Covalent Fixation of the Cyclic Tetramer of a Metallo-porphyrin Based on Self-complementary Quadruple Hydrogen Bonding

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The stability of quadruple hydrogen bonding in the cyclic tetramer of a metallo-porphyrin before and after a covalent fixation was investigated. According to competition and energy-transfer experiments, the exchange reaction between the cyclic tetramers of the metallo-porphyrin was fully suppressed by the covalent fixation. This spontaneous cyclization–covalent fixation strategy based on olefin metathesis can open the way to the use of cyclic assemblies in a solid phase.

Porphyrin-based supramolecules, which rely on a noncovalent strategy, have been extensively studied over the past decade, motivated by their potential functions, such as light-harvesting antenna[1,2] and hemoprotein-models.[3] The noncovalent approach to build porphyrin assemblies is quite advantageous, because it can take advantage of the porphyrin's preorganized structure to be a molecular junction while avoiding the porphyrin's synthetic difficulties. Very recently, we have reported the spontaneous formation of the cyclic tetramer from the synthetically accessible tetraphenylporphyrin derivative substituted with two strong self-complementary hydrogen-bonding units, 2-ureido-4[1*H*]-pyrimidinone (UPy).[4,5] However, we could not completely exclude the possibility of the cyclic tetramer's ring-opening upon concentrating because of the reversibility of the quadruple hydrogen bonding. Therefore, in regard to solid-state use of the cyclic tetramer, we investigated its stabilization by covalent fixation, as well as its tolerance against the ring-opening in terms of the exchange reaction of the quadruple hydrogen bonding.

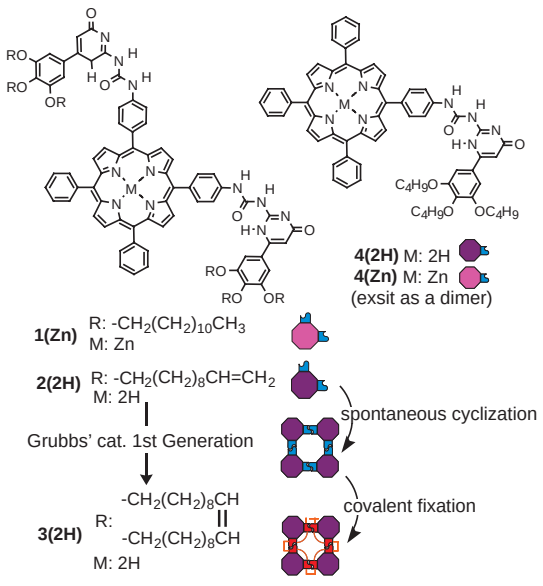

Figure 1. Porphyrins used in this study.

The porphyrin **1**, **2**, and **4** were synthesized by the reaction between the activated isocytosine and amino-substituted tetraphenylporphyrin. The covalent fixation of the porphyrin **2** was performed by olefin metathesis using Grubbs' catalyst first generation in a dilute condition (Figure 1).[2b,6] By diffusion-ordered spectroscopy (DOSY), each porphyrin derivative was reveled to exist as a tetramer in solution.[5]

The stability of the cyclic tetramer before and after the covalent fixation was examined by detecting the energy transfer (ET) between the donor and acceptor porphyrins. It has been shown already that ET is induced when an acceptor porphyrin exists adjacent to a donor porphyrin via the quadruple hydrogen bond.[5] We were able to monitor the exchange reaction successfully by the degree of the ET between the donor and acceptor porphyrins (Figure 2).[5,7] Without the covalent fixation, a slow exchange between the cyclic tetramer of **1(2H)** and **1(Zn)** was observed (case 1, red circles), which required 6 h until equilibration was reached. Compared to the lifetime of the dimer of the **4(2H)**, which was determined to be 120–130 ms by exchange spectroscopy (EXSY),[4a,8] this slow exchange is direct evidence for the cooperative quadruple hydrogen bonds in the tetramer. Furthermore, upon the addition of the donor porphyrin **4(Zn)**, the degree of ET was immediately equilibrated within 5 min

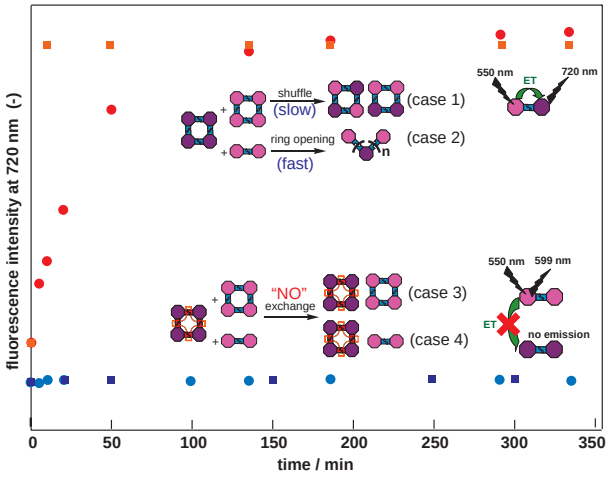

Figure 2. Time-dependency of the fluorescence intensity emitted from the acceptor zinc porphyrin. The equilibration profiles were examined for the equimolar mixture of the donor porphyrin (zinc) and the acceptor porphyrin (free base): (red circles) mixture of the porphyrin **1(Zn)** and **1(2H)**, (red squares) **4(Zn)** and **1(2H)**, (blue circles) **1(Zn)** and **3(2H)**, (blue squares) **4(Zn)** and **3(2H)**. Donor porphyrins were illuminated at $\lambda_{exc} = 550$ nm, with the constant concentration of at 3 μM in $CHCl_3$.

