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Solvent Programmable Polymers Based on Restricted Rotation

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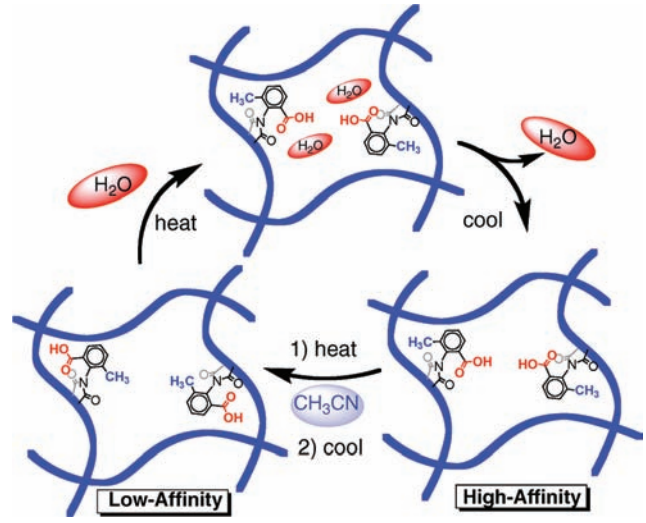
The ability to control and manipulate recognition properties of polymer gels is important for many applications including chromatography, drug delivery, and biosensors.[1] An attractive strategy has been to develop stimuli-responsive gels that can change their chemical properties in response to heat, solvent, and pH.[1d,f,2] A limitation of this strategy is that the stimuli-induced structural changes are typically fragile and unstable. Thus, the gels revert back to their equilibrium states upon removal of the stimuli. Reported, herein, is a new class of solvent programmable polymers (SPPs) based on restricted rotation with the ability to respond and remember their stimuli-induced properties (Scheme 1).[3] Like other stimuli-responsive polymers, the recognition properties can be modulated by heating in different solvents. At elevated temperatures, the carboxylic acid recognition groups have free rotation and can switch their relative orientations in response to the solvent. For example, heating the SPP in polar solvents increased the number of solvent accessible carboxylic groups. Conversely, heating in nonpolar solvents decreases the number of solvent accessible carboxylic acids. On cooling to rt, these solvent-induced changes were "saved" due to restricted rotation about the $C_{aryl}-N_{imide}$ bonds.[4] Thus, the orientation of the carboxylic acid groups were maintained even when the imprinting solvent is removed or exchanged. The solvent-induced changes are also reversible, and the binding properties can be modulated by cycling between heating the polymer in a polar and nonpolar solvent.

The SPP was prepared via ROMP polymerization of monomer **1** with restricted rotation and diimide cross-linker **2** (Scheme 2).[5] A high molar percentage of cross-linker (80%) was used to ensure that **1** was rigidly fixed within the polymer framework. The resulting polymer gel was not soluble in water or organic solvents. However, the interiors of the polymers were solvent accessible as they swelled to 30% v/v and 50% v/v in water and acetonitrile, respectively. A control polymer (CP) was prepared under the same conditions, using monomer **3** that has free rotation around its $C_{aryl}-N_{imide}$ bond. To verify that the polymerized ring opened products of **1** would also have restricted rotation, the conformational stability of model compound **4**, which has a similar *cis*-fused bicyclic framework as the ring-opened products of **1**, was studied.[6] The rotamers of **4** were stable at rt. A rotational barrier of 27.7 kcal/mol was measured by following the kinetics of isomerization. This barrier equates to a half-life of 0.58 y at 24 °C and 90 min at 83 °C.

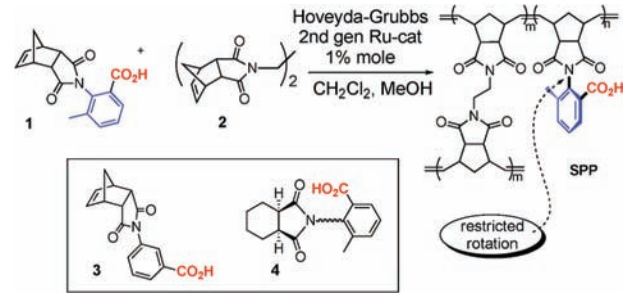
The switching and memory properties of the SPP were initially tested by heating the polymer (83 °C, 26 h) in solvents of varying polarity from cyclohexane to water (Figure 1). After heating, the polymers were cooled to rt and the imprinting solvents were removed *in vacuo*. The solvent-induced changes were assessed by measuring the binding capacities of the polymers for ethyl adenine-9-acetate (EA9A) in acetonitrile.[7] This basic guest is known to form strong H-bonding interactions with carboxylic acids.[4a−c,8] Thus, an increase or decrease in the number of solvent accessible carboxylic acids would result in an increase or decrease in the binding capacity of the polymers for EA9A. The solvent-induced

Scheme 1. A Solvent Programmable Polymer (SPP) That Modulates Its Recognition Properties When Heated in Different Polarity Solvents[a]



[a] The solvent induced changes are maintained after cooling and removal of solvent due to the presence of a monomer with restricted rotation.

Scheme 2. Synthesis of the SPP and Depictions of Control Monomer **3** Which Lacks Restricted Rotation and Atropisomeric Model Compound **4**



conformational changes were evident by the wide variation in binding properties of the polymers (Figure 1). The polymers heated in the most polar solvent (water) had a 50% higher binding capacity than the polymers heated in nonpolar solvent (cyclohexane). A sigmoidal correlation was observed between the polarities (E_T^N) of the imprinting solvent and the binding capacities of the solvent-imprinted polymers.[9] These solvent studies demonstrate the ability to attenuate and tailor the binding capacities of the SPP simply by heating in a solvent of appropriate polarity. The solvent trends were also consistent with the carboxylic acids favoring orientations that maximized their contact with solvents of matching polarity.

