Full Papers

Recl. Trav. Chim. Pays-Bas **110**, 265–270 (1991) 0165–0513/91/06265–06$2.00

Lipophilic diaza crown ethers in supported liquid membranes; influence of pH on transport rates and membrane stability

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(Received November 13th, 1990)

Abstract. Lipophilic diaza-18-crown-6 derivatives are used to transport potassium cations through supported liquid membranes. The influence of the pH of the aqueous phases on the rate of transport and membrane stability has been studied. At pH values lower than 10, the flux is reduced significantly because the ionophores are protonated and leach out of the membrane phase. With these carriers, proton-driven transport is possible. The length of the alkyl chain attached to the carrier has a pronounced effect on membrane stability. Carriers having two *n*-pentyl chains leach out to the aqueous phases at pH 10, whereas carriers with two *n*-decyl or *n*-tetradecyl chains result in a stable membrane system. Model calculations show that di-*n*-decyldiaza-18-crown-6 forms a 1:1 complex with potassium cations (K $3.1 \cdot 10^6$ $l \cdot mol^{-1}$) in 2-nitrophenyl *n*-octyl ether (NPOE). The calculated diffusion coefficient of the complex in NPOE is the same as the diffusion coefficient of the dibenzo-18-crown-6 potassium cation complex in NPOE ($1.1 \cdot 10^{-3}$ $cm^2 \cdot h^{-1}$). This means that the higher potassium fluxes for diaza crown ethers compared to dibenzo crown ethers are due to stronger complexation in the membrane phase with potassium cations. Very high carrier concentrations (and, therefore, very high fluxes) can be obtained using these lipophilic diaza crown ethers.

Introduction

Membrane technology is a relatively new and fast growing field of research[1]. Classic membranes consist of semipermeable porous polymers. Selectivities and fluxes through these conventional membranes may be rather low. Liquid membranes containing selective carriers may offer a solution to these problems.

A simple liquid membrane which has been investigated extensively is the bulk liquid membrane consisting of a hydrophobic organic phase, containing the carrier, which acts as a barrier between two aqueous phases. In bulk liquid membranes, macrocyclic compounds have been used as carriers to transport cations selectively from one aqueous to another aqueous phase[2-8]. However, these bulk liquid membranes require a large quantity of carrier solution in proportion to the interfacial area where phase transfer can take place. Supported liquid membranes (liquid immobilized membranes) do not have this disadvantage. They consist of a hydrophobic organic carrier solution immobilized in a thin microporous support that separates the two aqueous phases. In a way, they resemble biological membranes in which carrier molecules such as valinomycin facilitate selective transport of potassium ions. These supported liquid membranes are of interest both for possible technological applications (hollow fibers) and for fundamental studies of the transport process (model descriptions).

Previously, we have investigated the mechanism of transport of potassium and guanidinium salts through supported liquid membranes using (benzo) crown ethers as carriers[9-11]. The experimental fluxes could be described in terms of a general model. This model assumes diffusion-limited transport, electroneutrality in the membrane phase, thermodynamic equilibrium at the interfaces, and linear concentration profiles of crown ether and complex in the membrane phase. The flux can be expressed as a function of partition of the salt, partition of the carrier, and complexation constants both in the membrane and in the aqueous phases. We found that the stability of the membrane can be improved by increasing the lipophilicity of the carrier, *e.g.*, by introducing alkyl or aryl groups[9,10], or by attaching crown ethers to a polysiloxane backbone[11].

Hitherto, we have only studied passive transport through liquid membranes, a process with the chemical-potential difference of the primary ion (the ion to be transported) in the source and the receiving phase as the driving force. Active transport is driven by a chemical reaction or by a coupled co- or counter-transport of another (secondary) species and can be achieved, for instance, when a second function is present in the carrier. By active transport, primary species can be transported against their concentration gradient and can thus be concentrated. Electron-, light-, temperature-, and proton-driven transport have been applied in bulk liquid membranes containing macrocyclic

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carriers. For proton-driven transport, ionizable macrocycles (such as crown ethers bearing a pendant acidic group[12-17], aza crown ethers[18-19] and proton-ionizable calixarenes[20-25]) have been used.

