is proposed for the $Au(nucl)_3Cl_2$ complexes, implying six coordinate Au(III) ions, with the N(7) site of the nucleosides involved in bonding, based mainly on the ^{197}Au Mössbauer spectra. Polymeric structures were also proposed for the $Au(nucl\text{-}H^+)Cl_2$ complexes, from the combined IR and ^{197}Au Mössbauer spectra, involving in bonding the N(7) and O(6) sites of the ligands. The $Au(nucl)Cl_3$ complexes correspond to a square planar arrangement around Au(III) with the N(7) site again involved in bonding.

Finally, for the $Au(nucl)_2Cl$ the ^{197}Au Mössbauer spectra do not seem to agree with the other data, suggesting sp hydridization and two coordination of the type nucl–Au–Cl and not a three coordination of the type nucl–Au–Cl, as it was previously proposed
|
nucl
[3]. The results of the different techniques will be compared and discussed.

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T4

^{1}H-NMR Study on Self-Association and Macrochelate Formation in Metal Ion Systems of Nucleoside 5'-Diphosphates

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Nucleotides and their complexes are substrates for many enzymic reactions [1]. The self-association *via* aromatic ring stacking of nucleoside 5'-mono- [2] and 5'-triphosphates [3] is now well established and the structures for the complexes of these nucleotides (=N) in solution are relatively well characterized [3, 4]. Much less is known about nucleoside 5'-diphosphates (NDP^{3-}).

Therefore, the concentration dependence of the chemical shifts for the protons H-2, H-8, and H-1' of ADP^{3-} and IDP^{3-}, H-8 and H-1' of GDP^{3-}, and H-5, H-6, and H-1' of CDP^{3-} and UDP^{3-} has been measured in D_2O at 27 °C. The results are consistent with the isodesmic model [3] of indefinite non-cooperative stacking (eqn. 1); the association constants for

$$(N)_n + N \rightleftharpoons (N)_{n+1} \quad K = [(N)_{n+1}]/[(N)_n][N] \quad (1)$$

NDP^{3-} are between 1.8 (ADP^{3-}) and about 0.6 M^{-1} (UDP^{3-}). In agreement with earlier results [3] obtained under the same conditions for nucleosides and nucleoside 5'-triphosphates, the self-stacking tendency of the base moieties of the nucleic acids decreases in the series adenine > guanine $\gtrsim$ hypoxanthine > cytosine ~ uracil. Due to the repulsion of the negatively charged phosphate moieties, the self-association is always less pronounced for NDP^{3-} compared with the corresponding nucleoside.

Accordingly, the addition of Mg^{2+} to ADP^{3-} favors self-stacking, as is obvious from Fig. 1: the curvature of the lines is more pronounced for the $Mg(ADP)^-$ system ($K = 6.4\ M^{-1}$) than for the ADP^{3-} system. Generally, the self-stacking tendency of the NDP^{3-} systems is promoted by a factor of about 2–3 by the coordination of Mg^{2+} to the phosphate moiety. However, the self-association tendency of $Zn(ADP)^-$ and $Cd(ADP)^-$ or $Zn(IDP)^-$ and $Cd(IDP)^-$ is much larger than of $Mg(ADP)^-$; this is explained [5] by an increased tendency to form an *inter*molecular metal ion bridge in dimeric stacks, which may

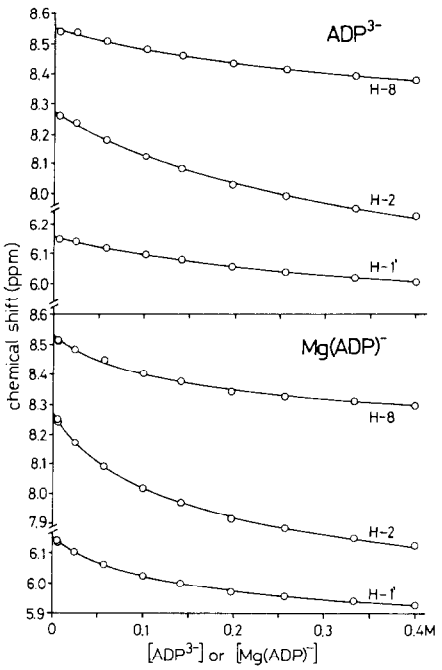
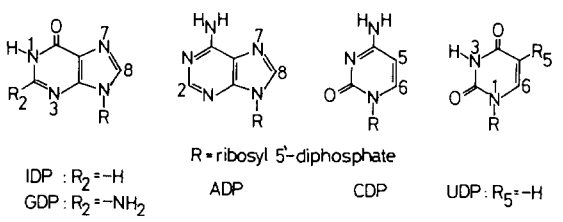
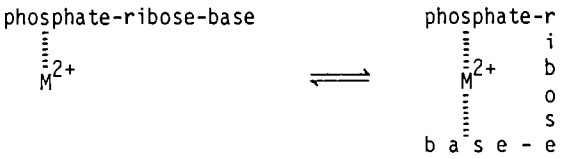


