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Communications to the Editor

A Bulk Mixture System of Cyclodextrin and Amine-Terminated Polyether: Observation of Reversible Thermoswitching Behavior between Fluid and Gel-like States

Yukio Isobe, Atsushi Sudo, and Takeshi Endo*

Molecular Engineering Institute, Kinki University, Kayanomori 11-6, Iizuka, Fukuoka, 820-8555, Japan

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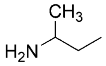
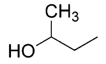
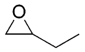
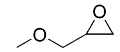
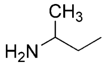
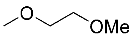
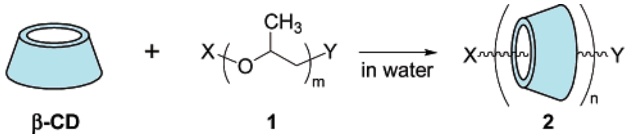
Cyclodextrins (CDs), which are cyclic oligomers of glucose with defined unit numbers and have an inner cavity with a defined diameter, recognize specific organic molecules by their sizes and accept them into the cavity to form the corresponding inclusion complexes.[1] Polyethers are also used as a guest molecule, which interpenetrate CD molecules to form necklace-shaped supramolecules. The family of such supramolecules is represented by the term "pseudo-polyrotaxane (PPRtx)".[2] They inherit the intrinsic equilibrium nature of the inclusion complexes between formation and dissociation, and thus the CD component can freely slip out from them by only a weak external stimulation. Recently, this stimuli-sensitive nature of the PPRtx has been attracted much attention as a fundamental concept for designing various smart materials involving those for drug-delivery systems and biodegradable materials.[3]

In this Communication, we report a new thermoresponsive system, which is simply prepared by mixing β-CD with a poly(propylene glycol) having amino groups in the both terminals. The thermoresponsive behavior of the system was confirmed by repeatable and keen response of its viscosity and transmittance of visible light to repeated heating-and-cooling cycles.

Table 1. Polyethers 1 and the Corresponding PPRtx 2

1	X-	-Y	m	2
1a		-NH_2	5.6	**2a**
1b		-OH	5.6	**2b**
1c			4.3	**2c**
1d			8.0	**2d**

Scheme 1



In general, PPRtx is prepared in aqueous media. Upon mixing an aqueous solution of CD with that of an appropriately selected guest polymer, the corresponding PPRtx will be precipitated out from the solution. This precipitation drives the successful formation of the thermodynamically unstable PPRtx. β-CD and an amine-terminated poly(propylene glycol) **1a** gave the corresponding PPRtx **2a** as a insoluble material in water, which can be easily isolated by filtration (Table 1). Generally, by one β-CD molecule, two propylene glycol units (PPG units) can be covered,[4] and this was true in the PPRtx 2a: Its ^{1}H NMR spectrum revealed that the composition ratio of [β-CD]:[**1a**] was ca. 2.9, which was comparable to the theoretical one (2.8) (Figure S-1). The other PPRtxs **2b**−**2d** were also prepared similarly. These experiments proved that the series of terminal structures employed herein are not sterically demanding to inhibit their penetration into the cavity of β-CD. One of our discoveries presented herein is that an initially heterogeneous mixture of powdery β-CD (1.14 g, 1.00 mmol) and a liquid polyether **1a** (the number-average molecular weight ($M_n = 400$; 4.00 g, ca. 10 equiv to β-CD) became homogeneous within a couple of hours at ambient temperature, to afford the corresponding mixture having viscosity of 257 P. This spontaneous dissolving phenomenon was observed exclusively when the guest polypropylene has amine terminals: β-CD was not

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* To whom correspondence should be addressed: e-mail tendo@me-henkel.fuk.kindai.ac.jp; Tel and Fax +81-238-26-3090.

