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Effect of Crown Ether Lipophilicity on the Facilitated Transport of Guanidinium Thiocyanate through an Immobilized Liquid Membrane

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Abstract: The flux of guanidinium thiocyanate through a supported liquid membrane has been measured for substituted benzo crown ethers and dibenzo crown ethers. This flux depends on the water solubility of the carrier. The more lipophilic crown ethers (**7–14** and **16**) show a higher flux and form more stable supported liquid membranes. The effect of the lipophilic substituents on the partition coefficient of the benzo crown ethers has been calculated and verified by partition experiments. The observed fluxes have been interpreted by a developed general model for the transport of salts through supported liquid membranes containing crown ethers. This thermodynamic model takes into account the interface equilibria, viz. the partition of crown ether and salt, as well as complexation equilibria in the membrane and aqueous phase. The model has been applied for the calculation of the complexation constants in the membrane phase. The lipophilic benzo crown ethers with 27 ring atoms show lower complexation constants than the corresponding benzo crown ether with 30 ring atoms. The complexation constants of the dibenzo crown ethers and guanidinium thiocyanate are smaller than those of the corresponding complexes of the substituted benzo crown ethers. During the diffusion process of the complex through the membrane phase complexation and decomplexation take place continuously as was concluded from the small value of the inverse Damköhler number.

The transport mechanism of carrier-mediated transport through bulk liquid membranes has been investigated extensively. Lamb et al.[1] suggested a cation-transport model which correctly predicts the change in the flux over an extended range of complexation constants. Behr et al.[2] reported a model description for each of the following transport mechanisms: (i) carrier-mediated transport of a single substrate species and of an ion pair and (ii) carrier-mediated exchange diffusion of two substrates against a counter-transported species. This resulted in a satisfactory equation for the transport rate. The bulk liquid membranes require a large quantity of carrier solution in proportion to the interfacial area. Therefore, in crown-ether-mediated transport through liquid membranes there is a tendency to replace these bulk liquid membranes by supported liquid membranes (liquid immobilized membranes). These are promising both for technological application (hollow fibers) and for fundamental studies of the relation of the flux with the partition, complexation, and the interaction of carrier molecules at the interfaces between the membrane and aqueous phases.

The published studies of facilitated transport through supported liquid membranes deal with the transport of gases,[3-10] such as oxygen,[3] nitric oxide,[4] carbon monoxide,[5] carbon dioxide,[6] and hydrogen sulfide[7] as well as metal salts, such as copper,[11-20] uranium,[21] zinc,[22,23] americum,[24] and europium.[25] From these studies various models have been developed to describe the steady-state flux for these supported liquid membrane systems. However, all these models cannot be applied to a membrane system that contains crown ethers as the carrier because they are limited to steady-state conditions *without leakage of the carrier from the membrane.* Furthermore, in contrast with the proton-coupled transport of metal cations,[11-25] the anion has to accompany the cation in the membrane phase according to the electrical neutrality of the system. Hitherto, the use of crown ethers in supported liquid membranes is limited.[26-31]

Previously we have reported that for the transport of potassium perchlorate through supported liquid membranes, the diffusion of the complex through the membrane phase is rate-limiting.[31] We also observed that the partition of the carrier between the membrane phase and the aqueous phases was fast (thermodynamic equilibrium), and this results in a lower actual crown ether concentration in the membrane phase under steady-state conditions. This leakage of the carrier from the membrane will be a severe limitation for the application of supported liquid membranes.

As part of our work on the selective separation of urea from aqueous solutions by macrocyclic carriers, dissolved in an organic membrane phase, we will need both receptor molecules which are selective for urea and liquid membranes with high stability. Our previous results showed that for complexation of urea macrocyclic polyethers with at least 27 ring atoms are needed that can encapsulate the guest molecule.[32-37] Moreover, they should be able

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to induce a (partial) positive charge on urea or form a strong hydrogen bond.[38-40]

In our work we have used guanidine as a model compound for urea because guanidine is isoelectronic with urea but more basic. Previously we have studied the crown-ether-mediated transport of guanidinium thiocyanate through a bulk liquid chloroform membrane.[41] We have established a quantitative relationship between the flux of guanidinium thiocyanate and the association constant of the complexes *in methanol*. The rate-limiting step in the overall transport is the diffusion of the complex through a stagnant layer at the interface between the membrane and aqueous phase.

In the present study the transport of guanidinium thiocyanate through the supported liquid membrane containing crown ethers of different lipophilicity by varying the ring size and substitution pattern was investigated. The observed fluxes have been interpreted by a developed general model for the facilitated transport of salts through supported liquid membranes, based on 1:1 stoichiometry of the complexes and electrical neutrality in the membrane phase, whereas the partition coefficient of the crown ether and the complexation constant in water are taken into account. This model makes the interpretation of the experimental data possible and allows also the *direct* calculation of the unknown parameter, viz. the complexation constant of the complex in the membrane phase.

A Theoretical Model That Describes the Membrane Flux as a Function of the Partition of the Crown Ether

Previously, a mathematical model for crown-ether-mediated transport has been derived by describing the transport mechanism with mathematical equations using the mass balances for the crown ether, the cation, and the anion.[31] In this model, based on 1:1 complexation, we assumed that predominantly free ions are present in the membrane phase. The partition coefficient of the salt was divided in a contribution of the anion and cation, respectively. We only used the partition coefficient of the cation on the condition that the anion is more lipophilic than the cation. This model was successfully verified by experiments with dibenzo-18-crown-6 in the membrane phase and potassium perchlorate in the source phase. However, in a general model the contribution of the anion to the partition coefficient of the salt will no longer be negligible. Further, we extended the set of equations with the restriction of electrical neutrality in both the aqueous and membrane phase (vide infra).[42]

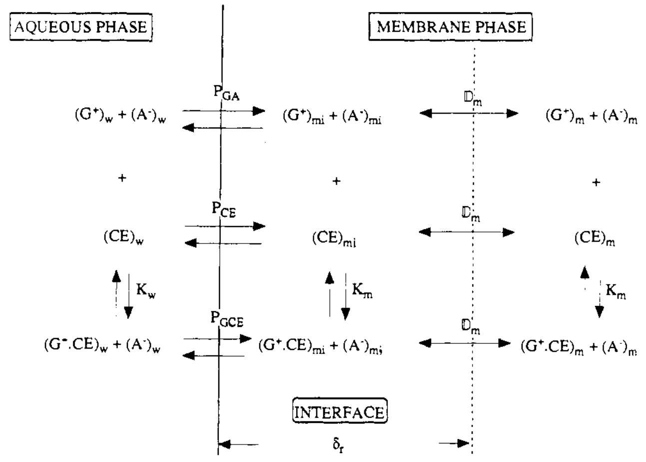

Figure 1. Schematic representation of the extraction equilibria at the interface.

In analogy with the transport of potassium perchlorate by dibenzo-18-crown-6 through the membrane phase[31] the flux of guanidinium thiocyanate through the liquid immobilized membrane can be described by a diffusion process of the complex. This means a fast complexation which mainly takes place at the source interface in a small reaction zone within a thickness of δ_r (Figure 1). Furthermore, it is assumed that the guanidinium complex and the thiocyanate anion are present in the membrane phase predominantly as free ions,[31,43] based on the association constant calculated from the theory of Fuoss and Kraus.[43] From previous studies it is reasonable to assume that crown ethers having at least 27 ring atoms form a 1:1 complex with guanidinium salts.[32-37,41] An expression for the complex concentration in the membrane phase can be derived and expressed in known or experimentally accessible data with the use of mass balances for the crown ether, and the cation, and the condition of electrical neutrality.

Both at the interface and in the bulk of the membrane there is a 1:1 complexation equilibrium with the same complexation constant K_m (eq 1). At the interface two other equilibria are important, viz., the partition of the salt, P_{GA} (eq 2), and the partition of the crown ether, P_{CE} (eq 3). In the equations the

$$K_m = \frac{[G^+ \cdot CE]_m}{[G^+]_m [CE]_m} = \frac{[G^+ \cdot CE]_{m1}}{[G^+]_{m1} [CE]_{m1}} \qquad (1)$$

$$P_{GA} = \frac{[G^+]_{m1} [A^-]_{m1}}{[G^+]_{w1} [A^-]_{w1}} \qquad (2)$$

$$P_{CE} = \frac{[CE]_m}{[CE]_w} \text{ for m is m1 and m2} \qquad (3)$$

subscripts m, m1, m2, w, w1, and w2 correspond with the membrane phase, membrane source interface, membrane receiving interface, aqueous phase, aqueous source phase, and receiving phase, respectively. The brackets [ ] and $[\,]^0$ refer to concentrations at equilibrium and to the initial concentrations, respectively. As a consequence of the partition of crown ether, also in the aqueous phase a 1:1 complex with the salt is formed, with an equilibrium constant K_w (eq 4). With these four equilibria, the partition of

$$K_w = \frac{[G^+ \cdot CE]_w}{[G^+]_w [CE]_w} \qquad (4)$$

the complex (P_{GCE}) can be expressed and calculated. The mathematical description of the membrane system is completed with the mass balances for the crown ether (eq 5) and cation (eq

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(42) Our experimental results with dibenzo-18-crown-6 in the membrane phase and potassium perchlorate in the source phase[31] have been verified with this model. For high crown ether concentrations these results can be described by a 2:1 stoichiometry of the complex (crown ether/cation) instead of a 1:1 stoichiometry. Recently, we also found a 2:1 complexation with potassium perchlorate for the polydimethylsiloxanes terminated with 18-crown-6. These results will be published.

