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Electron Transfer Reactions of Ru^{III}(edta) Containing the *N*−Heterocyclic Ligand Pyrazine: Kinetic and Mechanistic Studies

Debabrata Chatterjee[a,b@] and Rudi van Eldik[b,c,d]

[a]*Vice-Chancellor's Research Group, Zoology Department, University of Burdwan, 713104 Burdwan, India*
[b]*Department of Chemistry and Pharmacy, University of Erlangen-Nuremberg, 91058 Erlangen, Germany*
[c]*Faculty of Chemistry, Jagiellonian University, 30-387 Krakow, Poland*
[d]*Faculty of Chemistry, N. Copernicus University, 87-100 Torun, Poland*
[@]*Corresponding author E-mail: dchat57@hotmail.com*

Electron transfer reactions involving Ru(III) complexes pioneered by Nobel Laureate Henry Taube in the 'late sixties', has been an area of continued research for more than the past five decades. This review focuses on the research progress in the use of a Ru(III) complex containing the 'edta' ligand (edta^{4-} = ethylenediaminetetraacetate) in electron transfer processes, and mainly covers the electron transfer reaction of [Ru^{III}(edta)(pz)]$^{-}$ (pz = pyrazine) with biologically important reductants, viz. L-ascorbic acid, catechol, sulfite, sulfide and thiols, highlighting the authors' own research work. The scope of this review is to contribute to the mechanistic understanding of electron transfer reactions of [Ru^{III}(edta)(pz)]$^{-}$ with aforementioned biologically important electron donors, and to illustrate the preferential reaction pathway(s).

Keywords: Ru(edta), pyrazine, electron-transfer, redox reaction, biologically important reductants, reaction mechanism.

Реакции электронного переноса Ru^{III}(ЭДТА), содержащего *N*−гетероциклический пиразиновый лиганд: кинетическое и механистическое исследования

Д. Чаттерджи,[a,b@] Р. ван Элдик[b,c,d]

[a]*Кафедра зоологии, Университет Бурдвана, 713104 Бурдван, Индия*
[b]*Кафедра химии и фармации, Университет Эрланген-Нюрнберга, 91058 Эрланген, Германия*
[c]*Химический факультет, Ягеллонский университет, 30-387 Краков, Польша*
[d]*Химический факультет, Университет Н. Коперника, 87-100 Торунь, Польша*
[@]*E-mail: dchat57@hotmail.com*

Реакции переноса электрона с участием комплексов Ru(III), впервые разработанные лауреатом Нобелевской премии Генри Таубе в конце шестидесятых годов, являются предметом непрерывных исследований на протяжении более чем пяти последних десятилетий. Обзор охватывает результаты работ авторов по изучению комплекса Ru(III), содержащего в качестве лиганда ЭДТА$^{4-}$ (edta^{4-}, этилендиаминтетраацетат), главным образом [Ru^{III}(edta)(pz)]$^{-}$ (pz = пиразин), в процессах переноса электрона биологически важными восстановителями, а именно, L-аскорбиновой кислотой, катехолом, сульфитом, сульфидом и тиолами. Цель этого обзора – внести вклад в понимание механизмов реакций переноса электрона [Ru^{III}(edta)(pz)]$^{-}$ биологически важными донорами электронов, а также проиллюстрировать предпочтительный путь (пути) реакции.

Ключевые слова: Ru(edta), пиразин, перенос электронов, окислительно-восстановительные реакции, биологически важные восстановители, механизм реакции.

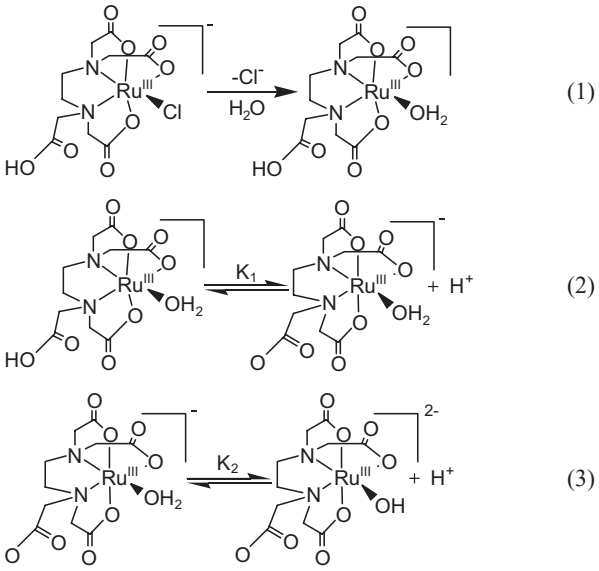
Introduction

The 'edta' ($edta^{4-}$ = ethylenediaminetetraacetate) complex of Ru(III) is of continued interest in regard to the kinetic and mechanistic studies for the past four decades in terms of the elucidation of inorganic reactions mechanism. A major impetus toward development of Ru^{III}(edta) chemistry has been bestowed by the authors of this article who have collaborated for the past two decades. Our collaborative work has resulted in many emissary papers on kinetic and mechanistic studies of Ru(edta) complexes. To me personally, Prof. Rudi van Eldik is an outstanding scientist and truly a wonderful friend, collaborator and mentor not only to me, but also to many of his colleagues and coworkers. I admire him for his intellectual curiosity, remarkable creativity and his warm and generous spirit. It is very nice and gratifying for me to dedicate this paper to Prof. Rudi van Eldik, co-author of this work on his 75th birthday. This paper necessarily reflects the active interest of my co-author even at his age of 75.

