Stepwise Assembly of Enantiomeric Poly(lactide)s on Surfaces

Takeshi Serizawa,[†] Hiroo Yamashita,[†] Tomoko Fujiwara,[‡] Yoshiharu Kimura,[‡] and Mitsuru Akashi*,[†]

Department of Applied Chemistry and Chemical Engineering, Faculty of Engineering, Kagoshima University, Korimoto 1-21-40, Kagoshima 890-0065, Japan, and Department of Polymer Science and Engineering, Faculty of Textile Science, Kyoto Institute of Technology, Goshokaido-Cho, Matsugasaki, Sakyo-Ku, Kyoto 606-8585, Japan

Received October 2, 2000; Revised Manuscript Received January 2, 2001

ABSTRACT: Enantiomeric poly(lactide)s were assembled on a quartz crystal microbalance (QCM) substrate, which detects the mass of the polymers from the frequency shift, following immersion of QCM into alternating acetonitrile solutions. A quantitative QCM analysis at each step and a differential scanning calorimetric study of the assembly showed racemic crystal (stereocomplex) formation on the substrate surface. Atomic force microscopic observation showed a dotted nanostructure of the assembly. The assembly amount was increased with increasing the PLA concentration and the immersion time, while that was decreased with increasing the assembly temperature. The heterogeneous assembly was also prepared by altering the immersion time. We found that racemic crystal formation was applied to the alternate deposition of certain structurally regulated polymers.

Introduction

Stepwise polymer deposition using alternate immersion of substrates into interactive polymer solutions promises the potential fabrication of polymeric assemblies with layered nanostructures.[1] Although there have been many studies on the alternate assembly of polymers based on ionic interaction[2−11] as well as hydrogen bonding[12] and charge transfer,[13,14] it is difficult to form polymeric assemblies in situ with molecularly regulated assembly structures. The main reason for this difficulty is due to the fact that the polymers usually adsorb with random-coiled conformations. (Ultrathin films have only layered structures.) It is therefore important to analyze whether these adsorbed polymers can be transformed into regular assemblies by utilizing other specific interactions between polymers, in which the appropriately prepared film can form higher ordered structures. If such a process can be realized, then further scientific investigation can be performed by alternate assembly. In addition, the drastic conformational change of the adsorbed polymers would really occur at the solid−solution interface.

In our previous study, stepwise assembly between isotactic (it-) and syndiotactic (st-) poly(methyl methacrylate)s (PMMAs) on surfaces resulted in stereocomplex formation following simple alternate immersion into their respective acetonitrile solutions.[15] In the resulting complex, it-PMMA was surrounded by twice the molar amount of st-PMMA with van der Waals contact, forming a double-stranded helical structure. Moreover, the assembly maintained a molecularly regulated nanostructure. From the mechanistic analysis, it was suggested that the complex formed at the step when st-PMMA interacted with a physically absorbed it-PMMA layer, possibly with dynamic conformational changes. The combinations of it-PMMA and st-poly(methacrylic acid)[16] or it-PMMA and st-poly(alkyl methacrylate)s,[17] which form stereocomplexes, were also applied to the stepwise assembly with a suitable solvent system. Quartz crystal microbalance (QCM) analysis, which detects the mass of adsorbed polymers from decreases in resonant frequency, was a useful technique for the quantitative analysis of the resulting assemblies.

A racemic crystal, comprising the stereocomplex, was formed between the poly(L-lactide) (PLLA) and the poly(D-lactide) (PDLA) by alternate packing of β-form 3_1-helices of the opposite absolute configuration (left- and right-handed, respectively) side by side with van der Waals contact.[18−26] The molecular conformation was significantly different from that of the PMMA complex. The stoichiometry, 1:1 for the poly(lactide)s (PLAs), was also different from the 1:2 ratio for it- and st-PMMAs. Although the PMMA complex could be applied in stepwise assembly, with the formation of a double-stranded helical structure,[15] it is of further interest to determine whether the complex system of enantiomeric PLAs is applicable to alternate assembly methods. If assembly of the PLAs could be successfully performed, this would suggest that the van der Waals contact between certain polymers (without conformational entanglement as in the PMMA complex system) is sufficient to drive stepwise polymer assembly on surfaces.

