Specific Cation-transport Abilities of New Macrocyclic Polyamine Compounds

Hiroshi Tsukube

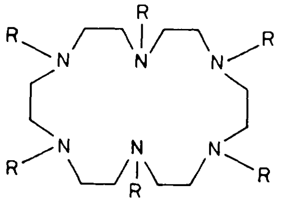
Department of Chemistry, College of Liberal Arts and Science, Okayama University, Okayama 700, Japan

The lipophilic macrocyclic polyamine carriers (1) and (2) mediated efficient ammonium-cation transport with characteristic properties not observed in previously reported crown ether systems.

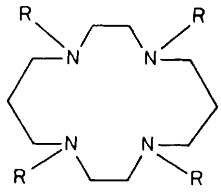
We report here that the lipophilic macrocyclic polyamine compounds (**1**) and (**2**) show unusually high transport efficiencies and selectivities towards the ammonium cations of biologically important amine compounds. Although several nitrogen-containing crown ethers have been recognized as specific cation carriers,[1] the present macrocyclic sytems could provide further possibilities for new selective site-controlled cation transport.

The nitrogen-containing macrocycles (**1**)—(**4**) were examined as cation carriers in a chloroform liquid membrane system.[2] The cycles (**1**) and (**2**) are polyamines, (**3**) a diaza-crown ether, and (**4**) a pyridino-crown ether. For comparison, a typical crown ether (**5**) was also examined. The carriers (**1**), (**2**), and (**3**), prepared by benzylation of the corresponding cyclic amines,† have limited solubilities in water which prevents loss of carrier to the aqueous phases.

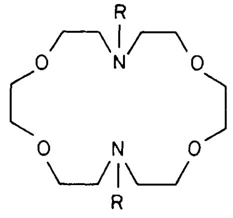
The macrocycles (**1**) and (**2**) showed selective transport of ammonium cations of some amino-acid esters and related amine compounds (Table 1). Of interest is the high discrimination of (**1**) and (**2**) for organic ammonium cations against K^+ in the transport process. In marked contrast, (**5**) transported both K^+ and the ammonium cations with seemingly less selectivity. Since the cavity size of the carriers cannot distinguish between ammonium and K^+ cations, our results indicate that the nature of donor sites in the macrocycles plays an important role in controlling selection for cations. The mixed-donor type crown ethers (**3**) and (**4**) exhibited transport properties intermediate between those of the polyamine- and polyether-type carriers. As reported before[3] they favoured the



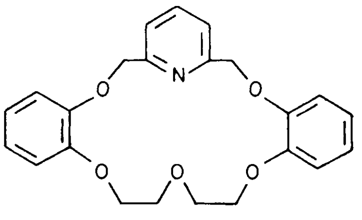
(1); R = CH_2Ph



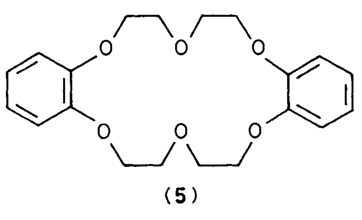
(2); R = CH_2Ph



(3); R = CH_2Ph



(4)



(5)

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† The cyclic amines were benzylated in a two-phase reaction system ($CHCl_3$–H_2O). A $CHCl_3$ solution (15 ml) of benzyl chloride (3.18 g) was added dropwise to an aqueous solution (15 ml) of Hexacyclen trisulphate (Aldrich, 1.9 g) and NaOH (2.0 g); after vigorous stirring at room temp. overnight the organic layer was separated and washed with HCl (0.05 M) and then water and dried over Na_2SO_4. The solvent was removed and the residue recrystallized from CH_2Cl_2–MeOH to give white crystals of (**1**) (m.p. 120—121 °C). The carriers (**2**) (m.p. 154—155 °C) and (**3**) (m.p. 82—83 °C) were similarly obtained.

Table 1. Passive transport of guest cations by macrocyclic carriers.[a]

		Transport rate[b] × 10^6 (mol h^{-1})				
Guest	Additive	**(1)**	**(2)**	**(3)**	**(4)**	**(5)**
LiCl	[c]	0	0	0	0	0.11
NaCl	[c]	0	0	0	0	0
KCl	[c]	0	0	1.13	0.64	2.90
NH_4Cl	[c]	0	0	0.96	0.27	0.27
$AgClO_4$	[c]	0.20	0	2.40	7.93	1.01
Phe-OEt·HCl	—	3.26	2.64	0	0.07	0
	[c]	2.67	0.56[d]	1.90	3.67	4.91
	NaSCN	2.98	0.57[d]	4.02	3.51	3.65
Tyr-OEt·HCl	[c]	5.90	2.83[d]	4.10	0.53	0
Trp-OEt·HCl	[c]	4.91	1.23[d]	2.25	3.98	6.59
Tyramine·HCl	[c]	0	0	0	0	0
$PhCH(OH)CH(Me)NH_2$·HCl	[c]	1.63	1.34	2.73	3.63	2.16
$Pro-OCH_2Ph$·HCl	—	3.46	3.04	0.80	0.38	0

[a] Initial conditions: aqueous phase 1, guest (0.25 mmol)–additive (0.5 mmol)–H_2O (5 ml); membrane, carrier (0.0372 mmol)–$CHCl_3$ (12 ml); aqueous phase 2, H_2O (5 ml). [b] Obtained from the initial rates of appearance of guest species in aqueous phase 2; reproducibility ±10% or better. [c] Additive = $LiClO_4$. [d] Suspension formed in these cases.

complexation of Ag^+ and ammonium cations, but their selectivities for the ammonium cations were much lower than those of **(1)** and **(2)**.

Table 1 also shows that **(1)** and **(2)** transported the 'secondary' ammonium cation of the proline ester with efficiencies comparable to those of 'primary' ammonium cations. Such an effective transport of a 'secondary' ammonium cation was not attained by using **(3)**, **(4)**, or **(5)**. Hence, incorporation of nitrogen donor atoms into the macrocycles may lead to new cation-transport properties.

Co-transported anions also have an effect on the cation-transport rates. For the crown ethers **(3)**, **(4)**, or **(5)** the rates of transport depended on the nature of the co-transported anion. As noted previously,[4] ClO_4^- and SCN^- are required for the promotion of interfacial cation-binding. The macrocycles **(1)** and **(2)**, though, effectively transported the ammonium cations in the absence of these hydrophobic anions. Although mechanistic details are unclear at present, these results do suggest that guest ammonium cations are more tightly bound to the nitrogen atoms of polyamines than to the oxygen atoms of polyethers. Further modifications of size and shape of macrocyclic systems could further their use in cation-transport and in related processes.

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