Transport of Potassium Picrate through a Liquid Membrane by Metal-Responsive Carriers

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Metal-responsive carriers having three receptors, and conformational variations were synthesized. The transport experiments of potassium picrate using these carriers were performed, and the mechanism was analyzed by numerical simulations. It was found that the rates and the mechanisms of transport of potassium picrate facilitated by these new carriers depend on the conformation of the carriers. That is, the transport rate of potassium picrate by carrier **I** was fast and potassium picrate was transported easily against its concentration gradient. On the other hand, when carrier **I** was coordinated by cupric ion, carrier **III** of cis conformation was formed and the transport rate by this carrier **III** was slower. The efficient uphill transport of potassium picrate by carrier **I** arises both from the different extraction equilibrium constants between the aqueous phase containing potassium chloride and the aqueous phase without potassium chloride, and the weak interaction between potassium picrate and carrier **I** in the organic phase. The numerical simulation of this uphill transport has been performed by using a diffusion-limited process, and the calculated result is consistent with the experimental result. It was also found that the transport rate of potassium picrate depends on the substituents of the nitrogen atoms of diazacrown ether, which affects the interaction between diazacrown ether and potassium picrate.

Introduction

Numerous multidentate complexing molecules for binding metal ions have been designed in order to mimic the biological transport system.[1] Since the complexing properties of diazacrown ether are dramatically modified by the introduction of suitable substituents on the nitrogen atom of diazacrown ether, many carriers using diazacrown ether have been synthesized. On the other hand, the role of metal ion in nature is very important and the metal ion often triggers subsequent reactions in biological systems. Therefore, we have combined the character of diazacrown ether with the metal ion in order to change the functionality of the carrier and have attempted to construct a new system of metal-responsive carriers.

The 2,2′-bipyridyl molecule is coordinated easily by metal ions, so many crown ether derivatives using 2,2′-bipyridyl have been prepared.[2] However, effective carrier systems using these molecules have not been constructed. Thus, we have synthesized new carrier molecules containing both the diazacrown ether and the 2,2′-bipyridyl moiety. The structures of these carriers incorporate three receptors: two diazacrown ether moieties and one 2,2′-bipyridyl moiety.

In this paper, we report the properties of new molecules used as metal-responsive carriers. The ability of these new carriers to transport molecules changes with conformational variations induced by the interaction between the carrier and the metal ion. The new metal-responsive carriers in this study resulted in a dramatic change in transport rates due to the conformational variations, and the efficient uphill transport of potassium picrate was realized by this system. This uphill transport arises from the difference in the extraction equilibrium constants at the two interfaces between the organic phase and the aqueous phase and from the weak interaction between the new carrier **I** and potassium picrate.

In order to clarify a detailed mechanism of uphill transport, the numerical simulation of uphill transport has been performed by using a diffusion limited model whose calculated result is consistent with the experimental result.

Experimental Section

Syntheses. Diazacrown ether (1,7,10,16-tetraoxa-4,13-diazacyclooctadecane) was used as received (Merck).

2,2′-Bipyridyl-6,6′-bis(diazacrown ether) (I). 2,2′-Bipyridyl-6,6′-dicarboxylic acid was prepared by lithiation of 6,6′-dibromo-2,2′-bipyridyl in ethyl ether and carboxylation with carbon dioxide (dry ice).[3,4] 2,2′-Bipyridyl-6,6′-diacid chloride was synthesized by the reaction of 2,2′-bipyridyl-6,6′-dicarboxylic acid with thionyl chloride in benzene. This diacid chloride was purified by the recrystallization, because high purity is necessary for the coupling reaction. New carrier **I** (2,2′-bipyridyl-6,6′-bis(diazacrown ether)) was synthesized by the coupling reactions of diazacrown ether with 2,2′-bipyridyl-6,6′-diacid chloride (H-NMR ($CDCl_3$, ppm): δ 8.92 (doublet), 8.19 (doublet), 8.10 (triplet)). A solution of 2,2′-bipyridyl-6,6′-diacid chloride (2.81 g, 0.01 mol) in dichloromethane (50 mL) was added to a dichloromethane solution (100 mL) containing diazacrown ether (6.9 g, 0.03 mol) and triethylamine (2.02 g, 0.02 mol) using a syringe pump for over 5 h. The reaction products were purified by silica-gel column chromatography after removal of the solvent, using chloroform–hexane as the eluent. This first product eluded is bipyridyl capped diazacrown ether (2,2′-bipyridyl-6,6′-diazacrown ether, **II**), as was previously reported.[4] The yield of this compound was low. The second product is 2,2′-bipyridyl-6,6′-bis(diazacrown ether) (**I**). This product was purified by recrystallization from benzene, and its structure was confirmed by NMR (270 MHz), infrared spectroscopy, mass spectroscopy, and elemental analyses. The yield was 45%. H-NMR ($CDCl_3$, ppm): δ 3.0–4.8 (m), 7.7–8.0 (m). Anal. Calcd for $C_{36}H_{56}N_6O_{10}$: C, 59.02; H, 7.65; N, 11.48. Found: C, 58.95; H, 7.70; N, 11.51.

