The Extraction and Transport of Metal Ions by 6,6'-Diamino-2,2'-bipyridine Derivatives

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6,6'-Disubstituted-2,2'-bipyridines were studied as to their ability to extract and transport transition- and heavy-metal ions. 6-Amino-6'-dodecylamino-2,2'-bipyridine (**3**) has been found to be an excellent synthetic carrier for the specific transport of Cu^{II} and Cd^{II} ions through a liquid membrane. The effective transport of Cd^{II} ion by (**3**), in spite of its less effective extraction into the organic phase than Cu^{II} or Zn^{II} ion, is notable. Moreover, (**3**) has been shown to have the ability to undergo up-hill transport of both Cu^{II} and Cd^{II} ions when the proton gradient is available.

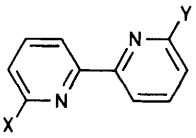
Specific metal-ion carriers such as valinomycin and the antibiotic X537A ($C_{34}H_{54}O_8$) play an important role in many biological processes.[1] Many artificial ligands such as crown ethers and their analogues have already been reported as model carriers to mimic biological transport systems.[2] They are known to transport alkali-metal and organic ammonium cations with a high selectivity and also with excellent efficiency.[3,4] In marked contrast, only a few synthetic carriers have been reported for the selective and up-hill transport of transition- or heavy-metal ions,[5] although it is important from the biological, medical, and environmental points of view.

In recent years, acyclic ionophores have been of interest in the transport system. The complexation and decomplexation of acyclic ionophores with metal ions are known to be generally faster than those of cyclic ones.[6] Not only the uptake process but also the release process of metal ions determines the overall rate of the metal ion transport, and acyclic ligands may have the advantage in the transport system over cyclic ones. 2,2'-Bipyridine (bipy) is well known as a typical ligand of transition- and heavy-metal ions, and many investigations of the excited state of $[Ru(bipy)_3]^{2+}$ have been carried out over the last 15 years.[7] However, there has been no report on the transport system using derivatives of bipy as a carrier to transport metal ions through a membrane. In a preliminary communication we recently reported the specific and up-hill transport of Cu^{II} using 6-amino-6'-dodecylamino-2,2'-bipyridine (**3**),[8] which was demonstrated to be an excellent carrier for the transport of Cu^{II} through a liquid membrane. We now report the full details in this paper.

Results

Carriers.—6-Bromo-6'-hexyloxy-2,2'-bipyridine (**1**) and 6,6'-bis(hexyloxy)-2,2'-bipyridine (**2**) were prepared from 6,6'-dibromo-2,2'-bipyridine (dbbp) and n-hexanol. 6,6'-Diamino-2,2'-bipyridine (dabp) was synthesized from dbbp and ammonia;[9] the ligands (**3**) and 6,6'-bis(dodecylamino)-2,2'-bipyridine (**4**) were obtained from the reaction of dabp with n-dodecyl bromide in the presence of base and catalytic amounts of tetra-n-butylammonium bromide.

The proton affinity of these ligands were examined by shaking a chloroform solution of each ligand with dilute hydrochloric acid. No dissolution of the ligands in the aqueous phase after shaking was confirmed spectroscopically. No spectral change of solutions of the ligands (**1**) and (**2**) in chloroform was observed after shaking with aqueous HCl solutions of various pH in the range 1—7. The absorption spectra of $CHCl_3$ solutions of (**3**) and (**4**) changed on shaking with aqueous hydrochloric acid solution (Figure 1) due to protonation of the bipyridine moieties.[9] Spectrometric titration



(**1**) X = Br, Y = OC_6H_{13}
(**2**) X = Y = OC_6H_{13}
(**3**) X = NH_2, Y = $NHC_{12}H_{25}$
(**4**) X = Y = $NHC_{12}H_{25}$

of (**3**) and (**4**) as a function of the pH of the aqueous phase showed that pK_a values of the ligands (**3**) and (**4**) in chloroform solution were *ca.* 4 (Figure 2).

The complexation of the ligand (**3**) with $Cu^{II}(O_2CMe)_2$, $Zn^{II}(O_2CMe)_2$, and $Cd^{II}(O_2CMe)_2$ in chloroform containing methanol (1% v/v) were studied by absorption spectroscopy. The addition of the methanol solution of a metal salt into the ligand solution caused a spectral change similar to that by protonation. Plots of the absorbance of the solution against composition indicated that the compositions of the complexes of (**3**) with metal ions were 1:1 (Figure 3).

