Self-exchange electron transfer in high oxidation state non-oxo metal complexes: amavadin†

Jeremy Lenhardt,[a] Bharat Baruah,[b] Debbie C. Crans*[b] and Michael D. Johnson*[a]

Received (in Berkeley, CA, USA) 27th July 2006, Accepted 20th September 2006
First published as an Advance Article on the web 12th October 2006
DOI: 10.1039/b610751f

The electron transfer self-exchange rate constant between the oxidized and reduced forms of amavadin equals ~1 × 10^5 dm^3 mol^{-1} s^{-1} at 25 °C and represents the first unambiguous example for a vanadium(IV/V) couple.

The determination of self-exchange electron transfer rate constants for vanadium(IV/V) couples remains a challenging problem that is overcome in studies of the natural product, amavadin. Two major impediments are: (1) coordination geometry changes between these two states[1] and (2) a competing inner-sphere pathway through their "yl" type oxygens.[2] These have led to inconsistent estimates of self-exchange rate constants for hydroxyoxovanadate(IV/V) of $\sim 10^{-3}$ and $\sim 10^3$ dm^3 mol^{-1} s^{-1}.[3,4] In amavadin the metal coordination geometry does not change when oxidized from the +4 to the +5 oxidation states.[5] Furthermore both amavadin and its oxidized form lack an "yl" type oxygen.[5] As a result, amavadin is an ideal system in which an unambiguous self-exchange rate constant may be determined for a vanadium(IV/V) couple.

Amavadin possesses an eight-coordinate, non-oxo vanadium center coordinated to two tetradentate ligands, 2,2′-(hydroxyimino)dipropionate (hidpa).[5] The unusual structure of this compound, its presence in mushrooms and its intriguing reactivity, including oxygen activation, have maintained scientists' interest in this class of compounds for decades.[6] Because vanadium forms very strong high oxidation state oxo-metal complexes, outer-sphere electron transfer studies of these systems are often problematic, but can be accessed with this ligand. Since additional metal ions such as Mo,[7] Ti,[8] Zr,[8] and others[9] yield similar coordination complexes, analogous studies may also be carried with other high oxidation state nonoxo-metal complexes with this ligand.

Before a fundamental kinetic study of amavadin's redox reactions was undertaken, the reaction stoichiometries were determined. Job plots for the oxidation of $[V(hidpa)_2]^{2-}$ with Ce^{4+} or $[IrCl_6]^{2-}$ and the reduction of $[V(hidpa)_2]^{-}$ by ascorbic acid (H_2Asc) in aqueous media all showed simple 1 : 1 (eqn 1 and 2) or 2 : 1 (eqn 3) stoichiometries.

$$[V(hidpa)_2]^{2-} + Ce^{4+} \rightarrow [V(hidpa)_2]^{-} + Ce^{3+} \quad (1)$$

$$[V(hidpa)_2]^{2-} + [IrCl_6]^{2-} \rightarrow [V(hidpa)_2]^{-} + [IrCl_6]^{3-} \quad (2)$$

$$2[V(hidpa)_2]^{-} + H_2Asc \rightarrow 2[V(hidpa)_2]^{2-} + Asc + 2H^{+} \quad (3)$$

While the Ce^{4+} oxidation rates were too fast to measure, the oxidation stoichiometry is truly 1 : 1 which has been used by others[10] to produce vanadium(V) containing amavadin. The reaction kinetics for eqn 2 and 3 each showed a first order dependence on both the vanadium complex and the oxidant (or reductant). No hydrogen ion dependence was observed for the $[IrCl_6]^{2-}$ oxidation between 0.10 mol dm^{-3} HCl ($k = 3.2 \pm 0.3 \times 10^6$ dm^3 mol^{-1} s^{-1}) and 0.0010 mol dm^{-3} HCl ($k = 3.3 \pm 0.2 \times 10^6$ dm^3 mol^{-1} s^{-1}). This is expected since amavadin has no site for protonation over this pH range. The following rate law can be written, eqn 4.