The 2,2′-Bipyridyl-6,6′-bis(diazacrown ether) Cu complex (**III**) was synthesized by the reaction of 2,2′-bipyridyl-6,6′-bis(diazacrown ether) (0.67 g, 0.001 mol) with an excess of copper acetate (1.1 g, 0.006 mol) in refluxing methanol. The copper complex was purified by silica-gel column chromatography (yield, 85%).

2,2′-Bipyridyl-6-mono(diazacrown ether) (IV) was synthesized by a method similar to that used for 2,2′-bipyridyl-6,6′-bis(diazacrown ether). First, 6-bromo-2,2′-bipyridyl was lithiated with butyllithium in ethyl ester, which formed 2,2′-bipyridyl-6-carboxylic acid after carboxylation by carbon dioxide (dry ice). Reaction of 2,2′-bipyridyl-6-carboxylic acid with thionyl chloride in benzene produced 2,2′-bipyridyl-6-acid chloride. 2,2′-Bipyridyl-6-acid chloride (1 g, 4.58×10^{-3} mol) in dichloromethane (10 mL) was added by a syringe pump to 30 mL of dichloromethane containing diazacrown ether (2.1 g, 9.15×10^{-3} mol) and triethylamine (0.46 g, 4.58×10^{-3} mol) slowly over a 5-h

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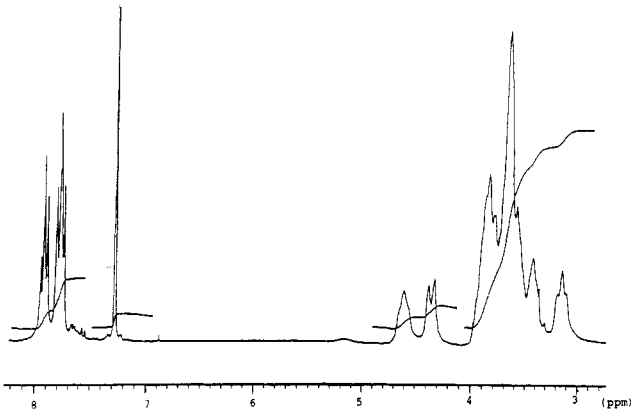


Figure 1. H-NMR (270 MHz) spectrum of bis(2,2′-bipyridyl)bis-(diazacrown ether) (**VI**) in $CDCl_3$: diazacrown ether methylene (δ, 3.05–4.0, 4.25–4.75); bipyridyl (δ, 7.93, 7.77); impurity chloroform (δ, 7.25).

period. After reaction, the solvent was evaporated to dryness. The product (**IV**) was purified by silica-gel column chromatography. The yield was 70%.

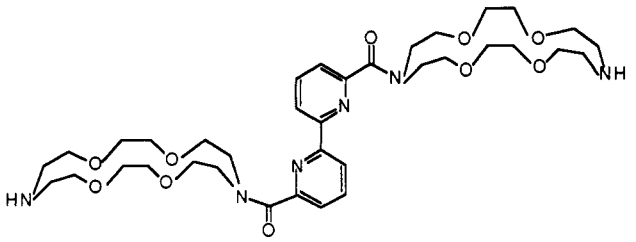
The 2,2′-Bipyridyl-6-mono(diazacrown ether) Cu complex (**V**) was prepared by a synthetic method using the copper complex **III**.

Bis(2,2′-bipyridyl) bis(diazacrown ether) (VI). The synthesis of the cyclic compound of bis(2,2′-bipyridyl)bis(diazacrown ether) (**VI**) was performed via the coupling reaction between 2,2′-bipyridyl-6,6′-bis(diazacrown ether) (**I**) and 2,2′-bipyridyl-6,6′-diacid chloride: 2,2′-bipyridyl-6,6′-bis(diazacrown ether) (0.5 g, 7.5×10^{-4} mol) and triethylamine (0.07 g, 7.5×10^{-4} mol) were dissolved in 10 mL of dichloromethane. 2,2′-Bipyridyl-6,6′-diacid chloride (0.21 g, 7.5×10^{-4} mol) was also dissolved in 10 mL of dichloromethane. Both solutions were added to dichloromethane (100 mL) in a 300-mL three necked flask using a syringe pump for over 6 h under argon. After addition, the reaction solution was refluxed for 1 h. After cooling, the solvent was evaporated to dryness. The product was purified by column chromatography on silica gel. The chloroform–hexane system was used as the eluent. The first fraction eluded is the product (yield, 36%). The structure was confirmed by NMR spectroscopy, (270 MHz), infrared spectroscopy, elemental analyses, and mass spectroscopy. The H-NMR of this cyclic compound (**VI**) is shown in Figure 1. H-NMR ($CDCl_3$; ppm): δ 3.05–4.0, 4.25–4.75 (48 H, m), 7.93 (4 H, m), 7.77 (8 H, m). Ir (KBr; cm^{-1}): 2930, 1640, 1560, 1480, 1440, 1360, 1290, 1200, 1100, 1000, 920, 820, 760. Anal. Calcd for $C_{48}H_{60}N_8O_{12}$: C, 61.28; H, 6.38; N, 11.91. Found: C, 61.10; H, 6.40; N, 11.87.

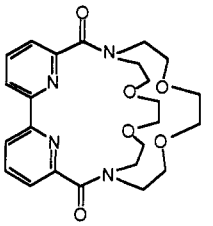
The structures of compounds **I**, **II**, **IV**, and **VI** described in the experimental section are shown in Chart 1.