Extraction of Metal Ions.—Figure 2 shows that the ligands (**3**) and (**4**) in chloroform in contact with an aqueous solution of pH 7 seem to exist in the free form, and protonated when in contact with a solution of pH 1. Ammonium acetate buffer (pH 7.0) and HCl–KCl buffer (pH 1.0) were used in the extraction and transport experiments. Ligands (**3**) and (**4**) in chloroform solution were protonated by contact with HCl–KCl buffer and deprotonated by contact with acetate buffer. The ability of these ligands to hold metal ions such as Cu^{II}, Ni^{II}, Co^{II}, Mn^{II}, Pb^{II}, Zn^{II}, and Cd^{II} was examined by equilibrating a chloroform solution of each ligand with buffer solutions containing metal ions. The metal ion release of the complexes was examined by shaking the chloroform solution with a fresh acidic buffer solution of pH 1. The results are listed in Table 1. Ligands (**1**) and (**2**) showed no ability for metal extraction; however, ligands (**3**) and (**4**) were found to be excellent particularly toward Cu^{II} and Zn^{II}. Naturally, the amount of Cu^{II} ion extracted into the organic phase by (**3**) did not exceed that of ligand (**3**) in the organic phase (Table 2). The nature of the counter anion in the Cu^{II} salts did not affect the extractability of ligand (**3**), but the effect of different buffer solutions was marked (Table 3).

Ligands (**3**) and (**4**) released metal ions extracted from a neutral buffer solution into an acidic one with high efficiency. However, no or very little release was observed into a neutral buffer solution.

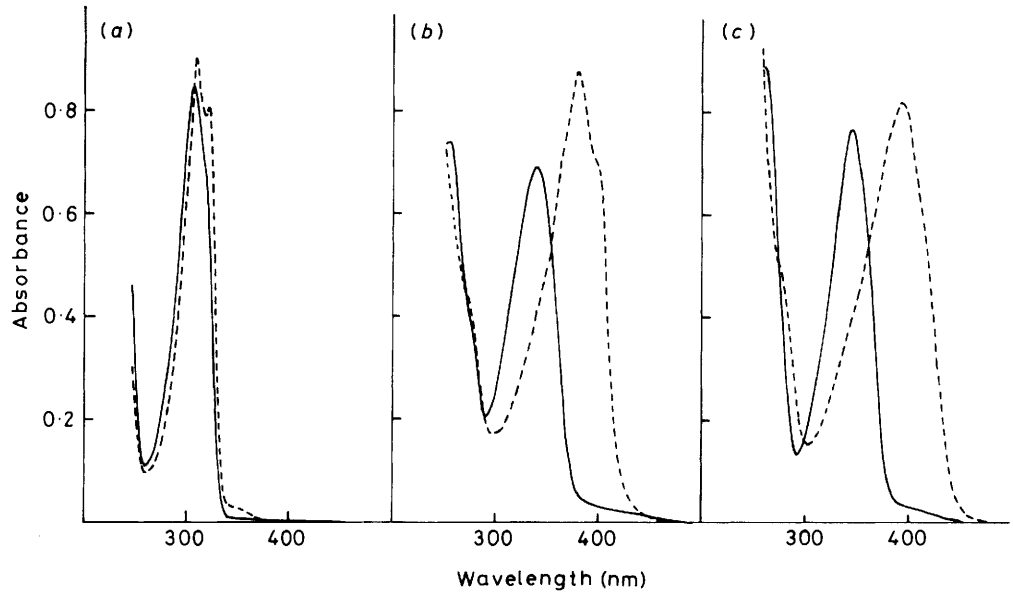


Figure 1. Absorption spectra of ligands (**1**)—(**4**) in chloroform: (*a*) (——) (**1**) (6.66 × 10^{-5} mol dm^{-3}), (– – – –) (**2**) (6.66 × 10^{-5} mol dm^{-3}); (*b*) (**3**) (6.66 × 10^{-5} mol dm^{-3}), (——) after contact with pH 7.0 buffer, (– – – –) after contact with pH 1.0 buffer; (*c*) (**4**) (6.66 × 10^{-5} mol dm^{-3}), (——) after contact with pH 7.0 buffer, (– – – –) after contact with pH 1.0 buffer

Table 1. Uptake and release of the metal ions (percent, relative to the initial concentration of metal ion in the buffer solution)*

	Uptake										Release				
	pH 7.0 buffer					pH 1.0 buffer					pH 1.0 buffer				
Ligand	None	(1)	(2)	(3)	(4)	None	(1)	(2)	(3)	(4)	None	(1)	(2)	(3)	(4)
Metal ion															
Cu^{II}	5	7	5	76	73	0	0	0	3	1	0	2	0	71	72
Ni^{II}	4	3	4	11	6	1	1	0	4	0	1	0	0	12	3
Co^{II}	7	9	9	13	11	0	0	1	0	0	1	1	1	6	10
Mn^{II}	7	8	9	9	8	1	1	3	4	3	0	0	0	0	0
Pb^{II}	3	2	3	5	2	4	3	2	1	1	2	3	2	3	3
Zn^{II}	1	1	1	52	50	2	1	0	2	2	1	1	0	52	27
Cd^{II}	0	0	1	12	7	0	0	0	0	0	0	0	0	9	5

* Uptake: organic phase, $CHCl_3$ (10 cm^3) containing 10^{-6} mol of ligand; aqueous phase, buffer solution (10 cm^3) containing 10^{-6} mol of metal ion. Release: organic phase, 5 cm^3 of the organic layer of the extract at pH 7.0; aqueous phase, 5 cm^3 of the buffer solution (pH 1.0). The aqueous and organic solutions were shaken in a capped bottle for 30 min using a mechanical shaker at room temperature and then the amount of a metal ion in the aqueous phase was measured.

