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Chiral Polyurea with L-Lysinyl Residue Aimed for Optical Resolution

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Abstract: Novel polyurea was synthesized from lysinyl residue, L-lysine-4-nitroanilide (L-Lys-4-NA) and 1,4-phenylene diisocyanate (1,4-PDI). The polyurea thus prepared gave durable self-standing membranes. The polyurea was converted into molecular recognition materials by using Z-D-Glu or Z-L-Glu as a print molecule. The Z-D-Glu molecularly imprinted membrane adsorbed the D-isomer of Glu in preference to the corresponding L-isomer and *vice versa*. Even though the polyurea consisted of L-lysinyl residue, both Z-D-Glu and Z-L-Glu worked as print molecules to construct molecular (chiral) recognition sites in the membrane. Those two types of molecularly imprinted membrane show chiral separation abilities, adopting a concentration gradient or an applied potential difference as a driving force for membrane transport.

Keywords: Chiral Separation, Membrane, Molecular Imprinting, Optical Resolution, Polyurea.

1. INTRODUCTION

In these days, the attentions of membranologists have been mostly focused on water treatment and reduction of carbon dioxide emission. Those are problems the globe has faced and have to be immediately solved. Furthermore, membrane separation is expected to contribute to solve the critical global issues we have faced; (1) environmental problems, such as water pollution by volatile organic compounds (VOCs), endcrine disruptors etc., air pollution, and so forth, (2) energy/resource problems, such as water resources, fuel cell, concentration difference power generation, utilization of biomass, etc., (3) health problems, such as artificial organs, production of pharmaceuticals, production and separation of optically pure drugs, and so forth. As enumerated above, membranes are expected to contribute to the globe as “Green Membranes”. Since membrane separation can be operated continuously under mild conditions and is perceived to be economically and ecologically competitive to other separation methods. Membranes are regarded as a promising separation media supporting safe, secure, and sustainable society.

Among problems, which can be solved by using membranes, separation of optically pure compounds from their racemic mixtures is not an urgent problem to be solved. However, it is an important subject to prepare for health problems, which will be soon emerged in the near future. As can be seen in various review papers [1-5], materials for membranes or stationary phases, which show optical resolution ability, are requisite to contain chiral environment or chiral selector (molecular recognition site) in them. To this end, the authors’ research group has been studied optical resolution with membranes, such as polymeric membranes [6-8] and nanofiber membranes [9-12] with molecular recognition sites introduced by an alternative molecular imprinting and those with chiral environment or chiral selector in a main chain [13, 14] or in a side chain [15-17].

In a link in the chain of studies on optical resolution with chiral polyurea [18-20], the chiral polyurea was prepared from L-lysine-4-nitroanilide (L-Lys-4-NA) as diamine component and 1,4-phenylene diisocyanate (1,4-PDI) as diisocyanate one. Its membrane performance was investigated adopting racemic mixture of glutamic acid (Glu) as a model racemate.

2. EXPERIMENTAL

2.1. Materials

L-Lys-4-NA dihydrobromide (L-Lys-4-NA/2HBr) was purchased from BACHEM AG and used without further purification. 1,4,-PDI was purified by sublimation under vacuum [21]. N-α-Benzyloxycrbonyl-D-glutamic acid (Z-D-Glu) and N-α-benzyloxycarbonyl-L-glutamic acid (Z-L-Glu) were purchased from Watanabe Chemical Ind., Ltd. (Hiroshima, Japan) and used without purification. Methanol, ethanol, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), D-glutamic acid (D-GLu), and L-glutamic acid (L-Glu) were obtained from commercial sources and used as received. Dimethylacetamide (DMAc), and triethylamine (TEA) were purified by the conventional methods [22]. Water purified with an ultrapure water

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system (Simpli Lab. Millilpore S. A., Molshein, France) was used.

2.2. Polyaddition

Requisite amounts of chemicals were placed in a reaction flask fitted with a condenser and a thermometer. The mixture was magnetically stirred at 0 °C for 18 h. The resulting solution was poured into water under rapid stirring, and the precipitate product was washed with water and then with methanol and dried *in vacuo*.

2.3. Characterization of the Polyurea

The viscosity number was determined with an Ubbelohde viscometer at a concentration of 5.0 x 10^{-3} g cm^{-3} in DMAc/LiCl (5 wt.%) at 25 °C.

The IR spectrum was recorded by using a Perkin-Elmer Spectrum GX; 64 scans at a resolution of 4 cm^{-1} were collected with a membrane, which was prepared from HFIP solution.

The ^1H NMR spectrum was recorded in DMF-d_7 using a BRUKER AV-300 with residual partially protonated solvent of DMF-d_7 as an internal standard (δ = 2.91 [23]).

The thermal stability of the polyurea was evaluated on a Hi-Res Modulated TGA 2950 (TA Instruments, Inc.) under nitrogen at heating rate of 10 °C min^{-1}.

Dynamic mechanical thermal analysis (DMTA) measurement was carried out with a dynamic mechanical analyzer, RSA III (TA Instruments, Inc.) in tension mode. The experiment was performed at a frequency of 1 Hz and a heating rate of 1.0 °C min^{-1} from 30 to 200 °C. The dimension of sample was 20.26 x 6.23 x 0.118 mm^3.

The specific rotations were obtained with Horiba SEPA-200 polarimeter at 589 nm at ambient temperature in DMF.