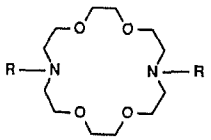
We decided to study proton-ionizable carriers because proton gradients are often used in nature in active transport systems. So far, only two examples have been reported in which macrocycle-mediated, proton-driven transport is used in supported liquid membranes. In one system, bis(monoaza crown ether)s are used for selective sodium transport[26-27]. The highest transport rates and selectivities are obtained at high pH, and proton-driven transport against a concentration gradient is described. In the second system, lipophilic 14-crown-4 derivatives, having a nitrophenol substituent, have been used for selective lithium transport[28-30]. In this case, the nitrophenol moiety is deprotonated in the source phase and serves as an anion cap for the cation complex, so that no counter-anions from the aqueous phase are needed. The influence of pH on cation transport has been investigated and proton-driven selective transport of Li^+ against its concentration gradient was observed. However, in both cases, a systematic study of the influence of pH on stability of the system, influence of lipophilicity of the carrier on transport, and a model description of the transport process are lacking. Therefore, we decided to perform a systematic study using proton-ionizable macrocyclic carriers in supported liquid membranes. We have used diaza crown ethers for three reasons: they possess basic nitrogen atoms in the macrocycle ring, the compounds can be easily modified, and they show good complexation properties with potassium cations. The transport of potassium ions further allows a comparison of the results with our previous experiments.

Results and discussion

Synthesis

The lipophilic diaza crown ethers **2** (di-*n*-pentyldiaza-18-crown-6, C_5), **4** (di-*n*-tetradecyldiaza-18-crown-6, C_{14}), and **5** (di-*n*-octadecyldiaza-18-crown-6, C_{18}) (Figure 1) were synthesized according to a published procedure[31]. Diaza-18-crown-6 **1** was reacted with an acid chloride and, subsequently, the amide function was reduced to yield the dialkyl diaza-18-crown-6 derivatives. Upon reduction with BH_3/THF, very stable crown ether borane complexes were formed and, therefore, when very low yields of free crown ethers were obtained, $LiAlH_4$ was used as the reducing agent. Di-*n*-decyldiaza-18-crown-6 (**3**) is commercially available.

The pK_a values of **3** and **4** were determined in methanol. The values for pK_{a1} and pK_{a2} are 10.14 and 8.26 for compound **3** and 10.34 and 8.30 for compound **4**, respectively.



1 R = H
2 R = $(CH_2)_4CH_3$
3 R = $(CH_2)_9CH_3$
4 R = $(CH_2)_{13}CH_3$
5 R = $(CH_2)_{17}CH_3$

Figure 1. Structures of diaza-18-crown-6 carriers used in supported liquid membranes.

Partition of carriers

Partition of unsubstituted diaza-18-crown-6 **1** between 1-octanol and an aqueous phase of pH 11.2 (KOH solution) gives a log(P) value of -0.97. In the transport experiments, KOH solutions are used and the partition determined at this pH actually gives the partition of the potassium complex. The partitions of the substituted crown ether potassium cation complexes were calculated from the partition of the unsubstituted complex and the hydrophobic substituent constants for the CH_2/CH_3 groups[32,33]. Since 2-nitrophenyl *n*-octyl ether (NPOE) was used as the membrane solvent, the octanol/water partitions were corrected for NPOE. The partition between NPOE and water could be calculated from the partition between 1-octanol and water using Eqn. 1[10,11,34].

$$\log(P_{NPOE/water}) = 0.84 \log(P_{octanol/water}) + 0.66 \quad (1)$$

Log($P_{NPOE/water}$) for **1**–K^+ was calculated to be -0.15; the calculated partitions for the substituted crown ether complexes are given in Table I.

Lipophilic diaza crown ethers were used as carriers for the transport of potassium perchlorate through a membrane that consisted of a solution of carrier in 2-nitrophenyl *n*-octyl ether (NPOE) immobilized in a porous polymeric support (Accurel^R). The membrane separates the source phase (s.p.) and the receiving phase (r.p.). KOH and $HClO_4$ solutions were used to adjust the pH of the aqueous phases in order to avoid the presence of competing ions in the aqueous phases. Except for high carrier concentrations and proton-driven transport, initial transport rates were measured.

