

Tuning Thermal Gelling Behavior of *N*-isopropylacrylamide Based Copolymer through Introducing Cucurbit[8]uril Ternary Complex on Side-chain*

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Abstract Thermo-gelation polymers have attracted increasing attention over decades. However, rare facile tuning method of sol-gel transition temperature restricted the wider application. Preceding study indicated that supramolecular interactions demonstrated a powerful means to control the structure and property of polymeric materials. Here we designed an *N*-isopropylacrylamide (NIPAM) based thermo-sensitive copolymer with naphthyl (Np) on its side chain. Positive-charged side-chain ternary complex was formed with cucurbit[8]uril (CB[8]) and methylviologen (MV²⁺) via CB[8]-enhanced intermolecular charge-transfer (CT) interaction. Introducing the ternary complex CB[8]/MV²⁺/Np on side-chain altered microstructure of macromolecular chains and led to a strong tendency for thermo gelation. Altering content of CB[8] and MV²⁺ changed content of the positive-charged side-chain ternary complex and varied gelation temperature. Therefore, introducing supramolecular interaction endowed the hydrogel with tunable gelation property.

Keywords: Thermo-sensitive copolymer; Supramolecular chemistry; Cucurbit[8]uril; Charge transfer interaction; Gelation.

INTRODUCTION

N-isopropylacrylamide (NIPAM) based polymer is an extensively used thermo-sensitive material which has low critical solution temperature (LCST) around 32 °C in aqueous solution^[1–3]. Below LCST, macromolecule chains stretch in water and form stable solution. While above LCST, they expel water and precipitate out of the solution. Main cause of this inconsecutive phase transition is the disruption of hydrogen bonding with water and increasing hydrophobic interactions among isopropyl groups^[4–6]. Because of this unique temperature sensitive property, NIPAM based polymer is very attractive for using as injectable hydrogel^[6–11] and potential benefits have been envisioned for a range of biologically applications^[5, 7, 12–15].

For NIPAM-based thermo-sensitive polymers, LCST can be controlled by copolymerizing with various comonomers^[5, 10, 16–18], adjusting ionic strength of solution^[6, 19], or changing cross-link density and architecture^[20]. Iwai *et al.*^[16] reported that thermo-responsive behavior of PNIPAM gel was affected by copolymerization with hydrophilic monomer *N,N*-dimethylacrylamide (DMAM) and hydrophobic monomer methacrylate (MMA). Incorporation of DMAM raised the LCST of PNIPAM gel, while MMA lowered it. Gupta *et al.*^[20] indicated that cross-linking density also caused a shift in LCST. For thermo-sensitive gels of PNIPAM cross-linked with 4,4'-di(2-methacryloylamide)azobenzene (DMAAB), high cross-link concentration resulted in lower LCST and decrease in the degree of equilibrium swelling. This shift in LCST was interpreted by an increase of the unfavorable interactions between the solvent (water) and the polymer network, while

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decrease in the degree of equilibrium swelling was due to an increase of topological constraints of the PNIPAM chains.

However, tuning gelation behavior *via* these processes leads to heavy workload in chemical synthesis. Supramolecular chemistry provides an effective and convenient way to adjust molecular structure and endow it with new properties^[21–23]. Preceding study indicated that introducing side-chain polypseudorotaxanes dramatically changed microstructure of macromolecular chains^[24]. In our previous work, NIPAM based cucurbit[7]uril (CB[7]) side-chain polypseudorotaxanes with low pseudorotaxane content were designed. These emulate rod-coil block copolymers demonstrated a strong tendency to aggregation and thermal gelation. Their mechanical properties were controlled *via* changing content of pseudorotaxane, meanwhile the gelation temperature was constant. In CB[n] family, CB[8] is another remarkable host molecule, giving a facile way to tune gelation behavior of these thermos-gelling hydrogels. Due to its suitable cavity size, CB[8] can selectively forms ternary complex *via* CT interaction with an electron-rich donor and an electron-deficient acceptor, such as naphthyl (Np) and methylviologen (MV²⁺)^[25]. High association constants ($K_a > 10^{11} \text{ L}^2 \cdot \text{mol}^{-2}$) in aqueous environment of this CT complex leads to the self-assembly of small molecular systems and architectures^[26–31]. In this work, we synthesized a NIPAM-based temperature-responsive copolymer within Np on its side-chain, which gave the possibility to form side-chain ternary complexes with CB[8] and MV²⁺. Introducing of electropositive CB[8]/MV²⁺/Np ternary complex on side-chain raised hydrophilicity of these macromolecular chains, leading to an increased gelation temperature. Changing content of MV²⁺ and CB[8] varied packaging ratio of this positively charged ternary complex, easily endowing the side-chain host-guest complexes with tunable thermal gelling property. Furthermore, they also showed low critical gelation concentration and excellent mechanical property.

EXPERIMENTAL

Materials

CB[8] was synthesized following literature procedure^[32]. NIPAM, 4,4'-dipyridyl, 2-naphthol, 4-vinylbenzyl chloride and 2,2-azobisisobutyronitrile (AIBN) were purchased from J&K Scientific. Diethyl ether (AR), toluene (AR), methyl alcohol (AR) and tetrahydrofuran (THF, HPLC) were obtained from Sinopharm Chemical Reagent Co., Ltd.