2.4. Membrane Preparation

The control membrane was prepared as follows: 60 mg of polyurea was dissolved in 1.20 cm^3 of DMAc. The polymer solution thus prepared was poured into a flat laboratory dish with 6.0 cm diameter, and the solvent was allowed to evaporate at 50 °C for 2 days. The thickness of the control membrane thus obtained was around 25.8 μm.

Molecularly imprinted polyurea membranes were also prepared. In the preparation of molecularly imprinted membranes, it was requisite to know the amount of the lysinyl residue in the polyurea, which was adopted as a candidate material for chiral separation membrane. To this end, it was necessary to know the amount of lysinyl residue in the polyurea to determine the molecular imprinting ratio, which was the mole ratio of the amount of print molecule to that of lysinyl residue in polyurea. Since the lysinyl residue in the polyurea was expected to dominantly show a role to construct chiral (molecular) recognition sites. In the present study, the polyurea was prepared by step-growth addition reaction, in other words, no by-product was emerged during polymerization. This simplified the polymerization process, even though biuret group was also formed in addition to urea linkage during the polymerization reaction [24, 25]. The amount of lysinyl residue in the candidate polyurea (Exp. No. 7 in Table **1**) was determined to be 2.18 x 10^{-3} mol Lys per g-polyurea, assuming that the polyaddition reaction was quantitatively proceeded, in other words, the composition of the obtained polyurea was exactly equal to the monomer composition. About 60.0 mg of (1.31 x 10^{-4} mol of lysinyl residue) of polyurea (Exp. No. 7 in Table **1**) and 18.4 mg (6.54 x 10^{-5} mol) of a print molecule (Z-D-Glu or Z-L-Glu) were dissolved in 1.20 cm^3 of DMAc. The imprinting ratio, the mole ratio of the amount of print molecule to that of lysinyl residue in polyurea, was fixed to be 0.50. The solution was poured into a flat laboratory dish with 6.0 cm diameter and dried at 50 °C for 2 days to evaporate the solvent. After drying, the print molecule was extracted from the resultant membrane by a large amount of 50 vol.-% aqueous ethanol until the print molecule was hardly detected in aqueous ethanol solution by UV analysis. In the present study, most of adopted print molecule was leached from the membrane. Thickness of the membrane thus obtained was around 28.4 μm for the Z-D-Glu molecularly imprinted membrane and 28.2 μm for the Z-L-Glu one, respectively.

2.5. Adsorption Selectivity

Membranes were immersed in racemic mixture of Glu solution, similar to the mixture studied in enantioselective transport and enantioselective electrodialysis, that is, aqueous solution of racemic Glu (each concentration of Glu, 1.0 x 10^{-3} mol dm^{-3}), and the membrane was allowed to be equilibrated at 40 °C. A 0.02 wt.-% of sodium azide was added as a fungicide. In the present study, the amount of racemic Glu adsorbed in the membrane was too low to be

Table 1: Polyaddition Reaction of L-Lys-4-NA/2HBr and 1,4-PDI[a]

Exp. No.	[L-Lys-4-NA]/[1,4-PDI]	L-Lys-pNA 2HBr	1,4-PDI	DMAc	TEA	Yield	η_i/C[b]
		g (mol dm^{-3})	g (mol dm^{-3})	cm^3	cm^3	g (%)	g^{-1}cm^3
1	1.00	0.6422 (1.50×10^{-1})	0.2402 (1.50×10^{-1})	9.55	0.45	0.5412 (84.61)	53.95
2	1.00	0.6423 (2.00×10^{-1})	0.2409 (2.00×10^{-1})	7.05	0.45	0.4828 (75.47)	28.53
3	1.00	0.6423 (2.50×10^{-1})	0.2403 (2.50×10^{-1})	5.55	0.45	0.5467 (85.47)	49.77
4	1.00	0.6421 (3.00×10^{-1})	0.2402 (3.00×10^{-1})	4.55	0.45	0.5451 (85.22)	65.19
5	0.83	0.5352 (1.25×10^{-1})	0.2403 (1.50×10^{-1})	9.3	0.7	0.5458 (95.25)	150.8
6	0.83	0.5352 (1.67×10^{-1})	0.2401 (2.00×10^{-1})	6.8	0.7	0.5460 (95.21)	200.0
7	0.83	0.5353 (2.08×10^{-1})	0.2401 (2.50×10^{-1})	5.3	0.7	0.5262 (91.83)	206.4
8	0.83	0.5351 (2.50×10^{-1})	0.2402 (3.00×10^{-1})	4.65	0.35	0.5427 (94.70)	186.5
9	0.67	0.4281 (1.00×10^{-1})	0.2401 (1.50×10^{-1})	9.4	0.6	0.4848 (95.72)	162.7
10	0.67	0.4282 (1.33×10^{-1})	0.2402 (2.00×10^{-1})	6.9	0.6	0.4899 (96.73)	202.5
11	0.67	0.4281 (1.67×10^{-1})	0.2402 (2.50×10^{-1})	5.4	0.6	0.4853 (95.82)	188.9
12	0.67	0.4282 (2.00×10^{-1})	0.2401 (3.00×10^{-1})	4.7	0.3	0.4715 (93.07)	167.5
13	0.50	0.3211 (7.50×10^{-2})	0.2402 (1.50×10^{-1})	9.60	0.40	0.4016 (91.30)	137.7
14	0.50	0.3211 (1.00×10^{-1})	0.2402 (2.00×10^{-1})	7.10	0.40	0.4037 (91.77)	141.7
15	0.50	0.3211 (1.25×10^{-1})	0.2403 (2.50×10^{-1})	5.60	0.40	0.4209 (95.67)	159.8
16	0.50	0.3211 (1.50×10^{-1})	0.2403 (3.00×10^{-1})	4.75	0.25	0.3984 (90.56)	171.0

[a] Polymerization temp., 0 ℃; polyrmerization time, 18 h.

