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Nitric oxide reactivity of a Cu(II) complex of an eneamine ligand that lead to the C=C bond breaking of the ligand to form amide compound

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A copper(II) complex with bidentate ligand **L** [**L**, N-4-(phenylimino)pent-2-en-2-yl)benzenamine] was synthesized as its perchlorate salt. The single crystal structure for ligand **L** was determined as its chloride salt. The nitric oxide reactivity of the complex was studied in acetonitrile solvent. The formation of thermally unstable [Cu(II)-NO] intermediate on reaction of the complex with nitric oxide in acetonitrile solution was observed prior to the reduction of copper(II) centres to copper(I). The reduction was found to result with a mono nitrosation at the secondary amine site as well as C=C bond breaking of the ligand leads to the formation of an amide product. All the products were isolated and characterized spectroscopically. The X-ray single crystal structure of the amide compound was determined.

Keywords: Bidentate ligand, nitrosation, amide, reductive nitrosation.

Introduction

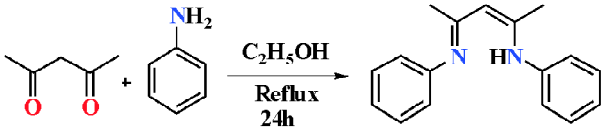
Nitric oxide is one of the simplest molecule and chemists have studied its structure and reactivity for many years. In the past decade nitric oxide, NO, has gain the attention of scientists as it is found to be an essential component in many physiological processes. Furchgott, Ignarro and Murad get Nobel Prize in 1998 due to their surprising and exciting discovery of the multiple roles nitric oxide plays in physiological and pathological functions in human body[1–4]. Nitric oxide has several biological and physiological activities like, it kills microorganisms, primary messenger in regulating blood pressure as well as neuro-transmitters. Dysfunction in NO metabolism has been associated with a number of diseases, such as arthritis, hypertension and septic shock[1–11]. Also, nitric oxide is believed to be the mediators of copper protein activity[12] which attributes to the formation of nitrosyl complex of metallo-proteins[13] mainly iron proteins[14,15]. The best characterized example is the ferroheme enzyme, soluble guanylyl cyclase (sGC)[16,17]. The Fe-NO complex formation changes the nature of histidine ligand in the protein conformation which activate the enzyme for catalytic formation of the secondary messenger cyclic-guanylyl monophosphate (cGMP) from guanylyl triphosphate (GTP). The enzymatic formation of cGMP results into the relaxation of smooth muscle tissue of blood vessels, hence lowering blood pressure. The interaction of nitric oxide with metal center has been of interest to chemist because of its flexibility to act either as an electron donor or acceptor during metal-NO binding[18,19]. The reduction of Cu(II) centres in cytochrome *c* oxidase and laccase, to Cu(I) on treating with NO gas has also been known for a long time[20]. In cytochrome *c* oxidase, the NO reduction of Cu(II) to Cu(I) is believed to play the role in regulating the electron transport activity of this protein[20]. Nitric oxide is also known to generate powerful nitrating and/or oxidizing agent peroxynitrite generation[20].

Experimental

*Synthesis of ligand **L**:*

Pentane-2,4-dione (1.001 g, 10 mmol) was dissolved in degassed and distilled ethanol and aniline (1.863 g, 20 mmol) was added. It was allowed to reflux for 24 h at 80°C. It was allowed to cool and dried over rotary evaporator and extracted and separated from chloroform-water mixture. The organic layer was dried to get pure ligand **L**, (2.12 g, yield, ~85%). FT-IR: 3354, 3032, 1597, 1572, 1498, 1312, 1278, 1189, 1025, 751, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 1.90–1.98 (3H, s), 2.04–2.10 (3H, s), 3.67 (1H, b), 5.16 (1H, s), 6.61–6.62 (2H, d), 6.68–6.72 (1H, t), 7.04–7.15 (5H, m), 7.21–

7.30 (2H, t); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 19.19, 28.60, 97.25, 114.47, 117.46, 123.96, 124.96, 128.70, 138.15, 146.53, 159.80, 195.48. ESI-Mass: (m+1)/z, 251.07.



Scheme 1

Synthesis of complex:

0.369 g (1 mmol) of $[Cu(II)(H_2O)_6](ClO_4)_2$ was dissolved in dry acetonitrile. To it, 0.250 g of ligand, **L** (1 mmol) was added with constant stirring. The reaction mixture was then stirred for 2 h. The solvent was evaporated and dried to get the crude complex. It was then washed with ether (10 ml×4 portions) to get pure solid complex **1** as dark red solid, (yield ~65%); FT-IR: 3437, 2924, 1576, 1522, 1493, 1383, 1143, 1110, 1087, 743, 626 cm^{-1}; UV-Vis (acetonitrile) λ_{max}: 512 nm (ε = 378 M^{-1} cm^{-1}); ESI-Mass: 395.43. The X-Band EPR data: $g_{||}$ = 2.4816, $g_{\perp}$ = 2.111, $A_{||}$ (cm^{-1}) = 120.86×10^{-4}. The $A_{||}$ value confirms the square planner geometry of the metal centre. The calculated magnetic moment is found to be 1.778 BM.

