The Role of NHC Ligands in Oxidation Catalysis

Thomas Strassner

Technische Universität Dresden, Physikalische Organische Chemie, Bergstrasse 66,
01069 Dresden, Germany
thomas.strassner@chemie.tu-dresden.de

Abstract During the last decade *N*-heterocyclic carbenes (NHC) have become a very important class of ligands for catalytic applications. They have been employed in reactions like C – C/C – N coupling, olefin metathesis, hydrosilylation and hydrogenation. Recently, also in the field of oxidation catalysis significant progress has been achieved. NHC ligands are known to efficiently activate metal centers and they are surprisingly resistant, even in acidic media. In contrast to phosphine ligands, the metal-NHC bond is also stable under oxidizing conditions. This review covers the oxidation of organic substrates by NHC catalysts as well as the fixation and activation of O_2 and CO_2 by NHC complexes. A variety of oxidation reactions have been studied using NHC catalysts, but the oxidation of alcohols and olefins was of particular interest. Most of the work in this area was conducted with palladium catalysts, which even allow the efficient oxidation of alcohols at ambient temperature using molecular oxygen. Bi- and tridentate NHC ligands are described as well as a variety of complexes with different metals other than palladium. Reactive intermediates like peroxo complexes have been characterized experimentally, while DFT calculations have been used to explain the mechanisms of the oxidation chemistry of transition metal NHC complexes.

Keywords Catalysis · DFT calculations · *N*-heterocyclic carbenes · Oxidation · Palladium

Abbreviations
acac   acetylacetonate
BDE   bond dissociation energy
CDA   charge decomposition analysis
CNC   2,6-bis(butylimidazole-2-ylidene)pyridine

| Cp	cyclopentadienyl
Cy	cyclohexyl
DFT	density functional theory
EDA	energy decomposition analysis
Hal	halogen
HF	Hartree–Fock
Me	methyl
NHC	*N*-heterocyclic carbene
OAc	acetate
Ph	phenyl
PPh₃	triphenylphosphine
post-HF	post-Hartree–Fock
TM	transition metal

1
Introduction

For a long time metal carbenes have been either classified as Fischer- or Schrock carbenes, depending on the oxidation state of the metal. Since the introduction of *N*-heterocyclic carbene complexes this classification needs to be extended because of the very different electronic character of these ligands. Carbenes—molecules with a neutral dicoordinate carbon atom—play an important role in all fields of chemistry today. The first examples in the field of organic chemistry were published by Doering and Hoffmann in the 1950s [1], while Fischer and Maasböl introduced them to organometallic chemists about ten years later [2, 3]. But it took another 25 years until the first carbenes could be isolated [4–8].

Especially the report of the successful isolation of a stable carbene by Arduengo [6, 7] (Scheme 1) and the publication of the solid-state structure of a stable imidazole-2-ylidene in 1991 led to a renaissance of these nucleophilic carbenes, which certainly also had an influence on the 2005 Nobel price in chemistry!

The realization of the extraordinary properties of these new ligands stimulated research in this area and many imidazole-2-ylidenes have been synthesized in the last 10 years [8]. The 1,3-diadamantyl derivative **1** of the imidazole-2-ylidenes is stable at room temperature and the 1,3-dimesityl-4,5-dichloroimidazole-2-ylidene [9] is reported to be even air-stable. A variety of stable carbenes has been synthesized in between and it could be shown that steric bulk is not a requirement for the stability (the 1,3-dimethylimidazoline-2-ylidene can be distilled without decomposition [10]), although it certainly influences the long-term stability by preventing dimerization.
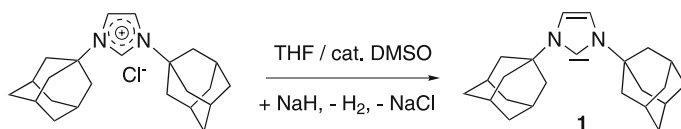
Scheme 1 Synthesis of a stable, "bottle-able" imidazole-2-ylidene

Those *N*-heterocyclic carbenes show a surprising stability which was of interest to organometallic chemists who started to explore the metal complexes of these new ligands. The first examples of this class had been synthesized as early as 1968 by Wanzlick [11] and Öfele [12], only four years after the first Fischer-*type* carbene complex was synthesized [2, 3] and six years before the first report of a Schrock-*type* carbene complex [13]. But at that time their potential as ligands had not been explored. Once the *N*-heterocyclic ligands are attached to a metal they show a completely different reaction pattern compared to the electrophilic Fischer- and nucleophilic Schrock-*type* carbene complexes.

Within the last decade many variations of the basic imidazole-2-ylidene structure (Scheme 2,A) have been synthesized [14–19]. They are not limited to sterically hindered unsaturated cyclic diaminocarbenes like **1**, also 1,2,4-triazolin-5-ylidenes (Scheme 2,B), saturated imidazolidin-2-ylidenes [6, 7, 20] (Scheme 2,C), tetrahydropyrimid-2-ylidenes [21, 22] (Scheme 2,D), acyclic structures [23, 24] (Scheme 2,E), systems with larger ring sizes [25, 26] (Scheme 2,F) or constrained geometry [27, 28] (Scheme 2,G). Reviews on the different possible synthetic routes from various precursors can be found in the literature [29–31].
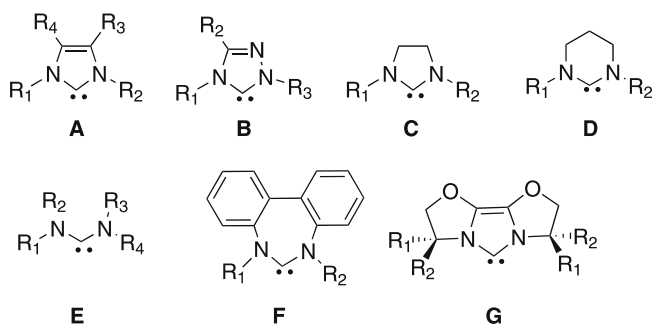
Scheme 2 Different classes of synthesized *N*-heterocyclic carbenes

2
Electronic Structure of *N*-Heterocyclic Carbenes

The electronic structure of the carbene center of an imidazole-2-ylidene can be approximated as a singlet carbene, where the carbene carbon atom is close to a sp^2-hybridization as shown in Scheme 3.

