Fabrication of mechanically improved hydrogels using a movable cross-linker based on vinyl modified polyrotaxane†

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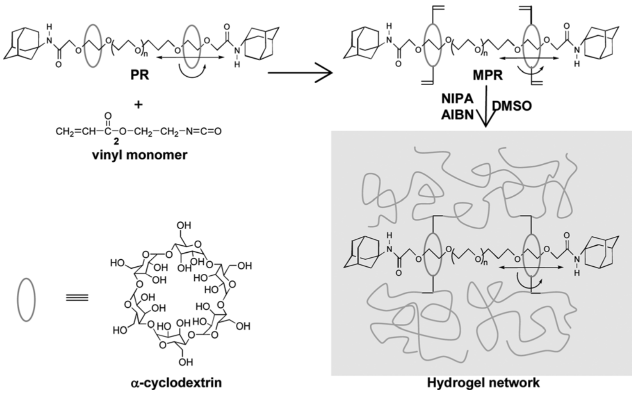
This manuscript describes the preparation of new slide-ring gels by using a polyrotaxane as a cross-linker.

Reversible stimuli-responsive polymers have aroused considerable interest for applications such as actuators, sensors, and drug delivery systems. The most extensive investigations of reversible stimuli-responsive polymers have been carried out on chemically cross-linked polymer gels, so-called "chemical gels."[1] However, as deformation is brought into the network, for instance, by the drastic change in the volume with a rapid change in the environment, the fixed cross-links cannot avoid the localization of the stress and the chemical gels soon lose their mechanical integrity. In contrast, physical gels, in which polymers interact with each other through reversible cross-linkages such as hydrogen bonding, and hydrophobic interaction, can exhibit strain relaxation *via* the reorientation of the non-covalent cross-link points under deformation. However, it is difficult for the physical gels to reveal reversible changes in their characteristic properties in response to the stimuli, since the networks cannot recover these original structures after major structural changes. This necessitates the innovation of novel reversible stimuli-responsive gels, which would be able to retain their original structure and properties without losing mechanical integrity under deformation. In this study, we aim to synthesize a novel type of movable cross-linker based on the sliding phenomenon, in which the cross-link architecture contains active vinyl modified cyclodextrin macrocycles capable of sliding and rotating about the polymer axle in the free state and with the covalently cross-linked polymer chains even in the gel state (Scheme 1).



Scheme 1 Schematic representation of the formation of the movable cross-linker and its gelation. For the sake of clarity only a few cross-link points are depicted in the scheme.

Gibson and co-workers[2] were the first to propose gels with sliding cross-link points, and recently the concept has been generalized.[3] The network structure of the sliding gels may be obtained by a cross-linking reaction among the threaded ring-like molecules, which are terminally-capped to the linear polymer chain on different polyrotaxane units. As the ring-like molecules can rotate and slide along the polymer chains, the lengths of the polymer chains in the network are averaged and, in an analogy to a pulley, the tension of the polymer chains can be equalized. Gels of this kind have shown definite progress in gel research and improvements in physical properties such as non-linear elasticity, softness, and higher mechanical strength have been achieved. To successfully exploit the sliding phenomenon in polymer gels for a particular polymer, the polymer chain needs to be tailored with a rotaxane-like architecture having a stable capping agent to prevent the dethreading of the macrocycles. However, this complicated and protracted process is not applicable to most polymer chains, and widespread use of a variety of polymer chains remains an elusive goal. Meanwhile, a sparse polyrotaxane solution exhibits three different types of diffusion: cooperative, self, and sliding diffusion. Interestingly, the mode of sliding diffusion for polyrotaxanes is noticeable even after gelation.[4] The fascinating characteristics of polyrotaxanes[5] have already been put to use in the syntheses of various smart materials, for instance, molecular tubes,[6] insulated molecular wires,[7] drug delivery systems,[8] light-induced energy transfer systems,[9] *etc.* We focused on polyrotaxane for its use as a cross-linker in syntheses of polymer gels having intriguing mechanical properties.