Table 2. Extraction of Cu^{II} ion by (**3**)*

Initial Cu^{II} (10^{-6} mol)	Extracted Cu^{II} (10^{-6} mol)
0.50	0.50
1.00	0.80
2.00	0.94
3.00	0.92

* Initial conditions: organic phase of $CHCl_3$ (10 cm^3) containing (**3**) (10^{-6} mol); aqueous phase, buffer (10 cm^3, pH 7.0) containing Cu^{II} ions. The two phases were shaken for 30 min at room temperature.

Table 3. Extraction of Cu^{II} ions by ligand (**3**) under various conditions

		Extracted Cu^{II} (%)*	
Salt	Buffer	Without (**3**)	With (**3**)
$CuCl_2$	NH_4O_2CMe	0	80
$Cu(O_2CMe)_2$	NH_4O_2CMe	2	80
$CuSO_4$	NH_4O_2CMe	7	81
$CuCl_2$	H_2SO_4–NH_3	0	5
$CuCl_2$	HCl–NH_3	0	13

* Relative to the initial amount of Cu^{II} ion. Initial conditions: organic phase, $CHCl_3$ (10 cm^3) containing ligand (**3**) (10^{-6} mol); aqueous phase, buffer solution (10 cm^3) containing a Cu^{II} salt. The two phases were shaken for 30 min at room temperature.

Transport of Transition- and Heavy-metal Ions.—This was examined using the ligands (**1**)—(**4**); aqueous phase I (aq.I) was a neutral buffer solution and aqueous phase II (aq.II) was an acidic one, unless otherwise cited. Metal ions were initially added in aq.I. The two aqueous phases were separated by a chloroform solution of the ligand. The distributions of metal ions in the system after standing for 20 h at 20 °C are listed in Table 4. Metal ions were not transported unless some ligand was added in the organic phase. Neither (**1**) nor (**2**) transport metal ions from aq.I into aq.II, nor take metal ions from aq.I

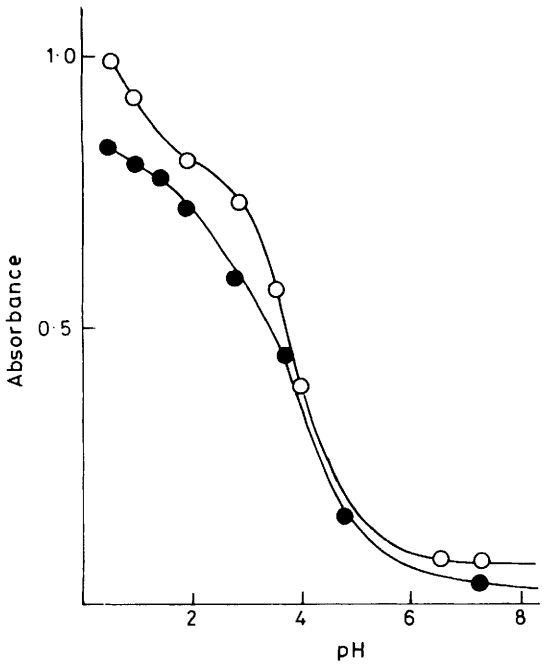


Figure 2. Plots of absorbances of (**3**) and (**4**) *vs.* pH: (○) (**3**) (6.66×10^{-5} mol dm^{-3}) at 380 nm, (●) (**4**) (6.66×10^{-5} mol dm^{-3}) at 400 nm

Table 4. Distribution of metal ions (percent, relative to the initial amounts of metal ion)*

	(3)		(4)	
Metal ion	aq.I	aq.II	aq.I	aq.II
Cu^{II}	25	54	92	2
Ni^{II}	95	2	97	0
Co^{II}	89	4	90	3
Mn^{II}	100	0	100	0
Pb^{II}	96	0	100	0
Zn^{II}	88	7	100	0
Cd^{II}	65	28	100	0

* Initial conditions: aq.I, ammonium acetate buffer solution containing a metal ion (10^{-6} mol); aq.II, HCl–KCl buffer solution; organic phase, $CHCl_3$ containing a ligand (2.5×10^{-7} mol). The amounts of a metal ion in the two aqueous phases were measured after running for 20 h.

Table 5. Distribution of the metal ions transported by ligand (**3**) (percent, relative to the initial amount of metal ion)*

Individual	aq.I	Organic phase	aq.II
Cu^{II}	25	21	54
Ni^{II}	95	3	2
Co^{II}	89	7	4
Mixture			
Cu^{II}	27	20	53
Ni^{II}	94	2	4
Co^{II}	95	3	2

* Initial conditions: aq.I, ammonium acetate buffer solution containing a metal ion (10^{-6} mol), or a mixture of metal ions (10^{-6} mol for each metal ion); aq.II, pH 1.0 buffer solution; organic phase, $CHCl_3$ containing ligand (**3**) (2.5×10^{-7} mol). After running for 20 h, the amounts of the metal ions in the two aqueous phases were measured.

