Porphyrin Isomers: Geometry, Tautomerism, Geometrical Isomerism, and Stability

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Density functional calculations have been carried out on free-base porphyrin (**1**) and its seven possible isomers (**2**−**8**) with an N_4-metal coordination core. A total of 27 structures resulting from geometrical isomerism ((*E*/*Z*)-configurations) and NH tautomerism were studied. Geometries were fully optimized with the nonlocal density functional approximation (BLYP) using the 3-21G and 6-31G** basis sets. The calculated geometries compare favorably with the available X-ray crystal structures. Porphycene (**2**) is predicted to be the most stable among the eight isomers and is about 2 kcal/mol more stable than porphyrin due to its exceptionally strong hydrogen bonding. Compounds **5**−**8** are much less stable than porphyrin due to severe ring strain in these compounds. When a -$(CH)_n$- linker is in a (*Z*)-configuration, each compound is planar or nearly planar with significant π-delocalization; the corresponding (*E*)-configured structures are predicted to be somewhat distorted into bowl-like geometries in order to avoid severe steric interactions involving the inner hydrogens.

Introduction

The fascinating structures of naturally occurring porphyrins and metalloporphyrins have been perfected by nature to give functional dyes *par excellence*.[1] The important roles these tetrapyrrolic macrocycles play in vital biological processes, in particular photosynthesis (chlorophyll), oxygen transport (hemoglobin), and oxygen activation (cytochrome), have led to their characterization as "Pigments of Life".[1c] Because porphyrins possess extended π-electron systems and exhibit high stability, they are finding use, to an increasing extent, in advanced materials as components in organic metals, molecular wires, and other devices.[2] In medicine, porphyrins are experiencing a renaissance due to the advent of photodynamic therapy of great promise in the treatment of cancer and dermatological diseases.[3] The interdisciplinary interest porphyrins thus generate has provided the impetus to develop novel porphyrin-like molecules anticipated to exhibit special properties, by structural variation of the tetrapyrrolic macrocycle while maintaining a $(4n + 2)\pi$ main conjugation pathway. As evidenced by the host of expanded,[4,5] reshuffled,[6] inverted,[7] contracted,[8] and otherwise modified porphyrins[9] brought to light in recent years, the pursuit of this concept has proven to be highly successful.

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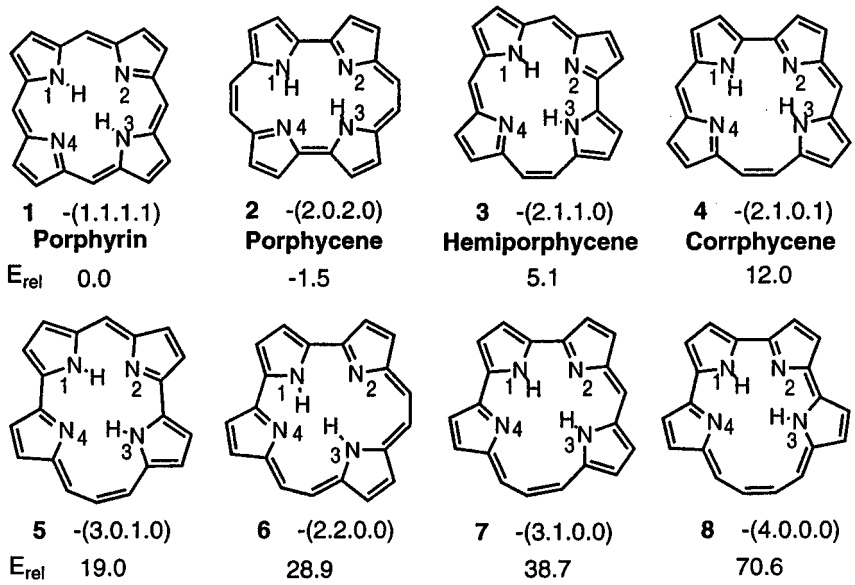

Figure 1. Porphyrin and its seven (*Z*)-configured constitutional isomers with an N_4-core metal-coordination center. The calculated relative energies (kcal/mol) by the BLYP/6-31G**//BLYP/3-21G are also shown (the formulae represent the most stable NH tautomer in each case).

One of the salient porphyrin structural variants is porphycene,[10,11] **2**, a brilliantly blue pigment with strongly reddish fluorescence. The synthesis of porphycene in 1986 marks the beginning of a new avenue of research in the porphyrin realm, since this molecule is the first and major representative of an entire family of cyclotetrapyrroles: the porphyrin isomers possessing an N_4 coordination site.[12] Shown in Figure 1 are porphyrin and its seven possible isomers which have four pyrrole nitrogen atoms arranged to coordinate a central metal ion. These isomers are referred to as porphyrins-(A.B.C.D).[6] They differ formally by the arrangement of the four methine units linking the pyrroles. The letters A−D denote the number of methines between adjacent pyrrole units. Recently, the syntheses of compounds **3** (hemiporphycene) and **4** (corrphycene) as octaethyl derivatives were reported.[11d,13,14] The X-ray crystal structures and NMR spectra indicate that, just like porphyrin, compounds **2**−**4** are all planar and aromatic. They all possess the ability to bind metal ions, and their redox properties are similar to those of porphyrin.[13,14] The synthesis of **5**−**8** is an obvious goal; whether the synthesis of these compounds can be achieved largely depends on their stability.

In view of potential practical applications of porphyrin structural variants in areas ranging from medicine to material science, theoretical understanding of the geometries and electronic and optical properties of such compounds is of great importance.[15] So far, theoretical investigations have mainly been focused on parent porphyrin (**1**). First calculations involved semiempirical quantum mechanical methods[16] and low levels of the Hartree−Fock method.[17] More recently, density func-

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tional methods and high levels of ab initio calculations including MP2 correlation energy have been applied to porphyrins and related systems.[18−20] Recent studies include calculation of the ground-state geometry and tautomerization of free-base porphyrin,[18] electronic spectra of both free-base and metalloporphyrins and porphyrin homologues,[19] and substituent effects on the electronic structures of free-base and metalloporphyrins.[20] Molecular mechanics force-fields have also been developed for the porphyrin system.[21]

By contrast, porphyrin isomers have not been studied much theoretically. Waluk and Michl used semiempirical CNDO/S, INDO/S, and PPP methods to explore the electronic structures of both free-base and metalloporphycenes.[22] These authors also used a perturbation molecular orbital perimeter model to analyze the electronic structures of porphyrin and its isomers (**1**−**8**). In that study, no geometrical optimizations were carried out.[23]

In this paper, we report a detailed theoretical study of porphyrin and its isomers (**1**−**8**) using nonlocal density functional theory.[24] The geometrical features of these compounds were calculated, and these were found to compare favorably with X-ray crystal structures of the compounds known. NH tautomerism and (*E*)/(*Z*)-geometrical isomerism were studied, and the influence of these changes on energy was analyzed. The relative stabilities of 27 tautomers and (*E*)/(*Z*)-geometrical isomers of porphyrin and its isomers were predicted. The results provide a guide to the porphyrin isomers which should be amenable to synthesis and to the geometrical features these molecules are predicted to possess.

