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Theoretical Study on Conformation and Electronic State of Hückel-Aromatic Multiply N-Confused [26]Hexaphyrins

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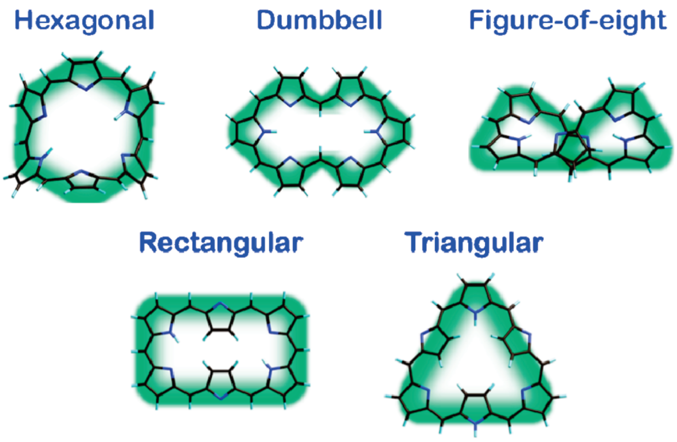

Conformations and electronic states of Hückel-aromatic regular, singly, doubly, and triply N-confused [26]hexaphyrins were investigated using density functional theory (DFT) calculations. A comparison of the molecular energies of 754 structures in all revealed that the most stable conformers depend on the degree of confusion, where ring strain and intramolecular hydrogen bonding would play a critical role. Consequently, regular and singly N-confused hexaphyrins prefer a dumbbell conformation, doubly N-confused hexaphyrin prefers a rectangular conformation, and triply N-confused hexaphyrin prefers a triangular conformation. Introduction of N-confused pyrrole rings into the hexaphyrin framework causes narrower HOMO−LUMO energy gaps, while it does not affect the NICS values or aromaticity significantly. The steric repulsion imposed by *meso*-aryl substituents largely affects the relative energies among the conformers.

Introduction

In recent years, research on expanded porphyrins has significantly grown.[1] Of special note, the discovery of a simple method for the synthesis of *meso*-aryl expanded porphyrins has stimulated rapid development in this field.[2] Depending on their structures, interesting properties such as multimetal coordination,[3] Möbius aromaticity,[4] splitting reactions,[5] nonlinear optics,[6] etc. have been discovered. In

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these studies, molecular shapes or conformations are undoubtedly key factors in understanding their unique properties. Thus, efforts to obtain a deeper insight into their conformations have become increasingly important.

Among expanded porphyrins, knowledge of hexaphyrins has been growing rapidly in the past decade, partly because of their accessibility.[2,7] The regular hexapyrrolic macrocycles have the privilege of conformational flexibility, allowing us to obtain a variety of metal complexes bearing unique 3D structures as well as electronic states.[8] In contrast, a prediction of their conformations is usually difficult. One experimental remedy for this conformational complication is the introduction of confusion. For example, C_2-symmetric doubly N-confused hexaphyrin preferentially takes a rectangular conformation, which is beneficial in forming bimetallic complexes.[7,9] Meanwhile, C_3-symmetric triply N-confused hexaphyrin takes a triangular conformation exhibiting unique photophysical properties.[10] This confusion approach brings not only conformational benefit but also molecular diversity in the macrocycles.[11] Thus, understanding the effect of confusion on the conformations and electronic properties of hexaphyrins is an interestingly important issue to be addressed.

Although theoretical calculations are powerful tools to study molecular conformations and electronic properties, considerable support of experimental evidence is essential to achieve meaningful discussion.[12] Among the expanded porphyrins thus far reported, the hexapyrrolic compounds are some of the most studied macrocycles and a fairly large amount of information on their conformations is available, especially owing to the great success in X-ray crystallographic analyses. Depending on the substituents at the *meso* positions and the β-pyrrolic positions, hexaphyrins take a variety of structures such as dumbbell, figure-eight, rectangular, and triangular conformations, where protonation, metal coordination, and oxidation states often play important roles.[8,10,13] Conformational changes imposed by the confusion described above are also intriguing. The rich experimental results in the hexapyrrolic compounds are favorable as the subject of a theoretical study.

In this study, conformations of regular, singly, doubly, and triply N-confused [26]hexaphyrins have been investigated using density functional theory (DFT)[14] calculations. The relative energies among conformers as well as NH tautomers are briefly discussed, and the relationship between the conformations and the electronic states is also examined. Here only Hückel-aromatic [26]hexaphyrins have been calculated to reveal their stability and electronic structures. The other members of the hexaphyrin family such as [28]hexaphyrins and Möbius-type conformers will be studied in a subsequent report. It should be noted that replacement of pyrrole rings by heteroaromatic rings,[15] benzene rings,[16] and other conjugated substructures have prompted further studies of the hexaphyrin family and the conformational issues are still rather important in these compounds.

Calculation Details

All DFT calculations were performed with the Gaussian03 program package.[17] The basis sets implemented in the program were used. The B3LYP density functional method[18] was used with the 6-31G** basis set for structural optimizations as well as frequency analyses. The 6-311++G** basis set was used for nucleus-independent chemical shift (NICS) calculations, since larger basis sets are recommended for reliability.[19] Initial structures have been arbitrarily constructed with the aid of semiempirical AM1 calculations. Equilibrium geometries were fully optimized and verified by the frequency calculations, where no imaginary frequency was found. The NICS values were calculated with a gauge invariant atomic orbitals (GIAO) method at the center of the 36 heavy atoms constructing the hexaphyrin framework of the optimized structure.

Structures

Regular hexaphyrin (**N0Hex**), singly N-confused hexaphyrin (**N1Hex**), C_2-symmetric doubly N-confused hexaphyrin (**N2Hex**), and C_3-symmetric triply N-confused hexaphyrin (**N3Hex**) were arbitrarily selected as the main candidates (Chart 1). Although there exist many isomers in multiply N-confused hexaphyrins related to the relative positions of N-confused pyrrole rings, only symmetrical structures

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CHART 1. Representative Structures of Regular Hexaphyrin and Its Confused Isomers

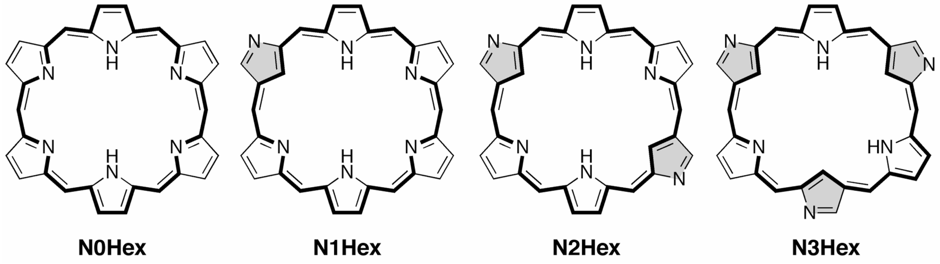
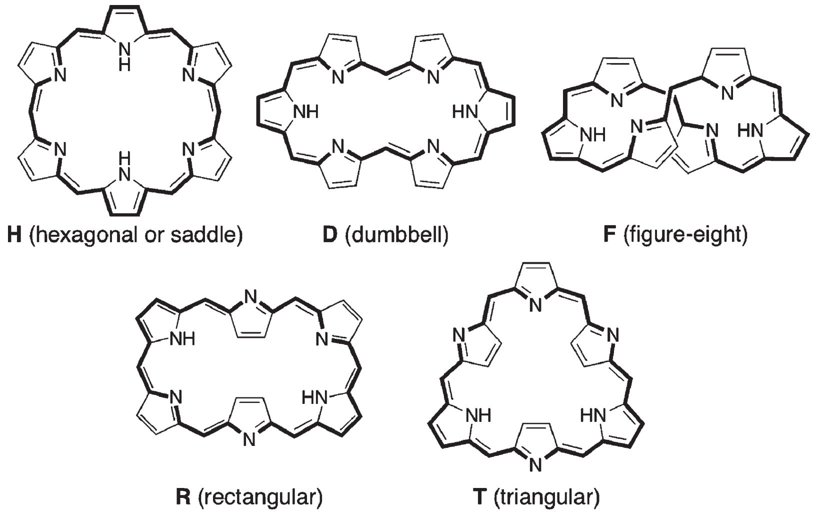


