

Some chelating C-donor ligands in hydrogen transfer and related catalysis

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Abstract

Recent work is discussed that throws light on synthetic, steric, and electronic aspects of NHC complexes as well as on outer sphere effects in their reactivity. The chemistry of the NHC ligand is much more complex than the more traditional phosphines and provides much greater possibilities for altering steric and electronic properties for tuning reactivity. In synthetic work the Lin Ag₂O method is shown to be inapplicable to the synthesis of abnormal NHCs bound via C-4(5) where the C2 position is blocked with CH₃, because Ag(I) oxidizes the CH₃ group to formate with formation of the normal C-2 bound Ag–NHC. Linker effects on the behavior of chelating NHCs depend on the linker locking the azole rings into a conformation that depends on linker length. This gives rise to different complexes being formed when different linker lengths are employed. The failure of M–NHC bonds to reversibly dissociate can prevent potentially chelating bis and tris NHC precursors from forming the desired products but instead being trapped in a kinetic nonchelate form. Imidazolium carboxylates prove to be synthetically useful in that they can act as excellent NHC transfer agents to a variety of transition metals. The Tolman electronic parameter of NHCs can be determined by a variety of experimental and computational methods. Anion dependent chemistry can give rise to a switching of the product of imidazolium salt metallation from normal (C-2) to abnormal (C-4(5)) forms.

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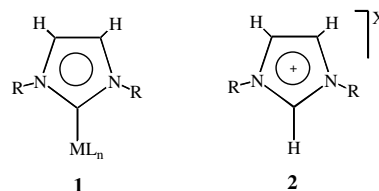
Keywords: NHC; Catalysis

1. Introduction

Phosphines have long been the workhorse spectator ligands of late transition metal homogeneous catalysis. Not only do their complexes promote rapid catalysis, but thanks to the understanding of steric and electronic effects contained in the Tolman ligand map, they can be tuned sterically and electronically to optimize a wide range of catalytic reactions.

Early work on metal carbene complexes emphasized their reactivity, but with the early work of Lappert co-workers [1] and the recent revival of the field [2], the promise of *N*-heterocyclic carbenes (NHCs, **1**) as spectator

ligands in catalysis has become widely recognized. A leading example of their potential is shown by the great improvement in the Grubbs metathesis catalyst caused by replacement of one of the PCy₃ ligands of the original standard catalysts by an NHC [3].



Originally considered as phosphine analogues, recent work [4] has increasingly emphasized the differences between NHCs and phosphines. One such difference is

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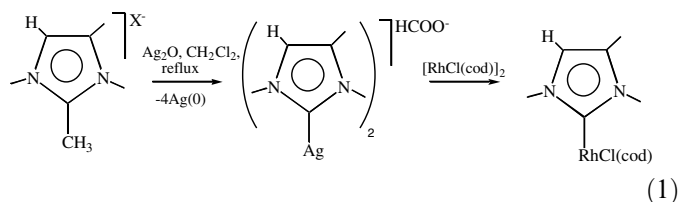
the contrast between the reversible dissociation common for $M-PR_3$ and the situation for $M-(NHC)$. This translates into a tendency to form kinetic NHC–metal products on attempted chelate formation. For example [5], chelating bis-imidazolium salts with short linkers typically give bis-rhodium complexes rather than chelates in metallation of $[RhCl(cod)]_2$. The presence of a $Ag(I)$ catalyst can lead to rearrangement to the chelate form, thus showing the chelate is the thermodynamic product (Scheme 1). In a similar vein, a potentially tripodal ligand precursor can fail to give a tripodal NHC [6].

In another general difference, the free carbene is typically much more nucleophilic than PR_3 and forms stronger $M-L$ bonds. Reversible dissociation of the sort found for phosphine complexes does not occur to a significant extent but when NHC dissociation does occur it is often irreversible, as in the reductive elimination of the azolium salt (2), typically leading to catalyst deactivation [7].

