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COMMUNICATION

Procedure-Dependent Construction of Two Isomers of Trimeric Self-Assembled Boronic Esters†

Cite this: DOI: 10.1039/x0xx00000x

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Received 00th January 2014,

Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

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Procedure-dependent selective construction of two isomers of trimeric boronic esters was realized. Capsule-like trimeric boronic ester was constructed by the direct connection of two kinds of self-assembled boronic esters by [3+2] cycloaddition, while tricyclic trimeric boronic ester was obtained by the self-assembly of pre-connected components.

Self-assembly of discrete molecular architectures has been attracting much attention due to their possible applications to storage material, separating agent, sensor, catalyst etc.^{1–3} To pursue new possibilities of the self-assembly, post-modification strategy is intriguing because of the possible formation of a new type of molecular architecture that cannot be prepared under simple self-assembling conditions. However, due to rather unstable nature of the self-assembled entity obtained by utilizing a hydrogen bond¹ or a coordination bond,² methods for the postmodification of such molecules are quite limited.^{4–6} In particular, connection of different self-assembled molecules has not been realized yet partly due to the difficulty in suppressing equilibrium between the component molecules during the connecting reactions. In this regard, utilization of dynamic covalent bonds is attractive due to their higher stability as covalent bond and their property to show dynamic nature under specific conditions. In this paper, we report a selective preparation of two isomeric, higher-order architectures either through postsynthetic direct connection of two kinds of discrete self-assembled boronic

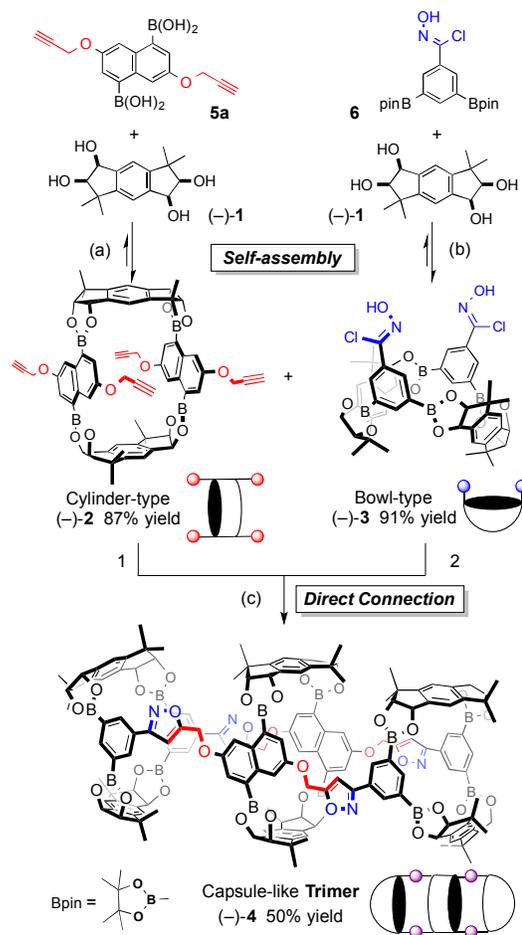


Fig. 1. Direct connection of self-assembled boronic esters (-2) and (-3) for the construction of capsule-like trimer (-4). Reaction conditions: (a) (-1), **5a** (1.0 mol. amount), MeOH/C₆F₆ (5:1), rt, 24 h, 87% yield. (b) (-1), **6** (1.0 mol. amount), MeOH/C₆F₆ (11:1), rt, 24 h, 91% yield. (c) (-2), (-3) (5.0 mol. amount), proton sponge (12 mol. amount), CHCl₃, rt, 7 days, 50% yield.

