CHAPTER 1. Introduction

1.1 History of *N*-Heterocyclic Carbene Chemistry

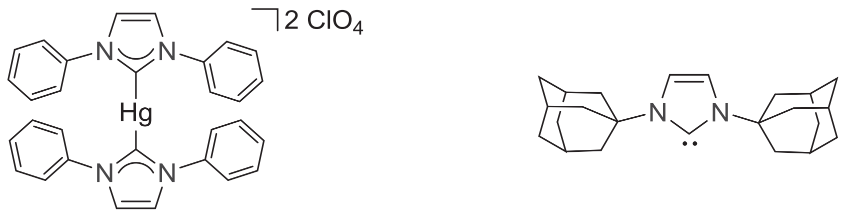
N-heterocyclic carbenes have found robust development in the past two decades,[1] and were widely used as ubiquitous ligands in organometallic catalysis[2] and organocatalysis.[3] Selected milestones in the history of *N*-heterocyclic carbene chemistry are shown in **Scheme 1.1**.

The first well-defined metal complex **1.1** based on an *N*-heterocyclic carbene ligand was reported by Wanzlick in 1968.[4] Yet, the importance of this new carbene type as ligands for metal complexes was not widely recognized in the following years until in 1991, Arduengo isolated the first stable crystalline imidazol-2-ylidene compound **1.2** from its imidazolium precursor, in which the bulky wingtip was thought to have provided crucial kinetic stabilization effect.[5] In 1995, the first class of *N*-heterocyclic carbene palladium complexes, such as complex **1.3** as homogeneous catalyst for Heck reaction, were synthesized and showed higher stability in the presence of oxygen and moisture, compared to the widely-used phosphine/phosphite ligands.[6] This discovery pulled a trigger to the robust development of *N*-heterocyclic carbene chemistry, especially for NHC metal complexes catalyzed organic reactions.[2a]

N-heterocyclic carbenes served as ligands not only for metal atoms, but also for non-metal atoms, such as carbon. For instance, bis(NHC) assisted bent allene **1.4**, also known as carbodicarbene, was synthesized and showed peculiar chemistry properties, which challenged the prevailing comprehension of carbon chemistry.[7]

In 2001, an unusual *N*-heterocyclic carbene iridium complex **1.5** was reported.[8] Different from imidazol-2-ylidenes, in the *N*-heterocyclic carbene ligand of **1.5**, the carbenic carbon located at the C4/5 position. Thereafter, more complexes with this type of ligands were reported and these ligands were referred to as ‘abnormal *N*-heterocyclic carbenes’. After the studies on abnormal *N*-heterocyclic carbene chemistry for almost one decade, the first free abnormal carbene species, *i. e.* imidazol-5-ylidene **1.6** was isolated.[9]

The transfer reaction from normal NHC iron complex **1.6a** to its abnormal NHC congener **1.7a** by heating suggested that encumbering substituents on the wingtip of the NHC could drive the rearrangement between these two isomers (**Scheme 1.1**).[10]



1.1

1968

first NHC metal complex

1.2

1991

first isolated free carbene

1.3

1995

NHC complex as catalyst for Heck reaction

1.4

2008

NHC substituted bent allene (carbodicarbene)

1.5

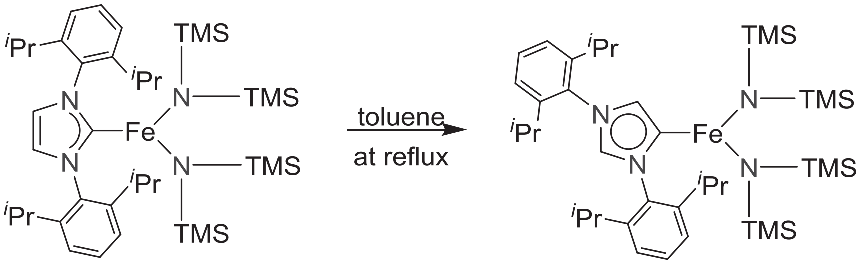
2001

first complex based on imidazol-5-ylidene

1.6

2009

first free imidazol-5-ylidene (abnormal NHC)



1.7a

1.8a

2013

rearrangement from abnormal NHC to normal NHC metal complex

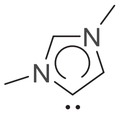
Scheme 1.1. Milestones of chemistry on *N*-heterocyclic carbenes.