CHART 2. Representative Description of Hexaphyrin Conformations



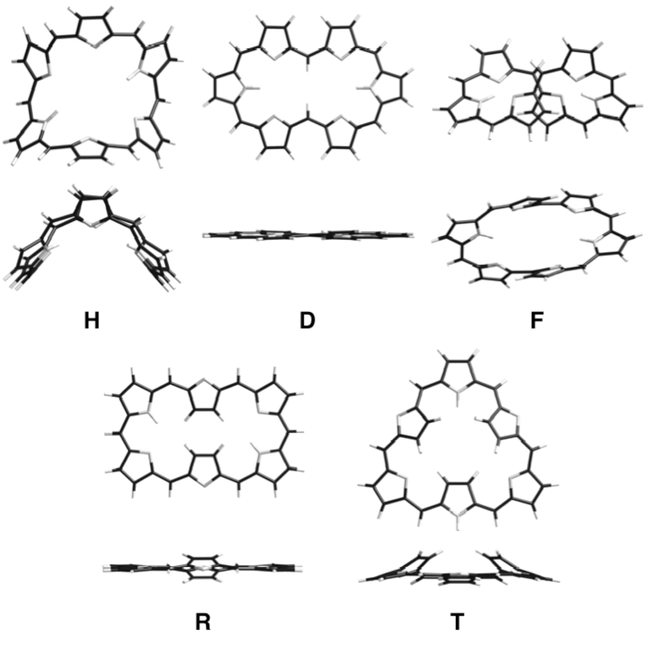


FIGURE 1. 3D structures (top and side views) of representative hexaphyrin conformers.

have been considered here. Syntheses of the C_2-symmetric doubly N-confused hexaphyrins and the C_3-symmetric triply N-confused hexaphyrins have been reported, but other types of multiply N-confused hexaphyrins have not yet been reported.[9,10]

On the basis of experimental evidence and preliminary investigations by semiempirical calculations, five conformations, namely, hexagonal (or saddle) (**H**), dumbbell (**D**), figure-eight (**F**), rectangular (**R**), and triangular (**T**) conformations were determined to be taken into consideration (Chart 2). For simplicity, each conformation is denoted by the initial letters. In brief, the calculated structures of hexaphyrins are represented as **N0Hex-D** and **N2Hex-R**. For protonated forms, the suffix "**-H$^+$**" is added as **N3Hex-T-H$^+$**. Although there exist four stages of protonation, only monoprotonated forms were taken into consideration to verify the relationship between conformation and intramolecular hydrogen bonding.

Representative optimized structures for each conformation are shown in Figure 1. Specifically, an H conformer would prefer to have a saddlelike structure rather than a planar structure. Severe distortion from planarity would imply significant ring strain. No example of this conformation has been reported. A D conformer has a nearly planar structure, and much less ring strain would be expected. This is the only conformer that possesses *meso*-CH moieties pointing inward the macrocycle and would be highly affected by the substituents at the *meso* positions. This conformation is frequently observed in the *meso*-unsubstituted derivatives.[20] An F conformer is obviously distorted from planarity. Nevertheless, such conformation is

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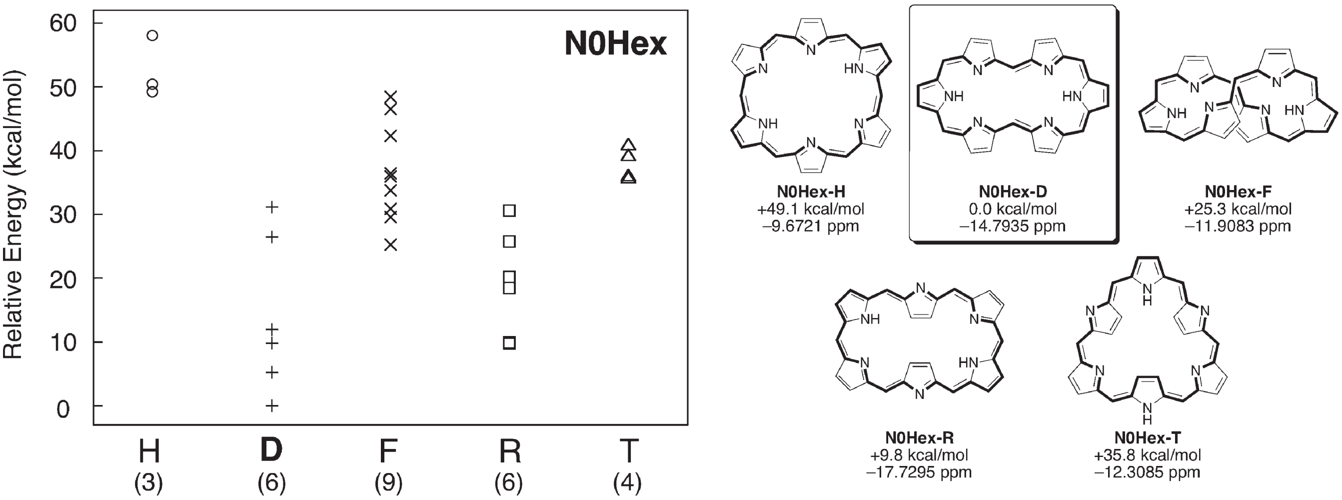

FIGURE 2. Relative energies of **N0Hex** tautomers and conformers. Numbers in parentheses denote the number of calculated NH tautomers. Structures, relative energies, and NICS values of the most stable tautomers are shown on the right.

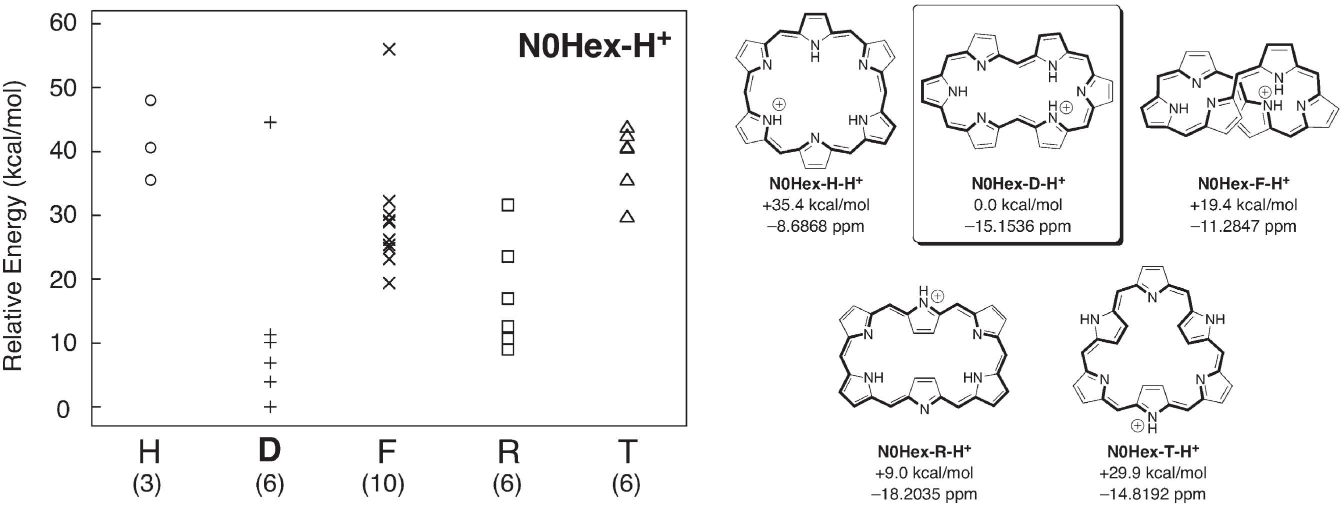

FIGURE 3. Relative energies of **N0Hex-H**$^+$ tautomers and conformers. Numbers in parentheses denote the number of calculated NH tautomers. Structures, relative energies, and NICS values of the most stable tautomers are shown on the right.

observed in *meso*-CF_3 [26]hexaphyrin as well as [28]hexaphyrins.[13,21] An R conformer is slightly deformed from the planar structures due to CH···CH repulsions inside the macrocycle. This conformation is popularly observed in the hexapyrrolic compounds.[9] A T conformer was recently reported in regular and triply N-confused hexaphyrins.[10] It deviates slightly from planarity due to the transannular CH···CH repulsions, quite similar to the case for the R conformer.

