Recent developments in the applications of palladium complexes bearing N-heterocyclic carbene ligands

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Abbreviations

AAS	atomic absorption spectroscopy
acac	acetylacetonate
atm	atmosphere
BINAM	binaphthyl-2,2′-diamine
Cy	cyclohexyl
dba	dibenzylideneacetonate
DCM	dichloromethane
DME	1,2-dimethoxyethane
DMSO	dimethylsulfoxyde
ee	enantiomeric excess
GC	gas chromatography
ICP-AES	inductively coupled plasma-atomic emission spectrometry
^{i}Pr	*iso* propyl
LHMDS	bis(trimethylsilyl)amide
m	*meta*
Mes	1,3,5-trimethylphenyl
MS	molecular sieves
NHC	N-heterocyclic carbene
o	*ortho*
OAc	acetate
OTf	trifluoromethanesulfonate
p	*para*
PAN	polyacrylonitrile
PDMS	polydimethylsiloxane
RT	room temperature
SBA-15	Santa Barbara Amorphous type material
^{t}Bu	*tert* butyl
TEG	tetraethylene glycol
TEOS	tetraethyl orthosilicate
THF	tetrahydrofurane
TMSCN	trimethylsilyl cyanide
TOF	turn over frequency
Ts	(4-methylphenyl)sulfonyl

Abstract

N-heterocyclic carbene (NHC) ligands have become ubiquitous ligands in the preparation of metal complexes with new catalytic applications. Mainly due to their applications in C-C bond formation reactions, a plethora of novel palladium-NHC complexes has been described, and a large number of review articles describing their chemistry have been published. In an attempt to provide a new vision of the topic, this article will focus our attention on the development of new palladium complexes with NHC ligands, paying special attention to their applications in catalytic processes other than the classical C-C coupling reactions. This article is divided in the following sections: i) design of reusable Pd-NHC complexes, ii) latest advances in the use of Pd-NHC complexes in homogenous catalysis and, iii) other applications of Pd-NHC complexes.

Keywords: N-heterocyclic carbenes, palladium, catalysis, homogeneous, reciclability, asymmetric, biomedical

1. Introduction

Over the last two decades, the popularity of N-heterocyclic carbene ligands (NHC) has dramatically increased mainly due to their use in the development of very active and versatile catalysts. Many aspects of the chemistry of NHC ligands have been extensively studied and comprehensively reviewed from any possible perspective including their preparation,[1-4] stability,[5] stereoelectronic properties[6-10] and coordination strategies.[4, 11, 12] The numerous applications of NHCs as supporting ligands of late transition metals[13-16] as well as in organocatalysis[17, 18] have been recently overviewed. The structural features and catalytic applications of metal complexes bearing poly-NHCs have also been reviewed.[19-23] Some excellent reviews have appeared dealing with the design of chiral-NHC systems and their applications in asymmetric catalysis.[24-27] Moreover, monographs[28, 29] and special issues[30, 31] have been entirely devoted to this research area.

More specifically, the chemistry of palladium-NHC complexes has attracted great interest due to their application in cross-coupling reactions and hence, is under continuous development. Palladium is, along with ruthenium, the most widely used transition metal with NHC ligands. Besides cross-coupling reactions, Pd-NHC systems display remarkable performances in many other organic transformations such as polymerization, C-H activation processes or olefin hydrogenation. The numerous applications of Pd-NHC systems have been comprehensively reviewed.[32-38]

The development of new Pd-NHC complexes and the study of their applications are so fast that new achievements are obtained every year. Although some overlap with the already published review articles is inevitable, we will try to focus on the most recent examples that have appeared in the literature, and will give an especial emphasis to catalytic examples that differ from the classical C-C bond formation processes.

We have organized this review article in three chapters. The first chapter deals with the design of reusable Pd-NHC complexes using different strategies. These strategies include the support of the Pd-NHC complex on a solid surface that can be separated from the reaction mixture once the reaction is complete, or the use of alternative solvents such as water, which allows the separation of the catalytic system by means of filtration or liquid-liquid extraction.

Trying to cover new aspects of the applications of Pd-NHC complexes in homogeneous catalysis, the second chapter includes palladium-catalyzed processes such as carbon-nitrogen and carbon-sulphur bond formation reactions, reduction and oxidation processes, and transformations through C-H activation. This chapter also includes the most recent examples of chiral Pd-NHC complexes applied to asymmetric catalysis and the design of new complexes with NHC-based linearly opposed ligands. The third chapter deals with other interesting applications described for Pd-NHC complexes.

2. Development of reusable palladium NHC-based catalysts

The green chemistry definition proposed by Anastas and Warner as "*the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products*"[39] has encouraged the scientific community to look for efficient ways to separate homogenous catalysts from the reaction media and their subsequent recycling.

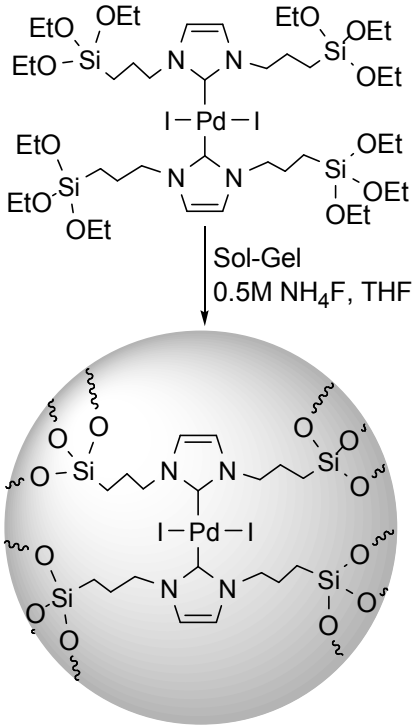
As stated in the introduction, organometallic NHC-based complexes have demonstrated their wide scope of application and thus, their usefulness in the synthesis of complex and valuable molecules. These important applications make NHC ligands good candidates for the preparation of reusable catalysts.

In this chapter, we will focus on the last strategies employed for catalyst recovery. Catalyst functionalisation and immobilization onto a solid support allows recycling by filtration. Additionally, the use of alternative solvents such as water, fluorinated solvents or ionic liquids has attracted great interest, as they allow the separation of the products from the reaction media by easy liquid-liquid extraction.

2.1. Supported Pd-NHC complexes and catalytic applications

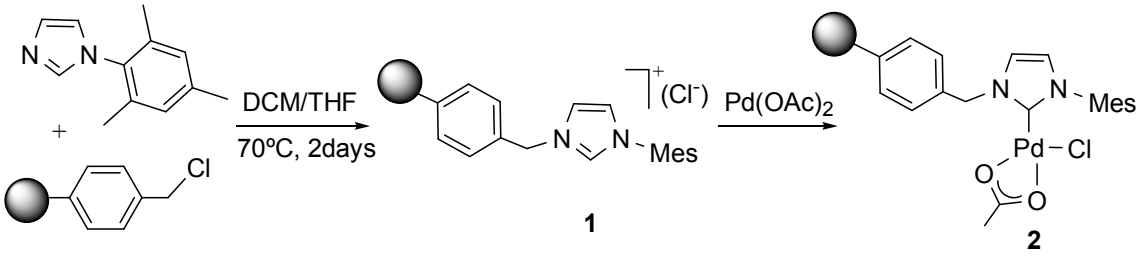
NHC-based complexes have been grafted onto different supports such as soluble and insoluble poly(styrene)s, silica, resins and clays. Many examples of supported Pd-NHC complexes can be found in the literature and these have been reviewed.[16, 40] The more recent examples will be discussed here.

In 2008, Varma and co-workers described the synthesis of a Pd-NHC organic silica (Scheme 1) and its application in the Heck and Suzuki carbon-carbon bond coupling reactions.[41] The synthesis of the organic silica did not require the use of any sol-gel precursor, thus increasing the number of catalytically active sites.



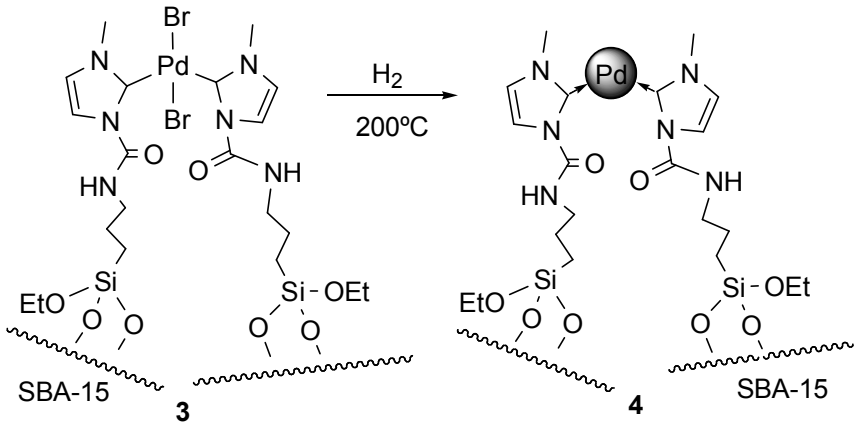
Scheme 1

As depicted in Scheme 2, macroporous polystyrene-supported (MPS) 1-mesitylimidazolium chloride **1** was prepared by reaction of macroporous chloromethyl polystyrene with 1-mesitylimidazole. Subsequent reaction with $Pd(OAc)_2$ afforded MPS-supported palladium system **2**, which was tested in the Suzuki reaction.[42] The immobilized palladium complex showed good catalytic activity in the coupling of aryl bromides and deactivated aryl chlorides with phenylboronic acid. More importantly, the catalytic activity (94 % isolated yield) and the initial catalyst loading levels (0.08 mmol/g) on the support remained almost unchanged after five runs. A small amount of leached palladium metal was detected in the filtrates by ICP-AES analysis.



Scheme 2

The immobilization of palladium complexes or nanoparticles in NHC modified mesoporous SBA-15 material was described.[43] Palladium complex and nanoparticles supported on the NHC-functionalized material (**3** and **4** in Scheme 3, respectively) were tested in the aerobic oxidation of benzyl alcohol in the presence of an external base. Supported nanoparticles **4** performed much better than **3** and could be reused up to eight times. No leaching of Pd species from the support could be detected during the reaction process. Furthermore, **4** showed good activity in the aerobic oxidation of other alcohols.



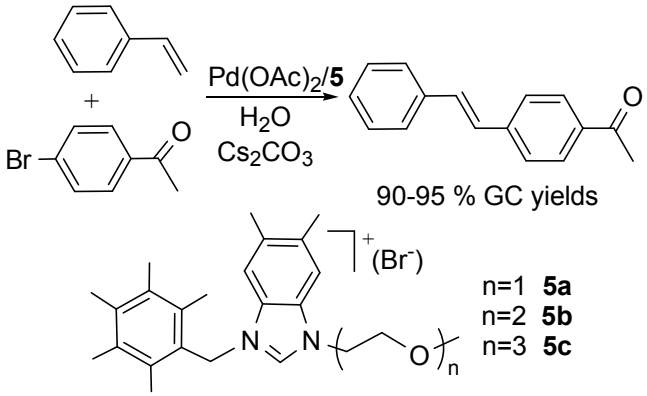
Scheme 3

2.2. Pd-catalyzed reactions in alternative solvents

i) Hydrophilic ligands and aqueous Pd-catalyzed reactions. The use of water as solvent has attracted great interest for economical and ecological reasons and so, water-soluble homogenous catalysts are highly desirable. This strategy requires that the metal remains bound to the water-soluble ligand in order to avoid loss of the metal to the organic phase or through decomposition. Micellar catalysis[44] and the introduction of hydrophilic functional groups in the molecular structure of the catalyst have emerged as good strategies. An excellent review by Shaughnessy gives a detailed account on the design of hydrophilic ligands and their catalytic applications in aqueous-phase metal-catalyzed reactions, devoting a part to hydrophilic NHC ligand precursors and their coordination.[45] Özdemir described the first hydrophilic NHC-based complex and its use as catalyst for the synthesis of 2,3-dimethylfuran via enynol intramolecular cyclization using water as solvent.[46] Water-soluble ruthenium-alkylidene complexes were described and successfully applied in olefin metathesis in aqueous media.[47, 48] Other interesting examples of hydrophilic NHC-based complexes have appeared in the literature.[49-54]

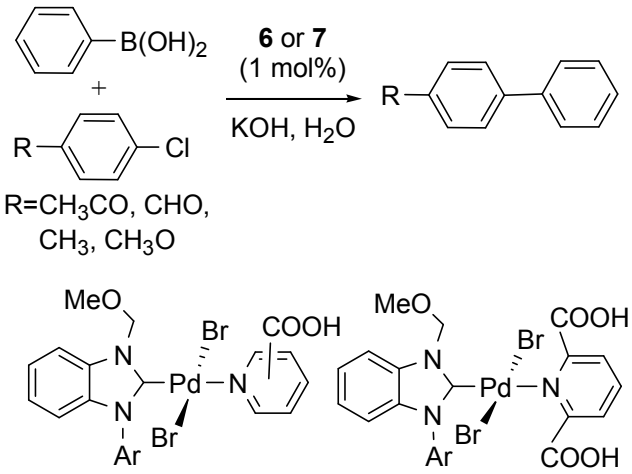
More recently, Çetinkaya and co-workers have focused their attention to the synthesis of water-soluble Pd(II)-NHC complexes and their application in catalysis. The group described the synthesis of oligoether-substituted benzimidazolium salts, their

coordination to Pd(II) and their test as catalysts for the Heck coupling reaction in water (Scheme 4).[55] In general, *in situ* formed complexes from $Pd(OAc)_2$ and the benzimidazolium salts performed better than the isolated Pd(II) complexes. Moreover, better catalytic activities were achieved with benzimidazolium salts with longer oligoether spacers. The potential reciclability of the $Pd(OAc)_2$/**5b** system was explored in a model reaction. The final products were extracted with an organic solvent and the aqueous phase transferred to a new reaction vessel for the next cycle. Notably, the catalyst was reused three times without significant loss of activity. Negligible Pd-leaching of 6 ppm was quantified by means of AAS.



