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Molecular Architecture with Nucleobases, Metal Ions and Water Molecules: Mixed Adenine, Hypoxanthine Quartet Containing *trans*-$(NH_3)_2Pt^{II}$ and Ag^+ and Harboring a Water Hexamer in Its Chair Conformation

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The formation and X-ray crystal structure of a molecular rectangle of 14.25(2) Å × 10.36(2) Å, comprised of two neutral 9-methyladenine (9-MeA) and two anionic 9-methylhypoxanthinate (9-MeHx) model nucleobases as well as two *trans*-$(NH_3)_2Pt^{II}$ and two Ag^+ entities, and further cross-linked intermolecularly by Ag^+ ions, is described: *trans*-$[\{(NH_3)_2Pt(9\text{-}MeA)(9\text{-}MeHx)Ag(NO_3)(H_2O)\}_2Ag](NO_3)_3 6H_2O$ (4). The water molecules are located between adjacent purine quartets and adopt a cyclic water hexamer structure in a chair conformation. In addition, the X-ray crystal structure of the precursor of 4, *trans*-$[(NH_3)_2Pt(9\text{-}MeA)(9\text{-}MeHxH)](NO_3)_2H_2O$ (2), is reported. 4 is discussed in terms of its relationship to proposals in the literature concerning possible structures of metalated forms of purine quartets.

Keywords: X-ray crystallograph; Purines; Nucleobases; Metals; Water hexamer

INTRODUCTION

Higher order DNA architectures beyond the well-known Watson–Crick duplex are an emerging feature of DNA structural chemistry [1,2]. It is now believed that these features are associated with regulation and DNA function and that, for example, quadruplex DNA plays both functional and dysfunctional roles in the cellular metabolism [3]. Guanine quartets (G_4) [4,5] appear to play a special role in DNA quadruplexes, but there exist meanwhile examples of many other quartets, including of thymine (T_4) [6,7] and uracil (U_4) [8] well as mixed guanine, cytosine (G_2C_2) [9] and mixed adenine, thymine quartets (A_2T_2) [10]. In most cases, it has been established that alkali metal ions are absolutely essential in stabilizing the base quartet structures. Interestingly, as early as 1980, it had been demonstrated by Shin and Eichhorn, that the nonphysiological Ag^+ ion is capable of converting poly(inosine), (polyI), into a highly ordered tetrastranded structure [11]. It had been shown by these authors, that one Ag^+ per purine base was bonded and that one proton in liberated by Ag^+. A model had been put forward, in which four Ag^+ ions are crosslinking four hypoxanthinate bases in a cyclic fashion via the deprotonated N(1) position as well as the exocyclic O(6) site (Fig. 1).

Over the years, our group has been conducting studies on model nucleobases quartets, involving both alkali metals ions [12,13] and nonphysiological metal entities such as substitutionally inert transition-metal complexes [14], linear metal entities such as *trans*-a_2Pt^{II} ($a = NH_3$ or amine) or other metal ions, e.g. Hg^{2+}, displaying linear coordination geometries [15–20]. A number of variants of artificial nucleobases quartet structures have thus been obtained. The “advantage” of artificial nucleobases quartets containing *trans*-a_2Pt^{II} entities over the natural nucleobase quartets in many cases was their chemical inertness in solution, hence the fact that they retained their solid-state structure also in solution.

Here we report on a mixed *trans*-$(NH_3)_2Pt^{II}$, Ag^+ purine quartet which bears relevance, at least from a structural point of view, to the tetrastranded polyI structure mentioned above. The X-ray crystal

