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

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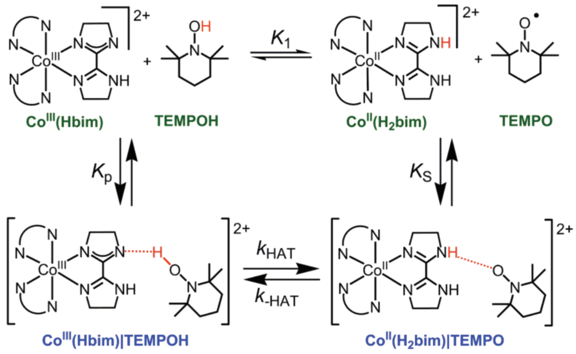
The transfer of a proton and an electron from the hydroxylamine 1-hydroxyl-2,2,6,6-tetramethylpiperidine (TEMPOH) to $[Co^{III}(Hbim)(H_2bim)_2]^{2+}$ (H_2bim = 2,2′-biimidazoline) has an overall driving force of $\Delta G° = -3.0 \pm 0.4$ kcal mol^{-1} and an activation barrier of $\Delta G^{\ddagger} = 21.9 \pm 0.2$ kcal mol^{-1}. Kinetic studies implicate a hydrogen-bonded "precursor complex" at high [TEMPOH], prior to proton−electron (hydrogen-atom) transfer. In the reverse direction, $[Co^{II}(H_2bim)_3]^{2+}$ + 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: $\Delta G°'$ for the proton−electron transfer step is only -0.3 ± 0.9 kcal mol^{-1}. Thus, formation of the precursor and successor complexes can be a significant component of the thermochemistry for intermolecular proton−electron transfer, 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] When Marcus theory is applied to bimolecular ET reactions, the reactants $A^+ + D$ are considered to proceed by the initial formation of a precursor or encounter complex, $A^+|D$. This undergoes ET to form a successor complex, $A|D^+$, 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 $\Delta G°'$ in Marcus theory treatments.[4] Precursor and successor complexes are likely to be more important for PCET reactions because the proton-transfer (PT) component must occur over a 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]

Scheme 1. Mechanism of HAT Involving Precursor and Successor Complexes[a]



[a] k_{HAT} is the rate-limiting step, and K_1 is the overall K_{eq}.

The deprotonated cobalt(III) tris(2,2′-biimidazoline) complex **Co^{III}(Hbim)** reacts reversibly with the hydroxylamine TEMPOH to slowly form the reduced protonated **Co^{II}(H$_2$bim)**

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(1) (a) *Hydrogen-Transfer Reactions*; Hynes, J. T., Klinman, J. P., Limback, H.-H., Schowen, R. L., Eds.; Wiley-VCH: Weinheim, Germany, 2007. (b) Huynh, M. H. V.; Meyer, T. *Chem. Rev.* **2007**, *107*, 5004–5064. (c) Mayer, J. M. *Annu. Rev. Phys. Chem.* **2004**, *55*, 363–390.

(2) (a) The terminology in this area is in flux. "CPET", coined by Costentin et al.,[2b] refers to any process in which electron and proton transfer are in the same kinetic step. The traditional term HAT is, in our view,[1c,2c] best used to include all reactions in which electron and proton 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, D. H.; Robert, M.; Savéant, J.-M.; Singh, P. S. *J. Am. Chem. Soc.* **2005**, *127*, 12490–12491. (c) Waidmann, C. R.; Zhou, Z.; Tsai, E. A.; Kaminsky, W.; Hrovat, D. A.; Borden, W. T.; Mayer, J. M. *J. Am. Chem. Soc.* **2009**, *131*, 4729–4743.

(3) (a) Hammes-Schiffer, S.; Soudackov, A. V. *J. Phys. Chem. B* **2008**, *112*, 14108–14123. (b) Tishchenko, O.; Truhlar, D. G.; Ceulemans, A.; Nguyen, M. T. *J. Am. Chem. Soc.* **2008**, *130*, 7000–7010.

