Quantum Chemical Calculations on the 'Macrocyclic Effect'

G. J. REIBNEGGER* and B. M. RODE

Institute of Inorganic and Analytical Chemistry, The University of Innsbruck, A-6020 Innsbruck, Innrain 52a, Austria

Quantum chemical calculations within the framework of the HF-LCAO-MO method have been performed in order to obtain insight into the nature of the well-known 'Macrocyclic Effect'. The results indicate the effect to be mainly due to the fact that the cyclic ligands are already 'pre-strained', i.e. they need not be contracted into another conformation better suited for complex formation with ions, in marked contrast to the behaviour of open chain analogues.

Introduction

Complexes of cyclic ligands such as polyamines or polyethers exhibit some remarkable properties, in particular an extra stability as compared to their open chain analogues which has been termed the 'Macrocyclic Effect' [1]. The existence of this effect is well established; its nature, namely the detailed balance between entropic and enthalpic contributions, is still a matter of some controversy, mainly due to the experimental difficulties arising from the kinetic lability of the complexes. Thus the answers to this question differ considerably from author to author [2–4].

Some groups [4, 5] have suggested that the extra enthalpic stabilization is due to the fact that the cyclic ligand is already 'pre-strained', which in turn also causes an entropic contribution arising from the smaller configurational entropy of the cyclic ligand.

In accordance with this assumption, X-ray investigations [6] have indicated a very similar structure of the free macrocycles as compared to their complexes with Ni(II) and Cu(II) ion. On the other hand, for the open chain analogues one has to expect a significant increase in the configurational energy

*Present address: Institute of Medical Chemistry and Biochemistry, University of Innsbruck, Fritz-Pregl-Str. 3, A-6020 Innsbruck, Austria.

TABLE I. Parameters Defining the Geometry of the Molecules.

C–C bond length	1.540 A
C–N	1.470 A
C–H	1.094 A
N–H	1.014 A
all bond angles:	109.47°

in the process of formation of the complex from the ion and the chain which should exist in one of various possible expanded conformations, when undisturbed by the ion.

In order to gain some insight into the problem of the nature of the enthalpic contribution to the macrocyclic effect, we have performed quantum chemical calculations in the framework of the *ab initio*-Hartree-Fock method on the complexes between the Li(I) ion and a) a macrocycle, 1,4,7,10-tetraaza-cyclododecane (L1), b) N,N'-bis-(2-methyl-aminoethyl)-1,2-diaminoethane (L2), c) N,N'-1,2-di-aminoethane (L3). Li(I) ion has been chosen to reduce the computational work to some extent. This choice seems to be further justified bearing in mind that macrocyclic ligands are able to form stable complexes also with alkaline and alkaline earth metal ions, in which cases most other complexing reagents fail.

The choice of the open chain analogues was determined to maintain all the nitrogen atoms secondary, so as to avoid any complications arising from possible differences in the behaviour of primary and secondary amino-groups as indicated in the literature [12].

Method

The calculations reported here are of the *ab initio*-MO-SCF type, employing a minimal Gaussian lobe

TABLE II. Results of the Calculation on the Complex betwen Li(I) and the Macrocyclic Ligand L1.

	total energy (aeu)	nuclear repulsion (aeu)	electronic energy (aeu)
Li(I) ion	−6.40997	−	−6.40997
L1	−451.90334	+844.96007	−1296.86341
L1 + Li(I)	−458.39059	+916.59567	−1374.98626

TABLE III. Results of the Calculation on the Complex between Li(I) and N,N'-bis-(2-methylaminoethyl)-1,2-diaminoethane (L2).

	total energy (aeu)	nuclear repulsion (aeu)	electronic energy (aeu)
L2(expand.)	−453.03256	+721.73897	−1174.77153
L2(contrac.)	−452.80394	+877.86432	−1330.66826
L2 + Li(I)	−459.29798	+950,80615	−1410.10413
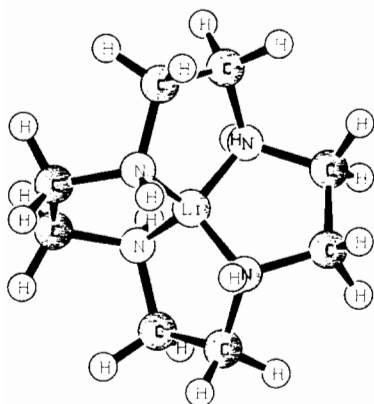
Fig. 1. Structure of the complex between Li(I) ion and the macrocyclic ligand 1,4,7,10-tetraaza-dodecane (L1).
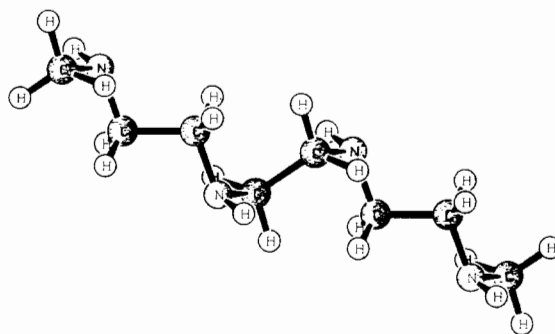

Fig. 2a. Assumed expanded structure of N,N'-bis-(2-methyl-aminoethyl)-1,2-diaminoethane (L2).

basis set, which has been shown to yield reasonable results for interaction energies due to complex formation of ions and similar organic molecules as well as for configurational energies of the latter [7, 8]. The program being used is discussed in the literature [10].

