Enantioselective Permeability through Membranes from a Poly(substituted phenylacetylene) Having a Chiral Helical Backbone and Achiral Bidentate Ligands as Pendant Groups

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A chiral helical poly(phenylacetylene) bearing *N*-(2-hydroxyethyl)aminomethyl groups as ligand sites was synthesized by helix-sense-selective polymerization. In the obtained polymeric membrane, the ligands could complex with Cu^{2+}. In permeation of aqueous solution of racemic phenylalanine, enantioselectivity in permeation through the Cu^{2+} complexing membrane was about 3 times higher than that of the original membrane.

Human bodies consist of biopolymers produced from some optically active compounds such as L-amino acids and D-saccharides. Therefore, each enantiomer often has different bioactivities to human bodies. For example, if one enantiomer shows good efficacy in use for medicine, the other may show toxicity. For this reason, optically pure compounds need to be used in pharmaceutical, agrochemical, and food industry. Optical resolution is an important method of obtaining pure single enantiomers. Particularly, high-performance liquid chromatography using chiral stationary phases is one of the most popular methods for optical resolution. Although optical resolution membranes have been studied by several researchers,[1] they have not been practically used. Since they have possibility separating a large amount of racemates, it is worthwhile to develop new ones.

In our laboratory, many kinds of chiral poly(substituted acetylene)s have been synthesized and applied for optical resolution membranes.[2] Because the chiral poly(substituted acetylene)s prepared from chiral monomers had two kinds of chiral recognition sites, i.e., a chiral main chain and chiral pendant groups, we could not confirm optical resolution abilities of the chiral helical main chain.[3] Recently, we succeeded in obtaining a chiral helical poly(substituted phenylacetylene) having an asymmetric structure only in the main chain. This polymer was synthesized by helix-sense-selective polymerization of achiral 4-dodecyloxy-3,5-bis(hydroxymethyl)phenylacetylene (DoDHPA) by use of a chiral catalytic system consisting of $[Rh(2,5\text{-norbornadiene})Cl]_2$ and chiral phenylethylamine ((*R*)- or (*S*)-PEA).[3] In addition, the polymer showed good membrane forming ability and its membrane exhibited enantioselective permeatbility. The fact indicated directly effectiveness of the main-chain's chirality on enantioselectivities.[4] To our knowledge, this is the first example to confirm the effectiveness.

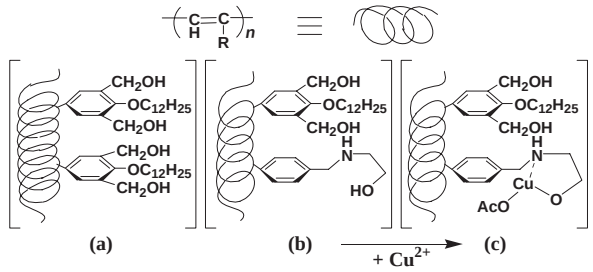

Figure 1. Chiral helical poly(phenylacetylene) membranes used in this study.

Since enantioselectivity of the chiral membrane from poly(DoDHPA) (Figure 1a) was not so high, achiral ligands were introduced to its pendants which can interact more effectively with permeants to improve enantioselectivity. We synthesized a new ligand having one-handed helical poly(substituted phenylacetylene) as a chiral source by helix-sense-selective copolymerization of DoDHPA and a new ligand containing phenylacetylene, *p*-((2-hydroxyethyl)aminomethyl)phenylacetylene (HAMPA) (Figure 1b).

The properties of three polymer membranes used in this study are listed in Table 1. Membrane (c) was obtained by complexing Cu^{2+} with the ligands in membrane (b). The amount of Cu^{2+} ion complexing with the ligands was estimated by adsorption experiment using a two-chamber cell which was also used for permeation experiment (Figure 2). $[Cu^{2+}]$ complexed in the membrane was calculated from $[Cu(OAc)_2]$ remained in the feed side determined by absorbance. $[Cu^{2+}]$/[HAMPA unit] was over 1.0 in membrane (c) (Table 1). On the other hand, $[Cu^{2+}]$ in the permeate side was almost zero after 5 weeks.

Permeations of aqueous solution of DL-phenylalanine driven by concentration gradient were carried out using the same cell (Figure 2). The experimental procedures and calculation of permeability coefficients (*P*), diffusion coefficients (*D*), and solubility coefficients (*S*) were carried out according to the same manner we reported previously.[5] The results for three membranes from poly(DoDHPA) (a), poly(DoDHPA-*co*-HAMPA) (b) and Cu^{2+}–poly(DoDHPA-*co*-HAMPA) complex (c) are shown in Figure 3 and Table 2.

Table 1. Properties of chiral helical poly(phenylacetylene) membranes used in this study

Membrane	HAMPA unit[a] /mol %	M_w[b] ($\times 10^5$)	M_w/M_n[b]	$[\alpha]_D^{20}$[c] /degree	$[Cu^{2+}]$/[HAMPA unit][d]	Thickness /μm
(a)	0	11.6	4.05	−238.7	0	26
(b)	3.76	397	5.22	−146.7	0	30
(c)	3.76	397	5.22	−146.7	1.23	30

[a]Calculated from elemental analysis. [b]By GPC correlating polystyrene standard. [c]$c = 0.031$ g/dL in THF. [d]Determined by adsorption exp.