In a conformational study on [26]hexaphyrins, NH tautomers should be also taken into consideration. Hence, all NH tautomers that maintain [26]annulenic substructures have been investigated. The compounds without [26]annulenic substructures are excluded, since they would have higher energies due to a loss of aromatic stabilization.

Results and Discussion

Relative Energies of Regular Hexaphyrins. Relative energies of NH tautomers and conformers of regular hexaphyrins are summarized in Figure 2. The vertical axis corresponds to relative energies, and each symbol represents one NH tautomer. NH tautomerism causes an energy difference of 10−30 kcal/mol in each conformer, suggesting that the selection of appropriate NH tautomers is crucially important for conformation analysis. Among the five conformers, a dumbbell structure (**N0Hex-D**) is the most stable and a rectangular structure (**N0Hex-R**) is the second most stable. The energy difference between **N0Hex-D** and **N0Hex-R** is 9.8 kcal/mol. The other three conformers (**N0Hex-H**, **N0Hex-F**, **N0Hex-T**) are much less stable. Similar calculations were also carried out on the protonated derivatives (Figure 3). In comparison to the free base hexaphyrins, no significant change is observed in relative energies among the conformers.

Relative Energies of Singly N-Confused Hexaphyrins. One pyrrole ring confusion in hexaphyrin frameworks mildly alters the relative energies among the NH tautomers and conformers (Figures 4 and 5). Similar to the case for the regular hexaphyrins, a dumbbell structure (**N1Hex-D**) is the most stable and a rectangular structure (**N1Hex-R**) is the second most stable. However, the energy difference between **N1Hex-D** and **N1Hex-R**

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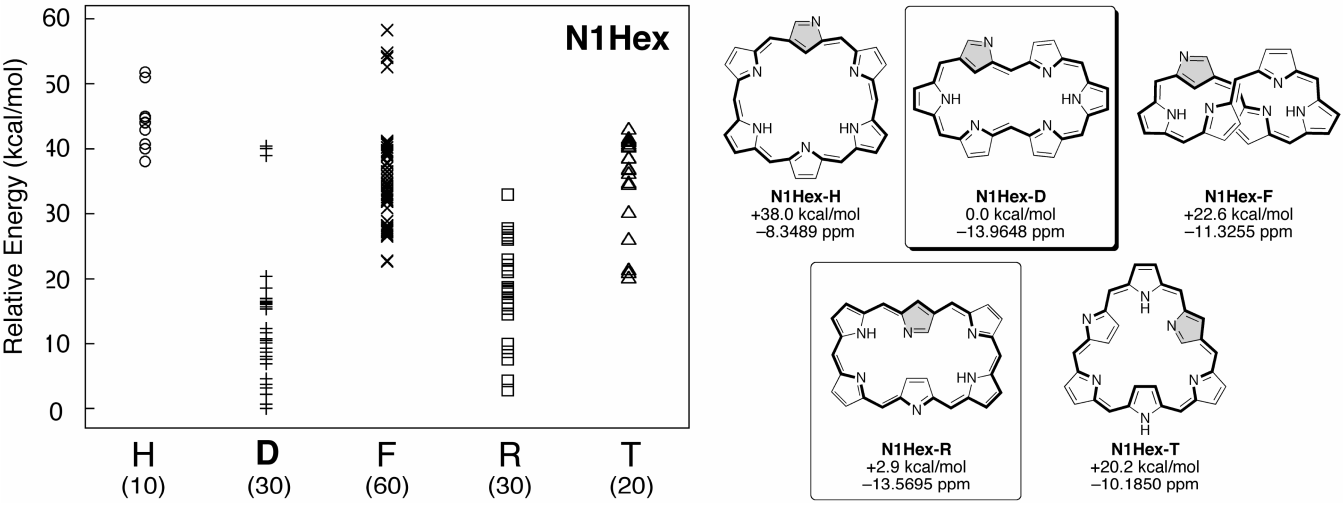

FIGURE 4. Relative energies of **N1Hex** tautomers and conformers. Numbers in parentheses denote the number of calculated NH tautomers. Structures, relative energies, and NICS values of the most stable tautomers are shown on the right.

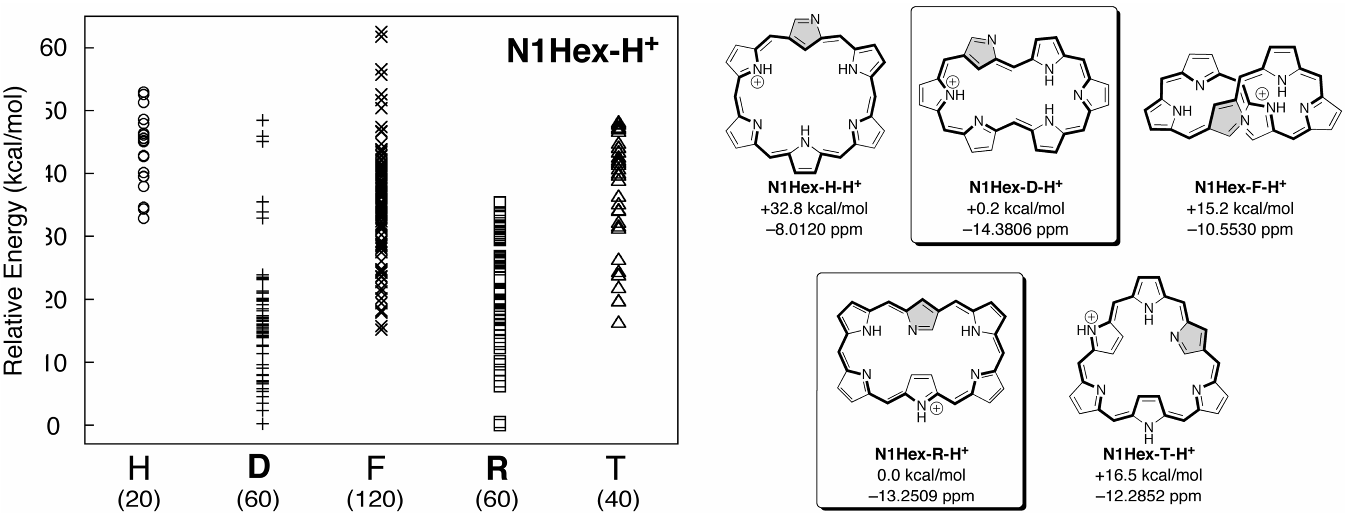

FIGURE 5. Relative energies of **N1Hex-H**$^+$ tautomers and conformers. Numbers in parentheses denote the number of calculated NH tautomers. Structures, relative energies, and NICS values of the most stable tautomers are shown on the right.

becomes smaller (2.9 kcal/mol). The other structures (**N1Hex-H**, **N1Hex-F**, **N1Hex-T**) are still much less stable. Upon protonation, energy differences among the conformers become significantly small, which would imply high flexibility of the singly N-confused hexaphyrin skeletons. Of special note, **N1Hex-R-H**$^+$ and **N1Hex-D-H**$^+$ show almost the same stability.