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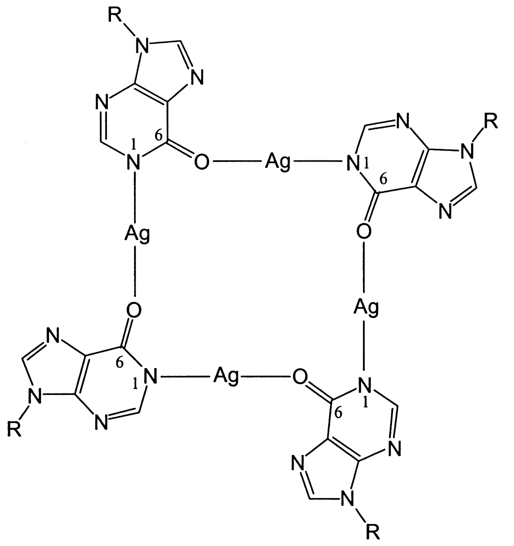

FIGURE 1 Schematic representation of proposed [Ag-hypoxanthinate]$_4$ quarter as formed between Ag$^+$ and poly(inosine) [11].

structure analysis of the metalated purine quartet reveals that the crystal water molecules form a cyclic hexamer structure in a chair conformation, located between layers of base quartets. This feature by itself is noticeable in the light of the high current interest in water clusters in all their variations [21,22].

EXPERIMENTAL

Syntheses

trans-[$(NH_3)_2$Pt(9-MeA)(9-MeHxH)]$(NO_3)_2\cdot H_2O$ (**2**): A sample of *trans*-[$(NH_3)_2$Pt(9-MeHxH)Cl]Cl (200 mg, 0.48 mmol), prepared from *trans*-$(NH_3)_2$-$PtCl_2$ and 9-MeHxH [23], was suspended in 80 ml of water and $AgNO_3$ (163 mg, 0.96 mmol) was added. A solution of 9-MeA (107 mg, 0.72 mmol) was brought to pH = 2 by means of HNO_3 and added to the suspension. The mixture was stirred for 5 days at 50°C in the dark, cooled to 4°C, and the precipitated AgCl was removed by filtration. The filtrate was concentrated to 10 ml. Slow evaporation gave colorless crystals of **2** suitable for X-ray analysis (yield 30%). Anal. Calc. for $C_{12}H_{20}N_{13}O_{7.5}Pt$ (hemihydrate) C: 21.8; H:3.0; N:27.5. Found: C: 21.9, H: 3.0, N: 27.5. In contrast, X-ray analysis showed the presence of one water molecule.

2:^{1}H NMR (D_2O, pD = 6.5, δ ppm, s) 8.75 (H(8)-A); 8.71 (H(8)-HxH); 8.36 (H(2)-A); 8.33 (H(2)-HxH); 3.96 (CH_3-A); 3.93 (CH_3-HxH); (DMSO-d_6 δ ppm, s) 13.20 (N(1)H-HxH); 8.79 (H(8)-A, H(8)-HxH); 8.60 (NH_2-A); 8.40 (H(2)-A, H(2)-HxH); 4.33 (Pt-NH_3); 3.94 (CH_3-A); 3.91 (CH_3-HxH). ^{195}Pt NMR (D_2O, δ ppm, s) −2462. IR (KBr) 3418 (s), 1680 (s), 1635 (s), 1598 (s), 1384 (s), 787 (w), 764 (w), 714 (w).

trans-[{$(NH_3)_2$Pt(9-MeA)(9-MeHx)Ag$(NO_3)(H_2O)$}$_2$Ag]$(NO_3)_3\cdot 6H_2O$ (**4**). The complex was obtained by reaction of **2** (7 mg, 0.01 mmol) in 500 µl D_2O (pD = 6.5) with 3 equivalents of $AgNO_3$. After the addition of the silver salt, the pD dropped to 2.6 and colorless crystals suitable for X-ray crystallography precipitated from solution (yield 20%).

4:^{1}H NMR (D_2O, pD = 2.6, δ ppm, s) 8.84, 8.73, 8.45, 8.35, 3.99, 3.97.

