RSC Advances

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

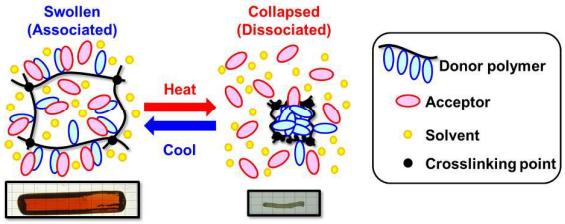
Graphical Abstract for Table of Contents (TOC)

Gel Thermoresponsiveness driven by Switch of Charge-Transfer Interaction

Desi H. Gharib,[a] Shogo Amemori,[a] Masami Naya,[a] Kenta Kokado,[a,b] and Kazuki Sada[a,b]

[a] *Department of Chemical Sciences and Engineering, Graduate School of Chemical Sciences and Engineering, Hokkaido University*

[b] *Department of Chemistry, Faculty of Science, Hokkaido University, Kita 10, Nishi 8, Kita-ku, Sapporo, 060-0810 Japan*



A novel gel LCST system was constructed by utilizing CT interaction between the gel and external effector, thus shrinking upon heating with hypochromic colour change.

Journal Name

COMMUNICATION

Gel Thermoresponsiveness driven by Switch of Charge-Transfer Interaction

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Desi H. Gharib,[a] Shogo Amemori,[a] Masami Naya,[a] Kenta Kokado*[,a,b] and Kazuki Sada*[,a,b]

A novel gel LCST system consisting of a pyrene containing acrylate network polymer and external effectors is demonstrated. The LCST behaviour was conducted by switch of CT interaction between the gel and effector, which was readily tuned by effector concentration or molecular structure of effector.

Introduction

Stimuli-responsive polymer gels, driven by environmental change such as light, pH, temperature, and solvent composition, have attracted considerable interest in the field of smart functional materials with large volumetric change.[1] Among various stimuli, heat controllable polymer gels possess a potential advantage derived from its facile operability without variation of chemical components.[2] Thus, many researches have focused on the application of thermoresponsive polymer gels for smart materials such as drug delivery,[3] gene therapy,[4] thermosensitive chromatography,[5] surface modifiers,[6] and cell cultivation sheets.[7] The basic structural feature of these thermoresponsive polymer gel lays on chemical crosslinking of linear polymer chain having thermoresponsiveness. For a typical example water, a solution of poly(N-isopropyl acrylamide (PNIPAM) exhibits lower critical solution temperature (LCST) type phase transition around at 32 °C, which shows sharp phase separation from solution to precipitation above the critical solution temperature.[8] Despite the convenience of thermoresponsive polymer gels at ambient temperature, the systematic molecular design of them are still unclear, especially in the media other than water.[9]

In this circumstance, we have recently reported LCST behaviour driven by charge-transfer (CT) interaction between electron-rich and poor aromatic compounds.[10] Therein, poly(1-pyrenemethyl acrylate) (**PPMA**) bearing pyrene side groups as a π electron donor showed LCST behaviour in toluene when a π electron acceptor (so-called effector) was added. The effector interacts with the pyrenyl group in the polymer chain via formation of CT complex to increase solubility, and heating induces formation of aggregates through decomposition of the CT complex. This result prompted us to design a novel gel LCST system driven by CT interaction. Herein, we demonstrate a synthesis of chemically crosslinked polymer gel consisting of **PPMA**, and its LCST behaviour using π accepting effectors.

[a] *Department of Chemical Sciences and Engineering, Graduate School of Chemical Sciences and Engineering, Hokkai-do University, Kita 13, Nishi 8, Kita-ku, Sapporo 060-8628, Japan.*
[b.] *Department of Chemistry, Faculty of Science, Hokkaido University, Kita 10, Nishi 8, Kita-ku, Sapporo, 060-0810 Japan.*
[c.] *Address here.*

† Electronic Supplementary Information (ESI) available: Experimental detail, swelling degree in organic solvents, UV-Vis absorption spectra of the CT complex and Benesi-Hildebrand plot. See DOI: 10.1039/x0xx00000x

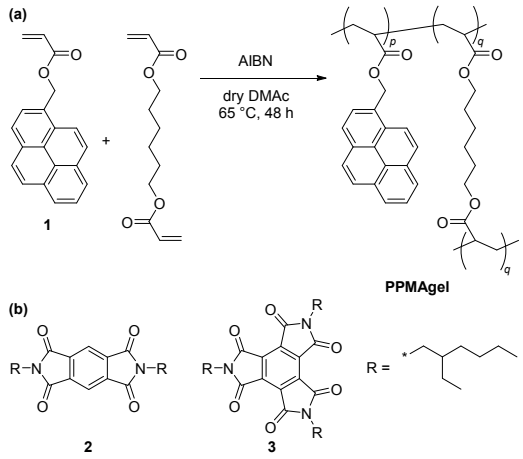


Fig. 1 (a) Synthetic method for **PPMAgel**. (b) Chemical structures of effectors **2** and **3**.