PLA is a well-known biodegradable polyester and has been widely studied as a solid or coating material for biomedical applications.[27] If the stepwise assembly of enantiomeric PLAs can be realized, a novel method for coating surfaces will be available. As the stepwise assembly is a "wetting" process using solutions, materials of various shapes could easily be coated. In addition, the amount of assembled polymer could be controlled with assembly step to the nanogram level. As the molecular conformation on surfaces is regulated, biological activity or affinity may be different from that of a PLA surface prepared by conventional techniques.

In the present study, we demonstrated the stepwise assembly of enantiomeric PLAs by stereocomplex formation. The assembly was quantitatively monitored by QCM with a silver electrode surface as well as by other qualitative analyses. We develop an alternate deposition technique using stereocomplex formation based on van

[†] Kagoshima University.
[‡] Kyoto Institute of Technology.

10.1021/ma001705o CCC: $20.00
Published on Web 02/10/2001

der Waals contacts between certain polymers without any conformational entanglement.

Experimental Section

Materials and Synthesis. L-Lactide and D-lactide were supplied from Purac Biochem (Netherlands) and Shimadzu (Kyoto), respectively, and were purified by recrystallization from ethyl acetate. Diethylene glycol monomethyl ether (DEGM) was purchased from Nacalai Tesque (Kyoto) and was distilled under a vacuum. Stannous 4-ethylhexanoate ($Sn(Oct)_2$) was purchased from Nacalai Tesque (Kyoto), distilled under reduced pressure, and dissolved in distilled toluene at a concentration of 0.1 g/mL. Chloroform and diethyl ether were commercially supplied and distilled before use. PLLA and PDLA, which had number-average molecular weights of 29 100 and 26 000, and distributions (M_w/M_n) of 1.45 and 1.44, respectively, were analyzed by gel permeation chromatography with a chloroform eluent using a polystyrene standard and were prepared in accordance with previous studies.[28] In brief, PLAs with a sharp molecular weight distribution were synthesized by ring-opening polymerization of the corresponding lactide in the presence of DEGM. Five grams of lactide and 30 mg of DEGM were charged into a 100 mL flask. After drying in vacuo for 3 h, 10 mg of $Sn(Oct)_2$ in toluene (10 mol % relative to DEGM) was added under a nitrogen atmosphere. The flask was heated, and the mixture was stirred at 120 °C for 7 h. The reaction mixture was cooled and dissolved in 50 mL of chloroform, and the solution was poured into a large excess of diethyl ether for reprecipitation of polymer. The polymer was filtered and vacuum-dried. Acetonitrile of spectral grade for stepwise assembly was purchased from Nacalai Tesque (Kyoto) and used for stepwise assembly without further purification.

Quartz Crystal Microbalance. An AT-cut quartz crystal with a parent frequency of 9 MHz was obtained from USI (Japan). A crystal (9 mm in diameter) was coated on both sides with silver electrodes 4.5 mm in diameter. The frequency was monitored by an Iwatsu frequency counter (model SC7201). The amount of PLAs assembled, Δm, could be calculated by measuring the frequency decrease in the QCM, ΔF, using Sauerbrey's equation[29] as follows:

$$-\Delta F = \frac{2F_0^{\,2}}{A\sqrt{\rho_q \mu_q}}\Delta m$$

where F_0 is the parent frequency of the QCM (9×10^6 Hz), A is the electrode area (0.159 cm^2), ρ_q is the density of the quartz (2.65 g cm^{-3}), and μ_q is the shear modulus (2.95×10^{11} dyn cm^{-2}). This equation is reliable when measurements are made in air as described in this study, because the mass of the solvents is never detected as the frequency shift, and the effect of the viscosity of the absorbent on the frequency can be ignored. Both sides of the electrodes were used in the present study.

Stepwise Assembly. Before assembly measurements, QCM electrodes were treated three times with a piranha solution (H_2SO_4:H_2O_2 = 3:1) for 1 min each time, followed by rinsing with pure water and drying with N_2 gas, to clean the surface. The QCM obtained was then immersed in a PLLA solution of adequate concentration for an adequate time at adequate temperature, taken out, thoroughly rinsed with the same solvent maintained at the same temperature, and dried with N_2 gas. The frequency decrease was then measured. The QCM was immersed again into a PDLA solution, and the same procedure was repeated. This stepwise cycle was repeated for PLA assembly. The PLAs were dissolved in acetonitrile at more than 40 °C and were precipitated by mixing both solutions, with subsequent stereocomplex formation.

