Selective Permeation of o-, m-, and p-Isomers of Benzene Derivatives Through Polymer Membranes Based on Cyclodextrin Complexation in the Bulk Aqueous Solution

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Synopsis

Transport behavior of several aromatic compounds through a poly(vinyl chloride) membrane and poly(vinyl alcohol)-poly(ethylenimine) composite membranes was studied in the presence of cyclodextrin in the aqueous solution. o-Isomers of nitrophenol, nitroaniline, and iodophenol were effectively separated from their mixture of regio isomers based on the preferential complexation between cyclodextrin and the m- and p-isomers over the o-isomers. Pumping of *p*-nitroaniline across the membrane was also observed by addition of cyclodextrin. The results were explained as a consequence of the selective complex formation between cyclodextrin and substrate and the low membrane permeability of the complexes.

INTRODUCTION

Membrane separation of ions and molecules has been extensively investigated from the viewpoints of biologic interest and practical application in industry.[1,2] To date, metal cations have been successfully separated by use of the ion-exchange and ion-carrier membranes.[3-11] Few reports, however, have appeared on the membrane separation of organic compounds with closely related structure, such as stereo and/or regio isomers.

Cyclodextrins (CD), which are known to selectively[12] form inclusion complexes with a variety of organic compounds, are promising materials for constructing the selective adsorbents and membranes. In this regard, some authors have already reported the successful use of CD in chromatography and liquid-liquid extraction in order to separate and purify several aromatic compounds.[13-21] Lee has prepared modified cellulose membranes containing α- and β-CD to separate the regio isomers of dichlorobenzene, nitrotoluene, and nitrochlorobenzene, for example, by liquid-liquid dialysis and pervaporation methods, but the separation factors he reported were 3 or 4 at best.[22] From biology Siegel et al. have studied ionic equilibria across the cellulose membrane in the presence of α-CD in the solution.[23] Recently, we have applied this idea to the membrane separation of organic compounds and have demonstrated that CD complexation in the solution significantly alters the the membrane permeability of *p*-nitroaniline.[24] We report here

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the membrane separation of several regio isomers of disubstituted benzenes based on CD complexation in the bulk aqueous solution. Pumping phenomena of the substrates cross the membrane are also described.

EXPERIMENTAL

Materials

Commercially available nitrophenols (NP), nitroanilines (NA), and iodophenols (IP) were used after recrystallization. Poly(vinyl chloride) (PVC; molecular weight, 70,000) poly(ethylenimine) (PEI; molecular weight, 60,000–80,000), and poly(vinyl alcohol) (PVA; molecular weight, 90,000) were commercial products and used without further purification. α-CD and γ-CD were gifts from Nihon Shokuhin Kako Co., Ltd. β-CD was purchased from Nakarai Chemical Co., Ltd. Double-distilled water was used throughout.

Membrane Preparation

PVC Membrane

A plasticized PVC membrane was prepared by evaporating the solvent from the mixture of 250 mg PVC, 0.5 ml diisodecylphthalate as a plasticizer, and 20 ml tetrahydrofuran on a flat Petri dish of 9.2 cm diameter. Thickness of the membrane thus obtained was approximately 0.1 mm.

PVA PEI Composite Membrane

This membrane was obtained by pouring the solution, composed of 900 mg PVA in water (20 ml) and 225 mg PEI in water (20 ml), onto a flat silicon rubber with a frame of 8.5 cm diameter. After evaporating the solvent, the membrane was immersed in the 5% glutaraldehyde solution for about 1 h for cross-linking the PEI moiety in the membrane.

Permeability Measurements

Selective Permeation of Substrates

All experiments were performed at 23°C using the glass cell illustrated in Figure 1. The effective membrane area of the cell was 2.54 cm^2. The left compartment of the cell was filled with 20 ml of an aqueous solution that dissolves the substrate mixture and an appropriate amount of CD. An equal volume of water was poured into the right side. Both compartments were magnetically stirred at a constant rate. The concentration of the substrates transported from the left to the right across the membrane was determined by high-performance liquid chromatography using ODS-120T (TOYO SODA) as column. The concentration of the substrates in the right-hand solution was plotted against time. The intrinsic membrane permeability of the substrates was determined from a similar measurements without CD.

