alent (assuming insignificant secondary effects[8]) to a primary isotope effect, $k_H/k_D = 5.3 \pm 1.4$, in good agreement with partitioning experiments.

All of the data reported here can be accounted for by the reversible formation of the adduct **5** between the dihydronicotinamide and the ketone, which is *not* on the pathway for the oxidation-reduction reaction. Evidence concerning the redox reaction itself is consistent with a simple hydride transfer ($k_H/k_D \sim 6$, considerable transfer of charge at the transition state[1b]). Discrepancies between isotope effects determined by kinetics and by partitioning experiments are thus *not* valid evidence for an intermediate on the path to hydrogen transfer in this reaction, and we must question the significance of such evidence in the case of other reactions of dihydronicotinamides[3] as well. Indeed, under conditions where formation of hydrated, neutral adducts like **5** is unlikely (because of solvent composition or steric effects[4]), agreement between isotope effects measured by the two methods has been observed.[11] However, although we have now discounted some of the evidence which has supported proposals for intermediates (cation radicals?) in the redox reactions of dihydronicotinamides, other evidence for complex mechanisms in such processes remains.[12]

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New Membrane Carrier for Selective Transport of Metal Ions

Sir:

Transport of metal ion across a membrane plays an important role in biology and may have useful practical applications to separation science. The selective and specific transport of alkali metal ions has already been realized by using synthetic or naturally derived cyclic multidentate ligands as membrane carriers.[1] On the other hand, little attention has been directed toward the transport of transition and heavy metal ions[2] which are important from the biochemical and medical points of view. Hence, the development of a new membrane carrier for selective transport of these metal ions is still a challenging problem.

We report here a selective liquid membrane system containing a new linear multidentate carrier for transporting transition and heavy metal ions, and present an example of an in vitro system which exhibits characteristics of biological transport. Previously we have reported the synthesis and metal binding properties of a new class of octameric oligomers having the structure $[CH_2CH_2N(CXNHPh)]_{n=8}$ (X = O or S). These linear octamers were prepared by ring-opening oligomerization[3,4] and could make complexes selectively with copper(II) and mercury(II) ions.[4,5] Such a specific binding property of the new octamers fits with the requirement for a selective carrier. Moreover, the intrinsic flexible nature of linear carrier may permit conformational changes in the binding and releasing processes of metal ions, as suggested by Tümmler et al.[6]

Two octameric carriers, **1** and **2**, and their analogue, **3**, were used as membrane carriers (see Figure 1). The "liquid membrane" system operated here is shown schematically in Figure 2.[7] The carriers, **1**-**3**, are much less soluble in the surrounding solutions (aqueous phases I and II) than in the CH_2Cl_2 "membrane". After complexation of the carrier with metal ion on the left side of the membrane, the complex slowly diffuses down its concentration gradient. On the right side of the membrane, metal ion may be extracted into the aqueous phase II, via formation of a ternary complex (carrier-metal ion-amino acid). Then the free carrier diffuses back across the membrane. The net result is that metal ion is moved from the aqueous phase I (left) to the aqueous phase II (right) across the bulk organic phase (liquid membrane).

The copper(II) ion was transported with surprisingly high

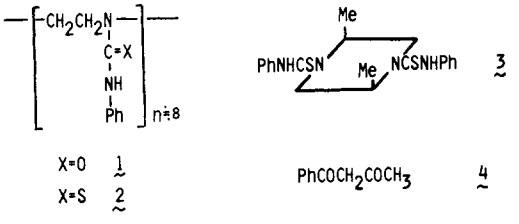

Figure 1. Structure of membrane carriers.

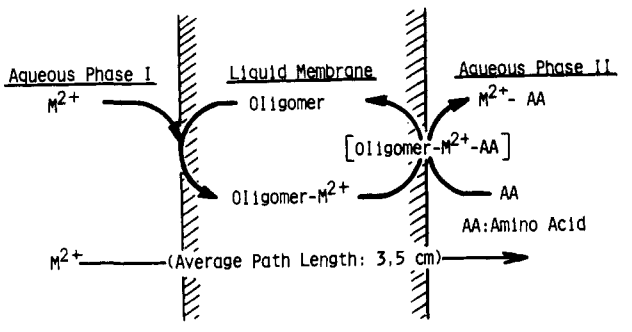

Figure 2. Liquid membrane system.