The kinetic behavior of Ru^{III}(edta) complexes towards coordinated water substitution and its catalytic ability to effect hydrocarbon oxidation, oxidation and S-nitrosylation of thiols, and its prospect in bio-inorganic application, have been adequately reviewed before.[1–4] However, the advancement of electron-transfer reactions involving Ru^{III}(edta) complexes to unravel mechanistic information, has not been systematically reviewed to date. This review mainly covers the reduction of the $[Ru^{III}(edta)(pz)]^-$ complex with biologically important electron transfer reagents, *viz*. *L*-ascorbic acid, catechol, sulfite and sulfide, and thiols. The scope of this review is to contribute to the mechanistic understanding of electron transfer reactions of $[Ru^{III}(edta)(pz)]^-$ with biologically important electron donors, and to rationalize the need of preferential reaction pathway(s).

Background Chemistry

The 'edta' ligand forms a very stable 1:1 metal complex with ruthenium. The $K[Ru^{III}(Hedta)Cl]$ complex rapidly converts into the $[Ru^{III}(Hedta)(H_2O)]$ species when dissolved in water.[5,6] It was established by crystallographic studies[7,8] that the 'edta' ligand functions as a pentadentate ligand towards Ru(III) with a protonated pendant acetate arm. The sixth coordination site of the ruthenium center in the Ru^{III}(edta) complex is occupied by a water molecule at low p*H* or by an hydroxide ion at high p*H* (Scheme 1). The pK_a values related to the acid-dissociation equilibria of the pendant carboxylic acid arm and the coordinated water molecule are 2.4 and 7.6, respectively, at 25 °C.[5,6]

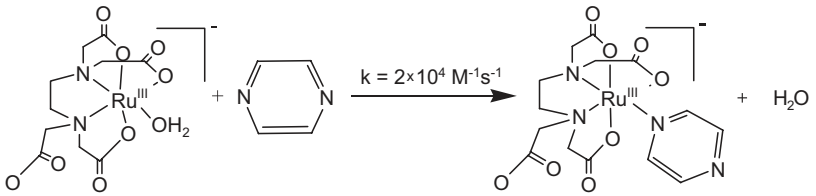


Scheme 1. Acid-dissociation equilibria of $[Ru^{III}(Hedta)(H_2O)]$.

The $[Ru^{III}(edta)H_2O]^-$ complex exhibited unusual lability towards aqua-substitution in the p*H* range 4–6.[5,6] It reacts with the aromatic *N*-heterocyclic ligand, pyrazine (pz) to form the $[Ru^{III}(edta)(pz)]^-$ complex, which has been involved in electron-transfer reactions reviewed herein, through a rapid ($k = 2{\cdot}10^4$ $M^{-1}{\cdot}s^{-1}$ at 25 °C)[5] and straightforward water displacement reaction as shown in Scheme 2.

While the spectrum of $[Ru^{III}(edta)(pz)]^-$ in aqueous solution is featureless (Figure 1A) in the entire visible range,[5] its Ru(II)-analogue exhibits a strong band (Figure 1B) in the visible range (λ_{max} = 462 nm, ε_{max} = 11000 $M^{-1}{\cdot}cm^{-1}$),[5] and thus offers an amenable way to monitor the electron-transfer reaction spectrophotometrically. The absorption band observed in the visible range was assigned to a metal to ligand charge transfer (MLCT) band. Such low energy and high intensity MLCT bands implicate strong mixing of metal-based dπ and ligand-based π* levels. Furthermore, the pyrazine ligand also prevents hydrolysis reactions of the Ru center. Electrochemical studies of the Ru^{III}(edta) complex has reportedly shown that the $[Ru^{III}(edta)(pz)]^-$ complex undergoes easy interconversion between low-spin Ru^{II}/Ru^{III} redox changes (d^6/d^5) without significant needs for structural changes that limit electron transfer steps, and the electron transfer process is rapid and reversible for the Ru^{III}/Ru^{II} couple ($E_{1/2}$ = 0.01 V *vs* SCE).[5]

The position of the band, however, changes with the p*H* of the solution due to protonation of the remote aromatic



Scheme 2. Formation of $[Ru^{III}(edta)(pz)]^-$ in the reaction of $[Ru^{III}(edta)(H_2O)]^-$ with pyrazine (pz).

