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Supramolecular Chemistry

Release and Recovery of Guest Molecules during the Reversible Borate Gel Formation of Guest-Included Macrocyclic Boronic Esters**

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Guest-induced self-assembly of host compounds based on dynamic covalent bond formation[1,2] or reversible metal–ligand coordination[3] has become a reliable method for the construction of isolable host compounds suitable for binding specific guest molecules. Meanwhile, dynamic covalent bond formation and reversible metal–ligand coordination have been utilized for the creation of smart gels,[4–7] which could respond to the external stimuli, such as temperature, pH, and light, owing to their dynamic nature. These smart gels are expected to find their practical applications in various fields, such as sensors, actuators, and self-healing materials. However, a relatively limited number of reported examples focused on the encapsulation or release of guest molecules in the gel state,[8] in contrast to the well-studied host–guest chemistry in solution state.[9,10] In the reported examples, guest molecules were covalently connected to the gelator[8a,e,f] or simply doped into the gels.[8b–d] Moreover, the recovery of the released guest molecule from the gel remains a challenging task. Therefore, the development of a new class of gelator, which enables both release and recovery of guest molecules, would further widen the possible application field of the smart gel. Herein, we realized the release and recovery of the guest molecule during the formation and collapse of the borate gel by utilizing the guest-induced self-assembly of macrocyclic boronic esters.

We have already reported the guest-induced self-assembly of discrete boronic esters from indacene-type bis(1,2-diol) **1** with di- or triboronic acid based on the reversible nature of boronic ester formation.[11] In this system, self-assembled boronic esters were obtained as precipitates, which was the key factor for the selective formation of the single boronic ester. Boronic esters are also well-known to form borates by the addition of an appropriate Lewis base, which causes the geometric change at the boron atom from sp^2 to sp^3.[12] Recently, the dynamic nature of borate formation was applied, for the first time, to the creation of thermoresponsive gel.[13] We envisaged that guest-included macrocyclic boronic esters would be utilized as a gelator with guest-releasing and recovering ability by taking advantage of the dynamic nature of both boronic ester formation and borate formation (Figure 1). The addition of an appropriate diamine to a suspension of a guest-included boronic ester in a suitable solvent is expected to yield oligomeric boronic esters cross-linked by the diamine through borate exchange reaction, which might lead to the formation of borate-based gel. Importantly, the included guest molecule should be released into the borate gel owing to the structural change of the boronic ester (Figure 1 a), and the released guest molecule could be recovered from the gel if the initial macrocyclic boronic ester were reconstructed by the removal of the diamine under appropriate conditions (Figure 1 b).

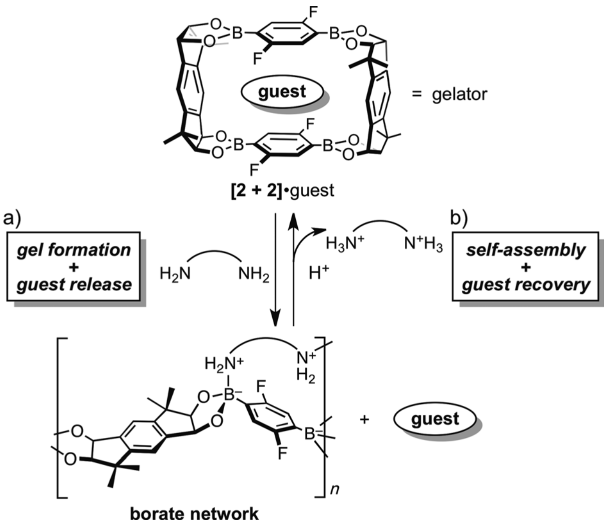
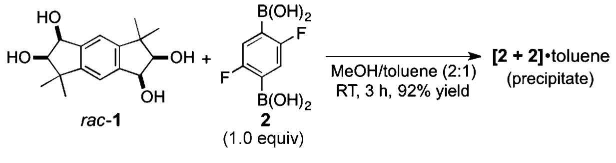


Figure 1. a) Formation of borate gel from the guest-included macrocyclic boronic ester along with release of the guest molecule into the gel. b) Reconstruction of the macrocyclic boronic ester and recovery of the guest molecule from the gel.

To realize this strategy, macrocyclic boronic ester [2+2]·toluene was prepared by the guest-induced self-assembly from bis(1,2-diol) **1** and 2,5-difluoro-1,4-phenylenediboronic acid (**2**; Scheme 1; Supporting Information, Table S1 and Figure S5).[14]



Scheme 1. Self-assembly of toluene-containing macrocyclic boronic ester [2+2]·toluene.

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The formation of borate gel from [2+2]·toluene was then examined by the "stable-to-inversion of a test tube" method.[15] When 1,3-diaminopropane (2 equiv) was added to a suspension of [2+2]·toluene (5.0 wt %) in methanol/toluene (2:1), a white borate gel was immediately formed at room temperature (Figure 2a). The amount of the gelator could be reduced to 2.2 wt % when the borate gel formation was carried out by a heating–cooling process.[16] Borate gel formation was also achieved in various solvents, including 1,4-dioxane, benzene, THF, and chloroform (Supporting Information, Table S2). The scanning electron microscope (SEM) image of [2+2]·toluene and xerogel, obtained by freeze-drying of the borate gel prepared in benzene, clearly exhibited the significant morphology change of the sample from plate-like morphology to mesh-like structure (Figure 2b,c).

