J. Am. Chem. Soc. **1995,** *117,* 2855–2861

The Mechanism of Inner-Hydrogen Migration in Free Base Porphyrin: *Ab Initio* MP2 Calculations

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Received July 26, 1994®

Abstract: *Ab initio* RHF SCF geometry optimizations and MP2 limited geometry optimizations are used to investigate the mechanism of inner-hydrogen migration in free base porphyrin. Previous approximate SCF results using AM1, MNDO, and PM3 methods predict the existence of a highly stable cis isomer close in energy to the most stable trans form and that trans ⇄ trans interconversion proceeds in an asynchronous two-step fashion via this intermediate. However, the calculated activation energies are very much greater than those observed. Here, at the *ab initio* MP2 level of correlation, it is found that all (classical) barriers are substantially reduced in height, becoming compatible with experiment: the trans to cis activation energy is 16.7 kcal/mol, the trans to trans saddle energy is 19.3 kcal/mol, and the relative energy of the cis isomer is 10 kcal/mol. Hence, an asynchronous path remains preferred. The reaction coordinate at small displacements is seen to correlate with the pyrrolic hindered rotation ν_{35}, observed at 109 cm^{-1}; for use in one-dimensional models, we find that the involvement of NH bending and stretching motions in the reaction at large displacements results in a globally optimized effective reactant reaction coordinate frequency of 600 cm^{-1}. Using PM3, zero-point energy considerations are shown to account for just over half of the observed inner-hydrogen isotope effect and to lower the classical activation energy by ca. 5 kcal/mol. The net activation energy is thus estimated to be 12 kcal/mol, no doubt fortuituously close to the value of 13 kcal/mol which has been deduced from experiment using simple tunneling theories.

Introduction

While porphyrins and their derivatives such as chlorins, bacteriochlorins, bacteriochlorophylls, pthalocyanines, etc., form one of the most important groups of chemical systems, the structural properties of the inner hydrogens in the simplest porphyrin, free base porphyrin (FBP), are relatively poorly understood. Experimentally,[1] the trans isomer is known to be the most stable, and no direct evidence of the existence of a cis isomer has been found; if such an isomer exists, its energy is at least 3 kcal/mol above that of the trans form. These and some possible interconnecting structures are sketched in Figure 1. Unfortunately, the crystal structure[1] for FBP is not completely definitive, and as a result there is ambiguity about the identity of the molecular point group for the trans isomer. It is generally believed that this isomer is of high symmetry, D_{2h}, but the possibility that a rapid equilibrium between two low-symmetry C_{2v} structures, in which the two inner hydrogen atoms become inequivalent, cannot be completely discounted. While Raman and infrared data[2-7] suggest that no distortion occurs, Self-Consistent-Field (SCF) Restricted-Hartree–Fock (RHF) theory using both *ab initio*[8] and semiempirical AM1,[2,9,10] MNDO,[10] and PM3[11] methods predict that it should. Unrestricted Hartree–Fock (UHF) theory,[12] however, favors high symmetry, but this result is not significant as a physically unrealistic triplet

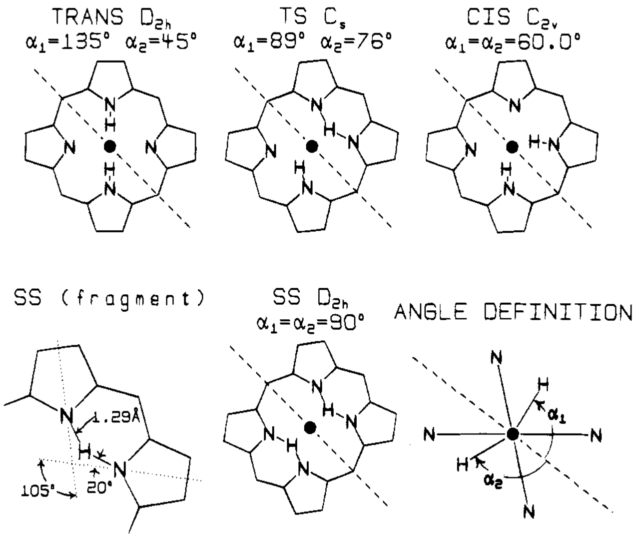

Figure 1. Calculated (planar) structures of the trans, cis, TS (trans ⇄ cis transition state), and SS (second-order saddle point, ie., a hilltop) structures of FBP: the trans, cis, and SS structures are *ab initio* RHF SCF high-symmetry structures, while the TS structure is an MP2-optimized linear combination of these three (15% trans, 24% cis, and 61% SS). The hydrogen locations are described by the angles α_1 and α_2 between the vectors joining the inner hydrogens to the ring center (shown as a solid circle) and the line (shown dotted) which bisects the two vectors joining opposite nitrogens.

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® Abstract published in *Advance ACS Abstracts.* February 15, 1995.

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Table 1. Energies, in kcal/mol, Relative to That of the Trans Structure, As Evaluated by Various Methods at Different Geometries and As Observed[a]

					ab initio SCF RHF			*ab initio* MP2						
	MNDO	AM1	PM3		PM3		SCF	PM3		SCF			observed	
	LS[10]	LS[9]	LS[11]	HS[11]	LS	HS	HS	LS	HS	HS	MP2[b]	MP2[b] + ZPT[c]	raw[14,15]	tunn. calcd[19]
cis	6	7	8	6	11	10	10	10	13	11	10	9	> 3	6
TS	43	35	26		31		31[b]	14			17	12	7−11	13
SS	69	61	45	40	49	47	38	20	25	19	19	9[d]	7−11	

[a] HS are high-symmetry structures, LS are low-symmetry structures. [b] Restricted optimization for the cis and TS structures obtained by forming linear combinations of the *ab initio* SCF HS structures for the trans, cis, and SS isomers. [c] ZPT is the zero-point energy correction evaluated using PM3. [d] The PM3 correction here is too large, see text.

ground state is also predicted. Almlöf *et al.*[8] showed that *ab initio* RHF Møller−Plesset second-order perturbation theory calculations (MP2) for the inclusion of electron correlation predict a D_{2h} structure, as does Local Density Functional (LDF) theory. Recently, Merchán, Ortí, and Roos[13] have verified this result using extensive multiconfigurational SCF and multireference configuration interaction approaches.

