

Surface-Modified Polysulfone Hollow Fibers. IV. Chloromethylated Fibers and Their Derivatives

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SYNOPSIS

A chloromethylated reaction was performed on the surfaces of polysulfone ultrafiltration hollow fibers and their derivative membranes, i.e., triethylaminated, ethylenediaminated, and acetylated fibers, were prepared. The modified fibers have a 30–60% insoluble region in chloroform, whereas nonmodified fibers can be dissolved in the chloroform. It is suggested that the insoluble parts of the fibers are highly cross-linked due to the high degree of chloromethylation. The modified fibers showed a 50–98% rejection of polyethylene glycol 6000 at a feed concentration of 0.5 wt %, except for the triethylaminated fibers, which gave a negative rejection from –91 to –96%. It was found that the modified segments significantly influenced the rejection behavior of the solutes. Absorption of bovine serum albumin on the ethylenediaminated fibers at pH 7.1 was estimated from permeation measurements to be less than that of the other modified and nonmodified fibers. This effect is attributed to the hydrophilic surface of the ethylenediaminated fibers.

INTRODUCTION

Surface reactions of active reagents on membranes are useful modifications to introduce various functional groups such as SO_3H , COOH , or OH .^{1–7} Several surface modifications^{1–7} of membranes have been designed to avoid the nonspecific adsorption of proteins. In our previous studies,^{4–7} we introduced a negatively charged group, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{SO}_3^-$, and a hydroxide group, $-\text{CH}(\text{CH}_3)\text{CH}_2\text{OH}$, on the surfaces of polysulfone hollow fibers from Friedel–Crafts reactions. We found that the novel modified fibers showed excellent results for antiabsorption of solutes compared to the nonmodified and conventionally sulfonated fibers.

Special attention has been focused on affinity membranes^{8–11} for the processes of protein purification due to the development of biotechnology. The affinity membranes are usually based on porous membranes activated by the covalent attachment of affinity ligands to their interior pore-wall surfaces.¹¹ When the membranes made of engineering plastics

such as polysulfone are used for the base membrane, the membranes must be activated during the first stage. One of the simplest reactions is chloromethylation from a Friedel–Crafts reaction. This research involves investigation of chloromethylated polysulfone membranes by surface reaction and their derivatives. The enzyme and affinity ligands will be easily immobilized from glutaraldehyde,^{12–14} succinimide,^{15,16} or carbodiimide¹⁷ reactions on the surfaces of the membranes. Ultrafiltration experiments for the modified membranes are also shown and discussed in this study.

EXPERIMENTAL

Membranes

The membranes used for chemical modification in this study were commercially available polysulfone hollow fibers (ultrafiltration membrane), SI-1 (Asahi Chemical Co.), the same grade of fibers used in previous studies.^{4–6} The inside and outside diameters of the fibers were approximately 0.75 and 1.3 mm, respectively. Water flux and rejection (R) of polyethylene glycol (PEG) 20,000 for the fibers were observed to be $10.8 \text{ m}^3/\text{m}^2$ per day at 3 kg/

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cm^2 and $R = 12.6\%$ at a feed concentration (C_f) of 0.5 wt % in this study.

Chemical Modifications

Chloromethylation¹⁸ of the polysulfone hollow fiber (i.e., Scheme 1) was performed by dipping in a solution of chlorodimethyl ether (CME), hexane, and Friedel-Crafts catalyst (ZnO or SnCl_4) at 20–28°C for several reaction times (1–168 h), as shown in Table I. Apparatus for the chemical modification of the fibers was described in a previous study⁴; the same procedures for the chemical modification were employed in this study.

Triethylamination and ethylenediamination of the chloromethylated polysulfone fibers (i.e., Scheme 1) were performed by dipping the chloromethylated fibers into triethylamine or ethylenediamine for 1–24 h at 20°C. The chloromethylated polysulfone fibers were refluxed in ethanol with acetic potassium for 6–48 h to prepare the acetylated polysulfone fibers (i.e., Scheme 1).

