Reversibility is a basic and crucial feature of supramolecular systems. In designing and fabricating new supramolecular materials, the realization of reversibility is particularly important as it could enable these substances to be superior to conventional materials. An excellent example is an elastomer reported recently, made of small functional molecules which form both long chains and cross-linkers through intermolecular multiple hydrogen bonding. When broken or cut, the elastomer can be simply repaired by just bringing together the fractured surfaces and allowing the recovery of the hydrogen bonding.

There are plenty of reports on supramolecular assemblies of polymers showing reversible responses to environmental changes; however, these are mostly based on the inherent stimuli-sensitive properties of the building blocks, such as the temperature-induced coil–globule transition of poly(N-isopropyl acrylamide) (PNIPAM) and pH-induced protonation of poly(vinyl pyridine), rather than the reversibility of the supramolecular interactions. Therefore, taking full advantage of the reversibility of the noncovalent interactions to construct supramolecular materials is still a big challenge. This has drawn increasing interest in recent years, and has led to a series of promising results. For example, some hydrophobically modified water-soluble polymers realized sol–gel transition as a result of the reversible interactions of cyclodextrin and alkyl chains. The assembly and disassembly of polymeric vesicles can be controlled by photosensitive interactions between cyclodextrin and azobenzene compounds.

The self-assembly of polyethylene glycol (PEG) and α-cyclodextrins (α-CDs) to form linear pseudopolyrotaxane (PPR), with PEG as the axis and α-CDs as threaded rings, was reported by Harada et al. Since the ability of PPR to form physical hydrogels was first reported in 1994, the system has been extensively studied as the hydrogels show very promising uses as biomedicine materials. There is now good understanding of the formation mechanisms and structures of such PPR hydrogels, but little has been explored concerning their dissociation and reassembly, though increasing temperature and shearing could make the hydrogel turn to a sol.

Herein, we demonstrate a facile photocontrollable supramolecular route to realize the disassembly and reassembly of the PPR hydrogels. The addition of a photoresponsive compound containing an azobenzene moiety to the PPR hydrogel was found to be effective in converting the hydrogels to transparent solutions. By subsequent alternation of UV and visible irradiation, reversible sol-to-gel and gel-to-sol transitions were observed. Thus, the widely investigated PEG/α-CD PPR hydrogel is proved to be “active” in supramolecular chemistry, and the reversible nature of supramolecular materials is fully realized.

In our study, the PPR hydrogel (Figure 1a) was prepared by using PEG10K (molecular weight 10000) and α-CD in water as described in reference [7c]. The concentrations of PEG and α-CD had to be higher than 0.1 g mL⁻¹, and the gel formed in about 4 h. The inclusion complexation between the PEG guest and CD host, and the threaded α-CD as competitive guest 1-[p-(phenylazo)benzyl]pyridinium bromide (Azo-Cl-N⁺) (see Figure 2, and Scheme S1 and Figure S1 in the Supporting Information) was synthesized. The presence of the quaternary pyridine group in Azo-Cl-N⁺ ensures its good solubility in water. Azo-Cl-N⁺, as expected, shows clear reversible cis–trans isomerization under UV and visible irradiation (Figure S2 in the Supporting Information). As equivalent molar amounts of trans-Azo-Cl-N⁺ to α-CD in water were added to the

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**Figure 1.** Hydrogels and sols: a) PEG/α-CD hydrogel; b) PEG/α-CD/Azo-Cl-N⁺ sol; c) sol in (b) after UV irradiation; d) gel in (c) after visible-light irradiation; e) sol in (b) after equivalent α-CD to Azo-Cl-N⁺ was added.
Communications