1.2 Imidazole Derived Carbenes

1.2.1 Imidazol-2-ylidene carbenes

Among all *N*-heterocyclic carbenes, imidazoly-2-lidenes, also referred to as Arduengo carbenes in early times, are certainly the most important. Synthesis of the imidazolium precursors, synthetic strategy of imidazole based carbene metal complexes (specially silver,[11] palladium,[12], ruthenium,[13] gold[14] and copper[14b] complexes) and their application in catalysis were well studied and summarized.[2, 15]

imidazol-2-ylidene
i.e. normal *N*-heterocyclic carbene



imidazol-4/5-ylidene
i.e. abnormal *N*-heterocyclic carbene

An early DFT calculation study on zirconium imidazol-2-ylidene complexes claimed that ‘the Arduengo carbene ligand acts as a pure σ-donor ligand at these very electrophilic group 4 metallocene complexes’.[16] The Arduengo carbene ligand acted as a pure donor in this special situation was probably because there were no d-electrons in the metal center to donate to the ligand *via* back-bonding. Later studies showed that, for complexes with d-orbital electrons at the metal center, Arduengo carbenes no longer served as ‘pure σ-donor ligand’ and they also had π acceptor character, just like other σ-donor ligands such as phosphine ligands (**Figure 1.1**).[17]

The π^* orbitals of the ligands could accept electrons from the electron-rich metal centers and the back-donation was not negligible. As for the electron-poor metal center, like that in d^0 complexes, the electron could also be donated from the π orbital of the ligand into the metal center, although the π orbital was normally not considered as a major donating party. Therefore, the electronic properties of imidazol-2-ylidene ligands were more complicated than ‘pure donors’. Yet, both theoretical and experimental studies still suggested that imidazol-2-ylidenes were stronger donor ligands than phosphines and phosphites in general.

For example, the donating capacity of an NHC ligand was evaluated by the CO vibrational frequency of the related NHC metal carbonyl complexes.[18] With other variables fixed in a metal complex, a stronger donating NHC ligand made the metal center to become more electron-rich. Therefore, the CO ligand obtained more back-donation from the metal into its anti-bonding π^* orbital, resulting in a weaker CO bond and thus a smaller value of its vibrational frequency.[18] Meanwhile, by comparison of the energies of HOMOs of different ligands, an early study confirmed the conclusion that imidazol-2-yliendes were better donating ligands than phosphine ligands.[18]

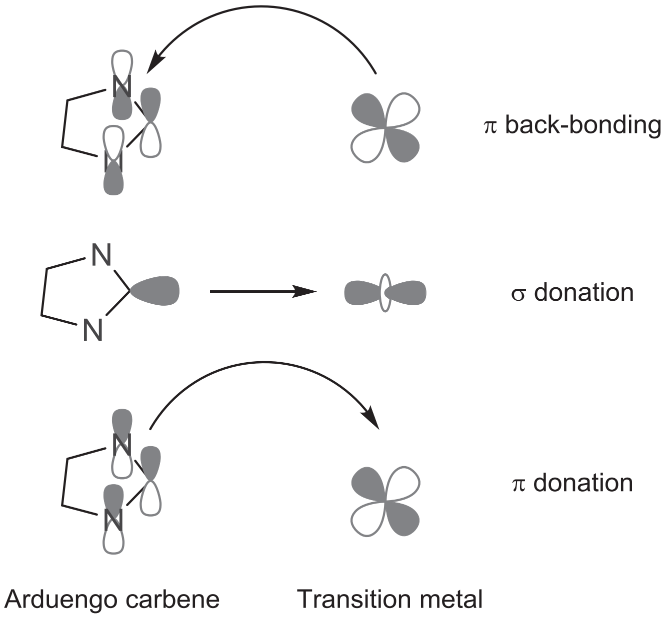
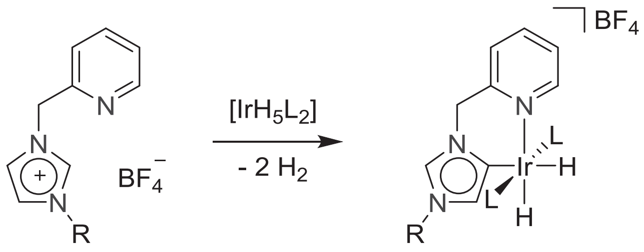


Figure 1.1. Selected molecular orbitals of *N*-heterocyclic carbene and their relationship to metal fragment.

