energy is 1.3 and 0.4 kcal/mol for α and β chains. These values are significant on the scale of the free energy of cooperativity, $\sim$3.4 kcal/mol (heme).[20] But the contribution is of the wrong sign, since the decrease in the Fe–Im bond energy implies a destabilization of the unligated heme in the T state and therefore an increase in the O_2 affinity, if everything else were equal. However, the H-bond effect is expected to be greater for O_2-heme and should outweigh the deoxy contribution. This is because the binding of the π-acid ligand O_2 should increase the polarization of the Fe–Im bond (there is much spectral evidence that the electron distribution in HbO_2 is similar to that in low-spin Fe^{III} hemes[17]) and thereby increase the strength of the N_δ H bond. Model calculations[11] suggest that the H-bond energy scale is more than adequate to support cooperativity. The key determinant is the strength of the H bond in the oxy forms of the R and T states. This could be monitored with ν_{Fe-Im}, but unfortunately, the Fe–Im mode has not yet been located in the RR spectrum of O_2-Hb.

Experimental. Aqueous (2-MeImH)Fe^{II}PP and (1,2-di-MeIm)Fe^{II}PP were prepared by adding an $\sim$3-fold excess of 2-MeImH and sodium dithionite to an aqueous solution ($\sim$1 mM) of hemin chloride. The 2-MeImH and 1,2-diMeIm adducts of Fe^{II}PPDME and OEP were prepared by shaking the porphyrin-iron(III) chloride in benzene with aqueous sodium dithionite (buffered with Na_2HPO_4) containing 2-MeImH or 1,2-diMeIm. (2-MeImH)Fe^{II}OEP ($\sim$2 mM) in dimethylformamide (DMF) was prepared as follows: Fe^{III}OEPCl and an $\sim$5-fold excess of 2-MeImH were dissolved in DMF and the solution was degassed by freeze–thawing in a transparent NMR tube in which Raman spectra were subsequently obtained via the spinning back scattering arrangement.[21] A small excess of solid sodium dithinoite and a small drop of water (for dithionite dissolution) were added to the frozen sample; the tube was evacuated and the sample was thawed under N_2. This complex was deprotonated by refreezing the sample, adding excess solid sodium *tert*-butoxide, sealing the tube under vacuum, and bringing the sample back to room temperature. A precipitate formed (probably sodium dithionite and hydroxide) and was spun to the bottom with a centrifuge. The Raman spectrum was obtained from the overlying solution via backscattering. The absorption spectrum showed peaks at 375, 427 (Soret), 515 (sh), 547 (β), 581 (α) nm compared to 361, 418 (Soret), 500 (sh), 543 (β) 575 (sh) nm for (2-MeImH)Fe^{II}OEP. These spectral shifts are similar to those observed by Mincey and Traylor[14] for the analogous PP complexes (but all PP specta are red-shifted relative to OEP due to the vinyl conjugation). The Raman spectrometer has been described elsewhere.[2]

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Correlation of Kinetic Isotope Effects with Free Energies of Reaction

Sir:

Marcus rate theory[1] provides a particularly useful formalism for correlating rates and equilibria of proton-transfer reactions.[2] Application of the simple theory to kinetic isotope effects, however, leads to an expression which might be interpreted in a way which violates a basic tenet of isotope effect theory. We wish to show

how this difficulty may be overcome.

Marcus theory relates the barrier for a chemical reaction, $\Delta G^{\ddagger}$, to its standard free energy change, ΔG°, through the parameter $\Delta G_0^{\ddagger}$, which is the value of $\Delta G^{\ddagger}$ when $\Delta G^{\circ} = 0$ (eq 1). This

$$\Delta G^{\ddagger} = (1 + \Delta G^{\circ}/4\Delta G_0^{\ddagger})^2 \Delta G_0^{\ddagger} \qquad (1)$$

parameter is therefore a purely kinetic barrier free of any thermodynamic drive or impediment; it is generally called the intrinsic barrier and its magnitude serves to characterize the potential energy surface for a reaction series; i.e., it identifies the series as consisting of inherently slow or inherently fast reactions.[2,3]

An equation relating kinetic isotope effects to ΔG° may be obtained by taking the difference between two Marcus theory expressions of the form of eq 1.[1,2a,4] The assumption that there is no isotope effect on ΔG° ($\Delta G_H^{\circ} = \Delta G_D^{\circ} = \Delta G^{\circ}$, i.e., no equilibrium isotope effect) then leads to eq 2. This expression

$$\Delta G_H^{\ddagger} - \Delta G_D^{\ddagger} = \\ (\Delta G_{0,H}^{\ddagger} - \Delta G_{0,D}^{\ddagger})[1 - (\Delta G^{\circ}/4(\Delta G_{0,H}^{\ddagger}\Delta G_{0,D}^{\ddagger})^{1/2})^2] \qquad (2)$$

predicts a parabolic dependence of the isotope effect $\Delta G_H^{\ddagger} - \Delta G_D^{\ddagger}$ upon ΔG° with a maximum effect, equal to the difference between H- and D-intrinsic barriers, $\Delta G_{0,H}^{\ddagger} - \Delta G_{0,D}^{\ddagger}$, occurring at $\Delta G^{\circ} = 0$. There is now considerable experimental support for such behavior.[4,5]

