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Altering the Reaction Pathways of Aminopyridine With 4,5-Diazafluorenone : Metal Ion Control

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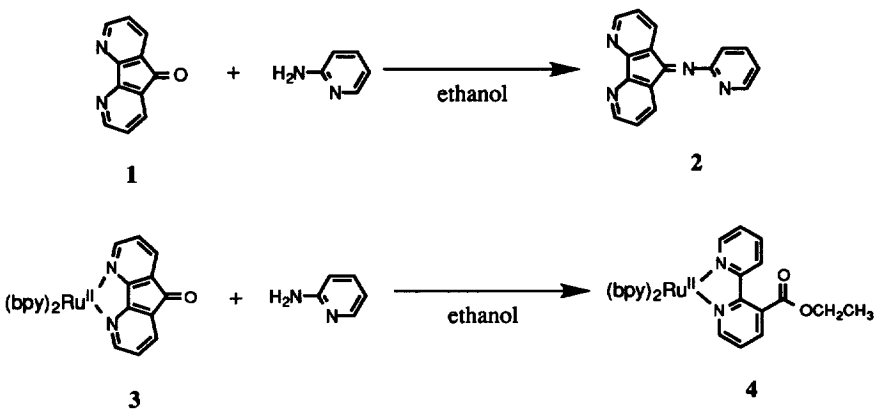
Abstract: A parallel study of the ligand 4,5-diazafluorenone reactivity in the presence and absence of ruthenium(II) ion revealed that the reaction pathway of the ligand 4,5-diazafluoren-9-one with aminopyridine can be altered from the normal Schiff-base reaction to an unusual ring opening reaction upon its coordination to ruthenium(II) ion.

Aminopyridine has two reactive sites: a primary amine and a ring nitrogen. Both can act as nucleophiles.[1] Therefore, when aminopyridine reacts with a ketone, two intermediates should exist. The two reaction pathways should be competitive and the resultant products should depend on the reaction rates. Normally, only the Schiff-base reaction pathway is observed.[2] We now demonstrate for the first time that a metal ion can be used to observe the other reaction pathway.

We have found that the chemical reactions of the ligand 4,5-diazafluoren-9-one (dafo) **1**[3] with 2–aminopyridine and its derivatives (4-aminopyridine, 2-aminopyrimidine, pyridine) differ when coordinated to Ru(II) than when uncoordinated. The free ligand **1** reacts with the primary amine of 2–aminopyridine to form a Schiff-base reaction product **2** as illustrated in Scheme 1; the coordinated ligand in the complex $Ru(bpy)_2(dafo)^{2+}$ **3**, on the other hand, does not react with primary amines under similar reaction conditions (No reactions were found between coordinated ligand **1** and aniline derivatives (aniline, 2-chloroaniline, 4-methoxyaniline, 4-nitroaniline)). Rather it reacts with the ring nitrogen to produce product **4**. Therefore, ruthenium ion acts as a switch to alter the reaction pathway.

