Inorganica Chimica Acta 366 (2011) 85–90

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

Coordinated nitroxyl anion is produced and released as nitrous oxide by the decomposition of iridium-coordinated nitrosothiols

Daniel Kazhdan [a], Laura L. Perissinotti [a], Bernardo Watanabe [a], Marcos N. Eberlin [b], Humberto M.S. Milagre [b], Boniek G. Vaz [b], Dario A. Estrin [a], Fabio Doctorovich [a,*]

[a] *Departamento de Química Inorgánica, Analitica y Química Física/INQUIMAE-CONICET, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Ciudad Universitaria, Pabellón II, C1428EHA Buenos Aires, Argentina*

[b] *ThoMSon Mass Spectrometry Laboratory, Institute of Chemistry, State University of Campinas, UNICAMP, CEP 13083-970, C.P. 6154, Campinas SP, Brazil*

ARTICLE INFO

Article history:
Received 1 July 2010
Received in revised form 27 September 2010
Accepted 11 October 2010
Available online 20 October 2010

Keywords:
Iridium
Nitroxyl
Bent NO
Nitrosothiol
Decomposition
Sulfenic acid

ABSTRACT

The aqueous decomposition of the iridium coordinated nitrosothiols (RSNOs) *trans*-K[$IrCl_4(CH_3CN)$NOS-Ph] (**1**), and $K_2[IrCl_5(NOECyS)]$ (**2**, ECyS = cysteine ethyl ester), was studied by MS analysis of the gaseous products, ESI-MS, NMR, and UV–Vis spectroscopy. Bent NO (NO^-, nitroxyl anion), sulfenic acids and nitrite were observed as coordinated products in solution, while nitrous oxide (N_2O) and nitrogen were detected in the gas phase. The formation of coordinated NO^- and N_2O, a nitroxyl dimerization product, allows us to propose the formation of free nitroxyl (HNO) as an intermediate. Complex **1** decomposes 300 times slower than free PhSNO does. In both cases (**1** and **2**) kinetic results show a first order decomposition behavior and a very negative $\Delta S^{\neq}$, which strongly indicates an associative rate-determining step. A proposed decomposition mechanism, supported by the experimental data and DFT calculations, involves, as the first step, nucleophilic attack of H_2O on to the sulfur atom of the coordinated RSNO, producing an NO^- complex and free sulfenic acid, followed by two competing reactions: a ligand exchange reaction of this NO^- with the sulfenic acid or, to a minor extent, coordination of N_2O to produce an NO^-/N_2O complex which finally renders free N_2 and coordinated NO_2^-. Some of the produced NO^- is likely to be released from the metal center producing nitroxyl by protonation and finally N_2O by dimerization and loss of H_2O. In conclusion, the decomposition of these coordinated RSNOs occurs through a different mechanism than for the decomposition of free RSNOs. It involves the formation of sulfenic acids and coordinated NO^-, which is released from the complexes and protonated at the reaction pH producing nitroxyl (HNO), and ultimately N_2O.

1. Introduction

The decomposition of *S*-nitrosothiols (RSNOs) in water to form NO is a biologically important reaction, since it is supposed to be involved in the transport and release of NO [1]. RSNOs' stability in solution varies as a function of, among other things, the pH, oxygen, and metal content of the solution [2–4]. RSNO compounds may be prepared by treatment of the precursor thiol (RSH) with nitrosating agents [5], including nitric oxide, in the presence of electron acceptors, such as nitrosonium salts, nitrous acid, inorganic nitrites, and metal nitrosyl complexes [6]. In cases when the nitrosating agent is a metal nitrosyl, the thiol reacts with the nitrosyl ligand to form an *S*-nitrosothiol ligand coordinated to the metal center, {M–N(O)SR}. Another method that has been used to prepare nitrosothiols complexes *in situ* consists of the reaction of the free thiolate anion with the ligand NO^+ coordinated to $[Fe(CN)_5]^{3-}$ or other coordinating moieties [7,8]. Ashby and coworkers have described time-resolved IR spectra in solution for the transient "red products", the adducts that are formed when nitroprusside reacts with thiols in aqueous media [9]. This reaction of nitroprusside with thiols has been extended to a great variety of nitrosyl complexes of formula type $\{(X)_5MNO\}^n$, with X comprising ligands of different donor–acceptor abilities and M = Fe, Ru, and Os. In most cases these complexes are unstable and decompose spontaneously to metal complexes and disulfides, with the lifetimes depending strongly on the thiol structure [10].

