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Molecularly Imprinted Nanofiber Membranes from Carboxylated Polysulfone by Electrospray Deposition[a]

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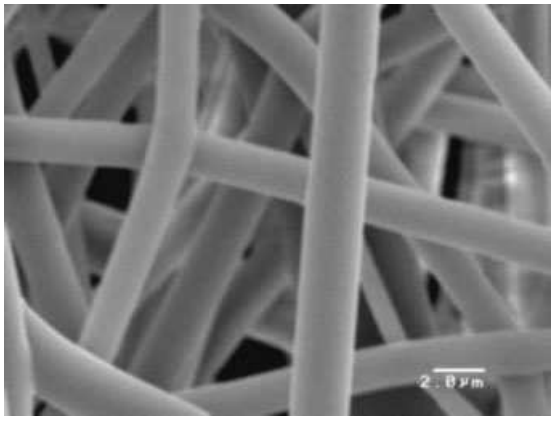
It is demonstrated that polymeric materials can be directly converted into molecular (chiral) recognition nanofiber membranes by simultaneously applying an electrospray deposition and an alternative molecular imprinting during the membrane preparation process. Polysulfone with a degree of substitution of 0.88 was adopted as the candidate polymeric material for molecularly imprinted nanofiber membranes. Molecularly imprinted nanofiber membranes imprinted by *Z*-D-Glu recognize the D-isomer in preference to the corresponding L-isomer and vice versa. The amino acid preferentially incorporated into the membrane is selectively permeated through the membrane by using a concentration gradient as a driving force for membrane transport.



Introduction

Molecular imprinting is perceived as a facile way to obtain molecular recognition materials, which can be applicable to chromatography, membranes, sensors, catalysts, and so forth.[1–3] Among those applications, interest in membranes has been increasing in various areas since membranes are expected to play an indispensable role for solving basic problems presently faced by the world such as resources, energy, information, environment, artificial organs, and so on. Specialty membranes can be prepared by applying molecular imprinting.[4–7] Various polymeric materials, which can construct and maintain their structure, such as synthetic polymers,[8–12] derivative of natural polymers,[13] oligopeptide derivatives,[14] and natural polymers,[15] were converted into molecular recognition materials or membranes by applying an alternative molecular imprinting.[16,17] In earlier work, we studied the chiral molecular recognition properties of molecularly imprinted dense membranes prepared from non-chiral carboxylated polysulfone (PSf).[8] Molecularly imprinted membranes with a higher surface area can be expected to give higher flux and permselectivity compared with those prepared by conventional methods. Electrospray deposition is one

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plausible method to obtain molecularly imprinted membranes with a large surface area. Electrospray deposition was expected to provide membranes consisting of polymeric nanofibers with diameters ranging from a few nanometers to several micrometers through the action of external electric field imposed on a polymeric solution or melt.[18–20] Electrosprayed nanofiber membranes with molecular recognition sites were reported previously by applying alternative molecular imprinting or molecular imprinting to the formed membrane.[12,21] However, it is of interest to convert polymeric materials directly into molecularly imprinted nanofiber membranes by simultaneously applying an electrospray deposition and an alternative molecular imprinting. To this end, molecularly imprinted electrosprayed nanofiber membranes were prepared from carboxylated PSf by adopting enantiomerically pure *N*-α-benzyloxycarbonyl-D-glutamic acid (*Z*-D-Glu) or *N*-α-benzyloxycarbonyl-L-glutamic acid (*Z*-L-Glu) as a print molecule. Their membrane performances, such as chiral recognition and optical resolution, were studied in the present paper.

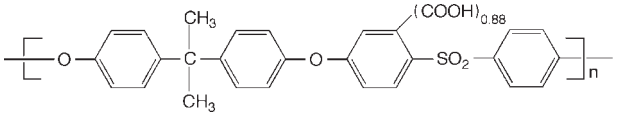
Experimental Part

Membrane Preparation

Carboxylated PSf, with a degree of substitution of 0.88 (Scheme 1), was prepared by the modification of PSf Udel P-3500 as reported previously.[22]

Tetrahydrofuran (THF) was adopted as a solvent and the polymer concentration was fixed at 15.0 wt.-% in the present study. Polymer solution containing either one of the print molecules was electrosprayed at ambient temperature using an applied voltage of 15.0 kV. The ESD device is the same as that used in a previous study.[23] The syringe used in the present study had a capillary tip of 0.52 mm diameter. A grounded aluminum foil used as a counter electrode was placed 10 cm from the tip of the capillary. The thicknesses of the electrosprayed molecularly imprinted membranes were around 200 μm. The print molecule was removed from the resultant membranes by a known large volume of methanol until the print molecule could be hardly detected in methanol by UV analysis. In the present study, 95–97% of added print molecule was removed from the membrane.

