Hydrogen bonding-assisted tautomerization of pyridine moieties in the coordination sphere of an Ir(I) complex†

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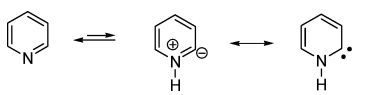
Ir(I)-induced tautomerization of a pyridine moiety to a carbene in 2,3-bipyridyls has been successfully achieved where an amide group plays a key role as a hydrogen-bonding acceptor and the carbene tautomer is stabilized by both chelation effect and by hydrogen-bonding.

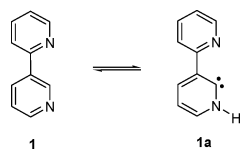
Transition metals can mediate remarkably the behavior of organic molecules. Organic moieties in metal complexes can undergo reactions that are otherwise thermodynamically and kinetically unfavorable. An important illustration is the tautomerization of acetylene to vinylidene (:C=CH_2) which has an activation barrier of 76 kcal mol^{-1} and the vinylidene is thermodynamically less stable by 44 kcal mol^{-1}.[1] Upon coordination to metals, the barrier of this tautomerization can drop significantly and the stabilization of the vinylidene by metals can invert the relative energy of these two tautomers.[2]

The tautomerization of pyridine has been thoroughly studied by computational methods (eqn (1)).[3] The N–H tautomer, an N-heterocyclic carbene, lies 45–50 kcal mol^{-1} higher than the C–H tautomer (pyridine) in energy.[3b] Despite the rather large dissociation energies of many transition metal–carbene bonds,[4] experimental examples of metal-mediated pyridine to carbene tautomerization have not been reported until very recently.[5–7] Examples of tautomerization of other heterocycles, such as imidazoles, are also rare.[8,9] This type of tautomerization is important not only in biological processes, where the energetically less stable tautomer is often responsible for the biological activity,[10] but also in important catalytic C–C coupling reactions of heterocycles, where the N-heterocyclic carbene tautomers are key intermediates.[11]



(1)

We recently reported the tautomerization of a substituted imidazole in the coordination sphere of a cationic iridium(III) complex,[9] and that the N-bound complex is thermodynamically more stable than the C-bound isomer. We now report Ir(I)-induced tautomerization of substituted pyridines to N-heterocyclic carbenes. Previous theoretical and experimental studies on the tautomerization of imidazoles have shown that either the N-bound imidazole complex or the C-bound carbene complex can be thermodynamically stable, depending on the nature of the metals and the ligands.[8,9,12] It is possible that similar thermodynamics may occur in the pyridine system. We reason that ligand **1** is a suitable candidate for this investigation. When bound to metals the carbene tautomer **1a** should be thermodynamically more stable (eqn (2)). The C–H tautomer **1** cannot serve as a bidentate chelating ligand, while **1a** should allow the formation of a stable metalacycle upon chelation. We have also selected $Ir(COD)_2BF_4$ as a metal source owing to the lability of one of the COD ligands, as observed in the rapid formation of $Ir(COD)(MeCN)_2BF_4$ from $Ir(COD)_2BF_4$ and MeCN. Here the carbene tautomer **1a** might readily substitute a COD ligand to give an isolable Ir(I) complex.



(2)

The reaction of ligand **1** and $Ir(COD)_2BF_4$ in CD_2Cl_2 was initially attempted but a complicated mixture was obtained on the basis of ^1H NMR analysis, which shows at least five hydride species obtained from C–H activation, together with a broad singlet at δ 12.1 ppm, tentatively ascribed to the N*H* of the carbene tautomer (see eqn (3)). While only the two C–H bonds *ortho* to the 2-pyridyl group can undergo feasible chelation-assisted C–H activation to give the hydride species, a various number of such species might result from the different stereoisomers of the C–H activation products (eqn (3)). To favor the selectivity of tautomerization, further improvement was made by using ligand **2** (Fig. 1) processing a 4-methyl group, which should prevent any oxidative addition at the 4-position and hence enhance the selectivity of tautomerization over C–H oxidative addition. Indeed we have found that although C–H oxidative addition and its product still exist, there is now only one hydride species (δ −12.95 ppm) with approximately a 5 : 1 molar ratio of the NH tautomer to hydride.

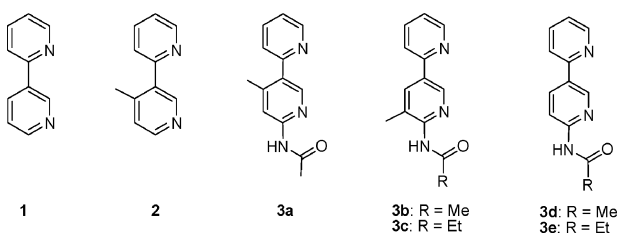


Fig. 1 Evolution of ligands for tautomerization studies.

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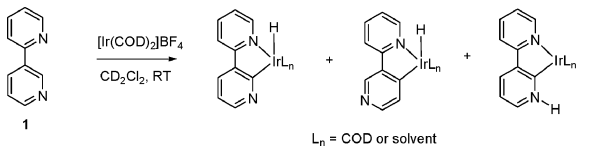
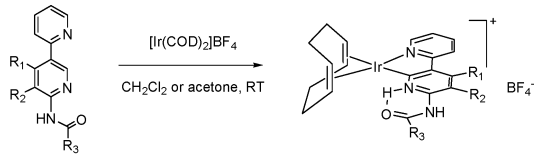
† Electronic supplementary information (ESI) available: Synthesis of all the ligands, metal complexes, NMR spectra, and crystallographic data for complex **4a** (CCDC 682697) in CIF format. See DOI: 10.1039/b804931a



