Molecular-Imprinted Nylon Membranes for the Permselective Binding of Phenylalanine as Optical-Resolution Membrane Adsorbents

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ABSTRACT: Nylon 6, nylon 6,6, and terephthalic phenylene polyamide (TPPP) were functionalized by phase-inversion molecular imprinting to add L-phenylalanine recognition ability. Formic acid containing 20 wt % nylon and 8 wt % L-phenylalanine was used as the solvent for the cast solution of the imprinting process. The resultant porous membranes behaved as membrane adsorbents that separated the L/D mixture of the substrate. The imprinted nylon 6 and nylon 6,6 presented high selectivity to the L-form substrate with respect to the TPPP membranes, but the imprinted TPPP membranes showed higher binding capacity with 0.57 μmol/g for L-phenylalanine. The apparent partition coefficients of L- and D-forms by the imprinted membranes were 6.8, 4.2, and 1.7 for nylon 6, nylon 6,6, and TPPP, respectively. The separation manner of the L- and D-forms from the mixture was also confirmed by membrane filtration under 1.5 kgf/cm^2 of applied pressure. The imprinted nylon 6, nylon 6,6, and TPPP membranes had separation factors of L- and D-phenylalanines of 1.1, 1.1, and 1.2, respectively. © 2005 Wiley Periodicals, Inc. J Appl Polym Sci 97: 620–626, 2005

Key words: membranes; molecular imprinting; molecular recognition; nylon; separation techniques

INTRODUCTION

Molecular imprinting is a very useful method for the preparation of recognition polymer materials, which selectively separate and concentrate a target molecule.[1–3] The technique imparts molecular recognition ability to polymer materials because it memorizes the target molecule with respect to its shape and functionality. In the noncovalent imprinting approach,[4] the hydrogen bonding between the polymer material and template molecule is the driving force for imprinting the target molecule. In an ordinary case, the recognition sites of the imprinted polymer are constructed by the common radical polymerization of a functional monomer and a crosslinking monomer in the presence of a template.[2–4] In template polymerization including a monomer–template complex, the resultant polymer matrix can complement the template molecule. However, without some modifications, this technique is unsuitable for the application of an imprinted matrix with a membrane shape. Some studies have addressed imprinted membranes, including those of Shea et al.[5] and Yoshikawa et al.[6,7] The latter reported that an imprinted amino acid polymer, which was highly crosslinked with styrene beads with oligopeptide chains, was embedded into a polyacrylonitrile–styrene copolymer membrane. On the other hand, to prepare imprinted membranes, we have developed phase-inversion imprinting,[8–10] which uses a polymer solution containing a template molecule. In the imprinting process, as shown in Figure 1, a polymer–template solution is coagulated and solidified in the nonsolvent water.[11,12] Then, template extraction enables the formation of imprinted sites in the polymer matrix. Hence, the resultant matrix can fix the volumetric size of the template during the solidification process. The resultant imprinted polymers have a porous membrane morphology and a higher binding capacity in permselective experiments for theophylline (THO)[10] and amino acid.[12,13] A high THO binding capacity and excellent recognition ability of THO analogues have been observed in THO imprinted membranes. Also, for amino acid recognition, nylon 6 has been functionalized with phase-inversion imprinting to form L-glutamine recognition sites in the polymer. These nylon membranes have amide hydrogen-bondable networks and show a stable membrane matrix for L- and D-glutamine recognition. However, little is known about the characteristics of imprinting matrices for various synthetic nylons with phase-inversion imprinting. Moreover, no separation behavior has been reported yet for the permselective bindings of optical-resolution membranes with imprinted properties.

