

Uphill Transport of Metal Picrate through a Liquid Membrane by Ylides¹

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New pH dependent carrier molecules, aminimides, were synthesized, and their properties were investigated by transport experiments of metal picrate through a liquid membrane. These aminimides have the nitrogen atom bearing a negative charge (ylidic nitrogen atom) and the oxygen atom of the carbonyl group, which interact with metal ions. Since this ylidic nitrogen atom can interact with a proton in solution and be conjugated to the carbonyl group, the extraction equilibrium constant is affected by the substituents of the aminimide and the pH in solution. Thus, the transport rate of metal picrate by the aminimide depended on the substituents and the pH in solution. By using this property of aminimides, a new uphill transport system was constructed and it was found that aminimides are efficient carrier molecules to transport metal picrate against its concentration gradient. The numerical simulation of uphill transport by this pH dependent carrier has been performed by using the improved transport rate equation, and the calculated result is consistent with the experimental result. These results indicate that the uphill transport arises from the difference in the extraction equilibrium constant at the two interfaces between the organic phase and the aqueous phases with different pH values.

Introduction

It has been known that ylides are important reagents in organic syntheses, even though ylides are usually very unstable. However, when the ylides have electron withdrawing groups as substituents, the electrons on the anionic atom (ylidic atom) can be delocalized and the ylides are stabilized.² These stabilized ylides have interesting properties as functionalized materials because of the unusual valency of the ylidic atom. A variety of multidentate macrocyclic compounds have been studied as model carriers for transport of cations across cell membranes, including naturally occurring ionophores, and their properties have been examined with liquid membrane model systems.^{3,4} The active transport observed in a cell membrane is very important to life, and the model system used is the pH dependent uphill transport.^{4,11}

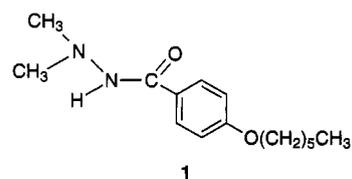
Since the ylidic atom of ylides has a negative charge and it is easy for this atom to interact with a proton, the properties of the ylide are very sensitive to the concentration of protons in solution. Thus, it is expected that the properties of ylides change largely with solution pH, and as a consequence, the ylide can be used as the pH dependent carrier of metal ions.

We have studied the properties of aminimides, which are one type of ylide.⁵ These compounds have adjacent nitrogens bearing positive and negative charges and are very stable under normal conditions, and we tried to clarify the properties of aminimides as carriers. As a consequence, we found that the aminimide functions well in this capacity. In this paper, we report the transport behavior of metal picrates through a liquid membrane containing the aminimide and their specific uphill transport phenomena.

Experimental Section

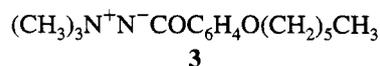
Syntheses. *N,N*-Dimethyl-*N'*-4-hexyloxybenzoylhydrazine **1**. A solution of 26 g (0.108 mol) of 4-hexyloxybenzoyl chloride in 50 mL of dry benzene was added to a mixture of 20 g (0.333 mol) of *N,N*-dimethylhydrazine and 5 mL of triethylamine in 100 mL of dry benzene at 5 °C during 2 h. This mixture was

stirred at room temperature for 3 h and then refluxed for 15 h. After cooling, the solvent was removed under vacuum and *N,N*-dimethyl-*N'*-4-hexyloxybenzoyl hydrazine **1** produced was recrystallized from benzene. The white needle type crystals (20.5 g) of hydrazine **1** were gained (yield 71.8%).



IR (KBr; cm^{-1}): 3240, 2950, 1640, 1608, 1540, 1509, 1480, 1320, 1260, 1180, 1020, 920, 850, 565. NMR: 7.9 (2H), 7.0 (2H), 4.1 (2H), 3.1 (1H), 2.78 (6H), 1.8 (2H), 1.48 (6H), 0.95 (3H) (ppm). Anal. Calcd for $\text{C}_{15}\text{H}_{24}\text{N}_2\text{O}_2$: C, 68.18; H, 9.09; N, 10.60. Found: C, 68.10; H, 8.89; N, 10.01.

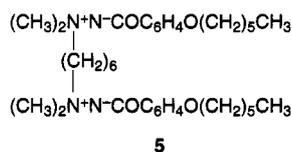
N,N,N-Trimethyl-*N'*-4-hexyloxybenzoylhydrazonium Salt **2** and Aminimide **3**. A mixture of 4.1 g (0.0155 mol) of hydrazine **1** and 6.6 g (0.0465 mol) of methyl iodide in 30 mL of benzene was refluxed for 20 h. After removal of partial solvents, the hydrazonium salt **2** was gained as precipitates. The salt **2** was recrystallized from benzene. The formation of this salt **2** was confirmed by infrared spectroscopy; that is, the absorption ν -(C=O) shifted from 1640 to 1690 cm^{-1} . Aminimide **3** was prepared from the reaction of hydrazonium salt **2** and sodium hydroxide. Hydrazonium salt **2** was dissolved in 30 mL of water, and 0.1 N sodium hydroxide solution was added to this solution until the neutral point of pH of the solution was confirmed. Chloroform (30 mL) was added to this aqueous solution, and the product was extracted. This extraction using chloroform was repeated three times. The combined chloroform solution was evaporated to dryness. The product was recrystallized from petroleum ether, and 3.2 g of aminimide **3** was gained (yield 46%).



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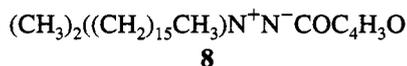
IR (KBr; cm^{-1}): 2950, 2870, 1610, 1560, 1510, 1470, 1340, 1260, 1170, 1020, 850, 780. NMR: 8.46 (2H), 7.50 (2H), 4.35 (2H), 3.8 (9H), 1.9 (2H), 1.5 (6H), 1.0 (3H) (ppm). Anal. Calcd for $\text{C}_{16}\text{H}_{26}\text{N}_2\text{O}_2$: C, 69.06; H, 9.35; N, 10.07. Found: C, 68.95; H, 9.65; N, 9.87.