Scheme 3 Electronic structure of an imidazole-2-ylidene

The two substituents and a pair of electrons occupy the three sp^2-hybrid orbitals, while a formally vacant p_π orbital remains at the carbene carbon atom. Because of the similar chemical behavior of these nucleophilic carbenes compared to phosphines, organometallic chemists have in many cases successfully replaced phosphines by stronger donating *N*-heterocyclic carbenes.

It is known today that it is absolutely not necessary to have a cyclic delocalization of π-electrons in those NHC ligands to be able to isolate stable carbenes, as was believed in the beginning, although this provides additional stability [32–34]. Contrary to Fischer-*type* or Schrock-*type* carbene complexes, these ligands generally are formally neutral two-electron donors, which are best described as pure σ-donor ligands without significant metal-ligand π-backbonding [35–38]. It has been proposed that this might be due to a rather high occupancy of the formally empty p_π orbital of the carbene carbon atom by π-delocalization [39].

The electronic structure of these carbenes was investigated by early theoretical studies [36, 40–48] to elucidate the reasons for the surprising stability, which came to different conclusions concerning the importance of the stabilizing effect of the π-delocalization. While early studies predicted that the C – N π-interaction does not play a major role [33], others found that the p_π population at the carbene carbon atom is 30% higher for the unsaturated case, indicating that cyclic delocalization is clearly enhanced in the unsaturated carbene [48].

Frenking [36] could show that the higher stability of the imidazoline-2-ylidenes is caused by enhanced p_π–p_π delocalization leading to a significant electronic charge in the formally "empty" p_π orbital of the carbene carbon atom. The unsaturated imidazoline-2-ylidenes as well as the saturated imidazolidin-2-ylidenes are strongly stabilized by electron donation from the nitrogen lone pairs into the formally "empty" p_π orbital. The cyclic 6π-electron delocalization shows some aromatic character according to energetic and magnetic analysis. The electronically less stable saturated imidazolidin-2-ylidenes need additional steric protection of the carbene carbon atom to become isolable.

3
Synthesis of Metal Complexes

During the last decade *N*-heterocyclic carbene complexes of transition metals have been developed for catalytic applications in many different organic transformations. The most prominent example is probably the olefin metathesis reaction (Nobel price in Chemistry in 2005). *N*-heterocyclic carbenes show a pure donor nature. Comparing them to other monodentate ligands such as phosphines and amines on several metal-carbonyl complexes showed the significantly increased donor capacity relative to phosphines, even to trialkylphosphines, while the π-acceptor capability of the NHCs is on the order of those of nitriles and pyridine [29]. Experimental evidence comes from the fact that it has been shown for several metals, that an exchange of phosphines versus NHCs proceeds rapidly and without the need of an excess quantity of the NHC. This also represents one general pathway for the synthesis of these complexes, the "free carbene pathway" (Scheme 4). After deprotonation of the imidazolium salt by bases like KO^{t}Bu or NaH, the free carbene replaces a weaker bonded ligand in the low valent metal precursor.
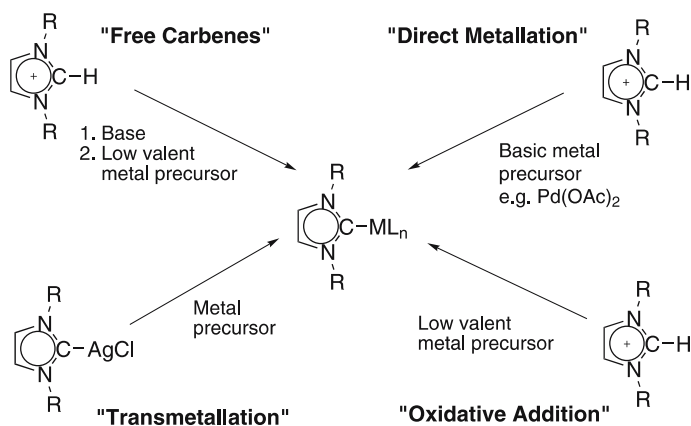
Scheme 4 Pathways for the synthesis of NHC metal complexes

This principle was used in the synthesis of the Grubbs/Herrmann metathesis catalysts [49]. As it was known that the exchange of the triphenylphosphine ligands of **2** by the more electron-donating tricyclohexylphosphines was accompanied by a significantly higher stability and reactivity [50–52], the development of complexes **3** and **4** (Scheme 5) was the logical extension of that concept. Although the metathesis reaction and NHC ligands are intimately connected and could be seen as oxidations, they are not included in this review.
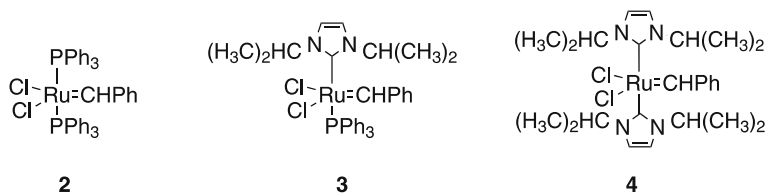
Scheme 5 Ruthenium-NHC complexes, active in the catalytic olefin metathesis

The synthesis of these complexes can easily be accomplished by substitution of one or both PPh_3 groups of **2** by NHC ligands. From the X-ray structure [53] of **4** the differences between the *N*-heterocyclic carbenes and Schrock carbenes becomes obvious just by looking at the significantly different bond lengths: the "Schrock double bond" to the CHPh group is 1.821(3) Å, while the "NHC bond" to the 1,3-diisopropylimidazoline-2-ylidene is 2.107(3) Å, more like a single bond.

The "direct metallation" is not in all cases useful as it depends on the availability of a suitable basic metal precursor, which is able to deprotonate the imidazolium salt. The advantage is that it allows one to deprotonate the imidazolium salts in the presence of groups which are labile towards stronger bases. We found $Pd(OAc)_2$ [54–56] and $Pt(acac)_2$ [57] especially useful in that regard. In cases where no basic metal precursor is available it is often successful to add NaOAc as an external base [58, 59].

Even though the "oxidative addition" pathway of imidazolium salts has been shown to be possible at certain metal complexes under special circumstances, it is far from being generally applicable to the synthesis of NHC complexes [60–67].

Widely applicable is the last pathway shown in Scheme 4, the "transmetallation reaction". Although other reagents have been proposed [68], the use of Ag_2O as introduced by Lin [69, 70] is currently the most important pathway for the synthesis of NHC metal complexes. The imidazolium halide forms a silverhalide-NHC complex which then transfers the carbene ligand to the metal precursor. Scheme 4 shows a general representation of possible pathways for the synthesis of transition metal NHC complexes.