Others. For differential scanning calorimetric (DSC) analysis, the PLAs were deposited onto the QCM in 60 steps. The QCM was crushed and put into a silver sample pan for DSC measurement. Bare quartz partitions as well as the QCM electrodes were applied to the measurement. We were unable to estimate the enthalpy change per unit, because it was difficult to accurately estimate the quantity of PLAs deposited. Atomic force microscopic (AFM) images were obtained in a Digital Instruments NanoScope III that was operated in a tapping or a contact mode in the air at ambient temperature. We did not perform any image processing other than flat leveling. The mean roughness (Ra) in given observed areas was estimated from the following equation:

$$Ra = \frac{1}{LxLy}\int_0^{Ly}\int_0^{Lx}|F(x,y)|\,dx\,dy$$

where $F(x,y)$ is the surface relative to the center plane which is a flat plane parallel to the mean plane, and Lx and Ly are the dimensions of the surface.

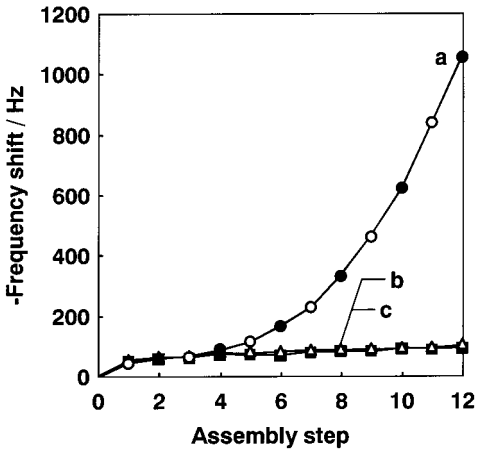

Figure 1. Frequency shift of QCM at each immersion time of 15 min at a concentration of 10 mg mL^{-1} at 50 °C: (a) alternately immersed into PLLA and PDLA solutions; (b) immersed into PLLA solution; (c) PDLA solution. The open and closed symbols show PLLA and PDLA steps, respectively (also in Figures 5−8).

Results and Discussion

Stepwise Stereocomplex Assembly. Acetonitrile was selected as the solvent for the stepwise assembly, because it is well-known to be a strong complex forming solvent.[18−26] Figure 1 shows the frequency shifts against each assembly step when the QCM was immersed into both PLLA and PDLA solutions alternately at each immersion time of 15 min at the concentrations of 10 mg mL^{-1} at 50 °C, as well as frequency shifts following immersion into enantiomer only. Alternate immersion showed an obviously larger shift, whereas slight shifts after one step were observed in the latter cases. The frequency shift of the former after a 12-step assembly was around −1000 Hz, which corresponds to a 2.7 μg cm^{-2} deposition onto the QCM electrodes. The ratio of the total frequency shift between the PLLA and PDLA steps (PLLA/PDLA) was 0.9. It is known that the stoichiometry of the PLA stereocomplex is 1.[18−26] Although the ratio is slightly smaller than the ideal one, this is attributed to stopping of the assembly process at the PDLA step, considering the possible assembly mechanism (see below). The stepwise assembly was observed even if the assembly was started at a PDLA step (data not shown). These observations demonstrated the stepwise process of stereocomplex formation at the solid−solution interface.

The frequency shift with alternate deposition increased exponentially with an increased number of assembly steps. This can be explained by an increase in the apparent surface area for PLA adsorption. Atomic force microscopic observations of a bare QCM undergo-

