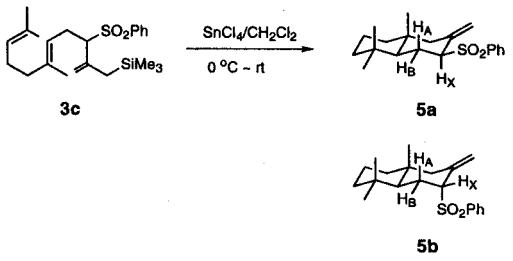
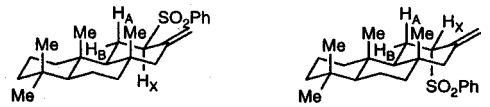
lsulfonyl group of the product **5a** clearly appears to be equatorial on the basis of the ^{1}H NMR data of the C-7 proton (δ 3.63, dd, J=12.2 and 3.8 Hz). The larger coupling constant (J=12.2 Hz) indicates that the proton Hx is located at the axial position. The shifts of the methyl protons to higher field in the cyclized product **5a** are also observed.



3c **5a**

5b

The cyclization of **3d** was not stereospecific, and gave a diastereomeric mixture of 13-methyleneperhydrophenanthrenes **6** in 62% yield.[7] The epimers **6a** and **6b** were isolated by the repeated chromatography (silica gel, hexane : ether=1 : 1), and the ratio was 2 : 1. In the ^{1}H NMR spectrum of **6a** the four methyl protons appear at δ 0.79 (6H), 0.83 and 0.86, and the Hx proton appears at δ 3.59 as a double doublet (J=12.2 and 4.0 Hz). The ^{1}H NMR spectrum of **6b** has four peaks at δ 0.78, 0.80, 0.81, and 0.87 for the methyl protons, and a doublet at δ 3.73 (J=6.6 Hz) for the proton (Hx).



6a **6b**

To our surprise all attempts to cyclize the allylsilane **7** having no phenylsulfonyl group with stannic chloride or other Lewis acids failed. Only desilyation was occurred to produce **8** from **7**.[5] It is noteworthy that the phenylsulfonyl group play an important role in the cyclization process, however, the role is not clear at present time.

7 **8**

Acknowledgment. The present studies were supported by the Basic Science Research Institute Program, Ministry of Education, 1995, Project No. BSRI-95-3408 and LG Chem. Research Park.

