# Proton-Assisted Electron Transfer

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The case for highly selective long range "proton assisted" electron transfer in biomolecules (PA-ET), involving the hopping of protons and hydrogen atoms along H-bond chains connecting two redox sites, is discussed and analyzed on systems closely resembling typical biochemical sequences. These systems consist of an electron acceptor, an H-bond/covalent-bridge chain and an electron donor, and monohydroparabenzoquinone as the electron acceptor and a xanthine-like molecule as the electron donor and acceptor species held together by one or more peptide bridges. It is shown that, in biochemical structures, despite the involvement of the imidol (oximine) form of the peptide link, (a) PA-ET is energetically efficient and (b) the rate constants for proton-transfer, which is arguably the rate-controlling step, are reasonably high, the transfer times being on the order of hundreds of picoseconds.

## Introduction

Long chains of hydrogen bonds are expected to play important roles in biochemistry. It is generally accepted that proton translocation over long distance, a basic process in the mechanism of energy conversion,[1,2] is mediated by chains of H-bridged proton acceptor and donor groups: a proton entering from one end of such a chain forms a ionic defect which propagates toward the opposite end by sequential hopping of successive protons. That view was later reinforced by evidence in favor of the claim that in the channel of gramicidin A the dominant mechanism for proton transport is not the diffusion of the hydronium ion through the membrane channels, but proton hopping along H-bond chains which span the membrane,[3] and by growing structural evidence of the presence of water chains in the interior of protein backbones.[4−7] Remarkably, the determination of the changes accompanying the formation of charge separation in the reaction centers of photosynthetic bacteria has shown, in the form crystallized under illumination, a measure of disorder which has been imputed to water motions associated with the formation of the charge separated state.[7]

Proton transport across biomembranes is not the only function that such chains of H-bonds can carry out. As we show here, proton hopping along a chain connecting two redox sites may also be a suitable path for long-range electron transfer (ET), a process of considerable importance in biochemistry, whose mechanism is still attracting much attention and stimulating many experimental and theoretical efforts.[8] In fact, fast ET in certain biomacromolecules, such as multiheme cytochromes,[9] poses special problems about its mechanism. For one thing, it is a long-distance process between groups (the hemes) not connected by a few highly polarizable bonds, indeed separated by many substructures, particularly amino acid residues. Now, (a) through-bond ET along a protein backbone segment of tens of units seems quite unlikely, and the overlap between the donor and acceptor molecular orbitals (MO) involved in ET, which is one among the parameters on which ET should depend critically,[10] should be exceedingly small; (b) the interposed residues have quite high-lying LUMOs, so that they are unlikely to function as efficacious virtual bridges in through-space ET.

These considerations and the remark that in proteins H-bond are present everywhere, led some of us to suggest that, as an extension of the proposed mechanism of proton transport in biological membranes[2] and the "imidazole pump" property of hemes,[11] intramolecular ET between two heme groups could be of a special type: a proton-assisted "there and back again" process.[12] Such a process would consist essentially of the following steps: (1) a negative charge is produced in the acceptor end A of the H-bond chain by the arrival of an electron from an outer electron donor (oED) species;[1] (2) A attracts an H-bond proton linked to the neighboring site of the H-bond chain (P), so that its negative charge is transferred to that site, without change in the number of electrons of A;[2] (3) a chain of proton shifts follows along the shortest hydrogen-bond peptide-bond chain connecting the acceptor A to the donor D, which becomes negative by losing the H-bond proton linked to it;[3] (4) D yields an electron to an outer electron acceptor (oEA) to be reduced;[4] (5) the reverse process (transfer of hydrogen by switching of the H-bonds) takes place, but this time it is hydrogen atoms, not protons, that move to restore the original bond arrangement.

$$\mathrm{oED^-} + \mathrm{A\cdots H{-}P\cdots H{-}D} \rightarrow \mathrm{oED} + \mathrm{A^-\cdots H{-}P\cdots H{-}D} \quad (1)$$

$$\mathrm{A^-\cdots H{-}P\cdots H{-}D} \rightarrow \mathrm{A{-}H\cdots P^-\cdots H{-}D} \quad (2)$$

$$\mathrm{A{-}H\cdots P^-\cdots H{-}D} \rightarrow \mathrm{A{-}H\cdots P{-}H\cdots D^-} \quad (3)$$

$$\mathrm{A{-}H\cdots P{-}H\cdots D^-} + \mathrm{oEA} \rightarrow \mathrm{A{-}H\cdots P{-}H\cdots D} + \mathrm{oEA^-} \quad (4)$$

$$\mathrm{A{-}H\cdots P{-}H\cdots D} \rightarrow \mathrm{A\cdots H{-}P\cdots H{-}D} \quad (5)$$