Results and discussion

A gel having CT interactive moiety was synthesized via ordinary free radical polymerization of 1-pyrenemethyl methacrylate (**1**)[10a] initiated by 2,2'-azobisisobutyronitrile (AIBN) in a sealed capillary tube under 65 °C for 48 hours (see also ESI). The obtained capillary gel (**PPMAgel**) was thoroughly washed and dried under vacuo. On Fourier transform infrared (FTIR) spectroscopy, disappearance of the peak assigned to stretching vibration of vinyl C=C ($\nu_{C=C}$, 1615 cm^{-1}) and deformation vibration of alkenyl C-H (δ_{C-H}, 1406 cm^{-1}) was confirmed after the gel formation, and hypsochromic shift of stretching vibration of ester C=O ($\nu_{C=O}$, 1716 $cm^{-1}\rightarrow$ 1724 cm^{-1}) was also observed, indicative of completion of the polymerization (Fig. S1). The dried gel with a length of ca. 3.5 mm were soaked and swollen in a wide range of organic solvents, such as hexane, toluene, chloroform, tetrahydrofuran (THF), acetone, N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and methanol, so as to evaluate an equilibrium swelling degree ($Q_1 = L_{wet}/L_{dry}$, L; length of the longer side, Fig. S2), implying compatibility of the solvent to the gel. In chloroform (Q_1 =1.6) or THF (Q_1 = 1.5), **PPMAgel** was moderately swollen, whereas it collapsed in toluene, hexane, methanol, and DMSO, due to the poor compatibility of the polymer chain to these organic solvents.

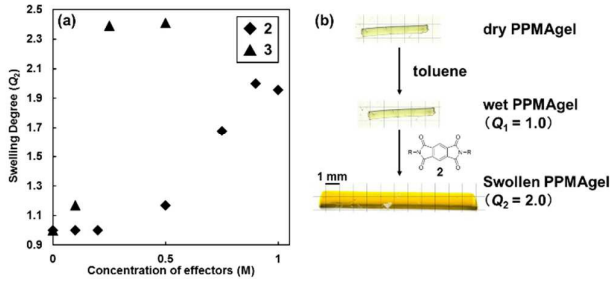


Fig. 2 (a) Q_2 of **PPMAgel** versus effector concentration in toluene, and (b) photographs representing the change of **PPMAgel** with effector **2** in toluene.

To elucidate the influence of effectors, we firstly chose toluene, which has poor compatibility (Q_1 = 1.0) to the polymer chain. In other words, **PPMAgel** was expected to swell in a poor solvent only by the aid of effectors. Additionally, toluene exhibits high boiling point (T_b = 111 °C) and good solubility of acceptors. **PPMAgel** was firstly soaked in toluene for 6 hours, and then transferred into different concentrations of effector **2** and **3** at 25 °C. After the addition of the effectors, Q_2 ($Q_2 = L_{wet2}/L_{wet1}$, a swelling degree in the presence (L_{wet2}) or absence (L_{wet1}) of effectors **2** and **3**) of **PPMAgel** gradually increased. For all gel samples, Q_2 increased with increment of effector concentration as shown in Fig. 2a, and swelling-saturation concentration of effector **2** (0.90 M) differed from that of **3** (0.25 M). Furthermore, the colour of **PPMAgel** was immediately changed after addition into the effector solution from light yellow to orange (**2**, Fig. 2b) or red (**3**), meaning a formation of CT complex. This observation simply shows that the improvement of swelling behaviour of **PPMAgel** after addition of effectors predominantly derived from disruption of strong π-π stacking between the polymer chains by CT complexation in **PPMAgel** and subsequent swelling. The saturation of swelling degree of **PPMAgel** in effector solution of toluene took ca. 4 days, probably due to slow diffusion of the effectors into the gel network, since the gel initially collapsed because of poor compatibility to toluene. At low concentration, Q_2 with **3** (0.25 M) was 2.4, while Q_2 with **2** (0.20 M) was 1.0 (Fig. 2a). This difference in CT complexation between **PPMAgel** and effectors can be explained from the association constant (K_a). Our previous study already showed CT complexation between **PPMA** and effectors derived from pyromellitic acid and mellitic acid, similar to **2** and **3**, with K_a of 0.74 M^{-1} and 4.68 M^{-1}, respectively.[10a] Therefore, the use of effector **2** with a lower association constant required a larger acceptor concentration for swelling of **PPMAgel** than that of **3** with a higher association constant.

