

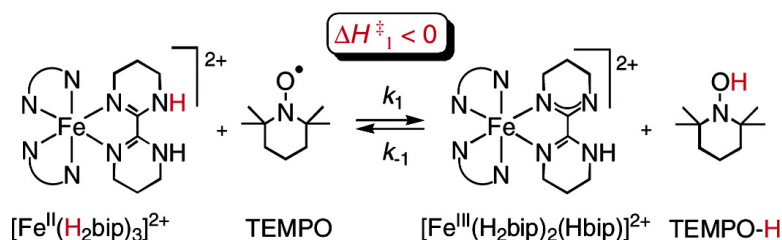
Communication

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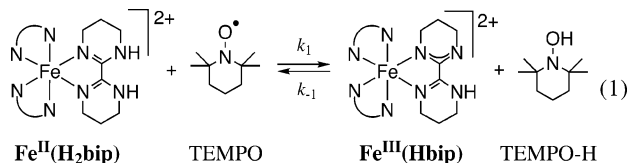
Hydrogen Atom Transfer from Iron(II)–Tris[2,2′-bi(tetrahydropyrimidine)] to TEMPO: A Negative Enthalpy of Activation Predicted by the Marcus Equation

Elizabeth A. Mader, Anna S. Larsen, and James M. Mayer*

Department of Chemistry, University of Washington, Box 351700, Seattle, Washington 98195-1700

Received February 11, 2004; E-mail: mayer@chem.washington.edu

Hydrogen atom transfer is one of the fundamental reactions of organic radical chemistry and is being increasingly implicated in reactions of transition-metal complexes and metalloenzymes. It is a key step in a variety of metal-mediated oxidations.¹ These reactions can also be termed proton-coupled electron transfer (PCET) because there is concerted movement of a proton and an electron.² We have previously shown that the rate constants of a number of metal-mediated and organic H-atom transfer reactions can be understood and predicted using Marcus theory, specifically the Marcus cross relation.³ This report describes studies of H-atom transfer between iron complexes with 2,2′-bi(tetrahydropyrimidine) (H₂bip) ligands and the stable nitroxyl radical TEMPO or its corresponding hydroxylamine, TEMPO–H (eq 1; N–N = H₂bip).⁴ The forward reaction has a very unusual temperature dependence, slowing as the temperature is raised. This result is predicted by the Marcus cross relation on the basis of the temperature dependences of the driving force and self-exchange rates.



[Fe(H₂bip)₃]²⁺ (Fe^{II}(H₂bip))⁵ reacts rapidly with TEMPO in anaerobic MeCN solution to give an equilibrium mixture with TEMPO–H and [Fe(Hbip)(H₂bip)₂]²⁺ (Fe^{III}(Hbip)).^{5,6} All four species are isolable.⁶ The kinetics in both directions have been studied by stopped-flow rapid-scanning UV–vis spectrophotometry under pseudo-first-order conditions.⁶ In the forward reaction, with an excess of TEMPO, the spectra show a decrease in concentration of Fe^{II}(H₂bip) (λ_{max} 510 nm) and a concomitant increase in the concentration of Fe^{III}(Hbip) (λ_{max} 636 nm). The derived second-order rate constants at 298 K are $k_1 = 260 \pm 30 \text{ M}^{-1} \text{ s}^{-1}$ and $k_{-1} = 150 \pm 20 \text{ M}^{-1} \text{ s}^{-1}$. Remarkably, the rate constants for the forward reaction show a small but definite decrease with increasing temperature. Eyring analysis of rate constants from 277 to 328 K (Figure 1) gives $\Delta H_1^\ddagger = -2.7 \pm 0.4 \text{ kcal mol}^{-1}$ and $\Delta S_1^\ddagger = -57 \pm 8 \text{ cal mol}^{-1} \text{ K}^{-1}$; $\Delta H_{-1}^\ddagger = 6.7 \pm 0.4 \text{ kcal mol}^{-1}$ and $\Delta S_{-1}^\ddagger = -26 \pm 2 \text{ cal mol}^{-1} \text{ K}^{-1}$. From the ratio of k_1 and k_{-1} , $K_{\text{eq}} = 1.7 \pm 0.3$ at 298 K; a van't Hoff plot (Figure 2, K_{eq}) gives $\Delta H^\circ = -9.4 \pm 0.6 \text{ kcal mol}^{-1}$ and $\Delta S^\circ = -30 \pm 2 \text{ cal mol}^{-1} \text{ K}^{-1}$. The equilibrium constants have been confirmed in independent experiments over a similar temperature range, by UV–vis determinations of the [Fe^{II}(H₂bip)]/[Fe^{III}(Hbip)] ratio in the presence of excess TEMPO and TEMPO–H.⁶

The negative enthalpy of activation is unusual for solution reactions but not unprecedented.^{5b,7} In most previous examples, $\Delta H^\ddagger < 0$ is attributed to the presence of a low-concentration intermediate ($\Delta G^\circ > 0$) that is enthalpically favored ($\Delta H^\circ < 0$). This pre-equilibrium can involve, for instance, a charge-transfer complex, a

