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Bioinspired Photo-Cross-Linked Nanofibers from Uracil-Functionalized Polymers

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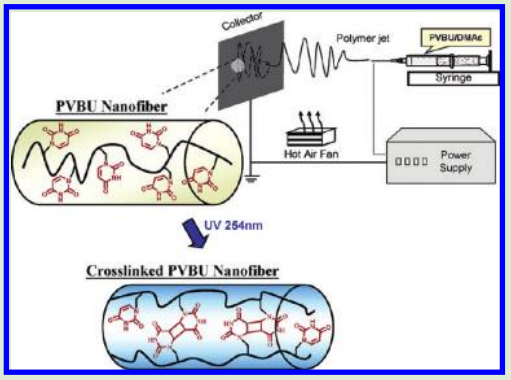
Supporting Information

ABSTRACT: In this study, we used electrospinning to fabricate nucleobase-functionalized and photo-cross-linkable poly[1-(4-vinylbenzyl uracil)] (PVBU) nanofibers. PVBU of high-molecular-weight (M_n > 250 550 g/mol) possessed a high thermal stability and sufficient chain entanglement to produce uniform fibers without forming beads. These uracil-functionalized nanofibers were further photo-cross-linked through exposure to UV light at a wavelength of 254 nm. After immersing in *N*,*N*-dimethylacetamide, the pristine PVBU fibers dissolved, while the cross-linked PVBU fibers maintained their shape; thus, the cross-linked PVBU nanofibers exhibited good dimensional stability and improved solvent resistance.



Hydrogen-bonding interactions found in DNA and RNA are useful for organizing novel structure through selective complementary nucleobase recognition [e.g., thymine−adenine (T−A), cytosine−guanine (C−G), and uracil−adenine (U−A) complexes].[1−4] The specific self-recognition properties of cDNA or RNA strands have widespread applications in various aspects of biotechnology and nanotechnology.[5,6] Nucleobase-functionalized polymers exhibiting similar self-recognition capabilities can also form interesting structures for advanced applications.[7−11] Indeed, several reports have appeared of nucleobase functionalities introduced into main- and side-chain polymers to take advantage of their biocomplementary hydrogen bonding.[12−14] Recently, we also reported the biocomplementary interactions between a nucleobase-like side-chain homopolymer and alkylated nucleobases, stabilized by T−A and U−A base pairs.[15,16] Such approaches are being used to prepare well-defined polymers with a broad range of applications.[17,18] The synthesis and utility of synthetic polymers bearing complementary nucleobases is an interesting subject in polymer fields and will likely expand further in the future.

Electrospinning is a technique, employing a strong electrostatic field, for the production of polymer fibers having diameters ranging from the nanometer to the submicrometer regimes.[19−23] The properties of electrospun fiber mats possessing high specific surface areas and high porosities are unlike those of their original polymers, making them very useful in a wide range of advanced applications (e.g., filtration,[24] drug delivery,[25] tissue engineering scaffolds,[26] sensors[27]). Through appropriate architectural design, nucleobase-functionalized fibers can be tailored for specific applications. Long et al.[28] used molten electrospinning to prepare biocompatible and biodegradable fibers from star-shaped poly(D,L-lactide) (PDLLA) polymers end-functionalized with complementary A/T base pairs. These nucleobase-functionalized fibers are, however, difficult to prepare, due to the limitations of the molecular weight (MW) or applicable solvents, potentially causing the polymeric jet to fail to extend during the electrospinning process. Therefore, the ability to prepare nucleobase-functionalized polymers of appropriate MWs or providing sufficient entanglement is of critical importance.

Uracil, a specific base of RNA, is a supramolecular functionality that has the ability to associate with A moieties of both DNA and RNA through complementary hydrogen bonding; it can also self-associate through self-complementary interactions.[29,30] We recently reported that the hydrogen bonding strength of the U−A base pair of RNA is stronger than that of the T−A base pair of DNA.[18] In addition, U is a photoactive pyrimidine base that can undergo $2\pi + 2\pi$ photodimerization.[31−34] Polymers functionalized with U bases potentially possess a number of interesting properties: (1) recognition capability between U and A units; (2) two or three parallel hydrogen bonding sites extending from the U units; and (3) UV-induced photo-cross-linking without the need for a photoinitiator or curing agent. To the best of our knowledge, electrospun fibers based on U-functionalized polymers and their photo-cross-linking properties have not been reported previously. Herein, we report a new method for the synthesis of high-MW poly[1-(4-vinylbenzyl uracil)] (PVBU) and the subsequent prepared of nanofibers through electrospinning. We then used ultraviolet−visible (UV−vis) spectroscopy, Fourier transform Raman (FT-Raman) spectroscopy, and field-emission scanning electron microscopy (FE-SEM) to

