Ab Initio Study of the Interaction of Guanine and Adenine with Various Mono- and Bivalent Metal Cations (Li^+, Na^+, K^+, Rb^+, Cs^+; Cu^+, Ag^+, Au^+; Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}; Zn^{2+}, Cd^{2+}, and Hg^{2+})

Jaroslav V. Burda, Jiří Šponer, and Pavel Hobza*

J. Heyrovský Institute of Physical Chemistry, Academy of Sciences of the Czech Republic,
Dolejškova 3, 182 23 Prague 8, Czech Republic

Received: October 3, 1995; In Final Form: January 2, 1996[⊗]

The interaction of guanine and adenine with ions of groups Ia, Ib, IIa, and IIb were studied at the Hartree−Fock and second-order Møller−Plesset levels employing all-electron (AE) and pseudopotential treatmetns. Christiansen's average relativistic effective pseudopotentials (AREP) were used for all the ions with the exception of Li^+. AE and AREP treatments were tested for the Na^+, K^+, Mg^{2+}, and Ca^{2+} complexes; very good agreement between the results suggests that pseudopotentials can be used with confidence also for other cations. Intermolecular X−N7 distances for complexes containing adenine are shorter than those for complexes containing guanine. The stabilization energies for guanine···X complexes are larger than those of adenine···X complexes. Relativistic effects are most pronounced for Au^+ and Hg^{2+} ions.

1. Introduction

The structure and function of DNA are, in general, dependent on metal ions. These ions can interact with many sites in DNA:[1−4] phosphate groups, the sugar moiety, as well as the DNA bases. Despite the fact that the metal cations usually interact with the phosphate group and, to a lesser extent, with the bases, cation−base interactions are expected to be involved in many important biophysical processes, such as different stabilization of DNA triple helices,[5] stabilization of quadruple helices,[6] and stabilization of the ribose−base stacking in Z-DNA.[7] It is assumed that the interaction of a divalent cation with the base can cause significant polarization of the bases associated with stabilization of certain H-bonded DNA base pairs and other interactions.[5,7,8]

Ab initio quantum-chemical calculations made at the Hartree−Fock (HF) theoretical level with a minimal basis set predicted polarization effects of the metal cations on the base caused by N7 coordination.[8] This was associated with a very significant increase in the stability of the base pairing. Ab initio calculations[9] (HF/minimal basis set) demonstrated that interaction of various cations with O6 of thymine leads to destabilization of the adenine···thymine pair. The approach of the cation to other available sites (thymine, O2; adenine, N1, N3) leads, on the other hand, to stabilization of the pair. The interactions of Li^+ with DNA bases were investigated by Del Bene[10] at HF levels.

Divalent cations stabilize the DNA double helix by neutralizing the negatively charged sugar−phosphate backbone. Coordination of transition metal cations to the sites of DNA bases that are not involved in hydrogen bonding increases the melting temperature of the DNA double helix.[11−13] However, a high metal/DNA ratio facilitates thermal denaturation, presumably because of through coordination to N3(C) and N1(A) atoms involved in base pairing.[12,14,15]

Monovalent alkaline cations seem to interact exclusively with the phosphate group of the backbone, and also the divalent alkaline metal cations (Mg^{2+}, Ca^{2+}, Ba^{2+}) interact mostly with the phosphate group.[1−4] This does not mean that interaction with bases is excluded. For example, a recent high-resolution X-ray study of Z-DNA hexamer shows a barium cation bridging two side-by-side Z-DNA helices in the crystal by simultaneously coordinating to the O6 and N7 atoms of two guanines. This cation is, at the same time, coordinated to four water molecules.[16] The phosphate-bound cations are frequently also involved in base coordination: they interact with the N7 position of adenine and guanine. Divalent transition metal cations have larger affinities to DNA bases, and the following affinity order holds for the nucleic acid monomers: N7(guanosine) > N3(cytidine) > N7(adenosine) > N1(adenosine) > N3(adenosine, guanosine).[3,4]

In the DNA double helix, the known sites for the cation coordination are mainly the N7 atoms of purines, while a simultaneous interaction with the guanine O6 atom is also known. Many other sites such as N3 of cytosine and N1 of adenine are blocked by the hydrogen bonding. It should be noted that the metal cation−base interactions do not involve only the metal cation and DNA base. The cation can interact with the phosphate group and is surrounded by water molecules. The metal cations can interact with the DNA base directly (inner-sphere coordination), or there is a water molecule between the DNA base and the metal cation (outer-sphere coordination).[4]

Experimental studies on 5′-monophosphates revealed the following order of macrochelate coordination involving the N7 position of purines: 5′-GMP > 5′-IMP (I = inosine) > 5′-AMP.[4] This order was explained as a result of different basicity of the N7 sites of guanosine, inosine, and adenine. This is well correlated with the dipole moments of DNA bases.