[b] Measured at a concentration of 5.0×10^{-3} g cm^{-3} in DMAc/LiCl (5 wt.%) at 25 ℃.

determined precisely by the aliquots of the solution after equilibrium had been reached. From this, that was determined by desorption method; the membrane, which had reached equilibrium with racemic Glu solution, was taken out from the immersing solution, blotted free solution adhering on the surface, and then transferred to a 0.02 wt.-% NaN_3 aqueous solution to desorb the racemic Glu from the membrane. Aliquots of the solution of adsorption after equilibrium had been reached and that for desorption were used for quantitative estimation by liquid chromatography (LC) [Jasco PU-2080, equipped with a UV detector （Jasco UV-2075)], using a CHIRALPAK MA(+) column [50 x 4.6 mm (id)] (Daicel Chemical Ind.) and aqueous copper sulfate solution as an eluent.

The amount of Glu in the desorption gave the amount of Glu adsorbed by the membrane. The adsorption selectivity $S_{A(i/j)}$ is defined as:

$$S_{A(i/j)} = ((\text{i-Glu}) / (\text{j-Glu})) / ([\text{i-Glu}] / [\text{j-Glu}]) \tag{1}$$

where (i-Glu) and [i-Glu] are the amount of Glu adsorbed in the membrane and the concentration in the solution after equilibrium had been reached. Hereafter, subscripts of D and L mean the D- and L-isomer, respectively.

2.6. Enantioselective Membrane Transport

A membrane with area of 3.0 cm^2 was fixed tightly with Parafilm between two chambers of a permeation cell. The volume of each chamber was 40.0 cm^3. An aqueous solution of racemic Glu was placed in the left-hand chamber (L-side) and an aqueous solution in the right-hand chamber (R-side). Each concentration of racemic Glu was fixed to be 1.0 x 10^{-3} mol dm^{-3}. In both chambers, 0.02 wt.% of sodium azide was added as a fungicide. All experiments were carried out at 40 °C with stirring. An aliquot was drawn from the permeate side at each sampling time. The amounts of D- and L-isomers transported by the membrane were determined by LC as described above.

The flux, J (mol cm^{-2} h^{-1}), is defined as:

$$J = Q / At \tag{2}$$

where Q (mol) is the amount of transported Glu, A (cm^2) the effective membrane area, and t (h) is the time.

The permselectivity $\alpha_{i/j}$ is defined as the flux ratio J_i/J_j divided by the concentration ratio [i-Glu] / [j-Glu]:

$$\alpha_{i/j} = (J_i/J_j) / ([\text{i-Glu}] / [\text{j-Glu}]) \tag{3}$$

2.7. Enantioselective Electrodialysis

An aqueous solution of racemic Glu was placed in each chamber of the permeation cell. Each concentration of racemic Glu was fixed to be 1.0 x 10^{-3} mol dm^{-3}. The electrodialysis was carried out with a prescribed applied potential difference between platinum electrodes (1.0 cm^2; distance between the electrodes, 7.0 cm) at 40 °C with stirring. An aliquot was drawn from the transport side (R-side) at each sampling time. The amounts of D-Glu and L-Glu transported through the membrane were determined by LC as described above.

3. RESULTS AND DISCUSSION

3.1. Syntheses of Polyurea

A novel chiral polyurea was prepared from L-Lys-4-NA with asymmetric carbon and 1,4,-PDI by polyaddition reaction. The polymerization scheme is shown in Figure **1**. In IR spectrum of newly prepared polyurea, characteristic absorption bands at 1656 cm^{-1} assigned to C=O stretching band of urea and amide I band, that at 1552 cm^{-1} assigned to asymmetric vibration of $–NO_2$, and that at 1341 cm^{-1} assigned to asymmetric stretching vibration of $–NO_2$ were detected. The ^{1}H NMR spectrum of polyurea (Exp. No. 7 in Table **1**) is shown in Figure **2**.

The IR and ^{1}H NMR spectra revealed that the expected polyurea was obtained from L-Lys-4-NA and 1,4-PDI. However, stereoregularity of the polyurea as given in Figure **1** and the composition of urea and biuret linkage [23,24] in the present polyurea were hardly determined.

