Medium effects on the redox properties of tris(2,2'-bipyridyl)ruthenium complexes

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Abstract

The electrochemistry of the 2,2'-bipyridyl ruthenium complexes $[Ru(Bipy)_3]^{n\pm}$ has been examined in a series of solvents with varying dielectric constant. The potential separation between the +1/0 and 0/−1 redox steps increases with decreasing solvent polarity and decreasing ionic strength of the supporting electrolyte. Electrochemically generated $[Ru(Bipy)_3]^n$ (where $n=0$ or -1) is kinetically labile in these low oxidation states and capable of reacting with the very high dielectric solvent *N*-methylacetamide via an E_rC_i mechanism; k_f for the following chemical reaction is 0.31 ± 0.15 s^{-1}. Relationship is drawn between the dependence of the $[Ru(Bipy)_3]$ potentials on solvent dielectric and the effect of local dielectric on protein redox potentials, and comment is made also on the solvent dependence of the potential of the ferricenium/ferrocene couple.

Introduction

The interesting chemistry of $Ru(Bipy)_3{}^{2+}$ (Bipy = 2,2'-bipyridyl) has stimulated the preparation and characterization of numerous ruthenium(II) complexes [1, 2] in order to examine the effects of moderate ligand structural changes on the reactivity and electronic properties of these complexes. In continuing our work [3] with Group 8 complexes of related ligands, we report herein the effects of solvent medium on the redox chemistry of the archetypal complex, $[Ru(Bipy)_3]^{2+}$.

Experimental

Reagents were used as received from Aldrich Chemical Co., Inc. and Fisher Scientific. Tetra-n-butylammonium hexafluorophosphate was prepared by the reaction of KPF_6 with NBu_4Br in water. The crude product was purified by recrystallization from ethyl acetate and dried *in vacuo* over P_4O_{10}. Propylene carbonate (PC) was dried overnight over calcined molecular sieves and then vacuum distilled. Pyridine (Pyr) was refluxed over phthalic anhydride and distilled at 1 atm. *N,N*-Dimethylformamide (DMF) was refluxed over CaH_2 and distilled at reduced pressure, while benzonitrile (PhCN) was purified according to Coetzee and McGuire [4], and dimethyl sulfoxide (DMSO) via the method of Casteel and Sears [5]. Acetonitrile (MeCN) and butyronitrile (PrCN) were refluxed over CaH_2 under dinitrogen and distilled at 1 atm. *N*-Methylformamide (NMF) was purified according to Held and Criss [6] and *N*-methylacetamide (NMA) was purified by refluxing with Na metal, followed by distillation at reduced pressure; no apparent solvent decomposition was observed in either case while electrochemical measurements were being carried out. NMA purified by this method has a potential window extending from −1.0 to −2.5 V (versus the Ag/Ag^+ reference electrode) at the rotating Hg electrode and +1.0 to −1.8 V at the rotating Pt electrode.

Electrochemical measurements were made with a three-electrode cell configuration controlled by a PAR-173 potentiostat, a PAR-176 i/E converter and a PAR-175 waveform generator. Potentials in non-aqueous solvent were measured and are quoted with respect to the Ag^+ (0.01 M; NEt_4ClO_4, 0.1 M)/Ag electrode. A Beckman rotating platinum disk electrode (area 0.300 cm^2) and a Beckman rotating gold electrode amalgamated and coated with Hg (0.289 cm^2) were used for stationary electrode cyclic voltammetry and rotating disk polarography; the latter is very well-suited to cathodic experiments. A platinum-bead electrode (0.400 cm^2) was also used for stationary electrode cyclic voltammetry. Measurements were carried out at 25.0 ± 0.2 °C for all solutions except PrCN (both 21.0 and 25.0 ± 0.2 °C) and NMA (32.0 ± 0.2 °C), which freezes at 26–28 °C. Solutions were deoxygenated by bubbling purified dinitrogen (MG Industrial Gases, boiling liquid N_2).

