Theoretical Study on the Structure, Stability, and Tautomerism of 2-Aza-21-carba-23-X(thia or oxa)-Porphyrin Isomers

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The structures and relative energies of all expected isomers and intermediates of new carbaporphyrin systems (2-aza-21-carba-23-X(thia or oxa)-porphyrin with or without 5,10,15,20-tetraphenyl) have been calculated using density functional theory (DFT) methods. The two tautomers having inside N−H turned out to be almost isoenergetic, with the relative energy difference less than 0.5−1.0 kcal/mol for both thiacarbaporphyrin and oxacarbaporphyrin. The tautomer having outside N−H is calculated to have only 1−3 kcal/mol higher energy than the lowest-energy isomer for the thiacarbaporphyrin, whereas the difference increases up to about 9−12 kcal/mol for the oxacarbaporphyrin system. The results explain why three isomers can coexist in the thiacarbaporphyrin, whereas only two isomers can be observed in the oxacarbaporphyrin. The calculated structures show that the relative stability of the isomers is not determined by the steric hindrance between two hydrogen atoms inside the core ring but by the degree of the π-electron resonance of the core framework. The relative energy of the intermediate structure having two hydrogen atoms at the C(21) atom is calculated to be about 3−6 and 11−15 kcal/mol for thiacarbaporphyrin and oxacarbaporphyrin, respectively. The overall energy barriers of the tautomerism between the isomers with inside N−H are estimated to be 12−15 and 20−22 kcal/mol for thiacarbaporphyrin and oxacarbaporphyrin, respectively. The shape of the core cavity made by the four inside ligand atoms (C, N, X, and N) is almost regular square in the oxacarbaporphyrin systems but rectangular or rhombic in the thiacarbaporphyrin systems.

1. Introduction

The porphyrin derivatives have attracted much attention because of their great importance in many vital biological processes, including photosynthesis (chlorophyll), oxygen transport (hemoglobin), and oxygen activation (cytochrome).[1] Numerous experimental and theoretical studies have been conducted on various aspects of porphyrin derivatives because of their potential in many practical areas, including molecular devices, light harvesting systems, photosynthesis, and phototheraphy.[2] Some aspects of these applications may be qualitatively understood and predicted based only on the unique construction of the model systems, i.e., the tetradentate macrocyclic systems can accommodate several types of metal ion in its core while maintaining aromatic systems. The current understanding of the relationship between their structures and chemical properties, however, is not sufficient, especially in the area of core-modified porphyrins. Thus, the important parts of the research activities in this area are designing a new framework of porphyrin core and studying the properties of those new systems.

The substitution of the nitrogen atoms of the porphyrin core by other heteroatoms[3−10] and the introduction of an inverted pyrrole ring in the core framework[11−14] can be a useful way to achieve the controlled modification of the basic framework without disturbing the aromaticity of porphyrin derivatives. Several such attempts have been successfully accomplished.[3−14] One of the present authors also has reported the synthesis of monooxaporphyrin (NCO) and monothiaporphyrin (NCS) bearing an inverted pyrrole ring and heteroatoms in the core,[7−9,13] and the existence of different tautomeric forms, as shown in Figure 1, was investigated by ^{1}H NMR spectroscopic experiments of the new porphyrin derivatives.[13c] An interesting fact emerging from the study is that while three isomers are observed in the monothiacarbaporphyrin derivatives, only two isomers are detected in the monooxacarbaporphyrin derivatives. Little information, however, was obtained on the identity, the relative stability, and the tautomerism of the isomers of the new systems.

In contrast to the new porphyrin derivatives, numerous extensive theoretical and experimental studies on the tautomerism of free-base porphyrin[15] as well as of choline[16] have been conducted. From the theoretical and experimental works on free base porphyrin, it is generally accepted that the tautomerism of free-base porphyrin occurs via a stepwise path. The transition state in the two-step mechanism has an inner hydrogen atom bridged between neighboring two N atoms, and the intermediate state has the cis form with each H atom attached to the adjacent N atoms. It also has been shown that the tautomerism of carbaporphyrin proceeds through a similar mechanism.[17] The new porphyrin system of the present work, however, has no such neighboring N atom to which the migrating H atom can bridge or attach. An updated mechanism is needed to explain the observed tautomerism.

Several extensive theoretical and experimental studies have been conducted on the structures of normal porphyrin systems[18,19] and on the flexible nature of the porphyrin ring[20] and their vibrational spectra.[21] Even the excited states and the

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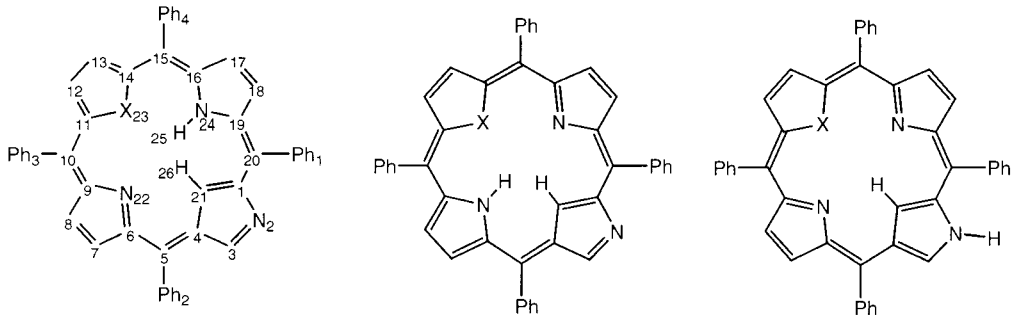

Figure 1. Structures of NCX-in1, NCX-in2, and NCX-out isomers.

photoinduced hydrogen atom transfer of free-base porphin derivatives have been studied recently.[22] Comparable theoretical studies are reported for free-base inverted porphyrins and carbaporphyrins[23] as well as for the porphyrin systems with double inverted-pyrrol units.[24] In contrast, almost no comparable information about the new carbaporphyrin system, which has both an inverted pyrrol unit and a heteroatom in the core, is available either from X-ray experiments or by a reliable theoretical method. The lack of such information on the new system can be an obstacle to understanding more details of the new system. Considering the fact that the new carbaporphyrin system may possibly be a new building block of large macromolecules for practical areas, further details on the new carbaporphyrin systems are highly desirable.

The prime object of the present study is to investigate the structure, stability, and tautomerism of the new porphyrin systems, 2-aza-21-carba-23-oxaporphyrin (NCO) and 2-aza-21-carba-23-thiaporphyrin (NCS), with or without 5,10,15,20-tetra-*meso*-phenyl. To design a new porphyrin system with some expected properties, proper understanding of previously observed experimental results is indispensable, and the goal can be attained with a reliable theoretical method. To attain this goal, the structures and energies of all predicted isomers and intermediates are calculated in the present study by using density functional theory (DFT) methods, and the calculated results are discussed in connection with previously observed experimental facts.

2. Computational Methods

Recent extensive studies on N−H tautomerism of the free-base porphyrin[15] have shown that theoretical studies using a nonlocal density functional theory (DFT) method[25] provide results almost comparable to elaborated experimental work[26] and the direct ab initio dynamic study.[15] DFT methods are used as the main tool in the present theoretical work, and the reliability of DFT methods is discussed elsewhere.[19b]

All calculations in the present work have been conducted by using DFT methods of three-parameter hybrid exchange correlation functional, the B3LYP[27] and the B3PW91,[28] implemented in the Gaussian 98 suit of programs.[29] Though the Hartree−Fock (HF) method is also applied as a starting point of the calculations, our major concern is placed on the results obtained by the DFT methods. Pople's 6-31G* basis[30] set of double-ζ plus polarization functions on heavy atoms is chosen as our major basis, and the 6-31G** basis[31] with p-type polarization functions on H atoms is used for a few selected cases.

