Multidentate DI-N-heterocyclic carbene ligands for transition metal catalyzed hydrogenation reactions
Sluijter, S.N.

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MULTIDENTATE DI-\(N\)-HETEROCYCLIC CARBENE LIGANDS FOR TRANSITION METAL CATALYZED HYDROGENATION REACTIONS

SORAYA SLUIJTER
Multidentate Di-N-Heterocyclic Carbene Ligands
for Transition Metal Catalyzed Hydrogenation
Reactions

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
Prof. dr. D. C. van den Boom
ten overstaan van een door het College voor Promoties ingestelde
commissie,
in het openbaar te verdedigen in de Agnietenkapel
op vrijdag 18 september 2015, te 10:00 uur
door

Soraya Nicole Sluijter
geboren te Amsterdam
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Promotor:  Prof. dr. C. J. Elsevier  Universiteit van Amsterdam
Copromotor:  Dr. ir. J. I. van der Vlugt  Universiteit van Amsterdam
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Faculteit der Natuurwetenschappen, Wiskunde en Informatica.

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<td>Metal-Ligand Cooperativity</td>
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<td>tz</td>
<td>1,2,3-triazole</td>
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<td>VT</td>
<td>Variable Temperature</td>
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Chapter 1

Introduction: Bidentate (di-)NHC Ligands bearing tzNHCs in Organometallic Chemistry and Homogeneous Catalysis
1.1 Organometallic Chemistry and Homogeneous Catalysis

Catalysis is essential to life on our planet. Enzymes, nature’s catalysts, enable chemical reactions in bio-systems, thereby making life possible in the first place. Moreover, catalysts are used in most industrial processes (>80%). Herein they facilitate the production of chemicals for various applications and products for everyday life, ranging from plastics and the fuel in our cars to pharmaceuticals. Catalysts can increase the rate at which reactions proceed. More importantly, they can prevent side reactions, making transformations more selective, which leads to fewer byproducts and less waste. To achieve a more sustainable chemical industry, much research in industry as well as academia is nowadays devoted to developing and improving catalytic systems. The research described in this thesis is a contribution to this end in the field of homogeneous catalysis.

In homogeneous catalysis the catalysts influence the rate and outcome of a reaction while being in the same phase as the reaction (usually in solution). Often they are organometallic compounds consisting of a (transition) metal surrounded by organic molecules, the ligands. These ligands influence the properties of the metal catalyst. Optimization of the steric and electronic characteristics of the ligands and their coordination to a suitable metal is therefore key to the performance of a catalyst. The accumulated knowledge on ligands and organometallic catalysts is extensive, including understanding of the mechanisms of catalytic reactions as well as the effects of certain ligand parameters. This makes it possible to design homogeneous catalysts in a rational manner. Traditional ligands in homogeneous catalysis were mostly based on oxygen, nitrogen, sulfur or phosphorus donor atoms, binding through a lone-pair on the atom. More recently, N-heterocyclic carbenes (NHCs), the class of ligands employed throughout this thesis, have been established as viable ligands.

1.2 N-heterocyclic Carbene Ligands

Nowadays, NHCs are paramount to organometallic chemistry and homogeneous catalysis. NHCs consist of a singlet carbene in a heterocyclic ring. The $sp^2$-hybridized carbon has a lone pair available for donation to the metal center of choice. Although free carbenes are very reactive, some can be isolated. Arduengo was the first to achieve this for a bulky imidazol-2-ylidene in the 1990's (Figure 1). Hence, these most well-known NHCs are also called Arduengo-type carbenes. The reactive carbene center was reasoned to be stabilized by steric shielding of the bulky side groups. The steric bulk can, for example, prevent the NHC from dimerization. Additionally, NHCs derive their relative stability from their structure having a “push-and-pull” system (Figure 1). The two nitrogen atoms adjacent to the carbene carbon donate electron-density from their lone pairs into the empty $p$-orbital of
the carbene ("push"). This causes the filled lone pair orbital, orthogonal to the stabilizing π-system, to be available for σ-donation. Besides, the nitrogen atoms also have an inductive mildly electron-withdrawing ("pull") effect.

Figure 1: Stabilization of the carbene moiety in NHCs; sterically in case of Arduengo’s bis-adamantyl-NHC (left) and electronically by the “push-and-pull” effect (right).

The first NHC metal complexes were reported by Öfele and Wanzlick in 1968. Since then, they have been coordinated to almost every metal in the periodic table. In the early days, NHCs were viewed as simple σ-donors, donating electron-density in an empty d-orbital of the metal. However, for the binding with electron-rich transition metals (TM) NHCs also accept electron-density in the π* orbital. The important orbital interactions that constitute the M-NHC bond are depicted in Figure 2.

Figure 2: Schematic representation of the relevant molecular orbital interactions constituting the M-NHC bond, left: imidazol-2-ylidene and right: 1,2,3-triazolylidene.
Several ways of making metal NHCs are known and a selection is depicted in Scheme 1. As most free NHCs are not shelf-stable, their metal complexes are mostly prepared via deprotonation of the corresponding imidazolium salts in the presence of the appropriate metal precursor. Various strong bases (at low temperatures) as well as internal bases at the metal precursor have been used to deprotonate the NHC precursors. Another popular synthetic route is transmetalation. Here, the imidazolium salt is coordinated to a metal, usually silver(I), that can subsequently transfer the carbene to a second metal center. Additionally, a metal can be inserted in the C=C bond of the Wanzlick carbene dimer, and oxidative addition of a C-X bond (e.g., X = halide, alkyl, H) can lead to an NHC-M complex. Lastly, the group of Hahn developed an entirely different approach. They obtained (asymmetrically substituted) saturated or benzimidazolylidene complexes by intramolecular cyclization (via nucleophilic attack of an amine to a functionalized isonitrile) on the metal center.

NHC metal complexes have been applied in medicinal chemistry, material science (photoluminescence) and organocatalysis, but above all in homogeneous transition metal catalysis (Scheme 1). One of the most well-known NHC...
catalysts is Grubbs’ second generation olefin metathesis catalyst. In this catalytic system the impact of the enhanced σ-donating properties is nicely illustrated. The replacement of one of the two tricyclohexylphosphine ligands in Grubbs’ first generation catalyst with an NHC leads to an enhanced catalytic rate by a factor of $10^2$-$10^3$ (Scheme 2). This rate enhancement is attributed to the weakened M-P bond; the increase in electron-density on the metal caused by the NHC ligand labilizes the metal-phosphine bond, facilitating dissociation of the phosphine ligand, which is necessary for the complex to enter the catalytic cycle.

Scheme 2: Grubbs’ first and second generation metathesis catalyst and dissociation of one PCy$_3$ leading to the active catalyst. This step is significantly faster when the phosphine ligand is replaced by an NHC (Grubbs II) with highly increased activity as a result. Cy = cyclohexyl, Mes = 2,4,6-trimethylphenyl.

Triazole-based mesoionic carbene ligands

Next to imidazole-2-ylidenes, several other types of NHCs have been developed in the last decade (Figure 3). The electron-donating properties of these NHCs are influenced to a large extent by the position of the nitrogen atoms in the ring.

Figure 3: Several NHCs arranged by increasing σ-donor properties according to their TEP (Tolman Electronic Parameter = ν$_{CO}$ of [Ni(CO)$_3$(NHC)]) data: phosphines, 1,2,4-triazolylidene, saturated imidazole-2-ylidene, imidazole-2-ylidene, six-membered expanded ring NHC, 1,2,3-triazolylidene, imidazole-4-ylidene and pyrazolin-4-ylidene. Calculated HOMO (highest occupied molecular orbital) energies reported by Frison and Huyn et al. are included.
Remarkably, for some of these NHCs formal charges have to be added in order to draw a valid Lewis structure of the free ligand, which led to the term meso-ionic carbenes (MICs).\textsuperscript{32,33} The formal negative charge is located partly on the carbene, which is in line with the higher electron-density at that position compared to "classic" NHCs (Figure 3).

The first MIC complex reported was an imidazole-4-ylidene published by Crabtree and co-workers in 2001.\textsuperscript{34} They described the "abnormal" coordination of the NHC, on the 4- instead of the 2-position, in an iridium-hydride complex. Hence, the term abnormal carbene (aNHC) is alternatively used for MICs. This mode of coordination is generally brought about by steric factors or on purpose by synthetically protecting the C2 position of the NHC.

Since the first serendipitous synthesis of a MIC complex, several successors have been developed and 1,2,3-triazol-5-ylidenes (tzNHCs) have advanced to one of the most widely studied and applied classes of "non-classical" NHCs. Triazoles can be easily prepared using Cu(I) catalyzed [3+2] cycloaddition of an alkyne and an azide (CuAAC; Scheme 3)\textsuperscript{35,36} and have been popular research subjects in several research fields such as bioconjugation, material science and medicinal chemistry.\textsuperscript{37} Recently, triazole-based ligands have also found their way into transition metal catalysis, either coordinating to the metal via one of the nitrogen atoms\textsuperscript{38} or as tzNHC (after alkylation of the N3 position).\textsuperscript{33,39,40} The popularity of the latter can be explained by the combination of their specific $\sigma$-donor properties, stronger than the most basic classic carbenes yet weaker than imidazole-4-ylidenes (Figure 3),\textsuperscript{1,6} their before-mentioned synthetic accessibility and the endless possibilities to vary the N1 and C4 position through "click" chemistry.\textsuperscript{42–44}

\begin{scheme}
\begin{align*}
R^1, N_3 + &\xrightarrow{\text{[Cu]}}[\text{click}] R^2 &\rightarrow N^\equiv N R^1 \rightarrow MeX &\rightarrow N^\equiv N^+ X^- \\
\text{Scheme 3: Synthesis of the most common tzNHC precursor, 1,3,4-substituted triazolium salt: Cu(I) catalyzed "click" cycloaddition of an alkyne and azide followed by alkylation of the N3 atom.}
\end{align*}
\end{scheme}

The versatility and huge potential of tzNHCs were already predicted in the first report on this highly modular class of MICs published by the group of Albrecht in 2008.\textsuperscript{41} They coordinated the tzNHCs to Pd(II) as well as Ag(I), and used the latter to transfer the carbene to Rh(I), Ir(I) and Ru(II), underlining the versatility of metal insertion.\textsuperscript{41,42} At the start of the research project described in this thesis, however, only few tzNHC complexes were known.\textsuperscript{45–47} Since then, tzNHCs have proven to be useful ligands for catalytic applications. Their metal complexes have been reported as active catalysts for a wide variety of reactions: oxidation, olefin metathesis and
transfer hydrogenation (TH) reactions facilitated by Ru(II);\textsuperscript{45,48-53} Ir(III) catalyzed water oxidations;\textsuperscript{49} Pd catalyzed C-C cross-coupling reactions\textsuperscript{51} and hydroarylation;\textsuperscript{57} and carbene transfer and cyclization reactions by gold complexes.\textsuperscript{58}

1.3 Bi- and Tridentate tzNHC Ligands and their Applications

Bidentate ligands have been often implemented in homogeneous catalysis. First of all because they generally improve the stability of complexes (chelate effect). More importantly, the combination of different donating atoms in synergy can lead to improved properties of the complex.\textsuperscript{59} The activity of the resulting catalyst may, for example, greatly exceed that of the analogous systems bearing two monodentate ligands.

**Bi- and Tridentate tzNHC Ligands with Heteroatom Donors**

Several chelate donor-functionalized tzNHC complexes have been reported and a selection is depicted in Figure 4.

**Figure 4:** Structures of selected examples of bidentate tzNHCs bearing heteroatom donors.
These complexes bear at least one anionic or neutral two-electron donor atom (C, N, O, or P) besides the NHC. They can act as bi- or tridentate ligands upon coordination to the metal center.

Gandelman et al. published pincer metal (Pd and Pt) complexes, bearing triazolylidene as central motif flanked by two phosphine donors (Figure 4).\(^\text{60}\) These complexes were prepared by post modification of the metal complexes, as depicted in Scheme 4. No catalytic applications have been reported for these systems to date.

![Scheme 4: Synthesis of the palladium triazolylidene complex by postmodification published by Gandelman.\(^\text{60}\)](image)

The majority of the functionalized tzNHC ligands have a secondary nitrogen donor. Sessler et al. combined two tzNHC ligands with ancillary pyrrole groups. Upon transmetalation of the silver(I) complex with a Ru \(\text{para-cymene (p-cym)}\) precursor the homodinuclear complex (Figure 4), which was active in the ring-opening metathesis polymerization of norbornene.

Pyridine functionalized tzNHC ruthenium complexes have been described by several groups. Košmrlj and co-workers synthesized several \([\text{Ru(\(\eta^6\text{-p-cym})\text{(tzNHC) Cl\}}]^+\) complexes bearing picolyl and pyridine substituents \(3-5\) via transmetalation of the corresponding Ag(I) complexes (Figure 4).\(^\text{61}\) Remarkably, the 1-(2-picolyl)-1,2,3-triazolium salt could not be coordinated following this route. The resulting complexes were applied in oxidation of alcohols with tert-butyl hydroperoxide in water and showed selectivity for benzylic compared to non-benzylic alcohols. The authors argued that this differentiation in combination with the mild conditions and the environmentally benign solvent makes this system superior to similar imidazole-2-ylidene catalysts. The group of Albrecht prepared a series of \([\text{Ru(bipy)}_2]\) analogues (bipy = 2,2-bipyridyl) as photosensitizers for solar energy conversion, including a tzNHC-pyr complex (5c; Figure 4).\(^\text{52}\) They reported that the tzNHC variant showed promising properties for this application, having the smallest HOMO-LUMO gap (2.41 eV; LUMO = lowest unoccupied molecular orbital) of the synthesized Ru NHC-pyr complexes and a long excited-state lifetime (188 ns).

The group of Albrecht also reported a series of bidentate tzNHC ruthenium \(\text{p-cym}\) complexes \(4-7\) with various donor substituents (Figure 4): phenyl anion, carboxylate, and again pyridine (connected via both the N1 and C4 atom of tzNHC).\(^\text{53}\) The catalysts were applied in alcohol dehydrogenation as well as transfer hydrogenation (TH) and
a significant influence of the donor functionalities was found. Complex 7a with the CC bidentate ligand led to the highest activity for alcohol dehydrogenation, whereas the complex bearing the pyridyl donor (5a) proved the best choice for TH. The authors explained these trends in terms of electron-density on the ruthenium center: neutral weakly donating chelated ligands (e.g. pyridine) lead to a relatively electron-poor metal center that readily binds anions (RO\textsuperscript{-} in this case), leading to good performance in TH, and vice versa. In addition, complexes 5a\textsuperscript{63} and 7b\textsuperscript{54} have successfully been applied for catalytic water oxidation with cerium ammonium nitrate (CAN) as the sacrificial oxidant.

CC chelating tzNHC complexes 7 and 8 are formed by so-called cyclometalation.\textsuperscript{49,64,65} Cyclometalation can be promoted by (weak) bases, but spontaneous C-H activation on the N-bound aryl ring occurs with electrophilic metal centers.\textsuperscript{64} Stephan et al. reported cyclometalated Ru(II) complexes 8b, derived from the corresponding ruthenium-hydride complex by C-H activation followed by liberation of H\textsubscript{2}.\textsuperscript{65} The complexes proved to be active catalyst precursors for the hydrogenation of olefins, while leaving other functional groups intact.

Recently, Sarkar et al. reported a series of Cp\textsuperscript{*}-Ir(III) complexes (Cp\textsuperscript{*} = pentamethylcyclopentadienyl) bearing ligands ranging from bipy, pyridyl-triazole, di-triazole to pyridyl-triazolylidene 5b, triazolyl-triazolylidene 9 (Figure 4) and di-triazolylidene 10b (Figure 5). The complexes were tested for the oxygenation of C-H bonds. The pre-catalyst with unsymmetrical donors, particularly 5b, proved to be the most suitable catalyst for the C-H oxygenation of cyclooctadiene with sacrificial oxidants, outperforming previously reported iridium systems. In this example unsymmetrical tzNHC ligands proved to give the most potent catalysts. However, excellent results have also been obtained with di-tzNHC complexes as described below.

**Bidentate di-NHC Ligands bearing tzNHCs**

Following the success of monodentate NHCs, chelating di-NHCs have become popular ligands in transition metal catalysis.\textsuperscript{66} Two strongly bound NHCs lead to enhanced stability of the complex due to the chelate effect as well as an electron-rich metal center. The ligands are good candidates for fine-tuning of catalytic properties by altering the wingtips, backbone and linker.\textsuperscript{67} More recently, also di-NHC ligands incorporating tzNHC have been reported, including a few examples of heteroditopic di-NHCs, bearing two different types of NHCs (Figure 5).

Bertrand et al. reported a tzNHC analogue to “bipy”: 1,4-bidentate bis(1,2,3-triazol-5-ylidene) “i-bitz” complex 10c (Figure 5).\textsuperscript{68} They isolated the free carbene ligand and a cationic rhodium complex. A similar diisopropylphenyl substituted ligand was
used to prepare half-sandwich Ru(p-cym), 10a, and Ir Cp*, 10b, complexes, that were applied in the transfer hydrogenation of nitrobenzenes. The products formed in the reactions were found to depend on the metal center: anilines for the ruthenium catalysts and azobenzenes when using iridium. The same ligand bearing para-tolyl substituents was used to prepare the heteroleptic Fe(II) complex 10d. The authors postulate that this iron complex, having a relatively long excited-state lifetime, could be the first step to possible future replacement of the expensive Ru(II) photosensitizer by Fe(II).

Another example of a di-carbene is the heteroditopic di-MIC iridium complex 11 that has been applied in water oxidation by Albrecht et al. (Figure 5). In this system a remote abnormal carbene based on pyridine is combined with a tzNHC. More recently, the same group published a homodinuclear version of this complex connected via a propylene linker on the N1. Both complexes were active precatalysts for water oxidation with CAN as sacrificial oxidant, the latter being more active than the monometallic species at low catalyst concentrations.

Series of heteroleptic bis(tridentate) Ru(II) complexes bearing a CNC pincer ditriaZolylidene ligand 12 have been developed (Figure 5). These photosensitizers showed excellent properties (e.g. long excited-state lifetime) and have also been immobilized on a TiO₂ surface without loss of charge transfer.

Crudden and co-workers have published complex 13 with two tzNHC wingtips on a 1,3-phenylene core (Figure 5). They synthesized and fully characterized a
dimeric Ag(I) (2:2 Ag:L) complex. Subsequent transmetalation to Rh(I) led to a homodinuclear species with the bidentate ligand acting as a bridge between the two metal centers. The group of Cowie reported homodinuclear rhodium and iridium and heterobimetallic Ir-Rh complexes with the same type of ligand (Figure 5). They recently also prepared heterobimetallic Pd-Rh complexes of this mixed NHC-tzNHC ligand by making use of the different acidities of the two NHCs (Figure 5). Very recent examples of multinuclear NHC complexes concern the phenyl-based di- and tri-tzNHC Pd complexes.

Cooperative Ligand Systems

The ligands described so far have been cleverly designed to steer the reactivity of the active metal center. The steric and electronic properties of the ligands determine the performance of the catalysts. The reaction, however, takes place at the metal center and the ligands do not actively participate in the catalytic cycle. Recently, it has become increasingly apparent that this traditional way of considering and utilizing ligands does not realize their full potential. Instead, some ligands can have an active role in the catalytic process, by participating directly in bond activation reactions. This concept, known as metal-ligand cooperativity (MLC), is illustrated by the example depicted in Scheme 5. Here, the benzylic linker of a pincer ligand is deprotonated while the pyridine ring is simultaneously dearomatized. Subsequently, an X-Y bond can be activated over the ligand and metal. The oxidation state of the latter consequently does not change in the process.

Scheme 5: Schematic representation of the active role of bifunctional ligand via aromatization/dearomatization (right) and hemilability (left).

The so-called “non-innocent” or “bifunctional” ligands in synergy with the metal center have led to unprecedented activities in known catalytic transformations and new catalytic reactions entirely, such as, for instance, coupling of alcohols with amines to form amides with liberation of H₂. In nature, evolution has led to similar cooperative mechanisms: the excellent efficiency and selectivity of enzymes is accredited to the active site being embedded in very specific surroundings. Within homogeneous catalysis, MLC is a relative new yet rapidly expanding field.
The pincer-type ligands containing a central pyridine ring flanked by other ligands, popularized by the group of Milstein, operate via the aromatization/dearomatization mechanism (Scheme 5). Metal complexes bearing these ligands exhibited reactivity in a broad range of useful and environmentally benign reactions. A selection of these, reported by Milstein, include dehydrogenative coupling of primary alcohols to produce esters, the reverse reaction: hydrogenation of esters to alcohols, the direct conversion of alcohols to imines (PNP), amides (PNN) and carboxylic acid salts with liberation of \( \text{H}_2 \) and water splitting.

In some of these catalytic reactions, the complexes with the PNN scaffold are excellent catalysts, whereas the PNP analogue is barely active. This has often been attributed to hemilability of the nitrogen donor, i.e. the ability to de- and recoordinate to the metal center (Scheme 5). This feature enables ligands to create vacant coordination sites on the metal, or preorganize or activate the substrate, which may benefit the performance of the catalyst.

The bifunctional approach has also been applied in combination with NHC ligands. One example concerns the bidentate NHC-amine ligands exploited by Morris’ and our group. The complexes 16, bearing such ligands, are active in the reduction of polar bonds (Scheme 6). The hydrogenation was found to proceed via an inner- or outer-sphere mechanism depending on the co-ligand: anionic \( \text{Cp}^* \) ligands lead to the faster outer-sphere mechanism while neutral 1,4-cyclooctadiene (cod) and \( p\text{-cvm} \) induce the inner-sphere route.

Scheme 6: Mode of action of NHC-amine ligands developed in our group. ML = Ru\( (p\text{-cym}) \). Rh- and Ir(cod) catalyze the hydrogenation of polar double bonds via the inner-sphere mechanism, while for ML = Rh- and Ir(Cp\(^*\)) the outer-sphere pathway is operative (box).

To the best of our knowledge, no tzNHC complexes capable of MLC via aromatization/dearomatization have been reported to date. This will be the subject of Chapter 5. More examples of catalytic applications of NHCs are discussed in the next paragraph.
1.4 Catalytic Transformations

As described above, bidentate tzNHC complexes have been applied in many catalytic reactions in the last few years. As these carbene complexes have strong electron-donating properties, they are especially suitable ligands for catalytic transformations that require an electron-rich metal center. The reactions that are studied in this thesis will be discussed below.

Hydrogenation of Unsaturated Bonds

Catalytic hydrogenation of unsaturated bonds is among the most widely studied reactions in chemistry. Reduction of a double or triple bond by the addition of hydrogen is a crucial reaction step in the synthesis of all kinds of chemicals. Traditionally, strong reducing agents like lithium aluminium hydride or sodium borohydride were used stoichiometrically for this transformation, resulting in large amounts of waste. Catalytic hydrogenation, on the other hand, is atom-efficient and generally environmentally benign.

Scheme 7: Two possible catalytic cycles for the hydrogenation: A: hydrogenation of C=C double bond catalyzed by Wilkinson’s catalyst, including the oxidative addition leading to metal hydrides; B: bifunctional mechanism in TH of ketones with isopropanol catalyzed by Noyori’s catalyst.
For catalytic hydrogenation, the splitting of molecular hydrogen or an alternative hydrogen source (*vide infra*) is essential. In homogeneous catalysis this can be achieved by oxidative addition of $H_2$ to the metal center (Scheme 7, cycle A), which is promoted by electron-rich ligands. Additionally, increased electron-density on the metal gives the hydrogens more hydridic character, due to the back-donation of electrons in the anti-bonding orbital of dihydrogen. Therefore, electron-rich NHC complexes are very suitable candidates to facilitate this reaction. The most well-known homogeneous catalyst for hydrogenation, however, remains Wilkinson’s $[\text{RhCl(PPh}_3)_3]$ complex. This catalyst is used to depict the general catalytic cycle for hydrogenation in Scheme 7.

Instead of dihydrogen gas, other hydrogen donors can be applied. In this so-called transfer hydrogenation (TH) reaction the donor source delivers hydrogen to the metal center, which in turn transfers it to the substrate. Popular alternative hydrogen donors are isopropanol and formic acid. The former has the advantage that it can serve as the solvent and hydrogen donor at the same time. In the example in Scheme 7 (cycle B), ketones are hydrogenated by Noyori’s ruthenium catalyst using isopropanol as hydrogen source. Here, a bifunctional mechanism is operative: dihydrogen is activated over both the metal and the ligand, as was explained in the previous paragraph. This pathway has led to greatly enhanced reaction rates and has been exploited by many groups over the years. Moreover, the same catalyst system has been expanded very successfully to asymmetric transfer hydrogenation (ATH). Enantioselective catalysis using NHC complexes will be discussed in more detail in the next paragraph.

Hydrogenation can be used to convert various substrates to useful products. In our group NHC-Pd systems for the transfer semihydrogenation of alkynes with HCOOH/$\text{NEt}_3$ as well as molecular hydrogen have been developed. Semi-hydrogenation of alkynes is a powerful tool to synthesize (Z)-alkenes, which are important building blocks for fine chemicals, such as bioactive molecules, flavors, and natural products.

Ketones are often used as benchmark substrates for the (transfer) hydrogenation of polar bonds. However, polar double bonds that are not readily reduced by hydrogen gas are of more interest. There is, for example, only a limited amount of catalytic systems known that are able to hydrogenate carboxylic acid derivatives. The relative reactivity in hydrogenation of C=O bonds is depicted in Figure 6.
Due to their thermodynamic stability, esters are a challenging substrate class for hydrogenation. The reduction of esters is formally called hydrogenolysis as the O-R bond is cleaved, leading to two alcohols (Scheme 8). Our group was among the first to convert esters to alcohols under reasonable temperature and pressure (100 °C and 70 bar) using a ruthenium triphosphine catalyst. In the last decade, a lot of progress has been made in catalytic ester hydrogenation. Two Ru di-NHC catalysts capable of facilitating this reaction are highlighted below (Scheme 8).

The first example is a system published recently by the group of Beller (Scheme 8). They screened several NHC ligands in combination with Ru(p-cym) and 30 mol% of base for the hydrogenation of methyl benzoate at 100 °C and 50 bar. The in situ prepared di-NHC catalysts, proved to be superior. Good conversions as well as functional group tolerance were observed for this system. The Ru(II) complex of Song et al. bearing a cooperative CNN ligand (Scheme 8), is active under milder conditions (5.3 bar and 105 °C). This pre-catalyst is slightly more active than the PNN predecessor developed by Milstein, with a TOF of 50 h⁻¹ compared to 8 h⁻¹. Moreover, even the very sterically hindered tert-butyl acetate could be reduced.
NHCs for Enantioselective Transformations

Enantioselective catalysis is an important tool within synthetic chemistry because it enables us to selectively produce a desired isomer (enantiomer or diastereomer). The ability to obtain one chiral form of a molecule selectively is essential, especially in the pharmaceutical field, as different stereoisomers often have different biological activity. Besides medicines, applications of chiral compounds include agrochemicals, flavors and materials (e.g. chiral polymers and liquid crystals). The widespread demand for chiral molecules has stimulated research into the development of chiral catalytic systems. This field is dominated by homogeneous catalysts, as these are very selective and can in principle give access to both enantiomers of a product (unlike enzymes).

Considering their popularity in homogeneous catalysis, there are relatively few examples of chiral (di-)NHC metal complexes that have been applied in enantioselective reactions. Efforts to induce chirality with NHCs have been described in some recent reviews. The most convenient way of introducing chirality in these ligands is to introduce chiral substituents on either the backbone or the nitrogen atoms of the NHC. The first chiral NHC complex, of the latter kind was already reported in 1983 by Lappert et al. through the transformation and ring closure of amino acids (Figure 7). However, research into this kind of complexes showed that, although good results were achieved with some catalysts, the general design for these types of ligands was not effective. Chiral induction was difficult because the chirality was too remotely located with respect to the metal atom, and the dynamic nature of the nitrogen substituents causes the chiral space to be ill-defined, which hinders the transfer of chirality to the substrates.

Bidentate ligands can be used to generate more rigid complexes. Several complexes have been published using chiral di-NHC complexes or an NHC in combination with a hetero-atom donor. Burgess et al. developed the chiral oxazoline-NHC iridium complex 18 for the asymmetric hydrogenation of alkenes (Figure 7).
Furthermore, some chiral di-NHC have proven to be useful in enantioselective catalysis. An example is the \( C_2 \)-symmetric binaphthyl-based Rh(I) complex 19 reported by Shi et al., which will be discussed in more detail in Chapter 6 (Figure 7).

The application of tzNHCs in enantioselective catalysis has barely been explored. In 2009 the first chiral palladium tzNHC complex 20 was obtained via Ag(I) transmetalation (Figure 8). Although this catalyst was active in the Suzuki-coupling for the synthesis of biphenyl derivatives, only deborylation of arylboronic acid was observed when it was tested in the asymmetric version of this C-C coupling reaction to produce chiral binaphthyl products.

![Figure 8: Examples of chiral tzNHC complexes.](image)

Aizpura and co-workers reported the axially chiral di-tzNHC complex 21 (Figure 8). Although the authors highlighted the potential of this chiral ligand in enantioselective catalysis, no catalytic application has been reported to date.

### 1.5 Outline of the Thesis

In this thesis the design and development of various bidentate di-NHC ligands for organometallic catalysis is described. The coordination to several late-transition metals is studied as well as the application of the resulting complexes in several catalytic transformations. As the employed ligands consist of highly electron-donating species, we focus mainly on hydrogenation reactions, for which such ligands have been shown to be very suitable. At the beginning of this project tzNHC complexes were relatively new ligands and only few applications were known. We aimed to gain fundamental knowledge about the properties of this class of carbenes and di-NHCs in general. By investigating the synthesis, stability and catalytic activity of several late-TM complexes bearing homo- or heteroleptic di-NHC ligands with various substituents, useful information can be obtained on both structure-activity relations and the potential and limits of di-NHCs and tzNHCs concerning complex synthesis and applications in homogeneous catalysis.

The first part of this thesis deals with chelating di-NHC complexes. In Chapter 2 the synthesis of zero- and divalent palladium complexes bearing di-NHC ligands
with various N-substituents is described. The resulting low-valent complexes are evaluated in the (transfer) semihydrogenation of alkynes to discover the effect of di-NHC ligands on the performance of the Pd pre-catalysts compared to mono-NHC analogues developed in our group.

Next, heteroditopic di-NHC ligands are introduced. The “click” procedures allows for the convenient synthesis of a series of ligands differing in side-groups, connectivity, chelating ring size and rigidity. In Chapter 3 the coordination of these mixed NHC-tzNHC ligands to Ag(I) Ru(II) and Pd(II) is investigated. The resulting complexes are tested in catalytic hydroarylation of alkynes (Pd) and the reduction of polar double bonds (Ru). Chapter 4 describes the Ir(I) and Rh(I) derivatives of these heteroditopic di-NHC ligands and NHC-triazole analogues thereof. Here, the electron-donating properties of the ligands are assessed further as well as the influence of the parameters mentioned above. The complexes are applied in the catalytic TH of unsaturated bonds with isopropanol as hydrogen donor, in which the effect of the secondary donor as well as the N-substituents on the catalytic activity are examined.

The last two chapters feature di-tzNHC complexes. In Chapter 5, the development of lutidine-based pincer complexes (Ag, Pd, Ru) is discussed. Although many cooperative pincer ligands are known and they have shown remarkable reactivity, there were no accounts of such compounds featuring a tzNHC moiety. We expect that this electron-rich donor in combination with the cooperative lutidine core possesses suitable characteristics for efficient Ru-catalyzed hydrogenation of esters.

Chapter 6 describes the design and synthesis of chiral \( C_2 \)-symmetric di-NHC complexes for enantioselective catalysis. Here, the successful binaphthyl backbone is combined with electron-rich 1,2,3-triazolylidene donors to obtain transition metal complexes for enantioselective hydrosilylation of ketones.

1.6 References

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Chapter 1


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Chapter 2
Pd(0) and -(II) Complexes with Chelating di-NHC Ligands and their Application in Semihydrogenation of Alkynes

Abstract
A transmetallation route, using silver(I) precursors, to several zero- and di-valent palladium complexes with chelating di-NHC ligands bearing various N-substituents has been established. The resulting complexes have been characterized by multinuclear NMR spectroscopy and mass spectrometry. The structures of two representative compounds, [Pd\textsuperscript{0}(di-(Mes)NHC)(η\textsuperscript{2}-ma)] \textit{3a} and [Pd\textsuperscript{II}(di-(Mes)NHC)(η\textsuperscript{3}-allyl)] \textit{3b} were determined by single-crystal X-ray crystallography. In contrast to the behavior in transfer semihydrogenation, wherein only low activity was observed, complex \textit{3a} exhibited similar activity (TOF = 49 mol\textsubscript{sub}/mol\textsubscript{cat}. h\textsuperscript{-1}) and selectivity as relevant monodentate analogues in the semihydrogenation of 1-phenyl-1-propyne with molecular hydrogen.

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2.1 Introduction

Following the success of their monodentate analogues, chelating N-Heterocyclic di-carbenes (di-NHCs; Figure 1) have become popular ligands in transition metal catalysis.\(^1,2\) Because of the chelate effect these di-NHCs lead to metal complexes with higher stability compared to their monodentate (di-)NHC counterparts.\(^1\) In addition to the advantages regarding stability, di-NHCs are good candidates for fine-tuning of catalytic properties by altering the wingtips, backbone and linker,\(^3\) the first of which is explored in this chapter. The influence of the linker length is briefly studied as well.

![Figure 1: General structure monodentate di-NHC and bidentate di-NHC complex.](image)

Di-NHCs have been coordinated to many transition metals, including ruthenium,\(^4\) rhodium,\(^3\) iridium,\(^6\) palladium\(^7\) and platinum.\(^8,9\) More recently also first-row transition metal complexes such as of nickel\(^10-12\) and iron have been reported.\(^13,14\)

We are interested in the properties and reactivity of low-valent late transition metal complexes, notably electron-rich zero-valent palladium NHC complexes, as these often play a vital role in the catalytic cycles of many reactions.\(^15-18\) Although a substantial amount of research has been devoted to di-NHC Pd(II)(halide)\(_2\) complexes, usually obtained by treating a bisimidazolium salt with Pd(OAc)\(_2\) at elevated temperatures,\(^7,15-19\) we are not aware of any previous reports on [Pd(0) (di-NHC)L] or [Pd(II)(di-NHC)(\(\eta^3\)-C\(_3\)H\(_5\)))]Cl complexes. Moreover, reports on zero-valent d\(^{10}\) metal complexes bearing a chelating di-NHC ligand are absent in literature, to the best of our knowledge.

2.2 Synthesis of bisimidazolium salts

The synthesis of bisimidazolium salts 1 has been documented; reacting a mono-substituted imidazole with 0.5 equivalent of dihaloalkane in several solvents at elevated temperatures gives the hygroscopic bisimidazolium salts in decent to good yields (Scheme 1).\(^20,21\) However, yields are dramatically improved for the methyl-linked bisimidazolium salts (1a, c-e) by heating the corresponding imidazole in an excess of dibromomethane, following a procedure by Lee et al.\(^19\)
2.3 Silver and Palladium complexes

Direct coordination by reacting the bisimidazolium salts with KOTBu in the presence of Pd(0) and Pd(II) precursors ([Pd(tBuDAB)(η²-ma)] (tBuDAB = 1,4-di-tert-butyl-1,4-diaza-1,3-butadiene, ma = maleic anhydride), [Pd(dvtms)]₂ (dvtms = 1,1,3,3-tetramethyl-1,3-divinylsiloxane) or [Pd(η³-C₃H₅)μ-Cl]₂), failed to give the palladium complexes in satisfactory yields. Instead, a carbene transfer route via Ag(I) complexes was applied, which was first adopted for the synthesis of zero-valent palladium complexes in 2009, providing excellent yields for chelate di-NHC Pd(II) complexes. The silver(I) complexes were obtained by reacting the corresponding bisimidazolium dibromide salts (1a-e) with Ag₂O at room temperature in dichloromethane (R = Mes) or methanol (R = Me, Benz, nBu; Scheme 2) according to literature procedures. The conversion can be monitored by the disappearance of the imidazolium-H peak around 9-10 ppm in the ¹H NMR spectra and the appearance of the ¹³CₙH₃-Ag(I) resonance around 180 ppm in the ¹³C NMR spectra. The silver complex derived from the mesityl bisimidazolium salt forms oligo- and polymeric structures, as was shown by Slaughter et al., whereas other substituents lead to dimeric complexes. The silver(I) di-carbene complexes were filtered over Celite, concentrated and used in the subsequent reaction without further purification.

Scheme 1: General synthesis of bisimidazolium salts.

Scheme 2: Synthesis of the [Pd⁰(di-NHC)(η²-ma)] complexes 3a-e via the silver complexes. i) Ag₂O in DCM or MeOH, 18h, ii) [Pd(tBuDAB)(η²-ma)] DCM, 2h.

Transmetallation of the Ag(I)NHCs by reacting 2a-e with one equivalent of [Pd(tBuDAB)(η²-ma)] relative to the di-carbene ligand in dichloromethane at room temperature provided a convenient route to the corresponding zero-valent
palladium maleic anhydride complexes 3a-e (42-99% yield; Scheme 2) The lower yields for the complexes with alkyl N-substituents (3c and 3e) can be explained by the instability of their Ag(I) precursors, demonstrated by Quezada et al. as well as of the Pd(0) complexes themselves (vide infra).

The resulting complexes 3 were characterized by NMR spectroscopy and mass spectrometry (FAB⁺). It has been reported that the mode of coordination (chelating or bridging) of di-NHCs is dictated by a combination of linker, N-substituents, counter-ion and reaction conditions. It has even been doubted whether chelated methylene linked di-NHC ligands would be able to support a zero-valent palladium center. However, we observed formation of chelate species exclusively for ligands bearing all wingtip substituents and for both linker lengths, as was concluded from the NMR spectra.

In the ¹H NMR spectra, the signals for the methylene linker hydrogens are split in an AB system with a geminal ²J_HH coupling constant of approximately 13 Hz, as is reported in Table 1. This observation can be attributed to the rigid boat structure of the complexes, having a plane of symmetry bisecting the di-carbene ligand and maleic anhydride. For 3b (n = 2) the same rigidity was evident from the ¹H NMR spectrum, that contained two doublets of doublets assigned to the ethyl-linker hydrogens. The ¹H NMR spectrum of 3e exhibits diastereotopic protons for the nBu groups as a result of their non-equivalence as was observed before for similar complexes. The ortho-methyl groups and meta-protons on the mesityl (3a) group both give rise to two singlets in the ¹H NMR spectrum as well.

The ¹³C_NHC-Pd(0) resonances all fall in the expected range (187-191 ppm) corresponding to shifts of monodentate di-carbene Pd(0) (η²-ma) equivalents (189 ppm), which is slightly upfield compared to their monocarbene analogues (193 ppm; Table 1). The stability of these complexes seems to depend on the N-substituents. Complexes 3c and 3e readily decomposed in solution and also for 3d formation of palladium black was observed after a couple of hours in dichloromethane. This instability, which has been observed for zero-valent monocarbene palladium complexes bearing alkyl substituents as well, can be attributed to the absence of steric protection of the electron-rich metal center. The decomposition of 3c in solution hampered the detection of the carbene signal in ¹³C NMR spectroscopy. Complexes with the bulkier mesityl analogues, on the other hand, were stable in solution and resistant towards air and moisture at room temperature for at least a week. In contrast to findings of Riederer et al., we did not observe a correlation between stability and linker length.
Chelating Di-NHC Late TM Complexes

Table 1: Chemical shifts and multiplicity in NMR spectra of 3a-e and 4a-e:

<table>
<thead>
<tr>
<th>Complex</th>
<th>C² (ppm)</th>
<th>H⁴ &amp; H⁵ (ppm)</th>
<th>H¹ &amp; H² (ppm, multiplicity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>187</td>
<td>7.38, 6.69</td>
<td>6.54 (d), 5.97 (d)</td>
</tr>
<tr>
<td>3b</td>
<td>191</td>
<td>7.13, 6.93</td>
<td>5.29 (dd), 4.34 (dd)</td>
</tr>
<tr>
<td>3c</td>
<td>-</td>
<td>7.68, 7.31</td>
<td>6.52 (d), 5.71 (d)</td>
</tr>
<tr>
<td>3d</td>
<td>186</td>
<td>7.11, 6.93</td>
<td>6.84 (d), 4.65 (d)</td>
</tr>
<tr>
<td>3e</td>
<td>184</td>
<td>7.10, 6.96</td>
<td>5.81 (dd)</td>
</tr>
<tr>
<td>4a</td>
<td>177</td>
<td>8.35, 6.99</td>
<td>7.46 (d), 6.56 (d)</td>
</tr>
<tr>
<td>4b</td>
<td>181</td>
<td>7.55, 6.82</td>
<td>5.29-5.07 (m)², 3.04 (dd)</td>
</tr>
<tr>
<td>4c</td>
<td>175</td>
<td>8.11, 6.96</td>
<td>7.05 (d), 6.19 (d)</td>
</tr>
<tr>
<td>4d</td>
<td>176</td>
<td>8.06, 6.93</td>
<td>6.46 (bs)</td>
</tr>
<tr>
<td>4e</td>
<td>175</td>
<td>8.01, 7.04</td>
<td>6.12 (bs)</td>
</tr>
</tbody>
</table>

a.) Not detectable, even with prolonged relaxation times. b.) Due to overlap with the signal of an allylic hydrogen the expected doublet of doublets could not be observed.

[Pd(II)(di-NHC)(η⁳-C₃H₅)]Cl complexes, 4a-e, have been synthesized via the same route as their zero-valent counterparts (Scheme 3). Transmetallation from the corresponding silver(I)complexes proceeded in reasonable to high yields. The resulting cationic complexes were all stable under aerobic conditions.