Bis(N,N-dimethyl-N'-4-hexyloxybenzoylhydrazonium)-N-hexamethylene Salt 4 and Aminimide 5. A mixture of 6.4 g (0.0189 mol) of 1,6-diiodohexane and 10 g (0.0378 mol) of *N,N*-dimethyl-*N'*-4-hexyloxybenzoylhydrazine **1** in 50 mL of absolute methanol was refluxed for 20 h. After cooling, the partial solvents were removed by rotary evaporator and the precipitates were gained. This product was recrystallized from ethanol-ethyl ether, and the salt **4** was obtained. The absorption of $\nu(\text{C}=\text{O})$ of this salt **4** was observed at 1680 cm^{-1} . This salt **4** was dissolved in 50 mL of water, and 0.1 N sodium hydroxide solution was added to a stirring aqueous solution of this salt **4** until neutral point of pH. Aminimide **5** was recovered by extraction with three 100 mL portions of chloroform. The combined extracts were dried over sodium sulfate, and the solvent was removed by a rotary evaporator. After recrystallization from chloroform-hexane, 5.7 g of aminimide **5** was obtained (total yield 25%).



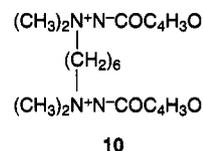
IR (KBr; cm^{-1}): 2920, 2850, 1600, 1550, 1500, 1400, 1340, 1240, 1170, 1020, 850, 770. NMR: 8.16 (4H), 7.10 (4H), 4.10 (4H), 3.90 (4H), 3.50 (12H), 2.8 (4H), 2.25 (4H), 1.85 (4H), 1.44 (12H), 0.96 (6H) (ppm). Anal. Calcd for $\text{C}_{36}\text{H}_{58}\text{N}_4\text{O}_4$: C, 70.82; H, 9.51; N, 9.18. Found: C, 71.01; H, 9.45; N, 9.25.

N,N-Dimethyl-N'-1-hexadecyl-N'-2-furoylhydrazonium Salt 7 and Aminimide 8. A solution of 20 g (0.154 mol) of 2-furoyl chloride in 50 mL of dry benzene was added to a mixture of 9.24 g (0.154 mol) of 1,1-dimethylhydrazine and 3 mL of triethylamine in 50 mL of dry benzene at $5\text{ }^\circ\text{C}$ during 3 h. This mixture was stirred at room temperature for 6 h. After reaction, the solvent was removed by rotary evaporator, and the product was dried under vacuum. The product was recrystallized from benzene, and the white crystals of *N,N*-dimethyl-*N'*-2-furoyl hydrazine **6** were gained (yield 12.1 g, 51%). A mixture of 1 g (0.0059 mol) of *N,N*-dimethyl-*N'*-2-furoylhydrazine **6** and 6.2 g (0.0176 mol) of 1-hexadecyl iodide in 20 mL of absolute methanol was refluxed for 15 h. After cooling, the solvent was removed by rotary evaporator and the product was dried under vacuum. This salt **7** was recrystallized from methanol-hexane (1.67 g, yield 56%). The salt **7** (1 g, 0.00198 mol) was dissolved in 50 mL of water, and 0.1 N sodium hydroxide was added to a stirring aqueous solution of this salt **7** until the neutral point of pH. Aminimide **8** was recovered by extraction with three 100 mL portions of chloroform. The combined extracts were dried over sodium sulfate, and the solvent was removed by rotary evaporator. After recrystallization from chloroform-hexane, aminimide **8** was obtained (0.52 g, yield 70%).



IR (KBr; cm^{-1}): 3190, 3050, 2850, 1650, 1570, 1470, 1320, 1160, 1050, 950, 890, 805, 780. NMR: 7.5-6.3 (3H), 3.6 (2H), 3.5 (6H), 2.8 (2H), 2.3 (2H), 1.9 (2H), 1.5 (2H), 1.5 (20H), 1.0 (3H) (ppm). Anal. Calcd for $\text{C}_{23}\text{H}_{42}\text{N}_2\text{O}_2$: C, 73.02; H, 11.11; N, 7.41. Found: C, 72.92; H, 11.01; N, 7.52.

Bis(N,N-dimethyl-N'-2-furoylhydrazonium)-N-hexamethylene Salt 9 and Aminimide 10. A mixture of 3.29 g (0.0097 mol) of 1,6-diiodohexane and 3 g (0.0194 mol) of *N,N*-dimethyl-*N'*-2-furoylhydrazine **6** in 30 mL of absolute methanol was refluxed for 48 h. After cooling, the partial solvents were removed by rotary evaporator, the white crystals of salt **9** were gained as the precipitate (4.57 g, yield 73%), and the absorption of $\nu(\text{C}=\text{O})$ of this salt **9** was observed at 1680 cm^{-1} . Aminimide **10** was gained by the synthetic method of aminimide **5** (yield 53%).



IR (KBr; cm^{-1}): 3200, 3050, 2850, 1660, 1580, 1480, 1330, 1200, 1170, 1020, 960, 900, 820, 790. NMR: 7.35-6.30 (6H), 3.5 (4H), 3.45 (12H), 2.9 (4H), 2.45 (4H) ppm. Anal. Calcd for $\text{C}_{20}\text{H}_{30}\text{N}_4\text{O}_4$: C, 61.53; H, 7.69; N, 14.36. Found: C, 61.60; H, 7.50; N, 14.20.

