since hydrogen bond chromatography can mimic various modes of DNA base pairing.

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Registry No. 4, 59495-22-6; 2′,3′,5′-tri-*O*-acetylguanosine, 6979-94-8; 3-methylthymidine, 958-74-7; thymidine, 50-89-5.

Porphyrin Vinyl Groups Act as Antennae for Electron Transfer within [Fe,Zn] Hemoglobin Hybrids

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Long-range electron transfer[1] at variable distance[2,3] between a donor and acceptor that are *not* small compared to their separation raises the question of the proper measure of intersite distance. If in fact a single value can be assigned,[4] when the process involves a metalloprotein should one consider the distance to the metal or to the atom(s) at the nearest edge of a conjugated ligand? The latter hypothesis would suggest that a heme vinyl group conjugated with the ring might act as an "antenna" and thereby increase the transfer rate.[5]

In most hemoprotein electron-transfer complexes[6] the vinyl groups are directed away from the redox partner (e.g., hemoglobin, cytochrome b_5)[7] and/or are reduced (e.g., cytochrome *c* peroxidase, cytochrome *c*)[8] and thus only influence electron transfer indirectly.[9] However, in the $[\alpha_1, \beta_2]$ electron-transfer complex of $[\mathrm{Fe^{III}P}, \mathrm{ZnP}]$[10] hemoglobin hybrids,[11] vinyl groups of the $\alpha_1(\mathrm{Fe^{III}P})$ and

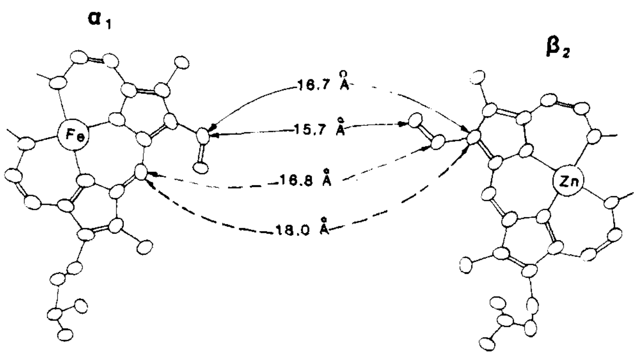

Figure 1. Schematic representation of distances between the α_1 and β_2 hemes within the T-state hemoglobin tetramer.[12] Preparation of the $[\alpha(\mathrm{Fe}),\beta(\mathrm{Zn})]$ hybrid with ZnD eliminates the vinyl group from the β-chain. The solid arrows indicate the shortest interporphyrin separations in the presence and absence of the vinyl group of the β-chain. The dashed arrows indicate the analogous distances for a ring-edge carbon of the α-chain heme.

