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Short communication

Trans-kinetic effects in ligand substitution processes of ruthenium polypyridyl complexes

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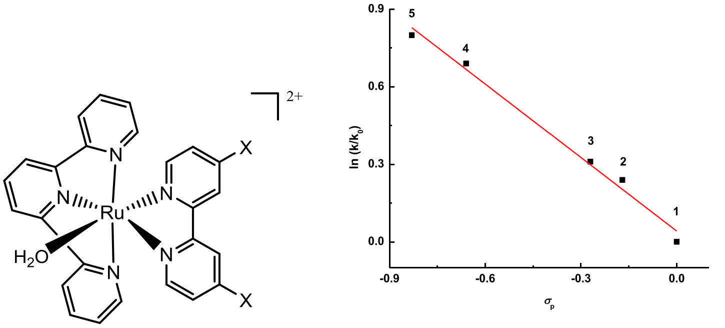
GRAPHICAL ABSTRACT



1 : X = H, **2** : X = CH_3, **3**: X = OCH_3, **4** : X = NH_2, **5** : X =$N(CH_3)_2$

ABSTRACT

A concerted mechanism is disclosed when studying *trans*-kinetic effects in substitution processes of complexes of formula $[Ru(trpy)(4,4'\text{-}(X)_2\text{-}bpy)(H_2O)]^{2+}$, with trpy = 2,2′:6′,2″-terpyridine, bpy = 2,2′-bipyridine and X = H, CH_3, OCH_3, NH_2 and $N(CH_3)_2$. The second order rate constants k_2 for substitution of water by acetonitrile increase with increasing donor ability of the X group. The correlation between ln k_2 and Hammett substituent constants σ_p of X gives a slope of near 1, indicating high sensitivity of the kinetic parameters for water replacement to the donor ability of the para-substituent attached to a bipyridine *trans*- to the water ligand and considerably separated from it. Besides, the activation enthalpies decrease with increasing pK_a values of the 4,4′-$(X)_2$-bpy ligands and the activation entropies have negative values almost one order of magnitude higher than those reported before in similar processes. These data indicate a concerted ligand interchange mechanism, infrequently found in substitution reactions of octahedral complexes which can be explained by the fact that H-bonds between the leaving ligand (H_2O) and the entering ligand (CH_3CN) will favor an intermediate transition state of increased order respect to the initial state. These results are pertinent for finding the best candidates in the quantitative detection of CH_3CN, an important contaminant in radiopharmaceuticals used in PET (positron emission tomography) studies.

Ruthenium polypyridyl complexes are relevant in systems involved in artificial photosynthesis [1]. Ligand substitution processes for the replacement of water by acetonitrile have already being studied in aquo (phosphine)ruthenium(II) complexes [2] and in complexes of the type $[Ru(H_2O)(N\text{-}N)(trpy)]^{2+}$ (with N-N = diimine ligand and trpy = 2,2′:6′,2″-terpyridine) [3], where steric effects for bidentate bipyridyl ligands were disclosed to be important in modulating the rate constants. However, since we were interested in detecting CH_3CN – an important contaminant in radiopharmaceuticals used in PET (positron emission tomography) studies [4] – by a rapid kinetic analytical method, we resorted to analyzing ligand substitution kinetics in similar complexes with 2,2′-bipyridines substituted in the 4,4′-positions with

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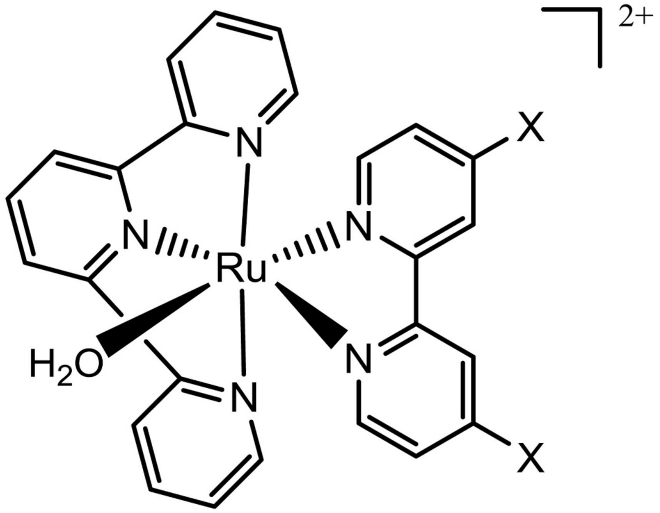

Scheme 1. Structure of complexes **1** (X = H), **2** (X = CH_3), **3** (X = OCH_3), **4** (X = NH_2) and **5** (X = $N(CH_3)_2$).

groups of different donor abilities, processes that had not been studied before.