1.2.2 Imidazol-4/5-ylidene carbenes

From the beginning of the new millennium, imidazol-4/5-ylidenes, constitutional isomers of the imidazol-2-ylidene counterparts, have attracted lots of attention. Several reviews were published to discuss various types of unconventional NHCs[1], the precursors[19], complexes[15b] and the application of their complexes in catalysis.[20]

In 2001, Crabtree and his co-workers serendipitously isolated an unusual NHC iridium complex **1.5** with the metal atom bound to the C5 of the imidazole ring (Eq 1.1), evidenced by the ^{1}H NMR spectroscopic data that the C2-H and C4-H signals remained.[8] This new type of NHC was then termed as ‘abnormal’ NHC, in order to be differentiated from normal NHC with the carbenic carbon atom at 2-position of the imidazole ring. Complex **1.5** was quite stable and showed no tendency to rearrange to the normal carbene isomer.

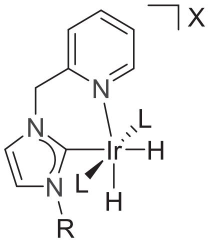
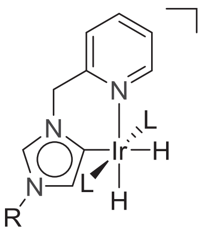


1.9 1.5 (1.1)

Considering that the C2 proton was more acidic than the C5 proton, the cleavage of C2-H was easier. Thus, the cause of the unexpected formation of complex **1.5** was generally not related to electronic reason.

The mechanism of the formation of the abnormal NHC iridium complex was then studied. A series of similar reactions (like that in Eq 1.1) with different variables (various R groups and counterions) indicated that both steric congestion of the wingtips on the azolium ring, and the counterions of the precursor influenced the selective formation of normal or abnormal NHC metal complexes (**Table 1.1**).[21]