Preparation of the Copolymer PVBN-co-NIPAM

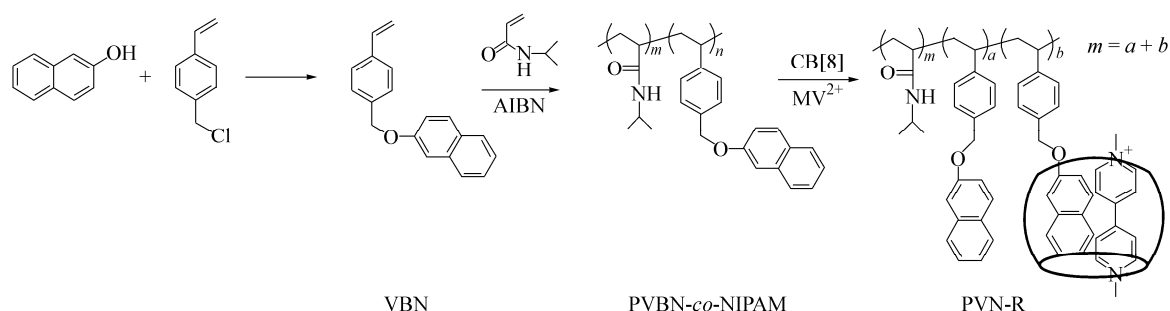
KOH (2 g, 0.0357 mol), 2-naphthol (1.73 g, 0.012 mol) and 4-vinylbenzyl chloride (1.53 g, 0.010 mol) were dissolved in dimethylsulfoxide (DMSO, 50 mL) under magnetic stirring. The reaction proceeded for 6 h at 60 °C. After the reaction, 20 mL of deionized water was added in and the mixture stirred for 1 h. Organic phase was extracted with diethyl ether (30 mL × 3) and washed with deionized water for three times. The solvent was removed by rotary evaporation at room temperature to obtain 2-((4-vinylbenzyl)oxy)naphthalene (VBN, 2.41 g, 81.1%). ¹H-NMR spectroscopy (CDCl₃, 400 MHz, δ): 5.18 (2H, s, Np–O–CH₂), 5.25–5.28 (2H, d, olefin–H), 5.75–5.79 (2H, d, olefin–H), 6.70–6.75 (2H, q, olefin–H), 7.22–7.24 (2H, m, Np–H), 7.32–7.36 (1H, t, Np–H), 7.41–7.45 (4H, m, Np–H), 7.71–7.77 (4H, m, aryl–H). ¹³C-NMR spectroscopy (CDCl₃, 400 MHz, δ): 69.8, 107.2, 114.2, 119.1, 123.7, 126.4, 126.5, 126.8, 127.7, 127.8, 129.1, 129.5, 134.5, 137.4, 156.7.

VBN (0.058 g, 0.0048 mol) and NIPAM (9.04 g, 0.08 mol) were dissolved in 100 mL of toluene, and this solution was heated to 65 °C and stirred to degas under nitrogen for 30 min. AIBN (0.045 g) dissolved in toluene was injected into the monomer solution and stood at 65 °C for 6 h. After the reaction, the solution was concentrated to 15 mL on rotary evaporator. The copolymer was precipitated in 300 mL of diethyl ether, and then dissolved in 5 mL methanol thrice to remove unreacted monomers and other impurities. The product was dried in a vacuum oven for 24 h at room temperature to have a yield of 67%. ¹H-NMR spectroscopy (CDCl₃, 400 MHz, δ): 0.71–1.46 (20.2H, br, NH–CH–(CH₃)₂), 1.46–3.38 (14.1H, br, polymer backbone), 3.69–4.35 (4.1H, br, NH–CH–(CH₃)₂), 4.91–5.18 (0.8H, br, Np–O–CH₂), 6.84–7.48 (2.3H, br, Np–H), 7.63–7.84 (1.1H, br, aryl–H). With the same synthesis condition, copolymers with different *R* and similar *M_n* (see Table 1) were obtained by changing only the ratio of VBN to NIPAM.

Table 1. Functional polymers used to prepare side-chain host-guest complex PVN-R

No.	Polymer	R^a (%)	M_n^b (kDa)	PDI ^b
1	PVBN- <i>co</i> -NIPAM-1	6.1	48.03	1.34
2	PVBN- <i>co</i> -NIPAM-2	4.5	54.04	1.37
3	PVBN- <i>co</i> -NIPAM-3	3.0	43.86	1.30

^a Determined by ¹H-NMR. $R = n/(m + n)$ in PVBN-*co*-NIPAM (Scheme 1); ^b Determined by gel permeation chromatography (GPC) using THF as eluent

**Scheme 1** Synthesis of temperature-responsive copolymers (PVBN-*co*-NIPAM) and preparation of NIPAM based CB[8] side-chain host-guest complexes PVN-R

Preparation of NIPAM-based CB[8] Side-chain Host-guest Complexes

To make a solution of PVBN-*co*-NIPAM, CB[8] and MV^{2+} , PVBN-*co*-NIPAM and CB[8], initially not soluble in water, were added in deionized water and the mixture was magnetically stirred for 1 h in an ice-water bath. The solution was allowed to stay at 2 °C overnight for complete loading. Due to CB[8]-enhanced CT interaction, Np/ MV^{2+} /CB[8] ternary complex was formed and yield red clarifying solutions. The content of each constituent was shown in Table 2.

Table 2. Preparation of CB[8]-based side-chain host-guest complexes PVN-R and their gelation temperature

Polymer	Sample	$C_{CB[8]}^a$ (mol%)	$C_{MV^{2+}}^a$ (mol%)	Gelation temperature ^b (°C)
PVBN- <i>co</i> -NIPAM-1	PVN-R11	3	3	29.3
	PVN-R12	2	2	29.4
	PVN-R13	1	1	27.8
PVBN- <i>co</i> -NIPAM-2	PVN-R21	3	3	30.5
	PVN-R22	2	2	29.4
	PVN-R23	1	1	28.1
	PVN-R24	0.5	0.5	26.4
PVBN- <i>co</i> -NIPAM-3	PVN-R31	3	3	34.6
	PVN-R32	2	2	33.4
	PVN-R33	1	1	32.4

^a $C_{CB[8]} = n_{CB[8]}/n_{copolymer\ units}$, and concentration of MV^{2+} was calculated *via* the same way; ^b Determined by rheological analysis under CD-auto strain mode with $\gamma = 0.01$, $f = 1$ Hz. The polymer content of each sample was 2.5 wt%.