The bond lengths and angles of all geometrical structures studied in the present study are optimized without any constraint under C_1 symmetry, which means that all of the structures correspond to stationary points in a potential energy surface. Because there are so many degrees of freedom in the large molecules of this work, especially those with four phenyl groups at meso sites, determining if the optimized geometry corresponds to true global minimum was difficult. All of the optimized three-dimensional structures were carefully examined not only by analyzing the calculated numbers but also by using computer graphic programs, such as the GaussView[32] and the CAChe.[33] Every effort has been taken to escape from a local minimum.

The solvent effect on total energy was estimated by using the Onsager model[34] of the self-consistent reaction field (SCRF) method implemented in Gaussian 98. By using the VOLUME keywords for Gaussian 98, a single-point calculation at optimized geometry in gas phase is performed to determine the radius of the cavity of the Onsager model for each molecule. Then the energy in the solvent is calculated by using the cavity radius and the dielectric constant of chloroform ($\epsilon = 4.90$), because the solvent was actually used in the previous NMR experiment.[13] All other aspects of the present calculations follow well-established procedures of using the Gaussian 98 package.

3. Results and Discussion

The isomers of the target molecules in this work that were actually synthesized and studied by using the ^{1}H NMR spectra are 2-aza-21-carba-23-X(thia or oxa)-porphyrin with four aryl groups (phenyls or mesityls) at meso sites (the 5,10,15,20 sites), and these molecules will be designated here as NCS(Ph_4) and NCO(Ph_4). Though the 2-aza-21-carba-23-X(thia or oxa)-porphyrin molecule with hydrogen atom at the four meso positions has not been synthesized, and might be very difficult to actually synthesize, it has the basic framework of our target systems. The carbaporphyrin with *meso*-H atoms is chosen as the model system of the target molecules and will be referred to as NCO(H_4) and NCS(H_4). Depending on the position of the hydrogen atoms attached to N atoms, the three N−H isomers shown in Figure 1 will be referred to by NCX-in1, NCX-in2, and NCX-out, respectively.

The relative energy between isomers will be discussed first for the NCX(H_4) systems, and then the relative energy for the NCX(Ph_4) systems will be analyzed. After that, the relative energy of a few anticipated intermediates will be discussed in connection with the mechanism of the N−H tautomerism. Finally, some features of the geometrical structures of the isomers and intermediates will be discussed at the end of this section. The zero-point energy correction on the relative energy is not included here because a recent extensive work on the tautomerism of the free-base porphyrin shows that the correction is only about 0.4 kcal/mol.[15]

TABLE 1: Total Energy (E_{tot} in Hartrees), Relative Energy (ΔE_{rel} in kcal/mol)[a], and Dipole Moment (in Debye) of the Theoretically Optimized Structures[b]

	NCS(H_4)[d]			NCO(H_4)[d]		
method	E_{tot} (in1)[c]	ΔE_{rel} (in2)[c]	ΔE_{rel} (out)[c]	E_{tot} (in1)[c]	ΔE_{rel} (in2)[c]	ΔE_{rel} (out)[c]
HF/6-31G**	−1325.7105	1.82	−1.66	−1003.0661	1.78	5.86
(dipole moment)	4.33 D	4.25 D	2.42 D	5.65 D	5.58 D	1.06 D
B3PW91/6-31G*	−1331.9319	0.51	3.27	−1008.9815	0.45	10.77
(dipole moment)	4.30 D	5.22 D	3.72 D	5.34 D	6.13 D	2.56 D
		(0.21)	(3.53)		(0.19)	(11.92)
B3LYP/6-31G*	−1332.3330	0.53	3.29	−1009.3649	0.47	10.95
(dipole moment)	4.26 D	5.18 D	3.67 D	5.29 D	6.07 D	2.51 D
		(−0.13)	(3.22)		(0.07)	(12.33)
B3LYP/6-31G**	−1332.3563	0.50	3.33	−1009.3880	0.45	10.92
(dipole moment)	4.25 D	5.17 D	3.65 D	5.27 D	6.05 D	2.49 D
	NCS(4Ph)[e]			NCO(4Ph)[e]		
B3PW91/6-31G*	−2255.7931	0.95	2.07	−1932.8370	0.37	9.20
(dipole moment)	3.54D	4.89 D	4.14 D	4.47 D	5.49 D	2.99 D
		(0.79)	(2.00)		(0.08)	(9.88)

[a] The relative energy is calculated with respect to the energy of the corresponding XCN-in1. [b] The relative energies calculated by using the Onsager model to incorporate the solvent effect (dielectric constant of chloroform ($\epsilon = 4.9$) is used) are given in parentheses. [c] See Figure 1 for the N−H position of in1, in2, and out isomers. [d] NCX(H_4) = 2-aza-21-carba-23-X(oxa or thia)-porphyrin. [e] NCX(Ph_4) = 2-aza-21-carba-23-X(oxa or thia)-5,10,15,20-tetraphenyl-porphyrin

3.1. The Relative Energy of NCO(H_4) and NCS(H_4) Isomers. The geometries and relative energies of three isomers of the NCS(H_4) and NCO(H_4) are optimized by using a few different calculation methods. Though the Hartree−Fock (HF) calculations are performed with several different basis sets, only the results with the 6-31G** basis set are given in the upper part of Table 1 because the other results contain little additional information.

The results of the HF/6-31G** method for the two systems, the NCS(H_4) and the NCO(H_4) systems, show the same order and magnitude of the relative stability between the two isomers, NCX(H_4)-in1 and NCX(H_4)-in2; the relative energy of the NCS-(H_4)-in2 is 1.82 kcal/mol while that of the NCO(H_4)-in2 is 1.78 kcal/mol. In contrast, the isomer with outer N−H is calculated to be the most stable one in the NCS(H_4) case, but it is the most unstable one in the NCO(H_4) case. The NCS(H_4)-out is calculated to be 1.66 kcal/mol more stable than the NCS(H_4)-in1. The result supports the simple explanation that the steric hindrance between two hydrogen atoms in the core region makes the NCS(H_4)-in1 and the NCS(H_4)-in2 higher in energy than the NCS(H_4)-out. The NCO(H_4)-out, however, is calculated to be 5.86 kcal/mol higher in energy than the NCO(H_4)-in1 or the NCO(H_4)-in2, which cannot be explained just by the steric effect. Because the effect of electron correlation on the relative energy is not included in the HF method, we need a more careful investigation before giving even a qualitative explanation for the relative stability among the isomers. It can be noticed that the dipole moment of the NCX-out is much smaller than that of the NCX-in1 and the NCX-in2.

It is well-known that the HF method does not properly account for the stabilization of the conjugated π-electron system. The importance of the electron correlation in the study of the π-electron stabilization of porphyrin systems is well demonstrated.[35−37] The DFT method is one of the most efficient ways to include the electron correlation effect. Several studies on the tautomerism of other porphyrin systems were made using several DFT methods.[16,17,21−24,38] To check the dependence of the relative energy on the functional forms and the basis sets of a DFT method, the geometries of NCX(H_4) isomers are optimized by using three DFT methods: the B3PW91/6-31G*, the B3LYP/6-31G*, and the B3LYP/6-31G**. The total energy of the NCX-(H_4)-in1, the relative energy of other isomers with respect to the NCX(H_4)-in1, and dipole moments are given in the middle part of Table 1 for the NCS and the NCO systems.

