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COMMUNICATION

New Benzylidene Oxazolone Derived Polymeric Photoswitches for Light-Induced Tunable Thermo-responsive Behaviors

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A series of thermo-responsive polymeric photoswitches containing benzylidene oxazolone moieties were successfully prepared. 3-vinylbenzaldehyde (VBA) and dimethylacrylamide (DMA) were copolymerized by reversible addition-fragmentation chain transfer (RAFT) polymerization to obtain statistical copolymers, poly(3-vinylbenzaldehyde-co-dimethylacrylamide) (PVBA-co-PDMA). The resulting PVBA-co-PDMA copolymers were reacted with hippuric acid to yield the target copolymers, poly(3-vinylbenzylidene oxazolones-co-dimethylacrylamide) (PVBO-co-PDMA). Successful synthesis of the desired copolymers was confirmed by ¹H-NMR spectroscopy and gel permeation chromatography (GPC). UV-Vis absorption measurements were employed to study the efficiency of photoisomerization of the benzylidene oxazolone moieties upon irradiation with UV and Visible light (365 nm and 650 nm) for various time intervals. Temperature-dependent optical transmission studies (turbidimetry) were also carried out on the aqueous solutions to investigate how the lower critical solution temperature (LCST) values were influenced by photoirradiation. The profiles of optical transmittance suggested that the LCST of the E isomer was higher than that of the Z isomer. The control of LCST by photoirradiation was observed to be repeatable over multiple cycles, demonstrating that photoisomerization is reversible. The LCST values measured by dynamic light scattering (DLS) correlated well with those determined by turbidimetry.

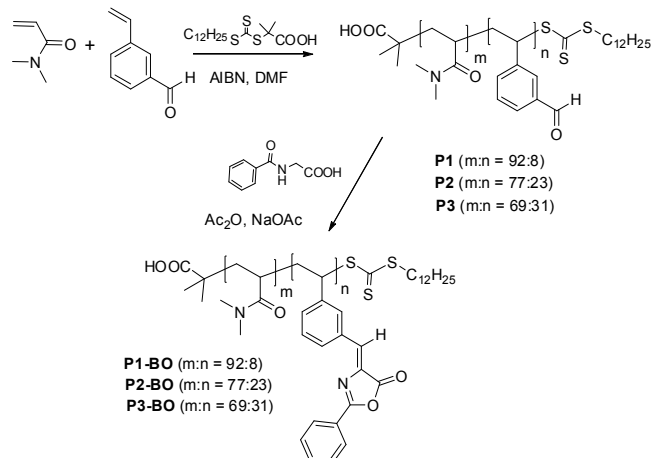
Stimuli-responsive polymers have attracted considerable interest over the past few decades in the fields of drug and gene delivery, imaging, sensors, and so on.¹⁻⁵ They undergo conformational or chemical changes in response to small variations in environmental conditions such as pH, light irradiation, temperature, ionic strength, etc.⁶⁻⁹ Thermo-responsive polymers with lower critical solution temperature (LCST) behavior undergo phase separation upon

heating above their LCST. These polymers are soluble in water through hydrogen bonding, but only below their LCST. When heated above the LCST, the polymers precipitate, leading to fast phase transitions. Light-responsive polymers possess photoresponsive groups such as azobenzene, spiropyran, and salicylideneaniline either in the main chain or in the side chain as a pendant group.¹⁰⁻¹⁶ For example, azobenzene units undergo cis-trans isomerization upon light irradiation, which results in large changes in the size and polarity of the units. Consequently, the cis isomer is more polar and less hydrophobic than the trans isomer.¹⁷

Recently, a great deal of effort has been made to prepare polymers with multiple-responsive components. For example, the LCST of thermo-responsive poly(N-isopropylacrylamide)s containing light responsive azobenzene groups in the side or end of the polymer chain was tuned by isomerization of the azobenzene moieties by photoirradiation.^{13, 17-21} For the cis-form of azobenzene, the higher dipole moment leads to an increase in the local polarity of the polymer chain, which causes a subsequent increase in the LCST. As a result, these copolymers can be precipitated or dissolved upon irradiation with UV light within a certain temperature range.