References

1. For reviews, see: (a) Schinzer, D. *Synthesis* **1988**, 263. (b) Fleming, I.; Dunogues, J.; Snithers, R. *Org. React.* **1989**, *37*, 57. (c) Thebtaranonth, C.; Thebtaranonth, Y. *Cyclization Reactions*; CRC Press: **1994**; Chap. 2 and 4.
2. Amstrong, R. J.; Harris, F. L.; Weiler, L. *Can. J. Chem.* **1982**, *60*, 673.
3. Kang, K.-T.; U, J. S.; Park, D. K.; Kim, J. G.; Kim, W. J. *Bull. Korean Chem. Soc.* **1995**, *16*, 464.
4. mp 97 ℃; ^{1}H NMR ($CDCl_3$) δ 0.08 (3H, s), 1.02 (3H, s), 1.78-1.98 (4H, m), 2.47-2.64 (2H, m), 3.63 (1H, d, J=5.6 Hz), 4.61 (1H, m), 4.88 (1H, s), 7.49-7.64 (3H, m), 7.82-7.87 (2H, m); ^{13}C NMR δ 22.15, 24.84, 29.15, 32.09, 34.61, 45.33, 67.84, 119.50, 129.17, 129.42, 133.87, 138.13, 139.23; MS m/e 264 (M^+, trace), 123 (100), 77 (38%).
5. For a comprehensive review, see: Lambert, J. B. *Tetrahedron* **1990**, *46*, 2677.
6. **5a**: mp 145-147 ℃; ^{1}H NMR ($CDCl_3$) δ 0.70 (3H, s), 0.78 (3H, s), 0.86 (3H, s), 0.99-1.96 (10H, m), 3.63 (1H, dd, J= 12.3, 3.8 Hz), 4.98 (1H, s), 5.53 (1H, s), 7.45-7.65 (3H, m), 7.91-7.95 (2H, m); ^{13}C NMR δ 18.88, 19.15, 21.55, 24.27, 32.76, 33.26, 36.11, 41.01, 42.13, 53.10, 55.46, 67.65, 113.08, 128.40, 129.00, 133.45, 136.90, 139.12; MS m/e 332 (M^+, trace), 191 (100), 77 (38%).
7. **6a**: mp 167 ℃; ^{1}H NMR ($CDCl_3$) δ 0.79 (6H, s), 0.83 (3H, s), 0.86 (3H, s), 0.87-1.95 (16H, m), 3.59 (1H, dd, J=12.2, 4.0 Hz), 4.97 (1H, s), 5.57 (1H, s), 7.52-7.65 (3H, m), 7.90-7.95 (2H, m); ^{13}C NMR δ 15.97, 18.41, 18.66, 20.41, 21.37, 23.20, 33.33, 36.53, 37.60, 39.48, 41.95, 42.35, 55.79, 56.90, 57.34, 67.50, 112.82, 128.39, 129.01, 133.44, 136.64, 139.10. **6b**: mp 165-167 ℃; ^{1}H NMR ($CDCl_3$) δ 0.78 (3H, s), 0.80 (3H, s), 0.81 (3H, s), 0.87 (3H, s), 0.97-1.87 (14H, m), 2.42-2.55 (2H, m), 3.73 (1H, d, J=6.1 Hz), 4.43 (1H, s), 4.89 (1H, s), 7.47-7.62 (3H, m), 7.82-7.87 (2H, m); ^{13}C NMR δ 15.16, 18.50, 18.69, 19.95, 21.82, 21.55, 33.33, 33.37, 35.58, 37.27, 39.36, 41.86, 42.65, 50.81, 50.99, 56.58, 68.55, 118.97, 128.64, 129.01, 133.33, 137.76, 137.89.
8. The allylsilane **7** was prepared from the palladium-catalyzed cross coupling reaction of 3-(tributylstannyl)-2-(trimethylsilylmethyl)propene with geranyl bromide. **7**: ^{1}H NMR δ 0.02 (9H, s), 1.54 (2H, s), 1.61 (6H, s), 1.69 (3H, s), 1.97-2.09 (8H, m), 4.53 (1H, s), 4.60 (1H, s), 5.01-5.16 (2H, m). **8**: ^{1}H NMR δ 1.55 (3H, s), 1.61 (6H, s), 1.68 (3H, s), 1.93-2.10 (8H, m), 5.04-5.20 (4H, m).

Rearrangement of 2,4-bisalkylpyrrole Unit to 2, 5-bisalkylpyrrole Unit in the Ligand-Modified Porphyrinogens

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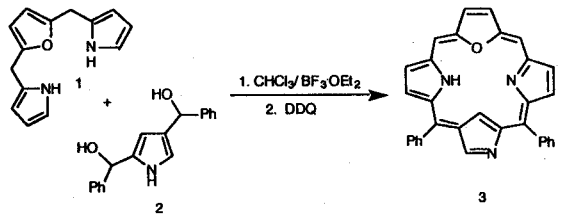
The porphyrins and related macro cyclic systems are the most widely studied of all macro cyclic compounds.[1] The convenience of meso-substituents as sites for functionalization, controlling the substituents geometry and the wealth of available meso-substituents make meso-substituted porphyrins ideally suited for use in various model systems. Although porphyrin is easily obtainable from pyrroles and aldehydes, generic methods are still limited to symmetric porph-



