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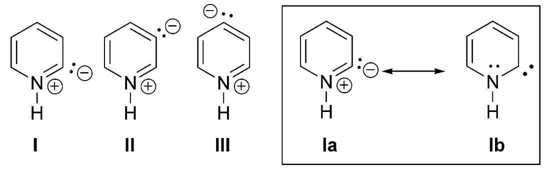
Iridium(III)-Induced Isomerization of 2-Substituted Pyridines to N-Heterocyclic Carbenes

Eleuterio Alvarez, Salvador Conejero, Margarita Paneque, Ana Petronilho, Manuel L. Poveda,*
Oracio Serrano, and Ernesto Carmona*

*Instituto de Investigaciones Químicas, Departamento de Química Inorgánica, CSIC and Universidad de Sevilla,
Avda. Américo Vespucio 49, 41092 Sevilla, Spain*

Received June 30, 2006; E-mail: guzman@us.es

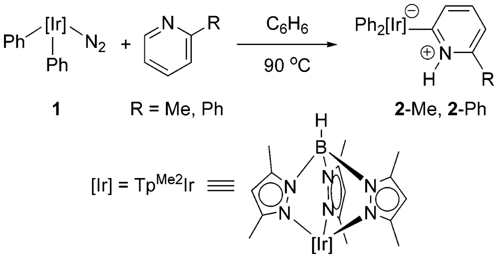
The pyridine tautomers **I**, **II**, and **III** are simple molecules that have been investigated thoroughly by computational methods. The 2-isomer **I**, first proposed almost 70 years ago,[1] has been generated recently in the gas phase by Schwarz an co-workers,[2a] who have additionally shown that **II** is stable on the microsecond time scale.[2b]



The intermediacy of the latter in the reaction of gaseous atomic carbon with pyrrole has also been ascertained.[3] Tautomer **I** is less stable than pyridine by more than 40 kcal•mol^{-1}, and **II** and **III** have even higher energies.[2] Therefore it is not surprising that isomerization of pyridine to metal-C-coordinated species **I**−**III** has not been reported, despite the stabilization that the carbene resonance contributors (e.g., **I**$_b$ for the 2-isomer **I**) may provide. However, a 2,6-lutidinium ylide bound to osmium(II) through the para carbon (therefore related to **III**) was produced from an isomeric η^2-*C*,*C*-2,6-lutidine complex,[4] and it is also known that complexes derived from class **I** ligands N(H)*C*:→M or N(R)*C*:→M, may be prepared indirectly from suitable precursors.[5,6] Very recently, Bergman and co-workers have reported a related Rh(I) mediated rearrangement of 3-methyl-3,4-dihydroquinazoline to the corresponding Rh−N-heterocyclic carbene complex.[7]

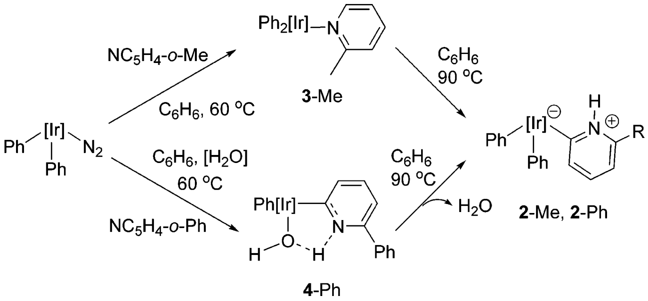
Extensive studies from our laboratories[8] have demonstrated that a variety of [Tp^{Me2}Ir(X)(Y)] fragments (Tp^{Me2} = hydrotris(3,5-dimethylpyrazolyl)borate), where X and Y are anionic ligands, are electronically and sterically suitable to stabilize carbene ligands with or without heteroatom substituents. This affinity seems to be responsible for the unusual isomerization of aromatic aldehydes to hydroxycarbene ligands,[9a] and of Ir−alkene termini to Ir−alkylidenes,[9b] among other unusual rearrangements. In this contribution we report that the reactions of some 2-substituted pyridines with the compound Tp^{Me2}Ir(C$_6$H$_5$)$_2$(N$_2$) (**1**),[10] yield N-heterocyclic carbenes[11,12] structurally akin to **I**. This unprecedented rearrangement is in part due to the decreased Lewis basicity of these 2-substituted pyridines toward sterically demanding Lewis acids as a consequence of F-strain, that is, steric interactions at the “front” of the Lewis base.[13]

