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Synthesis and characterization of a novel ruthenium nitrosyl complex and studies on photolability of coordinated NO

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ABSTRACT

In the present communication, we have reported the synthesis and characterization of a novel nitric oxide (NO) donating complex $[Ru(L^1)(PPh_3)_2(NO)](ClO_4)$ (**2**) derived from $[Ru(L^1)(PPh_3)_2(Cl)]$ (**1**) (L^1H_2 is pyridine 2,6-dicarboxylic acid and H stands for dissociable proton). Characterization of **2** by UV–Vis, IR and NMR spectral studies revealed the presence of $\{RuNO\}^6$ species with $S=0$ ground state. ESI-MS data also supported the formation of **2**. Electrochemical studies on complex **2** were investigated. The coordinated NO was found to be photolabile under visible as well as in UV light and photocleaved NO was transferred to reduced myoglobin.

Nitric oxide (NO) is highly reactive diatomic radical that is physiologically generated by organisms ranging from bacteria to humans [1]. This reactive radical has been found to be an important signaling molecule and is involved in several physiological processes namely blood pressure regulation, immune and endocrine response, neurotransmission and cell death [1,2]. In the cellular level NO is produced by the enzyme nitric oxide synthase (NOS) however, production of NO below or above the physiological level initiates different diseases like cardiovascular, neurologic and pulmonary diseases, atherosclerosis and cancer [2]. In the recent years, there has been considerable interest for the studies on interaction of NO with metal complexes [3]. Interaction of metal complexes with NO and synthesis of metal nitrosyl complexes are not only important for the synthesis of new NO donors but are also important for NO scavenging activity [4]. Metal complexes which could deliver NO upon illumination of light are important in photodynamic therapy (PDT) [3,5d].

This work stems from our interest in the synthesis of photolabile ruthenium nitrosyl complexes [6]. Recently Mascharak and coworkers reviewed [7] the research on photolabile ruthenium nitrosyl complexes by different research groups and such type of complexes derived from carboxylic acid and phosphine ligands are scarce [7,8]. We were interested to study the reactivity of ruthenium complexes having ligands containing one or more than one carboxylic acid (–COOH) donor(s) with nitric oxide. In the present study we report a novel ruthenium nitrosyl complex $[Ru(L^1)(PPh_3)_2(NO)](ClO_4)$ (**2**) (where L^1H_2 is pyridine 2,6-dicarboxylic acid and H stands for dissociable protons) derived from ligand pyridine 2,6-dicarboxylic acid (shown in Scheme 1). The complex was characterized by UV–Vis and IR spectral studies. NMR (^{1}H and ^{31}P) and ESI-MS spectral data and redox property of the metal center will be scrutinized. Photolability of the coordinated NO was determined by UV–Vis spectral studies. To confirm the photolability, the liberated NO after photocleavage was transferred to reduced myoglobin (Mb).

The precursor complex $[Ru(L^1)(PPh_3)_2(Cl)]$ (**1**) was synthesized by refluxing an ethanolic solution of $Ru(PPh_3)_3Cl_2$ and pyridine 2,6-dicarboxylic acid in 1:1 equivalent ratio. The brownish-red resultant complex was eluted through an alumina column and was recrystallized from benzene–ethanol mixture (1:1 v/v). Detail of the synthetic procedure was reported in the supporting information. The resultant complex was characterized by UV–Vis and IR spectral studies which authenticated the formation of $[Ru(L^1)(PPh_3)_2(Cl)]$ (**1**). These data were consistent with the data reported by Natarajan and coworkers [9] for the same resultant complex using $Ru(PPh_3)_3Cl_3$ as a starting material. Hence in our study during the reaction, aerial oxidation of the metal center in presence of hard carboxylic acid donors [10] (vide infra) and concomitant formation of **1** was observed.