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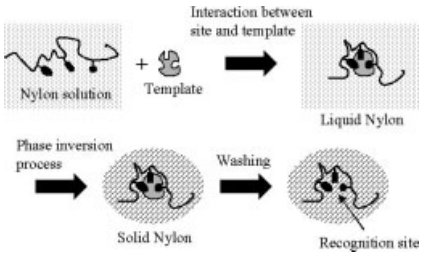


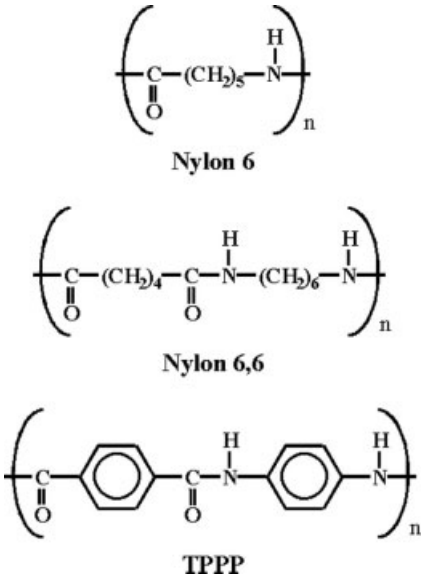
Figure 1 Illustration of the preparation process for molecular-imprinted membranes by phase-inversion imprinting.

This article specifically addresses phase-inversion imprinting for nylons with different chemical structures (Scheme 1). We report the separation behavior of L- and D-phenylalanines by imprinted nylon membranes, which have been characterized from the permselective binding of the target molecule. For the optical-resolution process of L- and D-phenylalanines, the first report of permeable separation imprinted membranes is made.

EXPERIMENTAL

Materials

Three types of nylons were used as imprinted membrane matrices: nylon 6 (Mitsubishi Chemical Corp., Japan), nylon 6,6 (Asahi Chemical Industry Co., Ltd., Japan), and terephthalic phenylene polyamide (TPPP; Novamid, Mitsubishi Chemical Corp.). L-Phenylalanine (Nacalai Tesque, Inc., Japan) was template molecule, and D-phenylalanine (Nacalai Tesque) was used as the binding substrate for recognition experiments.



Scheme 1 Chemical structures of nylon 6, nylon 6,6, and TPPP.

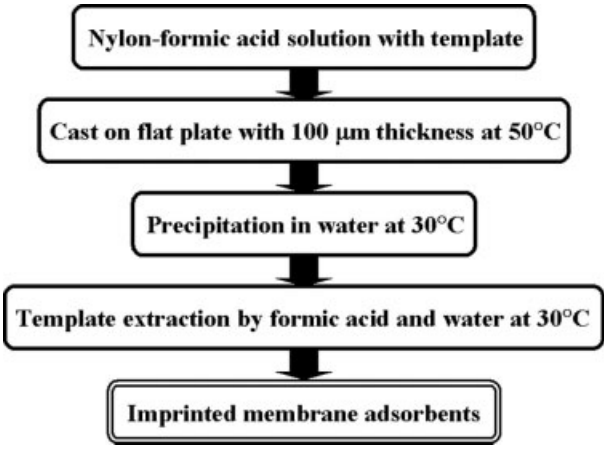


Figure 2 Schematic representation of imprinted nylon membranes preparation by the phase-inversion method.

Other reagents were analytical-grade chemicals and were used without further purification. Distilled water was employed as a coagulation nonsolvent for phase-inversion imprinting and for binding experiments of L- and D-phenylalanine aqueous solutions.

Preparation of the molecular-imprinted membranes

Molecular-imprinted nylon membranes were prepared by the phase-inversion method.[12,13] Figure 1 illustrates the imprint process, including phase inversion, for nylon 6. The imprint-including membrane formation process was performed during the phase inversion of a liquid nylon solution, which was converted into a solid matrix in water. For that purpose, a nylon cast solution was prepared with formic acid and a template, and then the phase-inversion process was carried out.[9,14] In the solidification of nylon, formic acid was highly soluble in water, but nylon was insoluble. Therefore, the nylon polymer precipitated in water. When the nylon solution contained a template, the resultant polymer membranes enveloped the template molecule in hydrogen-bonding networks of the precipitated nylons. The experimental procedure for imprinting membranes is presented schematically in Figure 2. A solution with 20 wt % nylon and 8 wt % L-phenylalanine was cast at 50°C onto a glass plate (200×200 cm^2) to a thickness of approximately 100 μm. Immediately, the solution coagulated in water at 30°C for 24 h. After nylon solidification, the membrane was washed well with distilled water to remove the formic acid solvent and the L-phenylalanine template at 30°C. In addition, the resulting nylon membrane was washed with a 0.1 wt % acetic acid aqueous solution for complete template extraction and then rinsed with an excess of water. For membrane characterization, Fourier transform infrared (FTIR) spectroscopy was used. The characterization of the nylon

membrane was performed before and after template extraction for the imprinted one. The FTIR spectra were measured with a transmittance setup with 20 accumulations with an FTIR spectrophotometer (FTIR 8100, Shimadzu Corp., Japan). Imprinted nylon samples without and with the L-phenylalanine template were obtained after freeze drying. We also used scanning electron microscopy (SEM; JSM-5310LVB, JEOL Co., Ltd., Japan) for the observation of the nylon membrane morphology.