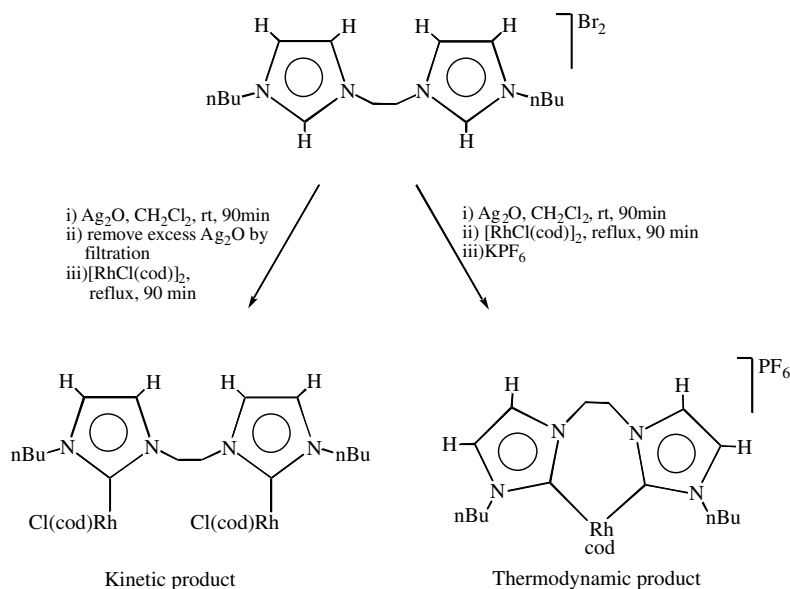
In early work, precursor azolium salt (2) was usually treated with a strong base to generate the free NHC (2) that can bind to a variety of metal precursors, but such harsh conditions limit the types of groups that can be present. To avoid this problem, a number of alternate procedures have been proposed for forming metal NHC complexes via mild procedures. Most notably, Lin and Vasam [8] pioneered the use of Ag_2O , as also exemplified in Scheme 1. The silver NHC complex of stoichiometry $[(NHC)AgX]$ ($X = \text{anion}$), obtained on reaction with 2 readily transmetallates to a variety of metal precursors. This procedure has proved extremely useful as illustrated by the large number of reports involving its use.

We noted an unexpected failure [9] of the Ag_2O procedure that led us to develop a new route to metal NHC

complexes. In an attempt to metallate 2-methyl imidazolium salts in the C-4(5) position for synthesis of an abnormal NHC complex, we noted that the methyl group at C-2 was cleaved (Eq. (1)) and replaced by Rh. Electro-spray MS data on the intermediate showed that the silver NHC complex had already lost the 2-methyl group, and that this group had now been converted into formate ion by oxidation. Silver ion was identified as the oxidant from the formation of the appropriate quantity of metallic silver. Even a 2-benzyl group could be cleaved, this time to form benzoate ion. The reaction presumably proceeds via the 2-acyl imidazolium ion because this species, prepared independently, proved competent to carry out the reaction, now without formation of $Ag(0)$. This implies that the 2-acyl imidazolium ion is competent to transfer the NHC to $Ag(I)$. Looking for alternatives to the Lin Ag_2O procedure, we first considered the 2-acyl imidazolium salts but these are somewhat troublesome to synthesize.



Instead, the carboxylates 3 seemed most promising, since they would liberate CO_2 , not the potentially ligating carboxylate ions on transfer. Carboxylate 3 is widely used as an ionic liquid and several syntheses are reported [10,11]. In our hands, Tommasi's procedure [10] (Eq. (2)) proved most useful for the N,N' -dimethyl case. The NHC carboxylate was found to readily transfer the NHC to a variety of



Scheme 1.

Table 1
Metal salts and their NHC adducts resulting from reaction with 1,3-dimethylimidazolium-2-carboxylate in MeCN at 75° for 0.3–12 h

Reactant	Product	Yield %
[Rh(cod)Cl] ₂	Rh(NHC)(cod)Cl	93
[Ir(cod)Cl] ₂	Ir(NHC)(cod)Cl	82
[Ir(PPh ₃) ₂ cod] ⁺ PF ₆ ⁻	[Ir(NHC) ₂ (cod)] ⁺ PF ₆ ⁻	84
[Ir(pyr) ₂ cod] ⁺ PF ₆ ⁻	[Ir(NHC) ₂ cod] ⁺ PF ₆ ⁻	76
RhCl ₃ · 3H ₂ O	[RhCl ₆] ³⁻ [Me ₂ C ₃ H ₄] ₃ ⁺	Quant.
IrCl ₃ · 3H ₂ O	[IrCl ₆] ³⁻ [Me ₂ C ₃ H ₄] ₃ ⁺	Quant.
Pd(OAc) ₂	Pd(OAc)(NHC) ₃	71
[Ru(ArH)Cl] ₂	[Ru(ArH)(NHC)Cl] ₂	85