Instruments

Nuclear magnetic resonance (NMR) tests were conducted by Bruker Avance 400 NMR spectrometer. Polymer molecular weight was measured by GPC with THF as the eluent at 39 °C and the flow rate was 1.000 mL/min. Samples were prepared in THF at 4 mg/mL. Sample detection was performed with a Waters515 refractive-index detector, and the setup was calibrated with eight narrow polystyrene samples from 2200 to 6.0×10^5 . The cloud point of NIPAM-based side-chain host-guest complexes were tested on a Persee TU1901 ultraviolet spectrophotometer. Rheological properties were conducted on a HAAKE MARS III rheometer. Gelation process and hydrogel properties were measured with C35/1° Ti L geometry. The gelation process was tested under CD-auto strain mode with $\gamma = 0.01$ at $f = 1$ Hz. The strain-dependent oscillatory rheology and frequency-

dependent oscillatory rheology of hydrogels were tested at 1 Hz and $\gamma = 0.01$ at 36 °C. The scanning electron micrography (SEM) images were obtained using Hitachi SU8010. SEM samples were prepared by lyophilization at -50 °C after direct freezing of heated supramolecular hydrogels in liquid nitrogen. The samples were imaged after sputtering.

RESULTS AND DISCUSSION

Synthesis and Characterization of NIPAM-based Host-guest Complexes

At the same concentration in hydrogels, CB[8] and PVBN-*co*-NIPAM were both white insolubles, and MV^{2+} was pale-yellow in aqueous solution. Simple mixing of PVBN-*co*-NIPAM and MV^{2+} , or PVBN-*co*-NIPAM and CB[8] both yielded swelling polymer phase at low temperature (quite similar condition as preparation of the hydrogels), but not a pellucid aqueous solutions. However, PVBN-*co*-NIPAM mixed with CB[8] and MV^{2+} showed entirely different phenomenon. The host-enhanced CT interaction led to formation of ternary complex CB[8]/ MV^{2+} /Np, a red solution. This color variation was considered as a visualized evidence for the existence of host-enhanced CT interaction and the formation of ternary complex^[33, 34].

As previous reported, CB[8] possessed a cavity large enough to accommodate two MV^{2+} molecules, but formation of this 1:2 host-guest complex was not observed. The electrostatic repulsion between two MV^{2+} ions in CB[8] cavity was considered to disfavor the formation of this ternary complex. However, when MV^{2+} and naphthyl existed simultaneously, CB[8] preferential bonded with MV^{2+} at first, then integrated with naphthyl to form the ternary complex *via* host-enhanced CT interaction^[33]. Formation of this ternary complex was further confirmed by ¹H-NMR spectra (Fig. 1). Peaks signed by blue triangle in Fig. 1 ($\delta = 7.21, 6.72, 4.37, 3.79, 2.54-0.32$) were assigned to proton of PVBN-*co*-NIPAM, and peaks signed by black square ($\delta = 5.62, 5.35, 4.05$) were assigned to proton of CB[8] (Fig. 1a). Chemical shifts of aromatic protons of MV^{2+} ($\delta = 8.96, 8.43$, Fig. 1b) were shifted to higher field ($\delta = 8.50, 7.63$, Fig. 1a) upon the formation of CB[8]/ MV^{2+} /Np ternary complex^[35-37]. In addition, these resonance peaks were broadened extensively due to complexation dynamics. It indicates that Np on side chain of PVBN-*co*-NIPAM and MV^{2+} were encapsulated inside the cavity of CB[8], and the NIPAM based CB[8] side-chain host-guest complexes were formed.

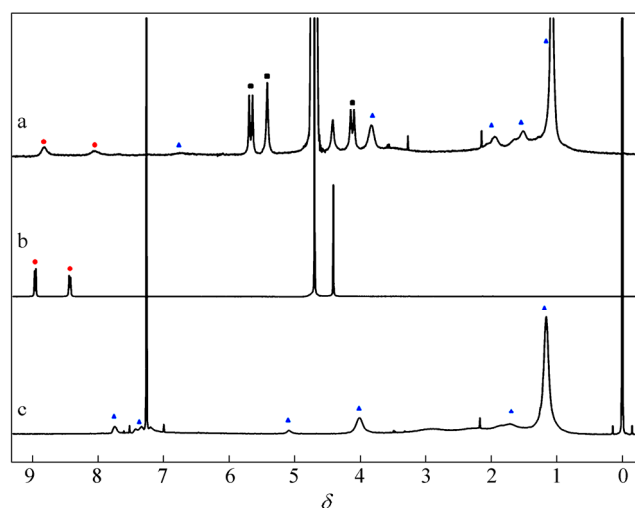
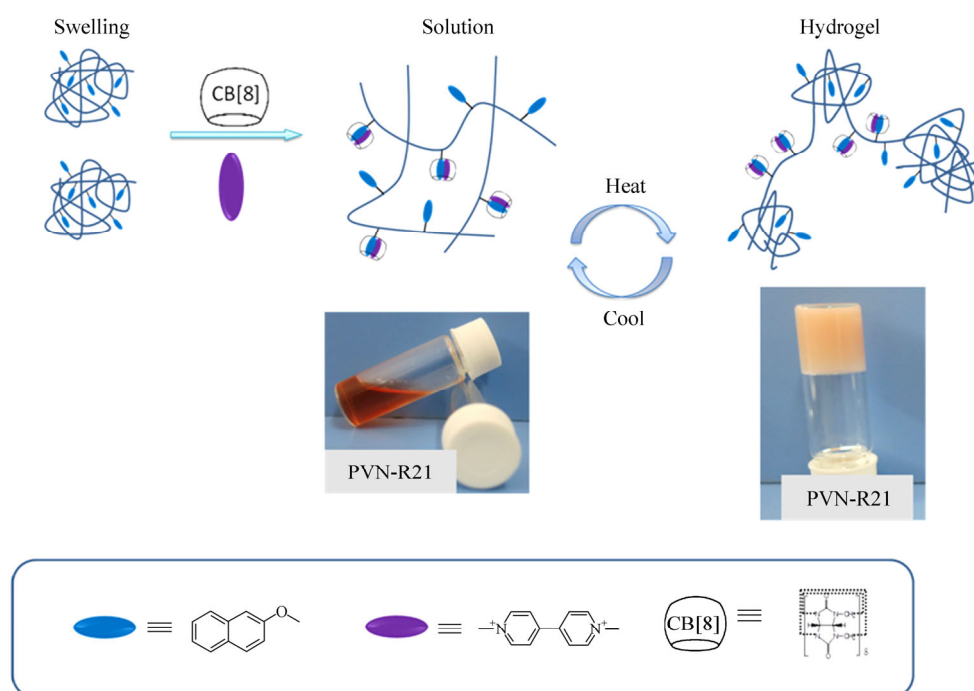


