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Specific recognition of copper ion by lipid-bound double armed crown ether

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Abstract

A lipid membrane aggregate, which showed specific binding ability for Cu^{2+} ion, was prepared by dispersing an aqueous solution of oligopyridine-armed diazacrown ether and a vesicle-forming surfactant. It selectively bound Cu^{2+} ion in the presence of Ni^{2+}, Co^{2+} and Zn^{2+} ions. Since the resulting Cu^{2+} complex was instantly recovered from the aqueous solution after addition of ClO_4^- ion, the present system can be considered as a simple immobilization of metal-specific ligand.

Introduction

A lipid membrane assembly can be formed from a variety of surfactants and possesses interesting properties similar to those of biological membranes [1]. It acts as a useful vehicle carrying functional reagents and provides a variety of integrated molecular systems. Since specific recognition and transportation of metal cations are often observed in the biomembrane processes, metal complexation on the synthetic membrane holds great promise for advances and new applications in inorganic, biomimetic and analytical chemistry [2].

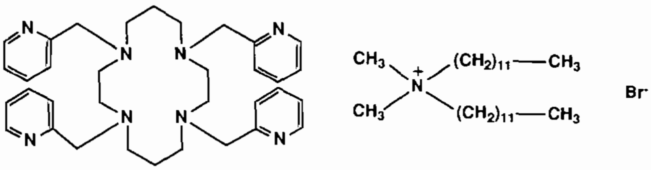

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Fig. 1. Previously reported macrocycle and lipid-surfactant.

We previously demonstrated that a lipid-bound macrocycle efficiently extracted Cu^{2+} ion from aqueous solution into a lipid aggregate [3]. This was simply prepared by dispersing an aqueous solution of lipophilic cyclam derivative **1** and a vesicle-forming ammonium-cation surfactant **2**, and was easily recovered after precipitation by the addition of perchlorate anion (Fig. 1). Unfortunately, its extraction ability was depressed in the presence of Ni^{2+}, Co^{2+} and Zn^{2+} ions, and competitive extraction has not yet been achieved. We now report that double armed crown ethers such as **4** specifically bind Cu^{2+} ion and efficiently extract it from an aqueous mixture of Cu^{2+}, Ni^{2+}, Co^{2+} and Zn^{2+} ions when they are incorporated in the lipid membrane (Fig. 2).

Experimental

Materials

N,N'-Bis(2,2':6',2'':6'',2'''-quaterpyridin-6-ylmethyl)diaza-18-crown-6 (**6**)

A mixture of quaterpyridinylmethyl bromide (2.64 mmol) [4], diaza-18-crown-6 (1.26 mmol) and *N,N*-diisopropylethylamine (12.6 mmol) was refluxed in EtOH (10 ml) for 2 h. After cooling, the solvent was evaporated off under reduced pressure. The residue was extracted with $CHCl_3$ (350 ml), washed with water (3 ml×3) and dried over $MgSO_4$. Column chromatography on alumina using 1–5% Et_3N in EtOAc gave the crown ether **6** in 60% yield; m.p. 208–210 °C ($CHCl_3$–Et_2O): ^1H NMR ($CDCl_3$): δ 2.98 (bs, 8H), 3.65 (s, 8H), 3.71 (t, $J=5.7$ Hz, 8H), 4.00 (s, 4H), 7.34 (ddd, $J=6.0$, 4.8 and 1.3 Hz, 2H), 7.59 (d, $J=7.3$ Hz, 2H), 7.83 (t, $J=7.9$ Hz, 2H), 7.87 (td, $J=7.7$ and 1.8 Hz, 2H), 7.97 (t, $J=7.7$ Hz, 2H). 7.98 (t, $J=7.9$ Hz, 2H), 8.46(dd, $J=7.7$ and 1.1 Hz, 2H), 8.49 (d, $J=8.1$ Hz, 4H), 8.61–8.64 (m, 6H), 8.70 (dm, $J=5.0$ Hz, 2H). FAB-HRMS: $[M+H]^+$ calc. for $C_{54}H_{55}N_{10}O_4$ 907.441, found 907.454.

Other crown ethers employed were similarly prepared [5], while surfactant **2** was purchased from Eastman Kodak Company.

Preparation of lipid-bound double armed crown ether

The lipid membrane was prepared by dissolving surfactant **2** (0.66 mmol) in $CHCl_3$ (2.0 ml). Subsequent to solvent evaporation, the thin lipid film was removed by shaking with distilled water (22 ml). The turbid suspension was sonicated for 3 min at ambient tem-

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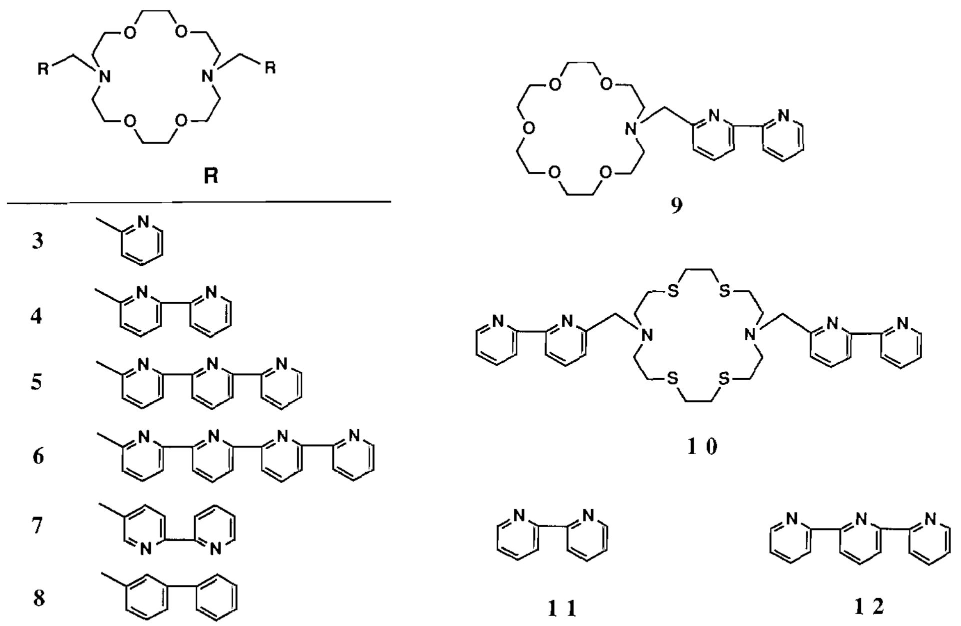

