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The Thermochemistry of Proton-Coupled Electron Transfer Reagents and its Implications

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1. Introduction

Many, if not most, redox reactions are coupled to proton transfers. This includes most common sources of chemical potential energy, from the bioenergetic processes that power cells to the fossil fuel combustion that powers cars. These proton-coupled electron transfer or PCET processes may involve multiple electrons and multiple protons, as in the $4 e^-$, $4 H^+$ reduction of dioxygen (O_2) to water (eq 1), or can involve one electron and one proton such as the formation of tyrosyl radicals from tyrosine residues (TyrOH) in enzymatic catalytic cycles (eq 2). In addition, many multi-electron, multi-proton processes proceed in one-electron and one-proton steps. Organic reactions that proceed in one-electron steps involve radical intermediates, which play critical roles in a wide range of chemical, biological, and industrial processes. This broad and diverse class of PCET reactions are central to a great many chemical and biochemical processes, from biological catalysis and energy transduction, to bulk industrial chemical processes, to new approaches to solar energy conversion. PCET is therefore of broad and increasing interest, as illustrated by this issue and a number of other recent reviews.^{12–3}

Proton-coupled redox reactions are by no means a new concept. The Nernst equation of 1889 describes how aqueous redox potentials vary with pH when protons are involved. Physical and organic chemists have been studying hydrogen atom transfer reactions of organic compounds for over a century, and a hydrogen atom is simply a proton and an electron. It has more recently been realized that these areas are connected; organic H-transfer reactions are part of a broader class of reactions in which $1 H^+$ and $1 e^-$ are transferred. As a result, the ubiquity of H^+/e^- transfers has come to the forefront of chemistry and biology.

The first issue that needs to be addressed in any PCET process is the thermochemistry of the electron, proton, and PCET processes. While many aspects of PCET are of great interest, from hydrogen tunneling and isotope effects to photoinduced processes, they all rely on knowledge of the thermochemistry. The thermochemical description is essentially a map of the system, showing each of the possible reactant, intermediate and product states where the system can reside (for at least a few vibrational periods), and the energies of each of these states. Having such a map is fundamental to understanding any PCET system.

In particular, the free energies of the various species will, in large part, answer one of the central questions in any PCET process: whether the electron and proton transfer ‘together,’ in a single kinetic step, or whether the process occurs by a sequence of electron transfer (ET) and proton transfer (PT) steps. In many cases, as described below, there is a large thermochemical bias that favors moving the two particles together, in a concerted process, since this can circumvent high energy intermediates formed in elementary ET or PT steps. While ET and PT are two of the most fundamental chemical reactions, the understanding of how H^+ and e^- transfer together is still emerging. In fact, even the concept of ‘transferring together’ can have a number of meanings, as discussed below and in a number of the other reviews in this issue.

This review provides, to the best of our abilities, the current “best” values for the solution thermochemistry of several classes of proton-coupled redox cofactors. Many of these PCET species are either involved in, or have been used to understand, key chemical and biochemical reactions. These thermochemical data can be used, as illustrated below, to analyze the mechanisms of specific H^+/e^- transfer reactions using common ‘square schemes.’ Analogous thermochemical data are available for some biochemical small molecules, allowing us to illustrate that the same approach can be used to analyze biochemical transformations. We begin with a discussion of definitions and thermochemical background.

2. Scope and Definitions

This review tabulates and analyzes the thermochemical properties of reagents that transfer electrons and protons. Our focus is on processes involving $1e^-$ and $1H^+$, and connecting this proton/electron perspective with hydrogen atom transfers and X–H homolytic bond strengths. We do not deal extensively here with processes involving multiple electron and/or proton transfers and heterolytic bond strengths, such as hydride ($2e^-/1H^+$) transfers, although the same type of analysis can be applied. A recent and elegant example can be found in the work of DuBois et al. using of the thermochemistry of H^- , $H^\bullet$, H^+ and e^- transfers to develop new transition metal-hydride catalytic processes.⁵

These H^+/e^- transfer processes all fall under the general term ‘proton-coupled electron transfer’ or PCET. This term has come to encompass any redox process where the rate or energetics are affected by one or more protons, including processes in which protons and electrons transfer among one or more reactants, by concerted or stepwise mechanisms, and processes in which protons modulate ET processes even if they do not transfer.⁶ This very broad definition is not what Meyer and co-workers intended when they coined the term in 1981,⁷ and many current researchers in the field use ‘PCET’ to mean something more specific. However, examination of the large literature citing ‘PCET’ – over 200 papers from 2006 to 2009⁸ – shows that the broad usage has taken hold. Therefore in our view, ‘PCET’ can no longer be used to refer to a single reaction class, and the mechanistic implications of this term have often been diluted. Thus, we support the broad use of PCET given above. We note that Meyer and Costentin have also recently emphasized this broad definition of PCET.¹⁻³

As ‘PCET’ has been used to describe many different redox reactions, researchers have coined new and more specific terms, which has led to some confusion in this area. The variety of nomenclature, while unfortunate, reflects the surge of interest in the field by workers from quite different disciplines, and the variety of PCET phenomena that have been investigated.

2.1 Concerted Proton-Electron Transfer (CPET) vs. stepwise pathways

As originally conceived,⁷ ‘PCET’ referred to reactions where a proton and electron are transferred in a single, concerted step. Since PCET has lost this mechanistic connotation, Savéant and coworkers have proposed a new term, ‘concerted proton-electron transfer’ (CPET), that makes the mechanistic implication explicit.⁹ We support using this term to refer to any chemical reaction where one H^+ and one e^- are transferred in a single kinetic step. CPET is equivalent to the ‘CEP’ term (concerted electron/proton) used by Hammarström and coworkers,¹⁰ and the ‘EPT’ moniker (electron/proton transfer) used by Meyer *et al.*^{1a} CPET (/CEP/EPT) processes contrast with stepwise processes involving either initial ET followed by PT, or PT followed by ET, as shown in Scheme 1. In this and the other Schemes in this review, proton transfer processes are horizontal lines, ET processes are vertical lines, and processes that involve protons and electrons are diagonal lines. Readers should be aware that other workers have chosen other representations that better illustrate their particular concerns (*cf.*, ref. 5).

The stepwise pathways in Scheme 1 for $1H^+/1e^-$ transfer reactions are proton transfer followed by electron transfer (PT-ET) and ET-PT. Many examples of PT-ET, ET-PT, and concerted reactions are known. For instance, the groups of Ingold and Foti have shown that acidic phenols can react by a PT-ET type mechanism termed ‘sequential proton-loss electron transfer’ or SPLET (adding to the list of acronyms).^{11–12} Hammarström *et al.* have shown that the aqueous ruthenium-tyrosine complexes can undergo ET-PT, CPET, or PT-ET processes depending on the pH.^{10–14} ET-PT pathways are particularly well documented in the electrochemical literature, where they are a type of EC mechanism (electrochemical then chemical).¹⁵ The factors that determine which path is followed are discussed in Section 6, below.

2.2 Hydrogen Atom Transfer (HAT)

Hydrogen atom transfer has been studied by physical and organic chemists for over a century.¹⁶ It is key to the rate and selectivity of a variety of free radical reactions, including radical chains as in autoxidation and combustion. The abstraction of $H^\bullet$ from organic compounds by peroxy radicals has been especially widely discussed and researched because they are important to disease states, aging and food preservation.¹⁷

In the older physical-organic literature there was no need to define HAT, as it was self-evident that this referred to reactions involving concerted transfer of $H^\bullet$ from a donor (XH) to an acceptor (Y, Scheme 2).¹⁸ We will use this definition here, noting that ‘concerted’ implies a single kinetic step for transfer of the two particles but does not necessarily imply synchronous transfer. By this definition, HAT is one class of CPET reactions.

In the last 25 years it has been recognized that transition metal coordination complexes and metalloenzymes can undergo HAT reactions, and that there is overlap between traditional HAT reactions and PCET. This has led to the appearance of a number of new definitions and new thinking about HAT.^{19–22} For instance, computationally there is a clear orbital distinction between degenerate $H^\bullet$ exchange between toluene and benzyl radical, versus exchange between phenol and phenoxyl radical.¹⁹ In toluene, the H^+ and e^- start in the same bond and end in the same bond. In the phenol/phenoxyl reaction, however, the proton is in the molecular plane but the transferring electron is in an orthogonal π symmetry orbital.¹⁹ To deal with such distinctions, Meyer *et al.* have proposed to restrict HAT to reactions where “the transferring electron and proton come from the same bond.”^{1–20} This contrasts with his earlier definition that “the term ‘H-atom transfer’ refers to what is transferred between reactants in the net sense and not to the mechanism of the event.”¹⁸ However, the restrictive definition is problematic in many cases. For instance, often the two particles come

from the same bond but are not in the same bond in the product. One example is hydrogen atom abstraction from C–H bonds by compound I in cytochrome P450 enzymes, where the proton transfers from carbon to the oxygen of the ferryl (Fe=O) group but the electron is transferred to the porphyrin radical cation.²³ Under the restrictive “same bond” definition the reaction would be HAT in the forward direction but not in the reverse, which is a problem. Furthermore, it is often difficult to determine whether the electron and proton are “in the same bond.” In removing H• from phenols, for example, the e^- and H^+ are in the same bond when the O–H bond lies in a plane perpendicular to the aromatic ring, but they are not in the same bond when the O–H lies in the plane of the aromatic ring. In phenol itself the hydrogen is in the plane, but how would reactions of the common 2,6-di-*tert*-butyl-substituted phenols be classified? Similarly, classification of H• removal from the vanadyl hydroxide complex $[(bpy)_2V^{IV}(O)(OH)]^+$ would depend on the $O\equiv V-O-H$ torsion angle.²⁴ In the minimum energy structure, the O–H bond is calculated to have a torsion angle of 45° vs. the orbital with the transferring electron, which precludes conclusions about ‘being in the same bond.’ To avoid these confusions, we prefer the definition implied in Scheme 2, that ‘hydrogen atom transfer’ indicates concerted transfer of H^+ and e^- from a single donor to a single acceptor.

2.3 Separated CPET

There are also concerted transfers of $1e^- + 1H^+$ in which the proton and electron transfer to (or from) different reagents. In Scheme 3, for instance, XH is oxidized with the electron being transferred to oxidant Y while the proton is transferred to base B. One of the more widely discussed biological examples is the photosynthetic oxidation of tyrosine-Z where an electron is transferred to a photoexcited chlorophyll (P680⁺) as the phenolic proton is thought to transfer to a nearby H-bonded histidine residue.²⁵ Babcock’s discussion of the thermochemistry of this process is a landmark in the development of biological PCET chemistry.²⁶ Such ‘separated CPET’ reactions are clearly distinct from HAT reactions. These have also been termed “multisite EPT.”^{1a} However, there are an increasing number of reactions that fall in a grey area between HAT and separated CPET, such as the reaction in eq 3.²⁷ This reaction involves concerted transfer of e^- and H^+ ($H^\bullet$) from the O–H bond of 2,4,6-tri-*t*-butylphenol to a ruthenium(III) complex, so this reaction could formally be called HAT. From another perspective, however, the proton is transferred to a carboxylate oxygen that is 11 Å removed from the ruthenium center that accepts the electron, and there is essentially no communication between these sites,²⁷ so in some ways this is better described as a separated CPET process.

(3)

3. Thermochemical Background

The thermochemistry of a $1H^+/1e^-$ PCET reagent XH in a given solvent is described by five parameters, as shown in Scheme 4. These are: the acidity/basicity of the oxidized and

reduced forms, given by the pK_a s of $XH^{\bullet+}/X^{\bullet}$ and XH/X^- pairs; the reduction potentials of the protonated and deprotonated substrate, $E^\circ[XH^{\bullet+}/XH]$ and $E^\circ[X^{\bullet}/X^-]$, and the homolytic bond dissociation free energy, the BDFE (see below). All of these parameters are free energies, and it is simple to convert them all into the same units (eqs 4 and 5, where R is the gas constant, T = temperature, and F = Faraday constant). The E° is a free energy for the chemical reaction that is the sum of the half reaction of interest, such as $X^{\bullet} + e^- \rightarrow X^-$, and the half reaction for the standard redox couple (NHE for aqueous values). For a reaction such as $HX + Y \rightarrow X + HY$, the pK_a and E° values for the HX and HY systems determine the free energies of PT, ET, and $H^\bullet$ transfer steps.

$$\begin{aligned}\Delta G^\circ_{PT} &= -RT\ln(K_a) = 2.303RT(pK_a) \\ &= -(1.37 \text{ kcal mol}^{-1})pK_a = -(5.73 \text{ kJ mol}^{-1})pK_a \quad (\text{at } 298 \text{ K})\end{aligned}\quad (4)$$

$$\Delta G^\circ_{ET} = -FE^\circ = -(23.06 \text{ kcal mol}^{-1}\text{V}^{-1})E^\circ = -(96.48 \text{ kJ mol}^{-1}\text{V}^{-1})E^\circ \quad (5)$$

The pK_a values in many cases can be determined by titration either versus pH (in aqueous media) or versus a standard acid or base (in organic solvents). As discussed below in more detail, there are extensive acid/base data available in organic solvents from the respective work of Izutsu,²⁸ Bordwell²⁹ and Kütt.³⁰ The redox potentials are typically determined electrochemically. The average of the anodic and cathodic peaks in the cyclic voltammogram, $E_{1/2}$, is typically used as a good measure of the thermodynamic potential E° .³¹ Parenthetically, we note that it is strongly preferred to reference non-aqueous potentials to the ferrocene ($\text{Cp}_2\text{Fe}^{+/0}$) couple.³² Aqueous potentials are reference to normal hydrogen (NHE) in this review. Useful conversions between common electrochemical references are available for acetonitrile³³ and water³⁴ and potentials of $\text{Cp}_2\text{Fe}^{+/0}$ in organic solvents versus aqueous NHE have been reviewed.³⁵

The thermodynamic parameters E° and pK_a , if they are to be used in the same Scheme or equation, should be determined under conditions that are as similar as possible. For instance, if the electrochemical data are determined using solutions containing supporting electrolyte (as is typical), then the pK_a values should ideally be determined in the presence of the same electrolyte. Because the data tabulated below often come from different sources and different types of measurements, this requirement for similar conditions is not always met, which introduces some (usually relatively small) uncertainty into any composite values. A valuable check on the consistency of the data can be obtained using Hess' law, which states that the energy change is independent of path, and that the energy change around any closed cycle is zero. This means that there are actually only 3 independent parameters in Scheme 4. It also implies, perhaps counter-intuitively, that in free energy terms the change in the pK_a values upon oxidation is identical to the change in redox potential upon deprotonation (eq 6).

$$2.303RT[pK_a(XH^{\bullet+}) - pK_a(XH)] = F[E^\circ(X^{\bullet/-}) - E^\circ(XH^{\bullet+}/0)] \quad (6)$$

3.1 X–H Bond Dissociation Free Energies

HAT reactions have historically been analyzed using the Bell-Evans-Polyani relation,³⁶ which uses bond dissociation *enthalpies* (BDEs, which are not exactly the same as bond dissociation *energies*³⁷). It is, however, more appropriate to use bond dissociation *free energies* (BDFEs) because all modern theories of ET, PT, and CPET use free energies rather than enthalpies. Our group has shown, for an iron system where the BDE and BDFE are

quite different, that CPET reactivity correlates with the free energy and not the enthalpy.
38·39 The use of BDFEs rather than BDEs is especially important for transition metal complexes because they can have large entropic contributions to the driving force for a PCET reaction.^{39·40}

One of the goals of this review is to encourage the use of solution BDFEs because these directly connect with the free energy of reaction which is the correct driving force. We discourage the (common) use of reduction potentials to describe PCET reagents because the E° or $E_{1/2}$ value does not indicate the proton stoichiometry. As noted above, a reduction potential is the free energy for a particular process and it is strictly speaking meaningful only when the stoichiometry of that process is well defined.

This review tabulates both solution BDFEs and BDEs. Most of the BDFEs are determined from known pK_a and E° following methods developed by Bordwell⁴¹ for organic compounds and later extended by Parker and Wayner⁴² and by Tilset⁴³ (eq 7). The methods are essentially identical, but Bordwell's method was derived explicitly to calculate BDEs while Tilset's derivation perhaps more clearly distinguishes between BDEs and BDFEs. Bordwell and coworkers were the first to popularize this approach and apply it to a range of compounds. They provide valuable discussion of the assumptions and potential errors involved,⁴¹ which were later analyzed in more detail by Parker and Tilset⁴⁴ and others.⁴⁵ It should also be noted that there are examples of the use of pK_a and E° values to derive bond strengths prior to Bordwell's broad use, including work by Breslow as early as 1969⁴⁶ and by Wiberg in 1961.⁴⁷ Similar thermochemical cycles have also been used in gas-phase thermochemical studies for some time.³⁷

This approach to calculating BDFEs uses Hess' Law and the pK_a and E° values on adjacent sides of a square scheme (Scheme 4, eqs 4 and 5). Essentially the same equation can be used for BDEs, with a constant denoted C_H (but see the comments in the next paragraph). The constants C_G and C_H were derived explicitly as described by Tilset,⁴³ and a similar derivation was given earlier by Parker.⁴⁸ A number of slightly different values of C_H can be found in the literature, depending on the assumptions and values used in the derivation.
41·42·43–44 The differences between these values are typically smaller than the estimated uncertainties in the bond strengths derived from this analysis, as briefly discussed in Section 4.1 below.

C_G in a given solvent is equivalent to the $H^+/H^\bullet$ standard reduction potential in that solvent (see Section 5.8.3). Following Tilset,⁴³ C_G includes the free energy for formation of $H^\bullet$ ($\Delta G_f^\circ(H^\bullet_g)=48.59 \text{ kcal mol}^{-1}$),⁴⁹ the free energy of solvation of $H^\bullet$ ($\Delta G_{\text{solv}}^\circ(H^\bullet)$), as well as the nature of the reference electrode. In Parker's early analysis,⁴⁸ $\Delta G_{\text{solv}}^\circ(H^\bullet)$ was approximated using solvation energies of the noble gases. Roduner has now shown that the solvation of $H^\bullet$ is better approximated as that of H_2 .⁵⁰ On that basis, we have calculated revised values for C_G in several different solvents (Table 1),^{39·51} using known values of $\Delta G_{\text{solv}}^\circ(H_2)$.^{52–53} The values for C_G and C_H in water in Table 1 are also different from those reported previously because we have corrected the standard state for $\Delta G_{\text{solv}}^\circ(H^\bullet)$ ($\cong \Delta G_{\text{solv}}^\circ(H_2)$) from 1 atm to 1 M.⁵⁵ These C_G and C_H values are, to the best of our abilities, the most accurate available, and they have been confirmed by comparison with BDEs and BDFEs derived from other methods such as equilibration or calorimetry. Readers should note that the constants in Table 1 in organic solvents are for redox potentials referenced to $CP_2Fe^{+/0}$, because we feel that these are more directly useful than those given previously vs. the standard hydrogen electrode.⁴³

$$\text{BDEF}_{\text{sol}}(X-H)=1.37pK_a+23.06E^\circ+C_{G,\text{sol}} \quad (7)$$

The calculation of bond dissociation *enthalpies* from free energy measurements (pK_a and E°) is accurate *only* when there are no significant entropic effects. Specifically, this analysis requires that the entropies of HX and $X^\bullet$ are essentially equal [$S^\circ(HX)_{\text{solv}} = S^\circ(X^\bullet)_{\text{solv}}$].^{39–40} This issue was discussed early on by Bordwell, Parker and Tilset,^{41–42} and entropic contributions were found to be small for the organic and organometallic systems they studied.^{37–39–40} Recently, however, it has been shown that $S^\circ(HX)_{\text{solv}}$ and $S^\circ(X^\bullet)_{\text{solv}}$ can be very different when the compounds contain high-spin transition metal ions.^{39–40} For such species, BDEs cannot be determined from pK_a and E° values. With the assumption that $S^\circ(HX)_{\text{solv}} = S^\circ(X^\bullet)_{\text{solv}}$, the solution BDE can be calculated from pK_a and E° values or from the $BDFE_{\text{sol}}$ (eqs 8, 9), with the constant C_H given by $C_G - T\Delta S^\circ(H^\bullet)_{\text{solv}}$.

Assuming $S^\circ_{\text{sol}}(HX) = S^\circ_{\text{sol}}(X^\bullet)$, then

$$BDE_{\text{sol}}(X-H) = 1.37pK_a + 23.06E^\circ + C_{H,\text{sol}} \quad (8)$$

$$BDE_{\text{sol}}(X-H) = BDFE_{\text{sol}}(X-H) + (C_{H,\text{sol}} - C_{G,\text{sol}}) \quad (9)$$

Equations 7 and 8 use the thermochemical standard potentials E° which are typically very close to the $E_{1/2}$ values measured by cyclic voltammetry. Bordwell has also shown that useful values can also often be obtained using electrochemical peak potentials from irreversible cyclic voltammograms.⁴¹ However, this introduces an additional uncertainty into the derived values (see Section 4.1). In the thermochemical tables below, it is explicitly noted when the BDFE or BDFE value has been derived using an irreversible peak potential.

A more direct way to determine a BDFE is by equilibration with a standard reagent, for instance, measurement of K_{eq} for $XH + 2,4,6\text{-}^t\text{Bu}_3\text{ArO}^\bullet \rightleftharpoons X^\bullet + 2,4,6\text{-}^t\text{Bu}_3\text{ArOH}$. $RT\ln(K_{\text{eq}})$ is then the difference between the BDFEs of XH and the standard reagent. This approach works very well for stable species such as aminoxyl radicals (Section 5.1) and transition metal complexes (Section 5.10), or for reactions of transients that reach equilibrium faster than they decay. Pedulli and co-workers, for instance, has used this approach to measure the bond strengths in a variety of phenols.⁵⁶ Kreevoy *et al.* used equilibration to measure the relative hydride affinities of NAD⁺ analogs (a type of heterolytic bond strength).⁵⁷

3.1.1 Solution vs. Gas Phase Bond Strengths—CPET reactivity in solution should be analyzed with solution BDFEs, but common tabulations of bond strengths are gas phase BDEs (as in many organic chemistry textbooks⁵⁸). A very extensive tabulation of such BDEs can be found in the recent book by Luo.⁵⁹ Gas phase BDEs are related to gas phase BDFEs by eq 10, using $S^\circ_g(H^\bullet) = 27.42 \text{ cal K}^{-1} \text{ mol}^{-1}$.⁴⁹ As noted above, for small molecules and organic molecules, $S^\circ(X^\bullet) \cong S^\circ(XH)$ because the species are roughly the same size and structure.^{37–40} For instance, $\{S^\circ_g(\text{HO}^\bullet) - S^\circ_g(\text{H}_2\text{O})\} = -1.2 \text{ cal mol}^{-1} \text{ K}^{-1}$,^{49–60} and $\{S^\circ_g(\text{PhO}^\bullet) - S^\circ_g(\text{PhOH})\} = -0.8 \text{ cal mol}^{-1} \text{ K}^{-1}$,⁶¹ so in both cases the magnitude of the $T\{S^\circ(X^\bullet) - S^\circ(XH)\}$ term is less than $0.4 \text{ kcal mol}^{-1}$. Note that when $S^\circ(X^\bullet) = S^\circ(XH)$, $BDFE_g(XH)$ is $8.17 \text{ kcal mol}^{-1}$ less than the corresponding $BDE_g(XH)$.

$$BDFE_g(XH) = BDE_g(XH) - TS^\circ(H^\bullet) - T\{S^\circ(X^\bullet) - S^\circ(XH)\} \quad (10)$$

Gas phase BDFEs are related to solution BDFEs as shown in Scheme 5 and eq 11. Determining the solution BDFE from the gas phase value requires (i) the free energy of solvation of $H^\bullet$ and (ii) the *difference* in the solvation free energies of $X^\bullet$ and XH . $\Delta G_{\text{solv}}^\circ(H^\bullet)$ is approximated as that of H_2 (see above).

$$\text{BDFE}_{\text{solv}}(\text{XH}) = \text{BDFE}_{\text{g}}(\text{XH}) + \Delta G_{\text{solv}}^{\circ}(\text{H}^{\bullet}) + \Delta G_{\text{solv}}^{\circ}(\text{X}^{\bullet}) - \Delta G_{\text{solv}}^{\circ}(\text{XH}) \quad (11)$$

For hydrocarbons and other relatively nonpolar substrates, the free energies of solvation of $\text{X}^{\bullet}$ and XH are close because the closed shell and radical species are approximately the same size and have the same charge. For this situation, $\Delta G_{\text{solv}}^{\circ}(\text{XH}) = \Delta G_{\text{solv}}^{\circ}(\text{X}^{\bullet})$, the difference between the solution and gas phase BDFEs is $\Delta G_{\text{solv}}^{\circ}(\text{H}^{\bullet})$ which is $\cong \Delta G_{\text{solv}}^{\circ}(\text{H}_2)$ (see above). This is, for example, 5.12 kcal mol⁻¹ in MeCN.⁵² For substrates with one H-bond donating/accepting group such as phenol, $[\Delta G_{\text{solv}}^{\circ}(\text{X}^{\bullet}) - \Delta G_{\text{solv}}^{\circ}(\text{XH})]$ can be approximated as the difference in solvation of the hydroxyl/oxy moiety. Following Ingold,⁶² this difference in solvation can be accurately estimated using Abraham's empirical hydrogen bonding model.^{63-64,65} This model relates the hydrogen bond acidity (α_2^{H}) and the hydrogen bond basicity (β_2^{H}) to the strength of a hydrogen bond (eq 12) and its application to estimate $[\Delta G_{\text{solv}}^{\circ}(\text{R}^{\bullet}) - \Delta G_{\text{solv}}^{\circ}(\text{RH})]$ is given in eq 13. We have shown that this procedure gives accurate solution BDFEs for several mono-hydroxylic substrates in several solvents.⁶⁶ However, given the approximations involved, this method should only be used when the relevant thermochemical data for the solvent of interest are not available. This method has been used sparingly in the Tables below and any BDFE estimated in this fashion is given in (parentheses).

$$\Delta G_{\text{HB}}^{\circ} = -10.02\alpha_2^{\text{H}}\beta_2^{\text{H}} + 1.492 \quad (12)$$

$$\Delta G_{\text{solv}}^{\circ}(\text{R}^{\bullet}) - \Delta G_{\text{solv}}^{\circ}(\text{RH}) = -10.02\alpha_2^{\text{H}}(\text{solv})\beta_2^{\text{H}}(\text{RO}^{\bullet}) + 10.02\alpha_2^{\text{H}}(\text{ROH})\beta_2^{\text{H}}(\text{solv}) \quad (13)$$

3.2 PCET Thermochemistry in Aqueous Solutions

In aqueous solution, proton transfer is extremely rapid and electrochemical measurements often give reduction potentials for half reactions including any proton addition or loss. The potential for a half reaction as a function of pH is given by the Nernst equation (eq 14). The Nernst factor RT/F is 59 mV at 298 K, so the potential of a one-electron, one-proton couple ($n = m = 1$) varies 59 mV per pH unit. For such a $1e^-/1\text{H}^+$ couple, the BDFE is simply given by the potential at pH 0 by eq 15, in which the $\text{p}K_{\text{a}}$ is not needed because $E^{\circ}(\text{X}^{\bullet}/\text{XH})$ includes the free energy of addition of the proton. For measurements at other pH's, the BDFE is given by eq 16. The $1.37(\text{pH})$ term in eq 16 in effect extrapolates a $1e^-/1\text{H}^+$ potential at a given pH to the standard state of pH 0.

$$E = E^0 - \frac{RT}{nF} \ln \frac{[\text{H}_m\text{A}^{(n-m)-}]}{[\text{A}][\text{H}^+]^m} \quad (14)$$

or:

$$E = E^0 - \frac{RT}{nF} \ln \frac{[\text{H}_m\text{A}^{(n-m)-}]}{[\text{A}]} - \frac{RT}{F} \frac{m}{n} \text{pH}$$

For a $1e^-/1\text{H}^+$ redox couple using E° at pH = 0:

$$\text{BDFE}(\text{XH}) = 23.06[E^\circ(\text{X}^\bullet/\text{XH})] + 57.6 \text{ kcal mol}^{-1} \quad (15)$$

For a $1e^-/1\text{H}^+$ redox couple using E° at another pH:

$$\text{BDFE}(\text{XH}) = 23.06[E_{\text{pH}}(\text{X}^\bullet/\text{XH})] + 1.37(\text{pH}) + 57.6 \text{ kcal mol}^{-1} \quad (16)$$

Pourbaix diagrams, which plot potential vs. pH, are one form of the thermochemical map described above, and an elegant application of the Nernst equation. Pourbaix assembled a compendium of these diagrams, describing the aqueous redox chemistry of each element.⁶⁷ Figure 1 shows a recent example of a Pourbaix diagram, constructed by Llobet and co-workers for a ligated dimeric ruthenium-aquo complex from electrochemical measurements.⁶⁸ Horizontal and diagonal lines on the diagram indicate the potentials separating the E/pH regions in which the various stable species predominate. As per eq 14, the lines have the slope of m/n and therefore indicate the proton/electron stoichiometry of the electrochemical measurements. For the $1e^-/1\text{H}^+$ couples, the BDFEs can be determined directly from the Pourbaix diagram from eq 16. Vertical lines (and points where diagonal lines change slope) indicate the $\text{p}K_{\text{a}}$ values of the species to the left of the line.