metal complexes [12]. For substitution patterns other than the dimethyl, deprotonation of **2** at C-2 followed by reaction with ClCO₂*i*Bu has now been found to give the ester NHC–CO₂*i*Bu **4** (R = mesityl) that proved to be competent for transfer of the *N,N'*-dimesityl NHC. Mild and general methods for synthesis of **3** and **4** are presently under development in our group.

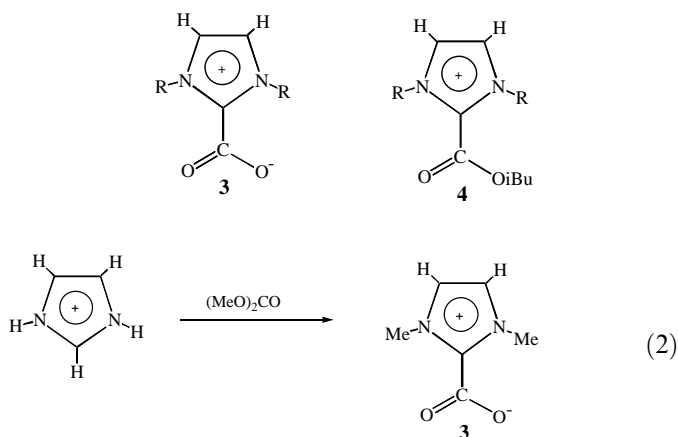
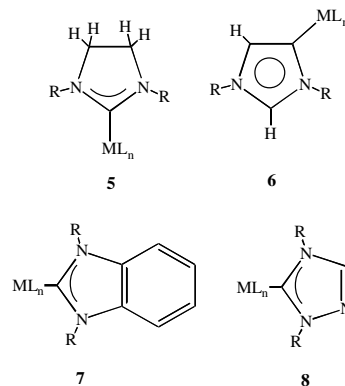


Table 1 shows some of the NHC complexes that are accessible in this way [12]. Sometimes the CO₂ is lost and the anionic metal halo-complex is precipitated as the imidazolium salt; presumably the lack of labile sites at the metal is responsible for the preference for protonation rather than metallation of the NHC liberated. The case of [Pd(NHC)₃OAc]OAc shows that multiple transfers are possible for this small *N,N'*-dimethyl case. The failure to form the tetra-NHC complex should not be taken to imply that it cannot exist. One proposed transition state for the NHC transfer, currently under study by Clot and Eisenstein, may require two *cis* vacant sites at the metal, one for the carboxylate oxygen, the other to allow formation of the new metal–NHC bond. We are currently examining the scope of this reaction.

2. Electronic effects

In a distinct difference between the PR₃ and NHC series, the electronic effects in NHCs seem to be principally

tuned by alteration of the azole ring (triazole, benzimidazole, imidazoline, etc.) [13]. In phosphines, in contrast, change of R is the sole available variable [14]. For example, hydrogenation of the C-4 and -5 backbone positions (**5**) or a move to the abnormal C4 (**5**) bound NHCs (**6**) enhance the electron donor power. A move to benzimidazole (**7**) or 1,2,4-triazole (**8**) based NHCs, in contrast diminish the electron donor power. The abnormal NHC (**6**) appears to be the most electron-donor so far seen [13].

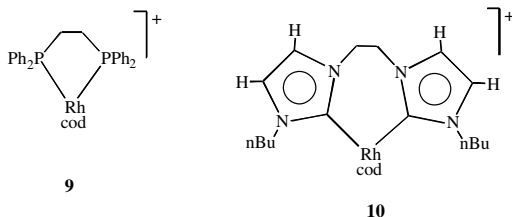


The Tolman electronic parameter (TEP) [14], the gold standard for ligand electronic effects, has been determined both computationally [15] and experimentally [16] for NHCs. The computational variant is of particular interest since it can be employed even in the planning stages of an investigation and for ligands which do not form the required LNi(CO)₃ derivatives. We have also used the [(CO)₂Rh(NHC)Cl] system to estimate the TEP experimentally for a number of NHCs using a correlation with values for LNi(CO)₃ [13].