$$d[V(V)]/dt = k_{Ir}[V(hidpa)_2{}^{2-}][IrCl_6{}^{2-}] \quad (4)$$

In contrast, in the ascorbic acid reduction of oxidized amavadin, a simple inverse dependence on H^+ was observed, Fig. 1. A rate law consistent with these observations can be written, eqn 5.

$$-d[V(V)]/dt = k_{asc}[V(hidpa)_2{}^{-}][H_2Asc][H^+]^{-1} \quad (5)$$

The zero y-intercept suggests that reduction proceeds solely *via* monohydrogen ascorbate, $HAsc^-$, since amavadin has no acidic hydrogens in the pH range studied, Scheme 1.

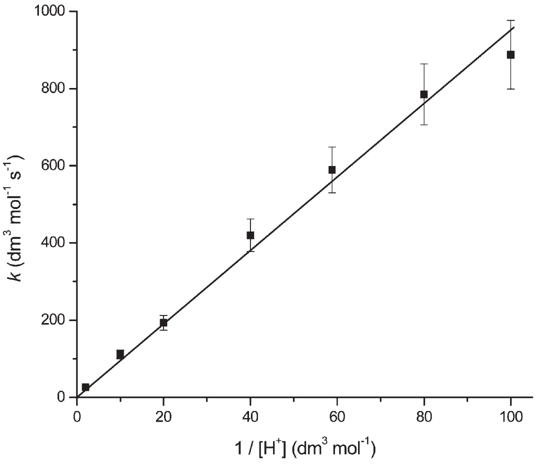

Fig. 1 Inverse hydrogen ion dependence of ascorbic acid reduction of amavadin. Conditions: I = 1.0 mol dm^{-3} LiCl, T = 25.0 °C.

---

[a] *Department of Chemistry and Biochemistry, New Mexico State University, Las Cruces, New Mexico, USA. E-mail: johnson@nmsu.edu; Fax: +1 505 646 2394; Tel: +1 505 646 3627*
[b] *Department of Chemistry, Colorado State University, Fort Collins, Colorado, USA. E-mail: crans@lamar.colostate.edu; Fax: +1 970 491 1801; Tel: +1 970 491 7635*

† Electronic supplementary information (ESI) available: Job plots, kinetic data. See DOI: 10.1039/b610751f

$$\mathrm{H_2Asc} \rightleftarrows \mathrm{H^+} + \mathrm{HAsc^-} \qquad K_{a1}$$

$$\mathrm{HAsc^-} + [\mathrm{V(hidpa)_2}]^- \rightarrow [\mathrm{V(hidpa)_2}]^{2-} + \mathrm{HAsc^\bullet} \qquad k_a$$

$$\mathrm{HAsc^\bullet} + [\mathrm{V(hidpa)_2}]^- \rightarrow [\mathrm{V(hidpa)_2}]^{2-} + \mathrm{H^+} + \mathrm{Asc} \qquad \text{fast}$$

Scheme 1

Based on Scheme 1, and using the pK_{a1} for ascorbic acid, 4.17,[11] a second order rate constant can be calculated since $k_{asc} = K_{a1}k_a$. The rate constant is given in Table 1.

Assuming that both these reactions are outer-sphere electron transfer processes allows the use of Marcus theory to calculate a self-exchange rate constant, k_{22}, for the V(IV/V) couple using the physical data provided in Table 1.[12] Values for k_{22}, of 1.6×10^4 and 2.8×10^4 dm^3 mol^{-1} s^{-1}, respectively, were calculated for the iridium and ascorbate reactions. These two rate constants are self-consistent and indicate the electron transfer reactions are adiabatic in nature.