Table 1. Calculated Total Energies (au) of Structures of Porphyrin and Porphyrin Isomers

structure	PM3	BLYP/ 3-21G	BLYP/ 6-31G**//3-21G	BLYP/ 6-31G**
9	0.269 28	−983.719 22	−989.201 06	−989.203 42
10	0.281 09	−983.710 23	−989.188 78	−989.170 60
11	0.372 57	−983.700 18	−989.170 60	−989.172 75
12	0.272 04	−983.729 10	−989.203 47	−989.206 67
13	0.294 56	−983.727 48	−989.200 49	−989.203 48
14	0.346 57	−983.726 55	−989.197 22	−989.198 85
15	0.288 93	−983.715 18	−989.192 92	−989.196 20
16	0.283 02	−983.713 93	−989.191 81	−989.195 14
17	0.289 89	−983.711 40	−989.186 90	−989.190 40
18	0.290 98	−983.710 14	−989.185 67	−989.188 95
19		−983.650 91	−989.138 66	
20	0.302 65	−983.700 04	−989.181 96	−989.184 63
21	0.310 63	−983.649 22	−989.173 93	−989.177 36
22	0.307 82	−983.693 88	−989.173 11	−989.176 20
23	0.317 18	−983.674 43	−989.155 25	
24	0.320 43	−983.671 39	−989.150 33	
25	0.306 84	−983.691 05	−989.170 76	
26	0.308 91	−983.674 19	−989.159 26	
27	0.329 19	−983.668 56	−989.155 02	
28	0.322 39	−989.663 25	−989.152 25	
29	0.332 54	−983.651 25	−989.139 40	
30	0.329 22	−983.646 85	−989.137 18	
31	0.316 78	−983.668 83	−989.154 02	
32	0.315 76	−983.666 68	−989.152 60	
33	0.355 09	−983.593 91	−989.088 59	
34	0.325 61	−983.651 78	−989.140 89	
35	0.324 74	−983.650 52	−989.139 85	

Method of Calculation

All calculations were performed with Pople's Gaussian 92/DFT program.[25] The nonlocal density functional approximation with Becke 88 exchange[26] and Lee−Yang−Parr correlation[27] functionals (BLYP) was used. For compounds **1**−**4**, geometries were optimized with the 3-21G and 6-31G** basis sets, respectively. For compounds **5**−**8**, geometries were optimized only with the 3-21G basis set. Energies were evaluated with the 6-31G** basis set on the 3-21G geometries. As demonstrated for compounds **1**−**4**, this method gives quite accurate relative energies. For comparison, the semiempirical PM3 method[28] was also used to optimize the structures. The calculated total energies of a total of 27 structures are collected in Table 1.

Results and Discussion

The porphyrin isomers **2**−**8** derive from porphyrin by reorganization of the ring skeleton, a type of constitutional isomerism. Two types of isomerism do not affect the connectivity of the molecules. The first is the (*Z*)/(*E*)-geometrical isomerism involving a cis (*Z*)/trans (*E*) configurational change of the -$(CH)_n$- linkage, when *n* is 2 or more. The second is the tautomerism involving the shifts of the N−H hydrogen atoms. We first describe the isomers which were calculated, and then discuss various

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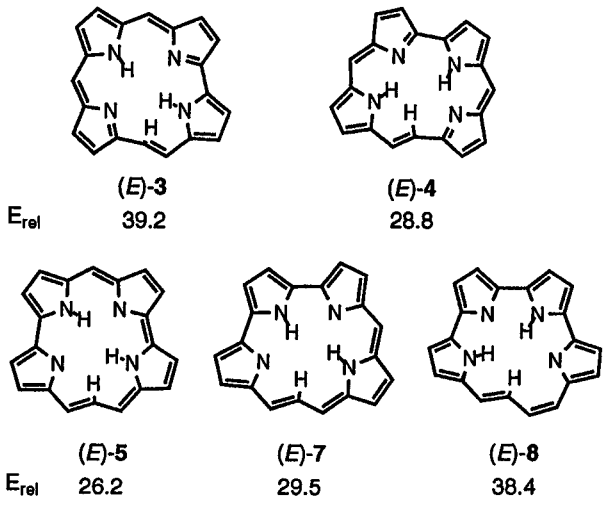
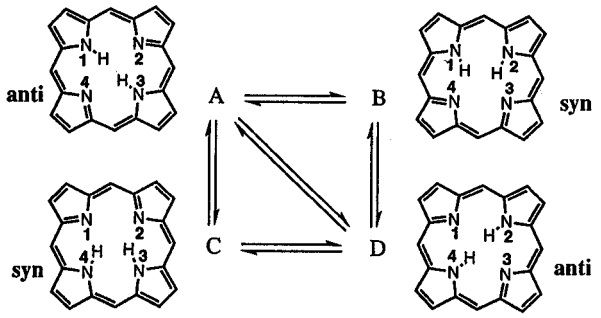


Figure 2. (*E*)-Configured porphyrin isomers and their relative energies (kcal/mol) with respect to porphyrin calculated by the BLYP/6-31G**//BLYP/3-21G method.

Scheme 1



computational methods, and then describe the geometry and energy patterns discovered in these calculations.

Geometrical Isomers. The (*Z*)/(*E*)-isomerism causes considerable geometrical change, as shown by comparing Figures 1 and 2. It especially affects the metal-binding properties of the ligand. Due to severe geometrical constraints, the formation of an (*E*)-double bond in **2** and **6** can be excluded. The (*E*)-isomer of corrphycene **4**, on the other hand, is conceivable, although attempts to synthesize (*E*)-corrphycene have failed so far, giving macrocyclic octapyrroles instead.[29] The (*E*)-isomer of hemiporphycene **3** is also possible. For compounds **5**, **7**, and **8**, the (*Z*)/(*E*)-isomerism should be more feasible because of the longer -$(CH)_n$- linkages in them.[30]

Syn and Anti Isomers. The N−H tautomerism of porphyrin has been studied most extensively. Experimentally, the D_{2h} anti tautomer[31] (Scheme 1) is found to be most stable.[32−35] There is rapid interconversion between the two anti tautomers, and the rate of exchange is sensitive to both temperature and isotopic substitution.[36−41] Two pathways for tautomerization are possible, as shown in Scheme 1. Tautomerization may pass through a symmetrically doubly bridged transition state in a one-step process or may occur as a two-step process with a syn tautomer[31] as an intermediate. Although the syn tautomer has not been observed directly, recent experiments with various substituted porphyrins give kinetics most consistent with the stepwise mechanism.[38]

Two theoretical calculations have been reported recently concerning the tautomerism of porphyrin. Ghosh and Almlöf optimized the syn tautomer of porphyrin using local density functional theory and found that it is about 7.6 kcal/mol less stable than the anti tautomer.[18b] Reimers et al. optimized the anti, syn, and bridged structures using the Hartree−Fock method; MP2 single-point energy evaluations predict the syn and the symmetrically bridged structures to be 10 and 19 kcal/mol, respectively, above the anti structure.[18c] The barrier for the stepwise mechanism was estimated as 12 kcal/mol, which is close to the experimental tautomerization barrier of 11−13 kcal/mol.[38,41]

Anti and syn tautomers and a symmetrically bridged structure were calculated for porphyrin (**1**) and porphycene (**2**), and these are shown as **9**−**11** and **12**−**14** in Figures3 and 4, respectively. The lowering of symmetry in hemiporphycene (**3**) makes all four nitrogen sites different. Therefore, a total of six tautomers is possible for the (*Z*)-isomer in this case. We only considered the two possible anti tautomers (**15**−**16**) and two of the four possible syn tautomers (**17**−**18**), as given in Figure 5. The other two syn tautomers with the two hydrogens attached on N_1 and N_2 or N_3 and N_4 (for numbering, see Figure 1) could be ignored, as they would have very short inner hydrogen distances and severe steric repulsions. The anti tautomer **19** of (*E*)-hemiporphycene was also calculated. For corrphycene (**4**), one anti and two syn tau-

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(30) For simplicity, throughout the paper, the configurational isomers in Figure 1 are referred to as (*Z*)-isomers and the isomers in Figure 2 are referred to as (*E*)-isomers, although more proper designation for **5**, **7**, and **8** in Figure 1 and Figure 2 should be (*Z*,*Z*)-**5**, (*Z*,*Z*)-**7**, (*Z*,*Z*,*Z*)-**8** and (*E*,*E*)-**5**, (*E*,*E*)-**7** and (*Z*,*E*,*E*)-**8**, respectively.

