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Synthesis of Well-Defined N-Heterocyclic Carbene (NHC) Complexes of Late Transition Metals

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Synthesis of Well-Defined N-Heterocyclic Carbene (NHC) Complexes of Late Transition Metals

A Dissertation

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To my mum

To Alexandre

To Elisha

Three loves, three pillars

À maman

À Alexandre

À Elisha

Trois amours, trois piliers

Acknowledgments

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Abstract

N-heterocyclic carbenes (NHCs) have emerged as appropriate replacements for phosphines to synthesized highly active metal complexes in homogeneous catalysis. The advantages of NHCs over phosphines include ease of handling, minimal toxicity and powerful electron donating properties. They bind transition metals with no need of back-donation and yield complexes with enhanced stability. The ability of NHCs to bind all metals from the periodic table, in low and high oxidation states, creates an unprecedented opportunity for the design of new complexes.

This dissertation is dedicated to the synthesis of well-defined organosilver and organogold complexes bearing NHC ligands. In addition, two short chapters describe briefly the synthesis of NHC acetylacetonate palladium(II) complexes, and the use of NHC ruthenium(II) indenylidene complexes in ring opening metathesis polymerization reactions.

New silver(I) and gold(I) halide mono-NHC complexes are synthesized, structurally characterized, and compared to other existing silver(I) and gold(I) complexes. The silver cation trends to form thermodynamically favored bis-NHC complexes and the success for the synthesis of kinetically favored silver(I) mono-NHC complexes is strongly dependant of the carbene, the solvent, and the silver salts used. In contrast, the synthesis of gold(I) mono-NHC complexes appears easier specially by transmetalation starting from silver(I) NHC complexes.

The reactivity of both metals NHC complexes is directly related to the strength of the metal-carbene bond. The gold(I) cation firmly bound to the carbene, undergoes oxidative addition

with halogens to afford gold(III) NHC complexes, or dehalogenation in presence of inorganic silver salts to afford cationic gold(I) mono-NHC complexes in coordinating solvent. The coordinating solvent can be replaced by a neutral or anionic group to yield gold(I) NHC complexes with unusual ligands such as olefins, pyridines, sugars. In contrast, the silver(I) cation is weakly bound to the carbene, and silver(I) NHCs decompose in presence of halogens or inorganic silver salts.

In conclusion the synthesis of the NHC complexes emphasizes deeply the similarities and the differences between silver and gold chemistries. While NHCs ideally stabilize gold(I) and(III) complexes, phosphines appears to be a more promising alternative than NHCs for the chemistry of silver.

Résumé

Les carbènes *N*-hétérocycliques se sont avérés être des candidats appropriés pour remplacer les phosphines dans la synthèse de complexes métalliques hautement actifs en catalyse homogène. Les NHCs présentent de nombreux avantages par rapport aux phosphines. Ils sont faciles à manipuler, faiblement toxiques, et surtout fortement donneurs en terme de densité électronique. Ils forment des liaisons avec les métaux de transition, ne nécessitant aucune rétro-donation, et donnent naissance à des complexes exceptionnellement stables. La particularité qu'ont les NHCs à se lier à tous les métaux du tableau périodique qu'ils aient un faible ou un haut degré d'oxydation, crée une réelle opportunité pour le design de nouveaux complexes, tant ils peuvent être nombreux.

Ce travail de thèse est dédié à la synthèse de complexes organométalliques d'argent et d'or portant des ligands NHC et de structure parfaitement définie. D'autre part, deux courts chapitres traitent de la synthèse de complexes NHC d'acétylacétonate de palladium(II), et de l'utilisation de complexes NHC d'indénylidène de ruthénium(II) pour amorcer des polymérisations par métathèse par ouverture de cycle (ROMP).

De nouveaux complexes mono-NHC d'halogénure d'argent(I) et d'or(I) ont été synthétisés, structurellement caractérisés, et comparés à d'autres complexes d'argent(I) et d'or(I) existants. Le cation argent a tendance à former des complexes bis-NHC thermodynamiquement favorisés et l'obtention de complexes exclusivement mono-NHC d'argent est fortement dépendant des carbènes, des solvants, et des sels d'argent utilisés.

La réactivité des complexes à base d'argent(I) et d'or(I) est directement liée à la stabilité de la liaison métal-carbène. L'or(I) qui est fortement complexé au carbène subit soit une réaction d'addition oxydante en présence d'halogènes pour donner des complexes NHC d'or(III), soit une déshalogénation en présence de sels d'argent inorganiques pour donner des complexes mono-NHC cationiques d'or(I) dans des solvants coordinants. Ce solvant coordinant a été remplacé par un ligand neutre ou anionique pour générer des complexes NHC d'or(I) avec des ligands originaux tels que des oléfines, des pyridines, ou même des sucres. En revanche, le cation argent(I) est faiblement complexé au carbène, et les complexes NHC d'argent(I) se décomposent en présence d'halogènes ou de sels d'argent inorganiques.

En conclusion, la synthèse de ces complexes NHC a permis de mettre en évidence les similitudes et les différences affichées par les chimies de l'argent et de l'or. Alors que les NHCs stabilisent idéalement les complexes d'or(I) et (III), les phosphines apparaissent comme étant une meilleure alternative que les NHCs pour la chimie de l'argent.

CHAPTER 1

NHC-LIGANDS AND ORGANOMETALLIC CHEMISTRY

1.1. The history of carbenes

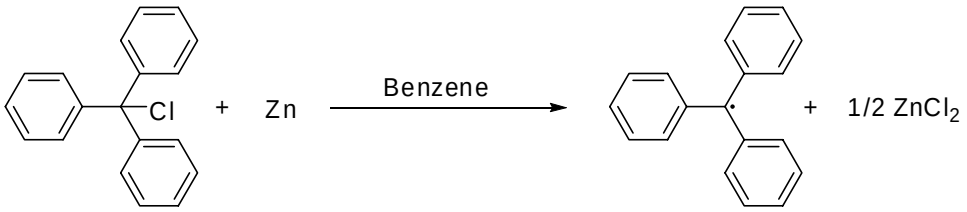
1.1.1. Early works, radical chemistry

A carbene is defined as a neutral, divalent carbon with 6 electrons on its valence shell.

The first assumption of a carbene species was made in 1862 by A. Geuther.[1] He suggested that the alkaline hydrolysis of chloroform proceeds though the formation of a reaction intermediate with a divalent carbon called dichlorocarbene. In 1897, J. Nef proposed the same reaction intermediate for the Reimer-Tiemann reaction[2] and the transformation of pyrrol to *β*-chloropyridine in chloroform. They both had a lot of intuition and courage for their postulations considering that most of the chemists did not even believe to the existence of free radicals at this time. Indeed three years later, M. Gomberg characterized the first example of free radical, the

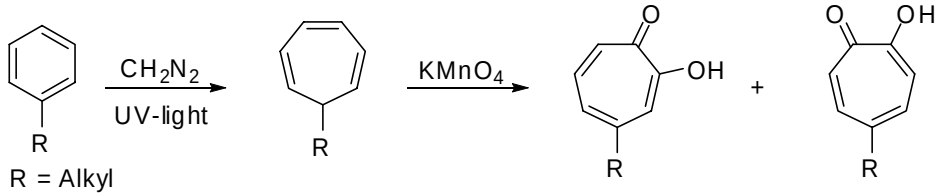
triphenylchloromethylene (Scheme 1.1), through elemental analysis and chemical reactivity.[3] Its discovery was freshly welcomed by the scientific community.[4]

Scheme 1.1. Generation of the first stable radical



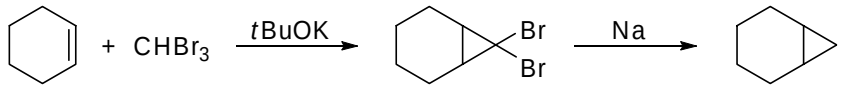
Prior to the Great War, H. Staudinger and O. Kupfer contributed to the recognition of the carbenic reaction-intermediates by studying on the formation of methylene derivatives[5] and diazomethane.[6] Throughout the 1920s and 1930s, the existence of free radicals was finally well recognized, and their use in organic chemistry as reaction intermediates was growing extremely rapidly. In this regard, carbene moieties were also regarded as diradicals.[7] The methylene carbene was seen as a linear species, with two degenerated *p*-orbitals inevitably leading to a triplet state.[8] At the beginning of the 1950s, there was a resurgence of interest in the organic chemical reactions of carbenes.[9] In 1953, W. Doering *et al.* proposed an elegant synthesis of tropolones *via* an addition of methylene to benzene.[10] (Scheme 1.2)

Scheme 1.2. Synthesis of tropolone-derivatives via a methylene intermediate



Doering and his collaborators' most important contribution came a year later when they proved the existence of a dibromomethylene intermediate, in the first synthesis of cyclopropane via the addition of bromoform to an alkene.[11] (Scheme 1.3)

Scheme 1.3. Olefin cyclopropranation via a methylene intermediate



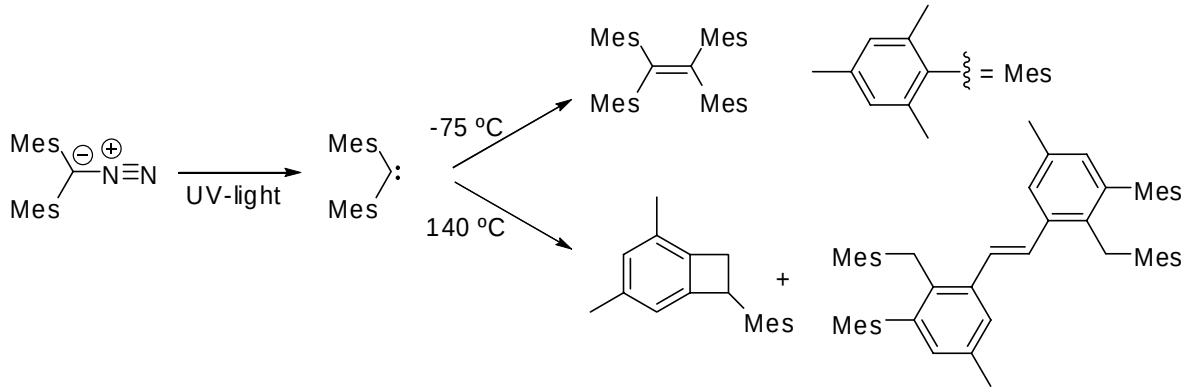
Then more organic synthesis involving the use of methylene were reported,[12] prompting chemists and physicists to have a closer look at this carbene intermediate.

1.1.2. Electronic configuration and geometry

In 1951, J. Lennard-Jones and J. Pole were using quantum mechanics to determine the geometric structures and properties of small molecules.[13] They assumed the existence of two different ground states for the methylene carbene (still seen as a diradical) but could not determine the one with the lowest energy. One of the ground states they proposed was a singlet

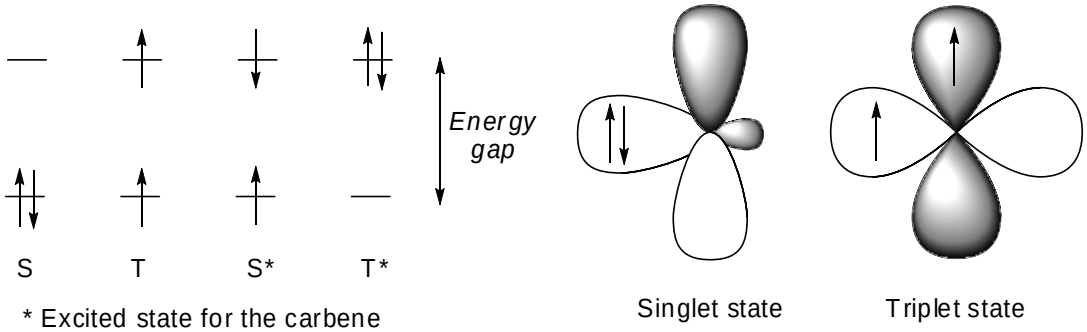
state with triangular geometry possessing three orbitals filled with two paired electrons and an empty orbital. The other proposed ground state was a triplet state with a linear geometry possessing two orbitals filled with paired electrons and two orbitals filled with unpaired electrons.[13,14] Two years later, J. Duschenne and L. Burnelle proved that :CF_2 had a singlet ground state with a sp^2 hybridization and the orbital bearing the nonbonding pair of electrons being nearly s.[15] In 1964, Zimmerman *et al.* assumed that steric protection would enhance the stability of carbenes. They successfully synthesized the dimesithylmethylene compounds, but could not isolate it.[16] Analysis of the rearrangements products suggested that the carbene had a triplet ground state with an unexpected nonlinear geometry (Scheme 1.4).

Scheme 1.4. Generation of a triplet carbene and rearrangement products



In 1968, Hoffmann *et al.* accurately determined the minimum splitting energy required between both ground states to have a methylene with a singlet state.[17] They also suggested that the singlet state could be favored by π-overlap between the *p*-orbitals of the carbene and the *α*-substituents (Scheme 1.5).

Scheme 1.5. Electronic states of a carbene



During the 1970s and 1980s, numerous theoretical works using *ab initio* quantum calculations were published to rationalize the electronic structures and the geometries of methylene moieties such as :CH_2, :CHF, :CHBr, :CF_2, :CCl_2.[18] It became more and more obvious that inductive and mesomeric effects act synergistically to determine the energy gap between both ground states.[19] In 1992, Goddard *et al.* were able to predict accurately the ground state configuration of a series of carbenes :CXY (X, Y = H, F, Cl, Br, I, SiH_3), with a method using only some slight calculations and which is applicable to other arbitrary carbenes.[20] It is important to predict the ground states of carbenes as it will directly affect their stability and reactivity.[21]

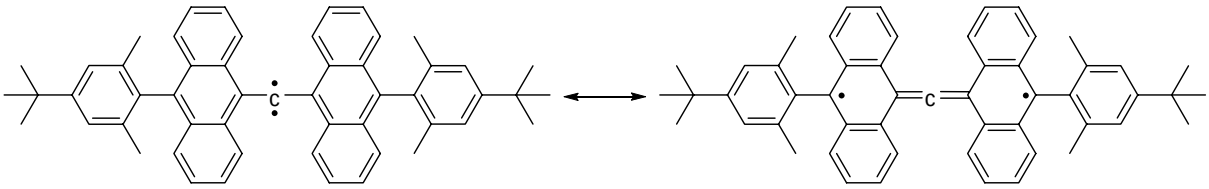
1.1.3. Stabilization and reactivity of carbenes

1.1.3.1. Triplet carbenes

Diazo compounds, which are very fragile and prone to degradation, are used to generate triplet carbenes by photolysis (UV-light or LASER-XeCl eximer). They usually bear two α-

phenyl groups, as most α-dialkylmethylenes appear to be singlet carbenes.[22] Their diradical behavior makes them very reactive and difficult to isolate.[23] Triplet carbenes are trapped by oxygen and form ketones via a ketone oxide intermediate.[24] They also rearrange/decompose by olefin dimerization,[16,25] C−H insertion,[25a,26] cyclopropanation of alkenes ([2+1]-cycloaddition),[27] H-abstraction from an alkene[28] or a C−H bond leading to a simple radical.[29] They are generated at low temperature (77 K) and can be characterized by ESR. More than thirty years after the unique (and unsuccessful) attempt by Zimmerman to isolate a triplet carbene, Tomioka *et al.* have overcome the challenge,[30] synthesizing a carbene in solution at room temperature stable up to one week (Scheme 1.6).[31]

Scheme 1.6. Stable triplet carbene



Contrary to their singlet cousins, the triplet carbenes do not react with carbon-halogen bonds[32] and they can be stabilized by steric protection with bromo and trifluoromethyl groups placed in their vicinity.[28c,33] Bulky alkyl groups are prohibited because any close C−H bond would be activated. Triplet carbenes can also be stabilized by delocalization of the unpaired electrons in an aromatic network such as an anthryl group. It is worthy to note that these stable carbenes can be linked together to form polycarbenes with interesting ferromagnetic properties.[34]

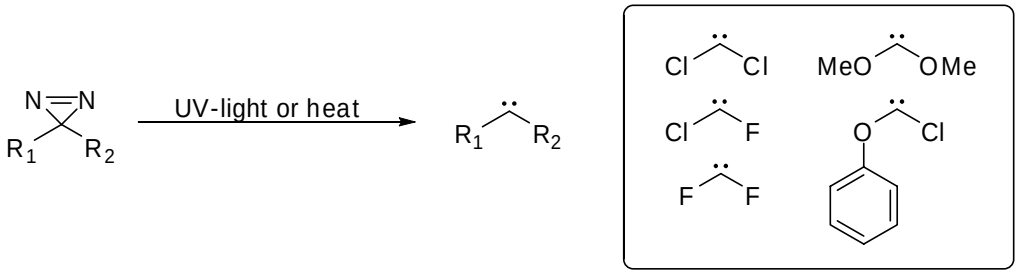
1.1.3.2. Singlet carbenes

Carbene multiplicity is greatly determined by the electronegativity of both α-substituents. σ-electron-withdrawing groups (negative inductive effect: –I) favor the singlet state by stabilizing the filled non-bonding orbital, increasing its *s* character.[19,20] On the other hand, electronic delocalizations (mesomeric effects: ±M) between the methylene and its α-substituents determine the carbene geometry (linear or bent) and play an active role in its thermodynamic stabilization.[17b] Depending upon the mesomeric effects and the stabilization brought by each *α*-group, singlet carbenes fall into three categories: +M/+M, –M/–M and –M/+M.[35] They are amphiphilic and can react as nucleophilic or electrophilic species.[36] Unstable singlet carbenes usually decompose/rearrange by olefin dimerization,[37] 1,2-shifts,[38] C−H insertion, fragmentation[39] or [2+1]-cycloaddition to alkenes.[40]

1.1.3.2.1. +M/+M α-groups

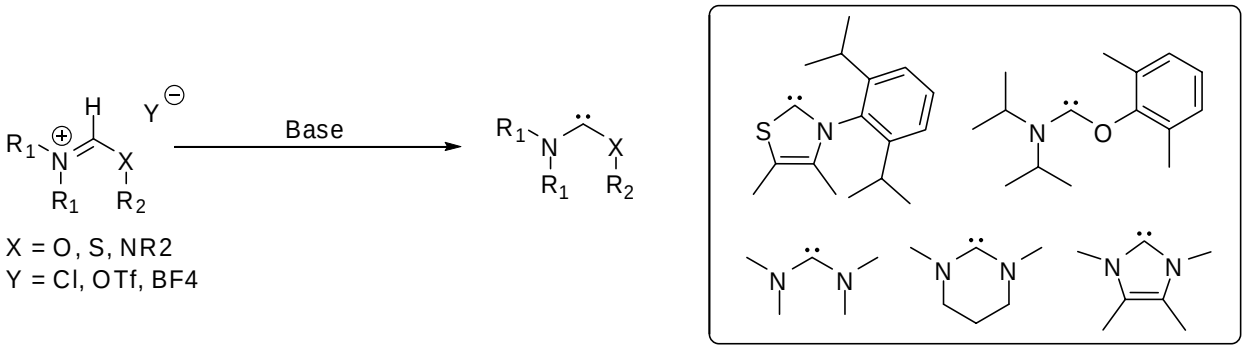
+M/+M singlet carbenes bear two electron-donating *α*-groups such as F, Cl, Br, I, OR, SR, SR_3, NR_2, PR_2. They are predicted to have a bent geometry.[19,20] Their stabilization occurs by back-donation from the *p* orbital of the substituents to the methylene empty *p*-orbital. Dihalocarbenes,[41] dimethoxycarbenes,[42] and alkoxyhalocarbenes[43] are transient species; they spontaneously dimerize. Their reactivity can be monitored in terms of their ability to promote the cyclopropanation of alkenes ([2+1]-cycloaddition).[42,43] They are cleanly generated by thermolysis or photolysis from the corresponding diazirines (Scheme 1.7).

Scheme 1.7. Generation of carbenes from diazarine precursors

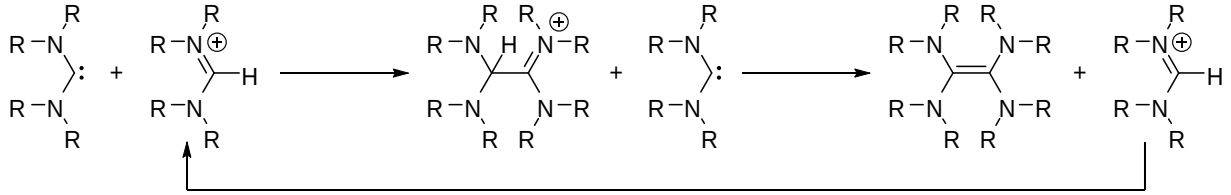


In contrast aminoxycarbenes,[44] aminothiocarbenes, diphosphinocarbenes[45] and especially diaminocarbenes (including NHCs) are kinetically stable in solution or as solids at ambient temperatures. While their dimerization is thermodynamically favored, it occurs only in presence of a Brønsted acid.[46] They are conveniently prepared by deprotonation of the corresponding salt (Scheme 1.8 and scheme 1.9).

Scheme 1.8. Generation of carbenes by deprotonation



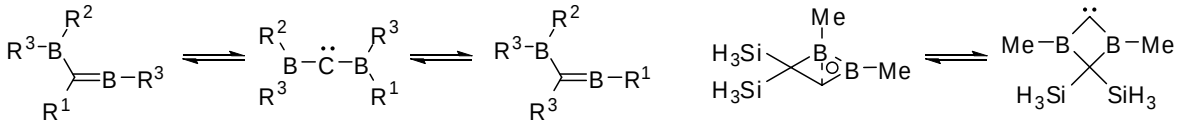
Scheme 1.9. Carbene dimerization assisted by a Brønsted acid



1.1.3.2.2. –M/–M α-groups

–M/–M singlet carbenes bear two electron-withdrawing *α*-groups such as COR, CN, CF_3, BR_2, SiR_3. They are predicted to have a linear geometry.[19,20] Stabilization occurs by back-donation from the methylene filled *p*-orbital to the substituents empty *p*-orbital. They have never been isolated. However, some masked analogues, such as the borinanylideneboranes,[47] have been synthesized and react like electrophilic carbenes toward trapping reactions with germylenes and stannylenes (Scheme 1.10).[48]

Scheme 1.10. Masked analogues of –M/–M carbenes



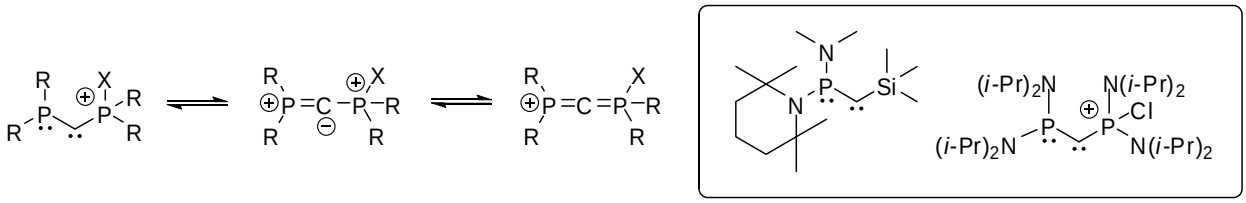
R^1 = Me, Et
R^2 = CR=C=C(SiMe3)2

R^3 = 2,3,5,6-tetramethyphenyl

1.1.3.2.3. +M/–M (or –I) α-groups

+M/–M singlet carbenes bear two α-groups with opposite electronic effects. Their geometry is predicted to be quasi linear.[19,20] They have to be stabilized simultaneously by a strong back-donation from the *p* orbital substituents to the methylene empty *p*-orbital and by a weaker back-donation from the methylene filled *p*-orbital to the substituents empty *p*-orbital (pull-push effect). At low temperatures alkoxycyanocarbenes[49] and alkoxytrifluoromethylcarbenes[50] are transient, while phosphinosylilcarbenes[51] and phosphinophosphoniocarbenes[52] are stable at ambient temperature. They are cleanly generated by photolysis or thermolysis of the corresponding diazarine or diazo compound. The phosphinocarbenes, stabilized by extensive delocalizations, can also react like phosphavinylylides or phosphacumulenes (Scheme 1.11).[35,53]

Scheme 1.11. Phosphinocarbenes and mesomeric forms

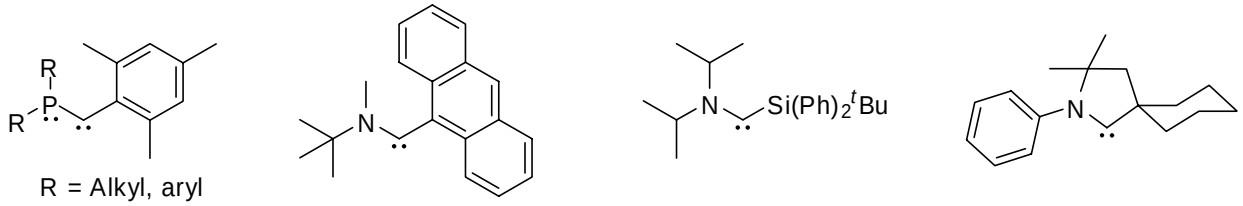


1.1.3.2.4. A recent new family of stable +M/-- carbenes

While alkylhalogenocarbenes are transient,[54] Bertrand *et al.* synthesized a series of stable arylphosphinocarbenes,[55] alkylaminocarbenes[56] and silylaminocarbenes (Scheme 1.12).[57] They

are stabilized by only one amino- or phosphino-group. The second α-group acts as a spectator and provides a marginal electronic effect toward the carbene center. They are nucleophiles and can be generated by depronation of the corresponding salt.

Scheme 1.12. New carbenes stabilized by only one *α*-group

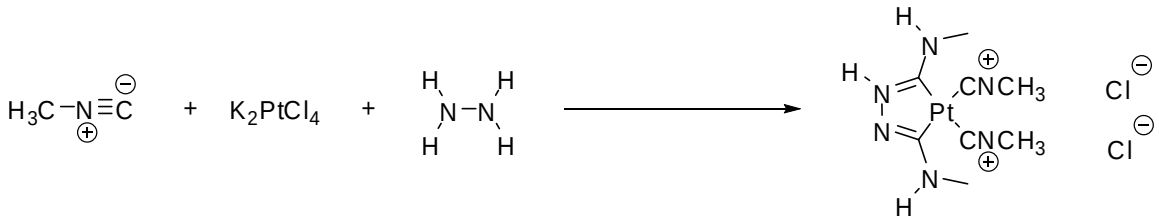


1.2. Carbenes and organometallic chemistry

1.2.1. Early works and first complexes

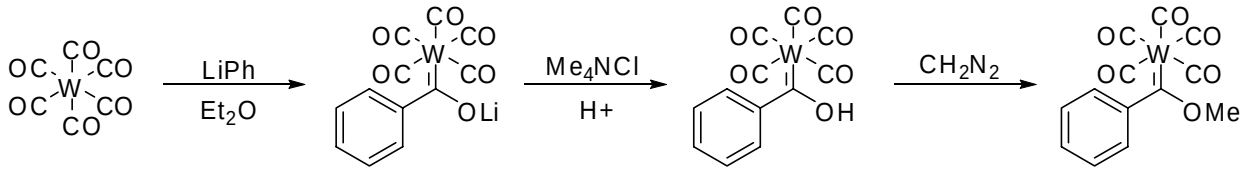
In 1915, Chugaev *et al.* reported that hydrazine reacts with isocyanides complexes of platinum(II) to yield a new hydrazine-bridged platinum complexes.[58] Unfortunately they did not have the required spectroscopic techniques to reveal, in fact, the first synthesized metal-carbene complex (Scheme 1.13). The structure was later resolved in 1973 by NMR and X-ray single crystal diffraction.[59]

Scheme 1.13. Synthesis of the Chugaev salt



During the 1960's, E. O. Fisher and K. Ölefe were working on alkene-metal-carbonyl (Mn, Re) complexes.[60] In 1964, while carbenes were en vogue in organic chemistry, Fisher reported and characterized unambiguously the first metal-carbene complex:[61] The methoxyphenylmethylene tungsten(0) pentacarbonyl (Scheme 1.14). He extended the synthesis to chromium(0), iron(0) and manganese(0) complexes with different alkoxy- and alkyl-groups.[62]

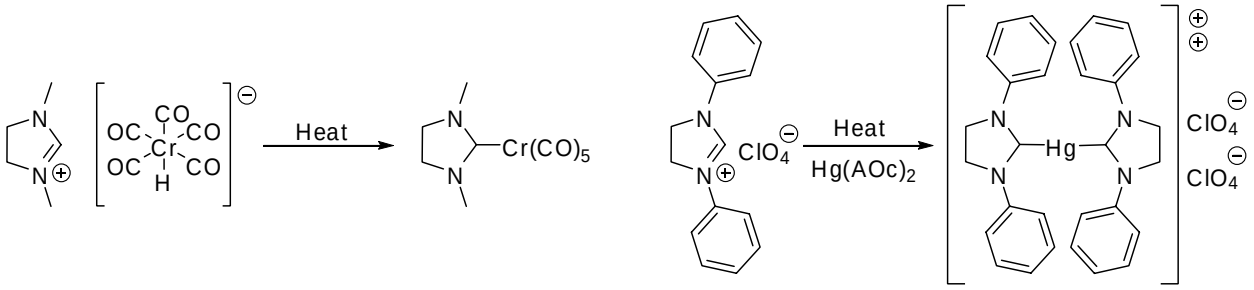
Scheme 1.14. Synthesis of the first recognized metal-carbene complex



During the same period, H. Wanzlick was interested in isolating carbenes and believed that diaminocarbenes would be stable. He proposed the synthesis of the 1,3-diphenyl-2-imidazolidinylidene via 1,3-diphenyl-2-trichloromethylimidazolidine.[63] The carbene was not isolated and only the corresponding enetetramine was recovered. He also reported different carbenes adducts by using thiophosgene, thionylchloride, cyclopentanone or benzaldehyde.[64] In

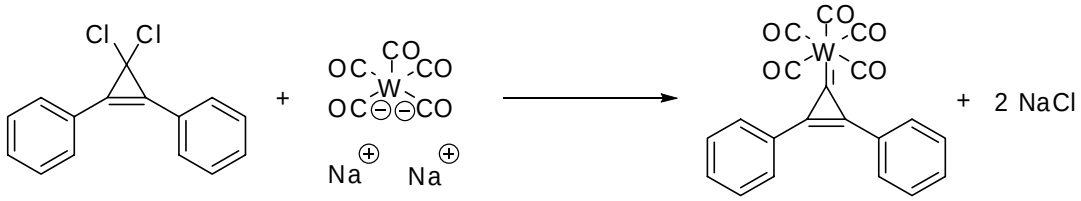
1968, H. Wanzlick and K. Öfele separately reported two different NHC-metal complexes[65] more than twenty years before the isolation of the first NHC (Scheme 1.15).

Scheme 1.15. Synthesis of the first NHC-metal complexes



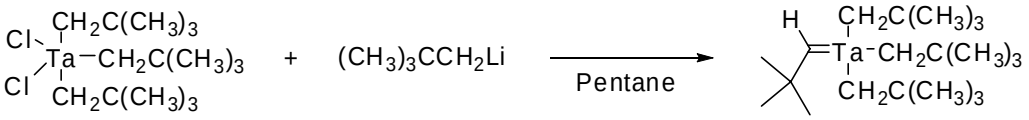
The same year, K. Öfele reported also the first complex bearing a non-stabilized carbene without any α-heteroatoms (Scheme 1.16).[66]

Scheme 1.16. Synthesis of the first alkylidene-metal complex



In 1974, R. R. Schrock reported the first synthesis of a high oxidation state (d^0) metal-alkylidene complex[67] by an α-hydrogen abstraction on the tri-(2,2-dimethylpropyl)methyl tantalum(V) dichloride precursor (Scheme 1.17).

Scheme 1.17. Synthesis of the first alkylidene-metal (d^0) complex



1.2.2. Carbenes and metal bond formation

1.2.2.1. Geometric considerations

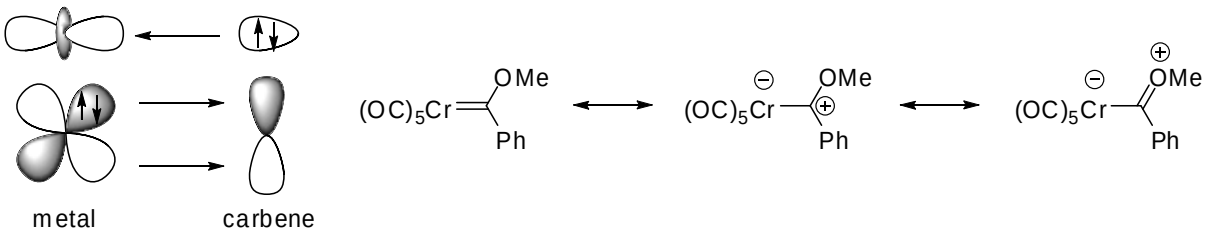
The formation of the metal-carbon bond of a metal-carbene complex by orbitals overlapping requires a narrowing of the valence angle (XCY) at the carbene center.[68] Carbenes stabilized by back-donation from both α-groups (+M/+M), such as diaminocarbenes or dialkoxycarbenes, adopt a bent geometry with a small valence angle (XCY) at the central carbon.[19,20] They have the required geometry to strongly and easily bind a metal fragment. In contrast push-pull carbenes, alkylidenes, and triplet carbenes adopt a widened valence angle and tend to be linear.[19,20] They do not have the adequate geometry to bind the metal fragment and any changes of conformation to narrow their valence angle (CXY) are energetically unfavourable. Consequently, they are very reluctant to form a metal-complex and give a weaker metal-carbon bond.

1.2.2.2. Electronic considerations

1.2.2.2.1. Fischer-carbene complexes

Well stabilized heteroatom singlet carbenes, such aminocarbenes and alkoxycarbenes have a significant gap between their singlet and triplet ground states. They form a metal-carbon bond constituted by mutual donor-acceptor interaction of two closed-shell (singlet) fragments. The dominant bonding arises from carbene-metal σ-donation and simultaneously from metal-carbene π-back-donation (Scheme 1.18).[69] The π-electrons are usually polarized toward the metal and the carbon-metal bond has a partial double bond character which diminishes with the stabilization of the carbene by its *α*-groups.[62,69] For instance, in diaminocarbenes, including NHCs, the metal-carbon bond is seen as a simple bond; the π-back-donation is usually weak because the carbonic carbon is already well stabilized by π-back donation from its amino-groups.[70,71] Fischer carbene complexes are electrophilic at the carbon-metal bond and are susceptible to nucleophilic attack at the carbene center (OMe/NMe_2 exchange for instance).[68-70] They are associated with low oxidation state metals.[69-71]

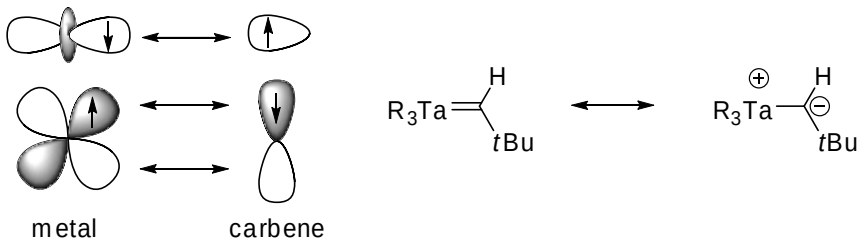
Scheme 1.18. Metal-carbon bonding in Fischer-carbene complexes



1.2.2.2.2. Schrock-carbene complexes

Poorly stabilized carbenes such as dialkylcarbenes or alkylidenes have a small gap between their singlet and triplet ground state. They form a covalent metal-carbon bond in nature created by the coupling of two triplet fragments.[68b,72] (Scheme 1.19) The π-electrons are nearly equally distributed between the carbon and the metal, and the metal-carbon is seen as a true double bond.[69,72] Schrock carbene complexes are nucleophilic at the carbon−metal bond and are susceptible to react at the carbene center with electrophiles as in a Wittig reaction involving an ylide instead of a carbene. They are found exclusively among early transition metals with the highest oxidation state (d^0).

Scheme 1.19. Metal-carbon bonding in Schrock complexes



1.2.2.2.3. Other type of metal-carbene complexes

Non-heteroatom stabilized carbenes can be bound to late transition metals and low oxidation state early transition metals. The complexes formed are usually electrophilic at the metal carbon bond in contrast with the Schrock carbenes complexes. They represent the borderline between traditional Fischer and Schrock type complexes, and they fit partially the

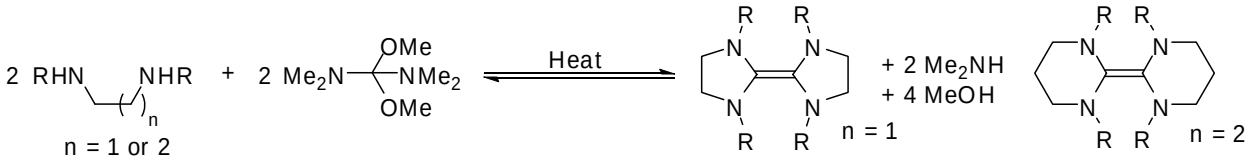
definition of both categories. R. R. Schrock mentioned that in such complexes the carbene moieties should be called phenylcarbenes and alkylcarbenes because benzylidenes and alkylidenes stand for Schrock carbene complexes.[73] Nevertheless, it is acceptable to call non-heteroatom stabilized carbenes alkylidenes and benzylidenes in complexes, regardless of the metal involved or its oxidation state.

1.2.3. Synthesis of Fischer-carbenes complexes

1.2.3.1. Enetetramines (ERO carbenoid precursor)

Enetetramines are electron-rich olefins (ERO).[74] They are synthesized from diamines and *N,N*-dimethylformamide. The reaction is an equilibrium which is driven towards the olefin by removal (distillation) of the methanol and the formation of dimethylamine.[75] (Scheme 1.20) The synthesis is restricted to primary alkyl- and unhindered aryl-diamines.[70,76]

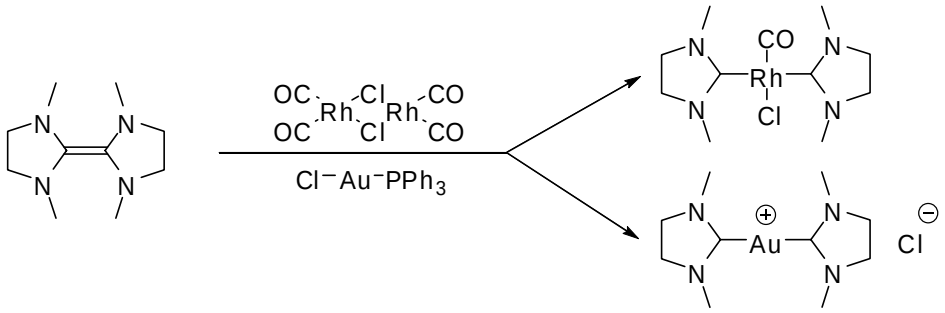
Scheme 1.20. Synthesis of enetetramines



They are generally oxygen- and moisture-sensitive, being chemiluminescent in air due to the formation and decay of dioxetane.[77] Their weak C=C bond reacts with electrophiles or protic reagents to yield the corresponding aminals. They are also strong reducing agents and form in

presence of alkyl-, organosilyl-, organogermanyl-, and organotin halides the corresponding radicals by halide abstraction. They generate imidazolinylidene (NHC) or tetrahydropyridinylidene transition metal complexes by di-μ-halogenodimetal bridge splitting or by the displacement of a neutral or anionic ligand depending upon the metal source chosen (Scheme 1.21).

Scheme 1.21. Carbene-metal complex derived from EROs

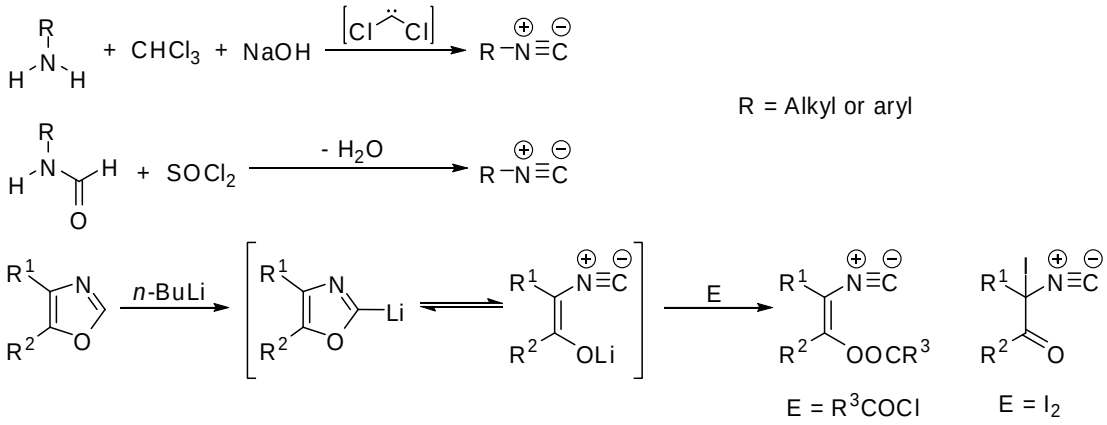


The mechanism of the metal-carbene formation is unlikely to proceed via generation and trapping of a free carbene. M. Lappert *et al.* have synthesized ERO-derived complexes, having between one and four carbene ligands, of Cr(0)/(I), Mo(0)/(II), W(0)/(II), Mn(I), Fe(-II)/(0)/(I)/(II), Ru(-II)/(0)/(II), Os(II), Co(-I)/(II)/(III), Rh(I)/(III), Ir(I)/(III), Ni(0)/(I)/(II), Pd(II), Pt(II), Au(I) and Hg(II).[70,78] Nevertheless, in some rare exceptions the C=C bond is not cleaved, and there is chelation with both the amino-groups. Also, in presence of metal-hydrides the imidazolidinium salt can be formed instead of the metal-carbene complex.

1.2.3.2. Isocyanide metal-complexes (carbenoid precursor)

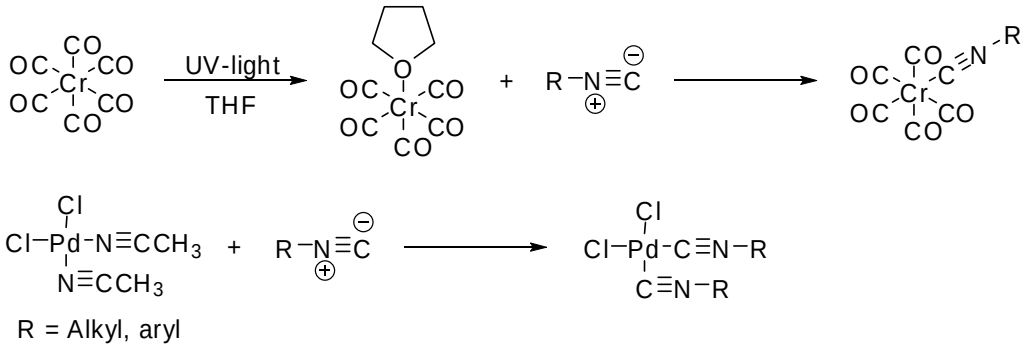
The first isocyanide was prepared by W. Lieke in 1859 by reaction of allyl iodide and silver cyanide.[79] They are usually synthesized by dehydration of formamides (Ugi's reaction),[80] by reaction of primary amines with dichlorocarbene[81] or by metalation of oxazoles (Scheme 1.22).[82]

Scheme 1.22. Synthesis of isocyanides



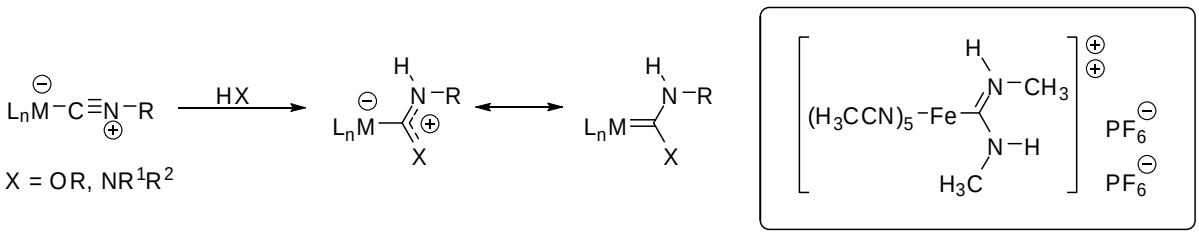
They are strong bases and either polymerize or hydrolyze under acidic conditions.[83] They can be stabilized via metal coordination and functionalized.[84] Isocyanides are notorious for their bad smell which might have seriously hindered their use by chemists. They are sufficiently obnoxious to have been included in non-lethal weapons![85] In terms of bonding they are isoelectronic with CO and react with metal salts or carbonyl to access the corresponding isocyanide-metal complexes (Scheme 1.23).[84,86]

Scheme 1.23. Synthesis of isocyanide metal complexes



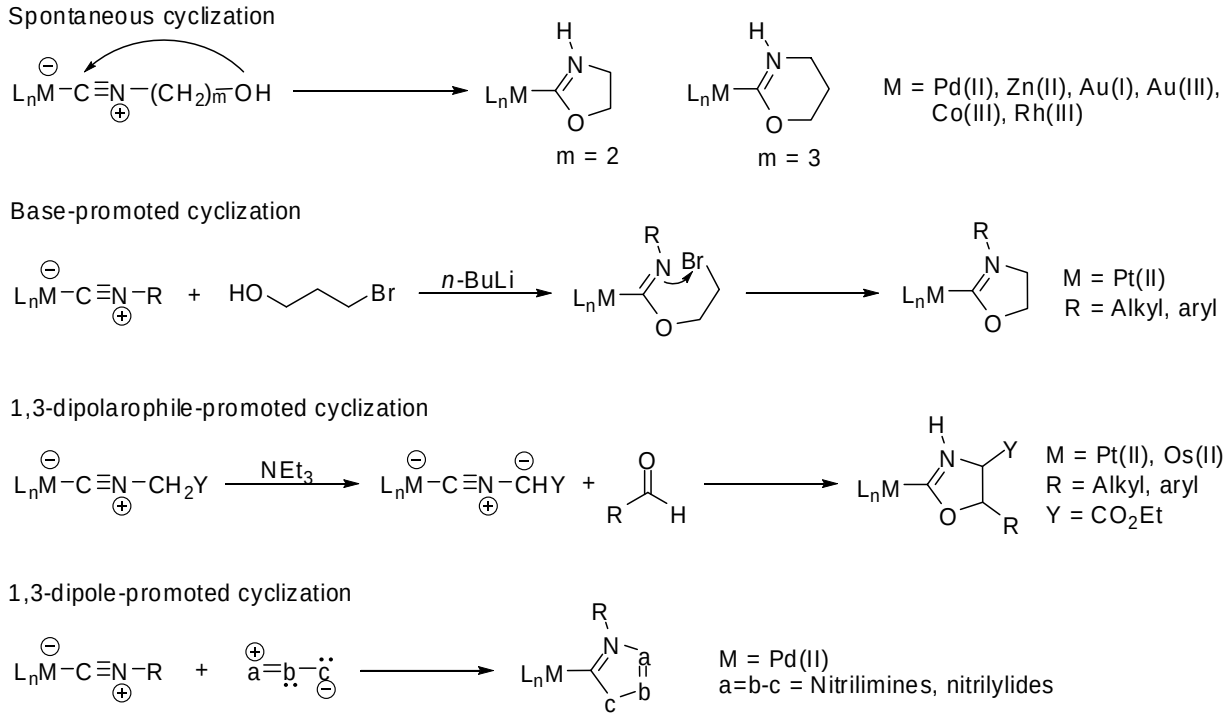
Isocyanide-metal complexes when the metal center is sufficiently acidic react promptly by nucleophilic attack at the coordinated carbon to form aminocarbene-metal complexes.[87] They react with protic nucleophiles such as primary and secondary amines or alcohols to yield acyclic diamino- and aminoalkoxycarbenes complexes (Scheme 1.24).[88]

Scheme 1.24. Synthesis of aminocarbenes complexes via isocyanides metal complexes



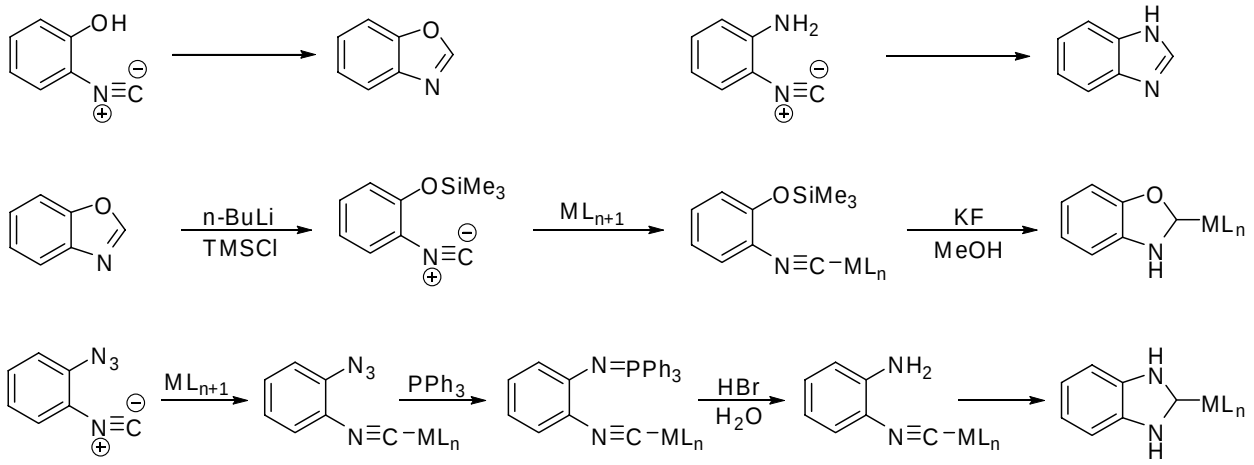
They also yield oxazolidinylidenes, thiazolinylidenes, tetrazolylidenes, triazolylidenes, imidazolylidenes and imidazolidinylidenes (NHCs) complexes by spontaneous cyclization, base-promoted cyclization, reaction with 1,3-dipolarophiles, and reaction with 1,3-dipoles (Scheme 1.25).[89]

Scheme 1.25. Mechanisms for the cyclization of isocyanides complexes



In the case of benzannulated carbenes, such as benzoxazolylidenes and benzimidazolinylidenes, the precursors 2-hydroxyaryl isocyanide and 2-aminoaryl isocyanide which undergo spontaneous cyclization, need to be protected before their metalation (Scheme 1.26).

Scheme 1.26. Benzannulated carbenes complexes formations

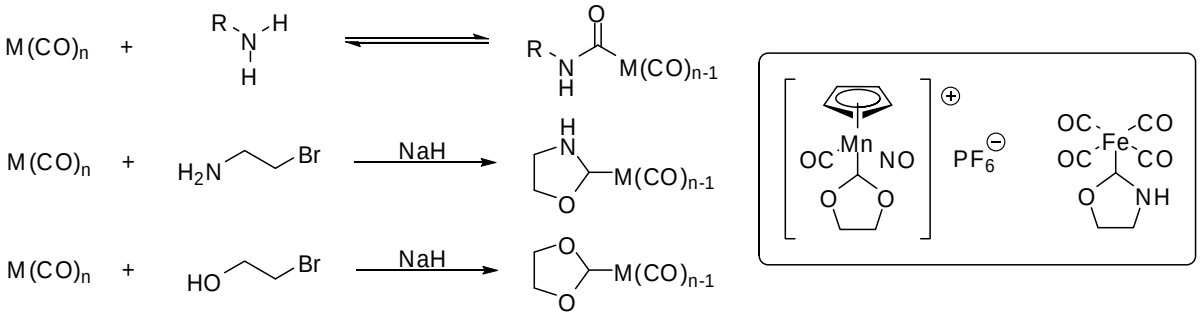


Isocyanide-metal complexes are valuable species because they give access to numerous carbene complexes derived from non-isolable carbenes, including acyclic aminoalkoxycarbenes, oxazolidinylidenes, 1,3-H,H-NHCs and 1,3-H,alkyl-NHCs. Moreover, NH,NH-carbenes can be alkylated stepwise leading to unsymetrically *N*,*N*'-substituted ligands. They also lead to high oxidation state metal complexes with an unusual large number of coordinated carbenes, such as tetra- or hexacarbene complexes.[90]

1.2.3.3. Carbonyl-metal complexes

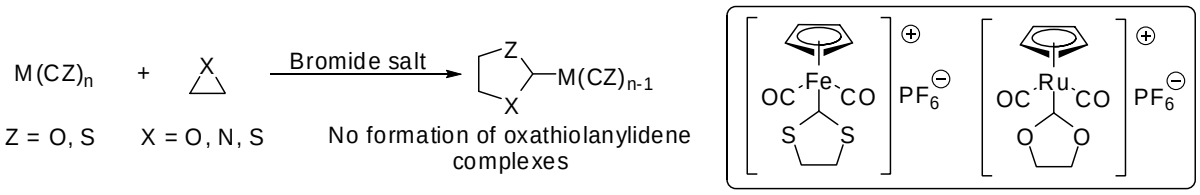
Complexes of acidic metals bearing an electron deficient carbonyl ligand react with aliphatic amines to give carbamoyl complexes.[91] Under basic conditions, they also react with amines and alcohols bearing a good leaving group in *β*-positions, leading to oxazolidinylidenes and dioxolanylidenes complexes (Scheme 1.27).[92]

Scheme 1.27. Synthesis of alkoxycarbenes complexes via carbonyl metal complexes



The reaction proceeds also with carbonyl ligands under neutral conditions by using oxiranes, aziridines and azetidines, and leads to the corresponding dioxolanylidenes, oxazolidinylidenes and oxazinanylidene complexes.[93] It is worthy to note that thiocarbonyl ligands can undergo the same type of reaction. In the presence of aziridines or thiiranes, they lead to thiazolinylidenes and dithiolanylidenes complexes, while oxathiolanylidenes complexes are not be formed (Scheme 1.28).

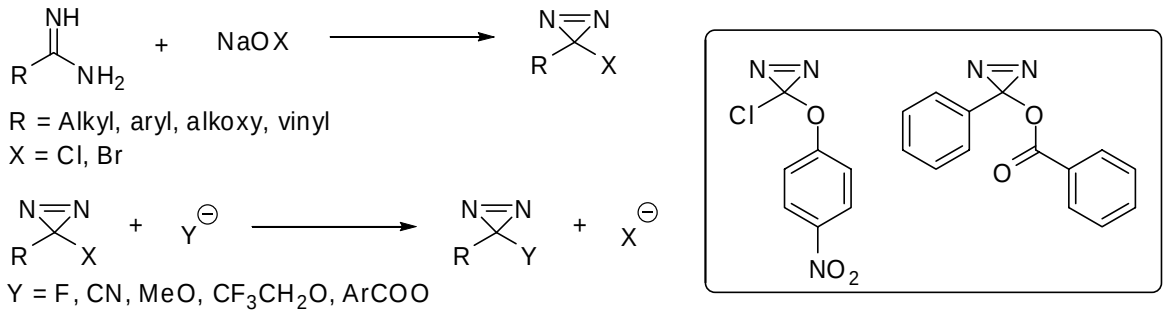
Scheme 1.28. Synthesis of carbenes complexes via heterocycles



1.2.3.4. Diazirines

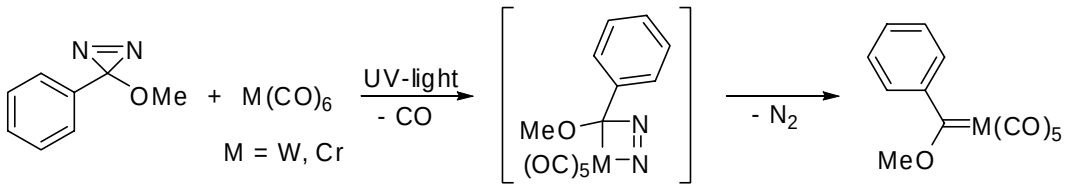
In 1965, W. Graham discovered a remarkable one-pot hypohalite oxidation of imidamides, leading to alkyl-, phenyl-, alkoxy-, or vinyl- halodiaziridines.[94] They can undergo further exchange reactions and be functionalized by nucleophilic attack to their halide moieties (Scheme 1.29).[95]

Scheme 1.29. Diazirines synthesis



Carbenes are afforded cleanly by thermal decomposition of diazirines (Scheme 1.7). Nevertheless, attempts to generate metal complexes directly from the diazirines have been quite unsuccessful, leading to very low yields (at the most 16%).[96] The reaction does not proceed via coupling between a metallic fragment and the free carbene but via an insertion route leading to a metal-diazo-intermediate (Scheme 1.30).[96b]

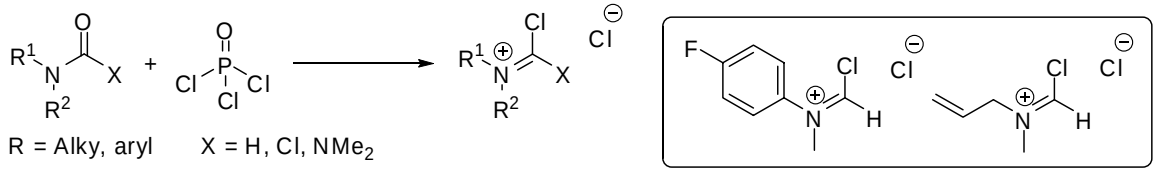
Scheme 1.30. Synthesis of carbene complexes via diazirines



1.2.3.5. Vilsmeyer's salts

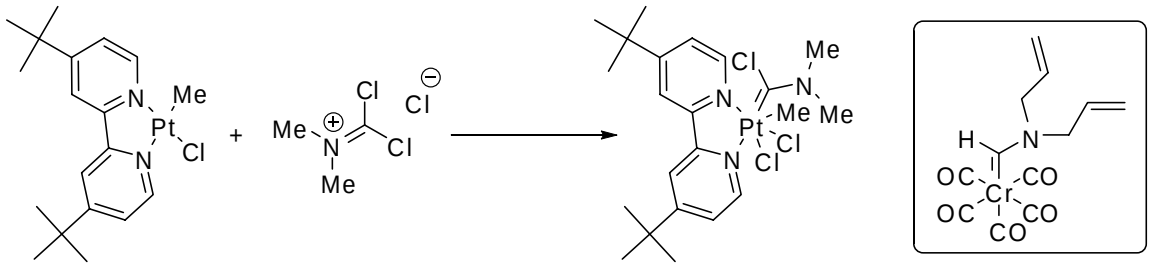
The first chloroiminium salt was prepared by A. Vilsmeyer in 1927, by the reaction of phophoryl trichloride and *N,N'*-dimethylformamide.[97] The synthesis has been extended to *N,N'*-dialkylcarbamic chloride and *N,N,N',N'*-tetraalkylurea (Scheme 1.31).[78c,98]

Scheme 1.31. Vilmeyer's salts synthesis



In presence of a tertiary amine, usually the Hünig's base,[99] iminium salts are deprotonated. The resulting unstable aminocarbenes can mediate the synthesis of isatins and quinolines.[100] When reacted with an electron rich metal center, Vilmeyers salts lead to stable aminocarbenes complexes (Scheme 1.32).[101]

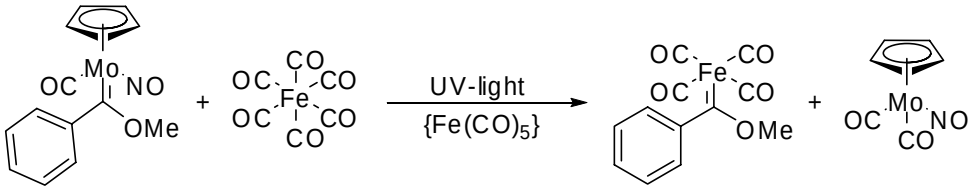
Scheme 1.32. Synthesis of aminocarbene complexes via Vilmeyer's salts



1.2.3.6. Transmetalation from Group 6 metal carbene complexes

The first example of stoichiometric carbene ligand transfer between metal ions was reported by Fischer *et al.* in 1970.[102] The reaction of a molybdenum carbene complex with photochemically generated pentacarbonyl iron(0), produced a new iron(0) complex by transmetalation (Scheme 1.33).