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† Electronic Supplementary Information (ESI) available: Experimental details, synthesis and characterization data of the compounds, crystallographic data and computational study. CCDC 869549–869452. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x/

esters via a reaction which proceeds without equilibration of the boronic esters or through self-assembly of pre-connected component molecules.⁷

We recently reported the construction of macrocyclic boronic esters simply by mixing a diboronic acid and indacene-type bis(1,2-diol) **1** in the presence of appropriate guest molecules under neutral conditions.⁸ In this system, in the presence of protic solvents such as MeOH, the boronic ester formation is in a very rapid equilibrium and gives the self-assembled products as thermodynamically stable compounds sometimes in a few seconds, while in the absence of protic solvents, the equilibration could be suppressed allowing the compound to be treated as a kinetically stable compound. These characteristics would be attractive to see the behavior of kinetically connected higher order architectures, however, the highly dynamic nature of this boronic ester linkage could be a problem during the connection of self-assembled structures. To realize this strategy, it is necessary to develop an orthogonal reaction, which proceeds under the conditions where equilibration of boronic esters does not occur.

Initially, we examined several reactions and found that the [3 + 2] cycloaddition of nitrile oxides with alkynes in the presence of proton sponge as base gave isoxazole derivatives in high yield suppressing the equilibration of the boronic ester linkage (Table S1 in the SI). With the reaction employable for connecting self-assembled boronic esters in hand, we designed functionalized macrocyclic boronic esters **2** and **3** for the construction of capsule-like trimeric architecture **4**.⁹ Our approach for the construction of trimer **4** is based on the end capping of cylinder-type boronic ester **2** having alkyne moieties^{8b} with two molecules of bowl-type boronic ester **3** having chlorooxime moieties (Fig. 1). Rigid structure of these boronic esters was considered to be suitable for the connection of two reaction sites of each macrocyclic boronic ester by the irreversible [3 + 2] cycloaddition.

The central cylinder framework (–)**2** and the end capping moiety (–)**3** were easily obtained as precipitates by the self-assembly of bis(1,2-diol) (–)**1** with 1,5-naphthalenediboronic acid derivative **5a** and 1,3-benzenediboronic acid derivative **6** in 87% and 91% yields, respectively (Fig. 1a,b). Enantiopure (–)**1** was used for the construction of (–)**2** and (–)**3** to avoid the formation of diastereomers of the connected product **4**. With the required two components in hand, the connecting reaction by [3+2] cycloaddition was examined. After the screening of the reaction conditions, it was found that the desired capsule-like trimeric product (–)**4** was obtained in 50% isolated yield by stirring a 1:5 mixture of (–)**2** and (–)**3** in the presence of 12 molar amounts of proton sponge in 1,2-dichloroethane at room temperature for 7 days, followed by the separation of oligomeric products by GPC (Fig. 1c).

The complete conversion of four alkyne moieties of (–)**2** into isoxazole rings and the formation of 1:2 adduct of (–)**2** and (–)**3** was confirmed by ¹H NMR and FAB-MS analyses (Fig. S1,3 in the SI). The structure was finally determined to be the desired capsule-like trimer (–)**4** by X-ray crystallographic analysis of the single crystal obtained by slow vapor diffusion of acetone into a toluene/chloroform solution of (–)**4** (Fig. 2).¹⁰ Three macrocyclic boronic esters, linked by isoxazole rings, are aligned in a straight line, thus forming the capsule-like structure, and the length of the molecular capsule is 31 Å. Disordered toluene molecules were observed in the cavity space, which were removed by the SQUEEZE¹¹ procedure in the PLATON¹² program to analyze the accurate structure of the capsule.

As the direct connection of different self-assembled boronic esters was realized, the self-assembly of pre-connected boronic acid derivative **7** with (+)**1** was then examined to see if the self-assembly of capsule-like trimer (+)**4** is possible (Fig. 3). Pre-connected hexaboronic acid **7** was prepared in 32% yield by the

same [3 + 2] cycloaddition between **5b** and **6** (Fig. 3a,b). Quite interestingly, when the pre-connected hexaboronic acid **7** was mixed