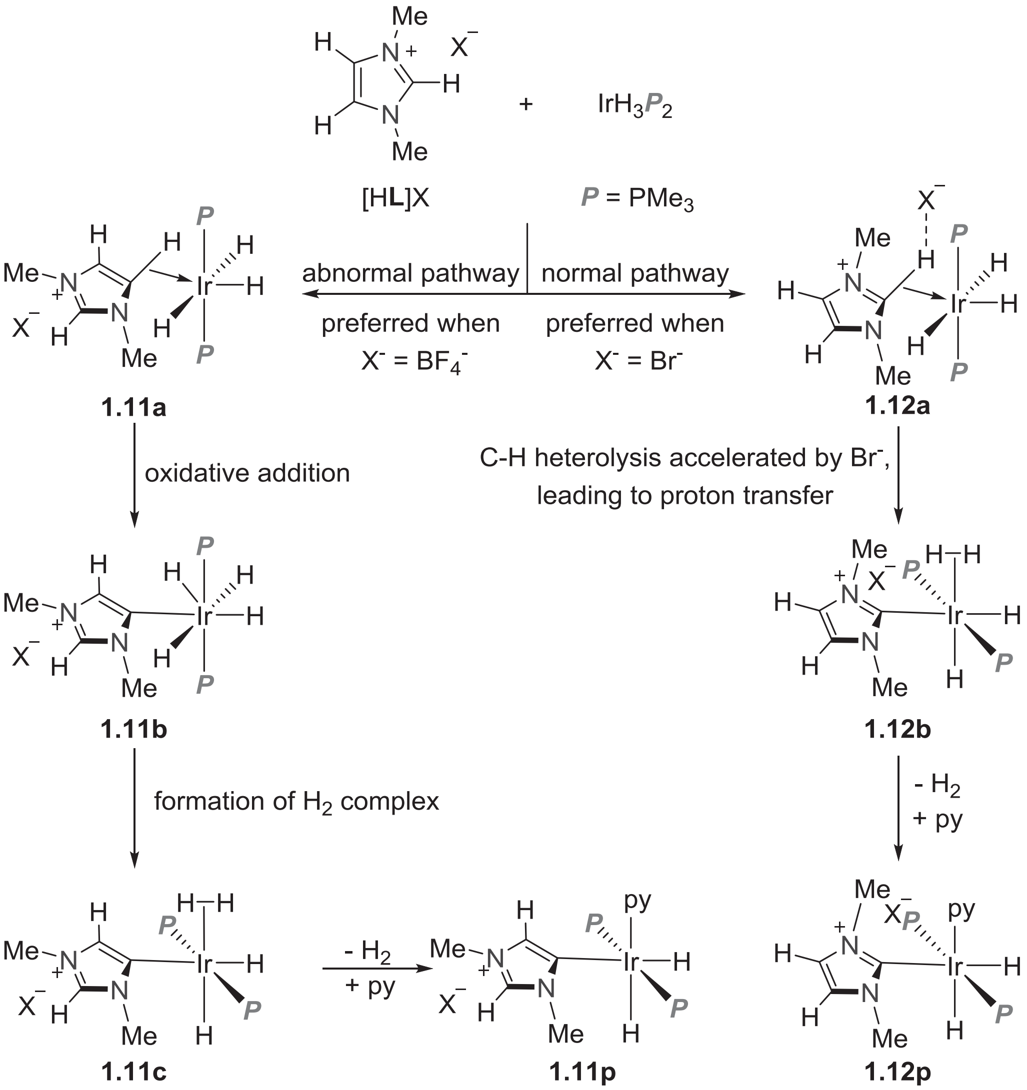
Table 1.1. Formation of normal/abnormal carbene complexes affected by counterions.

Entry	R	X	 **1.10a**	 **1.10b**
a	Me	Br	91	9
b	Me	OAc	80	20
c	Me	BF_4	45	55
d	Me	PF_6	50	50
e	Me	SbF_6	11	89
f	^{i}Pr	BF_4	0	100

Comparison of **Entry c** and **Entry f** implied that a ligand precursor with bulkier wingtips preferred to form abnormal NHC complex (**Entry f**). The steric repulsion between the wingtip and co-ligands of the product was significantly reduced in **Entry f**; while for the ligand precursor with less bulkier wingtip in **Entry c**, the normal NHC complex became more stable from thermodynamic point of view.

The counterions of the ligand precursor also had strong influence on the ratio of the normal and abnormal carbene complexes formed. With non-coordinating counterion

$[SbF_6]^-$ (**Entry e**), abnormal NHC metal complexes were preferred, while with Br^-, which could easily form H-bondings with protons of the imidazolium ring of the ligand precursors, normal NHC complexes were more likely to be generated. Note that, both of the products were reasonably stable and no transformation reaction between them was observed under various reaction conditions, even in highly acidic environment.



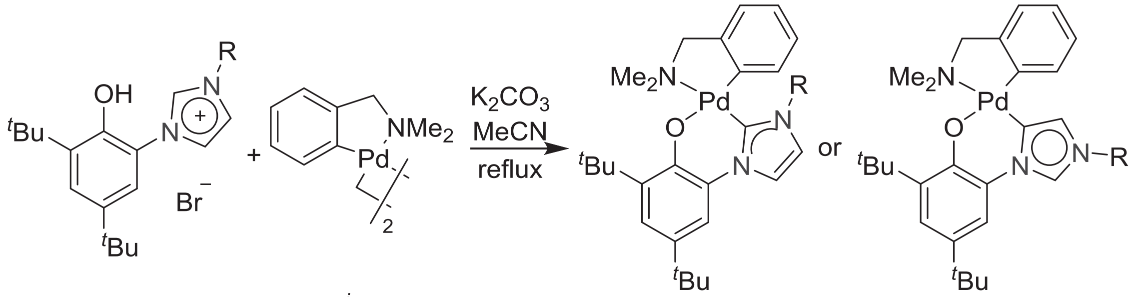
Scheme 1.2. Proposed mechanism of the selective formation of normal *versus* abnormal NHC metal complexes.

