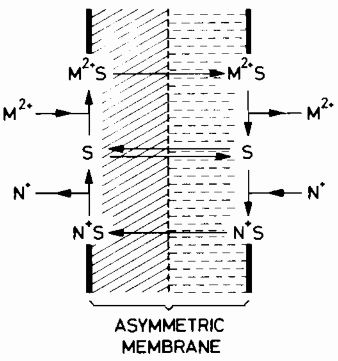

Fig. 1. Scheme of the idealized ion transport through an asymmetric membrane based on a neutral carrier S.

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H3

Solid–Liquid (S–L) and Liquid (L–L) Phase Transfer of Salts *via* 'Encapsulated' Crown Ether Cation Complexes

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In recent years crown ethers have been successfully used for the transport of salts, both inorganic and organic, from an aqueous phase to organic solvents. Our work has extended the applicability of these crown ethers to the transport of salts from the solid state into solution both aqueous and nonaqueous. For this purpose a number of novel crown ethers have been synthesized that have in addition to a polar 'cavity' formed by donor atoms of the macrocyclic ring, (an) additional anionic functional group(s) covalently bound to the macroring.

The first part of the lecture will deal with the design of such macrocycles that can encapsulate a spherical cation in a flexible cavity or that can encapsulate *non*-spherical cations, *e.g.* uronium cations, in a relatively rigid cavity.

Together with the synthesis results of complexation studies using ^{1}H NMR spectroscopy will be discussed.

In the second part the use of crown ethers for the transport of sparingly soluble salts from the solid state into aqueous solutions will be dealt with. The emphasis will be placed on theoretical models that can be used to describe such phase transfer processes and to predict thermodynamic stability constants of complexes required for solubilisation.

The lecture will conclude with a comparison of these models with experimental results.

H4

Ion Transport and Complex Formation Properties of Artificial Membrane Carriers

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Many natural compounds of antibiotic nature such as valinomycin [1], streptogramins (group B) [2] and calcimycin [3] exhibit the general structural properties of macrocyclic or pseudo-macrocyclic compounds. Such compounds act as artificial membrane carriers and increase the cation permeability of phospholipid bilayer membranes and of certain biological membrane systems. The study of these membrane-active compounds acting as multidentate ligands for cations has substantially contributed to our present knowledge of the basis of transport mechanisms and cation specificity.

Spectroscopic methods have been applied to the investigation of the physicochemical properties of these macrocyclic compounds as far as structural aspects and cation selectivity in homogeneous solution and in the membrane-bound state are concerned [4]. Thermodynamic parameters of the complex formation equilibria (stability constants, equilibrium enthalpies, stoichiometric coefficients) have been obtained from spectrophotometric titrations. For the fast and precise determination of these parameters a computer-controlled high performance titrator has been developed [5]. In order to identify the relevant groups of the antibiotics which are involved in the direct coordination of the cations, a large number of suitable model compounds have been synthesized and investigated. The experimentally observed alkali and alkaline earth cation selectivities are interpreted on the basis of the structural properties of these antibiotics.

Studies to determine the kinetic parameters of cation coordination employing stopped flow techniques and temperature-jump relaxation spectrometry have been carried out [1–4, 6]. The interpretation of kinetic data gives an insight into the mechanisms involved. Two cases are suggested for the mechanism of complex formation with alkali ions. One is characterized by a stepwise ligand exchange process where the rate-limiting step for certain compounds is a conformational change of the ligand occurring during the substitution of solvate molecules from the inner cation coordination sphere by the coordinating groups of flexible ligands. The second case is that of sterically fixed ligands in which only a partially stepwise ligand exchange can occur during coordination. However, the rate-limiting step is here attributed to the dissociation of more than one solvate molecule from the inner coordination sphere of the cation in a single reaction step. As far as complex formation of some of these ligands with alkaline earth cations is concerned, the determined kinetic parameters generally agree well with the known rates which characterize inner sphere solvate substitution.

The specificity of the cation transport across membranes in the presence of these carriers has been investigated using planar phospholipid bilayer membranes employing electrical techniques, and on unilamellar phospholipid vesicles of uniform size by carrying out flux and kinetic studies [6]. Special methods have been established for controlling the size, and the size distribution, of such spherical vesicles [7]. The relevance of these results concerning the cation specificity of certain biological transport systems in natural membranes will be discussed.

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