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and at the same time partly coordinated to its crown ether host.

As indicated in the Experimental section, despite numerous and extensive computational efforts, we could not extract from the experimental data kinetic parameters appropriate to the **3**$\cdot$Na$^+$ and to the Na$^+\cdot$**3**$\cdot$Na$^+$ systems. We were left in the quandary of having either too many parameters to extract from a limited number of experimental points or of cutting down drastically upon the number of rate constants to be determined, and finding that in the process of constraining our model on such a Procustean bed we killed it! Back of the envelope calculations show further that with diffusion-controlled values of k_+ in the 10^7–10^8 M^{-1} s^{-1} range, k_- for compounds **2** and **4** as estimated from the K_1 values (Tables II and IV) would be in the range of 10^4–10^6 s^{-1}, i.e., too fast to display intermediate exchange behavior—exactly as is found qualitatively in the temperature range accessible with pyridine solutions.

Conclusion

Like other crown ethers, spiro-bis-crown ethers form, at high ligand concentration, sandwich complexes having one Na$^+$ ion in between two ligand molecules. These 2:1 complexes coexist with 1:1 complexes. Conformational factors are important, besides cavity size, in determining the magnitude of K for these 1:1 complexes. But the distinctive feature of these ligands, with their two cavities offered as cation-binding sites, is formation of dicationic 1:2 complexes. These doubly occupied complexes of spiro-bis-crown ethers are *less* disfavored than could have been feared on the basis of strong electrostatic repulsions; furthermore, entropy variations appear to be more favorable to double occupancy than to single occupancy of the two binding sites. Hence, direct examination of the thermodynamics and kinetics of cation binding from nuclear magnetic resonance of the cation itself proves to be rewarding and to provide a wealth of information.

Note Added in Proof. The recent X-ray structure of the complex formed between O$_6$–O$_6$ and 2LiI, 4H$_2$O shows that each of the macrorings binds one of the water solvation molecules and an Li$^+$ ion in the same cavity, the metal ion being coordinated to three oxygens from the macroring and to two oxygens from water molecules.[21] This observation is consistent with our description of complex formation between O$_6$–O$_6$ and two Na$^+$ ions.

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Ab Initio SCF Studies of Interactions of Li$^+$, Na$^+$, Be^{2+}, and Mg^{2+} with H$_2$PO$_4^-$: Model for Cation Binding to Nucleic Acids

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Abstract: Phosphate anion–metal cation complexes of (OH)$_2$PO$_2^-$ with Li$^+$, Na$^+$, Be^{2+}, and Mg^{2+} have been studied by using ab initio self-consistent field methods with an extended, double ζ plus polarization, basis set. The most stable binding site for all cations is a symmetric C_{2v} complex with the metal interacting with two phosphate oxygen atoms, consistent with previous calculations. Significant electron transfer was found for all complexes except that involving Na$^+$, implying that Li$^+$, Be^{2+}, and Mg^{2+} interactions with phosphate are not totally electrostatic. Hydration of Li$^+$ and Be^{2+} does not significantly alter the extent of covalency of the metal–phosphate bond, although it weakens the direct complex formation by partial neutralization of the cation. All cations are found to affect both the geometry and electronic charge distribution of the phosphate group, consistent with their key role in determining nucleic acid conformational stability.

Nucleic acid structure is greatly influenced by the intrapolymer electrostatic forces involving the ionized phosphate groups of the backbone. Since the charges of these groups can be shielded by associated counterions, changes in ionic strength and ion type can trigger functionally important conformation changes in the polymer.

The sensitivity of nuclei acid structure to the concentration and type of cation with which it is associated has been established by a variety of experimental techniques. Well-defined conditions for obtaining DNA fibers in the A, B, and C forms have been determined by X-ray crystallographers.[1d] More recently, the identification of the circular dichroism spectrum for each of these forms in solution has allowed the observation of B → C + A transconformational reactions as a function of ion type and ionic strength.[2-4] The duplex rotation angle of closed circular DNA has been shown to depend on ion type and concentration.[5,6] The

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binding of Ca^{2+} to chromatin has been shown to induce a reversible transition from an uncondensed to a condensed state,[7] and the nulceoprotein core particles of chromatin have been shown to exhibit conformation changes as a function of ionic strength in NaCl solution.[8] Furthermore, the formation of certain complexes between polynucleotides and polypeptides has been shown to be mediated by Na^+ and Cu^{2+} ions.[9] Such changes in conformation and stability are of crucial importance to the biochemical functions of nuclei acids.

The extent of shielding of the phosphate group's charge depends on the nature of the association of counterion with the polyelectrolyte (nucleic acid). Although there is much activity directed at understanding this association, the nature of the association remains unclear.

The binding of counterions clearly alters the electrostatic potential of the phosphate groups, changing the intrapolymer energy and affecting the stability of various conformations. In addition to the decrease in phosphate–phosphate repulsions, calculations have suggested that counterion binding to the phosphate could induce base-sequential specific conformation changes in DNA.[10-12] The alteration of the phosphate potential can be described in terms of Debye–Hückel type screening[13-17] or by superposition of potentials of the spatially fixed, oppositely charged species (i.e., the phosphate and the cation).[18] A further alteration in the potential could occur if there is an electron donation from phosphate to cation resulting in a partial neutralization of the phosphate charge itself. This latter case would also be expected to show a stronger association due to the partial covalency of the phosphate–cation interaction.