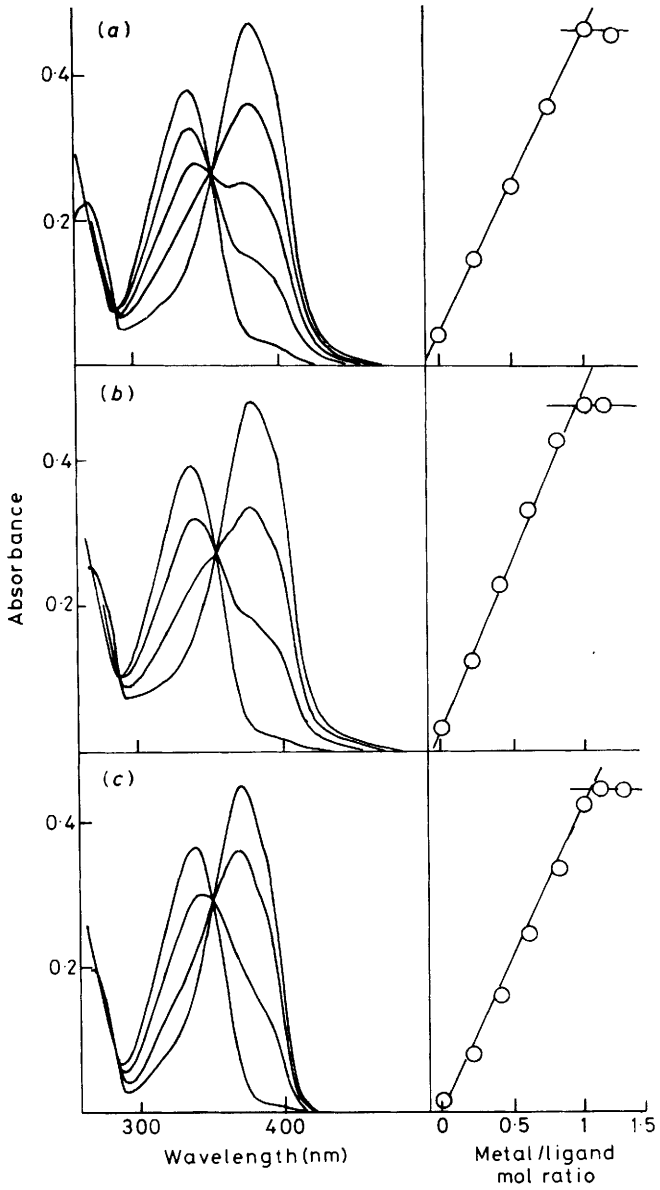


Figure 3. Change in the absorption spectra of (**3**) in chloroform by complexation and plots of absorbance of (**3**) *vs.* solution composition: (*a*) (**3**)–$Cu(O_2CMe)_2$ system at 380 nm; (*b*) (**3**)–$Zn(O_2CMe)_2$ system at 377 nm; (*c*) (**3**)–$Cd(O_2CMe)_2$ system at 372 nm

into the organic phase under the conditions. Ligand (**3**) showed excellent transport of metal ions, especially Cu^{II} and Cd^{II}. It is worth noting that Cd^{II} ions were efficiently transported by (**3**) in spite of its low extractability toward Cd^{II} ions, as shown in Table 1. When aq.I and aq.II were both neutral, (**3**) took metal ions from aq.I but did not release them into aq.II. Ligand (**3**) did not take nor transport metal ions when aq.I and aq.II were both acidic. The ligand (**3**) transported Cu^{II} ions selectively from a mixture of Cu^{II}, Ni^{II}, and Co^{II}, when aq.I was neutral and aq.II was acidic (Table 5). Highly selective transport of Cu^{II} was observed even in the presence of Cd^{II} (Table 6). Proton was found to be transported by (**3**) from acidic aq.II to neutral aq.I either in the presence or absence of metal ions.

The courses of the transport of Cu^{II} and Cd^{II} by (**3**) were followed with time (Figures 4 and 5). The patterns of transport phenomena were found to be different for Cu^{II} and Cd^{II}.

Table 6. Distribution of Cu^{II} and Cd^{II} ions after 20 h at 20 °C (percent, relative to the initial amount of metal ion)*

	aq.I	aq.II
Individual		
Cu^{II}	25	54
Cd^{II}	65	25
Mixture		
Cu^{II}	33	56
Cd^{II}	83	7

* Initial conditions: aq.I, ammonium acetate buffer solution containing a metal ion (10^{-6} mol), or a mixture of metal ions (10^{-6} mol for each metal); aq.II, pH 1.0 buffer solution; organic phase, $CHCl_3$ containing ligand (**3**) (2.5×10^{-7} mol).

