CHAPTER I

INTRODUCTION

The significance of macrocyclic ring systems and their solvation have been of interest to many chemists as they can serve as the simplest models for naturally occuring metal binding macrocyclic centers of proteins in solution and display a high degree of ion specificity [1-3]. The size of the cyclic ligand and its low solubility make diffraction studies and other spectroscopic techniques for the evaluation of such informations impossible.

1.1 Motivation

The solvation effect was suggested by Margerum et al. [4,5], to be one of the factors influencing the macrocyclic effect - an unusually high stability constants of metal complexes with cyclic polyamine and polyether ligands when compared to equivalent complexes with a non-cyclic ligands. The idea was that more solvent molecules are expected to bound to the open chain ligand than to the cyclic one. This suggestion was strongly opposed by other authors [6-9], but no final conclusion could be made until now. Some suggested that it is entirely due to the entropic contribution from both ligands and solvents [6] while others [10] assumed that the enthalpy term should predominate. Summarizing all data, both enthalpy and entropy contributions seem to participate in this effect [11].

In addition, quantitative consideration of the solvation effect of the macrocyclic ligands should be very useful in understanding the complexities of the interaction of metal ions and the solvent with large biological molecules where the solvation plays a very important role in determining the thermodynamic and kinetic of complex formations.

1.2 Factors Influencing the Macrocyclic Effect

Apart from the solvation effect, which is mentained before, the following factors were suggested to contribute to an existance of the macrocyclic effect :

a) the "*prestrained*" conformation of the cyclic ligands, which are already in a conformation most suitable for complex formation [11-14].
b the higher ligand field strength of the cyclic ligands due to the presence of more secondary nitrogen atoms [15], and
c) the larger number of fixed atoms of the cyclic ligands, and this led to the term "*multiple juxtapositional fixness*" as was suggested by Busch et al. [16].

1.3 Method for Studying the Macrocyclic Molecules and the Solvation Structure

1.3.1 Experimental Methods

Most of the investigations concerning the macrocyclic ligands always deal with the two common features, namely the structural and thermodynamic properties.

(a) Structural Investigations

The structural information together with the conformational change in complex formation of the crystallized systems have been mainly provided by X-ray and neutron diffraction techniques. In solution, nuclear magnetic resonance spectroscopy is a suitable method for the investigation of the molecular structure.

(b) Thermodynamic Measurements

The change of thermodynamic properties such as entropy, enthalpy and free energy of the chemical systems can give important information on the characterization of the solvation. The heat of formation can be obtained indirectly from the variation of logK (K = stability constant) with temperature in the polarographic or potentiographic method. The application of these methods in macrocyclic chemistry was mainly

contributed from Margerum [10] and Kodama and Kimura [17]. The most reliable method to obtain these primary quantities is the direct calorimetric method, contributed mainly from Paoletti et al. [11].

Optical spectroscopic methods such as ultraviolet-visible, infrared and Raman spectroscopy can also provide some important information about equilibrium constants, intermolecular interactions and conformational changes.

1.3.2 Theoretical Methods

(a) Quantum Chemical Methods

Among the quantum chemical methods, the *ab initio* MO SCF method is employed extensively for the prediction of the molecular geometry of many electron systems since they provide a sufficiently good approximated description. Although stabilization energies computed with small basis sets (normally, the extended basis sets are not used for large molecular systems) are usually overemphasized because of basis set superposition error, relative orders are mostly correct and the absolute data can be corrected partially using the method proposed by Boys and Bernardi [18].

An outstanding advantage of quantum chemical over experimental methods is the ability to perform calculations even on systems which is hard to access experimentally. In addition, the quantum chemical method can lead to a better understanding of chemical behavior on a microscopic or molecular basis.

(b) Statistical Mechanic Methods

Theoretical studies of chemical systems using statistical mechanics methods such as Monte Carlo (MC) [19] and molecular dynamics (MD) [20] techniques are required, whenever detailed description of the structure of solution and of energetic and dynamic characteristics of solute/solvent interaction are needed. A key issue underlying the success of both types of simulations is the need for potential functions that properly describe the intermolecular interactions in the systems under consideration. Therefore, the liability of the results of such simulations depend strongly on the accuracy of the quantum chemical calculation and, consequencely, on the pair potential function in use

(the pair potential function can be obtained empirically, by experimental [21] methods too).

1.4 Rationale for Studying the Solvation of Macrocyclic Compounds

Since the enhance complex stability of the macrocyclic ligands in comparison with the analogous open chain causes primarily by the, enthalpic contributions, mainly due to electronic binding phenomena and the specific molecular structure, as well as entropic effects related to solvation and desolvation phenomena but the experimental evaluation of the solvation structure of such compounds, by X-ray or neutron diffraction studies, is quite impossible due to the large number of very similar atoms and also atomic distances in the solution. To give access to detailed structure of such systems, however, computational techniques like Monte Carlo and molecular dynamics simulations are used successfully.

The aim of this work is to study structural properties of the system consisting of a cyclen (1,4,7,10-tetraazacyclododecane) molecule in water-methanol mixture. The intermolecular potential for cyclen-methanol has been developed recently using the *ab initio* MO SCF calculations with STO-3G basis set.. Monte Carlo simulation has been performed in order to investigate solvation structure around cyclen molecule and, consequently, their influence on the macrocyclic effect.

The results have been displayed in term of radial distribution functions, running integration numbers and their distributions.