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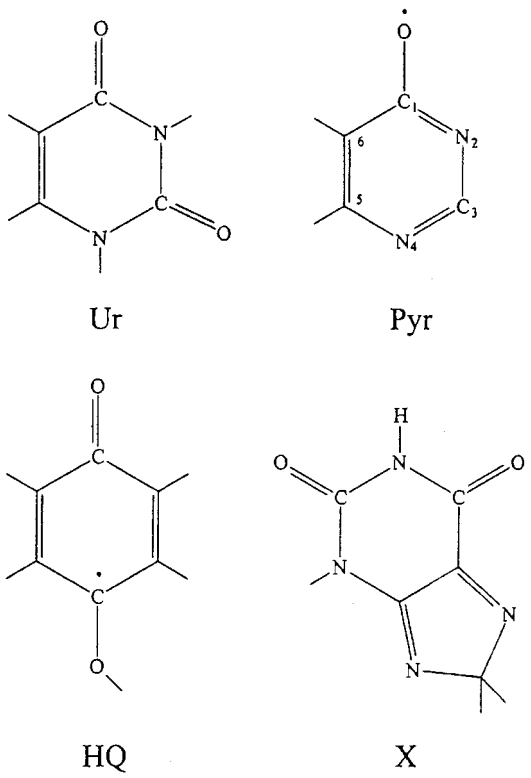
The net result is that the acceptor A, having received an electron plus a proton and lost a hydrogen atom, is back to its original form; the donor D, having lost first a proton and then an electron, and having received back a hydrogen atom, is again in the same form it was at the beginning. (Note that A and HD function as electron acceptor and donor with respect to some unspecified redox site, whereas they perform the opposite function with respect to one another. P stands for a chain of H-bonded molecules, each of which capable of tautomeric forms hp and ph). The PA-ET mechanism just described is formally plausible, since all the nuclear configurations involved obey the rules of valency, but to assess under what conditions it is a physically sound mechanism for long range ET one has to answer several questions: what kind of chemical perturbation at one site of the acceptor molecule would be sufficient to initiate the required proton-shift chain postulated by the PA-ET mechanism? Is the arrival of an electron a sufficient pertubation or other kinds of driving force are needed to initiate the proton hopping chain? Are A and D very special acid/base pair or does the postulated PA-ET mechanism work for a wide class of proton acceptor and donor pairs? What kind of molecules are suitable building blocks for the bridge connecting A to D?

Can PA-ET be fast enough to match experimentally observed ET rates? The present paper reports results obtained in an attempt to answer the above questions on suitable model compounds. They give insight into many critical features of the mechanism under consideration, and appear to provide strong support for the possibility of PA-ET.

**CHART 1**




## Modeling a Driving Force

Since PA-ET relies on the possibility of temporary switching of the H-bonds of a chain under a perturbation (driving force) applied at one end, a major problem is the proof that chemical events such as oxidation or reduction can produce such a driving force in a structure of the appropriate type. Now, proton-assisted electron transfer was originally suggested by the fact that in multiheme cytochromes it is possible to identify chains consisting of a histidine imidazole, H-bonds between peptide groups, peptide bonds, and another histidine imidazole, connecting the iron heme groups.[9,12] H-bond chains are also present in the reaction centers of photosynthetic bacteria,[13] and one of them connects the primary quinone to the secondary one. Unfortunately, the driving-force problem can hardly be discussed in terms of a model including all the main aspects of such a chain, for at least two reasons: (a) the electrostatic field of the protein backbone, which probably plays an important role, analogous to that of the solvent in outer sphere ET,[14] is difficult to model, due to the long-range nature of the Coulomb interaction; (b) the donor and acceptor groups would have to be entire iron-heme units. Therefore, we have analyzed the driving-force problem on model systems where the intermediate species are simple molecules not involving metal ions. The problem we will be concerned with can be formulated as follows: Is it possible to find a molecular pair D and A, resembling simple biomolecules, such that a pertubation consisting in the arrival of an electron on one end of the chain will cause the H-bond protons to switch their positions, localizing the additional electronic charge on the opposite end?

Concerning the building blocks of the H-bond chain, structural considerations on multiheme cytochrome $c_3$ suggest that the H-bond chain connecting the imidazole ligands of two iron−hemes should involve both peptide links and structural water molecules.[9,12] The involvement of a peptide link poses a problem, because its tautomeric form, namely, the imidol-like form, is a high-energy intermediate, which, to our knowledge, has never been observed in the gas phase or in solution, even though it has been postulated in the solid state.[15] The imidol form is expected to be a transient structure, so that the combination of short life and low concentration with respect to the normal amide form makes its detection by standard techniques difficult. This may explain why it has never been observed; however, it also raises another question: if the imidol form of a peptide bond is a short-lived species, is it not *so* short-lived that it will revert to the keto form before the probability has become sufficiently high that the next proton shift will take place?