Evidently, metal cations play an important role in stabilizing, as well as destabilizing, DNA bases, base pairs, and the DNA double helix. To understand the role of cations in the biophysics of DNA, it is necessary first to carry out a detailed interaction study of ions with isolated bases. This is the aim of the present study. In the future, we would like to investigate the interaction of ions with base pairs, as well as with fragments of the double helix. Water molecules will also be explicitly considered here. The present study makes a natural extension of our theoretical studies on DNA bases,[17a] H-bonded DNA base pairs,[17b−d] and stacked DNA base pairs.[17e]

[⊗] Abstract published in *Advance ACS Abstracts,* April 1, 1996.

0022-3654/96/20100-7250$12.00/0

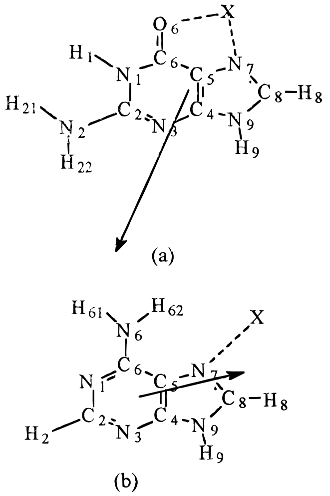

Figure 1. Structures of the guanine···X (a) and adenine···X (b) complexes. Arrows indicate the direction and magnitude of the dipole moments of isolated guanine and adenine.

2. Systems Studied

The interactions of guanine and adenine with the following metallic ions were considered: Li^+, Na^+, K^+, Rb^+, Cs^+, Cu^+, Ag^+, Au^+, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Cd^{2+}, and Hg^{2+}. For these elements from groups Ia, Ib, IIa, and IIb, the single-determinant Hartree−Fock approach is assumed to be sufficiently correct. The transition metal ions (i.e. Fe, Pt, Mo, ...), which will be studied in the future, require the use of a multideterminant approach. We limit the optimization to the planar C_s structures of the base···X^{n+} complexes, where metal cations X^{n+} interact with the nitrogen atom N7 of adenine or N7 and O6 atoms of guanine. This means that X interacts with two attractive centers of guanine, whereas in the case of adenine there is only one attraction center. These positions are known[8] to be the active sites for the interaction of metal ions with nucleic acids in the various biological systems. The structures and atom numbering of the complexes studied are depicted in Figure 1.

3. Calculations

The structures of all the systems were optimized using the analytical gradient method in the framework of the Hartree−Fock formalism. For the optimized geometries the correlation energies were calculated by the Møller−Plesset second-order perturbation theory (MP2). All the electrons were considered in the MP2 calculations; that is, no "frozen electrons" were taken into account. The interaction energy (ΔE) was determined as the difference of the optimized energy of the base···metal cation [E(B···X^{n+})] system and the sum of the energies of the base [E(B)] and the metal cation[E(X^{n+})]:

$$\Delta E = E(\mathrm{B}\cdots\mathrm{X}^{n+}) - [E(\mathrm{B}) + E(\mathrm{X}^{n+})] \qquad (1)$$

Since finite basis sets were used, the basis set extension effect must be eliminated. We used the standard Boys−Bernardi function counterpoise method,[18] in which all the occupied and virtual orbitals of the "ghost" subsystem were considered. The HF deformation energy (ΔE_{Def}) is defined as the difference between the energy of an optimized base and the energy of a base in the geometry of the optimized base···X^{n+} system.

TABLE 1: Optimized Intermolecular Parameters (in Å and deg) for Base···X^{n+} Complexes

	guanine[b]			adenine[b]	
X[a]	X−N7	X−N7−C2	X−O6	X−N7	X−N7−C4
Li(AE)	2.09	164.2	1.93	1.92	135.2
Na(AE)	2.41	159.2	2.26	2.30	137.2
Na(PS)	2.42	159.1	2.27	2.31	137.4
K(AE)	2.86	154.5	2.67	2.79	140.2
K(PS)	2.85	154.6	2.66	2.78	140.6
Rb(PS)	3.03	153.1	2.81	2.97	141.4
Cs(PS)	3.24	152.3	2.95	3.14	141.9
Mg(AE)	2.06	160.8	1.94	1.95	131.5
Mg(PS)	2.07	160.9	1.95	1.96	131.7
Ca(AE)	2.48	157.1	2.31	2.38	134.5
Ca(PS)	2.47	157.1	2.31	2.38	134.5
Sr(PS)	2.65	155.7	2.46	2.56	136.3
Ba(PS)	2.82	154.9	2.54	2.65	137.1
Cu(PS)	2.15	157.9	2.18	1.98	132.2
Ag(PS)	2.46	154.7	2.44	2.28	133.9
Au(PS)	2.31	147.8	2.64	2.17	131.7
Zn(PS)	1.98	160.3	1.91	1.87	130.2
Cd(PS)	2.24	157.0	2.18	2.12	131.5
Hg(PS)	2.26	155.4	2.22	2.11	130.6

[a] AE = all-electron calculation; PS = pseudopotential calculation. [b] Cf. Figure 1.