(43) The calculated value of K_{ass} (theory of Fuoss and Kraus) for guanidinium thiocyanate ($r^+ + r^- = 4.2$ Å) in NPOE ($\epsilon = 23.5$) is equal to 54. When [GuHSCN] in the membrane phase is equal to 1.6×10^{-4} M, then the fraction of free ions in NPOE is equal to 0.99.

$$V_m[\mathrm{CE}]_m^0 = V_m[\mathrm{CE}]_m + V_m[\mathrm{G^+{,}CE}]_m + V_{w1}[\mathrm{CE}]_{w1} + V_{w1}[\mathrm{G^+{,}CE}]_{w1} + V_{w2}[\mathrm{CE}]_{w2} + V_{w2}[\mathrm{G^+{,}CE}]_{w2} \quad (5)$$

$$V_{w1}[\mathrm{G^+}]_{w1}^0 = V_{w1}[\mathrm{G^+}]_{w1} + V_{w1}[\mathrm{G^+{,}CE}]_{w1} + V_m[\mathrm{G^+}]_m + V_m[\mathrm{G^+{,}CE}]_m + V_{w2}[\mathrm{G^+}]_{w2} + V_{w2}[\mathrm{G^+{,}CE}]_{w2} \quad (6)$$

6) and the expressions for electrical neutrality (eq 7 and 8). In the mass balances the concentrations of the complex and crown ether in the membrane phase represent *average* values, while the

$$[\mathrm{G^+}]_w + [\mathrm{G^+{,}CE}]_w = [\mathrm{A^-}]_w \qquad \text{for w is w1 and w2} \quad (7)$$

$$[\mathrm{G^+}]_m + [\mathrm{G^+{,}CE}]_m = [\mathrm{A^-}]_m \qquad \text{for m is m1 and m2} \quad (8)$$

equilibria reactions at the interface are expressed in terms of *local* concentrations. A relation between the average bulk and the interface concentrations can only be obtained when in the membrane phase the concentration profiles of the complex, crown ether, and the cation, respectively, are known. For the derivation of the expressions 10, 11, and 17 it is assumed that the diffusion coefficients of salt, crown ether, and complex in the membrane phase are approximately the same. In the membrane phase (thickness d_m) the transport of the cation is determined by diffusion described by Fick's first law (eq 9) with a linear concentration gradient of

$$J = \frac{\mathrm{D}_m}{d_m}\{[\mathrm{G^+{,}CE}]_{m1} + [\mathrm{G^+}]_{m1} - [\mathrm{G^+{,}CE}]_{m2} - [\mathrm{G^+}]_{m2})\} \quad (9)$$

the *sum of complex and cation as the driving force.* When at the receiving interface (m2) the rate of decomplexation and cation exchange is fast and complete, the local complex and cation concentrations are negligible compared to the respective concentrations at the source interface (m1). We can distinguish two possibilities (*models A and B*, respectively) of the concentration profile of the crown ether in the membrane phase.

According to *model A* both the cation and the complex have a linear concentration profile in the membrane phase. Consequently, there will be no concentration gradient of crown ether according to eq 1, and, therefore, the *average bulk* concentration of complex and crown ether can be expressed in the *interface concentrations* by eq 10 and 11. The flux is related to the complex

$$[\mathrm{G^+{,}CE}]_m = \frac{[\mathrm{G^+{,}CE}]_{m1} + [\mathrm{G^+{,}CE}]_{m2}}{2} = \frac{[\mathrm{G^+{,}CE}]_{m1}}{2} \quad (10)$$

$$[\mathrm{CE}]_m = [\mathrm{CE}]_{m1} \quad (11)$$

concentration in the membrane phase (eq 9). With the assumption that $[\mathrm{G^+}]_{w1} = [\mathrm{G^+}]_{w1}^0$ (during our experiments the amount of salt that is transferred is small in comparison with the initial salt concentration), an expression for the complex concentration can be derived from eq 1 to 11 (V_{w1} and V_{w2} are equal to V_w). With a salt activity coefficient $\gamma_\pm$ for high concentrations of guanidinium thiocyanate, eq 12 is obtained by substitution of an expression for $[\mathrm{G^+}]_{m1}$ (eq 2) in eq 1. In eq 13 the anion concentration in

$$[\mathrm{G^+{,}CE}]_{m1} = K_m P_{GA} \frac{\gamma_\pm^2 [\mathrm{G^+}]_{w1}^0 [\mathrm{A^-}]_{w1}^0}{[\mathrm{A^-}]_{m1}} [\mathrm{CE}]_{m1} \quad (12)$$

$$[\mathrm{G^+{,}CE}]_{m1} = K_m P_{GA} \frac{\gamma_\pm^2 [\mathrm{G^+}]_{w1}^0 [\mathrm{A^-}]_{w1}^0}{[\mathrm{G^+}]_{m1} + [\mathrm{G^+{,}CE}]_{m1}} [\mathrm{CE}]_{m1} \quad (13)$$

the membrane phase is replaced via eq 8. The complex concentration at the source interface can be expressed as a function of the initial salt concentration and $[\mathrm{CE}]_{m1}$ (eq 14). An expression for the local crown ether concentration at the source interface (eq 15) is derived from the mass balance (eq 5) together with eq 3,

$$[\mathrm{G^+{,}CE}]_{m1}^2\{1 + K_m[\mathrm{CE}]_{m1}\} - P_{GA}K_m{}^2\{\gamma_\pm^2[\mathrm{G^+}]_{w1}^0\}^2\left\{\frac{K_w}{P_{CE}}[\mathrm{CE}]_{m1}^3 + [\mathrm{CE}]_{m1}^2\right\} = 0 \quad (14)$$

$$[\mathrm{CE}]_{m1} = \frac{[\mathrm{CE}]_m^0 - \dfrac{[\mathrm{G^+{,}CE}]_{m1}}{2}}{1 + 2\dfrac{V_w}{V_m}\dfrac{1}{P_{CE}} + \dfrac{V_w}{V_m}K_w\gamma_\pm[\mathrm{G^+}]_{w1}^0\dfrac{1}{P_{CE}}} \quad (15)$$

4, 10, and 11, with the assumption that $[\mathrm{G^+{,}CE}]_{w2} = 0$. Within the limiting conditions there exists only one unique solution of eq 14 and 15. Equations 14 and 15 describe the extraction of a salt from the source phase into the membrane phase, assisted by a crown ether *when partition to the aqueous phase occurs.*

According to *model B* (eq 16) the concentration gradient in

$$[\mathrm{G^+{,}CE}]_{m1} - [\mathrm{G^+{,}CE}]_{m2} = [\mathrm{CE}]_{m2} - [\mathrm{CE}]_{m1} \quad (16)$$

crown ether is equal and opposite to the concentration gradient in complex. According to eq 1 a linear concentration profile of the crown ether means a linear relation between $[\mathrm{G^+{,}CE}]_m$ and $[\mathrm{G^+}]_m$. A combination with eq 9 results in nonlinear concentration profiles of both complex and cation. However, $[\mathrm{G^+}]_m$ is usually much lower than $[\mathrm{G^+{,}CE}]_m$, which results in a close to linear concentration gradient in $[\mathrm{G^+{,}CE}]_m$. The average bulk concentration of crown ether and complex are expressed in the interface concentrations by eq 17 and 10. In model B the expression of

$$[\mathrm{CE}]_m = \frac{[\mathrm{CE}]_{m1} + [\mathrm{CE}]_{m2}}{2} \quad (17)$$

the interfacial complex concentration is the same as in model A (eq 14). However, the expression of $[\mathrm{CE}]_{m1}$ (eq 18) is derived from the mass balance (eq 5) and eq 3, 4, 10, 16, and 17.

$$[\mathrm{CE}]_{m1} = \frac{[\mathrm{CE}]_m^0 - [\mathrm{G^+{,}CE}]_{m1}\left\{1 + \dfrac{V_w}{V_m}\dfrac{1}{P_{CE}}\right\}}{1 + 2\dfrac{V_w}{V_m}\dfrac{1}{P_{CE}} + \dfrac{V_w}{V_m}K_w\gamma_\pm[\mathrm{G^+}]_{w1}^0\dfrac{1}{P_{CE}}} \quad (18)$$

In the following section the experimental results of flux measurements of guanidinium thiocyanate with crown ethers that have different lipophilicities are reported. The complex concentrations have been calculated with eq 14, 15, and 18 by using an iterative procedure. The values of P_{GA}, P_{CE}, and D_m have been determined by independent experiments. On the basis of these experimental results a discrimination between models A and B has been made. The difference in the flux of guanidinium thiocyanate for the different crown ethers will be explained in terms of the partition coefficients of the crown ether and the complexation constants.

Results and Discussion

The carriers used in the experiments are the crown ethers depicted in Figure 2.