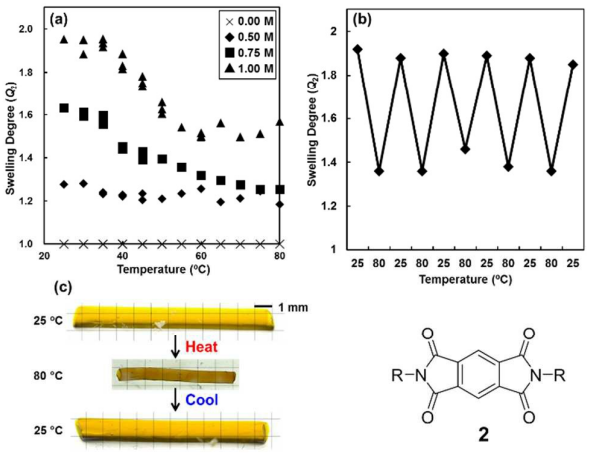


Fig. 3 (a) Q_2 of **PPMAgel** against temperature, with various effector **2** concentration in toluene, and (b) switching of Q_2 of **PPMAgel** between 25°C and 80°C and (c) photographs of **PPMAgel** along heating and cooling cycle under the existence of effector **2** (0.75 M) in toluene.

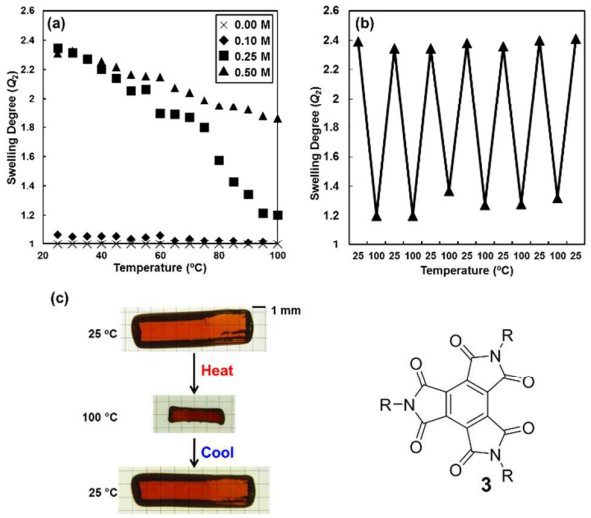


Fig. 4 (a) Q_2 of **PPMAgel** against temperature, with various effector **3** concentration in toluene, and (b) switching of Q_2 of **PPMAgel** between 25°C and 80°C, and (c) photographs of **PPMAgel** along heating and cooling cycle under the existence of effector **3** (0.25 M) in toluene.

When swollen **PPMAgel** in an effector solution was heated, the gel showed shrinkage at high temperature and hypochromic colour change, i.e., volume phase transition with dissociation of CT complex. To shed light on the thermal transition behaviour of **PPMAgel** in the presence of effectors, **PPMAgel** were steadily heated to 80 °C at 5 °C intervals. As shown in Fig. 3a and 4a, the swelling degree of the gel upon temperature elevation. In the case of effector **2**, the decrease of swelling degree occurred with above 0.75 M, while it was caused with above 0.25 M for effector **3**. The difference in K_a between **2** and **3** is probably responsible for this result. Higher concentration of the effectors resulted in high swelling degree, although **PPMAgel** with high effector concentration cannot shrink even at high temperature, due to too much amount of effectors surrounding the gel. Having successfully shown LCST behaviour of **PPMAgel**, we subsequently investigated recyclability of the gel LCST system. As a result, **PPMAgel** and **2** (0.75 M) exhibited reversible volume transition at 25 °C (Q_2 = 1.3-1.5) and 80 °C (Q_2 = 1.8-2.0), and the gel and **3** (0.25 M) also showed it at 25 °C (Q_2 = 1.2-1.4) and 100 °C (Q_2 = 2.3-2.5), respectively (Fig. 3b and 4b). These results illustrate that the gel LCST system can be reproduced on repeating cycles of heating and cooling, thus suitable for a long time usage.

