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Proofs of Macrocyclization of Gable Porphyrins as Mimics of Photosynthetic Light-Harvesting Complexes

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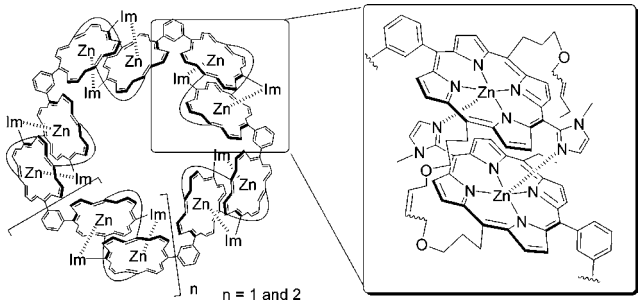
ABSTRACT



Porphyrin macrocycles composed of five and six units of *m*-gable imidazolylporphyrinatozinc (1-Zn) were synthesized by self-assembled cyclization followed by ring-closing metathesis linkings. Each porphyrin macrocycle was isolated by GPC chromatography, and their molecular weights were determined by MALDI-TOF mass spectroscopy. These structures represent mimics of light-harvesting complexes in photosynthetic bacteria.

X-ray crystallography, electron microscopy, and other analytical methods have been used to determine the structure of light-harvesting (LH) complexes obtained from photosynthetic bacteria.[1] Although the structures of several other LH systems have been elucidated, perhaps the most fascinating basic structure is that of the higher-ordered barrel of LH1 and B850 in LH2. These naturally occurring complexes have been constructed using only intermolecular forces, especially the coordination of imidazolyl to Mg centers in chlorophylls without the use of covalent bonding. Construction of such molecular systems has long been a challenging synthetic target in view of their importance in biological energy transformation events.[2] Successfully mimicking natural systems would be an important demonstration of the usefulness of supramolecular science. In LH complexes, transmembrane helices supply the matrix in which the chloro-

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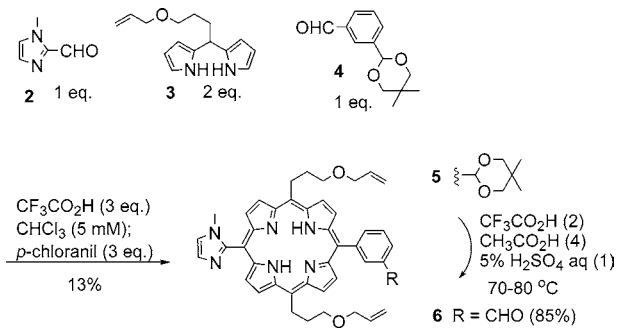
phylls are embedded. We have been interested in constructing LH complexes in the simplest way without using any peptide matrixes. A method of obtaining extremely stable complexes has been established applying the complementary coordination of imidazolylporphyrin Zn complexes[3], using an *m*-phenylene unit to bridge two porphyrins in a so-called gable porphyrin arrangement.[4] Six gable porphyrins were expected to coordinate into a hexagonal structure of six complementarily coordinated dimers.[5]

In this study, several methods of structural analysis were used to support the proposed structure of the macrorings and the hexamer. Even so, the smaller aggregate could not conclusively be assigned as the pentamer, in part because of large experimental errors associated with the small scattering intensities arising from the small size ring. However, the primary reason for the uncertainty was that the mass spectrometry was insufficiently powerful to give molecular ion peaks, even though the coordination interaction itself was strong enough in solution to retain almost 100% of the supramolecular structure. Mass spectrometry afforded predominantly a monomeric peak of small intensity due to the presence of the dimer.[6] In this report, we developed another methodology finally to confirm the formation of macrocyclic six- and five-membered rings. Here, each pair of complementarily coordinated dimers was connected to the other by its own template.

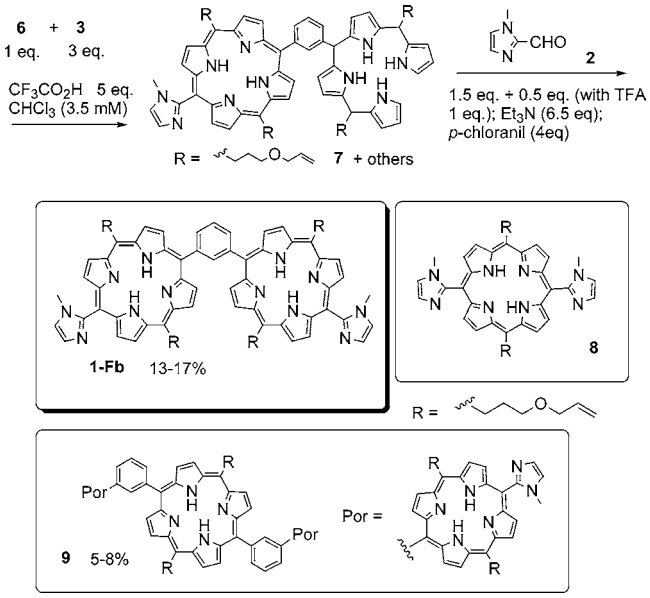
Olefin metathesis reactions have recently been utilized as a key reaction for C−C bond formation for a variety of synthetic targets.[7] This reaction has been applied to connect the complementary coordination pair, since all the meso substituents were brought into close proximity to each other in the corresponding positions in the coordination pair.[8] The substituents at the 10(10′)- and 20(20′)-meso positions of 5(5′)-*meta*-phenylene-bridged 15(15′)-imidazolyl porphyrin were then converted to allyloxypropyl substituents. The route for synthesis of *m*-bis(15-*N*-methylimidazolylporphynyl)-phenylene (gable porphyrin) **1-Fb** is illustrated in Schemes 1 and 2.