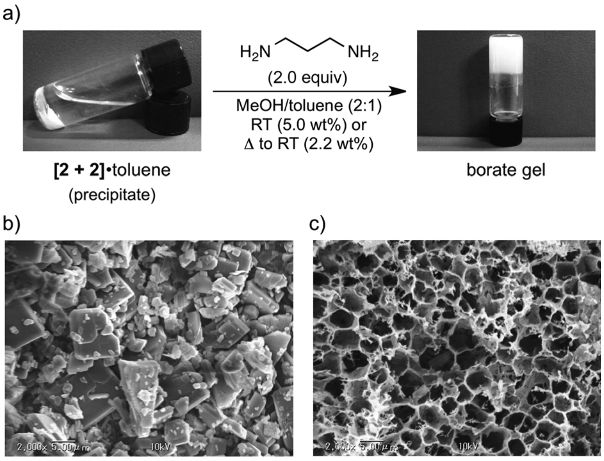

Figure 2. a) Borate gel formation using [2+2]·toluene as gelator. b) SEM image (10 kV, 2000×) of [2+2]·toluene. c) SEM image (10 kV, 2000×) of xerogel of the borate gel prepared in benzene.

Formation of sp^3 borate structure was confirmed by the solid-state single-pulse ^{11}B NMR analysis (Supporting Information, Figure S7). A sharp signal was detected at 5.4 ppm in the ^{11}B single-pulse NMR spectrum of the xerogel,[17] which supported the formation of sp^3 borate structure by the addition of diamine.[18] Although a broad signal of sp^2 boronic ester moieties was also observed around 22 ppm in the spectrum, which is more than 85 % of boron centers were sp^3-hybridized (Supporting Information, Figure S8). The chemical structure of boronic ester moieties, cross-linked by the diamine, was also analyzed. In contrast to relatively sharp signals observed in solid-state ^{13}C cross-polarization/magic angle spinning (CP/MAS) NMR spectrum of [2+2]·toluene, broad complex signals were observed in the spectrum of the xerogel (Supporting Information, Figure S9). Moreover, the gradual release of oligomeric boronic esters along with [2+2] was observed by ^{1}H NMR analysis of the xerogel in CDCl$_3$ solution with the addition of copper(II) chloride to remove 1,3-diaminopropane (Supporting Information, Figure S1).[19] Furthermore, solution-state NMR experiment in CD$_3$OD/[D$_8$]toluene revealed that the macrocyclic boronic ester [2+2] became a mixture of oligomeric borate species including the borate form of [2+2] in the presence of 1,3-diaminopropane (for details, see the Supporting Information, Figure S2 and Table S3). These results suggested that the boronic ester moieties in the xerogel are a complex mixture of oligomeric boronic esters, including [2+2]. That is, the role of the diamine is not simply linking the initial macrocyclic boronic ester [2+2] with its structure retained, but is inducing the conversion of [2+2] to oligomeric boronic esters and then cross-linking them (Figure 1).

Next, stimuli-responsive properties of the borate gel prepared in methanol/toluene (2:1) mixed solvent system were evaluated. Heating the borate gel triggered the transition of the gel to the clear solution owing to the reversible nature of the borate bond formation, and the sol–gel transition was reversible (Figure 3a). The gel also exhibited base-responsive behavior. When the gel was treated with 1M THF solution of tetra-*n*-butylammonium fluoride (TBAF) and heated until it became a clear solution, the gel was not reconstructed after the solution was cooled to room temperature. Similarly, a clear solution was obtained by the addition of 1M aqueous NaOH to the borate gel at room temperature (Figure 3b). The base-responsive property of the borate gel is attributed to the coordination of these bases to the boron center, thus resulting in the destruction of the cross-links by the diamine (Supporting Information, Figure S3). In contrast, the addition of 1M aqueous HCl (8.0 equiv) to the borate gel resulted in the collapse of the gel, and the mixture became a white suspension. Very importantly, [2+2]·toluene was recovered in 82 % when the precipitate was collected by filtration after stirring at room temperature for 24 h (Figure 3c). That is, the self-assembly of [2+2]·toluene from the oligomeric boronic esters occurred, and thus the reversible borate gel formation between [2+2]·toluene and borate gel was realized.[20]

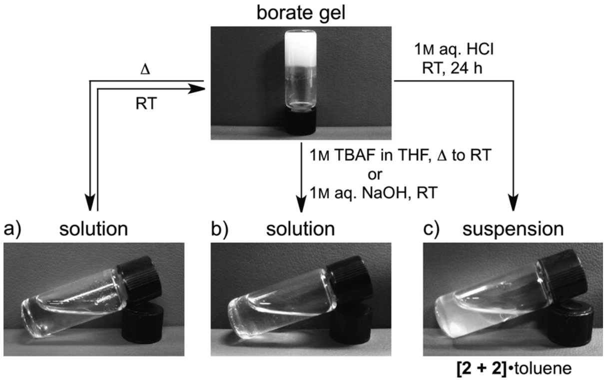

Figure 3. Multi-stimuli-responsive properties of the borate gel prepared from [2+2]·toluene with 1,3-diaminopropane in MeOH/toluene (2:1). a) Thermoresponsive property. b) Base-responsive property. The picture is from after the addition of NaOH. c) Acid-responsive property. In the cases of (b) and (c), TBAF (6.0 equiv), NaOH (4.0 equiv), or HCl (8.0 equiv) was added.