Measurements of Transport. Liquid membrane experiments were conducted using an open-ended double cylindrical glass cell as described previously.[5,6] The top of this cylinder was covered with a glass lid containing a three-way stopcock to minimize evaporation. A dichloromethane solution containing the carrier (2.7×10^{-4} M) was placed at the base of the cell. The source phase was a Tris buffer solution (pH = 7.20, 20 mL) containing potassium picrate (1×10^{-4} M) and potassium chloride (1×10^{-1} M), and this was added carefully to the dichloromethane solution in the outer cylinder. The receiving phase was a Tris buffer solution (pH = 7.20, 10 mL) which was placed in the inner cylinder, while the organic phase (dichloromethane membrane) was stirred magnetically. The vessels were maintained at 20 °C. The transport of potassium picrate was observed by monitoring the intensity of UV absorption of potassium picrate; that is, the parts of the receiving phase and the source phase were sampled by a syringe, and the UV–visible peak intensities of picrate in both phases were measured. After the UV–visible spectra were measured, the sampled solutions were returned to their respective phases. The potassium ion concentration was measured by means of ion chromatography, and the resulting concentrations were in good agreement with the concentrations of picrate measured by means of UV absorption.

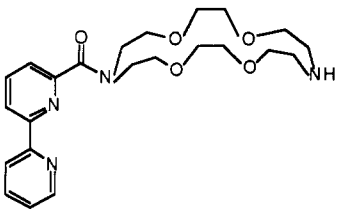
CHART 1



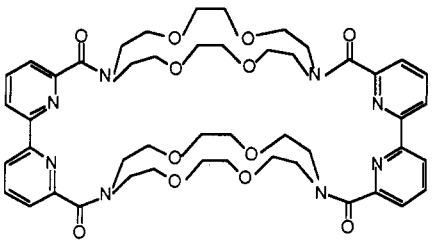
I



II



IV



VI

Instruments. UV–visible spectra were recorded on a Hitachi 340 recording spectrophotometer with the cell compartment thermostated at 20 °C. ^{1}H-NMR spectra were obtained with a JEOL X 270 spectrometer (270 MHz).

Results and Discussion

Relationship between the Conformation of the Carrier and the Transport Rate. 2,2′-Bipyridyl-6,6′-bis(diazacrown ether) (**I**) has two conformations of trans and cis form as shown in Chart 2. The trans form is more stable than the cis form under normal conditions. The trans form of carrier **I** may interact with two potassium picrate molecules, because some distance separates two diazacrown ether groups. On the other hand, there is a possibility that the interaction between the cis form of carrier **I** and the potassium picrate molecule is affected by the two diazacrown ether groups of carrier **I**, because the distance between these two diazacrown ether groups is short and two groups interact with each other. Therefore, it is expected that the efficiency of transport of potassium picrate is affected by the conformations of carrier **I**. Chelation of metal to the bipyridyl moiety of carrier **I** forces it into the cis form, resulting in restriction of freedom of two diazacrown ether groups and creating carrier **III** fixed by

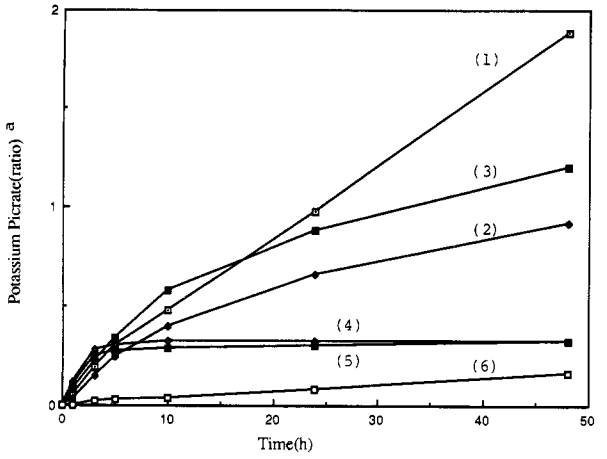
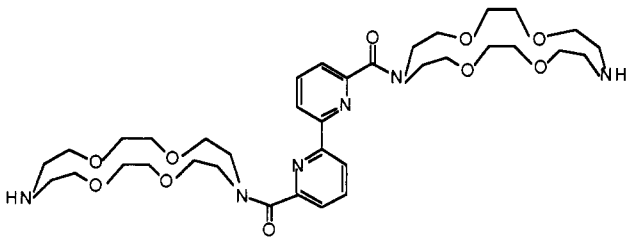
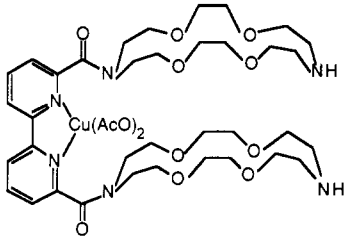


Figure 2. Transport behavior of potassium picrate. Source phase: tris buffer (pH = 7.20), 20 mL, potassium picrate (1×10^{-4} M); KCl (1×10^{-1} M). Receiving phase: Tris buffer (pH = 7.20), 10 mL. Organic phase: CH_2Cl_2, 30 mL; carrier (2.7×10^{-4} M). (1) Carrier I; (2) carrier III; (3) carrier I and $CuCl_2$ (1×10^{-2} M) in the source phase; (4) diazacrown ether; (5) diazacrown ether ($2 \times 2.7 \times 10^{-4}$ M) and 2,2'-bipyridyl (2.7×10^{-4} M); (6) *N,N'*-dibenzoyldiazacrown ether. [a]Concentration in the receiving phase. The ratio to initial concentration of source phase.