To show evidence of cleaving of CT complexation with increase in temperature, UV-Vis spectra of monomer **1** with acceptor **2** was measured with increased temperature (Fig. S3). When CT takes place between the donor to acceptor, then it leads to rise on absorption spectrum attributed to CT band with λ_{max} at around 430 nm. Mixing **1** and **2** in toluene ([**1**] = 2 mM and [**3**] = 100 mM) brought about formation of a distinct yellow solution. Increasing temperature of the solution gradually from 25 °C to 100 °C decreases the absorbance at 428 nm, presumably due to the decrease of concentration to form the CT complex with increasing temperature, resulting in its individual component monomer **1** and effector **2**. To obtain deeper insight, we assessed the association constants (K_a) between **1** and **2**, and the thermodynamic parameters for the association (ΔH and ΔS) by Benesi–Hildebrand and van't Hoff plots, respectively (Fig. S4 and Table S1), which founds ΔH = 16.4 kJ·mol^{-1} and ΔS = 47.5 J·mol^{-1}·K^{-1}.

Conclusions

In summary, we have demonstrated novel gel LCST system consisting of pyrene containing acrylate gel and external effectors. The LCST behaviour was driven by CT interaction between the gel and effector, which was readily tuned by effector concentration as well as molecular structure of effector. To the best of our knowledge, this is the first example of LCST polymer gels using donor-acceptor interactions. This study show that, through proper selection and design of intermolecular interactions, gels exhibiting ambient LCST temperatures can be prepared. Therefore, other intermolecular interactions will be explored in the design of thermoresponsive polymer gels.

Acknowledgement

The project was supported by JSPS Grant-in-Aid for Scientific Research (B) (26288054) and JSPS Grant-in-Aid for Young Scientists (B) (23750117).

Notes and references

1 T. Tanaka, Phys. *Rev. Lett.*, 1978, **40**, 820-823; Y. Osada and J. P. Gong, *Prog. Polym. Sci.*, 1993, **18**, 187-226; S.-k. Ahn, R. M. Kasi, S.-C. Kim, N. Sharma and Y. Zhou, *Soft Matter*, 2008, **4**, 1151-1157; M. A. Cohen Stuart, W. T. S. Huck, J. Genzer, M. Muller, C Ober, M. Stamm, G. B. Sukhorukov, I Szleifer, V. V. Tsukruk, M. Urban, F. Winnik, S. Zauscher, I. Luzinov and S. Minko, *Nat. Mater.*, 2010, **9**, 101-113; R. Yoshida and T. Okano, *Biomedical Applications of Hydrogels Handbook*, Springer Science + Business Media LLC, New York, 2010; K. Iseda, K. Kokado, K. Sada, *React. Funct. Polym.*, 2013, **73**, 951-957.

2 R. Pelton, *Adv. Colloid Interface Sci.*, 2000, **85**, 1-33; L. A. Lyon, Z. Meng, N. Singh, C. D. Sorrell and A. St. John, *Chem. Soc. Rev.*, 2009, **38**, 865-874.; A. V. Kabanov and S. V. Vinogradov, *Angew. Chem. Int. Ed.*, 2009, **48**, 5418-5429.

3 A. S. Hoffman, *J. Controlled Release*, 1987, **6**, 297-305; J. H. Chang, C. H. Shim, B. J. Kim, Y. Shin, G. J. Exarhos and K. J. Kim, *Adv. Mater.* 2005, **17**, 634-637; J. A. Yoon, S. A. Bencherif, B. Aksak, E. K. Kim, T. Kowalewski, J. K. Oh and K. Matyjaszewski, *Chem. Asian J.*, 2011, **6**, 128-136; Y. Dai, P. Ma, Z. Cheng, X. Kang, X. Zhang, Z. Hou, C. Li, D. Yang, X. Zhai and J. Lin, *ACS Nano*, 2012, **6**, 3327-3338; R. T. Chacko, J. Ventura, J. Zhuang, S. Thayumanavan, *Adv. Drug Delivery Rev.* 2012, **64**, 836-851.