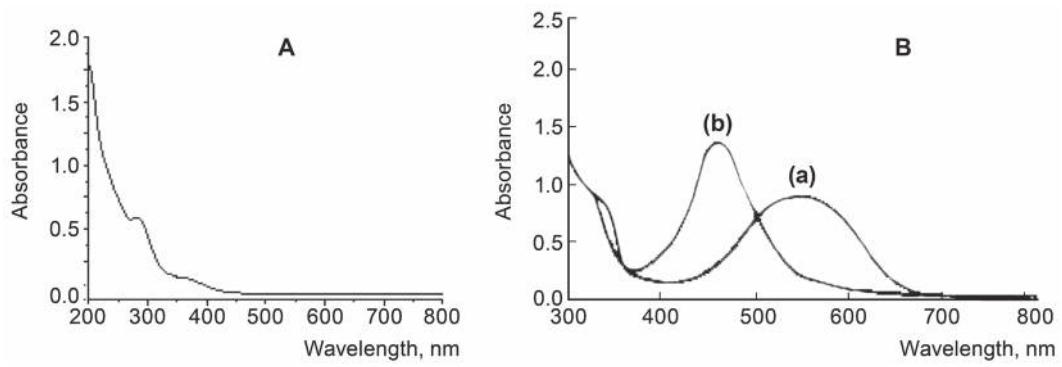
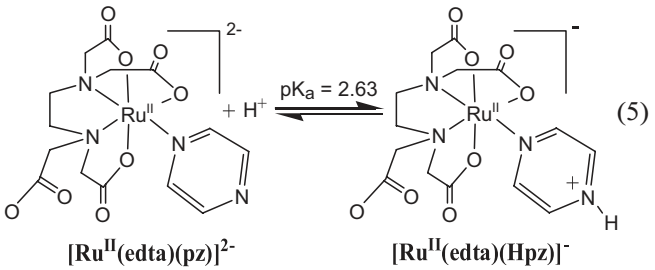


Figure 1. A: Spectrum of $[Ru^{III}(edta)(pz)]^-$, and B: spectra of (a) $[Ru^{II}(edta)(Hpz)]^-$ and (b) $[Ru^{II}(edta)(pz)]^{2-}$ in aqueous solution. Reprinted with permission from ref. [9]. Copyright the Royal Society of Chemistry

N atom of the coordinated pyrazine (Scheme 3) and the corresponding proton dissociation constant (pK_a) determined spectrophotometrically is 2.63 at 25 °C.[9] The $[Ru^{III}(edta)(pz)]^-/[Ru^{II}(edta)(pz)]^{2-}$ redox couple reportedly estimated from cyclic voltammetric studies, is 0.01 V (*vs* SCE).[5] The suitability of such complexes to study electron transfer reactions dates back to studies on the pentammine analogues of $[Ru(edta)pz]^-$ pioneered by Nobel Laureate Henry Taube in the late sixties.[10,11] The wide spectral difference between Ru(III)- and Ru(II)-species in $[Ru^{III}(NH_3)_5L]^{3+}$ (L = aromatic *N*-heterocyclic compounds like pyrazine, pyridine) complexes was also reported by Taube *et al*.[10,11]



(5)

Scheme 3. Protonation equilibrium of $[Ru^{II}(edta)(pz)]^{2-}$.

stoichiometry determined spectrophotometrically at p*H* 6.0 is outlined in Eq. 6.[9]

$$2[Ru^{III}(edta)(pz)]^- + HAA^- \longrightarrow 2[Ru^{II}(edta)(pz)]^{2-} + H^+ + DHA \quad (6)$$

Considering that the pK_1 and pK_2 of H_2AA are 4.1 and 11.4, respectively,[13] HAA^- is the predominant reacting species at p*H* 6.0. It has been reported that the rate of the aforementioned reaction is first-order with respect to the Ru(III)-complex concentration, and the values of the observed rate constants increased linearly with increasing ascorbic acid concentration in excess. Based on the experimental findings, the following mechanism involving two subsequent one-electron transfer steps, was proposed in Scheme 4 for the oxidation of ascorbic acid by $[Ru^{III}(edta)(pz)]^-$.[9]

$$[Ru^{III}(edta)(pz)]^- + HAA^- \xrightarrow{k_r} [Ru^{II}(edta)(pz)]^{2-} + HAA^\bullet \quad (7)$$

$$[Ru^{III}(edta)(pz)]^- + HAA^\bullet \longrightarrow [Ru^{II}(edta)(pz)]^{2-} + H^+ + DHA \quad (8)$$

Scheme 4. Suggested mechanism for the reduction of $[Ru^{III}(edta)(pz)]^-$ by HAA^-.

Electron Transfer Reaction of $[Ru^{III}(edta)(pz)]^-$ with *L*-Ascorbic Acid

Ascorbic acid (H_2AA) is a water soluble vitamin (*L*-ascorbic acid, the active form of vitamin C) and essential for human nutrition. Ascorbic acid is an excellent reducing agent and well known by its high anti-oxidant activity in cellular metabolism.[12] Oxidation of ascorbic acid to dehydroascorbic acid (DHA) can be induced by enzymes such as ascorbate oxidase. It has been reported that the Ru(edta) complex can mimic the enzymatic oxidation of ascorbic acid to dehydroascorbic acid.[9] Addition of ascorbic acid to the aqueous solution of $[Ru^{III}(edta)(pz)]^-$ resulted in an immediate reduction of the Ru(III)- to its Ru(II)-analogue with concomitant formation of dehydroascorbic acid. The reaction

As proposed in Scheme 4, in the rate-determining step (Eq. 7) the mono-protonated ascorbic acid anion (HAA^-) transfers one-electron to the Ru(III)-complex to produce its Ru(II)-analogue. The ascorbate radical ($HAA^\bullet$) so produced (Eq. 7), subsequently reduces another molecule of the Ru(III) complex to yield dehydroascorbic acid (DHA) in a rapid and kinetically indistinguishable step (Eq. 8). The effect of ionic strength on the reaction rate was studied and the reported experimental results are in agreement with the Bronsted-Bjerrum equation[14] for two likely charged reactants, and thereby validating the rate-determining step in the proposed mechanism (Scheme 4).