Relative Energies of Doubly N-Confused Hexaphyrins. In doubly N-confused hexaphyrins, a change from the regular and singly N-confused hexaphyrins is observed in the most stable conformer (Figures 6 and 7). Thus, an R conformer (**N2Hex-R**) is more stable than a D conformer (**N2Hex-D**) with a relative energy of 3.8 kcal/mol. Meanwhile, the other three conformers (**N2Hex-H**, **N2Hex-F**, **N2Hex-T**) are still rather unstable. Protonation further stabilizes R conformers. The energy difference between an R conformer (**N2Hex-R-H**$^+$) and a D conformer (**N2Hex-D-H**$^+$) extends to 9.1 kcal/mol.

Relative Energies of Triply N-Confused Hexaphyrins. Relative energies among the conformers are drastically changed in the case of triply N-confused hexaphyrins (Figures 8and 9). A T conformer (**N3Hex-T**) is the most stable, and an R conformer (**N3Hex-R**) is the second most stable. A D conformer (**N3Hex-D**) is no longer favorable, and the other two conformers (**N3Hex-H** and **N3Hex-F**) are consistently much less stable. Upon protonation, a T conformer (**N3Hex-T-H**$^+$) becomes rather favorable and the energy difference from the second most stable R conformer (**N3Hex-R-H**$^+$) is over 20 kcal/mol.

General Evaluation of Ring Strain. Ring strain energy is an important factor, which governs the relative energies in macrocyclic compounds. Generally, ring strain originates in (1) abnormal bond lengths, (2) abnormal bond angles, (3) unfavorable dihedral angles, and (4) transannular repulsions. In the case of large macrocyclic compounds such as hexaphyrins, abnormal bond lengths and bond angles are seldom observed, since those values are commonly averaged without considerable cross-linkage. Unfavorable dihedral

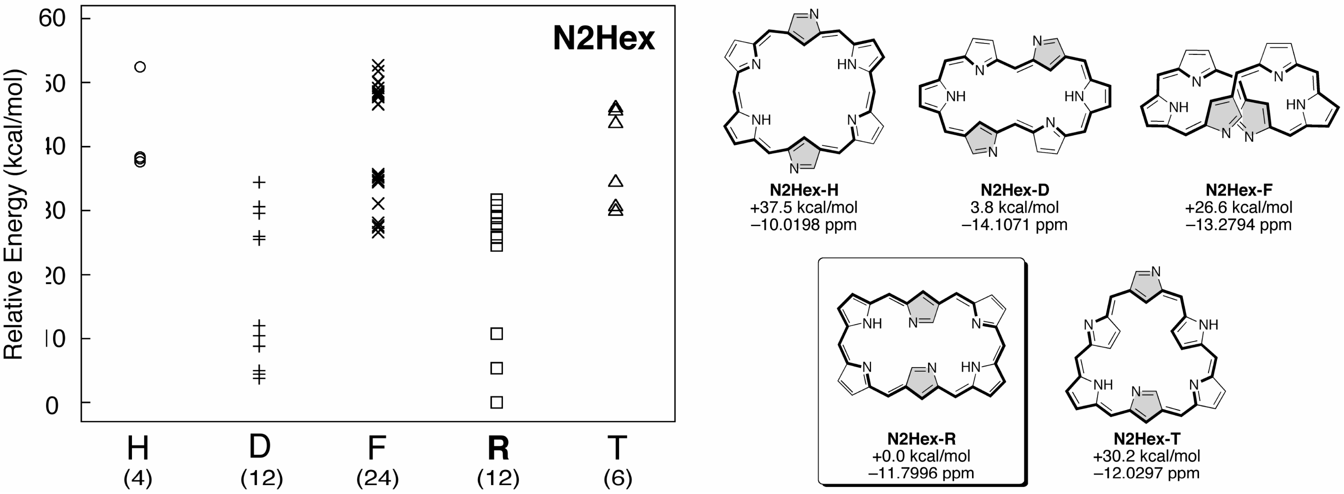

FIGURE 6. Relative energies of **N2Hex** tautomers and conformers. Numbers in parentheses denote the number of calculated NH tautomers. Structures, relative energies, and NICS values of the most stable tautomers are shown on the right.

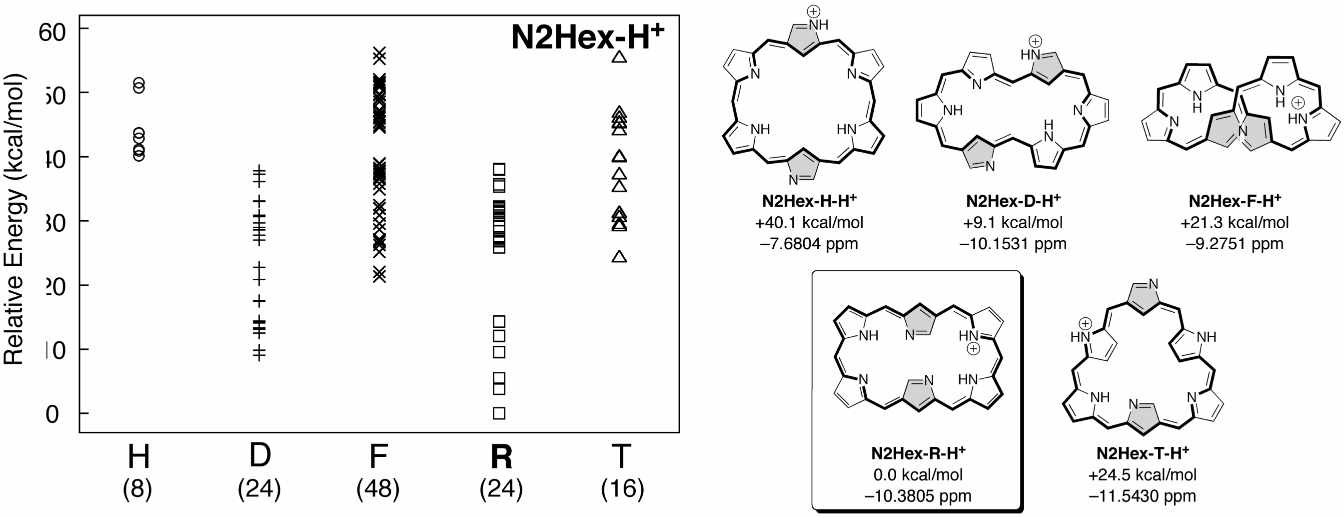

FIGURE 7. Relative energies of **N2Hex-H**$^+$ tautomers and conformers. Numbers in parentheses denote the number of calculated NH tautomers. Structures, relative energies, and NICS values of the most stable tautomers are shown on the right.