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Corrections for *iR* drop were estimated from the dependence of ΔE_p on $(|i_{p,a}|+|i_{p,c}|)$ for a Nernstian $n=1$ process in each of the different solvents, using $[Fe(Bipy)_3][BF_4]_2$ and $[Ru(Bipy)_3][PF_6]_2$. These corrections are based on a modification of the method of Parker [7], using the net cyclic voltammetric current rather than just the cathodic current to calculate values for the solution resistance. Viscosity measurements were made with a Cannon model 50 K677 viscometer for 0.1 M $[NBu_4][PF_6]$ solutions at 25.0 (or 32.0) ± 0.2 °C, and diffusion coefficients were calculated from the rotating disk polarography data by applying the Gregory–Riddiford method [8] to the limiting currents obtained at 2400 rpm. Elemental microanalyses were performed by Canadian Microanalytical Service Ltd. and Robertson Laboratory, Inc.

$[Ru(Bipy)_3][PF_6]_2$ was obtained by metathesis of the chloride salt, prepared in turn according to the literature procedure [9] and dried *in vacuo* et 155 °C. *Anal.* Calc. for $[Ru(Bipy)_3][PF_6]_2$, $C_{30}H_{24}N_6RuP_2F_{12}$: C, 41.9; H, 2.81; N, 9.78. Found: C, 41.8; H, 2.78; N, 9.66%.

Electrochemistry

The electrochemical behaviour of the $[Ru(Bipy)_3][PF_6]_2$ was examined using cyclic voltammetry. The Ru(II) to Ru(III) oxidation process involves the straightforward removal of a metal t_{2g} electron, while in reduction the added electrons are localized on individual ligand π^*-orbitals [10, 11–15], as outlined in Scheme 1.

E_1 $[Ru^{3+}(Bipy)_3]^{3+} + 1e^- \longrightarrow [Ru^{2+}(Bipy)_3]^{2+}$

E_2 $[Ru^{2+}(Bipy)_3]^{2+} + 1e^- \longrightarrow [Ru^{2+}(Bipy)_2(Bipy^-)]^+$

E_3 $[Ru^{2+}(Bipy)_2(Bipy^-)]^+ + 1e^- \longrightarrow [Ru^{2+}(Bipy)(Bipy^-)_2]^0$

E_4 $[Ru^{2+}(Bipy)(Bipy^-)_2]^0 + 1e^- \longrightarrow [Ru^{2+}(Bipy^-)_3]^-$

Scheme 1. The four redox steps for the tris(2,2′-bipyridyl)-ruthenium chelate.

The $[Ru(Bipy)_3]^{2+}$ cation undergoes a reversible one-electron oxidation and a series of reversible one-electron reductions in various non-aqueous solvents. In this context, germane properties of $[Ru(Bipy)_3][PF_6]_2$ are that (i) Ru is generally kinetically inert, (ii) the Ru is coordinatively saturated and should not exhibit any redox-state dependent bonding interactions with the solvent, (iii) several redox states exhibiting Nernstian behaviour are examinable using cyclic voltammetry and rotating disk polarography, (iv) the hexafluorophosphate salt affords adequate solubility in a broad range of solvents, and (v) Bipy (and $Bipy^{\bullet-}$) ligands seem relatively unreactive.

The consequences of differing solvent medium are related to the various approaches that historically have been taken by different groups of workers with regard to the connections amongst the free energies of transfer of ions between different solvents, the search for solvent-insensitive reference electrodes and junction potentials, the estimation of individual cation activities in different solvents, and the estimation of solvation free energy values for individual ions. Customarily, variously modified forms of the Born equation have been applied, for instance in computing the free energies of large complex ions such as within the $[Cr(Biphenyl)_2]^{+/0}$, ferricenium/ferrocene (Fc^+/Fc) [16] or other metallocene couples [17]. One of several arguably untenable extrathermodynamic assumptions is then introduced [18], not infrequently (though perhaps paradoxically) that the electrostatic component of the free energy of transfer of the Fc^+ ions is zero, perhaps because of the appeal of the Fc^+/Fc couple as a convenient reference in non-aqueous electrochemistry [19]. More recent work has continued to explore the contributions of solvent properties other than polarity to the redox thermodynamics of metal complexes [20, 21]. The simplest form [22] of the Born equation

$$\Delta G^0_{\text{solv}} = -(Nz^2e^2/8\pi\epsilon_0 r)(1-1/\epsilon)+7.9\ (\text{kJ mol}^{-1}) \qquad (1)$$

describes the standard free energy of solvation in charging a sphere of radius *r* immersed in a uniform continuum of dielectric constant ϵ. This is viewed as an appropriate (though far from precise) approximation of this major contribution to the net solvation free energy [23, 24], and indeed, it has been utilized extensively in modelling of the internal character of proteins [25, 26].