The polyrotaxane (PR),[10] consisting of α-cyclodextrin (α-CD), poly(ethylene glycol) carboxylic acid (MW = 35 000), and a capping agent, 1-adamantanamine, was used throughout this work. It contained *ca.* 103 α-CDs per molecule corresponding to an inclusion ratio of 26%. The PR was modified by 2-acryloyloxyethyl isocyanate (Showa Denko) having both isocyanate and vinyl groups in its parent structure. The isocyanate group forms a stable

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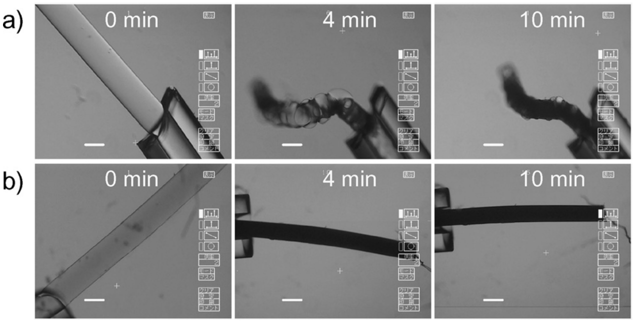

Fig. 1 Micrographs of the morphological changes of cylindrical (a) TN and (b) RN gels in water after a sudden temperature jump from 20 °C to 40 °C.

carbamate bond with the hydroxyl group of the α-CD of the PR to yield the cross-linker, which we refer to as MPR. The degree of substitution (DS) ($0 \leq DS \leq 18$), *i.e.*, the average number of substituted hydroxyl groups per α-cyclodextrin unit of the MPR, calculated using ^{1}H NMR spectra (see Fig. S1 in the ESI†), was found to be 8.4. The structure of the cross-linker is further evidenced from the FT-IR spectrum (see Fig. S2 in the ESI†). *N*-Isopropylacrylamide (NIPA) gels were prepared by free radical polymerization using MPR as a cross-linker (RN gels), maintaining the concentration of NIPA monomer at 2.0 M and varying the amount of the cross-linker MPR from 0.80 to 4 wt% (see Table S2 in the ESI†). Typical NIPA gels (TN gels) were also prepared under identical conditions using *N*,*N*′-methylene bis(acrylamide) (BIS) as a cross-linker instead of MPR and were used as references against the RN gels.

The synthesized RN and TN gels are transparent in dimethylsulfoxide, DMSO. The swelling behaviors of RN and TN gels in DMSO are similar to those in water. Since the RN gel structure is dominated mostly by poly(NIPA) chains, the swelling ratio in various solvents is also likely to be governed mainly by the poly(NIPA) chain. No volume changes with temperature occur for either gel in DMSO, but these gels show a sharp volume change above 32 °C in water.

To realize the effect of the novel cross-linker MPR on the kinetic process of shrinking and the mechanical properties of RN gel over conventional TN gel, we tailored RN and TN gels with similar degrees of swelling in water as well as in DMSO and used them as references for rheological studies.

RN gels display homothetic deformation during shrinking; in contrast, TN gels shrink anisotropically (Fig. 1). When the temperature of the gel rises above the lower critical solution temperature (LCST) of poly(NIPA), the RN gel shrinks isotropically without any bubble formation, and the rate of deformation is very fast. It has been known that general chemical gels like TN gels consist of lightly cross-linked and heavily cross-linked regions: there exist spatial network inhomogeneties in the chemical gels. Due to the presence of the inhomogeneties, the chemical gels reveal anisotropic volume changes. On the other hand, the mobile cross-links allow the homogenization of the spatial distributions of the cross-linked polymer regions in the network of the RN gel. This property may diminish the localization of the stress. Hence, the RN gel exhibits a homothetic change in the volume during shrinking.