The effect of lipophilicity or partition of the carrier complexes on potassium cation flux was determined using 10^{-2}M NPOE solutions of carriers with varying chain length, a 0.1M $KClO_4$, 10^{-4}M KOH source phase and a 10^{-4}M KOH (pH 10) receiving phase (Table I). At pH 10, the carriers are not protonated (*vide supra*) and, if carriers leach out at this pH, this will be due to low lipophilicity of the unprotonated carrier. As can be seen from Table I, the flux for the C_5 carrier was very low. After replacement of

Table I Influence of chain length of diaza-18-crown-6 on potassium ion flux[a].

Carrier	R	Flux[b] (10^{-8} mol · cm^{-2} · h^{-1})	log($P_{oct/water}$)	log($P_{NPOE/water}$)
1	H	–	−0.97	−0.15
2	C_5H_{11}	6.0 (3.5)[c]	4.03	4.05
3	$C_{10}H_{21}$	65 (65)[c]	9.03	8.25
4	$C_{14}H_{29}$	51 (51)[c]	13.0	11.6
5	$C_{18}H_{37}$	18 (18)[c]	17.0	15.0

[a] 10^{-2}M carrier in NPOE; source phase 0.1M $KClO_4$, pH 10. [b] Calculated from the K^+ concentration in the receiving phase after 24 hours by atomic absorption. [c] After replacement of the receiving phase.

the receiving phase by water, the flux decreased, which means that this carrier leaches out to the aqueous phases. This was not the case for the corresponding C_{10}, C_{14}, and C_{18} derivatives. We calculated that carriers with a partition coefficient higher than 10^5 leach out only slightly from the membrane, while carriers with a smaller value leach out substantially. This is in good agreement with the results found and with calculated partition coefficients. The fluxes for the C_{14} and C_{18} carriers were lower than for the C_{10} derivative. This may be caused by a lower diffusion rate for the larger carriers[9]. The C_{18} compound was only poorly soluble in NPOE: at 10^{-2}M carrier concentration, a saturated solution was obtained. Therefore, the lower flux with the C_{18} derivative may also be caused by a lower actual carrier concentration in NPOE.

Model description and calculations

Previously, we have reported a model description for macrocycle-mediated cation transport through supported liquid membranes[9-11]. We have shown that the transport is determined by diffusion through the membrane and can be described by Fick's first law. Because transport occurs predominantly via the complex and not via the free salt, the initial flux is proportional to the complex concentration at the membrane source interface, $[K^+CE]_m$.

$$J = \mathbb{D}_m \cdot d^{-1} \cdot [K^+CE]_m \qquad (2)$$

in which[9] J = flux, $\mathbb{D}_m$ = diffusion coefficient of the complex in the membrane phase, and d = membrane thickness. In this model, the crown ether potassium cation complex and the perchlorate anion are assumed to be present in the membrane phase predominantly as free ions[9]. Electroneutrality in the membrane phase, thermodynamic equilibrium at the interfaces and linear concentration profiles of crown ether and complex in the membrane phase are also assumed. For the potassium dibenzo-18-crown-6 complex, a diffusion coefficient of $1.2 \cdot 10^{-3}$ cm$^2 \cdot$h^{-1} was found[9]. In order to determine the diffusion coefficient of the potassium cation di-*n*-decyldiaza-18-crown-6 complex, the salt concentration of the source phase was varied, using a 10^{-2}M carrier solution and a pH 10 source and receiving phase. These conditions were chosen to obtain a high and stable flux. It was shown[9] that, by plotting $[a(KClO_4)]^{-1}$ *versus* $[CE]^0_m \cdot (d \cdot J)^{-1}$, a straight line should be obtained with an intercept $\mathbb{D}_m^{-1}$. From this variation of the salt concentration, the diffusion coefficient of the complex was determined. The results of these measurements are shown in Figure 2.