4. Introduction to the Thermochemical Tables

The following sections present an overview of the PCET reactivity of different classes of compounds, such as phenols, hydrocarbons, or transition metal-oxo/hydroxo/aquo complexes. Each section has brief comments about the importance of PCET reactivity of this class of compounds, and then provides an overview and highlights of the data available. Each section concludes with an extensive data Table. To assist the reader looking for a PCET reagent with a particular bond dissociation free energy (BDFE), and to give an overview of the following, this section has a Table with selected compounds from each class and their BDFE values.

The Table in each of the following sections present thermochemical data for PCET reagents from ascorbate to xanthene. They give, when available, the $E^\circ(\text{XH}^{\bullet+}/\text{XH})$, $E^\circ(\text{X}^\bullet/\text{X}^-)$, $\text{p}K_{\text{a}}(\text{XH}^{\bullet+})$, $\text{p}K_{\text{a}}(\text{XH})$, and the solution BDFE and BDE in various solvents (*cf.*, Scheme 4 above). All of the potentials in this review are *reduction potentials*, though arrows in the “square schemes” may appear to indicate oxidation. When the only redox potentials available are irreversible peak potentials from cyclic voltammetry (CV), the values are indicated by *italics* in the Tables. BDFEs and BDEs derived from such irreversible peak potentials should be viewed as more uncertain than those values derived from reversible $E_{1/2}$ measurements. Irreversible peak potentials often depend on the kinetics of the step preceding or following electron transfer and therefore are not necessary characteristic of the thermodynamics. While this is a concern, Bordwell addressed this issue in his early papers^{41,69} and showed that, at least for the systems studied, the use of irreversible potentials gave BDE values in agreement with those from other sources. In some cases, such as for hydrocarbons, gas phase bond strengths are given and the “solvent” is identified as “gas.”

Any value in the Tables below that is taken from the literature has a reference associated with it. Values without citations have been calculated from the other values in the Table; as noted above, there are only three unique values among the five free energy parameters for each compound (listed in a row of a Table or depicted in a square scheme). Typically, the $\text{p}K_{\text{a}}$ and E° values are experimentally determined and we have calculated the solution BDFE and BDE from those values using eqs 7, 8, 15 or 16 above. When E° and $\text{p}K_{\text{a}}$ values are

given in [square brackets], they have been calculated from the other values in the row using Hess' law (eqs 6, 7).

We note that some of the BDEs and BDFEs shown in this review have been revised from those previously reported. This may be due to new values of the pK_a or $E_{1/2}$, or more often to revision of the constants C_G and C_H as discussed above. A few BDFEs measured by equilibration with a standard reagent have been revised because the best BDFE value for the standard has been reevaluated. For instance, BDFEs derived from K_{eq} for $XH + 2,4,6\text{-}t\text{Bu}_3\text{ArO}^\bullet \rightleftharpoons X^\bullet + 2,4,6\text{-}t\text{Bu}_3\text{ArOH}$ may be revised to reflect the updated solution BDFE for 2,4,6-*t*Bu₃ArOH. Our goal has been to assemble a consistent set of values.

Most of the earlier data are reported as BDEs, but based on our recent discovery of large entropic contributions to PCET, we now encourage the use of BDFEs.^{39,40} Readers are urged to pay close attention to this distinction. If only a BDE or a BDFE has been reported, the Tables give the other value calculated using the difference between C_H and C_G (eq 9). As described above, this connection of a bond dissociation *enthalpy* (BDE) with measurements of *free energies* (BDFE, E° , and pK_a) requires the assumption that the entropies of HX and X[•] are equal (eqs 8, 9). Because this assumption does not hold well for some transition metal complexes, the calculation of BDEs in this fashion has not been done in Table 21. In some cases, a BDFE in one solvent has been estimated from a BDFE in a different solvent, using the Abraham model (eq 13); again, in these cases the BDFE is given in parentheses).

4.1 Estimated Errors

The thermochemical data given here come from a wide variety of sources and are derived from a variety of different measurements. It is beyond the scope of this review to provide error analyses for each value presented (particularly in light of the occurrence of systematic errors that have at times affected measurements of BDEs⁷⁰). Instead, we roughly estimate that typical uncertainties in the solution BDFE values given in this review of $\pm 2 \text{ kcal mol}^{-1}$. Accuracies may be better for well-studied, small molecules, particularly in their gas-phase bond dissociation enthalpies. For BDFEs derived from pK_a and $E_{1/2}$ measurements (eq 7 above), our error estimate is based on typical uncertainties in these values, and the uncertainties in the C_G constant. Relative values may be more accurate, as the uncertainty in C_G is eliminated. Bordwell estimated somewhat larger errors ($\leq \pm 3 \text{ kcal mol}^{-1}$) when irreversible peak potentials are used.⁴¹ In some cases, these estimated accuracies may be optimistic. We encourage the interested reader to examine the primary literature. All of the bond strengths are reported here to one decimal place to eliminate ambiguity due to rounding.

5. Thermochemistry of PCET Reagents

5.1 Hydroxylamines

Hydroxylamines and their $1e^-/1H^+$ oxidized partners, aminoxyl radicals, also known as nitroxyl radicals or nitroxides,⁷¹ have received considerable attention in the past 20 years.⁷² Thermochemical data for proton, electron, and H[•] transfers from hydroxylamines are given in Table 3. This section is focused on three of the most well studied hydroxylamine/aminoxyl radical pairs: 2,2'-6,6'-tetramethylpiperidine-1-ol (TEMPOH), *N,N*-di-*tert*-butylhydroxylamine (*t*Bu₂NOH) and *N*-hydroxyphthalimide (NHPI) (Scheme 6).

5.1.1 TEMPO(H) and *t*Bu₂NO(H)—The 2,2'-6,6'-tetramethylpiperidine-1-oxyl radical, TEMPO, and related derivatives have been widely used as spin labels, spin traps, MRI contrast agents, free radical polymerization promoters, and 'green' oxidation catalysts.⁷³

The radicals are typically air-stable, isolable, and commercially available (while the hydroxylamine 2,2',6,6'-tetramethylpiperidine-1-ol, TEMPOH, is reactive with air). The TEMPO/TEMPOH and related redox couples are particularly valuable for PCET studies because of their low O–H bond strengths, and their strong thermochemical bias towards concerted $\text{H}^\bullet$ transfer reactions (as discussed in greater detail below). HAT pseudo-self-exchange reactions of TEMPO and related alkyl aminoxyl radicals have been found to involve significant hydrogen tunneling (as do some cross reactions), in contrast to the related reactions of aryl aminoxyl radicals.^{74,75}

The BDFE and BDE of TEMPOH will serve as benchmarks for some of the following discussion. We have recently critically evaluated the BDE and BDFE of TEMPOH in MeCN and C_6H_6 solvents, using both reported calorimetric measurements⁷⁶ and E° and $\text{p}K_\text{a}$ data (Table 3).⁴⁰ The calorimetric measurements, for diphenylhydrazine + 2 TEMPO $\rightarrow$ azobenzene + 2 TEMPOH, were reinterpreted using the recently revised heat of formation of azobenzene.⁷⁷

The other noteworthy redox reaction of TEMPO is its oxidation to the corresponding nitrosonium cation. The nitrosonium cation has received attention for its superoxide dismutase-type reactivity⁷⁸ and catalytic alcohol oxidations,⁷⁹ both of which can be described as PCET processes. In water $E^\circ(\text{TEMPO}^{\bullet+}) = 0.74 \text{ V}$ (vs. NHE),⁸⁰⁻⁸¹ and in MeCN $E^\circ(\text{TEMPO}^{\bullet+}) = 0.61 \text{ V}$ ⁸² (vs. SCE; better: 0.24 V vs. $\text{Cp}_2\text{Fe}^{+/0}$ 33).

Several 4-substituted derivatives of TEMPO have been investigated, including 4-oxo-, 4-methoxy-, 4-amino-, and 4-hydroxy-TEMPO. Bond strengths for these and other aminoxyls in hexane have been reported by Malievskii *et al.* from kinetic and equilibrium measurements,⁸³ but little acidity or redox potential data are available for these other TEMPO derivatives.

As noted above, the $\text{TEMPO}(\bullet/\text{H}) \text{1H}^+/1\text{e}^-$ couple is an excellent example of a PCET reagent that favors concerted $\text{H}^\bullet$ transfer over stepwise ET-PT or PT-ET pathways. TEMPOH ($\text{p}K_\text{a} = 41$ in MeCN) is a very poor acid and TEMPO ($\text{p}K_\text{a} \sim -4$) is a poor base. Likewise, it is difficult to oxidize TEMPOH to $\text{TEMPOH}^{\bullet+}$ ($E_{\text{p,a}} = 0.71 \text{ V}$ vs. $\text{Cp}_2\text{Fe}^{+/0}$) and quite difficult to reduce TEMPO to TEMPO^- ($E_{\text{p,c}} = -1.95 \text{ V}$). These data indicate that under typical conditions, TEMPO^- and $\text{TEMPOH}^{\bullet+}$, the species at the top right and bottom left of the TEMPO square scheme (see Scheme 4), are high-energy species.

The preference for concerted transfer of $\text{H}^\bullet$ in reactions of TEMPO and TEMPOH can be illustrated by examining the energetics for the different pathways for the TEMPOH + TEMPO self exchange reaction (Scheme 7). HAT from TEMPOH to TEMPO has $\Delta G^\circ = 0$ because it is a degenerate process. In MeCN, initial PT from TEMPOH to TEMPO gives $\text{TEMPO}^- + \text{TEMPOH}^{\bullet+}$. This reaction has an equilibrium constant of 10^{-45} based on the $\text{p}K_\text{a}$ s of 41 and ~ -4 respectively (Table 3), indicating a very unfavorable free energy, $\Delta G^\circ_{\text{PT}} \sim +60 \text{ kcal mol}^{-1}$. Initial ET from TEMPOH to TEMPO is uphill by the same amount ($\sim 2.7 \text{ V}$ from the redox potentials). Note that for the unique case of a self-exchange reaction $\text{XH} + \text{X}$, these two values must be the same, because initial PT and ET both make the same intermediate state, $\text{XH}^+ + \text{X}^-$.⁸⁴ Thus, there is a very large (60 kcal mol^{-1}) bias favoring concerted transfer of e^- and H^+ . The self-exchange reaction occurs readily, proceeding on the stopped flow timescale with an Eyring barrier $\Delta G^\ddagger = 16.5 \text{ kcal mol}^{-1}$ in MeCN.^{38,74} On this basis, the self-exchange cannot be proceeding through an intermediate state that is 60 kcal mol^{-1} above the ground state; the two particles must transfer together. This type of thermochemical argument, probably first applied to PCET by Meyer and coworkers,¹ is quite powerful and is discussed in more detail for cross reactions in Section 6.

5.1.2 *N*-hydroxyphthalimide (NHPI)/phthalimide-*N*-oxyl radical (PINO)—The PINO radical has been broadly explored in organic free radical oxidations,^{85,86} especially as a ‘green’ alternative to the bromide co-catalyst in transition metal-catalyzed autoxidations.⁸⁷ Catalytic oxidations in PINO-containing systems are thought to proceed through a series of H-atom abstraction steps. Despite the wide attention that NHPI/PINO has received, relatively few thermochemical data are available. Koppel and co-workers have determined pK_a values for NHPI in water and DMSO,⁸⁸ and the DMSO value can be used to estimate a pK_a in MeCN.⁸⁹ NHPI is much more acidic than dialkyl hydroxylamines, as would be expected for a phthalimide.

There is little consensus between the published electrochemical studies of NHPI. In MeCN in the absence of base, a broad quasi-reversible oxidation is observed at +1.2 V vs. $\text{Cp}_2\text{Fe}^{+/0}$.⁹⁰ Addition of pyridine bases caused a shift to much lower potentials, which was attributed to the oxidation of deprotonated NHPI (the $\text{NHPI}^{•-}$ couple).^{90–91,92,93} However, this assignment is unlikely since the pyridine bases used ($pK_a = 12–16$ in MeCN³⁰) are not basic enough to deprotonate NHPI to any great extent ($pK_a = 23.5$ in MeCN, see Table 3). Furthermore, the potentials vary with the strength of the added base, with stronger bases leading to lower potentials – by roughly 59 mV per unit change in the pyridine pK_a , as would be expected for a PCET reaction.^{90–91,92,93} These data all suggest that the electrochemical process removes 1H^+ and $1e^-$ from NHPI, not simply an electron. We estimate, based on the reported electrochemical data extrapolated to $pK_a(\text{NHPI}) = 23.5$ (59 mV per pK_a), $E^\circ(\text{NHPI}^{•-}) = -0.1$ V and BDFE = 84.8 kcal mol⁻¹ in MeCN.

Lucarini, Pedulli and co-workers have employed their EPR radical equilibration technique to determine bond strengths (BDEs) of NHPI, substituted NHPI derivatives and other related hydroxylamines.^{94–95} The BDE of NHPI was determined to be 88.1 kcal mol⁻¹ in ^tBuOH solvent.⁹⁴ Later, bond strengths for substituted NHPI derivatives were determined in CH_3CN with respect to the parent NHPI, again using the EPR equilibration technique.⁹⁵ The reference BDE used in that study was 88.1 kcal mol⁻¹, the BDE of NHPI in ^tBuOH. However, based on the E° and pK_a data for NHPI in MeCN, we conclude that the BDE_{MeCN} of NHPI is 1.2 kcal mol⁻¹ higher than the corresponding BDE in ^tBuOH. Thus, BDEs for substituted NHPI derivatives have been adjusted upward by 1.2 kcal mol⁻¹ such that they are relative to the BDE of NHPI in MeCN determined here. One of the great advantages of the EPR equilibration technique is that the BDEs are usually very accurate with respect to each other, so that the uncertainty in the absolute BDE is essentially only dependent upon the accuracy of the reference compound BDE.

5.2 Phenols, Hydroquinones, Catechols and Ascorbate

This section presents thermochemical data for hydroxylic compounds where the OH group is attached to an unsaturated (sp^2) carbon. The redox chemistry of such compounds – phenols, quinones, ascorbate, etc. – has been the subject of intense interest for more than a half century. To give just a few examples, PCET reactions of these compounds are integral to biological energy production (e.g. quinone cycling in photosystems I and II and the bc_1 complex; tyrosine Z in photosystem II),^{106–107,108} biosynthesis (ribonucleotide reductases),¹⁰⁹ antioxidant activity (tocopherols),^{110–111} and food preservation (butylated hydroxytoluene).¹¹² The coverage in this section is not intended to be complete, but is rather focused on representative cases where there are extensive pK_a , E , and bond strength data. A reader interested in a particular substituted derivative that does not appear in Table 4 is encouraged to check the references cited there, and reference 56, as many of the primary papers cover a range of substituents.

5.2.1 Phenol (PhOH)—Phenol has been widely studied as the simplest of the aromatic hydroxylic compounds. The gas-phase O–H BDE in phenol has been a subject of much discussion.^{62,113,114} Heats of formation from the NIST Chemistry WebBook, $\Delta H_{\text{f}}^{\circ}(\text{PhO}^{\bullet}) = 13 \pm 1 \text{ kcal mol}^{-1}$ and $\Delta H_{\text{f}}^{\circ}(\text{PhOH}) = -23.03 \pm 0.14 \text{ kcal mol}^{-1}$, give $\text{BDE}_{\text{g}}(\text{PhOH}) = 88.0 \pm 1 \text{ kcal mol}^{-1}$.^{49,70} This value is in between alternative values of $86.7 \text{ kcal mol}^{-1}$ ¹¹⁴ and $88.7 \text{ kcal mol}^{-1}$.⁶² A clearer value for this important benchmark compound would be valuable.

A wealth of thermochemical data is available for phenols, in particular their acidity [$\text{p}K_{\text{a}}(\text{ArOH})$] and the phenoxyl radical/phenoxide reduction [$E^{\circ}(\text{ArO}^{\bullet}/-)$]. Protonated phenoxyl radicals are typically high energy species with aqueous $\text{p}K_{\text{a}}$ values > 0.115 . The most extensive studies of $E^{\circ}(\text{ArO}^{\bullet}/-)$ are by Bordwell *et al.* for DMSO solutions¹¹⁶ and by Lind *et al.* and Steenken and Neta in aqueous media.^{117,118} The aqueous measurements take advantage of the phenol potential becoming independent of pH above its $\text{p}K_{\text{a}}$ (see Section 3.2 above).

Phenols readily react by hydrogen atom transfer (HAT) and this pathway is implicated in the antioxidant properties of phenols both *in vivo* and *in vitro* (see below).¹¹⁹ For the more acidic phenols, or under basic conditions, a mechanism of sequential proton loss then electron transfer (SPLET) can occur.^{11–12,13} It is less common for phenols to react by initial outer-sphere electron transfer because of the high $E^{\circ}(\text{PhOH}^{\bullet+}/0)$ potentials. The $\text{ArO}^{\bullet}/\text{ArOH}$ potentials (or, better, BDFEs) are often above the thermodynamic requirement for water oxidation, as is necessary for the function of Tyrosine Z in photosystem II, mediating hole transfer from the chlorophyll radical cation to the oxygen evolving complex.

5.2.2 2,4,6-Tri-*tert*-butylphenol (tBu_3PhOH)—4-Substituted-2,6-di-*tert*-butyl-phenols are widely used in the research lab and as food preservatives, especially ‘butylated hydroxytoluene’ (BHT, 4-Me) and ‘butylated hydroxyanisole’ (BHA, 4-MeO). 2,4,6- tBu_3PhOH is an especially interesting and useful reagent for studies of PCET reactions because of the exceptional stability of the phenoxyl radical ($\text{tBu}_3\text{PhO}^{\bullet}$).¹²⁰ The radical is easily prepared from the corresponding phenol using NaOH and $\text{K}_3\text{Fe}(\text{CN})_6$, and can be isolated as dark blue crystals.¹²⁰ As discussed for TEMPOH above, we have recently reevaluated the solution BDE of $\text{tBu}_3\text{PhO}^{\bullet}$ in C_6H_6 to account for recent revision of the thermochemistry of the originally used diphenylhydrazine/azobenzene couple.⁴⁰ Our preferred value is $81.6 \pm 0.4 \text{ kcal mol}^{-1}$.

The $\text{tBu}_3\text{PhO}^{\bullet}/\text{H}$ PCET couple is a very useful benchmark for the determination of bonds strengths in other phenols. The clearest example is Pedulli and co-workers’ EPR method to measure equilibrium constants for $\text{ArOH} + \text{tBu}_3\text{PhO}^{\bullet}$.¹²¹ Please note that here and in Table 4, we have slightly adjusted Pedulli’s reported BDEs to reflect our recent critical evaluation of the BDE (and the BDFE) of tBu_3PhOH .⁴⁰ The EPR equilibration method provides a high degree of precision and the values are, in general, internally consistent.¹²² The values obtained agree very well with those from other methods, such as from E° and $\text{p}K_{\text{a}}$ measurements. For example, the adjusted Pedulli values for $\text{BDFE}(\text{PhOH})$ and $\text{BDFE}(2,6\text{-tBu}_2\text{PhOH})$ in C_6H_6 , = 83.8 and $78.3 \text{ kcal mol}^{-1}$ (Table 4), agree very closely with our conversion of Bordwell’s BDFEs in DMSO (from E° and $\text{p}K_{\text{a}}$ values)¹¹⁶ to C_6H_6 using the Abraham method, 83.7 and $78.1 \text{ kcal mol}^{-1}$, respectively.

5.2.3 Tyrosine—Redox reactions of the amino acid tyrosine are involved in biological energy transduction, charge transport, oxidative stress, and enzymatic catalysis.¹²³ The $1\text{H}^+/1\text{e}^-$ oxidized form, the tyrosyl radical, has been implicated in a variety of enzymatic systems, including ribonucleotide reductases,¹⁰⁹ photosystem II,¹⁰⁶ galactose oxidase,¹²⁴ prostaglandin-H-synthase¹²⁵ and perhaps cytochrome *c* oxidase.¹²⁶ Furthermore, tyrosine

oxidation products are thought to play deleterious roles in various disease states, including atherosclerosis and aging.¹²⁷

The proton-coupled redox chemistry of tyrosine (TyrOH) and related compounds has been widely reported.^{128–129,130,131} In aqueous solutions, the Pourbaix diagram shows a clear 59 mV per pH dependence for the oxidation of tyrosine below pH 10, indicative of a $1e^-/1H^+$ redox couple. As for phenol, above pK_a (tyrosine) the redox potential does not depend on pH because this is the proton-independent $TyrO^\bullet/TyrO^-$ redox couple. Other, more detailed, discussions of aspects of proton-coupled redox chemistry of tyrosine can be found in other contributions to this issue. As an aside, we encourage biochemical studies of PCET to use a nomenclature that explicitly shows the proton, such as 'TyrOH' for tyrosine, to avoid ambiguity. For instance, the commonly used "Y $^\bullet$ " for tyrosyl radicals could refer either to neutral radical $TyrO^\bullet$ or to the typically high-energy radical cation $TyrOH^{+\bullet}$.

5.2.4 α -Tocopherol and Related Phenols— α -Tocopherol (a main component of Vitamin E) is thought to be a key chain breaking antioxidant in biological systems. Since its discovery in 1922,¹³² vitamin E has received considerable attention from chemists, biologists, and clinicians, among others.¹¹⁰ Due to its insolubility in water, several small water soluble analogs such as Trolox C ($(\pm)$ -6-hydroxy-2,5,7,8-tetramethylchromane-2-carboxylic acid) and HPMC (6-hydroxy-2,2,5,7,8-pentamethylchroman) have been developed (Scheme 8; see references 133 and 134). As shown in Table 4, these three phenols show similar thermochemistry in the same solvent. This is in good agreement with their solution kinetic behavior and indicates that the analogs lacking the greasy phytol tails are good models for the redox chemistry of tocopherol. The BDFEs of these phenols are much lower than those of other phenols, by more than 10 kcal mol⁻¹ vs. unsubstituted phenol and by ~2 kcal mol⁻¹ vs. tBu_3PhOH in the same solvent. This relatively weak bond is the origin of the good biological reducing power of vitamin E. The weak bond is a result of the electron-donating substituents, which also reduces the acidity of these phenols. The combination of a weak O–H bond, low acidity, and a high outer-sphere redox potential [E° ($ArOH^{+/0}$)] give these molecules a strong preference to react by concerted transfer of e^- and H^+ (HAT). Njus and Kelley used such reasoning to conclude that Vitamin E donates $H^\bullet$ as opposed to e^- in biological reactions.¹³⁵ A characteristic of these and other systems that prefer to transfer $H^\bullet$ rather than react by stepwise paths (*cf.*, TEMPOH above) is the very large shift of the pK_a upon redox change and (equivalently) the large shift of E° upon protonation: for α -tocopherol, the pK_a changes by 25 units and E° changes by 1.5 V.

5.2.5 Quinones, Hydroquinones and Catechols—The PCET chemistry of hydroquinones and catechols (1,4- and 1,2-dihydroxybenzenes, respectively) is somewhat similar to that of 4-substituted phenols, but more extensive because there are two transferable hydrogen atoms and removal of both leads to stable quinones. This means that instead of the four species of the standard 'square scheme' that are formed upon PT, ET, or CPET from HX (Scheme 4), there are nine species derived from H_2Q , as shown in Figure 2. This is also the case for flavins, which are discussed below. In practice, the cationic forms, $H_2Q^{+\bullet}$, H_2Q^{2+} and HQ^+ , are not involved in typical PCET reactivity because they are high energy species under normal conditions.

In the reactions of the first O–H bond, hydroquinones follow the patterns outlined above for phenols. In general, the pK_a values for H_2Q and the oxidation potential of HQ^- fit on Hammett correlations with other 4-substituted phenols, both in aqueous¹¹⁷ and in organic media.¹¹⁶ For example, the BDFE of the first O–H bond in hydroquinone is 2–3 kcal mol⁻¹ weaker than that of *p*-methoxyphenol. With hydroquinones and catechols, however, loss of $H^\bullet$ yields the semiquinone radical that has a high propensity to lose a second $H^\bullet$.¹⁴⁸ Semiquinones and related species were among the first free radicals to be investigated in

detail: Michaelis' 1935 review in this journal points out that many systems commonly understood as $1e^-$ systems can actually undergo $1e^-$ or $1H^+/1e^-$ redox chemistry, and that the redox properties of semiquinone-type radicals are dependent upon pH – a very early recognition of the importance of PCET in biology.¹⁴⁹

While hydroquinones have reactivity patterns that are in part similar to phenols, with preferential loss of $H^\bullet$, quinones have a different PCET behavior, especially in water. Quinones are typically easily reduced to semiquinone radical anions in water, without the assistance of protons, and the $Q^{\bullet-}$ anions are not particularly basic (Table 6). Therefore quinone cofactors can readily mediate stepwise PCET reactions, with initial electron transfer followed by proton transfer. $Q/Q^{\bullet-}$ interconversion is well understood using semi-classical ET theory.¹⁵⁰ Such stepwise mechanisms have been discussed,¹⁵¹ and an example of stepwise PT-ET of quinones in biology is discussed in Section 6 below.

The aqueous $2H^+/2e^-$ potentials of many quinones have been reported, because they are easily measured and because they are important biological cofactors (ubiquinone, for instance, is so named because it is ubiquitous). Their electrochemistry is generally well behaved,¹⁵³ although there is still much to be learned in this area.¹⁵⁴ The electrochemical data directly give an average BDFE/BDE for each quinone system (Table 5). Interestingly, the average bond strength for most quinones lies between the relatively narrow range of 68 to 75 kcal mol⁻¹.

The *average* O–H bond strengths in Table 5 do not, however, always parallel the individual O–H bond strengths. Using the known pK_a s and reduction potentials for the quinones and semiquinones, the BDFEs (and BDEs) for many hydroquinones can be calculated (Table 6). The power of the thermochemical cycles (Hess' Law) is illustrated by the calculation of the $HQ^\bullet/HQ^-$ reduction potentials (Figure 2), which are difficult to obtain directly because of the rapid disproportionation of semiquinone radicals.¹⁵⁶ It should also be noted that the BDFEs of these quinones do not necessarily reflect the $1e^-$ quinone/semiquinone reduction potentials. For example, tetrachloro-*p*-benzoquinone is 0.5 V more oxidizing than *p*-benzoquinone,¹⁵⁷ even though the average BDFEs are not too different. One electron potentials for a variety of quinones in several different organic solvents are available in reference 157.

The *ortho*-substituted quinone/catechol redox couple has reactivity and thermochemistry that is somewhat distinct from the *para*-quinone/hydroquinone couple. *Ortho*-quinones and catechols (1,2-hydroxybenzenes) are also key biological cofactors, the most widely known of which are the catecholamines dopamine, epinephrine and norepinephrine.¹⁶⁷ The antioxidant and anti-cancer activities of *ortho*-quinone derivatives, known as 'catachins,' have recently received considerable attention.¹⁶⁸ Unfortunately, the data available for catechols are more limited than those for hydroquinones, and thus, the double square scheme in Figure 3 cannot be completely filled in. Still, sufficient results are available to show the important differences between hydroquinones and catechols.

The aqueous $2H^+/2e^-$ potential of catechol¹⁵⁵ indicates an average O–H BDFE of 75.9 kcal mol⁻¹, slightly higher than that of 1,4-hydroquinone (73.6 kcal mol⁻¹). From the known pK_a of the semiquinone¹⁶⁹ and the one electron potential of *ortho*-benzoquinone, the second BDFE is 65.4 kcal mol⁻¹, using eq 7. Thus, the first BDFE in catechol must be 86.2 kcal mol⁻¹ in water. The second O–H BDFEs for the hydroquinone and catechol semiquinones are very similar, 65.5 kcal mol⁻¹ and 65.4 kcal mol⁻¹, respectively.