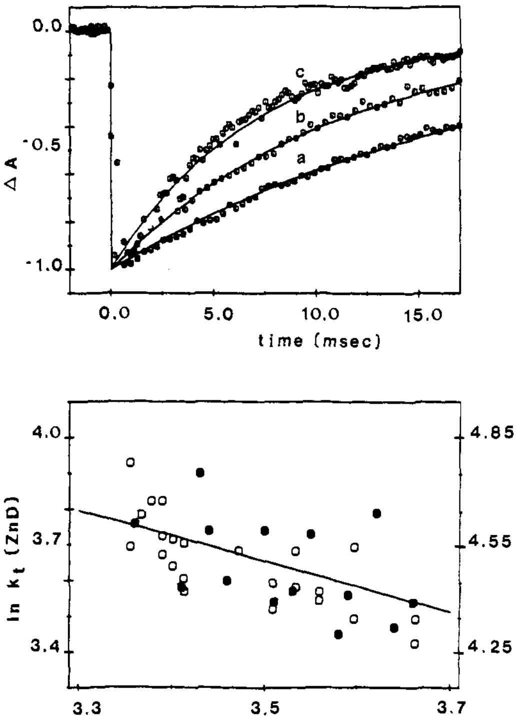

Figure 2. Kinetic properties of [Fe,Zn] hemoglobin hybrids. (upper) Normalized transient absorbance decay of $^3\mathrm{Zn}$ porphyrins within (a) $[\mathrm{Fe^{II}P,ZnD}]$; (b) $[\mathrm{Fe^{III}(H_2O)P,ZnD}]$; and (c) $[\mathrm{Fe^{III}(H_2O)P,ZnP}]$. Conditions: 415 nm; 25 °C; 10 mM $\mathrm{KP_i}$ buffer (pH 7.0). (lower) Temperature dependence of electron transfer rates: $k_t(\mathrm{ZnD})$ for the $[\mathrm{Fe^{III}(H_2O)P,ZnD}]$ hybrid (left ordinate, ●); $k_t(\mathrm{ZnP})$ for the $[\mathrm{Fe^{III}(H_2O)P,ZnP}]$ hybrid (right ordinate, ○). The right ordinate scale and the $k_t(\mathrm{ZnP})$ points have been shifted downward by 0.85 to facilitate comparison of the two data sets. The solid line corresponds to the best fit line for the $[\mathrm{Fe^{III}(H_2O)P,ZnD}]$ hybrid; $\Delta E^*(\mathrm{ZnD}) = 0.06$ eV.

$\beta_2(\mathrm{ZnP})$ point toward each other and are involved in the distances of closest approach (Figure 1).[12] Use of hybrid prepared with ZnD,[10] which lacks vinyl groups, rather than ZnP, lengthens the minimum distances between unsaturated carbons by 1 Å without significantly perturbing either the electron distribution of the zinc-porphyrin core[13] or, as shown by protein X-ray diffraction

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studies, the hemoglobin structure.[14] The comparison of photoinitiated (^{3}Zn porphyrin) → (Fe^{III} porphyrin) electron transfer within the mixed-metal [Fe^{III}P,ZnD] and [Fe^{III}P,ZnP] hybrids presented here has permitted us to identify a direct role of vinyl groups in determining the transfer distance within a biological system where donor/acceptor *orientation* and intervening protein *medium* are *fixed*.

The [α(FeP),β(ZnD)] hybrid and ZnDHb were prepared by procedures analogous to those for the ZnP-containing proteins.[15] The optical spectrum of the [α(Fe^{II}P),β(ZnD)] hybrid exhibits two maxima in the Soret region, one for the Fe^{II}P at 430 nm and one for ZnD at 412 nm. Oxidation of the Fe^{II}P to Fe^{III}P yields a normal [(Fe^{III}(H$_2$O)P)–(Fe^{II}P)] static difference spectrum,[11c] and the resultant hybrid has a single, combined Soret peak at 412 nm. The band for ZnD within the hybrid and ZnDHb is blue-shifted relative to the ZnP band in the corresponding proteins, in agreement with the trends observed for a series of Zn metalloporphyrins.[16] Similarly, the phosphorescence emission maximum for ZnDHb at ambient is blue-shifted to 708 nm from the value of 720 nm for ZnPHb.

Flash excitation of the [Fe^{II}P,ZnD] hybrid produces the ^{3}ZnD state, which decays with a rate constant, $k_D = 50(5)\ s^{-1}$ (Figure 2), essentially the same as that for ^{3}ZnP within the analogous hybrid.[11] When the [Fe^{III}P,ZnD] hybrid is photolyzed, electron-transfer quenching increases the decay rate to $k_{obsd} = 85\ (10)\ s^{-1}$, which corresponds to a ^{3}ZnD → Fe^{III}(H$_2$O)P electron-transfer rate of $k_t(\mathrm{ZnD}) = k_{obsd} - k_D = 35\ (10)\ s^{-1}$. This compares with an observed rate of $k_{obsd} = 150\ (10)\ s^{-1}$ for the [Fe^{III}(H$_2$O)P,ZnP] hybrid,[11c] which corresponds to $k_t(\mathrm{ZnP}) = 100\ (10)\ s^{-1}$ (Figure 2). Arguments presented elsewhere show that the measurement is not the result of spin or energy-transfer quenching;[11c] indeed the blue-shift of the ^{3}ZnD emission relative to that of ^{3}ZnP increases any spectral overlap with Fe^{III}P and would *increase* the quenching rate if Fe–Zn energy transfer were important, contrary to observation. Thus, elimination of the vinyl group on the ^{3}Zn-porphyrin donor through use of ZnD rather than ZnP reduces the nonadiabatic[11b] electron-transfer rate at ambient temperature by a factor of $k_t(\mathrm{ZnP})/k_t(\mathrm{ZnD}) \equiv \gamma \approx 2.8$.[17]