Based on the experimental observations and the subsequent computational studies with simplified models, a plausible mechanism for the selective formation of abnormal or normal NHC complexes **1.11p** and **1.12p** was proposed (**Scheme 1.2**).

In the proposed mechanism, $[BF_4]^-$ induced the oxidative addition of the C5–H onto $[Ir^{III}H_3(PMe_3)_2]$, forming an Ir^V intermediate **1.11b**, which then rearranged to the H_2-adduct complex **1.11c** and finally the abnormal NHC complex **1.11p**; while Br^- accelerated the heterolysis of the weaker C2–H bond (compared to the C5–H bond) in **1.12a** to form the H_2-adduct complex **1.12b** directly, eventually yielding the normal NHC complex **1.12p**.[21]

As a conclusion, ligand precursors with bulkier wingtip on the azolium rings and with non-coordinating counterion tended to form abnormal NHC complexes and ligand precursors with less hindered wingtips and with counterions that could easily form H-bonding preferred to form normal NHC complexes. The conclusion was consistent with other reports.

For example, in the reactions of ligand precursors **1.13a-1.13e** with palladium(II) species in the presence of potassium carbonate, when R was methyl, *iso*-propyl, phenyl or mesityl group, normal NHC palladium complexes **1.13a-1.13d** was formed; while when R group was the highly bulky *tert*-butyl group, abnormal NHC complex **1.13e** was formed (**Scheme 1.3**).[22]



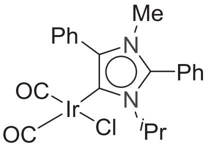
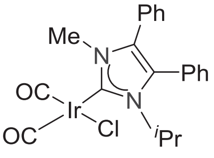
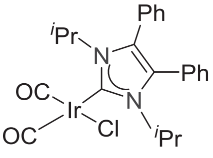
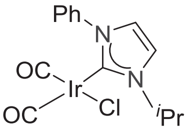
1.13a: R = Me, **1.13b**: R = ^{i}Pr,
1.13c: R = Ph, **1.13d**: R = Mes,
1.13e: R = ^{t}Bu