Discussion

Complexation in the Organic Phase.—These ligands are amphiphilic and, therefore, the possibility cannot be excluded that metal ions in the organic phase may exist in the 'water pools' of the reversed micelles[10] formed by the ligands rather than as a complex with the ligand. The results in Table 2 indicate that the ligand (**3**) takes Cu^{II} ions into the organic phase by no more than a 1:1 stoicheiometric amount even when there is excess of Cu^{II} ions in the aqueous phase. This clearly shows that the metal ion uptake takes place only by complex formation and not by formation of reversed micelles. This is also supported by the fact that the extractabilities of (**3**) and (**4**) are similar to the complexability of dabp.[9]

Ligand (**3**) forms only 1:1 complexes with Cu^{II}, Zn^{II}, and Cd^{II}. The situation is the same as for 6,6′-dimethyl-2,2′-bipyridine.[11] The complexation of either (**3**) or (**4**) is considered to occur at the bipyridine moiety in the same manner as for dabp;[9] they have extractabilities of the same order toward metal ions as that of dabp.

Table 3 indicates that Cu^{II} ion extraction into the organic phase is highly dependent on the buffer solution but not on the kind of Cu^{II} salt, suggesting that the counter anion which accompanies the metal ion into the organic phase is from the buffer solution, not the original anion of the metal salt.

Properties of the Carriers: the Ability to take and transport Metal Ions.—As described before, neither (**1**) nor (**2**) is protonated in the range above pH 1. Their low ability to extract metal ions seems to be due to the low basicity. On the other hand, ligands (**3**) and (**4**), which have higher proton affinity, showed excellent extractability (Table 1). Thus the extractability appears to be almost parallel to the proton affinity.

Though (**4**) extracts metal ions as efficiently as (**3**), (**4**) scarcely transports metal ions. This may be ascribed to the inefficient uptake of metal ions (*ca.* 6% even for Cu^{II} ions) under the conditions of the transport experiments. The low ability of metal ion uptake may be accounted for by the lower concentration of (**4**) in the interface between aq.I and the organic phase than that of (**3**) because of the higher lipophilicity of the former due to the two lipophilic moieties at the 6,6′-positions. In the metal ion extraction experiment, vigorous shaking appears to promote the uptake of metal ions.

Metal Ion–Ligand (**3**) *Transport Systems.*—The ligand (**3**) transported Cd^{II} ion (28% into aq.II) in spite of its low extractability of Cd^{II} ions (12% of initial amounts in Table 1). This suggests that the transport processes of Cu^{II} and Cd^{II} are different.

The transport of Cu^{II} ions consists of three stages, as shown in Figure 4: (*i*) the fast uptake process, (*ii*) the induction period before the stationary transport, and (*iii*) the stationary transport stage. Almost stoicheiometric amounts of Cu^{II} ions were taken into the organic phase by (**3**) at the first stage. The rate of the initial decrease of Cu^{II} ions in aq.I was much larger than that (2.3×10^{-7} mol h^{-1}) of the constant decrease in aq.I at stage (*iii*). The concentration of Cu^{II} ions in aq.I did not affect the rate of the stationary transport, which appears to depend on the concentration of the complex in the organic phase. Thus the process releasing Cu^{II} ions into aq.II is the rate-determining step in the overall transport of Cu^{II} ions.

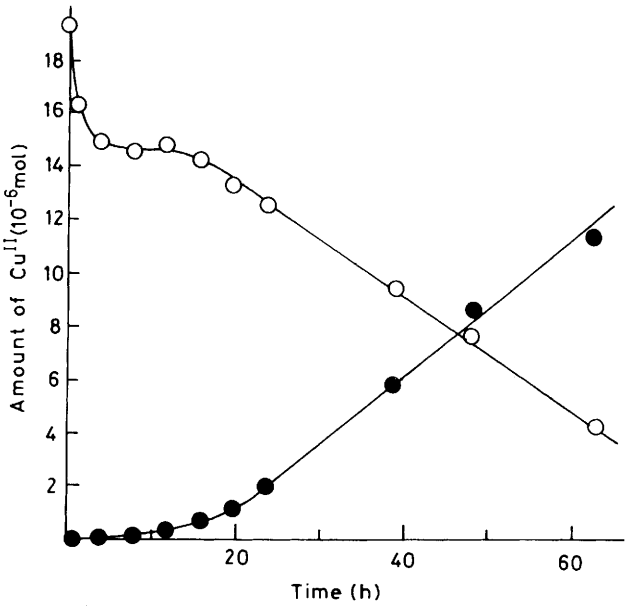


Figure 4. Plot of amount of Cu^{II} ion transported by (**3**) *vs.* time: (○) amount of Cu^{II} ions in aq.I, (●) amount in aq.II. Initial conditions: aq.I, ammonium acetate buffer (pH 7.0) with Cu^{II} (1.9×10^{-5} mol); aq.II, HCl–KCl buffer (pH 1.0); organic phase, $CHCl_3$ containing (**3**) (5.0×10^{-6} mol)

