

## Uniform Grafting of Poly(1,5-dioxepan-2-one) by Surface-Initiated, Ring-Opening Polymerization

Kuk Ro Yoon\*

Department of Chemistry, Hannam University, Daejeon 306-791, Korea

Ok Ja Yoon

Department of Physics, Chung-Ang University, Seoul 156-756, Korea

Young Shik Chi and Insung S. Choi\*

Department of Chemistry, KAIST, Daejeon 305-701, Korea

Received November 14, 2005; Revised February 10, 2006

**Abstract:** A polymeric film of a biodegradable poly(1,5-dioxepan-2-one) (PDXO) was formed on a gold surface by a combination of the formation of self-assembled monolayers (SAMs) presenting hydroxyl groups and the surface-initiated, ring-opening polymerization (SI-ROP) of 1,5-dioxepan-2-one (DXO). The SI-ROP of DXO was achieved by heating a mixture of Sn(Oct)<sub>2</sub>, DXO, and the SAM-coated substrate in anhydrous toluene at 55 °C. The resulting PDXO film was quite uniform. The PDXO film was characterized by polarized infrared external reflectance spectroscopy, X-ray photoelectron spectroscopy, time-of-flight secondary ion mass spectrometry, atomic force microscopy, ellipsometry, and contact angle goniometry.

**Keywords:** biodegradable, self-assembled monolayers, poly(1,5-dioxepan-2-one) (PDXO), surface-initiated, ring-opening polymerization (SI-ROP).

### Introduction

The coating of solid substrates with biocompatible and/or biodegradable polymers has drawn a great deal of attention because of its potential applicability to biomedical areas, such as passivation of prosthetic devices and implants, coating for drug-delivery devices, and scaffolds for tissue engineering.<sup>1</sup> For polymeric coating of substrates, the “grafting-from” approach, based on surface-initiated polymerization (SIP), has intensively been studied because of its inherent superiority to other conventional techniques, such as spin-casting and “grafting-onto” approach, in the aspects of robustness and controllability of density and thickness.<sup>2</sup> In the process of SIP, polymer brushes are grown from initiators bound to surfaces by reacting with monomers in solution. Among various types of polymers, polymeric films of biocompatible and biodegradable aliphatic polyesters, such as poly(lactic acid) (PLA), poly( $\epsilon$ -caprolactone) (PCL), and poly(*p*-dioxanone) (PPDX), were produced by surface-initiated, ring-opening polymerization (SI-ROP).<sup>3,4</sup>

There have been many efforts for polymeric coating of aliphatic polyesters on a variety of solid substrates via SI-ROP.<sup>3,4</sup> Similar to synthesis in solution or bulk, organometallic catalysts, such as Sn(Oct)<sub>2</sub> and AlEt<sub>3</sub>, have generally been employed for SI-ROP of biodegradable aliphatic polyesters from surfaces presenting hydroxyl or amino groups. For example, Choi and Langer explored the use of Sn(Oct)<sub>2</sub> to produce poly(L-lactide) (PLLA) brushes on gold and silicon oxide surfaces by ROP of L-lactide,<sup>3a</sup> and Husemann *et al.* used diethylaluminum alkoxides prepared from AlEt<sub>3</sub> as a catalyst to grow PCL brushes from gold surfaces presenting hydroxyl groups.<sup>3b</sup> Similar reaction conditions have widely been applied to SI-ROP for coating of various aliphatic polyesters, such as PLA,<sup>3a,3c</sup> PCL,<sup>3b,3c</sup> and PPDX,<sup>3d-f</sup> on various types of substrates, such as gold,<sup>3a-d</sup> silicon oxide,<sup>3a,3d</sup> particles,<sup>3e</sup> and nanotubes.<sup>3f</sup> To minimize harmful effects of metallic residues in polyester-coated biomedical devices, enzyme (lipase B)-catalyzed, SI-ROP of PCL and PPDX was also reported.<sup>4</sup>

One of the obstacles to the generation of a highly uniform film of aliphatic polyesters via SI-ROP is the high crystallinity of most aliphatic polyesters.<sup>3a,3d</sup> In the previous studies, SI-ROP of PLLA, a crystalline polymer, and PPDX, a