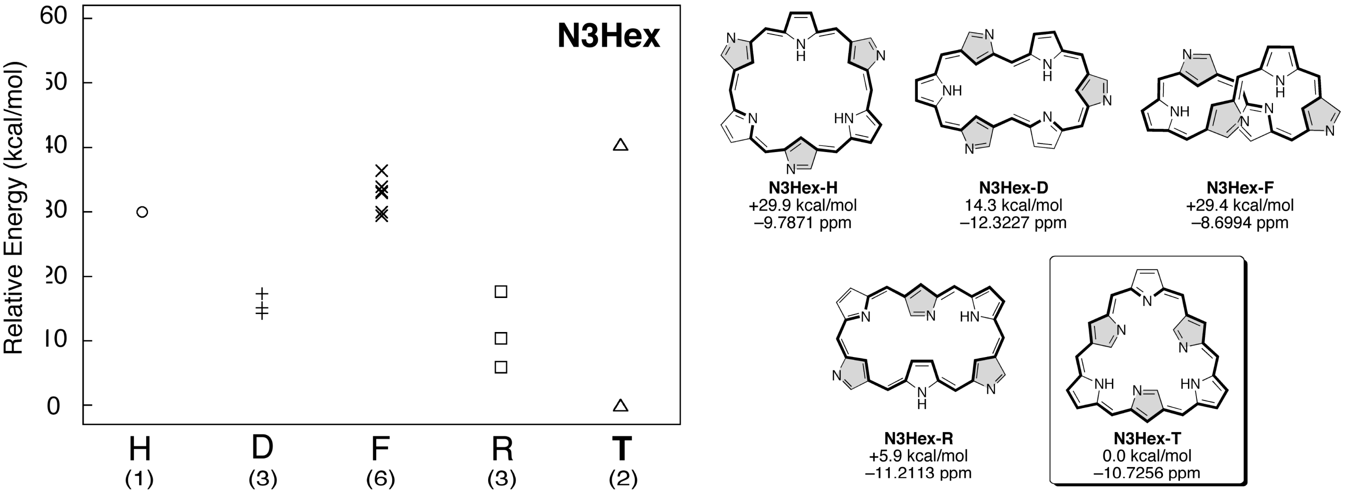

FIGURE 8. Relative energies of **N3Hex** tautomers and conformers. Numbers in parentheses denote the number of calculated NH tautomers. Structures, relative energies, and NICS values of the most stable tautomers are shown on the right.

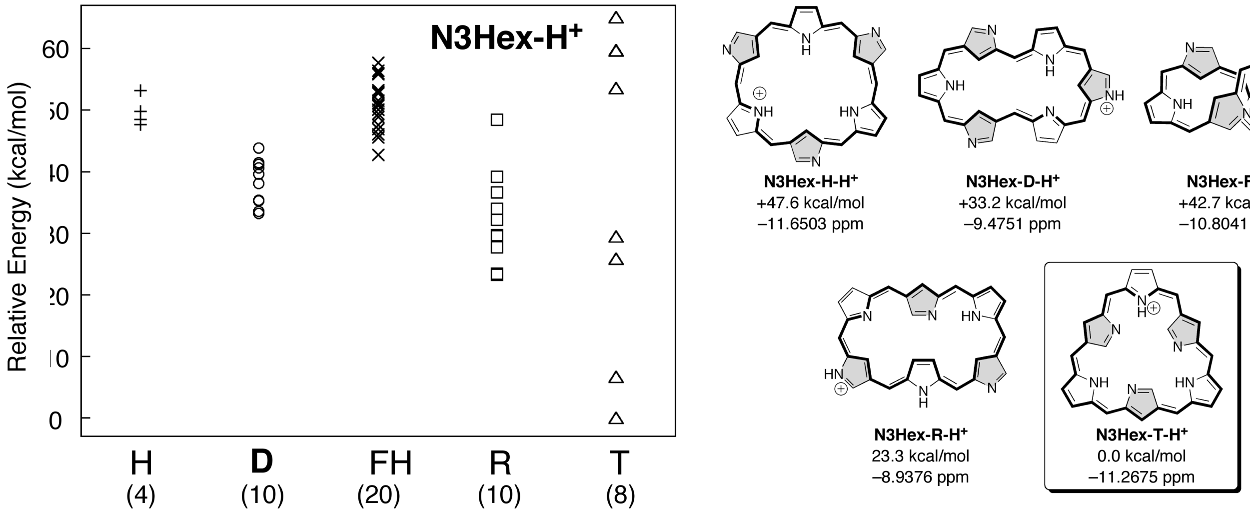

FIGURE 9. Relative energies of **N3Hex-H**$^+$ tautomers and conformers. The numbers in the parentheses mean the number of calculated NH-tautomers. Structures, relative energies, and NICS values of the most stable tautomers are shown on the right.

TABLE 1. Dihedral Angles between the Neighboring Pyrrole (Φ_P) Rings, Their Average (Φ_{AVG}), and Relative Energies (ΔE_{all} and ΔE_{rel}) of the Most Stable NH Tautomers in Hexaphyrins[a]

	Φ_P (deg)									
structure							Φ_{AVG} (deg)	ΔE_{all} (kcal/mol)	ΔE_{rel} (kcal/mol)	N_H
N0Hex-H	46.30	48.56	41.94	46.45	50.63	41.00	45.82	49.13	49.13	3
N0Hex-D	7.36	2.13	1.58	7.38	2.12	1.58	**3.69**	**0.00**	**0.00**	3
N0Hex-F	21.69	29.51	43.59	21.88	29.49	43.01	31.53	25.29	25.29	3
N0Hex-R	16.48	15.22	4.59	16.48	15.22	4.59	12.10	9.76	9.76	2
N0Hex-T	28.79	29.74	14.83	15.76	29.27	26.96	24.23	35.82	35.82	0
N1Hex-H	43.26	45.73	40.04	45.45	42.92	50.66	44.68	43.53	37.94	2.5
N1Hex-D	7.55	0.92	11.54	7.69	4.21	4.61	**6.09**	**5.59**	**0.00**	2.5
N1Hex-F	27.45	47.19	17.13	38.63	39.20	19.25	31.48	28.23	22.64	2.5
N1Hex-R	1.77	8.63	1.28	17.74	9.69	5.32	7.41	8.43	2.84	2.5
N1Hex-T	29.48	27.65	6.55	6.77	22.60	22.59	19.27	25.82	20.23	1
N2Hex-H	42.76	41.28	43.99	42.76	41.28	43.99	42.68	42.96	37.53	2
N2Hex-D	10.34	6.77	4.73	10.32	6.79	4.73	7.28	9.22	3.79	2
N2Hex-F	36.25	43.45	15.46	36.25	43.31	15.93	31.78	32.07	26.64	2
N2Hex-R	0.00	0.00	0.00	0.00	0.00	0.00	**0.00**	**5.43**	**0.00**	3
N2Hex-T	33.79	28.29	12.67	8.93	28.33	33.29	24.21	35.59	30.16	1
N3Hex-H	39.39	37.80	35.22	34.84	33.56	33.43	35.71	52.51	29.92	0
N3Hex-D	7.54	14.28	19.55	10.71	18.40	6.07	12.76	36.84	14.25	0
N3Hex-F	50.43	26.30	32.88	29.77	48.17	37.34	37.48	51.99	29.40	1
N3Hex-R	1.55	1.91	0.91	26.53	26.58	0.40	9.65	28.48	5.89	1
N3Hex-T	8.30	4.14	17.94	14.38	4.71	4.17	**8.94**	**22.59**	**0.00**	2

[a] Hydrogen bonding indexes (N_H) are also shown. Entries in boldface type indicate the most stable conformer in each degree of confusion.

angles could be expected in the hexapyrrolic macrocycles, as illustrated in Figure 1 and are discussed here. Transannular interactions are also important factors to be considered, especially in the case of *meso*- and/or β-substituted porphyrinoids. However, in the following discussion, unsubstituted derivatives are mainly examined and thus transannular interactions are less important. In addition to this, such interactions would be reflected also in the dihedral angles. Eventually, evaluation of the ring strain is based on the dihedral angles in this paper. The effect of *meso*-aryl groups is treated later.

In the case of macrocyclic hydrocarbons, a comparison of the energies between macrocyclic compounds and model linear compounds is an effective way to estimate the strain energies.[22] However, in the case of oligopyrrolic macrocycles, transannular intramolecular hydrogen bonding is particularly important in stabilizing the macrocycles. Thus, estimating the ring strain energy separately from the hydrogen bonding would be quite difficult. Consequently, the average dihedral angle between the neighboring pyrrole rings is utilized as a reference parameter for the ring strain in order to simplify the discussion.

