CHAPTER I

INTRODUCTION

It is generally accepted that solvent effects play an important role for chemical phenomena. To give a detailed description of the structure and energetic and dynamic characteristics of solute/solvent interactions at the molecular level, experimental evaluation, *e.g.*, by X-ray or neutron diffraction studies, is quite impossible due to the large number of very similar atoms and atomic distances in solutions. Theoretical studies of chemical systems using statistical mechanics methods such as Monte Carlo (MC) (1) and molecular dynamics (MD) (2) techniques are required. An outstanding advantage of these methods is the ability to perform simulations even on systems which are hard to access experimentally.

1.1   Ligand solvation: open questions regarding the macrocyclic effect

Enthalpic contribution:

Margerum and Hinz (3) originally suggested that the enhanced stability of macrocyclic ligand complexes compared with their open-chain analogs, known as the *macrocyclic effect*, is due almost entirely to an enthalpic contribution. The cyclic nature of a cyclic ligand physically prevents it from having as large a solvation number as its open-chain analog. This is reflected in the low solubility of the cyclic ligand. Consequently, more energy would be needed to break the hydrogen bonds between solvent molecules and open chain ligands than in the case of the cyclic ligands. However, Poaletti *et al.* (4) and Hancock and McDougall (5) have countered that the stabilization energy upon binding of solvent molecules to the cyclic ligand and to the open chain analog should be identical. A clear resolution of this conflict is not yet possible.

Entropic contribution:

Entropic effects are tentatively attributed to the entropic changes during complexation of the solvent and the ligand molecules and the metal ion. The release of solvent molecules from the metal ion and the ligand results in a positive entropy contribution because the number of independent particles has increased, but a negative contribution to the entropy change stems from the lower configurational entropy of the ligand upon coordination. The noncyclic ligand would be expected to suffer a much larger loss of configurational entropy upon coordination than the cyclic one where the geometry is already restricted (3). The favorable entropy change, due to the liberation of solvent molecules, and the loss in configurational entropy of the ligand are expected to be nearly equal in magnitude. For example, the net entropic change due to both contributions for 1,4,8,11-tetraazacyclotetradecane in water is 16 cal/K/mol less than that of its open chain analog (3,6).

In conclusion, the dominant factor responsible for the macrocyclic effect according to these assumptions is the degree of solvation of the macrocycle and the resulting enthalpic contribution. The relative enthalpy changes can be understood if *ligand solvation* is taken into consideration. The size of the cyclic ligand and its low solubility (3,6) make diffraction studies and other spectroscopic techniques for the evaluation of the solution structure impossible.

It has been suggested by the results of MC simulations of cyclen (7) and its complex with Mg(II) (8) in water that the solvation energy does not contribute to the macrocyclic effect (9). This conclusion was restricted only to a specific conformation of the cyclic ligand and a specific type of solvent. They have also suggested that the solvation structure of a cyclic ligand is strongly dependent on its conformation and on the relative size of the ligand's cavity and the solvent molecules. On the basis of available information, there is no way to ascertain whether the macrocyclic effect is caused primarily by the solvation effect. To overcome this problem, it is necessary to investigate the solvation structure of macrocyclic ligands in different solvents.

1.2   Factors influencing the macrocyclic effect

While all authors have agreed on the existence of the *macrocyclic effect*, efforts to establish more detailed contributions to this effect have led to conflicting results. The difficulties arise from the kinetic inertness of the cyclic ligands, regarding both the complex formation and decomposition (10).

The most frequent suggestions, apart from the solvation effect, postulate that the stability arises from:

i) the large number of fixed atoms of the cyclic ligands, hence the term *"multiple juxtapositional fixness"* (11),

ii) the *"higher ligand field strength"* of the cyclic ligands due to the presence of more secondary donor atoms than in non-cyclic analogs (12),

iii) the *"prestrained"* conformation of the cyclic ligands, which are already in a conformation most suitable for complex formation (13-17).

1.3   The significance of macrocyclic compounds

The significance of macrocyclic ring systems and their interaction with metal ions in aqueous solution have been of interest to many scientists as they can serve as the simplest models for understanding chemical and particularly biological processes which take place in solution (18-21). Solvation structures involving macrocyclic compounds have been widely studied (3-9,26) since they are especially important for the fundamental conception of ion transportation through cell walls (22).

There are many reasons why the behavior of polyamine and polyether macrocycles in solution is of interest. Typical properties of these compounds include: *a)* a marked kinetic inertness (for polyamine) regarding both the formation of the complex from a hydrated metal ion and ligand and its decomposition (10), *b)* a strong metal-donor interaction which is reflected in the spectrochemical parameters (11), *c)* the possibility of stabilization of high oxidation states for the metal ion (23), *d)* high thermodynamic stability, reflected in the stability constants which can be several orders of magnitude larger than those of the corressponding complexes of linear ligands (3,6), and *e)* the strong influence of the size of the macrocyclic cavity on metal complex stability, as the selectivity of macrocyclic ligands towards metal ions depends on the effective

fitting of the cation into the ring cavity and the ligand's ability to adjust itself to the electronic and geometrical requirements of the metal ion (24,25).

However, it has been reported that the above properties are strongly dependent on the type of solvent (26). Solvation of the ligands and their complexes is an important factor for the stability and reactivity of the complexes as well as the conformation of the ring structure in solution (26).

1.4   Specification of the model

The present study examines the solvation structure of a 1,4,7,10-tetraazacyclododecane (cyclen) in water-ammonia mixture. Monte Carlo simulations based on a modified Metropolis procedure (1) were performed (Chapter IV). Since a key issue underlying the success of the simulations is the need for potential functions that properly describe the intermolecular interactions in the systems under consideration, cyclen-ammonia and cyclen-water potential functions have been newly developed and comprehensively tested (Chapter IV). The remaining MCY [Matsuoka, O., Clementi, E., and Yoshimine, M. (27)], HISH [Hannongbua, S., Ishida, T., Spohr, E., and Heinzinger, K. (28)] and TR [Tanabe, Y., and Rode, B. M. (29)] potentials were taken from the literatures. Theoretical backgrounds of the quantum chemical (Chapter II) and the Monte Carlo (Chapter III) methods which are used for this study have been also outlined. The results of such simulations are evaluated in the form of radial and angular distribution functions together with the corresponding coordination numbers and their distributions (Chapter V). A solvation model for the solvation shell of the cyclen molecule has been proposed and the contribution of the solvation effect on the macrocyclic effect has been extrapolated and discussed (Chapter VI). Finally, the observed data have been extracted and summarized (Chapter VI).