Scheme 3: Synthesis of the [Pd(II)(di-NHC)(η³-C₃H₅)]Cl complexes 4a-e via the silver complexes.

The reduced electron-density at the metal in these stable Pd(II) complexes relative to the zero-valent analogues is reflected in their NMR spectra by a downfield shift for the backbone hydrogens and an upfield shift for the carbene carbon (Table 1). In the ¹³C NMR spectra two signals are present for the allyl group, indicating two-fold symmetry for the complexes with a non-coordinating chloride anion. Again,
the hydrogens of the linker give rise to two doublets in the $^1H$ NMR spectra for $4a$ and $4c$, and a doublet of doublets for $4b$, indicating the inequivalence of these protons and the non-fluxional behavior of the complexes at room temperature. Exceptions are complexes $4d$ and $4e$, that each show two broad singlets ($7.52/6.46$, and $6.82/6.12$ ppm, respectively), indicating fluxionality that could be caused by a lower barrier to allyl rotation compared to $4a$-$c$. Variable temperature $^1H$ NMR experiments showed that, as expected, these resonances become doublets upon cooling to $-20\,^\circ C$ for $4e$ in dichloromethane concomitant with broadening of the allyl peaks.

**Solid state structures of $3a$ and $4a$**

X-ray quality crystals of $3a$ were obtained by slow vapor diffusion of pentane to a concentrated dichloromethane solution of the complex $3a$. The crystal structure (Figure 2) confirmed that the di-NHC ligand is coordinated to the palladium center in a chelating fashion. The complex adopts a square planar geometry around the transition metal center, whereas the six-membered metallacycles, formed by the chelating di-carbene and palladium center, adopt a boat conformation (Figure 2). The NHCs are bent out of the metal coordination plane with dihedral angles of up to $32^\circ$. The di-carbene bite angle of the complex is $87.50(9)^\circ$, a small deviation from the ideal angle dictated by the methylene bridge.$^{31}$

The palladium(0)-carbene bond distances of $3a$ are shorter than those of the recently reported Y-shaped dissymmetric [Pd(0)(di-NHC)(ma)] complex containing two monodentate NHC ligands ($2.061(2)$-$2.067(3)$ Å)$^{28}$ but are in agreement with the values of chelate heteroditopic zero-valent palladium complexes ($2.0315(14)$-$2.045(2)$ Å)$^{22,32-34}$ In addition, Lee et al. reported unequal palladium-carbene bond lengths in the same range ($2.043(4)$-$2.070(3)$ Å) for zero-valent monodentate di-carbene palladium complexes.$^{35}$ The C=C double bond of the maleic anhydride, which is $\eta^2$ coordinated to the metal center and almost perpendicular to the coordination plane, is elongated compared to the free alkene due to $\pi$-backbonding from the palladium(0) center.

Suitable crystals of $4a$ were obtained as well, by slow vapor diffusion of pentane to a concentrated dichloromethane solution of the complex, but the structure could not be solved satisfactorily. A large number of solvent molecules was present in the crystal structure, which led to a high degree of disorder. The results did however show unequivocally that the carbene was coordinated in a bidentate fashion and that the chloride anion was not coordinated to the metal center (Figure 3).

Furthermore, the palladium-carbene distances of $4a$ are similar to bidentate NHC palladium allyl complexes bearing a nitrogen donor.$^{36,37}$Remarkably, the Pd-C$_{\text{NHC}}$
bond lengths for the complexes with different palladium oxidation states, 3a and 4a, do not differ significantly. This can be understood by considering the trans influence of the co-ligands. Yeung et al. found a trend of decreasing palladium-carbene bond distance with lower electron-donicity for their [Pd(II)(di-NHC)X₂] (X= I, NCS, CF₃CO₂) complexes and no influence of the overall charge with the same di-carbene ligand. The allyl and maleic anhydride ligand on 3a and 4a have similar electron donating capacities.

**Figure 2:** Molecular structure of complex 3a in the crystal, drawn at the 50% probability level. Hydrogen atoms and dichloromethane solvent molecule are omitted for clarity. The side-view of the structure (top right) is showing the conformation of the six-membered metallacycle in 3a and orientation of η²-maleic anhydride with respect to Pd plane. Mesityl substituents and hydrogens are omitted for clarity. Selected bond distances (Å) and (dihedral) angles (°) are depicted in the box.

<table>
<thead>
<tr>
<th>Bond Distance</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd1-C12</td>
<td>2.046(2) Å</td>
</tr>
<tr>
<td>Pd1-C16</td>
<td>2.045(2) Å</td>
</tr>
<tr>
<td>C26-C27</td>
<td>1.445(3) Å</td>
</tr>
<tr>
<td>∠C16-Pd1-C12</td>
<td>87.50(9)°</td>
</tr>
</tbody>
</table>

**Figure 3:** Molecular structure of complex 4a in the crystal, drawn at the 50% probability level. Only one of two independent molecules is shown. Hydrogen atoms, solvent molecules and anions are omitted for clarity. Selected bond distances (Å) and (dihedral) angles (°) are depicted in the box.

<table>
<thead>
<tr>
<th>Bond Distance</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd1-C12</td>
<td>2.036(3) Å</td>
</tr>
<tr>
<td>Pd1-C16</td>
<td>2.040(3) Å</td>
</tr>
<tr>
<td>C26-C27</td>
<td>1.445(3) Å</td>
</tr>
<tr>
<td>∠C16-Pd1-C12</td>
<td>87.50(9)°</td>
</tr>
</tbody>
</table>

35
2.3. Catalytic Semihydrogenation of 1-Phenyl-1-propyne

Palladium NHC complexes have been successfully applied in many reactions,\textsuperscript{38–40} including the (transfer) semihydrogenation of alkynes (Scheme 4).\textsuperscript{30,34,41,42} We applied complex 3a in this reaction, using 1-phenyl-1-propyne as the substrate with formic acid as a hydrogen donor at standard transfer hydrogenation conditions (70 °C in acetonitrile).\textsuperscript{41}

Unfortunately, complex 3a showed poor activity of only 18% conversion under these conditions (Table 2, entry 1). By considering the proposed mechanism for semihydrogenation of alkynes catalyzed by the very efficient mono-NHC Pd catalyst,\textsuperscript{42} it becomes apparent why the di-NHC is not such a suitable ligand. Two vacant sites or labile ligands at the Pd(0) center are required to allow coordination of both the formate and the alkyne, which is key in the reported cycle to reduce the substrate with formic acid.\textsuperscript{42} Complex 3a consists of a strongly coordinating di-NHC ligand occupying two sites on the metal center and only one more labile ma ligand. This corresponds to one available coordination site on the Pd center of 3a, whereas two are needed if the catalyst would operate through the aforementioned mechanism.

Table 2: Catalytic results for the semihydrogenation of 1-phenyl-1-propyne using precatalyst 3a.

<table>
<thead>
<tr>
<th>Hydrogen source</th>
<th>T (°C)</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>Z-/E-alkene/alkane</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HCO$_2$H/NEt$_3$</td>
<td>70</td>
<td>29</td>
<td>18</td>
<td>98/2/0</td>
</tr>
<tr>
<td>2 H$_2$</td>
<td>60</td>
<td>3</td>
<td>&gt;99</td>
<td>89/4/6</td>
</tr>
</tbody>
</table>

a.) Reaction conditions: 2.2 mmol substrate, 1 mol% catalyst; for entry 1: 5 equiv. HCO$_2$H/NEt$_3$; for entry 2: p(H$_2$) = 1 bar. b.) Product distribution as determined by GC at 18% and 99% conversion respectively.

When hydrogen gas was used as the source of dihydrogen, complex 3a proved to be more active (Table 2, entry 2). After an induction period of approximately four hours, presumably needed to ensure sufficient alkene dissociation or hydrogenation in order to create a vacant site, the reaction to Z-1-phenyl-2-propene proceeded to completion within two hours (TOF = 49 mol$_{\text{sub}}$/mol$_{\text{cat}}$/h).
Moreover, 3a showed high selectivity towards the Z-alkene with up to 89% conversion. When most of the alkyne was consumed, over-reduction to the alkane was observed (Figure 4). The catalyst was still active when adding new substrate at near-complete conversion of the alkyne.

![Figure 4: Selectivity of catalyst 3a in the semihydrogenation of 1-phenyl-1-propyne over time.](image)

Di-NHC complex 3a exhibited good activity and selectivity in the semihydrogenation of 1-phenyl-1-propyne. However, the results were similar to previously published systems in terms of selectivity and reaction rate. Catalytic tests with 4a in both transfer and direct semihydrogenation led to disappointing results, as no conversion was observed. The reason for this lack of catalytic activity may be that the allyl group is not easily removed by hydrogenation, thus inhibiting the formation of an active Pd-species.

Another explanation for the difference in activity for the two pre-catalysts may lie in the nature of the active catalyst. Both metal nanoparticles and molecular catalysts are known to reduce alkyynes. It was found recently by using a protocol combining partial poisoning studies with DLS measurements, that, in a [Pd(0)NHC] semihydrogenation system applying H₂, metal nanoparticles were the true catalyst instead of the proposed molecular catalyst. In this case the Pd(0) complex 3a may form active nanoparticles, whereas the stable Pd(II)(allyl) 4a species does not. This conjecture is yet to be corroborated.

### 2.4 Conclusion

We have described the synthesis and characterization of the first chelate di-NHC Pd(0) and Pd(II) allyl complexes via Ag(I) transmetalation with various substituents on the wingtip position of the NHC. The length of the linking moiety was also varied. Except for the Pd(0)(di-NHC) complexes bearing alkyl substituents, the formed di-carbene complexes showed prolonged stability towards air and in solution.

In contrast to their mono-carbene analogues these complexes 3a and 4a,
which lack a vacant coordination site, proved to be inactive in the transfer semihydrogenation of 1-phenyl-1-propyne. On the other hand the zero-valent palladium di-NHC complex 3a did catalyze the reaction when molecular hydrogen (1 bar) was used and comparable activity and initial selectivity as for systems employing mono-carbene palladium complexes were observed. The Pd(II)(η³-allyl) di-NHC 4a complex did not induce any conversion in the semihydrogenation reaction under the same conditions, which may be due to the reluctance of the allyl co-ligand to undergo dissociative processes or reduction to the active Pd(0) species. Possibly, as they principally constitute (re)active organometallic precatalysts, these Pd(di-NHC)(L) complexes (and close analogues thereof) could be amenable to carbon-carbon and other carbon-element coupling reactions.

2.5 Experimental

All reactions were carried out using standard Schlenk techniques under an atmosphere of dry nitrogen. Solvents were dried and distilled according to standard methods. All reagents were purchased from commercial suppliers and used without further purification. The following starting materials were synthesized according to literature procedures: mesitylimidazole, butylimidazole, the bisimidazolium dibromides and [Pd(tBuDAB)(η²-ma)]. The silver(I) complexes were also prepared following the reported procedures; in MeOH for R = Me, Benz, nBu or DCM for R = Mes. The NMR spectra were recorded on Varian Mercury 300 MHz, Bruker DRX 300 and Bruker AMX 400 MHz spectrometers. Mass spectra were recorded on a JEOL JMS SX/SX102A four-sector mass spectrometer and GC analyses were performed with an Interscience Trace GC Ultra instrument using a Rxi fused silica capillary column and p-xylene as internal standard.

**General procedure synthesis di-NHC palladium(0) maleic anhydride complexes:** [Pd(tBuDAB)(η²-ma)] (1 equiv.) was added to a solution (0.02 M) of the corresponding silver(I) complex in dichloromethane and the mixture was stirred for 3 hours at 20 °C upon which the greyish silver salt precipitated. The mixture was filtered over a pad of Celite and concentrated to a few mL. Then pentane was added to precipitate the product, which was isolated by decanting the solvent and washed twice with pentane to yield the product.

**Methyl-1,1-di(mesitylimidazol-2-ylidene) palladium(0) maleic anhydride; 3a.** Slightly yellow solid, 65 mg, 0.12 mmol, 80 %. $^1$H NMR (CD$_2$Cl$_2$, 300 MHz) δ 7.38 (2H, d, $^3$J$_{HH}$ = 1.5 Hz, CH$_2$), 7.14 (2H, s, m-Mes-H), 6.96 (2H, d, $^3$J$_{HH}$ = 1.5 Hz, CH$_2$), 6.92 (2H, s, m-Mes-H), AB system centered at δ$_A$: 6.54 (1H, d, $^3$J$_{HH}$ = 13.2 Hz, CH$_2$) & δ$_B$: 5.97 (d, $^3$J$_{HH}$ = 13.2 Hz, 1H, CH$_2$), 2.38 (6H, s, p-Mes-CH$_3$), 2.26 (2H, s, ma), 2.04 (6H, s, o-aryl-CH$_3$), 1.80 (6H, s, o-Mes-CH$_3$); $^{13}$C NMR (CD$_2$Cl$_2$, 300 MHz) δ 187.0 (C$_{NHC}$), 173.9 (CO), 138.5 (p-Mes-CH), 136.7 (i-aryl-C), 136.2 (o-Mes-C), 134.9 (o-aryl-C), 129.0 (CH), 128.1 (CH), 121.1 (m-Mes-CH), 120.8 (m-Mes-CH), 64.1 (CH$_2$), 38.4
(alkene), 20.8 (p-Mes-CH₃), 17.6 (o-Mes-CH₃), 17.5 (o-Mes-CH₃). MS(FAB⁺) for C₂₈H₁₈N₄O₅Pd: m/z calculated 561.1493 [M-CO+H]⁺, observed 561.1487.

**Ethyl-I, 1-di(mesitylimidazol-2-ylidene) palladium(0) maleic anhydride; 3b.**
Pale brown solid, 63 mg, 0.10 mmol, 99%. ¹H NMR (CD₂Cl₂, 300 MHz) δ 7.13 (2H, d, J₃₄ = 1.8 Hz, CH), 7.04 (2H, s, m-Mes-H), 6.93 (2H, d, J₃₄ = 1.8 Hz, CH), 6.86 (2H, s, m-Mes-H), 5.29 (2H, dd, J₃₄ = 13.2 Hz, J₃₄ = 6.2 Hz, CH₂), 4.34 (2H, dd, J₃₄ = 13.2 Hz, J₃₄ = 6.2 Hz, CH₂), 2.32 (6H, p-Mes-CH₃), 2.16 (2H, s, ma), 2.13 (6H, s, o-Mes-CH₂), 1.81 (6H, s, o-Mes-CH₂); ¹³C NMR (CD₂Cl₂, 300 MHz) δ 191.2 (Cₗ₉H₉), 171.2 (CO), 138.3 (p-Mes-CH), 136.7 (i-Mes-C), 136.2 (o-Mes-C), 128.9 (CH), 128.1 (CH), 122.6 (m-Mes-CH), 121.0 (m-Mes-CH), 49.5 (CH₂), 38.2 (alkene), 20.8 (p-Mes-CH₃), 17.7 (o-Mes-CH₃), 17.6 (o-Mes-CH₃). MS(FAB⁺) for C₂₉H₃₄N₄O₅Pd: m/z calculated 504.1516 [M-CO+H]⁺, observed 504.1516.

**Methyl-I, 1-di(methylimidazol-2-ylidene) palladium(0) maleic anhydride; 3c.**
Pale yellow solid, 64 mg, 0.17 mmol, 70%. ¹H NMR (300 MHz, CD₂Cl₂) δ 8.36 (2H, s, CH), 6.97 (2H, s, CH), AB system centered at δ₂; 6.60 (1H, d, J₃₄ = 12.1 Hz, CH₂), & δ₃; 5.63 (1H, d, J₃₄ = 12.1 Hz, CH₂), 3.82 (2H, s, ma) 3.36 (6H, s, CH₃); ¹³C NMR (75 MHz, CD₂Cl₂) δ 171.9 (CO), 124.5 (CH), 123.7 (CH), 64.4 (CH₂), 39.5 (alkene), 38.0 (CH₂). MS(FAB⁺) for C₂₉H₃₂N₄O₅Pd: m/z calculated 282.0100 [M-ma]⁺, observed 282.0121.

**Methyl-I, 1-di(benzylimidazol-2-ylidene) palladium(0) maleic anhydride; 3d.**
Brown solid, 83 mg, 0.16 mmol, 98%. ¹H NMR (CD₂Cl₂, 300 MHz) δ 7.41-7.26 (10H, m, Ar-H), 7.11 (2H, d, J₃₄ = 1.8 Hz, CH), 6.93 (2H, d, J₃₄ = 1.8 Hz, CH), AB system centered at δ₂; 5.89 (2H, d, J₃₄ = 17 Hz, CH₂), & δ₃; 5.41 (2H, d, J₃₄ = 17 Hz, CH₂), 3.69 (2H, s, ma); ¹³C NMR (CD₂Cl₂, 75 MHz) δ 186.5 (C₉H₈), 174.7 (CO), 136.8 (Ar-C), 129.2 (Ar-CH) 129.4 (CH), 128.8 (CH), 120.9 (Ar-CH), 119.9 (Ar-CH), 63.2 (CH₂), 54.8 (CH₂), 39.0 (alkene). MS(FAB⁺) for C₂₉H₃₂N₄O₅Pd: m/z calculated 505.0865 [M-CO+H]⁺, observed 505.0865.

**Methyl-I, 1-di(nButylimidazol-2-ylidene) palladium(0) maleic anhydride; 3e.**
Pale brown solid, 35 mg 0.08 mmol, 42%. ¹H NMR (CD₂Cl₂, 300 MHz) δ 7.10 (2H, d, J₃₄ = 1.8 Hz, CH), 6.96 (2H, d, J₃₄ = 1.8 Hz, CH), 5.81 (2H, dd, J₃₄ = 12 Hz, CH₂), 4.25 – 4.04 (4H, m, CH₂), 3.59 (2H, s, ma), 1.85 – 1.65 (4H, m, CH₂), 1.40 – 1.22 (4H, m, CH₂), 0.91 (6H, t, J₃₄ = 7.3 Hz, CH₂); ¹³C NMR (75 MHz, CD₂Cl₂) δ 183.9 (C₉H₈), 175.0 (CO), 119.9 (CH), 119.8 (CH), 63.0 (CH₂), 51.0 (CH₂), 38.4 (alkene), 33.6 (CH₂), 19.7 (CH₂), 13.61 (CH₃). MS(FAB⁺) for C₁₅H₂₄N₄Pd: m/z calculated 366.1042 [M-ma]⁺, observed 366.1053.
Chapter 2

General procedure for the synthesis of di-NHC palladium (II) η1-allyl chloride complexes: [Pd(η1-allyl) Cl2]2 (0.5 equiv.) was added to a solution (0.02 M) of the silver complex in dichloromethane and the mixture was stirred for 3 hours at room temperature upon which a greyish silver salt precipitated. The mixture was filtered over a pad of Celite and concentrated to yield the product.

Methyl-1,1-di(mesitylimidazol-2-ylidene) palladium(II) η1-allyl chloride; 4a. Off-white solid, 90 mg, 0.16 mmol, 99%. 1H NMR (CD2Cl2, 300 MHz) δ 8.35 (2H, d, 3JHH = 2.0 Hz, CH), AB system centered at δH = 7.46 (1H, d, 3JHH = 13 Hz, CH2) & δH = 6.56 (1H, d, 3JHH = 13 Hz, CH), 6.99 (2H, d, 3JHH = 2.0 Hz, CH), 6.92 (4H, s, m-Mes-H), 4.65 (1H, m, allyl-CH), 2.91 (2H, dt, 3JHH = 7.6, 3JHH = 1.1 Hz, allyl-CH2), 2.32 (6H, s, p-Mes-CH3), 1.94 (6H, s, o-Mes-CH3), 1.89 (6H, s, o-Mes-CH3), 1.67 (2H, dt 3JHH = 7.6, 3JHH = 1.1 Hz, allyl-CH2); 13C NMR (CD2Cl2, 300 MHz) δ 176.6 (C(NHC)), 139.9 (p-Mes-CH), 137.1 (i-Mes-C), 135.9 (o-Mes-C), 135.6 (o-Mes-C), 129.3 (m-Mes-CH), 124.0 (CH), 122.1 (CH), 119.2 (allyl-CH), 63.7 (CH3), 58.7 (allyl-CH3), 21.3 (p-aryl-CH3), 18.0 (o-Ar-CH3). MS(FAB+) for C28H33N4Pd: m/z calculated 531.1751 [M-Cl]+, observed 531.1757.

Ethyl-1,1-di(mesitylimidazol-2-ylidene) palladium(II) η1-allyl chloride; 4b. Off white solid, 102 mg, 0.18 mmol, 92%. 1H NMR (CD2Cl2, 300 MHz) δ 7.55 (2H, d, 3JHH = 1.8 Hz, CH), 7.03 (2H, s, m-Mes-H), 6.98 (2H, s, m-Mes-H), 6.82 (2H, d, 3JHH = 1.8 Hz, CH), 5.29-5.07 (3H, m, CH2, allyl-CH overlapping), 4.07 (2H, d, 3JHH = 7.4 Hz, allyl-CH2), 3.36 (2H, d, 3JHH = 5.4 Hz, allyl-CH2), 3.04 (2H, dd, 3JHH = 13.6 Hz, 3JHH = 6.0 Hz, CH3), 2.36 (6H, s, p-Mes-CH3), 2.23 (3H, s, o-Mes-CH3), 2.18 (3H, s, o-Mes-CH3), 2.08 (3H, s, o-Mes-CH3), 2.02 (3H, s, o-Mes-CH3); 13C NMR (CD2Cl2, 101 MHz) δ 181.7 (C(NHC)), 139.5 (p-Mes-CH), 136.8 (i-Mes-C), 136.2 (o-Mes-C), 136.0 (o-Mes-C), 129.5 (CH), 129.4 (CH), 124.3 (m-Mes-CH), 122.6 (m-Mes-CH), 49.6 (CH3), 21.4 (p-Mes-CH3), 18.7 (o-Mes-CH3), 18.6 (o-Mes-CH3). MS(FAB+) for C29H35N4Pd: m/z calculated 545.1908 [M-Cl]+, observed 545.1914. MS(FAB+): m/z = 545.1914 for C29H35N4Pd [M-Cl]+.

Methyl-1,1-di(mesitylimidazol-2-ylidene) palladium(II) η1-allyl chloride; 4c. Pale brown solid, 41 mg, 0.11 mmol, 63%. 1H NMR (CD2Cl2, 300 MHz) δ 8.11 (2H, s, CH), 7.05 (1H, bd, 3JHH = 13 Hz, CH2), 6.96 (2H, s, CH), 6.19 (1H, bd, 3JHH = 13 Hz, CH2), 5.26 (1H, m, allyl-CH), 4.18 (2H, bd, 3JHH = 10 Hz, allyl-CH2), 3.75 (6H, s, CH3), 2.85 (2H, d, 3JHH = 10 Hz, allyl-CH2); 13C NMR (CD2Cl2, 101 MHz) δ 175.1 (C(NHC)), 122.9 (CH), 120.8 (CH), 119.3 (allyl-CH), 62.4 (CH3), 58.2 (allyl-CH2), 38.5 (CH3). MS(FAB+) for C12H17N4Pd: m/z calculated 323.0493 [M-Cl]+, observed 323.0497.
Chelating Di-NHC Late TM Complexes

Methyl-1,1-di(benzylimidazol-2-ylidene) palladium(II) η⁴-allyl chloride; 4d.
Pale yellow/brown solid, 51 mg, 0.10 mmol, 99%. ¹H NMR (CD₂Cl₂, 300 MHz) δ 8.06 (2H, d, JHH = 1.8 Hz, CH), 7.52 (1H, bs, CH₂), 7.45 – 7.25 (6H, m, Ar-H), 7.21 – 7.09 (4H, m, Ar-H), 6.93 (2H, d, JHH = 1.8 Hz, CH), 6.44 (1H, bs, CH₂), 5.32 – 5.19 (1H, m, allyl-CH), 5.29 (4H, s, CH₂), 4.05 (2H, d, JHH = 6.0 Hz, allyl-CH₂), 2.78 (2H, bs, CH₂), 1.74 (2H, m, CH₂), 1.44 – 1.21 (4H, m, CH₂), 0.93 (6H, t, JHH = 7.4 Hz, CH₃);
¹³C NMR (CD₂Cl₂, 101 MHz) δ 176.4 (CNHC), 136.4 (Ar-C), 129.6 (Ar-C), 128.9 (Ar-CH), 127.8 (Ar-CH) 123.20 (C₃H), 119.99 (allyl-CH), 58.10 (allyl-CH₂), 51.32 (CH₂), 40.8 (CH₂), 33.4 (CH₂), 19.7 (CH₂), 13.4 (CH₃).
MS(FAB⁺) for C₂₄H₂₅N₄Pd: m/z calculated 475.1124 [M-Cl]⁺, observed 475.1127.

Methyl-1,1-di(nButylimidazol-2-ylidene) palladium(II) η⁴-allyl chloride; 4e.
Pale brown solid, 123 mg, 0.28 mmol, 99%. ¹H NMR (CD₂Cl₂, 300 MHz) δ 8.01 (2H, d, JHH = 1.9 Hz, CH), 7.04 (2H, d, JHH = 1.9 Hz, CH), 6.12 (2H, bs, CH₂), 5.38 – 5.24 (1H, m, allyl-CH), 4.17 (2H, d, JHH = 7.4 Hz, allyl-CH₂), 2.86 (2H, d, JHH = 13.2 Hz, allyl-CH₂), 1.74 (2H, m, CH₂), 1.44 – 1.21 (4H, m, CH₂), 0.93 (6H, t, JHH = 7.4 Hz, CH₃);
¹³C NMR (CD₂Cl₂, 75 MHz, CD₂Cl₂) δ 174.8 (CNHC), 123.3 (C₃H), 122.8 (CH), 119.99 (allyl-CH), 58.10 (allyl-CH₂), 51.32 (CH₂), 40.8 (CH₂), 33.4 (CH₂), 19.7 (CH₂), 13.4 (CH₃).
MS(FAB⁺) for C₁₂H₁₇N₄Pd: m/z calculated 407.1434 [M-Cl]⁺, observed 407.1432.

General procedure for catalytic transfer semihydrogenation. To a carrousel vial equipped with a cross-head stirring bar and 1 mol% of catalyst, 10 mL of a stock solution (c = 0.15 M) of 1-phenyl-1-propyne, p-xylene as an internal standard, triethylamine (5 equiv.) and formic acid (5 equiv.) in MeCN was added. The mixture was stirred under nitrogen at 70 °C and monitored by GC.

General procedure for catalytic semihydrogenation with H₂. To a two-necked Schlenk equipped with a cross-head stirring bar, a balloon with hydrogen gas and 1 mol% of catalyst, 10 mL of a stock solution (c = 0.15 M) of 1-phenyl-1-propyne in MeCN with p-xylene as an internal standard was added. The mixture was stirred under H₂ pressure at 60 °C and monitored by GC.

X-ray structural determination. X-ray intensities were measured on a Bruker Kappa ApexII diffractometer with sealed tube and Triumph monochromator (λ = 0.71073 Å). The intensities were integrated using Saint⁴⁹ (compound 3a) or Eval™⁵⁰ (compound 4a). Absorption correction and scaling was performed with SADABS.⁵¹ The structures were solved using Direct Methods in the program SHELXS-97.⁵² Least-squares refinement was performed refined with SHELXL-97⁵³ against F² of all reflections. Non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were located in difference Fourier maps (compound 3a) or included in calculated positions (compound 4a).
Hydrogen atoms of the maleic anhydride ligand in 3a were refined freely with isotropic displacement parameters, all other hydrogen atoms in 3a and 4a were refined with a riding model. Geometry calculations and checking for higher symmetry was performed with the PLATON program.

**Compound 3a:** Crystals suitable for X-ray analysis where obtained bij slow diffusion of pentane to a solution of the product in dichloromethane. C_{29}H_{30}N_{4}O_{3}Pd 0.5(CH_{2}Cl_{2}), Fw = 631.43, colourless needle, 0.29 x 0.07 x 0.07 mm\(^3\), triclinic, P (no. 2), a = 11.0535(6), b = 11.5821(7), c = 11.9965(6) Å, α = 101.2168(17), β = 99.4456(17), γ = 106.8020(17) º, V = 1401.91(13) Å\(^3\), Z = 2, D\(_x\) = 1.496 g/cm\(^3\), μ = 0.80 mm\(^{-1}\). 28028 reflections were measured up to a resolution of (sin θ/λ)\(_{\text{max}}\) = 0.65 Å\(^{-1}\) at a temperature of 150(2) K. 6357 Reflections were unique (R\(_{\text{int}}\) = 0.032), of which 5611 were observed [I>2σ(I)]. 366 Parameters were refined with no restraints. R1/wR2 [I > 2σ(I)]: 0.0315 / 0.0804. R1/wR2 [all refl.]: 0.0394 / 0.0845. S = 1.048. Residual electron density between -1.27 and 0.90 e/Å\(^3\).

**Compound 4a:** Crystals suitable for X-ray analysis where obtained by slow diffusion of pentane to a solution of the product in dichloromethane at room temperature. C_{28}H_{33}N_{4}Pd + disordered solvent, Fw = 531*, colourless plate, 0.21 x 0.19 x 0.10 mm\(^3\), triclinic, P(no. 2), a = 11.2900(3), b = 12.6503(3), c = 22.6818(7) Å, α = 76.310(2), β = 89.236(2), γ = 80.392(1) º, V = 3102.13(15) Å\(^3\), Z = 4, D\(_x\) = 1.139 g/cm\(^3\), μ = 0.62 mm\(^{-1}\). 48631 Reflections were measured up to a resolution of (sin θ/λ)\(_{\text{max}}\) = 0.65 Å\(^{-1}\) at a temperature of 150(2) K. 13890 Reflections were unique (R\(_{\text{int}}\) = 0.036), of which 10076 were observed [I>2σ(I)]. The structure contains solvent accessible voids (744 Å\(^3\)/ unit cell), filled with disordered solvent molecules. Their contribution to the structure factors (321 electrons / unit cell) was secured by back-Fourier transformation with the SQUEEZE routine of the PLATON software. 607 Parameters were refined with no restraints. R1/wR2 [I > 2σ(I)]: 0.0378 / 0.0919. R1/wR2 [all refl.]: 0.0561 / 0.0969. S = 1.060. Residual electron density between -0.49 and 0.92 e/Å\(^3\).

CCDC 908658 (compound 3a) and 908659 (4a) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

**Acknowledgements**

We thank Nig Pham and Basilia Pires for their synthetic contribution and Han Peeters for HR-MS measurements.

**2.6 References**


* Derived parameters do not contain the contribution of the disordered solvent.
Chelating Di-NHC Late TM Complexes


Chapter 3

Pd(II)(η^3-allyl) Complexes and Ru(II)(p-cym) Hydrogenation Catalysts bearing Chelating NHC-tzNHC Ligands

Abstract

1,2,3-Triazolylidenes (tzNHC) have become a popular class of NHC ligands in homogeneous catalysis. Herein, we introduce bidentate ligands that combine this tzNHC with an Arduengo-type NHC motif. The ligands vary with respect to linker rigidity and metallacycle ring size (6- vs 7-membered). In this chapter the coordination of the heteroditopic di-NHCs to Pd(II) and Ru(II) centers is described. The resulting complexes have been studied for the hydroarylation of alkynes and hydrogenation of unsaturated bonds, respectively. Unfortunately, the acidic conditions of the former reaction turned out to be incompatible with our system, which indicates that the Pd-tzNHC bond is not as strong as anticipated. The NHC-tzNHC Ru p-cymene complexes were active in the hydrogenation of ketones and an imine, whereas they converted esters significantly slower than a known ruthenium di-NHC system.

3.1 Introduction

Chelate complexes with two or more donating atoms can have improved stability and altered properties compared to their monodentate counterparts.\(^1\)\(^2\) This effect can be even more pronounced for catalysts with heteroditopic ligands due to the specific \textit{trans}-influences of the non-equivalent donors: a strong ligand can labilize the bond \textit{trans} to it and thereby affect the reactivity of the complex, i.e. the activity and/or selectivity of a catalyst.

In the previous chapter symmetric di-NHC complexes have been presented. Here, heteroditopic di-NHC complexes are introduced, combining the well-known imidazole-2-ylidenes with 1,2,3-triazolylidenes (tzNHC) in the ligand design (Figure 1, box). As described in the introductory chapter, there recently has been increasing interest in tzNHC ligands in transition metal catalysis.\(^3\)\(^-\)\(^5\) Their popularity can be explained by the combination of specific \(\sigma\)-donor properties (stronger than the most basic normal carbenes yet weaker than imidazol-4-ylidenes\(^3\)\(^,\)\(^6\)), synthetic accessibility and almost unlimited possibilities to vary the N1 and C4 position through “click” chemistry.\(^7\)\(^,\)\(^8\)

Bidentate triazole functionalized NHC complexes were previously developed in our group and proved to be good catalysts in the transfer semi-hydrogenation of alkyynes,\(^9\) the reaction that was also described in the previous chapter. In this system, the triazole moiety coordinates to the metal via N1 (Figure 1). However, when this position is protected, the C4 atom becomes the preferred position for coordination, leading to heteroditopic NHC-tzNHC complexes. Cowie and co-workers previously prepared hybrid NHC-tzNHC ligands to support bimetallic Pd/Rh complexes in a bridging fashion,\(^10\) but chelate complexes with these ligands have not yet been reported to date.

We were also interested in another NHC-tzNHC ligand bearing an aryl linker. Besides the electronic implications of an aromatic group next to the carbene donors, it has been found that an aryl linker can give more stability to metal complexes compared to alkyl linkers.\(^11\) Furthermore, the incorporation of this bridge between the two carbenes leads to a more rigid structure with restricted
geometry. The starting point for this structure was found in the NHC-NH$_2$ ligand that was recently developed in our group (Figure 1).\textsuperscript{12}

This chapter features two heteroditopic di-NHC ligands, 2 and 5. They vary with respect to linker rigidity, metallacycle ring size and side-groups. A synthetic route to the novel NHC-Ar-tzNHC has been developed, which will be discussed. Subsequent coordination to Pd(II) and Ru(II) is described as well as studies towards the application of the resulting pre-catalysts in the hydroarylation of alkynes and the hydrogenation of unsaturated bonds, respectively.

### 3.2 Synthesis of Heteroditopic di-NHC Ligands

**Synthesis imidazolium–triazolium salts with methylene linker**

The synthesis of the triazolyl functionalized imidazolium salt, 1, has been reported by our group\textsuperscript{9} and others.\textsuperscript{13} This building block can be conveniently prepared in high yields from [(1-(prop-2-ynyl)-3-mesityl)-imidazolium] bromide and 2-azido-1,3-diosopropylbenzene via a “click”-like copper-catalyzed cycloaddition (CuAAC) reaction, in either acetonitrile\textsuperscript{9} or a tert-butanol/water mixture.\textsuperscript{13} In order to obtain the di-NHC precursor, alkylation of N3 of the triazolyl is necessary, which can be achieved with various alkylation agents. In our hands methyl iodide proved to be ineffective,\textsuperscript{14} whereas treatment with methyl triflate did yield the desired compound 2 in high yield (Scheme 1).\textsuperscript{15}

**Scheme 1:** Synthesis of imidazolium-triazole 1 and imidazolium-triazolium salt 2 with methylene bridge. i) CuSO$_4$5H$_2$O, sodium ascorbate in H$_2$O:tBuOH (1:1), 50°C, ii) MeOTf, DCM, -78°C→RT.

**Synthesis imidazolium-triazolium salts with aryl linker**

The NHC-Ar-tzNHC ligand 5 was synthesized starting from the NHC-NH$_2$ ligand developed in our group.\textsuperscript{12} It could be transformed into the desired mixed di-NHC precursor in a three-step procedure with moderate to good yields (Scheme 2). The first step was the synthesis of imidazolium-azide 3 by reacting the amine group with tert-butyl nitrite and trimethylsilyl azide (Scheme 2). The formation of the desired product was confirmed by the disappearance of representative infrared (IR) signals around 3400 cm$^{-1}$ and the appearance of a sharp band at 2136 cm$^{-1}$ in the IR spectrum, characteristic for the amine and azide functionality, respectively.
Again, the CuAAC reaction was applied to convert 3 into the NHC-tz ligand 4. However, in this particular case a prolonged reaction time (5 days) was needed to obtain the compound in reasonable yield. The synthesis might be improved by further screening of the reaction conditions (particularly solvents), which has not been performed.

Finally, the desired ligand, imidazolium-triazolium hexafluorophosphate salt 5, was obtained by methylation of 4. The strong alkylating agent trimethyl oxonium tetrafluoroborate ((Me₃O)BF₄, Meerwein’s salt) was used for this purpose, followed by anion exchange with KPF₆. The triazolium salt 5 was identified in the ¹H NMR spectrum by a downfield shift of the triazole signal (to 9.52 ppm) and the methyl signal (at 4.29 ppm). All compounds were characterized by multinuclear NMR and HR-MS.

3.3 Heteroditopic NHC-tzNHC Ag, Pd and Ru Complexes

Synthesis and characterization of Ag(I) NHC-CH₂-tzNHC complex

Silver(I) NHC complexes are widely used as carbene transfer agents. The Ag(I) complexes are usually stable in air and they can be used to synthesize a large range of NHC-TM complexes without the use of an external base and at mild conditions.

The NHC-tzNHC silver(I) complex 6 could be obtained in high yield by reacting the ligand with Ag₂O in methanol (Scheme 3). As observed for the “classic” dicarbene this reaction was solvent dependent proving unsuccessful in DCM or...
The \(^1\)H NMR spectrum of the resulting Ag(I) complex exhibited an AB system corresponding to the two diastereotopic methylene linker hydrogens and multiple resonances for the mesityl and diisopropylphenyl N-substituents. The Ag(I) carbene carbons gave rise to two sets of doublets at 182.2 (\(J_{\text{NHCAg}} = 172.3\) Hz, \(J_{\text{tzNHCAg}} = 191.8\) Hz) and 172.3 ppm (\(J_{\text{NHCAg}} = 167.2\) Hz, \(J_{\text{tzNHCAg}} = 197.1\) Hz). HR-MS was in accordance with the dimeric structure of the silver complex.

The dimeric homobimetallic structure with two bridging dicarbene ligands, was also confirmed by X-ray crystal diffraction. Single crystals suitable for crystallographic analysis were obtained by slow diffusion of cyclopentane into a concentrated solution of 6 in THF. The solid-state structure of the silver complex is depicted in Figure 2.

**Scheme 3**: Synthesis of silver(I) di-carbene complex 6.

Figure 2: Molecular structure of 6 in the crystal, drawn at the 50% probability level. Only one of two independent molecules is shown. Triflate anions, disordered THF solvent molecules and hydrogen atoms are omitted for clarity.

The asymmetric unit contains two dimeric silver complexes, four triflate anions and severely disordered THF solvent molecules (see Experimental Section). The crystal structure of 6 largely resembles the dimeric Ag(I) di-NHC complex published...
by Slaughter and co-workers. The 12-membered bicyclic chelate ring adopts a twisted-boat conformation with both the CH$_2$ linkers pointing in one direction, while the N-substituents are perpendicular to the carbene rings. Moreover, a short Ag-Ag distance (3.1667(6) Å < twice the van der Waals radius (3.40 Å); Table 1) is observed, which points to “argentophilic” interactions between the two metal centers. Selected bond distances and angles in the two independent molecules of 6 are depicted in Table 1. The triazolylidene moieties of the ligands are coordinated trans to the imidazolylidenes (169.30(14)°-174.62(13)°). The Ag(I)-carbene bond lengths are in the expected range, but the similarity of the Ag–tzNHC and Ag-NHC distances in the X-ray structure of 6 is surprising.

Table 1: Selected bond lengths [Å] and angles [°] in the two independent molecules of 6.

<table>
<thead>
<tr>
<th></th>
<th>Ag1</th>
<th>Ag2</th>
<th>Ag3</th>
<th>Ag4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ag-C$_{NHC}$</td>
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<td>2.080(3)</td>
<td>2.074(3)</td>
<td>2.092(3)</td>
</tr>
<tr>
<td>Ag-C$_{tzNHC}$</td>
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<td>2.081(3)</td>
<td>2.083(3)</td>
<td>2.085(3)</td>
</tr>
<tr>
<td>Ag-Ag</td>
<td>3.1667(4)</td>
<td></td>
<td>3.1903(4)</td>
<td></td>
</tr>
<tr>
<td>∠C-Ag-C</td>
<td>173.07(14)</td>
<td>171.48(14)</td>
<td>174.62(13)</td>
<td>169.30(14)</td>
</tr>
</tbody>
</table>

Complex 6 could be stored under nitrogen atmosphere with exclusion of light. The complex has been employed to transfer the mixed di-carbene ligand to other transition metals as is described in the next paragraphs.

Synthesis and characterization of Pd(II) NHC-tzNHC complexes

Transmetalation of the Ag(I) complex 6 in dichloromethane at room temperature with [Pd($\eta^3$-$C_3H_5$)Cl]$_2$ was applied similarly as described for the classic di-NHCs in Chapter 2 (Scheme 4). This resulted in formation of the desired product 7, albeit in low yield after recrystallization. Alternatively, complex 7 could be obtained in higher yields (89%) by deprotonation of the ligand with KOtBu in the presence of half an equivalent of [Pd($\eta^3$-$C_3H_5$)Cl]$_2$, followed by purification by column chromatography using non-dried solvents.