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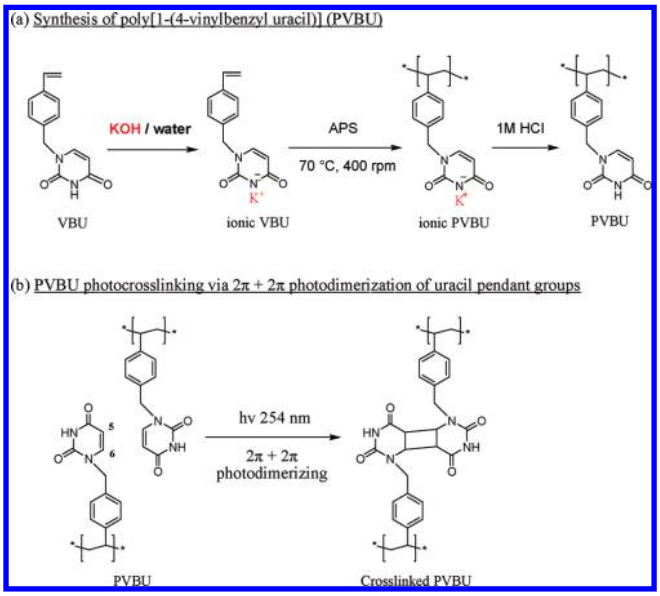
determine the physical characteristics and photoactive cross-linking capabilities of the PVBU fibers.

The VBU monomer, synthesized as described previously,[35,36] was subjected to free radical polymerization to produce high-MW PVBU. When Lutz et al.[37] attempted conventional radical polymerization of a homopolymer from VBU, the MW did not increase significantly, due to the high polarity and hydrogen bonding of the polymer. In previous studies performed in our laboratory, we have successfully synthesized nucleobase-functionalized polymers, with a high conversion and narrow polydispersity index (PDI), through atom transfer radical polymerization (ATRP).[15,16] The MWs of those nucleobase-functionalized polymers were, however, still too low for practical use; high MW is an important factor for determining the mechanical strength of a polymer. To overcome this problem, in this present study we have developed a strategy of synthesizing a styrenic monomer containing a U potassium salt and then converting it into a high-MW PVBU, resulting in a substantial increase in glass transition temperature (T_g) relative to that of low-MW PVBU (see Scheme 1a and Supporting Information). The increase in T_g was predictable because the rigid U groups inhibit the free rotation of the PVBU; that is, the rigid U groups possess a "connective effect" to assist the formation of intermolecular hydrogen bonds.

Scheme 1. Synthesis and Photo-Cross-Linking Reactions of PVBU



To investigate the effect of the PVBU concentration on the fiber morphology, we subjected different concentrations (5, 7.5, 10, and 20 wt %) of PVBU in *N*,*N*-dimethylacetamide (DMAc) to electrospinning under otherwise identical conditions. Figure 1 displays representative FE-SEM images of the resulting electrospun PVBU nanofibers. Table 1 lists the viscosities and fiber diameters obtained from the different concentrations of PVBU. The diameter of the fiber increased upon increasing the PVBU concentration. One of the most important parameters influencing the fiber diameter is the solution viscosity, which may have an effect on the morphology and continuous fiber forming ability. The SEM images reveal that bead-free and continuous fibers were spun from 10 and 20 wt % concentrations of PVBU. In other words, the increase in viscosity resulted in higher viscoelastic forces that prevented the break-up of the jet. When the solution viscosity was too low (7.5 or 5 wt %), we obtained beaded and irregularly shaped fibers, indicating that a low viscosity was insufficient to counter the high Coulombic force. Thus, the charged jet broke up into droplets and formed beaded structures.[38,39] Among the four tested concentrations of PVBU, the most uniformly distributed fibers with the narrowest diameter, without beaded structures, resulted from the used of 10 wt % PVBU; therefore, we used this concentration in our subsequent studies.