It is thus expected that more polar solvents should stabilize more highly charged Ru–Bipy species like $[Ru(Bipy)_3]^+$ and $[Ru(Bipy)_3]^-$ to a greater extent than less charged ones, such as $[Ru(Bipy)_3]^0$. Therefore, we might expect to observe a decrease in the potential separation $[E_3–E_4]$ as the solvent's bulk dielectric increases, if the free energies of the charged oxidation states $(+1/-1)$ are both consequently lowered relative to that of $[Ru(Bipy)_3]^0$, the approach here being similar to that of Ichimura and Kitagawa and others [23].

The results from the cyclic voltammetry data are presented in Table 1. $[E_3–E_4]$ (Scheme 1) represents the potential separation between the E_3 and E_4 redox steps of the $[Ru(Bipy)_3]$ complex, the $E_{1/2}$ values for the $+1/0$ and $0/-1$ redox couples. To a first approximation, this particular potential difference (i) averages any differential, specific stabilization effect of the solvent on the $+1$ versus the -1 redox states, (ii) approximates the solvent medium as an average dielectric, and (iii) eliminates the problem of attempting to realize a solvent-independent reference electrode which would be necessary if only one redox couple (e.g. the $+1/0$ couple) were examined (*vide infra*).

TABLE 1. Solvent dependence of $[Ru(Bipy)_3]^{n+}$ redox[a]

Solvent	$[NBu_4PF_6]$ (M)	Temp. (°C)	ϵ	$E_{1/2}$[b] (mV)	$E_{1/2}$[c] (mV)	$E_{1/2}$[d] (mV)	$[E_3–E_4]$ (mV)
Pyr	0.02	25	12	−1601	−1810	−2154	344
Pyr	0.10	25	12	−1575	−1796	−2115	319
Pyr	0.26	25	12	−1577	−1818	−2117	299
PrCN	0.10	21	20	−1592	−1795	−2097	302
PhCN	0.10	25	25	−1568	−1789	−2092	303
MeCN	0.02	25	36	−1636	−1840	−2101	261
MeCN	0.05	25	36	−1639	−1838	−2093	255
MeCN	0.10	25	36	−1642	−1831	−2076	245
DMF	0.10	25	37	−1671	−1854	−2108	254
DMSO	0.10	25	47	−1683	−1857	−2100	244
PC	0.10	25	65	−1681	−1854	−2077	224

[a] Potentials at 25 °C in mV vs. Ag^+(0.01 M), $[NEt_4ClO_4]$(0.1 M)/Ag electrode, the potential of which is about +0.54 V vs. the SHE. [b] +2/+1 Process. [c] +1/0 Process. [d] 0/−1 Process.

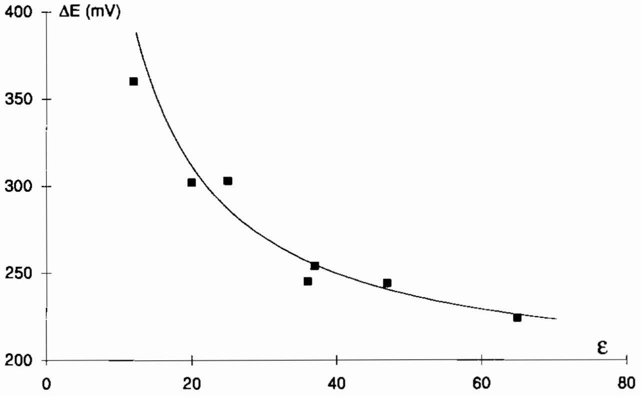

Fig. 1. Relationship between the potential difference $[E_3–E_4]$ (ΔE) for $[Ru(Bipy)_3][PF_6]_2$ and the dielectric constant ϵ of various solvents. The coefficient of determination for the linearized form (in $1/\epsilon$) is 0.91, excluding the datum for $\mu = 0$ pyridine.