In view of the uncertain state of knowledge concerning the nature of the phosphate–counterion interactions and its great significance in the understanding of nucleic acid structure and function, we report molecular-orbital calculations, more accurate than those of previous studies, on the nature of the bonds formed between each of Li^+, Na^+, Be^{2+}, Mg^{2+}, and $(OH)_2PO_2^-$ in direct complex formation. Specifically, we have calculated the stability, equilibrium geometry, and extent of electron transfer in each of these ion-pair complexes. The effect of retention of a water of hydration was also explored. Two types of interactions of cations with DNA have been proposed,[19-21] one involving nonspecific electrostatic interactions[19,20] and the other specific site binding.[21] It is the latter type, direct cation–phosphate complex formation, which is addressed in this study using molecular-orbital methods. The calculations were done by using an optimized extended atomic orbital basis set, with added polarization functions.

Previous ab initio calculations employing minimal basis sets have been performed.[22-24] Marynick and Schaefer[22] used the STO-3G basis, while Pullman et al.[23,24] used a relatively large Gaussian basis contracted to minimum for the phosphate and for the cation a modified STO-3G basis with the empty p orbitals suppressed and the remaining orbital exponents optimized. These pioneering calculations yielded the experimentally determined order of binding for Li^+, Na^+, and K^+ with DNA and showed that ab initio SCF calculations are useful in exploring the tight site-binding mode of cation DNA interactions.

The use of minimal basis set calculations, however, leads to questionable results when the nature of the binding interaction is considered. This basis set superposition error, discussed below, is substantial for minimal basis set calculations. Since the electronic structure of the $H_2PO_4^-$ and the cation will change when the complex is formed, a sufficiently complete basis set is needed to more accurately assess the detailed nature of the interaction. The studies of Umeyama and Morokuma[25] indicate that for $(H_2O)_2$ and $(HF)_2$ interactions, the calculated extent of charge transfer decreases as the size of the bais set increases from STO-3G to 4-31G to 6-31G. The use of polarization functions may be important because of the ionic nature of the species which are interacting.

The calculations reported here were designed to determine whether the binding of cations to $H_2PO_4^-$ is totally electrostatic or if it also involves a degree of covalency. The change in the phosphate charge distribution by electron donation and by polarization by the counterion is also addressed. Optimization of the OPO bond angle further allows any direct effect of the counterion on the phosphate group geometry to be considered. Finally, the effect of addition of a water molecule to the contact tight site-binding pair was also considered.

Method of Calculation and Procedure

All our results are from ab initio single configuration self-consistent field calculations, using the ALCHEMY program system which uses the MOLECULE integral generator of J. Almlof, in which molecular orbitals are expanded in the basis sets of Table I.[26] These basis sets are optimized for the constituent separated atoms but have the flexibility to accurately describe the atoms in their molecular environment. This is achieved by the use of two functions (so called double ζ) to describe the atomic valence shells plus polarization functions (p type for hydrogen and d type for the other atoms). We note that the oxygen basis set was optimized for the O^- negative ion and that the basis sets for sodium and magnesium contain low exponent p-type functions, optimized in atomic excited states, as is required for accurate calculation in systems containing these atoms. Polarization function exponents were optimized in the molecule in structures of C_{2v} symmetry shown in Figure 1. The phosphate geometry of Figure 1a is regularized from the crystal structure of B-DNA[27] so that it has two symmetry planes, thus greatly reducing computation time. Two hydrogen atoms were used in place of the C_3' and C_3' carbon atoms in the backbone of polynucleotides. Optimum d-function exponents were determined by using this geometry of $(HO)_2PO_2^-$, with the cation placed symmetrically between the two anionic oxygen atoms (C_{2v}) at the metal–oxygen (M–O) distance reported from STO-3G basis set calculations,[22] i.e., Li^+, Na^+, Be^{2+}, and Mg^{2+} M–O distances of 1.55, 1.98, 1.50, and 1.80 Å, respectively. The d exponent for Li^+ was fixed to obtain optimized d orbitals for P and O atoms, and those for the P and O atoms were allowed to vary to a minimum energy. These optimized values were then used to optimized the d-orbital exponents for all four cations, each time with respect to the total energy of the specific cation–$(OH)_2PO_2^-$ complex. This choice of basis should give results near the complete basis limit for the single-configuration wave functions we compute. One measure of this is the small superposition error[28] shown in Table II, which is the energy lowering of the separable fragments when they are computed in the full cation–phosphate basis. If the fragment basis sets were complete, there would be no energy lowering, although we must point out that the inverse is not true; the absence of energy lowering does not mean that a basis set is complete.

Our results for cation–phosphate interactions ignore correlation effects not contained in single-configuration wave functions. In comparing

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Table I. Contracted Gaussian-Type Function Basis Sets

	H		Li[a]		Be[a]		O[a]	
symmetry	exponent	contr. coeff.	exponent	contr. coeff.	exponent	contr. coeff.	exponent	contr. coeff.
s	48.7656	0.006068	1359.45	0.002035	3690.58	0.001565	10662.3	0.001906
	7.3365	0.045316	204.026	0.015642	551.066	0.012211	1599.71	0.014652
	1.6687	0.202846	46.5495	0.078324	123.771	0.064170	364.725	0.074198
	0.4692	0.503709	13.2326	0.283177	34.2308	0.254886	103.652	0.276102
			4.2862	0.710432	10.7237	0.749301	33.9877	0.718942
p	0.1479	1.0	1.4955	0.663781	3.5963	0.598985	12.3114	0.670073
			0.5422	0.377757	1.2419	0.449217	4.7413	0.366535
s			0.0740	1.0	0.1899	1.0	0.9541	1.0
s			0.0281	1.0	0.0678	1.0	0.2599	1.0
p	0.9	1.0	3.8263	0.010543	8.5168	0.012451	27.4344	0.025313
			0.7751	0.058882	1.8089	0.075567	6.1099	0.150480
			0.1976	0.269906	0.4898	0.211906	1.7636	0.418918
			0.0626	0.775839	0.1580	0.727652	0.5187	0.595137
p			0.0221	1.0	0.0534	1.0	0.1285	1.0
d			0.16	1.0	0.28	1.0	0.6	1.0

