Inorg. Chem. **2008**, *47*, 9122−9124

Inorganic Chemistry
Communication

Cu^{II}-Mediated Synthesis of a New Fluorescent Pyrido[1,2-*a*]quinoxalin-11-ium Derivative[†]

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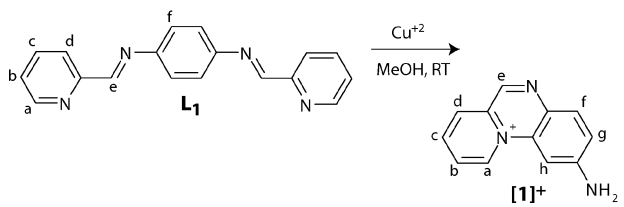
Received May 9, 2008

Quinoxalines are heterocyclic compounds with potential application as drugs or fluorophores. However, few quinoxalinylium salts have been reported in the literature. This manuscript describes the synthesis and structural characterization of a previously unknown quinoxalinylium derivative, 2-aminopyrido[1,2-*a*]quinoxalin-11-ylium ([**1**]$^+$), as perchlorate and thiocyanate salts from the Cu^{II}-mediated reaction of a Schiff base. The reaction is most efficient with Cu^{II}. The formation of a small quantity was observed spectroscopically in the presence of either a strong oxidizer or Mn^{II}. No product formation was observed with Zn^{II}, Cd^{II}, Fe^{II}, or Ni^{II}. [**1**]$^+$ emits at 580 nm, with a quantum yield estimated as 0.23, upon excitation at 470 nm.

Quinoxalines are an important class of heterocyclic compounds, some of which are found to be useful as fluorophores, dyes, and antibiotics.[1] There are different types of quinoxalines.[2] Among them, examples of pyrido[1,2-*a*]quinoxaline derivatives are rare and oxidized salt forms are unknown.[3] Syntheses of a few known closely related quinoxalines involve multiple steps.[3,4] In this manuscript, we report the single-step Cu^{II}-mediated synthesis of a previously unknown pyrido[1,2-*a*]quinoxalinylium derivative ([**1**]$^+$) and its structure (Scheme 1). The controlled reaction has been used to understand the role of metal ion in the reaction. The strong fluorescence observed increases the versatility of the application of the present compound.

Scheme 1. Formation of [**1**]$^+$ from $\mathbf{L_1}$ with Proton Labeling



Upon the addition of $Cu(ClO_4)_2 \cdot 6H_2O$ to the methanolic solution of $\mathbf{L_1}$,[5] an orange solution with yellow fluorescence was formed within minutes. Filtration of the solution followed by slow evaporation yielded the compound [**1**]ClO_4 as orange crystals.[6] Metathesis with KSCN in methanol yielded the crystals of [**1**]$SCN \cdot H_2O$.

[**1**]ClO_4[7] and [**1**]$SCN \cdot H_2O$[8] crystallized in the space

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[†] We dedicate this paper to Professor Rabindranath Mukherjee.

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(5) Characterization data for $\mathbf{L_1}$. Mp: 153−156 °C. UV/vis (MeOH): λ_{max}, nm (ϵ, M^{-1} cm^{-1}): 240 (20,800), 280sh, 364 (21 600). IR (KBr, cm^{-1}): $\nu_{C=N}$ 1617(s), ν(para-disubstituted benzene ring), 844. The synthesis and structure of $\mathbf{L_1}$ were reported before. (a) Chakraborty, S.; Munshi, P.; Lahiri, G. K. *Polyhedron* **1999**, *18*, 1437. (b) Chanda, N.; Mondal, B.; Puranik, V. G.; Lahiri, G. K. *Polyhedron* **2002**, *21*, 2033.