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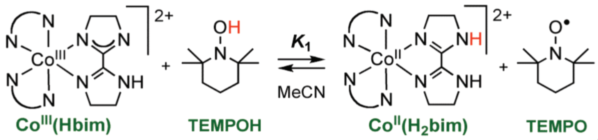
Table 1. Activation and Ground-State Thermodynamics for **Co^{III}(Hbim)** + TEMPOH in MeCN

	value at 298 K[a]	$\Delta G°$[b]	$\Delta H°$[b]	$\Delta S°$[c]
K_1[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		
		$\Delta G^‡$	$\Delta H^‡$	$\Delta S^‡$
$k_{-1} = k_{-HAT}K_S$	$(1.8 \pm 0.5) \times 10^{-4}$	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 ± 6

[a] Units: K_1, unitless; K_P, K_S, M^{-1}; k_{-1}, M^{-1} s^{-1}; k_{HAT}, s^{-1}. [b] In kcal mol^{-1} at 298 K. [c] In cal mol^{-1} K^{-1}. [d] Data from ref 6. [e] $\Delta H°_P$ and $\Delta S°_P$ from Hess' law.[9]

and the stable nitroxyl radical TEMPO (eq 1; N−N = 2,2′-biimidazoline = H_2bim). This is a net HAT reaction. Equilibrium measurements, as previously described, gave K_1 = 169 ± 23 at 298 K and the $\Delta H°_1$ and $\Delta S°_1$ values in Table 1.[6]



(1)

The kinetics of **Co^{III}(Hbim)** + TEMPOH have been measured by observing the conversion of **Co^{III}(Hbim)** to **Co^{II}(H$_2$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 [**Co^{III}(Hbim)**] and global analysis of the spectra from 350 to 800 nm over the course of 4−5 half-lives.[7] The pseudo-first-order rate constants k_{obs} vary linearly with [TEMPOH] at low concentrations but level off above 40 mM (Figure 1). The kinetics are well fit by a saturation rate law[8] (eq 2); k_{HAT} = (5.25 ± 0.08) × 10^{-4} s^{-1}, and K_P = 61.3 ± 0.8 M^{-1} ($\Delta G°_P$ = −2.44 kcal mol^{-1}) at 298 K.

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

The temperature dependences (278−313 K) of the rates from both the linear and saturated regions yield the activation parameters and the ground-state thermodynamics given in Table 1. The values for $\Delta H°_P$ and $\Delta S°_P$ 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 preequilibrium 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 values predicted for the sum of separated starting reagents. This indicates that the intermediate is a hydrogen-bonded **Co^{III}(Hbim)**| 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.

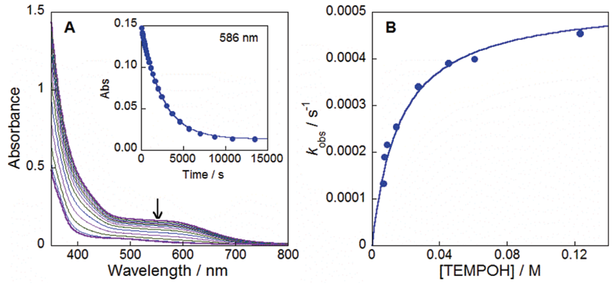


Figure 1. 0.3 mM **Co^{III}(Hbim)** + TEMPOH in MeCN at 298 K: (A) UV−vis spectra vs time (45.5 mM TEMPOH) (inset: first-order fit of absorbance at 586 nm). (B) Plot of pseudo-first-order rate constants vs [TEMPOH].

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

To probe the properties of the successor complex, the kinetics of the reverse reaction were measured both by ^{1}H NMR [5−10 mM **Co^{II}(H$_2$bim)** and 3−15 equiv of TEMPO] and by UV−vis [1−2 mM **Co^{II}(H$_2$bim)** and up to 0.38 M TEMPO].[7] The ^{1}H NMR spectra indicate good mass balance and that equilibrium is reached with ~10% conversion of

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(5) (a) HAT precursor complex formation is suggested to be rate-limiting in: Temprado, M.; McDonough, J. E.; Mendiratta, A.; Tsai, Y.-C.; Fortman, G. C.; Cummins, C. C.; Rybak-Akimova, E. V.; Hoff, C. D. *Inorg. Chem.* **2008**, *47*, 9380−9389. (b) For initial hydrogen-bonded complexes that inhibit HAT, see: Litwinienko, G.; Ingold, K. U. *Acc. Chem. Res.* **2007**, *40*, 222–230.