Several studies revealed that the biologically important green fluorescent protein (GFP) chromophore undergoes non-irradiative processes, such as E/Z isomerization, upon irradiation with light.²²⁻²⁶ Interestingly, familiar intermediates in the synthesis of GFP, such as oxazolone analogues, have been less explored in terms of their photoswitching ability.^{27, 28} More recently, Sampedro and co-workers synthesized a variety of benzylidene oxazolone analogues to investigate their photoswitching ability.²⁹ With their work as an inspiration, we turned to design dual responsive polymers in which thermo-responsive behaviors are further tuned by the E/Z isomerization of benzylidene oxazolone moieties by light irradiation.

For this purpose, we synthesized novel thermo- and photoresponsive random copolymers, poly(3-vinylbenzylidene oxazolones-*co*-dimethylacrylamide) (PVBO-*co*-PDMA), with different incorporation ratios of VBO units, and investigated the light controlled thermal phase transition behavior in detail. To the best of our knowledge, this is the first report employing benzylidene oxazolone chromophores as a switching element for the thermal transition of aqueous polymer solutions.



Scheme 1. Synthesis of polymeric photoswitches with pendant benzylidene oxazolones.

The strategy employed for the synthesis of polymeric photoswitches with pendant benzylidene oxazolones is schematically shown in scheme 1. A series of random copolymers containing benzylidene oxazolone moieties were prepared in two steps. In the first step, 3-vinylbenzaldehyde (VBA) and dimethylacrylamide (DMA) were copolymerized by reversible addition-fragmentation chain transfer (RAFT) polymerization, using 2-dodecylsulfanylthiocarbonylsulfanyl-2-methylpropionic acid (DMP) as the chain transfer agent (CTA) and 2,2'-azobisisobutyronitrile (AIBN) as the initiator, yielding statistical copolymers P1~P3. By controlling the initial feed ratio of VBA and DMA, a series of PVBA-*co*-PDMA copolymers with three different compositions were prepared (with inclusion of 8, 23, and 31 % VBA along the polymer chain). The successful formation of these polymers was confirmed by $^1\text{H-NMR}$ spectroscopy (Figure 1a & S1). For example, the disappearance of the vinyl protons and the presence of an aldehyde proton (a) confirmed the successful formation of P1. The ratio of VBA incorporation with respect to DMA was calculated by comparing the relative peak intensities corresponding to the aldehyde protons (a) and dimethyl protons (f) of DMA in the NMR spectrum of P1. The incorporation ratio of VBA to DMA was calculated to be 8:92. The final VBA incorporation ratio was higher than the initial feed ratio (5:95), which suggested that VBA is more reactive than DMA. It has been well reported that the reactivity of styrene type monomers is higher than that of dimethylacrylamide.³⁰ In the next step, the aldehyde groups of the copolymers were reacted with hippuric acid in the presence of sodium acetate, converting them into benzylidene oxazolones. The resulting polymeric photoswitches were denoted as P1-BO ~ P3-BO. The conversion of aldehyde groups into benzylidene oxazolones can be clearly seen in Figure 1b. The peak corresponding to aldehyde protons at 10.0 ppm (denoted as a in Figure 1a) disappeared completely after reaction, and new peaks (a'+d) representing vinyl and aromatic protons appeared at approximately 8.08 ~ 8.19 ppm (Figure 1b). The

molecular weights of the polymers were determined by gel permeation chromatography (GPC) (Figure S2). The number average molecular weight (M_n) of P1, P2 and P3 were obtained to be 24100, 16300, and 11800 with low polydispersity (M_w / M_n) of 1.07, 1.1 and 1.1, respectively.

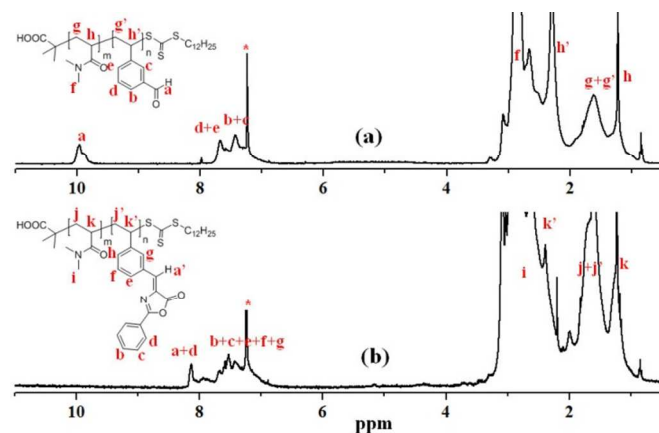


Figure 1. $^1\text{H-NMR}$ spectra of (a) P1 and (b) P1-BO.