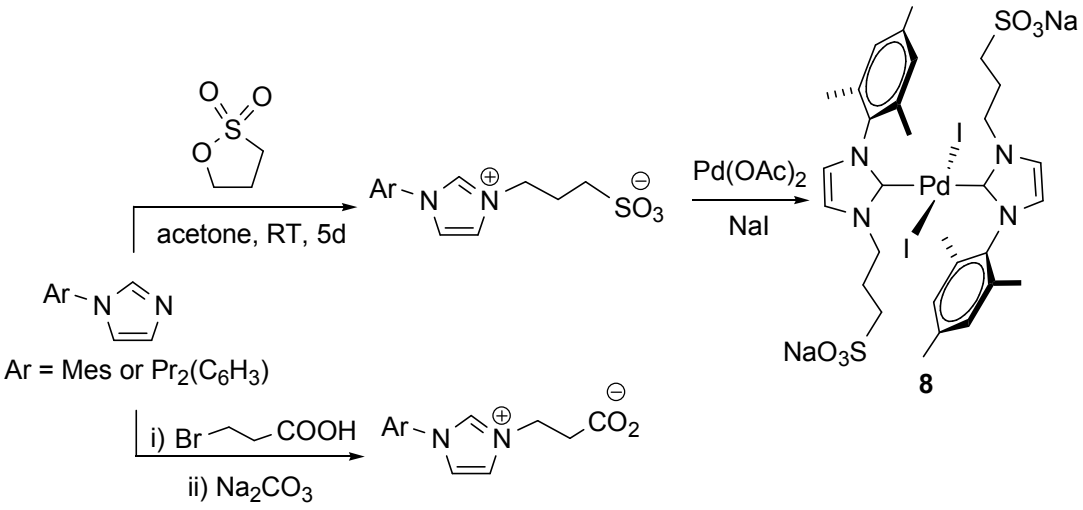
Scheme 4

In addition, they described a series of *trans*-[$PdBr_2$(NHC)L] complexes (NHC=1,3-dialkylbenzimidazol-2-ylidene; L=pyridinecarboxylic acid) which, due to deprotonation of the carboxylic acid functionality, are water soluble in basic conditions.[56] Complexes **6** and **7**, depicted in Scheme 5, were tested in the Suzuki-Miyaura coupling reaction of aryl chlorides with phenylboronic acid under aqueous basic conditions, showing good to excellent yields. In particular, complex **7** could be reused three times with 90% yield (determined by GC) in the model reaction of 4-bromoacetophenone and phenylboronic acid.



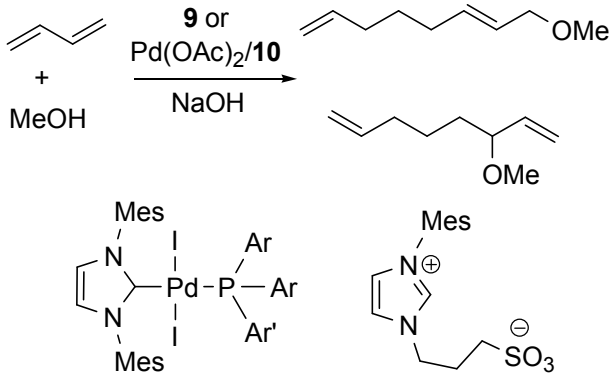
Scheme 5

Tsuji and co-workers reported the catalytic activity of Pd(II)-NHC complexes bearing hydrophilic chains in the Suzuki-Miyaura coupling reaction.[57] The study demonstrated that the introduction of hydrophilic tetraethylene glycol (TEG) chains dramatically enhances the catalytic activity in water. Pursuing the preparation of hydrophilic metal complexes, Shaughnessy and Schanz described the synthesis and coordination of imidazolium precursors bearing alkylsulfonate and alkylcarboxylate N-substituents.[58] Scheme 6 illustrates the synthesis of the carboxylate and sulfonate zwitterionic imidazolium salts and the coordination of the latter to Pd(II).



Scheme 6

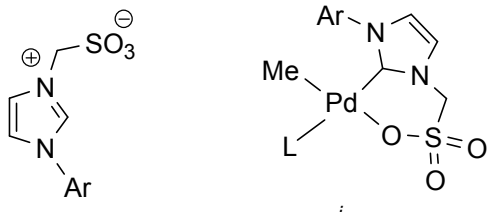
Mixed NHC and phosphine palladium complexes were described and studied as catalysts in telomerization of butadiene with methanol in the presence of water (Scheme 7).[59] However, neither water-soluble complexes **9** bearing sulfonated phosphines nor the complex prepared from imidazolium precursor **10** were found active in this reaction. Interestingly, other hydrosoluble phosphine-palladium complexes described by the same group exhibited very high activities in the telomerization of butadiene with methanol in aqueous medium.[60] Nozaki and co-workers have recently described imidazolium sulfonate salts **11** and NHC-sulfonate complexes **12** (Chart 1).[61] The molecular structure of complexes **12**, determined by single-crystal X-ray analysis, showed the ligand coordinated to the square-planar palladium centre in a bidentate way and the sulfonate unit *trans* to the methyl group. **12** constituted the first examples of complexes bearing a chelating bidentate NHC-sulfonate ligand.



9a Ar=$C_6H_4SO_3Na$; Ar'=C_6H_5
9b Ar=Ar'=$C_6H_4SO_3Na$

10

Scheme 7



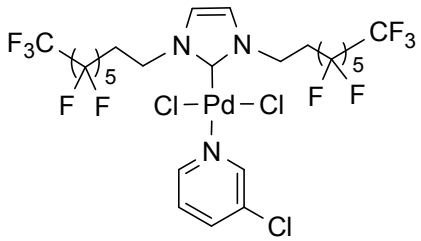
11a Ar=2,6-^{i}Pr$_2$(C_6H_3)
11b Ar=Mes

Ar=2,6-^{i}Pr$_2$(C_6H_3)
12a L=lutidine
12b L=PPh_3

Chart 1

ii) Fluorous NHC ligands and fluorous biphasic catalysis. Metal complexes with fluorous-based ligands have important features such as the possibility of catalyst recovery using fluorous solid phase extraction.[62] Very few examples of imidazolium salts bearing fluorinated chains can be found in the literature.[63-65] In 2000, Xiao and co-workers described the first fluorinated Pd-NHC complex, which was easy to prepare and did not require special handling precautions.[65]

Aiming to use fluorous biphasic catalysis, the fluorous palladium-NHC complex **13** (Chart 2) was described and tested in the Suzuki-Miyaura and Heck coupling reactions.[66] Although the catalyst performed well in both reactions, it could not be recycled using the typical fluorous separation methods.



13

Chart 2

iii) Use of ionic liquids as alternative solvents. The use of ionic liquids (ILs) in catalysis might imply the improvement of the catalytic performances (activity, selectivity or new chemistry). They also allow the catalyst separation and recycling by immobilization in the IL-phase. Several recent reviews provide an exhaustive view of the catalytic reactions occurring in ILs.[67-70] Ionic liquids based on 1,3-dialkylimidazolium salts are widely used although they have proved to be "non-innocent" solvents in organometallic chemistry. Several examples of Pd-catalyzed reactions using NHC ligands and mediated by ILs can be found in the literature.

Recently, the alcohol-functionalized imidazolium salts depicted in Chart 3 were synthesized and applied, in the presence of $PdCl_2$, in the Heck reaction of aryl bromides

with acrylates under mild and aerobic conditions.[71] The catalytic systems could be reused without much loss of activity after five cycles. The authors did not include data concerning the leaching of the catalyst.

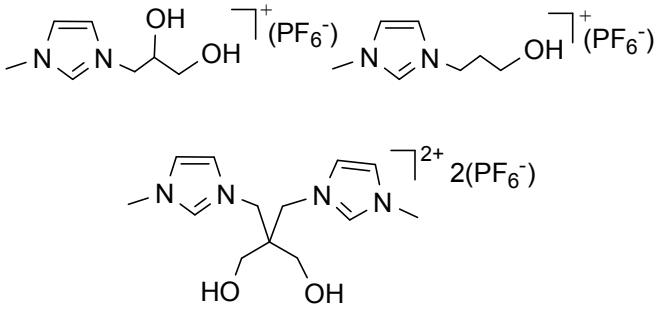


Chart 3

2.3. Other routes to reusable palladium NHC-based catalysts

Another approach for catalyst separation involves solvent-resistant nanofiltration.[72] A recent publication by Plenio and co-workers described the synthesis of mass-tagged NHC ligands and their coordination to $[PdCl(allyl)]_2$.[73] Enlarged complexes **14** and **15** (Chart 4) displayed excellent catalytic activity in the Suzuki coupling and the Buchwald-Hartwig amination. Moreover, the catalysts were efficiently separated from the final products by means of solvent-resistant nanofiltration using a PDMS (polydimethylsiloxane) membrane on PAN (polyacrylonitrile).

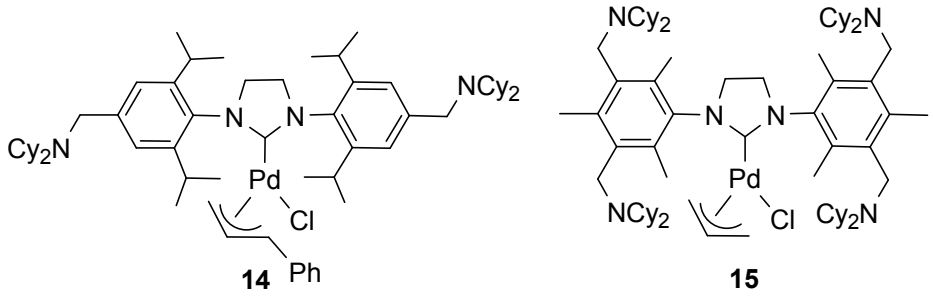
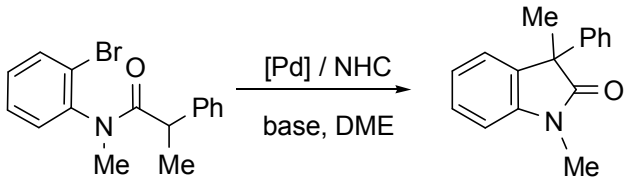


Chart 4

3. Applications of palladium-NHC complexes in homogenous catalysis

3.1. Chiral Pd-NHC systems for asymmetric catalysis

The preparation of new NHC ligands has involved the design of chiral NHC systems for asymmetric catalysis. Since the first examples reported by Herrmann and Enders,[74, 75] this area has grown dramatically and many chiral NHC systems have been described. Hartwig's group described the first palladium complex supported by an optically active NHC ligand and its application in the synthesis of valuable chiral oxindoles[76, 77] by amide α-arylation.[78, 79] Table 1 summarizes the best results for the asymmetric cyclization of amide **16** (Scheme 8) reported by that group, as well as the subsequent reports on this reaction.[80-82] The carbene precursors used in each case are depicted in Chart 5.

