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# A Mechanistically and Operationally Simple Route to Metal-N-Heterocyclic Carbene (NHC) Complexes

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Abstract: We have been puzzled by the involvement of weak organic and inorganic bases in the synthesis of metal-N-heterocyclic carbene (NHC) complexes. Such bases are insufficiently strong to permit the presumed required deprotonation of the azolium salt (the carbene precursor) prior to metal binding. Experimental and computational studies provide support for a base-assisted concerted process that does not require free NHC formation. The synthetic protocol was found applicable to a number of Transition Metal- and Main Group-centered NHC compounds and could become the synthetic route of choice to form M-NHC bonds.

Introduction

The use of N-heterocyclic carbenes (**NHC**) as a synthetic tool in organic and organometallic catalysis is nowadays ubiquitously found in the scientific literature.[1] Such carbenes have revolutionized modern homogeneous catalysis[1,2] as ligands in organometallic complexes and more recently as ligands on nanoparticles and surfaces.[3] Their exceptional reactivity and stability have rendered them *mainstream entities* in synthetic methodology. The most common synthetic routes leading to metal-NHC complexes are depicted in Scheme 1, as typical examples of accessing Au-NHC complexes. They make use of the free carbene generation (**route A**)[4] or transmetallation (**route B**)[5] approaches to obtain highly stable Au-NHC bonds.[6] These methodologies can be troublesome as the free carbene generated in **route A** can be quite sensitive/reactive and requires the action of strong bases,[4b] while **route B**, in most cases, makes use of light-sensitive silver as starting M-NHC complexes for transmetallation[5] to transfer the NHC group to its final bonding partner. These two approaches involve multiple steps and are not atom economical. Simpler, alternative synthetic strategies (**route C**) have been developed, where a built-in base is used.[5b,7] However, this approach is to date limited to the use of copper and silver oxides, and requires an

additional transmetallation step to install new metal-NHC bonds. Recently, we have reported a different approach that uses a weak base (K_2CO_3 or NEt_3, among others), the imidazolium salt and a common metal precursor directly leading to the targeted complex. We[8] and Gimeno[9] have reported initially our findings on gold complexes (**route D**, Scheme 1). While both groups have noted that simple weak bases could be employed in a reaction leading to Au-NHC complexes, we isolated an *aurate* intermediate that raised an important question as to the actual mechanism of this transformation. We have reported subsequently on the use of this weak base approach to isolate Cu[10] and Pd[11] complexes without addressing the mechanism in detail. More recently, Plenio has extended the use of the weak base methodology to the synthesis of Rh- and Ir-NHC complexes.[12]
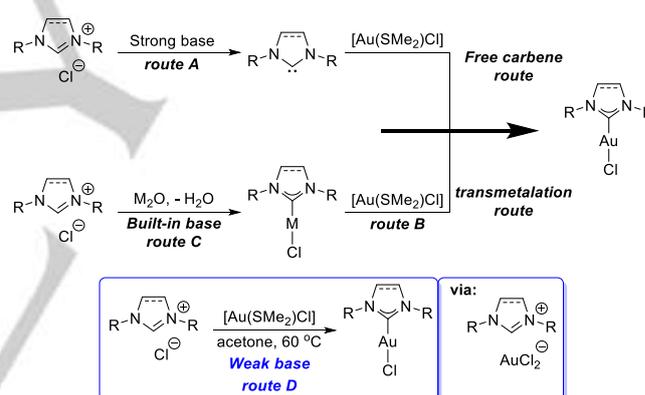
Scheme 1. Synthetic routes to Au-NHC complexes.

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In order to address the fundamental mechanistic questions associated with the role of a weak base in this transformation and in light of our own efforts in searching for simpler, more user-friendly synthetic protocols leading to metal-NHC complexes,[11] we examine here the intermediacy of metallates, easily obtained ionic species, as immediate precursors to M-NHC bonds and their possible role in a mechanism involving a weak base in the context of a metallation reaction.

