Chemical Education

A CHIMIA Column

Topics for Teaching: Proton-coupled Electron Transfer, Part 1

## Elephants in the Room, Part 1: Protons in Redox Reactions

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Abstract: Many oxidation and reduction reactions involve transfer of both electrons and protons. It is shown how this arises and how the energetics may be understood.

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You may not be familiar with the expression "The elephant in the room". It is used to designate something large and important that has been overlooked, neglected or forgotten. Although its use in English is quite recent, the origin of the expression is actually Russian: it comes from a fable written in 1814 by Ivan Krylov who wrote a story about a man visiting a museum and noticing a number of tiny things but failing to notice an elephant. I often feel that protons are the elephants in the room when we talk about oxidation and reduction (redox) reactions and these two articles (Part 2 will appear in the March issue) will look a little more closely at the role of protons and electrons in these reactions. Here we will show how electron and proton transfer are often coupled, and in a subsequent Education Column we will look at the dynamics of electron and proton transfer.

Early in their studies students learn that redox reactions involve transfer of electrons from the reductant to the oxidant and how to break down the reaction into two half-reactions such as reactions (1) and (2):

$$O_2 + 4\ e^- + 4\ H^+ \rightarrow 2\ H_2O \qquad (1)$$

$$N_2 + 6\ e^- + 8\ H^+ \rightarrow 2\ NH_4^+ \qquad (2)$$
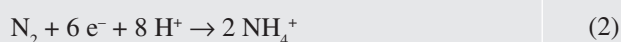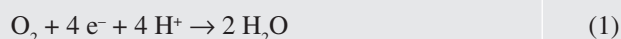
These are very important reactions. Reaction (1) is the basic reaction of oxygen metabolism in the human body. It requires a flow of electrons or current in the average human of about 80 Amperes which is quite considerable. The reverse of this reaction, in photosynthesis, generates the reducing equivalents needed to reduce CO_2 to sugars. Reaction (2) is perhaps even more important since, while life can exist without molecular oxygen, it cannot exist without nitrogen as a source of amino-acids and nucleobases. We notice that both reactions involve electrons *and* protons, and indeed reaction (2) involves *more* protons than electrons. Most of us can recall exercises writing balanced equations and using the Nernst equation to calculate the cell potential and hence the Gibbs (or free) energy change for a redox reaction in a variety of experimental conditions. Later one learns about electron transfer kinetics and Marcus theory, how to measure potentials with cyclic voltammetry and photo-induced electron transfer, all of which seems much more trendy. However, you will notice that in these more advanced subjects the reactions studied are usually simple electron transfer reactions involving couples such as ferrocenium/ferrocene, ferricyanide/ferrocyanide, or $[Ru(bipy)_3]^{3+,2+}$ (bipy = 2,2'-bipyridyl). The protons present earlier have mysteriously disappeared.

Of course not everyone has neglected the protons, and the study of transfer of both protons and electrons forms the field of *proton-coupled electron transfer* and is the subject of this article. Rather surprisingly there are only a few articles on this subject before 1990. A substantial proportion of the early work comes from the bioinorganic field where proton transport is known to be important (for example in reactions such as (1) and (2)). The field took off quite suddenly in 1991 with some 50 papers appearing and since then it has grown regularly, increasing sharply after 2010. In 2019 some 400 papers on the field were published. Some reviews written by pioneers in this field are given in the references.[1] A special issue of *Chemical Reviews* dedicated to the subject appeared in 2010.[2] Here I will try to give a brief introduction to the field.

Coupling of Electron and Proton Transfer

Why are these two processes so frequently coupled? Reduction by adding an electron to a molecule can generate a negative charge and the creation of charge is usually an energy-consuming process; adding a proton balances the negative charge and the coupled process is thus charge neutral. Consider a very simple couple involving oxidation of ferrous ion:

$$Fe^{2+} \rightarrow Fe^{3+} + e^- \qquad (3a)$$
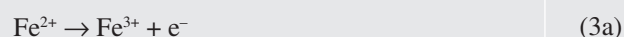
Reaction (3a) does not seem too shocking – as written it appears to take place in the gas phase, but we could simply add aq. or aqu to show it to be in aqueous solution. It is more instructive to write it as reaction 3b which includes the inner hydration shell.

$$[Fe(OH_2)_6]^{2+} \rightarrow [Fe(OH_2)_6]^{3+} + e^- \qquad (3b)$$
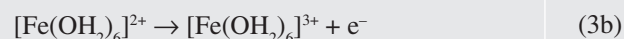
We should not forget the hydration energy of these ions: about 2000 kJ/mol for iron(II) and over 4000 kJ/mol for iron(III). A typical strong chemical bond corresponds to about 400 kJ/mol so there must be a big change in electronic structure associated with the oxidation. Indeed, the iron–oxygen distance changes from 2.21 Å for $[Fe(OH_2)_6]^{2+}$ to 2.05 Å for $[Fe(OH_2)_6]^{3+}$. The cations attract the electrons of the coordinated water molecules: principally the lone pairs of the oxygen but also the electrons of the O–H bond which thus becomes more polar. The greater polarity of the O–H bond for water coordinated to iron(II) leads to a proton being lost by the complex around pH 8; for iron(III) the effect is greater, and a proton is lost around pH 2. So at neutral pH the oxidation reaction is better written as reaction (3c):

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$$[Fe(OH_2)_6]^{2+} \rightarrow [Fe(OH_2)_5(OH)]^{2+} + H^+ + e^- \qquad (3c)$$