Scheme 4: Synthesis of [Pd($C_3H_5$)$_2$(NHC-tzNHC)]OTf 7. i. Ag$_2$O, MeOH 2. 0.5 equiv. [Pd($C_3H_5$)Cl]$_2$, DCM. ii. 2 equiv. KOtBu + 0.5 equiv. [Pd($\eta^3$-$C_3H_5$)Cl]$_2$. THF.
The higher donating properties of the NHC-tzNHC ligand in 7 compared to the di-NHC Pd(II) allyl complex reported in the previous chapter,\textsuperscript{17} are demonstrated by low chemical shifts for the allyl co-ligand (4.65-4.50, 2.63, 2.47 and 1.77 ppm in the \textit{^1}H NMR and 117.7, 58.8 and 56.6 ppm in the \textit{^{13}}C NMR spectrum; Table 2). Furthermore, a tzNHC carbon resonance is visible at 163.2 ppm in the \textit{^{13}}C NMR spectrum, besides the peak at 175.6 ppm corresponding to the NHC carbon. The asymmetry and restricted rotation of the ligand led to the observation of distinct signals for the meta and ortho hydrogens and substituents on the mesityl and diisoproplyphenyl wingtips in the NMR spectra as well as an AB system for the hydrogens on the methylene bridge linking the two carbene rings.

\textbf{Table 2}: Chemical shifts of carbenes and allyl in selected di-NHC Pd(\textit{^1}-C\textsubscript{3}H\textsubscript{5}) complexes:

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
Complex & \textbf{\textit{\delta}} C\textsubscript{NHC} in \textit{^{13}}C NMR (ppm) & \textbf{\textit{\delta}} Allyl-C in \textit{^{13}}C NMR (ppm) & \textbf{\textit{\delta}} Allyl-H in \textit{^1}H NMR (ppm) \\
\hline
\textit{[Pd(NHC(Mes))\textsubscript{2}(\textit{\eta}^3-C\textsubscript{3}H\textsubscript{5})]}Cl & 176.6 & 119.2, 58.7 & 4.65, 2.91 \\
\hline
\textit{7} & 175.6, 163.2 & 117.7, 58.9, 56.6 & 4.58, 2.63, 2.47 \\
\hline
\textit{8} & 180.7/180.3, 166.3/165.9 & 118.9/118.8, 59.6/58.4, 58.2/57.0 & 5.11/4.89, 3.98/3.80/3.51/3.16, 2.61/2.36/2.26/2.13 \\
\hline
\end{tabular}
\caption{Chemical shifts of carbenes and allyl in selected di-NHC Pd(\textit{^1}-C\textsubscript{3}H\textsubscript{5}) complexes.}
\end{table}

The values for the [Pd(NHC(Mes))\textsubscript{2}(\textit{\eta}^3-C\textsubscript{3}H\textsubscript{5})]Cl complex are taken from Chapter 2.

For the heteroditopic diNHC ligand connected via the aryl linker we chose to use the direct deprotonation procedure (Scheme 5). This method led to the isolation of the desired complex 8 in up to 95% yield after column chromatography.

\begin{scheme}
\centering
\includegraphics[width=0.8\textwidth]{Scheme_5.png}
\caption{Synthesis of [Pd(\textit{\eta}^3-C\textsubscript{3}H\textsubscript{5})(NHC-tzNHC)]PF\textsubscript{6} 8.}
\end{scheme}

In contrast to complex 7, two isomers of Pd complex 8 could be discerned in the NMR spectra in this case (Table 2). Duplicate signals for all allyl-protons and ligand hydrogens were observed in the \textit{^1}H NMR spectrum, which is depicted in Figure 3. This effect was attributed to the allyl fragment adopting a \textit{syn} or \textit{anti} orientation via
\(\pi\)-rotation.\(^{18}\) Variable temperature (VT) \(^1\)H NMR spectroscopy experiments (CD\(_3\)CN, <75°C) indicated a high barrier of rotation as no broadening or coalescence of the separate allyl signals was observed. Also two separate C\(_{\text{NHC}}\) and C\(_{\text{tzNHC}}\) resonances were found in the \(^{13}\)C NMR spectrum at downfield shifts compared to complex 7 (Table 2), due to the electron-withdrawing character of the aryl linker.

**Figure 3:** \(^1\)H NMR spectrum of 8. Allyl hydrogens are attributed by numbers (subscript s = syn, a = anti) and solvents are marked by “x”.

**Synthesis and characterization of Ru(II) NHC-tzNHC complexes**

Transmetalation could also be applied to obtain the corresponding Ru complexes. Synthesis of ruthenium complex 9 was achieved following a procedure of Sarkar and co-workers (Scheme 6).\(^{19}\) Again, two isomers were present in solution as concluded from multinuclear NMR spectroscopy. We attributed the difference in the two isomers (1:1.3 ratio) to the orientation of the p-cymene ligand caused by hindered rotation of this fragment. The AB systems for the hydrogens on the methylene bridge in \(^1\)H NMR and HR-MS pointed to a chelate coordination of the ligand.

**Scheme 6:** Synthesis of Ru(II) heteroditopic di-NHC complex 9. i) [Ru(p-cym)Cl\(_2\)] ii) KPF\(_6\).
The crystal structure of complex 9 (Figure 4) confirmed coordination of the ligand in a chelating fashion as well as the expected piano-stool geometry around the ruthenium center. The p-cym ligand is bound in an $\eta^6$-coordination mode with a ring-slippage of only 0.068 Å. The centroid of this fragment is located 1.7324(12) Å from the Ru center, which is in the expected range.²⁴-²⁶ The diisopropyphenyl and mesityl N-substituents are oriented perpendicular to the carbene rings. Notably, the 1,2,3-triazolylidene-ruthenium bond (2.074(2) Å) is shorter than the NHC-Ru bond (2.094(3) Å). Both these distances are among the longer ones reported for similar bidentate piano-stool ruthenium di-NHC²⁴ and (di-)tzNHC crystals,²³-²⁸ which may be due to the sterically demanding N-substituents.

![Crystal Structure of 9](image)

**Figure 4:** Crystal structure of 9 at the 50% probability level. The PF₆ anion, THF solvent molecule and hydrogens are omitted for clarity. Selected bond distances and angles are depicted in the box on the right.

Ruthenium complex 10 was prepared in the same manner as complex 9 (Scheme 7). Identification of this complex was performed by multinuclear NMR spectroscopy and HR-MS.

![Scheme 7](image)

**Scheme 7:** Synthesis of Ru(II) heteroditopic di-NHC complex 10.

*The ring-slippage is calculated with the PLATON software⁵³ and is defined as the distance between the ring centroid and the perpendicular projection of the metal on the ring least-squares plane.*

Ru-tzNHC: 2.074(2) Å
Ru-NHC: 2.094(3) Å
Ru-Cl: 2.3973(7) Å
Ru-cym(cent): 1.7324(12) Å
$\angle$CRuC: 85.90(10) °
In contrast to complex 9, complex 10 displayed one species in the $^1$H NMR spectrum. Presumably, the lack of steric hindrance in this ligand allows for rotation of the $p$-cymene ligand. This fragment gave rise to four different signals in the $^1$H as well as the $^{13}$C NMR spectrum of 10, while two resonances (2 x ddd, $J = 13.3, 11.3, 5.0$ Hz) were present corresponding to the diastereotopic N-CH$_2$ of the $n$-butyl group. Furthermore, similarly to the Pd(II) complexes, the carbene shifts of the NHC-Ar-tzNHC complex 10 were found downfield (182.2 and 165.3 ppm) in the $^{13}$C NMR spectrum compared to complex 9, illustrating the electron-withdrawing character of the linker. In the next chapter the electron-donating properties of the ligands will be studied further by means of the carbonyl IR stretching frequencies in the [(di-NHC)Rh(CO)$_2$]$^+$ complexes.

In summary, several Ag(I), Pd(II) and Ru(II) complexes bearing heteroditopic di-NHC ligands were successfully synthesized and characterized. The catalytic applications of the palladium and ruthenium complexes have been studied as is described below.

### 3.4 Catalytic Studies

**Di-NHC palladium catalyzed arylation of alkynes**

Carbon-carbon bond forming reactions are very important, as they are key for the development of new synthetic organic molecules as well as for the efficient production of known compounds. Catalytic aromatic C-H activation reactions provide an atom-efficient and “green” alternative to many other C-C coupling reactions, such as the Nobel prize-winning Heck reaction and Negishi or Suzuki couplings. These activations have therefore been studied intensively in the last decades and several examples have been reported, including the hydroarylation of alkynes. In this reaction the C-H bond of the aromatic substrate formally adds trans to the triple bond of the alkyne, usually leading to the corresponding cis alkene. Pioneering work on this reaction was reported by the group of Fujiwara, hence the alternative name “Fujiwara reaction”. Pd(II) salts were mainly used as catalysts.

Two proposed mechanisms exist for the hydroarylation of alkynes: A) a Friedel-Crafts-type alkenylation, and B) an arene metalation mechanism (Scheme 8). In the former pathway a triple bond is activated by coordination to the (cationic) palladium center, which subsequently undergoes an electrophilic substitution with an electron-rich arene. The resulting metal(arylvinyl) complex is subsequently protonated to form the product. Alternatively, a nucleophilic catalyst may facilitate C-H activation via oxidative addition of the arene. In the next step the triple bond adds to the metal(aryl) complex, leading to the substituted vinyl complex. Release of the product by reductive elimination closes this cycle.
Recently, also Pd NHC complexes have been applied in the hydroarylation of alkynes.\textsuperscript{31} The group of Biffis and Basato showed that di-NHC palladium halide complexes are very efficient catalysts for this reaction.\textsuperscript{32} A bidentate 1,2,3-triazolylidene (tzNHC) palladium complex was found to facilitate the Fujiwara reaction as well.\textsuperscript{14} We decided to test our complexes 7 and 8, having two different NHC donors, in the same reaction.

Unfortunately, initial catalytic results, reacting pentamethylbenzene with ethyl propiolate in 1,2-dichloroethane, were disappointing (Table 1). At room temperature the reactions catalyzed by complexes 7 and 8 only showed minor conversion after 24 hours (entries 1 and 3), whereas the known complex of Biffis et al. already showed 60\% conversion after 5 hours when silver trifluoroacetate (AgTFA) was added to abstract the halides (entry 5) or 76\% at 80 °C (entry 6). Even at elevated temperatures the activities of 7 and 8 were unsatisfactory (entries 2 and 4), yet for all trials selectivity to the $Z$ product was observed (>90\%).

An obvious difference between the known catalyst and complex 7 is the bulkiness of the substituents on the di-NHC. The allyl co-ligand might be another factor influencing the activity. To assess the impact of the bulky wingtips, we synthesized the mesityl substituted di-NHC palladium bromide complex, following a procedure of Herrmann et al.\textsuperscript{33} Attempts to make the halide analogue of 7 in this manner were unsuccessful. The bulky di-NHC(Mes) complex gave similar results to the heteroditopic di-NHC catalysts (entry 7). However, the ESI-mass spectrum of this complex indicated a dimeric composition for this compound as dimer $[L_2Pd_2Br_3]$. We then prepared the $[Pd(NHC(Mes))_2(O_2CF_3)_2]$ complex and tested this in catalysis with similar results.

Scheme 8: Proposed reaction mechanisms for the Fujiwara reaction: A) Friedel-Crafts-type alkenylation, B) arene metalation.
The disappointing catalytic results led us to investigate the stability of complex 7 under the strongly acidic reaction conditions during catalysis. Unfortunately, $^1$H NMR spectroscopy revealed decomposition of the complex upon addition of TFA, judging from the appearance of the characteristic imidazolium- and triazolium resonances between 8 and 10 ppm. In constrast, $[(\text{di-NHC})\text{PdBr}_2]$ complexes were extremely stable, displaying no decomposition under acidic conditions (stirring in concentrated hydrochloric or nitric acid or aqua regia) and elevated temperatures ($<160$ °C). It is difficult to generalize and predict the stability of tzNHC-M complexes. On the one hand, there have been various reports on tzNHC-M bonds with remarkable resistance against protonolysis: e.g. $[(\text{di-NHC})\text{PdBr}_2]$ withstood exposure to HI for several days, and cyclometalated Ru(II), Rh(III) and Ir(III) complexes displayed no decomposition upon treatment with HCl for 24h. On the other hand, lability of the tzNHC-M bond has been observed in certain cases. Pd nanoparticles were, for instance, formed from Pd(II)tzNHC complexes at moderate temperatures in Suzuki
and Heck cross-coupling reactions. Another example that actually exploits the acid lability of the tzNHC-M bond is an olefin metathesis system by Bertrand and Grubbs, wherein cleavage of the triazolylidene in a Ru(tzNHC)(NHC) complex under acidic conditions led to an exceptionally active catalyst. Our findings support the notion that the tzNHC-M bond may not always be as inert as previously regarded (under catalytic conditions). Protonolysis has been proposed to occur by protonation of the unsubstituted nitrogen atom (N2), which would cause dissociation of the triazole ring with a simultaneous 1,3-proton-shift to form the triazolium salt. It has been suggested that shielding C5-substituents may increase the stability of tzNHC-M bonds. Indeed, NMR experiments indicated that complex 8 was less prone to protonolysis compared to 7.

*Ruthenium catalyzed hydrogenation of polar bonds*

Complexes 9 and 10 were tested in the hydrogenation of polar double bonds. They can compete with the reported [(CNC)Ru(H)(CO)(PPh3)]Cl hydrogenation catalyst (capable of metal-ligand cooperativity) in terms of the reduction of N-benzylideneaniline (full conversion to benzylaniline within 6h at 70 °C under 5 bar H2). Acetophenone was not completely hydrogenated under the same conditions (Table 2, entries 1 and 4). Raising the hydrogen pressure to 25 bar (50 °C) improved conversion significantly (entries 2 and 5). In fact, pre-catalysts 9 and 10 were active in the hydrogenation of acetophenone to 1-phenylethanol at lower catalyst loadings (0.1 mol%) than previously reported Ru(NHC) systems. In contrast to the water-soluble Ru(p-cym) di-NHC complexes reported by Kühn and co-workers, complex 9 and 10 selectively hydrogenated the ketone functionality, leaving the aromatic ring intact.

*Table 4: Hydrogenation of acetophenone catalyzed by 9 and 10.*

<table>
<thead>
<tr>
<th>cat.</th>
<th>C/B/S</th>
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<th>t (h)</th>
<th>Conv. (%)</th>
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<tr>
<td>6</td>
<td>[Ru]</td>
<td>1/10/1000</td>
<td>25</td>
<td>6</td>
</tr>
</tbody>
</table>

a. C/B/S = catalyst/base/substrate ratio. b. Conversion was determined by GC analysis using p-xylene as internal standard. c. p(H2) = 5 bar. d. [Ru] = 0.5 equiv. of [Ru(p-cym) Cl2]2.
Addition of KOTBu was found to be necessary (Table 4, entry 2 vs 3), which points to a mechanism involving heterolytic cleavage of $H_2$. To gain more insight in the catalytically active species, $^1H$ NMR investigations were performed. A solution of complex 9 was studied under near-catalytic conditions (5 equiv. of KOTBu, 5 bar $H_2$, <65 °C in THF-$d_8$). The spectrum showed very broad signals for the ruthenium species, indicating exchange on the NMR time-scale, while sharp peaks (at 7.05, 2.82, 2.26 and 1.21 ppm) diagnostic for free $p$-cymene were visible. In contrast to studies on a Ru hydrogenation catalyst by Albrecht et al. and the Pd complex under hydroarylation conditions, no azolium peaks were observed in the $^1H$ spectrum during this experiment. This indicates that the ligand remains attached to the ruthenium center. Although direct evidence is lacking and assuming that putative Ru($\eta^2$-$H_2$) and $\eta^2$-hydride signals were not observed due to the broadened features of the spectrum, we propose that a mixture of an NHC-tzNHC Ru hydride and a Ru($\eta^2$-$H_2$) species is present in solution.

The substrate scope of pre-catalyst 9 was subsequently studied (at 50 °C, 25 bar $H_2$; Table 5). Aliphatic ketones and even the sterically congested substrate pinacolone were reduced within 6 hours (entry 1 and 2). Methyl levulinate was converted significantly slower, forming the ring-closed product $\gamma$-valerolactone (entry 3). When using 2-cyclohexenone as the substrate both the ketone and the C=C double bond functionality were hydrogenated (entry 4). By monitoring the reaction, it was determined that the substrate was first reduced to cyclohexanone before the ketone functionality was hydrogenated. Unfortunately, phthalic anhydride (entry 5) could not be reduced under these conditions.

**Table 5: Hydrogenation of several substrates catalyzed by 9.**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Conv. (%)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="substrate" /></td>
<td>100</td>
<td><img src="image2.png" alt="product" /></td>
</tr>
<tr>
<td>2</td>
<td><img src="image3.png" alt="substrate" /></td>
<td>100</td>
<td><img src="image4.png" alt="product" /></td>
</tr>
<tr>
<td>3</td>
<td><img src="image5.png" alt="substrate" /></td>
<td>12</td>
<td><img src="image6.png" alt="product" /></td>
</tr>
<tr>
<td>4</td>
<td><img src="image7.png" alt="substrate" /></td>
<td>100</td>
<td><img src="image8.png" alt="product" /></td>
</tr>
<tr>
<td>5</td>
<td><img src="image9.png" alt="substrate" /></td>
<td>0</td>
<td><img src="image10.png" alt="product" /></td>
</tr>
</tbody>
</table>

Reaction conditions: 0.4 mmol substrate, 1 mol% of 9, 8 mol% KOTBu, 25 bar $H_2$, 50 °C, THF, 6h. Conversion and yield were determined by GC analysis.
As explained in Chapter 1 anhydrides and esters are very challenging substrates for hydrogenation. Beller et al. showed that di-NHCs are suitable ligands for ester hydrogenolysis in combination with [Ru(p-cym)Cl₂]₂ (Table 6, entries 1-4).  

Table 6: Results of Ru catalyzed hydrogenolysis of methylbenzoate with di-NHC ligands.

<table>
<thead>
<tr>
<th>Cat/Ligand</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1ᵃ</td>
<td>MonoNHC</td>
<td>&lt;41</td>
</tr>
<tr>
<td>2ᵃ</td>
<td>11a + [Ru]ᵇ</td>
<td>98</td>
</tr>
<tr>
<td>3ᵃ</td>
<td>11b + [Ru]ᵇ</td>
<td>99</td>
</tr>
<tr>
<td>4ᵃ</td>
<td>[Ru(p-cym)(11a)Cl]Cl</td>
<td>79</td>
</tr>
<tr>
<td>5ᵇ</td>
<td>11b + [Ru]ᵇ</td>
<td>94</td>
</tr>
<tr>
<td>6ᵇ</td>
<td>1 + [Ru]ᵇ</td>
<td>9</td>
</tr>
<tr>
<td>7ᵇ</td>
<td>9</td>
<td>37</td>
</tr>
</tbody>
</table>

a. Adapted from reference [36]. b. [Ru] = 0.5 equiv. of [Ru(p-cym)Cl₂]₂.

We envisioned that our complex 9, bearing more electron-donating ligands, would also be a good candidate for the hydrogenation of esters. Therefore, we applied 9 in this reaction using methyl benzoate as substrate following the protocol described by Beller.  

Unfortunately, both the in situ prepared catalyst (Table 6, entry 6) and the isolated complex (entry 7) turned out to be significantly less active than the known system. The activated ester methyl trifluoroacetate however, was fully converted to the corresponding alcohol by our system.

Again, the disappointing conversion in the hydrogenolysis of methyl benzoate using a Ru complex with ligand 1 might be attributed to steric factors. Ligand 1 has bulky mesityl and diisopropylphenyl substituents that can for example hinder coordination of the substrate, whereas ligand 11 contained benzyl groups. However, in the report of Beller the di-imidazolium salt bearing the same bulky substituents also induced good conversion (better than ligand 1) for this reaction. Instead of testing the influence of N-substituents, we therefore decided to turn to a metal-ligand cooperative approach to hydrogenate esters more efficiently, which is described in Chapter 5.

3.5 Conclusions

Two novel bidentate ligands that combine a 1,2,3-triazolyl based NHC with an Arduengo-type NHC system have been developed. These heteroditopic di-NHCs
were coordinated to Ag(I) and Pd(II) centers. Transmetalation was an alternative route to Pd(II) complex 7 as well as to [Ru(II)(NHC-tzNHC)(p-cym)]PF₆ complexes 9 and 10. All complexes were characterized by multinuclear NMR spectroscopy and HR-MS, while the structures of Ag(I) complex 6 and Ru(II) complex 9 were unambiguously established by X-ray crystallography.

The Pd(II) complexes 7 and 8 were studied in the hydroarylation of alkynes. Unfortunately, the acidic conditions of the reaction turned out to be incompatible with the NHC-tzNHC complexes, as protonolysis of both of the M-C$_{\text{NHC}}$ bonds occurred. The ruthenium complexes 9 and 10, on the other hand, were successfully applied in the hydrogenation of polar bonds. While ketones and imines were readily reduced under 5 bar at low catalyst loadings, the NHC-tzNHC Ru complex proved to be less active than a previous Ru di-NHC system in the hydrogenation of the more challenging substrate methyl benzoate.

We have shown that, although caution is in order when considering tzNHCs as mere electron-rich and strongly coordinating NHCs, di-NHC triazolylidene complexes can have desirable properties and catalytic activities. However, this chapter only scratches the surface with respect to uncovering the potential of these highly accessible mixed NHC-tzNHC ligands: variation of side-groups is virtually endless and there are many more combinations with TMs conceivable (Ir and Rh complexes are discussed in the next chapter). Therefore, we are confident that di-NHCs including a 1,2,3-triazolylidene moiety are promising ligands for organometallic chemistry.

3.6 Experimental

Complex syntheses and catalytic experiments were performed using standard Schlenk techniques under an atmosphere of dry nitrogen. Solvents were dried and distilled according to standard methods. Acetophenone was vacuum-distilled from P$_2$O$_5$ under a nitrogen atmosphere and stored over 4 Å molecular sieves. All reagents were purchased from commercial suppliers and used without further purification. The azide, [(1-prop-2-nyl)-3-mesityl]imidazolium bromide, [1-((4-(2,6-diisopropylphenyl)-1H-1,2,3-triazolyl]-methylene-3-mesityl)]imidazolium bromide and 1-(2-aminophenyl)-3-(n-butyl) imidazolium hexafluorophosphate were prepared according to literature procedures. The NMR spectra were recorded on Varian Mercury 300 MHz, Bruker DRX Avance 300 and Bruker AMX 400 MHz spectrometers. $^{19}$F NMR was used to confirm the (non-coordinating) anion of the compounds: OTf (-78 ppm) and PF$_6$ (-70 ppm, d, $J_{PF}$ = 710 Hz). $^1$H-$^1$H COSY and/or $^1$H-$^{13}$C HSQC NMR spectroscopy was used to assign the peaks of several compounds. High resolution mass spectrometry was performed on a JEOL JMS SX/SX102A four-sector mass spectrometer (FAB$^*$) or Bruker MicrOTOF-Q (ESI$^*$) and GC analyses were performed with an Interscience Trace GC Ultra instrument using a Restek RTX®-200 (30 m, 0.25 mmID) capillary column.
[3-(2,6-diisopropylphenyl)-1-methyl-5-[(3-mesitylimidazolium)methyl] 1,2,3-triazolium] trifluoromethane sulfonate bromide; 2. To a cooled (-78 °C) solution of triazolylimidazolium bromide (125 mg, 0.3 mmol) in dichloromethane (5 mL) methyl triflate (120 mg, 0.73 mmol) was added drop-wise. The mixture was allowed to warm to room temperature and then stirred at room temperature for 16 more hours. Upon addition of ether (5 mL) a white crystalline solid precipitated from the mixture, which was collected on a glass frit and washed with ether (3 x 5 mL) to obtain the product (169 mg, 0.25 mmol, 84%). 1H NMR (CDCl3) δ 9.09 (s, 1H, NCHN), 7.76-7.73 (m, 2H, Ar-C), after which tert-butyl nitrite (295 µL, 2.5 mmol) was added. To this solution trimethylsilyl azide (260 µL, 2 mmol) was added. This solution was stirred at room temperature for 18 hours, after which solvent and excess reagents were evaporated in vacuo. The brown solid product was used without further purification (640 mg, 1.66 mmol, quantitative). 1H NMR (300 MHz, CDCl3) δ 8.84 (s, 1H, CH), 7.66-7.53 (m, 2H, Ar-CH), 7.46 (d, JHH = 1.6 Hz, 1H, CH), 7.44 (d, JHH = 1.6 Hz, CH), 7.40 – 7.30 (m, 2H, m, 2H, Ar-CH), 4.33 (t, JHH = 7.5 Hz, 2H, CH2), 1.94 (m, 2H, CH2), 1.50 – 1.35 (m, 2H, CH2), 0.98 (t, JHH = 7.3 Hz, 4H, CH2); 13C NMR (75 MHz, CDCl3) δ 136.4 (NCN), 134.8 (Ar-C), 132.4 (Ar-CH), 127.1 (Ar-CH), 126.4 (Ar-CH), 125.0 (Ar-C), 123.8 (CH), 122.1 (CH), 119.8 (Ar-CH), 50.6 (CH2), 32.0 (CH2), 19.6 (CH2), 13.5 (CH3). MS (FD+) for C29H37F3N5O5: m/z calculated 592.2569 [M-Br]+, observed 592.2564. 

[1-(2-azidophenyl)-3-(n-butyl)imidazolium] hexafluorophosphate; 3. A solution of 1-(2-aminophenyl)-3-(n-butyl)imidazolium hexafluorophosphate (600 mg, 1.66 mmol) in MeCN (30 mL) was cooled to 0 °C, after which tert-butyl nitrite (295 µL, 2.5 mmol) was added. To this solution trimethylsilyl azide (260 µL, 2 mmol) was added. This solution was stirred at room temperature for 18 hours, after which solvent and excess reagents were evaporated in vacuo. The brown solid product was used without further purification (640 mg, 1.66 mmol, quantitative). 1H NMR (300 MHz, CDCl3) δ 8.84 (s, 1H, CH), 7.66-7.53 (m, 2H, Ar-CH), 7.46 (d, JHH = 1.6 Hz, 1H, CH), 7.44 (d, JHH = 1.6 Hz, CH), 7.40 – 7.30 (m, 2H, m, 2H, Ar-CH), 4.33 (t, JHH = 7.5 Hz, 2H, CH2), 1.94 (m, 2H, CH2), 1.50 – 1.35 (m, 2H, CH2), 0.98 (t, JHH = 7.3 Hz, 4H, CH2); 13C NMR (75 MHz, CDCl3) δ 136.4 (NCN), 134.8 (Ar-C), 132.4 (Ar-CH), 127.1 (Ar-CH), 126.4 (Ar-CH), 125.0 (Ar-C), 123.8 (CH), 122.1 (CH), 119.8 (Ar-CH), 50.6 (CH2), 32.0 (CH2), 19.6 (CH2), 13.5 (CH3). MS (FD+) for C29H37F3N5O5: m/z calculated 242.1406 [M-PF6]+, observed 242.1400. IR (CDCl3) v(N3) 2136, 2107 cm⁻¹. 

[4-(p-toly)-1-phenyl-2-((n-butyl)imidazolium) 1,2,3-triazolium] hexafluorophosphate; 4. To a solution of [1-(2-azidophenyl)-3-(n-butyl)imidazolium] hexafluorophosphatate 3 (601.2 mg, 1.55 mmol) in H2O:tBuOH (1:1, 14 mL) CuSO4·5H2O (26 mg, 0.1 mmol), sodium ascorbate (39 mg, 0.2 mmol) and p-tolyl acetylene (265 µL, 2.09 mmol, 2.0 equiv.) were added. The resulting reaction mixture was stirred for 5 days at 50 °C. Tert-butanol was evaporated and the product was extracted with DCM (3x 10 mL), washed with H2O (3x 10 mL), dried over MgSO4 and concentrated in vacuo. The product was obtained as a brown solid (562 mg, 1.12 mmol, 72%). 1H NMR (300 MHz, CDCl3) δ 8.98 (s, 1H, NCHN), 8.29 (s, 1H, NCHC), 7.90 –
7.55 (m, 6H, CH and Ar-CH overlapping), 7.50 – 6.84 (m, 4H, Ar-CH), 4.16 (m, 2H, N-CH$_2$), 2.36 (s, 3H, CH$_3$), 1.75 (m, $^3$J$_{HH}$ = 7.4 Hz, 2H, CH$_2$), 1.25 – 1.07 (m, 2H, CH$_2$), 0.81 (t, $^3$J$_{HH}$ = 7.3 Hz, 3H, CH$_3$); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 148.6, 138.6 (Ar-C$_q$), 137.2 (NCH$_N$), 132.5, 132.1, 131.5 (Ar-C$_q$), 129.6, 129.5, 127.7, 127.4, 126.4, 125.7 (Ar-CH), 123.5, 121.9, 121.8 (CH), 50.3, 31.4 (CH$_2$), 21.20 (CH$_3$), 19.09 (CH$_3$), 13.07 (CH$_3$). MS (ESI$^+$) for C$_{32}$H$_{24}$N$_5$: m/z calculated 358.2026 [M-PF$_6$]$^+$, observed 358.2028.

[3-methyl-4-((p-tolyl)-1-phenyl-2-((n-butylimidazolium)1,2,3-triazolium]bis-hexafluorophosphate; 5. Meerwein’s salt ((Me$_2$O$_2$)BF$_4$, 249 mg, 1.7 mmol) and [4-(p-tolyl)-1-phenyl-2-((n-butylimidazolium)1,2,3-triazolium]hexafluorophosphate 4 (445.3 mg, 0.67 mmol) were dissolved in dry dichloromethane (10 mL) and the reaction mixture was stirred for 16 hours. The reaction was quenched with MeOH after which the solvent was removed. The resulting solid was redissolved in an acetone water mixture (1:1, 6 mL) and KPF$_6$ (375 mg, 5 mmol) was added. The mixture was stirred for 1 hour before acetone was removed under reduced pressure to yield an orange precipitate, which was washed with Et$_2$O to obtain the product as an orange solid (424 mg, 0.66 mmol, 95%). $^1$H NMR (300 MHz, DMSO-d$_6$) δ 9.61 (s, 1H, NCH$_N$), 9.52 (s, 1H, NCH$_C$), 8.21 – 8.03 (m, 4H, Ar-CH), 7.98 (s, 1H, CH), 7.90 (s, 1H, CH), 7.64 (d, $^3$J$_{HH}$ = 7.9 Hz, 2H, Ar-CH), 7.51 (d, $^3$J$_{HH}$ = 7.9 Hz, 2H, Ar-CH), 4.29 (s, 3H, N-CH$_3$), 4.23 (m, 2H, CH$_2$), 3.35 (m, 2H, CH$_2$), 2.42 (s, 3H, CH$_3$), 1.96 – 1.66 (m, 2H, CH$_2$), 1.26 (dt, $^3$J$_{HH}$ = 15.2, 7.3 Hz, 2H, CH$_2$), 0.87 (t, $^3$J$_{HH}$ = 7.3 Hz, 3H, CH$_3$). $^{13}$C NMR (101 MHz, DMSO-d$_6$) δ 148.4, 138.6 (Ar-C$_q$), 137.2 (NCH$_N$), 132.5, 132.2, 131.5 (Ar-C$_q$), 129.6, 129.5, 127.7, 127.4, 126.4, 125.7 (Ar-CH), 123.5, 121.9, 121.8 (CH), 50.3, 31.4 (CH$_2$), 21.2 (CH$_3$), 19.1 (CH$_3$). MS (ESI$^+$) for C$_{32}$H$_{24}$N$_5$: m/z calculated 372.2183 [M-PF$_6$]$^+$, observed 372.2176, m/z calculated 186.6128 [M-2PF$_6$]$^{2+}$, observed 186.6130.

[Ag(I)(NHC-CH$_2$-2NHC)$_2$]OTf; 6. Silver(I) oxide (91 mg, 0.4 mmol) was added to a solution of the imidazol-triazolium salt (100 mg, 0.2 mmol) in methanol (10 mL). The suspension was stirred for 16 hours at room temperature with exclusion of light. The pale brown suspension was filtered over Celite and the resulting slightly yellow solution was concentrated under vacuum to yield the product as a white solid (126 mg, 0.09 mmol, 92%). The compound was stored under nitrogen and with exclusion of light. $^1$H NMR (300 MHz, acetone-d$_6$) δ 7.81 (t, $^3$J$_{HH}$ = 1.5 Hz, 2H, CH), 7.71 (t, $^3$J$_{HH}$ = 7.8 Hz, 2H, DiPP-CH), 7.42 (2x d, $^3$J$_{HH}$ = 8.3 Hz, 4H, DiPP-CH), 7.28 (t, $^3$J$_{HH}$ = 1.4 Hz, 2H, CH), 7.11 (s, 2H, Mes-CH$_6$), 6.84 (s, 2H, Mes-CH$_6$), AB system centered at δ$_A$: 6.31 (d, $^3$J$_{HH}$ = 15.8 Hz, 2H, CH$_2$), & δ$_B$: 5.92 (d, $^3$J$_{HH}$ = 15.7 Hz, 2H, CH$_2$), 4.67 (s, 6H, CH$_3$), 2.81 – 2.44 (m, 2H, iPr-CH), 1.90 – 1.70 (m, 2H, iPr-CH), 1.53 (s, 6H, Mes-CH$_3$), 1.31 (s, 6H, Mes-CH$_3$), 1.27 (d, $^3$J$_{HH}$ = 6.9 Hz, 6H, iPr-CH$_3$), 1.10 (d, $^3$J$_{HH}$ = 6.9 Hz, 6H, iPr-CH$_3$), 0.98 (d, $^3$J$_{HH}$ = 6.9 Hz, 6H, iPr-CH$_3$), 0.46 (d, $^3$J$_{HH}$ = 6.8 Hz, 6H, iPr-CH$_3$); $^{13}$C NMR (75 MHz, acetone-d$_6$) δ 182.2 (2d, $^3$J$_{CAg}$ = 172.3 Hz, $^3$J$_{CAg}$ = 191.8 Hz, C$_N$-H), 172.3 (d, $^3$J$_{CAg}$ = 167.2 Hz, $^3$J$_{CAg}$ = 197.1 Hz, C$_{2nNHC}$), 145.7, 145.6, 145.4, 62
Chelating Heteroditopic Di-NHC Late TM Complexes

144.9, 139.1, 136.2, 135.2, 134.6 & 134.4 (C₉), 131.6 (DiPP-CH), 129.5 & 129.1 (Mes-CH), 124.6 (CH), 124.4 & 124.2 (DiPP-CH), 122.2 (CH), 119.0 (OTf), 44.6 (CH₂), 37.1 (N-CH₃), 28.2 (iPr-CH), 23.9 & 23.6 (iPr-CH₂), 23.2 (iPr-CH), 23.1 & 22.9 (iPr-CH₂), 20.2, 17.2 & 16.6 (Mes-CH₂). MS(ESI⁺) for C₅₆H₇₂Ag₁₁O₁₃F₃S: m/z calculated 549.2016 [M-2OTf]⁺, observed 549.1947 & for C₅₇H₇₂Ag₁₁O₁₃F₃S: m/z calculated 1247.3404 [M-OTf]⁺, observed 1247.3441.

General procedure synthesis di(NHC)Pd η³-allyl complex via transmetalation: [Pd(η³-allyl)Cl]₂ (1 equiv.) and the corresponding silver 6 complex (made in MeOH; 1 equiv.) were stirred in DCM for 2h, during which a grey precipitate formed. The mixture was filtered over Celite and concentrated in vacuo. The complex was purified by column chromatography (SiO₂, DCM : MeOH = 9:1) and recrystallized from THF/Et₂O at -20°C.

General procedure synthesis di(NHC)Pd η³-allyl complexes by direct deprotonation: The desired ligand (1 equiv.) and [Pd(η³-allyl)Cl]₂ (0.5 equiv.) were dissolved in THF. Potassium tert-butoxide was added to the solution and the mixture was stirred for 1 h. The resulting solution was filtered over Celite and concentrated in vacuo. In some cases, some excess of [Pd(η³-allyl)Cl]₂ could be separated by column chromatography (SiO₂, DCM : acetone = 3:1).

[Pd(II)(C₅H₃)(NHC-CH₃-tzNHC)]OTf. 7. Via transmetalation: yellow crystals (20 mg, 0.03 mmol, 27%) and via direct deprotonation (66 mg, 0.09 mmol, 89%). ¹H NMR (400 MHz, CD₂Cl₂) δ 7.98 (d, J_HH = 1.9 Hz, 1H, CH), 7.60 (t, J_HH = 7.8 Hz, 1H, DiPP-H), 7.34 (d, J_HH = 7.8 Hz, 2H, DiPP-H), 7.09 (d, J_HH = 1.9 Hz, 1H, CH), 7.00 (s, 2H, Mes-CH₂), AB system centered at δ_H: 5.95 (d, J_HH = 16.7 Hz, 1H, CH₂ & δ_H: 5.84 (d, J_HH = 16.7 Hz, 1H, CH₂), 4.65 – 4.50 (m, 4H, allyl-CH and N-CH₃), 2.63 (dt, J_HH = 7.2, 1.9 Hz, 1H, allyl-CHH), 2.47 (dt, J_HH = 7.2, 1.9 Hz, 1H, allyl-CHH), 2.41 – 2.31 (m, 4H, Mes-CH₂ and iPr-CH), 2.21 (q, J_HH = 6.8 Hz, 1H, iPr-CH), 1.98 (s, 3H, CH₃), 1.77 (d, J_HH = 14.4 Hz, 2H, allyl-CHH), 1.20 – 1.05 (m, 12H, iPr-CH₂); ¹³C NMR (101 MHz, CD₂Cl₂) δ 175.6 (C(CH₃), 163.2 (C_CC), 145.3, 145.0 (C_DiPP), 140.1, 139.4, 137.4, 136.1, 135.4, 135.1 (C₆Ar), 131.1 (DiPP-CH), 128.8 (Mes-CH), 123.8, 123.7 (DiPP-CH), 123.6, 121.9 (CH), 117.7 (allyl-CH), 58.9, 56.6 (allyl-CH₂), 45.0 (CH₂), 37.3 (N-CH₃), 28.4, 28.3 (iPr-CH), 24.7, 24.4, 22.4, 22.4 (iPr-CH₂), 20.68 (Mes-CH₂), 17.4, 17.3 (Mes-CH₃). MS(CSI⁺) for C₅₇H₇₄Ag₁₁N₅Pd: m/z calculated 588.2330 [M-PF₆⁻], observed 588.2316.

[Pd(II)(C₅H₃)(NHC-Ar-tzNHC)]PF₆. 8. This complex was synthesized following the direct deprotonation procedure for complex 7 from ligand 5. Yellow powder (62 mg, 0.09, 95%). ¹H NMR (300 MHz, CD₂Cl₂) δ 7.88 – 7.61 (m, 6H, Ar-CH), 7.57 (d, J_HH = 1.8 Hz, 1H, CH⁺), 7.55 – 7.52 (m, 1H, CH⁺), 7.41 (d, J_HH = 1.9 Hz, 1H, Ar-CH), 7.38 (dd, J_HH = 5.2, 2.2 Hz, 4H, Ar-CH), 7.30 (dd, J_HH = 3.9, 2.0 Hz, 2H, Ar-CH), 5.22 – 5.00 (m, 1H, allyl-H⁺), 4.89 (tt, J_HH = 13.3, 7.4 Hz, 1H, allyl-H⁺), 4.18 (s, 3H, N-CH₃), 4.14 (s, 3H, N-CH₃), 4.13 – 4.00 (m, 4H, N-CH₂), 3.98 (dt, J_HH = 7.0, 1.9 Hz, 1H, allyl-H⁺), 3.80 (dd, J_HH = 7.4, 2.4 Hz, 1H, allyl-H⁺), 3.51 (dd, J_HH = 6.6, 1.5 Hz, 1H, allyl-H⁺), 3.28 – 3.11 (m, 1H, allyl-H⁺), 2.61 (d, J = 12.9 Hz, 1H, allyl-H⁺), 2.46 (s, 6H, CH₃),
2.36 (d, $J_{HH} = 13.6$ Hz, 1H, allyl-H$^p$), 2.30 – 2.21 (m, 1H, allyl-H$^p$), 2.13 (dd, $J_{HH} = 13.5$, 1.0 Hz, 1H, allyl-H$^p$), 1.95 – 1.68 (m, 4H, CH$_2$), 1.48 – 1.32 (m, 4H, CH$_2$), 0.95 (td, $J_{HH} = 7.3$, 5.0 Hz, 6H, CH$_3$); $^{13}$C NMR (101 MHz, CD$_2$Cl$_2$) δ 180.7 ($C_{NHC}$), 180.3 ($C_{NHC}$), 166.3 ($C_{NHC}$), 165.9 ($C_{NHC}$), 146.3, 146.0, 140.8, 140.6, 133.6, 133.5 (Ar-C), 133.4, 131.5, 131.4, 130.0, 129.6, 129.5, 129.4, 129.3, 129.2, 127.9, 127.7, 127.7, 127.6 (Ar-CH), 123.8 (CH), 123.8, 123.7 (Ar-C$_6$H$_4$), 123.6, 122.4, 122.3 (CH), 118.9, 118.8 (allyl-CH), 59.6, 58.4, 58.2, 57.0 (allyl-CH$_3$), 51.7, 51.6 (N-CH$_3$), 37.7, 37.5 (N-CH$_3$), 33.3, 33.0 (CH$_3$), 21.1, 21.0 (CH$_3$), 19.7, 19.6 (CH$_3$), 13.3, 13.2 (CH$_3$). MS(ESI$^+$) for C$_{26}$H$_{30}$N$_2$Pd: m/z calculated 518.1546 [M-PF$_6$]$^+$, observed 518.1514.

**General procedure for the synthesis of NHC-tzNHC Ru(p-cym) complexes:** The desired ligand salt (1 equiv.), sodium chloride (8 equiv.) and silver(I) oxide (2.5 equiv.) were dissolved in MeCN and stirred with exclusion from light for 2 days at room temperature. The resulting suspension was filtered through Celite, and the solvent was removed under high vacuum to give a white solid. The solid was redissolved in DCM and [Ru(p-cym)Cl$_2$] (0.5 equiv.) was added. The mixture was stirred for 2 more days in the dark at room temperature. The mixture was subsequently filtered through Celite to remove silver chloride formed in the reaction. The solvent was evaporated, after which the yellow solid was dissolved in acetone (3 mL), Potassium hexafluorophosphate (8 equiv.) was added, and the resulting mixture was stirred for 10 min under air. Afterwards water was added to precipitate the desired complexes. If not all (di-NHC)Ag(I) had reacted this could be removed by precipitation from DCM by addition of Et$_2$O.