1.14a: R = Me, **1.14b**: R = ^{i}Pr
1.14c: R = Ph, **1.14d**: R = Mes,

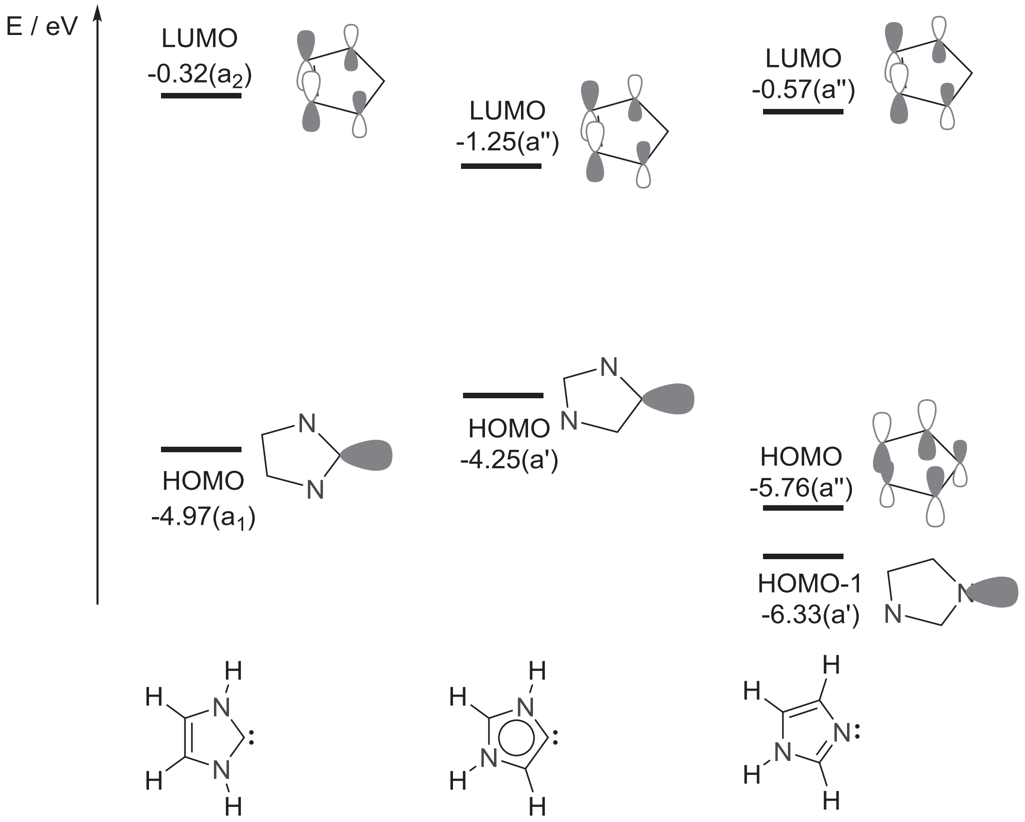
1.14e: R = ^{t}Bu

Scheme 1.3. Selective formation of normal/abnormal carbene complexes determined by bulkiness of R group.

Table 1.2. Vibration frequencies of CO in complex **1.15a-1.15d**.

	 **1.15a**	 **1.15b**	 **1.15c**	 **1.15d**
ν_{avg}(CO)/cm^{-1}	2003	2017	2017	2019

By means of comparing the vibrational frequency of CO of their metal carbonyl complexes, the new abnormal NHCs proved to be better donating ligands. For instance, the average CO vibrational frequency of the abnormal NHC iridium complex **1.15a** was considerably lower than those in the similar normal NHC complexes **1.15b-1.15d** (**Table 1.2**),[23] indicating that abnormal NHCs were stronger donors than normal NHCs.

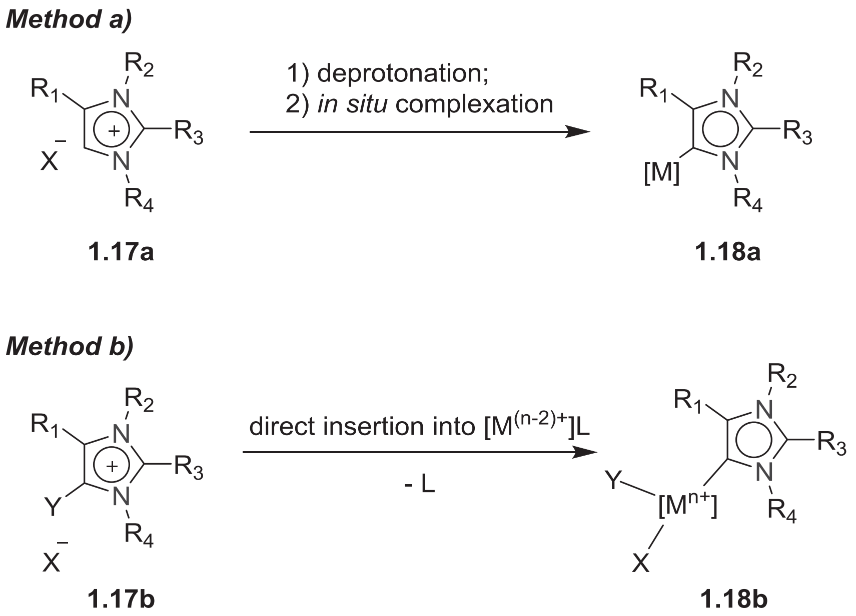


1.16a **1.16b** **1.16c**

Figure 1.2. LUMO and HOMO of imidazol-2-ylidene, imidazoly-4/5-ylidene and imidazolyl.