CHART 2



I (trans form)



III (cis form)

a copper atom. This molecule was prepared and the transport behaviors by carriers I and III were examined.

The transport experiments through the dichloromethane membrane containing new carriers I and III were conducted by the method used in previous studies.[5] A blank experiment was performed with potassium picrate in which the membrane contained no carrier; no detectable movement of potassium picrate across the dichloromethane membrane was observed. The results of the transport of potassium picrate by various carriers are shown in Figure 2, and the mean rates of transport of potassium picrate are summarized in Table 1. Table 2 lists the extraction equilibrium constants of potassium picrate by carriers from the aqueous Tris buffer solutions to the dichloromethane solutions under the same experimental condition.

The transport rate of potassium picrate by carrier I is very fast. On the other hand, the transport rate by carrier III is slower; after 24 h, the mean rate of transport by carrier I is about 4 times facter than that by carrier III, as shown in Table 1. The transport rate of potassium picrate by carrier I is constant after 10 h, but the rate by carrier III decreases with time. Even when the concentration of potassium picrate in the receiving phase is the same as that in the source phase after transport by carrier I, the transport rate of potassium picrate by carrier I remains nearly constant (4×10^{-8} mol/h). Eventually, potassium picrate is transported against its concentration gradient in an uphill transport. In contrast, the efficiency of transport of potassium picrate by carrier III is very low, and even when the transport experiment is continued for 48 h, its concentration in the receiving phase is almost the same as that in the source phase. This difference in the transport ability between carrier I and carrier III is remarkable.

TABLE 1: Mean Rate of Transport of Potassium Picrate through the Dichloromethane Membrane Containing Various Carriers

	rate for given time interval[a] (h), 10^{-8} mol/h					
	0–1	1–3	3–5	5–10	10–24	24–48
carrier I	5	7	5.5	4.0	3.7	3.7
carrier III	3	6	4.3	3.2	2.3	0.83
diazacrown[b]	12	8	1.0	0.6	0	0
dibenzocrown[c]	0	1	0.3	0.3	0.3	0.3

[a] Interval of time (h). The term 0–1 means the first hour, and 1–3 means from 1 to 3 h. [b] 1,7,10,16-Tetraoxo-4,13-diazacyclooctadecane. [c] *N,N'*-dibenzoyl-1,7,10,16-tetraoxo-4,13-diazacyclooctadecane.

TABLE 2: Extraction Equilibrium Constants (K_{so} and K_{ro}) between a Dichloromethane Solution Containing Carrier and a Tris Buffer Solution Containing Potassium Picrate[a]

carrier + K^+·picrate$^-$ $\rightleftharpoons$ (carrier–K^+·picrate$^-$ complex)

	K_{so}[b]	K_{ro}[c]
carrier I	291	246
carrier III	379	365

[a] The conditions of measurement of the equilibrium constant are the same as those in the transport experiments. [b] Extraction equilibrium constant between a Tris buffer solution containing KCl (1×10^{-1} M) and potassium picrate (1×10^{-4} M), and a dichloromethane solution containing carrier (2.7×10^{-4} M). [c] Extraction equilibrium constant between a Tris buffer solution containing potassium picrate (1×10^{-4} M) and a dichloromethane solution containing carrier (2.7×10^{-4} M): $K = (\text{carrier–potassium picrate})_{org}/(\text{carrier})_{org}\,(\text{potassium picrate})_{aq}$

These results suggest that the mechanism of transport by carrier I is different from that by carrier III. In order to clarify this mechanism, the organic phases containing the carrier were examined by UV–visible measurements after 48 h of transport, and the chemical species in the organic phase were determined by elemental analyses. The UV–visible spectrum of the organic phase containing carrier I showed a weak peak intensity for picrate, and the position of the peak did not change. On the other hand, the UV–visible spectrum of organic phase containing carrier III showed a strong peak intensity for picrate, and a slight red shift (3 nm) of the peak position was observed. In order to identify the species in the organic phase containing carrier III, the reaction of carrier III with an excess amount of potassium picrate was performed in methanol solution; this reaction led to successful isolation of fine crystals of the complex. The UV–visible spectrum of this complex was consistent with that of the organic phase in the transport experiment, and the elemental analysis of this complex indicated a 1:1 complex of carrier III and potassium picrate. On the other hand, the reaction of carrier I with potassium picrate in methanol did not give the product. This interaction would probably be too weak to form a stable complex.

