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Synthesis of cyclic chlorophyll oligomers

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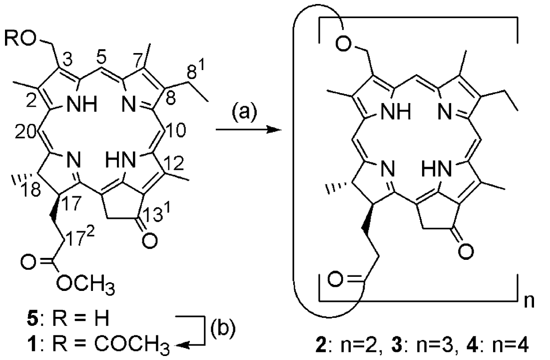
Abstract—As a new model of photosynthetic light-harvesting antennas, cyclic dimer, trimer, and tetramer of chlorophyllous moieties were prepared by intermolecular transesterification of a hydroxy-methoxycarbonyl-chlorin using 1,3-dichlorotetrabutyl distannoxane as a catalyst. ^{1}H NMR and UV–vis spectra showed that the cyclic oligomers tended to form stacked conformers through intramolecular π–π interactions of the chlorin macrocycles. It was demonstrated that the cyclic trimer could form a complex with fullerenes in $CDCl_3$.

In the initial stage of photosynthesis, dye molecules represented by chlorophylls are precisely arranged to form light-harvesting antennas, which enable absorption of sunlight, migration of harvested energy, and finally energy transfer to a reaction center.[1] As artificial mimics of such antenna systems, many (non)covalent multiporphyrin assemblies have been reported.[2] Construction of supramolecular structures based on self-assembling properties of synthetic zinc (bacterio)chlorins[3] and the development of dendrimers possessing chlorophyll-derived terminals[4] are other examples. Although several covalently-linked linear chlorophyll dimers have been reported,[5] there are only a few examples of cyclized chlorophyll dyads,[6] and no reports are available of synthetic cyclic oligomers having more than two chlorophyll moieties. In this letter, cyclic dimer, trimer, and tetramer of chlorophyll derivatives were synthesized, their structural properties were elucidated based on spectroscopic studies, and novel complexation ability of the cyclic trimer toward fullerenes was demonstrated.



Scheme 1. Reagents and conditions: (a) $(Bu_2ClSn)_2O$ (0.1 equiv), toluene, reflux, 12 h, **2**: 44%, **3**: 23%, **4**: 3%; (b) acetic acid, EDC·HCl, DMAP, CH_2Cl_2, rt, 98%.

To connect the 3 and 17 positions of chlorin macrocycle, chlorophyll-*a* extracted from *Spirulina geitleri* was converted to chlorin **5** (see left drawing of Scheme 1) by the reported procedure.[5f] 1,3-Dichlorotetrabutyl distannoxane [$(Bu_2ClSn)_2O$] was selected as a catalyst of transesterification.[7] Thus, intermolecular reaction between 3-hydroxymethyl and 17^2-methoxycarbonyl groups was performed in toluene at 2.5 mM of **5** in the presence of 10 mol % distannoxane catalyst (step (a) in Scheme 1). The product was separated by GPC to give cyclic dimer **2** (44% yield), trimer **3** (23%), and tetramer **4** (3%) together with recovered starting compound **5** (22%), as well as linear dimer (3%) and trimer (0.5%).[8] The efficient preparation of cyclic compounds over linear (70% vs 3.5%) is ascribed to the assumption that any π–π stacking interaction among chlorin macrocycles works under the present synthetic conditions to induce the formation of cyclic structures. The low yield of the larger size oligomers indicates that the resulting cyclic compounds are too stable to further expand through esterification, probably due to the sterical

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hindrance around the formed 17^2-ester group.[9] As a reference compound, monomer chlorin **1** was prepared by acetylation of the 3^1-hydroxy group in **5** (step (b) in Scheme 1).[10]

^{1}H NMR spectra of chlorins **1**–**4** measured in $CDCl_3$ are aligned in Figure 1. Because two chlorin macrocycles of dimer **2** are located close to each other, several protons show drastic upfield shifts compared to the corresponding protons of monomer **1**, due to the shielding of ring current effect. For example, chemical shifts of 5-H and 7-CH_3 in **2** were upfield shifted to $\delta = 6.99$ and 1.52 ppm, respectively, from the corresponding δs of **1** (9.44 and 3.28 ppm). On the contrary, upfield shifts of the proton signals in trimer **3** are small, and chemical shifts of **3** are similar to those of **1** as can be seen in Figure 1a and c. In view of the chemical shifts, the upfield shifts of proton peaks in the oligomer roughly decreased in the order of **2** > **4** > **3**. Because the ^{1}H NMR spectra of **2**–**4** showed simple signals, conformational transformation in each oligomer is rapid on a NMR time-scale to afford averaged signals. However, the observed changes of chemical shifts in **1** → **2**–**4** could be explained by their energy-minimized structures estimated from molecular model calculations.[11] Trimer **3** is in equilibrium between two conformers, three monomer units (left drawing of Fig. 2a) and a mixture of one dimeric and one monomeric unit (right drawing of Fig. 2a), while tetramer **4** can be regarded as two dimeric units (Fig. 2b). Some portions of chlorin ring in trimer **3** are located out of the shielding region. On the contrary, tetramer **4** having a larger cyclic structure seems relatively flexible, and therefore its structure would stabilize more easily through intramolecular π–π stacking than trimer **3** does.