Here, we further explore the applicability of MP2 theory to porphyrin systems by considering not just the trans structure, but also possible cis structures and the mechanism for inner-hydrogen migration. This may occur either synchronously, i.e. with there being just one transition state through which the reaction must pass, or asynchronously, i.e. via passage in a first step over a transition state from a trans to a cis isomer, followed by a second reaction to produce the rotated trans isomer. Semiempirical calculations at the RHF SCF level,[9,11] shown in Table 1, clearly predict that the reaction is asynchronous, passing through a cis isomer some 6−8 kcal/mol less stable in energy than that of the trans. Conversion of the trans isomer to the cis proceeds over a transition state (TS) barrier of 25−43 kcal/mol; synchronous trans−trans conversion is inhibited as this must proceed over a second-order saddle point (SS), or hilltop, of energy 45−69 kcal/mol. Experimentally, the barrier height is known to be very much less than this with $\Delta G^{\ddagger}$ being of the order[14−19] of 11 kcal/mol between 200 and 300 K. While earlier estimates interpreted this as arising from an activation entropy $\Delta S^{\ddagger}$ of −14 to −23[15] or −11 to −20[14] (cal mol^{-1})/K and an activation energy $\Delta E^{\ddagger}$ of 10.8 ± 0.8[15] or 7.8 ± 1[14] kcal/mol, later estimates[16,17,19] based on data taken at much lower temperatures include no significant activation entropy with $\Delta E^{\ddagger}$ = 12.9 kcal/mol, and this result is shown in Table 1. Indeed, from experimental evidence, the mechanism is in fact currently believed to be asynchronous (see refs 16−21 and references therein). We seek to determine whether or not *ab initio* MP2 theory predicts much lower barriers than do the semiempirical methods, and whether it predicts a synchronous or an asynchronous mechanism.

Computational Methods

All-electron *ab initio* SCF RHF and MP2 calculations are carried out on a CRAY Y-MP computer using direct schemes as implemented in GAUSSIAN-92.[22] Based on a systematic study of the basis-set dependence of the trans structure by Almlöf *et al.*,[8,23] we use, in their notation, a "DZ (8s4p)/[4s2p]" basis set for carbon, a "DZP (8s4p1d)/[4s2p1d]" basis set for nitrogen, and a "DZP (8s4p)/[4s2p]" basis set for hydrogen,[24] using the specified orbital exponents.[25] This set comprises a total of 330 basis functions. The polarization functions on the carbon atoms are omitted as these atoms are not directly involved in the reaction coordinate; at the RHF SCF level, this omission does not significantly affect the structure of the trans isomer from that obtained using a full DZP basis throughout.[8]

Table 2. *Ab Initio* SCF RHF High-Symmetry Optimized Coordinates, in Å, for the Heavy Atoms and Inner-Hydrogen Atoms in the Trans, Cis, and SS (Second Order Saddle) Structures of Free Base Porphyrin (FBP)

	trans (D_{2h})		cis (C_{2v})		SS (D_{2h})	
atom[a]	*x*	*y*	*y*	*z*	*x*	*y*
C_m	−2.4056	2.4286	0	−3.2552	0	−3.0702
N	0	±2.0437	±1.5561	−1.3606	±1.6681	−1.2239
C_α	−1.0805	±2.8465	±1.2636	−2.6764	±1.2711	−2.5187
C_α	1.0805	±2.8465	±2.8876	−1.2536	±3.0279	−1.1991
C_β	−0.6727	±4.2497	±2.4964	−3.4553	±2.4555	−3.3574
C_β	0.6727	±4.2497	±3.5129	−2.5655	±3.5362	−2.5441
C_m	±2.4056	±2.4286	±3.5605	−0.0207	±3.7216	0
N	±2.0984	0	±1.5786	1.3856	±1.6681	1.2239
H	±1.0968	0	±0.9855	0.5714	±1.2654	0
C_α	±2.8667	−1.1245	±1.2564	2.7036	±1.2711	2.5187
C_α	±2.8667	1.1245	±2.9436	1.2039	±3.0279	1.1991
C_β	±4.2286	−0.6814	±2.5058	3.4205	±2.4555	3.3574
C_β	±4.2286	0.6814	±3.5197	2.5159	±3.5362	2.5441
C_m	2.4056	−2.4286	0	3.2921	0	3.0702

[a] The carbon atoms are designated α, β, and m (*meso*).

Results and Discussion

Geometry optimizations are performed at the SCF RHF level for the trans, cis, and SS structures, constraining the symmetry to D_{2h}, C_{2v}, and D_{2h}, respectively (i.e., all high-symmetry structures in which the two inner hydrogen atoms are symmetry related). The resulting geometries are shown in Table 2 and Figure 1, and energies relative to the trans structure are shown in Table 1. Also shown in Table 1 are the MP2 energies evaluated at these geometries, as are the AM1,[9] MNDO,[10] and PM3[11] energies evaluated at their respective low-symmetry and high-symmetry geometries, and the *ab initio* SCF RHF and MP2 energies evaluated at the PM3 geometries.

