The Influence of Small Monovalent Cations on Neighbouring Hydrogen Bonds of Aquo-Protein Complexes

Kritsana P. Sagarik and Bernd M. Rode
Institut für Anorganische und Analytische Chemie, Universität Innsbruck, Austria

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The influence of small monovalent metal ions on hydrogen bonds of aquo-protein complexes is studied on $Li^+/HCONH_2\text{-}OH_2$ as an example. Using results obtained from ab initio calculations with minimal GLO basis sets, the remarkable changes in the hydrogen bond energy and charge distribution, due to metal ion complex formation, are discussed. The metal ion seems to enhance strongly the donor-acceptor interaction of the O ... H–N–C=O hydrogen-bonded system.

1. Introduction

Studies on metalloproteins in biological systems are of interest as it is known that the metal ions in metabolic reactions play an important role in maintaining the normal body functions. The main interest concerns the metal-protein interactions and the metal transport through membranes. Several works pertaining to this subject have been reported in Ref. [1, 2].

Hydrogen bond formation in biochemical reactions has also been widely studied because the hydrogen bond interaction is strong enough, relative to kT, to hold a reacting macromolecule, such as a protein, in a particular orientation suitable for a specific biochemical complex formation (for reviews see Ref. [3]), but weak enough to be broken easily by suitable reaction partners.

In preliminary theoretical studies on the effect of small metal ions on neighbouring hydrogen bonds, using the lithium-water-ammonia adduct as a model [4], it was also shown that the use of the minimal basis set is an acceptable way to reduce the computational effort in similar investigations on larger molecular systems, even when the intramolecular geometrical parameters are not optimized.

In the present work, we focus our interest on the above mentioned metal ion effect on the neighbouring hydrogen bond of the water-formamide adduct, using ab initio calculations with minimal basis set [5] for intermolecular geometrical parameter optimizations and relative energy calculations. More accurate energy calculations, using the previously employed [4] 8s, 4p + P(5111/31) basis set, were restricted by the size of our molecular systems to the smaller species within the series.

2. Method

The geometries of water and formamide, as given in Table 1, were kept constant throughout the calculations. The intermolecular geometry parameters reported here result from ab initio MO SCF calculations. The exponents of the basis set are given in Ref. [5] and have been used efficiently in several calculations on similar systems [5–8].

The position of the lithium ion was selected along the C=O axis according to Ref. [5], the molecular geometry of the system considered is given in Fig. 1. The water-formamide hydrogen bond formation takes place along the N–H bond, trans to the oxygen atom, according to [9]. The rotation of the water molecule about the N ... O axis was also investigated.

Some of the energy calculations, in the above optimized geometries, were carried out using ab initio calculations with extended basis 8s, 4p + P(5111/31) GLO sets for oxygen, nitrogen and

Bond length (Å)		Bond angle (degree)	
O–H	0.96	HOH	104.5
C–O	1.24	NCO	123.6
C–H	1.09	HCO	132.6
C–N	1.34	CNH	119.0
N–H	0.99	HNH	122.0

Table 1. Experimental geometrical parameters used in the calculations [12].

Reprint requests to Prof. B. M. Rode, Institut für Anorganische und Analytische Chemie, Universität Innsbruck, Innrain 52a, 6020 Innsbruck, Österreich.

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carbon, 4s+P for hydrogen atoms and 8s+P(5111) for lithium ion. The exponents for s and p functions were taken from Ref. [10]. The polarization functions of hydrogen, nitrogen, oxygen, carbon and lithium had the exponents 0.1, 0.3, 0.4, 0.2 and 0.3, respectively.

All calculations were performed at the CDC Cyber 170 computer of the Interuniversitary Computer Center at the Technical University of Vienna. The program used here is discussed in detail in Ref. [11].

3. Results and Discussion

Optimized intermolecular geometrical parameters and energies are reported in Table 2 and 3. The Mulliken population analysis of each chemical species is given in Table 4. The changes in charge distribution due to the complex formations are shown in Figure 2. In order to maintain reasonable computing times, ab initio calculations with extended basis sets on water-formamide and water-formamide-lithium complexes have not been performed.

3.1. The Lithium-Formamide Complex

A number of ab initio calculations on the lithium-amide complexes have been reported [5, 8]. Although the sizes of the basis sets used in these references were different, the predicted Li ... O distances were nearly the same (about 1.8 Å).