[Ru(II)(p-cym)](NHC-CH$_2$-tzNHC)PF$_6$; 9. 154 mg, 0.18 mmol, 90%. $^1$H NMR (300 MHz, CDCl$_3$) δ 7.61 (m, 2H, 2x DiPP-CH), 7.58 (d, $J = 2.0$ Hz, 1H, CH), 7.55 (d, $J = 2.0$ Hz, 1H, CH), 7.45 – 7.36 (m, 4H, 2x DiPP-CH), 7.09 (bs, 4H, 2x Mes-CH), 7.04 (d, $J_{HH} = 2.0$ Hz, 1H, CH), 7.00 (d, $J_{HH} = 2.0$ Hz, 1H, CH), AB system centered at δ$_a$ 5.78 (d, $J_{HH} = 17.3$ Hz, 1H, CH$_2$) & δ$_b$ 5.64 d, $J_{HH} = 17.3$ Hz, 1H, CH$_2$), AB system centered at δ$_a$ 5.71 (d, $J_{HH} = 16.8$ Hz, 1H, CH$_2$) & δ$_b$ 5.52 (d, $J_{HH} = 16.7$ Hz, 1H, CH$_2$), 5.32 – 5.26 (m, 2H, p-cym-CH), 5.21 (d, $J_{HH} = 6.1$ Hz, 2H, p-cym-CH), 4.34 (s, 3H, N-CH$_3$), 4.33 (s, 3H, N-CH$_3$), 4.28 – 4.19 (m, 2H, p-cym-CH), 3.74 – 3.62 (m, 2H, p-cym-CH), 3.20 – 3.08 (m, 1H, iPr-CH), 2.97 – 2.84 (m, 1H, iPr-CH), 2.52 – 2.45 (m, 1H, iPr-CH), 2.43 (s, 3H, CH$_3$), 2.42 (s, 3H, CH$_3$), 2.28 (s, 3H, CH$_3$), 2.22 (s, 3H, CH$_3$), 2.21 (s, 3H, CH$_3$), 2.17 (s, 3H, CH$_3$), 2.14 – 2.01 (m, 1H, iPr-CH), 1.79 (s, 3H, CH$_3$), 1.64 (s, 3H, CH$_3$), 1.48 (d, $J_{HH} = 6.7$ Hz, 3H, iPr-CH$_3$), 1.47 (d, $J_{HH} = 6.8$ Hz, 1H, 3H, iPr-CH$_3$), 1.33 (d, $J = 6.9$ Hz, 3H, iPr-CH$_3$), 1.29 – 1.20 (m, 12H, iPr-CH$_3$), 0.92 (d, $J = 6.9$ Hz, 6H, iPr-CH$_3$), 0.91 (d, $J = 6.9$ Hz, 6H, iPr-CH$_3$), 0.77 (d, $J = 7.0$ Hz, 3H, iPr-CH$_3$), $^{13}$C NMR (75 MHz, CDCl$_3$) δ 172.0, 171.9 ($C_{NHC}$), 159.6, 159.0 ($C_{NHC}$), 148.6, 146.8, 140.1, 139.9, 138.8, 138.7, 137.5, 137.3, 136.2, 135.9, 135.9, 135.6, 135.6, 135.1, 135.1, 131.9, 131.8, 130.0, 129.9, 128.8, 128.7, 125.5, 125.3 (Ar-CH), 124.4, 124.2, 123.5, 123.5 (CH), 115.0, 96.1, 94.6, 92.1, 91.9, 89.9, 86.0, 84.5, 84.5, 83.0, 82.6, 80.1, (p-cym-C), 45.2, 44.7 (CH$_3$), 37.2 (N-CH$_3$), 37.0 (N-CH$_3$), 31.0, 30.4, 29.6, 29.3, 28.9, 27.4, 27.2, 26.3, 24.9, 23.1, 22.0, 21.9, 21.7, 21.2 (iPr-CH, iPr-CH$_3$, & p-cym-
The catalyst (50 μmol, 4.8 mg) or the desired ligand (0.1 mmol) and [Ru(p-cym)Cl₂]₄ (25 μmol, 1.5 mg) and KOtBu (0.15 mmol, 16.8 mg) were weighed in a 4 mL GC-vial with a septum screw cap charged with a
stirring bar under an N₂ atmosphere. Subsequently, p-xylene (12.3 μL), the substrate (0.5 mmol) and 1,4-dioxane (2 mL) were added. A needle was used to puncture the cap and a set of four vials was placed in a stainless steel autoclave (200 mL) under argon. The autoclave was flushed 2 times with 10 bar of H₂ and then pressurized to 50 bar, after which it was placed in a preheated oil bath (140 °C; built-in thermometer indicated 100 °C as the internal temperature of the autoclave). The mixture was stirred for 6h after which the autoclave was cooled in an ice bath and the pressure was released. The crude reaction mixture was filtered through silica gel and analyzed by GC using p-xylene as internal standard. When methyl trifluoroacetate was employed as substrate the conversion was determined by ¹⁹F NMR spectroscopy using 1,3-bis(trifluoromethane)benzene as internal standard.

**NMR experiments under near-catalytic conditions:** Complex 9 (26 mg, 0.03 mmol) was dissolved in THF-d₈ (0.6 mL) and KOTBu was added (17 mg, 0.15 mmol) under nitrogen atmosphere. The mixture was transferred to a J-Y oung NMR pressure tube and pressurized with 5 bar H₂, after which a ¹H NMR spectra were recorded at various temperatures (<65 °C). The results of these experiments are discussed in paragraph 3.4.

**X-ray crystal structure determinations**

**Compound 6.** [C₇₆H₇₀Ag₂N₁₀][CF₃O₃S]₂ + disordered solvent, Fw = 1397.10,† colourless plate, 0.34 × 0.15 × 0.06 mm³, triclinic, P (no. 2), a = 14.5464(4), b = 22.2689(7), c = 25.2033(8) Å, α = 64.147(1), β = 75.447(1), γ = 80.344(1) °, V = 7095.5(4) Å³, Z = 4, Dₓ = 1.308 g/cm³, μ = 0.68 mm⁻¹.† 101708 Reflections were measured on a Bruker Kappa ApexII diffractometer with sealed tube and Triumph monochromator (λ = 0.71073 Å) at a temperature of 150(2) K up to a resolution of (sin θ/λ)max = 0.65 Å⁻¹. X-ray intensities were integrated with the Eval15 software. Multiscan absorption correction and scaling was performed with SADABS (correction range 0.67-0.75). 32528 Reflections were unique (Rint = 0.048), of which 21484 were observed [I>2σ(I)]. The structure was solved with Patterson superposition methods using SHELXT. Least-squares refinement was performed with SHELXL-2014 against F² of all reflections. The crystal structure contains large voids (1116 Å³ / unit cell) filled with severely disordered THF solvent molecules. Their contribution to the structure factors was secured by back-Fourier transformation with the SQUEEZE algorithm, resulting in 228 electrons / unit cell. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were introduced in calculated positions and refined with a riding model. Two of the isopropyl groups were refined with a disorder model. The disorder of the other isopropyl groups and of the triflate anions was not resolved. 1585 Parameters were refined with 903 restraints (distances, angles and displacement parameters of the isopropyl groups and triflate anions). R1/wR2 [I > 2σ(I)]: 0.0482 / 0.1164. R1/wR2 [all refl.]: 0.0852 / 0.1298. S = 1.075. Residual electron density between 1.02 and 1.86 e/Å³. Geometry calculations and checking for higher symmetry was performed with the PLATON program.†

† Derived values do not contain the contribution of the disordered solvent.
Compound 9. \([\text{C}_{38}\text{H}_{49}\text{ClN}_5\text{Ru}(\text{PF}_6)}\)\(_6\text{C}_{4\text{H}_8}\text{O}\). Fw = 929.41, orange block, 0.26 × 0.20 × 0.11 mm\(^3\), monoclinic, P2\(_1/c\) (no. 14), a = 17.3657(4), b = 14.9369(5), c = 16.9561(4) Å, β = 100.415(1) °, V = 4325.8(2) Å\(^3\), Z = 4, D\(_x\) = 1.427 g/cm\(^3\), µ = 0.53 mm\(^{-1}\). The crystal appeared to be cracked into two fragments. Consequently, two orientation matrices were used for the intensity integration with Eval15.\(^{48}\) 51488 Reflections were measured on a Bruker Kappa ApexII diffractometer with sealed tube and Triumph monochromator (λ = 0.71073 Å) at a temperature of 150(2) K up to a resolution of (sin θ/λ)\(_\text{max}\) = 0.65 Å\(^{-1}\). X-ray intensities were integrated with the Eval15 software.\(^{48}\) Multiscan absorption correction and scaling was performed with TWINABS\(^{49}\) (correction range 0.66-0.75) resulting in an HKLF-5 file.\(^{54}\) 9982 Reflections were unique (R\(_{\text{int}}\) = 0.030), of which 8616 were observed [I > 2σ(I)]. The structure was solved with automated Patterson methods using DIRDIF08.\(^{55}\) Least-squares refinement was performed with SHELXL-2014\(^{51}\) against F\(^2\) of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were introduced in calculated positions and refined with a riding model. The PF\(_6\) anion and the THF solvent molecule were refined with disorder models. 599 Parameters were refined with 484 restraints (distances, angles and displacement parameters of the disordered moieties). R\(_1\)/wR\(_2\) [I > 2σ(I)]: 0.0412 / 0.1065. R\(_1\)/wR\(_2\) [all refl.]: 0.0487 / 0.1100. S = 1.085. Residual electron density between 0.81 and 0.94 e/Å\(^3\). Batch scale factor for the two crystal components BASF = 0.193(2). Geometry calculations and checking for higher symmetry was performed with the PLATON program.\(^{53}\)

3.7 References


Pinter, P.; Biffis, A.; Tubaro, C.; Tenne, M.; Kaliner, M.; Strassner, T., Dalton Trans. 2015, DOI:10.1039/c5dt01067e


Sheldrick, G. M., SADABS and TWINABS: Area-Detector Absorption Correction, Universität Göttingen, Germany, 1999.


Chapter 4
Rh and Ir Complexes bearing Chelating NHC-tzNHC Ligands and their Application in Transfer Hydrogenation

Abstract

This chapter features a series of heteroditopic di-NHC ligands comprised of a 1,2,3-triazole based NHC and an Arduengo-type NHC, that were conveniently synthesized by CuAAC. The ligands have been coordinated to monovalent Rh(cod) and Ir(cod) complexes in a chelating fashion. From the NHC carbon resonances in $^{13}$C NMR and the IR carbonyl stretching frequencies of the corresponding [Rh(NHC-tzNHC)(CO)$_2$]X complexes, the electron-donating properties of the ligands were found to be higher than those of classic di-NHC ligands and dependent on the type of linker. The various NHC-tzNHC complexes have been applied in the transfer hydrogenation of a range of ketones, an imine and an alkene with isopropanol as the hydrogen donor. These systems show moderate activity (Ir > Rh). Although the various N-substituents did not have a large effect on the catalytic activity, the new di-carbene complexes were notably more active in this reaction than the analogues wherein the triazolyl moiety coordinates through a nitrogen donor.

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4.1 Introduction

In the previous chapter, heteroditopic di-NHCs were introduced that bear both a imidazolylidene and 1,2,3-triazolylidene moiety. The synthesis of ligand 1, 2 and 3 (Figure 1) has been described as well as their coordination to ruthenium and palladium centers via silver transmetalation. In this chapter, the coordination of these NHC-tzNHC ligands to monovalent Rh and Ir centers and the application of the resulting complexes in the transfer hydrogenation (TH) of unsaturated compounds are presented. In TH, the application of hydrogen gas is circumvented by employing an alternative hydrogen source, such as isopropanol or formic acid. This reaction was selected because it is aided by electron-rich catalysts. It has, for example, been described that the catalytic activity in this reaction is increased when Rh(III) complexes bearing di-imidazole-4-ylidenes instead of their di-imidazole-2-ylidenes analogues are used as catalyst. We expected that the incorporation of an electron-rich tzNHC moiety on a di-NHC ligand would also lead to enhanced activity in this reaction.

The activity of catalysts is determined by the structure of the ligand and a small structural change can have a pronounced effect on the activity and selectivity in a given reaction. The NHC-tzNHC ligands 2 and 3 described in the previous chapter vary with respect to linker rigidity, connectivity, metallocycle ring size and side-groups (Figure 1). To compare the ligands further we desired to expand the series by also preparing a mixed NHC-tzNHC that is connected via a methylene linker to the nitrogen on the triazole moiety (Figure 1, 4). Furthermore, we implemented various substituents on 2 and 3. This allows structural comparison of the influence of the following variables: 1) nitrogen versus carbene donor 2) substituents (alkyl/aryl), 3) connectivity/chelate ring size. $^{13}$C NMR carbene shifts and infrared (IR) carbonyl stretching frequencies have been evaluated to assess the electron-donating capacities of the various ligands in the corresponding $[M(CO)_2(di-NHC)]^+$ complexes. Furthermore, the activity of all complexes was studied in the TH of acetophenone with isopropanol as the hydrogen donor.

4.2 Synthesis of Heteroditopic di-NHC Ligands

Two hybrid di-NHC precursor ligands 2a and 3a have been described in Chapter
3. Ligands 2b-d and 3b, with various N-substituents, could generally be obtained following the same procedures (Figure 2). An exception was the synthesis of ligand 2d with methoxyphenyl as substituent on the triazolyl-N3, which could not be formed by methylation with methyl triflate. When the stronger alkylating agent trimethyloxonium tetrafluoroborate (Meerwein’s reagent) was applied according to a synthetic procedure described by Kilpin et al. the desired compound was obtained in 66% yield.\(^3\)

![Image of ligands 1, 2, and 3](image)

**Figure 2:** The ligands used in this chapter, 1-3.

*Synthesis imidazolium-triazolium salts connected via a methylene linker on the tz-nitrogen*

In order to compare the electronic properties of the ligands the mixed NHC-tzNHC ligand 4, connected via a methylene linker to the nitrogen on the triazole moiety (Scheme 1) was prepared as well. First, mesityl-imidazole was reacted with excess of iodochloromethane, leading to N-chloromethyl/N-iodomethyl mixtures of the product, as was observed previously.\(^4\) We decided to use this mixture in the subsequent tandem azidination-CuAAC\(^{5,6}\) reaction followed by methylation,\(^3\) with anion exchange as the last step.

![Image of Scheme 1](image)

**Scheme 1:** Synthesis of ligand 4. i) ClCH\(_2\)I  ii) p-methoxy acetylene, NaN\(_2\), Na\(_2\)CO\(_3\), CuSO\(_4\)\(_5\)\(\cdot\)H\(_2\)O, sodium scorbate, DMF/H\(_2\)O (4:1) iii) (Me\(_3\)O)BF\(_4\), followed by anion exchange with KPF\(_6\).

The resulting ligand 4, which is an isomer of ligand 2d (without the anion), was obtained in this manner. The novel ligand was characterized using multinuclear NMR spectroscopy and high resolution mass spectrometry (HR-MS). The most remarkable chemical shift difference between the \(^1\)H NMR spectra of ligands 4 and 2d relates to
the CH₂ hydrogen signal, which is observed at 7.22 ppm (Δ δ = 1.21 ppm).

**4.3 Heteroditopic NHC-tzNHC Rh(I) and Ir(I) complexes**

Using the new NHC-tzNHC ligands, one Ir(I)(cod) and several Rh(I)(cod) complexes, 5a and 6a-d respectively, were obtained in excellent yields (89-99%) by mixing the ligand and *in situ* generated [M(cod)(µ-OMe)]₂ with an additional equivalent of base at 50 °C. The resulting complexes were formulated as monometallic species with the mixed carbene ligands coordinating as a chelate framework, based on ¹H NMR and HR-MS analysis. Without applying additional base, the same chelating NHC-tzNHC complexes were found (together with residual ligand in a 1:1 ratio), rather than metal complexes with only one of the carbene units coordinating. This is in contrast to findings of Cowie et al., who reported monocoordination of the imidazolylidene moiety using the same ligand, an excess of KI, and [Rh(cod)(µ-OMe)]₂ for the synthesis of dinuclear complexes. Presumably, the addition of excess iodide leads to coordinatively saturated mono-NHC rhodium complexes in their case. However, when ligand 2c with BF₄⁻ as counterion was employed, we did observe monocoordination of the imidazolylidene moiety. The desired chelate species could be isolated after addition of one additional equivalent of base in this case.

The formation of the di-carbene complexes was confirmed by the disappearance of the imidazolium as well as the triazolium protons from the ¹H NMR spectra. The bright red (Ir) and orange (Rh) di-carbene compounds exhibited broad signals for the linker and cod hydrogens in ¹H NMR, implying there is some flexibility in the structure. In the respective ¹³C NMR spectra two signals for the cod-CH as well as two indicative carbene signals around 182-179 (NHC) and 170-166 ppm (tzNHC) were observed for all Rh complexes. Concerning the chemical shifts of the carbenes no trend could be detected considering the effect of the various N-substituents (*vide infra*). The relatively large Rh-C couplings (J_RhNHC = 53 Hz, J_RhNHC = 49 Hz for 6a) suggest strong rhodium-carbene bonds. The iridium-carbene carbon resonances (174 and 163 ppm) in the ¹³C NMR spectrum also fall in the expected range. The ¹⁹F NMR spectra showed resonances that are indicative for non-coordinating

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**Scheme 2:** Synthesis of [M(I)(NHC-tzNHC)(cod)] complexes 5a and 6a-e. i) NaH, [M(cod) µ- Cl]₂, MeOH, 30 min. ii) addition of the respective ligand, 2-3 hours at 50 °C.

<table>
<thead>
<tr>
<th>M</th>
<th>R</th>
<th>R’</th>
<th>X</th>
<th>Yield</th>
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<tbody>
<tr>
<td>5a</td>
<td>Ir</td>
<td>Mes</td>
<td>Dipp</td>
<td>OTf</td>
</tr>
<tr>
<td>6a</td>
<td>Rh</td>
<td>Mes</td>
<td>Dipp</td>
<td>OTf</td>
</tr>
<tr>
<td>6b</td>
<td>Rh</td>
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<tr>
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<td>Rh</td>
<td>Mes</td>
<td>4-C₆H₄- OMe</td>
<td>BF₄⁻</td>
</tr>
</tbody>
</table>
The bidentate coordination mode of the ligand was supported by the HR-MS (FAB⁺) corresponding to the entire cationic metal complex: rhodium, ligand and cod co-ligand in 1:1:1 ratio.

Unfortunately, the obtained complexes were not very stable under ambient conditions. Especially the iridium complex, 5a, showed decomposition, marked by a color change from bright dark-red to brown. The compound could be stored under argon at -20 °C up to one week, while the rhodium complexes could be stored under N₂ for at least a month. Therefore, the iridium complexes were prepared immediately prior to their application in the desired catalytic reaction.

In order to evaluate these systems more closely, we were also interested in the Ir and Rh NHC analogues wherein the triazolyl moiety coordinates to the metal via the nitrogen atom (NHC-tz), 7 and 8 (Scheme 3). During the course of this research, the group of Messerle reported the first rhodium complexes bearing this bidentate NHC-tz ligand and their application in the intramolecular hydroamination. The complexes could be obtained in the same manner as the NHC-tzNHC complexes, 5 and 6, using the in situ prepared precursors containing methoxide as internal base, or by addition of one equivalent of KOTBu in presence of the metal precursor [M(cod)μ-Cl]₂, followed by halide abstraction with silver triflate (Scheme 3).

The ¹H NMR spectra confirmed formation of the NHC fragment by disappearance of the imidazolium hydrogen, whereas the triazolyl-CH showed resonances (8.33 and 8.42 ppm) that are comparable to the Pd(II) analogue. These values for the triazolyl-CH are significantly shifted downfield compared to the Rh(I) complexes bearing a benzylic functionality that were reported by Messerle et al. (Δδ ≥ 1.58 ppm), which is probably caused by conjugation of the triazolyl moiety with the adjacent aryl group. The hydrogens of the methylene linker appear as a singlet in the ¹H NMR spectrum, indicating the hemilabile character of the nitrogen donor, as was observed by the group of Messerle. The chemical shift difference Δδ for the cod-CH signals of 7 and 8 was significantly larger in both the ¹H and ¹³C NMR spectra than for the NHC-tzNHC complexes, due to the lower donating capacity of the secondary nitrogen donor compared to a mesoionic carbene. The characteristic
13C-imidazolylidene carbon shifts were observed at 173.3 and 176.7 ppm (J_{RhNHC} = 52 Hz) for 7 and 8, respectively. Again, 19F NMR spectroscopy indicated the non-coordinating nature of the triflate anion and MS supported the mononuclear character of the complexes.

**Synthesis of tz-N-connected NHC-tzNHC Ir(I) and Rh(I)(cod) complexes**

The Rh(I) complexes 9a-b and 10 were prepared in a similar manner as complexes 6a-d (Scheme 4) by *in situ* synthesis of the methoxy bridged Ir(cod) or Rh(cod) dimer precursor followed by addition of the ligand. Upon addition of the phenyl-bridged ligands 3 the characteristic color change from a yellow suspension to a red (Ir) or bright orange (Rh) solution was observed immediately. This corresponds to the higher CH acidity of the triazolium ring in ligands 3 caused by the inductively σ-electron withdrawing aryl substituents.14

The resulting complexes 9a and b were obtained in excellent yields. The data obtained from multinuclear NMR spectroscopy and HR-MS analysis suggested the ligand to act as chelating species in both cases. The NMR spectra were largely in agreement with those of 5a and 6a-d. However, the tzNHC carbon peak (173.2 ppm; J_{RhNHC} = 47.4 Hz, for 9a) is found significantly downfield with respect to 6a-d (170-166 ppm) in the 13C NMR spectrum, which is in line with previous observations that the donor strength of tzNHC increases upon variation of N-substituents next to the carbene center in the order aryl< benzyl< alkyl.15-17 Besides, the phenyl linker gave rise to separate signals for all cod-CH atoms in the NMR spectra, which is attributed to the loss of symmetry caused by the phenyl ring that is rotated out of the coordination plane.

When ligand 4 was exposed to the same reaction conditions as 3, we did observe the disappearance of the peaks belonging to the azolium hydrogens in the 1H NMR spectrum, yet the spectrum displayed broad peaks. Unfortunately, both the 13C NMR spectrum and HR-MS did not correspond to the formation of complex 10 and the precise identity of this complex is currently unknown.

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**Scheme 4:** Synthesis of [M(I)(NHC-(Y)-tzNHC)(cod)] complexes. i) NaH, [M(cod)(μ-Cl)]_2, MeOH, 30 min. ii) addition of the respective ligand, 1-3 hours at rt or 50 °C.

<table>
<thead>
<tr>
<th>M</th>
<th>Y</th>
<th>R</th>
<th>Ar'</th>
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<td>PF_6</td>
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</tbody>
</table>

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4.3 Electronic Properties of [(NHC-tzNHC)M] Complexes

Electronic properties of [(NHC-tzNHC)Rh] complexes

The carbene carbon shifts of the rhodium complexes described in the previous paragraph are depicted in Table 1. As mentioned above, no clear trend considering the effect of the N-substituents on the chemical shifts of the carbones can be deduced. The difference between the shifts and corresponding electron-donating capacities of the NHCs with varying linkers is more apparent.

<table>
<thead>
<tr>
<th></th>
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<th>6b</th>
<th>6c</th>
<th>6d</th>
<th>8</th>
<th>9a</th>
<th>9b</th>
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<tbody>
<tr>
<td>δ^{13}C{NHC} in ppm</td>
<td>178.7</td>
<td>182.1</td>
<td>181.2</td>
<td>181.1</td>
<td>176.7</td>
<td>185.6</td>
<td>185.7</td>
</tr>
<tr>
<td>('J_{RhC} in Hz)</td>
<td>(53.5)</td>
<td>(52.2)</td>
<td>(53.1)</td>
<td>(43.3)</td>
<td>(51.8)</td>
<td>(52.6)</td>
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<tr>
<td>δ^{13}C{NHC} in ppm</td>
<td>166.1</td>
<td>166.7</td>
<td>170.4</td>
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<tr>
<td>('J_{RhC} in Hz)</td>
<td>(48.5)</td>
<td>(48.5)</td>
<td>(47.9)</td>
<td>(47.3)</td>
<td>(47.4)</td>
<td>(47.5)</td>
<td>(47.5)</td>
</tr>
</tbody>
</table>

Carbonyl stretching frequencies in IR provide an adequate measure of the donating strength of ligands in planar Ir/Rh(CO)$_2$ complexes. To this end, rhodium complexes 6a was first subjected to 5 bar of syngas (Scheme 5). Upon contact with the gas the solution immediately changed color from orange to yellow.

Scheme 5: General synthesis of [Rh(NHC-tzNHC)(CO)$_2$]X complexes.

The IR, $^1$H and $^{13}$C NMR spectra of the resulting species showed that the cyclooctadiene ligand was readily displaced by CO rendering complex 11a (Scheme 5); no hydrogenated ligand (cyclooctane or cyclooctene) was observed. The carbene resonances for the dicarbonyl complex appear at 173.7 ($'J_{RhNHC} = 48$ Hz) and 163.6 ppm ($'J_{RhNHC} = 42$ Hz) in $^{13}$C NMR while the carbonyl ligands give rise to a broad singlet at 185 ppm. The decrease in Rh-C coupling constants suggests weakening of the Rh-carbene bonds caused by the strongly π-accepting trans carbonyl co-ligand. The low average stretching frequency of the carbonyls ($v$(CO)$_{av} = 2034$ cm$^{-1}$) indicates that the NHC-tzNHC ligand is indeed a very strong electron-donor, compared to the “classic” di-NHCs,$^{18}$ “i-bitz”$^{19}$ and the 1,10-phenanthroline based “vegi” ligand.$^{20}$

Rh carbonyl complexes 11d and 12b were prepared in the same manner (Scheme 5), either in a J. Young NMR pressure tube or autoclave set-up. Their average carbonyl stretching frequencies are depicted in order of increasing σ-donor strength in Figure...
3. Unlike what was reported previously, substituent effects are notable in this particular series.\textsuperscript{15,17} The electron-donating methoxyphenyl N-substituent next to the triazolylidene carbon donor clearly but counter-intuitively led to a higher average CO stretching frequency corresponding to decreased electron-density on the metal. This may be attributed to compensating steric effects that are well-known to affect the Rh-CO bond.\textsuperscript{15,16,21} Nevertheless, the trend considering the linkers between the two carbene moieties corresponds to that found for the \textsuperscript{13}C carbene carbon shifts: the complex with the electron-withdrawing aryl moiety has lower electron-donating capacity according to both \textsuperscript{13}C and IR spectroscopy.

\begin{center}
\begin{tikzpicture}
\node [align=center] at (0,0) {\textbf{Figure 3:} \textup{[Rh(NHC-tzNHC)(CO)\textsubscript{2}]X complexes in order of increasing $\sigma$-donor strength according to their average CO stretching frequency in IR.}};
\end{tikzpicture}
\end{center}

\textit{Reactivity of iridium complex 5a with CO and H\textsubscript{2}}

When the iridium complex 5a was exposed to syngas under the same reaction conditions as 6a (Scheme 6, III), three separate signals for all ligand hydrogens (and the free cod ligand) were observed. This indicates the formation of a mixture of species: [Ir(NHC-tzNHC)(CO)\textsubscript{2}]OTf complex 12 and two octahedral [Ir(CO)\textsubscript{2}(H)\textsubscript{2}(NHC-tzNHC)]OTf complexes, 13 and 13', in a 3.2 : 2.8 : 1 ratio.

The difference in reactivity of the rhodium and iridium complexes with syngas can be explained by the higher basicity of the latter and its greater tendency to form coordinatively saturated octahedral d\textsuperscript{6} complexes. The \textsuperscript{1}H NMR spectrum showed two pairs of doublets in the hydride region (-10.33 and -12.36 ppm with $\delta_{\text{HH}} = 3.3$ Hz and -10.40 and -11.64 ppm with $\delta_{\text{HH}} = 2.8$ Hz), while the methylene linker gave rise to an AB system, which indicates that the faces above and below the iridium-ligand plane are not equivalent. Thus, one CO and one hydride (Scheme 6; \textsuperscript{1}H NMR $\delta$ -10.33 and -10.40 ppm) should occupy the axial positions, while the chelate di-NHC-Ir in the plane ring is not flat but presumably boat-shaped.\textsuperscript{9}

Complex 13 and 13' exhibited slow conversion to carbonyl complex 12 over time, while the cyclooctadiene was hydrogenated to give cyclooctane (coa; Scheme 6, IV). The depletion of 13 and 13' was monitored in time by \textsuperscript{1}H NMR at room temperature. The reaction followed first-order kinetics ($t_{\text{1/2}} \approx 7.5$ hour)
with respect to the disappearance of 13 and 13′. Reaction IV is reversible; when complex 12 was stirred under an atmosphere of hydrogen gas (1 bar), it was completely converted to a mixture of 13 and 13′. Due to this reactivity, we hypothesize that complex 12 may provide interesting catalytic properties.

Complex 12 could be obtained selectively by reacting 5a with carbon monoxide gas (Scheme 6, II) in quantitative yield or directly by reacting the ligand with [Ir(CO)\(_2\)(acac)] and 2 equivalents of potassium tert-butoxide. The IR spectrum showed two strong bands at 2056 and 1992 cm\(^{-1}\) (\(\nu(CO)_{\text{av}} = 2024 \text{ cm}^{-1}\)) corresponding to the two carbonyl stretching modes. In the \(^{13}\text{C} \text{ NMR spectrum}\) the NHC-Ir resonances were found at 171.3 and 162.0 ppm, while two separate signals for the carbonyl ligand were observed at 179.6 and 178.9 ppm, which are all well within the range of expected values.

* Dihydrogen is oxidatively added in a cis fashion as expected. The remaining equatorial carbonyl and hydride (\(^{1}H \text{ NMR: } \delta \approx -11.6\) and \(-12.3\) ppm) ligands can in theory be selectively bonded trans to one of the carbene donors, as depicted in Scheme 6. Alternatively, two species can be present: one in which the hydride is bound trans to the NHC and one in which it is bonded trans to the tzNHC. In an attempt to elucidate the precise structure, we employed 2D \(^{1}H-^{13}\text{C} \text{ heteronuclear multiple-bond correlation (HMBC) NMR experiments under syngas pressure}. The hydride of the minor complex 13′ showed coupling (2 Hz < \(J_{\text{CH}}\) < 12 Hz) with the imidazolylidene \(C_{\text{q}}\) only, indicating that this hydride is coordinated trans to the NHC moiety. Unfortunately, the results for the major complex 13 were inconclusive, as cross-peaks were observed for both the imidazolylidene and triazolylidene carbene when implementing the measured ranges of coupling constants. Further characterization was hampered by the fact that, upon release of hydrogen pressure, the mixture converts to complex 12.
4.4 Catalytic Transfer Hydrogenation

In order to exemplify the catalytic properties of the square planar Rh(I) and Ir(I) complexes, their application in the transfer hydrogenation of unsaturated compounds was studied using isopropanol (iPrOH) as hydrogen donor and solvent. Acetophenone was chosen as benchmark substrate, the conversion was followed by GC with p-xylene as internal standard and KOTBu was used to activate the hydrogen donor. All tested complexes were active in this reaction (Table 2) and the transformation proceeded to completion within 24 hours at 80 °C. For entries 1 and 2 (Table 2), dynamic light scattering (DLS) measurements of the catalytic mixtures before and after catalysis were performed to check for the presence of nanoparticles. As is described in reviews by Finke\textsuperscript{23} DLS is a powerful method to detect small particles (>1 nm) at concentrations far below those of our catalytic experiments. None of these measurements led to DLS signal, and therefore we trust that the catalysis is performed by molecular catalysts.

Table 2: Catalytic results 5 and 6a in the transfer hydrogenation of acetophenone.

<table>
<thead>
<tr>
<th>entry</th>
<th>Cat.</th>
<th>T (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{a}</td>
<td>5a</td>
<td>80</td>
<td>3</td>
<td>98</td>
</tr>
<tr>
<td>2\textsuperscript{a}</td>
<td>6a</td>
<td>80</td>
<td>3</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>98</td>
</tr>
<tr>
<td>3\textsuperscript{a}</td>
<td>6b</td>
<td>80</td>
<td>3</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>98</td>
</tr>
<tr>
<td>4\textsuperscript{b}</td>
<td>6c</td>
<td>80</td>
<td>3</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>98</td>
</tr>
<tr>
<td>5\textsuperscript{a}</td>
<td>6d</td>
<td>80</td>
<td>3</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>99</td>
</tr>
<tr>
<td>6\textsuperscript{a}</td>
<td>7</td>
<td>80</td>
<td>3</td>
<td>98</td>
</tr>
<tr>
<td>7\textsuperscript{a}</td>
<td>8</td>
<td>80</td>
<td>3</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>98</td>
</tr>
<tr>
<td>8\textsuperscript{b}</td>
<td>9b</td>
<td>80</td>
<td>3</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>100</td>
</tr>
<tr>
<td>9\textsuperscript{b}</td>
<td>10</td>
<td>80</td>
<td>3</td>
<td>44</td>
</tr>
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<td>3</td>
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<td>5a</td>
<td>25</td>
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<td>59</td>
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<tr>
<td>12\textsuperscript{a}</td>
<td>6a</td>
<td>25</td>
<td>22</td>
<td>38</td>
</tr>
</tbody>
</table>

Reaction conditions: 0.1 M acetophenone in isopropanol, 10 mol% KOTBu at indicated temperature. a) 0.5 mol% cat., b) 1 mol% catalyst.
At room temperature complexes 5a and 6a still converted the substrate (entries 12 and 13) albeit significantly slower. As expected for cationic (di)NHC complexes, the Ir complexes converted acetophenone faster to the corresponding alcohol than their Rh counterparts. Although there are several rhodium and iridium di-carbene species known that facilitate this transformation extremely efficiently reaching turnover frequencies (TOFs) of up to 50,000 h\(^{-1}\), \(^{25-27}\) the obtained results can compete with known, less active examples of other di-carbene complexes under comparable conditions. \(^{2,20,28-30}\)

Moreover, it is noteworthy that the di-carbene containing species 5a and 6a are more active than the NHC with secondary N donor, 7 and 8. The NHC-tzNHC outperform the NHC-tz complexes for both the rhodium (TOF = 190 h\(^{-1}\), determined around 15% conversion) and iridium catalysts (TOF = 641 h\(^{-1}\) against 338 h\(^{-1}\)). This might be explained by the higher electron-density on the metal for 5a and 6a compared to 7 and 8, which aids the formation of the metal-hydride in case the monohydride mechanism would be operative, as has been shown for monovalent group 9 TM catalysts. \(^{31,32}\)

The effects of the various N-substituents on the ligands of the rhodium complexes 6a-e were less pronounced for this reaction as is apparent from the reaction profiles. These are displayed in Figures 4 and 5.

**Figure 4:** Conversion acetophenone over time, catalyzed by [Rh(cod)(NHC\(^R\)-tzNHC\(^R\)) complexes with various N-substituents: 6a (purple diamonds, R = Mes, R’ = DiPP) vs 6b (yellow squares, R = Mes, R’ = Bn) vs 6c (red triangles, R = nBu, R’ = DiPP) vs 6d (grey diamonds, R = Mes, R’ = 4-C\(_6\)H\(_4\)-OMe).

**Figure 5:** Conversion acetophenone over time, catalyzed by various Rh catalysts bearing a methoxy phenyl substituent on the triazolylidene moiety: 6d (grey diamonds, methylene linker) vs 9b (green triangles, phenyl linker).
Catalyst 6b, bearing a benzyl substituent on the N3 position of the triazolylidene moiety, displayed somewhat slower conversion of acetophenone, while 6c seemed slightly more active. However, the differences are not large and no clear trend could be deduced. The metallacycle ring size did not seem to have a large influence either (Figure 5; 6d vs 9b).

A small library of substrates was tested for the transfer hydrogenation with complexes 5a and 6a (Table 3). Other aromatic ketones and cyclohexanone were converted readily by both complexes (entry 1-6), albeit faster by 5a than by 6a.

**Table 3**: Catalytic results 5 and 6a in the transfer hydrogenation of various substrates.

<table>
<thead>
<tr>
<th>entry</th>
<th>Cat.</th>
<th>Substrate</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>Product</th>
<th>Yield (%)</th>
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<tr>
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<td>5a</td>
<td>Acetophenone</td>
<td>1/2</td>
<td>92</td>
<td>OH Ph</td>
<td>92</td>
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<tr>
<td>2</td>
<td>6a</td>
<td>Acetophenone</td>
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<td>98</td>
<td></td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>5a</td>
<td>Cyclohexanone</td>
<td>3</td>
<td>90</td>
<td>OH Ph</td>
<td>90</td>
</tr>
<tr>
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<td>6a</td>
<td>Cyclohexanone</td>
<td>23</td>
<td>97</td>
<td></td>
<td>97</td>
</tr>
<tr>
<td>5</td>
<td>5a</td>
<td>2</td>
<td>1/6</td>
<td>100</td>
<td>OH Ph</td>
<td>&gt;99</td>
</tr>
<tr>
<td>6</td>
<td>6a</td>
<td>2</td>
<td>3</td>
<td>96</td>
<td></td>
<td>96</td>
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<td>7</td>
<td>5a</td>
<td>Acetone</td>
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<td>66</td>
<td>OH Ph</td>
<td>90</td>
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<tr>
<td>8</td>
<td>6a</td>
<td>Acetone</td>
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<td>90</td>
<td></td>
<td>34</td>
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<tr>
<td>9</td>
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<td>Methylglyoxal</td>
<td>23</td>
<td>74</td>
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<td>52</td>
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<td>2-Ketoglutarate</td>
<td>23</td>
<td>0</td>
<td>n.d.</td>
<td>23</td>
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<td>3</td>
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<td>PhN=Ph</td>
<td>23</td>
<td>82</td>
<td>PhN=Ph</td>
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</table>

Reaction conditions: 0.1 M acetophenone in isopropanol, 1 mol% cat., 10 mol% KOTBu at 80 °C. a) 1equivalent of NEt₃ was added to the reaction mixture, b) not determined, the substrate could not be detected on GC.
The limits of the more active Ir catalyst 5a were investigated further (Table 3); it also proved active for aliphatic ketones, even converting the very hindered pinacolone slowly (entry 8). To test the tolerance of the catalyst to other functional groups, methyl levulinate and levulinic acid were tested (entries 9 and 10). The former substrate, having both a ketone and ester functionality, was converted slowly to produce mainly γ-valerolactone. The acid functionality, on the other hand, was incompatible with the system, probably inhibiting the transfer hydrogenation by neutralizing the required base. When one equivalent of triethyl amine was added this substrate was converted slowly as well.

The substrate scope was subsequently expanded beyond ketones. In cinnamaldehyde mainly the aldehyde functionality was converted to yield cinnamylalcohol (Table 3, entry 11). Also some 3-phenylpropanal, due to the hydrogenation on the alkene moiety, and the completely hydrogenated product 3-phenylpropan-1-ol were observed. The fact that complex 5a can also be applied to reduce C=C double bonds using iPrOH as hydrogen donor is further confirmed by the hydrogenation of cyclooctadiene, which was eventually fully hydrogenated to cyclooctane (entry 12). Lastly, N-benzylideneaniline was readily reduced to benzylamine (82% conversion in 3 hours; entry 13) under the same reaction conditions.

4.5 Conclusion

A series of cationic chelate Rh and Ir complexes bearing mixed NHC-tzNHC ligands was developed. From the carbonyl stretching frequencies of the [(NHC-tzNHC)M(CO)₂]OTf complexes, the electron-donating properties of the ligand were determined to be stronger than for other examples of di-carbene ligands. In the course of making the carbonyl complexes, the difference in reactivity with syngas between iridium and rhodium became apparent, leading to interesting octahedral [Ir(CO)₂(H)₂(NHC-tzNHC)]OTf complexes.

All complexes showed moderate activity in the transfer hydrogenation of acetophenone with isopropanol as hydrogen donor at elevated temperatures. The different substituents on the tzNHC moiety did not have a large influence on the catalyst activity. As expected, the Ir(I) complexes were more active than their Rh(I) analogues in this transformation and the substrate scope for the iridium system could be expanded to more challenging ketones as well as cinnamaldehyde, N-benzylideneaniline and cyclooctadiene. More interestingly, the di-carbene NHC-tzNHC complexes converted the substrate significantly faster than the ones with one NHC and a secondary nitrogen donor. This has strengthened our trust in the potential of this electron-rich and accessible ligand in transition metal catalysis.

4.6 Experimental Section

Complex syntheses and catalytic experiments were performed using standard Schlenk
techniques under an atmosphere of dry nitrogen. Solvents were dried and distilled according to standard methods. Isopropanol was dried over CaCl₂, distilled and degassed prior to use. All reagents were purchased from commercial suppliers and used without further purification. The NMR spectra were recorded on Varian Mercury 300 MHz, Bruker DRX Advance 300 and Bruker AMX 400 MHz spectrometers. ¹⁹F NMR (unreferenced) was used to confirm the (non-coordinating) anion of the compounds: OTf (−78 ppm), BF₄ (−153 ppm) and PF₆ (−70 ppm, d, ¹JₚF = 710 Hz). ¹H-¹H COSY and/or ¹H-¹³C HSQC NMR spectroscopy was used to assign the peaks of several compounds. IR spectra were recorded on a Bruker Alpha-PFT-IR spectrometer. High resolution mass spectrometry was performed on a JEOL JMS SX/SX102A four-sector mass spectrometer (FAB⁺) or Bruker MicroTOF-Q (ESI⁻) and GC analyses were performed with an Interscience Trace GC Ultra instrument using an Rxi fused silica capillary column. The azides, prop-2-ynyl imidazolium bromide salts, 1,2,3-triazolymethyleneimidazolium bromide salts and [{MesImH}CH₂X]X (X = Cl/I) were prepared according to literature procedures. [4-(p-Methoxy)-1-phenyl-2-[(n-butylimidazolium)l,2,3-triazole] bishexafluoro-phosphate was prepared as described in Chapter 3.

