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Stability of phosphite coordinated to ruthenium(II) in aqueous media

Daniela R. Truzzi, Douglas W. Franco *

Departamento de Química e Física Molecular, Instituto de Química de São Carlos, Universidade de São Paulo, Av. Trabalhador São-carlense, 400, Centro, São Carlos, São Paulo, Brazil

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ABSTRACT

Changes in the reactivity of phosphorus(III) esters, which are promoted by coordination to the ruthenium(II) metal centre, were the focus of this study. Nuclear magnetic resonance data, which were acquired as a function of time, suggest that the phosphite coordination to the ruthenium(II) centre stabilises these molecules in terms of hydrolysis. This stabilisation is greater when the coordination occurs to the *trans*-$[Ru(H_2O)(NH_3)_4]^{2+}$ rather than to the *trans*-$[Ru(NO)(NH_3)_4]^{3+}$ fragment, and these results are interpreted considering the $4d\pi(Ru^{II}) \rightarrow 3d\pi(P(III))$ back-bonding interactions. The correlation between the data on alkyl phosphite hydrolysis constants in *trans*-$[Ru(NO)(NH_3)_4P(III)]^{n+}$ (P(III) = $P(OEt)_3$, $P(O)(OEt)_2$, $P(O^iPr)_3$ and $P(OBu)_3$) complexes and the δ_{13C} data show that the hydrolysis of phosphites that are coordinated to Ru(II) preferably occurs via the Michaelis–Arbuzov mechanism. Only the nitrosyl complex, where P(III) = $P(OMe)_3$, did not exhibit this correlation, which suggests that the hydrolysis likely occurs via the Aksnes mechanism in this case.

1. Introduction

The uses of phosphorus(III) to tailor metal complexes for catalysis and biochemistry applications have been extensively studied [1,2], and the emphasis was generally on the induced changes on the properties of the metal centre. However, few data discuss the ability of the metal centre to induce changes in the reactivity of the phosphorus(III) ligands.

Phosphites ($P(OR)_3$) are phosphorus(III) compounds that coordinates to metal centre through both a σ-donation of the lone electron pair of the phosphorus to empty orbital of the metal, and a π-backdonation from filled d-orbital of the metal to orbitals of appropriated energy and π-symmetry on phosphite ligand [3,4]. This π-acid character of the phosphites can be tuned according to the number and characteristics of the R groups [2,5–7].

The phosphites are easily oxidised by molecular oxygen, even without a catalyst, which leads to the corresponding phosphoryl derivatives [5,7]. In addition, these compounds are readily hydrolysed. The mechanism underlying this hydrolysis is an important focus of discussion because of its importance in nucleic acid chemistry and industrial processes [5,7]. Michaelis and Arbuzov [8] proposed that phosphite hydrolysis occurs through the electrophilic attack of the lone electron pair of phosphorus on water hydrogen and the subsequent nucleophilic attack of the water oxygen on the carbon in α-position, which subsequently breaks the O–C bond (Fig. 1a). However, based on the analysis of the phosphite hydrolysis product and data obtained using infrared spectroscopy and labelled water, Aksnes [9,10] suggested that the phosphite hydrolysis preferentially occurs via a nucleophilic attack on the phosphorus atom and the consequential breakage of the P–O bond (Fig. 1b).

The hydrolysis of phosphites and phosphates is also notably sensitive to acid catalysis [11]. Studies involving the retention of an alcohol configuration [12] have shown that acid hydrolysis in phosphanes occurs through both O–C [8] and P–O [9,10] bond-break mechanisms.

Metal complexes with coordinated phosphite, such as *trans*-$[Ru(H_2O)(NH_3)_4P(OR)_3](PF_6)_2$, where $P(OR)_3$ = $P(OMe)_3$, $P(OEt)_3$, $P(O^iPr)_3$ and $P(OBu)_3$ [13,14], are stable for days despite the high reactivity of phosphite molecules in aqueous medium. This result suggests that the coordination to metal centres, such as ruthenium(II), stabilises these phosphorus molecules against oxidation and hydrolysis. Indeed, the hydrolysis of triethyl phosphite was followed in solid-state *trans*-$[Ru(NO)(NH_3)_4P(OEt)_3](PF_6)_3$ over an eight-month period and produced *trans*-$[Ru(NO)(NH_3)_4P(OH)(OEt)_2](PF_6)_3$ and ethanol [15]. A similar behaviour was described for $[Mo(CO)_5P(OH)(OEt)_2]$, which is also hydrolysed in the solid-state to $[Mo(CO)_5(P(OH)_3)]$ [16]. Despite these observations, detailed information on the kinetics and the mechanisms of such hydrolyses have not been reported.

The phosphorus(III) ligands exhibit a high *trans* effect and *trans* influence when coordinated to metal centres. Thus, they are notably interesting ligands for tailoring metal complexes for

* Corresponding author. Tel./fax: +55 16 33739976.
E-mail address: douglas@iqsc.usp.br (D.W. Franco).