As soon as the carbene complex is formed it shows extraordinary stability, even against strong acids and oxidizing agents like peroxodisulfate [55–57, 59]. Therefore, these complexes can be used in catalytic processes which have not been possible before with the phosphine ligands, e.g. reactions under oxidizing conditions as the tendency to form phosphine oxides is too high.

4
Oxidation Catalysis

NHC transition metal complexes have been used in several different oxidation reactions, which are described in Scheme 6. This review will cover them by reaction type and I do apologize to any author whose work is not cited although I tried hard to include all contributions to the field of oxidation catalysis.

Quite recently transition metal oxo complexes with NHC ligands have been synthesized, e.g. for rhenium [71, 72] and uranium [73], but no oxygen transfer using those complexes has been reported yet.
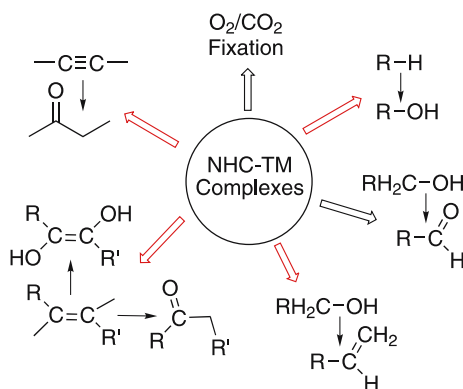
Scheme 6 Oxidation reactions catalyzed by NHC complexes

4.1
$O_2/CO/CO_2$ Fixation

Dioxygen activation at transition metal centers is a fundamentally important process and the catalytic aerobic oxidation by transition metal complexes is a challenging synthetic task. Several groups have succeeded in isolating and characterizing complexes where dioxygen, carbon monoxide or carbon dioxide are bound as ligands in empty coordination sites. One example is the cobalt peroxo complex isolated by Meyer [74]. There has been a longstanding interest in the dioxygen chemistry of cobalt and most of the complexes reported had shown the dioxygen molecule in an end-on binding mode. But cobalt(I) supported by a tripodal NHC ligand **5** binds dioxygen in a side-on, η^2-fashion (Scheme 7).
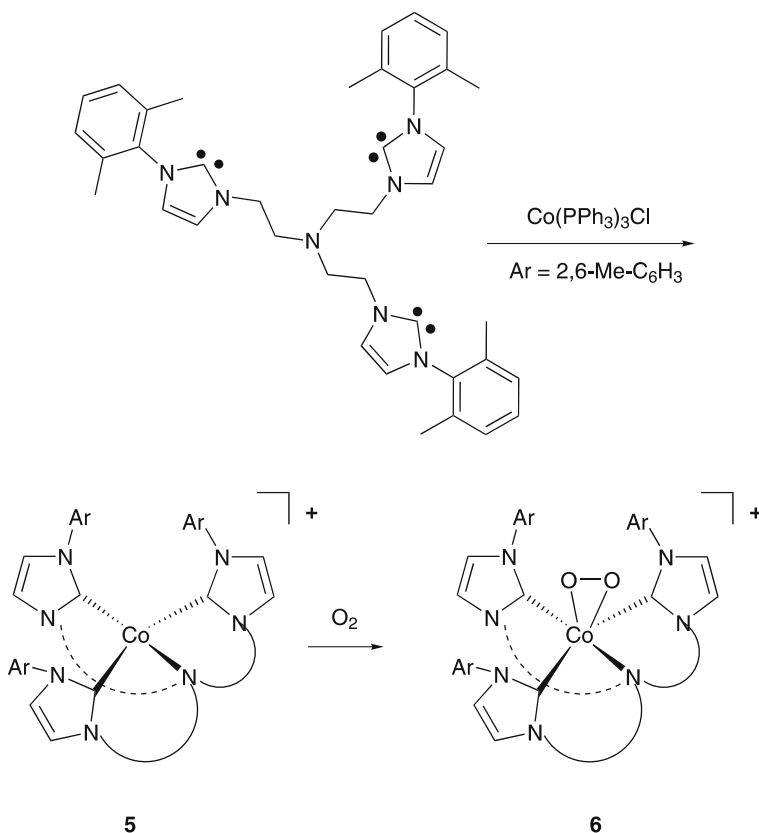
Scheme 7 Synthesis of [(TIMEN^xyl)Co(O_2)]BPh_4 (**6**)

The complex was synthesized by deprotonation of the corresponding im-
idazolium salt with potassium *tert*-butoxide under formation of the triscar-
bene ligand tris[2-(3-xylenimidazole-2-ylidene)ethyl]amine (TIMEN^xyl), fol-
lowed by the reaction with a cobalt-phosphine complex Co(PPh_3)_3Cl.
Under inert-gas atmosphere **5** is stable in the solid state, but in THF
or CH_3CN solution it slowly oxidizes to yield the cobalt (II) complex
[(TIMEN^xyz)CoCl]Cl (**7**). A solution of **5** reacts cleanly with dioxygen at room
temperature to form a 1 : 1 cobalt dioxygen adduct [(TIMEN^xyl)Co(O_2)]^+. On
the basis of the O – O stretching frequency observed in the infrared spectra it
is classified as a peroxo species. Additionally, the corresponding ^{18}O labelled
complex showed an isotopic shift of 50 cm^{-1}, which agrees well with theor-
etical predictions for a peroxo complex. When the reaction is carried out in
THF in the presence of NaBPh_4, the resulting complex **6** precipitates from the
reaction mixture.

The corresponding CO complex [(TIMEN^{xyz})Co(CO)]Cl (**8**) forms in 85% yield if **5** is reacted with an excess of CO gas. Structures of the complexes have been published [74] and are given in Fig. 1.
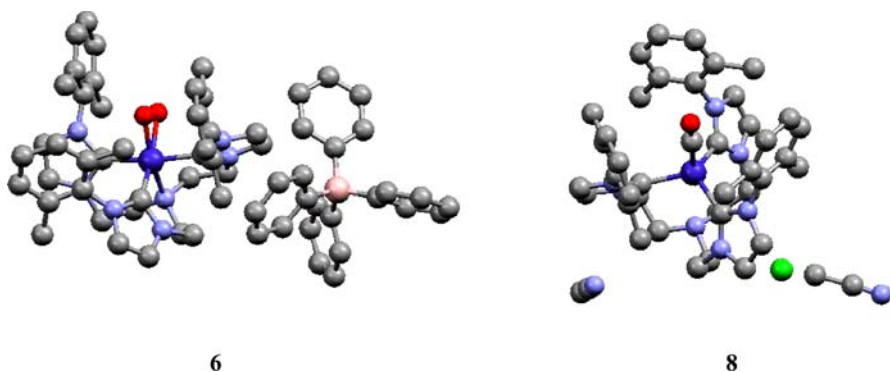

Fig. 1 Solid-state structures of the dioxygen complex **6** and carbon monoxide complex **8** (hydrogen atoms omitted for clarity)

The different ligand properties compared to phosphine ligands can be seen when comparing the NHC complexes with known analogous phosphine chelators. The differences become obvious from the coordination polyhedra and the electronic properties. The TIMEN ligands lead to high spin carbonyl complexes while the phosphine-based systems form diamagnetic complexes.