Since we were interested in the qualitative aspects of the problem rather than in quantitative predictions of actual enthalpies, changes in the ligand's geometries were ignored throughout the calculations. We employed standard bond lengths and bond angles [9], being aware of the lower degree of accuracy thus introduced. Parameters defining the geometry of the molecules are listed in Table I.
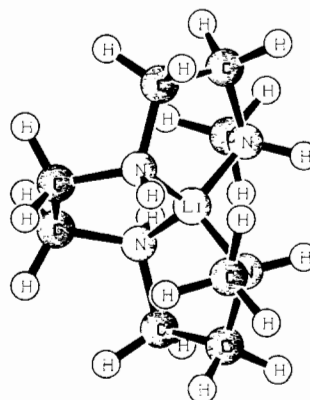

Fig. 2b. Structure of the complex between Li(I) and the contracted conformation of L2.

TABLE IV. Results of the Calculation on the Complex of Li(I) and two Molecules of N,N'-dimethyldiaminoethane (L3).

	total energy (aeu)	nuclear repulsion (aeu)	electronic energy (aeu)
L3 (*trans*)	−226.99862	+253.40143	−480.40005
L3 (*cis*)	−226.78970	+260.36029	−487.14999
2 L3[a]	−453.79612	+906.88354	−1360.67966
2 L3 + Li(I)	−460.29525	+981.08410	−1441.37935

[a]In suitable conformation for complex formation as shown in Fig. 3c.

In the calculations of the complexes with open chain ligands, we have tried to employ geometries implying favourable positions of adjacent methyl groups (see figures).

The quantum chemical calculations were performed on the CDC-CYBER 170 computer of the University computer center at the Technical University in Vienna. The computer-assisted plots of the complexes have been performed at the CDC-3300 computer of the University of Innsbruck, using the program SCHAKAL [11].

Results

Li(I) Ion and 1,4,7,10-Tetraaza-cyclododecane (L1)

Table II shows the results of the calculations on the complex between Li(I) ion and the macrocyclic ligand L1 (Fig. 1).

The complex formation process may thus be written:

$$Li^+ + L1 \rightarrow (LiL1)^+ + 48.5 \text{ kcal/mol}$$
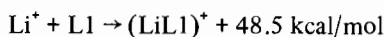
Li(I) Ion and N,N'-bis-(2-methylaminoethyl)-1,2-diaminoethane (L2)

There are many possible expanded conformations of nearly equal energy to be expected for this ligand molecule in an undisturbed state. The one chosen for this work is shown in Fig. 2a.

When involved in complex formation, the ligand has to be contracted to a structure like that shown in Fig. 2b.

The relevant energies are reported in Table III.

The contraction of the ligand molecule to the conformation suitable for subsequent complex formation is obviously very energy-consuming:

$$L2(\text{expanded}) + 143.5 \text{ kcal/mol} \rightarrow L2(\text{contracted}).$$
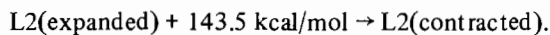
This large increase in configurational energy is mainly due to the high nuclear repulsion in the contracted conformation overcompensating the simultaneous gain in electronic energy. The sub-
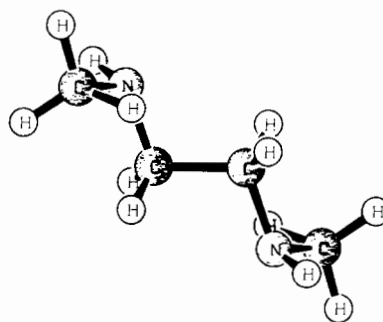

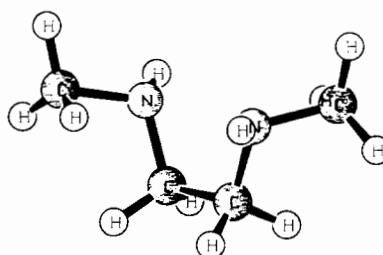Fig. 3a. N,N'-dimethyl-diaminoethane (L3) in *trans*-configuration.
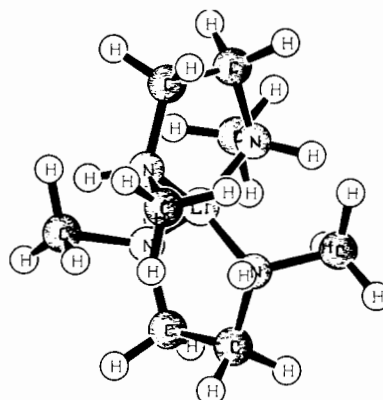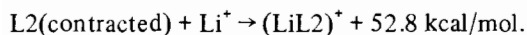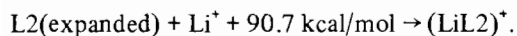

Fig. 3b. L3 in *cis*-configuration.