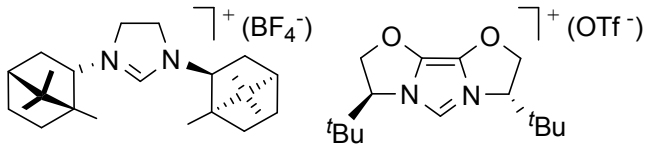


(±) **16** **17**

Scheme 8

Table 1. Selected results for the asymmetric cyclization of amide **16**

NHC precursor	Pd precursor	Base	Conditions	Yield of **17** (ee)	Ref.
18	$[Pd(dba)_2]$	NaO^tBu	25ºC, 24h	74% (57%)	[78, 79]
19	$[Pd(dba)_2]$	NaO^tBu	20ºC, 14h	95% (43%)	[80]
20	$Pd(OAc)_2$	LiO^tBu	100ºC, 12h	62% (61%)	[81, 82]



18 **19**

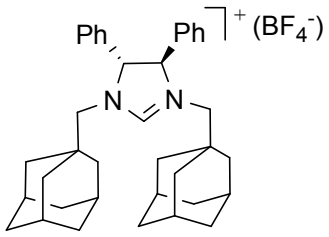


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Chart 5

More sterically demanding chiral NHC ligands have been described and successfully applied to this organic transformation. Remarkably, bulky chiral carbene precursors **21** provided the first highly enantioselective reaction (up to 95%) employing [Pd(dba)$_2$] as palladium source.[83] The same group reported the application of carbene precursor **23** (Chart 6) to the synthesis of oxindoles with heteroatoms at the stereogenic centre. Using [Pd(dba)]$_2$, chiral 3-alkoxyoxindoles and 3-aminooxindoles were synthesized with high yield and enantioselectivity.[84] More recently, Glorius and co-workers have described the extraordinary steric demand of IBiox[(−)-menthyl] (**22** in Chart 6) and its application in the amide α-arylation of aryl bromides and chlorides.[85] In the presence of [Pd(allyl)Cl]$_2$ and **22** it was performed the unprecedented conversion of aryl chlorides with high ee's (92-99%).

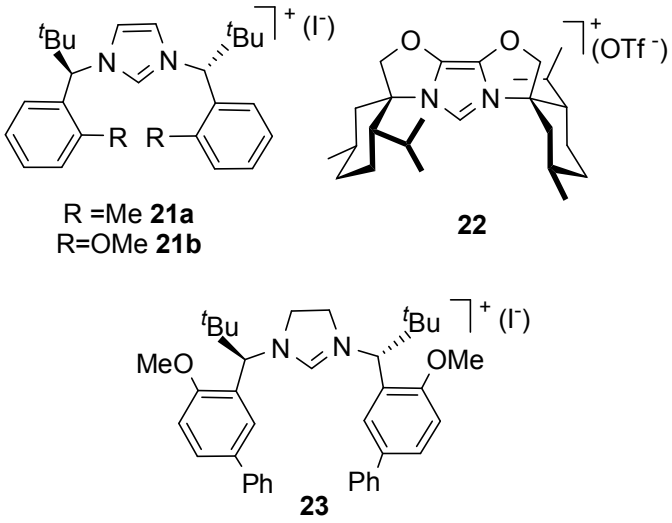
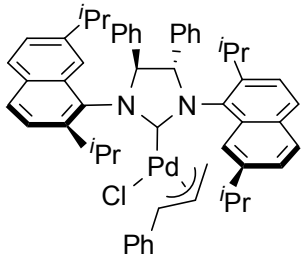


Chart 6

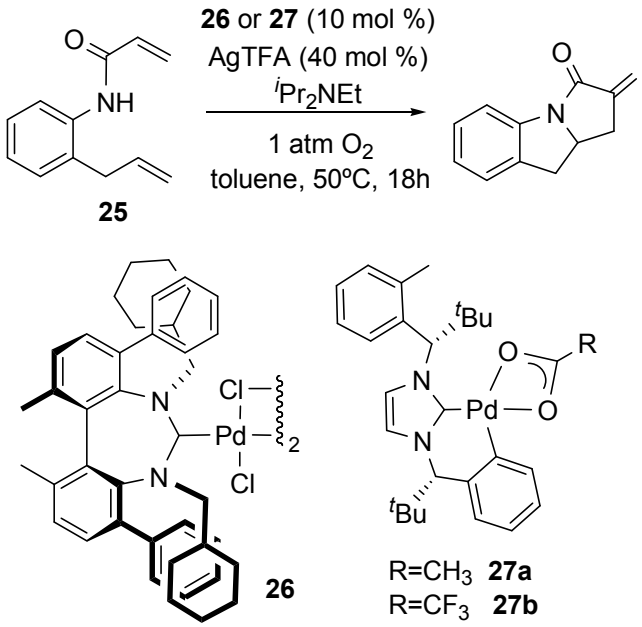
Well-defined Pd-NHC complexes have been applied in asymmetric amide α-arylation. A recent report by Dorta and co-workers showed that the absolute configuration of the chiral groups on the N-heterocycle determine the absolute configuration of the carbon centre in the final products, thus highlighting the importance of the ligand architecture.[86] In the asymmetric cyclization of amide **16** (Scheme 8), catalysts **24a** and **24b**, derived from the (*R, R*) and (*R, S*) isomers of the ligand, showed moderate to high enantiomeric excesses towards the *R*-configured final product whereas **24c**, derived from the (*S, S*) diastereomeric form, performed poorly and showed low enantiomeric excess.



(*R, R*)-**24a** 86% ee (*R, S*)-**24b** 67% ee (*S, S*)-**24c** 20% ee

Chart 7

Stahl and co-workers isolated a series of Pd(II) complexes bearing an enantiomerically resolved seven-membered NHC ligand and studied their possible application in intramolecular aerobic oxidative cyclization reactions.[87] The Pd(II) complex **26** achieved the best performance in the aerobic oxidative cyclization of substrate **25** (Scheme 9). Although the cyclization product was obtained in 63% ee, the yield was rather low. Other attempts at asymmetric aerobic oxidative cyclization led to nearly racemic mixtures. The authors also described the coordination of carbene precursor **21a** (Chart 6) to $[Pd(allyl)Cl]_2$ which afforded cyclometalated complexes **27** (Scheme 9). Catalytic performances of complexes **27** were better than that of complex **26** but, unfortunately, no asymmetric induction was observed.

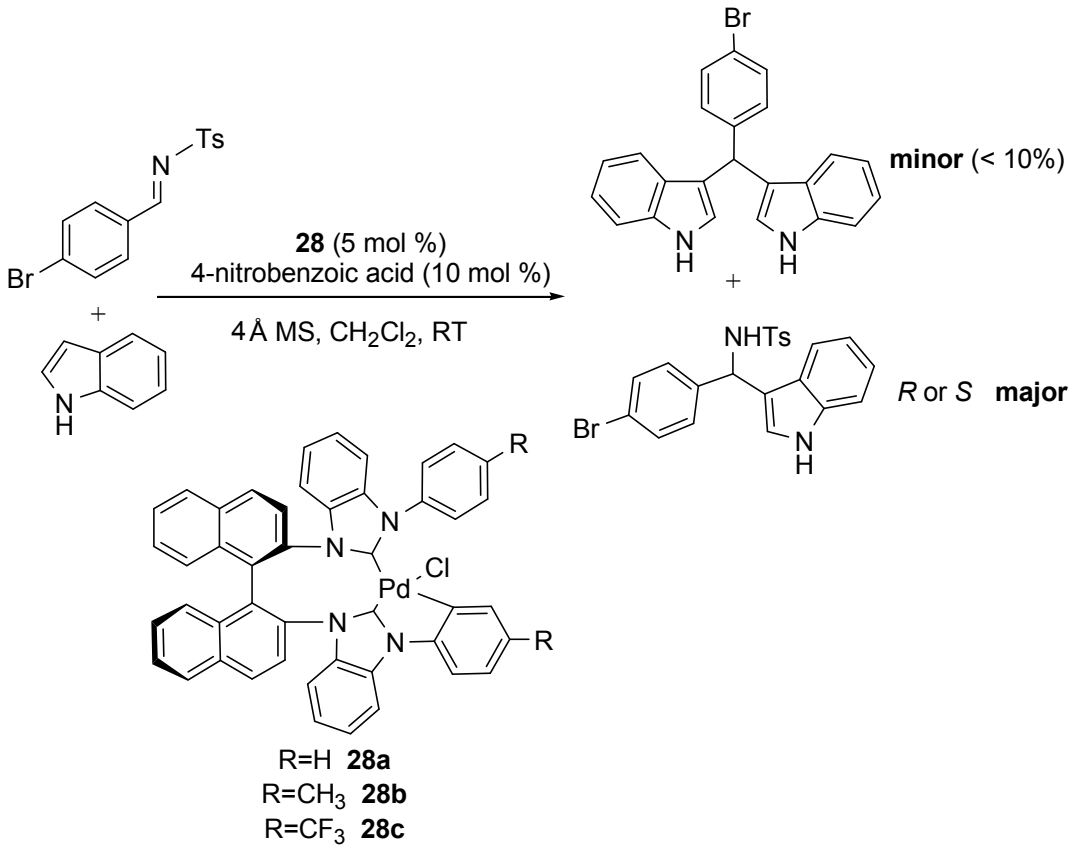


Scheme 9

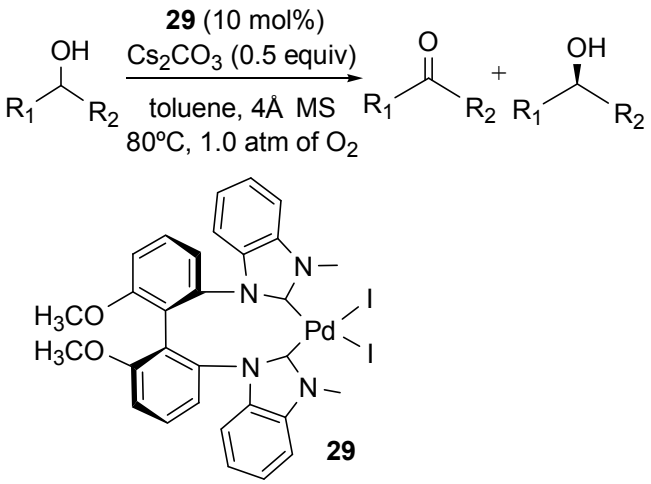
Yet another interesting example of asymmetric catalysis with palladium was recently described by the group of Min Shi using novel cyclometalated bidentate Pd(II)-NHC complexes derived from binaphthyl-2,2'-diamine (BINAM).[88, 89] Given the importance of indole derivatives in biology,[90-92] complexes **28** were tested in the asymmetric Friedel-Crafts reaction of indole with N-tosylarylimines (Scheme 10). The

best catalytic results were obtained using 4-nitrobenzoic acid as additive in the presence of molecular sieves. Notably, catalysts **28a** and **28b** with an (*R*)-configuration afforded the final product with an (*R*)-configuration as the major enantiomer, whilst catalyst **28c**, also with an (*R*)-configuration, produced the final product with an (*S*)-configuration as the predominant enantiomer. Hence, efficient stereocontrol on this reaction can be achieved by changing the R groups on the benzene rings of the Pd(II)-NHC complexes.

