4) is an active catalyst in the homoallylation of aldehydes or sulfonimines with allylstannane,[8a] but is not able to catalyze the stannylation reaction. Vice versa, NCN-pincer palladium complexes catalyze the stannylation reaction, but not the homoallylation.[10] On the other hand, SCS-pincer palladium complexes, like complex **C**, are able to catalyze each of the two reactions of the tandem reaction.[6]

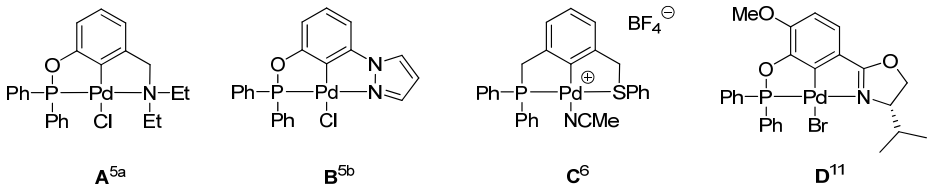
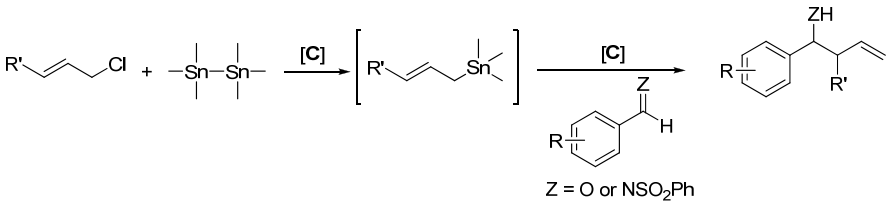


Figure 1. Representative examples of PCN- and PCS-pincer palladium complexes.



Scheme 1. Cationic PCS-pincer Pd complex **C** catalyzed stannylation/homoallylation tandem reaction.

These observations prompted us to study the syntheses of ECE'-pincer palladium complexes bearing other combinations of σ-donating (*i.e.*, N or S) and π-accepting (*i.e.*, P) donors in order to study their catalytic performances in the stannylation/homoallylation tandem reaction.

The use of isovanillin as the key building block, as pioneered by Nishiyama and co-workers (see complex **D** in Figure 1),[11] has allowed the regioselective introduction of oxazolinyl nitrogen donor and diphenylphosphinite phosphorus donor functionalities by chemoselective conversion of the two independent functional groups, *i.e.* the aldehyde and hydroxyl groups. Here, we report on the development of a synthetic methodology to synthesize ECE'-pincer arene and aryl bromide ligands along with their corresponding palladium complexes starting from isovanillin as the general building block (Figure 2).

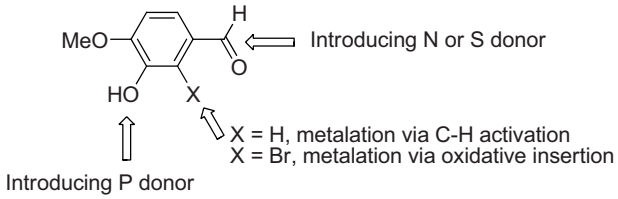
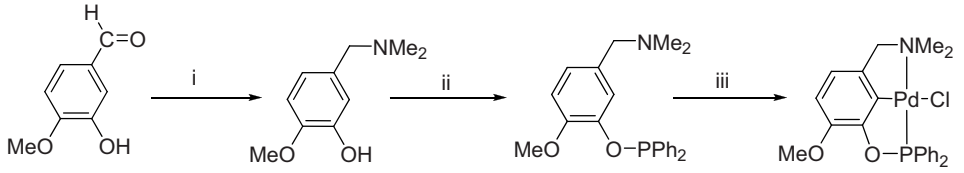


Figure 2. Strategy to access PCN- and PCS-pincer palladium complexes.

6.2 Results

6.2.1 Synthesis of PCN-Pincer Palladium Complex 1

Different from the literature procedure,[5a, 12] which involved subsequent reduction, bromination and amination reaction steps, in the present synthetic route to **6** the aldehyde group of isovanillin **5** was directly converted into a (dimethylamino)methyl moiety in moderate yield through a one-pot reductive amination reaction (Scheme 2).[13] Resulting **6** was then reacted with diphenylphosphine chloride in the presence of triethylamine to yield the corresponding ECE'-pincer arene ligand **7** in good yield and acceptable purity. Compound **7** was used in the next metallation step without further purification. A stoichiometric amount of $PdCl_2$ was added to a solution of **7** in toluene and the resulting reaction mixture was refluxed at 120 °C under N_2 for 18 h. After purification, the desired PCN-pincer palladium chloride complex **1** was obtained in 55% yield.



5 **6** **7** **1**

Scheme 2. The synthesis of PCN-pincer palladium chloride **1**. Reagents and conditions: i) $NMe_2H{\cdot}HCl$, NaOAc, $NaBH_3CN$, ethanol, 24 h, 53%; ii) Ph_2PCl, Et_3N, 0 °C to RT, 16 h, quantitative yield; iii) $PdCl_2$, toluene, 120 °C, 18 h, 55%.

The molecular geometry of **1** in the solid state was determined by single crystal X-ray diffraction analysis at 150(2) K. Suitable (colorless) single crystals of **1** were obtained by slow distillation of hexanes into a dichloromethane solution containing the complex at room temperature. As shown in Figure 3, the monoanionic pincer aryl ligand adopts the typical *mer*-PCN-pincer coordination mode. The palladium atom is located at the central position of a distorted square-planar structure, with the chloride group occupying the remaining *trans*-position with respect to C_{ipso}. The nitrogen donor and phosphorus donor are mutually *trans*-positioned, with a P1–Pd1–N1 angle of 159.53(5)°. The phenyl group C11/C16 is disordered. The value of the occupancy factor given for the major component of the disordered phenyl group refined to 0.646(14).

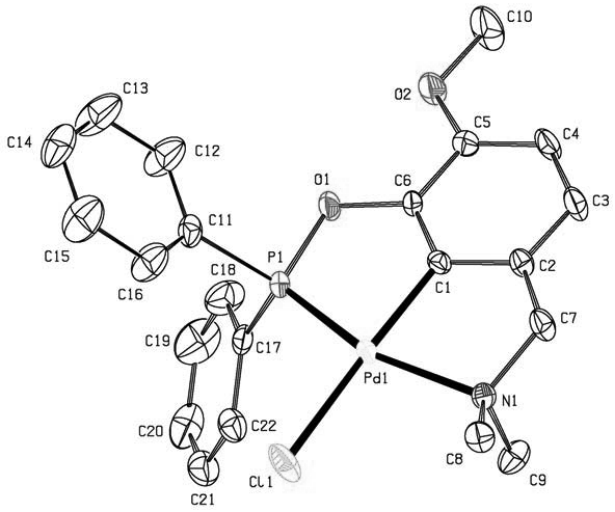
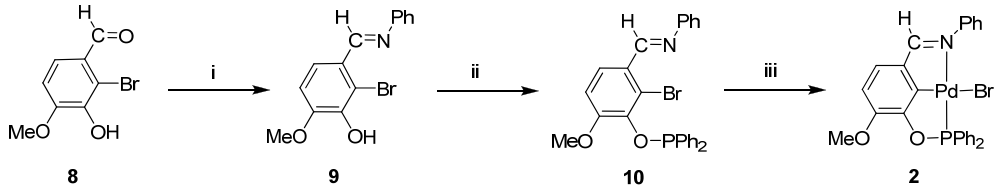


Figure 3. Displacement ellipsoid plot (50 % probability level) of the asymmetric unit of **1** at 150(2) K. H atoms and the minor component of the disordered phenyl ring C11/C16 are omitted for the sake of clarity. Selected bond lengths [Å] and angle [°]: Pd1-C1 1.957(2), Pd1-P1 2.1858(6), Pd1-N1 2.1592(17), Pd1-Cl1 2.3695(6), N1-C7 1.488(3), P1-O1 1.6380(16), P1-Pd-N1, 159.53(5), C1-Pd1-Cl1 177.26(7).

6.2.2 Synthesis of PCN-Pincer Palladium Complex 2

As depicted in Scheme 3, the novel PCN pincer palladium complex **2** has been derived from isovanillin bromide **8**.[14] Reaction of **8** with aniline in refluxing chloroform gave imine **9** in good yield. A subsequent reaction with diphenylphosphine chloride in the presence of triethylamine afforded the new PCN-pincer aryl bromide ligand **10** in quantitative yield. After removing $NEt_3 \cdot HCl$ by simple filtration and without further purification, a solution of **10** in toluene was added to a solution of a zerovalent Pd precursor (*i.e.*, $[Pd_2(dba)_3 \cdot CHCl_3]$) in toluene. The reaction mixture was warmed to 80 °C for 5 h to yield PCN-pincer palladium chloride complex **2** in 84% yield.



8 **9** **10** **2**

Scheme 3. Synthesis of PCN-Pincer complex **2**. Reagents and conditions: i) $PhNH_2$, $CHCl_3$, $MgSO_4$, reflux, 16 h, 85%; ii) Ph_2PCl, Et_3N, 0 °C to RT, 16 h, quantitative yield; iii) $Pd_2(dba)_3 \cdot CHCl_3$, toluene, 80 °C, 5 h, 84%.

The structure of **2** in the solid state (slow diffusion of hexanes into a dichloromethane solution of **2**) was determined by single crystal X-ray diffraction analysis at 150(2) K. As shown in Figure 4, **2** also adopts a typical *mer*-pincer coordination mode. Different to complex **1**, complex **2** possesses an almost perfect square-planar structure, as the double bond of the imine can become conjugated with the aromatic backbone. The palladium atom is located at the central position of this square-planar structure, while the bromine atom occupies a position *trans* to C_{ipso}. The nitrogen and phosphorus donors are mutually located in *trans*-positions with a P1-Pd1-N1 angle of 158.08(4)°, which is very similar to that of **1** (*vide supra*).

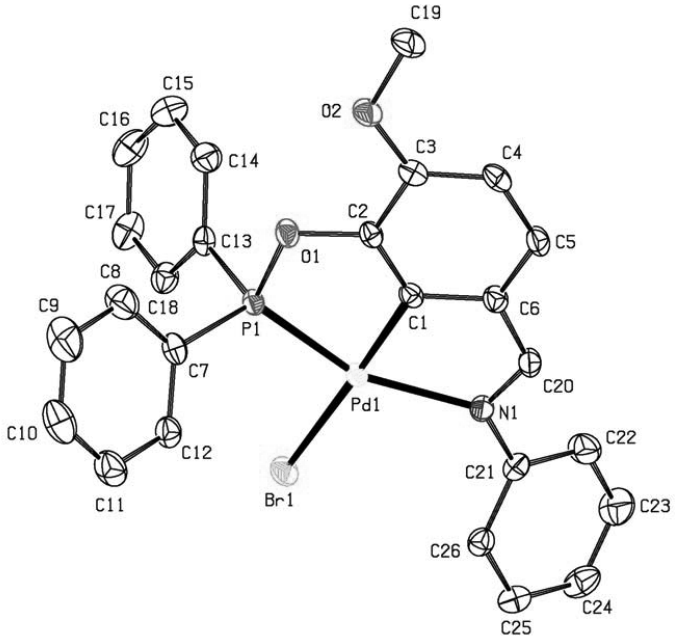
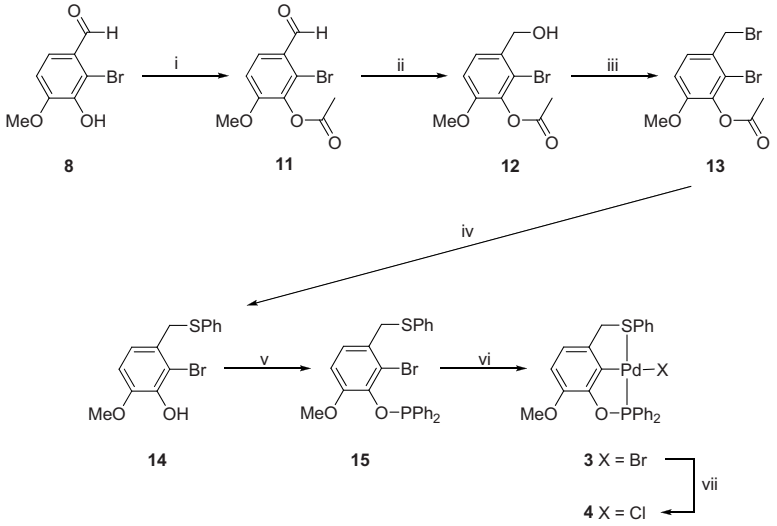


Figure 4. Displacement ellipsoid plot (50 % probability level) of the asymmetric unit of **2** at 150(2) K H atoms are omitted for the sake of clarity. Selected bond lengths [Å] and angle [°]: Pd1-C1 1.9658(16), Pd1-P1 2.2020(5), Pd1-N1 2.1777(14), Pd1-Br1 2.5037(2), N1-C20 1.297(2), P1-O1 1.6513(12), P1-Pd-N1, 158.08(4), C1-Pd1-Br1 177.68(5).

6.2.3 Synthesis of PCS-Pincer Palladium Complexes 3 and 4

Besides PCN pincer Pd complexes **1** and **2**, the novel PCS-pincer complexes **3** and **4** were synthesized as a proof of principle. As depicted in Scheme 4, the hydroxyl group of isovanillin bromide **8** was first protected by an acetyl group to prevent side product formation in the bromination step. Subsequently, aldehyde **11** was converted into alcohol **12** by reduction in the presence of $NaBH_4$ in ethanol. Benzylic bromine **13** was prepared by reacting alcohol **12** with a small excess of PBr_3 under mild conditions. These first three steps produced the respective

products in sufficient purity to enable their direct use in the next step. Thioether formation to afford compound **14** was accomplished by reacting **13** with NaSPh in dry THF at room temperature. Without purification, the resulting acetyl ester product was saponified and the resulting crude mixture was subjected to flash chromatography on silica gel to isolate compound **14** in promising yield. The phosphorus donor was introduced *via* a P-O coupling by reacting **14** with diphenylphosphine chloride in the presence of triethylamine. Finally, palladation was smoothly carried out by oxidatively inserting a zerovalent Pd species (*i.e.*, $[Pd_2(dba)_3{\cdot}CHCl_3]$) into the C-Br bond of **15**, which gave the novel PCS-pincer palladium complex **3** in good yields after purification.



8 **11** **12** **13** **14** **15**

Scheme 4. Synthesis of PCS-pincer palladium complexes **3** and **4**. Reagents and conditions: i) Ac_2O, pyridine, 80 °C, 40 min, 90%; ii) $NaBH_4$, EtOH, room temperature, 30 min, 95%; iii) 1.3 eq PBr_3, Et_2O, 0 °C, 2 h, 87%; iv) a) NaSPh, THF, room temperature, 16 h; b) 3 ml 2.5N NaOH water solution, EtOH, 30 min, 57%; v) $ClPPh_2$, Et_3N, THF, room temperature, 16 h, quantitative yield; vi) $Pd_2(dba)_3{\cdot}CHCl_3$, toluene, 80 °C, 5 h, 78%; vii) $AgBF_4$, wet acetone, aqueous NaCl solution, 1 h, 95%.

As we could not obtain suitable single crystals for **3**, complex **4** bearing a chloride anion was prepared.[15] Colorless crystals of this complex were obtained by slow diffusion of hexanes into a dichloromethane solution of **4** at room temperature. The structure of **4** was determined by single X-ray diffraction analysis at room temperature. As shown in Figure 5, the palladium atom is located at the central position of a distorted square-planar structure, in which the chloride group occupies a *trans* position with respect to the C_{ipso}. The sulfur and phosphorus donors are mutually located in *trans* positions, with a P1-Pd1-S1 angle of 165.02(3)°, which is larger than those of

PCN pincer complexes **1** (159.53(5)°) and **2** (158.08(4)°). The values of the occupancy factors given for the major components of the disordered phenyl groups C8/C13, C15/C20 and C21/C26 refined to 0.743(6), 0.504(10) and 0.52(2), respectively.

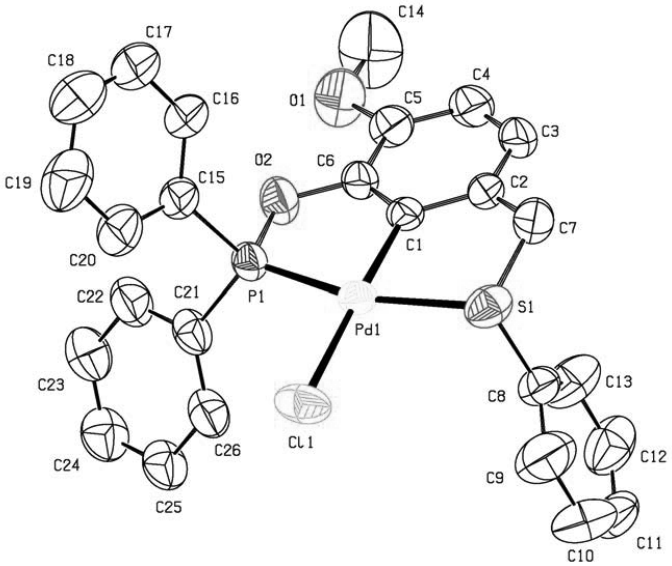
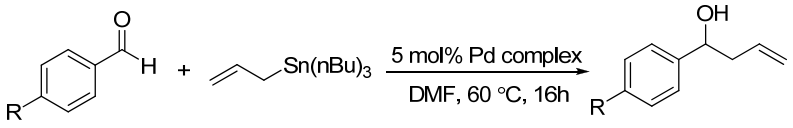


Figure 5. Displacement ellipsoid plot (50 % probability level) of the asymmetric unit of **4** at 295(2) K . H atoms and the minor components of the three phenyl groups are omitted for the sake of clarity. Selected bond lengths [Å] and angle [°]: Pd1-C1 1.982(3), Pd1-P1 2.2011(9), Pd1-S1 2.3774(10), Pd1-Cl1 2.3718(9), S1-C7 1.807(4), P1-O2 1.632(2), P1-Pd-S1, 165.02(3), C1-Pd1-Cl1 176.35(8).

6.2.4 PCN- and PCS-pincer Palladium Complex-Catalyzed Homoallylation

The catalytic performances of the new PCN- and PCS-pincer complexes were initially evaluated in the homoallylation of aryl aldehydes with allyl(tributyl)stannane (Table 1).

Table 1. Homoallylation reactions of aryl aldehydes and allyl(tributyl)stannane catalyzed by Pd complexes **1**-**3**.



16, R = H
17, R = NO_2
18, R = Me
19, R = Br

16a, R = H
17a, R = NO_2
18a, R = Me
19a, R = Br

Entry	Electrophile	Catalyst	Product	Yield(%)[a]
1	**16**	**1**	**16a**	68(75)
2	**16**	**2**	**16a**	21(30)
3	**16**	**3**	**16a**	84(90)
4	**17**	**1**	**17a**	90(>95)
5	**17**	**2**	**17a**	85(>95)
6	**17**	**3**	**17a**	93(>95)
7	**18**	**3**	**18a**	33 (40)
8	**19**	**3**	**19a**	71(75)

[a]: Isolated yields; chemical yields estimated by ^{1}H NMR spectroscopy with mesitylene as internal standard are presented in parentheses.

For the typical benchmark substrate benzaldehyde (**16**), PCS-pincer complex **3** affords the desired homoallylic alcohol **16a** in good yield (Table 1, entry 3), whereas complexes **1** and **2** merely gave promising and poor yields, respectively (Table 1, entries 1 and 2). Improved product yields were obtained for all three pincer complexes when *para*-NO_2 functionalized electrophile **17**, which is an activated substrate (*i.e.*, Hammett constant of *p*-NO_2 group is $\sigma_p = 0.78$[18]), was used (Table 1, entries 4-6 *vs.* entries 1-3). According to these initial tests, complex **3** showed the best catalytic activities amongst the three new pincer complexes. Remarkably, in the case of complexes **1** and **2**, some Pd black was found to be present in the reaction mixture after 5 h,

whereas no Pd black was observed for complex **3**. This observation strongly indicated that PCN complexes **1** and **2** decomposed during the catalytic processes at 60 °C in DMF. Another substrate, *p*-methylbenzaldehyde (*i.e.*, Hammett constant of *p*-methyl group is σ_p = -0.17[18]) **18** was evaluated as a slightly less electrophilic substrate using complex **3** as catalyst. The yield of its homoallylic alcohol product **18a** dramatically decreased to 33% (Table 1, entry 7). Finally, **3** catalyzes the conversion of *p*-bromobenzaldehyde **19** (*i.e.*, Hammett constant of *p*-Br group is σ_p = 0.23[18]) into homoallylic alcohol **19a** in promising yield (Table 1, entry 8).

6.2.5 PCN- and PCS-pincer Palladium Complex-Catalyzed in Tandem Catalysis

As cationic PCS-pincer palladium complex **C** was found to be an active catalyst for the stannylation/homoallylation tandem reaction,[6] we were interested in investigating the catalytic performance of the corresponding cationic PCN- and PCS-pincer palladium complexes **1a**-**3a**. These cationic complexes, comprising one equivalent of H_2O as co-ligand, were easily prepared by reacting the corresponding pincer halide complexes **1**-**3** with $AgBF_4$ in CH_2Cl_2 in the presence of water (Figure 6). The catalytic activities of these complexes in the tandem reaction are summarized in Tables 2-4.

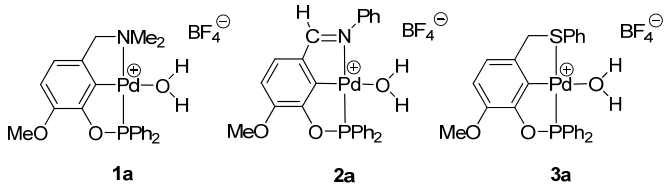
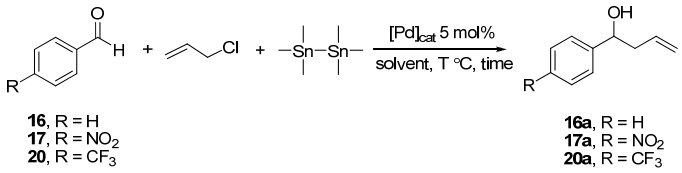


Figure 6. Cationic PCN- and PCS-pincer complexes **1a** – **3a**.

In order to compare their catalytic activities, the cationic PCN- and PCS-pincer complexes, **1a** - **3a** were tested in the tandem reaction of *p*-NO_2-benzaldehyde **17** and allyl chloride in the presence of hexamethyldistannane. Complexes **1a** and **3a** afforded comparable isolated yields as earlier reported (63 %) for the PCS-pincer complex **C** (see Figure 1),[6] while the PCN-pincer complex **2a** showed a slightly lower catalytic activity. Complex **3a** outperformed PCN-pincer complexes **1a** and **2a** as well as PCS-pincer complex **C** according to the conversions of electrophile **17** and the isolated yields of homoallyl product **17a** (Table 2, entry 3 *vs.* entries 1 and 2).

Table 2. Tandem reactions of aldehydes catalyzed by pincer complexes **1a**-**3a**.[a]



16, R = H
17, R = NO_2
20, R = CF_3

16a, R = H
17a, R = NO_2
20a, R = CF_3

Entry	Electrophile	Cat.	Conditions (solvent/T [°C]/time)	Product	Conversion(%)[b]	Yield(%)[c]
1	**17**	**1a**	DMF/RT/18 h	**17a**	70	59
2	**17**	**2a**	DMF/RT/18 h	**17a**	60	43
3	**17**	**3a**	DMF/RT/18 h	**17a**	85	70
4	**17**	**3a**	THF/RT/18 h	**17a**	80	65
5	**17**	**3a**	DCM/RT/18 h	**17a**	50	---
6	**17**	**3a**	Benzene/RT/18 h	**17a**	30	---
7	**17**	**3a**	DMF/40/18 h	**17a**	80	68
8[d]	**17**	**3a**	DMF/40/18 h	**17a**	80	71
9	**20**	**3a**	DMF/RT/16 h	**20a**	71[e]	68[e]
10	**16**	**3a**	DMF/RT/16 h	**16a**	19[e]	18[e]

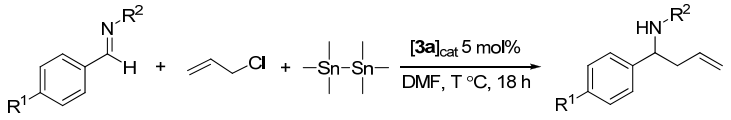
[a] Reagents and conditions: 0.1 mmol of aldehyde, 0.12 mmol of allyl chloride, 0.12 mmol of $Me_3SnSnMe_3$, 0.005 mmol of Pd complex, appointed solvent, reaction temperature and time. [b] Conversions of electrophiles were monitored by ^1H NMR with mesitylene as internal standard. [c] Isolated yields after column chromatography. [d] 2.0 equivalents of allyl chloride were used. [e] Detected by GC with mesitylene as internal standard.