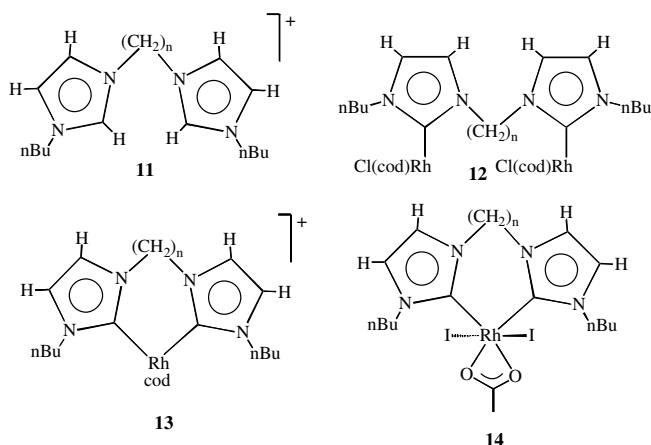
3. Steric effects

Phosphine substituents project away from the metal while NHC substituents project towards it, so that NHCs are expected to be able to achieve higher steric effects for a given substituent. The cone shape of PR₃ also contrasts with the fan shape of an NHC, so that the steric effect of the latter is expected to be highly dependent on the rotational conformation of the azole ring. Normally this difference would be muted by the ability of the NHC to rotate to minimize the steric clash with the other ligands, the azole having orthogonal slim and bulky axes. A special situation arises for chelate, pincer and tripod NHCs, however, where the linker length can fix the azole conformation within tight limits. Now, the orientational steric effect of the ligand can be tuned by changing the linker length [5], an effect with no close analogy in phosphine chemistry.

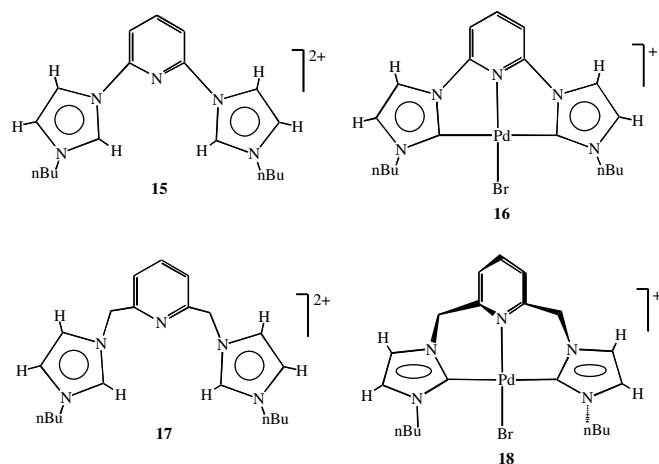
A linker of length n {e.g., $(\text{CH}_2)_n$ } in phosphine chemistry (e.g., **9**) produces a chelate ring of size $(n+3)$ with free rotation about every bond. The same linker in NHC chemistry produces a chelate ring of $(n+5)$ (e.g., **10**) with coplanarity imposed on two pairs of three bonds as a result of the presence of the twoazole rings.



We found an example of strong linker effects in the case of the reaction of ligand precursor **11** ($n=1-4$) with $[(\text{cod})\text{RhCl}]_2$. Under the conditions of Scheme 1, the short linkers ($n=1, 2$) lead to the formation of a 2:1 complex **12**, but long linkers ($n=3, 4$) lead to the chelate complex **13**. The outcome seems to be determined by the strong preference of the NHC to orient along the $\pm z$ axis where xy is the square plane of the complex. For a short linker, theazole rings can only achieve this orientation in a 2:1 complex, while a longer linker ($n=3, 4$) allows the two azoles to simultaneously adopt a $\pm z$ orientation while remaining chelated. Chelation is not forbidden for short linkers, however. In a related Rh(III) species, **14**, a chelate can always be achieved for any linker length and Scheme 1 shows how the $n=2$ ligand can do this.