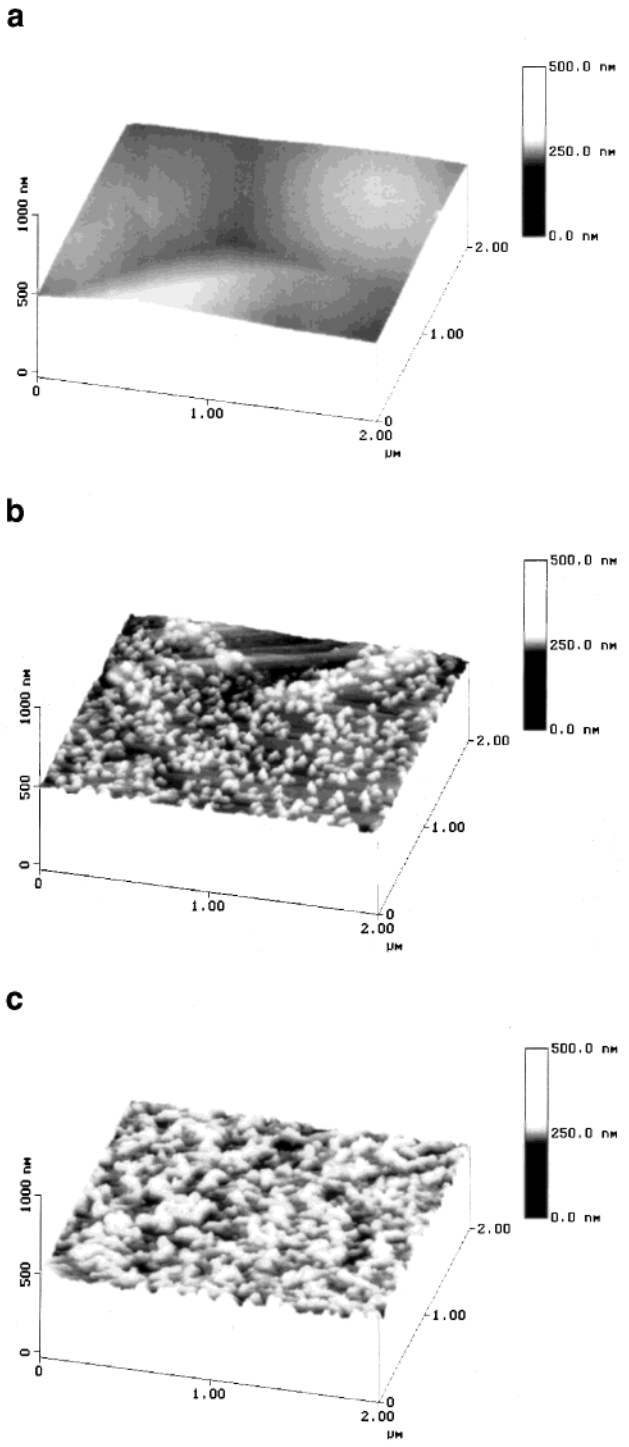

Figure 2. AFM observations of the surfaces of (a) a bare QCM, (b) a 6-step assembly, and (c) a 12-step assembly at each immersion time of 15 min at a concentration of 10 mg mL^{-1} at 50 °C.

ing stepwise assembly revealed that the enantiomeric PLAs were deposited along dotted nanostructures (Figure 2). An increase in the number of dotted assemblies on the QCM surface apparently increased the effective surface area for deposition at each step. The mean-square roughness for a bare QCM, 6-step, and 12-step assembly were 3.8, 11, and 15 nm, respectively. In addition, the static contact angles of the assembly at the 7 and 8 steps (PLLA and PDLA) were 75.8 ± 4.6° and 81.7 ± 1.5°, respectively. In fact, the angles of the surfaces of a bare QCM, PLLA, and PDLA cast films

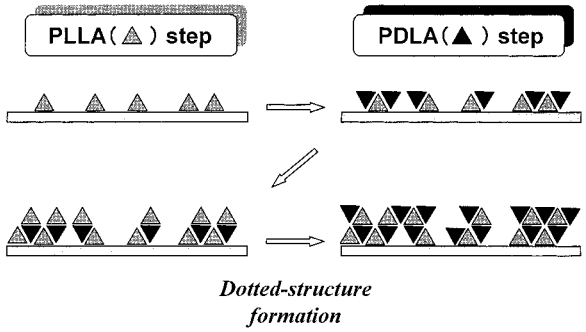

Figure 3. Schematic representation of stepwise assembly enantiomeric PLAs. The scheme was demonstrated until 4 steps. A triangle indicates a cross-sectional view of each enatiomeric PLA.

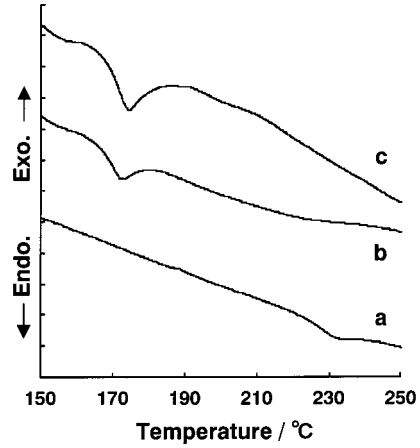

Figure 4. DSC analyses at a heating rate of 10 °C min^{-1}: (a) alternate assembly at each immersion time of 15 min at a concentration of 10 mg mL^{-1} at 50 °C; (b) cast film of PLLA; (c) PDLA.

