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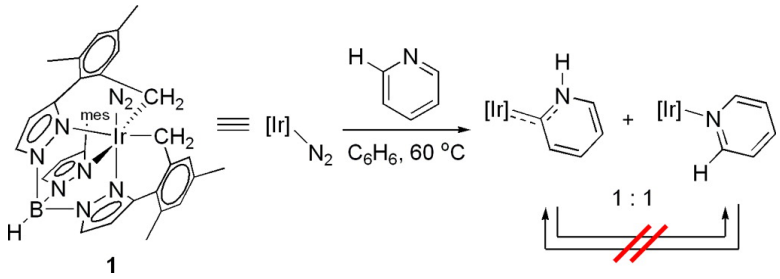

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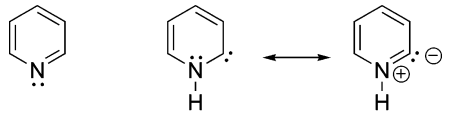
Rearrangement of Pyridine to Its 2-Carbene Tautomer Mediated by Iridium

Eleuterio Álvarez,[†] Salvador Conejero,[†] Patricia Lara,[†] Jorge A. López,[‡] Margarita Paneque,[†] Ana Petronilho,[†] Manuel L. Poveda,*[,†] Diego del Río,[†] 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, and Instituto de Investigaciones Científicas, Universidad de Guanajuato, Cerro de la Velada s/n, Pueblito de Rocha, Guanajuato, Mexico

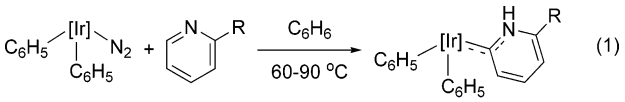
Received July 30, 2007; E-mail: guzman@us.es

The 2-carbene tautomer of pyridine (**I**), azacyclohexanetriene-2-ylidene (**II**), was first proposed by Hammick[1] 70 years ago to explain the facile decarboxylation of 2-picolinic acid. Recent theoretical calculations[2] have shown that **II** has energy about 45−50 kcal·mol^{-1} higher than **I** and that the transition state for the **I** to **II** rearrangement lies ca. 85 kcal·mol^{-1} above **I**. Accordingly, the **I** to **II** tautomerization has never been achieved, although **II** can be generated in the gas phase by mass spectrometric experiments[2] and as a ligand by protonation at the nitrogen atom of gold 2-pyridyl derivatives.[3]



I **IIa** **IIb**

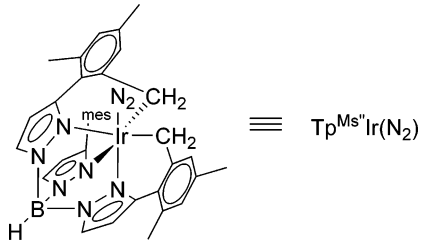
Recent work from our laboratories has shown that 2-substituted pyridines can be converted into their corresponding N-heterocyclic carbenes[4] (abbreviated as NHC) according to eq 1.



(1)

[Ir] = Tp^{Me2}Ir ; R = Me, Ph, *t*-Bu, NMe$_2$

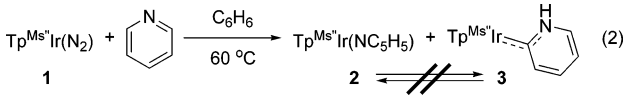
The bulky 2-substituted pyridines (R = Ph, *t*-Bu, NMe$_2$) gave exclusively the corresponding Ir−NHC complex, while 2-picoline allowed isolation of the N-bound adduct in route to the carbene. However, the intermediary role of this N-adduct in the tautomerization of the heterocycle could not be established.[4] Unsubstituted pyridine does not form an Ir−NHC complex but yields only a very stable N-coordinated adduct. Related isomerizations of the heterocycles 3-methyl-3,4-dihydroquinazoline (Rh),[5a] quinoline, and 8-methylquinoline (Ru, Os)[5b] have been also reported.[6] We considered plausible that a Tp′Ir(R)(R′) fragment could be found, capable of inducing the **I** to **II** tautomerization.