\*Corresponding Author. E-mail: kryoon@hannam.ac.kr, ischoi@kaist.ac.kr

semi-crystalline polymer, did not provide smooth polymeric films.<sup>3a,3d</sup> Because crystallinity of polymers must be considered in SI-ROP for uniform coating, we focused on amorphous poly(1,5-dioxepan-2-one) (PDXO).<sup>5</sup> PDXO has been known as a highly viscous and amorphous polymer with a glass transition temperature ( $T_g$ ) of  $-39^\circ\text{C}$ .<sup>6</sup> PDXO also shows characteristic behaviors, such as hydrolytic degradation and bioadsorption, and its main chain is composed of alternating ethylene glycol and  $\beta$ -hydroxypropionic acid.<sup>7</sup> In this study, we formed a polymeric film of PDXO on a gold surface by a combination of formation of self-assembled monolayers (SAMs) presenting hydroxyl groups and SI-ROP of 1,5-dioxepan-2-one (DXO) with  $\text{Sn}(\text{Oct})_2$  as a catalyst, and investigated the quality of the film, in particular, in the aspect of uniformity.

## Experimental

**Materials.** Toluene (from Aldrich) was purified by distillation over sodium. All other solvents and reagents were analytical-grade and used as received. The monomer DXO was prepared by the Baeyer-Villiger oxidation of tetrahydropyran-4-one (THP).<sup>6,8</sup> The crude product was purified by fractional distillation under reduced pressure. DXO was characterized by  $^1\text{H}$  NMR spectroscopy and its purity was determined by HP 5890 gas chromatograph. The gold substrates were prepared by thermal evaporation of 5 nm of titanium and 100 nm of gold onto silicon wafers.

Tri(ethylene glycol)-terminated alkanethiol [1-mercaptoundec-11-yl-tri(ethylene glycol),  $\text{HS}(\text{CH}_2)_{11}(\text{CH}_2\text{CH}_2\text{O})_3\text{OH}$ ] was prepared by following a previous report.<sup>9</sup> Reaction of 11-bromoundec-1-ene with a slight excess of 50% sodium hydroxide and 3-10 equiv. of oligo (ethylene glycol) provided the monoether in a reasonable yield (76%). Photochemical addition of thioacetic acid (2-4 equiv.) to the double bond (under a nitrogen atmosphere with a 450 W, medium-pressure mercury lamp; irradiation for 4-6 h) gave the thioacetate in a good yield (88%). To avoid oxidation of the thiol to the corresponding disulfide, methanolysis of the thioacetate was carried out in acid (0.1 M HCl in methanol) at reflux for 4 h (yield: 91%).

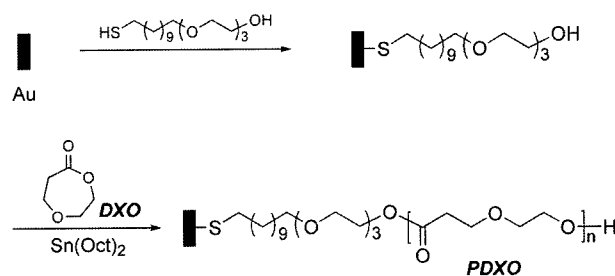
**Surface-Initiated, Ring-Opening Polymerization (SI-ROP) of DXO.** A hydroxyl-terminated SAM was formed on a gold surface by immersing the gold substrate in a 2 mM ethanolic solution of 1-mercaptoundec-11-yl-tri(ethylene glycol) for 12 h at room temperature. The SAM-coated gold substrate was treated with  $\text{Sn}(\text{Oct})_2$  (10  $\mu\text{mol}$ ) in 20 mL of dried toluene at  $55^\circ\text{C}$  for 1 h. The monomer, DXO (10 mmol), was then added by syringe and the mixture was heated at  $55^\circ\text{C}$ . The resulting substrate was intensively washed with chloroform, ethanol, THF and water, sonicated in chloroform for 30 min, and dried under a flow of nitrogen. Finally, the PDXO-coated film was dried under reduced pressure at room temperature for 24 h.

