



Cite this: *Chem. Commun.*, 2014, 50, 13683

Received 28th July 2014,
Accepted 9th September 2014

DOI: 10.1039/c4cc05836d

www.rsc.org/chemcomm

Procedure-dependent construction of two isomers of trimeric self-assembled boronic esters†

Kosuke Ono,^a Ryo Aizawa,^a Taiki Yamano,^a Suguru Ito,^a Nobuhiro Yasuda,^b Kohei Johmoto,^c Hidehiro Uekusa^c and Nobuharu Iwasawa^{*a}

A procedure-dependent selective construction of two isomers of trimeric boronic esters was realized. A capsule-like trimeric boronic ester was constructed by the direct connection of two kinds of self-assembled boronic esters via [3+2] cycloaddition, while the 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 in storage materials, separating agents, sensors, catalysts *etc.*^{1–3} To pursue new possibilities of achieving self-assembly, the post-modification strategy is intriguing because of the possibility of the formation of a new type of molecular architecture that cannot be prepared under simple self-assembling conditions. However, due to the 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 the 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 a covalent bond and their property of showing a dynamic nature under specific conditions. In this communication, we report a selective preparation of two isomeric, higher-order architectures either through postsynthetic

direct connection of two kinds of discrete self-assembled boronic esters *via* a reaction which proceeds without equilibration of the boronic esters or through the 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 yields 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 for observing 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 in which 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 a proton sponge as the base gave isoxazole derivatives in high yield suppressing the equilibration of the boronic ester linkage (Table S1 in the ESI†). 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 a capsule-like trimeric architecture **4**.⁹ Our approach for the construction of trimer **4** is based on the end capping of a cylinder-type boronic ester **2** having alkyne moieties^{8b} with two molecules of a bowl-type boronic ester **3** having chloro-oxime moieties (Fig. 1). The rigid structure of these boronic esters was considered to be suitable for the connection of two reaction sites of each macrocyclic boronic ester *via* 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

^a Department of Chemistry, Tokyo Institute of Technology and CREST, Japan Science and Technology Agency (JST), 2-12-1, O-okayama, Meguro-ku, Tokyo 152-8551, Japan. E-mail: niwasawa@chem.titech.ac.jp

^b Japan Synchrotron Radiation Research Institute/Spring-8, 1-1-1 Kouto, Sayo-gun, Hyogo 679-5198, Japan

^c Department of Chemistry and Materials Science, Tokyo Institute of Technology and CREST, Japan Science and Technology Agency (JST), 2-12-1, O-okayama, Meguro-ku, Tokyo 152-8551, Japan

† Electronic supplementary information (ESI) available: Experimental details, synthesis and characterization data of the compounds, crystallographic data and computational study. CCDC 1008723 and 1008724. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4cc05836d