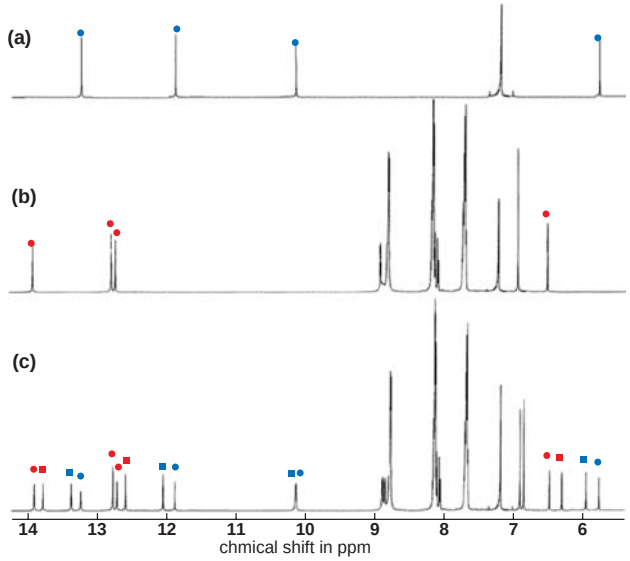

Figure 3. ^{1}H NMR spectra recorded in $CDCl_3$. (a) aliphatic UPy **5**, (b) porphyrin **4(2H)**, (c) the equimolar mixture of the porphyrin **4(2H)** and UPy **5**. The NMR signals indicated with red circles, red squares, blue circles, and blue squares correspond to the UPy of porphyrin in **4(2H)·4(2H)**, UPy of porphyrin in **4(2H)·5**, UPy of **5** in **5·5**, and UPy of **5** in **5·4(2H)**, respectively.

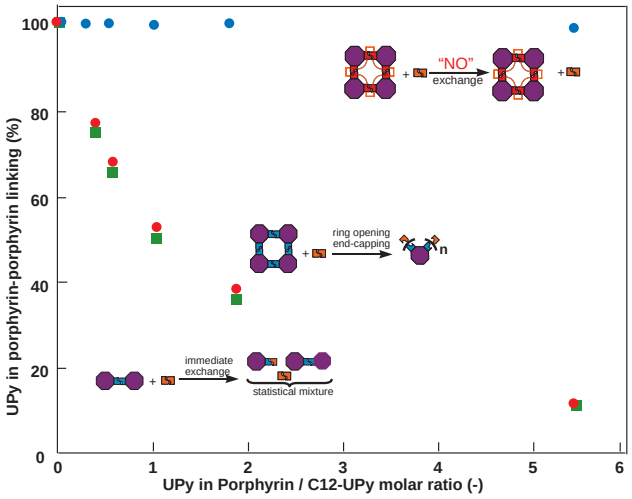

Figure 4. The percentage of the "UPy of the porphyrin" contributing to the "porphyrin–porphyrin linkage" upon addition of aliphatic UPy **5** as a competitor. The ratio was determined by ^{1}H NMR recorded in $CDCl_3$, at 300 K. (blue circles) mixture of porphyrin **3(2H)** and **5**, (red circles) mixture of porphyrin **1(2H)** and **5**, (green square) statistical ratio, anticipated when there is no selectivity or cooperativity in UPy dimerization. The concentration of the porphyrins was constant at 10 mM.

(case 2, red squares), which was ascribed to the fast ring-opening and the end-capping of the tetramer of **1(2H)**. This exchangeability in UPy–UPy linkage, as well as the direct detection of the ring-opening reaction, indicates that a tetramer without covalent fixation does not necessarily exist as a tetramer in a solid state. On the contrary, neither the shuffling between tetramers of **1(Zn)** and covalently fixed **3(2H)** nor the ring-opening of **3(2H)** upon the addition of the dimer of **4(Zn)** was observed (case 3, blue circles and case 4, blue squares, respectively), suggesting that a tetramer with covalent fixation would strongly resist ring-opening upon concentrating to the solid phase.

To investigate the stability of the tetramer in more severe conditions, we performed competition experiments, in which *N*-dodecyl-2-ureido-6-(1-ethylpentyl)-4-pyrimidinone (UPy, **5**) was added to break up the tetramer. As seen in Figure 3, the UPy moiety of the porphyrin bound to aliphatic UPy **5** was distinguishable from the one linking two porphyrins as a result of the strong ring current effect in ^{1}H NMR spectra. By using the integral values of the NMR signals of the UPy moiety of the porphyrin, we determined the percentage of the UPy contributing to the porphyrin–porphyrin linkage (Figure 4). The porphyrin **1(2H)** underwent the ring-opening and end-capping by **5**, despite the existence of a trace amount of the survived tetramer, which was indicated by the slight deviation of the plots (red circles) over statistical values. However, for the covalently fixed tetramer, no signals assigned as a **3(2H)·5** linkage were detected, which supports the finding that no exchange of the quadruple hydrogen bonding in the tetramer of **3(2H)** occurred. Moreover, even after evaporating the solution of **3(2H)** containing large excess of the competitor **5**, still no exchange was observed in the redissolved solution.[8] All these results demonstrate that the exchange reaction of the quadruple hydrogen bond in the covalently fixed porphyrin tetramer was frozen.

In conclusion, as a result of covalent fixation based upon olefin metathesis, inter-tetramer shuffling of the porphyrin was strongly suppressed. Our spontaneous cyclization–covalent fixation strategy can open the way to the use of cyclic assemblies in a solid phase. Currently, the incorporation of the "porphyrin tetramer" into the membrane is in progress.

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References and Notes

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8 EXSY spectrum of the mixture of the porphyrin **4(2H)** and aliphatic UPy **5**, plots to determine the lifetime, and experimental detail of competition experiment can be seen in the Supporting Information which is also available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett.

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