The same group has also studied the oxidative kinetic resolution of *sec*-alcohols using chiral Pd(II)-NHC complexes and molecular oxygen as a oxidant.[93-95] As an example, the axially chiral Pd(II)-NHC complex **29** was tested in the oxidative kinetic resolution of a wide range of *sec*-alcohols affording the corresponding alcohols in moderate conversions (48-68%) and moderate to high ee's (53-94%).[93]

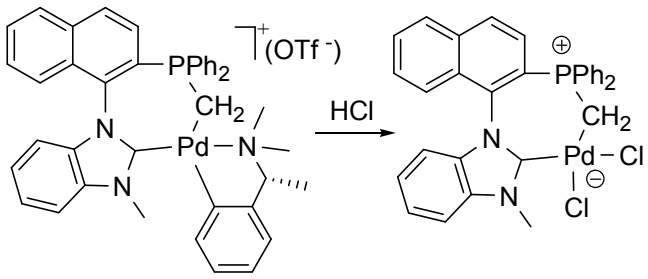


Scheme 10



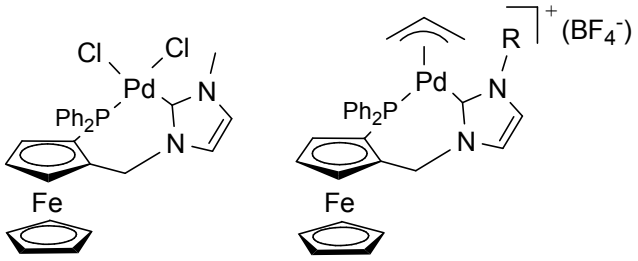
Scheme 11

Chiral bisimidazolium salts derived from amino acids have been reported and successfully coordinated to Pd(II).[96] Unfortunately, the complexes did not show any optical activity and racemization was always observed regardless of the synthetic route used. Another interesting example of the coordination of an atropochiral chelating NHC ligand to palladium has been recently proposed by Chauvin and Debono.[97] Complexes **30a** and **30b**, which are diastereoisomers, could be separated by fractional crystallization and their absolute configuration was unambiguously attributed by single-crystal X-ray crystallography. As depicted in Scheme 12, enantiomeric pure complexes **31a** and **31b** were synthesized by removing the chiral auxiliary amine under acidic conditions. Very recently, air-stable palladium(II) complexes bearing a planar chiral ferrocenyl phosphine-NHC ligand (Chart 8) have been described and successfully applied in the Suzuki-Miyaura reaction of aryl bromides with phenyl boronic acids. The chiral complexes were studied in the asymmetric version of mentioned reaction showing moderate but promising enantioselectivities.[98]



(*R,S*)-**30a** or (*S,S*)-**30b** (*R*)-**31a** or (*S*)-**31b**

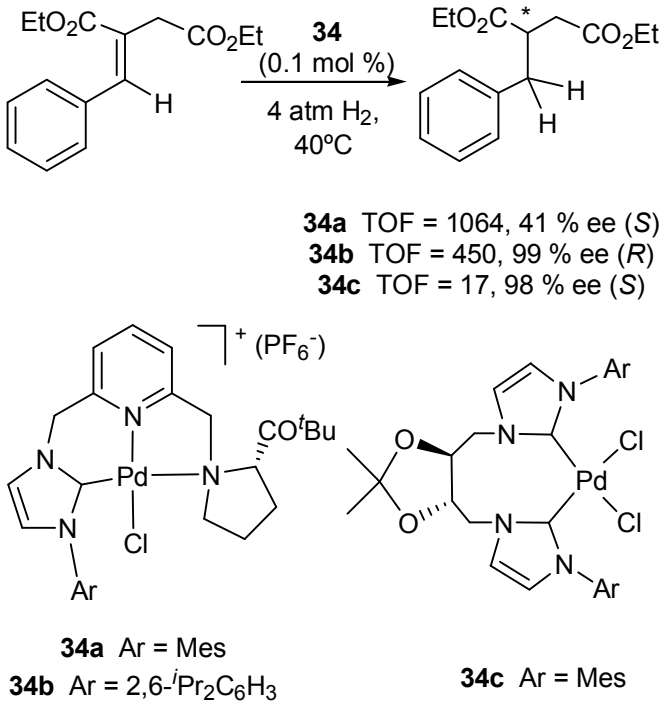
Scheme 12



32 **33**

Chart 8

Iglesias, Sánchez and co-workers have described the synthesis of chiral palladium CNN-pincer complexes **34a** and **34b** containing an NHC ligand and a (*S*)-proline moiety.[99] The complexes catalyze the asymmetric hydrogenation of prochiral alkenes with high reactivity in mild reaction conditions. The enantioselectivities were found to be very sensitive to the N-substituent on the NHC ligand, thus allowing the preparation of both isomers. For instance, in the hydrogenation of diethyl 2-benzylidene succinate catalyst **34a** led to the hydrogenated isomer *S* whereas catalyst **34b** afforded the *R* one (Scheme 13). The same group, have recently described the palladium bis-NHC complex **34c** with a chiral dioxolane backbone. Although the catalytic activity of **34c** in asymmetric hydrogenation was significantly lower than those of **34a** and **34b**, high ee's were achieved.[100]



Scheme 13

3.2. Pd complexes with linearly opposed NHC ligands

The presence of two metals in the design of new catalysts has led to a variety of applications that differ considerably from the monomeric forms.[101] Here we want to summarize the most recent examples based on ditopic NHC ligands with a facially opposed coordination (*Janus-Head* type), the morphology of which is depicted in Chart 9. The simplest is a triazolyldiylidene ligand **A**, so-called *ditz* ligand, derived from a dicationic triazolium salt. The rest of the ligands **B** to **D** are imidazolium-based linked by a π-conjugated system where the electronic and steric (metal-to-metal distance) properties have been modulated.[102]

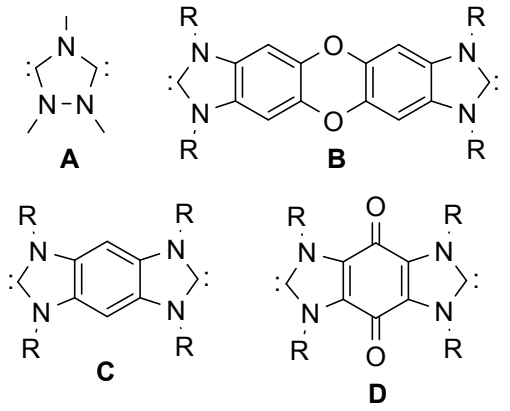
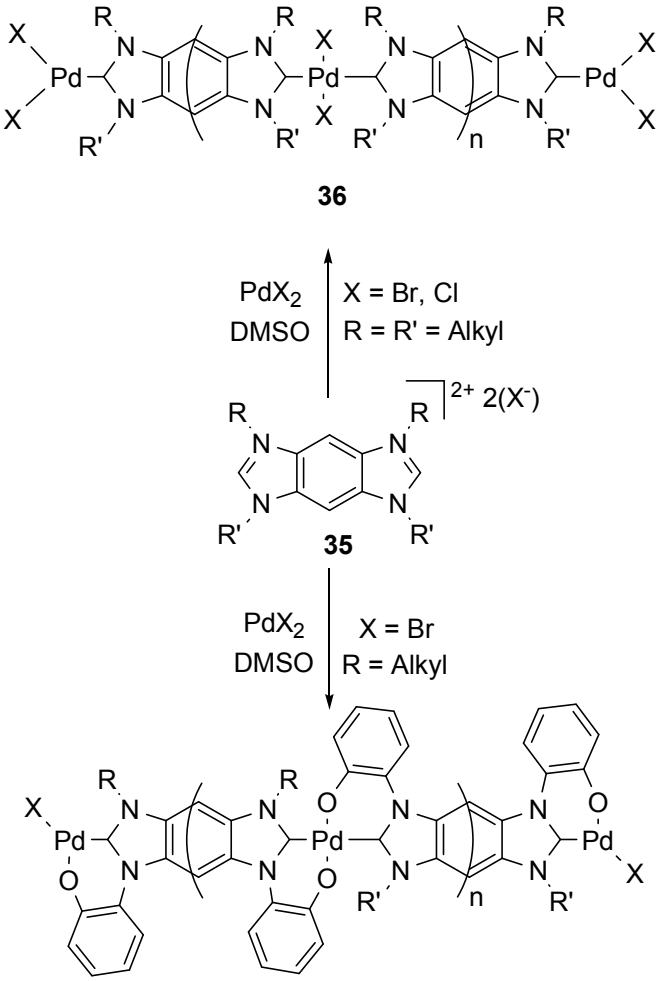


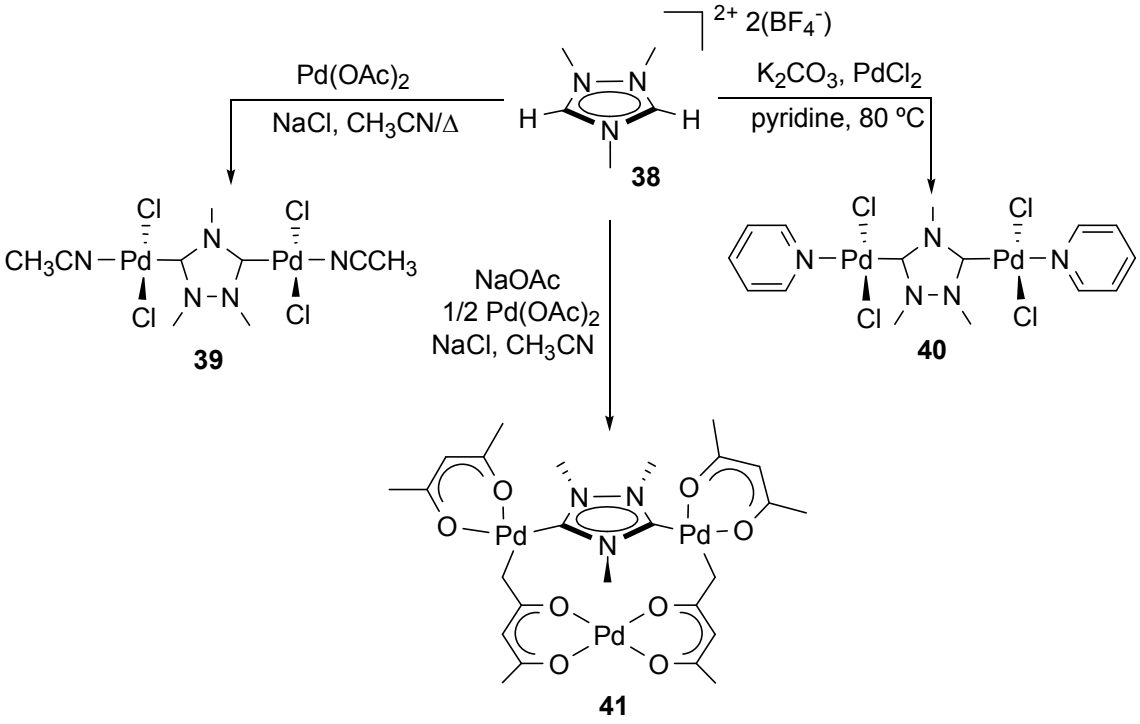
Chart 9

The first examples were introduced by Bielawski[103] and Bertrand[104] and were coordinated to palladium, platinum and silver. Ever since, the coordination of these ligands has been extended to other metals such as rhodium,[105] iridium,[106] ruthenium,[107] iron[108] and nickel.[109] The first palladium complexes with linearly-opposed coordination were polymeric in nature.[103] As illustrated in Scheme 14, ligand precursors **35** were coordinated to palladium salts yielding organometallic polymers.[110] Depending on the N-functionalization, non-chelated **36** or chelated **37** polymers were obtained.[111] Catalytic properties of the non-chelate polymer **36** were tested in the Suzuki-Miyaura coupling of aryl halides and boronic acids in water.[112] The polymer behaved as a self-supported catalyst and was active at least for six consecutive runs. The mercury test revealed that the catalytic experiment was homogeneous in nature. The polymer **37** was found to be stable, highly active and reusable, even with deactivated aryl chlorides and aryl fluorides using water as solvent.[109]



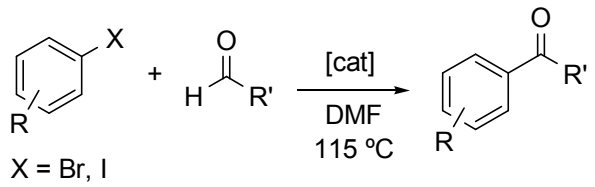
Scheme 14

The *ditz* ligand (**A** in Chart 9), which can potentially bind to two metal centers, has allowed the preparation of novel homo and heterobimetallic complexes.[104] The reaction of 1,2,4-trimethyltriazolium bis(tetrafluoroborate) with palladium salts in coordinating solvents avoided polymeric structures and led to homobimetallic palladium complexes **39** and **40** (Scheme 14).[113, 114] A slight modification in the reaction conditions using $Pd(acac)_2$ and Cs_2CO_3 afforded the trimetallic palladacycle **41**.[113] In this complex two of the palladiums are connected through the triazolyldiylidene ligand; the third metal center arises from a double C-H activation of the terminal methyl groups of two acac ligands.



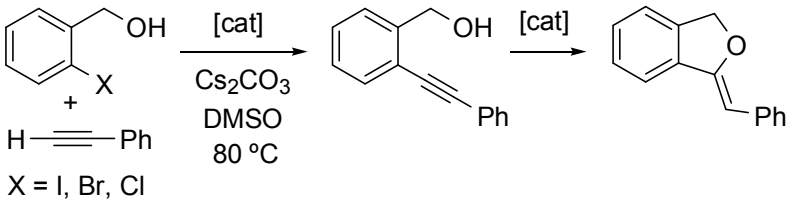
Scheme 14

The two palladium complexes **39** and **41** showed good activities in the Heck C-C coupling reaction of styrene and 4-bromoacetophenone. Full conversions were achieved at 100 ºC under aerobic conditions and with regular solvents. The direct acylation of aryl halides and aldehydes[115] (Scheme 15) was tested in order to widen the catalytic applications of the palladium complexes. Whilst complex **39** was found highly active in the acylation of aryl iodides and bromides with different aldehydes, complex **41** showed no activity. The reaction was regioselective as no other products as α-arylation of aldehydes were observed.[116] The main advantages of catalyst **39** are that no additives such as phosphines are needed and its high stability.