Evaluated at the SCF RHF level, the results for the activation energies obtained using *ab initio* and PM3 calculations are

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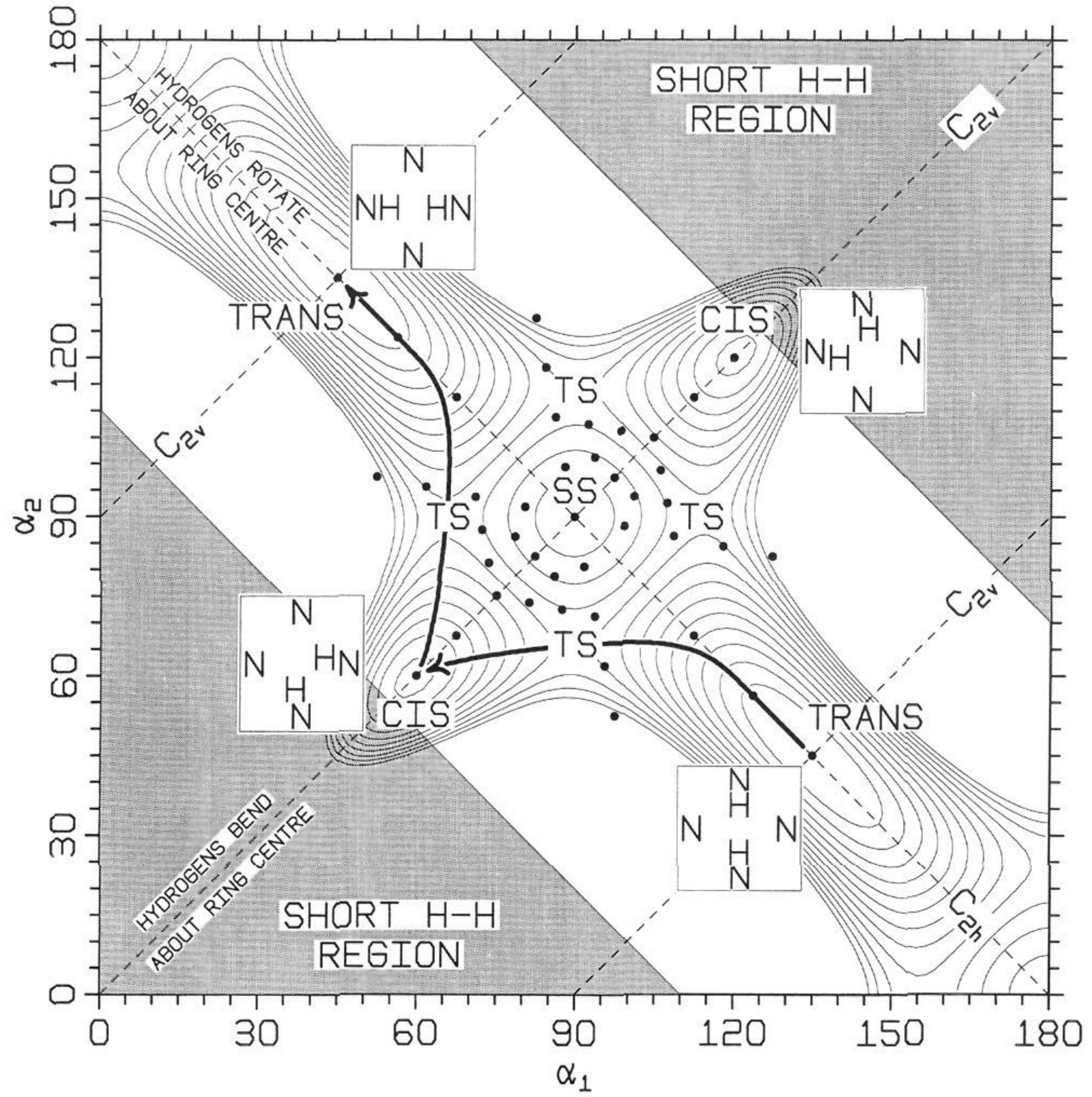

Figure 2. Contours of a six-parameter Fourier-series potential fitted to the calculated SCF RHF energies at geometries linearly interpolated between the calculated SCF RHF cis, trans, and SS structures. The circles indicate the points at which the function is fitted while the shaded regions indicate when the inner-hydrogen H−H separation becomes less than ca. 1.9 Å. The arrows indicate the predicted asynchronous inner-hydrogen rotation pathway over a transition state (TS) estimated to lie at $\alpha_1 = 90°$ and $\alpha_2 = 66°$ of relative energy 31 kcal/mol. Directions in which part of the motion involves the inner-hydrogen atoms either bending or rotating about the ring center are also indicated.

similar, see Table 1. Similarly, MP2 energies evaluated at the geometries obtained by the various SCF methods parallel each other. While symmetry-breaking distortions are predicted at the SCF level for the trans and cis isomers, the energy lowering is reduced from 7.4 and 6.1 kcal/mol, respectively, using PM3 to 1.6 and 1.2 kcal/mol, respectively; the semiempirical method thus shows similar qualitative behavior in these cases, but clearly has an increased tendency to distort. PM3 predicts some distortion for the SS structure, with the energy lowering reduced to only 2.4 kcal/mol, and for this structure it predicts no distortion from D_{2h}.

Inclusion of electron correlation at the MP2 level, however, has a profound effect on the energies of the cis, TS, and SS structures, as it is known[8,13] to have for the trans structure. High-symmetry structures globally become considerably lower in energy than the corresponding low-symmetry structures; for example, at the PM3 geometries, the high-symmetry structures become lower in energy by 16, 13, and 10 kcal/mol for the trans, cis, and SS structures, respectively. Further, as shown in Table 1, the greater is the distortion of the NH bonds, the greater is the relative importance of electron correlation: hence, at PM3 low- and high-symmetry geometries, the relative energies of the TS and SS structures with respect to the trans structures are considerably reduced while the cis energies are slightly increased. This effect is intuitively understandable as the SS and TS structures involve bond rearrangements and hence lower-energy σ excited states.