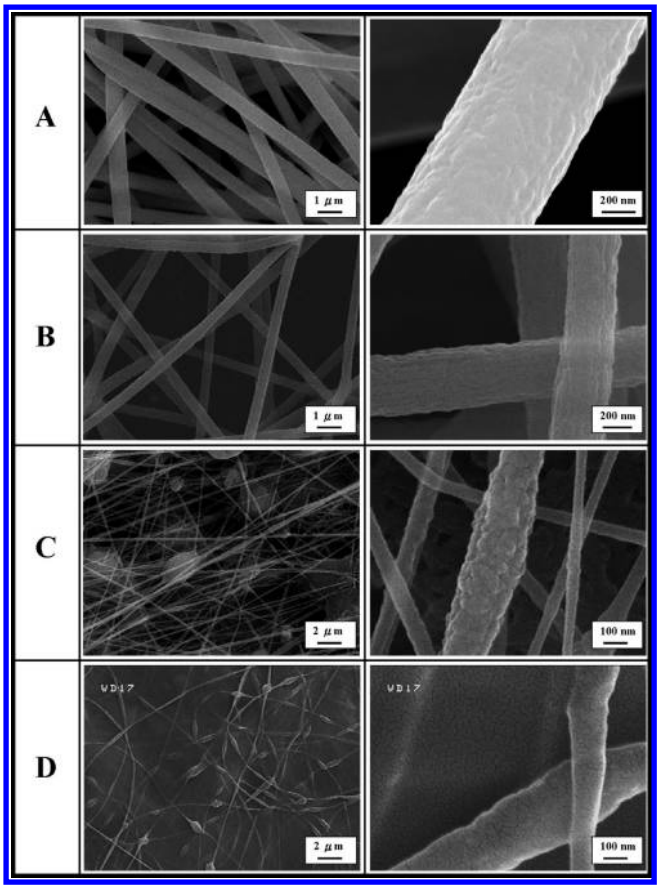


Figure 1. Representative FE-SEM images of as-electrospun fibers prepared from (A) 20, (B) 10, (C) 7.5, and (D) 5 wt % solutions of PVBU in DMAc.

Table 1. Representative Viscosities and Average Fiber Diameters of Electrospun PVBU Solutions

concentration of PVBU in DMAc (wt %)	viscosity (cp)[a] at 25 °C	avg fiber diameter (nm)
5.0	13.1	
7.5	51.6	90
10.0	202.5	420
20.0	539.2	800

[a]cp = centipoise (mPa·s).

Under UV radiation, pairs of U bases can undergo 2π + 2π photodimerizations to form cyclobutane rings.[31−34] We wished to use this cross-linking method to improve the dimensional stability of our PVBU fibers. Scheme 1b displays the structure of the photo-cross-linked PVBU fiber after exposure to UV light at a wavelength of 254 nm. We used UV−vis and Raman spectroscopy to investigate the structures formed after photo-cross-linking the U groups. Figure 2 presents the UV−vis

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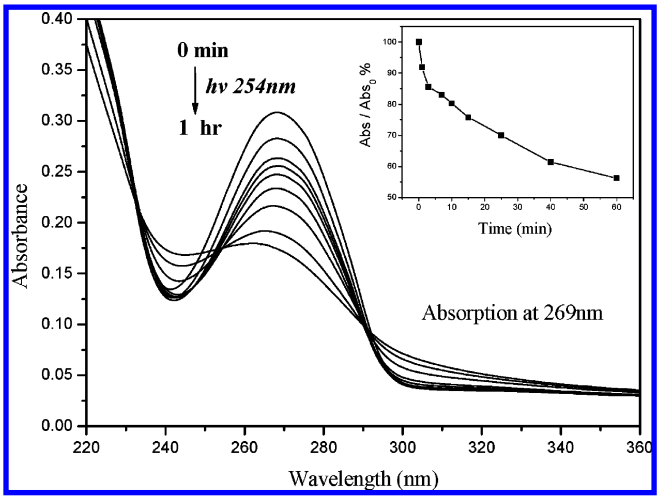

Figure 2. UV−vis spectra of the film formed from 10 wt % PVBU after exposing it to UV light at 254 nm for up to 1 h.

spectra of the PVBU film after exposure for up to 1 h. The initial signal at 269 nm is the absorption of the U functional groups. After exposure to the UV light, the intensity of this signal peak decreased gradually, suggesting the occurrence of $2\pi + 2\pi$ photodimerization.[31,40] We determined the extent of the cross-linking of the PVBU fibers in terms of the UV−vis intensity; the decrease in intensity of the peak at 269 nm revealed 44% cross-linking of the U units after exposure for 1 h (Figure 2 inset)—that is, a highly cross-linked network structure had formed.