The thermochemistry of catechols is different from hydroquinones partially due to the availability of an internal hydrogen bond (Scheme 9). The first pK_a of catechol (9.26170) is not too different from the first pK_a in hydroquinone (9.85), and for both the second pK_a is

larger, as expected for deprotonation of an anion. However, the second pK_a for catechol (13.4170) is two pK_a units larger than that of hydroquinone (11.4), because the catecholate is stabilized by the strong intramolecular hydrogen bond.

The intramolecular hydrogen bond appears to be more important in the gas phase and in non-hydrogen bond accepting solvents where it does not compete with hydrogen bonding to solvent. Theoretical work indicates that the intramolecular hydrogen bond in catechol has a free energy of about -4 kcal mol^{-1} and, importantly, that the analogous H-bond in the monoprotonated semiquinone radical is about twice as strong (Scheme 9).^{171,172} Thus the reactivity of catechols can be quite different in non-hydrogen bond accepting solvents vs. water. Lucarini¹⁷³ and Foti¹⁷⁴ have each shown that in non-hydrogen bond-accepting solvents, compounds with intramolecular hydrogen bonds are better $H^\bullet$ donors than analogous species without intramolecular hydrogen bonding. This is opposite to the thermochemistry in water where $BDFE(\text{catechol}) > BDFE(\text{hydroquinone})$.

5.2.6 Ascorbate—Ascorbic acid (Vitamin C) is a ubiquitous biological cofactor that is necessary for human health.¹⁷⁵ Ascorbate has traditionally been thought of as a one-electron reductant, but redox reactions of ascorbate almost always involve the loss of an electron and a proton (or a hydrogen atom), so it is really a PCET reagent. Njus¹⁷⁶ and Tsubaki¹⁷⁷ have shown that ascorbate donates hydrogen atoms in its reactions with cytochrome b_{561} . Njus has also demonstrated this for other ascorbate utilizing enzyme systems.¹⁷⁸ Ascorbate is also likely oxidized by loss of $H^+ + e^-$ in the catalytic cycle of ascorbate peroxidase (APX).¹⁷⁹ HAT from ascorbate may play a role in regeneration of vitamin E (tocopherol) radicals.^{135,180} Investigations from our group have shown that 5,6-isopropylidene ascorbate, a convenient, commercially available organic-soluble analog of ascorbate, reacts with TEMPO, $^t\text{Bu}_3\text{PhO}^\bullet$ and iron-porphyrin models via concerted transfer of $H^\bullet$.^{181,182}

The aqueous thermochemistry of ascorbate is well understood (Figure 4).^{135,183,184} In principle, a nine-membered square could be constructed for ascorbic acid because two electrons and two protons can be removed to make dehydroascorbate. However, similar to hydroquinones, the oxidized forms that have not lost a proton are high-energy species (very acidic) and are not relevant to ascorbate chemistry. Ascorbic acid becomes a stronger reducing agent at higher pH as it is converted to ascorbate (AscH^-) and then the doubly deprotonated form (Asc^{2-}).^{184,185} At physiological pH, AscH^- is the predominant species and the ascorbyl radical ($\text{Asc}^{\bullet-}$) is deprotonated (the pK_a of $\text{AscH}^{+\bullet}$ is -0.45). Therefore, the most important reaction is $\text{AscH}^- \rightarrow \text{Asc}^{\bullet-} + H^+ + e^-$. The thermochemical data for ascorbate and isopropylidene ascorbate in a few different solvents is given in Table 7. The ascorbyl radical rapidly disproportionates with consumption of a proton to give one equivalent of dehydroascorbate (Asc) and ascorbate,¹⁸⁶ so the very weak O–H BDFE of the ascorbyl radical is typically not relevant. Disproportionation is, however, much slower in ‘anhydrous’ solvents.¹⁸²

5.3 Alcohols and Water

Aliphatic alcohols and water have quite different PCET chemistry than the ‘enols’ discussed above (phenols, hydroquinones, catechols and ascorbate). O–H bonds in alcohols are much stronger than those in phenolic compounds (because the enolic π resonance stabilizes the oxyl radical much more than the σ -bond hyperconjugation). Thus, the gas phase O–H BDE in methanol ($96.4 \text{ kcal mol}^{-1}$)¹⁸⁸ is *ca.* 8 kcal mol^{-1} stronger than the analogous BDE in phenol (88 kcal mol^{-1} , see above). The alcohol O–H bond is usually stronger than the C–H bonds in the same molecule. Again using methanol as an example, the O–H BDE is more than 8 kcal mol^{-1} stronger than the C–H BDFE_g for $H\text{-CH}_2\text{OH}$, $87.9 \text{ kcal mol}^{-1}$.³⁷ For this

reason, hydrogen atom abstractors react with alcohols to give a hydroxyalkyl radical such as $\cdot\text{CH}_2\text{OH}$, rather than the alkoxyl radical ($\text{CH}_3\text{O}\cdot$).

5.3.1 *tert*-Butanol and *tert*-Butoxyl Radical—The *tert*-butoxyl radical ($\text{'BuO}\cdot$) has received considerable attention, in part because it does not have any easily abstracted α C–H bonds. $\text{'BuO}\cdot$ radicals can be generated via photolysis of 'BuOO'Bu in the gas phase¹⁸⁹ or in solution,¹⁹⁰ and by photolysis or thermal decomposition of *tert*-butylhyponitrite ('BuONNO'Bu),¹⁹¹ *tert*-butylhypochlorite,¹⁹² or *tert*-butylperoxalate.¹⁹³ The O–H bond in *tert*-butanol ('BuOH) is quite strong, with a gas-phase BDFE of $106.3 \text{ kcal mol}^{-1}$,³⁷ so $\text{'BuO}\cdot$ is a quite reactive H-atom abstractor. Photochemically generated $\text{'BuO}\cdot$ is therefore useful to rapidly form other oxyl radicals, such as phenoxyls, often within the duration of a nanosecond laser pulse.^{194–195} A large number of rate constants are available for HAT from various substrates to $\text{'BuO}\cdot$.¹⁹⁷ With less reactive X–H bonds, however, HAT must compete with β -scission of $\text{'BuO}\cdot$ to give methyl radical and acetone.¹⁹⁸ In neat acetonitrile, for instance, only β -scission is observed, because of the low reactivity of the H– CH_2CN bonds.¹⁹⁸

BDFEs for 'BuOH in water and DMSO have been estimated using Abraham's empirical method, described in Section 3.1.1 above. Combining these values with the known pK_a values provides estimates of the $1e^-$ reduction potentials of $\text{'BuO}\cdot$ in these solvents. The estimated $E(\text{'BuO}^{\cdot-})$ in DMSO is in reasonable agreement with Bordwell's estimate,¹⁰⁰ from the complex electrochemical response of 'BuO^- in DMSO (Table 8). In water, $\text{'BuO}\cdot$ is very oxidizing, substantially more than phenoxyl (1.2 V versus 0.78 V for the $\text{RO}^{\cdot-}$ couple). Electron transfer reactions of $\text{'BuO}\cdot$ have been briefly commented on,¹⁹⁹ although the product of these reactions is 'BuOH , apparently formed by protonation of the quite basic *tert*-butoxide anion.

5.3.2 Water/Hydroxyl radical—The first O–H bond in water is, to our knowledge, the strongest known O–H bond. It has a gas-phase BDFE of $110.64 \text{ kcal mol}^{-1}$ (a BDE_g of $118.81 \text{ kcal mol}^{-1}$).^{37,200} In aqueous solution, we calculate the $\text{BDFE}(\text{HO–H})$ to be $122.7 \text{ kcal mol}^{-1}$ based on the $\text{OH}^{\cdot-}$ redox potential and pK_a . The very high HO–H bond strength is due, at least in part, to the absence of any resonance or hyperconjugative stabilization in $\text{OH}\cdot$. The hydroxyl radical is therefore a very high energy species capable of extracting H-atoms from essentially all aliphatic C–H bonds (C–H bonds with an sp^3 -hybridized carbon). $\text{OH}\cdot$ is also a potent $1e^-$ oxidant and can add to unsaturated organic compounds, for instance converting benzene to phenol. The O–H bond in the hydroxyl radical (the second O–H bond in water) is significantly weaker, as given in Table 8 and shown in the square Scheme in Figure 5a.

5.4 Compounds with O–O Bonds

5.4.1 Overview of Dioxygen PCET Chemistry—PCET reactions involving dioxygen are of considerable research interest. The four electron/four proton reduction of O_2 to water is key to biological aerobic metabolism²⁰³ and is the “oxygen reduction reaction” (ORR) in fuel cells.²⁰⁴ The oxidation of water to dioxygen is an important component in many proposals for storage of electrical energy.²⁰⁵ The abundance and low environmental impact of dioxygen make it an attractive oxidant in industrial chemical processes.²⁰⁶ However, all $4e^-$ and 4H^+ cannot be added or removed at the same time, so the intermediate species of dioxygen reduction are also of great importance. These species, $\text{O}_2^{\cdot-}$, $\text{HO}_2\cdot$, HO_2^- , H_2O_2 , $\text{HO}\cdot$, and $\text{O}^{\cdot-}$, are all high-energy intermediates as can be seen in the Frost diagrams in Figure 6, and are known collectively as reactive oxygen species (ROS). In biology, ROS damage lipids, proteins, nucleic acids, and carbohydrates, and have been implicated in various diseases and aging.^{203,207,208} Many of these species are highly reactive with

organic molecules, making it difficult to study their chemistry in non-aqueous solvents. However, the aqueous thermochemistry of oxygen species has been studied extensively, and has been reviewed by Sawyer²⁰⁹ and Afanas'ev.²¹⁰ The properties of the species without an O–O bond have been summarized above; the PCET thermochemistry of the O–O bonded species are given in Table 9 and Figure 6.

The Pourbaix diagram for water (Figure 6c) does not show most of the reactive oxygen species. This is because, other than H_2O_2 and HO_2^- , the ROS are not the most thermodynamically stable species at any point in the diagram, at any pH or redox potential. The standard (pH 0) potential for the $4 e^-/4 \text{H}^+$ reduction of O_2 is always given as 1.23 V (eq 17) but from some perspectives it can be better to think about O_2 reduction or water oxidation as transferring hydrogen atoms. The free energy in these terms, following eqs 15 or 16 above, is given in eq 18 both for the full $4 e^-/4 \text{H}^+$ process and per hydrogen atom, as an effective BDFE. Thus, oxidizing water to O_2 , requires a 'system' with an effective BDFE of greater than 86 kcal mol^{-1} . Such a system could be a hydrogen atom abstracting reagent, or a combination of an oxidant and a base (Section 5.9 below). In photosystem II, the oxidizing equivalents pass through the tyrosine/tyrosyl radical couple which in aqueous solution has a BDFE of $87.8 \text{ kcal mol}^{-1}$ from Table 4. While this BDFE could be different within the protein, it shows that the tyrosyl radical has just enough free energy to accomplish water oxidation and shows the remarkable catalytic activity of the oxygen evolving complex at low overpotential.

5.4.2 Dioxygen—While the overall proton-coupled reduction of O_2 to water is quite favorable, transfer of the first electron is far less favorable. Dioxygen is a poor one-electron outer-sphere oxidant, with E° for reduction to superoxide ($\text{O}_2^{\bullet -}$) = -0.16 V vs. NHE in H_2O .²⁰⁹ Superoxide is also not very basic (aqueous $\text{p}K_a = 4.9$), so this combination of a low potential and low $\text{p}K_a$ means that $\text{HO}_2^\bullet$ (hydroperoxyl) has a very low O–H BDFE, $60.4 \text{ kcal mol}^{-1}$ in water. Because of this low BDFE, O_2 is not an effective H-atom abstractor (so the large majority of organic molecules are 'air stable'). It should be emphasized that H-atom abstracting ability typically correlates with the X–H BDFE that an oxidant can form and does not correlate with the 'radical character'.²¹¹ Thus, dioxygen is a triplet diradical but is quite unreactive toward HAT, while permanganate (MnO_4^-) with no unpaired spins is a reactive H-atom abstractor because it can form an O–H bond with a BDFE of $80.7 \text{ kcal mol}^{-1}$ (Section 5.10). In contrast, oxene (O), a neutral triplet radical like O_2 , is a far more potent H-atom abstractor because of the high BDFE of $^\bullet\text{O}-\text{H}$, $106.9 \text{ kcal mol}^{-1}$ (Table 8).

5.4.3 Superoxide/Hydroperoxyl—Superoxide radical anion ($\text{O}_2^{\bullet -}$) and its protonated form (the neutral perhydroxyl radical, $\text{HO}_2^\bullet$) are considered reactive oxygen species but do not undergo the chemistry typical of oxygen radicals.²¹² Superoxide generally does not act as a direct one electron oxidant due to the relatively high energy of the solvated peroxide dianion (O_2^{2-}).²¹³ Similarly, $\text{O}_2^{\bullet -}$ does not usually react as a direct H-atom abstractor since it forms a relatively weak O–H bond (aqueous $\text{BDFE}(\text{OO}-\text{H}) = 81.6 \text{ kcal mol}^{-1}$). The neutral perhydroxyl radical $\text{HO}_2^\bullet$ is a more reactive oxidant, in part because it forms a stronger O–H bond: $E(\text{HO}_2^{\bullet -}) = 0.76 \text{ V}$ and $\text{BDFE}_{\text{aq}}(\text{HOO}-\text{H}) = 91.0 \text{ kcal mol}^{-1}$ (Table 9). Thus, it is perhydroxyl, present in small quantities at biological pH ($\text{p}K_a \text{ HO}_2^\bullet = 4.9$),²⁰⁹ that is responsible for much of the oxidative damage associated with biological fluxes of

superoxide. Some of this damage also results from the H_2O_2 produced by superoxide dismutation or by HAT to $\text{HO}_2^\bullet$. Perhydroxyl, because of its high BDFE, can abstract H-atoms from weak C–H bonds such as the allylic C–H's in cyclohexadiene^{214,215} or linoleic acid.²¹⁶ Superoxide HAT reactions have also been reported with H-atom donors such as ascorbic acid²¹⁷ and di-*tert*-butylcatechol.²¹⁸

Superoxide is fairly stable to disproportionation in the absence of protons because the peroxide (O_2^{2-}) product is a high energy species. In the presence of protons, however, it rapidly decays to H_2O_2 and O_2 ($k = 1.0 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ at pH 7). This reaction likely occurs by the reaction of superoxide with perhydroxyl radicals to give hydroperoxide and dioxygen, which is a highly favorable process (eq 19).²¹⁹ This reaction has been described as the reduction of $\text{HO}_2^\bullet$ by superoxide, in other words as an ET reaction, but it could also occur by HAT from $\text{HO}_2^\bullet$ by superoxide, a net oxidation of $\text{HO}_2^\bullet$ that gives the same products. Superoxide disproportionation forms HO_2^- which is a moderate base ($\text{p}K_a$ 11.6),²²⁰ so aqueous superoxide in effect acts as a base despite its relatively low dissociation constant.

5.4.4 Hydrogen Peroxide—Peroxides are two-electron reduced from dioxygen. The peroxide dianion (O_2^{2-}) is found in ionic solids but is very basic, such that the two-electron electrochemical reduction of oxygen in DMSO produces deprotonated DMSO ($\text{p}K_{a,\text{DMSO}} = 3529$) and hydroperoxide.²²¹ Hydroperoxide (HO_2^-) is moderately basic in water [$\text{p}K_a(\text{H}_2\text{O}_2) = 11.6$]. In typical organic solvents such as DMSO, DMF, or acetonitrile, the $\text{p}K_a$ of H_2O_2 cannot be directly measured because HO_2^- readily reacts with sulfoxides, amides, and nitriles.^{221,222}

Hydrogen peroxide is increasingly attractive as a “green” oxidant and is being produced on a very large scale.²²³ It is almost always used as an aqueous solution.²²⁴ H_2O_2 is unstable with respect to disproportionation to water and dioxygen, but this is slow in the absence of light or a catalyst. The most famous example is the Fenton reaction, in which iron salts catalyze the decomposition in part by the inner-sphere reduction of H_2O_2 by Fe(II) (eq 20) which yields the very reactive hydroxyl radical ($\text{HO}^\bullet$).^{225,226} This and related reactions are a connection between the compounds with O–O bonds discussed in this section and the water/hydroxyl radical PCET chemistry described above. The proton-coupled reduction of H_2O_2 to $\text{H}_2\text{O} + \text{OH}^\bullet$ is thermodynamically quite favorable (eq 21). In practice, however, cleavage of H_2O_2 by outer-sphere electron donors and hydrogen atom donors often has a large kinetic barrier, likely associated with the cleavage of the O–O bond.²²⁷

5.4.5 Organic Hydroperoxides—Organic hydroperoxides have received considerable attention for their roles in synthesis, catalysis, and biochemical processes. Like H_2O_2 , the free radical chemistry of ROOH containing systems can proceed either by O–O or O–H homolysis. Here we only discuss the chemistry of the O–H bond; the interested reader is pointed to a review of the radiation and photochemistry of peroxides, which discusses a variety of O–O bond homolysis reactions.²³⁰ PCET reactions of organic peroxy radicals have almost always been understood as HAT reactions, especially the chain propagating step

in autoxidation.¹⁷ This makes sense because of the strong ROO–H bonds, while PT-ET or ET-PT pathways are disfavored by the low basicity of ROO• and the moderate ROO^{•/–} potentials (Table 10).

The most commonly employed organic hydroperoxide is *tert*-butyl hydroperoxide. The gas phase thermochemistry of organic peroxides has been widely discussed. Simmie *et al.*²³¹ recently gave $\Delta H_f^\circ(^t\text{BuOO}^\bullet) = -24.69 \text{ kcal mol}^{-1}$, which, together with $\Delta H_f^\circ(\text{H}^\bullet) = 52.103 \text{ kcal mol}^{-1}$ ²³² and $\Delta H_f^\circ(^t\text{BuOOH}) = -56.14 \text{ kcal mol}^{-1}$ ²³³, gives $\text{BDE}_g(^t\text{BuOOH}) = 83.6 \text{ kcal mol}^{-1}$.²³⁴

The pK_a s of several alkyl hydroperoxides and peracids have long been known,²³⁵ and pK_a values for several peroxybenzoic acid have been reported.²³⁶ However, until recently, the reduction potentials of the corresponding peroxy radicals have remained elusive. Das and co-workers indirectly measured the ROO^{•/–} couple for several peroxy compounds in water (Table 10).²³⁷ Their value for $E^\circ(^t\text{BuOO}^{\bullet/–})$ is in good agreement with an earlier estimate made using kinetic and pK_a data.²³⁸ In contrast, very little data exists on the redox potentials of percarboxylate anions. Peracids have gas phase BDFEs that are a little higher, and they are more acidic than the corresponding alkyl peroxides, which indicate that the $\text{RC}(\text{O})\text{OO}^{\bullet/–}$ potentials are probably more oxidizing ($\geq 1 \text{ V}$).²³⁹ Jonsson's estimate of $E^\circ(\text{CH}_3\text{C}(\text{O})\text{OO}^{\bullet/–}) = 1.14 \text{ V}$ ²⁴⁰ is in agreement with this estimate. Jonsson has also estimated thermochemical data for a variety of other peroxides but these need to be used with caution as they were extracted from electron transfer kinetic data²⁴⁰ and some of these values do not agree with those determined via more direct methods (*e.g.*, Jonsson gives $E^\circ(\text{Cl}_3\text{COO}^{\bullet/–}) = 1.17 \text{ V}$ while Das reports $E^\circ(\text{Cl}_3\text{COO}^{\bullet/–}) = 1.44 \text{ V}$ ²³⁷).

5.5 Simple Nitrogen Compounds: Dinitrogen to Ammonia, Amines, and Arylamines

The previous sections all focused on reagents with reactive O–H bonds. With this section we shift to N–H bonds, and those below deal with S–H and C–H bonds. While the same principles apply, there are some important differences. N–H bonds are less acidic than comparable O–H bonds, and in general *N*-lone pairs are higher in energy so nitrogen compounds are more basic and more easily lose an electron to form the radical cation. Therefore, stepwise PCET reactions of amines typically involve aminium radical cations ($\text{R}_3\text{N}^{\bullet+}$), particularly for arylamines, while those of alcohols and phenols involve alkoxides and phenoxides. We start with the simple gas phase species from N_2 to ammonia, then progress to alkyl and aryl amines, and finally to more complex aromatic heterocycles of biological interest.

5.5.1 Dinitrogen, Diazine, and Hydrazine—Dinitrogen (N_2) is one of the most abundant compounds on earth, making it an almost unlimited feedstock for the production of reduced nitrogen species such as ammonia. The overall reduction of dinitrogen to ammonia by dihydrogen is thermodynamically favorable under standard conditions both in the gas phase and in aqueous solution. However, this is a $6\text{H}^+/6e^-$ reaction and cannot occur in one step.²⁴³ The energetics of the intermediates are therefore important. Industrially, dinitrogen is reduced to ammonia via the Haber-Bosch process which is carried out at high temperatures and high pressures by an iron catalyst. The high temperature is needed to overcome the kinetic barrier, but makes the reaction less favorable so high pressures are needed. Combining the production of the H_2 and the operation of the Haber-Bosch process, it is said that industrial N_2 -fixation accounts for 1% or more of the total human energy consumption.²⁴⁴ In biology, N_2 -fixation is accomplished by nitrogenase enzymes in solution at room temperature using reduced ferredoxins and ATP.²⁴³ Most biochemical studies and biomimetic models for nitrogen fixation propose sequential single-electron and single-proton transfers to metal-bound nitrogen species, but the thermochemistry of these

steps is not experimentally known (only in the Schrock/Yandulov cycle is there good evidence for each of the various intermediates).²⁴⁵⁻²⁴⁶ Much less is known about the solution thermochemistry of simple $N_xH_y^{z\pm}$ species compared with the oxygen analogs. The known aqueous values are provided by Stanbury,²⁴⁷ and Koper has recently reviewed electrochemical studies.²⁴⁸

Dinitrogen is one of the most inert chemical compounds. The addition of a proton or an electron is not very favorable: N_2 has a gas phase proton affinity of 5.12 eV, slightly less than methane, and its electron affinity is negative (−1.8 eV).²⁴³ The BDE of NN–H is estimated to be close to or less than 0 kcal/mol (Table 11).²⁴⁹ These values make it unlikely that reduction of free dinitrogen can proceed through a free one-electron reduced species. The two H-atom reduced species of dinitrogen is diazene (HN=NH), also called diimide. Diazene is unstable, as it is powerful H-atom transfer agent with a first BDE of only ~60 kcal/mol.⁴⁹ The average gas phase BDFE for Z-diazene to $N_2 + 2H^\bullet$ is only 19.5 kcal mol^{−1} (average BDE = 26.7 kcal mol^{−1}), so decomposition to N_2 and H_2 is very favorable.⁴⁹ Moreover, diazene is thought to transfer both hydrogens in a concerted fashion to alkenes and alkynes, a very rare example of a $2e^-/2H^+$ reaction.²⁵⁰ Diazene, like dinitrogen, is a very poor base, with a pK_a of the conjugate acid of less than zero.²⁵¹

The reduction of diazene by one H-atom gives the hydrazyl radical (HNNH₂), a high-energy species with a very weak N–H bond. Hydrazyl is capable of abstracting an H-atom to yield the more stable hydrazine (H₂NNH₂) with BDFE_{aq}(H₂NNH₂) = 83 kcal mol^{−1}. In the gas phase the average BDFE for H₂NNH₂ to Z-diazene + $2H^\bullet$ is 58.7 kcal mol^{−1} (average BDE = 66.2 kcal mol^{−1}).⁴⁹ Like peroxides, hydrazine has a weak N–N bond (BDE = 66.2 kcal mol^{−1}) and can undergo homolytic N–N bond cleavage as well as PCET reactions. Hydrazine's lone pairs make it moderately basic, with a first pK_a of the conjugate acid similar to the pK_a of ammonium, though the addition of a second proton is very unfavorable.²⁴⁷ Electron transfer oxidation of tetraalkylhydrazines have been examined by Nelsen and others.²⁵² Hydrazine is a powerful, but kinetically slow oxidant, undergoing $2e^-/2H^+$ reduction to give two molecules of ammonium with $E^\circ = 1.2$ V in acidic aqueous solution.²⁵³ Hydrazine has also been used as a mild reducing agent in aprotic media, though the proton containing products are not clear.²⁵⁴

5.5.2 Ammonia and Alkylamines—Ammonia is the simplest amine and a critical commodity chemical; in 2005 global ammonia production was estimated at 168 million tons.²⁵⁸ Ammonia is a good base ($pK_a(NH_4^+)_{H_2O} = 9.24259$) so it primarily exists as ammonium salts at normal physiological conditions. The gas phase homolytic bond strengths for NH_3 , NH_4^+ , and $NH_3^{\bullet+}$ are very high (Table 12). H-abstraction from NH_3 requires very high energy species, such as hydroxyl radical.²⁶⁰ The pK_a of NH_3 has been estimated to be 38,²⁶¹ similar to that for H_2 (see below).

As indicated above, alkylamines can often be oxidized by one e^- to the protonated aminium radical cation $R_2NH^{\bullet+}$ (Table 12), which is substantially less acidic than a protonated alkoxy radical. As with alcohols, the N–H bonds in alkylamines are significantly stronger than the α -C–H bonds (because of dative stabilization of the carbon radical by the nitrogen lone pair). This is evident, for instance, in the N–H and C–H alkylamine BDEs in MeCN and C₆H₆ reported by Lalevée and co-workers.²⁶²

5.5.3 Arylamines and arylhydrazines—Arylamines are more easily oxidized to radical cations than phenols, because $-NH_2$ is a more electron-donating substituent to the aromatic ring than $-OH$ (in both cases the electron is lost from a π -symmetry orbital in large part on the aromatic ring). Therefore, for anilines the potential for oxidation of the neutral $ArNH_2$ is experimentally accessible $E^\circ(ArNH_2^{\bullet+/0})$, whereas for phenols the accessible outer-sphere

potential involves the phenoxide $E^\circ(\text{PhO}^{\bullet/-})$. Monoaryl and diaryl aminium radical cations are transient, but triarylamminium radical cations with *para*-substituents are isolable and very useful, for instance as chemical reagents²⁵⁴ and as ‘hole-transport’ electronic materials.²⁷⁰ Bordwell has tabulated data for complete ‘square schemes’ for several substituted anilines and diphenylamines.²⁷¹ Furthermore, Jonsson, Lind and Merényi have determined reduction potentials for anilinium radical cations, and $\text{p}K_\text{a}$ s for the corresponding radical cations in water.^{268,272,273} Selected data are shown in Table 13, but other examples are available in both DMSO and water in each respective reference.

The N–H BDE of aniline (PhNH_2) in C_6H_6 has been measured by MacFaul *et al.* using photoacoustic calorimetry (PAC), and they calculated the gas phase BDE using estimated solvation enthalpies.²⁷⁴ These values are consistent with the BDE derived from the reported E° and $\text{p}K_\text{a}$ data in DMSO when we extrapolate it to C_6H_6 using Abraham’s model.^{275,276} For diphenylamine, a number of slightly different BDEs have been reported,^{274,277,278} as summarized by Pratt *et al.*²⁷⁸ at this time we see no clear reason to favor one value.¹²²

The stable, isolable radical 2,2-diphenyl-1-picrylhydrazyl (DPPH) has long been used to study the antioxidant properties of organic compounds.^{11,12,279} DPPH–H (1,1-diphenyl-2-picrylhydrazine) has a bond strength *ca.* 80 kcal mol^{–1} making it well suited for studies of many antioxidants, such as phenols and thiols. The BDFE of DPPH–H is perhaps best known in benzene from the calorimetric determination by Ingold and co-workers.⁷⁶ Thermochemical data in other solvents are also shown in Table 13. From the work of Bordwell in DMSO,²⁸⁰ the bond strengths of aryl hydrazines are less than the BDFEs of arylamines, presumably because of stabilization of the radical by the delocalized π system.

5.6 Tryptophan, Flavins and Nucleosides

The nitrogen containing heterocycles tryptophan, flavin and the nucleotide guanine are important in biological redox chemistry. Tryptophan is thought to be important in long-range electron transfer in proteins^{123,285} and its oxidation products are often observed in oxidatively stressed proteins.²⁸⁶ Guanine is the most easily oxidized nucleoside and is therefore implicated in the much-studied long-range hole transfer through DNA. Guanine oxidation is also thought to be important in DNA damage/repair.²⁸⁷ Flavins are critical biological cofactors that mediate charge transfer in a variety of proteins.^{288,289} Although these cofactors are widely discussed in terms of electron transfer, their pH dependent redox potentials indicate that they should be viewed as PCET reagents, at least in certain circumstances.