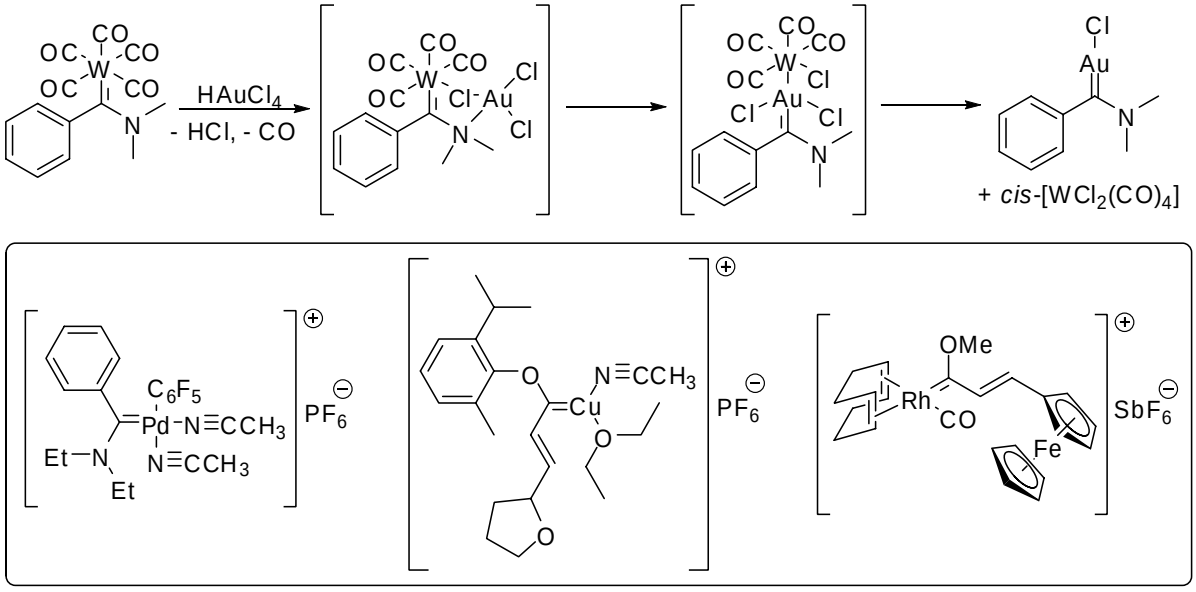
Scheme 1.33. Transmetalation and carbene transfer



Mechanistic studies have ruled out the involvement of free carbenes and the transmetalation process occurs via a carbene transfer between two metal centers.[103] In the case of alkene formation (decomposition products), these ones are not generated by carbenes dimerization, but

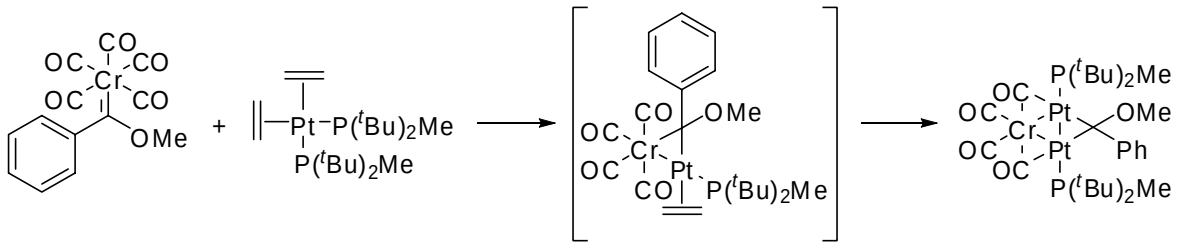
by elimination of a bis-carbene complex formed during a second transmetalation reaction.[104] Late transition metals complexes, including Rh(I), Rh(III), Ir(I), Pd(0), Pd(II), Pt(II), Cu(I), Ag(I), Au(I), Au(III) have been synthesized from Group 6 metal (Cr, Mo, W) complexes precursors (Scheme 1.34).[104,105]

Scheme 1.34. Carbene complexes synthesis via transmetalation



This method applies for all Fischer-type carbenes and is extremely efficient with diaminocarbenes complexes, including NHCs (Paragraph 1.3.9.5). In a few cases, carbene-bridged complexes are formed by transmetalation. They can be di- or even tri-nuclear, with a cluster core (Scheme 1.35).[104,106]

Scheme 1.35. Polynuclear carbene complex synthesis via transmetalation



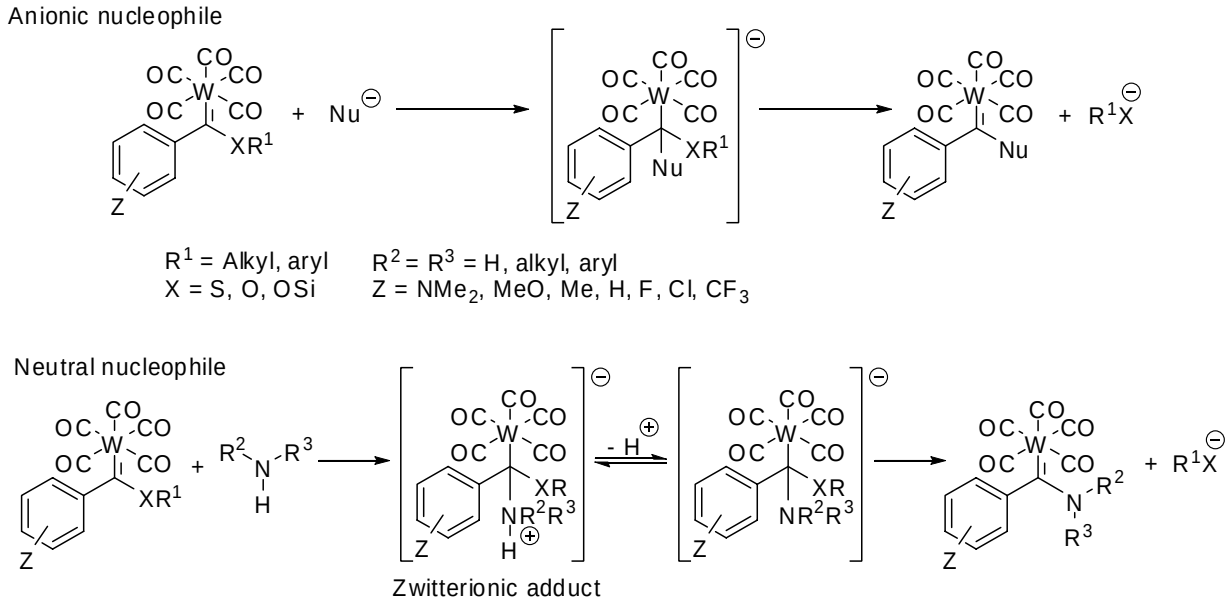
Interestingly, until 2000 the chemistry of the Group 6 metal Fischer carbene complexes was quite forsaken. Now the trend is reversed and a number of efficient catalysts for organic transformations such as carbene self dimerizations, C−H insertions, cyclizations, cyclopropanations are generated by transmetalation.[107]

1.2.3.7. Modification of complexes by nucleophilic attack

Most transition-metal carbene complexes of the Fischer type are electrophilic at the carbenic carbon (Scheme 1.18).[68-70,108] They can be easily modified by nucleophilic substitution when they bear some alkoxy-, alkylthio-, or silyloxygroups.[109] For aminocarbenes the substitution is more difficult as amines are not good leaving groups, and it does not occur with NHC-complexes.[110] Nucleophiles range from neutral to anionic, including ammoniac,[108,109a] amines,[108,109] hydrazines,[108,111] oximes,[108,112] alkoxides,[108,113] thiolates,[108,114] carbanions (usually aryl or alkyllithium),[115] malonitrile anion,[109b] imidazolide[116] and benzimidazolide anions. The first nucleophilic substitution was performed by Fischer *et al.* in 1967.[117] The mechanism is similar to the reaction of carboxylic esters with nucleophiles, involving a tetrahedral intermediate before extrusion of the leaving group.[118] For neutral nucleophiles a proton transfer is included as

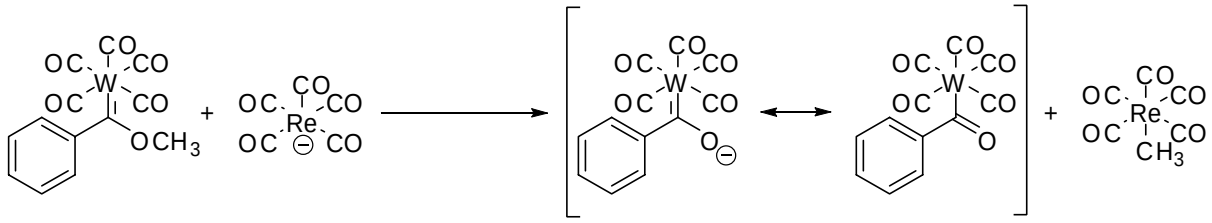
additional and mandatory step for the elimination. If there is no acidic proton available, the reaction stops at the zwitterion adduct stage (Scheme 1.36).

Scheme 1.36. Mechanism of nucleophilic substitution on Fischer carbenes complexes



In the presence of metal carbonyl anions, methoxycarbene complexes display an unusual reactivity. The nucleophilic attack occurs at the methyl group and leads to acylmetalate complexes by demethylation (Scheme 1.37).[119] Similar reactivity is encountered with silyloxycarbene complexes which undergo desilylation in presence of amines or sodium methoxide.[120]

Scheme 1.37. Formation of acylmetalate by demethylation

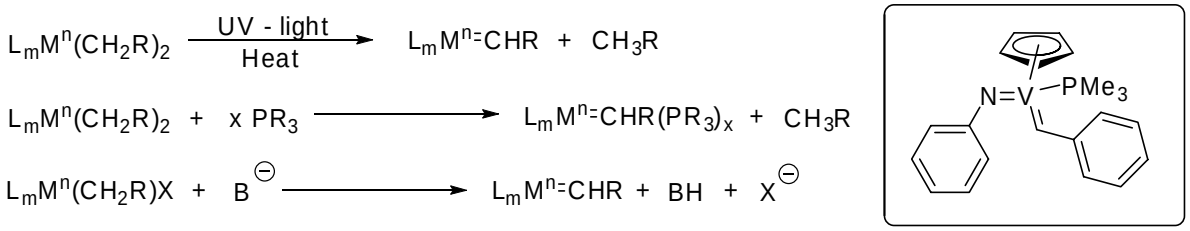


1.2.4. Synthesis of Schrock Carbene complexes

1.2.4.1. Metal alkyl complexes

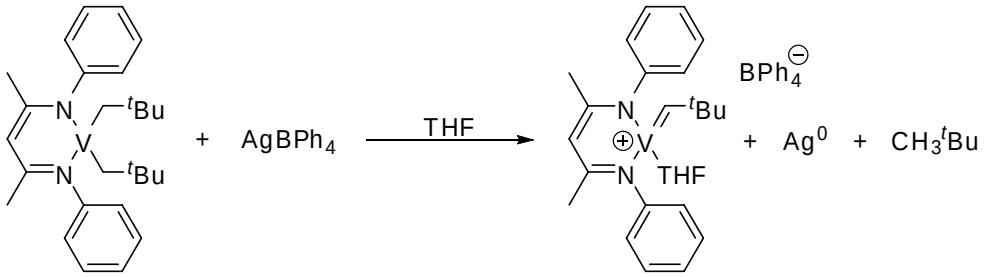
Alkyl metal complexes are easily prepared by reaction of halides metal with alkyl lithium or Grignard reagents.[121] Di- or polyalkyl complexes of coordinatively saturated early transition metals with high oxidation state (d^0) lead to alkylidene complexes by α-deprotonation.[122] The reaction requires the generation of a leaving group thermodynamically and entropically favored, usually an alkane or a week conjugated acid (Scheme 1.38). Complexes lacking *β*-hydrogens and bearing some methyl, neopentyl, or *ter*-butyl groups are preferred to avoid any competition between *α*- and *β*-deprotonation. The reaction can be promoted thermically, photochemically, sterically, or with a base. It is a general method to prepare alkylidene complexes of Ti(IV), Zr(IV), Hf(IV), V(V), Nb(V), Ta(V), Cr(VI), Mo(VI), W(VI) and Re(VII).[73,122]

Scheme 1.38. Formation of alkylidene complexes via α-hydrogen elimination



Di- and polyalkyl complexes of early transition metals which are not at their highest oxidation state, typically d^1 metals such as Ti(III), Zr(III) or V(IV), Nb(IV), can be oxidized to alkylidene complexes by Ag(I) salts or iodine (Scheme 1.39).[122e]

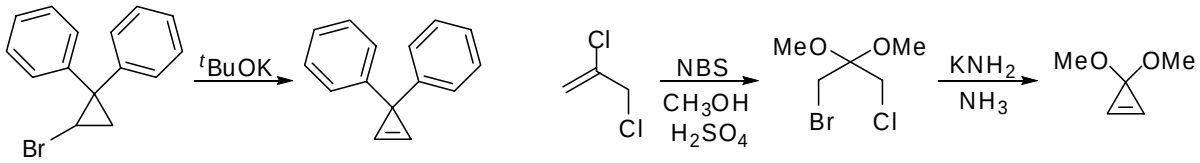
Scheme 1.39. Generation of alkylidene complexes via oxidation



1.2.4.2. Cyclopropenes

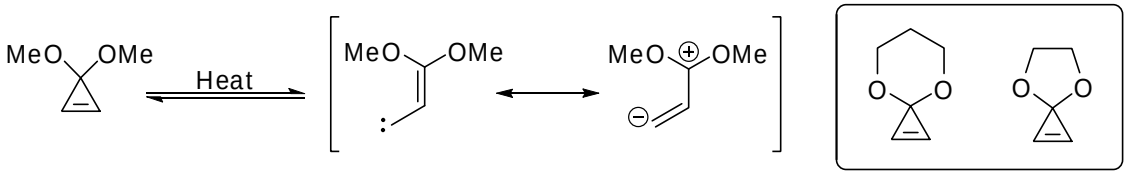
Cyclopropenes are conveniently prepared by dehalogenation of mono- or dihalocyclopropane precursors under strongly basic conditions, involving alkoxides, amides, or alkylithium reagents.[123] Cyclopropenone ketals are prepared by induced amide ring closure of 1-bromo-3-chloro-2,2-dimethoxypropane (Scheme 1.40).[124]

Scheme 1.40. Cyclopropenes and cyclopropenone ketals synthesis



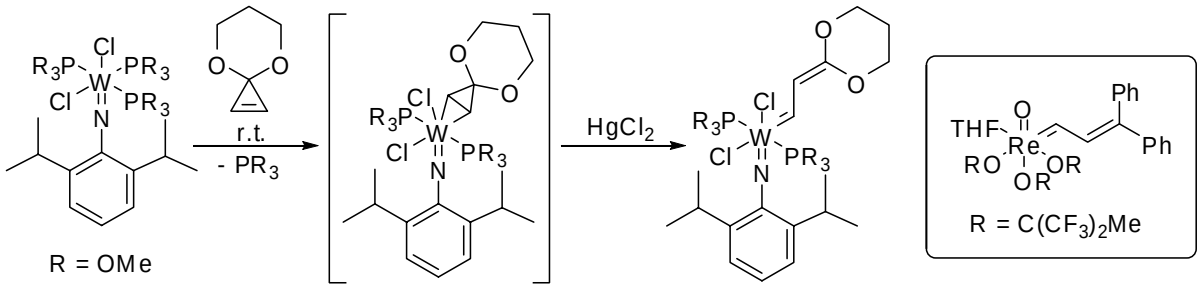
Investigations on the 1,3-dipolar cycloaddition of cyclopropenones ketals have shown that they are best characterized as a nucleophilic and π-delocalized singlet vinylcarbene. Both species are in thermal equilibrium (Scheme 1.41).

Scheme 1.41. Equilibrium between cyclopropenone ketals and vinylcarbenes



Following this reactivity, transition-metal vinylalkylidene complexes of Ti(IV), Zr(IV), W(VI) and Re(VII) have been synthesized by rearrangement of 3,3-diphenylcyclopropene, 3-methyl-3-phenylcyclopropene and 4,8-dioxaspiro[2,5]oct-1-ene.[125] The reaction can be induced thermically, photochemically or by using Hg(II) salts (Scheme 1.42).

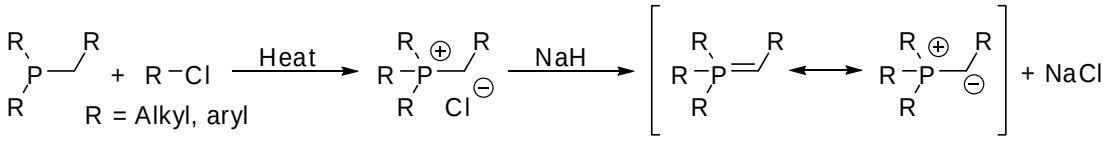
Scheme 1.42. Vinylalkylidenes formation by cyclopropene rearrangement



1.2.4.3. Phosphiranes

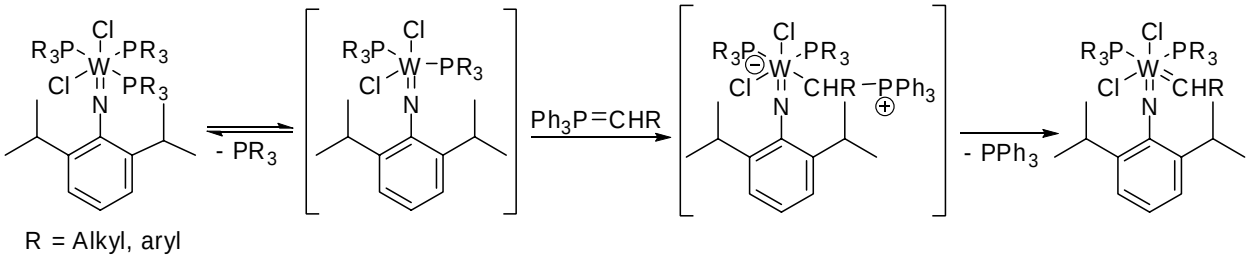
Phosphines react with organic halides forming phosphonium salts in high yield.[126] Further deprotonation by NaH yields phosphiranes (Scheme 1.43). They can be described as phosphorus ylides bearing a nucleophilic carbon and are commonly used for the Wittig reaction.[127]

Scheme 1.43. Synthesis of phophorus ylides



Phosphoranes react with phosphine reduced-metal complexes of Ti(II), Zr(II), V(III) and W(IV) to yield alkylidene complexes via a transfer reaction.[122b,128] The reaction proceeds through the loss of a phosphine from the metal center, followed by its nucleophilic attack by the ylide carbon.[128c] The zwitterionic adduct formed rearranges to alkylidene complex, relieving the steric crowding brought by the phosphirane group (Scheme 1.44).

Scheme 1.44. Transfer of alkylidene from phosphorus ylides

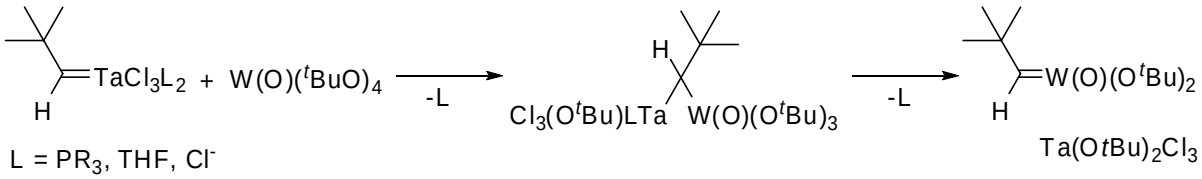


Transfers from partially resonance-stabilized phosphorus ylides are greatly favored because the formed alkylidenes (such as benzylidenes, and vinylylidenes) have their nucleophilic carbon stabilized by delocalization.[128c]

1.2.4.4. Transmetalation from Group 5 metal alkylidenes

In 1982, R. R. Schrock *et al.* readily obtained a series of tungsten(VI) oxoneopentylidene complexes by alkylidene transfer from the tantalum(V) alkylidene precursors.[129] The reaction proceeds via a bridged alkylidene intermediate between tungsten and tantalum. Since then no other examples of transmetalation have been reported between alkylidene complexes (Scheme 1.45).

Scheme 1.45. Transmetalation of alkylidenes complexes

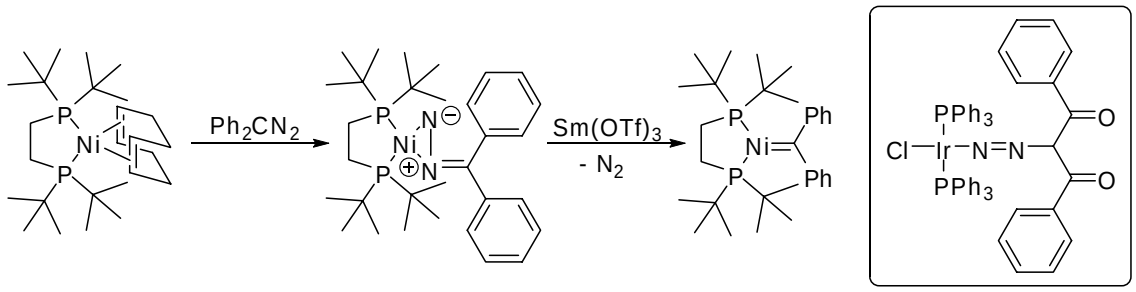


1.2.5. Synthesis of alkyl- and phenylcarbene complexes

1.2.5.1. Diazo compounds

In 1906, bronze copper and copper(II) salts were found to catalytically promote the decomposition of diazoalkanes.[130] The catalyst development for diazo decomposition reactions began in earnest in the 1960s with the introduction of well defined phosphite or acetylacetonate copper complexes.[131] The reaction proceeds via the formation of a diazo-metal adduct.[132] Depending upon the metal complexes used, this adduct can be stable or rearrange to a carbene complex by nitrogen extrusion.[133] (Scheme 1.46) For instance Cu(I),[132,134] Rh(II),[135] Ru(II), Ni(0),[136] Co(II),[137] Pd(II),[138] Ag(I),[139] Au(I)[140] complexes lead to carbenic species while Ta(V),[141] Nb(V), Mo(IV),[142] Fe (II),[143] Ir(I)[144] lead to stable diazo-complexes.

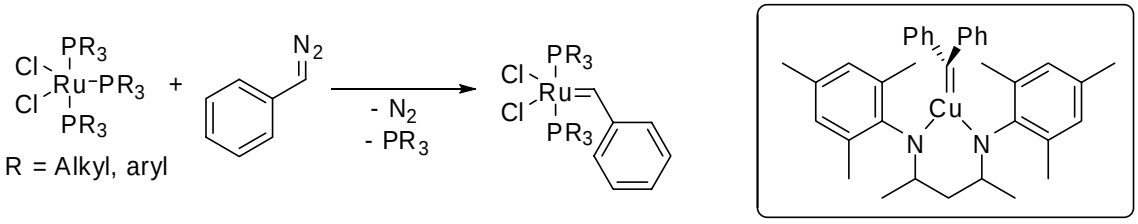
Scheme 1.46. Mechanism of diazo decomposition



Most of the carbene complexes formed by decomposition are used to promote carbene transfer reactions such as: cyclopropanations of alkenes,[145] cyclopropenations of alkynes, cycloadditions to aromatic rings, ylides formations, ketenes formations[146] and insertions into metal and hydrogen bonds.[145,147] They are generally very reactive but are sufficiently stabilized by binding

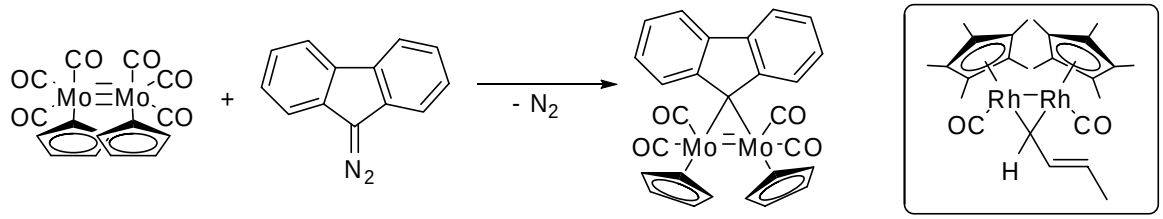
with the metal to avoid any competing carbene dimerization.[148] Actually, some phenylcarbenes complexes of Ni(0),[149] Cu(I),[150] Ru(II)[151] including the Grubbs catalyst, Ru(IV),[152] Fe(IV)[153] and Os(IV)[154] porphyrins were stable enough to be structurally characterized by single crystal X-ray diffraction (Scheme 1.47)

Scheme 1.47. Synthesis of the Grubbs catalyst



Diazoalkanes react also with metal-metal double or triple bonds compounds and form some metal-diazo adducts, which undergo thermally or photochemically induced loss of nitrogen, to rearrange to bridged metal-carbene complexes.[155] The reaction usually proceeds via a 1,3-dipolar cycloaddition pathway and allows the formation of dimetallacyclopropane and dimetallacyclopropene functional groups (Scheme 1.48).[156]

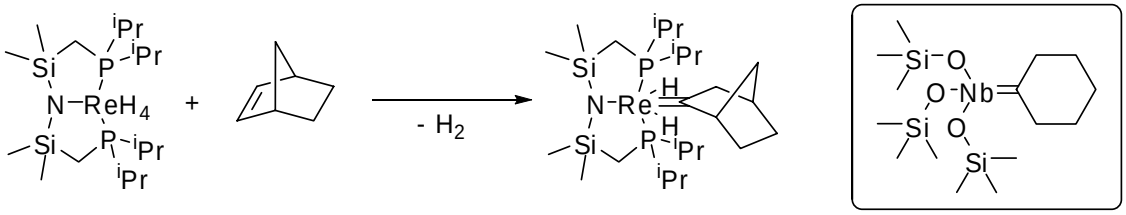
Scheme 1.48. Reaction of a diazo-group with metal-metal multiple bonds



1.2.5.2. Alkenes isomerisation

Recently, powerful π-donor ligands, such as the anionic PNP[157] or silox ligands,[158] have been used to bind early transition metals and form π-basic metal centers. In presence of olefins, they lead to alkylcarbenes[159] or alkylidenes[160] via an isomerization reaction. Back donation from the metal stabilizes the carbene and favors its formation. In that case the alkene-metal complex is not formed (Scheme 1.49).

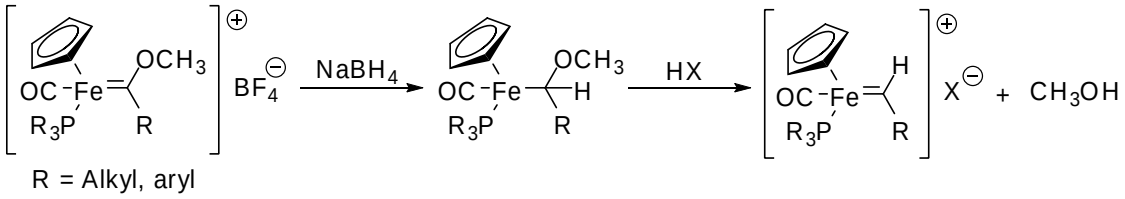
Scheme 1.49. Isomerisation of olefins to alkylcarbenes



1.2.5.3. α-Ionization

Metal *α*-ethers and α-thioethers are conveniently synthesized by hydride reduction of the parent Fischer alkoxy- and thiocarbenes complexes.[161] They undergo *α*-ionization in the presence of Lewis or Brønsted acids to form alkyl- and phenylcarbene complexes via the dissociation of alcohols or thiols (Scheme 1.50).[162] Complexes of W(0), Fe(II) and Ni(II) have been synthesized from metal *α*-ethers and used for cyclopropanations.

Scheme 1.50. α-Ionization of metal α-ethers



1.2.5.4. Cyclopropenes

R. H. Grubbs *et al.* have reported and patented the synthesis two vinylcarbene complexes of Ru(II) and Os(II) by thermal rearrangement of 3,3-diphenylcyclopropene.[163] (Paragraph 1.2.4.2, for an insight on the mechanism of reaction) Nevertheless, this route has not been applied to synthesize further vinylcarbene complexes since.

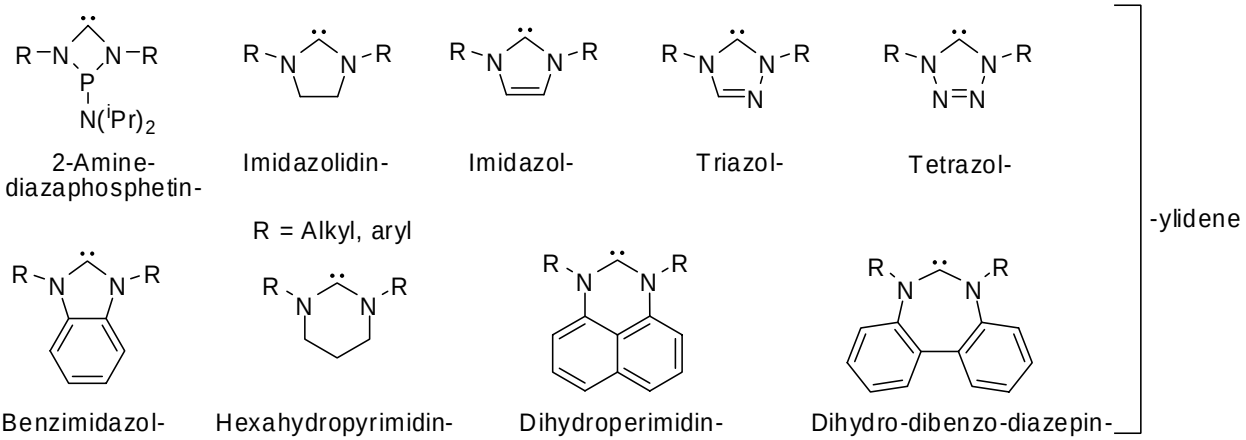
1.3. *N*-heterocyclic carbenes (NHC)

1.3.1. Definition

N-heterocyclic carbenes, also called Arduengo carbenes, are diaminocarbenes and form Fischer-type complexes with transition metals. Since the seminal work of Wanzlick[63-65] during the 1960s, plenty of NHC-metal complexes have been synthesized following the traditional route to Fischer complexes without the involvement of any free carbene ligand. (Paragrah 1.2.3) Nevertheless, the real breakthrough came in 1991, when Arduengo *et al.* synthesized and isolated the first stable *N*-heterocyclic carbene: the 1,3-bis(adamantyl)imidazol-2-ylidene.[164] Since then, a

great variety of NHCs bearing different scaffolds have been synthesized and reacted with transition metals leading to well-defined complexes (Scheme 1.51).[165] Today, these carbenes are recognized as an exciting alternative to the limitations of phosphine ligands in the field of organometallic chemistry and its related catalysis.

Scheme 1.51. Scaffolds of NHCs currently in the literature



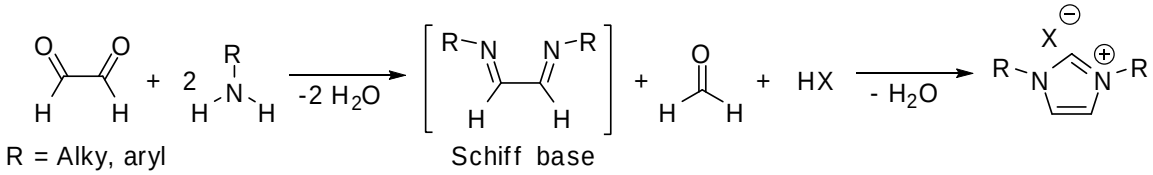
Slight changes to the NHC architectures have a dramatic change on the electronic donor properties of the carbene moieties and impose geometric constraints on the *N*-substituents, influencing their steric impact.[166] These *N*-substituents allow for a modulation of the steric pressure on both the carbene and the coordinated metal. Nevertheless, five member rings, imidazolylidenes and imidazolinylidenes are widely used to generate NHC-complexes, while the other frameworks are rarely employed.

1.3.2. Synthesis of 5-membered ring NHCs and precursors

1.3.2.1. Imidazolium salts and imidazolylidenes

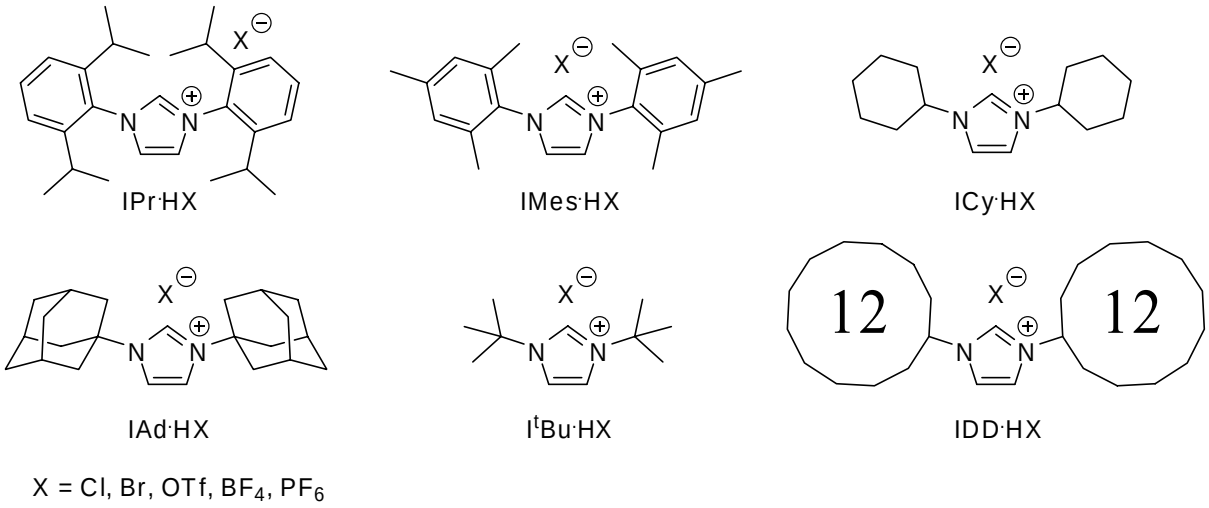
Various reliable routes are available to prepare imidazolium precursors.[167] A straightforward one is the one-pot synthesis starting from glyoxal, primary amine, and formaldehyde.[168] Under acidic conditions the reaction proceeds through a coupling between amine and glyoxal and forms the corresponding Schiff base. Condensation with formaldehyde leads to the imidazolium salt (Scheme 1.52).

Scheme 1.52. One-pot synthesis of imidazolium salts



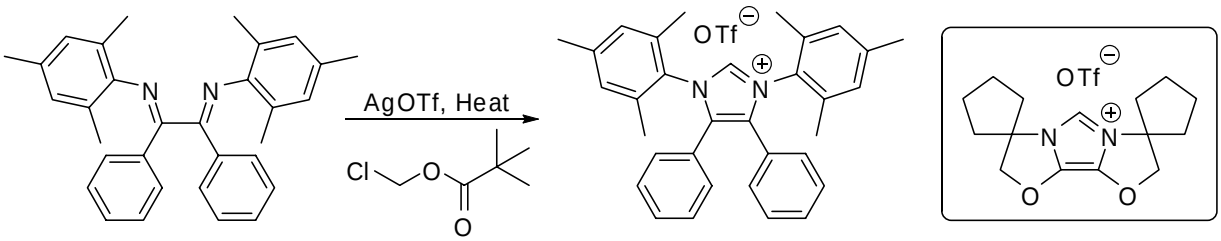
The reaction can be split in two distinct steps, with the isolation of the Schiff base (diimine).[169] It allows for the synthesis of symmetrically *N,N'*-substituted imidazolium salts with various aryl- and alkyl-groups such as the 1,3-bis(2,6-diisopropylphenyl)imidazolium (IPr•HX), 1,3-bis(2,4,6-trimethylphenyl)imidazolium (IMes•HX), 1,3-bis(cyclohexyl)imidazolium (ICy•HX), 1,3-bis(adamantyl)imidazolium (IAd•HX), 1,3-bis(isobutyl)imidazolium (IsB•HX) and 1,3-bis(dodecyl)imidazolium (IDD•HX) for instance (Scheme 1.53).[170]

Scheme 1.53. Imidazolium salts used as carbene precursors



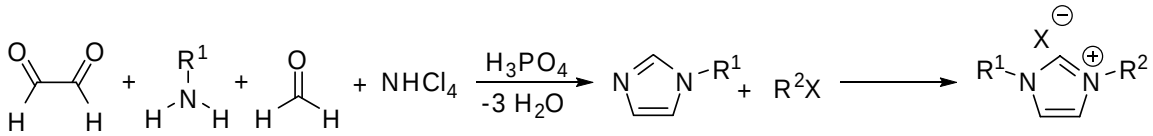
Nevertheless, with sterically demanding salts the cyclization step becomes disfavored and reveals the limitation of this route.[171] Recently, Glorius *et al.* proposed an alternative approach for the synthesis of sterically hindered imidazolium salts.[172] The reaction of silver triflate with chloromethyl pivalate generates, in situ, an alkylating reagent which efficiently cyclizes hindered and non-hindered diimines (Scheme 1.54).

Scheme 1.54. Synthesis of encumbered imidazolium salts



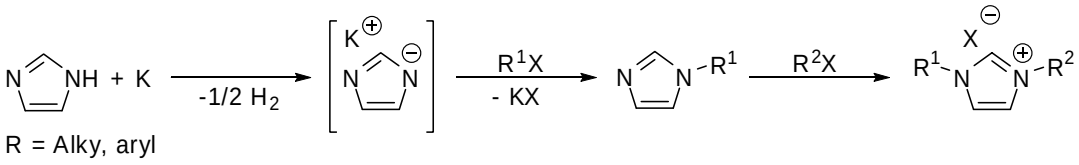
The one-pot reaction between glyoxal, ammonium chloride, paraformaldehyde, and only one equivalent of primary amine leads to the mono *N*-substituted imidazole. This one can be *N*-alkylated by reaction with an alkyl halide to form an unsymmetric *N,N'*-substituted imidazolium salt (Scheme 1.55).

Scheme 1.55. Synthesis of *N*-alkylimidazoles and further *N*-alkylation



Another route to synthesize unsymmetric imidazolium salts is the step-by-step alkylation of an imidazolide anion generated from the reaction of imidazole with potassium (Scheme 1.56).

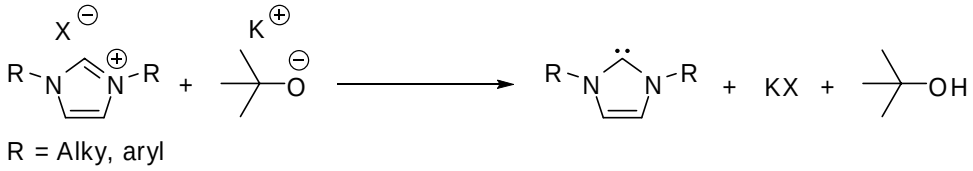
Scheme 1.56. Stepwise alkylations of imidazoles



Imidazolium salts lead to imidazolylidenes by depronation. The reaction is carried out in ammonia or in non-protic solvents such as THF or ethers. The depronation requires anhydrous conditions and the bases used are very strong, with pKa values above 14. Usually, potassium or sodium hydride with a catalytic amount of *tert*-butoxide is employed, but *tert*-butoxide itself,

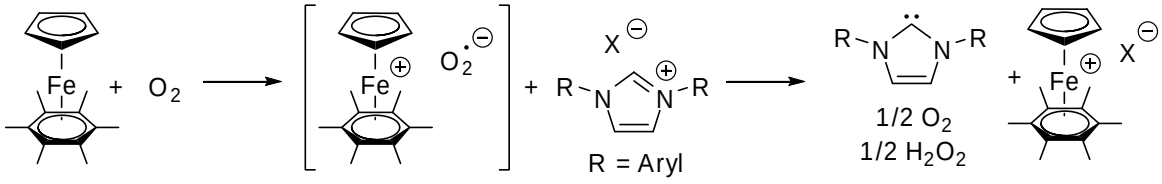
lithium aluminium hydride, *n*-butyllithium, potassium hexamethyldisilazide (HMDS) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) are also efficient alternatives (Scheme 1.57).[167,169,173]

Scheme 1.57. Imidazolylidene formation via deprotonation



Last year, Astruc *et al.* proposed a surprising route to deprotonate a series of imidazolium salts via a radical anion superoxide formed by reduction of ambient dioxygen with a 19-electron sandwich complex of Fe(I) (Scheme 1.58).[174]

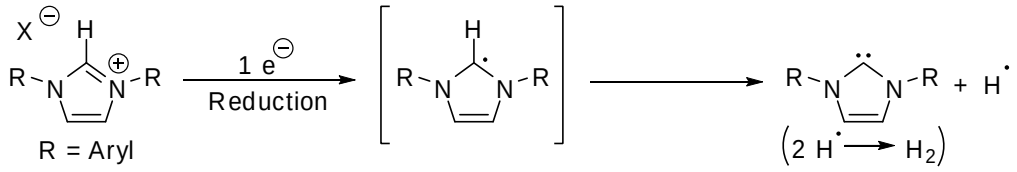
Scheme 1.58. Deprotonation of imidazolium salts by the radical anion superoxide



Finally, imidazolylidenes can be synthesized by electrochemical or chemical reduction of imidazolium salts.[169a,175] Cyclic voltammograms indicate a very negative potential at – 2.28 V, and an excess of potassium in boiling THF is required to perform the chemical reduction. Coulometric analysis reveals a single electron event and the reduction is likely to proceed via a

radical imidazole intermediate which undergoes a further loss of radical hydrogen (Scheme 1.59).

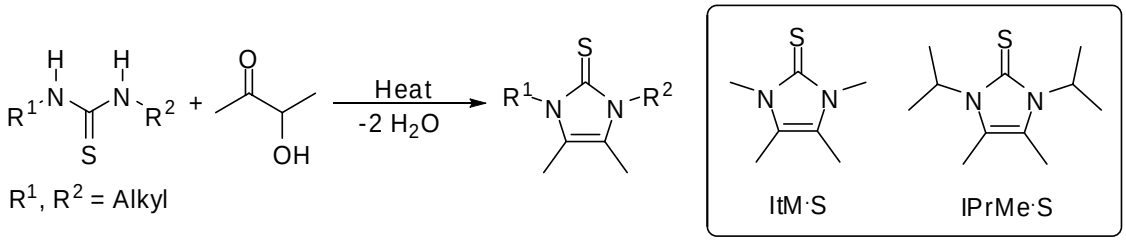
Scheme 1.59. Reduction of imidazolium salts



1.3.2.2. Imidazole-2-thiones and imidazolylidenes

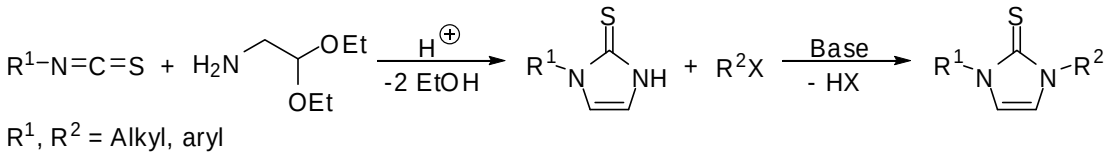
The condensation reaction of thioureas with 3-hydroxy-2-butanone in refluxing hexanol leads to 4,5-dimethyl-1,3-dialkylimidazole-2-thiones.[176] The reaction requires harsh conditions, but it is a general route to produce, in one step, tetraalkylimidazole-2-thiones with good yields. For instance, 1,3,4,5-tetramethylimidazole-2-thione (ITM•S), 1,3-diisopropyl-4,5-dimethylimidazole-2-thione (IPrMe•S) and 1,3-diethyl-4,5-dimethylimidazole-2-thione (IEtMe•S) are conveniently synthesized by this method (Scheme 1.60).

Scheme 1.60. Synthesis of imidazole-2-thiones by condensation



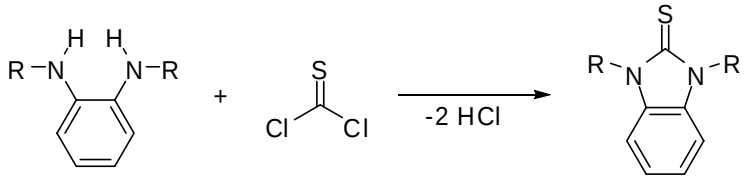
Under acidic conditions, aryl- or alkyl isothiocyanates react with 2,2-diethoxyethaneamine to form mono *N*-substituted imidazole-2-thiones. These can react further with an alkyl halide to form *N,N'*-substituted imidazole-2-thiones (Scheme 1.61).[177]

Scheme 1.61. Synthesis of imidazole-2-thione in two steps



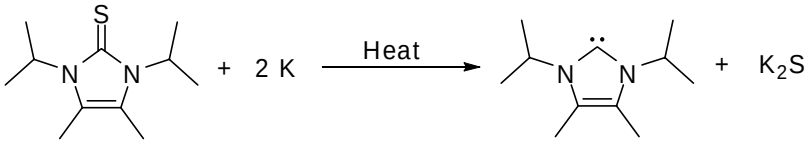
Alternatively, the cyclization reaction of *N,N'*-dialkylbenzene-1,2-diamines with thiophosgene leads to benzimidazole-2-thiones in high yield (Scheme 1.62).[167,178]

Scheme 1.62. Synthesis of benzimidazole-2-thione



Imidazole-2-thiones lead to imidazolylidenes by reduction. The reaction is carried out in boiling THF with an excess of potassium. Despite the drastic conditions required, the yields are generally almost quantitative (Scheme 1.63).[176,178,179]

Scheme 1.63. Imidazolylidene formation by reduction with potassium

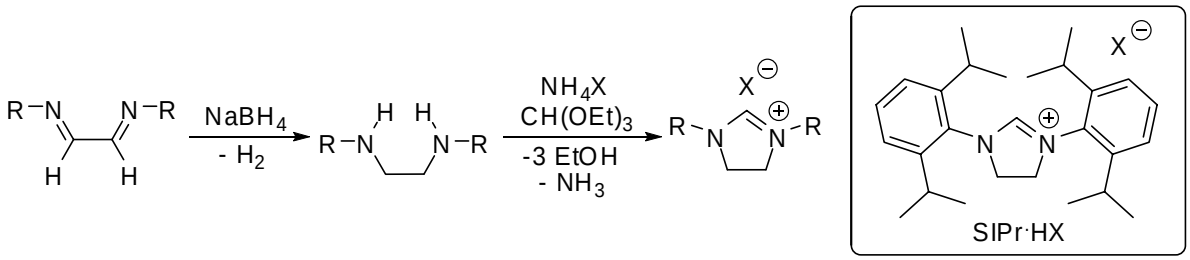


Finally it is worthy to note that imidazole-2-thiones are easily formed by reaction of imidazolium halides with elemental sulfur under basic conditions.[180] However, this route is not appealing as working with potassium metal is cumbersome.

1.3.2.3. Imidazolinium salts and imidazolidinylidenes

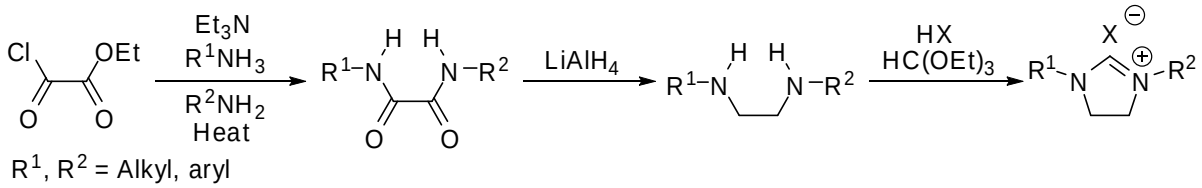
Diazobutadienes (Schiff bases) obtained by condensation of glyoxal with two equivalents of primary amine are reduced to ethane-1,2-diamines by action of sodium borohydride or Red-Al. [181] They react with triethyl orthoformate under acidic conditions to form imidazolinium salts. The cyclization is an equilibrium which is driven to the right by removal (distillation) of the ethanol. The reaction time can be reduced from hours to a few minutes using a microwave.[182] It allows for the synthesis of symmetrically *N,N'*-substituted imidazolinium salts with various aryl groups such as the 1,3-bis(2,6-diisopropylphenyl)imidazolinium (SIPr•HX) and 1,3-bis(2,4,6-trimethylphenyl)imidazolinium (SIMes•HX) for instance (Scheme 1.64).

Scheme 1.64. Synthesis of imidazolinium salts



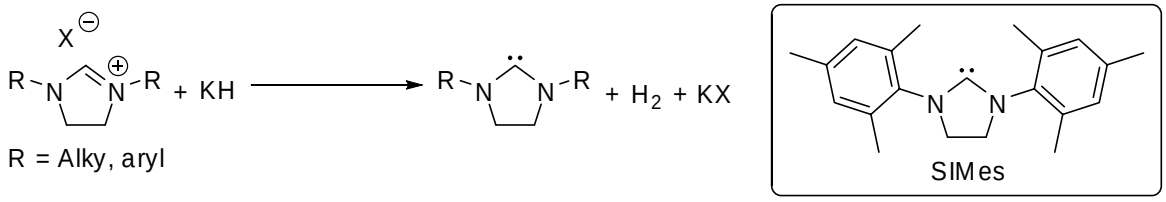
Ethyl-2-chloro-2-oxoacetate can react with two different amines, stepwise, to form an oxalamide. Its reduction with borane•THF or lithium aluminium yields some ethane-1,2-diamine which can be cyclized to form unsymmetric *N,N'*-substituted imidazolinium salts (Scheme 1.65).[183]

Scheme 1.65. Synthesis of unsymmetric of *N,N'*-substituted imidazolinium salts



Imidazolinium salts lead to imidazolidinylidenes by deprotonation. The reaction conditions are the same as with imidazolium salts. Nevertheless, ammonia, alcoxides and any other nucleophilic bases have to be avoided because they form adducts with imidazolidinylidenes (Scheme 1.66).[184]

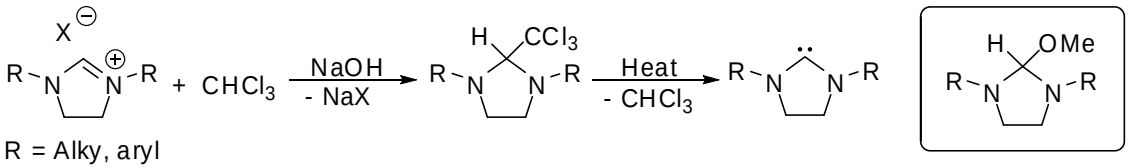
Scheme 1.66. Imidazolidinylidenes formation via deprotonation



1.3.2.4. Imidazolidine-adducts and imidazolidinylidenes

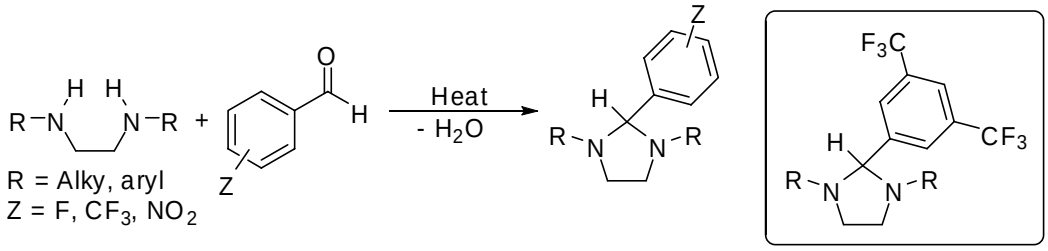
Imidazolinium halides can be converted to 2-methoxyimidazolidine,[185] 2-*tert*-butanolimidazolidine[185,186] and 2-trichloromethylimidazolidine[187] with methanol, *tert*-butanol, and chloroform under basic conditions. These adducts act as masked carbenes and can be chemically manipulated under air conditions. They generate imidazolidinylidenes by thermolysis without the need for a strong base (Scheme 1.67).[185-187]

Scheme 1.67. Synthesis of imidazolidine adducts under basic conditions



Another route is the condensation-cyclization of ethane-1,2-diamines with benzaldehydes. The reaction leads to benzyl-, pentafluorophenyl-, *p*-nitrophenyl-2-imidazolidine adducts (Scheme 1.68).[188]

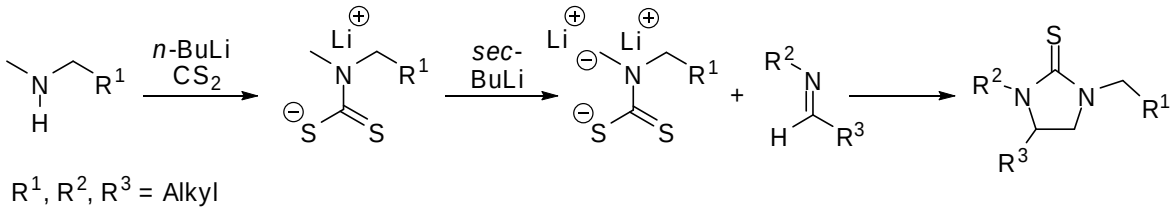
Scheme 1.68. Synthesis of imidazolidine adducts by condensation of diamines



1.3.2.5. Imidazolidine-2-thiones and imidazolidinylidenes

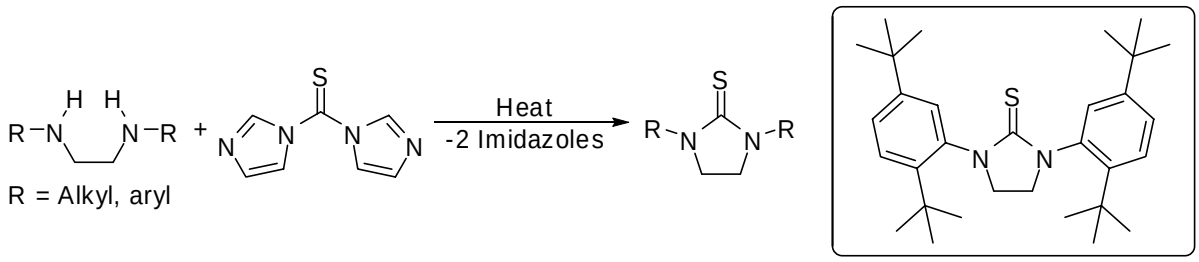
In a one-pot reaction secondary amines are depronated with *n*-butyllithium and treated with carbon disulfide to yield lithium dithiocarbamates. A second lithiation with *sec*-butyllithium yields to lithium *N*-lithiomethyldithiocarbamates. Finally, addition of an aldimine,[189] easily prepared from aldehydes and primary amines, yields imidazolidine-2-thiones (Scheme 1.69).[190] Even if this route leads to mediocre yields of thiones (around 50%), it remains a rapid synthesis for *N,N'*-unsymmetrically imidazolidinylidene precursors.

Scheme 1.69. Synthesis of imidazolidine-2-thiones by condensation of aldimines



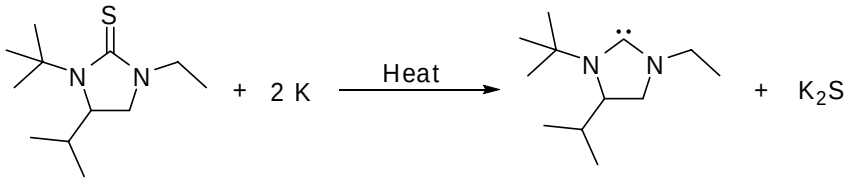
An alternate route to yield imidadozilidine-2-thiones in better yield is the cyclization reaction of ethane-1,2-diamines with thiophosgene or 1,1'-thiocarbonyldiimidazole (Scheme 1.70).[191]

Scheme 1.70. Synthesis of imidazolidine-2-thiones by condensation of diamines



Imidazolidine-2-thiones are reduced similarly to imidazole-2-thiones with an excess of potassium in boiling THF. The reaction leads to imidazolidinylidenes in high yield (Scheme 1.71).[176,190]

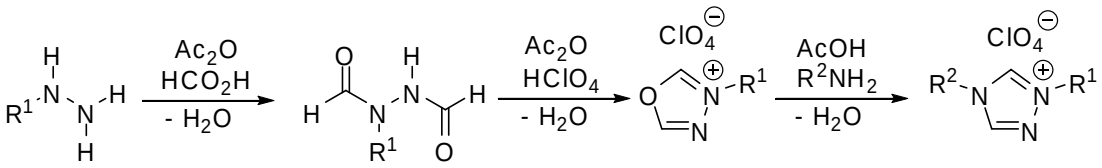
Scheme 1.71. Imidazolidinylidenes formation by reduction with potassium



1.3.2.6. Triazolium salts and triazolylidenes

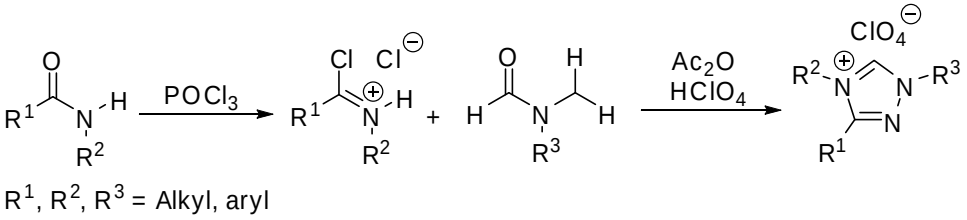
1,4-disubstituted triazolium salts can be synthesized in a three-step procedure described by G. Boyle.[192] In presence of formic acid and acetic anhydride, aryl- or alkylhydrazines form bisformylhydrazines. Further condensation with a mixture of acetic anhydride and perchloric acid affords the corresponding oxadiazolium salts. The last step of the synthesis is the ring-opening / ring-closure reaction (RORC-reaction) using a primary amine, in which the oxygen atom is substituted by the amine (Scheme 1.72).

Scheme 1.72. Synthesis of 1,4-disubstituted triazolium salts



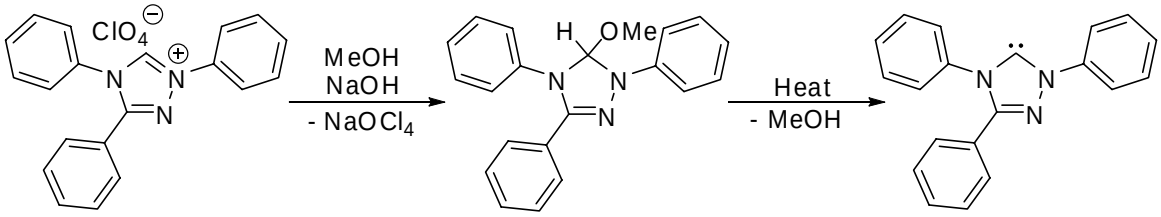
1,3,4-trisubtisituted triazolium salts can be synthesized in a one-pot procedure patented by J. H. Teles.[193] *N*-alkyl-*N*-formylhydrazines, prepared by condensation reaction of alkylhydrazines with methylformate, react with an imidoylchloride, which can be prepared in situ. Then, the cyclization is achieved using acetic anhydride and perchloric acid (Scheme 1.73).

Scheme 1.73. Synthesis of 1,3,4-trisubstituted triazolium salts



Triazolium halides or perchlorate salts are converted to 5-methoxytriazolines in methanol under basic conditions. Whereas the deprotonation of triazolium salts result in carbene decomposition, these adducts yield quantitatively triazolylidenes by thermolysis (Scheme 1.74).[35,167,194]

Scheme 1.74. Triazolylidenes formation by thermolysis



1.3.3. Six and seven-membered ring iminium salts and NHCs

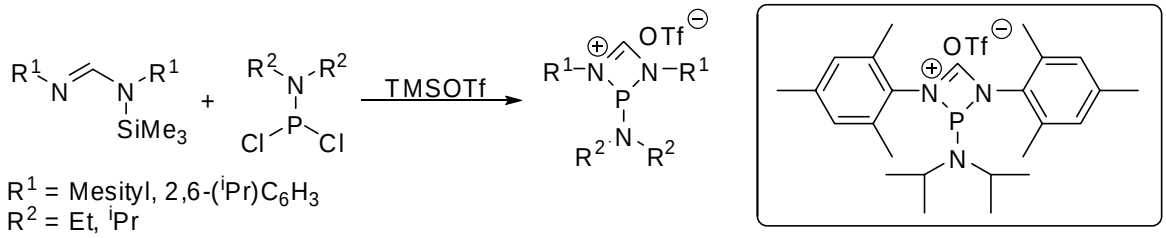
Only a few examples of six- and seven-membered ring NHCs have been reported.[195,196] The synthesis of the precursor salts follows the one proposed for imidazolinium salts: the propane-1,3- and butane-1,4-diamines are condensed with triethyl orthoformate under acidic conditions. The carbenes are generated by deprotonation with potassium hexamethyldisilazide

(HMDS) or bis(trimethylsilyl)mercury while *tert*-butoxide forms adducts (Scheme 1.65 and Scheme 1.66).[197]

1.3.4. Four-membered ring iminium salts and NHCs

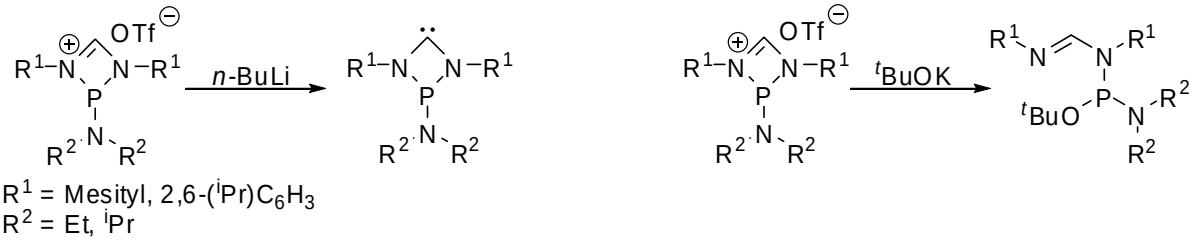
The only examples of four-membered ring NHCs were reported by Grubbs *et al.* in 2004. Two equivalents of primary amine react with triethyl orthoformate under acidic conditions to form *N,N*-disubstituted formamidines.[198] They are converted to silylamidines by addition of *n*-butyllithium and trimethylsilyl chloride. They form the four-membered ring iminium salts by cyclization in presence of diethylaminodichlorophosphine and trimethylsilyl-trifluoromethanesulfonate (TMSOTf) at room temperature (Scheme 1.75).

Scheme 1.75. Synthesis of four-membered ring iminium salts



Iminium salts are depronated with mesityllithium or hexamethyldisilazide (HMDS) to generate the four-membered-ring NHCs. When a less hindered or more nucleophilic base is employed, the ring opens by P−N bond cleavage and forms an *N*-phosphino-*N,N'*- disubstituted formimidamide rather than a NHC (Scheme 1.76).

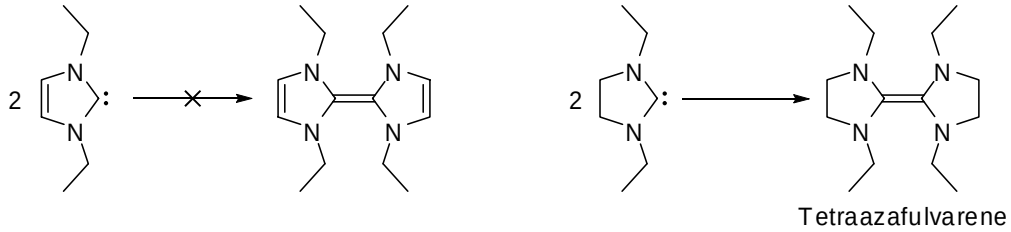
Scheme 1.76. Synthesis of four-membered ring NHCs



1.3.5. Stability of NHCs toward dimerization

The major limitation to the design of stable diaminocarbenes is their dimerization into enetetramines.[180c,199] This reaction has likely prevented the isolation of the 1,3-diphenylimidazolinylidenes by the Wanzlick group more than 40 years ago. The dimerization follows a nonleast motion pathway that involves the attack of the occupied σ lone pair of one carbene center on the vacant p_π orbital of a second carbene.[200] Whereas imidazolinylidenes required sterically demanding ligands to prevent their dimerization to tetraazafulvalenes,[201] imidazolylidenes exhibit a thermodynamically unfavorable dimerization even for small ligands such as methyl groups (Scheme 1.77).[201,202]

Scheme 1.77. Dimerization of NHCs



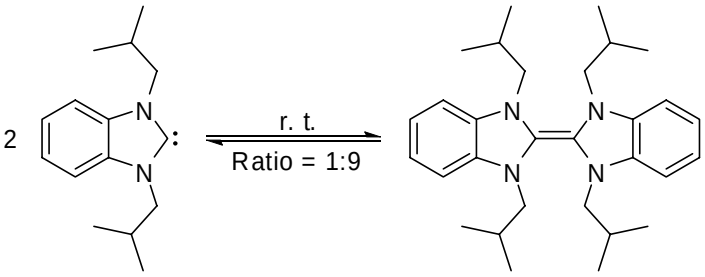
The strength of the C=C bond in the enetetramines can be approximated by the strength of the (sp^2-sp^2)σ and the (p-p)π bonds in ethylene (172 kcal.mol^{-1}),[203] minus the sum of the singlet-triplet energy gap for both dissociated carbenes.[204] The energy gap between singlet and triplet state is higher for imidazolylidenes (85 kcal.mol^{-1}) than for imidazolinylidenes (70 kcal.mol^{-1}) due to an extra-stabilization provided by the aromatic character of the imidazole ring.[,205] Consequently imidazolylidenes do not form enetetramines easily as the C=C bond would be very weak or even energetically disfavored. In contrast, imidazolidinylidenes readily form enetetramines which are difficult to dissociate. The dimerization reaction has to be kinetically hampered by steric protection. For symmetrically *N,N'*-substituted imidazolinylidenes, the demarcation line separating stable from unstable carbenes is established as $^{t}Bu_2/^{i}Pr_2$ and Mes_2/Ph_2.

1.3.6. Wanzlick Equilibrium

H. Wanzlick believed that imidazolinylidenes could be generated from tetraazafulvalenes. He assumed that both species were present together through an equilibrium reaction. Nevertheless, Winberg *et al.* showed that metathesis reaction between acyclic and cyclic enetetramines did not lead to cross metathesis products,[206] while Lemal *et al.* showed that cross metathesis could only proceed in presence of electrophiles;[207] finally, Wanzlick's postulate was rejected in the mid-1960s. In 1999, Denk *et al.* reinvestigated the cross metathesis reaction between two enetetramines and uncovered some cross metathesis products formed at high temperature (150º C) without the presence of any electrophiles.[208] They supported a Wanzlick equilibrium, but could not prove it, as the cross metathesis products could have been formed by a [2+2]-cycloaddition / [2+2]-cycloreversion of the enetetramines, favored at high temperatures.

One year later, Hahn *et al*. demonstrated the existence of the Wanzlick equilibrium by evidencing the formation of some benzimidazolylidene by partial dissociation of the corresponding dimer dibenzotetraazafulvalene, at room temperature without the use of any electrophile (Scheme 1.78).[209] It is important to note that if benzannulated NHCs exhibit the topology of imidazolydenes, they are prompt to dimerize and have the reactivity of imidazolinylidenes.[190,210]

Scheme 1.78. Equilibrium between a NHC and its dimer



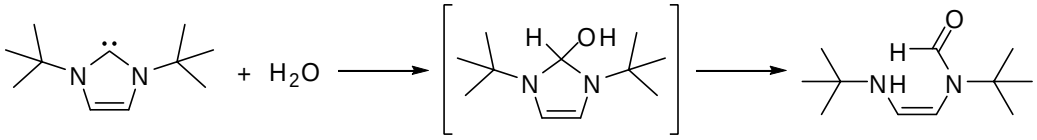
Finally the rate of dimerization for some unsymmetrically substituted imidazolinylidenes has been reduced, making possible the observation of the carbene and its dimers over weeks by adjusting the steric constraint of *N*-alkyl groups.

1.3.7. General reactivity of the NHCs

Imidazolylidenes and sterically stabilized imidazolinylidenes are thermodynamically stable. They do not react with triplet dioxygen for kinetic reasons, even if the formation of ketones appears to be very exothermic.[211,212] They are inert toward carbon monoxide (no formation of ketenes) and oxidating agents such as CuO and HgO. They react slowly with

dihydrogen to form aminals by 1,1-addition in the presence of a catalytic amount of palladium or platinum. They are extremely sensitive to moisture and have to be handled under dry atmosphere. They hydrolyze through the insertion of the carbene into H_2O, or by nucleophilic attack of OH^-. Both pathways lead to a formamide by ring opening of a cyclic α-diaminomethanol intermediate (Scheme 1.79).