The addition of Azo-C1-N\(^+\) to the hydrogel causes remarkable changes (Figure 2, curve c), that is, the aromatic proton signals of Azo-C1-N\(^+\) shift to a low field (from \(\delta = 8.00\) ppm of Figure 2, curve e, to \(\delta = 8.11\) ppm) and the proton signals of \(\alpha\)-CD to a high field (from \(\delta = 3.92\) ppm of Figure 2, curve b, to \(\delta = 3.66\) ppm). Such changes are exactly the same as that observed for the reference system containing Azo-C1-N\(^+\) and \(\alpha\)-CD only as a result of the formation of the host–guest complex (Figure 2, curve d). In this ternary system of PEG/\(\alpha\)-CD/Azo-C1-N\(^+\), the most interesting observation is that the integral area of PEG signals returns to the initial value (9.70, S1.6 and Figure S3 in the Supporting Information) shown in Figure 2, curve a, before gelation. It means that after mixing Azo-C1-N\(^+\) with the hydrogel, all the PEG chains that were bound to the hydrogel become free chains. In other words, the complexed \(\alpha\)-CD molecules were pulled out from the PEG chains driven by the host–guest interaction between \(\alpha\)-CD and Azo-C1-N\(^+\). This argument is confirmed by a supplementary experiment as follows. In the PEG/\(\alpha\)-CD/Azo-C1-N\(^+\) solution (Figure 1b), in which all the \(\alpha\)-CD forms a complex with Azo-C1-N\(^+\), additional \(\alpha\)-CD equivalent to Azo-C1-N\(^+\) was added. The hydrogel (Figure 1c) re-formed in 2 h as a result of the PEG chains threading into the cavities of the newly added host \(\alpha\)-CD. In addition, the \(^1\)H NMR spectrum of PEG/Azo-C1-N\(^+\) was recorded (Figure 2, curve h). No shift was observed, thus showing that Azo-C1-N\(^+\) had no interactions with PEG.

Dynamic laser light scattering (DLS) performed in very dilute solutions was used to monitor the formation of linear PPR and its dissociation. The concentration of PEG was 0.01 g•mL\(^{-1}\), much lower than that used to form the hydrogel, so the PPR could form but no precipitation and gelation took place. As shown in Figure 3, curve a, the solution of PEG alone shows a relatively narrow hydrodynamic radius distribution with a peak value of 3 nm. Mixing this PEG10K solution with \(\alpha\)-CD causes a remarkable change in the distribution curve, that is, three peaks appear (Figure 3, curve b). The middle one is the same as that of Figure 3 curve a, which is obviously associated with the free PEG10K. The right-hand peak, with a size ranging from about 50 to 200 nm, is attributed to the PEG/\(\alpha\)-CD linear complex and its...
aggregate PPR. In addition, a small peak of size less than 1 nm is observed, which is no doubt from the free $\alpha$-CD. Finally, Figure 3 curve c clearly shows the great change caused by adding Azo-Cl-N$^+$ to the solution of $\alpha$-CD and PEG10K: the peak associated with the PPR aggregates completely disappears. This reflects PPR dissociation caused by pulling the complexed $\alpha$-CD molecules out of the PEG chains, driven by the inclusion complexation of $\alpha$-CD and Azo-Cl-N$^+$. The presence of the small molecular complex is indicated by the small peak located at less than 1 nm. Therefore, in the ternary system only free PEG chains and the complex of $\alpha$-CD and Azo-Cl-N$^+$ exist.

All the results from $^1$H NMR spectroscopy and DLS indicate that the host–guest interaction between trans-Azo-Cl-N$^+$ and $\alpha$-CD was so strong that, in the ternary system, trans-Azo-Cl-N$^+$ competed with and replaced PEG forming the trans-Azo-Cl-N$^+$/trans-CD complex and releasing the PEG chains. However, when the ternary solution underwent UV irradiation for about 1.5 h and was then kept in the dark at 4°C overnight, PPR hydrogel was regenerated (Figure 1c). The regeneration of the hydrogel implies that the interaction between $\alpha$-CD and Azo-Cl-N$^+$ becomes much weaker when the latter is converted from the trans to the cis form. This point of view is confirmed by our 2D NMR measurements.

As shown in Figure 4, the $^1$H NOESY spectrum of Azo-Cl-N$^+$/trans-CD in D$_2$O clearly displays a series of NOE correlation peaks between H3/H5 of $\alpha$-CD, which point to the cavity, and the protons Ha–Hd of the azobenzene moiety: peaks A between H3/H5 and Hb as well as He, peaks B between H3/H5 and Hd, and peak C between H5 and Ha. These NOE correlation peaks indicate that the trans form of the azobenzene moiety in Azo-Cl-N$^+$ is deeply included in the hydrophobic cavity of $\alpha$-CD. However, all of these correlation peaks disappeared after UV irradiation of the solution, as shown in Figure S4 in the Supporting Information, which indicates that the azobenzene moiety of cis-Azo-Cl-N$^+$ was excluded from the cavity of $\alpha$-CD. This provides opportunities for the free $\alpha$-CD molecules to move and be threaded by the PEG chains again.

