A Cyclic Nucleobase Phosphate: Fast Atom Bombardment Studies on a 1 : 1 Mixture of *cis*-$[Pt(NH_3)_2(OH_2)_2](CF_3SO_3)_2$ and Guanosine 5′-Monophosphoric Acid†

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The fast atom bombardment mass spectrum of a 1 : 1 mixture of *cis*-$[Pt(NH_3)_2(OH_2)_2](CF_3SO_3)_2$ and guanosine 5′-monophosphoric acid demonstrates the existence of a cyclic Pt-*N*(7),α-*O*PO_3 complex.

The kinetics of the reaction of *cis*-$[Pt(NH_3)_2(OH_2)_2]^{2+}$ with 5′-$GMPH_2$ are very different from those with 3′-$GMPH_2$; in the first case[1] two reactions, (i) and (ii), can be followed; in the second,[2] step (ii) is too fast to be observed kinetically. When B is 3′-$GMPH_2$, there is little doubt that X is the straightforward complex, *cis*-$[Pt(NH_3)_2(OH_2)(3'\text{-}GMPH)]^+$. However, on the basis of kinetic data we[3] have postulated that in the case of d-5′-$GMPH_2$, X is an *N*(7),α-*O*PO_3 cyclic species (**1**; Y = H), as opposed to (**2**; Y = H). Similar phosphate complexes of a variety of more labile metal(II) ions and derivatives of, in particular, adenosine have been studied by Sigel's group.[3] ^{31}P N.m.r. studies by Reily and Marzilli[5] demonstrate the formation of a cyclic complex from *cis*-$[Pt(NH_2Me)_2(OH_2)_2]^{2+}$ and 5′-$IMPH_2$. Here we present evidence which confirms that 5′-$GMPH_2$ forms a cyclic complex.

$$cis\text{-}[Pt(NH_3)_2(OH_2)_2]^{2+} + B \longrightarrow X \qquad \text{(i)}$$

$$X + B \longrightarrow cis\text{-}[Pt(NH_3)_2B_2]^{y+} \qquad \text{(ii)}$$

cis-$[Pt(NH_3)_2(OH_2)_2](CF_3SO_3)_2$ was prepared following the method of Tobias *et al.*[6] A 1 : 1 mixture of this complex and 5′-$GMPH_2$ was dissolved in a minimum of a 1 : 1 (v/v) mixture of glycerol and water at room temperature. (The complex dissolves slowly.) Fast atom bombardment (f.a.b.) spectra were run on a Kratos MS-30 instrument with a DS-55 data system. Samples were sputtered into the gas phase as ions by bombardment with 6 keV neutral xenon atoms. Runs were made after the 1:1 mixture had been standing at room temperature for 10, 20, 30, and 60 min. The four spectra are similar in general features; Figure 1 shows that obtained after 20 min.

The observation of a fairly intense cluster of ions corresponding to $[Pt(NH_3)_2(GMPH)]^+$ (centred at *m/z* 591; Figure 1) demonstrates that the reaction between the platinum complex and 5′-$GMPH_2$ takes place to a significant extent. (The assignments are for ^{195}Pt, the natural abundance of which is 34%. Other isotopes are present in the proportions ^{194}Pt, 33%; ^{196}Pt, 25%; and ^{198}Pt, 7%.) This reaction is

Table 1. Principal peaks in Figure 1.

m/z	Assignment
591	$Pt(NH_3)_2(GMPH)^+$
575	$Pt(NH_3)(GMPH_2)^+$
511	$[Pt(NH_3)_2(GMPH_2) - OP(OH)_2]^+$
495	$[Pt(NH_3)_2(GMPH_2) - O_2P(OH)_2]^+$
460	$[Pt(NH_3)_2(Gua - H) + OP(OH)_2]^+$
443	$[Pt(NH_3)_2(Gua - H) + OP(OH)_2]^+$ or $[Pt(NH_3)(Gua - H) + P(OH)_2 - H]^+$
379	$Pt(NH_3)_2(Gua - H)^+$
363	$Pt(NH_3)(Gua)^+$
346	$Pt(Gua)^+$
320	$[Pt(NH_3)_2(gly) - H]^+$
303	$[Pt(NH_3)(gly) - H]^+$
264	$[Pt(NH_3)_2(OH_2)_2 - H]^+$
246	$[Pt(NH_3)_2(OH_2) - H]^+$
229	$Pt(NH_3)_2^+$
212	$Pt(NH_3)^+$

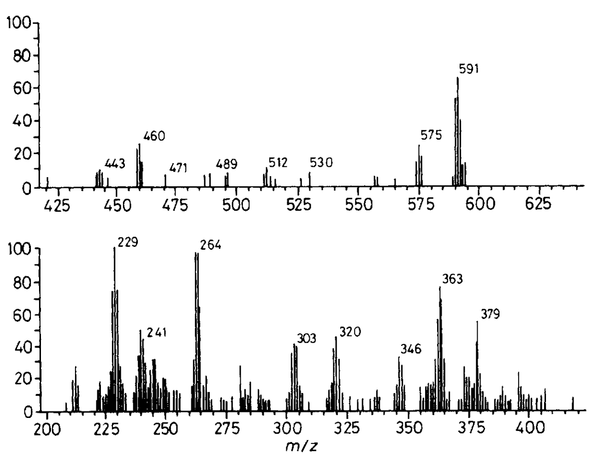
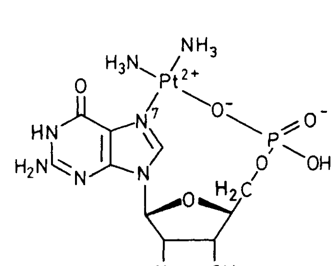
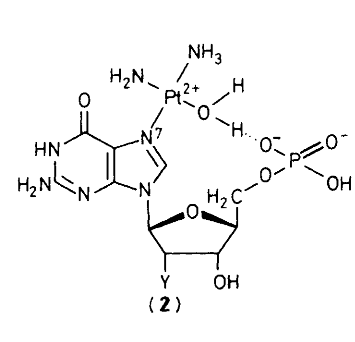