The dihedral angles between neighboring pyrrole rings (Φ_P) and their average (Φ_{AVG}) and relative energies among the most stable NH tautomers (ΔE_{all} and ΔE_{rel}) are summarized in Table 1. The ΔE_{all} value represents the energy difference from the most stable hexaphyrin (**N0Hex-D**), and the ΔE_{rel} value represents the energy difference from the most stable conformer in each degree of confusion. Roughly speaking, the conformers possessing smaller Φ_{AVG} values are more stable in energy. This means that Φ_{AVG} would be an appropriate value for a general estimation of the stability in the oligopyrrolic aromatic macrocycles. In the case of hexaphyrins, the desirable Φ_{AVG} values

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[22] (a) Ali, M. K.; Krishnan, M. S. *J. Org. Chem.* **2010**, *75*, 5797. (b) Segawa, Y.; Omachi, H.; Itami, K. *Org. Lett.* **2010**, *12*, 2262.

seem to be less than 10°. Usually, a conformation having a small Φ_{AVG} value would be favorable, since a strainless dipyrromethene unit takes a conformation of $\Phi_P = 0$.

Intramolecular Hydrogen Bondings. In porphyrinoids, intramolecular hydrogen bonding inside the macrocycles would be one of the dominative factors governing their stabilities.[23] Hence, the relationship between the plausible intramolecular hydrogen bonding and the relative energies in hexaphyrins is another important factor to be addressed. The numbers of plausible intramolecular hydrogen bonds are arbitrarily represented by a hydrogen bonding index (N_H), which is postulated as shown in Figure 10. Basically, one dipyrromethene unit corresponds to $N_H = 1$ (**A**). When, two dipyrromethene units share one pyrrole ring in common as in **B** or **C**, $N_H = 1.5$.

On the basis of the above hydrogen bonding indices, relative energies for each conformer have been plotted for all the NH tautomers and linear regression analyses performed (Figure 11). Regular and a series of N-confused hexaphyrins are lumped together on the assumption that the changes in the ring strain energy imposed by confusion would be less effective or offset in the regression analyses (vide infra). In the dumbbell ($r = 0.9508$), figure-eight ($r = 0.9479$), and rectangular ($r = 0.9254$) conformers, correlation coefficients are considerably high and the slopes of regression lines are around 10. This might mean that one hydrogen bond would cause stabilization of the macrocycle by ca. 10 kcal/mol. Although the correlation coefficient is relatively low ($r = 0.6979$), a similar trend is observed in the triangular conformers. In the hexagonal conformer, the number of samples is small and a statistical analysis is less reliable. Nevertheless, moderate stabilization by hydrogen bonding could be recognized with $r = 0.5988$. When a regression line is tentatively calculated without the cases of $N_H = 0$, the correlation coefficient is modified to $r = 0.9654$.

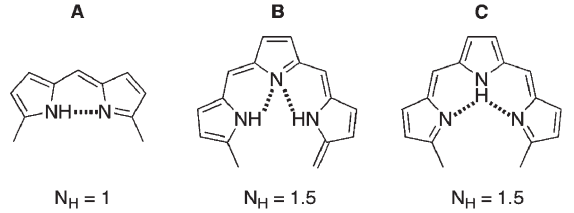

FIGURE 10. Definition of intramolecular hydrogen bonding index (N_H).

The same trend is observed in the protonated hexaphyrins (Figure 12). Correlation coefficients between the relative energies and N_H values are considerably high, and the slopes of regression lines are around 10. This means that the number of pyrrolic hydrogen atoms and positive charge would not affect the whole trend. It should be noted that the hydrogen bonds between NH moieties and counteranions should play crucial roles in the relative energies among conformers experimentally.

In brief, N_H is an important factor in determining the stable NH tautomers in each conformation. In general, formation of one hydrogen bond would cause stabilization of the macrocycles by ca. 10 kcal/mol, which is large enough to determine the preferential NH tautomers. Intramolecular hydrogen bonding might be also important in determining the most stable conformers in each degree of confusion, although the effect of ring strain seems to be dominant (Table 1).

Effect of Confusion on Relative Energies. The effect of confusion on the relative energies (ΔE_{con}) is discussed by comparison of a series of hexaphyrins possessing the same conformation on the basis of Φ_{AVG}, N_H, and NICS values (Table 2). The ΔE_{con} value represents the energy difference from the most stable hexaphyrin in each conformation. First of all, the N_H values are dependent on the degree of confusion. The larger N_H values usually mean higher stability in each conformation, suggesting each conformation possesses

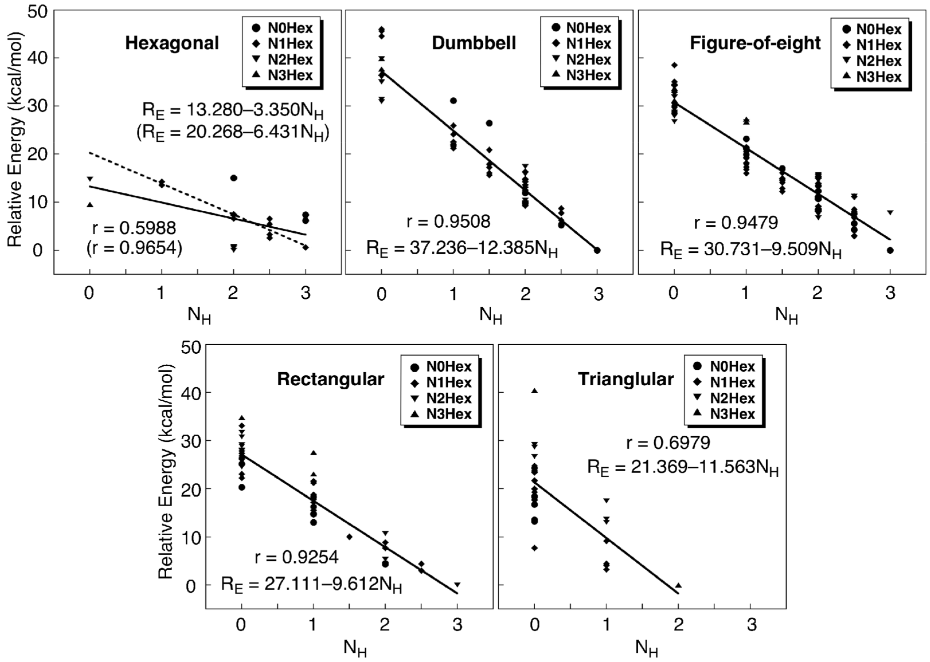

FIGURE 11. Relative energies and hydrogen bonding indices of free-base hexaphyrin conformers with regression lines (data for $N_H = 0$ were removed for the dotted line in the hexagonal conformer).