(31) In this paper, a tautomer is referred to as anti when the two NH groups are separated and syn when the two NH groups are adjacent (as shown in Scheme 1). In the literature, these tautomers have been referred to as trans and cis, respectively. The current nomenclature is adopted in order to avoid confusion with cis (*Z*)/trans (*E*) configurational isomerism.

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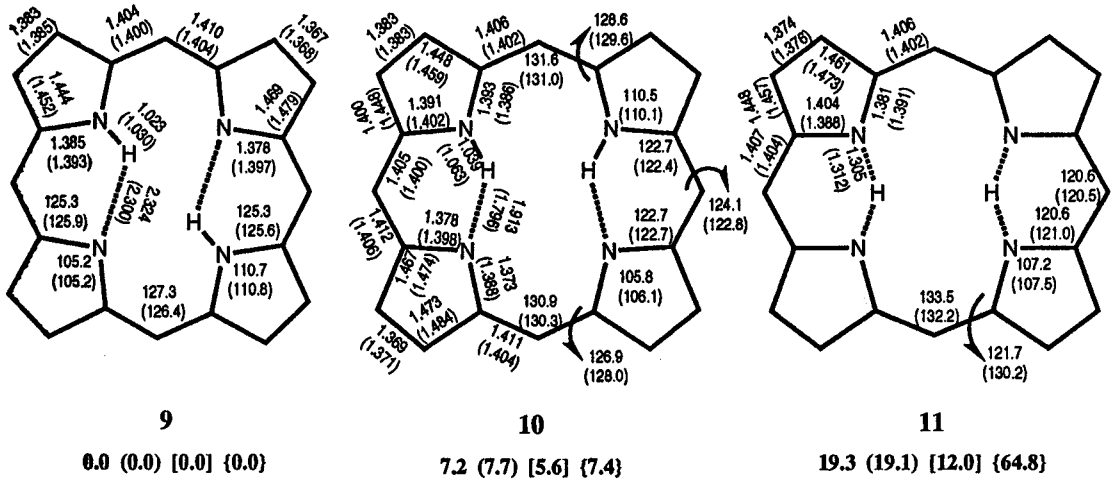

Figure 3. Calculated BLYP/3-21G (in parentheses) and BLYP/6-31G** geometries of anti (**9**), syn (**10**), and symmetrically bridged (**11**) structures of free-base porphyrin. The bond lengths are in angstroms and the bond angles are in degrees. The bond lengths and angles in the X-ray crystal structure of free-base porphyrin are $C_\alpha-N$ 1.380 (1.376), $C_\alpha-C_\beta$ 1.431 (1.452), $C_\beta-C_\beta$ 1.365 (1.345), $C_\alpha-C_{meso}$ 1.387 (1.376), $N-C_\alpha-C_\beta$ 108° (110°), $C_\alpha-N-C_\alpha$ 108° (106°), $N-C_\alpha-C_{meso}$ 125° (126°), and $C_\alpha-C_{meso}-C_\alpha$ 127°. The values in the parentheses are for pyrroles whose N atoms are not protonated. Relative energies are in the order BLYP/6-31G**, (BLYP/6-31G**//BLYP/3-21G), [BLYP/3-21G], and {UHF/PM3}.

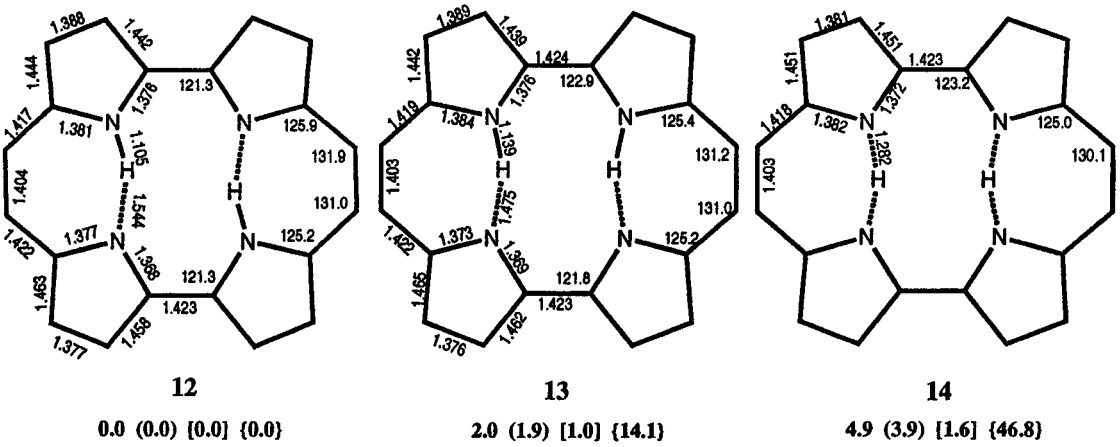

Figure 4. Calculated BLYP/6-31G** geometries of anti (**12**), syn (**13**), and symmetrically bridged (**14**) structures of the free-base porphycene. The average bond lengths from the X-ray crystal structure of porphycene are $C_\alpha-N$ 1.358, $C_\alpha-C_\beta$ 1.433, $C_\beta-C_\beta$ 1.348, $C_\alpha-C_\alpha$ 1.397, $C_\alpha-C(H)$ 1.399, $C(H)-C(H)$ 1.387. Energies are as described in Figure 3.

tomers (**20**−**22**) were calculated for the (*Z*)-isomer. Another syn tautomer is also possible, with the two hydrogens residing at N_1 and N_4 (or N_2 and N_3). However, this tautomer is significantly destabilized by the steric interactions between the two very close hydrogens. The PM3 calculation indicates that it is 23 kcal/mol less stable than structure **20**, and therefore, no DFT calculations were performed. Calculations were performed for one anti and one syn tautomer (**23**−**24**) of the (*E*)-corrphycene.

The calculations indicated that the anti tautomers are all more stable than the syn tautomers. As will be discussed later, this is a general feature which is due mainly to relatively unfavorable electrostatic interactions in the syn tautomers. Therefore, for the rest of the compounds only anti tautomers were studied. Thus, for porphyrin-(3.0.1.0), **5**, only the two anti tautomers (**25**−**26**) were calculated. Two anti tautomers (**27**−**28**) are possible for porphyrin-(2.2.0.0), **6**. For porphyrin-(3.1.0.0), **7**, two anti tautomers were studied for both the (*E*)- and (*Z*)-isomers (**29**−**32**). Three structures were calculated for porphyrin-(4.0.0.0), **8**, one with a (*Z*)-configuration (**33**) and two with a (*E*)-configuration (**34**−**35**).