Results and discussion

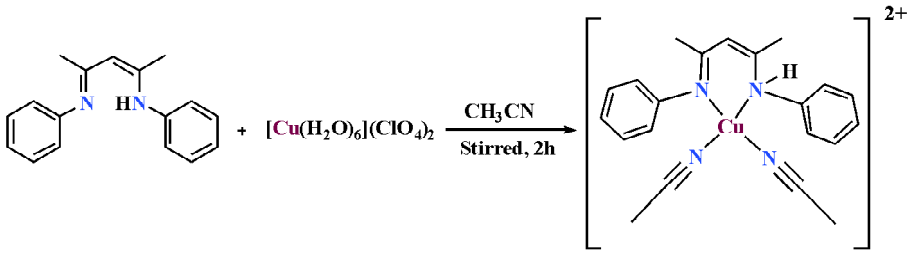
Synthesis and characterization of the complex:

Ligand **L** was synthesized following general procedure (Experimental section, Scheme 1). It was characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, Mass spectrometry and X-ray single crystal structure determination (Experimental section). The complex was synthesized by the reaction of hexa-aquacopper(II) perchlorate with the ligand **L** and isolated as solid (Scheme 2). It was characterized by various spectroscopic methods such as FT-IR, UV-Visible spectroscopy and ESR spectroscopical studies as well as by single crystal X-ray structure determination. The single crystal structure for ligand **L** was determined as its chloride salt. The perspective ORTEP view of ligand **L** is shown in Fig. 4. The ligand **L** is a mono-anionic bidentate β-diketiminate ligand; it's properties can be changed by choosing the various types of amine and diketone during synthesis. The ligand **L** is a pincer type ligand which can be revealed from the crystal structure and is sterically crowded. The modified ligand, **L′** is a simple amide compound which has been characterized by various spectroscopic techniques (Supporting Information) as well as by X-ray crystallographic structure determination (Fig. 5). The *d-d* transition for complex **1** appears at 512 nm in acetonitrile solvent (Supporting Information). The complex shows the axial ESR pattern at 77 K that reveals the square planar nature of the complex (Supporting Information). The complex was found to exhibit one electron paramagnetism at room temperature (Experimental section).

Nitric oxide reactivity:

Nitric oxide reduces the Cu(II) center of the complex **1** in acetonitrile solvent to copper(I) and was experimentally evidenced by various spectroscopic techniques like UV-Visible, ESR and solution FTIR spectroscopy.

The *d-d* transition band that appears at 512 nm has been shifted to 500 nm after purging NO gas reveal the development of unstable [Cu(II)-NO] intermediate as shown in Fig. 1. The band that appears at 500 nm was found to decrease with time showing the formation of Cu(I) complex with pseudo-first order kinetics (Fig. 1, inset). In UV region of the spectra, the higher energy band correspond to $\pi \rightarrow \pi^*$ transition shows the shifting and diminishing the peak at 295 nm to 275 nm, indicating the change in the ligand structure after reaction is complete. The solution FT-IR spectrum, the peak that ap-



Scheme 2

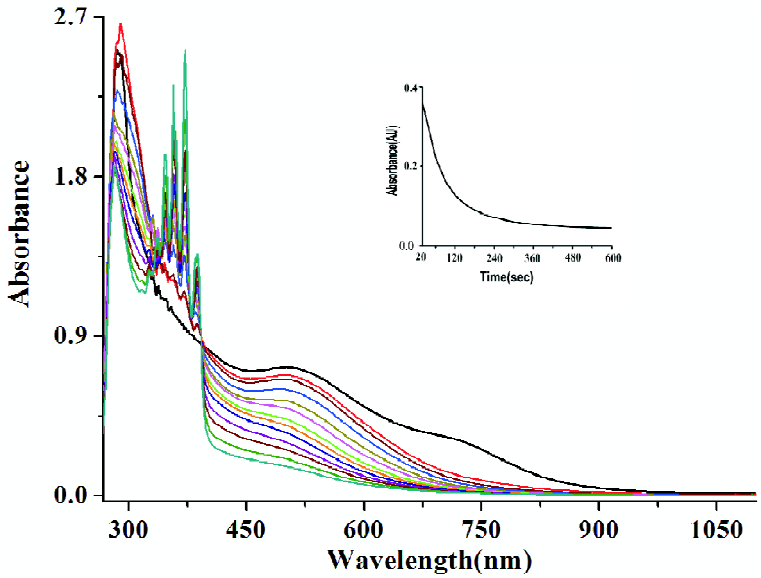


Fig. 1. UV-Visible spectra of complex **1** after purging NO in acetonitrile.