(6) Mader, E. A.; Manner, V. W.; Markle, T. F.; Wu, A.; Franz, J. A; Mayer, J. M. *J. Am. Chem. Soc.* **2009**, *131*, 4335–4345.

(7) See the Supporting Information.

(8) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw Hill, Inc.: New York, 1995.

(9) $\Delta H°_1 = \Delta H°_P + \Delta H^‡_{HAT} - (\Delta H^‡_{-HAT} + \Delta H°_S)$. $\Delta H°_P$ can be derived using the independently determined values for $\Delta H°_1$, $\Delta H^‡_{HAT}$, and $(\Delta H^‡_{-HAT} + \Delta H°_S)$. An equivalent entropic relationship can be defined. The calculated values of $\Delta H°_P$ (Table 1) are consistent with those measured directly ($\Delta H°_P = -6 \pm 4$ kcal mol^{-1}; $\Delta S°_P = -13 \pm 12$ cal mol^{-1} K^{-1}) but have smaller error bars.

(10) Roth, J. P.; Yoder, J. C.; Won, T. J.; Mayer, J. M. *Science* **2001**, *294*, 2524–2526.

(11) (a) King, E. L. *Int. J. Chem. Kinet.* **1982**, *14*, 1285–1286. (b) Pladziewicz J. R.; Lesniak, J. S.; Abrahamson, A. J. *J. Chem. Educ.* **1986**, *63*, 850–851.

(12) (a) In bimolecular reactions, equilibrium constants for weak encounter complexes are typically estimated from the average collisional distance.[4] The estimate of 0.16 M^{-1} follows: (b) Eberson, L. *Electron Transfer reactions in Organic Chemistry*; Springer-Verlag: Berlin, Germany, 1987; pp 32−34. (c) If the value for K_S were smaller than 0.16 M^{-1}, the discrepancy between $\Delta G°'_{HAT}$ and $\Delta G°_1$ would be even larger.

(13) Radius of {**Co^{II}(H$_2$bim)** + TEMPO} ≈ 0.8 nm: (a) Yoder, J. C.; Roth, J. P.; Gussenhoven, E. M.; Larsen, A. S.; Mayer, J. M. *J. Am. Chem. Soc.* **2003**, *125*, 2629–2640. (b) Roth, J. P.; Lovell, S.; Mayer, J. M. *J. Am. Chem. Soc.* **2000**, *122*, 5486–5498.

$\mathbf{Co^{II}(H_2bim)}$. The data are well fit by an opposing second-order approach-to-equilibrium kinetic model (eq 3),[11] with $k_{-1} = (1.8 \pm 0.5) \times 10^{-4}$ M^{-1} s^{-1} at 298 K. Eyring analysis of the rate constants from 273 to 313 K is shown in Table 1. No saturation was observed up to 0.38 M TEMPO.

$$-\frac{d[\mathrm{Co^{III}}]}{dt} = \frac{k_{\mathrm{HAT}}K_{\mathrm{P}}[\mathrm{Co^{III}}][\mathrm{TEMPOH}] - k_{-\mathrm{HAT}}K_{\mathrm{S}}[\mathrm{Co^{II}}][\mathrm{TEMPO}]}{1 + K_{\mathrm{P}}([\mathrm{Co^{III}}] + [\mathrm{TEMPOH}])} \qquad (3)$$