The results of the DFT methods show a somewhat different trend compared with the HF results. First of all, detailed analyses are warranted for the results by using different DFT methods. The relative energies by the B3LYP/6-31G* method are almost the same as those by the B3LYP/6-31G** method, for both the NCS and the NCO systems. This means that relative stability is not affected by the p-type polarization functions for H atoms in the 6-31G** basis set. Also noticed is that there is almost no difference between the B3PW91/6-31G* results and the B3LYP/6-31G* results, which means that the choice of different functional forms, either the B3PW91 or the B3LYP functional, produces no difference in the relative energy. As for the result, the three methods (the B3PW91/6-31G*, the B3LYP/6-31G*, and the B3LYP/6-31G**) show virtually the same order and magnitude of relative stability between isomers, for both the NCS and the NCO systems. The results of the other two methods are within 0.18 kcal/mol deviation from those of the B3PW91/6-31G* results. Our discussions are conducted mainly by referring to the B3PW91/6-31G* results because only the B3PW91/6-31G* method is applied in the calculations for the NCX systems bearing *meso*-tetraphenyl groups.

In the B3PW91/6-31G* results, the relative energies with respect to the NCX-in1 are 0.51 and 3.27 kcal/mol for the NCS-in2 and the NCS-out, respectively. Those of the NCO-in2 and the NCO-out are 0.45 and 10.77 kcal/mol. The energy difference between NCX-in1 and NCX-in2 is about 0.5 kcal/mol regardless of the presence of oxygen or sulfur atom at the 23 position. In contrast to the HF results, where the NCS-out is most stable in the NCS systems and the NCO-out is most unstable in NCO systems, both the NCS-out and the NCO-out turned out to be the least unstable isomers in the DFT results. To provide more understanding for this outcome, we performed the PM3 semiempirical calculation with a UHF reference function. As was used in a previous work,[39] the resultant spin-density maps uncovered different π-electron resonance in the three isomers shown in Figure 2.

The π-electron resonance path in the NCX-in1 and the NCX-in2 isomers satisfies the 4n+2 rule of the aromaticity and forms

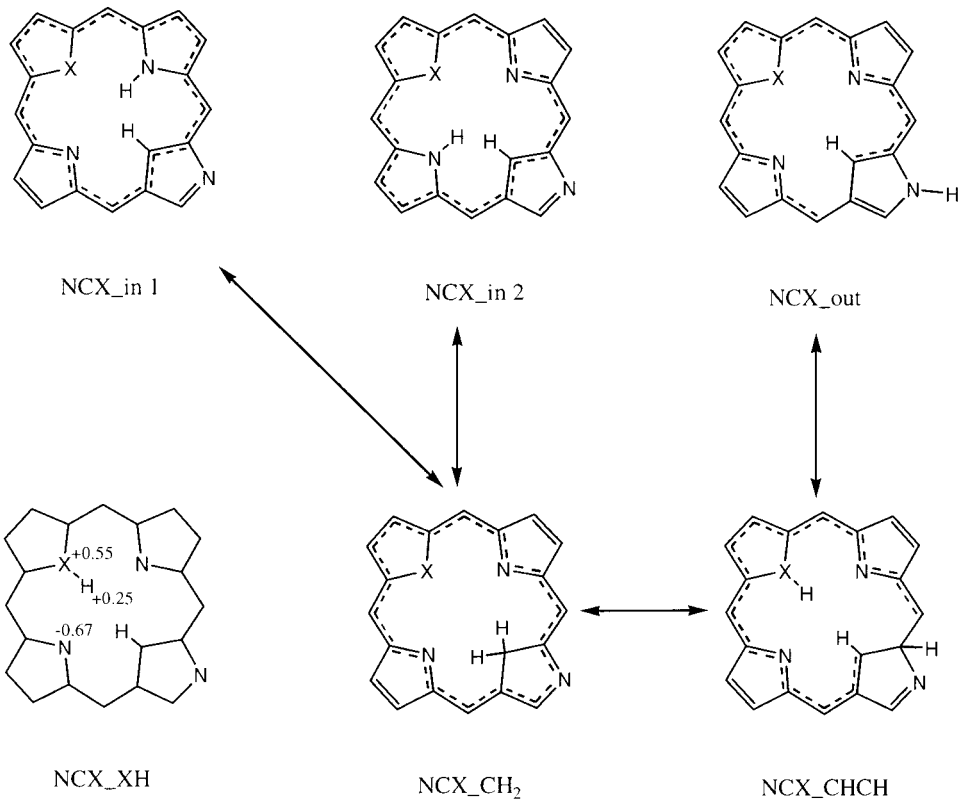

Figure 2. Isomers and intermediates in N−H tautomerism.

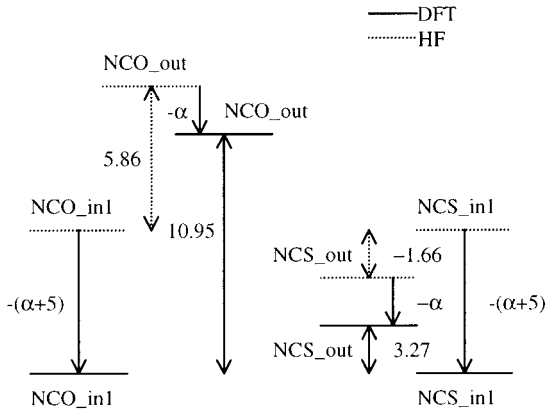

Figure 3. Effect of electron correlation on the relative energy. Dotted lines represent the HF results, whereas the solid lines stand for the DFT results.

an [18] annulene substructure. The path of the NCX-out isomer, however, cannot satisfy the 4n+2 rule and is disconnected at the inverted pyrrole moiety. More evidence supporting the broken path of the resonance will be given in the final part of the section discussing the structural features. The resonance effect for the NCX-in1 and NCX-in2 isomers, which satisfies the (4n+2) rule, is expected to be larger than that for NCX-out. We estimate the effect of the π-electron resonance (or electron correlation) on the relative stability by using the difference between DFT and HF results. The change in the energetic order of isomers, as going from the HF to the DFT results, is depicted in Figure 3. The dotted lines represent the HF result whereas the solid lines stand for the DFT results. The relative energies are given with respect to the NCX-in1 isomer.

If we take the π-electron resonance effect on the total energy of the NCX-out to be $-\alpha$ kcal/mol, then the effect on NCX-in1 (or NCX-in2) seems to be about $-(\alpha+5)$ kcal/mol. As a result, the HF energy gap of 5.86 kcal/mol between NCO-out and NCO-in1 increases to 10.77 kcal/mol by the inclusion of the π-electron resonance effect with the DFT method. In the case of NCS systems, the HF energy difference of −1.66 kcal/mol between NCS-out and NCS-in1 changes its sign, and NCS-in1 becomes 3.27 kcal/mol more stable than the NCS-out, as shown in Figure 3. The present results mean that the core frame of the porphyrin systems is flexible enough to accommodate the steric effect between the H atoms inside the core ring, and that the relative energy between isomers is determined not by the steric effect but by the difference between the π-electron resonance.