TABLE 2: Optimized Energy Characteristics[a] (in kcal/mol) for Base···X^{n+} Complexes

	guanine				adenine			
X[b]	ΔE^{HF}	ΔE_{Def}	ΔE_{BSSE}	ΔE^{MP2}	ΔE^{HF}	ΔE_{Def}	ΔE_{BSSE}	ΔE^{MP2}
Li(AE)	−85.4	5.2	0.6	−78.3	−43.2	2.0	1.2	−40.4
Na(AE)	−62.6	2.6	3.8	−56.8	−27.4	1.4	2.4	−25.6
Na(PS)	−62.5	2.6	4.0	−56.8	−27.2	1.4	2.4	−25.6
K(AE)	−45.2	1.4	4.0	−40.7	−15.6	0.9	2.0	−14.6
K(PS)	−45.2	1.4	4.0	−40.1	−15.6	0.9	2.1	−14.5
Rb(PS)	−40.1	1.1	3.8	−35.7	−12.6	0.7	2.0	−11.6
Cs(PS)	−38.5	1.2	5.8	−37.4	−11.4	0.7	3.5	−12.6
Mg(AE)	−227.1	15.7	−5.3[c]	−212.6	−126.7	7.8	−2.2[c]	−122.3
Mg(PS)	−221.6	15.4	−4.4[c]	−206.0	−119.4	6.2	−1.4[c]	−112.2
Ca(AE)	−149.2	8.4	0.5	−137.0	−70.2	4.6	0.2	−66.8
Ca(PS)	−149.2	8.4	0.5	−136.6	−70.2	4.6	0.3	−66.7
Sr(PS)	−128.3	6.8	1.7	−116.6	−56.5	3.9	0.7	−53.2
Ba(PS)	−125.4	7.5	4.1	−120.3	−54.6	4.0	2.7	−55.5
Cu(PS)	−76.5	4.2	3.6	−80.3	−46.4	2.3	2.9	−56.6
Ag(PS)	−62.8	2.6	6.8	−63.8	−33.7	1.8	4.7	−37.8
Au(PS	−67.2	2.8	6.7	−75.7	−45.3	2.6	5.2	−57.3
Zn(PS)	−248.7	17.6	−4.9	−245.5	−155.3	9.4	−2.3	−161.3
Cd(PS)	−199.0	12.0	3.0	−196.9	−119.3	7.7	1.3	−123.8
Hg(PS)	−205.3	12.3	1.8	−212.2	−137.0	9.2	0.0	−149.3

[a] ΔE^{HF} and ΔE^{MP2} are the interaction energies evaluated at HF and MP2 levels using the function counterpoise method; ΔE_{Def} is the HF deformation energy; and ΔE_{BSSE} means the total basis set superposition error (sum of HF and MP2 parts). [b] AE = all-electron calculation; PS = pseudopotential calculation. [c] The negative BSSE comes from the fact that only HF energy was optimized.

For all the metal cations (with the exception of Li^+) the Christiansen average relativistic effective pseudopotentials (AREP)[19] were used. For the base···X^{n+} (X^{n+} = Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}) complexes the all-electron (AE) treatment was also applied. Guanine and adenine were described by the standard 6-31G** basis sets,[20] and DZ basis sets of Schaefer[21] were employed for the metal cations. The Gaussian 92 set of programs[22] was used utilizing the direct mode for both the SCF and MP2 parts.

4. Results and Discussion

The optimized geometry parameters, energy, and population characteristics for all the complexes of guanine and adenine are summarized in Tables 1−4.

4.1. Reliability of the Pseudopotentials. For the Na^+, K^+, Mg^{2+}, and Ca^{2+} complexes, both AE and AREP treatments were adopted. Because the relativistic effects could be neglected for these elements, any difference in the calculated characteristics indicates inadequacies in the pseudopotentials used. The

TABLE 3: Intramolecular Changes in Base Geometry Parameters in Guanine···X and Adenine···X Complexes in Comparison with the Isolated Base: Five Greatest Deviations of Bond Length (in Å)