Fig. 1 ¹H-NMR spectra obtained in D₂O: (a) PVN-R21 (diluted to 1 wt%), (b) MV^{2+} and (c) PVBN-*co*-NIPAM-2 obtained in CDCl₃ at room temperature

Thermo-gelling Process of NIPAM Based CB[8] Side-chain Host-guest Complexes

When heated above LCST, the liquid solutions of PVN-Rs became turbid and transformed into hydrogels, which was totally different from unmodified poly(*N*-isopropylacrylamide). Gelation process and formation mechanism of these supramolecular hydrogels is shown in Scheme 2. Below LCST, The thermo-sensitive polymer PVBN-

co-NIPAM swelled in water, while CB[8] side-chain host-guest complex PVN-R stretched. Above LCST, swelling PVBN-*co*-NIPAM expelled water molecules and precipitated out from the aqueous solution, while the CB[8] side-chain host-guest complex PVN-R demonstrated strong tendency for aggregation and thermo-gelling. In our previous work, we studied gelation behavior and formation mechanism of NIPAM based CB[7] side-chain polypseudorotaxanes which had a quite similar molecular structure to the hydrogels in this paper^[24]. This unique aggregation behavior can be attributed to rigid-soft block structure of the side-chain host-guest complex. Scheme 2 shows the gelation process *via* visualized and convenient vial inversion method. The hydrogels were stable and maintain integrity after fiercely shake. In addition, With increasing content of CB[8]/MV²⁺, high ratio of host-enhanced CT ternary molecular complex led to deepen color both for the solutions and for the hydrogels, demonstrating the existence of the ternary molecular complex over gelation process.



Scheme 2 Schematic gelation process and description of the formation mechanism for the thermo-gelling supramolecular hydrogels PVN-R21

Well design of the thermo-gelling supramolecular hydrogels affords opportunity to use various characterization techniques for the materials, such as rheological tests. In order to probe the molecular dynamics of the thermo-gelling supramolecular hydrogels and to quantify mechanical properties, rheological characterization was performed. Figures 2(a) and 2(b) show the oscillatory temperature sweep profiles at constant shear frequency and strain. At room temperature, the storage modulus (G') was low, indicating a sol state; and it increased dramatically at temperature around LCST, indicative of the transition to a gel. The onset of this sharp increase in storage modulus was used as a measurement of gelation temperature. A slow increase of G' followed over the transition temperature and reached its maximum at 35 °C. Cloud points of PVN-Rs shown in Figs. 2(c) and 2(d) indicated an obvious phase transition in the gelation process.

As reported, LCST can be controlled by copolymerizing hydrophilic or hydrophobic comonomers. Copolymers of NIPAM and VBN are expected to have lower LCST than homo-PNIAA (32 °C), because both phenyl and naphthyl groups of VBN monomer unit are hydrophobic. Figures 2(a) and 2(c) show that low copolymerization ratio of hydrophobic monomer units in thermo-sensitive copolymers demonstrated high gelation temperature at constant CB[8]/MV²⁺ content (3 mol%). When CB[8] and MV²⁺ were added, formation

of CB[8]/MV²⁺/Np side-chain electropositive complex would partially alter the hydrophilicity of PVBN-*co*-NIPAM macromolecular chain. With increased content of CB[8] and MV²⁺, introducing positive charge on side chain, the hydrophilicity of the copolymer chain was raised, leading to an elevation for the gelation temperature. In Figs. 2(b) and 2(d), the gelation temperature ranged from 24.6 °C to 28.9 °C following the increased content of CB[8] and MV²⁺ while the same copolymerization ratio (4.5%) of PVBN-*co*-NIPAM was kept the same. Another two series of hydrogels with different copolymerization ratio of PVBN-*co*-NIPAM showed analogical gelation temperature changing behavior (see Table 2). Therefore, gelation temperature has a quite wide scope (26.4 °C to 34.6 °C) and can be further changed by modifying ratio of PVBN-*co*-NIPAM in the copolymers and by varying content of CB[8] and MV²⁺.

