Thermoreversible sol–gel transition of an aqueous solution of polyrotaxane composed of highly methylated α-cyclodextrin and polyethylene glycol†

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Novel thermo-gelling aqueous solution systems are developed with a polyrotaxane, consisting of methylated α-cyclodextrin and polyethylene glycol, based on the slide-ring properties of the macrocycles along the linear chain.

Polymers having novel molecular architectures have been of great interest in recent years due not only to their structures and properties but also to their potential applications as smart and stimuli-responsive materials.[1] Polyrotaxane is one of supramolecular polymers in which a number of cyclic molecules are threaded onto a linear polymer chain. The most characteristic feature of polyrotaxanes is that each macrocycle slides and rotates on the polymer chain. This feature gives us fascinating molecular materials, such as the molecular tube formed by cross-linking macrocycles in a single polyrotaxane,[2] insulated molecular wires incorporating conductive polymers,[3] and a drug delivery system.[4] We also reported a novel gel, called a topological gel or a slide-ring gel, which has movable figure-of-eight crosslinks formed by crosslinking among cyclic molecules on different polyrotaxanes.[5]

In particular, polyrotaxanes comprised of α-cyclodextrin (α-CD) and polyethylene glycol (PEG) have been studied extensively due to their facile synthesis and biocompatibility.[1,4–6,8,10] Additionally, the α-CD moiety is very convenient for functionalisation because an α-CD has 18 hydroxyl groups that can be subject to modification with variety of functional groups.

Methylation is one of the simple examples of modification and functionalisation of CDs. Methylated CDs are known to show peculiar solubility as well as to form inclusion complexes with various compounds in water.[7] It is interesting to notice that methylated CDs exhibit higher water solubility than unmodified CDs, although their surface is hydrophobic in character. Moreover, highly methylated CDs exhibit the negative temperature coefficient of the solubility in water: they are well-soluble in cold water (for example, 200 g L^{-1} at 25 °C for permethylated α-CD), but they are hardly soluble and form aggregates or crystals in hot water.[7]

Here we design, synthesise and characterise temperature-responsive polyrotaxane, composed of methylated α-CDs and a polyethylene glycol end-capped with adamantanes (Fig. 1a). This thermoresponsiveness arises from the combination of the slide-ring nature of polyrotaxane and thermally aggregating behaviour of methylated α-CDs in aqueous systems. Thermal changes in conformation of the polyrotaxane as shown in Fig. 1b is expected to provide stimuli-responsive materials.

Polyrotaxane **5** was prepared by a previously reported method.[8] The number of α-CD in a polyrotaxane is estimated at *ca.* 110, corresponding to 28% coverage of PEG chains with α-CDs. The controlled coverage is important to our molecular design because the α-CDs should have enough space to move along the PEG chain. To investigate the effect of methylation ratio on the thermoresponsive behaviour, polyrotaxanes **1**, **2**, **3** and **4** (87%, 74%, 52% and 19% of methylation ratio to the OH groups of the polyrotaxane **5**, respectively) were prepared.[9]†

Methylation of the polyrotaxane **5** brings drastic change in its solubility. The methylated products **1–4** are soluble in neutral water, although native polyrotaxane **5** is insoluble in neutral water and most organic solvents due to the strong inter- and intramolecular hydrogen bonding among the α-CDs in the polyrotaxanes.[10] The substituted methyl groups would suppress the hydrogen bonding between CDs. **1** is soluble in chloroform and dichloromethane, but not in DMSO. However, **2–4** are soluble in DMSO, *N*,*N*-dimethylformamide and *N*,*N*-dimethylacetamide.

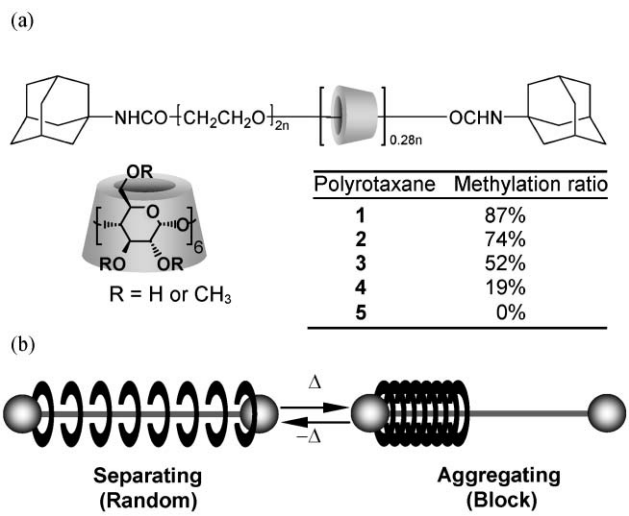

Fig. 1 (a) Chemical structure of methylated polyrotaxane. (b) Stimuli (temperature)-induced change in distribution of methylated CDs in a polyrotaxane.