General procedure for the methylation of 1,2,3-triazolymethylene imidazolium bromide salts with MeOTf: To a cooled (-78 °C) solution of triazolymethylene imidazolium bromide (1 equiv.) in dry dichloromethane (c = 0.1M), methyl triflate (2 equiv.) was added dropwise under a nitrogen atmosphere. The mixture was allowed to warm to room temperature and stirred at room temperature for 16 hours. After precipitation with diethyl ether and filtration the product was obtained.

[3-(benzyl)-l-methyl-5-((3-mesitylimidazolium)methyl)] 1,2,3-triazolium trifluoromethanesulfonate/bromide; 2b. White solid (358 mg, 0.60 mmol, 70%). ¹H NMR (400 MHz, DMSO-d₆) δ 9.49 (s, 1H, NCHN), 9.09 (s, 1H, tz-H), 8.13 (s, 1H, CH), 8.04 (s, 1H, CH), 7.50-7.46 (m, 5H, Ar-H), 7.17 (s, 2H, Mes-H), 5.94 (s, 2H, CH₂), 5.90 (s, 2H, CH₂), 4.35 (s, 3H, N-CH₃), 2.34 (s, 3H, p-Mes-CH₃), 2.04 (s, 6H, o-Mes-CH₃), 1³C NMR (101 MHz, DMSO-d₆) δ 140.5 (p-Mes-C), 138.5 (tq-C), 137.2 (NCHN), (p-Mes-C), 134.3 (o-Mes-C), 132.7 (Ar-C), 131.3 (i-Mes-C), 130.9 (tq-CH), 129.4 (m-Mes-CH), 129.3 (tq-CH), 129.1 (Ar-C), 123.0 (Ar-C), 124.4 (CH), 123.5 (CH), 56.3 (CH₂), 40.9 (CH₂), 38.5 (N-CH₃), 20.6 (o-Mes-CH₃), 17.0 (p-Mes-CH₃), MS(FAB⁺) for C₂₄H₂₇F₃N₅O₅S: m/z calculated 522.1787 [M-Br]⁺, observed 522.1791.

[3-(2,6-diisopropylphenyl)-l-methyl-5-((3-n-butylimidazolium)methyl)] 1,2,3-triazolium trifluoromethanesulfonate/bromide; 2c. Brown oil (533.4 mg, 0.87 mmol, 65%). ¹H NMR (400 MHz, CDCl₃) δ 10.74 (s, 1H, NCHN), 8.50 (s, 1H, tz-H), 7.80 (t, 1H, Jc₃ḥ₃ = 7.8 Hz, Ar-H), 7.49 (d, 2H, Jc₃ḥ₃ = 7.5 Hz, Ar-H), 7.26 (s, 1H, CH), 7.14 (s, 1H, CH), 6.15 (s, 2H, CH₂), 4.55 (s, 3H, N-CH₃), 4.13 (t, 2H, Jc₃ḥ₃ = 7.5 Hz, CH₂), 2.17 (t, 2H, Jc₃ḥ₃ = 7.1 Hz, CH₂), 1.92 (t, 2H, Jc₃ḥ₃ = 7.5 Hz, CH₂), 1.29 (m, 2H, Jc₃ḥ₃ = 7.0 Hz, iPr-CH), 1.10 (d, 12H, Jc₃ḥ₃ = 7.5 Hz, iPr-CH₂), 0.99 (t, 3H, Jc₃ḥ₃ = 6.8 Hz, CH₂), 1³C NMR (101 MHz, CDCl₃) δ 145.7 (Ar-C), 139.5 (tq-C), 137.3 (CH), 132.9 (Ar-CH), 132.4 (tq-CH), 130.6 (Ar-C), 124.5 (Ar-CH), 124.2 (CH), 123.3 (CH), 50.2
(CH₃), 42.2 (N-CH₃), 39.27 (CH₃), 31.6 (CH₃), 28.4 (iPr-CH), 23.5 (iPr-CH₂), 19.3 (CH₃), 13.2 (CH₂). MS (ESI⁺) for C₅₂H₃₂N₅: m/z calculated 380.2809 [M-OTF-Br]⁺, observed 380.2800.

General procedure for the methylation of 1,2,3-triazolylmethane imidazolium bromide salts with Me₃OTf: Triazolylmethane imidazolium bromide (1 equiv.) and Meerwein’s salt (1.5 equiv.) were dissolved in dry dichloromethane and the reaction mixture was stirred for 16 hours, during which a white solid precipitated. This was collected on a glass frit and washed with dichloromethane and ether to obtain the product.

[3-(4-methoxyphenyl)-1-methyl-5-(3-mesitylimidazolium)methyl] 1,2,3-triazolium] tetrafluoroborate/bromide; 2d. Hygroscopic white powder (234 mg, 0.42 mmol, 66%). ¹H NMR (300 MHz, DMSO-d₆) δ 9.58 (s, 1H, NCHN), 9.50 (s, 1H, tz-H), 8.16 (s, 1H, CH), 8.07 (s, 1H, CH), 7.93 (d, Jₘₙ = 8.6 Hz, 2H, Ar-CH), 7.31 (d, Jₘₙ = 8.5 Hz, 2H, Ar-H), 7.17 (s, 2H, Mes-H), 6.01 (s, 2H, CH), 4.45 (s, 3H, N-CH₃), 3.89 (s, 3H, O-CH₃), 2.33 (s, 3H, Mes-CH₃), 2.06 (s, 6H, Mes-CH₃); ¹³C NMR (101 MHz, DMSO-d₆) δ 161.7, 154.9, 140.5, 138.2, 137.3, 134.3 (Ar-C), 130.9 (Ar-CH), 129.3, 129.2 (tz-CH), 127.6 (Ar-Cq), 124.4, 123.7 (CH), 123.1, 115.6 (Ar-CH), 56.0 (O-CH₃), 40.9 (CH₃), 38.7 (N-CH₃), 20.6 (CH₃), 17.1 (CH₃). MS (FAB⁺) for C₆₂H₅₂N₅OBF₄: m/z calculated 476.2249 [M-Br]⁺, observed 476.2243.

[3-(4-methoxyphenyl)-1-phenyl-2-(3-n-butylimidazolium) 1,2,3-triazolium] bis(hexafluorophosphate; 3b. [4-(p-methoxy)-1-phenyl-2-(n-butylimidazolium) 1,2,3-triazole] hexafluorophosphate (1 equiv.) and Meerwein’s salt (2 equiv.) were dissolved in dry dichloromethane (8 mL) and the reaction mixture was stirred for 16 hours. The reaction was quenched by the addition of one drop of methanol after which the solvent was removed. The resulting solid was redissolved in acetone:water = 1:1 (4 mL), KPF₆ was added and the mixture was stirred for 10 min. The acetone was evaporated and the resulting precipitate was filtered and washed with water and Et₂O to obtain the product as brown solid (259 mg, 0.38 mmol, 64%). ¹H NMR (500 MHz, DMSO-d₆) δ 9.64 (s, 1H, NCHN), 9.51 (s, 1H, CCHN), 8.19 – 8.06 (m, 4H, Ar-H), 8.00 (t, Jₘₙ = 1.9 Hz, 1H, CH), 7.93 (t, Jₘₙ = 1.9 Hz, 1H, CH), 7.76 – 7.69 (d, Jₘₙ = 8.8 Hz, 2H, Ar-H), 7.31 – 7.23 (d, Jₘₙ = 8.8 Hz, 2H, Ar-CH), 4.31 (s, 3H, N-CH₃), 4.27 (t, Jₘₙ = 7.2 Hz, 2H, CH₂), 3.90 (s, 3H, O-CH₃), 1.90 – 1.80 (m, 2H, CH₂), 1.35 – 1.23 (m, 2H, CH₂), 0.91 (t, Jₘₙ = 7.4 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO-d₆) δ 161.8 (Cq), 142.9, 137.9 (Cq), 133.6 (Ar-CH), 132.6 (Ar-CH), 131.0 (Ar-CH), 130.5 (tz-CH), 129.5 (Cq), 129.2 (Ar-CH), 128.7 (Cq), 127.3 (Ar-CH), 123.7 (CH), 123.2 (CH), 115.0 (Ar-CH), 55.6 (O-CH₃), 49.2 (CH₂), 31.0 (CH₃), 18.7 (CH₃), 13.2 (CH₃). MS (ESI⁺) for C₅₂H₃₂N₅O₅PF₆: m/z calculated 534.1857 [M-OTF]⁺, observed 534.1867.

[4-(4-methoxyphenyl)-1-((3-mesitylimidazolium)methyl] 1,2,3-triazole] hexafluorophosphate. To a solution of [(MesIm)CH₂]X (X = Cl⁺/I⁻) (363 mg, 1 mmol) in DMF:H₂O mixture (5 mL:4:1) was added NaN₃ (68 mg, 1.05 mmol), Na₂CO₃ (53 mg, 0.5 mmol) and ethynyl anisole (136 µL, 138 mg, 1.05 mmol) and a catalytic amount of CuSO₄·5H₂O
(50 mg, 0.2 mmol) and natrium ascorbate (80 mg, 0.4 mmol). The resulting white suspension was stirred overnight at room temperature, during which it turned bright yellow and was subsequently poured into a solution of EDTA in NH₄OH (65 mL). The suspension was extracted with DCM (3 x 10 mL), washed with water (2 x 10 mL) and brine (15 mL), dried over MgSO₄ and concentrated. The yellow oil was dissolved in an acetone:water mixture (6 mL, 2:1) and stirred with an excess of KPF₆. After stirring the reaction mixture for 1 hour, the acetone was removed and the product extracted with DCM (3 x 5 mL), washed with H₂O and ether and dried in vacuo to obtain the product. Yield not determined.

\[ 1\]H NMR (500 MHz, CDCl₃) δ 8.96 (s, 1H, NC₅H₄N), 8.42 (s, 1H, CC₅H₄N), 7.90 (s, 1H, C₅H₄N), 7.73 (d, 3JHH = 8.3 Hz, 2H, Ar-CH₂), 7.24 (s, 1H, C₅H₈), 6.98 – 6.84 (m, 4H, Ar- & Mes-C₅H₄), 6.22 (s, 2H, C₆H₂), 3.81 (s, 3H, O-C₅H₃), 2.30 (s, 3H, C₅H₃), 2.03 (s, 3H, C₅H₃);

\[ 13\]C NMR (126 MHz, CDCl₃) δ 160.0 (Ar-C₅q), 141.6, 136.0, 134.4 (C₅q), 130.4 (CH), 128.9 (Ar-CH), 124.9, 122.2 (C₅q), 114.4 (Ar-CH), 56.6 (CH₃) 55.4 (O-CH₃), 21.1 (CH₂), 17.0 (CH₃). MS(CSI⁺) calculated m/z = 374.1981 for C₃₂H₂₄N₅O [M-X]⁺, observed 374.1825.

\[ 4-(4-methoxyphenyl)-3-methyl-1-((3-mesitylimidazolium)methyl)1,2,3-triazolium \] bishexafluorophosphate; 4. Meerwein’s salt (71 mg, 0.47 mmol) and [4-(4-methoxyphenyl)-1-((3-mesitylimidazolium)methyl) 1,2,3-triazolium] hexafluorophosphate (148 mg, 0.29 mmol) were dissolved in dry dichloromethane (5 mL) and the reaction mixture was stirred for 16 hours. A drop of methanol was added to quench the reaction. Diethyl ether was subsequently added upon which a pale pink solid precipitated. The solid was redissolved in an acetone:water mixture (10 mL, 1:1) and stirred with an excess of KPF₆ (285 mg, 3.8 mmol) for one hour. Upon removal of the acetone a white solid precipitated, which was collected on a glass frit and washed with H₂O and diethyl ether and dried in vacuo to obtain the product. (200 mg, 0.29 mmol, quantitative). \[ 1\]H NMR (500 MHz, CDCl₃) δ 9.82 (s, 1H, NC₅H₄N), 9.37 (s, 1H, NC₅H₄N), 8.31 (s, 1H, CH), 8.14 (s, 1H, CH), 7.72 (d, 3JHH = 8.8 Hz, 2H, Ar-CH₂), 7.22 (d, 3JHH = 8.8 Hz, 2H, Ar-CH₂), 7.20 (s, 2H, Mes-H), 4.36 (s, 3H, N-C₅H₃), 3.89 (s, 3H, O-C₅H₃), 2.36 (s, 3H, Mes-CH₃), 2.07 (s, 6H, Mes-CH₃);\n
\[ 13\]C NMR (75 MHz, DMSO-d₆) δ 161.8, 140.6 (Ar-C₅q), 139.3 (NCN), 134.1 (Ar-C₅q), 131.0 (Ar-CH), 130.9 (Ar-C₅q), 130.8 (Ar-CH), 129.3 (tz-CH), 129.2 (Mes-CH), 128.3 (Ar-C₅q) 124.3, 123.0 (CH) 115.0 (Ar-C₅q), 61.9 (CH₂), 55.6 (O-CH₃), 38.0 (N-CH₃), 20.5, 17.0 (Mes-CH₃). MS (CSI⁺) for C₃₃H₃₇F₁₆N₇OP: m/z calculated 534.1857 [M-PF₆⁻], observed 534.1821.

General procedure synthesis [M(cod)(NH₅-tzNHC₅H₄)]X 5 and 6: NaH (2 equiv., 60 wt%) was washed three times with pentane. Subsequently, [M(cod)Cl]₂ (M= Ir, Rh, 0.5 equiv.) in MeOH (c = 20 mM) was added and the resulting suspension was stirred for half an hour at room temperature. After addition of the appropriate imidazole-triazolium salt (1 equiv.), the mixture was stirred for 3 hours at 50 °C, after which the resulting orange (rhodium) or red (iridium) solution was concentrated, redissolved in dichloromethane and filtered over Celite. The solvent was evaporated to yield the product.
Chelating Heteroditopic Di-NHC Late TM Complexes

[Ir(I)(cod)(NHC⁵Mes-tzNHC⁵DiPP)]OTf; 5a. Dark red powder (89 mg, 0.1 mmol, 99%). ¹H NMR (300 MHz, CD₂Cl₂) δ 7.87 (d, JHH = 2.0 Hz, 1H, CH), 7.55 (t, JHH = 7.8 Hz, 1H, DiPP-H), 7.33 (d, JHH = 7.8 Hz, 2H, CH₂), 6.98 (s, 2H, Mes-H), 6.92 (d, JHH = 2.0 Hz, 1H, CH), 5.66 (bs, 2H, CH₂), 4.42 (s, 3H, N-C₂H₅), 3.58 (s, 4H, cod-CH₂), 2.34 (s, 3H, Mes-CH₃), 2.11 (s, 6H, Mes-CH₂), 2.05-2.00 (m, iPr-CH), 1.71-1.45 (bm, 8H, cod-CH₂), 1.28 (d, JHH = 6.7 Hz, 12H, iPr-CH₂); ¹³C NMR (101 MHz, CD₂Cl₂) δ 174.5 (C NH₃), 162.5 (C₂NHC₂H₅), 145.3, 139.2, 138.0, 135.9, 135.1, 134.8 (C), 131.2, 128.8, 123.9 (CH Ar), 123.3, 122.4 (CH), 119.2 (OTf), 73.4 (cod-CH), 44.6 (CH₂), 37.3 (N-CH₃), 30.9 (cod-CH₂), 29.6 (iPr-CH₂), 28.6 (cod-CH₂), 25.3 (iPr-CH), 22.1 (iPr-CH₃), 20.6, 18.5 (Mes-CH₂). MS (FAB⁺) calculated m/z = 742.3463 for C₃₆H₄₇N₅Ir [M-OTf]⁺, observed 742.3387.

[Rh(I)(cod)(NHC⁵Mes-CH₃-tzNHC⁵DiPP)]OTf; 6a. Bright orange powder (180 mg, 0.22 mmol, 99%). ¹H NMR (300 MHz, CDCl₃) δ 8.06 (d, JHH = 1.8 Hz, 1H, CH), 7.53 (t, JHH = 7.8 Hz, 1H, DiPP-H), 7.30 (d, JHH = 7.8 Hz, 2H, DiPP-H), 6.97 (s, 2H, Mes-H), 6.77 (d, JHH = 1.8 Hz, 1H, CH), 5.93 (bs, 2H, CH₂), 4.49 (s, 3H, N-C₂H₅), 3.87 (bs, 4H, cod-CH₂), 2.44 – 2.38 (m, 2H, iPr-CH), 2.35 (s, 3H, Mes-CH₃), 2.12 (s, 6H, Mes-CH₂), 1.88-1.62 (bm, 8H, cod-CH₂), 1.28 (d, JHH = 6.7 Hz, 6H, iPr-CH₃) 1.05 (d, JHH = 6.7 Hz, 6H, iPr-CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 178.7 (d, JHCC = 53.5 Hz, C NH₃), 166.1 (d, JHCC = 48.5 Hz, C₂NHC₂H₅), 145.4, 139.5, 139.3, 136.3, 135.5, 135.1 (tz/Ar-C₃), 131.4, 129.2, 128.8, 124.1 (Ar-CH), 123.4, 123.0 (CH), 118.9 (OTf), 86.08 (d, JHCC = 8.3 Hz, cod-CH), 45.2 (CH₂), 37.8 (N-CH₃), 29.8 (cod-CH₂), 28.8 (iPr-CH₂), 28.5 (cod-CH₂), 25.8 (iPr-CH), 22.6 (iPr-CH₃), 21.2 (Mes-CH₃), 18.8 (Mes-CH₂). MS (FAB⁺) calculated m/z = 652.2886 for C₃₆H₄₇N₅Rh [M-OTf]⁺, observed 652.2885.

[Rh(I)(cod)(NHC⁵Mes-CH₃-tzNHC⁵Benz)]OTf; 6b. Orange powder (78 mg, 0.089 mmol, 92%). ¹H NMR (300 MHz, CDCl₃) δ 7.72 (bs, 1H, CH), 7.48 – 7.28 (m, 4H, Benz-CH), 7.19-7.16 (m, 1H, Benz-CH), 6.97 (s, 2H, Mes-CH₃), 6.81 (bs, 1H, CH), 5.62 (bs, 2H, CH₂), 5.55 (s, 2H, CH₂), 4.89 (bs, 2H, cod-CH₂), 4.31 (s, 3H, N-C₂H₅), 3.66 (bs, 2H, cod-CH₂), 2.37 (s, 6H, CH₃), 2.10 (s, 3H, CH₃), 1.93-1.87 (m, 8H, cod-CH₂); ¹³C NMR (101 MHz, CD₂Cl₂) δ 182.1 (d, JHCC = 52.2 Hz, C NH₃), 166.7 (d, JHCC = 48.5 Hz, C₂NHC₂H₅), 140.4, 139.5, 138.9, 135.0, 134.4 (tz/ Ar-C₃), 129.0, 128.9, 128.2, 127.2 (Ar-CH), 122.4, 122.2 (CH), 119.1 (OTf), 95.9 (d, JHCC = 7.7 Hz, cod-CH), 78.4 (d, JHCC = 12.2 Hz, cod-CH), 56.5, 55.3 (CH₂), 36.9 (N-CH₃), 29.5, 28.7 (cod-CH₂), 20.6, 18.0 (Mes-CH₂). MS (FAB⁺) calculated m/z = 568.1947 for C₃₀H₃₅N₅Rh [M-OTf-CH₂]⁺, observed 568.1932.

[Rh(I)(cod)(NHC⁵Mes-CH₃-tzNHC⁵DiPP)]OTf; 6c. Brown solid (203 mg, 0.27 mmol, 92%). ¹H NMR (300 MHz, CDCl₃) δ 7.69 (s, 1H, CH), 7.59 (t, 1H, JHH = 7.2 Hz, Ar-CH), 7.37 (d, 2H, JHH = 7.2 Hz, Ar-CH), 6.82 (s, 1H, CH), 5.85 (bs, 2H, CH₂), 4.58 (s, 4H, cod-CH₂), 4.35 (s, 3H, N-C₂H₅), 2.22-1.84 (m, 12H, 2 × CH₂ and cod-CH₂), 2.22 (m, 2H, CH₂), 2.17 (m, 2H, CH₂), 1.84 (m, 8H, cod-CH₂), 1.41 (m, 2H, JHH = 6.5 Hz, iPr-CH), 1.17 (d, 6H, JHH = 6.8 Hz, iPr-CH₃), 1.12 (d, 6H, JHH = 6.8 Hz, iPr-CH₃), 0.84 (t, 3H, JHH = 6.5 Hz, CH₃); ¹³C NMR (101
MHZ, CD$_2$Cl$_2$ δ 181.2 (d, $J_{\text{Rh-C}} = 53.1$ Hz, C$_{\text{NHC}}$), 170.4 (d, $J_{\text{Rh-C}} = 47.9$ Hz, C$_{\text{tznHC}}$), 146.3 (Ar-C$_{pp}$), 135.0 (CH$_3$), 132.9 (Ar-CH$_{3}$), 131.6 (Ar-C$_{pp}$), 129.1 (Ar-CH$_{2}$), 123.8 (CH$_{3}$), 120.3 (CH$_{3}$), 89.0 (d, $J_{\text{Rh-C}} = 9.2$ Hz, cod-CH$_{2}$), 55.0 (CH$_{3}$), 51.1 (N-CH$_{3}$), 45.6 (CH$_{3}$), 37.8 (N-CH$_{3}$), 34.2 (iPr-CH$_{3}$), 28.6 (iPr-CH$_{3}$), 20.6 (CH$_{2}$), 14.0 (CH$_{3}$). MS(ESI$^+$) for C$_{30}$H$_{43}$N$_{5}$Rh: m/z calculated 576.2568 [M-O$^{+}TF$]$^+$, observed 576.2575.

[$\text{Rh}(I)(\text{cod})(\text{NHC-Mes-CH$_{2}$}_2\text{tzNHCH}^{+}_{\text{C},\text{H},6\text{GMe}})]\text{BF}_{4}^-$ 6d. Orange powder (98.5 mg, 0.14 mmol, 96%). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.80 (bs, 1H, CH$_{3}$), 7.58 (d, $J_{\text{HH}} = 8.8$ Hz, 2H, Ar-CH$_{2}$), 7.02 (d, $J = 8.8$ Hz, 4H, Ar-CH and overlapping) (mes-CH$_{2}$), 6.77 (s, 1H, CH$_{3}$), 5.59 (bs, 2H, CH$_{2}$), 4.39 (s, 3H, N-CH$_{3}$), 4.02 – 3.76 (m, 2H, cod-CH$_{2}$), 3.90 (s, 3H, O-CH$_3$), 3.49 (bs, 2H, cod-CH$_{2}$), 2.37 (s, 6H, cod-CH$_{2}$) and CH$_{3}$ overlapping). $^{13}$C NMR (75 MHz, CDCl$_3$) δ 181.1 (d, $J_{\text{Rh-C}} = 53.3$ Hz, C$_{\text{NHC}}$), 166.3 (d, $J_{\text{Rh-C}} = 47.3$ Hz, C$_{\text{tznHC}}$), 161.1 (Ar-C-O), 140.1, 139.2, 136.0, 131.8, 130.4 (tz/Ar-C$_{pp}$), 129.3, 125.8, 123.2, 122.5, 114.4 (Ar-CH and CH$_{2}$), 77.4 (d, $J_{\text{bc}} = 3.5$ Hz, cod-CH), 55.9 (O-CH$_{3}$), 45.4 (CH$_{3}$), 37.3 (N-CH$_{3}$), 28.2, 22.0 (cod-CH$_{2}$), 21.2, 17.7 (Mes-CH$_{2}$). MS(FAB$^+$) for C$_{31}$H$_{47}$N$_{5}$ORh: m/z calculated 598.2053 [M-BF$_4^-$]$^+$, observed 598.2054.

General procedure synthesis [M(cod)(NHC-tz)]X: NaH (1 equiv., 60 wt%) was washed three times with pentane. Subsequently [M(cod)(µ-Cl)$_2$] (M= Ir or Rh, 0.5 equiv.) in MeOH (c = 20 mM) was added and the resulting suspension was stirred for half an hour at room temperature. After addition of the appropriate triazolyl-imidazolium bromide (1 equiv.), the mixture was stirred for 3 hours at 50 °C, after which the resulting orange (rhodium) or red (iridium) solution was concentrated, redissolved in dichloromethane and filtered over Celite. AgOTf (1.1 equiv.) was added to the solution and the mixture was stirred in the dark for 2 hours at room temperature during which it turned to a pale brown suspension. The reaction mixture was filtered over Celite and concentrated to yield the product.

Alternative procedure synthesis [M(cod)(NHC-tz)]X: The triazolyl-imidazolium bromide salt (1 equiv.) was dissolved in THF. Potassium tert-butoxide was added and the mixture was stirred for 3 hours, after which the solution was filtered over Celite and concentrated. Subsequently a solution of AgOTf (1.1 equiv.) in DCM was added and the resulting mixture was stirred for another 2 hours at room temperature in the dark during which it turned to a pale brown suspension. The reaction mixture was filtered over Celite and concentrated to yield the product.

[$\text{Ir}(I)(\text{cod})(\text{NHC-Mes-CH$_{2}$}_2\text{tzDiPP})]^{\text{OTf}}^-$ 7. Red solid (88 mg, 0.11 mmol, 76%). $^1$H NMR (300 MHz, CD$_2$Cl$_2$) δ 8.42 (s, 1H, tz-CH$_{3}$), 7.70 (d, $J_{\text{HH}} = 2.0$ Hz, 1H, CH$_{3}$), 7.59 (t, $J_{\text{HH}} = 7.7$ Hz, 1H, DiPP-CH$_{2}$), 7.35 (d, $J_{\text{HH}} = 7.9$ Hz, 2H, DiPP-CH$_{3}$), 7.03 (s, 2H, Mes-CH$_{2}$), 6.94 (d, $J_{\text{HH}} = 2.0$ Hz, 1H, CH$_{3}$), 5.75 (s, 2H, CH$_{2}$), 4.59 (bs, 2H, cod-CH$_{2}$), 3.54 (bs, 2H, cod-CH$_{3}$), 2.37 (s, 3H, Mes-CH$_{3}$), 2.07 (s, 6H, Mes-CH$_{3}$), 2.08-1.61 (m, 10H, cod-CH$_{2}$ and iPr-CH overlapping), 1.19 (d, $J_{\text{HH}} = 6.8$ Hz, 6H, DiPP-CH$_{3}$), 1.06 (d, $J_{\text{HH}} = 6.8$ Hz, 6H, DiPP-CH$_{3}$). $^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) δ 173.3 (C$_{\text{NHC}}$), 146.2, 141.2, 140.3, 135.8, 134.3 (Ar/tz-C$_{pp}$), 132.4 (DiPP-CH$_{3}$), 129.6 (Mes-CH$_{2}$), 127.3
(tz-CH), 124.8 (DiPP-CH), 122.6, 123.3 (CH), 117.9 (OTf), 83.8 (cod-CH), 66.3 (cod-CH), 45.2 (CH2), 33.7 (cod-CH2), 30.1 (cod-CH2), 29.4 (iPr-CH), 24.9, 23.4 (DiPP-CH), 22.6, 18.6 (Mes-CH3). MS(FAB+) for C35H46N5Rh: m/z calculated 638.2730 [M-OTf]+, observed 638.2725.

[Rh(I)(cod)(NHCMes-CH2-tz(Dpp)])OTf; 8. Bright orange solid (52 mg, 0.07 mmol, 73%). 'H NMR (300 MHz, CD2Cl2) δ 8.33 (s, 1H, tz-CH), 7.67 (d, JHH = 1.9 Hz, 1H, CH), 7.58 (d, JHH = 7.8 Hz, 1H, DiPP-CH), 7.36 (d, JHH = 7.8 Hz, 2H, DiPP-CH), 7.08 (s, 2H, Mes-CH2), 6.89 (d, JHH = 1.8 Hz, 1H, CH), 5.86 (s, 2H, CH2), 5.01 – 4.75 (m, 2H, cod-CH), 3.91 – 3.61 (m, 2H, cod-CH2), 2.40 (s, 3H, Mes-CH3), 2.12 (s, 6H, Mes-CH3), 2.11-1.93 (m, 8H, iPr-CH and cod-CH2 overlapping), 1.84-1.78 (m, 2H, cod-CH2), 1.20 (d, JHH = 6.8 Hz, 6H, iPr-CH2), 1.07 (d, JHH = 6.8 Hz, 6H, iPr-CH2); 13C NMR (75 MHz, CD2Cl2) δ 176.7 (d, JCC = 51.8 Hz, C(NHC)), 146.3, 141.4, 140.2, 136.19, 135.7 (Ar/tz-C6), 132.8, 132.3 (DiPP-CH), 129.7 (Mes-CH3), 126.6 (tz-CH), 124.7 (DiPP-CH), 123.6, 123.2 (CH), 118.9 (OTf), 96.7 (d, JRC = 7.8 Hz, cod-CH), 79.6 (d, JRC = 12.3 Hz, cod-CH), 45.4 (CH2), 32.7 (cod-CH2), 29.5 (cod-CH2), 29.3 (DiPP-CH), 24.8, 23.4 (DiPP-CH), 21.4, 18.5 (Mes-CH3). MS(FAB+) for C35H46N5Rh: m/z calculated 638.2730 [M-OTf]+, observed 638.2725.

[Rh(I)(cod)(NHCAr-tzNHCp-Tol)]PF6; 9a. This complex was synthesized in analogy to complex 6 from ligand 3a with a reduced reaction time of 1 hour. Orange powder (66 mg, 0.1 mmol, 98%). 'H NMR (500 MHz, CDCl3) δ 7.86 – 7.73 (m, 3H, Ar-CH), 7.68 (d, JHH = 8.1 Hz, 2H, Tol-CH), 7.70 – 7.64 (m, 1H, Ar-CH), 7.46 (d, JHH = 7.9 Hz, 2H, Tol-CH), 7.36 (d, JHH = 2.0 Hz, 1H, CH), 7.21 (d, JHH = 2.0 Hz, 1H, CH), 4.39 (m, 3H, CH2 and cod-CH overlapping), 4.31 – 4.24 (m, 1H, cod-CH), 4.15 (s, 3H, NCH3), 4.12 (m, 1H, cod-CH), 2.53 (s, 3H, Tol-CH), 2.30 – 2.08 (m, 2H, cod-CH2), 2.00 – 1.70 (m, 2H, CH2), 1.60-1.50 (m, 4H, cod-CH2 and CH2 overlapping), 1.10 (t, J = 7.4 Hz, 1H, CH3); 13C NMR (75 MHz, CD2Cl2) δ 185.6 (d, JRC = 52.6 Hz, C(NHC)), 173.2 (d, JRC = 47.4 Hz, C(tzNHC)), 144.8, 140.8, 135.3, 134.7 (Ct-Ar), 131.3, 129.4, 129.4, 128.6, 126.8, 126.5, 123.6 (Ar-CH), 123.1, 121.8 (CH), 91.7 (d, JRC = 8.0 Hz, cod-CH), 90.7 (d, JRC = 8.6 Hz, cod-CH), 90.4 (d, JRC = 7.2 Hz, cod-CH) & 84.4 (d, JRC = 7.5 Hz, cod-CH), 50.7 (N-CH3), 37.9 (N-CH3), 33.3 (CH3), 32.0, 31.6, 29.0, 28.5 (cod-CH2), 21.2 (Ar-CH), 20.2 (CH3), 13.5 (CH3). MS(ESI+) for C31H37N5Rh: m/z calculated 582.2099 [M-PF6]+, observed 582.2081.

[Rh(I)(cod)(NHCAr-tzNHCp-H4OMe)]PF6; 9b. This complex was synthesized in analogy to complex 6 from ligand 3b with a reduced reaction time of 1 hour. Brown solid (71 mg, 0.1 mmol, 95%). 'H NMR (300 MHz, CD2Cl2) δ 7.89 – 7.61 (m, 6H, Ar-CH), 7.34 (d, J = 2.2 Hz, 1H, CH), 7.22 – 7.12 (m, 3H, CH and Ar-CH), 4.41-4.38 (m, 4H, N-CH2 and cod-CH overlapping), 4.37-4.35 (m, 1H, cod-CH), 4.13 (s, 3H, N-CH3), 4.13-4.11 (m, 1H, cod-CH), 3.96 (s, 3H, O-CH3), 2.26 – 2.08 (m, 2H, CH2), 2.04-1.47 (m, 10H, cod-CH2 and CH2 overlapping), 1.09 (t, J = 7.3 Hz, 3H, CH3); 13C NMR (75 MHz, CD2Cl2) δ 185.7 (d, JRC = 52.8 Hz, C(NHC)), 173.0 (d, JRC = 47.5 Hz, C(tzNHC)), 161.1, 144.6, 135.3, 134.6, 131.3, 131.0, 130.4, 129.6, 128.6, 126.7, 126.5, 123.1, 121.8, 118.6, 113.3, 113.6,
91.8 (d, $J_{RC} = 7.9$ Hz, cod-CH), 90.7 (d, $J_{RC} = 8.7$ Hz, cod-CH), 90.5 (d, $J_{RC} = 7.4$ Hz, cod-CH), 84.4 (d, $J_{RC} = 7.6$ Hz, cod-CH), 55.6 (O-CH$_3$), 50.6 (N-CH$_3$), 41.5 (CH$_2$), 37.8 (N-CH$_3$), 32.1, 31.7, 28.9, 28.4, 28.0, 27.9, 25.5, 24.7 (cod-CH$_2$), 20.2 (CH$_3$), 13.5 (CH$_3$). MS(CSI$^-$) for $C_{31}H_{37}N_5O\text{Rh}$: m/z calculated 598.20531 [M-PF$_3$]$^-$, observed 598.20634.

**General procedure synthesis** $[M(CO)_3(NHC-tzNHC)]X$: A pressure NMR tube containing the desired complex (~10 mg) in CD$_2$Cl$_2$ (0.5 mL) was pressurized with syngas (5 bar). After shaking the tube a color change was generally observed.

**Alternative procedure synthesis** $[M(CO)_3(NHC-tzNHC)]X$: Two septum screw cap vial (4 mL, punctured with a small needle) containing the desired complexes in CD$_2$Cl$_2$ (1 mL) were placed in an autoclave. After pressurizing with syngas (5 bar), the solutions were allowed to stir for 10 min., after which the autoclave was vented and the carbonyl complexes could be analyzed.

The formation of the resulting complexes was confirmed by $^1$H NMR spectroscopy, in which free cod was observed. IR measurements were performed to obtain the CO stretching frequencies.

$[\text{Rh}(I)(CO)_2(NHC}_{\text{mes-tzNHC}}^{\text{dipp}}\text{)]OTf$; **11a**. A pressure NMR tube containing $[\text{Rh}(I)(\text{cod})\text{(NHC-Trzl}^+)]\text{OTf}$ 6a (9.2 mg) in CD$_2$Cl$_2$ (0.5 mL) was pressurized with syngas (5 bar). After shaking the tube a color change from bright orange to a darker shade of orange was observed. The NMR spectra showed complete conversion to the carbonyl complex. $^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 8.03 (s, 1H, CH), 7.60 (t, $J_{HH} = 7.8$ Hz, 1H, CH-DiPP), 7.36 (d, $J_{HH} = 7.8$ Hz, 2H, CH-DiPP), 7.10 (s, 1H, CH), 7.02 (s, 2H, Mes-CH$_3$), 5.92 (s, 2H, CH$_2$), 5.62 – 5.52 (m, 4H, free cod), 4.51 (s, 3H, NH$_2$), 2.44 – 2.26 (m, 8H, free cod), 2.27-2.21 (m, $J_{HH} = 13.5$, 6.7 Hz, 2H, iPr-CH$_2$), 2.03 (s, 6H, Mes-CH$_3$), 1.27 (s, 3H, Mes-CH$_3$), 1.22 (d, $J_{HH} = 6.8$ Hz, 6H, iPr-CH$_2$), 1.10 (d, $J_{HH} = 6.8$ Hz, 6H, iPr-CH$_2$); $^{13}$C NMR (101 MHz, CD$_2$Cl$_2$) $\delta$ 185.3 (bs, CO), 173.7 (d, $J_{RC} = 47.5$ Hz, C$_{\text{NHC}}$), 163.6 (d, $J_{RC} = 42.4$, C$_{\text{tzNHC}}$), 145.7, 141.0, 140.2, 135.9, 135.7, 134.6 (tz/Ar-C$_{\text{H}}$), 131.9, 129.2, 124.2 (Ar-CH) 124.2 (CH) 123.0 (CH), 118.9 (OTf), 44.8 (CH$_3$), 37.7 (N-CH$_3$), 28.5 (iPr-CH$_2$), 24.7 (DiPP-CH$_2$), 22.4 (CH$_3$), 20.7 (Mes-CH$_3$), 17.9 (Mes-CH$_3$). MS(FAB$^+$) for $C_{30}H_{36}N_5O_2\text{Rh}$: m/z calculated 602.2002 [M-OTf]$^+$, observed 602.2038/ $C_{30}H_{36}N_5O_2\text{Rh}$: m/z calculated 601.1924 [M-OTf-H]$^-$, observed 601.1929. IR v(CO) 2064, 2005 cm$^{-1}$.

$[\text{Ir}(I)(CO)_2(NHC}_{\text{mes-tzNHC}}^{\text{dipp}}\text{)]OTf$; **12a**. A pressure NMR tube containing $[\text{Ir}(I)(\text{cod})\text{(NHC-Trzl}^+)]\text{OTf}$ 7a (40 mg) in CD$_2$Cl$_2$ (0.5 mL) was pressurized with carbon monoxide gas (5 bar). After shaking the tube the color changed from red to bright yellow. The NMR spectra showed complete conversion to the carbonyl complex. $^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 8.08 (d, $J_{HH} = 1.9$ Hz, 1H, CH), 7.68 – 7.52 (t, $J_{HH} = 7.9$ Hz, 1H, DiPP-CH), 7.37 (d, $J_{HH} = 7.9$ Hz, 2H, DiPP-CH), 7.13 (d, $J_{HH} = 2.0$ Hz, 1H, CH), 7.02 (s, 2H, Mes-CH$_3$), 6.00 (s, 2H, CH$_2$), 5.62 – 5.52 (m, 4H, free cod), 4.53 (s, 3H, N-CH$_3$), 2.44 – 2.26 (m, 8H, free cod), 2.23 (p, $J_{HH} = 6.8$ Hz, 2H, iPr-CH$_2$) 2.13 (s, 3H, Mes-CH$_3$), 2.03 (s, 6H, Mes-CH$_3$), 1.35 – 1.21 (m, 18H, DiPP-
CH₃), 1.10 (d, 3JHH = 6.9 Hz, 6H, DiPP-CH₃); ¹³C NMR (126 MHz, CD₂Cl₂) δ 179.6, 178.9 (CO), 171.3 (C₄H₈), 162.0 (C₅H₈), 146.6, 141.9, 141.1, 136.7, 135.9, 134.6 (tzz/Ar-C), 132.8, 129.9, 127.7 (Ar-CH), 125.2 (CH), 125.0 (Ar-CH), 124.9 (CH), 124.0 118.9 (OTf), 45.6 (CH₂), 38.5 (N-CH₂), 29.2 (iPr-CH), 25.4 (DiPP-CH₃), 23.11 (DiPP-CH₃), 21.42 (Mes-CH₃), 18.68 (Mes-CH₃). MS (ESI⁺) for C₅₀H₃₅N₃O₂Ir: m/z calculated 690.2416 [M-OTf]+, observed 690.2401. IR ν(CO) 2056, 1992 cm⁻¹.

Alternate synthesis [Ir(I)(CO)₂(NHCMes-tzNHCDiPP)]OTf; 12. Potassium tert-butoxide was added to a solution of Ir(CO)₂(acac) (35 mg, 0.1 mmol) and 2a (671 mg, 0.1 mmol) in THF (5 mL) and the resulting brown solution was stirred for 2 hours at 50 °C. After the solution was allowed to cool to room temperature, the mixture was filtered over Celite. Then the solution was concentrated to 2 mL and Et₂O (10 mL) was added to precipitate the remaining ligand. The solution was decanted and concentrated under vacuum to yield the product (50 mg, 0.06 mmol, 60%).

[Ir(l)(CO)₂(H)₂(NHC-tzNHC-DiPP)]OTf; 13 and 13*. A pressure NMR tube containing [Ir(l)(COD)(NHC-Trzl)]OTf 5a (~ 40 mg) in CD₂Cl₂ (0.5 mL) was pressurized with syngas (5 bar). After shaking the tube a color change from bright red to yellow. The NMR spectra showed a mixture of [Ir(I)(CO)₂(NHC-Trzl)]OTf 12 and two different isomers of [Ir(l)(CO)₂(H)₂(NHC-Trzl)]OTf 13 in a 3.2 : 2.8 : 1 ratio. Upon release of the syngas pressure, complex 13 converts to 12 by losing H₂, which prevented us from further characterization, and the mixture of products prevented us from assigning all ¹³C resonances. ¹H NMR (300 MHz, CD₂Cl₂) δ 8.03 (d, 3JHH = 2.0 Hz, 1H, CH), 8.01 (d, 3JHH = 1.9 Hz, 1H, CH'), 7.65 – 7.49 (m, 2H, DiPP-CH and DiPP-CH'), 7.34 – 7.28 (m, 4H, DiPP-CH and DiPP-CH'), 7.12 (d, 3JHH = 2.0 Hz, 1H, CH), 7.09 (d, 3JHH = 2.0 Hz, 1H, CH'), 7.00 (s, 2H, Mes-CH), 6.97 (s, 2H, Mes-CH'), 6.33 (d, 3JHH = 16.8 Hz, 1H, CH'), 6.33 (d, 3JHH = 16.8 Hz, 1H, CH').