The morphology and diameter of the electrosprayed molecularly imprinted nanofiber membranes were determined with a SM-200 scanning electron microscope (SEM, Topcon). A small section of the membrane was placed on the SEM sample holder and sputter coated with gold, prior to the analysis.



Scheme 1. Chemical structure of PSf.

Adsorption Selectivity

The membrane samples were immersed in a 1.0×10^{-3} mol · dm^{-3} racemic glutamic acid (D-Glu and L-Glu) solution, and the mixture was allowed to equilibrate at 40 °C. A 0.02 wt.-% of sodium azide was added as a fungicide. It took the membrane 5–7 d to reach equilibrium. Quantitative measurements of aliquots of the solution at the initial stage and after equilibrium had been reached were made using HPLC employing a Chiralpak MA(+) column (50 mm × 4.6 mm id) (Daicel Chemical Ind. Ltd). The amount of amino acid in the supernatant subtracted from the amount initially in the solution gave the amount of Glu adsorbed in the membrane.

The adsorption selectivity $S_{A(i/j)}$ is defined as

$$S_{A_{(i/j)}} = \frac{[(i\text{–Glu})/(j\text{–Glu})]}{[(i\text{–Glu}]/[j\text{–Glu})]} \quad (1)$$

where (*i*-Glu) and [*i*-Glu] are the amount of *i*-Glu adsorbed in the membrane and concentration in the solution after equilibrium had been reached, respectively.

Enantioselective Permeation

A membrane with an area of 3.0 cm^2 was tightly secured with Parafilm between two chambers of a permeation cell. The volume of each chamber was 40.0 cm^3. A racemic Glu solution was placed in the left-hand chamber (L-side) and aqueous solution in the right-hand chamber (R-side). Each concentration of racemic Glu was fixed at 1.0×10^{-3} mol · dm^{-3}. In both chambers, 0.02 wt.-% of sodium azide was added as a fungicide. Permeation 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-Glu permeated through the membrane were determined by HPLC as described above.

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

$$J = Q/At \quad (2)$$

where Q (mol) is the amount of permeated 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],

$$\alpha_{(i/j)} = \frac{J_i/J_j}{[i\text{–Glu}]/[j\text{–Glu}]} \quad (3)$$

Results and Discussion

The SEM photographs of the electrosprayed nanofiber membranes with different molecular imprinting ratios are shown in Figure 1–3. Those three types of membranes were electrosprayed in the presence of *Z*-D-Glu as a print molecule. The SEM photographs of the nanofiber membranes imprinted by the L-isomer gave similar morphology

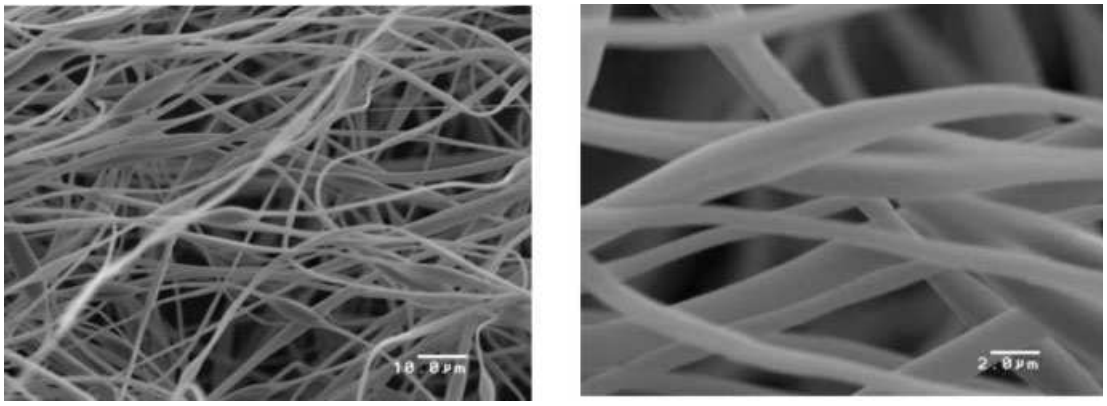


Figure 1. SEM images of the electrosprayed PSf membrane imprinted by *Z*-D-Glu [(*Z*-D-Glu)/(PSf) = 0.50].