As shown in Table 1, the NCX-in2 isomer has a little larger dipole moment than the NCX-in1, whereas the NCX-out has a much smaller electric dipole, both in the NCS and the NCO cases. To provide more reliable results, the solvent effect on energy is estimated by using the Onsager model, and the relative energies with the solvent effect are given in parentheses in Table 1. The inclusion of the solvent effect with the B3PW91/6-31G* method stabilizes the relative energy of NCX-in2 about 0.3 kcal/mol, but the relative energy of NCX-out was destabilized at about 0.3−1.0 kcal/mol. It can be seen that the B3LYP/6-31G* method produces a little larger solvent effect. The NCS-in2 becomes even more stable (−0.13 kcal/mol) than NCS-in1, and the NCO-in2 becomes almost isoenergetic (0.07 kcal/mol) to the NCO-in1. Considering the small energy difference, as well as the inherent error bar of the present theoretical method, the two isomers (the NCX-in1 and the NCX-in2) can be considered isoenergetic. Because the electric dipole moment of the NCX-in2 is about 1.0−1.5 D larger than that of the NCX-in1, the actual relative stability between them may depend on the dielectric constant of a solvent. It might be worthwhile to note that the dipole moments of the present systems are larger than those of the 2-aza-21-carbaporphyrin (1.5−2.0 D) and the free-base porphyrin (∼0.3 D) systems.

As mentioned above, the results on model systems by the B3PW91/6-31G* method are virtually the same as those by the B3LYP/6-31G* method and show good agreement with that of the B3LYP/6-31G** method which needs more computation time than the B3PW91/6-31G* method. Based on the facts, we have chosen the B3PW91/6-31G* method as our main computation tool for studying our target molecules, the NCS and NCO porphyrin systems with phenyl groups at the four meso sites.

3.2. The Relative Energy of the NCO(Ph_4) and the NCS-(Ph_4) Isomers. The relative stability of the phenyl-substituted NCX(Ph_4) isomers with respect to the NCX(Ph_4)-in1 are calculated by using the B3PW91/6-31G* method, and the results are presented in the lower part of Table 1. The values of the NCS(Ph_4)-in2 and the NCS(Ph_4)-out are 0.95 and 2.07 kcal/mol, respectively, which can be compared with the corresponding values, 0.51 and 3.27 kcal/mol, of the NCS(H_4)-in2 and the NCS(H_4)-out, respectively. As the H atoms at meso sites are substituted by the phenyl groups, the energy gap between the NCS-in1 and the NCS-in2 increases 0.44 kcal/mol, but the gap between the NCS-in1 and the NCS-out decreases 1.2 kcal/mol.

In the case of the NCO(Ph_4) systems, the relative energies of the NCO(Ph_4)-in2 and the NCO(Ph_4)-out are 0.37 and 9.20 kcal/mol; the same order and magnitude as the NCO(H_4)-in2 and the NCO(4H)-out, 0.45 and 10.77 kcal/mol, respectively. We can see that the effects of the substitution on the order and magnitude of the relative stability among isomers are virtually the same for both NCS and NCO systems.

There are, however, some noticeable changes in the electric dipole moment. The values of the NCS(Ph_4) system by the DFT methods are 3.54, 4.89, and 4.14 D for NCS-in1, NCS-in2, and NCS-out, respectively, whereas those of NCS(H_4) are 4.30, 5.22, and 3.72 D. When the H atoms at meso positions atoms are replaced by phenyl groups, the dipole moments decrease about 0.8 and 0.3 D for the NCS-in1 and the NCS-in2, respectively, but increase about 0.4 D for NCS-out. It was noticed that the dipole moment of the NCS-out becomes even larger than that of the NCS-in1. Though similar changes in the magnitude have been induced in the NCO(Ph_4) isomers by the meso-phenyl groups, the dipole moment of NCO(Ph_4)-out is still smaller than that of NCO(Ph_4)-in1.

When the solvent effect is included, the relative energies of NCS-in1, NCS-in2, and NCS-out become 0.00, 0.79, and 2.00 kcal/mol, respectively. The energy differences between these three isomers are within 2.0 kcal/mol. According to the present theoretical results, the NCS-out is the most unstable species whereas the NCS-in1 and NCS-in2 are virtually isoenergetic. However, we cannot confirm which one of the two NCS-in isomers is the most stable isomer because the inherent error bar of the present calculation method, especially of the Onsager model, might be comparable to or could be even larger than the energy gap, 2.0 kcal/mol. Considering the facts that the Onsager model used in the present work is the simplest method of incorporating the solvent effect and that the dipole moments of the NCS(Ph_4)-in2 and the NCS(Ph_4)-out are larger than those of the NCS(Ph_4)-in1, the relative stability among the three isomers can be changed if the solvent effect is treated more rigorously. It is, however, clear that the present theoretical results explain and confirm the fact that the three isomers can coexist at room temperature. It has been shown that the single NMR resonance line at room temperature is divided into three different lines at low temperature with the ratio of area 1:1:0.3,[13] which is in good accord with the present calculation result. Based on the agreement between the present theoretical result and the previous experimental observation, we tentatively estimate the maximum error bar of the present calculation method, the B3PW91/6-31G* method, for the relative stability to be less than 2.0 kcal/mol.

In contrast to the above NCS(Ph_4) systems, the relative energies of NCO(Ph_4) systems, including the solvent effect, are 0.00, 0.08, and 9.88 kcal/mol for NCO(Ph_4)-in1, NCO(Ph_4)-in2, and NCO(Ph_4)-out, respectively. Even if the error of the present calculation method is considered, it is clear that the NCO(Ph_4)-out form is somewhat more unstable than the other two isomers. Based on the present result, we expect that the one broad NMR signal of the NCO(Ph_4) at room temperature will split into two lines at low temperature. The two isomers are calculated to have almost the same energy. We can now confirm that the two isomers experimentally observed in the NCO system are the NCO-in1 and the NCO-in2, which was understood based on the experimentally observed chemical shift.

We have found that the results by the B3PW91/6-31G* method have provided a reasonable and complete explanation of the experimentally observed number of isomers. We can expect the same level of confidence for the calculated values for the relative energy difference of not only the isomers but also some anticipated intermediate that might be observed experimentally.

3.3. The Stability of Possible Intermediates in the N−H Tautomerism. To study the N−H tautomerism of the monothia- and monooxacarbaporphyrin systems, we have considered the three most probable intermediates, which are depicted in the lower part of Figure 2. The first intermediate is expected to appear when the N−H hydrogen atom migrates via oxygen atom or sulfur atom to the neighboring nitrogen atom, and the intermediate will be referred to by NCX−XH (X = O, S). The second intermediate may occur when the H atom is moving via the inner methine (C21) of the inverted pyrrole, and it will be designated as NCX−CH2 (X = O, S). We may assume the third intermediate (NCX−CHCH), in which one of the H atoms in the second intermediate migrates to the neighboring carbon, C(1). Successive transfer of hydrogen to outer nitrogen affords the NCX-out isomer. The geometries of the three intermediates are optimized by using the B3PW91/6-31G* method without any geometrical constraint. The relative energy is calculated with respect to the corresponding NCX-in1 isomer, and the results are collected in Table 2. For easier reference, the relative energies of NCX-in2 and NCX-out isomers are included again in Table 2. The comparable values of the 2-aza-21-carbaporphyrin, which will be referred to as NCN(H_4), are also shown in the lower part of the table.

If we take the NCX-in1 or NCX-in2 of the present study to correspond to the Cph2 of the NCN(H_4) system, then the NCX-out of this study corresponds to the 2NHcph structure of the NCN(H_4).[17,23] The numbers in Table 2 show that the relative energy of the NCN(4H)-2NHcph (4.56 kcal/mol) is larger than the relative energy of the NCS-out isomer (3.27 kcal/mol) but smaller than the NCO-out (10.95 kcal/mol). As will be shown in the next section, the difference stems from the different size of the core cavity, i.e., the size of the NCN(H_4) core is small than the NCS(H_4) core but larger than the NCO(H_4) core.