The values of $\Delta H^{\neq} = 38 \pm 1$ kJ·mol^{-1} and $\Delta S^{\neq} = -65 \pm 3$ J·K^{-1}·mol^{-1}, estimated from the temperature dependence of the second-order rate constant for the reduction of $[Ru^{III}(edta)(pz)]^-$ by HAA^- (Figure 2) are consistent with the

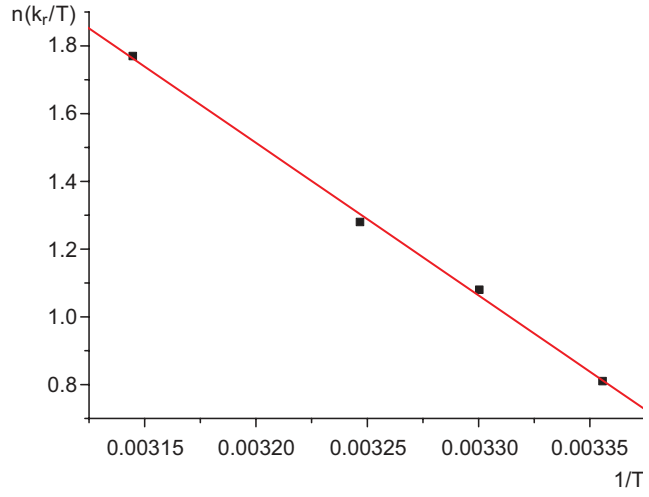


Figure 2. Eyring plot for the reduction of $[Ru^{III}(edta)(pz)]^-$ with HAA^-.

proposed outer-sphere electron transfer process as outlined in Scheme 4.

The effect of p*H* on the reduction of $[Ru^{III}(edta)(pz)]^-$ by ascorbic acid was examined in the p*H* range from 3.8 to 8.2. The p*H* dependence of the rate of the reaction was found to be consistent with the reactivity of various protonated and deprotonate species of ascorbic acid which decreases in the following order: $AA^{2-} >> HAA^- > H_2AA$.[15] While ascorbic acid is predominantly present as HAA^- in the p*H* range 6–8,[13] a sharp increase in the reaction rate with increasing p*H* from 6.0 to 8.0 suggests the participation of the highly reactive ascorbate anion (AA^{2-}), although present in very small concentrations in the reduction of $[Ru^{III}(edta)(pz)]^-$ by ascorbic acid.[9]

An attempt was reportedly made to correlate experimental rate constant data with the data calculated by using the simplified Marcus cross-reaction relationship.[16] The close agreement between the calculated rate constant data (477 $M^{-1}\cdot s^{-1}$) with that obtained experimentally (450 ± 30 $M^{-1}\cdot s^{-1}$ at 25 °C),[9] further supports the outer-sphere electron transfer process proposed in Scheme 4.

Electron transfer reaction of $[Ru^{III}(edta)(pz)]^-$ with catechol

Oxidation of catechol by metallo-enzymes is known to play an important role in biological systems.[17] In order to gain mechanistic insight of such enzymatic reactions, a brief study exploring the ability of $[Ru^{III}(edta)(pz)]^-$ towards catechol oxidation was performed, as an extension of the aforementioned studies on ascorbic acid oxidation.[9] It had been reported that $[Ru^{III}(edta)(pz)]^-$ could effectively oxidize catechol to benzoquinone. The rate of oxidation was found to be first-order, both with respect to the Ru(III)-complex and catechol concentrations. The values of the first-order rate constant increased linearly with increasing catechol concentration, and the value of the second-order rate constant (k_r), determined from the plot of k_{obs} *versus* catechol concentration, was found to be 570 ± 30 $M^{-1}\cdot s^{-1}$ at 25 °C and p*H* 6.0.[9]

Electron Transfer Reaction of $[Ru^{III}(edta)(pz)]^-$ with Sulfite

The reaction between sulfite and different metal ions and metal complexes is important in view of the different mechanistic aspects and electron transfer processes resembling sulfite oxidase.[18,19] A report on the oxidation of sulfite by $[Ru^{III}(edta)(pz)]^-$ resulting in the formation of both sulfate and dithionate as major oxidation products, is available in the literature.[20] Formation of $[Ru^{II}(edta)(pz)]^{2-}$ in the reaction of $[Ru^{III}(edta)(pz)]^-$ and sulfite was reportedly ascertained by spectral analysis of the resultant product. The time course of the reaction was followed spectrophotometrically as function of sulfite concentration, p*H* and temperature.[20] At a lower concentration of sulfite over the Ru(III) complex, both sulfate and dithionate were identified as major products of the oxidation of sulfite by $[Ru^{III}(edta)(pz)]^-$, however, dithionate was reported to be the only oxidation product at higher concentrations of sulfite over the Ru(III) complex. The values of the observed first-order rate constant were reported to depend linearly on the sulfite concentration under the specified conditions.[20] Considering that deprotonated sulfite (SO_3^{2-}) is the dominant reacting species at p*H* 8.0 (pK_1 and pK_2 values of H_2SO_3 are 1.78 and 6.99, respectively),[21] the following mechanism (Scheme 5) was proposed for the reduction of $[Ru^{III}(edta)(pz)]^-$ by SO_3^{2-}.

$$[Ru^{III}(edta)(pz)]^- + SO_3^{2-} \xrightarrow{k} [Ru^{II}(edta)(pz)]^{2-} + SO_3^{\bullet -} \quad (9)$$

$$SO_3^{\bullet -} + SO_3^{\bullet -} \longrightarrow S_2O_6^{2-} \quad (10)$$

$$[Ru^{III}(edta)(pz)]^- + SO_3^{\bullet -} \longrightarrow [Ru^{II}(edta)(pz)]^{2-} + SO_3 \quad (11)$$

$$SO_3 + OH^- \longrightarrow HSO_4^- \quad (12)$$

Scheme 5. Suggested mechanism for the reduction of $[Ru^{III}(edta)(pz)]^-$ by SO_3^{2-}. Reprinted with permission from ref. [20]. Copyright Springer Nature.

