

shifts are to low field, and must be due to a combination of charge, magnetic anisotropy and polarization effects of the angular MoO_2^{2+} species. The relative magnitude of the shifts indicates that MoO_2^{2+} binds to an oxygen atom of the phosphate group, the oxygen atom of the ribose ring and possibly interacts with the adenine base through the N_7 and/or NH_2 group. However, molybdate does not bind to adenine in D_2O . UO_2^{2+} has been found [6] to bind to the phosphate and $-\text{OH}$ groups of 5'-AMP but not to the base. Further studies are in progress, using nucleosides, ribose, ribose-phosphates and the bases in order to define the binding sites of 5'-mononucleotides to molybdate.

We have observed similar interactions of 5'-AMP with tungstate, WO_4^{2-} , and vanadate, VO_4^- , in solution. However the percentage of metal complexes formed is always much smaller than with molybdate, possibly due to the more extensive polymerization of tungstate and vanadate in aqueous solution [7].

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PS5.54 — TU

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METAL COMPLEXES OF 3d IONS WITH 5'-AMP, 3'-AMP AND 2'-AMP: SYNTHESIS, CHARACTERIZATION AND STUDY OF RABBIT MUSCLE GLYCOGEN PHOSPHORYLASE b ACTIVATION

INTRODUCTION

As a follow-up to work on the synthesis and characterization of compounds of metal ions with nucleotides [1-4], complexes of Co(II) , Co(III) , Ni(II) , Cu(II) and Zn(II) with 5'-, 3'- and 2'-AMP were prepared and were enzyme tested on rabbit muscle glycogen phosphorylase b as analogues of the allosteric activator.

RESULTS

The complexes were synthesized in a water medium and a dimethylsulfoxide medium. They were characterized by elementary C,H,N,P and metal analysis and by infrared, ultraviolet-visible and fluorescent spectroscopy.

The bonding of cations to nucleotides may be effected through the phosphate group, the ribose ring and the base. The Ns of the purine ring are right for the formation of covalent bonds with the metal ions; on the other hand, few complexes were observed between the ribose ring oxygens and a 3d cation. The nucleotide metal stability constants have a large component of electrostatic attraction

between the metal cation and the phosphate group [5]. In earlier studies [2] it was seen that the position of the phosphate group (5', 3' or 2') influenced the stability of the metal-N bond of the adenine ring.

From the study of the infrared spectra of the synthesized complexes, shiftings and changes in intensity were observed on the bands due to the purine ring, which seem to indicate metal ion-base interaction, probably through N(7), in accordance with crystallographic data [6].

On the 5'-AMP bands peculiar to the phosphate group, shiftings and splittings of the mode of stretching $\nu\text{-PO}_3^{2-}$ (deg) were observed in all the complexes except the $\text{Co(5'-AMP).7H}_2\text{O}$ and $\text{Co(5'-AMP)NO}_3\cdot\text{C}_2\text{H}_6\text{SO}\cdot 5\text{H}_2\text{O}$ derivatives. This might indicate coordination to the phosphate group in the cases where splitting occurs.

For the complexes obtained with 3'-AMP it was observed that in the phosphate group vibration zone the only complex which does not present splitting of the $\nu\text{-PO}_3^{2-}$ (deg) band is the formula $\text{Co(3'-AMP).3H}_2\text{O}$ complex. This rules out direct metal-phosphate interaction in this complex and implies it in the others where splitting does occur. For the derivatives of 2'-AMP it was observed that, in the zone corresponding to the phosphate group, the only complex in which splitting of the band ascribable to the phosphate group degenerate stretching band occurs is the formula $\text{Co(2'-AMP).(OH)}_2\cdot 3\text{H}_2\text{O}$ complex. So this is the only one which seems to present direct metal cation-phosphate group interaction. Variations of the adenine bands were observed in all the cases. The ultraviolet-visible and fluorescent spectroscopy study is in conformity with the coupling of the metal ion to the purine ring in all cases [7].

ENZYME TEST

The test for the activity of rabbit muscle glycogen phosphorylase b in the presence of the 17 new synthesized complexes and of the $\text{Ni(5'-AMP).6H}_2\text{O}$ [6] and $\text{Cu(5'-AMP).2H}_2\text{O}$ [8] complexes already described in the literature resulted in the activation of the enzyme in the presence of the formula $\text{Co(5'-AMP).7H}_2\text{O}$, $\text{Ni(5'-AMP).6H}_2\text{O}$ and $\text{Co(5'-AMP)NO}_3\cdot\text{C}_2\text{H}_6\text{SO}\cdot 5\text{H}_2\text{O}$ complexes.

The structural data in the literature [6] for the Ni(II) complex report the absence of direct Ni(II)-phosphate interaction and the infrared study leads to the same conclusion for the derivatives of cobalt which activate the enzyme. Since the structures of Cu(II) and Zn(II) complexes with nucleotides reveal the presence of direct metal cation phosphate group bonding, it may be concluded that there exists a direct correlation between the activation of the enzyme and the free phosphate group. The complexes synthesized with 3'-AMP and 2'-AMP do not activate the enzyme as it is an essential condition for the phosphate group to be coordinated in the 5'-position [9,10] as shown in earlier studies.

The conclusion of this study is that the activation of rabbit muscle glycogen phosphorylase b occurs through the 5'-AMP phosphate group in the presence of metal ions not directly coordinated to it.

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PS5.55 — TH

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REACTION OF RADIOLYTICALLY FORMED HYDROPEROXIDES ON DNA AND PRECURSOR COMPOUNDS WITH REDOX-ACTIVE METAL IONS AND COMPLEXES

The exposure of oxygenated aqueous solutions of nucleic acids and related compounds to ionising radiation leads to the formation of peroxidic products (H_2O_2 and organic hydroperoxides). Analytical techniques [1] previously developed for determination of peroxides at concentrations of 10^{-6} – 10^{-5} mol dm^{-3} have allowed study of the post-radiolytic decay of such species in systems ranging in complexity from the pyrimidine bases to RNA and DNA.

The metal ion-catalysed decomposition of peroxides is a well documented phenomenon, and the possible involvement of contaminating metal ions in the decay processes was considered. The influence of both chelating agents and a variety of redox-active metal ions on peroxide stability has therefore been examined.

Preliminary data concerning the interaction of the glycopeptide antibiotic, bleomycin, with DNA hydroperoxide have been obtained. The results may have important implications with regard to synergism in the DNA-cleaving activities of bleomycin combined with ionising radiation.

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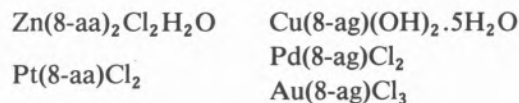
PS5.56 — MO

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TRANSITION METAL COMPLEXES WITH 8-AZAADENINE AND 8-AZAGUANINE

The biological properties of the azaderivatives of nucleic acid bases and nucleosides have been extensively studied and a number of them were found to be active chemotherapeutic agents. However very few reports have been published on complexes of metal ions with azapurines.

We have prepared and characterized a number of complexes of transition metal ions with 8-azaadenine and 8-azaguanine. These complexes were prepared by mixing equimolar aqueous solutions of the azapurines with the metal chloride or nitrate solution at an appropriate pH. On standing precipitated the complexes which were of the following composition:



These complexes were characterized by elemental analyses, conductivity and magnetic measurements, diffuse reflectance spectra and infrared spectroscopy. In the complexes prepared the 8-azapurines are acting as monodentate or bridging ligands, binding through the nitrogen of the imidazole ring.