	Na[b]		Mg[b]		P[b]	
symmetry	exponent	contr. coeff.	exponent	contr. coeff.	exponent	contr. coeff.
s	36166.4	0.000623	43866.5	0.000659	77492.4	0.000627
	5372.6	0.004864	6605.4	0.005056	11605.8	0.004854
	1213.21	0.025425	1513.26	0.025836	2646.0	0.025048
	339.62	0.102300	432.32	0.101390	753.98	0.098740
	109.55	0.311048	142.15	0.307599	248.75	0.304553
	38.777	0.652313	51.398	0.653564	91.157	0.657557
	14.5759	0.859985	19.9196	0.788626	36.226	0.718987
	5.2699	0.163649	8.0247	0.237074	15.211	0.309062
	1.8278	0.625162	2.5082	0.562705	4.7139	0.497060
	0.6199	0.423660	0.8715	0.485763	1.7825	0.544561
	0.0572	1.0	0.1082	1.0	0.3427	1.0
	0.0240	1.0	0.0401	1.0	0.1247	1.0
	146.33	0.005289	194.67	0.004741	447.04	0.002853
	34.177	0.038426	45.600	0.035171	108.30	0.021481
	10.571	0.153661	14.198	0.144457	34.767	0.096358
	3.6908	0.349215	5.0224	0.341818	12.583	0.279576
	1.3194	0.443529	1.8359	0.452191	4.6988	0.470775
	0.4636	0.254554	0.6688	0.252282	1.7528	0.331236
p	0.0690	1.0	0.1412	1.0	1.7528	0.046703
					0.4221	0.973260
p	0.0209	1.0	0.0438	1.0	0.1253	1.0
d	0.33	1.0	0.28	1.0	0.6	1.0

[a] Unpublished basis sets generated by G. S. Chandler and A. D. McLean. [b] Details and evaluation of these basis sets is given in ref 26.

fragment and complex energies, these effects largely cancel, except for any correlation effects in the bonding of the cation to the phosphate.

Equilibrium geometries, energies, and electron distributions were calculated by the following procedure. (1) For each metal-phosphate complex, a symmetric approach of the cation to two nonprotonated oxygen atoms was investigated, as shown in Figure 1b, leading to a complex with C_{2v} symmetry. (2) The geometry of the C_{2v} complex was optimized with respect to energy by varying r, the phosphate–metal distance, and α, and O_1PO_2 bond angle (Figure 1b). (3) For Li^+ and Be^{2+}, an alternative path to complex formation was also investigated with the cation asymmetrically approaching one of the oxygen atoms (Figure 1c). In this geometry, leading to a complex of C_s symmetry, α was fixed at the experimental value, and the metal–oxygen distance (r_1) and PO_1M bond angle (β) were varied. (4) The energies of the $(OH)_2PO_2^-$ species at the experimental geometry and of each cation were calculated. (5) The interaction energy of each complex was calculated as the energy difference between the optimized complex and the isolated $(OH)_2PO_2^-$ and cation species. (6) Net atomic charges were calculated for the isolated species and the optimized complexes by a Mulliken population analysis[29]

Table II. Energies of the Cation and Phosphate Fragments Computed in the Fragment Basis Alone and in the Full Cation–Phosphate Basis

	energy, hartree	
species	fragment basis	cation–phosphate basis[b]
$H_2PO_4^-$	−641.5623[a]	−641.5658 (Li^+)
		−641.5662 (Be^{2+})
		−641.5645 (Na^+)
		−641.5627 (Mg^{2+})
H_2O[c]		−76.0462 $(Be\cdot H_2PO_4^-)^+$
		−76.0455 $(Li\cdot H_2PO_4)^0$
Li^+	−7.2361	−7.2361
Be^{2+}	−13.6107	−13.6107
Na^+	−161.6444	−161.6444
Mg^{2+}	−198.8084	−198.8084

[a] Geometry of Figure 1a. [b] Geometry of Figure 1b with α = 115.5° and r equal to the computed equilibrium energy. [c] Energy of H_2O with the experimental geometry in (cation·phosphate) optimum complex basis.

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Table III. Equilibrium Geometries[a] and Energies of a Series of Metal Cation-$(OH)_2PO_4^-$ Complexes

M	$\angle O_1PO_2$	d(PM)	$d(MO_1)$	$\angle PO_1M$	energy, hartree
Li^{+c}	115.55	2.29	1.95	82.2	−649.0516
Li^{+d}	107 (103)[b]	2.33	1.88 (1.77)[b]	87.1	−649.0573 (−640.7909)[b]
Be^{2+c}	115.55	1.92	1.69	73.8	−655.9000
Be^{2+d}	95 (89)[b]	2.00	1.48 (1.50)[b]	85.0	−655.9614 (−647.7363)[b]
Na^{+c}	115.55	2.66	2.25		
Na^{+d}	110 (105)[b]	2.70	2.21 (1.98)[b]		−803.4261 (−793.2700)[b]
Mg^{2+c}	115.55	2.34	1.99		−840.9210
Mg^{2+d}	102 (94)[b]	2.43	1.89 (1.80)[b]	91.5	−840.9432 (−830.4676)[b]
LiH_2O^{+e}	107 (103)[b]	2.33	1.88 (1.77)[b]	87.1	−725.1289 (−715.8309)[b]
BeH_2O^{2+e}	95 (89)[b]	2.00	1.48 (1.50)[b]	85.0	−732.1092 (−722.8654)[b]