The above MP2 energies are not evaluated at MP2-optimized geometries, and provide only an approximation. It would be beneficial if MP2-optimized geometries were obtained using a DZP basis set throughout (or one even larger), followed by a normal mode analysis to completely characterize the stationary points thus obtained. Unfortunately, neither operation is feasible given currently available computer resources, but it is possible to perform geometry optimizations at the MP2 level in just two geometric variables. Specifically, we generate the Cartesian coordinates for an arbitrary (planar) configuration of FBP as a (normalized) linear combination of the trans, cis, and SS high-symmetry structures; such structures can be uniquely characterized in terms of the resulting inner-hydrogen orientation angles α_1 and α_2 defined in Figure 1. In terms of these angles, the two trans structures have $\alpha_1 = 45°$, $\alpha_2 = 135°$ and $\alpha_1 = 135°$, $\alpha_2 = 45°$, while the SS structure has $\alpha_1 = \alpha_2 = 90°$, and the two cis structures have $\alpha_1 = \alpha_2 = \Theta$ and $\alpha_1 = \alpha_2 = 180° - \Theta$ for some optimizable variable Θ which is found to be 60.0° at the SCF level. We have evaluated the molecular energy at the SCF RHF and MP2 levels at 15 (unique) points on the α_1–α_2 surface, and the results are given in Figure 1, Figure 2, and, for the (estimated) stationary points, Table 1.

Results obtained for the α_1/α_2 surface at the SCF RHF level are shown in Figure 2. The energies obtained in this fashion are intuitively thought to be more reliable than those that could be obtained by optimizing the geometry at the SCF level at fixed α_1 and α_2, as this would introduce contamination due to

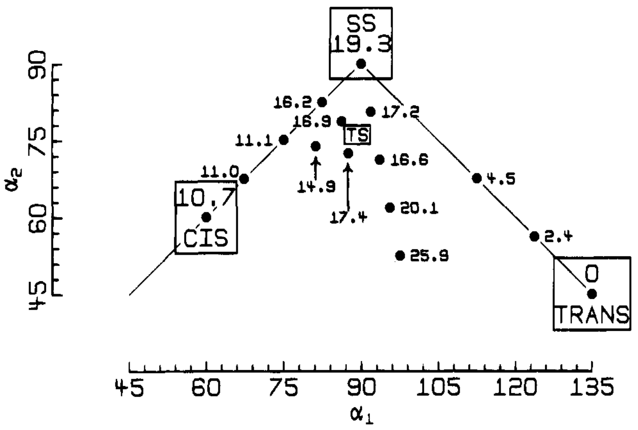

Figure 3. MP2 calculated energies, in kcal/mol, as a function of the inner-hydrogen angles α_1 and α_2 (see Figure 1), in degrees; data are shown in only one of the symmetry-related regions of Figure 2. The transition state (TS) is estimated to be at $\alpha_1 = 89°$ and $\alpha_2 = 76°$ of relative energy 16.7 kcal/mol.

the operation of the forces which cause SCF to distort the trans and cis structures from high symmetry. In Figure 2, the solid circles indicate the points at which the energy is evaluated, but the energy itself is represented schematically as contours of a six-parameter second-order Fourier series best-fit approximation to the raw data. Wells for the trans and cis structures are apparent, as are transition states (TS) linking them and a second-order saddle point (SS). These results are quantitatively similar to those from AM1, MNDO, and PM3, as previously remarked, and an asynchronous trans to trans reaction path, through two different TS structures, is indicated. From interpolation, the TS structures are predicted to have $\alpha_1 = 90°$ and $\alpha_2 = 66°$, very close to the values of 91° and 64°, respectively, obtained using unconstrained PM3 optimization. Also marked on this figure are repulsive regions in which the two hydrogens approach each other by less than ca. 1.9 Å. Arbitrary points on the surface have C_s symmetry; lines on which the symmetry is C_{2h} or C_{2v} are marked, and the points of intersection of these lines have D_{2h} symmetry.

Analogous results obtained using MP2 are shown in Figure 3, but there the discrete energies of the raw data points in just one of the symmetry-related sections of Figure 2 are shown. The MP2 results are not as smooth as the SCF results, and interpolation with simple functions is much more difficult. The changes in shape are most noticeable around the cis well, which is now very flat with steep walls.