Scheme 1.79. Hydrolysis of NHC ligands



NHCs react with acids and form iminium salts quantitatively due to their high pK_a values, ranging from 20 to 30 (in water).[213] They are among the most powerful neutral organic bases and their strength is comparable to DBU and pentacyclic vinamidines.[214]

1.3.8. Organometallic chemistry of the NHCs

1.3.8.1. Bonding to metal and π-back donation

The distance between the carbenic carbon and the metal in organometallic complexes gives an insight on the ability of the carbene to accept any transfer of electronic density from the metal (π-back donation).[109a] A short distance accounts for a partially metal−carbon double bond due to a π-back donation. Studies of different types of carbenes show that the π-accepting ability

decreases from Schrock-type to Fischer-type (non diaminocarbenes) to NHCs.[215] It is well accepted that NHCs bind strongly metals by σ-bonding while the π-back-bonding is negligible.[216] Only copper, silver and gold from Group 11 exhibit a significant π-back-bonding from the metal to the NHC.[217] It is important to add that the 6π-delocalization in NHCs, such as imidazolylidenes, does not have a significant effect in the bonding nature of NHCs.

1.3.8.2. Bonding properties, comparison with phosphines

In metal complexes, NHCs share with phosphines the characteristics of being monodendate two-electron ligands.[218] Carbonyl-metal complexes bearing a CO group *trans* position to an NHC or a phosphine ligand are of special interest in infrared spectroscopy. The vibrational frequency of C–O stretching is thought to be proportional to the π-back donating ability of the NHC or phosphine ligand. In a totally symmetric vibrational mode more basic ligands (σ donors) induce smaller vibrational frequencies. Studies of different complexes of Ni(0) have shown that NHCs appear to be more electron-donating than most basic phosphines.[219] They bind more firmly the metal center than phosphines ligands. Finally, contrary to the phosphines, NHCs bind with alkaline, lanthanides and high oxidation state metals in which π-back donation is not possible.[220]

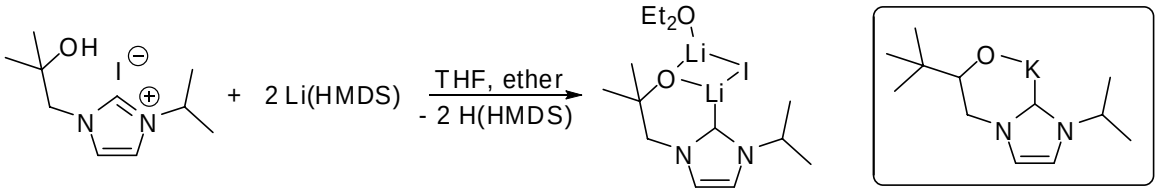
1.3.8.3. Reaction between metals and isolated NHCs

Isolated carbenes react with metal to form well-defined complexes by controlling the stoichiometry of the reagents.

1.3.8.3.1. Alkali metals (group 1)

In THF, the 4,5-dimethyl-1,3-diisopropylimidazolium salt is depronated with lithium, sodium, or potassium hexamethyldisilazide to form the corresponding carbene alkali metal adducts.[195a] The bonding with the metal induces a slight shift upfield for the signals of the carbenic carbon (^{13}C NMR) and can be suppressed by trapping the alkali metals with crown ethers. Interactions between the metals and imidazolylidenes appear to be purely electrostatic, but are sufficient to enhance the stability of the carbene in air.[195a] Recently, the synthesis of a bidentate alkoxy-*N*-imidazolylidene has allowed for the isolation of lithium and potassium NHC adducts with a good thermal stability (Scheme 1.80).[221]

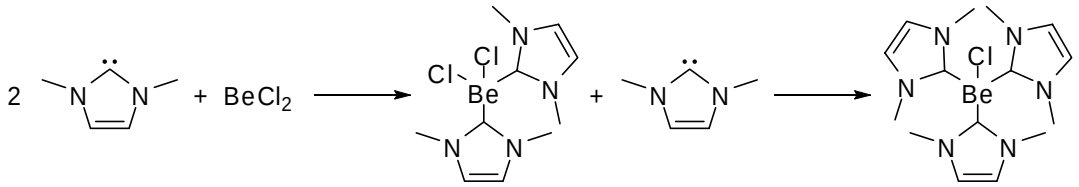
Scheme 1.80. NHC alkali metals complexes



1.3.8.3.2. Alkaline earth metals (Group 2)

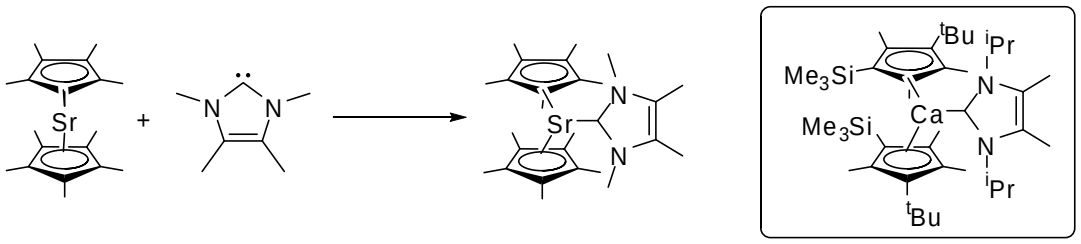
Beryllium chloride, one of the strongest Lewis acids known, reacts with three equivalents of sterically unencumbered NHCs, or two equivalents of bulkier NHCs, to form the corresponding adducts (Scheme 1.81).[222]

Scheme 1.81. NHC beryllium complexes



Metallocenes of magnesium, calcium, strontium, and barium react with one equivalent of NHC to form the corresponding adducts.[223] The metal-carbon bond has a pronounced covalent character for magnesium, and become more ionic for the heavier alkaline earth metals. Using an excess of carbene with calcium, strontium, and barium leads to the bis-NHC adduct in which the second NHC is weakly bound to the metal (Scheme 1.82).[216a,223]

Scheme 1.82. NHC alkaline earth metal complexes

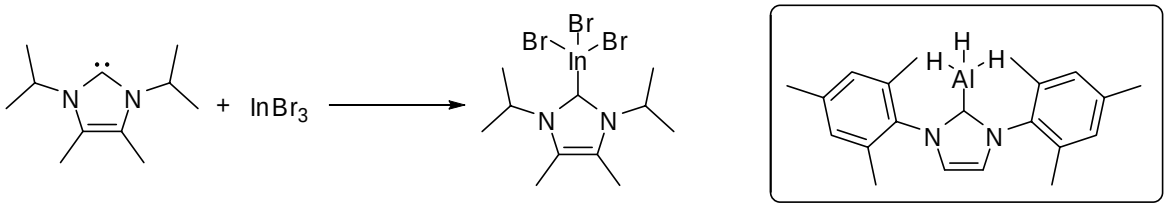


1.3.8.3.3. Metals from Group 13

Aluminum(III) and gallium(III) trihalides react with one equivalent of NHC to form a four-coordinate adduct.[224] Indium(III) and thallium(III) trihalides react with one or two equivalents of NHC to form respectively a four-coordinate adduct or a five-coordinate (hyper

valent) bis-NHC adduct (Scheme 1.83).[225] The electronic structure of the imidazole fragment is an intermediate between those of the free carbene and imidazolium ion.[35,226]

Scheme 1.83. NHC Group 13 metal complexes



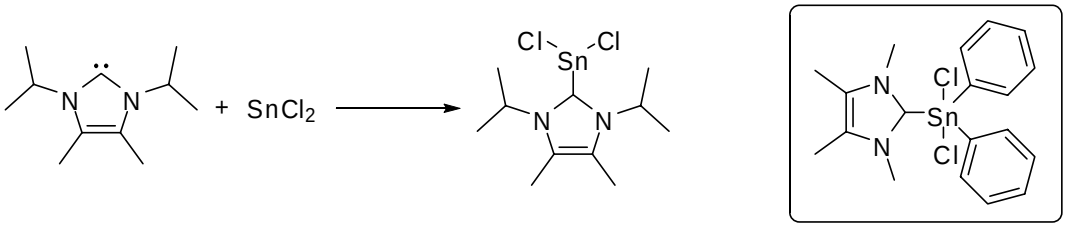
Alanes, galanes, and indanes are well stabilized by bulky NHCs. The formed adducts are thermally stable in contrast with the phosphines.[227] The only known complex of thallium(I) exhibits a metal center coordinated with three NHCs from the same pincer ligand.[228]

1.3.8.3.4. Metals from Groups 14 & 15

The carbene chemistry of these metals appears to be extremely undeveloped. Complexes of tin have been described only in two reports while there is no reference available for lead and bismuth. Tin(II) dichloride leads to a tetravalent bis-NHC adduct with sterically unencumbered carbenes and to a trivalent mono-NHC adduct with bulkier carbenes.[216a,229] The carbon−tin bond is strongly polarized and fragile. Although the complexes are stable in solid state, they decompose slowly in solution and rapidly in gas phase. They do not belong to the stannene family because there is no π-back-donation from tin to the carbene.[230] A mono-NHC adduct of

pentavalent tin(IV) has been synthesized by reaction of diphenyltin(IV) dichloride and tetramethylimidazolylidene (Scheme 1.84).[216a]

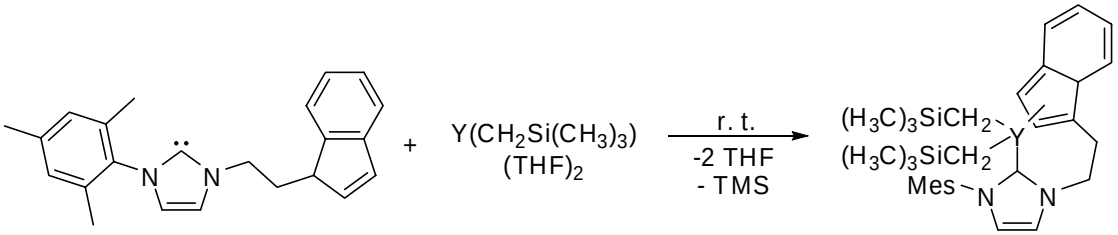
Scheme 1.84. NHC tin complexes



1.3.8.3.5. Rare earths: lanthanides and Group 3 transition metals

Metallocenes or tris(silylamido) complexes of yttrium, scandium, lanthanum, and of the lanthanides series bearing at least one tetrahydrofuran ligand form some NHC adducts by substitution of the tetrahydrofuran.[35,231] Following this method, complexes bearing one, two, or three carbene ligands have been characterized. The metal−carbene bond is primarily electrostatic and longer than in σ-bonded alkyl lanthanide complexes.[232] The ^{13}C NMR spectra of yttrium(III) NHCs display a characteristic resonance for the carbene around 195 ppm,[216a,233] with a well defined coupling constant $\{^{1}J(^{13}C\text{-}^{89}Y)\}$ suggesting that the NHC does not dissociate from the rare earths, on the NMR time scale (Scheme 1.85).

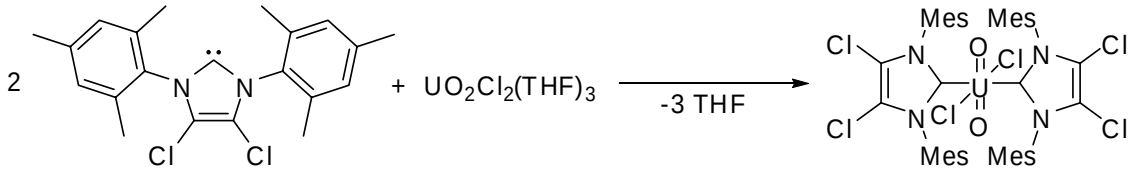
Scheme 1.85. NHC lanthanides complexes



1.3.8.3.6. Actinides

In 2001, D. A. Costa *et al.* synthesized the first actinide NHC complexes by reacting two equivalents of 1,3-bis(2,4,6-trimethylphenyl)imidazolylidene (IMes) with uranyldichloride.[234] Although a thorium(IV) methylidene complex has been recently synthesized,[235] there is no example of thorium NHC complex. Globally, examples of actinide complexes remain extremely scarce and are restrained to uranium(III) and (VI). The bonding between the carbene and uranium exhibits some highly unusual properties. The NHC ligands are among the weakest σ-donor for uranyl complexes in contrast to their strong donor character in transition metal complexes. In the meantime, actinyl ions (MO_2^{2+}, M = U, Np, Pu) are hard Lewis acids and the coordination of the uranyl ion with a soft σ-donor NHC is unprecedented. With electron-rich uranium(III), π-back bonding occurs and accounts for the stabilization of the complexes in contrast with transition metals. There is a transfer of electronic density from the uranium *f* orbitals to the empty *p* orbital of the carbene (Scheme 1.86).[236]

Scheme 1.86. NHC actinides complexes



Spent nuclear fuel contains some lanthanides formed from the nuclear fission of actinides.[237] Recent work has shown the stronger affinity of NHCs for 5*f* ions than for 4*f* ions, and they might find an application in the partitioning/recycling of nuclear waste.[238]

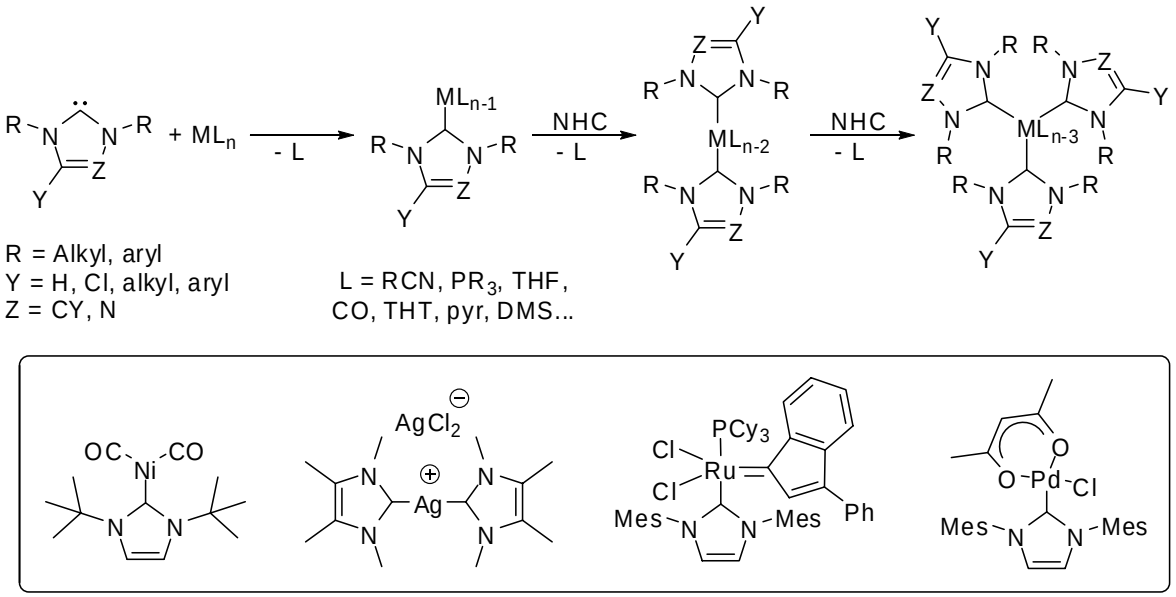
1.3.8.3.7. Transition metals: Group 4 to 12

1.3.8.3.7.1. Overview

There is an amazing diversity of transition metal NHC-complexes with a variety of ligands and oxidation states. All metals from groups 4 through 12 have been covered, including the radioactive technetium.[239] The motivation for such a large volume of work is the stability/availability of the NHC ligands and the outstanding performances of their metal complexes in catalysis. This paragraph is intended to provide only an overview on the synthesis of metal-transition NHC complexes whereas two detailed reviews on the topic have been written by W. A. Hermann and G. Bertrand.[35,216a,240] NHCs react with a broad range of organometallic precursors by direct addition or by replacement of two-electron donor ligands. Nitriles, phosphines, tetrahydrofurane, carbonyl (CO), tetrahydrothiophene (THT), pyridines, and dimethylsulfide (DMS) are among the most common ligands displaced by the NHCs. Dinuclear

precursors featuring halo or aceto bridges are also split by the NHCs to form the corresponding monomeric complexes. Depending upon the metal and the stoichiometry of reagent employed, complexes bearing up to three carbene ligands are commonly synthesized (Scheme 1.87).

Scheme 1.87. NHC transition metals complexes; examples from Nolan research

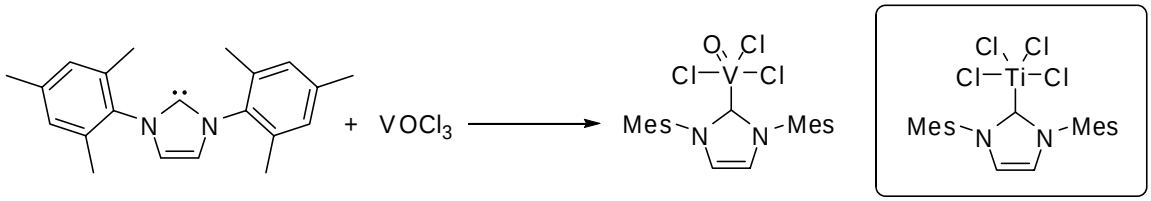


1.3.8.3.7.2. High oxidation state early transition metals

In 2002, Abernathy *et al.* have reported the synthesis of stable tetrachloro titanium(IV) and trichloro-oxo-vanadium(V) NHC complexes.[241] These complexes demonstrate that both alkylidenes (Schrock-type carbenes) and NHCs (Fischer-type carbene) can stabilize transition metals at their highest oxidation state. These complexes exhibit an unusual back-bonding from the lone electron pairs of the *cis*-chloride ligand to the empty *p* orbital of the carbene. Indeed, the metals centers are strong Lewis acids and the σ-bond between the carbene and the metal is more

polarized. This results in a partial positive charge on the carbene carbon, which is stabilized by bonding interactions with the chlorides lone pairs (Scheme 1.88).

Scheme 1.88. Synthesis of a NHC vanadium(V) complex

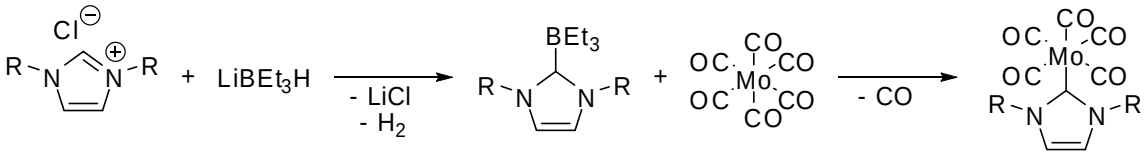


1.3.9. Reaction of metal masked carbenes

1.3.9.1. Trialkylborane-2-imidazole

Imidazolium salts are deprotonated by lithium trialkylborohydride and form trialkylborane-2-imidazoles in good yield.[242] These boron-NHC complexes are thermally and air stable as expected for an NHC-group 13 acid-base adducts.[227,243] In boiling toluene, they react with hexacarbonylmolybdenum(0) and form the corresponding molybdenum(0) NHC complex without the need for any base. It is not clear if the reaction proceeds or not by the generation of a free NHC from the boron adduct because its mechanism has not been studied (Scheme 1.89).

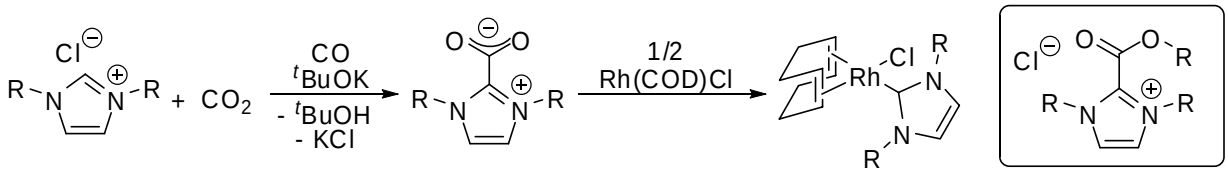
Scheme 1.89. NHC complex formation via trialkylborane-2-imidazole precursors



1.3.9.2. Carboxylate-2-imidazole

Imidazolium salts react with carbon dioxide or alkyl chloroformates under basic conditions to yield 2-carboxylate or 2-esterimidazoles.[244] They are air stable and can transfer NHCs to a variety of metals salts without the need for any base. At 80 ºC, they lead to rhodium, iridium, and palladium complexes in high yield in less than one hour. The mechanism likely proceeds through a metal coordination of the carboxylate via oxygen followed a *β*-elimination (Scheme 1.90).[244b]

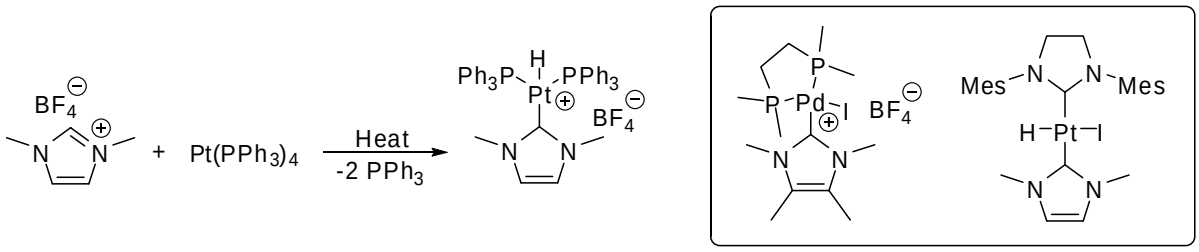
Scheme 1.90. NHC complex formation via carboxylate-2-imidazole precursors



1.3.9.3. Oxidative addition on imidazolium and 2-haloimidazolium salts

Zerovalent Group 10 metals, especially platinum and nickel complexes, are prompt to react with imidazolium and 2-haloimidazolium salts to form NHC-complexes by oxidative addition.[245] The activation energy barrier of the reaction is very low for bromo- and iodoimidazolium salts. The reaction is also favored with metal(0) complexes bearing bis-chelating ligands and/or basic ligands, such as phosphines.[245a] The oxidative addition of imidazolium salts is an interesting approach to generate metal hydride NHC complexes (Scheme 1.91).[246] Recently, Peris *et al.* have extended the reaction to the Group 9 metals with the synthesis of an iridium(III) hydride complex by oxidative addition of an imidazolium salt to the chloro(1,5-cyclooctadiene) iridium(I) dimer.[247]

Scheme 1.91. NHC complex formation via oxidative addition

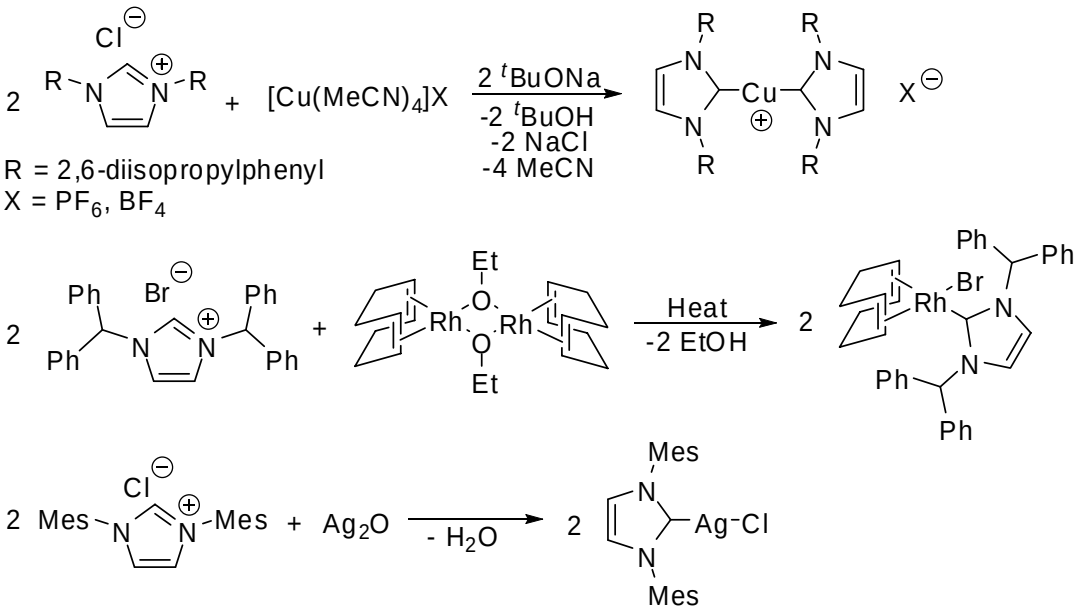


Finally, it is important to note that metal-mediated catalysis in ionic liquids is very likely to proceed via the formation of metal NHC complexes by oxidative addition.

1.3.9.4. In situ, deprotonation of imidazolium salts

NHC complexes can be obtained by in situ deprotonation of the corresponding imidazolium salts in the presence of metal precursors under basic conditions. An organic base, such as triethylamine, *tert*-butoxide or carbonate can be added directly to the reaction media[35,248] or the depronation can arise from an organometallic fragment bearing basic ligands, such as alkoxides, hydride, or acetate.[249] Simple metal oxides, such as silver(I) oxide, can also act as the base and the metal source (Scheme 1.92).[170,250]

Scheme 1.92. In situ deprotonation of imidazolium salts

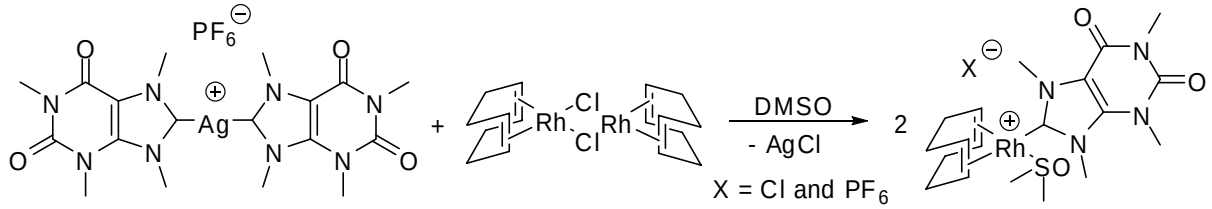


1.3.9.5. Transfer of NHC by transmetalation

1.3.9.5.1. Silver(I) NHC halide complexes

The air stability and the straightforward synthesis of silver(I) NHC halide complexes render them attractive for transmetalation reactions.[250,251] In the presence of an organometallic fragment bearing a metal more electronegative than silver, the carbon−silver bond is broken and the carbene transferred while the reaction is thermodynamically favored by the precipitation of solid silver(I) halide. Complexes of ruthenium(IV), rhodium(I), iridium(I), palladium(II), platinum(II) and gold(I) have been synthesized in excellent yields following this procedure (Scheme 1.93).[250,251] Recently Abernathy *et al.* have attempted to transfer some NHCs from silver(I) complexes to titanium(IV) and zirconium(IV) salts. The reaction failed and led to the formation of a bis-NHC silver(I) complex by abstraction of a chloride ion from the silver to the early transition metal center.[252]

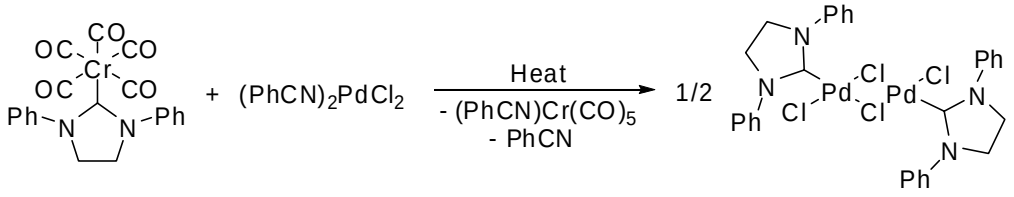
Scheme 1.93. Synthesis of a caffeine rhodium(I) complex by transmetalation



1.3.9.5.2. Group 6 metal(0) NHC complexes

Group 6 metal Fischer-type carbene complexes, including NHCs, are efficient transmetalating agents.[253] (Scheme 1.33) Rhodium(I), palladium(II), copper(I), silver(I) and gold(I) NHC complexes have been synthesized in good yield from the corresponding pentacarbonyl chromium(0), molybdenum(0) and tungsten(0) NHC precursors.[253a] Nevertheless, these complexes are air sensitive and consequently less employed than silver(I) complexes (Scheme 1.94).

Scheme 1.94. Synthesis of a palladium(II) complex by transmetalation



1.3.9.5.3. Unusual transmetalating agents

Finally, it should be noticed that three separate recent works describe the synthesis of cerium(III), rhodium(III) and gold(I) complexes from respectively a lithium(I) NHC adduct, a zirconium(IV) pincer NHC complex, and a manganese(0) NHC complex.[254]

1.4. Closing remarks

This chapter overviews the synthesis and the properties of carbenes and is dedicated to all the chemists who have contributed to the development of carbene chemistry. These highly active species have slowly emerged from laboratory curiosities to powerful tools in organic, organometallic and material chemistry. They can be reagents, reaction intermediates, or ligands for metal complexes.

N-heterocyclic carbenes (NHC) have a very special place in the carbene family thanks to their stability and their straightforward synthesis. They bind metals with various oxidation states and generate organometallic complexes with enhanced stability and unique properties in the field of catalysis. In this regard, NHC complexes are outstanding catalysts for a broad array of organic transformations including cross-coupling reactions, metathesis, hydrogenations, polymerizations, hydrosilylations… for the most famous ones.[255]

For almost fifteen years, Nolan group has been highly active with the chemistry of transition metal NHC complexes, covering the synthesis of well-defined complexes and their applications in catalysis. During my doctoral studies, I have brought my humble contribution to the field of NHC chemistry with the synthesis of various well-defined complexes of palladium(II), silver(I), gold(I) and gold(III). Since, some of them have already found some promising applications in organic catalysis.

1.5. References and notes

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CHAPTER 2

N-HETEROCYCLIC CARBENE PALLADIUM COMPLEXES [(NHC)Pd(acac)Cl]: IMPROVED SYNTHESIS AND CATALYTIC ACTIVITY IN LARGE-SCALE CROSS-COUPLING REACTIONS

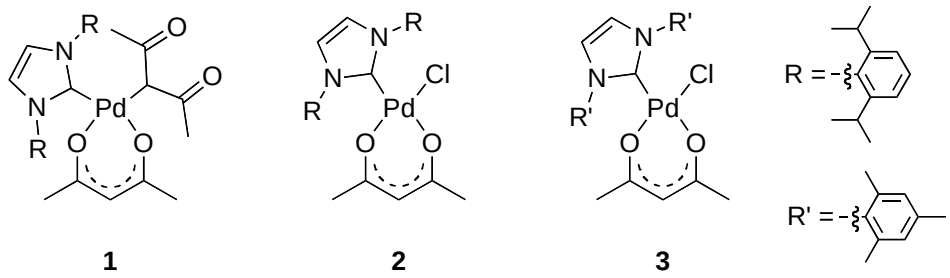
2.1. Introduction

The use of NHC ligands (NHC = *N*-heterocyclic carbene) is now widespread in numerous areas of organometallic catalysis.[1] Their impressive involvement in ruthenium-catalyzed alkene metathesis[2] is only one of their many possible applications in ligand-supported organometallic transformations.[3] Therefore, simple and efficient protocols to synthesize NHC-containing transition metal complexes are of wide interest.

In the last few years, we have developed several user-friendly procedures leading to diverse families of [(NHC)Pd(L)Cl] (where L = allyl, R-allyl, palladacycle).[4] These protocols allow for the synthesis of air- and moisture-stable palladium precatalysts possessing high activities in cross-coupling reactions.[5,6] Along these lines, we recently described the synthesis of

two air- and moisture-stable NHC-bearing acetylacetonato complexes, shown in Figure 2.1, with formulae [(IPr)Pd(acac)$_2$] **1** and [(IPr)Pd(acac)Cl] **2** (IPr = *N*,*N*'-bis(2,6-diisopropylphenyl)imidazol-2-ylidene; acac = acetylacetonate).[7] Complex **1**, bearing an η^1-*C*-bound and an κ^2-*O*,*O*-bound acac, was prepared from free IPr and Pd(acac)$_2$, while complex **2** was prepared by reacting stoichiometrically **1** with HCl.

Figure 2.1. Structures of complexes **1**, **2** and **3**



Complexes **1** and **2** were found to be active in the Buchwald-Hartwig reaction[8] and the α-arylation of ketone[9] involving a wide array of substrates.[10] The higher activity of **2** in these reactions when compared to **1** prompted us to design a one-pot synthesis to avoid the isolation of **1**. The remaining drawback of this early synthetic pathway was the use of the free carbene. We subsequently showed that the NHC salt (i.e. NHC•HCl) could be used in lieu of the free NHC.[10] Nevertheless, in this synthetic procedure all reagents had to be thoroughly dried under vacuum prior to the reaction being carried out, the use of anhydrous dioxane was mandatory and the reaction had to be performed under inert atmosphere. Herein, we report an improved synthesis of two [(NHC)Pd(acac)Cl] complexes by simply mixing and heating NHC•HCl with Pd(acac)$_2$ in

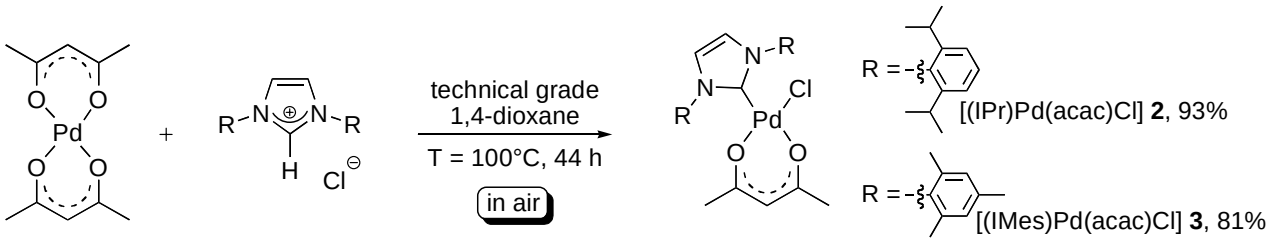
technical grade dioxane and without any precautions to avoid air. Furthermore, large-scale cross-coupling reactions have been performed successfully using the most active precatalyst, **2**.

2.2. Results and discussion

2.2.1. Synthesis of palladium(II) complexes

Our desire to design organometallic complexes with potential commercial and industrial applications prompted us to develop a synthetic pathway that would circumvent all the aforementioned drawbacks. The new synthetic pathway leading to precatalyst **2** and **3** is illustrated in Scheme 2.1.

Scheme 2.1. Improved Synthesis of [(NHC)Pd(acac)Cl]



Direct reaction of a slight excess of the imidazolium salt IPr·HCl with $Pd(acac)_2$ in refluxing 1,4-dioxane for 44 hours led to the formation of **2** in high yield (90%). This procedure has been improved since our last report and no longer requires a large excess of NHC•HCl salt (from 1.4 equiv to 1.1 equiv).[11] Furthermore, it was discovered that anhydrous conditions are no longer mandatory to obtain the desired complexes. The reaction can be carried out in air with technical

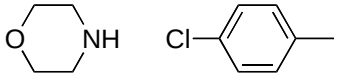
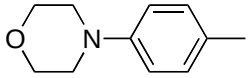
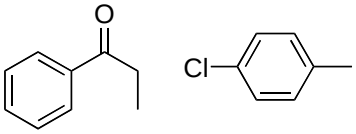
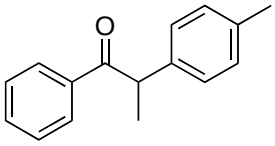
grade 1,4-dioxane with no loss of yield. We carried out a synthesis, starting with 7.16 g of $Pd(acac)_2$to obtain 14.1 g of [(IPr)Pd(acac)Cl] precatalyst (i.e. 93% yield).

The same protocol, albeit in shorter reaction time, can be applied to the synthesis of [(IMes)Pd(acac)Cl] **3** (IMes = *N*,*N*'-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) again in very good yield (81%) starting from the corresponding NHC salt, IMes•HCl. Complex **3** has been characterized by ^{1}H and ^{13}C NMR spectroscopies and its purity further established by elemental analysis and HRMS. Overall, this improved procedure simply requires the aerobic addition of technical grade 1,4-dioxane to a round-bottom flask previously loaded with a 1:1.1 mixture of $Pd(acac)_2$ and NHC·HCl, followed by heating. Every manipulation is done in air and none of the chemicals needs to be dried prior to use.

2.2.2. Cross-coupling reactions

Next, we examined the activity of these complexes in the Buchwald-Hartwig and the α-ketone arylation reactions. The IPr-bearing complex was found more effective in both palladium-catalyzed couplings (Table 2.1), presenting superior turnover numbers (TON) and turnover frequencies (TOF). Hence, in reaction A, a difference in TONs was observed for **2** and **3** (98 and 34 respectively), which was even larger in TOFs (196 h^{-1} and 5.7 h^{-1}). The same trend was noticed in reaction B (TONs of 97 and 21, TOFs of 97 h^{-1} and 3.5 h^{-1}). However, if the reaction temperature was increased, pre-catalysts **2** and **3** were found to have comparable performance.

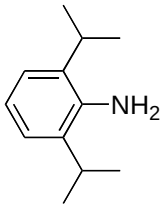
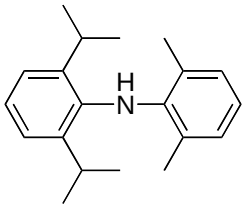
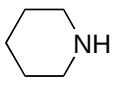
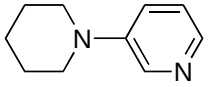
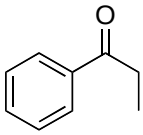
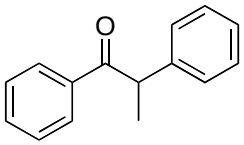
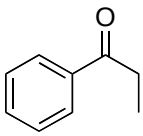
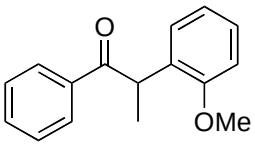
Table 2.1. Activity of **2** and **3** in cross-coupling reactions

substrates	product	[Pd]	T (°C)	time (h)	conv. (%)[b]
		2	50	0.5	98
reaction A		**3**	50	0.5	0
		**3**	50	6	34
		2	100	0.5	100[c]
		3	100	0.5	97[c]
		2	60	1	97
reaction B		**3**	60	1	4
		**3**	60	6	21
		2	100	0.5	98
		3	100	0.5	87

[a] Reaction conditions: reaction A: morpholine (1.1 mmol); 4-chlorotoluene (1 mmol); **2** or **3** (1 mol %); KO^{t}Bu (1.1 mmol); DME (1 mL). Reaction B: propiophenone (1.1 mmol); 4-chlorotoluene (1 mmol); **2** or **3** (1 mol %); NaO^{t}Bu (1.5 mmol); toluene (1 mL). [b] GC conversions are the average of 2 runs. [c] Reaction performed in 1,4-dioxane.

We previously showed that **2** performs efficiently in *N*-aryl amination and α-ketone arylation reactions with a variety of substrates, including unactivated aryl chlorides, hindered amines or heteroaromatic ketones.[10] To extend further the scope of our catalytic system and make it an appealing tool for synthetic chemists at an academic or industrial level, we carried out four cross-coupling reactions on a 10-mmol scale (Table 2.2).

Table 2.2. Large-scale cross-coupling reactions

entry	substrates	product	t (h)	yield (%)[b]	amount of product (g)
1			8	92	2.58
2			4	96	1.43
3			3	93	1.95
4			6	88	2.12

[a] Reaction conditions: for entries 1 and 2: amine (10 mmol); aryl halide (10 mmol); **2** (1 mol %); KO^{t}Bu (11 mmol); DME (10 mL); T = 50°C. For entries 3 and 4: ketone (10 mmol); aryl chloride (10 mmol); **2** (1 mol %); NaO^{t}Bu (15 mmol); toluene (10 mL); T = 60°C. [b] Isolated yields, average of 2 runs.

Overall, the present catalytic system was found to be highly efficient in large-scale couplings, yielding at least 88% of pure isolated arylated product. We deliberately chose challenging substrates to highlight the generality and the efficiency of the process (see Table 2.2). For example, two extremely hindered partners could be coupled in high yield, producing more

than 2.5 g of a tetra-*ortho*-substituted diarylamine (Table 2.2, entry 1). Strongly unactivated heteroaromatic chlorides[12] reacted also in high yield (entry 2). As an added advantage, the coupling products of both *N*-aryl amination reactions were found to be of very good purity (> 95%) by ^{1}H and ^{13}C NMR spectroscopies after a simple extraction with *tert*-butylmethyl ether followed by a filtration through a plug of celite, therefore avoiding further purification by flash chromatography on silica gel.

For the *α*-ketone arylation reactions, we performed the same trend in NHC ligand control on catalyst activity was observed as above. Aryl chlorides, inexpensive and widely available when compared to bromides or iodides, reacted smoothly with propiophenone on a 10-mmol scale (entries 3 and 4). Even the strongly unactivated and sterically hindered 2-chloroanisole could be coupled in near 90% yield.[13]

2.3. Conclusion

In summary, a synthetically appealing (one-pot/in air/gram-scale) procedure, from two commercially available materials (i.e. $Pd(acac)_2$ and NHC·HCl), leading to two NHC-Pd complexes has been described. These indefinitely air-stable complexes are useful pre-catalysts for a number of C–C and C–N bond forming reactions. Studies aimed at capitalizing on this simple protocol and synthesizing related [(NHC)Pd(acac)Cl] complexes are currently ongoing in our laboratories.

2.4. Experimental section

2.4.1. General considerations

- All aryl halides, amines and ketones were used as received.
- All solvents (anhydrous and technical grade) and the bases (potassium *tert*-butoxide and sodium *tert*-butoxide) were used as received and stored under argon in a glovebox.
- Flash chromatography was performed on silica gel 60 (230-400 mesh).
- ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on a 300 or a 400 MHz spectrometer at ambient temperature in $CDCl_3$, C_6D_6 or DMSO-d_6.
- Assignments of some ^{1}H and ^{13}C NMR signals rely on COSY and/or HMBC experiments.

2.4.2. Synthesis of palladium(II) Complexes

*Synthesis of [(IPr)Pd(acac)Cl] (**2**):* [in square bracket, figures for the *large-scale synthesis*] In a round-bottom flask equipped with a magnetic stir bar and a condenser, $Pd(acac)_2$ (0.716 g, 2.35 mmol) [7.16 g, 23.50 mmol], IPr·HCl (1.10 g, 2.59 mmol) [11.00 g, 25.85 mmol] and technical grade 1,4-dioxane (15 mL) [150 mL] were loaded and the reaction mixture was refluxed for 44 h. 1,4-Dioxane was then evaporated in vacuo and diethyl ether was added. The mixture was filtered over a plug of Celite to afford a clear yellow solution. Ether was removed and the orange/yellow powder obtained was washed with pentane and dried, affording the desired complex as a pale yellow powder. Yield: 1.36 g (90%) [14.1 g (93%)]. NMR data were found in good agreement with previously reported characterization data. [7a,10]

*Synthesis of [(IMes)Pd(acac)Cl] (**3**):* In a round-bottom flask equipped with a magnetic stir bar and a condenser, $Pd(acac)_2$ (0.893 g, 2.93 mmol), IMes·HCl (1.000 g, 2.93 mmol) and technical grade 1,4-dioxane (15 mL) were loaded and the reaction mixture was refluxed for 24 hours. 1,4-Dioxane was then evaporated in vacuo and cold diethyl ether was added leading to the formation of a yellow precipitate. The mixture was filtered over a plug of silica (immobilizing the precipitate) and washed with cold diethylether until the solvent came through colorless. The filtrate was discarded and the plug of silica was washed with dichloromethane affording a bright yellow solution. After evaporation of the DCM, the desired complex was obtained as a yellow powder. Yield: 1.342 g (81%). ^{1}H MNR (500 MHz, $CDCl_3$): δ 7.06 (s, 2H, N–C*H*), 7.01 (s broad, 2H, H^{Ar}), 6.97 (s broad, 2H, H^{Ar}), 5.10 (s, 1H, C(O)–C*H*), 2.34 (s, 6H, CH_3), 2.30 (s broad, 6H, CH_3), 2.14 (s broad, 6H, CH_3), 1.75 (s, 3H, C(O)–CH_3), 1.74 (s, 3H, C(O)–CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.5 (C, *C*=O), 183.6 (C, *C*=O), 154.1 (C, N–*C*–N), 139.6 (C, N–C^{Ar}), 137.4 (C, C^{Ar}), 136.1 (C, C^{Ar}), 135.3 (C, C^{Ar}), 130.1 (CH, C^{Ar}), 129.2 (CH, C^{Ar}), 124.2 (CH, N–*C*H), 100.1 (CH, C(O)–*C*H), 27.5 (CH_3, C(O)–*C*H_3), 26.0 (CH_3, C(O)–*C*H_3), 21.6 (CH_3), 19.2 (CH_3), 18.2 (CH_3). Calcd. HRMS for $C_{28}H_{34}N_3O_2Pd$ (M+MeCN-Cl^-): 550.1707. Found: 550.1686. Elemental analysis calcd. (%) for $C_{28}H_{31}N_2O_2PdCl$ (MW 545.41): C, 57.26; H, 5.73; N, 5.14. Found: C, 57.21; H, 5.87; N, 5.11.

2.4.3. General procedure for Buchwald-Hartwig reactions

In a glovebox, [(IPr)Pd(acac)Cl] 2 (0.1 mmol, 63 mg, 0.01 equiv), potassium *tert*-butoxide (11 mmol, 1.24 g, 1.1 equiv) and anhydrous 1,2-dimethoxyethane (DME) (10 mL) were added in turn to a vial equipped with a magnetic stir bar, and sealed with a screw cap fitted with a septum.

Outside the glove-box, the amine (10 mmol, 1 equiv) and the aryl halide (10 mmol, 1 equiv) were injected in turn through the septum. The reaction mixture was then stirred at 50 °C and monitored by GC. When the reaction was found complete, water was then added to the reaction mixture, the organic layer was extracted with *tert*-butylmethyl ether (MTBE), dried over magnesium sulfate and the solvent was evaporated in vacuo. The crude product was dissolved in pentane and filtered through a plug of Celite, yielding the desired product. The reported yields and quantities are the average of two runs.

N-(2,6-Diisopropylphenyl)-*N*-(2,6-dimethylphenyl)amine (Table 2, entry 1): Following the above general procedure with *N*-(2,6-diisopropylphenyl)amine (10 mmol, 1.88 mL) and 2-bromo-*m*-xylene (10 mmol, 1.33 mL), the reaction yielded 2.58 g (92%) of the title compound. NMR data were found in good agreement with previously reported characterization data. [10,14]

N-(3-Pyridyl)piperidine (Table 2, entry 2): Following the above general procedure with piperidine (10 mmol, 0.99 mL) and 3-chloropyridine (10 mmol, 0.95 mL), the reaction yielded 1.43 g (96%) of the title compound. NMR data were found in good agreement with previously reported characterization data. [10,15]

2.4.4. General procedure for α-ketone arylation reactions

In a glovebox, [(IPr)Pd(acac)Cl] 2 (0.1 mmol, 63 mg, 0.01 equiv), sodium *tert*-butoxide (15 mmol, 1.44 g, 1.5 equiv) and anhydrous toluene (10 mL) were added in turn to a vial equipped with a magnetic bar, and sealed with a screw cap fitted with a septum. Outside the glovebox, the ketone (10 mmol, 1 equiv) and the aryl halide (10 mmol, 1 equiv) were injected in turn through the septum. The reaction mixture was then stirred at 60°C and monitored by GC. When the reaction was found complete, water was then added to the reaction mixture, the organic layer was

extracted with *tert*-butylmethyl ether (MTBE), dried over magnesium sulfate and the solvent was evaporated in vacuo. The product was purified by flash chromatography on silica gel.

1,2-Diphenylpropan-1-one (Table 2, entry 3): Following the above general procedure with propiophenone (10 mmol, 1.33 mL) and chlorobenzene (10 mmol, 1.02 mL), the reaction yielded, after flash chromatography on silica gel (pentane/MTBE, 80/20), 1.95 g (93%) of the title compound. NMR data were found in good agreement with previously reported characterization data. [10,16]

2-(2-Methoxyphenyl)-1-phenylpropan-1-one (Table 2, entry 4): Following the above general procedure with propiophenone (10 mmol, 1.33 mL) and 2-chloroanisole (10 mmol, 1.27 mL), the reaction yielded, after flash chromatography on silica gel (pentane/MTBE, 85/15), 2.12 g (88%) of the title compound. NMR data were found in good agreement with previously reported characterization data. [10,17]

2.5. Acknowledgements

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CHAPTER 3

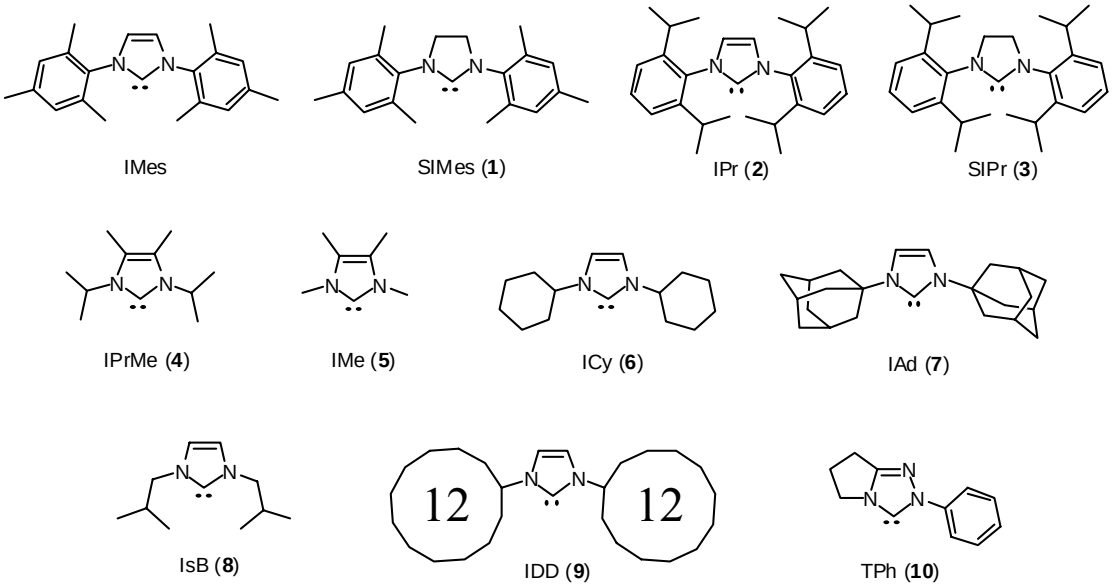
SYNTHESIS OF WELL-DEFINED *N*-HETEROCYCLIC CARBENE SILVER(I) COMPLEXES

3.1. Introduction

It is now widely accepted that the saga of *N*-heterocyclic carbene (NHC) chemistry began in 1968 when Ölefe[1] and Wanzlick[2] successfully isolated the first chromium and mercury *N*-heterocyclic carbene complexes. In 1991, Arduengo's seminal discovery of a stable *N*-heterocyclic carbene[3] led to incredible activity and development in the coordination chemistry of NHCs. With better sigma donor ability than most phosphines, NHCs strongly bind and stabilize transition metals,[4] leading to a wide variety of well-defined catalytic systems. NHC complexes of late transition metals especially those of Groups 8, 9 and 10 have been employed to catalyze Heck[5], cross coupling reactions (such as the Suzuki-Miyaura reaction[6]), olefin metathesis,[7] and hydrogenation[8] reactions, among the most significant. From Group 11, copper and gold NHCs are known to catalyze a more limited number of organic transformations,[9-10] but silver-NHC complexes have been reported recently to behave as efficient catalysts in transesterification

reactions.[11] While tungsten-NHC complexes can be used as carbene transfer reagents,[12] silver-NHC compounds are the most popular complexes used for NHC transfer.[12,13] Their common use as transfer agents is due to their straightforward synthesis, usually circumventing the need for free NHC isolation, and the relative stability of the Ag-NHC complexes toward air and light.[12,15] NHC-silver complexes are known to adopt different architectures depending on the synthetic conditions employed. Most of the reported complexes are homoleptic with two carbene units bound to the silver in a linear fashion.[11,12,14,15,16,17] In the case of argentophilic interactions, some polymeric and bridged structures have been elucidated.[18,19] On the other hand, monocarbene silver halides remain rare with only a handful of reported examples.[20,21,22] We report here the synthesis of a series of two-coordinate NHC-silver(I) chloride complexes of general composition (NHC)AgCl. The NHC ligands used in the present study are shown in Scheme 3.1 and are commonly used saturated and unsaturated ligands: (1,3-bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene) SIMes (**1**), (1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) IPr (**2**), (1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene) SIPr (**3**), (1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene) IPrMe (**4**), (1,3,4,5-tetramethylimidazol-2-ylidene) IMe (**5**), (1,3-bis(cyclohexyl)imidazol-2-ylidene) ICy (**6**), (1,3-bis(adamantyl)imidazol-2-ylidene) IAd (**7**), (1,3-bis(isobutyl)imidazol-2-ylidene) IsB (**8**), (1,3-bis(dodecyl)imidazol-2-ylidene) IDD (**9**), as well as the triazolium ligand (2,5,6,7-tetrahydro-2-phenyl-3H-pyrrolo[2,1-c]-1,2,4-triazol-3-ylidene) TPh (**10**). All new Ag(I)–NHC complexes were characterized by ^{1}H and ^{13}C NMR spectroscopy, elemental analysis and X-ray diffraction.

Scheme 3.1. NHC ligands used in this study



Although the synthesis of the two-coordinate silver(I) chloride complex (IMes)AgCl[22] has been already reported, we noticed that the use of a more polar solvent favors the formation of $[(IMes)_2Ag]^+[AgCl_2]^-$ (**21**). Finally, by studying the synthesis of (IMes)AgI in a polar solvent, we have obtained the unusual $[(IMes)_2Ag]_2[Ag_4I_6]$ (**22**) complex.

3.2. Results and Discussion

3.2.1 Synthesis of silver(I) complexes

Refluxing the imidazolium chloride salts SIMes•HCl (**1**), IPr•HCl (**2**), SI•Pr (**3**), ICy•HCl (**6**), IAd•HCl (**7**), IsB•HCl (**8**) and TPh•HCl (**10**) in dichloromethane (DCM) in the presence of a slight excess of Ag_2O yields complexes [(SIMes)AgCl] (**11**), [(IPr)AgCl] (**12**), [(SIPr)AgCl] (**13**),

[(ICy)AgCl] (**16**), [(IAd)AgCl] (**17**), [(IsB)AgCl] (**18**) and [(TPh)AgCl] (**20**) according to equation 1:

$$2\ \text{NHC}\cdot\text{HCl} + \text{Ag}_2\text{O} \xrightarrow{\text{DCM}} 2\ (\text{NHC})\text{AgCl} + \text{H}_2\text{O} \quad (1)$$

Using the same conditions with the bulky salt IDD•HCl (**9**) leads to a mixture of 55% of the desired complex [(IDD)AgCl] (**19**) and 45% of the starting salt **9**. In order to increase the kinetics of the reaction, a solvent with a higher boiling point was selected and after 12 hours at reflux in THF, total conversion to **19** was obtained. It is noteworthy that contrary to the method described by Wang and Lin[12], all syntheses can be carried out without exclusion of light with no deleterious effect on yields.

In anhydrous THF, under argon and in the dark, the free carbenes IPrMe (**4**) and IMe (**5**) are stirred overnight at room temperature in the presence of a slight excess of AgCl to yield complexes [(IPrMe)AgCl] (**14**) and [(IMe)AgCl] (**15**) and traces of metallic silver according to the equation 2:[12]

$$\text{NHC} \xrightarrow[\text{THF}]{\text{AgCl}} (\text{NHC})\text{AgCl} \quad (2)$$

All complexes can be obtained in good yields in this manner with the notable exception of [(IMe)AgCl] (**15**). For this particular complex, and to a lesser extent for [(SIMes)AgCl] (**11**), the lower yields are due to the formation of a side product. Separation of the desired complexes and the side products is easily achieved by crystallization. Interestingly, when we examine the ^{1}H NMR spectrum of the side products, we find similarities with spectra of $[(IMe)_2Au]Cl$ and $[(IMes)_2Au]Cl$, two complexes that we have previously encountered while synthesizing a series of NHC gold(I) chloride complexes.[23] Usually homoleptic halide silver(I) carbene complexes have the formulation $[Ag(NHC)_2]^+[AgX_2]^-$[11,12,15] and we propose the following formulation

$[Ag(IMe)_2]^+[AgCl_2]^-$ and $[Ag(SIMes)_2]^+[AgCl_2]^-$ for both side products. While complexes **11**, **12**, **13**, **15**, **16**, **20** display high stability toward light and air, complexes **14**, **17**, **18**, **19** slowly decompose within a week to a month under air and light. Once again, ^{1}H NMR spectra of the decomposed products indicate a mixture of (NHC)AgCl and $[Ag(NHC)_2]^+[AgX_2]^-$.

3.2.2. NMR Study of silver(I) complexes

The ^{1}H NMR spectra of complexes [(SIMes)AgCl] (**11**) and [(SIPr)AgCl] (**13**) give a single resonance at 4.00 and 4.07 ppm respectively for the saturated imidazole ring. [(IPrMe)AgCl] (**14**) and [(IMe)AgCl] (**15**) give a single high field resonance at 2.16 and 2.12 ppm respectively for the methyl group on the unsaturated imidazole ring and the corresponding signal for the *N*-alkyl chains. [(IPr)AgCl] (**12**), [(ICy)AgCl] (**16**), [(IAd)AgCl] (**17**), [(IsB)AgCl] (**18**) and [(IDD)AgCl] (**19**) display a single resonance signal at low field between 6.95 and 7.21 ppm for the unsaturated imidazole ring and the corresponding signals for the *N*-aryl and *N*-alkyl chains. The ^{13}C NMR spectra give a low field signal, attributed to the carbenic carbene at 207 ppm for both saturated complexes **11** and **13** while unsaturated complexes **12** and **14-20** exhibit a signal between 173 and 185 ppm (Table 3.1). [(SIMes)AgCl] (**11**) gives a carbenic signal at 207.5 ppm as a doublet of doublets with an observable coupling between carbon and silver of ($J^1(^{13}C\text{-}^{109}Ag)$ = 256 Hz and $J^1(^{13}C\text{-}^{107}Ag)$ = 222 Hz). [(SIPr)AgCl] (**13**) gives a signal at 207.7 ppm as a doublet of doublets with a coupling between silver and carbon ($J^1(^{13}C\text{-}^{109}Ag)$ = 271 Hz and $J^1(^{13}C\text{-}^{107}Ag)$ = 253 Hz). The similar values in chemical shift for (**11**) and (**13**) indicate no significant difference in the electronic donor properties existing for the saturated carbenes (SIMes and SIPr) in these silver systems. Nevertheless, both signals are 20 ppm downfield from that of the saturated complexes, confirming that saturated complexes might exhibit a better electron

donor ability to the metal in the present system.[24] For the unsaturated NHCs, *N*,*N*-bis(alkyl)-imidazol-ylidenes are generally considered better sigma donors than *N*,*N*-bis(aryl)-imidazol-ylidenes, however in the present silver(I) complexes, this trend is reversed. Surprisingly (IPr)AgCl (**12**) and (IMes)AgCl[22] display the highest downfield signal for the unsaturated series. This signal appears at 184.6 ppm as a doublet of doublets with an observable coupling between carbon and silver of $J^1(^{13}C\text{-}^{109}Ag)$ = 253 Hz and $J^1(^{13}C\text{-}^{107}Ag)$ = 219 Hz. Usually complexes exhibiting strong coupling are known to exhibit no exchange or very slow exchange[12,24] (on the NMR time scale) of their carbene moieties with the silver centers and are poor carbene transfer agents for transmetalation.[25] This quasi-static behavior in solution might also be correlated to the downfield signal of the carbenic carbon proving a stronger donation to the silver and indicates a stronger Ag–C bond.[24] This stronger bond decreases the lability of the carbene moieties and inhibits the formation of $[(NHC)_2Ag]^+$, preventing the formation of an equilibrium between (NHC)AgCl and $[(NHC)_2Ag]^+$.[24] (IDD)AgCl (**19**) displays a broad doublet at 177.8 ppm, due to a weak coupling between carbon and silver which is characteristic of a slightly faster exchange between IDD moieties and the silver centers. The upper field value of the signal shows that the IDD carbene does not exhibit strong donating abilities and the exchange should be faster.[24] We believe that this slow dynamic behavior is not due to electronic considerations but to the steric bulk of the dodecyl groups. Indeed, we have noticed that the formation of (IDD)AgCl (**19**) was slower and under synthetic conditions required a higher reaction temperature, possibly due to the difficulty of the silver center to reach the carbenic center which is protected by two large dodecyl groups. It is clear that having four dodecyl groups around the same silver center is very unlikely due to the overwhelming steric hindrance of such a situation. (IPrMe)AgCl (**14**), (ICy)AgCl (**16**), (IAd)AgCl(**17**), display signals at 172.3, 179.1 and 173.8 ppm respectively, as broad singlets characteristic of a slow exchange between the carbene moieties and the silver centers.[17,24] This

exchange is nevertheless faster than in the case of (IDD)AgCl (**19**). While the signal of (ICy)AgCl (**16**) is the most downfield (5 ppm from (IPr)AgCl (**12**)) and the IAd carbene leads to strong steric hindrance around the silver, the absence of coupling shows that these two parameters provide a small contribution indicating a significantly slower exchange for these two complexes. (IMe)AgCl (**15**) and (IsB)AgCl (**18**) exhibit a ^{13}C NMR signal at 177.6 ppm and 179.8 ppm respectively, as two sharp singlets characteristic of a fast exchange of the carbene moieties[17,24] with the silver centers. This rapid equilibrium must be facilitated by the relative small hindrance of both carbene moieties. The triazolium complex (TPh)AgCl (**20**) displays a ^{13}C NMR signal at 176.9 ppm illustrating an average donating ability similar to the previously discussed unsaturated NHC-silver complexes. The signal is a sharp singlet indicating a fast exchange of the triazolium moieties with the silver centers. The carbenic carbons of these new silver(I) complexes display resonances between 172 and 208 ppm and these are good indicators of the donating properties of the carbene to silver. While some silver(I) carbene halide complexes are known to establish a dynamic equilibrium between (NHC)AgCl and $[(NHC)_2Ag]^+$,[12,17,24] a routine ^{13}C NMR can give specific indications about the rate of the exchange indicated by the pattern associated with the carbenic signal. For all complexes we have examined, steric and/or electronic factors lead to a wide range of exchange rates as gauged by NMR signal positions and patterns.

Table 3.1. Chemical shifts of the carbenic carbon in NMR for the (NHC)AgCl complexes

Complex	Solvent[a]	δ (*C*–Ag) ppm	Appearance of the signal	$J^1(^{107\text{-}109}Ag–^{13}C)$ Hz
(IMes)AgCl[22]	$CDCl_3$	185.0	Doublet of doublet	270/234
(SIMes)AgCl (**11**)	$CDCl_3$	207.5	Doublet of doublet	256/222
(IPr)AgCl (**12**)	$CDCl_3$	184.6	Doublet of doublet	271/253
(SIPr)AgCl (**13**)	CD_2Cl_2	207.7	Doublet of doublet	253/219
(IPrMe)AgCl](**14**)	CD_2Cl_2	172.3	Broad singlet	---
(IMe)AgCl (**15**)	CD_2Cl_2	177.6	Sharp singlet	---
(ICy)AgCl (**16**)	$CDCl_3$	179.1	Broad singlet	---
(IAd)AgCl (**17**)	CD_2Cl_2	173.8	Broad singlet	---
(IsB)AgCl (**18**)	$CDCl_3$	179.8	Sharp singlet	---
(IDD)AgCl (**19**)	$CDCl_3$	177.8	Broad doublet	Unresolved
(TPh)AgCl (**20**)	$CDCl_3$	176.9	Sharp singlet	---

[a] Complexes partially soluble in $CDCl_3$ were fully solubilized in CD_2Cl_2

3.2.3. Structures of silver(I) complexes

While NMR data give specific information about the complexes and their dynamic properties in solution, X-ray diffraction was used to unambiguously determine the structure of NHC-Ag containing complexes in the solid state. Selected bond distances and bond angles are given in Table 3.2.