This question requires a detailed dynamical study. The energy difference between the keto and imidol form of the peptide bond is ca. 14 kcal/mol.[16] If the driving force for the steps (1−3) is higher than this value, there should be no problem concerning the lifetime of the imidol intermediate: the keto−enol isomerization will probably be the rate-determining step of the whole ET process, but the imidol form will correspond to the lowest energy state of the charge relay system and therefore its lifetime will be long enough to allow $D^-$ to release an electron to its neighboring site in the redox chain. For a lower value of the driving force, or when several peptide links are involved in the H-bond chain connecting the two redox partners, the proton-shifted configuration will be a high-energy intermediate, and then the question concerning its lifetime becomes of crucial importance. An analysis of the lifetime of the imidol form in the formamide dimer—a case where no driving force for proton switching is present, so that the proton-shifted form corresponds to a higher energy intermediate—showed that, if a perturbation forces that molecule pair to switch to the imidol form, the return time is of the order of a period of the stretching vibration of the heavy atoms of the H-bond, tenths of picoseconds.[17] This is probably too short a time to allow the process to continue, an analysis of more realistic systems is therefore in order.

The simplest model system which appears to embody all the critical features to be studied is the acceptor−relay−donor chain:

$$A\cdots H-N(CH_3)-C(H)=O\cdots H-D$$

As the proton acceptor species, we have considered the pyrimidinol (Pyr) and the monohydroquinone (HQ) radicals and uracyl (Ur); a xanthine-like molecule (X) has been chosen as proton donor species, Chart 1. These systems provide examples of small (D = Pyr), medium (D = Ur), and strong (D = HQ) driving force. Electron releasing and/or withdrawing substituents have then be introduced in order to determine to what extent the driving force for the CT steps (2 and 3) can be chemically modulated, keeping the basic components of the chain fixed.

## Computational Details

Estimates of the energies of the metastable states and of the potential energy barriers for interconversion can be obtained by MNDO/PM3 computations,[18−20] because they give reliable results for simple compounds as those of Chart 1 in their equilibrium nuclear configurations. A few ab initio computations confirm that expectation.[21] On the other hand, as is well-known, this method highly overestimates proton-hopping barriers. Unfortunately, fully reliable experimental data about the latter are not available, and all one can say is that a reasonable evaluation of the latter could probably be obtained by highly correlated methods.[22] Therefore, we have based our analysis on probabilities and lifetimes estimated by PM3 computations, keeping in mind that they should be considered as upper limits.

The geometries assigned to the initial states have been the fully optimized ones obtained from our computations, whereas for the other nuclear configurations the mutual orientations of different molecular blocks have been kept fixed, to better simulate a rigid chain and to avoid unrealistic long distances between minimum energy structures along the reaction paths.

The transition probabilities for proton hopping have been estimated assuming, as is customary in most rate-process studies, evolution along a one-dimensional reaction path. In particular, proton hopping has been assumed to follow the least-motion path,[23] the path which connects the two minima along a straight line.[24] The potential energy profiles along those paths, in mass weighted coordinates, have been interpolated by polynomial functions, and the H-bond vibrational states have been computed variationally, using a set of harmonic oscillator basis functions localized in either well. All Hamiltonian matrix elements have been evaluated analytically.

The time evolution of the initial states has ben evaluated using the following, standard, procedure: (1) the initial states, which, according to the Franck−Condon principle are assumed to be the vibrational states associated with the proton oscillations in the single-well potential of the neutral systems, have been projected on the eigenstates of the double-well potentials of the negatively charged systems; (2) the time dependence of the expansion coefficients $c$ is evaluated by multiplying by the appropriate phase factors: $c_i(t) = c_i(t = 0)\exp(-i\epsilon_i t/\hbar)$), where $\epsilon_i$ is the energy of the $i$th eigenstate; (3) the resulting vibrational states at the time $t$ are then projected on the basis functions, and the Born probability for the system being localized in either of the two wells determined by summing over all the states localized in that well.

## Results

**Driving Force for CT and ET.** We consider first H-bond A···H−D complexes without any interconnecting bridge. The estimated energies for the stationary states of either the neutral and the negatively charged complex are reported in Table 1. All the complexes containing an unsubstituted A species of the type selected for our study possess two stable nuclear configurations depending on the absence or presence of an additional electron. The more stable nuclear configurations of the neutral complexes (their "normal forms") are those with the H-bond proton bound to site D; the proton-shifted form lies at a higher energy, as expected because of the accompanying charge separation, which is not compensated by the resulting electrostatic attraction. The arrival of an additional electron reverses the situation: in the negatively charged complexes, the proton shifted forms are the more stable ones.