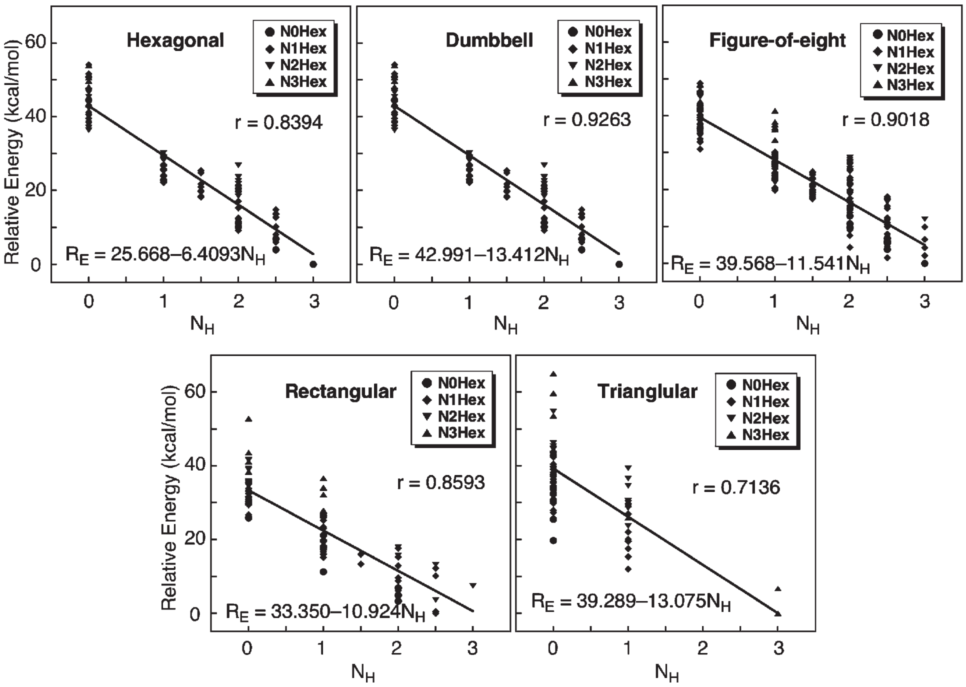

FIGURE 12. Relative energies and hydrogen bonding indices of monoprotonated hexaphyrin conformers with regression lines.

TABLE 2. Relative Energies in Each Conformer (ΔE_{con})[a]

structure	ΔE_{con} (kcal/mol)	Φ_{AVG} (deg)	N_H	NICS (ppm)
N0Hex-H	6.17	45.82	**3**	−9.6721
N1Hex-H	0.57	44.68	**2.5**	−8.3489
N2Hex-H	0.00	42.68	2	−10.0198
N3Hex-H	9.55	35.71	0	−9.7871
N0Hex-D	0.00	3.69	**3**	−14.7935
N1Hex-D	5.59	6.09	**2.5**	−13.9648
N2Hex-D	9.22	7.28	2	−14.1071
N3Hex-D	36.84	12.76	0	−12.3227
N0Hex-F	0.00	31.53	**3**	−11.9083
N1Hex-F	2.94	31.48	**2.5**	−11.3255
N2Hex-F	6.78	31.78	2	−13.2794
N3Hex-F	26.70	37.48	1	−8.6994
N0Hex-R	4.33	12.10	2	−17.7295
N1Hex-R	3.00	7.41	**2.5**	−13.5695
N2Hex-R	0.00	0.00	**3**	−11.7996
N3Hex-R	23.05	9.65	1	−11.2113
N0Hex-T	13.23	24.23	0	−12.3085
N1Hex-T	3.23	19.27	1	−10.1850
N2Hex-T	13.00	24.21	1	−12.2097
N3Hex-T	0.00	8.94	**2**	−10.7256

[a] Structural parameters (Φ_{AVG}, N_H) and NICS values are also shown. Values givien in boldface indicate the largest N_H values in each degree of confusion.

an appropriate degree of confusion, although a slight exception is found in the H conformers. For example, the R conformer favors double confusion (N_H = 3) and the T conformer favors triple confusion (N_H = 2). Regular and singly N-confused hexaphyrins seem to be suitable for various conformations from the viewpoint of N_H, which implies the flexibility of those skeletons. Namely, a high degree of confusion would restrict compatible conformations or could control the conformation of oligopyrrolic macrocycles through introduction of appropriate numbers of N-confused pyrrole rings. Obviously, the relative positions of N-confused pyrrole rings are also important in the multiply N-confused hexaphyrins. Meanwhile, the Φ_{AVG} values are barely dependent on the degree of confusion. Thus, confusion would not affect the ring strain energies considerably. Of course, the formation of intramolecular hydrogen bonds causes smaller Φ_P values and thus smaller Φ_{AVG} values and should be taken into account in part.

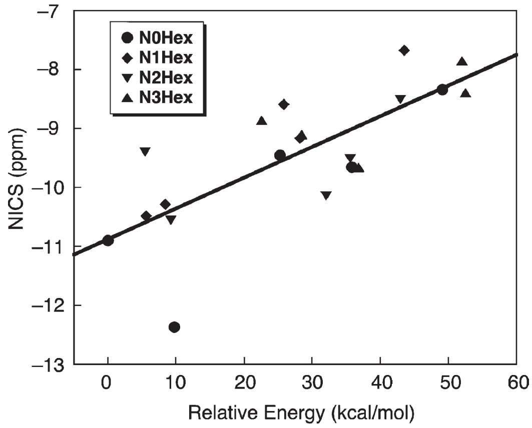

FIGURE 13. Relative energies and NICS values of hexaphyrins with the regression line (r = 0.7603).

All relative energies among regular, singly N-confused, doubly N-confused, and triply N-confused hexaphyrins are summarized in Figure 13. A correlation between the relative energies and the NICS values is also shown. The most stable NH tautomers in each conformation have been applied. Although the correlation coefficient is not very high (r = 0.7603), a distinct positive correlation between the relative energies and the NICS values (namely, aromaticity) is recognized. The NICS values are not greatly affected by the conformations and are a trivial factor. More importantly, the degree of confusion or number of N-confused pyrrole rings does not affect the relative energies as well as aromaticity largely in the hexapyrrolic systems, which can be recognized by the dispersed symbols

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(23) Toganoh, M.; Furuta, H. *J. Phys. Chem. A* **2009**, *113*, 13953.

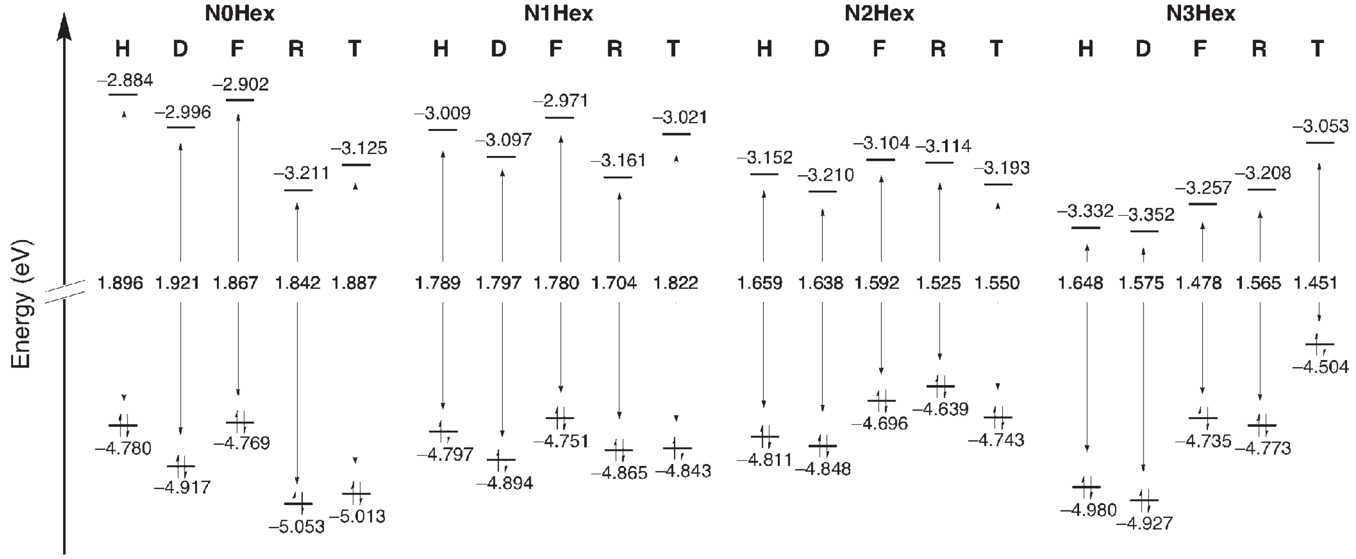

FIGURE 14. HOMO and LUMO orbital energies of hexaphyrins.

in Figure 13.[24] When they take the appropriate conformation, destabilization due to confusion is less than 10 kcal/mol. This is in sharp contrast with the case for the tetrapyrrolic systems, where the degree of confusion affects the relative energies abruptly.[25] Introduction of one N-confused pyrrole ring commonly destabilizes the tetrapyrrolic skeletons by ca. 20 kcal/mol.