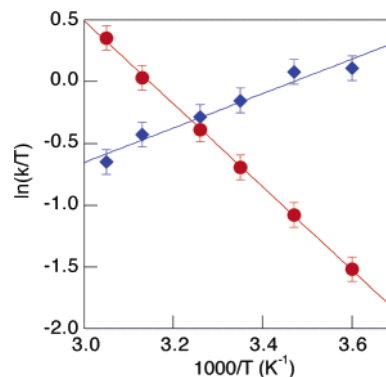


Figure 1. Eyring plots of PCET between (blue \blacklozenge) Fe^{II}(H₂bip) + TEMPO (k_1) and (red \bullet) Fe^{III}(Hbip) + TEMPO–H (k_{-1}) in MeCN.

precursor complex for electron transfer, or spin inversion.⁷ Pre-equilibrium isomerization of Fe^{II}(H₂bip) from high- to low-spin was suggested as the origin of ΔH_2^\ddagger of $-1.5 \pm 0.5 \text{ kcal mol}^{-1}$ (260–300 K) for the hydrogen atom self-exchange between Fe^{II}(H₂bip) and Fe^{III}(Hbip) (eq 2).^{5b}



In 1975, Marcus and Sutin showed that Marcus Theory, the classical Marcus equation $\Delta G^\ddagger = 1/4\lambda(1 + \Delta G^\circ/\lambda)^2$, predicts $\Delta H^\ddagger < 0$ for electron-transfer reactions that have $\Delta G^\circ \approx 0$ and substantially negative ΔH° and ΔS° values.⁸ In the case of eq 1, the quadratic term in the Marcus equation can be ignored because $|\Delta G^\circ|$ is much less than λ ($|\Delta G^\circ| < 1.1 \text{ kcal mol}^{-1}$, $\lambda \cong 56 \text{ kcal mol}^{-1}$). Also ignored here, for simplicity, are work terms and nonadiabatic effects.^{8,9} Under these conditions, the Marcus cross relation applied to eq 1 (eq 3) has $f \cong 1^9$ and can be written in free energy terms as in eq 4. The subscripts Fe/s.e. and TEMPO/s.e. refer to the self-exchange reactions involving iron (eq 2) or TEMPO (eq 6). (The self-exchange barriers provide the intrinsic barrier λ according to the additivity postulate.⁹) Equation 4 implies an equivalent relation in enthalpic terms (eq 5⁸), when $\partial(\Delta H)/\partial T \cong 0$, as is assumed in the Eyring and van't Hoff treatments.

$$k_1 = \sqrt{k_{\text{Fe/s.e.}} k_{\text{TEMPO/s.e.}} K_{\text{eq}} f} \quad (3)$$

$$\Delta G_{\text{calcd}}^\ddagger = 1/2(\Delta G_{\text{Fe/s.e.}}^\ddagger + \Delta G_{\text{TEMPO/s.e.}}^\ddagger + \Delta G_1^\circ) \quad (4)$$

$$\Delta H_{\text{calcd}}^\ddagger = 1/2(\Delta H_{\text{Fe/s.e.}}^\ddagger + \Delta H_{\text{TEMPO/s.e.}}^\ddagger + \Delta H_1^\circ) \quad (5)$$

Direct measurement of the rate of hydrogen atom self-exchange between TEMPO and TEMPO–H (eq 6) by dynamic NMR line broadening has proven problematic, as multiple relaxation mechanisms are indicated. As an alternative, the pseudo-self-exchange H-atom transfer reaction between TEMPO–H and 4-oxo-TEMPO has been examined (eq 7). Equilibrium constants for eq 7 from

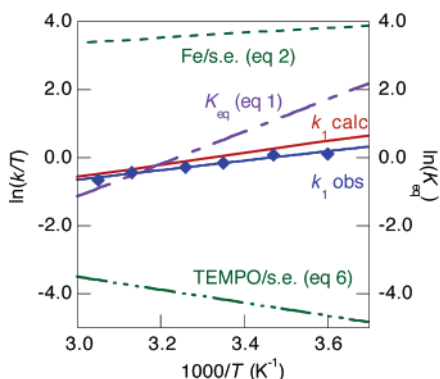
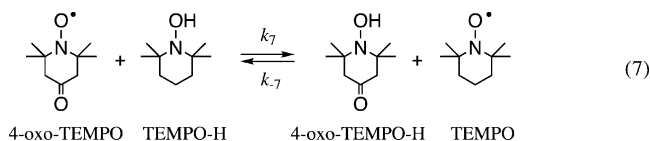


Figure 2. Comparison of measured second-order rate constants for $\text{Fe}^{\text{II}}(\text{H}_2\text{bip}) + \text{TEMPO}$ (\blacklozenge , k_1 obsd) to rate constants calculated from $k_1 = (k_{\text{Fe/s.e.}} k_{\text{TEMPO/s.e.}} K_{\text{eq}})^{1/2}$ (eq 3) (\bullet , k_1 calcd). The calculation uses the illustrated equilibrium constants ($-\cdot-\cdot-$, K_{eq}) and the iron and TEMPO self-exchange (s.e.) rate constants ($-\cdot-\cdot-$ and $-\cdot-\cdot-$).