A reaction condition optimization was then carried out with complex **3a** and electrophile **17**. It was found that the conversions of **17** depended highly on the polarity of the solvent in which the reaction was carried out. Polar solvents like THF and DMF afforded good conversions and isolated yields (Table 2, entries 3 and 4), whereas non-polar solvents like benzene and dichloromethane gave moderate conversions of 30-50% (Table 2, entries 5 and 6). Accordingly, DMF was kept as the optimal solvent in further catalytic tests. The reaction temperature was then slightly elevated to 40 °C using 2.0 equivalents of allyl chloride, which did not show an improvement of the conversions (Table 2, entry 3 *vs.* entries 7 and 8). The catalytic activities of **3a** in reactions with two other electrophiles were then investigated. The trifluoromethyl

functionalized electrophile **20** (*i.e.*, Hammett constant of *p*-CF_3 group is $\sigma_p = 0.54$[18]) gave a slightly decreased conversion and isolated yield compared to those of benchmark electrophile **17** (Table 2, entry 9). In contrast, the conversion and isolated yield dramatically decreased to less than 20% for benzaldehyde **16** (R=H) (Table 2, entry 10).

Next to aryl aldehyde substrates, a series of sulfonimines were tested as electrophiles in the tandem reaction by using the optimized conditions (Table 3). *N*-(4-nitrobenzylidene)benzenesulfonamide **21** was converted into its homoallylic amine product **21a** in 63% isolated yield at room temperature. This yield increased to 77% when the reaction was carried out at 40 ^{o}C (Table 3, entries 1 and 2). Surprisingly, the conversions and yields were not significantly affected by using less electrophilic sulfonimines. For instance, *N*-benzylidenebenzenesulfonamide **22** achieved 80% conversion and 65% isolated yield, which is considerably different than the conversion and isolated yield observed in the tandem reaction for benzaldehyde (Table 3, entry 3 *vs.* Table 2, entry 10). Even the *N,N*-dimethylsulfamoyl protected sulfonimines **23** and **24** were converted providing reasonable yields of the corresponding allylic products (Table 3, entries 4 and 5). These two homoallylsulfonamides belong to a novel class of homoallylic compounds that allow facile deprotection to yield primary allylamines.[16]

Table 3. Cationic PCS-pincer palladium complex **3a** catalyzed tandem allylation of sulfonimines.[a]



21, $R^1 = NO_2$, $R^2 = SO_2C_6H_5$
22, $R^1 = H$, $R^2 = SO_2C_6H_5$
23, $R^1 = NO_2$, $R^2 = SO_2NMe_2$
24, $R^1 = H$, $R^2 = SO_2NMe_2$

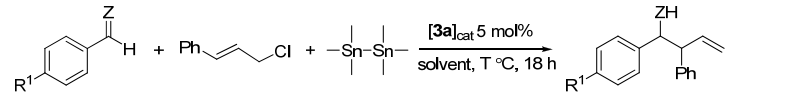
21a, $R^1 = NO_2$, $R^2 = SO_2C_6H_5$
22a, $R^1 = H$, $R^2 = SO_2C_6H_5$
23a, $R^1 = NO_2$, $R^2 = SO_2NMe_2$
24a, $R^1 = H$, $R^2 = SO_2NMe_2$

Entry	Electrophile	Product	Conversion[%][b]	Yield[%][c]
1[d]	**21**	**21a**	80	63
2	**21**	**21a**	90	77
3	**22**	**22a**	80	65
4	**23**	**23a**	75	60
5	**24**	**24a**	60	45

[a] Reagents and conditions: 0.1 mmol of sulfonimine, 0.12 mmol of allyl chloride, 0.12 mmol of $Me_3SnSnMe_3$, 0.005 mmol of Pd complex, 1 mL of DMF, 40 °C unless otherwise stated. [b] Conversions of electrophiles were monitored by ^{1}H NMR with mesitylene as internal standard. [c] Isolated yields. [d] The reaction was performed at room temperature.

In addition, cinnamyl chloride was examined as allylic reagent in order to reveal the diastereoselectivity of **3a** in the tandem catalysis. Entries 1 and 2 in Table 4 show that both the isolated yield and diastereoselectivity of this reaction are dependent on the nature of the solvent in which the reaction was carried out. For *p*-NO_2-benzaldehyde **17** both the yield and diastereomeric ratio (*i.e., anti/syn*) were remarkably improved by using DMF instead of THF as the solvent (Table 4, entry 1 *vs.* entry 2). In contrast to the strong solvent-effect, an increase of the temperature did not significantly affect the yield and diastereoselectivity (Table 3, entry 2 *vs.* 3). Moreover, the desired homoallylsulfonamide product **21b** was isolated in the same yield and similar stereoselectivity as the homoallylic product **17b** but with opposite steric configuration when *N*-(4-nitrobenzylidene)benzenesulfonamide **21** was used as electrophile. Interestingly, as earlier observed by Szabó *et al*.,[8a, 17] formation of the *anti*-product is favored for aldehyde electrophile **17**, whereas sulfonimine electrophile **21** prefers formation of the *syn* product.

Table 4. PCS-pincer complex **3a** catalyzed tandem allylation reactions with cinnamyl chloride.[a]



17, $R^1 = NO_2$, Z = O
21, $R^1 = NO_2$, $Z = NSO_2C_6H_5$

17b, $R^1 = NO_2$, Z = O
21b, $R^1 = NO_2$, $Z = NSO_2C_6H_5$

Entry	Electrophile	Product	Conditions (solvent/T[°C])	Conversion[%][b]	Yield[%][c]	dr[d]
1	**17**	**17b**	THF/RT	50	30	3:2
2	**17**	**17b**	DMF/RT	85	65	5:1
3	**17**	**17b**	DMF/40	85	63	6:1
4	**21**	**21b**	DMF/40	80	48[e]	1:5

[a] Reagents and conditions: 0.1 mmol of aldehyde or sulfonimine, 0.12 mmol of cinnamyl chloride, 0.12 mmol of $Me_3SnSnMe_3$, 0.005 mmol of Pd complex **3a**, appointed solvent, temperature and reaction time. [b] Conversions of electrophiles were detected by ^1H NMR with mesitylene as internal standard. [c] Isolated yields. [d] Diastereomeric ratio: anti/syn. [e] Only the pure *syn* product was isolated.

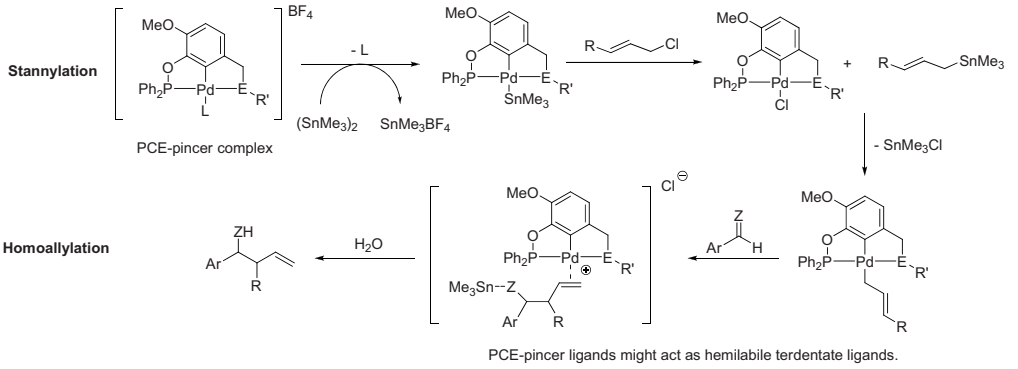
6.3 Discussion

In general, the entitled ECE'-pincer palladium complexes are able to catalyze the homoallylation and stannylation/homoallylation tandem reactions with aldehydes and sulfonimines as electrophiles. Probably due to the combination and cooperation of two different donor moieties, these pincer complexes display quite dissimilar catalytic activities not only to each other and but also to the previously reported symmetrical ECE-pincer complexes. For instance, PCN-pincer complexes **1** and **2** showed low catalytic activities towards the benchmark electrophile benzaldehyde in the homoallylation reactions, and Pd black formed during the course of the reactions. Presumably, PCN-pincer ligands are hemi-labile under the reaction conditions (60 °C, DMF), and the Pd atoms might dissociate from the complexes during the catalysis (See Scheme 5). Differently, PCS-pincer complex **3** could take advantage of the combination of S and P donors, and conserves its configuration during the catalysis. Thus, it shows better catalytic activities without the concomitant formation of Pd black.

The catalytic use of complex **3** in the homoallylation is limited to relatively strong eletrophiles bearing electron-withdrawing groups and shows a rather low catalytic activity towards weak

electrophilic substrates in comparison with earlier reported phosphite or phosphonite PCP-pincer Pd complexes (Table 1, entries 7 and 8).[8a, 8b, 8e, 8f, 9] Importantly, it was found that the increasing order of yields agreed with the increasing order of Hammett constants of the *para*-functional groups in the aldehyde substrates, which implies that the electrophilic character of the aldehydes can affect the rate-determining step in homoallylation of aldehydes. This observation strongly suggests that the catalytic activity of ECE'-pincer complexes in homoallylation reactions might not be further improved by simply combining one electron-enriched donor and one electron-deficient donor.

The stannylation/homoallylation tandem reaction involves three independent steps (Scheme 5): 1) stannylation of allyl chloride, which is favored by an electron-enriched Pd metal center;[10] 2) transmetalation of allylstannane and pincer Pd complex to generate an η^1-allyl Pd intermediate, which requires an electron-deficient Pd metal center; [8a – 8c] and 3) an aryl aldehyde or aryl sulfonimine substrate electrophilically attacks the γ position of the η^1-allyl moiety, which is enhanced by an electron-enriched Pd metal center.[8a – 8c] Clearly, these reactions proceed under very complicated electronic demandings, and thus the rational design of pincer ligands and the fine-tuning of the electronic properties of their donor moieties are crucial for the further development of these catalyzed reactions. Electronically tunable ECE'-pincer metal complexes seem to be an ideal choice in this respect, particularly when the complexes bear both σ-donating (*i.e.*, N or S) and π-accepting (*i.e.*, P) donors.



Scheme 5. Reaction pathway of PCE-pincer Pd complexes catalyzed stannylation/homoallylation tandem reaction.

In the tandem reactions of aldehydes, allyl chloride and hexamethyldistannane, cationic aqua PCS-pincer complex **3a** also outperformed PCN-pincer complexes **1a** and **2a**, albeit that its catalytic activity towards less electrophilic substrates is still not ideal, which is consonant with

the results observed for the corresponding, neutral PCS-pincer palladium chloride **3** in homoallylation reactions (*vide supra*). Interestingly, the catalytic activity of complex **3a** was not significantly affected by using less electrophilic sulfonimine substrates, which indicates that the electrophilic character of sulfonimines cannot predominate the rate-determining step in their homoallylation. Importantly, under mild ambient conditions Pd-black was not formed in any of the tandem catalysis reactions. Electron-deficient phosphinite PCS-pincer complex **3a** overall showed comparable catalytic activities and stereoselectivities to the relatively electron-enriched phosphine cationic PCS-pincer complex **C** [Pd{$C_6H_3(CH_2PPh_2)$-2-(CH_2SPh)-6}(MeCN)](BF_4),[6] regardless of the combination of electrophile (*i.e.*, *p*-NO_2-benzaldehyde and *N*-(4-nitrobenzylidene)benzenesulfonamide) and allyl chloride (*i.e.*, allyl chloride and cinnamyl chloride). Yet, **3a** is outperformed by SCS-pincer complex [Pd{$C_6H_3(CH_2SPh)_2$-2,6}(MeCN)](BF_4) bearing an electron-donating SCS-pincer ligand in both catalytic activity and diastereoselectivity.[6] These observations imply that the better catalytic activity in the tandem reaction could require pincer complexes bearing relatively stronger electron-donating pincer ligands and less electrophilic Pd metal centers.

According to the Hammett constant for a *meta*-OMe group with respect to the C-Pd σ-bond, *i.e.*, $\sigma_m = 0.12$,[18] the *meta*-OMe groups in the ECE'-pincer complexes **1-3** and **1a-3a** withdraw electron density from the C_{ipso}-Pd bonds and thus polarize the C_{ipso}-Pd bonds in the direction of C_{ipso}, consequently, it makes the Pd metal centres more positively charged. Therefore, these pincer complexes can be considered as relatively electron-deficient and they are expected to accelerate the transmetallation step in the allylation process but to slow down both the stannylation of allyl chlorides and homoallylation of Pd η^1-allyl moieties according to previous reports.[8a, 8d, 8c] Efforts are currently ongoing to corroborate this line of reasoning with the analogous complex that does not have a OMe group.

6.4 Conclusions

In this paper, we have developed a series of unsymmetrical PCN- and PCS-pincer palladium complexes starting from isovanillin as the common building block, by using tunable and straightforward synthetic routes. Their syntheses enjoy good yields, mild reaction conditions, and excellent flexibility. Additionally, the detailed structures of the PCN- (**1** and **2**) and PCS- (**3a**) pincer palladium complexes in the solid state have been determined by single crystal X-ray analyses. The catalytic performances of these complexes have been examined in homoallylation reactions of aldehydes with allyl(tributyl)stannane as well as the tandem reactions of allyl chlorides, aldehydes or sulfonimines, and hexamethyldistannane in order to understand the influence of the combination of different E-donors on the course of these reactions. In the homoallylation reactions, PCS-pincer complex **3** outperforms PCN-pincer complexes **1** and **2** to afford promising to good yields for strong electrophiles, although its catalytic activity is rather low towards less electrophilic substrates. In the tandem reaction, it was also found that cationic PCS-pincer complex **3a** is superior to cationic PCN-pincer complexes **1a** and **2a** in terms of catalytic activities towards both aryl aldehydes and aryl sulfonimines. Remarkably, aryl sulfonimines generally present higher reactivities in comparison with aryl aldehydes when PCS-pincer complex **3a** is used as the catalyst. These investigations have shown the remarkable catalytic properties of PCS-pincer palladium complexes in the stannylation/homoallylation tandem reaction, but also showed that these are inferior to the activity of symmetrical SCS-pincer palladium complexes. Due to the flexible synthetic strategy, the catalytic performances of PCS-pincer complexes could be further improved by varying either the thioether or the phosphinite functionalities with different substituents. Current efforts in our laboratory aim at both the development of more active PCS-pincer complexes and of their chiral analogues in asymmetric tandem catalysis, as well as at the understanding of the subtle electronic demand of the catalytic stannylation/homoallylation reaction.

6.5 Experimental section

General remarks: All reactions were performed under a dry N_2 atmosphere using standard Schlenk techniques unless stated otherwise. Glassware was oven dried or flame dried prior to use. Diethyl ether and THF were freshly distilled over metallic sodium prior to use. Toluene, Et_3N, and DMF were distilled over CaH_2 and stored under N_2 at –30 °C. Diphenylphosphine chloride was freshly distilled under reduced pressure prior to use. 2-bromo-3-hydroxy-4-methoxybenzaldehyde **8** was prepared according to a reported procedure.[14] All other reagents were purchased from ACROS Organics and Sigma-Aldrich Chemical Co. Inc, and used as received. ^{1}H-NMR (400.0 MHz), ^{13}C-NMR (100.6 MHz), and ^{31}P-NMR (161.9 MHz) spectra were recorded at room temperature in $CDCl_3$ on a Varian spectrometer at 400 MHz. Chemical shift values are reported in ppm (δ) relative to $(CH_3)_4Si$ (^{1}H and ^{13}C NMR) or a capillary containing 85% H_3PO_4 in D_2O ($^{31}P\{^1H\}$ NMR). Flash chromatography was performed using ACROS silica gel, 0.06-0.200 mm, pore diameter ca. 6 nm. MS measurements were carried out on an Applied Biosystems Voyager DE-STR MALDI-TOF MS. Elemental microanalyses were performed by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim a/d Ruhr, Germany.

5-((dimethylamino)methyl)-2-methoxyphenol (6) Isovanillin (2 g, 13.15 mmol) was reacted with dimethylamine hydrochloride (2.32 g, 28.45 mmol) and sodium cyanoborohydride (1.44 g, 22.85 mmol) in methanol (100 mL) in the presence of sodium acetate (1.82 g, 22.20 mmol). The pH value of the solution was maintained in the range of 7-8 throughout the reaction, if necessary by the addition of concentrated HC1. The solution was stirred at room temperature during 24 h. Acetone (x mL) was then added, followed by 6 N HCl (until pH 2-3 was reached). The solvent was removed *in vacuo*, and the residue was dissolved in water (50 mL) and extracted with EtOAc (4 x 15 mL). The combined organic layers upon evaporation of the solvent yielded a mixture of starting aldehyde and the corresponding alcohol. The remaining aqueous phase was made basic (pH 8-9) and extracted with EtOAc (5 x 25 mL). The organic extracts were dried over $MgSO_4$, and the solvent was removed *in vacuo*, thus yielding an amber oil residue. An analytical sample was recrystallized from a saturated hot hexanes solution of the crude product. Yield : 53% (1.27g, white solid) ^{1}H NMR ($CDCl_3$, 400MHz): δ 6.83-6.91 (m, 3H, Ar*H*), 6.05 (br s, 1H, O*H*), 3.91 (s, 3H, OCH_3), 3.39 (s, 2H, CH_2NMe$_2$), 2.28 (s, 6H, NMe_2); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 146.2, 145.8, 131.5, 121.0, 116.0, 110.7, 63.9, 56.2, 45.2; Anal. Calcd. for C, 66.27; H, 8.34; N, 7.73; Found : C, 66.26; H, 8.40; N, 7.69;

(3-(diphenylphosphinooxy)-4-methoxyphenyl)-*N,N*-dimethylmethanamine(7) Compound **6** (0.182 g, 1 mmol) was in dissolved dry toluene (20 mL) and precooled to 0 °C on an ice bath. To this solution was consecutively added Et_3N (280 µL, 2 mmol) and Ph_2PCl (189 µL, 1 mmol) *via* an air-tight syringe. After the addition, the reaction mixture was allowed to warm to room temperature and was vigorously stirred for 16 h. The resulting white suspension was filtered through a short pad of Celite, after which the filtrate was concentrated under reduced pressure to give crude compound **7**, which was obtained in quantitative yield and used in the next step without further purification. Yield: quantitative (0.037 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.66-7.74 (m, 4H, PPh*H*), 7.35-7.48 (m, 6H, PPh*H*), 6.71 (d, ^3J=8.0 Hz, 1H, Ar*H*), 6.42 (d, ^3J=8.0 Hz, 1H, Ar*H*), 6.38 (s, 1H, Ar*H*), 3.98 (s, 3H, OCH_3), 3.41 (s, 2H, CH_2NMe$_2$), 2.34 (s, 6H, NMe_2); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 168.6, 153.9 (d, *J*=3.0 Hz), 148.5, 144.7, 142.5 (d, *J*=18

Hz), 131.2 (d, *J*=7.6 Hz), 131.0 (d, *J*=7.6 Hz), 129.8 (d, *J*=4 Hz), 128.3 (d, *J*=7.5 Hz), 126.1, 123.4, 110.9, 53.6, 50.7; $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 126.4 (s).

PCN-pince Pd complex 1 To a solution of compound **7** (0.19 g, 0.5 mmol) in dry toluene (15 mL) was added $PdCl_2$ (0.09 g, 0.5 mmol) and this mixture was refluxed at 120 °C under N_2 for 18 h. After cooling, the reaction mixture was filtered through a short pad of Celite and the filtrate was concentrated under reduced pressure to yield a yellowish solid. The solid was subjected to flash chromatography with EtOAc/hexanes (9:1, (v/v)) as eluent. Analytically pure product was obtained as a slightly yellow and air stable solid. Yield : 55% (0.139 g, 0.275 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.97-8.03 (m, 4H, PPh*H*), 7.47-7.49 (m, 6H, PPh*H*), 6.70 (d, ^{3}J=8.0 Hz, 1H, Ar*H*), 6.64 (d, ^{3}J=8.0 Hz, 1H, Ar*H*), 4.05 (s, 2H, CH_2NMe_2), 3.86 (s, 3H, OCH_3), 2.89 (s, 6H, NMe_2); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 50.5 (d, *J*=11 Hz), 146.8, 144.5 (d, *J*=20 Hz), 140.3, 133.5 (d, *J*=54 Hz), 131.8-132.2 (m), 128.8 (d, *J*=20 Hz), 117.6, 110.9, 56.6, 50.5; $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 155.4 (s). MS (MALDI-TOF): m/z calcd for $C_{22}H_{23}NO_2PPd$: 470.82 $[M\text{-}Cl]^+$; found: 470.81; Anal. Calcd. for C, 52.19; H, 4.58; N, 2.77; P, 6.12; Pd, 21.02; Found : C, 52.22; H, 4.61; N, 2.71; P, 6.09; Pd, 21.01;

2-bromo-6-methoxy-3-((phenylimino)methyl)phenol (9) Compound **8** (0.4620 g, 2 mmol),[13] aniline (184 μL, 2 mmol), and $MgSO_4$ (1 g) were suspended in $CHCl_3$ (20 mL) and refluxed at 75 °C under N_2 for overnight. After cooling, the reaction mixture was filtered through a short pad of Celite and the filter cake was washed with CH_2Cl_2 (3 x 5 mL). The combined filtrate was concentrated to dryness in vacuo to yield a yellow-brown solid that was used for the next step without further purification. An analytical sample was recrystallized from a saturated hot hexanes solution of the crude product. Yield: 85% (0.52 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.81 (s, 1H, PhN=C*H*Ar), 7.91 (d, ^{3}J=8.4 Hz, 1H, Ar*H*), 7.40 (m, 2H, NPh*H*), 7.27 (m, 3H, NPh*H*), 6.93 (d, ^{3}J=8.4 Hz, 1H, Ar*H*), 6.06 (br s, 1H, O*H*), 3.98 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 159.4, 151.9, 149.7, 143.3, 129.4, 128.0, 126.4, 121.0, 112.7, 109.9, 56.7; Anal. Calcd. for C, 54.92; H, 3.95; N, 4.58; Found : C, 54.96; H, 3.91; N, 4.53;

***N*-(2-bromo-3-(diphenylphosphinooxy)-4-methoxybenzylidene)benzenamine (10)** Compound **9** (0.3062 g, 1 mmol) was azeotropically dried on dry toluene (3 x X mL), and afterwards dissolved in dry toluene (20 mL) and precooled to 0 °C on an ice bath. To this solution was consecutively added Et_3N (280 μL, 2 mmol) and Ph_2PCl (189 μL, 1 mmol) *via* an air-tight syringe. After addition, the reaction mixture was allowed to warm to room temperature and was vigorously stirred for 16 h. The resulting white suspension was filtered through a short pad of Celite and the filter cake was washed with EtOAc (3 x 5 mL). The filtrate was concentrated under reduced pressure and was fully dried in vacuum to give crude compound **10**, which was used in the next step without further purification. Yield: quantitative (0.496 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.84 (s, 1H, C*H*=NPh), 7.80 (t, ^{3}J=4.4 Hz, 4H, PPh*H*), 7.43-7.47 (m, 6H, PPh*H*), 7.24-7.41 (m, 6H, Ar*H* + NPh*H*), 6.94 (d, ^{3}J=8.8 Hz, 1H, Ar*H*), 3.64 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 159.6, 151.1, 142.1 (d, *J*=18 Hz), 132.0 (d, *J*=11Hz), 131.3 (d, *J*=23 Hz), 129.4 (d, *J*=12 Hz), 128.6, 128.5, 128.4, 126.3, 124.5, 122.4, 121.3, 111.6, 56.2; $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 126.8 (s).

PCN-pincer Pd complex 2 To a solution of compound **10** (0.2450 g, 0.5 mmol) in dry toluene (15 mL) was added [$Pd_2(dba)_3{\cdot}CHCl_3$] (0.258 g, 0.25 mmol) and this mixture was warmed to 80 °C under N_2 for 5 h. After cooling, the reaction mixture was filtered through a short pad of Celite and the filtrate was concentrated under reduced pressure to yield a yellowish solid mixture. The solid was subsequently subjected to flash chromatography with EtOAc/hexanes (3:7 (v/v)) as eluent. The product was obtained as a light yellow and air stable solid. Yield : 80% (0.2387 g, 0.4 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.07 (q, ^3J=6.4 Hz, 4H, PPh*H*), 7.46-7.54 (m, 6H, PPh*H*), 7.40 (t, ^3J =7.2 Hz, 2H, NPh*H*), 7.26-7.31 (m, 3H, NPh*H*), 8.24 (d, $^4J_{P,H}$=4.8 Hz, 1H, C*H*=NPh), 7.22 (d, ^3J=8.0 Hz, 1H, Ar*H*), 6.70 (d, ^3J=8.0 Hz, 1H, Ar*H*), 3.94 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 173.0, 156.5, 150.3 (d, *J*=10.4 Hz), 148.3 (d, *J*=20.7 Hz), 148.6, 138.1, 132.2-132.9 (m), 128.8-129.2 (m), 127.7, 125.6, 123.7, 109.5, 56.4; ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 159.2 (s). MS (MALDI-TOF): m/z calcd for $C_{26}H_{21}NO_2PPd$: 516.84 $[M\text{-}Br]^+$; found: 516.86; Anal. Calcd. for C, 52.33; H, 3.55; N, 2.35; P, 5.19; Pd, 17.83; Found : C, 52.28; H, 3.65; N, 2.38; P, 5.14; Pd, 17.81;

2-bromo-3-formyl-6-methoxyphenyl acetate (11) Compound **8** (1.16 g, 5 mmol) and Ac_2O (0.47 mL, 5 mmol) were dissolved in pyridine (15 mL) and vigorously stirred at room temperature under N_2 for 1 h. Afterwards, pyridine was removed from the mixture under reduced pressure on a rotary evaporator. The resulting oily product was redissolved in demineralized water (20 mL) and the pH value of the mixture was then adjusted to 7 by adding saturated aqueous $NaHCO_3$ solution. The neutralized aqueous solution was extracted with EtOAc (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$. After filtration, filtrate solution was evaporated to dryness to afford a white solid. The product was enough pure to be used in the next step without further purification. Yield: 90% (1.22 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 10.14 (s, 1H, ArC=O*H*), 7.76 (d, ^3J=8.8 Hz, 1H, Ar*H*), 6.94 (d, ^3J=8.8 Hz, 1H, Ar*H*), 3.83 (s, 3H, OCH_3), 2.33 (s, 3H, OAc); ^{13}C NMR ($CDCl_3$, 100.6 MHz): 190.3, 167.8, 157.4, 138.2, 128.9, 127.2, 122.6, 111.2, 56.8, 20.5; Anal. Calcd. for C, 43.98; H, 3.32; Br, 29.26; Found: C, 43.91; H, 3.28; Br, 29.31.