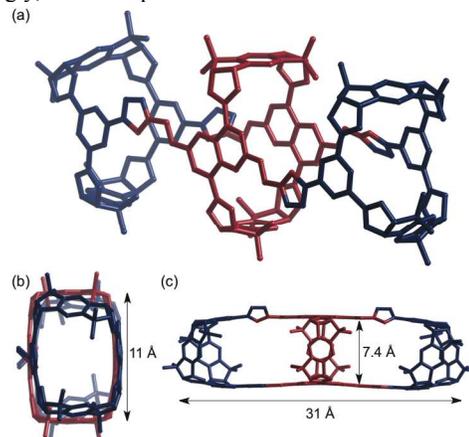


Fig. 2. Single crystal structure of capsule-like trimer (–)**4** (cylinder-type boronic ester moiety = red, bowl-type boronic ester moieties = blue). (a) Overview. (b) Front view. (c) Top view.

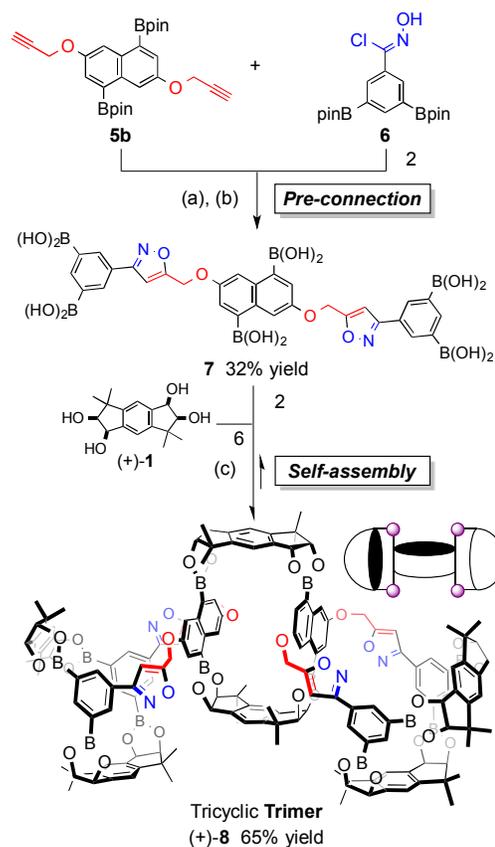


Fig. 3. Self-assembly of tricyclic trimer (+)**8** from (+)**1** with pre-connected hexaboronic acid **7**. Reaction conditions: (a) **5b**, **6** (2.1 mol. amount), triethylamine, 1,2-dichloroethane, reflux, 25 h, 75% yield. (b) Diethanolamine (31 mol. amount), MeOH/CHCl₃ (1:1), rt, 24 h then 1M aq. HCl/CH₂Cl₂ (1:1), rt, 8 h, 42% yield. (c) **7**, (+)**1** (2.9 mol. amount), MeOH/*p*-xylene (2:1), rt, 24 h, 65% yield.

with (+)**1** in MeOH/*p*-xylene (2:1) and the resulting precipitate was dissolved in CHCl₃ to remove insoluble polymer, another boronic

ester was obtained in 65% yield containing almost one molecule of *p*-xylene along with a trace amount of capsule-like trimer (+)-**4** (Fig. 3c). Although FAB-MS analysis of the product supported the formation of trimeric product, ^1H NMR spectrum of the self-assembled product was different from that of trimer **4** (Fig. S3 in the SI). The structure of this product was revealed by X-ray analysis of the single crystal prepared by slow vapor diffusion of *n*-hexane into a toluene/chloroform solution of the product to be tricyclic trimer **8** (Fig. 4),¹³ in which each boronic acid moiety on the two benzene rings of **7** was intramolecularly linked by two molecules of **1** and the central diboronic acid on the naphthalene ring was intermolecularly linked by **1**. Selective self-assembly of capsule-like trimer (+)-**4** was not achieved even after the extensive screening of the reaction conditions (Table S2, 3 in the SI). Thus, two isomeric trimers **4** and **8** could selectively be constructed by choosing an appropriate order of assembling protocols, and in particular, capsule-like trimer **4** could only be prepared selectively by using the direct connection of two kinds of self-assembled products developed in the present study.