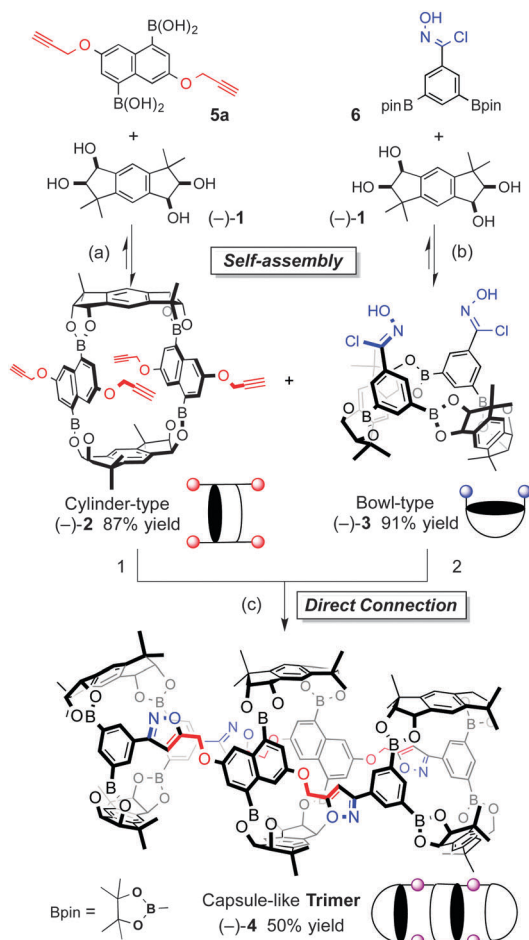


Fig. 1 Direct connection of self-assembled boronic esters (–)-2 and (–)-3 for the construction of capsule-like trimer (–)-4. Reaction conditions: (a) (–)-1, **5a** (1.0 mol. amount), MeOH/C₆F₆ (5:1), r.t., 24 h, 87% yield. (b) (–)-1, **6** (1.0 mol. amount), MeOH/C₆F₆ (11:1), r.t., 24 h, 91% yield. (c)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

bis(1,2-diol) (–)-1 with the 1,5-naphthalenediboronic acid derivative **5a** and the 1,3-benzenediboronic acid derivative **6** in 87% and 91% yields, respectively (Fig. 1(a) and (b)). The enantiopure compound (–)-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 was examined *via* [3+2] cycloaddition. After the screening of the reaction conditions, it was found that the desired capsule-like trimeric product (–)-4 was obtained in a 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. 1(c)).

The complete conversion of four alkyne moieties of (–)-2 into isoxazole rings and the formation of a 1:2 adduct of (–)-2 and (–)-3 was confirmed using ¹H NMR and FAB-MS analyses (Fig. S1 and S3 in the ESI†). 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

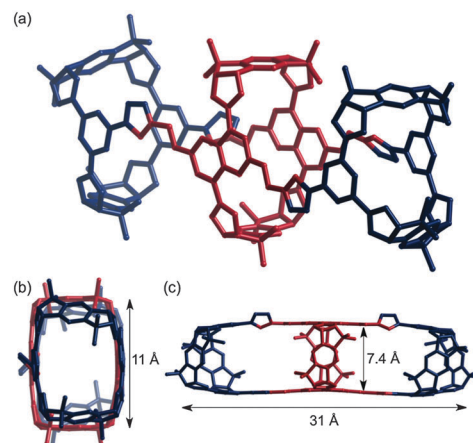


Fig. 2 Single crystal structure of capsule-like trimer (–)-4 (cylinder-type boronic ester moiety = red, bowl-type boronic ester moieties = blue). (a) Overview. (b) Front view. (c) Top view.

isoxazole rings, are aligned in a straight line, thus forming a capsule-like structure, and the length of the molecular capsule was 31 Å. Disordered toluene molecules were observed in the cavity space, which were removed using the SQUEEZE¹¹ procedure in the PLATON¹² program to analyze the structure of the capsule accurately.

As the direct connection of different self-assembled boronic esters was realized, the self-assembly of the pre-connected hexaboronic acid derivative **7** with (+)-1 was then examined to see whether the self-assembly of the capsule-like trimer (+)-4 is possible (Fig. 3). Pre-connected hexaboronic acid **7** was prepared in 32% yield *via* the same [3+2] cycloaddition reaction between **5b** and **6** (Fig. 3(a) and (b)). Quite interestingly, when the pre-connected hexaboronic acid **7** was mixed with (+)-1 in MeOH-*p*-xylene (2:1) and the resulting precipitate was dissolved in CHCl₃ to remove the insoluble polymer, another boronic ester was obtained in 65% yield containing almost one molecule of *p*-xylene along with a trace amount of the capsule-like trimer (+)-4 (Fig. 3(c)). Although FAB-MS analysis of the product supported the formation of a trimeric product, the ¹H NMR spectrum of the self-assembled product was different from that of trimer **4** (Fig. S3 in the ESI†). 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 the capsule-like trimer (+)-4 was not achieved even after an extensive screening of the reaction conditions (Table S2 and S3 in the ESI†). Thus, two isomeric trimers **4** and **8** could be selectively constructed by choosing an appropriate order of assembling protocols, and in particular, the 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.