Orbital Energies and Band Gaps. Orbital energies of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) in the hexaphyrins are summarized in Figure 14. In each degree of confusion, the HOMO and LUMO orbital energies are dependent on the conformations, while any characteristic trend could not be recognized. Meanwhile, the HOMO−LUMO gap energies do not differ much, depending on the conformations. It should be noted that only the Hückel-aromatic [26]annulenic compounds have been considered in this study and this situation might change when nonaromatic and/or antiaromatic compounds are taken into consideration. On the other hand, the degree of confusion significantly affects the HOMO−LUMO gap energies. Introduction of the N-confused pyrrole rings resulted in narrower HOMO−LUMO band gaps. For example, in the D conformers, the HOMO−LUMO gap energies decreased from 1.921 eV (**N0Hex**) through 1.797 and 1.638 eV (**N1Hex** and **N2Hex**) to 1.575 eV (**N3Hex**).

Effect of *meso*-Aryl Groups. The rapid expansion of hexaphyrin chemistry has mainly relied on the availability of the *meso*-aryl derivatives. Therefore, the relative energies of *meso*-phenyl and *meso*-pentafluorophenyl derivatives were also calculated (Table 3). Since there exist numerous structures even in each conformer relating the dihedral angles between the *meso*-aryl groups and the hexaphyrin plane, these values might contain minor errors, although several initial structures were examined in each case. Nevertheless, we can at least discuss a prevalent trend due to the *meso*-aryl groups.

TABLE 3. Relative Energies of *meso*-Aryl Hexaphyrins

	ΔE_{all}(kcal/mol)				ΔE_{all}(kcal/mol)		
structure	H	Ph	C_6F_5	structure	H	Ph	C_6F_5
N0Hex-H	49.13	35.68	32.62	**N0Hex-H-H$^+$**	35.44	31.18	30.45
N0Hex-D	**0.00**	7.37	10.00	**N0Hex-D-H$^+$**	**0.00**	10.95	10.72
N0Hex-F	25.29	**0.00**	**0.00**	**N0Hex-F-H$^+$**	19.41	**0.00**	**0.00**
N0Hex-R	9.76	13.80	2.42	**N0Hex-R-H$^+$**	9.01	15.04	8.81
N0Hex-T	35.82	15.40	12.44	**N0Hex-T-H$^+$**	29.90	11.75	13.98
N1Hex-H	43.53	33.16	33.84	**N1Hex-H-H$^+$**	38.48	31.75	31.66
N1Hex-D	5.59	8.45	10.77	**N1Hex-D-H$^+$**	5.95	9.83	10.39
N1Hex-F	28.23	2.75	1.96	**N1Hex-F-H$^+$**	20.88	0.01	1.17
N1Hex-R	8.43	11.25	4.86	**N1Hex-R-H$^+$**	5.72	11.29	8.76
N1Hex-T	25.82	7.50	7.32	**N1Hex-T-H$^+$**	22.18	7.57	10.87
N2Hex-H	42.96	34.56	33.54	**N2Hex-H-H$^+$**	49.40	43.40	43.58
N2Hex-D	9.22	8.57	12.42	**N2Hex-D-H$^+$**	18.42	19.79	20.04
N2Hex-F	32.07	6.81	5.23	**N2Hex-F-H$^+$**	30.67	8.93	10.81
N2Hex-R	5.43	9.21	6.23	**N2Hex-R-H$^+$**	9.33	14.08	12.92
N2Hex-T	35.59	13.47	13.50	**N2Hex-T-H$^+$**	33.84	15.36	17.71
N3Hex-H	52.51	43.63	44.28	**N3Hex-H-H$^+$**	57.59	53.94	53.58
N3Hex-D	36.84	29.64	27.55	**N3Hex-D-H$^+$**	43.32	38.73	34.87
N3Hex-F	51.99	22.39	24.21	**N3Hex-F-H$^+$**	52.90	28.13	29.41
N3Hex-R	28.48	27.26	20.81	**N3Hex-R-H$^+$**	33.42	34.20	31.02
N3Hex-T	22.59	10.64	9.06	**N3Hex-T-H$^+$**	10.16	5.27	5.79

The substituent effect is discussed with respect to each conformation. The H conformation is invariably unstable, which is consistent with the absence of experimental examples. In the D conformation, as described above, considerable transannular aryl−aryl interactions can be expected, since two *meso* positions point inside the macrocycle. Expectedly, the advantage of the D conformation is commonly lost. On the other hand, no significant transannular aryl−aryl interactions are found in the F conformation and, surprisingly, it becomes the most stable conformer in the regular, singly N-confused, and doubly N-confused hexaphyrins. Although the R conformers are the second most stable in the regular, singly N-confused, and doubly N-confused hexaphyrins, the energy differences from the most stable F conformers are less than 3 kcal/mol, suggesting that the R conformations are still favorable in the *meso*-aryl hexaphyrins. The T conformation is relatively stable in all cases and is still the most stable conformation for the triply N-confused hexaphyrins. Because no distinct transannular aryl−aryl repulsion is

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[24] Although the aromaticity of the F conformers should be considered carefully, only the NICS values at the center of the molecule are adopted in this discussion. See ref 12a.

[25] (a) Furuta, H.; Maeda, H.; Osuka, A. *J. Org. Chem.* **2000**, *65*, 4222. (b) Furuta, H.; Maeda, H.; Osuka, A. *J. Org. Chem.* **2001**, *66*, 8563.

expected except in the D conformations, the changes in relative energies aroused by the *meso*-aryl groups are derived predominantly from the interactions between the β-pyrrolic hydrogen atoms and the *ortho* hydrogen (or fluorine) atoms of the *meso*-aryl moieties.

Summary

A series of [26]annulenic hexaphyrins have been theoretically investigated, and revealing their relative energies and electronic states. The findings from this study are as follows.

(1) The most stable conformers depend on the degree of confusion (**N0Hex**, D conformer; **N1Hex**, D conformer; **N2Hex**, R conformer; **N3Hex**, T conformer).
(2) The effect of simple monoprotonation on the conformation is negligible.
(3) The ring strain estimated from the dihedral angles between the neighboring pyrrole rings (Φ_{AVG}) is useful in predicting the stable conformers.
(4) One intramolecular hydrogen bond affords stabilization by ca. 10 kcal/mol, which governs the stability of NH tautomers.
(5) The introduction of N-confused pyrrole rings causes narrower HOMO−LUMO energy gaps, while it does not affect the NICS values or aromaticity significantly.

The calculations shown here were mainly achieved only on the hexapyrrolic skeletons, and considerable effects motivated by the substituents, solvents, and counteranions should play crucial roles in the actual experiments. Nevertheless, a growing knowledge of the conformations of oligopyrrolic macrocycles should bring about a positive effect in the field of structural organic chemistry. Although we are well aware of the difficulty of studying conformations for the macrocyclic compounds, a thorough investigation is necessary in understanding the important conformation−function relationship. In addition to this, we believe that these studies should stimulate intriguing molecular design of new macrocycles. Further study, including the conformations of [28]hexaphyrins, is now underway.

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Supporting Information Available: Figures and tables giving chemical structural formulas for all the calculated hexaphyrins and Cartesian coordinates and the results of frequency analyses for the optimized structures. This material is available free of charge via the Internet at http://pubs.acs.org.