General procedure catalytic transfer hydrogenation: To a carrousel vial or Schlenk equipped with a magnetic stirrer, 0.5 or 1 mol % of catalyst, and 10 mol % of KOtBu were added a degassed stock solution (c = 0.1 M) of the appropriate substrate and p-xylene as internal standard in isopropanol. The mixture was stirred at 80 °C. Aliquots were taken from the mixture during the reaction, subsequently filtered over a plug of silica, and analyzed by GC.

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4.7 References

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Chapter 5
Cooperative Lutidine-based Tridentate tzNHC Ru(II) Complexes for Catalytic Ester Hydrogenolysis

Abstract
In this chapter the development of CNC and CNN pincer ligands bearing tzNHCs is described as an expansion to the library of cooperative lutidine-derived ligands. Coordination of these ligands via transmetallation of the respective Ag(I) complexes led to [(L)Ru(H)(CO)(PPh$_3$)] complexes displaying rare facial coordination of the tridentate ligand. The Ru and Pd complexes exhibit the expected reactivity (reversible deprotonation/dearomatization) of the benzylic “arm”. The ruthenium complexes were active in catalytic ester hydrogenation at 100 °C in the presence of minimally 20 mol% of KOTBu. The sterically congested tBu-benzoate ester was converted considerably faster than the methyl analogue. Although transesterification of the substrate to the tert-butyl ester may play a role, the reason for the requirement of the critical minimum amount of KOTBu (≥20 mol%) remains unknown. Furthermore, potentially active CNC Ru hydride species have been elucidated by NMR spectroscopy under near-catalytic conditions.

Soraya N. Sluijter, Ties J. Korstanje, Jarl Ivar van der Vlugt and Cornelis J. Elsevier, manuscript in preparation.
5.1 Introduction

In Chapter 3 heteroditopic di-NHC ruthenium catalysts have been described that are active in the hydrogenation of ketones and imines. However, these catalytic systems were not able to reduce non-activated esters, which are more challenging substrates than ketones, in satisfactory yields. The hydrogenation, formally called hydrogenolysis, of carboxylic esters leading to alcohols (Scheme 1) is more difficult compared to ketones because the C=O double bond is a weak electrophile that is stabilized by resonance.

Ester hydrogenation is an industrially important transformation as it is commercially used to produce several alcohols from esters.\(^1\)\(^2\) Furthermore, interesting biomass feedstocks such as vegetable fats and oils contain many ester functionalities. Considering the depletion of fossil fuels, ester hydrogenation may therefore become an even more important transformation. In industry, non-selective heterogeneous catalysts (typically based on copper chromite) are used at high pressures and temperatures to perform this reaction.\(^3\) Hence, a more selective and environmentally friendly homogeneous replacement of these catalysts is desirable. Early reports on such catalysts for the hydrogenation of esters required additives, harsh conditions and/or were only suitable for activated esters.\(^4\)\(^–\)\(^6\)

Our group was among the first to convert esters to alcohols at reasonable temperature and pressure (100 °C and 70 bar) using a homogeneous ruthenium Triphos catalyst (Triphos = 1,1,1-tris(diphenylphosphinomethyl)ethane; Scheme 1).\(^7\)\(^–\)\(^9\) In the last decade, much progress has been made in ester hydrogenolysis catalyzed by well-defined transition metal complexes.\(^10\) Even first-row transition metals have now been successfully applied in this transformation.\(^11\)\(^–\)\(^15\) Several
breakthroughs can be attributed to the emergence of metal-ligand cooperativity (MLC) in the homogeneous catalysis field. As explained in the introductory chapter, MLC can create alternative catalytic pathways as the ligand participates actively in the process.

Although the mechanisms for ester hydrogenation have hardly been unequivocally proven, a plausible catalytic cycle for ester hydrogenation catalyzed by a cooperative Ru hydride complex is depicted in Scheme 2. Addition of $\text{H}_2$ to the dearomatized pincer complex leads to the formation of a trans-dihydride species. In the following step the first hydride transfer to the stabilized ester carbonyl leading to a hemi-acetal, is generally considered to be rate-limiting. To facilitate this step electron-rich ligands can be employed to enhance the nucleophilicity of the hydride towards the substrate. The hemi-acetal, unstable under the reaction conditions, subsequently splits in the first alcohol product and an aldehyde, which is then hydrogenated to produce the second alcohol product. Alternatively, an outer-sphere bifunctional mechanism could be operative as shown by Morris et al. On the basis of DFT calculations, another pathway involving direct H/OR metathesis was proposed by Hasanayn and Baroudi.

Scheme 2: Proposed catalytic cycle of the hydrogenation of esters to alcohols using MLC.
The first example of an ester hydrogenation catalyst making use of MLC by deprotonation/dearomatization (Scheme 1) was the PNN Ru catalyst developed by the group of Milstein.\textsuperscript{18} Notably, the PNP Ru analogue was significantly less active, which was attributed to the lack of a hemilabile donor, which likely hampers substrate (pre-)coordination.\textsuperscript{18} By replacing the phosphine donor in the PNN design for a more electron-rich NHC moiety, Song \textit{et al.} were able to increase the rate of the reaction (Scheme 1).\textsuperscript{22} The CNN complex reported by Milstein in 2011 was slightly more active than its predecessor as well (Scheme 1). The lutidine-based CNC Ru pincer complex (Scheme 1) reported very recently by Pidko \textit{et al.} hydrogenated methyl benzoate and other esters in the presence of KOMe (C/B/S = 1/20/200) at 50 bar H\textsubscript{2} pressure and a relatively low temperature of 70 °C in 4 hours.\textsuperscript{23} The same group recently demonstrated that the cooperativity of the deprotonated NHC-based CNC is more pronounced compared to its phosphine analogue, which was attributed to a combination of electronic properties and flexibility of the larger CNC chelate.\textsuperscript{24}

In this chapter we describe the development of CNC and CNN pincer ligands bearing 1,2,3-triazolylidenes, which are envisioned to be an expansion to the library of cooperative lutidine-derived ligands. The corresponding Ru(II) complexes have been synthesized and characterized and applied in catalytic ester hydrogenolysis. The ability of these ruthenium complexes and the related [(CNC)PdCl] compound to undergo deprotonation/dearomatization has been studied. As described, a correlation between electron-density and catalytic ester hydrogenation activity has been observed previously: the PNP ligand leads to a less active catalyst than CNC ligand (C = imidazole-2-ylidene). It is therefore hypothesized that the more electron-rich tzNHC donors on our ligands may accordingly lead to enhanced activity, due to an expected increase of hydricity of the Ru-hydride.

\textbf{5.2 Synthesis of the CNC and CNN ligands}

The desired CNC ligand was efficiently synthesized in two steps (Scheme 3). First, 2,6-bis(bromomethyl)pyridine was converted to ditriazole 1 in high yields following a one-pot multicomponent tandem azidination and CuAAC procedure published by Crowley and Bandeen.\textsuperscript{25,26} As the \textit{in situ} prepared azide reacts with the terminal alkyne, handling of potentially dangerous azides could be circumvented and cumbersome work-up was avoided.

Second, N3 of the triazole was methylated using 2 equivalents of (Me\textsubscript{3}O)BF\textsubscript{4} leading to CNC ligand 2 (Scheme 3). The formation of the compound was confirmed by a downfield shift of the triazole peak to 9.19 ppm and the methyl resonance at 4.22 ppm in the \textsuperscript{1}H NMR spectrum.
We were also interested to obtain the CNN analogue 3, because the potential
hemilability of the triazole moiety might have a positive effect on the catalytic
ester hydrogenolysis.\textsuperscript{18} When only one equivalent of methylating agent was used,
a mixture of starting material, mono- and bis-methylated product was obtained.
The three different species could easily be separated by column chromatography
(DCM : acetone = 1:1), providing access to the CNN pincer ligand (Scheme 3).
Although the yield of ligand 3 is low (34%), this procedure allowed for recovery
of the starting material 1 as well as isolation of ligand 2. Ligand 1, 2 and 3 have been
characterized by multinuclear NMR spectroscopy and HR-MS. In contrast to ligands
1 and 2, the \textsuperscript{1}H and \textsuperscript{13}C NMR spectra of 3 indicated a non-symmetric structure with
distinct signals for all hydrogen and carbon atoms.

5.3 Synthesis of CNC Ag(I), Pd(II) and Ru(II) complexes

\textit{Synthesis of the CNC metal complexes}

Initial attempts to coordinate symmetric ligand 2 to ruthenium by direct
deprotonation of the triazolium fragments using various bases (K\textsubscript{OT}Bu, KHMDS and
2-\textit{tert}-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine;
BEMP) in the presence of several precursors ([RuCl\textsubscript{2}(MeCN)\textsubscript{4}], [RuCl(CO)(H)
(PPh\textsubscript{3})\textsubscript{3}], [RuCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{4}] and [Ru(p-cym)(CO)Cl\textsubscript{2}]) were unsuccessful.\textsuperscript{23,27} Therefore,
we turned to the Ag(I)-transmetalation route, which previously proved suitable for
the heteroditopic Ru(II) NHC complexes in Chapter 3.

\textbf{Scheme 3}: Synthesis of 1 and non-innocent CNC and CNN ligands, 2 and 3. i) NaN\textsubscript{3},
Na\textsubscript{2}CO\textsubscript{3}, CuSO\textsubscript{4}.5H\textsubscript{2}O, Sodium ascorbate, DMF/H\textsubscript{2}O (4:1), ii) 2 equivalent of (Me\textsubscript{3}O)BF\textsubscript{4}, iii) 1 equivalent of (Me\textsubscript{3}O)BF\textsubscript{4}, followed by separation by column chromatography.
Silver(I) complex 4 could be obtained by stirring the CNC ligand 2 in the presence of Ag$_2$O in MeOH for two days (Scheme 4).\textsuperscript{28} The formation of the desired complex was confirmed by the disappearance of the triazolium hydrogen in the $^1$H NMR spectrum. In contrast to the other silver(I) di-NHC complexes described in this thesis, mass spectrometry pointed to a mononuclear structure in this case. Apparently, the structure of ligand 2 allows the two tzNHC groups to coordinate to the silver center in a linear fashion.

![Scheme 4: Synthesis of Ag(I) complex 4, Ru(II) complex 5 and Pd(II) complex 6. i) Ag$_2$O, MeOH, 48h, ii) [Ru(CO)HCl(PPh$_3$)$_3$], THF, 55 °C, 48h, iii) [Pd(PhCN)Cl]$_2$, DCM, 3h.](image)

The silver complex was subsequently transmetalated following a procedure published by Suárez et al.,\textsuperscript{29} by stirring 4 with [RuCl(CO)(H)(PPh$_3$)$_3$] in THF at 55 °C for 2 days (Scheme 4) to produce [Ru(CNC)(CO)(H)(PPh$_3$)]BF$_4$, complex 5. Remarkably, the CNC ligand was coordinated in a facial (fac) coordination mode to the ruthenium center, as was evident from the $^1$H and $^{13}$C NMR spectra. The inequivalent sides of the ligand gave rise to separate signals for all hydrogen and carbon atoms. Most indicative were the distinctive signals for both triazolylidene carbons at 172.2 ($^{2}$J$_{CP}$ = 7.2 Hz, cis to PPh$_3$) and 164.9 ppm ($^{2}$J$_{CP}$ = 75.7 Hz, trans to PPh$_3$) in the $^{13}$C NMR spectrum. The carbonyl ligand was also detected as a doublet in the $^{13}$C NMR spectrum at 208.5 ppm ($^{2}$J$_{CP}$ = 14.8 Hz) and it gave rise to a CO vibrational band at 1926 cm$^{-1}$ in the IR spectrum. The hydrido and PPh$_3$ ligands were observed as a doublet at -7.04 ($^{2}$J$_{PH}$ = 28.9 Hz) and a singlet at 46.7 ppm in the $^1$H NMR and $^{31}$P($^1$H) NMR spectrum, respectively. These data are consistent with the only previous report of a fac-CNC Ru complex by Suárez.\textsuperscript{12} Interestingly, Triphos is also known to adopt a facially coordination mode to octahedral Ru centers in our previously reported active ester hydrogenation system.\textsuperscript{30}
Most lutidine-based pincer complexes, including those with more flexible six-membered chelate rings, adopt a meridional (mer) conformation. However, a recent DFT and experimental study has shown that for [Ru(PNP)(PhCOO)$_2$] the fac coordination mode was significantly more stable (yet inactive in direct insertion of CO$_2$ into the C-H bonds of arenes). To gain insight in the reason for fac coordination in our case, we performed DFT calculations. The mer conformation turned out to be more thermodynamically favorable by 2.2 kcal/mol at the BP86/def2-TZVP level (Figure 1). This points to the fac configuration being the kinetic product, produced by these specific reaction conditions. Attempts to obtain the mer analogue synthetically have not been successful to date (combinations of various bases mentioned above or Ag(I) complex and several ruthenium precursors ([RuCl$_2$(MeCN)$_4$], [RuCl(CO)(H)(PPh$_3$)$_3$], [RuCl$_2$(PPh$_3$)$_4$] and [Ru(p-cym)(CO)Cl$_2$]) in various solvents (THF/DCM/MeCN) and temperatures (25-70 °C).

![Figure 1: Computed DFT (BP86/def2-TZVP) structures of Ru CNC complexes with meridional (left) and facial (right) coordination. Hydrogen atoms, except for hydride and CH$_2$, are omitted for clarity.](image)

In Pd(II) complex 6, which could be obtained by transmetalation of the Ag(I) complex 4 with [Pd(PhCN)$_2$Cl$_2$] in 92% yield (Scheme 4), planar coordination of the ligand 2 was observed. The square planar complex was characterized by multinuclear NMR spectroscopy and HR-MS. In CD$_2$Cl$_2$ the hydrogens of the linker were split in the $^1$H NMR spectrum [AB system centered at $\delta_A$ 6.10 and $\delta_B$: 5.98 ppm; $^3$J$_{HH}$ = 15 Hz] and the tzNHC carbon was found in the expected range at 168.0 ppm in the $^{13}$C NMR spectrum.

Dearomatization/deprotonation of complexes 5 and 6

The deprotonation/dearomatization abilities of the complexes were investigated next (Scheme 5). The benzylic position of both complex 5 and 6 could be deprotonated with one equivalent of KOTBu, marked by a characteristic color change to dark red.
The $^1$H NMR spectra of the symmetric CNC Pd(II) 6 and non-symmetric dearomatized CNC* Pd(II) complex 6’ are depicted in Figure 2. Upon deprotonation of the benzylic arm, dearomatization of the pyridine ring occurred, characterized by an upfield shift for the pyridine hydrogens (5.92-4.93 and 6.45-5.70 ppm) and the appearance of the vinylic protons (5.52 and 6.27 ppm for 5’ and 6’, respectively) in the $^1$H NMR spectra. The complexes were not very stable upon dearomatization and could consequently not be completely characterized. The deprotonation/dearomatization reaction was reversible, as addition of hydrochloric acid (1 M in dioxane) led to rearomatization of the pyridine ring (Scheme 5).

![Scheme 5](image)

**Scheme 5**: Reversible deprotonation/dearomatization of CNC complexes. 5: $ML_n$ = Ru(CO)H(PPh$_3$)$_3$ and 6: $ML_n$ = PdCl.

The $^1$H NMR spectra of the symmetric CNC Pd(II) 6 and non-symmetric dearomatized CNC* Pd(II) complex 6’ are depicted in Figure 2. Upon deprotonation of the benzylic arm, dearomatization of the pyridine ring occurred, characterized by an upfield shift for the pyridine hydrogens (5.92-4.93 and 6.45-5.70 ppm) and the appearance of the vinylic protons (5.52 and 6.27 ppm for 5’ and 6’, respectively) in the $^1$H NMR spectra. The complexes were not very stable upon dearomatization and could consequently not be completely characterized. The deprotonation/dearomatization reaction was reversible, as addition of hydrochloric acid (1 M in dioxane) led to rearomatization of the pyridine ring (Scheme 5).

![Figure 2](image)

**Figure 2**: $^1$H NMR spectra of CNC Pd complex 6 (top; in CD$_2$Cl$_2$) and the deprotonated 6’ (bottom; in THF-d$_8$). Pyridine hydrogens of 6’ are assigned by letters (a-e; see Scheme 5) and solvents are marked by “x”.

**Synthesis of Ag(I) and Ru(II) CNN metal complexes**

[Ru(CNN)(CO)(H)(PPh$_3$)$_3$] complex 7 was synthesized in the same way as complex 5 via the silver transmetalation route from ligand 3 (Scheme 6). The formation of the carbene was indicated by the disappearance the triazolium hydrogen in $^1$H NMR and by CSI-HR-MS, which indicated the presence of the [(CNN)$_2$Ag]$^+$ ion, suggesting that two ligands are coordinated to one silver atom in 7.
Transmetalation to the Ru complex 8 proceeded smoothly in the same manner as for 5 using [RuCl(CO)(H)(PPh₃)]₃. Again, NMR spectroscopy pointed to facial coordination of the ligand. Compared to complex 5, the hydrido and PPh₃ ligand both appeared as upfield signals at -13.0 ppm (JPH = 28 Hz, cis to PPh₃) and 40.9 ppm in the ′H NMR and ′P{′H} NMR spectrum, respectively. The upfield shift of the former is in agreement with the hydride in trans position to the weak-field triazole ligand. In the ′C NMR spectrum, the large coupling of the tzNHC carbon (166.0 ppm; JCP = 76.9 Hz) with the phosphorus atom indicates that the NHC is located trans to the PPh₃ ligand. The CO stretching frequency of 8 of 1949 cm⁻¹ in the IR spectrum is higher than for 5. We correlate this value to the reduced electron density on the metal center (triazole is a weaker donor than a triazolylidene) of complex 8 compared to 5.

5.4 Ruthenium Catalyzed Ester Hydrogenolysis

Ruthenium catalyzed hydrogenolysis of esters

The application of 5 in the catalytic hydrogenolysis of esters was initially studied using methyl benzoate as the substrate, following the protocol as described by Beller and co-workers. When applying 30 mol% of KOTBu full conversion was observed within 6 hours at 100 °C under 50 bar of H₂ pressure in 1,4-dioxane (Table 1). The reaction time as well as the catalyst loading could be reduced to 2 hours and 0.75 mol%, respectively, without a decrease in yield (Table 1, entries 2-4). At lower pressure (5 bar) the system also converted methyl benzoate, albeit significantly slower (entries 5 and 6). The amount of base, on the other hand, proved to be crucial. The concentration could be reduced to 20 mol% (entry 2), but when 10 mol% of base was added (entry 3), only traces of benzyl alcohol were detected. Beller et al. also reported a sharp decrease in conversion at lower base concentrations (<20 mol%), but did not provide any explanation for this critical concentration of base. The experiments described below are conducted with 20 mol% of KOTBu, whereas the role of the base is investigated further in the next paragraph.
The substrate scope was expanded beyond methyl benzoate. The aliphatic ester n-butyl benzoate could be hydrogenated by complex 5 as well under the same reaction conditions (Table 2, entry 1). Longer alkyl chains did not provide a problem either: methyl stearate was nearly completely reduced to octadecanol within 2 hours (entry 2).

Methyl oleate, which contains both a carbon-carbon double bond and ester functionality, was subsequently tested in the ester hydrogenolysis catalyzed by 5 to test the chemoselectivity of the system (Table 2, entry 3). Almost full conversion of the unsaturated fatty carboxylic ester and formation of both the saturated and unsaturated product in a 2.6 : 1 ratio was observed. This indicates that the ester functionality is hydrogenated first. Saudan et al. reported this selectivity to a larger extent for their system, in which the double bond was only minimally affected (<99:1 ratio).\textsuperscript{19} They found that the ester reduction path is kinetically favored over the olefin hydrogenation. The triglyceride triolein was also converted, but many (often unidentified) products, including octadecanol (~5%) and oleyl alcohol (~4%), were detected using GC analysis.

**Table 1:** Methyl benzoate hydrogenolysis catalyzed by complex 5.

<table>
<thead>
<tr>
<th>(t) (h)</th>
<th>(p) (bar)</th>
<th>mol% KOTBu</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>50</td>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>50</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>50</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>50</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>18</td>
<td>5</td>
<td>20</td>
</tr>
</tbody>
</table>

Conditions: 0.5 mmol methyl benzoate, 1.5 mol% (entry 1) or 0.75 mol% of 5, indicated amount of KOTBu, pressure and reaction time in 1,4-dioxane at 100 °C. Conversion and yield were determined by GC analysis with \(p\)-xylene as internal standard.
The hydrogenation of the cyclic ester γ-valerolactone led to a moderate yield of 1,4-pentanediol (Table 2, entry 4). Carboxylic acids were incompatible with the system (entry 5 and 6), as even the activated acid trifluoroacetic acid (TFA) was not converted at all. This is probably due to the acid functionality neutralizing the base that is needed for the reaction, which was observed by a color change of the catalytic mixture from the characteristic bright orange to yellow upon addition of the substrate. As expected the methyl ester of TFA was completely converted to trifluoroethanol (entry 7). When phenyl benzoate was used as substrate no benzyl alcohol was detected on the GC, instead some transesterification products (tert-butyl benzoate and benzyl benzoate) were observed. This might be explained by the acidity of the formed phenol, neutralizing the required base.

Table 2: Substrate scope for hydrogenation catalyzed by complex 5.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Conv. (%)a</th>
<th>Product</th>
<th>Yield (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>93</td>
<td>OH</td>
<td>93</td>
</tr>
<tr>
<td>2</td>
<td>93</td>
<td>C17H35OH</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>98</td>
<td>C17H35OH</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C6H17OH</td>
<td>27</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>OH</td>
<td>54</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>OH</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>F3C-OH</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>100</td>
<td>F3C-OH</td>
<td>100</td>
</tr>
<tr>
<td>8</td>
<td>17</td>
<td>OH</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>100</td>
<td>OH</td>
<td>100</td>
</tr>
</tbody>
</table>

Conditions: 0.5 mmol ester, 0.75 mol% 5, 20 mol% of KOTBu, stirred under 50 bar H₂ in 1,4-dioxane at 100 °C for 2 hours. a.) Conversion and yield were determined by GC analysis with p-xylene as internal standard (entries 1-5 & 9) or by ¹⁹F NMR spectroscopy using 1,3-bis(trifluoromethane)benzene as internal standard (entry 6 & 7).
Last but not least, the sterically hindered tert-butyl benzoate was hydrogenated to benzyl alcohol within 2 hours (Table 2, entry 9). In fact, we found that this substrate was converted significantly faster than methyl benzoate. This finding is very remarkable, as very few ester hydrogenation catalysts are known to convert this substrate.\(^{19,37}\)

The role of KOtBu in the hydrogenolysis of esters

Catalyst 5 showed good activity in the hydrogenolysis of aryl esters, but only when 20 mol% of KOtBu was used (Table 1, entry 2 and 3). Also for alkyl esters the base dependence was apparent (93% conversion of methyl butyrate to n-butanol using 20 mol% KOtBu vs 4% using 10 mol%). It has been previously observed that base can be required or have a tremendous accelerating effect on the rate of catalytic hydrogenolysis of esters,\(^{15,17,36,38}\) yet the role of the base has hardly been investigated.\(^*\)

To obtain more insight in the role of the base in catalytic ester hydrogenolysis, we tested different bases (KOH, KHMDS, \(K_2CO_3\)). None of these were beneficial for the reaction and notably, even different batches of KOtBu led to varying results.

The amount of base (10 or 20 mol%) and catalyst (1.5 mol% or 0.75 mol%) was varied, leading to full conversion at 20 mol% KOtBu, whereas only traces of product (<2%) were observed for both catalyst loadings when 10 mol% base was applied. This indicates that 20 mol% base is required with respect to the ester and not the catalyst. For the reduction of \(N\)-benzylideneaniline (100% conversion to benzylaniline after 2 hours under 5 bar hydrogen pressure at 100 °C) no excess of KOtBu with respect to the substrate was necessary. These observations, together with the remarkable activity of complex 5 for tert-butyl benzoate led us to investigate whether transesterification to this substrate induced by KOtBu plays a role.

Stirring methyl benzoate with 20 mol% of KOtBu at 100 °C (without catalyst) led to formation of 8% tert-butyl benzoate, whereas with 10 mol% only traces (~1%) were observed. Thus, transesterification followed by hydrogenation of tert-butyl benzoate could be a plausible explanation for the need for 20 mol% of KOtBu. From Table 3 it becomes apparent that tert-butyl benzoate is hydrogenated significantly faster than the corresponding methyl ester (entry 1 and 2). Furthermore, methyl benzoate showed no conversion when KHMDS was applied as base, whereas the tert-butyl analogue was fully converted (entry 3 vs entry 5).\(^\dagger\)

\(^*\) Exceptions include Milstein and co-workers, who recently proposed a mechanism for Co-catalyzed ester hydrogenation involving the enolate form of the ester, which is only present (in equilibrium with the ester) under basic conditions.\(^{15}\) This mechanism is not suitable for our system, as this mechanism was based on the fact that the Co-catalyst did not convert “non-enolizable” esters (e.g. methyl benzoate and methyl trifluoracetate), whereas complex 5 does. According to Bergens et al. the base facilitates substitution of the alkoxide for \(H_2\) on the metal through deprotonation of the NH group in their proposed mechanism.\(^{38}\)
Table 3: Catalytic hydrogenation of methyl vs tert-butyl benzoate with complex 5.

<table>
<thead>
<tr>
<th>R=</th>
<th>base</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>KOtBu</td>
<td>53</td>
</tr>
<tr>
<td>tBu</td>
<td>KOtBu</td>
<td>99</td>
</tr>
<tr>
<td>Me</td>
<td>KHMDS</td>
<td>0</td>
</tr>
<tr>
<td>Me</td>
<td>KOtBu</td>
<td>66</td>
</tr>
<tr>
<td>tBu</td>
<td>KHMDS</td>
<td>100</td>
</tr>
<tr>
<td>tBu</td>
<td>KOtBu (10 mol%)</td>
<td>13</td>
</tr>
</tbody>
</table>

Conditions: 0.5 mmol ester, 0.75 mol% of 5, 20 mol% of KOtBu (except for entry 6), 50 bar H\textsubscript{2} in 1,4-dioxane at 100 °C for 2 hours. The experiments in entries 1-2 and 3-6 are performed with different batches of 5.† The yield was determined by GC analysis with p-xylene as internal standard.

Unfortunately, decreasing the amount of base for the substrate tert-butyl benzoate did result in a large decrease of conversion (Table 3, entry 6). Thus, although transesterification seems to play a role in the hydrogenation of esters with 5, it does not fully explain the need for the critical amount of base.

The effect of possible vacant sites on Ru in the hydrogenolysis of esters

The previously developed NHC Ru ester hydrogenation pre-catalysts either bear a halide co-ligand that is abstracted during the deprotonation of the benzylic arm on the ligand or, in case of the complexes that are viable at low hydrogen pressure, contain a CNN motif with a hemilabile nitrogen donor. Complex 5, on the other

†Remarkably, the yield of several entries containing the same conditions differ significantly, such as entry 1 vs entry 4 in Table 3 vs previous results from Table 1. These experiments were performed with different batches of complex 5. We therefore suspected these differences in activity of the pre-catalyst to be due to trace impurities in complex 5 that are not visible in the NMR spectra. Such an impurity could be silver salts that are still present after transmetallation. In control experiments wherein AgCl or AgBF\textsubscript{4} (1 mol%) was added to the catalytic mixture, no benzylalcohol was formed at all. Fluctuations in activity between different batches of 5 are consequently attributed to the presence of trace amounts of silver. Comparisons are made between experiments performed with the same batch of catalyst throughout the entire chapter.
hand, is completely coordinatively saturated, which might initially prevent it from entering the catalytic cycle. Hence, we attempted to create a vacant site on complex \(5\). When trimethylamine \(N\)-oxide (\(\text{Me}_3\text{NO}\); excess) was added to a solution of the complex in \(\text{CD}_2\text{Cl}_2\) in order to remove the carbonyl ligand as \(\text{CO}_2\), the \(^{31}\text{P} \text{NMR}\) spectrum exhibited a peak at 27 ppm, characteristic for free \(\text{Ph}_3\text{P}=\text{O}\). This indicates that the phosphine instead of the carbonyl moiety of \(5\) is oxidized and subsequently dissociates. The corresponding \(^1\text{H} \text{NMR}\) spectrum was unclear, presumably due to instability of the resulting unsaturated complex. Next, we added this reagent as an additive to the catalytic mixtures in ester hydrogenation trials (Table 4).

**Table 4:** The influence of additives on the catalytic hydrogenation of methyl benzoate.

<table>
<thead>
<tr>
<th>Additive</th>
<th>Conv (%)</th>
<th>Yield (%)</th>
<th>Additive</th>
</tr>
</thead>
<tbody>
<tr>
<td>(-)</td>
<td>62</td>
<td>49</td>
<td>(-)</td>
</tr>
<tr>
<td>(\text{Me}_3\text{NO})</td>
<td>67</td>
<td>66</td>
<td>(\text{Me}_3\text{NO})</td>
</tr>
<tr>
<td>(\text{Me}_3\text{NO})</td>
<td>57</td>
<td>56</td>
<td>(\text{Me}_3\text{NO})</td>
</tr>
</tbody>
</table>

The addition of \(\text{Me}_3\text{NO}\) (0.5 mol\%) led to slightly increased yield (Table 4, entry 1 vs 2). Interestingly, use of this additive allowed for the reduction of the amount of \(\text{KOTBu}\) to 10 mol\% without significant loss in yield (entry 3), yet when the amount of base was lowered to 2 mol\% no reaction occurred (entry 4). Increasing the amount of \(\text{Me}_3\text{NO}\) did not improve the results.

Complex \(8\), bearing the CNN motif with the potentially hemilabile triazole donor, could result in a vacant site on the Ru center upon decoordination of this moiety. In Table 5 the results of complex \(8\) vs complex \(5\) in methyl and \(\text{tert}\)-butyl benzoate hydrogenation have been compiled. As no significant differences between the conversion of the two pre-catalysts was observed, we conclude that either the 1,2,3-triazole donor is more strongly bound than anticipated (hence not displaying
hemilability) or this feature does not play a critical role in the rate determining step of this catalytic reaction.

**Table 5:** Catalytic hydrogenation of methyl vs tert-butyl benzoate with complex 5 and 8.

<table>
<thead>
<tr>
<th>R</th>
<th>cat</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>tBu</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>tBu</td>
<td>8</td>
</tr>
</tbody>
</table>

Conditions: 0.5 mmol ester, 0.75 mol% of catalyst, 20 mol% of KOtBu, 50 bar H₂ in 1,4-dioxane at 100 °C for 2 hours. The yield was determined by GC analysis with p-xylene as internal standard.

### 5.5 NMR Investigations of Complex 5 under Near-Catalytic Conditions

To gain more insight in the catalytically active species, ¹H NMR investigations were performed. A solution of complex 5 in THF-d₈ was studied under near-catalytic conditions (20 equiv. of KOtBu, 5 bar of H₂) in a J. Young pressure tube. At room temperature, the dearomatized complex 5' was present in solution according to the ¹H NMR spectrum (Scheme 5). After the tube was warmed at 100 °C for 2 hours, a mixture of products was detected by NMR spectroscopy at room temperature. In the ³¹P NMR spectrum four peaks were visible at 59.6, 22.9, 14.9 and -5.5 ppm, the latter being characteristic for free PPh₃. The hydridic region of the ¹H NMR spectrum is depicted in Figure 3 and suggests the presence of three hydride-containing Ru complexes (~1:1:1 ratio).

The doublet at -6.90 ppm has a large coupling constant Jₚₚ₃ of 122 Hz, which according to proton-coupled ³¹P NMR spectroscopy couples with the resonance at 23 ppm in the ³¹P spectrum. These values are in agreement with mutual trans arrangement of the hydride and PPh₃ and they compare well with those reported by Milstein et al. for a similar [(CNN)Ru(CO)H(PPh₃)] complex.²⁷ Since the phosphine and hydride ligand are attached trans to each other, the CNC ligand consequently must be coordinated in a mer fashion, which leads to the proposed
structure of 5A in Figure 3. Apparently, fac-mer isomerization of the flexible CNC chelate, for instance via a five-coordinated Ru species, is possible under these conditions. Attempts to induce this isomerization thermally without base were unsuccessful.

$^{1}$H-$^{1}$H COSY combined with $^{1}$H{$^{31}$P} NMR spectroscopy indicated that the hydride signals at -11.77 and -15.09 ppm (d, $^{2}$J$_{HH}$ = 8.4 Hz) belong to a Ru cis dihydride bearing no phosphine ligand (5B in Figure 3). The remaining two signals in the hydride region at -7.53 (1H) and between -8.67 and -9.11 ppm (2H) belong to complex 5C, which gives rise to the peak at 59.6 ppm in the $^{31}$P NMR spectrum. Based on integration and $^{1}$H-$^{1}$H COSY, $^{1}$H($^{31}$P) and $^{31}$P($^{1}$H) spectra and the observed patterns, which are indicative of an ABMX spin system, this species presumably concerns the trihydride species fac-5c (Figure 3). The peak at 14.9 ppm in the $^{31}$P NMR spectrum could not be assigned.

When the H$_{2}$ pressure was released, the mixture of species converted to the mer- and fac-ruthenium complexes 5A and 5’ in a ratio of approximately 2:1, which confirms that either 5B or 5C contain a mer coordinated CNC ligand, assuming that no fac-mer isomerization occurs at room temperature. However, more data (preferably single crystal X-ray diffraction) are required to verify the exact stereochemistry around the metal centers of 5B and 5C.

When applying 10 equivalents of KOrBu and H$_{2}$ to 5 the same species were observed in solution, albeit in a slightly different ratio (5A : 5B : 5C = 1.5 : 2 :1).
These NMR experiments provide initial insight in the potential structure of the active species during the catalytic hydrogenation of esters. Additionally, access to the meridional coordination mode of ligand 2 has been found.

5.6 Conclusions

Novel lutidine-derived CNC and CNN pincer ligands 2 and 3 bearing tzNHCs have been developed. The ligands could be conveniently synthesized using a one-pot multi-component reaction followed by methylation of the triazole ring. Coordination of these ligands via transmetalation of the corresponding Ag(I) complex led to the rare fac-[(L)Ru(H)(CO)(PPh₃)] complexes 5 and 8. According to DFT calculations this facial coordination mode is thermodynamically less stable than the mer form and presumably forms as the kinetic product under the reaction conditions. Planar coordination of the tridentate ligand was observed in the symmetric [(CNC)Pd(II)Cl] complex 6, which was also obtained via transmetalation. All complexes showed the expected (reversible) deprotonation/dearomatization reactivity upon addition of one equivalent of KOTBu.

The ruthenium complexes 5 and 8 were active pre-catalysts in the hydrogenolysis of a range of aromatic and aliphatic esters at 100 °C in the presence of 20 mol% KOTBu. Surprisingly, the sterically congested tBu-benzoate ester was converted more rapidly than the methyl analogue. Although transesterification of the substrate to the tert-butyl ester may play a role, the exact reason for the critical minimal amount of KOTBu remains unknown in spite of near-catalytic and high pressure in situ NMR spectroscopic investigations. Nevertheless, more insight in potentially active Ru hydride species in the catalytic ester hydrogenolysis reaction was obtained by these experiments.

5.7 Experimental

All reactions were carried out using standard Schlenk techniques under an atmosphere of dry nitrogen. Solvents were dried and distilled according to standard methods. Methyl benzoate was degassed and dried over 4 Å molsieves. All other chemicals were purchased from commercial suppliers and used without further purification. The NMR spectra were recorded on Varian Mercury 300 MHz, Bruker DRX Avance 300 and Bruker AMX 400 MHz spectrometers. ¹⁹F NMR was used to confirm the (non-coordinating nature of the) BF₄⁻ anion (-152 ppm). ¹H-¹H COSY and/or ¹H-¹³C HSQC NMR spectroscopy was used to assign the signals of several compounds. High resolution mass spectrometry was performed on a Bruker MicrOTOF-Q (ESI) GC analysis for esters was performed on a Thermo Scientific Trace GC Ultra equipped with a Restek RTX-200 column (30 m x 0.25 mm x 0.5 μm). Temperature program: Initial temperature 50 °C, hold for 4 min, heat to 130 °C with 30 °C/min, hold for 2 min, heat to 250 °C with 50 °C/min, hold for 9 min.
Inlet temperature 200 °C, split ratio of 60, 1 mL/min carrier flow, FID temperature 250 °C. GC analysis for fatty esters and benzoic acid was performed on a Thermo Scientific Trace GC Ultra equipped with a Restek Stabilwax-DA column (30 m x 0.25 mm x 0.25 μm). Temperature program: initial temperature 40 °C, heat to 175 °C with 6 °C/min, heat to 250 °C with 50 °C/min, hold for 18 minutes. Inlet temperature 280 °C, split ratio of 40, 1.5 mL/min carrier flow, FID temperature 250 °C. Conversion of trifluoroacetic acid and methyl trifluoroacetate were determined by 19F NMR spectroscopy using 1,3-bis(trifluoromethyl)benzene as internal standard.

**Synthesis of 3,3-[pyridine-2,6-diylbis(methylene)]bis(4-para-tolyl-1,2,3-triazole); 1.** To a solution of 2,6-bis(bromomethyl)pyridine (397 mg, 1.5 mmol) in DMF/H$_2$O (7.5 mL, 4:1) was added NaN$_3$ (205 mg, 3.1 mmol), para-tolylacetylene (357 mg, 3.1 mmol), Na$_2$CO$_3$ (159 mg, 1.5 mmol), CuSO$_4$.5H$_2$O (150 mg, 0.6 mmol) and sodium ascorbate (238 mg, 1.2 mmol). The reaction mixture was stirred at room temperature for 16 h, after which the suspension was poured into an EDTA/NH$_4$OH solution (100 mL, 0.5 M). The product was extracted with dichloromethane (3 x 15 mL) and washed with water (2 x 50 mL) and brine (50 mL). The organic phase was dried over MgSO$_4$ and concentrated in vacuo to yield the product as a white solid (480 mg, 1.1 mmol, 76%). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.85 (s, 2H, NC=CH), 7.75-7.65 (m, 6H, pyr-C$_6$H$_5$, Tol-C$_6$H$_5$), 7.22 (m, 8H, Pyr-C$_6$H$_5$, Tol-C$_6$H$_5$), 5.71 (s, 4H, C$_2$H$_4$), 2.40 (s, 6H, Tol-C$_3$H$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 155.0 (C$q$), 139.0 (Pyr-C$_6$H), 138.3 (C$q$), 136.1 (C$q$), 129.8 (Tol-CH$_2$), 127.7 (C$q$), 125.9 (Tol-CH$_2$), 122.2 (pyr-CH), 120.1 (tz-CH), 55.51(CH$_3$), 21.51(CH$_3$). MS(El$^+$) for C$_{25}$H$_{23}$N$_7$: m/z calculated 421.2009 [M$^+$], observed 421.2013.

**Synthesis of 3,3-[pyridine-2,6-diylbis(methylene)]bis(3-methyl-4-para-tolyl-1,2,3-triazolium) bistetrafluoroborate; 2.** Meerwein's salt ((Me$_3$O)BF$_4$, 137 mg, 0.92 mmol) was added to a solution of ligand 1 (155 mg, 0.37 mmol) in dichloromethane (10 mL) and the reaction mixture was stirred at room temperature for 16 h. A few drops of methanol were added to quench the reaction. The precipitate was collected on a glass frit and washed with small amounts of DCM and Et$_2$O, yielding the product as a white solid (185 mg, 0.30 mmol, 81%). $^1$H NMR (300 MHz, DMSO-d$_6$) δ 9.19 (s, 2H, NCHC), 8.08 (t, 3$^2$J$_{HH}$ = 7.8 Hz, 1H, Pyr-CH$_2$), 7.70 (d, 3$^2$J$_{HH}$ = 7.8 Hz, 2H, Pyr-CH$_2$), 7.54 (d, 3$^2$J$_{HH}$ = 8.0 Hz, 4H, Tol-CH$_2$), 7.37 (d, 3$^2$J$_{HH}$ = 8.0 Hz, 4H, Tol-CH$_2$), 6.07 (s, 4H, CH$_2$), 4.22 (s, 6H, N-CH$_2$), 2.40 (s, 6H, Tol-CH$_2$); $^{13}$C NMR (75 MHz, acetonitrile-d$_3$) δ 152.6, 144.2, 143.4 (C$q$), 140.7 (pyr-CH), 131.0, 130.1 (Tol-CH), 130.0 (tz-CH), 124.9 (Pyr-CH), 120.1 (C$q$), 58.2 (CH$_3$), 39.6 (N-CH$_2$), 21.5 (CH$_3$). MS(CSI$^+$) for C$_{27}$H$_{29}$N$_7$BF$_4$: m/z calculated 538.2513 [M-BF$_4$]$^+$, observed 538.2482.
Synthesis of 3,3-[pyridine-2,6-diylbis(methylene)](4-para-tolyl-1,2,3-triazolyl) (3-methyl-4-para-tolyl-1,2,3-triazolium) tetrafluoroborate; 3. Meerweins’ salt ((Me₂O)BF₄, 126 mg, 0.85 mmol) was added to a solution of ligand I (360 mg, 0.85 mmol) in DCM (30 mL) and the reaction mixture was stirred at room temperature for 16 h. A few drops of methanol were added to quench the reaction. After the solvent was removed under reduced pressure, the product was purified by column chromatography (SiO₂, DCM:acetone = 1:1) yielding the product (151 mg, 0.29 mmol, 34%) as a white powder.