Spectroscopy

^{1}H NMR spectra were recorded on Bruker 200 FT NMR and DRX 400 FT spectrometers using D_2O (TSP as internal reference) as well as DMSO-d_6 (non-deuterated DMSO as reference, $\delta = 2.53$ relative to TMS) as solvents. The ^{195}Pt NMR spectrum (43.02 MH$_z$) was recorded on an AC 200 spectrometer in D_2O (Na_2PtCl_6 external reference). The IR spectrum was recorded on a Bruker IFS 28 instrument.

X-ray Crystallography

Crystal data for **2**: $C_{12}H_{21}N_{13}O_8Pt$ $M_r = 670.51$, monoclinic, space group $P2_1/n$, $a = 13.961(3)$, $b = 11.769(2)$, $c = 14.220(3)$, $\beta = 111.29(3)$, $V = 2177.0(8)\,\text{Å}^3$, $Z = 4$, $D_c = 2.046\,\text{g cm}^{-3}$, $\mu(\text{MoK}\alpha) = 6.516\,\text{mm}^{-1}$, $T = 293(2)\,\text{K}$, Enraf–Nonius–KappaCCD [24] with graphite monochromator, φ-scans, 5159 independent reflections, $R_{\text{int}} = 0.070$, structure solved by standard Patterson methods [25] and refined by full matrix least squares on F^2 using ShelXL-97 [26]. All nonhydrogen atoms were refined anisotropically. Hydrogens were placed at calculated positions and not further refined. 317 refined parameters gave $R_1 = 0.0348$ and $wR_2 = 0.0459$ for 2000 reflections with $I \geq 2\sigma(I)$ and $wR_2 = 0.0537$ for all data, maximum and minimum features in difference Fourier map were 1.15 and $-0.70\,\text{e Å}^{-3}$ (near Pt(1)).

Crystal data for **4**: $C_{12}H_{25}Ag_{1.5}N_{13.5}O_{12}Pt$ $M_r = 907.35$, triclinic, space group P-1, $a = 7.520(2)$, $b = 12.025(2)$, $c = 14.962(3)$, $\alpha = 99.92(3)$, $\beta = 92.93(3)$, $\gamma = 102.87(3)$, $V = 1293.6(4)\,\text{Å}^3$, $Z = 2$, $D_c = 2.329\,\text{g cm}^{-3}$, $\mu(\text{MoK}\alpha) = 6.609\,\text{mm}^{-1}$, $T = 293(2)\,\text{K}$, Enraf–Nonius Kappa CCD [24] with graphite monochromator, φ-scans, 4694 independent reflections, $R_{\text{int}} = 0.094$, structure solved by standard Patterson methods [25] and refined by full matrix least squares on F^2 using ShelXL-97 [26]. All nonhydrogen atoms were refined anisotropically except N(3N), O(7); O(8), O(9) and O(1W). Hydrogens were placed at calculated positions and no further refined. Three hundred and sixty nine refined parameters gave $R_1 = 0.0508$ and $wR_2 = 0.0795$ for 2264 reflections with $I \geq 2\sigma(I)$ and $wR_2 = 0.0955$ for all data, maximum and minimum features in

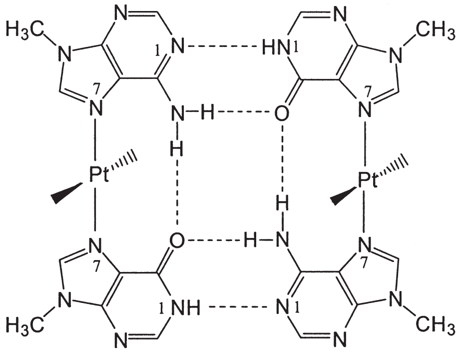

FIGURE 2 Drawing of solid state structure of *trans* [$(NH_3)_2$Pt(9-MeA)(9-MeHxH)]$(ClO_4)_2$ (**1**) [19].

difference Fourier map were 1.07 and $-1.78\,e\,\text{Å}^{-3}$ (near N(1) and Pt(1), respectively).

