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Characteristic Transport Properties of Diaza-crown Ethers for Primary and Secondary Ammonium Cations

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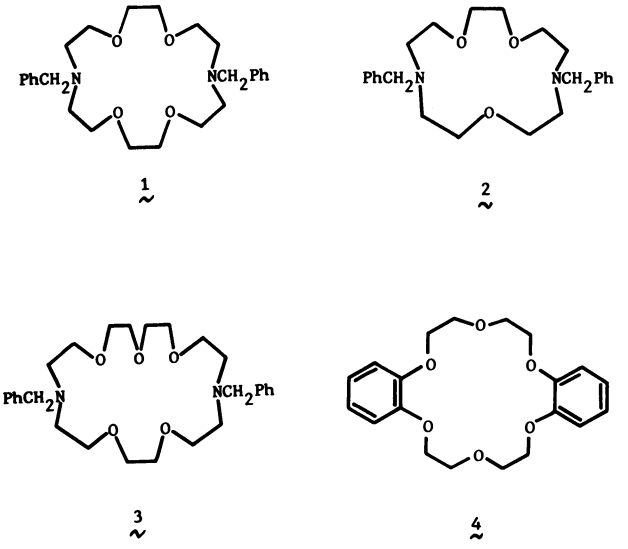
Synopsis. Simple lipophilic diaza-crown ethers show unique transport properties for primary and secondary ammonium salts, which are markedly different from those observed with common crown ether systems.

An important advantage of aza-crown ethers over oxa-crown ethers is the presence of soft nitrogen donor atoms which can offer characteristic complexing and transporting abilities.1) Recently, pyrido-crown ethers and their analogues have received much attention as specific ligand and/or carrier for primary ammonium cations and some metal ions.2) Here we report that simple diaza-crown ethers show new and unique cation transport properties, especially for a series of amino acid ester salts. They were demonstrated to transport both primary and secondary ammonium cations with high efficiency and unique selectivity, which were not attained in the oxa-crown ether systems.

Three kinds of lipophilic diaza-crown ethers having 15- to 21-membered rings, **1**—**3**, were employed as cation carriers (Fig.). They were easily prepared from benzyl chloride and corresponding diaza-crown ethers (see Experimental), and have limited solubilities in water. In the liquid membrane system employed,3) the crown ether carrier dissolved in the chloroform membrane phase mediates the transport of guest cation and co-transported anion from the source aqueous phase through the membrane phase into the receiving aqueous phase by complexing and solubilizing guest salt into the membrane phase.

The diaza-crown ethers **1**—**3** showed high transport abilities for various ammonium cations of amino acid esters, while they offered low transport rates for K$^+$ and other metal ions (Table). It is of particular importance that they transport "secondary" ammonium cation of proline ester with efficiency comparable to those observed for primary ammonium cations. Although many kinds of oxa-crown ethers are known to transport primary ammonium cations effectively like the carrier **4**, such an effective transport of secondary ammonium cation has not been achieved in these oxa-crown ether systems. Since the employed diaza-crown ethers have various cavity sizes (diameter: *ca.* 2.0—4.0 Å), our results strongly suggest that nitrogen donor atoms in the macrocycles play an important role in complexation and transportation of ammonium cations. Probably, guest ammonium cation would be tightly attached by "two" hydrogen bonds to two diametrical nitrogen donor atoms in the diaza-crown ether. Similar complex structures have been proposed in the diazametacyclophane and related systems.4)



1 **2** **3** **4**

Fig. Macrocyclic carriers examined.

Table also indicates that diaza-crown ethers **1**—**3** have largely different transport selectivities from those observed in the oxa-crown ether **4** system. When the crown ether **4** was employed, hydrophobic primary ammonium salts such as phenylalanine and tryptophan esters were much more effectively transported than the hydrophilic glycine and alanine esters. On the other hand, diaza-crown ethers **1**—**3** offered high transport rates for a variety of ammonium salts including glycine, alanine, and proline esters. Recently we demonstrated that lipophilic macrocyclic polyamine-type carriers showed parallel transport trend for a series of amino acid esters.5) Hence, introduction of the nitrogen donor atoms into the macrocycles would offer not only

