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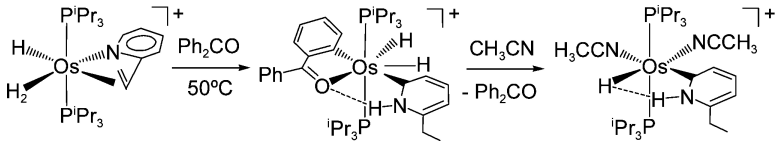

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Understanding the Formation of N−H Tautomers from α-Substituted Pyridines: Tautomerization of 2-Ethylpyridine Promoted by Osmium

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N−H tautomers of α-substituted pyridines, postulated 70 years ago[1] and experimentally proved in the gas phase for pyridine,[2] have been recently synthesized by means of an iridium mediated process that involves formally a 1,2-H shift from carbon to nitrogen.[3] At the same time, we showed the stabilization of N−H tautomers of quinoline and 8-methylquinoline by coordination to osmium and ruthenium and an additional Cl···HN interaction between the NH hydrogen and a chlorine of the metal fragment.[4] A few months later, Whittlesey[5] et al. reported ruthenium isomers resulting from the N- or C-bond tautomers of isopropyl-4,5-dimethylimidazol, in agreement with the paper of Crabtree, Eisenstein, and Sini about the possibility that C-bound imidazoles could have some existence in metalloprotein chemistry.[6]

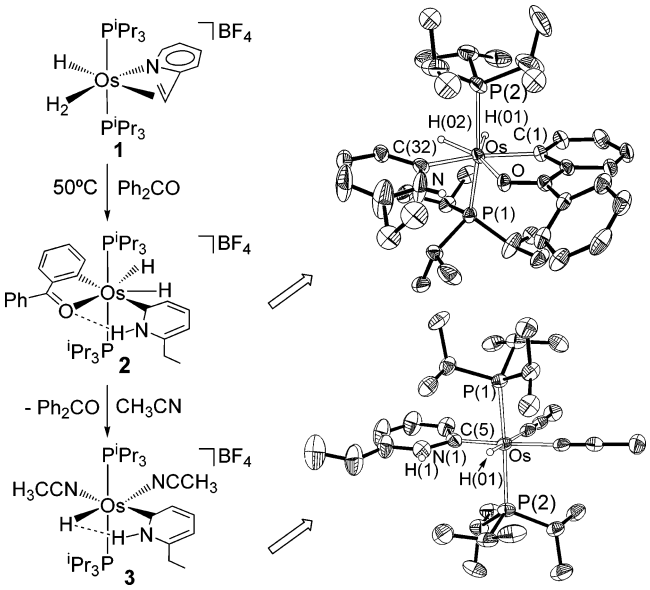
This type of tautomerization is important not only in biological processes, where the energetically less stable tautomer is often an active intermediate that dictates the mechanism and the formed product, but also in some relevant catalytic reactions,[7] in particular those involving N-aromatic compounds.[8] Thus, Bergman, Ellman et al.[9] have proposed that the C,N-1,2-H rearrangement is the key step for the Rh(I) catalyzed ortho alkylation of pyridines and quinolines. An exciting question arises now: Are such tautomerizations more frequent than previously thought?

A process related to the ortho alkylation of pyridines and quinolines is the Murai's reaction for the insertion of olefins in an ortho-CH bond of aromatic ketones. Like for the nitrogen heterocycles, the ortho-CH addition of the aromatic ring to the ruthenium catalyst is a fundamental step.[10] In agreement with the trend of osmium to provide stable models of reactive intermediates proposed in transformations with ruthenium counterparts,[11] osmium−polyhydride compounds have proven to activate an ortho-CH bond of aromatic ketones to give orthometalated derivatives, which are reminiscent species of the intermediates proposed for the Murai's reaction.[12]