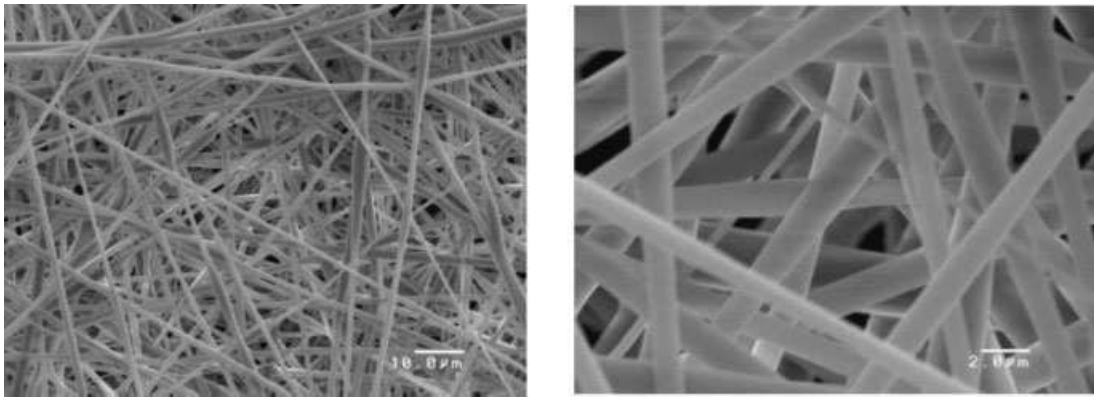


Figure 2. SEM images of the electrosprayed PSf membrane imprinted by *Z*-D-Glu [(*Z*-D-Glu)/(PSf) = 1.00].

like those given in Figure 1–3. The morphology and the diameter of the electrosprayed membranes could be effectively controlled. The authors aimed to investigate the possibility that electrosprayed molecularly imprinted nanofiber membranes, which are directly converted from a given candidate material, can be applicable to chiral separation membranes. Optimization of electrospray deposition condition has not been studied. In the present study, those membranes shown in the figures were adopted for the following studies of chiral recognition and optical resolution.

The amounts of racemic Glu adsorbed in the electrosprayed molecularly imprinted nanofiber membranes and adsorption selectivities for those membranes are summarized in Table 1. The adsorbed Glu's are given not only as the absolute amounts per g-membrane [$(Glu)_M$/

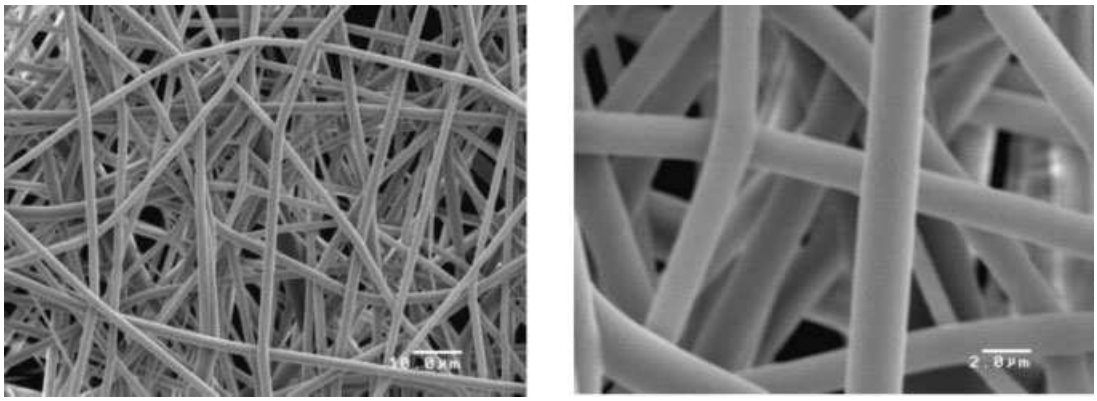


Figure 3. SEM images of the electrosprayed PSf membrane imprinted by *Z*-D-Glu [(*Z*-D-Glu)/(PSf) = 2.00].

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Table 1. Adsorption selectivity of molecularly imprinted membranes toward racemic Glu mixtures.