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Results and Discussion

Our initial reasoning in trying to explain the conversion of **2** into **3** focused on the counteranion, the obvious difference between **1** and **2** (Scheme 2). We speculated that the counterion might have an effect on the acidity (pKa) of the imidazolium salt C-2 C-H bond; the one whose removal leads to the free carbene. It should be stated that in the *aurate* route, presented in Scheme 2, the commonly used organic base, triethylamine (NEt₃) is operationally efficient (**2**→**3** or **1**→**3**) leading to an 80% yield of **3**.[8] Experiments have shown clearly that weak bases alone such as K_2CO_3 or NEt₃ are ineffective in generating a free carbene from the imidazolium salt precursor. The role of the counterion in the aurate complex was suspected to enable or facilitate the imidazolium C-2 proton removal by a weak base.
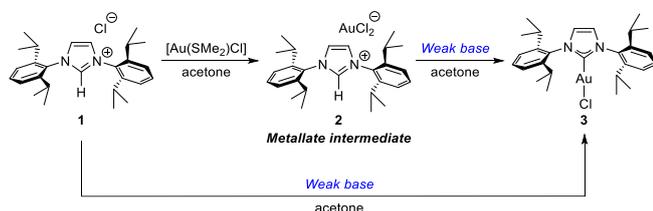
Scheme 2. Key components leading to complex **3**.

Experimental pKa determination by nuclear magnetic resonance (NMR) spectroscopy[14] showed that this hypothesis proved invalid as both **1** and **2** have the same pKa value (20.6 in CH₃CN/water). Deprotonation does not appear to be the reaction route taken. Although we have attempted to observe the free NHC under the weak inorganic and organic base conditions, this has been frustratingly unsuccessful. We were unable to obtain unequivocal spectroscopic evidence to support the conversion of the aurate (**2**) into the Au-NHC complex (**3**) via the generation of a free NHC ligand generated *in situ*. In spite of our inability to observe the free NHC, we understand that this does not preclude its actual formation.[15] Intrigued by recent reports questioning the need for a free carbene to enable organocatalysis,[16] we examined the thermodynamic feasibility of a possible alternative synthetic pathway, by DFT methods, to probe not a stepwise deprotonation/metallation sequence but rather a concerted bond-making/bond-breaking event where the base (possibly irrespective of its strength) could play a crucial role.

Starting from **1**, the mechanistic scenario leading to **3** was investigated using NMe₃ as the base, for ease of computation (see Scheme 3). The formation of **2** is energetically favored by 6.0 kcal/mol, in agreement with the experimentally observed intermediacy and isolation of the stable metallate species. The following transition state, **2-3**, is the key species along the reaction pathway allowing deprotonation of the imidazolium cation concomitantly with formation of the Au-NHC bond

(Scheme 3). The energy barrier on going from **2** to **2-3** amounts to 28.2 kcal/mol, and should be affected by the steric hindrance of the base and of the carbene precursor involved in the reaction. Evolution of transition state **2-3** leads to the [Au(NHC)Cl] complex by the spontaneous dissociation of one Cl atom from Au and the formation of the ionic salt [Cl⁻][HNMe₃⁺]. The thermodynamics of the transformation favor **3** with a gain of 14.9 kcal/mol with respect to **2**.
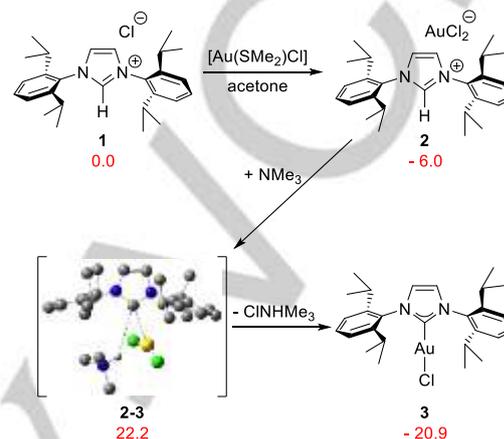
Scheme 3. Computed reaction pathway from **1** to **3**. Values reported are δG in acetone in kcal/mol.

The base itself may act to assemble this loosely bound template intermediate, helping to overcome opposing entropic forces and bringing together key components required for **2-3** formation. The driving force leading to M-NHC bond formation using a weak base has practical consequences. The possibility to deploy this procedure as a general synthetic route was next examined as a function of the nature of the NHC to delineate the impact of the NHC structure on the reaction barriers (see Table 1 and related energy diagrams in the Supporting Information). To correlate the data with specific NHC properties, thus placing these on a common quantitative scale, we calculated their percent buried volume,[17] %V_{Bur}, as a steric descriptor, and the snapping energy of the NHC-H bond.