2-bromo-3-(hydroxymethyl)-6-methoxyphenyl acetate (12) To a solution of **11** (1.22 g, 4.5 mmol) in absolute ethanol (20 mL) was added $NaBH_4$ (0.1 g, 2.5 mmol) in one portion. The reaction mixture was stirred at room temperature for 1 h. Ethanol was removed on a rotary evaporator and the resulting mixture was diluted with water (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, followed by filtration. A white solid product was obtained after removing the solvent under vacuum. The product was enough pure to be used in the next step without further purification. An analytical sample was recrystallized from a saturated hot hexanes solution of the crude product. Yield: 95% (1.18 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.23 (d, ^3J=8.4 Hz, 1H, Ar*H*), 6.86 (d, ^3J=8.4 Hz, 1H, Ar*H*), 4.59 (s, 2H, ArCH_2OH), 3.78 (s, 3H, OCH_3), 2.93 (s very br., 1H, CH_2O*H*), 2.34 (s, 3H, OAc); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 168.4, 153.2, 151.8, 137.9, 130.5, 126.3, 117.6, 109.7, 64.6, 56.5, 21.2; Anal. Calcd. for C, 43.66; H, 4.03; Br, 29.05; Found : C, 43.70; H, 3.98; Br, 29.09;

Synthesis of 2-bromo-3-(bromomethyl)-6-methoxyphenyl acetate (13) To a solution of **12** (1.18 g, 4.3 mmol) in dry THF (20 mL) precooled at 0 °C on an ice bath was added freshly distilled PBr_3 (0.50 mL, 5 mmol) *via* syringe. After the addition, ice bath was removed and the reaction was quenched by carefully adding saturated aqueous $NaHCO_3$ (10 mL) after being stirred at room temperature for 1.5 h. Afterwards, the mixture was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried over $MgSO_4$. Removal of all volatiles under vacuum yielded a yellowish oily product. The product was enough pure to be used in the next step without further purification. An analytical sample was obtained by high vacuum flash distillation (0.5 mmHg/185 ℃). Yield: 87% (1.26 g, 3.74 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.26 (d, ^3J=8.8 Hz, 1H, Ar*H*), 6.84 (d, ^3J=8.8 Hz, 1H, Ar*H*), 4.56 (s, 2H, ArCH_2Br), 3.77 (s, 3H, OCH_3), 2.32 (s, 3H, OAc); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 164.8, 138.3, 129.4, 129.1, 122.0, 114.3, 56.2, 26.7, 20.3; Anal. Calcd. for C, 35.54; H, 2.98; Br, 47.28; Found : C, 35.44; H, 3.05; Br, 47.23;

2-bromo-6-methoxy-3-(phenylthiomethyl)phenol (14). Compound **13** (0.25 g , 0.76 mmol) and NaSPh (0.1 g, 0.76 mmol) were stirred in of dry THF (20 mL) at room temperature for 16 h. After quenching the reaction with demineralized water (20 mL), the crude product was extracted with EtOAc (3 x 30 mL) and the combined organic layers were dried over $MgSO_4$. A yellow oily mixture was obtained after removing of all volatiles. Without further purification, it was directly treated with 2.5 N NaOH (3 mL) and ethanol (10 mL) at room temperature for 30 min. The reaction mixture was then diluted with demineralized water (50 mL) and neutralized with acetic acid. The mixture was extracted with EtOAc (3 x 30 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated on a rotary evaporator after filtration. The resulting beige oily product was subjected to flash chromatography with EtOAc/hexanes (1:1 (v/v)) as eluent, R_f = 0.85. The desired product was obtain as a beige viscous oil. Yield: 57% (0.14 g, 0.43 mmol) ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.33 (apparent d, ^3J=7.6 Hz, 2H, SPh*H*), 7.24 (t, ^3J=7.6 Hz, 2H, SPh*H*), 7.19 (apparent t, ^3J=7.2 Hz, 1H, SPh*H*), 6.78 (d, ^3J=8.4 Hz, 1H, Ar*H*), 6.68, (d, ^3J=8.4 Hz, 1H, Ar*H*), 6.04, (s br, 1H, ArO*H*), 4.19 (s, 2H, ArCH_2SPh), 3.85 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 158.0, 141.9, 136.4, 129.9, 129.0, 126.8, 125.2, 123.6, 116.0, 114.7, 58.2, 37.8; Anal. Calcd. for C, 51.70; H, 4.03; Br, 24.57; S, 9.86; Found : C, 51.61; H, 3.98; Br, 24.59; S, 9.79;

(2-bromo-6-methoxy-3-(phenylthiomethyl)phenoxy)diphenylphosphine (15) Compound **14** (0.1630 g, 0.5 mmol) was azeotropically dried on dry toluene 3 times, dissolved in dry toluene (20 mL) and precooled to 0 °C on an ice bath. To this solution was consecutively added Et_3N (140 µL, 1 mmol) and Ph_2PCl (94.5 µL, 0.5 mmol) *via* an air-tight syringe. After addition, the reaction mixture was allowed to warm to room temperature and was vigorously stirred for 16 h. The resulting white suspension was filtered through a short pad of Celite, and the filtrate was concentrated under reduced pressure and thoroughly dried in vacuum to give crude compound **15**, which was obtained in quantitative yield and used in the next step without further purification. Yield: quantitative (0.260 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.83 (q, ^3J=8.0 Hz, 4H, PPh*H*), 7.58-7.75 (m, 2H, SPh*H*), 7.37-7.48 (m, 6H, PPh*H*), 7.24-7.31 (m, 3H, CH_2SPh*H*), 6.71 (d, ^3J=7.6 Hz, 1H, Ar*H*), 6.43 (d, ^3J=7.6 Hz, 1H, Ar*H*), 4.34 (s, 2H, ArCH_2SPh), 3.95 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 163.4, 153.9 (d, *J*=3.6 Hz), 148.5, 144.9, 142.1 (d, *J*=18 Hz), 131.7 (d, *J*=7.5 Hz), 131.4 (d, *J*=7.5 Hz), 129.8 (d, *J*=4 Hz), 128.3 (d, *J*=7.8 Hz), 129.7, 128.6, 117.5, 110.5, 57.1, 23.4, 14.9; ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 126.9 (s).

PCS-pincer Pd complex 3 To a solution of compound **15** (0.2550 g, 0.5 mmol) in dry toluene (15 mL) was added $Pd_2(dba)_3.CHCl_3$ (0.258 g, 0.25 mmol) and the mixture was warmed to 80 °C under N_2 for 5 h. After cooling, the reaction mixture was filtered through a short pad of Celite and the filtrate was concentrated under reduced pressure to yield a yellowish solid mixture. The solid was subjected to flash chromatography with EtOAc/hexanes (3:7 (v/v)) as eluent. An analytic sample was obtained as a light yellow and air stable solid. Yield : 78% (0.2400 g, 0.39 mmol) ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.03 (q, ^3J=8.0 Hz, 4H, PPh*H*), 7.79-7.82 (m, 2H, SPh*H*), 7.45-7.52 (m, 6H, PPh*H*), 7.34-7.36 (m, 3H, CH_2SPh*H*), 6.85 (d, ^3J=8.0 Hz, 1H, Ar*H*), 6.70 (d, ^3J=8.0 Hz, 1H, Ar*H*), 4.62 (s, 2H, ArCH_2SPh), 3.86 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 174.4, 157.8, 152.0 (d, *J*=14 Hz), 148.0, 142.5 (d, *J*=2 Hz), 142.0, 133.3, 133.0, 132.5 (d, *J*=3 Hz), 132.0 (d, *J*=14 Hz), 130.0, 129.6 (d, *J*=14 Hz), 118,9, 111.4, 57.1, 50.5; ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 153.0 (s). MS (MALDI-TOF): m/z calcd for $C_{26}H_{21}NO_2PPd$: 535.91 $[M\text{-}Br]^+$; found: 535.90; Anal. Calcd. for C, 50.71; H, 3.60; P, 5.03; Pd, 17.28; S, 5.21; Found : C, 50.68; H, 3.51; P, 5.04; Pd, 17.27; S, 5.25;

PCS-pincer Pd complex 4 To a solution of **3** (0.2400 g, 0.39 mmol) in acetone (20 mL), $AgBF_4$ (0.082 g, 0.42 mmol) was added and the reaction mixture was stirred at room temperature for 1 h. The resulting suspension was filtered over Celite and the residue was subsequently washed with CH_2Cl_2 (15 mL) and demineralized water (10 mL). A saturated aqeuous NaCl solution was added and the biphasic mixture was stirred at room temperature for 1 h. Afterwards, the two layers were separated and the aqueous layer was further washed with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and evaporated to dryness. The residue was redissolved in a minimal amount of CH_2Cl_2, from which the product precipitated upon addition of hexanes. After centrifugation, **4** was isolated as a slightly yellow powder. Yield: 95% (0.2120 g, 0.37 mmol) ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.03 (q, ^3J=8.0 Hz, 4H, PPh*H*), 7.79-7.82 (m, 2H, SPh*H*), 7.45-7.52 (m, 6H, PPh*H*), 7.34-7.36 (m, 3H, CH_2SPh*H*), 6.82 (d, ^3J=8.0 Hz, 1H, Ar*H*), 6.69 (d, ^3J=8.0 Hz, 1H, Ar*H*), 4.59 (s, 2H, ArCH_2SPh), 3.86 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 171.4, 158.6, 151.8 (d, *J*=14 Hz), 147.9, 142.5 (d, *J*=2 Hz), 141.7, 133.3, 132.8, 132.5 (d, *J*=3 Hz), 131.5(d, *J*=14 Hz), 129.8, 129.5 (d, *J*=14 Hz), 118,9, 110.8, 56.5, 50.0; ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 150.8 (s). MS (MALDI-TOF): m/z calcd for $C_{26}H_{21}NO_2PPd$: 535.91 $[M\text{-}Cl]^+$; found: 535.90; Anal. Calcd. for C, 54.65; H, 3.88; P, 5.42; Pd, 18.63; S, 5.61; Found : C, 54.70; H, 3.91; P, 5.34; Pd, 18.27; S, 5.52;

General procedure of synthesizing cationic pincer palladium complexes 1a-3a.

PCN- or PCS-pincer palladium complexes **1-3** (0.1 mmol) and $AgBF_4$ (0.020g, 0.1 mmol) were suspended in dichloromethane (5 mL). A few drops of demineralized water were added to the reaction mixture and the resultant mixture was stirred at room temperature for 1 h. To the mixture was added $MgSO_4$ (0.5 g) and the white suspension was further stirred for some time. Afterwards, the suspension was filtered over a short pad of Celite and the filter cake was washed with freshly distilled dichloromethane (3 x 5 mL). The combined solutions were concentrated in vacuo and the product was precipitated from the solution by the addition of hexanes or ether. A white solid was then collected by centrifuge and was completely dried under vacuum.

Spectral data for complex 1a: Yield : 87% (0.050 g, 0.087 mmol), white solid. ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.96-8.02 (m, 4H, PPh*H*), 7.47-7.50 (m, 6H, PPh*H*), 6.71 (d, ^{3}J=8.0 Hz, 1H, Ar*H*), 6.65 (d, ^{3}J=8.0 Hz, 1H, Ar*H*), 4.06 (s, 2H, CH_2NMe$_2$), 3.84 (s, 3H, OCH_3), 2.89 (s, 6H, NMe_2); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 171.9, 155.8, 150.5 (d, *J*=10 Hz), 146.8, 144.5 (d, *J*=18.8 Hz), 140.3, 133.5 (d, *J*=50 Hz), 131.7-132.1 (m), 128.9 (d, *J*=18.8 Hz), 118.6, 110.9, 56.7, 50.5; ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 152.3 (br s). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -153.1 (s). MS (MALDI-TOF): m/z calcd for $C_{22}H_{25}NO_3PPd$: 488.83 $[M\text{-}BF_4]^+$; found: 488.86; calcd for $C_{22}H_{23}NO_2PPd$: 470.82 $[M\text{-}BF_4\text{-}H_2O]^+$; Found: 470.80; Anal. Calcd. for C, 45.90; H, 4.38; N, 2.43; P, 5.38; Pd, 18.49; Found: C, 45.85; H, 4.44; N, 2.40; P, 5.35; Pd, 18.51;

Spectral data for complex 2a: Yield : 80% (0.049 g, 0.08 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.23 (d, $^{4}J_{P,H}$=5 Hz, 1H, C*H*=NPh), 8.10 (q, ^{3}J=6.8 Hz, 4H, PPh*H*), 7.46-7.54 (m, 6H, PPh*H*), 7.38 (t, ^{3}J=7 Hz, 2H, NPh*H*), 7.26-7.33 (m, 3H, NPh*H*), 7.23 (d, ^{3}J=8.0 Hz, 1H, Ar*H*), 6.71 (d, ^{3}J=8.0 Hz, 1H, Ar*H*), 3.93 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 172.8, 156.5, 150.1 (d, *J*=10 Hz), 148.6, 148.4 (d, *J*=21 Hz), 138.5, 132.3-132.7 (m), 129.1 (m), 128.7, 127.9, 125.6, 123.8, 109.5, 56.3; ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 156.2 (br s). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -153.3 (s). MS (MALDI-TOF): m/z calcd for $C_{26}H_{23}NO_3PPd$: 534.86 $[M\text{-}BF_4]^+$; found: 534.80; calcd for $C_{26}H_{21}NO_2PPd$: 516.84 $[M\text{-}BF_4\text{-}H_2O]^+$; found: 516.88; Anal. Calcd. for C, 50.23; H, 3.73; N, 2.25; P, 4.98; Pd, 17.12; Found : C, 50.30; H, 3.78; N, 2.20; P, 4.91; Pd, 17.14;

Spectral data for complex 3a: Yield : 90% (0.058 g, 0.09 mmol) ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.02 (q, ^{3}J=8.0 Hz, 4H, PPh*H*), 7.80-7.83 (m, 2H, SPh*H*), 7.46-7.53 (m, 6H, PPh*H*), 7.32-7.35 (m, 3H, CH_2SPh*H*), 6.88 (d, ^{3}J=8.4 Hz, 1H, Ar*H*), 6.72 (d, ^{3}J=8.4 Hz, 1H, Ar*H*), 4.63 (s, 2H, ArCH_2SPh), 3.87 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 174.2, 152.1 (d, *J*=14 Hz), 148.0, 142.5 (d, *J*=2 Hz), 142.1, 133.3, 133.0, 132.7 (d, *J*=3 Hz), 132.5 (d, *J*=14 Hz), 130.3, 129.9 (d, *J*=14 Hz), 118,7, 111.5, 57.1, 50.6; ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 151.7 (br s). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -153.2 (s). MS (MALDI-TOF): m/z calcd for $C_{26}H_{24}O_3PPdS$: 553.93 $[M\text{-}BF_4]^+$; found: 553.85; calcd for $C_{26}H_{22}O_2PPdS$: 535.91 $[M\text{-}BF_4\text{-}H_2O]^+$; found: 535.85; Anal. Calcd. for C, 48.74; H, 3.78; P, 4.83; Pd, 16.61; Found : C, 48.65; H, 3.80; P, 4.81; Pd, 16.58;

General procedure for catalytic homoallylation reactions. In a flame dried Schlenk flask, aryl aldehyde (0.1 mmol), allylstannane (37 μL, 0.12 mmol), pincer complex (0.005 mmol), dry DMF (1 mL) and a stirring bar were loaded and the resulting mixture was vigorously stirred at 60 °C for 16 h. The reaction was quenched by the addition saturated aqueous KF solution (1 mL) and the reaction mixture was stirred at room temperature for another 12 h. Afterwards, the reaction mixture was extracted with EtOAc (3 x 2 mL) and the combined organic layers were dried over $MgSO_4$. The dry solution was concentrated on a rotary evaporator and was subjected to flash chromatography with EtOAc/hexanes (3:7 (v/v)) as eluent. Chemical conversions were estimated by ^{1}H NMR with mesitylene as internal standard. The ^{1}H and ^{13}C NMR spectral data of the resulting allylic alcohols agreed with those of reported compounds.[7c]

General procedure for catalytic tandem reactions. In a flame dried Schlenk flask, aryl aldhyde or sulfonimine (0.1 mmol), hexamethyldistannane (25 μL, 0.12 mmol), pincer complex (0.005 mmol), solvent (1 mL), and a stirring bar were loaded and the resulting mixture was vigorously stirred at the indicated temperature for 16-18 h. The reaction was quenched by addition saturated aqueous KF solution (1 mL) and the reaction mixture was stirred at room temperature for another 12 h. Afterwards, the reaction mixture was extracted with EtOAc (3 x 2 mL) and the combined organic layers were dried over $MgSO_4$. The dry solution was concentrated on a rotary evaporator and was subjected to flash chromatography with EtOAc/hexanes (3:7 (v/v)) as eluent. Chemical conversions were estimated by ^{1}H NMR or GC with mesitylene as internal standard. The ^{1}H and ^{13}C NMR spectral data of the resulting allylic alcohols agreed with those of reported compounds.[6, 8c]

X-ray diffraction analysis. All reflection intensities were measured using a Nonius KappaCCD diffractometer equipped either with a rotating anode (**1** and **2**) or a sealed tube (**4**) with graphite-monochromated Mo *K*α radiation (λ = 0.71073 Å) under the program *COLLECT*.[19] The programs *PEAKREF*[20] or *HKL2000*[21] were used to refine the cell dimensions. Data reduction was done using the programs *EVALCCD*[22] or *HKL2000*. The structures were solved either with the programs *DIRDIF08*[23] or *SHELXS-97*[24] and were refined on F^2 [20] with *SHELXL-97*[24]. Multi-scan semi-empirical absorption corrections based on symmetry-related measurements were applied to all sets of data with the program *SADABS*.[25] The temperature of data collection was controlled using the system *OXFORD CRYOSTREAM 600* (manufactured by *OXFORD CRYOSYSTEMS*). The H-atoms (except for the H atom attached to C20 in **2**) were placed at calculated positions (*AFIX 23* or *AFIX 43* or *AFIX 137*) with isotropic displacement parameters having values 1.2 or 1.5 times *U*eq of the attached C atom. The coordinates and the isotropic displacement parameter of the H atom attached to C20 (**2**) were refined freely.

For **1**, data were collected at 150 K after the crystal had been flash cooled from room temperature. One phenyl ring of complex **1** is disordered. Restraints were applied so that the minor and major components of the disordered phenyl group have similar geometries (*FLAT*, *SADI* and *SAME* instructions). The *SIMU* instruction (*i.e.*, a restraint for which neighboring atoms have similar U_{ij}) had to be applied to all disordered atoms in order to get a satisfactory refinement.

For **2**, data were collected at 150 K after the crystal had been flash cooled from room temperature. The structure of complex **2** is ordered.

For **4**, crystals shattered if the temperature was set at 200 K or below. This behavior may result from the existence of a destructive phase transition. Subsequently, no data could be collected at 150 K. Near 230 K, a few frames were collected but the diffraction pattern looked rather complicated (*i.e.*, extra spots were not integrated correctly during the process of cell determination). Data were then collected near 295 K, at which the diffraction corresponds to that of a single crystal. It seems to be likely that a solid-solid phase transition occurs somewhere between room temperature and 230 K, but its study is beyond the scope of this paper. The structure of **4** is disordered: the phenyl groups attached to the P and S atoms are disordered. The anisotropic displacement parameters for the disordered C_{phenyl} atoms attached directly to P and S atoms (*e.g.*, C8 and C8') were constrained to be the same using the *EADP* instruction. The *ISOR* and *SIMU* instructions were applied to all disordered atoms in order to get a satisfactory refinement. Restraints were applied so that the minor and major components of the disordered rings have similar geometries using the *SADI* and *SAME* instructions.

Table 5. Crystallographic data for **1**, **2** and **4**.

	1	**2**	**4**
Formula	$C_{22}H_{23}ClNO_2PPd$	$C_{26}H_{21}BrNO_2PPd$	$C_{26}H_{22}ClO_2PPdS$
Fw	506.23	596.72	571.32
cryst syst	Monoclinic	Monoclinic	Triclinic
space group	$P2_1/c$	$P2_1/c$	$P\bar{1}$
T /K	150 (2)	150 (2)	295 (2)
a, b, c /Å	11.9919 (4) 9.9825 (7) 18.1045 (6)	10.0370 (1) 13.6684 (1) 17.5004 (2)	9.4992 (6) 10.2754 (8) 13.7361 (7)
α, β, γ /°	90.00 101.180 (3) 90.00	90.00 102.9902 (4) 90.00	93.012 (3) 104.715 (3) 108.664 (3)
V /Å^3	2126.15 (18)	2339.43 (4)	1215.41 (14)
Z	4	4	2
D_x /Mg m^{-3}	1.581	1.694	1.561
μ /mm^{-1}	1.09	2.59	1.05
crystal form, colour	Irregular block, colorless	Needle, yellow	Thick plate, pale yellow
crystal size /mm	0.43 × 0.27 × 0.22	0.60 × 0.24 × 0.12	0.36 × 0.22 × 0.10
T_{min}, T_{max}	0.62, 0.79	0.29, 0.73	0.68, 0.90
meas refls	29758	64860	30752
indep refls	4885	5349	5575
$I > 2\sigma(I)$ refls	3973	4869	4735
R_{int}	0.036	0.037	0.025
θ_{max} /°	27.5	27.5	27.5
$R[F^2 > 2\sigma(F^2)]$	0.026	0.019	0.034
$wR(F^2)$	0.058	0.046	0.085
S	1.10	1.06	1.08
refined params	311	294	437
$(\Delta/\sigma)_{max}$	<0.0001	0.001	0.001
$\Delta\rho$ /e Å^{-3}	0.79, –0.63	0.43, –0.37	0.64, –0.37

6.6 References

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Chapter 7

PCN-Pincer Palladium and Platinum Complexes [MBr{C_6H_2-(OPR'$_2$)-2-(OMe)-3-(CH=NR)-6}] and Investigation of their Relative Lewis Acidity

Abstract

A series of PCN-pincer palladium and platinum complexes [MBr{C_6H_2-(OPR'$_2$)-2-(OMe)-3-(CH=NR)-6)], **4a**-**4f**, have been synthesized in moderate to good yields (55 − 88%) starting from 2-bromo-3-hydroxy-4-methoxybenzaldehyde **1** as the common building block. The structures in solution (NMR) and in the solid state (X-ray crystal structure determination) of **4a**-**4f** have been studied. Their corresponding cationic acetonitrile complexes **5a**-**5f** and **6a**-**6f** were prepared in good to excellent yields (88-98%). The relative Lewis acidities of these cationic PCN-pincer metal complexes were investigated by means of NMR techniques, IR spectroscopy, and reaction profiles of the catalyzed aza-Michael addition reaction of morpholine with acrylonitrile. These studies showed that the normal probe, *i.e.* nitrile ligands, employed for studying the effect of a *trans*-ligand on Lewis acidity does not work with PCN-pincer metal complexes in which the *cis*-ligands are changed. Furthermore, it was observed that the relative rate of the PCN-pincer Pd- or Pt-complex catalyzed aza-Michael reaction is inversely related to their Lewis acidity as concluded from the NMR investigations, which pointed at the C–N bond formation not being rate-determining step in the catalyzed aza-Miachael addition.

7.1 Introduction

The synthesis and application of ECE-pincer metal complexes have attracted much attention in the past decades.[1] A variety of structures containing the mono-anionic ECE-pincer motif with various donor atom containing groups, *e.g.* E = NR_2, SR, PR_2, SeR, OPR_2, $OP(OR)_2$, *etc*. have been developed.[1c,1d] Notably, many ECE-pincer metal complexes show remarkable catalytic performances in various catalytic reactions, which has initiated the use of these complexes as catalysts in organic synthesis.[1-4] Recently, the development of ECE'-type (E ≠ E') pincer complexes has become a new aspect of pincer chemistry.[5-8] A few examples of PCN- and PCS-pincer palladium, platinum, and rhodium complexes and their application in C–C cross coupling reactions,[5] aldol condensations, and tandem catalysis[6] have already been reported by different groups. It has been shown that the new catalytic activities found for these ECE'-type pincer metal complexes originates from cooperative effects and interplay of the two different *ortho*-chelating E- and E'-donor moieties.[5-6]

Recently, we reported the preparation of a series of PCN- and PCS-pincer Pd complexes starting from isovanillin as the common intermediate, see Figure 1.[9] The use of isovanillin as key building block has also been described by Nishiyama *et al.* and allows for regioselective introduction of different nitrogen and phosphorus donor groups by taking advantage of two independent functional groups, *i.e.* aryl aldehyde and aryl hydroxyl groups.