Figure 1. Fast atom bombardment mass spectrum of a 1 : 1 mixture of *cis*-$[Pt(NH_3)_2(OH_2)_2](CFSO_3)_2$ and 5′-$GMPH_2$ in 1 : 1 (v/v) glycerol–water after 20 min.

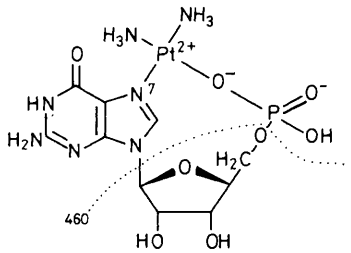


(**1**)



(**2**)

† *Abbreviations:* $GMPH_2$ = guanosine monophosphoric acid, d = 2′-deoxy, $IMPH_2$ = inosine monophosphoric acid, Gua = guanine, p = phosphate, A = adenosine, G = guanosine, gly = glycerol.



(3)

further supported by the fragment ions such as $Pt(NH_3)_2(Gua)^+/Pt(NH_3)_2(Gua - H)^+$, $Pt(NH_3)(Gua)^+/Pt(NH_3)(Gua - H)^+$ and $Pt(Gua)^+/Pt(Gua - H)^+$ (centred at *m/z* 379, 363, and 346). Partial and complete losses of the phosphate group from *m/z* 591 lead to peaks at *m/z* 511 and 495 (Table 1).

The strong peaks observed at *m/z* 264 and 229, which are also detected in the positive ion spectrum of the complex itself, can be rationalized as $[Pt(NH_3)_2(OH_2)_2 - H]^+$ and $[Pt(NH_3)_2]^+$, respectively. Thus the water ligands are not necessarily lost from the complex during the ionization process. The absence of water in ions containing Pt and GMPH suggests strongly that these ligands have been replaced by a new group during the reaction between the Pt complex and 5′-$GMPH_2$. It is proposed that the new group is a phosphate, so that the cyclic species (**1**; Y = OH) is formed.

The evidence for a cyclic structure such as (**1**) is further supported by the ions observed at *m/z* 460 and 443. These are particularly significant since they cannot readily be rationalized by the fragmentation of a non-cyclic structure but can be easily explained if the ribose ring is eliminated completely from a cyclic structure such as (**1**; Y = OH) while the phosphate and guanine groups are retained. The elimination is illustrated in structure (**3**), giving *m/z* 460, followed by loss of ammonia (or possibly O and H) to give *m/z* 443.

However, although (**1**; Y = H) exists in the mass spectrometer, it is almost certainly not present in solution in significant quantity prior to fast atom bombardment. Only a trace of the cyclic species $[Pt(NH_2Me)_2(IMP)]$ is present 20 min after mixing *cis*-$[Pt(NH_2Me)_2(OH_2)_2]^{2+}$ and 5′-IMP^{2-} in water, a significant quantity only being formed after heating at 50 °C for 30 min.[5] The same is true of *cis*-$[Pt(NH_3)_2(OH_2)_2]^{2+}$ and d-5′-$GMPH_2$.[7] [The phosphate in the cyclic complex of Reily and Marzilli is not protonated; *cf.* (**1**) for which there is f.a.b. evidence.] In reaction (i), the initial product X must be *cis*-$[Pt(NH_3)_2(OH_2)$(d-5′-GMPH)$]^+$. Thus this reaction resembles a typical substitution process involving platinum(II) in which there is no kinetic *trans* effect. Hence the water ligand in $[Pt(NH_3)_2(OH_2)$(d-5′-GMPH)$]^+$, if not particularly stable, is inert.

An implication of the preceding paragraph is that the abnormal kinetic behaviour of *cis*-$[Pt(NH_3)_2(OH_2)_2]^{2+}$ and excess of d-5′-$GMPH_2$ compared with d-3′-GMPH cannot be accounted for in terms of (**1**) as we originally proposed.[3] In both systems X (in the reaction scheme above) must be the aqua complex, *cis*-$[Pt(NH_3)_2(OH_2)$(d-GMPH)$]^+$. However only in the case of d-5′-$GMPH_2$ (and also 5′-$GMPH_2$) is the second step slow enough to be detected kinetically;[1,2] it is still too fast for a significant amount of (**1**, Y = H or OH) to be formed. This also indicates that *cis*-$[Pt(NH_3)_2(OH_2)$(d-5′-GMPH)$]^+$ must be somewhat inert (namely compared with its 3′-isomer). Perhaps the hydrogen bonding is unusually strong in (**2**, Y = H or OH).

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