Both the capsule-like trimer (–)-4 and the tricyclic trimer (+)-8 contain intrinsic cavities, and thus should be utilized as porous organic materials.^{14,15} Nitrogen adsorption measurements were

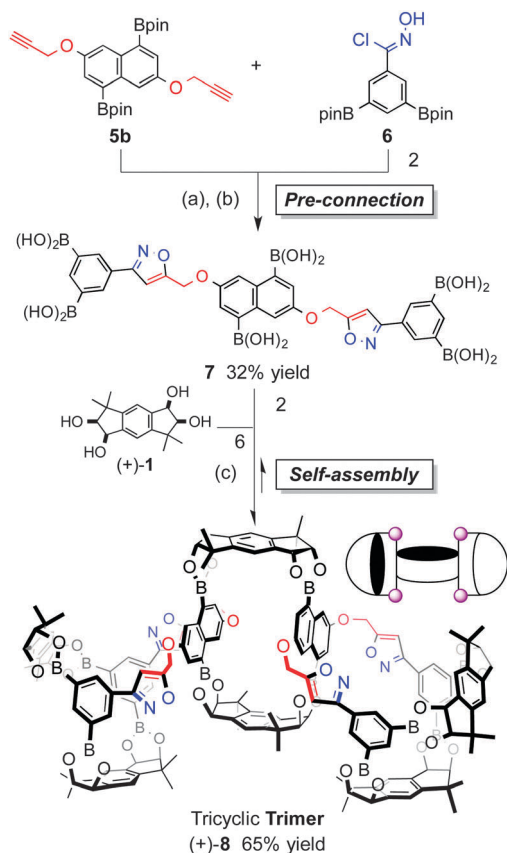


Fig. 3 Self-assembly of tricyclic trimer (+)-8 from (+)-1 with pre-connected hexaboronic acid **7**. Reaction conditions: (a) **5b**, **6** (2.1 mol. amount), triethylamine, 1,2-dichloroethane, reflux, 25 h, 75% yield. (b) Diethanolamine (31 mol. amount), MeOH/CHCl₃ (1:1), r.t., 24 h then 1M aq. HCl/CH₂Cl₂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

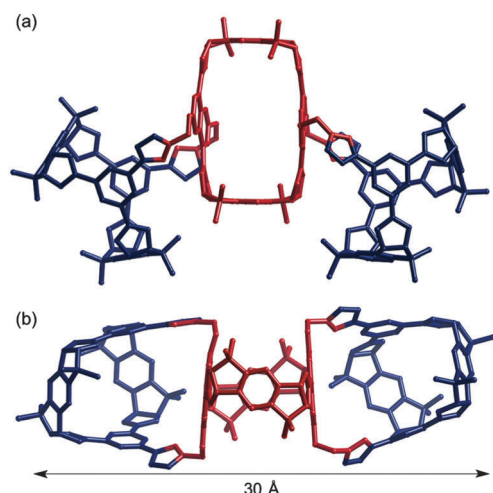


Fig. 4 Single crystal structure of tricyclic trimer *rac*-8 (cylinder-type boronic ester moiety = red, bowl-type boronic ester moieties = blue). (a) Top view. (b) Side view.

performed for amorphous solids of trimers (–)-4 and (+)-8. The adsorption isotherms of (–)-4 and (+)-8 (Fig. 5) were classified as

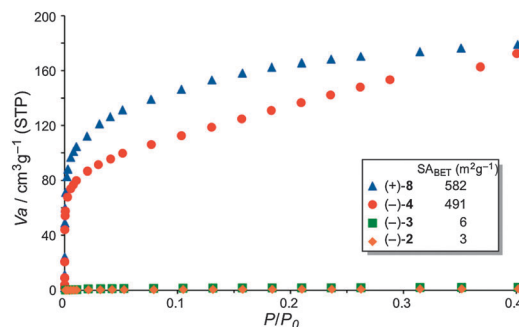


Fig. 5 Nitrogen adsorption isotherms of trimers and monomeric components at 77 K.