A hydroxide type of polysulfone fiber (i.e., Scheme 1) was prepared from the saponification of

the acetylated polysulfone fibers with 0.5 M NaOH solution for 12 h. The fibers were subsequently rinsed in 0.5 M HCl solution and ultrapure water. All the modified fibers were dried and stored under vacuum at 25°C.

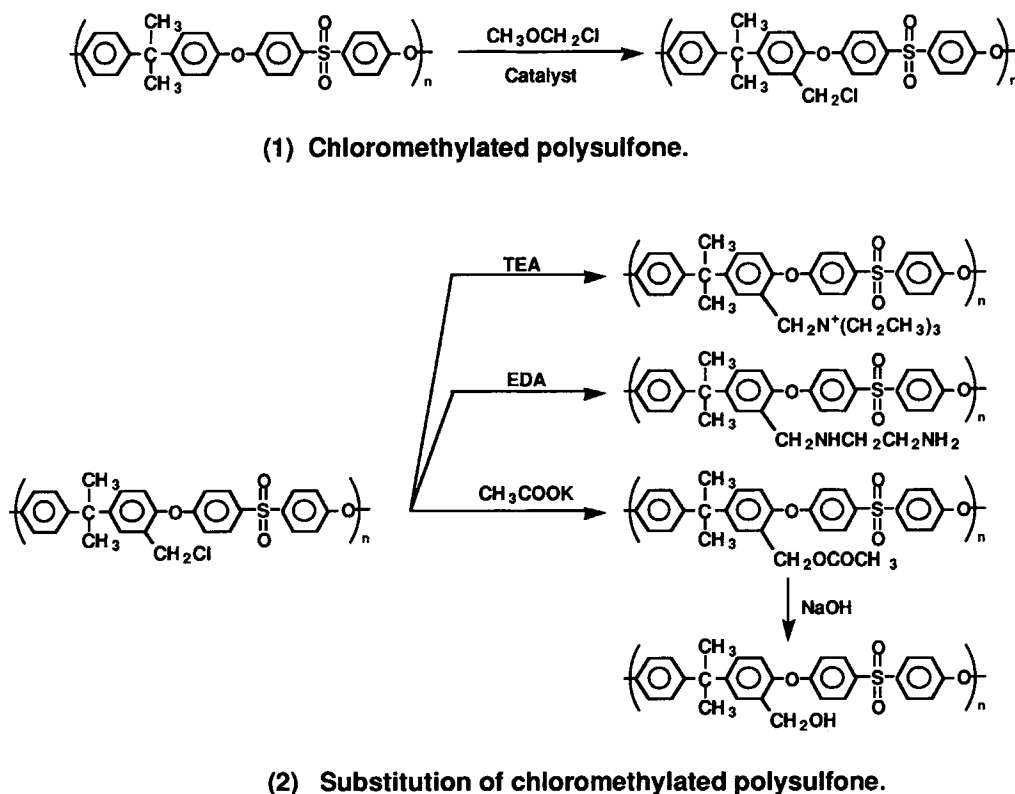
Transport Measurements

The ultrafiltration apparatus and procedures have been described in a previous paper.⁴ The transpressure drop at the fiber, Δp , was fixed at 3 kg/cm², and speed of the feed solution at the inlet of the fiber was fixed at 12 cc/min throughout the experiments. The ultrafiltration measurements were performed at $20 \pm 0.5^\circ\text{C}$. The standard deviations for flux (J) and rejection measurements were found to be 3 and 5%.

RESULTS AND DISCUSSION

Characterization

The chloromethylated polysulfone fibers were dissolved in CDCl_3 , and insoluble parts of the fibers