Fig. 1. Variation of the chemical shift for H-2, H-8, and H-1' of ADP with varying concentrations of ADP^{3-} (pD 8.9) or $Mg(ADP)^-$ (pD 7.5). The spectra were measured on a Bruker FT 90 at 90.025 MHz (D_2O; 27 °C; I = 0.1 to ~1.7, $NaNO_3$). The curves are the computer-calculated best fits of the experimental data, using the indefinite non-cooperative stacking model: $K_{ADP} = 1.8 \pm 0.5\ M^{-1}$ and $K_{Mg(ADP)} = 6.4 \pm 0.9\ M^{-1}$).



then further associate. In these dimeric stacks Zn^{2+} or Cd^{2+} is coordinated to the phosphate moiety of one NDP^{3-} and to N-7 of the purine residue of the other NDP^{3-}. The shifts of H-8 (and H-2) for complete stacking (δ_∞) agree with this interpretation.

Comparison of the shifts of H-8 at infinite dilution (δ_0) reveals that an M^{2+}/N-7 interaction exists in the monomeric Zn^{2+} and Cd^{2+} complexes of purine-NDP^{3-}; *i.e.* a macrochelate is at least partially formed by an *intra*molecular coordination of the metal ion to the phosphate moiety *and* to N-7. The NMR study gives no hint for such an interaction in the corresponding $Mg(NDP)^-$ complexes or in any of the pyrimidine-NDP^{3-} complexes [5]. An evaluation of the stability data available [6] gives further evidence for the existence of the concentration-independent



(2)

equilibrium 2 between an open and a macrochelated isomer in purine-NDP^{3-} complexes. For the $M(ADP)^-$ complexes of Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}, about 60, 70, 80, 95, and 75 percent respectively exist in the macrochelated form [5]. No evidence for such an isomer is found for $Mg(ADP)^-$ and $Ni(CDP)^-$.

The ambivalent coordinating properties of nucleotides and their structural versatility is evident from these results. It should be emphasized that in studies aiming to evaluate the properties of monomeric nucleotides and their complexes, low concentrations must be employed (often $< 10^{-3}$ *M*). In addition, it seems clear that in natural systems self-association of nucleotides must be expected, *e.g.*, in the adrenal chromaffin granules which contain substantial amounts [7] of metal ions and nucleotides. That metal ions may promote not only the self-association of nucleotides, but also their stacking and hydrophobic interactions with amino acids, has already been proven [8].

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T5

Metal Complex Induced Changes in DNA Conformation and Template Activity

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It is now well-known that the interaction of metal ions with DNA leads to dramatic changes in nucleic acid structure [1] and recently it has become apparent that even the handedness of the double helix [2] and its compaction into aggregates [3, 4] is affected by such interaction. As recently demonstrated, DNA can exist in left-handed (Z) as well as the familiar right-handed conformations. The Z-structure is produced by DNA molecules containing alternating guanine (G) and cytosine (C) bases [poly(dGdC)·poly(dGdC)] [5]. Compacted states have been known for some time to exist *in vivo*, and it is believed that these as well as left-handed conformations may be involved in the control of genetic information transfer. It is therefore important to understand how transitions between the DNA conformers take place, and whether such transitions affect the biological activities of DNA. We have addressed both of these problems.

We have found that $[Co(NH_3)_6]Cl_3$ brings about reversible transitions in the structure of poly(dGdC)·poly(dGdC) so that the right-handed B-form is first converted to Z-DNA and then to another structure that resembles A-DNA and finally to the highly compacted ψ-DNA [6]. The metal complex is thus able to induce three transitions among four conformers of DNA. By manipulating the concentrations of $[Co(NH_3)_6]Cl_3$ and poly(dGdC)·poly(dGdC), as well as other factors such as reaction time and temperature, each of these conformations can be stabilized, and identified by its circular dichroism spectrum; or labilized and converted into another structure. We believe that the mechanism for these interconversions depends on the fact that increasing concentrations of the Co(III) complex stabilize conformations in which the phosphate groups of DNA are closer together.