The snapping energy is defined as the energy required to separate the two fragments in **2-3** and is used as an electronic descriptor (Table 1). The energy barrier rises by increasing the ligand steric bulk, as clearly illustrated by the IPr/IMes comparison; a decrease of %V_{Bur} from 43.5 to 34.5 leads to a decrease in the barrier by 3.4 kcal/mol for the snapping energy. A strong effect of the NHC-H bond strength is also noted. For example, eventhough TPT-Me has a %V_{Bur} only slightly smaller than IMe (24.0 vs 25.8), TPT-Ph possesses an energy barrier of only 18.9 kcal/mol compared to 25.6 kcal/mol for IMe. This is due to the much weaker NHC-H bond, i.e. the snapping energy is almost 12 kcal/mol lower for TPT-Me than for IMe.

Table 1. δG (kcal/mol) for the key transition state **2-3** and %VBur and δE_{snap}(kcal/mol) of the NHC-H bond calculated for five NHCs.
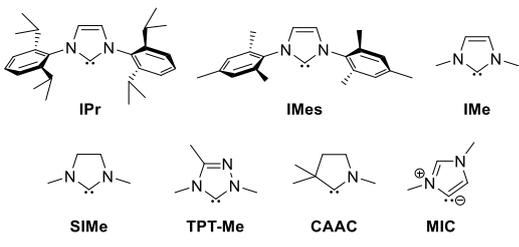
| NHC	$\delta G^{\ne}_{2-3}$	%V_{Bur}	$\delta E_{snap}([NHC-H]^+ = NHC^+ + H^+)$
IPr	28.2	43.5	286.1
IMes	24.9	34.3	286.5
IMe	25.6	25.8	276.5
SIMe	27.4	26.3	278.2
TPT-Me	18.9	24.0	264.6
CAAC	24.3	27.9	277.5
MIC	33.5	23.2	295.5

To confirm the predicted ease of synthesis of the triazolyl complex, the gold-triazol-2-ylidene (**6**) was synthesized (Scheme 4). High yield and purity of the desired complex were obtained using NEt$_3$ (or K$_2$CO$_3$) as base. The aurate intermediate (**5**) could also be isolated when the reaction was conducted in the absence of base (see Supporting Information for experimental details). The aurate **5** could be readily converted to the neutral Au-NHC (**6**) by action of a weak base (NEt$_3$ or K$_2$CO$_3$).
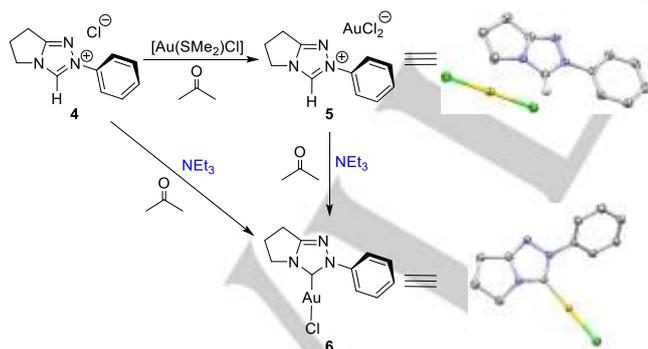
**Scheme 4.** Conditions leading to aurate **5** and gold-NHC complex **6**.

To test the limits of the method, the MIC (**7**) case was examined using NEt$_3$ as base and, as suggested by the computed high-energy barriers found along the reaction pathway, no product formation was observed after 20 hours at 60 °C (Scheme 5). The weak base method does however lead to the desired metallated

product (**8**) if K$_2$CO$_3$ is employed.[12,18] The exact role of K$_2$CO$_3$ in the method is presently being investigated mechanistically, and appears to proceed through a pathway that permits the expansion of the ligand precursor-type allowed under these initial NEt$_3$ conditions. The identity of the weak base appears to have a profound influence on reaction outcome.
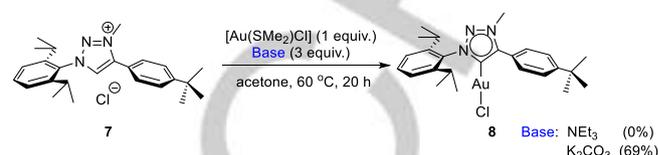

Scheme 5. Conditions leading to the Au-MIC complex (**8**).