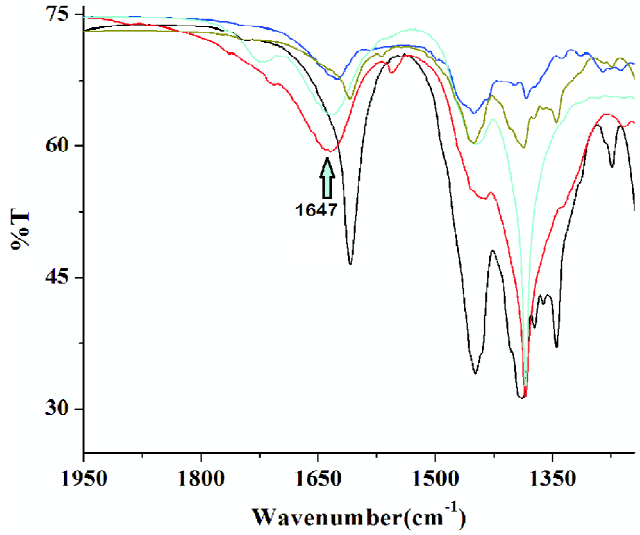


Fig. 2. Solution FT-IR spectra of complex **1** before (black trace) and after (red, green, blue and dark yellow traces respectively) NO treatment in acetonitrile.

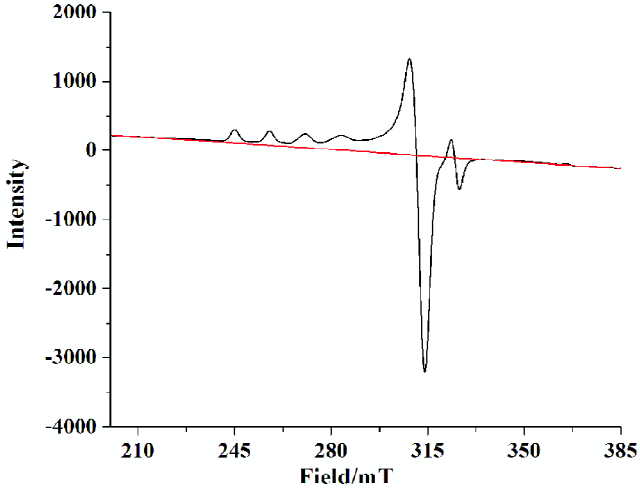
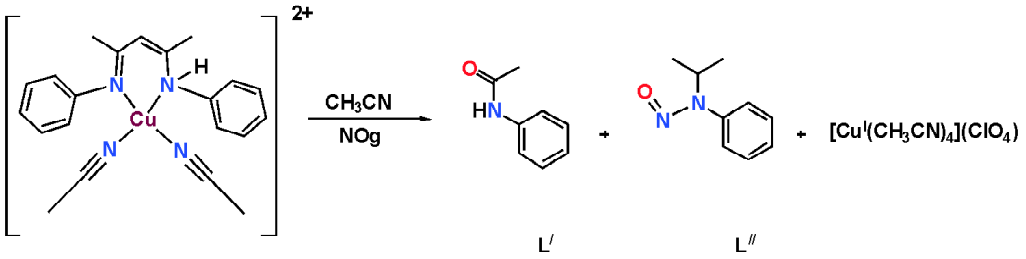


Fig. 3. The ESR spectra showing the complex **1** (black) in acetonitrile and the complex after purging NO gas (red trace) in acetonitrile at 77 K.

peared at 1647 cm^{-1} in acetonitrile solvent (Fig. 2) corresponds to the frequency of [Cu(II)-NO] which was found to diminish with time showing the unstable nature of the intermediate. The complex displayed four line X-band ESR at 77 K in acetonitrile solvent, $g_{||}$ and $g_{\perp}$ values are found to be 2.48 and 2.11 (Fig. 3), respectively. This unstable and short lived [Cu(II)-NO] intermediate is ESR silent at 77 K.

*Isolation of the modified ligand **L′** and **L″***:

395 mg of the complex was dissolved in a Schlenk tube in ~30 ml degassed acetonitrile. NO gas was purged to the solution for about one minute and the reaction mixture was kept undisturbed for around 10 min. The organic layer was then extracted, collected and dried in rotary evaporator. The compounds were separated by column chromatography to



Scheme 3

obtain the modified ligands **L′** and **L″**. The single crystal structure for ligand **L′** was determined. The perspective ORTEP view of the modified ligand **L′** is shown in Fig. 5.