Reduced pressure, the product was purified by column chromatography (SiO₂, DCM:acetone = 1:1) yielding the product (151 mg, 0.29 mmol, 34%) as a white powder. After the solvent was removed under reduced pressure, the product was purified by column chromatography (SiO₂, DCM:acetone = 1:1) yielding the product (151 mg, 0.29 mmol, 34%) as a white powder. After the solvent was removed under reduced pressure, the product was purified by column chromatography (SiO₂, DCM:acetone = 1:1) yielding the product (151 mg, 0.29 mmol, 34%) as a white powder.

Synthesis of [Ag(CNC)]BF₄; 4. Ag₂O (87 mg, 0.3 mmol) was added to a solution of ligand 3 (95 mg, 0.15 mmol) in acetone (10 mL) in a Schlenk flask charged with 4Å molsieves. The resulting suspension was stirred for 2 days at room temperature during which it changed color to pale grey/brown. The mixture was filtered over Celite (to obtain good yields the filtrate was thoroughly flushed with MeOH and acetone) and dried in vacuo yielding the product (87 mg, 0.13 mmol, 90%) as a pale yellow solid. The compound was stored under nitrogen and with exclusion of light. 

Synthesis of [Ru(CO)(H)(PPh₃)(CNC)]BF₄; 5. A mixture of silver complex 4 (78.2 g, 0.12 mmol) and [RuHCl(CO)(PPh₃)₂] (115 g, 0.12 mmol) in THF (8 mL) was heated at 55 °C for 2 days. The resulting pale brown suspension was filtered, evaporated to dryness and extracted with MeOH (2 × 5 mL). The solvent was evaporated, and the product was obtained by precipitation from DCM with Et₂O as pale beige powder (76.2 mg, 0.08 mmol, 68%). IR ν(CO) 1926 cm⁻¹; ³¹P {¹H} NMR (162 MHz, CD₂Cl₂) δ 46.7; ¹H NMR (400 MHz, CD₂Cl₂) δ 7.94 (t, δ JHH = 7.7 Hz, 1H, Pyr-CH), 7.76 (d, δ JHH = 7.5 Hz, 1H, Pyr-CH), 7.58 – 7.12 (m, 16H, PPh₃ & Pyr-CH), 6.97 (d, δ JHH = 2.8 Hz, 4H, Tol-CH), 6.90 (d, δ JHH
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= 7.8 Hz, 2H, Tol-CH), 6.53 – 6.44 (m, 3H, Tol-CH & CH2) 6.05 (d, Jcp = 13.8 Hz, 2H, CH2), AB system centered at δH 5.51 (d, JHH = 15.7 Hz, 1H, CH2) & δH 4.82 (d, JHH = 15.7 Hz, 1H, CH2), 3.73 (s, 3H, N-CH3), 3.54 (s, 3H, N-CH3), 2.46 (s, 3H, Tol-CH3), 2.40 (s, 3H, Tol-CH3), -7.04 (d, Jph = 28.9 Hz, 1H, Ru-H): 13C NMR (101 MHz, CD2Cl2) δ 208.51 (d, Jcp = 14.8 Hz, Ru-CO), 172.2 (d, Jcp = 7.2 Hz, CznH2), 164.9 (d, Jcp = 75.7 Hz, CznH2) 155.4 & 155.2 (Pyr-C), 148.7 (Pyr-CH), 148.3 (d, Jcp = 7.1 Hz, PPh3,CH3) 139.6 (d, Jcp = 6.0 Hz, PPh3-CH3) 138.1 (Pyr-CH), 136.7 (d, Jcp = 38.0 Hz, PPh3-CH3), 136.2, 134.3, 133.7, 133.5, 132.61, 131.8, 131.7, 130.2 (Tol-CH), 129.4 (Tol-CH), 129.3, 129.2, 129.1, 128.9, 128.4 (d, Jcp = 7.7 Hz, 6 CH arom, PPh3), 128.3, 128.1, 128.0, 127.9, 127.4, 127.4, 125.3, 125.1, 125.0, 124.3, 124.1, 61.5 (CH2), 58.3 (CH2), 37.0, 36.8 (N-CH3), 21.4, 21.1 (Tol-CH3). MS(CSI+) for C46H43NNOPRu: m/z calculated 842.2323 [M-H-BF4]+ observed 842.2323.

Synthesis of [Pd(CNC)(Cl)]BF4. 6. To a solution of complex 4 (75 mg, 0.12 mmol) in MeCN (7 mL) was added [Pd(NCPh)2Cl2] (45 mg, 0.10 mmol) and the resulting mixture was stirred for 2 h. The resulting suspension was filtered over Celite and the solvent was removed under reduced pressure. The product was precipitated from DCM with pentane to obtain the product as a yellow solid (72 mg, 0.11 mmol, 92%). 1H NMR (300 MHz, acetone-d6) δ 8.40 (t, JHH = 7.8 Hz, 1H, Pyr-CH), 8.22 (d, JHH = 7.8 Hz, 2H, Pyr-CH), 7.61 (d, JHH = 7.9 Hz, 4H, Tol-CH), 7.24 (d, JHH = 7.9 Hz, 4H, Tol-CH), 6.26 (s, 3H, CH3), 4.16 (s, 6H, N-CH3), 2.35 (s, 6H, CH3); 1H NMR (300 MHz, CD2Cl2) δ 8.27 (t, JHH = 7.7 Hz, 1H, Pyr-CH), 7.97 (d, JHH = 7.7 Hz, 2H, Pyr-CH), 7.48 (d, JHH = 7.8 Hz, 4H, Tol-CH), 7.29 (d, JHH = 7.8 Hz, 4H, Tol-CH), AB system centered at δH 6.10 (d, JHH = 15.1 Hz, 1H, CH2) & δH; 5.98 (d, JHH = 14.8 Hz, 1H, CH2), 4.02 (s, 6H, N-CH3), 2.42 (s, 6H, CH3); 13C NMR (75 MHz, CD2Cl2) δ 168.0 (CznH2), 154.2, 148.3, 146.5 (Cq), 142.5 (Pyr-CH), 140.9 (Cq), 130.9, 129.4 (Tol-CH), 127.24 (Pyr-CH), 123.7 (Cq), 59.38 (CH3), 37.65 (N-CH3), 21.61 (CH3). MS(CSI+) for C46H43NNOPRu: m/z calculated 590.1058 [M-BF4]+ observed 590.1012.

General procedure for deprotonation/dearomatization of complexes: To a solution of the CNC complex (1 equiv.) in THD-d8 was added KOTBu (1 equiv.) upon which an immediate color change to dark-red was observed.

[[CNC®Ru(CO)(H)(PPh3)]: 5°. Dark-red solution. Low stability of the complex prevented its isolation and full characterization. 31P {1H} NMR (162 MHz, THF-d8) δ 55.3; 1H NMR (300 MHz, THF-d8) δ 7.74 – 7.04 (m, 19H, PPh3 & 4H Tol-CH), 6.93 (d, JHH = 7.8 Hz, 2H, Tol-CH), 6.64 (d, JHH = 7.7 Hz, 2H, Tol-CH), 6.12 (d, JHH = 13.1 Hz, 1H, CH2), 5.90 (d, JHH = 8.0 Hz, 1H, Pyr-CH), 5.57 – 5.43 (m, 2H, CH and Pyr-CH overlapping), 5.13 (d, JHH = 13.1 Hz, 1H, CH2), 4.90 (d, JHH = 8.8 Hz, 1H, Pyr-CH), 4.02 (s, 3H, N-CH3), 3.17 (s, 3H, N-CH3), 2.42 (s, 3H, Tol-CH3), 2.39 (s, 3H, Tol-CH3), -7.19 (d, JHH = 21.9 Hz, 1H, Ru-H); 13C NMR (75 MHz,THF) δ 138.8 (Cq), 137.6 (d, Jcp =12.1 Hz, PPh3), 134.8, 110.
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133.8, 133.7, 133.6, 133.4, 131.8 (d, \( J_{CP} = 9.5 \) Hz, PPh\(_3\), 131.3, 130.6 (pyr-CH), 130.3, 129.4, 128.7, 128.4, 128.3, 128.2, 128.0, 127.5, 127.4 (d, \( J_{HH} = 4.5 \) Hz, PPh\(_3\), 126.9, 126.7, 116.8 (Pyr-CH), 100.4 (Pyr-CH), 94.5 (CH), 64.1 (CH\(_2\)), 35.6 (N-CH\(_3\), 34.5 (N-CH\(_3\)), 20.4 (Tol-CH\(_3\)), 20.3 (Tol-CH\(_3\)).

\([(\text{CNC}^6)\text{Pd(Cl)}] \cdot 6\). Dark-red solution. \(^1\)H NMR (300 MHz, THF-d\(_8\)) \( \delta \) 7.44 (d, \( J_{HH} = 8.0 \) Hz, 2H, Tol-CH\(_3\)), 7.35 (d, \( J_{HH} = 8.0 \) Hz, 2H, Tol-CH\(_3\)), 7.15 – 7.01 (m, 4H, Tol-CH\(_3\)), 6.45 (dd, \( J_{HH} = 9.0 \) Hz, 6.1 Hz, 1H, Pyr-CH), 6.27 (s, 1H, CH\(_3\)), 6.10 (d, \( J_{HH} = 9.0 \) Hz, 1H, Pyr-CH), 5.70 (d, \( J_{HH} = 6.2 \) Hz, 1H, Pyr-CH), AB system centered at \( \delta \_A \) 5.28 (d, \( J_{HH} = 14.2 \) Hz, 1H, CH\(_3\)) & \( \delta \_B \) 5.11 (d, \( J_{HH} = 12.7 \) Hz, 1H, CH\(_3\)), 3.96 (s, 3H, 1H, NCH\(_3\)), 3.80 (s, 3H, NCH\(_3\)), 2.32 (s, 6H, CH\(_3\)).

Synthesis of [Ag(CNN)]BF\(_4^–\). 7. This complex was synthesized in analogy to complex 4 from ligand 3. Pale beige solid (58 mg, 0.05 mmol, 78%) \(^1\)H NMR (300 MHz, methanol-d\(_4\)) \( \delta \) 7.99 (s, 1H), 7.72 (t, \( J_{SH} = 7.7 \) Hz, 1H, Pyr-CH), 7.43 (d, \( J_{HH} = 7.9 \) Hz, 1H, Pyr-CH), 7.34 (d, \( J_{HH} = 8.0 \) Hz, 2H, Tol-CH\(_3\)), 7.28 (d, \( J_{HH} = 8.0 \) Hz, 2H, Tol-CH\(_3\)), 7.20 (d, \( J_{HH} = 7.9 \) Hz, 1H, Pyr-CH), 7.16 (d, \( J_{HH} = 7.8 \) Hz, 2H, Tol-CH\(_3\)), 6.96 (d, \( J_{HH} = 7.8 \) Hz, 2H, Pyr-CH), 5.61 (s, 2H, CH\(_2\)), 5.38 (s, 2H, CH\(_2\)), 4.01 (s, 3H, NCH\(_3\)), 2.45 (s, 3H, Tol-CH\(_3\)), 2.30 (s, 3H, Tol-CH\(_3\)); \(^{13}\)C NMR (101 MHz, methanol-d\(_4\)) \( \delta \) 154.2, 154.1, 148.4 (C\(_q\)), 139.6 (Pyr-CH), 138.6 (Tol-CH), 138.2 (Tol-CH), 137.6, 131.7, 129.7, 129.1, 128.9, 128.9, 127.0, 124.9, 124.8, 124.5, 122.0, 121.8 (C\(_q\)), 47.9, 47.5 (CH\(_3\)), 36.2 (N-CH\(_3\)), 19.9 (Tol-CH\(_3\)), 19.7 (Tol-CH\(_3\)). MS(CSLI) for \( \text{C}_{52}\text{H}_{50}\text{AgN}_{14} \): m/z calculated 979.3390 [\( \text{L}_2\text{Ag-BF}_4^+ \)], observed 979.3445.

Synthesis of [Ru(CO)(H)(PPh\(_3\))(CNN)]BF\(_4^–\). 8. This complex was synthesized in analogy to complex 5 from Ag(I) complex 7 (0.5 equiv). Pale beige powder (23 mg, 0.025 mmol, 64%) IR v(CO) 1949 cm\(^{-1}\). \(^{31}\)P \(^1\)H NMR (162 MHz, CDCl\(_3\)) \( \delta \) 40.9; \(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 8.59 (s, 1H, tz-CH), 7.90 (t, \( J_{HH} = 7.7 \) Hz, 1H, Pyr-CH), 7.78 – 7.64 (m, 4H, Tol-CH\(_3\)), 7.59 – 7.14 (m, 20H, Tol-CH\(_3\), PPh\(_3\) and Pyr-CH overlapping), 7.07 – 6.95 (m, 1H, Pyr-CH), 6.18 (d, \( J_{HH} = 13.7 \) Hz, 1H, CH\(_2\)), 6.07 (d, \( J_{HH} = 15.4 \) Hz, 1H, CH\(_2\)), 5.90 (d, \( J_{HH} = 14.1 \) Hz, 1H, CH\(_2\)), 4.82 (d, \( J_{HH} = 15.8 \) Hz, 1H, CH\(_2\)), 3.79 (s, 3H, CH\(_3\)), 2.60 (s, 3H, CH\(_3\)), 2.46 (s, 3H, CH\(_3\)), -12.96 (d, \( J_{HH} = 27.9 \) Hz, 1H, Ru-H); \(^{13}\)C NMR (101 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 166.0 (d, \( J_{CP} = 76.9 \) Hz, C\(_{ntz-NHC}\)), 155.7 & 154.2 (Pyr-C\(_q\)), 148.5, 148.4, 139.8 (d, \( J_{CP} = 3.7 \) Hz, PPh\(_3\)), 138.4, 133.7, 133.6, 132.9, 132.8, 131.2, 129.7, 129.2, 129.2, 129.1, 128.5, 128.5, 128.4, 128.3, 128.2, 127.1, 126.6, 125.7, 124.8, 124.4, 123.9 (tz-CH), 60.8 & 54.4 (CH\(_3\)), 36.6 (N-CH\(_3\)), 21.3 (Tol-CH\(_3\)), 21.0 (Tol-CH\(_3\), Ru-CO not observed. MS(FD\(^+\)) for \( \text{C}_{45}\text{H}_{42}\text{N}_{40}\text{OPRu} \): m/z calculated 828.22104 [\( \text{M-BF}_4^+ \)] , observed 828.21537.
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General procedure for catalytic ester hydrogenation reactions: The catalyst (3.75 μmol), KOtBu (11 mg, 0.1 mmol for 20 mol%), ME₃NO (if applicable, 1.9 mg) and the substrate (if solid; 0.5 mmol) were weighed in a 4 mL GC-vial with a septum screw-cap charged with a stirring bar under an N₂ atmosphere. Subsequently, p-xylene (23.2 μL), the substrate (if liquid; 0.5 mmol) and THF (2 mL) were added. A needle was used to puncture the cap and a set of four vials was placed in a stainless steel autoclave (200 mL) under argon gas. The autoclave was flushed 2 times with 10 bar of H₂ and then pressurized to the desired pressure (5 or 50 bar), after which it was placed in a preheated oil bath (140 °C; built-in thermometer indicated 100 °C as the internal temperature of the autoclave). After allowing the autoclave to warm up (approximately 30 min.) the mixture was stirred for 2h after which the autoclave was cooled in an ice bath and the pressure was released. The conversions were determined by GC analysis.

NMR experiment on the effect of possible vacant sites on Ru in the hydrogenolysis of esters. Trimethylamine N-oxide (Me₃NO; 5 mg, 0.07 mmol) was added to a solution of complex 5 (10 mg, 0.01 mmol) dissolved in CD₂Cl₂ (1 mL) under N₂ atmosphere and stirred for 18 hours. The resulting solution was characterized by NMR spectroscopy as is described in paragraph 5.5.

NMR experiments under near-catalytic conditions: Complex 5 (~20 mg) was dissolved in THF-d₈ (0.6 mL) and KOtBu was added (0, 10 or 20 equiv.) under nitrogen atmosphere. The mixture was transferred to a J. Young NMR pressure tube and pressurized with 5 bar H₂, after which a ¹H NMR spectrum was recorded. The tube was subsequently heated in an oil bath at 100 °C for two hours and analyzed by multinuclear NMR spectroscopy at room temperature.

5.7 References
(11) Korstanje, T. J.; van der Vlugt, J. I.; Elsevier, C. J.; de Bruin, B. 2015, manuscript submitted.


Chapter 6

Synthesis of Chiral BINAM-based di-tzNHC Complexes and Application in Rh Catalyzed Enantioselective Hydrosilylation

Abstract

Despite the prolific use of (di-)NHC complexes in homogeneous catalysis, there are relatively few reports of their successful application in asymmetric transformations. In this chapter the atropisomeric binaphthyl backbone is combined with readily accessible 1,2,3-triazolylidene groups to obtain a strongly electron-donating $C_2$-symmetric ligand. The target ligand was efficiently synthesized in a three step synthesis with an overall yield of 91% starting from commercially available starting materials. The corresponding di-NHC silver(I), palladium(II), rhodium(I) and iridium(I) complexes were synthesized and characterized. The Rh(I) complex 5 was applied in the catalytic asymmetric hydrosilylation of ketones, providing good conversions at catalyst loadings as low as 0.2 mol% and giving chiral inductions of up to 51% ee.

6.1. Introduction

Enantioselective catalysis is one of the key areas in homogeneous catalysis. It enables the production of chiral molecules, needed for many purposes, mostly bio-related applications. Most catalytic enantioselective reactions are facilitated by well-defined metal complexes bearing chiral ligands. In contrast to the successful application of a wide range of chiral phosphorus-based ligands for a variety of enantioselective transformations, efforts to induce chirality by means of chiral N-heterocyclic carbene (NHC) ligands have met with only limited attention and success. This is remarkable considering the continued popularity of NHCs in homogeneous catalysis. The relatively few transition metal complexes of chiral (di-)NHCs applied in enantioselective transformations have been described in recent reviews\(^1\)-\(^4\) and some general strategies in ligand design have been put forward, that are depicted in Figure 1.\(^4\)

![Figure 1](image)

**Figure 1**: General structure of selected examples of chiral NHC metal complexes illustrating different design strategies. **A**: Chirality in N-substituents,\(^5\) **B**: Chirality in backbone, **C**: Heteroditopic bidentate coordination of the ligand with axial chirality in linker, **D**: \(C_2\)-symmetric di-NHC complex with chirality in the linker. In box: general structure of the target complexes in this chapter.

As the imidazole ring itself is inherently planar, the most convenient way of introducing chirality in these ligands is via the incorporation of chiral substituents either at the nitrogen atoms or on the backbone of the NHC (Figure 1, A and B). The latter approach was, amongst others, suitable for Ru catalysts active in ring-closing metathesis.\(^6\) Although good results were achieved with such catalysts, the general design for these types of ligands proved to be ineffective. This has been attributed to the dynamic nature of the N-substituents on an NHC: the nitrogen substituents can rotate freely and rotation is also possible around the M-C\(_{\text{NHC}}\) bond. This causes the chiral space to be ill-defined, which hampers adequate chiral induction during transfer of relevant reactant moieties to coordinated substrates.\(^3\) Incorporation of chiral auxiliaries or stereogenic centers in the remote locations on the backbone often results in poor chiral induction at the metal center.\(^7\) Therefore, very large substituents are required to ensure efficient chiral definition using these approaches.\(^3,7\)
As has been argued throughout this thesis, bidentate ligands provide more rigid (chiral) environments around the metal center compared to their monodentate analogues.\textsuperscript{8,9} Several such chiral bidentate ligands consist of an NHC donor in combination with another hetero-atom donor.\textsuperscript{10–17} An example of such a ‘hybrid’ system is Burgess’ oxazoline functionalized NHC iridium hydrogenation catalyst (Figure 1, C).\textsuperscript{18} This system is active in the hydrogenation of unfunctionalized alkenes under 1 bar of H\textsubscript{2} with excellent enantiomeric excesses (ee). Furthermore, the group of Bellemin and Gade reported a similar NHC-oxazoline rhodium complex that catalyzed hydrosilylation of even the challenging dialkyl ketones enantioselectively.\textsuperscript{19}

Lastly, chelated di-NHC catalysts have been used for enantioselective transformations (Figure 1, D).\textsuperscript{11–16,20} In particular, the catalysts reported by Shi et al. have been successfully employed in several reactions.\textsuperscript{21–34} High ee’s were obtained in a range of catalytic reactions, including hydrosilylation of ketones and esters,\textsuperscript{35,36} addition of arylboronic acids to N-Boc imines\textsuperscript{37,38} and umpolung allylation aldehydes with cyclohexenyl acetate.\textsuperscript{39}

Inspired by this C\textsubscript{2}-symmetric system, we set out to combine the success of the atropisomeric binaphthyl backbone with the straightforward synthetic (”click” chemistry-based) routes available for 1,2,3-triazolylidenes.\textsuperscript{40,41} This could allow for the development of a modular toolbox of chiral di-NHC ligands based on this motif. The superior donor-strength of triazolylidenes over imidazole-2-ylidenes might prove critical in the pursuit of successful enantioselective catalysis where oxidative addition reactivity is rate-limiting. Here, we describe the synthesis and coordination chemistry of the first chiral di(1,2,3-triazolylidene) ligand (Figure 1, box), based on 2,2’-diamino-1,1’-binaphthylene (BINAM) as well as its application in Rh-catalyzed hydrosilylation of ketones.

### 6.2. Synthesis of C\textsubscript{2}-symmetric di-tzNHC Ligand

To warrant the most efficient chiral induction, the triazoles are introduced directly at the 2 and 2’ positions of the binaphthyl moiety, closest to the atropisomeric center. We decided to connect the triazole to the binaphthyl unit through the nitrogen atoms as the commercially available enantiopure BINAM is easily converted into the corresponding bis-azide via nucleophilic aromatic substitution. Besides, this route has the advantage of extending the scope of viable substituents to include alkyl groups at the heterocycle without having to use hazardous alkyl azides.

The desired ligand 3 could be synthesized from commercially available chiral (R)-BINAM, which was first reacted with tert-butyl nitrite, to generate the diazonium intermediate and subsequently with trimethylsilyl azide to obtain bis-azide 1 in 96% yield (Scheme 1). Substitution of the diazonium fragment proceeds via an S\textsubscript{N}1-
mechanism, generating a carbocation, which may decrease the steric interaction between the 2 and 2' positions of the binaphthyl system and might consequently lead to racemization. To suppress this process, the (R)-2,2'-diamino-1,1'-binaphthalene solution was cooled to -15 °C prior to the addition of both reagents. Analysis using chiral high-performance liquid chromatography (HPLC) indicated that the enantiomeric excess of the product 1 was >99% ((R)-enantiomer).

The formation of the desired bis-azide was confirmed using ¹H NMR, ¹³C NMR, infrared (IR) spectroscopy and high resolution mass spectrometry (HR-MS). Most indicative for the formation of the product was the disappearance of the signals around 3500 cm⁻¹ in the IR spectrum, ascribed to the amine functionality, and the appearance of a sharp peak at 2098 cm⁻¹, characteristic of the azide group.

Bis-azide (R)-1 was reacted with an alkyne to afford bis-triazole (R)-2 via a copper catalyzed ‘click’-reaction (Scheme 1). An aromatic acetylene was selected for this [3+2] cycloaddition, because aromatic groups stabilize the NHC formed in the corresponding complexes. After screening several solvent systems, performing the reaction in an acetonitrile/water mixture (4:1) and in the presence of triethylamine resulted in 95% yield of (R)-2 after column chromatography. Interestingly, the intermediate product containing only one triazole ring and one azide moiety was neither isolated nor observed by ¹H NMR spectroscopy. This implies that the second ‘click’ reaction is much faster than the first reaction, which might be

Scheme 1: Synthesis of chiral ditriazolium salt 3. i) tBuONO, TMSN₃, MeCN, -15 °C, 40h, ii) p-tolyl acetylene, CuSO₄,SH₂O, sodium ascorbate, NEt₃, MeCN : H₂O (4:1), 50 °C, 60h, iii) MeOTf, DCM, -78 °C → rt, 12h.

The formation of the desired bis-azide was confirmed using ¹H NMR, ¹³C NMR, infrared (IR) spectroscopy and high resolution mass spectrometry (HR-MS). Most indicative for the formation of the product was the disappearance of the signals around 3500 cm⁻¹ in the IR spectrum, ascribed to the amine functionality, and the appearance of a sharp peak at 2098 cm⁻¹, characteristic of the azide group.

Bis-azide (R)-1 was reacted with an alkyne to afford bis-triazole (R)-2 via a copper catalyzed ‘click’-reaction (Scheme 1). An aromatic acetylene was selected for this [3+2] cycloaddition, because aromatic groups stabilize the NHC formed in the corresponding complexes. After screening several solvent systems, performing the reaction in an acetonitrile/water mixture (4:1) and in the presence of triethylamine resulted in 95% yield of (R)-2 after column chromatography. Interestingly, the intermediate product containing only one triazole ring and one azide moiety was neither isolated nor observed by ¹H NMR spectroscopy. This implies that the second ‘click’ reaction is much faster than the first reaction, which might be
caused by ligation of the copper catalyst to the initially formed triazole, resulting in a favorable proximity effect for the conversion of the remaining azide.\textsuperscript{42}

Lastly, the desired ligand, bis-triazolium salt (R)-3, was obtained by methylation of (R)-2 (Scheme 1). Methyl iodide is most often used for methylation of NHCs. However, we previously noted (see previous chapters) that methyl iodide is generally not nucleophilic enough to effectively methylate a triazole ring in high yields.\textsuperscript{43} Therefore, methyl triflate was applied in this step, leading to (R)-3 in quantitative yield after evaporation of the excess reagent. The triazolium salt was identified in the \textsuperscript{1}H NMR spectrum by a substantial downfield shift of the triazole peak to 8.71 ppm compared to (R)-2 (\(\Delta\delta = 0.62\) ppm) and the appearance of a signal at 4.04 ppm for the methyl groups. A small downfield shift of the triazolyldienium carbon atom was also observed by \textsuperscript{13}C NMR spectroscopy.

Overall, ligand precursor (R)-3 could be synthesized in three steps starting from the commercially available bis-amino precursor with an overall yield of 91\%. The synthetic route is deemed quite efficient, while still allowing facile ligand modification. The (S)-enantiomer was also successfully synthesized using the same route with similar results.

6.3. Chiral di-tzNHC Complexes

\textit{Synthesis and characterization of chiral di-tzNHC Ag(I) complex}

Silver complex 4 was synthesized in a similar fashion as di-NHC silver complexes described in Chapters 2 and 3 (Scheme 2), by stirring the ligand with Ag\(_2\)O in acetonitrile at room temperature. To drive the reaction to completion 4 Å molecular sieves were added to the reaction mixture.

\textbf{Scheme 2: Synthesis of silver(I) complex (R)-4.}

The formation of silver (I) complex (R)-4 was confirmed by the disappearance of the hydrogen signal of the triazolium ring in the \textsuperscript{1}H NMR spectrum. The protons of the ligand were observed in pairs of equivalent protons in the \textsuperscript{1}H NMR spectrum, indicating that the complex is still \(C_2\)-symmetric. The exact mass of the parent ion obtained from HR-CSI-MS suggests a dimeric structure for this complex,
(corresponding to a \([M_2L_2\text{-2OTf}]^{2+}\) fragment). Unfortunately, no single crystals suitable for X-ray diffraction have been obtained to support this assumption.

A pair of doublets was observed in the \(^{13}\text{C}\) NMR spectrum at characteristic carbene shifts (\(\delta = 167.2\) ppm, \(J_{107}^{\text{AgC}} = 171.2\) Hz and \(J_{109}^{\text{AgC}} = 197.5\) Hz).\(^{44,45}\) These well resolved Ag-C\(_{NHC}\) couplings indicate a strong bond between the metal and the carbene in solution.\(^{45}\) Attempts to transmetalate complex \((R)-4\) to e.g. palladium(II) were unsuccessful, which is likely due to this strong Ag-C bond. Therefore, we turned to a direct deprotonation route to obtain other chiral di-tzNHC metal complexes.

**Synthesis and characterization of chiral di-tzNHC Ir(I), Rh(I) and Rh(III) complexes**

Rhodium(I) 1,5-cyclooctadiene (cod) complex \((R)-5\) was synthesized via direct deprotonation of the ligand with KOTBu in the presence of half a molar equivalent of \([\text{Rh(cod)}\text{Cl}]_2\) (Scheme 3). The resulting complex was purified using column chromatography with regular silica and non-dried solvents, leading to an isolated yield of 80\%, which illustrates the high stability of the complex towards water and aerobic conditions. The \(^1\text{H}\) NMR spectrum of \((R)-5\) indicated \(C_2\)-symmetry, as each signal must be assigned to two equivalent protons for the ligand as well as the cod fragment. Coupling of the rhodium with the carbene carbon is observed at 173.2 ppm (\(J_{\text{RhC}} = 50.9\) Hz) in the \(^{13}\text{C}\) NMR spectrum, which is in accordance with the shifts and coupling constants found in rhodium di-tzNHC\(^{46}\) and aryl-linked NHC-tzNHC complexes (Chapter 4). ESI HR-MS detection of the correct mass (minus the triflate anion) confirmed the formation of the desired mononuclear species. In contrast to Shi et al.,\(^{35}\) we did not observe the formation of dinuclear species, which explains the lower yield (25\%) in their case.

![Scheme 3: Synthesis of rhodium(I)- and iridium(I)(cod) complexes (R)-5 and (R)-6.](image)

Iridium complex \((R)-6\) was prepared using the same procedure as for \((R)-5\), using the corresponding \([\text{Ir(cod)}\text{Cl}]_2\) precursor (Scheme 3). Full conversion of the ligand was observed after three hours. The isolated yield for the desired complex after
regular column chromatography is significantly lower (21%) than for the analogous rhodium complex \((R)-5\). This may indicate that the iridium species is inherently less stable than the rhodium species or more sensitive under the chosen work-up conditions. Again, the formation of the desired \(C_2\)-symmetric Ir(I) complex was confirmed by \(^1\text{H}\) and \(^{13}\text{C}\) NMR and HR-MS analysis. The NHC carbon peak was observed at 170.7 ppm in the \(^{13}\text{C}\) NMR spectrum. This value is quite low field compared to the tzNHC peak of the \([\text{Ir(tzNHC-CH}_2\text{-tzNHC})(\text{cod})]\)\(X\) complex from Chapter 4 (162.5 ppm),\(^{43}\) which can be attributed to the slightly electron withdrawing binaphthyl linker.

To assess the electron-donating capabilities of the novel di-tzNHC ligand, Rh(I) carbonyl complex \((R)-7\) was synthesized by stirring complex \((R)-5\) under 5 bar of syngas pressure (Scheme 4). Characterization of the resulting complex revealed the formation of the desired species with preservation of the \(C_2\)-symmetry. Two doublets are observed in the \(^{13}\text{C}\) NMR spectrum at 185.5 ppm (\(J_{\text{RhC}} = 56.8\) Hz) and 161.8 ppm (\(J_{\text{RhC}} = 43.7\) Hz) that correspond to the carbonyl carbon and tzNHC-carbon, respectively. The rhodium-carbon coupling constant is smaller than was observed in complex \((R)-5\), which is attributed to the presence of the strongly π-accepting CO ligands.

**Scheme 4:** Synthesis of Rh(I) carbonyl complex \((R)-7\) and Rh(III) complex \((R)-8\). The possible (symmetric and asymmetric) isomers of \(8\) are represented in the box.
The IR adsorption spectrum of (R)-7 showed two adsorption bands ($\nu_{\text{CO}} = 2066$ cm$^{-1}$ and 2005 cm$^{-1}$) for the carbonyl ligands, which is in line with the frequencies found for the ligands described in Chapter 4 ($2075 < \nu_{\text{CO}} < 2005$ cm$^{-1}$). Furthermore, these values correspond to strong electron-donating properties for the di-tzNHC (R)-3 ligand compared to BINAP (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl; $\nu_{\text{CO}} = 2094$ and 2048 cm$^{-1}$) chiral di-imidazolylidene and di-benzimidazolylidene ligands ($2086 < \nu_{\text{CO}} < 2011$ cm$^{-1}$) and the “i-bitz” ligand ($2076 < \nu_{\text{CO}} < 2019$ cm$^{-1}$).

The rhodium(III) complexes reported as (pre)catalysts by Shi’s group contain two iodido ligands as well as an $\kappa^2$-acetato ligand. When following the reported synthetic procedure to prepare the analogous complex (R)-8, i.e. stirring the ligand with [Rh(cod)Cl]$_2$, 2 equivalents of KI and excess NaOAc under reflux in acetonitrile, no product was obtained. A protocol to oxidize an Ir(III) di-NHC complex of Miecznikowski and Crabtree did result in the desired rhodium(III) complex (R)-8 (Scheme 3). This complex was purified using column chromatography, showing that also this rhodium complex is stable under aerobic conditions. The $^1$H NMR spectrum indicated that the isolated complex exists as a mixture of isomers. Assuming that the ligand will only coordinate in a cis-fashion, occupying two coordination sites in the equatorial plane of the complex, there are two possibilities for coordination of the acetate group: i) at the two remaining sites in the equatorial plane, leading to the symmetric isomer, or ii) an equatorial-apical coordination mode, yielding the asymmetric isomer (box, Scheme 4). The $^1$H NMR spectrum is consistent with the presence of one $C_2$-symmetric and one asymmetric isomer. HR-MS showed data corresponding to the parent complex, minus either the acetate or one iodine ligand.

**Synthesis and characterization of chiral di-tzNHC palladium(II) complex**

Palladium complex (R)-9 was synthesized using the protocol described in Chapter 2 and 3, by stirring ligand (R)-3 with KOTBu and half a molar equivalent of [Pd($\eta^3$-C$_3$H$_5$)Cl]$_2$ (Scheme 5). Full conversion of (R)-3 was observed within two hours.

![Scheme 5: Synthesis of palladium(II) complex (R)-9.](image)
The palladium complex (R)-9 was obtained in quantitative yields after isolation using column chromatography with regular silica and solvents, indicating the stability of this complex. The complex can be stored under nitrogen for several months and even in solvents exposed to oxygen for several weeks without decomposition. NMR spectroscopy revealed that the introduction of the allyl group breaks the symmetry of the complex, leading to a non-symmetric complex. The protons of the allyl moiety are observed as three separate signals in the $^1$H NMR spectrum while all ligand hydrogens give rise to distinctive signals. The presence of two carbene carbon signals at 163.2 and 164.4 ppm in the $^{13}$C NMR spectrum confirmed the loss of $C_2$-symmetry in this complex.

In summary, Ag(I), Pd(II), Ir(I) and Rh(I) complexes of ligand (R)-3 were successfully synthesized and characterized using NMR and HR-MS. The complexes were stable enough to be purified using regular column chromatography and most complexes were obtained in high yields. They have been tested for enantioselective catalysis as will be described in the next section.

### 6.4. Catalytic Application of Chiral di-tzNHC Complexes

The strong electron-donating properties of NHC ligands make them very suitable ligands for transformations in which oxidative addition is the key (slow) step, such as in hydrogenation, hydrosilylation and allylic alkylation processes. All these transformations are also amenable to asymmetric catalysis when using prochiral substrates and are therefore ideal cases to evaluate the novel di-triazolylidene ligand, as will be described in this paragraph.

Initially, we tested palladium(II) complex (R)-9 in the asymmetric allylic alkylation reaction of 1,3-diphenylprop-3-enyl acetate and dimethyl malonate, but no conversion was noted at room temperature. This might be caused by an inhibiting effect of the strongly coordinated allyl ligand, preventing formation of an active Pd species.

Rh(I) catalyst (R)-5 was also tested in the hydrogenation of methyl Z-2-acetamido-3-phenylacrylate under 25 bar hydrogen pressure at 40 °C overnight, which resulted in only minor conversion to the racemic product. Rh complex (R)-5 and Ir complex (R)-6 were active in the transfer hydrogenation of acetophenone in isopropanol in the presence of catalytic amount of base. Full conversion of the starting material was observed after stirring at 80 °C overnight. Unfortunately, chiral HPLC analysis revealed that a racemic mixture of the product was formed under these conditions.

**Rhodium catalyzed enantioselective hydrosilylation of ketones**

Enantioselective hydrosilylation of ketones is a valuable reaction to produce chiral silyl ethers or secondary alcohols after hydrolysis. The conditions required for this
reaction are milder than for most hydrogenations and the bulky nature of silanes compared to $H_2$ may lead to improved chiral induction. Complexes based on various metals, with rhodium as prime example, are known to facilitate hydrosilylation.

The group of Shi reported very efficient hydrosilylation reactions of prochiral ketones using a Rh(III) complex with a chiral bidentate di-benzimidazolylidene ligand. Given the resemblance of ligand to these systems, we decided to probe the activity of complex (R)-5 for this application. Acetophenone was chosen as the benchmark substrate using similar reaction conditions as reported by Shi: stirring the substrate ($c = 0.25 \text{ mmol/L}$) with 2 mol% catalyst, 2 equivalents of $H_2SiPh_2$ for 24 hours at room temperature followed by hydrolysis with HCl. A solvent screening indicated that THF was the best solvent for our system. Varying the temperature had no beneficial effect. The results of the complexes in the hydrosilylation at different catalyst loadings are depicted in Table 1.

**Table 1:** Results of the hydrosilylation of acetophenone catalyzed by (R)-5 and (R)-8.

<table>
<thead>
<tr>
<th>Catalyst loading</th>
<th>T (°C)</th>
<th>Conv. (Yield)$^a$</th>
<th>ee$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.1% of (R)-5</td>
<td>25</td>
<td>33% (17%)</td>
</tr>
<tr>
<td>2</td>
<td>0.2% of (R)-5</td>
<td>25</td>
<td>78% (78%)</td>
</tr>
<tr>
<td>4</td>
<td>1.1% of (R)-5</td>
<td>25</td>
<td>90% (90%)</td>
</tr>
<tr>
<td>5</td>
<td>2.0% of (R)-5</td>
<td>25</td>
<td>92% (78%)</td>
</tr>
<tr>
<td>6</td>
<td>2.0% of (R)-8</td>
<td>25</td>
<td>42% (13%)</td>
</tr>
<tr>
<td>7</td>
<td>2.0% of Shi’s catalyst</td>
<td>15</td>
<td>87% (87%)</td>
</tr>
</tbody>
</table>

$^a$ Determined by GC analysis using para-xylene as an internal standard.

$^b$ Determined by chiral GC

$^c$ Values reported by Shi et al.

We were able to decrease catalyst loadings significantly to 0.2 mol % without loss of enantiomeric excess (ee) and little loss in conversion (Table 1, entry 2). Shi reported reactions with a catalyst loading of 1 mol% leading to 77% yield after 48 hours, while several signals of high-boiling compounds were also detected in GC results. This indicates that the hydrolysis step is not very reproducible.
similar to the results achieved at 0.2 mol% catalyst loading with complex (R)-5 after 24 hours (entry 2). The increased activity in our case might be caused by the electron-donating properties of the ligand. The enantioselectivity on the other hand, was significantly lower for our system compared to Shi, yet higher than the imidazolylidene-naphthoxy Rh(I) complex of Crabtree et al.

Surprisingly, complex 8, which is more closely related to the pre-catalyst of Shi, proved less active in the hydrosilylation reaction under the same conditions and a racemic mixture of 1-phenylethanol was observed (entry 6). Therefore, we assume that the difference in ee between the benzimidazolylidene and triazolylidene complexes is caused by steric effects (vide infra).

We performed a small substrate screening including bulky substrates and substrates with various electronic properties to obtain insight in the catalyst performance (Table 2). This screening showed higher conversions for more electron-rich ketones, while adding an electron-withdrawing group on the phenyl ring led to slightly reduced conversion. The 4-bromoacetophenone (entry 2) was converted with similar ee as acetophenone.

Table 2: Substrate scope of hydrosilylation of aryl alkyl ketones catalyzed by (R)-5.

<table>
<thead>
<tr>
<th>R</th>
<th>R'</th>
<th>Conv. (Yield)</th>
<th>ee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>H</td>
<td>92%(78%)</td>
<td>26%</td>
</tr>
<tr>
<td>Me</td>
<td>Br</td>
<td>79%(78%)</td>
<td>32%</td>
</tr>
<tr>
<td>Me</td>
<td>MeO</td>
<td>100%(0%)</td>
<td>-</td>
</tr>
<tr>
<td>iPr</td>
<td>H</td>
<td>100%(100%)</td>
<td>51%</td>
</tr>
</tbody>
</table>

a) Determined by GC analysis using para-xylene as an internal standard  
b) Determined by chiral GC  
c) Determined by chiral HPLC.

The hydrosilylation of 4-methoxyacetophenone (Table 2, entry 3) resulted in full conversion of the starting compound, but no traces of the product could be observed in the GC. This might be explained by the nature of the substrate, as the methoxy group might not be stable under the catalytic conditions in the presence of the highly oxophilic silicon species. The conversion of phenyl isopropyl ketone (entry 4) gave significantly better results in terms of ee than for the reaction with
acetophenone. The higher enantioselectivity obtained with this sterically congested ketone indicates that increasing the steric bulk around the triazolylidenes aids the transfer of chirality in this reaction. This bulkiness could be introduced in the side groups on the triazolylidene (in the direct vicinity of the metal centre). Another possibility is the introduction of groups at the 2 and 2’ positions on the binaphthyl backbone that may decrease rotational freedom of the triazolylidene moieties, yielding an even more rigid complex and possibly enhanced chiral definition.

6.5. Conclusion
A new chiral $C_2$-symmetric di-1,2,3-triazolylidene ligand with a binaphthyl backbone was successfully obtained via an efficient three-step synthesis from commercially available starting materials in 91% overall yield. Silver(I), palladium(II), iridium(I) and rhodium(I) complexes were synthesized and characterized using multinuclear NMR spectroscopy and mass spectrometry. The complexes were stable enough to be purified by column chromatography and most complexes were obtained in high yields. Rhodium complex ($R$)-7 allowed for the assessment of the electron-donating properties of the ligands and the $\nu_{\text{avg}}$(CO) observed was lower than for similar di-imidazol-2-ylidene complexes, indicating stronger electron-donating properties of the new ligand.