To test the general validity of the weak base approach, we deemed it necessary to examine whether NEt$_3$ can be used for the synthesis of TM-NHC complexes with metal centers other than gold. Remarkably, when the palladium dimer-cleaving reaction was launched using imidazolium salt **1** and NEt$_3$, the desired Pd-NHC complex (**9**) was obtained in a 77% isolated yield, under non-optimized reaction conditions (Scheme 6).[11a]
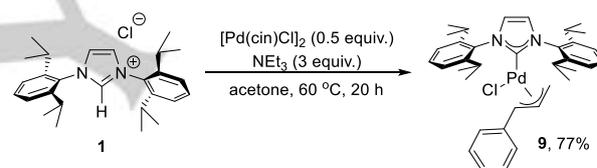
Scheme 6. Conditions leading to the [Pd(IPr)(cin)Cl] complex (**9**).

We next turned our attention to Main Group elements and reasoned that these could also be synthesized using a weak base such as NEt$_3$.[19] We targeted a thione and selenol compounds bearing the IPr ligand under reaction conditions identical to those deployed for transition metal systems presented above. The outcome of these reactions is presented in Scheme 7.
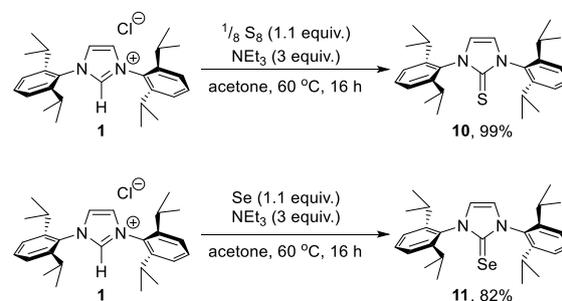
Scheme 7. Reaction conditions leading to thione (**10**) and selenol (**11**).

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Pleasingly, the use of a very weak base does allow isolation in high yield of the desired compounds. The importance of these has been addressed in recent reviews and reports on their use as S and Se synthons in materials science.[20] A detailed mechanistic and synthetic scope of the use of other weak bases in these and related transformations is presently being finalized in our laboratories and will be communicated shortly.

The concerted mechanism proposed above is reminiscent of a recent report by Hollóczki[16] who suggested a similar mechanism might be at play in organocatalytic reactions mediated by NHC precursors in the presence of weak bases. The free carbene is never generated under this scenario but a weak base/substrate-assisted activation is proposed to take place that allows the NHC precursor to enter the catalytic cycle directly without existing as a free NHC. The present mechanism is also reminiscent of the Concerted Metallation Deprotonation (CMD) mechanism proposed by Fagnou[21] but in its present incarnation the base is external and the substrate is a ligand precursor. This substrate-assisted transformation involves a metal complex that binds the NHC moiety without the need to invoke the generation or existence of a free NHC. The experimental approach is simple and does not require any air and moisture exclusion, conditions that may further assist in bringing a multitude of metal (and non-metal)-NHC species into the synthetic mainstream.

Conclusion

We have illustrated why the weak base synthetic route is so attractive and could prove a general, simple and cost-effective synthetic method to access various M-NHC (M= metal or non-metal) complexes. This simple approach and the mechanism at play also offer insights into longstanding questions of how metal salts interact with ionic liquids to yield catalytically active species.[22]

We have long favored the use of catalysts with well-defined composition and the general synthetic method using a mild base is a reminder to homogeneous catalysis novices and experienced practitioners alike, that fundamental knowledge of catalyst reaction mechanism, even at the catalyst synthesis stage, is key to understanding reactivity. The ease of catalyst synthesis permitted by the use of the weak base route will permit more rapid deployment and discovery using NHC-based transition metal catalysis. Ongoing work in our laboratories addressing mechanistic and synthetic uses of the weak base approach continues.

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Entry for the Table of Contents

Layout 1:

RESEARCH ARTICLE

No Free Carbene Required: Computational and experimental investigations of a weak base- assisted synthetic route leading to metal-NHC complexes suggest a concerted mechanism is at play. The method is exemplified with metal and non-metal centers and establishes its synthetic utility.

The "Weak Base" Approach

Weak Base / Metal synthon

Via Free Carbene or Concerted Metallation?
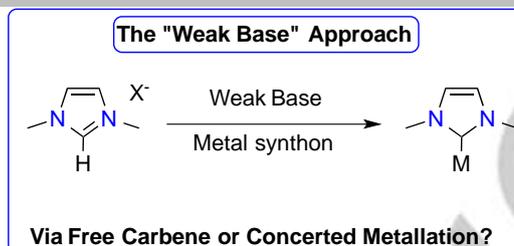
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