Scheme 1

Table I Surface Reaction Conditions of Chloromethylated Polysulfone Membranes^a

Membrane	Reagent (mol %)	Catalyst (mol %)	Solvent (mol %)	Temp (°C)	Reaction Time (h)	Substitution
(a)						
Z1	CME (1.12)	ZnO (0.040)	Hexane (98.84)	28.1	40	^b
Z2	CME (1.06)	ZnO (0.19)	Hexane (98.74)	28.1	40	^b
Z3	CME (1.25)	ZnO (0.40)	Hexane (98.35)	28.1	40	^b
C1	CME (12.35)	SnCl ₄ (12.38)	Hexane (75.28)	28.1	1	^c
C2	CME (7.50)	SnCl ₄ (7.50)	Hexane (85.00)	28.1	1	0.071
C3-1	CME (5.00)	SnCl ₄ (5.00)	Hexane (90.00)	28.1	1	0.054
C3-2	CME (5.00)	SnCl ₄ (5.00)	Hexane (90.00)	28.1	6	0.139
(b)						
C4-1	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	28.1	1	^b
C4-2	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	28.1	12	0.0301
C4-3	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	28.1	24	0.0675
C4-4	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	28.1	30	0.072
C4-5	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	28.1	40	0.106
C4-5P	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	28.1	40	0.155
C5-1	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	20.5	24	0.030
C5-2	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	20.5	48	0.032
C5-3	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	20.5	72	0.064
C5-4	CME (0.97)	SnCl ₄ (0.98)	Hexane (98.05)	20.5	96	0.072
C6-1	CME (0.50)	SnCl ₄ (0.50)	Hexane (99.00)	28.1	1	^b
C6-2	CME (0.50)	SnCl ₄ (0.50)	Hexane (99.00)	28.1	24	^b
C6-3	CME (0.50)	SnCl ₄ (0.50)	Hexane (99.00)	28.1	168	0.0678

^a Substitution was estimated by NMR measurements.^b CH₂Cl peak was not detected in NMR spectrum.^c Sample was not dissolved in CDCl₃.

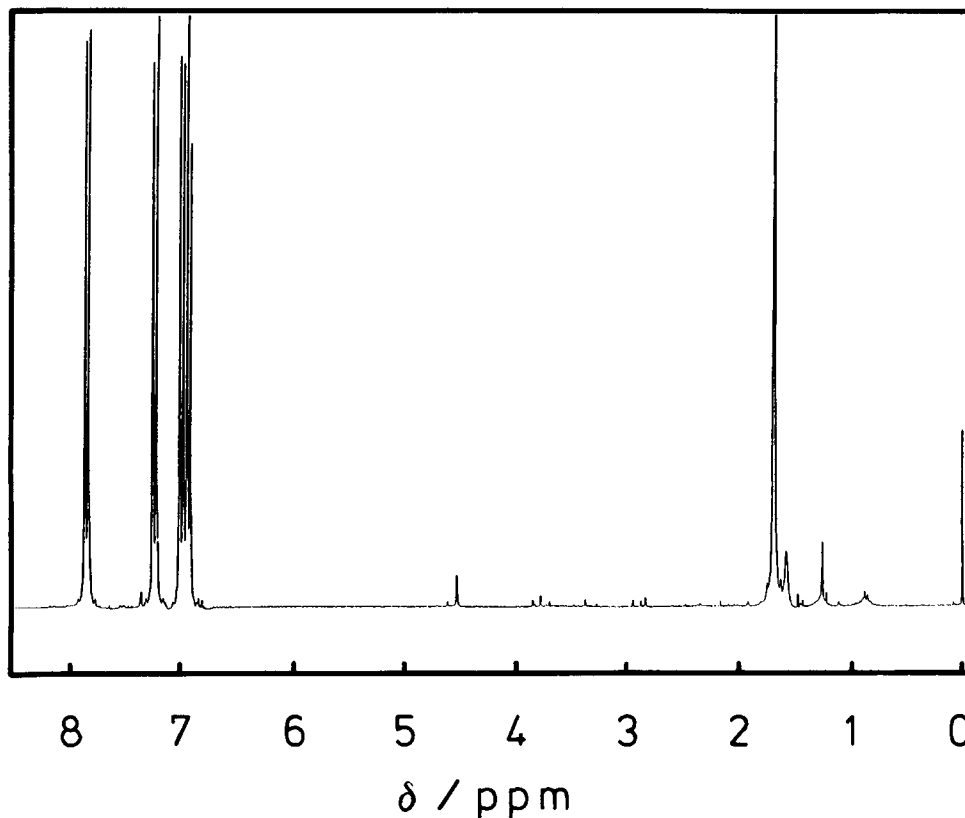


Figure 1 $^1\text{H-NMR}$ spectrum of chloromethylated polysulfone membrane (C4-4).