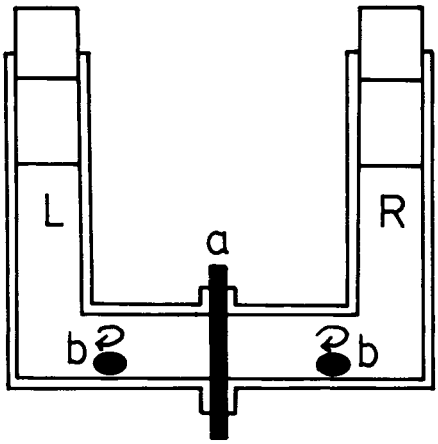

Fig. 1. Schematic representation of the cell for the permeability measurements: (a) membrane, (b) stirring bar.

Pumping of Substrates

Both compartments of the cell in Figure 1 were filled with 20 ml of an aqueous solution that dissolves 0.1 mM of substrate, and an appropriate amount of CD was added to the solution in the right-hand compartment. Both compartments were stirred magnetically at a constant rate. The temperature was kept at 23°C. The concentration changes of the substrate in both solutions were monitored by measuring the absorbances at the wavelength of isosbestic points and the absorption maxima for the cases of PVA-PEI membrane and PVC membrane, respectively. The concentrations of the substrate in both compartments were plotted against time.

RESULTS AND DISCUSSION

Selective Permeation of *o*-, *m*-, and *p*-Isomers

The results of liquid-liquid dialysis permeation of *o*-, *m*-, and *p*-nitroaniline (o-, m-, and p-NA, respectively) through the PVC membrane in the presence or absence of α-CD are depicted in Figure 2. It is clear that, in the absence of α-CD, NA isomers permeate through the PVC membrane from the left to the right along the concentration gradient, but the permeation selectively among the isomers is low. The concentration ratio of the isomers on the right was 1.4:1.2:1.0 for o-NA-m-NA-p-NA 23 h later. On the contrary, in the presence of $5 \times 10^{-2} M$ α-CD, the isomers permeated the membrane selectively, and the concentration ratio on the right at 23 h was 44:14:1.0 for o-NA-m-NA-p-NA. An important characteristic of permeation in the presence of α-CD is that the permeation rate of p-NA remarkably decreased compared with that in the absence of α-CD. Although α-CD addition also depressed the permeation of m-NA and o-NA, the effects were relatively small. These data imply that one can separate o-NA and m-NA from o-NA-p-NA and m-NA-p-NA mixtures, respectively, with the present α-CD-PVC membrane system.

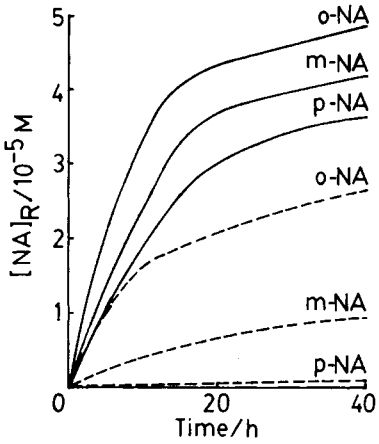

Fig. 2. Permeation of *o*-, *m*-, and *p*-nitroaniline through the PVC membrane in the presence (- - - -) and absence (—) of α-CD. Initial conditions: left, [*o*-nitroaniline] = [*m*-nitroaniline] = [*p*-nitroaniline] = 1×10^{-4} *M*, [α-CD] = 5×10^{-2} *M* (20 ml); right, water (20 ml).