**TABLE 1: Energy Differences (eV) with Respect to the Neutral Normal Form and Charges (me) for Neutral and Negatively Charged A···H−D Complexes. Ph Stands for a Phenyl Group**

| | neutral | | | charged | | | |
|---|---|---|---|---|---|---|---|
| | normal | tautomer | | normal | | tautomer | |
| A/D | $Q_A$ | $\Delta E$ | $Q_D$ | $\Delta E$ | $Q_A$ | $\Delta E$ | $Q_D$ |
| Ur−X | 29 | 1.780 | −866 | −1.711 | −948 | −2.238 | −922 |
| HQ−X | 15 | 1.047 | 59 | −2.305 | −886 | −3.151 | −910 |
| Pyr−X | 25 | 0.932 | −36 | −3.492 | −907 | −3.895 | −920 |
| Pyr−X(F) | 26 | 0.935 | −50 | −3.566 | −901 | −4.074 | −926 |
| 3−Ph−Pyr−X | 29 | 1.524 | −69 | 3.590 | −829 | −3.751 | −991 |
| 6−Ph−Pyr−X | 43 | 1.065 | 62 | −3.538 | −915 | −3.562 | −919 |
| 3−$NH_2$ −Pyr−X | 28 | 1.637 | −30 | −3.513 | −904 | −3.705 | −954 |
| 6−$NH_2$ −Pyr−X | 27 | 1.977 | −872 | −2.860 | −907 | −3.252 | −922 |

In the normal form, after the reception of an electron, a high negative charge appears on the proton acceptor group A (Table 1); in the proton-shifted configuration the negative charge is on D. This means that proton transfer from site D to A induces migration of a negative charge in the opposite direction (CT); although ET has not yet taken place, D has now been activated to yield an electron to the environment, for the ionization potential of $D^-$ is certainly be significantly lower than that of H−D. As explained in the general description of the PA-ET mechanism (above), upon release of an electron from D, the normal nuclear configuration is restored by successive shifts of the H-bond protons *plus* an electron to their original sites, so that an electron is physically transferred from A to D. This "backward" process is expected to be fast, since for the neutral complexes the proton shifted configuration corresponds to a labile minimum of the potential energy hypersurface or, in some cases, to a maximum.

The energy differences between the normal and the proton-shifted configurations of the negatively charged complexes represent the chemical driving forces for CT from A to D. For unsubstituted A−D complexes, computations yield values in the range 0.35−0.8 eV (0.40, 0.53, and 0.85 for Pyr−X, Ur−X and HQ−X, respectively). The driving force for proton switching can be varied by as much as 0.5 eV by introducing suitable substituents at appropriate positions. For instance, substitution of the $C_6$ hydrogen of the pyrimidinol cycle by a phenyl group causes the CT driving force to vanish. The effect is smaller if the same substitution is done at the $C_3$ carbon. On the contrary, substitution of the $N_7$ hydrogen of X, that not involved in the H-bond with A, by fluorine increases the driving force for CT by ca. 0.1 eV. This finding is important, because it suggests that the PA-ET mechanism could be of much wider applicability than implied by the few examples given here.

The ionization potentials of the proton-shifted configurations lie in the range 4−5 eV (4.0, 4.6, and 5.0 for Ur−X, HQ−X, and Pyr−X, respectively, Table 1). The PM3 vertical ionization potential of X in the gas-phase is 10.3 eV, which means that

**TABLE 2: Energy Differences (eV) with Respect to the Neutral Normal Form, Charges (me), and Vertical Ionization Potentials of the Proton Shifted Forms for Negatively Charged A···H−D Complexes with a NMF Bridge. Ph Stands for a Phenyl Group**

| | normal | | intermediate | | tautomer | | |
|---|---|---|---|---|---|---|---|
| A/D | $\Delta E$ | $Q_A$ | $\Delta E$ | $Q_{br}$ | $\Delta E$ | $Q_D$ | IP |
| Ur−X | −1.759 | −939 | −1.639 | −792 | −2.175 | −920 | 4.653 |
| Pyr−X | −4.154 | −942 | −3.740 | −752 | −4.305 | −918 | 5.520 |
| HQ−X | −2.410 | −930 | −2.451 | −804 | −3.098 | −924 | 5.027 |
| HQ−X(F) | −2.494 | −929 | −2.545 | −793 | −3.312 | −928 | 5.706 |
| 6−$NH_2$ −Pyr−X(F) | −3.327 | −939 | −2.831 | −761 | −3.392 | −919 | 5.090 |
| 3−$NH_2$ −Pyr−X(F) | −3.668 | −942 | −3.492 | −785 | −4.032 | −924 | 6.23 |
| 6−Ph−Pyr−X | −3.711 | −948 | −2.894 | −744 | −3.446 | −920 | 5.87 |

the PA-CT process has more than halved the potential energy required for X to release an electron to an external partner. A further energy gain of ca. 1 eV is associated with the restoration of the initial situation by return of H-bond hydrogen atoms from A to D.