Transport Measurements. Liquid membrane experiments were performed by using the same system as described previously.⁸

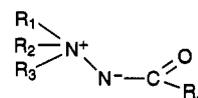
A chloroform solution (30 mL) containing aminimide ($1 \times 10^{-3}\text{ M}$) was placed at the base of the cell as the organic phase. The source phase was a Tris buffer solution (10 mL) containing metal picrate ($1 \times 10^{-4}\text{ M}$) and metal chloride ($1 \times 10^{-1}\text{ M}$), and the receiving phase was a Tris buffer solution (10 mL). Metal ion transport was examined by observing changes in the UV-visible absorption of metal picrate, and the procedures of measurements were the same as the method as described previously.⁸ The metal ion concentration in the receiving phase was also measured by means of atomic absorption analyses.

The uphill transport was performed by the same system. Tris buffer solutions (pH 7.20 and 8.05) of each aqueous phase contained metal picrate ($1 \times 10^{-4}\text{ M}$) and metal chloride ($1 \times 10^{-1}\text{ M}$), respectively.

Instruments. The infrared spectra were obtained on a Perkin Elmer 1600 series FTIR. UV-visible spectra were recorded on a Hitachi 340 recording spectrometer with the cell compartment thermostated at $20\text{ }^\circ\text{C}$. The atomic absorption analyses were performed by Instrumentation Laboratory Model IL 551 AA/EE. ^1H -NMR spectra were recorded on a JEOL X 270 spectrometer (270 MHz).

Results and Discussion

The ylides used here are carbonyl-stabilized aminimides, which are very stable under normal conditions. The general structure of a carbonyl-stabilized aminimide is shown in below.



As shown, the aminimide has a nitrogen atom bearing a positive charge and a nitrogen atom bearing a negative charge. The oxygen atom of the carbonyl group is conjugated to the anionic nitrogen atom (ylidic nitrogen atom), and the oxygen atom and the ylidic nitrogen atom can interact with metal ions. It is easy for the ylidic nitrogen atom to react with acid such as hydrochloric acid and form the salt, and the formation of this salt can be confirmed by the shift to higher frequency of the $\nu(\text{C}=\text{O})$ absorption in the infrared spectrum. Since the oxygen

TABLE 1: Data of Carbonyl Stretching Band $\nu(\text{C}=\text{O})$ in the Infrared Spectra of Hydrazines, Aminimides, and Their Salts

	$\nu(\text{C}=\text{O}) \text{ cm}^{-1}$
hydrazine 1 (CH_3) ₂ NNHCOC ₆ H ₄ O(CH ₂) ₅ CH ₃	1640
hydrazonium salt 2 (CH_3) ₃ N ⁺ NHCOC ₆ H ₄ O(CH ₂) ₅ CH ₃ ·I ⁻	1690
aminimide 3 (CH_3) ₃ N ⁺ N ⁻ COC ₆ H ₄ O(CH ₂) ₅ CH ₃	1610
hydrazonium salt 4 (CH_3) ₂ N ⁺ NHCOC ₆ H ₄ O(CH ₂) ₅ CH ₃ ·2I ⁻	1680
↓ (CH ₂) ₆	
(CH_3) ₂ N ⁺ NHCOC ₆ H ₄ O(CH ₂) ₅ CH ₃	
aminimide 5 (CH_3) ₂ N ⁺ N ⁻ COC ₆ H ₄ O(CH ₂) ₅ CH ₃	1600
↓ (CH ₂) ₆	
(CH_3) ₂ N ⁺ N ⁻ COC ₆ H ₄ O(CH ₂) ₅ CH ₃	
hydrazine 6 (CH_3) ₂ NNHCOC ₄ H ₃ O	1670
hydrazonium salt 7 (CH_3) ₂ ((CH ₂) ₁₅ CH ₃)N ⁺ NHCOC ₄ H ₃ O·I ⁻	1675
aminimide 8 (CH_3) ₂ ((CH ₂) ₁₅ CH ₃)N ⁺ N ⁻ COC ₄ H ₃ O	1650
hydrazonium salt 9 (CH_3) ₂ N ⁺ NHCOC ₄ H ₃ O·2I ⁻	1680
↓ (CH ₂) ₆	
(CH_3) ₂ N ⁺ NHCOC ₄ H ₃ O	
aminimide 10 (CH_3) ₂ N ⁺ N ⁻ COC ₄ H ₃ O	1660
↓ (CH ₂) ₆	
(CH_3) ₂ N ⁺ N ⁻ COC ₄ H ₃ O	

atom of the carbonyl group is conjugated to the ylidic nitrogen atom as noted above, the degree of interaction between the oxygen atom and the metal ion is affected by the concentration of protons in solution. Thus, it is expected that the carbonyl-stabilized aminimide has the property of being a pH dependent carrier of metal ions. It seems that the evaluation of the pK_a value of the ylidic nitrogen is very important in order to design carrier molecules using aminimides, because the degree of interaction between the proton and the ylidic nitrogen of the aminimide depends on the pK_a of the ylidic nitrogen atom which is controlled mainly by the substituents (R₄) shown above. This molecule also has another specific property of a carrier; that is, typical carriers such as crown ethers transport the anion as a gegen anion of a cation.⁶ However, since the aminimides possess a positive charge in the molecule, these can be used as carriers for anions.

Since it is expected that the aminimide has characteristic properties of a carrier, several new aminimides 3, 5, 8, and 10 were synthesized and their properties as carriers were investigated. Their structures are shown below.