The first-order kinetic behavior in [TEMPO] indicates that under these conditions the successor complex $\mathbf{Co^{II}(H_2bim)}$|TEMPO is formed only to a small extent. Analysis with a full kinetic model based in Scheme 1 (see the 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 $\mathbf{Co^{II}(H_2bim)}$ to the nitroxyl radical. This analysis assumes that the formation of the precursor and successor complexes is fast on the time scale of the HAT reaction, which is reasonable given that the formation of hydrogen-bonded adducts is usually fast and that k_{HAT} is small, $< 10^{-3}$ s^{-1}. A standard collisional model[12] can be used to estimate a lower limit for the formation of the successor complex, $K_S \approx 0.16$ M^{-1}, using molecular radii roughly estimated from crystallographic data.[13] The range 2.6 M^{-1} $> K_S >$ 0.16 M^{-1} indicates that the free energy of formation of the successor complex is $1.1 > \Delta G°_S > -0.56$ kcal mol^{-1} or $\Delta G°_S = 0.27 \pm 0.83$ 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, $\Delta G°'_{HAT}$, is given by the overall free energy $\Delta G°_1$ minus the difference between the energies of forming the precursor (P) and successor (S) complexes, $\Delta G°_S$ and $\Delta G°_P$ (eq 4).[4] $\Delta G°'_{HAT}$ is clearly very different from the overall free energy change, $\Delta G°_1$. Quantitatively, $\Delta G°'_{HAT} = -0.3 \pm 0.9$ kcal mol^{-1}, roughly isoergic. In contrast, the overall $\Delta G°_1$ is significantly downhill, -3.0 ± 0.4 kcal mol^{-1} ($K_1 = 169$). The 2.7 ± 0.9 kcal mol^{-1} difference between $\Delta G°'_{HAT}$ and $\Delta G°_1$ is due to the much higher equilibrium constant for the precursor complex than for the successor complex. This is likely due to the TEMPOH → $\mathbf{Co^{III}(Hbim)}$ hydrogen bond being stronger than the $\mathbf{Co^{II}(H_2bim)}$ → TEMPO hydrogen bond.

$$\Delta G°'_{HAT} = \Delta G°_1 + \Delta G°_S - \Delta G°_P \qquad (4)$$

The precursor and successor (P and S) complexes for PCET are quite different from those for ET. Electrons can tunnel over multiple-angstrom 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 angstroms, 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 $\Delta G°_P = \Delta G°_S$ because no net charge is transferred [for reaction (1), there is no electrostatic work because TEMPO and TEMPOH are neutral reactants].

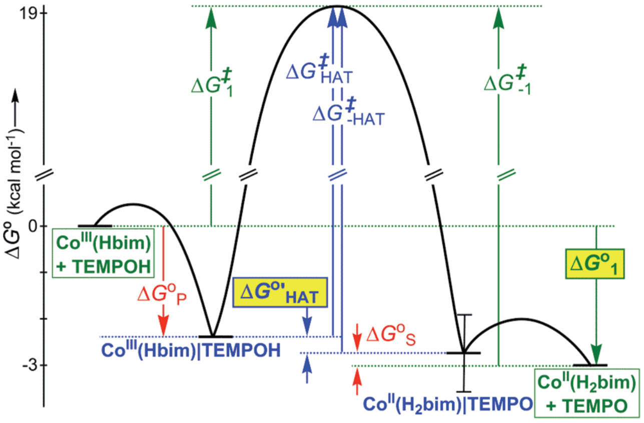

Figure 2. Free-energy surface for the reaction of $\mathbf{Co^{III}(Hbim)}$ + TEMPOH in MeCN (eq 1). The uncertainty in $\Delta G°_S$ for the formation of $\mathbf{Co^{II}(H_2bim)}$|TEMPO is indicated by the error bar. The top half of the figure is not to scale, as indicated by the breaks in the lines.

Precursor and successor complexes for PCET (and PT) likely have specific orientation requirements in which both steric interactions and hydrogen bonding are energetically significant. The $\mathbf{Co^{III}(Hbim)}$|TEMPOH complex implicated here is likely to be structurally very similar to the precursor complex although that may not always be the case. The energetics of PCET precursor and successor 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 HAT reactions, but for a somewhat different reason: a hydrogen-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 that are important to the PCET process. The energetics of their formation, as indicated by the $\mathbf{Co^{III}(Hbim)}$ + 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] Because 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 the application of the Marcus cross relation[10,16] to sophisticated quantum theories.[1,3a]

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Supporting Information Available: Experimental details and kinetic thermochemical analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Compare refs 1, 13, 16, and: Concepcion, J. J.; Brennaman, M. K.; Deyton, J. R.; Lebedeva, N. V.; Forbes, M. D. E.; Papanikolas, J. M.; Meyer, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 6968–6969.

(16) Warren, J. J.; Mayer, J. M. *Proc. Natl. Acad. Sci. U.S.A.*, doi:10.1073/pnas.0910347107.