Published in final edited form as:

Inorg Chem. 2010 April 19; 49(8): 3685–3687. doi:10.1021/ic100143s.

The Importance of Precursor and Successor Complex Formation in a Bimolecular Proton-Electron Transfer Reaction

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Abstract

The transfer of a proton and an electron from the hydroxylamine TEMPOH (1-hydroxyl-2,2,6,6-tetramethylpiperidine) to $[\text{Co}^{\text{III}}(\text{Hbim})(\text{H}_2\text{bim})_2]^{2+}$ (H_2bim = 2,2'-bi-imidazoline) has an overall driving force $\Delta G^\circ = -3.0 \pm 0.4 \text{ kcal mol}^{-1}$ and an activation barrier of $\Delta G^\ddagger = 21.9 \pm 0.2 \text{ kcal mol}^{-1}$. Kinetic studies implicate a hydrogen-bonded 'precursor complex' at high $[\text{TEMPOH}]$, prior to proton-electron (hydrogen atom) transfer. In the reverse direction, $[\text{Co}^{\text{II}}(\text{H}_2\text{bim})_3]^{2+} + \text{TEMPO}$, a similar 'successor complex' was not observed, but upper and lower limits on its formation have been estimated. The energetics of formation of these encounter complexes are the dominant contributors to the overall energetics in this system: the ΔG° for the proton-electron transfer step is only $-0.3 \pm 0.9 \text{ kcal mol}^{-1}$. Thus formation of precursor and successor complexes can be a significant component of the thermochemistry for intermolecular proton-electron transfers, particularly in the low driving force regime, and should be included in quantitative analyses.

Proton-coupled electron transfer (PCET) reactions are critical steps in a variety of biologically and industrially important processes.¹ Reactions in which one electron and one proton transfer in a single kinetic step can be called hydrogen atom transfer (HAT) or, more generally, concerted proton-electron transfer (CPET).² Most current theoretical models for proton-electron transfer have their roots in electron transfer (ET) theories such as Marcus Theory.³ In applying Marcus Theory to bimolecular ET reactions, the reactants $\text{A}^+ + \text{D}$ are considered to proceed by initial formation of a precursor or encounter complex, $\text{A}^+|\text{D}$. This undergoes ET to form a successor complex, $\text{A}|\text{D}^+$, which then dissociates to products.⁴ It has long been recognized that the energetics of the ET step must be corrected for the energetics of formation of these precursor and successor complexes, as indicated by the use of ΔG° in Marcus treatments.⁴ Precursor and successor complexes are likely to be more important for PCET reactions, because the proton transfer component must occur over very short range,¹ yet they have not been included in most analyses to date. Described here, for the first time, are the energetics of a bimolecular PCET reaction including the precursor and successor complexes (Scheme 1), showing that the formation of these complexes can be energetically significant.⁵

The deprotonated cobalt(III)-tris(2,2'-bi-imidazoline) complex $\text{Co}^{\text{III}}(\text{Hbim})$ reacts reversibly with the hydroxylamine TEMPOH to slowly form the reduced protonated $\text{Co}^{\text{II}}(\text{H}_2\text{bim})$ and the stable nitroxyl radical TEMPO (eq 1, N-N = 2,2'-bi-imidazoline = H_2bim). This is a net hydrogen atom transfer reaction. Equilibrium measurements, as previously described, gave $K_1 = 169 \pm 23$ at 298 K and the ΔH°_1 and ΔS°_1 values in Table 1.⁶

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(1)

The kinetics of $\text{Co}^{\text{III}}(\text{Hbim}) + \text{TEMPOH}$ have been measured by observing the conversion of $\text{Co}^{\text{III}}(\text{Hbim})$ to $\text{Co}^{\text{II}}(\text{H}_2\text{bim})$ using UV-Vis spectroscopy.⁷ Under conditions of excess TEMPOH, the reactions proceed to completion and are first-order in cobalt based on studies with varying $[\text{Co}^{\text{III}}(\text{Hbim})]$ and global analysis of spectra from 350 - 800 nm over the course of 4-5 half-lives.⁷ The pseudo-first order rate constants k_{obs} vary linearly with $[\text{TEMPOH}]$ at low concentrations, but level off above 40 mM (Figure 1). The kinetics are well fit by a saturation rate law⁸ (eq 2), $k_{\text{HAT}} = (5.25 \pm 0.08) \times 10^{-4} \text{ s}^{-1}$, and $K_{\text{P}} = 61.3 \pm 0.8 \text{ M}^{-1}$ ($\Delta G^\circ_{\text{P}} = -2.44 \text{ kcal mol}^{-1}$) at 298 K. The temperature dependence (278 - 313 K) of the rates from