From the plot in Fig. 1, it is evident that the Born dielectric function $(1 - 1/\epsilon)$ is well-correlated ($r = 0.96$) with $[E_3–E_4]$ for $[Ru(Bipy)_3]^{+/-}$. The dependence of $[E_3–E_4]$ in Pyr and MeCN on the square root of the ionic strength of the supporting electrolyte also yields the expected linear trend [27], where the increasing salt concentration (i.e. increasing ionic atmosphere) again stabilizes the charged redox states and decreases $[E_3–E_4]$. The effect of the supporting electrolyte is more pronounced in the lower-ϵ solvent Pyr than in the higher-ϵ solvent MeCN as evidenced by the steeper slope of the Pyr data versus the MeCN data (-123 ± 11 versus -92 ± 10 mV $mol^{-1/2}$ $l^{1/2}$). The $[E_3–E_4]$ values for a zero ionic strength medium may be obtained from the ordinate intercepts of these data; in Pyr the intercept value is 360 ± 4 mV while in MeCN the value is 275 ± 2 mV. However, the effect of the ionic strength on the net solution polarity is of course much less significant in higher dielectric solvents like MeCN.

Measurement of the experimental values for the potential separation in solvents with extremely large dielectric constants (about double that of water) was non-trivial. In NMF and NMA, an irreversible chemical reaction following the electrochemical generation of the $[Ru(Bipy)_3]^-$ anion was observed. The kinetics of this reaction were examined in NMA at 32 °C by cyclic voltammetry. At scan rates below 0.5 V s^{-1} the process is under kinetic control, while faster scan rates ($v > 1$ V s^{-1}) bring the process under diffusion control. The application of appropriate diagnostic criteria to the cyclic voltammetry data, taken over a broad range of scan rates ($0.01 < v < 20$ V s^{-1}), verified this to be an E_rC_i mechanism [28]. The rate constant for this following reaction, k_f, was determined by the method of Nicholson and Shain [29] from the $i_{p,a}/i_{p,c}$ data [30], the mean value of k_f being 0.31 ± 0.15 s^{-1}. It thus appears that these lower oxidation levels are more kinetically labile than Ru(II) or Ru(III), so that the most polar solvents may be Lewis basic enough to effect fast substitution at Ru (or perhaps react with $Bipy^{\bullet -}$).

The diffusivity constant ($D\eta$) values (Table 2) are in good internal agreement, with a mean value across the solvent series (exclusive of NMF and NMA) of 3.4 ± 0.1 ($\times 10^{-8}$ g cm s^{-2}). The indication is that $[Ru(Bipy)_3][PF_6]_2$ is behaving rather uniformly in a wide range of solvents with varying dielectric constant and donor/acceptor ability properties, with little specific differentiation by the solvents; the noteworthy exceptions are those two in which the chemical following reaction occurs.

When redox potentials for various metal complexes are compared, there are often uncertainties because of $E_{1/2}$ shifts generated by the use of different solvents by different investigators [31], a situation arising commonly from solubility limitations, for example. Such

TABLE 2. Hydrodynamic properties of $[Ru(Bipy)_3]^{2+}$ in various solvents

Solvent[a]	Temp. (°C)	v[b] (cm^2 s^{-1})	10^6 D[c] (cm^2 s^{-1})	η[d] (g s^{-1} cm^{-1})	10^8 $D\eta$ (g cm s^{-2})
Pyr	25	0.0101	3.9	0.00993	3.8
PrCN	25	0.0078	5.7	0.00617	3.5
PhCN	25	0.0138	2.3	0.0138	3.2
MeCN	25	0.0047	9.7	0.00370	3.6
DMF	25	0.0093	3.9	0.00879	3.4
DMSO	25	0.0195	1.6	0.0213	3.5
PC	25	0.0228	1.2	0.0273	3.4
NMF	25	0.0184	2.6	0.0184	4.9
NMA	32	0.0103	1.3	0.0392	4.9