Partition Coefficient of Crown Ether. The partition coefficients of the crown ethers **1–6** for the system 1-octanol/water have been reported previously.[44] Functionalization of the benzo crown ethers with a substituent in the aromatic ring will influence the partition of the crown ether, while the complexation properties are hardly affected.[41,45] The partition coefficients of the substituted benzo crown ethers **7–14** were calculated with the substituent model (eq 19) from the experimental value of the corresponding unsubstituted

$$\log P_{CE}(\mathbf{7\text{–}14}) = \log P_{CE}(\mathbf{1,2}) + \sum_{1}^{n}\Pi(X_n) \quad (19)$$

benzo crown ether **1** or **2**, log P_{CE}(**1**,**2**). Further, the partition coefficients of crown ethers **15–18** were calculated from the known partition coefficients with the fragmental and/or substituent constants from the literature.[44,46,47] For comparison the partition coefficients of **7** and **8** have also been determined experimentally (Table I). The difference between the experimental values of log P_{CE} of **7** and **8** is −0.20, in agreement with the fragmental constant for an oxyethylene unit.[44] The calculated values of log P_{CE} are close to the experimental value. The values of log P_{CE} for the crown ethers **9–14** could not be determined experimentally

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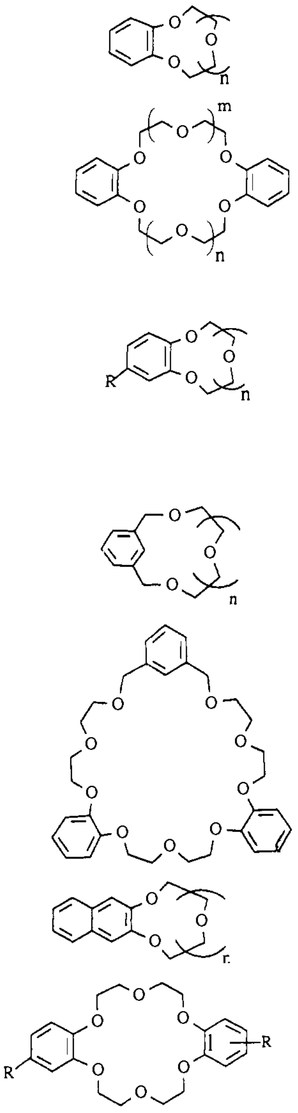

1 n=7: B27C9
2 n=8: B30C10
3 n=9: B33C11

4 n=0, m=5: [2,7]DB27C9
5 n=0, m=6: [2,8]DB30C10
6 n=2, m=5: [4,7]DB33C11

7 n=7: R= $(CH_3)_3C$
8 n=8: R= $(CH_3)_3C$
9 n=7: R= $CH_3(CH_2)_3C(CH_3)_2$
10 n=8: R= $CH_3(CH_2)_3C(CH_3)_2$
11 n=7: R= $(CH_3CH_2CH_2)_3C$
12 n=8: R= $(CH_3CH_2CH_2)_3C$
13 n=7: R= $CH_3(CH_2)_8C{=}O$
14 n=7: R= $CH_3(CH_2)_9$

15 n=6: X27C8

16 [3,3,3]XDB30C9

17 n=7: N27C9

18 R= $CH_3(CH_2)_{17}$

Figure 2. Structures of crown ethers. Abbreviated names: C = crown, B = benzo, N = naphtho, X = xyleno, D = di (or bis), [ ] = code for the number of hetero atoms between the functionalities.

Table I. Measured and Calculated Values of the Partition Coefficient for the Lipophilic Benzo Crown Ethers[a]

crown ether	n[b]	log P_{CE}[c]	log P_{CE}(II)[d]
7	7	1.89[e]	2.0
9	7	nd	3.5
11	7	nd	5.0
13	7	nd	4.0
14	7	nd	5.0
8	8	1.69[e]	1.8
10	8	nd	3.3
12	8	nd	4.8

[a] The partition coefficient measured and calculated for the system 1-octanol/water; n.d. means not determined. [b] The number of ethylene oxide bridges. [c] The partition coefficient measured at T = 293–298 K. [d] The partition coefficient calculated with eq 19. [e] Standard deviation ±5%.

because of the low solubility of these crown ethers in water.

Simon et al.[48] have derived an empirical relation (eq 20) between the measured values of log P(NPOE) and the calculated values of log P(oct) with the hydrophobic substituent constants. We have calculated the log P values of the ionophores used by Simon with the hydrophobic fragmental constants[46] including our experimentally derived fragmental constant of an oxyethylene moiety.[44] This resulted in a new correlation between log P(NPOE) and log P(oct) with a higher accuracy (eq 21, r = 0.97). The values of log P_{CE}(NPOE) as given in Table IV have been used in our further calculation of the fluxes.

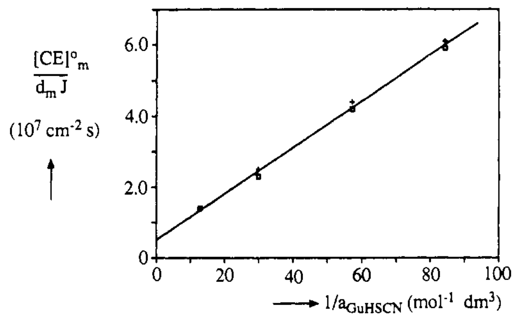

Figure 3. $[CE]^0_m/(d_m J)$ as function of the reciprocal salt activity for **11** (+) and **12** (□), according to eq 26.

$$\log P(\mathrm{NPOE}) = (0.8 \pm 0.1) \log P(\mathrm{oct}) + (0.4 \pm 0.4);\ r = 0.95 \quad (20)$$

$$\log P(\mathrm{NPOE}) = (0.84 \pm 0.06) \log P(\mathrm{oct}) + (0.66 \pm 0.17);\ r = 0.97 \quad (21)$$

Partition Coefficient of Guanidinium Salt.[49] The value of P_{GA} was estimated from the value of the flux of guanidinium thiocyanate *in the absence of crown ether.* We have assumed that the diffusion coefficient of guanidinium thiocyanate with the hydration shell is equal to the effective diffusion coefficient of the complex because in a first approximation the ligand acts in the complex as the first solvation layer of the cation.[52] The salt concentration in the membrane interface, $[G^+]_{ml} = [A^-]_{ml} = 1.6 \times 10^{-4}$ M, follows directly from the observed flux in the absence of crown ether. The value of P_{GA} was obtained from the salt concentrations in the membrane interface and the source phase, corrected for the activity[53] [$P_{GA} = (4.2 \pm 2.6) \times 10^{-6}$].

Diffusion Coefficient. Because we needed an accurate value of the diffusion coefficient for the calculation of the complex concentration from the value of the flux, the diffusion coefficient of the complex was determined by measuring the flux as a function of the initial salt concentration.[31] A more simplified equation for the complex concentration was used in which the dependency of the flux from the salt concentration is easy to recognize. When it is assumed that the crown ether is completely retained in the membrane phase, the complexation can be simply described by an extraction equilibrium at the interface between membrane and source phase (eq 22), given by an extraction equilibrium constant K_{ex} (eq 23A). According to Danil de Namor et al.[50] and Marcus[51]

$$(G^+)_{wl} + (A^-)_{wl} + (CE)_{ml} \xrightleftharpoons{K_{ex}} (G^+{\cdot}CE)_{ml} + (A^-)_{ml} \quad (22)$$

$$K_{ex} = \frac{[G^+{\cdot}CE]_{ml}[A^-]_{ml}}{[G^+]_{wl}[A^-]_{wl}[CE]_{ml}} \quad (23A)$$

$$K_{ex}' = \frac{[G^+{\cdot}CE]_{ml}}{[G^+]_{wl}[CE]_{ml}} \quad (23B)$$

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(48) Oesch, U.; Simon, W. *Anal. Chem.* **1980**, *52*, 692.

(49) The partition coefficient of guanidinium salts can in principle be determined in an experiment that is independent of the flux measurements. Danil de Namor[50] and Marcus[51] have described a method for the determination of the partition coefficients of both the cation and the anion separately by using the tetraphenylarsonium tetraphenylborate (TATB) method. They describe the transfer of species from water to the organic solvent (NPOE) in the membrane in terms of standard Gibbs free energy, and the difference between G_{NPOE} and G_{H_2O} can be derived from the solubility product of the

$$\Delta G^{tr}(X) = G_{NPOE}(X) - G_{H_2O}(X); \qquad X = \text{salt, cation, or anion}$$

salt in the respective solvents. However, the solubilities of guanidinium tetraphenylborate, guanidinium thiocyanate, and tetraphenylarsonium tetraphenylborate are too low for accurate determinations (see Experimental Section). Therefore, we have tried to determine the partition coefficient P_{GA} by equilibration of an aqueous solution of guanidinium thiocyanate and NPOE, but the amount of guanidinium salt transferred to NPOE was below the limit of detection which means that P_{GA} (eq 2) is smaller than 6×10^{-6}.

Table II. Experimental ($\mathbb{D}_m$),[a] Normalized ($\mathbb{D}_{m,n}$),[b] and Calculated ($\mathbb{D}_{m,1}$ and $\mathbb{D}_{m,2}$) Diffusion Coefficients and Extraction Equilibrium Constants of the Complexes of Crown Ethers **11** and **12** with Guanidinium Thiocyanate

	11	**12**
$\mathbb{D}_m$ (cm^2 s^{-1})	$(2.4 \pm 0.6) \times 10^{-7}$	$(2.1 \pm 0.4) \times 10^{-7}$
$\mathbb{D}_{m,n}$ (cm^2 s^{-1})	$(7.5 \pm 2.6) \times 10^{-7}$	$(6.6 \pm 1.9) \times 10^{-7}$
$\mathbb{D}_{m,1}{}^c$ (cm^2 s^{-1})	5.5×10^{-7}	5.3×10^{-7}
$\mathbb{D}_{m,2}{}^d$ (cm^2 s^{-1})	2.7×10^{-7}	2.6×10^{-7}
K'_{ex} (cm^3 mol^{-1})	$(0.7 \pm 0.2) \times 10^4$	$(0.7 \pm 0.2) \times 10^4$

[a] $[\mathrm{GuHSCN}]^0_{w1} = 10^{-2}$–$10^{-1}$; $[\mathrm{carrier}]^0_m = 10^{-2}$ M; $T = 298$ K. [b] Calculated with eq 27 for $\theta = 0.64$ and $\tau = (2.1 \pm 0.1)$ (see text). [c] Diffusion coefficient calculated from the Wilke and Chang equation[54] with $\eta_2 = 12.63$ cP ($=10^{-2}$ g cm^{-1} s^{-1}); $\Phi = 1$; $T = 298$ K. [d] Diffusion coefficient calculated from the Stokes–Einstein equation[54] with $\eta_2 = 12.63 \times 10^{-2}$ g cm^{-1} s^{-1}; $T = 298$ K.

