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# Acidity and photolability of ruthenium salen nitrosyl and aquo complexes in aqueous solutions

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## Abstract

The photochemical behavior of nitrosyl complexes Ru(salen)(NO)$(OH_2)^+$ and Ru(salen)(NO)Cl (salen = N,N′-ethylenebis-(salicylideneiminato) dianion) in aqueous solution is described. Irradiation with light in the 350–450 nm range resulted in nitric oxide (NO) release from both. For Ru(salen)(NO)Cl secondary photoreactions also resulted in chloride aquation. Thus, in both cases the final photoproduct is the diaquo cation $Ru^{III}(salen)(OH_2)_2{}^+$, for which p$K_a$'s of 5.9 and 9.1 were determined for the coordinated waters. The p$K_a$ of the Ru(salen)(NO)$(OH_2)^+$ cation was also determined as 4.5 ± 0.1, and the relative acidities of these ruthenium aquo units are discussed in the context of the bonding interactions between Ru(III) and NO.

*Keywords:* Chloride; Photolability; Photorelease; Ruthenium; Salen; Schiff base; Nitrosyl; Complexes; Photochemistry; Nitric oxide; Donor; Nitrosonium; Acidity; Coordinated water; Sequential photoreactions

## 1. Introduction

Nitric oxide (NO) has numerous important roles in mammalian biology including activity in blood pressure regulation, as a neurotransmitter and as a toxic agent formed in immune response to pathogens [1–5]. The physiological functions of NO are complicated and depend on thermodynamic, kinetic and concentration considerations [6,7]. NO can be either beneficial or harmful, depending on the circumstances [1,3,4,6–9]. For instance, at high concentration NO can induce cell death, but in low concentrations NO reduces metastasis in pulmonary tissues [8,10–14]. The importance of NO as a bioregulator suggests potential applications for controlled and site specific NO delivery agents. In this regard, several NO donors and scavengers, many of these being metal complexes, have been reported [15–44]. Of parallel interest are potential applications of photochemistry in the treatment of various disease states, including cancer [45–48]. Such photochemotherapy would involve irradiation-induced production of a biologically active species in elevated concentrations at a specific locale from photoactive compounds introduced into the patient. Similar concepts should be able to generate NO photochemically.

Ruthenium nitrosyl ammine complexes such as the *trans*-Ru(NO)$(NH_3)_4L^{3+}$ cations have been shown to have biological activity and low toxicity [49–53]. They also release NO photochemically (Eq. (1)). Net quantum yields for this reaction are dependent on the irradiation wavelength and the solution pH. Although these complexes are not very photoactive to visible irradiation, near-UV excitation may be effective for topical applications or in a solid-state implant [54–56].

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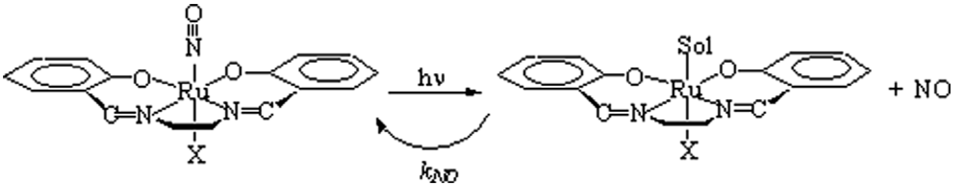
$$trans\text{-}Ru(NH_3)_4(NO)L^{3+} \xrightarrow{h\nu} trans\text{-}Ru(NH_3)_4(H_2O)L^{3+} + NO \quad (1)$$

Ruthenium salen nitrosyls of the type Ru(salen-Y)(X)(NO) (X = $Cl^-$ or ONO, salen-Y = various substituted salen dianions, where salen = *N*,*N*′-ethylenebis(salicylideneiminato) dianion) have also been shown to be photoactive toward NO labilization in various solvents (Eq. (2)) [33,57]. However, with regard to potential medical applications, it is important to understand the aqueous media reactivities, so in this context, we report the photochemistry of the water-soluble complexes Ru(salen)(NO)Cl (**I**) and $Ru(salen)(NO)(OH_2)^+$ (**II**) in aqueous solution.