A straight line was obtained and from the intercept, $\mathbb{D}_m$ was calculated to be $1.1 \cdot 10^{-3}$ cm$^2 \cdot$h^{-1}. This means that the diffusion coefficients of the potassium cation complexes of

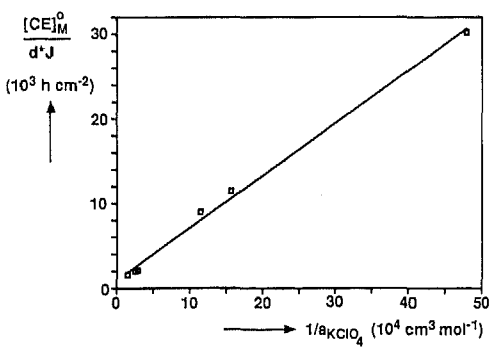


Figure 2. Model calculations used for the determination of the diffusion coefficient of the di-n-decyldiaza-18-crown-6–K^+ complex in NPOE.

di-*n*-decyldiaza-18-crown-6 and dibenzo-18-crown-6 are equal.

The complexation constant for a 1:1 complex is defined as:

$$K = \frac{[K^+CE]_m}{[K^+]_m \cdot [CE]_m} \qquad (3)$$

in which $[K^+]_m$ is the concentration of free potassium ions in the membrane phase and $[CE]_m$ is the concentration of free crown ether in the membrane phase. When $[K^+CE]_m$, $[K^+]_m$, and $[CE]_m$ are known, the complexation constant in NPOE can, therefore, be calculated. The values for $[K^+CE]_m$, $[K^+]_m$, and $[CE]_m$ can be calculated directly from the flux using Eqns. 4, 5, and 6[11].

$$[K^+]_m = \frac{P_K \cdot [K^+]^2_w \cdot \mathbb{D}_m}{J \cdot d} \qquad (4)$$

$$[K^+CE]_m = \frac{d \cdot J}{\mathbb{D}_m} - [K^+]_m \qquad (5)$$

$$[CE]_m = [CE]^0_m - [K^+CE]_m \qquad (6)$$

P_K is the partition of the salt, determined in blank experiments ($8.6 \cdot 10^{-7}$), $[K^+]_w$ is the potassium ion concentration in the source phase, and $[CE]^0_m$ is the initial carrier concentration. In this case, we can assume that the carrier does not leach out to the aqueous phases.

To verify the model and to calculate the complexation constant in NPOE, the flux can be measured for different carrier concentrations. When, for each carrier concentration, $[K^+CE]_m$, $[K^+]_m$, and $[CE]_m$ are calculated using Eqns. 4–6 and $[K^+CE]_m$ is plotted *versus* $[K^+]_m \cdot [CE]_m$, a straight line should be obtained with a slope being the complexation constant K, when 1:1 complexation takes place. We have varied the di-*n*-decyldiaza-18-crown-6 concentration (using a 0.1M $KClO_4$, pH 10 source phase and a pH 10 receiving phase, to avoid loss of carrier to the aqueous phases) and found that the carriers were very soluble in NPOE so that high carrier concentrations could be reached and, therefore, very high potassium cation fluxes (see Figure 3).

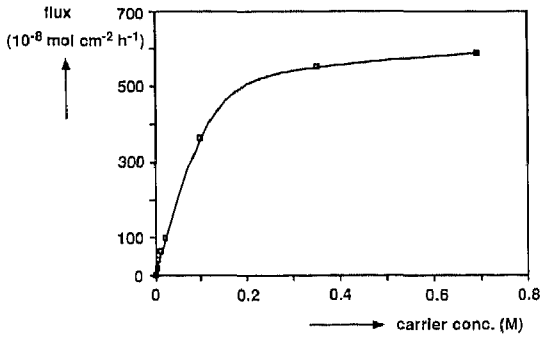


Figure 3. Influence of the di-n-decyldiaza-18-crown-6 concentration on the potassium ion flux through supported liquid membranes.

At higher carrier concentrations, the flux levels off because the NPOE solution is saturated with carrier. This was concluded from the appearance of small crystals in the NPOE solutions after leaving to stand for a few days. This means that 0.2 M carrier concentrations in NPOE are the maximum allowable. $[K^+CE]_m$ was calculated and plotted *versus* $[K^+]_m \cdot [CE]_m$ (see Figure 4).