the contribution of the anion partition is considered to be a constant, which simplifies K_{ex} to eq 23B. With the mass balance for $[CE]_{ml}$, viz. $[CE]_{ml} = [CE]^0_{ml} - [G^+\cdot CE]_{ml}$, and the assumption that $[G^+]_{wl} = [G^+]^0_{wl}$ (the amount of transported guanidinium thiocyanate is at most 0.1% of the initial salt concentration), an expression for the complex concentration at the source interface is derived (eq 24). The complex concentration

$$[G^+\cdot CE]_{ml} = \frac{K_{ex}'\gamma_\pm[G^+]^0_{wl}}{1 + K_{ex}'\gamma_\pm[G^+]^0_{wl}}[CE]^0_m \qquad (24)$$

is related to the flux via eq 9. The contribution of crown-ether-mediated transport to the total flux is expressed in eq 25, and when this equation is transformed into eq 26 the left-hand

$$J = \frac{\mathbb{D}_m}{d_m}[G^+\cdot CE]_{ml} = \frac{\mathbb{D}_m \; K_{ex}'\gamma_\pm[G^+]^0_{wl}}{d_{ml} + K_{ex}'\gamma_\pm[G^+]^0_{wl}}[CE]^0_m \qquad (25)$$

$$\frac{[CE]^0_m}{d_m J} = \frac{1}{\mathbb{D}_m} + \frac{1}{\mathbb{D}_m K_{ex}' a_{G^+}} \qquad (26)$$

term is a function of the reciprocal activity of the salt. For the lipophilic carriers **11** and **12** we have measured the flux as a function of the initial salt concentration in the source phase (Figure 3). A linear correlation between $[CE]^0_m/(d_m J)$ and $1/a_{G^+}$ agrees with eq 26. The intercept and the slope of Figure 3 correspond to $1/\mathbb{D}_m$ and $1/\{\mathbb{D}_m K_{ex}'\}$, respectively. Table II shows the *experimental* values of $\mathbb{D}_m$ and K_{ex}'. The values of $\mathbb{D}_m$ for **11** and **12** are nearly the same ($2.3 \pm 0.5 \times 10^{-7}$ cm^2 s^{-1}). This value is slightly smaller than the value previously reported for dibenzo-18-crown-6 ($\mathbb{D}_m = 3.2 \times 10^{-7}$ cm^2 s^{-1}).[31]

We have also *calculated* the diffusion coefficients of the complexes with two different equations, viz., the empirical equation of Wilke and Chang[54] (27) and the Stokes–Einstein eq (28).[54]

$$\mathbb{D}_m = 7.4 \times 10^{-8}\left\{\frac{(\Phi M_2)^{0.5}T}{\eta_2 V_1^{0.6}}\right\} \qquad (27)$$

$$\mathbb{D}_m = kT/6\pi\eta_2 r \qquad (28)$$

The molal volume V_1 of the crown ethers is *not* known but can be calculated with the Schroeder's increments,[54] and in Table III the calculated values of V_1 are given. In the case of **1**, **2**, **4**, and **5** these calculated values can be compared with the values of V_1 obtained from crystallographic data of the complexes of **1** with guanidinium perchlorate[35] or uronium perchlorate,[38] the complex of **2** with imidazolium perchlorate,[55] and the complex of **4** and **5** with guanidinium perchlorate,[36,41] respectively. There is a good agreement between the *calculated* and *experimental* values irrespective of the state of aggregation if we take into account that the calculated values refer to the molal volume at the boiling point and the experimental values to a crystalline structure. According to eq 28 the complex is regarded as a sphere moving through a continuum, and the validity of this equation is limited to cases in which the solute is larger than the solvent. The radius of the solute can be obtained from the molal volume and Avogadro's constant, assuming a spherical shape. The calculated values of the diffusion coefficients are summarized in Table III. The values of both $\mathbb{D}_{m,1}$ (Wilke and Chang, eq 27) and $\mathbb{D}_{m,2}$ (Stokes–Einstein, eq 28) decrease when the lipophilicity of the substituent in the benzo crown ether increases. Although we observe a difference in the absolute values of the diffusion coefficients calculated with the Stokes–Einstein or the Wilke and Chang equation (approximately a factor of 2.2), the variation of the diffusion coefficient with the lipophilicity of the crown ether is the same.

Table III. Values of the Diffusion Coefficient Calculated from the Molal Volumes of the Crown Ethers

carrier	n^a	$V_1{}^b$ (cm^3 mol^{-1})	$\mathbb{D}_{m,1}{}^c$ (cm^2 s^{-1})	$\mathbb{D}_{m,2}{}^d$ (cm^2 s^{-1})
1	27	A: 483	6.8×10^{-7}	3.0×10^{-7}
		B: 440[e]	7.2×10^{-7}	3.1×10^{-7}
2	30	A: 532	6.4×10^{-7}	2.9×10^{-7}
		B: 502[f]	6.6×10^{-7}	3.0×10^{-7}
3	33	A: 581	6.1×10^{-7}	2.8×10^{-7}
4	27	A: 525	6.5×10^{-7}	2.9×10^{-7}
		B: 465[g]	7.0×10^{-7}	2.7×10^{-7}
5	30	A: 574	6.1×10^{-7}	2.8×10^{-7}
		B: 508[h]	6.6×10^{-7}	3.0×10^{-7}
6	33	A: 623	5.8×10^{-7}	2.8×10^{-7}
15	27	A: 476	6.9×10^{-7}	3.0×10^{-7}
16	30	A: 609	5.9×10^{-7}	2.8×10^{-7}
17	27	A: 532	6.4×10^{-7}	2.9×10^{-7}
7	27	A: 567	6.2×10^{-7}	2.8×10^{-7}
8	30	A: 616	5.9×10^{-7}	2.8×10^{-7}
9	27	A: 630	5.8×10^{-7}	2.7×10^{-7}
10	30	A: 679	5.5×10^{-7}	2.7×10^{-7}
11	27	A: 693	5.5×10^{-7}	2.7×10^{-7}
12	30	A: 742	5.3×10^{-7}	2.6×10^{-7}
13	27	A: 686	5.5×10^{-7}	2.7×10^{-7}
14	27	A: 693	5.5×10^{-7}	2.7×10^{-7}
18	18	A: 693	5.5×10^{-7}	2.7×10^{-7}

[a] Crown ether ring size. [b] Calculated from Schroeder's increments (A) and from crystallographic data (B). [c] Diffusion coefficient calculated from the Wilke and Chang equation[54] with $\eta_2 = 12.63$ cP ($=10^{-2}$ g cm^{-1} s^{-1}); $\Phi = 1$; $T = 298$ K. [d] Diffusion coefficient calculated from the Stokes–Einstein equation[54] with $\eta_2 = 12.63 \times 10^{-2}$ g cm^{-1} s^{-1}; $T = 298$ K. [e] The average value of two complexes, viz., **1**–guanidinium perchlorate ($V_1 = 432$ cm^3 mol^{-1}; $T = 156$ K), and **1**–uronium perchlorate ($V_1 = 448$ cm^3 mol^{-1}; $T = 269$ K). [f] Complex **2**–imidazolium perchlorate; $T = 167$ K. [g] Complex **4**–guanidinium perchlorate; $T = 146$ K. [h] Complex **5**–guanidinium perchlorate; $T = 161$ K.

The empirical values of $\mathbb{D}_m$ can only be compared with the calculated values ($\mathbb{D}_{m,1}$, $\mathbb{D}_{m,2}$) when the empirical diffusion coefficients are normalized for the porosity θ (0.64 for Accurel)[31] and the tortuosity τ[56] (eq 29).[57] On the basis of these results

$$\mathbb{D}_{m,n} = \mathbb{D}_m\tau/\theta \qquad (29)$$

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(50) (a) Danil de Namor, A. F.; Hill, T.; Sigstad, E. *J. Chem. Soc., Faraday Trans. 1* **1983**, *79*, 2713. (b) Danil de Namor, A. F.; Ghousseini, L. *J. Chem. Soc., Faraday Trans. 1* **1984**, *80*, 2843.

(51) Marcus, Y. *J. Chem. Soc., Faraday Trans. 1* **1987**, *83*, 2985.

(52) (a) Meot-Ner (Mautner), M. *Acc. Chem. Res.* **1984**, *17*, 186. (b) Meot-Ner (Mautner), M. *J. Phys. Chem.* **1987**, *91*, 417.

(53) Serjeant, E. P. *Potentiometry and Potentiometric Titrations*; John Wiley & Sons: New York, 1981; Vol. 69.

(54) Reid, R. C.; Sherwood, T. K. *The Properties of Gases and Liquids; Their Estimation and Correlation*; McGraw-Hill Book Company: New York, 1966. $\mathbb{D}_m$ = diffusion of solute 1 in solvent 2 at very low solute concentration, cm^2 s^{-1}; M_2 = molecular weight of the solvent; T = temperature, K; η_2 = viscosity of solution (solvent), 10^{-2} g cm^{-1} s^{-1} (eq 23), g cm^{-1} s^{-1} (eq 24); V_1 = molal volume of the solute at its normal boiling point, cm^3 mol^{-1}; Φ = "association parameter of the solvent"; k = the Boltzmann constant, 1.38×10^{-16}, g cm^2 s^{-2} K^{-1}; r = radius of the solute, cm.

(55) Stolwijk, T. B.; Sudhölter, E. J. R.; Reinhoudt, D. N.; van Eerden, J.; Harkema, S. *J. Org. Chem.* **1989**, *54*, 1000.