Aminimides 3, 5, and 8 have a long hydrocarbon chain as the concomitant insolubility in the aqueous phase protects the liquid membrane system from degradation. As aminimide 5 has four metal binding points to a metal ion, it is expected that aminimide 5 shows not only high transport efficiency but also enhancement of transport ability between binding points. Aminimides 8 and 10 have the furoyl group, of which the oxygen atom interacts with the metal ion. Since the absorption positions of the carbonyl group of aminimides 8 and 10 are very different from those of aminimides 3 and 5 as shown in

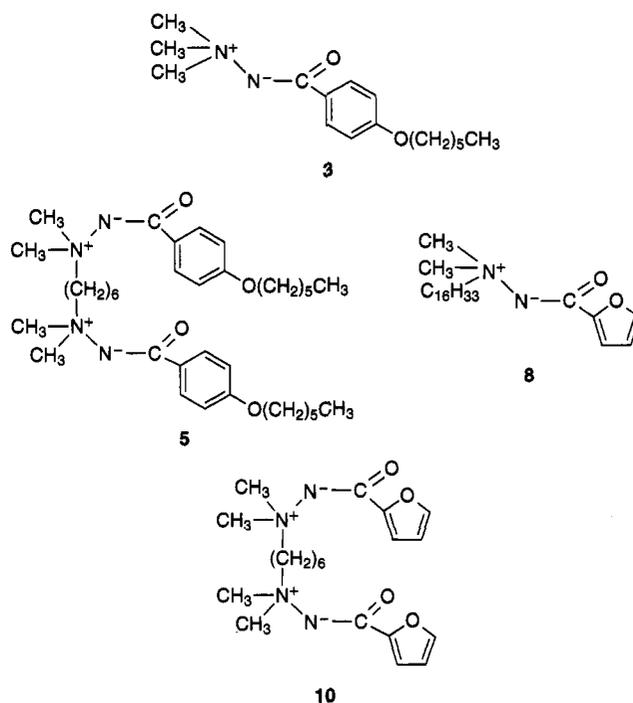
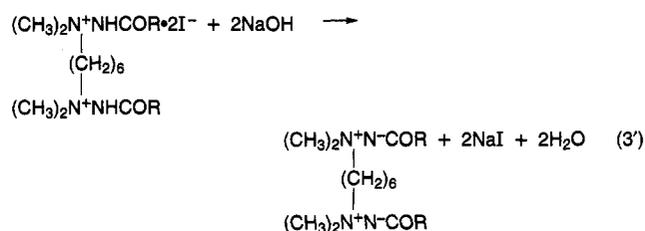
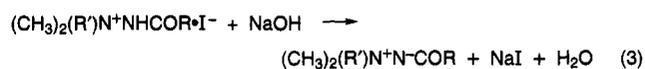
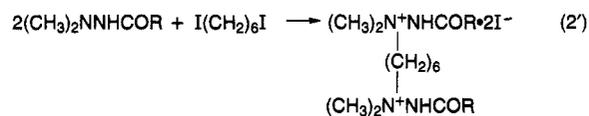
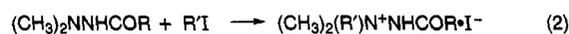
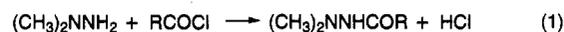


Table 1, the effect of the carbonyl group on the interaction between the aminimide and the metal ion can be also investigated clearly by using these aminimides 3, 5, 8, and 10.

Syntheses of Aminimides and Their Properties. The synthetic methods of these aminimides are shown below.



The structures of aminimides 3, 5, 8, and 10 were assigned from their infrared, H-NMR, and mass spectra and elemental analyses. H-NMR spectra of aminimides show the downshift of methyl groups or methylene groups compared with those of hydrazine derivatives, because aminimides have the nitrogen atom with a positive charge, which binds methyl groups or methylene groups. The infrared absorptions of $\nu(\text{C}=\text{O})$ of aminimides are lower than those of the corresponding hydrazine derivative and hydrazonium salts as shown in Table 1. This indicates that the carbonyl group is conjugated to the ylidic nitrogen atom bearing a negative charge and the electron is delocalized over the carbonyl group and the ylidic nitrogen atom. The nitrogen–nitrogen bond of this aminimide has specific properties; that is, the displacement of bonding electrons between the positive nitrogen atom and the negative nitrogen atom occurs and the degree of positive charge of the quaternary nitrogen atom becomes lower compared with that of typical

quaternary ammonium salts (electron displacement effect).^{5,7} In reverse, the ylidic nitrogen atom (anionic nitrogen atom) of the aminimide is stabilized by this effect with the conjugation of the carbonyl group and the ylidic nitrogen atom.

As described above, aminimides are very stable due to both effects (the electron displacement effect and the conjugation effect) and their properties are very sensitive to the concentration of protons in solution. Thus, these molecules are good candidates for functionalized carriers such as pH dependent carriers.

In order to clarify their ability as carriers, the interaction between the carrier and the metal ion was investigated. The addition of KClO_4 to deuteriomethanol solutions of the aminimide caused significant changes in the chemical shifts of the methyl groups attached to the quaternary nitrogen atom. This shift of the methyl group is very distinct: $[\Delta\delta(\text{Me}_2\text{N}^+) = 0.10$ ppm for aminimide **5** and $\Delta\delta(\text{Me}_3\text{N}^+) = 0.15$ ppm for aminimide **3**]. The interaction between the potassium ion and the aminimide probably affects the conjugation, which affects the displacement of bonding electrons between the nitrogen–nitrogen bond. As a consequence, the shifts of methyl groups would be observed in H-NMR spectra. The shape of the peak of a methyl group in H-NMR spectra was broadened by the addition of KClO_4 to a deuteriomethanol solution of the aminimide. More evidence of interaction between the potassium ion and the aminimide was found in the Fourier transform infrared spectra. The peak of the carbonyl group of the aminimide– KClO_4 complex in methanol was much broader than that of original aminimide in methanol solution. This absorption also shifts to lower wavenumber ($\Delta\nu(\text{C}=\text{O}) = 5\text{--}10\text{ cm}^{-1}$). These results acquired by NMR and infrared measurements suggest that some interactions between the aminimide and potassium perchlorate exist in methanol. The potassium ion probably interacts with the oxygen atom.