Scheme 1. Synthesis of Porphyrin **6**



The reaction of *N*-methylimidazole aldehyde **2** (1 equiv), dipyrromethane **3** (2 equiv), and monoprotected isophthalaldehyde, **4**, (1 equiv) in the presence of CF_3CO_2H (TFA, 3 equiv) followed by oxidation with chloranil gave porphyrin, **5**, in 13% yield. Deprotection of the acetal group on **5** by

Scheme 2. Synthesis of Gable Porphyrin **1-Fb**



hydrolysis afforded porphyrin, **6**, in 85% yield. Second cyclization to obtain a gable porphyrin, **1-Fb**, was improved over the previous method.[5] It was realized that the reactivity of porphyrin-substituted benzaldehyde **6** was lower than that of imidazole aldehyde, **2**. When the three components, **2**, **3**, and **6**, were mixed at once, even though a significant amount of bisimidazolylporphyrin **8** was produced, porphyrin-substituted benzaldehyde **6** was left unreacted. Therefore, imidazole aldehyde, **2**, was added portionwise by monitoring the mixture's mass spectrum. When only dipyrromethane, **3**, and aldehyde **6** were mixed in the presence of TFA (5 equiv), aldehyde **6** was gradually consumed and tetrapyrrole, **7**, formed. **2** (1.2 equiv) was added once the aldehyde, **6**, had disappeared (normally after 1.5 h). If unreacted tetrapyrrane **7** was observed after 1 h, an additional aliquot of **2** (0.5 equiv) was added along with TFA (1 equiv). After disappearance of tetrapyrrane, **7**, the reaction mixture was neutralized by the addition of Et_3N, and then chloranil was added. The reaction mixture contained bisimidazolylporphyrin, **8**, *m*-gable porphyrin, **1-Fb** (13−17%), and porphyrin trimer, **9** (5−8%). A first purification by column chromatography using SiO_2 (10−40% (v/v) acetone in $CHCl_3$) gave a mixture of *m*-gable porphyrin **1-Fb** and trimer **9**, eliminat-