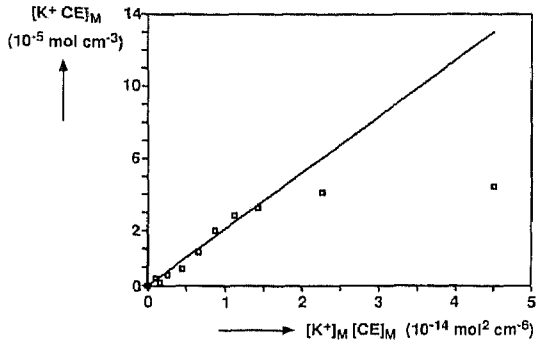


Figure 4. Complex concentration plotted versus *free salt and free carrier concentration for the determination of the association constant for di-*n*-decyldiaza-18-crown-6 with potassium cations in NPOE.*

The KOH concentrations were negligible with respect to the $KClO_4$ concentrations and had no influence on the model calculations. A straight line with a slope of $K = 3.1 \cdot 10^6$ l·mol^{-1} ($R_{sq} = 0.97$) was obtained for carrier concentrations smaller than 0.2 M, which confirms 1:1 complexation for these concentrations. Because of the saturation effect, the model calculations are not valid for concentrations higher than 0.2 M. For dibenzo-18-crown-6 (10^{-2} M, 0.1M $KClO_4$ source phase and a neutral receiving phase), a complexation constant of $2.0 \cdot 10^5$ l·mol^{-1} was found[35]. This means that the potassium cation forms a stronger complex in NPOE with di-*n*-decyldiaza-18-crown-6 than with dibenzo-18-crown-6. This is in agreement with the complexation constants of these crown ethers measured in methanol, $\log(K) = 5.0$ for dibenzo-18-crown-6 and $\log(K) = 5.3$ for dimethyldiaza-18-crown-6[36].

Influence of pH of aqueous phases on transport

The influence of pH of the receiving phase on potassium ion transport was examined, using 0.1M $KClO_4$ in 10^{-4}M KOH as a source phase solution (pH 10), because it is expected that, on account of the pK_a values of the carriers measured in methanol, no protonation will take place under these conditions. When a more basic source phase is used, KOH transport is no longer negligible as shown by an increase in pH of neutral aqueous receiving phases, when a source phase of pH 12 or 13 was used. The carried used was di-*n*-decyldiaza-18-crown-6 (3) and the carrier concentration was kept constant at 10^{-2} M. The receiving phase was either $HClO_4$ solution (pH 1, 2, 4), doubly distilled and deionized water (pH 6), or 10^{-4}M KOH (pH 10). The results are given in Table II.
It can be seen that the pH of the receiving phase has a dramatic effect on the observed potassium ion flux. The fluxes drop significantly when the pH of the receiving phases is decreased from pH 10 to pH 4. Below pH 4, almost no decrease in flux takes place on lowering the pH. At pH 6 and lower, the carrier will be protonated. This protonation may have an effect on the complexation of potassium ions (inhibition of complexation because of the protonation of the carrier) and/or the partition of the carrier (leaching out of the protonated carrier from the membrane phase).
In order to study the influence of pH on the loss of the carrier from the membrane phase, the receiving phase was replaced several times by a new solution of pH 4, 6, and 10. When the carrier leaches out to the aqueous phases, equilibrium is reached within an hour. This means that, when the protonated carrier leaches out from the membrane phase, replacement of the receiving phase will further reduce the flux (Table III).

Table II Influence of pH of receiving phase on observed potassium ion flux in supported liquid membranes[a].

pH	Flux[b] (10^{-8} mol·cm^{-2}·h^{-1})
1	0.14
2	0.15
4	0.68
6	22
10	65

[a] 10^{-2}M di-n-decyldiaza-18-crown-6 in NPOE; source phase: 0,1 M $KClO_4$, pH 10. [b] Calculated from the K^+ concentration in the receiving phase after 24 hours by atomic absorption.

Table III Influence of pH of receiving phase on loss of carrier from a supported liquid membrane[a].

Number of replacements	Flux[b] (10^{-8} mol·cm^{-2}·h^{-1})		
	pH 4	pH 6	pH 10
0	0.68	22	65
1	0.17	4.8	65
2	0.10	3.2	65
3	0.10	2.9	65

[a] 10^{-2}M di-n-decyldiaza-18-crown-6 in NPOE; source phase: 0.1M $KClO_4$, pH 10. [b] Calculated from the K^+ concentration in the receiving phase after 24 hours by atomic absorption.