$$k_{\text{obs}} = \frac{K_{\text{P}} k_{\text{HAT}} [\text{TEMPOH}]}{1 + K_{\text{P}} [\text{TEMPOH}]}$$
(2)

both the linear and saturated regions, yield the activation parameters and the ground state thermodynamics given in Table 1. The values for $\Delta H^\circ_{\text{P}}$ and $\Delta S^\circ_{\text{P}}$ are in agreement with those independently (and more precisely) determined from the overall thermochemistry and activation parameters using a thermochemical cycle (Hess' Law).⁹

The simplest kinetic saturation model is the pre-equilibrium formation of an intermediate prior to the rate limiting step. Optical spectra of reactions at short times and TEMPOH concentrations up to 0.2 M, conditions where the intermediate is the dominant species present in solution, are within error of the λ_{max} and ϵ predicted for the sum of separated starting reagents. This indicates that the intermediate is a hydrogen bonded $\text{Co}^{\text{III}}(\text{Hbim})|\text{TEMPOH}$ precursor complex, only slightly perturbed from the starting materials, rather than a charge transfer complex or a species with a different coordination about cobalt.

Alternative formulations of the intermediate involving pre-equilibrium electron transfer (ET) or proton transfer (PT) are ruled out by the optical spectra and thermodynamic arguments.⁷ In these cases, reactions with high $[\text{TEMPO}]$ at short times would predominantly contain $\text{Co}^{\text{II}}(\text{Hbim})$ or $\text{Co}^{\text{III}}(\text{H}_2\text{bim})$, but these have distinct optical spectra from what is observed.^{13a} In addition, ET from TEMPOH to $\text{Co}^{\text{III}}(\text{H}_2\text{bim})$ would be endoergic by 30 kcal mol⁻¹, based on the known $E_{1/2}$ values for $\text{Co}^{\text{III}}(\text{Hbim})$ ¹⁰ and TEMPOH.⁶ Proton transfer (PT) from TEMPOH to $\text{Co}^{\text{III}}(\text{Hbim})$ is even more endoergic, 44 kcal mol⁻¹ based on the known $\text{p}K_{\text{a}}$ values.^{6,10}

To probe the properties of the successor complex, the kinetics of the reverse reaction were measured both by ¹H NMR, [5-10 mM $\text{Co}^{\text{II}}(\text{H}_2\text{bim})$ and 3-15 equiv TEMPO], and by UV-vis [1-2 mM $\text{Co}^{\text{II}}(\text{H}_2\text{bim})$ and up to 0.38 M TEMPO].⁷ The ¹H NMR spectra indicate good mass balance and that equilibrium is reached with ~10% conversion of $\text{Co}^{\text{II}}(\text{H}_2\text{bim})$. The data are well fit by an opposing second-order approach-to-equilibrium kinetic model (eq 3),¹¹ with

$k_{-1} = (1.8 \pm 0.5) \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ at 298 K. Eyring analysis of the rate constants from 273 - 313 K is shown in Table 1. No saturation was observed up to 0.38 M TEMPO.

$$-\frac{d[\text{Co}^{\text{III}}]}{dt} = \frac{k_{\text{HAT}} K_p [\text{Co}^{\text{III}}] [\text{TEMPOH}] - k_{-\text{HAT}} K_s [\text{Co}^{\text{II}}] [\text{TEMPO}]}{1 + K_p ([\text{Co}^{\text{III}}] + [\text{TEMPOH}])} \quad (3)$$