**Role of Covalent Bridges.** The above energy analysis applies in its essential lines to all those cases where the A/H−D pairs are connected by a H-bond chain whose building blocks are molecules capable of two nearly degenerate tautomeric forms. This is the case with chains formed by water molecules or hydroxyl groups, as discussed by Nagle and Morowitz,[2] but also amino and carboxylic groups can easily exchange protons in a polarizable H-bond chain, as inferred from the IR spectra of some H-bond chains.[25] Of course, the activation energy for proton hopping depends on the chemical nature of the molecules forming the bridge, but the chemical driving force for CT should not be significantly affected.

Let us now consider the case of an H-bond chain including a covalent bridge, in particular a peptide bond, which, upon proton transfers, will take the higher energy imidol form. The relative energies for the initial, final and intermediate states of the negatively charged A···H−D complexes considered before, but now separated by a peptide bond, are shown in Table 2. The peptide bond has been modeled by *N*-methylformamide (NMF).

In most cases, although the peptide bridge lowers the driving force for CT by roughly 0.2−0.3 eV, the CT process is still exoergonic. The only case for which the CT process is predicted to be endoergonic (ca. 0.3 eV) is when D is the 6-phenyl−pyrimidinol radical, since the phenyl group stabilizes the initial nuclear configurations, with the negative charge localized on A.

The double proton transfer will occur either by a stepwise or a concerted mechanism. The latter is ruled out by the consideration (supported by PM3 estimates) that the concerted motion of both protons would involve the simultaneous crossing of the barrier without any compensating energy change at other structural elements, as might be the case if the two H-bonds involved a common heavy atom. As to the stepwise mechanism, two intermediate configurations are possible, depending on which proton moves first. The configuration corresponding to transfer of the proton from NMF to A turns out to be the lower energy one, as expected on the grounds that it does not require charge separation, as is instead the case with the intermediate state obtained by moving the X proton first.

In certain cases (A = HQ, Ur, 3$NH_2$−Pyr), the driving force for CT after introducing a peptide linkage is high enough to make the lengthening of the proton wire possible by insertion of another peptide linkage.[21] Further increase in the H-bond chain length by suitable amino acid residues, those of tyrosine and aspartic acid, should pose no problem, at least as the energetics of the process is concerned.

## Dynamical Features of the PA-ET Mechanism

We now analyze the kinetic features of the PA-ET mechanism for the two extreme cases of Table 2: A = HQ and A = 6-phenyl−Pyridinol radicals, corresponding to strong and very weak chemical driving force respectively (0.85 and 0.002 eV, respectively, Table 1).

The preceding analysis suggests that the possible rate determing steps are the two proton transfers and the ET step from $D^-$ to the external partner oEA. The last step, the reverse hydrogen transfer, is expected to be much faster, because upon removal of the additional electron, the proton relay chain is in a high-energy nuclear configuration: the neutral proton-shifted configuration is predicted to be ca. 2 eV higher in energy than the initial form (Tables 1 and 2: an estimate of the energy difference between the normal and the proton-shifted form of neutral complexes can be obtained by summing the relative energy and the vertical ionization potential of the negatively charged proton-shifted forms, reported in Table 2).

Since the electron affinity of NMF is lower than that of A, it is not surprising that the first proton transfer should be endoergonic for most A species. This is the case for all the structures studied by us, with the notable exception of $HQ^-$; the latter is a particularly strong proton acceptor because its negative charge is mainly localized on the oxygen to restore ring aromaticity, so that in this case the intermediate state with the negative charge localized on NMF is predicted to be slightly at lower energy than the starting point. The second proton transfer is always exoergonic, because the electron affinity of D is higher than that of NMF; according to our estimates, the energy gained in this step is of the order of 0.5 eV. The rate-determining step should thus be either the first proton transfer or the transfer of the additional electron to oEA. We will not deal with the latter process here, and we will confine ourselves to show that the lifetime of the proton-shifted configurations may be long enough to allow $D^-$ to release an electron to oEA, even in those cases in which it is a high-energy intermediate, as when A is the 6-phenyl−pyrimidinol radical.

In principle, the proton transfer in an H-bond X−H−Y can take place both by thermal activation and by tunneling. In both cases the process involves at least two large amplitude coordinates: the X−H bond and the X···Y distance.[26−30] In fact, the minimum energy path (MEP), the most important path for the thermally activated process, consists, in the transition state region, of the proton motion and approaches the region nearest to the two minima along the X−Y stretching coordinate.[24] The latter is important not only because it decreases the potential energy barrier for proton hopping but because it modulates the distance between the two potential energy minima, and therefore the coupling between the vibrational wave functions associated with proton oscillations in the sites near X and Y.