were removed from the dissolved solution for measurement of $^1\text{H-NMR}$ (270 MHz, JNM GX-270, JEOL Ltd.). The $^1\text{H-NMR}$ spectrum of the chloromethylated fiber is shown in Figure 1. Doublet peaks at $\delta = 6.92, 6.95, 6.98, 7.02, 7.22, 7.26, 7.83,$ and 7.86 ppm are attributed to protons in the aromatic rings of polysulfone.¹⁹ The peak at $\delta = 1.69$ ppm is attributed to methyl protons of bisphenol A in polysulfone. The peak at $\delta = 4.53$ ppm is attributed to the proton in the chloromethylated region in the chloromethylated polysulfone fiber. The $^1\text{H-NMR}$ spectrum suggests that the surface reaction surely occurs according to Scheme 1 under the present conditions.

The dependence of the degree of chloromethylation on reaction time at 20 and 28°C is shown in Figure 2. SnCl_4 was used as a catalyst in this case, since no peak at $\delta = 4.53$ ppm was observed when ZnO was used as the catalyst [see Table I(a)]. The degree of chloromethylation was obtained from the comparison of the areas at $\delta = 1.69$ and 4.53 ppm from the NMR measurements. It was found that the degree of chloromethylation increases with increasing reaction time and that the chloromethylation of

polysulfone progresses faster at a higher reaction temperature. It was also found that the fibers treated by plasma-glow charge at 10W for 1 min before the chloromethylation (C4-5P) showed a higher degree of chloromethylation when compared to the fibers without the plasma treatment [C4-5, see Table I(b)]. The plasma treatment of the fibers were not,

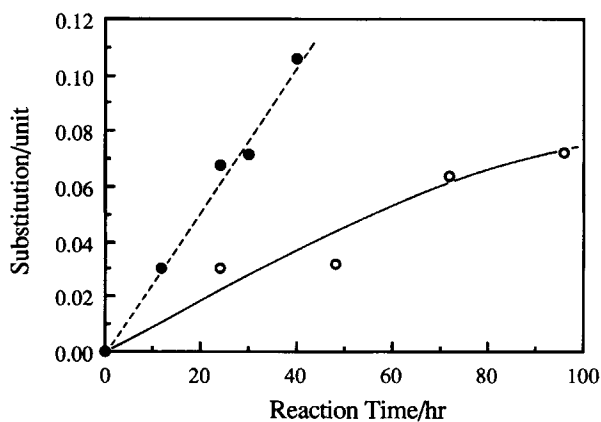
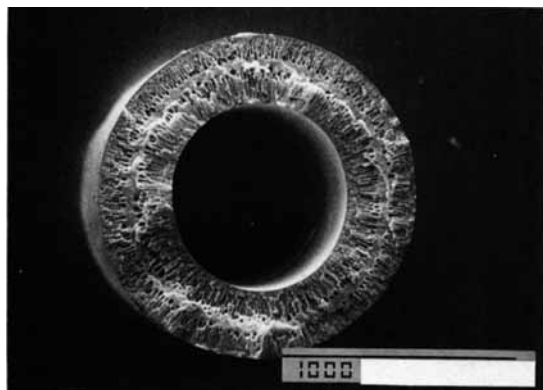
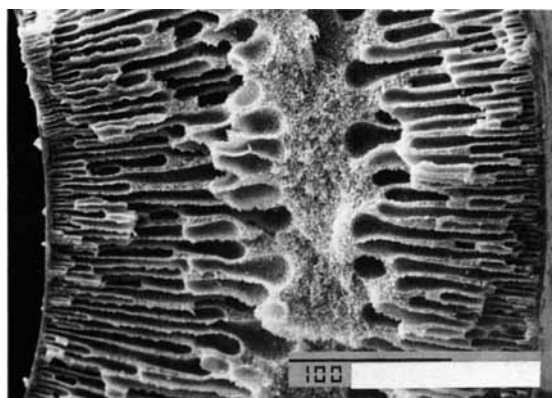