Basis Set Effects on Geometries. For compounds **1**−**4**, geometry optimizations were performed with both the 3-21G and 6-31G** basis sets. As exemplified with porphyrin (**1**) in Figure 3, the 3-21G geometries (in parentheses) are quite similar to the 6-31G** geometries. With the 6-31G** basis set, there is a shortening of bonds in the pyrrole rings and a lengthening of the $C_\alpha-C_{meso}$ bonds. The unprotonated pyrrole $C_\alpha-N$ bond lengths show the largest difference, i.e., 0.01−0.02 Å. Bond angles are very similar, with the largest difference about 2°. Overall, the largest geometrical difference occurs in the NH---N hydrogen-bonding system. There is a decrease in the N−H bond lengths of 0.02−0.05 Å and an increase in the NH---N hydrogen-bonding distances of 0.12 Å upon improving the basis set. This can be traced to the lack of polarization functions in the 3-21G basis set. The lack of polarization functions leads to an overestimation of electrostatic interactions and thus to an overemphasis of hydrogen bonding. Inclusion of polarization functions on N and H in the 6-31G** basis set causes geometrical changes which signal a more faithful representation of hydrogen bonding.[42] The overestimate of hydrogen bonding weakens the $C_\alpha-N$ bonds,

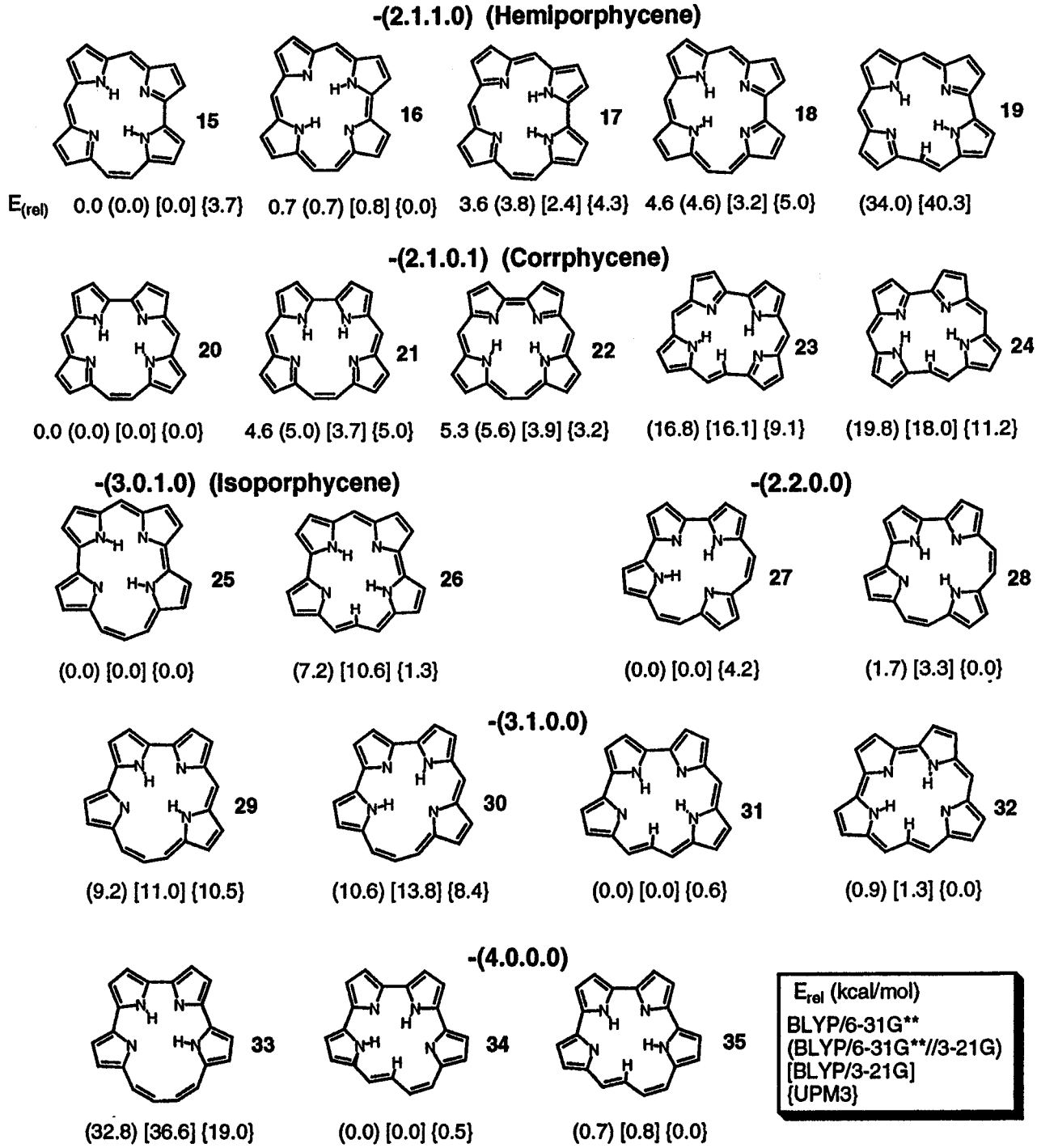

Figure 5. Calculated structures of porphyrin isomers porphyrin-(2.1.1.0), -(2.1.0.1), -(3.0.1.0), -(2.2.0.0), -(3.1.0.0), and -(4.0.0.0). The relative energies (kcal/mol) of structures of each isomer are given below the formulae.

causing these bonds to be too long with the 3-21G basis set. This is also responsible for the shrinkage of the central cavity in the 3-21G geometries. These features are also found for other isomers. Therefore, for compounds **2**−**4**, only the 6-31G** geometrical parameters are given in Figures 4, 6, and 7. Because there are only these small and systematic basis set effects, geometry optimizations for compounds **5**−**8** were only carried out with the BLYP/3-21G method.

Effect of Tautomerization on Skeletal Geometries. Structures **9**−**11** (Figure 4) have very similar bond lengths, especially in the pyrrole rings. The syn and bridged structures are different from the anti structure mainly in the $C_\alpha-C_{meso}-C_\alpha$ bending angles, due to different hydrogen bonding modes in these structures. While the anti tautomer (**9**) has weak hydrogen bonding (N---H = 2.32 Å), the syn (**10**) has stronger hydrogen bonding as indicated by a normal N---H hydrogen-bonding distance of 1.91 Å (vide infra). The symmetrically bridged structure (**11**) involves the largest ring skeletal deformation because the two partially formed N---H bonds are only 1.305 Å.[43]

(42) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; John Wileys & Sons: New York, 1986.

(43) The N---H distance is similar to those found in the transition structures of many proton-transfer reactions. For examples, see: Florian, J.; Hrouda, V.; Hobza, P. *J. Am. Chem. Soc.* **1994**, *116*, 1457.