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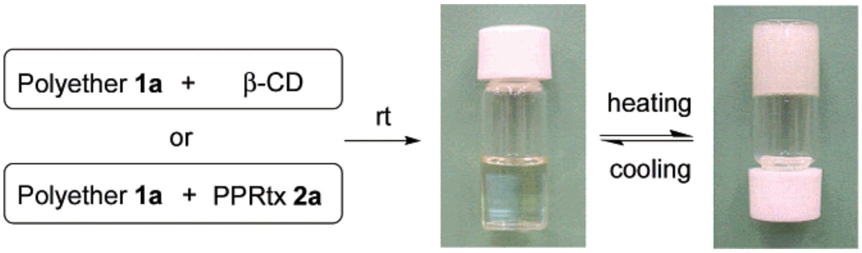

Figure 1. Photographic images showing the change in appearance of the mixture of **1a** with *β*-CD upon heating and cooling.

dissolved in **1b** or **1c** at all, although their chain ends should not sterically interfere the interpenetration as is supported by the successful formation of the corresponding PPRtxs in aqueous media. On the other hand, *β*-CD (0.18 g, 0.16 mmol) was dissolved in **1d** (M_n = 600; 2.40 g, 4.00 mmol, ca. 25 equiv to *β*-CD**)** having an amino group at one side of the chain ends, even though it took 6 h for dissolving. These results made us to speculate that the dissolving process would not be induced simply by solvating *β*-CD by poly(propylene glycol) but would involve spontaneous interpenetration of the polyether **1a** to form the corresponding PPRtx **2a** in the mixture. Recently, spontaneous interpenetration in a bulk system has been independently reported by two research groups.[5] They have reported that the poly(ethylene glycol) having hydroxyl terminals and α-CD spontaneously form the corresponding complex. Compared to this α-CD−poly(ethylene glycol) system, the distinctive point of our target system, the *β*-CD−poly(propylene glycol) system, is that the amino group is the only functional group on the polyether terminals that permits the dissolution phenomenon. The importance of the amino group was also supported by the following experiment: Employment of **1a** having a larger molecular weight (M_n = 2000) and accordingly containing a lower amount of amino group leads to serious deceleration of the dissolving process. It required 12 h for complete dissolution of *β*-CD (0.23 g, 0.20 mmol) in **1a** (4.00 g, [*β*-CD]/[**1a**] = 0.1) at ambient temperature. In addition, the following experiment confirmed that amino group must be located at the polyether terminals: To the heterogeneous mixture of *β*-CD and **1b** (with hydroxyl terminals), a low-molecular-weight amine, 2-amino-1-methoxypropane (AMP), was added ($[\mathrm{AMP}]_0/[\beta\text{-CD}]_0/[\mathbf{1b}]_0$ = 1.0/0.1/1.0). However, the dissolution phenomenon was not observed in a range of temperature from 20 to 100 °C.

We also examined dissolving behavior of PPRtx **2**, prepared by the conventional method in aqueous media, in the each guest polymer **1**. PPRtx **2a** (1.26 g) was easily dissolved in **1a** (3.87 g). The viscosity of the resulting solution was virtually the same as that of the solution prepared by mixing the components in bulk, suggesting that the two solutions could be identical. On the other hand, the other PPRtxs **2b**−**d** were not soluble in the corresponding guest polymers. In other words, the amino group at the terminals is indispensable to promote dissolving of the PPRtxs in the polyether. One of the possibilities is that the amino terminal would promote transfer of the CD molecules from one polyether chain to others, leading to homogeneous distribution of CD molecules in the mixture.

We next focused on the thermoresponsive behavior of the homogeneous bulk mixture of CD and the polyether **1a**. Upon heating the mixture in a test tube up to 100 °C, it suddenly became a turbid and gel-like material, suggesting that this process could involve dissociation of the PPRtx with releasing CD component out of the mixture (Figure 1). It was quite striking to find that such a simple system exhibited the transition from the fluid state into gel-like state. To date, there have been various reports on gelation behaviors of cyclodextrin polyrotaxanes.[6] However, in these reports, gelation has been achieved only when an aqueous medium was used, which is totally different from our bulk system. Another interesting phenomenon was recovery of the initial homogeneous state upon cooling the mixture to ambient temperature; i.e., the mixture became fluid and transparent again. We repeated this heating-and-cooling cycle several times and observed that the changes in the viscosity and transparency responded to the thermal stimuli repeatedly. The recovery of the initial homogeneous state could be arisen by spontaneous rethreading of CD with **1a** to form PPRtx **2a**.