The spectroscopic data for the modified ligands are mentioned below. **L′**: Yield, 25 mg (~18%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 2.143 (3H, s), 7.06–7.09 (1H, t), 7.24–7.30 (2H, t), 7.46–7.48 (2H, d); ^{13}C NMR (400 MHz, $CDCl_3$) δ_{ppm}: 24.699, 120.183, 124.477, 129.114, 138.113, 168.855; FT-IR: 3294, 2924, 1663, 1600, 1557, 1435, 1370, 1324, 1264, 753, 694 cm^{-1}; ESI-Mass: (m+1)/z, 135.98. **L″**: Yield, 28 mg (~17%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 2.11 (6H, s), 3.65–3.67 (1H, m), 6.62–6.64 (2H, d), 6.71–6.72 (1H, t), 7.09–7.13 (2H, t); ^{13}C NMR (400 MHz, $CDCl_3$) δ_{ppm}: 30.543, 46.631, 114.784, 117.865, 128.948, 146.632; FT-IR: 3440, 2929, 2850, 1623, 1411, 1341, 688 cm^{-1}; ESI-Mass: (m+1)/z, 164.88.

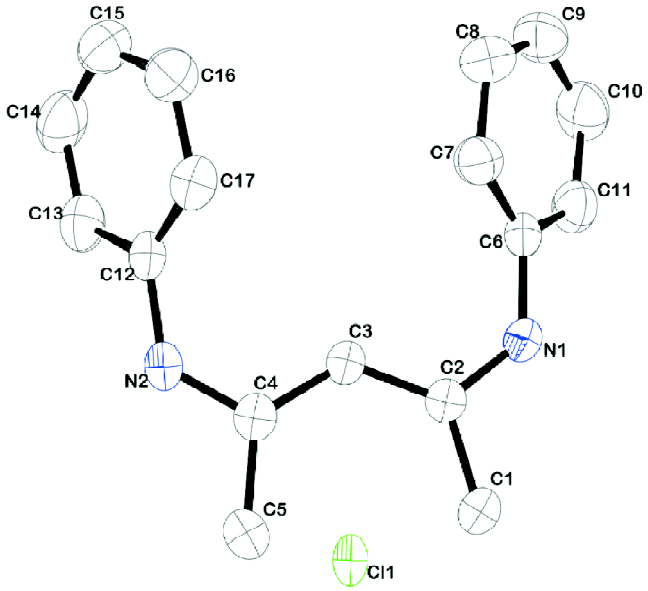


Fig. 4. ORTEP diagram of chloride salt of ligand **L** (50% thermal ellipsoid plot, hydrogen atoms are omitted for clarity).

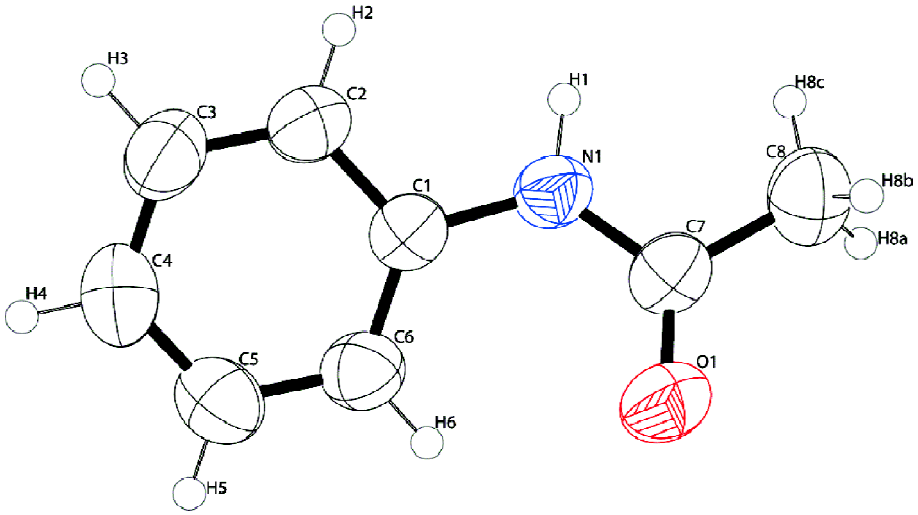


Fig. 5. ORTEP diagram of modified ligand **L** (50% thermal ellipsoid plot).

Conclusion

A Cu(II) complex is synthesized and characterized. Nitric oxide reactivity of the synthesized complex is studied and the concomitant reduction of the metal center i.e. Cu(II) centre to Cu(I) center is observed. The modified N-nitrosated product and the amide products are isolated and characterized spectroscopically and structurally.

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