The first-order kinetic behavior in [TEMPO] indicates that under these conditions, the successor complex $\text{Co}^{\text{II}}(\text{H}_2\text{bim})|\text{TEMPO}$ is formed only to a small extent. Analysis with a full kinetic model based on Scheme 1 (see Supporting Information) indicates that K_s must be less than 2.6 M^{-1} . The successor complex, although not observed, likely involves a hydrogen-bond from $\text{Co}^{\text{II}}(\text{H}_2\text{bim})$ to the nitroxyl radical. This analysis assumes that the formation of the precursor and successor complexes is fast on the timescale of the HAT reaction, which is reasonable given that formation of hydrogen bonded adducts is usually fast and that k_{HAT} is small, $< 10^{-3} \text{ s}^{-1}$. A standard collisional model¹² can be used to estimate a lower limit for formation of the successor complex, $K_s \approx 0.16 \text{ M}^{-1}$, using molecular radii roughly estimated from crystallographic data.¹³ The range $2.6 \text{ M}^{-1} > K_s > 0.16 \text{ M}^{-1}$ indicates that the free energy of formation of the successor complex is $1.1 > \Delta G^\circ_s > -0.56 \text{ kcal mol}^{-1}$, or $\Delta G^\circ_s = 0.27 \pm 0.83 \text{ kcal mol}^{-1}$.

The free energies of activation and complex formation for reaction 1 are illustrated in Figure 2. The free energy for unimolecular HAT, $\Delta G^{\circ'}_{\text{HAT}}$, is given by the overall free energy ΔG°_1 minus the difference between the energies of forming the precursor (P) and successor (S) complexes, ΔG°_s and ΔG°_p (eq 4).⁴ $\Delta G^{\circ'}_{\text{HAT}}$ is clearly very different from the overall free energy change, ΔG°_1 . Quantitatively, $\Delta G^{\circ'}_{\text{HAT}} = -0.3 \pm 0.9 \text{ kcal mol}^{-1}$, roughly isoergic. In contrast, the overall ΔG°_1 is significantly downhill, $-3.0 \pm 0.4 \text{ kcal mol}^{-1}$ ($K_1 = 169$). The $2.7 \pm 0.9 \text{ kcal mol}^{-1}$ difference between $\Delta G^{\circ'}_{\text{HAT}}$ and ΔG°_1 is due to the much higher equilibrium constant for the precursor complex than for the successor complex. This is likely due to the $\text{TEMPOH} \rightarrow \text{Co}^{\text{III}}(\text{Hbim})$ hydrogen bond being stronger than the $\text{Co}^{\text{II}}(\text{H}_2\text{bim}) \rightarrow \text{TEMPO}$ H-bond.

$$\Delta G^{\circ'}_{\text{HAT}} = \Delta G^\circ_1 + \Delta G^\circ_s - \Delta G^\circ_p \quad (4)$$

The precursor and successor (P and S) complexes for proton-coupled electron transfer (PCET) are quite different than those for ET. Electrons can tunnel over multiple Ångstrom distances so there are usually no orientation requirements for the P and S complexes. These are typically treated as weak 'encounter' complexes whose energies of formation can be estimated by electrostatic models.¹² In PCET, however, the transfer of the proton occurs over tenths of Å, typically along a specific axis and often within a hydrogen bond. Therefore the simple electrostatic models used for ET are not appropriate for PCET. For instance, they predict that $\Delta G^\circ_p = \Delta G^\circ_s$ because no net charge is transferred (for reaction 1, there is no electrostatic work because TEMPO and TEMPOH are neutral reactants).

P and S complexes for PCET (and PT) likely have specific orientation requirements where both steric interactions and hydrogen bonding are energetically significant. The $\text{Co}^{\text{III}}(\text{Hbim})|\text{TEMPOH}$ complex implicated here is likely to be structurally very similar to the precursor complex, though that may not always be the case. The energetics of PCET P and S complexes could in some cases be estimated using empirical models for hydrogen bond energies,^{7,14} although the parameters needed are often not available for metal complexes or organic radicals. Hydrogen bonds are also important in organic hydrogen atom transfer

reactions, but for a somewhat different reason: an H-atom donor such as phenol must shed its hydrogen-bonded solvent prior to reaction with an organic radical.^{5b}