UV-Vis absorption measurements of 0.6 mL aqueous solutions of P2-BO and P3-BO (1.0 wt. %) were obtained to study the photoisomerization behavior of benzylidene oxazolone moieties upon irradiation with UV and visible light (365 and 650 nm) with various time intervals. The Z isomer was the only product initially detected. Irradiation with UV light led to photoisomerization and subsequent conversion of the Z isomer to the E isomer. As expected, UV irradiation led to a decrease in the optical density of the 368 nm absorption bands (Figure 2a and S3). The decrease in optical density observed with increasing irradiation time suggested the gradual formation of E isomers. The optical density of the absorption band at 368 nm did not demonstrate further change after irradiation for 3h, indicating the photostationary state had been reached (Figure 2b). Similarly, irradiation with visible light (650 nm) isomerized the E form back to the Z form, as was confirmed by the spectra gradually reverting to the original absorption profile (Figure S4).

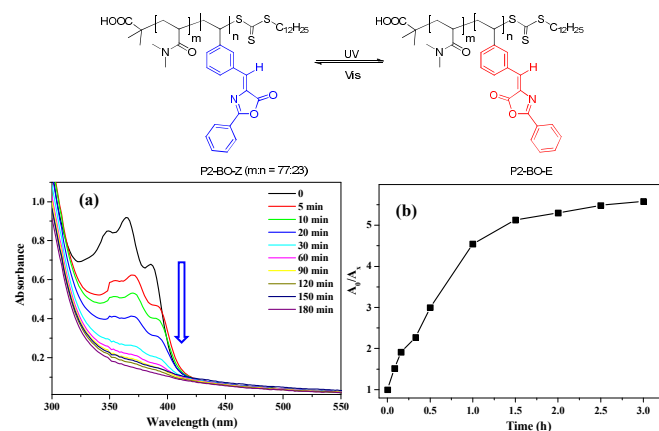


Figure 2. (a) UV-Vis absorption responses of P2-BO with UV irradiation (365 nm) at different time intervals. (b) The plot of A_0/A_x versus irradiation time (A_0 = initial absorbance, A_x = absorbance after x h UV irradiation).

Generally, the Z to E isomerization efficiency of benzylidene oxazolone moieties can be assessed by ^1H NMR spectroscopy.²⁹ Unfortunately, it was not possible to calculate the isomerization efficiency of the benzylidene oxazolone moieties in the polymers studied, since no noticeable change in the ^1H NMR spectrum was observed upon UV irradiation. For this reason, the structurally identical monomer VBO was chosen as a model compound to estimate the isomerization efficiency by ^1H NMR spectroscopy. The quantitative isomerization efficiency determined by ^1H NMR spectroscopy was correlated with the changes in the UV-Vis absorption spectra. This correlation was in turn employed to assess the isomerization efficiency from the UV-Vis absorption spectra of the polymers. The NMR and UV-Vis absorption spectral changes of VBO are shown in Figures S5 & S6. Since Z and E isomers have distinctive ^1H NMR signals, the isomer ratio could be calculated by integration of the peaks corresponding to each isomer. The efficiency for the conversion of Z to E isomer was calculated to be approximately 49 % after UV irradiation for 3h. Since the A_0/A_3 values (where A_0 is the initial absorbance and A_3 is the absorbance after 3h of UV irradiation) of VBO and P2-BO (also P3-BO) were approximately the same, 4.9 - 5.3, we assumed that the isomerization efficiency of benzylidene oxazolone moieties of VBO and P2-BO (also P3-BO) may also be similar, at 49 %.

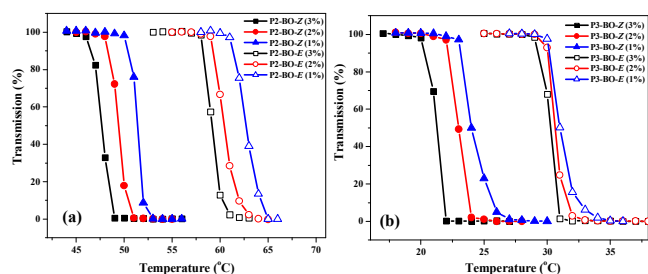


Figure 3. Plot of the % transmission vs temperature of (a) P2-BO and (b) P3-BO with different concentrations of solutions.