In addition to the Marcus estimations, a direct measurement was also carried out using ^{51}V NMR line broadening.[2] The vanadium(V) form of amavadin was produced by addition of one equivalent of Ce(IV) to a solution of amavadin. Fig. 2 shows the ^{51}V spectrum of oxidized amavadin in D_2O at acidic pH. Since a racemic mixture of the hidpa ligand was used to synthesize the complex, the three signals observed presumably represent three different isomers of the oxidized form of amavadin. The ^{51}V line broadening experiment measures the line broadening induced by vanadium(IV) of each signal. Fig. 2 (insert) shows that the amount of broadening is directly proportional to the amavadin (vanadium(IV)) concentration. A value for k_{22} can be calculated from the slope of these lines, Table 2.[13,14] An average self-exchange rate constant of $1 \pm 0.5 \times 10^5$ dm^3 mol^{-1} s^{-1} was observed for each isomer. Within experimental error, there was no difference in self-exchange rate constants for these three isomers.

Table 1 Kinetic and thermodynamic data for amavadin redox reactions

Reactant	$k_{12}{}^a$/dm^3 mol^{-1} s^{-1}	K_{11}/dm^3 mol^{-1} s^{-1}	$E°$/V, NHE	$k_{22}{}^b$/dm^3 mol^{-1} s^{-1}
$\mathrm{HAsc^\bullet/HAsc^-}$	1.4×10^5	$1.0 \times 10^{5\,c}$	0.70^d	2.8×10^4
$[\mathrm{IrCl_6}]^{2-}$	3.2×10^6	$2.0 \times 10^{5\,e}$	0.96^f	1.6×10^4

[a] $k_{12} = k_a$ or k_{Ir} in text, T = 25.0 °C, I = 1.0 M (LiCl). [b] Calculated using $E°$ ($\mathrm{V^{V/IV}}$) = 0.75 V, NHE, ref. 3. [c] See ref. 18. [d] See ref. 19 for the $\mathrm{HAsc^\bullet/HAsc^-}$. [e] See ref. 20. [f] See ref. 21.

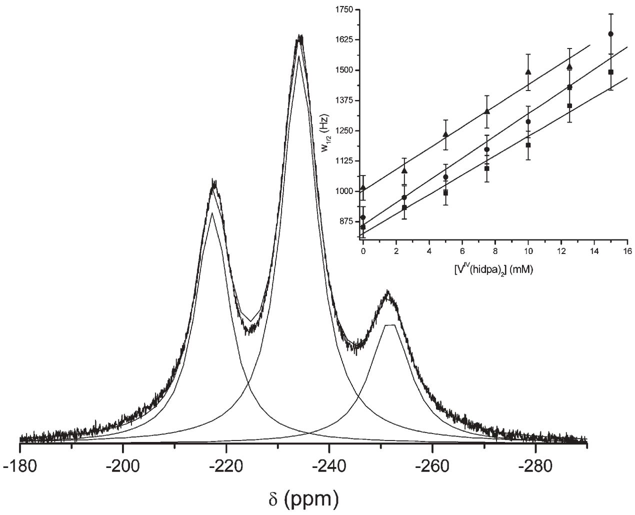

Fig. 2 The ^{51}V NMR spectrum of 0.050 mol dm^{-3} oxidized amavadin, $VOCl_3$ used as reference. Conditions: 0.10 mol dm^{-3} HCl, I = 1.0 mol dm^{-3} LiCl, T = 25.0 °C. Insert: line width broadening as a function of vanadium(IV) concentration. Inset linear fits correspond to: −252 ppm ▲, −234 ppm ●, −217 ppm ■.

The line broadening experiment was carried out at 0.10 and 10^{-3} mol dm^{-3} HCl. As found for the iridium(IV) oxidation study above, no difference was observed, thereby eliminating a proton dependence in this acid range. This observation supports Scheme 1 where the observed proton dependence was ascribed to the deprotonation of ascorbic acid and not deprotonation of amavadin.