Therefore, we report here the kinetic parameters of substitution of water (H_2O) by acetonitrile (CH_3CN) in complexes of formula $[Ru(trpy)(4,4'\text{-}(X)_2\text{-}bpy)(H_2O)]^{2+}$, with trpy = 2,2′:6′,2″-terpyridine, bpy = 2,2′-bipyridine and X = H, CH_3, OCH_3, NH_2 and $N(CH_3)_2$. The structure of complexes **1**–**5** are disclosed in Scheme 1.

All chemicals used in this work were analytical-reagent grade. Acetonitrile was freshly distilled over P_4O_{10} prior to use. Water used in all experiments was triply distilled; the second distillation was performed over $KMnO_4$ on a slightly basic media. Chemical analyses were carried out at INQUIMAE, University of Buenos Aires, Argentina, with an estimated error of ± 0.5%. $[Ru(terpy)Cl_3]$ was prepared by following reported techniques [5]. All the $[Ru(trpy)(4,4'\text{-}(X)_2\text{-}2,2'\text{-}bpy)Cl]Cl$ complexes were synthesized as described before, by heating at reflux $Ru(terpy)Cl_3$ and the corresponding $4,4'\text{-}(X)_2$-bpy ligand for 3 h in ethylene glycol [6]. The recrystallization in concentrated $HCl_{(aq)}$ was avoided for the bipyridines substituted with ammine groups; instead, a recrystallization in ethanol/ether was done. The reaction yields were between 70% and 80%.

In order to synthetize complexes of formula $[Ru(trpy)(4,4'\text{-}(X)_2\text{-}2,2'\text{-}bpy)(H_2O)](CF_3SO_3)_2$, 100 mg of the corresponding $[Ru(trpy)(4,4'\text{-}(X)_2\text{-}2,2'\text{-}bpy)Cl]Cl$ complex were poured onto 10 mL of an acetone/water (3:1) mixture. Then, an equivalent quantity of $Ag(CF_3SO_3)$ was added, and the resulting solution was refluxed for 4 h under subdued light. The precipitated AgCl was then removed by filtration and the filtrate was roto-evaporated to dryness. The obtained solid was recrystallized twice in acetone/ether. The reaction yields were between 60% and 75%. Complex **1** has been characterized before [7]. Anal. % found (calculated) for (**2**)·$(CF_3SO_3)_2$·$5/2(CH_3)_2CO$ or $C_{36.5}H_{40}F_6N_5O_{9.5}RuS_2$: C, 44.6 (44.7); N, 7.5 (7.2); H, 4.0 (4.1); for (**3**)·$(CF_3SO_3)_2$·H_2O or $C_{29}H_{27}F_6N_5O_{10}RuS_2$: C, 39.0 (39.4); N, 7.7 (7.9); H, 3.1 (3.1); S, 7.6 (7.3); for (**4**)·$(CF_3SO_3)_2$·$4H_2O$·$2(CH_3)_2CO$ or $C_{33}H_{43}F_6N_7O_{13}RuS_2$: C, 38.4 (38.7); N, 9.0 (9.6); H, 3.4 (4.2); S, 6.0 (6.3); for (**5**)·$(CF_3SO_3)_2$·$2H_2O$ or $C_{31}H_{35}F_6N_7O_9RuS_2$: C, 39.9 (40.1); N, 10.5 (10.6); H, 3.7 (3.8); S, 6.8 (6.9).

Electrochemical experiments were performed using a BAS Epsilon EC equipment, with vitreous C as working electrode, Pt wire as auxiliary electrode and Ag/AgCl(3 M KCl) as reference electrode. The cyclic voltammograms were measured at a scan rate of 100 mV/s, in aqueous solutions at pH = 1 (0.1 M HNO_3) and [complex] ~10^{-3} M. Only the redox potentials on the oxidative side were determined.

