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Boronic Esters as a System for Crystallization-Induced Dynamic Self-Assembly Equipped with an "On−Off" Switch for Equilibration

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Dynamic self-assembly involves the recognition of organic guest molecules by spontaneous rearrangement of the structure of host molecules constructed from a single set of building blocks.[1] Most of the reported examples are based on the coordination of multidentate nitrogen ligands to metal ions,[2] only a few cases being known in which covalent links[3] such as S−S[4] or C═N[5] bonds are reversibly formed. In these cases, the reaction is usually carried out under either acidic or basic conditions, and the yield and selectivity of host molecule formation are not necessarily good. Here we show that boronic ester formation can be used to achieve the dynamic self-assembly of organic molecules through dynamic covalent bond formation,[6,7] which has the following novel features; that is (1) dynamic self-assembly of two kinds of host boronic ester occurs in nearly quantitative yield simply by mixing boronic acid and alcohol under neutral conditions in the presence of appropriate guest molecules, (2) precipitation plays a key role in the selective preparation of the two kinds of host molecule,[8] and (3) it is possible to freeze or free the equilibration between these two host molecules under appropriate conditions.

We selected a racemic polyol **1**[9] containing two sets of fixed, 1,2-diol units oriented on the same face of a nearly planar molecule. 1,4-Benzenedi(boronic acid) **2** was chosen as the boron component because of its rigid, planar structure. When equimolar amounts of these two were mixed in methanol, an insoluble material precipitated instantaneously. This is thought to be a polymeric boronate,[10] made up of tetrol and di(boronic acid) in 1:1 ratio, a composition supported by elemental analysis. This material was insoluble in all solvents examined.

We next looked at adding an appropriate guest molecule that could work as template for the formation of a cyclic boronic ester. In particular, we examined some typical aromatic solvents in the expectation that $\pi-\pi$ interactions between the component molecules would facilitate formation of a supramolecular structure. To our delight, when a 2:1 mixture of methanol and toluene was employed as solvent in the same reaction, the mixture again became heterogeneous, but this time the solid isolated was soluble in several organic solvents. ^{1}H and ^{13}C NMR spectra in $CDCl_3$, together with FAB-MS data for the newly formed compound, suggest that it is a 2:2 complex of the di(boronic acid) and the tetrol (abbreviated as [2 + 2]). Furthermore, the presence of one molecule of toluene contained within [2 + 2] was confirmed by integration of ^{1}H NMR and elemental analysis, suggesting that toluene really is acting as a template in the formation of [2 + 2].

Extensive trials to obtain single crystals suitable for X-ray analysis finally bore fruit when recrystallization was performed using toluene. As shown in Figure 1, the complex has the expected structure and is composed of two molecules each of the di(boronic acid) and the tetrol, while one molecule of toluene is included in the center of the host, suggesting the presence of $\pi-\pi$ interactions with the phenyl rings of two di(boronic acid) groups. The distance between these phenyl rings and the toluene is 3.5 Å, which is ideal

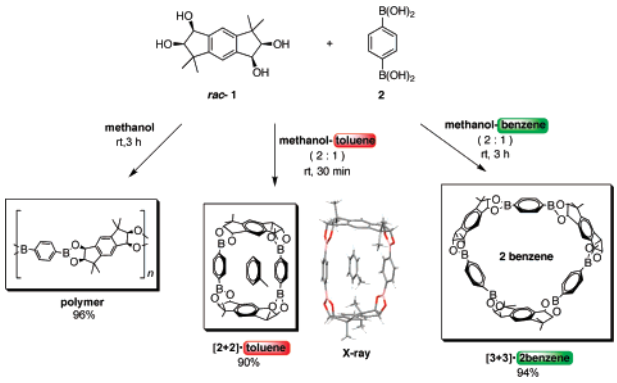

Figure 1. Dynamic self-assembly based on the formation of boronic ester. The reaction of racemic tetrol **1** and 1,4-benzenedi(boronic acid) **2** in methanol (left), in methanol/toluene (2:1) (middle), and methanol/benzene (2:1) (right), and the X-ray structure of [2 + 2]·toluene (white, hydrogen; pink, boron; gray, carbon; red, oxygen).

for this.[11] It should be emphasized that the two tetrol units in this 2:2 complex are both derived from the same enantiomer of the starting material, suggesting that recognition of the enantiomers occurs during complex formation.[12] Within the crystals, neighboring [2 + 2]·toluene units are formed from opposite enantiomers of the tetrol, and it is noteworthy that use of optically active tetrol starting material under the same reaction conditions resulted in the formation of insoluble, polymeric boronic esters instead of the [2 + 2]·toluene complex. These results suggest that the equilibrium of the system is driven toward formation of [2 + 2] by precipitation of its complex out of solution with appropriate packing of units derived from the pair of tetrol enantiomers.

Even more interestingly, when benzene was employed instead of toluene (methanol/benzene = 2:1), the mixture again became instantaneously heterogeneous and once again a product was obtained that is soluble in several organic solvents. FAB-MS data for this product clearly supported the formation of a 3:3 complex (abbreviated as [3 + 3]), while elemental analysis and integration of ^{1}H NMR spectra demonstrated the inclusion of two molecules of benzene in a host molecule comprises three molecules each of 1,4-benzenedi(boronic acid) and tetrol. In particular, careful analysis of the ^{1}H and ^{13}C NMR spectra showed that this [3 + 3] is composed of two molecules of one enantiomer and one molecule of the other enantiomer of the tetrol, suggesting that enantiomer recognition once again operates during the precipitation process.