**Instrumentation.** Polarized infrared external reflectance spectroscopy (PIERS) spectra were obtained in a single reflection mode using a  $\text{N}_2$ -purged Thermo Nicolet Nexus Fourier transform infrared spectrometer. The  $p$ -polarized light was incident at  $80^\circ$  relative to the surface normal of the substrate and a narrow band mercury-cadmium-telluride (MCT) detector was used. An ellipsometer (Gaertner L116s) equipped with a He-Ne Laser (632.8 nm) was used to determine the thickness of the PDXO films, and a contact angle goniometer (Phoenix 300, Surface Electro Optics Co. Ltd, Korea) to determine the water contact angle of the films. Atomic force microscopy (AFM) images were recorded by a Nanoscope IIIa (Digital Instruments) using tapping mode. The X-ray photoelectron spectroscopy (XPS) study was performed with a VG-Scientific ESCALAB 250 spectrometer (UK) with monochromatized Al  $K_\alpha$  X-ray source. Time-of-flight secondary ion mass spectrometry (TOF-SIMS) spectra were recorded by a PHI 7200 time-of-flight secondary ion mass spectrometer.

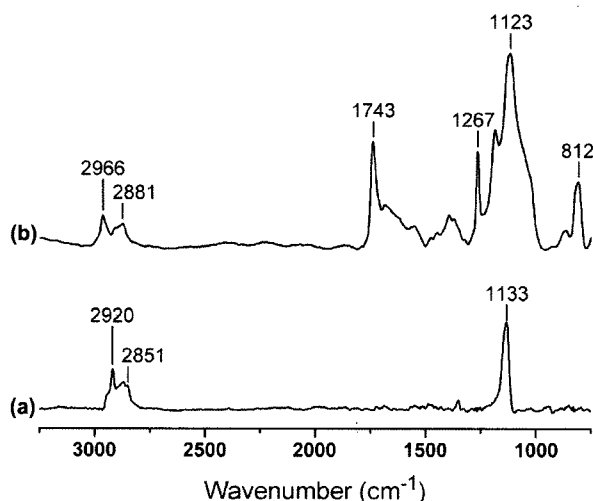
## Results and Discussion

As a platform for surface-initiated, ring-opening polymerization (SI-ROP), we prepared the SAM of 1-mercaptoundec-11-yl-tri(ethylene glycol) on gold by immersing a gold substrate in a 1 mM ethanolic solution of 1-mercaptoundec-11-yl-tri(ethylene glycol) overnight and characterized the resulting SAM by PIERS and ellipsometry (Figure 1). The IR spectrum of the SAM showed several characteristic bands, such as C-O stretching band at  $1133\text{ cm}^{-1}$  and  $\text{CH}_2$  stretching bands at 2920, 2873, and  $2851\text{ cm}^{-1}$  (Figure 2(a)). The thickness of the SAM was measured to be 20 Å by ellipsometric measurement, in accordance with the reported value.<sup>9</sup> The terminal ethylene glycol (EG) group plays two important roles in SI-ROP. Terminal hydroxyl group acts as an initiation site for SI-ROP, and the flexible nature of EG moiety is critical in the successful SI-ROP.<sup>3a,3d</sup>

After the formation of the SAM, SI-ROP of DXO was performed by heating a mixture of the gold substrate presenting the SAM, DXO and  $\text{Sn}(\text{Oct})_2$  in anhydrous toluene at  $55^\circ\text{C}$ . We chose the reaction temperature at  $55^\circ\text{C}$  because of thermal