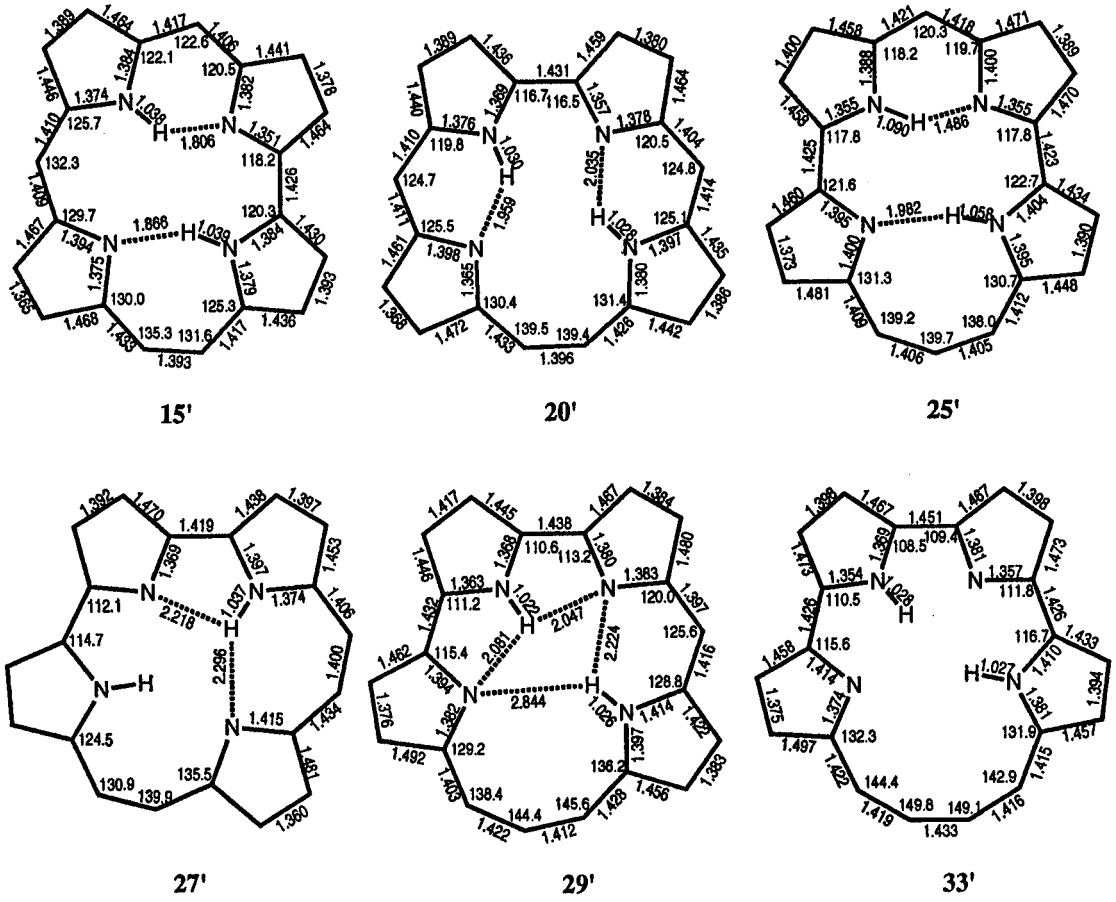

Figure 6. Geometries of the most stable (*Z*)-configured porphyrin isomers porphyrin-(2.1.1.0), -(2.1.0.1), -(3.0.1.0), -(2.2.0.0), -(3.1.0.0), and -(4.0.0.0). Geometries are optimized with the BLYP/6-31G** method for **15′** and **20′** and with the BLYP/3-21G method for **25′**, **27′**, **29′**, and **33′**.

In the case of porphycene (**2**), the three structures **12**−**14** shown in Figure 4 have very similar ring skeletons. The corresponding C−C bond lengths differ less than 0.02 Å, and the corresponding C−C−C bond angles are all within 2°. Here the hydrogen shift can occur without much ring skeletal distortion. Similar situations are also found for compounds **3**−**8**. Therefore, we conclude that tautomerism of the two inner hydrogens has little effect on the geometry of the ring skeleton and thus on the π-electron system.

Bond Lengths and Planarity: Comparison with X-ray Crystal Structures. Crystal structures of compounds **1**−**4** (**3** and **4** as alkyl derivatives) have been determined by X-ray crystallography.[10a,13,14,28] All of them are planar and exhibit delocalized π-electron systems. That is, the C−C bond lengths (not involving those of the pyrrole rings) are nearly equal. It has been shown that the restricted Hartree−Fock (RHF) method gives a bond length alternating geometry for porphyrin with a C_2 symmetry primarily due to the lack of electron correlation.[17] Both MP2 and local density functional methods have been shown to give better geometries for porphyrin.[18] The BLYP functional used here gives a D_{2h} delocalized structure for porphyrin.

The calculated structures for (*Z*)-configured compounds **1**−**4** are all planar. In each structure the C−C bond lengths in the linkage are nearly equalized. Even in the structures of compounds **5**−**8** which contain the $(CH)_3$ and $(CH)_4$ linkages, there is significant bond length equalization (see Figures6 and 7). For example, in structure **33′** the five C−C bonds range from 1.415 to 1433 Å.[10a,13,14,28] The calculated structures are very close to the X-ray crystal structures for **1**−**4**. The BLYP/6-31G** calculated bond lengths are systematically longer by 0.01−0.03 Å.[44] The X-ray crystal structure of corrphycene also reveals a stretching of the $C_\alpha-C_\alpha$ bond (1.423 vs 1.397 Å), relative to porphycene, a contraction of the $N-C_\alpha-C_\alpha$ angles (114° vs 118°), and a widening of $C_\alpha-C(H)-C(H)$ angles (139° vs 131°).[14] The calculated increase in length of the $C_\alpha-C_\alpha$ bond is too small (0.01 Å), but the other features are well reproduced by the calculations.

Compounds **5**−**8** are predicted to be planar or nearly planar when they are in the (*Z*)-configurations (see Figure 6), although they suffer severely from angle strain. For example, structure **33** (or **8**) is about 71 kcal/mol less stable than **9** (or **1**) (see Table 3) but is still essentially planar. For compound **6**, both anti tautomers were optimized with a C_s planar constraint with the symmetry plane running through N_1 and N_3. While structure **27** retains a planar ring skeleton, slight nonplanarity is found in structure **28**. The ring distortion mainly reduces the inner H---H interaction. When the ring skeleton is forced to be planar, the H---H distance is only 1.95 Å and this structure is less stable than the fully optimized one by 0.4 kcal/mol. For structure **27**, the H---H distance is 2.39 Å, and no significant steric interaction is expected. We believe that this is the main reason structure **27** is more stable than structure **28** by about 2 kcal/mol.

(44) Johnson, B. G.; Gill, P. M. W.; Pople, J. A. *J. Chem. Phys.* **1993**, *98*, 5612.