Complex **1** was reacted with *in situ* generated NO by an acidified $NaNO_2$ solution [11]. The brownish-red color was turned to yellow after 1 h of stirring. The resultant yellow compound **2** was isolated as perchlorate salt (detail of the synthetic procedure was reported in supplementary material). No change was observed when **1** was treated with same acidic solution without $NaNO_2$.

Complex **1** possesses a band near 400 nm in UV–Vis spectrum. This band was disappeared in complex **2** and a peak near 320 nm was observed. Molar extinction coefficients of the above two bands indicated that the peaks were due to charge transfer transition. IR spectrum of **2** provided ν_{NO} at ~1890 cm^{-1} and the presence of

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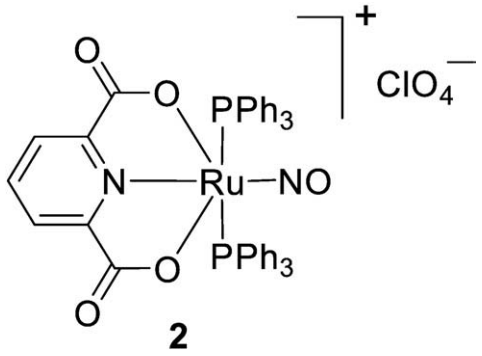

Scheme 1. Schematic drawing of complex **2**.

perchlorate ion was confirmed by peaks near 1090 and 623 cm^{-1} (Fig. S2 in supplementary material). The peak near 1890 cm^{-1} was consistent with the data reported by Karidi et al. [12] where coordinated NO was *trans* to pyridine nitrogen donor and hence we obtained a ruthenium nitrosyl complex having $\{RuNO\}^6$ moiety [13] via the substitution of chloride ion by non-innocent NO ligand. The ν_{NO} value indicated $\{Ru^{II}NO^+\}^6$ description of $\{RuNO\}^6$ moiety [7,12]. Complex **2** was diamagnetic and NMR spectra of **2** were recorded. ^1H NMR spectrum clearly depicted the presence of protons from ligand and phosphine groups in **2** (Fig. 1(a)). Moreover *trans* disposition of PPh_3 ligands was confirmed by single peak near 20 ppm in ^{31}P NMR spectrum (Fig. 1(b)) [14].