In conclusion, precursor and successor complexes are an important part of PCET reactions. These complexes have specific orientations which are important to the PCET process. The energetics of their formation, as indicated by the $\text{Co}^{\text{III}}(\text{Hbim}) + \text{TEMPOH}$ reaction analyzed here, can be a substantial component of the overall energy change. This is particularly the case in the low driving force regime that is important in biological and energy-conversion PCET processes.¹ Since the precursor and successor complexes have both steric interactions and hydrogen bonds, their energies of formation cannot be estimated with the electrostatic models common for ET reactions. These conclusions have important implications for analyses of PCET systems, from mechanistic arguments^{1,15} to application of the Marcus cross relation^{10,16} to sophisticated quantum theories.^{1a,3a}

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank the U.S. National Institutes of Health (GM50422 to JM) and from the Natural Sciences and Engineering Research Council of Canada (NSERC PGS-D2 to EM) for financial support. The authors are also indebted to Drs. J. P. Roth and J. C. Yoder for their prior studies on this system.

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- (2). (a) The terminology in this area is in flux. ‘CPET,’ coined by Costentin *et al.*,^{2b} refers to any process in which e^- and H^+ transfer in the same kinetic step. The traditional term HAT is, in our view, ^{1c,2c} best used to include all reactions in which $e^- + H^+$ transfer from one reactant to a single product. There are also narrower definitions of HAT, for instance restricting it to processes “in which the transferring electron and proton come from the same bond.”^{1b} Reaction 1 is HAT under both definitions (although according to the latter the reverse reaction is not HAT). (b) Costentin C, Evans DH, Robert M, Savéant J-M, Singh PS. *J. Am. Chem. Soc* 2005;127:12490–12491. [PubMed: 16144387] (c) Waidmann CR, Zhou Z, Tsai EA, Kaminsky W, Hrovat DA, Borden WT, Mayer JM. *J. Am. Chem. Soc* 2009;131:4729–4743. [PubMed: 19292442]
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Figure 1. 0.3 mM $\text{Co}^{\text{III}}(\text{Hbim})$ + TEMPOH in MeCN at 298 K: (A) UV-vis spectra vs. time (45.5 mM TEMPOH), inset: 1st-order fit of absorbance at 586 nm. (B) Plot of pseudo-first-order rate constants vs. [TEMPOH].

Figure 2.

Free energy surface for reaction of $\text{Co}^{\text{III}}(\text{Hbim}) + \text{TEMPOH}$ in MeCN (eq 1). The uncertainty in $\Delta G^\circ_{\text{S}}$ for formation of $\text{Co}^{\text{II}}(\text{H}_2\text{bim})|\text{TEMPO}$ is indicated by the error bar. The top half of the Figure is not to scale, as indicated by the breaks in the lines.

Scheme 1.

Mechanism of HAT involving precursor and successor complexes; k_{HAT} is the rate limiting step and K_1 is the overall K_{eq} .

Table 1Activation and Ground State Thermodynamics for **Co^{III}(Hbim) + TEMPOH in MeCN**

	Value at 298 K ^a	ΔG° ^b	ΔH° ^b	ΔS° ^c
K_I ^d	169 ± 23	-3.0 ± 0.4	9.3 ± 0.4	41 ± 2
K_P ^e	61.3 ± 0.8	-2.44 ± 0.05	-4 ± 2	-9 ± 4
K_S	$0.16 < K_S < 2.6$	0.27 ± 0.83		

		$\Delta G^\ddagger$	$\Delta H^\ddagger$	$\Delta S^\ddagger$
$k_{-1} = k_{\text{HAT}}K_S$	$(1.8 \pm 0.5) \times 10^{-4}$	22.5 ± 0.3	9.0 ± 0.8	-47 ± 3
k_{HAT}	$(5.25 \pm 0.08) \times 10^{-4}$	21.9 ± 0.2	23 ± 2	3.3 ± 0.6

^aUnits: K_I : unitless; K_P , K_S : M^{-1} ; k_{-1} : $\text{M}^{-1} \text{s}^{-1}$; k_{HAT} : s^{-1} .^b kcal mol^{-1} at 298 K.^c $\text{cal mol}^{-1} \text{K}^{-1}$.^dData from ref. 6.^e ΔH°_P and ΔS°_P from Hess' Law⁹.