278 to 328 K were determined by integration of ^1H NMR spectra, using Lorentzian line-shape analysis.⁶ K_{eq} values are small ($\Delta H_7^\circ = -2 \pm 2 \text{ kcal mol}^{-1}$, $\Delta S_7^\circ = -3 \pm 4 \text{ cal mol}^{-1} \text{ K}^{-1}$), indicating that this is a good approximation for TEMPO/TEMPO–H self-exchange. The optical spectra of TEMPO and 4-oxo-TEMPO are sufficiently resolved to allow monitoring of the hydrogen atom transfer kinetics. Global fitting of the spectra using SPECFIT and second-order approach to equilibrium kinetics¹⁰ gives $k_7 = 10 \pm 1 \text{ M}^{-1} \text{ s}^{-1}$ and $k_{-7} = 2.2 \pm 0.2 \text{ M}^{-1} \text{ s}^{-1}$ at 298 K, with activation parameters $\Delta H_7^\ddagger = 3.0 \pm 0.5 \text{ kcal mol}^{-1}$ and $\Delta S_7^\ddagger = -43 \pm 20 \text{ cal mol}^{-1} \text{ K}^{-1}$ (278–318 K). TEMPO self-exchange rate constants (eq 6) are estimated as the geometric mean of k_7 and k_{-7} .¹¹



Application of the Marcus cross relation (eq 3) to eq 1 uses the equilibrium constants and the rate constants for iron and TEMPO self-exchange (eqs 2, 6). The calculated rate constants are the same within error as those observed, over the entire temperature range (Figure 2). A negative enthalpy of activation is calculated, $\Delta H_{\text{calcd}}^\ddagger = -3.5 \pm 0.5 \text{ kcal mol}^{-1}$, within error of the observed $\Delta H_1^\ddagger = -2.7 \pm 0.4 \text{ kcal mol}^{-1}$. This is a striking confirmation of the applicability of the cross relation to hydrogen atom transfer reactions.

Figure 2 illustrates that while the iron self-exchange and the equilibrium constant both contribute to the inverse temperature dependence, the K_{eq} term is dominant ($\Delta H_1^\circ = -9.4 \text{ kcal mol}^{-1}$ while $\Delta H_{\text{Fe/s.e.}}^\ddagger = -1.5 \text{ kcal mol}^{-1}$). In essence, reaction 1 has a negative enthalpy of activation because $\Delta G_1^\circ \cong 0$ and $\Delta H_1^\circ \ll 0$. $\Delta G_1^\circ \cong 0$ implies that the transition state is midway along the reaction coordinate. The high point on the enthalpy surface is earlier (because $\Delta H_1^\circ < 0$), and therefore at the transition state the enthalpy is below that of the starting materials. This situation has been found and more quantitatively explored in another context.¹² This explanation does not require the presence of an intermediate but does not exclude its presence.

The thermochemistry of hydrogen atom transfer from $\text{Fe}^{\text{II}}(\text{H}_2\text{bip})$ to TEMPO (eq 1) is unusual in its substantial negative entropy, $\Delta S_1^\circ = -30 \pm 2 \text{ cal mol}^{-1} \text{ K}^{-1}$. Most H-atom transfers, at least for the organic reactions where values are available, occur with

small values of $|\Delta S^\circ|$.¹³ The large entropy in this case results in part⁶ ($\sim 60\%$) from conversion of mostly high-spin $\text{Fe}^{\text{II}}(\text{H}_2\text{bip})$ to largely low-spin $\text{Fe}^{\text{III}}(\text{Hbip})$.^{5b}

In conclusion, hydrogen atom transfer (PCET) from $\text{Fe}^{\text{II}}(\text{H}_2\text{bip})$ to TEMPO has a negative enthalpy of activation: the rate constants decrease with increasing temperature. The dominant contribution to this effect is the large enthalpic driving force, even though $|\Delta G^\circ| \cong 0$. Using independently measured equilibrium constants and self-exchange rates, Marcus theory quantitatively predicts the rate constants and the unusual temperature dependence. This result, part of ongoing work in our laboratory,^{2,3,5b,14} shows the applicability of Marcus theory to hydrogen-atom transfer/proton-coupled electron transfer. This study also raises interesting questions about entropic contributions and spin-state changes in H-atom transfer and PCET reactions in chemistry and biology. For example, the widely used determination of bond dissociation enthalpies from redox potential and $\text{p}K_{\text{a}}$ measurements assumes small entropic differences between the reagents.^{2,3,15} For $\text{Fe}(\text{H}_2\text{bip})$, this assumption introduces an error of 9 kcal mol⁻¹. Studies are currently underway to probe the significance of this issue in other systems.

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Supporting Information Available: Synthesis of compounds and experimental details on kinetic measurements. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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