The dioxygen complex **6** shows almost no electrophilicity as it does not react with alkenes like styrene, cyclohexene or α,β-unsaturated alkenes such as 2-cyclohexene-1-one or 1,4-naphthochinones. Only with electron-deficient alkenes like TCNE or with benzoyl chloride reactivity was observed.

In the case of a π-allylnickel(NHC)chloride complex (**9**) a different re-action with oxygen was observed [75]. The active complex is formed in a one-pot reaction (Scheme 8). Solutions of complex **9** which are exposed to molecular oxygen undergo rapid color changes under precipitation of a purple solid, which has been identified as a μ-hydroxo Ni(II) dimer which is air-stable, but moisture-sensitive. It also was reported to be unstable in solution [75].
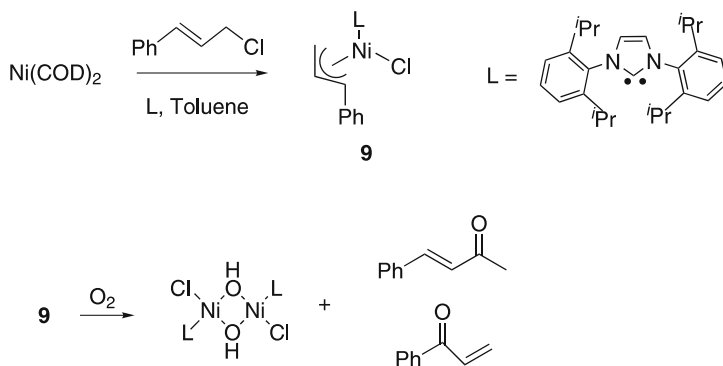
Scheme 8 Synthesis of the π-allylnickel(NHC)chloride complex **9** and its reaction with dioxygen

From the observed products and from studies using labelled material (^{18}O) it can be concluded that the nickel center promotes the splitting of the oxygen–oxygen bond. The proposed mechanism is given in Scheme 8. Reversible binding of dioxygen to the nickel center leads to the activated complex, which then undergoes rate-determining decomposition. Plausible intermediates according to kinetic studies include a Ni(III) peroxide intermediate and a monomeric hydroxonickel compound. Oxygenation of the allyl fragment leads to cinnamaldehyde and phenyl vinyl ketone in a 5 : 3 ratio.
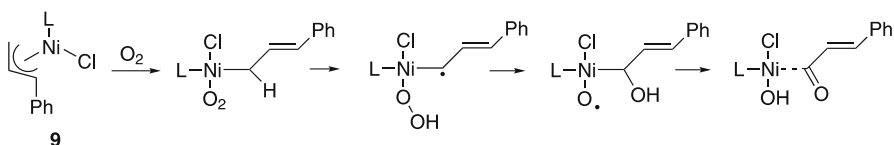

Scheme 9 Proposed mechanism of the observed allylic oxidation

The same group reported the rapid aerobic oxidation of planar bis-μ-hydroxynickel(I) dimers to yield bis-μ-hydroxonickel(II) dimers with concomitant ligand dehydrogenation [76].
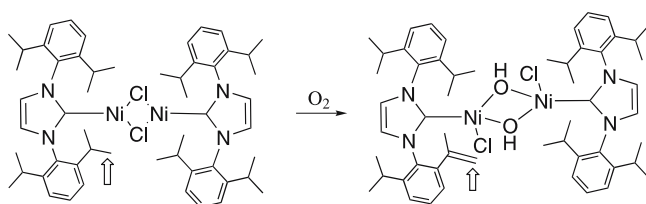
Scheme 10 Oxidation leading to ligand dehydrogenation

In contrast to the biological CO_2 fixation during the dark reaction of photosynthesis where very low concentrations of CO_2 from air can be fixed at room temperature, most reactions with transition-metal complexes or with organic substrates either require high partial pressure of CO_2 or high temperatures. An exception was published quite recently, the rapid fixation of CO_2 and O_2 from air at a palladium(0) complex **10** (Scheme 11) [77].
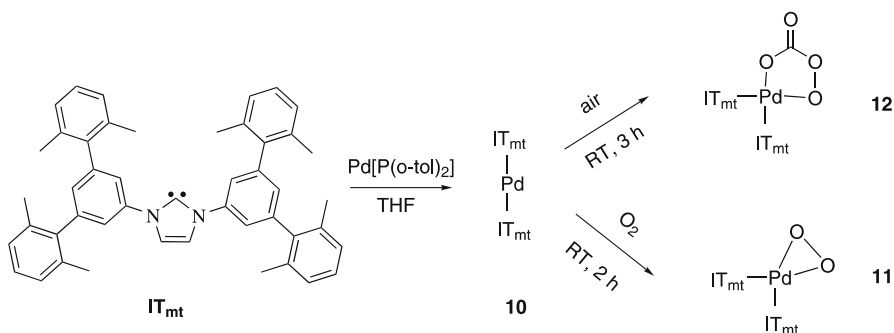

Scheme 11 Fixation of O_2 and CO_2 at a palladium(0) complex **10**

The ligand 1,3-bis(2,2″, 6,6″-tetramethyl-*m*-terphenyl-5′-yl)imidazole-2-ylidene) IT_{mt} was designed to facilitate the formation of low-coordinate species. It has a much higher overall degree of bulkiness than the well-known 1,3-bis(2,4,6-trimethylphenyl)imidazoline-2-ylidene (IMes), but in the vicinity of the carbene center it is less severe because of the absence of substituents in the ortho-position.