Imprinting conditions	Substrate	$[Glu]_M$	$(Glu)_M/(PSf)$	$S_{A(D/L)}$	$S_{A(L/D)}$
		10^5 mol · (g membrane)$^{-1}$			
(*Z*-D-Glu)/(PSf = 0.50)	D-Glu	3.08	0.0148	1.20	0.83
	L-Glu	2.58	0.0124		
(*Z*-L-Glu)/(PSf = 0.50)	D-Glu	3.41	0.0164	0.84	1.19
	L-Glu	4.03	0.0194		
(*Z*-D-Glu)/(PSf = 1.00)	D-Glu	6.70	0.0322	1.35	0.74
	L-Glu	4.97	0.0239		
(*Z*-L-Glu)/(PSf = 1.00)	D-Glu	7.02	0.0338	0.77	1.30
	L-Glu	9.12	0.0439		
(*Z*-D-Glu)/(PSf = 2.00)	D-Glu	7.23	0.0348	1.01	0.99
	L-Glu	7.17	0.0345		
(*Z*-L-Glu)/(PSf = 2.00)	D-Glu	4.45	0.0214	0.97	1.04
	L-Glu	4.57	0.0220		

g-membrane], but also relative to PSf repeating unit $[(Glu)_M/(PSf)]$. Adsorption selectivity depends on the absolute configuration of the print molecule used in the electrosprayed process; in other words, the *Z*-D-Glu imprinted membrane recognized the D-isomer in preference to the corresponding L-isomer and vice versa. Generally, adsorption selectivity depends on molecular imprinting conditions and it is usually observed to increase with a decrease in the imprinting ratio, the mole ratio of the print molecule to the constitutional repeating unit of the polymer.[13,14] In contrast to previous results,[13,14] the membranes with the imprinting ratio of 1.0 gave higher adsorption selectivity among those three types of membranes. Adsorption selectivity depends on an amount of chiral recognition site, which was formed in the presence of a given print molecule and an area of non-specific wall, which does not contribute to chiral recognition. Adsorption selectivity is governed by the combination of above two factors. This is the reason why the membrane with the imprinting ratio of 1.0 gave the highest adsorption selectivity in the present study.

The adsorption amount of Glu for the molecularly imprinted dense carboxylated PSf membranes previously reported[8] was about one order of magnitude more than that for those electrosprayed in the present study. It is difficult to compare the chiral adsorption phenomena observed in the present study with those for the previous results[8] because the experimental conditions for adsorption selectivity were not similar. At the moment, a precise explanation for this difference cannot be specified. As for adsorption selectivity, the present and previous membranes gave comparable adsorption selectivity.

Chiral separation of racemic Glu with those six types of membranes was investigated by adopting a concentration gradient as a driving force for the membrane transport. Time–transport curves of D- and L-Glu through the mem-

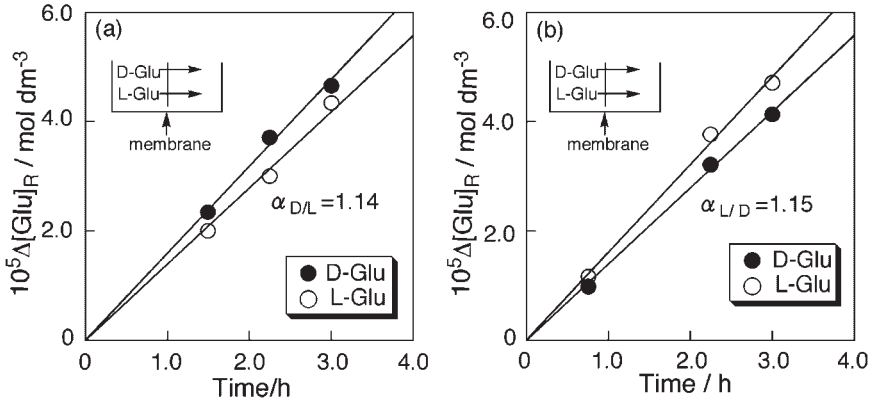

Figure 4. Time-transport curves of D-Glu and L-Glu through the molecularly imprinted nanofiber membrane imprinted by (a) *Z*-D-Glu and that by (b) *Z*-L-Glu (*Z*-L-Glu)/(PSf) = 1.0; $[D\text{-Glu}]_{L,0} = [L\text{-Glu}]_{L,0} = 1.0 \times 10^{-3}$ mol · dm^{-3}; $[NaN_3]_{L,0} = [NaN_3]_{R,0} = 2.77 \times 10^{-3}$ mol · dm^{-3}).

Table 2. Permselectivity of molecularly imprinted membranes toward racemic Glu mixtures.