When we study the stability and structures of anticipated intermediates, the first noticeable result is that the NCO−OH structure turns out to be not an intermediate but a transient structure. We made several efforts to find a local minimum corresponding to the NCO−OH structure, but the efforts were not successful. It means that the NCO−OH does not correspond

TABLE 2: Relative Energies (in kcal/mol) of Isomers and Expected Intermediates Calculated by Using the B3PW91/6-31G* Method

	isomers			intermediates		
NCX(R_4)	in1	in2	out	XH	CH2	CHCH
			Present Systems			
NCS(H_4)	0.00	0.51	3.27	42.9	2.73 (3.81)[b]	35.0
NCS(Ph_4)	0.00	0.95	2.07		5.77	37.1
NCO(H_4)	0.00	0.45	10.77	(53.55)[a]	11.07 (12.06)[b]	
NCO(Ph_4)	0.00	0.37	9.20		13.41	
			Other Systems			
	Cph2	2NHcph			21-H-cph	
NCN(H_4)[c]	0.00	4.56			3.0	
		5.7[d]				

[a] No local minimum structure is found for this intermediate. The number in parentheses is the lowest relative energy we have seen. [b] The relative energy obtained by using the B3LYP/6-31G** method. [c] The relative energy of NCN(H_4), the 2-aza-21-carba-porphyrin, is calculated by using the B3LYP/6-31G**//B3LYP/6-31G method. [d] The result by Ghosh et al. in ref 23.

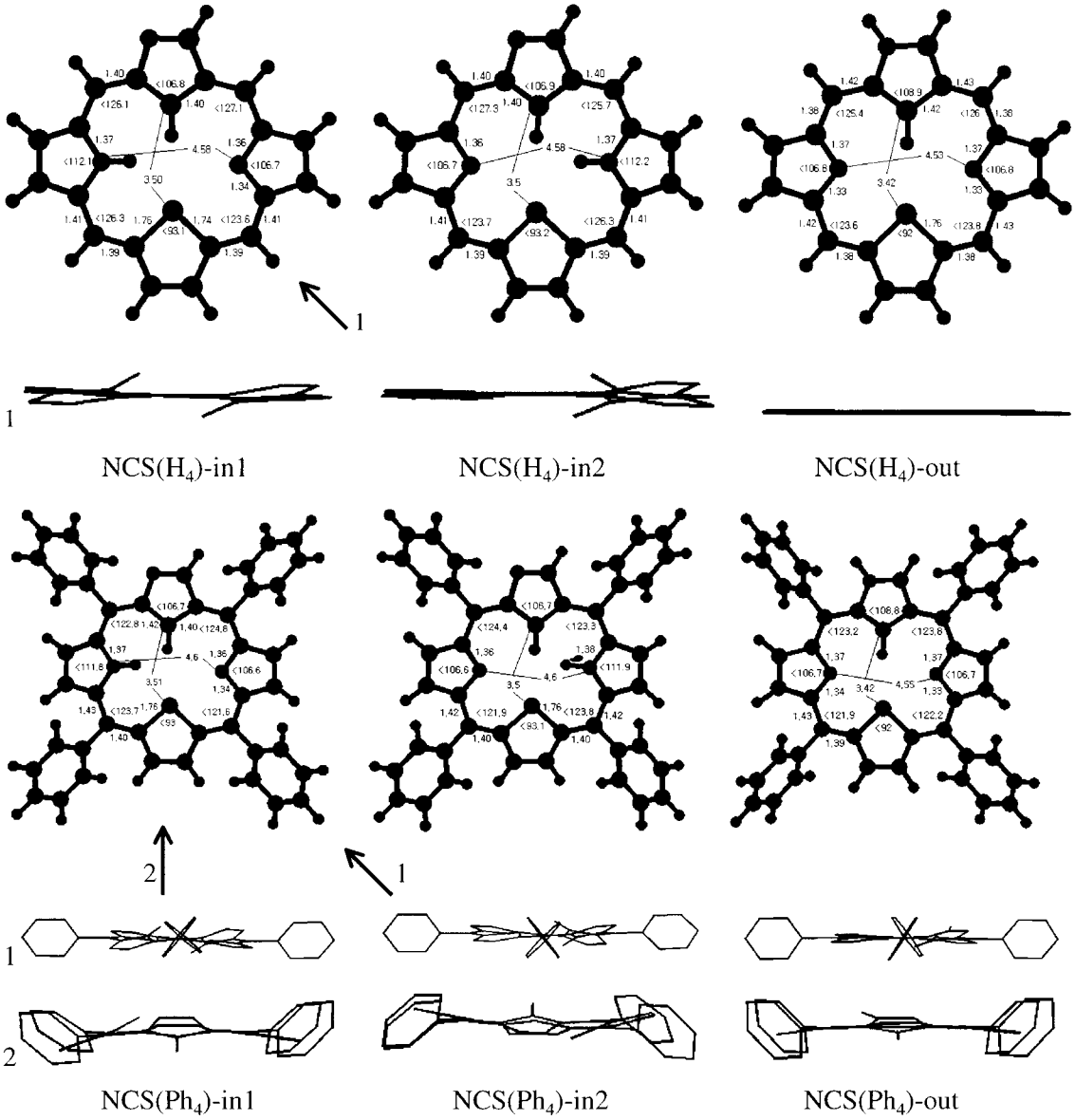

Figure 4. Optimized structures of monothiacarbaporphyrin isomers.

to a local minimum. The minimum relative energy we have seen of the transient structures occurring when the inner N−H atom approaches the O atom is at least 53.5 kcal/mol higher than the corresponding NCO-in1. In the case of the NCS systems, the NCS−SH structure is optimized to be an intermediate, and its relative energy is calculated to be 42.9 kcal/mol for NCS(H_4)-SH and 45.4 kcal/mol for NCS(Ph_4)-SH. The S−H part has large positive partial charges and the corresponding negative charges are equally distributed to the two N atoms in the core ring, as shown in Figure 2. Because of their high relative energy, the NCX-XH structures can hardly be an intermediate in the N−H tautomerism between NCX-in1 and NCX-in2.