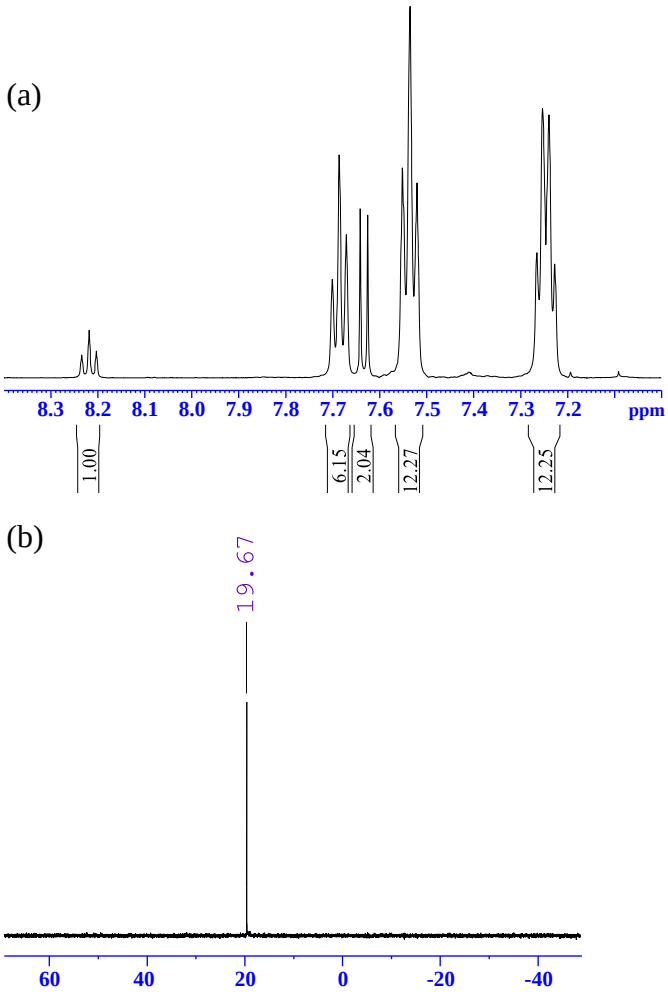

Fig. 1. ^1H NMR spectrum (a) and ^{31}P NMR spectrum (b) of complex **2** at room temperature. ^1H NMR ($(CD_3)_2SO$, 500MHz): δ 8.219 (dd, 1H), 7.634 (d, 2H), and 7.228–7.701 (m, 30H) ppm. ^{31}P NMR (CD_3CN, 500MHz): δ 19.67 ppm.

We have investigated the ESI-MS of **2** and the experimental spectrum is shown in Fig. 2. The proposed fragmentation pattern was shown in the supporting information (Scheme S2). The molecular ion peak for $m/z = 919.5$ (M^+) was not detected in ESI-MS spectrum, however the most abundant peak at $m/z = 820.99$ $(M–ClO_4)^+$ corresponding to the mono-positive complex cation was found. This data clearly indicated the dissociation of the perchlorate ion, however, all these data confirmed the formation of the nitrosyl complex $[Ru(L^1)(PPh_3)_2(NO)](ClO_4)$ (**2**). The peak at $m/z = 558.13$ $[(M–ClO_4)–PPh_3]^+$ was probably due to the dissociation of one of the PPh_3 groups [15].

We have performed the electrochemical investigation of complex **2** in dichloromethane. Complex **2** exhibited quasireversible cyclic voltammogram with $E_{1/2}$ at −0.021 V versus Ag/AgCl reference electrode (shown in Fig. 3). Cyclic voltammogram clearly showed that the initial electrode process was cathodic during the scan starting from −0.4V. This behavior was consistent with the data reported by Patra et al. [16]. Hence it has been found out that Ru(III) in **2** was stabilized in presence of hard carboxylic acid donors [10].

Complex **2** was soluble in dichloromethane, methanol and acetonitrile and was stable under heat in those solvents. Photolability of the coordinated NO was determined by UV–Vis spectral studies using two different light sources. Methanolic solution of **2** was irradiated with visible light from a tungsten lamp (100 W), on the other hand acetonitrile solution of **2** was irradiated with UV light from the low intensity UV lamp ($\lambda = 302$ nm) and spectral changes are depicted in Fig. 4. Spectral changes due to light irradiation afforded isosbestic points at 242 nm and 275 nm in Fig. 4a and at 244 nm, 275 nm and 363 nm in Fig. 4b. Time dependent absorption changes (inset of Fig. 4a and b) clearly showed the higher rate of photo dissociation of NO under UV light than in visible light. This may be due to the absence of proper absorption peak in the visible range [16]. We added excess of tetraethyl ammonium chloride to methanolic solution of **2** after photo dissociation of NO (Fig. S4 in the supplementary material). Generation of peak near 400 nm in UV–Vis spectra clearly supported the formation of **1** and hence formation of a solvento species $[Ru(L^1)(PPh_3)_2(S)]^+$ (where S is solvent) was suggested after photocleavage of NO. This solvento species gave rise to **1** after reacting with excess of tetraethyl ammonium chloride.

