particular hydroxyl group *specifically* releases that hydroxyl, making it available for whatever subsequent transformations might be required. This enlarges considerably the scope of the method: α *C*-mannosides, for example, could, in principle, be made by inversion of the C-2 hydroxyl of the glucose-derived **4** and, similarly, β *C*-glucosides are accessible, not only as shown in **6** to **7**, or **8** to **9**, but also by inversion of the C-2 hydroxyl of **11**.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for their support of this work.

High-Driving-Force Electron Transfer in Metalloproteins: Intramolecular Oxidation of Ferrocytochrome *c* by Ru(2,2'-bpy)$_2$(im)(His-33)$^{3+}$

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Received May 6, 1991

Electron-transfer (ET) theory describes rates in terms of nuclear-reorganization (λ) and electronic-coupling (H_{AB}) parameters.[1] These parameters are most directly determined from the driving-force dependence of the ET rate (ideally at high driving forces in the neighborhood of λ).[2] Remarkably slow ET rates have been observed at low driving forces ($-\Delta G° < 0.3$ eV) in certain iron–sulfur[3] and blue copper proteins,[4] and at high driving forces in Ru(bpy)$_2$L(His-33) (bpy = 2,2'-bipyridine; L = imidazole, pyridine, H_2O; His = histidine) derivatives of cytochrome *c* (cyt *c*).[5] Since the latter results conflict sharply with the much faster ET rates reported for Ru-modified Zn-substituted cytochrome *c* (Ru-Zn-cyt *c*)[2,6] and Ru(bpy)$_2$(dcbpy)-labeled ferrocytochrome *c* (dcbpy = dicarboxybipyridine),[7,8] we have determined the Ru(bpy)$_2$L(His-33)-cyt *c* kinetics by using a novel flash-quench method that allows the observation of rates over an extremely wide range.[9-11]

The rate of intramolecular oxidation of horse heart ferrocytochrome *c* by Ru(bpy)$_2$(im)(His-33)$^{3+}$ (im = imidazole)[12,13] was measured as outlined in Scheme I. The quencher (Q) used

Scheme I

$$\text{D–A} + h\nu \rightarrow \text{D–A}^* \quad (1a)$$

$$\text{D–A}^* + \text{Q} \rightarrow \text{D–A}^+ + \text{Q}^- \quad (1b)$$

$$\text{D–A}^+ \rightarrow \text{D}^+\text{–A} \quad (1c)$$

$$\text{D}^+\text{–A} + \text{Q}^- \rightarrow \text{D–A} + \text{Q} \quad (1d)$$

in this study was Ru_6^{3+} (a = NH_3). The excited-state decay rates of Ru(bpy)$_2$(im)$_2^{2+*}$ and Ru(bpy)$_2$(im)(His-33)$^{2+*}$-Fe^{II}-cyt *c* do not differ greatly (1.4×10^7 and 1.25×10^7 s^{-1}, respectively), demonstrating a minor role for direct photoinduced ET. The second-order rate constant for oxidative quenching of Ru(bpy)$_2$(im)(His-33)$^{2+*}$-Fe^{II}-cyt *c* by Ru_6^{3+} is 4.9×10^8 M^{-1} s^{-1}. Transient absorption measurements[14] on solutions of Ru(bpy)$_2$(im)(His-33)$^{2+}$-Fe^{II}-cyt *c* (18 μM) and Ru_6^{3+} (7 mM)[15] exhibit biphasic kinetics. The rate constants of both kinetic components are independent of protein concentration. The first process represents decay of Ru(bpy)$_2$(im)(His-33)$^{2+*}$, accelerated by the bimolecular quenching reaction with Ru_6^{3+}. The second process corresponds to the intramolecular oxidation of the ferroheme by Ru(bpy)$_2$(im)(His-33)$^{3+}$ ($k_{ET} = 2.6 \times 10^6$ s^{-1}, T = 298 K, pH = 7, sodium phosphate buffer, μ = 0.1).[16] Identical kinetics were measured at wavelengths characteristic of the heme oxidation state and the Ru oxidation state (306, 400, 500, and 550 nm; Figure 1). This ET rate contrasts with the previously reported rate of 55 s^{-1} measured by pulse radiolysis.[5] The transient absorption spectrum measured upon completion of the second process is identical with the Fe$^{III/II}$-cyt *c* difference spectrum (Figure 2).[17] Over a period of seconds, the photogenerated Ru_6^{2+} reduces the Fe^{III}-cyt *c* formed by intramolecular ET to regenerate the original complex.