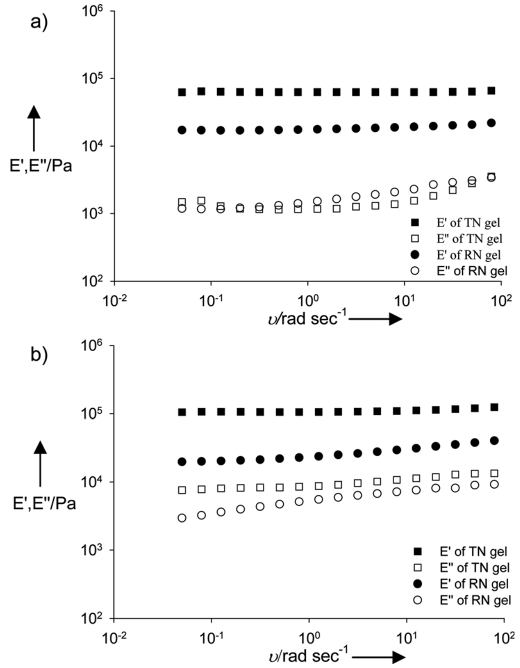

Fig. 2 Strain-controlled dynamic frequency sweep test of storage moduli (closed symbols) and loss moduli (open symbols) for TN gel (square) and RN gel (circle) at 26 °C (a) in water (where both gels are in swollen states) and (b) in DMSO.

The values of storage moduli, E', are always greater than loss moduli, E'', in the frequency range for both gels studied in water and DMSO (Fig. 2), a finding that substantiates the formation of a stable polymer network inside the gels. The E' value for RN gel is significantly smaller than that for TN gel in the whole frequency range; however, in both cases the E' values do not show appreciable changes with changes in frequency. The RN gel in water at this particular temperature is, therefore, very soft and flexible in nature. When a frequency is applied to the gels, the poly(NIPA) chains inside both gels squeeze sufficiently, but owing to the sliding effect of the MPR of the RN gel, the poly(NIPA) chains can gradually equalize their tension. This viscoelastic behavior implies that the RN gel is more liquid-like than the TN gel. The rheological studies of these gels in DMSO also show identical behaviors (Fig. 2b). However, the E' and E'' values at all frequencies for the RN gel in DMSO are slightly higher than those in water. Despite the better solubilization of the precursors of MPR in DMSO than in water, the unmodified hydroxyl group of the α-CDs of MPR in DMSO facilitates the formation of a cyclodextrin tube,[11] which to some extent suppresses the sliding and rotating ability of α-CDs through MPR. If we compare these values to TN gel in DMSO, this effect is imperceptible because the RN gel has very small storage and loss moduli in comparison to the TN gel. These small modulus values, *i.e.*, softness, must come from the inherent sliding ability of poly(NIPA) chain through the cross-links.

The storage moduli and loss moduli of the RN gel increase with increasing temperature (Fig. 3a). When the temperature is increased the thermo-sensitive poly(NIPA) chains turn to the collapsed state along with sliding cross-linking points which facilitate reaching the contractile state. Hence with increasing

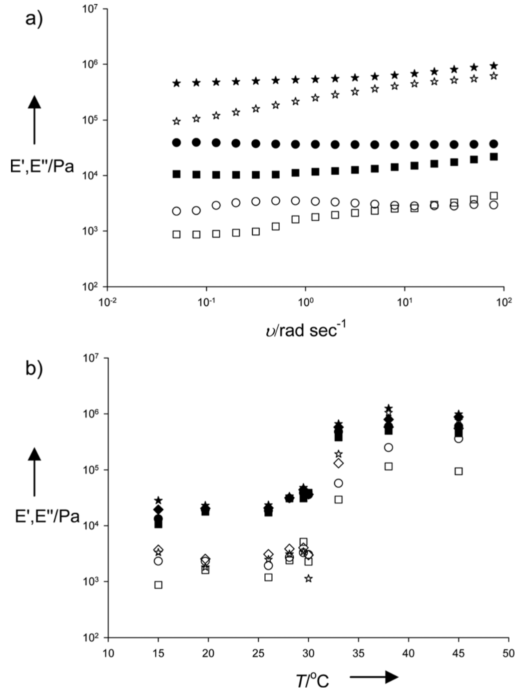

Fig. 3 Strain-controlled dynamic frequency sweep test of storage moduli (closed symbols) and loss moduli (open symbols) of RN gel in water (a) at 15 °C (square), 30 °C (circle), and 45 °C (star) as a function of frequencies and (b) at 0.05 rad s^{-1} (square), 5 rad s^{-1} (circle), 50 rad s^{-1} (diamond), and 125.6 rad s^{-1} (star) as a function of temperature.