(56) The value of τ(Accurel) is not equal to 1 as reported previously[12] but must be (2.1 ± 0.1). We recalculate this value from the same experiments described in ref 12 after normalization of the flux for actual crown ether concentration, membrane thickness, and porosity. A better value of τ(Celgard 2500) from literature is used for the calculation of τ(Accurel): τ(Celgard 2500) = 2.47[a] or 2.23.[b] (a) Prasad, R.; Kiani, A.; Bhave, R. R.; Sirkar, K. K. *J. Membr. Sci.* **1986**, *26*, 79. (b) Bhave, R. R.; Sirkar, K. K. *J. Membr. Sci.* **1986**, *27*, 41.

Table IV, Fluxes of Guanidinium Thiocyanate and Partition Coefficient of the Crown Ethers **1–18**

carrier^{a}	n^{b}	10^{8} J^{c} (mol cm^{-2} h^{-1})	log P_{CE}(NPOE)^{d}	F^{e}
f		(1.3 ± 0.1)		
1	27	(1.3 ± 0.1)	0.9	1
2	30	(1.3 ± 0.1)	0.7	1
3	33	(1.3 ± 0.1)	0.6	1
4	27	(3.9 ± 0.1)	2.0	(3.0 ± 0.3)
5	30	(4.3 ± 0.2)	2.2	(3.3 ± 0.4)
6	33	(4.0 ± 0.4)	1.9	(3.1 ± 0.5)
15	27	(1.3 ± 0.1)	1.0^{g}	1
16	30	(4.4 ± 0.3)	4.4^{g}	(3.4 ± 0.5)
17	27	(4.3 ± 0.2)	1.9^{g}	(3.3 ± 0.4)
7	27	(6.0 ± 0.5)	2.3	(4.6 ± 0.7)
8	30	(5.1 ± 0.5)	2.1	(3.9 ± 0.7)
9	27	(22.8 ± 1.1)	3.6^{h}	(17.5 ± 2.2)
10	30	(22.2 ± 0.9)	3.3^{h}	(17.1 ± 2.0)
11	27	(24.4 ± 1.0)	4.9^{h}	(18.8 ± 2.2)
12	30	(27.6 ± 1.8)	4.7^{h}	(21.4 ± 3.0)
13	27	(20.4 ± 0.8)	4.0^{h}	(15.7 ± 1.8)
14	27	(26.1 ± 1.2)	4.9^{h}	(20.1 ± 2.5)
18	18	(1.3 ± 0.1)	17.0^{i}	1

^{a}The structures of the crown ethers are displayed in Figure 2. ^{b}Crown ether ring size. ^{c} $[\mathrm{GuHSCN}]^{0}_{\mathrm{w1}} = 10^{-1}$ M; $[\mathrm{carrier}]^{0}_{\mathrm{m}} = 10^{-2}$ M; T = 298 K. ^{d}Partition coefficient calculated for the system NPOE/water using eq 19; standard deviation ±15%. ^{e}Facilitation factor (see text). ^{f}Equal to transport in a blank system. ^{g}Value of log P_{CE}(oct) calculated from the measured value of **1**. ^{h}Value of log P_{CE}(oct) calculated from the measured value of **2**. ^{i}Value of log P_{CE}(oct) calculated from the measured value of dibenzo-18-crown-6.[44]

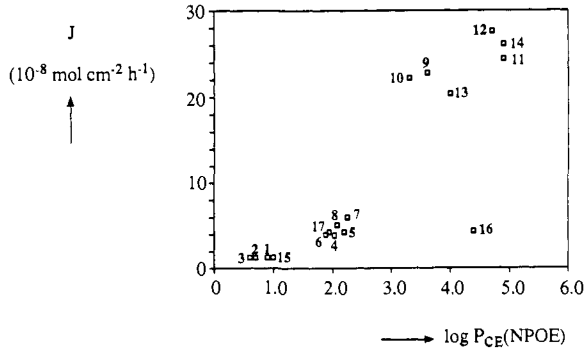

Figure 4, Effect of carrier lipophilicity on the flux.

we conclude that the diffusion coefficient calculated with the Wilke and Chang equation results in a better approximation of the experimental values of $\mathbb{D}_{m,n}$ for **11** and **12** than calculated with Stokes–Einstein.

Crown Ether Assisted Transport of Guanidinium Thiocyanate, The experimentally determined fluxes of transport of guanidinium thiocyanate assisted by the crown ethers **1–18** are given in Table IV together with the partition coefficients of the carrier. The observed fluxes, after equilibration of the distribution of the crown ether over the organic and aqueous phases, are displayed in Figure 4 as a function of the partition coefficient of crown ether. The fluxes increase with the lipophilicity of the 27-, 30-, and 33-crown ethers. The highest flux is found with crown ether **12**, and no enhancement of the flux was measured with the crown ethers **1**, **2**, **3**, **15**, and **18**. A substantial transfer of crown ether from the membrane phase to the aqueous phases was noticed for the unsubstituted benzo crown ethers **1**, **2**, and **3** and the 1,3-xyleno crown ether **15**.

Introduction of an additional aromatic ring in the 27-, 30-, and 33-crown ethers (**4**, **5**, **6**, and **17**) resulted in enhanced steady-state fluxes, although the complexation constants are expected to decrease as a result of the enforced assistance of the less basic oxygen atoms of the second catechol moiety in the hydrogen bonding with the guanidinium cation and the increased rigidity of the crown ethers.[41] Incorporation of a third aromatic ring (**16**) has hardly an effect on the transport of guanidinium thiocyanate. The reason of the higher fluxes is that aromatic rings will increase the partition coefficients and consequently the actual crown ether concentration in the membrane phase at equilibrium. The low flux of guanidinium thiocyanate observed with the lipophilic crown ether **18** (log P_{CE}(NPOE) = 17.0) is due to a low complexation constant.[41]

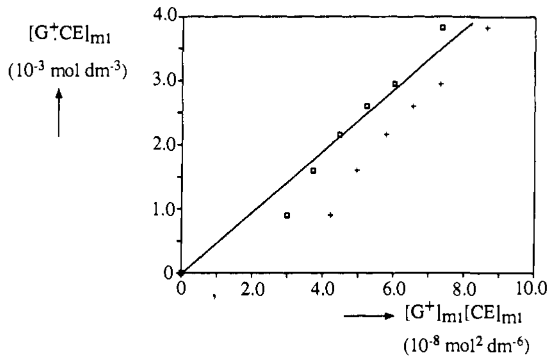

Figure 5, $[\mathrm{G^{+}{\cdot}CE}]_{ml}$ as function of $[\mathrm{G^{+}}]_{ml}[\mathrm{CE}]_{ml}$ for crown ether **11** by variation of the initial crown ether concentration, according to model A (+) and B (□).

The introduction of a lipophilic chain in the benzo crown ethers results in higher fluxes (Figure 4), attributed in first approximation to the increased value of P_{CE}, although Smid et al.[45] and Ikeda et al.[58] have shown that substituents in the aromatic ring might influence the stability of such complexes.

In Table IV a facilitation factor F is introduced which is defined as the ratio between the total flux in the presence and in the absence of crown ether. The maximal value of F (21.4) was found for **12**. The facilitation factor changes with the experimental flux for the different crown ethers in the same manner. However, it is only allowed to compare F with values of other systems, when the actual carrier concentration in the membrane phase is the same. Consequently, the resulting sequence of increasing F for the crown ethers parallels the increasing complexation constants.

In our theoretical description of the transport process two models were distinguished based on the difference in concentration profile of the crown ether in the membrane phase (vide supra). These two models can be distinguished by measuring the flux as function of the initial crown ether concentration because the relation between $[\mathrm{G^{+}{\cdot}CE}]_{ml}$ and $[\mathrm{G^{+}}]_{ml}[\mathrm{CE}]_{ml}$ will be different for models A and B. With the values of P_{CE}, $\mathbb{D}_{m}$, and P_{GA} together with the experimental value of the flux it is possible to calculate $[\mathrm{G^{+}{\cdot}CE}]_{ml} + [\mathrm{G^{+}}]_{ml}$ (eq 9), $[\mathrm{G^{+}}]_{ml}$ (eq 2 and 8), and consequently $[\mathrm{G^{+}{\cdot}CE}]_{ml}$. The unknown parameters K_m and $[\mathrm{CE}]_{ml}$ can be calculated from eq 14 and 15 (model A) or from eq 14 and 18 (model B) when the complexation constant in the aqueous phase is small. From the literature data the value of K_w is estimated a factor 10^{3}–10^{4} lower[59] than the value of K_m of the complexes of compound **1** (K_m = 59 M^{-1}) and **2** (K_m = 68 M^{-1}) in methanol.[41] Consequently, *the value of K_w will be too small to influence the values calculated from eq 14, 15, and 18*. In Figure 5 $[\mathrm{G^{+}{\cdot}CE}]_{ml}$ is given as a function of $[\mathrm{G^{+}}]_{ml}[\mathrm{CE}]_{ml}$ for both models A and B. According to eq 1 the relation between $[\mathrm{G^{+}{\cdot}CE}]_{ml}$ and $[\mathrm{G^{+}}]_{ml}[\mathrm{CE}]_{ml}$ must be linear with a slope equal to K_m, and $[\mathrm{G^{+}{\cdot}CE}]_{ml}$ must be 0 when $[\mathrm{G^{+}}]_{ml}[\mathrm{CE}]_{ml}$ is 0. From these results we concluded that model B provides a better fit and, consequently, that the gradient in crown ether concentration is equal to the gradient in complex concentration. The flux was also calculated as a function of the initial crown ether concentration for model B (Figure 6), and the experimental results are reproduced very well. The nonlinear behavior of the flux as a function of the initial crown ether concentration can be attributed to the presence of

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(57) Babcock, W. C.; Baker, R. W.; Lapochelle, E. D.; Smith, K. L. *J. Membr. Sci.* **1980**, *7*, 89.