At both the SCF and MP2 levels, we see that, for the cis and trans structures in our reduced coordinate space, the reaction coordinates correspond to symmetric or antisymmetric combinations of the two local motions, α_1 and α_2. For the trans structure, the combination $\alpha_2 - \alpha_1$ results in an apparent rotation of the hydrogen atoms (anticlockwise in Figure 1) about the ring center, heading in a path toward the TS and SS structures, see Figure 2, while $\alpha_2 + \alpha_1$ combination produces an apparent bending about the ring center. Frequencies for all structures, estimated crudely using six-parameter second-order Fourier-series potentials fitted to SCF RHF and MP2 energies, are shown in Table 3. Note that, as shown in Figure 2, the effective reaction coordinate at the trans structure has the direction $\alpha_2 - \alpha_1$; this would remain unchanged if the path were to proceed via the SS structure, but at large displacement, it deflects, passing instead over the TS structure. For the trans isomer, the effective reaction coordinate frequency is estimated to be 800 cm^{-1} (SCF) or 600 cm^{-1} (MP2); the MP2 frequency provides a reasonable value for use in any simple one-dimensional model of the inner-hydrogen migration process. These frequencies do not refer to any specific normal mode, but rather to an effective reaction coordinate which is a weighted sum of the normal modes important to the reaction, optimized to describe the surface globally rather than just at the center of the trans well. Specifically, the relative displacements of all atoms involved in our reaction coordinate $\alpha_2 - \alpha_1$ are shown in Figure 4, along with the most important (D_{2h} PM3) normal coordinates of the trans isomer; for FBP, Li and Zgierski[2] have recently detailed the nomenclature used to describe the normal modes and compiled lists of observed in-plane frequencies. The most important normal coordinate is clearly identified to be the hindered pyrrole rotation ν_{35} of b_{1g} symmetry, observed[2] at 109 cm^{-1}; significant involvement is also found for totally-symmetric hindered pyrrole translation ν_8, the asymmetric pyrrole half-ring deformation ν_{22}, the symmetric hydrogen rotation δ_s(NH), and the totally-symmetric stretch ν_s(NH). Qualitatively, this result is expected as the SS and trans structures shown in Figure 1 differ principally by a pyrrole rotation of 15°, a hydrogen rotation of 19°, and a NH bond extension of 0.29 Å. Quantitatively, the PM3-calculated and observed frequencies of these bands are shown in Table 4, as well as the percentage contributions by length and by energy of these normal modes to the effective reaction coordinate. From this table, the true form of the reaction coordinate appropriate in the vicinity of the trans structure is clearly identified as ν_{35} (109 cm^{-1}): it is thus not possible to obtain a qualitatively correct description of the inner-hydrogen migration without explicit consideration of the skeletal modes, as concluded previously by Sarai.[26] While early theories which treated the reaction as simply the breaking of one NH bond and the formation of another (e.g., see refs 15 and 27−31) have been revised and improved (e.g., refs 19−21), one-dimensional models are quite approximate and multidimensional models should be further developed. Globally, the NH stretching motions may be better represented in terms of ring-center to hydrogen coordinates rather than by the normal coordinates of any single isomer. In such a coordinate system, the symmetric and asymmetric stretch frequencies would be expected to be reduced (perhaps to ca. 1800 cm^{-1}) in the TS and SS states but remain real.

Table 3. Vibration Frequencies, in cm^{-1}, for the Effective Modes Spanned by α_1 and α_2 Motion, Crudely Estimated from Second-Order Fourier-Series Potentials Fitted to the Calculated Data Points (see Figures 2 and 3)[a]

	SCF RHF potential		MP2 potential	
isomer	rotate	bend	rotate	bend
trans	800	2000[b]	600[e]	1700[b]
cis	1200	2900[b]	900[c]	2000[b,c]
TS[d]	1300*i*	1600	1300*i*	1400
SS	1000*i*	1500*i*	700*i*	1000*i*

[a] These effective (global) modes overestimate the local frequencies when real and underestimate them when imaginary. [b] The data points do not examine this motion directly and hence the frequency is less reliable. [c] This fit is quite poor for the MP2 cis well in particular. [d] Eigenvectors are local in nature; others are delocalized and produce motions which, ignoring skeletal motions, perceive the inner hydrogens as either *rotating* or *bending* about the ring center, see Figure 2. [e] This effective mode correlates here with the pyrrole hindered rotation ν_{35} of the trans isomer observed[2] at 109 cm^{-1}.

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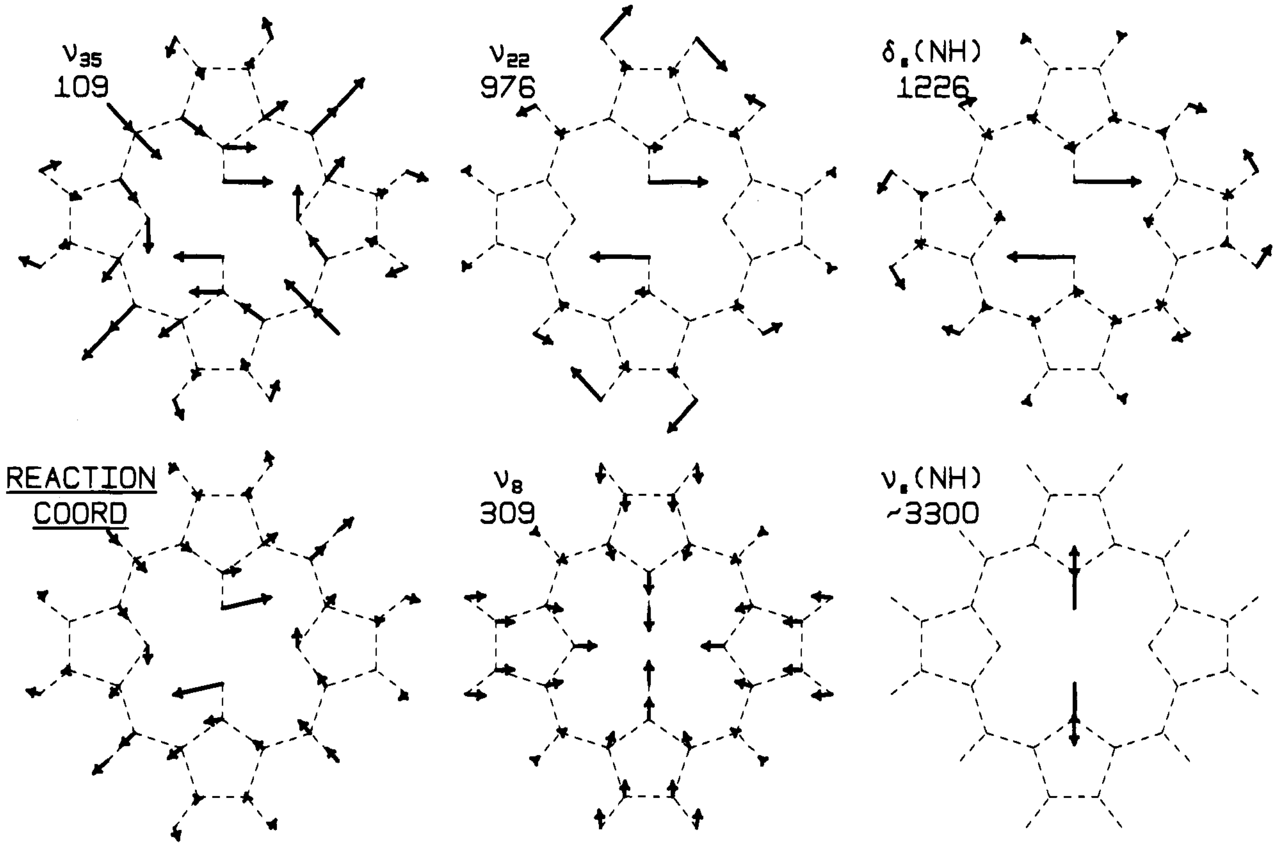