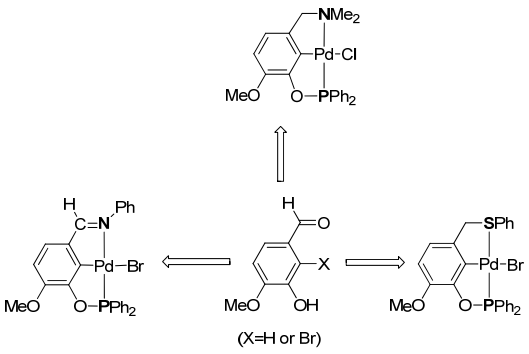


Figure 1. Development of PCN- and PCS-pincer Pd complexes starting from isovanillin.

In this chapter, we report on the further use of this protocol, giving ready access to another series of PCN-pincer palladium and platinum complexes. As depicted in Figure 2, 2-bromo-3-hydroxy-4-methoxybenzaldehyde **1** has three functional groups, which are potentially available for organic transformations. Firstly, various imine nitrogen donors can be introduced by reacting

1 with different primary amines. Secondly, various phosphorus donors can be introduced by reacting the hydroxyl group of **1** with phosphite or phosphine chlorides *via* electrophilic substitution in the presence of an appropriate base (Et_3N or DMAP). Eventually, metalation can be efficiently carried out by an oxidative insertion of a suitable zerovalent palladium or platinum species (*i.e.*, $[Pd_2(dba)_3 \cdot CHCl_3]$ or $[Pt_2(dba)_3]$) into the aryl-Br bond.

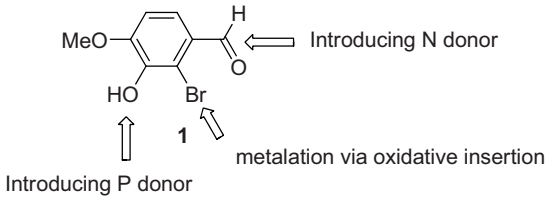


Figure 2. Strategy to access PCN-pincer palladium and platinum complexes.

The development of new and efficient Lewis acids catalysts for carbon-carbon bond forming reactions has received extensive and growing attention in the fields of organic chemistry and homogeneous catalysis.[10] Pincer metal complexes have been reported as active Lewis acid catalysts to accelerate several organic transformations under very mild conditions.[11 – 17] With the design of new catalysts in mind, some efforts have been made to understand the relative Lewis acidity of NCN-pincer Ni-, Pd-, and Pt-complexes by means of NMR spectroscopy and theoretical calculations.[2a, 14, 15, 17] For example, we have earlier prepared a series of *para*-functionalized NCN-pincer Pt-complexes and theoretical calculations showed that both the ^{195}Pt chemical shift and the calculated natural population charge on the platinum metal center correlate linearly with the σ_p Hammett substituent constants.[2a] On the other hand, Fossey and Richards reported a convenient and practical spectroscopic method (*i.e.*, using ^1H NMR spectroscopy) to study the relative Lewis acidity of pincer metal complexes (Figure 3).[15] After converting neutral pincer complexes into their corresponding cationic complexes bearing MeCN as co-ligand, the characteristic protons of this co-ligand are suitable spectroscopic probes. The downfield chemical shifts of the coordinated MeCN moieties are proportional to the relative Lewis acidity of the corresponding pincer complexes. In these studies, it was found that the pincer metal complexes comprising strong electron-withdrawing *para*-functional groups display larger downfield chemical shifts, which indicates that these complexes are stronger Lewis acids than their non-substituted analogues. Connell *et al.* recently employed this method to study the relative Lewis acidity of a series of *para*-functionalized NCN-pincer nickel complexes[17] and their conclusion was consistent with the results reported by Fossey and Richards. These findings nicely illustrate that *para*-functional groups can directly and strongly influence the electronic density on pincer metal centers.

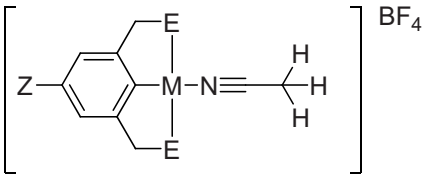


Figure 3. Cationic ECE-pincer metal acetonitrile compounds used for studying the relative Lewis acidity of ECE-pincer metal complexes by means of ^{1}H NMR.

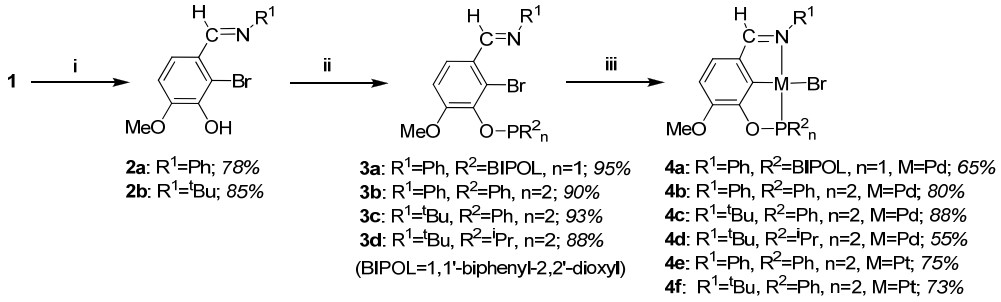
Previous work has mainly focused on *para*-functionalized NCN-pincer complexes in which the functional groups do not bind to the metal center and on the differences amongst symmetrical ECE-pincer metal complexes. The influence of two different E-donor moieties that coordinate in mutual *trans*-positions to the metal center on its relative Lewis acidity has not yet been studied. Whereas the *para*-functionalized aryl moiety is located *trans* with respect to the nitrile "reporter" ligand, the two E-donor moieties are both situated in *cis*–positions with respect to the nitrile ligand and could, therefore, lead to rather different electronic effects on the nitrile "reporter" ligand. By taking advantage of the structurally and electronically tunable PCN-pincer complexes reported in this chapter, we have now studied the relative Lewis acidity of these PCN-pincer Pd- and Pt-complexes by following the NMR protocol proposed by Fossey and Richards. The results of this study were correlated with the relative rates of Lewis acid-catalyzed aza-Michael reactions in which the PCN-pincer metal complexes act as the catalysts. This chapter describes both the synthesis and characterization of a series of unsymmetrical PCN-pincer Pd- and Pt-complexes, next to the investigation of their relative Lewis acidic properties.

7.2 Results

7.2.1 Synthesis of PCN-Pincer Palladium and Platinum Complexes

As described in Scheme 1, the series of PCN-pincer Pd- and Pt-complexes **4a**-**4f** can be efficiently synthesized *via* a modular synthetic approach that starts with 2-bromo-isovanillin (**1**) as the common precursor. Imine adducts **2a,b** were prepared in good yields by reacting primary amines such as $PhNH_2$ and *t*-$BuNH_2$ with **1** in chloroform at refluxing temperature for 16 h. Afterwards, the resulting compounds **2a,b** were reacted with phosphite or phosphine chlorides such as (1,1'-biphenyl-2,2'-diyl)chlorophosphite, diphenylphosphine chloride, and diisopropylphosphine chloride in the presence of triethylamine or *N,N*-dimethyl-4-aminopyridine (DMAP) to afford a series of PCN-pincer ligands **3a**-**3d** in good yields. Notably, the use of DMAP was crucial for achieving full conversion when di(iso-propyl)phosphine chloride was employed as the reactant. After removal of either [Et_3N·HCl] or [DMAP·HCl] salts by simple

filtration, the solution of ligands **3a-3d** in toluene was added without further purification to a solution of the zerovalent Pd- or Pt-precursors $[Pd_2(dba)_3 \cdot CHCl_3]$ or $[Pt_2(dba)_3]$, respectively, in toluene. Warming the resulting reaction mixture to 80 °C for 5-16 h yielded the PCN-pincer Pd- and Pt-complexes **4a-4f** in promising to good isolated yields after column chromatography or recrystallization.[18]



Scheme 1. Synthesis of PCN-pincer Pd- and Pt-complexes. Reagents and conditions: i) $PhNH_2$ or $^tBuNH_2$, $CHCl_3$, $MgSO_4$, reflux, 16 h; ii) 1,1'-biphenyl-2,2'-diyl phosphite chloride, Ph_2PCl or $^iPr_2PCl$, and Et_3N or *N,N*-dimethyl-4-aminopyridine, 0 °C to RT, 16 h; iii) $[Pd_2(dba)_3 \cdot CHCl_3]$ or $[Pt_2(dba)_3]$, toluene, 80 °C, 5-16 h.

7.2.2 Structural studies of complexes 4a-4f

Besides full characterization of complexes **4a-4f** by NMR techniques, mass spectrometry, and elemental analysis, their solid state structures were established by X-ray crystal structure determination. Suitable single crystals were obtained by slow distillation of hexanes or diethyl ether into a dichloromethane solution of the complex at room temperature. The compounds crystallize either as a racemic twinned crystal in a non-centrosymmetric space group (**4e**) or in centrosymmetric space groups (**4a-4d, 4f**), thus, they are either achiral or racemic. As shown in Figures 4 and 5, these PCN-pincer Pd- and Pt-complexes generally adopt the typical meridonal pincer coordination mode. Complexes **4a-4f** possess almost perfect square-planar structures, most probably due to the double bonds of the imines being conjugated with the aromatic backbones. The metal atoms are located at the central positions of these square-planar structures, for which the halogen atoms occupy the *trans*-positions with respect to the *ipso*-carbon atoms of the aromatic backbones. The nitrogen and phosphorus donors are mutually located in *trans*-positions with very similar P-Pd-N bond angles. Full structural details on complex **4b** were previously reported and are not shown in detail here.[9]

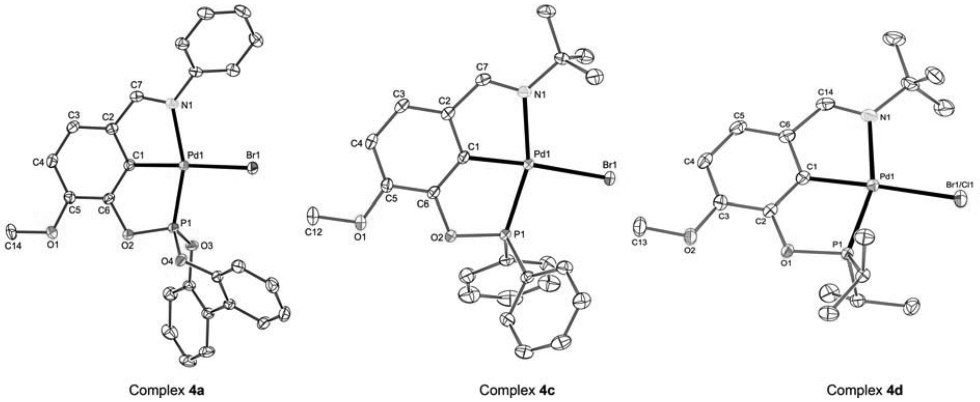


Figure 4. Displacement ellipsoid plots (50 % probability level) of complex **4a**, **4c** and **4d**. H atoms are omitted for the sake of clarity. Only the major disorder component with the bromine ligand is shown (for **4a**: 98% occupancy; for **4c**: 95% occupancy; for **4d**: 92% occupancy).

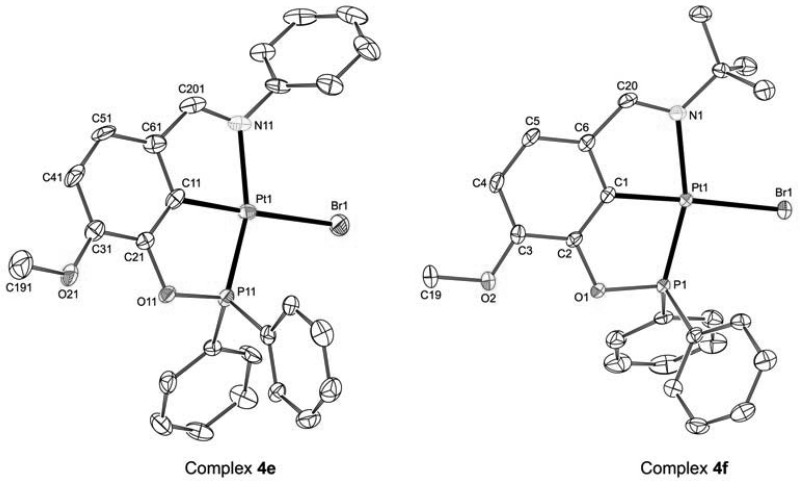
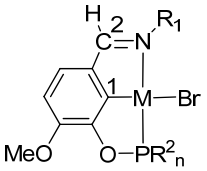


Figure 5. Displacement ellipsoid plots (50 % probability level) of complex **4e** and **4f**. H atoms are omitted for the sake of clarity. For **4e**, only the major disorder component with the bromine ligand (95% occupancy) of one of two independent molecules is shown.

In order to compare the solid state structures of PCN-pincer complexes **4a**-**4f**, selected bond lengths are summarized in Table 1 and the substructure of these pincer complexes was redefined for the sake of convenience. The bond lengths of the *t*-Bu-functionalized imine double bonds (C2=N) in complexes **4c**, **4d**, and **4f** are shorter than those of phenyl-functionalized complexes **4a**, **4b**, and **4e**, respectively. This strengthening of the C=N double bond is due to the presence of the stronger electron-donating *t*-Bu- group. In contrast, the bond lengths of the P–O bonds in complexes **4a**-**4d** are lengthened upon the introduction of an electron-donating substituent on the P-donor. For instance, the phosphite P–O bond in complex **4a** (*i.e.*, 1.6174(12) Å) is significantly shorter than those in phosphinite complexes **4b**-**4d**. Similarly, the diphenylphosphinite P–O bonds of complexes **4b** and **4c** (i.e., 1.6513(12) Å and 1.6462(9) Å) are shorter than the di(iso-propyl)phosphinite P–O bond in complex **4d** (*i.e.*, 1.6625(11) Å). Furthermore, the M–P bond lengths in complexes **4a**-**4d** are gradually shortened upon reinforcing the electron-withdrawing ability on the P-donor. For example, the M–P bond in complex **4a** (*i.e.*, 2.1734(3) Å), which comprises an electron-poor phosphite donor, is shorter than those in complexes **4b** and **4c**, and is particularly shorter than that in di(iso-propyl)phosphinite complex **4d** (*i.e.*, 2.2139(4) Å). Similarly, the M–N bond lengths in phenyl-imine functionalized complexes **4a**, **4b**, and **4e** are shorter than those of *t*-Bu-imine functionalized complexes **4c**, **4d**, and **4f**, respectively. The M–N bond of complex **4d** (*i.e.*, 2.2130(13) Å) is particularly longer than those of other PCN-pincer Pd-complexes. This could be due to the *trans*-influence of the strong σ-donating P donor, which lengthens the M–N bond. In terms of the P–M–N angles, regardless of the electron properties and geometries of the substituents on P- and N-donors, complexes **4a-4f** possess very similar angles because of the rigid structural configurations of the pincer motif. Unfortunately, since the Br counter anions in the single crystals were contaminated by small amounts of chloride[19] a comparison of M–X (X = Cl or Br) bonds and the corresponding C1–M bond lengths appeared to be impossible.

Table 1. Selected bond lengths (Å) for complexes **4a**-**4f**.

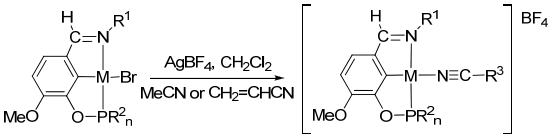


	4a	**4b**[a]	**4c**	**4d**	**4e**[b]	**4f**
C1-M	1.9549(16)	1.9658(16)	1.9527(12)	1.9612(16)	1.952(4)	1.950(2)
M-N	2.1743(13)	2.1777(14)	2.1889(10)	2.2130(13)	2.143(3)	2.1749(19)
M-P	2.1734(4)	2.2020(5)	2.1987(4)	2.2139(4)	2.1767(8)	2.1786(6)
M-Br	2.4786(3)[c]	2.5037(2)	2.5108(2)[c]	2.5215(2)[c]	2.4905(6)[c]	2.5120(3)
C2-N	1.293(2)	1.297(2)	1.2855(16)	1.284(2)	1.296(6)	1.285(3)
P-O	1.6174(12)	1.6513(12)	1.6462(9)	1.6625(11)	1.651(2)	1.6451(17)

[a] Data taken from ref. 9. [b] The bond lengths are averaged from two independent molecules. The standard uncertainties are calculated according to the propagation of error. [c] The position of the bromine was partially occupied by chlorine. Restraints and/or constraints were used to refine this disorder.

7.2.3 Synthesis and characterization of cationic PCN-pincer Pd- and Pt-complexes

As described in Scheme 2, a series of cationic PCN-pincer Pd- and Pt-complexes **5a**-**5f** and **6a**-**6f** were prepared by reacting the corresponding neutral pincer complexes **4a**-**4f** with $AgBF_4$ in the presence of acetonitrile or acrylonitrile in dry dichloromethane. The resulting, off-white or pale yellow cationic nitrile complexes were fully characterized by NMR techniques and MALDI-TOF mass spectrometry.



4a: R^1=Ph, R^2=BIPOL, n=1, M=Pd;
4b: R^1=Ph, R^2=Ph, n=2, M=Pd;
4c: R^1=^{t}Bu, R^2=Ph, n=2, M=Pd;
4d: R^1=^{t}Bu, R^2=^{i}Pr, n=2, M=Pd;
4e: R^1=Ph, R^2=Ph, n=2, M=Pt;
4f: R^1=^{t}Bu, R^2=Ph, n=2, M=Pt;

5a: R^1=Ph, R^2=BIPOL, R^3=Me, n=1, M=Pd; *98%*
5b: R^1=Ph, R^2=Ph, R^3=Me, n=2, M=Pd; *93%*
5c: R^1=^{t}Bu, R^2=Ph, R^3=Me, n=2, M=Pd; *95%*
5d: R^1=^{t}Bu, R^2=^{i}Pr, R^3=Me, n=2, M=Pd; *90%*
5e: R^1=Ph, R^2=Ph, R^3=Me, n=2, M=Pt; *93%*
5f: R^1=^{t}Bu, R^2=Ph, R^3=Me, n=2, M=Pt; *88%*

6a: R^1=Ph, R^2=BIPOL, R^3=vinyl, n=1, M=Pd; *95%*
6b: R^1=Ph, R^2=Ph, R^3=vinyl, n=2, M=Pd; *91%*
6c: R^1=^{t}Bu, R^2=Ph, R^3=vinyl, n=2, M=Pd; *99%*
6d: R^1=^{t}Bu, R^2=^{i}Pr, R^3=vinyl, n=2, M=Pd; *88%*
6e: R^1=Ph, R^2=Ph, R^3=vinyl, n=2, M=Pt; *95%*
6f: R^1=^{t}Bu, R^2=Ph, R^3=vinyl, n=2, M=Pt; *90%*

Scheme 2. Synthesis of cationic PCN-pincer Pd- and Pt-complexes.

In addition, we succeeded in growing single crystals of complexes **5b** and **5e**, which have isomorphous crystal structures. As depicted in Figures 6, both complexes possess the typical pincer structural motif and comprise a tightly coordinated MeCN unit located at the *trans*-positions with respect to the C_{ipso}–M bonds. The characteristic bond lengths and angles had not significantly changed after introduction of the MeCN units in comparison with their parent, neutral complexes **4e** and **4f**. Remarkably, for these two complexes, all the bond lengths of the coordinated MeCN units are not significantly different from those in free MeCN. Therefore, the relative Lewis acidity of these pincer complexes could not be established by comparing these crystallographic data.

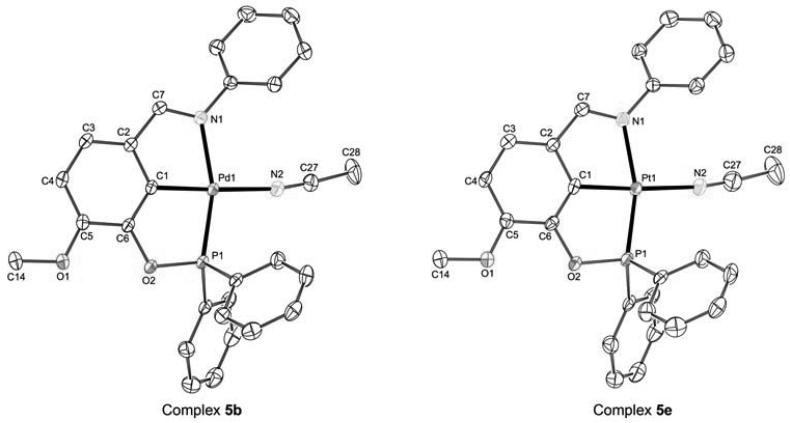


Figure 6. Displacement ellipsoid plots (50 % probability level) of the cationic complex **5b** and **5e**. H atoms and BF_4 anion are omitted for the sake of clarity. Selected bond lengths [Å] and angles [°]: for **5b**: Pd1-C1 1.9511(12), Pd1-P1 2.2213(3), Pd1-N1 2.1640(11), Pd1-N2 2.0876(12), N1-C7 1.2981(17), O2-P1 1.6550(10), C27-N2 1.1336(19), P1-Pd1-N1, 158.10(3), C1-Pd1-N2 175.34(5); for **5e**: Pt1-C1 1.950(3), Pt1-P1 2.2000(8), Pt1-N1 2.127(3), Pt1-N2 2.066(3), N1-C7 1.298(4), O2-P1 1.654(2), C27-N2 1.129(5), P1-Pt1-N1, 159.26(7), C1-Pt1-N2 174.46(12).

7.2.4 NMR investigation of the relative Lewis acidity of cationic pincer complexes

The relative Lewis acidities of cationic complexes **5a**-**5f** and **6a**-**6f** were indirectly determined by recording the chemical shifts of characteristic H- and C-nuclei of the coordinated nitrile moieties. According to previous reports,[15, 17, 20] the downfield chemical shifts of these NMR signals, relative to those of the free nitrile are proportional to the Lewis acidity of the corresponding pincer complexes. Table 2 and Table 3 separately list the characteristic chemical shifts of complexes **5a**-**5f** and **6a**-**6f** recorded at 25 °C in $CDCl_3$ on a 400 MHz NMR spectrometer.

Table 2. ^{1}H and ^{13}C NMR chemical shifts of the methyl groups of the coordinated MeCN units in complexes **5a**-**5f**. [a, b]

Entry	Complexes	δ CH_3 [c]	Δδ CH_3	δ CH_3 [c]	Δδ CH_3
1	**5a**	2.00	+ 0.02	2.5	+ 0.4
2	**5b**	2.23	+ 0.25	3.0	+ 0.9
3	**5c**	2.43	+ 0.45	3.1	+ 1.0
4	**5d**	2.48[d]	+ 0.50	2.9[d]	+ 0.8
5	**5e**	2.31	+ 0.33	3.5	+ 1.4
6	**5f**	2.58	+ 0.60	3.6	+ 1.5

[a] NMR measurements were preformed at 25 °C in deacidified and predried $CDCl_3$. Samples concentrations were approximately 0.01M. Values are reported in ppm (δ) relative to $(CH_3)_4Si$. [b] The ^{1}H and ^{13}C NMR chemical shifts of the methyl group of free MeCN at 25 °C in $CDCl_3$ are 1.98 ppm and 2.1 ppm, respectively. [c] Broad signal. [d] Very broad signal.

As shown in Table 2, the general trend of the chemical shifts of the acetonitrile methyl groups of complexes **5a**-**5f** is to gradually move downfield for more electron-enriched PCN-pincer ligands. For instance, complex **5a** comprises the most electron-poor pincer ligand **3a** and gave a ^{1}H NMR signal at δ = 2.00 ppm, which is just 0.02 ppm downfield shifted compared to free MeCN (Table 2, entry 1). The complexes **5b**, **5c**, and **5d** comprise the more electron-enriched pincer ligands **3b**, **3c**, and **3d**, respectively, and displayed ^{1}H NMR signals that are significantly downfield shifted compared to free MeCN (Table 2, entries 2-4). These data would imply an increasing order in the relative Lewis acidity of cationic PCN-pincer complexes **5a**-**5d** as **5a**<**5b**<**5c**<**5d**., *i.e.*, the more σ-donating one of the donor sites of the ECE'-pincer ligands becomes, while keeping the other E-donor and C_{ipso} the same, the stronger Lewis acid a resulting ECE'-pincer metal complex is. The general trend of the ^{13}C NMR chemical shifts differences in this series of compounds agrees with that found by ^{1}H NMR, although the ^{13}C NMR downfield chemical shift of the acetonitrile methyl C-nucleus in complex **5d** is smaller than that in complexes **5b** and **5c** (Table 2, entry 4 *vs.* entries 2 and 3). This could be due to the steric interference of the *t*-Bu and *i*-Pr groups with the nitrile ligand, leading to the fast exchange of coordinated and non-coordinated MeCN. It is worth pointing out that the differences between these chemical shifts are much larger than the accuracy of the NMR experiments and also of the previously reported data.[17]

Besides the PCN-pincer Pd complexes, the cationic PCN-pincer Pt-complexes **5e** and **5f** followed the same trend as their Pd-analogues. For example, complexes **5e** and **5f** gave signals at δ=2.31 ppm and δ=2.58 ppm, respectively, for the protons of the coordinated MeCN units, which are 0.33 and 0.60 ppm downfield shifted compared to free MeCN (Table 2, entry 5 *vs*. entry 6). ^{13}C NMR data agreed with these results. According to these chemical shifts, the Pt complexes are supposed to be stronger Lewis acids than their Pd analogues, which is in accordance with the observations reported by Fossey and Richards.[15]

Table 3. ^{1}H and ^{13}C NMR chemical shifts of the vinyl groups of the coordinated acrylonitrile units in complexes **6a**-**6f**. [a, b]

Entry	Complexes	δ C*H* and CH_2	Δδ C*H* and CH_2	δ *C*H_2	Δδ *C*H_2
1	**6a**	6.10 (d, *J*=18 Hz) 6.22 (d, *J*=11.6 Hz)	+ 0.08 + 0.07	137.6	+ 0.1
2	**6b**	6.15 (d, *J*=17.6 Hz) 6.35 (d, *J*=10.8 Hz)	+ 0.13 + 0.20	137.9	+ 0.4
3	**6c**	6.35 (d, *J*=18 Hz) 6.51 (d, *J*=11.6 Hz)	+ 0.33 + 0.36	138.6	+ 1.1
4	**6d**	6.46 (m)[c]	—	138.4[c]	+ 0.9
5	**6e**	6.24 (d, *J*=18 Hz) 6.41 (d, *J*=11.6 Hz)	+ 0.22 + 0.26	138.3	+ 0.8
6	**6f**	6.47 (d, *J*=17.6 Hz) 6.60 (d, *J*=12 Hz)	+ 0.45 + 0.45	139.5	+ 2.0

[a]: The NMR measurements were preformed at 25 °C in deacidified and predried $CDCl_3$. Sample concentrations were approximately 0.01M. Values are reported in ppm (δ) relative to $(CH_3)_4Si$. [b]: The ^{1}H and ^{13}C NMR chemical shifts of the terminal proton and carbon in the vinyl group of free CH_2=CHCN are 6.02 ppm (d, *J*=12 Hz), 6.15 ppm (d, *J*=16 Hz) and 137.5 ppm, respectively. [c]: Broad signal.