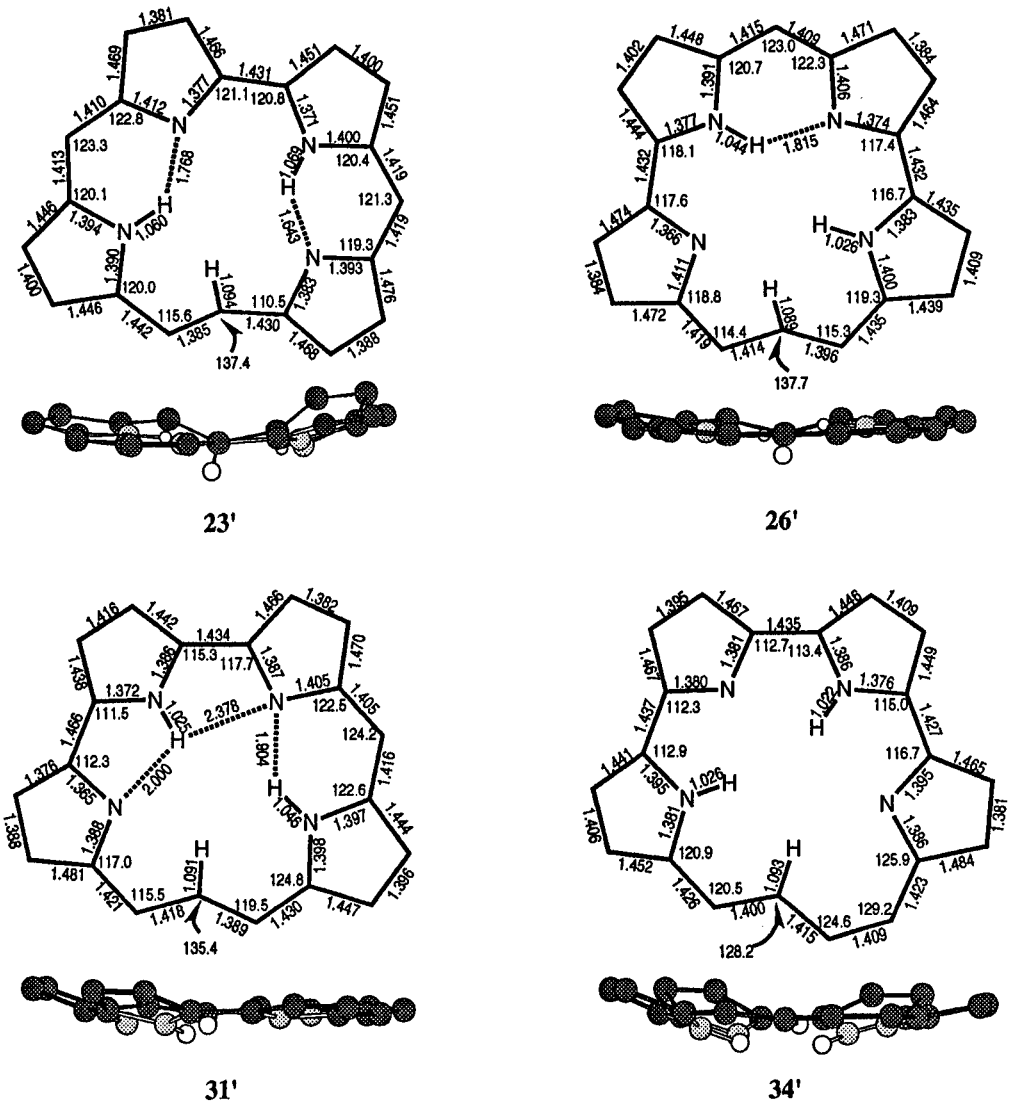

Figure 7. Geometries of the most stable (*E*)-configured porphyrin isomers porphyrin-(2.1.0.1), -(3.0.1.0), -(3.1.0.0), and -(4.0.0.0). Geometries were optimized with the BLYP/3-21G method.

Although these calculations predict a strong preference for planarity, the BLYP method is known to overemphasize the stability of cyclic delocalized structures.[45] The strained molecules may have a greater tendency toward bond localization and nonplanarity than is found in the BLYP results.

All (*E*)-structures are somewhat distorted away from planarity, as shown in Figure 7 for the most stable ones.[46] In each structure, there is an inner C−H bond which causes steric interactions with the adjacent N and N−H groups. The overall gain in stabilization due to nonplanar distortion is small. The largest is for structure **34** (**34′**), which is about 1.4 kcal/mol.

Hydrogen Bonding. Due to the close proximity of the four nitrogen atoms, there are some strong hydrogen bonds in several structures. Short X---H−Y distances and more linear X−H−Y angles are generally understood to give rise to stronger hydrogen bonding. In the most stable anti porphyrin tautomer **9**, the N---H−N distance is 2.32 Å, indicating only weak hydrogen bonding. Each N−H is equidistant from two hydrogen-bond-accepting imino nitrogens, however, so the net electrostatic attraction in the anti conformation is larger, only reduced by the H−H repulsion. Shortening one N---H−N distance would necessarily increase the other. The anti porphycene tautomer (**12**) features strong hydrogen bonding: the N−H bond lengths are 1.064 Å, the H---N distances are 1.670 Å, and the N−H---N angles are 153°. Strong hydrogen bonding also exists in structures **15′**, **20′**, and **25′**. On the other hand, structures **27′**, **29′**, and **33′** benefit little from hydrogen bonding either because of long N---H−N distances or small N−H−N angles. In general, syn tautomers have two strong hydrogen bonds, while the corresponding anti tautomers have NH bonding to two nitrogens, with each individual bond being less strong.

Central Cavity and Metal Complexation Propensities. The four adjacent N−N distances of structures **9**−**35** are collected in Table 2. Several features are noted. (1) The four N−N distances in *anti*-porphycene (2.66 and 2.87 Å) are all smaller than those in *anti*-porphyrin (2.95 Å), indicating that porphycene has a smaller and rectangular cavity. While porphycene is predicted to be more

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(46) The (*E*)-configured hemiporphycene, structure **19**, is not shown because it is about 34 kcal/mol less stable than the (*Z*)-configured structure **15**. It is unlikely to be synthesized.

Table 2. Calculated Adjacent N---N Distances and Imino H−H Distance (Å) of Porphyrin Isomers. The BLYP/6-31G Geometries for Structures 9−18 and 20−22 and the BLYP/3-21G Geometries for Structures 19 and 23−35**

structure	N_1-N_2	N_2-N_3	N_3-N_4	N_3-N_4	H−H
9	2.954	2.954	2.954	2.954	2.225
10	3.154	2.718	2.718	3.154	2.131
11	3.361	2.488	2.488	3.361	2.572
12	2.664	2.865	2.865	2.664	2.380
13	2.619	2.919	2.864	2.619	2.331
14	2.520	2.924	2.924	2.520	2.450
15	2.602	2.764	2.931	3.241	2.366
16	2.596	2.760	2.929	3.256	2.281
17	2.530	2.852	2.842	3.275	2.229
18	2.519	2.790	2.829	3.376	2.308
19	2.947	2.586	3.668	2.828	2.445
20	2.651	2.749	3.585	2.742	2.287
21	2.761	2.657	3.628	2.657	2.080
22	2.702	2.641	3.773	2.641	2.348
23	2.855	2.598	4.260	2.469	2.932
24	2.846	2.640	4.200	2.519	2.787
25	2.419	2.811	3.009	2.790	2.287
26	2.627	2.686	3.661	2.715	2.253
27	2.518	3.722	3.722	2.518	2.388
28	2.542	3.242	3.242	2.542	2.062
29	2.463	2.855	3.664	2.523	2.000
30	2.463	2.800	3.635	2.547	2.350
31	2.669	2.723	4.307	2.474	2.428
32	2.661	2.741	4.335	2.453	2.638
33	2.343	2.565	3.845	2.517	2.141
34	2.517	2.638	4.278	2.504	2.229
35	2.512	2.580	4.262	2.520	2.428

Table 3. Calculated Relative Stabilities (kcal/mol) of Compounds 1−8

isomer	structure	PM3	BLYP/3-21G	BLYP/6-31G**//3-21G	BLYP/6-31G**
1	**9**	0.0	0.0	0.0	0.0
2	**12**	1.7	−6.2	−1.5	−2.0
3	**15**	8.6[a]	2.5	5.1	4.5
(*E*)-**3**	**19**		42.9	39.2	
4	**20**	20.9	12.0	12.0	11.8
(*E*)-**4**	**23**	30.1	28.1	28.7	
5	**25**	23.6	17.7	19.0	
(*E*)-**5**	**26**	24.9	28.3	26.2	
6	**27**	37.6	31.8	28.9	
7	**29**	39.7	42.7	38.7	
(*E*)-**7**	**31**	29.8	31.6	29.5	
8	**33**	53.9	78.6	70.6	
(*E*)-**8**	**34**	34.8	43.1	38.4	

[a] The data here correspond to structure **16** which is the most stable PM3 structure of **3**-(2.1.1.0).

stable as a free ligand than porphyrin, the central cavity of porphyrin provides a more perfect geometry for ligation of a metal ion. (2) For compounds **4**, **5**, and **8**, the central cavity in the (*Z*)-configured structures is of a trapezoid shape. The N_1-N_2 distances are much smaller than the N_3-N_4 distances, while N_2-N_3 and N_1-N_4 distances are of similar values. (3) Compared to porphyrin, all of the (*Z*)-configured structures have somewhat smaller central cavities. (4) The (*E*)-configured structures have larger central cavities than the corresponding (*Z*)-configured structures.