The scaling as well as the global refinement of crystal parameters for both **2** and **4** were preformed by SCALEPACK [24]. Reflections, which were partly measured on previous and following frames, were used to scale these frames on to each other. Merging of redundant reflections eliminates in part absorption effects, and also a crystal decay if present is considered.

RESULTS AND DISCUSSION

Starting Compound

We have recently described the model nucleobase complex *trans*-[$(NH_3)_2$Pt(9-MeA-*N*7)(9-MeHxH-*N*7)]$(ClO_4)_2$ (**1**) (with $9-\text{MeA}=9-$ methyladenine; $9-\text{MeHxH}=9-$ methylhypoxanthine) [19]. This compound has been prepared with the aim of finding out whether the ADAD (A = acceptor; D = donor) hydrogen bonding capability of the cation in its expected *hh* (*hh* = head–head) arrangement, which makes it self-complementary, would lead to dimerization and consequently quartet formation. Indeed, this was the case, as established by X-ray crystallography (Fig. 2).

As has now seen found, $[ClO_4]^-$ anion are essential in generating the quartet structure: The corresponding nitrate compound, *trans*-[$(NH_3)_2$-Pt(9-MeA-*N*7)(9-MeHxH-*N*7)]$(NO_3)_2$·H_2O (**2**), despite its essentially identical cation structure (Fig. 3), displays a different packing pattern, which does not permit interaction H bonds (Fig. 4). Rather, a nitrate anion blocks the N(1)H site of the hypoxanthine base, leading to a centrosymmetric dimer with stacking (3.3 Å, av.) of the purine bases of two cations. As a consequence of this difference, the dihedral angle between the two bases is larger in **2** (9.7(1)°) as compared to **1** (1.5(2)°) and the intramolecular H bond between O(6) of 9-MeHxH and NH_2(6) of 9-MeA becomes longer in the case of **2** (3.092(7) Å in **2** vs. 3.016(6) Å in (**1**).

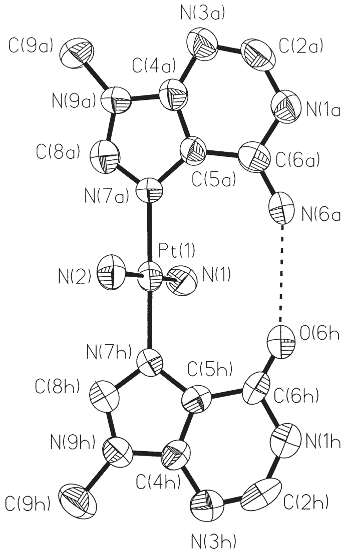

FIGURE 3 View of cation of *trans*-[$(NH_3)_2$Pt(9-MeA)(9-MeHxH)] $(NO_3)_2$·H_2O (**2**).

The crystallographic differentiation of the two purine bases in **1** and **2** is straightforward on the basis of the following considerations: first, the internal ring angles differ significantly (8–9 σ).* The angle is expectedly larger in the case of the hypoxanthine base (which has a proton at this site) as compared to adenine (which has a lone electron pair at N1): 124.5(4)° (**1**) and 125.8(6)° (**2**) vs. 119.5(4)° (**1**) and 118.4(5) (**2**). Second, bond lengths of the exocyclic groups differ likewise significantly, with C(6)–O(6) of the hypoxanthine base being significantly shorter (8–9 σ) than that of C(6)–N(6) of adenine (Table I). The values observed in **1** and **2** not only are in agreement with similar differences in the free bases [27], but also with those of metal complexes of a large series of adenine and guanine model nucleobases, e.g. [15–18,20].

^{1}H and ^{195}Pt NMR spectra (D_2O; DMSO-d_6) of **1** and **2** are identical, as expected. The chemical shift of the adenine NH_2 protons at 8.60 ppm (DMSO-d_6) is consistent with intramolecular H bond formation with O(6) of 9-MeHxH [28], and therefore suggests a preferential *head–head* orientation of the two nucleobases of **1** and **2** in solution. The ^{195}Pt NMR chemical shift of $\delta=-2462$ ppm is in agreement with a PtN_4 coordination sphere. As already pointed out [19], there is no indication for any significant dimerization of **1** (or **2**) in DMSO solution.