5.6.1 Indole and Tryptophan—The biological importance of electron transfer reactions of tryptophan has prompted thorough studies of its solution thermochemistry (Table 14). Merényi and co-workers have reported aqueous redox potentials and $\text{p}K_\text{a}$ values for a series of indoles,²⁹⁰ although their measurement of $E^\circ(\text{TrpH}^{*+/0})$ is different from the value reported by both Harriman¹²⁸ and from DeFilippis.¹³¹ (Table 14 does not give the $\text{p}K_\text{a}$ s for the amine or the carboxylate moieties of tryptophan.) Indoles and tryptophan are more acidic than alkylamines and anilines, but are still less acidic than phenols [in DMSO, $\text{p}K_\text{a}(\text{indole}) = 20.9291$ while $\text{p}K_\text{a}(\text{phenol}) = 18.0116$ (see Tables 4 and 14 for more extensive data)]. The more striking difference between indole and phenol is the acidity of the radical cation: PhOH^{*+} is a very strong acid (aqueous $\text{p}K_\text{a} = -2115$) while indole^{*+} is a weak acid (aqueous $\text{p}K_\text{a} = 4.9290$). Thus oxidations of indoles and tryptophan often form the radical cation (like the amines discussed above), while oxidations of phenols typically form the neutral phenoxyl radical.

This comparison of indole and phenol is particularly interesting because tryptophan and tyrosine are the most important redox-active amino acids, and their thermochemistry proves

the framework for understanding their roles in biological catalysis and charge transfer. Tyrosine radical cations ($\text{TyrOH}^{\bullet+}$) are too high in energy to be involved in a biological system, even in photosystem II that is said to contain the strongest oxidant in biology.²⁹² Thus, in biological systems (and in the large majority of chemical systems as well) tyrosine and other phenols are oxidized to the neutral phenoxyl radical. However, $\text{TrpH}^{\bullet+}$ is a much more accessible species, being much less acidic than $\text{TyrOH}^{\bullet+}$ and having a reduction potential 0.25 V lower than that of $\text{TyrOH}^{\bullet+}$. Therefore oxidations of tryptophan (and indoles) often involve the radical cation. In this way, indoles resemble the alkylamines and anilines discussed in Section 5.5.3. While tryptophan is easier to oxidize by outer-sphere electron transfer, tyrosine is easier to oxidize by PCET because its BDFE is about 3 kcal mol⁻¹ weaker than the N–H BDFE in tryptophan. Again, given the critical importance of the proton in these chemical transformations, we strongly encourage those working on redox-active amino acids to not just refer to the oxidized forms as, for instance, $\text{Y}^{\bullet}$ or $\text{W}^{\bullet}$, but to explicitly show the proton, for instance as $\text{TyrO}^{\bullet}$ vs. $\text{TrpH}^{\bullet+}$.

5.6.2 Flavins—Flavin is the common name for a family of 7,8-dimethyl-substituted isoalloxazines (isoalloxazine = 10-substituted alloxazine). The reader should be warned that the current IUPAC flavin numbering scheme is different from much of the flavin literature published before *ca.* 1980.²⁹⁵ There are four biologically relevant flavins, which differ only in the nature of the alkyl substituent at N10: lumiflavin, riboflavin, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) (Scheme 10).²⁹⁶ These cofactors exhibit essentially identical redox¹⁵⁵ and acid/base chemistry (Figure 7). Both the fully oxidized and fully reduced forms are stable, and are typically referred to using nomenclature analogous to quinones/hydroquinones.²⁸⁹ For example, the fully reduced form can be referred to as the “flavohydroquinone.” Flavins also exhibit stable “flavosemiquinone” radicals at low pH.²⁸⁹ Also like hydroquinones, flavins can undergo $2\text{H}^+/2e^-$ chemistry, thus a 9-membered square scheme is needed to describe the PCET thermodynamics.

The proton-coupled redox chemistry of flavins has long been known. Michaelis in the late 1930s^{297,298} and Lowe in 1956²⁹⁹ reported that lumiflavin, FMN, and FAD all have the Nernstian dependence of the redox potential on pH (~60 mV per pH unit) below the pK_a of the flavohydroquinone, which indicates that they can undergo $1e^-/1\text{H}^+$ and $2e^-/2\text{H}^+$ PCET reactions. Starting from the reduced anion, flavins can also mediate $1\text{H}^+/2e^-$ (hydride) transfer to give the fully oxidized form. The net hydride transfer from NAD(P)H to a flavin is a fundamental biological reaction that can be found in nearly any biochemistry text book. PCET chemistry of NADH and related compounds is discussed below. There is evidence that the mechanism of such net hydride transfers can be concerted in some instances.³⁰⁰ A recent study of the enzyme glucose oxidase, using chemically modified flavin-type cofactors, concluded that glucose is most likely oxidized by concerted hydride ($2e^-/\text{H}^+$) transfer.³⁰¹ Flavins can also mediate single electron transfer reactions, such as has been implicated in the electron transport chain of NADPH oxidase, to name just one example.³⁰² The flavin cofactor in glucose oxidase has been shown to react with O_2 by electron transfer, showing the power of using a series of modified flavins in mechanistic studies.³⁰³ The interested reader is directed to these references for the thermochemical properties of flavins, deazaflavins and related derivatives. While electron and hydride transfer reactions of flavins are well known, to our knowledge single hydrogen atom transfer reactions of flavins have not been widely discussed.

The acid/base chemistry of flavins has been extensively studied. The first pK_a s of flavins are generally much lower than that of many quinones, and are below neutral pH, so that they are mostly ionized under biological conditions. The pK_a for the flavohydroquinone and the flavosemiquinone have not been drastically revised since their first reports in the early 20th century.^{289,297–298,299} Land and Swallow reported a pK_a of 0.25 for protonation of

oxidized riboflavin and $pK_a = 2.3$ for protonation of the flavin semiquinone.³⁰⁴ We note that pK_a s of the transient flavosemiquinones, like those of most transient radicals, are not simple to determine; the values quoted here are the most widely employed. Many reports of pH 7 midpoint one electron potentials for flavins have emerged, but perhaps the most widely accepted values were reported by Anderson.³⁰⁵ Those data were later used to fit E versus pH data for flavins and obtain $1H^+/1e^-$ potentials at pH 0.³⁰⁶ Using the known dissociation constants (Figure 7) we have calculated the standard $1e^-$ (not proton-coupled) reduction potentials shown along the vertical arrows in Figure 7. The derived bond strengths are in excellent agreement with the average bond strength calculated from the pH 7 midpoint potential (-0.21 V, 155 equivalent to $+0.2$ V at pH 0 upon extrapolation with the Nernstian 59 mV per pH).

The free energy to lose $1H^+/2e^-$ (or H^-) is also shown in Figure 7, as the long steep diagonal. As with BDFEs, hydride affinities can be determined from thermodynamic square schemes.⁵ In a given solvent, the hydride affinity is calculated from the sum of two free energies for reduction/oxidation ($23.06E^\circ$), the free energy for protonation/deprotonation ($1.37pK_a$), and $23.06E^\circ(H^{+/-}) (= 23.06(E^\circ(H^{+/\bullet}) + E^\circ(H^{\bullet/-})))$, see Table 19 and Section 5.8.3, below).⁵ By Hess' law, it does not matter which two reduction potentials and pK_a are used to calculate a hydride affinity so long as together they connect the two species differing by H^- .

The $2H^+/2e^-$ potentials for non-biological substituted flavins do not vary drastically with respect to substitution,^{155,307} ranging from $E^\circ = 0.30$ V to $E^\circ = 0.19$ V (the later for the biological flavins discussed above). This implies a range of average N–H BDFEs from 64.5 kcal mol⁻¹ to 62 kcal mol⁻¹. Unfortunately, there are no individual pK_a/E° data for many of these compounds, precluding construction of complete thermochemical cycles.

As noted above, the thermochemistry of flavins allows them to mediate a wide range of redox reactions, including hydride transfers and single electron transfers. The ability of flavins to transfer H^- is in contrast with hydroquinones, which do not normally react by hydride transfer presumably because the hydroquinone anion (HQ^-) is a high energy species, and difficult to generate under typical conditions (see above). In contrast, the reduced flavin anion is much lower in energy. In this way flavins are also unique from the other nitrogen containing compounds discussed above. Inspection of Figure 7 shows that the thermochemical landscape for flavins is more “flat” than other compounds discussed here. Because the redox potentials of flavins are less sensitive to their acid/base chemistry (and vice versa), they are able to mediate a wider range of reactions, and are not limited to $H^\bullet$ transfer like phenols or ascorbate.

5.6.3 Nucleosides—The redox chemistry of nucleotides, nucleosides, and nucleobases has been of great interest because of its relevance to the effects of free radicals, oxidants, and ionizing radiation on DNA, and to understand long-range charge transport along DNA.³⁰⁸ This section summarizes the PCET thermochemistry of individual nucleosides. These data are a foundation for understanding the redox chemistry of DNA, although the properties of the nucleosides can be different within the DNA helix. There is some evidence that charge transport along DNA can be a PCET process.^{308f,309}

Guanine is the most easily oxidized nucleobase and therefore has received the most attention. At pH 7, one-electron oxidation of guanine occurs with loss of the N1 proton (Scheme 11; the radical density in the product is mostly at O6, as drawn). The most authoritative value for this redox potential is 1.29 V at pH 7.³¹⁰ It should be emphasized that *this is the potential for a $1H^+/1e^-$ transfer process and cannot be used in analyses of*

pure electron transfer – although this has been done. The nature of the charge carrier in oxidized DNA is still a matter of debate, as summarized in a very recent review:^{308e}

“in the context of hopping and drift, the nature of the states that mediate charge transport vary with the sequence and sequence-dependent dynamics. What these states are, localized radical cations, localized neutral radicals, large polarons, delocalized domains, or a combination, will be different on the basis of the properties of the specific donor, DNA bridge, and acceptor.”

Table 15 gives the PCET thermochemical data for the four nucleosides at pH 7 and the bond strengths derived from these values. Steenken also extrapolated these measured pH 7 potentials for guanosine and adenosine to standard pH 0 E° values, accounting for the complex pH dependence of the neutral and radical species.³¹⁰ The bond strengths are quite high, and highlight the propensity of the nucleobases to undergo reactions other than HAT with powerful oxidants, such as $\text{OH}^\bullet$ addition to guanosine to produce 8-oxo-guanosine. Reagents that abstract hydrogen atoms tend to react with the weak C–H bonds in the ribose portion of DNA. The nucleobase N–H bonds may also be kinetically unreactive because those hydrogen atoms are in strong hydrogen bonds, a possible effect analogous to Ingold’s kinetic solvent for HAT from O–H bonds in small molecules in solution.¹¹

5.7 Thiols

The redox chemistry of thiols is important in many areas of biology. The oxidation of the thiol side chain of the amino acid cysteine, $^-\text{O}_2\text{CCH}(\text{NH}_3^+)\text{CH}_2\text{SH}$, forms disulfide linkages that are critical to the proper folding and function of peptides and proteins. Thiols are also important to the function of the hormone insulin to catalysis by ribonucleotide reductases to the structural keratin in hair and other biomaterials. Thiols are important biological antioxidants, with the prototypical example being glutathione (GSH), a tripeptide of glycine, cysteine and glutamic acid.³¹³ GSH has long been understood as an important biological antioxidant, and it has more recently been shown to have other important biological roles.³¹⁴ The redox chemistry of thiols typically involves net $\text{H}^\bullet$ loss to give the thiyl radical $\text{RS}^\bullet$, with subsequent disulfide formation or oxidation to sulfenic (RSOH), sulfinic [$\text{RS}(\text{O})\text{OH}$] and/or sulfonic acids [$\text{RS}(\text{O})_2\text{OH}$].

Thiols are in general more acidic than corresponding alcohols, more easily oxidized, and have weaker X–H bonds. For example, in DMSO thiophenol is 7.7 $\text{p}K_\text{a}$ units more acidic and PhS^- is 35 mV easier to oxidize than phenol and phenoxide, which results in an 11 kcal mol^{-1} weaker BDFE (Tables 4 and 16). In water, the differences are less because PhS^- is not as strongly solvated as PhO^- : the differences are 3.4 $\text{p}K_\text{a}$ units, 0.1 V in $E^\circ(\text{PhE}^{\bullet/-})$, and 7 kcal mol^{-1} in BDFE ($E = \text{S}$ or O). Extensive $\text{p}K_\text{a}$ data available for thiols³¹⁵ but fewer redox potentials are known, presumably because of the rapid dimerization of thiyl radicals. Representative available data are given in Table 16 for selected compounds. We can find no data for thiol radical cations, which suggests that these are high energy species with $E^\circ(\text{RSH}^{\bullet+/0}) > 1$ V and $\text{p}K_\text{a}(\text{RSH}^{\bullet+}) < 0$ in water.

Armstrong and Surdhar used gas phase RS–H BDEs, estimated heats of solution and the $\text{p}K_\text{a}$ s to calculate $\text{RS}^{\bullet/-}$ redox couples in water.³¹⁶ They used $\text{BDE}(\text{RS–H}) = 81.2$ kcal mol^{-1} , but these values have since then been determined to be larger, *ca.* 87 kcal mol^{-1} (Table 16). Using Armstrong’s thermochemical cycle with the revised gas phase BDFEs shown in Table 16 gives $E^\circ(\text{MeS}^{\bullet/-}) = 0.73$ V and $E^\circ(\text{EtS}^{\bullet/-}) = 0.74$ V. These values are in good agreement with later estimates of $E^\circ(\text{RS}^{\bullet/-})$ for deprotonated β -mercaptoethanol (= $\text{HOCH}_2\text{CH}_2\text{SH}$)³¹⁷ and cysteine.³¹⁸

β -mercaptoethanol has better solubility in water than other alkyl thiols, and serves as a reasonable model of aqueous thiol chemistry since the thiol and alcohol moieties are not too

near to each other. The aqueous potential for $\text{HOCH}_2\text{CH}_2\text{S}^\bullet + \text{H}^+ + e^- \rightarrow \text{HOCH}_2\text{CH}_2\text{SH}$ is $E^\circ = 1.33 \pm 0.02 \text{ V}$ ($\text{HOCH}_2\text{CH}_2\text{SH} = \beta$ -mercaptoethanol).³¹⁷ Applying eq 15 above gives $\text{BDFE}_{\text{H}_2\text{O}}(\text{HOCH}_2\text{CH}_2\text{S-H}) = 88.3 \text{ kcal mol}^{-1}$ (and $\text{BDE}_{\text{H}_2\text{O}}(\text{HOCH}_2\text{CH}_2\text{S-H}) = 86.5 \text{ kcal mol}^{-1}$ with the assumption that $S^\circ_{\text{H}_2\text{O}}(\text{HOCH}_2\text{CH}_2\text{S}^\bullet) = S^\circ_{\text{H}_2\text{O}}(\text{HOCH}_2\text{CH}_2\text{SH})$, see above). This value is in excellent agreement with the bonds strengths calculated above from thermochemical cycles.

The $\text{p}K_{\text{a}}$ of the S-H group in cysteine has long been known³¹⁹ and was recently determined as a function of temperature and ionic strength.³²⁰ It is very similar to the $\text{p}K_{\text{a}}$ of other alkyl thiols,³¹⁵ which is not surprising since the side chain is fairly separated from the amine and carboxylate groups. The $\text{RS}^\bullet + \text{H}^+ + e^- \rightarrow \text{RSH}$ redox potential of cysteine, determined by Prütz and co-workers, is also very similar to the values determined by Surdhar and Armstrong (see above). Thus, the PCET thermochemistry of cysteine, glutathione, and alkyl thiols are very similar. Like phenols and ascorbate, the intermediates of single proton or electron transfer of RSH species are high in energy, indicating that thiols preferentially lose $\text{H}^\bullet$ under normal physiological conditions.

5.8 C-H bonds and H_2

Bell, Evans, and Polanyi showed in the 1930s that the facility of hydrogen atom abstraction from hydrocarbons parallels the gas phase homolytic BDE of the C-H bond being cleaved. Ever since then, BDEs have been central to organic free radical chemistry, and have been widely used for solution as well as gas-phase radical reactions: the gas phase BDE is the typical starting point for understanding the reactivity of C-H bonds. However, it should be noted that other factors besides C-H bond strength affect radical reactivity. For instance, the polar effect³²⁸ of electron withdrawing substituents makes C-H bonds much less reactive towards electrophilic radicals such as $^\bullet\text{BuO}$, as illustrated above in the lack of reactivity of acetonitrile solvent with this radical.¹⁹⁸

This portion of the review is divided into three subsections. The first presents selected thermochemical data for simple hydrocarbons and small alkylaromatic compounds. Readers interested in a wider range of compounds are referred to specialized reviews on the acidities, redox potentials, and bond dissociation energies of organic compounds. In particular, Bordwell and co-workers measured $\text{p}K_{\text{a}}$ s in DMSO for many compounds with weak C-H bonds, as well as a number of redox potentials of the corresponding anions.^{29,69,329} One version of this is available online.²⁹ Kochi and others have discussed outer-sphere electron transfer reactions of organic compounds³³⁰ and Ebersson's book on electron transfer in organic chemistry is particularly useful.³³¹ Recently, Luo has assembled an excellent and very extensive monograph on bond dissociation energies (which is also in part available online).⁵⁹ The second section below discusses the thermochemistry of nicotinamide derivatives and analogs, which are perhaps the most important biological PCET reagents with reactive C-H bonds. There are a number of other redox-active C-H bonds in biology that we would like to include, such as the glycine that is oxidized to a glycy radical in the catalytic cycle of pyruvate formate-lyase activating enzyme³³² and the adenosine methyl C-H bond that is formed and cleaved in the catalytic cycles of vitamin B_{12} and radical-SAM enzymes.³³³ However, little experimental thermochemistry is available for these systems; the interested reader is referred to computational studies.³³⁴ Finally, this section concludes with a discussion of the PCET thermochemistry of H_2 .

5.8.1 Hydrocarbons—Gas phase C-H BDEs of hydrocarbons have been repeatedly reviewed, but the reader is cautioned that the “best” values have changed over time (the reasons for this are nicely explained by Tsang⁷⁰). Two of the more valuable current sources are a review by Blanksby and Ellison of gas phase BDEs of common organic and inorganic

compounds³⁷ and Luo's monograph mentioned above.⁵⁹ Table 17 presents some of these data for hydrocarbons (and xanthene), as well as a few pK_a and E values. For a number of entries in the Table, the solution bond strength has been calculated from the gas phase value using Abraham's model, which is expected to work well here. In the absence of strong hydrogen bonding, the energies of solution are small and the differences in these energies should be very small [*e.g.*, $\Delta G_{\text{solv}}^\circ(\text{R}^\bullet) - \Delta G_{\text{solv}}^\circ(\text{RH}) \cong 0$]. This means that the solution bond strengths differ from the gas phase values primarily by the different solvation energies of $\text{H}^\bullet$ (see eq 11 above). Using this method, we estimate $\text{BDFE}(\text{H}_3\text{C-H}) \cong 106 \text{ kcal mol}^{-1}$ in water and, using eq 16, $E^\circ(\text{CH}_3^{\bullet-}) = -0.7 \text{ V vs. NHE}$.

For several aromatic hydrocarbons, redox potentials $E(\text{R}^{+/0})$ are available in MeCN solvent.³³⁵ For toluene, *p*-xylene and fluorene there are also data for the reduction of the neutral radical $\text{R}^\bullet$, and estimates can be made of the pK_a s in MeCN. Thus, a complete cycle can be made for these reagents. However, readers should be cautioned that potentials and pK_a s that are very high or very low are difficult to measure and may have larger errors.

These hydrocarbons, as exemplified by toluene, are extreme examples of reagents that prefer to react by $\text{H}^\bullet$ transfer rather than the stepwise paths of ET-PT or PT-ET. Few reagents are basic or oxidizing enough to mediate single electron or single proton transfers with toluene and other alkyl aromatics, yet the toluene C–H is of modest strength and is relatively easily abstracted. As discussed in more detail below, toluene is oxidized by a variety of transition metal complexes and most of these reactions must proceed via concerted transfer of $\text{H}^\bullet$ because the stepwise electron transfer or proton transfer intermediates are simply too far uphill. However, an interesting exception involving stepwise ET-PT is also discussed in Section 6, below. As noted above for hydroxylamines and phenols, one of the hallmarks of a reagent that prefers to transfer an electron and proton together is that the pK_a of the changes dramatically upon redox change (and, equivalently, the E° changes dramatically upon deprotonation). For toluene, the pK_a s of PhCH_3 and $\text{PhCH}_3^{\bullet+}$ differ by more than 50 orders of magnitude!

5.8.2 Nicotinamide derivatives—One of the archetypal biological redox reactions of C–H bonds is the $\text{H}^+/2e^-$ couple in reactions of nicotinamide adenine nucleotide (NAD^+/H) and nicotinamide adenine dinucleotide phosphate (NADP^+/H , Figure 8). As noted above, NADH and NADPH commonly transfer hydride to flavins in many different enzyme catalytic cycles. Kreevoy and coworkers have beautifully explored the hydride transfer chemistry of NADH analogs, and shown that the kinetics of these reactions are related to the thermochemistry of hydride transfer.⁵⁷ More recently, other cellular roles of nicotinamides have been uncovered.³⁴⁹ *In vitro*, nicotinamide derivatives and analogs can undergo electron transfer, hydrogen atom transfer, and hydride transfer reactions (similar to flavins), as has been shown in a number of studies.³⁵⁰

The reactivity of NADH and related compounds, such as *N*-benzyl-1,4-dihydronicotinamide (BNAH) and 10-methyl-9,10-dihydroacridine (AcrH_2), has been widely studied, and there are a few reports of the redox potential and pK_a data necessary to draw complete thermochemical scheme. Nicotinamides are oxidized by two electrons with loss of one proton, to give the corresponding pyridinium ion, so a double square scheme is needed to describe each system (Figure 9). Nicotinamide radical cations are quite acidic, like the hydrocarbon radical cations discussed above, and the closed shell (reduced) nicotinamides are very poor acids, highlighting the typical preference of these compounds to undergo PCET rather than ET or PT. Cheng *et al.* have presented thermochemical data for aqueous NADH³⁵¹ and for 10-methyl-9,10-dihydroacridine (AcrH_2) in DMSO³⁵² and MeCN (Figure 9),³⁵³ although questions have been raised about some of these results.³⁵⁴ For AcrH_2 in MeCN, there is reasonable agreement between Cheng's values and those reported

earlier by Savéant and Neta, but there is a substantial disagreement in the values for BNAH. 355 There is also a discrepancy between Cheng *et al.*'s data³⁵¹ and other literature values³⁵⁶⁻³⁵⁷ for NADH in water. The E° and pK_a data can be converted to BDFEs and hydride affinities ($\Delta G^\circ(H^-)$), as discussed above. The derived hydride affinities for AcrH₂ and benzyl nicotinamide BNAH (Figure 8) in MeCN are in reasonable agreement with those obtained from equilibrium measurements,³⁵⁸ and the difference between them similarly agrees with the relative hydride affinities reported by Wayner.³⁵⁹ Methylated BNAH derivatives show thermochemistry that is similar to the parent compound in MeCN.³⁶⁰

5.8.3 Hydrogen—The H–H bond in dihydrogen is in many ways very similar to the C–H bond in methane. The gas phase BDE³⁶¹ and BDFE⁴⁹ of H₂ are known (Table 19). These gas phase values are within 1 kcal mol^{−1} of methane. These BDEs and BDFEs, along with the known enthalpies and entropies of solution, are used to calculate BDEs and BDFEs in various solvents, using Roduner's 2005 demonstration that the solvation of H[•] is energetically roughly equal to that of H₂.⁵⁰ As described in Section 3.1 above, use of this approximation has led to revision of the H⁺/H[•] reduction potentials in different solvents. The H[•]/H[−] reduction potentials in water³⁶² and in DMSO and MeCN³⁶³ have been reported, allowing the pK_a of H₂ to be estimated by eq 22. H₂ is very weakly acidic, though significantly more acidic than methane. Recently Kelly has proposed new values for $pK_a(H_2)$ and $E^\circ(H^\bullet/H^-)$, some of which are very different from the values that have long been used.³⁶⁴

$$pK_a(H_2)_{(solv)} = [BDFE(H_2)_{solv} - F[E^\circ(H^\bullet/H^+)_{solv} + E^\circ(H^\bullet/H^-)_{solv}]]/1.37 \quad (22)$$

5.9 Separate Proton and Electron Donors/Acceptors

This review primarily deals with PCET reagents, that is individual chemical compounds that can donate or accept proton(s) and electron(s). *From a thermodynamic perspective*, this is equivalent to two reagents, one of which accepts or donates proton(s) and the other of which accepts or donates electrons. For instance, ferrocene-carboxylic acid is a single PCET reagent that can donate $e^- + H^+$ (H[•]) to give the zwitterionic ferrocene carboxylate, with an effective BDFE of 68 kcal mol^{−1} in 80/20 MeCN/H₂O solvent [assuming that $C_G(\text{MeCN}) \sim C_G(\text{MeCN}/\text{H}_2\text{O})$].³⁶⁵ Similarly, the combination of ferrocene and benzoic acid can donate $e^- + H^+$. One can even define a formal BDFE for the Cp₂Fe + benzoic acid combination in MeCN, 83.3 kcal mol^{−1}, using the same eq 7 as used above for a single PCET reagent. The thermodynamic calculation is independent of whether the proton and electron come from a single reagent or two reagents. The most famous example of a separate outer-sphere oxidant and a base accomplishing a PCET reaction is the oxidation of tyrosine Z in photosystem II, in which the proton is transferred from tyrosine Z to a nearby histidine while the electron is transferred to the chlorophyll radical cation P680^{•+} about 14 Å away.¹⁰⁸

The use of a “BDFE” for two separated reagents is perhaps a bit peculiar, because there is no X–H bond that is being homolytically cleaved. It is, however, a very useful way to characterize the thermochemistry of a PCET system, and it emphasizes the thermodynamic equivalence of H⁺/ e^- acceptors and H[•] acceptors [H⁺/ e^- donors and H[•] donors]. The literature for water oxidation, for example, typically quantifies the free energy required as a minimum redox potential of $E^\circ = 1.23$ V (pH 0). However, this puts emphasis on the electron, while the thermochemistry depends equally on the e^- and the H⁺. What is needed to convert H₂O to O₂ is a PCET reagent *or* PCET system with an average BDFE of ≥ 86 kcal mol^{−1} (eq 18, described above). This free energy can be obtained with a single PCET reagent or with a combination of an oxidant and a base. The required free energy can be obtained with a strong oxidant plus a weak base, or a weak oxidant plus a strong base. While

this area has not received the same detailed study as traditional H-atom transfer reactions, we believe that it is a very important and versatile approach to PCET, and will prove to be widely used in biology and valuable in the development of new chemical processes.

A huge number of possibilities are possible for oxidant/base combinations ($H^\bullet$ acceptors) and reductant/acid combinations ($H^\bullet$ donors). This is because there are many one-electron redox reagents and a huge number of possible acids/bases. A few examples are listed in Table 20, with an emphasis on $H^\bullet$ acceptors in MeCN, based on our experience (*cf.*, reference 366). The same principles should apply to other solvents and to " $H^\bullet$ donors." Listings are available of stable, isolable one-electron oxidants and reductants and their potentials in MeCN,²⁵⁴ as well as tabulations of organic acids and bases and their pK_a s.²⁸⁻³⁰⁻⁸⁹ There are, however, practical limitations at both the extremes of strong $H^\bullet$ acceptors (high BDFEs) and strong $H^\bullet$ donors (low BDFEs). In general, bases are electron-rich and can be oxidized, and in our experience this limits the combinations that are available at high BDFE. Similarly, strong reductants are electron rich and are often protonated by acids, and acids are often easily reduced to H_2 . Some of the challenges are illustrated by the Schrock/Yandulov nitrogen reduction system, which uses decamethylchromocene as the very strong reductant (E° for $CrCp^*_2 = -1.47$ V in THF *vs.* $Cp_2Fe^{+/0}$ [$Cp^* = C_5Me_5$]) and [2,6-lutidinium]BAR'₄ [$Ar' = 3,5-(CF_3)_2C_6H_3$] as the acid.^{245b} As Schrock wrote: "Heptane was chosen as the solvent to minimize the solubility of [2,6-lutidinium]BAR'₄ and thereby minimize direct reduction of protons by $CrCp^*_2$ in solution. Slow addition of the reducing agent in heptane to an Mo complex and [2,6-lutidinium]BAR'₄ in heptane (over a period of 6 h with a syringe pump) was chosen to minimize exposure of protons to $CrCp^*_2$ at a high concentration."^{245b}

Waidmann *et al.* have explored combinations of triarylaminium oxidants and substituted pyridine bases as strong $H^\bullet$ acceptors in CH_2Cl_2 .³⁶⁶ One of the key observations in these studies is that trace reducing impurities in the pyridine base can lead to decay of the aminium oxidant. Thus, careful purification of the base appears to be important. Furthermore, some oxidant-base combinations may not be compatible. For example, the $N(4-Br-C_6H_4)_3^{3+}$ ($E_{1/2} = 0.67$ V versus $Cp_2Fe^{+/0}$ in MeCN²⁵⁴) is stable in the presence of pyridine ($pK_a = 12.530$) at 298 K, but decays in the presence of 4-NH₂-pyridine ($pK_a = 17.630$). [For the reader not accustomed to this electrochemical scale, $Cp_2Fe^{+/0}$ in MeCN is roughly +0.63 V *vs.* aqueous NHE.³³] By using different combinations of oxidant and base, effective BDFEs ranging from 76 to 100 kcal mol⁻¹ can be achieved (Table 20). Roughly the same BDFE can often be achieved with different combinations of oxidants and bases, which allows flexibility in selecting oxidant/base combinations based on the requirements or limitations of a given PCET system and which can be a valuable mechanistic test.