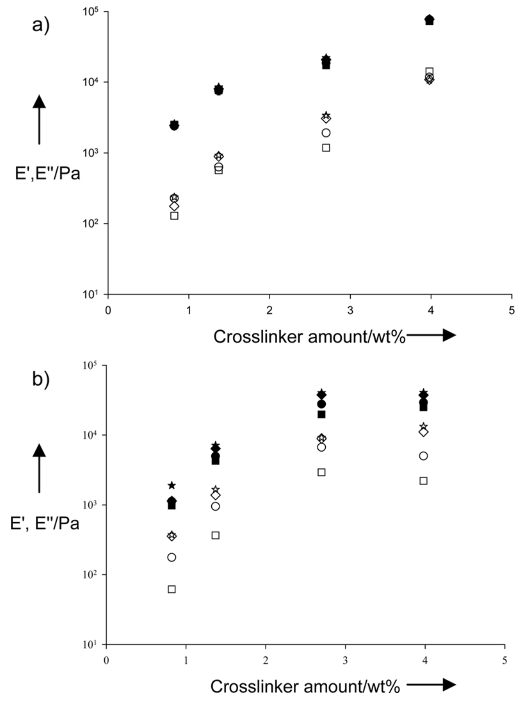

Fig. 4 Storage moduli (closed symbols) and loss moduli (open symbols) dependencies on the cross-linker amount of RN gels at 26 °C at the frequencies 0.05 rad s^{-1} (square), 5 rad s^{-1} (circle), 50 rad s^{-1} (diamond), and 79.2 rad s^{-1} (star) (a) in water (b) in DMSO.

temperature the RN gel gives higher modulus values in the whole frequency range. The RN gel has little frequency dependence on its moduli values but the modulus value increases significantly with temperature (Fig. 3b). Above the volume phase transition temperature, a sharp increase in the modulus value is observed and the difference between storage and loss moduli decrease greatly, *i.e.*, the gel loses its viscous behavior markedly, which indicates the rigid behavior of the gel in that state.

An increase in the amount of cross-linker in the RN gels results in increases in both storage and loss moduli in water as well as in DMSO (Fig. 4). In water the modulus values increase proportionally with the crosslinker amount, but in DMSO the features are slightly different. At a higher ratio of cross-linker amount, the modulus values increase for the RN gel in water or the TN gel in water and DMSO. The better solubility of the cross-linker, MPR, in DMSO gives the poly NIPA chains many more degrees of freedom than that in water which brings the gel a somewhat soft nature. The softness or hardness of the RN gel may, therefore, be well controlled by changing the amount of cross-linker or temperature.

The rheological studies of the RN gel show no evidence of cracking or breaking, while cracking has sometimes been observed in TN gels, especially at high concentrations of cross-linker at high frequencies. At high frequencies, the covalently bonded fixed cross-links divide the long poly(NIPA) chains into several segments: hence, the tension is solely centered on the shortest poly(NIPA) chains, and the gel network can not adjust its cross-link distribution or polymer length; eventually the TN gel loses its mechanical integrity at the micro and macro level. In contrast, MPR exhibits a characteristic sliding effect; α-CDs with the long poly(NIPA) chains of RN gel can slide and rotate *via* the MPR, which gradually equalizes its experienced tension and gives the gel a very soft and mechanically stable nature.

The phenomenon of sliding gels may successfully be exploited for the development of materials for diverse applications, such as photosensitive materials, biomedical applications *etc*. Extensive work is currently underway to extend these novel cross-links to other polymer network systems.

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