	guanine[a]					adenine[a]				
X[b]	N1−C6	C6−O6	C5−C6	N3−C4	C2−N2	C8−N9	N7−C8	C5−N7	N3−C4	C4−N9
Li(AE)	1.374	1.226	1.400	1.337	1.331	1.339	1.300	1.401	1.316	1.371
Na(PS)	1.383	1.219	1.410	1.338	1.333	1.345	1.296	1.398	1.318	1.368
K(PS)	1.390	1.214	1.417	1.340	1.335	1.351	1.292	1.395	1.320	1.367
Rb(PS)	1.392	1.212	1.419	1.341	1.336	1.353	1.290	1.394	1.320	1.367
Cs(PS)	1.391	1.214	1.417	1.341	1.336	1.353	1.291	1.394	1.320	1.367
Mg(PS)	1.353	1.262	1.376	1.317	1.315	1.311	1.327	1.425	1.303	1.383
Ca(PS)	1.363	1.245	1.391	1.322	1.320	1.324	1.313	1.415	1.308	1.375
Sr(PS)	1.367	1.240	1.396	1.324	1.321	1.328	1.309	1.412	1.310	1.373
Ba(PS)	1.365	1.247	1.390	1.323	1.321	1.326	1.309	1.411	1.309	1.375
Cu(PS)	1.378	1.222	1.405	1.337	1.331	1.338	1.299	1.401	1.315	1.370
Ag(PS)	1.383	1.219	1.410	1.338	1.332	1.341	1.298	1.399	1.316	1.370
Au(PS)	1.385	1.212	1.414	1.338	1.332	1.336	1.300	1.400	1.315	1.372
Zn(PS)	1.350	1.267	1.373	1.315	1.314	1.307	1.329	1.428	1.301	1.385
Cd(PS)	1.357	1.258	1.381	1.316	1.315	1.311	1.325	1.420	1.303	1.383
Hg(PS)	1.356	1.259	1.381	1.316	1.315	1.309	1.327	1.422	1.301	1.385
isol. base	1.416	1.194	1.434	1.353	1.347	1.371	1.280	1.382	1.328	1.362

[a] Cf. Figure 1. [b] AE = all-electron calculation; PS = pseudopotential calculation.

TABLE 4: Net Atomic Charges (in *e*) on Selected Atoms of the Guanine···X and Adenine···X Complexes Obtained by Mulliken Population Analysis

	guanine[a]					adenine[a]			
X[b]	X	N7	O6	H21	H1	X	N7	N1	H21
Li(AE)	0.86	−0.73	−0.75	0.34	0.36	0.90	−0.88	−0.63	0.36
Na(AE)	0.90	−0.69	−0.74	0.34	0.36	0.92	−0.81	−0.63	0.35
Na(PS)	0.89	−0.69	−0.74	0.34	0.36	0.92	−0.80	−0.63	0.35
K(AE)	0.93	−0.65	−0.71	0.34	0.35	0.95	−0.74	−0.64	0.35
K(PS)	0.93	−0.65	−0.71	0.34	0.35	0.95	−0.74	−0.63	0.35
Rb(PS)	0.94	−0.64	−0.71	0.33	0.35	0.95	−0.71	−0.64	0.35
Cs(PS)	0.88	−0.62	−0.70	0.33	0.35	0.92	−0.70	−0.64	0.35
Mg(AE)	1.70	−0.95	−0.89	0.37	0.39	1.76	−1.13	−0.60	0.39
Mg(PS)	1.77	−0.98	−0.92	0.37	0.39	1.83	−1.18	−0.60	0.39
Ca(AE)	1.86	−0.88	−0.88	0.36	0.38	1.89	−1.02	−0.61	0.38
Ca(PS)	1.85	−0.88	−0.88	0.36	0.38	1.89	−1.02	−0.61	0.38
Sr(PS)	1.88	−0.84	−0.87	0.36	0.37	1.91	−0.97	−0.61	0.38
Ba(PS)	1.75	−0.78	−0.83	0.36	0.38	1.81	−0.90	−0.61	0.38
Cu(PS)	0.92	−0.79	−0.74	0.34	0.36	0.92	−0.95	−0.63	0.36
Ag(PS)	0.78	−0.67	−0.69	0.34	0.36	0.81	−0.79	−0.63	0.36
Au(PS)	0.75	−0.71	−0.65	0.34	0.36	0.73	−0.82	−0.63	0.36
Zn(PS)	1.75	−1.04	−0.91	0.37	0.39	1.73	−1.21	−0.59	0.39
Cd(PS)	1.48	−0.81	−0.77	0.36	0.39	1.55	−0.93	−0.60	0.39
Hg(PS)	1.44	−0.80	−0.74	0.37	0.39	1.44	−0.90	−0.60	0.39
isol. base		−0.51	−0.60	0.32	0.33		−0.57	−0.66	0.33

[a] Cf. Figure 1. [b] AE = all-electron calculation; PS = pseudopotential calculation.

geometry parameters for the complexes of guanine and adenine with Na$^+$, K$^+$, Mg^{2+}, and Ca^{2+} evaluated by the all-electron and pseudopotential methods (cf. Table 1) differ negligibly; the energy characteristics (cf. Table 2) of these complexes differ slightly more. The largest difference was found for Mg^{2+} complexes, where pseudopotentials give smaller stabilization energies; the respective difference is 2.4% for guanine and 5.8% for adenine. The agreement between the AE and AREP results for the Na$^+$, K$^+$, Mg^{2+}, and Ca^{2+} complexes is very good and suggests that AREP can also be used with the confidence for complexes of guanine and adenine with the other cations.