The difference in the binding ability of the trans- and cis-Azo-Cl-N$^+$ with $\alpha$-CD was also estimated by isothermal titration calorimetry (ITC). The enthalpy changes ($\Delta H$) during mixing of the guest Azo-Cl-N$^+$ solution (0.3 $\mu$mol) and the host $\alpha$-CD solution (1 equiv) before and after UV irradiation are recorded in Figure 5. Here, the single-injection mode (SIM) was used. The heat of dilution of the $\alpha$-CD solution was measured as a control and subtracted from the corresponding data. The heat released before UV irradiation was 939 $\mu$cal, whereas after irradiation it decreased to 323 $\mu$cal only. However, this finding cannot be simply attributed to the contribution of the cis form. As is well known, trans and cis isomers of the azobenzene moiety undergo dynamic balance. By $^1$H NMR measurements it was calculated that the trans isomer of Azo-Cl-N$^+$ is present at about 90 and 22% before and after UV irradiation, respectively (Figure S5 in the Supporting Information), which is generally in agreement with data reported in the literature. Considering that after UV irradiation, about a fifth of the azobenzene groups remain in the trans form, which makes the major contribution to the measured very low $\Delta H$, the association between the cis form and $\alpha$-CD is very weak. Figure S6 (Supporting Information) shows the titration curve for $\alpha$-CD and Azo-Cl-N$^+$ before UV irradiation, from which the association constant of 1.46 $\times$ 10$^7$ M$^{-1}$ was obtained. This value is very close to those reported for other azobenzene compounds in the literature. For $\alpha$-CD and cis-Azo-Cl-N$^+$, the association constant is not detectable from the ITC titration curve as the interaction is too weak.

We also studied the complexation between Azo-Cl-N$^+$ and $\alpha$-CD by circular dichroism spectroscopy. As shown in Figure 6a, the spectrum of Azo-Cl-N$^+$/trans-CD in water shows a large positive band at 330 nm and a small negative band at 450 nm, which are assigned to the $\pi-\pi^*$ transition of Azo-Cl-N$^+$ and n-\pi$^*$ transition of cis-Azo-Cl-N$^+$, respectively. This result indicates that the azobenzene moiety of trans-Azo-Cl-N$^+$ inserts in the $\alpha$-CD cavity with its electronic transition moment parallel to the $\alpha$-CD axis. Meanwhile, the azobenzene moiety of cis-Azo-Cl-N$^+$ just lies on the $\alpha$-CD axis.

![Figure 4](image.jpg) 

**Figure 4:** NOESY spectrum of Azo-Cl-N$^+$/trans-CD aqueous solution before UV irradiation.

![Figure 5](image.png) 

**Figure 5:** Heat observed by ITC in the titration of Azo-Cl-N$^+$ by $\alpha$-CD in SIM mode, before (----) and after (-----) UV irradiation.
ternary system prepared by adding Azo-C
azobenzene moiety. After subsequent visible-light (435 nm) irradiation, the spectrum recovers almost to its original value, which suggests that α-CD moves back to the azobenzene moiety.

Figure 6 displays the circular dichroism spectra of the ternary system prepared by adding Azo-C1-N+ (1 equiv) to PEG/α-CD (a) and then diluting the mixture. It is remarkable to see that Figure 6b shows exactly the same spectra and variation with irradiation as those shown in Figure 6a. This means that in the solution formed by mixing Azo-C1-N+ with the PPR hydrogel (curve “initial”), all of the α-CD species are pulled out from the PPR to form a complex with trans-Azo-C1-N+. In other words, the presence of PEG chains does not show any effect on the complexation between α-CD and the azobenzene moiety in either the trans or cis forms.

In conclusion, photoreversible PPR hydrogels were simply achieved through competition of three host–guest interactions (Scheme 1). Our studies proved that the strength of the interactions is in the sequence trans-Azo-C1-N+/α-CD > PEG/α-CD > cis-Azo-C1-N+/α-CD. PEG10K and α-CD form PPR hydrogel in water. The hydrogel transfers into solution by simply adding the competitive guest trans-Azo-C1-N+, which replaces PEG units to form complexes with α-CD. After UV irradiation, the PPR hydrogel regenerates because Azo-C1-N+ in the cis form loses its ability to complex with α-CD and then the latter is threaded by the PEG chain again. Subsequent irradiation by visible light makes the hydrogel convert to a solution. The photocontrollable gel-to-sol and sol-to-gel processes can be repeated for cycles. The simplicity of preparation, commercial availability, and biocompatibility of the materials bode well for future applications of the hydrogels in various fields.

Keywords: cyclodextrins · host–guest systems · rotaxanes · sol–gel processes · supramolecular chemistry

References