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 m² g^{–1}, respectively, both of which were of moderately high value compared with the 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 to trimers, S_{BET} values of (–)-2 and (–)-3 were only 3 and 6 m² g^{–1}, respectively, indicating the absence of micropores. Thus, a great improvement of S_{BET} was realized *via* 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. The capsule-like trimer was synthesized by the direct connection of self-assembled boronic esters, while the 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 an effective method for the construction of a 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 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).

Notes and references

- For reviews on the discrete architectures constructed by hydrogen bonds, see (a) M. Alajarin, R.-A. Orenes, J. W. Steed and A. Pastor, *Chem. Commun.*, 2010, **46**, 1394–1403; (b) L. Avram, Y. Cohen and J. Rebek Jr., *Chem. Commun.*, 2011, **47**, 5368–5375; (c) A. Scarso and G. Borsato, *Self-Assembly of Organic Supramolecular Capsules*, in *Supramolecular Chemistry: From Molecules to Nanomaterials*, ed. P. A. Gale and J. W. Steed, John Wiley & Sons, Ltd, New York, 2012, vol. 5, pp. 2085–2147.
- For reviews on the discrete architectures constructed by reversible coordination bonds, see (a) M. J. Wiester, P. A. Ulmann and C. A. Mirkin, *Angew. Chem., Int. Ed.*, 2011, **50**, 114–137; (b) R. Chakrabarty,