As shown in Table 3, the ^{1}H NMR and ^{13}C NMR signals of the terminal protons and carbons of the vinyl groups (*i.e*., *C*H_2=CHCN) of the cationic acrylonitrile complexes **6a**-**6f** gradually gave larger downfield chemical shifts for the complexes derived from more electron-enriched PCN-pincer ligands. The cationic complexes **6a**-**6f** followed the same trend as their analogous Pd-complexes **5a**-**5f**. Like for the acetonitrile complexes, the acrylonitrile Pd-complex **6d** does not fit in this trend.

To provide further insight in the correlation between the electron-donating ability of pincer ligands and the effective electron density on the metal center in pincer metal complexes, the Pt-P coupling constants (J_{Pt-P}) of the PCN-pincer Pt complexes were studied. It was found that the J_{Pt-P} of Pt complexes **4e** and **4f** are 4862 Hz and 4830 Hz, respectively. This indicates that complex **4f** possesses a relatively less positive metal center.[32-34] Similarly, the Pt-P coupling constants (J_{Pt-P}) of Pt complexes **5e** and **5f** (*i.e.,* J_{Pt-P}=4652 Hz *vs*. J_{Pt-P}=4586 Hz) along with those of complexes **6e** and **6f** (*i.e.,* J_{Pt-P}=4660 Hz *vs*. J_{Pt-P}=4576 Hz) also indicate that more electron-enriched pincer ligands lead to less positive Pt metal centers in the cationic complexes **5f** and **6f**.

7.2.5 Infrared study of the cationic PCN-pincer Pd complexes

Besides NMR techniques, IR spectroscopy offers an alternative approach to investigate the electronic property of the coordinated C≡N moieties.[21] As shown in Table 4, the frequencies of the coordinated C≡N units increased with respect to those of the free nitrile compounds for all complexes, although no convincible trend was found. Therefore, we were not able to assign a relative Lewis acidity of the cationic pincer metal complexes based on these IR wavenumber studies.

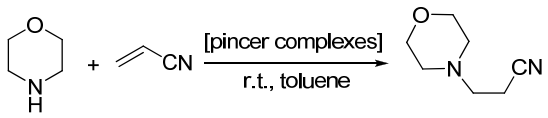
Table 4. IR stretches of the C≡N units in the cationic PCN-pincer Pd complexes.

Entry	Complex	$\upsilon(C\equiv N)_{coord}$[a]	$\Delta\upsilon$
1	**5a**	2287	+ 34
2	**5b**	2292	+ 39
3	**5c**	2292	+ 39
4	**5d**	2288	+ 35
5	**6a**	2268	+ 39
6	**6b**	2265	+ 36
7	**6c**	2261	+ 32
8	**6d**	2262	+ 33

[a]: Values are reported in cm^{-1}. The $\upsilon(C\equiv N)$ of free MeCN and CH_2=CHCN are 2253 cm^{-1} and 2229 cm^{-1}, respectively.

7.2.6 Aza-Michael additions catalyzed by PCN-pincer Pd and Pt complexes

Catalytic amination of olefins, especially transition metal-catalyzed olefin hydroamination processes, has attracted great attention since these processes are environmentally friendly approaches that allow easy access to industrially important amines.[24, 25] The aza-Michael addition of amines to activated olefins resembles olefin hydroamination. Whereas these reactions have been shown to proceed without catalysts under solvent-free conditions,[26] uncatalyzed addition of amines to acrylonitrile were proven to be much more sluggish in diluted media and especially in non-polar solvents.[27] Accordingly, a large diversity of Lewis acids such as $AlCl_3$, $InCl_3$, and $TiCl_4$ have been applied to efficiently increase the rate of these reactions.[28, 29] Recently, Togni's group has reported a series of Ni- and Pd-complexes derived from novel terdentate PPP-phosphine ligands and PCP carbene phosphine fused ligands, and their use as catalysts in the anti-Markovnikov additions of aniline, piperidine, and morpholine to acrylic acid derivatives.[30, 31] In 2007, Zargarian *et al.* firstly reported that cationic P'CP'-pincer Ni-complexes can efficiently promote aza-Michael additions of morpholine, cyclohexyl amine, and aniline to acrylonitrile, methacrylonitrile, and crotonitrile with TON's up to 2000.[16] These results prompted us to investigate the catalytic activities of the present cationic PCN-pincer Pd and Pt complexes in the representative aza-Michael addition of morpholine to acrylonitrile (Scheme 3). Especially, we were interested to understand the correlation between the reaction rate of this reaction and the relative Lewis acidity of these pincer metal complexes as determined by the NMR studies (*vide supra*).



Scheme 3. Cationic PCN-pincer complexes catalyzed aza-Michael addition.

Using 0.5 mol% pincer complex loading under mild conditions, the trends observed for both the reaction rate and overall the conversion of the starting material (Chart 1) agreed with the order of the relative Lewis acidity of the complexes based on the NMR studies, *i.e.* the more electron-enriched pincer ligands result in a more positive metal center and more active Lewis acidic catalysts (*vide supra*). For instance, pincer complex **6a** comprising the most electron-deficient ligand **3a** with the weakest σ-donating donor moieties actually gave the lowest reaction rate and the lowest conversion of starting material. In contrast, complexes **6c** and **6d** which

possess more electron-enriched pincer ligands showed much higher catalytic activities and the reactions went to completion within 10 min and 5 min, respectively.

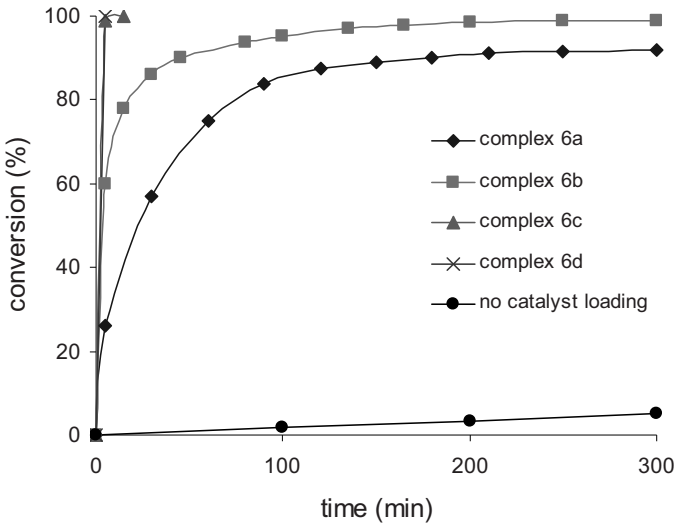


Chart 1. Reaction profiles for the aza-Michael addition of morpholine and acrylonitrile catalyzed by cationic PCN-pincer complexes **6a**-**6d**. Reaction conditions: 1 mmol of morpholine, 1 mmol of acrylonitrile, 0.5 mol% [Pd], toluene (2 mL), and room temperature; substrate conversions to the anti-Markovnikov product were monitored by GC.

To obtain more information on the reaction profiles for complexes **6c** and **6d**, additional tests were carried out with a lower catalyst loading, *i.e.*, 0.05 mol%, and the corresponding reaction profiles are shown in Chart 2. It was found that for complex **6c** a 10-fold decrease in catalyst loading resulted in a decreased catalytic activity and conversion. The reaction was found to merely achieve 85% conversion after 5 h, which is much slower than the full conversion within 10 min when 0.5 mol% of catalyst was applied. For complex **6d**, whilst 0.05 mol% catalyst loading also significantly decreased the catalytic activity, the reaction still proceeded to full conversion (completion time < 5min for 0.5 mol% *vs*. ~30 min for 0.05 mol%).

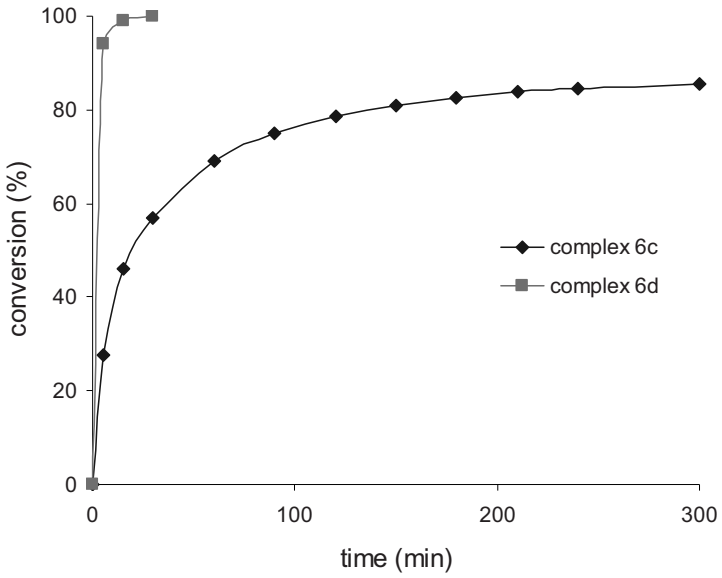


Chart 2. Reaction profiles for the aza-Michael addition of morpholine and acrylonitrile catalyzed by cationic PCN-pincer complexes **6c** and **6d**. Reaction conditions: 1 mmol of morpholine, 1 mmol of acrylonitrile, 0.05 mol% [Pd], toluene (2 mL), and room temperature; substrate conversions to the anti-Markovnikov product were monitored by GC.

Much like the Pd analogues, Pt complex **6f** bearing the more electron-enriched pincer ligand performed at higher catalytic activity and conversion than complex **6e** (Chart 3). However, these reactions were slower than those of their Pd-analogues (compare the reaction profiles of **6b** and **6c** in Chart 1 to the profiles of **6e** and **6f** in Chart 3).

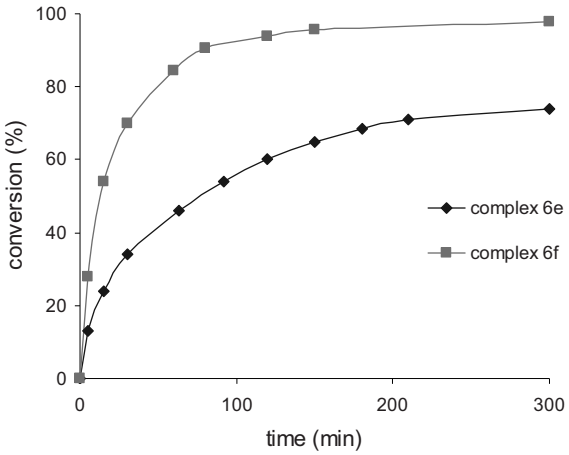


Chart 3. Reaction profiles for the aza-Michael addition of morpholine and acrylonitrile catalyzed by cationic PCN-pincer complexes **6e** and **6f**. Reaction conditions: 1 mmol of morpholine, 1 mmol of acrylonitrile, 0.5 mol% [Pt], toluene (2 mL), and room temperature; substrate conversions to the anti-Markovnikov product were monitored by GC.

7.3 Discussion

We have reported the synthesis of a series of PCN-pincer palladium and platinum complexes comprising isovanillin derivative **1** as the common intermediate by using a modular synthetic route. The entitled pincer complexes **4a**-**4f** bearing various donor units with variable electron properties and geometries were obtained in moderate to good yields (55-88%). Their structures in the solid state were investigated by means of X-ray analysis, which unambiguously showed their structural integrity. Several characteristic bond lengths in these complexes are significantly affected by the electronic properties and geometries of the substituents on the E-donors of their ligands. Generally, electron-deficient P and N donor units shorten the M–P, M–N and P–O bonds, respectively. In contrast, electron-enriched N donor units shorten the C=N bond lengths of the aldimine functionalities in the coordinated pincer ligands.

The analogous cationic pincer complexes **5a**-**5f** and **6a**-**6f** were prepared in good to excellent yields by reacting the neutral pincer complexes **4a**-**4f** with $AgBF_4$ in the presence of MeCN or CH_2=CHCN. ^1H and ^{13}C NMR studies on these complexes were carried out to provide information on their relative Lewis acidities. It was found that the pincer complexes bearing more electron-enriched pincer ligands generally displayed larger downfield chemical shifts for the α-H and α-C nuclei of the coordinated MeCN and CH_2=CHCN moieties. According to previously

reported correlations between the characteristic chemical shifts and relative Lewis acidity,[15, 17, 20] this would mean that more electron-enriched pincer ligands would result in more positive metal centers and increased Lewis acidity, which is entirely opposite to general intuitive considerations on metal-based Lewis acidity.

In previous investigations on *para*-functionalized NCN-pincer metal complexes it was found that electron-withdrawing *para*-functional groups lead to a decreased electron density at the metal center.[15, 17] As a consequence, these metal centers displayed a higher electrophilicity towards external lone pair electron donors, which follows intuitive Lewis acidity considerations. The fact that we now seem to find an opposite effect in the new PCN-pincer metal complexes may have several reasons. In the case of NCN-pincer complexes, the nitrile probe ligand is located *trans* with respect to the variable *para*-functional group, which does not directly bind to metal center and affects the electronic properties on metal center through changing the polarization of the C_{ipso}-metal bonds. Differently, in the case of PCN-pincer complexes, the nitrile probe ligand is situated in *cis*–positions with respect to the variables, *i.e.,* both E-donor moieties, which directly bind to metal center and affect the electronic properties of metal center through varying their σ-donating and π-accepting characters. On the other hand, the *para*-functional group is free of steric effects towards the nitrile probe ligand, whereas the various substituents on two E-donor moieties may enforce steric congestion on the nitrile ligand. Definitely, these factors lead to rather different electronic effects on the nitrile probe ligand.

Based on these considerations we, therefore, conclude that the general approach of using a metal coordinated nitrile molecule as a probe for the effect of a *trans*-ligand on Lewis acidity of the metal *via* NMR techniques (^{1}H and ^{13}C NMR) is not applicable to systems in which a ligand in mutual cis-position with respect to the nitrile probe is varied. The current PCN-pincer metal complexes are a clear example of this conclusion, which may have more general ground. Instead, one would need to rely on other spectroscopic means to probe the Lewis acidity in such cases. As shown here, the ^{195}Pt-^{31}P coupling constant in NMR is an appropriate alternative.

The acrylonitrile complexes **6a**-**6f** were found to be active catalysts for aza-Michael addition of morpholine to acrylonitrile, where the complexes derived from the more electron-enriched pincer ligands again seemed to behave as the stronger Lewis acids towards external, two-electron donor molecules. At first sight, these observations also contradict general Lewis acidity considerations. Yet, the overall rate of a (catalyzed) reaction is determined by its rate-determining step (rds). Our observations on the pincer-catalyzed aza-Michael addition, therefore, should be interpreted as providing information on the rate-determining step of this reaction. Based on this consideration, our data provide evidence for the C–N bond forming step, *i.e.* attack of a morpholine nucleophile

on a metal-ccordinated acrylonitrile moiety, not being the rate determing step of this reaction. In the case that this step would be rate-determining indeed, one would expect the pincer complexes comprising more electron-enriched pincer ligands and less positive metal centers to be inferior catalysts for this reaction. On the other hand, the complexes bearing less positive metal centers outperformed the complexes which possess more positive metal centers (*vide supra*), this would imply that the dissociation of formed product from the metal center, *i.e.* the product release, could be the rate-determining step of these PCN-pincer complex catalyzed aza-Michael addition reactions.

7.4 Conclusion

In conclusion, we have reported the synthesis of a series of PCN-pincer palladium and platinum complexes **4a-4f** along with their cationic pincer complexes **5a-5f** and **6a-6f** bearing acetonitrile or acrylonitrile as co-ligands in moderate to excellent yields by using a modular synthetic route. By taking advantage of the structurally and electronically tunable cationic PCN-pincer complexes, we have studied the relative Lewis acidity of these PCN-pincer Pd- and Pt-complexes by means of NMR techniques. Interestingly, ^{1}H and ^{13}C NMR investigations revealed an opposite trend to general intuitive considerations on metal-based Lewis acidity. Subsequently, ^{195}Pt-^{31}P coupling constants studies corrected the controversial findings. It is clear that the general approach of using a metal coordinated nitrile molecule as a probe is not applicable to PCN-pincer complexes in which two E-donor moieties in the pincer ligand in mutual *cis*-position with respect to the nitrile probe are varied. In addition, we tentatively propose that the product releasing step, instead of C–N bond formation step, is the rate-determining step of PCN-pincer-catalyzed aza-Michael addition, which is in contrast to previously documented Lewis acidic metal complex catalyzed aza-Michael addition reactions.[28,29] Apparently, the assignment of relative Lewis acidity by NMR techniques has some drawbacks and limitations. As it was proposed by Laszlo *et al*.,[35] MO calculations seem to provide an alternative and supplementary method, giving direct access to a quantitative determination of the strength of a Lewis acid. Therefore, current efforts in our laboratory aim at theoretical calculations in order to understand the relative Lewis acidity of different types of pincer complexes at the MO level.

7.5 Experimental Section

General remarks: All reactions were performed under a dry N_2 atmosphere by using standard Schlenk techniques unless otherwise stated. Glassware was oven dried or flame dried prior to use. Diethyl ether and THF were freshly distilled over metallic sodium prior to use. Toluene, Et_3N and DMF were distilled over CaH_2 and stored under N_2 at –30 °C. Diphenylphosphine chloride and diisopropylphosphine chloride were freshly distilled under reduced pressure prior to use. 2-bromo-3-hydroxy-4-methoxybenzaldehyde **1** was prepared according to a reported procedure.[36] $[Pd_2(dba)_3{\cdot}CHCl_3]$[37] and $[Pt_2(dba)_3]$[38] were prepared according to literature procedures. 1,1'-biphenyl-2,2'-diyl chlorophosphite was prepared as reported.[39] All other reagents were purchased from ACROS Organics and Sigma-Aldrich Chemical Co. Inc, and used as received. ^{1}H-NMR (400.0 MHz), ^{13}C-NMR (100.6 MHz), ^{31}P-NMR (161.9 MHz) and ^{19}F-NMR (376.3 MHz) spectra were recorded at room temperature in $CDCl_3$ on a Varian spetrometer at 400 MHz. $CDCl_3$ was deacidified by treatment with Al_2O_3 and was subsequently distilled over $MgSO_4$. The pretreated $CDCl_3$ was stored in a Schlenk flask under N_2 in the absence of light. Chemical shift values are reported in ppm (δ) relative to $(CH_3)_4Si$ (^{1}H and ^{13}C NMR) or a capillary containing 85% H_3PO_4 in D_2O, (^{31}P{^{1}H} NMR). Flash chromatography was performed using ACROS silica gel, 0.06 – 0.200 mm, pore diameter ca. 6 nm. MS measurements were carried out on an Applied Biosystems Voyager DE-STR MALDI-TOF MS. Elemental microanalyses were performed by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim a/d Ruhr, Germany.

Compound 2b: A mixture of **1** (0.4620 g, 2 mmol), $tBuNH_2$ (420 µL, 4 mmol) and $MgSO_4$ (1 g) suspended in $CHCl_3$ (20 mL) was refluxed at 75 °C under N_2 for overnight. After cooling, the reaction mixture was filtered through a short pad of Celite and the filter cake was washed with CH_2Cl_2 (3 x 5 mL). The combined filtrate was stripped to dryness on a rotary evaporate. Finally, a slightly pink solid was obtained after standing at room temperature and the product was used for the next step without further purification. An analytical sample was obtained by flash chromatography with EtOAc/hexanes (1:9 (v/v)) as eluent. Yield: 85% (0.48 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.57 (s, 1H, ArC*H*=NtBu), 7.57 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.84 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.93 (s, 3H, O*Me*), 1.30 (s, 9H, tBu*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 56.4, 154.7, 148.6, 142.9, 135.1, 129.1, 119.9, 111.8, 109.9, 30.0. Anal.Calcd for: C, 50.37; H, 5.64; N, 4.89; found: C, 50.31; H, 5.66; N, 4.91;

Compound 3a: Compound **2a** (0.3062 g, 1 mmol) was dissolved in dry toluene (20 mL) and precooled to 0 °C on an ice bath. To this solution were consecutively added Et_3N (280 µL, 2 mmol) and 1,1'-biphenyl-2,2'-diyl chlorophosphite[39] (1 mmol) *via* an air-tight syringe. After addition, the reaction mixture was allowed to warm to room temperature and was vigorously stirred for 16 h. The resulting white suspension was filtered through a short pad of Celite and the filter cake was washed with freshly distilled toluene (3 x 5 mL). The filtrate was concentrated under reduced pressure and was thoroughly dried in vacuum to give crude compound **3a**, which was obtained in 95% isolated yield and used in the next step without further purification. Yield: 95% (0.495 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.88 (s, 1H, ArC*H*=NPh), 7.35-7.40 (m, 5H, NPh*H*), 7.05-7.30 (m, 9H, Ar*H* + BIPOL *H*), 6.96 (d, *J*=8.8 Hz, 1H, Ar*H*), 3.70 (s, 3H, O*Me*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 160.1, 156.2, 155.9, 146.3, 135.4, 130.1, 129.1, 127.3, 126.4, 125.0, 122.3, 121.9, 117.7, 116.4, 114.8, 56.2. ^{31}P{^{1}H} NMR (d^8-toluene, 161.9 Hz): δ 153.6 (s).

Compound 3c: Compound **2b** (0.2865 g, 1 mmol) and *N*,*N*-dimethyl-4-aminopyridine (DMAP) (0.1225g, 1 mmol) were dissolved in 20 mL of dry THF and the mixture was precooled to 0 °C on an ice bath. To this solution was added Ph_2PCl (189 μL, 1 mmol) *via* an air-tight syringe. After addition, the reaction mixture was allowed to warm to room temperature and was vigorously stirred for 16 h. The resulting white suspension was filtered through a short pad of Celite and the filter cake was washed with freshly distilled toluene (3 x 5 mL). The filtrate was concentrated under reduced pressure and was thoroughly dried in vacuum to give crude compound **3c**, which was obtained in 93% isolated yield and used in the next step without further purification. Yield: 93% (0.437 g). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.57 (s, 1H, ArC*H*=NtBu), 7.71-7.80 (m, 4H, PPh*H*), 7.38-7.44 (m, 7H, Ar*H* + PPh*H*), 6.85 (d, 1H, *J*=8.8 Hz, Ar*H*), 3.44 (s, 3H, O*Me*), 1.34 (s, 9H, tBu*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 154.9, 154.0, 142.1 (d, *J*=18 Hz), 131.9 (d, *J*=11 Hz), 131.5, 131.2, 129.8, 129.3, 128.3 (d, *J*=7.5 Hz), 123.6, 111.6, 58.0, 56.1, 30.1. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 126.3 (s).

Compound 3d: Compound **2b** (0.2865 g, 1 mmol) and DMAP (0.1225g, 1 mmol) were dissolved in dry THF (20 mL) and the mixture was precooled to 0 °C on an ice bath. To this solution was added iPr_2PCl (160 μL, 1 mmol) *via* an air-tight syringe. After addition, the reaction mixture was allowed to warm to room temperature and was vigorously stirred for 24 h. The resulting white suspension was filtered through a short pad of Celite under N_2 and the filter cake was quickly washed with toluene (3 x 5 mL). The filtrate was concentrated under reduced pressure and was thoroughly dried in vacuum to give crude compound **3c**, which was obtained in 88% isolated yield and used in the next step without further purification. Yield: 88% (0.354 g).^{1}H NMR ($CDCl_3$, 400MHz): δ 8.23 (s, 1H, ArC*H*=NtBu), 7.15 (d, *J*=8.8 Hz, 1H, Ar*H*), 6.63 (d, *J*=8.8 Hz, 1H, Ar*H*), 3.73 (s, 3H, O*Me*), 1.80-2.10 (m, 2H, iPr*H*), 1.28 (s, 9H, tBu*H*), 0.90-1.10 (m, 12H, iPr*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 155.9, 153.1, 146.3, 135.1, 125.0, 117.7, 114.8, 58.3, 56.2, 31.9, 19.3, 15.3. ^{31}P{^{1}H} NMR (d^8-toluene, 161.9 Hz): δ 175.3 (s).