were 29.3 ± 1.5°, 61.3 ± 2.0°, and 69.2 ± 2.3°, respectively. This observation also supports the observation of dotted assembly because the angle of a dotted surface tends to be larger than that of a smooth surface. Furthermore, a chiral PLA is surrounded by three of its enantiomers in the triclinic crystal system of the stereocomplex.[26] When we suppose the stepwise assembly on surfaces, the polymer may interact with two enatiomers because one site for interaction has been already utilized. If this manner proceeds, the amount of assembled polymer will increase exponentially. In fact, the assembling ratio from an adequate step to the next step was within 2 in the stepwise assembly (except for the initial two step; a direct influence of the substrate). Based on this interpretation and using a schematic drawing of PLAs reported by Brizzolara et al.,[26] a scheme for the assembly mechanism is shown in Figure 3. DSC analysis was applied to a 60-step alternate assembly (around 20 000 Hz) and to cast films of both PLLA and PDLA (Figure 4). The cast films showed an endothermic peak at 174.4 and 172.4 °C, respectively. However, the assembly showed a peak at 231.7 °C, which was consistent with that of stereocomplex films (230 °C) previously reported.[18] This observation also supports stereocomplex formation on a QCM substrate. No significant peak was observed for assembly at around 170 °C, which corresponds to the melting point of each enantiomer. Accordingly, we can state that all of the enantiomeric PLAs had formed stereocomplex during assembly. Unfortunately, we could

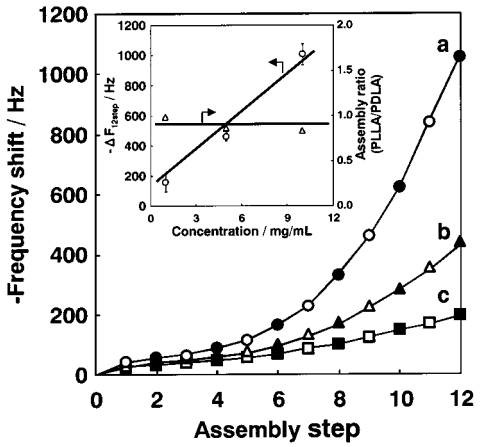

Figure 5. Stepwise assembly of PLAs at each immersion time of 15 min at 50 °C at different concentrations of (a) 10, (b) 5, and (c) 1 mg mL^{-1}.

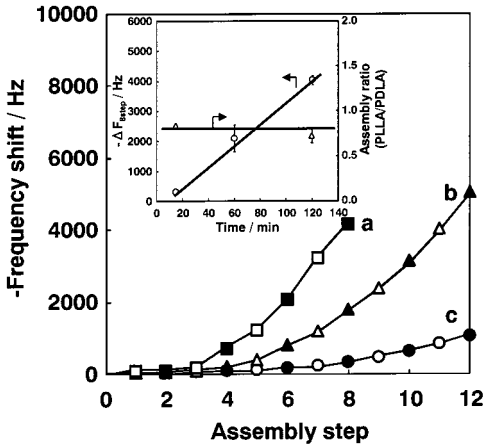

Figure 6. Stepwise assembly of PLAs at a concentration of 10 mg mL^{-1} at 50 °C at different each immersion times of (a) 120, (b) 60, and (c) 15 min.

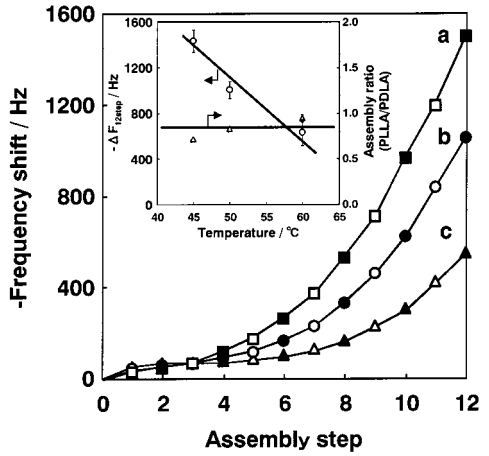

Figure 7. Stepwise assembly of PLAs at each immersion time of 15 min at a concentration of 10 mg mL^{-1} at different temperatures of (a) 45, (b) 50, and (c) 60 °C.

not analyze the enthalpy changes of the assembly because we did not estimate the accurate mass of the assembly for DSC analysis (see Experimental Section). However, the peak area was reproducible by regulating the frequency change to be the same. This means relative analysis is useful in the present system. Careful deposition onto the electrodes will enable an estimation of these changes in the near future.