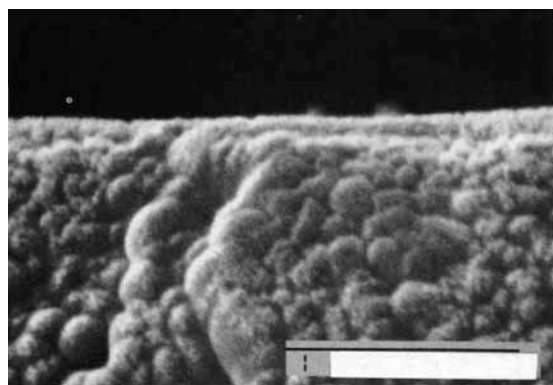
Figure 2 Dependence of degree of chloromethylation on reaction temperature: (O) 20.5°C, (●) 28.1°C.



(a)



(b)



(c)

Figure 3 Scanning electron micrographs of cross section of chloromethylated polysulfone fiber (C4-4): (a) 50 \times magnification; (b) 350 \times magnification; (c) 50,000 \times magnification (internal skin layer region).

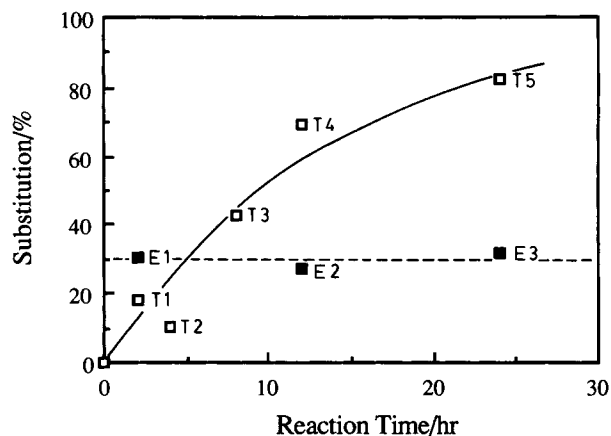


Figure 4 Dependence of substitution of triethylamine (\square) and ethylenediamine (\blacksquare) on reaction time at 20°C.

however, performed in further experiments, since the C4-5P fiber showed zero rejection of PEG 6000.

SEMs of the cross section of the chloromethylated polysulfone fiber (C4-4) are shown in Figure 3. The modified fiber shows essentially no difference from the nonmodified one in the 50,000 \times SEM observations, as no change in the SEM observations was reported for the modified fibers with propane sulfone and SnCl_4 catalyst.⁴

The dependence of the degree of triethylamination ($= \text{TA}/[\text{TA} + \text{CM}]$; TA = mol % of the triethylamine group, CM = mol % of the chloromethyl group) on reaction time is shown in Figure 4. C4-4 fibers were used as base fibers for the triethylamination. The degree of triethylamination was found to increase with increasing reaction time and to be 82% substitution at a reaction time of 24 h. The dependence of ethylenediamination ($= \text{EA}/[\text{EA} + \text{CM}]$; EA = mol % of the ethylenediamine group) on reaction time is also shown in Figure 4. The degree of ethylenediamination was found to be independent of reaction time and to be $30 \pm 3\%$ for a reaction time of 2–24 h. It is suggested that substitution of ethylenediamine from the chloromethyl group is a difficult reaction when compared to the substitution of triethylamination.

The dependence of the degree of acetylation ($= \text{AC}/[\text{AC} + \text{CM}]$; AC = mol % of the acetyl group) on reaction time is shown in Figure 5. It was also found that the degree of acetylation increased with increasing reaction time and became 79% substituted at a reaction time of 48 h.