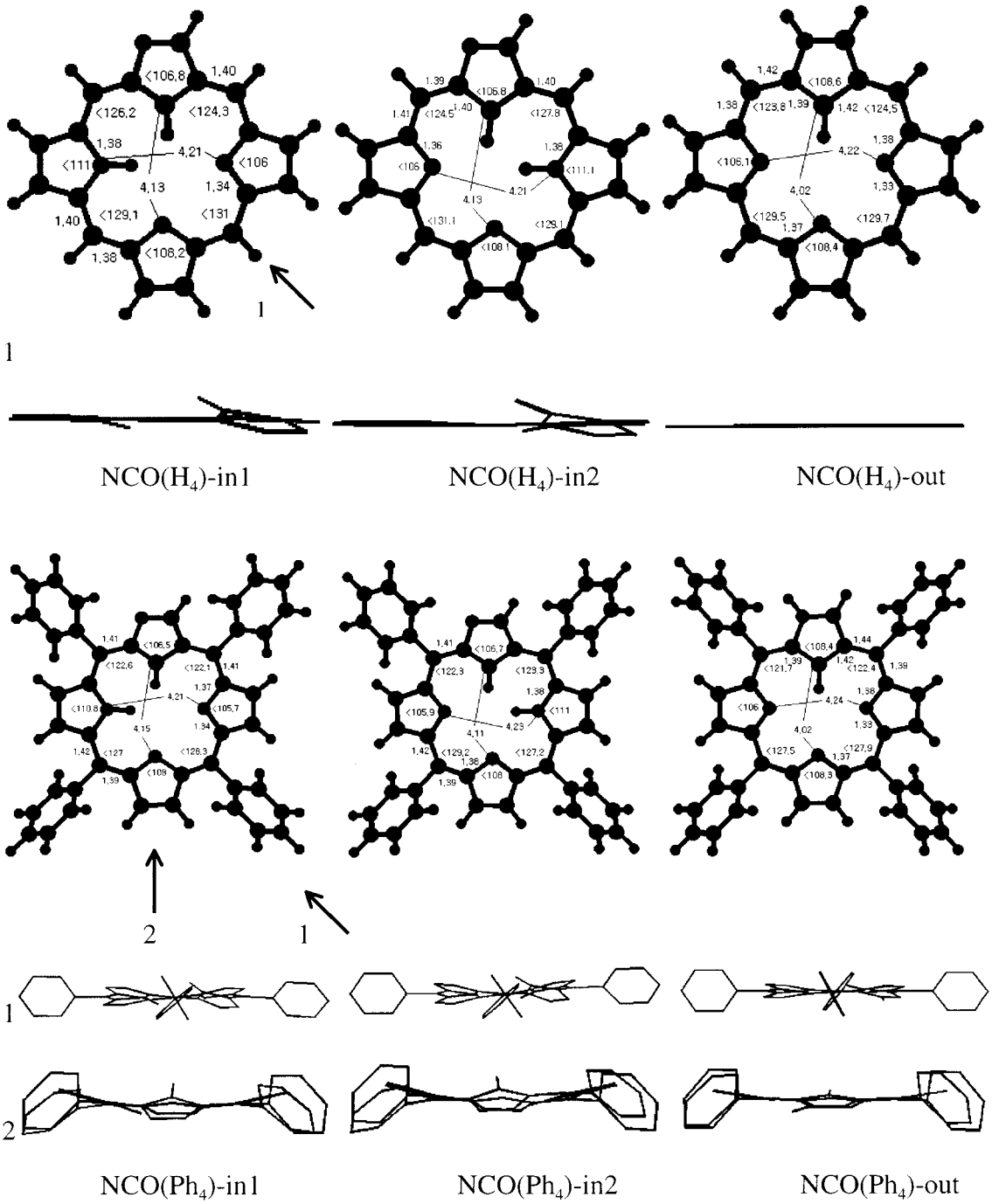

Figure 5. Optimized structures of monooxacarbaporphyrin isomers.

The structures of the second intermediates, NCX-CH2, are optimized with little difficulty. The relative stabilities of NCS-(H_4)−CH2 and NCO(H_4)−CH2 by the B3PW31/6-31G* method are 2.73 and 11.07 kcal/mol, respectively. It also can be seen that these values differ by only about 1 kcal/mol from the corresponding results in the parentheses by the B3LYP/6-31G** method. As was shown in Figure 2, the resonance path of the NCX−CH2 structure can satisfy the $(4n+2)\pi$ rule, and it might be the reason of the exceptional stability of this intermediate structure. The relative stabilities of the intermediates with *meso*-tetraphenyl groups are 5.77 and 13.41 kcal/mol for NCS(Ph_4)−CH2 and NCO(Ph_4)−CH2, respectively. It was noticed that the NCS(H_4)−CH2 has energy similar to the NCS(H_4)-out, whereas the NCS(Ph_4)−CH2 has energy 3.7 kcal/mol higher than the NCS(Ph_4)-out. A similar change is induced in the NCO systems by the *meso*-tetraphenyl substituents, i.e., the relative energy of the NCO(H_4)−CH2 11.07 kcal/mol is similar to that of NCO-(4H)-out, but the relative energy of the NCO(Ph_4)−CH2 is 4.21 kcal/mol higher than the NCO(Ph_4)-out isomer.

According to the study on the tautomerism of 2-aza-21-carbaporphyrin NCN(H_4),[17] the relative energy of its intermediate with two H atoms at C(21), 21-H−CPH, is 3.0 kcal/mol, which is very close to the relative energy of the NCS(H_4)−CH2 2.78 kcal/mol, but much smaller than that of NCO(H_4)−CH2 11.07 kcal/mol.

The optimization of a structure with no constraint under C_1 symmetry usually means that the optimized structure corresponds to an intermediate. To be more certain, however, we have calculated the harmonic frequencies by the B3PW91/6-31G* method, and no imaginary frequency appeared for the

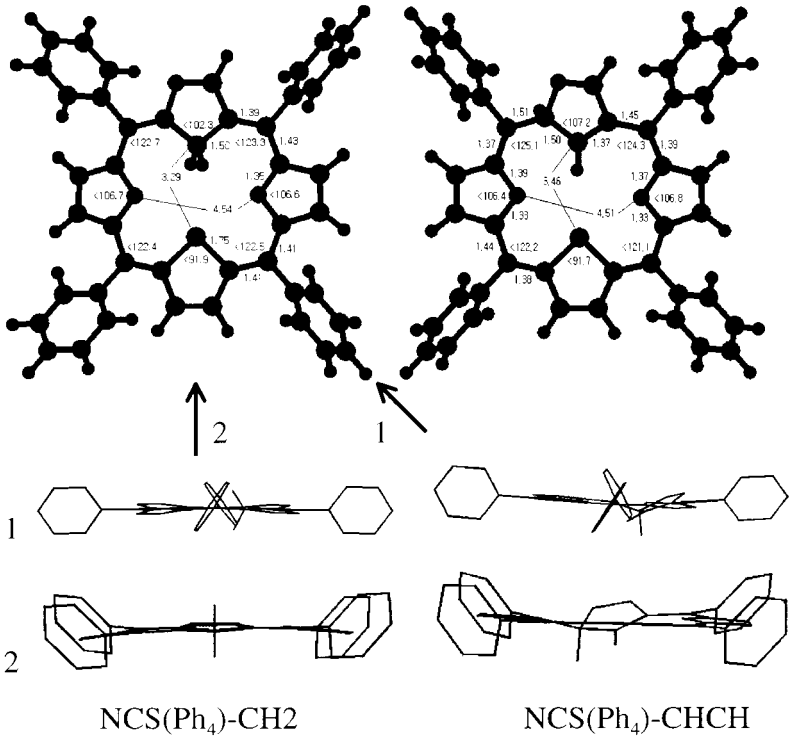

Figure 6. Optimized structures of intermediates in the tautomerism of the monothiacarbaporphyrin system.

$NCS(H_4)-CH2$ or the $NCO(H_4)-CH2$. Though we have not checked the possibility on the $NCS(Ph_4)-CH2$ and the $NCO(Ph_4)-CH2$, we believe not only the $NCX(H_4)-CH2$ but also the $NCX(Ph_4)-CH2$ could be an intermediate in the N−H tautomerism between the two isomers with inside N−H.