4.2. Geometry Parameters. For the sake of consistency, only results obtained using pseudopotentials will be discussed; for Li$^+$ complexes, the all-electron results will be considered.

Intermolecular Parameters. All the intermolecular distances X−N7 for adenine-containing complexes are shorter than the corresponding distances in guanine. This can be explained by the fact that there is a second attractive side in guanine, i.e. not only nitrogen N7 but also oxygen O6. The competitive X−O6 attraction is rather strong, and the X−O6 distances are, with the exception of Au$^+$ complexes, even shorter than the corresponding X−N7 distances. The intermolecular X−N7 distance monotonically increases with the atomic number for the alkali metals and metals of alkali earths (cf. Figure 2 and Table 1). This increase is more pronounced for the former metals, where it amounts to more than 1 Å (from Li$^+$ to Cs$^+$). The calculated X−N7 distances for both types of metals correlate with the known ionic radii.[23]

The dependence of the X−N7 distances on the atomic number for coin metals is not monotonic for guanine and adenine but exhibits extremes. Au−N7 distances are shorter than Ag−N7 (cf. Figure 2 and Table 1). This is clearly due to relativistic effects. For IIb transition metals, the relativistic effects for Hg^{2+} are less pronounced than for Au$^+$ (but are still important), and therefore, the Hg−N7 distances are comparable to Cd−N7 distances.

The influence of the relativity on the 5s, 4d, and 5p electrons (Cs$^+$, Ba^{2+}) is not as marked as for 5d electrons (Au$^+$, Hg^{2+}).[24] This is the reason that relativistic effects were not so visible in previously discussed alkali groups. It must be mentioned here that, for coin metals and IIb transition metals, there is no correlation between the calculated X−N7 distances and experimental ionic radii.[23] The experimental ionic radii[23] for coin metals and IIb transition metals also increase linearly with the atomic number. We do not have an explanation for this phenomenon.

All the complexes studied were kept planar; that is, metal ions approach guanine and adenine in the molecular plane. In the case of guanine···X$^+$ and adenine···X$^+$ (X = Li, Cu) also the nonplanar structures were investigated at the MP2 level, but their stabilization energies were lower.

Intramolecular Parameters. The geometries of isolated bases and bases in the complexes differ considerably (cf. Table 3). We have analyzed only bond lengths and bond angles among heavy atoms because only these geometric parameters could be determined from X-ray measurements. Because the complexes were held planar, the dihedral angles were not allowed to change. The five largest bond length deviations of guanine···X and adenine···X complexes are summarized in Table 3. With the exception of the C6−O6 and C2−N2 bond lengths, the most prominent bond length changes in guanine under the influence of the ion are in the six-membered ring. All the bond lengths in the ring become shorter; the same is true also for the C2−N2 and C6−O6 bonds. The bond angles in guanine are affected less by the ions; the most important change occurs in the C5−C6−O6 angle, which, due to the direct interaction of O6 with