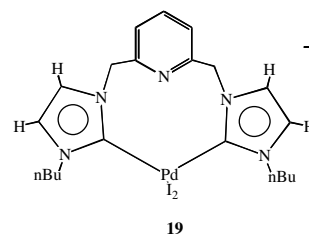


In another example of a linker effect [17–20], $n=0$ pincer precursor **15**, capable of giving five-membered chelate rings, gives a planar Pd(II) complex **16**, while $n=1$ pincer precursor **17** gives the seven-membered twisted complex **18**. The catalytic chemistry of **16** vs. **18** also shows considerable differences [17–20].



4. Outer sphere effects

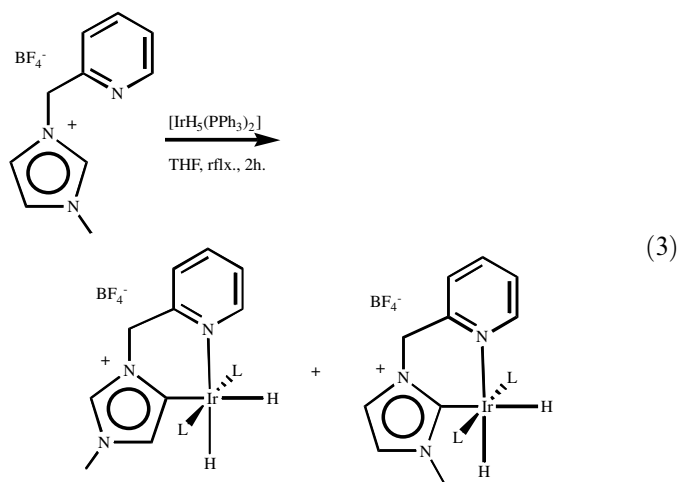
Nonrigidity of the twisted conformation in **18** was shown to be sensitive to the nature of the outer sphere anion. Good nucleophiles like I^- can replace the pyridine element of the pincer to produce a transient intermediate **19**. This conclusion was supported by a comparison between anions of varying nucleophilicity and by computational work. The barriers found from dynamic NMR data tracked the nucleophilicity of the anion and the calculated transition state energies matched the observed ones [18].



Another example of an anion effect emerged in studies on abnormal (C-4 bound) NHC complexes [21]. The synthetic route of Eq. (3) gives a ca. 55:45 mixture of normal (nNHC) and abnormal (aNHC) isomers, but is this thermodynamic or kinetic in origin? We therefore needed to know the relative stability of the two isomers. The nature of the counterion was predicted by Clot and Eisenstein to be critical to the energetics. The free carbenes strongly favor the nNHC by ca. 15 kcal/mol. Inclusion of the metal alters the balance only slightly, the nNHC now being favored by ca. 10 kcal/mol. The main effect was shown to be inclusion of the anion, the nNHC now being favored by only 1–3 kcal/mol. Binding of the anion to the protonic C-2 C–H bond of the aNHC was found to be responsible. This CH bond, not available in the nNHC has a highly protonic H and therefore hydrogen bonds to the anion

particularly strongly. NOE data obtained by Macchioni and his group confirmed the dose C–H···A contact (A = BF₄) experimentally.

Remarkably, change of anion from SbF₆ to Br switched the kinetic product of Eq. (3) from 10:1 aNHC to nNHC to 1:10 aNHC to nNHC. In a parallel theoretical study [21], Clot and Eisenstein found that the metallation at C5 is a true oxidative addition, and hence essentially independent of anion. The metallation at C-2, in contrast, involves proton transfer from C-2 to an adjacent hydride as the rate determining step. The role of the anion is to accompany this proton in its motion in an anion-coupled proton transfer (ACPT). This anion coupling is strongly favored in polar solvents and polar media give aNHC only.



5. Conclusions

The chemistry of the NHC ligand is much more complex than that of the more traditional phosphine ligand set and provides many more possibilities for altering steric and electronic properties for tuning reactivity. Synthetic pathways are also complex as shown by the anion dependence of a route to abnormal and normal NHCs by direct metallation of an imidazolium salt. The failure of M–NHC bonds to reversibly dissociate can prevent potentially chelating bis and tris NHC precursors from forming the desired products but instead being trapped in a kinetic non-chelate form. Imidazolium carboxylates prove to be synthetically useful in that they can act as excellent NHC transfer agents to a variety of transition metals. The Tolman electronic parameter of NHCs can be determined by a variety of experimental and computational methods.

Acknowledgments

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