At pH 10, the flux is high and stable upon three consecutive replacements of the receiving phase. At this pH, no protonation takes place. At pH 6, the carriers are protonated; the flux is significantly lower and rapidly drops further upon replacement of the receiving phase. At pH 4, the carriers are also protonated and a very low flux was observed. After replacement of the receiving phase, the flux decreased to the level of the blank flux measured in the absence of carriers. These results strongly suggest that the protonated carrier leaches out from the membrane phase.
This leaching out of the protonated carrier was confirmed by first replacing the receiving phase (pH 4) with an acidic solution (pH 4) and then with a basic solution (pH 10) (Table IV).

Table IV Influence of protonation of carrier on stability of potassium ion flux through a supported liquid membrane[a].

Replacements	pH receiving phase	Flux[b] (10^{-8} mol·cm^{-2}·h^{-1})
0	4	503
1	4	337
2	10	268

[a] Saturated di-n-decyldiaza-18-crown-6 solution in NPOE (0.35 M). [b] Calculated from the K^+ concentration in the receiving phase after 24 hours by atomic absorption; source phase: 0.1M $KClO_4$, pH 10.

This means that a stable flux can be obtained by using basic aqueous phases. This flux ($65 \cdot 10^{-8}$ mol·cm^{-2}·h^{-1}, Table II) is more than a factor ten higher than in the case of no pH adjustment (both aqueous phases pH 6, 10^{-2}M di-*n*-decyldiaza-18-crown-6; flux $4.3 \cdot 10^{-8}$ mol·cm^{-2}·h^{-1}).

We have also investigated whether proton transport could be achieved and whether this proton transport influences the potassium ion flux. In these experiments, a 0.35M (saturated) di-*n*-decyldiaza-18-crown-6 solution in NPOE and an acidic receiving phase (0.1M $HClO_4$, pH 1) were used. The experimental fluxes were compared with those obtained using a receiving phase of pH 10 and the results are given in Table V.

Table V Influence of proton counter-transport on potassium ion flux using di-n-decyldiaza-18-crown-6[a].

Carrier concn. (M)	Flux[b] (10^{-8} mol·cm^{-2}·h^{-1})	
	r.p. pH 10	r.p. pH 1
0.35[c]	552	1617

[a] Source phase: 0.1M $KClO_4$, pH 10. [b] Calculated from the K^+ concentration in the receiving phase after 24 hours by atomic absorption. [c] Saturated carrier solution.

Although part of the carrier leached out to the acidic receiving phase, the potassium ion fluxes were significantly higher using a receiving phase of pH 1 than using a pH 10 receiving phase. At this carrier concentration, only a relative small percentage of carrier was transferred to the aqueous receiving phase because of the saturation of this aqueous phase. After these experiments, the pH of the source phase was significantly decreased: from pH 10 to pH 3.5 after 24 hours.

Finally, we studied whether proton-driven transport could be used to transport potassium ions against a concentration gradient. Experiments were carried out using source and receiving phases with equal $KClO_4$ concentrations (0.05 M) and different pH (source phase pH 10, receiving phase pH 1), for a 0.35M (saturated) di-*n*-decyldiaza-18-crown-6 solution in NPOE. A potassium cation flux of $30 \cdot 10^{-8}$ mol·cm^{-2}·h^{-1} was found. After these experiments, the pH of the source phase was decreased from pH 10 to pH 3.4 (24 hours). These results show that proton-driven transport of potassium ions against a concentration gradient using diaza crown ethers is possible, although part of the carrier leaches out to the aqueous phases.