The method was then applied to the release and recovery of an equimolar amount of guest molecule, as the above guest molecule (toluene) was the co-solvent used in the reversible formation of the borate gel (Figure 2a and Figure 3c). Azulene, a blue-colored organic dye, was used as a model guest compound and found to act as an effective guest molecule for the formation of [2+2] (Supporting Information, Table S1). Blue-colored borate gel was obtained when [2+2]·azulene (5.0 wt %) was treated with 2 molar amounts of 1,3-diaminopropane in methanol/THF (4:1) mixed solvent system at room temperature (Figure 4a,b). Azulene was released from the host molecule at this state, which was confirmed by ^{1}H NMR analysis of the borate gel prepared in CD_3OD/[D_8]THF (4:1) (Supporting Information, Figure S4). The released azulene was efficiently recovered from the borate gel as [2+2]·azulene in 84 % when the gel was treated with 1 M aqueous HCl (8.0 equiv) at room temperature and stirred for 24 h (Figure 4c). Similarly, naphthalene and benzothiophene could also be used as the equimolar guest molecule (Supporting Information, Table S4).[14]

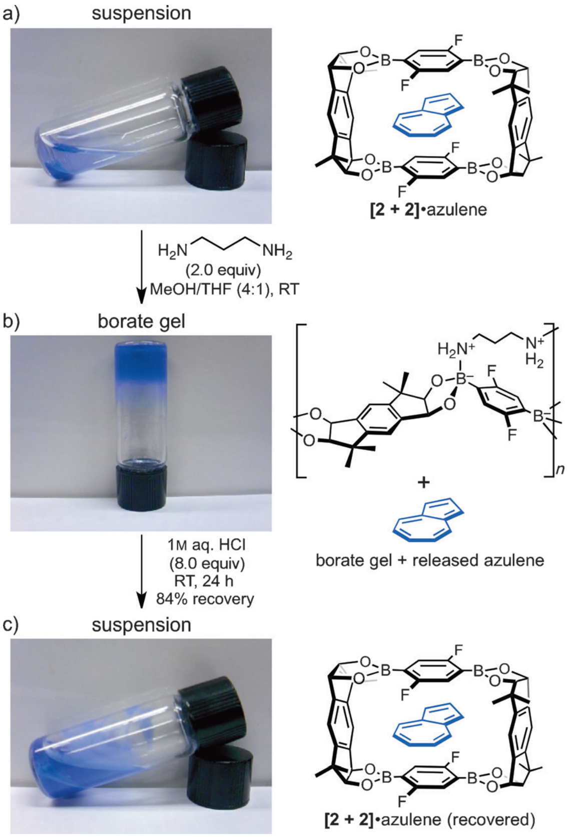

Figure 4. Release and recovery of the guest molecule during the reversible borate gel formation of [2+2]·azulene with 1,3-diaminopropane in MeOH/THF (4:1).

In summary, reversible borate gel formation was realized by utilizing the guest-included macrocyclic boronic esters as gelator. The borate gel exhibited thermo-, base-, and acid-responsive properties owing to the reversible nature of the borate bond. Furthermore, release and recovery of the equimolar amount of the guest molecule was realized during the formation and collapse of the borate gel based on the dynamic nature of both boronic ester formation and borate formation. The method developed herein provides a new concept for the application of smart gels, which enable a temporary release of guest compounds into the gel. We believe that this concept should not be specific to the macrocyclic boronic esters, and would be applied for a wide variety of guest-included self-assembled structures to create such smart gels in the near future. Although the current proof-of-concept system is only applicable for the creation of organogel, the interconversion between self-assembled boronic ester and borate-based hydrogel might be realized by using a suitable combination of substrates since the sp^3 borate structure is stable in water,[21] which would open the door to the practical use of borate gel. Further investigations on the creation of self-assembled boronic esters, which encapsulate larger guest molecules and exhibit higher gelation ability, are now in progress.

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[20] When 1 M aqueous HCl was added to the borate gel prepared in dioxane or benzene, oligomeric boronic esters were obtained as precipitate along with [2+2], indicating that the self-assembly of [2+2] did not occur efficiently in the absence of methanol which facilitates the equilibrium of the boronic ester. This result also supported that the formation of borate gel is caused by the cross-linking of oligomeric boronic esters and [2+2] by the diamine.

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