Transport of Metal Picrate by Various Aminimides. The transport experiments of metal picrate through a chloroform membrane containing aminimides were conducted by the method used in previous studies.⁸ A blank experiment was performed with metal picrate in which the membrane contained no carrier; the movement of metal picrate across the membrane was not observed. The transport behaviors of metal picrate by aminimides **3** and **5** are shown in Figures 1 and 2, and the data of transport by aminimides **3**, **5**, **8**, and **10** are summarized in Table 2. Table 3 lists the extraction equilibrium constants of metal picrate by aminimides from the aqueous Tris buffer solutions to the chloroform solutions under the same experimental condition.

Aminimide **3** has a long hydrocarbon tail, the insolubility protects the liquid membrane from degradation, and is used as a good carrier. Aminimide **5** has two ylidyne moieties, and it is expected that these parts give the enhanced interaction between the carrier and the metal ion by their many binding points. Aminimide **8** has a furoyl group which interacts with the metal ion. Then, it is expected that the interaction of aminimide **8** with the metal ion is much stronger than that of aminimide **3**, and the largest interaction between aminimide and metal ion is found for aminimide **10**, because this aminimide **10** has the most binding points among the four aminimides synthesized in this study. Table 2 shows that the order of increasing transport rate of potassium picrate by aminimide is $5 > 10 > 3 > 8$ and the transport rate by aminimide **5** is extremely high.

Since the general transport formula of the carrier-mediated transport of an ion pair in a diffusion-limited process gives a definite relationship between the transport rate and the concentration of the carrier, the transport rate should depend on the

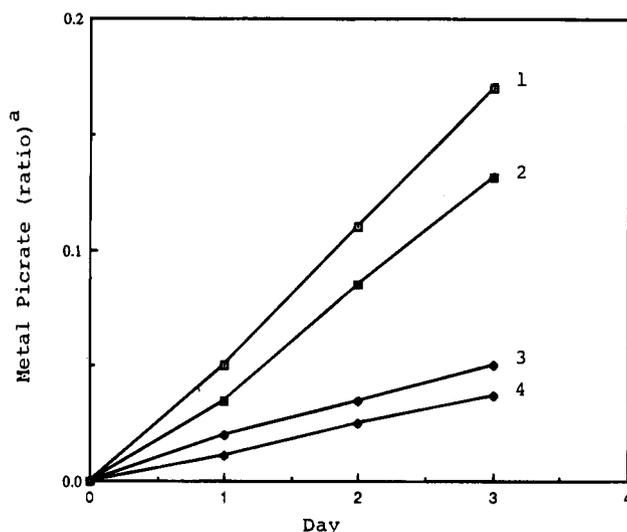


Figure 1. Transport behavior of metal picrates by aminimide **3**. (1) pH = 7.20, potassium picrate, (2) pH = 7.20, calcium picrate, (3) pH = 8.05, potassium picrate, (4) pH = 8.05, calcium picrate. Source phase: Tris buffer, 10 mL; metal picrate (1×10^{-4} M); KCl, 1×10^{-1} M. Receiving phase: Tris buffer, 10 mL. Organic phase: chloroform, 30 mL; aminimide **3** (1×10^{-3} M). (a) The ratio to initial concentration of source phase.

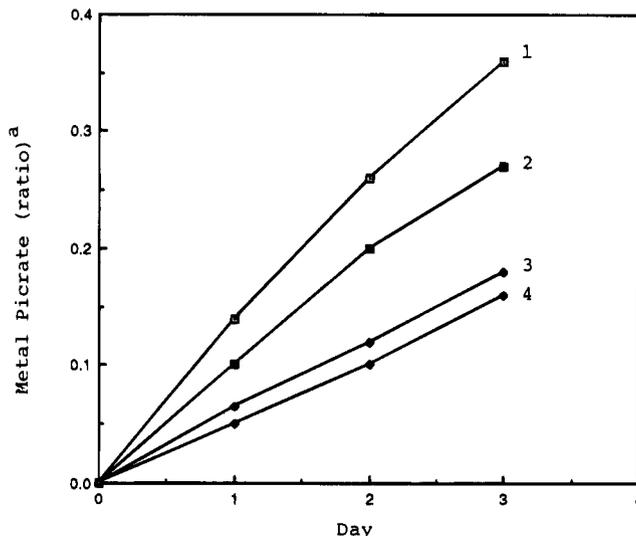


Figure 2. Transport behavior of metal picrate by aminimide **5**. (1) pH = 7.20, potassium picrate, (2) pH = 7.20, calcium picrate, (3) pH = 8.05, potassium picrate, (4) pH = 8.05, calcium picrate. Source phase: Tris buffer, 10 mL; metal picrate (1×10^{-4} M); KCl, 1×10^{-1} M. Receiving phase: Tris buffer, 10 mL. Organic phase: chloroform, 30 mL; aminimide **5** (1×10^{-3} M). (a) The ratio to initial concentration of source phase.

TABLE 2: Mean Rate of Transport of Potassium Picrate through the Chloroform Membrane Containing Aminimide^a

aminimide	rate (10^{-9} mol/h)	
	pH 7.20	pH 8.05
3	2.08	0.83
5	5.83	2.70
8	1.01	0.63
10	2.50	1.04

^a These values are the mean rate for the first day.