Heteronuclear Pt, Ag Derivatives of 1 And 2

Addition of an excess of $AgNO_3$ (3 equivalent) to aqueous solutions of **1** or **2** causes a marked drop in

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*The esd is calculated according to $\sigma=(\sigma_1^2+\sigma_2^2)^{1/2}$ with σ_1 and σ_2 being the errors in bond lengths and angles which are compared.

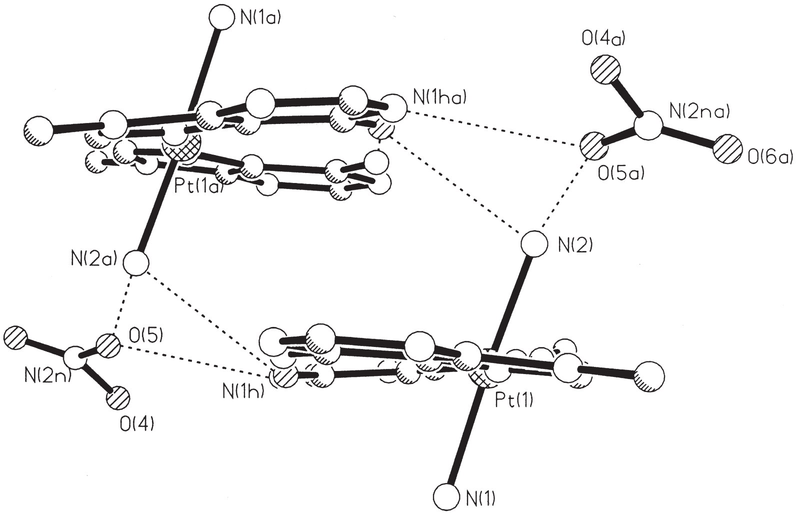

FIGURE 4 Side views of arrangement of cations of **2** with H bonds involving also nitrate ions shown.

pH, usually from ca. 6 to ca. 2. As demonstrated in a control experiment, and consistent with the high pK_a value of the aqua ligand in $Ag(H_2O)^+$ (ca. 10), this feature is not due to hydrolysis but rather due to deprotonation of **1** (**2**). The most likely site of deprotonation is the N(1) position of the hypoxanthine ligand. In other words, the change in pH indicates that Ag^+ ions are displacing protons of **1** (**2**). ^1H NMR chemical shifts of the aromatic protons of **1** (**2**) in the presence of excess Ag^+ are essentially the same as those of **1** (**2**) at identical acidic pH (e.g. at pD 2.6:8.84, 8.73, 8.45, 8.35, 3.99, 3.97 (δ, ppm, s)). The suggest that there is rapid exchange between Ag^+ and H^+ on the NMR time scale.

Crystallization of species from $AgNO_3$ containing solutions of **1** on one hand and **2** on the other provided a surprise in that compounds of different stoichiometries and different structures were obtained. The only difference between the two preparations was that **1** contained ClO_4^- in addition to NO_3^- (from $AgNO_3$), while in the second preparation NO_3^- was the only anion.