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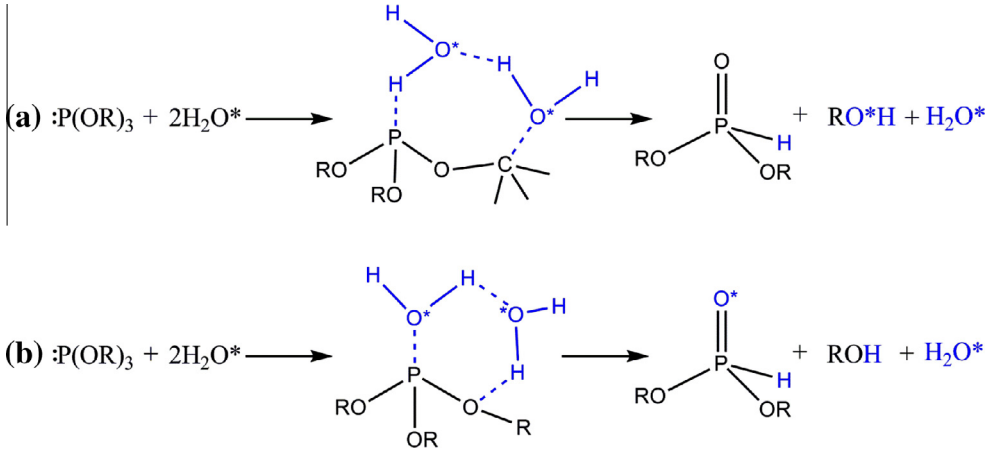


Fig. 1. Mechanisms of phosphite hydrolysis: (a) Michaelis–Arbuzov and (b) Aksnes (similar to organic ester hydrolysis). $O^* = {}^{18}O$.

specific applications [2,6]. In ruthenium nitrosyl complexes, the triethyl phosphite coordinated to the *trans*-$[Ru(NO)(NH_3)_4]^{3+}$ fragment makes the reduction of the nitrosyl group accessible to biological reduction ($E_{NO^+/NO} = -0.24$ V versus SCE) and promotes a fast liberation of nitric oxide ($k_{-NO} = 0.97\ s^{-1}$) [17]. *In vitro* and *in vivo* tests that used *trans*-$[Ru(NO)(NH_3)_4P(OEt)_3](PF_6)_3$ showed that this complex promotes vasodilation [18,19] and exhibits activity against cancer cells [20], Leishmaniasis [21] and Chagas' disease [22]. However, the hydrolysis of the phosphorus ligand reduces the efficacy of *trans*-$[Ru(NO)(NH_3)_4P(OEt)_3]^{3+}$ in biological media. Thus, a better knowledge of the phosphorus(III) ligand hydrolysis is required to improve the design of such complexes.

This work aimed to better understand the changes in the reactivity of phosphorus(III) compounds that are induced by coordination. Because of their properties [2], ruthenium(II) tetraammines were selected as a model to investigate the induced reactivity changes in the selected ligands. A series of phosphites were studied in aqueous medium as free molecules and as ligands coordinated to *trans*-$[Ru(H_2O)(NH_3)_4]^{2+}$ and *trans*-$[Ru(NO)(NH_3)_4]^{3+}$ fragments.

Because the equatorial ammines remain unchanged, the coordination of phosphorus(III) to *trans*-$[Ru(H_2O)(NH_3)_4]^{2+}$ and *trans*-$[Ru(NO)(NH_3)_4]^{3+}$ offers an interesting opportunity to compare the effects of the metal centre on the phosphorus ligand reactivity in notably different environments. On the *trans*-$[Ru(NO)(NH3)4]^{3+}$ fragment where the nitrosyl (strong π-acceptor) is present, the metal centre became a good π-acceptor exhibiting an accentuated Ru(III) character and stronger ligand polarisability than on the *trans*-$[Ru(H2O)(NH3)4]^{2+}$ fragment (where the nitrosyl is replaced by the water molecule), in which the metal centre is a poor π-acceptor.

2. Experimental

2.1. General

The chemicals used in the present study were of reagent grade (Aldrich or Merck). And the *trans*-$[Ru(NH_3)_5Cl](Cl)_2$ [23], *trans*-$[Ru(H_2O)(NH_3)_5](PF_6)_2$ [24], *trans*-$[Ru(NO)(NH_3)_4P(OR)_3](PF_6)_2$, where $P(OR)_3 = P(O^iPr)_3$, $P(OBu)_3$, $P(OEt)_3$, and $P(OMe)_3$ [17,25], and *trans*-$[Ru(NO)(NH_3)_4P(O)(OEt)_2](PF_6)_2$ [26] complexes were synthesised using procedures described in the literature.

2.2. Instrumentation

2.2.1. Infrared spectroscopy

The infrared spectra in aqueous medium were recorded on a Bomem-102 using a silicon window with a Teflon spacer of 0.10 mm; the number of scans was 16, the resolution was ±2 cm^{-1}, and the range was 2000–1750 cm^{-1}.

2.2.2. Electrochemical measurements

A Princeton Applied Research 264A instrument was used to acquire the cyclic voltammetry (CV) and the differential pulse voltammetry (DPV) data. In the electrochemical cell, a saturated-calomel-electrode (SCE), a platinum-plate, and a glassy-carbon were the reference, the auxiliary, and the working electrodes, respectively.

2.2.3. NMR

The ^1H NMR spectra were recorded in a BRUKER AC-200 spectrometer with a proton frequency of 200.13 MHz using a 5-mm probe, 3-(trimethylsilyl)-2,2′,3,3′-tetradeuteropropionic acid (TMSP-D4) as the internal reference ($\delta = 0$ ppm), and 40 scans per spectrum. The ^{31}P NMR spectra were acquired on an Agilent 400/54 Premium Shielded with a phosphorus frequency of 161.90 MHz using a 5-mm probe and 1024 scans for each spectrum. The internal reference was NH_4PF_6 salt ($\delta = -144$ ppm). The solutions were degassed with argon (purified and dried) using standard inert atmosphere techniques [27]. Spectral processing was performed using the exponential function (LB = 3.0 Hz) for apodisation.

2.3. Kinetic measurements

The NMR kinetics experiments were performed using D_2O solutions, which were prepared with deuterated trifluoroacetic (CF_3COOD) and acetic (CD_3COOD) acids to maintain the solution pH at 1.0 and 3.0. The temperature was maintained at 25.0 ± 0.5 °C. The spectral processing and area calculation were performed using the KnowItAll(R) Informatic System 8.0 software.