In our previous study, the stepwise assembly of isotactic (it) and syndiotactic (st) poly(methyl methacrylate)s (PMMAs) was performed by the alternate immersion of a QCM substrate into acetonitrile solutions;[15] the procedure was essentially the same as the method employed in the present study. The driving force was stereocomplex formation between the PMMAs, which have a double-stranded nanostructure as described above. In this case, there is strong entanglement between the PMMAs in the stereocomplex undergoing stepwise deposition. However, stereocomplex formation between the enantiomeric PLAs was based only on van der Waals contact between PLAs. This means that this type of racemic crystal formation between structurally well-defined polymers could be applied to alternate deposition. Accordingly, the deposition process could be applied to other stereocomplex systems such as enantiomeric poly(γ-benzyl glutamate)s,[30−33] enantiomeric poly(α-methyl-α-ethyl-β-propiolactone)s,[34] and polymers of *R*-(+)-/*S*-(−)-α-methybenzyl methacrylates.[35] These applications lead not only to further understanding of stereocomplex systems but also to the functional modification of suitable substrates. Furthermore, the assembly of the PMMAs had a molecularly smooth surface, whereas that of the PLAs had a dotted surface. This difference may be due to the differences in the molecular assembly structures.

Other Parameters for Stepwise Assembly. To regulate the stepwise assembly of enantiomeric PLAs, it is significant to analyze the effect of other parameters such as the concentration of PLAs, immersion time of the QCM, and assembly temperature. Each parameter was altered on the basis of the conditions discussed above.

Figure 5 shows the frequency shift against each assembly step at the different concentrations. The frequency exponentially decreased with increasing assembly step in all cases, as discussed above. The shift increased with increasing the concentration. The inset shows the dependence of a frequency shift after a 12-step assembly and the ratio of the frequency shift (PLLA/PDLA) against the concentration. The shift after a 12-step assembly, which corresponds to the assembly amount, increased linearly with increased concentration. The surface coverage by PLAs might therefore be increased by increasing the concentration. The ratio was, however, independent of the concentration and was around 1. This indicates that stepwise stereocomplex assembly is achieved even though the concentration was changed.

Figure 6 shows the frequency shift against each assembly step with different immersion times. The frequency similarly decreased with increasing assembly step in all cases. The shift increased with increasing time. The inset shows the dependence of a frequency shift after an 8-step assembly and the ratio on time. The shift increased almost linearly with increasing time. Why we obtained this result is difficult to explain, although Tsuji et al. demonstrated that it takes more than 1 day to obtain the stereocomplex precipitate.[22] The increase in assembly amount with a lengthy immersion time is discussed further in the following section. The ratio was similarly around 1, indicating stepwise stereocomplex assembly.

Figure 7 shows the frequency shift against each assembly step at different solution temperatures. The frequency similarly decreased with increasing assembly

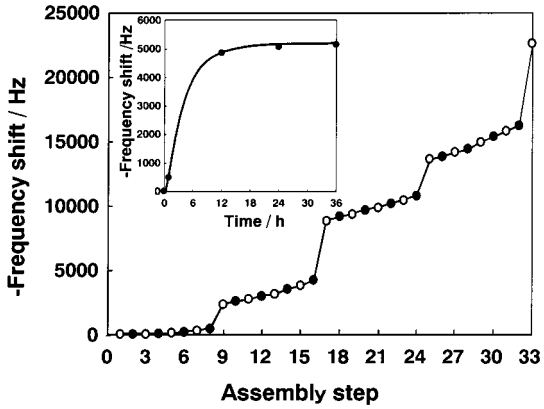

Figure 8. Heterogeneous assembly of PLAs at a concentration of 10 mg mL^{-1} at 50 °C. QCM was immersed for 12 h in a PLLA solution after every 8-step alternate assembly, for each 15 min immersion time.

step in all cases, and the shift decreased with increasing temperature. The inset shows the dependence of a frequency shift after a 12-step assembly and the ratio on temperature. The shift decreased almost linearly with increasing temperature. The PLAs used could be dissolved in acetonitrile above 40 °C. The enhanced solubility at higher temperature seemed to decrease the assembly amount. In fact, it is well-known that physisorption of polymers is enhanced from a poor solvent.[36] The ratio was also around 1, indicating stepwise stereocomplex assembly.