Conclusions

Diaza-18-crown-6 carriers can be used as potassium ion carriers in proton-driven transport through supported liquid membranes. When the pH of the aqueous phases is lower than 10, the carriers are protonated and leach out of the membrane. Using basic aqueous phases, very high and stable fluxes can be obtained using di-*n*-decyl- and di-*n*-tetradecyldiaza-18-crown-6. The partition coefficient of the potassium cation di-*n*-pentyldiaza-18-crown-6 complex [$\log(P_{NPOE/water}) = 4.05$] is low and, therefore, this complex leaches out even at high pH. With the carriers that have longer alkyl chains, proton-driven potassium ion transport against a concentration gradient can be achieved, although part of the carrier leaches out to the aqueous phases. The 1:1 complexation constant of the di-*n*-decyldiaza-18-crown-6 potassium cation complex is $3.1 \cdot 10^6$ l·mol^{-1} ($2 \cdot 10^5$ l·mol^{-1} for the dibenzo-18-crown-6 complex) and the diffusion coefficient $1.1 \cdot 10^{-3}$ cm^2·h^{-1} ($1.2 \cdot 10^{-3}$ cm^2·h^{-1} for the dibenzo carrier). This means that the higher fluxes with the diaza carrier ($65 \cdot 10^{-8}$ mol·cm^{-2}·h^{-1} compared to $26 \cdot 10^{-8}$ mol·cm^{-2}·h^{-1}) can be explained by stronger complexation of potassium ions with the diaza crown ether. Since these substituted diaza crown ethers are much more soluble in NPOE than dibenzo crown ethers, the potassium ion fluxes obtained are much higher.

Experimental

Melting points were determined using a Reichert melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded using a Bruker WP-80 spectrometer with $(CH_3)_4Si$ as an internal standard. Mass spectra were obtained using a Varian Mat 311A spectrometer. Infrared spectra were recorded on a Nicolet 5SXC spectrophotometer. Benzene was dried on molecular sieves prior to use. THF was distilled from sodium/benzophenone before use. All reactions were carried out under an argon atmosphere.

Materials

The synthesis of **2–5** was carried out by N-acylation of 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (diaza-18-crown-6 **1**, Merck–Schuchardt) with an acid chloride, followed by reduction with BH_3/THF according to a published procedure[31], except for **3** which was commercially available from Merck–Schuchardt. Compounds **4** and **5** have been described before[37]. Compound **4** was also prepared from 7,16-bis(1-oxotetradecyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane by reduction with $LiAlH_4$ to avoid the formation of borane complexes. Pentanoyl chloride was distilled before use. Potassium perchlorate was obtained from Janssen Chimica and was used without further purification. The polymeric film Accurel^R was obtained from Enka Membrana. 2-Nitrophenyl *n*-octyl ether (NPOE) was obtained from Fluka and was used without further purification.

Synthesis of diaza-18-crown-6 ethers **2** *and* **4**

7,16-Bis(1-oxopentyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane. A solution of pentanoyl chloride (0.51 g, 4.2 mmol) in benzene (6 ml) was added dropwise over a period of 30 min to a stirred solution of 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**1**) (0.51 g, 1.9 mmol) and triethylamine (0.46 g, 4.6 mmol) in benzene (14 ml) at 50 °C. The mixture was stirred for 30 min at 50 °C. The mixture was then filtered and the filtrate was evaporated to give the crude diamide. Yield 0.57 g (70%). Transparent oil. ^{1}H NMR ($CDCl_3$): δ (ppm) 3.9–3.4 (m, 24 H, OCH_2, NCH_2), 2.3 (t, 4 H, $CH_2C{=}O$), 1.6–1.3 (m, 8 H, CH_2), 0.88 (t, 6 H, CH_3). IR (KBr) 1670 cm^{-1} (C=O). Mass spectrum *m/e* 430.299 (M^+, calcd. for $C_{22}H_{42}N_2O_6$ 430.304).

7,16-Dipentyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**2**). 6 ml of a BH_3 solution in THF (6 mmol) was added dropwise over a period of 40 min to a solution of 7,16-bis(1-oxopentyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (0.25 g, 0.58 mmol) in THF (10 ml) at 0 °C. The mixture was refluxed for 2 h. Water (2 ml) was added and the solvent was evaporated. After addition of 6M hydrochloric acid (2.5 ml), the mixture was kept at 125 °C for 3 h. The solvent was evaporated, water (12 ml) was added and the mixture was treated with aqueous tetraethylammonium hydroxide. The product was extracted three times with dichloromethane (15 ml). The organic layer was dried ($MgSO_4$). After filtration and evaporation of the solvent, the product was purified by column chromatography (Al_2O_3–$CHCl_3$/EtOH 99/1). Yield 0.13 g (55%). Transparent oil. ^{1}H NMR ($CDCl_3$): δ (ppm) 3.8–3.4 (m, 16 H, OCH_2), 2.8 (t, 8 H, ring NCH_2), 2.5 (t, 4 H, NCH_2), 1.7–1.0 (m, 12 H, CH_2), 0.89 (t, 6 H, CH_3). Mass spectrum *m/e* 402.343 (M^+, calcd. for $C_{22}H_{46}N_2O_4$ 402.346).