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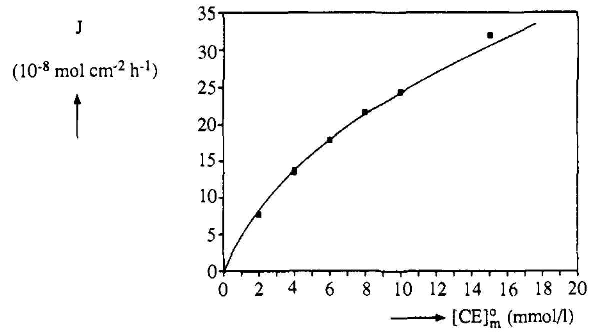

Figure 6. Theoretical curve of the flux vs the initial crown ether concentration, according to model B, and the experimental (■) values for carrier **11**.

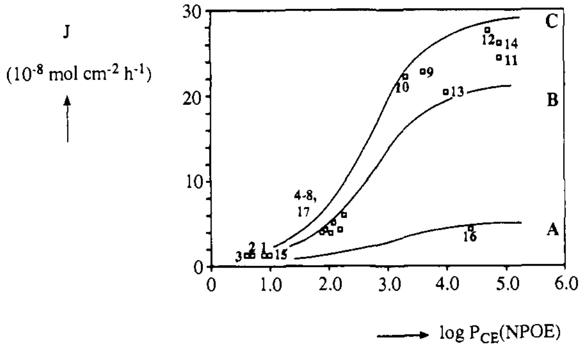

Figure 7. Effect of carrier lipophilicity on the flux for different values of K_m: (A) $K_m = 10^3$ M^{-1}; (B) $K_m = 10^4$ M^{-1}; (C) $K_m = 5 \times 10^4$ M^{-1}.

free ions in the membrane phase. In the case of an apolar organic solvent ion pairs are present predominantly, and, consequently, the flux would vary linearly with the initial crown ether concentration.[41]

Figure 4 demonstrates clearly that the differences in flux measured for **1–18** cannot only be attributed to the differences in partition coefficient of the crown ethers. Therefore, the complexation constants between the crown ethers and guanidinium thiocyanate must be different. The relation between J (calculated with eq 14 and 18) and log P_{CE}(NPOE) is plotted for five different values of K_m (Figure 7). This figure also includes the experimental data from Table IV for the different crown ethers. The calculated values of K_m (eq 14 and 18) for the crown ethers exhibiting a measurable active transport are listed in Table V. The values of K_m for the different crown ethers vary between 1.1×10^4 M^{-1} and 6.8×10^4 M^{-1}, except **16** ($K_m = 1.1 \times 10^3$ M^{-1}), but this is not unexpected in view of the values of K_m determined in methanol.[41] There are no large differences in K_m for the different ring sizes, viz., 27-, 30-, and 33-membered macrocycles.

K_m varies both with the number of aromatic rings in the macrocyclic polyether and the lipophilicity of the substituent. The latter is confirmed by the difference in K_m, determined by transport measurements of guanidinium, for the crown ethers **7**, **9**, **11**, **13**, and **14**. The lower value of K_m for compound **13** in comparison with **14** agrees with the previous results of Smid et al.[45] They found that the stability of a complex of Na$^+$ with the 4′-methylbenzo crown ether decreased with a formyl substituent at the 4′-position. For the most lipophilic crown ethers **9–12** and **14**, approximately the same value for K_m is found. The substituted benzo crown ethers exhibit a small effect of the ring size on the value of K_m. The complexation constants of the 27-membered macrocycles **7**, **9**, and **11** are lower than the values of K_m of the corresponding 30-membered macrocycles **8**, **10**, and **12**. In contrast to the partition coefficient P_{CE}, the complexation constant K_m decreases upon incorporation of an additional aromatic ring in the crown ether ring (**4**, **5**, and **16**). Crown ether **16**, a 30-membered macrocycle, has a high lipophilicity but a low complexation constant, because of the destabilizing effect of the 1,3-xyleno moiety and the presence of four catecholic oxygens in the ring.

Table V. The Calculated Values of K_m and log K_m from the Complex Concentration in the Membrane Phase

crown ether	n^a	$[G^+{\cdot}CE]_{ml} + [G^+]_{ml}{}^b$ (M)	$K_m{}^c$ (M^{-1})	log K_m
7	27	7.3×10^{-4}	2.2×10^4	4.34
9	27	2.8×10^{-3}	5.5×10^4	4.74
11	27	3.0×10^{-3}	4.8×10^4	4.68
13	27	2.5×10^{-3}	3.6×10^4	4.55
14	27	3.2×10^{-3}	5.7×10^4	4.76
4	27	4.7×10^{-4}	1.3×10^4	4.11
17	27	5.2×10^{-4}	2.2×10^4	4.34
8	30	6.2×10^{-4}	2.3×10^4	4.36
10	30	2.7×10^{-3}	6.8×10^4	4.83
12	30	3.3×10^{-3}	6.6×10^4	4.82
5	30	5.2×10^{-4}	1.1×10^4	4.03
16	30	5.3×10^{-4}	1.1×10^3	3.04
6	33	4.8×10^{-4}	2.2×10^4	4.34

[a] Crown ether ring size. [b] Average value, calculated from the measured flux; $[\mathrm{GuHSCN}]^0_{wl} = 10^{-1}$ M, activity coefficient 0.783 (calculated with the Debye–Hückel equation);[53] $[\mathrm{carrier}]^0_m = 10^{-2}$ M; T = 298 K. [c] Calculated with eq 14 and 18.

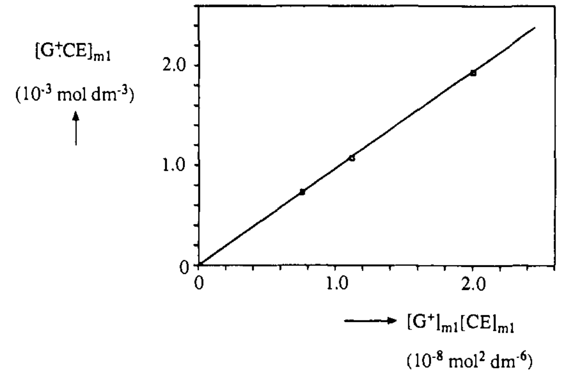

Figure 8. $[G^+{\cdot}CE]_{ml}$ as a function of $[G^+]_{ml}[CE]_{ml}$ for crown ether **11** by changing the initial guanidinium thiocyanate concentration, according to model B.

In separate series of experiments the initial salt concentration in the source phase was varied for the crown ethers **9**, **11**, **12**, and **14** in order to correlate the experimental fluxes to the theoretical model by a specific value of K_m for each crown ether. In Figure 8 $[G^+{\cdot}CE]_{ml}$ is plotted as a function of $[G^+]_{ml}[CE]_{ml}$ for **11**, and the slope of the line is equal to K_m. In Figure 9 both the experimentally determined and calculated fluxes are presented as a function of the salt activity. The theoretical curves in Figure 9A (carrier **9**, and **11**, $K_m = 9.6 \times 10^4$ M^{-1}), and 9B (carrier **12**, $K_m = 8.9 \times 10^4$ M^{-1}; carrier **14**, $K_m = 8.7 \times 10^4$ M^{-1}), calculated for the specific value of K_m, fit the experimental values very well, except for high salt concentrations. The values of K_m, which are used for the calculation of the theoretical curve, deviate from the values summarized in Table V for the corresponding crown ethers by a factor of 1.4–2.0. This small deviation is probably caused by the incorrectness of the calculated activity coefficients and/or the fact that the solubility limit of the salt in the membrane phase is reached at high salt concentrations.

The thermodynamic stability of a complex, K_m, is equal to the rate of complexation divided by the rate of decomplexation. The complexation process involves conformational reorganization of the macroring of the crown ether prior to complexation. The decomplexation process involves breaking of the hydrogen bonds and diminishing the electrostatic interactions. From literature[60–67]

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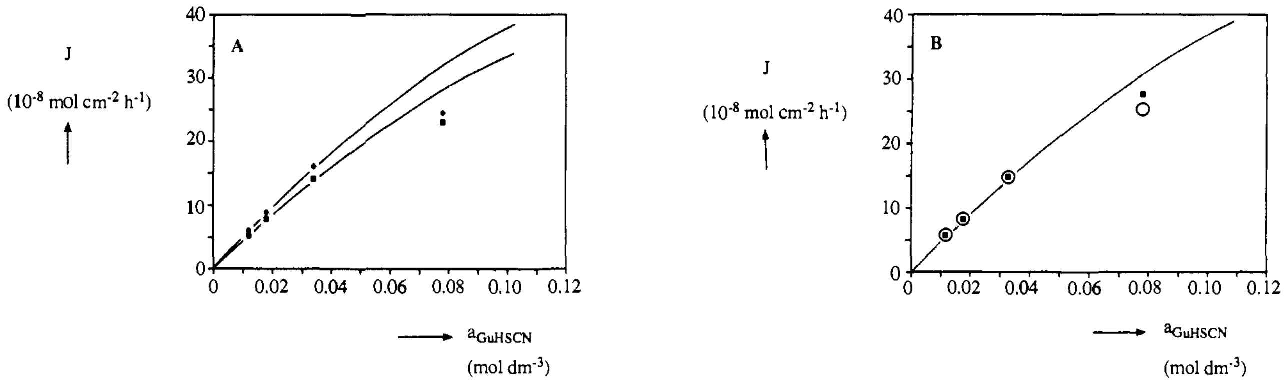


Figure 9. Theoretical curves of the flux vs the initial salt concentration (aqueous phase) and the experimental fluxes for the carriers: (A) **9**, $K_m = 9.6 \times 10^4$ M^{-1} (■), **11**, $K_m = 9.6 \times 10^4$ M^{-1} (♦); (B) **12**, $K_m = 8.9 \times 10^4$ M^{-1} (■), **14**, $K_m = 8.7 \times 10^4$ M^{-1} (○).