Figure 4. The arrows for the effective reaction coordinate indicate the calculated relative magnitudes of the Cartesian displacements between the trans and SS structures; they are compared to the zero-point-energy-scaled normal coordinates (obtained using PM3 at its D_{2h}-optimized structure) for key pyrrole hindered rotation (ν_{35}), hindered translation (ν_8), half-ring deformation (ν_{22}), hydrogen rotation (δ_s(NH)), and stretch (ν_s(NH)) motions of the trans isomer. Observed[2] vibration frequencies, in cm^{-1}, are also given.

Table 4. Description of the Effective Reaction Coordinate $\alpha_2-\alpha_1$ in Terms of the PM3-Calculated Normal Modes of the Trans Isomer[a]

		frequency/cm^{-1}		percentage contribution	
mode	symmetry	obsd	PM3	coordinate	energy
ν_{35}	b_{1g}	109	123	95.7	75.0
ν_8	a_g	309	325	1.3	2.7
ν_{22}	b_{1g}	976	1036	0.6	3.9
δ_s(NH)	b_{1g}	1226	1252	0.6	5.1
ν_s(NH)	a_g		3284	0.2	4.0

[a] Percentage contributions are given based on the length of the raw mass-weighted normal coordinates and the length scaled by the zero-point displacement so as to reflect the relative contributions to the energy of the effective mode.

Table 5. Lowest Six Singlet (S) or Triplet (T) Eigenvalues (in atomic units) of the SCF Stability Matrix

trans	cis	~TS[a]	SS
0.0815 (T)	−0.0559 (T)	−0.0653 (T)	−0.0609 (T)
−0.0281 (T)	−0.0545 (T)	−0.0470 (T)	−0.0159 (T)
0.0174 (T)	0.0238 (T)	0.0204 (T)	−0.0058 (T)
0.0338 (S)	0.0387 (S)	0.0384 (S)	0.0527 (S)
0.0408 (S)	0.0393 (S)	0.0402 (S)	0.0736 (S)
0.1772 (S)	0.1784 (S)	0.1786 (S)	0.1573 (S)

[a] At the point $\alpha_1 = 87.5°$, $\alpha_2 = 60°$ (relative energy = 17.4 kcal/mol) close to TS.

Quantitatively, our partially optimized MP2 results predict that a cis isomer should exist, lying 10 kcal/mol in energy above the trans isomer; TS and SS structures both remain and are predicted to lie at relative energies of 17 and 19 kcal/mol, respectively, as indicated Figure 3 and Table 1, with an energy difference of 2.7 kcal/mol. While the barrier height is much closer to the raw observed[14,15,32] value of $\Delta E^{\ddagger} = 8-11$ kcal/mol, significant discrepancies appear to remain. These may be interpreted in terms of shortcomings in the MP2 approximation, shortcomings in the implementation of MP2, or quantum effects such as zero-point energy corrections and proton tunnelling; we address these issues in turn.

(i) Precision of the MP2 Method. As mentioned earlier, sharp features are found in the MP2 surface in the vicinity of the cis well. These could arise artefactually if the nature of the SCF orbitals change abruptly, e.g., if a low-symmetry electronic structure produces a lower energy than a high-symmetry electronic structure for a high-symmetry geometry, or if a change in the orbital assignment occurs. The SCF results show none of these features, however, and no artefacts have been found. Also, for all of the points considered, the HOMO and LUMO orbitals remained of π type, and the band gap varies by less than 2%. Another criterion which must be satisfied in order for MP2 to be applicable is that the singlet eigenvalues of the SCF stability matrix must be positive. Almlöf *et al.* have shown that for the trans isomer the lowest triplet eigenvalues are negative, indicating the presence of a triplet instability, while the singlet eigenvalues remain positive, albeit with two rather low eigenvalues indicating that configuration interaction is likely to be important—shown in Table 5 and the lowest six eigenvalues evaluated at the trans, cis, SS, and at the point near the TS at $\alpha_1 = 87.5°$, $\alpha_2 = 60°$ (relative energy 17.4 kcal/mol) indicated in Figure 3. These eigenvalues do not vary significantly as the hydrogen atoms move inside the ring and hence no great variations in the accuracy of the MP2 method are expected.

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(32) Harding, M. J. Ph.D. Thesis, University of Sydney, 1986.

(ii) Implementation of the MP2 Method. In our implementation of the MP2 method, errors may arise from inadequacies in the basis set used, from restriction to planar structures only, and from the restricted geometry optimization procedure. Out-of-plane distortions would be expected to preferentially stabilize the cis structure as this has the shortest H−H bond length, see Figure 2, but even in this case, the inner-hydrogen separation is ca. 2 Å, however, and significant forces are not expected. Note that we find the trans and SS structures to be stable with respect to out-of-plane displacements of the two inner-hydrogen atoms at a fixed geometry for all the other atoms.

