X-Ray Evidence for Metal–N-7 Bonding in a Hydrated Manganese Derivative of Guanosine 5'-Monophosphate

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Single-crystal X-ray studies of a manganese(II) derivative of guanosine 5'-monophosphate, $[\text{Mn}(5'\text{-GMP})(\text{H}_2\text{O})_5]\cdot 3\text{H}_2\text{O}$, have shown that it is isostructural with its nickel analogue. The manganese atom therefore is bonded to five water molecules with the remaining octahedral co-ordination site being occupied by N-7 of the nucleotide base. No direct metal–phosphate bonding is involved, but there are structure-stabilizing intramolecular hydrogen bonds between two phosphate oxygen atoms and co-ordinated water molecules.

The effects of bivalent metal ions in stabilizing or destabilizing the structures of DNA or tRNA have been well established (Eichhorn & Shin, 1968; Fresco *et al.*, 1966). Moreover they are thought to influence protein synthesis (Szer & Ochoa, 1964) and to be involved in nucleotide-transport processes (Stillwell & Winter, 1974). Because of their constructive or potentially disruptive role the interaction of metal ions with nucleotides and their bases has been the object of intensive study for several years (Izatt *et al.*, 1971). Spectral methods, especially n.m.r., have been favoured hitherto. Unfortunately the interpretation of the results of these studies have not always been unambiguous and the identification of the co-ordination sites has been a subject of disagreement (Tu & Friedrich, 1968; Glassman *et al.*, 1971; Shin *et al.*, 1972; Ogawa *et al.*, 1971; Kotowycz & Suzuki, 1973).

In principle these problems could be resolved by full X-ray investigation. For nucleotide bases there is now a satisfactory body of such structural evidence (de Meester *et al.*, 1973), but this definitive information has been lacking for nucleotide derivatives because of greater difficulty in obtaining suitable crystals. We have recently determined the structure of a hydrated nickel complex of guanosine 5'-monophosphate, $[\text{Ni}(5'\text{-GMP})(\text{H}_2\text{O})_5]\cdot 3\text{H}_2\text{O}$ (de Meester *et al.*, 1974). A striking feature of the structure of this compound is that the metal ion does not bind directly to the phosphate, but to N-7 of the base. We have now obtained the corresponding manganese(II) derivative, $[\text{Mn}(5'\text{-GMP})(\text{H}_2\text{O})_5]\cdot 3\text{H}_2\text{O}$, and on the basis of single-crystal X-ray evidence have found it to be isostructural with the nickel analogue.

Experimental

Manganese(II) nitrate tetrahydrate (0.07 g) in water (2 ml) was added to an aqueous solution of $\text{Na}_2(5'\text{-GMP})\cdot \frac{1}{2}\text{H}_2\text{O}$ (Aldrich Chemical Co., Milwaukee, Wis., U.S.A.) (0.1 g in 8 ml). A white

precipitate formed. The mixture was stirred and the pH lowered to 4.19, when a clear solution was obtained. This solution was heated to 60°C for a few minutes and then kept at room temperature (22°C). Colourless plate-like crystals formed, and were collected, washed with a little water, and air-dried. Microanalysis was performed by the Pregl method.

Single-crystal X-ray oscillation and Weissenberg photographs were used to establish the unit cell and space group of the manganese derivative. Accurate unit-cell dimensions were obtained by measuring high-angle reflexions on a Siemens four-circle diffractometer and performing a least-squares calculation.

Results and discussion

The crystal data of the manganese derivative are compared with those of the analogous nickel compound for which a complete structure determination has been carried out (Table 1); the data are alike. More significantly, there is a very close similarity in the distribution of reflexion intensities in corresponding Weissenberg photographs, and this establishes that the two compounds are strictly isostructural. The slightly larger unit-cell volume (by approx. 3%) of the manganese compound is in line with the bigger size of the manganese atom relative to nickel. The stoichiometry of the compound is confirmed by the analytical results (Found: C, 21.55; H, 4.97. Calc. for $\text{Mn}(\text{C}_{10}\text{H}_{12}\text{N}_5\text{O}_8\text{P})\cdot 8\text{H}_2\text{O}$: C, 21.44; H, 5.04%).

Fig. 1 shows the molecular structure, common to both the nucleotide complexes, in which the metal atom bonds to the guanine moiety at the N-7 position. Five co-ordinated water molecules complete the octahedral metal environment, and the remaining water molecules are interspersed in the crystal lattice as water of crystallization. Although there is no direct metal–phosphate bonding, two of the phos-

Table 1. *Comparison of the crystal data of a hydrated manganese derivative of 5'-GMP with that of its nickel analogue*

Estimated standard deviations are quoted in parentheses.

Crystal data	[Mn(5'-GMP)- (H ₂ O) ₅], 3H ₂ O	[Ni(5'-GMP)- (H ₂ O) ₅], 3H ₂ O
System	Monoclinic	(de Meester <i>et al.</i> , 1974) Monoclinic
<i>a</i>	27.809 (3) Å [2.7809 (3) nm]	27.604 (4) Å (2.7604 (4) nm)
<i>b</i>	11.230 (1) Å [1.1230 (1) nm]	11.087 (2) Å [1.1037 (2) nm]
<i>c</i>	6.757 (1) Å [0.6757 (1) nm]	6.715 (2) Å [0.6715 (2) nm]
β	93.11 (1)°	93.94 (1)°
<i>U</i>	2107.0 Å ³ [2.1070 nm ³]	2050.2 Å ³ [2.0502 nm ³]
<i>Z</i>	4	4
Space group	C2	C2

Fig. 1. *Schematic view of the structure of the [Mn(5'-GMP)-(H₂O)₅] molecule*

phate oxygens are connected indirectly by means of intramolecular hydrogen bonds to co-ordinated water molecules.

Ogawa & Sakaguchi (1971) reported the isolation of a manganese 5'-GMP derivative of stoichiometry Mn(5'-GMP)₂·2H₂O. A possible cause of the large

difference in water content of their compound could be the more intensive drying conditions that they used (vacuum drying at 50°C over P₂O₅). I.r. criteria were used to infer direct metal-phosphate bonding in this lower hydrate. The low symmetry of the nucleotide phosphate renders such an i.r. criterion of very doubtful use and hydrogen-bonding effects would further limit the validity of this method. However, in view of the lower number of water molecules present in the sample obtained by Ogawa & Sakaguchi (1971), direct metal-phosphate bonding cannot, of course, be ruled out for their strongly dried material.

If the structure type shown in Fig. 1 proves to be of widespread occurrence this may be of biological relevance, since conditions *in vivo* would favour a high degree of hydration about a metal ion.

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