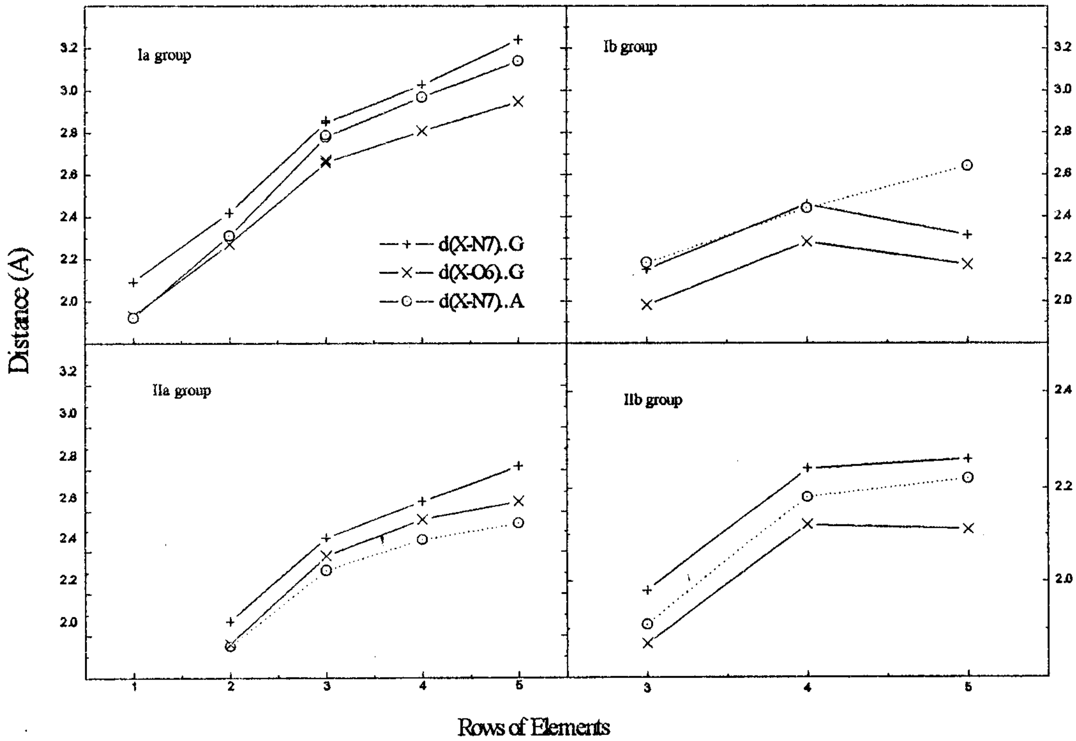

Figure 2. Dependencies of intermolecular distances on the atomic number of the ion for guanine···X and adenine···X complexes for ions of groups Ia, Ib, IIa, and IIb. Solid line with + symbols indicates the X−N7 distance in guanine, dotted line with × symbols indicates the X−O6 distance in guanine, and solid line with ○ symbols indicates the X−N7 distance in adenine.

metal cations, decreases by about 6°. The situation differs considerably in adenine-containing complexes. Here, all the most important bond length changes take place in the five-membered ring. The only exception is the changes in amino group caused by direct repulsion between the metals and the NH_2 group. The C5−C6−N6 bond angle decreases by about 3.0°, while the C6−N6 distance is almost not changed. Correlation between the bond length changes and stabilization energy was found for both types of complexes; consequently, the bond length changes in guanine are larger than in adenine.

We can only speculate about the reasons that it is the six-membered ring in guanine and five-membered ring in adenine which are predominantly affected by the ions. It could indicate that the X−O6 interaction in guanine is stronger than the X−N7 interaction. The internuclear X−O6 distances were found to be mostly shorter than the X−N7 distances. The favored orientation of charge and dipole in guanine complexes (see Figure 1) probably also plays a role. The Cartesian coordinates of all the optimized complexes are available upon request.

4.3. Energy Characteristics. The stabilization energies of guanine···X complexes are systematically larger than those of adenine···X complexes (cf. Table 2). This is due to the large dipole moment of guanine and, further, also to the more favorable orientation of the ions and guanine dipole moment (see Figure 1). Another argument for larger stabilization energy for guanine complexes is the existence of two attraction centers (O6 and N7); in adenine complexes there is only one attraction center (N7). The stabilization energies of the complexes with bivalent ions are larger than those with monovalent ions, and as expected, the stabilization energies of the guanine and adenine metal complexes decrease with increasing atomic number of the metal ions. The only exceptions are the Au^+ and Hg^{2+} complexes, in which, due to relativistic effects, the respective stabilization energies are larger than those of complexes with the preceding ions (Ag^+ and Cd^{2+}).

The role of electron correlation could be evaluated by comparing ΔE^{HF} and ΔE^{MP2}. For cations of the alkali metals and alkaline earth metals, ΔE^{MP2} is systematically larger (i.e. smaller stabilization energy), due to reduction of the dipole moment of the base when passing from the HF to the MP2 treatment. The intersystem correlation energy, which is always negative (stabilizing), is small in these complexes and does not compensate the positive (repulsive) intrasystem correlation term originating in the above-mentioned change in the dipole moment. For coin metals, ΔE^{MP2} is smaller (i.e. more stable) than ΔE^{HF}, reflecting the larger (stabilizing) role of the intersystem correlation energy, as well as the larger extent of covalent character of the intermolecular bond (see below). ΔE^{MP2} is also more stable than ΔE^{HF} for Hg^{2+} complexes with both adenine and guanine.

The largest stabilization energy (at the MP2 level) for guanine and adenine was found for the bivalent transition ions, the only exception is the guanine···Mg^{2+} complex. The stabilization energies of coin metals and alkali metals are smaller.

The deformation energy of bases reflects deformability of the base in the field of an ion. The deformation energy of guanine is larger than that of adenine, corresponding to the larger stabilization energy of guanine-containing complexes. The deformation energies of the complexes of bivalent ions are larger than those of monovalent ions. The increase in the ion atomic number leads to a decrease in the deformation energy; the heavy elements (Cs, Ba, Au, Hg) constitute an exception. The base···ion deformation energies are considerably larger than those of DNA base pairs which lie between 0.6 and 2.5 kcal/mol.[17d]

Values of the basis set superposition error (BSSE) are also presented in Table 2. Clearly, for the complexes of both types the total (SCF+MP2) BSSE is rather small, not exceeding 16% of the MP2 stabilization energy. Deformation energy and BSSE are roughly comparable in size.