Fig. 3c. Structure of the complex between two molecules of L3 and Li(I).

sequent formation of the complex is, as one would expect, favourable:

L2(contracted) + Li$^+$ → (LiL2)$^+$ + 52.8 kcal/mol.

The overall reaction remains energy-consuming, however:

L2(expanded) + Li$^+$ + 90.7 kcal/mol → (LiL2)$^+$.

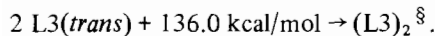### *Li(I) Ion and Two Molecules of N,N'-dimethyldi-aminoethane (L3)*

We have done computations on the following systems: a) L3 in *trans* conformation (Fig. 3a); b) L3 in *cis* conformation (Fig. 3b); c) two L3 in the geometry suitable for complex conformation (Fig. 3c) without and with the cation.

The resulting energies are listed in Table IV.

The comparison between the energies of the *trans* and *cis* conformations clearly demonstrates the preference of the former structure:
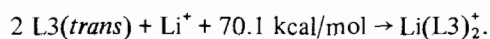
L(3)(*cis*) → L3(*trans*) + 131.1 kcal/mol.
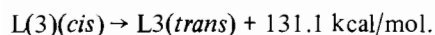
If — again partitioning the overall reaction into two consecutive steps — two ligand molecules are to form a dimer of suitable geometry (indicated by '§'), one obtains:

2 L3(*trans*) + 136.0 kcal/mol → (L3)$_2$ §.

The second step yields:

(L3)$_2^§$ + Li$^+$ → Li(L3)$_2^+$ + 55.9 kcal /mol.
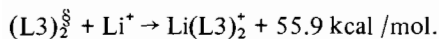
The overall process can be written as

2 L3(*trans*) + Li$^+$ + 70.1 kcal/mol → Li(L3)$_2^+$.

Discussion

The absolute energy values reported in the foregoing section should be considered with some caution, since there are a lot of assumptions and simplifications introduced and, consequently, the model character of the calculations has to be emphasized.

Among the assumptions the following examples seem to be most important:

  Restriction to the frame of Hartree-Fock method.
  Use of a very small basis set.
  Employment of fixed bond parameters.
  Complete neglect of solvent influence.

The rather large energy differences indicated for the various processes by our results will, most probably, be appreciably smaller in real chemical

systems, mainly due to solvent interactions and geometrical relaxations which are supposed to compensate some effects and soften the geometrical strain implied in complex formation. Furthermore, when using very small basis sets (which is absolutely necessary for reasons of computational economy when dealing with systems of this size) there is the danger of introducing some artificial stabilization of one part of the system due to the basis functions of the remainder.

However, bearing in mind all these reservations, we can make the conclusion — at least in a semi-quantitative sense — that the reason for the enthalpic contribution to the macrocyclic effect is in fact, most probably the one suggested in [4, 5]. The conformationally fixed and 'pre-strained' macrocyclic ligand molecules are strongly favoured as complexing agents as compared to open chain analogues for energetic reasons. The open structured ligands interact in a way quite similar or even stronger than that of the ion, when being brought into a suitably contracted conformation. The process of forming this conformation starting with one of the far more probable expanded conformations is very energy-consuming, however, and thus overcompensates the stabilization energy gain due to the second step, *i.e.* the complex formation.

References

1 D. K. Cabbiness and D. W. Margerum, *J. Am. Chem. Soc., 91*, 6540 (1969).
2 F. P. Hinz and D. W. Margerum, *Inorg. Chem., 13*, 2941 (1974).
3 M. Kodama and E. Kimura, *J. Chem. Soc. Dalton*, 1081 (1978).
4 L. Fabbrizzi, P. Paoletti and R. M. Clay, *Inorg. Chem., 17*, 1042 (1978).
5 G. J. McDougall, R. D. Hancock and J. C. A. Boeyens, *J. Chem. Soc. Dalton*, 1438 (1978).
6 S. M. Peng and V. L. Goedken, unpublished results, quoted in N. F. Curtis, G. A. Melson (ed.), 'Coordination Chemistry of Macrocyclic Compounds', Plenum Press, New York, 1979, ch. 4, p. 237.
7 B. M. Rode, *Monatsh. Chemie, 106*, 339 (1975).
8 B. M. Rode and G. J. Reibnegger, *J. Chem. Soc. Faraday II, 75*, 178 (1979).
9 L. E. Sutton, 'Tables of Interatomic Distances', London, The Chemical Society, 1958.
10 R. Ahlrichs, *Theoret. Chim. Acta (Berlin), 33*, 157 (1974).
11 E. Keller, Univ. Freiburg, Germany.
12 R. D. Hancock and G. J. McDougall, *Adv. Mol. Relax. Interact. Proc., 18*, 99 (1980).