(6) $Cu(ClO_4)_2 \cdot 6H_2O$ (0.097 g, 0.262 mmol) was added to a solution of $\mathbf{L_1}$ (0.150 g, 0.524 mmol) in 10 mL of MeOH and stirred for 2 h. The solution was filtered. The filtrate was evaporated to dryness and washed with diethyl ether. The solid obtained was recrystallized from MeOH to obtain [**1**]ClO_4 as dark-orange crystals. Yield: 65 mg. Metathesis: KSCN (0.016 g, 0.169 mmol) was added to a methanolic solution of [**1**]ClO_4 (0.050 g, 0.169 mmol). The solution was stirred for 20 min and filtered to remove undissolved $KClO_4$. A dark-brown crystalline product was obtained from slow evaporation of the filtrate. Yield: 30 mg. Characterization data for [**1**]ClO_4. Anal. Calcd for $C_{12}H_{10}N_3ClO_4$: C, 48.80; H, 3.41; N, 14.24. Found: C, 46.75; H, 3.41; N, 14.21. Λ_M (MeOH): 99 S cm^{-2} mol^{-1}. ESI-MS (M^+): calcd 196.08747; found 196.0870. UV/vis (MeOH): λ_{max}, nm (ϵ, M^{-1} cm^{-1}): 260 (55 400), 316 (10 800), 367 (8900), 470 (25 300). IR (KBr, cm^{-1}): $\nu_{perchlorate}$ 1114, 1077, $\nu_{C=N}$(bend) 1615, ν_{amine} 3297, 3185. ^1H NMR (CD_3OD, ppm): H^a 9.76d, H^b 8.25m, H^c 8.56m, H^d 8.61m, H^e 9.18s, H^f 8.01d, H^g 7.38dd, H^h 7.66d (all protons integrate to a single proton), J_{ab} = 7, J_{bc} = 7.5, J_{cd} = 8, J_{fg} = 9, J_{gh} = 2.4, J_{ac} = 2, J_{bd} = 2.

(7) Crystal data for [**1**]ClO_4: $C_{12}H_{10}N_3ClO_4$, monoclinic, $P2_1/c$, a = 6.32910(10) Å, b = 12.9283(3) Å, c = 15.4054(4) Å; β = 100.0910(10)°, V = 1241.04(5) Å^3, Z = 4, ρ_{calcd} = 1.583 Mg m^{-3}, μ = 0.326 mm^{-1}, reflections collected 12 571, independent 2939, R1 = 0.0388, wR2 = 0.0801 [$I > 2\sigma(I)$]; R1 = 0.0935, wR2 = 0.1006 (all data), GOF = 0.871. Data collected on a Siemens (Bruker) SMART CCD diffractometer at 296 K.

10.1021/ic8008464 CCC: $40.75

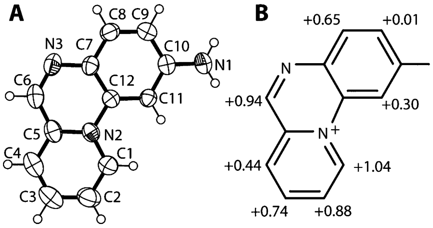

Figure 1. (a) Molecular structure of [**1**]$^+$ in [**1**]SCN with thermal ellipsoids set to the 50% probability level. (b) ^{1}H NMR shifts compared to $\mathbf{L_1}$. Selected bond distances (Å): C10−N1 1.357(3), C6−N3 1.300(4), N3−C7 1.372(3), C12−N2 1.424(3), C5−N2 1.377(3), N2−C1 1.369(3).

groups $P2_1/c$ and $P\bar{1}$, respectively. The structures of [**1**]$^+$ are identical in both of the crystals, but the thermal parameters of several atoms in [**1**]ClO$_4$ are high (Supporting Information). Thus, the bond lengths of [**1**]SCN are used in the discussion. The ORTEP diagram and selected bond lengths of the [**1**]$^+$ ion in [**1**]SCN are shown in Figure 1.