Table. Cation transport properties of diaza-crown ether carriers

Guest	Additive	Transport rate $\times 10^6$ mol/h			
		1	2	3	4
NaCl	$NaClO_4$	0.5	0.5	0.7	0.2
KCl	$NaClO_4$	0.8	0.4	0.4	5.6
NH_4Cl	$NaClO_4$	2.5	0.9	1.0	0.4
PheOEt·HCl	None	1.2	0.2	0.8	0
	$NaNO_3$	3.3	1.6	3.9	1.2
	NaSCN	6.3	8.6	8.1	9.6
	$NaClO_4$	3.8	4.3	6.8	11.9
TrpOEt·HCl	$NaClO_4$	6.0	5.7	5.4	13.2
LeuOEt·HCl	$NaClO_4$	5.6	6.2	7.2	12.3
AlaOEt·HCl	$NaClO_4$	8.2	6.6	7.2	1.4
GlyOEt·HCl	$NaClO_4$	8.7	8.7	9.3	1.0
ProOMe·HCl	$NaClO_4$	5.3	6.7	6.6	0.2

Transport conditions: Source aqueous phase; guest salt, 0.5 mmol. Additive, 1.0 mmol/H_2O, 5 ml. Membrane; carrier, 0.0372 mmol/$CHCl_3$, 12 ml. Receiving aqueous phase; H_2O, 5 ml.

high efficiency but also unique selectivity in the transport process.

The nature of co-transported anion has a pronounced effect on the cation-transport rate. As frequently reported in the crown ether-type carrier systems,⁶⁾ ClO_4^-, SCN^-, and other hydrophobic anions were required to promote this cation-transport process. Since we confirmed that diaza-crown ethers having 15- to 21-membered ring sizes showed potential transport properties for ammonium salts, they may provide wide applications in the cation-transport and in the related biomimetic systems.

Experimental

Materials. Diaza-crown ethers **1**—**3** were prepared in a two-phase reaction system (chloroform/water). Typically, a chloroform solution (15 ml) of benzyl chloride (3.48 g) was added dropwise to an aqueous solution (15 ml) of "Kryptofix 22" (Merck Japan, 3.00 g) and NaOH (2.00 g). After vigorous stirring at room temperature overnight, the organic layer was washed with aqueous HCl solution and water, and dried over Na_2SO_4. The solvent was removed, and recrystallization from ether gave colorless crystals **1**: Mp 82 °C (lit, 80 °C).1b) Yield, 80%. IR (Nujol) 1602, 1498, 1125, 755, and 705 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$) δ=2.83 (8H, t, $NC\underline{H}_2CH_2$), 3.50—3.73 (20H, m, $OC\underline{H}_2CH_2$, $NC\underline{H}_2C_6H_5$), 7.23—7.40 (10H, m, $CH_2C_6\underline{H}_5$).

The carriers **2** and **3** were similarly prepared and purified by column chromatography on alumina (elute, $CHCl_3$). **2**: yellowish oil, 65%. IR (neat) 1600, 1495, 1450, 1125, 735, and 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ=2.67—2.95 (8H, t+t, $NC\underline{H}_2CH_2$), 3.52—3.73 (16H, m, $OC\underline{H}_2CH_2$, $NC\underline{H}_2C_6H_5$), 7,17—7.45 (10H, m, $CH_2C_6\underline{H}_5$). **3**: yellowish oil, 58%. IR (neat) 1600, 1495, 1455, 1100, 740, and 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ=2.83 (8H, t, $NC\underline{H}_2CH_2$), 3.53—3.77 (24H, m, $OC\underline{H}_2CH_2$, $NC\underline{H}_2C_6H_5$), 7.20—7.47 (10H, m, $CH_2C_6\underline{H}_5$). Satisfactory elemental analyses were obtained for these carriers.

Phenylalanine ethyl ester, leucine ethyl ester, alanine ethyl ester, and glycine ethyl ester were obtained from Nakarai Chem. Ltd., and other employed esters were purchased from Tokyo Chem. Ind. Ltd.

Transport Procedure. The transport experiments were carried out at room temperature in a U-tube glass cell (2.0 cm, i.d.) as reported before.³⁾ The carrier in chloroform (12 ml) was placed in the base of the U-tube, and two aqueous phases (5 ml, each) were placed in the arms of the U-tube, floating on the chloroform phase. The membrane phase was stirred with a magnetic stirrer. The transport rates were calculated from the initial rates of appearance of co-transported anion, ClO_4^-, into the receiving aqueous phase, which were determined by means of ion-selective electrode (Orion Model 93-81). Phenylalanine and tryptophan esters were also monitored spectroscopically. Reproducibility was confirmed as ±15% or better.

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