≡ Tp$^{Ms''}$Ir(N$_2$)

1

Here we show that complex **1** that contains two Ir−CH$_2$ bonds as a result of the metalation of two *ortho*-Me groups of two of the three 3-mesityl substituents of the Tp^{Ms} ligand[7] (Tp$^{Ms''}$ represents the dimetalated Tp^{Ms} ligand) reacts with an excess of pyridine (eq 2) to give a 1:1 kinetic mixture of the N-adduct **2** and the NHC derivative **3**.[8] Prolonged heating of this mixture under the conditions of eq 2 does not change the product ratio, and furthermore, solutions of isolated samples of **2** and **3** remain unaltered in C_6H_6 at 60 °C, in the presence of pyridine, but decompose to complex mixtures of products at higher temperatures (90 °C). Thus, at variance with the Rh−quinazoline system,[5a] the N-adduct **2** is not an intermediate in the route to the NHC complex **3**. Instead, as discussed below, **2** and **3** form through different, competitive reaction pathways.



(2)

Carbene **3** can be readily characterized by spectroscopy. Similarly to related NHC derivatives of the Tp^{Me2}Ir unit,[4] **3** features an IR absorption at 3375 cm^{-1} and a broad ^{1}H NMR signal at δ 10.3 ppm, both associated with the NH group. A characteristic ^{13}C resonance at 183 ppm can be attributed to the metal-bound ylidic carbon atom. In the solid state, molecules of **3** exhibit Ir−CH$_2$ distances of 2.093(3) Å (average value) and a somewhat shorter Ir−carbene bond length (Figure 1) of 1.975(2) Å. Bonds lengths within the pyridine ring show significant differences, with a long C37−C38 distance of 1.493 (3) Å and smaller separations of ca. 1.363 (4) Å for C38−C39 and C40−C41. Similar, albeit less pronounced, differences have been found in somewhat related NHC complexes.[9a] In free pyridine, the C−C bonds have a length of 1.39 Å.[9b]

Use of $^{15}NC_5H_5$ allows isolation of **2**-^{15}N and **3**-^{15}N. The ^{15}N NMR resonance of the former has a chemical shift of 4.7 ppm (CH_3NO_2 as external reference), comparable to that of the related $^{15}NC_5H_5$ adduct of the Tp^{Me2}Ir(C$_6$H$_5$)$_2$ fragment (δ 1.9 ppm). The ^{1}H signal of **3** at 10.3 ppm due to the NH proton splits into a doublet in the spectrum of **3**-^{15}N, with a one-bond ^{1}H−^{15}N coupling of 95 Hz. The ^{15}N-labeled carbene features a ^{15}N{^{1}H} resonance at δ −7.15 ppm that converts into the expected doublet in the proton-coupled ^{15}N NMR spectrum.

^{1}H NMR monitoring of the reactions of **1** with NCMe,[7] NC_5H_5, and NC_5D_5 shows they proceed with identical rate (independent of L and [L]) and are characterized by $t_{1/2} \sim 80$ min, at 50 °C. Reactions with pyridine-d_5 provide relevant mechanistic information regarding the route leading to the NHC complex **3**. First, adduct **2** doubles its proportion in the deuterated **2**:**3** mixture, which allows an estimation of $k_H/k_D = 2$ (±0.2) for the C−H activation route. This value is identical within experimental error to that found for the Tp^{Me2}Ir system[4] and indicates that pyridine C−H bond cleavage controls the rate of the individual pathway leading to the NHC complex **3**. Second, while **2**-d_5 contains all deuterium atoms in the

[†] CSIC and Universidad de Sevilla.
[‡] Universidad de Guanajuato.