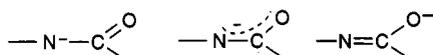
number of binding points to the metal ion.^{9,10} If this is the case, the transport rate by aminimide **5** is 2 times faster than that by aminimide **3**. However, the data of the transport rate as shown in Table 2 does not show such a trend and a much faster transport rate is observed for aminimide **5**. There is a possibility

TABLE 3: Extraction Equilibrium Constants between a Chloroform Solution Containing Aminimide and a Tris Buffer Solution Containing Potassium Picrate^a

aminimide	<i>K</i> (pH 7.20)
3	301
5	637
8	152
10	350

^a The conditions of measurements of the equilibrium constants are the same as those in the transport experiments. Extraction equilibrium constant between a Tris buffer solution containing potassium chloride (1×10^{-1} M) and potassium picrate (1×10^{-4} M), and a chloroform solution containing aminimide (1×10^{-3} M). $K = (\text{aminimide-potassium picrate complex})_{\text{org}}/(\text{aminimide})_{\text{org}}(\text{potassium picrate})_{\text{aq}}$.

that some cooperative effects between binding points occurs and more metal ions are transported. The transport rate by aminimide **8** is slower than that by aminimide **3**. Though aminimide **8** has more binding points, its extraction equilibrium constant is smaller than that of aminimide **3**. One of explanations for this result can be gained from the infrared spectroscopic data. The difference (80 cm^{-1}) in the absorption of $\nu(\text{C}=\text{O})$ between aminimide **3** and its salt **2** is much larger than that (25 cm^{-1}) between aminimide **8** and its salt **7**. The absorption of $\nu(\text{C}=\text{O})$ of aminimide **3** is 40 cm^{-1} lower than that of aminimide **8**. This indicates that the degree of delocalization of electrons of aminimide **3** is higher than that of aminimide **8** as shown below.



This part is probably easily coordinated by the metal ion and as a consequence, a higher extraction equilibrium constant will be observed for aminimide **3**. This result also suggests that the conjugation between the ylidic nitrogen atom and the carbonyl group is an important factor of metal coordination and more effective for coordination of the metal compared with the oxygen atom of the furoyl group. The difference in the transport rate between aminimides **5** and **10** can also be explained by this effect. The transport rate by aminimide **10** is higher than that by aminimide **8**, and this difference in transport rate would come simply from the number of binding sites.

In order to probe the selectivity for metal ions, calcium picrate was transported by using the same system. The transport rate of calcium picrate is much slower than that of potassium picrate as shown in Figures 1 and 2. These differences in transport rates are due to differences in the extraction equilibrium constant; for example, at pH 7.20, the extraction equilibrium constants of potassium picrate and calcium picrate with aminimide **5** were 637 and 451. It is also reported that the equilibrium constant of calcium picrate is smaller than that of potassium picrate for crown ether carriers.^{6,10} This result indicates that the aminimide as a carrier molecule has the same selectivity.

Details of the Transport of Metal Picrate by Aminimides 3 and 5. The detailed transport behaviors of metal picrate by aminimides **3** and **5** are shown in Figures 1 and 2. The transport rate of potassium picrate by aminimide **5** is much faster than that by aminimide **3**. It is noticed that the transport rate by the aminimide is very fast and the ratio of potassium picrate in the organic phase to that in the aqueous phase is very small. This is the evidence that the aminimide is a good carrier of metal picrate. Assuming that the complexation between the metal picrate and the aminimide was 1:1, the extraction equilibrium constants of aminimides **3** and **5** at pH 7.20 were 301 and 637, respectively. The order of increasing transport rate follows that

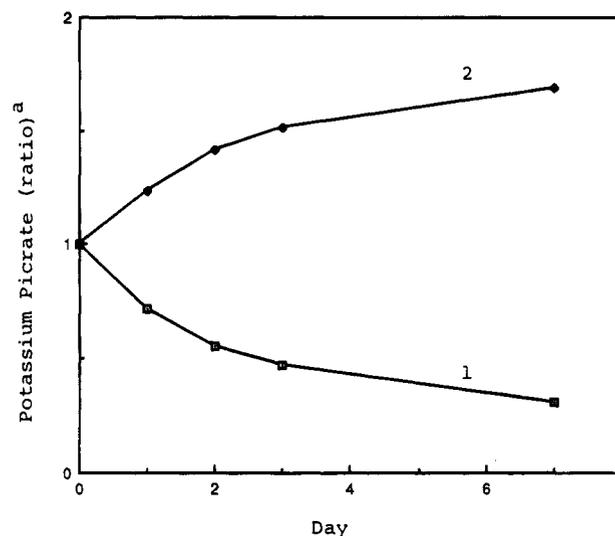


Figure 3. Uphill transport of potassium picrate by aminimide **5**. (1) Tris buffer pH 7.20 solution: Tris buffer (pH = 7.20), 10 mL; potassium picrate (1×10^{-4} M); potassium chloride (1×10^{-1} M). (2) Tris buffer pH 8.05 solution: Tris buffer (pH = 8.05), 10 mL; potassium picrate (1×10^{-4} M); potassium chloride (1×10^{-1} M). Organic phase: chloroform, 30 mL; aminimide **5** (1×10^{-3} M). (a) The ratio to initial concentration of both aqueous phases (Tris buffer solutions).

of the extraction equilibrium constant of aminimide as shown in Tables 2 and 3. Therefore, the ion uptake is the rate-determining step in the transport of metal picrate.

The large difference between the transport rate at pH 7.20 and that at pH 8.05 is also noticed. As shown in Figures 1 and 2, the transport rate by aminimide at pH 7.20 is much faster than that at pH 8.05; after 3 days, the ratio of transport at pH 7.20 is about two times larger than that at pH 8.05. As noted above, this result comes from the fact that the concentration of protons affects the conjugation of the ylidic atom and the carbonyl group. These results indicate that aminimides **3** and **5** have the property of being pH dependent carriers of metal picrate as already expected. This fact also suggests that the system of uphill transport of potassium picrate can be constructed by using aminimides.