Increasing the basis set is likely to stabilize the structures with long NH bonds, thus reducing the energies of the SS and TS structures and hence the difference between theory and experiment. In a full MP2 geometry optimization, the energies for all structures would be lowered. The trans structure and the SS structure appear as fixed points on the $\alpha_1 - \alpha_2$ surface and are not affected by optimization with respect to these variables. As the energy of the SS structure is reduced considerably by configuration interaction, constraint-free optimization of its geometry may further reduce its energy. The optimizations for the cis structure, which is constrained to lie on the $\alpha_1 = \alpha_2$ line, and the TS structure, which may have any value of α_1 and α_2, are in terms of variables α_1 and α_2 which each effect the skeletal deformations, the hydrogen bending, and the NH stretches *uniformly*. A full geometry optimization could significantly lower their energies.

It is conceivable that the classical energy of the SS structure could fall below that for the TS structure, thus changing the nature of the proton migration from an asynchronous process to a synchronous one. This possibility exists because the difference between their energies is just 2.6 kcal/mol, see Figure 3. Note that the location of the TS structure at the MP2 level ($\alpha_1 = 89°$, $\alpha_2 = 76°$) lies between the SS structure ($\alpha_1 = \alpha_2 = 90°$) and the TS structure at the SCF RHF level ($\alpha_1 = 90°$, $\alpha_2 = 66°$), see Figures 2 and 3; the two structures thus become more similar as a result of electron correlation, and indeed the TS and SS structures sketched in Figure 1 clearly are closely related.

(iii) Zero-Point Energy Corrections. A significant correction to the barrier energy arises from the change in the quantum zero-point energy of the reactant and transition states.[33] By performing a full MP2 geometry optimization and vibrational analysis, this correction could be calculated explicitly, but this is not currently feasible at the *ab initio* MP2 level. We proceed first by evaluating zero-point corrections using PM3-calculated structures and (positive) frequencies and second by considering the contributions, presumed dominant, from the six modes associated with inner-hydrogen motion using both PM3 and *ab initio* MP2 methods.

PM3 predicts that the zero-point energy of the TS state is less than that of the trans isomer by 5 kcal/mol; applying this correction to the MP2 activation energy produces an estimated barrier of just 12 kcal/mol, close to the observed values shown in Table 1. Similarly, PM3 predicts a lowering of just 1 kcal/mol for the relative energy of the cis isomer.

For many chemical reactions,[33] the total zero-point contribution to the activation energy can be approximated by considering just the reaction coordinate, whose real frequency component is reduced to zero in the transition state. Using either the true reaction coordinate frequency of 109 cm^{-1} or our effective mode frequency of 600 cm^{-1} produces a contribution of only 1−2 kcal/mol to the zero-point energy lowering. For FBP, it is essential to consider explicitly the contributions from all six vibrations involving inner-hydrogen motion. From the PM3 results, we evaluate this contribution to be 4 kcal/mol, or 80% of the value obtained using all modes. It may be directly measured experimentally by replacing the inner-hydrogen atoms with deuterium atoms. This results in an increase in the raw observed[15,31,32] activation energy increase of 2.1 kcal/mol, considerably larger than the value of 1.2 kcal/mol which we calculate using PM3. If the reaction mechanism were synchronous rather than asynchronous, than this would be increased by 0.6 kcal/mol, still falling short of the experimental value. While more accurate calculations are clearly required, this suggests that, *independent*[31] of whether the mechanism is synchronous or asynchronous, zero-point energy changes are not of sufficient magnitude to describe the entire observed hydrogen isotope effect: this implies that some part of the shift must be attributable to quantum mechanical tunneling effects, and this is pursued further in the following subsection. Indeed, the most-recent[19] interpretations of the hydrogen isotope effect attribute ca. 1.7 kcal/mol of the observed 2.1 kcal/mol to tunneling corrections, leaving an intrinsic activation energy of just 0.45 kcal/mol which is somewhat *less* than the PM3 value.

To further check the accuracy of the above PM3 results, we performed some *ab initio* MP2 single-point calculations, each with a displacement of only the inner-hydrogen atoms from each of the *ab initio* SCF high-symmetry trans and SS structures. This results in a calculated zero-point energy change between these structures for the four preserved inner-hydrogen vibrations of 5 kcal/mol; from Table 3, the calculated zero-point energy change for α_1 and α_2 motions between the trans and TS states is 1.3 kcal/mol, but the use of data for SS rather than TS for the other four modes would probably overestimate the change by at least 1 kcal/mol. We thus estimate from these MP2 calculations that the inner hydrogens contribute 5 kcal/mol to the zero-point energy lowering, 1 kcal/mol greater than the value calculated (using a complete force field analysis) by PM3. Qualitatively, the same picture remains, however. Indeed, as the PM3 frequencies for the trans isomer (and, by implication, for all structures) are on average ca. 10% greater than those observed, PM3 would intuitively be thought to overestimate slightly the zero-point energy contribution. More significantly, the PM3 results could be in error by up to say 2 kcal/mol, as contributions from the modes of imaginary frequency are not included.

We also evaluated the zero-point energy correction using PM3 for the SS structure and obtained the value of 10 kcal/mol, thereby adjusting the MP2 calculated relative energy from 19 to 9 kcal/mol as shown in Table 1. If this result is reliable, then it would predict that the lowest quantum energy level at the SS structure would be less than that of the TS structure: i.e., classically, the reaction would be asynchronous, but quantum-mechanically the reaction would be extremely complicated, following both classically synchronous and asynchronous paths. In kinetics models (e.g., refs 20 and 21), such complexity is not usually postulated, however. As PM3 considerably overestimates the energy of the SS structure, and as it predicts[11] a TS structure with a fully intact NH bond, the calculated difference in zero-point energy between the TS and SS structures will be considerably overestimated by PM3, and this prediction is thus presumably incorrect. Using the calculated MP2 frequency of 1400 cm^{-1} for TS, see Table 3, the SS structure is expected to have a zero-point energy only at most 2 kcal/mol less than that of the trans structure. While this lowering is less than that required to change the nature of the reaction mechanism, a rather complicated picture still remains.