[**1**]$^+$ is essentially planar with a short C10−N1 distance of 1.357(3) Å, compared to the usual $C_{aro}-N_{amine}$ single-bond distance of 1.43 Å.[9] This might be due to the electron-withdrawing effect of positively charged pyridine, which increased the $C-N_{amine}$ bond order. Other C−C and C−N bond distances are well within the limits expected for aromatic rings.[9]

In [**1**]SCN•H$_2$O, amine NH, water, and N of SCN$^-$ form two different types of hydrogen-bonded networks, resulting in two nonidentical SCN$^-$ units in the crystal (Supporting Information). The FT-IR of [**1**]SCN shows two stretches at 2062 and 2031 cm^{-1} for ν_{CN} of SCN$^-$.[10] In [**1**]ClO$_4$, the perchlorate ion hydrogen-bonded with the free amine hydrogens (N•••O, 3.1−3.2 Å) forms a 2D network (Supporting Information). [**1**]ClO$_4$ shows strong absorption at ~1100 cm^{-1} due to the perchlorate ion.[6,10] Both compounds show two ν_{NH} stretches between 3100 and 3300 cm^{-1}, characteristic of a primary amine, while that of ν_{imine} in the ring occurs at ~1620 cm^{-1}.[6,10] The elemental analysis, mass spectrum, and molar conductance of [**1**]ClO$_4$ are consistent with the formula.[6,11]

In the ^{1}H NMR of [**1**]ClO$_4$ in CD$_3$OD, protons were identified from relative positions, coupling, and integration (Supporting Information). Compared to $\mathbf{L_1}$, both H^e and H^a in [**1**]$^+$ shifted considerably downfield by 0.94 and 1.04 ppm, respectively, presumably because of their proximity with quaternary nitrogen (Figure 1b, labeling in Scheme 1). The protons in the pyridine ring are shifted more downfield compared to the protons in the aniline ring. Thus, the pyridine ring is more electron-deficient compared to the aniline ring, which probably led to strong intramolecular charge transfer (see below).

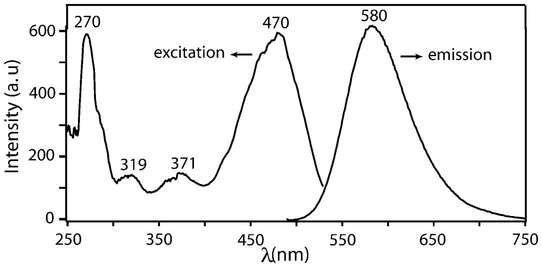

Figure 2. Excitation and emission spectra of [**1**]ClO$_4$ in MeOH.

The solution of [**1**]ClO$_4$ in MeOH shows strong charge-transfer bands.[6] Upon excitation at 470 nm, the molecule fluoresces at 580 nm (Figure 2). The quantum yield was estimated using a micromolar methanolic solution and found to be 0.23.[12] The reasonable quantum yield and emission in the useful 500−600 nm region for [**1**]$^+$ is comparable with those of popular fluorescent dyes like acridine orange (λ_{em} = 525 nm, quantum yield = 0.20), fluorescein (λ_{em} = 500−600 nm, quantum yield = 0.79), and quinine sulfate (λ_{em} = 400−600 nm, quantum yield = 0.54).[13] The fluorescence emission at 580 nm is due to the intramolecular charge transfer between the relatively electron-rich amine ring and the electron-deficient pyridinium ring.

[**1**]ClO$_4$ shows an irreversible oxidation at 1.43 V and an irreversible reduction at −0.78 with respect to SCE in MeCN.[14] Thus, the molecule is redox-stable over a wide range.

The reaction of Cu^{II} and $\mathbf{L_1}$ most likely proceeds through complexation (Scheme 2). Electron paramagnetic resonance (EPR) of the frozen solution at the beginning of the reaction shows a strong signal at 77 K for typical a Cu^{II} tetragonal complex with $g_{\parallel}$, $g_{\perp}$, and $A_{\parallel}$ values of 2.37, 2.02, and 177 G, respectively.[15] The formation of [**1**]$^+$ monitored using fluorescence spectroscopy showed the completion of the reaction within 15 min (Supporting Information). The amount of [**1**]$^+$ produced decreases with an increase in the metal ion concentration presumably because of the formation of side product **III** (Scheme 2). Binuclear complexes of $\mathbf{L_1}$ with Ru^{II} and Zn^{II} similar to **III** are known that support the formation of side product **III**.[5,16]