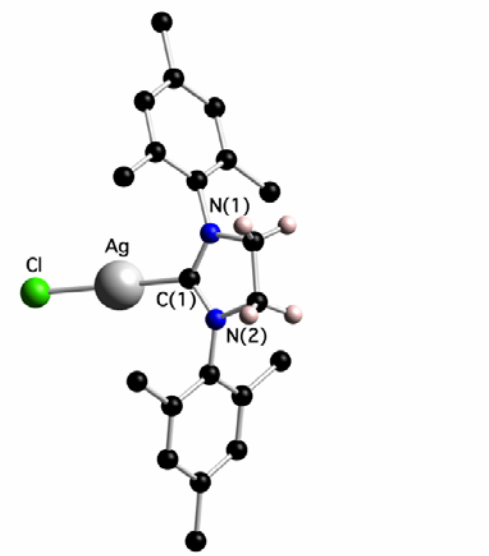
Table 3.2. Selected bond lengths and angles for the (NHC)AgCl complexes.

Complex	Ag–C (Å)	Ag–Cl (Å)	Ag•••Ag (Å)	C–Ag–Cl (deg)
(SIMes)AgCl (**11**)	2.0832(19)	2.3358(5)	---	173.70(6)
(IPr)AgCl (**12**)	2.056(6)	2.316(17)	---	175.2(2)
(SIPr)AgCl (**13**)	2.081(9)	2.320(2)	---	173.3(2)
(IPrMe)AgCl (**14**)	2.087(3)	2.3184(8)	---	180.00(9)
(IMe)AgCl (**15**)	2.091(2) 2.077(2)	2.3608(7) 2.3382(7)	3.0673(3)	172.56(7) 168.98(7)
(ICy)AgCl (**16**)	2.091(5) 2.075(6) 2.096(5) 2.085(5)	2.3335(14) 2.3290(15) 2.3593(14) 2.3293(14)	3.0650(6) 3.0181(6)	170.06(15) 177.46(16) 166.27(16) 170.91(15)
(IAd)AgCl (**17**)	2.094(6)	21350(16)	---	176.08(14)
(IsB)AgCl (**18**)	2.073(17) 2.087(17) 2.060(19) 2.067(18)	2.314(5) 2.332(5) 2.324(5) 2.359(5)	3.108(2) 3.124(2)	175.9(5) 178.7(5) 178.1(6) 176.9(5)
(IDD)AgCl (**19**)	2.067(4)	2.3200(9)	---	174.96(11)
(TPh)AgCl (**20**)	2.121(1) 2.105(2) 2.089(2)	2.4458(6) 2.7978(6) 2.4045(6) 2.3753(6) 2.8685(6)	3.0242(2) 3.0752(2) Cl–Ag–Cl (deg) 102.177(19) 96.159(18)	150.34(6) 109.61(6) C–Ag–C (deg) 169.51(9) Ag-Ag-Ag (deg) 147.295(7)

All complexes, with the exception of (TPh)AgCl (**20**), have a two-coordinate silver(I) atoms in a close linear environment with a C–Ag–Cl bond close to 180°. All C–Ag bond distances are in the range of 2.056 and 2.094 Å which is in line with other silver bis- or mono-carbene complexes previously reported.[12,14,20,22,24,26] As expected, the silver–carbon bonds are longer than the gold–carbene bonds reported for analogous (NHC)Au(I)Cl complexes (bond lengths between 1.987 and 1.999 Å).[23] All Ag–Cl bond distances are between 2.332 and 2.360 Å which is in the range of other silver(I) chloride complexes reported.[20,22] None of the C–Ag bond lengths are shortened with a simultaneous elongation of the Ag–Cl. The absence of a *trans*-effect for the complexes does not allow any comparisons of the electronic donating abilities for different carbene moieties. It is noteworthy, that the shorter length of the Ag–C (2.057 Å) bond and the more downfield value of the carbenic signal (184.6 ppm) in (IPr)AgCl (**12**) hint at the better donating properties of the carbene IPr over other unsaturated carbene ligands. Complexes **11**, **12**, **13**, **14**, **17**, **19** are monomeric with no evident argentophilic (Ag(I)•••Ag(I)) interactions (Figure 3.1, 3.2 and 3.3). Indeed, all distances between silver(I) centers are greater than 3.44 Å, the sum of twice the Van Der Waals radius of Ag(I).[12] (IMe)AgCl (**15**) has two molecules in the asymmetric unit and forms a dimer linked by argentophilic interactions with a Ag(I)•••Ag(I) distance of 3.067 Å (Figure 3.2). (ICy)AgCl (**16**) and (IsB)AgCl (**18**) have four molecules in the asymmetric unit and display a dimeric structure with Ag(I)•••Ag(I) distances between dimer centers longer than 3.44 Å.[12] For each dimer, two molecules of the complex are linked by argentophilic interactions with two Ag(I)•••Ag(I) distances of 3.065 and 3.108 Å for (ICy)AgCl (**16**) and 3.108 and 3.124 Å for (IsB)AgCl (**18**) (Figure 3.2). (TPh)AgCl (**20**) has a unique structure where (TPh)AgCl coexists with $[(TPh)_2Ag]^+[AgCl_2]^-$ in the asymmetric unit. $[(TPh)_2Ag]^+$ is linked to (TPh)AgCl by an argentophilic interaction with a Ag(I)•••Ag(I) distance of 3.042 Å to form a trimer. $[(TPh)_2Ag]^+$ is also linked to $[AgCl_2]^-$ by argentophilic interactions

with a Ag(I)•••Ag(I) distance of 3.075 Å, while $[AgCl_2]^-$ is linked to the silver and the chloride of (TPh)AgCl to form a bridge. In fact, the structure can also be envisaged as a polymer with each $[(TPh)_2Ag]^+$ unit bound by $[(TPh)Ag–(\mu Cl)_2–AgCl]^-$ units (Figure 3.3 and 3.4). It is interesting to note that in the bridged $[(TPh)Ag–(\mu Cl)_2–AgCl]^-$ moiety, even though there is no direct argentophilic interaction, a Ag(I)•••Ag(I) distance of 3.510 Å can induce a preferential orientation in the packing of the structure.[19] For (TPh)AgCl, the Ag–C distance is slightly longer than others with a value of 2.121 Å but is reasonable if compared with the 2.772 Å of the silver(I) carbene described by Calano *et al.*[18] The two Ag–Cl bond distances of the bridge have values of 2.798 and 2.869 Å which are marginally longer than the 2.535 Å value found for $[AgCl_2]^-$. The solid state structure of (TPh)AgCl (**20**) confirms the sharp singlet found in ^{13}C NMR for the carbenic carbon and it also justifies our expectations of a dynamic equilibrium between (TPh)AgCl, and $[(TPh)_2Ag]^+$ $[AgCl_2]^-$ in solution. For all complexes, no agostic interactions between silver–hydrogen or even silver–methyl groups have been observed as described in the silver(I) phosphine carborane complexes synthesized by Weller *et al*[27] with Ag–H and Ag–C(H_3) distances greater than 2.49 and 3.29 Å respectively.[27]

Figure 3.1. Ball and stick representations of complexes (SIMes)AgCl (**11**), (IPr)AgCl (**12**) (SIPr)AgCl (**13**) and (IPrMe)AgCl (**14**). Most hydrogen atoms have been omitted for clarity



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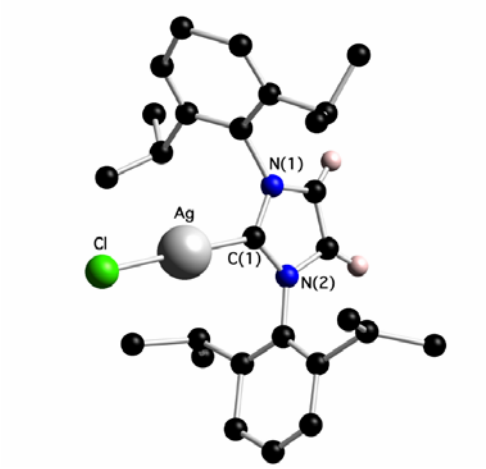

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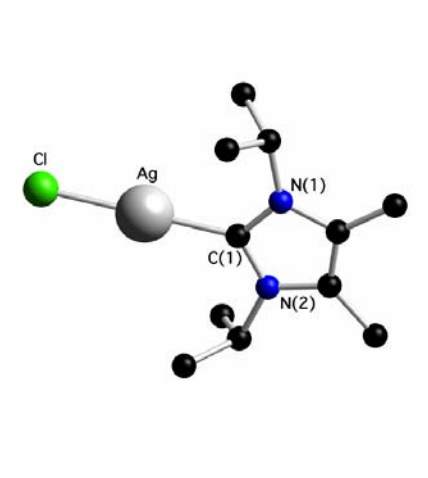

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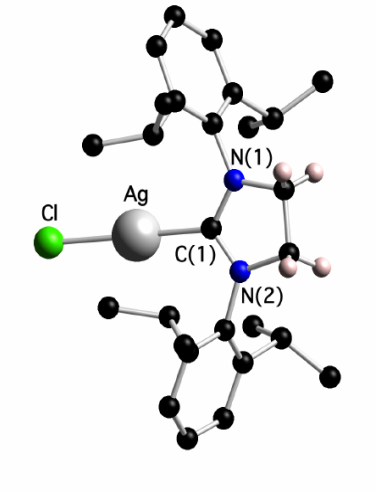
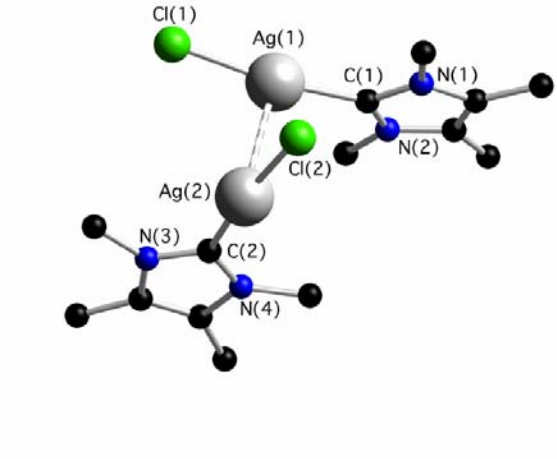


14

Figure 3.2. Ball and stick representations of complexes (IMe)AgCl (**15**) and (ICy)AgCl (**16**), (IAd)AgCl (**17**) and (IsB)AgCl (**18**). Most hydrogen atoms have been omitted for clarity



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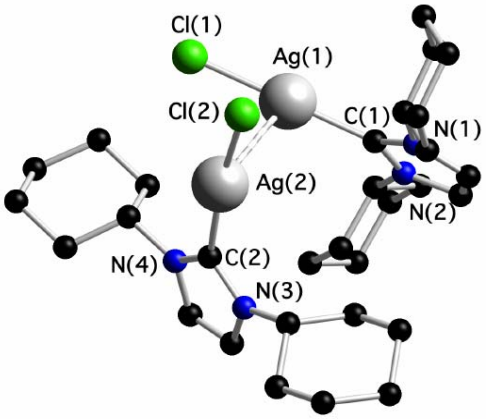

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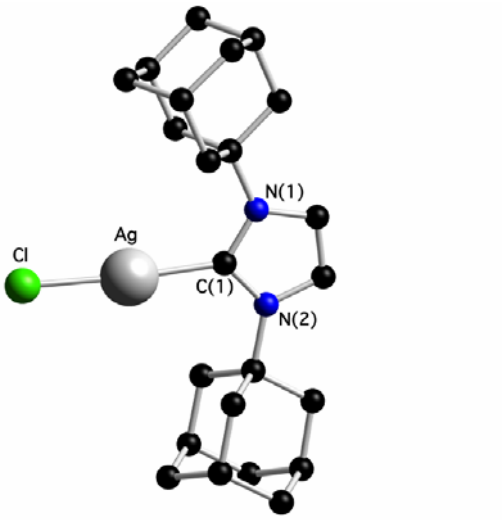
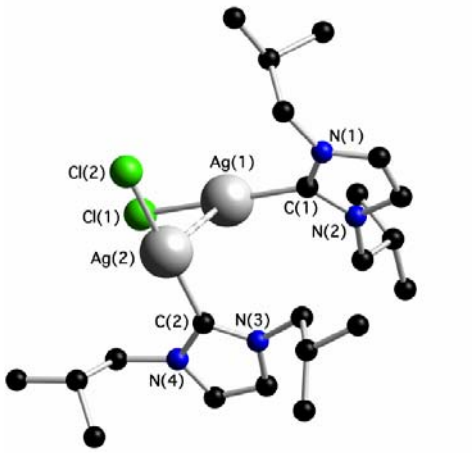
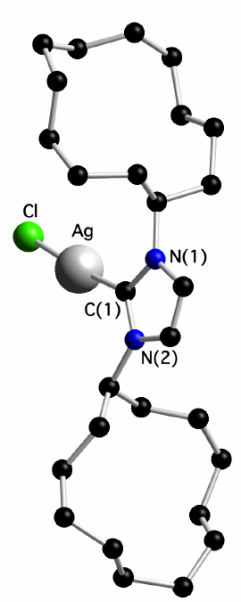


17



18

Figure 3.3. Ball and stick representations of complexes (IDD)AgCl (**19**), (TPh)AgCl as a trimer (**20a**). Hydrogen atoms have been omitted for clarity



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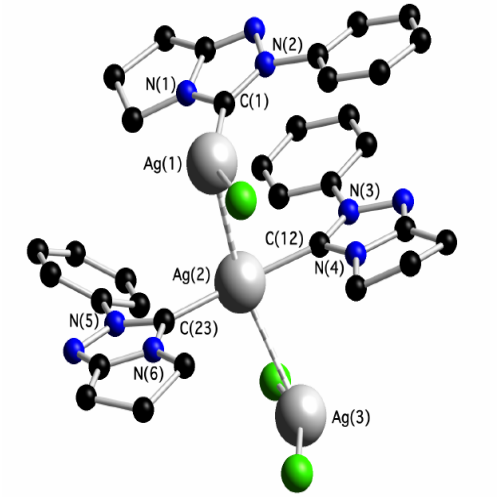
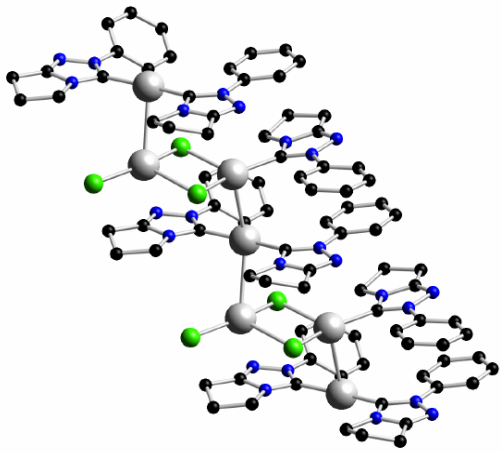


20a

Figure 3.4. Ball and stick representations of complex (TPh)AgCl as a bridged Ag-(μCl$_2$)-Ag polymer (**20b**). Hydrogen atoms have been omitted for clarity



20b

3.2.4. Solvent effect on the synthesis of silver(I) complexes

In order to improve the yields of (NHC)AgCl complexes obtained, especially for (SIMes)AgCl (**11**) and (IMe)AgCl (**15**), the effect of the solvent polarity used in the synthesis was studied for the already well-defined (IMes)AgCl complex.[22] Three different solvents, chloroform, acetonitrile and dimethylsulfoxide, with a gradient of polarity, are used under similar experimental conditions. When NMR characterization of the crude reactions are carried out, a side product is observed and its NMR spectrum is consistent with the previously reported bis-NHC $[(IMes)_2Ag]^+[AgCl_2]^-$ (**21**) complex.[11] After separation by crystallization, X-ray studies of the crystals grown confirmed that the side-product was $[(IMes)_2Ag]^+[AgCl_2]^-$ (**21**) (Figure 3.5) and confirmed our hypothesis for the formation of $[(SIMes)_2Ag]^+[AgCl_2]^-$ and $[(IMe)_2Ag]^+[AgCl_2]^-$ as side products from the syntheses of [(SIMes)AgCl] (**11**) and [(IMe)AgCl] (**15**). The three assays show that increasing the polarity of the solvent, leads to an increase in the amount of bis-carbene complex formed (Table 3.3). It is reasonable to state that polar solvents must stabilize the ionic $[(IMes)_2Ag]^+$ form better than non polar solvents, and might shift the equilibrium {(IMes)AgCl / $[(IMes)_2Ag]^+$} toward bis–NHC–Ag complex.

Table 3.3. Product distribution of $[(IMes)_2Ag]^+[AgCl_2]^-$ and (IMes)AgCl.

Solvent (Dielectric Constant)[28]	$[Ag(IMes)_2]^+[AgCl_2]^-$	(IMes)AgCl
Chloroform (4.2)	15%	85%
Acetonitrile (37.5)	25%	75%
Dimethylsulfoxide (46.7)	34%	66%

^{1}H NMR spectrum of **21** displays a single resonance at 7.23 ppm for the unsaturated imidazole ring and the corresponding signals for the *N*-mesityl groups.[11] The ^{13}C NMR spectrum does not exhibit any signal between 160 and 200 ppm, an observation also made by Hedrick *et al*.[11] Solid state structural data showed a two coordinate silver(I) atom in a linear environment with a C–Ag–C bond of 180°. The Ag–C bond distances are 2.066 Å and 2.084 Å while both Ag–Cl bond distances are 2.534 Å (Table 3.4). All these values are in good agreement with the other bis-carbene complexes previously reported.[12,14,26] There is one cation $[(IMes)_2Ag]^+$ and one anion$[AgCl_2]^-$ present in the asymmetric unit. This complex is monomeric with no argentophilic interactions and no Ag-(μCl_2)-Ag bridging present with the minimal Ag(I)•••Ag(I) distance being 6.397 Å (Figure 3.5).

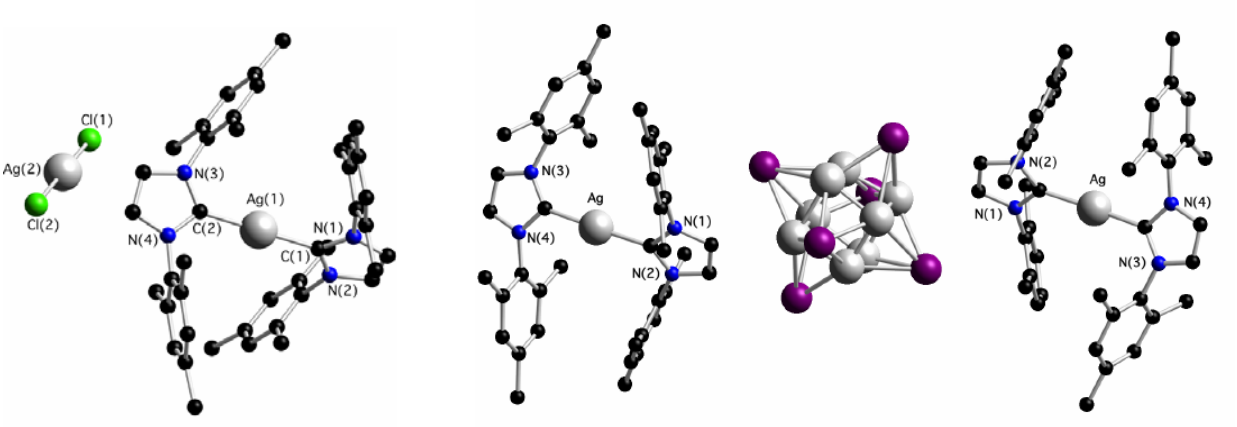
We also attempted to synthesize the complex (IMes)AgI in acetonitrile to investigate the effect of the halide and the solvent polarity on the structure of the complex. We anticipated a mixture of mono- and bis-carbene. The ^{1}H NMR and the ^{13}C NMR spectra of the reaction crude matched those of $[(IMes)_2Ag]^+[AgCl_2]^-$ (**21**) leading us to conclude that only the bis-NHC complex **22** is formed in acetonitrile. The fact that Zhang *et al*. have reported a polymeric mono-carbene silver(I) iodide, without any trace of bis-carbene, in non polar dichloromethane[19] leads us to believe that polarity of the solvent must be the dominating factor in directing the structure adopted by an iodide silver complex between mono- and bis-carbene. X-ray studies confirm that the silver(I) atom is surrounded by two carbon atoms in near linear environment with a C–Ag–C bond angle of 180°. There are two $[(IMes)_2Ag]^+$ cations and one $[Ag_4I_6]^{2-}$ anion in the asymmetric unit, leading to a $[(IMes)_2Ag]_2[Ag_4I_6]$ formulation for **22**. This complex is monomeric with no argentophilic interactions (Figure 3.5). The most surprising feature comes from the massive octahedral anion $[Ag_4I_6]^{2-}$ cluster. Inside this cage, the Ag(I)•••Ag(I) distances are between 2.0915 and 3.1453 Å and the Ag–I distances are between 2.7052 and 2.8507 Å

(Table 3.4). The structure is centrosymmetric with an inversion center located at the origin of the octahedron. This remarkable structure is the first silver halide complex reported with a general formula of $[(NHC)_2Ag]^+_2$ $[Ag_4X_6]^{2-}$.

Table 3.4. Selected bond lengths and angles for $[(IMes)_2Ag]^+_2$ complexes.

Complex	Ag–C (Å)	Ag–Cl / Ag–I (Å)	Ag•••Ag (Å)	C–Ag–C (deg)
$[(IMes)_2Ag]^+[AgCl_2]^-$ (**21**)	2.066(5) 2.084(5)	2.534(5)	---	180.000(1)
$[(IMes)_2Ag]^+_2[Ag_4I_6]^{2-}$ (**22**)	2.079(5) 2.082(5)	2.7556(14)-2.7774(14) 2.8121(14)-2.7212(12) 2.7468(12)-2.7751(13) 2.7157(13)-2.7627(14) 2.8507(14)-2.7025(14) 2.7175(14)-2.8397(14) 2.7052(14)-2.7627(14)	---	172.5(2)

Figure 3.5. Ball and stick representations of complexes $[(IMes)_2Ag]^+[AgCl_2]^-$ (**21**) and $[(IMes)_2Ag]^+_2[Ag_4I_6]^{2-}$ (**22**). Hydrogen atoms have been omitted for clarity.



21 **22**

3.3. Conclusion

We report the synthesis of ten new silver mono-carbene complexes. Their straightforward synthesis can be accomplished by simple reaction of an imidazolium chloride salt with silver oxide or by reaction of a free NHC with silver chloride. The NMR and crystallographic data do not permit unambiguous determinations of electronic differences between the various NHC–Ag moieties as a function of NHC. We have observed a dynamic equilibrium between (NHC)AgCl and $[(NHC)_2Ag]^+[AgCl_2]^-$ species in solution as gauged by a simple analysis of the ^{13}C NMR spectrum. It has also been observed that (TPh)AgCl (**20**) exhibits both forms of mono and bis-carbene complexation in the solid state. In addition, by increasing the solvent polarity, formation of the bis-NHC complex can be favored. This trend looks more pronounced with the more easily

polarizable iodide than with the harder chloride, allowing the synthesis of the first $[(NHC)_2Ag]^+_2$ $[Ag_4X_6]^{2-}$ (**22**) complex. Catalytic activity of this new series of well-defined silver–NHC complexes in a number of organic transformations is presently underway.

3.4. Experimental Section

3.4.1. General Considerations

- All reactions using an imidazolium salt as starting material were carried out in aerobic condition.
- All reactions using a free carbene as starting material were carried out using standard Schlenk techniques under an atmosphere of dry argon or in a MBraun glovebox containing dry argon and less than 1 ppm oxygen. Anhydrous solvents were either distilled from appropriate drying agents or purchased from Aldrich and degassed prior to use by purging with dry argon and kept over molecular sieves.
- Solvents for NMR spectroscopy were degassed with argon and dried over molecular sieves. NMR spectra were collected on a 400 MHz Varian Gemini spectrometer.
- Elemental analyses were performed by Robertson Microlit Labs. Carbene ligands **1**-**10** were synthesized following literature procedures.[29-30]

3.4.2. Synthesis of silver(I) complexes

Synthesis of (SIMes)AgCl ***(11):*** A 50 mL flask was charged with SIMes·HCl (750 mg, 2.19 mmol) and 15 mL of dichloromethane, to this solution was added silver(I) oxide (583 mg, 2.52 mmol). The resulting solution was refluxed for 12 h then filtered over celite and the filtrate reduced to 10 mL. The solution was cooled to 0 °C and heptane was slowly added until white crystals appeared. The solid was filtered, washed with pentane (10 mL) and dried under vacuum. Yield: 699 mg (71 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 6.95 (s, 4H, C*H*-aromatic), 4.00 (s, 4H, CH_2-imidazole), 2.30 (s, 12H, CH_3), 2.29 (s, 6H, CH_3); ^{13}C NMR (CD_2Cl_2): δ (ppm) = 207.5 (dd, J^1(^{109}Ag, ^{13}C) = 256 Hz, J^1(^{107}Ag, ^{13}C) = 222 Hz, *C*-carbene), 139.0 (s, *C*H-aromatic), 135.7 (s, *C*H-aromatic), 135.3 (s, *C*H-aromatic), 130.0 (s, *C*H-aromatic), 51.3 (s, *C*H_2-imidazole), 21.2 (s, CH_3), 18.1 (s, CH_3). Elemental analysis calcd for $C_{21}H_{26}N_2AgCl$ (450.77): C, 55.96; H, 5.77; N, 6.21. Found: C, 56.27 H, 5.94; N, 6.08.

Synthesis of (IPr)AgCl ***(12):*** A 50 mL flask was charged with IPr·HCl (1 g, 2.35 mmol) and 15 mL of dichloromethane, to this solution was added silver(I) oxide (328 mg, 1.41 mmol). The resulting solution was stirred at room temperature for 12 h then filtered over celite and the filtrate reduced to 10 mL. Pentane (30 mL) was added to the solution to precipitate a white solid. The solid was washed further with pentane (3 x 10 mL) and dried under vacuum to afford a white powder. Yield: 2.160 g (88 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.50 (m, 2H, C*H*-aromatic), 7.30 (m, 4H, C*H*-aromatic), 7.21 (s, 2H, C*H*-imidazole), 2.54 (septet, *J* = 6.8 Hz, 4H, C*H*(CH_3)$_2$), 1.28 (d, *J* = 6.8 Hz, 12H, CH (CH_3)$_2$), 1.22 (d, *J* = 6.8 Hz, 12H, CH (CH_3)$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 184.6 (dd, J^1(^{109}Ag, ^{13}C) = 271 Hz, J^1(^{107}Ag, ^{13}C) = 235 Hz, *C*-carbene), 145.6 (s, *C*H-

aromatic), 130.8 (s, *C*H-aromatic), 124.4 (s, *C*H-aromatic), 123.7 (s, *C*H-aromatic), 123.6 (s, *C*H-imidazole), 28.7 (s, *C*H ($CH_3)_2$), 24.7 (s, CH ($CH_3)_2$), 24.0 (s, CH ($CH_3)_2$). Elemental analysis calcd for $C_{27}H_{36}N_2AgCl$ (531.59): C, 61.00; H, 6.77; N, 5.27. Found: C, 61.20; H, 7.05; N, 5.22.

Synthesis of (SIPr)AgCl ***(13):*** A 50 mL flask was charged with SIPr·HCl (1 g, 2.60 mmol) and 15 mL of dichloromethane, to which was added silver(I) oxide (356 mg, 1.61 mmol). The resulting solution was stirred at room temperature for 12 h then filtered over celite and the filtrate reduced to 10 mL. Pentane (30 mL) was added to immediately precipitate a white solid. The solid was further washed with pentane (3 x 10 mL) and dried under vacuum to afford a white powder. Yield: 1.019 g (74 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.41 (m, 2H, C*H*-aromatic), 7.25 (m, 4H, C*H*-aromatic), 4.07 (s, 4H, CH_2-imidazole), 3.06 (septet, *J* = 6.8 Hz, 4H, C*H*($CH_3)_2$), 1.35 (d, *J* = 6.8 Hz, 12H, CH (C$H_3)_2$), 1.35 (d, *J* = 6.8Hz, 12H, CH (C$H_3)_2$); ^{13}C NMR (CD_2Cl_2): δ (ppm) = 207.7 (dd, J^1(^{109}Ag, ^{13}C) = 253 Hz, J^1(^{107}Ag, ^{13}C = 219 Hz, *C*-carbene), 147.0 (s, *C*H-aromatic), 134.9 (s, *C*H-aromatic), 130.1 (s, *C*H-aromatic), 124.8 (s, *C*H-aromatic), 54.1 (s, *C*H_2-imidazole), 29.0 (s, *C*H ($CH_3)_2$), 25.3 (s, CH ($CH_3)_2$), 24.0 (s, CH ($CH_3)_2$). Elemental analysis calcd for $C_{27}H_{38}N_2AgCl$ (533.59): C, 60.77; H, 7.12; N, 5.25. Found: C, 60.64; H, 7.38; N, 5.04.

Synthesis of (IPrMe)AgCl ***(14):*** In a glovebox, a 50 mL Schenk flask was charged with 120 mg (0.66 mmol) of IPrMe and 10 mL of THF and then 143 mg (0.14 mmol) of silver(I) chloride was added. The resulting solution was kept in the dark and stirred at room temperature for 12 h. The remaining steps were then carried out in air. The solution was filtered over celite and the filtrate reduced to 10 mL. Pentane (30 mL) was added to the solution resulting in an immediate precipitation of a white solid. The solid was further washed with pentane (2 x 10 mL) and dried

under vacuum, to afford a white powder. Yield: 63 mg (71 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 4.55 (septet, *J* = 6.9 Hz, 2H, NC*H*-isopropyl), 2.16 (s, 6H, CH_3-imidazole), 1.56 (d, *J* = 6.9 Hz, 12H, CH (CH_3)$_2$); ^{13}C NMR (CD_2Cl_3): δ (ppm) = 172.3 (s, *C*-carbene), 124.9 (s, *C*H-imidazole), 51.5 (s, *C*H (CH$_3$)$_2$), 23.9 (s, CH (*C*H$_3$)$_2$), 9.5 (s, *C*H$_3$-imidazole). Elemental analysis calcd for $C_{11}H_{20}N_2AgCl$ (323.43): C, 40.85; H, 6.18; N, 8.66. Found: C, 40.96; H, 5.92; N, 8.57.

Synthesis of (IMe)AgCl ***(15):*** In a glovebox, a 50 mL Schenk flask was charged with 100 mg (0.81 mmol) of IMe and 10 mL of THF and then 230 mg (0.16 mmol) of silver(I) chloride was added. The resulting solution was kept in the dark and stirred at room temperature for 12 h. The remaining steps were then carried out in air. The solution was cooled to –78 ºC and rapidly filtered over celite. The celite was rinsed first with cold THF. The clear green solution obtained was discarded. Then the celite was washed with 10 ml of dichloromethane resulting in a bright yellow solution. Heptane was slowly added until appearance of yellow clears crystals. The solid were filtered off and rinsed with pentane and dried under vacuum. Yield: 80 mg (28 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 3.65 (s, 6H, N*CH*$_3$), 2.12 (s, 6H, *CH*$_3$); ^{13}C NMR (CD_2Cl_2): δ (ppm) = 177.5 (s, *C*-carbene), 125.8 (s, *C*H-imidazole), 36.5 (s, *CH*$_3$), 9.2 (s, *CH*$_3$). Elemental analysis calcd for $C_7H_{12}N_2AgCl$ (267.69): C, 31.43; H, 4.48; N, 10.46. Found: C, 31.21; H, 4.38; N, 10.19.

Synthesis of (ICy)AgCl ***(16):*** A similar method of preparation to that used for compound (SIMes)AgCl **(11)** gave a white solid**.** Yield: 754 mg (72 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 6.98 (s, 2H, C*H*-imidazole), 4.22 (m, 2H, NC*H*-cyclohexyl), 2.02 (m, 4H, C*H*$_2$), 1.87 (m, 4H, C*H*$_2$), 1.74 (m, 2H, C*H*$_2$), 1.58 (m, 4H, C*H*$_2$), 1.43 (m, 4H, C*H*$_2$), 1.19 (m, 2H, C*H*); ^{13}C NMR ($CDCl_3$): δ (ppm) = 179.1 (broad s, *C*-carbene), 119.9 (s, *C*H-imidazole), 63.9 (s, N*C*H-cyclohexyl), 36.6

(s, *C*H_2), 27.5 (s, *C*H_2), 27.2 (s, *C*H_2). Elemental analysis calcd for $C_{15}H_{24}N_2AgCl$ (375.42): C, 47.99; H, 6.39; N, 7.46. Found: C, 48.17; H, 6.56; N, 7.40.

Synthesis of (IAd)AgCl ***(17):*** A 50 mL flask was charged with IAd·HCl (300 mg, 0.81 mmol) and 10 mL of dichloromethane, to which was added silver(I) oxide (112 mg, 0.48 mmol). The resulting solution was refluxed for 12 h then filtered over celite and the filtrate reduced to 5 mL. The solution was cooled to 0 °C and pentane was slowly added until appearance of white crystals. The solid was filtered off, washed with pentane (3 x 5 mL) and dried under vacuum to afford a white powder. Yield: 699 mg (71 %). ^{1}H NMR (CD_2Cl_2): δ (ppm) = 7.19 (s, 2H, C*H*-imidazole), 2.35-22 (broad m, 20H, adamantyl), 1.75 (m, 10H, C*H*$_2$-adamantyl); ^{13}C NMR (CD_2Cl_2): δ (ppm) = 173.8 (broad s, *C*-carbene), 116.3 (s, *C*H-imidazole), 58.2 (s, N*C*H-adamantyl), 44.9 (s, *C*H_2), 36.0 (s, *C*H_2), 30.2 (s, *C*H_2). Elemental analysis calcd for $C_{23}H_{32}N_2AgCl$ (478.92): C, 57.68; H, 6.68; N, 5.85. Found: C, 57.88; H, 6.82; N, 5.59.

Synthesis of (IsB)AgCl ***(18):*** A similar method of preparation to that used for compound (SIMes)AgCl **(11)** gave a white solid**.** Yield: 838 mg (75 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 6.95 (s, 2H, *C*H-imidazole), 3.88 (d, *J* = 7.3 Hz, 4H, *CH*$_2$), 2.12 (m, 2H, *CH*), 0.91 (d, *J* = 6.3 Hz, 12H, *CH*$_3$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 179.3 (s, *C*-carbene), 121.6 (s, *C*H-imidazole), 53.4 (s, *C*H_2), 30.5 (s, *C*H), 20.0 (s, *C*H_3). Elemental analysis calcd for $C_{11}H_{20}N_2AgCl$ (323.39): C, 40.85; H, 6.18; N, 8.66. Found: C, 41.12; H, 6.34; N, 8.60.

Synthesis of (IDD)AgCl ***(19):*** A 50 mL flask was charged with IDD·HCl (500 mg, 1.15 mmol) and 10 mL of THF, to which was added silver(I) oxide (305 mg, 1.32 mmol). The resulting

solution was stirred at reflux for 16 h then filtered over celite and the filtrate reduced to 5 mL. The solution was cooled to –40 °C and cold pentane was slowly added until appearance of a white precipitate. The solid was filtered off, washed with cold pentane (10 mL) and dried under vacuum. Yield: 415 mg (67 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 6.96 (s, 2H, C*H*-imidazole), 4.52 (m, 2H, NC*H*-cyclododecyl), 2.04 (m, 4H, CH_2), 1.69 (m, 4H, CH_2), 1.55-1.27 (m, 36H, CH_2); ^{13}C NMR ($CDCl_3$): (ppm) δ = 177.8 (broad d, *C*-carbene), 118.6 (s, *C*H-imidazole), 59.0 (s, NCH-cyclododecyl), 31.7 (s, *C*H_2), 23.8 (s, *C*H_2), 23.7 (s, *C*H_2), 23.6 (s, *C*H_2), 23.5 (s, *C*H_2), 21.8 (s, *C*H_2). Elemental analysis calcd for $C_{27}H_{48}N_2AgCl$ (543.43): C, 59.67; H, 8.83; N, 5.15. Found: C, 59.46; H, 8.71; N, 4.94.

Synthesis of (TPh)AgCl ***(20):*** A similar method of preparation to that used for compound (IPr)AgCl **(12)** gave a white solid**.** Yield: 590 mg (82 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.79 (m, 2H, C*H*-aromatic), 7.41 (m, 3H, C*H*-aromatic), 4.39 (m, CH_2-pyrrolidine), 3.10 (m, 2H, CH_2-pyrrolidine), 2.73 (m, 2H, CH_2-pyrrolidine); ^{13}C NMR ($CDCl_3$): δ (ppm) = 176.9 (s, *C*-carbene), 160.7 (s, N*C*=N), 140.1 (s, N*C*-aromatic), 129.5 (s, *C*H-aromatic), 129.0 (s, *C*H-aromatic), 122.9 (s, *C*H-aromatic), 46.6 (s, C*C*HN-pyrrolidine), 26.1 (s, *C*H_2-pyrrolidine), 21.5 (s, *C*H_2-pyrrolidine). Elemental analysis calcd for $C_{11}H_{11}N_3AgCl$ (329.43): C, 40.10; H, 3.34; N, 12.75. Found: C, 40.51; H, 3.13; N, 12.51.

Synthesis of $[(IMes)_2Ag]^+[AgCl_2]^-$ ***(21):*** A 50 mL flask was charged with IMes·HCl (340 mg, 0.99 mmol) and 10 mL of acetonitrile, to which was added silver(I) oxide (120 mg, 0.50 mmol). The resulting solution was refluxed for 24 h then filtered over celite and the filtrate reduced to 5 mL. The solution was left to crystallize and brown pale crystals were obtained. Yield: 750 mg (85

%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.23 (s, 2H, C*H*$_2$-imidazole), 6.97 (s, 4H, C*H*-aromatic), 2.42 (s, 6H, C*H*$_3$), 1.71 (s, 12H, C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 140.2 (s, *C*H-aromatic), 135.9 (s, *C*H-aromatic), 135.5 (s, *C*H-aromatic), 129.8 (s, *C*H-aromatic), 123.9 (s, *C*H-imidazole), 21.1 (s, C*H*$_3$), 17.3 (s, C*H*$_3$). Elemental analysis calcd for $C_{42}H_{48}N_4Ag_2Cl_2$ (894.96): C, 56.33; H, 5.40; N, 6.26. Found: C, 56.01; H, 5.67; N, 6.57.

Synthesis of $[Ag(IMes)_2]^+{}_2[Ag_4I_6]^{2-}$ ***(22):*** A similar method of preparation to that used for compound $[(IMes)_2Ag]^+[AgCl_2]^-$ (**21**) gave pale brown crystals**.** Yield: 299 mg (23 %). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.23 (s, 2H, C*H*$_2$-imidazole), 6.97 (s, 4H, C*H*-aromatic), 2.42 (s, 6H, C*H*$_3$), 1.71 (s, 12H, C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 140.1 (s, *C*H-aromatic), 135.9 (s, *C*H-aromatic), 135.5 (s, *C*H-aromatic), 129.8 (s, *C*H-aromatic), 124.0 (s, *C*H-imidazole), 21.1 (s, C*H*$_3$), 17.3 (s, C*H*$_3$). Elemental analysis calcd for $C_{84}H_{96}N_8Ag_6I_8$ (2625.46): C, 39.41; H, 3.68; N, 4.27. Found: C, 39.59; H, 3.98; N, 4.56.

3.5. Acknowledgments

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3.6. References and Notes

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CHAPTER 4

SYNTHESIS AND STRUCTURAL CHARACTERIZATION OF *N*-HETEROCYCLIC CARBENE GOLD(I) COMPLEXES

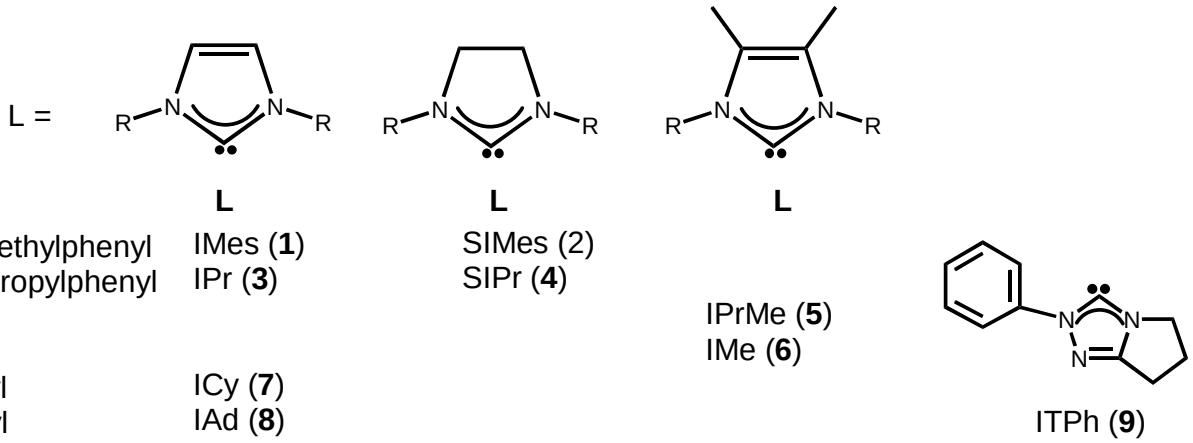
4.1. Introduction

The development of *N*-heterocyclic carbene (NHC) metal complexes has now become a well-established area of research.T[1] As a result a large variety of metal-NHC complexes are known, many of which have been successfully used in catalytic applications.[2] Interestingly, most studies of catalysts incorporating NHC ligands have evolved around the platinum group metals and in many cases simple substitution of phosphines with NHCs led to higher catalytic activity as well as higher thermal stability of the catalysts. The working hypothesis is that NHCs are more powerfully σ-donating than the closely related phosphine ligands and therefore form stronger bonds to transition metal centres.[3] Recently we reported a detailed steric and electronic investigation of the NHC and phosphine ligand classes involving the square planar complex $(L)Ni(CO)_3$ which allowed a direct comparison of the two ligand families and also led to the experimental determination of Ni-C(NHC) bond strengths.[4,5] Contrary to the wealth of

information available for such late transition metal NHC compounds, the chemistry of linear two-coordinate coinage metal-NHC compounds in general, and gold(I)-NHC complexes in particular, has remained relatively unexplored.[6,7,8,9] Complexes of general formula Au(NHC)(X) (X = halide) are especially scarce and this prompted us to develop reliable synthetic methods for the preparation of such monocarbene-gold(I) compounds, to investigate their solid state and solution behavior and to explore their chemistry. It should be noted that gold complexes have received considerable attention in medicinal chemistry, where they can act as antitumor and antimicrobial agents.[10] Moreover, Au(I) complexes often show interesting photophysical properties by displaying strongly luminescent behavior.[11] Finally, whereas the use of Au(I) complexes in homogeneous catalysis is a relatively new field of research, it has already witnessed spectacular achievements.[12,13]

We report here the synthesis of a series of two-coordinate gold(I) chloride complexes of general composition Au(NHC)Cl. The NHC ligands used are shown in Figure 4.1 and comprise commonly used saturated and unsaturated ligands such as IMes (**1**), SIMes (**2**), IPr (**3**), SIPr (**4**), IPrMe (**5**), IMe (**6**), ICy (**7**), IAd (**8**) as well as the triazolium ligand ITPh (**9**). All new Au(I)–NHC complexes were characterized by X-ray crystallography, elemental analysis and by spectroscopic methods. Both X-ray crystallography as well as NMR spectroscopy allowed us to gain some insight into the electronic characteristics of the resulting complexes. ^{13}C NMR measurements of the carbenic carbon proved to be especially useful. We present a comparison of NMR shift values of the free NHC ligands **1**-**9**, the (NHC)-AuCl complexes as well as their isolobal counterparts (NHC)-$Ni(CO)_3$ and [(NHC)-H]Cl and discuss the results obtained. It should be noted that complex [Au(IPr)Cl] (**12**) has been previously published in a communication.[14]

Figure 4.1. NHC ligands used in this study



4.2. Results and discussion

4.2.1. Synthesis of gold(I) complexes

A direct reaction between one equiv. of AuCl and free carbene was initially attempted but was not successful resulting in very low yields of Au(NHC)Cl in addition to the by-products $[Au(NHC)_2]Cl$ and gold(0). Similar by-products have been observed in the attempted preparation of [Au(ItBu)(X)] (X = BF_4, ClO_4). For that reason an exchange reaction between a THF solution containing IPr (**3**), SIPr (**4**), IPrMe (**5**), IMe (**6**), ICy (**7**), IAd (**8**) and ItBu with $[Au(SMe_2)Cl]$ gave the complexes [Au(IPr)Cl] (**12**), [Au(SIPr)Cl] (**13**), [Au(IPrMe)Cl] (**14**), [Au(IMe)Cl] (**15**), [Au(ICy)Cl] (**16**), [Au(IAd)Cl] (**17**) and the already reported [Au(ItBu)Cl] as white solids in high yield (eq 1).

$$[Au(SMe_2)Cl] + NHC \longrightarrow [Au(NHC)Cl] + SMe_2 \qquad (1)$$

NHC = IPr (3), SIPr (4), IPrMe (5), IMe (6), ICy (7) and IAd (8)

Although SIMes (**2**) and ITPh (**9**) were not attempted with this method, it was not successful with IMes (**1**) affording a mixture of products similar to that found initial attempt using AuCl and free carbene. An alternative route treating an equal molar ratio of $Au(SMe_2)Cl$ to the respective *in situ* generated Ag(I)-NHC salt (NHC = IMes (**1**), SIMes (**2**), ITPh (**9**)) gave rise to the complexes [Au(IMes)Cl] (**10**), [Au(SIMes)Cl] (**11**) and [Au(ITPh)Cl] (**18**) in moderate to high yield. The advantages of this method are that no exclusion of air and moisture and no decomposition of **10** to Au(0) was observed (eq. 2).

$$\text{NHC.HCl} \xrightarrow{Ag_2O} \text{Ag(NHC)Cl} \xrightarrow{Au(SMe_2)Cl} \text{Au(NHC)Cl} \quad (2)$$

NHC = IMes (**1**), SIMes (**2**), ITPh (**9**)

4.2.2. NMR Study of gold(I) complexes

The ^{1}H NMR spectrum of complexes **10**, **12**, **16** and **17** containing unsaturated NHC ligands is characterized by a single resonance at low field for the two imidazole protons (6.98 - 7.08 ppm), as well as signals characteristic for their corresponding side-chain R groups. For the unsaturated complexes **14** and **15**, the ^{1}H NMR spectra is characterized by a single resonance at low field for the two methyl groups (2.19 and 2.13 ppm respectively) on the unsaturated imidazole backbone, in addition to their side-chain R groups. The ^{13}C NMR spectra give rise to signals attributable to the side-chain R groups in addition to characteristic low-field resonances for the carbenic carbon ranging from 166.0 - 173.4 ppm. Saturated complexes **10** and **11** result in ^{1}H NMR spectra with resonances for the imidazole ring protons occurring at 3.98 and 4.06 ppm respectively, and the expected signals for the mesityl and isopropyl phenyl side chain groups.

The ^{13}C spectra of the saturated NHC complexes display one resonance for the carbenic carbon atom at a marginally lower field (ca. 195 ppm) compared to that observed for the unsaturated complexes. For **16**, the ^{1}H NMR spectrum shows resonances attributable to the phenyl side arm substituent as well as those associated with the pyrrolidine cycle. The ^{13}C NMR spectrum shows one characteristic low-field resonance for the carbenic carbon (167.8 ppm) that is similar the unsaturated NHC complexes in addition to a low-field signal attributable to the quaternary C4 carbon on the triazolium backbone. Elemental analyses for the complexes confirm their composition.

The carbene carbons in the new gold(I) complexes resonate between 166 and 195 ppm and appear closer to the corresponding upfield imidazolium salt carbene (NHC•HCl) resonance (Table 4.1) than that of the low field free carbene. This contrasts that seen for the isolobal counterpart $Ni(CO)_3$-NHC series of complexes (Table 4.1). Since the isolobal principle[15] which suggests close analogies between species with protons H^+ and the cationic fragment $[ClAu]^+$ it is interesting to note that our (NHC)-AuCl complexes are much closer to those obtained for the imidazolium salt [(NHC)-H]Cl. Raubenheimer *et al.* found that oxidation of bis(carbene)gold(I) species to bis(carbene)di(halo)gold(III) species resulted in upfield shifts of ca. 30 to 40 ppm for the carbene carbon resonance.[16] However no explanation for this behaviour was presented. In general, both the ancillary ligands surrounding and the oxidation state of the metal center has been known to directly influence the Lewis aciditiy of the metal center. This is evidenced by the substantial difference in $^{13}C_{carbenic}$ resonances among the isolobal partners Au(NHC)Cl and $Ni(CO)_3$(NHC). In Au(NHC)Cl, the increase in NHC donor ability should directly effect the chemical shift of the carbene carbon due to the slight change in Lewis acidity of the metal. Such a difference should be able to be quantified by subtraction of this value from the corresponding free NHC and imidazolium salt resonances, as shown in Table 4.1.

Table 4.1. ^{13}C NMR data for [Au(NHC)Cl] complexes

Complexes	Solvent	δ_c Au–C(1)	δ_c NHC	Ref.	Solvent	$\Delta\ \delta_c$	δ_c NHC.HCl[a]	Solvent	$\Delta\ \delta_c$
[Au(IMes)Cl] (**10**)	$CDCl_3$	173.4	219.7	17	C_6D_6	46.3	134.76	DMSO-d_6	38.6
[Au(SIMes)Cl] (**11**)	$CDCl_3$	195.0	243.8	18	C_6D_6	48.8	160.2	DMSO-d_6	34.8
[Au(IPr)Cl] (**12**)	CD_2Cl_2	175.1	220.6	18	C_6D_6	45.5	132.22	DMSO-d_6	42.9
[Au(SIPr)Cl] (**13**)	$CDCl_3$	196.1	244.0	18	C_6D_6	47.9	160.0	DMSO-d_6	36.1
[Au(IPrMe)Cl] (**14**)	$CDCl_3$	166.0	207.9	19	C_6D_6,	41.9			
[Au(IMe)Cl] (**15**)	CD_2Cl_2	168.4	213.7	19	C_6D_6,	45.3			
[Au(ICy)Cl] (**16**)	CD_2Cl_2	168.0	210.1	20	C_6D_6	42.1	134.51	DMSO-d_6	33.5
[Au(IAd)Cl] (**17**)	CD_2Cl_2	166.3	211.4	17	C_6D_6	45.1	132.11	DMSO-d_6	34.2
[Au(ITPh)Cl] (**18**)	$CDCl_3$	167.8					135.26	DMSO-d_6	32.5
[Au(ItBu)Cl] [a]	$CDCl_3$	168.2	213.2	21	C_6D_6	45.0	132.7	DMSO-d_6	35.5
[Au(Me_2-imy)Cl] [b]	DMSO-d_6	169.0	213.7	22	C_6D_6	44.7			
$Ni(CO)_3$(IMes)	C_6D_6	198.73	219.7	17	C_6D_6	21.0	134.76	DMSO-d_6	64.0
$Ni(CO)_3$(SIMes)	C_6D_6	220.40	244.0	18	C_6D_6	23.6	160.2	DMSO-d_6	60.2
$Ni(CO)_3$(IPr)	C_6D_6	198.21	220.6	18	C_6D_6	22.4	132.22	DMSO-d_6	66.0
$Ni(CO)_3$(SIPr)	C_6D_6	223.16	244.0	18	C_6D_6	20.8	160.0	DMSO-d_6	63.2
$Ni(CO)_3$(ICy)	C_6D_6	199.48	210.1	20	C_6D_6	10.6	134.51	DMSO-d_6	65.0

[a] Samples of NHC.HCl salts were prepared and ^{13}C NMR resonance recorded; Ref. 7; [c] Ref. 8

Overall, these values indicate that there are no significant differences among the NHC ligand class with the gold(I) center. However, the saturated SIMes and SIPr gold(I) complexes exhibit the largest upfield shift from the free carbene of Δ 48.8 and 47.9 ppm respectively, Within the unsaturated NHC class, the alkyl-substituted NHCs are expected to be better donors than their aryl-counterparts however it appears that the aryl-substituted NHC ligands are slightly more donating. Analysis of the Au–C(NHC) bond lengths as determined from the structural studies (see below) also suggest that their are no major electronic differences of the studied NHC ligand class and the gold centre.

4.2.3. Structures of gold(I) complexes

To unambiguously characterize these complexes and to get a possible insight into fine structural differences between different NHCs and the gold(I) centre, X-ray quality crystals were grown of [Au(IMes)Cl] (**10**), [Au(SIMes)Cl] (**11**), [Au(IPr)Cl] (**12**), [Au(SIPr)Cl] (**13**), [Au(IPrMe)Cl] (**14**), [Au(IMe)Cl] (**15**), [Au(ICy)Cl] (**16**), [Au(IAd)Cl] (**17**) and [Au(ITPh)Cl] (**18**). Ball and stick representations are shown in Figure 4.2 (**10**-**13**), Figure 4.3 (**14**-**17**) and Figure 4.4 (**18**) and a comparison of selected bond distances and angles can be found in Table 4.2.

Table 4.2. Selected bond lengths and angles for [Au(NHC)Cl] complexes

Complexes	Au–C(1)	Au–Cl	C(1)–Au(1)–Cl
[Au(IMes)Cl] (**10**)	1.998(5)	2.2756(12)	180 (-)
[Au(SIMes)Cl] (**11**)	1.983(4)	2.2766(10)	177.68(11)
[Au(IPr)Cl][b] (**12**)	1.942(3)	2.2698(11)	177.0(4)
[Au(SIPr)Cl] (**13**)	1.979(3)	2.2761(10)	180 (-)
[Au(IPrMe)Cl] (**14**)	1.996(9)	2.279(2)	180 (-)
[Au(IMe)Cl] (**15**)	1.987(8)	2.288(2)	178.9(3)
[Au(ICy)Cl] (**16**)[a]	1.990(13),1.996(12)	2.306(3), 2.281(3)	178.2(4), 177.2(3)
[Au(IAd)Cl] (**17**)	1.989(2)	2.2761(6)	178.07(7)
[Au(ITPh)Cl] (**18**)[a]	1.979(5), 1.972(5)	2.2880(13), 2.2835(13)	175.59(15), 178.74(16)
[Au(ItBu)Cl][c]	2.018(3)[c]	2.2742(7)[c]	180 (-)[c]
[Au(Me_2-imy)Cl][d]	1.979(11)	2.288(3)	178.8(2)
[Au(R_2-imy)Cl][e]	1.965(5)	2.3061(11)	177.41(15)

[a] Contains two molecules in the asymmetric unit; [b] Ref.14; [c] Ref.7; [d] Ref.8; [e] Ref. 9, R = R_2-imy = 1-di-phenylmethyl-3-methyl-imidazol-2-ylidene)

All these complexes show the gold(I) atom is two-coordinate in an essentially linear environment with C–Au–Cl bond angles close to 180°. In **10, 13** and **14,** one half of the molecule comprises the asymmetric unit of the structure, with a crystallographic 2-fold axis along the C–Au–Cl array (which are obligate linear) which bisects the NHC ligand. For **16** and **18**, two independent molecules comprise the asymmetric unit; in all other cases, a single molecule comprises the asymmetric unit. For all the compounds (except **12**), the Au–C(NHC)

distances lie in the range 1.979 - 1.998 Å. While the saturated NHC complex **11** shows a slightly shorter bond distance than its corresponding unsaturated analogue **10** (1.983 (4) Å for **11** versus 1.998 (5) Å for **10**), the saturated NHC complex **13** was found to have a larger Au–C(NHC) bond length than its corresponding unsaturated analogue **12** (1.979(3) Å for **13** versus 1.942(3) Å for **12**). These results are not very significant and lie within experimental error to other Au–C(NHC) bond lengths. For all compounds **10 - 18** the Au–C(NHC) distance suggests a single-bond character, in good accordance with their strong σ-donor characteristics.[3c,23] They are comparable to those reported for other Au(I)(carbene) complexes [6a,7,8,24] and, as also found in solution studies (see above), the electronic difference governing the NHC ligand class is relatively small. The Au–Cl distances in **10-18** lie in the range 2.2756(12) Å - 2.306(3) Å and are marginally longer that found for $[AuCl_2]^-$ (2.257 Å),[25] a consequence of the *trans*-influence of the carbene.[6c,9,24d,24e,24g]

As seen for other crystallographically characterized complexes containing NHC ligands with aryl substituents, the R-groups are rotated near perpendicular with respect to the imidazole backbone plane, resulting in a favourable arrangement around the metal centre. In addition, the saturated imidazole backbones in SIMes and SIPr compounds, due to the presence of two sp^3 carbons in the hetercyclic ring, show torsion angles of 8.2(4)° (for complex **11**) and 5.8(2)° (for complex **13**). These torsion values are significantly lower than for free SIMes (13.4°) suggesting that some restriction in rotation is present on coordination with the gold centre. For the unsaturated NHC complexes **14** and **15** the methyl substituents are positioned in the same plane as the imidazole backbone. The disposition of the *iso*-propyl substituents in **14** is such that the two methyl substituents straddle the ring plane to either side and are directed toward the gold atom, with associated hydrogen atoms contacting it at 2.713 Å (Au···H5A of C5) and 2.948 Å (Au···H6C of C6). Closer Au···H–C contacts can be found in complexes **17** and **18** with the

former having two α-carbon atoms from both side-chain adamantly groups approaching the metal centre (Au···H23A 2.652 Å; Au···H24A 2.694 Å; Au···H11A 2.675 Å; Au···H12A 2.708 Å). This Au…H–C interaction has been reported by others however for intermolecular association.[26] For the triazolium NHC complex **18**, the plane of phenyl side arm substituent is rotated 32.8(2)° with respect to the triazolium backbone plane. As a result, one *ortho*-carbon atom approaches the gold atom with a distance (Au···H7 2.892 Å and Au···H22 2.946 Å) that is within range for reported Au···H interactions. This rotation may also be a result of π-π stacking from the phenyl ring of neighboring molecules that are aligned in a head-to-tail fashion, as illustrated in Figure 4.4b, with the closest π-π contact of 3.307 Å indicating such an interaction. Furthermore the packing diagram also shows that there are also sets of two molecules that have a Au1···Au1' interaction of 3.580(3) Å. Adjacent to this is a one directional linear chain that is linked through intermolecular gold-gold contacts (3.851 Å, 4.059 Å). Although these contacts are longer than the sum of van der Waals radii for two gold atoms of 3.6 Å, they are sufficiently strong to influence the packing of the molecules in the solid state. For the other complexes (**10**-**17**) no case of Au···Au interactions or other notable packing features are observed.

