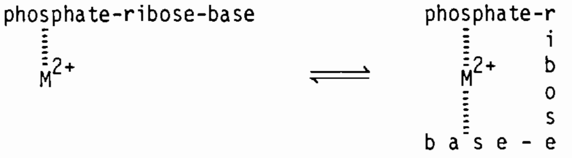
then further associate. In these dimeric stacks Zn^{2+} or Cd^{2+} is coordinated to the phosphate moiety of one NDP^{3-} and to N-7 of the purine residue of the other NDP^{3-}. The shifts of H-8 (and H-2) for complete stacking (δ_∞) agree with this interpretation.

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.

Conformational change in DNA, as demonstrated for the $B \rightarrow Z$ conversion leads to the biologically important consequence that the ability of the DNA to act as a template for RNA synthesis is affected. Figure 1 illustrates the correlation of the $B \rightarrow Z$ transition of poly(dGdC)•poly(dGdC) which occurs at ~60 μM $Co(NH_3)_6{}^{3+}$, with a decrease in RNA synthesis to ~1/2 the original rate, in the presence of *E. coli* RNA polymerase. A decrease in RNA synthesis also accompanies the conversion of a similar double helix in which the guanines are methylated, poly(dGdm^{5}C)•poly(dGdm^{5}C), from the B to the Z form, even though this transition occurs at a much lower (~3 *μM*) Co(III) concentration. Clearly the metal complex has profound effects on the DNA conformation, and the DNA conformation affects the ability of the DNA to act as a template for RNA synthesis.

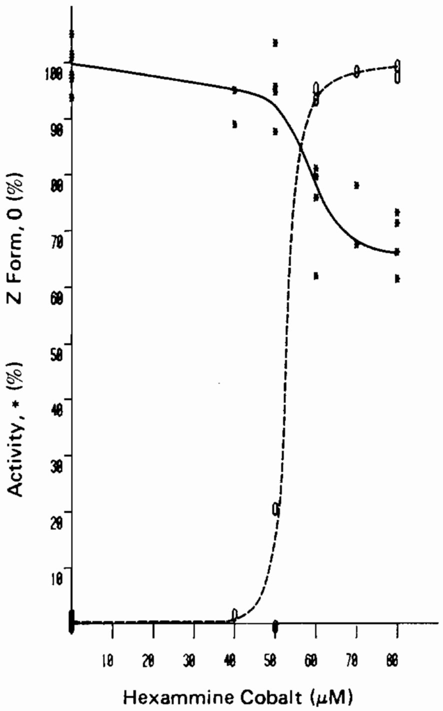

Fig. 1. Correlation between conformational transition (- - -) of poly(dGdC)•poly(dGdC) and change in activity to act as template in RNA synthesis (——).

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T6

A Spectrophotometric Study of tRNA-Cu(II) Complex

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The spectrum of the aqueous copper(II) ion is changed in the presence of the tRNA molecule: a marked increase in absorption and a shift in its maximum from 800 to 740 nm is observed (Fig. 1). This effect is similar to the one observed on coordination of Cu(II) with ammonia and ethylene diamine [1] and is due to the stronger ligand field of the nitrogen derivatives. Therefore our data seem to indicate that the copper hydrated ion exchanges a water molecule with a heterocyclic base of tRNA at one of its nitrogen donor sites creating a coordination complex. The ΔA_{710} value obtained from the differential spectrum (2) in Fig. 1 is proportional to the bound copper concentration. We observed that ΔA_{710} increased immediately as Cu(II) ions were added and the process shows a saturation only for a $[Cu^{2+}]/[PO_4{}^-]$ ratio greater than 0.5 (Fig. 2). An increase in the NaCl concentration from 0.1 to 0.7 *M* has some influence, however small, on the formation of

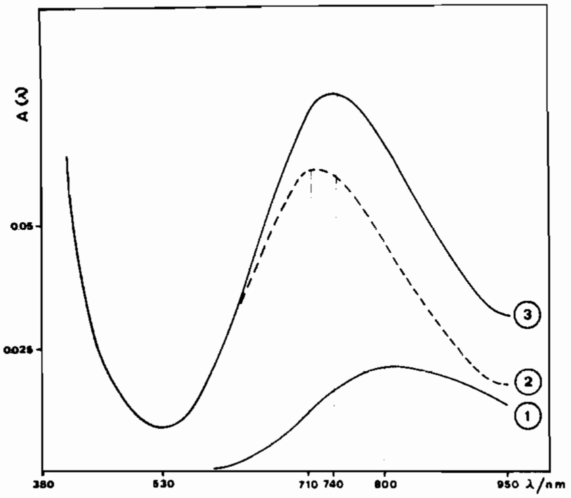

Fig. 1. Absorption and differential spectra for tRNA–Cu(II) complex: Curve 1 the $[Cu(H_2O)_6]^{2+}$ absorption spectrum $A_1(\lambda)$; curve 2 the differential spectrum $\Delta A(\lambda) = A_3(\lambda) - A_1(\lambda)$; curve 3 the tRNA–Cu(II) absorption spectrum $A_3(\lambda)$ for $[Cu^{2+}]/[PO_4{}^-]$ equal to 0.24.