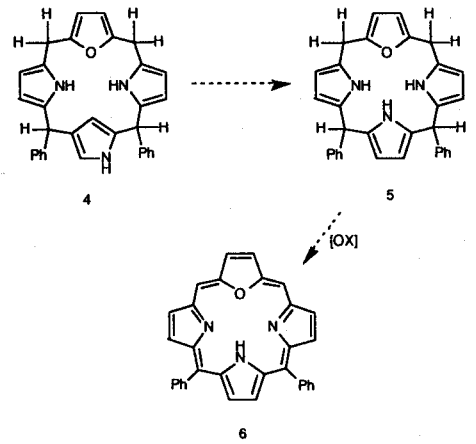
Scheme 1.

yrins because of the isomeric porphyrin formation from mixed condensation and consequent difficulties in separation and identification. Thus, methods for the synthesis of meso-substituted porphyrins with predesignated orientation of core-ligands or meso-substituents still need to be developed, especially in creating sophisticated models of porphyrin-based enzymes and in medicinal applications.

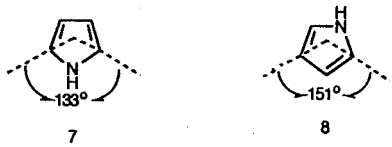
Recently, we reported a synthesis of 12-aza-21-oxa-23-carba-24H-10,15-diphenylporphyrin (**3**) (ONCN-porphyrin) in regioisomerically pure form.[2] The reaction utilized the [3+1] type condensation of 16-oxa-5,10,15,17-tetrahydrotripyrrin (**1**) with 2,4-bis[α-hydroxy-α-phenyl]methylpyrrole (**2**) as shown in Scheme 1. This new compound which is core-ligand modified and 2-aza-21-carba-5,10,15,20-tetraphenylporphyrin (N-confused porphyrins) is a typical example of a porphyrin isomer. The convenience of the synthesis and its unique structural characteristic led us to study the mechanistic point of the condensation and wider applicability.

The condensation of 16-oxa-5,10,15,17-tetrahydrotripyrrin (**1**) with 2,4-bis-[α-hydroxy-α-phenyl]methylpyrrole (**2**) was carried out in chloroform in the presence of catalytic amount of borontrifluoride etherate at room temperature. It was observed that the products isolated after oxidative workup contain both ONCN-porphyrin (**3**) and unexpected isomeric 21-oxa-23H-10,15-diphenylporphyrin (**6**) (ONNN-porphyrin). The isolation of ONNN-porphyrin (**6**) from the reaction indicates that initially used 2,4-bis-substituted pyrrole unit (**2**) rearranges to 2,5-bis-substituted pyrrole unit during the condensation processes. The formation of (**6**) could be explained by considering one of the alkyl group migration of the 2,4-substituted pyrrole unit into the 2,5-substituted pyrrole at the porphyrinogen stage during condensation (vide infra). The proton nmr spectrum taken after chromatographic separation of crude reaction mixture indicates that the fraction of (**6**) is significantly increased by extending the reaction time. For example, the ratio of the two porphyrins (**3**)/(**6**) is almost 1/1 based on the proton nmr spectra when work-up of the reaction mixture is done after 50 min. But only traces of (**3**) were detected when the reaction was run for more than 12 hours. The stirring of individual reactant (**1**) or (**2**) alone under the porphyrin-forming condition did not result in any observable porphyrin-like components. Each porphyrin component was easily identifed by proton nmr spectroscopy; the proton nmr spectra of porphyrin (**6**) was quite simple due to inherent symmmetry of the molecule. The proton nmr spectrum of porphyrin (**6**) isolated from the reaction mixture was identical with the spectrum of an authentic sample which was independently synthesized from the condensation of **1** with 2,6-bis-[α-hydroxy-α-phenyl]methylpyrrole.

The proton nmr spectrum of porphyrin (**6**) showed an inner N-H proton at −2.0 ppm as a broad singlet. The protons



Scheme 2.