The hydroxide type of polysulfone fibers that were prepared from the saponification of acetylated polysulfone fibers would not dissolve in CDCl_3 ;

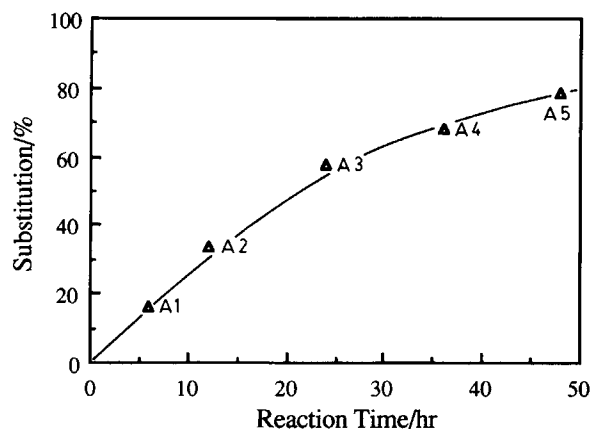


Figure 5 Dependence of substitution of acetylation (Δ) on reaction time at 20°C.

therefore, NMR measurements could not be carried out. The surface modification of polysulfone fibers with propylene oxide⁶ is, however, a more desirable reaction for the preparation of the hydroxide type of polysulfone fibers, since the surface modification with propylene oxide is only a one-step reaction and the hydroxide type of fibers prepared in this study showed zero rejection of PEG 6000.

Table II Gelation Ratio for Various Membranes^a

Membrane	Gelation Ratio (%)
<u>No reaction</u>	
SI-1	0.0
SI-1V	0.0
SI-1M	0.0
<u>Chloromethylated fibers</u>	
C5-2	31.0
C5-3	35.2
C4-3	36.4
C4-4	43.1
C4-5	38.2
<u>Triethylaminated fiber</u>	
T5	37.5
<u>Ethylenediaminated fiber</u>	
E1	57.7
<u>Acetylated fibers</u>	
A1	36.8
A2	34.3

^a SI-1: nonmodified fibers. SI-1V: The fiber was stored under vacuum. SI-1M: The fiber was immersed in ethanol and then stored under vacuum.

The insoluble parts of the fibers (i.e., gelation ratio) were measured for modified polysulfone fibers as follows: The fibers were immersed in chloroform for 48 h at $20 \pm 0.5^\circ\text{C}$. The insoluble parts of the fibers were dried under vacuum and their weight was subsequently measured. The gelation ratio (weight of insoluble part [g]/weight of initial fiber [g]) is summarized in Table II. The chloromethylated (C4 and C5 series), triethylaminated (T5), and acetylated (A1) fibers show $37 \pm 5\%$ of the gelation ratio, while nonmodified fibers (SI-1, SI-1V, SI-1M) can be completely dissolved in chloroform.

It is known that a side reaction (i.e., $\text{Ar}-\text{CH}_2-\text{Ar}$; Ar = aromatic ring) occurs with chloromethylation of a polymer having aromatic rings by the Friedel-Crafts reaction.^{20,21} The intermolecular side reaction leads to a cross-linking of the fibers, and the fibers become insoluble in chloroform to some extent.

The degree of chloromethylation was also estimated from elemental analysis (EA) and was compared to the degree of chloromethylation obtained from NMR measurements as shown in Figure 6. It is surprising that the degree of chloromethylation from the elemental analysis is 6–11 times higher than the degree of chloromethylation from NMR measurements. The degree of chloromethylation obtained from the elemental analysis represents the average values of insoluble and soluble parts of the chloromethylated fibers, whereas the degree of chloromethylation obtained from NMR measurements is an estimate of only the soluble parts of the fibers in the chloroform. It is, therefore, suggested that the

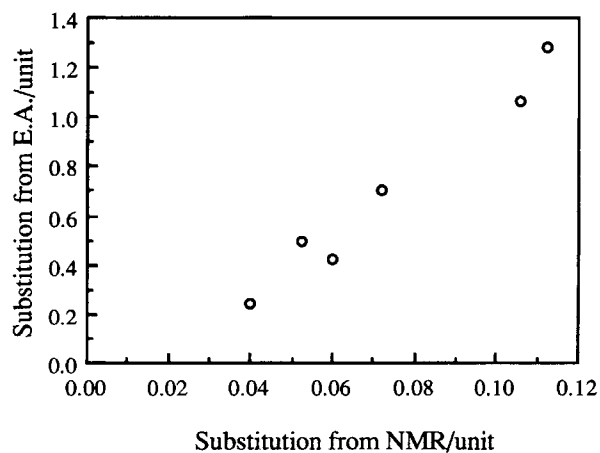


Figure 6 Relationship between degree of chloromethylation measured from elemental analysis and NMR measurements.

