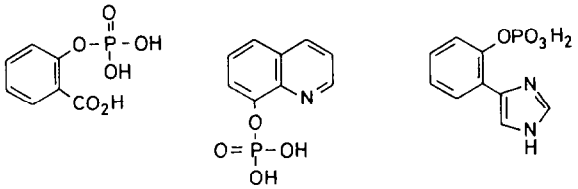
subject to metal ion catalysis. However, the role of the metal ion in promoting the hydrolysis reactions of phosphate derivatives including phosphate esters has been the subject of considerable speculation.

Copper(II) ions have been observed to catalyse the hydrolysis of a number of phosphate monoesters including salicyl phosphate (I) [1, 2], 8-quinolyl phosphate (II) [3, 4] and 2-(4(5)-imidazoyl)phenyl phosphate (III) [5]. The catalytic effect observed



(I) (II) (III)

with salicyl phosphate and 8-quinolyl phosphate was apparently quite small (*ca.* 10 fold).

We have studied the copper(II) promoted hydrolysis of salicyl phosphate over a range of copper(II) concentrations at pH 4.72, 5.14 and 5.30 at 30 °C and I = 0.1 *M* ($KNO_3$). Copper(II) ions exert a very marked effect on the hydrolysis of the normally unreactive phosphate monoester dianion of salicyl phosphate (*ca.* $10^{10}$ rate acceleration). Previous work in this area had indicated only small rate accelerations, as comparisons were made between the metal ion promoted reaction and the *intramolecular general acid catalysed hydrolysis* of the phosphate monoester dianion.

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## T21

## Physico-Chemical Investigation of Nucleoside-Containing Pt(II) Triamines

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The discovery of the antitumor activity of *cis*-Pt-$(NH_3)_2Cl_2$ has aroused considerable interest in the study of Pt(II) complexes with nucleosides [1]. Most of the compounds investigated contain two nucleoside molecules and are of the nonelectrolyte or cation type [2–5].

We have synthesized and investigated isomeric Pt(II) triamines of composition $[Pt(NH_3)_2LCl]Cl$, where L = adenosine(ado), inosine(Ino), and *cis*-$[Pt(NH_3)_2L'Cl]Cl$, where L' = cytidine(Cyd).

The coordination formulae have been proved by the measurement of molecular conduction (Λ in aqueous solution = 100–110 ($ohm^{-1}$ $cm^2$ $mol^{-1}$) and by long-wave IR spectroscopy ($\nu_{Pt\text{-}Cl}$ lies in the range 330–337 $cm^{-1}$). The hydrolysis constant $K_h$ of the above triamines and $[Pt(NH_3)_3Cl]Cl$ has been determined potentiometrically with the use of Ag/AgCl and chloroselective electrodes.

$K_h \times 10^4$:

$[Pt(NH_3)_3Cl]Cl$ 2.3 *trans*-$[Pt(NH_3)_2InoCl]Cl$ 7.0

*trans*-$[Pt(NH_3)_2Clado]Cl$ 9.0 *cis*-$[Pt(NH_3)_2CydCl]Cl$ 20.6

*cis*-$[Pt(NH_3)_2adoCl]Cl$ 19.0

The substitution of $NH_3$ by a purine or pyrimidine molecule leads to an increase in $K_h$ which is likely to be due to steric factors. The hydrolysis constant $K_h$ is slightly affected by the nature of the nucleoside.

The geometric structure of the complexes affects $K_h$: *cis*-isomers are approximately 2–3 times less stable than *trans*-isomers. The lower stability of the Pt–Cl bond in the *cis*-triamine $[Pt(NH_3)_2$·adoCl]Cl also follows from the comparison of $\nu_{Pt\text{-}Cl}$ in isomers: *cis*, 330 $cm^{-1}$; *trans*, 337 $cm^{-1}$.

The acidic properties of isomers $[Pt(NH_3)_2InoCl]$-Cl have been investigated by the method of potentiometric titration with an alkali in the presence of 0.3 *N* KCl (Fig. 1). Coordination leads to the enhancement of the acidic properties of inosine: $pK_a$ of the

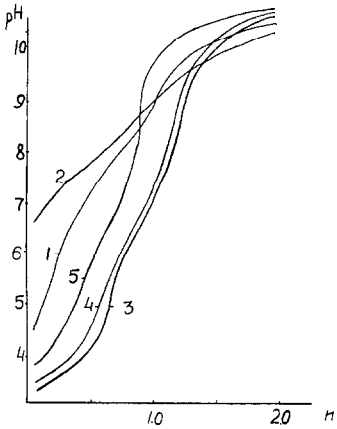
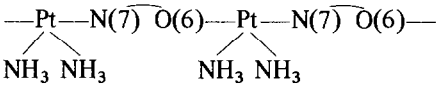



Fig. 1. pH values *versus* the number of added equivalents of OH-ions (n). $[Pt(NH_3)_2InoCl]Cl$: 1-*trans*, 2-*cis*; $[Pt(NH_3)_2$-$InoH_2O]$·$(NO_3)_2$: 3-*trans*, 4-*cis*; 5-*cis*$[Pt(NH_3)_2Ino](NO_3)_2$. Concentration of complexes = $1.10^{-3}$ *M*.