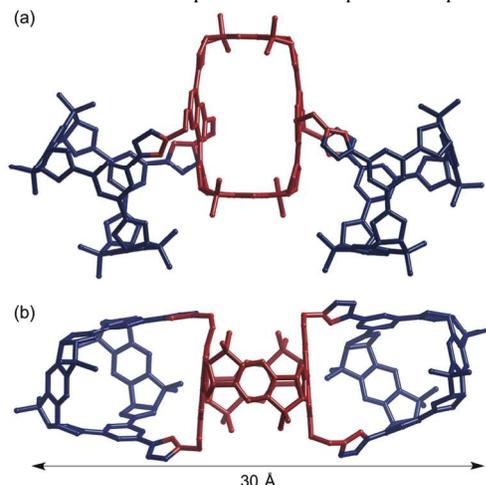


Fig. 4. Single crystal structure of tricyclic trimer *rac*-**8** (cylinder-type boronic ester moiety = red, bowl-type boronic ester moieties = blue). (a) Top view. (b) Side view.

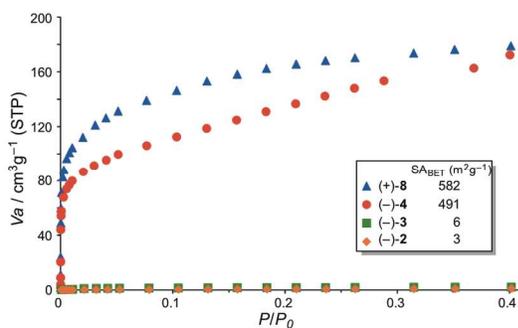


Fig. 5. Nitrogen adsorption isotherms of trimers and monomeric components at 77 K.

Both capsule-like trimer (-)-**4** and tricyclic trimer (+)-**8** contain intrinsic cavities, thus should be utilized as porous organic materials.^{14,15} Nitrogen adsorption measurements were performed for amorphous solid of trimer (-)-**4** and (+)-**8**. The adsorption isotherms of (-)-**4** and (+)-**8** were classified as type-I forms, which are characteristic of microporous materials. The Brunauer-Emmett-Teller (BET) surface areas (S_{BET}) of (-)-**4** and (+)-**8** were 491 and

582 m^2g^{-1} , respectively, both of which were moderately high value compared with reported values of amorphous porous organic materials.¹⁵ The specific surface areas of monomeric macrocyclic boronic esters (-)-**2** and (-)-**3** were also measured by nitrogen adsorption experiments. In sharp contrast with trimers, S_{BET} of (-)-**2** and (-)-**3** were only 3 and 6 m^2g^{-1} , respectively, indicating the absence of micropores. Thus, the great improvement of S_{BET} was realized by the construction of trimeric architectures with intrinsic cavities.

In conclusion, we achieved the selective construction of isomers of trimeric self-assembled boronic esters depending on the order of assembling protocols. Capsule-like trimer was synthesized by the direct connection of self-assembled boronic esters, while tricyclic trimer was obtained by the self-assembly of pre-connected hexaboronic acid with bis(1,2-diol) **1**. Therefore, the direct connection of two kinds of self-assembled products developed in this study was found to be the effective method for the construction of higher order architecture, which could not be obtained by the simple self-assembly of pre-connected components. Moreover, the specific surface areas of these trimeric boronic esters were greatly enhanced compared with the monomeric macrocyclic boronic esters. Further studies are now in progress to create structurally defined molecular tubes by using functional macrocyclic boronic esters.

This work was supported by a CREST (Core Research for Evolution Science and Technology) project from the Japan Science and Technology Agency (JST). The synchrotron radiation experiment was performed at the BL40XU of SPring-8 with the approval of the Japan Synchrotron Radiation Research Institute (JASRI) (Proposal No. 2013A1052).

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