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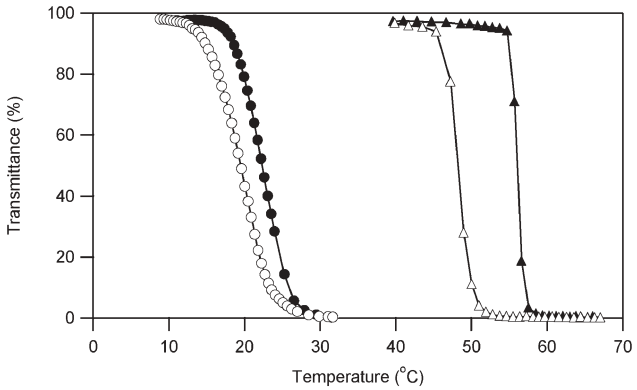

Fig. 2 The temperature dependence of transmittance for 2 wt% aqueous solutions of **1** (circles) and **2** (triangles). Open and closed marks represent cooling and heating processes (1 °C min^{-1}), respectively.

Fig. 2 shows the temperature dependence of the turbidity for a 2 wt% aqueous solution of **1** and **2** during transmittance change. These solutions become opaque with increasing temperature. The transition temperature depends remarkably on the degree of substitution. The solutions of **1** and **2** show a transition temperature around 22 °C and 53 °C, respectively, while **3** and **4** show no thermo-response. These results indicate that the transition temperatures can be controlled by increasing the ratio of methyl group substitution. This kind of solubility change is known as lower critical solution temperature (LCST). The LCST behaviour has been frequently reported for water-soluble polymers having hydrophobic groups in their molecular structures, such as methylcellulose,[11] PEO–PPG–PEO triblock copolymers,[12] and poly(*N*-isopropylacrylamide).[13] On the other hand, there are only few reports on LCST based on polyrotaxane structure.[14]

Interestingly, the aqueous solutions of **1** and **2** show not only LCST but also a thermoreversible sol–gel transition at higher concentrations. Fig. 3 shows a 5 wt% solution of **1** at 10 °C (sol) and 50 °C (gel), respectively. The 5 wt% solutions of **1** and **2** become turbid around 20 °C and 55 °C, respectively. Their viscosity increases with increasing temperature and the solutions eventually form an elastic gel above 50 °C and 75 °C, respectively. To the best of our knowledge, this is the first report on a polyrotaxane which exhibits thermo-gelling behaviour through LCST. On the other hand, there are several reports on thermo-gelling systems of polyrotaxanes based on upper critical solution temperature (UCST).[15,16]

A X-ray diffraction preliminary study for a 10 wt% solution of **1** shows remarkable diffraction peaks above 40 °C, indicating that the formation of a crystalline-like structure which may play an important role in the gelation.† A similar crystalline-like structure was confirmed at low temperature for an inclusion complex showing UCST.[15] Physical crosslinks are most likely formed by intermolecular aggregates between the methylated α-CDs, due to their hydrophobic interaction in an aqueous system at high temperatures. As a result, the α-CDs threaded onto each PEG chain would form aggregates with a tube-like structure (exemplified in Fig. 1b) promoted by the rings moving along a PEG chain. At high temperature, the polyrotaxane, therefore, acts as a block copolymer comprising of two segments, the hydrophilic naked PEG and the hydrophobic methylated CD-tube.

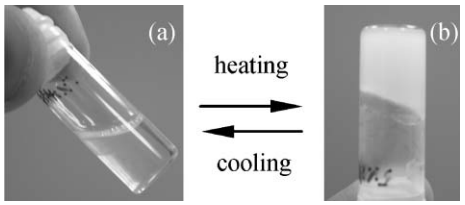

Fig. 3 Photographs of thermally induced sol-gel transition for 5 wt% aqueous solution of **1** at 10 °C (a) and 50 °C (b).

In conclusion, we demonstrated the novel sol–gel transition system based on polyrotaxane structure, which undoubtedly provides new opportunities in the field of thermoresponsive systems. Detailed structure analysis in the sol–gel transition and the mechanical properties of the gels will be published elsewhere.

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9 Methylation of α-CDs in the polyrotaxane was carried out by a method based on the well-known Williamson reaction by adding 110%, 80%, 60% and 20% (for **1**, **2**, **3** and **4**, respectively) equivalent of iodomethane and sodium hydride with respect to the OH groups of polyrotaxane **5** in DMSO. The methylation ratio for **1–4** was estimated from 1H NMR spectra by comparing the integration of the OH and H1 signals of CD with that of other protons. GPC measurements show that the products are pure enough without decomposition.

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