The activation barrier between the NCX-in1 (or NCX-in2) and the NCX−CH2 has not been explicitly obtained yet, but the barriers in NCS systems can be expected to be much lower than in NCO systems. To estimate the barrier, we notice the fact that the activation barrier from the cis to trans isomer of free-base porphyrin is confirmed to be about 9 kcal/mol in the recent work.[15] The H atom of the cis isomer, initially deviating outward from the core plane, has to bridge to the neighboring N atom on the core plane. The situation is quite similar here. The C−H bond at the C(23) site of the NCX−CH2 intermediate is also deviating outward from the plane and has to bridge to the neighboring N atom on the plane. Therefore, the overall barrier of the N−H tautomerism, NCX-in1→NCX−CH2→NCX-in2, of the present system can be estimated by adding the same amount of barrier, ∼9 kcal/mol, to the relative energy of NCX−CH2. The estimated overall barriers become about 12−15 and 20−22 kcal/mol for the monothia- and monooxacarbaporphyrin, respectively, which can be compared with the barrier of the free-base porphyrin, 22 kcal/mol. We are now quite sure that the tautomerism between the two isomer with inside N−H atom occurs via the intermediate having the two H atoms at the C(21) site. We also anticipate that the kinetics of the tautomerism of the monothiacarbaporphyrin (NCS) is faster than free-base porphyrin, whereas the kinetics of the monooxacarbaporphyrin (NCO) is comparable to free-base porphyrin.

As the third intermediate, we have selected the NCX−CHCH structure that can be expected to appear when an H atom of the NCX−CH2 structure moves to the N atom of the inverted pyrrole ring, resulting in the NCX-out isomer. Because the NCS-out isomer has energy comparable to the NCS-in isomers, the structure of the NCS−CHCH, depicted in Figure 2 and shown in Figure 6, is optimized, and their relative energies are calculated to be 35.0 and 37.1 kcal/mol for $NCS(H_4)-CHCH$ and $NCS(Ph_4)-CHCH$, respectively. Though the values are lower than the relative energies of the corresponding NCS−SH structure, they are still very high to be overcome at room temperature. The nonclassical tunneling effect can play an important role here. The possibility of other intermediates or paths connecting to the NCS-out isomer also cannot be excluded. The corresponding NCO−CHCH intermediate is not considered here because the NCS-out isomer is not observed experimentally due to its high relative energy.

3.4. The Structural Features of the Isomers and Intermediates. The actual shape of the optimized structures of the NCS and NCO isomers are shown in Figure 4 and Figure 5, respectively. The structures of $NCS(Ph_4)-CH2$ and $NCS(Ph_4)-CHCH$ intermediates are shown in Figure 6. The plane view of each isomer contains some bond length, interatomic distance, and angles. To provide more insight, the side-view of each isomer is given under the corresponding plane view. All protons, except the methine and nitrogenic protons, are not shown in the side views for clearer understanding. The direction of the side view is indicated by the numbered-arrow in the plane view and the number at the left of the side view. Only one side view is given for $NCX(H_4)$ isomers, but two side views are given for $NCX(Ph_4)$ isomers for better understanding. To make quantitative analysis on the structures, some of the selected bond lengths and angles of $NCS(Ph_4)$ and $NCO(Ph_4)$ isomers are presented in Table 3, and the corresponding values of $NCS(H_4)$ and $NCO(H_4)$ are given in the parentheses of the table. Though the comparison of the calculated geometrical parameters with experimental values is impossible for the present isomers due to the lack of any experimental X-ray result for them, several previous theoretical works on experimentally determined structures have shown that the results by DFT methods are accurate enough.[15,17,19b] The deviations in bond lengths and angles are within 0.01 Å and 0.3°, respectively. Similar accuracy can be expected for the present results.

TABLE 3: The Bond Length (Å), Non-bonded Distance (Å), and Dihedral Angle (degrees) of NCX(Ph_4) (corresponding values for NCX(H_4) in parentheses)

	NCS(Ph_4)			NCO(Ph_4)		
	-in1	-in2	-out	-in1	-in2	-out
L_1: C(1)−C(21)	1.419	1.408	1.392	1.409	1.402	1.389
	(1.414)	(1.403)	(1.390)	(1.404)	(1.401)	(1.387)
L_2: C(21)−C(4)	1.401	1.411	1.420	1.397	1.402	1.417
	(1.398)	(1.407)	(1.417)	(1.395)	(1.397)	(1.415)
L_3: C(4)−C(5)	1.422	1.418	1.444	1.415	1.411	1.440
	(1.405)	(1.404)	(1.431)	(1.402)	(1.399)	(1.429)
∠P0(5−10−15−20)	−0.58	2.52	−0.34	0.76	0.05	0.55
	(1.00)	(−1.41)	(0.00)	(−0.38)	(1.21)	(0.00)
∠Pcorr(23−24−21−22)	7.51	7.96	3.81	6.68	4.11	5.26
	(4.08)	(4.01)	(0.00)	(4.05)	(3.98)	(0.02)
∠Py1(10−15−20−2)	−16.80	14.42	−10.89	15.91	12.81	8.68
	(−9.91)	(−6.65)	(−0.02)	(8.12)	(5.49)	(−0.01)
∠Py2(15−20−5−7)	10.58	−10.51	6.88	−11.65	−9.88	−8.23
	(1.51)	(4.58)	(0.00)	(0.17)	(−0.26)	(0.04)
∠Py3(20−5−10−12)	−7.84	5.10	−4.08	12.02	6.81	8.79
	(−3.60)	(−0.51)	(0.00)	(1.53)	(−0.83)	(0.00)
∠Py4(5−10−15−17)	16.35	−7.83	6.41	−14.36	−3.92	−9.05
	(9.50)	(−1.86)	(0.00)	(−3.66)	(1.60)	(−0.02)
∠CH(25−5−10−15)	−13.97	12.43	−9.14	16.11	12.19	6.37
	(−11.60)	(−9.28)	(−0.04)	(13.36)	(10.93)	(−0.02)
∠NH[a]	13.53	−10.46	9.26	−7.73	−7.29	−7.96
	(11.97)	(8.65)	(0.03)	(−4.34)	(−2.68)	(0.00)
D_1: C(21)-X(23)[b]	3.510	3.512	3.418	4.146	4.110	4.020
	(3.498)	(3.501)	(3.417)	(4.131)	(4.130)	(4.017)
D_2: N(22)−N(24)[b]	4.600	4.596	4.548	4.210	4.228	4.244
	(4.585)	(4.581)	(4.528)	(4.208)	(4.207)	(4.225)

[a] See the text for the definition. [b] The D1/D2 of free-base porphyrin and 2-aza-21-carbaporphyrin, by the B3PW91/631-G*, are 4.045/4.227 Å and 3.991/4.375 Å, respectively.

First of all, there was an argument that the bond length L1: C(1)−C(21) might be longer than L2:C(21)−C(4).[40] This assumption was the starting point in the discussion about the NCS-in1 and NCS-in2 observed by the ^{1}H NMR spectra.[13] The L1 is longer than L2, as was previously assumed, in the case of NCS(Ph_4)-in1; the length of L1 is 1.419 Å and L2 is 1.401 Å. The results in Table 3, however, show that the length of L1 and L2 are flexible enough depending on the position of the inner nitrogenic proton, N−H. When the inner N−H atom moves to the N atom at the other side, resulting in the NCS-in2 structure, the lengths of L1 and L2 become 1.408 and 1.411 Å, respectively, resulting in L2 being longer than L1. The same changes appear in L1 and L2 of the NCO isomers. The difference between L1 and L2, however, is very small (0.00−0.18 Å) due to the resonance of π-electrons as shown in Figure 2. In contrast, the difference between L1 and L2 in NCX-out isomer is about 0.03 Å due to the broken resonance path, as mentioned before. The bond length L3:C(4)−C(5) also supports the different resonance path, as seen in Figure 2; the L3 is longer in NCX-out than NCX-in1 or NCX-in2.