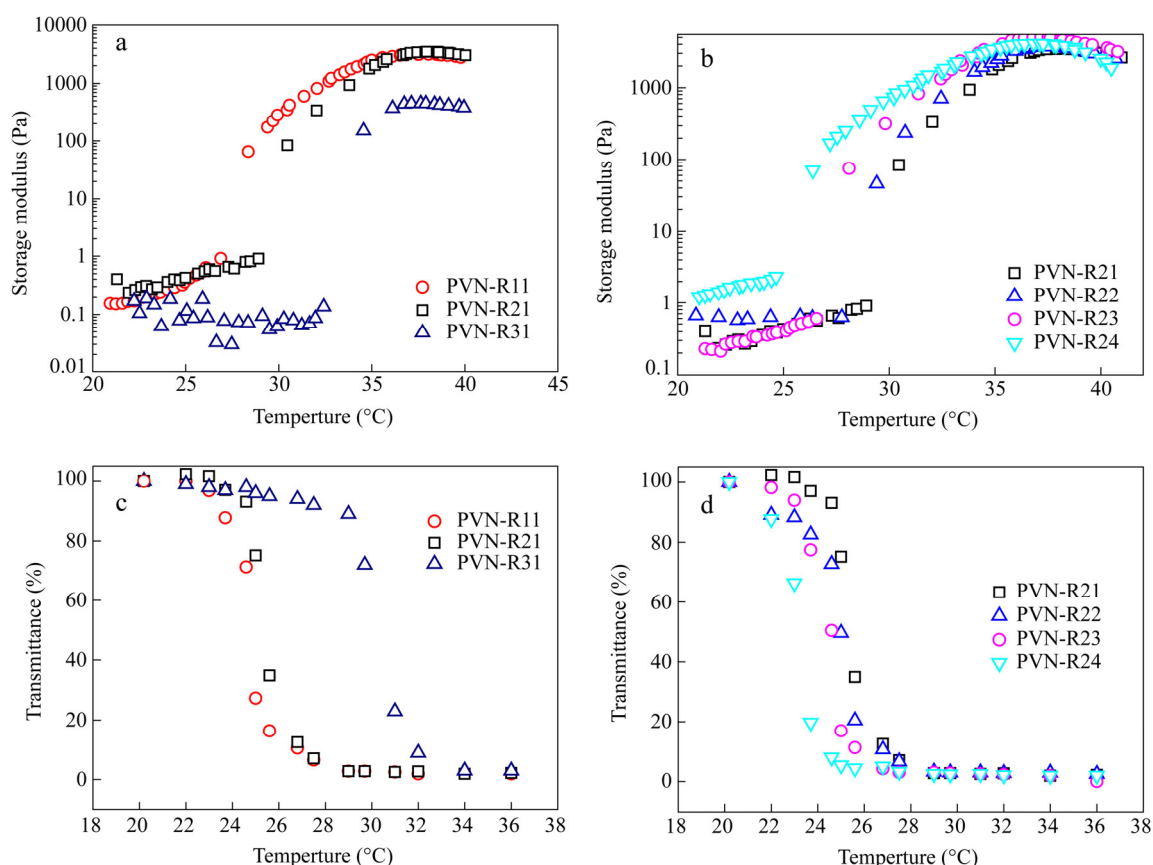


Fig. 2 (a, b) Tunable gelation behavior of NIPAM-based side-chain host-guest complexes PVN-Rs measured *via* oscillatory rheological analysis and (c, d) their cloud point obtained *via* UV-Vis spectrophotometry at 500 nm wavelength (c, d, samples diluted to 0.5 wt%)

Rheological Properties of the Thermo-gelling NIPAM-based CB[8] Side-chain Host-guest Complexes

The frequency-dependent oscillatory rheology performed at linear viscoelastic region is shown in Fig. 3, in which both viscous and elastic responses to mechanical perturbation were given, providing insight into dynamic mechanical properties of the thermo-sensitive hydrogels. The elastic component (storage modulus, G') is a measurement of energy stored in the hydrogel network when perturbation occurred, while the viscous component (loss modulus, G'') is a complementary measurement of energy loss in material through relaxations or dissipated heat. In Fig. 3(a), G' and G'' increased when the frequency changed from 0.01 Hz to 100 Hz at different rates, leading to an intersection. The frequency (f) of this intersection is the bulk relaxation rate β . At short time scales, $f > \beta$, these thermo-sensitive hydrogels are elastic, the elastic component G' dominates as the reversible aggregations are active and capable of responding to the deformation energy. While at long time scales, $f < \beta$,

they are viscous. The bulk relaxation rate β changes a little among different CB[8] and MV^{2+} contents. At the same frequency, storage and loss modulus both increase with the rising percentage of CB[8] and MV^{2+} .

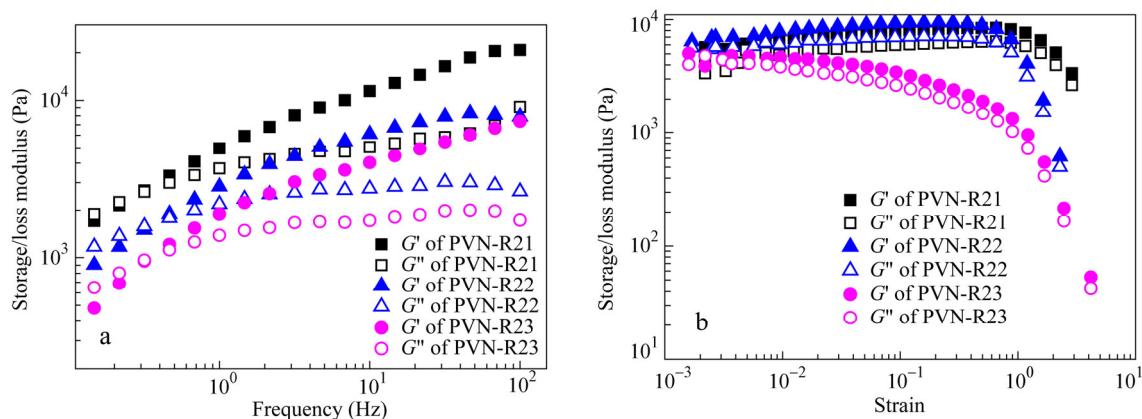


Fig. 3 Oscillatory rheological analysis at 36 °C: (a) frequency-dependent and (b) strain-amplitude sweep storage and loss modulus at different loading ratio of CB[8]/ MV^{2+} /Np

Figure 3(b) depicts the moduli of hydrogels versus applied strain. The linear viscoelastic region (plateau region), where the moduli are independent of strain, can therefore be identified. The wide linear viscoelastic region indicated that the hydrogels were not brittle. Breakdown strain amplitude of hydrogels demonstrated a parallel rule compared to the result of moduli. For hydrogels with PVBN-co-NIPAM of 4.5% ratio with varied content of CB[8]/ MV^{2+} , high assembling content (PVN-R21) yielded high moduli and wide breakdown strain amplitude, and vice versa. This rule obtained from the sample series PVN-R2 also was also validated in the series PVN-R1 and PVN-R3, indicating that changing the copolymerization ratio in an appropriate scope did not affect stable thermo-gelling PVN-R with tunable gelation temperature.