In order to confirm the phenomenon of uphill transport, a double cylindrical cell was set up with an outer aqueous phase of a Tris buffer solution (pH 7.20) and an inner phase of a Tris buffer solution (pH 8.05) both with the same concentration of potassium picrate (1×10^{-4} M) and potassium chloride (1×10^{-1} M). A chloroform solution containing the aminimide (1×10^{-3} M) was placed at the base of the cell. The results are shown in Figure 3. The concentration of potassium picrate in the pH 7.20 solution decreased with time as shown in Figure 3. On the other hand, the concentration of potassium picrate in the pH 8.05 solution increased with time. Eventually, the concentration gradient of potassium picrate between the pH 7.20 solution and the pH 8.05 solution increased with time. This is definite evidence that potassium picrate is transported against its concentration gradient by new carrier molecule, aminimide.

Uphill Transport of Potassium Picrate and Its Numerical Simulation. As shown in Figure 3, potassium picrate is efficiently transported against its concentration gradient. In addition, the concentration of the complex of the aminimide and potassium picrate in the organic phase is very low. This result indicates that aminimides are efficient pH dependent carrier molecules for uphill transport of potassium picrate. We reported the uphill transport system using diazacrown ether bipyridine carriers⁸ and showed that the uphill transport by this carrier arises from the difference in the extraction equilibrium

constants of two interfaces between the organic phase and the aqueous phase. In this case, since the difference in the extraction equilibrium constants came from potassium chloride in the source phase, the driving force of uphill transport was potassium chloride in the source phase.

In order to confirm the reason for uphill transport using aminimide which is the pH dependent carrier, the extraction equilibrium constants were measured as in the previous case. The extraction equilibrium constants of aminimide **5** at pH 7.20 and 8.05 were 637 and 313, respectively. This suggests that the uphill transport is caused by the extraction equilibrium constant which depends on the pH in solution.

We reported eq 1 for the transport rate of potassium picrate using a model of diffusion-limited transport as shown in below.⁸

$$V = \left(\frac{D}{2l}\right) (L_o) \left(\frac{K_1 S_{out}^2 - K_2 S_{in}^2}{(1 + K_1 S_{out}^2)(1 + K_2 S_{in}^2)} \right) \quad (1)$$

This equation (1) means that the uphill transport depends on the difference between the extraction equilibrium constants K_1 and K_2 . In order to confirm a detailed mechanism of uphill transport by the aminimide, eq 1 was applied for this system; that is, the values of K_1 and K_2 were 637 and 313, respectively, and the experimental value of V for the first day was used to determine $(D/l)(L_o)$.

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

Where K_1 = the extraction equilibrium constant between the pH 7.20 solution and the organic phase; K_2 = the extraction equilibrium constant between the pH 8.05 solution and the organic phase; $L_{i,out}$ = the concentration of the aminimide at the interface between the pH 7.20 solution and the organic phase; $LS_{i,out}$ = the concentration of the complex at the interface between the pH 7.20 solution and the organic phase; S_{out} = the concentration of potassium picrate in the pH 7.20 solution; $L_{i,in}$ = the concentration of the aminimide at the interface between the pH 8.05 solution and the organic phase; $LS_{i,in}$ = the concentration of the complex at the interface between the pH 8.05 solution and the organic phase; and S_{in} = the concentration of potassium picrate in the pH 8.05 solution.

However, the calculated result using eq 1 is slightly different from the experiment result. The reason for this is the small difference between the extraction equilibrium constants K_1 and K_2 . Then, improvement of the calculation method of uphill transport is required. In the case of eq 1, we assume that the total carrier concentration (L_o) is constant through the liquid membrane.⁹

$$L_o = LS_{i,out} + L_{i,out} = LS_{i,in} + L_{i,in} \quad (2)$$

However, since the extraction equilibrium constant K_1 is larger than K_2 , it is expected that the concentration of the complex ($LS_{i,out}$) at the interface between the pH 7.20 aqueous phase and the organic phase is much higher than that ($LS_{i,in}$) at the interface between the pH 8.02 aqueous phase and the organic phase. We assume that the ratio of concentration of the carrier-potassium picrate complex at the interface is proportional to the extraction equilibrium constant. Thus, eq 2 is replaced by eq 3.

$$LS_{i,out} + L_{i,out} = (K_1/K_2) L_o \quad (3)$$

$$LS_{i,in} + L_{i,in} = (K_2/K_1) L_o$$

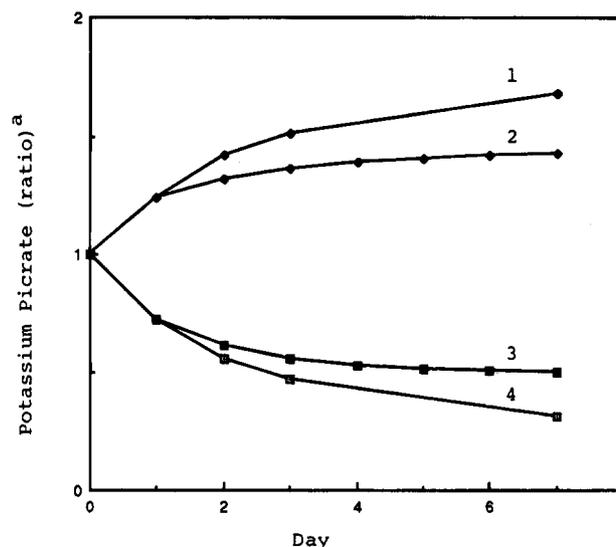


Figure 4. Numerical simulation of uphill transport of potassium picrate by aminimide **5**. (1,2) Tris buffer pH 8.05 solution, (3,4) Tris buffer pH 7.20 solution, (2,3) calculation (these data were calculated by eq 6. The experimental data of V for the first day were used for determination of the $(D/l)(L_o)$ value. The values for the organic phase were gained from the transport experiments), and (1,4) experiment. (a) The ratio to the initial concentration of both aqueous phases (Tris buffer solutions).