The discussion above has emphasized the *thermodynamics* of oxidant/base and reductant/acid combinations of reagents, and that they are equivalent to the thermochemistry of single PCET reagents. However, equivalent BDFEs does not necessarily mean that the *kinetic behavior* will be the same for single PCET reagents *vs.* combinations, or even that similar pathways – stepwise *vs.* concerted – will be followed. A few studies have shown that two separate reagents can accomplish concerted transfer of H^+ and e^- , termed separated CPET (or multisite EPT). In perhaps the first clear example, Linschitz and co-workers oxidized phenols hydrogen-bonded to pyridines, using photogenerated triplet C_{60} as the oxidant (eq 23).³⁶⁷ They showed that proton transfer to the pyridine is concerted with electron transfer to the oxidant. Hammarström and Nocera have studied reactions in which a tethered tyrosine is oxidized by a photoexcited transition metal complex (Ru or Re), with proton transfer to an intramolecular carboxylate or to the aqueous solvent or buffer.^{10,14,368} Both separated CPET and stepwise proton transfer then electron transfer mechanisms have been observed. Rhile, Markle and co-workers have examined oxidations of phenols with an attached base,

in which outer-sphere electron transfer to an oxidant A^+ is concerted with intramolecular proton transfer (eq 24).³⁶⁹ Hammarström and Savéant have examined similar systems.^{368b,e,f,370} Costentin has very thoroughly and clearly reviewed electrochemical CPET reactions, in which electron transfer to/from an electrode is concerted with proton transfer.³

(24)

The examples in the previous paragraph show that combinations of oxidant and base, or reductant and acid, can in some circumstances accomplish concerted transfer of an electron and a proton. Thus, considering these combinations as having an ‘effective BDFE’ is reasonable. More studies are needed to examine the generality and utility of these combination PCET reagents. In addition, as illustrated in the next section, the distinction between a single PCET reagent and two separate reagents is not always so clear.

5.10 Selected Transition Metal Systems

The PCET chemistry of a wide range of transition metal systems has been investigated over the last few decades. No individual system has received the scrutiny of many of the classic organic systems discussed above, such as phenol, but there are examples for most of the transition metals that readily undergo one-electron redox change. A comprehensive account of all known transition metal PCET systems is beyond the scope of this review, which just presents selected examples, particularly from our laboratories.

Transition metal containing systems can mediate a range of PCET reactions. Most of these systems undergo redox change at the metal coupled to protonation or deprotonation at a ligand. A classic example is the interconversion of a metal hydroxide complex with a one-electron oxidized metal-oxo compound (eq 25). This could be viewed as analogous to the oxidation of a phenol to a phenoxyl radical, in which the aromatic ring is oxidized by $1e^-$. HAT reactions involving metal hydride complexes, which are well known, are somewhat different because both the redox and acid/base chemistry occur at the metal center. In some ways, HAT from metal hydrides is similar to that of C–H bonds.

The thermochemistry of transition metal PCET reagents is typically determined by pK_a and E° measurements (Scheme 12), and sometimes by equilibration with other PCET reagents. In the same manner as done above, these free energy measurements yield BDFE values using eqs 7, 15, or 16, as listed in Table 21 below. Unlike the data for organic reagents above, data are typically available for a given transition metal system only in one solvent, because of experimental limitations. BDFEs can not be adjusted as above because the Abraham model is untested and difficult to apply for metal complexes. Table 21 also does

not include data for BDEs unless they have been directly measured via calorimetry or van't Hoff analysis. This is because, as discussed in Section 3.1, ground state entropy changes in transition metal PCET systems can be substantial. Thus, use of BDFEs is especially important in these cases.

5.10.1 Metal-Oxo and Hydroxo Complexes—The aqueous redox chemistry of transition metal ions has long been known to be critically dependent on the solution pH, and to involve aquo, hydroxo, and oxo species. Pourbaix first assembled a compendium of diagrams summarizing the aqueous behavior of each metal in 1945.⁶⁷ There are two excellent books on the properties of aqueous metal ions.³⁷² The chemical reactivity of transition metal-oxo complexes in particular have been of special interest to chemists and biochemists for many years.³⁷³ Compounds such as KMnO_4 , OsO_4 and RuO_4 are important reagents for organic oxidations,³⁷⁴ and many of their reactions are proton coupled. Metal-oxo intermediates are similarly implicated in a range of biological oxidations, in particularly the oxo-iron(IV) (ferryl) intermediates found in the catalytic cycles of peroxidases, cytochromes P450, and many other heme and non-heme iron enzymes.³⁷⁵ The dissolution/precipitation of many oxide/hydroxide minerals in the environment can also be a PCET process.³⁷⁶ For these reasons and others, there may be more interest in PCET reactions of the metal-oxo/hydroxo/aquo complexes than any other class of compounds.

For the simple aquo ions of metal cations, and for oxyanions of both main-group and transition-metal elements, most redox processes are proton-coupled.⁶⁷ A simple example is the oxidation of aqueous ferrous ion, $[\text{Fe}(\text{H}_2\text{O})_6]^{2+}$, in mildly acidic solutions to give – at least in principle – the ferric hydroxo ion $[\text{Fe}(\text{OH})(\text{H}_2\text{O})_5]^{2+}$. This transformation is loss of $\text{H}^\bullet$ and has a BDFE of $79.5 \text{ kcal mol}^{-1}$ based on the well-known $\text{Fe}(\text{H}_2\text{O})_6^{3+/2+}$ aqueous redox potential (0.77 V) and the $\text{p}K_a$ of aqueous Fe^{III} .³⁷² In practice, such reactions are challenging to study because of the hydrolysis of the cations – the $[\text{Fe}(\text{OH})(\text{H}_2\text{O})_5]^{2+}$ product under most conditions loses additional protons and precipitates a hydrous oxide/hydroxide. Using transient methods, Bakac has studied aqueous PCET reactions of simple metal-oxo aquo ions, for example showing that oxidations of organics by $\text{Fe}^{\text{IV}}\text{O}^{2+}$ occurs by either HAT or hydride transfer.³⁷⁷ The chromium(III) superoxo complex $(\text{H}_2\text{O})\text{CrOO}^{2+}$ was found to undergo various PCET reactions and, starting from Anson's $1\text{H}^+/1\text{e}^-$ electrochemical data,³⁷⁸ a bond strength for $(\text{H}_2\text{O})_5\text{CrOO}-\text{H}^{2+}$ (BDFE = $81.4 \text{ kcal mol}^{-1}$) was determined.³⁷⁹ Bakac has also discussed the BDFEs in $(\text{H}_2\text{O})_5\text{CrO}-\text{H}^{2+}$, $(\text{Me}_6\text{cyclam})(\text{H}_2\text{O})\text{Rh}(\text{OO}-\text{H})^{2+}$, $(\text{Me}_6\text{cyclam})(\text{H}_2\text{O})\text{Co}(\text{OO}-\text{H})^{2+}$, and $(1,4,8,11\text{-tetraazacyclotetradecane})(\text{H}_2\text{O})\text{Co}(\text{OO}-\text{H})^{2+}$, ($\text{Me}_6\text{cyclam} = \text{meso-hexamethylcyclam}$).³⁸⁰⁻³⁸¹ The BDFEs given for these species in Table 21 are slightly different than those in Bakac's original reports because of reevaluation of the value for $E^\circ(\text{H}^+/\text{H}^\bullet)_{\text{aq}} [\text{C}_G(\text{H}_2\text{O})]$ as noted in Sections 3.1 and 5.8.3.

Probably the best studied metal PCET system, and one of the earliest studied in detail, is the ruthenium polypyridyl complex $[\text{cis}-(\text{bpy})_2(\text{py})\text{Ru}^{\text{IV}}\text{O}]^{2+}$ (abbreviated $[\text{Ru}^{\text{IV}}\text{O}]$), developed by Meyer and coworkers ($\text{bpy} = 2,2'$ -bipyridine, $\text{py} = \text{pyridine}$).³⁸² An extensive 2007 *Chemical Reviews* article is focused on this and other closely related complexes.^{1b} Various reactions have been investigated including ET,³⁸³ PCET,³⁸⁴ C–H bond oxidations by HAT,³⁸⁵ and by hydride abstraction,³⁸⁶ HAT from O–H bonds,³⁸⁷ and others.³⁸⁸ Related compounds are of much current as catalysts for the oxidation of water to O_2 .⁶⁸⁻³⁸⁹ The thermochemical landscape of this system has been thoroughly worked out by Meyer and coworkers³⁸³⁻³⁹⁰ and is summarized in Figure 10 and Table 21. $[\text{Ru}^{\text{IV}}\text{O}]$ has a very strong preference to accept H^+ and e^- together; no well defined $\text{p}K_a$ for its protonation or E° for its non-proton-coupled reduction could be determined.³⁸³ The limits on these values are included in Figure 10 in parentheses. The relatively large bond strengths in the $[\text{Ru}^{\text{IV}}\text{O}]$ system allow it to oxidize a number of strong bonds C–H bonds via H-atom abstraction.

The PCET properties of a number of other transition metal oxo complexes have been examined. Borovik and co-workers have prepared unusual non-heme manganese and iron hydroxo/oxo systems stabilized by a hydrogen-bonding ligand, and has reported a number of O–H bond strengths.^{391–392} Stack *et al.* have determined O–H bond strengths for H₂O–ligated or MeOH–ligated iron and manganese complexes (Py5)M(ROH)²⁺ as models for lipoxygenase enzymes which use a non-heme iron(III) hydroxide to oxidize fatty acids by an HAT mechanism (Py5 = 2,6-bis(bis(2-pyridyl)methoxymethane)-pyridine).^{393–395}

Oxidized iron-heme active sites are perhaps the most important and most studied PCET reagents. The so-called “compound I” and “compound II” intermediates are the reactive species in the catalytic cycles of cytochromes P450, peroxidases, and other enzymes that accomplish a wide range of important transformations.³⁹⁶ Compound I species are two redox levels above the iron(III) resting state, and are usually described as iron(IV)–oxo complexes with an oxidized ligand, usually a porphyrin radical cation. Compound II species are one-electron oxidized and were traditionally viewed all as iron(IV)–oxo compounds. However, Green and co-workers have recently described a number of lines of evidence that some Compound II's are basic ($pK_a > 8.2$) and are actually iron(IV)–hydroxo species.^{397–398} In these cases, the conversion of compound I to compound II is an unusual PCET process, in which the proton is transferred to the oxo group and the electron to the porphyrin radical cation (Scheme 13). Based on the apparent pK_a values for of compound II in myoglobin, horseradish peroxidase, cytochrome *c* peroxidase and catalase, it was concluded that only thiolate-ligated Compound IIs have substantial basicity. As should be clear to readers of this review, the basicity of Compound II is a key component of the free energy of PCET or HAT to compound I. Thus, the ability of cytochrome P450 enzymes to abstract H[•] from strong C–H bonds is intimately tied to the basicity of Compound II, as well as its redox potential. Behan and Green have also estimated, using equation 7 above, the minimum redox potentials and pK_a s necessary for ferryl containing systems to achieve a BDE of 99 kcal mol^{−1} (so that HAT from cyclohexane would be isothermal).³⁹⁸

Small-molecule metal-oxo porphyrin species have been widely studied, both as models for heme proteins and as reactive intermediates in catalytic oxidation processes. These systems are very oxidizing, reacting via ET, PCET, oxygen atom transfer and other pathways, which makes direct determination of redox and acid/base properties challenging. Groves *et al.* have reported aqueous pK_a values for manganese(V)–oxo–hydroxo complexes with water-soluble porphyrins, 7.5 for the *tetra*-(*N*-methyl-2-pyridyl)porphyrin (complex and 8.6 for the isomeric *N*-methyl-4-pyridyl (4TMPy) derivative.³⁹⁹ They have also estimated, using rate constants for HAT reactions and the Brønsted-Evans-Polanyi relationship, O–H bond dissociation enthalpies of ~100 kcal mol^{−1} for [(5,10,15,20-*tetra*-(*N*-methyl-4'-pyridyl)porphyrin))Fe^{IV}OH]⁵⁺, ~92 kcal mol^{−1} for [(5,10,15,20-*tetra*-(*mesityl*)porphyrin)Fe^{IV}OH]⁺, and ~86 kcal mol^{−1} for [(5,10,15,20-*tetra*-(*pentafluorophenyl*))porphyrin)Fe^{IV}OH]⁺.⁴⁰⁰ Shaik *et al.* have computed an O–H BDE of ~86 kcal mol^{−1} for a gas-phase Fe^{IV}OH complex of a simplified protoporphyrin IX model.^{396a} Goldberg's porphyrinoid Mn^VO(corrolazine) complex has a relatively low redox potential in MeCN ($E_{1/2}(\text{Mn}^{\text{V/IV}}) = -0.43$ V vs. Cp₂Fe⁺⁰) yet is able to abstract H[•] from fairly strong phenolic O–H bonds.⁴⁰² Based on these results and eq 7, they concluded that the reduced Mn^{IV}O species must be quite basic.

Related ruthenium compounds with porphyrin, salen or tetramine macrocycles have also been studied in detail, as has been reviewed elsewhere.⁴⁰³ For instance, Lau and coworkers have studied in detail oxidation reactions of *trans*-[Ru^{VI}(tmc)(O)₂]²⁺, *trans*-[Ru^{IV}(tmc)(O)(solvent)]²⁺, and *trans*-[Ru^{II}(tmc)(H₂O)₂]²⁺, where *tmc* is the macrocyclic tertiary amine ligand 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane.⁴⁰⁴ A full Pourbaix diagram was developed from aqueous electrochemical data, which indicates BDFEs of 74.3 kcal mol^{−1}

for $\text{Ru}^{\text{V}}(\text{O})(\text{O}-\text{H})$ and $82.5 \text{ kcal mol}^{-1}$ for $\text{Ru}^{\text{IV}}(\text{O})(\text{HO}-\text{H})$.⁴⁰⁵ Consistent with these values, this and related complexes abstract $\text{H}^\bullet$ from alkylaromatic compounds.⁴⁰⁶ Lau *et al.* have also shown that Lewis acids can greatly enhance the ability of oxo reagents to abstract $\text{H}^\bullet$ from C–H bonds, due to the stabilization of the reduced oxidant by the Lewis acid and therefore the larger O–H BDFE in the presence of the acid.⁴⁰⁷

The first studies of metal-mediated HAT in our labs involved chromyl chloride (CrO_2Cl_2) and permanganate.^{211,408,409} The known aqueous $E^\circ(\text{MnO}_4^{2-/-}) = 0.564 \text{ V}$ and $\text{p}K_{\text{a}}(\text{HMnO}_4^-) = 7.4$ give, using equation 7, $\text{BDFE}(\text{O}_3\text{MnO}-\text{H}^-) = 80.7 \text{ kcal mol}^{-1}$ (which was reported originally as a BDE of $80 \pm 3 \text{ kcal mol}^{-1}$). The ability of CrO_2Cl_2 and MnO_4^- to abstract $\text{H}^\bullet$ from hydrocarbons was rationalized on the basis of this bond strength, which is high for isolable, stable species. More recently, H-transfer reactions of *cis*-vanadium dioxo complexes, $(\text{bpy})_2\text{V}^{\text{V}}(\text{O})_2^+$, have been examined,²⁴ and a VO–H BDFE of $70.6 \text{ kcal mol}^{-1}$ was obtained by equilibration with 2,6-di-*tert*-butyl-4-methoxyphenol. This system has unusually large barriers to HAT which are due to the substantial inner-sphere reorganization that occurs between $(\text{bpy})_2\text{V}^{\text{V}}(\text{O})_2^+$ and $(\text{bpy})_2\text{V}^{\text{IV}}(\text{O})(\text{OH})^+$.²⁴

Bridging oxo and hydroxo ligands can also be involved in PCET reactions. Pecoraro, Baldwin, and Caudle,^{410,411} and independently Brudvig, Crabtree and Thorp,⁴¹² showed that dimeric μ -oxo manganese compounds such as $[(\text{phen})_2\text{Mn}^{\text{IV}}(\mu\text{-O})_2\text{Mn}^{\text{III}}(\text{phen})_2]^{3+}$ ($[\text{Mn}^{\text{IV}}\text{Mn}^{\text{III}}_2(\text{O})_2]^{3+}$, phen = 1,10-phenanthroline) are reduced with addition of protons to make $[\text{Mn}^{\text{III}}_2(\text{O})(\text{OH})]^{3+}$ and $[\text{Mn}^{\text{III}}\text{Mn}^{\text{II}}(\text{OH})_2]^{3+}$. Pecoraro *et al.* derived BDE values and showed that these hydroxide complexes could donate $\text{H}^\bullet$ to a phenoxyl radical, and thus suggested that these are potential models for the manganese cluster in Photosystem II (the oxygen evolving cluster) which is oxidized by the nearby tyrosine Z radical. A more recent report has described transfer of $\text{H}^\bullet$ from a μ -hydroxide to 2,4,6-*t*-Bu₃PhO $^\bullet$.⁴¹³ It was later shown that $[\text{Mn}^{\text{IV}}\text{Mn}^{\text{III}}_2(\text{O})_2]^{3+}$ can abstract $\text{H}^\bullet$ from alkylaromatic hydrocarbons with weak C–H bonds, consistent with the thermochemistry summarized in Figure 11.⁴¹⁴ The more highly oxidized dimer, $[\text{Mn}^{\text{IV}}_2(\text{O})_2]^{4+}$, has a much higher $1e^-$ redox potential and oxidizes aromatic hydrocarbons either by ET or by hydride abstraction.⁴¹⁵ $\text{H}^\bullet$ abstraction by $[\text{Mn}^{\text{IV}}_2(\text{O})_2]^{4+}$ is not observed because the one-electron reduced product $[\text{Mn}^{\text{IV}}\text{Mn}^{\text{III}}_2(\text{O})_2]^{3+}$ is not basic, and therefore the thermodynamics are not favorable to form “ $[\text{Mn}_2(\text{O})(\text{OH})]^{4+}$ ”.⁴¹⁶ More recently, a number of laboratories have shown that dimeric $\text{Cu}^{\text{III}}\text{-}\mu$ -oxo complexes abstract $\text{H}^\bullet$ from C–H and O–H bonds, as has been reviewed and discussed elsewhere.⁴¹⁷ Unfortunately, this system has not proven amenable to detailed thermodynamic measurements, despite considerable effort.⁴¹⁷

5.10.2 Metal Complexes with N–H Bonds—Metal-imido, –amide, and –amine complexes, MNR , MNR_2 and MNR_3 , are isoelectronic with metal–oxo, –hydroxo, and –aquo species. These appear to undergo analogous PCET processes, although far fewer systems have been examined. The nitrogen derivatives have an additional substituent and are therefore more sterically encumbered than their oxygen relatives. Che,⁴¹⁸ Holland⁴¹⁹ and others have shown that metal-imido species can abstract $\text{H}^\bullet$ from C–H bonds, analogous to the oxo complexes above, but little thermochemical data are available. In principle, oxidizing metal amide complexes MNR_2 could be good $\text{H}^\bullet$ acceptors due to the basicity of the amide ligand. For instance, De Santis and co-workers have reported E° and $\text{p}K_{\text{a}}$ data for $\text{Ni}^{\text{II}}(\text{cyclam})$ which indicate $\text{BDFE} = 89.1 \text{ kcal mol}^{-1}$ to give the Ni^{III} with a deprotonated cyclam ligand.⁴²⁰ However, the amide ligand itself is often susceptible to oxidation, losing hydrogen from the α -carbon to form imines or nitriles.⁴²¹ Che has used the oxidation-protected 2,3-diamino-2,3-dimethylbutane ligand ($\text{H}_2\text{NCMe}_2\text{CMe}_2\text{NH}_2$) to prepare oxidizing Ru^{IV} amides (and reported their Pourbaix diagrams).⁴²²

Anilido ligands, NHAr^- , can not be oxidized by loss of α -hydrogens (but they can be susceptible to nucleophilic attack in oxidizing compounds⁴²³). The Os^{IV} anilido complex $\text{TpOs}(\text{NHPh})\text{Cl}_2$ (Tp = hydrotris(1-pyrazolyl)borate, HBpz_3) converts to the Os^{III} -aniline derivative $\text{TpOs}(\text{NH}_2\text{Ph})\text{Cl}_2$ on addition of one electron and one proton.⁴²⁴ In the thermochemical square scheme in MeCN, there is a remarkably large shift of the pK_a of the aniline ligand from -3 when bound to Os^{IV} to 22.5 on Os^{III} . The redox potential shifts from strongly oxidizing for the protonated forms, $E_{1/2}(\text{TpOs}(\text{NH}_2\text{Ph})\text{Cl}_2^{+/0}) = +0.48 \text{ V}$ vs. $\text{Cp}_2\text{Fe}^{+/0}$, to quite reducing for the anilide, $E(\text{TpOs}(\text{NHPh})\text{Cl}_2^{0/-}) = -1.05 \text{ V}$. The 1.53 shift in potential is, in free energy terms, exactly the same as 25 unit shift in pK_a , as it has to be by Hess' Law since these are all part of the same square scheme (Scheme 12). This large shift is reminiscent of the $[\text{cis}-(\text{bpy})_2(\text{py})\text{Ru}^{\text{IV}}\text{O}]^{2+}$ system (Figure 10) and probably has the same origin, that the oxidized form has a metal-ligand π bond that is disrupted upon reduction. In the osmium system, the rate constants for degenerate ET, PT, and HAT self-exchange were all obtained.⁴²⁴

There are a number of metal-imidazole and related PCET systems where protonation/deprotonation occurs at the nitrogen not bound to the redox-active metal center. In such systems there is a formal separation between the redox and the acid/base sites (see also Section 6): there are 3 chemical bonds and $\sim 4 \text{ \AA}$ separation between the metal center and the acidic/basic nitrogen (Figure 12). Even with this separation the redox and acid/base chemistry is still coupled. In general, protonation/deprotonation of metal-imidazole complexes results in a change of 0.3 to 0.5 V in reduction potential (Table 21 and reference 425). Even though this 'thermochemical communication' is substantially less than in compounds where the proton is bound to an atom directly bonded to the metal, as discussed above, imidazole complexes are still able to mediate concerted H-transfer reactions.

Of these systems perhaps the most well explored are the iron(II)tris(2-2'-biimidazoline)²⁺ ($\text{Fe}^{\text{II}}\text{H}_2\text{bip}$) and iron(II)tris(2,2'-(tetrahydro)pyrimidine)²⁺ ($\text{Fe}^{\text{II}}\text{H}_2\text{bip}$).⁸⁴ 426–427 428 The $\text{Fe}^{\text{II}}(\text{H}_2\text{bim})$ and $\text{Fe}^{\text{II}}(\text{H}_2\text{bip})$ systems have similar acid/base properties in MeCN, with $\text{pK}_a = 17.5$. The systems have slightly different redox potentials in MeCN, $E_{1/2}(\text{Fe}^{\text{III/II}}(\text{H}_2\text{bim})) = -0.31 \text{ V}$ ⁸⁴ and $E_{1/2}(\text{Fe}^{\text{III/II}}(\text{H}_2\text{bip})) = -0.55 \text{ V}$ ⁴²⁸ (both vs. $\text{Fc}^{+/0}$). Application of eq 7 gives $\text{BDFE}(\text{Fe}^{\text{II}}\text{H}_2\text{bim}) = 71.7 \text{ kcal mol}^{-1}$ and $\text{BDFE}(\text{Fe}^{\text{II}}\text{H}_2\text{bip}) = 66.2 \text{ kcal mol}^{-1}$. The $\text{Fe}^{\text{II}}\text{H}_2\text{bip}$ and $\text{Fe}^{\text{III}}\text{H}_2\text{bip}$ compounds are both mixtures of high-spin and low-spin forms at ambient temperatures in MeCN, which indirectly affects their hydrogen atom self-exchange rate.⁴²⁷ The related cobalt- H_2bim complexes have similar thermochemistry, with a BDFE of $70.5 \text{ kcal mol}^{-1}$.⁴²⁹ In this system, $\text{Co}^{\text{II}}\text{H}_2\text{bim}$ is high spin while $\text{Co}^{\text{III}}\text{H}_2\text{bim}$ is low spin, and HAT reactions that interconvert these two are very slow.⁴²⁸ 429 These iron and cobalt H_2bim and H_2bip systems all have large ground-state entropy changes (ΔS°) associated with their $1e^-/1\text{H}^+$ redox couples, so the initial analyses of these systems using BDEs has been revised.³⁹ 40

Related ruthenium systems have been developed using a bidentate 2-(2'-pyridyl)-imidazole ligand (py-imH) and with either acac (2,4-pentanedionato) or 1,1,1,5,5,5-hexafluoro-acac (hfacac) as supporting ligands.⁴³⁰ In both sets of compounds, deprotonation of the imidazole reduces the redox potential by 0.36 V (and, equivalently, oxidation from Ru^{II} to Ru^{III} makes the imidazole proton more acidic by 6.1 pK_a units). The BDFEs in $(\text{acac})_2\text{Ru}^{\text{II}}(\text{py-imH})$ and in $\text{TpOs}^{\text{III}}(\text{NH}_2\text{Ph})\text{Cl}_2$, 62.1 and $61.5 \text{ kcal mol}^{-1}$ respectively, are unusually low for N–H bonds. HAT reactions of $(\text{acac})_2\text{Ru}^{\text{II}}(\text{py-imH})$ show large H/D kinetic isotope effects and involve substantial hydrogen tunneling.⁷⁵

Replacing acac with hfacac increases the BDFE by a remarkable $17.6 \text{ kcal mol}^{-1}$.⁴³⁰ This is principally the result of differences in the reduction potentials; the pK_a of the imidazole ligand is not strongly affected. This illustrates that the effect of ligands and substituents on

BDFEs is not always straightforward. Electron-withdrawing groups, for instance, will make a complex more oxidizing but also more acidic, and these two effects are in opposite directions in terms of the BDFE. This is perhaps most clearly illustrated for substituted toluenes, where substituents strongly affect E° and pK_a values, but the benzylic C–H bond strengths are much more constant.³⁴⁶ In phenols, however, electron donating substituents lower the redox potential more than they raise the pK_a , and therefore these substituents lower the BDFE (Table 4). This is probably because the “hole” created upon oxidation of phenols resides mostly on the aromatic ring, rather than on the phenolic oxygen. Similarly, replacing $-\text{CH}_3$ for $-\text{CF}_3$ in the acac ligands of $(\text{acac})_2\text{Ru}^{\text{II}}(\text{py-imH})$ has a much larger effect on the ruthenium center than the distant imidazole ligand.⁴³⁰

The PCET chemistry of metal-imidazole compounds has been extended to models for biologically important bis(histidine) ligated hemes. Starting from initial studies of Quinn, Nappa, and Valentine on *meso*-tetraphenylporphyrin-iron complexes with 4-methylimidazole, $(\text{TPP})\text{Fe}^{\text{III}}(\text{MeImH})_2^+$,⁴³¹ we have generated all of the compounds in the $\text{Fe}^{\text{II/III}}$ imidazole/imidazolate square scheme.¹⁸¹ The thermochemistry and concerted H-transfer reactivity is similar to the $\text{Fe}^{\text{II}}\text{H}_2\text{bip}$, $\text{Fe}^{\text{II}}\text{H}_2\text{bim}$ and $(\text{acac})_2\text{Ru}^{\text{II}}\text{py-imH}$ systems discussed above.