- P. S. Mukherjee and P. J. Stang, *Chem. Rev.*, 2011, **111**, 6810–6918; (c) M. M. J. Smulders, I. A. Riddell, C. Browne and J. R. Nitschke, *Chem. Soc. Rev.*, 2013, **42**, 1728–1754.
- 3 For reviews on the discrete architectures constructed by dynamic covalent bonds, see (a) P. T. Corbett, J. Leclaire, L. Vial, K. R. West, J.-L. Wietor, J. K. M. Sanders and S. Otto, *Chem. Rev.*, 2006, **106**, 3652–3711; (b) N. E. Borisova, M. D. Reshetova and Y. A. Ustynyuk, *Chem. Rev.*, 2007, **107**, 46–49; (c) M. Mastalerz, *Angew. Chem., Int. Ed.*, 2010, **49**, 5042–5053; (d) R. Nishiyabu, Y. Kubo, T. D. James and J. S. Fossey, *Chem. Commun.*, 2011, **47**, 1124–1150.
 - 4 For some postsynthetic functional group modification of a discrete architecture with a monofunctionalized reactant, see (a) D. Zhao, S. Tan, D. Yuan, W. Lu, Y. H. Rezenom, H. Jiang, L.-Q. Wang and H.-C. Zhou, *Adv. Mater.*, 2011, **23**, 90–93; (b) M. Wang, W.-J. Lan, Y.-R. Zheng, T. R. Cook, H. S. White and P. J. Stang, *J. Am. Chem. Soc.*, 2011, **133**, 10752–10755; (c) R. Chakrabarty and P. J. Stang, *J. Am. Chem. Soc.*, 2012, **134**, 14738–14741; (d) M. W. Schneider, I. M. Oppel, A. Griffin and M. Mastalerz, *Angew. Chem., Int. Ed.*, 2013, **52**, 3611–3615.
 - 5 For postsynthetic treatment with a multifunctionalized reactant or a multidentate ligand, see (a) J. K. Clegg, S. S. Iremonger, M. J. Hayter, P. D. Southon, R. B. Macquart, M. B. Duriska, P. Jensen, P. Turner, K. A. Jolliffe, C. J. Kepert, G. V. Meehan and L. F. Lindoy, *Angew. Chem., Int. Ed.*, 2010, **49**, 1075–1078; (b) S. Mirtschin, A. Slabon-Turski, R. Scopelliti, A. H. Velders and K. Severin, *J. Am. Chem. Soc.*, 2010, **132**, 14004–14005; (c) A. Granzhan, C. Schouwey, T. Riis-Johannessen, R. Scopelliti and K. Severin, *J. Am. Chem. Soc.*, 2011, **133**, 7106–7115; (d) J. Fan, M. L. Saha, B. Song, H. Schönherr and M. Schmittel, *J. Am. Chem. Soc.*, 2012, **134**, 150–153.
 - 6 For some postsynthetic covalent bond formations within a discrete architecture, see (a) L. Wang, M. O. Vysotsky, A. Bogdan, M. Bolte and V. Böhmer, *Science*, 2004, **304**, 1312–1314; (b) M. S. Kaucher, W. A. Harrell, Jr. and J. T. Davis, *J. Am. Chem. Soc.*, 2006, **128**, 38–39; (c) S. Hiraoka, Y. Yamauchi, R. Arakane and M. Shionoya, *J. Am. Chem. Soc.*, 2009, **131**, 11646–11647.
 - 7 To the best of our knowledge, there has been no report on the direct connection of different discrete self-assembled architectures, whereas multifunctionalized linkers or ligands have been used for the connection of two or more identical discrete self-assembled architectures. See ref. 6.
 - 8 (a) N. Iwasawa and H. Takahagi, *J. Am. Chem. Soc.*, 2007, **129**, 7754–7755; (b) Y. Kikuchi, H. Takahagi, K. Ono and N. Iwasawa, *Chem. – Asian J.*, 2014, **9**, 1001–1005.
 - 9 In this communication, 1 : 2 adducts of cylinder-type boronic ester 2 and bowl-type boronic ester 3 are referred to as trimer.
 - 10 CCDC 1008723 contains the supplementary crystallographic data of (–)-4.
 - 11 P. van der Sluis and A. L. Spek, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 1990, **46**, 194–201.
 - 12 A. L. Spek, *Acta Crystallogr., Sect. D: Biol. Crystallogr.*, 2009, **65**, 148–155.
 - 13 Single crystal was obtained by using *rac*-8, which was constructed from *rac*-1 with 7 in a lower yield (Table S3 in the ESI†). Because the diffraction from the crystal was very weak, the single crystal X-ray diffraction data were collected using synchrotron radiation ($\lambda = 0.78215 \text{ \AA}$) on SPring-8 BL40XU with Rigaku Saturn CCD area detector (for details, see the ESI†). CCDC 1008724 contains the supplementary crystallographic data of *rac*-8.
 - 14 For reviews, see (a) A. I. Cooper, *Angew. Chem., Int. Ed.*, 2012, **51**, 7892–7894; (b) M. Mastalerz, *Chem. – Eur. J.*, 2012, **18**, 10082–10091; (c) Y. Jin, Y. Zhu and W. Zhang, *CrystEngComm*, 2013, **15**, 1484–1499.
 - 15 For some examples of amorphous porous organic materials, see (a) J. H. Chong, S. J. Ardakani, K. J. Smith and M. J. MacLachlan, *Chem. – Eur. J.*, 2009, **15**, 11824–11828; (b) J. Tian, P. K. Thallapally, S. J. Dalgarno, P. B. McGrail and J. L. Atwood, *Angew. Chem., Int. Ed.*, 2009, **48**, 5492–5495; (c) Y. Jin, B. A. Voss, A. Jin, H. Long, R. D. Noble and W. Zhang, *J. Am. Chem. Soc.*, 2011, **133**, 6650–6658; (d) M. W. Schneider, H.-J. S. Hauswald, R. Stoll and M. Mastalerz, *Chem. Commun.*, 2012, **48**, 9861–9863; (e) T. Hasell, S. Y. Chong, K. E. Jelfs, D. J. Adams and A. I. Cooper, *J. Am. Chem. Soc.*, 2012, **134**, 588–598.