Tautomerism. The relative energies of the three structures of porphyrin are given in Figure 4. The BLYP/6-31G** geometry optimizations performed here give a 7.2 kcal/mol preference for the anti tautomer over the syn tautomer. This is close to the value of 7.6 kcal/mol reported by Ghosh et al.[18b] but is lower than the value of 10 kcal/mol reported by Reimers.[18c] Allinger's latest MM3 calculations gave an 8 kcal/mol preference to anti over syn.[21e] The symmetrically bridged transition structure is calculated to be less stable than the anti tautomer by 19.2 kcal/mol. This is nearly identical with the value reported by Reimers et al.[18c] Three points concerning our results are notable: (1) The 3-21G basis set gives a smaller preference for the anti tautomer over the syn and symmetrically bridged tautomers (values in brackets), because the 3-21G basis set overestimates hydrogen-bonding interactions in structures **10** and **11**. (2) The BLYP/6-31G** calculations on the 3-21G geometries give nearly identical relative energies (values in parentheses) to the BLYP/6-31G** full geometry optimizations. The same is also found for porphycene, corrphycene, and hemiporphycene. This indicates that for systems with low symmetry the BLYP/3-21G geometry optimization might be sufficiently accurate. (3) The PM3 method predicts much too large a destabilization of the symmetrically bridged structure. A similar situation applies to the AM1 calculations by Merz et al.[16f]

The positions of the imino hydrogens of porphycene have not been determined explicitly by experiment. The tautomerism of crystalline porphycene was studied using the ^{15}N-CPMAS NMR technique by Limbach et al.[37] An extremely fast two-step mechanism of isomerization was proposed. Early PPP calculations predicted a 7 kcal/mol preference for the syn tautomer.[22] As shown in Figure 4, our calculations with the BLYP/6-31G** full geometry optimization indicate that the anti tautomer (**12**) is about 2 kcal/mol more stable than the syn tautomer (**13**).[47] The symmetrically bridged structure, **14**, a possible transition structure for the synchronous mechanism, is 5 kcal/mol less stable than **12**. Since the syn tautomer is about 2 kcal/mol less stable than the anti tautomer, it is expected that the classical barriers for both stepwise and concerted mechanisms of tautomerism are likely to be in the range of 3−5 kcal/mol. Since the NH---N distance is quite short in porphycene, tunneling may play an important role in the tautomerism. In comparison to porphyrin, the tautomerization of porphycene requires a much smaller geometrical deformation (see the N---N distances in Table 2) and has a very low barrier due to strong hydrogen bonding in the ground state.

Among the four tautomers of hemiporphycene (**3**), structure **15** is predicted to be most stable with each level of density functional calculation but not with the PM3 method. Structure **15** is about 0.7 kcal/mol more stable than the other anti tautomer (**16**). The two syn tautomers are less stable than the two anti tautomers by 3−4 kcal/mol. These results are in accord with the observation by an NMR study that two tautomers are in fast equilibrium, differing in energy by about 0.6 kcal/mol.[13b] It is interesting that structure **17** with two hydrogens on the bipyrrole nitrogens is more stable than structure **18** by 0.7 kcal/mol, which has the two hydrogens attached to the two nitrogens with the largest separation.

The ^{1}H NMR spectra of octaethylcorrphycene indicate the presence of two equivalent anti-NH tautomers in solution, with a free energy of activation of 8.3 kcal/mol for tautomerization.[14a] However, a syn tautomer was observed in the X-ray crystal structure of the compound. Our calculations indicate that the anti tautomer is more

(47) In an early stage of the study, the local density functional method was employed to optimize the porphycene structures using the DMol program of BIOSYM. This predicts an essentially symmetrically bridged structure starting from either anti or syn structure using both the JMW/DN and JMW/DND methods. It is known that the local density functional approximation overestimates the strength of hydrogen-bonding interactions (see ref 50).

stable than the two syn tautomers by about 4−5 kcal/mol, in agreement with the solution data. Similar to hemiporphycene, the syn tautomer with the two hydrogens attached to the bipyrrole nitrogens (**21**) is more stable than that with hydrogens on the two nitrogens with the largest separation (**22**).

Since tautomerization has little effect on the geometry and electronic structure of the ring skeleton, it is likely that the tautomeric preference of **1**−**4** is mainly caused by electrostatic effects; both hydrogen-bonding and lone-pair, lone-pair repulsions are involved. Although the D−D−A−A pattern of the syn tautomers generally allows stronger hydrogen bonds as indicated by shorter N---H−N distances, the D−A−D−A pattern of the anti tautomer allows each of the two hydrogens to be attracted by the two imino nitrogens (D's). Therefore, the anti tautomers enjoy better overall electrostatic attractions. In addition, the syn tautomers are destabilized by the electrostatic repulsion between the two adjacent imino nitrogen lone-pair donors. Similar situations have been analyzed by Jorgensen et al. for base pairing.[48] The preference for the anti tautomer should hold in compounds **5**−**8** as well. Therefore, for compounds **5**−**8**, only the anti tautomers were studied.

Geometrical Isomerism. (*Z*)- and (*E*)-configurations were calculated for compounds **3**, **4**, **5**, **7**, and **8**. Compounds **2** and **6** would have very high energy (*E*)-isomers because of restrictive geometrical constraints, and therefore were not calculated. All structures were optimized with the BLYP/3-21G method, and energies were further calculated with the BLYP/6-31G** method. As shown in Figure 7 for the most stable structures, the introduction of (*E*)-double bond(s) causes a deviation from planarity to a nonplanar, bowl-like conformation, due to the steric interactions caused by the inner C−H group.

The introduction of the (*E*)-double bond(s) leads to considerable extension of the $(CH)_n$ linkage, and therefore a much larger separation between N_3 and N_4. This results in a large difference in the ring strain between the (*E*)- and (*Z*)-isomers. For corrphycene (**4**), the most significant geometrical differences cause stronger hydrogen bonding in the (*E*)-corrphycene than in the (*Z*)-corrphycene. The NH---N distances decrease from 1.898 and 1.813 Å in the anti tautomer of (*Z*)-corrphycene (**20′**) to 1.768 and 1.643 Å in the anti tautomer of (*E*)-corrphycene (**23′**), and even further to 1.489 and 1.697 Å in the syn tautomer of (*E*)-corrphycene (**24**).