(2)

We also report the $pK_a$ values for several new ruthenium aquo complexes and compare these to the $pK_a$ values of other known ruthenium complexes, and discuss these in terms of the relative electron acceptor/donor characters of the nitrosyl and other ligands.

## 2. Materials and methods

### 2.1. Reagents

All chemicals used were reagent grade or of comparable purity. All manipulations were carried out under inert atmosphere, except where noted. Milli-Q grade or doubly distilled water was used throughout the work. Commercially available argon (Air Liquid) was passed through a drying column and through a column of MnO for deoxygenation prior to use. Dimethylformamide (Aldrich), methanol (Synth), dichloromethane (Synth), ethylenediamine (Merck), salicylaldehyde (Merck), acetonitrile (Acros) were dried and distilled prior to use as described [58]. $RuCl_3 \cdot nH_2O$ (Strem), $AgNO_3$ (Aldrich), and silica gel (Acros) were used as received. NaH, 60% in Nujol (Aldrich), was washed three times with dry hexane before use. The nitric oxide gas was generated by the reaction of 30% nitric acid with metallic copper. The NO gas evolved was then passed through a trap with a 8 mol $L^{-1}$ NaOH solution and through a drying column of silica prior to use. For quantitative photolysis studies the $[Ru(salen)(NO)(OH_2)](SbF_6)$ salt was prepared according to a literature procedure [59].

### 2.2. [Ru(NO)Cl(salen)] and $[Ru(NO)(OH_2)(salen)]NO_3$ syntheses

The compounds $H_2$salen and $Na_2$salen [60,61] and the complexes [40] were prepared as described. IR band, $\nu_{NO}$, strong, 1848 $cm^{-1}$. $^1H$ NMR (dmso-$d_6$): $\delta$ 8.72 (s) (imine protons), 7.46–7.44 (d) ($J$ = 10 Hz), 7.42–7.38 (t) ($J$ = 10 Hz), 6.98–6.96 (d) ($J$ = 10 Hz), 6.69–6.67 (t) ($J$ = 5 Hz) (aromatic protons), 4.23 (m) (methylenic protons) (**I**). IR band, $\nu_{NO}$, strong, 1855 $cm^{-1}$. $^1H$ NMR (dmso-$d_6$): $\delta$ 8.88 (s) (imine protons), 7.56–7.54 (d) ($J$ = 10 Hz), 7.50–7.46 (t) ($J$ = 10 Hz), 7.06–7.05 (d) ($J$ = 5 Hz), 6.80–6.77 (t) ($J$ = 5 Hz) (aromatic protons), 4.20 (s) (methylenic protons) (**II**).

### 2.3. Instrumentation and techniques

UV–Vis spectra in the range 200–800 nm were recorded on a Beckman Coulter DU 650 and on a Hewlett–Packard 8452A diode array spectrophotometer. The pH values were determined using a Corning 430 pH-meter. A Bomem BM 102 model FTIR spectrophotometer was used for infrared spectra with Attenuated Total Reflectance or KBr pellets. NMR spectra were obtained on a Bruker WH500 MHz spectrometer. The CVI neutral filter was used to measure the initial Ru(salen)(NO)Cl phototransformation rate as a function of the irradiation intensity, which was controlled by Spectra Physics 407A power meter.

### 2.4. Photolysis

The photolysis experiments were performed at pH’s 3.0, 7.5 and 11.0, in a 1.0 cm path length cell, capped with a rubber septum. The solutions of **I** and **II** ($\approx 1 \times 10^{-4}$ mol $L^{-1}$) were deaerated by bubbling with argon prior to photolysis, and stirred during irradiation at 25 °C. The samples were irradiated in the spectral range from 350 to 450 nm (filter band path) using a 150 W tungsten lamp and a 5–57 KOPP glass filter (transmission region: 350–500 nm). A standard quartz 1.0 cm cuvette with water was used behind the sample cell as a thermal infrared filter. The intensity of irradiation of the sample was 22 $mW/cm^2$, as measured by a Spectra-Physics 407A radiometer. Monochromatic irradiations at 365 nm (10 nm band path) were carried out using a 150 W Xenon lamp in a 6253 Oriel Uni-