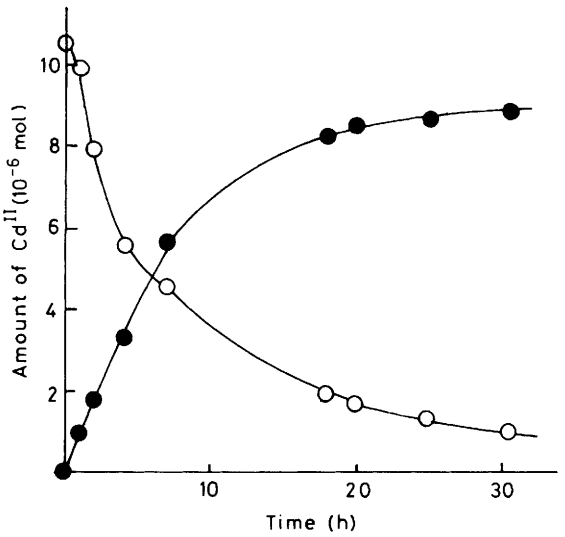


Figure 5. Plot of Cd^{II} ion transported by (**3**) *vs.* time: (○) amount of Cd^{II} ions in aq.I, (●) amount in aq.II. Initial conditions: aq.I, ammonium acetate buffer (pH 7.0) with Cd^{II} (1.0×10^{-5} mol); aq.II, HCl–KCl buffer (pH 1.0); organic phase, $CHCl_3$ containing (**3**) (5.0×10^{-6} mol)

Figure 5 indicates that the time course of the transport of Cd^{II} ions is markedly different from that of Cu^{II} ions. The most distinctive difference is in that no induction period was observed in the increase of Cd^{II} ions in aq.II, *i.e.* Cd^{II} is released into aq.II as soon as it is taken into the organic phase from aq.I. The curves in Figure 5 indicate that the rate of decrease of Cd^{II} ion in aq.I and also that of the increase of Cd^{II} in aq.II are dependent on the amount of Cd^{II} ion in aq.I; this is in contrast to the situation with Cu^{II} (Figure 4). Therefore, the process of taking Cd^{II} ions into the organic phase is the rate-determining step in the Cd^{II}–(**3**) system.

Figures 4 and 5 clearly show that the ligand (**3**) has the ability to undergo up-hill transport of either Cu^{II} or Cd^{II} ions, when the proton gradient is available. Thus the up-hill transport of Cu^{II} and Cd^{II} ions by (**3**) against its reverse concentration gradient is coupled with the counter flow of proton from aq.II to aq.I. In addition, it is worth noting that the amounts of Cu^{II} and Cd^{II} ions transported from aq.I to aq.II were more than that of (**3**) in the organic phase, indicating that (**3**) played a role as mediator.

Ligand (**3**) transported Cu^{II} ions selectively even from the aqueous solution of a mixture of Cu^{II}, Ni^{II}, and Co^{II} ions (Table 5) corresponding to the extractability of (**3**). Also, the amounts of Cu^{II} ions transported into aq.II are hardly affected by the presence of Cd^{II} ions (Table 6). Thus the selectivity of transport by (**3**) is determined by the uptake process of metal ions into the organic phase, and not only the extractability of the ligand but also the rates of uptake appear to determine the specificity in the system.

Conclusions

We have demonstrated specific and up-hill transport using a simple ligand, 6-amino-6′-dodecylamino-2,2′-bipyridine, (**3**). We have shown that the extractability of a ligand does not always parallel its ability to transport metal ions. The balance of lipophilic and polalophilic moieties is important for the effective transport and ligand (**3**) has such a balance as to effect not only excellent extractability but also excellent ability to transport metal ions. The ligand (**4**) has higher lipophilicity, lowering the polalophilicity and giving limited ability to transport metal ions. It is remarkable that (**3**) transported not only Cu^{II} but also Cd^{II}, though the extractability of (**3**) for Cd^{II} is not as high as for Cu^{II}.

Experimental

Melting points were measured using a micro-melting-point measuring apparatus (Yazawa Co. Ltd.) and are uncorrected. I.r. spectra were recorded with a JASCO IRA-1 spectrometer. Mass spectra were recorded with a Hitachi RMU-7L spectrometer. ^1H N.m.r. spectra were measured with a JEOL JMN-MH 100 spectrometer, and chemical shifts are reported in p.p.m. from internal $SiMe_4$. Absorption spectra were recorded with a JASCO UVIDEC-505 spectrophotometer at 20 °C.

The metal salts $CuCl_2$, $NiCl_2$, $CoCl_2$, $MnCl_2$, $PbCl_2$, and $CdCl_2$ were of analytical reagent grade. Solutions of $ZnCl_2$ were prepared from zinc metal with dilute aqueous HCl solution, unless otherwise stated. Analyses of metal ions were carried out by atomic absorption spectrophotometry using a Instrumentation Laboratory Inc. model IL551 AA/AE spectrophotometer.