(3)

Noting that Carmona and Poveda have proposed that hydrogen bonding in an Ir(III)–OH intermediate stabilizes the carbene tautomer and lowers the barrier of tautomerization,[6] we reason that an amide group proximal to the incipient NH species should provide a similar stabilization of the NH tautomer in our system. In this regard we then designed ligand **3a** (Fig. 1). This reacted immediately with $Ir(COD)_2BF_4$ in acetone or CH_2Cl_2 to give a dark green solution, from which complex **4a** was isolated in nearly quantitative yield (eqn (4)). Complex **4a** was fully characterized. In the ^{1}H NMR spectrum (CD_2Cl_2), the NH$\cdots$O resonates at δ 13.88 ppm as a broad singlet and the amide NH appears at δ 10.25 ppm. Two distinct olefinic proton peaks were observed [δ 5.01 (m, 2H) and 3.86 (m, 2H) ppm], suggesting that **4a** is C_s symmetric. The Ir–$C_{carbene}$ resonates at δ 180.0 ppm, comparable to those in related iridium complexes. The identity of **4a** was further confirmed by X-ray crystallography (Fig. 2).†[13] Complex **4a** has a distorted square planar structure. The Ir–carbene bond has a normal length of 1.999(2) Å.[6,7] The calculated NH$\cdots$O distance is 1.960 Å and is shorter than the sum of the van der Waals radii of hydrogen and nitrogen, suggestive of an intramolecular NH$\cdots$O hydrogen bond. The amide plane also offsets the adjacent pyridine ring by only 11.09° to allow this hydrogen bond. The length of C(14)–C(15), 1.425(3) Å, is longer than the other three C–C bonds in the carbene ring ranging from 1.377 to 1.407 Å. Similar observations have been found in related pyridine-based carbene complexes.[6,14] The Ir(1)–C(1) [2.205(11) Å] and Ir(1)–C(2) [2.212(10) Å] distances are longer than those of Ir(1)–C(5) [2.123(2) Å] and Ir(1)–C(6) [2.125(2) Å], as a result of the high *trans* influence of the carbene. It is clear that ligand **3a** can readily isomerize to the corresponding carbene *via* the activation of the C–H bond adjacent to the N, with the H atom being formally transferred to the nitrogen atom.



(4)

3a: R_1 = Me, R_2 = H, R_3 = Me
3b: R_1 = H, R_2 = Me, R_3 = Me
3c: R_1 = H, R_2 = M3, R_3 = Et
3d: R_1 = R_2 = H, R_3 = Me
3e: R_1 = R_2 =H, R_3 = Et

4a: R_1 = Me, R_2 = H, R_3 = Me
4b: R_1 = H, R_2 = Me, R_3 = Me
4c: R_1 = H, R_2 = Me, R_3 = Et
4d: R_1 = R_2 = H, R_3 = Me
4e: R_1 = R_2 =H, R_3 = Et

In fact, it is not necessary to have a blocking group at the 4-position to prevent the undesired C–H oxidative addition. Directly analogous reactions yielding **4b–e** can also be achieved by starting from ligands **3b–e** and $Ir(COD)_2BF_4$, respectively. In all these products the N*H*$\cdots$O protons resonate in a range of δ 13.8 to 14.3 ppm in the ^{1}H NMR spectra and the Ir–$C_{carbene}$ signals appear in a narrow range of δ 175 to 180 ppm. These comparisons indicate that the presence of an amide group as a hydrogen bond acceptor can remarkably enhance the selectivity of tautomerization over C–H oxidative addition. A hydride species (δ −14.9 ppm in the ^{1}H NMR spectrum) was observed in the reaction of **3a** and $[Ir(COD)]BF_4$ carried out in CD_2Cl_2 at −20 °C. However, it still remains a question whether the tautomerzation proceeds through iridium hydride oxidative addition intermediates[11] or goes directly *via* a concerted mechanism.

In summary, we have demonstrated that Ir(I)-induced tautomerization of a pyridine moiety can be successfully achieved. The carbene tautomer is both stabilized by the chelation effect and by hydrogen bonding with a proximal amide group. The amide group also enhances the selectivity of tautomerization over C–H oxidative addition. These results may find applications in catalyst design featuring non-covalent interactions to enhance the selectivity and reactivity of catalytic reactions, as in molecular recognition. Theoretical investigations of this tautomerization process and the tautomerization of monodentate pyridines are currently in progress.

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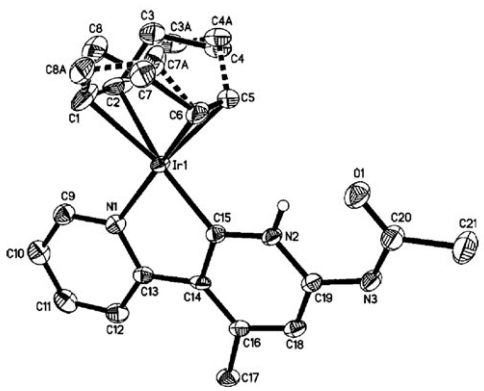

Fig. 2 Molecular structure of the cation of **4a** shown with 50% thermal ellipsoid. Selected lengths (Å) and angles (°): Ir(1)–C(15) 1.999(2), Ir(1)–N(1) 2.0860(19), Ir(1)–C(1) 2.205(11), Ir(1)–C(2) 2.212(10), Ir(1)–C(5) 2.123(2), Ir(1)–C(6) 2.125(2), C(14)–C(15) 1.425(3), O(1)–H[N(2)] 1.960, N(1)–Ir(1)–C(15) 78.44(8), C(14)–C(15)–N(2) 116.66(19).

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