[a] Distances in angstroms, angles in degrees. [b] The numbers in parentheses are previously reported results for theses complexes using a minimum basis set and total geometry optimization (ref 22). [c] These are for the experimental geometry of $H_2PO_4^-$ in DNAB with experimental P_1PO_2 angle and optimized MP distance only. [d] These results are for O_1PO_2 bond angle and MP distance optimization. [e] Metal–H_2O was not reoptimized. See text.

and used as a measure of electron transfer from the cation to $(OH)_2PO_2^-$.

(7) To determine the effect of hydration on charge transfer, we added symmetrically a H_2O molecule to the optimized C_{2v} complexes of Li^+ and Be^{2+} with $(OH)_2PO_2^-$, as shown in Figure 1b. The experimental geometry was used for the H_2O. The Li^+–O and Be^{2+}–O distances chosen were 1.89 and 1.54 Å, respectively, corresponding to optimized values calculated for the cation-monohydrates from extended bases set ab initio calculations.[30-32]

Results

Energies of the cation and phosphate fragments computed in the fragments basis alone and in the full cation–phosphate base are given in Table II. As mentioned, results in this table indicate a very small superposition error.

Calculated values of cation–phosphate complex total energies are given in Table III in two approximations, with the O_1PO_2 bond angle fixed as in B-DNA and with this value as well as the metal–phosphorus distance optimized. For comparison, previously reported results[22] from an STO-3G calculation with total geometry optimizations are also given. This table shows that both studies obtained significant decrease of the O_1PO_2 bond sangle upon complex formation. While the results obtained from an STO-3G basis with total geometry optimization[22] give a somewhat larger decrease in O_1PO_2 angle, both sets of results give the same order of effect of the cation, i.e., $Na^+ < Li^+ < Mg^{2+} < Be^{2+}$.

In Table IV, we list heats of formation for three processes: process A includes the heats of complex formation which show increasing stability in the order of $Na^+ < Li^+ < Mg^{2+} < Be^{2+}$, with Be^{2+} forming a complex nearly 4 times more stable than Na^+. The results from the previous STO-3G basis set calculation,[22] shown for comparison, while overestimating the stability of the complexes, give the same relative behavior. Process B includes the heats of hydration of Li^+ and Be^{2+} with a single water molecule. Assuming that the zero-point energy correction is negligible, the calculated energy of Li^+ aggrees extremely well with the experimental gas phase value[33] and lends credence to this level of calculation. Process C includes the heats of formation of complexes between hydrated Li^+ and Be^{2+} with $(OH)_2PO_2^-$. Both cations form significantly weaker complexes with $(OH)_2PO_2^-$ when hydrated but retain their relative stabilities.

In order to further characterize the energy surface for cation–phosphate complex formation, estimates of the change of energy about the minimum value of the phosphate–metal distance, d(PM), were obtained for displacements in two different directions in the O_1PO_2 plane: along and perpendicular to the C_2 axis. The results are given in Table V.

Table IV. Heats of Formation (ΔE) of [Metal Cation-$(OH)_2PO_2^-$] C_{2v} Complexes

A. Direct Metal-Phosphate Complex Formation: $(OH)_2PO_2^{-a} + M^{z+} \rightarrow [(OH)_2PO_2M]^{z-1\,b}$

M^{z+}	ΔE, kcal/mol	
	this work	STO-3G[c]
Na^+	−138.2	−202.1
Li^+	−162.5	−308.7
Mg^{2+}	−359.5	−497.0
Be^{2+}	−494.7	−711.0

B. Heat of Monohydration: $H_2O^d + M^{z+} \rightarrow (H_2O{\cdot}M)^{z-}$

M^{z+}	ΔE, kcal/mol	
	this work	exptl
Li^+	−33.3	−34[e]
Be^{2+}	−143.8	

C. Ternary Complex Formation: $(OH)_2PO_2^- + (H_2O{\cdot}M)^{z+} \rightarrow [(OH)_2PO_2{\cdot}M{\cdot}H_2O]^{z-1}$

M^{z+}	ΔE, kcal/mol this work
Li^+	−145.6
Be^{2+}	−414.7

[a] Experimental geometry (Figure 1a). [b] Optimized α, r (Figure 1b). [c] Reference 22. [d] Experimental water geometry (Figure 1b). [e] Reference 33.

Table V. Increase in Metal Cation-$OH_2PO_2^-$ Complex Energy with the Cation Displaced Perpendicular to[a] and along[b,c] the C_2 Axis in the O_1PO_2 Plane

cation	M–O distance, Å	ΔE,[a] kcal/mol	ΔE, kcal/mol	
Na^+	2.11	0.8	2.4[b]	2.0[c]
Li^+	1.76	1.4	4.6	3.0
Mg^{2+}	1.77	10.3	13.0	3.6
Be^{2+}	1.38	10.9	22.6	2.12

[a] Energy above the minimum complex energy for 0.2-Å displacement perpendicular to C_2 axis. [b] Energy above the minimum complex energy for 0.2-Å displacement of cation towards the P atom along the C_2 axis. [c] Energy above the minimum complex energy for 0.2-Å displacement of cation away from the P atom along the C_2 axis obtained from partial difference approximations to the derivatives using energies calculated at $\Delta X = 0.05$ Å for Li^+ and 0.1 Å for Na^+, Be^{2+}, and Mg^{2+}.