Heterogeneous Assembly. When the QCM immersion time was increased in the former section, the assembly amount increased linearly, as shown in Figure 6. Here, the heterogeneous assembly was analyzed after much longer immersion times in certain PLA solutions.

Figure 8 shows the frequency shift against assembly step when the QCM was immersed for 12 h in a PLLA solution after every 8-step alternate assembly, for each 15 min immersion period. At the lengthy immersion steps, an obviously larger frequency shift was observed, indicating homogeneous deposition of PLLA on the stereocomplex assembly. The heterogeneous assembly, which includes an 8-step stepwise assembly (stereocomplex formation) and homogeneous PLLA deposition, was achieved by repeating the process. The homogeneous deposition reached equilibrium after around 12 h, as shown in the inset of Figure 8 (that is why we immersed for 12 h). It is significant to discuss why heterogeneous assembly was observed. As discussed in the former section, the polymer conformation on the assembly surface should be strictly regulated by stereocomplex formation. It is therefore reasonable to suggest that the homogeneous assembly of PLLA grew epitaxially on the complex surface. To further analyze the results, the heterogeneous assembly was analyzed by DSC. We observed only one peak at around 230 °C. The peak area was smaller than that observed in Figure 4a, when the total assembly amount was similar. If a conventional homocrystal of PLLA was formed on the assembly, the corresponding peak should be observed at around 170 °C. The PLLA in the homocrystal is closely packed with 10_3-helices, while the PLAs in the stereocomplex is with 3_1-ones. These data suggest that PLLA was grown epitaxially on the stereocomplex assembly. On the basis of this suggestion, the saturation curve of the inset suggests that the 3_1-helices of PLLA were gradually transformed to random conformations because of limitations in the epitaxial growth of PLLA. Further research on this heterogeneous assembly including structural analyses and functions will be needed in the near future. Regardless, it should be noted that the heterogeneous assembly of enantiomeric PLAs was achieved by using the present methodology.

Conclusion

Alternate immersion of a QCM substrate resulted in the stepwise assembly of enantiomeric PLAs by stereocomplex formation, which was further confirmed by DSC analysis. A dotted assembly was observed by AFM analysis, as this observation was further supported by the static contact angle measurement. The assembly amount was affected by certain parameters such as concentration, immersion time, and immersion temperature. Heterogeneous assembly was achieved by suitable altering of the immersion time. We found that a stereocomplex based on van der Waals contact between the polymers, without any entanglement, could be the basis of this alternate assembly. The present study advanced not only scientific knowledge related to polymeric behavior at the solid−liquid interface but also the practical application of substrate modification by biodegradable PLAs. Further research on biodegradability of the present assembly and applications to other polymer systems are now in progress.

Acknowledgment. We acknowledge Dr. A. Kishida (Kagoshima University, Japan) for fruitful discussions. This work was financially supported in part by a Grant-in-Aid for Scientific Research in the Priority Area of "Molecular Synchronization for Design of New Materials System" (No. 404/11167270) and by a Grant-in-Aid for Scientific Research (No. 12750802) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