The fact that this expression contains different intrinsic barriers, however, might be taken to mean that the H and D reactions are intrinsically different in the sense that they occur on different potential energy surfaces. This, of course, is in violation of the fundamental principle upon which isotope effect theory is built, namely, that isotopic substitution does not alter the potential energy of a chemical system (Born–Oppenheimer approximation).[6] These intrinsic barriers as written in eq 2, however, are free energy quantities measured from vibrational energy levels which lie above potential energy minima, and isotopic substitution does alter vibrational energy levels. All of the difference between $\Delta G_{0,H}^{\ddagger}$ and $\Delta G_{0,D}^{\ddagger}$ may therefore be attributed to differences in isotopically sensitive vibrational energy levels situated in the same isotopically-invariant potential energy wells, and the principle of isotopically different reactions occurring on a single potential energy surface may thus be preserved. Unfortunately, it is not clear from the model upon which simple Marcus theory is based why isotopic vibrational energy differences should depend upon ΔG° in the parabolic fashion required by eq 2. Such dependence, however, can be obtained by combining Marcus theory with the Melander–Westheimer principle.[7]

Consider a system in which hydrogen is transferred between two heavy atoms, eq 3. Replacement of H by D will change the

$$A-H + B \rightarrow [A-H-B]^{\ddagger} \rightarrow A + H-B \qquad (3)$$
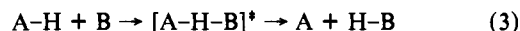
zero-point energy of the transition state of this reaction by an amount $\delta(ZPE)^{\ddagger}$ whose magnitude, according to an idea first put forward by Melander and Westheimer,[7] will vary with the symmetry of the transition state. When the transition state is symmetrical in the sense that the partial bonds holding the atom being transferred are equal, $\delta(ZPE)^{\ddagger}$ will have a minimum value, $\Delta(ZPE)^{\ddagger}_{min}$. As dissymmetry is introduced in the form of reactant-like or product-like character, $\delta(ZPE)^{\ddagger}$ will increase from this minimum value, and, in the limit of a completely reactant-like transition state, it will be equal to the isotopic zero-point energy

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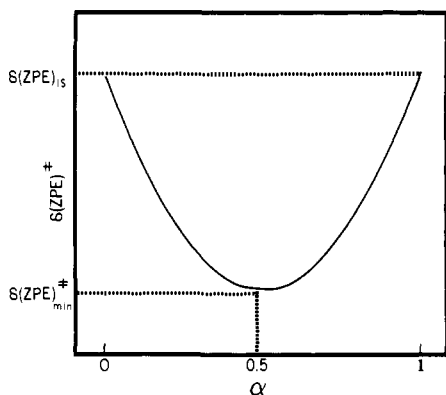
Figure 1. Variation of zero-point energy differences between isotopic transition states, $\delta(ZPE)^{\ddagger}$, with transition-state symmetry, α, in accordance with the Melander–Westheimer principle.

difference of the initial state, $\delta(ZPE)_{IS}$; in the absence of an equilibrium isotope effect, the product-like limit will be the same.

These ideas may be quantified by introducing a parameter α to denote transition-state symmetry: $\alpha = 0$ for a completely reactant-like transition state, $\alpha = {}^{1}/_{2}$ for a symmetrical transition state, and $\alpha = 1$ for a completely product-like transition state.[8] The simplest continuous function relating α and $\delta(ZPE)^{\ddagger}$ consistent with the limits imposed by the Melander–Westheimer principle is then the parabolic one shown in Figure 1 and stated by eq 4.

$$\delta(ZPE)^{\ddagger} = \delta(ZPE)^{\ddagger}_{min} + [\delta(ZPE)_{IS} - \delta(ZPE)^{\ddagger}_{min}](2\alpha - 1)^2 \quad (4)$$

Marcus theory provides an expression for α in terms of ΔG° and $\Delta G_0^{\ddagger}$, eq 5, and insertion of this into eq 4 leads to eq 6. For-

$$\alpha = (1 + \Delta G^{\circ}/4\Delta G_0^{\ddagger})/2 \quad (5)$$

$$\delta(ZPE)^{\ddagger} =$$
$$\delta(ZPE)^{\ddagger}_{min} + [\delta(ZPE)_{IS} - \delta(ZPE^{\ddagger})_{min}](\Delta G^{\circ}/4\Delta G_0^{\ddagger})^2 \quad (6)$$

mulation of the kinetic isotope effect in the usual way as the difference between transition-state and initial-state zero-point energy differences then leads to eq 7.