Synthesis.—*6,6′-Dibromo-2,2′-bipyridine.* This was prepared by the literature method.[12] Yield 61%, m.p. 225—226 °C (lit.,[12] 226—227 °C).

6-Bromo-6′-hexyloxy-2,2′-bipyridine, (**1**). The compound dbbp (1.0 g), n-$C_6H_{13}OH$ (2 mol equiv.), and KOH (0.3 g) in dioxane (20 cm^3) were refluxed for 15 h. After the removal of the solvent, the residue was extracted with chloroform. The u.v.-active fraction was collected by column chromatography (Wakogel C200–benzene), condensed and then recrystallized from n-hexane. Yield 0.16 g (15%), m.p. 54.5—55.5 °C (Found: C, 57.25; H, 6.00; N, 8.50%; M^+, 334.0650. $C_{16}H_{19}BrN_2$ requires C, 57.3; H, 5.70; N, 8.35%; M^+, 334.0727); δ_H (100 MHz, $CDCl_3$, $SiMe_4$) 8.06 (1 H, d, ring 3-H), 7.51—7.15 (3 H, m, ring 4-, 4′-, and 5′-H), 7.05 (1 H, d, ring 3′-H), 6.56 (1 H, d, ring 5-H), 4.07 (2 H, t, CH_2–O), 1.79—1.35 (8 H, br, m, CH_2), and 0.89 (3 H, t, CH_3).

6,6′-Bis(hexyloxy)-2,2′-bipyridine, (**2**). The compound dbbp (1.0 g) and n-$C_6H_{13}OH$ (0.662 g) with sodium hydride (0.28 g) in dioxane (20 cm^3) were refluxed for 15 h. After removal of solvent, the residue was extracted with n-hexane. The extract was then separated by column chromatography (Wakogel C200–benzene). The u.v.-active fraction was concentrated and recrystallized from n-$C_6H_{13}OH$. Yield 0.418 g (36.8%), m.p. 77—79 °C (Found: C, 73.9; H, 9.25; N, 8.10%; M^+, 356.2354. $C_{22}H_{32}N_2O_2$ requires C, 74.1; H, 9.05; N, 7.85%; M^+, 356.2556); δ_H (100 MHz, $CDCl_3$, $SiMe_4$), 7.72 (2 H, d, ring 3-H), 7.42 (2 H, t, ring 4-H), 6.52 (2 H, d, ring 5-H), 4.29 (4 H, t, OCH_2), 1.76—1.36 (16 H, br, m, CH_2), and 0.86 (6 H, t, CH_3).

6,6′-Diamino-2,2′-bipyridine. A quantity of dbbp (3.0 g, 9.6 mmol) was placed in a glass ampoule. Liquid ammonia (30 g) was also placed in another ampoule. The unsealed ampoules were placed in an 500-cm^3 autoclave, and heated up to 220 °C. The inner pressure rose to 100 kg cm^{-2}; heating was continued for 6 h. After the reaction, the solid in the glass ampoule was dissolved in dilute aqueous HCl (50 cm^3) and filtered in order to remove unreacted starting material and any other insoluble matter. Aqueous ammonia was added into the filtrate to precipitate a solid which was collected by filtration, washed with aqueous ammonia and water, and dried under vacuum. The crude products were sublimed under vacuum [2 mmHg (≈267 Pa), 150—200 °C] to give 1.42 g (80%) of purified dabp, m.p. 185—186 °C (lit.,[13] 186 °C) (Found: C, 64.7; H, 5.2; N, 30.2. $C_{10}H_{10}N_4$ requires C, 64.5; H, 5.4; N, 30.1%).

6-Amino-6′-dodecylamino-2,2′-bipyridine, (**3**). The compound dabp (0.30 g) and tetra-n-butylammonium bromide (0.034 g) with KOH (0.3 g) in dioxane (10 cm^3) were refluxed for *ca.* 30 min. After the solution became yellowish, n-dodecyl bromide (1 cm^3) was added and further refluxed for 10 h. After removal of solvent, chloroform (20 cm^3) was added to the residue, and the solution was washed with dilute aqueous HCl and then with aqueous ammonia. The chloroform layer was separated and concentrated. The residue was worked-up by column chromatography (Wakogel C 200–chloroform then –ethanol), the ethanol fraction was concentrated and recrystallized from n-hexane. Yield 0.376 g (66%), m.p. 72—73.5 °C (Found: C, 74.35; H, 9.70; N, 15.8%; M^+, 354.2693. $C_{22}H_{34}N_2$ requires C, 74.55; H, 9.65; N, 15.8%; M^+, 354.2786); δ_H (100 MHz, $CDCl_3$, $SiMe_4$) 7.63—7.52 (4 H, m, ring 3-, 3′-, 4-, and 4′-H), 6.55—6.41 (2 H, m, ring 5-, and 5′-H), 4.54 (3 H, br, s, NH and NH_2), 3.34 (2 H, t, N–CH_2–), 1.22 (20 H, s, –CH_2–), and 0.84 (3 H, t, Me).