*cis*-isomer = 7.9, *trans*-isomer = 7.2, whereas for free inosine it is 9.0. The difference in acidity of isomers and in the stability of the Pt–Cl bond may be accounted for by the higher *trans*-effect of $NH_3$ compared with inosine.

Solutions of isomeric aquocomplexes $[Pt(NH_3)_2InoH_2O]^{2+}$ have been obtained by the action of $AgNO_3$ on isomeric triamines. The curves of potentiometric titration with an alkali of isomeric aquoions practically coincide and correspond to titration of the mixture of a strong acid (the first portion of the curve) and coordinated water (the second portion). The titration curve of the synthesized complex $[Pt(NH_3)_2Ino](NO_3)_2$ obtained in solid state by the action of inosine on the solution of *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ is of the same type. Since the acidic properties of isomeric aquocomplexes and $[Pt(NH_3)_2Ino](NO_3)_2$ are similar it may be concluded that in the aqueous solutions of these compounds there are no complexes with inosine bidentate coordinated through N(7), O(6) atoms. At the first portion of the curve the strong acid is titrated, it being formed in solution due to partial polymerization of complexes according to the type:



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## T22

## The Interplay of Hydrogen Bonding and Metal–Nucleic Acid Interactions

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Since hydrogen bonding plays a crucial role in the structure and function of nucleic acids and metal ions are involved in many biological processes involving nucleic acids, it is of interest to look at the interplay of these two features. The crystal structures of several metal complexes of nucleic acid components have been reported in the literature [1, 2] and they demonstrate such an interplay. This article briefly reviews this aspect.

Metal ions can interact directly with the phosphate back bone (M–O–P–) and also through water bridged interactions (M–O–H···O–P–); both types have been realised in the crystal structures of nucleotides [2].

The interligand hydrogen bond is a common feature in the metal complexes of purines [1, 2].

| | |
|---|---|
| N(6)–H····X–M–N(7) | in adenine X = H-bond |
| N(6)–H····X–M–N(1) | acceptor |
| O(6)···HX–M–N(7) | in guanine X = H-bond |
| O(6)···HX–M–N(1) | donor |
| | N(1) = deprotonated |

The ability of $Rh_2(CH_3COO)_4$, an antitumor agent, to interact specifically with adenine and not with guanine has been attributed to its indirect chelation with the former but not with the latter [3]. A similar interligand hydrogen bond has been implicated in the mode of action of *cis*-Pt(amine)$_2$ [2]. A coordinated $H_2O$ molecule can function as a H-bond acceptor and/or donor and consequently can participate in the complexes of guanine as well as adenine.

When M binds to N(7) of A, W.C. sites are available for base pairing and A:A pairing involving W.C. sites has been observed in some metal complexes [4]. In the crystal structure of $[(Pt(NH_3)_2(9\text{-EtG})(1\text{-MeC})]^{2+}[(Pt(NH_3)_2(9\text{-EtG-H})(1\text{-MeC})]^{+}(ClO_4)_3$, coordination of Pt to N(7) (a non W.C. site) has changed the pK of the base from 9.8 to 8.2 facilitating deprotonation at N(1); the $(G–G)^-$ pair exists in the crystal lattice rather than the (G–C) pair [5] (9-EtG-H = the deprotonated base).

In certain metal complexes, protons are transferred to other sites on the bases by incoming metal ions [6] suggesting that the metal ion can alter the relative stability of different tautomers. Metal induced activation or deactivation of C–H protons in purines has been reported [7, 9]; this suggests that metal ions can also influence C–H···X types of interactions [8] commonly observed in the crystal structures of nucleobases. Metal ion-nucleic acid interaction *vis-a-vis* hydrogen bonding is emerging as a fascinating structural feature [7].

"I believe that as the methods of structural chemistry are further applied to physiological problems it will be found that the significance of the hydrogen bond for physiology is greater than that of any other single structural feature." Linus Pauling [10].

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