Table 2. Optimized geometrical parameters.

System	Θ	O ... N (Å)	Li ... O (Å)
$(H_2NCHOLi)^+$	—	—	1.77
(H_2OH_2NCHO)	60	2.73	—
$(H_2OH_2NCHOLi)^+$	60	2.62	1.76

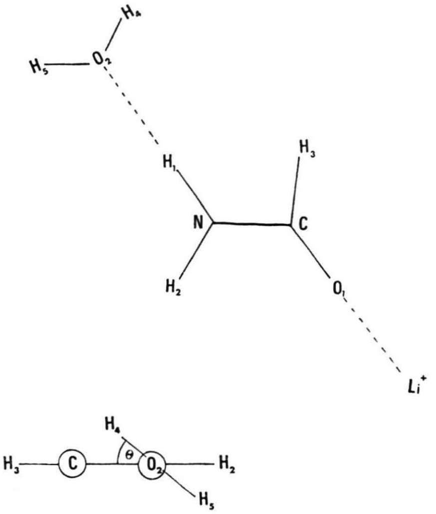

Fig. 1. Geometry of water-formamide-lithium complex; Θ = Angle between HOH and formamide planes.

The binding energies obtained, using 2s, 1p, 4s, 2p [13] and 8s, 4p+P(5111/31) basis sets, are 38.7, 55.9 and 52.2 kcal/mole, respectively. Comparing the complex formation of $Li^+/HCONH_2$ with $Li^+/HCOOH$ [14], the calculated binding energy, using the same minimal basis set, is by 2.1 kcal/mole lower in the case of $HCONH_2$.

Considering the changes in the charge distributions for both complex formations, the charge transfer from formic acid and formamide to lithium ions seem to be almost identical. The discrepancy in the binding energy can be attributed to a difference in the base strength between the $CO-NH_2$ and $CO-OH$ functional groups.

Table 3. Total, binding and hydrogen bond energies.

System	Calc. Tech.	Total energy (kcal/mole)	Binding energy (kcal/mole)	H-Bond energy (kcal/mole)
Li^+	A	− 7.2361 [a]	—	—
	B	− 6.4100 [a]	—	—
H_2O	B	− 64.5189 [a]	—	—
H_2NCHO	A	− 168.8536	—	—
	B	− 143.3421	—	—
$H_2NCHOLi^+$	A	− 176.1728	52.2	—
	B	− 149.8137	38.7	—
H_2OH_2NCHO	B	− 207.8840	—	14.4
$H_2OH_2NCHOLi^+$	B	− 214.3695	—	23.2

[a] A = ab initio 8s/4p+P(5111/31); B = ab initio minimal basis set 2s, 1p; Value taken from Reference [2].

3.2. The Formamide-Water Adduct

The optimized O ... N distance is 2.73 Å. This value agrees quite well with that of Ref. [9] (using STO-3G basis).

The investigation of the rotational energy barrier predicted that, within kT, the formamide-water adduct allows free rotation, the energy barrier being only 0.5 kcal/mole. The favourable form seems to be $\Theta = 60°$ (see Fig. 1).

The hydrogen bond energy of this equilibrium geometry is 14.4 kcal/mole. This value is about 1.8 kcal/mole lower than that of the most favourable form of the formamide dimer [13].

The net charge of the hydrogen bond proton (see Fig. 2 and Table 4.) is about 0.038 lower. The nitrogen of the formamide molecule gains about 0.061 in charge. This seems to be a correct prediction of the charge transfer resulting from a hydrogen-bonded complex formation.