5.10.3 Separating the Redox and Protonation Sites—In the metal-oxo systems above, the oxo group that accepts the proton is only one bond away from the metal center that formally accepts the proton. In the imidazole compounds, the two sites are three bonds and *ca.* 4 Å removed. It is interesting to ask how far the two sites can be separated in a PCET reagent. From one perspective this is related to the issues raised in the discussion of PCET by separate proton and electron donors in Section 5.9 above. These concerns are probably very relevant to biological PCET, where proton acceptors may be able to be placed somewhat distant from redox cofactors.

Ruthenium systems developed by Manner *et al.*, shown in Scheme 14, are perhaps the clearest examples of a proton-electron accepting reagent with a long and fixed separation between the redox and acid/base sites. The complex with a trpy-carboxylate ligand, $\text{Ru}^{\text{III}}\text{COO}$, has a 6.9 Å separation between the ruthenium and the carboxylate oxygen atoms, 27 and in the trpy-benzoate analog $\text{Ru}^{\text{III}}\text{PhCOO}$ the distance is *ca.* 11 Å (trpy = 2,2',6',2''-terpyridine).⁴³² As this distance gets larger, there is less ‘communication’ between the redox and acid/base sites, as indicated by the thermochemical measurements. For $\text{Ru}^{\text{III}}\text{CO}_2\text{H}$ the redox potential decreases by only 0.13 V upon deprotonation and for RuPhCO_2H the changes is only 0.02 V and the pK_a of the carboxylate is almost the same as that for benzoic acid in MeCN. However, even though the two sites behave essentially independently, $\text{Ru}^{\text{III}}\text{PhCOO}$ is still able to undergo concerted $\text{H}^\bullet$ transfer from TEMPOH (see below).

5.10.4 Selected Metal Hydrides—Metal hydride complexes can transfer e^- , H^+ , $\text{H}^\bullet$, or H^- to substrates, and therefore they can be considered to be PCET reagents. Metal hydrides are key intermediates in various homogeneous catalytic processes involved in the production of petrochemicals to fine chemicals as well as laboratory-scale reactions. Their thermochemistry has been investigated by a number of groups, especially by Parker, Tilset, 43 Norton,⁴³³ Bullock,⁴³⁴ DuBois,^{5·435} and Hoff.⁴³⁶ The cited references provide excellent reviews of these data; in Table 21 we include only a few examples that illustrate some general features of metal hydride systems. In general, metal hydrides have M–H bond strengths that are somewhat weaker than the X–H bond strengths summarized above. Furthermore, H^+ and e^- transfers of many metal hydrides are highly coupled, meaning that there is a large change in pK_a with reduction/oxidation of the metal, and that the redox potential drops dramatically upon deprotonation. For example, the oxidation/reduction of

CpCr(CO)₃H changes the p*K*_a by more than 20 orders of magnitude. These very large changes in acidity with redox state are reminiscent of the chemistry of C–H bonds, above.

6. Mechanistic Implications

The thermochemistry of individual PCET reagents provides a foundation for understanding *cross reactions* between two potential PCET reagents. The following sections address how the individual *E*^o, p*K*_a, and BDFE values are informative about the mechanism of a reaction, whether it occurs by PT, ET, HAT, or otherwise (*e.g.*, hydride transfer). The discussion above indicated that, in general, reagents that exhibit a large change in p*K*_a upon redox change (equivalently, a large change in *E*^o upon protonation state change) preferentially undergo concerted rather than stepwise transfer of H⁺ and e[−]. In two examples emphasized above, TEMPOH and toluene, the p*K*_a values in MeCN change more than 40 orders of magnitude upon oxidation/reduction and these reagents in most cases react by HAT.

The following sections outline situations where concerted H[•] transfer or stepwise H⁺/e[−] transfers are more likely based on thermochemical arguments. One example is also discussed in which thermochemical arguments do not give a clear indication of mechanism. We emphasize here that it is best to use of solution bond dissociation free energies to understand solution hydrogen atom transfer reactions, despite the century-old use of gas-phase bond enthalpies for this purpose. For all-organic PCET reactions this is usually a minor concern, as the entropic change is usually small, however this is not the case for some metal mediated PCET reactions.^{39,40}

6.1 Using Thermochemical Data to Understand PCET Mechanisms

In any net one-electron/one-proton transfer reaction, there are three simple mechanisms, as shown in Scheme 1 at the start of this review: proton transfer (PT) followed by electron transfer (ET), ET followed by PT, and concerted transfer of the two particles (CPET or HAT). The thermochemical data in the Tables above can be used to calculate the ground state free energy changes, Δ*G*^o, for each of these mechanisms, following eqs 26–28. The activation energies Δ*G*[‡] must be at least as high as these free energy changes, so the Δ*G*^o values are a conservative lower limit to Δ*G*[‡]. It should be noted that electron transfer theories use a slightly different free energy barrier, Δ*G*^{*}, because a different pre-exponential factor is used.⁴⁴² Since this prefactor is smaller than the Eyring *kT/h*, the ET Δ*G*^{*} is always higher than the Eyring Δ*G*[‡], and Δ*G*^o is still a good conservative lower limit.

For X–H + Y,

$$\Delta G^{\circ}(\text{PT}) = -RT \ln(K_{\text{eq}}) = -(1.37 \text{ kcal mol}^{-1})[\text{p}K_{\text{a}}(\text{YH}^{+}) - \text{p}K_{\text{a}}(\text{XH})] \quad (26)$$

$$\Delta G^{\circ}(\text{ET}) = -FE^{\circ} = -(23.06 \text{ kcal mol}^{-1} \text{ V}^{-1})[E^{\circ}(\text{XH}^{+/0}) - E^{\circ}(\text{Y}^{0/-})] \quad (27)$$

$$\Delta G^{\circ}(\text{CPET}) = \text{BDFE}(\text{X} - \text{H}) - \text{BDFE}(\text{Y} - \text{H}) \quad (28)$$

The reaction of Fe^{II}H₂bim²⁺ + TEMPO will serve to illustrate this approach (Figure 13). The analysis uses the thermochemical data in MeCN for TEMPOH (Table 3) and Fe^{II}H₂bim (Table 21). Initial PT from Fe^{II}H₂bim²⁺ to TEMPO to yield Fe^{II}Hbim⁺ + TEMPOH^{•+} has Δ*G*^o = +41 kcal mol^{−1} from the relevant p*K*_a values. Similarly, Δ*G*^o for initial ET to give Fe^{III}H₂bim³⁺ + TEMPO[−], from the redox potentials, is +52 kcal mol^{−1}. The observed

Eyring barrier ($\Delta G^\ddagger$) is much lower, only 17.7 kcal mol⁻¹, so the reaction cannot be going through either of the stepwise pathways. Thus, the reaction of Fe^{II}H₂bim + TEMPO most likely proceeds via concerted proton-electron transfer (CPET). This same treatment can be applied to any H-transfer reaction, provided the relevant reduction potentials and pK_as are known.

It should be noted that Figure 13 is a simplification of the actual multi-dimensional free energy surface for a PCET reaction. The stepwise intermediates are in different regions of the multi-dimensional space, particularly when the solvent coordinates are included. This has been discussed by Hammes-Schiffer⁴⁴³ and Truhlar⁴⁴⁴ and is mentioned in other contributions to this special issue.

Many studies have used this thermochemical approach to show that the transfer of an electron and a proton must occur in the same kinetic step. This section is meant to be illustrative, not comprehensive. A particularly elegant example is the comproportionation of related ruthenium oxo and -aquo complexes to make the hydroxo derivative (eq 29), which has an H/D kinetic isotope effect of 16.1.^{7,18,445} The aquo complex has an aqueous pK_a of 10.3 and the oxo species is not protonated even in strong acid (Figure 10 above), so initial proton transfer is too endoergic to account for the observed rate. In this case, the large kinetic isotope effect and its linear dependence on the mole fraction of deuterium provide strong additional evidence against a mechanism of initial electron transfer and for a CPET pathway. The pseudo-self exchange reaction between the aquo complex and a related hydroxo complex (eq 30) proceeds by a similar mechanism, except at high pH when the aquo complex is deprotonated and the reaction becomes a pure electron transfer.

Reducing PCET reactions to the three mechanistic alternatives of Figure 13, eqs 26–28 and Scheme 1 is also a simplification. First of all, many PCET reagents form hydrogen bonds to solvent, and Ingold and co-workers have shown that for reagents such as phenols, this hydrogen bond must be broken prior to HAT.^{11,12} Second, the reaction of two PCET reagents likely involves precursor and successor complexes, by analogy to electron transfer theory, whether the reaction proceeds by ET, PT, or HAT/CPET. Such complexes may have hydrogen bonds and be energetically significant.⁴⁴⁶ In addition, one can envision a stepwise path of initial ET, for instance, which forms a successor complex that undergoes PT prior to dissociation to the products. The energetics of this situation are more complicated to analyze than eqs 26–28 above, as described in reference 447. Finally, PCET reactions can be mechanistically more complex, for instance being catalyzed by trace acid or base, or trace oxidant or reductant, as in the mechanism shown in eq 31.⁴²⁴ Thermochemical analysis of a reaction such as eq 31 requires the pK_a of the catalytic acid, as well as the properties of the HY and HX systems.

6.2 Characteristics and Examples of Concerted vs. Stepwise Pathways

In general, the concerted mechanism is favored when one or both of the reagents have strong 'thermodynamic coupling' between the proton and the electron, as indicated by large changes in pK_a upon oxidation/reduction and large changes in E° upon protonation/deprotonation. In the $\text{Fe}^{\text{II}}\text{H}_2\text{bim}^{2+} + \text{TEMPO}$ case analyzed in Figure 13, in the ruthenium-oxo system in eq 29, and in the TEMPOH/TEMPO self-exchange reaction analyzed in Scheme 7, both reagents have large ΔpK_a and ΔE° values. It is not necessary, however, for both reagents to have this property. For instance, TEMPOH transfers $\text{H}^\bullet$ in a concerted fashion to the ruthenium carboxylate complexes in Scheme 14, even though the Ru complexes have very little thermodynamic 'communication.' The very strong preference for CPET by TEMPOH is sufficient to make the PT-ET and ET-PT paths very high in energy.

On the other hand, stepwise mechanisms for net PCET occur when there is a good match between the pK_a s of HX and HY^+ , or between the E° 's of $\text{HX}^{+/0}$ and $\text{Y}^{0/-}$. If the two pK_a s are similar, then initial proton transfer will be accessible. A particularly clear example of this comes from Ingold's studies of acidic phenols + the DPPH radical (DPPH = 2,2-diphenyl-1-picrylhydrazyl radical).^{11,12} In MeCN, DMSO and THF there is a pK_a mismatch and proton transfer is thermodynamically unfavorable, so a CPET mechanism is operative. In alcohol solvents, however, the mismatch is much smaller and the reaction proceeds by initial H^+ transfer. These thermodynamic effects are compounded in this case by the unusual kinetic facility of proton transfer in hydroxylic solvents. As this example illustrates, solvent can alter the E°/pK_a properties of a compound, so that there is no one set of mechanistic "rules" for a given PCET reagent.

Ebersson has described a particularly clear example of a stepwise ET/PT mechanism, in the oxidation of aromatic hydrocarbons by polyoxometallates containing Co^{III} ions such as $\text{Co}^{\text{III}}\text{W}_{12}\text{O}_{40}^{5-}$.⁴⁴⁸ (Jönsson has extended these studies to Ni^{IV} and Mn^{IV} containing oxidants.⁴⁴⁹) Although these reactions show primary H/D kinetic isotope effects, consistent with CPET, they actually occur via fast, pre-equilibrium electron transfer, followed by rate limiting proton transfer (the origin of the isotope effect). The hallmark of this mechanism is that the reactions are inhibited by addition of the reduced Co^{II} species, which shifts the pre-equilibrium toward the reactants.^{448b} This is an excellent example of the limits of thermochemical analyses, as this ET-PT mechanism would have been eliminated without the careful kinetics studies, and without considering the unusual stabilization of the ET successor complex by the strong attraction between the aromatic cation radical and the polyanionic polyoxometallate.

In biology, perhaps the clearest example of a stepwise PCET reaction is the $2\text{H}^+/2e^-$ reduction of the quinone Q at the end of the ET cascade in the reaction centers of photosynthetic bacteria.⁴⁵⁰ The first electron transfer ($\text{Q} + e^- \rightarrow \text{Q}^{\bullet-}$) occurs via conformational gating, as indicated by the absence of a driving force dependence for this step.⁴⁵¹ The second reducing equivalent is added in a PCET process, $\text{Q}^{\bullet-} + \text{H}^+ + e^- \rightarrow \text{QH}^-$, which was indicated to occur by fast, pre-equilibrium proton transfer, followed by rate limiting electron transfer, PT-ET.^{450a} The cycle is completed by the addition of one proton, not coupled to electron transfer ($\text{QH}^- + \text{H}^+ \rightarrow \text{QH}_2$).

Finally, this section would be remiss without mentioning electrochemical PCET processes, which have been examined in detail by Savéant, Costentin, Robert, Finklea, Evans, and others.^{3,9,15,142,154b,452} Often, the electrochemical reactions of organic molecules proceed by electrochemical-chemical (EC) mechanisms, akin to a ET-PT mechanism (and often by more complex paths such as ECE etc.). However, some electrochemical processes

have recently been shown to occur by concerted transfer of e^- and H^+ , as summarized in an excellent recent review in this journal.³

7. Conclusions

The primary goals of this review are (1) to assemble thermochemical data – reduction potentials, pK_a values, and bond dissociation free energies and enthalpies – from disparate sources, and (2) to illustrate the utility of these data in understanding proton-coupled redox chemistry. We hope to have illustrated the value and power of thermochemical cycles (“square schemes”), and made them accessible to readers. For example, the square schemes for tyrosine and tryptophan indicate why biochemical oxidations of tyrosine residues form tyrosyl radicals directly, while those of tryptophan residues typically proceed via indole radical cations. The square schemes are particularly valuable in analyzing mechanistic pathways for H-transfers. A detailed knowledge of all of the microscopic steps (ET, PT and $H^\bullet$ transfer) is a key part of understanding a PCET process. We hope that this review will have value for workers developing and understanding proton-coupled redox phenomena. This area has grown tremendously in scope and depth in the past 25 years, and there is still much to be learned about PCET in chemistry and biology, and much to be done utilizing PCET processes in chemical synthesis and chemical energy transduction.

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Biographies

Jeff Warren was born in Spokane, WA in 1982. He received his Bachelor of Science Degree in Chemistry from Washington State University in 2005, at which time he joined Professor James M. Mayer's research group at the University of Washington. He earned his PhD in March, 2010 and is currently a Postdoctoral Scholar in Chemistry at Caltech under the mentorship of Harry Gray. He is currently interested in understanding biological redox reactions, especially coupled redox reactions, using a combination of small molecule and biochemical tools.

Tristan Tronic was born in Falls Church, Virginia in 1985. He received his B. S. in chemistry from the College of William and Mary in 2007, performing undergraduate research with Robert Pike. He then joined the group of James Mayer at the University of Washington, where he is currently studying redox reactions related to catalytic dioxygen/water interconversion.

James Mayer was born in New York City in 1958 and did undergraduate research at Hunter College with Edwin Abbott, and with William Klemperer while earning his A.B. at Harvard. He completed a PhD at Caltech under the direction of John Bercaw in 1982, and after two years as a Visiting Scientist at DuPont moved to the University of Washington, where he is now Alvin L. and Verla R. Kwiram Professor of Chemistry. His interests in redox chemical reactions span inorganic, bioinorganic, organometallic, and physical organic chemistry.

Figure 1. Pourbaix diagram for the *in,in*- $\{[\text{Ru}^{\text{II}}(\text{trpy})(\text{H}_2\text{O})_2(\mu\text{-bpp})]\}^{3+}$ water oxidation catalyst (trpy is 2,2':6',2''-terpyridine, bpp is bis(2-pyridyl)-3,5-pyrazolate)). Reprinted with permission from Ref. 68. © 2009 American Chemical Society.

Figure 2.

Thermochemistry of the hydroquinone/benzoquinone system (a) in water and (b) in DMSO, from Table 6. Numbers above horizontal arrows give pK_a values; numbers beside vertical arrows give electrochemical potentials (vs. NHE in water and vs. $\text{Cp}_2\text{Fe}^{+/0}$ in DMSO); numbers bisecting diagonal lines are BDFEs in kcal mol⁻¹. In (a), the values in parentheses were estimated by Laviron;¹⁵² in (b) the values in square brackets are estimates using eq 7 and Hess' Law.

Figure 3. Thermochemistry of the catechol/*ortho*-quinone system in water, with pK_a values above horizontal arrows, redox potentials (in V vs. NHE) beside vertical arrows, and BDFE values (in kcal mol^{-1}) bisecting diagonal lines. The values in square brackets are estimates using eq 7 and Hess' Law.

Figure 4.

Aqueous thermochemistry of ascorbic acid, with pK_a values above horizontal arrows, redox potentials (in V vs. NHE) beside vertical arrows, and BDFE values (in kcal mol⁻¹) bisecting diagonal lines. Data from references 135, 183, 184 and 187 (see Table 7).

Figure 5. Aqueous PCET thermochemistry of (a) aqueous H_2O and (b) aqueous hydrogen peroxide, with $\text{p}K_{\text{a}}$ values above horizontal arrows, redox potentials (in V vs. NHE) beside vertical arrows, and BDFE values (in kcal mol^{-1}) bisecting diagonal lines.

Figure 6.

Frost diagram for dioxygen reduction to water showing the free energy (nE) of the various reactive oxygen species at (a) pH 0 and (b) pH 7. (c) Pourbaix diagram for water, showing the potentials for oxidation to O_2 and reduction to H_2 as a function of pH and the pressure of O_2 and H_2 (from M. Pourbaix, *Atlas of Electrochemical Equilibria in Aqueous Solutions*, reference 67, with permission, © NACE International 1974).

Figure 7.

Double square scheme showing the PCET thermochemistry of flavins. While only one resonance form is drawn for each species, many are better described by multiple structures. Numbers above horizontal arrows give pK_a values; numbers beside vertical arrows give electrochemical potentials vs. NHE in water; numbers bisecting diagonal lines are BDFEs in kcal mol⁻¹. The values in square brackets are estimates using eq 7 and Hess' Law. For definitions of R, see Scheme 10. References for the values in this scheme, and descriptions of how they were derived, are given in the text.

Figure 8. Structures of nicotinamide adenine nucleotide (NADH), nicotinamide adenine dinucleotide phosphate (NADPH) and the model complexes *N*-benzyl-1,4-dihydronicotinamide (BNAH) and 10-methyl-9,10-dihydroacridine (AcrH₂).

Figure 9.

Square schemes showing the PCET thermochemistry of 10-methyl-9,10-dihydroacridine (AcrH₂) in (a) DMSO and (b) MeCN from Cheng;352:353 see text. Values above horizontal arrows give pK_a values; numbers beside vertical arrows give electrochemical potentials vs. Cp₂Fe^{+/0}; numbers bisecting diagonal lines are BDFEs in kcal mol⁻¹; and numbers along the steep diagonals are hydride affinities. The values in square brackets are estimates using eq 7 and Hess' Law. For definitions of R, see Figure 8.

Figure 10.

Double square scheme showing the PCET thermochemistry of $[cis-(bpy)_2(py)RuOH_x]^{n+}$ from reference(s) 383 and 390. Numbers above horizontal arrows give pK_a values; numbers beside vertical arrows give electrochemical potentials *vs.* NHE in water; numbers bisecting diagonal lines are BDFEs in kcal mol⁻¹ except for the long diagonal at left which is a hydride affinity, determined following reference 385a. Values in parentheses are limits derived from experimental results in 383.

Figure 11.

PCET thermochemistry of the $[(\text{phen})_4\text{Mn}_2(\text{O})_2]^{3+}$ system in MeCN, from reference 415. The phen ligands are omitted from the formulae for brevity. Numbers above horizontal arrows give $\text{p}K_{\text{a}}$ values; numbers beside vertical arrows give electrochemical potentials vs. $\text{Cp}_2\text{Fe}^{+/0}$; numbers bisecting diagonal lines are BDFEs in kcal mol^{-1} except for the long diagonal at left which is a hydride affinity.

Figure 12.

Examples of transition metal PCET systems with three bonds between the redox site and acid/base site. The ancillary ligands in Fe^{II}H₂bim and Fe^{II}H₂bip are the same as the ligand shown in full. The ancillary O-O ligands are acac (= 2,4-pentanedionato). The black bar in (TPP)Fe^{II}(MeImH)₂ represents *meso*-tetraphenylporphyrin.

Figure 13.

Potential energy surface showing free energy changes for different mechanisms of H-transfer for the reaction of $\text{Fe}^{\text{II}}\text{H}_2\text{bim} + \text{TEMPO}$. Not drawn to scale.

Scheme 1.
Concerted vs. stepwise transfer of $e^- + H^+$.

Scheme 2.
Hydrogen atom transfer.

Scheme 3.
Concerted proton-electron transfer that is not HAT.

Scheme 4.

Thermochemical square scheme for a PCET reagent.

Scheme 5.

Relationship between gas-phase and solution bond dissociation free energies.

TEMPOH

t BuNOH

NHPI

Scheme 6.
Hydroxylamines.

Scheme 7.

Thermochemical analysis of stepwise vs. concerted pathways for the TEMPO + TEMPOH self-exchange reaction.

Trolox C, R = CO₂H (mixture of isomers)

HMPC, R = Me

Scheme 8.

α -Tocopherol (vitamin E) and analogs Trolox C, and HPMC.

Scheme 9.

$\text{H}^\bullet$ loss and intramolecular H-bonding in *ortho*-quinones.

6,7-dimethyl-isoalloxazine

R = H (lumichrome)

Me (lumiflavin)

$\text{CH}_2(\text{CHOH})_3\text{CH}_2\text{OH}$ (riboflavin)

$\text{CH}_2(\text{CHOH})_3\text{CH}_2\text{O}(\text{PO}_3^-)$ (flavin mononucleotide, FMN)

$\text{CH}_2(\text{CHOH})_3\text{CH}_2\text{O}(\text{PO}_3^-)_2$ -adenine (flavin adenine dinucleotide (FAD))

Scheme 10.

Nomenclature and structures of biologically relevant flavins.

Scheme 11.
 $1\text{H}^+/1\text{e}^-$ reaction of guanosine.

Scheme 12.

Thermochemical cycle for transition metal PCET systems.

Scheme 13.
PCET Reactions of High-Valent Heme Species.

Scheme 14.

Ruthenium complexes with large separations between basic and redox sites.

Table 1Summary of constants C_G and C_H in common solvents.^a

solvent	C_G	$T(\Delta S^\circ)_{\text{solv}}^b$	C_H	Electrochemical Reference
acetonitrile	54.9	4.62	59.4	$\text{Cp}_2\text{Fe}^{+/0}$
DMSO	71.1	4.60	75.7	$\text{Cp}_2\text{Fe}^{+/0}$
DMF	69.7	4.56	74.3	$\text{Cp}_2\text{Fe}^{+/0}$
methanol	65.3	3.81	69.1	$\text{Cp}_2\text{Fe}^{+/0}$
water	57.6	-1.80	55.8	normal hydrosen

^a Values in kcal mol^{-1} at 298 K from references 39, 51.^b $T(\Delta S^\circ)_{\text{solv}} = T(S^\circ(\text{H}^\bullet)_{\text{g}} + \Delta S_{\text{solvation}}^\circ(\text{H}_2)_{\text{soiv}})$.

Table 2Selected PCET reagents and their X–H bond dissociation free energies.^a

Compound (XH)	solvent	BDFE	Table below
TEMPOH	H ₂ O	71.0	Table 3
TEMPOH	DMSO	67.5	Table 3
TEMPOH	MeCN	66.5	Table 3
TEMPOH	C ₆ H ₆	65.2	Table 3
PhOH	H ₂ O	89.5	Table 4
2,4,6- ^t Bu ₃ PhOH	MeCN	77.1	Table 4
hydroquinone (H ₂ Q)	H ₂ O	first OH: 81.5 average: 73.6	Tables 5, 6
ascorbate	H ₂ O	73.6	Table 7
MeO–H	DMSO	102.5	Table 8
OO–H	H ₂ O	42.7	Table 9
HOO–H	H ₂ O	91.0	Table 9
^t BuOO–H	H ₂ O	91.5	Table 10
H ₂ NNH–H	H ₂ O	83.4	Table 11
PhNH ₂	MeCN	94.1	Table 13
tryptophan	H ₂ O	90.6	Table 14
guanosine	H ₂ O	106.8	Table 15
PhS–H	DMSO	76.9	Table 16
C ₆ H ₅ CH ₂ –H	MeCN	87	Table 17
9,10-dihydroanthracene	DMSO	76.0	Table 17
NADH	H ₂ O	79.3	Table 18
N(2,4-Br ₂ -C ₆ H ₄) ₃ ⁺ + 2,6-Me ₂ -pyridine	MeCN	100.5	Table 20
MnO ₃ (O–H) [–]	H ₂ O	80.4	Table 21
[(bpy) ₂ pyRu ^{III} O–H] ²⁺	H ₂ O	84.8	Table 21

^aFor more examples, more data, and the origin of these values, see the individual Tables below.^bBDFE values in kcal mol^{–1}.

Table 3

PCET thermochemistry of hydroxylamines.^a

Compound (ROH)	solvent	$E(\text{RO}^{\bullet-})$	$E(\text{ROH}^{+\bullet})$	$\text{p}K_a(\text{ROH}^{+\bullet})$	$\text{p}K_a(\text{ROH})$	BDFE	BDE
H ₂ NOH	H ₂ O	0.0996	1.396	[-6.7]	13.797	78.4	76.7
TEMPOH	H ₂ O	-0.17581	--	--	12.998-99	71.0	69.4
TEMPOH	DMSO	-1.997100	--	--	31.100	67.5	72.1
TEMPOH	MeCN	-1.9582-101	0.71 102	[-4]	41 ^b	66.5 ^c	70.6
TEMPOH	C ₆ H ₆	--	--	--	--	65.240	70.040
TEMPOH	hexane	--	--	--	--	64.7	69.783
TEMPOH	EtOH	--	--	--	--	(65.4) ^d	(69) ^d
4-oxo-TEMPOH	hexane	--	--	--	--	62.5	67.583
4-oxo-TEMPOH	CCl ₄	--	--	--	--	67.3	72.076
4-oxo-TEMPOH	MeCN	--	--	--	--	65.674	70.1
4-MeO-TEMPOH	MeCN	--	--	--	--	65.074	69.5
4-OH-TEMPOH	hexane	--	--	--	--	66.3	71.383
4-NH ₂ -TEMPOH	hexane	--	--	--	--	66.0	71.083
4-Cl-TEMPOH	hexane	--	--	--	--	66.2	71.283
^t Bu ₂ NOH	MeCN	[-2] ^b	--	--	41 100, ^e	65.274	69.7
^t Bu ₂ NOH	DMSO	-2.070100	--	--	31.3100	66.2	70.8
Et ₂ NOH	DMSO	-1.645100	--	--	29.6100	73.7	78.3
PhN(Bz)OH ^f	DMSO	-1.354103	--	--	23.87103	72.6	77.2
<i>p</i> -BrC ₆ H ₄ N(Bz)OH ^f	DMSO	-1.259103	--	--	22.7103	73.2	77.8
<i>p</i> -NCC ₆ H ₄ N(Bz)OH ^f	DMSO	-0.976103	--	--	19.4103	75.2	79.8
<i>c</i> -C ₃ H ₁₀ NOH	DMSO	-1.610103	--	--	26.93103	70.9	75.5
NHPI	H ₂ O	[1]	--	--	6.388	88.8104	87.0
NHPI	DMSO	≤ -0.079105, ^g	--	--	12.988	≤87 ^g	≤92 ^g
NHPI	^t BuOH	--	--	--	--	83.3	88.194
NHPI	MeCN	-0.1 ^h	1.290	[1.4]	23.588, ^e	84.8	89.3
NHPI	C ₆ H ₆	--	--	--	--	(83.8)	(88.6)

Compound (ROH)	solvent	$E(\text{RO}^{\cdot-})$	$E(\text{ROH}^{\cdot+})$	$\text{p}K_a(\text{ROH}^{\cdot+})$	$\text{p}K_a(\text{ROH})$	BDFE	BDE
4-AcO-NHPI	MeCN	--	--	--	--	85.6	90.1 ⁱ
3-F-NHPI	MeCN	--	--	--	--	85.3	89.8 ⁱ
4-Me-NHPI	MeCN	--	--	--	--	84.9	89.4 ⁱ
4-MeO-NHPI	MeCN	--	--	--	--	84.0	88.5 ⁱ
3-MeO-NHPI	MeCN	--	--	--	--	84.6	89.1 ⁱ
3,6-(MeO) ₂ -NHPI	MeCN	--	--	--	--	83.8	88.3 ⁱ

^a Potentials are in V vs. NHE for aqueous measurements and vs. Cp₂Fe^{+/0} in non-aqueous solvents. E° and $\text{p}K_a$ values in [square brackets] have been calculated from the other values in the row using Hess' law (eqs 6, 7). *Italicized* values are irreversible potentials, $E_{\text{p,a}}$ or $E_{\text{p,c}}$, measured by cyclic voltammetry. BDFE and BDE in kcal mol⁻¹, when neither has a reference the BDFE has been calculated from E° and $\text{p}K_a$ values (eqs 7, 15, 16); when one of these has a reference, the other has been calculated from it using eq 9. BDE or BDFE values in (parentheses) have been estimated from a value in another solvent using the Abraham model (eq 13).