Fig. 2. Employed armed crown ethers and reference compounds

perature by means of the probe of a Nissei US 300 ultrasonic generator. To this aqueous dispersion (5.0 ml) was added crown ether (0.0045 mmol) as a solid or an oil (0.0090 mmol of oligopyridine **11** or **12** was employed), and the mixture was sonicated again to give an almost clear solution.

Extraction with lipid-bound double armed crown ether

An aqueous mixture (1.0 ml) of $Cu(ClO_4)_2$, $Ni(ClO_4)_2$, $Co(ClO_4)_2$ and $Zn(ClO_4)_2$ (0.0045 mol/l, each) was added to the aqueous dispersion prepared above, and the resulting solution was stirred mechanically for 50 min at room temperature. Addition of $Mg(ClO_4)_2$ (0.50 mmol) immediately gave a powdery precipitate. After stirring for 100 min, the insolubilized lipid aggregate was filtered. The amount of metal perchlorate extracted was calculated from the concentration of metal perchlorate remaining in the filtrate. Liquid–liquid extraction experiments (CH_2Cl_2/H_2O) were carried out under similar concentration conditions. Typical results are summarized in Table 1.

TABLE 1. Competitive extraction of metal cation by lipid-bound crown ether

Crown ether	Extraction (%)[a]			
	Cu^{2+}	Ni^{2+}	Co^{2+}	Zn^{2+}
3	0	3	0	1
4	93	7	2	1
5[b]	93	45	2	0
6[b]	78	0	0	0
7	3	0	0	0
8	3	3	0	0
9	4	0	0	0
10[b]	88	40	0	0
11	1	4	3	1
12	2	4	31	1
4[c]	50	25	7	4
5[c]	99	10	38	34

[a] Extraction % = [metal perchlorate]$_{insol}$/[metal perchlorate]$_{added}$ × 100 [b] Slightly turbid. [c] Liquid–liquid extraction: crown, 0.0045 mmol in CH_2Cl_2 6.0 ml; metal perchlorate, 0.0045 mmol (each) $Mg(ClO_4)_2$, 0.50 mmol in H_2O 6.0 ml. stirred for 100 min.

Results and discussion

Oligopyridine-armed diaza-crown ethers **4**–**6** extracted Cu^{2+} ion very efficiently from an aqueous mixture of Cu^{2+}, Ni^{2+}, Co^{2+} and Zn^{2+} ions into the lipid aggregate. Their extraction selectivity and efficiency were higher than those observed in liquid–liquid extraction experiments. Lipid immobilization clearly enhanced the extraction ability of these double armed crown ethers. Bipyridine-armed diaza-crown ether **7** rarely extracted any of the metal cations examined, though its structural elements are like those of crown ether **4**. Since crown ethers, **3** and **8**, and oligopyridines, **11** and **12**, were not as effective, introduction of the bis-pyridine-functionalized sidearm into the diaza-crown ring system in the proper geometrical arrangement offered specific complexation with Cu^{2+} ion.

Bipyridine-armed lariat ether **9** and thia-crown ether **10** were compared and showed extraction profiles greatly different from bipyridine-armed diaza-crown ether **4**:

thia-crown ether **10** efficiently extracted Ni^{2+} ion as well as Cu^{2+} ion; lariat ether **9** extracted little of either. As frequently reported in crown ether complexation systems, the nature of the parent crown ring strongly influenced cation recognition and extraction profiles in the lipid membrane assembly.

Cu^{2+} ion binding behavior of the bipyridine-armed diazacrown ether **4** was studied by electronic spectroscopy. A spectrum of an aqueous dispersion of the surfactant **2**, $Cu(ClO_4)_2$ and crown ether **4** exhibited the d–d transition band of a Cu^{2+} complex at 658 nm. Since the intensity of this band was rarely changed by addition of $Ni(ClO_4)_2$, $Co(ClO_4)_2$ and $Zn(ClO_4)_2$, the crown ether **4** must bind the Cu^{2+} ion specifically in the lipid membrane system. A similar d–d transition band was observed at 689 nm in an H_2O/EtOH (vol./vol. = 1/5) solution. It showed a certain decrease in the presence of Ni^{2+}, Co^{2+} or Zn^{2+} salt, indicating that the order of binding strength was $Cu^{2+} > Zn^{2+} = Co^{2+} > Ni^{2+}$. Thus, a lipid membrane assembly offers an effective microenvironment for enhancing Cu^{2+} ion specificity.

In conclusion, we have presented the first example of lipid-bound armed crown ethers which bind a specific metal cation and effectively extract it from an aqueous mixture of metal cations. Although several membrane assemblies have been employed in the detection and separation of metal cations [6], our system can be considered as a simple immobilization of metal–ligand and should have broad applicability.

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