PDMA is a water-soluble polymer, and does not exhibit LCST transitions on its own. However, LCST behavior can be induced by copolymerizing DMA with hydrophobic monomers. In this manner, the PVBO-co-PDMA copolymers were expected to demonstrate such thermoresponsive behavior. Since P1-BO was too hydrophilic to show an LCST transition, this study was limited to P2-BO and P3-BO. The temperature dependent transmission measurement at 650 nm was analyzed for different concentrations of the aqueous solution of P2-BO and P3-BO before and after UV irradiation (Figure 3). The cloud point was defined as the middle point of the transmittance change. Before UV irradiation, the aqueous solution of P2-BO (1.0 wt %) exhibited LCST behavior with a cloud point of 52 °C. The cloud point of the aqueous solution of P3-BO (1.0 wt %) was 24 °C, since P3-BO contains more hydrophobic VBO units. As P2-BO and P3-BO both contain photoswitchable BO units, we further investigated the light-induced thermal transition behaviors of these polymers in aqueous solutions. The cloud points of the aqueous solutions of P2-BO and P3-BO, at the same concentration (1.0 wt %), were measured after irradiation with UV light for 3h. For both P2-BO and P3-BO solutions, the cloud points increased to 63 and 32 °C by a shift of 11 and 8 °C, respectively, compared to those without UV irradiation. This indicated that UV irradiation led to change in the molecular geometry (Z to E isomerization of BO units), which was accompanied by a significant increase in hydrophilicity. In order to analyze the thermal stability of the E isomer, the aqueous solutions of P2-BO and P3-BO were heated at 65 °C for several

hours to see if the E isomer would be thermally isomerized back to the Z isomer. It was found that the absorption spectra of the E isomer of both P2-BO and P3-BO solutions were unchanged after heating (Figure S7 and S8). This implies that these photoswitches are thermally stable at 65 °C, and can be operated without interference from thermal processes. The effect of the polymer concentration in water on the thermal transition behavior was also investigated. It was found that the cloud points decreased with increasing concentrations of the aqueous solutions, irrespective of the photoisomeric state of BO, which is a typical characteristic of LCST phase transition (Figure 3).

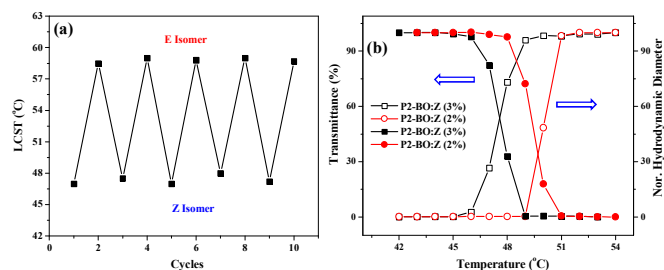


Figure 4. (a) The reversibility plot of LCST of P2-BO solution (3.0 wt %) versus the number of cycles of alternating irradiation with UV and Visible light. (b) Comparison plot of optical transmission and DLS data of P2-BO at concentrations of 2.0 and 3.0 wt %.

To investigate the reversibility of the photo-induced thermoresponsive behavior, the cloud points of the aqueous solutions of P2-BO and P3-BO were measured after alternating irradiation with UV (365 nm) and Visible light (650 nm) (Figure 4a and Figure S9). The control of the thermal transition by light irradiation was observed to be reversible for at least five cycles for both P2-BO and P3-BO samples. To provide additional evidence of the photo-tunable thermal transition behavior, temperature-dependent dynamic light scattering (DLS) analysis was conducted. It is expected that the hydrodynamic diameter of all polymer samples increases with increasing temperature. As shown in Figure 4b, the cloud points measured by DLS for the aqueous solutions of P2-BO (2.0 and 3.0 wt %) with two different isomerization states matched well with those obtained by turbidimetry.