Substrate recognition and binding by heterogeneous batch experiments to imprinted nylon membranes

Batch-binding experiments with the L-phenylalanine-imprinted nylon membranes were carried out in 40-mL aqueous solutions of 5 μM phenylalanine at 30°C. In these cases, both the L- and D-forms of the substrates were mixed; the concentration of each was 2.5 μM. The pH of the phenylalanine solution was adjusted to 6.5 with diluted NaOH and HCl. Before the substrate binding, the membrane was stored in water at a neutral pH (6.5). During the substrate binding, the L- and D-phenylalanine concentrations in the solution were determined by the monitoring of the UV absorbance of the substrate at 210 nm by high-performance liquid chromatography (HPLC; CCPS, Tosoh Corp., Japan) with a UV8000 UV detector and an optical-resolution column (4.0-mm i.d. and 15-cm length; Daicel Crownpack, Daicel Chemical Industries, Ltd.); the mobile phase composition was an $HClO_4$ aqueous solution at pH 2, and the rate of the flow into the column was 1 mL/min under 60 kgf/cm^2 of pressure. The concentrations of the L- and D-phenylalanines bound to the imprinted membranes ($[S]_L$ and $[S]_D$, respectively) were calculated as follows:

$$[S]_{L\text{ or }D} = (C_0 - C_t)V/W$$

where C_0 and C_t are the molar concentrations of phenylalanine measured at the initial time and the saturated binding time, respectively. In each imprinted membrane, the substrate binding concentrations were saturated at 2 h. V and W are the volume (L) of the phenylalanine aqueous solution and the weight (g) of the dry polymer used for the binding experiments, respectively. The apparent partition coefficient [$(P_{L/D})_{app}$] of the L- and D-forms for the imprinted membranes was calculated with $[S]_L$ and $[S]_D$ as follows:

$$(P_{L/D})_{app} = [S]_L/[S]_D$$

Permselective binding experiments of substrate solutions through L-phenylalanine-imprinted membranes

A 50-mL ultrafiltration (UF) cell (UF-8050, Amicon, Inc., Beverly, MA) was used to permeate the L- and D-phenylalanine mixed solution through the imprinted membranes. The experimental procedure was performed similarly to that reported in a previous article.[10] An imprinted membrane with a 43-mm diameter was mounted in a UF cell, and 40 mL of a phenylalanine aqueous solution was fed into the cell. The solution permeated through the membrane under an applied pressure of 1.5 kgf/cm^2. The permeation solution was collected at different time intervals. For L/D mixtures of phenylalanine in the permeation solution, the separation factor (α_s) of the imprinted membrane was defined and calculated as follows:[14,15]

$$\alpha_s = (C_{Lp}/C_{Dp})/(C_{Lf}/C_{Df})$$

where C_{Lp} and C_{Dp} are the L- and D-phenylalanine concentrations in the permeation solution and C_{Lf} and C_{Df} are the L- and D-phenylalanine concentrations in the feed solution. When α_s was 1, no separation was achieved; $\alpha_s > 1$ indicated that permselective binding was in the L-form by the membrane.