Scheme 1



1 2

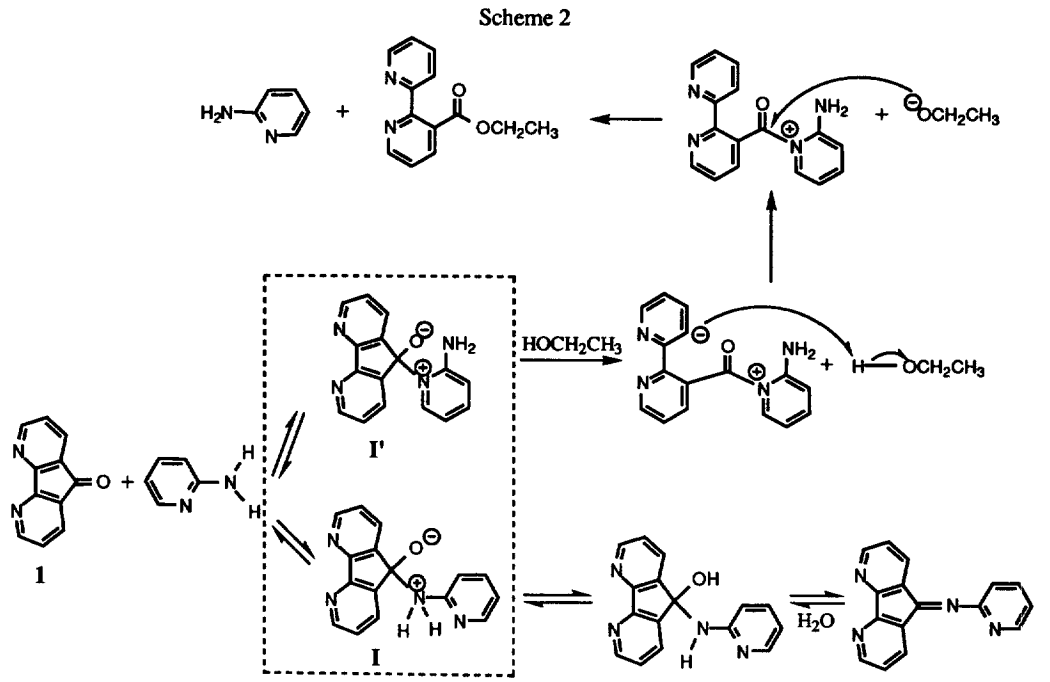
3 4

Product **4** had the following properties: (1) A strong absorption band in the infrared at 1700 cm^{-1} indicated that a carbonyl functional group was still present; (2) The ^1H NMR spectrum contained two peaks in the aliphatic region located at δ 4.50 (quartet, 2 H) and 1.45 (triplet, 3 H) corresponding to the $-OCH_2CH_3$ group; (3) The product luminescenced strongly whereas the starting material **3** luminescenced weakly;[4] and (4) The products obtained from the reaction of $Ru(bpy)_2(dafo)^{2+}$ in ethanol with different aminopyridine derivatives (4-aminopyridine, 2-aminopyridine, 2-aminopyrimidine, pyridine) gave the same properties and elemental analyses. Elemental analysis: Calcd. for $RuC_{33}H_{28}N_6O_2F_{12}P_2$: C, 42.53%; H, 3.03%; N, 9.02%. Found: C, 42.36; H, 3.06%; N, 9.08%. The complex absorbs vis/uv light at 450 nm (1.3×10^4 M^{-1} cm^{-1}), 287 nm (5.7×10^4 M^{-1} cm^{-1}) and 244 nm (2.6×10^4 M^{-1} cm^{-1}) and emits light at 680 nm (λ_{ex} = 450 nm, $\phi_{em} = 3.3 \times 10^{-3}$) in water at room temperature.

To account for these observations, the mechanism in Scheme 2 has been postulated. The difference in reactivity between the free ligand **1** and the coordinated ligand in **3** can be understood by considering formation of two possible intermediates, **I** and **I'**, for the reaction of the carbonyl group with aminopyridine. The Schiff-base reaction pathway is normally observed in organic reactions.[5] But the presence of the metal center alters the electron density on the carbonyl carbon atom as noted from infrared spectrum where the -C=O stretching frequency shifts from 1720 cm^{-1} for the free ligand to 1740 cm^{-1} for the coordinate ligand. The increase in electron density from the metal center shuts down the Schiff-base reaction pathway, but allows the alternate route **I'** to occur. In this case, following attack by the ring nitrogen,[6] collapse of the tetrahedral intermediate leads to the formation of the intermediate anion and the acylpyridinium ion due to release of the coordination-induced ring strain. Rapid proton transfer from ethanol to the pyridinyl anion yields ethoxide ion which, upon further reaction with the highly reactive acylpyridinium ion, results in the formation of the observed product. An attempt was

made to identify I' by infrared spectroscopy. However, its concentration was too low to observe spectroscopically.

Scheme 2



The effect of the metal ion is two fold: First, it adds electron density to the carbonyl carbon atom passivating the Schiff-base reaction pathway. Second, it promotes a nucleophilic induced ring-opening process. The driving force for this reaction is due to structural modifications. Molecular mechanics calculations indicate a 15 kcal/mol decrease in energy occurs upon conversion of the coordinated dafo ligand to the coordinated bipyridine ligand. These calculations were based on x-ray crystal structure data.[4] The Ru-N(dafo) bond distance of 2.125 Å was allowed to shorten to 2.056 Å as found in $[Ru(bpy)_3]^{2+}$ and the N-Ru-N bite angle of 81.9° for Ru(dafo) in $[Ru(bpy)_2(dafo)]^{2+}$ was allowed to relax to 78.7° as found for the N-Ru-N bite angle in $[Ru(bpy)_3]^{2+}$. Similar calculations for ring opening of the free ligand resulted in a 4 kcal/mole lowering of energy. Thus, the energy change needed for ring opening must be greater than 4 kcal/mole in order for it to occur, and therefore, the driving force for ring opening is not only due to release of the steric strain associated with bond cleavage of the five membered ring on dafo, but also requires the energy associated ruthenium-ligand bond distance changes that occur upon ring opening when the ligand is coordinated. An effort was made to test the generality of the reaction with protons and other 3d transition metal complexes. Unfortunately the only complex isolated was $Cu(dafo)_2Cl_2$, but it did not undergo the ring opening reaction.

The metal ion effect discussed here is different from its effect in typical organometallic reactions where a reaction pathway is normally activated through the interaction of a functional group bonded directly with the metal ion or a site adjacent to one of the coordinating atoms.[7] To our knowledge, there are no examples of attack at ligand sites remote from the metal center other than the normally expected organic chemical reactions. The probable reason for this is the remote sites are less preturbed by the metal center and hence, retain their usual reactivity.

In summary, we demonstrated the reaction pathways of aminopyridine with dafo were altered by ruthenium(II) ion. The free ligand reacts with the primary amine of aminopyridine to form azo compounds; whereas upon coordination to Ru(II), it reacts with the ring nitrogen of aminopyridine to undergo ring opening. At this point the reaction appears specific to ruthenium(II), but other heavy transition metal complexes are still being examined.

Acknowledgments

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