In the proposed mechanism, reduction of the Ru(III) complex takes place in a rate-determining step (Eq. 9) involving one-electron transfer [from sulfite to the Ru(III) complex] in an outer-sphere manner to yield the Ru(II) complex and the SO_3^- radical. In the presence of an excess of sulfite, the SO_3^- radicals can subsequently dimerize (Eq. 10) to produce dithionate ($S_2O_6^{2-}$) exclusively in the reaction mixture. The formation of sulfate was observed at lower concentration of SO_3^{2-} ($[Ru^{III}] > [SO_3^{2-}]$), which is understandable in terms of Eqs. (11) and (12). The SO_3^- radical formed as shown in Eq. 9, reduces another molecule of the Ru(III) complex (Eq. 11) to form SO_3 in a rapid and kinetically unresolved step, which further reacts with OH^- to produce HSO_4^- in the reaction solution as outlined in Eq. (12). The effect of p*H* on the reduction of $[Ru^{III}(edta)(pz)]^-$ was reportedly studied in the p*H* range 5.0 to 8.5, and in the studied p*H* range the rate of reduction was found to increase with increasing p*H* of the solution.[20] This is consistent with the fact that increase in p*H* enhances the concentration of SO_3^{2-} which is a stronger reducing species

than HSO_3^-, and therefore an increase in reaction rate was observed.[20] The lower reactivity of HSO_3^- was attributed to the lower electron density on the sulfur atom due to the associated proton in HSO_3^-.[20]

The reduction of $[Ru^{III}(edta)(pz)]^-$ with sulfite was studied at four different temperatures and the values of the second order rate constants (k_r) are 23 ± 4, 32 ± 3, 39 ± 3 and 67 ± 7 M^{-1} s^{-1} at 25, 30, 35 and 45 °C, respectively.[20] The values of the activation parameters ($\Delta H^{\neq}$ = 43 ± 4 kJ·mol^{-1} and $\Delta S^{\neq}$ = –73 ± 12 J·K^{-1}·mol^{-1}) are comparable to that reported for ascorbate reduction.[9]

The effect of alkali metal cations on the aforementioned reaction was also studied and the reported results (Table 1) are consistent with an outer-sphere electron transfer reaction between two negatively charged reacting species. The results in Table 2 may be understood on the basis that the cation (M^+) acts as a bridge, or by means of allowing the two negatively charged reacting ions $[Ru^{III}(edta)(pz)]^-$ and SO_3^{2-}, to come close enough to form a triple ion, $\{[Ru^{III}(edta)(pz)]^-\cdots M^+\cdots SO_3^{2-}\}$, in order to accelerate electron transfer through the solvent. The increase in the reaction rate on going from Li^+ to Na^+ to K^+ (Table 1) essentially provides evidence that the specific effect[22,23] of alkaline metal cations is operative in the reported reaction.[20] Considering the size of the hydrated cations,[22,23] which is in the order $Li^+ > Na^+ > K^+$, the K^+ would be more effective than Na^+ or Li^+ in bringing the reacting species close enough to form a triplet-ion species and to facilitate the electron transfer process as typically revealed by the increase in the reaction rate in the present studies.

Though the value of the experimentally determined rate constant (k = 23 ± 4 M^{-1}·s^{-1} at 25 °C) is reportedly larger than the calculated value (k = 3.03 M^{-1}·s^{-1}) by using the simplified Marcus cross-relationship,[16] the difference is not unusual[24] considering the uncertainties inherent in the input numbers in the Marcus calculations.[16] The considerably slower electron transfer rate (k = 23 ± 4 M^{-1}·s^{-1} at 25 °C) observed in case of the $[Ru^{III}(edta)(pz)]^-/SO_3^{2-}$ reaction as compared to that in the $[Ru^{III}(edta)(pz)]^-/HAA^-$ reaction (k = 450 ± 30 M^{-1}·s^{-1} at 25 °C)[9] may be well explained on the basis of thermodynamic (reduction potential) as well as kinetic (self-exchange rate) considerations. While the reduction potential values of the SO_3^-/SO_3^{2-} (E^0 = 0.72 V)[25] and HAA/HAA^- (E^0 = 0.72 V)[26] couples are very close, the self-exchange rate constant for the SO_3^-/SO_3^{2-} couple is much lower (by a factor of $2.5\cdot10^5$)[27] than that of the HAA/HAA^- couple, and as a consequence, a substantially lower reduction rate is observed for the reduction of $[Ru^{III}(edta)(pz)]^-$ by SO_3^{2-}.[20]

Table 1. Effect of alkali cations on the reduction of $[Ru^{III}(edta)(pz)]^-$ ($2.5\cdot10^{-4}$ M) by $[SO_3^{2-}]$ ($1\cdot10^{-2}$ M) at pH = 8.0 and 25 °C. Reprinted with permission from ref. [20] Copyright Springer Nature.