Rhodium(I) complex ($R$)-5 was successfully applied in the asymmetric hydrosilylation of prochiral ketones. Good yields were obtained at catalyst loadings as low as 0.2 mol%, indicating the increased activity of complex ($R$)-5 compared to the complexes reported by Shi. Chirality was efficiently transferred onto various aryl ketone substrates. Furthermore, we observed increased enantioselectivity when bulkier substrates were used. This indicates that using even bulkier substrates may lead to higher ee while modification of the ligand may allow for effective transfer of chirality to smaller substrates.

Because of the combination of interesting electronic properties and the straightforward synthetic route, chiral 1,2,3-triazolylidene-based ligands are deemed very interesting subjects for further research. The possibilities in design and diversity of side-groups of (chiral) tzNHCs has barely been explored, and the before-mentioned benefits promise future applications for this type of ligands in asymmetric catalysis.

6.6. Experimental Section
All experiments were carried out under an atmosphere of purified nitrogen using standard Schlenk techniques. Solvents were freshly distilled under an argon atmosphere from sodium benzophenoneketyl (toluene, THF, pentane and diethyl ether) and from CaH$_2$ (DCM and MeCN). Acetophenone was vacuum-distilled and stored over 4 Å molecular sieves under a
nitrogen atmosphere. NMR spectra were recorded on either a Bruker AV400 MHz, Bruker DRX300 MHz, Varian Mercury 300 MHz, Bruker IMC500 MHz. $^1$H-$^1$H COSY and/or $^1$H-$^{13}$C HSQC NMR spectroscopy was used to assign the peaks of several compounds. Thin layer chromatography was carried out using Merck aluminium TLC sheets (Silica gel 60 F254). Column chromatography was carried out using Screening Devices 60-200 μm (60 Å pore size) silica gel and using technical grade solvents. HR-MS was performed on a Bruker MicrOTOF-Q machine in ESI mode. IR spectra were recorded on a Bruker Alpha-PFT-IR spectrometer. GC analyses for determination of conversions and yields were performed with a Thermo Scientific Trace GC Ultra system with a Restek RTX®-200 (30 meters, 0.25 mmID) capillary column with a split injection method, using p-xylene as an internal standard. Determination of the ee of the products formed using HPLC was carried out using a Shimadzu LC-10AT VP with a Chiralcel OD-H column (0.9 mL/min flowrate, heptane/isopropanol=95/5) except for acetonophene. The products of the acetonophene hydroisilylation were analysed using chiral GC using a Supelco β-dex 225 column (30m x 0.25mm, 92 °C to 95 °C with a ramp 0.1 °C per minute, holding at 95 °C for 10 minutes).

The ligand synthesis starting from both BINAM enantiomers from racemic BINAM. The results of the synthesis of the (R)-ligand are reported, as all complexes were synthesized using the (R)-ligand. It was found that using starting from (S)-BINAM or (+/-)-BINAM did not have a significant effect on any of the ligand synthesis steps.

(S) or (R)-2,2'-bis(4-(p-tolyl)-1H-1,2,3-triazolyl)-1,1'-binaphthyl; (S)- or (R)-1. A solution of 1,1'-binaphthyl-2,2'-diamine (280 mg, 0.98 mmol, 1.0 equiv.) in MeCN (7.5 mL) was cooled to 0 °C, after which tert-butyl nitrite (305 mg, 2.95 mmol, 3.0 equiv.) was added. To this solution trimethylsilyl azide (272 mg, 2.36 mmol, 2,4 equiv.) was added, upon which the color changed from brown to a bright red solution. This solution was stirred at room temperature for 40 hours before the solution was filtered, the solvents were evaporated and the mixture was purified using column chromatography (SiO$_2$, hexane : Et$_2$O= 1:0 → 10:1). Concentration _in vacuo_ yielded the product (316 mg, 0.94 mmol, 96% yield) as a red solid. $^1$H NMR (CDCl$_3$) $\delta$ 8.08 (d, $^3$J$_{HH}$ = 8.8 Hz, 2H, Ar-C$_H$), 7.95 (d, $^3$J$_{HH}$ = 8.1 Hz, 2H, Ar-Ch), 7.53 (d, $^3$J$_{HH}$ = 8.8 Hz, 2H, Ar-Ch), 7.47 (ddd, $^3$J$_{HH}$ = 8.2 Hz, $^3$J$_{HH}$ = 6.9 Hz, $^3$J$_{HH}$ = 1.2 Hz, 2H, Ar-Ch), 7.33 (ddd, $^3$J$_{HH}$ = 8.4 Hz, $^3$J$_{HH}$ = 6.9 Hz, $^3$J$_{HH}$ = 1.3 Hz, 2H, Ar-Ch), 7.08 (d, $^3$J$_{HH}$ = 8.5 Hz, 2H, Ar-Ch); $^{13}$C NMR (CDCl$_3$) $\delta$ 153.0 (Ar-C$_q$), 136.0 (Ar-C$_q$), 133.5(Ar-C$_q$), 130.9 (Ar-C$_q$), 130.4 (Ar-Ch), 128.3 (Ar-Ch), 127.4 (Ar-Ch), 125.6 (Ar-Ch), 125.5 (Ar-Ch), 117.2 (Ar-Ch). HR-MS (ESI) for C$_{20}$H$_{12}$N$_6$: m/z calculated 336.1123, [M]+, observed 336.1122. IR: 2098, 2042, 1285, 801, 743 cm$^{-1}$.

(S) or (R)-2,2'-bis(4-(p-tolyl)-1H-1,2,3-triazolyl)-1,1'-binaphthyl; (S)- or (R)-2. To a solution of 2,2'-diazido-1,1'-binaphthalene (212 mg, 0.63 mmol, 1.0 equiv.) in MeCN:H$_2$O (4:1, 10 mL) was added copper(II)sulfate pentahydrate (11 mg, 0.063 mmol, 0.1 equiv.), sodium ascorbate (63
mg, 0.32 mmol, 0.5 equiv.), p-tolyl acetylene (146 mg, 1.26 mmol, 2.0 equiv.) and triethyl amine (32 mg, 0.32 mmol, 0.5 equiv.). The resulting red mixture was stirred for 60 hours at 50 °C. The MeCN and triethylamine were removed in vacuo and the product was purified using column chromatography (SiO₂, PE : EtOAc = 4:1 → 1:1) yielding the product (340 mg, 0.60 mmol, 95% yield) as an orange oil. ¹H NMR (CDCl₃) δ 8.09 (d, 3JH-H = 8.7 Hz, 2H, Ar-CH), 7.96 (d, 3JH-H = 8.2 Hz, 2H, Ar-CH), 7.55 (ddd, 3JH-H = 8.1 Hz, 2H, Ar-CH), 7.47 (d, 3JH-H = 8.1 Hz, 4H, Tol-CH), 7.41 (ddd, 3JH-H = 8.3 Hz, 3JH-H = 6.7 Hz, 3JH-H = 1.2 Hz, 2H, Ar-CH), 7.35 (d, 3JH-H = 8.6 Hz, 2H, Ar-CH), 7.13 (d, 3JH-H = 8.0 Hz, 4H, Tol-CH), 2.33 (s, 6H, Tol-CH₃). HR-MS (ESI) for C₃₈H₂₉N₆: m/z calculated 569.2448, [MH]+, observed 569.2451.

(S) or (R)-2,2'-bis(3-methyl-4-(p-tolyl)-1H-1,2,3-triazolium)-1,1'-binaphthyl triflate; (S)- or (R)-3. Under inert conditions 2,2'-bis(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)-1,1'-binaphthalene (282 mg, 0.50 mmol, 1.0 equiv.) was dissolved in dried DCM (10 mL) and the solution was cooled to -78 °C. Methyl triflate (156 mg, 1.375 mmol, 2.75 equiv.) and Ag₂O (32 mg, 0.32 mmol, 0.5 equiv.) were added to a Schlenk, after which the mixture was allowed to heat up to room temperature and stirred for 15 minutes. The mixture was stirred for 12 hours, after which the mixture was concentrated in vacuo and the product was purified using column chromatography (SiO₂, PE : EtOAc = 1:1) yielding the product (340 mg, 0.50 mmol, quantitative yield). HR-MS (ESI) for C₃₈H₂₉N₆: m/z calculated 569.2448, [MH]+, observed 569.2451.

(Bis[[(R)2,2'-bis(3-methyl-4-(p-tolyl)-1H-1,2,3-triazol-5-ylidene)-1,1'-binaphthyl]] silver(I) triflate; (R)-4. Under inert conditions (R)-3 (198.0 mg, 0.22 mmol, 1.0 equiv.) and Ag₂O (203.4 mg, 0.88 mmol, 4.0 equiv.) were added to a Schlenk, after which 4Å molsieves were added followed by dry MeCN (15 mL). The mixture was stirred in the dark at 50 °C for 48h, after which the mixture was filtered over Celite and concentrated in vacuo yielding the product as an off-white solid (269.4 mg, quantitative yield). HR-MS (ESI) for C₃₈H₂₉N₆: m/z calculated 569.2448, [MH]+, observed 569.2451.
(R)-2,2′-bis(3-methyl-4-(p-tolyl)-1,2,3-triazol-5-ylidene)-1,1′-binaphthyl

η⁴-cyclooctadiene iridium(II) triflate; (R)-5. Under inert conditions a solution of (R)-3 (102 mg, 0.11 mmol, 1.0 equiv.), [Ir(cod)Cl]₂ (28.1 mg, 0.06 mmol, 0.5 equiv.) and KOtBu (49.4 mg, 0.44 mmol, 4.0 equiv.) in THF (10 mL) was stirred for 3 hours at room temperature, after which the solution was filtered over Celite and concentrated in vacuo. Purification using column chromatography (SiO₂, DCM:acetone=3:1) yielded the product as an orange solid (83.7 mg, 0.09 mmol, 80% yield). HR-MS (ESI) for C₈₀H₆₄Ag₄N₁₂CF₃SO₃: m/z calculated 1557.3008, [M+OTf]⁺, observed 1557.3601 and for C₈₀H₆₄Ag₄N₁₂: m/z calculated 703.1739, [M-2OTf]⁻, observed 703.1740.

\[
\text{(R)-2,2′-bis(3-methyl-4-(p-tolyl)-1,2,3-triazol-5-ylidene)-1,1′-binaphthyl} \\
\text{η⁴-cyclooctadiene iridium(II) triflate} \\
\text{Chelating Di-tzNHC Late TM Complexes}
\]
Under inert conditions a Rh(I) complex (10.6 mg, 0.11 mmol, 1.0 equiv.), I \textsubscript{2} (100.6 mg, 0.34 mmol, 3.0 equiv.) and NaOAc (62.0 mg, 0.55 mmol, 5.0 equiv.) were dissolved in dry MeCN and stirred at room temperature overnight, after which the product was purified using column chromatography (SiO\textsubscript{2}, Hexane:DCM=1:1 for the elution of excess iodine, DCM:acetone=1:1 for product elution) yielding the product as a red solid (no yield determined). \textsuperscript{1}H NMR (CD\textsubscript{2}Cl\textsubscript{2}) \( \delta \) 8.67 (d, \( J_{\text{HH}} \) = 8.7 Hz, 1H, Ar-CH), 8.56 (d, \( J_{\text{HH}} \) = 8.7 Hz, 1H, Ar-CH), 8.43 (d, \( J_{\text{HH}} \) = 8.7 Hz, 2H, Ar-CH), 8.27 (d, \( J_{\text{HH}} \) = 8.4 Hz, 1H, Ar-CH), 7.51-7.67 (m, 6H, Ar-CH), 7.33-7.42 (m, 6H, Ar-CH/Tol-CH), 6.90-7.17 (m, 20H, Ar-CH/Tol-CH), 6.46 (d, \( J_{\text{HH}} \) = 7.8 Hz, 1H, Ar-CH), 6.03 (d, \( J_{\text{HH}} \) = 7.4 Hz, 1H, Ar-CH), 3.21 (s, 6H, N-CH\textsubscript{3}), 2.88 (s, 3H, N-CH\textsubscript{3}), 2.84 (s, 3H, N-CH\textsubscript{3}), 2.39 (s, 6H, Tol-CH\textsubscript{3}), 2.34 (s, 3H, Tol-CH\textsubscript{3}), 2.30 (s, 3H, Tol-CH\textsubscript{3}); \textsuperscript{13}C NMR (CD\textsubscript{2}Cl\textsubscript{2}) \( \delta \) 146.2 (Ar-C\textsubscript{q}), 139.8 (Ar-C\textsubscript{q}), 137.9 (Ar-C\textsubscript{q}), 134.0 (Ar-C\textsubscript{q}), 133.0 (Ar-C\textsubscript{q}), 131.8 (Ar-C\textsubscript{q}), 130.8 (Ar-C\textsubscript{q}), 128.4 (Tol-CH), 128.2 (Ar-CH), 128.1 (tol-CH), 127.6 (Ar-CH), 127.2 (Ar-CH), 126.9 (Ar-CH), 123.9 (Ar-CH), 37.1 (N-CH\textsubscript{3}), 21.7 (Tol-CH\textsubscript{3}). HR-MS (ESI) for \( \text{C}_{45} \text{H}_{33} \text{N}_{6} \text{O}_{2} \text{Rh} \): m/z calculated 1011.9966 [M+], observed 1012.0030.
temperature, after which the solution was purified using column chromatography (SiO$_2$, DCM:acetone=1:1) yielding the product (96.0 mg, 0.11 mmol, quantitative yield) as a yellow solid. 

$^1$H NMR (CD$_2$Cl$_2$) $\delta$ 8.25 (d, $^3$J$_{HH}$ = 8.6 Hz, 1H, Ar-CH), 8.14 (d, $^3$J$_{HH}$ = 8.4 Hz, 1H, Ar-CH), 7.99 (d, $^3$J$_{HH}$ = 8.3 Hz, 1H, Ar-CH), 7.89-7.94 (m, 2H, Ar-CH), 7.78 (d, $^3$J$_{HH}$ = 8.9 Hz, 1H, Ar-CH), 7.49-7.65 (m, 6H, Ar-CH), 7.19-7.22 (m, 4H, Tol-CH), 6.89-6.92 (m, 4H, Tol-CH), 4.45-4.59 (m, 1H, allyl-CH), 3.46 (s, 3H, N-C$_3$H$_3$), 3.41 (s, 3H, N-C$_3$H$_3$), 2.84-2.86 (m, 1H, allyl-CH), 2.36-2.38 (m, 6H, Tol-CH), 2.10-2.05 (m, 1H, allyl-CH), 1.28-1.36 (m, 2H, allyl-CH); 

$^{13}$C NMR (CD$_2$Cl$_2$) $\delta$ 164.4 (C$_{tzNHC}$), 163.2 (C$_{tzNHC}$), 147.4 (Ar-C$_4$), 147.3 (Ar-C$_4$), 140.5 (Ar-C$_4$), 140.4 (Ar-C$_4$), 136.9 (Ar-C$_4$), 136.7 (Ar-C$_4$), 133.7 (Ar-C$_4$), 133.5 (Ar-C$_4$), 131.4 (Ar-C$_4$), 131.1 (Ar-C$_4$), 131.1 (Ar-C$_4$), 130.6 (Ar-CH), 130.5 (Ar-CH), 129.8 (Tol-CH), 129.4 (Tol-CH), 129.2 (Ar-CH), 129.2 (Ar-CH), 128.0 (Ar-CH), 127.3 (Ar-CH), 125.0 (Ar-C$_4$), 124.9 (Ar-C$_4$), 122.5 (Ar-CH), 122.4 (Ar-CH), 117.9 (allyl-CH), 63.0 (allyl-CH), 58.9 (allyl-CH), 36.4 (N-CH$_3$), 36.1 (N-CH$_3$), 21.1 (CH$_3$). HR-MS (ESI) for C$_{44}$H$_{37}$PdN$_6$: m/z calculated 743.2115 [M-O'PF$_6$], observed 743.2130.

Rhodium catalyzed hydrosilylation. In a dried Schleck flask equipped with a magnetic stirrer, the rhodium catalyst (0.1-2 mol%, weighed in a small aluminium weighing vessel) was dissolved in dry THF (2 mL), after which the substrate (62 $\mu$L, 0.5 mmol), p-xylene (61 $\mu$L, 0.5 mmol) and diphenylsilane (139 $\mu$L, 0.75 mmol) were added. After stirring for 24 hours at the desired temperature, water (2 mL) and 2M HCl (1 mL) were added, the product was extracted using diethyl ether (2 x 10 mL) and the resulting solution was used for GC and HPLC analysis.

Palladium catalyzed asymmetric allylic alkylation. In a dried Schlenk flask equipped with a magnetic stirrer, the palladium catalyst (0.01 equiv., weighed using a small aluminium weighing vessel), 1,3-diphenylprop-3-enyl acetate (1.0 equiv.), dimethyl malonate (3.0 equiv.), bis-trimethylsilyl acetamide (3.0 equiv.) KOAc (0.1 equiv.) and p-xylene (1.0 equiv.) were dissolved in DCM (1.0 equivalent at 0.1 M) and the mixture was stirred at room temperature for 5 hours. After this, a saturated solution of NH$_4$Cl (5 times initial V$_{solv}$.) was added and the mixture was extracted with diethyl ether (2 x 10 mL) and the resulting solution was used for GC and HPLC analysis.

Rhodium catalyzed hydrogenation of alkenes. In an autoclave (150 mL) with six inserts glass GC vials were placed with a septum cap, pierced by a small needle, containing a magnetic stirrer; the rhodium catalyst (0.01 equivalents, weighed in a small aluminium weighing vessel) and the substrate (1.0 equivalents, weighed in a small aluminium weighing vessel) dissolved in DCM (1.0 equivalent at a concentration of 1.0 M) and the mixture was stirred at room temperature for 5 hours. After this, a saturated solution of NH$_4$Cl (5 times initial V$_{solv}$.) was added and the mixture was extracted with diethyl ether (1.5 times initial V$_{solv}$.) and the crude organic layer was analyzed.

Rhodium catalyzed transfer hydrogenation of acetophenone. In a dried Schleck flask equipped with a magnetic stirrer, the rhodium catalyst (0.01 equiv., weighed using a small aluminium weighing vessel) and KOtBu (0.1 equiv., weighed using a small aluminium weighing vessel)
were dissolved in a degassed stock of substrate and internal standard in isopropanol (0.1 M solution of acetophenone and \( p \)-xylene in isopropanol). The mixture was stirred at 80 °C overnight, after which the crude sample was analyzed.

6.7 References

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Summary

Multidentate Di-N-Heterocyclic Carbene Ligands for Transition Metal Catalyzed Hydrogenation Reactions
Synthetic catalysts play an important role in creating a more sustainable society. The use of catalysts has environmental as well as economic advantages. They speed up reactions without being consumed in the reaction itself. Moreover, they reduce the amount of byproducts and waste significantly. Catalysts are applied in various chemical processes, ranging from the manufacturing of products for daily use, such as plastics, fuels and pharmaceuticals to the reduction of poisonous sideproducts, for instance, the exhaust gasses from cars. In order to warrant an environmentally viable chemical industry, a lot of research on catalysis is being and has been conducted in this field. Both at universities and in industry, more efficient catalytic systems for a variety of processes are under development. The research that is described in this thesis is part of this endeavor. It relies on organometallic and coordination chemistry as an essential input for the design of suitable catalysts for homogeneous catalysis.

Homogeneous catalysts often exist as complexes consisting of a metal center surrounded by organic molecules, the ligands. These ligands, in synergy with the metal, determine the properties of the complexes for a large part. Nowadays, the accumulated knowledge about organometallic catalysts is extensive, including understanding of reaction mechanisms and the influence of certain ligand parameters. This enables the design of homogeneous catalysts in a rational manner.

The research described in this thesis aimed to develop new catalysts based on N-heterocyclic carbene (NHC; Figure 1) ligands. More specifically, it focused on late-transition metal complexes with multidentate ligands and the subclass of 1,2,3-triazolylidenes (tzNHCs; Figure 1). At the start of this research project few metal complexes of the latter and applications thereof were known in organometallic chemistry.

![Figure 1: General structure of NHC and tzNHC ligand. The mesoionic character of the latter is illustrated by the additional formal charges. Box: The general structure of the metal complexes described in this thesis.](image)

In the introductory Chapter 1 relevant characteristics of NHC and tzNHC ligands and applications of the corresponding metal complexes are discussed. Additionally, the advantages of multidentate ligands are described. Such ligands lend increased stability to metal complexes compared to their monodentate counterparts and more handles (rigidity of the linker and chelate ring size) to steer the properties of
the catalysts. The convenient synthesis of tzNHC ligands by the copper catalyzed alkyne-azide cycloaddition (Scheme 1) allows the incorporation of virtually every side-group. Because of their strong and tunable $\sigma$-donating capacity, these ligands are very suitable for catalytic reactions in which oxidative addition is a key step, such as hydrogenation. Several examples of chelate tzNHC metal complexes from literature and their applications are also discussed in this chapter.

Scheme 1: General synthesis of tzNHC precursor by copper-catalyzed “click” cycloaddition of an azide and alkyne, followed by methylation.

The first experimental part of this thesis focuses on di-NHC compounds. In Chapter 2 the coordination of several $\zeta_5$-symmetric ligands, consisting of two NHCs, to Pd(0) and Pd(II) via transmetalation of the corresponding Ag(I) complexes is presented (Scheme 2). This is a frequently used route to synthesize (di-)NHCs, which is applied more often throughout the thesis.

Scheme 2: General synthesis of the di-NHC Pd(0) complexes via Ag(I) transmetalation.

Extremely electron-rich di-NHC Pd(0) complexes were isolated for the first time. The chelate coordination of the ligands to palladium has been confirmed by NMR spectroscopy and single crystal X-ray diffraction. The application of the obtained pre-catalysts is studied in the semihydrogenation of alkynes. The zero-valent Pd complex with mesityl side-groups exhibits similar activity and initial selectivity towards the $Z$-alkene in the hydrogenation of 1-phenyl-1-propyne using H$_2$ as a known monodentate Pd NHC analogue. The Pd(II)(allyl) complex, on the other hand, is inactive under the same reaction conditions and both complexes are not very suitable for transfer hydrogenation using formic acid as hydrogen donor.

In the next part of the thesis, complexes of hybrid di-NHC ligands, combining an NHC and tzNHC donor in one ligand, are introduced (Scheme 3, B and C). In Chapter 3 the coordination of these ligands to palladium and ruthenium is studied. Again, chelation of the ligand in the metal complexes has been verified by single crystal X-ray diffraction and NMR spectroscopy. Moreover, these methods indicated strong $\sigma$-donating properties of the tzNHC moiety. Although
the resulting complexes are stable under aerobic conditions and in solution, the Pd complexes are not compatible with the acidic reaction conditions required for catalytic hydroarylation of alkynes. Under these conditions protonolysis of both the Pd-NHC and Pd-tzNHC bond is observed. The (NHC-tzNHC)Ru(II) pre-catalysts proved to be good candidates for the hydrogenation of polar bonds (Scheme 3); ketones and imines are reduced under 5 bar of hydrogen pressure at low catalyst loadings (0.1 mol%). Methyl trifluoroacetate, an activated ester, is also converted to the corresponding alcohol by the ruthenium catalyst (p(H₂) = 50 bar and T = 100 °C). These results however, cannot compete with known di-NHC ruthenium systems for the hydrogenolysis of esters.

Iridium and rhodium compounds are the topic of Chapter 4. Synthetic procedures for NHC-tzNHC Ir and Rh complexes and their NHC-tz analogues have been established. Additionally, the impact of several substituents and linkers between the carbenes on the electron-donating capacities of the ligands is studied by means of NMR and IR spectroscopy. The complexes are active in the transfer hydrogenation of polar bonds using isopropanol as hydrogen source. Notably, the electron-rich NHC-tzNHC pre-catalysts (Scheme 3, B) proved to facilitate this reaction significantly faster than the NHC-tz analogue (Scheme 3, A).

The final part of this thesis discusses various di-tzNHC ligands. The systems developed in Chapter 5 consist of tridentate CNC and CNN ligands bearing tzNHC donors (Scheme 4). As esters are not reduced to alcohols very efficiently by the heteroditopic di-NHC ruthenium complexes (Chapter 3), cooperative functionalities have been introduced in these ligands. The benzylic linker of the lutidine-based ligands can be deprotonated, while the pyridine ring is simultaneously dearomatized (Scheme 4, box). Substrates, such as H₂, can subsequently be activated over the metal and the ligand, which has led to unprecedented catalytic activities in amongst others catalytic ester hydrogenation.
Summary

Transmetalation of the respective Ag(I) complexes led to rare facial coordination of the tridentate ligands to Ru(II). Both these resulting ruthenium complexes and the palladium CNC analogue exhibit the expected reactivity of the benzylic "arm". Furthermore, the Ru pre-catalysts are active in the hydrogenolysis of methyl benzoate and other ester in the presence of a minimum of 20 mol% of KOTBu (Scheme 4; p(H₂) ≥ 5 bar, T = 100 ºC). The reason for this critical amount of KOTBu has not been unambiguously established, yet high pressure in situ NMR spectroscopic investigations revealed potentially active CNC Ru hydride species under catalytic conditions.

The development of chiral di-NHC transition metal complexes for enantioselective catalysis is described in Chapter 6. Enantioselective catalysis is essential for the selective synthesis of chiral products that are for example of vital importance for pharmaceuticals. Despite the extensive use of NHCs in homogeneous catalysis, relatively few applications are known in enantioselective transformations making use of this ligand class. A chiral di-tzNHC ligand has been obtained in a three-step synthetic route in 91% yield from the atropisomeric BINAM molecule. The corresponding di-tzNHC Ag(I), Pd(II), Ir(I) and Rh(I) complexes have been successfully synthesized. The Rh complex is active in the hydrosilylation of ketones. Moreover, chirality of the ligand is transferred to the substrate in this reaction leading to enantiomeric excess of up to 51% (Scheme 5).

Scheme 4: The catalytic hydrogenation of esters and the CNC ruthenium catalysts from Chapter 5. Box: reversible deprotonation/dearomatization.

Scheme 5: The chiral Rh(cod) pre-catalyst from Chapter 6 (box) for the catalytic hydrosilylation of ketones.
The research described in this thesis has demonstrated that (bidentate) tzNHC ligands are new assets in organometallic chemistry and homogeneous catalysis. This thesis exemplifies that these ligands can be efficiently synthesized and coordinated to several late-transition metals. The potential applications of the developed electron-rich complexes have been illustrated by various catalytic double bond reductions, including enantioselective transformations and the hydrogenolysis of challenging ester substrates. Moreover, the knowledge about transition metal complexes with triazolylidene and di-NHC ligands has been expanded. This research shows, for instance, that the bond between the metal and chelating carbene ligands is not always as robust as was generally thought. Because of the convenient synthetic route and the endless possibilities to vary tzNHC ligands, it is plausible that these ligands will facilitate interesting new applications in the future.
Samenvatting

Multidentaat Di-N-Heterocyclische Carbeen Liganden voor Overgangsmetaal-gekatalyseerde Hydrogeneringsreacties

Synthetische katalysatoren leveren een positieve bijdrage aan het streven naar een duurzamere maatschappij. Ze worden gebruikt in allerlei chemische processen, variërend van het vervaardigen van producten voor dagelijks gebruik, zoals plastics, brandstof en medicijnen, tot het verminderen van de uitstoot van schadelijke gassen van bijvoorbeeld auto’s. Katalysatoren versnellen reacties zonder er zelf in opgebruikt te worden. Bovendien zorgen ze ervoor dat er minder bijproducten gevormd worden. Het gebruik van katalysatoren heeft dus niet alleen economische voordelen, maar zeker ook voordelen voor het milieu. Om een gezonde en duurzame chemische industrie te waarborgen wordt er veel onderzoek naar gedaan. Zowel binnen universiteiten als in de industrie worden continue efficiëntere katalysatoren ontwikkeld. Ook het onderzoek dat is beschreven in dit proefschrift heeft hieraan een bijdrage geleverd.

De homogene katalyse is grotendeels gebaseerd op organometaal- en coördinatiechemie. Homogene katalysatoren, met uitzondering van organokatalysatoren, zijn doorgaans opgebouwd uit een metaalcentrum met daaraan gekoppeld organische moleculen, de liganden. Liganden bepalen voor een groot deel de eigenschappen van de katalysator. Inmiddels is de vergaarde kennis over organometaalkatalysatoren (o.a. begrip van katalytische reactiemechanismen en het effect van ligandparameters) dusdanig groot, dat het mogelijk is deze verbindingen volgens een rationele aanpak te ontwerpen. Het onderzoek dat staat beschreven in dit proefschrift, richt zich op het ontwikkelen van nieuwe katalysatoren gebaseerd op N-heterocyclische carbeen (NHC; Figuur 1) liganden. In het bijzonder staan late-overgangsmetaalverbindingen met multidentaat liganden en de subklasse van 1,2,3-triazolylidenen (tzNHCs; Figuur 1) centraal. De laatstgenoemde ligandsoort was bij de start van dit onderzoek nog maar net in opkomst en er waren slechts weinig toepassingen van dergelijke verbindingen in de organometaalchemie bekend.

Figuur 1: Algemene structuur van NHC en tzNHC liganden. Het mesoionische karakter van het tweede type wordt geïllustreerd door de toegevoegde formele ladingen. In het kader: de algemene structuur van de metaalverbindingen die zijn ontwikkeld in dit onderzoek.
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In het inleidende Hoofdstuk 1 komen de belangrijkste kenmerken van NHC en tzNHC verbindingen, evenals de voordelen van multidentaat liganden aan de orde. Multidentaat liganden verlenen een grotere stabilititeit aan metaalverbindingen dan hun monodentaat equivalenten en bevatten meer “handvatten”, zoals stijfheid van het bruggende deel en de chelaat-ringgrootte, om de eigenschappen van de katalysatoren te sturen. De efficiënte synthese van tzNHCs door middel van de koper-gekatalyseerde “klik” cyclo-additie (Schema 1), maakt het mogelijk om deze liganden met bijna elke gewenste zij-groep te vervaardigen. Door hun sterke en regelbare σ-donerende eigenschappen zijn dergelijke liganden erg geschikt voor katalytische reacties waarin oxidatieve additie een belangrijke stap is, zoals bijvoorbeeld in hydrogeneringsreacties. Verscheidene succesvolle voorbeelden van (de toepassing van) chelerende tzNHC metaalverbindingen uit de literatuur worden eveneens behandeld in dit hoofdstuk.

Schema 1: Algemene synthese van het tzNHC ligand door middel van de koper-gekatalyseerde “klik” cycloadditie van een azide en alkyn, gevolgd door methylering.

In het eerste experimentele deel van dit proefschrift komen di-NHC verbindingen aan bod. In Hoofdstuk 2 wordt de coördinatie van verscheidene C₅-symmetrische liganden met twee NHCs aan Pd(0) en Pd(II) beschreven. De resulterende metaalverbindingen zijn gesynthetiseerd door transmetallering van de bijbehorende zilver(I) verbindingen (Schema 2). Dit is een veelvuldig gebruikte methode voor de synthese van (di-)carbenen, die ook in het vervolg van dit proefschrift vaak terugkeert.

Schema 2: Algemene synthese van een di-NHC Pd(0) verbinding via Ag(I) transmetalering.

Deze extreem elektronenrijke complexen zijn de eerste geïsoleerde di-NHC Pd(0) verbindingen. Door middel van NMR spectroscopie en éénkristal Röntgen diffractie is bewezen dat de twee carbeengroepen een chelaatring vormen met het Pd-centrum. Daarnaast is de toepassing van de verkregen pre-katalysatoren in de semihydrogenering van alkynen bestudeerd. De nulwaardige palladiumverbinding
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met mesityl N-substituenten vertoont vergelijkbare activiteit en initiële selectiviteit voor het Z-alkeen in de hydrogenering van 1-fenyl-1-propyn met H₂ als reeds bekende katalysatoren met monodentaat NHC liganden. Het Pd(II)(allyl) complex daarentegen is niet actief onder dezelfde reactiecondities en beide verbindingen bleken niet erg geschikt te zijn voor de transferhydrogenering met mierenzuur als waterstofdonor.

In het volgende deel van deze thesis worden hybride di-NHC complexen geïntroduceerd die bestaan uit een NHC gekoppeld aan een tzNHC (Schema 3, B en C). In Hoofdstuk 3 wordt de coördinatie van deze liganden aan Pd en Ru centra bestudeerd. Ook voor deze verbindingen is chelaatvorming aangetoond door middel van éénkristal Röntgen-diffractie en NMR spectroscopie. Bovendien toonden deze methoden de sterke σ-donatie van de tzNHC groep aan. Hoewel de gesynthetiseerde verbindingen stabiel zijn zowel aan de lucht als in oplossing, bleken de Pd complexen niet resistent tegen de zure condities in de katalytische hydroarylering van alkynen met arenen. Gedurende deze reactie vond protonolyse van zowel de Pd-NHC als Pd-tzNHC binding plaats.

De (NHC-tzNHC)Ru(II) pre-katalysatoren zijn zeer geschikt voor de hydrogenering van polaire bindingen (Schema 3); ketonen en imines kunnen worden gereduceerd bij 5 bar waterstofdruk met lage katalysatorconcentraties (0.1 mol%). Hoewel methyltrifluoroacetataat, een geactiveerde ester, ook wordt omgezet tot de overeenkomstige alcohol onder invloed van de ruthenium verbinding (p(H₂) = 50 bar en T = 100 °C), bleven de prestaties in ester-hydrogenolyse helaas achter bij de resultaten beschreven in een eerdere publicatie over Ru systemen met andere di-NHCs.

![Schema 3](image)

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Iridium- en rhodiumverbindingen vormen het onderwerp van Hoofdstuk 4. Synthesemethoden voor NHC-tzNHC Ir- en Rh-cod verbindingen en hun NHC-tz equivalenten worden hier beschreven. De invloed van verschillende substituenten en verbindingen tussen de carbenen op de elektronendonatie van de liganden is ook onderzocht aan de hand van $^{13}$C NMR en IR spectroscopie. De complexen zijn actief in de transferhydrogenering van polaire bindingen met isopropanol als waterstofdonor. Bovendien bleken de elektronenrijke NHC-tzNHC verbindingen (Schema 3, B) het substraat acetofenon significant sneller om te zetten dan de NHC-tz analoog (Schema 3, A).

Het laatste deel van dit proefschrift gaat over verscheidene di-tzNHC liganden. Hoofdstuk 5 betreft tridentaat CNC en CNN liganden met tzNHC donoren (Schema 4). Omdat esters niet erg efficiënt worden gereduceerd tot alcoholen met de ontwikkelde di-NHC ruthenium verbindingen uit Hoofdstuk 3, is in deze liganden een coöperatieve functionaliteit ingebouwd. De benzyïsche “arm” van de op lutidine gebaseerde liganden kan worden gedeporteerd, waarbij tegelijkertijd de aromaticiteit van de pyridinering verloren gaat (Schema 4, kader). Vervolgens kunnen (ver)bindingen, bijvoorbeeld $H_2$, over het metaal én het ligand geactiveerd worden. Deze aanpak heeft in het verleden tot ongeëvenaarde katalytische activiteit geleid in onder andere ester hydrogerenlyse.

Transmetalering van het Ag(I) complex leidt tot ongebruikelijke faciale coördinatie van de tridentaat liganden aan Ru(II). Zowel de ruthenium verbindingen als de palladium equivalenten vertonen zoals verwacht reactiviteit van de benzyïsche linker. De ruthenium complexes zijn bovendien actief in de hydrogerenlyse van methylbenzoaat en andere esters onder invloed van minimaal 20 mol% KOtBu ($p(H_2) > 5$ bar, $T = 100$ ºC; Schema 4).

De reden voor de cruciale minimum concentratie van KOtBu (<20 mol%) is onderzocht in dit hoofdstuk, maar helaas niet onomstotelijk vastgesteld. Desalniettemin is er meer inzicht verkregen in het mechanisme van Ru-
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gekatalyseerde ester hydrogenering. Door middel van hoge druk in situ NMR spectroscopische experimenten zijn CNC Ru hydride verbindingen aangetoond die mogelijk actief zijn onder de katalytische omstandigheden.

Tot slot behandelt **Hoofdstuk 6** het ontwerp van chirale di-carbeen metaalverbindingen voor enantioselectieve katalyse. Enantioselectieve katalyse is onmisbaar voor de selectieve synthese van chirale producten, die bijvoorbeeld essentieel zijn voor geneesmiddelen. Ondanks het wijdverbreide gebruik van NHCs in homogene katalyse waren er nog relatief weinig toepassingen bekend in enantioselectieve transformaties met behulp van deze liganden. Het chirale di-tzNHC ligand in dit proefschrift, dat is gebaseerd op het antropisomere BINAM molecuul, kan in drie synthetische stappen worden verkregen met een opbrengst van 91%. De bijbehorende di-tzNHC Ag(I), Pd(II), Ir(I) en Rh(I) verbindingen zijn met succes gesynthetiseerd. De laatstgenoemde is actief in de hydrosilylering van ketonen. Bovendien is de chiraliteit van het ligand overgebracht op het substraat met een enantiomere overmaat (ee) van maximaal 51% (Schema 5).

**Schema 5:** De chirale Rh(cod) pre-katalysator uit Hoofdstuk 6 (kader) voor de katalytische hydrosilylering van ketonen.

Het onderzoek dat is beschreven in dit proefschrift toont aan dat (bidentaat) tzNHC liganden een aanwinst zijn voor de organometaalchemie en homogene katalyse. De liganden zijn eenvoudig te synthetiseren en aan vele late overgangsmetalen te coördineren. De mogelijke toepassingen van de verkregen elektronenrijke metaalverbindingen zijn gedemonstreerd aan de hand van verscheidene katalytische reducties van dubbele bindingen, inclusief enantioselectieve transformaties en hydrogenolysis van lastige ester substraten. Bovendien is er meer kennis vergaard over triazolylideen- en di-carbeenverbindingen. Zo is bijvoorbeeld aangetoond dat de binding tussen het metaal en chelerende dicarbenen niet altijd even robuust is. De efficiënte synthetische route garandeert dat een veelvoud aan nieuwe tzNHC liganden kan worden verkregen. Hierdoor is het aannemelijk dat er een glansrijke toekomst voor de toepassing van dergelijke liganden is weggelegd.
Dankwoord

Na 4 jaar, waarin evenveel labjournaals zijn gevuld met tenminste 575 experimenten, is het nu tijd om iedereen te bedanken die, op wat voor manier dan ook, een bijdrage heeft geleverd aan dit proefschrift. Daarnaast wil ik even laten weten aan alle lieve, leuke mensen in mijn leven hoe blij ik met ze ben.

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Dankwoord

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I had the opportunity to perform some of my research in la bella Italia! Andrea Biffis, Paulo, Chiara, Marco x2, Cristina & Casa Duccesci, grazie mille! I hope that we will have another spritz together some day! Andrea Volpe, although our collaboration was not as fruitful as we would have hoped, we sure have had a lot of fun (good thing Italians do not get drunk from beer)! In bocca al lupo/DOEI!

The strongest collaboration was obviously with the Homkat group. Everyone, thanks for all your input/help/enthusiasm/nice coffee and lunch breaks/(non-home-made)cakes/borrels and above all companionship! Joost, bedankt voor het openstellen van de mini- en group meetings en voor alle suggesties over de jaren heen. Esther, Juju (finally time to go to the Casablanca?!), SHAM, Paul, Monalisa, Saeed, Andrei, Zhou, Qiquang, Wojciech, Snurti, Andrea en de gin-tonic/weerwolf crew: Danny, Fenna, Linda, Martin, René, SanderO & Vincent (bedankt voor vele mooie herinneringen, ook naast Camerino!), InCatT (bedankt voor jullie hulp bij mijn eerste autoclaaf experimenten!): Zohar, Detz (mijn practicumbegeleider!), Lidy & Kluwer and former Homcats: Rafa, Pauline, NMri (superpisvis/abadia!) and last but not least, Bartje (altijd gezellig als je langs kwam voor cola of EHBO en je was het leukste paranimf-maatje ever!).

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The best thing about doing a PhD is that you get to go to conferences! I met a lot of people there that contributed to the PhD experience (in a scientific discussion or afterwards during the conference dinner/after party). Especially Clementine en Eva (go-yen!) are thanked for the awesome times we had. I hope we stay in touch!
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Dan kom ik bij mijn **βy-matties (+Thomas)**, ik ken jullie nu bijna 10 jaar! Wow! Thanks voor alle leuke activiteiten samen (wintersport, sinterklaas, feestjes, etc.), ik hoop dat er nog veel volgen! **Andrea, Aukje, Jessie & Lisa**: lieve patzers, of we nou samen in Dare rijden naar Dubrovnik, spontaan liften naar Berlijn, reizen door ZO-Azië of gewoon chillen in Amsterdam, het is altijd leuk samen en jullie zijn geweldige vriendinnen!

Alle chicks van **SV de Meer Vr3**, elke week kijk ik uit naar zaterdag: lekker potje voetballen! In het begin verloren we alles met 10-0, maar inmiddels zijn we BEST goed (dankzij **Ian, Remko, Konna & Vincent** (ik heb je de laatste jaren zeer gemist als lunchbuddie))). Vorig jaar het kampioenschap was de kers op de taart!! Bedankt voor heel veel afleiding en gezelligheid.

De andere sportieve afleiding in mijn leven: skifahren! Als ik in de sneeuw (of op de rolband) sta, denk ik nooit aan de chemie (hetzelfde geld trouwens voor de Kuhstal & schirm ;-)). Dank aan iedereen van de **Ski-Inn & skischule Krimml** (pferti!).

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Amsterdam, mei 2015

Soraya