When the other relationship is the same as those of a previous paper,⁸ the formula at the interfaces between the aqueous phase and the organic phase is as follows.

$$LS_{i,out} = L_o \frac{K_1}{K_2} \left(\frac{K_1 S_{out}}{1 + K_1 S_{out}} \right) \quad LS_{i,in} = L_o \frac{K_2}{K_1} \left(\frac{K_2 S_{in}}{1 + K_2 S_{in}} \right) \quad (4)$$

The transport rate is

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

From formula 4

$$V = \left(\frac{D}{2l}\right) \left(L_o \left(\frac{K_1^2}{K_2} \right) \left(\frac{S_{out}}{1 + K_1 S_{out}} \right) - L_o \left(\frac{K_2^2}{K_1} \right) \left(\frac{S_{in}}{1 + K_2 S_{in}} \right) \right) \\ = \left(\frac{D}{2l}\right) (L_o) \left(\frac{1}{(1 + K_1 S_{out}^2)(1 + K_2 S_{in}^2)} \right) \left(\left(\frac{K_1^2}{K_2} S_{out}^2 - \frac{K_2^2}{K_1} S_{in}^2 \right) + \right. \\ \left. (K_1^2 - K_2^2) S_{out} S_{in} \right) \quad (5)$$

In the case of facilitated diffusion of an ion pair, the transport rate equation is written as

$$= \left(\frac{D}{2l}\right) (L_o) \left(\frac{1}{(1 + K_1 S_{out}^2)(1 + K_2 S_{in}^2)} \right) \left(\left(\frac{K_1^2}{K_2} S_{out}^2 - \frac{K_2^2}{K_1} S_{in}^2 \right) + \right. \\ \left. (K_1^2 - K_2^2) S_{out}^2 S_{in}^2 \right) \quad (6)$$

The result of a calculation using eq 6 is shown in Figure 4, which contains the experimental result. The trend of the calculated result is the same as that of the experimental result. Equation 6 contains the correction to the concentration of the complex at the interface between the aqueous phase and the

organic phase, but eq 1 does not. This result suggests that the transport rate equation (6) represents the behavior of uphill transport of potassium picrate by aminimide **5** correctly. The correction to the concentration of the complex at the interfaces between the aqueous phase and the organic phase is an important factor in order to simulate the uphill transport. This fact indicates that the uphill transport by the aminimide also arises from the difference in the extraction equilibrium constants of the two interfaces between the aqueous phase and the organic phase.

Conclusions

The aminimides are good carrier molecules for the transport of metal picrates. Since the interaction between the aminimide and potassium picrate in the organic phase is weak, potassium picrate is transported from the source phase to the receiving phase through a chloroform membrane efficiently. The aminimide is a pH dependent carrier that is caused by the change of conjugation between the carbonyl group and the ylidic nitrogen atom. As a consequence, an efficient uphill transport system can be constructed by using aminimide carrier molecule. The equation of numerical simulation previously reported by us is improved by using the correction to the concentration of the complex at the interfaces, and the result of the calculation using the new equation (6) is almost the same as the experimental result. This indicates that the uphill transport is caused by the difference in the extraction equilibrium constants of the two

interfaces between the organic phase and the aqueous phases with different pH values.

References and Notes

- (1) A preliminary communication has appeared. *J. Chem. Soc., Chem. Commun.* 1983, 995.
- (2) (a) Gilchrist, T. L.; Moody, C. J. *Chem. Rev.* **1977**, *77*, 40. (b) Trost, B. M.; Melvin, L. S., Jr. *Sulfur Ylides*; Academic Press: New York, 1975.
- (3) (a) Dang, L. X.; Kollman, P. A. *J. Am. Chem. Soc.* **1990**, *112*, 5716. (b) Chen, Z.; Schall, O. F.; Alcalo, M.; Li, Y.; Gokel, G. W.; Echegoyen, L. *J. Am. Chem. Soc.* **1992**, *114*, 444. (c) Malhotra, N.; Roepstoff, P.; Hansen, T. K.; Becher, J. *J. Am. Chem. Soc.* **1990**, *112*, 3709. (d) Hosseini, M. W.; Lehn, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 3525. (e) Rebek, J., Jr. *Science* **1987**, *235*, 1478.
- (4) (a) Izatt, R. M.; Christensen, J. J. *Synthetic Multidentate Macrocyclic Compounds*; Academic Press: New York, 1978. (b) Vogtle, F., Ed. *Host Guest. Chemistry II*; Springer-Verlag: Berlin-Heidelberg, 1982.
- (5) (a) Tsuchiya, S.; Senō, M. *J. Org. Chem.* **1979**, *44*, 2850. (b) Tsuchiya, S.; Senō, M.; Lwowski, W. *J. Chem. Soc., Perkin Trans. 2* **1983**, 887. (c) Tsuchiya, S.; Senō, M. *J. Chem. Soc., Dalton Trans.* **1984**, 731.
- (6) Lamb, J. D.; Christensen, J. J.; Izatt, S. R.; Bedke, K.; Astin, M. S.; Izatt, R. M. *J. Am. Chem. Soc.* **1980**, *102*, 3399.
- (7) Tsuchiya, S.; Mitomo, S.; Senō, M.; Miyamae, H. *J. Org. Chem.* **1984**, *49*, 3556.
- (8) Tsuchiya, S.; Senō, M. *J. Phys. Chem.* **1994**, *98*, 1682.
- (9) Behr, J. P.; Kirch, M.; Lehn, J. M. *J. Am. Chem. Soc.* **1985**, *107*, 241.
- (10) Lamb, J. D.; Christensen, J. J.; Oscarson, J. L.; Nielsen, B. L.; Asay, B. W.; Izatt, R. M. *J. Am. Chem. Soc.* **1980**, *102*, 6820.
- (11) (a) Tabushi, I.; Kobuke, Y.; Imuta, J. *J. Am. Chem. Soc.* **1980**, *102*, 1744. (b) Frederick, L. A.; Fyles, T. M.; Malik-Diemer, V. A.; Whitfield, D. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1211.