As previously reported, the product isolated from a mixture of **1** and $AgNO_3$ proved to be a one-dimensional helical polymer, *trans*-[{$(NH_3)_2$-Pt(9-MeA)(9-MeHxH)}Ag(NO_3)(H_2O)](ClO_4)(NO_3) (**3**) [19]. In **3**, Ag^+ ions cross-link the N(1) and N(3) positions of adenine nucleobases of adjacent cations of **1**. Both Ag–N bonds are rather long, 2.321(4) (Ag(1)–N(1a)) and 2.351(4) Å (Ag(1)–N(3a)). Hypoxanthine is not involved in Ag^+ coordination at all and both nucleobases are neutral. Thus, the solid-state structure of **3** does not reflect the situation in solution, where ligand deprotonation is evident (c.f. above). There can be no doubt that the two purine bases in **3** are correctly assigned. For example, the short C(6)–O(6) bond (1.225(6) Å)) of 9-MeHxH as opposed to the longer C(6)–N(6) bond (1.340(6) Å) of 9-MeA and the large internal ring angle of N(1) of 9-MeHxH (125.4(5)°) clearly prove that the hypoxanthine ligand is neutral and does not bind Ag^+. Moreover, there is no reason to assume that the adenine base is deprotonated at the exocyclic amino group. Neither does the number of anions support such a situation, nor does the high pK_a of this group (17.6 [29]) favor such a scenario, not even with metal ions coordinated [30,31].

The Ag^+ adduct isolated from an aqueous solution of **2** and $AgNO_3$, hence with ClO_4^- being absent, resulted in a compound of different structure, different stoichiometry, and above all in a compound containing indeed the 9-methylhypoxanthine anion (9-MeHx) (Fig. 5). The compound was shown by X-ray crystallography to

TABLE I Comparison of selected bond lengths (Å) and angles (deg) of **1**, **2**, **3**, **4**

	1	2	3	4*
C(6h)–O(6h)	1.253(6)	1.219(6)	1.225(6)	1.29(1)
C(6a)–N(6a)	1.317(5)	1.327(6)	1.340(6)	1.30(1)
C(6h)–N(1h)–C(2h)	124.5(4)	125.8(6)	125.4(5)	119.4(9)
C(2h)–N(3h)–C(4h)	110.6(4)	110.3(5)	110.8(5)	110.2(10)
C(6a)–N(1a)–C(2a)	119.5(4)	118.4(5)	119.4(4)	120.3(9)
C(2a)–N(3a)–C(4a)	111.1(4)	108.8(5)	110.4(4)	112.3(10)

*Model with Ag^+ bonded to 9-MeHx (c.f. text).

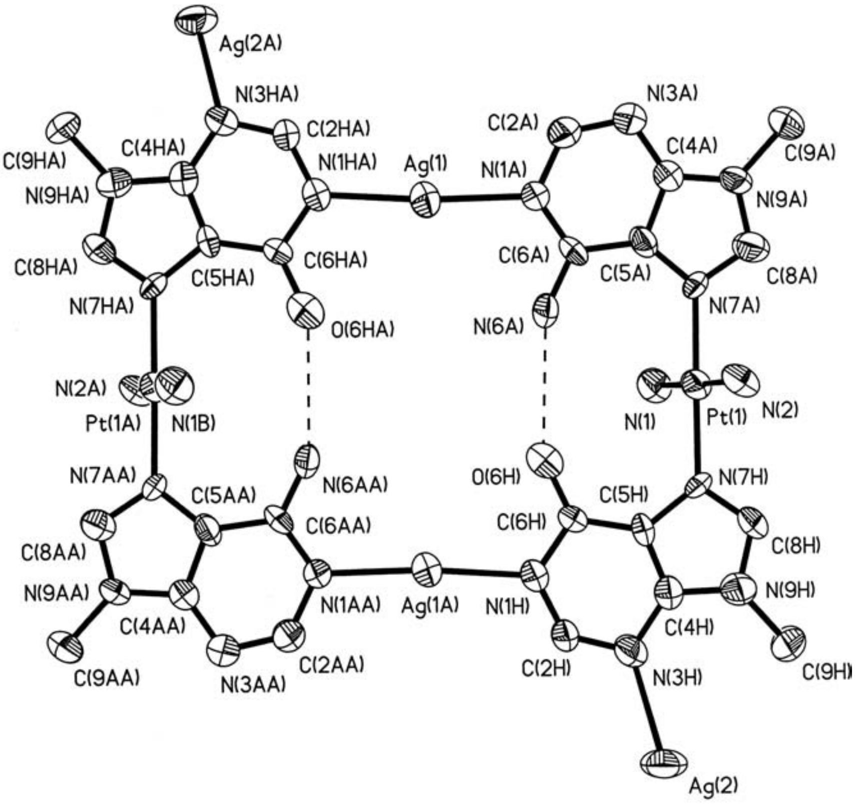

FIGURE 5 Section of metalated purine base quartet *trans*-[{$(NH_3)_2$Pt(9-MeA)(9-MeHx)Ag$(NO_3)(H_2O)$}$_2$Ag]$(NO_3)_3$·$6H_2O$ (**4**).