These results indicate that the interaction between carrier III and potassium picrate is stronger than that between carrier I and potassium picrate. That is, since carrier III coordinated by a copper atom has two diazacrown ether groups of cis form, these groups strongly interact with picrate, and one picrate molecule would exist between two diazacrown ether groups of carrier III. This interaction may be a charge transfer from the diazacrown ether to the picrate, although picrate has a negative charge on

TABLE 3: Extraction Equilibrium Constants (K) between a Dichloromethane Solution Containing Carrier I and An Aqueous Solution Containing Potassium Picrate and Potassium Chloride[a]

concn of potassium chloride,[b] M	1.0	1×10^{-1}	0.0
K	458	154	75.6

[a] The organic solution: CH_2Cl_2 (10 mL), 2.7×10^{-4} M carrier I. The aqueous solution: H_2O (10 mL), 1×10^{-4} M potassium picrate. [b] The concentration of potassium chloride in the aqueous solution.

the oxygen atom. The red shift of the peak in the UV–visible spectrum described above supports a strong interaction between picrate and the diazacrown ether groups of carrier III. A similar charge-transfer interaction between crown ether and quaternary bipyridyl was reported already.[7] In contrast, the interaction between carrier I and potassium picrate would be weak, since the conformation of carrier I is not fixed completely. The extraction equilibrium constant in Table 2 supports smaller interaction between carrier I and potassium picrate; the extraction equilibrium constants of carrier I are smaller than those of carrier III. Thus, one of the reasons that the transport behavior of carrier I is very different from that of carrier III is the difference in the interaction between the carrier and potassium picrate.

The general transport formula of the carrier mediated transport of an ion pair in a diffusion limited process gives the relationship between the transport rate and the concentration of carrier (L_o).[8] If two molecules of potassium picrate are transported by two diazacrown ether groups of carrier I, the transport rate by carrier I is 2 times faster than that by carrier III. However, the data of the transport rate as shown in Table 1 does not show such a trend. Only one molecule of potassium picrate is probably transported by carrier I, and the difference in the transport rate between two carriers comes from the term of extraction equilibrium constant.[8] The reason for this fact is the weak interaction between carrier I and potassium picrate. Thus, the concentration of the complex of carrier I and potassium picrate in the organic phase is very low, and potassium picrate is transported against its concentration gradient efficiently (uphill transport).

As described above, the transport rate depends on the changes in the conformation of the carrier molecule; that is, a metal-responsive transport system is realized by new carriers. This may also be inferred as one of the allosteric effects in the transport system.[9]

Uphill Transport by the New Carrier (I). Generally, an unsymmetric gradient between the source phase and the receiving phase across the organic membrane is required for uphill transport. Thus, in order to clarify the mechanism of uphill transport observed in this experiment, the extraction equilibrium constant (K_{so}) from the source phase to the organic phase and the extraction equilibrium constant (K_{ro}) from the receiving phase (containing 1×10^{-4} M potassium picrate) to the organic phase were measured, and the results were summarized in Table 2. The extraction equilibrium constant K_{so} of carrier I is 291, which is larger than the K_{ro} of carrier I (246), while the extraction equilibrium constant K_{so} (379) of carrier III is slightly larger than K_{ro} (365) of carrier III. The difference between the extraction equilibrium constants K_{so} and K_{ro} may be due to the effect of potassium chloride (1×10^{-1} M) in the source phase.

In order to confirm this, the extraction equilibrium constants between the dichloromethane solution containing 2.7×10^{-4} M carrier I and the aqueous solution containing various concentrations (0.0–1.0 M) of potassium chloride were measured. In this experiment, pure water was used in place of the Tris buffer solution, since there is a possibility that the extraction equilibrium constant is affected by tris(hydroxymethyl)aminomethane in Tris buffer. As shown in Table 3, the extraction equilibrium constant depends on the concentration of potassium chloride in the aqueous solution. In addition, transport experiments using various concentrations of potassium chloride in the source phase were performed, and their results were shown in Figure 3. This indicates that the efficiency of uphill transport increases with an increasing concentration of potassium chloride in the source phase.

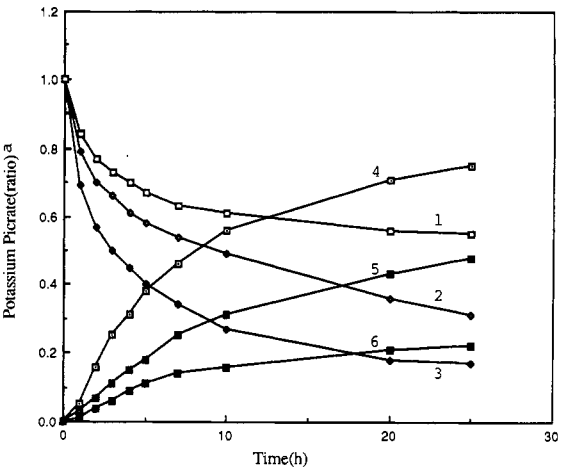


Figure 3. Transport behavior of potassium picrate by carrier I. Effect of concentration of potassium chloride in the source phase. Source phase: H_2O, 10 mL; potassium picrate (1×10^{-4} M); KCl, 1, 1×10^{-1}, and 1×10^{-2} M. Receiving phase: H_2O, 10 mL. Organic phase: CH_2Cl_2, 30 mL; carrier I (2.7×10^{-4} M). (1–3) Source Phase; (4–6) receiving phase; (3, 4) KCl 1 M in the source phase; (2, 5) KCl, 1×10^{-1} M in the source phase; (1, 6) KCl, 1×10^{-2} M in the source phase. [a]The ratio to initial concentration of source phase.