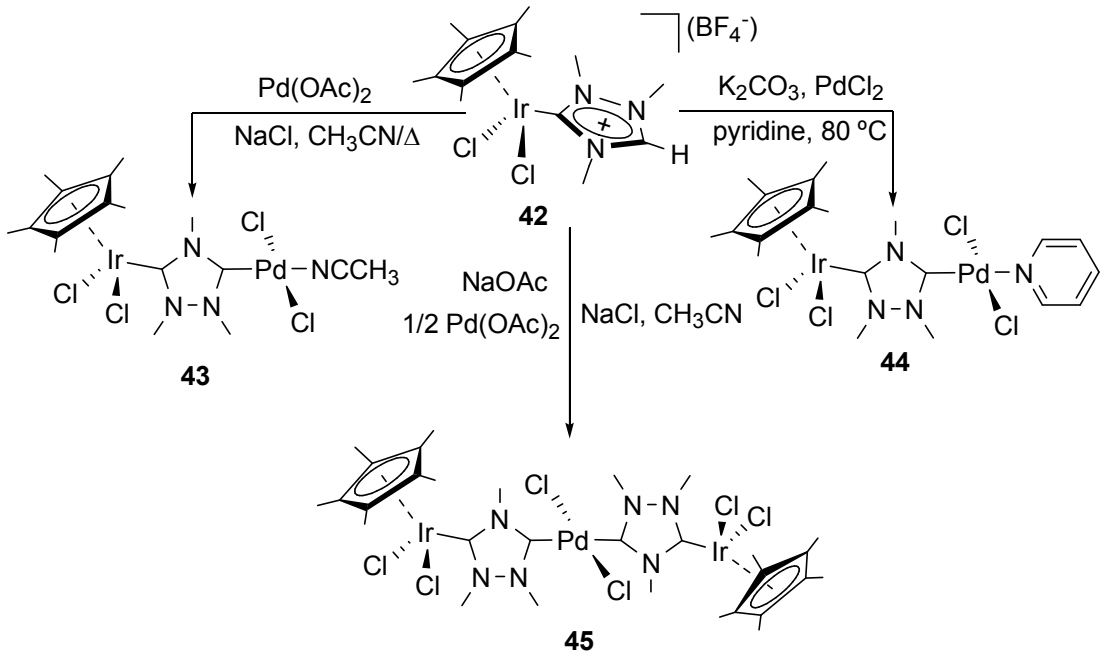
Scheme 15

Additionally, complex **40** was active in the tandem process depicted in Scheme 16, that comprises an intermolecular Sonogashira coupling and an intramolecular cyclic hydroalkoxylation.[114] The carbon-carbon bond formation worked without the need of additives other than the base. The cyclization process was highly selective towards the *Z* isomer and five member ring. Neither the *E* isomer nor the six member were observed. Full conversions (95% yield) to the final product were observed in less than one hour for the *o*-iodobenzyl alcohol. The catalytic activity of complex **40** was higher than that of the ubiquitous $Pd(OAc)_2$ and $PdCl_2(PPh_3)_3$ under the same reaction conditions.



Scheme 16

The molecular complexes based on ditopic NHC ligands with a facially opposed coordination are not restricted to homobimetallic species. Recently, a series of iridium-palladium complexes have been described.[117] The synthetic strategy for the preparation of the heterobimetallic Ir/Pd complexes consist of the monofunctionalization of the dicationic salt 1,2,4-trimethyltriazolium bis(tetrafluoroborate) to obtain the cationic iridium complex **42**. In complex **42**, the *ditz* ligand acts as a monocarbene and still has other acidic proton that can be activated to generate a second heterobimetallic complex. As shown in Scheme 17, the reaction of **42** with different palladium precursors under basic conditions afforded heterobimetallic complexes **43** and **44** or even trimetallic species **45** with two azole rings.

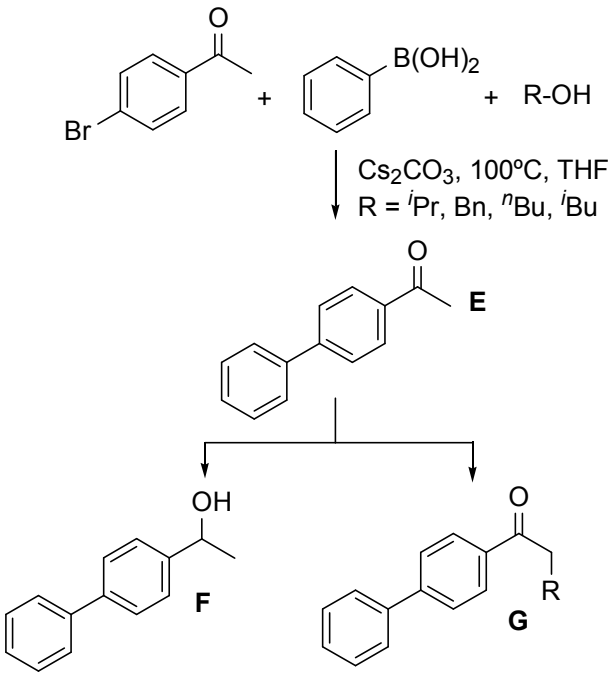


Scheme 17

The heterobimetallic complexes were tested in tandem processes typically catalyzed by iridium and palladium. Suzuki coupling and dehalogenation of haloacetophenones, typically palladium-catalyzed transformations, were successfully combined with transfer hydrogenation and ketone α-alkylation reactions, typically iridium-catalyzed reactions.

Complexes **43**, **44** and **45** performed very well in three tandem processes, namely dehalogenation and transfer hydrogenation of haloacetophenones, Suzuki coupling and transfer hydrogenation of *p*-bromoacetophenone and Suzuki coupling and α-alkylation of *p*-bromoacetophenone. As an example, the last two processes have been summarized in Scheme 18. The reaction of *p*-bromoacetophenone with phenylboronic acid in the presence of catalyst **44** afforded the carbon-carbon coupling product **E**. Then, ketone reduction was achieved under hydrogen transfer conditions using ^{i}PrOH, yielding alcohol **F**. When a primary alcohol was used instead of ^{i}PrOH, the product that arises from the α-alkylation of the ketone (compound **G**) was observed. Remarkably, these heterobimetallic complexes are more active than the sum of the corresponding

homobimetallic species most probably due to some iridium-palladium cooperation process.



Scheme 18

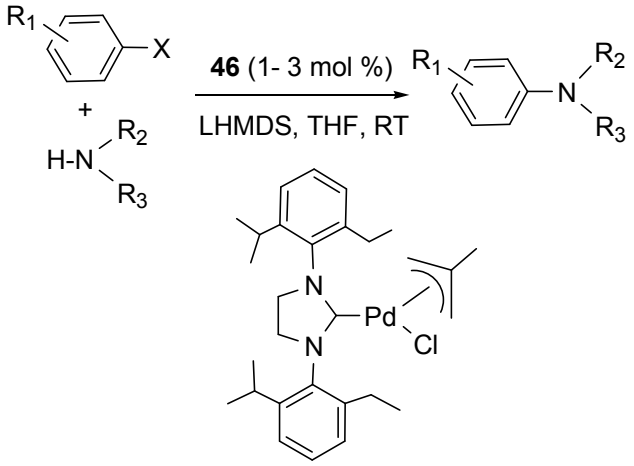
3.3. Other palladium-catalyzed reactions using NHC ligands

As stated in the Introduction, although Pd-NHC systems are mainly known for their application in carbon-carbon coupling reactions, their application in other organic transformations are several and remarkable.[13, 14, 19, 20] In this section we will try to highlight the latest advances in this latter regard.

3.3.1. Carbon-nitrogen bond formation reactions

i) Amination of aryl halides (Buchwald-Hartwig reaction). The Buchwald-Hartwig amine arylation reaction is a useful and versatile method to obtain aryl amines and thus, is of great interest in modern synthetic chemistry. Many efforts have been made to simplify the practical protocols and avoid the use of extreme inert conditions. Air- and moisture-stable (NHC)Pd(R-allyl)Cl catalysts can be prepared without using the glovebox and even the need of dry solvents and have shown high activity in the Buchwald-Hartwig coupling.[118, 119] Keen to develop a practical protocol efficient at

room temperature and applicable to a wide range of amines and aryl halides, Caddick and co-workers have designed a new variant of (NHC)Pd(R-allyl)Cl catalysts and have applied them to aryl amination.[120] Air-stable complex **46** (Scheme 19) was found very active in the coupling of a wide range of aryl halides with primary and secondary alkyl amines at moderate (70ºC) or room temperature. The use of lithium bis(trimethylsilyl)amide (LHMDS) as base was found to be crucial to catalyst turnover.

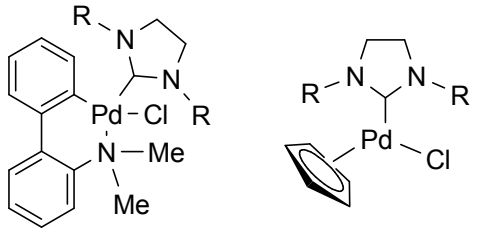


46

Scheme 19

The group of Nolan has recently described the synthesis of air- and moisture-stable NHC-based *N,N*-dimethyl biphenylamine palladacycle complexes and their evaluation in the Buchwald-Hartwig amination.[121] For instance, complex **47** was active in the coupling of aryl and alkyl primary and secondary amines with several unactivated aryl chlorides. Interestingly, **47** was found to be active in the synthesis of the biaryl compound employed in its own preparation. Well-defined Cp-containing Pd(II)-NHC complexes (**48** in Chart 10) were successfully applied in the cross-coupling of aryl chlorides with a series of primary and secondary amines at room temperature.[122] Noteworthy, the reactions with sterically demanding substrates proceeded in high yields at room temperature. Complex **49**, bearing a highly electron-donating carbene

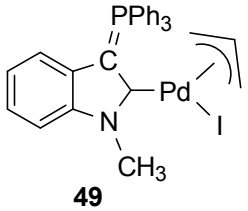
phosphorous-ylide ligand, was active in the arylation of morpholine with bromotoluene.[123]



47

48

R = 2,6-^{i}Pr$_2$C$_6$H$_3$

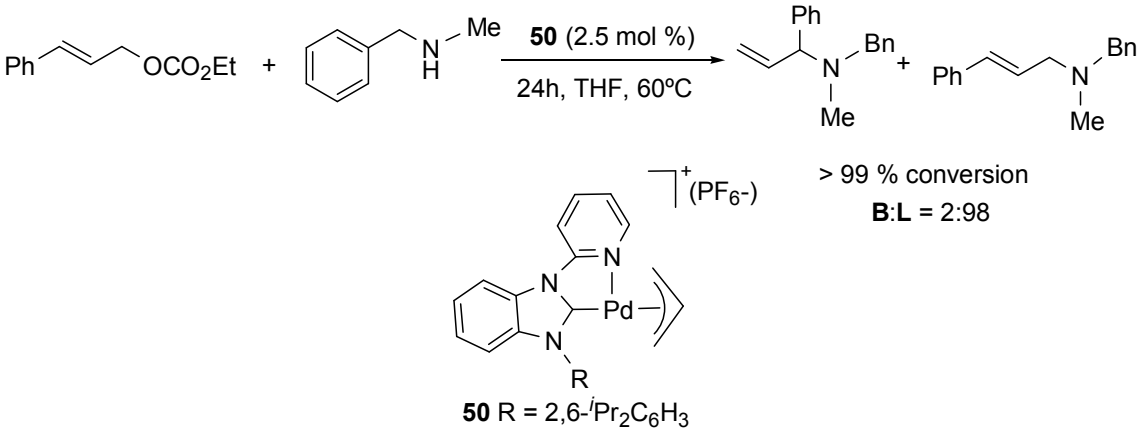


49

Chart 10

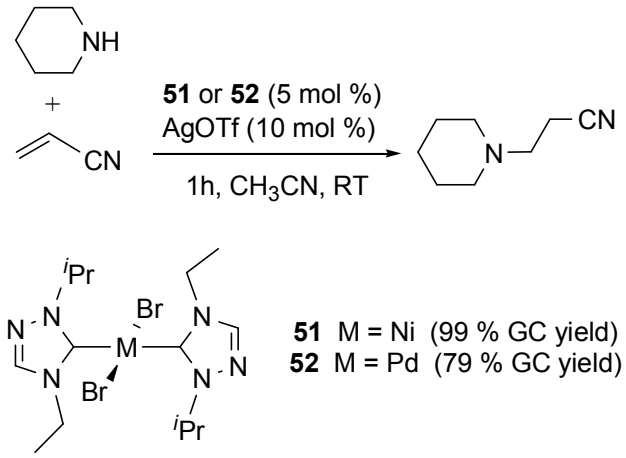
ii) Allylic amination. The palladium-catalyzed nucleophilic substitution of allylic electrophiles such as acetates or carbonates provides a useful synthetic method to prepare highly valuable substrates. In the particular case of palladium, the selectivity towards branched versus linear products has probed to be ligand dependent. With regard to NHC ligands, Chianese and co-workers described a series of rigid chelating palladium-allyl complexes as well as their application in alkylation and amination of allylic carbonates.[124] The best result is shown in Scheme 20; complex **50** achieved full conversion in the amination of cinnamyl ethyl carbonate using N-methylbenzylamine after 24h. The reaction was found to be selective towards the linear product. Roland and co-workers described other well-defined palladium-allyl complexes and applied them in the same reaction.[125, 126] In this case, the reaction only proceeded in the presence of PPh_3, thus suggesting the *in situ* formation of cationic $[(NHC)Pd(allyl)(PPh_3)]^+$ complexes, which are more electrophilic than their counterparts and allow the attack of the amine at the allyl fragment. Good to excellent performances were achieved with

various nitrogen nucleophiles and allylic acetates. Noteworthy, the catalytic system was also active in the amination of an allylic alcohol, albeit in a very low yield.