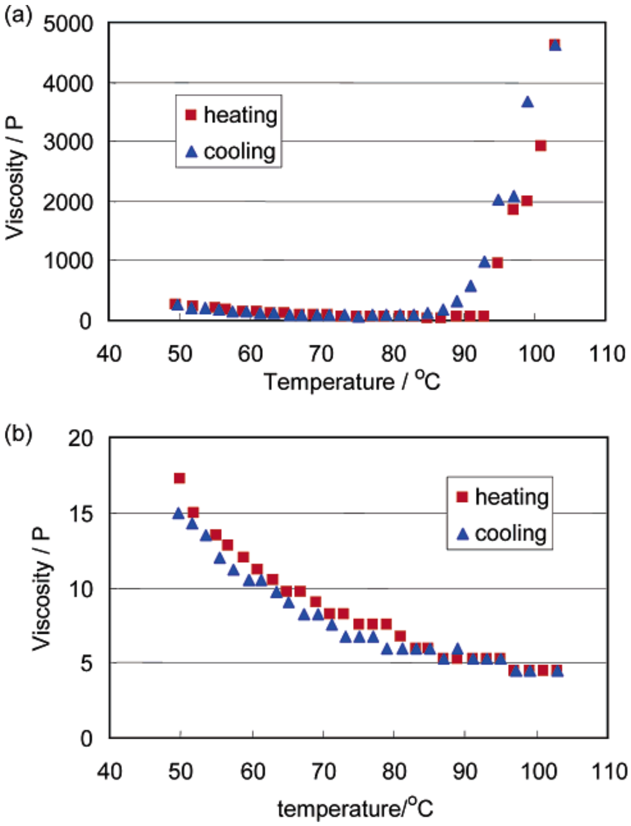

Figure 2. Temperature−viscosity relationships for the **1a**−*β*-CD bulk mixture system (a) and for the **1b**−*β*-CD bulk mixture system.

The reversible thermoresponsible behavior of the **1a**−*β*-CD mixture system was studied more precisely by monitoring viscosity change in the process. Figure 2a shows the corresponding temperature−viscosity plots. In the heating process, the viscosity gradually decreased upon heating, and it clearly increased at 94 °C, as was expected from the observation of the phase transition from the liquid state to the gel-like state. Such a drastic change in viscosity was also observed in the cooling process, and the temperature−viscosity profile for the cooling process virtually traced that of the heating process. On the other hand, the mixture of the hydroxyl-terminated polyether **1b** and *β*-CD showed a totally different temperature−viscosity profile (Figure 2b). This mixture was heterogeneous in a range from ambient temperature to 150 °C and never showed immediate increase as that observed for the **1a**−β-CD system. The viscosity of the heterogeneous **1b**−β-CD system was quite low as 5 P, suggesting that the immiscibility of β-CD in polyether cannot explain the surprisingly high viscosity of the **1a**−β-CD system beyond 100 °C. These observations lead us to postulate that the turbid and gel-like state of the **1a**−β-CD system at high temperature is created not by immiscibility of the thermally released β-CD, but by formation of a hydrogen-bonding network, in which the hydroxyl groups of the released CD molecules and the amino terminals of **1a** would participate. In contrast, the **1b**−β-CD system would be a simple dispersion of β-CD in **1b** with negligible interaction between them.

Differential scanning calorimetric (DSC) analysis of the **1a**−β-CD mixture indicated transitions in both the heating and cooling processes (Figure S-2). In the heating process, an endothermic peak was observed, and its peak top was at 95 °C, being in good agreement with the transition temperature for the drastic change in viscosity. In the cooling process, a broad exothermic peak was observed, indicating the regeneration of **2a** in the mixture. The scans with heating and cooling were repeated to find that the corresponding endo- and exothermic peaks reproducibly appeared without significant change of the positions of the peaks, strongly supporting the reversible thermoswitching behavior of the present system.

It is noteworthy that the virtually same thermoswitching behavior as those of the mixture prepare by mixing β-CD and **1a** was exhibited by the homogeneous mixture prepared by dissolving **2a** into **1a**: The mixture, which was fluid and transparent below 90 °C, became turbid and gel-like above 95 °C.

In summary, new aspects of the PPRtxs composed of CD and polyethers were discovered: (1) It can be formed spontaneously upon mixing the two components at ambient temperature by appropriate design of the terminal functionality of the polyether. (2) On the basis of this spontaneous formation of the PPRtx and its dissociation upon heating, a reversible and repeatable thermoresponse of its physical properties was observed. The response is highly sensitive to the thermal stimuli, giving us opportunity to design various systems with thermoswitching behavior.

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Supporting Information Available: Details for the preparation of PPRtx **2a** and its ^{1}H NMR analysis (Figure S-1), the method for measurement of viscosity, and the DSC profile for **1a**−β-CD (Figure S-2). This material is available free of charge via the Internet at http://pubs.acs.org.

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