In a previous work, we presented the reaction between a free thiol, benzyl mercaptan, and K[$IrCl_5NO$], leading to the formation of the stable coordinated nitrosothiol *trans*-K[$IrCl_4(CH_3CN)$-N(O)SCH_2Ph] [11,12]. This was the first time that a nitrosothiol complex was isolated and fully characterized, including a structural determination by X-ray crystallography. This finding represents a good example of how the coordination chemistry of RSNOs uncovers new aspects of the nitrosation processes, since coordination to metal centers considerably change the stability of

---

* Corresponding author.
E-mail address: doctorovich@qi.fcen.uba.ar (F. Doctorovich).

0020-1693/$ - see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.ica.2010.10.013

the RSNOs. In a more recent work we presented a complete and detailed experimental characterization and theoretical study of these novel compounds bearing a variety of coordinated nitrosothiols: cysteine derivatives, mercaptosuccinic acid, benzyl thiol and phenyl thiol [13]. Although the free forms of some of these nitrosothiols are extremely unstable and sensitive, upon coordination they become very stable even in aqueous solution. The report of several stable coordinated nitrosothiols which can be isolated as pure materials, allows for a careful study of their decomposition and implies new and interesting intermediates that were not seen before for free RSNOs. Herein we present detailed studies for the decomposition of two coordinated RSNOs with distinct structures and stabilities: *trans*-K[$IrCl_4(CH_3CN)NOSPh$], (**1**) and $K_2[IrCl_5(NOECyS)]$, (**2**) (Fig. 1) supported by MS analysis of the gaseous products, ESI-MS, NMR, UV–Vis spectroscopy, and DFT calculations.

2. Experimental

2.1. Materials

$K_2[IrCl_5NO]$(cysteine-ethyl-ester), *trans*-K[$IrCl_4(CH_3CN)NOSPh$] and their ^{15}N counterparts were made as previously described [13]. $Na^{15}NO_2$ was purchased from Aldrich and used as received.

2.2. UV/Visible spectroscopy and kinetic measurements

Absorption spectra were acquired on a Hewlett-Packard HP8453 diode array spectrometer with 1 cm path length cells, under N_2 preparing the solutions using Schlenk methods. A thermal bath was used to vary temperatures and the solvent was allowed to equilibrate for half an hour prior to use. After the experiment was done the temperature was measured externally. The reaction rates were measured in milliQ water (pH 7, $T = 20–75\,°C$, $\lambda = 475–581$ nm) without buffering the solution to avoid secondary reactions with buffer compounds (the pH decreased ca. 2 units during the decomposition). The kinetic rate constants were calculated from the first order plots (ln (Ir-coordinated nitrosothiol concentration) versus time), which in all cases showed $R^2 > 0.99$. The activation parameters were obtained from Eyring plots in the range 300–350 K, with $R^2 = 0.99$ for **1** and 0.98 for **2**, respectively.

In a typical experiment, samples were prepared by placing 0.2–1.2 mg of solid **1** or **2** in a quartz cuvette equipped with a Schlenk adapter and degassing the cuvette. About 3.0 mL degassed milliQ water was placed in another cuvette. Both cuvettes were placed in a water bath to equilibrate to the temperature at which the UV–Vis was to be measured. The cuvette with **1** or **2** was then placed in the UV–Vis spectrometer, with the appropriate temperature maintained by a hot water bath, and the water was added with a syringe. UV–Vis spectra were then measured every 3 min for 3–12 h.