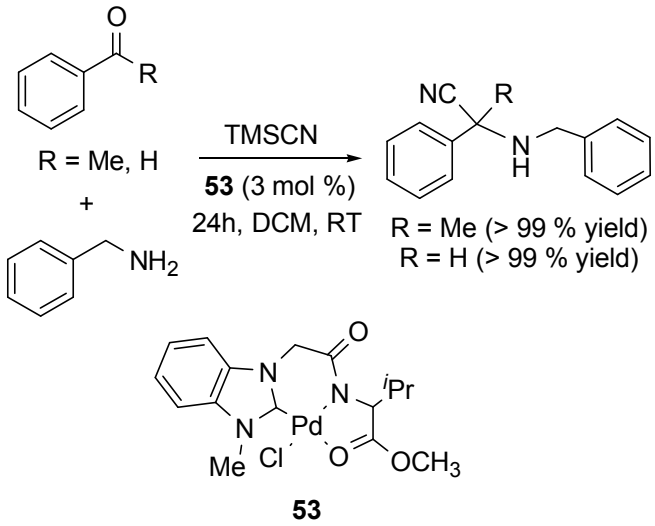
Scheme 20

iii) Hydroamination. The hydroamination of olefins provides an easy and highly atom-economical route to alkylamines since readily available starting materials are converted in valuable products without generating any by-products. Hence, many efforts have been made to develop active catalysts for this process.[127, 128] Very recently, Gosh and co-workers have focused their interest on C-N bond formation through the hydroamination reaction using palladium and nickel complexes of 1,2,4-triazole based NHCs.[129] Nickel and palladium complexes **51** and **52** (Scheme 21) were tested in the hydroamination of secondary amines with activated olefins at room temperature. The authors suggested that the higher activity of the nickel complexes compared to the palladium ones could be explained by the more electron deficiency of the nickel centre as extracted from the computational studies.



Scheme 21

iv) Synthesis of α-aminoniriles (Strecker reaction). The Strecker reaction, which employs aldehydes or ketones, amines and a cyanide source, is a well-established method to prepare α-aminonitriles which are versatile intermediates for the synthesis of amino acids via hydrolysis of the nitrile group. This reaction using ketones remains a challenging transformation as harsh reaction conditions and difficult manipulations are generally required.[130, 131] New chelating NHC-amidate Pd(II) complexes have been applied in the synthesis of α-aminonitriles using either aldehydes or ketones and amines with trimethylsilyl cyanide (TMSCN).[132] Complex **53** promoted one-pot multicomponent Strecker reactions involving a wide range of aldehydes and ketones with moderate to excellent yields (Scheme 22). One of the benefits of the methodology employed was its simplicity as chromatographic purification of the products was not necessary in most of the cases.

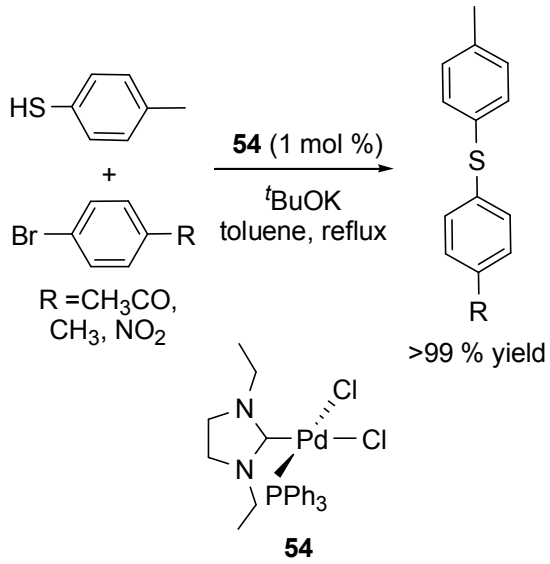


53

Scheme 22

3.3.2. Carbon-sulphur bond formation reactions

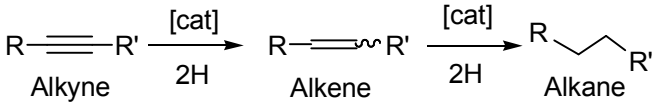
Given the importance of organosulphur molecules for pharmaceutical purposes, the C-S bond formation has become an important process in synthetic chemistry. The first reports on the activity of NHC-based complexes in such a challenging reaction were published in 2007 using nickel precursors.[133] Very recently, NHC ligands supporting palladium complexes have also been investigated in this coupling reaction.[134] Monocarbene complex **54** was found to be highly active in the C-S coupling of a wide range of aryl bromides and thiols (Scheme 23). The authors pointed out that the ligands about the metal centre have a dramatic influence in the catalytic activity and so, fine-tuning of the ligand features would lead to improved catalytic systems.



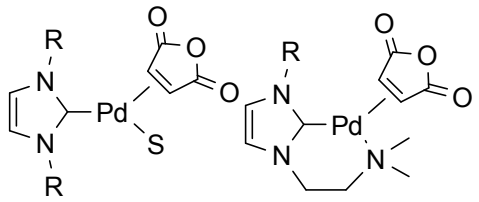
Scheme 23

3.3.2. Reduction reactions

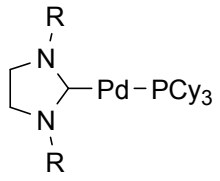
Hydrogenation of unsaturated organic molecules is a very useful organic transformation in laboratory and industry.[135, 136] While the hydrogenation of carbon-heteroatom multiple bonds is well known due to the difference in polarity, the hydrogenation of alkynes and alkenes is more challenging. The general reaction pathway could be summarized as depicted in Scheme 24. Chemioselectivity is an important factor to consider as different products can be obtained. Starting from alkynes, a complete hydrogenation process leads to alkanes but partial hydrogenations produce alkenes. In the last years, several Pd(0)-NHC complexes have been developed to reduce alkynes or alkenes specifically (Chart 11).



Scheme 24



55 S = solvent **56**



57

Chart 11

Complex **55** and the chelate version **56**, were tested in the hydrogenation reaction of alkynes.[137, 138] The hydrogen donor source used was HCOOH/NEt_3, so the process is best described as a transfer hydrogenation being CO_2 the only secondary product generated. Under these conditions, catalyst **55** showed excellent activity in the reduction of aromatic, aliphatic, internal and terminal alkynes. The reaction was highly stereoselective to the *Z* alkene and almost no over-reduction to the alkane was observed.[138] Chelating complexes as **56** showed similar semihydrogenation activity and performed very well in the coupling of phenylboronic acid with aryl bromides.[137] Compound **57**, which under molecular hydrogen undergoes an oxidative addition to form a *trans*-hydride, was found very active in the hydrogenation of alkenes and alkynes under mild reaction conditions (RT, low Pd loadings and 1 atm of H_2).[139]

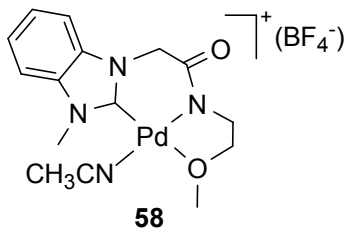
3.3.3. Oxidation reactions

The oxidation of alcohols to their corresponding carbonyl products is a very important and useful reaction in organic synthesis. Although molecular oxygen is an environmental friendly and cheap oxidant, the hazards of oxygen pressure when running oxidations in flammable organic solvents make this option rather inconvenient. A very attractive alternative for the selective oxidation of alcohols is the use of aryl halides as

oxidants.[140-142] The aryl halide acts as a hydride acceptor and forms the corresponding dehalogenated compound as the only by-product of the reaction. In this particular sense, Navarro's group has described the use of commercially available palladium and nickel complexes with NHC ligands in the oxidation of secondary alcohols using chlorobenzene as oxidant.[143] The reactions were carried out in anaerobic conditions and at very mild temperatures (RT or 60ºC), and good to excellent yields were achieved using a wide variety of secondary alcohols.

3.3.4. C-H activation reactions

N-heterocyclic carbene ligands have allowed for the preparation of new and improved catalysts for C-H activation, which remains a great challenge. Several late transition metal complexes supporting NHC ligands have shown good catalytic activity toward C-H activation during the last years.[144-148] With regard to palladium, an air/water stable NHC-based complex has recently been described as an efficient catalyst for C-H activation of hydrocarbons *via* H/D exchange using D_2O as deuterium source. Air and water stable complex **58** (Chart 12) showed high activity in the deuteration of a wide range of molecules including saturated hydrocarbons (cyclohexane and cyclopentane), ethers and ketones.[149] Remarkably, the reactions were carried out under mild reaction conditions (55 or 100ºC) and the catalytic activity was not inhibited by the coordination of water to the palladium compound.



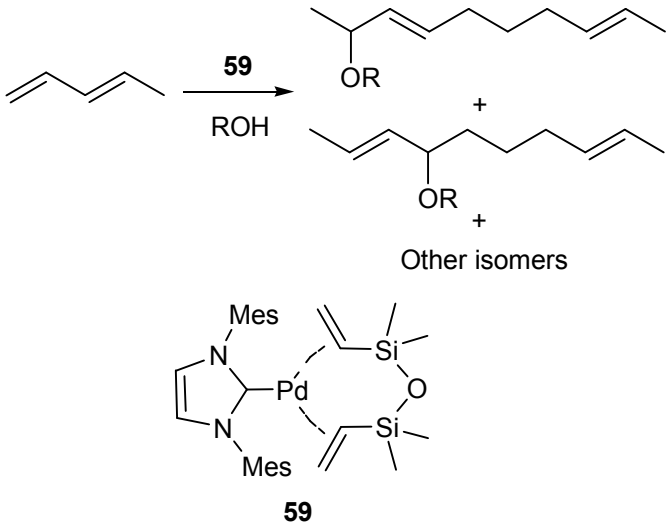
58

Chart 12

3.3.5. Miscellaneous reactions

Other important organic transformations can be performed by Pd-NHC systems; we will point out here those which cannot be included in any of the subgroups proposed above.

Palladium-catalyzed reactions using alcohols as substrates or reagents have extensively been studied.[150] A series of Pd(0)-NHC complexes have been described and tested in the telomerization reaction of 1,3-pentadiene with different alcohols (Scheme 25).[151] In particular, complex **59** displayed moderate conversions and very high selectivity towards the telomerization products using long chain alcohols such as 1-propanol and 1-butanol.

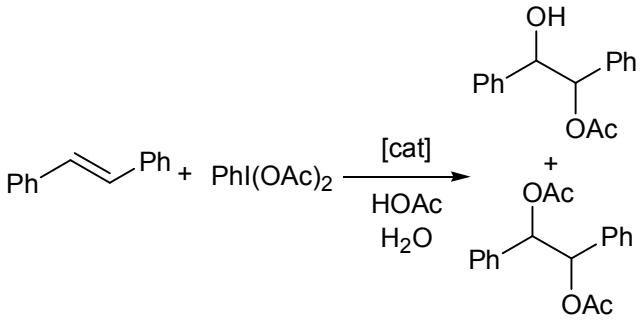


59

Scheme 25

The group of Min Shi has recently described the unprecedented application of a bis(NHC)-palladium(II) complex derived from BINAM in dioxygenation of alkenes. The dicationic diaquo complex displayed good activity and high *syn*-diastereoselectivity in the dioxygenation of 1,2-disubstituted alkenes (Scheme 26).[152] Notably, the reactions proceeded under mild reaction conditions and were tolerant to air and moisture.