A first-order reaction model was used to treat the kinetic data; thus, the rate constants (k) were calculated from the plots of $\ln(A_\infty - A_t)$ as a function of time.

2.4. k_{-NO} calculation [28]

NO is readily liberated from *trans*-$[Ru(NO)(NH_3)_4P(III)]^{3+}$ ions after a one-electron reduction centred on the nitrosyl ligand. Therefore, this reaction involves a charge transfer followed by an irreversible reaction, which enables the measurement of the rate constants for liberation of NO (k_{-NO}) through the Nicholson and Shain electrochemical method [28]. In this method, the i_{pa}/i_{pc} ratio is correlated with the kinetic parameter through the working curve of i_{pa}/i_{pc} as a function of $k\tau$ [28]. The electrochemical measurements were performed using solutions with pH 2.0,

μ = 0.1 mol L^{-1}, a temperature of 25 ± 0.1 °C, and scan rates from 20 mV s^{-1} to 2 V s^{-1}.

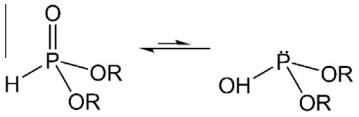
3. Results

3.1. $P(OR)_3$ and $(O)P(H)(OR)_2$ reactivity in aqueous medium

Aqueous solutions that contained triisopropyl ($P(O^iPr)_3$), tributyl ($P(OBu)_3$), triethyl ($P(OEt)_3$), and trimethyl ($P(OMe)_3$) phosphites were monitored using ^1H NMR as a function of time at pH 3.0. In the first spectra of these solutions, only the chemical shifts from the corresponding dialkyl phosphite ($(O)P(H)(OR)_2$) and alcohol (ROH) were observed (reaction 1), which precluded a detailed observation of the hydrolysis of the trialkyl phosphite under these experimental conditions. Because the first spectra was recorded after 20 min, the estimated upper limit of the half-life of $P(O^iPr)_3$, $P(OBu)_3$, $P(OEt)_3$, and $P(OMe)_3$ in an aqueous solution at pH 3.0 and 25.0 ± 0.5 °C (reaction 1) was 1.2 × 10^2 s ($k \sim 6 \times 10^{-3}$ s^{-1}).

$$P(OR)_3 + H_2O \rightarrow (O)P(H)(OR) + ROH \quad (1)$$

The hydrolysis of diethyl phosphite ($(O)P(H)(OEt)_2$) also was followed in aqueous medium at pH 3.0 using ^1H NMR. Fig. 2 shows a quintet at 4.20 ppm and a triplet at 1.35 ppm, which correspond to the CH_2 and CH_3 groups of the diethyl phosphite molecule, respectively. Instead of the expected quartet, the quintet (Fig. 2a) was observed due to the ^3J coupling between ^1H and ^{31}P. A doublet at 5.17 and 8.77 ppm also appeared in the spectrum with a coupling constant (J) of 720 Hz, and this doublet resulted from the ^1J coupling between the ^1H and ^{31}P nuclei. This doublet is characteristic of diethyl phosphite in the tetracoordinate form (reaction 2) [29–31].



(2)

In addition to the signals of the diethyl phosphite molecule, the spectra showed a quartet at 3.64 ppm and a triplet at 1.17 ppm due to the CH_2 and CH_3 groups of the ethanol molecule (Fig. 2c). This result was confirmed by the addition of ethanol to the sample. The intensities of the peaks from ethanol increased over time, whereas the intensities of the peaks from diethyl phosphite decreased, which indicates the hydrolysis of diethyl phosphite in this medium. A quintet at 3.94 ppm and a triplet at 1.26 ppm were also observed because diethyl phosphite was converted to monoethyl phosphite ($(O)P(H)(OH)(OEt)$, Fig. 2b).

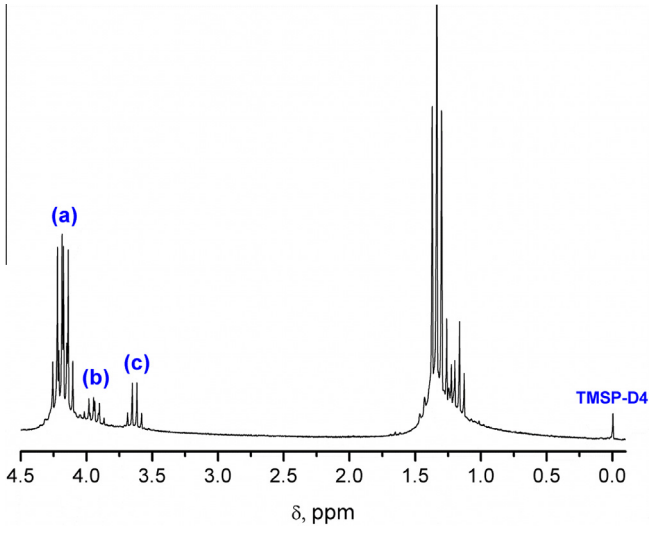


Fig. 2. ^1H NMR spectra of (a) diethyl phosphite, (b) monoethyl phosphite, and (c) ethanol after 20 h in solution in D_2O at pH = 3.0 (CD_3COOD), $C_{P(OH)(OEt)2}$ = 2.0 - × 10^{-4} mol L^{-1}, 25.0 ± 0.5 °C (BRUKER AC-200).