Complex $OsH_6(P^iPr_3)_2$ also activates a $C(sp^2)$-H bond of the CH_2 group of the substituent of 2-vinylpyridine to yield $\overline{OsH_3(NC_5H_4\text{-}o\text{-}CH{=}CH)}(P^iPr_3)_2$, which reacts with HBF_4 to give **1** as a result of the regeneration of the 2-vinylpyridine molecule and the transformation of the Os-trihydride unit into Os-hydride-dihydrogen.[13] Now, we have observed that the treatment at 50 °C of the white complex **1** with 5.0 equiv of benzophenone in the absence of solvent gives rise after 24h to a red melt that, by stirring in diethyl ether at room temperature, affords **2** (Scheme 1) as a red solid in 55% yield. The addition of some drops of acetonitrile or acetone to the discarded diethyl ether solution produces the precipitation of the side complexes $[\overline{Os\{C_6H_4C(O)C_6H_5\}}(\eta^2\text{-}H_2)L(P^iPr_3)_2]BF_4$ (L = CH_3CN, $(CH_3)_2CO$), which were characterized by X-ray diffraction analysis.

The formation of **2** is a one-pot tandem process of three reactions: (i) hydrogenation of the vinyl substituent of the pyridine as a result of the transfer of the coordinated hydrogen molecule from the metal center to the C−C double bond; (ii) ortho-CH bond activation of the ketone by the resulting monohydride, in agreement with the trend shown by the osmium−hydride complexes to add aromatic ketones; and (iii) C,N-1,2-H rearrangement of 2-ethylpyridine.

Scheme 1



The tautomerization appears to be favored by the steric hindrance experienced between the ethyl substituent and the orthometalated ketone. In agreement with this, the reaction of **1** with methyl vinyl ketone does not lead to a N−H tautomer, the species $[\overline{OsH\{CH{=}CHC(O)CH_3\}}_2(P^iPr_3)_2]BF_4$ is isolated instead. The presence of the substituent in α-position is certainly determinant for the tautomerization of the heterocycle. Recently, we have also observed that 2-methylpyridine reacts with $MH_2Cl_2(P^iPr_3)_2$ (M = Ru, Os) to give N−H tautomers related to those isolated with quinoline and 8-methylquinoline, while under the same conditions pyridine affords the usual species coordinated by the nitrogen atom.

2-Ethylpyridine is the third pyridine undergoing C,N-tautomerization, after 2-methylpyridine and 2-phenylpyridine,[3] and the tautomerization is the first one of a pyridine promoted by a metal of the eighth group.[14] A 2,6-lutidinium ylide bound to osmium through the carbon atom at 4-position has been produced by isomerization of an η^2-C,C-2,6-lutidine species.[15] A few pyridine- or *N*-alkylpyridine-2-ylidene and -4-ylidine complexes of other metals than osmium have been also prepared by indirect methods from suitable precursors.[16]

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The X-ray structure of **2** proves the orthometalation of the ketone and the stabilization of the N−H tautomer of the pyridine, which coordinates through C(32). Furthermore it suggests that, like in the previous quinoline complexes,[4] a hydrogen bond involving the NH group plays an important role in the stabilization of **2**. Thus, the NH-hydrogen points out the oxygen atom of the ketone, the separation between them being (2.05(5) Å) shorter than the sum of the van der Waals radii of hydrogen and oxygen.[12b,17]

The coordination geometry around the osmium atom can be rationalized as a distorted pentagonal bipyramid with axial phosphines (P(1)−Os−P(2) = 163.79(4)°) and the hydride ligands lying in the equatorial plane between the metalated carbon atom of the ketone and the heterocycle, which are *transoid* disposed (C(1)−Os−C(32) = 158.11(17)°). In the ^{1}H NMR spectrum in CD_2Cl_2 at room temperature, they give rise to a broad signal at −9.8 ppm. This resonance is temperature dependent. At 263 K decoalescence occurs, and at temperatures lower than 253 K an ABX_2 spin system is observed. The value of the H−H coupling constant (55.7 Hz) suggests the operation of a weak quantum exchange coupling[18] between the hydride ligands, in addition to the thermally activated site exchange process. The $\Delta H^{\ddagger}$ (13.6 ± 0.5 kcal mol^{-1}) and $\Delta S^{\ddagger}$ (4.7 ± 1.2 eu) values compare well with those found for the other Os−H_2 compounds with the hydride ligands separated by less than 1.6 Å.[17,19] In agreement with this, at 300 MHz, a T_1(min) value of 59 ms was obtained, which corresponds to a H−H distance of 1.40 Å (1.59(6) Å by X-ray) assuming slow spinning.[20]