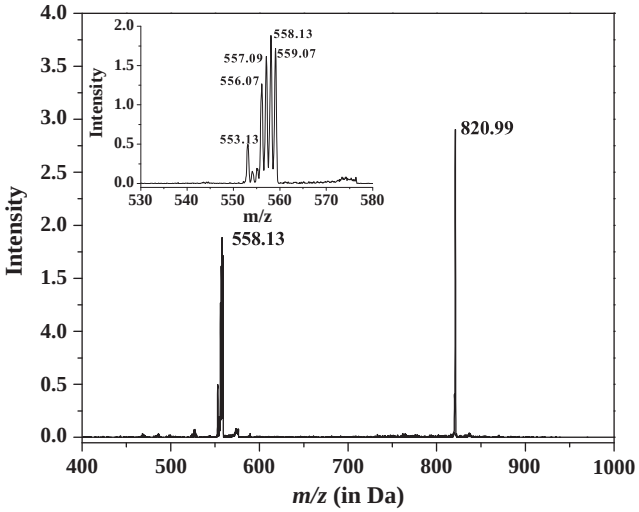

Fig. 2. ESI-MS positive ion specrtum of complex **2** (methanol solvent was used). Units m/z in Da. The calculated pattern of the peak near m/z 558.13 (formula, $C_{25}H_{18}N_2O_5PRu$; exact mass, 559; molecular weight, 558.46) was found to be m/z 559.00, 558.00, 561.00, 557.00, and 553.00.

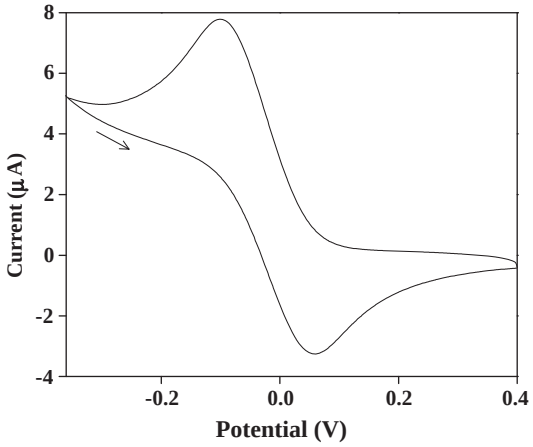

Fig. 3. Cyclic voltammogram of a 10^{-3} M solution of **2** in dichloromethane, in the presence of 0.1 M tetrabutylammonium perchlorate (TBAP), using working electrode: glassy-carbon, reference electrode: Ag/AgCl, auxiliary electrode: platinum wire, scan rate 0.05 V/s. ($E_{1/2}$) = −0.021 V *vs.* Ag/AgCl.