3.3. The Lithium-Formamide-Water Adduct

The main consequence of the metal ion on the shape of the complex seems to be the shortening of the O ... N distance by about 0.11 Å. At the same time, the hydrogen bond energy is increased to 23.2 kcal/mole, which corresponds to a net stabilization effect (NSE) of 8.8 kcal/mole. The order of the NSE value, as predicted by this and the previous works [4, 15], is

$$\mathrm{NSE}(H_2O/NH_3) > \mathrm{NSE}(H_2O)_2 > \mathrm{NSE}(HCONH_2/OH_2).$$

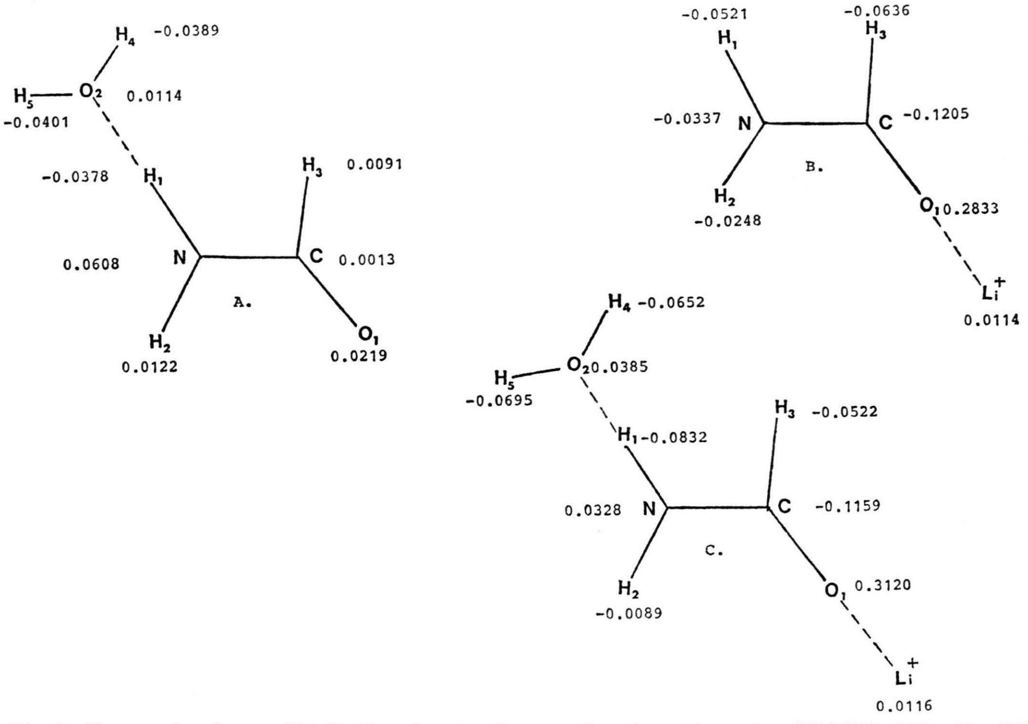

Fig. 2. Changes in charge distribution due to the complex formations A = $CHONH_2$-OH_2, B = $Li^+/CHONH_2$, C = $Li^+/CHONH_2$-OH_2.

Table 4. Electron populations obtained from ab initio calculations with 2s, 1p basis sets. H_1(b) = Hydrogen bond proton.

System	H_1(b)	H_2	H_3	N	C	O_1	O_2	H_4	H_5	Li
H_2O	—	—	—	—	—	—	8.3776	0.8112	0.8112	—
$HCONH_2$	0.6185	0.6064	0.9633	8.0043	5.5525	8.2550	—	—	—	—
$Li^+/HCONH_2$	0.5664	0.5816	0.8997	7.9706	5.4320	8.5383	—	—	—	2.0114
$HCONH_2$-OH_2	0.5807	0.6186	0.9724	8.0651	5.5538	8.2769	8.3890	0.7723	0.7711	—
$Li^+/HCONH_2$-OH_2	0.5353	0.5975	0.9111	8.0371	5.4366	8.5670	8.4161	0.7460	0.7417	2.0116

This order seems to depend on the number of the nuclei between the metal ion binding site and the donor-acceptor pair of the hydrogen-bonded system. Considering the changes of the electron population due to ternary complex formation, the charge transfer to the lithium ion is still the same as in $Li^+/HCONH_2$ but, in this case, the metal ion seems to induce a higher donor ability at the nitrogen atom. This inductive effect is also transmitted along the hydrogen bond to the oxygen atom of the water molecule, leading to a decrease of electron density at both H_4 and H_5 hydrogen atoms. The results obtained can thus be described as a transfer of the effect of the metal ion along the O=C—N backbone and the hydrogen bond to the water molecule. This seems to be one more good example for the observation that ion effects can be transferred by solvents or other suitable molecular structures over a considerable number of bonds [16].

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