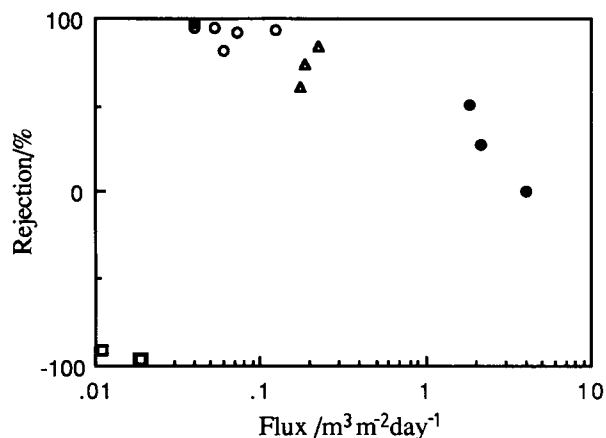


Figure 7 Relationship between flux and rejection of PEG 6000 in chemically modified and nonmodified hollow fibers at $C_f = 0.5$ wt % and 20°C : (○) chloromethylated fibers; (□) triethylaminated fibers; (■) ethylenediaminated fibers; (△) acetylated fibers; (●) nonmodified fibers (SI-1, SI-1V, and SI-1M).

insoluble parts of the fibers are highly cross-linked due to the high degree of chloromethylation.

The ethylenediaminated fiber (E1) shows a

rather higher gelation ratio (e.g., $58 \pm 5\%$) than do the chloromethylated, triethylaminated, and acetylated fibers. The ethylenediamine has two NH_2 in a molecule that can react with a chloromethyl group. It is considered that the ethylenediaminated fiber is also cross-linked to some extent by ethylenediamine, and the cross-linking leads to a higher gelation ratio of the fibers compared to the chloromethylated, triethylaminated, and acetylated fibers.

Transport Experiments

Figure 7 shows the relationship between flux and rejection of PEG 6000 in chemically modified and nonmodified fibers at $C_f = 0.5$ wt %, where C_f is the concentration of the feed solution. The fiber stored under vacuum for 48 h, SI-1V, shows 28% rejection of PEG 6000, and the fiber immersed in ethanol for 24 h and subsequently dried under vacuum for 48 h, SI-1M, shows 50% of PEG 6000, while the nonmodified fiber (SI-1) shows no rejection of PEG 6000 (see Table III). Although the physically treated fibers, however, cannot give more than 51% rejection

Table III Transport Characteristics of Several Membranes at $\Delta p = 3$ kg/cm²; feed solution = PEG 6000; 5000 ppm^a

Membrane	$J_0/\text{m}^3\text{m}^{-2}\text{ day}$	$J/\text{m}^3\text{m}^{-2}\text{ day}$	$J\eta/J_0\eta_0$	R (%)
<u>No reaction</u>				
SI-1	10.80	4.12	0.399	0.0
SI-1V	5.01	2.14	0.447	27.5
SI-1M	4.30	1.82	0.443	50.4
<u>Chloromethylated fibers</u>				
C5-2	0.286	0.123	0.450	94.8
C5-3	0.153	0.064	0.438	94.9
C4-3	0.444	0.269	0.434	81.5
C4-4	0.410	0.271	0.490	92.5
C4-5	0.327	0.137	0.439	94.1
<u>Triethylaminated fibers</u>				
T1	n.d.	n.d.		
T2	n.d.	n.d.		
T3	n.d.	n.d.		
T4	0.058	0.019	0.343	-96.1
T5	0.061	0.011	0.189	-91.3
<u>Ethylenediaminated fiber</u>				
E1	0.057	0.040	0.735	97.9
<u>Acetylated fiber</u>				
A1	0.425	0.225	0.554	73.6
A2	0.407	0.187	0.481	50.3
A3	0.404	0.175	0.454	61.8

^a n.d. indicates no drop of water through the membrane.