Based on the decay in the area of the quintet at 4.20 ppm as a function of time, the observed rate constant (k) for the diethyl phosphite molecule decay (reaction 3) in the aqueous medium at pH 3.0 and 25.0 ± 0.5 °C was calculated to be (7.10 ± 0.42) × 10^{-6} s^{-1} ($t_{1/2} \sim 27.0$ h). The diethyl phosphite molecule was also monitored at pH 1.0, and the observed rate constant associated with the hydrolysis of this molecule under this condition was (1.80 ± 0.08) × 10^{-4} s^{-1} ($t_{1/2} \sim 1.1$ h).

$$(O)P(H)(OEt)_2 + H_2O \rightarrow (O)P(H)(OH)(OEt) + EtOH \quad (3)$$

^1H NMR was chosen for this study instead of ^{31}P NMR because the spectrum is readily acquired and the chemical shifts are easily identified and sufficiently separated to calculate the area of the individual resonances.

3.2. Reactivity of $P(OR)_3$ and $P(OH)(OR)_2$ coordinated to the trans-$[Ru(H_2O)(NH_3)_4]^{2+}$ fragment

According to previous spectrophotometric data, *trans*-$[Ru(H_2O)(NH_3)_4P(OEt)_3]^{2+}$ is stable for two weeks ($k < 5 \times 10^{-7}$ at pH 3.0 and 25 ± 0.1 °C) [14]. In *trans*-$[Ru(NH_3)_4(P(OEt)_3)_2]^{2+}$, although the hydrolysis of the coordinated triethyl phosphite is not noted, it is observed the phosphorus ligand dissociation, which produces *trans*-$[Ru(H_2O)(NH_3)_4P(OEt)_3]^{2+}$ ($k = 2.6 \times 10^{-5}$ s^{-1} at pH 3.0 and 25 ± 0.1 °C [14]).

In this study, the *trans*-$[Ru(H_2O)(NH_3)_4P(O^iPr)_3]^{2+}$, *trans*-$[Ru(H_2O)(NH_3)_4P(OBu)_3]^{2+}$, and *trans*-$[Ru(H_2O)(NH_3)_4P(OH)(OEt)_2]^{2+}$ complexes and the phosphite molecules were investigated to determine their hydrolysis under the same experimental conditions (at pH 3.0 and 25.0 ± 0.5 °C).

The ^1H NMR spectra of *trans*-$[Ru(H_2O)(NH_3)_4P(O^iPr)_3]^{2+}$ as a function of time exhibited a decrease in the doublet area at 1.30 ppm, which corresponds to the CH_3 groups of the coordinated triisopropyl phosphite, and an increase in the doublet area at 1.16 ppm, which corresponds to the CH_3 groups of isopropanol. This result indicates the hydrolysis of the coordinate triisopropyl phosphite (reaction 4), which occurs with a rate constant of k = (4.45 ± 0.16) × 10^{-7} s^{-1} ($t_{1/2} \sim 18$ days). Under the same experimental conditions, the calculated rate constant of the *trans*-$[Ru(H_2O)(NH_3)_4P(OBu)_3]^{2+}$ ion hydrolysis was k = (7.36 ± 0.21) × 10^{-7} s^{-1} ($t_{1/2} \sim 11$ days).

$$\textit{trans}\text{-}[Ru(H_2O)(NH_3)_4P(OR)_3]^{2+} + H_2O \rightarrow \textit{trans}\text{-}[Ru(H_2O)(NH_3)_4P(OH)(OR)_2]^{2+} + ROH \quad (4)$$

Similar to the aquo complexes of trialkyl phosphites, *trans*-$[Ru(H_2O)(NH_3)_4P(OH)(OEt)_2]^{2+}$ was also hydrolysed to produce ethanol and the corresponding monoethyl phosphite complex (reaction 5). According to the ^1H NMR data, this hydrolysis occurs with a rate constant of (4.80 ± 0.15) × 10^{-7} s^{-1} ($t_{1/2} \sim 17$ days) at pH 3.0 and 25.0 ± 0.5 °C.

$$\textit{trans}\text{-}[Ru(H_2O)(NH_3)_4P(OH)(OEt)_2]^{2+} + H_2O \rightarrow \textit{trans}\text{-}[Ru(H_2O)(NH_3)_4P(OH)_2(OEt)]^{2+} + EtOH \quad (5)$$

3.3. Reactivity of $P(OR)_3$ and $P(OH)(OR)_2$ coordinated to trans-$[Ru(NO^+)(NH_3)_4]^{3+}$ fragment

The stabilities of the trimethyl ($P(OMe)_3$), triethyl ($P(OEt)_3$), triisopropyl ($P(O^iPr)_3$), and tributyl ($P(OBu)_3$) phosphites coordinated

to the *trans*-$[Ru(NO)(NH_3)_4]^{3+}$ fragment were also evaluated in an aqueous medium. In contrast to the results found for the free ligands, the ^1H NMR chemical shifts of these complexes and their hydrolysis products are near one another, which made their identification and the calculation of their areas complicated. Thus, ^{31}P NMR was used to follow the reactions.

According to the ^{31}P NMR spectra, *trans*-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$ in a solution at pH 3.0 and 25.0 ± 0.5 °C initially exhibited only one peak at 85 ppm, and this peak decayed with a rate constant of $(3.01 \pm 0.05) \times 10^{-5}\ s^{-1}$ ($t_{1/2} = 6.4$ h). Concurrently, the peak at 71 ppm, which is related to the *trans*-$[Ru(NO)(NH_3)_4P(OH)(OMe)_2]^{3+}$ species, grew with an identical rate constant ($k = (3.03 \pm 0.05) \times 10^{-5}\ s^{-1}$) (Fig. 3).

The *trans*-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$ decay was also monitored in aqueous solution at pH 3.0 using infrared spectroscopy (Fig. 4). The initial ν_{NO^+} at 1922 cm^{-1} decreased in intensity with the concurrent appearance of a new ν_{NO^+} at 1891 cm^{-1} as a function of time. The isosbestic point shown in Fig. 4 also suggests that the $P(OMe)_3$ ligand in *trans*-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$ was hydrolysed to quantitatively produce *trans*-$[Ru(NO)(NH_3)_4P(OH)(OMe)_2]^{3+}$.