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Table I. Transport Rate of Various Metal Perchlorates[a]

entry	membrane system: carrier (mmol)	membrane system: amino acid	transport rate × 10^6 (mol/h)[b]: Cu^{2+}	Ni^{2+}	Co^{2+}	Zn^{2+}	Cd^{2+}	Hg^{2+}	Fe^{3+}
1	**1** (0.15)[c]	His	6.20	0	0	0	0	0.68	0
2	**1** (0.10)	His	3.72	0	0	0.04	0.04	0.40	0
3		Ala	1.20	0	0	0.04	0.04	0.08	0
4		None	0.52	0	0	0	0	0.08	0
5	**2** (0.10)	His	4.84	0.20	0	0	0	2.24	1.32
6		Ala	3.40	0.08	0	0.04	0	1.40	0.72
7		None	1.56	0	0	0	0	0.56	0.32
8	**3** (0.15)	His	2.56	0	0	0	0	0.24	0.24
9		Ala	0.72	0	0	0	0	0.04	0.08
10		None	0.20	0	0	0	0	0	0
11	**4** (0.30)	His	0	0	0				
12		*d*	7.52	7.84	7.16				
13	none	His	0	0	0	0	0	0	0
14		Ala	0	0	0	0	0	0	0
15		None	0	0	0	0	0	0	0
		Extraction of Metal Perchlorate from Aqueous to Organic Phase, %[e]							
16	**2**		30	7	4	6	5	58	
17	**3**		25	10	7	6	11		

[a] Aqueous phase I: metal perchlorate, 0.4 mmol; H_2O, 4 mL. Organic phase: carrier-CH_2Cl_2, 8 mL. Aqueous phase II: amino acid, 2.0 mmol; H_2O, 10 mL. [b] The amounts of the transported metal ions in the aqueous phase II were determined by absorptiometry method. The rates were calculated from the transported amounts after 12 h. [c] Values in parentheses indicate the amounts of carriers in organic phase. [d] Aqueous phase I: 0.5 N NH_4OH. Aqueous phase II: 0.5 N HCl. Other conditions were the same as given in *a* (see ref 8). [e] Organic phase: monomeric units in the ligand, 1.2×10^{-4} mol; CH_2Cl_2, 3 mL. Aqueous phase: metal perchlorate, 3.0×10^{-5} mol: H_2O, 3 mL. See ref 4.

selectivity by use of a "liquid membrane" containing the new carriers **1** and **2**. Typical results are shown in Table I. When using oligomeric carrier **1**, copper ion was transported from the aqueous phase I to the aqueous phase II in an amount equal to 37% of the total after 24 h under the conditions stated (entry 1). On the other hand, other metal ions such as nickel(II), cobalt(II), zinc(II), cadmium(II), and iron(III) ions were hardly transported, and mercury(II) ion was transported only slightly. While high selectivity was maintained in transport, the rate of transport could increase with increasing concentration of the carriers in the membrane (entries 1 and 2).

Other experiments show that the permeability of the membrane for copper ion depends largely on the nature of the amino acid in the aqueous phase II (entries 2-10). Free histidine was found to be more effective for enhancement of the transport rate. Amino acids (metal acceptor) which were relatively insoluble in the membrane were scarcely moved into aqueous phase I during the transport. We showed that, in the absence of carrier, metal ion could not be transported to the aqueous phase II (entries 13-15); further the amino acid seemed to play an important role in the metal-releasing process on the right side of the membrane as shown in Figure 2.

Sulfur-containing oligomer **2** was a more powerful carrier for transport. The "soft" character of sulfur groups on its side chain would be effective for developing a higher efficiency of transport (entries 5-7), but its stronger coordination character was not favorable for selective transport of copper ion. In other words, carrier **1** was believed to fulfill the requirements for a carrier better; it had a suitable binding efficiency and a high selectivity for complexation.

The transport selectivity in this system is almost parallel to that observed in the extraction experiments[4] (entry 16), except for the mercury ion. This selectivity in transport, therefore, seemed to be dependent on the same factors governing the metal-extraction process into the membrane. The transport rate of mercury ion was unexpectedly suppressed. This fact may suggest that the mercury complex is too stable in the membrane to be extracted into aqueous phase II.

Similar transport behavior was observed by using bidentate carrier **3** (entries 8-10). Although an extraction experiment[4] indicated that its complexing activity was comparable with that of multidentate carrier **2**, its transport rate was low.

To check the applicability of the findings of Evans et al.,[8] a β-diketone-type carrier, benzoylacetone **4**, was also examined (entries 11 and 12). They reported that **4** could transport copper ion selectively over nickel and cobalt ions, followed by simultaneous countertransport of protons. Although a direct comparison is difficult,[9] no selective transport of copper ion could be realized (entry 12).

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