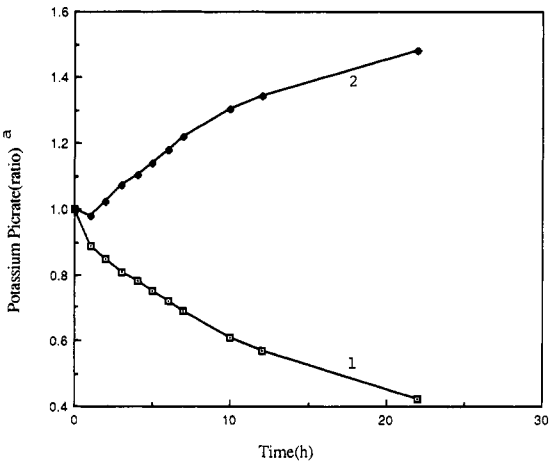


Figure 4. Transport behavior of potassium picrate by carrier I. Effect of potassium chloride in the source phase. Source phase: Tris buffer (pH = 7.20), 10 mL; potassium picrate (1×10^{-4} M); KCl (1×10^{-1} M). Receiving phase: Tris buffer (pH = 7.20), 10 mL; potassium picrate (1×10^{-4} M). Organic phase: CH_2Cl_2, 30 mL; carrier I (2.7×10^{-4} M). (1) Source phase; (2) receiving phase. [a]The ratio to initial concentration of source phase.

In order to confirm the effect of potassium chloride, another transport experiment was performed; in this experiment, the source phase initially contains 1×10^{-4} M potassium picrate and 1×10^{-1} M potassium chloride and the receiving phase also contains 1×10^{-4} M potassium picrate. As shown in Figure 4, the concentration of potassium picrate in the source phase decreased with time. At the same time, the concentration of potassium picrate in the receiving phase also decreased. However, after the initial decrease, the concentration of potassium picrate in the receiving phase began to increase. The initial decrease is caused by partial transfer of potassium picrate from the receiving phase to the organic phase to form a complex with carrier I and potassium picrate. Eventually, the concentration gradient of potassium picrate between the source phase and the receiving phase increased with time, as shown in Figure 4. This is definite evidence that uphill transport is caused by potassium chloride in the source phase.

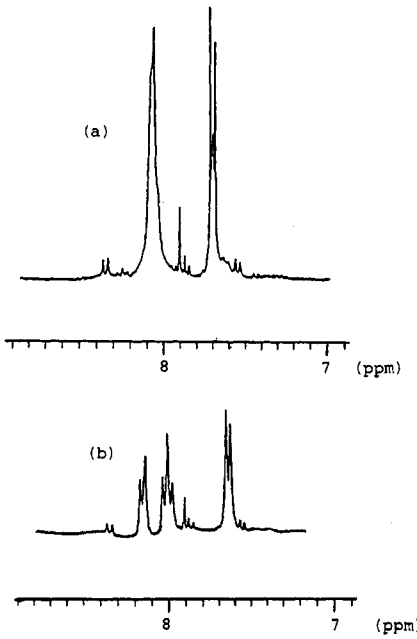


Figure 5. H-NMR (270 MHz) spectra of bis(2,2'-bipyridyl)bis-(diazacrown ether) (VI) in CD_3OD. (a) VI in CD_3OD; (b) VI + KI in CD_3OD.

Evidence for the formation of a carrier I–potassium complex is required as additional data. However, since this complex is unstable, it is difficult to confirm this complex by usual spectroscopic methods. Thus, a related cyclic carrier VI (bis-(bipyridyl)bis(diazacrown ether)) was used to make a stable carrier–potassium complex, since the two diazacrown ether groups of carrier VI are fixed by the two bipyridyl moieties as shown in Chart 1. The formation of the carrier VI–potassium complex was examined by NMR measurements. The H-NMR spectrum of the bipyridyl group of carrier VI in CD_3OD shows a single broad peak at 8.06 ppm and a double peak at 7.69 ppm. After addition of potassium iodide to this solution, the single broad peak splits into two peaks and, eventually, into three peaks: 8.15 ppm (doublet), 8.03 ppm (triplet), and 7.64 ppm (doublet), as shown in Figure 5. It was reported by Buhleier that a similar NMR spectrum is observed when the complex of carrier II and sodium ion is formed.[4] These results suggest that the bipyridyl of carrier VI is coordinated by the potassium ion. Further evidence for the formation of the carrier I–potassium complex was obtained by measuring the UV–visible spectrum. A shift in the peak position and an increase in peak intensity were observed during the formation of the complex.

Numerical Simulation of Uphill Transport. In order to clarify the mechanism of the uphill transport of potassium picrate by carrier I, a numerical simulation using a model for diffusion-limited transport was performed on the results of the transport experiment using 1 M potassium chloride in the source phase shown in Figure 3.