Figure 3 presents the Raman spectra of the PVBU fibers before and after photo-cross-linking for 1 h. Table S1 of the

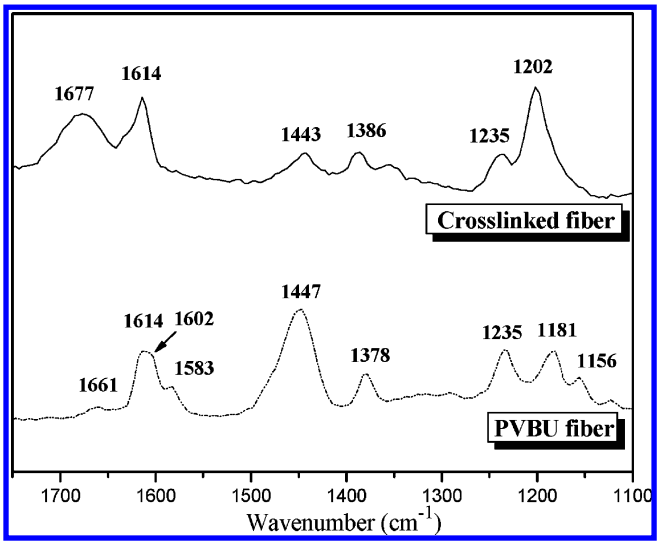

Figure 3. Raman spectra of fibers formed from 10 wt % PVBU before and after photo-cross-linking for 1 h.

Supporting Information lists the assignments of the pertinent Raman bands.[41−48] The intensities of the C(5)=C(6) stretching modes at 1583 and 1602 cm^{-1} decreased significantly after UV exposure, consistent with the double bond between atoms C(5) and C(6) being involved in cyclobutane ring formation. In addition, a wide band appeared near 1677 cm^{-1}, corresponding to C(4)=O and C(5)=C(6) in-phase stretching of the U groups of the cross-linked fiber, implying that the cross-linking of the structures did indeed occur predominantly through the formation of U−U dipyrimidines.

Figure 4 displays FE-SEM images of the cross-linked PVBU fibers after 1 h of exposure to 254 nm UV light. Notably, the

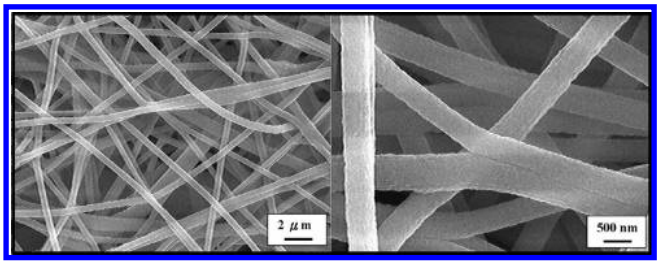

Figure 4. FE-SEM images of PVBU fibers after exposure to 254 nm UV light for 1 h.

surface features of the fibers remained unchanged. We performed solvent-resistance studies to confirm the presence of specific cross-linking structures within the fibers and to test the expected resulting improvement in dimensional stability. The pristine and cross-linked PVBU fibers were immersed into DMAc for 10 min at room temperature and then dried under vacuum. The pristine fibers lost their original shape (Figure

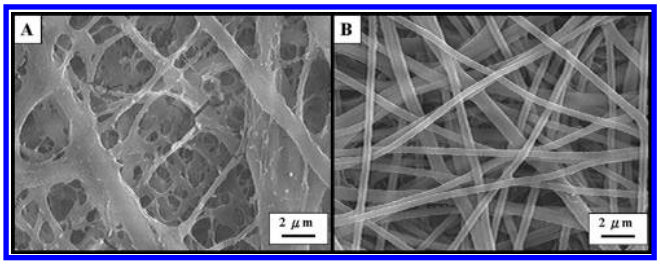

Figure 5. FE-SEM images of (A) noncross-linked and (B) cross-linked PVBU fibers that had been immersed in DMAc for 10 min.