Scheme 3.

on the furan appeared as a singlet at 9.67 ppm. The β-pyrrolic protons appear as doublets at 9.17 and 8.85 ppm. Chemical shift of the meso-protons appear at 10.22 ppm, a typical value for the meso-unsubstituted porphyrin. The proton nmr spectrum of (**3**) was rather complex due to the unsymmetric nature of the compound. The inner C-H proton was shown at −3.74 ppm and the outer β-H of the flipped pyrrole showed a singlet at 8.70 ppm. The inner C-H proton was not exchanged upon exposure to acidic deuterium oxide over 36 hour period. The inner N-H proton signal was observed at −0.57 ppm as a broad singlet and completely disappeared by addition of D_2O. The Soret band of the porphyrin (**3**) appeared at 432 nm and porphyrin (**6**) at 408 nm.[3] This observation indicates that the structure of (**3**) is distorted from planarity due to the two ajacent inner hydrogens possibly causing repulsion between each other. On the other hand, porphyrin (**6**) is closer to planarity than meso-tetraphenylporphyrin (TPP) due to the presence of one less inner hydrogen and consequent reduction of resonance interaction with two meso-phenyl group. This is possibly why the Soret band of porphyrin (**6**) shows such a large blue shift.

From a mechanistic point of view, one can consider the sum of all the internal bond angles of each porphyrinogen. Structure (**4**) takes up a greater portion of the sum of internal angles than does (**5**). This is because the imaginary angle which is formed by extrapolation of 2- and 5-alkyl substitutents (**7**) in the pyrrole unit is 133°, while 2- and 4-alkyl substituents (**8**) is 151°.[4] (Figure 1) Thus porphyrinogen (**4**) has increased size of the macrocycle due to an inversion of one pyrrole unit causing increased ring strain. Thus, acid catalyzed reversible cleavage between meso-carbon and 3-position of the inverted pyrrole ((**9**)→(**10**)) will release the strain somewhat and followed by recyclization which will result in porphyrinogen (**5**) (Scheme 3). Sessler and Latos-Grazynskyi have suggested that the formation of N-confused porphy-

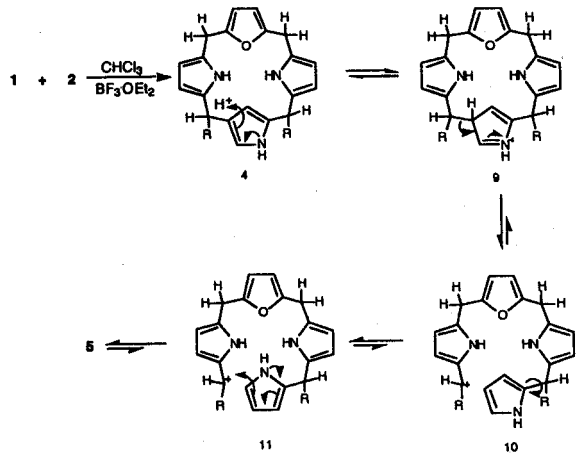


Figure 1.

rin is the result of macrocyclization of filpped pyrrole,[5,6] which is consistent with earlier suggestion.[7,8] But current results clearly indicate that normal macrocyclization is thermodynamic while 'flipped' macrocyclization is kinetic in nature.

This process must be thermodynamically favorable and inherent characteristics of pyrrole nuclei. This is why the thermodynamic equilibration between **4** through **11** must prefer normal porphyrinogen **5**. If the reaction stops before the equilibration reaches on the other hand, **4** is preferred and consequently results in porphyrin **3** as predominant product.