Figure 4.2. Ball and stick representations of aryl-substited NHC ligated complexes; [Au(IMes)Cl] (**10**) (a), [Au(SIMes)Cl] (**11**) (b), [Au(IPr)Cl] (**12**) (c) and [Au(SIPr)Cl] (**13**) (d). Hydrogen atoms have been omitted for clarity

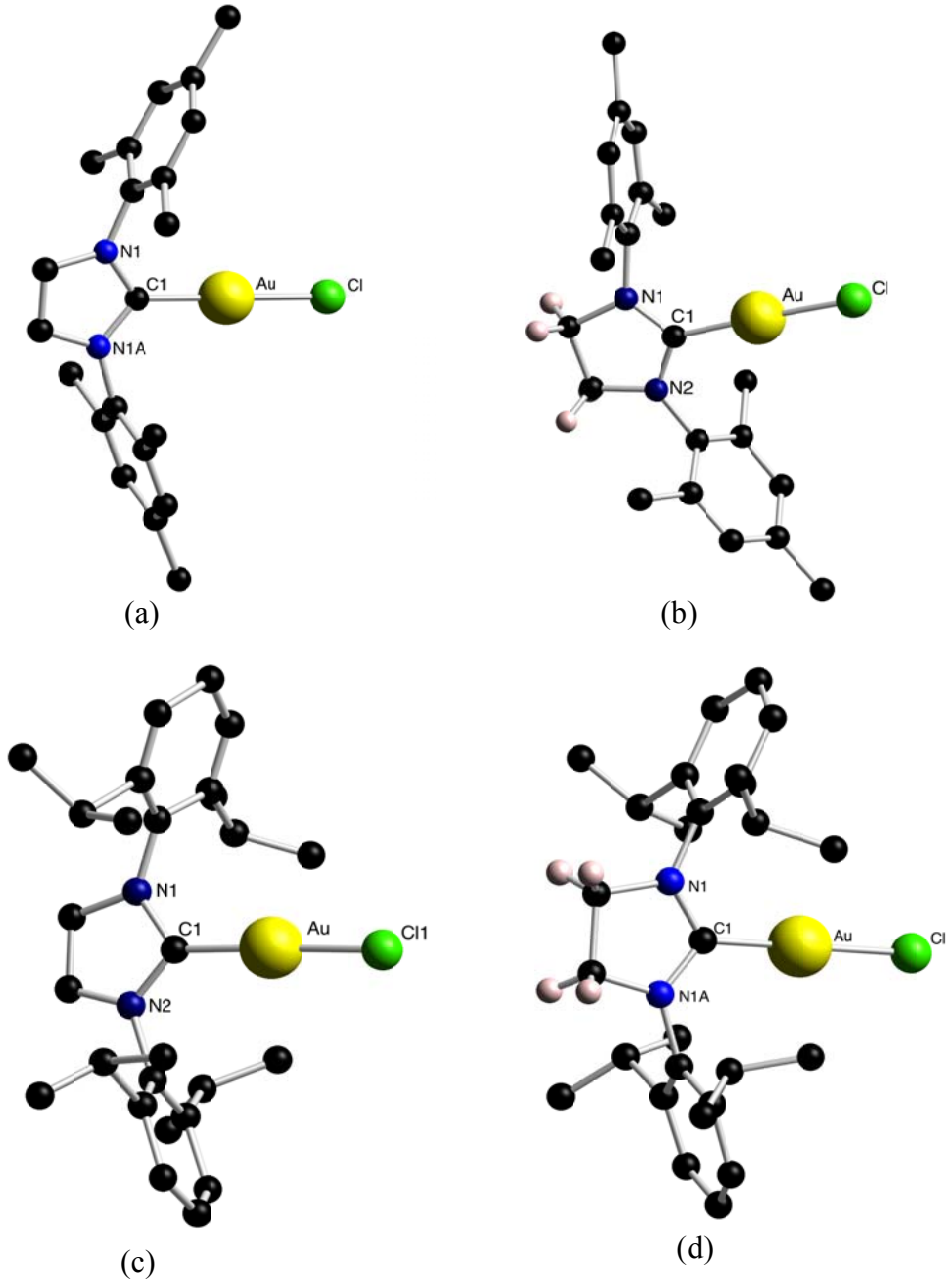
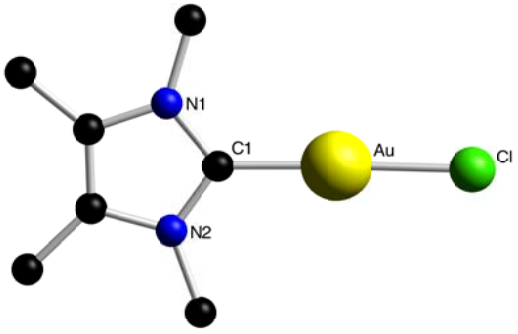


Figure 4.3. Ball-and-Stick representations of alkyl-substituted NHC ligand complexes [Au(IPrMe)Cl] (**14**) (a), [Au(IMe)Cl] (**15**) (b), [Au(ICy)Cl] (**16**) (c) and [Au(IAd)Cl] (**17**) (d). Hydrogen atoms have been omitted for clarity



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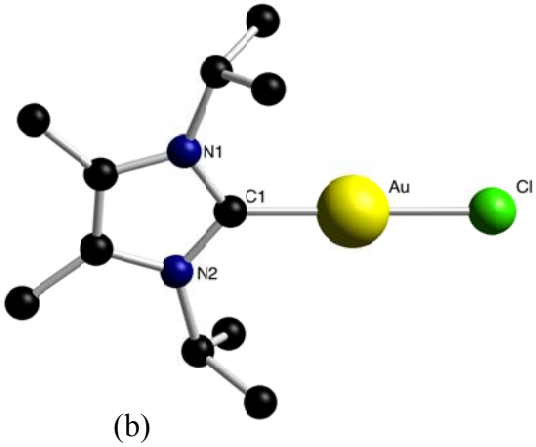

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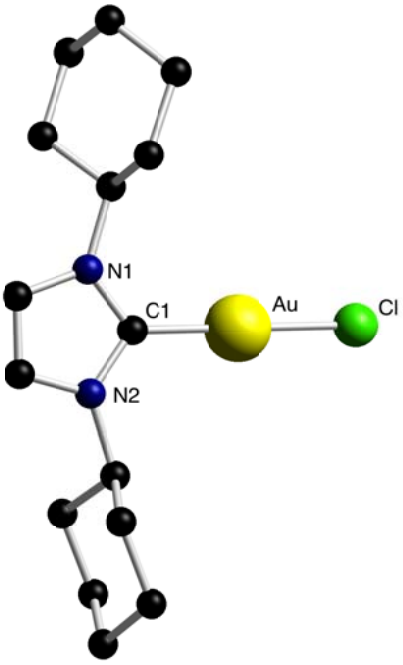
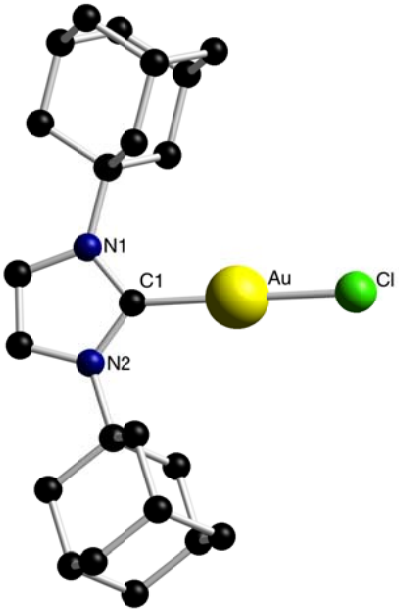


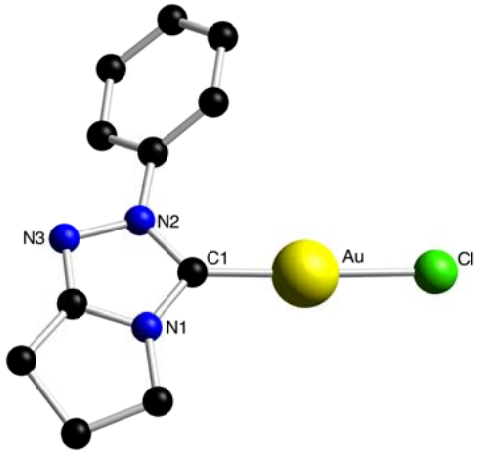
(c)



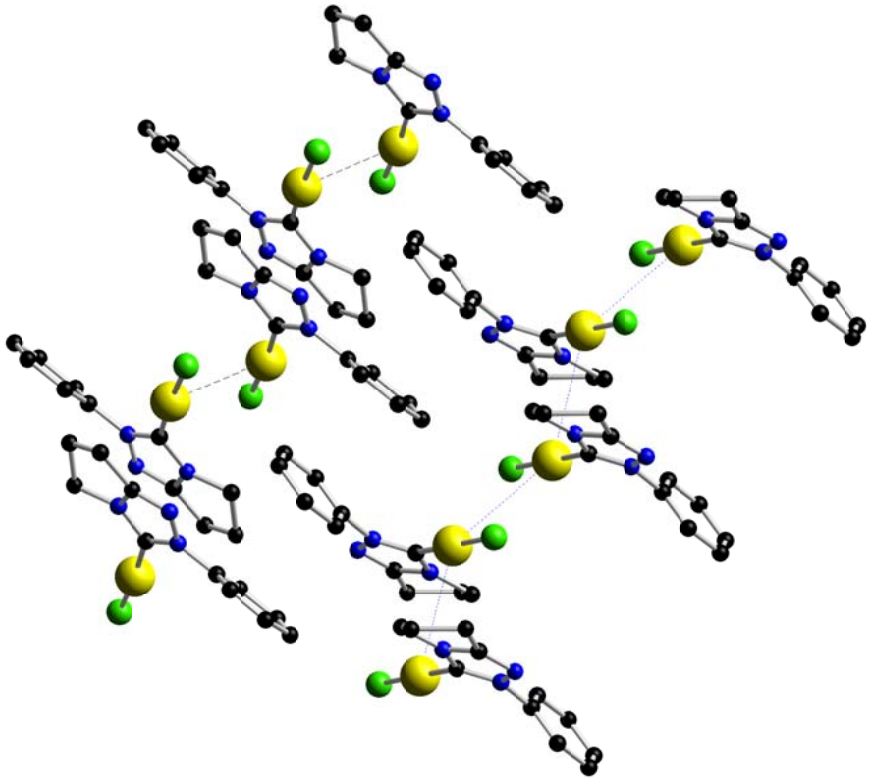
(d)

Figure 4.4. (a) Ball-and-Stick representation and of triazol-NHC ligand complex [Au(ITPh)Cl] (**18**), hydrogen atoms have been omitted for clarity. (b) Staking of [Au(ITPh)Cl showing head-to-tail ring-ring interactions as well as intermittent Au···Au contacts among the molecules

(a)



(b)



4.3. Conclusion

An understanding of how the electronic properties of N-heterocyclic ligands govern the coordination chemistry of the resulting gold(I) chloride complexes is of fundamental importance for the displacement of the chloride atom in future NHC gold chemistry. Although competing disproportionation and decomposition reactions were observed between AuCl and free carbene we have gained success via two routes for the synthesis of a series of [Au(NHC)Cl] complexes. They were synthesized in high yield by transfer of either free carbene or the *in situ* generated silver(I) NHC salt with [Au(SMe_2)Cl]. A greater understanding of Au(I)-NHC interactions has been achieved through NMR and structural analysis of all reported [Au(NHC)Cl] complexes and interestingly no significant difference in donor ability between the saturated and unsaturated NHC ligands was observed. Since the chloride ligand can be readily substituted by another donor atom, the series of [Au(NHC)Cl] complexes serve as very useful starting materials for the development of new NHC-Au(I) compounds that can be utilized for a variety of medicinal and catalytic applications. Differences between the NHC-metal bonds may also become more apparent in such systems and help our continuing efforts in a better understanding of this ligand class.

4.4. Experimetal Section

4.4.1. General Considerations

- All reactions were carried out using standard Schlenk techniques under an atmosphere of dry argon or in MBraun gloveboxes containing dry argon and less than 2 ppm oxygen.
- Anhydrous solvents were either distilled from appropriate drying agents or purchased from Aldrich and degassed prior to use by purging with dry argon and kept over molecular sieves.
- Solvents for NMR spectroscopy were degassed with argon and dried over molecular sieves. NMR spectra were collected on a 400 MHz Varian Gemini spectrometer.
- Elemental analyses were performed by Robertson Microlit Labs. Carbene ligands **1**-**9** were synthesized following literature procedures.[18,19]
- AuCl and SMe_2 were purchased were obtained from Strem and Acros respectively, and [Au(SMe_2)Cl] was prepared according to the reported procedure.[27]

4.4.2. Synthesis the gold(I) complexes

Synthesis of [Au(IMes)Cl] ***(10):*** A mixture of silver(I) oxide (50 mg, 0.21 mmol) and 1,3-dimesityl-imidazolium chloride (122 mg, 0.36 mmol) in dichloromethane (50 mL) was stirred for 4 h. The mixture was filtered and dimethylsulfide gold (I) chloride (100 mg, 0.34 mmol) was added. The resulting mixture was stirred for 3 h, filtered and activated carbon was added to the filtrate. The mixture was filtered over celite and the solvent was removed *in vacuo* then dichloromethane (3 mL) was added. Pentane (10mL) was added to the solution resulting in an immediate precipitation of a bright white solid. The solid was further washed with pentane (3 x 5

mL) and dried under vacuum. Yield: 116 mg (63 %). ^{1}H NMR ($CDCl_3$): δ = 7.09 (s, 2H, C*H*-imidazole), 6.99 (s, 4H, C*H*-aromatic), 2.35 (s, 6H, CH_3), 2.10 (s, 12H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 173.4 (s, *C*-carbene), 139.8 (s, *C*H-aromatic), 134.7 (s, *C*H-aromatic), 134.6 (s, *C*H-aromatic), 129.5 (s, *C*H-aromatic), 122.1 (s, *C*H-imidazole), 21.1 (s, *C*H_3), 17.7 (s, CH_3) ppm. Elemental analysis calcd for $C_{21}H_{24}N_2AuCl$ (537.62): C, 46.91; H, 4.46; N, 5.21. Found: C, 47.13; H, 4.32; N, 5.13.

*Synthesis of [Au(SIMes)Cl] (**11**):* A similar preparation method to that used for compound **10** gave a white solid of **11.** Yield: 72 mg (51 %). ^{1}H NMR ($CDCl_3$): δ = 6.94 (s, 4H, C*H*-aromatic), 3.98 (s, 4H, CH_2-imidazole), 2.31 (s, 12H, CH_3), 2.29 (s, 6H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 195.0 (s, *C*-carbene), 138.9 (s, *C*H-aromatic), 135.5 (s, *C*H-aromatic), 134.6 (s, *C*H-aromatic), 129.8 (s, *C*H-aromatic), 50.6 (s, *C*H_2-imidazole), 21.1 (s, CH_3), 17.9 (s, CH_3) ppm. Elemental analysis calcd for $C_{21}H_{26}N_2AuCl$ (539.62): C, 46.74; H, 4.81; N, 5.19. Found: C, 46.71; H, 5.01; N, 5.12.

*Synthesis of [Au(IPr)Cl] (**12**):* In a glove box a 100 mL schenk flask was charged with IPr (686 mg, 1.76 mmol) and 50 mL of THF, then dimethylsulfide gold (I) chloride (500 mg, 1.70 mmol) 50 mg (0.17 mmol) was added. The resulting solution was kept in the dark and stirred at room temperature for 12h. The remaining steps were then carried out in air. The resulting solution was filtered over celite and activated carbon was added to the filtrate which was stirred for 4 hours. The colorless solution was filtered over celite and the solvent was reduced to dryness under vacuum and 10 ml of dichloromethane was added. Pentane (20mL) was added to the solution resulting in an immediate precipitation of a white solid. The solid was further washed with pentane (3 x 10 mL) and dried under vacuum, to afford a bright white powder. Yield: 820 mg

(75 %). ^{1}H NMR (CD_2Cl_2): δ = 7.57 (t, J=7.8Hz, 2H, C*H*-aromatic), 7.35 (d, J=7.8Hz, 4H, C*H*-aromatic), 7.24 (s, 2H, C*H*-imidazole), 2.57 (septet, J=6.8Hz, 4H, C*H*$(CH_3)_2$), 1.34 (d, J=6.8Hz, 12H, CH (C*H*$_3)_2$), 1.23 (d, J=6.8Hz, 12H, CH (C*H*$_3)_2$); ^{13}C NMR (CD_2Cl_2): δ = 175.1 (s, *C*-carbene), 145.7 (s, *C*H-aromatic), 134.0 (s, *C*H-aromatic), 130.6 (s, *C*H-aromatic), 124.2 (s, *C*H-aromatic), 123.3 (s, *C*H-imidazole), 28.7 (s, *C*H $(CH_3)_2$), 24.1 (s, CH (*C*H$_3)_2$), 23.7 (s, CH (*C*H$_3)_2$) ppm. Elemental analysis calcd for $C_{27}H_{36}N_2AuCl$ (621.69): C, 52.11; H, 5.79; N, 4.50. Found: C, 51.70; H, 5.61; N, 4.38.

*Synthesis of [Au(SIPr)Cl] (**13**):* In a glove box a 100 mL schenk flask was charged with 63 mg (0.16 mmol) of SIPr and 15 mL of THF and then 50 mg (0.17 mmol) of dimethylsulfide gold (I) chloride was added. The resulting solution was kept in the dark and stirred at room temperature for 12h. The remaining steps were then carried out in air. The resulting solution was filtered over celite and activated carbon was added to the filtrate which was stirred for 4 hours. The colorless solution was filtered over celite and the solvent was reduced to dryness under vacuum and 5 ml of dichloromethane was added. Pentane (10mL) was added to the solution resulting in an immediate precipitation of a bright white solid. The solid was further washed with pentane (3 x 5 mL) and dried under vacuum. Yield: 80 mg (81 %). ^{1}H NMR ($CDCl_3$): δ = 7.43 (t, J=7.8Hz, 2H, C*H*-aromatic), 7.25 (d, J=7.8Hz, 4H, C*H*-aromatic), 4.06 (s, 4H, C*H*$_2$-imidazole), 3.07 (septet, J=6.8Hz, 4H, C*H*$(CH_3)_2$), 1.43 (d, J=6.8Hz, 12H, CH (C*H*$_3)_2$), 1.36 (d, J=6.8Hz, 12H, CH (C*H*$_3)_2$); ^{13}C NMR ($CDCl_3$): δ = 196.1 (s, *C*-carbene), 146.5 (s, *C*H-aromatic), 134.1 (s, *C*H-aromatic), 130.1 (s, *C*H-aromatic), 124.6 (s, *C*H-aromatic), 53.4 (s, *C*H$_2$-imidazole), 28.9 (s, *C*H $(CH_3)_2$), 25.1 (s, CH (*C*H$_3)_2$), 24.1 (s, CH (*C*H$_3)_2$) ppm. Elemental analysis calcd for $C_{27}H_{38}N_2AuCl$ (623.69): C, 51.99; H, 6.09; N, 4.49. Found: C, 52.02; H, 6.22; N, 4.27.

*Synthesis of [Au(IPrMe)Cl] (**14**):* A similar preparation method to that used for compound **13** gave a bright white solid of **14.** Yield: 63 mg (58 %). ^{1}H NMR ($CDCl_3$): δ = 4.97 (m, 2H, NC*H*-isopropyl), 2.19 (s, 6H, C*H*$_3$-imidazole), 1.61 (d, J=7.32Hz, 12H, CH (C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ = 166.0 (s, *C*-carbene), 124.4 (s, *C*=*C*-imidazole), 53.7 (s, *C*H (CH$_3$)$_2$), 22.8 (s, CH (*C*H$_3$)$_2$), 9.9 (s, *C*H$_3$-imidazole) ppm. Elemental analysis calcd for $C_{11}H_{20}N_2AuCl$ (413.48): C, 31.95; H, 4.83; N, 6.77. Found: C, 31.80; H, 4.71; N, 6.57.

*Synthesis of [Au(IMe)Cl] (**15**):* A similar preparation method to that used for compound **13** gave a bright white solid of **15.** Yield: 180 mg (58 %). ^{1}H NMR (CD_2Cl_2): δ = 3.68 (s, 6H, NC*H*$_3$), 2.13 (s, 6H, *CH*$_3$); ^{13}C NMR (CD_2Cl_2): δ = 168.4 (s, *C*-carbene), 125.1 (s, *C*H-imidazole), 35.4 (s, *CH*$_3$), 8.9 (s, *CH*$_3$) ppm. Elemental analysis calcd for $C_7H_{12}N_2AuCl$ (357.44): C, 23.52; H, 3.33; N, 7.82. Found: C, 23.73; H, 3.00; N, 7.77.

*Synthesis of [Au(ICy)Cl] (**16**):* A similar preparation method to that used for compound **13** gave a bright white solid of **16.** Yield: 87 mg (67 %). ^{1}H NMR (CD_2Cl_2): δ = 6.98 (s, 2H, C*H*-imidazole), 4.55 (tt, J_1=3.9Hz , J_2=11.7Hz , 2H, NC*H*-cyclohexyl), 2.07 (m, 4H, C*H*$_2$), 1.86 (m, 4H, C*H*$_2$), 1.74 (m, 2H, C*H*$_2$), 1.65-1.41 (m, 8H, C*H*$_2$) , 1.27-1.15 (m, 2H, C*H*); ^{13}C NMR (CD_2Cl_2): δ = 168.0 (s, *C*-carbene), 117.3 (s, *C*H-imidazole), 60.9 (s, N*C*H-cyclohexyl), 34.0 (s, *C*H$_2$), 25.3 (s, *C*H$_2$), 25.0 (s, *C*H$_2$) ppm. Elemental analysis calcd for $C_{15}H_{24}N_2AuCl$ (464.57): C, 38.78; H, 5.16; N, 6.02. Found: C, 38.90; H, 5.12; N, 5.85.

*Synthesis of [Au(IAd)Cl] (**17**):* A similar preparation method to that used for compound **13** gave a bright white solid of **17.** Yield: 103 mg (78 %). ^{1}H NMR (CD_2Cl_2): δ = 7.08 (s, 2H, C*H*-

imidazole), 2.57 (m, 14H, C*H*$_2$), 2.28 (s, 6H, C*H*$_2$), 1.77 (m, 10H, C*H*$_2$); ^{13}C NMR (CD_2Cl_2): δ = 166.3 (s, *C*-carbene), 115.5 (s, *C*H-imidazole), 59.2 (s, N*C*H-adamantyl), 44.1 (s, *C*H$_2$), 35.8 (s, *C*H$_2$), 30.1 (s, *C*H$_2$) ppm. Elemental analysis calcd for $C_{23}H_{32}N_2AuCl$ (568.65): C, 48.58; H, 5.63; N, 4.92. Found: C, 48.53; H, 5.64; N, 4.66.

*Synthesis of [Au(ITPh)Cl] (**18**):* A mixture of silver(I) oxide (37 mg, 0.16 mmol) and 2-phenyl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,3]triazol-2-ium chloride (61 mg, 0.28 mmol) in dichloromethane (10 mL) was stirred for 4 h at room temperature. The mixture was filtered and dimethylsulfide gold (I) chloride (100 mg, 0.34 mmol) was added. The resulting mixture was stirred for 3 h, filtered and activated carbon was added to the filtrate. The mixture was filtered over celite and the solvent was removed *in vacuo* then dichloromethane (3 mL) was added. Pentane (10mL) was added to the solution resulting in an immediate precipitation of a bright white solid. The solid was further washed with pentane (3 x 5 mL) and dried under vacuum. Yield: 72 mg (63 %). ^{1}H NMR ($CDCl_3$): δ = 7.96 (m, 2H, C*H*-aromatic), 7.48 (m, 3H, C*H*-aromatic), 4.26 (t, J = 7.32Hz, 2H, C*H*$_2$-pyrrolidine), 3.15 (t, J = 7.81Hz, 2H, C*H*$_2$-pyrrolidine), 2.77 (m, 2H, C*H*$_2$-pyrrolidine); ^{13}C NMR ($CDCl_3$): δ = 167.8 (s, *C*-carbene), 160.5 (s, N*C*=N), 139.2 (s, N*C*-aromatic), 129.4 (s, *C*H-aromatic), 129.4 (s, *C*H-aromatic), 123.4 (s, *C*H-aromatic), 46.3 (s, C*C*HN-pyrrolidine), 25.7 (s, *C*H$_2$-pyrrolidine), 21.8 (s, *C*H$_2$-pyrrolidine) ppm. Elemental analysis calcd for $C_{11}H_{11}N_2AuCl$ (417.48): C, 31.64; H, 2.63; N, 10.06. Found: C, 31.74; H, 2.30; N, 9.72.

4.5. Acknowledgment

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4.6. References and notes

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CHAPTER 5

SYNTHESIS, CHARACTERIZATION AND REACTIVITY OF *N*-HETEROCYCLIC CARBENE GOLD(III) COMPLEXES

5.1. Introduction

Although, historically, organogold complexes have been underutilized in organic synthesis, numerous publications have recently emphasized the beneficial role of gold(I) in catalysis.[1] Organic transformations such as skeletal rearrangements (cycloisomerizations),[2] carbene transfer reactions,[3] indolizations,[4] oxidations,[5] and hydrosilylations,[6] are examples of the diverse chemistry mediated by organogold catalysts. Such transformations have been achieved with low catalyst loading and high turnover numbers. The gold(I) center must have two coordination sites occupied to ensure stability of the complexes and thereby avoid reduction to gold(0).[7] The most commonly employed ligands so far have been phosphines (PR_3),[8] and most recently *N*-heterocyclic carbenes (NHC).[9] Both ligand families exhibit strong σ-donation and coordination of such ligands result in good stability of the Au(I) complexes towards air, moisture

and thermolysis. It is interesting to note that gold has even a stronger affinity for *N*-heterocyclic carbene than for phosphine and other Fisher acyclic carbenes.[10] A broad range of catalyzed transformations by inorganic gold(III) salts has been reported in the literature, examples include hydroaminations,[11] [4+2] benzannulations,[12] functionalization of aromatic C-H bonds,[13] cycloisomerizations,[14] and addition reactions to heterocycles.[15] Most often AuX_3 (X=Cl or Br) salts are directly used[11-16] and only a limited number of examples of well-defined organogold(III) complexes acting as catalysts are known.[17] No catalysis mediated by (PR_3)- or (NHC)Au(III) complexes has been reported so far. This is quite surprising since the chemistry of the arsine,[18] stilbine,[19] phosphine,[18b,18c,20] and carbene[21] gold (III) complexes, was first examined in the mid-1970's. Since these initial studies only a limited number of publications have focused on this chemistry. Notable exceptions are the extensive studies performed on gold(III) phosphine complexes by Schmidbaur *et al.*[22] Since then, C-tetrazolato,[23] bis-thiazolinylidene and bis-(NHC) gold(III) complexes bearing carbene moieties, have been published.[24] Nevertheless, no example of mono-(NHC)Au(III) complex has been reported, the mono-(4-methylthiazol-2-ylidene)$AuCl_3$ being the closest related complex reported so far.[24a] In order to expand the range of Au(III) complexes known and hopefully to provide access to novel Au(III) architectures, we reasoned that our prior expertise in NHC and Au(I) chemistry could be put to use in the synthesis of novel Au(III) complexes bearing the electron rich NHC ligands.

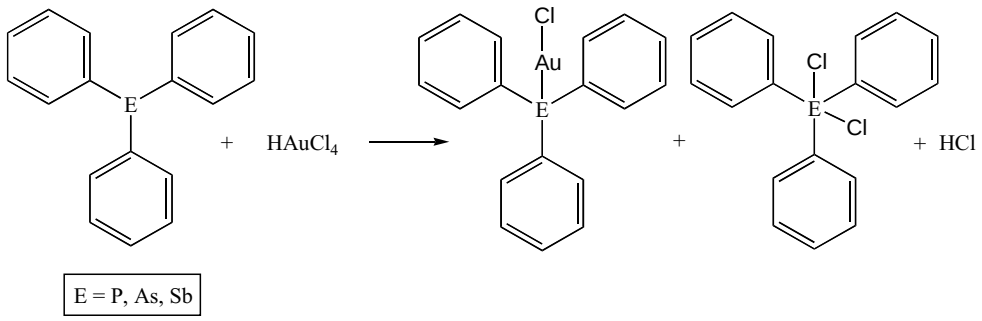
5.2. Results and Discussion

To eventually develop a general synthetic route leading to a family of (NHC)AuX_3 (X= halide) complexes, we initially examined possible approaches to a single target compound:

(IPr)AuX_3. Previously, chlorine gas had been used to convert (thiazolinylidene)AuCl to (thiazolinylidene)$AuCl_3$.[24] Because of the very aggressive nature of chlorine gas, liquid bromine was selected as a halogenation agent as it does not require special safety equipment and allowed for a fairly straightforward and general synthetic protocol.

We first attempted to generate a NHC-Au(III) complex from a gold(III) salt, by direct reaction of the free carbene IPr (IPr =1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) with $AuCl_4^-$. The reaction led to the formation of yellow metallic gold(0). Study of the reaction mixture by ^{1}H NMR spectroscopy, showed extensive sign of decomposition of the carbene and formation of (IPr)AuCl, in a low yield (20%). This result is not surprising as the gold(III) cation possesses a very strong oxidant character.[25] Indeed, reduction of tetrachloroauric acid ($HAuCl_4$) with a 2-fold excess of stibine, arsine, or phosphine ligands, is known to generate the corresponding gold(I) complexes in good yield.[25] (Scheme 5.1)

Scheme 5.1. Formation of gold(I) complexes by reduction of $HAuCl_4$

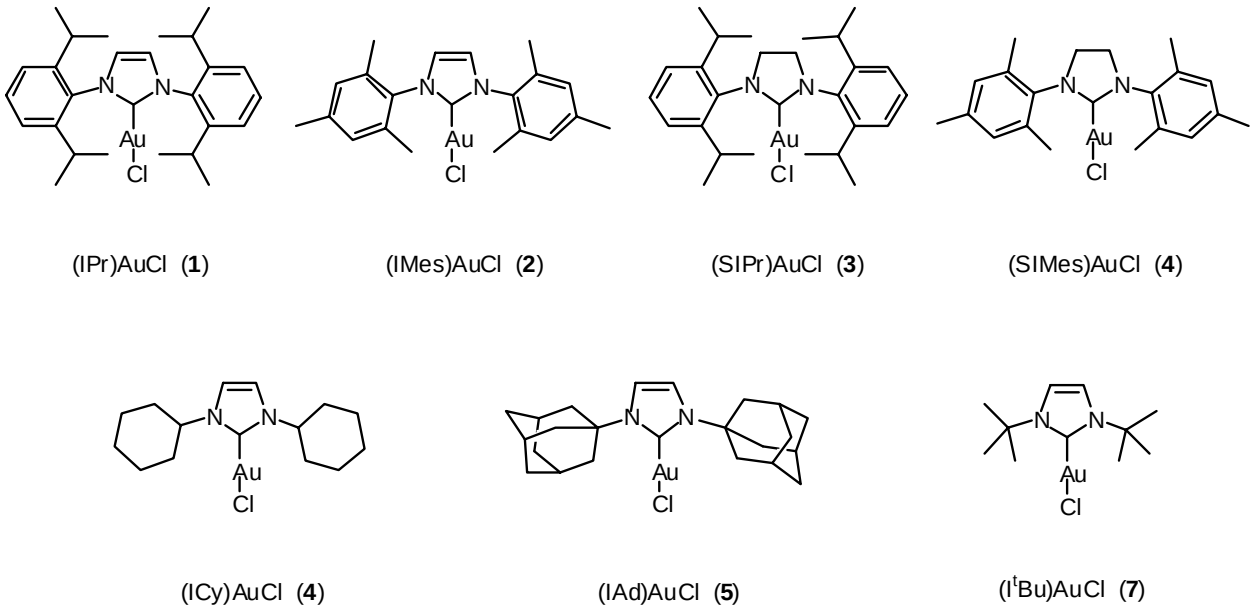


Oxidative addition of bromine by (IPr)AuCl (**1**) gave an orange powder in high yield. ^{1}H NMR analysis provided a spectrum with the same pattern as the one found for (IPr)AuCl, but with significant change in the chemical shifts for all protons. We also noticed that the septuplet assigned to the protons from the diisopropyl group, was split into two distinct multiplets at 2.99 and 2.96 ppm. We attribute this small splitting to the existence of two different complexes:

(IPr)$AuBr_3$ and (IPr)$AuBr_2Cl$. ^{13}C NMR spectra also support this hypothesis as two complexes with a similar carbon skeleton and very close signals are observed.

To exclude the formation of a mixture of (IPr)$AuBr_{3-x}Cl_x$, we proceeded to convert the reported[7a,26] (NHC)Au(I) chloride complexes (**1**-**7**) : (1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) gold(I) chloride (IPr)AuCl[26] (**1**), (1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) gold(I) chloride (IMes)AuCl[26] (**2**), (1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene) gold(I) chloride (SIPr)AuCl[26] (**3**), (1,3-bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene) gold(I) chloride (SIMes)AuCl[26] (**4**), (1,3-bis(cyclohexyl)imidazol-2-ylidene) gold(I) chloride (ICy)AuCl[26] (**5**), (1,3-bis(adamantyl)imidazol-2-ylidene) gold(I) chloride (IAd)AuCl[26] (**6**), (1,3-bis(*tert*-butyl)imidazol-2-ylidene) (I^tBu)AuCl[7a] (**7**) (Figure 5.1) into their (NHC)Au(I) bromide relatives (**8**-**14**) by use of a metathetical reaction with LiBr. The gold(I) cation being one of the softest available acids, we suspected the bromide anion would easily replace the chloride anion.

Figure 5.1. (NHC)Au(I)Cl complexes used as starting material in this study



5.2.1. Synthesis of gold(I) complexes

The complexes (NHC)AuCl (**1**-**7**) were stirred with a large excess of lithium bromide, at room temperature, with acetone or THF as solvent. The reactions are not sensitive to air and provide the desired bromide complexes (IPr)AuBr (**8**), (IMes)AuBr (**9**), (SIPr)AuBr (**10**), (SIMes)AuBr (**11**), (ICy)AuBr (**12**), (IAd)AuBr (**13**) and (I^{t}Bu)AuBr (**14**) as white powders (Equation **1**). The protocol furnishes the products in good yields after stirring for 24 hours.

$$\text{(NHC)AuCl} + \text{LiBr} \xrightarrow{\text{acetone}} \text{(NHC)AuBr} + \text{LiCl} \quad (1)$$

It is interesting to note that while these complexes are air-stable, the presence of water leads to rapid decomposition with appearance of purple colloidal gold(0) and formation of imidazolium salts. This trend is strongly accentuated for complexes bearing saturated carbene moieties (**10** and **11)**. While Baker *et al.*[7a] reported a reaction time of 16 hours to convert (I^{t}Bu)AuCl (**7**) into (I^{t}Bu)AuBr (**14**), we selected a longer reaction time of 24 hours as a general reaction time as we noticed that the metathesis reaction could require longer time to reach completion as a function of the NHC. This reaction time is then general and not optimized for each NHC employed.

5.2.2. NMR Study of gold(I) complexes

The ^{1}H NMR spectra of complexes **8**, **9**, **12**, **13** and **14** display a low field singlet between 6.95 and 7.17 ppm assigned to the two protons located on the unsaturated imidazole backbone. Spectra of complexes **10** and **11** display a more upfield singlet at 4.04 and 3.97 ppm respectively, assigned to the four protons located on the saturated imidazole backbone. For all complexes, all

signals expected for the *N*-aryl, and *N*-alkyl chains are present. As expected, no significant change in the chemical shift (less than 0.1 ppm) is visible for the signals attributed to congeners of the (NHC)AuCl and (NHC)AuBr series. The substitution of a chloride by a bromide has a very small effect on the environment seen by the protons of the different complexes. ^{13}C NMR spectra display resonances for the different carbenic carbons between 166.3 and 175.1 ppm for the unsaturated imidazole moieties and around 195 ppm for the saturated imidazole moieties. (Table 5.1) The intensity of this resonance is weak since the carbenic carbon is a quaternary center and is affected by the quadrupolar moment of the gold atom (I=3/2).

Table 5.1. Chemical shifts of the carbenic carbon in NMR for the gold(I) halides complexes

(NHC)AuCl	δ_C (ppm)	(NHC)AuBr	δ_C (ppm)	$\Delta\ \delta_C$ (ppm)
(IPr)AuCl[a] (**1**)	175.1	(IPr)AuBr[b] (**8**)	179.0	+ 3.9
(IMes)AuCl[b] (**2**)	173.4	(IMes)AuBr[b] (**9**)	176.7	+ 3.3
(SIPr)AuCl[b] (**3**)	196.1	(SIPr)AuBr[b] (**10**)	199.0	+ 2.9
(SIMes)AuCl[b] (**4**)	195.0	(SIMes)AuBr[b] (**11**)	198.1	+ 3.1
(ICy)AuCl[a] (**5**)	168.0	(ICy)AuBr[b] (**12**)	172.1	+ 4.1
(IAd)AuCl[a] (**6**)	166.3	(IAd)AuBr[b] (**13**)	170.2	+ 3.9
(I^{t}Bu)AuCl[a] (**7**)	168.2	(I^{t}Bu)AuBr[b] (**14**)	172.4	+ 4.2

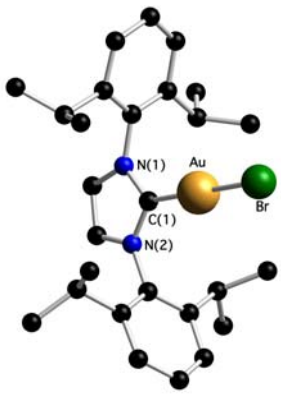
[a] NMR recorded in CD_2Cl_2. [b] NMR recorded in $CDCl_3$.

Herrmann *et al*.[27] have postulated that the chemical shift of the carbenic carbon can be correlated to the acidity of the metal to which the NHC is bound. Indeed a free NHC ligand, with no electronic donation toward a Lewis acid would have a very low-field signal, usually above 200 ppm, reflecting the availability of an excess of electron density on the carbene carbon. In contrast, a bond with a metal will displace the chemical shift to a higher field value when the electronic density from the carbene is partially transferred to the metal by sigma donation. By comparing the chemical shifts of the carbenic carbon, between the chloride and the bromide series of the gold(I) complexes, a consistent shift of 3 to 4 ppm to lower field due the halide exchange was observed that we attribute to a small variation of the acidity of the gold center. We reasoned that the metal acidity is less due to the lower electronegativity of bromine versus chlorine. This result is in good agreement with the study published by Baker *et al.*[7a]

5.2.3. Structure of gold(I) complexes

Crystals of (IPr)AuBr (**8**) were grown by slow diffusion in a mixture of DCM/hexane and allowed us to perform a single crystal X-ray diffraction study. (Figure 5.2)

Figure 5.2. Ball and stick representation of (IPr)AuBr. Hydrogen atoms have been omitted for clarity



The gold atom is two coordinate, as usual for gold(I) complexes, and exhibits a linear geometry with a C(1)–Au–Br bond angle value of 180.0°. The C(1)–Au bond length (1.975 Å) is in good agreement with reported NHC gold(I) complexes.[7a,26,28] The Au–Br bond length (2.381 Å) is in the range of known bromide gold(I) salts and complexes.[7a,29] The minimal Au•••Au distance is 8.431 Å, excluding any aurophilic interactions, which require a distance shorter than 3.60 Å between gold(I) cations.[30] There is no major structural difference between the (IPr)AuCl (**1**) and (IPr)AuBr (**8**). Crystals of other (NHC)AuBr complexes, described in this paper, can be grown in a mixture of DCM/heptane.

5.2.4. Synthesis of gold(III) complexes

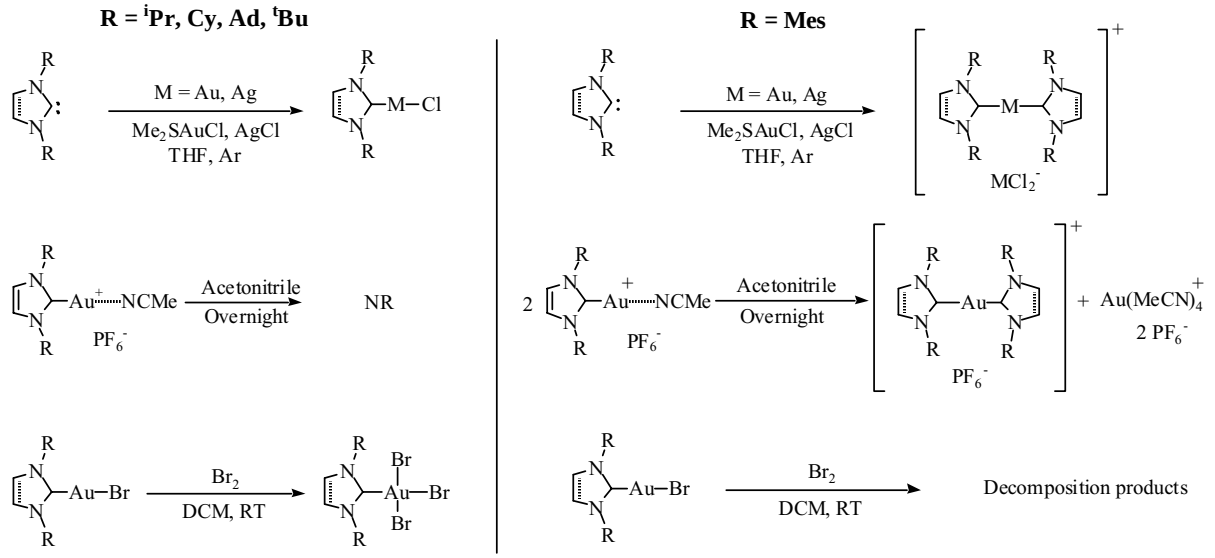
Direct addition of a slight excess of elemental bromine (Br_2) to a solution of (IPr)AuBr (**8**), (IMes)AuBr (**9**), (SIPr)AuBr (**10**), (SIMes)AuBr (**11**), (ICy)AuBr (**12**), (IAd)AuBr (**13**) and (I^{t}Bu)AuBr (**14**) complexes, gives the desired (IPr)$AuBr_3$ (**15**), (IMes)$AuBr_3$ (**16**), (SIPr)$AuBr_3$ (**17**), (SIMes)$AuBr_3$ (**18**), (ICy)$AuBr_3$ (**19**), (IAd)$AuBr_3$ (**20**) and (I^{t}Bu)$AuBr_3$ (**21**) complexes in good yields, as yellow or orange powders stable in air. (Equation 2)

$$\text{(NHC)AuBr} + Br_2 \xrightarrow[\text{oxidative addition}]{CH_2Cl_2} \text{(NHC)}AuBr_3 \qquad (2)$$

Initially, the reactions were allowed to proceed overnight but we noticed that the reactions were very fast at room temperature (even at –78° C), and completed in less than half hour. This is not surprising since redox reactions involving metals, are known to proceed with a rapid kinetic. We did not observe any NHC-Au bond cleavage or rearrangement by using bulky carbenes, such as IAd and I^{t}Bu, as reported for the oxidation of sterically demanding gold(I) phosphines.[22b] Attempts to synthesize (IMes)$AuBr_3$ (**16**) and (SIMes)$AuBr_3$ (**18**) at room temperature failed and

gave decomposition product with no trace of the desired complexes, even when a sub-stoichiometric amount of bromine was used. At –78° C, the reaction proceeded smoothly without any trace of decomposition product. These particular synthetic conditions for the complexes bearing the IMes and SIMes moieties, again illustrate the difference in reactivity encountered with these two carbenes on the chemistry of metals from group 11.[26,28c,31] (Scheme 5.2)

Scheme 5.2. Reactivity of complexes bearing different NHC moieties



5.2.5. NMR study the gold(III) complexes

The ^{1}H NMR spectra of the complexes **15**, **16**, **19**, **20,** and **21** display a low field singlet between 7.21 and 7.53 ppm assigned to the two protons located on the unsaturated imidazole backbone. The chemical shifts are slightly shifted down-field, when compared to the (NHC)AuBr series, likely due to a double bond being less rich in electron density. It is reasonable to assume that gold(III) being more acidic than gold(I) induces a greater delocalization of the electronic

density from the carbon-carbon double bond to the carbenic carbene, through the entire aromatic system. There is no sign of attack by the bromine on the double bond. ^{1}H NMR Spectra of **17** and **18** display a more up field singlet at 4.29 and 4.23 ppm respectively, assigned to the four protons located on the saturated imidazole backbone. For all complexes, signals expected for the *N*-aryl, and *N*-alkyl chains are present. ^{13}C NMR resonances of the different carbenic carbons are characterized by a weak upfield signal between 132.9 and 146.2 ppm for the unsaturated imidazole moieties and around 173 ppm for the saturated imidazole moieties. (Table 5.2)

Table 5.2. NMR Chemical shifts of the carbenic carbon for the Au-Br complexes

(NHC)AuBr	δ_C (ppm)	(NHC)$AuBr_3$	δ_C (ppm)	$\Delta\delta_C$ (ppm)
(IPr)AuBr[a] (**8**)	179.0	(IPr)$AuBr_3$[a] (**15**)	146.2	- 32.8
(IMes)AuBr[a] (**9**)	176.7	(IMes)$AuBr_3$[a] (**16**)	144.4	- 32.3
(SIPr)AuBr[a] (**10**)	199.0	(SIPr)$AuBr_3$[a] (**17**)	174.1	- 24.9
(SIMes)AuBr[a] (**11**)	198.1	(SIMes)$AuBr_3$[a] (**18**)	172.3	- 25.8
(ICy)AuBr[a] (**12**)	172.1	(ICy)$AuBr_3$[a] (**19**)	136.8	- 35.3
(IAd)AuBr[a] (**13**)	170.2	(IAd)$AuBr_3$[a] (**20**)	132.9	- 37.3
(I^{t}Bu)AuBr[a] (**14**)	172.4	(I^{t}Bu)$AuBr_3$[a] (**21**)	134.2	- 38.3

(NHC)•HCl	δ_C (ppm)	$\Delta\ \delta_C$ (ppm)
(IPr)•HCl[b]	132.2	+ 14.0
(IMes)•HCl[b]	134.8	+ 9.6
(SIPr)•HCl[b]	160.0	+ 14.1
(SIMes)•HCl[b]	160.2	+ 12.1
(ICy)•HCl[b]	134.5	+ 2.3
(IAd)•HCl[b]	132.1	+ 0.8
(I^{t}Bu)•HCl[b]	132.7	+ 1.5

[a] NMR recorded in $CDCl_3$. [b] NMR recorded in DMSO-d_6.

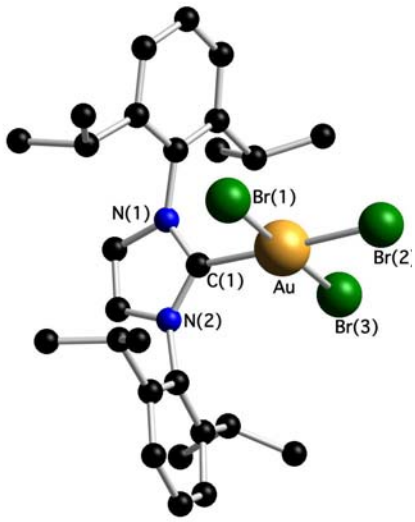
The differences of the carbenic carbon shifts between the two series of gold bromide complexes are found between 24.9 and 38.3 ppm. However, it is within the range reported for the oxidation of chloride gold(I) thiazolinylidene by Raubenheimer *et al.*[24] Expectedly, it indicates an increase of acidity of the gold atom associated with an increase in oxidation state. (Table 5.2) It is reasonable to assume that a smaller upfield shift indicates an attenuated acidity of the gold atom, likely due to a better donation of the carbene moieties. If this is correct, the saturated SIPr and SIMes carbenes provide the greatest electronic density to the gold(III) cation. A comparison between unsaturated carbenes bearing aromatic and alkyl R-groups, is also possible. Interestingly, IPr and IMes appear to be better σ-donors than IAd, ICy and I^{t}Bu. All NHC-ligands display the same donor property trend as seen for the gold(I) complexes.[26] It is also interesting to note that the chemical shifts of the carbenic carbon in these gold(III) complexes, especially the alkyl *R*-group bearing complexes, are extremely close to the reported value for the imidazolium salts, with a difference of 0.9 to 2.3 ppm. Unfortunately, we cannot unequivocally quantify in an

absolute sense the electronic effect associated with electronic density residing on the carbenic carbene as the –Au(III)Br_3 moiety is not isolobal with the acidic proton born by imidazolium salts.[7a]

5.2.6. Structures of gold(III) complexes

To unambiguously characterize all these new gold(III) complexes, X-ray quality crystals were grown in a mixture of DCM/heptane. Ball and stick representations are provided in Figures 5.3, 5.4 and 5.5.

Figure 5.3. Ball and stick representation of (IPr)$AuBr_3$ (**15**) and (IMes)$AuBr_3$ (**16**). Hydrogen atoms have been omitted for clarity



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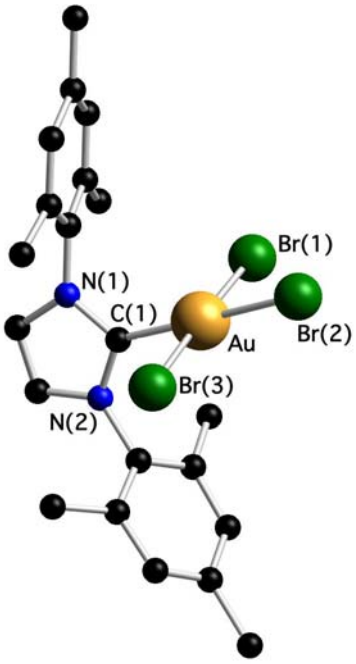
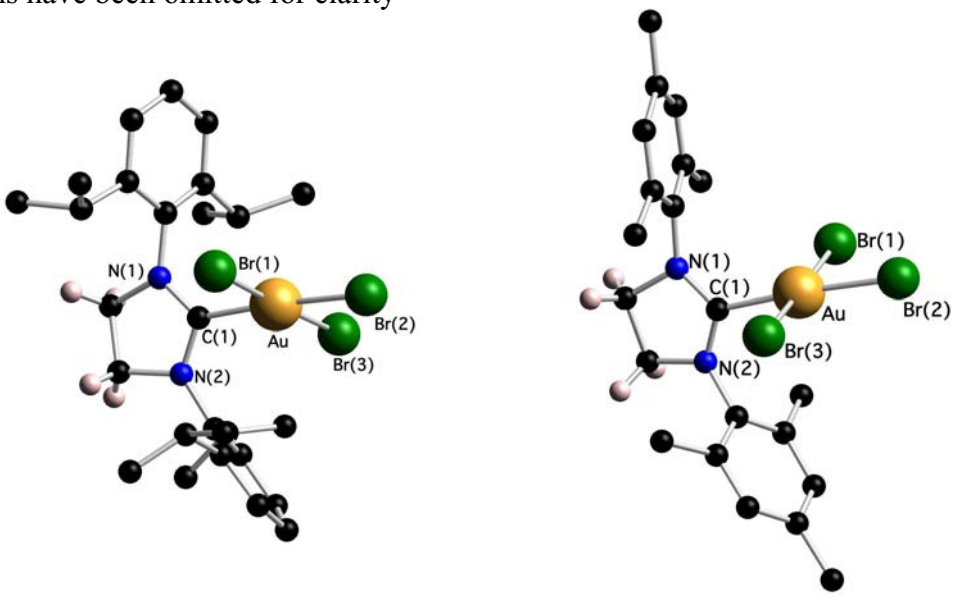


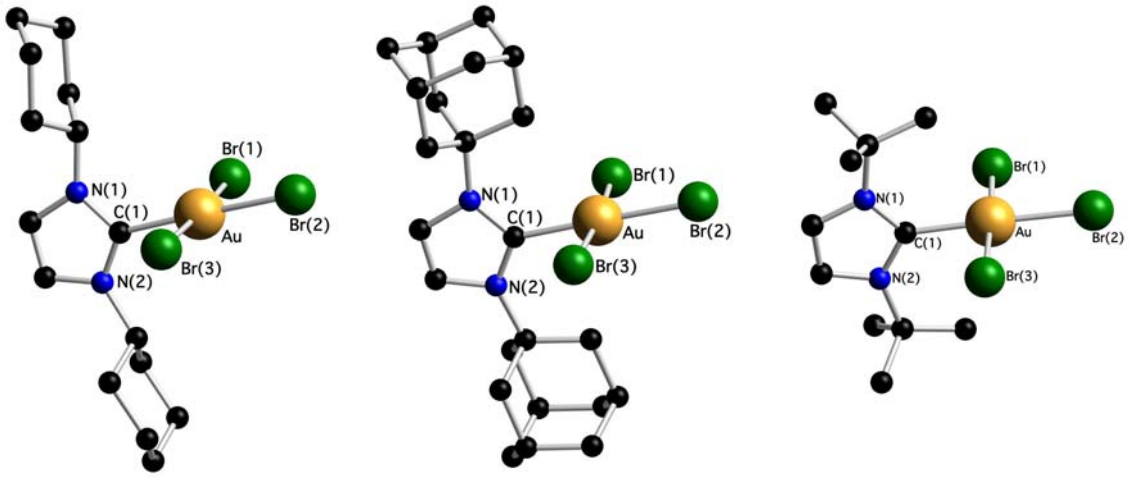
16

Figure 5.4. Ball and stick representation of (SIPr)$AuBr_3$ (**17**) and (SIMes)$AuBr_3$ (**18**). Most hydrogen atoms have been omitted for clarity



17 **18**

Figure 5.5. Ball and stick representation of (ICy)$AuBr_3$ (**19**) and (IAd)$AuBr_3$ (**20**) and (I^{t}Bu)$AuBr_3$ (**21**). Hydrogen atoms have been omitted for clarity



19 **20** **21**

All (NHC)$AuBr_3$ complexes have a four-coordinate gold atom, in a square planar environment, as expected for d^8 metals. The C(1)–Au–Br(2) and Br(1)–Au–Br(3) bonds are nearly linear with angles between 173.73º and 178.66º (Table 5.3).

Table 5.3. Selected bond angles values (deg) for (NHC)$AuBr_3$ complexes

(NHC)$AuBr_3$	C(1)–Au–Br(1)	C(1)–Au–Br(2)	C(1)–Au–Br(3)
(IPr)$AuBr_3$ (**15**)	92.3(5)	178.2(5)	88.8(5)
(IMes)$AuBr_3$ (**16**)	91.4(2)	178.0(2)	89.1(2)
(SIPr)$AuBr_3$ (**17**)	88.0(4)	174.9(4)	93.0(4)
(SIMes)$AuBr_3$ (**18**)	91.0(4)	175.9(4)	90.9(4)
(ICy)$AuBr_3$ (**19**)	89.2(6)	178.3(6)	86.4(6)
(IAd)$AuBr_3$ (**20**)	87.80(15)	178.66(16)	85.93(15)
(I^{t}Bu)$AuBr_3$ (**21**)	90.69(14)	177.97(14)	87.16(14)
(NHC)$AuBr_3$	Br(1)–Au–Br(2)	Br(1)–Au–Br(3)	Br(2)–Au–Br(3)
(IPr)$AuBr_3$ (**15**)	87.66(15)	178.79(12)	91.21(16)
(IMes)$AuBr_3$ (**16**)	89.69(7)	177.78(5)	89.83(6)
(SIPr)$AuBr_3$ (**17**)	89.89(7)	177.76(4)	89.28(7)
(SIMes)$AuBr_3$ (**18**)	88.71(7)	176.60(7)	89.66(7)
(ICy)$AuBr_3$ (**19**)	91.92(11)	175.45(11)	92.51(10)
(IAd)$AuBr_3$ (**20**)	93.53(2)	173.73(3)	92.73(2)
(I^{t}Bu)$AuBr_3$ (**21**)	91.32(2)	177.82(2)	90.83(3)

All C(1)–Au distances lie in the range of 2.01 and 2.05 Å, whether the gold center bears a saturated or unsaturated imidazol motif. (Table 5.4) These metrical parameters are in close agreement with reported organogold(III) complexes[20c,32] possessing carbon-gold bond lengths between 2.01 and 2.07 Å. There is no discernable correlation between the gold-carbon bond length and the electronic or steric parameters associated with the NHCs employed.

Table 5.4. Selected Au-X bond distanced (Å) in (NHC)$AuBr_3$ complexes

(NHC)$AuBr_3$	Au–C(1)	Au – Br(1)	Au–Br(2)	Au–Br(3)
(IPr)$AuBr_3$ (**15**)	2.048(19)	2.384(3)	2.386(4)	2.397(3)
(IMes)$AuBr_3$ (**16**)	2.009(8)	2.4156(15)	2.4224(12)	2.4123(14)
(SIPr)$AuBr_3$ (**17**)	2.042(13)	2.405(2)	2.4452(18)	2.408(2)
(SIMes)$AuBr_3$ (**18**)	2.052(13)	2.4108(15)	2.4468(17)	2.4169(17)
(ICy)$AuBr_3$ (**19**)	2.04(2)	2.405(3)	2.444(3)	2.410(3)
(IAd)$AuBr_3$ (**20**)	2.052(6)	2.4465(8)	2.4496(7)	2.4426(7)
(I^tBu)$AuBr_3$ (**21**)	2.015(5)	2.4209(6)	2.4403(6)	2.4638(6)

All Br–Au distances were found to be between 2.38 and 2.47 Å. (Table 5.4) They are similar to reported Br–Au(III) complexes where the bromide-gold(III) bond lengths are between 2.38 and 2.65 Å.[22b,33] The carbene ligands (except IPr and IAd) induce a *trans*-influence with a lengthening of the Au–Br(2) bond. This effect is less pronounced than the one observed for the phosphine-$AuBr_3$ complexes described by Schmidbaur *et al.*[22b] It is surprising to observe that while there is no visible *trans*-effect for the complex (IAd)$AuBr_3$ (**20**), the three different Au-Br bonds are slightly longer than expected when compared to our other gold(III) complexes. There is

no close contact between gold atoms. This is not surprising since aurophilic interactions only apply for d^{10} gold(I) cations.[34] There is no insertion of bromine in the crystals lattices, as reported for some phosphine gold(III) tribromide complexes.[22b]

Table 5.5. Crystallographic data for complexes **8** and **15-21**

Complex	**8**	**15**	**16**	**17**
Formula	$C_{27}H_{36}N_2AuBr$	$C_{27.50}H_{37}N_2AuBr_3$	$C_{21}H_{24}N_2AuBr_3$	$C_{28}H_{40}N_2AuBr_3Cl_2$
M_r	665.45	867.74	741.12	912.22
Crystal system	orthorhombic	monoclinic	orthorhombic	monoclinic
Space group	Pccn	P2(1)/n	P2(1)2(1)2(1)	P2(1)/c
Cells constants				
a (Å)	10.9117(6)	16.950(2)	10.6845(6)	10.677(2)
b (Å)	12.6771(7)	19.403(3)	14.2833(8)	16.593(4)
c (Å)	19.9643(10)	20.417(3)	15.7115(9)	19.306(4)
α (deg)	90.00	90.00	90.00	90.00
β (deg)	90.00	110.421(3)	90.00	99.664(4)
γ (deg)	90.00	90.00	90.00	90.00
V (Å^3)	2761.6 (3)	6293.0(15)	2397.7(2)	3371.5(12)
Z	4	8	4	4
λ (Å)	0.71073	0.71073	0.71073	0.71073
ρ (calcd) (g/cm^3)	1.601	1.832	2.053	1.797
μ, mm^{-1}	6.789	8.588	11.143	8.096
F(000)	1304	3336	1392	1760

T (K)	295(2)	295(2)	295(2)	295(2)
$2\theta_{max}$ (deg)	55.04	52.774	46.718	53.004
No. of rflns measd	17717	39800	25184	16323
No. of indep rflns	3140	8206	3137	4009
R_{int}	0.0505	0.0574	0.0410	0.0820
No. of data/ restraints/params	2026/ 0/146	5509/ 563/638	2891/ 705/330	2934/ 335/377
R_w (F^2 all rflns)	0.0758	0.0967	0.0701	0.0992
$R(F, > 4\sigma(F))$	0.0321	0.0495	0.0300	0.0589
Max $\Delta\rho$ (e Å^{-3})	0.928 and -0.986	0.925 and -1.413	0.744 and -0.530	1.130 and -0.775

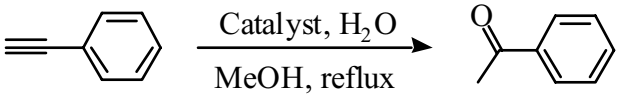
Complex	**18**	**19**	**20**	**21**
Formula	$C_{21.50}H_{27.01}N_2AuBr_3Cl_{1.01}$	$C_{15.50}H_{25}N_2AuBr_3Cl$	$C_{23}H_{32}N_2AuBr_3$	$C_{11}H_{20}N_2AuBr_3$
M_r	785.90	711.52	773.20	616.99
Crystal system	monoclinic	orthorhombic	monoclinic	monoclinic
Space group	P2(1)/c	Pccn	P2(1)/c	P2(1)/c
Cells constants				
a (Å)	8.7226(8)	15.0878(9)	16.4445(16)	9.2947(5)
b (Å)	16.0470(15)	19.9495(13)	11.1131(10)	15.3944(8)
c (Å)	19.7576(18)	14.6881(9)	12.9782(12)	12.1528(7)

α (deg)	90.00	90.00	90.00	90.00
β (deg)	95.611(2)	90.00	90.044(2)	96.7460(10)
γ (deg)	90.00	90.00	90.00	90.00
V (Å^3)	2752.3(4)	4421.0(5)	2371.8(4)	1726.86(16)
Z	4	8	4	4
λ (Å)	0.71073	0.71073	0.71073	0.71073
ρ (calcd) (g/cm^3)	1.897	2.138	2.165	2.373
μ, mm^{-1}	9.808	12.198	11.270	15.445
F(000)	1485	2664	1472	1136
T (K)	295(2)	295(2)	295(2)	295(2)
$2\theta_{max}$ (deg)	61.21	58.484	46.718	52.846
No. of rflns measd	39906	36155	21229	21428
No. of indep rflns	3600	2892	3429	3569
R_{int}	0.0603	0.0586	0.0494	0.0418
No. of data/ restraints/params	3197/ 240/278	2609/ 186/217	2888/ 280/390	3107/ 491/235
R_w (F^2 all rflns)	0.1291	0.1339	0.0725	0.0548
$R(F, > 4\sigma(F))$	0.0490	0.0438	0.0295	0.0259
Max $\Delta\rho$ (e Å^{-3})	1.610 and -0.797	0.778 and -1.198	1.244 and -1.443	1.127 and -0.907

5.2.7. Catalytic activity the gold(III) complexes

We were interested to test the catalytic activity of our new well-defined gold(III) complexes to mediate the addition of water to alkynes. As gold(I) and gold(III) salts are known to catalyze this reaction, we used the reported work[1a,17a,35] as references to gauge the catalytic activity of our system. Of the many Au(III) complexes synthesized, (IPr)$AuBr_3$ displays the best catalytic activity. (Table 5.6)

Table 5.6. Screening of (NHC)$AuBr_3$ complexes in addition of water to alkynes

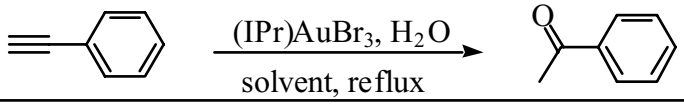


entry	catalyst	time	yield[b]
1	-	-	NR
2	IPr	-	NR
3	$AuCl_3$	24h	94%
4	(IPr)$AuBr_3$	24h	95%
5	(IMes)$AuBr_3$	24h	91%
6	(IAd)$AuBr_3$	48h	35%
7	(ItBu)$AuBr_3$	48h	92%

[a]Reaction conditions: 10 mol% of catalyst, 0.5 mL of H_2O, 0.5 mL of methanol, 1 mmol of phenylacetylene. [b]GC yields, an average of two runs.

The solvent screening indicates that an alcohol is required for the catalysis to proceed efficiently. (Table 5.7) There is no trace of enol ethers or acetals resulting from the addition of alcohol to the alkynes as a competing reaction.

Table 5.7. Solvent screening in addition of water to alkynes

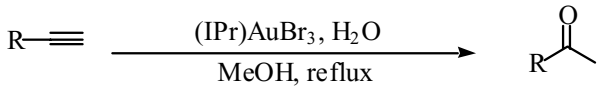


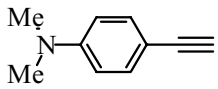
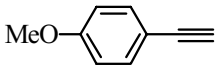
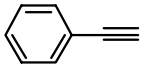
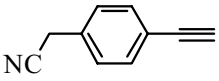
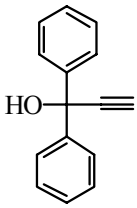
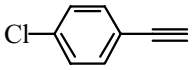
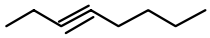
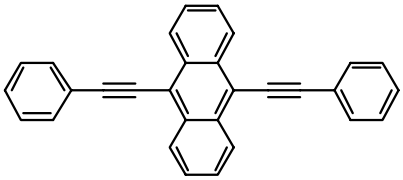
entry	solvent	time	yield[b]
1	MeOH	24h	95%
2	IPA	36h	47%
3	H_2O	48h	62%[c]
4	MeCN	-	NR
5	THF	-	NR

[a]Reaction conditions: 10 mol% of catalyst, 0.5 mL of H_2O, 0.5 mL of methanol, 1 mmol of phenylacetylene. [b]GC yields, an average of two runs. [c]Small amount of acetone added to solubilize the catalyst.

The present complexes were inefficient with internal alkynes, confirming the likely formation of a gold(III) vinyl secondary carbocation as an early reaction intermediate[14d,35] (Table 5.8).

Table 5.8. Various alkynes screened in addition of water to alkynes

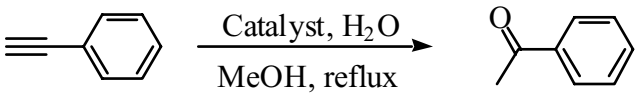


entry	alkyne	cat. loading	time	yield (%)[b]
1		10 mol%	1h	100 (92)[c]
2		10 mol%	6h	96 (90)
3		10 mol%	24h	95 (88)
4		10 mol%	36h	92 (86)
5		10 mol%	3h	40 (36)
6		10 mol%	36h	80 (77)
7		10 mol%	-	NR
8		20 mol%	-	NR

[a]Reaction conditions: 0.5 mL of H_2O, 0.5 mL of methanol, 1 mmol of alkyne. [b]GC yields, isolated yields in parentheses, an average of two runs. [c]Temperature = 25°C.

But the most dramatic result is the acceleration obtained when one equivalent of a silver(I) salt is added as co-catalyst. This permits the rapid and quantitative formation of products while reducing catalyst loading from 10 mol% to 2 mol%. (Table 5.9)

Table 5.9. Effect of a silver salt on catalytic addition of water to alkynes



loading mol%	catalyst	time	yield[b]
10	$(IPr)AuBr_3$	24h	95%
2	$(IPr)AuBr_3+AgPF_6$	1h	99%
10	$AgPF_6$	24h	NR

[a]Reaction conditions: 0.5 mL of H_2O, 0.5 mL of methanol, 1 mmol of phenylacetylene. [b]GC yields, an average of two runs.

These initial catalytic observations raise many questions in term of mechanism of activation and nature of the true catalytic species. Ongoing studies in our laboratories are aimed at answering these questions.

5.3. Conclusion

We report the synthesis of the first series of well-defined (NHC)Au(III) complexes. Their straightforward synthesis can be carried out under aerobic conditions by oxidative addition of elemental bromine to the corresponding (NHC)Au(I) precursor. NMR and crystallographic data provide detailed information concerning the steric constraints and electronic effects produced by the different carbene environments around the Au(III) center. We also report the first use of a (NHC)Au(III) complex to catalyze an organic transformation. While the initial catalytic tests provide modest results, addition of a silver salt as a co-catalyst allowed the formation of a very

efficient catalytic system. We are currently investigating the possible mechanism at play in this and related reactions.

5.4. Experimental Section

5.4.1. General Considerations

- All reactions using (NHC)AuCl or (NHC)AuBr as starting material were carried out in air.
- All alkynes were used as received (Aldrich, Acros).
- All reactions were carried out open to air unless indicated otherwise.
- Solvents for NMR spectroscopy were dried over molecular sieves.
- NMR spectra were collected on a 500 or a 400 MHz Varian Gemini spectrometer.
- Flash chromatography was performed on silica gel (230-400 mesh) (Natland International Corporation).
- Elemental analyses were performed by Robertson Microlit Labs. (NHC)AuCl complexes were synthesized according to literature procedures.[26]

5.4.2. Synthesis of gold(I) complexes

*Synthesis of [(IPr)AuBr] (**8**):* In a flask, (IPr)AuCl (**1**) (1.00 g, 1 equiv, 1.61 mmol) is dissolved in 5 mL of acetone with LiBr (1.19 g, 8.5 equiv, 13.70 mmol) and the solution is stirred at room temperature for 24 h. The acetone is removed by vacuum and 2 mL of DCM added to the residue. The organic phase is dried over $MgSO_4$ since LiBr is extremely hygroscopic. The solution is

filtered over a plug of silica gel (3 g). After, reduction of the volume of DCM to 0.5 mL, 5 mL of pentane are added that lead to the appearance of a white precipitate. This precipitate is filtered, washed with 5 mL of cold pentane and dried to afford the desired complex. Yield: 0.94 g (87%). ^{1}H NMR ($CDCl_3$): δ 7.50 (t, *J* = 8.0 Hz, 2H, C*H*-aromatic), 7.28 (d, *J* = 8.0 Hz, 4H, C*H*-aromatic), 7.17 (s, 2H, C*H*-imidazole), 2.56 (septet, *J* = 7.0 Hz, 4H, C*H*$(CH_3)_2$), 1.34 (d, *J* = 7.0 Hz, 12H, CH (C*H*$_3)_2$), 1.22 (d, *J* = 7.0 Hz, 12H, CH (C*H*$_3)_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 179.0 (s, *C*-carbene), 145.8 (s, *C*H-aromatic), 134.2 (s, *C*H-aromatic), 131.0 (s, *C*H-aromatic), 124.5 (s, *C*H-imidazole), 123.3 (s, *C*H-aromatic), 29.0 (s, *C*H $(CH_3)_2$), 24.7 (s, CH (*C*H$_3)_2$), 24.2 (s, CH (*C*H$_3)_2$). Elemental analysis calcd for $C_{27}H_{36}N_2AuBr$ (665.21): C, 48.74; H, 5.41; N, 4.21. Found: C, 48.68; H, 5.17; N, 3.94.