These results demonstrate that formation of a supramolecular structure is strongly dependent on the presence of an appropriate guest molecule and is controllable by slight changes in the structure of that guest.

We next examined the stability of [2 + 2] and [3 + 3]. When isolated [2 + 2]·toluene was suspended in methanol/benzene (2:1), perfect conversion to [3 + 3]·2 benzene occurred within 36 h. The opposite conversion could also be carried out by treatment of

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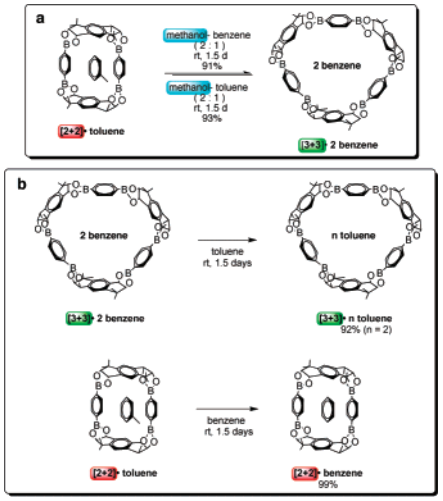

Figure 2. The ability to "freeze or free". (a) Interconversion between [2 + 2] and [3 + 3] in the presence of methanol. (b) Kinetic stability of [2 + 2] and [3 + 3] in the absence of methanol.

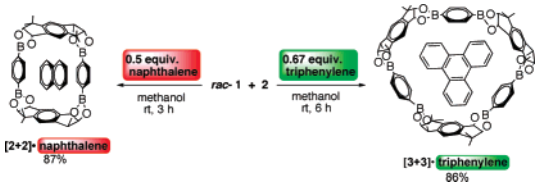

Figure 3. Naphthalene-induced self-assembly of [2 + 2]•naphthalene and triphenylene-induced self-assembly of [3 + 3]•triphenylene.

[3 + 3]•2 benzene with methanol/toluene (2:1) for 36 h. Thus, [2 + 2] and [3 + 3] can be interconverted in the presence of methanol and an appropriate guest molecule. On the other hand, when [2 + 2]•toluene was dissolved in benzene only, then the solvent was removed under reduced pressure, [2 + 2]•benzene was obtained in quantitative yield. This structure was confirmed by elemental analysis and the presence of equal amounts of benzene and [2 + 2] in the ^{1}H NMR spectrum. It should be emphasized that this host−guest complex cannot be prepared under thermodynamically controlled, equilibrating conditions. In a similar manner, treatment of [3 + 3]•2 benzene in toluene only gave [3 + 3]•*n* toluene (*n* = ∼2) almost quantitatively. This ability to "freeze or free" the conversion between [2 + 2] and [3 + 3] depending on the presence or absence of a protic solvent, in this case methanol, is an extremely attractive feature of this system. Thus, each boronic ester host could be either kinetically stabilized or thermodynamically equilibrated by the appropriate choice of conditions (Figure 2).

We have looked for even more effective guest molecules for this dynamic self-assembly and found that both naphthalene and triphenylene work very well in methanol, precipitating out [2 + 2]•naphthalene and [3 + 3]•triphenylene, respectively, in high yield. Thus, treatment of equimolar amounts of the di(boronic acid) and tetrol with only a half molar amount of naphthalene (the theoretical minimum amount) gave [2 + 2]•naphthalene in 87% yield, while use of only 0.67 molar amounts of triphenylene (twice the theoretical minimum amount) gave [3 + 3]•triphenylene in 86% yield (Figure 3).

The high yield, exquisite selectivity, and ready on−off ability of this system suggest that it may be possible to develop it into a method for the efficient recovery of a pure compound from a mixture, provided that a combination of tetrol and di(boronic acid)

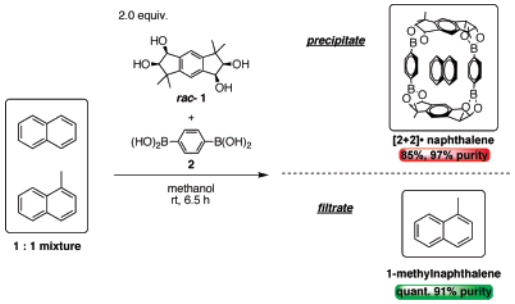

Figure 4. Separation system based on selective guest inclusion and precipitation of the host−guest complex.

can be found that forms a complex with the compound to be purified, precipitating it from solution.[13] With the pair of reagents described here, we were able to separate naphthalene from the structurally very similar 1-methylnaphthalene in solution in methanol, the former precipitating as its [2 + 2] complex in 85% yield and over 97% purity (Figure 4).

We are currently trying to develop this system into selective functionalization of a complexed aromatic molecule, followed by release in an iterative, "molecular assembly line"-like process.

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Supporting Information Available: Experimental details and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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