RESULTS AND DISCUSSION

Characterization of the imprinted nylon membranes

To study the interaction between L-phenylalanine and nylons, we measured FTIR spectra for the imprinted membranes. The samples were lyophilized overnight to dry the wet membranes completely. We previously reported that FTIR data gave evidence of interactions between the imprinted nylon and template molecule via hydrogen bonding.[13] In the spectroscopic data of the nylon samples, IR bands of amide–carbonyl hydrogen bands appeared near the 1000–2000-cm^{-1} region.[16] Figure 3(a,b) shows typical FTIR spectra of the TPPP membrane before and after template extraction; spectrum c was measured after 2 h of equilibrium binding of L-phenylalanine. The wave-number region is known to be characteristic of the amide–carbonyl absorption band of nylon.[17,18] Bands appeared near 1650 and 1550 cm^{-1} and were assigned to the C═O stretching vibration and N—H deformation, respectively. The bandwidth of the amide and carbonyl peaks differed for the spectral traces in Figure 3(a,b). That is, the IR peak width became sharp after the extraction of the template molecule with respect to that measured before substrate extraction. Also, comparing Figure 3(b,c), we find that broad peaks appear in Figure 3(c) for the imprinted membrane after L-phenylalanine rebounded. This fact indicates that the hydrogen-bonding network of TPPP nylon interacted with L-phenylalanine when the template molecule was incorporated into the membrane.

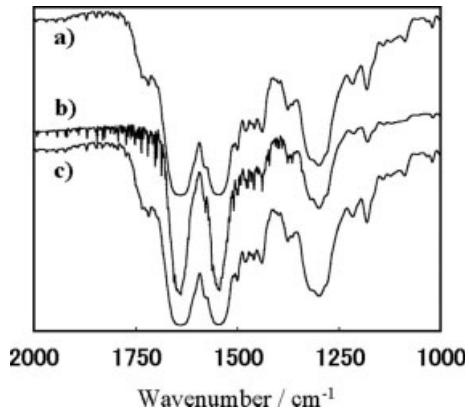


Figure 3 FTIR spectra of L-phenylalanine-imprinted TPPP membranes: (a) before the extraction of the template molecule from the polymer, (b) after the extraction of the template molecule from the polymer, and (c) after the incorporation of the template molecule.

Binding of L- and D-phenylalanine to the imprinted nylon membranes by heterogeneous batch experiments

$[S]_L$ has been compared with $[S]_D$ to determine the recognition characteristics of the L-phenylalanine-imprinted nylon membranes. Table I shows $[S]_L$, $[S]_D$, and $(P_{L/D})_{app}$. Batch-binding experiments were carried out for L-phenylalanine-imprinted and unimprinted membranes. $[S]_L$ and $[S]_D$ were calculated from the peak reduction of chromatographic data of L- and D-phenylalanines. The L-phenylalanine unimprinted membranes showed lower $[S]_L$ values than the imprinted membranes. Thus, $[S]_L$ and $[S]_D$ were 0.06–0.15 μmol/g in the unimprinted membranes. For the L-phenylalanine-imprinted membranes, $[S]_L$ was higher than $[S]_L$ for the unimprinted membranes, which had a binding capacity of 0.29–0.57 μmol/g. For D-form binding, the imprinted membranes had $[S]_D$ values of 0.06 and 0.07 μmol/g for nylon 6 and nylon 6,6, respectively. However, the imprinted TPPP membranes had high values of the binding capacity with $[S]_L = 0.57$ μmol/g for the L-form and $[S]_D = 0.33$ μmol/g for the D-form. Therefore, $(P_{L/D})_{app}$ was 1.7 for the imprinted TPPP and was lower than that of the other nylon membranes (6.8 and 7.2 for nylon 6 and nylon 6,6, respectively). This difference indicates that the imprinted nylon 6 and nylon 6,6 had somewhat better recognition ability for L-phenylalanine.

Figure 4 presents SEM pictures of cross sections of L-phenylalanine-imprinted membranes made of nylon 6, nylon 6,6, and TPPP. Figure 4(d–f) presents SEM pictures of unimprinted membranes made of nylon 6, nylon 6,6, and TPPP, respectively. These membranes showed porous structures in the cross sections. Nylon 6 and nylon 6,6 also showed similar porous morphologies, but the assembled nylon 6 layer looked somewhat dense with respect to that of nylon 6,6. Because the template was enveloped by nylon networks during phase-inversion imprinting, the solidification might be effective for a slightly higher selectivity of the L-form with respect to the D-form. The porous morphology of the membranes changed slightly in the absence and presence of the template molecule during the phase-inversion process. There was a tendency for unimprinted membranes to show a dense structure in the cross sections of nylon 6 and nylon 6,6. Therefore, a comparison of the SEM data indicated that the porous morphology was enhanced in the presence of the template molecule. We performed preliminary experiments with different template concentrations of 2, 4, 8, and 10 wt % in the cast solutions for the membrane preparation. These results indicated that the higher template concentration in the cast solutions engendered a highly porous structure of the membranes. However, a lower template concentration was unsuitable for permeation experiments. In addition, when the concentration of the template was higher than 10 wt %, membrane weakness was caused under a high pressure of permeation. As a result, we attempted permeation experimentation with nylon membranes prepared with nylon concentrations of 8 wt % for the L-phenylalanine template.