For the C_s complex of Li^+ and Be^{2+} with $(OH)_2PO_2^-$ (Figure 1c), an incomplete search was made for the equilibrium geometry. No minimum was found with either complex. The lowest energy $(Li\text{-}(OH)_2PO_2)$ complex that we computed has a Li–O distance of 1.7 Å and a value of β of 150° with α fixed at the experimental B-DNA value and a total energy ~16 kcal/mol above the lowest C_{2v} complex. Similarly, the lowest energy $(Be\text{–}(OH)_2PO_2)^+$ complex which we computed with r = 1.4 Å and β = 150° has an energy 73 kcal/mol higher than the minimum energy C_{2v} complex. Since this is a very high energy region, location of a local minimum was not completed for the C_s complex. However,

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Table VI. Gross Atomic Charges[a] and Extent of Charge Transfer in Metal Cation-$(OH)_2PO_2^-$ Complexes

		phosphate group								H_2O		
species	sym	q_P	q_{O_1}	q_{O_2}	q_{O_3}	q_H	Σ_q	q_M	Δe_1[b] phos → M	q_O	q_H	Δe_2[c] H_2O → M
$H_2PO_4^-$	C_{2v}	+1.71	−0.97	−0.97	−0.75	+0.35	−1.00					
H_2PO_4Li	C_{2v}	+1.81	−0.88	−0.88	−0.65	+0.36	−0.54	+0.54	0.46			
H_2PO_4Na	C_{2v}	+1.71	−1.01	−1.01	−0.68	+0.36	−0.95	+0.95	0.05			
$(H_2PO_4Be)^+$	C_{2v}	+1.80	−0.52	−0.52	−0.57	+0.39	+0.40	+0.60	1.40			
$(H_2PO_4Mg)^+$	C_{2v}	+1.71	−0.77	−0.77	−0.59	+0.38	−0.25	+1.25	0.75			
H_2PO_4Li	C_s[d]	+1.69	−0.89	−0.99	−0.69	+0.36	−0.85	+0.85	0.15			
$(H_2PO_4Be)^+$	C_s[e]	+1.56	−0.76	−0.78	−0.62	+0.38	+0.16	+0.84	1.16			
H_2O										−0.69	+0.35	
$(LiH_2O)^+$	C_{2v}							+0.80		−0.62	+0.41	0.20
$(H_2PO_4LiH_2O)$	C_{2v}	+1.83	−0.88	−0.88	−0.66	−0.36	−0.53	+0.38	0.46	−0.62	+0.39	0.16
$(BeH_2O)^{2+}$	C_{2v}							+1.30		−0.25	+0.48	0.70
$(H_2PO_4BeH_2O)^+$	C_{2v}	+1.74	−0.56	−0.56	−0.58	+0.38	+0.22	+0.32	1.22	−0.38	+0.42	0.46

[a] Calculated from Mulliken population analysis. [b] Number of electrons transferred from anionic $H_2PO_4^-$ to Li^+, Na^+, Be^{2+}, and Mg^{2+} cations in complex. [c] Number of electrons transferred from H_2O to Li^+ and Be^{2+}. [d] Atomic charges for the C_s complex with $\angle PO_1Li = 180°$ and LiO_1 distance of 1.7 Å are reported here. [e] Atomic charges for the C_s complex with $\angle PO_1Be = 180°$ and BeO_1 distance of 1.4 Å are reported here.

Table VII. Net Bond Overlap Population[a] in Metal Cation-$(OH)_2PO_2^-$ Complexes

species	sym	P-O_1	P-O_2	P-O_3	O_3-H	M-O_1	M-O_{H_2O}	$(O\text{-}H)_{H_2O}$
$H_2PO_4^-$[b]	C_{2v}	1.22	1.22	0.53	0.73			
H_2PO_4Li	C_{2v}	0.83	0.83	0.73	0.69	0.35		
H_2PO_4Na	C_{2v}	0.99	0.99	0.70	0.70	0.02		
$(H_2PO_4Be)^+$	C_{2v}	0.59	0.59	0.89	0.67	0.74		
$(H_2PO_4Mg)^+$	C_{2v}	0.73	0.73	0.82	0.68	0.47		
H_2PO_4Li	C_s[c]	0.54	1.37	0.67	0.72	0.30		
$(H_2PO_4Be)^+$	C_s[c]	0.21	1.33	0.67	0.70	0.91		
H_2O[b]								0.69
$(LiH_2O)^+$	C_{2v}						0.16	0.65
$(H_2PO_4LiH_2O)$	C_{2v}	0.81	0.81	0.73	0.68	0.36	0.22	0.65
$(BeH_2O)^{2+}$	C_{2v}						0.87	0.63
$(H_2PO_4BeH_2O)^+$	C_{2v}	0.62	0.62	0.99	0.67	0.67	0.87	0.63

[a] Calculated from a Mulliken population analysis. [b] Calculated for experimental geometry of $H_2PO_4^-$ and H_2O. [c] See footnotes *d* and *e* of Table VI for C_s complex geometry used.

while the geometry optimization was incomplete, these results very strongly suggest that symmetric C_{2v} cation–phosphate complex formation is preferred, in agreement with previous calculations.[22]

Table VI gives the calculated gross atomic charges from a Mulliken population analysis for $(OH)_2PO_2^-$, for optimized (cation–$H_2PO_4^-$) complexes in C_{2v} and C_s symmetry, and for hydrated Li^+ and Be^{2+} complexes with $(OH)_2PO_2^-$. These results can be used as a measure of electron donation from anion to cation in the complex. From this table, we see that in C_{2v} symmetry, the extent of electron transfer from the $(OH)_2PO_2^-$ to the cation is 0.05, 0.46, 0.75, and 1.4 e^-, respectively, for $Na^+ < Li^+ < Mg^{2+} < Be^{2+}$. In C_s symmetry, the less stable complex, there is less charge transfer to both Li^+ and Be^{2+}.