^b Estimated in ref. 40.

^c The E and $\text{p}K_a$ data yield BDFE(TEMPOH) = 66.1 kcal mol⁻¹, slightly lower than the preferred value from our recent critical evaluation of BDFE(TEMPOH) in MeCN.⁴⁰

^d Estimated from the value in C₆H₆ using Abraham's model.

^e Extrapolated from DMSO to MeCN using the method of Kütt and coworkers.⁸⁹

^f Bz = benzyl (-CH₂C₆H₅).

^g Ref. 105 states that the CV of deprotonated NHPI in DMSO shows an odd concentration dependence and that the true E° may be lower than the given value, so the BDFE is also an upper limit.

^h Estimated from MeCN electrochemical data with added pyridine bases, references 90/192-93, see text.

ⁱ Determined at -10°C in MeCN with respect to NHPI in ref. 95. Modified relative to our value for BDEMeCN(NHPI). The corresponding BDFEs are obtained using equation 9.

Table 4

PCET thermochemistry of phenols.^a

Compound	solvent	$E(\text{RO}^{\bullet(-)})$	$E(\text{ROH}^{\bullet(0)})$	$\text{p}K_a(\text{ROH}^{\bullet(+)})$	$\text{p}K_a(\text{ROH})$	BDFE	BDE
PhOH	gas	--	--	--	--	79.849	88.049
PhOH	H ₂ O	0.79117	1.5136	[-2] 115	10.0137	89.5	87.7
PhOH	DMSO	-0.325116	1.2116	[-7.7]	18.0116	88.3	92.7
PhOH	C ₆ H ₆	--	--	--	--	83.8	88.6121, ^b
4-Me-PhOH	H ₂ O	0.68117	1.4136	[-2] 115	10.3137	87.4	85.6
4-Me-PhOH	DMSO	-0.428116	1.1116	[-4]	18.9116	87.1	91.7
4-Me-PhOH	C ₆ H ₆	--	--	--	--	81.7	86.5121, ^b
4-MeO-PhOH	H ₂ O	0.54117	1.1136	[0.7]	10.1137	83.9	82.1
4-MeO-PhOH	DMSO	-0.618116	0.85116	[-5.6]	19.1116	83.0	87.6
4-MeO-PhOH	C ₆ H ₆	--	--	--	--	78.3	83.1121, ^b
4-NO ₂ -PhOH	H ₂ O	1.22117	--	--	7.1137	95.5	93.7
4-NO ₂ -PhOH	DMSO	0.314116	1.9116	[-9.5]	10.8116	93.1	97.7
4-F-PhOH	H ₂ O	0.76117	--	--	9.9137	88.7	86.9
4-Cl-PhOH	H ₂ O	0.80117	--	--	9.4137	88.9	87.1
4-Cl-PhOH	DMSO	-0.232116	1.4116	[-11]	16.75116	88.7	93.3
4-Br-PhOH	H ₂ O	0.82117	--	--	9.4137	89.4	87.6
4-Br-PhOH	DMSO	-0.19116	1.3116	[-8.7]	16.36116	89.1	93.7
4-I-PhOH	H ₂ O	0.82117	--	--	9.3137	89.3	87.5
4-CO ₂ ⁻ -PhOH	H ₂ O	0.90117	--	--	9.4137	91.2	89.4
4-Me(O)C-PhOH	H ₂ O	1.00117	--	--	8.0137	91.6	89.8
4-Me(O)C-PhOH	DMSO	0.04116	1.6116	[-12]	14.0116	91.2	95.8
4-CN-PhOH	H ₂ O	1.12117	--	--	7.9137	94.3	92.5
4-CN-PhOH	DMSO	0.15116	1.7116	[-13]	13.2116	92.6	97.2
4-NH ₂ -PhOH	H ₂ O	0.217117	--	--	10.4137	76.9	75.0
4-NH ₂ -PhOH	DMSO	-1.031116	-0.065116	[4.5]	20.75116	75.8	80.4
4-NMe ₂ -PhOH	H ₂ O	0.174	--	--	10.1137	75.4	73.6
4-NMe ₂ -PhOH	DMSO	-0.847116	-0.045116	[6.3]	19.8116	78.7	83.3

Compound	solvent	$E(\text{RO}^{\cdot-})$	$E(\text{ROH}^{+/0})$	$pK_a(\text{ROH}^{+/+})$	$pK_a(\text{ROH})$	BDFE	BDE
1-naphthol	H ₂ O	0.59138	--	--	9.3138	83.9	82.1
1-naphthol	DMSO	-0.473116	0.95116	[-7.8]	16.2116	82.4	87.0
2-naphthol	H ₂ O	0.69138	--	--	9.6138	86.7	84.9
2-naphthol	DMSO	-0.353116	1.0116	[-5.7]	17.1116	86.4	91.0
tyrosine	H ₂ O	0.71117	[1.4]	~-2.115	10.1137	87.8	86.0
Trolox C ^c	H ₂ O	0.192118	--	--	12139	78.5	76.7
HPMC ^d	C ₆ H ₆	--	--	--	--	73.7	78.5121, ^b
TocOH ^e	DMSO	-0.87140	--	--	20.2140	78.7	83.3
TocOH ^e	MeCN	-0.90141	0.6141	[4.7]	30 140, ^f	75.2	79.7
TocOH ^e	C ₆ H ₆	--	--	--	--	73.7	78.5121, ^b
2,4,6-'Bu ₃ PhOH	H ₂ O	0.21142	1.28142	[-5] 142	13 142-143	80.3	78.5
2,4,6-'Bu ₃ PhOH	DMSO	-0.645116	1.0116	[-10]	17.8116	80.6	85.2
2,4,6-'Bu ₃ PhOH	MeCN	-0.70144145146	1.18147	[-3]	28 116, ^f	77.1	81.6
2,4,6-'Bu ₃ PhOH	C ₆ H ₆	--	--	--	--	76.7	81.640
2,4,6-'Bu ₃ PhOH	CCl ₄	--	--	--	--	77.2	82.040
2,6-'Bu ₂ PhOH	DMSO	-0.619116	--	--	17.3116	80.5	85.1
2,6-'Bu ₂ PhOH	C ₆ H ₆	--	--	--	--	78.3	83.1121, ^b
4-Me-2,6-'Bu ₃ PhOH	DMSO	-0.755140	--	--	17.7140	77.9	82.5
4-Me-2,6-'Bu ₃ PhOH	C ₆ H ₆	--	--	--	--	76.9	81.7121, ^b
4-MeO-2,6-'Bu ₃ PhOH	DMSO	-0.806140	--	--	18.2140	77.4	82.0
4-MeO-2,6-'Bu ₃ PhOH	C ₆ H ₆	--	--	--	--	73.8	78.6121, ^b

^a Potentials are in V vs. NHE for aqueous measurements and vs. Cp2Fe^{+/0} in non-aqueous solvents. E° and pK_a values in [square brackets] have been calculated from the other values in the row using Hess' law (eqs 6, 7). *Italicized* values are irreversible potentials, $E_{p,a}$ or $E_{p,c}$, measured by cyclic voltammetry. BDFEs (kcal mol⁻¹) are from the cited reference or calculated from E and pK_a values (eqs 7, 15, 16); BDEs (kcal mol⁻¹) are typically calculated from BDFEs using eq 9.

^b The values reported in reference 121 are relative to ^tBu₃PhOH. The values given here have been adjusted to reflect our critical re-evaluation of BD(F)E of ^tBu₃PhOH in reference 40.

^c Trolox C = (±)-6-hydroxy-2,5,7,8-tetramethylchromane-2-carboxylic acid.

^d HPMC = 6-hydroxy-2,2,5,7,8-pentamethylchroman.

$\epsilon_{\text{TocOH}} = \alpha\text{-tocopherol}$.

$f_{\text{Extrapolated}}$ from DMSO to MeCN using the method of Kiitt and coworkers.⁸⁹

Table 5

Average O–H BDFEs and BDEs of substituted 1,4-hydroquinones in water.^a

Quinone	E155	Avg. BDFE	Avg. BDE	Quinone	E155	Avg. BDFE	Avg. BDE
benzoquinone (BQ)	0.700	73.6	71.8	methyl-BQ	0.644	72.5	70.7
chloro-BQ	0.712	74.0	72.2	2,5-dimethyl-BQ	0.596	71.3	69.5
2,6-dichloro-BQ	0.721	74.2	72.4	2,3-dimethyl-BQ	0.588	71.2	69.4
2,5-dichloro-BQ	0.723	74.3	72.5	2,3,5-trimethyl-BQ	0.527	69.8	68.0
2,3-dichloro-BQ	0.706	73.9	72.1	2-Me-5- <i>i</i> -Pr-BQ	0.589	71.2	69.4
bromo-BQ	0.715	74.1	72.3	2,5-Me ₂ -3-Cl-BQ	0.595	71.3	69.5
2-Br-5-Me-BQ	0.656	72.7	70.9	2,5-dimethoxy-BQ	0.590	71.2	69.4
2-Cl-5-Me-BQ	0.654	72.7	70.9	2,6-dimethoxy-BQ	0.514	69.5	67.7
tetrachloro-BQ	0.68	73.3	71.5	tetramethyl-BQ	0.48	68.7	66.9
naphthoquinone (NQ)	0.48	68.7	66.9	2,3-dimethyl-NQ	0.34	65.4	63.6
2-methyl-NQ	0.415	67.2	65.4				

^a BQ = 1,4-benzoquinone; NQ = 1,4-naphthoquinone. Potentials in V versus NHE. BDFE and BDE in kcal mol⁻¹. The BDFEs are derived from the *E*^o values using an analog of eq 15, and the BDEs are 1.8 kcal mol⁻¹ lower than the BDFEs according to eq 9.

Table 6

PCET thermochemistry of 1,4-hydroquinones.^a

Hydroquinone	solvent	$E(\text{HQ}^{\bullet-})$	$E(\text{H}_2\text{Q}^{\bullet+0})$	$pK_a(\text{H}_2\text{Q}^{\bullet+})$	$pK_a(\text{H}_2\text{Q})$	$pK_a(\text{HQ}^-)$	BDFE	BDE
hydroquinone (H ₂ Q)	H ₂ O	0.46117	1.1158	[-1.1]152	9.85159	11.4159	81.5	79.7
hydroquinone (H ₂ Q)	DMSO	-0.79116	--	--	19.8116	26.5116	80.0	84.6
methyl-HQ	H ₂ O	[0.40]	--	--	10.1159	11.6159 12.1160	80.7	78.9
2,3-dimethyl-H ₂ Q	H ₂ O	[0.36]	--	--	10.4161	12.6161	80.1	78.3
2,5-dimethyl-H ₂ Q	H ₂ O	[0.36]	--	--	10.4161	12.5161	80.2	78.4
2,3,5-Me ₃ -H ₂ Q	H ₂ O	[0.28]	--	--	10.8161	12.9161	79.0	77.2
tetramethyl-H ₂ Q	H ₂ O	[0.075]	--	--	11.3161	13.2161	74.8	73.0
2-methyl-H ₂ NQ	H ₂ O	--	--	--	--	--	75.5	73.7
2,3-Me ₂ -H ₂ NQ	H ₂ O	--	--	--	--	--	72.8	71.0

Semiquinone	solvent	$E(\text{Q}^{\bullet-})$	$E(\text{HQ}^{\bullet-})$	$pK_a(\text{HQ}^{\bullet+})$	$pK_a(\text{HQ}^{\bullet})$	BDFE	BDE
HQ [•]	H ₂ O	0.099162	0.76	[-7]	4.1163164	--	65.5 63.7
HQ [•]	DMSO	-0.91116	--	--	[11]	--	65.2 69.8
methyl-HQ [•]	H ₂ O	0.023162	--	--	4.5165	--	64.3 62.5
2,3-dimethyl-HQ [•]	H ₂ O	-0.074162	--	--	4.7165	--	62.3 60.5
2,5-dimethyl-HQ [•]	H ₂ O	-0.067162	--	--	4.6165	--	62.4 60.6
2,3,5-Me ₃ -HQ [•]	H ₂ O	-0.165162	--	--	5.0165	--	60.6 58.8
tetramethyl-HQ [•]	H ₂ O	-0.235166	--	--	5.0165	--	59.0 57.2
2-methyl-HNQ [•]	H ₂ O	-0.203166	--	--	4.4165	--	58.9 57.1
2,3-Me ₂ -HNQ [•]	H ₂ O	-0.240162	--	--	4.3165	--	58.0 56.2

^a H₂Q = 1,4-hydroquinone; H₂NQ = 1,4-naphthalenediol; HQ[•] and HNQ[•] are the monoprotonated semiquinones derived from these two hydroquinones. Potentials are in V vs. NHE for aqueous measurements and vs. Cp₂Fe⁺⁰ in DMSO. *Italicized* values are irreversible potentials, $E_{p,a}$ or $E_{p,c}$, measured by cyclic voltammetry. E° and pK_a values in [square brackets] have been calculated from the other values in the row using Hess' law (eqs 6, 7). BDFE and BDE in kcal mol⁻¹, the former calculated from eq 7 and converted to the latter using eq 9.

Table 7

PCET thermochemistry of ascorbates.^a

Compound	solvent	$E(\text{Asc}^{\bullet-}/2^-)$	$E(\text{AscH}^{\bullet-}/^-)$	$pK_a(\text{Asc}^*)$	$pK_a(\text{AscH}^-)$	BDFE	BDE
AscH ⁻	water	0.015183·184	0.72183·184	-0.45187	11.4183·184	73.6	71.8
AscH ⁻	MeCN	--	--	--	--	67.7	65.9
AscH ⁻	DMSO	--	--	--	--	67.6	65.8
<i>i</i> AscH ⁻	MeCN	-1.30182	-0.41182	[14] ^b	26.8182	65.4 ^c	63.6
<i>i</i> AscH ⁻	DMSO	--	--	--	--	67.5	65.7
Compound	Solvent	$E(\text{AscH}_2^{\bullet+0})$	$E(\text{AscH}^{\bullet-}/^-)$	$pK_a(\text{AscH}_2)$	$pK_a(\text{AscH}_2^{\bullet+})$	BDFE	BDE
AscH ₂	water	--	0.72183·184	4.1183·184	--	79.8	78.0
<i>i</i> AscH ₂	MeCN	--	-0.41 182	18.3182	--	70.5	75.0
Compound	Solvent	$E(\text{Asc}^{0/+})$	NA	$pK_a(\text{Asc}^*)$	NA	BDFE	BDE
Asc ^{•+}	water	-0.14183·184	--	-0.45187	--	53.6	52.0

^a Potentials are in V versus NHE for aqueous measurements and versus Cp₂Fe^{+/0} in MeCN. The BDFEs (kcal mol⁻¹) are calculated from E° and pK_a values (eqs 7, 15, 16) and the BDEs calculated from them using eq 9.

^b Calculated from a thermochemical cycle (Hess' Law).

^c For the BDFE of 5,6-isopropylidene ascorbate in MeCN we prefer the use of the BDFE obtained from equilibration with TEMPO, BDFE(*i*AscH⁻) = 66.4 kcal mol⁻¹, BDE = 70.9 kcal mol⁻¹.

Table 8

PCET thermochemistry of water and common alcohols.^a

Compound	solvent	$E(\text{RO}^{\bullet/})$	$E(\text{ROH}^{\bullet+/0})$	$\text{p}K_{\text{a}}(\text{ROH}^{\bullet+/})$	$\text{p}K_{\text{a}}(\text{ROH})$	BDFE	BDE
HO-H	gas	--	--	--	--	111.0 ^b	118.8200
HO-H	H ₂ O	1.89209	--	--	15.7209	122.7	-- ^c
O-H	gas	--	--	--	--	96.2 ^b	102.8200
O-H	H ₂ O	1.43209	--	--	11.9209	106.9	-- ^c
O-H ⁻	gas	--	--	--	--	103.1 ^b	110.237
O-H ⁻	H ₂ O	--	1.89209	11.9209	--	117.5	-- ^c
MeOH	gas	--	--	--	--	96.4	104.637
MeOH	DMSO	0.368100	--	--	29.1201	102.5	107.1
EtOH	gas	--	--	--	--	96.5	104.737
EtOH	DMSO	0.483100	--	--	29.8201	100.8	105.4
^t PrOH	gas	--	--	--	--	97.5	105.737
^t PrOH	DMSO	0.471100	--	--	30.3201	101.7	106.3
ⁱ BuOH ^d	DMSO	0.512100	--	--	32.2201	103.4	108.0
^t BuOH	gas	--	--	--	--	98.1	106.337
^t BuOH	DMSO	[-0.40]	--	--	32.2201	(106)	(111)
^t BuOH	H ₂ O	[≤1.2]	--	--	≥15.5137-202, ^e	(107)	(105)

^a Potentials are in V, vs. NHE for aqueous measurements and vs. Cp₂Fe^{+/0} in DMSO. *Italicized* values are irreversible potentials, $E_{\text{p,a}}$ or $E_{\text{p,c}}$, measured by cyclic voltammetry. BDEs (kcal mol⁻¹) are from the cited reference or are calculated from the BDFEs using eq 9. BDFEs (kcal mol⁻¹) are from the gas-phase BDEs using $S^{\circ}_{\text{gas}}(\text{H}^{\bullet})$ or are calculated from E and $\text{p}K_{\text{a}}$ values (eqs 7, 15, 16). BDFEs BDE or BDFE values in (parentheses) have been estimated from a value in another solvent using the Abraham model (eq 13).

^b BDFEs for these species are calculated using $S^{\circ}_{\text{gas}}(\text{X-H})$ and $S^{\circ}_{\text{gas}}(\text{X}^{\bullet})$ from ref. 49.

^c BDEs are not given for these species because it is not clear that equation 9 holds for very small molecules in water where the solvation of the closed shell and radical species may be complicated.

^d ^tBuOH = isobutyl alcohol, (CH₃)₂CHCH₂OH.

^e $\text{p}K_{\text{a}}(^i\text{BuOH})$ is taken to be at least that of MeOH or EtOH.

Table 9

PCET thermochemistry of dioxygen, superoxide, and hydrogen peroxide.^a

HO ₂ [•] /HOOH	solvent	E(HOOH ^{••(b)})	E(HOO ^{•(-)})	pK _a (HOOH ^{••})	pK _a (HOOH)	BDFE	BDE
HO ₂ [•] /HOO-H	Gas	--	--	--	--	79.6	87.5228
HO ₂ [•] /HOO-H	H ₂ O	--	0.76 ^b	--	11.6220	91.0	-- ^c
O ₂ [•] /OOH	solvent	E(HOO ^{••})	E(O ₂ ^{•(-)})	pK _a (HO ₂ [•])	pK _a (HO ₂ [•])	BDFE	BDE
O ₂ [•] /OO-H	gas	--	--	--	--	42.7	49.2228
O ₂ [•] /OO-H	H ₂ O	--	-0.16209	--	4.9209	60.6	-- ^c
O ₂ [•] /OO-H	DMSO	--	-1.27209	--	~12229	~58	~63
O ₂ ^{••} /OO-H	solvent	E(HOO ^{•(-)})	E(O ₂ ^{••(-2-)})	pK _a (HO ₂ [•])	pK _a (HOO ⁻)	BDFE	BDE
O ₂ ^{••} /OO-H	H ₂ O	0.76 ^b	--	4.9209	--	81.6	-- ^c

^a Potentials are in V versus NHE for aqueous measurements and versus Cp₂Fe^{+/0} in DMSO. BDFEs and BDEs in kcal mol⁻¹. Gas-phase BDFEs calculated from gas-phase BDEs and S^o_{gas}(H[•]), S^o_{gas}(X-H), and S^o_{gas}(X[•]) from ref. 49. Solution BDFEs calculated from E and pK_a values (eqs 7, 15, 16)

^b Calculated using the 1H⁺/1e⁻ potential (1.44 V versus NHE at pH 0209) and extrapolating to pH = pK_a(H₂O₂) assuming a 59 mV per pH unit dependence.

^c BDEs are not given for these species because it is not clear that equation 9 holds for very small molecules is water where the solvation of the closed shell and radical species may be complicated.

Table 10

PCET thermochemistry of organic hydroperoxides.^a

Compound	solvent	$E(\text{ROOH}^{\bullet+}/0)$	$E(\text{ROO}^{\bullet-})$	$\text{p}K_a(\text{ROOH}^{\bullet+})$	$\text{p}K_a(\text{ROOH})$	BDFE	BDE
MeOOH	gas	--	--	--	--	79.6	87.8234a
MeOOH	H ₂ O	[1.62] ^b	0.94237	[0] ^b	11.5235	95.0	93.2
EtOOH	gas	--	--	--	--	76.6	84.8234a
EtOOH	H ₂ O	[1.57] ^b	0.91237	[0] ^b	11.8235	94.8	93.0
<i>i</i> -PrOOH	gas	--	--	--	--	76.9	85.1231
<i>i</i> -PrOOH	H ₂ O	[1.51] ^b	0.81237	[0] ^b	12.1235	92.8	91.0
<i>t</i> -BuOOH	gas	--	--	--	--	76.1	84.3234a
<i>t</i> -BuOOH	H ₂ O	[1.47] ^b	0.71237	[0] ^b	12.8235	91.5	89.7
HC(O)OOH	gas	--	--	--	--	86.8	95.0241
HC(O)OOH	H ₂ O	--	[>1] ^c	--	7.1235	[>90.4]	[>88.6]
CH ₃ C(O)OOH	gas	--	--	--	--	82.3	90.5242
CH ₃ C(O)OOH	H ₂ O	--	[1.14] ^d	--	8.2235	95.1	93.3
ⁿ PrC(O)OOH	H ₂ O	--	--	--	8.1235	--	--
ⁿ BuC(O)OOH	H ₂ O	--	--	--	8.2235	--	--
<i>m</i> -CPBA	H ₂ O	--	--	--	7.5236	--	--

^aPotentials are in V vs. NHE and BDFE and BDE are in kcal mol⁻¹. Gas phase BDFEs are calculated from gas-phase BDEs and $S^\circ_{\text{gas}}(\text{H}^\bullet)$ from ref. 49. Aqueous BDFEs calculated from E° and $\text{p}K_a$ values (eqs 15, 16) and the solution BDEs are estimated from those values using eq 9.

^bFrom ref. 237 assuming that $\text{p}K_a \text{ ROOH}^{\bullet+} \sim 0$.

^cMinimum value, see text.

^dEstimated from electron transfer kinetic data (see text).240

Table 11

PCET thermochemistry for N_2H_x derivatives.^a

Compound	solvent	$E^\circ(-NH^{+}/0)$	$pK_a(-NH^{+})$	$pK_a(-NH)$	BDFE	BDE
NN-H	gas	--	--	--	--	~ -4 , b , 249
HNN-H	gas	--	--	--	52.6	60.849
HNN-H	H ₂ O	--	--	34.3255	--	-- ^c
HNNH-H	gas	--	--	--	35.6	43.8256
HNNH-H	H ₂ O	[-0.22] ^d	-1.5247	--	50.5	-- ^c
H ₂ NNH-H	gas	--	--	--	72.6	80.8256
H ₂ NNH-H	H ₂ O	0.69	7.2257	--	83.4	-- ^c

^aPotentials in V referenced to NHE. Gas-phase BDFEs (kcal mol⁻¹) calculated from gas-phase BDEs and $S^\circ_{\text{gas}}(H^\bullet)$ from ref. 49. Solution BDFEs calculated from E° and pK_a values (eqs 7, 15, 16).

^bApproximate value based on DFT calculations.

^cBDEs are not given for these species because it is not clear that equation 9 holds for very small molecules in water where the solvation of the closed shell and radical species may be complicated.

^dCalculated from the $1e^-/1H^+$ potential of -0.31 V vs. NHE.

Table 12

PCET thermochemistry of ammonia and alkylamines.^{a,b}

Compound	solvent	$E(\text{RR}'\text{NH}^{+/0})$	$\text{p}K_a(\text{RR}'\text{NH}^{+/+})$	BDFE	BDE
$\text{H}_3\text{N}^+\text{-H}^+$	gas	--	--	116.9	125.1263-264
$^+\text{H}_2\text{N-H}$	gas	--	--	121.9	130.1263
$\text{H}_2\text{N-H}$	gas	--	--	99.4	107.6265
MeNH_2	gas	--	--	93.4	101.6266
PrNH_2	MeCN	1.12267	[5.7]	88.6	93.1262
PrNH_2	C_6H_6	--	--	86.2	91.0262
PrNH_2	MeCN	1.10267	[7.6]	90.7	95.5262
PrNH_2	C_6H_6	--	--	86.0	90.5262
$\text{Me}_2\text{N-H}$	gas	--	--	86.4	94.6266
$\text{Me}_2\text{N-H}$	H_2O	1.27268	6.8268	96.2	94.4
$\text{Et}_2\text{N-H}$	H_2O	1.36268	5.3268	96.2	94.4
$\text{Et}_2\text{N-H}$	MeCN	0.97269 0.75268	[5.0] [8.7]	84.1	88.6262
$\text{Et}_2\text{N-H}$	C_6H_6	--	--	82.2	87.0262
piperidine	H_2O	1.34268	5.8268	96.5	94.6
$^n\text{Bu}_2\text{N-H}$	C_6H_6	--	--	86.0	90.8262
$^n\text{Bu}_2\text{N-H}$	MeCN	0.83269	[7.6]	84.4	88.9262
$^t\text{BuNH}_2$	C_6H_6	--	--	90.2	95.0262
$^t\text{BuNH}$	MeCN	1.13267	[5.7]	88.8	93.3262

^aPotentials are in V vs. NHE for aqueous values and vs. $\text{Cp}_2\text{Fe}^{+/0}$ in MeCN; BDFE and BDE in kcal mol^{-1} . Gas-phase BDFEs calculated from gas-phase BDEs and $S^\circ_{\text{gas}}(\text{H}^\bullet)$ from ref. 49 [assuming $S^\circ_{\text{gas}}(\text{XH}) = S^\circ_{\text{gas}}(\text{X}^\bullet)$]. Solution BDFEs calculated from E and $\text{p}K_a$ values (eqs 7, 15, 16) and the solution BDEs calculated from those values using eq 9.

^bWe have found no values for $E^\circ(\text{RR}'\text{N}^{\bullet+}/-)$ or $\text{p}K_a(\text{RR}'\text{NH})$ for simple amines.