Figure 2 also presents Arrhenius plots of k_t for the [Fe^{III}(H$_2$O)P,ZnP] and [Fe^{III}(H$_2$O)P,ZnD] hybrids; for comparison, the scale of ln[k_t(ZnP)] is shifted by a constant amount of −0.85. The points for the ZnP and ZnD hybrids as plotted in this way clearly overlap, and the small activation energies obtained by least-squares fits agree within experimental error: $\Delta E^*(\mathrm{ZnD}) = 0.06\ (5)$ eV; $\Delta E^*(\mathrm{ZnP})^{11b} = 0.10\ (5)$ eV.[18] Thus, k_t(ZnD) is reduced from k_t(ZnP) by a change in the temperature-independent, electron-tunnelling preexponential term for the rate constant.[1]

The present results show that a vinyl group of a ^{3}ZnP donor can conjugate with the ring sufficiently well to serve as an electron-transfer antenna. The preexponential factor of the rate constant[1] for nonadiabatic electron transfer is suggested to represent a weighted contribution from the electron densities on all conjugated atoms,[4] and we may write the following: $k_t(\mathrm{ZnP}) = k_t(\mathrm{vinyl}) + k_t(\mathrm{other})$; $k_t(\mathrm{ZnD}) = k_t(\mathrm{other})$.[13] Even though the electron density associated with a conjugated vinyl moiety is small,[13] the value, $\gamma \approx 2$–3, as seen in Figure 2, implies that the term associated with the shortest distance between redox centers, k_t(vinyl), represents over $^2/_3$ of the measured rate for the [Fe^{III}(H$_2$O)P,ZnP] hybrid. This suggests that often it will be a good approximation to discuss long-range electron-transfer measurements in terms of a single parameter, the distance of closest approach between conjugated atoms. In fact, Gray and co-workers[3] conclude that the rate constant can be described in terms of a single distance (d), with $k_t \propto \exp(-0.9d)$. This would predict $k_t(\mathrm{ZnP})/k_t(\mathrm{ZnD}) = \exp(0.9\Delta d) \sim 2.5$ for $\Delta d \sim 1$ Å, in accordance with our experiments.

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Total Synthesis of a C$_{15}$ Ginkgolide, (±)-Bilobalide

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The ginkgo tree, *Ginkgo biloba*, which has existed in its present form for thousands of centuries, produces a collection of unusual polycyclic structures (ginkgolides) which are C$_{15}$[1] and C$_{20}$[2] polylactones.[3] Extracts of the ginkgo, which have long been recommended in Chinese medicine, are now commonly used in Europe for the treatment of cerebrovascular and peripheral circulatory problems of the elderly. Reported herein is the first total synthesis of a member of the ginkgolide family (±)-bilobalide (**1**), a C$_{15}$-trilactone.

Enone **2**, which contains all the carbon atoms needed for the synthesis of **1**, was prepared by a remarkably simple, single-step process.[4] Reaction of the dilithio derivative of dimethyl *cis*-4-cyclohexen-1,2-dicarboxylate[5] in THF containing 3 equiv of hexamethylphosphoric triamide with 1 equiv of phenyl 3-*tert*-butylpropiolate[6] at −45 °C for 30 min and 0 °C for 4 h produced after extractive isolation and silica gel (sg) chromatography enone **2** in 72% yield.[7] Reduction of **2** with sodium borohydride in 1:1.5 methanol–isopropyl alcohol at 0 °C for 7 h furnished stereoselectively allylic alcohol **3** (75%). Ozonolysis of **3** at −78 °C in 1:1 methylene chloride–methanol containing 5 equiv of sodium bicarbonate, reduction of the intermediate with dimethyl sulfide, and extractive isolation gave aldehyde lactol **4** in 80% yield. The acetal **5**[8] was obtained from **4** by treatment with 0.05 equiv of p-toluenesulfonic acid in 5:1 methanol–methyl orthoformate at 23 °C for 24 h (72% after sg chromatography in the presence of

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