7,16-Ditetradecyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**4**). $LiAlH_4$ (0.04 g, 1.1 mmol) was added to a solution of 7,16-bis(1-oxotetradecyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (0.09 g, 0.13 mmol) in THF (3 ml). The mixture was refluxed for 2 h. After cooling to room temperature, 2M NaOH (5 ml) was added. The mixture was filtered and the solvent was evaporated. The crude product was dissolved in ethyl acetate (5 ml). The organic phase was washed with saturated NaCl solution. The organic layer was dried ($MgSO_4$). After filtration, the solvent was

removed by evaporation to obtain the pure product. Yield 0.09 g (99%). M.p. 55–57°C. ^{1}H NMR ($CDCl_3$): δ (ppm) 3.7 (t, 16 H, OCH_2), 2.8 (t, 8 H, ring NCH_2), 2.5 (t, 4 H, NCH_2), 1.3 (pseudo-s, 48 H, CH_2), 0.87 (t, 6 H, CH_3). Mass spectrum *m/e* 654.626 (M^+, calcd. for $C_{40}H_{82}N_2O_4$ 654.628).

Determination of the pK_a *values of di-n-decyldiaza-18-crown-6 and di-n-tetradecyldiaza-18-crown-6*

The pK_{a1} and the pK_{a2} values of di-*n*-decyldiaza-18-crown-6 (**3**) and di-*n*-tetradecyldiaza-18-crown-6 (**4**) were determined in methanol by titration with 0.1 M trifluoromethanesulphonic acid in *tert*-butanol at 25°C. The measurements were checked by a mass balance.

Determination of the octanol/water partition coefficient of diaza-18-crown-6

Diaza-18-crown-6 **1** (0.5 mmol) was dissolved in 1-octanol (50 ml), which was saturated with an aqueous KOH solution (pH 11.2). A KOH solution (pH 11.2) (5 ml), saturated with 1-octanol, was added. With this amount of KOH solution, a phase transfer of about 50% of the crown ether complex into the aqueous phase was estimated. The liquids were vigorously stirred for 1 h at room temperature. After separation of both phases by centrifugation (1500 rpm) over 2 h, both phases were analyzed by titration with a 0.1 M trifluoromethanesulphonic acid solution in *tert*-butanol. The measurements were checked by a mass balance for the two phase system. The measurements were repeated at least twice. From the concentrations of crown ether complex in the aqueous and octanol phase, the partition coefficient could be calculated from Eqn. 7.

$$P_{\text{octanol/water}} = \frac{[\text{CE}]_{\text{octanol}}}{[\text{CE}]_{\text{water}}} \quad (7)$$

Transport experiments

The permeation cell consisted of two identical cylindrical compartments (half-cell volume: 50 ml; effective membrane area: 12.4 cm^2). Details of this cell have been previously described[9,11]. The supported liquid membrane consisted of a thin microporous polypropylene film (Accurel^R; thickness d_m 100 μm, porosity 64%) immobilizing the solution of crown ether in 2-nitrophenyl *n*-octyl ether (NPOE). A potassium perchlorate solution was used as the source phase. The pH of this source phase was adjusted to pH 10 by using a 10^{-4}M KOH solution. The receiving phase consisted of either doubly distilled and deionized water (pH 6), a 10^{-4}M KOH solution (pH 10), or $HClO_4$ solutions (pH 4, 2,1). The measurements were performed at a constant temperature of 25°C. The transported potassium perchlorate was determined by monitoring the conductivity of the receiving phase as a funtion of time (Philips PW 9527 conductivity meter and a Philips PW 9512/61 electrode with a cell constant of 0.76 cm^{-1}) and/or by atomic absorption measurements of samples taken after 24 h. All experiments were carried out at least twice. The standard deviation was about 15%.

Acknowledgement

Financial support from the Koninklijke/Shell-Laboratorium Amsterdam (KSLA), is gratefully acknowledged.

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