The reduction of Cu^{II} during the reaction was indicated by a significant reduction of the EPR signal intensity at the end of the reaction. Involvement of the redox state of metal was also indicated by the reaction in the presence of a redox-inactive metal ion. The formation of [**1**]$^+$ was not observed in the presence of Zn^{2+} and Cd^{2+} even after prolonged

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(8) Crystal data for [**1**]SCN: C$_{12}$H$_{10}$N$_4$SCN, triclinic, $P\bar{1}$, a = 9.3055(9) Å, b = 11.6353(11) Å, c = 12.8604(13) Å; α = 106.728(6)°, β = 90.896(7)°, γ = 108.176(6)°, V = 1258.4(2) Å^3, Z = 2, ρ_{calcd} = 1.385 Mg m^{-3}, μ = 0.249 mm^{-1}, reflections collected 13 215, independent 6383, R1 = 0.0728, wR2 = 0.1949 [$I > 2\sigma(I)$]; R1 = 0.1137, wR2 = 0.2211 (all data), GOF = 1.057.

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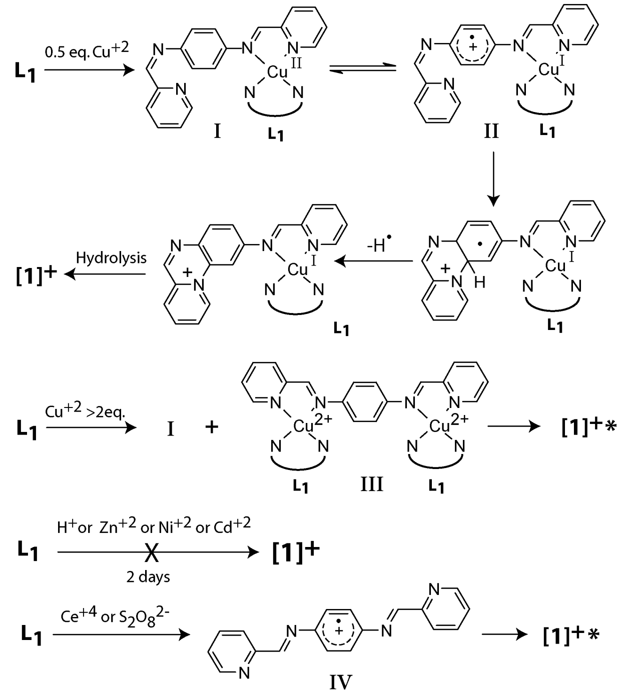
Scheme 2. Proposed Path of the Reaction



* observed spectroscopically

stirring for 2 days. $\mathbf{L_1}$ is known to stabilize the lower oxidation state of the metal (the Ru^{III}/Ru^{II} potential for $[(bpy)_2Ru(\mathbf{L_1})Ru(bpy)_2]$ is 1.59 V vs SCE).[5a,17] Thus, reduction of the metal ion with concomitant oxidation of the ligand forming an intermediate **II** is conceivable (Scheme 2). The reaction proceeded further with ring closure followed by hydrolysis of the imine bond (Scheme 2).

If a cation radical indeed is the intermediate, then a proper oxidizer might be able to form $[\mathbf{1}]^+$. To check this possibility, we have reacted $\mathbf{L_1}$, which gets oxidized[5a] at 1.79 V (vs SCE in MeCN) with strong oxidizers, Ce^{IV} and $S_2O_8^{2-}$ salts. Electrospray ionization mass spectrometry (ESI-MS) and fluorescence measurements of the resulting solution indicate the formation of a small quantity of $[\mathbf{1}]^+$ (Supporting Information) in comparison with the reaction in the presence of Cu^{II}. The formation of $[\mathbf{1}]^+$ supports the ligand oxidation as a key step for the formation of $[\mathbf{1}]^+$. The tendency of $\mathbf{L_1}$ to stabilize Cu^{I} [17] possibly helps in the formation of intermediate **II**. Thus, the role of Cu^{II} is to form the intermediate **II** (Scheme 2) and thereby facilitate the formation of $[\mathbf{1}]^+$ in a larger quantity. Cu^{II} has been reported to stabilize radicals in other systems.[18] Our attempt to isolate the product from these reaction mixtures proved futile.