Imprinting conditions	Permeant	Flux	$\alpha_{D/L}$	$\alpha_{L/D}$
		10^7 mol · cm^{-2} · h^{-1}		
(*Z*-D-Glu)/(PSf = 0.50)	D-Glu	1.44	1.03	0.97
	L-Glu	1.39		
(*Z*-L-Glu)/(PSf = 0.50)	D-Glu	1.15	0.93	1.08
	L-Glu	1.24		
(*Z*-D-Glu)/(PSf = 1.00)	D-Glu	2.11	1.14	0.88
	L-Glu	1.86		
(*Z*-L-Glu)/(PSf = 1.00)	D-Glu	1.86	0.87	1.15
	L-Glu	2.14		
(*Z*-D-Glu)/(PSf = 2.00)	D-Glu	2.23	1.00	1.00
	L-Glu	2.23		
(*Z*-L-Glu)/(PSf = 2.00)	D-Glu	1.76	1.00	1.00
	L-Glu	1.76		

brane with the imprinting ratio of 1.00 are shown in Figure 4. As shown in the figure, D-Glu was selectively transported through the D-isomer imprinted membrane and vice versa. The permselectivity toward the D-isomer for the *Z*-D-Glu imprinted membrane was determined to be 1.14, and that for the L-isomer imprinted membrane to be 1.15, respectively. The flux values for the present membranes were about two orders of magnitude higher than the previous results, while the permselectivity in the present study was slightly lower than the previous results. The membrane transport results are summarized in Table 2. The membrane with the imprinting ratio of 0.50 only gave slight permselectivity. As for the membrane with the imprinting ratio of 2.00, optical resolution was hardly observed. Using permselectivity and adsorption selectivity, diffusivity selectivity $S_{D(i/j)}$ was obtained by the following equation:

$$S_{D_{(i/j)}} = \frac{\alpha_{(i/j)}}{S_{A(i/j)}} \quad (4)$$

The estimated diffusivity selectivity and other results for the *Z*-D-Glu imprinted membranes are summarized in Table 3, and those for the *Z*-L-Glu imprinted membranes in Table 4. The diffusivity selectivity toward the isomer, which was preferentially incorporated into the membrane, was determined to be below unity. In other words, the mobility of the substrate showing a high affinity toward membrane was retarded as usually observed in membrane transport phenomena. As observed in the present study, adsorption selectivity surpassed diffusivity selectivity; as a result, the isomer selectively adsorbed in the membrane was transported in preference to the opposite enantiomer.

Although the membrane performance in the present study was lower than some earlier studies, it can be improved by the optimization of electrospray conditions, molecular imprinting ratio, and other experimental parameters. The purpose of the present study is to present the possibility that electrospray deposition may lead to a new frontier as a means to prepare molecularly imprinted nanofiber membranes, as described in the previous articles.[12,21]

Conclusion

We have demonstrated that non-chiral polymeric materials can be directly converted into molecular (chiral) recognition

Table 3. Summary of chiral separation of *Z*-D-Glu molecularly imprinted membranes.

Imprinting conditions	Substrate	$\alpha_{(D/L)}$	$S_{A(D/L)}$	$S_{D(D/L)}$
(*Z*-D-Glu)/(PSf = 0.50)	Glu	1.03	1.20	0.86
(*Z*-D-Glu)/(PSf = 1.00)	Glu	1.14	1.35	0.84
(*Z*-D-Glu)/(PSf = 2.00)	Glu	1.00	1.01	0.99

Table 4. Summary of chiral separation of *Z*-L-Glu molecularly imprinted membranes.

Imprinting conditions	Substrate	$\alpha_{(L/D)}$	$S_{A(L/D)}$	$S_{D(L/D)}$
(*Z*-L-Glu)/(PSf = 0.50)	Glu	1.08	1.19	0.91
(*Z*-L-Glu)/(PSf = 1.00)	Glu	1.15	1.30	0.88
(*Z*-L-Glu)/(PSf = 2.00)	Glu	1.00	1.04	0.96

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nanofiber membranes by simultaneously applying an electrospray deposition and an alternative molecular imprinting during the membrane preparation process. In the present study, carboxylated PSf with a degree of substitution of 0.88 was adopted as the candidate polymeric material for molecularly imprinted nanofiber membranes. Molecularly imprinted nanofiber membranes imprinted by *Z*-D-Glu recognize the D-isomer in preference to the corresponding L-isomer and vice versa. The amino acid preferentially incorporated into the membrane is selectively permeated through the membrane by using a concentration gradient as a driving force for membrane transport.

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