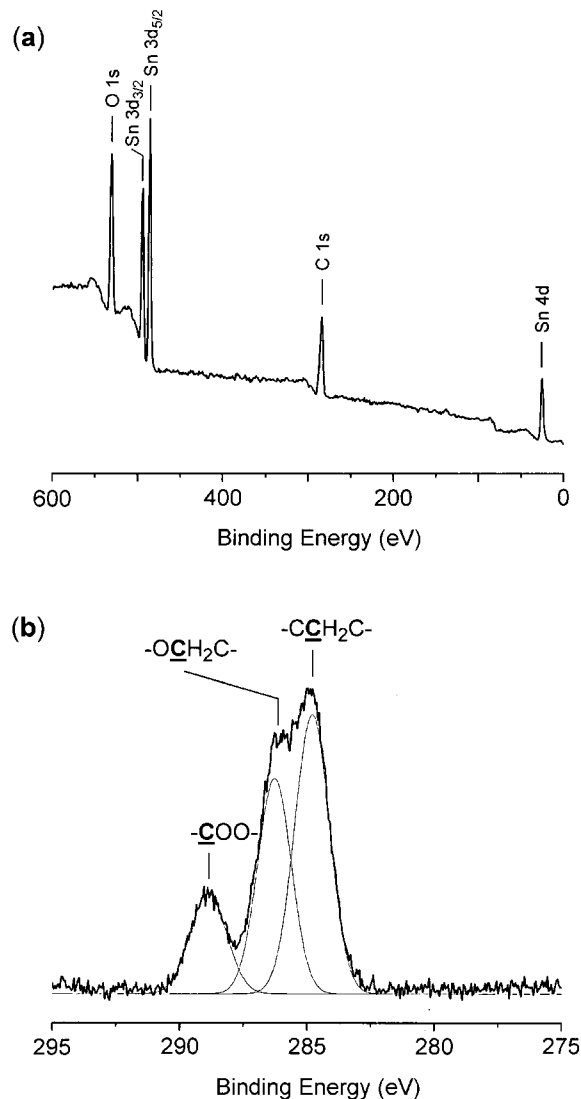
**Figure 1.** Schematic representation for surface-initiated, ring-opening polymerization of 1,5-dioxepan-2-one (DXO) on a gold surface.



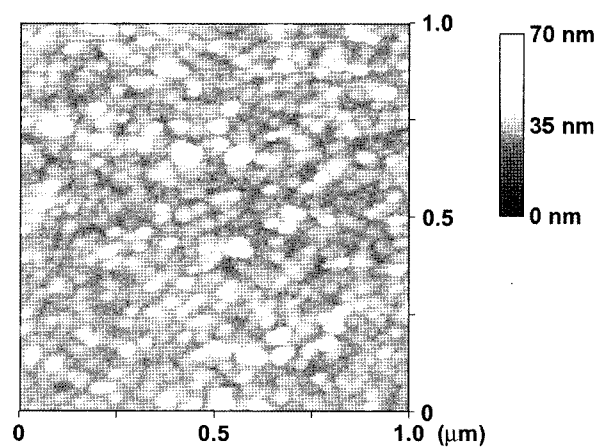
**Figure 2.** FTIR spectra of (a) tri(ethylene glycol)-terminated SAMs and (b) PDXO films.

instability of the Au-S bond.<sup>10</sup> After washing the substrate thoroughly to remove any physisorbed PDXO, the resulting PDXO film was characterized by ellipsometry, contact angle goniometry, PIERS, XPS, TOF-SIMS, and AFM. The thickness of the film was measured to be 4.5 nm by ellipsometry after 1 h reaction and the film thickness seemed to be dependent on the reaction time. The film thicknesses increased to 10 nm after 2 h reaction and 25 nm after 6 h reaction. We conducted further characterizations with the 25 nm-thick film as a representative.