*Synthesis of [(IMes)AuBr] (**9**):* A protocol similar to that used for **8** gave **9** (from 0.90 g, 1.68 mmol of **2**) as a white solid. Yield: 0.780 g (80%). ^{1}H NMR ($CDCl_3$): δ 7.09 (s, 2H, C*H*-imidazole), 6.98 (s, 4H, C*H*-aromatic), 2.33 (s, 6H, C*H*$_3$), 2.10 (s, 12H, C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 176.7 (s, *C*-carbene), 139.7 (s, *C*H-aromatic), 134.6 (s, *C*H-aromatic), 134.5 (s, *C*H-aromatic), 129.4 (s, *C*H-aromatic), 122.0 (s, *C*H-imidazole), 21.1 (s, C*H*$_3$), 17.7 (s, C*H*$_3$). Elemental analysis calcd for $C_{21}H_{24}N_2AuBr$ (581.02): C, 43.39; H, 4.16; N, 4.82. Found: C, 43.51 H, 3.88; N, 4.66.

*Synthesis of [(SIPr)AuBr] (**10**):* In a flask (SIPr)AuCl (**3**) (1.00 g, 1 equiv, 1.61 mmol) is dissolved in 5 ml of acetone and LiBr (1.19 g, 8.5 equiv, 13.70 mmol) is added. This solution is stirred at room temperature for 48 h. The acetone is removed by vacuum and replaced by DCM. Solution is filtered over a plug of silica gel and dried over $MgSO_4$. After filtration and reduction

of the volume of DCM to 0.5 mL, 5 mL of pentane were added until appearance of a white precipitate. This one is filtered, washed with pentane and dried out to afford the desired complex. It is worthy to note that washing the complex with water leads to its decomposition to the corresponding imidazolium salt. Yield: 0.610 g (57%). ^{1}H NMR ($CDCl_3$): δ 7.41 (t, *J* = 7.5 Hz, 2H, C*H*-aromatic), 7.23 (d, *J* = 7.5 Hz, 4H, C*H*-aromatic), 4.04 (s, 4H, CH_2-imidazole), 3.05 (septet, *J* = 6.5 Hz, 4H, C*H*$(CH_3)_2$), 1.41 (d, *J* = 6.5 Hz, 12H, CH (C$H_3)_2$), 1.33 (d, *J* = 6.5 Hz, 12H, CH (C$H_3)_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 199.0 (s, *C*-carbene), 146.7 (s, *C*H-aromatic), 134.1 (s, *C*H-aromatic), 130.2 (s, *C*H-aromatic), 124.8 (s, *C*H-aromatic), 53.7 (s, *C*H_2-imidazole), 29.2 (s, *C*H $(CH_3)_2$), 25.3 (s, CH (*C*$H_3)_2$), 24.3 (s, CH (*C*$H_3)_2$). Elemental analysis calcd for $C_{27}H_{38}N_2AuBr$ (667.14): C, 48.58; H, 5.74; N, 4.20. Found: C, 48.60; H, 5.60; N, 4.05.

*Synthesis of [(SIMes)AuBr] (**11**):* A protocol similar to that used for **10** provided **11** (from 1.00 g, 1.86 mmol of **4**) as a white solid. Yield: 0.780 g (72%). ^{1}H NMR ($CDCl_3$): δ 6.93 (s, 4H, C*H*-aromatic), 3.97 (s, 4H, CH_2-imidazole), 2.31 (s, 12H, CH_3), 2.29 (s, 6H, CH_3); ^{13}C NMR ($CDCl_3$): δ (ppm) = 198.1 (s, *C*-carbene), 139.1 (s, *C*H-aromatic), 135.7 (s, *C*H-aromatic), 134.7 (s, *C*H-aromatic), 130.0 (s, *C*H-aromatic), 50.9 (s, *C*H_2-imidazole), 21.3 (s, CH_3), 18.2 (s, CH_3). Elemental analysis calcd for $C_{21}H_{26}N_2AuBr$ (583.08): C, 43.24; H, 4.49; N, 4.80. Found: C, 43.14 H, 4.22; N, 4.69.

*Synthesis of [(ICy)AuBr] (**12**):* A protocol similar to that used for **8** gave **12** (from 1.15 g, 2.47 mmol of **5**) as a white solid. Yield: 0.980 g (78%). ^{1}H NMR ($CDCl_3$): δ 6.95 (s, 2H, C*H*-imidazole), 4.57 (m, 2H, NC*H*-cyclohexyl), 2.07 (m, 4H, CH_2), 1.86 (m, 4H, CH_2), 1.73 (m, 2H, CH_2), 1.56 (m, 4H, CH_2), 1.43 (m, 4H, CH_2), 1.22 (m, 2H, C*H*); ^{13}C NMR ($CDCl_3$): δ (ppm) =

172.1 (s, *C*-carbene), 117.3 (s, *C*H-imidazole), 61.0 (s, N*C*H-cyclohexyl), 34.3 (s, *C*H_2), 25.5 (s, *C*H_2), 25.3 (s, *C*H_2). Elemental analysis calcd for $C_{15}H_{24}N_2AuBr$ (509.20): C, 35.38; H, 4.75; N, 5.50. Found: C, 35.50; H, 4.73; N, 5.30.

Synthesis of [(IAd)AuBr] ***(13):*** A protocol similar to that used for **8** gave **13** (from 1.00 g, 1.76 mmol of **6**) as a white solid. Yield: 0.590 g (55%). ^{1}H NMR ($CDCl_3$): δ 7.08 (s, 2H, C*H*-imidazole), 2.56 (m, 14H, C*H*$_2$-adamantyl), 2.26 (m, 6H, C*H*$_2$-adamantyl), 1.75 (m, 10H, C*H*$_2$-adamantyl); ^{13}C NMR ($CDCl_3$): δ (ppm) = 170.2 (*C*-carbene), 115.2 (s, *C*H-imidazole), 59.2 (s, N*C*H-adamantyl), 44.0 (s, *C*H_2), 35.7 (s, *C*H_2), 29.8 (s, *C*H_2). Elemental analysis calcd for $C_{23}H_{32}N_2AuBr$ (613.10): C, 45.04; H, 5.26; N, 4.57. Found: C, 44.97; H, 5.01; N, 4.44.

Synthesis of [(I^{t}Bu)AuBr][7a] ***(14):*** A protocol similar to that used for **8** gave **14** (from 1.00 g, 2.42 mmol of **7**) as a white solid. Yield: 0.810 g (73%). ^{1}H NMR ($CDCl_3$): δ 7.09 (s, 2H, C*H*-imidazole), 1.87 (s, 18H, C(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 172.4 (s, *C*-carbene), 116.4 (s, *C*H-imidazole), 59.2 (s, *C*(CH$_3$)$_3$), 31.9 (s, C(*C*H$_3$)$_3$).

5.4.3. Synthesis of gold(III) complexes

Synthesis of [(IPr)AuBr$_3$] ***(15):*** In a flask (IPr)AuBr (**8**) (0.840 g, 1 equiv, 1.262 mmol) is dissolved in 5 mL of DCM with bromine (0.240 g, 1.2 equiv, 1.514 mmol). The solution is stirred at room temperature for 1 hour. The volume of DCM is reduced to 0.5 mL by vacuum, removing at the same time the excess bromine. Then 5 mL of pentane is added to produce an orange precipitate. This solid is collected on a filter, washed with 5 mL of pentane and dried to afford the

desired complex. Yield: 0.870 g (84%). ^{1}H NMR ($CDCl_3$): δ 7.54 (t, *J* = 7.5 Hz, 2H, C*H*-aromatic), 7.35 (d, *J* = 7.5 Hz, 4H, C*H*-aromatic), 7.35 (s, 2H, C*H*-imidazole), 2.99 (septet, *J* = 6.5 Hz, 4H, C*H*$(CH_3)_2$), 1.41 (d, *J* = 6.5 Hz, 12H, CH (C*H*$_3)_2$), 1.13 (d, *J* = 6.5 Hz, 12H, CH (C*H*$_3)_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 146.2 (s, *C*-carbene), 145.8 (s, *C*H-aromatic), 132.6 (s, *C*H-aromatic), 131.6 (s, *C*H-aromatic), 126.1 (s, *C*H-aromatic), 124.7 (s, *C*H-imidazole), 29.1 (s, *C*H $(CH_3)_2$), 26.5 (s, CH (*C*$H_3)_2$), 23.0 (s, CH (*C*$H_3)_2$). Elemental analysis calcd for $C_{27}H_{36}N_2AuBr_3$ (825.27): C, 39.30; H, 4.40; N, 3.39. Found: C, 39.26; H, 4.12; N, 3.28.

*Synthesis of [(IMes)AuBr$_3$] (**16**):* In a flask (IMes)AuBr (**9**) (0.100 g, 1 equiv, 0.179 mmol) is dissolved in 1 mL of DCM and cooled to –78 °C, then bromine (0.040 g, 1.2 equiv, 0.214 mmol) is added and the solution is stirred for 20 min. The excess bromine is removed by vacuum while the temperature is allowed to increase slowly to room temperature. Then 0.5 mL of DCM is added followed by 5 mL of pentane until the appearance of an orange precipitate. This suspension is filtered, the solid washed with pentane and dried to afford the desired complex. Yield: 0.120 g (94%). ^{1}H NMR ($CDCl_3$): δ 7.32 (s, 2H, C*H*-imidazole), 7.06 (s, 4H, C*H*-aromatic), 2.37 (s, 6H, C*H*$_3$), 2.29 (s, 12H, C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 144.4 (s, *C*-carbene), 140.9 (s, *C*H-aromatic), 135.2 (s, *C*H-aromatic), 132.8 (s, *C*H-aromatic), 130.1 (s, *C*H-aromatic), 125.9 (s, *C*H$_2$-imidazole), 21.3 (s, C*H*$_3$), 19.7 (s, C*H*$_3$). Elemental analysis calcd for $C_{21}H_{24}N_2AuBr_3$ (740.82): C, 34.03; H, 3.26; N, 3.78. Found: C, 34.13; H, 3.49; N, 3.52.

*Synthesis of [(SIPr)AuBr$_3$] (**17**):* A protocol similar to that used for **15** gave **17** (from 0.280 g, 0.448 mmol of **10**) as a orange solid. Yield: 0.360 g (97%). ^{1}H NMR ($CDCl_3$): δ 7.43 (t, *J* = 7.0 Hz, 2H, C*H*-aromatic), 7.26 (d, *J* = 7.0 Hz, 4H, C*H*-aromatic), 4.29 (s, 4H, C*H*$_2$-imidazole), 3.41

(septet, *J* = 6.5 Hz, 4H, C*H*$(CH_3)_2$), 1.46 (d, *J* = 6.5 Hz, 12H, CH (C*H*$_3)_2$), 1.25 (d, *J* = 6.5 Hz, 12H, CH (C*H*$_3)_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 174.1 (s, *C*-carbene), 147.0 (s, *C*H-aromatic), 132.9 (s, *C*H-aromatic), 131.1 (s, *C*H-aromatic), 125.4 (s, *C*H-aromatic), 55.0 (s, *C*H_2-imidazole), 29.3 (s, *C*H $(CH_3)_2$), 27.4 (s, CH (*C*$H_3)_2$), 24.2 (s, CH (*C*$H_3)_2$). Elemental analysis calcd for $C_{27}H_{38}N_2AuBr_3$ (827.94): C, 39.20; H, 4.63; N, 3.39. Found: C, 39.52; H, 4.66; N, 3.32.

*Synthesis of [(SIMes)AuBr$_3$] (**18**):* A preparation similar to that used for **9** gave **18** (from 0.100 g, 0.185 mmol of **11**) as a orange solid. Yield: 0.128 g (94%). ^{1}H NMR ($CDCl_3$): δ 6.96 (s, 4H, C*H*-aromatic), 4.23 (s, 4H, C*H*$_2$-imidazole), 2.54 (s, 12H, C*H*$_3$), 2.31 (s, 6H, C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 172.3 (s, *C*-carbene), 140.1 (s, *C*H-aromatic), 135.8 (s, *C*H-aromatic), 132.1 (s, *C*H-aromatic), 130.3 (s, *C*H-aromatic), 53.3 (s, *C*H_2-imidazole), 21.2 (s, C*H*$_3$), 20.3 (s, C*H*$_3$). Elemental analysis calcd for $C_{21}H_{26}N_2AuBr_3$ (742.88): C, 33.94; H, 3.53; N, 3.77. Found: C, 34.19; H, 3.57; N, 3.66.

*Synthesis of [(ICy)AuBr$_3$] (**19**):* A protocol similar to that used for **15** gave **19** (from 0.365 g, 0.789 mmol of **12**) as a yellow solid. Yield: 0.470 g (89%). ^{1}H NMR ($CDCl_3$): δ 7.21 (s, 2H, C*H*-imidazole), 4.50 (m, 2H, NC*H*-cyclohexyl), 2.24 (m, 4H, C*H*$_2$), 1.90 (m, 4H, C*H*$_2$), 1.77 (m, 2H, C*H*$_2$), 1.51 (m, 4H, C*H*$_2$), 1.46 (m, 4H, C*H*$_2$), 1.21 (m, 2H, C*H*); ^{13}C NMR ($CDCl_3$): δ (ppm) = 136.8 (s, *C*-carbene), 120.5 (s, *C*H-imidazole), 61.1 (s, N*C*H-cyclohexyl), 33.4 (s, *C*H_2), 25.3 (s, *C*H_2), 25.1 (s, *C*H_2). Elemental analysis calcd for $C_{15}H_{24}N_2AuBr_3$ (668.82): C, 26.93; H, 3.63; N, 4.19. Found: C, 26.89; H, 3.56; N, 3.99.

*Synthesis of [(IAd)AuBr$_3$] (**20**):* A procedure similar to that used for **15** gave **20** (from 0.185 g, 0.325 mmol of **13**) as a yellow solid. Yield: 0.240 g (95%). ^{1}H NMR ($CDCl_3$): δ 7.53 (s, 2H, C*H*-imidazole), 2.57 (m, 14H, C*H*$_2$-adamantyl), 2.32 (m, 6H, C*H*$_2$-adamantyl), 1.75 (m, 10H, C*H*$_2$-adamantyl); ^{13}C NMR ($CDCl_3$): δ (ppm) = 132.9 (*C*-carbene), 121.4 (s, *C*H-imidazole), 63.8 (s, NC*H*-adamantyl), 44.1 (s, *C*H$_2$), 35.6 (s, *C*H$_2$), 30.2 (s, *C*H$_2$). Elemental analysis calcd for $C_{23}H_{32}N_2AuBr_3$ (778.93): C, 35.73; H, 4.17; N, 3.62. Found: C, 35.43; H, 4.05; N, 3.54.

*Synthesis of [(I^{t}Bu)AuBr$_3$] (**21**):* A protocol similar to that used for 1**5** gave **21** (from 0.360 g, 871 mmol of **14**) as a yellow solid. Yield: 0.500 g (93%). ^{1}H NMR ($CDCl_3$): δ 7.49 (s, 2H, C*H*-imidazole), 1.92 (s, 18H, C(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 134.2 (s, *C*-carbene), 122.7 (s, *C*H-imidazole), 62.6 (s, *C*(CH$_3$)$_3$), 32.2 (s, C(*C*H$_3$)$_3$). Elemental analysis calcd for $C_{11}H_{20}N_2AuBr_3$ (616.78): C, 21.41; H, 3.27; N, 4.54. Found: C, 21.59; H, 3.28; N, 4.47.

5.4.4. Screening of substrates in catalytic addition of water to terminal alkynes

Into a reaction vessel equipped with a magnetic stirring bar and a reflux condenser were placed catalyst [(IPr)AuBr$_3$, 10 mol%, 83 mg] distilled water (0.5 mL), and methanol (5 mL). 1 mmol of the indicated alkyne was then added. The resulting mixture was refluxed and stirred using a magnetic plate in an oil bath for the indicated time. The reactions were monitored by gas chromatography. After reaching maximum conversion, the reaction mixture was allowed to cool to room temperature. Prior to workup, the reaction mixture was passed through a short silica column. The resulting filtrate was concentrated under reduced pressure and the residue diluted with methyl *tert*-butyl ether or diethyl ether and washed with brine. The ethereal solution was

dried over magnesium sulfate. The solvent was then evaporated *in vacuo*. When necessary the product was purified by flash chromatography on silica gel with hexanes or 2-10% mixture of ethyl acetate in hexanes.

5.4.5. Isolated Products

1-(4-Dimethylamino-phenyl)-ethanone[36] (Table 7, entry 1) The procedure afforded 133 mg (92%) of the product.

1-(4-Methoxy-phenyl)-ethanone[37] (Table 7, entry 2) The procedure afforded 118 mg (90%) of the product.

1-Phenyl-ethanone[38] (Table 7, entry 3) The procedure afforded 105 mg (88%) of the product.

(4-Acetyl-phenyl)-acetonitrile[39] (Table 7, entry 4) The procedure afforded 121 mg (86%) of the product.

1-Hydroxy-1,1-diphenyl-propan-2-one[40] (Table 7, entry 5) The procedure afforded 74 mg (36%) of the product.

1-(4-Chloro-phenyl)-ethanone[41] (Table 7, entry 6) The procedure afforded 118 mg (77%) of the product.

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5.6. References and Notes

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CHAPTER 6

SYNTHESIS, ISOLATION AND CHARACTERIZATION OF CATIONIC GOLD(I) *N*-HETEROCYCLIC CARBENE (NHC) COMPLEXES

6.1. Introduction

As part of an ongoing program aimed at examining the role of *N*-heterocyclic carbenes (NHC) in transition metal-mediated reactions, we have recently studied the stabilizing effects of NHCs surrounding unsaturated and "reactive" metal centers. Since the isolation of the first free stable NHC, bearing two sterically demanding adamantyl groups on the nitrogens of an imidazolyl framework, by Arduengo,[1] sterically encumbering NHCs have allowed for the isolation of unusual 3-coordinate (NHC)Ni(CO)$_2$ complexes,[2] highly unsaturated 14-electron Ir(I) species,[3] a number of orthometallated ruthenium[4] and iridium[5] species, well-defined monomeric copper(I) species[6] and formally 16-electron second generation ruthenium-based olefin metathesis catalysts.[7] In view of the steric and electronic properties of this ligand class, the NHCs have been employed to prepare efficient and robust catalysts for transformations such as palladium-catalyzed cross-coupling reactions,[8] platinum-mediated hydrosilation,[9] palladium telomerization

of butadiene and methanol,[10] copper-catalyzed hydrosilylation[11] and ruthenium-based olefin metathesis,[12] to name a few.

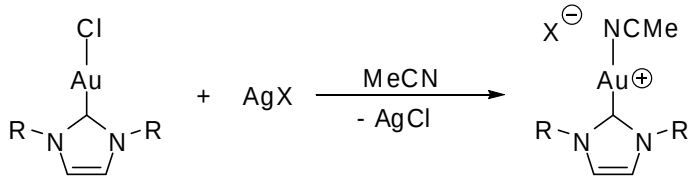
We recently became involved in the synthesis and isolation of well-defined (NHC)gold(I) complexes.[13] The first NHC gold(I) complexes were reported in 1989[14] and these usually bore two strongly bound ligands arranged in a linear fashion around a gold cation. These can be neutral or cationic and have the [(NHC)AuX][13] or $[(NHC)_2Au^+][X^-]$[15] composition. Until recently, catalytic organogold chemistry appeared to have been somewhat forgotten. The "noble" character of the metal was possibly at the origin of the misconception that it would perform poorly in catalysis. This misconception has now been shattered as numerous examples of gold-phosphines[16] and gold-NHC[17] mediated transformations have recently appeared. Gold(I) halide complexes are especially efficient at activating alkyne moieties toward nucleophilic addition under mild reaction conditions.[16,17] A recent example by He also shows these complexes to be excellent co-catalysts in intra- and intermolecular hydroamination of unsaturated olefins.[18] The use of silver salts, with an accompanying non-coordinating anion, is usually required to generate the active catalyst. It is commonly accepted that silver assists in halide abstraction from the gold center generating a highly electrophilic monoligated cationic gold complex.[19] While Echavarren has reported the isolation of a monoligated complex with a very bulky phosphine [(2-(di-*t*-butylphosphino)biphenyl)$Au^+(CH_3CN)][SbPF_6^-]$ as an active catalyst for cycloisomerization,[19] attempts to synthesize or isolate $I^tBuAuBF_4$ by Baker[20] and PPh_3AuPF_6 by Gagosz[21] have so far failed due to the rapid decomposition of these complexes to colloidal gold(0). In this communication, we report the isolation and characterization of such complexes by using a NHC ligand of sufficient bulk and a weakly coordinating solvent such as acetonitrile or THF leading to relatively stable yet reactive cationic gold(I) complexes.

6.2. Results and Discussion

6.2.1. Synthesis of (NHC)Au(MeCN)X complexes

The previously reported IPrAuCl[13] (IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene) , IMesAuCl[13] (IMes = 1,3- bis(2,4,6-trimethylphenyl)imidazol-2-ylidene), I^{t}BuAuCl[20] (I^{t}Bu = 1,3-di-*t*-butylimidazol-2-ylidene) and IAdAuCl[13] (IAd = 1,3-diadamantylimidazol-2-ylidene) were dissolved in acetonitrile and $AgPF_6$, $AgSbF_6$, $AgBF_4$, or AgFABA (FABA$^-$ = tetrakis(perfluorophenyl)borate) was added in slight excess leading to the rapid formation of a precipitate (AgCl). After stirring the solutions for one minute, the suspensions were filtered through a plug of celite to give the novel complexes,in solution (Scheme 6.1).

Scheme 6.1. Synthesis of cationic (NHC)Au(MeCN)X complexes



R = Aryl, alkyl
X = PF_6, SbF_6, BF_4, FABA

(IPr)Au(MeCN)PF_6 (**1**)
(IPr)Au(MeCN)SbF_6 (**2**)
(IPr)Au(MeCN)BF_4 (**3**)
(IPr)Au(MeCN)FABA (**4**)
(IAd)Au(MeCN)PF_6 (**5**)
(I^{t}Bu)Au(MeCN)PF_6 (**6**)
(IMes)Au(MeCN)PF_6 (**7**)

Attempts to obtain solid materials for all complexes by simply removing the solvent under vacuum led to a white powder turning greyish with the appearance of colloidal silver(0). To remove the excess of silver, complexes were dissolved in cold DCM and filtered over a plug of silicagel. All complexes are stable in air and can be kept as a white powder indefinitely in a

freezer. They are stable in acetonitrile and chlorinated solvents at room temperature, with the exception of (IMes)Au(MeCN)PF_6 (**6**) and (I^tBu)Au(MeCN)PF_6 (**7**) which rearrange into $(NHC)_2Au(PF_6)$ and $Au(MeCN)_4PF_6$. Interestingly, the carbene−gold bond remains intact, and no formation of gold(0) was observed.

6.2.2. NMR study of (NHC)Au(MeCN)X complexes

Under these synthetic conditions, ^1H and ^{13}C NMR spectra of the neutral precursors and the novel products were recorded. While the pattern of the ^1H NMR spectra remained the same with no trace of decomposition products between neutral and expected complexes, we observed a slight downfield shift for the backbone protons of the imidazole fragment. We attributed this change to a loss of electronic density in the aromatic heterocyclic system, due a delocalization of the π-electrons toward the more acidic gold center. The ^{13}C NMR spectra present signals for the carbenic carbons that are significantly shifted upfield for all complexes (Table 6.1).

Table 6.1. ^{13}C NMR data for (NHC)AuCl and (NHC)Au(MeCN)X complexes

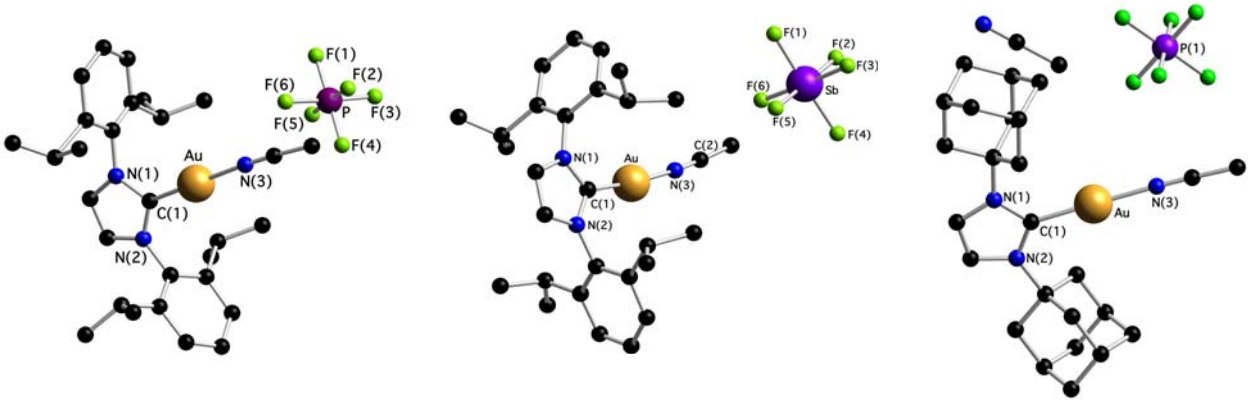
Complexes	solvent	δ_c Au−C	Complexes	solvent	δ_c Au−C
IPrAuCl	$CDCl_3$	175.1	(IPr)Au(MeCN)PF_6	$CDCl_3$	166.1
			(IPr)Au(MeCN)SbF_6	$CDCl_3$	166.0
			(IPr)Au(MeCN)BF_4	$CDCl_3$	165.9
			(IPr)Au(MeCN)FABA	$CDCl_3$	166.1
IAdAuCl	$CDCl_3$	166.3	(IAd)Au(MeCN)PF_6	$CDCl_3$	157.7
I^tBuAuCl	$CDCl_3$	168.2	(I^tBu)Au(MeCN)PF_6	CD_3CN	159.7
IMesAuCl	$CDCl_3$	173.4	(IMes)Au(MeCN)PF_6	CD_3CN	165.3

Once again, this observation confirmed a more acidic gold center. Both ^{1}H and ^{13}C NMR studies support the presence of an electron deficient gold center, confirming the very likely presence of monoligated gold(I) complexes.

6.2.3. Structures of (NHC)Au(MeCN)X complexes

To unambiguously establish the solid state structure of these complexes, suitable X-ray quality crystals for single crystal diffraction studies were grown from a saturated acetonitrile solution of (IPr)Au(CH_3CN)PF_6 (**1**), (IPr)Au(CH_3CN)SbF_6 (**2**) and (IAd)Au(CH_3CN)PF_6 (**5**). For **3**, **4**, **6** and **7** no suitable crystals could be obtained for X-ray diffraction. Results from the diffraction studies confirmed the NMR determined structure and coordination of one acetonitrile to the gold centre (Figure 6.1).

Figure 6.1. Ball-and-stick representations of (IPr)Au(CH_3CN)PF_6 (**1**), (IPr)Au(CH_3CN)SbF_6 (**2**) and (IAd)Au(CH_3CN)PF_6 (**5**). Hydrogens are omitted for clarity



The three complex structures revealed a nearly linear NHC–Au–NCMe arrangement with a C–Au–N angle close to 180°. The C–Au bond distances range between 1.952(2) and 1.990(2) Å; they are similar to those found for the neutral corresponding (NHC)AuCl[13]. The N–Au bond distances range between 2.008(2) and 2.022(2) Å in the range of reported gold complexes with nitrogen donor ligands,[22] but slightly longer than known gold (I) complexes with coordinated acetonitrile such as $[Au^{+}(MeCN)_2][X^{-}]$[23] with a Au–N distance bond equal to 1.96 Å.

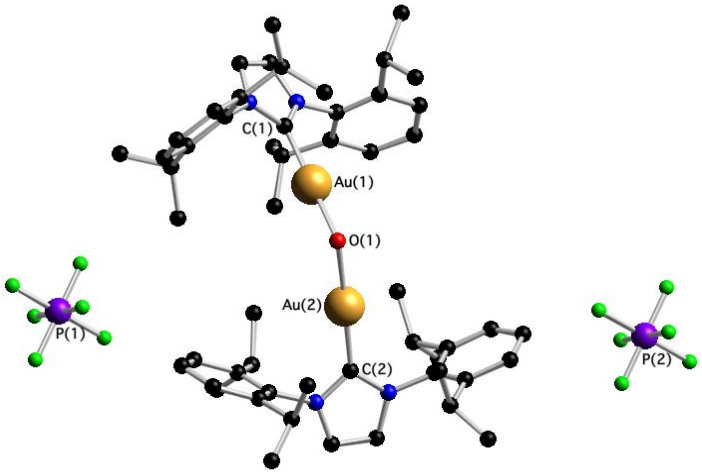
6.2.4. Solvent effect and stabilization of cationic gold(I) complexes

We were interested in further testing the stability of such complexes. Attempts to synthesize the complex **1** in dichloromethane or chloroform with anhydrous silver salts lead to the rapid appearance of large amounts of colloidal gold(0). The ^{1}H NMR spectra of these products indicate the existence of two different NHC environments attributed to at least two NHC-gold species in solution. We confirmed in this manner the necessity of a coordinating solvent to stabilize the cationic gold centre. Ample precedents exist for coordinating solvent stabilization in Pt and Pd complexes.[24,25]

Reproducing the same stability test for **1** with wet silver salts leads to a white precipitate poorly soluble in chlorinated solvents, and no formation of colloidal gold(0). Extensive NMR acquisitions in $CDCl_3$ give a ^{1}H spectrum with broad signals and a ^{13}C spectrum with a new carbenic species reasoning at 162.2 ppm. X-ray quality crystals were grown from a $CDCl_3$ solution. Diffraction study reveals a new complex displaying two $(IPr)Au^{+}$ moieties bound to one molecule of water and two PF_6^{-} counter ions to ensure the electroneutrality of the structure (Figure 6.2). $[((IPr)Au)_2(H_2O)^{2+}][PF_6^{-}]_2$ (**8**) emphasizes the strong Lewis acidic character of the $(IPr)Au^{+}$ cation and is analogous to the complex $[((PR_3)Au)_4O^{2+}][BF_4^{-}]_2$ (PR_3 = triarylphosphine)

described by Schmidbaur.[26] To the best of our knowledge, there is no H_2O-containing gold(I) NHC or phosphine complexes described in the literature.

Figure 6.2. Ball-and-stick representations of $[((IPr)Au)_2(H_2O)^{2+}][PF_6^-]_2$ (**8**). Hydrogens are omitted for clarity



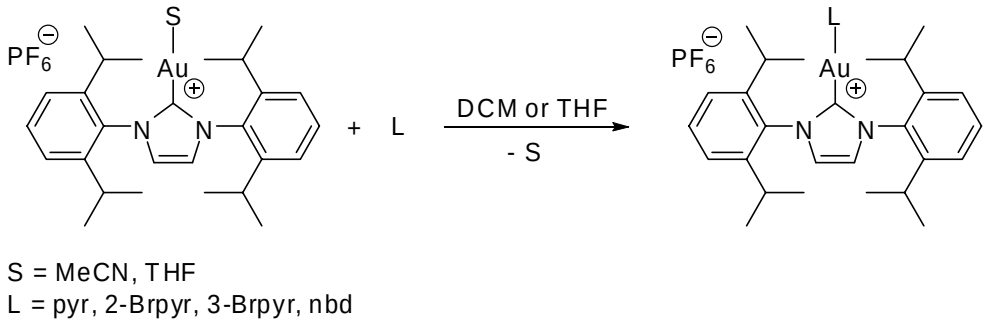
Tetrahydrofuran (THF) was employed as an alternative to acetonitrile to generate $(IPr)Au(S)PF_6$ (S= coordinating solvent). In THF, no decomposition was observed even after 24 h in solution in air, but surprisingly a gel was obtained, attributed to the ring opening polymerization of THF.[27] On the other hand, any attempt to dried or replace the THF by another solvent led to decomposition of $(IPr)Au(THF)PF_6$ (**13**). The ^{13}C NMR spectrum indicated a gold species in THF that is even more acidic than in acetonitrile with a carbenic carbon appearing at a more upfield position (δ = 159.7 ppm *vs* 167.6 ppm in CD_3CN). The complex in THF also displayed a second, more downfield, signal with a low intensity (after a few hours) for the deuterated THF that confirmed the formation of poly-THF.[28] It is worthy of note that the cationic polymerization of THF by ring opening, in the presence of a Lewis acid such as $FeCl_3$ or the trityl cation is well known.[28] In the present case, this polymerization behaviour confirms the presence

of a cationic gold centered complex capable of acting as a Lewis acid, an interesting reaction profile we are presently examining. We also noticed that adding IPrAu(S)PF_6, synthesized from acetonitrile, into THF led to THF polymerization. While the acetonitrile needs to be displaced by the THF to initiate its polymerization, this result shows that in solution the molecules of solvent are weakly bound, labile and can be easily displaced from gold.

6.2.5. Synthesis of pyridine and norbonadiene cationic gold(I) complexes

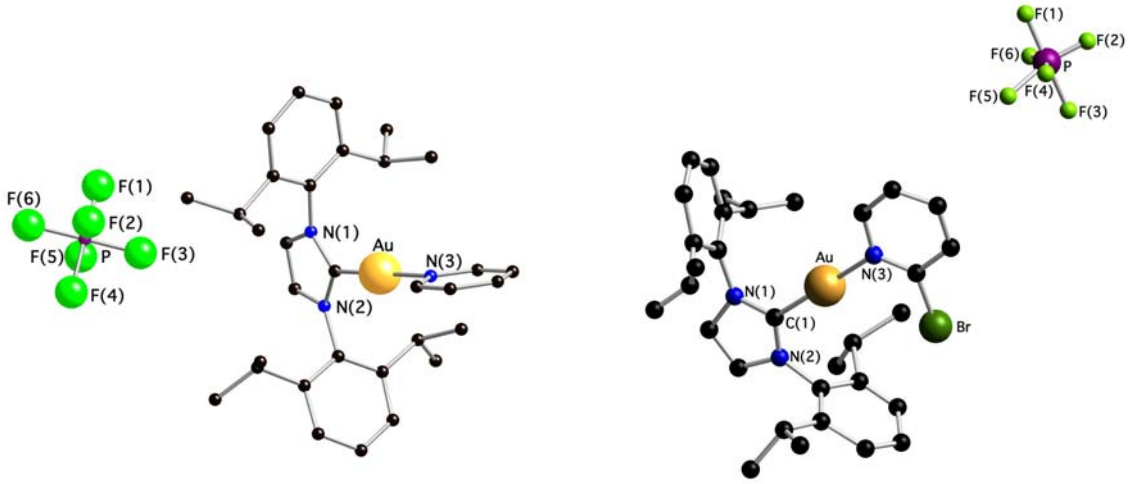
To broaden the scope of available cationic NHC gold(I) complexes, pyridine, 2-bromopyridine, 3-bromopyridine and norbonadiene were employed to generated respectively the new complexes (IPr)Au(pyr)PF_6 (**9**), (IPr)Au(2-Brpyr)PF_6 (**10**), (IPr)Au(3-Brpyr)PF_6 (**11**) and (IPr)Au(nbd)PF_6 (**12**). These new complexes were obtained in high yield from (IPr)Au(S)PF_6 (**1**) and (**8**) by substitution of acetonitrile or THF. In the case of **12** a large excess of norbonadiene and a longer reaction time were required (Scheme 6.2).

Scheme 6.2. Synthesis of cationic (NHC)Au(L)PF_6 complexes



Complexes **9**, **10**, **11** are stable in air and can be kept as a white powder indefinitely in a freezer. They are also stable in acetonitrile, THF, and chlorinated solvents, at room temperature. They display similar ^{1}H and ^{13}C NMR spectra pattern. The carbenic carbons resonate between 166.0 and 167.1 ppm. The bromide group does not appear to noticeably influence the electronic properties of the pyridine ligands. X-ray quality crystals suitable for single crystal diffraction studies were grown from a saturated DCM solution of (IPr)Au(pyr)PF_6 (**9**) and (IPr)Au(2-Brpyr)PF_6 (**10**) (Figure 6.3).

Figure 6.3. Ball-and-stick representations of (IPr)Au(pyr)PF_6 (**9**) and (IPr)Au(2-Brpyr)PF_6 (**10**). Hydrogens are omitted for clarity

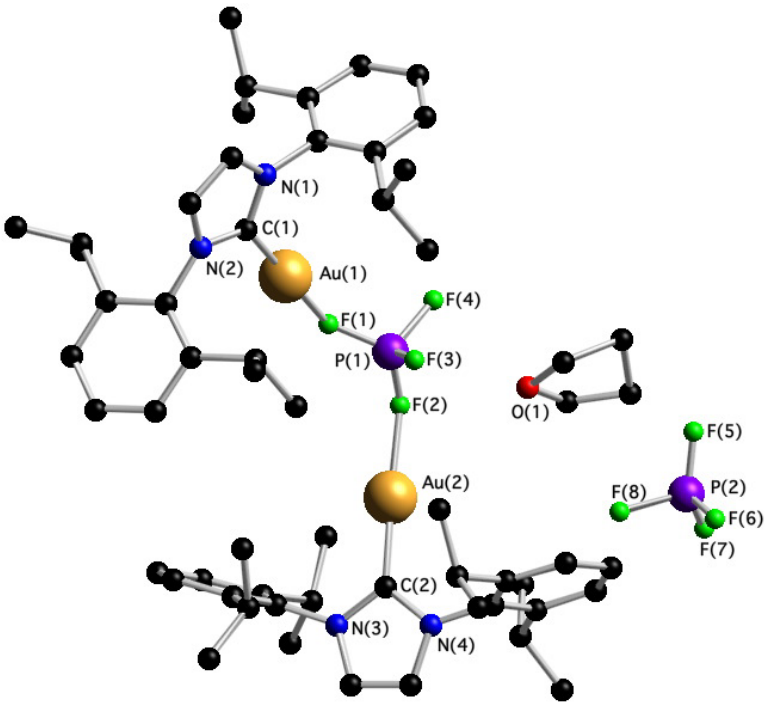


(IPr)Au(nbd)PF_6 (**12**) is stable in air, on the contrary to other gold(I) olefin complexes described.[29] It can be kept as a white powder in the freezer but slowly decomposes in THF or DCM. After a few days in solution, the ^{1}H NMR spectrum of **12** keeps the same aspect while the characteristic septuplet of PF_6^- at -141.3 ppm on the ^{31}P NMP spectrum disappears to be replaced by a broad triplet at -11.5 ppm. From both spectra, it can be assumed that **12** is degraded by decoordination of $(IPr)Au^+$ from norbonadiene followed by reaction with PF_6^-. ^{1}H and ^{13}C NMR spectra of **12** exhibit a norbonadiene ligand with two non equivalent olefin sides characterized by

two different sets of broad signals. One set exhibits the chemical shift of free norbonadiene while the second one is slightly up-field. Such NMR spectra are characteristic of a gold(I) center bound with norbonadiene by only one double bond. On the NMR time scale, the gold(I) center swaps from one double bond to another one, but remains coordinated to the same norbonadiene molecule. The small shift up-field for the olefin signals indicates that the olefin is acting almost as a pure electron donor with negligeable back-bonding from the gold(I) center.[30]

Attempts to crystallize **12** in a saturated solution of dried THF, gave white crystals suitable for X-ray diffraction study. Nevertheless, the structure of **12** was not confirmed and the complex $[((IPr)Au)_2(PF_4)^+][PF_4^-]$ (**14**) was isolated. Such complex can be seen as an intermediate product in the pathway decomposition of **12**. It is worthy to note that described structures with a PF_4^- anion are extremely scarce[31] and unknown in gold chemistry (Figure 6.4).

Figure 6.4. Ball-and-stick representations of $[((IPr)Au)_2(PF_4)^+][PF_4^-]$ (**14**). Hydrogens are omitted for clarity



6.2.6. Catalysis

Previous work form our laboratories has shown a very interesting catalytic behaviour of the complex IPrAuCl in the presence of $NaBAr_4$ (BAr_4 = tetrakis(3,5-bis(trifluoromethyl)phenyl)borate) for the decomposition of ethyl diazoacetate (N_2=$CHCO_2Et$) and the subsequent transfer of the :$CHCO_2Et$ unit to organic substrates.[17] This procedure has led to the functionalization of aromatic sp^2 and primary sp^3 C-H bonds of alkanes in moderate to high yields in a process that requires the assistance of the halide scavenger. Attempts to fully characterize a well-defined complex with the BAr_4 counterion has proven yet unsuccessful. Therefore, the availability of **1,** in solution or as an isolated solid, now allows for the study of its catalytic properties toward this transformation. In reactions with catalytic amounts of **1**, ethyl diazoacetate was reacted with several substrates (Table 6.2).

Table 6.2. Reaction of ethyl diazoacetate and several substrates in the presence of IPrAu(MeCN)PF_6 (**1**) as catalyst.

Substrate	Product	Time[a]	Yield[b]
Methanol	$CH_3OCH_2CO_2Et$	0.2	>99
Ethanol	$CH_3CH_2OCH_2CO_2Et$	0.2	>99
Aniline	$PhN(H)CH_2CO_2Et$	24	>99
t-butylamine	*t*-$BuN(H)CH_2CO_2Et$	24	55
Styrene	Cyclopropanes	120	>99
Benzene	no reaction[c]	120	---
2,3-dimethylbutane	no reaction[c]	120	---

[a] In hours. [b] Determined by GC, diethyl fumarate and maleate accounted for 100%. [c] EDA not consumed

In the case of good nucleophiles such as alcohols, quantitative conversion was obtained within minutes. Longer times were required for aniline whereas for *t*-butylamine incomplete conversion was observed even after 24 h. A similar result was found with styrene, for which three days were required for complete conversion into cyclopropanes. This trend could be attributed to the ease of replacement of the coordinated acetonitrile in **1** by the substrate. In accord with this, the use of more weakly coordinating molecules such benzene or 2,3-dimethylbenzene has led to undetectable yields: only very minor amounts of diethyl fumarate and maleate were detected by GC after several days, with most of the initial EDA remaining in the solution. But an additional experiment strongly suggests that this coordination of the substrate is not the only factor at play. The use of an equimolar mixture of IPrAuCl and $NaBAr_4$ as the catalyst in the reaction of styrene and EDA with a five-fold excess of CH_3CN added did not affect the course of the reaction, and led to the same mixture of products found in the absence of nitrile. We strongly suspect at this point that the counterion plays an important role in this catalytic transformation, a feature that is currently under investigation.

6.3. Conclusion

We have isolated and characterized by NMR spectroscopy and for by X-ray diffraction study well-defined cationic (NHC)Au(I)(S)X and (NHC)Au(L)X complexes which are postulated as the active pre-catalysts in numerous gold mediated organic transformations. The well-defined, isolated species (IPr)Au(MeCN)PF_6 (**1**) has been tested as the catalyst for the carbene transfer reaction from ethyl diazoacetate. The results suggest a large effect of the counterion in this transformation, when compared to the already reported *in situ* generated IPrAuCl + $NaBAr_4$

system.[17] Studies aimed at exploring this relative stability issue as well as investigations focusing on the reactivity of (NHC)Au complexes in organic chemistry are presently ongoing in our laboratories.

6.4. Experimental Section

6.4.1. General conditions

- All reactions were carried out open to air unless indicated otherwise.
- Solvents for NMR spectroscopy were dried over molecular sieves.
- NMR spectra were collected on a 500 or a 400 MHz Varian Gemini spectrometer.
- Flash chromatography was performed on silica gel (230-400 mesh) (Natland International Corporation).

6.4.2. Synthesis of cationic gold(I) complexes

*Synthesis of [(IPr)Au^{+}(CH$_3$CN)][PF$_6^{-}$] (**1**):* In a scintillation vial, IPrAuCl (2.000 g, 1 equiv, 3.22 mmol) is partially dissolved in 10 mL of dried acetonitrile and $AgPF_6$ (0.855 g, 1.05 equiv, 3.38 mmol) is added. The solution is stirred for one minute. All the acetonitrile is removed by vacuum pump and replaced by 10 mL of DCM. Filtration over a plug of silicagel gives a clear greenish solution. After removal of the DCM by vacuum pump, the desired complex is recovered as a white powder. Yield: 2.102 g (92%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.55 (t, *J* = 8.0 Hz, 2H, C*H*

aromatic), 7.40 (s, 2H, C*H* imidazole), 7.32 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 2.44 (septet, *J* = 7.0 Hz, 4H, C*H*(CH_3)$_2$), 2.30 (s, 3H, C*H*$_3$ acetonitrile), 1.27 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$), 1.24 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 166.1 (s, *C* carbene), 145.8 (s, *C*H aromatic), 133.2 (s, *C*H aromatic), 131.3 (s, *C*H aromatic), 125.0 (s, *C*H aromatic), 124.7 (s, *C*H imidazole), 120.5 (s, N*C* acetonitrile), 29.0 (s, CH(*C*H$_3$)$_2$), 24.5 (s, CH(*C*H$_3$)$_2$), 23.8 (s, CH(*C*H$_3$)$_2$), 2.8 (s, *C*H$_3$ acetonitrile); ^{31}P NMR ($CDCl_3$): δ (ppm) = -141.4 (septet, J^1(^{31}P–^{19}F) = 712.0 Hz, *P*F_6^-); ^{19}F NMR ($CDCl_3$): δ (ppm) = -73.5 (d, J^1(^{19}F–^{31}P) = 712.0 Hz, P*F*$_6^-$).

*Synthesis of [(IPr)Au$^+$(CH$_3$CN)][SbF$_6^-$] (**2**):* In a scintillation vial, IPrAuCl (0.250 g, 1 equiv, 0.40 mmol) is dissolved in 2 mL of dried acetonitrile and $AgSbF_6$ (0.152 g, 1.05 equiv, 0.43 mmol) is added. The solution is stirred for one minute. All the acetonitrile is removed by vacuum pump and replaced by 2 mL of DCM. Filtration over a plug of silicagel gives a clear greenish solution. After removal of the DCM by vacuum pump, the desired complex is recovered as a white powder. Yield: 0.310 g (90%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.57 (t, *J* = 8.0 Hz, 2H, C*H* aromatic), 7.36 (s, 2H, C*H* imidazole), 7.34 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 2.45 (septet, *J* = 7.0 Hz, 4H, C*H*(CH_3)$_2$), 2.31 (s, 3H, C*H*$_3$ acetonitrile), 1.28 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$), 1.23 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 166.0 (s, *C* carbene), 145.7 (s, *C*H aromatic), 133.1 (s, *C*H aromatic), 131.5 (s, *C*H aromatic), 125.0 (s, *C*H aromatic), 124.6 (s, *C*H imidazole), 120.5 (s, N*C* acetonitrile), 28.9 (s, CH(*C*H$_3$)$_2$), 24.8 (s, CH(*C*H$_3$)$_2$), 24.1 (s, CH(*C*H$_3$)$_2$), 2.6 (s, *C*H$_3$ acetonitrile); ^{19}F NMR ($CDCl_3$): No signals visible, due the antimony nucleus (I = 7/2).

*Synthesis of [(IPr)Au$^+$(CH$_3$CN)][BF$_4^-$] (**3**):* In a scintillation vial, IPrAuCl (300 mg, 1 equiv, 0.48 mmol) is dissolved in 2 mL of dried acetonitrile and $AgBF_4$ (94 mg, 1 equiv, 0.48 mmol) is added in the dark. The solution is stirred for one minute. All the acetonitrile is removed by vacuum pump and replaced by 2 mL of DCM. Filtration over a plug of silicagel gives a colorless solution. After removal of the DCM by vacuum pump, the desired complex is recovered as a white powder. Yield: 328 mg (96%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.56 (t, *J* = 8.0 Hz, 2H, C*H* aromatic), 7.41 (s, 2H, C*H* imidazole), 7.32 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 2.43 (septet, *J* = 7.0 Hz, 4H, C*H*$(CH_3)_2$), 2.37 (s, 3H, C*H*$_3$ acetonitrile), 1.27 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3)_2$), 1.23 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3)_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 165.9 (s, *C* carbene), 145.6 (s, *C*H aromatic), 133.2 (s, *C*H aromatic), 131.4 (s, *C*H aromatic), 125.1 (s, *C*H aromatic), 124.6 (s, *C*H imidazole), 121.0 (s, N*C* acetonitrile), 28.9 (s, CH(*C*H$_3)_2$), 24.8 (s, CH(*C*H$_3)_2$), 24.1 (s, CH(*C*H$_3)_2$), 2.6 (s, *C*H$_3$ acetonitrile); ^{11}B NMR ($CDCl_3$): δ (ppm) = -1.1 (s, B, *B*F$_4^-$); ^{19}F NMR ($CDCl_3$): δ (ppm) = -153.7 (s, F, BF$_4^-$).

*Synthesis of [(IPr)Au$^+$(CH$_3$CN)][FABA$^-$] (**4**):* In a scintillation vial, IPrAuCl (150 mg, 1 equiv, 0.24 mmol) is dissolved in 2 mL of dried acetonitrile and AgFABA•0.5 toluene (246 mg, 1.05 equiv, 0.25 mmol) is added. The solution is stirred for one minute. All the acetonitrile is removed by vacuum pump and replaced by 2 mL of DCM. Filtration over a plug of silicagel gives a clear greenish solution. After removal of the DCM by vacuum pump, the desired complex is recovered as a white powder. Yield: 307 mg (98%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.56 (t, *J* = 8.0 Hz, 2H, C*H* aromatic), 7.36 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 7.32 (s, 2H, C*H* imidazole), 2.47 (septet, *J* = 7.0 Hz, 4H, C*H*$(CH_3)_2$), 2.22 (s, 3H, C*H*$_3$ acetonitrile), 1.29 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3)_2$), 1.25 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3)_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 166.1 (s, *C* carbene), 149.5

(broad s, *para*-*C*F aromatic), 147.1 (broad s, *C*F aromatic), 145.7 (s, *C*H aromatic), 139.5 (broad s, *C*B aromatic), 137.6 (broad s, *C*F aromatic), 137.0 (broad s, *C*F aromatic), 135.2 (broad s, *C*F aromatic), 133.0 (s, *C*H aromatic), 131.5 (s, *C*H aromatic), 124.7 (s, *C*H aromatic), 124.7 (s, *C*H imidazole), 119.6 (s, N*C* acetonitrile), 29.0 (s, CH(*C*H_3)$_2$), 24.6 (s, CH(*C*H_3)$_2$), 23.9 (s, CH(*C*H_3)$_2$), 2.4 (s, *C*H_3 acetonitrile); ^{11}B NMR ($CDCl_3$): δ (ppm) = -16.7 (s, B, *B*$(C_6F_5)_4^-$); ^{19}F NMR ($CDCl_3$): δ (ppm) = -132.7 (s, *ortho*-C*F* aromatic), -163.3 (t, $J^3(^{19}F–^{19}F)$ = 21.0 Hz, s, *para*-C*F* aromatic), -167.0 (broad t, $J^3(^{19}F–^{19}F)$ = 21.0 Hz, *meta*-C*F* aromatic).

*Synthesis of [(IAd)Au$^+$(CH$_3$CN)][PF$_6^-$] (**5**):* In a scintillation vial, IAdAuCl (0.100 g, 1 equiv, 0.18 mmol) is partially dissolved in 2 mL of dried acetonitrile and $AgPF_6$ (0.047 g, 1.05 equiv, 0.18 mmol) is added. The solution is stirred for one minute. All the acetonitrile is removed by vacuum pump and replaced by 2 mL of DCM. Filtration over a plug of silicagel gives a clear greenish solution. After removal of the DCM by vacuum pump, the desired complex is recovered as a white powder. Yield: 0.113 g (88%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.35 (s, 2H, C*H* imidazole), 2.47 (m, 14H, C*H*$_2$), 2.25 (s, 6H, C*H*$_2$), 2.18 (s, 3H, C*H*$_3$ acetonitrile), 1.77 (m, 10H, C*H*$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 157.7 (s, *C*-carbene), 120.4 (s, N*C* acetonitrile), 118.6 (s, *C*H-imidazole), 60.5 (s, N*C*H-adamantyl), 45.3 (s, *C*H_2), 36.4 (s, *C*H_2), 31.0 (s, *C*H_2), 2.8 (s, *C*H_3 acetonitrile); ^{31}P NMR ($CDCl_3$): δ (ppm) = -141.3 (septet, $J^1(^{31}P–^{19}F)$ = 712.0 Hz, *P*F_6^-); ^{19}F NMR ($CDCl_3$): δ (ppm) = -74.0 (d, $J^1(^{19}F–^{31}P)$ = 712.0 Hz, P*F*$_6^-$).

*[(I^{t}Bu)Au$^+$(CH$_3$CN)][PF$_6^-$] (**6**):* In a scintillation vial, I^{t}BuAuCl (1 equiv., 50 mg, 121 μmol) is dissolved in 2 mL of acetonitrile and $AgPF_6$ (1 equiv., 31 mg, 121 μmol) is added. The solution is stirred one minute and filtered over celite to give a colorless solution. In acetonitrile, the complex

slowly decomposes within a few days. After removal of acetonitrile in vacuum, a white powder is isolated. ^{1}H NMR (CD_3CN) δ (ppm) = 7.38 (s, 2H, C*H*-imidazole), 1.83 (s, 18H, C(CH_3)$_3$); ^{13}C NMR (CD_3CN) δ (ppm) = 159.7 (s, *C*-carbene), 60.6 (s, N*C*(CH_3)$_3$), 32.7 (s, NC(*C*H$_3$)$_3$.

*[(IMes)Au^{+}(CH$_3$CN)][PF$_6^{-}$] (**7**):* In a scintillation vial, IMesAuCl (1 equiv., 50 mg, 93 μmol) is dissolved in 2 mL of acetonitrile and $AgPF_6$ (1 equiv., 24 mg, 93 μmol) is added. The solution is stirred one minute and filtered over celite to give a colorless solution. After one day in acetonitrile, extra signals appear in the ^{13}C NMR spectrum and are attributed to [(IMes)$_2$Au^{+}][PF$_6^{-}$]. After removal of acetonitrile in vacuum, a white powder is isolated which decomposes, turning purple, after few hours. ^{1}H NMR (CD_3CN) δ (ppm) = 7.50 (s, 2H, C*H*-imidazole), 7.15 (s, 4H, C*H*-aromatic), 2.38 (s, 6H, CH_3), 1.31 (s, 12H, CH_3); ^{13}C NMR (CD_3CN) δ (ppm) = 165.3 (s, *C*-carbene), 141.9 (s, *C*H-aromatic), 136.4 (s, *C*H-aromatic), 135.6 (s, *C*H-aromatic), 130.6 (s, *C*H-aromatic), 125.6 (s, *C*H-imidazole), 21.5 (s, *C*H (CH_3)$_2$), 18.2 (s, CH (CH_3)$_2$), 25.1 (s, CH (CH_3)$_2$).

*[((IPr)Au)$_2$(H$_2$O)$^{2+}$][PF$_6^{-}$]$_2$ (**8**):* In a scintillation vial, IPrAuCl (50 mg, 1 equiv, 0.081 mmol) is partially dissolved in 2 mL of DCM and wet $AgPF_6$ (31 mg, 1.5 equiv, 0.121 mmol) is added. The solution is stirred for one minute. Filtration over a plug of celite gives a clear greenish solution. After removal of the DCM by vacuum pump, the desired complex is recovered as a white powder. ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.55 (t, *J* = 8.0 Hz, 2H, C*H* aromatic), 7.25 (s, 2H, C*H* imidazole), 7.32 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 2.49 (septet, *J* = 7.0 Hz, 4H, C*H*(CH_3)$_2$), 1.23 (d, *J* = 7.0 Hz, 12H, CH(CH_3)$_2$), 1.22 (d, *J* = 7.0 Hz, 12H, CH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 162.2 (s, *C* carbene), 145.8 (s, *C*H aromatic), 133.2 (s, *C*H aromatic), 131.3 (s, *C*H

aromatic), 125.0 (s, *C*H aromatic), 124.7 (s, *C*H imidazole), 24.5 (s, CH(*C*H_3)$_2$), 24.5 (s, CH(*C*H_3)$_2$), 23.8 (s, CH(*C*H_3)$_2$), 2.8 (s, *C*H_3 acetonitrile); ^{31}P NMR ($CDCl_3$): δ (ppm) = -153.8 (septet, J^1(^{31}P–^{19}F) = 979.8 Hz, *P*F_6^-).

*Synthesis of [(IPr)Au$^+$(pyr)][PF$_6^-$] (**9**):* In a scintillation vial, [(IPr)Au$^+$(CH_3CN)][PF_6^-] (**1**) (100 mg, 1 equiv, 0.13 mmol) is partially dissolved in 2 mL of dried DCM and the pyridine (12 µl, 1.1 equiv, 1.44 mmol) is added. The solution is stirred for six hours. The DCM and the excess of pyridine are removed by pump vacuum. The desired complex appears to be a white powder. Yield: 91 mg (91%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 8.05-7.80 (broad m, 3H, C*H* pyridine), 7.58-7.52 (broad m, 2H, C*H* pyridine), 7.55 (t, *J* = 8.0 Hz, 2H, C*H* aromatic), 7.46 (s, 2H, C*H* imidazole), 7.33 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 2.53 (septet, *J* = 7.0 Hz, 4H, C*H*(CH$_3$)$_2$), 1.30 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$), 1.24 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 167.1 (s, *C* carbene), 150.6 (s, *C* pyridine), 145.8 (s, *C*H aromatic), 133.2 (s, *C*H aromatic), 131.3 (s, *C*H aromatic), 127.7 (broad s, *C* pyridine), 126.8 (s, *C* pyridine), 125.0 (s, *C*H aromatic), 124.7 (s, *C*H imidazole), 29.0 (s, CH(*C*H_3)$_2$), 24.5 (s, CH(*C*H_3)$_2$), 23.8 (s, CH(*C*H_3)$_2$); ^{31}P NMR ($CDCl_3$): δ (ppm) = -141.4 (septet, J^1(^{31}P–^{19}F) = 711.0 Hz, *P*F_6^-); ^{19}F NMR ($CDCl_3$): δ (ppm) = -74.2 (d, J^1(^{19}F–^{31}P) = 711.0 Hz, P*F*$_6^-$).

*Synthesis of [(IPr)Au$^+$(2-Brpyr)][PF$_6^-$] (**10**):* In a scintillation vial, [(IPr)Au$^+$(CH_3CN)][PF_6^-] (**1**) (200 mg, 1 equiv, 0.26 mmol) is partially dissolved in 2 mL of dried DCM and the 2-bromopyridine (26 µl, 1.05 equiv, 0.27 mmol) is added. The solution is stirred for six hours and the DCM is removed by pump vacuum. Pentane is added, and a filtration is made to remove the excess of 2-bromopyridine. Solids are washed with more pentane (2 x 2 mL). The desired

complex appears to be a white powder. Yield: 192 mg (82%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.95 (broad m, 1H, C*H* pyridine), 7.71 (broad m, 2H, C*H* pyridine), 7.65 (broad m, 1H, C*H* pyridine), 7.57 (t, *J* = 8.0 Hz, 2H, C*H* aromatic), 7.45 (s, 2H, C*H* imidazole), 7.35 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 2.53 (septet, *J* = 7.0 Hz, 4H, C*H*(CH_3)$_2$), 1.31 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$), 1.26 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 166.9 (s, *C* carbene), 152.7 (s, *C* pyridine), 145.3 (s, *C*H aromatic), 143.2 (s, *C* pyridine), 143.1 (s, *C* pyridine), 133.7 (s, *C*H aromatic), 131.7 (s, *C* pyridine), 131.3 (s, *C*H aromatic), 126.0 (s, *C* pyridine), 125.6 (s, *C*H imidazole), 124.9 (s, *C*H aromatic), 29.0 (s, CH(*C*H$_3$)$_2$), 24.7 (s, CH(*C*H$_3$)$_2$), 24.2 (s, CH(*C*H$_3$)$_2$); ^{31}P NMR ($CDCl_3$): δ (ppm) = -141.3 (septet, $J^1(^{31}P–^{19}F)$ = 711.0 Hz, *P*F_6^-); ^{19}F NMR ($CDCl_3$): δ (ppm) = -74.2 (d, $J^1(^{19}F–^{31}P)$ = 711.0 Hz, P*F*$_6^-$).

*Synthesis of [(IPr)Au$^+$(3-Brpyr)][PF$_6^-$] (**11**):* In a scintillation vial, [(IPr)Au$^+$(CH_3CN)][PF_6^-] (**1**) (200 mg, 1 equiv, 0.26 mmol) is partially dissolved in 2 mL of dried DCM and the 3-bromopyridine (26 µl, 1.05 equiv, 0.27 mmol) is added. The solution is stirred for six hours and the DCM is removed by pump vacuum. Pentane is added, and a filtration is made to remove the excess of 3-bromopyridine. Solids are washed with more pentane (2 x 2 mL). The desired complex appears to be a white powder. Yield: 188 mg (80%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 8.14 (broad m, 1H, C*H* pyridine), 7.91 (broad m, 2H, C*H* pyridine), 7.70 (broad m, 1H, C*H* pyridine), 7.59 (t, *J* = 8.0 Hz, 2H, C*H* aromatic), 7.45 (s, 2H, C*H* imidazole), 7.36 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 2.53 (septet, *J* = 7.0 Hz, 4H, C*H*(CH_3)$_2$), 1.32 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$), 1.27 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = δ 166.0 (s, *C* carbene), 150.9 (s, *C* pyridine), 149.5 (broad s, *C* pyridine), 145.6 (s, *C*H aromatic), 144.6 (broad s, *C* pyridine), 133.3 (s, *C*H aromatic), 128.9 (broad s, *C* pyridine), 131.4 (s, *C*H aromatic), 125.2 (s, *C*H imidazole),

124.6 (s, *C*H aromatic), 122.9 (broad s, *C* pyridine), 28.9 (s, CH(*C*H_3)$_2$), 24.8 (s, CH(*C*H_3)$_2$), 24.0 (s, CH(*C*H_3)$_2$); ^{31}P NMR ($CDCl_3$): δ (ppm) = -141.3 (septet, J^1(^{31}P–^{19}F) = 711.0 Hz, *P*F_6^-); ^{19}F NMR ($CDCl_3$): δ (ppm) = -73.5 (d, J^1(^{19}F–^{31}P) = 711.0 Hz, P*F*$_6^-$).

*Synthesis of [(IPr)Au$^+$(nbd)][PF$_6^-$] (**12**):* In a scintillation vial, [(IPr)Au$^+$(CH_3CN)][PF_6^-] (**1**) (500 mg, 1 equiv, 0.66 mmol) is partially dissolved in 5 mL of dried DCM and norbonadiene (nbd) (612 mg, 0.68 mL, 10 equiv, 6.6 mmol) is added. The solution is stirred overnight. All the DCM and the excess of norbonadiene is removed by vacuum pump and replaced by 10 mL of DCM. Filtration over a plug of silicagel gives a clear greenish solution. After removal of the DCM by vacuum pump, the desired complex is recovered as a white powder. Yield: 457 mg (84%). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.53 (t, *J* = 8.0 Hz, 2H, C*H* aromatic), 7.50 (s, 2H, C*H* imidazole), 7.30 (d, *J* = 8.0 Hz, 4H, C*H* aromatic), 6.85 (s, 2H, C*H* norbonadiene), 6.52 (s, 2H, C*H* norbonadiene), 3.62 (s, 2H, C*H* norbonadiene), 2.40 (septet, *J* = 7.0 Hz, 4H, C*H*(CH$_3$)$_2$), 1.40 (s, 2H, C*H*$_2$ norbonadiene), 1.25 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$), 1.23 (d, *J* = 7.0 Hz, 12H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): δ (ppm) = 182.0 (s, *C* carbene), 145.7 (s, *C*H aromatic), 143.2 (broad s, *C*H norbonadiene), 134.4 (very broad s only seen by HMQC sequence, *C*H norbonadiene), 133.1 (s, *C*H aromatic), 131.5 (s, *C*H aromatic), 125.1 (s, *C*H aromatic), 124.9 (s, *C*H imidazole), 52.2 (s, *C*H norbonadiene), 30.3 (s, *C*H norbonadiene), 28.9 (s, CH(*C*H_3)$_2$), 25.0 (s, CH(*C*H_3)$_2$), 24.0 (s, CH(*C*H_3)$_2$); ^{31}P NMR ($CDCl_3$): δ (ppm) = -141.4 (septet, J^1(^{31}P–^{19}F) = 713.0 Hz, *P*F_6^-); ^{19}F NMR ($CDCl_3$): δ (ppm) = -73.7 (d, J^1(^{19}F–^{31}P) = 713.0 Hz, P*F*$_6^-$).