A tentative mechanism by which the permeation rates of NA isomers were altered by addition of α-CD is presented in Figure 3. NA can inherently permeate through the membrane by the solution-diffusion mechanism, in which solute transverses the membrane by the process involving solute dissolution into the membrane phase followed by diffusion along the membrane thickness. In this type of permeation, the partition coefficient of the solute between the membrane phase and the aqueous phase, and the diffusion coefficient in the membrane phase as well, plays a dominant role in determining the overall permeation rate. It is reasonable to assume that, under the present experimental conditions, dissolution of NA-α-CD complexes and α-CD itself from the left-hand solution into the hydrophobic membrane phase was rejected because of their hydrophilic nature. The free NA isomers are the species that can dissolve into and permeate the hydrophobic membrane phase. These interpretations are strongly supported by the fact that, by sulfuric acid-phenol colorimetry[25], we found no α-CD in the right-hand solution even at the end of each measurement. Consequently, the permeation rates of NA isomers depend mainly on the free NA concentration, which is determined by complexation equilibria in the left-hand solution. Considering from the data obtained from the permeation

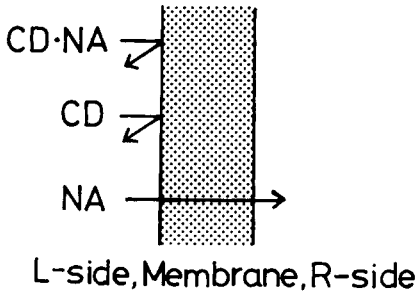

Fig. 3. A tentative mechanism of CD-induced selective permeation of nitroaniline isomers through a plasticized PVC membrane.

experiment without α-CD (Fig. 2), o-, m-, and p-isomers of NA seem to have similar values of diffusion constants in the membrane. The severely reduced permeation rate of p-NA can be rationalized on the basis of the reported values of complex formation constants between α-CD and p-NA, m-NA, and o-NA, which are $65M^{-1}$, $15M^{-1}$, and too small to determine, respectively.[26] As expected from the permeation mechanism, we can find an obvious inverse relationship between the permeation efficiency of the isomers and the stability of the α-CD-NA complexes.

Figure 4 shows the results obtained by using 1×10^{-2} M α-CD, β-CD, and γ-CD. The extent of separation among o-, m-, and p-isomers is enlarged by α-CD and β-CD but it is scarcely affected by γ-CD. The difference observed among α-CD, β-CD, and γ-CD seems reasonable in view of the fact that CD bind more preferably those compounds with the size and shape to fit their hydrophobic cavities. α-CD and β-CD bind p-NA efficiently, but the cavity size of γ-CD is too large to form a stable complex with p-NA.

By comparison of the data in Figure 4A with those in Figure 2, it becomes obvious that the permeation behavior of NA isomers depends significantly on the CD concentration in the solution. A higher CD concentration seems to be required for attaining selective permeation.

The permeation characteristics of nitrophenol (NP) and iodophenol (IP) through the PVC membrane in the presence of α-CD were also studied (Table I). The permeation behavior of NP isomers resembles that of NA isomers. The permeation efficiency of m-NP and p-NP was reduced significantly by α-CD addition, but the effect of α-CD was rather small in the case of o-NP. We can see a noticeable example in the permeation of IP isomers. Namely, nearly no leakage of m-IP and p-IP across the membrane was observed after 23 h, but at that time, the concentration of o-IP in the right-hand solution measured approximately 7×10^{-6} M. This means that