$$\Delta G_H^{\ddagger} - \Delta G_D^{\ddagger} = \delta(ZPE)^{\ddagger} - \delta(ZPE)_{IS} =$$
$$[\delta(ZPE)^{\ddagger}_{min} - \delta(ZPE)_{IS}][1 - (\Delta G^{\circ}/4\Delta G_0^{\ddagger})^2] \quad (7)$$

Comparison of this expression with eq 2 shows that the two are identical in form. The maximum isotope effect which occurs at $\Delta G^{\circ} = 0$ is now $\delta(ZPE)^{\ddagger}_{min} - \delta(ZPE)_{IS}$ rather than $\Delta G_{0,H}^{\ddagger} - \Delta G_{0,D}^{\ddagger}$ and the quantity $\Delta G_{0,H}^{\ddagger}\Delta G_{0,D}^{\ddagger}$, which governs how rapidly the isotope effect changes with changing ΔG°, is now replaced by a single intrinsic barrier, $\Delta G_0^{\ddagger}$. The presence of only one intrinsic barrier in eq 7 is an advantage in that it avoids any implication that two reaction series which differ only by an isotopic substitution may take place on different potential energy surfaces.

Although this expression was derived from the Melander–Westheimer principle, it is not incompatible with the alternative idea that it is not this principle but rather the tunnel effect which produces isotopic effect maxima at $\Delta G^{\circ} = 0$.[5a] Tunneling, and its influence on isotope effects, is expected to be greatest when $\Delta G^{\circ} = 0$ and to fall off on either side of this value, becoming negligible for systems with reactant-like or product-like transition states.[5a] A parabolic dependence of the tunneling isotope effect on α consistent with this expectation will then lead to a relationship of the same form as eq 7. Such a simple parabolic dependence is, of course, an oversimplification, for the tunnel effect is a complex phenomenon; but the factors which determine isotopic zero-point energy differences are complex as well, and eq 4 must also be an oversimplification. These approximations, however, crude though they may be, do lead to a simple expression which

(8) The parameter α could be the exponent in the Brønsted relation or the order of the forming bond; in simple Marcus theory these two quantities are equal.

allows easy correlation of experimental data.

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Hydroxymercuration of Nonconjugated Dienes in Aqueous Micelles[1]

Sir:

Among the reports of micellar catalysis of organic reactions,[2] there are only a few examples of a micelle partitioning a reaction among a variety of pathways[3] and none have demonstrated a general synthetic utility for selective micellar catalysis. We would like to report preliminary results of our attempts to use an anionic surfactant in aqueous medium to (a) catalyze the mercuration of simple olefins, (b) control the selective monofunctionalization of nonconjugated dienes, and (c) promote effective partitioning of a reaction intermediate into a disfavored manifold, in a predictable and synthetically useful way.

The hydroxymercuration of olefins is a reaction that is compatible with aqueous medium and ambient temperatures.[4] Its products (olefins, alcohols, and ethers) can be readily analyzed, and it is a system of proven synthetic utility.[4b] The standard mercuration procedure, involving $Hg(OAc)_2$ in THF/H_2O,[4a] was modified by replacing the THF with a solution of sodium lauryl sulfate (SLS) at concentrations ≥ 2.5 times its critical micelle concentration. This allowed the conversion of 1-octene to 2-octanol, with both the hydroxymercuration of the olefin and the $NaBH_4$ reduction of the alkylmercurial proceeding smoothly in the micellar medium. The exclusive formation of the Markovnikoff alcohol was comparable to the specificity of the THF/H_2O system. The SLS reaction was somewhat faster than that in THF/H_2O, but no attempt was made to precisely compare rates. Interestingly, the corresponding reaction using a cationic surfactant (hexadecyltrimethylammonium bromide) in place of SLS resulted in almost no reaction, even after extended reaction times. Our observation of the enhanced approach of mercurating agent to olefin in an anionic system and severely retarded reaction with cationic micelles is consistent with a well-precedented Coulombic attraction or repulsion at the micelle surface.[2,5]

We next turned our attention to the hydroxymercuration of nonconjugated dienes. Random attack on two noninteracting

(1) Portions of this work were presented at the International Symposium on Solution Behavior of Surfactants, June 30–July 3, 1980, Potsdam, NY.

(2) An excellent review of the literature on micellar catalysis can be found in: Fendler, J. H.; Fendler, E. J. "Catalysis in Micellar and Macromolecular Systems"; Academic Press: New York, 1975. Two useful recent symposia are: "Micellization, Solubilization and Microemulsions"; Mittal, K. L., Ed.; Plenum: New York, 1977; and "Solution Chemistry of Surfactants"; Mittal, K. L., Ed.; Plenum: New York, 1979.

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