5A), and the cross-linked PVBU fibers maintained their original shape (Figure 5B). Thus, the cross-linking of PVBU nanofibers through photodimerization of U groups significantly improved the dimensional stability.

In summary, we have successfully synthesized high-MW nucleobase-functionalized PVBU (M_n > 250 550) through free radical polymerization in aqueous solution. This high-MW PVBU exhibited significantly improved thermal properties as a result of increased entanglement of its polymer chains. We used electrospinning of PVBU in DMAc at a controlled concentration to fabricate continuous bead-free PVBU fibers, which were further photo-cross-linked upon exposure to UV light at a wavelength of 254 nm. After immersion in DMAc, the pristine fibers were seriously damaged, due to dissolution, while the cross-linked PVBU fibers maintained their original shape; thus, the cross-linked PVBU nanofibers exhibited good dimensional stability and solvent resistance. We suspect that this novel PVBU fiber will have great potential for use in many applications (e.g., drug binding and delivery and metal ion adsorption).[49−51]

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■ ASSOCIATED CONTENT

Supporting Information

Synthetic procedures; electrospinning details; characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Saenger, W. *Principles of Nucleic Acid Structures*; Springer: Berlin, 1984.
(2) Soyfer, V. N.; Potaman, V. N. *Triple-Helical Nucleic Acids*; Springer: New York, 1995.
(3) Binder, W. H.; Zirbs, R. *Adv. Polym. Sci.* **2007**, *207*, 1.
(4) Mueller, A.; Talbot, F.; Leutwyler, S. *J. Am. Chem. Soc.* **2002**, *124*, 14486.
(5) Mirkin, C. A.; Letsinger, R. L.; Mucic, R. C.; Storhoff, J. J. *Nature* **1996**, *382*, 607.
(6) Jain, K. K. *Science* **2001**, *294*, 621.
(7) Takemoto, K.; Mochizuki, E.; Wada, T.; Inaki, Y. *Biomimetic Polym.* **1990**, 253.
(8) Inaki, Y. *Prog. Polym. Sci.* **1992**, *17*, 515.
(9) Smith, W. T. *Prog. Polym. Sci.* **1996**, *21*, 209.
(10) Bauerle, P.; Emge, A. *Adv. Mater.* **1998**, *10*, 324.
(11) Mather, B. D.; Baker, M. B.; Beyer, F. L.; Berg, M. A. G.; Green, M. D.; Long, T. E. *Macromolecules* **2007**, *40*, 6834.
(12) Khan, A.; Haddleton, D. M.; Hannon, M. J.; Kukulj, D.; Marsh, A. *Macromolecules* **1999**, *32*, 6560.
(13) Lutz, J. F.; Thuenemann, A. F.; Rurack, K. *Macromolecules* **2005**, *38*, 8124.
(14) Noro, A.; Nagata, Y.; Takano, A.; Matsushita, Y. *Biomacromolecules* **2006**, *7*, 1696.
(15) Cheng, C. C.; Huang, C. F.; Yen, Y. C.; Chang, F. C. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 6416.
(16) Cheng, C. C.; Yen, Y. C.; Ye, Y. S.; Chang, F. C. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 6388.
(17) Trakhtenberg, S.; Warner, J. C.; Nagarajan, R.; Bruno, F. F.; Samuelson, L. A.; Kumar, J. *Chem. Mater.* **2006**, *18*, 2873.
(18) Saito, K.; Ingalls, L. R.; Lee, J.; Warner, J. C. *Chem. Commun.* **2007**, *24*, 2503.
(19) Reneker, D. H.; Chun, I. *Nanotechnology* **1996**, *7*, 216.
(20) Norris, I. D.; Shaker, M. M.; Ko, F. K.; MacDiarmid, A. G. *Synth. Met.* **2000**, *114*, 109.