4.4. Analyses of Wave Functions. *Mulliken Population.* Mulliken net atomic charges of selected atoms of guanine$\cdots$X and adenine$\cdots$X complexes are presented in Table 4. The atoms chosen (with the exception of X) participate in H-bonding between DNA bases. The amount of charge transfer (CT) between a base and an ion is easily determined as the difference between the charge of the isolated ion and the net atomic charge of the metal. The CT for guanine$\cdots$X complexes is systematically larger than that for adenine$\cdots$X complexes. The only exceptions are Au and Zn atoms, where slightly less positive metals were found in adenine complexes. For complexes of alkali metals and the alkaline earth metals, the smallest CT was found for elements Rb and Sr. The fact that dependence of CT on the atomic number for both types of complexes exhibits an extreme could be interpreted in terms of higher covalent contributions by Cs and Ba ions (compared to Rb and Sr). This point is briefly discussed in the next paragraphs. Partial charges on atoms O6 and N7 in guanine and adenine complexes decrease monotonically with increasing atomic number of metal ions. The only exception is atom N7 of the Au−guanine complex, where strong relativistic effects in Au play a key role. The O6 charges in the guanine complex change, however, monotonically. The reason is the same as for the above-mentioned larger Au−O distance and will also be discussed later. Atomic charges on the hydrogen atoms in guanine and adenine as well as on the N1 nitrogen of adenine differ only slightly in the complexes of mono- and divalent ions.

Molecular Orbitals. The aim of the present analysis is to elucidate the above-mentioned behavior of energy, geometry, and net charge dependencies on the atomic number in individual groups of metals studied. The wave function contains all the necessary information on various system properties including energy. Analyses of the MOs of alkali metal complexes revealed no mixing of Li cation orbitals with the orbitals of the bases. For Na and K ions, slight mixing of ion $(n-1)$s and $(n-1)$p orbitals was detected in the MOs of the base with a main contribution of N7 and, in the case of guanine, O6 electron pairs (back-donation). The most important contribution comes from the localized lone pair orbitals of the guanine N7 and O6 and adenine N7 atoms interacting with orbitals of metals. This "donating" mixing become even stronger for the Rb and Cs ions. Further, another type of mixing appears for these ions, where the AOs of the base N7 and O6 lone pairs penetrate into the MO containing localized electrons of the ion. Finally, for the Cs ion, an additional type of MO bonding combination occurred, where two or one new σ-bonding orbitals (for guanine and adenine, respectively) were created. These new orbitals are clearly of covalent nature. All this elucidates the highly ionic character of base$\cdots$Li$^+$ bonding and increasingly covalent character of bonding when passing from Na$^+$ to Cs$^+$. The decreasing ionic character corresponds to decreasing ΔE^{HF} (cf. Table 2).

The interaction of the AOs of the ion and the MOs of the base is basically not changed, when passing from the alkali metals to the alkaline earth metals.

In coin metal complexes, the bonding interaction becomes stronger due to the presence of higher energy d-orbitals (compared with the p-orbitals of the alkali metals), enabling better donation interaction of these orbitals with the lone pair orbitals of bases. One of the five d-orbitals of the coin metals is completely involved in the "σ-bonding" orbital of the complex. This leads to the increased coordination covalent character of the bonding and thus explains the basic difference between K$^+$ and Cu$^+$ bonding. The peculiar behavior of the Au$^+\cdots$guanine complex, especially the Au−O6 bond distance (see above), could be interpreted in terms of the bonding or antibonding character of the N7 and O6 in one of the MOs describing the metal−guanine interaction. Whereas for the Cu$^+$ and Ag$^+$ complexes this MO contains only the bonding combination of the metal d-orbitals with the orbitals of the lone pair of guanine N7, for Au$^+$, a comparable amount of antibonding combination of O6 also takes place. The antibonding character gives rise to a quite strong repulsion interaction between the Au and O6 atoms. Consequently, the Au$^+$ ion is pushed away from O6 (cf. Table 1 and Figure 2, Ib), and O6 partial charge becomes less negative and Au$^+$ less positive (cf. Table 4). In the complexes of group IIb cations we found trends which combine the behavior of metals of both groups IIa and Ib, i.e. strong Coulombic interaction via the 2+ charge and high covalent d-orbital−lone pair bonding interaction, resulting in very strong bond interaction.

5. Conclusions

(1) The geometry and energy characteristics for guanine$\cdots$X and adenine$\cdots$X complexes where X = Na$^+$, K$^+$, Mg^{2+}, and Ca^{2+} were evaluated using the pseudopotential and all-electron treatments; the agreement between the results was very good and gave us the confidence to use pseudopotentials for heavier cations.

(2) The X−N7 distances for adenine-containing complexes are shorter than those in guanine-containing complexes. This is due to the existence of a second attractive site in guanine-containing complexes; the X−O6 distances are mostly shorter than the corresponding X−N7 ones.

(3) The most important intramolecular geometry changes induced by ions occurred (with the exception of exocyclic groups) in the six-membered ring of guanine and five-membered ring of adenine.

