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HIGHLY SELECTIVE TRANSPORT OF BIOGENETIC AMINES AND DRUGS BY USING FUNCTIONALIZED "ACYCLIC CROWN ETHER"

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Acyclic crown ether 1, containing quinoline terminal groups, showed effective transport selectivity for some kinds of biogenetic amines and drugs of biological significances over alkali metal cations, which was not attained by using a typical cyclic crown ether 3.

Recently many types of "acyclic crown ethers" have been presented as models for acyclic antibiotics.[1] Although these acyclic crown ethers could offer the advantages of facile synthesis, of versatility of ligand structure, and of fast complex formation, we have known only a few acyclic crown ethers displaying more excellent abilities than corresponding cyclic crown ethers as ion-transport carriers.[2]

Here we present the first successful example of liquid membrane transport in which some organic ammonium cations are effectively discriminated from K^+ cation by "acyclic crown ether" carrier. Our employed acyclic crown ether 1 contains quinoline unit as terminal groups, and provides several adequate properties as a potential carrier, especially for ammonium cations: (1) Its terminal groups act as powerful hydrogen bonding sites for ammonium cations; (2) The quinoline moiety also functions as anchoring points with locally fixed donor sites on which guest cation can take hold; (3) The flexible nature of acyclic carrier may permit effective conformational changes in the binding and releasing processes.[3] Although some thermodynamic and kinetic data of the carrier 1-alkali metal complexes have been reported,[3] so far as we know, this is the first application of this type of acyclic crown ether to the ion-transport process.

Transport experiments were performed by using a liquid membrane cell (Figure 1).[4] The cell consisted of 8 ml membrane phase (chloroform containing 0.0372 mmol carrier, stirred constantly by magnetic stirrer), interfaced to 3 ml source phase (salt solution) and 9 ml receiving phase (distilled water). After a period of 12 h, the transported amounts into the receiving phase were determined for individual guest cation. Three types of carriers were employed below (Figure 2): quinoline-bearing acyclic crown ether 1, butyl-bearing acyclic crown ether 2, and typical cyclic crown ether 3. As guest ammonium cations, we chose phenethylammonium type cations to which the biogenetic amines and various drugs of great biological importance belong. Typical results are shown in Table. Blank experiments, no carrier present, were performed for each system to determine membrane leakages. The obtained amounts of cation leakages varied with used cations, but were generally much smaller than those indicated in Table.

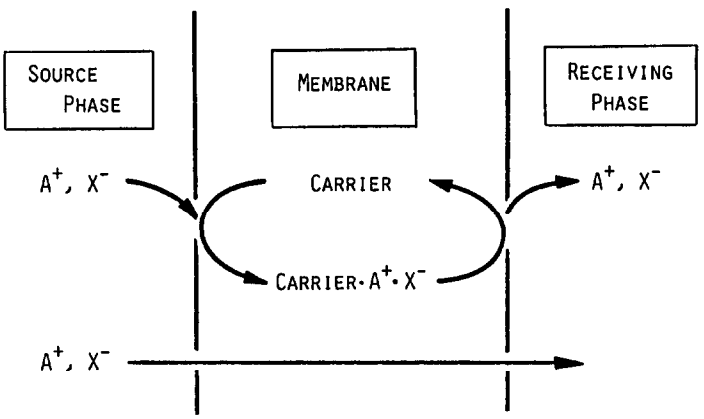
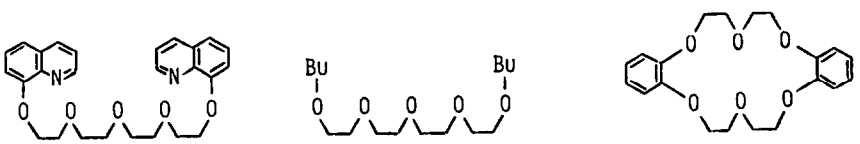


Figure 1. Cation-Transport Membrane. (A^+: Guest Cation; X^-: Symport Anion)



1 2 3

Figure 2. Synthetic Carriers.

Table. Selective Cation-Transport Mediated by "Acyclic Crown Ether".

Salt		Transport Rate $\times 10^6$ (mol/h)		
		1	2	3
$LiClO_4$	(A)	0	1.5	0.5
$NaClO_4$	(A)	0.1	0.4	0.3
$KClO_4$	(A)	0.1	0.1	4.7
NH_4ClO_4	(A)	0.3	0.2	0.3
KCl	(B)	0.9	0.2	28.5
NH_4Cl	(B)	3.0	0.2	8.6
$C_6H_5\underset{CH_3}{\overset{}{C}}HNH_3Cl$	(B)	10.7	1.0	11.6
$C_6H_5CH_2CH_2NH_3Cl$	(B)	12.5	1.2	12.9
$C_6H_5CH_2\overset{CH_3}{\underset{CH_3}{C}}NH_3Cl$ (phentermine)	(B)	17.1	0.1	18.5
$C_6H_5\underset{OH}{CH}-\underset{CH_3}{CH}NH_3Cl$ (norephedrine)	(B)	6.2	0.5	6.9
$(CH_3O)_2C_6H_3CH_2CH_2NH_3Cl$ (homoveratrylamine)	(B)	12.7	1.0	14.1
$HOC_6H_4CH_2CH_2NH_3Cl$ (tyramine)	(B)	0.6	1.0	1.4
$(HO)_2C_6H_3CH_2CH_2NH_3Cl$ (dopamine)	(B)	0.2	0.3	1.0

Initial Concentrations: Source Phase; Salt, 0.3 mmol. Additive($NaClO_4$), 0 mmol (A) or 1.5 mmol (B) / H_2O, 3 ml. Membrane; Carrier, 0.0372 mmol / $CHCl_3$, 8 ml. Receiving Phase; H_2O, 9 ml.

Quinoline-bearing acyclic crown ether 1 showed excellent transport selectivities for some organic ammonium cations over alkali metal cations examined. Of particular, it was noted that the carrier 1 highly discriminated organic ammonium cations from K^+ ion in the transport process. Compared to this acyclic crown ether 1, dibenzo-18-crown-6, 3, typical cyclic crown ether-type carrier,[5] facilitated effectively the transport of K^+ ion as well as that of ammonium cations, and seemed to be a non-selective carrier in a sense. Butyl-bearing acyclic crown ether 2, which has similar polyether linkages to the carrier 1,

was confirmed to hardly transport ammonium cations and other examined metal ions. Therefore, quinoline nitrogen atoms of the acyclic crown ether 1 can play essential roles as effective hydrogen bonding sites, and their coordination may induce pseudocyclic conformation of the acyclic carrier, leading to the successive interactions of polyether sequence with ammonium cations. Although pyridine-containing cyclic crown ethers have been reported[6] to form more stable complexes with ammonium cations, the present study clearly demonstrates that introduction of the potential binding sites such as quinoline moiety into the acyclic crown ether can offer not only high efficiency but also excellent selectivity in the transport phenomena.

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