As reported, polymer content affected the property of hydrogels. In this session, as varying pattern of PVN-Rs performed under quite the same way, PVN-R21 was chosen to explain the general rule in rheological characterizations. The frequency, temperature and strain dependent storage and loss modulus plots are shown in Fig. 4. As expected, storage and loss modulus increased with increasing polymer content, while their linear viscoelastic regions, gelation temperature and moduli-frequency trend were similar, indicating that the structure of hydrogels were independent from polymer content. Therefore, by simply varying the concentration of these polymers, one can modulate the mechanical property without changing their structure and intrinsic properties. A further illustration of the relationship between polymer content and moduli is shown in Fig. 4(d). For PVN-R21, critical gelation concentration was 0.75 wt%, which was much lower than most of those reported on thermo-gelling hydrogels (usually above 10 wt%). The critical gelation concentration point of these well designed hydrogels was even lower than hydrogels with a similar structure reported in our previous work. Furthermore, these hydrogels demonstrated exceptional high mechanical property even at low concentration.

Microstructure of the Thermo-gelling NIPAM-based CB[8] Side-chain Host-guest Complexes

The microstructure of these supramolecular hydrogels was investigated using SEM. After heated and transformed into hydrogels, the supramolecular hydrogels were cryo-dried and retained the characteristic red color of ternary complex charge-transfer band, indicating that the supramolecular side-chain complex was still intact. Figure 5 shows the SEM images of PVN-R21, PVN-R22, PVN-R23 and PVN-R24, from which highly ordered microstructure was seen in all the hydrogels. As loading ratio of side-chain ternary complex CB[8]/ MV^{2+} /Np was increased, the pore size of PVN-R with the side-chain host-guest complex decreased from approximately 7 μm to 2 μm , endows therefore PVN-R with a high rheological strength, which corroborated well the observations in the “rheological properties of the thermo-gelling nipam-based cb[8] side-chain host-guest complexes” part.

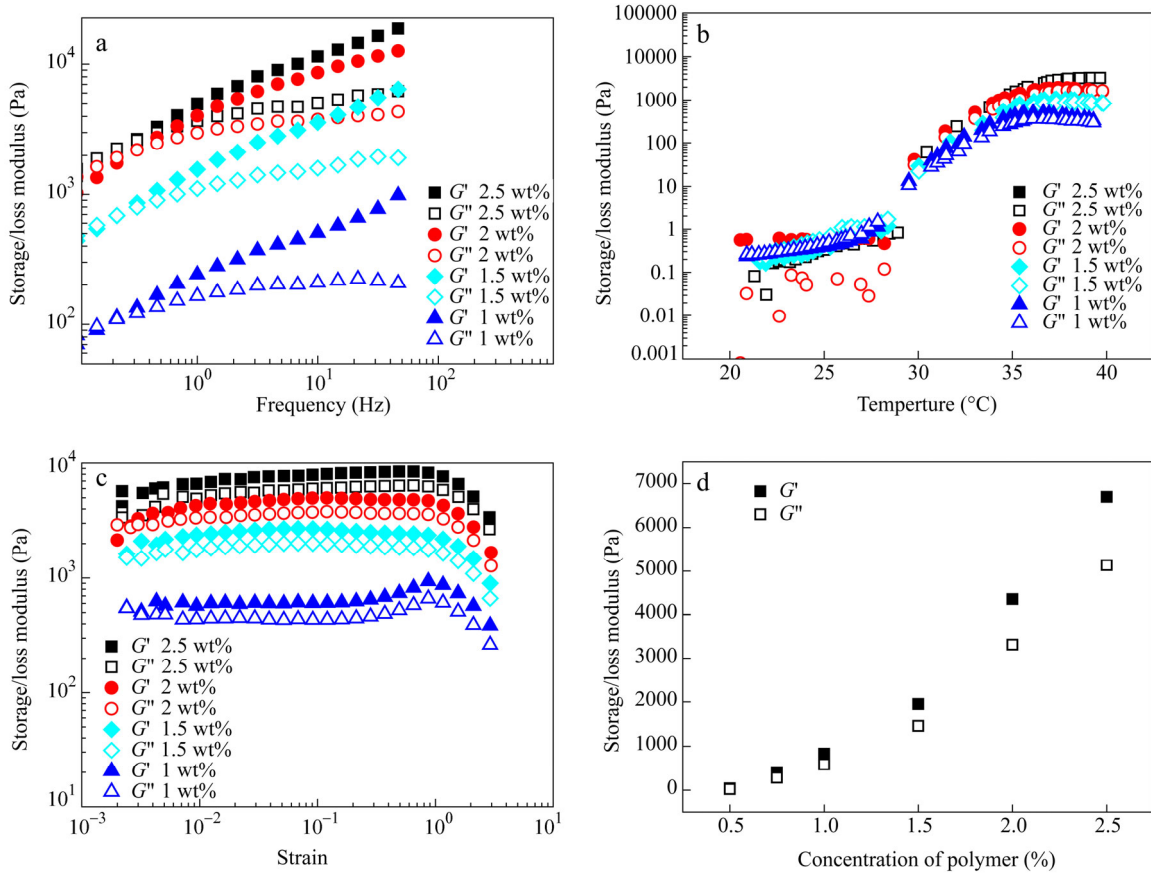


Fig. 4 Oscillatory rheological analysis of the PVN-R demonstrating effect of polymer content on the thermogelling property at 36 °C: (a) Frequency dependent storage and loss modulus of different polymer content of PVN-R21; (b) Temperature dependent and (c) strain dependent storage and loss modulus of different polymer content of PVN-R21 at 1 Hz; (d) Summary of moduli of different polymer content