The conclusion was consistent with a DFT computational study (**Figure 1.2**).[24] The energies of HOMOs of the calculated normal and abnormal NHC models (**1.16a** and **1.16b**, respectively) were -4.97 eV and -4.25 eV, respectively, indicating that the abnormal NHC had a stronger tendency to act as an electron donor; the energy gaps between LUMO and HOMO for normal and abnormal NHC were 4.65 eV and 4.00 eV, respectively, suggesting that the normal NHC was more stable than the abnormal NHC. It was noteworthy that the σ-donating orbital of **1.16c**, which would coordinate to metal fragments, was HOMO-1 instead of HOMO. The HOMO-1 energy (-6.33 eV) was much smaller than those of HOMOs of **1.16a** and **1.16b**, implying that imidazole as a nitrogen-coordinating ligand was a reasonably poor σ-donor compared to the isomeric carbene donors.[24]

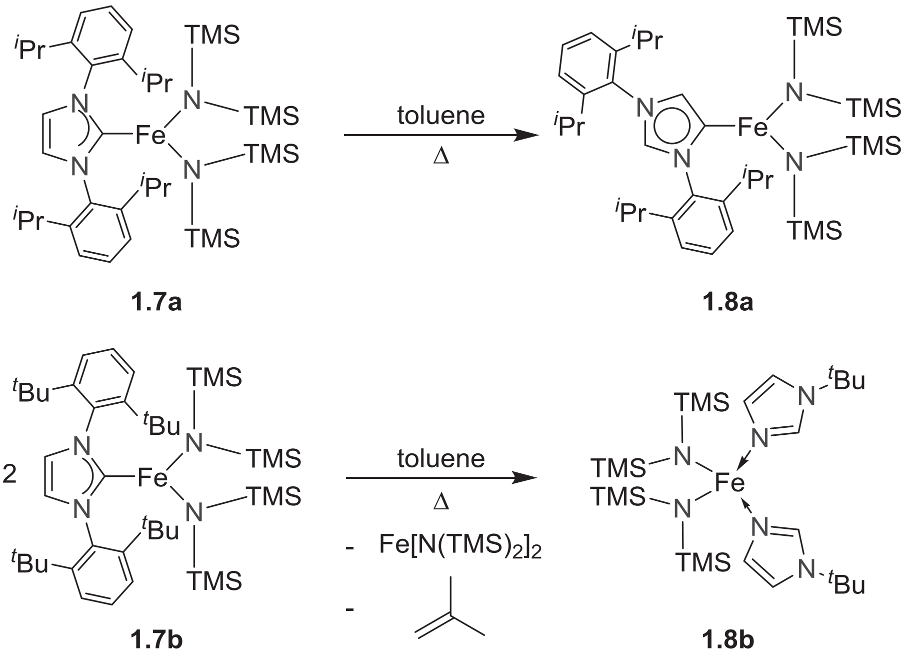
Synthesis of abnormal NHC metal complexes became more attractive after their stronger donating capacity had been revealed. Besides several fortuitous isolations of abnormal carbene species,[25] general strategies were also developed to synthesize abnormal NHC metal complexes. Basically, abnormal NHC complexes could be prepared either a) from the imidazolium precursors **1.17a** with their C2 positions blocked with inert funcational groups [23, 26] to form complex **1.18a**, or b) by oxidative addition of C4/5–X (X = hydrogen[27] or halogen atoms[28]) bonds of the imidazolium precursors **1.17b** onto low-valence metal fragments (**Scheme 1.4**) to generate **1.18b**, in which the value of oxidation state of the central metal ion was increased by two units.



Scheme 1.4. Two synthetic methods to abnormal NHC metal complexes **1.18a-1.18b**.

The transformation between normal and abnormal NHC complexes was quite rare.[29] Recent research found that an iron normal NHC complex **1.7a** was easily transferred to its abnormal NHC isomer **1.8a** by heating at reflux in toluene.[10] A plausible driving force was the release of the steric congestion caused by the bulky wingtip group, 2,6-di(isopropyl)phenyl, in **1.7a**. Meanwhile, the rearrangement pathways were also strongly influenced by the wingtip; when the wingtip was *tert*-butyl group, the normal NHC complex **1.7b** was transformed to a tetrahedral bis(*N*-*tert*-butylimidazole) iron complex **1.8b** under the same reaction condition (**Scheme 1.5**).

The transformation between normal and abnormal NHC metal complexes was a relatively new topic and the reaction mechanism was still unclear.



Scheme 1.5. Reactions of normal NHC complex to the abnormal NHC metal complex or imidazole metal isomer.