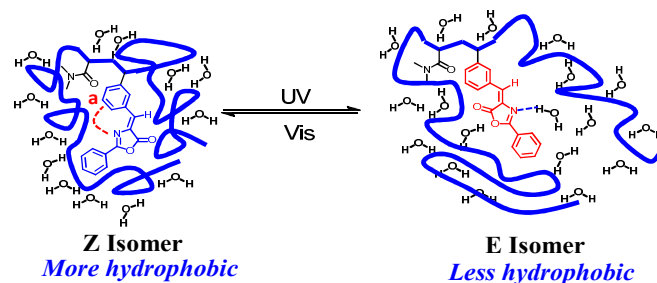


Figure 5. Possible mechanism for photo-induced LCST properties.

A possible reason for the significant increase in LCST of the solutions of polymers after irradiation with UV light is schematically shown in Figure 5. The non-bonding electron of the nitrogen atoms on the Z isomers may interact with the π electrons of the adjacent aromatic ring (denoted as 'a'). In contrast, the nitrogen atoms of the E isomers are located slightly away from the aromatic ring. As a consequence, the nitrogen atoms of the E isomers are readily

exposed to the external aqueous environment, and serve as possible sites for hydrogen bonding with water molecules, rendering the system less hydrophobic.³¹ The polarity change of the benzylidene oxazolone moiety could be another reason for increase in cloud point of the polymer solutions after irradiation with UV light.³²

Conclusions

Novel benzylidene oxazolone-derived polymeric photoswitches with phototunable thermal transition behaviors were successfully synthesized via RAFT polymerization, followed by post modification with hippuric acid. It was demonstrated that the LCST of the polymeric photoswitches could be tuned by isomerization of the benzylidene oxazolone moieties, accomplished with photoirradiation. The LCSTs of the polymer solutions containing E isomers are higher than those with only the Z isomers. The fine control of the thermal transition by light irradiation was repeated several times, indicating the reversible nature of the photoisomerization. These benzylidene oxazolone-containing polymers, with phototunable thermoresponsiveness, are anticipated to have broad applications in switching devices and sensors.

Notes and references

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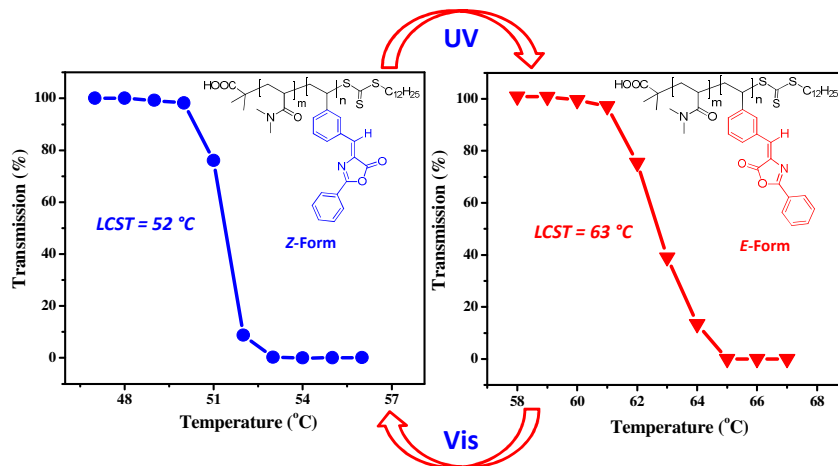
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Electronic Supplementary Information (ESI) available: [Experimental procedures, NMR, GPC curves, UV-Vis absorption spectra, transmission plot and DLS measurement for P3-BO and VBA]. See DOI: 10.1039/c000000x/