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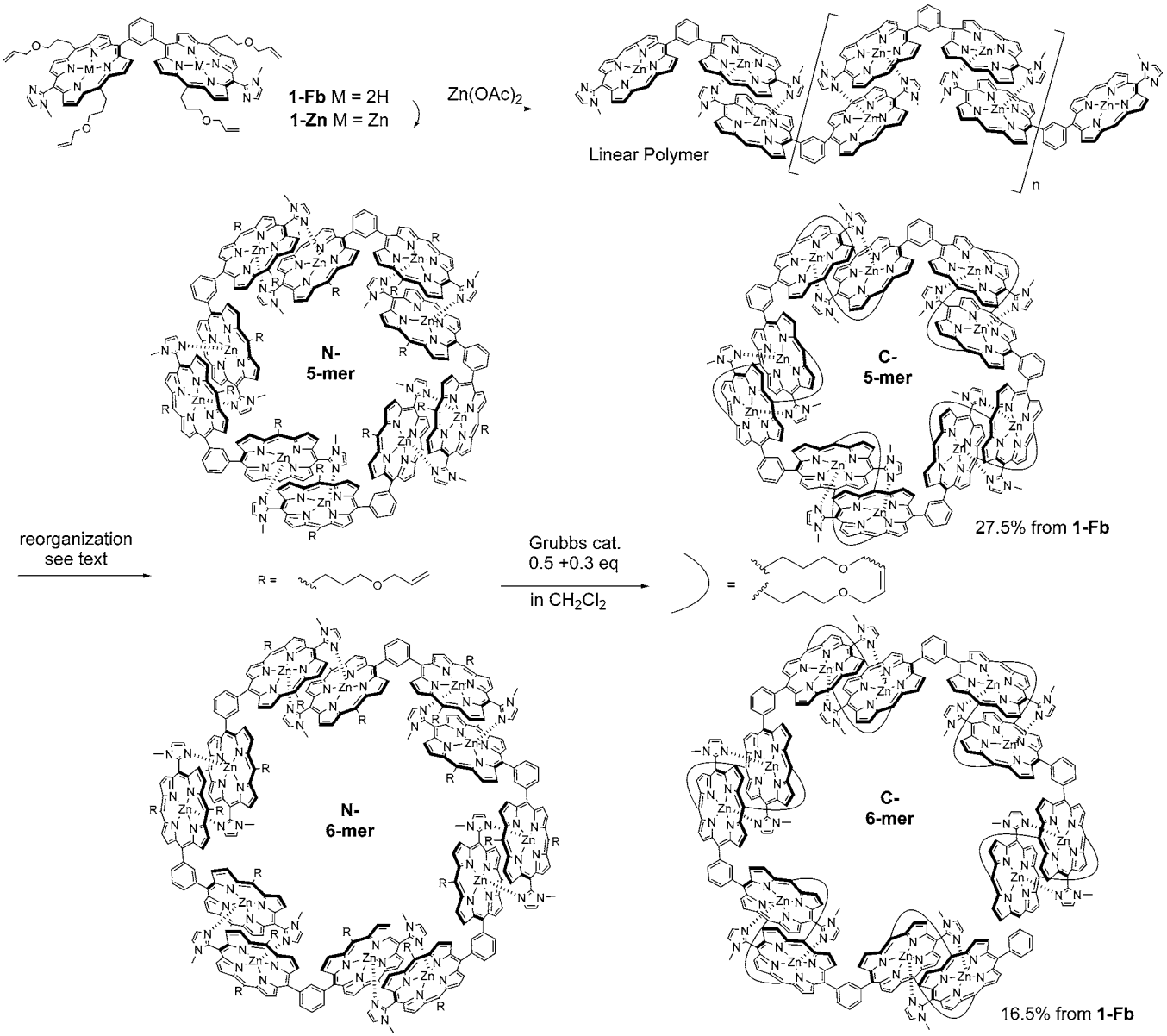
(6) All attempts to detect macroring formation by soft ionization mass spectrometries, which included FAB, ion spray, and cold electrospray mass spectrometries, were unsuccessful.

(7) Review: Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001,** *34*, 18−29.

(8) For a more general application of olefin metathesis reactions to our supramolecular systems by its own template assistance, see: Ohashi, A.; Satake, A.; Kobuke, Y. *Bull. Chem. Soc. Jpn.* **2004**, in press.

Scheme 3. Reorganization of **1-Zn** and Covalent Linkage



ing bisimidazolylporphyrin **8** and any other polymeric compounds. The mixture of **1-Fb** and **9** was purified by a recycling GPC systerm (Japan Analytical Industry Co., Ltd.) using a Tosoh GM2500H_{HR} column (exclusion limit 20 000 Da) with $CHCl_3$/MeOH 10/1 as an eluent to give the trimer (5−8% based on aldehyde **6**) and *m*-gable porphyrin (13−17%). (Figure S1 in Supporting Infomation)

Introduction of Zn assembled imidazolylporphyrinatozinc gable into a mixture of oligomers and macrocycles. The coordination bond weakened in a $CHCl_3$−MeOH solution (7:3 (v/v), 0.02 mM) and the complex reorganized according to the procedure established in a previous communication.[5] After this procedure, GPC analysis showed the disappearance of almost all the oligomers and demonstrated a convergent peak at 11.79 min (Figure S2 in Supporting Information). The behavior and retention times of this peak were very similar to that observed previously in gable porphyrins with *meso*-*n*-heptyl substituents, except that the two split peaks coalesced to a single peak. However, this problem was overcome by using a recycling GPC system. At this point, the reaction mixture was subjected directly to the olefin metathesis reaction by the addition of Grubbs catalyst. Reaction of the reorganized components with Grubbs catalyst (0.5 equiv based on 1 unit of gable porphyrin) was carried out in CH_2Cl_2. This time, macrocyclic compounds could be observed directly by MALDI-TOF mass spectra. In a typical case, peaks at *m*/*z* 6592 and 7909, corresponding to the macrocyclic pentamer and hexamer, covalently linked by the ring-closing metathesis substituents, were observed after 2 h along with peaks at *m*/*z* 6621, 6649, 7937, and 7961, corresponding to macrocyclic pentamers and hexamers. This left two or four allylic moieties unreacted. These unreacted allylic moieties were gradually consumed, but the rate of reaction became very slow at the last stage. To consume the

unreacted olefins, an additional 0.3 equiv of Grubbs catalyst was added. Finally, the convergent peaks at *m*/*z* 6592 (pentamer) and 7910 (hexamer) were obtained as dominant peaks together with small peaks at 9228, 13 199, 14 524, and 15 817, corresponding to seven, ten, eleven, and twelve units of the *m*-gable porphyrin, respectively. The relative intensities of the peak maxima in a typical experiment were 100 (pentamer):62 (hexamer):1.8 (heptamer):7.0 (decamer): 5.8 (undecamer):4.0 (dodecamer) (Figure 1). Neither the