Permselective binding of L-phenylalanine in permeation experiments of the imprinted nylon membranes

As mentioned previously, imprinted nylon membranes prepared by the phase-inversion process had a porous structure. Thus, porous nylon membranes

TABLE I
[S] and $(P_{L/D})_{app}$ Values Obtained in Batch-Binding Experiments in 5 μM L- and D-phenylalanine Mixture Solutions for Imprinted Nylon Membranes for 2 h

	Imprinted			Unimprinted		
	[S] (μmol/g of polymer)			[S] (μmol/g of polymer)		
Polymer	L-form	D-form	$(P_{L/D})_{app}$	L-form	D-form	$(P_{L/D})_{app}$
Nylon 6	0.39	0.06	6.8	0.08	0.06	1.3
Nylon 6,6	0.29	0.07	4.2	0.10	0.15	0.7
TPPP	0.57	0.33	1.7	0.10	0.07	1.5

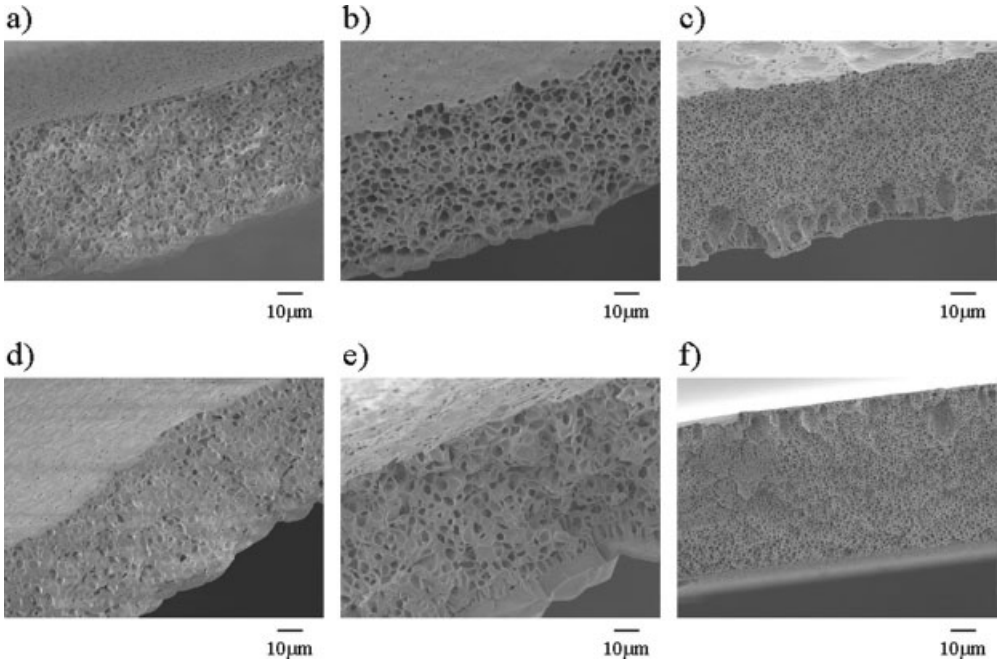


Figure 4 SEM cross sections of L-phenylalanine-imprinted nylon membranes by phase-inversion imprinting: (a) imprinted nylon 6 membrane, (b) imprinted nylon 6,6 membrane, (c) imprinted TPPP membrane, (d) unimprinted nylon 6 membrane, (e) unimprinted nylon 6,6 membrane, and (f) unimprinted TPPP membrane.