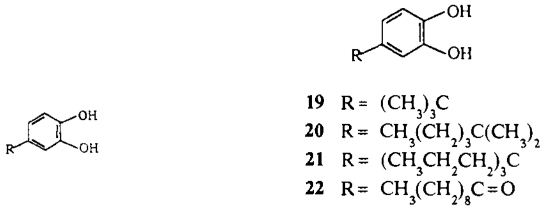
the conclusion is drawn that the rates of complex formation (k_f, s^{-1} M^{-1}) are very similar, k_f is estimated to be about 10^8 s^{-1} M^{-1}, while the differences in thermodynamic stability are almost fully accounted for by the differences in rates of decomplexation (k_d, s^{-1}). This means that most of the crown ethers studied have a value of k_d equal to 10^3–10^4 s^{-1}. With this approximated value of k_d one additional characteristic of the carrier-mediated transport mechanism can be checked with the so-called inverse Damköhler number N, with $N = D_m/(k_d d_m^2)$. The Damköhler number is a measure of the relationship between the characteristic reverse reaction and diffusion times. The small value of N (10^{-7}–10^{-6}) for our membrane system indicates a diffusion-limited process with a reaction equilibrium in the membrane phase. This means a continuous complexation and decomplexation of the salt during the diffusion through the membrane phase. We can calculate from eq 30 the average distance, which a crown ether salt complex

$$d = \sqrt{2D_m t} \qquad (30)$$

moves before decomplexation takes place.[68] With $t = 1/k_d$, and D_m is the diffusion coefficient of the complex, d is about 1000 Å. Consequently, during transport of the salt from the source to the receiving interface ($d_m = 10^6$ Å) decomplexation and complexation takes place for at least 1000 times. From the estimated distance between the crown ether molecules in the membrane phase (about 70 Å when $[\mathrm{CE}]^0_m = 10^{-2}$ M) and from a complexed fraction of 30%, it is reasonable that the cation complexed by a crown ether molecule at the source interface will be different from the cation decomplexed from the same crown ether molecule at the receiving interface.

Conclusions

In crown-ether-mediated transport through supported liquid membranes, leakage of crown ether carriers from the membrane phase causes a decrease in the flux until equilibrium has been reached. The transport rate of guanidinium thiocyanate by different carriers shows a correlation with the partition coefficient and the complexation constant. The substitution of an alkyl chain on the benzo crown ether results in an increased lipophilicity and therefore in a more stable membrane system. The diffusion coefficient of the carrier hardly changes with increasing lipophilicity. Complexation constants of complexes between guanidinium salts and the various crown ethers have been estimated from a thermodynamic model. This model predicts the change in the steady-state flux of guanidinium thiocyanate very well for a change in crown ether concentration and in salt concentrations, respectively. With the value of the inverse Damköhler number we have confirmed the previous assumption that the transport through the membrane is a diffusion-limited process with a reaction equilibrium in the membrane phase. On the basis of our results we can conclude that the difference in the flux through a supported liquid membrane has to be attributed to both the partition coefficient of the crown ether and the complexation constant.



19 R= $(CH_3)_3C$
20 R= $CH_3(CH_2)_3C(CH_3)_2$
21 R= $(CH_3CH_2CH_2)_3C$
22 R= $CH_3(CH_2)_8C{=}O$

Figure 10. Structures of substituted catechol compounds.

Experimental Section

Melting points were determined with a Reichert melting point apparatus and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded with a Bruker WP-80 and a Nicolet NT-200 WB spectrometer, respectively, with $(CH_3)_4Si$ as an internal standard. Mass spectra were obtained with a Varian Mat 311A. Elemental analyses were carried out by the department of Analytical Chemistry. Infrared spectra were recorded on a Perkin Elmer 257 spectrophotometer.

Materials. The synthesis of **1–6**, **15**, **16**, and **18** has been carried out according to known procedures.[31-33,35,36,42,69,70] The substituted benzo crown ethers **7–14** were obtained by reaction of the substituted catechols **19–22** (Figure 10) with the corresponding polyethylene glycol dimesylates. Catechols were alkylated with tertiary alcohols in trifluoroacetic acid[71] in the presence of a small amount of sulfuric acid at 40 °C. Acylation of catechol was carried out by reaction of an aliphatic acid in the presence of boron trifluoride etherate[72] at 80 °C. A Clemmensen reduction of **13** resulted in crown ether **14**. The naphtho crown ether **17** was synthesized from 2,3-naphthalenediol under the same conditions as described for the benzo crown ethers.[70] Guanidinium thiocyanate was obtained from Fluka and used without further purification. The polymeric film Accurel was obtained from Enka Membrana. *o*-Nitrophenyl octyl ether (Fluka) was distilled before use.

General Procedure for the Synthesis of 4-Alkylcatechol 19, 20, and 21. Catechol (5 g, 45 mmol) was dissolved in trifluoroacetic acid (50 mL) at room temperature. To this solution were added 1 equiv of the tertiary alcohol and 1 mL of concentrated sulfuric acid, and the mixture was stirred in a nitrogen atmosphere at 40 °C for 16 h. The crude product was dissolved in dichloromethane and washed subsequently with water and a saturated aqueous sodium bicarbonate solution. After drying ($NaHCO_3$), filtration, and evaporation of the solvent the product was distilled under vacuum.

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4-(1,1-Dimethylethyl)-1,2-benzenediol (19). This compound was prepared according to the general procedure. The product was obtained in 50% yield as an oil: ^{1}H NMR (CDCl$_3$) δ 6.9–6.7 (m, 3 H, ArH), 5.9 (s, 2 H, ArOH), 1.3 (s, 9 H, CH$_3$); ^{13}C NMR δ 144.9, 142.7, 140.6 (ArC-1, C-2, C-4), 118.0 (ArC-5), 115.9 (ArC-6), 113.4 (ArC-3), 34.0 (C), 31.3 (CH$_3$); mass spectrum, *m/e* 166.098 (M$^+$; calcd 166.099).

4-(1,1-Dimethylpentyl)-1,2-benzenediol (20). After addition of 2-methyl-2-hexanol to catechol, according to the general procedure, the product was obtained as an oil in a yield of 36%: ^{1}H NMR (CDCl$_3$) δ 6.9–6.6 (m, 3 H, ArH), 5.3 (s, 2 H, ArOH), 1.8–1.0 (m, 12 H, (CH$_2$)$_3$C(CH$_3$)$_2$), 0.8 (t, 3 H, CH$_3$); ^{13}C NMR δ 143.4, 142.9, 140.7 (ArC-1, C-2, C-4), 118.4 (ArC-5), 114.9 (ArC-6), 113.5 (ArC-3), 44.5, 27.0, 23.4 (CH$_2$), 37.2 (C), 29.1, 14.1 (CH$_3$); mass spectrum, *m/e* 208.147 (M$^+$; calcd 208.146).

4-(1,1-Dipropylbutyl)-1,2-benzenediol (21). This compound was prepared using tri(*n*-propyl)carbinol, according to the general procedure. The product was obtained as an oil in a yield of 35%: ^{1}H NMR (CDCl$_3$) δ 6.9–6.6 (m, 3 H, ArH), 5.2–4.2 (br s, 2 H, ArOH), 1.8–0.5 (m, 21 H, H-alkyl); ^{13}C NMR (CDCl$_3$) δ 142.9, 141.9, 140.5 (ArC-1, C-2, C-4), 119.2 (ArC-5), 114.8 (ArC-6), 114.1 (ArC-3), 42.8 (C), 40.3, 16.8 (CH$_2$), 14.1 (CH$_3$); mass spectrum, *m/e* 250.191 (M$^+$; calcd 250.193).

4-Decanoyl-1,2-benzenediol (22). To a mixture of catechol (5.0 g, 45 mmol) and decanoic acid (7.8 g, 45 mmol) at 80 °C, boron trifluoride etherate (6.5 g, 45 mmol) was slowly added, and the mixture was stirred for 2 h. After the reaction hot water was added, and the mixture was extracted with diethyl ether. The organic layer was washed twice with water and dried over MgSO$_4$. After filtration the solvent was evaporated in vacuo, and the residue was distilled under vacuum. The product was recrystallized from cyclohexane: yield 19%; mp 102–104 °C; ^{1}H NMR (CDCl$_3$) δ 8.9–8.0 (br s, 2 H, ArOH), 7.7–6.8 (m, 3 H, ArH), 2.9 (t, 2 H, CH$_2$CO), 1.9–1.0 (m, 14 H, CH$_2$), 0.9 (t, 3 H, CH$_3$); ^{13}C NMR (CDCl$_3$) δ 201.5 (CO), 149.7 (ArC-1), 143.7 (ArC-2), 129.9 (ArC-4), 123.2 (ArC-5), 115.0, 114.5 (ArC-3, C-6), 38.3, 31.9, 29.5, 24.8, 22.7 (CH$_2$), 14.1 (CH$_3$); mass spectrum, *m/e* 264.174 (M$^+$; calcd 264.173).