References and Notes

(1) Decher, G. *Science* **1997**, *277*, 1232.
(2) Linford, M. R.; Auch, M.; Möhwald, H. *J. Am. Chem. Soc.* **1998**, *120*, 178.
(3) Kong, J.; Lu, Z.; Lvov, Y. M.; Desamero, R. Z. B.; Frank, H. A.; Rusling, J. F. *J. Am. Chem. Soc.* **1998**, *120*, 7371.
(4) Lvov, Y.; Onda, M.; Ariga, K.; Kunitake, T. *J. Biomater. Sci. Polym. Ed.* **1998**, *9*, 345.
(5) He, J.-A.; Samuelson, L.; Li, L.; Kumar, J.; Tripathy, S. K. *Langmuir* **1998**, *14*, 1674.
(6) Serizawa, T.; Takeshita, H.; Akashi, M. *Langmuir* **1998**, *14*, 4088.
(7) Zhao, M.; Liu, Y.; Crooks, R. M.; Bergbreiter, D. E. *J. Am. Chem. Soc.* **1999**, *121*, 923.
(8) Harris, J. J.; DeRose, P. M.; Bruening, M. L. *J. Am. Chem. Soc.* **1999**, *121*, 1978.
(9) Caruso, F.; Lichtenfeld, H.; Donath, E.; Möhwald, H. *Macromolecules* **1999**, *32*, 2317.
(10) Kaschak, D. M.; Lean, J. T.; Waraksa, C. C.; Saupe, G. B.; Usami, H.; Mallouk, T. E. *J. Am. Chem. Soc.* **1999**, *121*, 3435.
(11) Wu, A.; Yoo, D.; Lee, J.-K.; Rubner, M. F. *J. Am. Chem. Soc.* **1999**, *121*, 4883.
(12) Stockton, W. B.; Rubner, M. F. *Macromolecules* **1997**, *30*, 2717.
(13) Shimazaki, Y.; Mitsuishi, M.; Ito, S.; Yamamoto, M. *Langmuir* **1997**, *13*, 1385.
(14) Shimazaki, Y.; Mitsuishi, M.; Ito, S.; Yamamoto, M. *Langmuir* **1998**, *14*, 2768.
(15) Serizawa, T.; Hamada, K.; Kitayama, T.; Fujimoto, N.; Hatada, K.; Akashi, M. *J. Am. Chem. Soc.* **2000**, *122*, 1891.
(16) Serizawa, T.; Hamada, K.; Kitayama, T.; Katsukawa, K.; Hatada, K.; Akashi, M. *Langmuir* **2000**, *16*, 7122.
(17) Hamada, K.; Serizawa, T.; Kitayama, T.; Fujimoto, N.; Hatada, K.; Akashi, submitted.

(18) Ikada, Y.; Jamshidi, K.; Tsujii, H.; Hyon, S.-H. *Macromolecules* **1987**, *20*, 906.
(19) Tsujii, H.; Horii, F.; Hyon, S.-H.; Ikada, Y. *Macromolecules* **1991**, *24*, 2719.
(20) Tsujii, H.; Hyon, S.-H.; Ikada, Y. *Macromolecules* **1991**, *24*, 5651.
(21) Tsujii, H.; Hyon, S.-H.; Ikada, Y. *Macromolecules* **1991**, *24*, 5657.
(22) Tsujii, H.; Hyon, S.-H.; Ikada, Y. *Macromolecules* **1992**, *25*, 2940.
(23) Tsujii, H.; Ikada, Y. *Macromolecules* **1992**, *25*, 5719.
(24) Tsujii, H.; Horii, F.; Nakagawa, M.; Ikada, Y.; Odani, H.; Kitamaru, R. *Macromolecules* **1992**, *25*, 4114.
(25) Tsujii, H.; Ikada, Y. *Macromolecules* **1993**, *26*, 6918.
(26) Brizzolara, D.; Cantow, H.-J.; Diederichs, K.; Keller, E.; Domb, A. J. *Macromolecules* **1996**, *29*, 191.
(27) For example: Wise, D. L.; Fellmann, T. D.; Sanderson, J. E.; Wentworth, R. L. *Drug Carrier in Biology and Mehicine*; Gregoriadis, G., Ed.; Academic Press: New York, 1979; pp 237−270.
(28) For example: Amass, W.; Amass, A.; Tighe, B. *Polym. Int.* **1998**, *47*, 89.
(29) Sauerbrey, G. *Z. Phys.* **1959**, *155*, 206.
(30) Fukuzawa, T.; Uematsu, I. *Polym. J.* **1974**, *6*, 537.
(31) Takahashi, T.; Tsutsumi, A.; Hikichi, K.; Kaneko, M. *Macromolecules* **1974**, *7*, 806.
(32) Baba, Y.; Kagemoto, A. *Macromolecules* **1977**, *10*, 458.
(33) Heitz, F.; Cary, P. D.; Crane-Robinson, C. *Macromolecules* **1977**, *10*, 526.
(34) Grenier, D.; Prud'homme, R. E. *J. Polym. Sci., Polym. Phys. Ed.* **1984**, *22*, 577.
(35) Hatada, K.; Shimizu, S.; Terawaki, Y.; Ohta, K.; Yuki, H. *Polym. J.* **1981**, *13*, 811.
(36) Fleer, G. D.; Stuart, M. A. C.; Scheutjens, J. M. H. M.; Cosgrove, T.; Vincent, B. In *Polymers at Interfaces*; Chapman & Hall: London, 1993.

MA001705O