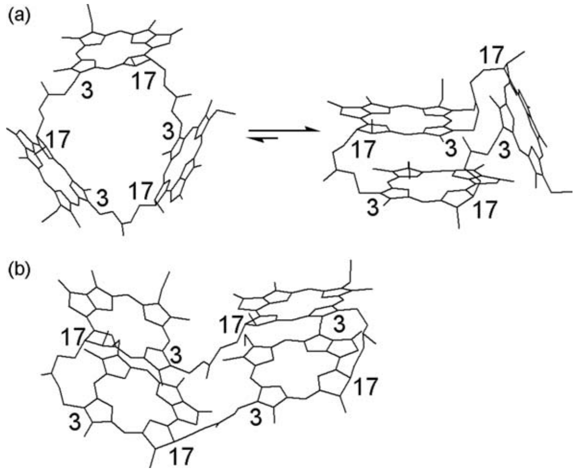

Figure 2. Proposed structures of (a) trimer **3** and (b) tetramer **4** based on molecular modeling study.

To further investigate the proposed conformation of the oligomers, absorption spectra were recorded using the same sample solutions as for ^{1}H NMR measurements. Figure 3 compares the absorption spectra of **1**–**4** and their absorption maxima are summarized in Table 1. Both Q_x (508, 540 nm) and Q_y peaks (668 nm) of dimer **2** showed slight red-shifts compared to those of monomer **1** (Q_x: 506, 537; Q_y: 666 nm). The difference is apparently ascribable to the stacking interaction of **2**, which was also observed for other types of cyclic chlorophyll dyad.[5c] On the other hand, characteristic similarities of peak maxima and shape between dimer **2** and tetramer **4** indicate that stacked conformation of **4** through intramolecular interaction (Fig. 2b) is a dominant species in this solution state.

Inspired by the recent development of fullerene–porphyrin constructs,[12] the interaction between **1**–**4** and

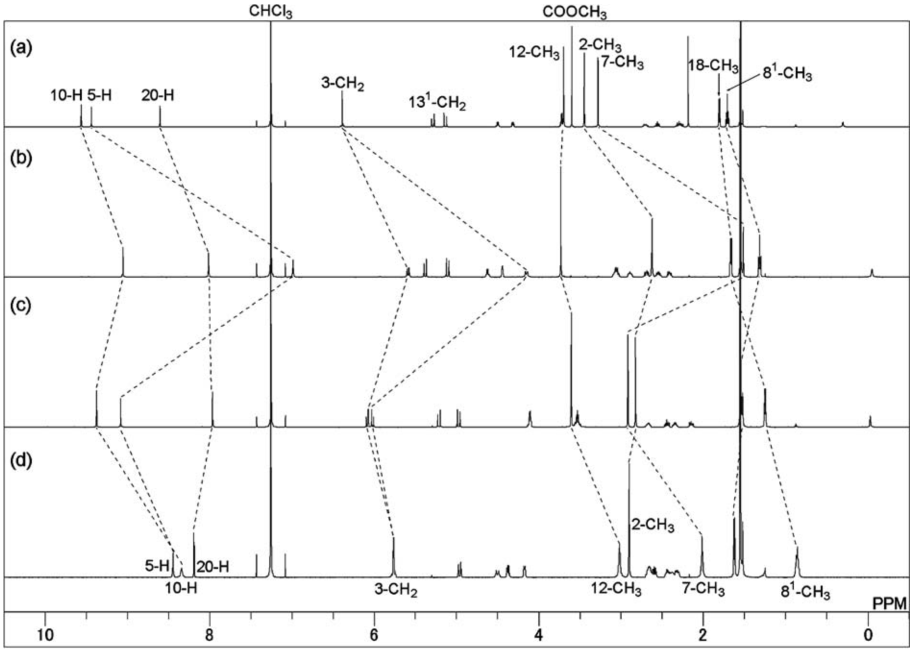

Figure 1. ^{1}H NMR spectra of (a) monomer **1** (1.0 mM), (b) dimer **2** (0.50 mM), (c) trimer **3** (0.33 mM), and (d) tetramer **4** (0.25 mM) in $CDCl_3$.