Exposure of the crystalline palladium(0) complex **10** to air at room temperature caused a color change from deep red to pale yellow. The formation of the palladium(II)peroxocarbonate complex **12** was confirmed by spectroscopic analysis as well as a solid-state structure. Control reactions revealed that the first intermediate is a palladium(II)peroxo complex **11**.

The analogous dioxygen species $(IMes)_2Pd(O_2)$ was isolated for the $Pd(IMes)_2$ complex, confirming the above analysis [78]. But in this case the peroxo complex does not react with CO_2. Addition of acetic acid to a toluene solution of the peroxo complex produces a hydroperoxopalladium(II) complex species $(IMes)_2Pd(OAc)(OOAc)$. Further protonolysis to yield hydrogen peroxide proceeds quite slowly (Scheme 12). Details are described in another article of this issue by S. Stahl.
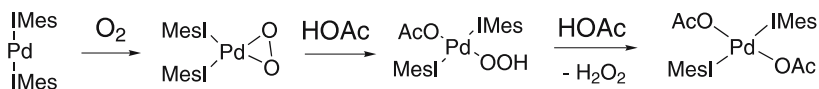
Scheme 12 Palladium dioxo intermediate

A general simplified mechanism for palladium-catalyzed aerobic oxidation reactions and the different intermediates is given in Scheme 13.
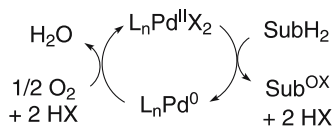

Scheme 13 Palladium-catalyzed aerobic oxidations

4.2
## Transformation of Alcohols

But not only palladium(0) complexes can activate CO or O_2, also palladium(II) complexes have been reported to be active in the presence of carbon monoxide or dioxygen as it was shown in the direct synthesis of polycarbonate from CO and phenol or bisphenol A [79, 80]. The authors could confirm the positive influence of the NHC ligand comparing the activity and reactivity of the palladium-carbene complex with the corresponding $PdBr_2$ catalyst. The molecular weights and yields of the polycarbonates improved with increasing steric hindrance of the substituents in the 1,1′-position of the carbene complex.
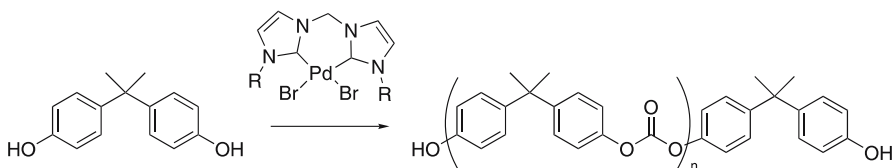
Scheme 14 Palladium(II)biscarbenes as catalysts for the oxidative carbonylation

The oxidation of alcohols to carbonyl compounds is one of the most important transformations in organic synthesis. Although many different methods have been developed, some of the most popular reactions suffer from the necessity to use toxic reagents in stoichiometric amounts or the production of large quantities of waste. Therefore, catalytic reactions using a simple oxidant like oxygen or air are still of interest to the community. Many different metals have been used in the last years, but palladium seems to be the most promising transition metal. While there is a long history for the use of palladium in the oxidation of alcohols [81–84], the benchmarks might be the Uemura system [85–87] (pyridine/Pd(OAc)$_2$) and the Sheldon system [88] (phenantroline/Pd(OAc)$_2$). Although they already succeeded in using low catalyst loadings there was still room for improvement by NHC-palladium complexes. Quite recently reports appeared where carbene ligands
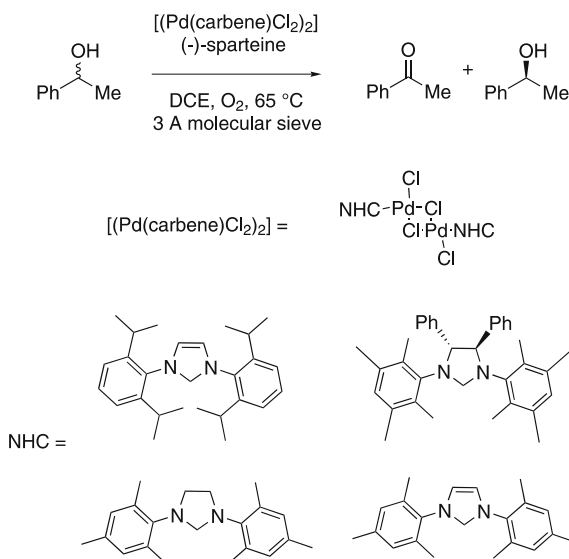
promoted the aerobic oxidation of alcohols even at room temperature [89–91]. A key role is attributed to the acetate counterions in **13**, which according to the authors allow intramolecular hydrogen transfer. The optimized catalytic system is comprised of 0.5 mol % **13**, 2 mol % HOAc, and 3 Å molecular sieve in toluene at 60 °C under a balloon pressure of oxygen. For activated substrates up to 1000 turnovers have been observed. This system converts primary as well as secondary benzylic, allylic and aliphatic substrates to the corresponding carbonyl compounds in high yields.
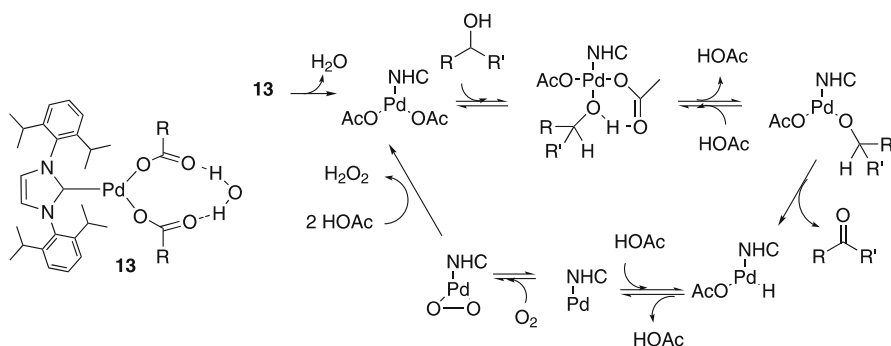
Scheme 15 Alcohol oxidation by a 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene) palladium(II) complex **13**