Thermal activation is not expected to play an important role in proton hopping, since the potential energy barriers are expected to be high, at least of the order of tens of thermal quanta at room temperature.[22] Therefore, we will focus our attention on the Born transition probabilities for proton tunneling. Since we are only interested in orientative estimates of the proton-transfer rates, it will be sufficient to refer to a simple one-dimensional model, taking as the reaction path the "least-motion" path, the straight line joining the two minima associated with the two bound sites of the moving proton. With this choice the effects due to the large amplitude vibration of the two heavy

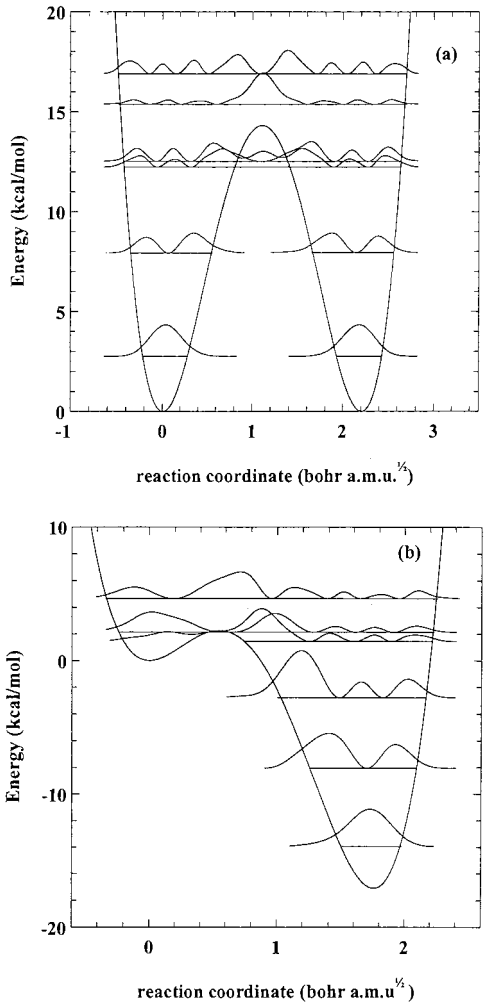



**Figure 1.** Potential energy profile for proton transfer (a) from NMF to HQ and (b) from X to NMF, for the [HQ···NMF···X]$^-$ complex.

atoms is lost, but it can be taken into account by using a statically weighted average of the tunneling probabilities obtained for different values of the X−Y bond distances.

**Potential Energy Profiles.** The potential energy profiles for the shift of the first proton from NMF to A and of the second proton from D to NMF along the least motion path are shown in figures 1a and b, respectively. Both profiles refer to X−Y distances fixed at their equilibrium values (2.77 and 2.73 Å for HQ··· −NMF and NMF··· X, respectively).

The probability that the system, initially prepared in the Boltzmann distribution ($T = 298$ K) of the vibrational states of a harmonic well with the same force constant and equilibrium position of the left-hand ($|L\rangle$) well of Figure 1a, which simulates the single-well potential energy profile expected for the neutral complex, is found after a certain time in any of the vibrational states associated to the right-hand well ($|R\rangle$) is shown in Figure 2a. The maximum probability occurs after ca. 140 ps. This is an upper limit of the interconversion time because of the assumed initial distribution of states and because, as mentioned, the potential energy barriers for proton hopping are certainly overestimated.

Proton switching is triggered by injection of an electron to the left end of the H-bond chain. The electron affinity of HQ is ca. 2.3 eV (Table 1). This energy will be partly spent to extract the electron from the external electron donor oED; the rest will be distributed over the vibrational degrees of freedom of the whole system (oED included), particularly those modes