Table 13

PCET thermochemistry of arylamines.^a

Compound	solvent	$E(\text{R}_2\text{N}^{\bullet(-)})$	$E(\text{R}_2\text{NH}^{+/0})$	$\text{p}K_a(\text{R}_2\text{NH}^{+/+})$	$\text{p}K_a(\text{R}_2\text{NH})$	BDFE	BDE
PhNH ₂	gas	--	--	--	--	81.5	89.7274
PhNH ₂	H ₂ O	--	1.02272	7.05272	--	90.8	88.0
PhNH ₂	DMSO	-0.992271	0.5271	6.4271	30.6271	90.1	94.7
PhNH ₂	MeCN	[-1.1]	0.66268	17.5 ^b	44 ^b	94.1	98.6
PhNH ₂	C ₆ H ₆	--	--	--	--	87.4	92.2274
4-MePhNH ₂	H ₂ O	--	0.92272	8.5272	--	90.9	89.1
4-MePhNH ₂	DMSO	-1.072271	0.305271	8.5271	31.7271	89.8	94.4
4-MePhNH ₂	C ₆ H ₆	--	--	--	--	85.2	90.0274
4-MeOPhNH ₂	H ₂ O	--	0.79272	9.6272	--	89.0	87.2
4-MeOPhNH ₂	DMSO	-1.188271	0.125271	10.271	32.5271	87.6	92.2
4-CIPhNH ₂	H ₂ O	--	1.01272	~7.272	--	90.5	88.7
4-CIPhNH ₂	DMSO	-0.915271	0.535271	5.0271	29.4271	90.3	94.9
4-CNPhNH ₂	H ₂ O	--	1.32272	4.272	--	93.5	91.7
4-CNPhNH ₂	DMSO	-0.550271	0.795271	2.6271	25.3271	93.0	97.6
4-CF ₃ PhNH ₂	H ₂ O	--	1.38272	4.8272	--	96.0	94.2
4-CF ₃ PhNH ₂	DMSO	-0.597271	0.723271	4.7271	27.0271	94.3	98.9
Ph ₂ NH	H ₂ O	--	1.0268	3.8268	--	85.9	84.1
Ph ₂ NH	DMSO	-0.865271	0.455271	2.7271	25.0271	85.3	89.9
Ph ₂ NH	MeCN	[-0.82] [-0.92]	0.61268 0.51281	13.5 ^b	37.5 ^b	87.5 85.2	92.0 89.7
Ph ₂ NH	C ₆ H ₆	--	--	--	--	84.4 81.3	89.2274 86.2 ^c
(4-MePh) ₂ NH	DMSO	-0.923271	0.415271	2.9271	25.5271	84.8	89.4
(4-MePh) ₂ NH	MeCN	[-1.0]	0.40281	13.7 ^b	38 ^b	82.9	87.4
DPPH-H ^d	H ₂ O/EtOH	0.52282	--	--	8.6283	81 ^e	83 ^e
DPPH-H ^d	DMSO	-0.093280	--	--	--	--	--
DPPH-H ^d	C ₆ H ₆	--	--	--	--	75.2	80.076 ^f

Compound	solvent	$E(R_2N^{+/•})$	$E(R_2NH^{+/0})$	$pK_a(R_2NH^{+/•})$	$pK_a(R_2NH)$	BDFE	BDE
DPPH-H ^d	hexane	--	--	--	--	[77] ^f	[82] ^g
2,4-(NO ₂)C ₆ H ₃ NNHPh ₂	DMSO	-0.292280	--	--	12.1280	80.9	85.5
PhNHNPh ₂	DMSO	-1.117280	--	--	24.5280	78.9	83.5
PhNHNHPh	DMSO	-1.730280	--	--	26.2280	67.1	71.7
PhNHNH ₂	DMSO	-1.740280	--	--	28.8280	70.4	75.0

^a Potentials are in V vs. NHE for aqueous measurements and vs. Cp₂Fe^{+/0} in non-aqueous solvents. E° and pK_a values in [square brackets] have been calculated from the other values in the row using Hess' law (eqs 6, 7). *Italicized* values are irreversible potentials, $E_{p,a}$ or $E_{p,c}$, measured by cyclic voltammetry. BDFE and BDE in kcal mol⁻¹, when neither has a reference the BDFE has been calculated from E and pK_a values (eqs 7, 15, 16); when one of these has a reference, the other has been calculated from it using eq 9.

^b Extrapolated from DMSO to MeCN using the method of Kütt and coworkers.⁸⁹

^c The value reported in reference 277 is relative to ^tBu₃PhOH. The value given here has been adjusted to reflect our critical re-evaluation of BD(F)E of ^tBu₃PhOH in reference 40.

^d DPPH-H = 1,1-diphenyl-2-picrylhydrazine.

^e Assumes that $CG(H_2O/EtOH) \cong CG(H_2O)$ (and similarly for CH₃(H₂O)).

^f Corrected for the revised heat of formation of azobenzene as described in reference 40.

^g BDFE(DPPH) in hexane is +1.17 kcal mol⁻¹ larger than BDFE(^tBu₃PhOH) in hexane, 284 which we have estimated to be 76 kcal mol⁻¹ using the Abraham model and the data in Table 4.

Table 14

Thermochemical data for indoles and tryptophan.^a

Compound	solvent	$E(R_2N^{\cdot-})$	$E(R_2NH^{\cdot+})$	$pK_a(R_2NH^{\cdot+})$	$pK_a(R_2NH)$	BDFE	BDE
indole	DMSO	-0.35291, 293	--	--	20.94291	91.7	96.3
indole	H ₂ O	[0.52]	1.24290	4.9290	17.0294	92.9	91.1
tryptophan	H ₂ O	[0.43]	1.15128 1.24290	4.7128	16.8294	90.6 92.6	88.8 90.8
2-CH ₃ -indole	H ₂ O	--	1.10290	5.7290	--	90.8	89.0
3-CH ₃ -indole	H ₂ O	[0.38]	1.07290	5.0290	16.6294	89.1	87.3
2,3-CH ₃ -indole	H ₂ O	--	0.93290	6.1290	--	87.4	85.6

^aPotentials are in V vs. NHE for aqueous measurements and vs. Cp2Fe^{+/0} in DMSO; BDFE and BDE values are in kcal mol⁻¹. *Italicized* values are irreversible potentials, $E_{p,a}$ or $E_{p,c}$, measured by cyclic voltammetry. The BDFEs are calculated from the E and pK_a values using eqs 7, 15, 16; BDEs are calculated from the BDFEs using eq 9.

Table 15

PCET thermochemistry of nucleosides in water.^a

Compound	$E(\text{RN}^{\cdot}/\text{RNH})^a$	$\text{p}K_a(\text{RNH}^{++})$	$\text{p}K_a(\text{RNH})$	BDFE	BDE
guanosine	1.29310	3.9311	9.3310	96.9	95.1
adenosine	1.42310	≤ 1	12.5310	99.9	98.1
cytidine	1.6310	--	--	104.0	102.2
thymidine	1.7310	--	--	106.3	104.5

^aPotentials are in V vs. NHE at pH 7; BDFE and BDE values are in kcal mol⁻¹. The BDFEs are calculated from the E values using eq 16; BDEs are calculated from the BDFEs using eq 9.

Table 16

PCET thermochemistry of thiols.^a

Compound	solvent	$E(\text{RS}^{\bullet-})$	$\text{p}K_{\text{a}}(\text{RSH})$	BDFE	BDE
HS-H	gas	--	--	83.0	91.237
HS-H	H ₂ O	1.15316	7.0137	93.7	91.9
MeS-H	gas	--	--	79.2	87.4321
MeS-H	H ₂ O	0.73 ^b	10.3137	88.6	86.8
EtS-H	gas	--	--	79.1	87.3322
EtS-H	H ₂ O	0.74 ^b	10.6137	89.3	87.5
^t BuS-H	gas	--	--	78.4	86.6323
HOCH ₂ CH ₂ S-H	H ₂ O	[0.77] 0.75317	9.5 ^c	88.3 ^d	86.5
cysteine	H ₂ O	0.73318	8.5319 ^e 9.1319 ^f	86.2 ^e 87.0 ^f	84.4 ^e 85.2 ^f
glutathione	H ₂ O	0.81324	9.3325	89.0	87.2
PhS-H	gas	--	--	75.3	83.5326
PhS-H	H ₂ O	0.69327	6.6137	82.6	80.8
PhS-H	DMSO	-0.3641	10.341	76.9	81.5
PhS-H	C ₆ H ₆	--	--	81.6	86.4326
4-MePhS-H	H ₂ O	0.64327	6.8137	83.9	82.1
4-MeOPhS-H	H ₂ O	0.57327	6.8137	80.1	78.3
4-BrPhS-H	H ₂ O	0.71327	6.0137	82.2	80.4

^aPotentials are in V vs. NHE for aqueous measurements and vs. Cp₂Fe^{+/0} in DMSO. *Italicized* values are irreversible potentials, $E_{\text{p,a}}$ or $E_{\text{p,c}}$, measured by cyclic voltammetry. BDFEs (kcal mol⁻¹) are calculated from E and $\text{p}K_{\text{a}}$ values (eqs 7, 15, 16) or (for gas-phase values) from the BDE(g) using eq 10. Solution BDEs (kcal mol⁻¹) are calculated from the corresponding BDFEs using eq 9. The application of either eqs 9 or 10 requires the assumption that $S^{\bullet}(\text{RS}^{\bullet}) = S^{\bullet}(\text{RSH})$.

^bCalculated using the relevant gas phase BDFE following Sordhar in reference 316.

^cAverage of several reported values; see ref. 315.

^dCalculated from the 1H⁺/1e⁻ potential (1.33 V) reported in ref. 317.

^e $\text{p}K_{\text{a}}$ (and therefore BDFE and BDFE) for zwitterionic form of cysteine.

pK_a (and therefore BDFE and BDE) of $\text{HSCH}_2\text{CH}(\text{CO}_2\text{Et})\text{NH}_2$.

Table 17

PCET thermochemistry of C–H bonds in selected compounds.

Compound	solvent	$E(R^{\bullet}/R^{\bullet-})^a$	$E(RH^{\bullet+}/RH)^a$	$pK_a(RH^{\bullet+})^a$	$pK_a(RH)^a$	BDFE ^b	BDE ^b
CH ₄	gas	--	--	--	--	96.8	105.0336
CH ₄	H ₂ O	[-0.75]	--	--	~48 259, ^c	(106)	(104)
CH ₄	DMSO	[-2]	--	--	~56 29	(102)	(107)
CH ₃ CH ₂ -H	gas	--	--	--	--	92.9	101.1337
(CH ₃) ₂ CH-H	gas	--	--	--	--	90.4	98.6337
(CH ₃) ₃ C-H	gas	--	--	--	--	88.3	96.5337
CH ₂ =CH-H	gas	--	--	--	--	102.5	110.7338
HC≡C-H	gas	--	--	--	--	125.2	133.3339
cyclo-C ₃ H ₆ ^d	gas	--	--	--	--	73.2	81.4340
cyclo-C ₃ H ₆ ^d	H ₂ O	[0.11]	--	--	16 341	(82)	(80)
cyclo-C ₃ H ₆ ^d	DMSO	-0.778329	--	--	18.0329	77.8	82.4
1,4-cyclohexadiene	gas	--	--	--	--	67.8	76.0342
C ₆ H ₅ -H	gas	--	--	--	--	104.7	112.9338
C ₆ H ₅ CH ₂ -H	gas	--	--	--	--	81.6	89.8343
C ₆ H ₅ CH ₂ -H	H ₂ O	[-0.93]	--	--	~40 259, ^e	(91)	(89)
C ₆ H ₅ CH ₂ -H	DMSO	[-1.9]	--	--	~43	(87)	(92)
C ₆ H ₅ CH ₂ -H	MeCN	-1.85344	1.87335	[-~8] ^f	[-54] ^f	(87)	(92)
(CH ₃) ₆ C ₆	MeCN	--	1.11335	2.0 345	--	83.2	87.7
<i>p</i> -(CH ₃) ₂ C ₆ H ₄	MeCN	-2.0346	1.45335	[-4.3]	53.8346	82.5	87.0
(CH ₃) ₅ C ₆ H	MeCN	--	1.19335	2.0 345	--	85.1	89.6
1,2,4,5-Me ₄ C ₆ H ₂	MeCN	--	1.20335	3.0 345	--	86.8	91.3
Indene	DMSO	-0.952329	--	--	20.1329	76.7	81.3
Fluorene	DMSO	-1.069329	--	--	22.6329	77.4	82.0
Fluorene	MeCN	-1.16344	1.16335	[-~3] ^f	[-35] ^f	(77)	(82)
DHA ^g	DMSO	-1.575329	--	--	30.1329	76.0	80.6
xanthene	DMSO	-1.685329	--	--	30.0329	73.3	77.9

Compound	solvent	$E(R^{\bullet+})^a$	$E(RH^{+0})^a$	$pK_a(RH^{+0})^a$	$pK_a(RH)^a$	BDFE ^b	BDE ^b
Ph ₃ CH	DMSO	-1.466329	--	--	30.6329	78.8	83.4
Ph ₂ CH ₂	DMSO	-1.54329	--	--	32.2329	79.7	84.3

^aPotentials are in V vs. NHE for aqueous measurements and vs. Cp2Fe^{+/0} in non-aqueous solvents. *Italicized* values are irreversible potentials, $E_{p,a}$ or $E_{p,c}$, measured by cyclic voltammetry. E and pK_a values in [square brackets] have been calculated from the other values in the row using Hess' law (eqs 6, 7).

^bBDFEs (kcal mol⁻¹) are calculated from E and pK_a values (eqs 7, 15, 16) or (for gas-phase values) from the BDE(g) using eq 10. Solution BDEs (kcal mol⁻¹) are calculated from the corresponding BDFEs using eq 9. The application of either eqs 9 or 10 requires the assumption that $S^\circ(R^\bullet) = S^\circ(RH)$. BDE or BDFE values in (parentheses) have been estimated from a value in another solvent using the Abraham model (eq 13).

^cGiven in ref. 259, calculated from data in 347.

^d_{cyclo}-C₅H₆ = 1,3-cyclopentadiene.

^eGiven in ref. 259, from data in 348.

^fFor toluene and fluorene, there are measurements of the pK_a in DMSO (41–4329a-344 and 22.6,329-344 respectively), and values can be estimated from those in MeCN using the method of Klitt and co-workers.⁸⁹ but we believe that it is likely to be more accurate to estimate the pK_{as} from the E° and BDFE values. Wayner *et al.* have also used thermochemical cycles to estimate C–H pK_{as} in MeCN.³⁴⁴

^gDHA = 9,10-dihydroanthracene.

Table 18

PCET thermochemistry of nicotinamides and related compounds.^a

Compound	solvent	$E(R^{+/•})$	$E(RH^{+/0})$	$E(R^{+/•})$	$pK_a(RH^{+/•})$	$pK_a(RH)$	BDFE(RH) ^b	BDFE(RH ⁺⁺) ^b	$\Delta G^\circ(H^-)$
AcH ₂	DMSO	-1.96352	0.497352	-0.876352	[-9.9]	31.5352	69.0	37.3	73.9
AcH ₂	MeCN	[-2]	0.492353	-0.819353	2.2353	[44] ^c	69.2353	39.0	76.4
AcH ₂	MeCN	--	0.475355	-0.845355	0.8355	[44] ^c	67.0	36.5	74.5
BNAH	DMSO	--	0.182352	-1.53352	-3.3352	--	70.8	31.3	55.0
BNAH	MeCN	--	0.406355	-1.49355	4.7355	--	86.9	43.2	62.3
NADH	H ₂ O	--	0.94356/357	-0.92357	-3.5357	--	74.3	31.4	56.8
							79.3351, ^e	36.3351, ^e	53.6351, ^e

^aDrawings of the compounds are shown in Figure 8. Potentials are in V vs. NHE for aqueous values and vs. Cp2Fe^{+/0} in non-aqueous solvents. E and pK_a values in [square brackets] have been calculated from the other values in the row using Hess' law (eqs 6, 7).

^bBDE Only BDFEs (in kcal mol⁻¹) are given in this Table due to space constraints. Assuming $\Delta S^\circ(RH) = \Delta S^\circ(R^\bullet)$, the BDE is obtained from the BDFE by adding 4.5 (MeCN), 4.6 (DMSO) or -1.8 (H₂O) kcal mol⁻¹.

^cEstimated using the method of Kiitt and co-workers.⁸⁹

^d $E(NADH^{*+}/0) = 1.05$ V in propanol/water.³⁵⁷

^eValues are bond dissociation *enthalpies*, from thermochemical cycles and calorimetric measurements in 351.

Table 19

PCET thermochemistry of hydrogen.^a

Solvent	$E(\text{H}^+/\text{H}^\bullet)$	$E(\text{H}^\bullet/\text{H}^-)$	$\text{p}K_a(\text{H}_2)^b$	BDFE ^{c,d}	BDE ^d
Gas	--	--	--	97.2	104.2361
Water	-2.5051	0.18363	[32]	106.2	103.2
DMSO	-3.0851	-1.09363	[42]	102.8	106.2
MeCN	-2.3851	-1.13363	[54]	102.3	105.8
MeOH	-2.8351	--	--	102.4	105.0

^aPotentials are in V vs. NHE for aqueous measurements and vs. $\text{Cp}_2\text{Fe}^{+/0}$ in non-aqueous solvents. BDFEs and BDEs in kcal mol^{-1} . Ref. 364 has proposed alternative values.

^b $\text{p}K_a$ values calculated from reduction potentials and BDFEs according to eq. 22.

^cGas phase BDFE calculated from BDE and gas phase $S^\circ(\text{H}^\bullet)$ and $S^\circ(\text{H}_2)$ from ref. 49.

^dSolution BDFEs and BDEs calculated from gas phase values according to eq. 3 assuming $\Delta G_{\text{solV}^\circ}(\text{H}^\bullet) = \Delta G_{\text{solV}^\circ}(\text{H}_2)$.⁵⁰

Table 20

PCET thermochemistry of a few oxidant/base or reductant/acid pairs in MeCN for separated CPET.

Oxidant	$E_{1/2}^{a,b}$	base	pK_a^c	BDFE ^d
$N(4\text{-MeO-C}_6\text{H}_4)_3^{*+}$	0.16	pyridine	12.5	75.7
$N(4\text{-MeO-C}_6\text{H}_4)_3^{*+}$	0.16	2,6-Me ₂ -pyridine	14.1	77.9
$N(4\text{-Me-C}_6\text{H}_4)_3^{*+}$	0.40	pyridine	12.5	81.3
$N(4\text{-Me-C}_6\text{H}_4)_3^{*+}$	0.40	2,6-Me ₂ -pyridine	14.1	83.5
$N(4\text{-Me-C}_6\text{H}_4)_3^{*+}$	0.40	4-N(Me) ₂ -pyridine	18.0	88.8
$N(4\text{-Br-C}_6\text{H}_4)_3^{*+}$	0.67	pyridine	12.5	87.5
$N(4\text{-Br-C}_6\text{H}_4)_3^{*+}$	0.67	2,6-Me ₂ -pyridine	14.1	89.7
$N(2,4\text{-Br}_2\text{-C}_6\text{H}_4)_3^{*+}$	1.14	pyridine	12.5	98.3
$N(2,4\text{-Br}_2\text{-C}_6\text{H}_4)_3^{*+}$	1.14	2,6-Me ₂ -pyridine	14.1	100.5
Reductant	$E_{1/2}^{a,b}$	Acid	pK_a^c	ΔG_H^d
Cp ₂ Fe	0	pyridinium	12.5	71.5
(C ₅ Me ₅) ₂ Fe	-0.48	pyridinium	12.5	61.0
Cp ₂ Fe	0	acetic acid	22.3	85.5
Cp ₂ Co ^e	-1.34371	acetic acid	22.3	55.5 ^e

^aPotentials are in V versus Cp₂Fe^{+/0}.^bFrom reference 254 unless otherwise noted.^c pK_a of baseH⁺ from reference 30.^dEffective BDFE in kcal mol⁻¹ from equation 7.^eFor illustrative purposes; the stability of this combination is not known.

Table 21

PCET thermochemistry of selected transition metal systems.^a

Compound (ML-H)	solvent	$E(\text{M}^{\text{II}}-\text{L})^{0/-}$	$E(\text{M}^{\text{II}}-\text{LH})^{+/0}$	$\text{p}K_{\text{a}}(\text{M}^{\text{II}}-\text{LH})$	$\text{p}K_{\text{a}}(\text{M}^{\text{II}}-\text{LH})$	BDFE
$\text{Fe}^{\text{II}}(\text{H}_2\text{O})_6^{2+}$	H_2O	[0.39]	0.77372	3.372	9.5372	79.5
$(\text{H}_2\text{O})_5\text{CrOOH}^{2+}$	H_2O	--	--	--	--	81.4379, ^b
$(\text{H}_2\text{O})_5\text{CrOH}^{2+}$	H_2O	--	--	--	--	≥ 91.6380 , ^b
$(\text{Me}_6\text{cyclam})\text{Rh}(\text{H}_2\text{O})(\text{OOH})^{2+}$ ^b	H_2O	--	--	--	--	80.0381, ^b
$(\text{Me}_6\text{cyclam})\text{Rh}(\text{HO})(\text{OOH})^{2+}$ ^b	H_2O	--	--	--	--	79.5381, ^b
$(\text{Me}_6\text{cyclam})\text{Co}(\text{H}_2\text{O})(\text{OOH})^{2+}$ ^b	H_2O	--	--	--	--	81.9381, ^b
$([\text{14}]\text{aneN}_4)\text{Co}(\text{HO})(\text{OOH})^{2+}$ ^b	H_2O	--	--	--	--	80.9381, ^b
$[(\text{bpy})_2\text{pyRu}^{\text{II}}\text{OH}_2]^{2+}$	H_2O	0.46390	1.02390	0.85390	10.6390	82.3
$[(\text{bpy})_2\text{pyRu}^{\text{III}}\text{OH}]^{2+}$	H_2O	<0.48383	>1.6383	<0.383	>13.383	84.8
$\text{trans}[\text{Ru}^{\text{V}}(\text{tmc})(\text{O})(\text{O}-\text{H})]^{2+}$ ^c	H_2O	0.56404	>0.67	<1.404	2.8404	74.3
$\text{trans}[\text{Ru}^{\text{IV}}(\text{tmc})(\text{O})(\text{HO}-\text{H})]^{2+}$ ^c	H_2O	0.80404	--	--	4.7404	82.5
$\text{MnO}_3(\text{OH})^-$	H_2O	--	0.564415	7.4415	--	80.7
$[\text{Mn}_2(\text{OH})_2(\text{phen})_4]^{3+}$	MeCN	-0.03415	--	--	11.5415	70.0
$[\text{Mn}_2(\text{O})(\text{OH})(\text{phen})_4]^{3+}$	MeCN	-0.01415	--	--	14.6415	74.7
$(\text{salpn})_2(\text{Mn}_2(\text{O})(\text{OH}))$ ^d	MeCN	-0.89410	-0.21410	24.5410	13.4410	68.4
$(\text{L}^{\text{A}})_2(\text{Mn}_2(\text{O})(\text{OH}))$ ^e	MeCN	-0.63410	0.01410	20.5410	10.8410	69.9 ^e
$(\text{L}^{\text{B}})_2(\text{Mn}_2(\text{O})(\text{OH}))$ ^e	MeCN	-0.12410	0.47410	13.3410	5.0410	68.5 ^e
$(\text{L}^{\text{C}})_2\text{Mn}_2\text{OH}_2$ ^f	-- ^e	-0.52411	-0.09411	10.411	19.411	-- ^f
$(\text{L}^{\text{C}})_2\text{Mn}_2\text{OH}_2$ ^{+f}	-- ^e	0.32411	>0.97411	<0.411	10.411	-- ^f
$[(\text{L}^{\text{D}})\text{Mn}^{\text{II}}\text{OH}]^{2-}$ ^g	DMSO	<-2392	-1.51391	28.3391	[>37]	75.1
$[(\text{L}^{\text{D}})\text{Mn}^{\text{III}}\text{OH}]^{2-}$ ^g	DMSO	-1.0391	[-0.2]	~15.392	28.3391	86.8
$[(\text{L}^{\text{D}})\text{Fe}^{\text{II}}\text{OH}]^{2-}$ ^g	DMSO	--	-1.79391	25.0391	--	64.1

Compound (ML-H)	solvent	$E(\text{M}^{\text{II}}-\text{L})^{0/-}$	$E(\text{M}^{\text{II}}-\text{LH})^{+/0}$	$\text{p}K_{\text{a}}(\text{M}^{\text{II}}-\text{LH})$	$\text{p}K_{\text{a}}(\text{M}^{\text{II}}-\text{LH})$	BDFE
$[(\text{L}^{\text{D}})\text{Fe}^{\text{II}}\text{OH}]^{-g}$	DMSO	0.34391	--	--	25.0391	113
$(\text{Py}5)\text{Fe}^{\text{II}}(\text{MeOH})^{2+,h}$	MeOH	0.12394	0.32394	[7.6]	9.1394	83.1
$(\text{Py}5)\text{Fe}^{\text{II}}(\text{OH}_2)^{2+,h}$	DMSO	-0.095395	--	--	8.1395	63.8
$(\text{Py}5)\text{Mn}^{\text{II}}(\text{OH}_2)^{2+,h}$	MeCN	0.186393	0.636393	[5.4]	13.393	77.0
$(\text{bpy})_2\text{V}^{\text{IV}}(\text{O})(\text{OH})^+$	MeCN	--	--	--	--	70.624
$\text{Ni}^{\text{II}}(\text{cyclamN-H})$	H_2O	--	0.984420	7.1420	--	89.1
$\text{TpOs}^{\text{III}}(\text{NH}_2\text{Ph})\text{Cl}_2^i$	MeCN	-1.05424	0.48424	[-3] 424	22.5424	61.5
$\text{Fe}^{\text{II}}\text{H}_2\text{bim}^j$	MeCN	~ -0.884	-0.3184	17.584	~26.84	71.7 (BDE: 67.0) ^k
$\text{Fe}^{\text{II}}\text{H}_2\text{bip}^j$	MeCN	--	-0.55428	17.5428	--	66.2 (BDE: 62.0) ^k
$\text{Co}^{\text{II}}\text{H}_2\text{bim}^j$	MeCN	--	-0.53429	20.3429	--	70.5 (BDE: 63.0) ^k
$(\text{acac})_2\text{Ru}^{\text{II}}(\text{pyImH})^j$	MeCN	-1.00430	-0.64430	16.0430	[22.1] 430	62.1 (BDE: 68.1) ^k
$(\text{hfacac})_2\text{Ru}^{\text{II}}(\text{pyImH})^j$	MeCN	-0.07430	0.29430	[13.2] 430	19.3430	79.7
$(\text{TPP})\text{Fe}^{\text{II}}(\text{MeImH})_2^j$	MeCN	[-0.95]181	-0.585181	20.8181	26.9181	69.9
$\text{Ru}^{\text{II}}\text{CO}_2\text{H}^l$	MeCN	0.04727	--	--	18.527	81.3
$\text{Ru}^{\text{II}}\text{PhCO}_2\text{H}^l$	MeCN	0.17432	--	--	20.5432	86.9
$\text{CpCr}(\text{CO})_3\text{H}$	MeCN	-0.688437	0.668438	[-9.5]	13.3439	57.3 (BDE: 61.5) ^m
$\text{CpMo}(\text{CO})_3\text{H}$	MeCN	-0.501437	0.800438	[-8.0]	13.9439	62.4
$\text{CpW}(\text{CO})_3\text{H}$	MeCN	-0.491437	0.758438	[-5.0]	16.1439	65.6
$\text{Mn}(\text{CO})_5\text{H}$	MeCN	-0.555437	--	--	15.1440	62.8
$\text{Re}(\text{CO})_5\text{H}$	MeCN	-0.690437	--	--	21.1440	67.9
$\text{CpFe}(\text{CO})_2\text{H}$	MeCN	-1.352437	--	--	19.4440	50.3
$\text{CpRu}(\text{CO})_2\text{H}$	MeCN	-1.057437	--	--	20.2440	58.2

^a BDFE and BDE in kcal mol⁻¹. Potentials are in V vs. NHE for aqueous values and vs. Cp₂Fe^{+/0} in non-aqueous solvents. *Italicized* values are irreversible potentials, *E*_{p,a} or *E*_{p,c}, measured by cyclic voltammetry.

^b These values differ from those originally reported because they have been re-evaluated using the revised $E^\circ(\text{H}^+/\text{H}^\bullet)$ given in Table 19. Me₆cyclam = Me₆cyclam = *meso*-hexamethylcyclam; [14]aneN₄ = 1,4,8,11-tetraazacyclotetradecane.

^c tmc = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetra-decane.

^d salpn = 1,3-bis(salicylideneamino)propane.

^e L^A = 1,3-bis(3,5-dichloro-salicylideneamino)-propane and L^B = 1,3-bis(3,5-dinitrosalicylideneamino)propane. Slightly different bond strengths are calculated from consecutive sides of a square scheme using the reported data.

^f L^C = 2-hydroxy-1,3-bis(salicylideneamino)propane. Determined under various conditions in MeCN or mixed MeCN/water. See reference 411 for full details and additional examples. BDFEs can not be calculated from these data because CG is not known in mixed solvent systems.

^g L^D = tris[(*N'*-tert-butylureaylato)-N-ethyl]aminato.

^h Py5 = 2,6-bis(bis(2-pyridyl)methoxymethane)-pyridine.

ⁱ Tp = hydrotris(1-pyrazolyl)borate.

^j Complex drawn in Figure 12.

^k BDE determined from variable temperature equilibration methods and/or by calorimetry.⁴⁰

^l Complex drawn in Scheme 12.

^m From solution calorimetry in toluene solvent, ref. 441.