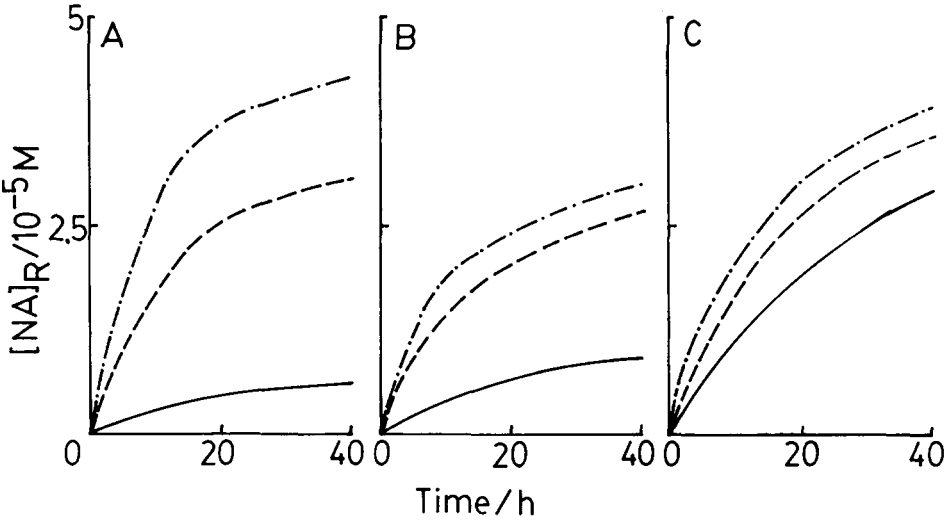

Fig. 4. Permeation of o-, m-, and p-nitroaniline through the PVC membrane in the presence of α-CD (A), β-CD (B), or γ-CD (C). Initial conditions: left, [o-nitroaniline] = [m-nitroaniline] = [p-nitroaniline] = $1 \times 10^{-4}M$, [CD] = $1 \times 10^{-2}M$ (20 ml); right, water (20 ml).

TABLE I
Selective Permeation of Nitrophenols, Nitroanilines, and Iodophenols in the Presence of 5×10^{-2} M α-CD[a]

Substrate[b]	10^6 [substrate]/M on right after 23 h		
	o-	m-	p-
NP	23	2.7	0.7
NA	22	7.0	0.5
IP	6.9	<0.3	—
IP	7.4	—	<0.3

[a] Initial conditions: left; [substrate] = 1×10^{-4} M, [α-CD] = 5×10^{-2} M (20 ml); right, water (20 ml).

[b] NP = nitrophenol, NA = nitroaniline, and IP = iodophenol. o-IP = m-IP or o-IP = p-IP mixture was fed because of the difficulty in simultaneous determination of m-IP and p-IP with HPLC.

one can separate o-IP in a reasonably pure form from a o-IP-m-IP or o-IP-p-IP mixture by use of the present system.

Pumping of Substrates

We have already reported that p-NA permeates the PVC membrane from the left to the right when CD is added to the right-hand solution in spite of the equal initial concentration of p-NA in both compartments.[24] The detailed results are described below.

Figure 5 shows the permeation of p-NA through the membrane in the presence of 1×10^{-2} M CD in the right-hand compartment. The p-NA concentration on the right increased with time to reach 1.52×10^{-4}, 1.46×10^{-4}, and 1.10×10^{-4} M at 50 h for α-CD, β-CD, and γ-CD addition,

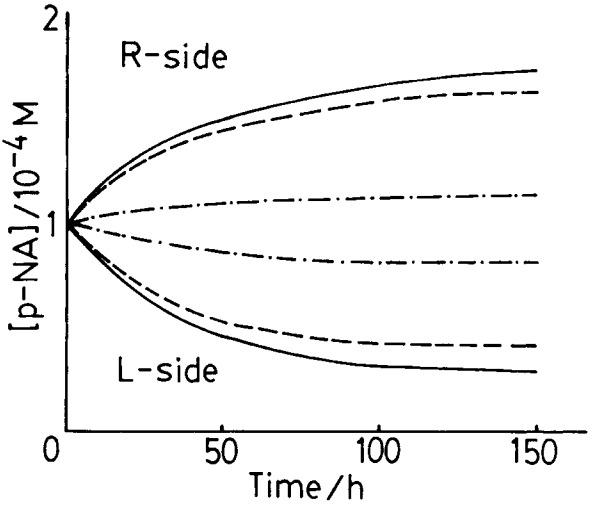

Fig. 5. CD-induced permeation of p-nitroaniline through the PVC membrane: α-CD (—), β-CD (- - -), γ-CD (- · · -). Initial conditions: right, [p-nitroaniline] = 1×10^{-4}–4 M, [CD] = 5×10^{-2} M; left, [p-nitroaniline] = 1×10^{-4} M.