Due to the aforementioned problems in determining self-exchange rate constants for vanadium(IV/V) couples, there is a paucity of data for comparison. The self-exchange electron transfer rate constant for aqueous alkaline vanadium(IV/V), $[\mathrm{VO(OH)_3}]^{0/-}$, has been reported using the Marcus cross relation. Two very different values were reported, ($k_{22} \sim 10^{-3}$ dm^3 mol^{-1} s^{-1}) and ($k_{22} \sim$ 10–10^3 dm^3 mol^{-1} s^{-1}).[3,4] The inconsistency was attributed to non-adiabaticity of the cross reactions.[3] In contrast, the self-exchange rate constants in the present study, obtained by both Marcus calculation and direct measurement, vary by less than a factor of four. Despite the ambiguity in the values for $[\mathrm{VO(OH)_3}]^{0/-}$, the self-exchange rate constant in the amavadin system is at least 2 orders of magnitude higher than the corresponding aqueous oxohydroxide couple. This reflects the smaller structural differences between the oxidized and reduced forms of amavadin than those in the aqueous vanadium(IV/V) system.[2] These smaller changes reduce the inner sphere reorganization energy barrier and thereby increase the self-exchange rate constant for amavadin.

Iron containing enzymes have been reported to enhance biological electron transfer processes compared to aqueous iron. For example, the observed self-exchange rate constant for the $[\mathrm{Fe(OH_2)_6}]^{2+/3+}$ couple is 33 dm^3 mol^{-1} s^{-1} [15] whereas for the cytochrome c couple, rate constants above 10^4 dm^3 mol^{-1} s^{-1} are reported.[16,17] These rate enhancements have been attributed primarily to reductions in reorganization energies within the protein matrix.[17] Similarly, the natural product, amavadin, shows significantly enhanced electron transfer processes compared to the aqueous vanadium(IV/V) system.

In summary, this work provides a self-consistent vanadium(IV/V) self-exchange rate constant, $k = 1.0 \pm 0.2 \times 10^5$ dm^3 mol^{-1} s^{-1} using Marcus theory and line broadening experiments. As the first example of a non-oxo vanadium(IV/V) redox system in aqueous

Table 2 Self-exchange rate constants for amavadin enantiomers

Isomer (resonance frequency, ppm)^a	$k_{22}{}^b$/dm^3 mol^{-1} s^{-1}
−217	$1.0 \pm 0.5 \times 10^5$
−234	$1.2 \pm 0.5 \times 10^5$
−252	$1.3 \pm 0.5 \times 10^5$

[a] Chemical shifts reported in reference to $VOCl_3$, 50 mM amavadin used for kinetic study. Conditions: 0.10 mol dm^{-3} HCl, I = 1.0 mol dm^{-3} LiCl, T = 25.0 °C. [b] Calculated as in ref. 13.

media, it is significantly faster than the oxo containing analog. The electron transfer enhancement observed for amavadin should be considered in elucidation of its biological function.

Notes and references

1 D. C. Crans, J. J. Smee, E. Gaidamauskas and L. Q. Yang, *Chem. Rev.*, 2004, **104**, 849.

2 K. Okamoto, W. Jung, H. Tomiyasu and H. Fukutomi, *Inorg. Chim. Acta*, 1988, **143**, 217; C. Guiliano and H. McConnell, *J. Inorg. Nucl. Chem.*, 1959, **9**, 171.

3 D. H. Macartney, *Inorg. Chem.*, 1986, **25**, 2222.

4 D. H. Macartney, A. McAuley and O. A. Olubuyide, *Inorg. Chem.*, 1985, **24**, 307.

5 E. M. Armstrong, R. L. Beddoes, L. J. Calviou, J. M. Charnock, D. Collison, N. Ertrok, J. H. Naismith and C. D. Garner, *J. Am. Chem. Soc.*, 1993, **115**, 807.