For the cation–water complexes, $(LiH_2O)^+$ and $(BeH_2O)^{2+}$, the gross atomic populations show that the H_2O donates 0.20 e and 0.70 e, respectively, to the cation. These are significantly greater than the values previously reported for these complexes. The larger electron transfer found in the presence calculations apparently results from the inclusion here of d polarization functions on the first-row cations. The previous calculations[30-32] on these systems utilized extended basis sets with d functions on the oxygen atoms but without d functions on the first-row cations and yielded an electron transfer of 0.018[31] and 0.48[32] e, respectively, for $(LiH_2O)^+$ and $(BeH_2O)^{2+}$. In the $(H_2PO_4{\cdot}Li{\cdot}H_2O)$ complex, the extent of charge transfer to Li^+ from both $(OH)_2PO_2^-$ and H_2O is about the same as in the individual complexes with each donor. In the $(H_2PO_4\text{-}Be\text{-}H_2O)^+$ complex, electron transfer is diminished from each donor when both are present in the complex.

The extent of covalent character of the metal–phosphate complex formed is also manifest by the bond overlap population in the M–O bond. As shown in Table VII, these values are 0.02, 0.35, 0.47, and 0.74 e for Na+, Li^+, Mg^{2+}, and Be^{2+} respectively. Table VII also shows that the phosphate–anionic oxygen (O_1,O_2) bond is weakened by cation binding to these oxygens, while, conversely, the phosphate–backbone oxygen bond is strengthened. Hydration of the cation appears to somewhat weaken the Be^{2+}–phosphate bond but has little effect on the Li^+–phosphate bond.

Table VIII. Comparison of the Distance of Approach from Summing Ionic Radii of the Cation and the Oxygen with the Metal–Oxygen Distance Obtained in this Work

cation	ionic radius[a]	contact[b]	*r*(M–O)[c]	diff
Na^+	0.95	2.35	2.21	0.14
Li^+	0.60	2.00	1.88	0.12
Mg^{2+}	0.65	2.05	1.89	0.16
Be^{2+}	0.31	1.71	1.48	0.23

[a] Reference 27. [b] The van der Waal's radius of O atom is 1.4 Å as is the ionic radius of O^{-2} ion. [c] This work.

Discussion

No direct experimental evidence exists to determine whether counterions exert their effect on polynulceotide conformation and stability by altering the charge distribution or the electrostatic potential of the constituent units of the polymer. Our calculations indicate that different ions may have different mechanisms of influence. As seen in Tables VI and VII, Na^+ has very little charge transferred to it, and the overlap population in the Na^+–O bond is negligible. Thus Na^+, which is virtually completely ionic in its binding to phosphate, would change the internal stability of nucleic acids mainly by the superposition of its potential on that of the phosphate, while Li^+, Be^{2+}, Mg^{2+} form covalent complexes with significant amounts of electron transfer and overlap population in the cation–oxygen bond. Li^+ accepts nearly half an electron (0.46 e^-, Table VI) and can form a partial covalent bond (0.35 e shared, Table VII) with each oxygen. The electron donation is equally shared by the four oxygen atoms and the