2.3. NMR spectroscopy

The ^1H, ^{13}C, and ^{15}N NMR spectra were obtained at room temperature on a Bruker 500 MHz instrument, with deoxygenated D_2O and DMSO-d_6. ^{15}N NMR spectra were referenced to an external standard of $Na^{15}NO_2$ at 232 ppm. ^1H and ^{15}N NMR spectra were measured by dissolving the compound in degassed deuterated solvent. When measurements were done over a period of time the NMR tubes were stored wrapped in tinfoil to protect from decomposition due to light and the NMR caps were protected with parafilm to minimize the entry of oxygen. In a typical experiment, the decomposition of **1** or **2** were followed in an NMR tube purged with Ar or N_2 and closed with a cap protected with parafilm, by dissolving the corresponding coordinated nitrosothiol in degassed D_2O at r.t. to obtain 0.5 mL of a 0.1 M solution. A first measurement was recorded immediately, and the reaction was followed by taking successive spectra for a period of several days (ca. 1 spectrum per day).

(**1**) *trans* – $[IrCl_4(CH_3CN)N(O)S\,Ph]^-$

(**2**) $[IrCl_5N(O)ECyS]^{2-}$ ECyS:

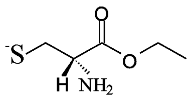

Fig. 1. Structures of the studied iridium coordinated RSNOs.

2.4. Mass spectrometry

2.4.1. Gases

Qualitative and quantitative measurements of the gas production (extracted from the headspace of the reaction mixtures) were conducted using a thermostated homemade flow reactor (volume 0.07 dm^3) linked to a vacuum system and to an Extrel Emba II quadrupolar mass spectrometer through a thin thermostated capillary. The reactor was also supplied with an absolute pressure transducer, MKS Baratron 622 A, and with a mechanical stirrer.

2.4.2. ESI-MS

All fragmentation of the nitrosothiol complexes and the reaction mixtures were performed under exactly the same conditions. Mass spectrometric measurements were performed using a high-resolution hybrid quadrupole (Q) and orthogonal time-of-flight (TOF) mass spectrometer (QTOF from Micromass, UK) operating in the negative ion electrospray ionization mode set from 2100 to 3500 V. Samples dissolved in appropriate anhydrous solvents at room temperature (RT) under an inert atmosphere were injected through an uncoated fused-silica capillary, using a syringe pump (Harvard Apparatus, Pump 11, 15 $\mu L\ min^{-1}$). The temperature of the nebulizer and desolvation gas was set at 100 °C, and the cone voltage was set between 25 and 35 V. Tandem mass spectra (ESI-MS/MS) were acquired using the product ion scan mode via mass selection of the ion of interest, followed by collision-induced dissociation (CID) with Ar using energies varying from 15 to 35 eV with high-accuracy orthogonal TOF mass analysis of the CID ionic fragments. For comparison with experimental data, isotopic patterns were calculated using the MassLynx software.

2.5. Theoretical calculations

All the calculations performed in this work were carried out using the GAUSSIAN 98 [14] package. We have fully optimized the geometries of all species at the pbe1pbe [15] level with sddall basis set without symmetry constraints. Each stationary point in the gas phase was characterized by performing a normal modes analysis. The energetics for the reactions obtained form the pbe1pbe functional with sddall basis set, were validated by single-point energy calculations, using the sddall reference geometries, with the extended SDB-cc-pVDz basis set. The SDB-cc-pVDZ basis set, combines the Dunning cc-p-VDZ basis set [16] on the main group elements with the Stuttgart–Dresden basis set-RECP combination on the transition metals, with an *f*-type polarization exponent [17].

3. Results

3.1. Reaction products and intermediates

When **1** and **2** are allowed to decompose anaerobically in water, in the absence of light, for a period of around 1 week at room tem-