*[(IPrAu)$^+$(THF)][PF$_6^-$] (**13**):* In a scintillation vial, IPrAuCl (1 equiv., 200 mg, 322 μmol) is dissolved in 2 mL of THF and $AgPF_6$ (1 equiv., 81 mg, 322 μmol) is added. The solution is

stirred one minute and filtered over celite to give a colorless solution. Overnight, the THF becomes a gel and two extra signals appear for the deuterated THF at 2.7 and 1.0 ppm downfield from the two normal THF signals. Appearance of colloidal gold(0) is observed after 3 days. After removal of THF in vacuum, a white powder is isolated and decomposes turning grey after a few hours. ^{1}H NMR (THF_{d8}) δ (ppm) = 7.82 (s, 2H, C*H*-imidazole), 7.59 (t, *J* = 8.0 Hz, 2H, C*H*-aromatic), 7.42 (d, *J* = 8.0 Hz, 2H, C*H*-aromatic), 2.57 (sept, *J* = 6.8 Hz, 4H, C*H*$(CH_3)_2$), 1.33 (d, *J* = 6.8 Hz, 12H, CH(C*H*$_3)_2$), 1.26 (d, *J* = 6.8 Hz, 12H, CH(C*H*$_3)_2$); ^{13}C NMR (THF_{d8}) δ (ppm) = 159.7 (s, *C*-carbene), 146.7 (s, *C*H-aromatic), 134.8 (s, *C*H-aromatic), 131.7 (s, *C*H-aromatic), 126.3 (s, *C*H-aromatic), 125.1 (s, *C*H-imidazole), 29.7 (s, *C*H $(CH_3)_2$), 25.8 (s, CH (*C*$H_3)_2$), 24.7 (s, CH (*C*$H_3)_2$).

6.4.3. Catalysis Protocol

0.01 mmol of (IPr)Au(MeCN)PF_6 were dissolved in 3 mL of the neat substrate in the case of alcohols, styrene, benzene or in a mixture of the substrate (5 mL) and dicholoromethane (5 mL) for amines or 2,3-dimethylbutane. EDA (0.25 mmol) was added in one portion (or with a syringe pump for 6 h in the case of the alkane). Reactions were monitored by GC, at time intervals shown in Table 1, and also the product identity confirmed by NMR spectroscopy. Yields were obtained following procedures described in previous work from this laboratory (see reference 17).

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6.6. Notes and references

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CHAPTER 7

SYNTHESIS AND CHARACTERIZATION OF GOLD(I) *N*-HETEROCYCLIC CARBENE COMPLEXES BEARING MOIETIES OF BIOLOGICAL INTEREST

7.1. Introduction

The use of gold salts in medicinal chemistry was first described in 2500 BC.[1] In modern chemistry, the interest in these salts as potential pharmacophores emerged in 1890 with the discovery of $Au(CN)_2^-$ and its bacteriostatic properties.[2] Almost forty years later, Forestier reported the first gold-based treatment against tuberculosis.[3] Today *in vivo* biochemistry of gold remains enigmatic, mainly due to a lack of adequate models and a lack of understanding of the reactivity of gold.[4] Moreover, as gold is not a metal naturally used in metabolism, it is believed that its chemistry *in vivo* differs from other transition metals such as iron and copper, which are carefully transported and stored by enzymatic processes.[5] The biochemistry of gold with D-penicillamine,[6] gluthadione,[7] thiomalic acid,[8] 2,3-dimercaptopropanol,[9] albumin[10] has been studied. The reactivity of gold occurs though the thiolate function of these biological molecules

and leads to the formation of gold(I) thiolates, also called chrysotherapy agents. These complexes are efficient against rheumatoid arthrisis and even HIV[11] and are commercialized under different trade names such as Myochrysine®, Solganol®, Krysolgan® and Allochrysine® for instances.[12] Other types of gold complexes used in medicinal chemistry are gold(I) mono- or bisphosphines. They can bind to DNA via the guanine and cytosine bases[13] and act as antitumor agents against L1210 leukemia and M5076 reticulum cell sarcoma.[14] In 1972, Sutton synthesized a gold complex with a thiolate and a phosphine ligand: the 2,3,4,6-tetra-O-acetyl-1-thio-β-D-pyranosato-S-(triethylphosphine)-gold(I) compound also known by the trade name Auranofin®. It became one of the most promising gold complexes in medicinal chemistry,[15] with a great potency against rheumatoid arthritis and cancer cells such as P388 leukemia and B16.[16]

In 1991, Arduengo showed that free *N*-heterocyclic carbenes (NHCs) are stable enough species to be isolated,[17] sparking an evergrowing interest in their chemistry. Since then, these ligands have been used extensively to stabilize transition metal complexes.[18] Their unusual and tunable electronic and steric properties have allowed for enhanced catalytic systems performance in palladium-catalyzed cross coupling reactions,[19] olefin metathesis,[20] and copper-catalyzed hydrosilylation[21], as most prominent examples. Gold(I) NHCs are known since 1989 and they can be neutral or cationic with the respective formulae (NHC)AuX and $(NHC)_2AuX$.[22] They are now widely used as catalysts for organic transformations such as nucleophilic additions on alkynes.[23] Nevertheless their potential applications in pharmacology have only recently started to be examined, thanks to the work of Baker *et al.* who have reported the antitumor activity of a cationic gold(I) bis-carbene by a mithocondrial membrane permeabilization (MMP) mechanism[24] and even synthesized the first carbenic aurofin mimics by substituting the phosphine ligand by different NHCs.[25]

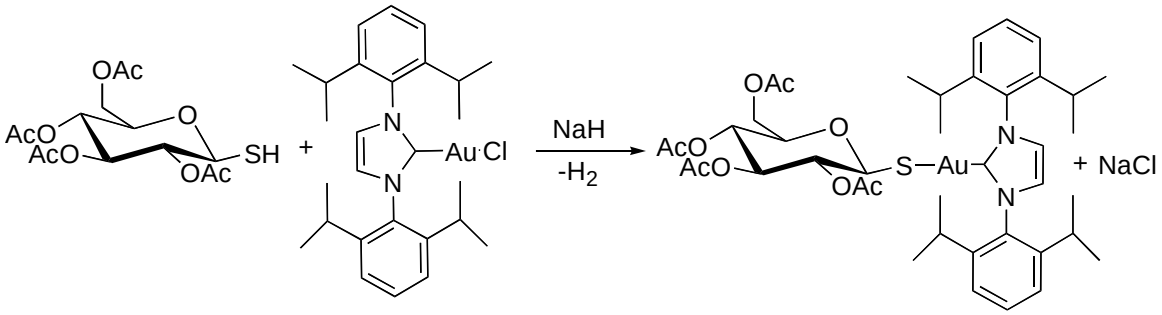
In this Note, we report the synthesis of a new NHC auranofin® mimic using an alternative approach than that recently employed by Baker. We also report the synthesis of a carbenic gold(I) saccharin complex by using for the first time a cationic monoligated NHC gold (I) as reagent.[26] This unstable complex been usually been proposed as an intermediate in gold-catalyzed transformations.[27]

7.2. Results and Discussion

7.2.1. Synthesis of gold(I) complexes

We first attempted to synthesize (IPr)AuTgt (**1**) (Tgt = 1-thio-*β*-D-glucose tetraacetate) by reacting directly the thiosugar with (IPr)AuCl[28] in refluxing dichloromethane (DCM). While the formation of HCl was expected to act as a driving force, no reaction was observed and the two starting materials were recovered. To enhance the nucleophilic behavior of the thio-carbohydrate, we generated the thiolate *in situ* using NaH. Addition of IPrAuCl permitted the bond formation between the electrophilic gold(I) and the nucleophilic thiolate. The overall reaction is favored by precipitation of sodium chloride. (Scheme 7.1) After filtration over a plug of silica gel and evaporation of the DCM, the desired complex was obtained in a good yield and analytically pure form as an off-white, air-stable powder. It is interesting to note that reaction of the cationic $[(IPr)Au^{+}(MeCN)][PF_6^{-}]$, generated *in situ* from IPrAuCl and $AgPF_6$, with either the thiol or the thiolate failed, the NMR spectra indicating a decomposition pathway.

Scheme 7.1. Synthesis of (IPr)AuTgt (**1**)



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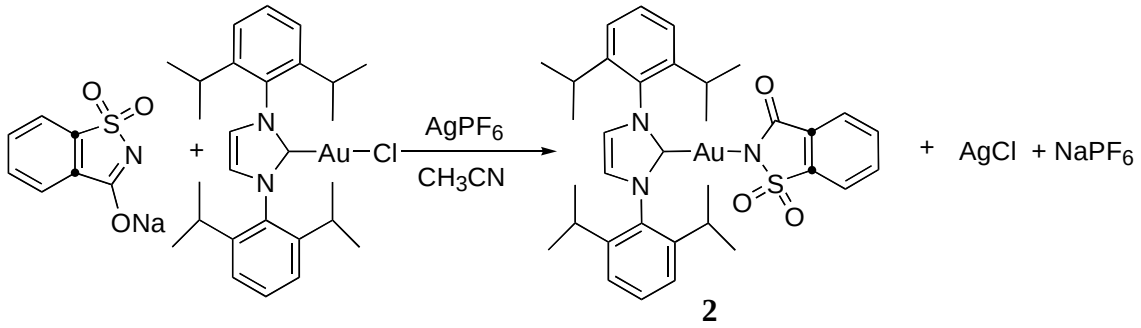
We first attempted to synthesize (IPr)AuSac (**2**) (Sac = saccharin) by directly reacting the sodium saccharin salt with (IPr)AuCl in DCM. While the formation of a gold-oxygen bond and the precipitation of NaCl were expected, no reaction was observed and the two starting materials were recovered. We attributed this lack of reactivity to the very poor affinity of gold for oxygen. To enhance the acidic character of the gold center, we generated the stable cationic $[(IPr)Au^{+}(MeCN)][PF_6^{-}]$ complex, by adding $AgPF_6$ in the presence of (IPr)AuCl. Addition of the saccharin salt allowed the slow formation of the desired complex with appearance of $NaPF_6$ as a white precipitate. (Scheme 7.2) To increase the kinetics of the reaction, an excess of saccharin salt (2:1) was used. After filtration over a plug of silica gel and the evaporation of the volatiles, the desired complex was obtained in good yield and analytically pure form as an off-white air-stable powder.

Scheme 7.2. Synthesis of (IPr)AuSac (**2**)



In order to unambiguously characterize both complexes NMR and X-Ray diffraction studies were performed. A mass spectroscopy IA-MALDI-TOF study of both complexes was performed in order to study their stability in the gas phase.

7.2.2. NMR Study of gold(I) complexes

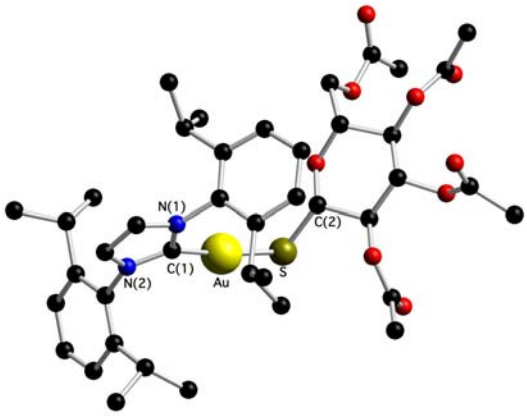
The ^{1}H NMR spectra of both complexes give a single resonance at 7.15 and 7.25 ppm respectively for the imidazole ring. The same pattern as IPrAuCl is observed for the two diisopropylphenyl groups, indicating that neither sugars prevents the free rotation of the isopropyl groups by steric hinderance.[28] For (IPr)AuTgt (**1**), the signal of the thiolate proton at 2.24 ppm disappears, indicating the bond formation between gold and sulfur while the four acetate groups appear as four well-defined singlets between 2.03 and 1.87 ppm. Moreover, all protons associated with the β-D-glucopyranose ring are shifted upfield and appear between 3.37 and 4.93 ppm.[25] For (IPr)AuSac (**2**), all aromatic protons are inequivalent. Two of these give well-defined doublets, shifted downfield while the others give a broad multiplet overlapping the triplet from the aromatic protons assigned to the IPr moiety. The ^{13}C NMR spectra of both

complexes exhibit a signal for their carbene carbon at 186.7 and 165.6 ppm respectively. A good indication of the influence of the ligands, especially of their electronic effects, toward the gold(I) center can be correlated to the chemical shift of the carbene carbon signal.[29] A strong electron donating ligand will trigger a downfield shift of the carbene carbon position. While the carbene carbon of (IPr)AuCl appears at 175.1 ppm,[28] it is obvious that both sugars for complexes (**1**) and (**2**) trigger two very different electronic environments around the gold(I) center. The sulfur appears to increase the electronic density at the gold(I) cation and appears to be strongly bound, as expected from its soft base character and its great affinity for gold. By comparing the carbene carbon signal of (IPr)AuSac (**2**) with the one reported for the cationic complex $[(IPr)Au^{+}(MeCN)][PF_6^{-}]$,[26] we can confirm that the nitrogen adds a small amount of electronic density on the gold(I) center and is probably weakly bound, as expected from its hard base character.

7.2.3. Structures of gold(I) complexes

Suitable crystals for X-ray diffraction were grown by slow diffusion of a mixture DCM / heptane for (IPr)AuTgt (**1**) and (IPr)AuSac (**2**). In the solid state, both complexes (Figure 7.1) exhibit a two-coordinate gold(I) atom in a nearly linear environment with a C–Au–S bond angle of 173.49° and a C–Au–N bond angle of 177.09°. The respective Au–C(1) distances of 1.986(6) Å and 1.973(4) Å are in good agreement with previously reported structures of neutral and cationic Au(I)NHC.[25-29]. The Au–S distance of 2.2873(16) Å for (IPr)AuTgt (**1**) is close to the ones found in anionic thiolate gold complexes,[30] and the Au–N distance of 2.031(3) Å for (IPr)AuSac (**2**) is similar to that found in complexes with nitrogen donor ligands.[31]

Figure 7.1. Ball and stick representations of complexes (IPr)AuTgt (**1**), (IPr)AuSac (**2**). Hydrogen atoms have been omitted for clarity



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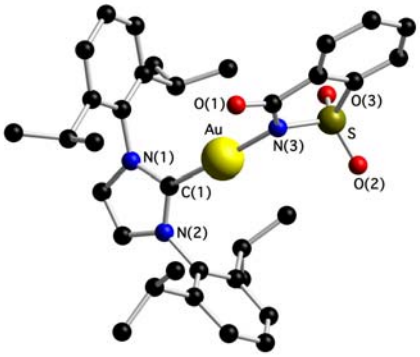

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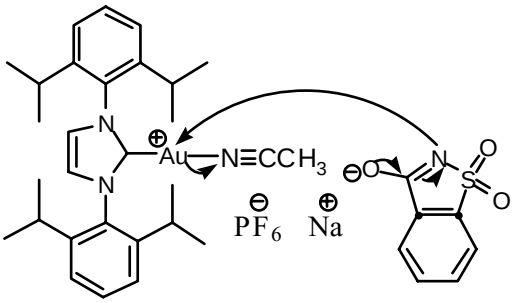
It is noteworthy that the gold(I) center binds the saccharin by the nitrogen due to the very poor affinity of gold for binding oxygen, and triggers a rearrangement between both possible resonance forms of the saccharin salt, enabling the moiety binding reaction (Scheme 7.3). For both complexes, there is no noticeable *trans*-effect of the carbene moiety toward the sugar ligands and no aurophilic interaction detected with a minimum Au•••Au distance of 7.392 Å and 9.451 Å, respectively, between gold centers.[32]

Scheme 7.3. Rearrangement of the sugar upon binding with the gold cation



We decided to investigate the stability of both complexes in the gas phase by using the mass spectroscopy technique. Inert-atmosphere MALDI-TOF mass spectrometric analysis[33] of (IPr)AuTgt (**1**) and (IPr)AuSac (**2**) was carried out using pyrene as a charge-transfer matrix. (Table 7.1)

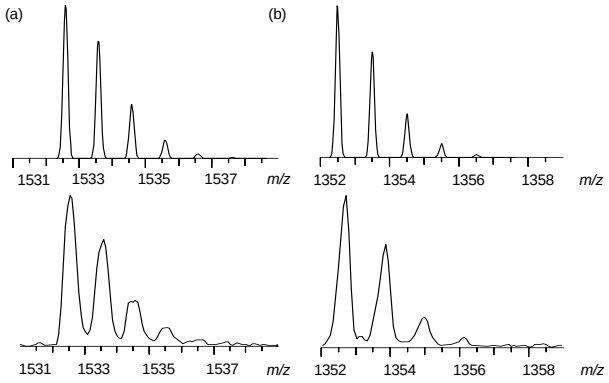
Table 7.1. Summary of MALDI mass spectrometric data obtained from analysis of (IPr)AuTgt (**1**) and (IPr)AuSac (**2**) in positive ion mode. (The asterisk indicates the base peak in each spectra)

	(IPr)AuTgt (1)		**(IPr)AuSac (2)**	
	m/z	Assignment	*m/z*	Assignment
Molecular ion	948.3	Not detected	767.3	Not detected
Agglomeration	1819.1	$[(IPr)_3Au_3S_2]^+$		
	*1787.2	$[(IPr)_3[Au_3S]^+$		
	1564.4	$[(IPr)_2Au_2S(Tgt)-H]^+$		
	1532.5	$[(IPr)_2Au_2(Tgt)-H]^+$	1352.1	$[(IPr)_2Au_2(Sac)]^+$
	1266.3	$[(IPr)_2Au_2S_3]^+$		
	1202.8	$[(IPr)_2Au_2S]^+$		
Fragments	847.1	$[H(IPr)_2Cl_2]^+$	*847.1	$[H(IPr)_2Cl_2]^+$
	787.1	$[(IPr)Au(pyrene)]^+$	787.1	$[(IPr)Au(pyrene)]^+$

Analysis in negative ion mode revealed signals due to $[CH_3COO]^-$ for (**1**) (presumably arising from fragmentation of the thiolate ligand, Tgt), as well as signals for the $[Sac]^-$ ligand for (**2**). In neither case could the intact molecular cations be observed in positive ion mode. Instead, prominent signals are present in each spectrum due to dinuclear Au complexes, resulting from

agglomeration in the gas phase. Ample precedents exist for aggregation of coordinatively unsaturated ions via ion-molecule interactions in the gas phase.[34] Of particular interest are peaks assigned to $[(IPr)_2Au_2(Tgt)\text{-}H]^+$ (**1a**) and $[(IPr)_2Au_2(Sac)]^+$ (**2b**), respectively, on the basis of the match between their simulated and observed isotope patterns (Figure 7.2). The complexity of the patterns is due to the isotopic composition of the ligands, as gold is monoisotopic.

Figure 7.2. Inert-atmosphere MALDI-MS spectra (pyrene matrix) showing simulated (top) and observed (bottom) isotope patterns for (a) $[(IPr)_2Au_2(Tgt)\text{-}H]^+$ (**1a**) (observed *m/z* 1532.5, calculated *m/z* 1532.3) and (b) $[(IPr)_2Au_2(Sac)]^+$ (**2b**) (observed *m/z* 1352.1, calculated *m/z* 1352.3)



While numerous peaks for aggregated Au complexes are evident in the spectrum of (**1**), including the peak for (**1a**), (**2b**) is the sole agglomeration product observed in the spectrum for (**2**) (see Table 1 for a summary of mass spectrometric data). Additional signals at high *m/z* in the mass spectrum of (**1**) are due to aggregation products resulting from the cleavage of the sugar moiety from the thiolate ligand, rather than loss of the entire (Tgt) ligand. Prominent among these are signals for $[(IPr)_3[Au_3S]^+$ (which is observed as the base peak) and $[(IPr)_2Au_2S]^+$. Retention of the sulfur donor, whether by rearrangement or by recapture following fragmentation reflects the

thiophilic nature of gold. It is worthy to note that for (**2**), there is no retention of nitrogen emphasizing the low affinity of gold to bind nitrogen. The gold(I) cation, present in the ion fragments, remains bound to the IPr ligand highlighting the very strong bond between gold and NHCs ligand, responsible for the exceptional stability of the complexes types. Present in the MALDI spectra for both (**1**) and (**2)** are peaks corresponding to $[H(IPr)_2Cl_2]^+$ (indeed, this signal is the base peak in the spectrum of (**2**)). Presumably this results from dimerization of the N-heterocyclic carbene, IPr, and capture of chloride ions from residual AuCl and/or starting material. It should be noted that the relative intensity of ion peaks in mass spectra does not necessarily correlate with abundance, the kinetic stability of the ion also playing a key role. The proportion of AuCl in the analyte itself is negligible, as judged from microanalysis. Also evident in the positive ion spectra are peaks due to $[(IPr)Au(pyrene)]^+$, which we attribute to scavenging of the coordinatively unsaturated $[(IPr)Au]^+$ by pyrene in the gas phase.

7.3. Conclusion

We report the synthesis, in good yield, of two new neutral gold(I) complexes with ligands of biological interest. Generation of the nucleophilic thiolate or the electrophilic cationic gold(I) center have allowed the reactions to proceed smoothly and efficiently. Structures of the new complexes have been confirmed by NMR and XRD. IA-MALDI-TOF mass spectroscopy provides information as to stability of (**1**) and (**2**) and decomposition routes accessible to compounds of this composition. Both complexes exhibit expected decomposition pathways in the gas phase in agreement with the chemistry of organogold complexes in solution and in the solid state. Further NMR studies have emphasized the difference of electronic donation between the sugars toward gold(I) centers and relies on the affinity of gold to bind these more or less basic

ligands. The ability of these (and related congener) complexes to bind DNA and act as potential chemotherapeutic agents is currently under study.

7.4. Experimental Section

7.4.1. General Considerations

- Complexes were synthesized using standard Schlenk techniques under an atmosphere of dry argon.
- Anhydrous solvents were either distilled from the appropriate drying agents or purchased from Aldrich and kept over molecular sieves.
- IA-MALDI-MS analyses were performed using a Bruker OmniFlex® MALDI TOF mass spectrometer equipped with a nitrogen laser (337 nm) and interfaced to an MBraun Labmaster® 130 glovebox.
- Data were collected in both positive and negative reflectron mode, with the accelerating voltage held at 20 kV for all experiments.
- Matrix (pyrene) and analyte solutions were prepared in acetontrile at concentrations of 20 and 1 mg/mL, respectively; samples were mixed in a matrix to analyte ratio of 20:1. Pyrene (99% purity) was used as received from Aldrich.
- Solvents for NMR spectroscopy were dried over molecular sieves. NMR spectra were collected on a 400 MHz Varian Gemini spectrometer.
- Elemental analyses were performed by Robertson Microlit Labs. (IPr)AuCl was synthesized following the literature procedure.[26]

7.4.2. Synthesis of gold(I) complexes

*Synthesis of (IPr)AuTgt (**1**):* In a oven-dried Schlenk flask under argon, 1-thio-β-D-glucose tetraacetate (59 mg, 0.16 mmol, 1 equiv.) was dissolved in 2 mL of DCM and the solution cooled at 0°C with the aid of an ice bath. NaH (6 mg, 0.24 mmol, 1.5 equiv.) was then added and allowed to react for 30 minutes after which time (IPr)AuCl (100 mg, 0.16 mmol) was added as a solid. The reaction was stirred overnight at room temperature. After filtration over a plug of silica gel and evaporation of volatiles, a white analytically pure powder was obtained (120 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (t, J = 8.0 Hz, 2H, C*H*-aromatic), 7.31 (m, 4H, C*H*-aromatic), 7.15 (s, *C*H-imidazole), 4.93 (t, J = 9.2 Hz, 1H, CH(C*H*)CH), 4.68 (t, J = 9.2 Hz, 1H, CH(C*H*)CH), 4.54 (d, J = 9.2 Hz, 1H, O(C*H*)S), 4.41 (t, J = 9.2 Hz, 1H, CH(C*H*)CH), 3.92 (m, 1H, CH(CH_2)O), 3.82 (m, 1H, CH(CH_2)O), 3.37 (m, 1H, CH_2(C*H*)O, 2.63-2.55 (m, 4H, C*H*(CH_3)$_2$), 2.03 (s, 3H, OCH_3), 2.02 (s, 3H, OCH_3), 1.95 (s, 3H, OCH_3), 1.87 (s, 3H, OCH_3), 1.35 (m, 12H, CH (CH_3)$_2$), 1.22 (m, 12H, CH (CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7 (s, *C*-carbene), 171.2 (s, O*C*O), 170.6 (s, O*C*O), 169.8 (s, O*C*O), 169.4 (s, O*C*O), 146.1 (s, *C*H-aromatic), 146.0 (s, *C*H-aromatic), 134.4 (s, *C*H-aromatic), 130.9 (s, *C*H-aromatic), 124.4 (s, *C*H-aromatic), 124.3 (s, *C*H-aromatic), 123.1 (s, *C*H-imidazole), 82.8 (s, O(*C*H)S), 75.2 (s, CH(*C*H)CH), 74.4 (s, CH(*C*H)CH), 69.7 (s, CH(*C*H)CH), 63.8 (s, CH(*C*H)CH), 29.0 (s, *C*H (CH_3)$_2$), 28.9 (s, *C*H (CH_3)$_2$), 24.6 (s, CH (*C*H_3)$_2$), 24.2 (s, CH (*C*H_3)$_2$), 21.1 (s, O*C*H_3), 21.0 (s, O*C*H_3), 20.9 (s, O*C*H_3), 20.8 (s, O*C*H_3).). Anal. calcd. for $C_{41}H_{55}N_2O_9SAu$ (948.44): 51.92 C, 5.80 H, 2.95 N, found: 51.74 C, 5.59 H, 2.67 N.

*Synthesis of (IPr)AuSac (**2**):* In an oven- dried Schlenk flask under argon, (IPr)AuCl (75 mg, 0.12 mmol, 1 equiv.) was dissolved in 2 mL of acetonitrile. $AgPF_6$ (31 mg, 0.12 mmol, 1 equiv.) was

added and the solution was stirred for 30 seconds, with the rapid appearance of a precipitate (AgCl). Then the saccharin sodium salt (54 mg, 0.24 mmol, 2 equiv.) was added and the solution was stirred overnight at rt. Acetonitrile was removed under reduced pressure and replaced by cold DCM. While the excess of saccharin sodium and AgCl salts are not soluble in cold DCM, the solution was filtered over celite and the solids were discarded. Evaporation of the DCM gave a white powder (60 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 6.4 Hz, 1H, C*H*-aromatic), 7.62 (d, J = 6.8 Hz, 1H, C*H*-aromatic), 7.52 (m, 4H, C*H*-aromatic), 7.32 (d, J = 7.2 Hz, 4H, C*H*-aromatic), 7.25 (s, 2H, *C*H-imidazole), 2.59 (sept, J = 6.8 Hz, 4H, C*H*$(CH_3)_2$), 1.42 (m, J = 6.8 Hz, 12H, CH (C*H*$_3)_2$), 1.25 (m, J = 6.8 Hz, 12H, CH (C*H*$_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2 (s, N*C*O), 165.6 (s, *C*-carbene), 145.9 (s, *C*H-aromatic), 142.0 (s, *C*H-aromatic), 133.9 (s, *C*H-aromatic), 132.8 (s, *C*H-aromatic), 132.7 (s, *C*H-aromatic), 132.1 (s, *C*H-aromatic), 131.1 (s, *C*H-aromatic), 124.5 (s, *C*H-imidazole), 124.1 (s, *C*H-aromatic), 123.5 (s, *C*H-aromatic), 120.2 (s, *C*H-aromatic), 29.2 (s, *C*H $(CH_3)_2$), 24.7 (s, CH (*C*$H_3)_2$), 24.3 (s, CH (*C*$H_3)_2$). Anal. calcd. for $C_{41}H_{55}N_2O_9SAu$ (948.44): 53.14 C, 5.21 H, 5.47 N, found: 52.97 C, 5.30 H, 5.37 N.

7.5. Acknowledgments

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CHAPTER 8

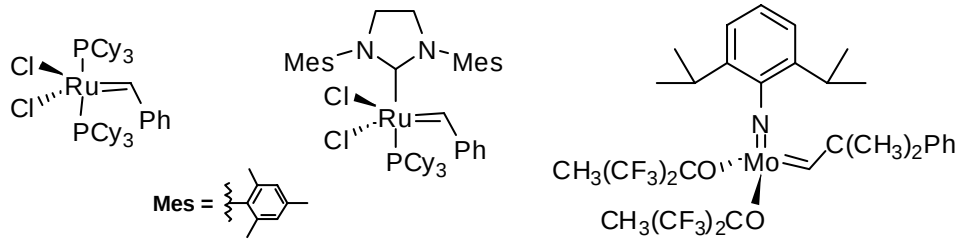
RUTHENIUM-INDENYLIDENE COMPLEXES IN RING OPENING METATHESIS POLYMERIZATION (ROMP) REACTIONS

8.1. Introduction

Metal catalyzed carbon-carbon bond forming reactions represent very powerful tools in organic and polymer chemistry.[1] The olefin metathesis reaction represents one such important C-C bond forming method. The versatility of the method, in its many incarnations: Ring Closing Metathesis (RCM), Cross Metathesis (CM), Ring Opening Polymerization Metathesis (ROMP), or Acyclic Diene Metathesis Polymerization (ADMET) cannot be overstated. In 2005, Chauvin, Grubbs and Schrock received the Nobel Prize for their contributions to the development of this reaction and of the associated eponymous catalysts[2] (Scheme 8.1). Developed in the early 1990's, the Schrock catalyst based on Molybdenum was found extremely active.[3] But its use was limited by its air sensitive nature as well as by its low tolerance to functional groups.[4] In the mid 1990's, Grubbs *et al*. developed a series of active ruthenium alkylidene catalysts, including **G-I**, with enhanced tolerance toward functionalized alkenes.[5] In the late 1990's, Hermann *et al.*[6] developed

a new class of ruthenium catalyst, bearing two *N*-heterocyclic carbene ligands (NHC). He was then followed a few months later by Nolan and Grubbs reporting separately some ruthenium catalysts, bearing some mixed phosphine / *N*-heterocyclic carbene ligands, with enhanced activity, stability and great tolerance toward functionalized olefins.[7]

Scheme 8.1. Commercially available Grubbs and Schrock Catalysts



Grubbs catalyst 1st generation — **G-I**

Grubbs catalyst 2nd generation — **G-II**

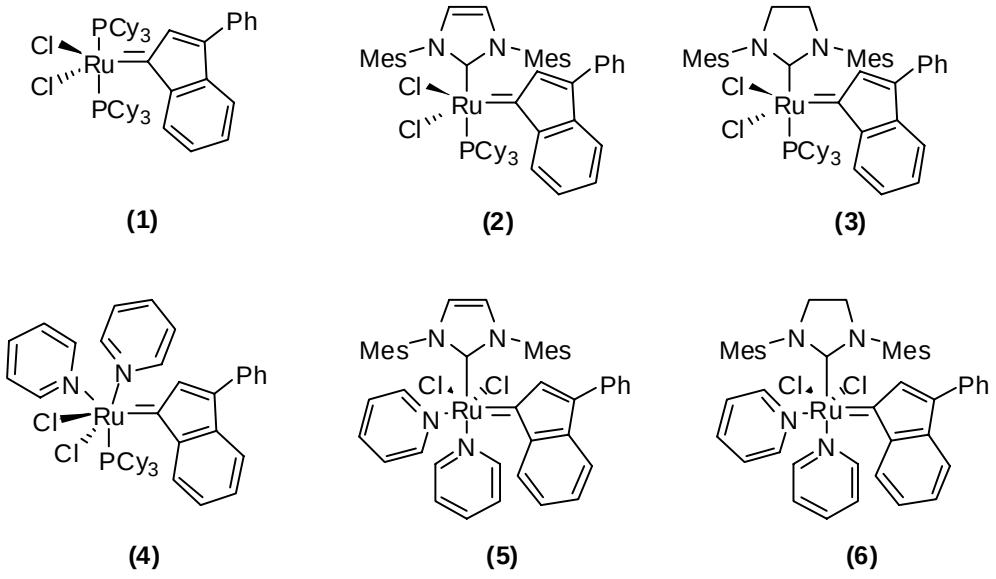
Schrock catalyst

The metathesis reaction is comprised of an initiation and a propagation step with two distinct reaction intermediates.[8] Contrary to the RCM and CM reactions, the rate of initiation is a critical feature for controlled ROMP and the synthesis of well-defined polyolefins.[9] The controlled behavior of a catalyst depends on a subtle mix of its ability to provide good initiation and the stability of the generated propagating species. Tremendous efforts have been undertaken to rationalize the mechanism of the metathesis reaction and to design a most efficient catalyst.[8b,10] Among the numerous scaffolds available, we focused our study on the synthesis and application of the less investigated indenylidene ruthenium-based catalysts. This class of catalyst was synthesized initially by Hill in its phosphine-based version[11] and by Nolan,[12] in its NHC derived version. The second-generation Ruthenium NHC complexes were found more active in RCM and

CM, and more thermally stable than Grubbs' catalysts bearing the benzylidene moiety.[13] The ROMP of strained cyclo-olefins is a very efficient route to access a wide range of unsaturated functionalized polymers with common poly-isoprene or 1,4-poly-butadiene backbones.[9,14] Suitable monomers for ROMP include, for example, norbornene, cyclopentadiene, cyclobutadiene, cyclooctene and cycloocta-1,5-diene (COD).[6,9b,15] Due to its moderately strained cyclic structure, COD reacts smoothly in ROMP and is commonly used to benchmark new catalyst reactivity.[16]

In the present paper, we report the evaluation in ROMP of six well-defined ruthenium-indenylidene based catalysts (**1-6**) (Scheme 8.2) and a reactivity comparison with the two commercially available Grubbs 1st (**G-I**) and 2nd (**G-II**) catalysts. Reactions were monitored by ^{1}H NMR and SEC. These ruthenium-indenylidene catalysts were synthesized according the literature procedures[13a,17] with the exception of (**3**) being commercial.[18]

Scheme 8.2. Indenylidene catalysts used to polymerize cycloocta-1,5-diene (COD)



8.2. Results and discussion

8.2.1. General procedure for monitoring the polymerizations

Under argon, in deuterated chloroform, a stock solution of catalyst and a stock solution of COD containing CH_2Br_2 were prepared. In a NMR tube sealed with a septum, a desired volume of each solution was injected, in order to keep the monomer / initiator ratio [M]/[I] near 50 and the final volume equal to 400 µL with a constant concentration of COD. At 20 ºC, the progress of the polymerization was monitored by ^{1}H NMR by following the disappearance of the characteristic signal associated with the unsaturation of the COD at 5.52 ppm.

8.2.2. General procedure for the kinetic study of polymerizations

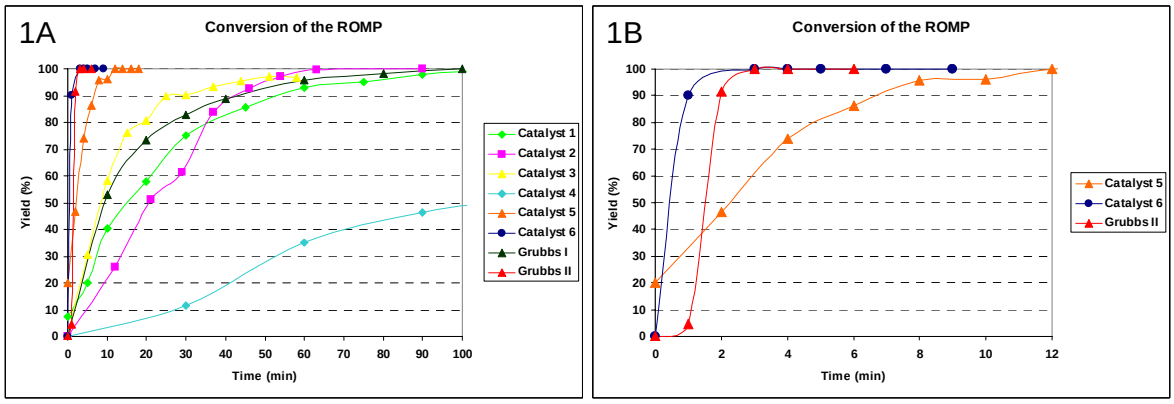
Under argon, using chloroform, a stock solution of catalyst and a stock solution of COD containing CH_2Br_2 were prepared. At 20 ºC, the catalyst solution was injected into the COD solution keeping the [M]/[I] ratio and the COD concentration equal to 50.[18] At the indicated time intervals, a 100 µL aliquot of the crude reaction mixture (roughly 10 mg of polymers) was sampled and injected in a NMR tube containing 10 µL of ethyl vinyl ether to quench the polymerization (30 equiv. compared to the COD present in the aliquot). The progress of the polymerization was monitored by ^{1}H NMR by following the disappearance of the characteristic signal associated to the COD unsaturation at 5.52 ppm. The solution contained in each tube, was then dried in vacuum and acetone was added to trigger the precipitation of the polybutadiene. The polymer was immobilized on a plug of silica gel, and the acetone solution was discarded. Rinsing

the plug with DCM followed by its evaporation, gave clean polybutadiene as a white solid. This polymer sample was then dissolved in a 1:1000 solution of THF:toluene, then filtered and injected in the SEC column.

8.2.3. NMR study of polymerizations

At room temperature, all catalysts give nearly quantitative conversion of the COD, with the notable exception of **4** that requires much longer reaction times to reach high consumption of COD. Catalysts can be divided in two groups based on reaction time. The first group comprised of **1**, **2**, **3** and **G-I** allow reactions to reach completion within 2 hours (Figure 8.1A), while the second group, made up of **5**, **6** and **G-II**, exhibits very high activity with reaction times shorter than 10 minutes (Figure 8.1B).

Figure 8.1. Catalyst reactivity profile in ROMP as a function of time



As expected, **G-I** and its indenylidene analogue **1** exhibit similar kinetic behavior and represent the most sluggish reactions. Complex **2** exhibits higher activity than **1** and **G-I**, as a phosphine

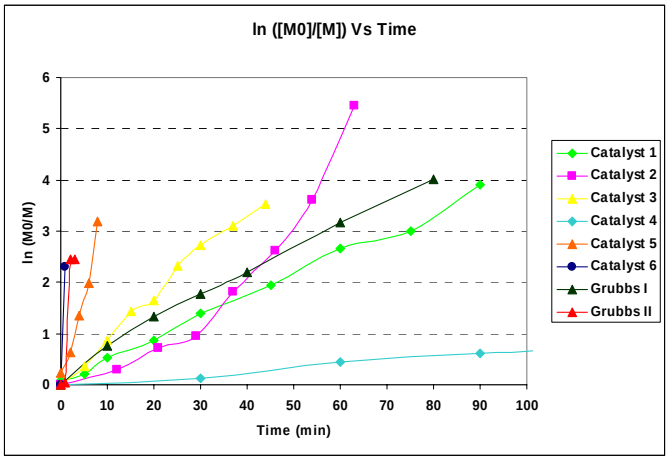
ligand has been replaced by *N,N'*-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes). Complex **3** gives the fastest ROMP activity, for the first group of catalysts. However this performance is unexpectedly slow compared to its benzylidene congener **G-II**. Interestingly, examination of the reaction profiles within this "slow group" shows that replacing a benzylidene by an indenylidene does not guarantee increased catalytic activity, as is reported for RCM reactions.[13b]

Among the second group of catalysts, **5** is the least active, and contrary to **6** and **G-II** bears a saturated NHC, *N,N'*-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene (SIMes). A closer look, at the kinetic plots for **6** and **G-II** (Figure 8.1B) shows that while both catalysts quantitatively polymerize the COD in less than 3 minutes, **6** initiates faster than **G-II**. This result emphasizes the fact that Ru-pyridine based catalysts initiate very fast due to an easy dissociation of the pyridine from the Ru center leading the 14 electrons active species.[10c] This argument is of course also valid for ROMP. In contrast to **G-II**, the dissociation of the phosphine from the Ru center is not so rapid, resulting in slower initiation.[10e] The study of this second group of catalysts ultimately demonstrates that using the (NHC)-ligands SIMes and pyridine allows the formation of highly active catalytic species for ROMP. In view of its structure, we expected **4** to display reactivity between **5** and **G-I**. In fact, this catalyst shows poor conversion after extended reaction time. We believe that this atypical behavior is due to the instability of the propagating species, as postulated previously in RCM.[17c]

While having high conversion for RCM and CM is acceptable, synthesizing polymers with well-defined structures by ROMP requires a controlled polymerization. A living polymerization, where the concentration of propagating species remains constant without any termination, is a key step to control. If the polymerization is "living"[10a,20] the time dependence of the log concentration of the monomer disappearance ($\ln [M]_{t=0}/[M]_t$) should be linear, indicating

first order kinetics for the monomer consumption. The plots for each catalyst are drawn in Figure 8.2.

Figure 8.2. Logarithmic plot of the COD concentration [M] versus time ([M0] = $[M]_{t=0}$) during ROMP of COD



Catalysts **G-1** and **1** exhibit a nearly linear behavior indicating a lack of termination and a correct initiation. In contrast **2** and, to a lesser extent **5**, exhibit a curved plot typical of a low rate of initiation compared to the propagation. Complex **3** exhibits some weak signs of early termination. Surprisingly, **4** does not exhibit any sign of early termination. This suggests that part of the catalyst decomposes during the initiation step. Depending on the propagation rate, a more significant amount of **4** might decompose to keep the overall rate of COD consumption small. Finally, **G-II** exhibits delayed initiation compared to **6**, but a very similar rate of polymerization is observed for both catalysts.

8.2.4. Size Exclusion Chromatography study of polymerizations

Very active ruthenium catalysts suffer from a lack of control in ROMP due to extensive transfers (or secondary metathesis reactions) between growing polymer chains. In 1998, Grubbs *et al*. stated that the ROMP of COD with first generation catalyst gave kinetic data too complicated to be rationalized.[15b] Two years later, they were still producing polybutadienes with high PDIs, but with a partial control of the number-average molecular weight.[21] If the polymerization is living and transfer free, the number-average molecular weight of the polybutadiene should increase linearly with the conversion (or consumption of COD) and the PDI value should remain as low as 1.05. Surprisingly, we were not able to find any published examples of controlled ROMP of COD using a ruthenium catalyst.

For each catalyst, we followed by size exclusion chromatography the evolution of the polybutadiene number-average molecular weight ($\overline{Mn}$) and the PDI value, as the polymerization was proceeding (Figures 8.3A, 8.3B, and Table 8.1). These values were corrected to account the difference between the hydrodynamic radius of the analyzed polybutadiene chains and the polystyrene chains used to calibrate the SEC column.[22]

Figures 8.3A & 8.3B. Evolution of the $\overline{Mn}$ versus conversion

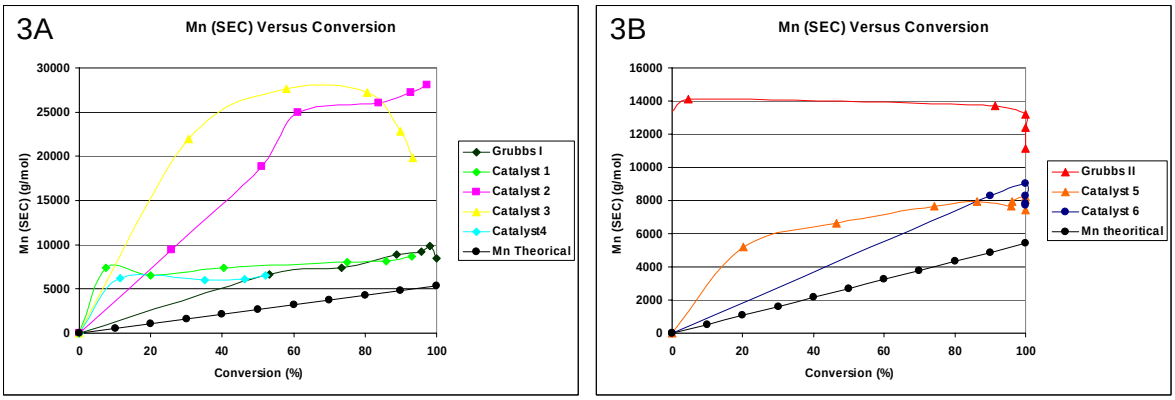


Table 8.1. Catalyst efficiency and PDI of the polymers

Catalyst	Yield (%)	$\overline{Mn}$ [b] (SEC)	$\overline{Mn}$ [c] (theoric)	PDI [b]	f [c]
1	98	8700	5290	1.46	0.61
2	100	28065	5400	3.88	0.19
3	97	22005	5240	1.93	0.24
4	46	6495	2485	1.25	0.38
5	100	8075	5400	1.43	0.67
6	100	7810	5400	1.47	0.69
G-I	100	8480	5400	1.43	0.63
G-II	100	11120	5400	1.70	0.49

[a] General conditions: Ratio [M]/[I] = 50, T = 20 ºC, t_{max} = 100 min (polymerization incomplete). [b] $\overline{Mn}$ reported are corrected as the SEC column is calibrated with polystyrene. [c] Initiation efficiency: $f = \overline{Mn}_{theoric}/\overline{Mn}_{SEC}$ with $\overline{Mn}_{theoric} = \{[M]/[I]\}_{t=0} \times M_{monomer} \times (Yield/100)$.

For all catalysts, the experimental data are characteristic of an uncontrolled polymerization with extensive chain transfer. At low conversion, the number-average molecular weight ($\overline{Mn}$) of all polybutadienes are very important and grow fast, compared to the theoretical $\overline{Mn}$ calculated for a controlled polymerization. They highlight a partial initiation of the catalyst, generating very active propagating species. As transfers, to polymers, begin to compete with polymerization, the lengths of the polymers chains stop growing after 20 % conversion for **1**, **4**, **G-II** and after 50 % conversion for **2**, **3**, **5**, **G-I** while the PDI values keep increasing. The mass are statistically redistributed depending upon the location of chain transfer on the polymer backbone. At higher or quantitative conversion, the transfers become predominant as the COD

become scarce, and the number-average molecular weigh tend to slightly decrease. All catalysts exhibit low initiation efficiency (*f*). Interestingly the best results come from the highly active catalysts **5** and **6**. As a result of this strong tendency to catalyze cross metathesis (transfers), at 100 % conversion, adding 100 equivalents of COD does not promote any significant chain growth. As the catalyst is still active, we observe even more transfers, with an associated increase in the PDI (Table 8.2). These results seem to indicate that surprisingly, after a limit size for the chains, only transfer reactions occur independently of the monomer concentration.

Table 8.2. Evolution of the $\overline{Mn}$ and PDI of a polymerization in two steps

	1		5		6		G-II	
	$\overline{Mn}$	PDI	$\overline{Mn}$	PDI	$\overline{Mn}$	PDI	$\overline{Mn}$	PDI
Block 1	9470	1.46	8070	1.43	7810	1.47	11110	1.70
Block 2	10700	1.62	6700	1.66	10720	1.53	6910	2.54

8.2.5. Stereochemistry of polybutadienes

For low strained cyclic monomers, benzylidene catalysts usually don't allow for control of the stereochemistry (*cis*/*trans*) of the polyolefins.[9] Nevertheless, a high proportion of chains transfer and/or secondary metathesis isomerization can increase the proportion of *trans*-stereoisomers up to 70-90%.[9] The stereochemistry of the polybutadienes synthesized with the indenylidene based catalysts **1**-**6**, was determined by using a ^{13}C NMR INVERSE GATE

sequence (Table 8.3). Complexes **2** and **4** gave polyolefin with a surprisingly low proportion of *trans*-stereoisomoers. We are further investigating these anomalous results.

Table 8.3. Percentage (%) of *cis* and *trans* stereoisomers present in the ROMP product.

Catalyst	1	2	3	4	5	6
$\%_{cis}$	17	51	24	60	22	18
$\%_{trans}$	83	49	76	40	78	82

8.3. Conclusion

In this study, we have used the low strained cycle COD as monomer to test eight well-defined ruthenium pre-catalysts including Grubbs 1st and 2nd generation complexes. We have observed that ligand/structural variations on the catalysts do have a profound effect on polymerization kinetic behavior. While all catalysts, with the exception of **4**, were highly active for the ROMP of COD, none performs the polymerization in a controlled manner due to important chain transfer behavior. This astonishing lack of control on an apparently very straightforward polymerization highlights the remaining challenge of catalyzing efficiently the ROMP of low strained cycles without sacrificing the control of the polymeric architecture. The synthesis of new indenylidene ruthenium catalysts, more specifically dedicated to the controlled ROMP of low strained monomers, is under investigation in our laboratories.

8.4. Experimental section

8.4.1. General considerations

- All solvents, the cycloocta-1,5-diene (COD) and the ethyl vinyl ether were purchased from ACROS.
- Deuterated chloroform ($CDCl_3$) was purchased from Cambridge Isotope Laboratories, Incorporation.
- Chloroform was washed with distilled water, dried and distilled from $CaCl_2$ under argon. Acetone, COD, dibromomethane, dichloromethane (DCM) were dried and distilled according to standard procedures.[19]
- Catalysts **G-I** and **G-2** were purchased from Aldrich. Catalyst **3** was bought from STREM Inc.[18] while catalysts **1**, **2**, **4**, **5** and **6** were synthesized according to literature procedures.[13a,17]
- All chemicals used for the kinetic studies were degassed under argon.
- Dibromomethane was used as the internal reference to follow the kinetics by ^1H NMR spectroscopy.

8.4.2. Measurements and spectroscopy

- NMR spectra were recorded on a Bruker AC-400 spectrometer for ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz).
- Chemical shifts are reported in ppm relative to the tetramethylsilane (TMS) resonance.

- Number-average molecular weights ($\overline{Mn}$) and polydispersity indexes (PDI) were measured using size exclusion chromatography (SEC) on a system equipped with a SpectraSYSTEM AS 1000 autosampler, with a guard column (polymer laboratories, PL gel 5 μm guard column, 50 x 7.5 mm) followed by two columns polymer laboratories, 2 PL gel 5 μm MIXED-D columns, 2 x 300 x 7.5 mm), with a SpectraSYSTEM RI-150.
- The eluent used was THF at a flow rate of 1 $ml.min^{-1}$ at 35 ºC. Polystyrene standards (580-483 x 10^3 $g.mol^{-1}$) were used to calibrate the SEC.

8.4.3. Procedures for the kinetic study of polymerizations

*Catalyst **1**:* At 20 ºC, in a 25 mL Schlenk flask under argon, **1** was dissolved in 2.97 ml of $CDCl_3$ (50 mg, 1 equiv., 0.018 $mmol.ml^{-1}$), then the COD (293 mg, 49.9 equiv., 0.912 $mmol.ml^{-1}$) was added. NMR tubes were loaded with 10 μL of ethyl vinyl ether, 10 μL CH_2Br_2 as internal reference, and $CDCl_3$. At defined time, 100 μL of the reaction crude were injected in a tube and NMR was performed. The solution contained into each tube, was dried out and 2 mL acetone was added triggering the precipitation of the polybutadiene. The polymer was immobilized on a plug of silica gel, and washed with more acetone (5 ml). Rinsing the plug with DCM (5 mL) followed by its evaporation, gave clean polybutadiene as a white solid. This one was dissolved in a 1:1000 solution of THF:toluene, then filtered to be injected in the SEC column. All polybutadiene solutions were purged with nitrogen and kept in the freezer to avoid degradation of the polymer by oxidation.

*Catalyst **2**:* At 20 ºC, in a 25 mL Schlenk flask under argon, **2** was dissolved in 4.01 ml of $CDCl_3$ (60 mg, 1 equiv., 0.018 $mmol.ml^{-1}$), then the COD (343 mg, 50.1 equiv., 0.913 $mmol.ml^{-1}$) was added. NMR tubes were loaded with 10 µL of ethyl vinyl ether, 10 µL CH_2Br_2 and $CDCl_3$. At defined time, 100 µL of the reaction crude were injected in a tube and NMR was performed. The remainder of the procedure is similar to that described for catalyst **1**.

*Catalyst **3**:* At 20 ºC, in a 25 mL Schlenk under argon, **3** was dissolved in 3.29 ml of $CDCl_3$ (57 mg, 1 equiv., 0.018 $mmol.ml^{-1}$), then the COD (325 mg, 50.1 equiv., 0.913 $mmol.ml^{-1}$) was added. NMR tubes were loaded with 10 µL of ethyl vinyl ether, 10 µL CH_2Br_2 and $CDCl_3$. At defined time, 100 µL of the reaction crude were injected in a tube and NMR was performed. The remainder of the procedure is similar to that described for catalyst **1**.

*Catalyst **4**:* At 20 ºC, in a 25 mL Schlenk flask under argon, **4** was dissolved in 1.38 ml of $CDCl_3$ (20 mg, 1 equiv., 0.018 $mmol.ml^{-1}$), then the COD (136 mg, 50.3 equiv., 0.911 $mmol.ml^{-1}$) was added. NMR tubes were loaded with 10 µL of ethyl vinyl ether, 10 µL CH_2Br_2 and $CDCl_3$. At defined time, 100 µL of the reaction crude were injected in a tube and NMR was performed. The remainder of the procedure is similar to that described for catalyst **1**.

*Catalyst **5**:* At 20 ºC, in a 25 Schlenk flask under argon, **5** was dissolved in 3.12 ml of $CDCl_3$ (47 mg, 1 equiv., 0.018 $mmol.ml^{-1}$), then the COD (308 mg, 50.0 equiv., 0.913 $mmol.ml^{-1}$) was added. NMR tubes were loaded with 10 µL of ethyl vinyl ether, 10 µL CH_2Br_2 and $CDCl_3$. At defined time, 100 µL of the reaction crude were injected in a tube and NMR was performed. The remainder of the procedure is similar to that described for catalyst **1**.

*Catalyst **6**:* At 20 ºC, in a 25 Schlenk flask under argon, **6** was dissolved in 2.93 ml of $CDCl_3$ (44 mg, 1 equiv., 0.018 $mmol.ml^{-1}$), then the COD (289 mg, 50.2 equiv., 0.912 $mmol.ml^{-1}$) was added. NMR tubes were loaded with 10 µL of ethyl vinyl ether, 10 µL CH_2Br_2 and $CDCl_3$. At defined time, 100 µL of the reaction crude were injected in a tube and NMR was performed. The remainder of the procedure is similar to that described for catalyst **1**.

*Catalyst **G-I**:* At 20 ºC, in a 25mL Schlenk flask under argon, **G-I** was dissolved in 2.33 ml of $CDCl_3$ (35 mg, 1 equiv., 0.018 $mmol.ml^{-1}$), then the COD (289 mg, 50.0 equiv., 0.913 $mmol.ml^{-1}$) was added. NMR tubes were loaded with 10 µL of ethyl vinyl ether, 10 µL CH_2Br_2 and $CDCl_3$. At defined time, 100 µL of the reaction crude were injected in a tube and NMR was performed. The remainder of the procedure is similar to that described for catalyst **1**.

*Catalyst **G-II**:* At 20 ºC, in a 25 mL Schlenk flask under argon, **G-II** was dissolved in 2.13 ml of $CDCl_3$ (33 mg, 1 equiv., 0.018 $mmol.ml^{-1}$), then the COD (289 mg, 49.9 equiv., 0.911 $mmol.ml^{-1}$) was added. NMR tubes were loaded with 10 µL of ethyl vinyl ether, 10 µL CH_2Br_2 and $CDCl_3$. At defined time, 100 µL of the reaction crude were injected in a tube and NMR was performed. The remainder of the procedure is similar to that described for catalyst **1**.

8.4.4. Polymerizations in two steps (Table 8.2)

Under argon, when the full conversion was reached, 200 µL of the crude polymerization mixture was transferred into a capped vial. Then COD was added (100 equiv.). Time of reaction was doubled then ethyl vinyl ether was added (30 equiv.). The solution was dried out and 2 mL acetone was added triggering the precipitation of the polybutadiene. The polymer was

immobilized on a plug of silica gel, and washed with more acetone (5 ml). Rinsing the plug with DCM (5 mL) followed by its evaporation, gave clean polybutadiene as a white solid. This one was dissolved in a 1:1000 solution of THF:toluene, then filtered to be injected in the SEC column. All polybutadiene solutions were blanketed with nitrogen and kept in the freezer to avoid oxidation of the polymer.

8.4.5. NMR data

Cycloocta-1,5-diene (COD): ^{1}H NMR ($CDCl_3$): δ = 5.52 (m, 4H,), 2.30 (m, 8H)

Polybutadiene: ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 5.31 (broad m, 4H), 2.00 (broad m, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 130.1 (*C*H), 129.5, (*C*H), 32.7 ($C_{trans}H_2$), 27.4 ($C_{cis}H_2$)

8.5. Acknowledgments

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CHAPTER 9

SUMMARY AND CONCLUSION

The main area of research was the synthesis of well-defined palladium(II), silver(I), gold(I), gold(III) and ruthenium(II) N-heterocyclic carbene complexes, as potential catalysts for organic transformations. Carbenes with different steric and electronic properties were synthesized and employed whereas the resulting complexes were characterized by ^{1}H, ^{11}B, ^{13}C, ^{19}F, ^{31}P NMR and X-ray diffraction. Analytical techniques showed that the behavior of the metal centers were strongly dependant on the NHC employed, in term of stability and structure of the complexes.

We synthesized palladium(II) complexes with good activity in cross-coupling reactions,[1] in high yield, following a simple one-pot reaction between imidazolium salts and bis-acetylacetonate palladium(II), carried in air with technical grade solvents.[2] This straightforward synthetic route could be scaled up without any loss of yield.

We synthesized mono-NHC silver(I) chloride complexes in high yield by direct addition of silver chloride to NHCs or by reaction of imidazolium salts with silver(I) oxide, according to a

method described by Lin.[3] By carefully monitoring the reaction conditions, we succeeded to avoid the thermodynamically favored formation of cationic silver(I) bis-NHC complexes.[4] Our complexes were used as transmetallating agents to access gold(I) and rhodium(I) NHCs.[5,6]

We synthesized mono-NHC gold(I) chloride complexes in high yield by reaction of dimethylsulfide gold(I) chloride with NHCs or by transmetalation from a silver(I) NHC precursors, a method described by Lin.[7] The gold(I) cation is extremely well stabilized by the NHC ligand and the complexes were air and light stable.[5] They could not undergo electrochemical reduction to gold(0) even with a potential as low as -3.2 V.[8]

We synthesized mono-NHC gold(III) complexes in excellent yield by oxidative addition of bromine to mono-NHC gold(I) halide complexes.[9] These gold(III) complexes catalyzed the addition of alcohol onto alkynes as the first example of organic transformation mediated by gold(III) NHCs.[9] They were still strong oxidants and were reduced by primary alcohols to the corresponding gold(I) NHCs.[8] In this regard, the redox couple (NHC)Au(III)X_3/(NHC)Au(I)X (X = halide) might find an application to catalyze 2-electron transfer reactions.

We synthesized and isolated cationic mono-NHC gold(I) complexes by reaction of silver or sodium salts with the neutral mono-NHC gold(I) halide complexes.[10] They are the actual catalytically active species in organic transformations mediated by gold(I) NHC and were thought to be too unstable to be isolated.[11] Our complexes were efficient for alkynes, allenes and alkenes activation and catalyzed the cyclopropanation of enynes, or the hydroarylation of allenes notably.[12] They are strong Lewis acids and reacted with various nucleophiles, yielding unusual NHC-gold(I) complexes of pyridines, olefins (norbonadiene), water and thiosugar.[8,13]

We synthesized ruthenium(II) complexes bearing indenylidene moieties, monitored their activity in ring opening metathesis polymerization and compared them with the commercially available Grubbs catalysts.[14] Our complexes were efficient to initiate fast but uncontrolled polymerization of olefins.