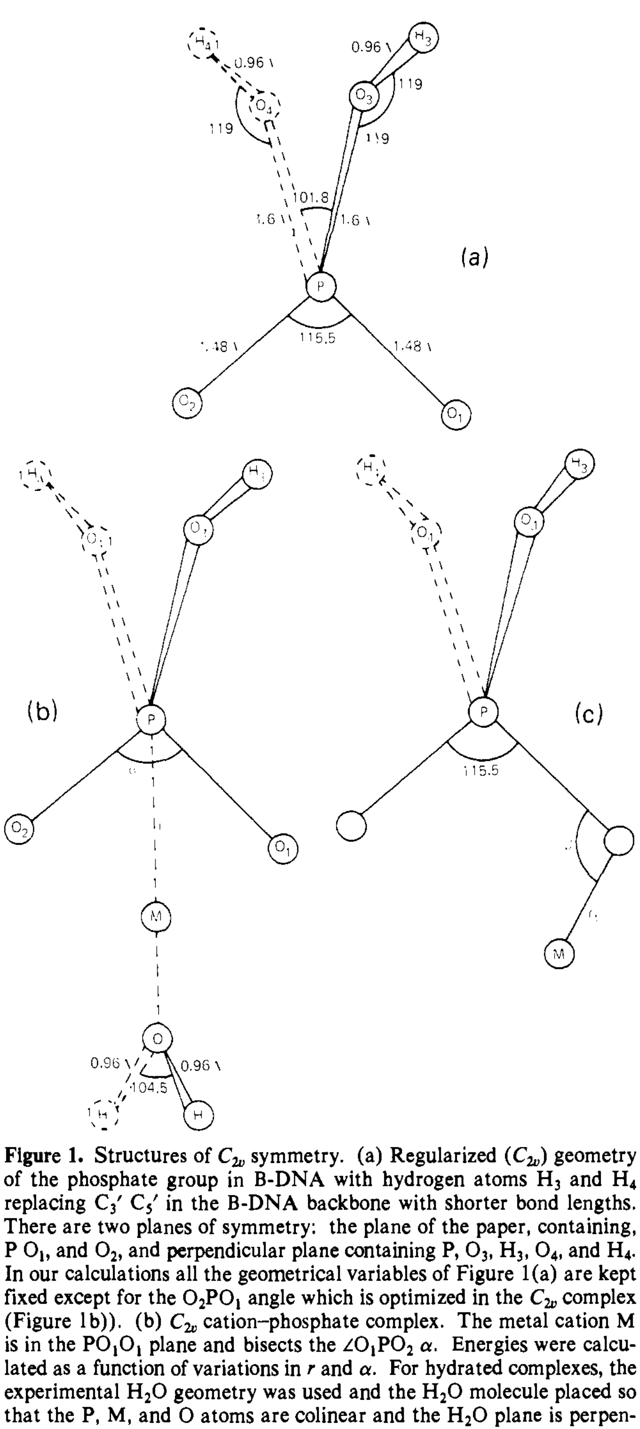

Figure 1. Structures of C_{2v} symmetry. (a) Regularized (C_{2v}) geometry of the phosphate group in B-DNA with hydrogen atoms H_3 and H_4 replacing C_3' C_5' in the B-DNA backbone with shorter bond lengths. There are two planes of symmetry: the plane of the paper, containing, P O_1, and O_2, and perpendicular plane containing P, O_3, H_3, O_4, and H_4. In our calculations all the geometrical variables of Figure 1(a) are kept fixed except for the O_2PO_1 angle which is optimized in the C_{2v} complex (Figure 1b)). (b) C_{2v} cation–phosphate complex. The metal cation M is in the PO_1O_1 plane and bisects the $\angle O_1PO_2$ α. Energies were calculated as a function of variations in r and α. For hydrated complexes, the experimental H_2O geometry was used and the H_2O molecule placed so that the P, M, and O atoms are colinear and the H_2O plane is perpendicular to the O_1PO_2 plane. The metal–OH_2 distances were fixed at 1.89 Å for Li^+ and 1.53 Å for Be^{2+} cation complex. (c) C_s cation-phosphate complex. The metal cation M approaches one of the phosphate atoms preferentially. Energies were calculated as a function of r_l and β with α fixed at the experimental value of 115.5°.

phosphorus atom of the phosphate group. The charge distribution of the phosphate remains virtually unchanged with the binding of a water of hydration.

Compared to the monovalent cations, the divalent cations Mg^{2+} and Be^{2+} both have a greater influence on the phosphate charge distribution, Mg^{2+} accepting 0.75 e^- and Be^{2+} accepting 1.4 e^-. The backbone oxygen atoms (O_3 and O_4) of the phosphate become less negative in both cases by nearly 0.2 e. The most striking feature of the interaction is in the Be^{2+} complex which draws off enough electron density from the "anionic" phosphate to make the phosphate 0.40 e positive. This is diminished to 0.22 e, but still positive, when a water of hydration is included. Again, while more pronounced than in the Li^+ complex, the water has little effect on the charge distribution of the phosphate.

From the correlation between ion size and extent of covalency obtained for the two series, it would appear that alkali metal ions larger (more electronegative) than Na^+ would also form ionic complexes, while alkaline earth ions such as Ca^{2+} and Sr^{2+} could still form complexes with charge transfer comparable to that of Li^+ ion complexes.

In addition to their effects on electronic structure, the binding of each cation studied results in a specific conformation of the O_1PO_2 angle. These angles, which are 110°, 107°, 102°, and 95°, respectively, for Na^+, Li^+, Mg^{2+}, and Be^{2+}, differ significantly from the 115.5° observed in DNA fibers.[27] (See Table III.) This order is the same as the relative extent of electron transfer from phosphate to cation in each complex and reflects the decrease in the O_1–O_2 repulsion. Table VI shows that these oxygens have net atomic charges of −1.01, −0.88, −0.77, and −0.52 in the Na^+, Li^+, Mg^{2+}, and Be^{2+} complexes, respectively. The decrease in charge on each oxygen atom allows them to approach more closely resulting in a decrease in the angle. This change in the external phosphate geometry could be propagated along the backbone of the polymer if, as the O_1PO_2 angle closes, the O_3PO_4 angle opens and causes changes which would affect the nuleic acid conformation. It should be emphasized that the calculation was done for an O_3PO_4 angle constrained to be that observed in B-DNA fibers. The magnitude of the effect which cation binding would have on the backbone conformation can only be assessed by using a larger portion of the DNA backbone and by including the complementary polynucleotide strand.

The larger electron transfer to Li^+ and larger decrease in the O_1PO_2 bond angle, compared to Na^+, might explain its anomalous position in ^{31}P NMR data for the alkali metal cation complexes with polyphosphates.[34] The magnitude of chemical shifts are $Na^+ < K^+ < Li^+ < Rb^+ < Cs^+$, with the effect of the Li^+ ion anomalously large. Such effects have been correlated with changes in the phosphate ester bond angle,[35] evidence that a change in O_1PO_2 bond angle can be translated to a change in backbone angle. This order of cation specificity is also found for the unwinding of closed circular DNA, from sedimentation studies on B $\rightarrow$ C + A conformational changes as observed by circular dichroism.[3,4]

The addition of a water molecule to either a mono or divalent cation does not significantly diminish the bond overlap of the metal–oxygen bond. The overlap population changing from 0.3 to 0.36 e for Li^+ and from 0.74 to 0.67 for Be^{2+} (Table VII). Nevertheless, the complex formed between the metal and the phosphate is somewhat weakened by the outside binding of a water. The Li^+ complex decreases in strength from −162.5 to −145.6 kcal/mol while the Be^{2+} complex changes from −494.7 to −414.7 kcal/mol (Table IV). This results from a weakening in the electrostatic component of the interaction. Table VI shows that the charge on Li in the complex decreases from +0.54 to +0.38, and the charge on Be from +0.60 to +0.32 on additon of a single water, causing weakening of the ionic component of the interaction with phosphate. This weakening is particularly pronunced in the case of hydrated Be, which is less positive than the monovalent Li when complexed.