6 E. Bayer and H. Kneifel, *Z. Naturforsch., B*, 1972, **27**, 207; M. F. C. Guedes da Silva,, J. A. L. da Silva, J. J. R. Fraústo da Silva, A. J. L. Pombeiro, C. Amatore and J. N Verpeaux, *J. Am. Chem. Soc.*, 1996, **118**, 7568; R. Gillard and R. Lancashire, *Phytochemistry*, 1984, **23**, 179; E. Bayer and H. Kneifel, *J. Am. Chem. Soc.*, 1986, **108**, 3075; E. Bayer, E. Koch and G. Anderegg, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 545; R. Berry, E. M. Armstrong, R. L. Beddoes, D. Collison, S. N. Ertok, M. Helliwell and C. D. Garner, *Angew. Chem., Int. Ed.*, 1999, **38**, 795; C. D. Garner, E. M. Armstrong, R. E. Berry, R. L. Beddoes, D. Collison, J. J. A. Cooney, S. N. Ertok and M. Helliwell, *J. Inorg. Biochem.*, 2000, **80**, 17; E. Armstrong, D. Collison, N. Ertok and C. D. Garner, *Talanta*, 2000, **53**, 75; M. Nawi and T. Reichel, *Inorg. Chim. Acta*, 1987, **136**, 33; G. S. Mishra and A. J. L. Pombeiro, *J. Mol. Catal. A: Chem.*, 2005, **239**, 96.

7 H. Yadav, E. M. Armstrong, R. L. Beddoes, D. Collison and C. D. Garner, *J. Chem. Soc., Chem. Commun.*, 1994, 605.

8 S. M. Harben, P. D. Smith, M. Helliwell, D. Collison and C. D. Garner, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1897.

9 P. D. Smith, S. M. Harben, R. L. Beddoes, M. Helliwell, D. Collison and C. D. Garner, *J. Chem. Soc., Dalton Trans.*, 1997, 685; S. M. Harben, P. D. Smith, R. L. Beddoes, D. Collison and C. D. Garner, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1897; S. M. Harben, P. D. Smith, R. L. Beddoes, D. Collison and C. D. Garner, *J. Chem. Soc., Dalton Trans.*, 1997, 4517.

10 P. D. Smith, R. E. Berry, S. M. Harben, R. L. Beddoes, M. Helliwell, D. Collison and C. D. Garner, *J. Chem. Soc., Dalton Trans.*, 1997, 4509.

11 *The Merck Index, 12th Edition*, ed. S. Budavari, M. J. O'Neil, A. Smith, P. E. Heikelman and J. F. Kinnerary, Merck & Co., Inc., Whitehouse Station, NJ, 1996.

12 The relationship $k_{12} = (k_{11}k_{22}K_{12}f_{12})^{1/2}$ was used to calculate the value of k_{22} for the amavadin couple. J. H. Espenson, *Chemical Kinetics and Reaction Mechanisms*, 2nd edn, McGraw-Hill, Inc, New York, 1995, p. 243.

13 D. Macartney, *Inorg. Chem.*, 1991, **30**, 3337.

14 P. D. Metelski and T. W. Swaddle, *Inorg. Chem.*, 1999, **38**, 301; H. Tagaki and T. W. Swaddle, *Inorg. Chem.*, 1992, **31**, 4669.

15 G. E. Kozerski, M. A. Fiorentino and M. E. Ketterer, *Anal. Chem.*, 1997, **69**, 783; W. H. Jolly, D. R. Stranks and T. W. Swaddle, *Inorg. Chem.*, 1990, **29**, 1948.

16 D. Cummins and H. Gray, *J. Am. Chem. Soc.*, 1977, **99**, 5158.

17 N. Legrand, A. Bondon and G. Simonneaux, *Inorg. Chem.*, 1996, **35**, 162.

18 D. Macartney and N. Sutin, *Inorg. Chim. Acta*, 1983, **74**, 221.

19 C. Creutz, *Inorg. Chem.*, 1981, **20**, 4452.

20 P. Hurwitz and K. Kustin, *Trans. Faraday Soc.*, 1966, **62**, 427.

21 W. Drury and J. DeKorte, *Inorg. Chem.*, 1983, **22**, 121.