(4) The stabilization of guanine$\cdots$X complexes are systematically larger than those of adenine$\cdots$X complexes. This is due to the larger dipole moment of guanine and more favorable orientation of the ions and the guanine dipole moment.

(5) The strongest bonding interactions for both guanine$\cdots$X and adenine$\cdots$X complexes were found for the metal cations of group IIb.

(6) Charge transfer for guanine$\cdots$X complexes is mostly larger than that for adenine$\cdots$X complexes.

(7) Relativistic effects are pronounced for Au$^+$ and Hg^{2+} ions; dependencies of energy and geometry characteristics on the atomic number exhibit dramatic irregularities for these ions.

References and Notes

(1) Eichhorn, G. L. *Adv. Inorg. Biochem.* **1981**, *3*, 1.

(2) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984.

(3) Martin, R. B. *Acc. Chem. Res.* **1985**, *18*, 32.

(4) Sigel, H. *Chem. Soc. Rev.* **1993**, *22*, 255.

(5) Potaman, V. N.; Soyfer, V. N. *J. Biomol. Struct. Dyn.* **1994**, *11*, 1035.

(6) Guschlbauer, W.; Chantot, J. F.; Thiele, D. *J. Biomol. Struct. Dyn.* **1990**, *8*, 491.

(7) Egli, M.; Gessner, R. V. *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 180.

(8) Anwander, E. H. S.; Probst, M. M.; Rode, B. M. *Biopolymers* **1990**, *29A*, 757.

(9) Hobza, P.; Sandorfy, C. *J. Biomol. Struct. Dyn.* **1985**, *2*, 1245; *Biophys. Chem.* **1984**, *19*, 201.

(10) Del Bene, J. E. *J. Phys. Chem.* **1984**, *88*, 5927.

(11) Jia, X.; Marzilli, L. G. *Biopolymers* **1991**, *31*, 23.

(12) Michenkova, L. E.; Ivanov, V. I. *Biopolymers* **1967**, *5*, 615.

(13) Shin, Y. A.; Eichhorn, G. I. *Biochemistry* **1968**, *7*, 1026.

(14) Duguid, J.; Bloomfield, V. A.; Benevides, J.; Thomas, G. J., Jr. *Biophys. J.* **1993**, *65*, 1916.

(15) Langlais, M.; Tajmir-Riahi, H. Q.; Savoie, R. *Biopolymers* **1990**, *30*, 743.

(16) Jean, Y.-C.; Gao, Y.-G.; Wang, A. H. *J. Biochem.* **1993**, *32*, 381.

(17) (a) Šponer, J.; Hobza, P. *J. Phys. Chem.* **1994**, *98*, 3161. (b) Hobza, P.; Šponer, J.; Polášek, M. *J. Am. Chem. Soc.* **1995**, *117*, 792. (c) Šponer, J.; Hobza, P. *Chem. Phys.*, in press. (d) Šponer, J.; Leszczynski, J.; Hobza, P. *J. Phys. Chem.* **1996**, *100*, 1965. (e) Šponer, J.; Leszczynski, J.; Hobza, P. *J. Phys. Chem.* **1996**, *100*, 5590.

(18) Boys, F. S.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.

(19) (a) Pacios, L. F.; Christiansen, P. A. *J. Chem. Phys.* **1985**, *82*, 2664. (b) Hurley, M. M.; Pacios, L. F.; Christiansen, P. A.; Roos, R. B.; Ermler, W. C. *J. Chem. Phys.* **1986**, *84*, 6840. (c) LaJohn, L. A.; Christiansen, P. A.; Roos, R. B.; Atashroo, T.; Ermler, W. C. *J. Chem. Phys.* **1987**, *87*, 2812. (d) Roos, R. B.; Powers, J. M.; Atashroo, T.; Ermler, W. C.; LaJohn, L. A.; Christiansen, P. A. *J. Chem. Phys.* **1990**, *93*, 6654.

(20) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257.

(21) Schaefer, A.; Horn, H.; Ahlrichs, R. *J. Chem. Phys.* **1992**, *93*, 2571.

(22) *Gaussian 92*, Revision A; Frisch, J., Truck, G. W., Head-Gordon, M., Gill, P. M., Wong, M. W., Foresman, J. B., Schlegel, H. B., Robb, M. A., Gomperts, R., Andres, L., Raghavachari, K., Binkley, J. S., Gonzalez, C., Martin, R. L., Fox, D. J., Defrees, D. J., Steward, J. J. P., Pople, J. A., Eds.; Gaussian Inc.: Pittsburgh, PA, 1992.

(23) *CRC Handbook of Chemistry and Physics*, 57th ed.; Weast, R. C., Ed.; CRC Press: Cleveland, OH, 1976−1977.

(24) Pyykko, P. *Chem. Rev.* **1988**, *88*, 563.

JP952941H