As has been previously shown,[22-24] some insight into the possible hydration state of the metal–phosphate complex may be gained from such molecular-orbital calculations. It is evident from the bond overlap populations shown in Table VII that the Be–OH_2 bond with 0.87 e is quite covalent. The large value of −143.8 kcal/mol calculated as the monohydration energy (Table IV) is consistent with such a covalent complex. On the other hand, the Li–OH_2 bond is much less covalent (0.16 e) and weaker (−33.3 kcal/mol). Although a fully hydrated ion would have less electron sharing with each associated water, the results indicate that the primary hydration of Be^{2+} is stronger than that of Li^+ and involves more charge transfer.

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In assessing the ability of the phosphate group to replace waters of hydration of the cations to form direct-binding complexes, one may conclude that both Li^+ and Be^{2+} could from such direct complexes if one assumes additivity and that a single phosphate replaces two H_2O molecules.

Further comparison of the enthalpies of monohydration of Li^+ and of Be^{2+} (Table IVB) with the enthalpies of metal–phosphate complex formation (Table IVA) indicates that the phosphate Li^+ interaction is 4.4–4.9 times as great as the H_2O–Li^+ interaction, while the same ratio is 2.9–3.4 for Be^{2+}. Thus it appears that Li^+ can lose more waters of hydration than Be^{2+} during direct-site binding with the phosphate. It might thus be conjectured that Li^+ would more readily form direct complexes with the phosphate, while Be^{2+} might interact in a way which allows it to retain its primary hydration shell.

Although the question of ion mobility is not addressed directly in these calculations, estimates of the ease of cation dissociation in two perpendicular directions, given in Table V, indicate that monovalent cations would move more readily perpendicular to the C_2 axis, while divalent cations would have a tendency for separation along the C_2 axis.

Conclusions

Cations with significant charge transfer appear to have three important effects on the phosphate group: significant change in O_1PO_2 bond angle; significant atomic charge redistribution, i.e., decrease in positive charge of the phosphate group and negative charge on the backbone and anionic oxygen atoms; and significant change in bond density, i.e., strengthening of the phosphate–ester oxygen bond and weakening of the phosphate–anionic oxygen bonds. In spite of the ionic nature of its interaction, Na^+ also seems to have these same three direct effects on the phosphate group but to a lesser extent. Even without electron transfer, there is polarization of the charge distribution, particularly resulting in less negative charge at backbone oxygen atoms.

These calculated changes in phosphate anion charge distribution indicate the mechanism by which the presence of counterions can significantly alter interstrand backbone repulsion as well as specific base–backbone interactions leading to the observed structural changes. The tendency of the divalent cation to form partial covalent linkages with the phosphate oxygens and with water may play a major role in their association with nucleic acids. A tendency of Li^+ to form partial covalent linkages with these oxygens while Na^+ (and presumably large alkali metals) interacts totally electrostatically also suggests a cation specificity both in nature and in the extent of interaction with the phosphate group.

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Registry No. Li^+, 17341-24-1; Na^+, 17341-25-2; Be^{+2}, 22537-20-8; Mg^{+2}, 22537-22-0; $(OH)_2PO_2^-$, 14066-20-7; H_2O, 7732-18-5.

(π-Allyl)palladium Complex Ion Pairs Containing Two Different, Mobile π-Allyl Groups: NMR and X-ray Crystallographic Studies

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Abstract: The reaction of (π-allyl)palladium chloride dimer with TMEDA in THF produced an unusual complex ion pair **1**, in which two different π-allyl groups were present. This complex was characterized by high-field (360-MHz) NMR spectroscopy in solution and by solid-state ^{13}C NMR spectroscopy. In solution the two allyl groups in complex **1** underwent facile exchange with each other. The kinetic parameters E_a, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta G^{\ddagger}$ for this exchange were determined. The proposed structure of complex **1** was confirmed by a single-crystal X-ray structure determination of the related complex **7**, which crystallized in the monoclinic space group $P2_1/c$ with $a = 11.55$ (1) Å, $b = 13.04$ (1) Å, $c = 13.98$ (1) Å, $\beta = 123.86$ (3)°, and $Z = 4$. Compound **7** was found to consist of discrete complex ion pairs, with allyl ligands bound to palladium in both the cation and the anion. Least-squares refinement of this structural model for 1833 unique, observed reflections resulted in $R = 0.063$ and $R_w = 0.077$.

Reactions of both (π-olefin)-[2-6] and (π-allyl)palladium[7-11] halide complexes with nucleophiles have found extensive application in organic synthesis. With both types of complexes, the addition of several equivalents of an external ligand is required to produce reasonable yields of products resulting from nucleophilic attack on the π-bound functional group. The course of these reactions is remarkably dependent upon the specific ligand used. For example, tertiary amines are required for the successful alkylation of (π-olefin)palladium complexes by carbanions,[5] whereas phosphines completely inhibit this reaction. In contrast, allylic alkylation of (π-allyl)palladium halide complexes requires tertiary phosphines as ligands, and the regiochemistry of alkylation is

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