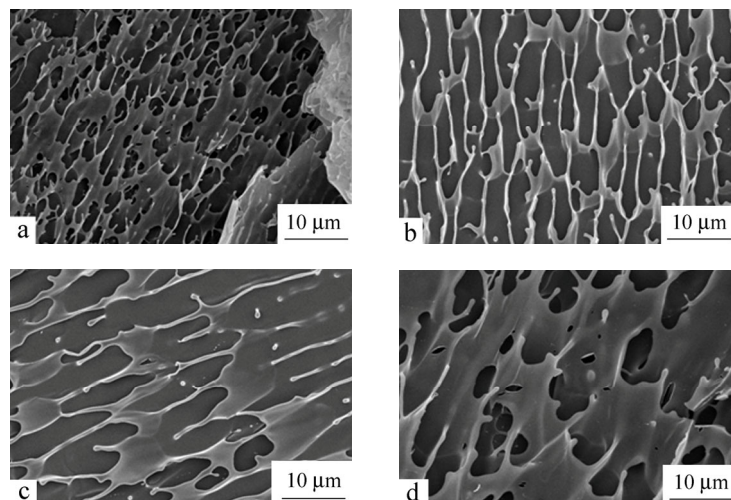


Fig. 5 Scanning electron microscopy (SEM) images of the cryo-dried supramolecular hydrogels: (a) PVN-R21, (b) PVN-R22, (c) PVN-R23 and (d) PVN-R24

Tuning Sol-gel Transition Behavior of PVN-R via Competing Guests

The above experiments show that presence of CB[8]/MV²⁺/Np ternary complex was a key condition for sol-gel transition. Therefore, the thermo-gelling behavior of PVN-R could be controlled *via* adding competing guests through the complex-dissociation process of CB[8]/MV²⁺/Np ternary complex. At room temperature, adding 1-adamantanamine hydrochloride (Ad·HCl, 50 mol% to CB[8]), white solids precipitated from PVN-R aqueous solution. The red liquid solution became pink-turbid (Fig. 6b), indicating a partial dissociation of charge-transfer complex CB[8]/MV²⁺/Np. Increasing content of Ad·HCl to equal amount to CB[8], the red color disappeared and the complex CB[8]/MV²⁺/Np was totally dissociated (Fig. 6c). The transformation into hydrogels did not occur when heating above the gelation temperature of PVN-R21. Besides, very similar results were observed when changing the competing guest (1,6-hexanediamine dihydrochloride).

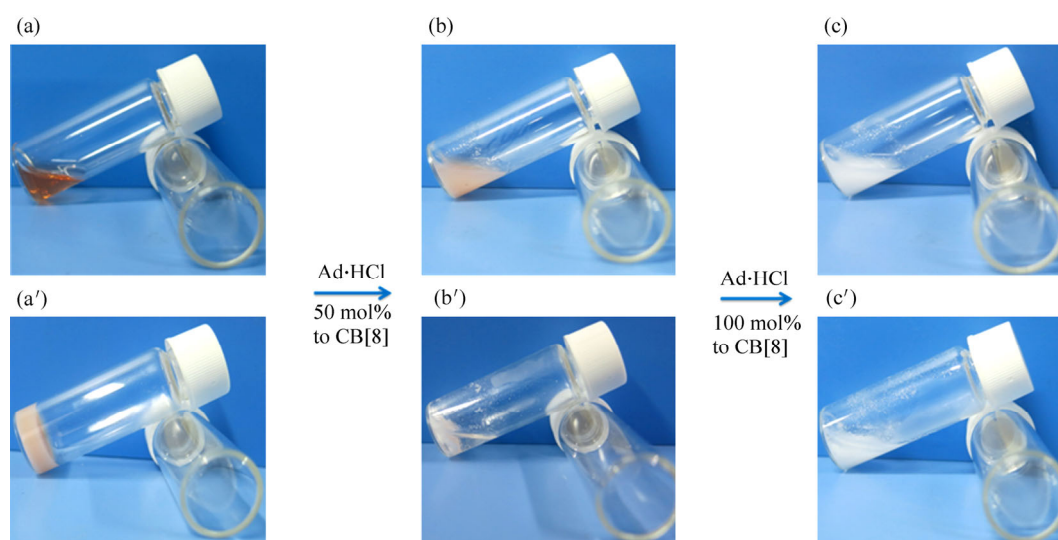


Fig. 6 Tuning gelation behavior of PVN-R *via* competing guests: (a) PVN-R21, (b) adding competing guest 1-adamantanamine hydrochloride (Ad·HCl), 50 mol% to CB[8], (c) increasing the content of Ad·HCl to 100 mol% to CB[8] at room temperature, (a'), (b') and (c'): heating at 45 °C for 2 min

CONCLUSIONS

This work demonstrates that supramolecular materials as thermo-gelling hydrogel can be constructed from rigid and bulky structure of hydrophilic ternary complex formed *via* CB[8]-enhanced CT interaction, and the gelation property can be also modified. The present study is focused on the tunable gelation behavior and rheological characterization of the materials. By changing the copolymerization ratio of PVBN-*co*-NIPAM from 3% to 6% and varying content of CB[8] and MV²⁺, one can alter the ratio of electropositive side-chain host-guest complex and modify hydrophilicity and microstructure of copolymer macromolecular chain. Gelation temperature can be regulated from 26.4 °C to 34.6 °C. These PVN-R copolymers maintain excellent mechanical property at relatively low polymer content and exhibit stimuli-responsive gelation behavior. The high mechanical property, low critical gelation concentration and tunable gelation behavior provide a possibility to further enlarge potentially application range of these thermo-gelling hydrogels, such as smart coating agent and injectable system for drug release.