Figure 2(b) shows the IR spectrum of the PDXO film. The characteristic peaks of PDXO were observed: at 2966 and 2881  $\text{cm}^{-1}$  due to the C-H stretching, at 1743  $\text{cm}^{-1}$  due to the C=O stretching, at 1267  $\text{cm}^{-1}$  due to the C-O stretching of ester, at 1123  $\text{cm}^{-1}$  due to the C-O stretching of ether, and at 812  $\text{cm}^{-1}$  due to the CH<sub>2</sub> deformation. The polymer film was further characterized by XPS (Figure 3). Three elements -carbon, oxygen, and tin- were investigated from survey spectrum (Figure 3(a)). Carbon and oxygen are elements for the composition of PDXO and the SAM, and tin was used as a catalyst for polymer growth. In the previous report on SI-ROP of dioxanone, it was found that tin remained at surfaces after the polymerization, and the result supported the coordination-insertion mechanism in Sn(Oct)<sub>2</sub>-catalyzed SI-ROP.<sup>11</sup> The C(1s) region of the XPS spectra confirms the chemical structure of the PDXO film. Three carbon peaks were found at 284.6 eV (C-C-C), at 288.6 eV (C=O), and at 286.1 eV (C-C-O) (Figure 3(b)). The SIMS spectrum showed peaks at  $m/z$  58 (C<sub>2</sub>H<sub>2</sub>O<sub>2</sub>),  $m/z$  59 (C<sub>2</sub>H<sub>3</sub>O<sub>2</sub>),  $m/z$  71 (C<sub>3</sub>H<sub>3</sub>O<sub>2</sub>),  $m/z$  87 (C<sub>3</sub>H<sub>3</sub>O<sub>3</sub>), and  $m/z$  115 (C<sub>3</sub>H<sub>7</sub>O<sub>3</sub>), which are characteristic fragments of PDXO. The grafting of PDXO also induced the change in water contact angles on gold. The water contact angle of the SAM-coated gold surface was 32° and it was changed to 60° after grafting the polymer. The increase of



**Figure 3.** (a) Survey XPS spectrum and (b) high-resolution XPS spectrum of C(1s) region of PDXO films.



**Figure 4.** AFM image of PDXO films.

contact angle may be due to the hydrophobic methylene backbone of PDXO, different from the hydroxyl-terminated, EG moiety of the SAM-coated surface.

We used a tapping-mode AFM to investigate microstructures and uniformity of the PDXO film (Figure 4). The PDXO film was quite uniform: the root-mean-square (RMS) was about 1 nm with the 25 nm-thick film. In the previous reports, the surfaces coated with PLLA or PPDX were not smooth, indicating microscopic nonuniformity of the films: the RMS values of 38 and 34 nm were observed in the 70 nm-thick PLLA film and 90 nm-thick PPDX film, respectively.<sup>3a,3d</sup> From the comparison of the results, we confirm that crystallinity of polymer at room temperature is crucial for a uniform coating of biodegradable aliphatic polyesters on solid substrate by SI-ROP, because PDXO has been known as a highly viscous and amorphous polymer<sup>6</sup> in contrast to crystalline structure of PLLA<sup>12</sup> and semi-crystalline structure of PPDX.<sup>13</sup>

## Conclusions

We demonstrated the surface-initiated, ring-opening polymerization (SI-ROP) of 1,5-dioxepan-2-one (DXO) on a gold surface catalyzed by Sn(Oct)<sub>2</sub>. A polymeric film of a biodegradable PDXO was grown from a gold surface by combination of formation of SAMs presenting hydroxyl groups and SI-ROP of DXO. The resulting surface presenting PDXO films was quite uniform because of the amorphous nature of PDXO.

PDXO is a promising candidate as a biodegradable and biocompatible coating material. The coating of solid substrates with biodegradable polymers will be important for fundamental studies in biological fields, such as cell biology, and for fabrication of prosthetic devices, implants, drug-delivery devices, and scaffolds for tissue engineering. In particular, the uniformity of PDXO films grown in this study will provide great advantages for the use of solid substrates coated with biodegradable polymers.

**Acknowledgements.** This work was supported by the research fund from Hannam University. The authors thank Dr. Won in Korea Basic Science Institute (KBSI) for the XPS analysis.