The proposed mechanism is given in Scheme 15. Initially the dissociation of water, maybe trapped by the molecular sieve, initiates the catalytic cycle. The substrate binds to the palladium followed by intramolecular deprotonation of the alcohol. The alkoxide then reacts by β-hydride elimination and sets the carbonyl product free. Reductive elimination of HOAc from the hydride species followed by reoxidation of the intermediate with dioxygen reforms the catalytically active species. The structure of **13** could be confirmed by a solid-state structure [90]. A similar system was used in the cyclization reaction of suitable phenols to dihydrobenzofuranes [92]. The mechanism of the aerobic alcohol oxidation with palladium catalyst systems was also studied theoretically [93–96].
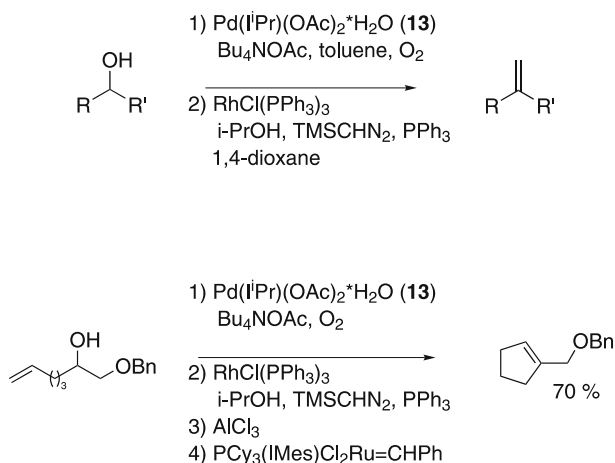
Even more interesting is the oxidative kinetic resolution of alcohols under aerobic conditions. The system Pd(II)/sparteine/O_2 was reported to convert a racemic alcohol with high selectivity into the ketone and the alcohol [97–99]. This has also been shown to work with palladium carbene complexes (Scheme 16).

Scheme 16 Aerobic oxidative kinetic resolution of secondary alcohols

Using the catalyst system described above in combination with a rhodium phosphine catalyst Lebel reported the de novo synthesis of alkenes from alcohols [100]. They developed a one-pot process, avoiding the isolation and purification of the potentially instable aldehyde intermediate. They combined the oxidation of alcohols developed by Sigman [89] with their rhodium-catalyzed methylenation of carbonyl derivatives. The cascade process is compatible with primary and secondary aliphatic as well as benzylic alcohols in good yields. They even added another reaction catalyzed by a NHC complex, the metathesis reaction, which has not been addressed in this review as there are many good reviews, which exclusively and in great depth describe all aspects of the reaction.

The three-reaction one-pot procedure allows the conversion of suitable alcohols to cyclic alkenes in relatively good yields, one example is given in Scheme 17.

1) Pd(I^{i}Pr)(OAc)$_2$*H$_2$O (**13**)
   Bu$_4$NOAc, toluene, O$_2$

2) RhCl(PPh$_3$)$_3$
   i-PrOH, TMSCHN$_2$, PPh$_3$
   1,4-dioxane

1) Pd(I^{i}Pr)(OAc)$_2$*H$_2$O (**13**)
   Bu$_4$NOAc, O$_2$

2) RhCl(PPh$_3$)$_3$
   i-PrOH, TMSCHN$_2$, PPh$_3$

3) AlCl$_3$

4) PCy$_3$(IMes)Cl$_2$Ru=CHPh

70 %

**Scheme 17** Multicatalytic oxidation of alcohols

Iridium complexes like [Cp*IrCl$_2$]$_2$ have been found to catalyze the Oppenauer-*type* oxidation of alcohols. However, the catalytic activity was not really satisfactory as the turnover numbers were less than 200. But when NHC ligands were introduced, the catalytic activity increased considerably. Treatment of [Cp*IrCl$_2$]$_2$ with two equivalents of free carbene resulted in the formation of air-stable complexes of the type Cp*Ir(NHC)Cl$_2$ in good yields [101]. With AgOTf in acetonitrile they could be converted to the dicationic complexes [Cp*Ir(NHC)(CH$_3$CN)$_2$]$^{2+}$. It turned out that the neutral complexes do not show any activity while for the dicationic complexes (0.10 mol % Ir, 0.10 mol % K$_2$CO$_3$, acetone, 40 °C, 4 h) turnover numbers up to 6600 were measured [102]. Control experiments with isoelectronic phosphine ligands revealed the importance of the NHC ligands, as there was no catalytic activity observed for the phosphines. The postulated mechanism together with the most active catalyst **14** is given in Scheme 18 [101].
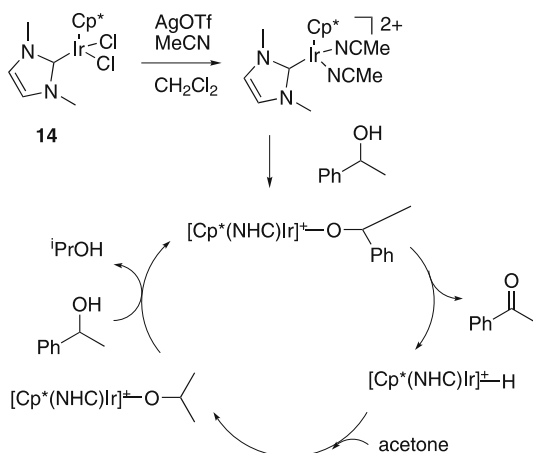
Scheme 18 Oppenauer-*type* oxidation catalyzed by Cp*Ir(NHC) complexes

4.3
Alkyne Oxidation

The hydration of unsaturated carbon-carbon bonds is one of the most environmentally friendly oxidation reactions. It had been reported that highly polar phosphane Au(I) complexes catalyze the addition of nucleophiles to non activated alkynes [103, 104]. Consequently the replacement of the phosphine by a NHC ligand was attempted and tested in the catalytic addition of water to 3-hexyne (Scheme 19). The catalyst (NHC)Au(I)OAc was synthesized from the corresponding chloride complex by addition of AgOAc [105]. Tris-(pentafluorophenyl)borane $B(C_6F_5)_3$ was needed as a co-catalyst to successfully catalyze the water addition. The authors mention that the chloride complex itself had been tested and was not active, indicating the need for a weakly coordinating ligand. The catalysis could be accomplished, but in this case the phosphine ligands provide better conversions.
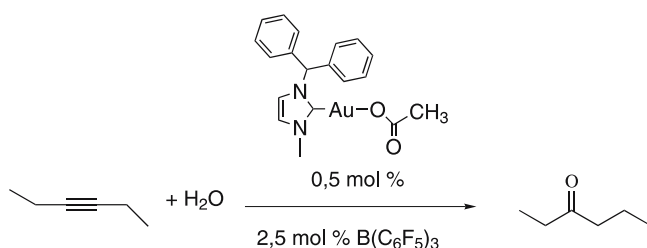
Scheme 19 Catalytically active gold carbene