Complex **1** reacts with 2-picoline and 2-phenylpyridine (1.2 equiv, C$_6$H$_6$, 90 °C) to give carbenes **2**-Me and **2**-Ph (eq 1) in high spectroscopic yields (>80%). While pyridine and 4-(dimethylamino)pyridine give rise exclusively (60−150 °C) to the N-bound adducts related to **3**-Me (Scheme 1), the reaction of eq 1 seems to be general for 2-substituted pyridines. Indeed, the bulkier 2-*tert*-butylpyridine yields carbene **2**-*t*-Bu under milder reaction conditions (60 °C), and even 2-(dimethylamino)pyridine, for which a heteroatom-stabilized carbene resulting from a double C−H bond activation at one of the methyl N-Me$_2$ groups could be expected,[14] rearranges to a C-bound carbene, **2**-NMe$_2$, also under mild conditions (60 °C). Interestingly, the reaction leading to **2**-Ph is very sensitive to the presence of traces amounts of water, (vide infra) that at 60 °C appreciably slow the formation of **2**-Ph in favor of the side-product **4**-Ph (see Scheme 1 later). No similar water effect has been detected for the other carbene forming reactions; all compounds **2** form reproducibly under the specified conditions. It is thus clear that 2-substituted pyridines isomerize readily to carbene ligands by C−H bond activation at the available aromatic C−H bond adjacent to N, with the H atom being formally transferred to nitrogen.



(1)

Scheme 1



The four carbenes **2** can be easily purified by silica gel chromatography and have been fully characterized by IR and NMR spectroscopy (see Supporting Information). In solution they exist as mixtures of two interchanging rotamers with relevant spectroscopic broad ^{1}H NMR resonances around δ 13 (one kind of rotamer) and at 10 ppm (the other) attributed to the N-bound proton, and a carbene ^{13}C signal at ca. 175 ppm. In addition, the molecular structures of **2**-Me and **2**-Ph have been determined by X-ray crystallography (see Figure 1 and Supporting Information). The Ir−carbene bond has a normal length of ca. 1.98 Å,[9b,14] somewhat shorter than the corresponding Ir−C(phenyl) distances of ca. 2.05 Å. This distance is comparable to corresponding separations found in NHC iridium compounds.[12a]

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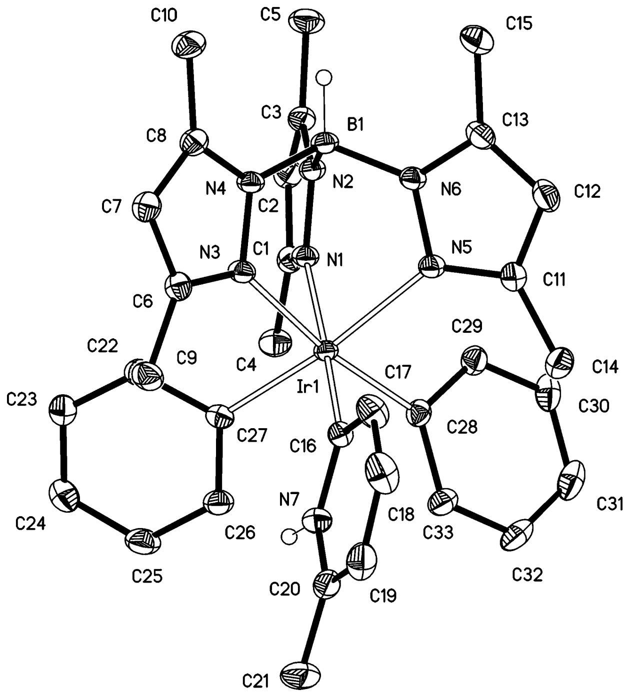