Intramolecular ET reactions involving Ru–ammine complexes coordinated to His-33 of Zn-substituted cytochrome *c* (Ru$_4$L-(His-33)-Zn-cyt *c*; L = NH_3, pyridine, isonicotinamide) are best described by an electronic coupling matrix element of 0.12 (2) cm^{-1} and a 1.2 (1)-eV reorganization energy.[2] A large part of this reorganization energy involves solvent reorientation around the Ru–ammine complex. It is known, however, that the solvent reorganization energies associated with the ET reactions of Ru–bipyridine complexes are substantially smaller than those of ammine complexes.[18] The self-exchange reorganization energies (λ_{11}) for Ru$_5$(pyridine)$^{3+/2+}$ and Ru(bpy)$_3^{3+/2+}$ are 1.20 and 0.57 eV, respectively.[18] By using the Marcus cross-relation ($\lambda_{12} = {}^1/_2\lambda_{11} + {}^1/_2\lambda_{22}$)[1] and these same reorganization energies for Ru$_4$L-(His-33) and Ru(bpy)$_2$(im)(His-33), we estimate λ = 0.89 (10) eV for intramolecular ET in Ru(bpy)$_2$(im)(His-33)-Fe-cyt *c*. The predicted rate of ferroheme oxidation by Ru(bpy)$_2$(im)(His-33)$^{3+}$, 3.5×10^6 s^{-1} (λ = 0.89 eV; H_{AB} = 0.12 cm^{-1}; $-\Delta G°$ = 0.74 eV), is in excellent agreement with that measured by the flash-quench technique. An important advantage of the reduced reorganization energy in Ru(bpy)$_2$(im)(His) (compared to the Ru(a)$_4$L(His)

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(15) Under these conditions, the equilibrium concentrations of solution species are the following: [Ru(bpy)$_2$(im)(His-33)$^{2+}$-Fe^{II}-cyt *c*] = 18 μM; [Ru(bpy)$_2$(im)(His-33)$^{2+}$-Fe^{III}-cyt *c*] = 5 μM; [Ru_6^{3+}] = 7 mM. Thus, 22% of the ET quenching reactions generate Ru(bpy)$_2$(im)(His-33)$^{3+}$-Fe^{III}-cyt *c*. Independent measurements with the fully oxidized protein exhibit no transient kinetics on the time scale (i.e., $\leq$10 μs) of the intramolecular ET reaction.
(16) We also observe identical ET kinetics for the same reaction when Ru(bpy)$_2$(im)(His-33)$^{3+}$-Fe^{II}-cyt *c* is produced (in low yield) by direct electron transfer from Ru(bpy)$_2$(im)(His-33)$^{2+*}$ to the ferriheme center. This observation provides strong support for our interpretation of the flash-quench kinetics. The photoinduced ET rate does not significantly accelerate the Ru(bpy)$_2$(im)(His-33)$^{2+*}$ decay so that a reliable rate constant for this reaction cannot be extracted from the decay kinetics. Estimates based on the yield of Ru(bpy)$_2$(im)(His-33)$^{3+}$-Fe^{II}-cyt *c* suggest a rate constant of $\sim 2 \times 10^5$ s^{-1}.
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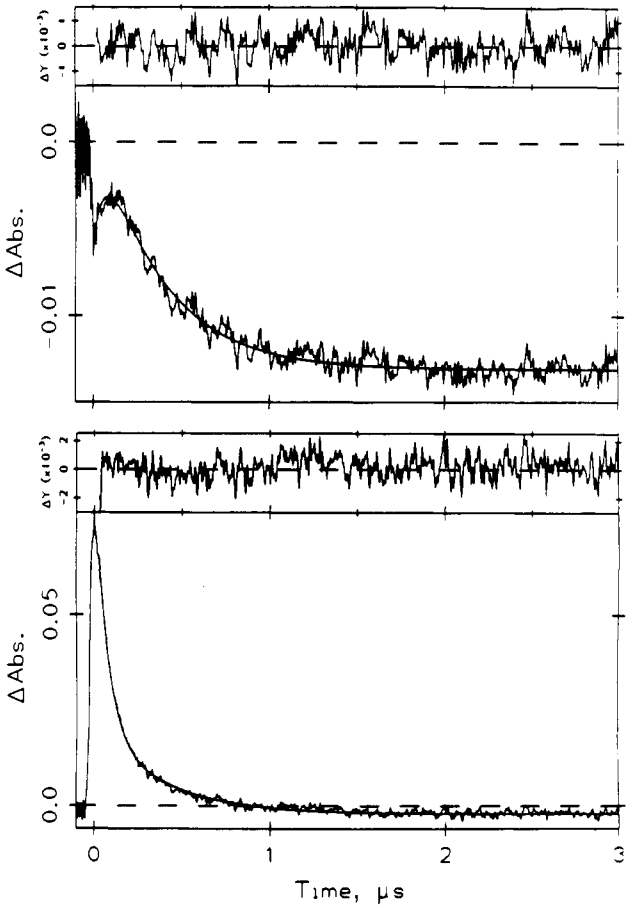