An identical behaviour was observed for the nitrosyl complexes of triethyl, triisopropyl, and tributyl phosphite (reaction 6). The rate constants associated with the hydrolysis of each of these complexes at pH 3.0 and 25.0 ± 1.0 °C are summarised in Table 1.

$$trans\text{-}[Ru(NO)(NH_3)_4P(OR)_3]^{3+} + H_2O \rightarrow trans\text{-}[Ru(NO)(NH_3)_4P(OH)(OR)_2]^{3+} + ROH \quad (6)$$

3.4. Electrochemical properties of the nitrosyl complexes of phosphorus(III) and k_{-NO}

The biological activity of the ruthenium nitrosyl complexes is related to their ability to release nitric oxide after a one-electron reduction (reaction 7) and nitroxyl after a two-electron reduction (reaction 8) [33]. Recently, the *trans*-$[Ru(NO)(NH_3)_4P(OEt)_3]^{3+}$ ion was described to generate NO or HNO under controlled-reduction conditions ($E_{NO^+/NO} = -0.10$ V and $E_{NO/HNO} = -0.70$ V versus SCE) [33]. This ability was also investigated in the *trans*-$[Ru(NO)(NH_3)_4P(III)]^{n+}$ ions in this study. The cyclic voltammogram in an aqueous medium exhibited an identical profile for all of the complexes (Fig. 5a). The $[Ru(NO^+)]/[Ru(NO)]$ and $[Ru(NO)]/[Ru(HNO)]$ reduction processes (reactions 7 and 8, Table 2) are clearly observed in the differential pulse voltammogram (Fig. 5b).

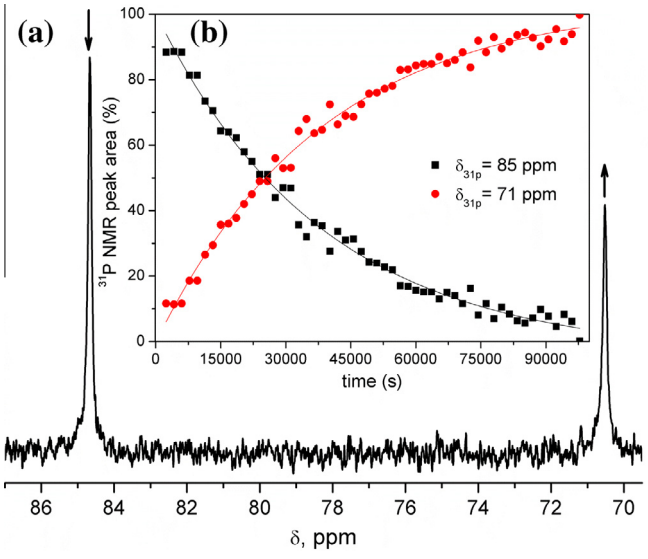


Fig. 3. *trans*-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$ in D_2O at pH = 3.0 (CD_3COOD) and 25.0 ± 0.5 °C. (a) ^{31}P NMR spectra (using NH_4PF_6 as the internal reference); (b) variation in the area of the ^{31}P NMR peaks as a function of time.

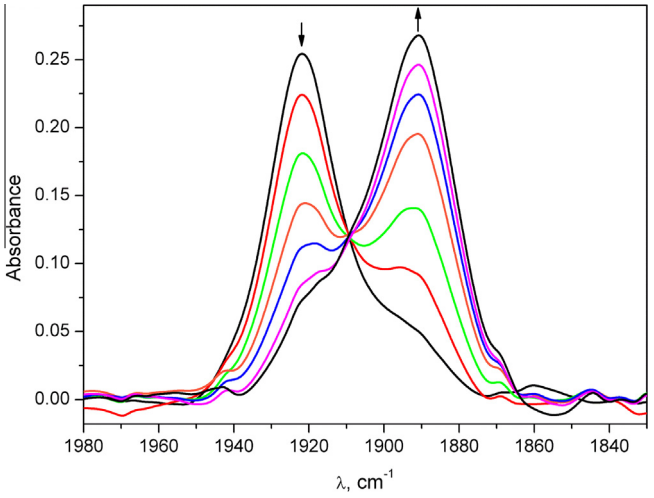


Fig. 4. Infrared spectra of *trans*-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$ in pH 3.0, $\mu = 0.1$ mol L^{-1}, and 25.0 ± 1.0 °C.

Table 1
Hydrolysis rate constants of phosphites that were bonded to an $[Ru(NO)(NH_3)_4]^{3+}$ fragment at pH 3.0 and 25.0 ± 0.5 °C.

Complex ions	k (s^{-1})	Reference
t-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$	3.01×10^{-5}	This work
t-$[Ru(NO)(NH_3)_4P(OEt)_3]^{3+}$	2.90×10^{-6}	This work
t-$[Ru(NO)(NH_3)_4P(O^iPr)_3]^{3+}$	1.35×10^{-5}	This work
t-$[Ru(NO)(NH_3)_4P(OBu)_3]^{3+}$	6.04×10^{-6}	This work
t-$[Ru(NO)(NH_3)_4P(O)(OH)_2]^{2+}$	$2.10 \times 10^{-4*}$	[32]
t-$[Ru(NO)(NH_3)_4P(O)(OEt)_2]^{2+}$	$8.90 \times 10^{-7**}$	[26]

Rate constant calculated for the nitrosyl complex decay as a consequence of the phosphorus ligand isomerisation* or dissociation**.