Figure 1. ORTEP representation of complex **2**-Me. Selected bond lengths (Å) and angles (deg): Ir1−C16 = 1.9821(2), Ir1−C27 = 2.0463(2), Ir1−C28 = 2.0567(2), C16−N7 = 1.366(2), Ir1−N1 = 2.1174(1), Ir1−N3 = 2.1570(1), Ir1−N5 = 2.1873(1), N7−C16−Ir1 = 122.87(1), N7−C16−C17 = 112.54(1), C17−C16−Ir1 = 124.54(1).

While no intermediates can be detected in the reactions leading to carbenes **2**-*t*-Bu and **2**-NMe_2, for 2-picoline at 60 °C, a N-bound adduct **3**-Me can be isolated and in the case of 2-phenylpyridine, also at 60 °C, adventitious water permits the trapping of compound **4**-Ph with a O···H···N hydrogen bond (Scheme 1). The latter can be formulated as a N-heterocyclic carbene related to **2**, but with a hydroxyl ligand in place of a phenyl group, or alternatively, as the water adduct of a compound containing an *o*-metalated molecule of the pyridine. While it is clear that **4**-Ph is not a real intermediate on the path to **2**-Ph, both this complex and **3**-Me convert cleanly into the corresponding carbenes when heated in benzene at 90 °C. The structures of the two compounds **3**-Me and **4**-Ph are fully in accord with the spectroscopic data and have been confirmed by X-ray studies to be reported elsewhere.

In the Rh(I)-quinazoline system of Bergman and co-workers,[7] an isolable N-coordinated adduct intermediate seems to convert intramolecularly into the N-heterocyclic carbene. To shed light on this mechanistic step, we have undertaken some isotopic studies and found that the N-adduct **3**-Me undergoes exchange when treated at 60 °C with 5 equiv of 2-picoline-d_7 (the adduct **3** of the unsubstituted pyridine does not exchange with NC_5D_5 even at 150 °C). Furthermore, if the exchange reaction is performed at 90 °C, carbene **2**-Me-d_6 is obtained (the NH functionality of this deuterated complex probably originates by an exchange reaction with adventitious water during the final silica gel chromatographic separation). Finally in this regard, a kinetic isotope effect of $k_H/k_D = 2.0\ (\pm 0.2)$ has been determined when **1** was allowed to react with an excess of a 1:1 mixture of 2-picoline and 2-picoline-d_7. A definite mechanistic proposal for the pyridines rearrangement of eq 1 cannot be drawn from these data. To gain additional information we are pursuing further theoretical and experimental studies.

In summary, 2-substituted pyridines transform into the respective carbene tautomers in an iridium mediated process that involves formally a 1,2-H shift from carbon to nitrogen. It seems evident that the increased bulkiness of the 2-substituted pyridines destabilizes the N-adduct by F-strain,[13] while the isomeric carbene structures do not suffer from this kind of steric repulsion. In fact, the Ir−C carbene bond lengths in **2**-Me and **2**-Ph are normal (ca. 1.98 Å),[9b,14] whereas the Ir−N distance in the N-adduct **3**-Me of 2.135(3) Å is about 0.15 Å longer, despite the somewhat smaller covalent radius of Nsp^2 in comparison with Csp^2. Clearly, these factors contribute to the comparatively more favorable thermodynamics of the carbene forming reaction. In this regard, it is worth recalling that while 2-*tert*-butylpyridine is more basic than pyridine against H^+ (pK_a values of 5.17 and 5.76, respectively) the reaction of pyridine with BMe_3 is exothermic by about 15 kcal·mol^{-1}, whereas that of 2-*tert*-butylpyridine is endothermic.[13]

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Supporting Information Available: Synthesis and characterization of complexes **2**−**4**; crystallographic data for **2**-Me and **2**-Ph. This material is available free of charge via the Internet at http://pubs.acs.org.

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