6,6′-Bis(dodecylamino)-2,2′-bipyridine, (**4**). The compound dapb (100 mg) and tetra-n-butylammonium bromide (10 mg) with sodium hydride (0.3 g) in dioxane (10 cm^3) were refluxed for *ca.* 30 min. After the solution became dark green, n-dodecyl bromide (1 cm^3) was added to the solution and refluxed for 8 h. After the removal of the solvent, chloroform (10 cm^3) was added to the residue, and the solution was washed with dilute aqueous HCl then aqueous ammonia. The solution was concentrated and separated by column chromatography (Wakogel C 200–chloroform), and then recrystallized from ethanol. Yield 94 mg (34%), m.p. 82—85 °C (Found: C, 78.0; H, 11.55; N, 10.35%; M^+, 522.4532. $C_{34}H_{58}N_4$ requires C, 78.1; H, 11.2; N, 10.7%; M^+, 522.4665); δ_H (100 MHz, $CDCl_3$, $SiMe_4$) 7.35 (4 H, m, ring 3- and

4-H), 6.22 (2 H, d, ring 5-H), 4.44 (2 H, br, t, NH), 3.22 (4 H, q, NCH_2), 1.62—1.22 (40 H, br, m, CH_2), 0.83 (6 H, t, CH_3).

Ion Extraction and Release Experiments.—All uptake and release experiments were carried out at room temperature.

Uptake. A buffer solution (10 cm^3, pH 7.0 or 1.0) containing 10^{-6} mol of a metal ion and 10 cm^3 of a chloroform solution containing 10^{-6} mol of ligand were placed in a 50-cm^3 cylindrical capped bottle, and shaken for 30 min (200 r.p.m.) using a Yamato shaker model SA-31 and then left to settle for 30 min. The amount of the metal ion extracted from the aqueous phase into the organic phase was determined by atomic absorption analysis of the aqueous phases for metal ion.

Release. A portion (5 cm^3) of the organic phase of the uptake experiments at pH 7.0 and a fresh buffer solution (5 cm^3, pH 1) were shaken in a 50-cm^3 cylindrical bottle for 30 min and left to stand for 30 min. The extent of release of the metal ion from the organic phase into the aqueous phase was also determined by atomic absorption analysis of the aqueous phase.

Metal Ion Transport Experiments.—All transport experiments were carried out at 20 °C. A cylindrical glass cell (diameter 4 cm, height 6 cm) was divided into two parts by a glass plate, except for the bottom portion (1 cm). The two aqueous phases were separated from each other by the glass plate and the chloroform layer placed at the bottom. During one transport experiment, the chloroform layer was slowly stirred with a small magnetic stirrer to allow the interface of the aqueous and organic layers to swirl slowly (*ca.* 60 r.p.m.). The distribution of the metal ions was determined by atomic absorption analysis of the two aqueous phases.

References

1 J. W. Westley, R. H. Evans, jun., T. Williams, and A. Stempel, *Chem. Commun.*, 1970, 71; C. A. Maier and I. C. Paul, *ibid.*, 1971, 181.
2 Yu. A. Ovchinnikov, V. T. Ivanov, and A. M. Shkrob, 'Membrane-Active Complexones,' Elsevier, Amsterdam, 1974.
3 K. Matsushima, H. Kobayashi, Y. Nakatuji, and M. Okahara, *Chem. Lett.*, 1983, 792.
4 E. Schchori and J. J. Grodzinskira, *J. Appl. Polym. Sci.*, 1976, **20**, 773; E. M. Choy, D. F. Evans, and E. L. Cussler, *J. Am. Chem. Soc.*, 1974, **96**, 7085.
5 R. W. Baker, M. E. Tuttle, D. J. Kelly, and H. K. Lonsdale, *J. Membrane Sci.*, 1977, **2**, 213; K. Maruyama, H. Tsukube, and T. Araki, *J. Chem. Soc., Dalton Trans.*, 1981, 1486.
6 M. Kirch and J. M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 555.
7 K. Kalyanasundarum, *Coord. Chem. Rev.*, 1979, **46**, 159.
8 N. Kishii, K. Araki, and S. Shiraishi, *J. Chem. Soc., Chem. Commun.*, 1984, 103.
9 N. Kishii, K. Araki, and S. Shiraishi, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 2121.
10 J. H. Fendler, 'Membrane Mimetic Chemistry,' John Wiley, New York, 1982.
11 E. Bielli, P. M. Gidney, R. D. Gillard, and B. T. Heaton, *J. Chem. Soc., Dalton Trans.*, 1974, 2133.
12 J. E. Parks, B. E. Wagner, and R. H. Holm, *J. Organomet. Chem.*, 1973, **56**, 53.
13 F. H. Burstall, *J. Chem. Soc.*, 1938, 1662.

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