M^+	$[M^+]$, M	k_{obs}, s^{-1}
Li^+	0.2	0.11
	0.3	0.21
	0.5	0.32
	1.0	0.53
Na^+	0.2	0.20
	0.3	0.36
	0.5	0.51
	1.0	0.83
K^+	0.2	0.32
	0.3	0.58
	0.5	0.84
	1.0	1.43

Electron Transfer Reaction of $[Ru^{III}(edta)(pz)]^-$ with Sulfide

Hydrogen sulfide (H_2S), the smallest thiol, has recently been shown to be an important redox-signaling molecule, and its various beneficial effects in our bodies have been recognized lately.[28,29] The use of hydrogen sulfide, an obnoxious industrial pollutant as an effective electron transfer agent in the reduction of $[Ru^{III}(edta)(pz)]^-$ has been reported quite recently.[30] Detailed kinetic and mechanistic studies of the reduction of $[Ru^{III}(edta)(pz)]^-$ to $[Ru^{II}(edta)(pz)]^{2-}$ with hydrogen sulfide was performed strictly under argon atmosphere.

Addition of a solution of NaHS to the pale-yellow solution of $[Ru^{III}(edta)(pz)]^-$ at pH 8.5 (phosphate buffer) resulted in rapid spectral changes (Figure 3a) that were ascribed to the formation of $[Ru^{II}(edta)pz]^{2-}$ *via* reduction of $[Ru^{III}(edta)(pz)]^-$ by HS^-. The effect of the HS^- concentration on the kinetic profile (time *versus* absorbance traces at 462 nm) is typically displayed in Figure 3b.

It had been reported that the rate of reduction increased linearly with increasing concentration of HS^- at a constant pH (8.5).[30] The observed decrease in the rate of the reduction of $[Ru^{III}(edta)(pz)]^-$ at lower pH could be explained in terms of the lower reducing ability of hydrogen sulfide (which is the major reacting species at pH < 7.0) than its conjugate base HS^- (pK_1 of H_2S is 7.02).[31] Considering that HS^- is the predominant reacting species at pH 8.5, the overall experimental observations[30] can be accounted for in terms of the following reaction scheme (Scheme 6).

$$[Ru^{III}(edta)(pz)]^- + HS^- \xrightarrow{k_r} [Ru^{II}(edta)(pz)]^{2-} + HS^\bullet \quad (13)$$

$$[Ru^{III}(edta)(pz)]^- + HS^\bullet \longrightarrow [Ru^{II}(edta)(pz)]^{2-} + S + H^+ \quad (14)$$

$$HS^\bullet + HS^\bullet \longrightarrow H_2S_2 \quad (15)$$

$$H_2S_2 \longrightarrow H_2S + S^o \quad (16)$$

Scheme 6. Suggested mechanism for the reduction of $[Ru^{III}(edta)(pz)]^-$ by HS^-.

The rate determining step (13) proposed in the above mechanism involves an one-electron transfer from HS^- to the Ru(III) complex in an outer-sphere manner to yield the Ru(II) complex and the $HS^\bullet$ radical. The $HS^\bullet$ radical subsequently reduces another molecule of $[Ru^{III}(edta)(pz)]^-$ to yield elemental sulfur in a rapid and kinetically indistinguishable step as outlined in Eq. (14). Formation of colloidal sulfur

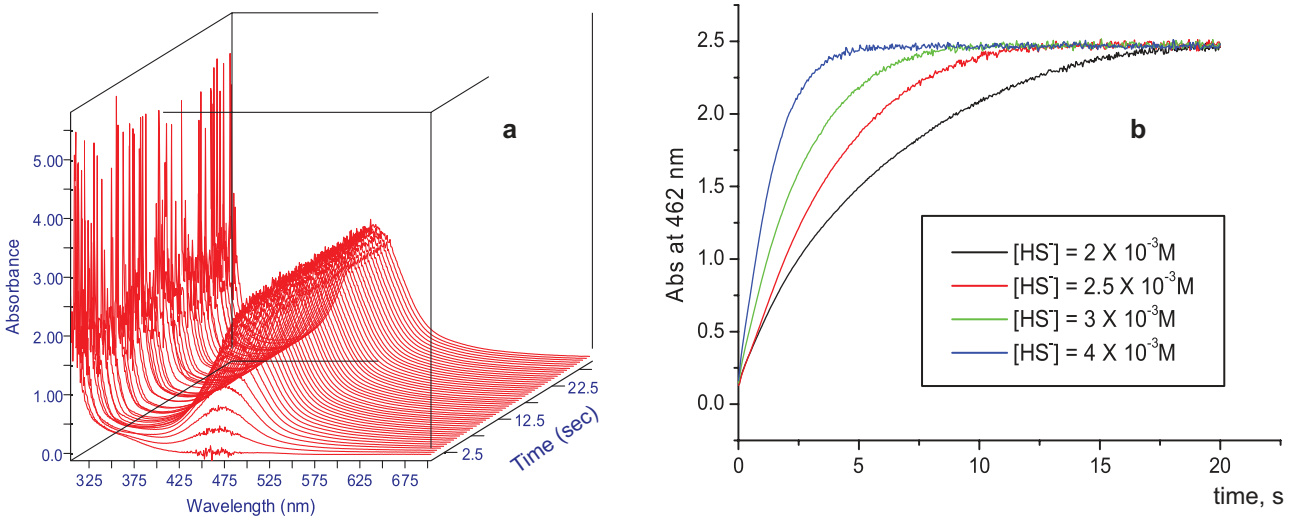


Figure 3. (a) UV-Vis spectral changes for the reaction of $[Ru^{III}(EDTA)(pz)]^-$ (0.2 mM) with HS^- (2.0 mM), (b) kinetic traces (recorded at 462 nm) at various $[HS^-]$ at 25 °C and p*H* 8.5 (phosphate buffer). Reprinted with permission from ref. [30] Copyright the Royal Society of Chemistry.