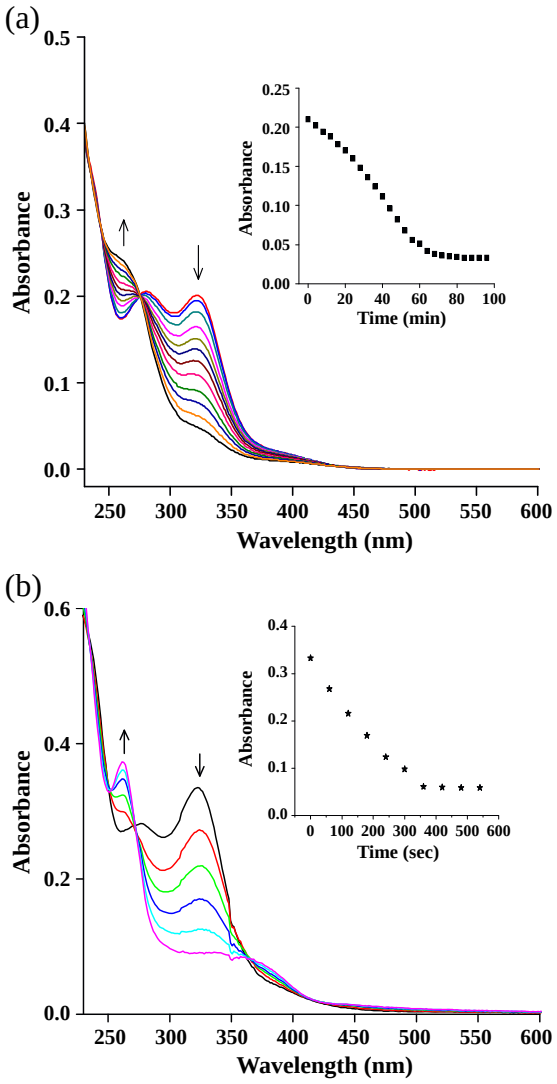

Fig. 4. (a) Photodissociation of **2** (~9×10^{-6} M) in methanol under illumination of 100 W tungsten lamp. Repetitive scans were taken in 5 min intervals. Inset: Time dependent change in absorbance at λ = 321 nm. (b) Photodissociation of **2** (~2×10^{-5} M) in acetonitrile under illumination of a low intensity UV lamp (λ = 302 nm) with isosbestic points near 244 nm, 275 nm and 363 nm. Repetitive scans were taken in 1 min intervals. Inset: Time dependent change in absorbance at λ = 321 nm.

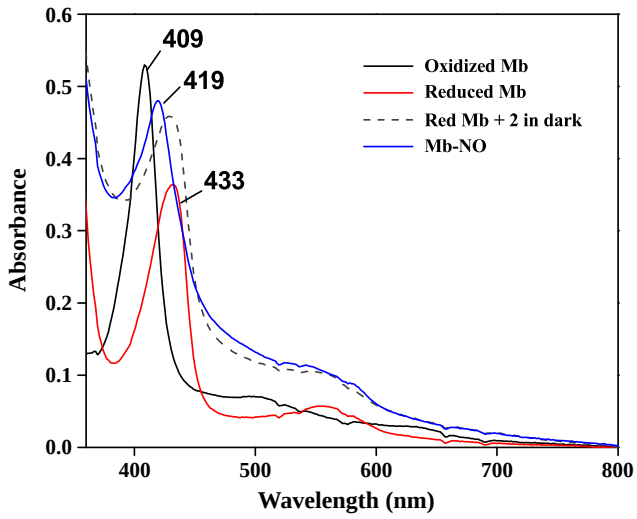

Fig. 5. Electronic spectra of conversion of reduced myoglobin (Mb) to Mb–NO adduct upon reaction with **2** in buffer solution (50 mM phosphate buffer, pH 6.8) under exposure to low intensity UV light (λ = 302 nm). Black line, oxidized Mb (intense band at 409 nm); red line, reduced Mb (at 433 nm, with excess of sodium dithionite); gray dashed line, Mb + solution of **2** (~3×10^{-5}M) in dark for 30 min; blue line, Mb–NO adduct (at 419 nm), obtained by Mb + solution of **2** exposed to the light of a low intensity UV lamp (λ = 302 nm) for 1 min.

It is known in the literature that nitric oxide acts as a biological messenger and NO binds to heme iron and cysteine sulfur for the regulation of biological processes [17]. NO donating property for this complex was investigated by transferring the coordinated NO to reduced myoglobin (Fig. 5) after photolytic cleavage of Ru–NO bond under UV light (λ = 302 nm). Formation of new peak at 419 nm clearly showed the formation of myoglobin–NO species [16]. We have performed the same experiment under illumination with visible light (100 W tungsten lamp). Similar spectra were obtained by visible light irradiation, however longer irradiation was needed in this case.

In conclusion, we synthesized and characterized a novel nitric oxide (NO) donating complex $[Ru(L^1)(PPh_3)_2(NO)](ClO_4)$ (**2**). Complex **2** was found to be diamagnetic having $\{RuNO\}^6$ moiety with $S = 0$ ground state. The complex was characterized by ^1H and ^{31}P NMR spectra which were also supported by ESI-MS data. We have investigated the redox property of the complex. Coordinated NO was found to be photolabile under visible light as well as in UV light and higher rate of photodissociation was observed under UV light. Liberated NO was transferred to reduced myoglobin. Details of NO interaction, modification of the ligand, biological applications of this complex and its other related complexes are under progress.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.inoche.2010.10.008.

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