respectively. On the other hand, the concentration of p-NA in the left-hand compartment decreased gradually. The transport of p-NA driven by CD addition was thought to come from the depressed permeation of p-NA from right to left because of CD complexation in the right-hand solution (Fig. 6). In other words, p-NA permeated the membrane from the left to the right along the concentration gradient of the uncomplexed form, which is the only species that can permeate the membrane. The formation of inclusion complexes was ascertained by the fact that the absorption maxima of the right-hand solutions, upon CD addition, shifted from 378 nm (original spectrum of p-NA) to longer wavelengths, that is, 395, 386, and 380 nm for α-CD, β-CD, and γ-CD addition, respectively. The permeation behavior of p-NA was closely related to CD concentration in the right-hand solution (Fig. 7). The permeation efficiency of p-NA was enhanced with increasing the CD concentration. These results also suggest that the permeation of p-NA is driven by CD complexation. As shown in Table I, α-CD induced the permeation of p-NA effectively but the effects on m-NA and o-NA were rather small. This originates from the difference in the complex formation constants between α-CD and o-, m-, and p-NA.[25]

Figures 8 and 9 show the results obtained using PVA-PEI membranes. Although the outline of the permeation is similar to that of PVC membrane, some differences between the two kinds of membranes can be found; in the case of the PVA-PEI membrane, (1) after attaining the maximum concentration difference at about 30 h, the concentration of the substrate on the right gradually decreased with time, and (2) the increased concentration of CD did not enhance the permeation efficiency. The former may be due to the diffusion of CD and its inclusion complexes from the right to the left through the membrane pore along their concentration gradient. Siegel et al. also reported that CD and its inclusion complex permeate the pore of a cellulose membrane.[23] To clarify this point, we estimated the permeability of α-CD for the PVA-PEI membrane. Based on sulfuric acid-phenol colorimetry[25] and the equation of Flynn et al.[27], we obtained the permeability constant of approximately 3.3×10^{-7} cm^2 s^{-1}. This means that CD and its inclusion compolexes permeate the PVA-PEI membrane concurrently with the substrate. The latter was also interpreted by the permeation of CD itself through the membrane. A higher concentration of CD was found

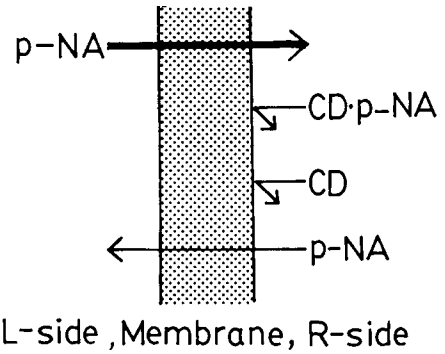

Fig. 6. A tentative mechanism of CD-induced permeation through the PVC membrane.