The anti tautomer of (*E*)-corrphycene is 16.1 kcal/mol higher in energy than the anti tautomer of (*Z*)-corrphycene, and the lowest-energy syn NH tautomer (**24**) is another 3 kcal/mol higher in energy. There is less angle strain in the $-(CH)_2-$ linkage for the (*Z*)-isomer than the (*E*)-isomer. In addition, the (*E*)-isomer is prevented from achieving the fully aromatic planar conformation by CH−NH interactions. The offending CH repulsion could be avoided by replacing the CH by an imine N, and the resulting compound might offer five nitrogens for coordination of a central metal ion.

A 40 kcal/mol destabilization is predicted for the (*E*)-hemiporphycene (**19**) with respect to the (*Z*)-hemiporphycene (**15**). There is significant distortion about the $(CH)_2$ linkage, and the dihedral angle about the bridging CH−CH bond is 125°, far from planarity.

For porphyrin-(3.0.1.0) (**5**), there is angle strain in both the (*Z*)-isomer (**25′**) and the (*E*)-isomer (**26′**). Although the (*Z*)-isomer is predicted to be more stable than the (*E*)-isomer (see **25** and **26** in Figure 5) by about 7 kcal/mol at the BLYP/6-31G** level, we propose that this (*Z*)-preference is not due to a larger angle strain in the (*E*)-isomer. Instead, the (*E*)-isomer is destabilized by the steric interactions caused by the inner C−H, since it is 2.106, 1.798, and 2.258 Å away from the N_3, $H(N_3)$, and N_4, respectively. In addition, the (*Z*)-isomer enjoys better hydrogen bonding (cf. **25′** and **26′**). Both (*Z*)- and (*E*)-porphyrin-(3.0.1.0)−Pd(II) complexes have been synthesized recently.[6d] On exposure to light, the two structural isomers interconvert readily.[49]

Although porphyrin-(3.1.0.0) (**7**) resembles porphyrin-(3.0.1.0) (**5**) in that it also has a $-(CH)_3-$ linkage, it is predicted to favor an (*E*)-configuration. The two (*E*)-configured structures (**31** and **32**) are more stable than the two (*Z*)-configured structures (**29** and **30**) by about 10 kcal/mol.

The (*E*)-configured structures (**34** and **35**) of compound **8** are predicted to be much more stable than the (*Z*)-isomer (**33**). Structure **33** suffers from severe angle strain as indicated by small $N-C_\alpha-C_\alpha$ angles (**33′**) and very large C(H)−C(H)−C(H) angles in the $-(CH)_4-$ linkage.

Relative Stabilities. Table 3 gives the calculated relative stabilities of the seven porphyrin isomers with respect to the parent porphyrin. Only the most stable tautomer of each isomer is listed. While porphyrin is most stable with PM3 calculations, porphycene is found to be slightly more stable than porphyrin with the BLYP method. The best calculation predicts a 2 kcal/mol preference. Judging from the optimized structural parameters, porphycene should have larger angle strain than porphyrin, but the strong hydrogen bonding in porphycene makes it more stable. This is also reflected by the exaggerated preference of 6 kcal/mol with the 3-21G basis set, since 3-21G overestimates the strength of hydrogen bonding.[50]

Hemiporphycene (**3**) and corrphycene (**4**), the other two known porphyrin isomers, are less stable than porphyrin by 4.5 and 11.8 kcal/mol, respectively. Ring strain differences are the main reasons for the destabilization of the two compounds. The difference between the stabilities of corrphycene and hemiporphycene can also be traced to ring strain and because hemiporphycene is better hydrogen-bonded than corrphycene.

Isomers **5**−**8** are much higher in energy than porphyrin and porphycene. They are destabilized by the presence of severe angle strain in the $C_\alpha-C_\alpha$ and $-(CH)_n-$ linkages, as shown in Figures 6 and 7. The most stable of the four isomers is **5**. This isomer favors a $(Z)-(CH)_3$ arrangement. While angle strain is clearly present, this isomer has strong inner hydrogen bonding. We also note that isomer **5** has two separated pyrrole/pyrrole connections, while the isomers **6**−**8** have two or three contiguous pyrrole/pyrrole connections. Whether or not such contiguous pyrrole/pyrrole connections cause inherent destabilization needs to be studied further.

Compound **8** is the least stable of the eight isomers. In its favored (*Z*)-configuration, despite the fact that there is not much angle strain in the $-(CH)_4-$ linkage, severe

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angle strains exist in the pyrrole/pyrrole linkages. In addition, the structure is destabilized by the presence of an inner CH group.

Comment on the PM3 Method. It has been shown that the unrestricted AM1 method gives a reasonable geometry for porphyrin.[16g] We used the unrestricted PM3 method to study compounds **1**−**8**. As with the BLYP method, the PM3 method gives planar and delocalized structures for compounds **1**−**4**. The calculated geometrical parameters are quite comparable to those obtained by the BLYP method. However, for compounds **5**−**8**, the PM3 method gives structures with significant ring skeletal deformations. In these structures, there are also substantial bond length alternations. Contrary to the BLYP method, the structures with the constraint of a planar ring skeleton are significantly less stable than the fully optimized nonplanar structures. It has been recognized that PM3 underestimates the energies of planar delocalized aromatic structures.[45]

Table 3 indicates that the relative stabilities of porphyrin and its seven isomers calculated with the PM3 method are similar to the BLYP/6-31G** values. However, as can be seen in Figures 3−5, the calculated relative energies of different NH isomers are quite different from the DFT results. This problem is especially serious for the symmetrically bridged porphyrin and porphycene. Therefore, caution is recommended when the PM3 method is used for the study of large conjugated π-systems.

Summary

We have presented a detailed density functional study of the geometry, tautomerism, geometrical isomerism, and stability of porphyrin and its seven isomers with an N_4-metal coordination core. Density functional theory calculations using both the BLYP/3-21G and BLYP/6-31G** methods give geometries which compare quite favorably with the available X-ray crystal structures. All these compounds are predicted to have a planar or nearly planar ring skeleton with significant π-delocalization when in a (*Z*)-configuration, even in the presence of significant angle strain as is the case in compounds **5**−**8**. A small ring distortion is introduced in the (*E*)-configured structures in order to reduce the steric interactions involving the inner CH group. Each compound favors an anti tautomeric form (anti NH/NH) instead of a syn form primarily due to electrostatic repulsion between the two adjacent pyrrolenine nitrogen atoms in the syn tautomer and the reduction in the number of hydrogen bonds from four to two. The N−H tautomerism is found to have little effect on geometry. The cis (*Z*)−trans (*E*) isomerism about the -$(CH)_n$- linkage considerably extends the cavity and causes variation in angle strain. Compounds **2**−**4** and **6**, which have -$(CH)_2$- linkage(s), significantly favor a (*Z*)-configuration. (*Z*)-**5** is calculated to be only about 7 kcal/mol more stable than (*E*)-**5**. This (*Z*)-preference may be due to the steric interactions involving the inner CH group in (*E*)-**5** and a favorable hydrogen bonding in (*Z*)-**5**. Compounds **7** and **8** strongly favor (*E*)-configurations. Porphycene (**2**) is the most stable among the seven isomers and is about 2 kcal/mol more stable than porphyrin due to its exceptionally strong hydrogen bonding. Porphyrin isomers **5**−**8** are much less stable than porphyrin, since they suffer from ring strain that sharply increases from **5** to **8**. While these compounds may not be stable enough to permit isolation, they may still form stable metal complexes.[49]

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