Optimization of polyaddition reaction is indispensable to obtain durable membranes from the present polyurea. To this end, first, effect of monomer concentration on polyaddition reaction was studied

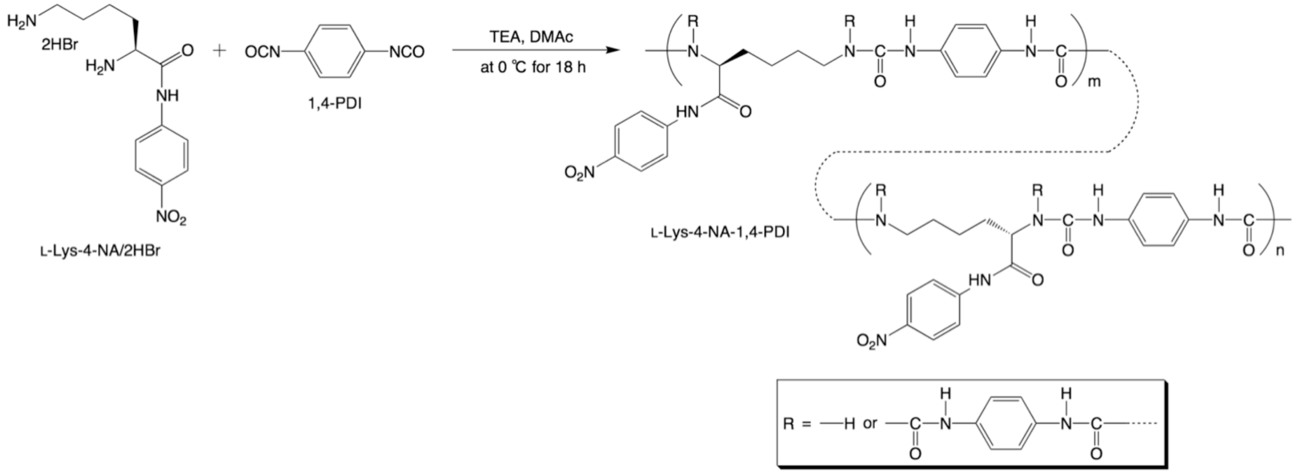

Figure 1: Polymerization scheme of chiral polyurea (L-Lys-4-NA-1,4-PDI).

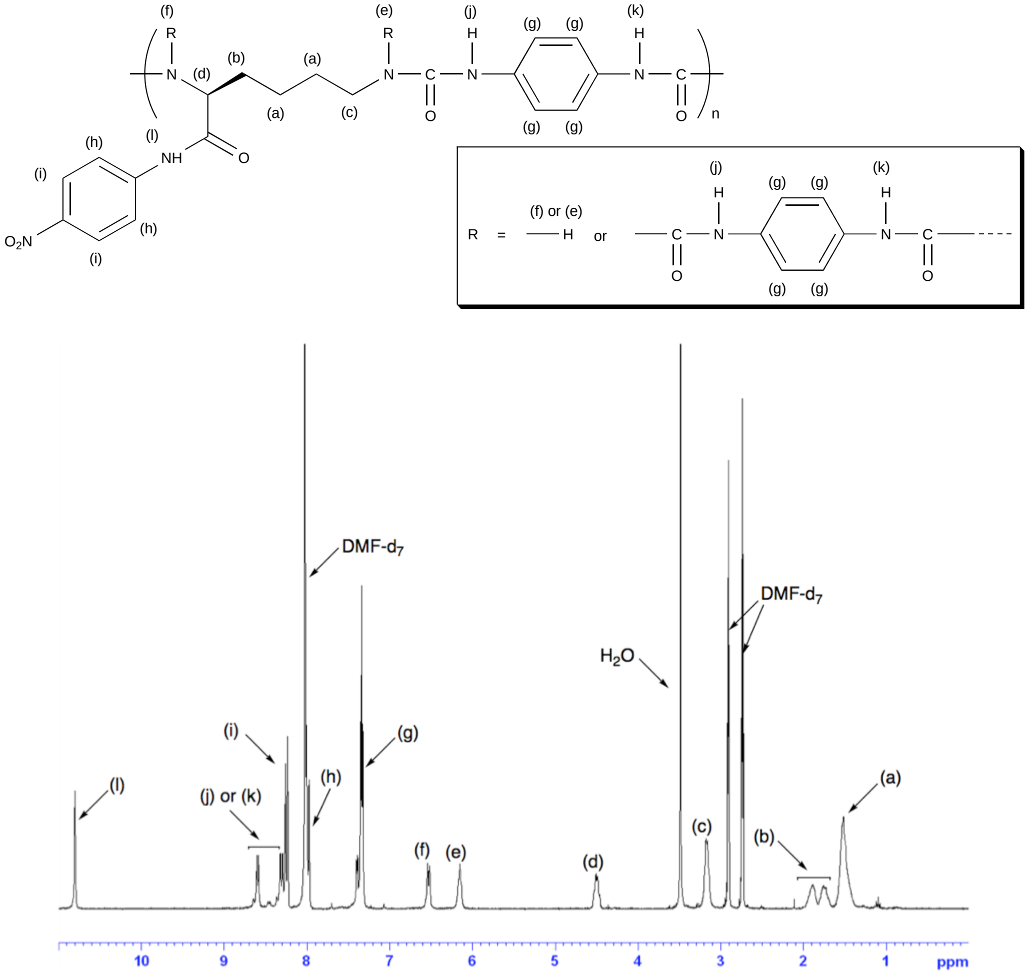

Figure 2: ^{1}H NMR spectrum of L-Lys-4-NA-1,4-PDI (Exp. No. 7 in Table **1**).

adopting equimolar amount of each monomer (Exp. No. 1 – 4 in Table **1**). The viscosity number, which can be correlated to molecular weight, was adopted as an index to the present study. The molecular weight (viscosity number) of polyurea (Exp. No. 1 – 4 in Table **1**) was too low to give a durable self-standing membrane. From the reaction conditions that the molar ratio of two types of monomer, [L-Lys-4-NA]/[1,4-PDI], was unity, most linkage formed in the polyurea was though to be a urea unit. The introduction of long side chains is expected to both increase the molecular weight and enhance the entanglement of polymer chains. This would be one of smart ways to obtain durable self-standing membranes from the present chiral polyureas. To this end, the introduction of biuret linkage into the polyurea was attempted.