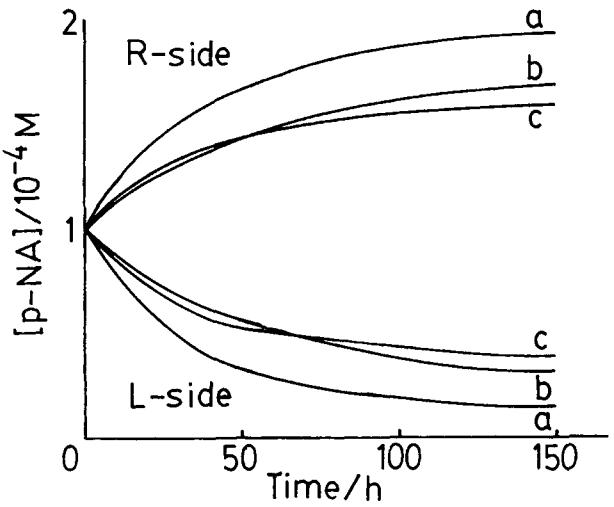

Fig. 7. Effects of α-CD concentration on the permeation of *p*-nitroaniline through the PVC membrane. Initial conditions: right, [*p*-nitroaniline] = 1×10^{-4} *M*, [α-CD] = 5×10^{-2} *M* (a), 2×10^{-2} *M* (b), or 5×10^{-3} *M* (c); left, [*p*-nitroaniline] = 1×10^{-4} *M*.

to be ineffective to enhance the unequality of the substrate concentration between the right-hand and left-hand solutions. In such a situation, the driving force of permeation would diminish significantly.

CONCLUSIONS

CD complexation in the bulk aqueous solution was found to be effective to separate the o-, m-, and p-isomers of disubtituted benzenes from the mixture of regio isomers by taking advantages of the preferential permeation of uncomplexed substrate through the membrane. The concentration

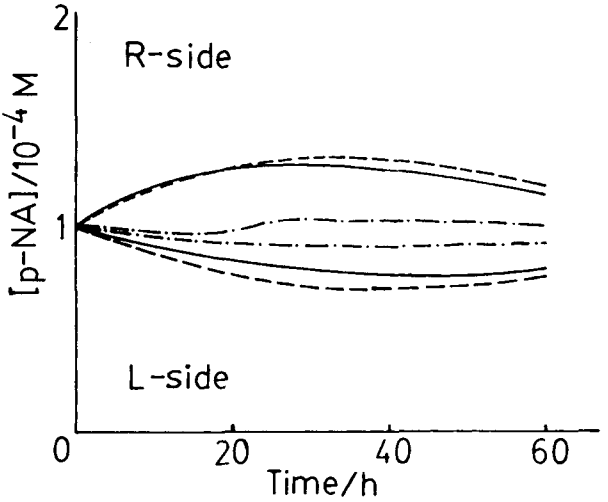

Fig. 8. CD-induced permeation of *p*-nitroaniline through the PVA-PEI composite membrane: α-CD ( ), β-CD (—), γ-CD (-.-.-). Initial conditions are the same as in Figure 5.

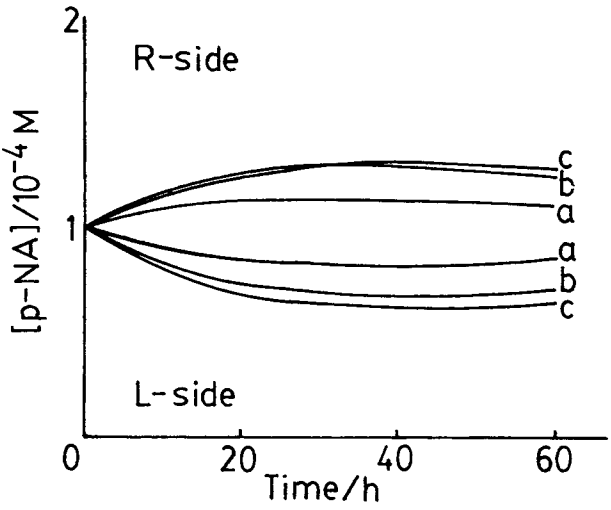

Fig. 9. Effects of α-CD concentration on the permeation of *p*-nitroaniline through the PVA-PEI composite membrane. (a) 5×10^{-2} *M*, (b) 2×10^{-2} *M*, and (c) 5×10^{-3} *M* α-CD. Initial conditions are the same as in Figure 7.

of the substrate across the membrane was also induced by CD addition into the solution. The present CD membrane systems will find some potential applications.

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