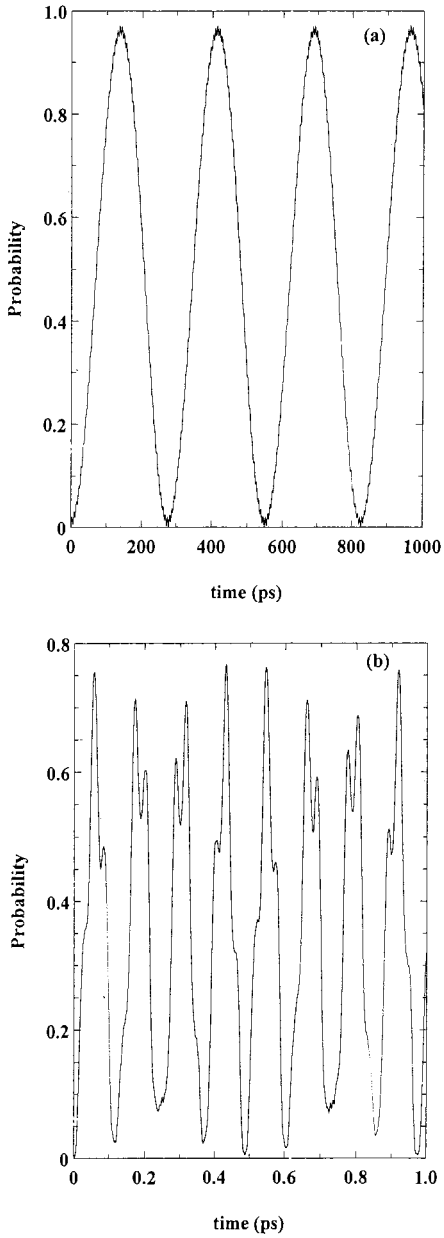



**Figure 2.** Born transition probability for proton transfer (a) from NMF to HQ and (b) from X to NMF, for the [HQ···NMF···X]$^-$ complex.

whose equilibrium positions change as a result of electron rearrangement. Pending further investigations, which for one thing require experimental information, we have assumed that the vibrational energy redistribution (IVR)[26] is faster than proton hopping, so that that the excess energy is removed from the active modes and redistributed on all the vibrational degrees of freedom, particularly on the low frequency modes. This assumption is not fully justified by the computed interconversion times; the nature of the (vibrational) state from which PA-ET begins is therefore a critical piece of information in the discussion of those cases in which tunneling from the ground vibrational state is not possible, see infra.

The second proton transfer, from the xanthine ring to the NMF oxygen, appears to be faster, the transition time being ca. 50 fs (Figure 2b), so that, after the first proton switches its position, the system will rapidly pass in a high excited vibrational state of the final state, from which it may either go back to the intermediate state and begin to oscillate between these two states, or decay to a lower vibrational state, the excess energy being redistributed among the other vibrational degrees

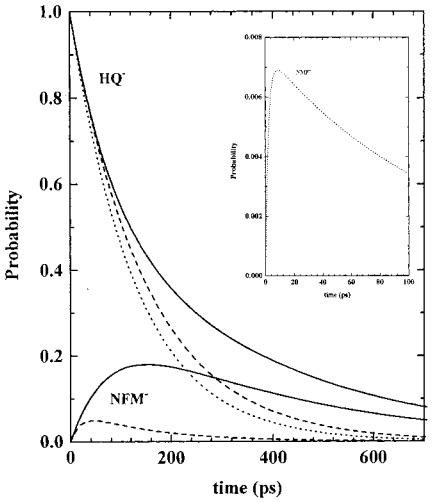



**Figure 3.** Time variation of concentration of the initial [HQ$^-$···NMF···X] and intermediate [HQ···NMF$^-$···X] states, for different values of $k_{ivr}$. Full lines, $k_{ivr} = 1$ ps$^{-1}$; dashed lines, $k_{ivr} = 0.1$ ps$^{-1}$; dotted lines, $k_{ivr} = 0.01$ ps$^{-1}$

of freedom, so that it will be irreversibly trapped in the final state:

$$HQ^-\cdots hp\cdots H-X \overset{k_1}{\rightleftharpoons} HQ-H\cdots p^-\cdots H-X$$

$$HQ-H\cdots p^-\cdots H-X \overset{k_2}{\rightleftharpoons} HQ-H\cdots p-H\cdots X^-*$$

$$HQ-H\cdots p-H\cdots X^-* \xrightarrow{k_{ivr}} HQ-H\cdots p-H\cdots X^-$$

where the star denotes a molecule in a high vibrational state. The decay rate of the initial distribution of states $|HQ^-\rangle$ can be obtained by letting $k_1 = 1/140$, and $k_2 = 1/0.05$ ps$^{-1}$, the reciprocal of the transition times for the first and the second proton transfer respectively, taking the same values for the backward processes, assuming reasonable values for $k_{ivr}$,[31,32] and solving the above set of kinetic equations by standard methods.[33] The results are shown in Figure 3. A half-life of ca. 100 ps is predicted for CT from HQ- to X. The intermediate species HQ−NMF−X is present only at the very beginning of the process, and its survival time depends crucially on the value of $k_{ivr}$, the IVR rate (Figure 3).