REFERENCES

- 1 Fujishige, S., Kubota, K. and Ando, I., J. Phys. Chem., 1989, 93(8): 3311
- 2 Kubota, K., Fujishige, S. and Ando, I., Polym. J., 1990, 22(1): 15

- 3 Roy, D., Brooks, W.L.A. and Sumerlin, B.S., *Chem. Soc. Rev.*, 2013, 42(17): 7214
- 4 Temtem, M., Casimiro, T., Mano, J.F. and Aguiar-Ricardo, A., *Green. Chem.*, 2007, 9(1): 75
- 5 Overstreet, D.J., Dhruv, H.D. and Vernon, B.L., *Biomacromolecules*, 2010, 11(5): 1154
- 6 Gan, T.T., Zhang, Y.J. and Guan, Y., *Biomacromolecules*, 2009, 10(6): 1410
- 7 Alexander, A., Ajazuddin, Khan, J., Saraf, S. and Saraf, S., *Eur. J. Pharm. Biopharm.*, 2014, 88: 575
- 8 Stile, R.A., Burghard, W.R. and Healy, K.E., *Macromolecules*, 1999, 32(22): 7370
- 9 Li, L., Yan, B., Yang, J.Q., Chen, L.Y. and Zeng, H.B., *Adv. Mater.*, 2015, 27(7): 1294
- 10 Cao, Z., Chen, T.Y., Guo, X.L., Zhou, X.J., Nie, J.J., Xu, J.T., Fan, Z.Q. and Du, B.Y., *Chinese J. Polym. Sci.*, 2011, 29(4): 439
- 11 Li, Z.Q., Wang, F., Roy, S., Sen, C.K. and Guan, J.J., *Biomacromolecules*, 2009, 10(12): 3306
- 12 Ayano, E. and Kanazawa, H., *Anal. Sci.*, 2014, 30(1): 167
- 13 Yang, Y. and Li, J.B., *Adv. Colloid Interface Sci.*, 2014, 207: 155
- 14 Alexander, C., *Expert Opin. Drug Deliv.*, 2006, 3(5): 573
- 15 Bulmus, V., Dind, Z.L., Long, C.J., Stayton, P.S. and Hoffman, A.S., *Bioconjugate Chem.*, 2000, 79(1): 78
- 16 Iwai, K., Hanasaki, K. and Yamamoto, M., *J. Lumin.*, 2000, 87: 1289
- 17 Ma, Z.W., Nelson, D.M., Hong, Y. and Wagner, W.R., *Biomacromolecules*, 2010, 11(7): 1873
- 18 Hacker, M.C., Klouda, L., Ma, B.B., Kretlow, J.D. and Mikos, A.G., *Biomacromolecules*, 2008, 9(6): 1558
- 19 Liu, H.J., Xu, Y.Y. and Chen, Y., *Chinese J. Polym. Sci.*, 2016, 34(5): 585
- 20 Kang, M. and Gupta, V.K., *J. Phys. Chem. B*, 2002, 106(16): 4127
- 21 Ma, Q., Yang, H., Kim, K. and Tan, Y.B., *Chinese J. Polym. Sci.*, 2012, 30(4): 578
- 22 Chen, Y. and Liu, Y., *Adv. Mater.*, 2015, 27(36): 5403
- 23 Wojtecki, R.J. and Nelson, A., *J. Polym. Sci., Part A: Polym. Chem.*, 2016, 54: 457
- 24 Chen, H., Ma, H.L., Chieng, Y.Y., Hou, S.Z., Li, X. and Tan, Y.B., *RSC Adv.*, 2015, 5(27): 20684
- 25 Kim, H.J., Heo, J., Jeon, W.S., Lee, E., Kim, J., Sakamoto, S., Yamaguchi, K. and Kim, K., *Angew. Chem.*, 2001, 113: 1574
- 26 Jeon, Y.J., Bharadwaj, P.K., Choi, S., Lee, J.W. and Kim, K., *Angew. Chem. Int. Ed.*, 2002, 41: 4474
- 27 Jeon, W.S., Kim, E., Ko, Y.H., Hwang, I., Lee, J.W., Kim, S.Y., Kim, H.J. and Kim, K., *Angew. Chem. Int. Ed.*, 2005, 44: 87
- 28 Ko, Y.H., Kim, K., Kang, J.K., Chun, H., Lee, J.W., Sakamoto, S., Yamaguchi, K., Fettingner, J.C. and Kim, K., *J. Am. Chem. Soc.*, 2004, 126(7): 1932
- 29 Kim, K., Kim, D., Lee, J.W., Ko, Y.H. and Kim, K., *Chem. Commun.*, 2004, 848
- 30 Jeon, W.S., Ziganshina, A.Y., Lee, J.W., Ko, Y.H., Kang, J.K., Lee, C. and Kim, K., *Angew. Chem. Int. Ed.*, 2003, 115(34): 4231
- 31 Ko, Y.H., Kim, E., Hwang, I. and Kim, K., *Chem. Commun.*, 2007, 1305
- 32 Day, A., Arnold, A.P., Blanch, R.J. and Snushall, B., *J. Org. Chem.*, 2001, 66(24): 8094
- 33 Appel, E.A., Biedermann, F., Rauwald, U., Jones, S.T., Zayed, J.M. and Scherman, O.A., *J. Am. Chem. Soc.*, 2010, 132(40): 14251
- 34 Appel, E.A., Loh, X.J., Jones, S.T., Biedermann, F., Dreiss, C.A. and Scherman, O.A., *J. Am. Chem. Soc.*, 2012, 134(28): 11767
- 35 Yang, L.L., Yang, H., Li, F. and Zhang, X., *Langmuir*, 2013, 29(40): 12375
- 36 Kin, H.J., Heo, J., Jeon, W.S., Lee, E., Kim, J., Sakamoto, S., Yamaguchi, K. and Kim, K., *Angew. Chem. Int. Ed.*, 2001, 40(8): 1526
- 37 Rauwald, U. and Scherman, O.A., *Angew. Chem. Int. Ed.*, 2008, 47(21): 3950