In conclusion, during the core-modified porphyrin synthesis, 21-oxa-23H-10,15-diphenylporphyrin (**6**) was unexpectedly isolated. The rearranged product provided simple evidence for the angle strain and relative thermodynamic stability of the two porphyrins. Furuta *et al.* reported the synthesis of *N*-confused porphyrin using acid catalyzed condensation of benzaldehyde and pyrrole. They considered the formation of *N*-confused porphyrin as anion template effects.[9] When we tried to condense **1** with **2** in the presence of conc-HBr as catalyst, no porphyrin components was observed. This observation strongly support the proposal made by Furuta *et al.* The detailed kinetic studies are under investigation.

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References

1. (a). Lindsey, J. S. in *Metalloporphyrins-Catalyzed Oxidations*; F. Montanari and L. Casella, Eds.; Kluwer Academic Publishers: The Netherlands; **1994**, pp 49-86. (b) *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, **1975**. (c) Gribkova, S. E.; Evistigneeva, R. P.; Luzgina, V. N. *Russian Chem. Rev.* **1993**, *62*, 963. (d) Suslick, K. S.; Reinert, T. J. *J. Chem. Edu.* **1985**, *62*, 974.
2. Heo, P. Y.; Shin, K.; Lee, C. H. *Tetrahedron Lett.* **1996**, *37*, 197.
3. Spectroscopic data for the porphyrins are follows; 12-aza-21-oxa-23-carba-24*H*-10,15-diphenylporphyrin (**3**), ^{1}H NMR ($CDCl_3$) δ 9.02 (s, 1H, meso-H), 9.00 (s, 1H, meso-H), 8.95 (s, 2H, furan-β-H), 8.70 (s, 1H, pyrrole(13)-H), 8.59 and 8.43 (AA'BB', 2H, J=4 Hz, pyrrole-H), 8.53 and 8.50 (AA'BB', 2H, J=5 Hz, pyrrole-H), 8.25-8.21 (m, 2H, Ar-(o)-H), 8.18-8.13 (m, 2H, Ar-(o)-H), 7.88-7.79 (m, 6H, Ar-(m,p)-H), −0.57 (bs, 1H, N-H), −3.72 (s, 1H, inner C-H). UV-vis (CH_2Cl_2) λ_{max} ($\varepsilon\times10^3$); 432 (67), 468 (27), 535 (8), 570 (4), 614 (2), 712 (2), LDMS Calcd for $C_{32}H_{21}N_3O$ 463.54, Found 464.2.
21-oxa-23*H*-10,15-diphenylporphyrin (**3**) ^{1}H NMR ($CDCl_3$) δ 10.22 (s, 2H, meso-H), 9.88 (s, 2H, furan-H), 9.16 (d, 2H, pyrrole-H), 8.97 (s, 2H, pyrrole-H), 8.85 (d, 2H, pyrrole-H), 8.23-8.19 (m, 4H, Ar-H), 7.81-7.74 (m, 6H, Ar-H), −2.01 (bs, 1H, inner N-H); UV-vis (CH_2Cl_2) λ_{max} ($\varepsilon\times10^3$), 408 (171), 495 (14), 557 (1), 596 (2), 654 (1). HRMS Calcd for $C_{32}H_{21}N_3O$ 463.1685, Found 463.1706.
4. Frank, B.; Nonn, A. *Angew. Chem. Int. Ed. Eng.* **1995**, *34*, 1795.
5. Sessler, J. L. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1348.
6. (a) Chmilewski, P. J.; Latos-Grazynsi, L.; Rachlewicz, K.; Glowiak, T. *Angew. Chem.* **1994**, *106*, 805. (b) Chmilewski, P. J.; Latos-Grazynsi, L.; Rachlewicz, K.; Glowiak, T. *Angew. Chem. Int. Ed. Eng.* **1994**, *33*, 779.
7. Frank, B. *Angew. Chem. Int. Ed. Eng.* **1982**, *21*, 343.
8. Schmacher, K. H.; Frank, B. *Angew. Chem. Int. Ed. Eng.* **1989**, *28*, 1243.
9. Furuta, H.; Asano, T.; Ogawa, T. *J. Am. Chem. Soc.* **1994**, *116*, 767.