$$trans\text{-}[Ru(NO^+)(NH_3)_4P(OR)_3]^{3+} \underset{-e^-}{\overset{+e^-}{\rightleftharpoons}} trans\text{-}[Ru(NO_3)_4P(OR)_3]^{2+} \quad (7)$$

$$trans\text{-}[Ru(NO)(NH_3)_4P(OR)_3]^{2+} + H_3O^+ \underset{-e^-}{\overset{+e^-}{\rightleftharpoons}} trans\text{-}[Ru(HNO)(NH_3)_4P(OR)_3]^{2+} + H_2O \quad (8)$$

Based on the rate constant data for the NO liberation (k_{-NO}), which was calculated for the *trans*-$[Ru(NO)(NH_3)_4L]^{n+}$ series [2,34], the k_{-NO} value can be associated with the *trans* effect exhibited by the ligand *trans* to NO. The esters of phosphorus(III) are known to exert high *trans* effects; thus, a fast NO release is expected for *trans*-$[Ru(NO)(NH_3)_4L]^{n+}$, where L = P(III) [2].

Because *trans*-$[Ru(NO)(NH_3)_4P(OR)_3]^{3+}$ ions can be hydrolysed at pH 5.0, which may affect the k_{-NO} measurement associated with reaction 9, the k_{-NO} calculation was performed at pH 2.0 and 25.0 ± 0.1 °C (Table 2). The k_{-NO} values found for *trans*-$[Ru(NO)(NH_3)_4P(OEt)_3]^{3+}$ at pH 5.0 (previous reported) [17] and pH 2.0 were essentially identical within the experimental error limits (0.97 and 0.98 s^{-1}, respectively).

$$trans\text{-}[Ru(NO)(NH_3)_4P(OR)_3]^{2+} \overset{k_{-NO}}{\rightarrow} trans\text{-}[Ru(H_2O)(NH_3)_4P(OR)_3]^{2+} + NO \quad (9)$$

The process that corresponds to HNO/NO oxidation was not clearly observed even at high scan rate (2 V s^{-1}) and 5 °C, which prohibited the calculation of k_{-HNO} using the Nicholson and Shain [28] method.

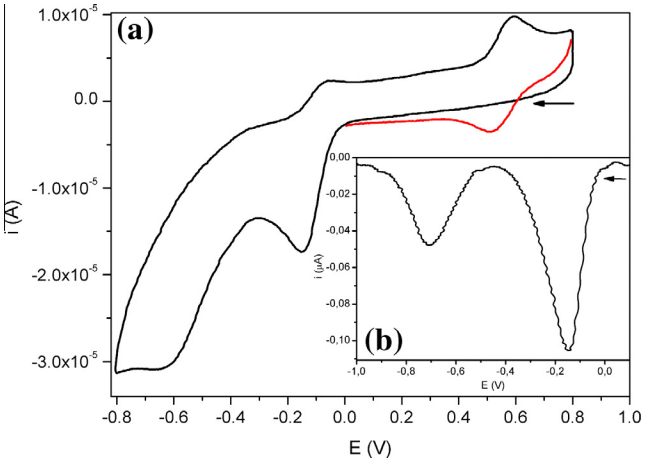


Fig. 5. *trans*-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$ ion in aqueous solution at pH 2.0, $\mu = 0.1$ mol L^{-1}, $C_{Ru} = 1.5 \times 10^{-3}$ mol L^{-1}, and $T = 5 \pm 0.1$ °C (a). The cyclic voltammogram was obtained at a scan rate of 100 mV s^{-1}; and (b) the differential pulse voltammogram was performed at a scan rate of 20 mV s^{-1}.

Table 2
Electrochemical data and the calculated k_{-NO} for some *trans*-$[Ru(NO)(NH_3)_4P(III)]^{3+}$ ions at pH 2.0 and 25.0 ± 0.1 °C.

Complex ions	$E_{NO^+/NO}$*	$E_{NO/HNO}$*	k_{-NO}
t-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$	−0.12	−0.68	0.26
t-$[Ru(NO)(NH_3)_4P(OEt)_3]^{3+}$	−0.10 [17]	−0.70 [33]	0.97 [17]
t-$[Ru(NO)(NH_3)_4P(O^iPr)_3]^{3+}$	−0.19	−0.39	2.85
t-$[Ru(NO)(NH_3)_4P(OBu)_3]^{3+}$	−0.10	−0.47	0.91
t-$[Ru(NO)(NH_3)_4P(O)(OH)_2]^{2+}$	−0.52 [32]	−0.79	0.22
t-$[Ru(NO)(NH_3)_4P(O)(OEt)_2]^{2+}$	−0.50 [26]	−0.80 [26]	0.24 [26]

* Values vs. SCE.

4. Discussions

The free trialkyl phosphites were quickly hydrolysed in the aqueous media at pH 3.0 and 25.0 ± 0.1 °C. There is indeed a considerable difference in the reaction time scale (from seconds to hours) between the hydrolysis of triethyl phosphite and that of diethyl phosphite.

Diethyl phosphite hydrolyses faster at pH 1.0 ($k = (1.80 \pm 0.08) \times 10^{-4}$ s^{-1}; $t_{1/2} = 1.1$ h) than at pH 3.0 ($k = (7.1 \pm 0.42) \times 10^{-6}$ s^{-1}; $t_{1/2} = 27.0$ h) by forming a phosphonium salt before the water nucleophilic attack, as suggested by the acid catalysis pathway [35,36].

All phosphites tested in this study are substantially stabilised against hydrolysis when they are coordinated to the Ru(II) metal centre. The triisopropyl, tributyl, and diethyl phosphites coordinated to the *trans*-$[Ru(H_2O)(NH_3)_4]^{2+}$ fragment were found to hydrolyse with rate constants of the same order of magnitude ($4.4–7.3 \times 10^{-7}$ s^{-1}). The increased stability against hydrolysis of the phosphite molecules coordinated to the *trans*-$[Ru(H_2O)(NH_3)_4]^{2+}$ fragment may be explained by Ru(II) → P(III) back-bonding, which increases the electronic density on the phosphorus(III) ligand and deactivates this ligand against nucleophilic attack and the consequential hydrolysis.