in the reaction system was reportedly noticed at the end of the reaction. [30] However, formation of colloidal sulfur may also take place via dimerization of the HS• radical to yield H_2S_2 (Eq. 15), followed by the decomposition of H_2S_2 to produce H_2S and S° (Eq. 16).

The temperature dependence of the reduction of $[Ru^{III}(edta)(pz)]^-$ with HS^- was investigated at four different temperatures and at constant p*H* 8.5.[30] The reported values of the second order rate constant (k_r) are 29 ± 1, 41 ± 2, 50 ± 2 and 70 ± 2 $M^{-1}\cdot s^{-1}$ at 15, 20, 25 and 30 °C, respectively.[30] The calculated values of $\Delta H^{\neq}$ (39 ± 2 kJ·mol^{-1}) and $\Delta S^{\neq}$ (–60 ± 6 J·K^{-1}·mol^{-1}) are quite comparable with those reported for the reduction of $[Ru^{III}(edta)(pz)]^-$ by negatively charged reductants,[9,20] and consistent with an outer-sphere electron transfer process as proposed in Scheme 6.

The effect of alkali metal cations[22,23] on the electron transfer rate of the aforementioned electron transfer reaction between two negatively charged reactants, was also studied. The reported increase in the reaction rate on going from Li^+ to Na^+ to K^+ essentially signifies the operation of an outer-sphere electron transfer process taking place between the two negatively charged reactants closely held by the alkali metal cations in form of a triple ion, $\{[Ru^{III}(edta)(pz)]^-\text{--}M^+\text{--}HS^-\}$. Electron transfer rate is governed by the size of the hydrated alkali metal cation. Considering the size of hydrated cations which are in the order $Li^+ > Na^+ > K^+$,[22,23] the K^+ would be more effective than Na^+ or Li^+ in bringing the negatively charged species close enough to form the triplet-ion species and thus to facilitate the electron transfer process as observed by the increase in the reaction rate.[30]

Electron Transfer Reaction of $[Ru^{III}(edta)(pz)]^-$ with Thiols

The redox reaction of thiol-disulfide conversions is of immense biological significance.[32] In this context reports on the application of the $[Ru^{III}(edta)(pz)]^-$ complex in the oxidation of thiols (RSH = cysteine, glutathione) to disulfide (RSSR), are available in the literature.[33] The reaction of $[Ru^{III}(edta)(pz)]^-$ with RSH resulted in the formation of $[Ru^{II}(edta)(pz)]^{2-}$ and RSSR as reaction products. The kinetics of the reaction of $[Ru^{III}(edta)(pz)]^-$ with RSH was performed as a function of [RSH], p*H*, temperature and pressure.[33] The reaction rate was reported to be first-order in $[Ru^{III}]$ and [RSH], and under pseudo-first order conditions of excess RSH (over $[Ru^{III}]$), the values of the observed rate constant increased linearly with increasing [RSH]. The following reaction scheme (Scheme 7) was proposed to account for the experimental results.

$$[Ru^{III}(edta)(pz)]^- + RSH \xrightarrow{k_r} [Ru^{II}(edta)(pz)]^{2-} + RS^{\cdot} + H^+ \quad (17)$$

$$2RS^{\cdot} \longrightarrow RSSR \quad (18)$$

Scheme 7. Suggested reaction mechanism for the reduction of $[Ru^{III}(edta)pz]^-$ to $[Ru^{II}(edta)pz]^{2-}$ by RSH. Reprinted with permission from ref. [33] Copyright the Royal Society of Chemistry.

In the rate-determining electron transfer step (Eq. 17), RSH reduces the Ru(III) complex in an outer-sphere manner to produce the Ru(II) complex and RS• radical concomitantly. In the subsequent and kinetically indistinguishable step (Eq. 18), the RS• radical rapidly transforms into RSSR (the oxidized form of RSH).

The role of alkali cations in the reduction of $[Ru^{III}(edta)(pz)]^-$ by RSH was studied and an increase in the reaction rate on going from Li^+ to Na^+ to K^+ was reported.[33] Formation of a bridged intermediate species **I**, as shown typically in Figure 4, was postulated for the reaction of the negatively charged $[Ru^{III}(edta)(pz)]^-$ and zwitterionic cysteine. Since the size of the hydrated cations follow the order $Li^+ > Na^+ > K^+$,[22,23] the K^+ would be more effective than Na^+ or Li^+ in bringing the reacting species close enough in **I**, and thereby facilitate the electron transfer process, as observed in the increase in reaction rate with K^+ in the

reported study.[33] Although the effect of p*H* on the reaction rate was reported to be somewhat insignificant at lower p*H*, at higher p*H* (> 8) the reaction rate increased markedly[33] due to increase in the concentration of deprotonated thiol RS^- (which is stronger reducing than RSH).