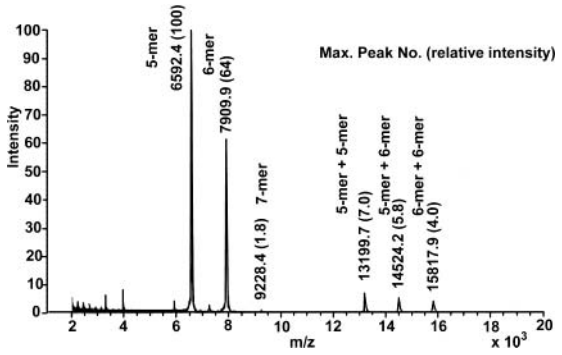


Figure 1. Mass spectrum of covalently linked macrocycles prepared by ring-closing metathesis.

octamer nor the nonamer could be detected. Since two porphyrin moieties were connected at the 1- and 3-positions of benzene, the angle between the two porphyrins was near to 120°. Therefore, the thermodynamically stable structure should be a hexamer. However, dynamic processes explain the observed product distribution. Since oligomer units grow from a smaller number of units as a result of a reorganization process, the pentamer can be cyclized kinetically under these conditions, albeit at the expense of angle strain. This hypothesis was supported by the presence of a small amount of the heptamer. The decamer, undecamer, and dodecamer were likely formed by intermolecular connection between pentamer and hexamer moieties. The mixture was purified by recycling GPC system with a Tosoh G3000H_{HR} column (exclusion limit 60 000 Da) with $CHCl_3$/MeOH 10/1 as an eluent. The chromatogram of the purification process is shown in Figure 2. After three recycle purifications, one shoulder and two major peaks were collected (fractions 1−3) in the order of eluted samples. Mass spectroscopy gave parent peaks (M + 1) of 6590 and 7909 for the fractions 2 and 3, respectively (Figures S3 and S4, Supporting Information). These figures show a macrocyclic hexamer (C-hexamaer, 16.5%) and a pentamer (C-pentamer, 27.5%). Fraction 1 contained the heptamer and larger macrocycles.

The stability constant of the complementary coordination of imidazolyl-Zn in $CHCl_3$ was very large, reaching 10^{10} M^{-1}, but the dimer can be dissociated into monomeric units in coordinating solvents such as MeOH and pyridine.[3,8] Thus, the characteristic split Soret band arising from an exciton

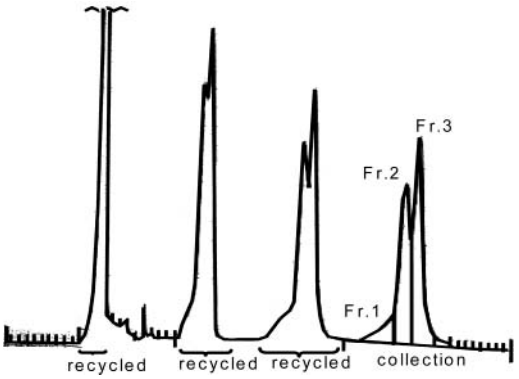


Figure 2. Chromatograms of covalently linked macrorings using recycling GPC systems. After three recycling processes, fractions 1−3 (Frs. 1−3) were collected. Mass spectra of Fr. 2 and Fr. 3 are shown in Figure S4 and S5 in Supporting Information.

interaction[9] for N-macro-rings in $CHCl_3$ changed into a sharp single peak in pyridine. The spectrum of C-macrorings after metathesis did not show any difference in two solvents (Figure S5). This was a remarkable feature considering that the imidazole can compete favorably for coordination even in the presence of 10^7 molar excess of strongly coordinating pyridine (log K = 3.8).[10] This was brought about by the intramolecular coordination of the imidazolyl moieties in parallel alignment with slipped cofacial porphyrin groups.

In summary, efficient supramolecular macrocyclization of an *m*-gable porphyrin was demonstrated. Intramolecular ring-closing metathesis reactions between complementary coordination pairs connected all of the ring components to ensure the observation of molecular ion peaks, finally proving the macrocyclic structure of the gable porphryn. It was demonstrated that a smaller ring formed in the process of reorganization under highly dilute conditions was a pentameric macroring. These substrates could afford excellent materials for studying and understanding the mechanisms operating in natural photosynthetic light-harvesting systems and further developing highly efficient artificial photosynthesis systems.

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Supporting Information Available: Experimental details for synthetic procedures, spectroscopic data, and gel permeation chromatographic analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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