were successfully applied as permeable membrane materials for low-pressure permeation for high-efficiency desalination.[16] In this work, permeation experiments with the membranes were carried out at 1.5 kg/cm^2 of pressure for a 5 μM phenylalanine solution with 2.5 μM concentrations of the L- and D-forms. When imprinted membranes prepared with a 8 wt % template concentration were used for the permeation experiments of the phenylalanine solution, we collected the permeation solution and measured the concentrations of the phenylalanines at different time intervals. The L- and D-phenylalanine concentrations in the permeation solution were determined by HPLC analysis. Also, the water permeation confirmed that no leak of the L-phenylalanine template from the membranes occurred before L- and D-phenylalanine separation. For the permeation for each membrane, the volume flux was determined from the solution volume permeated per unit of time.[14] The volume flux values were 9.7×10^{-8}, 8.8×10^{-8}, and 7.4×10^{-8} m^3/m^2 s for nylon 6, nylon 6,6, and TPPP membranes, respectively. During the permeation experiments for 10 h under a high applied pressure, the volume flux was almost constant. Figure 5 shows the L- and D-phenylalanine concentrations of the permeation solution and α_s obtained in permeation experiments for L-phenylalanine-imprinted membranes. In Figure 5(a), the closed symbols represent the L-form, and the open symbols represent the D-form. At time zero, the concentrations of the L- and D-forms were 2.5 μM. The concentration of phenylalanine in the permeation so-

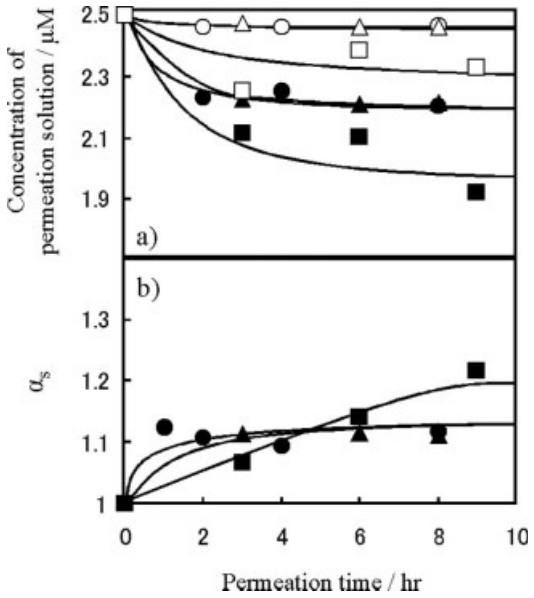


Figure 5 Time profiles of (a) the concentrations of L- and D-phenylalanines in permeation solutions and (b) the α_s values obtained for imprinted nylon membranes: (○,●) nylon 6 membranes, (△,▲) nylon 6,6 membranes, and (□,■); TPPP membranes. The applied pressure in the filtration was 1.5 kgf/cm^3. The permeation solutions contained L- and D-phenylalanines, each at a concentration of 2.5 μM at time zero. The open and closed symbols represent the binding experiments for L-phenylalanine and D-phenylalanine, respectively.

lution decreased as the permeation time increased. This tendency was remarkable in the L-form with respect to that in the D-form for each imprinted membrane. The reduction of the L- and D-phenylalanine concentrations in the permeation solution was due to substrate binding to the imprinted membrane. α_s, measured at various permeation times, was 1.1–1.2 in the nylon 6 and nylon 6,6 membranes. The values of α_s obtained for nylon 6 and nylon 6,6 were constant throughout the permeation experiments. However, the value of α_s for the imprinted TPPP membrane increased as the permeation time increased. The binding sites were eventually saturated because the imprinted membranes contained substrate binding sites for the target molecule. Therefore, no separation proceeded because of substrate saturation. Then, we found $\alpha_s = 1$. However, the time dependence of α_s in Figure 5(a) shows that α_s was greater than 1. This suggests the possibility of facilitated transport of the bound substrates through the imprinted membranes. That is, the substrate transport was followed by the mechanism of facilitated or carrier-mediated transport of the imprinted target molecule.[19] On the other hand, the imprinted TPPP membrane showed a somewhat different dependence of α_s on the permeation time. The imprinted TPPP membrane exhibited an increased α_s value with time. The binding capacity in the batch-binding experiments showed high binding concentrations of phenylalanine for the TPPP membrane. In addition, a low permeate flux of 7.4×10^{-8} m^3/m^2 s was observed for the TPPP membrane in comparison with those of the other membranes (9.7×10^{-8} and 8.8×10^{-8} m^3/m^2 s for nylon 6 and nylon 6,6, respectively). Therefore, the TPPP membrane remained in an unsaturated condition of the imprinted sites after even 10 h of permeation. This fact strongly suggests that the TPPP membrane provided inefficient separation for the permeation experiment under a high applied pressure. That is, the permselective binding of the TPPP membrane depended on a low residence time of solute molecules. In other words, a low permeable flux of the TPPP membrane caused low binding and a long time for the saturation of imprinted sites when a solute solution permeated. This tendency of the TPPP membrane resulted from the membrane morphology, which had very fine pores of less 1 μm in diameter [Fig. 4(c,f)]. Consequently, the imprinted TPPP showed low permeation ability under a high applied pressure.