[a] 0.1 M $TBAPF_6$ supporting electrolyte in each case. [b] v is solution kinematic viscosity, η/ρ. [c] Gregory–Riddiford diffusion coefficient from rotating disk polarographic data. [d] Solution η values are better than ±0.2%. $1cP = 10^{-3}$ kg m^{-1} s^{-1}, so the above $D\eta$ values are in units of 10^{-13} kg m s^{-2}.

potential shifts have their origins mainly in (a) variation in solvent polarity, (b) specific peripheral solvation effects, such as donor–acceptor interactions with ligands, and (c) solvent coordination at coordinatively unsaturated metal centres. Correction for, or at least standardization of these has often been sought by referring $E_{1/2}$ values to those observed experimentally for a couple such as Fc^+/Fc, $[Ru(Bipy)_3]^{3+/2+}$ or $[(Biphenyl)_2Cr]^{+/0}$ [16, 17, 19, 32] rather than, for example, disregarding the variation of an SCE's liquid junction potential with solvent. We propose that an allowance for the gross dielectric contribution, (a) above, may be made using the relationships obtained here, with the effective molecular radius in the given solvent being most sensibly estimated from the diffusion coefficient by use of the Stokes–Einstein relationship [33]; the effective hydrodynamic radius of $[Ru(Bipy)_3]^{2+}$ is thus 0.57 nm in comparison to 0.31 nm for Fc. From

$$\delta E \approx 3.64\times10^{10} D\eta(\epsilon_1^{-1}-\epsilon_2^{-1}) \qquad (2)$$

(where δE is the mV shift in $E_{1/2}$ for a ±1/0 molecular couple in passing from a solvent of dielectric ϵ_1 to a solvent of dielectric ϵ_2, the more polar solvent stabilizing the higher-charged state, and $D\eta$ (in g cm s^{-2}; see Table 2) is assumed to be solvent-independent) we therefore estimate that in passing from MeCN ($\epsilon=36$) to PrCN ($\epsilon=20$), the absolute $E_{1/2}$ of the Fc^+/couple would decrease by 38 mV, as opposed to the presumption that it is unchanged [19, 32]. Furthermore, the original proposals [34, 35] that dielectric constant is poorly correlated with $E_{1/2}$ would appear to be vitiated by all the data having been referred to a redox couple (such as $[Biphenyl]_2Cr^{+/0}$), of which the $E_{1/2}$ is assumed to be constant, but which will in fact be dependent on solvent dielectric, so that any effects of ϵ on other $E_{1/2}$ values would thus effectively suffer cancellation.

The local dielectric at a metalloprotein active site

The lower limit of the dielectric constant inside a folded protein has been calculated to fall between 2.5 and 4.0, establishing a quite non-polar environment [25]. The redox potential associable with a metal ion active site will be influenced by the effect of the surrounding medium on the charge of the redox state [36–38]. For example, if a redox center with a formal charge of +1 is buried inside a folded protein, then a one-electron reduction is expected to be associated with a more positive redox potential than the same redox center exposed to an aqueous (or other polar) environment with a high dielectric constant. We suggest that the potential/dielectric correlation above be extended to a metal ion active site in a protein as a factor governing redox state changes of the metal ion. In fact, several reports [36–38] have proposed theoretical models to account for the effect of polar versus nonpolar environment on redox potential. One experimental model, using data from a nickel macrocycle [39] has shown that increasing the solvent polarity indeed stabilizes the charged redox state relative to the uncharged state. Another study [40] estimated the equivalent solution dielectric constant inside an enzyme active site cleft by correlating the stability constants of mixed-ligand complexes in solvents of varying dielectric.

Horse heart cytochrome *c* has a redox potential, $E^{0\prime}$, of approximately +260 mV for reduction of the iron(III) heme active site to the iron(II) oxidation state, representing an overall change in charge at the active site from +1 to 0. (The contribution from the charge of the ionizable propionate side chains is excluded from this argument.) The methionine–octapeptide complex formed by hydrolysis of cytochrome *c* has a redox potential 300 mV more negative; the corresponding $E^{0\prime}$ is approximately −40 mV [36]. The difference in redox potentials is proposed to be due to the removal of the protein 'overcoat' by hydrolysis, exposing the redox center to a high dielectric aqueous environment, which is attributed with lowering the free energy of the exposed active site by stabilizing the higher-charged redox state. The $E^{0\prime}$ values reported for cytochrome *c* and the methionine–octapeptide complex can also be expressed as ΔG^0 values which describe the difference in free energy between two redox states, +1 and 0. The absolute difference between these two ΔG^0 values, $\Delta(\Delta G^0)$, is 300 mV and is a reflection of the difference in the dielectric constants of the media to which the active site is exposed since the electrostatic component was assumed to be the only variable.*