General procedure of the synthesis of complexes 4a-4f.

To a solution of **3a** − **3d** (0.5 mmol) in dry toluene (15 mL) was added [$Pd_2(dba)_3$·$CHCl_3$] (0.258 g, 0.25 mmol) or [$Pt_2(dba)_3$] (0.274 g, 0.25 mmol) and the reaction mixture was warmed to 80 °C under N_2 for 5 or 16 h, respectively. After cooling, the reaction mixture was filtered through a short pad of Celite and the filtrate was concentrated under reduced pressure to yield a yellowish solid mixture. Complexes **4a-4c** and **4e-4f** were obtained by repeating the addition of hexanes into a concentrated dichloromethane solution of the crude products. Complex **4d** was obtained by flash chromatography with EtOAc/hexanes (3:7 (v/v)) as eluent. Analytic samples were obtained as light yellow and air stable solids in 55% − 88% isolated yields.

Complex 4a: Yield : 65% (0.204 g, 0.325 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.52 (d, *J*=9.6 Hz, 2H, NPh*H*), 7.48 (m, 10H, NPh*H* + BIPOL *H*), 7.36- 8.28 (d, *J*=7.2 Hz, 1H, ArC*H*=NPh), 7.34 (d, *J*=8 Hz, 1H, NPh*H*), 7.30 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.78 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.91(s, 3H, O*Me*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 173.3 (d, *J*=6 Hz), 156.4, 149.0, 148.4, 138.0, 130.4, 130.1, 129.2, 128.9, 127.9, 127.2, 126.4, 123.6, 122.7, 110.7, 56.5. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 144.6 (s). MS (MALDI-TOF): m/z calcd for $C_{26}H_{19}NO_4PPd$: 546.83 $[M\text{-}Br]^+$; found: 546.78; Anal.Calcd for: C, 49.83; H, 3.06; N, 2.23; P, 4.94; Pd, 16.98; found: C, 49.78; H, 3.01; N, 2.29; P, 5.02; Pd, 17.02;

Complex 4c: Yield : 88% (0.254 g, 0.44 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ8.02-8.10 (m, 5H, PPh*H* + ArC*H*=NtBu), 7.42-7.52 (m, 6H, PPh*H*), 7.09 (d, *J*=8 Hz, 1H, Ar*H*), 6.66 (d, *J*=8 Hz, 1H, Ar*H*), 3.90 (s, 3H, O*Me*), 1.58 (s, 9H, tBu*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 167.3 (d, *J*=4.3 Hz), 154.9, 150.3 (d, *J*=11 Hz), 148.1 (d, *J*=21 Hz), 138.7, 135.7, 131.4, 128.9 (d, *J*=14 Hz), 126.7, 124.1, 109.2, 62.3, 56.3, 29.6. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 156.1 (s). MS (MALDI-TOF): m/z calcd for $C_{24}H_{25}NO_2PPd$: 496.85[M-Br]$^{+}$; found: 496.86; Anal.Calcd for: C, 49.98; H, 4.37; N, 2.43; P, 5.37; Pd, 18.45; found: C, 50.04; H, 4.31; N, 2.49; P, 5.30; Pd, 18.41;

Complex 4d: Yield : 55% (0.140 g, 0.275 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.05 (d, *J*=4.8 Hz, 1H, ArC*H*=NtBu), 7.03 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.61 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.87 (s, 3H, O*Me*), 2.56-2.61 (m, 2H, iPr*H*), 1.54 (s, 9H, tBu*H*), 1.47 (dd, *J*=7.2 Hz, *J*=9.2 Hz, 6H, iPr*H*), 1.33 (dd, *J*=7.2 Hz, *J*=9.2 Hz, 6H, iPr*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 166.7 (d, *J*=4.4 Hz), 151.6 (d, *J*=7 Hz), 147.4 (d, *J*=19 Hz), 138.9, 128.8 (d, *J*=58 Hz), 123.7, 109.1, 61.8, 56.3, 29.8 (t, $J_{P\text{-}C}$=12.5 Hz), 18.3, 17.1. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 206.9 (s). MS (MALDI-TOF): m/z calcd for $C_{18}H_{29}NO_2PPd$: 428.82 [M-Br]$^{+}$; found: 428.80; Anal.Calcd for: C, 42.50; H, 5.75; N, 2.75; P, 6.09; Pd, 20.92; found: C, 42.55; H, 5.79; N, 2.69; P, 6.13; Pd, 20.95;

Complex 4e: Yield : 75% (0.257 g, 0.375 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.45 (dt, $J_{P\text{-}H}$=6.8 Hz, $J_{Pt\text{-}H}$=96 Hz, ArC*H*=NPh), 8.06 (q, *J*=7.6 Hz, 4H, PPh*H*), 7.41-7.53 (m, 10H, PPh*H* + NPh*H*), 7.28-7.32 (m, 1H, NPh*H*), 7.24 (d, *J*=8 Hz, 1H, Ar*H*), 6.71 (d, *J*=8 Hz, 1H, Ar*H*), 3.95 (s, 3H, O*Me*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 176.3 (s with Pt satellite, $J_{Pt\text{-}C}$=82 Hz), 156.7, 150.1 (d, *J*=15 Hz), 149.0 (d, *J*=6.8 Hz), 148.1, 137.1, 135.8, 132.6, 132.4, 128.9 (d, *J*=12.5 Hz), 128.6, 127.7, 126.0, 124.2, 108.7, 56.5. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 123.5 (s with Pt satellite, $J_{Pt\text{-}P}$=4862 Hz). MS (MALDI-TOF): m/z calcd for $C_{26}H_{21}NO_2PPt$: 605.50 [M-Br]$^{+}$; found: 605.49; Anal.Calcd for: C, 45.56; H, 3.09;N, 2.04; P, 4.52; Pt, 28.46; found: C, 45.48; H, 3.13;N, 2.07; P, 4.47; Pt, 28.41;

Complex 4f: Yield : 73% (0.243 g, 0.365 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.37 (dt, $J_{H\text{-}H}$=7.6 Hz, $J_{Pt\text{-}H}$=104 Hz, 1H, ArC*H*=NtBu), 8.02 (apparent q, *J*=8 Hz, 4H, PPh*H*), 7.40-7.55 (m, 6H, PPh*H*), 7.10 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.95 (s, 3H, O*Me*), 6.66 (d, *J*=8.4 Hz, 1H, Ar*H*), 1.64 (s, 9H, tBu*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 169.7 (Pt satellite, $J_{Pt\text{-}C}$=100 Hz), 149.5 (d, *J*=9.6 Hz), 148.7 (d, *J*=15 Hz), 144.4 (d, *J*=5 Hz), 136.5, 133.2, 132.4, 132.3, 128.9 (d, *J*=12 Hz), 124.6, 108.4, 63.5, 56.4, 29.5. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 118.9 (s with Pt satellite, $J_{Pt\text{-}P}$=4830 Hz). MS (MALDI-TOF): m/z calcd for $C_{24}H_{25}NO_2PPt$: 585.51[M-Br]$^{+}$; found: 585.50; Anal.Calcd for: C, 43.32; H, 3.79; N, 2.10; P, 4.65; Pt, 29.32; found: C, 43.25; H, 3.70; N, 2.14; P, 4.58; Pt, 29.35;

General procedure of the synthesis of complex 5a-5f and 6a-6f.

To a solution of complex **4a-4f** (0.05 mmol) in dry dichloromethane (2 mL), a few drops of MeCN or CH_2=CHCN and $AgBF_4$ (0.0100 g, 0.05 mmol) were added in one portion. The reaction mixture was then stirred at room temperature for 2 h. The resulting white suspension was filtered over a short pad of Celite and the filtrate cake was washed with dichloromethane (3 x 2 mL). After removing all volatiles in vacuum, the desired products were obtained in good isolated yields as yellowish or brown solids after recrystallization from CH_2Cl_2/pentane or CH_2Cl_2/diethyl ether. The products were stored under N_2 to prevent from being affected by moisture in air for long term conservation.

Complex 5a: Yield: 98% (0.033 g, 0.049 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.30 (d, *J*=8 Hz, ArC*H*=Ph), 7.69 (d, *J*=7.2 Hz, 2H, NPh*H*), 7.67 (d, *J*=8.4Hz, 1H, Ar*H*), 7.43-7.55 (m, 8H, BIPOL *H*), 7.41 (t, *J*=7.2 Hz, 1H, NPh*H*), 7.31 (d, *J*=7.2 Hz, 2H, NPh*H*), 6.92 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.96 (s, 3H, O*Me*), 2.00 (s, 3H, NC*Me*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 174.5, 152.3, 149.8, 149.5, 147.9, 147.4 (d, *J*=11 Hz), 144.0 (d, *J*=21.6 Hz), 138.0, 130.9 (d, *J*=21 Hz), 129.8, 129.1, 128.6 (d, *J*=18 Hz), 128.1, 123.8, 121.9 (d, *J*=28.7 Hz), 112.0, 56.8, 2.5. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 139.0 (s). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -153.2 (s). MS (MALDI-TOF): m/z calcd for $C_{28}H_{22}N_2O_4PPd$: 587.88; found: 587.90 $[M\text{-}BF_4]^+$;

Complex 5b: Yield: 93% (0.029 g, 0.046 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.19 (d, *J*=4.8 Hz, 1H, ArC*H*=NPh), 7.82 (q, *J*=4.4 Hz, 4H, PPh*H*), 7.47 (t, *J*=8 Hz, 2H, NPh*H*), 7.64 (br s, 6H, PPh*H*), 7.25-7.35 (m, 3H, NPh*H*), 7.31 (d, *J*=8 Hz, 1H, Ar*H*), 6.73 (d, *J*=8 Hz, 1H, Ar*H*), 3.93 (s, 3H, O*Me*), 2.23 (s, 3H, NC*Me*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 173.8, 151.3 (m), 149.8 (d, *J*=21 Hz), 148.0, 138.1, 133.8, 132.0 (d, *J*=15 Hz), 129.9 (m), 129.1, 128.5, 127.3, 122.3, 119.4, 110.6, 56.5, 3.0. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 157.9 (s). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -153.4 (s). MS (MALDI-TOF): m/z calcd for $C_{28}H_{24}N_2O_2PPd$: 557.90 $[M\text{-}BF_4]^+$; found 557.88;

Complex 5c: Yield: 95% (0.030 g, 0.048 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.07 (d, *J*=5.6 Hz, 1H, ArC*H*=NtBu), 7.81 (dd, $J_{H\text{-}H}$=7.2 Hz, $J_{P\text{-}H}$=6 Hz, 4H, PPh*H*), 7.60-7.67 (m, 6H, PPh*H*), 7.15 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.71 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.90 (s, 3H, O*Me*), 2.43 (br s, 3H, NC*Me*), 1.56 (s, 3H, tBu*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 168.3, 151.4 (d, *J*=10.4 Hz), 150.0, 148.5 (d, *J*=5.8 Hz), 138.6, 133.9, 132.1 (d, *J*=15 Hz), 130.2, 130.0, 129.9, 125.6, 121.5, 110.3, 61.5, 56.4, 29.1, 3.1. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 156.5 (s). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -153.4 (s). MS (MALDI-TOF): m/z calcd for $C_{26}H_{28}N_2O_2PPd$: 537.91 $[M\text{-}BF_4]^+$; found: 537.90;

Complex 5d: Yield: 98% (0.025 g, 0.045 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.03 (d, *J*=4.8 Hz, 1H, ArC*H*=NtBu), 7.08 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.65 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.88 (s, 3H, O*Me*), 2.68 (q, *J*=6.4 Hz, 2H, iPr*H*), 2.48 (very br s, 3H, NC*Me*), 1.44 (d, *J*=7.2 Hz, 6H, iPr*H*), 1.40 (s, 9H, tBu*H*), 1.36 (d, *J*=6.8 Hz, 6H, iPr*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 167.9, 152.6 (d, *J*=8 Hz), 148.1 (d, *J*=23 Hz), 138.8, 129.6 (d, *J*=50 Hz), 125.0, 119.7, 110.1, 61.1, 56.3, 29.6 (t, *J*=12 Hz), 17.8, 17.0, 2.9 (very br). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 207.3 (s). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -153.3 (s). MS (MALDI-TOF): m/z calcd for $C_{20}H_{32}N_2O_2PPd$: 469.87 $[M\text{-}BF_4]^+$; found: 469.90;

Complex 5e: Yield: 93% (0.034 g, 0.047 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.47 (d with Pt satellites, $J_{P\text{-}H}$=7.2 Hz, $J_{Pt\text{-}H}$=98 Hz, 1H, ArC*H*=NPh), 7.78-7.82 (m, 4H, PPh*H*), 7.58-7.62 (m, 6H, PPh*H*), 7.49 (t, *J*=7.6 Hz, 2H, NPh*H*), 7.33-7.39 (m, 4H, Ar*H* + NPh*H*), 6.71 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.93 (s, 3H, O*Me*), 2.31 (s, 3H, NC*Me*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 176.8 ($J_{Pt\text{-}C}$=110 Hz), 150.6, 150.3, 147.5, 141.0, 136.3, 133.8, 131.4, 130.5, 129.8, (d, *J*=12 Hz), 128.1, 125.2, 122.7, 120.1, 118.5, 110.2, 56.6, 3.5. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 123.2 (s with Pt satellites, $J_{Pt\text{-}P}$=4652 Hz). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -152.6 (s). MS (MALDI-TOF): m/z calcd for $C_{28}H_{24}N_2O_2PPt$: 646.55 $[M\text{-}BF_4]^+$; found: 646.58;

Complex 5f: Yield: 88% (0.031 g, 0.044 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.42 (d with Pt satellites, $J_{P\text{-}H}$=7.6 Hz, $J_{Pt\text{-}H}$=99 Hz, 1H, ArC*H*=NtBu), 7.75-7.81 (m, 4H, PPh*H*), 7.60-7.63 (m, 6H, PPh*H*), 7.22 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.71 (d, *J*=8.4 Hz, 1H, Ar*H*), 3.91 (s, 3H, O*Me*), 2.58 (s, 3H, NC*Me*), 1.58 (s, 3H, *t*Bu). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 171.6 (s with Pt satellites, $J_{Pt\text{-}C}$=105 Hz), 150.4, 149.2 (d, *J*=5 Hz), 139.5, 137.0, 133.8, 131.9 (d, *J*=11.3 Hz), 131.4, 130.2 (d, *J*=14 Hz), 127.2, 126.8, 110.3, 62.9, 56.4, 29.2, 3.6. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 120.8 (s with Pt satellites, $J_{Pt\text{-}P}$=4586 Hz). $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376.3 Hz): δ -152.7 (s). MS (MALDI-TOF): m/z calcd for $C_{26}H_{28}N_2O_2PPt$: 626.56 $[M\text{-}BF_4]^+$; found: 626.60;

Complex 6a: Yield: 95% (0.032 g, 0.047 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.40 (d, *J*=7.6 Hz, 1H, ArC*H*=NPh), 7.67 (d, *J*=8 Hz, 1H, Ar*H*), 7.41-7.59 (m, 8H, BIPOL *H*), 7.23-7.40 (m, 5H, NPh*H*), 6.87 (d, *J*=7.6 Hz, Ar*H*), 6.22 (d, *J*=11.6 Hz, 1H, NCCH=CH_2), 6.10 (d, *J*=18 Hz, 1H, NCCH=CH_2), 5.65 (dd, *J*=12 Hz, *J*=5.6 Hz, 1H, NCC*H*=CH_2), 3.89 (s, 3H, O*Me*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 174.4, 150.8, 149.5, 148.4, 147.8 (d, *J*=11 Hz), 140.6 (d, *J*=21.6 Hz), 138.4, 137.6, 135.4, 130.9 (d, *J*=21 Hz), 129.8, 129.5, 128.9 (d, J=18 Hz), 128.7, 122.9 (d, *J*=28.7 Hz), 119.7, 112.0, 106. 6, 56.7. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 139.2 (s). $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376.3 Hz): δ -152.8 (s). MS (MALDI-TOF): m/z calcd for $C_{29}H_{22}N_2O_4PPd$: 599.89 $[M\text{-}BF_4]^+$; found: 599.92;

Complex 6b: Yield: 91% (0.030 g, 0.045 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.22 (d, *J*=4.8 Hz, 1H, ArC*H*=NPh), 7.55-7.78 (m, 4H, PPh*H*), 7.40-7.49 (m, 5H, NPh*H*), 7.32-7.38 (m, 7H, PPh*H* + Ar*H*), 6.76 (d, *J*=8.8 Hz, 1H, Ar*H*), 6.35 (d, *J*=10.8 Hz, 1H, NCCH=CH_2), 6.15 (d, *J*=17.6, 1H, NCCH=CH_2), 6.02 (apparent t, *J*=12 Hz, 1H, NCC*H*=CH_2), 3.94 (s, 3H, O*Me*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 173.9, 150.9, 149.7 (d, *J*=25 Hz), 148.1, 138.6, 137.9, 133.7, 132.0 (d, *J*=15 Hz), 130.5, 129.7, 128.2, 127.4, 126.1, 122.4, 119.4, 110.6, 106.8, 56.5. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 157.6 (s). $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376.3 Hz): δ -153.4 (s). MS (MALDI-TOF): m/z calcd for $C_{29}H_{24}N_2O_2PPd$: 569.91 $[M\text{-}BF_4]^+$; found: 569.90;

Complex 6c: Yield: 99% (0.032 g, 0.0495 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.11 (d, *J*=3.6 Hz, 1H, ArC*H*=NtBu), 7.75-7.81 (br m, 4H, PPh*H*), 7.58-7.64 (br m, 6H, PPh*H*), 7.22 (d, *J*=7.6 Hz, 1H Ar*H*), 6.73 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.51 (d, *J*=11.6 Hz, 1H, NCCH=CH_2), 6.35 (d, *J*=18 Hz, 1H, NCCH=CH_2), 6.19 (m, 1H, NCC*H*=CH_2), 3.89 (s, 3H, O*Me*), 1.42 (s, 9H, tBu*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 168.9, 151.2 (d, *J*=10.5 Hz), 150.0, 148.7 (d, *J*=21 Hz), 144.3 (br s), 138.6, 135.7, 134.0, 132.1 (d, *J*=15 Hz), 130.8, 129.8 (d, *J*=12 Hz), 127.1, 126.1, 123.2, 120.1, 110.6, 61.5, 56.5, 29.1. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 156.0 (s). $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376.3 Hz): δ -153.7 (s). MS (MALDI-TOF): m/z calcd for $C_{27}H_{28}N_2O_2PPd$: 549.92 $[M\text{-}BF_4]^+$; found: 549.90;

Complex 6d: Yield: 88% (0.025 g, 0.044 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.07 (d, *J*=4 Hz, 1H, ArC*H*=NtBu), 7.14 (d, *J*=8 Hz, 1H, Ar*H*), 6.67 (d, *J*=8 Hz, 1H, Ar*H*), 6.46 (very br, m, 2H, NCCH=CH_2), 6.11 (very br s, 1H, NCC*H*=CH_2), 3.87 (s, 3H, O*Me*), 2.63 (q, *J*=6.4 Hz, 2H, iPr*H*), 1.32-1.43 (m, 21H, tBu*H* + iPr*H*). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100.6Hz): δ 168.1, 153.0 (d, *J*=8 Hz), 148.2 (d, *J*=20 Hz), 139.4, 138.4, 135.0, 130.5 (d, *J*=48 Hz), 125.2, 122.5, 120.3, 110.0, 61.0, 56.4, 29.7 (t, *J*=12 Hz), 17.7, 16.9. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, 161.9 Hz): δ 206.3 (s). $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 376.3 Hz): δ -153.6 (s). MS (MALDI-TOF): m/z calcd for $C_{21}H_{32}N_2O_2PPd$: 481.88 $[M\text{-}BF_4]^+$; found: 481.90.

Complex 6e: Yield: 95% (0.035 g, 0.0475 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ8.46 (d with Pt satellites, J_{P-H}=6.8 Hz, J_{Pt-H}=104 Hz, ArC*H*=NPh), 7.75-7.84 (m, 4H, PPh*H*), 7.54-7.66 (m, 6H, PPh*H*), 7.48 (t, *J*=7.6 Hz, 2H, NPh*H*), 7.30-7.38 (m, 4H, NPh*H* + Ar*H*), 6.71 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.41 (d, *J*=11.6 Hz, 1H, NCCH=CH_2), 6.24 (d, *J*=18 Hz, 1H, NCH=CH_2), 6.12 (d, *J*=2 Hz, 1H, NC*H*=CH_2), 3.95 (s, 3H, O*Me*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): δ 177.0 (s with Pt satellites, J_{Pt-C}=107 Hz), 153.9, 150.7, 147.6 (d, *J*=18 Hz), 144.5, 141.5, 138.3, 136.2, 134.8, 132.2, 129.8 (d, *J*=13 Hz), 128.7, 127.9, 122.5, 119.8, 110.2, 106.3, 56.4. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 123.4 (s with Pt satellites, J_{Pt-P}=4660 Hz). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -152.8 (s). MS (MALDI-TOF): m/z calcd for $C_{29}H_{24}N_2O_2PPt$: 658.56 $[M-BF_4]^+$; found: 658.60.

Complex 6f: Yield: 90% (0.033 g, 0.045 mmol). ^{1}H NMR ($CDCl_3$, 400MHz): δ 8.47 (d with Pt satellites, J_{P-H}=7.6 Hz, J_{Pt-H}=112 Hz, 1H, ArC*H*=NtBu), 7.77 (dd, J_{H-H}=7.6 Hz, J_{P-H}=3.6 Hz, 4H, PPh*H*), 7.61-7.65 (m, 6H, PPh*H*), 7.29 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.74 (d, *J*=8.4 Hz, 1H, Ar*H*), 6.60 (d, *J*=12 Hz, 1H, NCCH=CH_2), 6.47 (d, *J*=17.6 Hz, 1H, NCCH=CH_2), 6.30 (dd, *J*=11.6 Hz, *J*=5 Hz, 1H, NCC*H*=CH_2), 3.91 (s, 3H, O*Me*), 1.49 (s, 9H, tBu*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6Hz): 171.5 (s with Pt satellites, J_{Pt-C}=105 Hz), 151.7, 150.5 (d, *J*=6.6 Hz), 149.2 (d, *J*=15 Hz), 145.2, 139.5, 137.0, 134.0, 132.3 (d, *J*=14 Hz), 129.7 (d, *J*=12 Hz), 129.3 (d, *J*=15 Hz), 128.7 (d, *J*=32 Hz), 126.3, 119.7, 110.1, 63.0, 56.3, 29.1. ^{31}P{^{1}H} NMR ($CDCl_3$, 161.9 Hz): δ 121.1 (s with Pt satellites, J_{Pt-P}=4576 Hz). ^{19}F{^{1}H} NMR ($CDCl_3$, 376.3 Hz): δ -152.8 (s). MS (MALDI-TOF): m/z calcd for $C_{27}H_{28}N_2O_2PPt$: 638.58 $[M-BF_4]^+$; found: 638.62;

General procedure of the catalytic aza-Michael additions.

At room temperature, morpholine (87.5 µL, 1 mmol) and acrylonitrile (65.8 µL, 1 mmol) were quickly added to a solution of pincer complex in dry toluene (2 mL). In the case of 0.05 mol% [Pd] loading ratio, a stock-solution of the Pd complexes in dry toluene was prepared. The resulting mixture was vigorously stirring at room temperature and the progress of the reaction was monitored by GC analysis.

X-ray crystal structure determinations

X-ray intensities were measured on a Nonius Kappa CCD diffractometer with rotating anode (graphite monochromator, λ = 0.71073 Å). The integration of the data was performed with EvalCCD[40] (compounds **4a**, **4c**, **4e**, **4f**, **5b**, **5e**) or HKL2000[41] (compounds **4b** and **4d**). For absorption correction and scaling the program SADABS[42] was used. The structures were solved with automated Patterson Methods (DIRDIF-99 or DIRDIF-08,[43] compounds **4a**, **4c**, **4e**, **4f**, **5b**, **5e**) or Direct Methods (SHELXS-97,[44] compounds **4b** and **4d**) and refined with SHELXL-97[44] against F^2 of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. Hydrogen atoms were located in difference-Fourier maps (compound **4a**) or introduced in calculated positions and refined with a riding model. Geometry calculations and checking for higher symmetry was performed with the PLATON program.[45] Further details are given in Table 5.

Compound 4a: The halogen position was occupied by 98% Br and 2% Cl. The Pd-Br and Pd-Cl distances were restrained to expected values. Additional restraints were used for the displacement parameters of Br and Cl.

Compound 4c: The halogen position was occupied by 95% Br and 5% Cl. The Pd-Br and Pd-Cl distances were restrained to expected values. Additional restraints were used for the displacement parameters of Br and Cl.

Compound 4d: The halogen position was occupied by 92% Br and 8% Cl. Br1 and Cl1 were constrained to the same position and displacement parameters.

Compound 4e: The crystal structure was refined as a racemic twin. The halogen position was occupied by 94% Br and 6% Cl. The Pt-Br and Pt-Cl distances were restrained to expected values. The displacement parameters of the Br and the corresponding Cl atoms were constrained to the same values.