A typical concentration profile for the model is shown in Figure 6.[8c] When the rates for complex formation and dissociation between carrier I and potassium picrate are very fast compared to the diffusion rate through the organic membrane, the extraction equilibrium constants K are related to the concentrations (L and LS) at the organic membrane interfaces and the concentration (S) of aqueous phases according to the following formula.

$$K_1 = \frac{LS_{i,out}}{L_{i,out}S_{out}} \quad K_2 = \frac{LS_{i,in}}{L_{i,in}S_{in}} \tag{1}$$

where K_1 = extraction equilibrium constant between the source phase and the organic phase; K_2 = extraction equilibrium constant between the receiving phase and the organic phase; $L_{i,out}$ = concentration of carrier I at the interface between the source phase and the organic phase; $LS_{i,out}$ = concentration of complex at the interface between the source phase and the organic phase; S_{out} = concentration of potassium picrate in the source phase; $L_{i,in}$ = concentration of carrier I at the interface between the receiving phase and the organic phase; $LS_{i,in}$ = concentration of complex at the interface between the receiving phase and the organic phase; and S_{in} = concentration of potassium picrate in the receiving phase.

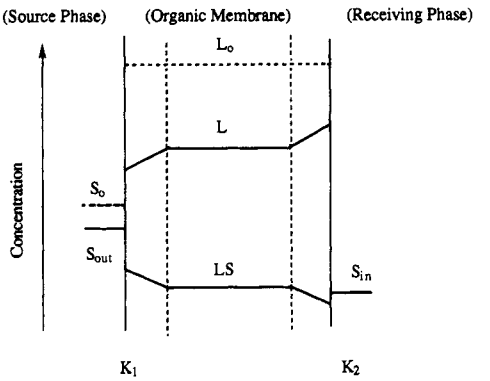


Figure 6. Concentration profile of uphill transport of potassium picrate in the steady state.

Under steady-state condition,[8c]

$$\frac{LS_{i,out} - LS}{LS - LS_{i,in}} = 1 \qquad LS = {}^1/_2(LS_{i,out} + LS_{i,in}) \tag{2}$$

The transport rate V is written as

$$V = D/l(LS_{i,out} - LS) = D/2l(LS_{i,out} - LS_{i,in}) \tag{3}$$

When we assume that the total carrier I concentration (L_o) is constant through the membrane,

$$L_o = LS_{i,out} + L_{i,out} = LS + L = LS_{i,in} + L_{i,in} \tag{4}$$

From eqs 1 and 4,

$$LS_{i,out} = L_o\left(\frac{K_1S_{out}}{1 + K_1S_{out}}\right) \qquad LS_{i,in} = L_o\left(\frac{K_2S_{in}}{1 + K_2S_{in}}\right)$$

Thus, the equation of the transport rate becomes

$$V = \left(\frac{D}{2l}\right)(L_o)\left(\frac{K_1S_{out} - K_2S_{in}}{(1 + K_1S_{out})(1 + K_2S_{in})}\right) \tag{5}$$

The equation of transport rate for an ion pair such as potassium picrate is

$$V = \left(\frac{D}{2l}\right)(L_o)\left(\frac{K_1S_{out}^2 - K_2S_{in}^2}{(1 + K_1S_{out}^2)(1 + K_2S_{in}^2)}\right) \tag{6}$$

The values of K_1 and K_2 shown in Table 3 were used for eq 6, and the experimental value of V for the first hour was used to determine $(D/l)(L_o)$. The result of the numerical simulation using eq 6 is shown in Figure 7, which agrees with the experimental results. This result also indicates that the uphill transport of potassium picrate arises from the difference in the extraction equilibrium constants of the two interfaces between the organic phase and the aqueous phase.

Effect of Other Factors on Transport Rate. In order to examine the effect of the stability of the complex on the transport rate of potassium picrate, transport experiments using related compounds were performed. When diazacrown ether (1,7,10,16-tetraoxa-4,13-diazacyclooctadecane) is used as the carrier, the efficiency of transport is very low and potassium picrate is not transported after 10 h. This is caused by strong interaction between diazacrown ether and potassium picrate as indicated by the result of UV–visible measurements. This transport behavior of diaz-

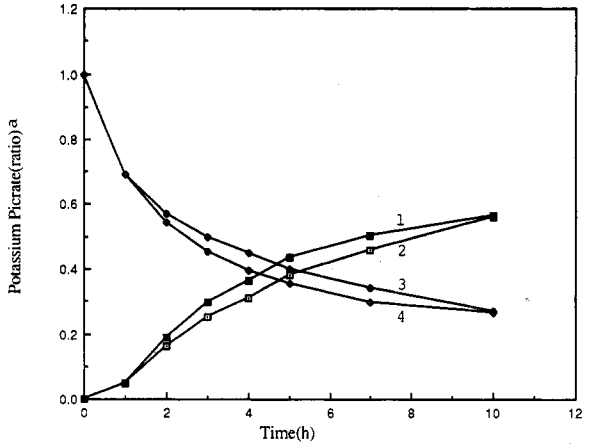


Figure 7. Numerical simulation of uphill transport of potassium picrate by carrier I. (1, 2) Receiving phase; (3, 4) source phase; (1, 4) calculation,[b] (2, 3) experiment.[c] [a]The ratio to initial concentration of source phase. [b]These data were calculated by eq 6. The experimental data of V for the first hour were used for determination of $(D/l)(L_0)$ value. The values of organic phase were gained from the transport experiment. [c]The experimental data shown in lines 3 and 4 of Figure 3.

acrown ether is very similar to that of carrier **III**. The transport behavior of the cyclic carrier **VI** (bis(bipyridyl)bis(diazacrown ethers)) is also almost the same as carrier **III**, although the transport rate of potassium picrate by carrier **VI** is faster than that by carrier **III**. Because the distance between the two diazacrown ether moieties of carrier **VI** is fixed by two bipyridyl moieites, the complex is weaker than with carrier **III**. As a consequence, as potassium picrate is released easily from the organic phase to the receiving phase, a faster transport rate is observed for carrier **VI**.