In the cytochrome *c* example, where the ΔG^0 values for the iron(III)/iron(II) heme redox center can be measured in two different dielectric environments, one known (the aqueous environment) and the other unknown (the protein environment), then the latter might be estimated from a linear regression on the data in Fig.1 ($[E_3\text{–}E_4] = -1731\,(1-1/\epsilon)+1942$ mV), which also is an ultimate source of eqn. (2). For example, an aqueous environment has a dielectric constant of about 79, yielding a ΔE^0 value of 230 mV from the plot; the dielectric constant inside the protein is unknown; however, there is a 300 mV-J separation between the two redox situations on the ΔG^0 scale, yielding a ΔE^0 value of 530 mV and consequently a dielectric constant value inside the protein of about 6. An analysis such as this illustrates one source of the 300 mV range in redox

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*The ΔG^0 value is not adjusted for the different Stoke's radius of heme octapeptide, and thus supplies an upper limit to the magnitude of ΔG^0.

potentials observed for different cytochromes possessing similar heme units and axial ligands [36].

In cases where the active site cannot be excised from the protein, a model complex can be used to determine the dielectric constant of the active site. Caution must be exercised, however, since a model complex may not faithfully duplicate every structural detail of the actual protein site. For example, the structure [41] of the blue copper protein, *Pseudomonas æruginosa* azurin has been determined by X-ray diffraction and several structural features of the active site modeled [42] with a Cu(II) coordination complex of irregular geometry. The redox potential of *P. æruginosa* azurin is +377 mV [43], while the model complex has a redox potential of approximately +530 mV in methanol ($\epsilon = 33$) versus the SHE [44]. The ligands incorporated in the model complex differ from those in the protein by the substitution of an *N*-methylbenzimidazole for an imidazole, a thioether for a thiolate* and a water molecule for a peptide carbonyl [45]. The redox potential of the model compound can be adjusted by using the appropriate empirical factors to correct for the substitution of thioether for thiolate [46], *N*-methylbenzimidazole for imidazole [47] and recognizing that the $D\eta$ values of most metal complexes are about 3×10^{-8} g cm s^{-2}, yielding an $E^{0\prime}$ of +85 mV**. The remaining difference in potential of the model complex and the azurin redox center is 292 mV. Using the method described above, but recognizing the difference in Cu–O distances between protein and model, a minimum effective dielectric constant of 5 is estimated for the medium immediately surrounding the redox center in *P. æruginosa* azurin.

Conclusions

The $E_{1/2}$ values of the redox states of the [Ru(Bipy)$_3$][PF$_6$]$_2$ complex have been obtained in a series of solvents with varying dielectric constants. The potential separation defining the uncharged redox state has been plotted as a function of the dielectric constant, yielding a relationship which can be utilized as a predictive tool to estimate the effective dielectric constant inside a protein. The dielectric constants of the media surrounding the redox centers of the electron transfer proteins cytochrome *c* and *P. æruginosa* azurin have been estimated to be about 6. In closing, it should be noted that the absolute $E_{1/2}$ of the $\mathrm{Fc^+/Fc}$ couple is solvent dependent and will vary significantly as a function of the dielectric constant of the medium.

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*The Cu ion in *Pseudomonas æruginosa* azurin has a coordination ensemble of one cysteine, one methionine, and two histidine residues in addition to a peptide carbonyl. The Cu(II) ion in the model complex is ligated by two thioether sulfurs, two *N*-methylbenzimidazoles and a water molecule.

**The substitution of a methanol for a peptide carbonyl will raise the redox potential by 0.06 V, as judged by the difference in $E_{1/2}$ values observed for tetrabenzo[*b,f,j,n*][1,3,9,13]-tetraazacyclohexadecinecopper(II) nitrate in MeOH and in DMF [49].

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