To establish that the changes in the binding capacity of the SPP were coupled to restricted rotation, the rates of the solvent imprinting processes were measured (Figure 2) and compared with the rotational barriers of atropisomer model system **4**. A high-

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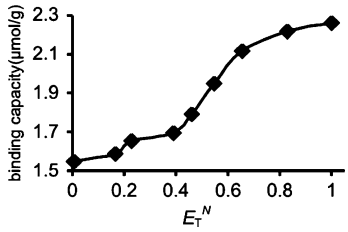

Figure 1. Binding capacities of SPP for EA9A in acetonitrile after heating (83 °C, 26 h) in solvents of varying polarity (From left to right: cyclohexane, dioxane, ethyl acetate, *tert*-butanol, acetonitrile, 2-propanol, ethanol, ethanol/water (1:1), water).

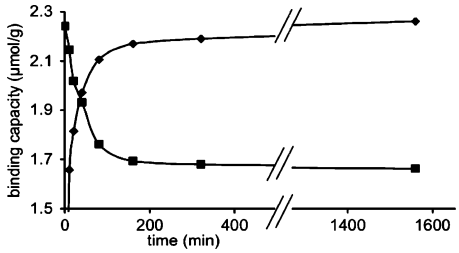

Figure 2. Change in binding capacity over 26 h for a high-affinity SPP heated (83 °C) in acetonitrile (■) and a low-affinity SPP heated (83 °C) in water (◆).

affinity SPP (prepared by heating in water) was heated in a less polar solvent (acetonitrile) at 83 °C. The systematic transformation into a low-affinity SPP was followed over 26 h (Figure 2, ■). The complementary experiment was also performed in which a low-affinity SPP (prepared by heating in CH_3CN) was heated in water. The systematic transformation into a high-affinity polymer appeared to occur at the same rate. This was confirmed by kinetic analyses of the rate curves. Both rate curves could be fit to first-order kinetic equations, yielding rates of 3.1 and 3.6 × 10^{-4} s^{-1}. The rate order and activation energies (27.1 and 27.0 kcal/mol) of the solvent-imprinting processes were of similar magnitudes to the rotational barrier of **4** and other structurally similar *N*-arylimides.[4,10] The high activation barriers were also consistent with the ability of the SPPs to maintain their solvent-induced changes for a week without a measurable change in binding capacity.[11]

We have previously demonstrated that the conformational changes of atropisomeric systems are reversible, allowing the properties to be repeatedly "written" and "erased".[4a−c] To test whether similar levels of reversibility could be observed in the SPP, a sample was repeatedly heated (83 °C, 26 h) in acetonitrile and water (Figure 3, ◆). The solvent-induced switching was shown to be reversible and proceeded with high fidelity. The binding capacities of the high- and low-affinity SPP states remained constant over 5 cycles. Control studies were also carried out to verify that the solvent-induced changes were due to rotation about the $C_{aryl}-N_{imide}$ bonds and were not due to differences in hydration or swelling of the polymers after heating in the different solvents. First, the SPP was subjected to the same cycle of immersion in CH_3CN and water but without heating (Figure 3, ▲). Second, a control polymer (CP) made with monomer **3** was tested that lacked restricted rotation. Both cases did not display the solvent-memory effects, as the binding capacities remained relatively constant (Figure 3, ■). The control studies showed that (1) the combination of solvent **and** heat were necessary to change the binding properties, (2) the presence of monomer **1** with restricted rotation was essential, and (3) the switching process cannot be explained by the presence of residual solvent in the polymers gels.

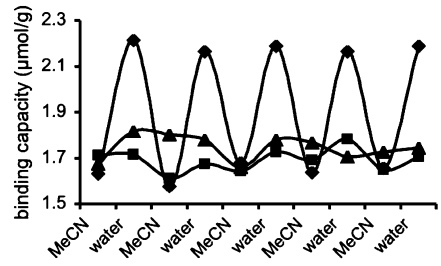

Figure 3. Measured EA9A binding capacities of SPP (◆) and CP (■) after repeatedly heating (83 °C, 26 h) in acetonitrile and then in water. The SPP was also repeatedly shaken in acetonitrile and then water without heating (▲).

In summary, the programmable polymers based on restricted rotation were developed that can be reversibly shaped at elevated temperatures and can maintain these solvent-induced conformational changes on cooling to room temperature.

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Supporting Information Available: Experimental details, NMR spectra, and crystallographic data. These material is available free of charge via Internet at http://pubs.acs.org.

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(6) The rotational barrier of **1** could not be measured because the bicyclic bridge sterically biases the atropisomer to form only a single isomer. After polymerization, this steric bias is removed as the bicyclic ring is broken in the ROMP. Thus, the fused ring system of compound **4** is a more appropriate model for the C−N rotational barrier in the ROMP product.

(7) For a binding study, 60 mg of polymer were shaken with 0.1 mM EA9A in CH_3CN (2.5 mL). The concentration of EA9A in the supernatant was measured by UV−vis (257 nm) and compared with the original stock solution.

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(10) A number of studies have established that barriers of atropisomers in polymer matrices and films are very similar to those measured in solution, and in some cases, the rotational barriers in polymer matrices can be lower. See: Park, J. W.; Green, M. M.; Morawetz, H. *Macromolecules* **2001**, *34*, 5719–5722, and references therein.

(11) Using the Eyring equation, a barrier of 27.1 kcal/mol equates to a half-life of 56 days at 25 °C.

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