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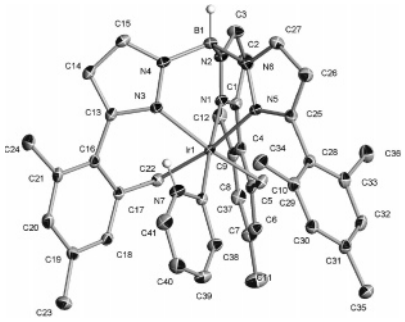
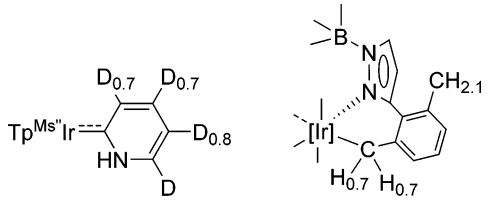


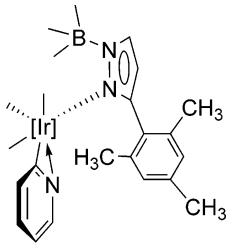
Figure 1. ORTEP representation of complex **3** (50% thermal ellipsoids).

N-coordinated pyridine ligand, NHC derivative **3** has ca. 0.3D less probably as a consequence of facile N−D to N−H exchange during chromatographic workup of the **2** plus **3** reaction mixture. More importantly, **3**-$d_{4.7}$ exhibits an odd deuterium distribution, within the carbene and one of the metalated arms of the $Tp^{Ms''}$ ligand (see **III** and **IV**), that clearly does not correspond to thermodynamic control of the D scrambling. This distribution is the same regardless of the use of 1.5 equiv or neat NC_5D_5 in the experiment.



III **IV**

The above results indicate that the rate of eq 2 is determined by N_2 dissociation from **1** to give the unsaturated $Tp^{Ms''}$ Ir fragment,[7] which can then progress through two independent pathways of comparable activation energy[8] that lead to compounds **2** and **3**, respectively. Formation of **3** requires C−H activation of pyridine, facilitated by one of the two inequivalent Ir−CH_2 linkages of **1**. Definite mechanistic details cannot be offered at this early stage, but it seems probable that, as found for somewhat related systems,[10] the C−H activations needed for the generation of **3** occur in a concerted manner, through the intermediacy of σ-C−H complexes.[11] Pyridine C−H activation could take place at any of the ring C−H



V

bonds, yielding corresponding pyridyl derivatives in which one of the Ir−CH_2 arms becomes temporarily disengaged (Tp^{Ms} becomes monometalated, see structure **V** of the 2-pyridyl intermediate).

Subsequent restoration of the original dimetalated structure should be a facile process entropically facilitated by the chelate effect, given the close vicinity of the two equivalent (by C−C bond rotation) *ortho*-methyl groups of the demetalated mesityl. The 2-pyridyl intermediate **V** could be kinetically favored over the 3- and 4-isomers due to the somewhat higher acidity of the 2-C−H bond[12] and also thermodynamically as a consequence of the plausible coordination of the N atom. The process would end when methyl C−H activation places one of its H on the N atom of **V**, generating the NHC complex **3**. Thus the unsaturated $Tp^{Ms''}$ Ir fragment acts as a selective molecular shuttle by means of one of its Ir−CH_2 bonds and drives the 1,2-H shift from C to N needed for the **I** to **II** rearrangement.

In summary, a simple reaction system has been found that permits isomerization of pyridine to its 2-carbene tautomer by means of C−H activation chemistry mediated by an Ir−CH_2 bond within a chelate structure. In this way, pyridine tautomerization becomes kinetically competitive with the traditionally facile N coordination of the heterocycle. Evidently, these results are relevant to the metal-catalyzed functionalization of pyridine and related heterocycles.[13]

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Supporting Information Available: Synthesis and characterization of complexes **2** and **3**. Crystallographic data for **3**. DFT calculation details. This material is available free of charge via the Internet at http://pubs.acs.org.

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