In summary, several families of well-defined NHC complexes of various transition metals were prepared. They can be used as reagents for organometallic synthesis or to mediate catalysis; and some of them have already been commercialized.[15] We believe that the extraordinary potency of NHCs to stabilize gold at a +I or +III oxidation state will open more applications in organogold chemistry. Moreover, we are ultimately convinced that NHCs might even lead to gold(V) complexes[16] with enhanced stability and potential application in oxidation chemistry…

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APPENDIX

Cristal data and structure refinement for SIMesAgCl (Chapter 3, complex **11**)

Empirical formula	$C_{42}H_{52}N_4Ag_2Cl_2$	
Formula weight ($g.mol^{-1}$)	899.52	
Crystal system	orthorhombic	
Space group	$Cmc2_1$	
Unit cell dimensions (Å)	a = 21.0382(10)	α = 90.00
	b = 9.7005(5)	β = 90.00
	c = 9.9477(5)	γ = 90.00
Volume ($Å^3$)	2030.14(18)	
Z	2	
Calculated density ($g.cm^{-3}$)	1.472	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	920	
$2\theta_{max}$ for data collection (º)	61.058	
Limiting indices	-24<=h<=24, -11<=k<=11, -11<=l<=11	
Reflection collected / unique	11204/1840	
No. data/restraints/param.	1840/106/122	
Final R indices	R = 0.0111	wR = 0.0296
File type	cif	
CCDC reference number	279034	

Cristal data and structure refinement for IPrAgCl (Chapter 3, complex **12**)

Empirical formula	$C_{28.86}H_{39.74}N_2AgCl_{4.74}$	
Formula weight ($g.mol^{-1}$)	690.59	
Crystal system	monoclinic	
Space group	$P2_1$	
Unit cell dimensions (Å)	a = 9.7940(10)	α = 90.00
	b = 16.2939(16)	β = 103.488(2)
	c = 10.9680(11)	γ = 90.00
Volume ($Å^3$)	1702.0(3)	
Z	2	
Calculated density ($g.cm^{-3}$)	1.348	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	709	
$2\theta_{max}$ for data collection (º)	61.330	
Limiting indices	-10<=h<=10, -17<=k<=17, -11<=l<=11	
Reflection collected / unique	12571/4318	
No. data/restraints/param.	4318/557/344	
Final R indices	R = 0.0519	wR = 0.1295
File type	cif	
CCDC reference number	279035	

Cristal data and structure refinement for SIPrAgCl (Chapter 3, complex **13**)

Empirical formula	$C_{14.50}H_{21}NAg_{0.50}Cl_{2.50}$	
Formula weight ($g.mol^{-1}$)	351.88	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions (Å)	a = 9.7788(15)	α = 90.00
	b = 16.334(3)	β = 101.986(4)
	c = 21.755(3)	γ = 90.00
Volume ($Å^3$)	3399.1(9)	
Z	8	
Calculated density ($g.cm^{-3}$)	1.375	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1448	
$2\theta_{max}$ for data collection (º)	61.156	
Limiting indices	-11<=h<=9 , -19<=k<=19, -25<=l<=21	
Reflection collected / unique	17992/5901	
No. data/restraints/param.	5901/273/343	
Final R indices	R = 0.0868	wR = 0.2239
File type	cif	
CCDC reference number	279036	

Cristal data and structure refinement for IPrMeAgCl (Chapter 3, complex **14**)

Empirical formula	$C_{11}H_{18}N_2AgCl$	
Formula weight ($g.mol^{-1}$)	321.59	
Crystal system	tetragonal	
Space group	$P4_12_12$	
Unit cell dimensions (Å)	a = 8.1431(2)	α = 90.00
	b = 8.1431(2)	β = 90.00
	c = 20.5450(8)	γ = 90.00
Volume ($Å^3$)	1362.34(7)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.568	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	648	
$2\theta_{max}$ for data collection (º)	61.022	
Limiting indices	-9<=h<=9, -9<=k<=9, -24<=l<=24	
Reflection collected / unique	15153/1206	
No. data/restraints/param.	1206/53/74	
Final R indices	R = 0.0144	wR = 0.0453
File type	cif	
CCDC reference number	279037	

Cristal data and structure refinement for IMeAgCl (Chapter 3, complex **15**)

Empirical formula	$C_7H_{12}N_2AgCl$	
Formula weight ($g.mol^{-1}$)	267.51	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions (Å)	a = 10.5104(4)	α = 90.00
	b = 16.0633(6)	β = 100.5640(10)
	c = 11.2920(4)	γ = 90.00
Volume ($Å^3$)	1874.13(12)	
Z	8	
Calculated density ($g.cm^{-3}$)	1.896	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1056	
$2\theta_{max}$ for data collection (º)	61.122	
Limiting indices	-10<=h<=10, -15<=k<=15, -10<=l<=10	
Reflection collected / unique	12132/1744	
No. data/restraints/param.	1744/167/208	
Final R indices	R = 0.0144	wR = 0.0388
File type	cif	
CCDC reference number	279038	

Cristal data and structure refinement for ICyAgCl (Chapter 3, complex **16**)

Empirical formula	$C_{15}H_{24}N_2AgCl$	
Formula weight ($g.mol^{-1}$)	375.68	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions (Å)	a = 9.3033(6)	α = 93.6870(10)
	b = 17.3304(11)	β = 92.5790(10)
	c = 20.6786(13)	γ = 99.6820(10)
Volume ($Å^3$)	3274.4(4)	
Z	8	
Calculated density ($g.cm^{-3}$)	1.524	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1536	
$2\theta_{max}$ for data collection (º)	57.758	
Limiting indices	-8<=h<=8, -16<=k<=16 , -19<=l<=19	
Reflection collected / unique	18859/6091	
No. data/restraints/param.	6091/662/685	
Final R indices	R = 0.0319	wR = 0.0737
File type	cif	
CCDC reference number	279039	

Cristal data and structure refinement for IAdAgCl (Chapter 3, complex **17**)

Empirical formula	$C_{23}H_{32}N_2AgCl$	
Formula weight ($g.mol^{-1}$)	479.83	
Crystal system	orthorhombic	
Space group	$Pna2_1$	
Unit cell dimensions (Å)	a = 11.5347(15)	α = 90.00
	b = 26.847(4)	β = 90.00
	c = 6.4849(9)	γ = 90.00
Volume ($Å^3$)	2008.2(5)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.587	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	992	
$2\theta_{max}$ for data collection (º)	61.060	
Limiting indices	-11<=h<=11, -25<=k<=25, -6<=l<=6	
Reflection collected / unique	12591/1871	
No. data/restraints/param.	1871/280/245	
Final R indices	R = 0.0260	wR = 0.0657
File type	cif	
CCDC reference number	279040	

Cristal data and structure refinement for IsBAgCl (Chapter 3, complex **18**)

Empirical formula	$C_{11}H_{20}N_2AgCl$	
Formula weight ($g.mol^{-1}$)	323.61	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 19.1151(12)	α = 90.00
	b = 17.1519(11)	β = 97.1180(10)
	c = 17.3503(11)	γ = 90.00
Volume ($Å^3$)	5644.6(6)	
Z	16	
Calculated density ($g.cm^{-3}$)	1.523	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	2624	
$2\theta_{max}$ for data collection (º)	61.786	
Limiting indices	-18<=h<=18, -16<=k<=16, -16<=l<=16	
Reflection collected / unique	34631/5247	
No. data/restraints/param.	5247/462/557	
Final R indices	R = 0.0879	wR = 0.1866
File type	cif	
CCDC reference number	279041	

Cristal data and structure refinement for IDDAgCl (Chapter 3, complex **19**)

Empirical formula	$C_{28}H_{50}N_2AgCl_3$	
Formula weight ($g.mol^{-1}$)	628.92	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions (Å)	a = 16.1296(6)	α = 90.00
	b = 13.0986(5)	β = 116.7990(10)
	c = 16.5205(6)	γ = 90.00
Volume ($Å^3$)	3115.5(2)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.341	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1320	
$2\theta_{max}$ for data collection (º)	61.044	
Limiting indices	-15<=h<=15, -12<=k<=12, -15<=l<=15	
Reflection collected / unique	19837/2900	
No. data/restraints/param.	2900/232/308	
Final R indices	R = 0.0264	wR = 0.0600
File type	cif	
CCDC reference number	279042	

Cristal data and structure refinement for TPhAgCl (Chapter 3, complex **20**)

Empirical formula	$C_{8.25}H_{8.25}N_{2.25}Ag_{0.75}Cl_{0.75}$	
Formula weight ($g.mol^{-1}$)	246.41	
Crystal system	triclinic	
Space group	P1	
Unit cell dimensions (Å)	a = 7.3050(3)	α = 75.3660(10)
	b = 11.0525(4)	β = 81.8210(10)
	c = 11.3905(5)	γ = 85.8790(10)
Volume ($Å^3$)	880.15(6)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.860	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	486	
$2\theta_{max}$ for data collection (º)	61.014	
Limiting indices	-8<=h<=8, -13 <=k<=13, -13<=l<=13	
Reflection collected / unique	10010/6147	
No. data/restraints/param.	6147/431/434	
Final R indices	R = 0.0143	wR = 0.0360
File type	cif	
CCDC reference number	279043	

Cristal data and structure refinement for $[(IMes)_2Ag][AgCl_2]$ (Chapter 3, complex **21**)

Empirical formula	$C_{21}H_{24}N_2AgCl$	
Formula weight ($g.mol^{-1}$)	447.74	
Crystal system	orthorhombic	
Space group	Pbcn	
Unit cell dimensions (Å)	a = 17.0221(11)	α = 90.00
	b = 14.0448(9)	β = 90.00
	c = 17.2731(11)	γ = 90.00
Volume ($Å^3$)	4129.5(5)	
Z	8	
Calculated density ($g.cm^{-3}$)	1.440	
Temperature (K)	173(2)	
Radiation wavelength (mm^{-1})	0.71069	
F(000)	1824	
$2\theta_{max}$ for data collection (º)	55.000	
Limiting indices	-22<=h<=22 , -18<=k<=18, -22<=l<=22	
Reflection collected / unique	38340/4772	
No. data/restraints/param.	4772/0/235	
Final R indices	R = 0.0403	wR = 0.1217
File type	cif	
CCDC reference number	279044	

Cristal data and structure refinement for $[(IMes)_2Ag]_2[Ag_4I_6]$ (Chapter 3, complex **22**)

Empirical formula	$C_{42}H_{48}N_4Ag_3I_3$	
Formula weight ($g.mol^{-1}$)	1313.15	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions (Å)	a = 11.8323(7)	α = 65.5310(10)
	b = 14.6993(8)	β = 69.4360(10)
	c = 15.6755(9)	γ = 70.8040(10)
Volume ($Å^3$)	2269.0(2)	
Z	2	
Calculated density ($g.cm^{-3}$)	1.922	
Temperature (K)	298(2)	
Radiation wavelength (mm^{-1})	0.71069	
F(000)	1256	
$2\theta_{max}$ for data collection (º)	49.760	
Limiting indices	-15<=h<=15, -19<=k<=19, -20<=l<=20	
Reflection collected / unique	22387/10452	
No. data/restraints/param.	10452/0/499	
Final R indices	R = 0.0472	wR = 0.1257
File type	cif	
CCDC reference number	279130	

Cristal data and structure refinement for IMesAuCl (Chapter 4, complex **10**)

Empirical formula	$C_{21}H_{24}N_2AuCl$	
Formula weight ($g.mol^{-1}$)	536.84	
Crystal system	orthorhombic	
Space group	Fd22	
Unit cell dimensions (Å)	a = 14.7275(5)	α = 90.00
	b = 28.8179(9)	β = 90.00
	c = 9.7016(3)	γ = 90.00
Volume ($Å^3$)	4117.5(2)	
Z	8	
Calculated density ($g.cm^{-3}$)	1.732	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	2080	
$2\theta_{max}$ for data collection (º)	70.136	
Limiting indices	-23<=h<=23, -45<=k<=45, -15<=l<=15	
Reflection collected / unique	21578/4415	
No. data/restraints/param.	4415/106/164	
Final R indices	R = 0.0161	wR = 0.0387
File type	cif	
CCDC reference number	263603	

Cristal data and structure refinement for SIMesAuCl (Chapter 4, complex **11**)

Empirical formula	$C_{21}H_{26}N_2AuCl$	
Formula weight ($g.mol^{-1}$)	538.85	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions (Å)	a = 8.4242(3)	α = 90.00
	b = 21.9330(9)	β = 91.0600(10)
	c = 11.2534(5)	γ = 90.00
Volume ($Å^3$)	2078.91(15)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.722	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1048	
$2\theta_{max}$ for data collection (º)	71.344	
Limiting indices	-9<=h<=9, -23<=k<=23, -12<=l<=12	
Reflection collected / unique	24387/2701	
No. data/restraints/param.	2701/217/233	
Final R indices	R = 0.0173	wR = 0.0438
File type	cif	
CCDC reference number	263604	

Cristal data and structure refinement for IPrAuCl (Chapter 4, complex **12**)

Empirical formula	$C_{34}H_{44}N_2AuCl_2$	
Formula weight ($g.mol^{-1}$)	713.13	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 22.0888(14)	α = 90.00
	b = 9.7434(6)	β = 113.9410(10)
	c = 16.5776(10)	γ = 90.00
Volume ($Å^3$)	3260.9(3)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.453	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1432	
$2\theta_{max}$ for data collection (º)	59.846	
Limiting indices	-29<=h<=29, -13<=k<=13, -22<=l<=22	
Reflection collected / unique	19675/7819	
No. data/restraints/param.	7819/350/352	
Final R indices	R = 0.0307	wR = 0.0568
File type	cif	
CCDC reference number	263611	

Cristal data and structure refinement for SIPrAuCl (Chapter 4, complex **13**)

Empirical formula	$C_{27}H_{38}N_2AuCl$	
Formula weight ($g.mol^{-1}$)	623.01	
Crystal system	orthorhombic	
Space group	Pccn	
Unit cell dimensions (Å)	a = 10.9098(5)	α = 90.00
	b = 12.5994(6)	β = 90.00
	c = 19.3635(9)	γ = 90.00
Volume ($Å^3$)	2661.6(2)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.555	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1240	
$2\theta_{max}$ for data collection (º)	61.024	
Limiting indices	-15<=h<=15, -18<=k<=18, -27<=l<=27	
Reflection collected / unique	42383/4060	
No. data/restraints/param.	4060/130/147	
Final R indices	R = 0.0187	wR = 0.0426
File type	cif	
CCDC reference number	263605	

Cristal data and structure refinement for IPrMeAuCl (Chapter 4, complex **14**)

Empirical formula	$C_{11}H_{20}N_2AuCl$	
Formula weight ($g.mol^{-1}$)	412.71	
Crystal system	tetragonal	
Space group	$P4_32_12$	
Unit cell dimensions (Å)	a = 8.0840(3)	α = 90.00
	b = 8.0840(3)	β = 90.00
	c = 20.6310(15)	γ = 90.00
Volume ($Å^3$)	1348.26(12)	
Z	4	
Calculated density ($g.cm^{-3}$)	2.033	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	784	
$2\theta_{max}$ for data collection (º)	69.570	
Limiting indices	-8<=h<=8, -8<=k<=8, -22<=l<=22	
Reflection collected / unique	8694/889	
No. data/restraints/param.	889/53/110	
Final R indices	R = 0.0201	wR = 0.0494
File type	cif	
CCDC reference number	263606	

Cristal data and structure refinement for IMeAuCl (Chapter 4, complex **15**)

Empirical formula	$C_7H_{12}N_2AuCl$	
Formula weight ($g.mol^{-1}$)	356.60	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions (Å)	a = 10.405(2)	α = 90.00
	b = 8.4073(18)	β = 90.00
	c = 11.068(2)	γ = 90.00
Volume ($Å^3$)	968.3(4)	
Z	4	
Calculated density ($g.cm^{-3}$)	2.446	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	656	
$2\theta_{max}$ for data collection (º)	61.428	
Limiting indices	-14<=h<=14, -12<=k<=12, -15<=l<=15	
Reflection collected / unique	16002/2962	
No. data/restraints/param.	2962/0/104	
Final R indices	R = 0.0477	wR = 0.1035
File type	cif	
CCDC reference number	263607	

Cristal data and structure refinement for ICyAuCl (Chapter 4, complex **16**)

Empirical formula	$C_{30}H_{48}N_4Au_2Cl_2$	
Formula weight ($g.mol^{-1}$)	929.56	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 9.5570(5)	α = 90.00
	b = 19.4416(10)	β = 103.1440(10)
	c = 17.6956(9)	γ = 90.00
Volume ($Å^3$)	3201.8(3)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.928	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1792	
$2\theta_{max}$ for data collection (º)	61.320	
Limiting indices	-9<=h<=9, -18<=k<=18, -17<=l<=17	
Reflection collected / unique	19002/2987	
No. data/restraints/param.	2987/38/154	
Final R indices	R = 0.0371	wR = 0.0881
File type	cif	
CCDC reference number	263608	

Cristal data and structure refinement for IAdAuCl (Chapter 4, complex **17**)

Empirical formula	$C_{23}H_{32}N_2AuCl$	
Formula weight ($g.mol^{-1}$)	568.92	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 14.5735(7)	α = 90.00
	b = 11.7626(6)	β = 111.4490(10)
	c = 12.9098(6)	γ = 90.00
Volume ($Å^3$)	2059.76(17)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.835	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1120	
$2\theta_{max}$ for data collection (º)	60.932	
Limiting indices	-20<=h<=20, -16<=k<=16, -18<=l<=18	
Reflection collected / unique	32039/6242	
No. data/restraints/param.	6242/273/245	
Final R indices	R = 0.0207	wR = 0.0524
File type	cif	
CCDC reference number	263609	

Cristal data and structure refinement for TPhAuCl (Chapter 4, complex **18**)

Empirical formula	$C_{11}H_{11}N_3AuCl$	
Formula weight ($g.mol^{-1}$)	417.64	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions (Å)	a = 7.3539(4)	α = 91.9290(10)
	b = 10.8603(5)	β = 91.3230(10)
	c = 14.5517(7)	γ = 101.5470(10)
Volume ($Å^3$)	1137.48(10)	
Z	4	
Calculated density ($g.cm^{-3}$)	2.439	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	776	
$2\theta_{max}$ for data collection (º)	61.546	
Limiting indices	-7<=h<=7, -11<=k<=11, -15<=l<=15	
Reflection collected / unique	10117/2972	
No. data/restraints/param.	2972/278/290	
Final R indices	R = 0.0214	wR = 0.0634
File type	cif	
CCDC reference number	263610	

Cristal data and structure refinement for IPrAuBr (Chapter 5, complex **8**)

Empirical formula	$C_{27}H_{36}N_2AuBr$	
Formula weight ($g.mol^{-1}$)	665.45	
Crystal system	orthorhombic	
Space group	Pccn	
Unit cell dimensions (Å)	a = 10.9117(6)	α = 90.00
	b = 12.6771(7)	β = 90.00
	c = 19.9643(10)	γ = 90.00
Volume ($Å^3$)	2761.6(3)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.601	
Temperature (K)	295(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1304	
$2\theta_{max}$ for data collection (º)	55.040	
Limiting indices	-14<=h<=14, -16<=k<=16, -25<=l<=22	
Reflection collected / unique	17717/3140	
No. data/restraints/param.	3140/0/146	
Final R indices	R = 0.0321	wR = 0.0758
File type	cif	
CCDC reference number	621434	

Cristal data and structure refinement for $IPrAuBr_3$ (Chapter 5, complex **15**)

Empirical formula	$C_{27.50}H_{37}N_2AuBr_3$	
Formula weight ($g.mol^{-1}$)	867.74	
Crystal system	monoclinic	
Space group	P2(1)/n	
Unit cell dimensions (Å)	a = 16.950(2)	α = 90.00
	b = 19.403(3)	β = 110.421(3)
	c = 20.417(3)	γ = 90.00
Volume ($Å^3$)	6293.0(15)	
Z	8	
Calculated density ($g.cm^{-3}$)	1.832	
Temperature (K)	295(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	3336	
$2\theta_{max}$ for data collection (º)	52.774	
Limiting indices	-18<=h<=18, -20<=k<=20, -21<=l<=21	
Reflection collected / unique	39800/8206	
No. data/restraints/param.	5509/638/563	
Final R indices	R = 0.0495	wR = 0.0967
File type	cif	
CCDC reference number	621435	

Cristal data and structure refinement for $IMesAuBr_3$ (Chapter 5, complex **16**)

Empirical formula	$C_{21}H_{24}N_2AuBr_3$	
Formula weight ($g.mol^{-1}$)	741.12	
Crystal system	orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions (Å)	a = 10.6845(6)	α = 90.00
	b = 14.2833(8)	β = 90.00
	c = 15.7115(9)	γ = 90.00
Volume ($Å^3$)	2397.7(2)	
Z	4	
Calculated density ($g.cm^{-3}$)	2.053	
Temperature (K)	295(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1392	
$2\theta_{max}$ for data collection (º)	46.718	
Limiting indices	-11<=h<=11, -15<=k<=15, -16<=l<=16	
Reflection collected / unique	25184/3137	
No. data/restraints/param.	3137/705/330	
Final R indices	R = 0.0300	wR = 0.0701
File type	cif	
CCDC reference number	621436	

Cristal data and structure refinement for $SIPrAuBr_3$ (Chapter 5, complex **17**)

Empirical formula	$C_{28}H_{40}N_2AuBr_3Cl_2$	
Formula weight ($g.mol^{-1}$)	912.22	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 10.677(2)	α = 90.00
	b = 16.593(4)	β = 99.664(4)
	c = 19.306(4)	γ = 90.00
Volume ($Å^3$)	3371.5(12)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.797	
Temperature (K)	295(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1760	
$2\theta_{max}$ for data collection (º)	53.004	
Limiting indices	-11<=h<=11, -17<=k<=17, -20<=l<=20	
Reflection collected / unique	16323/4009	
No. data/restraints/param.	4009/355/377	
Final R indices	R = 0.0589	wR = 0.0992
File type	cif	
CCDC reference number	621437	

Cristal data and structure refinement for $SIMesAuBr_3$ (Chapter 5, complex **18**)

Empirical formula	$C_{21.50}H_{27.01}N_2AuBr_3Cl_{1.01}$	
Formula weight ($g.mol^{-1}$)	785.90	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 8.7226(8)	α = 90.00
	b = 16.0470(15)	β = 95.611(2)
	c = 19.7576(18)	γ = 90.00
Volume ($Å^3$)	27.52(3)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.897	
Temperature (K)	295(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1485	
$2\theta_{max}$ for data collection (º)	61.210	
Limiting indices	-9<=h<=9, -17<=k<=17, -21<=l<=21	
Reflection collected / unique	39906/3600	
No. data/restraints/param.	3600/240/278	
Final R indices	R = 0.0490	wR = 0.1291
File type	cif	
CCDC reference number	621438	

Cristal data and structure refinement for $ICyAuBr_3$ (Chapter 5, complex **19**)

Empirical formula	$C_{15.50}H_{25}N_2AuBr_3Cl$	
Formula weight ($g.mol^{-1}$)	711.52	
Crystal system	orthorhombic	
Space group	Pccn	
Unit cell dimensions (Å)	a = 15.0878(9)	α = 90.00
	b = 19.9495(13)	β = 90.00
	c = 14.6881(9)	γ = 90.00
Volume ($Å^3$)	4421.0(5)	
Z	8	
Calculated density ($g.cm^{-3}$)	2.138	
Temperature (K)	295(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	2664	
$2\theta_{max}$ for data collection (º)	58.480	
Limiting indices	-16<=h<=16, -21<=k<=21, -15<=l<=15	
Reflection collected / unique	36155/2892	
No. data/restraints/param.	2892/186/217	
Final R indices	R = 0.0438	wR = 0.1339
File type	cif	
CCDC reference number	621439	

Cristal data and structure refinement for $IAdAuBr_3$ (Chapter 5, complex **20**)

Empirical formula	$C_{23}H_{32}N_2AuBr_3$	
Formula weight ($g.mol^{-1}$)	773.20	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 16.4445(16)	α = 90.00
	b = 11.1131(10)	β = 90.044(2)
	c = 12.9782(12)	γ = 90.00
Volume ($Å^3$)	2371.8(4)	
Z	4	
Calculated density ($g.cm^{-3}$)	2.165	
Temperature (K)	295(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1472	
$2\theta_{max}$ for data collection (º)	46.718	
Limiting indices	-18<=h<=18, -12<=k<=12, -14 <=l<=14	
Reflection collected / unique	21229/3429	
No. data/restraints/param.	3429/280/390	
Final R indices	R = 0.0295	wR = 0.0725
File type	cif	
CCDC reference number	621440	

Cristal data and structure refinement for $I^tBuAuBr_3$ (Chapter 5, complex **20**)

Empirical formula	$C_{11}H_{202}N_2AuBr_3$	
Formula weight ($g.mol^{-1}$)	616.99	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 9.2947(5)	α = 90.00
	b = 15.3944(8)	β = 96.7460(10)
	c = 12.1528(7)	γ = 90.00
Volume ($Å^3$)	1726.86(16)	
Z	4	
Calculated density ($g.cm^{-3}$)	2.373	
Temperature (K)	295(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1136	
$2\theta_{max}$ for data collection (º)	52.846	
Limiting indices	-11<=h<=11, -19<=k<=19, -15<=l<=15	
Reflection collected / unique	21428/3569	
No. data/restraints/param.	3569/491/235	
Final R indices	R =0.0259	wR = 0.0548
File type	cif	
CCDC reference number	621441	

Cristal data and structure refinement for (IPr)Au(MeCN)PF_6 (Chapter 6, complex **1**)

Empirical formula	$C_{31}H_{42}N_4AuPF_6$	
Formula weight ($g.mol^{-1}$)	812.62	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions (Å)	a = 8.9662(6)	α = 90.00
	b = 18.3466(13)	β = 96.8410(10)
	c = 21.6925(15)	γ = 90.00
Volume ($Å^3$)	3543.0(4)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.523	
Temperature (K)	298(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1616	
$2\theta_{max}$ for data collection (º)	46.660	
Limiting indices	-9<=h<=9, -19 <=k<=19, -23 <=l<=23	
Reflection collected / unique	53909/4625	
No. data/restraints/param.	4625/351/398	
Final R indices	R = 0.0442	wR = 0.1084
File type	cif	
CCDC reference number	296436	

Cristal data and structure refinement for (IPr)Au(MeCN)SbF_6 (Chapter 6, complex **2**)

Empirical formula	$C_{29}H_{39}N_3AuSbF_6$	
Formula weight ($g.mol^{-1}$)	862.35	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions (Å)	a = 9.0520(18)	α = 90.00
	b = 17.531(4)	β = 97.280(6)
	c = 20.949(4)	γ = 90.00
Volume ($Å^3$)	3297.5(11)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.737	
Temperature (K)	100(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1672	
$2\theta_{max}$ for data collection (º)	79.100	
Limiting indices	-14<=h<=15, -23<=k<=31, -37<=l<=36	
Reflection collected / unique	65186/19150	
No. data/restraints/param.	19150/0/387	
Final R indices	R = 0.0505	wR = 0.1409
File type	cif	
CCDC reference number	not deposited	

Cristal data and structure refinement for (IAd)Au(MeCN)PF_6 (Chapter 6, complex **5**)

Empirical formula	$C_{27}H_{38}N_4AuPF_6$	
Formula weight ($g.mol^{-1}$)	760.55	
Crystal system	orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions (Å)	a = 7.2205(2)	α = 90.00
	b = 17.6382(5)	β = 90.00
	c = 22.2743(7)	γ = 90.00
Volume ($Å^3$)	2836.78(14)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.781	
Temperature (K)	100(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1504	
$2\theta_{max}$ for data collection (º)	78.88	
Limiting indices	-12<=h<=5, -31<=k<=31, -34<=l<=38	
Reflection collected / unique	45545/16295	
No. data/restraints/param.	16295/0/334	
Final R indices	R = 0.0320	wR = 0.0738
File type	cif	
CCDC reference number	not deposited	

Cristal data and structure refinement for $[(IPrAu)_2(H_2O)][PF_6]_2$ (Chapter 6, complex **8**)

Empirical formula	$C_{54}H_{74}N_4Au_2P_2OF_{12}$	
Formula weight ($g.mol^{-1}$)	1479.05	
Crystal system	monoclinic	
Space group	C2/c	
Unit cell dimensions (Å)	a = 27.0937	α = 90.00
	b = 21.2028	β = 106.116
	c = 23.1607	γ = 90.00
Volume ($Å^3$)	X	
Z	4	
Calculated density ($g.cm^{-3}$)	X	
Temperature (K)	100(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	X	
$2\theta_{max}$ for data collection (º)	X	
Limiting indices	-X<=h<=X, -X<=k<=X, -X<=l<=X	
Reflection collected / unique	26088/17633	
No. data/restraints/param.	17633/6/662	
Final R indices	R = 0.0699	wR = 0.1098
File type	res	
CCDC reference number	not deposited	

Cristal data and structure refinement for $(IPr)Au(pyr)PF_6$ (Chapter 6, complex **9**)

Empirical formula	$C_{32}H_{41}N_3AuPF_6$	
Formula weight ($g.mol^{-1}$)	809.61	
Crystal system	orthorhombic	
Space group	Pbca	
Unit cell dimensions (Å)	a = 15.8918(10)	α = 90.00
	b = 16.7009(10)	β = 90.00
	c = 24.5616(15)	γ = 90.00
Volume ($Å^3$)	6518.8(7)	
Z	8	
Calculated density ($g.cm^{-3}$)	1.650	
Temperature (K)	100(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	3216	
$2\theta_{max}$ for data collection (º)	72.38	
Limiting indices	-16<=h<=24, -26<=k<=27, -9<=l<=40	
Reflection collected / unique	75024/14337	
No. data/restraints/param.	14337/0/396	
Final R indices	R = 0.0588	wR = 0.1617
File type	cif	
CCDC reference number	not deposited	

Cristal data and structure refinement for (IPr)Au(2-Brpyr)PF_6 (Chapter 6, complex **10**)

Empirical formula	$C_{32}H_{40}N_3AuPBrF_6$	
Formula weight ($g.mol^{-1}$)	888.51	
Crystal system	monoclinic	
Space group	C2	
Unit cell dimensions (Å)	a = 11.3656	α = 90.00
	b = 14.0795	β = 91.125
	c = 22.7103	γ = 90.00
Volume ($Å^3$)	X	
Z	4	
Calculated density ($g.cm^{-3}$)	X	
Temperature (K)	100(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	X	
$2\theta_{max}$ for data collection (º)	X	
Limiting indices	-X<=h<=X, -X<=k<=X, -X<=l<=X	
Reflection collected / unique	10305/9539	
No. data/restraints/param.	9539/1/482	
Final R indices	R = 0.0437	wR = X
File type	res	
CCDC reference number	not deposited	

Cristal data and structure refinement for $[(IPrAu)_2(PF_4)]PF_4$ (Chapter 6, complex **14**)

Empirical formula	$C_{54}H_{72}N_4Au_2P_2F_8$	
Formula weight ($g.mol^{-1}$)	1385.04	
Crystal system	P-1	
Space group	triclinic	
Unit cell dimensions (Å)	a = 10.3907	α = 84.251
	b = 17.1438	β = 84.439
	c = 17.9774	γ = 77.098
Volume ($Å^3$)	X	
Z	8	
Calculated density ($g.cm^{-3}$)	X	
Temperature (K)	100(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	X	
$2\theta_{max}$ for data collection (º)	X	
Limiting indices	-X<=h<=X, -X<=k<=X, -X<=l<=X	
Reflection collected / unique	32182/25136	
No. data/restraints/param.	25136/0/692	
Final R indices	R = 0.0771	wR = X
File type	res	
CCDC reference number	not deposited	

Cristal data and structure refinement for IPrAuTgt (Chapter 7, complex **1**)

Empirical formula	$C_{41}H_{55}N_2AuSO_9$	
Formula weight ($g.mol^{-1}$)	948.90	
Crystal system	orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions (Å)	a = 10.9509(4)	α = 90.00
	b = 13.9651(5)	β = 90.00
	c = 28.3700(11)	γ = 90.00
Volume ($Å^3$)	4338.6(3)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.453	
Temperature (K)	150(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1928	
$2\theta_{max}$ for data collection (º)	52.780	
Limiting indices	-12<=h<=13, -17<=k<=17, -35<=l<=34	
Reflection collected / unique	31184/8886	
No. data/restraints/param.	8886/463/547	
Final R indices	R = 0.0392	wR = 0.0912
File type	cif	
CCDC reference number	615644	

Cristal data and structure refinement for IPrAuSac (Chapter 6, complex **2**)

Empirical formula	$C_{35}H_{41}N_3AuSO_3Cl_3$	
Formula weight ($g.mol^{-1}$)	887.08	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions (Å)	a = 15.4337(9)	α = 90.00
	b = 16.4214(9)	β = 101.5660(10)
	c = 15.8384(9)	γ = 90.00
Volume ($Å^3$)	3932.6(4)	
Z	4	
Calculated density ($g.cm^{-3}$)	1.498	
Temperature (K)	298(2)	
Radiation wavelength (mm^{-1})	0.71073	
F(000)	1768	
$2\theta_{max}$ for data collection (º)	52.958	
Limiting indices	-19<=h<=19, -20<=k<=20, -19<=l<=19	
Reflection collected / unique	48191/8093	
No. data/restraints/param.	8093/0/575	
Final R indices	R = 0.0325	wR = 0.0720
File type	cif	
CCDC reference number	615645	

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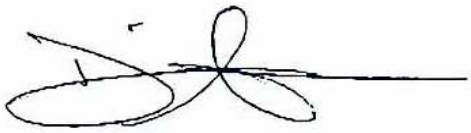

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de Frémont, P.; Scott, N. M.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2005**, *24*, 2411-2418.

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de Frémont, P.; Stevens, E. D.; Eelman, M. D.; Fogg, D. E.; Nolan, S. P. *Organometallics* **2006**, *25*, 5824-5828.

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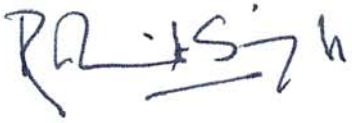

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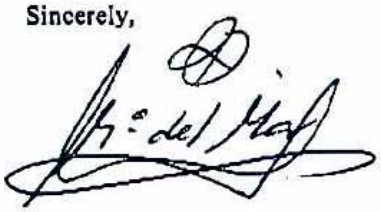

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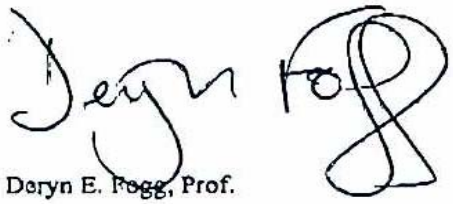

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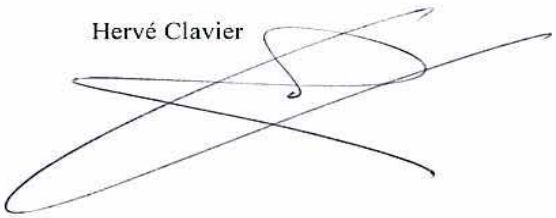

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Synthesis and Structural Characterization of *N*-Heterocyclic Carbene Gold(I) Complexes

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Received February 16, 2005

A series of *N*-heterocyclic carbene Au(NHC)Cl complexes (NHC = IMes (**1**), SIMes (**2**), IPr (**3**), SIPr (**4**), IPrMe (**5**), IMe (**6**), ICy (**7**), IAd (**8**), ITPh (**9**)) have been synthesized either through reaction of the corresponding imidazol-2-ylidene carbene with [Au(SMe_2)Cl] or by transmetalation of the respective Ag(I)−NHC complex in the presence of 1 equiv of [Au(SMe_2)Cl]. All of the gold(I) complexes [Au(IMes)Cl] (**10**), [Au(SIMes)Cl] (**11**), [Au(IPr)Cl] (**12**), [Au(SIPr)Cl] (**13**), [Au(IPrMe)Cl] (**14**), [Au(IMe)Cl] (**15**), [Au(ICy)Cl] (**16**), [Au(IAd)Cl] (**17**), and [Au(ITPh)Cl] (**18**) have been characterized spectroscopically and structurally by X-ray diffraction. The ^{13}C chemical shifts of the carbene carbon have been compared through subtraction of the corresponding imidazol-2-ylidene carbene and suggest that there is little difference in donor ability of the NHC ligands bound to gold(I). Crystal structure analysis reinforces this notion, with no obvious change in Au−C(NHC) bond length on going from saturated and unsaturated NHC ligands. For complexes **14**, **17**, and **18** Au···H−C interactions were observed from the sidearm substituents on the NHC ligand. Furthermore, the triazolium complex **18** also contains Au···Au interactions as well as head-to-tail $\pi-\pi$ stacking of the phenyl sidearm substituent from neighboring molecules.

The development of *N*-heterocyclic carbene (NHC) metal complexes has now become a well-established area of research.[1] As a result, a large variety of metal−NHC complexes are known, many of which have been successfully used in catalytic applications.[2] Interestingly, most studies focusing on catalysts incorporating NHC ligands have revolved around the platinum metal groups. In numerous instances simple substitution reaction routes involving replacement of phosphines by NHC ligands lead to higher catalytic activity as well as improved thermal stability of the resulting organometallic complex. The working hypothesis is that NHCs are more powerfully σ-donating than the closely related phosphine ligands, forming stronger bonds to transition metals and thereby also leading to electron-rich metal centers.[3] Recently we reported a detailed steric and electronic investigation of the NHC and phosphine ligand classes involving the square-planar complex (L)-$Ni(CO)_3$, which allowed a direct comparison of the two ligand families and also led to the experimental determination of Ni−C(NHC) bond energies.[4,5] In contrast to the wealth of information available for such late-transition-metal NHC compounds, the chemistry of linear two-coordinate coinage-metal−NHC compounds in general, and gold(I)−NHC complexes in particular, has remained relatively unexplored.[6−9] Complexes of the general formula Au(NHC)(X) (X = halide) are especially scarce, and this prompted us to develop reliable synthetic methods for the preparation of such monocarbene−gold(I) compounds. This was initiated to provide a better understanding of the (NHC)Au^I solid-state and solution behavior and to explore their reaction chemistry. It should be noted that gold complexes have received considerable attention in medicinal chemistry, where they display interesting antitumor and antimicrobial activity.[10] Moreover, Au(I) complexes often exhibit interesting photophysical properties by displaying strongly luminescent behavior.[11] Finally, the use of Au complexes in homogeneous catalysis has undergone a renaissance as of late and spectacular achievements have recently been reported.[12,13]

We report here the synthesis of a series of two-coordinate Au(I) chloride complexes of general composition Au(NHC)Cl. The NHC ligands used are shown in

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Carbene Chemistry

DOI: 10.1002/anie.200501056

A Gold Catalyst for Carbene-Transfer Reactions from Ethyl Diazoacetate**

Manuel R. Fructos, Tomás R. Belderrain, Pierre de Frémont, Natalie M. Scott, Steven P. Nolan, M. Mar Díaz-Requejo,* and Pedro J. Pérez**

The use of transition-metal-based catalysts for the transfer of carbene units from diazo compounds constitutes a powerful tool in organic synthesis.[1] Several metals have been reported to mediate this transformation effectively, and the appropriate selection of ligands has permitted excellent selectivities. Highly chemo-, diastereo-, and/or enantioselective systems have been reported with rhodium-, copper-, or cobalt-containing catalysts. In fact, nearly all 12 elements of Groups 8–11 have been found to decompose diazo compounds and transfer a carbene unit to saturated or unsaturated organic substrates,[2] leading to the insertion or addition product, respectively (Scheme 1). Only one of these 12 elements remains unexplored in this chemistry: gold.[3] Although the other members of Group 11—copper and, to a lesser extent, silver—have been described to induce such transformations, conducting this type of catalytic reaction with gold remains a challenge. We therefore focused our attention on the development of a gold-based catalyst, as a result of our experience in the area of metal-catalyzed carbene transfer from ethyl diazoacetate (EDA).[4]

We recently reported the catalytic behavior of [(IPr)CuCl] (**1**, IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene) for the transfer of carbene from ethyl diazoacetate to olefins, amines, and alcohols to form cyclopropanes, amino acid derivatives, and ethers, respectively.[5] These promising results

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Supporting information for this article (general experimental procedures and product characterization data) is available on the WWW under http://www.angewandte.org or from the author.

Articles

Synthesis of Well-Defined *N*-Heterocyclic Carbene Silver(I) Complexes

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A series of *N*-heterocyclic carbene (NHC)AgCl complexes [NHC = SIMes (**1**), IPr (**2**), SIPr (**3**), IPrMe (**4**), IMe (**5**), ICy (**6**), IAd (**7**), IsB (**8**), IDD (**9**), and TPh (**10**)] have been synthesized through reaction of the imidazolium chloride salts with Ag_2O or by direct metalation of the corresponding imidazol-2-ylidene carbene in the presence of AgCl. All silver(I) complexes [(SIMes)AgCl] (**11**), [(IPr)AgCl] (**12**), [(SIPr)AgCl] (**13**), [(IPrMe)AgCl] (**14**), [(IMe)AgCl] (**15**), [(ICy)AgCl] (**16**), [(IAd)AgCl] (**17**), [(IsB)AgCl] (**18**), [(IDD)AgCl] (**19**), and [(TPh)AgCl] (**20**) have been spectroscopically and structurally characterized. The structure of these silver complexes is dependent on the halide and the solvent used for the synthesis. Adjusting these parameters has led to the previously reported complex, $[(IMes)_2Ag]^+[AgCl_2]^-$ (**21**), and to a new silver complex, $[(IMes)_2Ag]^+{}_2[Ag_4I_6]^{2-}$ (**22**).

Introduction

It is now widely accepted that the saga of *N*-heterocyclic carbene (NHC) chemistry began in 1968 when Ölefe[1] and Wanzlick[2] successfully isolated the first chromium and mercury *N*-heterocyclic carbene complexes. In 1991, Arduengo's seminal discovery of a stable *N*-heterocyclic carbene[3] led to incredible activity and development in the coordination chemistry of NHCs. With better sigma donor ability than most phosphines, NHCs strongly bind and stabilize transition metals,[4] leading to a wide variety of well-defined catalytic systems. NHC complexes of late transition metals especially those of groups 8, 9, and 10 have been employed to catalyze Heck reactions,[5] cross-coupling reactions (such as the Suzuki−Miyaura reaction[6]), olefin metathesis,[7] and hydrogenation[8] reactions, among the most significant. From group 11, copper- and gold-NHCs are known to catalyze a more limited number of organic transformations,[9,10] but silver-NHC complexes have been reported recently to behave as efficient catalysts

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Synthetic Methods

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Au^{I}-Catalyzed Tandem [3,3] Rearrangement–Intramolecular Hydroarylation: Mild and Efficient Formation of Substituted Indenes**

*Nicolas Marion, Silvia Díez-González, Pierre de Frémont, April R. Noble, and Steven P. Nolan**

Recent reports have highlighted the use of gold(I) and gold(III) complexes as efficient homogeneous catalysts in several organic transformations.[1] Notably, gold catalysts, in both oxidation states, enable the cycloisomerization of enynes.[2] Based on these earlier studies, we reasoned that the electron-rich phenyl ring could replace an alkene moiety and lead to

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Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

Alkane Carbon−Hydrogen Bond Functionalization with (NHC)MCl Precatalysts (M = Cu, Au; NHC = N-Heterocyclic Carbene)

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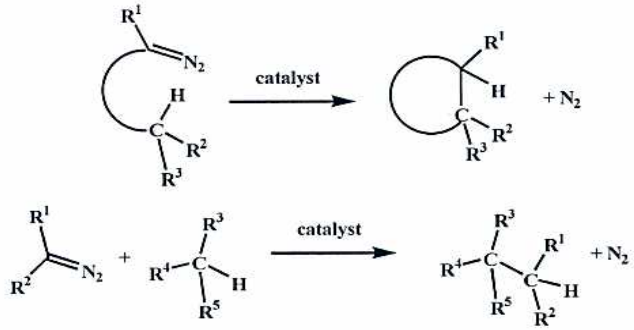
Facile alkane functionalization by means of the insertion of :$CHCO_2Et$, from ethyl diazoacetate, into carbon−hydrogen bonds mediated by catalytic amounts of (NHC)MCl (NHC = N-heterocyclic ligand; M = Cu, Au) and a halide scavenger MX has been achieved. This chemistry includes the insertion of the carbene fragment into alkane primary positions with Cu- and Au-based catalysts. The nature of the counterion X and of the NHC ligand have a significant effect on the overall yields and regioselectivity of the reaction.

Introduction

The metal-catalyzed transfer of a carbene unit, :CR^1R^2, from diazo compounds $N_2CR^1R^2$ has been extensively studied during the last few decades.[1] The main transformations involving this fragment have centered on its addition to unsaturated bonds or, alternatively, its insertion into saturated X−H bonds. The most interesting example is when X is carbon, a case that results in the functionalization of carbon−hydrogen bonds by carbene insertion.[2] This procedure (Scheme 1) has been extensively employed in intramolecular reactions; however the intermolecular counterpart has been described only with a few metal-based catalysts. The first examples were performed with simple copper salts.[3] The seminal work by Noels and co-workers[4] with rhodium acetate was followed by work from several other groups[5] that aimed at developing new catalysts based on rhodium. This methodology was quite limited in scope, and it was not until the end of the past decade when work by Davies and co-workers[2,6] led to the renaissance of this method for the functionalization of carbon−hydrogen bonds. Interestingly, systems based on copper[7a−d] and silver[7d−f] have also been reported to insert a :$CHCO_2Et$ unit from ethyl diazoacetate into the C−H bonds of several saturated substrates.

Scheme 1. Intra- and Intermolecular C−H Bond Functionalization by Carbene Insertion from Diazo Compounds



We have very recently reported on the catalytic properties of the complex (IPr)CuCl (**1**) [IPr: 1,3-bis(diisopropylphenyl)imidazol-2-ylidene] (Scheme 2) in the transfer of the :$CHCO_2Et$ unit from ethyl diazoacetate to olefins, amines, and alcohols.[8] We have also prepared and characterized the gold analogue (IPr)AuCl (**2**) and reported its catalytic competency for carbene transfer reactions, in what to the best of our knowledge represents the first example of this metal mediating

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Synthesis, isolation and characterization of cationic gold(I) *N*-heterocyclic carbene (NHC) complexes†

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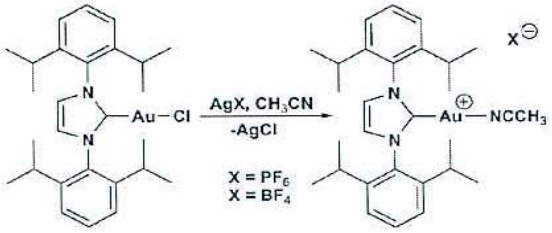
A number of cationic gold(I) complexes have been synthesized and found to be stabilized by the use of *N*-heterocyclic carbene ligands. These species are often employed as *in situ*-generated reactive intermediates in gold catalyzed organic transformations. An isolated, well-defined species was tested in gold-mediated carbene transfer reactions from ethyl diazoacetate.

As part of an ongoing program aimed at examining the role of *N*-heterocyclic carbenes (NHC) in transition metal-mediated reactions, we have recently studied the stabilizing effects of NHCs surrounding unsaturated and "reactive" metal centers. Since the isolation of the first free stable NHC, bearing two sterically demanding adamantyl groups on the nitrogens of an imidazolyl framework, by Arduengo *et al.*,[1] sterically encumbering NHCs have allowed the isolation of unusual three-coordinate $(NHC)Ni(CO)_2$ complexes,[2] highly unsaturated 14 electron Ir(I) species,[3] a number of orthometalated ruthenium[4] and iridium[5] species, well-defined monomeric copper(I) species[6] and formally 16 electron second generation ruthenium-based olefin metathesis catalysts.[7] In view of the steric and electronic properties of this ligand class, NHCs have been employed to prepare efficient and robust catalysts for transformations such as palladium-catalyzed cross-coupling reactions,[8] platinum-mediated hydrosilylation,[9] palladium telomerization of butadiene and methanol,[10] copper-catalyzed hydrosilylation[11] and ruthenium-based olefin metathesis,[12] to name a few.

We recently became involved in the synthesis and isolation of well-defined NHC–gold(I) complexes.[13] The first NHC–gold(I) complexes were reported in 1989,[14] and these usually bore two strongly bound ligands arranged in a linear fashion around a gold cation. These can be neutral or cationic and have either $[(NHC)AuX]$[13] or $[(NHC)_2Au^+][X^-]$[15] composition. Until recently, catalytic organogold chemistry appeared to have been somewhat forgotten. The "noble" character of the metal was possibly the origin of the misconception that it would perform poorly in catalysis. This misconception has now been shattered, as numerous examples of gold–phosphines[16] and gold–NHC[17]-mediated transformations have recently appeared. Gold(I) halide complexes are especially efficient at activating alkyne moieties towards nucleophilic addition under mild reaction conditions.[16,17] A recent example by He *et al.* also shows these complexes to be excellent co-catalysts in the intra- and intermolecular hydroamination of unsaturated olefins.[18] The use of silver salts, with an accompanying non-coordinating anion, is usually required to generate the active catalyst. It is commonly accepted that silver assists in halide abstraction from the gold center, generating a highly electrophilic monoligated cationic gold complex.[19] While Ferrer and Echavarren have reported the isolation of a monoligated complex, with a very bulky phosphine, [(2-(di-*tert*-butylphosphino)biphenyl)Au^+(NCMe)][SbF_6^-], as an active catalyst for cycloisomerization,[19] attempts to synthesize or isolate $I^tBuAuBF_4$ by Baker *et al.*[20] and PPh_3AuPF_6 by Gagosz *et al.*[21] have so far failed, due to the rapid decomposition of these complexes into colloidal gold(0). In this communication, we report the isolation and characterization of such complexes by using a NHC ligand of sufficient bulk and a weakly coordinating solvent, such as acetonitrile or tetrahydrofuran (THF), leading to relatively stable yet reactive cationic gold(I) complexes.

The previously reported IPrAuCl[13] (IPr = 1,3-bis(di-*iso*-propylphenyl)imidazol-2-ylidene), IMesAuCl[13] (IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) and $I^tBuAuCl$[20] (I^tBu = 1,3-di-*tert*-butylimidazol-2-ylidene) were dissolved in acetonitrile, and $AgPF_6$ or $AgBF_4$ was added in stoichiometric amounts, leading to the rapid formation of a precipitate (AgCl). After stirring the solutions for one minute, the suspensions were filtered through Celite to give the novel complexes in solution (Scheme 1).[22] The appearance of colloidal gold(0) was noticeable after a few hours for all solutions. Attempts to obtain solid materials for all complexes by simply removing the solvent under vacuum only led to rapid decomposition of the materials, obvious as the white material turns to a greyish powder. Carrying out these



Scheme 1 Synthesis route to cationic NHC–Au(I) complexes.

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† Electronic Supplementary Information (ESI) available: Detailed experimental details with full NMR characterization data and catalytic procedures.

Au^I-catalyzed cycloisomerization of 1,5-enynes bearing a propargylic acetate: formation of unexpected bicyclo[3.1.0]hexene†

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The use of *N*-heterocyclic carbene (NHC) as a ligand in the gold(I)-catalyzed cycloisomerization of enyne results in the assembly of a new carbocyclic product.

Recent reports have employed gold(I) and gold(III) complexes as homogeneous catalysts capable of facilitating several organic transformations.[1] For instance, gold catalysts in both oxidation states perform enyne cycloisomerization,[2] one of the most efficient means of converting acyclic precursors into complex polycyclic structures.[3] The reactivity of gold complexes toward enynes leads notably to the formation of bicyclic [*n*.1.0] derivatives[4] that are of great synthetic interest, since the cyclopropane ring is a widely encountered motif in natural products.[5]

As we recently reported the syntheses of several air- and moisture-stable (NHC)AuCl complexes[6] (NHC = *N*-heterocyclic carbene) (Fig. 1), we were interested in testing these in such cycloisomerization reactions. We focused our attention on the specific dienyne **1**, which bears an acetate at the propargylic position, since we previously reported its reactivity in the presence of $PtCl_2$ (Scheme 1).[7,8] Substrate **1** formally contains 1,6 and 1,5 enynes that lead, after 1,2 migration of the acetate, to **2** and **3**, respectively. With $PtCl_2$, the bicyclo[4.1.0]heptene **2** is formed preferentially, while the bicyclo[3.1.0] compound **3** is only a minor product. Fürstner *et al.* showed that this transformation with simple enynes was catalyzed equally well by Pt^{II} or Au^I.[9] Since ligand effects have been studied only scarcely in this chemistry, it was of interest to examine whether Au^I would provide a similar selectivity to Pt^{II} in this specific system, and furthermore if ligands such as NHCs could support such a transformation. To the best of our knowledge, the influence of only a limited set of tertiary phosphine and NHC ligands has been studied in this reaction to date.[2e,10]

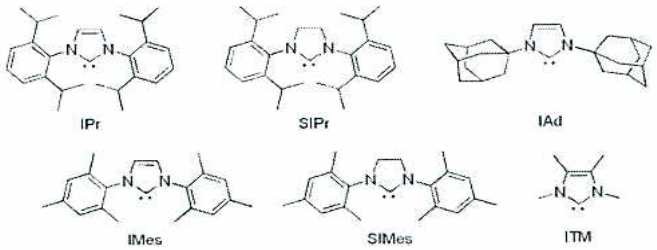

Fig. 1 Structures of NHC ligands.

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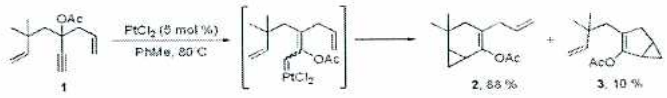

Scheme 1 $PtCl_2$-catalyzed cycloisomerization of **1**.

We subjected dienyne **1** to an equimolar mixture of IPrAuCl and $AgBF_4$ (2 mol%) in CH_2Cl_2 at rt. After 5 minutes, no starting material remained; isolation and purification yielded **2** and **3** in moderate yields, and a novel compound **4** as the major product. The ^1H NMR data suggested **4** was a cycloisomerized product displaying three propanoid and one extra vinylic protons. ^1H–^1H and ^1H–^{13}C HSQC (heteronuclear single quantum correlation) NMR experiments did not permit the unequivocal assignment of the structure of the new product. To determine unambiguously the atom connectivity in **4**, we prepared **1′**, the *para*-nitrobenzoate analogue of **1**, and subjected it to cycloisomerization conditions.[11] Suitable crystals of the purified product were grown and the structure was elucidated by X-ray diffraction (Fig. 2). Surprisingly, in **4′** the cyclopropane ring has migrated to the former propargylic position, making **4** a formal vinylcyclopropane rearrangement of **3**.

To examine the influence of the NHC ligand, we carried out reactions with various (NHC)AuCl complexes in conjunction with $AgBF_4$ (Table 1). The widely studied IMes (*N,N′*-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) and SIMes (*N,N′*-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene) ligands[12] presented similar reactivities (Table 1, entries 1 and 2), affording, in good overall yields, the three bicyclic compounds in comparable ratios; **4** remaining the major product. Slightly more encumbered than IMes, IPr (*N,N′*-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) showed a comparable reactivity (Table 1, entry 3), while its saturated counterpart SIPr yielded **2** and **4** in equal proportion (Table 1, entry 4). When the extremely sterically demanding[13] IAd (*N,N′*-1,3-bis(adamantyl)imidazol-2-ylidene) was used, the cyclohexene compound became major and both cyclopentene derivatives were obtained in smaller amounts (Table 1, entry 5). At this point, it seemed that the formation of **4** was disfavored for ligand steric reasons. We then examined the sterically unencumbering ITM

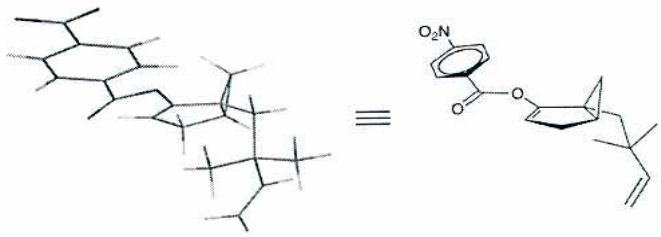

Fig. 2 Stick representation of **4′**.

Notes

Synthesis and Characterization of Gold(I) *N*-Heterocyclic Carbene Complexes Bearing Biologically Compatible Moieties

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Summary: Two new gold(I) complexes bearing the bulky N-heterocyclic carbene IPr (IPr = bis(2,6-diisopropylphenyl)-imidazol-2-ylidene) and respectively 2,3,4,6-tetra-O-acetyl-1-thio-β-D-pyranosatothiolato [(IPr)AuTgt (1)] and a saccharin ligand [(IPr)AuSac (2)] have been synthesized in good yield and are fully characterized by NMR spectroscopy and by inert-atmosphere MALDI-TOF. These complexes are well-behaved compounds analogous to gold drugs such as Auranofin and Solganol.

Introduction

The use of gold salts in medicinal chemistry was first described in 2500 B.C.[1] In modern chemistry, the interest in these salts as potential pharmacophores emerged in 1890 with the discovery of $Au(CN)_2^-$ and its bacteriostatic properties.[2] Almost 40 years later, Forestier reported the first gold-based treatment against tuberculosis.[3] Today in vivo biochemistry of gold remains enigmatic, mainly due to a paucity of adequate models and an inadequate understanding of the reactivity of gold.[4] Moreover, as gold is not a metal naturally used in metabolism, it is believed that its chemistry in vivo differs from other transition metals such as iron and copper, which are carefully transported and stored by enzymatic processes.[5] The biochemistry of gold with D-penicillamine,[6] gluthadione,[7] thiomalic acid,[8] 2,3-dimercaptopropanol,[9] and albumin[10] has been studied. The reactivity of gold occurs though the thiolate function of these biological molecules and leads to the formation of gold(I) thiolates, also called chrysotherapy agents. These complexes are efficient against rheumatoid arthrisis and even HIV[11] and are commercialized under different trade names such as Myochrysine, Solganol, Krysolgan, and Allochrysine.[12] Other types of gold complexes used in medicinal chemistry are gold(I) mono- or bis-phosphines. They can bind to DNA via the guanine and cytosine bases[13] and act as antitumor agents against L1210 leukemia and M5076 reticulum cell sarcoma.[14] In 1972, Sutton synthesized a gold complex with a thiolate and a phosphine ligand: the 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-pyranosato-*S*-(triethylphosphine)gold(I) compound also known by the trade name Auranofin. It became one of the most promising gold complexes in medicinal chemistry,[15] with a great potency against rheumatoid arthritis and cancer cells such as P388 leukemia and B16.[16]

In 1991, Arduengo showed that free *N*-heterocyclic carbenes (NHCs) are stable enough species to be isolated,[17] sparking an ever-growing interest in their chemistry. Since then, these ligands have been used extensively to stabilize transition metal complexes.[18] Their unusual and tunable electronic and steric

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Synthesis, Characterization and Reactivity of *N*-Heterocyclic Carbene Gold(III) Complexes

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A series of (NHC)Au^{I}Cl (**1**, NHC = *N*,*N*′-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr); **2**, NHC = *N*,*N*′-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes); **3**, NHC = *N*,*N*′-bis(2,6-diisopropylphenyl)-imidazolin-2-ylidene (SIPr); **4**, NHC = *N*,*N*′-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene (SIMes); **5**, NHC = *N*,*N*′-dicyclohexylimidazol-2-ylidene (ICy); **6**, NHC = *N*,*N*′-diadamantylimidazol-2-ylidene (IAd); **7**, NHC = *N*,*N*′-di-*tert*-butylimidazol-2-ylidene (I^{t}Bu)) complexes were reacted with LiBr to generate [(IPr)AuBr] (**8**), [(IMes)AuBr] (**9**), [(SIPr)AuBr] (**10**), [(SIMes)AuBr] (**11**), [(ICy)AuBr] (**12**), [(IAd)-AuBr] (**13**), and [(I^{t}Bu)AuBr] (**14**). These (NHC)Au^{I}Br complexes undergo oxidative addition of elemental bromine, leading to the new Au(III) complexes [(IPr)AuBr$_3$] (**15**), [(IMes)AuBr$_3$] (**16**), [(SIPr)AuBr$_3$] (**17**), [(SIMes)AuBr$_3$] (**18**), [(ICy)AuBr$_3$] (**19**), [(IAd)AuBr$_3$] (**20**), and [(I^{t}Bu)AuBr$_3$] (**21**). Complete characterization by NMR spectroscopy and single-crystal X-ray diffraction were performed in order to discern structural differences between organogold(I/III) congeners. A preliminary study examining the activity of (NHC)Au^{III} species on the addition of water to alkynes is also presented.

Introduction

Although, historically, organogold complexes have been underutilized in organic synthesis, numerous publications have recently emphasized the beneficial role of gold(I) in catalysis.[1] Organic transformations such as skeletal rearrangements (cycloisomerizations),[2] carbene transfer reactions,[3] indanization,[4] oxidations,[5] and hydrosilylations[6] are examples of the diverse chemistry mediated by organogold catalysts. Such transformations have been achieved with low catalyst loading and high turnover numbers. The gold(I) center must have two coordination sites occupied to ensure stability of the complexes and thereby avoid reduction to gold(0).[7] The most commonly employed ligands so far have been phosphines (PR_3)[8] and, most recently, N-heterocyclic carbenes (NHC).[9] Both ligand families exhibit strong σ-donation, and coordination of such ligands results in good stability of the Au(I) complexes toward air, moisture, and thermolysis. It is interesting to note that gold has

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[(NHC)Au^{I}]-Catalyzed Formation of Conjugated Enones and Enals: An Experimental and Computational Study

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Abstract: The [(NHC)Au^{I}]-catalyzed (NHC = N-heterocyclic carbene) formation of α,β-unsaturated carbonyl compounds (enones and enals) from propargylic acetates is described. The reactions occur at 60 °C in 8 h in the presence of an equimolar mixture of [(NHC)AuCl] and $AgSbF_6$ and produce conjugated enones and enals in high yields. Optimization studies revealed that the reaction is sensitive to the solvent, the NHC, and, to a lesser extent, to the silver salt employed, leading to the use of [(I*t*Bu)AuCl]/$AgSbF_6$ in THF as an efficient catalytic system. This transformation proved to have a broad scope, enabling the stereoselective formation of (*E*)-enones and -enals with great structural diversity. The effect of substitution at the propargylic and acetylenic positions has been investigated, as well as the effect of aryl substitution on the formation of cinnamyl ketones. The presence or absence of water in the reaction mixture was found to be crucial. From the same phenylpropargyl acetates, anhydrous conditions led to the formation of indene compounds via a tandem [3,3] sigmatropic rearrangement/intramolecular hydroarylation process, whereas simply adding water to the reaction mixture produced enone derivatives cleanly. Several mechanistic hypotheses, including the hydrolysis of an allenol ester intermediate and S_N2' addition of water, were examined to gain an insight into this transformation. Mechanistic investigations and computational studies support [(NHC)AuOH], produced in situ from [(NHC)AuSbF$_6$] and H_2O, instead of cationic [(NHC)AuSbF$_6$] as the catalytically active species. Based on DFT calculations performed at the B3LYP level of theory, a full catalytic cycle featuring an unprecedented transfer of the OH moiety bound to the gold center to the C≡C bond leading to the formation of a gold–allenolate is proposed.

Keywords: carbenes · density functional calculations · enones · gold · potential energy surface

Introduction

Conjugated enones arguably represent one of the most useful building blocks in organic synthesis;[1] two of their main uses are as reactants in 1,4 addition and Diels–Alder reactions.[2,3] α,β-Unsaturated ketones and aldehydes are usually obtained by aldol- or Knoevenagel-type condensation reactions[4] and by the Horner–Wadsworth–Emmons reaction.[5,6] These methods generally require strong basic media and therefore functional group compatibility and selectivity issues can be problematic. Other methods that afford enones include the use of widely available propargylic alcohols.[7] The Meyer–Schuster rearrangement[8] of propargylic alcohols, involving a formal 1,3-shift of the hydroxy moiety, and the Rupe rearrangement,[9] proceeding via a 1,3-enyne, produce isomeric α,β-unsaturated carbonyl compounds (Scheme 1). Despite some reports on the utilization of the Meyer–Schuster reaction under mild conditions,[10,11] these isomerization reactions have not been widely used or

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N-Heterocyclic Carbene–Palladium Complexes [(NHC)Pd-(acac)Cl]: Improved Synthesis and Catalytic Activity in Large-Scale Cross-Coupling Reactions

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Abstract: From two commercially available starting materials, improved one-step, multigram-scale syntheses of [(IPr)Pd(acac)Cl] [IPr = *N*,*N*′-bis(2,6-diisopropylphenyl)imidazol-2-ylidene; acac = acetylacetonate] and [(IMes)Pd(acac)Cl] [IMes = *N*,*N*′-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] are described. The catalytic activity of both complexes in cross-coupling reactions has been examined. The most active pre-catalyst, [(IPr)Pd(acac)Cl], has allowed for efficient large-scale (10 mmol) Buchwald–Hartwig and α-ketone arylation reactions to be carried out.

Keywords: *N*-aryl amination; cross-coupling; N-heterocyclic carbene; α-ketone arylation; large-scale; palladium

Introduction

The use of NHC ligands (NHC = N-heterocyclic carbene) is now widespread in numerous areas of organometallic catalysis.[1] Their impressive involvement in ruthenium-catalyzed alkene metathesis[2] is only one of their many possible applications in ligand-supported organometallic transformations.[3] Therefore, simple and efficient protocols to synthesize NHC-containing transition metal complexes are of wide interest.

In the last few years, we have developed several user-friendly procedures leading to diverse families of [(NHC)Pd(L)Cl] (where L = allyl, R-allyl, palladacycle).[4] These protocols allow for the synthesis of air- and moisture-stable palladium precatalysts possessing high activities in cross-coupling reactions.[5,6] Along these lines, we recently described the synthesis of two air- and moisture-stable NHC-bearing acetylacetonato complexes, shown in Figure 1, with the formulae [(IPr)Pd(acac)$_2$] **1** and [(IPr)Pd(acac)Cl] **2** [IPr = *N*,*N*′-bis(2,6-diisopropylphenyl)imidazol-2-ylidene; acac = acetylacetonate].[7] Complex **1**, bearing a η^1-*C*-bound and a κ^2-*O*,*O*-bound acac, was prepared from free IPr and Pd(acac)$_2$, while complex **2** was prepared by reacting stoichiometrically **1** with HCl.

Complexes **1** and **2** were found to be active in the Buchwald–Hartwig reaction[8] and the α-arylation of ketone[9] involving a wide array of substrates.[10] The higher activity of **2** in these reactions when compared to **1** prompted us to design a one-pot synthesis to avoid the isolation of **1**. The remaining drawback of this early synthetic pathway was the use of the free carbene. We subsequently showed that the NHC salt (that is, NHC·HCl) could be used *in lieu* of the free NHC.[10] Nevertheless, in this synthetic procedure all reagents had to be thoroughly dried under vacuum prior to the reaction being carried out, the use of anhydrous dioxane was mandatory and the reaction had to be performed under an inert atmosphere. Herein, we report an improved synthesis of two [(NHC)Pd-(acac)Cl] complexes by simply mixing and heating NHC·HCl with Pd(acac)$_2$ in technical grade dioxane and without any precautions to avoid air. Furthermore, large-scale cross-coupling reactions have been

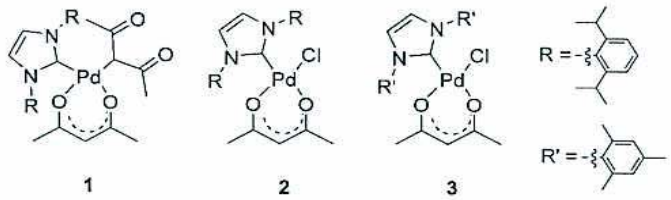

Figure 1. Structures of complexes **1**, **2** and **3**.

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