(21) Deitzel, J. M.; Kleinmeyer, J.; Harris, D.; Beck Tan, N. C. *Polymer* **2001**, *42*, 261.
(22) Bognitzki, M.; Czado, W.; Frese, T.; Schaper, A.; Hellwig, M.; Steinhart, M.; Greiner, A.; Wendorff, J. H. *Adv. Mater.* **2001**, *13*, 70.
(23) Dzenis, Y. *Science* **2004**, *304*, 1917.
(24) Yoon, K.; Kim, K.; Wang, X.; Fang, D.; Hsiao, B. S.; Chu, B. *Polymer* **2006**, *47*, 2434.
(25) Kenawy, E.-R.; Bowlin, G. L.; Mansfield, K.; Layman, J.; Simpson, D. G.; Sanders, E. H.; Wnek, G. E. *J. Controlled Release* **2002**, *81*, 57.
(26) Yoshimoto, H.; Shin, Y. M.; Terai, H.; Vacanti, J. P. *Biomaterials* **2003**, *24*, 2077.
(27) Yoon, J.; Chae, S. K.; Kim, J. M. *J. Am. Chem. Soc.* **2007**, *129*, 3038.
(28) Hunlely, M. T.; Karikari, A. S.; Mckee, M. G.; Mather, B. D.; Layman, J. M.; Fornof, A. R.; Long, T. E. *Macromol. Symp.* **2008**, *270*, 1.
(29) Sivakova, S.; Rowan, S. J. *Chem. Soc. Rev.* **2005**, *34*, 9.
(30) Lin, I. H.; Cheng, C. C.; Yen, Y. C.; Chang, F. C. *Macromolecules* **2010**, *43*, 1245.
(31) Setlow, R. B. *Science* **1966**, *153*, 379.
(32) Lamola, A. A.; Mittal, J. P. *Science* **1966**, *154*, 1560.
(33) Blackburn, G. M.; Davies, R. J. H. *J. Chem. Soc. C* **1966**, *23*, 2239.
(34) Wang, S. Y. *Photochemistry and Photobiology of Nucleic Acids*; Academic Press: New York, 1976.
(35) Grasshoff, J. M.; Warner, J. C.; Taylor, L. D. U.S. Patent 5,455,349, October 3, 1995.
(36) Cheng, C. M.; Egbe, M. I.; Grasshoff, J. M.; Guarrera, D. J.; Pai, R. P.; Warner, J. C.; Taylor, L. D. *J. Polym. Sci., Part A: Polym. Chem.* **1995**, *33*, 2515.
(37) Lutz, J.-F.; Thunemann, A. F.; Nehring, R. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 4805.
(38) Buchko, C. J.; Chen, L. C.; Shen, Y.; Martin, D. C. *Polymer* **1999**, *40*, 7397.
(39) Mit-uppatham, C.; Nithitanakul, M.; Supaphol, P. *Macromol. Chem. Phys.* **2004**, *205*, 2327.
(40) Tominaga, M.; Konishi, K.; Aida, T. *Chem. Lett.* **2000**, *4*, 374.
(41) Singh, J. S. *J. Mol. Struct.* **2008**, *876*, 127.
(42) Nishimura, Y.; Haruyama, H.; Nomura, K. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1340.
(43) Tsuboi, M.; Komatsu, M.; Hoshi, J.; Kawashima, E.; Sekine, T.; Ishido, Y.; Russell, M. P.; Benevides, J. M.; Thomas, G. J. *J. Am. Chem. Soc.* **1997**, *119*, 2025.
(44) Li, C.; Huang, J.-G.; Liang, Y.-Q. *Spectrochim. Acta, Part A* **2001**, *57*, 1587.
(45) Ghosh, M.; Chakrabarti, S.; Misra, T. N *J. Phys. Chem. Solids* **1998**, *59*, 753.
(46) Li, C.; Huang, J.-G.; Liang, Y.-Q. *Langmuir* **2001**, *17*, 2228.
(47) Farquharson, S.; Gift, A.; Shende, C.; Inscore, F.; Ordway, B.; Farquharson, C.; Murren, J. *Molecules* **2008**, *13*, 2608.
(48) Otto, C.; Van Den Tweel, T. J. J.; de Mul, F. F. M.; Greve, J. *J. Raman Spectrosc.* **1986**, *17*, 289.
(49) Chakraborty, S.; Liao, I.-C.; Adler, A.; Leong, K. W. *Adv. Drug Delivery Rev.* **2009**, *61*, 1043.
(50) Lin, Y. X.; Cai, W. P.; Tian, X. Y.; Liu, X. L.; Wang, G. Z.; Liang, C. H. *J. Mater. Chem.* **2011**, *21*, 991.
(51) Navarathne, D.; Ner, Y.; Jain, M.; Grote, J. G.; Sotzing, G. A. *Mater. Lett.* **2011**, *65*, 219.