of PEG 6000, the chloromethylated fibers, where the substitution is more than 0.032% (based on NMR measurements), gave more than 80% rejection of PEG 6000. The acetylated fibers (A1, A2, and A3) had a higher flux but rather lower rejection than the chloromethylated fibers before acetylation. The ethylenediaminated fiber (E1) gave the highest rejection ($R = 98\%$) in this study. The triethylaminated fibers (T4 and T5) showed a different rejection behavior from the other fibers. Rejection of these fibers gave negative values from -91 to -96% , although the flux of pure water, J_0 , for triethylaminated fibers was approximately the same as J_0 for the ethylenediaminated fibers (see Table III). It is known that the fibers modified with propane sultone at 70 – 80°C also give negative rejection ($R = -16.2$ to -106.3%). It is suggested that the modified segments significantly influence the rejection behavior of solutes.

Antiabsorption of Solutes

$J_\eta/J_0\eta_0$ is known to give a measure of the absorption layer thickness of solutes on the pore wall,^{4–6} where η_0 is the viscosity of pure water and η is the viscosity of the feed solution. Absorption of PEG 6000 and bovine serum albumin (BSA) on the fibers was tested in this study.

$J_\eta/J_0\eta_0$, where the feed solution is 5000 ppm of PEG 6000, is summarized in Table III. $J_\eta/J_0\eta_0$ of nonmodified and chloromethylated fibers was 0.45 ± 0.05 , whereas $J_\eta/J_0\eta_0$ of acetylated fibers showed slightly better results (i.e., 0.50 ± 0.05). The ethylenediaminated fiber gave the best value of $J_\eta/J_0\eta_0$

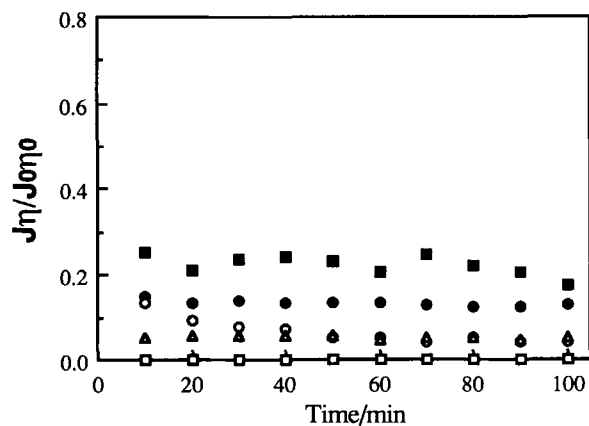


Figure 8 Dependence of $J_\eta/J_0\eta_0$ on running time for (■) E1, (●) SI-1, (○) C4-4, (△) A1, and (□) T4 at 20°C . Feed solution is 0.5 wt % BSA solution at pH 7.1.

(i.e., 0.735) in this study. This probably originated from the fact that the NH_2 group in ethylenediaminated fibers contributes to generate a more hydrophilic surface on the fibers than do the chloromethylated and acetylated groups. It is generally known that the hydrophilic surfaces of membranes show greater antiabsorption behavior of proteins than do the hydrophobic surfaces of membranes.^{1,2,4–7} The triethylaminated fibers, which also have hydrophilic surfaces, however, showed the lowest value of $J_\eta/J_0\eta_0$ (i.e., 0.189 and 0.343) among the nonmodified and modified fibers in this study. This observation may be related to the phenomenon that the fibers show negative rejection of PEG 6000.

The triethylaminated fibers having a positive charge on the surface are probably apt to have a significantly higher concentration polarization²² than have other fibers, which reduces the flux and increases the concentration on the surface inside the fiber. It is suggested that the increased concentration on the surface leads to the apparent observation of negative rejection in the triethylaminated fibers.

Figure 8 shows the dependence of $J_\eta/J_0\eta_0$ on running time at $C_f = 0.5$ wt % of BSA in the phosphate-buffer solution at pH 7.1. The figure suggests that the ethylenediaminated fiber gives less absorption of BSA than does the nonmodified fiber, although the triethylaminated, acetylated, and chloromethylated fibers are found to absorb more BSA than does the nonmodified fiber. This effect can be attributed to the hydrophilic surface of the ethylenediaminated fiber originating from the NH_2 group.

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