## References

- (1) (a) N. Nath and A. Chilkoti, *Adv. Mater.*, **14**, 1243 (2002). (b) J. Lahann, I. S. Choi, J. Lee, K. F. Jensen, and R. Langer, *Angew. Chem. Int. Ed.*, **40**, 3166 (2001). (c) B. D. Klugherz, P. L. Jones, X. Cui, W. Chen, N. F. Meneveau, S. DeFelice, J. Connolly, R. L. Wilensky, and R. J. Levy, *Nat. Biotechnol.*, **18**, 1181 (2000). (d) F. E. Black, M. Hartshorne, M. C. Davies, C. J. Roberts, S. J. B. Tendler, P. M. Williams, K. M. Shakesheff, S. M. Cannizzaro, I. Kim, and R. Langer, *Langmuir*, **15**, 3157 (1999).
- (2) (a) S. Edmondson, V. L. Osborne, and W. T. S. Huck, *Chem. Soc. Rev.*, **33**, 14 (2004). (b) Y. S. Chi, J. K. Lee, K.-B. Lee, D. J. Kim, and I. S. Choi, *Bull. Korean Chem. Soc.*, **26**, 361 (2005). (c) Y.-W. Lee, S. M. Kang, K. R. Yoon, Y. S. Chi, S.-P. Hong, B.-C. Yu, H.-J. Paik, W. S. Yun, and I. S. Choi, *Macromol. Res.*, **13**, 356 (2005).
- (3) (a) I. S. Choi and R. Langer, *Macromolecules*, **34**, 5361 (2001). (b) M. Husemann, D. Mecerreyes, C. J. Hawker, J. L. Hedrick, R. Shah, and N. L. Abbott, *Angew. Chem. Int. Ed.*, **38**, 647 (1999). (c) M. Möller, F. Nederberg, L. S. Lim, R. Kånge, C. J. Hawker, J. L. Hedrick, Y. D. Gu, R. Shah, and N. L. Abbott, *J. Polym. Sci., Part A: Polym. Chem.*, **39**, 3529 (2001). (d) K. R. Yoon, Y. S. Chi, K.-B. Lee, J. K. Lee, D. J. Kim, Y.-J. Koh, S.-W. Joo, W. S. Yun, and I. S. Choi, *J. Mater. Chem.*, **13**, 2910 (2003). (e) K. R. Yoon, Y.-J. Koh, and I. S. Choi, *Macromol. Rapid Commun.*, **24**, 207 (2003). (f) K. R. Yoon, W.-J. Kim, and I. S. Choi, *Macromol. Chem. Phys.*, **205**, 1218 (2004).
- (4) K. R. Yoon, K.-B. Lee, Y. S. Chi, W. S. Yun, S.-W. Joo, and I. S. Choi, *Adv. Mater.*, **15**, 2063 (2003).
- (5) K. R. Yoon, Y.-W. Lee, J. K. Lee, and I. S. Choi, *Macromol. Rapid Commun.*, **25**, 1510 (2004).
- (6) T. Mathisen, K. Masus, and A.-C. Albertsson, *Macromolecules*, **22**, 3842 (1989).
- (7) A. Kafrawy and S. W. Shalaby, *J. Bioact. Compat. Polym.*, **1**, 431 (1986).
- (8) R. Arentzen, Y. T. Yan Kui, and C. B. Reese, *Synthesis*, 509 (1975).
- (9) C. Pale-Grosdemange, E. S. Simon, K. L. Prime, and G. M. Whitesides, *J. Am. Chem. Soc.*, **113**, 12 (1991).
- (10) (a) J.-B. Kim, M. L. Bruening, and G. L. Baker, *J. Am. Chem. Soc.*, **122**, 7616 (2000). (b) R. R. Shah, D. Merreces, M. Husemann, I. Rees, N. L. Abbott, C. J. Hawker, and J. L. Hedrick, *Macromolecules*, **33**, 597 (2000). (c) C. D. Bain, E. B. Troughton, Y. Tao, J. Evall, G. M. Whitesides, and R. G. Nuzzo, *J. Am. Chem. Soc.*, **111**, 321 (1989).
- (11) K. R. Yoon, Y. Kim, and I. S. Choi, *J. Polym. Res.*, **11**, 265 (2004).
- (12) K. A. M. Thakur, R. T. Kean, J. M. Zupfer, N. U. Buehler, M. A. Doscotch, and E. J. Munson, *Macromolecules*, **29**, 8844 (1996).
- (13) H. R. Kricheldorf and D.-O. Damrau, *Macromol. Chem. Phys.*, **199**, 1089 (1998) and references therein.