The use of metal-NHC complexes, including those palladium-based, as catalysts for alkene oligomerization and polymerization, has recently been reviewed by McGuinness.[153]



Scheme 26

4. Other applications

Along with their proven extraordinary catalytic versatility, other interesting properties of palladium-NHC complexes have been described that widen their scope of application. In a pioneering work, Ghosh and co-workers described the potential anticancer activity of two *trans*-dichloro Pd(II)-NHC complexes (**60** and **61**, Chart 13).[154] In particular, complex **60** had stronger inhibition effect than worldwide employed cisplatin in the proliferation of three different human tumour cells, namely, cervical cancer (HeLa), breast cancer (MCF-7) and colon adenocarcinoma (HCT 116).

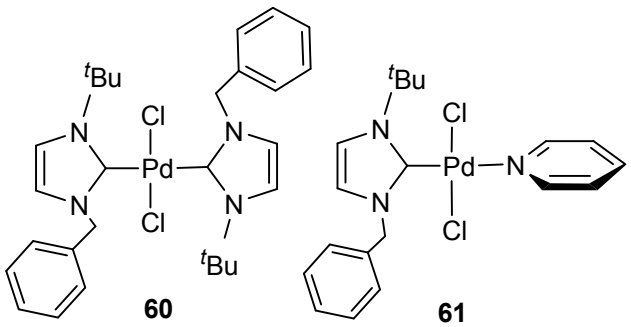


Chart 13

Perspectives

Since the first catalytic application of a Pd-NHC complex was described, several and remarkable applications have been proposed for this type if complexes. The continuous development of new ligand architectures has allowed the preparation of a plethora of Pd-NHC complexes with new catalytic performances.

Along with their many catalytic applications, these systems have found their place in the design of metal-based drugs, thus opening a new and exciting field.

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References

[1] Herrmann, W. A.; Kocher, C. *Angew. Chem. Int. Edit.* **1997**, *36*, 2162-2187.
[2] Hahn, F. E.; Jahnke, M. C. *Angew. Chem. Int. Edit.* **2008**, *47*, 3122-3172.
[3] Herrmann, W. A.; Weskamp, T.; Bohm, V. P. W., Metal complexes of stable carbenes. Advances in Organometallic Chemistry*;* Academic Press Inc: San Diego, **2001**; Vol. 48, pp. 1-69.
[4] Hahn, F. E. *Angew. Chem. Int. Edit.* **2006**, *45*, 1348-1352.
[5] Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39-91.
[6] Diez-Gonzalez, S.; Nolan, S. P. *Coord. Chem. Rev.* **2007**, *251*, 874-883.
[7] Cavallo, L.; Correa, A.; Costabile, C.; Jacobsen, H. *J. Organomet. Chem.* **2005**, *690*, 5407-5413.
[8] Strassner, T. *Top. Organomet. Chem.* **2004**, *13*, 1-20.
[9] Scott, N. M.; Nolan, S. P. *Eur. J. Inorg. Chem.* **2005**, 1815-1828.
[10] Dorta, R.; Stevens, E. D.; Scott, N. M.; Costabile, C.; Cavallo, L.; Hoff, C. D.; Nolan, S. P. *J. Am. Chem. Soc.* **2005**, *127*, 2485-2495.
[11] Peris, E. *Top. Organomet. Chem.* **2007**, *41*, 83-116.
[12] Ofele, K.; Herrmann, W. A.; Mihalios, D.; Elison, M.; Herdtweck, E.; Priermeier, T.; Kiprof, P. *J. Organomet. Chem.* **1995**, *498*, 1-14.
[13] Diez-Gonzalez, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612-3676.
[14] Normand, A. T.; Cavell, K. J. *Eur. J. Inorg. Chem.* **2008**, 2781-2800.
[15] Herrmann, W. A. *Angew. Chem. Int. Edit.* **2002**, *41*, 1290-1309.
[16] Sommer, W. J.; Weck, M. *Coord. Chem. Rev.* **2007**, *251*, 860-873.

[17] Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606-5655.
[18] Marion, N.; Diez-Gonzalez, S.; Nolan, I. P. *Angew. Chem. Int. Edit.* **2007**, *46*, 2988-3000.
[19] Mata, J. A.; Poyatos, M.; Peris, E. *Coord. Chem. Rev.* **2007**, *251*, 841-859.
[20] Poyatos, M.; Mata, J. A.; Peris, E. *Chem. Rev.* **2009**, *109*, 3677-3707.
[21] Pugh, D.; Danopoulos, A. A. *Coord. Chem. Rev.* **2007**, *251*, 610-641.
[22] Peris, E.; Crabtree, R. H. *Coord. Chem. Rev.* **2004**, *248*, 2239-2246.
[23] Peris, E.; Crabtree, R. H. *Comptes Rendus Chimie* **2003**, *6*, 33-37.
[24] Cesar, V.; Bellemin-Laponnaz, S.; Gade, L. H. *Chem. Soc. Rev.* **2004**, *33*, 619-636.
[25] Gade, L. H.; Bellemin-Laponnaz, S. *Top. Organomet. Chem.* **2007**, *41*, 117-157.
[26] Perry, M. C.; Burgess, K. *Tetrahedron-Asymmetry* **2003**, *14*, 951-961.
[27] Gade, L. H.; Bellemin-Laponnaz, S. *Coord. Chem. Rev.* **2007**, *251*, 718-725.
[28] Glorius, F. N-Heterocyclic Carbenes in Transition Metal Catalysis; Topics in Organometallic Chemistry. Springer-Verlag: Berlin/Heidelberg, **2007**.
[29] Nolan, S. P. N-Heterocyclic Carbenes in Synthesis. Wiley-VCH: New York, **2006**.
[30] Bertrand, G., Ed. *J. Organomet. Chem.* **2005**, *690*.
[31] Crabtree, R. H., Ed. *Coord. Chem. Rev.* **2007**, *251*.
[32] Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Angew. Chem. Int. Edit.* **2007**, *46*, 2768-2813.
[33] Herrmann, W. A.; Ofele, K.; Von Preysing, D.; Schneider, S. K. *J. Organomet. Chem.* **2003**, *687*, 229-248.
[34] Hillier, A. C.; Grasa, G. A.; Viciu, M. S.; Lee, H. M.; Yang, C. L.; Nolan, S. P. *J. Organomet. Chem.* **2002**, *653*, 69-82.
[35] Marion, N.; Nolan, S. P. *Acc. Chem. Res.* **2008**, *41*, 1440-1449.
[36] Wurtz, S.; Glorius, F. *Acc. Chem. Res.* **2008**, *41*, 1523-1533.
[37] Diez-Gonzalez, S.; Nolan, S. P. *Top. Organomet. Chem.* **2007**, *21*, 47-82.
[38] Bedford, R. B.; Cazin, C. S. J.; Holder, D. *Coord. Chem. Rev.* **2004**, *248*, 2283-2321.
[39] Anastas, P. T.; Warner, J. C. Green Chemistry: Theory and Practice. Oxford University Press: Oxford, **1988**.
[40] Cazin, C. S. J. *Comptes Rendus Chimie* **2009**, *12*, 1173-1180.
[41] Polshettiwar, V.; Varma, R. S. *Tetrahedron* **2008**, *64*, 4637-4643.
[42] Lee, D. H.; Kim, J. H.; Jun, B. H.; Kang, H.; Park, J.; Lee, Y. S. *Org. Lett.* **2008**, *10*, 1609-1612.
[43] Hou, Y. Z.; Ji, X. T.; Liu, G.; Tang, J. Y.; Zheng, J.; Liu, Y.; Zhang, W. X.; Jia, M. J. *Catal. Commun.* **2009**, *10*, 1459-1462.
[44] Dwars, T.; Paetzold, E.; Oehme, G. *Angew. Chem. Int. Edit.* **2005**, *44*, 7174-7199.
[45] Shaughnessy, K. H. *Chem. Rev.* **2009**, *109*, 643-710.
[46] Ozdemir, I.; Yigit, B.; Cetinkaya, B.; Ulku, D.; Tahir, M. N.; Arici, C. *J. Organomet. Chem.* **2001**, *633*, 27-32.
[47] Hong, S. H.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 3508-3509.
[48] Gallivan, J. P.; Jordan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **2005**, *46*, 2577-2580.
[49] Ozdemir, I.; Gurbuz, N.; Gok, Y.; Cetinkaya, E.; Cetinkaya, B. *Synlett* **2005**, 2394-2396.
[50] Ozdemir, I.; Demir, S.; Yasar, S.; Cetinkaya, B. *Appl. Organomet. Chem.* **2005**, *19*, 55-58.

[51] Furstner, A.; Krause, H. *Adv. Synth. Catal.* **2001**, *343*, 343-350.
[52] Zhao, Y. H.; Zhou, Y. Y.; Ma, D. D.; Liu, J. P.; Li, L.; Zhang, T. Y.; Zhang, H. B. *Org. Biomol. Chem.* **2003**, *1*, 1643-1646.
[53] Kascatan-Nebioglu, A.; Panzner, M. J.; Garrison, J. C.; Tessier, C. A.; Youngs, W. J. *Organometallics* **2004**, *23*, 1928-1931.
[54] Melaiye, A.; Sun, Z. H.; Hindi, K.; Milsted, A.; Ely, D.; Reneker, D. H.; Tessier, C. A.; Youngs, W. J. *J. Am. Chem. Soc.* **2005**, *127*, 2285-2291.
[55] Gulcemal, S.; Kahraman, S.; Daran, J. C.; Cetinkaya, E.; Cetinkaya, B. *J. Organomet. Chem.* **2009**, *694*, 3580-3589.
[56] Turkmen, H.; Can, R.; Cetinkaya, B. *Dalton Trans.* **2009**, 7039-7044.
[57] Ohta, H.; Fujiharaa, T.; Tsuji, Y. *Dalton Trans.* **2008**, 379-385.
[58] Moore, L. R.; Cooks, S. M.; Anderson, M. S.; Schanz, H. J.; Griffin, S. T.; Rogers, R. D.; Kirk, M. C.; Shaughnessy, K. H. *Organometallics* **2006**, *25*, 5151-5158.
[59] Mesnager, J.; Lammel, P.; Jeanneau, E.; Pinel, C. *Appl. Catal., A* **2009**, *368*, 22-28.
[60] Mesnager, J.; Kuntz, E.; Pinel, C. *J. Organomet. Chem.* **2009**, *694*, 2513-2518.
[61] Nagai, Y.; Kochi, T.; Nozaki, K. *Organometallics* **2009**, *28*, 6131-6134.
[62] Gladysz, J. A.; Curran, D. P.; Horvath, I. T. Handbook of Fluorous Chemistry. Wiley-VCH: Weinheim, **2004**.
[63] Kysilka, O.; Rybackova, M.; Skalicky, M.; Kvicalova, M.; Cvacka, J.; Kvicala, J. *Collect. Czech. Chem. Commun.* **2008**, *73*, 1799-1813.
[64] Furstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. *Chem. Eur. J.* **2001**, *7*, 3236-3253.
[65] Xu, L. J.; Chen, W. P.; Bickley, J. F.; Steiner, A.; Xiao, J. L. *J. Organomet. Chem.* **2000**, *598*, 409-416.
[66] Skalicky, M.; Rybackova, M.; Kysilka, O.; Kvicalova, M.; Cvacka, J.; Cejka, J.; Kvicala, J. *J. Fluor. Chem.* **2009**, *130*, 966-973.
[67] Welton, T. *Chem. Rev.* **1999**, *99*, 2071-2083.
[68] Olivier-Bourbigou, H.; Magna, L.; Morvan, D. *Appl. Catal., A* **2010**, *373*, 1-56.
[69] Zhang, Z. C., Catalysis in ionic liquids. Advances in Catalysis. **2006**; Vol. *49*, pp. 153-237.
[70] Welton, T. *Coord. Chem. Rev.* **2004**, *248*, 2459-2477.
[71] Cai, Y. Q.; Liu, Y. *Catal. Commun.* **2009**, *10*, 1390-1393.
[72] Vandezande, P.; Gevers, L. E. M.; Vankelecom, I. F. J. *Chem. Soc. Rev.* **2008**, *37*, 365-405.
[73] Schoeps, D.; Sashuk, V.; Ebert, K.; Plenio, H. *Organometallics* **2009**, *28*, 3922-3927.
[74] Enders, D.; Gielen, H. *J. Organomet. Chem.* **2001**, *617*, 70-80.
[75] Herrmann, W. A.; Goossen, L. J.; Kocher, C.; Artus, G. R. J. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2805-2807.
[76] Nicolaou, K. C.; Hao, J. L.; Reddy, M. V.; Rao, P. B.; Rassias, G.; Snyder, S. A.; Huang, X. H.; Chen, D. Y. K.; Brenzovich, W. E.; Giuseppone, N.; Giannakakou, P.; O'Brate, A. *J. Am. Chem. Soc.* **2004**, *126*, 12897-12906.
[77] Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, 2209-2219.
[78] Culkin, D. A.; Hartwig, J. F. *Acc. Chem. Res.* **2003**, *36*, 234-245.
[79] Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, *66*, 3402-3415.
[80] Glorius, F.; Altenhoff, G.; Goddard, R.; Lehmann, C. *Chem. Commun.* **2002**, 2704-2705.
[81] Arao, T.; Kondo, K.; Aoyama, T. *Chem. Pharm. Bull.* **2006**, *54*, 1743-1747.