Compound 5b: The methyl group of the coordinated acetonitrile molecule was rotationally disordered over two orientations.

Compound 5e: The difference Fourier map contains one positive peak of 2.65 e/Å^3 with a distance of 0.99 Å to Pt1.

Table 5. Details of the X-ray crystal structure determinations.

	4a	**4b**	**4c**
formula	$C_{26}H_{19}Br_{0.98}Cl_{0.02}NO_4PPd$	$C_{26}H_{21}BrNO_2PPd$	$C_{24}H_{25}Br_{0.95}Cl_{0.05}NO_2PPd$
fw	625.81	596.72	574.51
crystal colour	pale yellow	yellow	colourless
crystal size [mm^3]	0.27x0.25x0.16	0.60x0.24x0.12	0.37x0.27x0.15
T [K]	150	150	150
crystal system	triclinic	monoclinic	monoclinic
space group	$P\overline{1}$ (no. 2)	$P2_1/c$ (no. 14)	$P2_1/c$ (no. 14)
a [Å]	7.7128(3)	10.0370(1)	10.0501(3)
b [Å]	11.8806(6)	13.6684(1)	12.9046(13)
c [Å]	13.9990(3)	17.5004(2)	17.6344(5)
α [°]	109.104(2)	-	-
β [°]	103.747(2)	102.9902(4)	93.378(3)
γ [°]	98.611(2)	-	-
V [$Å^3$]	1140.66(8)	2339.43(4)	2283.1(2)
Z	2	4	4
D_x [g/cm^3]	1.822	1.694	1.671
μ [mm^{-1}]	2.638	2.593	2.572
abs. corr. method	multi-scan	multi-scan	multi-scan
abs. corr. range	0.41-0.66	0.29-0.73	0.35-0.68
$(\sin\theta/\lambda)_{max}$ [$Å^{-1}$]	0.65	0.65	0.70
refl. (meas./unique)	25645 / 4901	64860 / 5349	40131 / 6648
param./restraints	312 / 4	294 / 0	279 / 4
R1/wR2 [$I>2\sigma(I)$]	0.0173 / 0.0421	0.0193 / 0.0442	0.0165 / 0.0393
R1/wR2 [all refl.]	0.0198 / 0.0430	0.0232 / 0.0455	0.0197 / 0.0404
S	1.079	1.063	1.087
$\rho_{min/max}$ [$e/Å^3$]	-0.37 / 0.71	-0.37 / 0.43	-0.61 / 0.40

Continue **Table 5**.

	4d	**4e**	**4f**
formula	$C_{18}H_{29}Br_{0.92}Cl_{0.08}NO_2PPd$	$C_{26}H_{21}Br_{0.94}Cl_{0.06}NO_2PPt$	$C_{24}H_{25}BrNO_2PPt$
fw	505.15	682.68	665.42
crystal colour	yellow	yellow	yellow
crystal size [mm^3]	0.42x0.24x0.15	0.18x0.13x0.11	0.44x0.18x0.10
T [K]	150	150	150
crystal system	monoclinic	orthorhombic	monoclinic
space group	$P2_1/c$ (no. 14)	$P2_12_12_1$ (no. 19)	$P2_1/c$ (no. 14)
a [Å]	11.9955(1)	14.4592(4)	10.0497(6)
b [Å]	14.3754(1)	14.7567(3)	12.9048(2)
c [Å]	15.6395(1)	21.5903(5)	17.6290(12)
β [°]	130.0556(3)	-	93.059(2)
V [$Å^3$]	2064.24(3)	4606.72(19)	2283.0(2)
Z	4	8	4
D_x [g/cm^3]	1.625	1.969	1.936
μ [mm^{-1}]	2.778	7.821	7.987
abs. corr. method	multi-scan	multi-scan	analytical
abs. corr. range	0.37-0.66	0.19-0.42	0.12-0.47
$(\sin\theta/\lambda)_{max}$ [$Å^{-1}$]	0.65	0.65	0.65
refl. (meas./unique)	38555 / 4722	36599 / 10571	35624 / 5234
param./restraints	229 / 0	588 / 4	275 / 0
R1/wR2 [$I>2\sigma(I)$]	0.0193 / 0.0466	0.0301 / 0.0430	0.0156 / 0.0336
R1/wR2 [all refl.]	0.0215 / 0.0475	0.0484 / 0.0465	0.0207 / 0.0352
Flack x parameter[46]	-	0.247(5)	-
S	1.050	1.016	1.062
$\rho_{min/max}$ [$e/Å^3$]	-0.60 / 0.52	-0.72 / 0.83	-0.74 / 0.89

Continue **Table 5**.

	5b	**5e**
formula	$[C_{28}H_{24}N_2O_2PPd](BF_4)$	$[C_{28}H_{24}N_2O_2PPt](BF_4)$
fw	644.67	733.36
crystal colour	yellow	yellow
crystal size [mm^3]	0.31x0.26x0.19	0.22x0.20x0.16
T [K]	150	110
crystal system	monoclinic	monoclinic
space group	$P2_1/c$ (no. 14)	$P2_1/c$ (no. 14)
a [Å]	15.5374(5)	15.6012(4)
b [Å]	9.5779(2)	9.4964(2)
c [Å]	20.9458(6)	21.0455(8)
β [°]	120.087(2)	120.598(2)
V [$Å^3$]	2697.08(13)	2683.85(14)
Z	4	4
D_x [g/cm^3]	1.588	1.815
μ [mm^{-1}]	0.804	5.345
abs. corr. method	multi-scan	analytical
abs. corr. range	0.71-0.85	0.33-0.49
$(\sin\theta/\lambda)_{max}$ [$Å^{-1}$]	0.70	0.65
refl. (meas./unique)	47428 / 7871	44721 / 6175
param./restraints	354 / 0	354 / 0
R1/wR2 [$I>2\sigma(I)$]	0.0209 / 0.0503	0.0226 / 0.0495
R1/wR2 [all refl.]	0.0268 / 0.0536	0.0309 / 0.0528
S	1.084	1.049
$\rho_{min/max}$ [$e/Å^3$]	-0.42 / 0.46	-0.75 / 2.65

7.6 References

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Summary

The synthesis and application of PCP-pincer metal complexes have attracted much attention in the past decades due to their remarkable catalytic performances in many catalytic reactions. More recently, the development of chiral PCP-pincer metal complexes has also received much attention because of very promising to good enantioselective behavior in catalysis. With the design of new catalysts in mind, the development of novel non-oxygen sensitive phosphite and phosphoramidite-derived P'CP'-pincer metal complexes and of chiral P'CP'-pincer metal complexes along with the evaluation of their catalytic behavior are the main aims of the present study (Figure 1). In addition, the development of novel ECE'-type (E ≠ E') pincer metal complexes has become a new aspect of pincer chemistry. The synthesis of such complexes often suffers from tedious ligand synthesis. In this study, some efforts for the development of efficient and flexible synthetic routes to easily accessible PCE-type (E = N or S) pincer metal complexes are described (Figure 1). These PCE-pincer metal complexes were investigated as catalysts in organic transformations, and their catalytic performance was compared to those of more conventional ECE-pincer metal complexes in order to reveal the effect of combining different donor atoms within one pincer ligand framework.

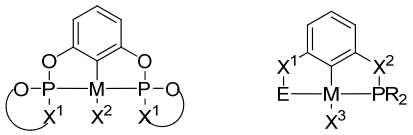
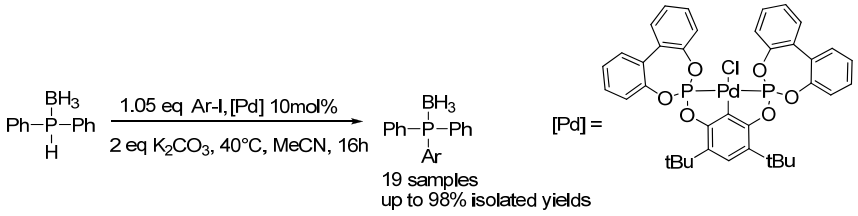


Figure 1. General structure of P'CP'-pincer and PCE-pincer metal complexes (P'CP' indicates an aryl to E-donor bridge different than $–CH_2$-/-CR_2- in the pincer ligand).

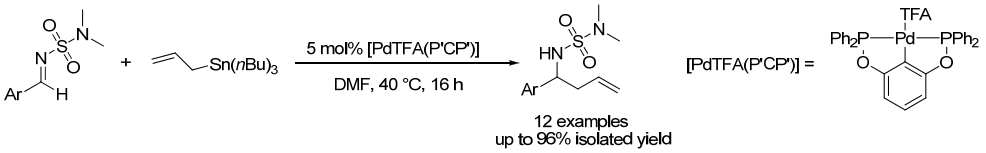
After an overview of the synthesis and catalytic applications of chiral PCP-pincer metal complexes and PCE-pincer metal complexes (including planar chiral complexes) in Chapter 1, the synthesis of a series of mono- and bidentate phosphite ligands and their Pd complexes are described in Chapter 2. These ligands were constructed by reacting 2,2'-biphenol with PCl_3 followed by reaction of the resulting phosphorochloridite with either phenol or 4,6-di-tert-butyl-resorcinol. Palladation of these ligands was accomplished with either $PdCl_2(MeCN)_2$ or $PdCl_2$. The resulting complexes were investigated in C-P cross coupling reactions between diphenylphosphineborane and a variety of different aryl iodides. In particular, the P'CP'-pincer Pd-complex was found to be as active as many other previously reported bidentate phosphine

complexes with a wide scope of substrates (Scheme 1). Additional kinetic investigations have indicated that the phosphite pincer complex merely acts as a precatalyst and that Pd nanoparticles are the actual catalytically active species in these reactions.



Scheme 1. Phosphite P'CP'-pincer Pd-complex catalyzed C-P cross coupling reactions.

In Chapter 3, the P'CP'-pincer (P'=diphenylphosphinite) Pd complex-catalyzed allylation of *N,N*-dimethylsulfamoyl-protected aldimines with allyl(tributyl)stannane was investigated (Scheme 2). The experiments showed that N,N-dimethylsulfamoyl-protected aldimines can be allylated smoothly under mild conditions and isolated in moderate to excellent yields They showed good functional group tolerance, albeit that the isolated yields obtained with these substrates are generally 10-15% lower than in the case of tosyl-protected aldimines. The presence of the strongly electron-donating Me_2N group instead of the *p*-tolyl group most likely decreases the electrophilicity of corresponding aldimine. The *N,N*-dimethylsulfamoyl protected reaction products can be conveniently deprotected by refluxing in 1,3-diaminopropane for 1 h to yield the homoallylic primary amines in high yield (95%). Overall, the present procedure represents an efficient and straightforward approach toward towards the synthesis of homoallylic amines.



Scheme 2. [Pd(TFA)P'CP']-catalyzed homoallylation of aldimines.

Chapter 4 describes the synthesis of novel P-stereogenic P'CP'-pincer palladium complexes derived from (*S*)-(−)-α,α-diphenyl-2-pyrrolidinemethanol and (*S*)-(+)-indolinemethanol via a flexible modular synthetic approach (Figure 2). The P-chiral building block derived from (*S*)-(+)-indolinemethanol is reported here for the first time. Its epimerization energy barrier is high enough to prevent racemization upon heating at 110 °C for 1 h, which illustrates the perspective for employing this building block in further P-chiral ligand design. Interestingly, through X-ray diffraction analysis of the new P'CP'-pincer metal complexes, it was found that the new indoline-

derived P-chiral building block provides an opposite steric congestion with respect to previously reported S-proline derived P-chiral ligands (Figure 2).

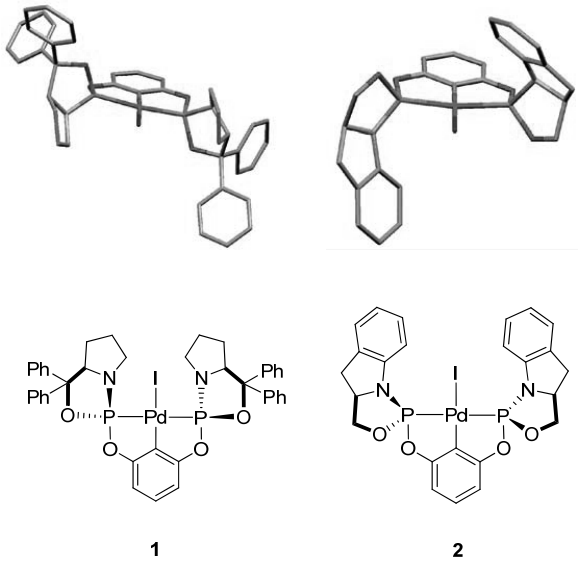
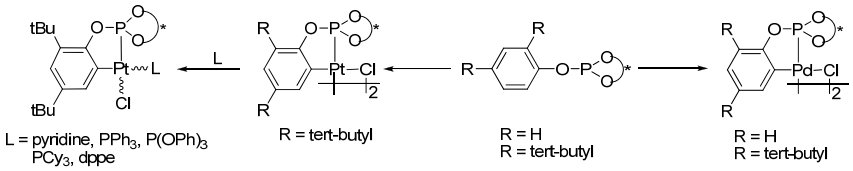


Figure 2. X-ray structures of novel P-chiral P'CP"-pincer Pd complexes.

These new P-chiral P'CP'-pincer palladium complexes were found to be active catalysts in the asymmetric homoallylation of sulfonimines bearing different protecting groups with allyl(tributyl)stannane giving 60-81% yields and up to 33% ee. The stereoselectivities of these reactions were found to be very dependent on both the electronic properties and the geometries of the sulfonimines substrates, and on the geometries of the chiral catalysts. These findings could lead to the synthesis of novel P-chiral pincer metal complexes bearing well-tailored bulky substituents in order to further improve enantioselectivities and yields in these reactions.

In Chapter 5, a series of chiral bis-phosphite complexes and chiral ortho-metallated phosphite complexes have been synthesized by using enantiopure (*R*)-BINOL-derived chiral phosphite ligands, which are easily prepared from (*R*)-BINOL, PCl_3, and either phenol or 2,4-di-*tert*-butylphenol (Scheme 3). It was found that both the bulkiness of these BINOL-derived phosphite ligands and the metal species play important roles in the formation of *C,P*-cyclometallated complexes. Reacting the chiral phosphite ligands with $PdCl_2$ in refluxing toluene furnished the dimeric *C,P*-cyclometallated Pd-complexes in 55-65% yields. In contrast, only the reaction of the chiral phosphite ligand derived from 2,4-di-*tert*-butylphenol with K_2PtCl_4 yielded the dimeric *C,P*-cyclometallated Pt complex in a similar yield. The latter complex smoothly reacts with monodentate or bidentate ligands to generate the corresponding monomeric ortho-platinated

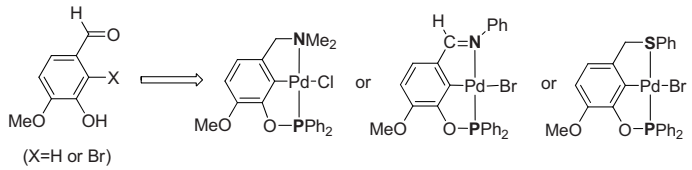
complexes. ^{31}P NMR and X-ray diffraction analyses revealed that strong electron-withdrawing or moderately electron-donating ligands are preferentially located at the *cis*-position with respect to the BINOL-phosphite moiety in these complexes. The potential of employing the *ortho*-platinated complex either as a resolution reagent or as a chiral NMR shift reagent was shown by the resolution of (*rac*)-α-methylbenzylamine.



Scheme 3. Chiral ortho-palladated and -platinated arylphosphite complexes.

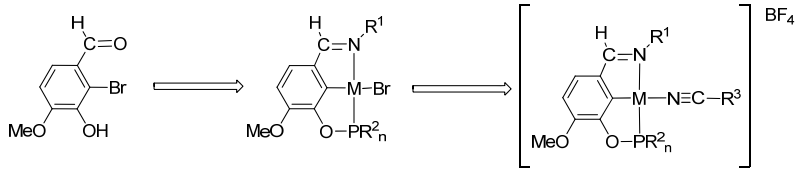
Chapter 6 describes the synthesis of a series of PCN- and PCS-pincer palladium complexes starting from isovanillin as the common precursor (Scheme 5). Initial reduction of the aldehyde moiety of isovanillin produced a benzyl alcohol moiety, which was converted into a benzyl bromide grouping. Nitrogen and sulfur donor groupings were introduced by nucleophilic substitution reactions on the benzyl bromide. Alternatively, different imine nitrogen donor groupings were directly introduced by reacting isovanillin with primary amines. In each case different phosphorus donor groupings were introduced by reacting the arylhydroxyl group with commercially available phosphine chlorides. Palladation of the resulting set of ligands was carried out by reacting the ligands either with $PdCl_2$ via a C-H activation mode (X = H) or with $[Pd_2(dba)_3 \cdot CHCl_3]$ via an oxidative insertion mode (X = Br; Scheme 4). The catalytic activities of the resulting complexes were investigated in homoallylation reactions of aldehydes with allyl(tributyl)stannane and of their corresponding cationic complexes in the stannylation/homoallylation tandem reaction of aldehydes or sulfonimines with allyl chlorides and hexamethyldistannane. The catalytic activities of the complexes were found to be very dependent on the combination of different donor moieties. It was found that the PCS-pincer Pd-complex outperformed the PCN-pincer Pd-complexes in both homoallylation and tandem stannylation/homoallylation. In homoallylation reaction, good to very good product yields (~70-95%) were obtained with electron-deficient electrophiles, although electron-enriched electrophiles gave rather low yields (~30%). In the tandem reaction, the product yields were not significantly affected by using more electron-enriched sulfonimines as electrophiles. The cationic PCS-pincer Pd complex was even able to catalyze the tandem reactions of strongly electron-enriched *N,N*-dimethylsulfamoyl-protected sulfonimines with moderate to promising yields (45-60%). These allylsulfonamides belong to a novel class of allyl compounds that allow facile

deprotection to yield primary allylamines (see Chapter 3). Clearly, PCS-complex Pd complexes could take advantage of the combination of S and P donor atoms.



Scheme 4. PCN- and PCS-pincer Pd complexes derived from isovanillin.

Chapter 7 describes the synthesis of a different series of PCN-pincer palladium and platinum complexes which were isolated in moderate to good yields (55-88%) by following the synthetic route reported in Chapter 6 (Scheme 5). Their corresponding cationic complexes bearing acetonitrile or acrylonitrile as co-ligands were easily prepared in good to excellent yields (88-98%) by reacting neutral pincer complexes with $AgBF_4$ in CH_2Cl_2 in the presence of acetonitrile or acrylonitrile.



Scheme 5. PCN-pincer Pd or Pt complexes.

Several NMR and IR studies were carried out in order to scale the relative Lewis acidities of the cationic complexes. Standard ^{1}H and ^{13}C NMR experiments in which the δ (α-CH) is monitored and IR experiments in which the $\upsilon(C\equiv N)$ are monitored did not provide a good measure of the relative Lewis acidity of the complexes. In contrast, the ^{31}P-^{195}Pt NMR coupling constants were a good measure. Both the PCN-pincer Pd- and Pt-complexes were found to be active catalysts for the aza-Michael addition between morpholine and acrylonitrile. Reaction profiles showed the Pd-complexes to be the more active catalysts than Pt-complexes. In addition, the relative order of activity amongst the Pd-complexes pointed out the complexes bearing more electron-enriched pincer ligands are more active catalysts. For a general Lewis acid-catalyzed reaction, such as the aza-Michael reaction studied here, this strongly pointed at the product releasing step to be the rate-determining as opposed to the Lewis acid promoted C–N bond forming step.

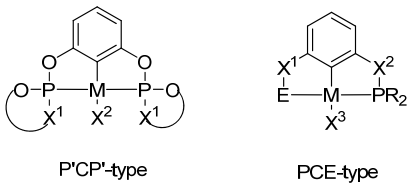
General Conclusions and Perspectives

This thesis reports about a novel series of PCN- and PCS-pincer Pd- and Pt-complexes, phosphite P'CP'-pincer Pd complexes, *C,P*-cyclometalated Pd- and Pt-complexes, and P-chiral phosphoramidite-pincer Pd-complexes. It provides an overview of the fine-tuning of the geometrics and electronic properties of these phosphorus-based pincer metal complexes through appropriate organic transformations of the pincer ligand. The newly reported pincer complexes were found to be active catalysts in C-P cross coupling, homoallylation, tandem catalytic, and aza-Michael addition reactions. Several aspects of this study deserve special attention. First of all, the development of new P-chiral pincer complexes derived from readily available chiral amino alcohols provide access to a library of new P-chiral phosphoramidite pincer complexes with great potential in enantioselective catalysis. Moreover, the synthetic protocol toward a series of electronically and structurally fine-tuned PCE-pincer metal complexes (E = N and S) using isovanillin as the common intermediate holds a great promising for the synthesis of new tailor-made ECE'-type pincer complexes. The combination and possible cooperativity of different E-donors has proven potential to alter the catalytic activities of pincer complexes. The further development of PCE-pincer complexes could, therefore, provide a stepping stone to improve and extend the catalytic application of pincer metal complexes.

Samenvatting

De opmerkelijke katalytische eigenschappen van PCP-tang metaalcomplexen in een scala aan verschillende katalytische reacties heeft in de laatste decennia geleid tot een verhoogde interesse in de synthese en nieuwe toepassingen van dit type organometaalcomplexen. Een recente veel belovende ontwikkeling op dit gebied is het gebruik van chirale PCP-tang metaalcomplexen in de katalytische enantioselectieve synthese.

Het onderzoek beschreven in dit proefschrift is gericht op het ontwerp, de synthese en de verdere ontwikkeling van fosforamidiet P'CP'-tang metaalcomplexen (Figuur 1). Deze complexen zijn vervolgens onderzocht op hun katalytische activiteit in een aantal verschillende katalytische reacties. Recentelijk heeft ook de ontwikkeling van ECE'-type (E ≠ E') tangmetaalcomplexen veel aandacht gekregen. Een nadeel van dit type ligand is dat de synthese ervan moeilijk en erg tijdrovend kan zijn. Een nieuwe, flexibele en efficiënte syntheseroute voor PCE-type (E = N of S) tangmetaalcomplexen is daarom ontwikkeld en beschreven in dit proefschrift. Deze PCE-tang metaalcomplexen zijn vervolgens onderzocht op hun katalytische activiteit in organisch chemische transformaties en zijn vergeleken met de activiteit van de standaard tangmetaalcomplexen.

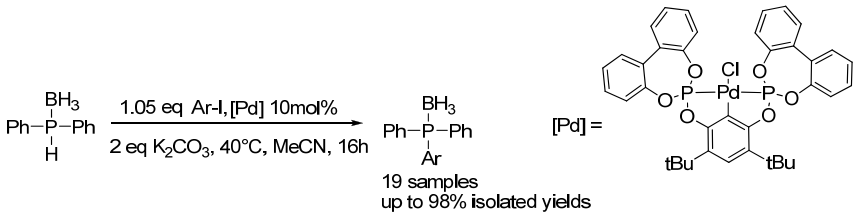


Figuur 1. De algemene structuur van P'CP'- en PCE-tangmetaalcomplexen (P'CP' geeft een aryl naar E-donor brug aan die anders is dan $-CH_2-/-CR_2-$ in het tangligand).

Hoofdstuk 1 van dit proefschrift geeft een overzicht van de synthese en katalytische toepassingen van chirale PCP-tang en PCE-tangmetaalcomplexen, inclusief planair chirale complexen.

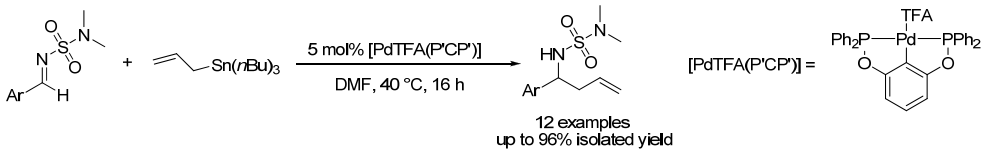
De synthese van een serie mono- en bidentaat fosfietliganden en hun overeenkomstige Pd-complexen wordt beschreven in *Hoofdstuk 2*. Deze liganden werden gesynthetiseerd door 2,2'-biphenol te laten reageren met PCl_3 tot de vorming van een fosforochloridiet. Dit reactieproduct is vervolgens omgezet naar het gewenste fosfietligand door middel van een reactie met fenol of 4,6-di-tert-butyl-resorcinol. De synthese van de gewenste palladiumcomplexen werd

bewerkstelligd door reacties van de betreffende liganden met $PdCl_2(MeCN)_2$ of $PdCl_2$. De complexen die op deze wijze werden verkregen zijn onderzocht op hun activiteit als katalysator in de C–P koppelingsreacties tussen difenylfosfineboraan en verschillende aryljodides. Het P'CP'-tang Pd-complex bleek een gelijke katalytische activiteit te bezitten als een aantal andere tangmetaalcomplexen beschreven in de literatuur. Daarnaast tolereert het complex een brede varieteit aan aryljodidesubstraten (Schema 1). Verder kinetisch onderzoek aan deze katalytische reactie toonde aan dat de fosfiet-tang metaalcomplexen voornamelijk fungeren als prekatalysator en dat de actieve deeltjes tijdens de katalyse voornamelijk bestaan uit palladiumnanodeeltjes.



