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T16

Conformation of d(ATGG)–*cis*Pt(NH_3)$_2$ in Aqueous Solution by Proton Magnetic Resonance Spectroscopy

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The conformation of an adduct d(ATGG)–*cis*Pt resulting from the interaction of the antitumor *cis*Pt(NH_3)$_2$Cl$_2$ with a short DNA fragment dApTpGpG has been investigated by ^{1}H NMR at 500 MHz and at various temperatures. The chemical shift and coupling constant measurements confirm the CD and UV results that divalent platinum binds covalently to the N-7 atoms of the two adjacent guanines in the same strand as in the case of diguanosine monophosphates [1, 2]. Analysis of the coupling constants between the deoxyribose protons (Fig. 1) shows that the sugar ring of the internal dG adopts the N conformation ($C_{3'}$-endo) (91% N) while the external dG and the other residues adopt the S conformation ($C_{2'}$-endo) (70–80% S). In the case of unplatinated oligomer, the S conformation is largely predominant (>70%) for all residues of d(ATGG).

The relaxation time and nuclear Overhauser measurements indicate that the orientation of the two guanines is *anti*, in agreement with the previous results obtained for the dimers r(GpG)–*cis*Pt, d(GpG)–*cis*Pt [1, 2]. Surprisingly, on decreasing temperature from 80 to 25 °C, the $H_{1'}$, resonance of the internal dG (Fig. 1) and the $H_{4'}$ resonance of the internal dT (not shown) shift and broaden substantially and finally disappear at t < 40 °C. These results suggest that d(ATGG)–*cis*Pt tends to associate with neighbouring molecules and the conformation of this adduct changes with temperature. It seems likely that at low temperature the base protons (H-6 and CH_3) of dT are situated

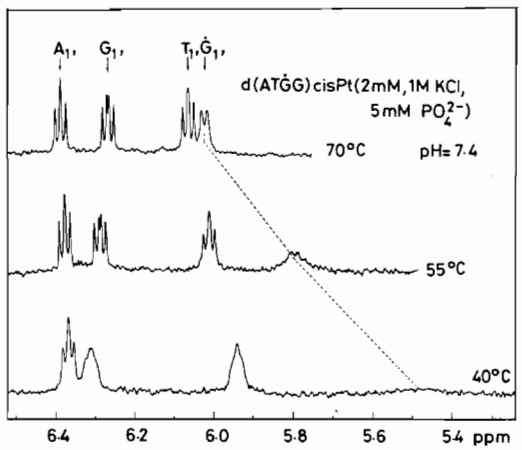

Fig. 1. 500 MHz ^{1}H NMR spectra of the $H_{1'}$ protons of d(ATGG)–*cis*Pt in aqueous solution at various temperatures.

'inside' the adenine ring whereas the sugar protons of dT are very close to the guanine ring of the internal dG.

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T17

Structural Studies on Metal-ATP Complexes: X-Ray Structures of Mg(II), Ca(II), Mn(II) and Co(II) Ternary Complexes with ATP and Dipyridylamine

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The enzyme-catalyzed reactions of transferring simple and substituted phosphoryl groups, such as nucleotidyl groups, are among the most fundamental biochemical processes. Enzymes which utilize one of the nucleotides as a cofactor or substrate usually require a specific complex of the nucleotide with metal ion for activity. The metal ions are involved in a number of mono-, bi- and tri-dentate coordination geometries and some of the forms may be preferred by specific enzymes over the others as substrates. X-ray studies of several metal-polyphosphate

compounds have provided a substantial knowledge about modes of interaction between metal ions and phosphoryl groups [1–3]. However, there are only few solid-state studies [4, 5] of metal complexes with adenosine triphosphate (ATP) in spite of the importance of this nucleotide polyphosphate for many biochemical reactions.

In a previous note we reported the syntheses of a series of ternary complexes between ATP, dipyridylamine (DPA) and the metal ions Mg(II), Mn(II), Co(II), Cu(II) and Zn(II) [6]. Subsequently we prepared ternary complexes with the ions Ca(II), Sr(II), Ba(II), Fe(II), Ni(II), Cd(II) and Pb(II).

In order to provide further information about coordination geometry of the metal–ATP system, the X-ray structure analysis of the ternary complexes Mg(II)–ATP–DPA (1), Ca(II)–ATP–DPA (2), Mn(II)–ATP–DPA (3) and Co(II)–ATP–DPA (4) has been performed. The compounds were crystallized from solutions containing a mixture of the appropriate components in the molar ratio 1:1:1. All four compounds crystallize in the orthorhombic space group $C222_1$ (Table I).

TABLE I. Some Significant Crystal Data for the M(II)(ATP)-(DPA) Complexes.

	Mg	Ca	Mn	Co
a (Å)	10.233(3)	10.154(3)	10.234(3)	10.218(3)
b (Å)	22.734(3)	22.965(3)	22.699(3)	22.717(3)
c (Å)	30.997(4)	32.390(4)	31.351(4)	31.027(4)
V (Å^3)	7,211.05	7,552.91	7,282.89	7,202.06
Z	8	8	8	8
Diffractometer	Philips PW1100 (MoK_α)	Philips PW1100 (MoK_α)	Cad-4 (MoK_α)	Cad-4 (MoK_α)
No. of observed reflections ($F > 3\sigma(F)$)	1050	1200	3534	1850

Some attempts to solve the structures of the compounds (1) and (2) by direct methods, using MULTAN 80 [7] and SHELX 76 [8] packages were unsuccessful. The structures were solved by the SIR program [9] through the extensive use of phase semivariants in the starting set. The structures of the compounds (3) and (4) were independently solved by means of heavy-atom techniques using regular and anomalous Patterson maps.

The analysis clearly showed the existence of two different sites occupied by metal ions in the structures.

In all four structures the ATP molecule is bonded to one of the metal ions by oxygen atoms from the α-, β- and γ-phosphate groups. There is no bonding interaction between the metal ions and the adenine base.

The structure analysis of the compounds (1) and (2) showed the presence of a twofold orientational disorder of the DPA molecules.

Further work is in progress to establish the remaining details of the structures.

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T18

Macromolecular Nature of Nucleic Acids in Metal Interactions

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The conformational changes of nucleic acid macromolecules as a result of rotation around C–C, C–O, C–N covalent bonds occur without destruction of the chains, but they can lead to the loss of biological function; this can be seen in interactions with metal ions of nucleic acids. The latter are ambidentate ligands and supply by complex formation different sites of binding, sometimes cooperatively, in polyfunctional chains. This leads to the formation in nucleic acid macromolecules of different coordination centers, among them the unsaturated, deformed type: pure phosphate, mixed phosphate-base, pure base, crosslinked base, sandwich, complementary paired base and others. The probability of the centers is discussed.

As a result of complex formation with nucleic acid macromolecules there are mutual influences between functional groups of the chain, those of electronic origin, conjugations, field effects, dispersion interactions, hydrogen bonding, solvation, supermolecular structure formation and so on.