Lipid-bound Macrocycles as New Immobilized Ligand Systems for Effective Separation of Metal Cations

Horishi Tsukube,*[a] Takehiro Yoden,[b] Tadashi Iwachido[a] and Michio Zenki[b]

[a] *Department of Chemistry, College of Liberal Arts & Science, Okayama University, Okayama 700, Japan*
[b] *Department of Chemistry, Faculty of Science, Okayama University of Science, Ridai-Chou, Okayama 700, Japan*

Lipid-bound macrocycles, prepared by dispersing an aqueous solution of lipophilic polyamine ligand and a vesicle-forming lipid, showed specific binding abilities for transition metal cations, the resulting complex being instantly precipitated by addition of perchlorate anion and easily recovered, as for insoluble immobilized systems.

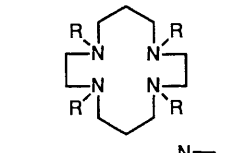
There is the expectation that the immobilization of metal-specific ligands on insoluble polymer supports will enhance their usefulness for separation of valuable and/or toxic metal cations. Many efforts to bind certain ligands covalently to polystyrene, silica gel and other insoluble supports have been reported,[1] but their immobilization has usually involved sequences of laborious chemical reactions and has often reduced the metal binding ability of the parent ligand systems.

We now report that a lipid-bound macrocycle can be used as a new type of immobilized ligand system. This was simply prepared by dispersing an aqueous solution of a lipophilic macrocyclic polyamine and a vesicle-forming lipid, and was easily recovered as for insoluble immobilized systems. Further, our lipid-bound macrocycle showed higher extraction selectivity and efficiency towards transition metal cations than those observed in liquid–liquid and solid–liquid extraction experiments. Thus, the present study offers a new application of lipid-based aggregates in host–guest separation processes.[2]

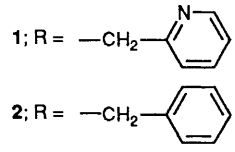
We compared the cation extraction behaviour of three kinds of ligands **1**–**3**.[3] A typical extraction experiment with a lipid-bound macrocycle was as follows. To an aqueous dispersion (3 ml) of the lipid **X** (0.09 mmol) was added the ligand as a solid (0.0027 mmol), and the mixture was sonicated at 30–40 °C for 5 min. An aqueous solution of the transition metal perchlorate (0.0027 mmol in 0.6 ml) was added, and the resulting solution was stirred for 30 min at room temperature. Addition of $Mg(ClO_4)_2$ (0.3 mmol) immediately gave a powdery precipitate. After stirring for 30 min, the insolubilized lipid-bound macrocycle was easily separated from the aqueous solution by filtration. The amount of metal perchlorate extracted by the lipid-bound macrocycle was calculated from the concentration of metal perchlorate remaining in the aqueous solution. Solid–liquid and liquid–liquid extraction experiments were also carried out under similar concentration conditions. Typical results are summarized in Table 1.

The lipid-bound macrocycle **1** extracted Cu^{2+} cation very effectively from the bulk aqueous phase into the lipid-aggregate phase, while Ni^{2+}, Co^{2+} and Zn^{2+} cations were bound only slightly, or not at all. Its Cu^{2+} extraction ability was much higher than observed in solid–liquid and liquid–liquid extraction experiments. Since the macrocycle **1** bound Ni^{2+}, Co^{2+} and Zn^{2+} cations strongly in liquid–liquid and solid–liquid extraction experiments, the metal selectivity was thus markedly enhanced by lipid-immobilization. The coordination chemistry of tetra-armed macrocycles is quite complicated owing to the range of potential donor atoms,[4] but the lipid-bound armed macrocycle **1** clearly exhibited selective binding for Cu^{2+} ion. Such specific cation binding behaviour is unusual in comparison with the aggregate systems reported.[2,5] The extraction activity of the lipid-bound macrocycle was also dependent on the nature of the ligand employed. The macrocycle **2** showed no extraction ability for the metal cations studied, while the polyamine ligand **3** showed modest extraction for Zn^{2+}.† The structure of the complex formed, stoichiometry, binding kinetics and lipophilicity of the ligand employed all affected the extraction profile of the lipid-bound ligand system.

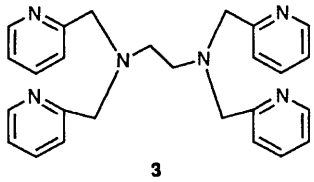
The cation complexation behaviour of the macrocycle **1** was studied by means of electronic spectroscopy. The spectrum of an aqueous dispersion of the lipid **X**, $Cu(ClO_4)_2$ and ligand **1** exhibited the d–d transition band of the Cu^{2+} complex at 664 nm. Since the macrocycle **1**–Cu^{2+} complex was slightly soluble



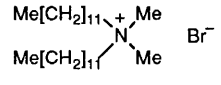
1; R = —CH_2—



2; R = —CH_2—



3



Lipid **X**

Table 1 Cation extraction of lipid-bound macrocycles and related systems[a]