Selective recognition of D-phenylalanine by the D-form imprinted nylon membrane

To examine D-form phenylalanine imprinting, we attempted to imprint the nylon 6 membrane, which showed better performance of L-form imprinting. The preparation and estimation of the selectively recognized ability of the resultant D-form imprinted membrane were similar to those of the L-form imprinting. Figure 6 shows $[S]_D$, $[S]_L$, and $(P_{D/L})_{app}$. The D-form imprinted membranes had selective recognition ability for D-phenylalanine because the imprinted membranes showed a high binding capacity of the D-form with respect to the L-form. In addition, $[S]_D$ was 0.33 and $(P_{D/L})_{app}$ was 6.6 for the D-form imprinted membrane. Those values were almost the same as those for the L-form imprinted nylon 6 membrane in Table I: $[S]_L = 0.39$ and $(P_{D/L})_{app} = 6.8$. Therefore, it was confirmed that both D-phenylalanine and L-phenylalanine could imprint with the phase-inversion process of nylon 6.

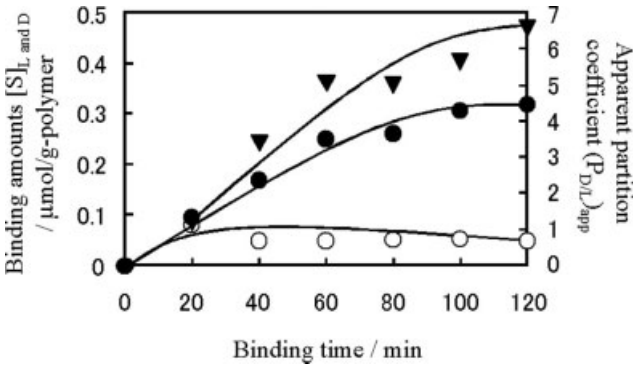


Figure 6 $[S]_D$, $[S]_L$, and $(P_{D/L})_{app}$ for D-form imprinted nylon 6 membranes in batch-binding experiments: (●) $[S]_D$, (○) $[S]_L$, and (▼) $(P_{D/L})_{app}$.

CONCLUSIONS

This article includes evidence of the first report of L- and D-phenylalanine separation in permeation experiments with imprinted membranes. A porous morphology of the membranes was observed for L- and D-phenylalanine binding in batch and permeation experiments. In addition, selective recognition and separation binding of L- and D-phenylalanines were confirmed for nylon 6, nylon 6,6, and TPPP membranes. The L-form imprinted nylon 6 and nylon 6,6 showed somewhat high recognition and selective binding to the L-form. Thus, the membranes had characteristics of adsorbent membranes in batch experiments. In addition, when D-phenylalanine was imprinted to the nylon 6 membrane, we confirmed the recognition and selective binding abilities of the D-form. In the permselective binding of phenylalanines, an α_s value of 1.1–1.2 was observed throughout the operation time. We concluded that the imprinted sites of the porous nylon membranes prepared by phase-inversion imprinting behaved as facilitated transport of the adsorbed L-phenylalanine in the separation process. In the future, the behavior of the permselective binding of porous imprinted membranes will be investigated

with respect to enantioselectivity for amino acid analogues under various conditions, such as different pHs and salt concentrations. Further efforts are now in progress.

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