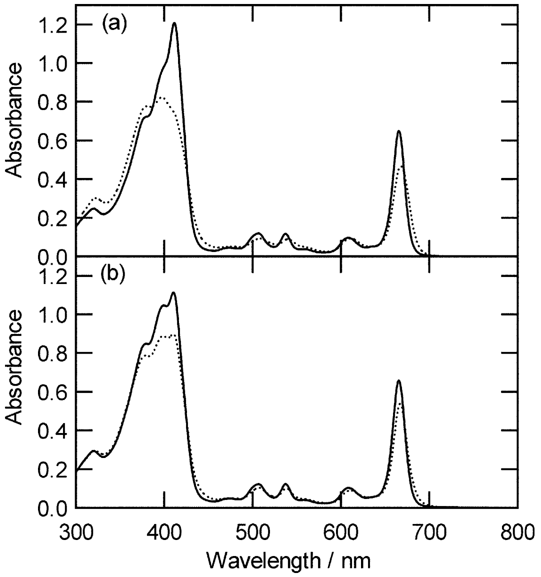

Figure 3. Electronic absorption spectra of (a) monomer **1** (solid line, 1.0 mM) and dimer **2** (dotted line, 0.50 mM) and (b) trimer **3** (solid line, 0.33 mM) and tetramer **4** (dotted line, 0.25 mM) in $CDCl_3$.

Table 1. Absorption maxima (λ_{max}/nm) of free-base chlorins **1**–**4** in $CDCl_3$[a]

	Soret	Q_x	Q_y
1	378(sh), 397(sh), 411	506, 537	666
2	380, 397, 410(sh)	508, 540	668
3	378, 398, 410	506, 538	666
4	378, 398, 410	507, 539	667

[a] Concentrations of **1**, **2**, **3**, and **4** were 1.0, 0.50, 0.33, and 0.25 mM, respectively.

C_{60}/C_{70} was also examined. When solid C_{60} was extracted with $CDCl_3$ solutions of **1**–**4**, trimer **3** showed some peak shifts in the ^1H NMR spectrum while **1**, **2**, and **4** did not show any spectral changes. It turned out that C_{70} causes more drastic changes as summarized in Table 2. Similarly, only trimer **3** showed spectral changes in electronic absorption and CD measurements with addition of fullerenes,[13] and the changes were larger for C_{70} than for C_{60}. By treatment with C_{70}, Q_y peak of **3** showed a red-shift (666→671 nm) and CD signal changes at the Q_y region (S → reversed S-shape) was observed as can be seen in Figure 4. The observed selectivity would be explained by the supramolecular model where the C_{70} molecule is well-accommodated into the cavity of **3** surrounded by three chlorin macrocycles (see Supplementary data).

Table 2. Selected ^1H NMR chemical shift (ppm) of trimer **3** with(out) fullerenes in $CDCl_3$[a]

Proton	Without	C_{60}	C_{70}
10-H	9.38	9.32	9.22
5-H	9.09	9.10	9.03
20-H	7.97	8.10	8.32
12-CH_3	3.61	3.58	3.53
7-CH_3	2.92	2.97	2.97
2-CH_3	2.83	2.99	3.22
8^1-CH_3	1.54	1.48	1.45
18-CH_3	1.25	1.58	1.80

[a] [Trimer **3**] = 0.33 mM. Solid C_{60} or C_{70} was added to the sample solution, sonicated for 1 min, filtered, and subjected to measurement.

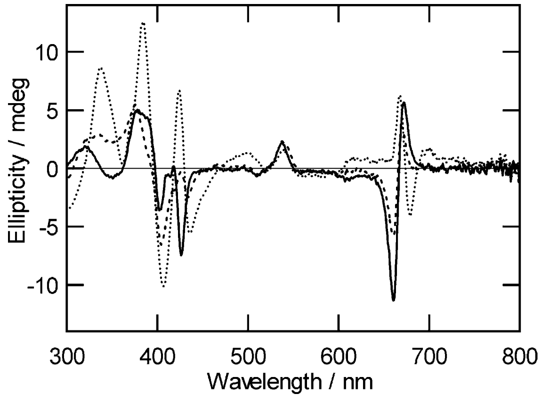

Figure 4. CD spectra of trimer **3** (solid line), **3** with C_{60} (dashed line), and **3** with C_{70} (dotted line) in $CDCl_3$. [**3**] = 0.33 mM. C_{60} or C_{70} was saturated in the solution.

In summary, we synthesized new cyclic chlorin oligomers by intermolecular transesterification using a distannoxane catalyst under a high dilution condition. The chlorin macrocycles of tetramer **4** are found to be stacked through intramolecular π–π interaction as in dimer **2**, and more flexible trimer **3** accommodated fullerenes in its cavity. Development of other types of chlorin oligomers and elucidation of their physical properties are in progress.

Acknowledgements

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Supplementary data

Supplementary data available via Science-Direct: http://www.sciencedirect.com. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.04.159.

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8. Total yield of the identified products was 95.5%. The loss is mainly due to the incomplete separation during GPC, where each valley was cut off to obtain the pure compounds.
9. It is reported that the bulkiness around the ester group strongly influences the rate of transesterification using this catalyst (Ref. 7). Therefore, less hindered methyl ester terminal at the 17^2-position of **5** and linear oligomers can be assumed to be the only active site for the reaction.
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13. Fluorescence emission intensity I_f at 668 nm of trimer **3** in $CHCl_3$ (0.33 μM) excited at 410 nm was quenched by the addition of C_{70} (10 μM). The quenching ratio $[= (I_f^0 - I_f)/I_f^0]$ in **3** was about 30% and twice larger than 15% in **1** (1 μM).