Kinetic measurements were carried out on a Hewlett-Packard 8453 Diode-Array Spectrophotometer connected to a bath thermostatized to ± 0.5 °C. An aqueous solution of $NaClO_4$ 0.1 M was used to adjust the ionic strength. The complex concentrations were about 4.6×10^{-5} M. The measured pH values for all solutions were between 4.7 and 4.9. The experiments were developed at different acetonitrile concentrations (0.74, 1.42 and 2.05 M) and for each concentration, the absorbance changes were determined at 50°, 60°, 70° and 80 °C. The pseudo-first order constants (k_{obs}) for the substitution were obtained by fitting an exponential function for the decay obtained at 4 selected wavelengths and computing the average values. All experiments were done by duplicate. Activation parameters were obtained by using the Eyring equation [8]:

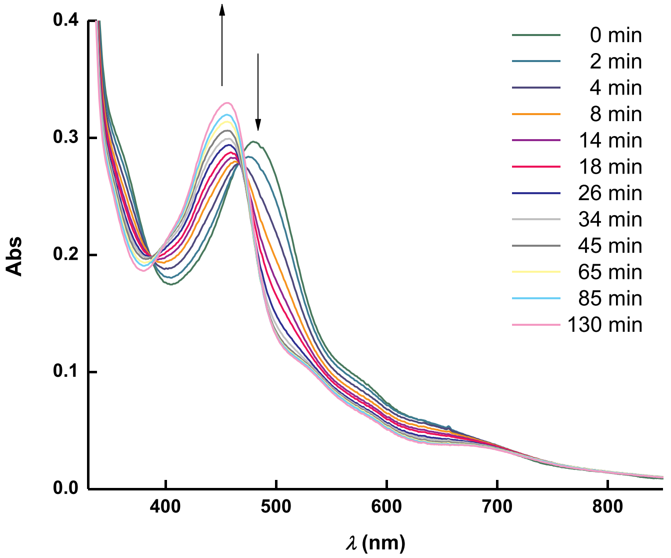

Fig. 1. Changes of absorbance with time for complex **3** (X = OCH_3), at $C \sim 4.5 \times 10^{-5}$, $[CH_3CN] = 0.74$ M and $T = 50$ °C.

$$\ln\left(\frac{k}{T}\right) = -\frac{\Delta H^*}{RT} + \ln\frac{k_B}{h} + \frac{\Delta S^*}{R} \qquad (1)$$

where k is the rate constant at temperature T, k_B is the Boltzmann constant, h is the Planck constant, R is the universal gas constant, ΔH^* is the activation enthalpy and ΔS^* is the activation entropy. Errors in activation parameters are estimated to be ± 5% in ΔH^* and ± 20% in ΔS^*.

The substitution of water by acetonitrile is disclosed by changes in the UV/absorption spectra, as shown in Fig. 1, for the case of X = OCH_3 as a representative example. The maximum absorption wavelengths (in nm) in aqueous solutions of the initial complexes $[Ru(trpy)(4,4'\text{-}(X)_2\text{-}bpy)(H_2O)]^{2+}$ are: λ_{max} = 475 nm (X = H), 476 nm (X = CH_3), 482 nm (X = OCH_3), 485 nm (X = NH_2) and 493 nm (X = $N(CH_3)_2$). These bands can be assigned to metal-to-ligand charge transfer (MLCT) transitions d_π (Ru) → π^*(bpy, trpy) [7]. As expected, the HOMO-LUMO gap decreases with increasing donor ability of the substituent X. The corresponding values in acetonitrile solutions for the final complexes $[Ru(trpy)(4,4'\text{-}(X)_2\text{-}bpy)(CH_3CN)]^{2+}$ are: λ_{max} = 454 nm (X = H), 456 nm (X = CH_3), 457 nm (X = OCH_3), 467 nm (X = NH_2) and 463 nm (X = $N(CH_3)_2$).

In all cases, substitution of water by acetonitrile causes an hypsochromic shift of the absorption band maxima. Since CH_3CN is a good π-acceptor, in contrast to H_2O, it competes for the metal electronic density with the polypyridyl ligands and thus the HOMO-LUMO gap increases, as already discussed in a previous work on the hydrolysis of coordinated acetonitrile in $[Ru(trpy)(bpy)(CH_3CN)]^{2+}$ [9].

Isosbestic points are detected in all cases (as shown in Fig. 1 for X = OCH_3 and in Supplementary Fig. 1 for the other complexes) and indicate the co-existence of two species in solution, according to the substitution process:

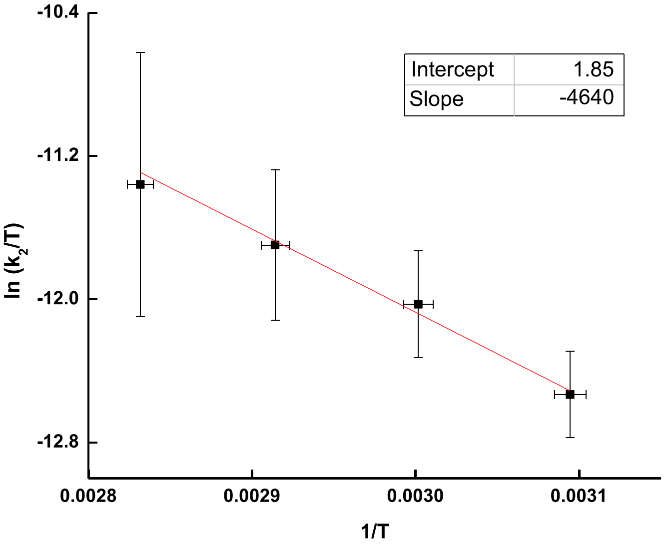

Fig. 2. Linear fitting of ln (k_2/T) vs. ($1/T$) for complex **3** (X = OCH_3). Using Eq. (1), a value of $\Delta H^* = 39(3)$ kJ/mol was determined from the slope, and a value of $\Delta S^* = -182(99)$ J/mol K was obtained from the intercept.

$$[Ru(trpy)(4,4'\text{-}(X)_2\text{-}bpy)(H_2O)]^{2+} + CH_3CN \xrightarrow{k_2} [Ru(trpy)(4,4'\text{-}(X)_2\text{-}bpy)(CH_3CN)]^{2+} + H_2O \quad (2)$$

where the second order-rate constants k_2 are obtained as $k_2 = k_{obs}$ [CH_3CN].

Previous studies by Takeuchi et al. [3] have shown that substitution of water by acetonitrile in complexes of the type $[Ru(H_2O)(N\text{-}N)(trpy)]^{2+}$ occur by a dissociative interchange mechanism, as supported by the values obtained at different concentrations. In our studies, however, we found evidence of a concerted mechanism, as discussed below.

Supplementary Table 1 shows the determined values of k_2, averaged over all the three used acetonitrile concentrations, for complexes **1**–**5** at four different temperatures.

The activation parameters were obtained by a linear fitting of ln(k_2/T) vs. $1/T$, according to Eq. (1). Fig. 2 shows the correlation obtained for complex **3** as a representative example. Supplementary Fig. 2 shows the fittings obtained for the other complexes.

In Table 1, values of the averaged second-order rate constants k_2 at $T = 50$ °C are shown together with the activation parameters. It can be deduced that the rate constants increase with increasing donor power of the substituents X in para-positions of the bipyridyl rings of complexes **1**–**5**, as measured by their sigma Hammett values σ_p [10], also included in Table 1. Fig. 3 shows the variation of ln (k/k_0), where k is the second-order rate constant displayed in Table 1 and k_0 is the value corresponding to complex **1** (X = H) vs. σ_p.

Linear fitting of the points represented in Fig. 3 gives a slope of (-0.95 ± 0.05), indicating extreme sensitivity of the rate constants to the donor ability of the substituent X *trans*- to the leaving water molecule (see Scheme 1) and considerably separated from it (estimated as ca. 10 Å). The value of the slope is rather high in this type of complexes; for example in substitution of water by acetonitrile in aquo(phosphine) ruthenium(II) complexes the obtained slope was -0.57 [2]. Thus, the rate constant almost doubles when going from X = H (complex **1**) to X = $N(CH_3)_2$ (complex **5**), a result which may prove useful for increasing the sensibility of detection of acetonitrile, a relevant contaminant in radiopharmaceuticals used for PET studies.

Table 1
Second-order rate constants (at $T = 50$ °C) and activation parameters of substitution processes (Eq. (2)) in complexes of the type $[Ru(trpy)(4,4'\text{-}(X)_2\text{-}bpy)(H_2O)]^{2+}$, together with the corresponding sigma Hammett values (σ_p) of X, the pK_a values of 4,4′-(X)$_2$-bpy, and the reduction potentials $E_{1/2}(Ru^{III}/Ru^{II})$ vs. NHE for each complex.