[82] Arao, T.; Sato, K.; Kondo, K.; Aoyama, T. *Chem. Pharm. Bull.* **2006**, *54*, 1576-1581.
[83] Kundig, E. P.; Seidel, T. M.; Jia, Y. X.; Bernardinelli, G. *Angew. Chem. Int. Edit.* **2007**, *46*, 8484-8487.
[84] Jia, Y. X.; Hillgren, J. M.; Watson, E. L.; Marsden, S. P.; Kundig, E. P. *Chem. Commun.* **2008**, 4040-4042.
[85] Wurtz, S.; Lohre, C.; Frohlich, R.; Bergander, K.; Glorius, F. *J. Am. Chem. Soc.* **2009**, *131*, 8344-8345.
[86] Luan, X. J.; Mariz, R.; Robert, C.; Gatti, M.; Blumentritt, S.; Linden, A.; Dorta, R. *Org. Lett.* **2008**, *10*, 5569-5572.
[87] Scarborough, C. C.; Bergant, A.; Sazama, G. T.; Guzei, I. A.; Spencer, L. C.; Stahl, S. S. *Tetrahedron* **2009**, *65*, 5084-5092.
[88] Liu, Z.; Shi, M. *Tetrahedron-Asymmetry* **2009**, *20*, 119-123.
[89] Liu, Z.; Zhang, T.; Shi, M. *Organometallics* **2008**, *27*, 2668-2671.
[90] Somei, M.; Yamada, F. *Nat. Prod. Rep.* **2004**, *21*, 278-311.
[91] Faulkner, D. J. *Nat. Prod. Rep.* **2002**, *19*, 1-48.
[92] Bosch, J.; Bennasar, M. L. *Synlett* **1995**, 587-596.
[93] Liu, L. J.; Wang, F. J.; Shi, M. *Organometallics* **2009**, *28*, 4416-4420.
[94] Liu, S. J.; Liu, L. J.; Shi, M. *Appl. Organomet. Chem.* **2009**, *23*, 183-190.
[95] Chen, T.; Jiang, J. J.; Xu, Q.; Shi, M. *Org. Lett.* **2007**, *9*, 865-868.
[96] Meyer, A.; Taige, M. A.; Strassner, T. *J. Organomet. Chem.* **2009**, *694*, 1861-1868.
[97] Abdellah, I.; Debono, N.; Canac, Y.; Duhayon, C.; Chauvin, R. *Dalton Trans.* **2009**, 7196-7202.
[98] Debono, N.; Labande, A.; Manoury, E.; Daran, J.-C.; Poli, R. *Organometallics* **2010**, *DOI: 10.1021/om100125k.*
[99] Boronat, M.; Corma, A.; Gonzalez-Arellano, C.; Iglesias, M.; Sanchez, F. *Organometallics* **2010**, *29*, 134-141.
[100] Arnanz, A.; Gonzalez-Arellano, C.; Juan, A.; Villaverde, G.; Corma, A.; Iglesias, M.; Sanchez, F. *Chem. Commun.* **2010**, *46*, 3001-3003.
[101] Broussard, M. E.; Juma, B.; Train, S. G.; Peng, W. J.; Laneman, S. A.; Stanley, G. G. *Science* **1993**, *260*, 1784-1788.
[102] Tennyson, A. G.; Ono, R. J.; Hudnall, T. W.; Khramov, D. M.; Er, J. A. V.; Kamplain, J. W.; Lynch, V. M.; Sessler, J. L.; Bielawski, C. W. *Chem. Eur. J.* **2010**, *16*, 304-315.
[103] Boydston, A. J.; Williams, K. A.; Bielawski, C. W. *J. Am. Chem. Soc.* **2005**, *127*, 12496-12497.
[104] Guerret, O.; Sole, S.; Gornitzka, H.; Teichert, M.; Trinquier, G.; Bertrand, G. *J. Am. Chem. Soc.* **1997**, *119*, 6668-6669.
[105] Khramov, D. M.; Boydston, A. J.; Bielawski, C. W. *Angew. Chem. Int. Edit.* **2006**, *45*, 6186-6189.
[106] Mas-Marza, E.; Mata, J. A.; Peris, E. *Angew. Chem. Int. Edit.* **2007**, *46*, 3729-3731.
[107] Viciano, M.; Sanau, M.; Peris, E. *Organometallics* **2007**, *26*, 6050-6054.
[108] Mercs, L.; Neels, A.; Stoeckli-Evans, H.; Albrecht, M. *Dalton Trans.* **2009**, 7168-7178.
[109] Boydston, A. J.; Rice, J. D.; Sanderson, M. D.; Dykhno, O. L.; Bielawski, C. W. *Organometallics* **2006**, *25*, 6087-6098.
[110] Boydston, A. J.; Bielawski, C. W. *Dalton Trans.* **2006**, 4073-4077.

[111] Williams, K. A.; Boydston, A. J.; Bielawski, C. W. *Chem. Soc. Rev.* **2007**, *36*, 729-744.
[112] Karimi, B.; Akhavan, P. F. *Chem. Commun.* **2009**, 3750-3752.
[113] Zanardi, A.; Mata, J. A.; Peris, E. *Organometallics* **2009**, *28*, 1480-1483.
[114] Zanardi, A.; Mata, J. A.; Peris, E. *Organometallics* **2009**, *28*, 4335-4339.
[115] Ruan, J. W.; Saidi, O.; Iggo, J. A.; Xiao, J. L. *J. Am. Chem. Soc.* **2008**, *130*, 10510-10511.
[116] Vo, G. D.; Hartwig, J. E. *Angew. Chem. Int. Edit.* **2008**, *47*, 2127-2130.
[117] Zanardi, A.; Mata, J. A.; Peris, E. *J. Am. Chem. Soc.* **2009**, *131*, 14531-14537.
[118] Navarro, O.; Nolan, S. P. *Synthesis* **2006**, 366-367.
[119] Jensen, D. R.; Sigman, M. S. *Org. Lett.* **2003**, *5*, 63-65.
[120] Cawley, M. J.; Cloke, F. G. N.; Fitzmaurice, R. J.; Pearson, S. E.; Scott, J. S.; Caddick, S. *Org. Biomol. Chem.* **2008**, *6*, 2820-2825.
[121] Broggi, J.; Clavier, H.; Nolan, S. P. *Organometallics* **2008**, *27*, 5525-5531.
[122] Jin, Z.; Guo, S. X.; Gu, X. P.; Qiu, L. L.; Song, H. B.; Fang, J. X. *Adv. Synth. Catal.* **2009**, *351*, 1575-1585.
[123] Nakafuji, S. Y.; Kobayashi, J.; Kawashima, T. *Angew. Chem. Int. Edit.* **2008**, *47*, 1141-1144.
[124] Chianese, A. R.; Bremer, P. T.; Wong, C.; Reynes, R. J. *Organometallics* **2009**, *28*, 5244-5252.
[125] Roland, S.; Cotet, W.; Mangeney, P. *Eur. J. Inorg. Chem.* **2009**, 1796-1805.
[126] Flahaut, A.; Roland, S.; Mangeney, P. *J. Organomet. Chem.* **2007**, *692*, 5754-5762.
[127] Muller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795-3892.
[128] Muller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675-703.
[129] Dash, C.; Shaikh, M. M.; Butcher, R. J.; Ghosh, P. *Dalton Trans.* **2010**, *39*, 2515-2524.
[130] Najera, C.; Sansano, J. M. *Chem. Rev.* **2007**, *107*, 4584-4671.
[131] Yet, L. *Angew. Chem. Int. Edit.* **2001**, *40*, 875-877.
[132] Jarusiewicz, J.; Choe, Y.; Yoo, K. S.; Park, C. P.; Jung, K. W. *J. Org. Chem.* **2009**, *74*, 2873-2876.
[133] Zhang, Y. G.; Ngeow, K. C.; Ying, J. Y. *Org. Lett.* **2007**, *9*, 3495-3498.
[134] Fu, C. F.; Liu, Y. H.; Peng, S. M.; Liu, S. T. *Tetrahedron* **2010**, *66*, 2119-2122.
[135] Klomp, D.; Hanefeld, U.; Peters, J. A. Handbook for Homogenous Hydrogenation. Wiley-VCH: Weinheim, **2007**.
[136] Dobereiner, G. E.; Crabtree, R. H. *Chem. Rev.* **2010**, *110*, 681-703.
[137] Warsink, S.; Hauwert, P.; Siegler, M. A.; Spek, A. L.; Elsevier, C. J. *Appl. Organomet. Chem.* **2009**, *23*, 225-228.
[138] Hauwert, P.; Maestri, G.; Sprengers, J. W.; Catellani, M.; Elsevier, C. J. *Angew. Chem. Int. Edit.* **2008**, *47*, 3223-3226.
[139] Jurcik, V.; Nolan, S. P.; Cazin, C. S. L. *Chem. Eur. J.* **2009**, *15*, 2509-2511.
[140] Bei, X. H.; Hagemeyer, A.; Volpe, A.; Saxton, R.; Turner, H.; Guram, A. S. *J. Org. Chem.* **2004**, *69*, 8626-8633.
[141] Guram, A. S.; Bei, X. H.; Turner, H. W. *Org. Lett.* **2003**, *5*, 2485-2487.
[142] Bouquillon, S.; Henin, F.; Muzart, J. *Organometallics* **2000**, *19*, 1434-1437.
[143] Berini, C.; Brayton, D. F.; Mocka, C.; Navarro, O. *Org. Lett.* **2009**, *11*, 4244-4247.

[144] Burling, S.; Paine, B. M.; Nama, D.; Brown, V. S.; Mahon, M. F.; Prior, T. J.; Pregosin, P. S.; Whittlesey, M. K.; Williams, J. M. J. *J. Am. Chem. Soc.* **2007**, *129*, 1987-1995.
[145] Ahrens, S.; Strassner, T. *Inorg. Chim. Acta* **2006**, *359*, 4789-4796.
[146] Fructos, M. R.; de Fremont, P.; Nolan, S. P.; Diaz-Requejo, M. M.; Perez, P. J. *Organometallics* **2006**, *25*, 2237-2241.
[147] Corberan, R.; Sanau, M.; Peris, E. *J. Am. Chem. Soc.* **2006**, *128*, 3974-3979.
[148] Muehlhofer, M.; Strassner, T.; Herrmann, W. A. *Angew. Chem. Int. Edit.* **2002**, *41*, 1745- 1747.
[149] Lee, J. H.; Yoo, K. S.; Park, C. P.; Olsen, J. M.; Sakaguchi, S.; Prakash, G. K. S.; Mathew, T.; Jung, K. W. *Adv. Synth. Catal.* **2009**, *351*, 563-568.
[150] Muzart, J. *Tetrahedron* **2005**, *61*, 9423-9463.
[151] Torrente-Murciano, L.; Lapkin, A.; Nielsen, D. J.; Fallis, I.; Cavell, K. J. *Green Chem.* **2010**, DOI: 10.1039/b921573e.
[152] Wang, W.; Wang, F.; Shi, M. *Organometallics* **2010**, *29*, 928-933.
[153] McGuinness, D. *Dalton Trans.* **2009**, 6915-6923.
[154] Ray, S.; Mohan, R.; Singh, J. K.; Samantaray, M. K.; Shaikh, M. M.; Panda, D.; Ghosh, P. *J. Am. Chem. Soc.* **2007**, *129*, 15042-15053.