The Os−C(32) bond length (2.110(5) Å) is similar to the distances reported for the scarce Os−imidazolylidene complexes characterized by X-ray diffraction analysis.[21] Although the Os−C(1) distance (2.084(4) Å) is lightly shorter than the Os−C(32) bond length, and despite the chelate nature of the orthometalated ligand, the elimination of the ketone from **2** is favored with regard to the *retrotautomerization* of the heterocycle[22] or the elimination of 2-ethylpyridinium. Thus, at room temperature in acetonitrile, **2** evolves to **3** (90% yield).

Complex **3** has been also characterized by X-ray diffraction analysis. The geometry around the osmium atom can be rationalized as a distorted octahedron with trans phosphines (P(1)−Os−P(2) = 160.98(5)°) and the N−H tautomer of the heterocycle (Os−C(5) = 1.993(6) Å) cis disposed to the hydride ligand (H(01)). The NH-hydrogen H(1) atom points out the latter. The separation between both atoms is short (2.26 Å) and lies within the range reported for the H−H distance in rings of the type LH···HN with an electrostatic hydrogen−hydrogen interaction.[23] The hydrogen bond maintains in solution. In CD_2Cl_2, at 300 MHz, the T_1(min) value of the hydride resonance (δ = −16.22; J_{H-P} = 19.5 Hz) is lower than that of $[OsH(CH_3CN)_3(P^iPr_3)_2]BF_4$ (198 ms versus 257 ms). Assuming that the excess relaxation rate (1.16 s^{-1}) is due to the proximity of the NH hydrogen atom, and that the H(01)···H(1) vector rotates with the molecule as a whole, one can calculate a H(1)···H(01) separation of 2.2 Å, in good agreement with that obtained by X-ray diffraction analysis.

In conclusion, the steric hindrance experienced by the substituent and the co-ligands of the complex is a strong determining factor for the promotion of the metal mediated rearrangement of α-substituted pyridines into N−H tautomers. The retrotautomerization and release of the heterocycle from the metal center is disfavored with regard to the elimination of strongly coordinating ligands, including orthometalated aromatic ketones.[24] Like in the previously reported Os- and Ru-quinoline derivatives,[4] hydrogen bonds involving the NH group appear to play an important role in the stabilization of this type of compounds. In the light of these results, one should expect a rapid growth of the number of transition-metal complexes containing N−H tautomers of α-substituted pyridines in the near future.

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Supporting Information Available: Experimental details for the synthesis, characterization and crystallographic data for **2**, **3**, and $[Os\{C_6H_4C(O)C_6H_5\}(\eta^2\text{-}H_2)L(P^iPr_3)_2]BF_4$ (L = CH_3CN, $(CH_3)_2CO$). This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) Note that complex $[Os\{C_6H_4C(O)C_6H_5\}(\eta^2\text{-}H_2)(CH_3CN)(P^iPr_3)_2]BF_4$ formally resulting from the replacement of the heterocycle by acetonitrile in **2** is stable and has been characterized by X-ray diffraction analysis (see Supporting Information).
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(24) Complexes $[OsH_2\{C(Ph)=CHC(O)R\}\{\kappa\text{-}C\text{-}[HNC_5H_3Et]\}(P^iPr_3)_2]^+$ (R = Me, Ph) react in the same manner as **2** to give **3**.

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