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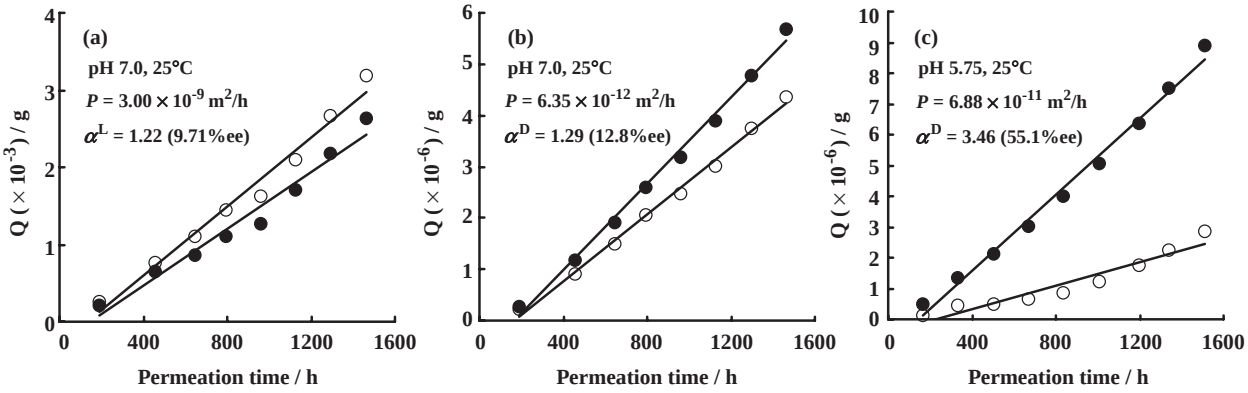

Figure 3. Plots of quantity (Q) of permeated D-phenylalanine (●) and L-phenylalanine (○) vs permeation time through a polymeric membrane (a), (b), and (c), respectively; feed = 0.5 wt % aqueous solution of DL-phenylalanine, permeation area = 7.07×10^{-6} m^2.

Table 2. Enantioselective permeation of 0.5 wt % aqueous solution of DL-phenylalanine through a polymeric membrane at 25 °C

Membrane	pH	$P \times 10^{11}$ [a] /m^2·h^{-1}	α (=P_D/P_L)	e.e. /%	$D_D \times 10^{12}$ [b] /m^2·h^{-1}	D_D/D_L	$S_D \times 10^{2}$ [c]	S_D/S_L
(a)	7.0	300	0.82 (1.22)[d]	9.71 (L)	0.76	0.65 (1.54)[e]	1760	1.23
(b)	7.0	0.64	1.29	12.8 (D)	0.86	0.95	4.16	1.36
(c)	5.7	0.69	3.54	56.0 (D)	1.03	1.52	5.21	2.33

[a]Permeation coefficient. [b]Diffusion coefficient of D-isomer. [c]Solubility coefficient of D-isomer. [d]P_L/P_D. [e]D_L/D_D.

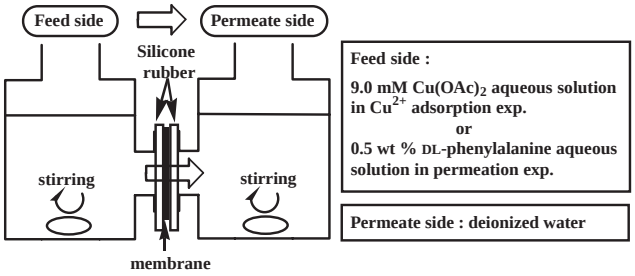

Figure 2. Schematic diagram of a two-chamber cell.

As we reported in the other papers, the main chain chirality of poly(DoDHPA) had enantioselectivity.[4] However, the α (=P_D/P_L) values of membrane (a) and (b) were not high because of weak interaction with DL-phenylalanine. Membrane (c) exhibited the best enantioselectivity in this study by introducing the complex sites.

Interestingly, the sign of the enantioselectivity was opposite for membranes (a) (L-selective) and (b), (c), (D-selective) (Figure 3 and Table 2). This may be caused by the change of permeation mechanism. The α of membrane (a) ($P_L/P_D = 1.22$) was mainly determined by the diffusion selectivity ($D_L/D_D = 1.54$). On the other hand, the D_D/D_L of membrane (b) was almost 1.0 and the selectivity was mainly governed by the solution selectivity. One of the reasons may be the change of the chiral helical structures.[6] In case of membrane (c), the S_D/S_L was enhanced by complexing Cu^{2+}, resulting in the best selectivity.

The P values of membranes (b) and (c) were significantly lowered in comparison with that of membrane (a) (Table 2). Both the P and α values of membrane (c) were better than those of membrane (b). This phenomenon is unexpected because simultaneous improvement of enantioselectivity and permeability was generally difficult. As shown in Table 2, the good α value of membrane (c) was due to the highest S_D/S_L value. In addition, the chiral helical structure of membrane (c) was not changed by complexation from the CD and UV–vis spectra.[6] Therefore, it is considered that the complex site acted as a chiral selector that may facilitate the permeability of D-phenylalanine.

In conclusion, a new ligand-containing chiral poly(phenylacetylene) membrane was prepared, and its Cu^{2+}-complexing membrane exhibited better enantioselective permeability than the original membrane.

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