4 S. Vinogradov, E. Batrakova and A. Kabanov, *Colloids Surf. B*, 1999, **16**, 291-304; P. Lemieux, S. Vinogradov, C. Gebhart, N. Guerin, G. Paradis, H.-K. Nguyen, B. Ochietti, Y. Suzdaltseva,

E. Bartakova, T. Bronich, Y. St-Pierre, V. Alakhov and A. Kabanov, *J. Drug Targets*, 2000, **8**, 91-105; V. Vinogradov, A. D. Zeman, E. V. Batrakova and A. V. Kabanov, *J. Controled Release*. 2005. **107**, 143-157; F.-J. Xu, H. Li, J. Li, Z. Zhang, E.-T. Kang and K.-G. Neoh, *Biomaterials*, 2008, **19**, 3023-3033; J. Moselhy, T. Vira, F.-F. Liu and X. Y. Wu, *Int. J. Nanomed*, 2009, **4**, 153-164.

5 T. Yakushiji, K. Sakai, A. Kikuchi, T. Aoyagi, Y. Sakurai and T. Okano, *Anal. Chem.*, 1999, **71**, 1125-1130; A. Kikuchi and T. Okano, *Prog. Polym. Sci.*, 2002, **27**, 1165-1193; L. Qin, X.-W. He, M. Jia, W.-Y. Li and Y.-K. Zhang, *Chem. Eur. J.*, 2011, **17**, 1696-1704; F. Song, X.-L. Wang and Y.-Z. Wang, *Eur. Polym. J.*, 2011, **47**, 1885-1892; K. Nagase, J. Kobayashi, A. Kikuchi, Y. Akiyama, H. Kanazawa and T. Okano, *ACS Appl. Mater. Interfaces*, 2012, **4**, 1998-2008.

6 F. Zhang and C.-C. Wang, *Langmuir* 2009, **25**, 8255-8262; F. Tang, N. Ma, X. Wang, F. He and L. Li, *J. Mater. Chem.*, 2011, **21**, 16943-16948; Y. Stetsyshyn, J. Zemla, O. Zolobko, K. Fornal, A. Budkowski, A. Kostruba, V. Donchak, K. Harhay, K. Awsiuk, J. Rysz, A. Bernasik and S. Voronov, *J. Colloid Interface Sci.*, 2012, **387**, 95-105;

7 N. Yamada, T. Okano, H, Sakai, F. Karikusa, Y. Sawasaki and Y. Sakurai, *Makromol. Chem., Rapid Commun.*, 1990, **11**, 571-576; T. Okano, N. Yamada, H. Sakai and Y. Sakurai, *J. Biomed. Mater. Res.*, 1993, **27**, 1243-1251; C. Li, Y. Tang, S. P. Armes, C. J. Morris, S. F. Rose, A. W. Lloyd and A. L. Lewis, *Biomacromolecules*, 2005, **6**, 994-999; K. Haraguchi, T. Takehisa and M. Ebato, *Biomacromolecules*, 2006, **7**, 3267-3275; A. Kumar, A. Srivastava, I. Y. Galaev and B. Mattiasson, *Prog. Polym. Sci.*, 2007, **32**, 1205-1237.

8 H. G. Schild, Prog. Polym. Sci., 1992, **17**, 163-249; M. Heskins and J. E. Guillet, *J. Macromol. Sci. A Chem.*, 1968, **2**, 1441-1455; K. Otake, H. Inomata, M. Konno and S. Saito, *Macromolecules*, 1990, **23**, 283-289.

9 T. Ono, T. Sugimoto, S. Shinkai and K. Sada, *Nat. Mater.*, 2007, **6**, 429-433; T. Ono, S. Shinkai and K. Sada, *Soft Matter* 2008, **4**, 748-750; T. Ono, T. Sugimoto, S. Shinkai and K Sada, *Adv. Funct. Mater.*, 2008, **18**, 3936-3940; J. Krishnamurthi, T. Ono, S. Amemori, H. Komatsu, S. Shinkai and K. Sada, *Chem. Commun.*, 2011, **47**, 1571-1573; K. Iseda, M. Ohta, T. Ono and K Sada, *Soft Matter*, 2011, **7**, 5938-5940; K. Iseda, Y. Haketa, K. Kokado, H. Maeda, H. Furuta and K. Sada, Soft Matter, 2012, **8**, 7490-7494; T. Ono, M. Ohta, K. Iseda and K Sada, *Soft Matter*, 2012, **8**, 3700-3704.

10 (*a*) S. Amemori, K. Kokado and K. Sada, *Angew. Chem. Int. Ed.*, 2013, **52**, 4174-4178; (*b*) S. Amemori, K. Kokado and K. Sada, *J. Am. Chem. Soc.*, 2012, **134**, 8344-8347.