	Extraction (%)			
	Cu^{2+}	Ni^{2+}	Co^{2+}	Zn^{2+}
Lipid **X**	3	3	0	0
Lipid–**1**	89	4	0	3
Lipid–**2**	0	0	0	0
Lipid–**3**	0	1	1	17
1[b]	21	26	76	100
1[c]	57	3	3	87

[a] Extraction conditions: lipid, 0.09 mmol; ligand, 0.0027 mmol; guest metal perchlorate, 0.0027 mmol; $Mg(ClO_4)_2$, 0.3 mmol in H_2O, 3.6 ml. Details are in the text. [b] Liquid–liquid extraction: ligand 0.0027 mmol in CH_2Cl_2, 3.6 ml; guest metal perchlorate, 0.0027 mmol; $Mg(ClO_4)_2$, 0.30 mmol in H_2O, 3.6 ml; stirred for 1 h. [c] Solid–liquid extraction: ligand, 0.0027 mmol; guest metal perchlorate, 0.0027 mmol; $Mg(ClO_4)_2$, 0.30 mmol in H_2O, 3.6 ml; stirred for 1 h.

† The ligand **3** also formed a Cu^{2+} complex in the aqueous dispersion system, the d–d transition band of which was at 676 nm, but the resulting complex was hardly detectable in the insolubilized lipid aggregate.

in water and showed a similar d–d transition band, the macrocycle **1** is dynamically immobilized by the lipid-based aggregate and acts as a supramolecular extractor.

In conclusion, we have described an easy and direct measurement of selective metal complexation in a lipid-based aggregate. Although bilayer membranes and related aggregates have been widely employed in the detection and separation of metal cations,[6] our method should have broad applicability and is regarded as a simple immobilization of the metal-specific ligand.

This research was supported in part by a Grant-in-Aid for Scientific Research on Priority Areas ('Multiplex Organic System') from the Ministry of Education, Science, and Culture, Japan.

Received, 8th May 1991; Com. 1/02159A

References

1 Review: M. Takagi and H. Nakamura, *J. Coord. Chem.*, 1986, **15**, 53. Recent example: J. S. Bradshaw, R. L. Bruening, K. E. Krakowiak, B. J. Tarbet, M. L. Bruening, R. M. Izatt and J. J. Christensen, *J. Chem. Soc., Chem. Commun.*, 1988, 812.

2 Several macrocyclic ligands have been characterized in molecular aggregates. Recent examples: H. Fasoli, L. E. Echegoyen, J. C. Hernandez, G. W. Gokel and L. Echegoyen, *J. Chem. Soc., Chem. Commun.*, 1989, 578; J. Malthete, D. Poupinet, R. Vilanove and J.-M. Lehn, *J. Chem. Soc., Chem. Commun.*, 1989, 1016; S. Shinkai, T. Nishi, A. Ikeda, T. Matsuda, K. Shimamoto and O. Manabe, *J. Chem. Soc., Chem. Commun.*, 1990, 303; K. Kurihara, K. Ohto, Y. Tanaka, Y. Aoyama and T. Kunitake, *J. Am. Chem. Soc.*, 1991, **113**, 444.

3 Ligands **1** and **2**: N. W. Alcock, K. P. Balakrishnan and P. Moore, *J. Chem. Soc., Dalton Trans.*, 1986, 1743; H. Tsukube, K. Yamashita, T. Iwachido and M. Zenki, *Tetrahedron Lett.*, 1989, **30**, 3983; *J. Chem. Soc., Perkin Trans. 1*, 1991, 1661. Ligand **3**: G. Anderegg, E. Hubmann, N. G. Podder and F. Wenk, *Helv. Chim. Acta*, 1977, **60**, 123; P. Arslan, F. D. Virgilio, M. Beltrame, R. Y. Tsien and T. Pozzan, *J. Biol. Chem.*, 1985, **260**, 2719.

4 Typical examples of tetra-armed cyclams: K. P. Wainwright, *J. Chem. Soc., Dalton Trans.*, 1980, 2117; C. M. Madeyski, J. P. Michael and R. D. Hancock, *Inorg. Chem.*, 1984, **23**, 1487; G. M. Freeman, E. K. Barefield and D. G. Van Derveer, *Inorg. Chem.*, 1984, **23**, 3092; I. Murase, M. Mikuriya, H. Sonoda, Y. Fukuda and S. Kida, *J. Chem. Soc., Dalton Trans.*, 1986, 953.

5 Most reported systems showed cation recognition patterns parallel to those observed in homogeneous solution or liquid–liquid extraction: N. Nakashima, I. Moriguchi, K. Nakano and M. Takagi, *J. Chem. Soc., Chem. Commun.*, 1987, 617; Y. Ishikawa, T. Kunitake, T. Matsuda, T. Otsuka and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, 1989, 736; S. Yoshida, Y. Okawa, T. Watanabe. S. Inokuma and T. Kuwamura, *Chem. Lett.*, 1989, 243.

6 I. Rubinstein, S. Steinberg, Y. Tor, A. Shanzer and J. Sagiv, *Nature*, 1988, **332**, 426; S. Nagase, M. Kataoka, R. Komatsu, R. Naganawa, K. Odashima and Y. Umesawa, *Anal. Chem.*, 1990, **62**, 1252.