General Procedure for the Synthesis of the Lipophilic Crown Ethers 7–13. The 4-substituted catechol (30 mmol) was dissolved in freshly distilled THF (1000 mL). Two equivalents of NaH were added, and the mixture was stirred at room temperature. When the production of hydrogen had ceased, the mixture was refluxed for 1 h. After the addition of 1 equiv of Cs$_2$CO$_3$ refluxing was continued for another 2 h. A solution of the corresponding polyethylene glycol dimesylate (1 equiv) in freshly distilled THF (50 mL) was added dropwise over a period of 2 h. The mixture was refluxed for at least 3 days. The mixture was allowed to cool to room temperature and filtered, and the solvent was evaporated. The residue was mixed with CH$_2$Cl$_2$ and extracted with water, sodium bicarbonate solution, and water. After drying over MgSO$_4$ the solvent was evaporated in vacuo. The residual oil was extracted with refluxing petroleum ether 40–60 several times, followed by evaporation of the petroleum ether. The crown ethers were then purified by column chromatography and vacuum distillation.

4′-(1,1-Dimethylethyl)benzo-3(*n* + 2)-crown-(*n* + 2) (7, *n* = 7; 8, *n* = 8). These crown ethers were prepared using octa- and nonaethylene glycol dimesylate, respectively, according to the general procedure. Purification was effected by column chromatography (neutral Al$_2$O$_3$, activity II/III, CHCl$_3$) and vacuum distillation. The products were obtained in yields of 30–40%: ^{1}H NMR δ 7.0–6.8 (m, 3 H, ArH), 4.3–3.5 (m, 32 H (**7**), 36 H (**8**), OCH$_2$), 1.3 (s, 9 H, CH$_3$); ^{13}C NMR (CDCl$_3$) δ 148.3, 146.8, 144.7 (ArC-1, C-2, C-4), 118.1 (ArC-5), 114.1, 113.1 (ArC-2, C-6), 71.0–69.0 (OCH$_2$), 34.3 (C), 31.4 (CH$_3$); mass spectrum, **7** *m/e* 500.300 (M$^+$; calcd 500.299), **8** *m/e* 544.328 (M$^+$; calcd 544.325).

4′-(1,1-Dimethylpentyl)benzo-3(*n* + 2)-crown-(*n* + 2) (9, *n* = 7; 10, *n* = 8). The crown ethers **9** and **10** were synthesized using octa- and nonaethylene glycol dimesylate, respectively, according to the general procedure. Purification was accomplished by column chromatography (neutral Al$_2$O$_3$, activity II/III, CHCl$_3$) and vacuum distillation; the products were obtained as an oil in a yield of 25% (**9**) and 20% (**10**): ^{1}H NMR (CDCl$_3$) δ 6.9–6.7 (m, 3 H, ArH), 4.3–3.5 (m, 32 H (**9**), 36 H (**10**), OCH$_2$), 1.8–0.9 (m, 15 H, H-alkyl); ^{13}C NMR (CDCl$_3$) δ 148.2, 146.7, 143.2 (ArC-1, C-2, C-4), 118.8 (ArC-5), 113.8, 113.4 (ArC-3, C-6), 71.0–68.7 (OCH$_2$), 37.2 (C), 44.4, 26.9, 23.3 (CH$_2$), 29.1, 14.0 (CH$_3$); mass spectrum, **9** *m/e* 542.346 (M$^+$; calcd 542.346), **10** *m/e* 586.376 (M$^+$; calcd 586.372).

4′-(1,1-Dipropylbutyl)benzo-3(*n* + 2)-crown-(*n* + 2) (11, *n* = 7; 12, *n* = 8). These two crown ethers were prepared from the corresponding functionalized catechol derivative and octaethylene glycol dimesylate and nonaethylene glycol dimesylate, respectively, according to the general procedure. Purification was effected by column chromatography (neutral Al$_2$O$_3$, activity II/III, CHCl$_3$) and vacuum distillation, and the product was obtained as an oil in a yield of 20–30%: ^{1}H NMR (CDCl$_3$) δ 6.9–6.7 (m, 3 H, ArH), 4.3–3.5 (m, 32 H (**11**), 36 H (**12**), OCH$_2$), 1.7–0.5 (m, 21 H, H-alkyl); ^{13}C NMR (CDCl$_3$) δ 148.1, 146.5, 142.6 (ArC-1, C-2, C-4), 119.8 (ArC-5), 114.1, 113.4 (ArC-3, C-6), 71.0–68.7 (OCH$_2$), 42.9 (C), 40.2, 16.8 (CH$_2$), 14.9 (CH$_3$); mass spectrum, **11** *m/e* 584.395 (M$^+$; calcd 584.392), **12** *m/e* 628.422 (M$^+$; calcd 628.419).

4′-Decanoylbenzo-27-crown-9 (13). This crown ether was prepared from **22** and octaethylene glycol dimesylate according to the general procedure. Purification was effected by column chromatography (neutral Al$_2$O$_3$, activity II/III, EtOH) and recrystallization from ether in a yield of 30%: mp 31–33 °C; ^{1}H NMR (CDCl$_3$) δ 7.6–6.8 (m, 3 H, ArH), 4.4–3.5 (m, 32 H, OCH$_2$), 2.9 (t, 2 H, CH$_2$CO), 2.1–1.0 (m, 14 H, CH$_2$), 0.9 (t, 3 H, CH$_3$); ^{13}C NMR (CDCl$_3$) δ 199.2 (CO), 153.1 (ArC-1), 148.6 (ArC-2), 130.6 (ArC-4), 122.9 (ArC-5), 113.1, 112.2 (ArC-3, C-6), 71.1–68.7 (OCH$_2$), 38.2, 31.9, 29.4, 24.8, 22.7 (CH$_2$), 14.1 (CH$_3$); mass spectrum, *m/e* 598.366 (M$^+$; calcd 598.372); IR (KBr) 1670 cm^{-1} (ν CO).

4′-Decylbenzo-27-crown-9 (14). A Clemmensen reduction of **13**, dissolved in EtOH, gave product **14** in quantitative yield. This compound was used without further purification: ^{1}H NMR (CDCl$_3$) δ 6.9–6.7 (m, 3 H, ArH), 4.3–3.5 (m, 32 H, OCH$_2$), 2.5 (t, 2 H, ArCH$_2$), 1.8–1.0 (m, 16 H, CH$_2$), 0.9 (t, 3 H, CH$_3$); ^{13}C NMR (CDCl$_3$) δ 148.8, 146.9 (ArC-1, C-2), 136.5 (ArC-4), 121.0 (ArC-5), 115.0, 114.8 (ArC-3, C-6), 70.9–68.9 (OCH$_2$), 35.4, 31.9, 31.6, 29.6, 29.5, 29.3, 22.7 (CH$_2$), 14.1 (CH$_3$); mass spectrum, *m/e* 584.393 (M$^+$; calcd 584.392).

Naphtho-27-crown-9 (17). This crown ether was prepared from the corresponding 2,3-naphthalenediol and octaethylene glycol dimesylate according to the general procedure. Purification was accomplished by column chromatography (neutral Al$_2$O$_3$, activity I, CHCl$_3$) and recrystallization (EtOH) to give the product (15%) as white crystals: mp 33–36 °C; ^{1}H NMR (CDCl$_3$) δ 7.7–7.0 (m, 6 H, ArH), 4.4–3.4 (m, 32 H, OCH$_2$); ^{13}C NMR (CDCl$_3$) δ 149.1, 129.3, 126.3, 124.1, 108.3 (ArC), 71.1–68.9 (OCH$_2$); mass spectrum, *m/e* 494.255 (M$^+$; calcd 494.252). Anal. Calcd for C$_{26}$H$_{38}$O$_9$: C, 63.14; H, 7.75. Found: C, 62.78; H, 7.95.

Determination of the Partition Coefficients of the Crown Ethers for the System 1-Octanol/Water. A solution of the compound was prepared in 1-octanol, saturated with water ([H$_2$O] = 3.1 M),[73] with a concentration of about 1 mM. The amount of the organic phase and water phase, distilled deionized water saturated with 1-octanol, were estimated by a preliminary calculation on the basis of a phase transfer of about 50% of the crown ether to the aqueous phase. From each stock solution a series of five different dilutions was made. An appropriate amount of water was added, and the solutions were shaken for at least 2 min (about 100 inversions) at room temperature. After separation of both phases by centrifugation (2000 rpm) during 2 h both phases were analyzed by UV-spectroscopy (Varian Cary 17, Carl Zeiss PMQII). For the lipophilic crown ethers it was necessary to concentrate the aqueous phase by evaporation of water and dissolving the residue in a small volume of chloroform. Because the determination of the solute concentration in the aqueous phase is less accurate than in the organic phase, the former is checked by a mass balance for the two phase system. When the solute concentration in 1-octanol is plotted against the solute concentration in water, the slope of the straight line will be equal to the partition coefficient. Finally, the measurements were checked by an experiment with a freshly prepared solution of the solute in 1-octanol.

Determination of the Partition Coefficient of the Guanidinium Cation. The solubilities of guanidinium tetraphenylborate in water and NPOE and the solubility of tetraphenylarsonium tetraphenylborate in NPOE were determined by addition of an excess amount of salt to *o*-nitrophenyl octyl ether (NPOE) in order to obtain a saturated solution. The mixtures were stirred for at least 5 days at 25 °C, followed by a filtration through a Millipore Millex-HV filter. The determination of the tetraphenylborates was performed by a titration with a standard solution of AgNO$_3$ by using a Metrohm 636 Titroprocessor with a Ag/Ag$_2$SO$_4$ electrode. A blank experiment was carried out on NPOE.

Apparatus. The transport experiments were carried out in a permeation cell previously described.[31] The supported liquid membrane consisted of a thin microporous polypropylene film (Accurel; thickness d_m = 100 μm, porosity θ = 64%) immobilizing the solution of crown ether in *o*-nitrophenyl octyl ether (NPOE). A guanidinium thiocyanate solution was used as the source phase, and doubly distilled and deionized water was used as the receiving phase. The transported guanidinium thiocyanate was determined by monitoring the conductivity of the receiving phase solution as a function of time.