The extension of the Ru(II) → P(III) back-bonding in the *trans*-$[Ru(L)(NH_3)_4P(III)]^{n+}$ compounds depends on the ligand (L) in the position *trans* to the phosphorus ester. Thus, this back-bonding tends to be smaller in nitrosyl complexes than in aquo species because the nitrosonium ligand is a strong π-acceptor. In this case, the nitrosonium competes for the Ru(II) 4dπ electrons, which decreases the electronic density in the phosphite ligand. This reasoning is consistent with the observed faster hydrolysis of phosphites coordinated to a *trans*-$[Ru(NO)(NH_3)_4]^{3+}$ fragment than that of phosphites coordinated to a *trans*-$[Ru(H_2O)(NH_3)_4]^{2+}$ fragment.

Although the hydrolyses of the trialkyl phosphite ligands in the *trans*-$[Ru(H_2O)(NH_3)_4P(OR)_3]^{2+}$ and *trans*-$[Ru(NO)(NH_3)_4P(OR)_3]^{3+}$ species produce the respective dialkyl phosphite complexes, the trialkyl phosphite ligands in the bisphosphito complex (*trans*-$[Ru(NH_3)_4(P(OR)_3)_2]^{2+}$) do not hydrolyse as long as they remain coordinated [13,14]. Instead, the aquation of one of the trialkyl phosphite groups is observed ($k = 1.90–8.02 \times 10^{-5}$ s^{-1} at pH 3.0 and 25 ± 1 °C for *trans*-$[Ru(NH_3)_4(P(OR)_3)_2]^{2+}$, where P(OR) = $P(O^iPr)_3$, $P(OBu)_3$, $P(OEt)_3$, and $P(OMe)_3$ [13,14]). For *trans*-$[Ru(H_2O)(NH_3)_4P(OH)(OEt)_2]^{2+}$, phosphite hydrolysis is observed, whereas in *trans*-$[Ru(NO)(NH_3)_4P(O)(OEt)_2]^{2+}$, the deprotonated diethyl phosphite ligand dissociates without prior hydrolysis (Table 1) [26].

Indeed, the phosphorus ester ligands can undergo both hydrolysis and dissociation. Thus, when $k_{diss} > k_{hyd}$, phosphorus(III) dissociation is observed, but when $k_{diss} < k_{hyd}$, hydrolysis is observed. The more favourable reaction (hydrolysis or dissociation) for each complex may be related to intrinsic factors of the system, such as the degree of susceptibility of the phosphite ligand to nucleophilic attack and the *trans* effect of the ligand *trans* to the phosphite.

Hence, if the rate constant of the diethyl phosphite dissociation in *trans*-$[Ru(NO)(NH_3)_4P(O)(OEt)_2]^{2+}$ is $k_{diss} = 8.90 \times 10^{-7}$ s^{-1}, its estimated hydrolysis rate constant may be $k_{hyd} < 8.90 \times 10^{-7}$ s^{-1}. Then, the stability of phosphites in nitrosyl complexes against hydrolysis follows the sequence of $P(O)(OEt)_2 > P(OEt)_3 > P(OBu)_3 > P(O^iPr)_3 > P(OMe)_3$. This sequence does not match the ^{31}P NMR chemical shift sequence, which is $\delta_{31P} = 68$, 80, 79, 75, and 84 ppm, respectively. However, with the exception of $P(OMe)_3$ ($\delta_{13C} = 61$ ppm), this sequence is consistent with the ^{13}C NMR chemical shift sequence for phosphite α-carbon atoms, namely $\delta_{13C} = 64$, 70, 75, and 81 ppm (Fig. 6).

In *trans*-$[Ru(NO)(NH_3)_4P(III)]^{3+}$, the phosphite is already activated by the Ru-P bond; thus, nucleophilic attack by the water molecule may be more favourable at the phosphite α-carbon than at the phosphorus atom (Fig. 7a). Therefore, the hydrolysis mechanism in *trans*-$[Ru(NO)(NH_3)_4P(III)]^{3+}$ for P(III) = $P(O)(OEt)_2$, $P(OEt)_3$, $P(OBu)_3$, and $P(O^iPr)_3$ (Fig. 7a) likely occurs via the Michaelis–Arbuzov proposal. In contrast, in the *trans*-$[Ru(NO)(NH_3)_4P(OMe)_3]^{3+}$ ion, which exhibits the most positive phosphorus atom ($\delta_{31P} = 84$ ppm) and the smallest steric effect among the studied

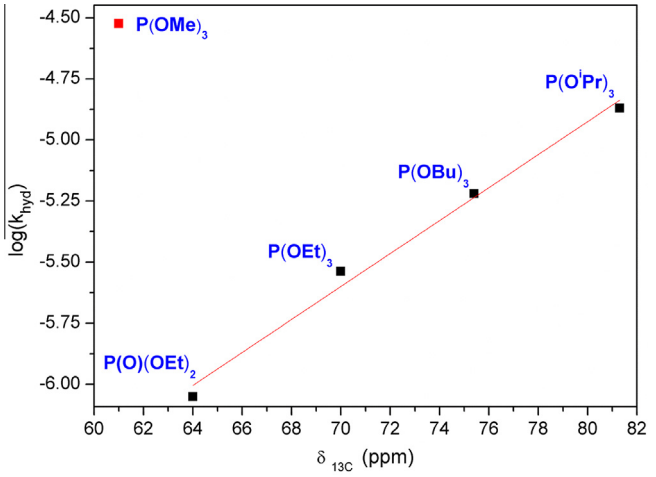


Fig. 6. Correlation between the k_{hyd} values and δ_{13C} (ppm) for phosphite α-carbon in a ruthenium nitrosyl complex.