The deformation of the porphyrin plane as well as the deviation of the inner methine proton C−H and nitrogenic proton N−H from the plane require further discussion. Though there is no unique way of defining the planarity of the porphyrin's imaginary plane, our optimized structure has shown that the four meso positions, C(5), C(10), C(15), C(20), usually reside on the same plane, and we are going to use that plane as the reference plane. The planarity of the reference plane is given by the dihedral angle ∠P0:C(5)−C(10)−C(15)−C(20) in Table 3. Another dihedral angle, ∠Pcore:X(23)−N(24)−C(21)−N(22), is also examined to observe the planarity of the four ligand atoms that will coordinate to an incoming transition element. The deformations of four pyrrole rings from the reference plane are defined by the dihedral angles ∠Py1:C(10)−C(15)−C(20)−N(2), ∠Py2:C(15)−C(20)−C(5)−C(7), ∠Py3:C(20)−C(5)−C(10)−C(12), and ∠Py4:C(5)−C(10)−C(15)−C(17). The deviation of the inner C−H from the plane is defined by the dihedral angles ∠CH:H(25)−C(5)−C(10)−C(15), whereas the deviation of the N−H is determined by the dihedral angles ∠NH:H(26)−C(20)−C(5)−C(10), ∠NH:H(26)−C(10)-C(15)−C(20), and ∠NH:H(26)−C(5)−C(10)−C(15) for NCX-in1, NCX-in2, or NCX-out, respectively. More visual guess can be gained from the side views in Figures 4 and 5.

From the side views as well as from the values of ∠P0, ∠Pcore, and ∠Py*n*, it can be seen that all atoms in the NCS-(4H)-out and the NCO(4H)-out isomer reside on the same plane. When the N−H atom resides inside the core, however, the inverted pyrrole ring (Py1) and the pyrrole ring with the N−H (the Py4 in NCX-in1 or the Py2 in NCX-in2) deviate from planarity. As can be seen from the figures and from the different signs of the ∠CH and ∠NH, the two pyrrole rings direct opposite sides of the plane. It is also noticeable that the magnitude of ∠CH is much larger than that of ∠NH in NCO-in1 and NCO-in2, but the difference between ∠CH and ∠NH is very small in NCS-in1 and NCS-in2. By the introduction of the *meso*-phenyl groups, the planes are distorted further, but overall features remain the same. Though the change of the sign of ∠Pyn of NCX(Ph_4) isomers shows that the optimized structures of this work correspond to the saddle type,[23] other structures corresponding to the ruffle, wave, or dome types of dodeca-substituted porphyrins[23] also can be expected in actual experiments of the present systems, due to the high flexibility of the porphyrin's core framework. When the bond lengths of NCX(Ph_4) isomers are compared with the corresponding values in parentheses of NCX(H_4), it can be seen the changes in bond lengths and angles by the *meso*-phenyls are not so large, except for the deformation from the planarity.

The dihedral angle ∠Pcore defines the planarity of the core plane made by the four ligand atoms. As expected, the dihedral angles of NCS(H_4)-out and NCO(H_4)-out are almost zero, and

those of NCX(H_4)-in1 and NCX(H_4)-in2 are all about 4° due to the repulsion between the two inner H atoms. Little difference is there between the NCS and NCO systems. When the *meso*-H atoms are substituted with the *meso*-phenyl groups, however, some differences between them are induced. The deformations from planarity increase by about the same amount, 3.43−3.95°, in all the three NCS(Ph_4) isomers. In contrast, the changes in NCO(Ph_4) isomers differ: 2.63°, 0.13°, and 5.24° for OCN-(Ph_4)-in1, OCN(Ph_4)-in2, and OCN(Ph_4)-out, respectively.

To predict the binding character of the core ligands toward an incoming transition metal element, the size of the core cavity is estimated by the diagonal distances D1 and D2, where D1 is the distance between two N atoms in the core ring and D2 is the distance between the S(23) or O(23) atom and the C(21) atom of the inverted pyrrole ring. The distances are not changed much by the *meso*-phenyls. In the case of NCO(Ph_4) systems, the lengths of D1/D2 are 4.146/4.210 Å, 4.110/4.228 Å, and 4.020/4.244 Å for NCO-in1, NCO-in2, and NCO-out, respectively. The shape of the core cavity is approximately square. In the case of NCS(Ph_4) systems, by contrast, the distances are 3.509/4.600 Å, 3.512/4.596 Å, and 3.418/4.548 Å for NCS-in1, NCS-in2, and in NCS-out, respectively. It means that when the O(23) atom is replaced by the S(23) atom, the internuclear distances between the two inside N atoms increase about 30−40 pm, and the distance between C(21) and X(23) atoms decreases about 60 pm, resulting in a rectangular or rhombic shape of the core cavity. The D1/D2 values of free-base porphyrin and 2-aza-21-carbaporphyrin are calculated to be 4.045/4.227 Å and 3.991/4.375 Å, respectively, by the B3PW91/6-31G* method. The different shape of the core cavity deserves to be noted in anticipating the metal coordination property of the new carbaporphyrin derivatives.

The optimized structure in Figure 6 shows that the porphyrin plane of the NCS(Ph_4)−CH2 is almost planar. The planar structure and the preservation of the $(4n+2)\pi$ rule for aromaticity might be the reason of the exceptionally small relative energy, 3−6 kcal/mol, of this intermediate. The structure of NCS(Ph_4)−CHCH in Figure 6 corresponds to the dome type, in which the methine proton, C−H, resides on the plane of the inverted pyrrole and the H atom on the C(1) site directs outward of the dome. The large bond lengths of C(1)−C (20) and C(4)−C(5), 1.51 and 1.45 Å, respectively, demonstrate the broken resonance path, which might be the main reason for the large relative energy, 37.1 kcal/mol.

4. Conclusions

By using density functional theory methods, we have shown that the energy difference between the three isomers of the 2-aza-21-carba-23-thia-porphyrin (NCS) is less than 2 kcal/mol, which explains the coexistence of the three isomers at room temperature. In contrast, the isomer of 2-aza-21-carba-23-oxa-porphyrin (NCO) with outer N−H is calculated to have energy about 9−11 kcal/mol higher than the two isomes with inside N−H having almost the same energy. The result explains why only two isomers can be detected experimentally. It also has been shown that the relative stability among the isomers is governed not by the steric hindrance between the two hydrogen atoms inside the core but by the difference in the resonance path of π-electrons. The isomers with inside N−H do satisfy the (4n+2) rule of aromaticity but the isomer with outside N−H does not.

It has also been shown that the monothia- and monooxacarbaporhyrin systems have a larger dipole moment than the cabaporphyrin without heteroatom and the free-base porphyrin, and this fact could be useful in designing or predicting experimental work with the new porphyrin systems.

The most plausible intermediate between the two N−H isomers with inside N−H turned out to have a structure with two hydrogen atoms at the C(21) atom of the inverted pyrrole ring. The relative energies of the intermediates with respect to the isomers with inside N−H are calculated to be about 3 and 11 kcal/mol for the NCS and the NCO systems without tetra-*meso*-phenyl groups, respectively. The presence of the phenyl groups increases the relative energies about 3 kcal/mol. We estimated the overall barrier of the tautomerism between the isomers with inside N−H to be about 12−15 and 20−22 kcal/mol for the NCS and NCO systems, respectively. The relative energy of another intermediate, expected to appear during the migration of the inside N−H to the outer N−H, is calculated to be about 33−35 kcal/mol for the NCS systems.

Considering the possible metal coordination property, it is worth noting that the shape of the porphyrin's core cavity made by the four ligand atoms is calculated to be almost square in the oxacarbaporphyrin (NCO) systems but rectangular or rhombic in the thiacarbaporhpyrin (NCS) systems.

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