The loss of a proton from coordinated water is called the *hydrolysis* of the cation since an O–H bond is broken. You can verify this experimentally: a sample of pure solid ferric nitrate is almost colourless with a pale violet colour due to $[Fe(OH_2)_6]^{3+}$ but if you dissolve it in water you will observe a yellow brown colour due to $[Fe(OH_2)_5(OH)]^{2+}$ and the pH of the solution is strongly acid. You will notice that the simple electron transfer reaction of (3a) has become in (3c) a reaction in which both electron and a proton are transferred. What would happen if we further oxidised the metal to Fe(IV)? The attraction of the metal would be even stronger and species of the type Fe(IV)=O (where a second proton has been lost) are indeed formed as intermediates in many iron-containing enzymes. TiO^{2+} and VO^{2+} are well established species in Ti(IV) and V(IV) chemistry respectively. The loss of protons avoids the build-up of large positive charge.

One Reaction, Three Definitions

You may feel that adding in the protons makes life more complicated, but it can actually simplify some things. At the beginning of their studies, students are told by inorganic chemists that oxidation corresponds to loss of electrons, but organic chemists will often define oxidation as a gain of oxygen (as in the transformation $CH_3CHO \rightarrow CH_3COOH$) *or* a loss of hydrogen (as in $CH_3CH_2OH \rightarrow CH_3CHO$). It is not very satisfactory to use the same word, oxidation, for what appear to be three quite different transformations. If we rewrite these reactions with electron *and* proton transfer they become:

$$CH_3CH_2OH \rightarrow CH_3CHO + 2\ e^- + 2\ H^+ \qquad (4)$$

$$CH_3CHO + H_2O \rightarrow CH_3COOH + 2\ e^- + 2\ H^+ \qquad (5)$$
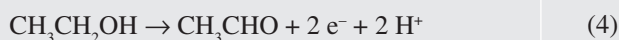
Reactions (4) and (5) involve a loss of electrons and are thus oxidations in the language of inorganic chemistry. The three apparently different definitions are now equivalent. Reactions (4) and (5) may seem a little artificial but many oxidations, including the oxidation of glucose in the body, the principal source of physiological energy, indeed involve separate transfer of protons and electrons.

Looking at Energies

We can look at the energetics of proton-coupled electron transfer using a *square scheme* as shown in Scheme 1 for the oxidation of iron(II) described in reaction (3c). Electron transfer processes correspond to horizontal shifts and proton transfers to vertical shifts. Note that it is not necessary for electron and protons to have the same origin or destination. In this example the electron comes from an iron atom and the proton from coordinated water. In reactions studied by electrochemistry, the electron is exchanged with the electrode while the proton is usually exchanged with the solvent.
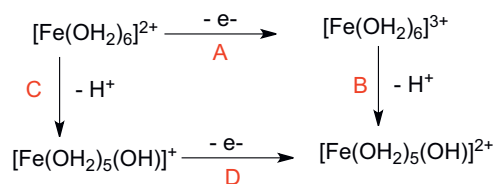

Scheme 1. A square scheme for a proton-coupled electron transfer reaction.

In the example above, the reaction could occur in the sequence A – B or C – D; the overall energy change must be the same. We saw above that reaction B is more favourable than reaction C, so reaction D must be more favourable than reaction A. The negative free energy change of B makes the hydrolysed species $[Fe(OH_2)_5(OH)]^{2+}$ more stable than the simple ferric aqua-ion. Oxidation of iron(II) will be easier if preceded by hydrolysis.

Multi-electron Reactions

Reactions involving the transfer of several electrons and protons will take place in many steps which may be represented by an expanded square scheme (Scheme 2).
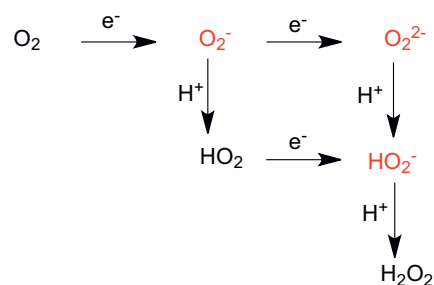
Scheme 2. A square scheme for a two electron transfer reaction. Intermediate unstable species in red may be stabilised by coordination to metal ions.

It is favourable to accompany one electron reduction with protonation in order to avoid the generation of highly charged species such as O_2^{2-}. Positively charged species other than protons can of course equally be used to stabilize otherwise unstable intermediates and metal cations are frequently used for this in enzymes which catalyse reactions of molecular oxygen since they can stabilize species such as O_2^- and O_2^{2-} which are then protonated in subsequent steps.

In conclusion, redox reactions are not simply a question of electron accounting but must also take into account the protonation equilibria if one is to understand the free energy changes.

[1] a) M. H. V. Huynh, T. J. Meyer, *Chem. Rev.* **2007**, *107*, 5004; b) D. R. Weinberg, C. J. Gagliardi, J. F. Hull, C. F. Murphy, C. A. Kent, B. C. Westlake, A. Paul, D. H. Ess, D. G. McCafferty, T. J. Meyer, *Chem. Rev.* **2012**, *112*, 4016; c) J. M. Mayer, *Ann. Rev. Phys. Chem.* **2004**, *55*, 363; d) R. I. Cukier, D. G. Nocera, *Ann. Rev. Phys. Chem.* **1998**, *49*, 337; e) S. Hammes-Schiffer, *J. Am. Chem. Soc.* **2015**, *137*, 8860.
[2] *Chem. Rev.* **2010**, *110*, 6937–7099.