- F. D. Jochum and P. Theato, *Chem Soc Rev*, 2013, **42**, 7468 - 7483.
- F. Liu and M. W. Urban, *Prog. Polym. Sci.*, 2009, **35**, 3-23.
- D. Roy, J. N. Cambre and B. S. Sumerlin, *Prog. Polym. Sci.*, 2010, **35**, 278-301.
- P. S. Stayton, T. Shimoboji, C. Long, A. Chilkoti, G. Chen, J. M. Harris and A. S. Hoffman, *Nature*, 1995, **378**, 472 - 477.
- M. A. C. Stuart, W. T. S. Huck, J. Genzer, M. Mueller, 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.
- S. Dai, P. Ravi and K. C. Tam, *Soft Matter*, 2008, **4**, 435-449.
- E. S. Gil and S. M. Hudson, *Prog. Polym. Sci.*, 2004, **29**, 1173-1222.
- J. P. Magnusson, A. Khan, G. Pasparakis, A. O. Saeed, W. Wang and C. Alexander, *J. Am. Chem. Soc.*, 2008, **130**, 10852-10853.
- N. Murthy, J. Campbell, N. Fausto, A. S. Hoffman and P. S. Stayton, *Bioconjugate Chem.*, 2003, **14**, 412-419.
- C. Li, Y. Zhang, J. Hu, J. Cheng and S. Liu, *Angew. Chem. Int. Ed.*, 2010, **49**, 5120-5124.
- J. Xu, S. Luo, W. Shi and S. Liu, *Langmuir*, 2005, **22**, 989-997.
- O. Boissiere, D. Han, L. Tremblay and Y. Zhao, *Soft Matter*, 2011, **7**, 9410 - 9415.
- F. D. Jochum, L. zur Borg, P. J. Roth and P. Theato, *Macromolecules*, 2009, **42**, 7854-7862.
- D. Wang and X. Wang, *Prog. Polym. Sci.*, 2013, **38**, 271-301.
- P. Xue, R. Lu, G. Chen, Y. Zhang, H. Nomoto, M. Takafuji and H. Ihara, *Chem. Eur. J.*, 2007, **13**, 8231-8239.
- Y. Zhao, L. Tremblay and Y. Zhao, *J. Polym. Sci. Polym. Chem.*, 2010, **48**, 4055-4066.
- H.-i. Lee, J. Pietrasik and K. Matyjaszewski, *Macromolecules*, 2006, **39**, 3914-3920.
- H. Akiyama and N. Tamaoki, *Macromolecules*, 2007, **40**, 5129-5132.
- H. Dai, X. Li, Y. Long, J. Wu, S. Liang, X. Zhang, N. Zhao and J. Xu, *Soft Matter*, 2009, **5**, 1987-1989.
- H.-i. Lee, W. Wu, J. K. Oh, L. Mueller, G. Sherwood, L. Peteanu, T. Kowalewski and K. Matyjaszewski, *Angew. Chem. Int. Ed.*, 2007, **46**, 2453-2457.
- Y. Li, Y. Deng, X. Tong and X. Wang, *Macromolecules*, 2006, **39**, 1108-1115.
- R. Heim, D. C. Prasher and R. Y. Tsien, *Proc. Natl. Acad. Sci.*, 1994, **91**, 12501-12504.
- P. Naumov, J. Kowalik, K. M. Solntsev, A. Baldrige, J.-S. Moon, C. Kranz and L. M. Tolbert, *J. Am. Chem. Soc.*, 2010, **132**, 5845-5857.
- S. Rafiq, B. K. Rajbongshi, N. N. Nair, P. Sen and G. Ramanathan, *J. Phys. Chem. A*, 2011, **115**, 13733-13742.
- V. Voliani, R. Bizzarri, R. Nifosi, S. Abbruzzetti, E. Grandi, C. Viappiani and F. Beltram, *J. Phys. Chem. B*, 2008, **112**, 10714-10722.
- J.-S. Yang, G.-J. Huang, Y.-H. Liu and S.-M. Peng, *Chem. Commun.*, 2008, 1344-1346.
- N. Baumann, M.-T. Sung and E. F. Ullman, *J. Am. Chem. Soc.*, 1968, **90**, 4157-4158.
- E. F. Ullman and N. Baumann, *J. Am. Chem. Soc.*, 1970, **92**, 5892-5899.
- M. Blanco-Lomas, P. J. Campos and D. Sampedro, *Org. Lett.*, 2012, **14**, 4334-4337.
- T. Iwamura and M. Sakaguchi, *Macromolecules*, 2008, **41**, 8995-8999.
- Y. Zheng, G. Li, H. Deng, Y. Su, J. Liu and X. Zhu, *Polym. Chem.*, 2014, 2521-2529.
- C. A. B. Rodrigues, I. F. A. Mariz, E. M. S. Macoas, C. A. M. Afonso and J. M. G. Martinho, *Dyes Pigments*, 2012, **95**, 713-722.

TOC Graphic:



TOC Synopsis:

Thermoresponsive polymeric photoswitches containing benzylidene oxazolone moieties were successfully synthesized and characterized. The LCST of the polymeric photoswitches could be tuned by isomerization of the benzylidene oxazolone moieties, accomplished with photoirradiation.