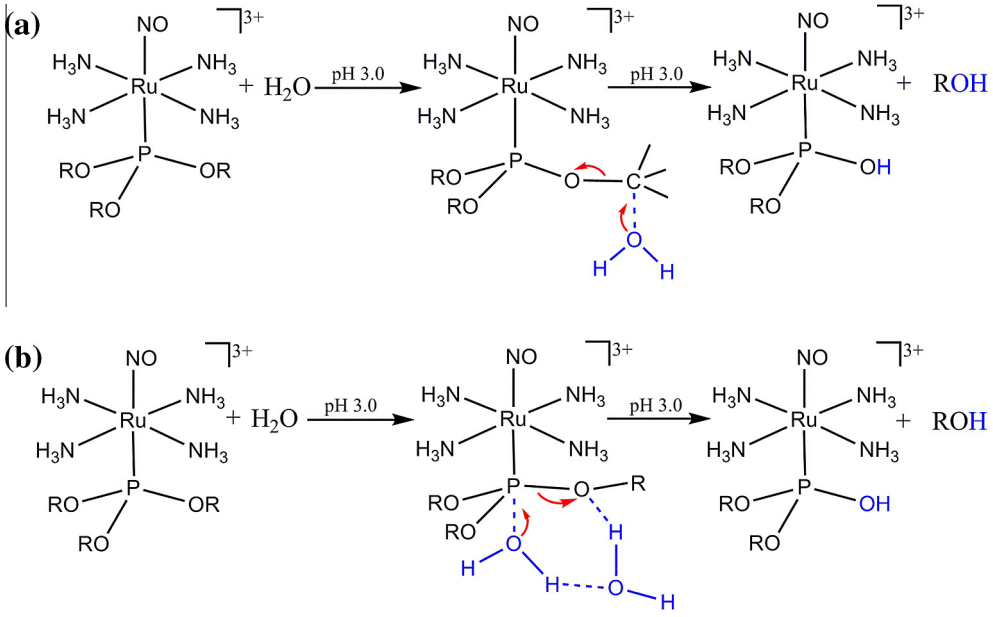


Fig. 7. Mechanism of phosphite hydrolysis in ruthenium nitrosyl complexes: (a) O–C bond break and (b) P–O bond break.

ions, the nucleophilic attack appears more likely to occur at the phosphorus atom, i.e., via the Aksnes mechanism (Fig. 7b).

Regarding the electrochemical properties, all five phosphite nitrosyl complexes can selectively generate NO or HNO upon reduction. From the first to the second reduction process, which are centred on the nitrosonium ligand, the potential values exhibited at least a 200-mV difference, which enables the selective nitrosonium reduction to NO or HNO according to the selected chemical reducing or electrochemical potential applied.

The rate of NO release (k_{-NO}) in the aqueous medium follows the sequence $P(O^iPr)_3 \gg P(OEt)_3 > P(OBu)_3 \gg P(OMe)_3 > P(O)(OEt)_2 > P(O)(OH)_2$. This sequence is identical to the observed sequence for the aquation of the pyrazine ligand in *trans*-$[Ru(pz)(NH_3)_4P(III)]^{n+}$ using these phosphite molecules as ligands [2,6]. In general, an increase in the σ-inductor groups that are bonded to the phosphite α-carbon substantially increases the *trans*-labilising effect of this phosphite ligand. In addition, the removal of σ-inductors groups that are bonded to the phosphite oxygen, such as in diethyl phosphite and phosphorous acid, substantially decreases the *trans*-labilising effect.

Although the rates of HNO release have not been directly measured, based on the absence of an anodic wave ($E_{HNO/NO}$) even at 5 °C and 2 V s^{-1}, k_{-HNO} should be higher than k_{-NO} for all complexes described herein.

5. Conclusion

The coordination of phosphites to ruthenium(II) centres stabilises these molecules against hydrolysis. The rate of the trialkyl phosphite hydrolysis changed from $k \sim 6 \times 10^{-3}$ s^{-1} to $k = 7.36–4.45 \times 10^{-7}$ s^{-1} and $0.30–6.04 \times 10^{-6}$ s^{-1} when the phosphite was coordinated to the *trans*-$[Ru(H_2O)(NH_3)_4]^{2+}$ and *trans*-$[Ru(NO)(NH_3)_4]^{3+}$ fragments, respectively. This increased stability is explained by the π-back-donation $4d\pi(Ru^{II}) \rightarrow 3d\pi(P^{III})$ extension. The experimental data suggest that, with the exception of trimethyl phosphite, the hydrolysis constant rate for phosphites that are coordinated to *trans*-$[Ru(NO)(NH_3)_4]^{3+}$ is related to the ^{13}C NMR chemical shifts of the phosphite α-carbon, which indicates that hydrolysis occurs via the Michaelis–Arbuzov mechanism.

The described nitrosyl complexes quickly release nitric oxide ($k_{-NO} = 0.22 – 2.87$ s^{-1} for $P(O)(OH)_2$ and $P(O^iPr)_3$, respectively) or nitroxyl ($k_{-NO}^{-} \gg k_{-NO}$) when they are activated by reduction centred on the nitrosyl ligand.

In summary, in addition to providing information that will increase our knowledge of phosphorus chemistry, these findings may be useful for tailoring new complexes for catalytic and medical applications.

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This manuscript is dedicated in memoriam of our friend and colleague José Cardoso do Nascinemento Filho.

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