We have tried the reaction in the presence of Mn^{II}, Ni^{II}, Fe^{II}, Fe^{III}, and $[Fe(CN)_6]^{3-}$. In the presence of Mn^{II}, traces of **1** were formed only after 2 days. Product formation was not observed with Ni^{II}, Fe^{II}, or $[Fe(CN)_6]^{3-}$. The formation of $[\mathbf{1}]^+$ was observed with Fe^{III} spectroscopically. However, the formation of a purple-colored solution indicated a mixture of products. The fact that both Cu^{II} (0.16 V vs NHE in water) and Fe^{III} (Fe^{III}/Fe^{II} 0.77 V vs NHE in water) salts form $[\mathbf{1}]^+$ but $[Fe(CN)_6]^{3-}$ (0.36 V vs NHE in water)[19] does not indicates that metal ions that are capable of binding with the ligand and stabilizing the radical intermediate upon reduction have the potential to facilitate this reaction. While $[Fe(CN)_6]^{3-}$ has the redox potential between Cu^{II} and Fe^{III}, its inability to bind to the ligand inhibits the reaction. On the other hand, oxidizers that are strong enough to oxidize the ligand directly can also form $[\mathbf{1}]^+$, but the instability of the intermediate **IV** decreases the amount of cyclized product. Our efforts are ongoing to study the reaction with other metal ions.

The overall reaction stoichiometry of the reaction is likely to be as follows:

$$\underset{C_{18}H_{14}N_4}{\mathbf{L_1}} + H_2O \rightarrow \underset{C_{12}H_{10}N_3}{[\mathbf{1}]^+} + \underset{C_6H_5NO}{\text{pyridine-2-carboxaldehyde}} + \{H^+ + 2e^-\}$$

The ESI-MS spectrum of the reaction mixture from a Cu^{II}-mediated reaction at the end of the reaction shows the presence of $\{C_6H_5NO\}^+$ and $\{Cu^I(C_6H_5NO)\}^+$ at 107.0 and 169.9, respectively, supporting the above reaction.

Cu^{II} has earlier been used as a mediator in heterocyclic compound formation[20] but was never used as a mediator in any quinoxaline derivative. Recently, a fluorescent triazinium compound has been reported where pyridinium salt formation occurred via the addition of an acid followed by loss of H_2.[21] However, we have not observed the formation of $[\mathbf{1}]^+$ in the presence of an acid (Supporting Information).

In conclusion, we have synthesized and characterized a new pyrido[1,2-*a*]quinoxalin-11-ium derivative. The reaction proceeds through a primarily Cu^{II}-mediated pathway hitherto unobserved for similar reactions. Strong fluorescence in the visible region and solubility of the compound in a wide range of solvents increase the potential of the compound as a fluorescent dye.

Acknowledgment. We thank the DST, DST-FIST, and CSIR, India, for financial support, Rajib Choudhuri for initial observations, Babulal Das for X-ray data collection, and Prof. A. Chattopadhdya for discussion. Reviewers' suggestions at the revision stage were very helpful.

Supporting Information Available: CIF for $[\mathbf{1}]ClO_4$ and $[\mathbf{1}]SCN$ and ^1H NMR, ESI-MS, UV−visible spectra, FT-IR, fluorescence, X-ray tables, and figures. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) The Cu^{II}/Cu^{I} potential for $Cu(bpy)_2PF_6$, which has a coordination environment similar to that of **I**, is 0.52 V vs SCE. The Ru^{III}/Ru^{II} potential of $[Ru(bpy)_3]^{2+}$ is 1.29 V. Kourkine, I. V.; Mirkin, C. A. *J. Am. Chem. Soc.* **2000**, *122*, 2659.

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