Let us now consider the case when A is the 6-phenyl−pyrimidinol radical. In that case the proton-shifted configuration is expected to lie at a higher energy than the initial state. The first proton transfer is endoergonic by 18 kcal/mol, yet the possibility of ET is not ruled out. In fact, as recalled above, the initial state is prepared by injection of an additional electron at the pyridinol side of the neutral H-bond chain. Now, the estimated electron affinity of the pyrimidinol radical is significantly higher than that of HQ (Tables 1 and 2) the difference being well above the estimated proton barrier for the hopping of the first proton. The vibrational component of the initial state, therefore, will be a superposition of highly excited vibrational states of A. A fraction of this energy will be localized on the active modes for proton hopping, in agreement with the computational prediction of a significant change in the equilibrium value of the X···Y distance, which changes from 2.86 to 2.76 Å upon reception of an electron by A. Under the quantum mechanical "sudden approximation" (which, in our case, is analogous to the Franck−Condon principle), this means that the X···Y oscillator is prepared by reduction of A in a state having an expectation value of its vibrational amplitude of ca.

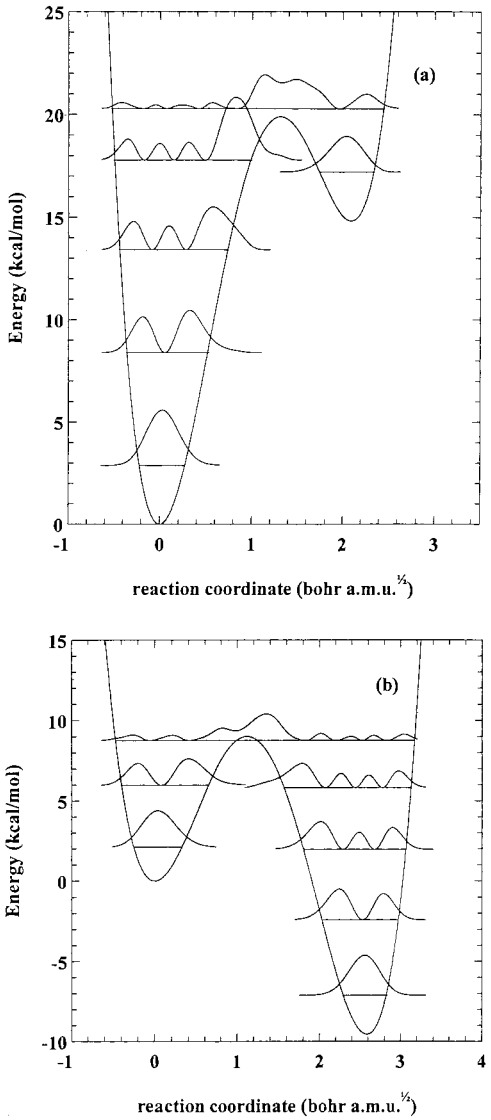



**Figure 4.** Potential energy profile for proton transfer (a) from NMF to 6-ph−Pyr and (b) from X to NMF, for the [6-ph−Pyr···NMF···X]$^-$ complex.

0.2 Å. The potential energy profile for the X···Y distance of 2.66 Å is shown in Figure 4a; the energy needed to cross the potential energy barrier is now 15 kcal/mol. Moreover, evaluation of Franck−Condon integrals, using harmonic approximation and $\nu = 250$ cm$^{-1}$, shows that the initial distribution of vibrational states contains more than 25% of states whose vibrational mean amplitude is higher than 0.25 Å. At a X···Y distance of 2.50 Å, the energy difference between the intermediate and the initial state is only 8 kcal/mol. It is then possible that the internal energy gained by the system upon arrival of an electron from oED is high enough to allow the passage of the first proton from NMF to pyridinol. The second proton transfer should be much easier, the two lowest vibrational states of the intermediate state being nearly degenerate with two excited states of the final form. If the excess energy is now removed from the active modes by thermal redistribution, the system could be trapped there for a sufficiently long time, since the return back to the initial state by tunneling would require the simultaneous motion of both protons and therefore it should be, if not unlikely, at least slower than the first proton transfer in HQ.

## Conclusions

Since Mitchell's initial proposal of proton translocation driven by ET[34] and our suggestion that "polarizable" H-bond chains may function as electron wires,[12] the evidence supporting the notion that proton motion is coupled to long range electron transfer (PA-ET) has rapidly grown,[7,13,35] and it is now believed to be a feature of several energy conversion processes in biosystems. The concrete case study reported above shows that the energy and time requirements for the special mechanism thus introduced are likely to be realized in systems closely resembling redox enzyme substructures. We can thus say that, as far as speculations based on the general theory of structure−property relations in molecules and on quantum-chemical estimates go, the plausibility of PA-ET has been fully proven. In particular, the existence of structures capable of sending an electron to one another via an H-bond−peptide link chain seems to be established, pending ad hoc experimental studies. The above results should be useful not only in attempts to understand selective long-range electron transfer in redox enzymes but also in the design of supramolecular assemblies exhibiting long-lived charge separated states.

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