4.4
Olefin Oxidation

The well-known Wacker oxidation of terminal alkenes to methylketones has been used for many years on a large scale. It requires a catalytic amount of Pd(II) together with stoichiometric $CuCl_2$ under aerobic conditions. But it is limited by palladium decomposition and chlorinated byproducts. Therefore, a lot of research has been devoted to modifying the reaction, but most of the time copper cocatalysts were necessary. Another problem is the often observed cleavage of the double bond and the production of aldehydes.
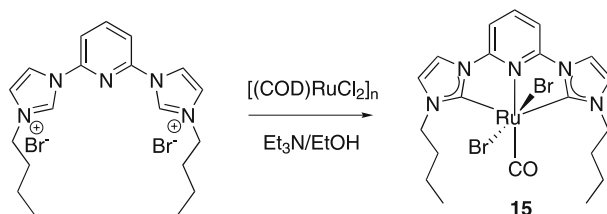

Scheme 20 Synthesis of Ru(CNC)(CO)Br$_2$ **15**

This was observed for a ruthenium(II) pincer complex Ru(CNC)(CO)Br$_2$ **15** (CNC = 2,6-bis(butylimidazole-2-ylidene)pyridine), which can be obtained in moderate yield from the direct reaction of $[(COD)RuCl_2]_n$ and 2,6-bis(1-n-butylimidazolium-3-yl)pyridine bromide in refluxing ethanol in the presence of NEt$_3$ (Scheme 20) [106]. The source of the CO in this reaction is believed to be oxidative addition of CH$_3$CHO followed by CH$_3$ migration and reductive CH$_4$ elimination. A similar mechanism is known from the synthesis of RuHCl(CO)(PPh$_3$)$_3$ [107]. Reaction of RuCl$_3$ with the ligand under similar conditions leads to the formation of [Ru(CNC)$_2$](PF$_6$)$_2$ (CNC = 2,6-bis(butylimidazole-2-ylidene)pyridine) **16**, where two pincer ligands occupy all six positions of a distorted octahedral geometry. This compound proved to be very stable and no catalytic activity was reported, but **15** catalyzes hydrogen transfer as well as the clean oxidation of olefins to aldehydes without unwanted byproducts. The catalytic system consists of 1 mol % catalyst and NaIO$_4$ in CDCl$_3$/H$_2$O (9 : 1).

The oxidation to methyl ketones without cleavage of the double bond was reported recently for a palladium NHC complex [108]. When the authors used the previously described catalyst **13** in THF with dioxygen for the oxidation of styrene they found that together with the phenylmethylketone a significant amount of γ-butyrolactone was formed. Analysis of the mechanism led to the conclusion that THF is oxidized to a hydroperoxide species which is the real oxidant. They therefore tried *tert*-butylhydroperoxide (TBHP) and found immediate conversion without any induction period. Optimized conditions include 0.75 mol % of the previously described dimeric complex

[(Pd(NHC)Cl$_2$)$_2$] (Scheme 16) together with 3 mol % AgOTf and 5.5 eq. TBHP in methanol under aerobic conditions at 35 °C.

The oxidation of alkenes to diols via 1,2-bis(boronate) esters was reported for a silver(I) NHC complex **17** [109]. 1-Methyl-3-(+)-methylmenthoxide imidazolium chloride was used as the precursor together with an excess of Ag$_2$O (Scheme 21). The resulting complex was significantly more active than when prepared in situ from Ag$_2$O and the imidazolium salt.
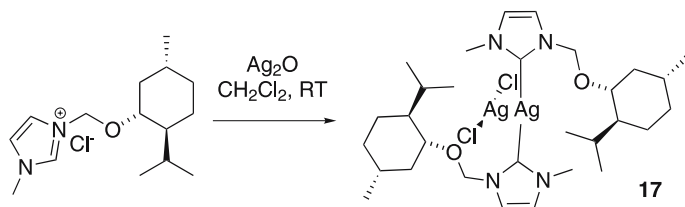
Scheme 21 Catalytically active silver carbene complex **17**

Bis(catecholato)diboron was added to internal and terminal alkenes in the presence of 5 mol % catalyst **17** in THF at room temperature. The resulting diborane complex was oxidized to the corresponding diol by a NaOH/H$_2$O$_2$ mixture. The conversions are strongly dependent on the electronic situation of the double bond. Vinylcyclohexane proved to be the most active substrate at 90% conversion compared to 76% conversion of styrene. Substituents in the para position of the styrene dramatically reduced the conversion (F: 12%; Cl: 14%; CF$_3$: 10%). Although the ligand is chiral, no asymmetric induction was observed in the reaction.

4.5
Alkane Oxidation

The CH-activation of alkanes and especially of methane and their catalytic conversion to alcohols is one of the major challenges for chemists. Methane as the major part of natural gas is currently the cheapest source of hydrocarbons and the need for methanol will increase in the near future. Methane conversion to methanol would make a conveniently transportable fuel and also a new carbon source for the chemical industry.

The catalytic homogeneous oxidation at low temperatures is therefore economically interesting, but also very difficult to achieve due to the high stability of CH-bonds. Partial oxidation is particularly hard in alkanes as classical oxidation procedures tend to overoxidize them. In the case of methane this would result in the formation of CH$_2$O, CO and CO$_2$. Low valent transition metals, however, are capable of activating the CH bond and rendering that problem less important as the difference in reactivity between the CH bond in methane and methanol is not that big.

Palladium- and platinum compounds have been successfully used for the functionalization of alkanes [110–112]. An efficient and highly selective catalytic system is a platinum complex with a bipyrimidine ligand [Pt(bpym)Cl$_2$], which provides up to 72% yield of methanol. The major drawback of the system is the reaction medium. Oleum leads to a large amount of diluted sulfuric acid when the formed ester is hydrolized.

While the research in the direction of the CH activation had its advances, the central problem is still not solved. There is no selective and efficient catalytic functionalization reaction known for unactivated sp^3 CH bonds. Only a small number of systems have been published that are capable of functionalizing methane catalytically [113–115], many of them dealing with the direct carbonylation to acetic acid [116–119].