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In summary, we believe that, given all of the approximations used in the *ab initio* calculations, as well as the use of PM3 to evaluate vibrational frequencies, the calculated activation energy can be considered to be within range of the experimental value. Hence, based on these activation energy calculations alone, we cannot comment on the possible importance of tunneling contributions. The hydrogen isotope effect is, however, calculable with greater precision using PM3 and *ab initio* MP2 estimates: these results indicate that tunneling must have some influence.

(iv) Proton Tunneling. Early suggestions that proton tunneling is important, effectively reducing the observed activation energy, *inter alia*, were made by Henning and Limbach (see refs 18, 27, and 28 and references therein) and Stilbs and Moseley.[29,30] Initially, this was envisaged to arise through interactions between quantized NH stretching motions within in the various potential wells. Some key signatures of the tunneling have not been found in some or all of the different substituted porphyrins considered (eg., see[14,15,34]), however, but their absence does not necessarily eliminate the possibility that tunneling does indeed occur.[33] Certainly, the observation that the inner-hydrogen migration does not change in nature due to asymmetric substitution[14] is strong evidence suggesting that direct trans to trans tunneling is not a major factor. Based on the conclusion that large skeletal deformations are intricately involved in the migration, Sarai[26,35] has argued that tunneling would be impeded as the skeletal motions would limit the coherence of the proton motion. Indeed, our calculated structures shown in Figure 1 do show large skeletal deformations at the TS and SS structures, as deduced by Sarai, and our calculations of the zero-point energy contribution to the activation energy and hydrogen isotope effect indicate that tunneling can only have a small effect, much less than is often observed[33] in other situations. Using more sophisticated calculational methods, Smedarchina, Siebrand, and Wildman[20] have shown that synchronous tunneling could not account for non-Arrhenius kinetics, when observed, but that asynchronous tunneling could indeed account for it. Recently, evidence supporting the involvement of weak tunneling in an asynchronous pathway has been found from studies of oxalimidines,[36] substituted porphyrins,[17,18] and FBP at low temperatures in polycrystaline solids[19] and Shpol'skii matrices,[16,21] as well as from the most recent tunneling calculations;[37,38] a similar mechanism is also proposed[39] for inner-hydrogen migration in the lowest excited triplet state of FBP.

Based on asynchronous tunneling models,[19-21] values for the relative energy of the cis isomer, the height of the TS barrier, and the TS imaginary frequency have been extracted from experimentally observed temperature dependences of the rate constant. The most recent value shown in Table 1 for the relative energy of the cis isomer[19] is 6 kcal/mol, close to our calculated zero-point corrected value of 9 kcal/mol; for the activation energy, the estimate[19] is 13 kcal/mol, again close to our zero-point corrected value of 12 kcal/mol; the estimated barrier frequency[21] is 1800 ± 400*i* cm^{-1}, compatible with our calculated underestimate of 1400*i* cm^{-1} shown in Table 3. These MP2 results thus support the results obtained from models which assume that the inner-hydrogen migration proceeds via an asynchronous pathway, aided somewhat by quantum mechanical tunneling effects.

Conclusion

The *ab initio* prediction of the experimental rate constant for the inner-hydrogen migration process, as a function of temperature, requires not only calculation of an accurate potential energy surface but also detailed vibrational analyses, the completion of a full RRKM analysis, and sophisticated (e.g., refs 20, 37, 38, and 40) quantum tunneling calculations which should include a large number of vibrational modes. Results for the potential energy surface indicate that our constrained MP2 approach predicts properties in agreement with the best-available interpretations of the raw experimental data. This is in contrast to predictions made using either *ab initio* SCF or semiempirical SCF methods which, while providing a qualitatively similar picture, considerably overestimate the activation energies involved. Our results tentatively confirm a classically asynchronous mechanism for the inner-hydrogen migration. We also find that zero-point energy considerations provide important contributions to the activation energies, and that they alone are insufficient to account for *all* of the observed inner-hydrogen isotope effect, implying that tunneling indeed is involved to some extent in the reaction mechanism. They may also make the quantum energy difference between synchronous and asynchronous paths quite small, suggesting that the reaction kinetics may be very complicated indeed.

While *ab initio* MP2 calculations do promise to lead to full characterization of the inner-hydrogen migration, they are extremely computationally intensive, and it would also be of interest to determine the structure predicted using the PM3 RHF SCF combined with a MP2 calculation performed using PM3 integrals. This would be significantly more computationally efficient and may lead to accurate energies for the various isomers with the distinct possibility of the feasible evaluation of vibrational force fields. Alternatively, LDF calculations may provide a computationally efficient route. This method is known[8] to produce a high-symmetry structure for the trans isomer so that zero-point energy calculations obtained using this method are likely to be more accurate than those obtained using PM3. It is interesting to note from Table 1 that, even compared to *ab initio* MP2 results, the relative energies of the various low-symmetry PM3 isomers appear reasonably well represented. Also, except for the variables in which symmetry lowering occurs, the geometries are also in good agreement. Hence, this very simple method may be useful for estimating the relative energies of complex structures such as oligoporphyrin dimers, tetramers, octamers, etc.,[11,41,42] for which meaningful *ab initio* calculations, even at the SCF level, are prohibitive.

Acknowledgment. We are indebted to the Cooperative Research Centre for Molecular Engineering and Sensor Technology (Sydney) for funding of this project and for the CSIRO supercomputer facility for the provision of computer resources; M.J.C. and J.R.R. gratefully acknowledge support from the Australian Research Council.

Registry Number supplied by author: free base porphyrin (FBP), 101-60-0.

JA9424538

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