The polyaddition reaction with the monomer ratio, [L-Lys-4-NA]/[1,4-PDI], of 0.83, 0.67, and 0.50 was studied in addition to that of unity. Those results are also summarized in Table **1** (Exp. No. 5 – 16), as well. Those results are visually shown in Figure **3** for convenience. Among those sixteen experiments, the polyurea prepared under the polyaddition reaction of the monomer ratio of 0.83 and the 1,4-PDI concentration of 2.50 x 10^{-1} mol dm^{-3} (Exp. No. 7 in Table **1**) gave the highest viscosity number. In the present paper, hereafter, this polyurea was adopted as a candidate material for membrane study.

3.2. Characterization of Polyurea

Thermogravimetric analysis of polyurea (Exp. No. 7 in Table **1**) was carried out and its thermograph is shown in Figure **4**. The degradation temperature of the present polyurea was determined to be 216.5 °C. L-Lys-4-NA-2,4-TDI, which consisted of the same lysine derivative of L-Lys-4-NA and 2,4-toluene diisocyanate (2,4-TDI), showed the degradation temperature of 231.4 °C [20], which was around 15 °C higher than that of the present polyurea. This might be due to the bulkiness of methyl group in 2,4-TDI unit rather than to the rigidness of 1,4-PDI unit [24,26]. Contrary to this, the T_d of the present polyurea was aroud 9 °C higher

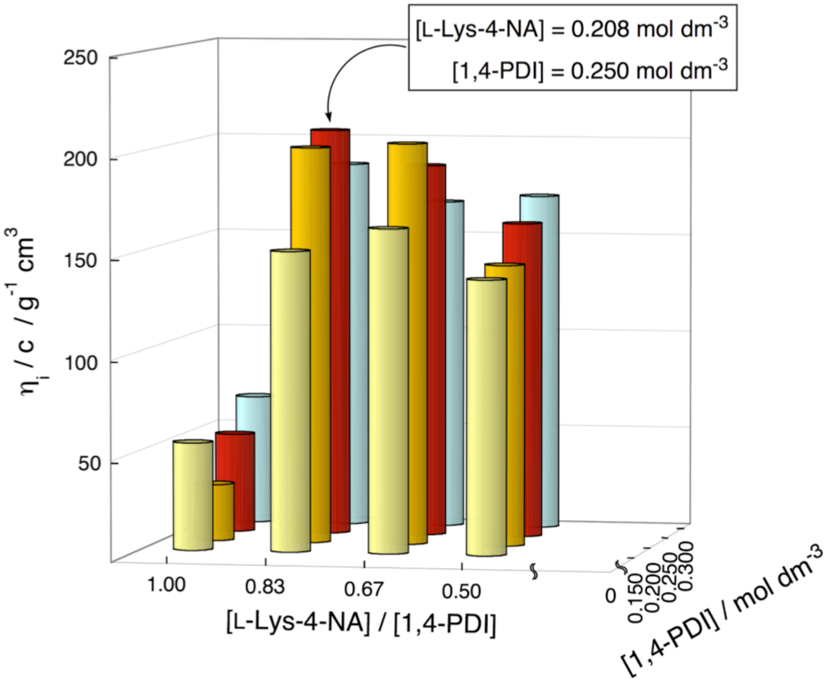

Figure 3: Results of polyaddition reaction of L-Lys-4-NA and 1,4-PDI.

than that of L-Lys-OEt-1,4-PDI (T_d, 207.7 °C), which was prepared from the same diisocyanate monomer, 1,4-PDI, and L-lysine ethyl ester (L-Lys-OEt) [18]. This is thought to be due to the steric hindrance of the bulkiness of a protecting group of 4-nitroanilide in L-Lys-4-NA unit.

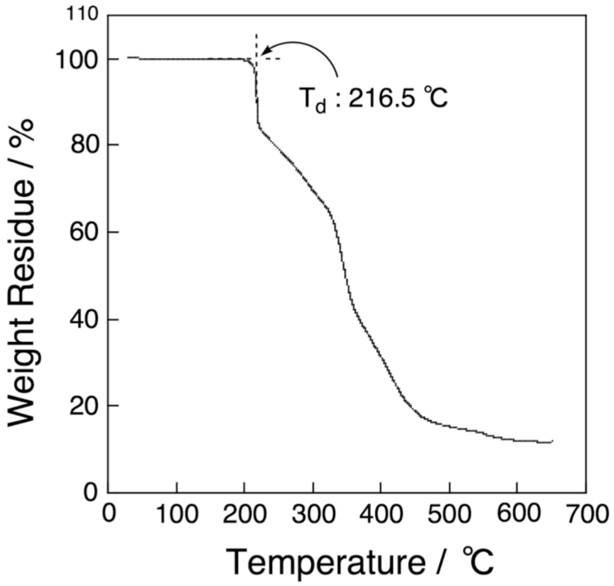

Figure 4: Thermogravimetric analysis curve of L-Lys-4-NA-1,4-PDI (Exp. No. 7 in Table **1**). (Heating rate, 10 °C min^{-1}).