We reported the use of N-heterocyclic carbene complexes (NHC) for the catalytic activation of methane [55, 56]. We found that solutions of N-heterocyclic carbene complexes of palladium(II) in carboxylic acids catalyze the conversion of methane to the corresponding methylesters. The high thermal stability of palladium(II) carbene complexes could be shown for complex **18** (Scheme 22), which we also structurally characterized [120]. An extraordinary feature is the unprecedented resistance of the palladium-NHC-complexes **18–22** under the acidic oxidizing conditions which are necessary for the CH-activation and functionalization.

18: R = tBu, X = Br
19: R = tBu, X = I
20: R = Me, X = Br
21: R = Me, X = I
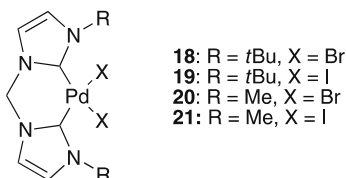
Scheme 22 Palladium biscarbene complexes **18–22**

A suspension of potassiumperoxodisulfate in a mixture of trifluoroacetic acid and trifluoroacetic acid anhydride at a methane pressure of 20–30 atmospheres methane and 80–100 °C in the presence of catalytic amounts of **18** and **20** leads to the formation of the trifluoroacetic acid methylester. Scheme 23 shows the oxidative character of the reaction which formally can be described as CH$_4$ → [CH$_3$]$^+$ + H$^+$ + 2e$^-$.

$$CH_4 + CF_3COOH \xrightarrow{\textbf{18 / 20}} CF_3COOCH_3$$

K$_2$S$_2$O$_8$ 2 KHSO$_4$
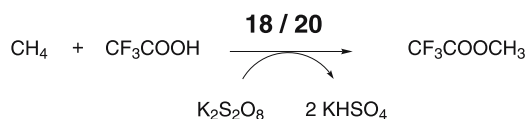
Scheme 23 Conversion of methane into the methylester of the trifluoroaceticacid

The analogous platinum complexes could be synthesized by a new synthetic route and have been structurally characterized [58], but can not be used as catalysts, since they immediately decompose in trifluoroacetic acid under formation of platinum black, whereas compounds **18–22** form clear yellow solutions in the same solvens, which even after 20 hours do not show signs of decomposition according to a NMR analysis. Reprotonation of the carbene ligands to the corresponding bisimidazolium salts can be excluded. The complexes are also stable against the addition of strong oxidants and no precipitation of palladium(II) salts was observed.

Therefore, these palladium-NHC-complexes fulfill the requirements for catalysts which are suitable for the CH-activation: a strong acid can be used as the reaction medium to protect the formed alcohols against overoxidation by forming an ester; the NHC-ligands stabilize the strong *Lewis*-acidic metal centers, which can bind the methyl species formed from methane by activation of a CH-bond and the extraordinary thermal and chemical stability allows reactions at higher temperatures in the presence of strong oxidants.

For the catalytic functionalization of methane 0.21 mmol of compound **18** and 100 equivalents $K_2S_2O_8$ are suspended in a mixture of 60 mL trifluoroacetic acid and 10 mL trifluoroacetic acid anhydride and are transferred into an autoclave. With an initial methane pressure of 20 atmospheres and a temperature of 80 °C the only product is trifluoroacetic acid methylester (510% yield relative to palladium).

The choice of the counterion has a significant influence on the activity of the catalyst, no methylester is produced by complex **19**. Similar results were obtained for compounds **20** (980%) and **21** (0%), where the steric demand of the ligands R (= methyl) is significantly lower. Additional reactions under different conditions show that the yields can be improved. After 14 hours at 90 °C catalyst **20** yielded 3000% relative to palladium (TON 30) [55].

The use of trifluoroacetic acid has the additional advantage that the formed ester can easily be removed from the reaction mixture by distillation due to the difference in boiling point between the acid and the ester. After hydrolysis, the recovered acid together with unreacted methane can be transferred back into the reactor, the catalysis could be run as a cyclic process.

DFT calculations indicated that the mechanism most likely involves three steps: electrophilic substitution, oxidation and reductive elimination. The inactivity of the iodine complexes prompted us to investigate the counterion dependence. For the methyl-substituted complexes (Scheme 23, R = CH_3) we synthesized the acetate (X = $OCOCH_3$) **22** and the chloride complex (X = Cl) **23**. The catalytic conversions are within experimental error identical to the results of the bromide complex **20**. This indicates that the dissociation of a counterion is a necessary condition for the activity of the complex [59].

We recently succeeded in synthesizing platinum-NHC complexes which are stable under the reaction conditions [57]. Introduction of aromatic substituents (Scheme 24, R= NO_2, Cl, Br, OCH_3, COOEt) in the imidazole changed the properties of the complexes quite significantly.
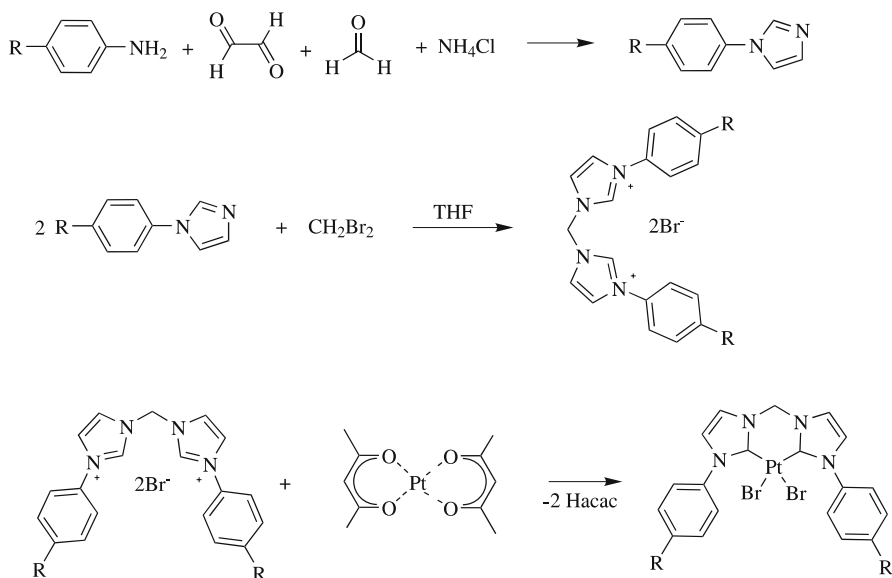
Scheme 24 Synthesis of acid stable platinum-NHC-complexes

Unfortunately, these new complexes do not show higher activities than the palladium complexes **18** and **20**, further optimization of the catalysts and reaction conditions is necessary to improve the reaction to a point where it becomes economically interesting.

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