Figure 1. Transient kinetics following laser flash excitation (480 nm, 25 ns, 4 mJ) of a mixture of $Ru(bpy)_2(im)(His\text{-}33)^{2+}$-$Fe^{II}$-cyt *c* (18 μM) and Ru_a^{3+} (7 mM). Smooth lines are fits to a biexponential decay function. The faster component corresponds to decay of the excited Ru complex (k_{obsd} = 1.6 (1) × 10^7 s^{-1}); the slower component arises from the intramolecular ET reaction (k_{obsd} = 2.6 (3) × 10^6 s^{-1}). Top: Kinetics recorded at 550 nm. Bottom: Kinetics recorded at 306 nm.

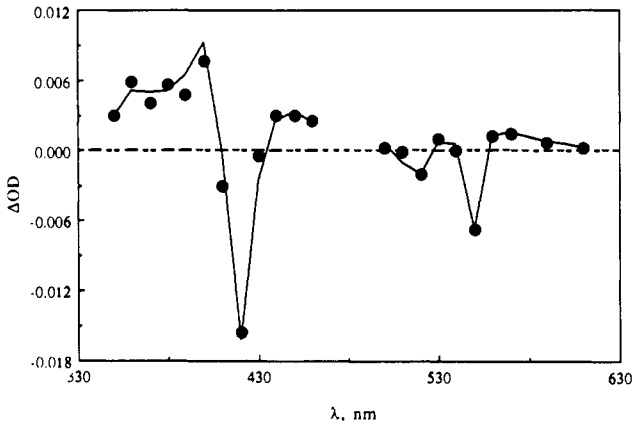

Figure 2. Difference spectrum (●) of the product of the intramolecular ET reaction. The solid line is the [Fe^{III}]-[Fe^{II}] cytochrome *c* difference spectrum (ref 17).

systems) is that the inverted region for ET (i.e., $-\Delta G° > \lambda$) is more accessible.

Up to this time, high-driving-force intramolecular ET rates in proteins and protein-protein complexes have been extracted mainly from studies of excited-state reactions.[2,6,7,19-21] Extremely fast ET rates can be measured by this technique, but the lower limit is always determined by the intrinsic excited-state lifetime (~1 μs for transition-metal complexes; ~10 ms for metalloporphyrins). This limit restricts the range of donor-acceptor distances that can be probed, as well as the nature of the proteins that can be examined (heme proteins substituted with unnatural metals). The flash-quench approach opens the way for studies of intramolecular ET at high driving forces over a wide range of distances in *both heme and nonheme proteins in which the natural metal is still in place.*

Acknowledgment. This work was supported by grants from the National Science Foundation and the National Institutes of Health.

Supplementary Material Available: Chromatograms from the preparation and purification of $Ru(bpy)_2(im)(His\text{-}33)$-Fe-cyt *c*, absorption spectra of $Ru(bpy)_2(im)(His\text{-}33)$-Fe-cyt *c*, and spectra from the reactions of Fe-cyt *c* and $Ru(bpy)_2(im)(His\text{-}33)$-Fe-cyt *c* with diethyl pyrocarbonate (5 pages). Ordering information is given on any current masthead page.

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Metallacyclobutanes from Kinetic Nucleophilic Addition to η^3-Allyl Ethylene Complexes of Iridium. Regioselectivity Dependence on Nucleophile and Allyl Orientation

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Received March 27, 1991

The addition of nucleophiles to transition metal complexes of unsaturated hydrocarbons has been extensively investigated, leading to a number of synthetically useful organic reactions.[1] For unsaturated organometallic systems that possess several potentially reactive electrophilic sites, Davies, Green, and Mingos have developed a series of rules governing the regioselectivity of kinetic nucleophilic additions.[2] For complexes coordinating both η^2-alkene and η^3-allyl ligands, these rules predict addition preferentially to the olefin functionality. This prediction is supported both on theoretical grounds[2] and in many systems by experimental results.[2,3] Possible exceptions have, however, been noted for geometrically constrained complexes of the form $(C_5R_5)M[(1\text{-}3)\text{-}\eta^3\text{:}(5,6)\text{-}\eta^2\text{-cycloalkadienyl}]^+X^-$ (**1**, R = Me, H; M = Co, Rh,

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