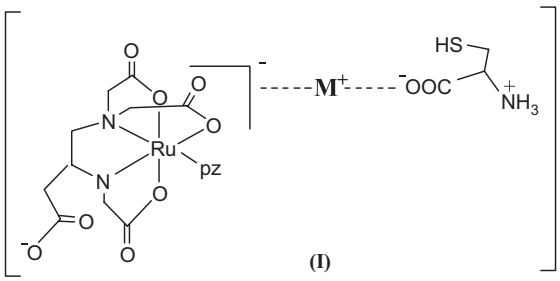
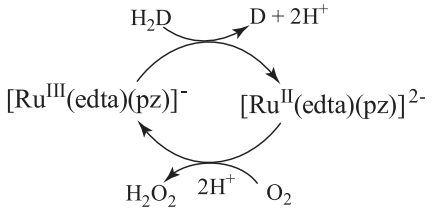


Figure 4. Structural representation of the intermediate, **I**. Reprinted with permission from ref. [33] Copyright the Royal Society of Chemistry

The reduction of $[Ru^{III}(edta)(pz)]^-$ by RSH was studied as function of temperature and pressure. At constant pressure (P = 1 atm), the reported values of the second-order rate constant (k_r) are 1.63 ± 0.11, 2.85 ± 0.14, 4.17 ± 0.13 and 5.82 ± 0.14 $M^{-1}\,s^{-1}$ at 10, 15, 21 and 25 °C.[33] The values of $\Delta H^{\neq}$ (56 ± 3 $kJ{\cdot}mol^{-1}$) and $\Delta S^{\neq}$ (–44 ± 8 $J{\cdot}K^{-1}{\cdot}mol^{-1}$) reported for the reduction of $[Ru^{III}(edta)(pz)]^-$ by RSH are quite comparable to those for the reduction of $[Ru^{III}(edta)(pz)]^-$ by acorbate,[9] sulfite[20] and sulfide[30] reported in the preceding sections, and consistent with the proposed outer-sphere electron transfer process. The pressure dependence of the reduction rate was studied at constant temperature (25 °C), and the reported values of the second-order rate constant (k_r) are 3.67 ± 0.02, 3.26 ± 0.02, 2.90 ± 0.01 and 2.47 ± 0.01 at P = 100, 500, 900 and 1300 atm, respectively.[33] The positive value for $\Delta V^{\neq}$ (+8.1 ± 0.5 $cm^3{\cdot}mol^{-1}$) reflects an increase in volume on the formation of the transition state within the intermediate, **I**. Since, no bond cleavage or bond formation take place in the activation process of the outer-sphere electron transfer the intermediate (**I**), the small values of $\Delta V^{\neq}$ (+8.1 ± 0.5 $cm^3{\cdot}mol^{-1}$) are consistent with the mechanistic scheme (Scheme 7) proposed for the reduction of $[Ru^{III}(edta)(pz)]^-$ with RSH. Partial reduction of Ru(III) to Ru(II) is expected to be accompanied by an increase in molar volume in the transition state. Noteworthy here, is that reports for positive values of $\Delta V^{\neq}$ for outer-sphere electron transfer processes are available in the literature.[34,35]

Catalytic Implications

The results of the present studies could be of significance for the mechanistic understanding of the action of a group of enzymatic reactions for redox regulation. Noteworthy here, is that the $[Ru^{II}(edta)(pz)]^{2-}$ complex, the one-electron reduction product of the Ru(III) analogue, is very unstable when exposed to oxygen by which it is re-oxidized to $[Ru^{III}(edta)(pz)]^-$. The results of the aforementioned studies taken together allow rationalization of the Ru(edta) mediated catalytic cycle (Scheme 8) for dioxygen (O_2) reduction to hydrogen peroxide (H_2O_2) using biologically important electron donors (H_2D) as reducing agent.



Scheme 8. Suggested mechanism for the reduction of O_2 by H_2D mediated by $[Ru^{III}(edta)(pz)]^-$.

It has already been reported that the $[Ru^{III}(edta)(pz)]^-$/HS^- system could produce H_2O_2 with a 88 % yield and catalytic turn-over number (TON) of 4.2.[30] The reported results validate the above catalytic scheme (Scheme 8) involving $[Ru^{II}(edta)(pz)]^{2-}$ as the catalytically active species responsible for H_2O_2 production.[30] It has also been confirmed that the $[Ru^{III}(edta)(pz)]^-$ catalyst does not undergo any degradation under the specified turn-over conditions.[30]

Conclusion

Following a brief description and background of Ru(edta) chemistry, the work described in this short review confirms the ability of Ru(edta) towards participating in electron transfer reactions – an important feature that governs its catalytic activities. This review has systematically summarized the performance of $[Ru^{III}(edta)(pz)]^-$ towards oxidizing various biologically significant reducing agents like *L*-ascorbic acid, catechol, sulfite, sulfide and thiols. The results discussed in this review afford a significant scope for an increased mechanistic understanding of outer-sphere electron transfer processes, and provide a basis towards the development of more efficient ruthenium-based catalysts containing the aromatic *N*-heterocyclic ligand for the selective reduction of O_2 *via* two one-electron outer-sphere reductions to produce H_2O_2, which is a promising candidate for a renewable energy source.

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