X	$10^3\ k_2$ ($M^{-1}\ s^{-1}$)	ΔH^* (kJ/mol)	ΔS^* (J/mol K)	σ_p	pK_a	$E_{1/2}$ (V)
H	0.86	45	−166	0	4.44	1.04
CH_3	1.09	44	−167	−0.17	4.92	0.94
OCH_3	1.17	39	−182	−0.27	5.74	0.91
NH_2	1.71	37	−183	−0.66	5.98	0.74
$N(CH_3)_2$	1.92	34	−191	−0.83	6.44	0.74

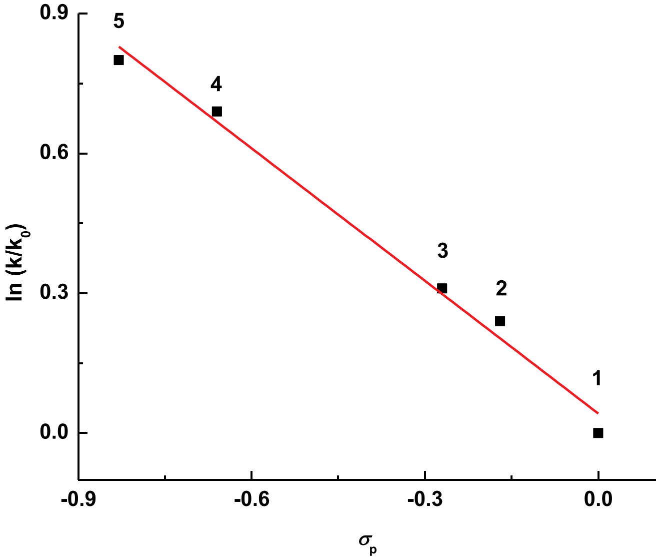

Fig. 3. Correlation between logarithm of the relative rate constants and sigma Hammett values σ_p of X for complexes **1**–**5**.

Fig. 4 shows that the activation enthalpies decrease with increasing basicity of the 4,4′-(X)$_2$-bpy ligand, as measured by the pK_a values, also displayed in Table 1 [11,12]. This correlation indicates an enthalpic control of the kinetics: the bond strength between Ru and the O atom of the leaving water molecule becomes weaker when increasing the electronic density of the metal by introducing a *trans*-substituent X with stronger donor strength. This fact is consistent with increasing Ru—O bond lengths with increasing donor ability of X; for instance, the distance Ru—O is 2.097 Å in complex **1** (X = H) [13] and 2.147 Å in complex **3** (X = OCH_3) [14].

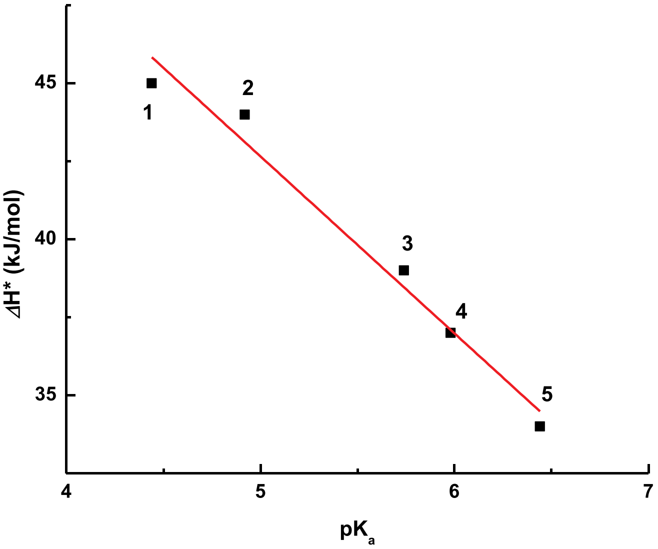

Fig. 4. Correlation between the activation enthalpies of processes (Eq. (2)) and pK_a values of 4,4′-(X)$_2$-bpy for complexes **1**–**5**.

The activation entropies also decrease with increasing values of pK_a but with a much lower slope. Moreover, all the activation entropies have negative values and they almost an order of magnitude higher than those observed in similar processes; for example, the negative activation entropies reported in the aquation of Co(III) complexes of the type $[Co(en)_2ACl]^{n+}$ (en = ethylenediamine) [15]. Almost all *trans*-effects in ligand substitution processes in octahedral complexes can be explained by a dissociative mechanism [16], so that positive activation entropies are usually expected. Negative ΔS^* values have been determined before in substitution reactions of octahedral Ru complexes, but only when charged species were produced from uncharged precursors [17], which is not the present case. The results found in this work may indicate a concerted mechanism with some associative character, possibly due to H-bonds between the leaving water molecule and the entering acetonitrile molecule (an interaction already described in [18]), which causes an increased order of the transition state respect to the ground state and a concomitant negative activation entropy.

In conclusion, we have demonstrated the existence of a concerted mechanism when studying *trans*-effects in ligand substitution processes in octahedral Ru polypyridyl complexes, a result that can be eventually applied to the determination of traces of acetonitrile, an important contaminant in radiopharmaceuticals used in PET studies.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.inoche.2018.09.043.

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