In order to confirm the effect of the cis form of carrier **I** on the transport rate, the process of complexation of carrier **I** with cupric ion was examined. Cupric chloride (1×10^{-2} M) was added to the source phase (1×10^{-4} M potassium picrate and 1×10^{-1} M KCl), and the transport rate by carrier **I** was measured. The transport behavior of this system is shown in Figure 2. During the first 0–17 h, the transport rate using the source phase with cupric ions was faster than that without cupric ions. This indicates that the transport rate of potassium picrate is accelerated by cupric ions in the source phase. This result was observed in other cases.[10] However, the transport rate of potassium picrate by this system decreased with time, as shown in Figure 2, and the transport rate using the source phase without cupric ions exceeded that with cupric ions after 17 h.

This result could be explained as follows. The cupric ions in the source phase react gradually with carrier **I** on the interface between the source phase and the organic phase, and its copper complex, carrier **III**, is formed. That is, carrier **I** is gradually transformed to carrier **III**, and the transport rate decreases due to strong interaction between the diazacrown ether groups of carrier **III** and potassium picrate. This indicates that the change in conformation of carrier from trans to cis form in the same solution causes a decrease in the transport rate of potassium picrate. This also supports our explanation of the relationship between the conformation of the carrier and the transport rate.

Since the carrier **III** includes a bipyridyl moiety coordinated by cupric ion, there is a possibility that the rate of transport by carrier **III** is affected by cupric ion. In order to examine the effect of cupric ion on the transport rate, 2,2′-bipyridyl-6-mono-(diazacrown ether) (**IV**) and its copper complex (**V**) were synthesized. The transport rate by carrier **IV** (4.5×10^{-8} mol/h, for the first hour) is very similar to that by carrier **I** (5×10^{-8} mol/h) and the difference in the transport rate between carrier **IV** (4.5×10^{-8} mol/h) and carrier **V** (4.3×10^{-8} mol/h) is very small. Thus, the transport rate of potassium picrate by carrier **III** would not be affected by cupric ion.

These experimental results also suggest that the ability of diazacrown ether to act as a carrier is changed by the introduction of suitable substituents on the nitrogen atom of diazacrown ether. In order to examine the effect of the substituents of diazacrown ether on the rate of transport, *N*,*N*′-dibenzoyldiazacrown ether was chosen for comparison, and the rates of transport by diazacrown ether were compared with that of *N*,*N*′-dibenzoyldiazacrown ether, and their results were shown in Figure 2. The total rates of transport by both carriers were very slow. The initial rate of transport by diazacrown ether (0–3 h) was very fast, but potassium picrate was not transported after 10 h (as described above). This indicates that potassium picrate is not transported, because the interaction between diazacrown ether and potassium picrate is very strong. This conclusion was confirmed by the high peak intensity of picrate in the UV–visible spectrum of the organic membrane phase. On the other hand, though the initial rate of transport by *N*,*N*′-dibenzoyldiazacrown ether was very slow, the concentration of potassium picrate in the receiving phase gradually increased with time. The concentration of potassium picrate increased in the receiving phase even after the transport experiment was continued for 48 h. This initial transport behavior by *N*,*N*′-dibenzoyldiazacrown ether is similar to that by carrier **I**, though the transport rate of potassium picrate through the organic membrane by carrier **I** is very fast. This suggests that the interaction between *N*,*N*′-dibenzoyldiazacrown ether and potassium picrate is very weak and that both the stability of this complex and the extraction equilibrium constant are small. Thus, although potassium picrate is released easily from the organic phase to the receiving phase, it is difficult for potassium picrate to be transported from the source phase to the organic phase. This result indicates that the transport rate is affected by the substituents on the nitrogen atom of diazacrown ether.

The transport experiments using dichloromethane membrane containing diazacrown ether ($2 \times 2.7 \times 10^{-4}$ M) and 2,2′-bipyridyl-(2.7×10^{-4} M) were conducted to probe the effect of 2,2′-bipyridyl on the transport rate of potassium picrate, but their rates are almost the same as with the diazacrown ether.

Conclusion

The results indicate that the stability of these complexes and the extraction equilibrium constants of these carriers are changed by the conformational variations of carriers and the substituents on the nitrogen atoms of diazacrown ether of the carriers. Especially, the transport rates of potassium picrate through the dichloromethane membranes by new carrier **I** depend on its conformational changes. The uphill transport is caused by the difference in the extraction equilibrium constants at the two interfaces; this is confirmed by the numerical simulation using a diffusion-limited model. Since carrier **I** has suitable extraction equilibrium constants and since the interaction between carrier **I** and potassium picrate in the organic phase is small, potassium picrate is transported quickly from the source phase to the receiving phase through the dichloromethane membrane. Therefore, new carrier **I** is unique as a carrier of potassium picrate and as a metal-responsive carrier.

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