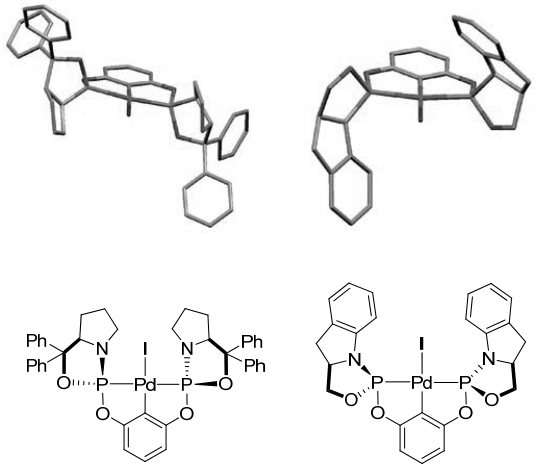
Schema 1. Fosfiet P'CP'- tang Pd- complexen als katalysator in C–P koppelingsreacties.

Hoofdstuk 3 beschrijft het gebruik van een P'CP'-tang (P'=difenylfosfiniet) Pd-complex als katalysator voor de allylering van *N,N*-dimethylsulfamoyl-beschermde aldimines met allyl(tributyl)stannaan (Schema 2). De experimenten lieten zien dat *N,N*-dimethylsulfamoyl-beschermde aldimines eenvoudig en onder milde condities omgezet kunnen worden tot hun allylderivaten in redelijke tot zeer goede opbrengsten. Het tangmetaalcomplex tolereert daarbij een grote variatie aan functionele groepen in de substraten, ondanks dat de opbrengst van de geïsoleerde producten over het algemeen 10 tot 15% lager was dan in de gevallen van de tosyl-beschermde aldimines. De aanwezigheid van de sterke elektrondonerende Me_2N-groep in plaats van de *p*-tolyl groep verlaagt de electrofiliciteit van het overeenkomstige aldimine en is zeer waarschijnlijk van invloed op deze reactie. De *N,N*-dimethylsulfamoyl-beschermde reactieproducten kunnen eenvoudig en in hoge opbrengsten (95%) en in een korte reactietijd ontschermd worden door middel van verhitten in 1,3-diaminopropaan als oplosmiddel. Deze gecombineerde procedures zijn een nieuwe en efficiëntere methode voor de synthese van gesubstitueerde homoallylische amines.



Schema 2. [Pd(TFA)P'CP']-gekatalyseerde homoallylering van aldimines.

Hoofdstuk 4 beschrijft de synthese van P-stereogene P'CP'-tang palladiumcomplexen op basis van (*S*)-(−)-α,α-difenyl-2-pyrrolidinemethanol en (*S*)-(+)-indolinemethanol door middel van een flexibele synthesemethode (Figuur 2). Het gebruik van de P-chirale uitgangstof verkregen uit (*S*)-(+)-indolinemethanol wordt voor het eerst beschreven in dit proefschrift. Het verwarmen van een oplossing van deze verbinding tot 110 °C gedurende 1 uur leidt niet tot racemisatie van deze verbinding, wat deze verbinding tot een veelbelovende P-chirale uitgangsstof maakt. De P'CP'-tang palladiumcomplexen die op basis van bovengenoemde uitgangsmaterialen gesynthetiseerd werden vertonen opmerkelijke geometrische verschillen. Zoals aangetoond door röntgenkristallografische analyse van beide nieuwe P'CP'-tang metaalcomplexen, resulteert het gebruik de nieuwe, P-chirale indolinebouwsteen in een ligandconformatie rond om Pd die tegenovergesteld is aan die zoals die verkregen wordt met de *S*-proline P-chirale liganden beschreven in de literatuur (Figuur 2).

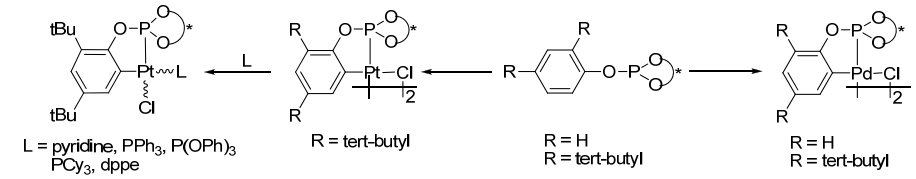


Figuur 2. X-ray structuren van nieuwe P-chiral P'CP"-pincer Pd complexen.

Deze nieuwe P-chirale P'CP'-tang palladiumcomplexen bleken actieve katalysatoren te zijn in de asymmetrische homoallylering van diverse beschermde sulfonimines met allyl(tributyl)stannaan met opbrengsten van 60-81% en een enantioselectiviteit tot 33%. De stereoselectiviteit van deze reacties bleek zeer afhankelijk te zijn van zowel de elektronische eigenschappen en de geometrie van de sulfoniminesubstraten, als van de geometrie van de chirale katalysatoren. Deze bevindingen kunnen leiden tot de synthese van nieuwe P-chirale tangmetaalcomplexen met op maat gemaakte (grotere) substituenten om zo de enantioselectivitieit en de opbrengsten in deze reacties verder te kunnen vergroten.

De synthese van een serie chirale bisfosfietcomplexen en van chirale ortho-gemetalleerde fosfietcomplexen, uitgaande van chirale fosfietliganden gebaseerd op (*R*)-BINOL, is beschreven in *Hoofdstuk 5*. De (*R*)-BINOL-gebaseerde chirale phosphietliganden werden verkregen door (*R*)-BINOL te laten reageren met PCl_3 en fenol of 2,4-di-tert-butylfenol (Schema 3). Uit deze studie is gebleken dat zowel de grootte van de BINOL-fosfietliganden als het metalleringsreagens een belangrijke rol spelen in de vorming van de uiteindelijke *C,P*-cyclogemetalleerde complexen. De *C,P*-cyclogemetalleerde Pd-complexen werden gesynthetiseerd door de chirale fosfietliganden te laten reageren met $PdCl_2$ in kokende tolueen (55-65% opbrengst). Voor de platina-complexen blijkt dat alleen het complex gemaakt uit de reactie van het chirale fosfietligand gebaseerd op 2,4-di-tert-butylphenol met K_2PtCl_4, resulteert in een dimeer, *C,P*-cyclogemetalleerde Pt-complex. Dit complex reageert onder milde omstandigheden met monodentaat en bidentaat liganden tot de overeenkomstige mono Pt-complexen.

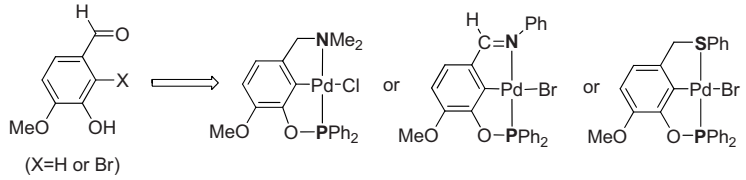
^{31}P-NMR en röntgenkristallografische analyse lieten zien dat sterk elektronzuigende of elektrondonerende liganden voorkeur hebben voor een cis-positie ten opzichte van de BINOL-fosfiet groep in deze complexen. De toepassingsmogelijkheden van de Pt complexen als een resolutie agens of als chiraal shiftreagens in NMR werden aangetoond door deze toe te passen op racemisch α-methylbenzylamine.



Schema 3. Chirale Pd- en Pt-arylphosphietcomplexen.

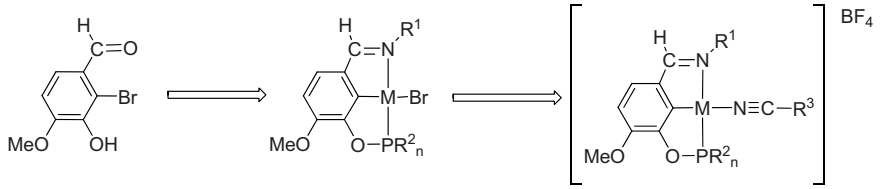
Hoofdstuk 6 beschrijft de synthese van een aantal PCN- en PCS-tangmetaalcomplexen uitgaande van isovaniline (Schema 5). Reductie van de aldehydegroep in isovaniline resulteerde in een alcoholgroep die verder omgezet kon worden tot een benzylbromidegroep. Stikstof- en zwaveldonorgroepen werden vervolgens geïntroduceerd door middel van nucleofiele substitutiereacties. De reactie van de aldehydegroep in isovanilline met primaire amines vormt een alternatieve route voor stikstofderivaten. In alle gevallen werden de arylhydroxylgroepen gefunctionaliseerd met commercieel verkrijgbare fosfinechloriden. Palladering van de liganden werd daarna bewerkstelligd door de liganden te laten reageren met $PdCl_2$ (C-H activering, X = H) of met $[Pd_2(dba)_3 \cdot CHCl_3]$ (oxidatieve additie, X = Br; Scheme 4)). De katalytische activiteit van deze nieuwe tangcomplexen werd onderzocht in de reactie van aldehyden met allyl(tributyl)stannaan. Bovendien werden de overeenkomstige kationische complexen

onderzocht op hun activiteit als katalysator in de stannyllering/homoallylering tandemreactie van aldehyden of sulfoniminen met allylchloriden en hexamethyldistannaan. De katalytische activiteit van de complexen bleek erg afhankelijk te zijn van de combinatie van de verschillende donoratomen in het tangligand. Uit het onderzoek bleek tevens dat de PCS-tang Pd-complexen veruit de beste resultaten gaven in zowel de homoallylering als in de tandemreactie. In de katalystische homoallylerings reactie werden goede tot zeer goede conversies bereikt (~70-95%) met elektron-arme electrofielen, terwijl het gebruik van elektronrijke electrofielen lage conversies opleverde (~30%). De conversies van de tandemreacties werden niet beïnvloed door het gebruik van elektronrijke sulfonimines. Het kationische PCS-tang Pd-complex was zelfs in staat om de tandemreactie met sterk elektronrijke *N,N*-dimethylsulfamoyl-beschermde sulfonimines te katalyseren met redelijke tot gemiddelde opbrengsten (45-60%). Deze allylsulfonamides behoren tot een interessante groep allylverbindingen die toegepast kunnen worden als eenvoudige beschermingsgroep van allylamines (zie *Hoofdstuk 3*).



Schema 4. PCN- en PCS-tang Pd-complexen gemaakt vanuit een isovanillinederivaat.

In *Hoofdstuk 7* wordt de synthese van verschillende PCN-tang Pd- en Pt-complexen beschreven. Daarbij is gebruik gemaakt van de methode zoals beschreven in *Hoofdstuk 6*. De complexen werden verkregen in gemiddelde tot goede opbrengsten (55-88%). De overeenkomstige kationische complexen die een acetonitril danwel een acrylonitril co-ligand bevatten, werden gesynthetiseerd in hoge opbrengsten (88-98%) door de neutrale complexen te laten reageren met AgBF4 in CH2Cl2 in de aanwezigheid van acetonitril of acrylonitril.



Schema 5. PCN-tang Pd- en Pt-complexen.

De Lewiszuursterkte van deze complexen werd onderzocht met behulp van NMR en IR spectroscopie. Standaard ^{1}H and ^{13}C NMR experimenten waarin de (-CH) van het nitril co-ligand

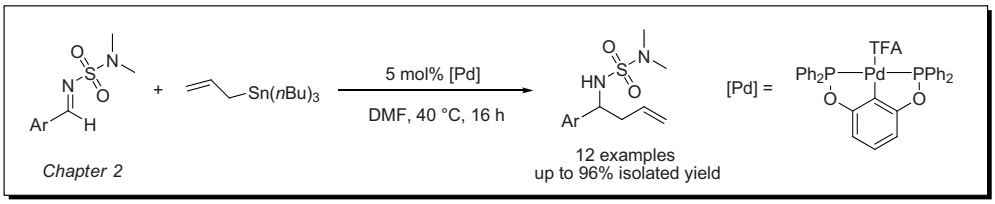
werd bestudeerd en IR-spectroscopisch onderzoek naar de verschuiving van de υ(C≡N) vibratie resulteerde niet in voldoende informatie over de relatieve Lewiszuursterkte van de complexen. In tegenstelling tot de genoemde methoden bleek de analyse van ^{31}P-^{195}Pt NMR koppelingsconstantes van de complexen wel een goede methode te zijn om de Lewiszure eigenschappen van de complexen te onderzoeken. Zowel de PCN-tang Pd- als de Pt-complexen bleken actief te zijn als katalysator in de aza-Michael additiereactie tussen morfoline en acrylonitril, waarin de Pd-complexen het meest actief waren. Tevens bleek uit de volgorde van activiteit van de Pd-tangcomplexen dat de complexen met een elektronrijk tangligand een hogere activiteit als katalysator bezitten. Voor een algemene Lewiszuur gekatalyseerde reactie, zoals bijvoorbeeld de hier onderzochte aza-Michael additie, duiden deze bevindingen sterk in de richting van de dissociatie van het product als snelheidbepalende stap, in tegenstelling tot de verwachte Lewiszuur-versnelde vorming van de C-N binding.

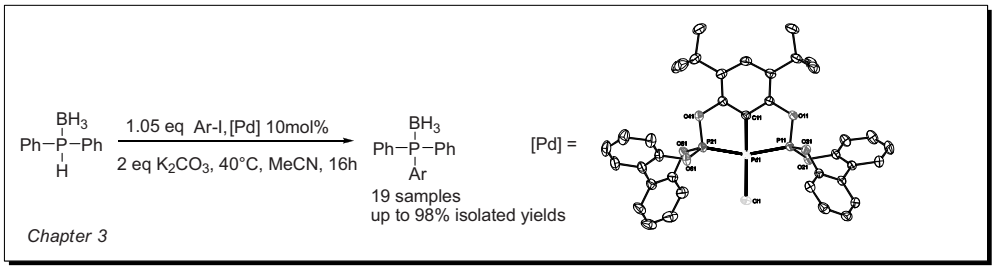
Algemene Conclusies en Perspectief

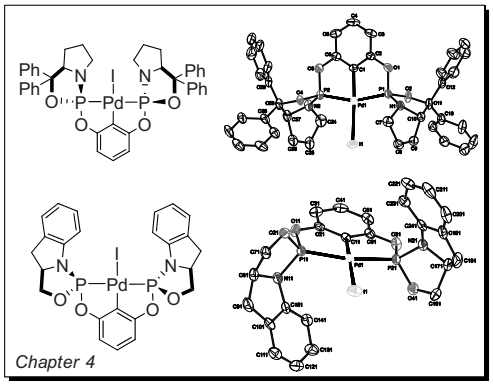
De synthese en eigenschappen van nieuwe PCN- en PCS-tang Pd- en Pt-complexen, fosfiet-P'CP'-tang Pd-complexen, *C,P*-cyclogemetalleerde Pd- en Pt-complexen en P-chirale fosforamidiet-tang Pd-complexen zijn beschreven in dit proefschrift. De ontwikkelde methoden maken het mogelijk om de geometrische en elektronische eigenschappen van deze fosfor-type tangmetaalcomplexen te verfijnen door middel van de juiste organische transformaties op het tangligand. De nieuwe tangmetaalcomplexen zijn actief als katalysator in C-P koppelingsreacties, homoallyleringen, stannyleringen, tandemreacties, en aza-Michael additiereacties.

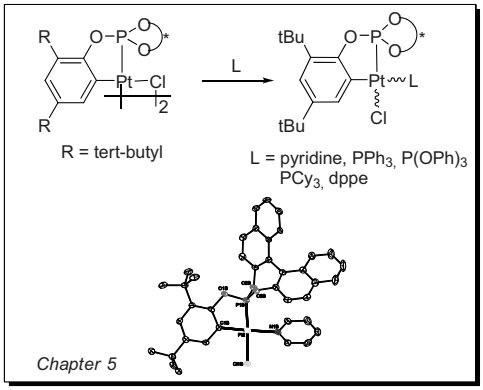
Een aantal interessante aspecten die uit deze studie naar voren zijn gekomen verdienen extra aandacht. Allereerst geven de ontwikkelde methoden voor de synthese van P-chirale tangcomplexen vanuit eenvoudig toegankelijke chirale aminoalcoholen toegang tot een serie nieuwe P-chirale fosforamidiet-tangcomplexen die te gebruiken zijn als enantioselectieve katalysatoren. Ten tweede geven de methoden voor de synthese van verschillende elektronisch en geometrisch verfijnde PCE-tang metaalcomplexen (E = N of S) uitgaande van isovanillinederivaten eenvoudige en goede mogelijkheden voor de synthese van op maat gemaakt ECE'-tangcomplexen. De combinatie van de positieve samenwerking en interactie van de verschillende donor E-atomen in het tangmetaalcomplex systeem geeft, tenslotte, de mogelijkheid tot het verder verfijnen en optimaliseren van de katalytische activiteiten van tangmetaalcomplexen. De verdere ontwikkeling van de in dit proefschrift beschreven PCE-tangmetaalcomplexen kan dan ook ook gezien worden als een interessante en uitdagende bijdrage tot de verbetering en toepasbaarheid van de katalytische eigenschappen van tangmetaalcomplexen.

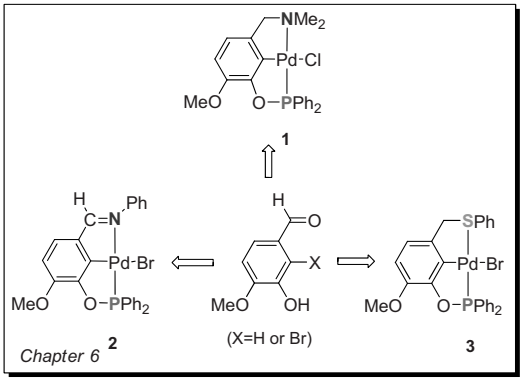
Graphical Abstract

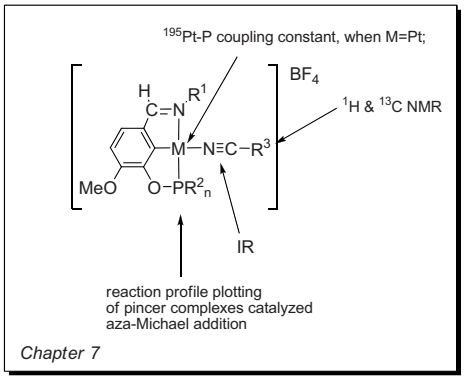












Acknowledgement

This thesis arose in part out of years of research that has been done since I came to Chemical Biology and Organic Chemistry group at University Utrecht. By that time, I have worked with a great number of people whose contribution in assorted ways to the research and the making of the thesis deserved special mention. It is a pleasure to convey my gratitude to them all in my humble acknowledgment.

In the first place, I would like to express my sincere appreciation and gratitude to Prof. dr. Gerard van Koten and Prof. dr. Bert Klein Gebbink for their support, guidance and encouragement during more than four years of this thesis's work. Above all and the most needed, they provided me unflinching encouragement and support in various ways. Their truly scientist intuition has made them as a constant oasis of ideas and passions in science, which exceptionally inspire and enrich my growth as a student, a researcher and a scientist want to be. I am indebted to them more than they know. Their uncompromising quest for excellence significantly shapes everyone in the group.

I gratefully acknowledge Dr. Gerard van Klink for his advice, supervision, and crucial contribution during the first two and a half years of my Ph.D study, which made him a backbone of this research and so to this thesis. His involvement with his originality has triggered and nourished my intellectual maturity that I will benefit from, for a long time to come.

I gratefully thank Prof. dr. Adriaan J. Minnaard at University of Groningen for his guidance and assistance in the joint project and his constructive comments on the publication. I enjoyed the cooperation very much and I am grateful in every possible way and hope to keep up our collaboration in the future.

I was extraordinarily fortunate in having Dr. Maxime Siegler, Dr. Martin Lutz and Prof. dr. Anthony L. Spek on the same floor. Without their kind help and guidance, I could never have had all those beautiful crystal structures.

My sincere appreciation also extends to all my colleagues and others who have provided assistance at various occasions. Milka, thank you very much for a lot of paper work in the course of preparing this thesis and the promotion. Henk, thank you very much for buying many chemicals and for many useful tips in manipulations with your excellent experience. It is a pleasure to express my gratitude wholeheartedly to Morgane and her parents for their kind hospitality during the unforgettable stay in Renne, France. Kees, thank you very much for helping me translating the summary of this thesis into

Dutch. Furthermore, I would like to thank Prof. dr. Shengmin Ma for creating a pleasant working atmosphere in Shanghai during my short visit in China Academy of Sciences in 2007.

Collective and individual acknowledgments are also owed to my colleagues at University Utrecht whose present somehow perpetually refreshed, helpful, and memorable. Many thanks go in particular to Harm, Sylvestre, Kees, Bart, Guido, Sipke, Birgit, Dennis, Maaike, Elena, Niels, Ties, Aidan, Erwin, Marcel, Yves, Sohail, Vital, Marcella, Nilesh, Pieter, Silvia and Preston for their advice and their willingness to share their bright thoughts with me, which were very fruitful for shaping up my ideas and research.

Where would I be without my family? I owe special gratitude to my family for continuous and unconditional support of all my undertakings, scholastic and otherwise.

My parents deserve special mention for their inseparable support and prayers. My Father, Fang Li, in the first place is the person who put the fundament my learning character, showing me the joy of intellectual pursuit ever since I was a child. My Mother, Meiyun Wang, is the one who sincerely raised me with her caring and gently love. I miss her very much.

Words fail me to express my appreciation to my wife Jin whose dedication, love and persistent confidence in me, has taken the load off my shoulders. I owe her for being unselfishly let her intelligence, passions, and ambitions collide with mine. Therefore, I would also thank my parents-in-law for letting me take their daughter's hands in marriage, and accepting me as a member of the family, warmly.

Finally, I would like to thank everybody who was important to the successful realization of thesis, as well as expressing my apology that I could not mention personally one by one.

Curriculum Vitae

Jie Li was born on the 26th of September 1978 in Shanghai, China. After graduating from high school in 1997, he studied Pharmaceutical Engineering at East China University of Science and Technology. In 2002, he got a fellowship from Rhodia and went to Ecole Nationale Supérieure des Ingénieurs en Arts Chimiques et Technologiques, Toulouse, France, where he obtained his MSc with a major in Chemical Engineering and a minor in Agrochemistry in 2004.

During master degree study, he completed two internships at the Research Center of Rhodia in Lyon, where he worked on research projects about Pd-catalyzed C-C cross coupling reactions with Dr. Johann Vastra and new phosphite ligands for asymmetric hydrogenation with Dr. Jean-Marc Paris.

In December 2004, he started his Ph.D study at the Utrecht University, under supervision of Prof. dr. Bert Klein Gebbink and Prof. dr. Gerard. van Koten. There he developed a novel series of phosphite P'CP'-pincer Pd-complexes, P-chiral phosphoramidite-pincer Pd-complexes, PCN- and PCS-pincer Pd- and Pt-complexes, which were applied as catalysts in C-P cross coupling, homoallylation, tandem catalysis, and aza-Michael addition reactions.

Part of the work described in this thesis were presented at several national (N3C 2005-2008) and international congresses (IFOMC 2007, Heidelberg & ICOMC 2008, Rennes).

List of Publications

Asymmetric PCP-Pincer and PCE-Pincer Metal Complexes: Synthesis and Applications.
Jie Li, Gerard van Koten , Robertus J. M. Klein Gebbink
manuscript in preparation (Chapter 1)

P'CP'-Pincer palladium complex catalyzed allylation of N,N-dimethylsulfamoyl-protected aldimines.
Jie Li, Adriaan J. Minnaard, Robertus J. M. Klein Gebbink , Gerard van Koten. (*Chapter 2*)
Tetrahedron letts. **2009***,* 50, 2232-2235.

Novel Phosphite Palladium Complexes and their Application in C–P Cross Coupling Reactions.
Jie Li, Martin Lutz, Anthony L. Spek, Gerard P.M. van Klink, Gerard van Koten, Robertus J. M. Klein Gebbink
To be submitted for publication (Chapter 3)

Chiral Amino Alcohol Derived Bis-Phosphoramidite Pincer Metal Complexes and Their Applications in Asymmetric Allylation of Aldimines.
Jie Li, Martin Lutz, Anthony L. Spek, Gerard P.M. van Klink, Gerard van Koten, Robertus J. M. Klein Gebbink
To be submitted for publication (Chapter 4)

Chiral Ortho-palladated and -platinated Arylphosphite Complexes.
Jie Li, Maxime A. Siegler, Martin Lutz, Anthony L. Spek, Robertus J. M. Klein Gebbink, Gerard van Koten
submitted for publication (Chapter 5)

PCN- and PCS-Pincer Palladium Complexes as Tandem Catalysts in Homoallylation Reactions.
Jie Li, Maxime Siegler, Martin Lutz, Anthony L. Spek, Robertus J. M. Klein Gebbink, Gerard van Koten
submitted for publication (Chapter 6)

PCN-Pincer Palladium and Platinum Complexes [MBr{C_6H_2-(OPR'$_2$)-2-(OMe)-3-(CH=NR)-6}] and Investigation of their Relative Lewis Acidity.
Jie Li, Maxime Siegler, Martin Lutz, Anthony L. Spek, Gerard P.M. van Klink, Gerard van Koten, Robertus J. M. Klein Gebbink
manuscript in preparation (Chapter 7)

Synthesis and Resolution of Planar–Chiral Ruthenium–Palladium Complexes with ECE'-Pincer Ligands.
Sylvestre Bonnet, Jie Li, Maxime A. Siegler, Lars S. von Chrzanowski, Anthony L. Spek, Gerard van Koten, and Robertus J. M. Klein Gebbink.
Chem. Eur. J. **2009**, 15, 3340-3343.