Figure **5** shows dependences of dynamic storage modulus E', dynamic loss modulus E'', and tan δ on temperature for the polyurea (Exp. No. 7 in Tanle **1**). The single peak of tan δ, assigned to the glass transition temperature, can be found at 198.1 °C, which was higher than those of L-Lys-4-NA-2,4-TDI (162.9 °C [20]) and L-Lys-OEt-1,4-PDI (186.1 °C [18]). The 2,4-TDI, which was a component of L-Lys-4-NA-2,4-TDI, is more flexible than the 1,4-PDI in the present polyurea and the protecting group of ethoxy moiety in L-Lys-OEt unit is smaller than that of 4-nitroanilide in L-Lys-4-NA unit. Therefore, the present polyurea L-Lys-4-NA-1,4-PDI gave higher glass transition temperature than those polyureas.

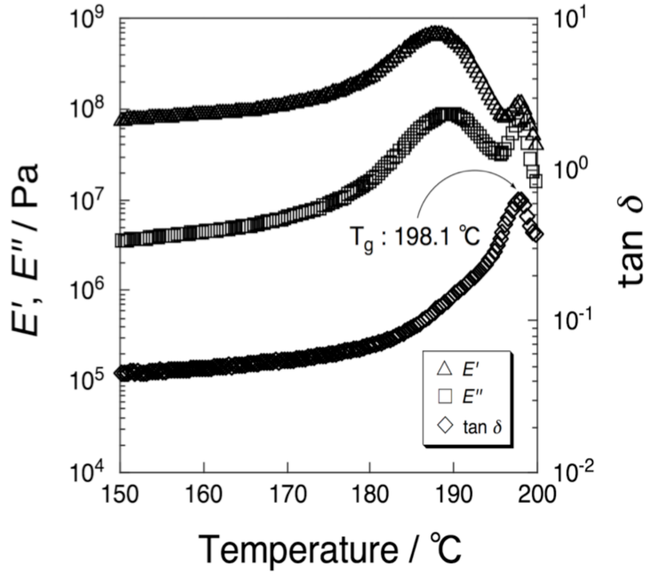

Figure 5: Temperature dependence of E', E'', and tan δ for the chiral polyurea (Exp. No. 7 in Table **1**) at a frequency of 1 Hz and a heating rate of 1.0 °C min^{-1}.

The optical rotation, $[\alpha]_D$, of the polyurea and the corresponding starting material of L-Lys-4-NA/2HBr are shown in Table **2**. The results revealed that optically active polyurea was obtained. From this, the membranes from the present polyurea were expected to express chiral separation ability since there can be found chiral environment in the present polyurea.

Table 2: Specific Rotations of Diamine Monomer and Chiral Polyurea

	$[\alpha]_D$ deg cm^2 g^{-1}
L-Lys-4-NA/2HBr[a]	45.0
L-Lys-4-NA-1,4-PDI[b]	-51.8

[a] in DMF, c = 5.00 g dL^{-1}, L = 10 cm.
[b] in DMF/LiCl (5 wt.%), c = 1.00 g dL^{-1}, L = 10 cm.

3.3. Adsorption Selectivity

Adsorption selectivity of the present polyurea membrane was studied adopting racemic mixture of Glu as model racemates. The results of adsorption selectivity are summarized in Table **3**. As observed in adsorption studies on other chiral polyurea membranes [18-20], the control polyurea membrane incorporated into the L-isomer of Glu in preference to the corresponding D-isomer. Even though the present control membrane showed adsorption selectivity, the value was not so prominent and determined to be 1.05. As reported [27-32], molecular imprinting is a facile way to bestow molecular recognition ability on polymeric materials. However, in the present study, conventional molecular imprinting could not be applicable to give molecular recognition ability into the present polyurea, since polymeric materials were already prepared. In such a case, an alternative molecular imprinting is an effective and a suitable method to introduce molecular recognition sites into polymeric materials, which were already polymerized [6-12,33]. Applying an alternative molecular imprinting, the present polyurea will be directly converted into molecular recognition materials (membranes). To this end, molecularly imprinted membranes were prepared from the present polyurea adopting N-α-protected glutamic acid, such as Z-D-Glu or Z-L-Glu, as a print molecule.

The adsorption selectivities for those molecularly imprinted membranes are also shown in Table **3** together with that for control non-imprinted membrane. As expected, the membrane imprinted by Z-D-Glu showed opposite adsorption selectivity to the control non-imprinted membrane. In other words, the Z-D-Glu molecularly imprinted membrane preferentially adsorbed D-Glu and the adsorption selectivity toward the D-isomer was determined to be 1.09. Contrary to this, the Z-L-Glu molecularly imprinted membrane showed the adsorption selectivity of 1.10 toward the L-isomer of Glu. In the authors' previous studies, molecularly imprinted membranes from synthetic achiral polymers, such as carboxylated polysulfone [9,34], polyamide [7], and polysulfone with aldehyde group [12], the chiral print molecule and the antipode equally worked as a print molecule; the adsorption selectivity for the membrane imprinted by the D-isomer gave nearly same selectivity expressed by that imprinted by the antipode.

In the case of molecularly imprinted membranes from tetrapeptide derivatives [8], the formation of molecular recognition site was strictly dependent on the absolute configuration of candidate materials. The tetrapeptide derivative consisting of D-amino acid residues was converted into the D-isomer recognition materials by adopting the D-isomer of print molecule and *vice versa*, and the print molecule, of which absolute configuration was opposite to that of the tetrapeptide derivative, hardly worked as a print molecule. However, in the present study, the polyurea was flexible enough to construct molecular recognition sites toward the D-isomer by adopting a print molecule of D-isomer derivative and *vice versa*. The flexibility of the present polyurea was advantageous to construct D-isomer and L-isomer recognition membrane depending

Table 3: Adsorption Selectivity of Three Types of Membrane Toward Racemic Mixture of Glu in H_2O

Membrane	D-Glu		L-Glu		$S_{A(D/L)}$	$S_{A(L/D)}$
	10^5(mol / g-mem.)	10^2(mol / mol(Lys-residue))	10^5(mol / g-mem.)	10^2(mol / mol(Lys-residue))		
Z-D-Glu imprinted mem.	2.05	0.94	1.89	0.86	1.09	0.92
control mem.	3.95	1.81	4.13	1.89	0.96	1.05
Z-L-Glu imprinted mem.	2.44	1.12	2.70	1.24	0.91	1.10

on the selection of print molecules, but disadvantageous to obtain higher substrate specificity in adsorption selectivity.

3.4. Enantioselective Transport

From the results of adsorption selectivity, those membranes were expected to show chiral separation ability. To this end, first, enantioselective transport ability of those three types of membrane were studied adopting racemic mixture of Glu as model racemates and concentration gradient as a driving force for membrane transport. Time-transport curves of racemic mixture of Glu through those membranes are shown in Figure **6**.

Two types of molecularly imprinted membrane, such as Z-D-Glu (a) and Z-L-GLu (c) molecularly imprinted ones, showed chiral separation ability. However, against expectation from adsorption selectivity, the observed permselectivities were opposite to their adsorption selectivities. Such a discrepancy between adsorption selectivity and permselectivity is often observed in membrane separation, especially, in optical resolution [6,8,35-38]. This discrepancy was rationalized by the retarded membrane transport of the enantiomer, which was preferentially incorporated into the membrane. The diffusion of the enantiomer selectively adsorbed in the membrane was retarded by a relatively high affinity between the enantiomer and the membrane. As a result, the antipode was transported faster than the enantiomer preferentially incorporated into the membrane.

Against expectation from adsorption selectivity, the control non-imprinted membrane hardly showed permselectivity. This might be also explained by the reduction of diffusivity due to a relatively strong interaction between the membrane and the L-isomer of Glu. If the magnitude of the reduction of diffusivity of the L-isomer had been higher than that observed, permselectivity toward antipode would have been expressed as observed [6, 8, 12].

It is interesting to transport the enantiomer, which was selectively incorporated into the membrane, faster than the antipode. In other words, it is interesting to construct membrane transport system, of which permselectivity reflects its adsorption selectivity. In the next chapter, such an approach will be described.

3.5. Enantioselective Electrodialysis

In order to transport the eanantiomer preferentially adsorbed in the membrane faster than the antipode, the applied potential difference was adopted as a driving force for the membrane transport of racemic Glu through the two types of molecularly imprinted membrane. In other words, enantioselective electrodialysis was applied so that the permselectivity would reflect its adsorption selectivity.

Time-transport curves of racemic Glu at the applied potential difference of 6.0 V are shown in Figure **7**. As can be seen in Figure **7**, D-Glu, which was preferentially incorporated into the Z-D-Glu imprinted membrane, was selectively transported through it and *vice versa*.

The membrane performance, such as permselectivity and flux, was expected to be dependent on the applied potential difference as reported previously [8,15,18]. To this end, the membrane performance was investigated at an applied potential difference of 3.0 V and 9.0 V and results are summarized in Figure **8** together with that of 6.0 V. In

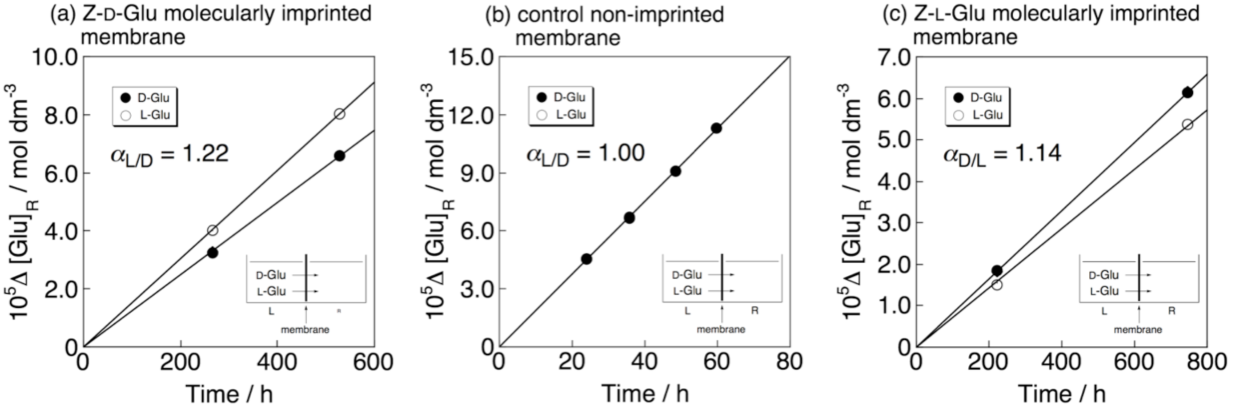

Figure 6: Time-transport curves of racemic mixture of Glu through Z-D-Glu molecularly imprinted (**a**), control non-imprinted (**b**), and Z-L-Glu molecularly imprinted (c) membranes at 40 °C in H_2O solution adopting a concentration gradient as a driving force for membrane transport.

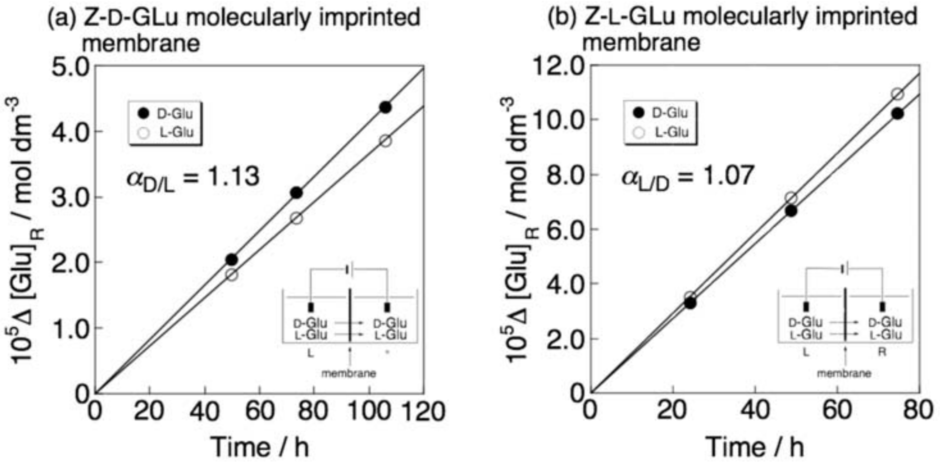

Figure 7: Time-transport curves of racemic mixture of Glu through Z-D-Glu molecularly imprinted (**a**) and Z-L-molecularly imprinted (**b**) membranes at 40 °C in aqueous solution adopting a potential difference as a driving force for membrane transport. (ΔE = 6.0 V).

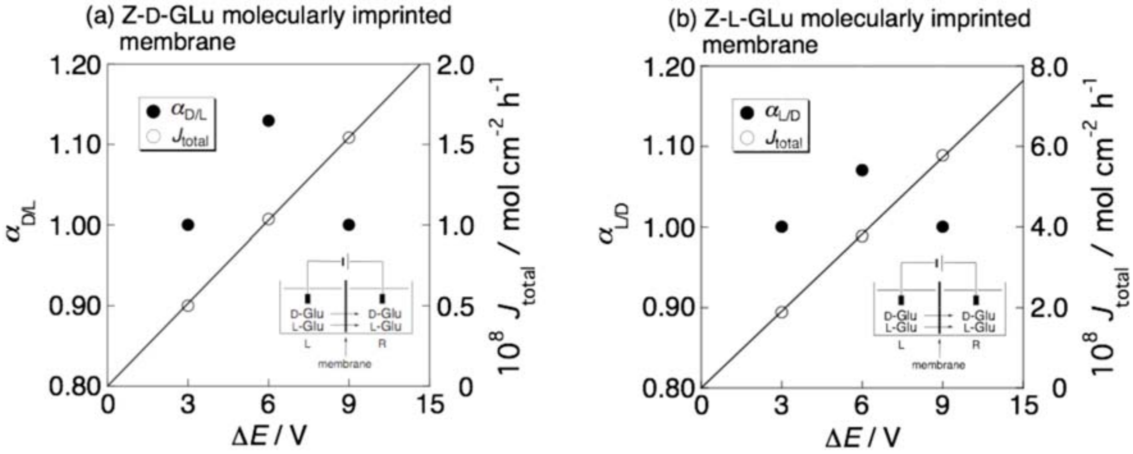

Figure 8: Effect of a potential difference on enantioselective electrodialysis of a racemic mixture of Glu through the Z-D-Glu molecularly imprinted membrane (**a**) and the Z-L-Glu molecularly imprinted one (**b**) at 40 °C in aqueous solution.

both membrane systems, the total flux increased with the increase in the potential difference, passing through origin. The permselectivities for both membranes were determined to be unity at the applied potential difference of 3.0 V and 9.0 V. From previous results [8,15,18], below the applied potential difference of 3.0 V, opposite permselectivity would be observed.

4. CONCLUSIONS

Novel polyurea was synthesized from lysinyl residue, L-lysine-4-nitroanilide (L-Lys-4-NA) and 1,4-phenylene diisocyanate (1,4-PDI). The optimum polyaddition condition was determined as follows; [L-Lys-4-NA] = 2.08 x 10^{-1} mol dm^{-3} and [1,4-PDI] = 2.50 x 10^{-1} mol dm^{-3} ([L-Lys-4-NA]/ [1,4-PDI] = 0.83. The polyurea thus prepared gave durable self-standing membranes and were converted into molecular recognition materials (membranes) adopting Z-D-Glu or Z-L-Glu as a print molecule. The Z-D-Glu molecularly imprinted membrane adsorbed the D-isomer of Glu in preference to the corresponding L-Glu and *vice versa*. Even though the present polyurea consisted of L-lysinyl residue, both the D-isomer and the L-isomer of print molecules worked as a print molecule to construct molecular recognition site in the membrane. Those two types of molecularly imprinted membrane showed chiral separation ability adopting a concentration gradient or applied potential difference as a driving force for membrane transport. The permselectivity was dependent on the magnitude of the driving force.

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