be *trans*-[{$(NH_3)_2$Pt(9-MeA)(9-MeHx)Ag$(NO_3)(H_2O)$}$_2$Ag]$(NO_3)_3$·$6H_2O$ (**4**). The compound consists of a purine quartet with the four bases cross-linked by two *trans*-$(NH_3)_2Pt^{II}$ units and two Ag^+ ions. Individual metalated base quartets, which have dimensions of 14.25(2) Å × 10.36(2) Å (separations between adjacent 9-methyl groups), are joined through additional Ag^+ ions into an infinite array (Fig. 6). Selected interatomic distances and angles of **4** are listed in Table II.

Unlike in **1**, **2**, and **3**, the differentiation of the two kinds of purine bases in **4** proved difficult. The structure was originally refined under the assumption that a similar Ag^+ binding pattern as seen in **3** might be expected, hence that it was the adenine base that carried a Pt^{II} at N(7) and two Ag^+ at N(1) and N(3). However, the result of the refinement gave an unreasonably long C(6)–O(6) bond of 1.33(1) Å and a likewise unexpectedly short C(6)–N(6) bond of 1.27(1) Å. While N(1) deprotonation of the hypoxanthine base is expected to cause a lengthening of the bond to the carbonyl group (albeit counteracted by the coordination of a metal at N(1)), experience with N(7) platinated, N(1) deprotonated guanine [32] as well as N(1) platinated [33] and N(7), N(1) diplatinated guanine [34] rules against such a dramatic increase. Furthermore, to the best of our knowledge, there is no example of any adenine metal complexes where the C(6)–N(6) bond is anything

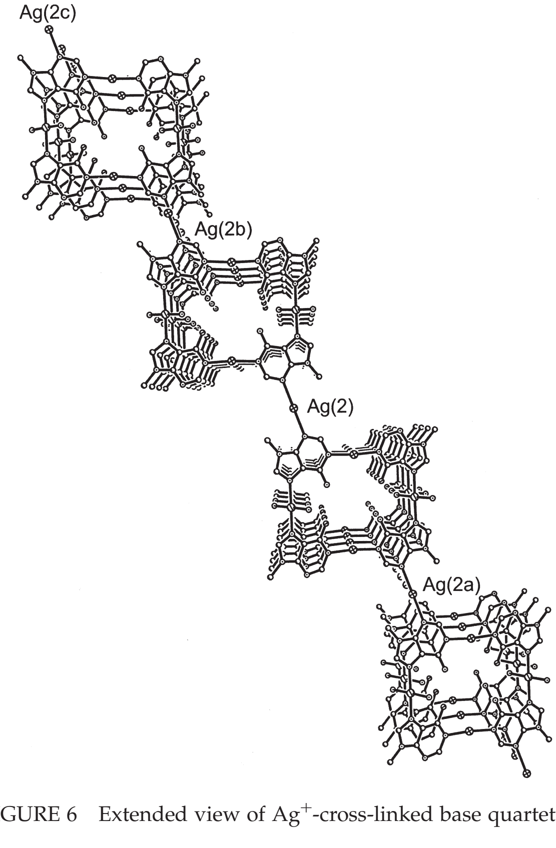

FIGURE 6 Extended view of Ag^+-cross-linked base quartets **4**.

TABLE II Selected bond lengths (Å) and angles (deg) of **4**

Pt(1)–N(7h)	2.022(8)	N(7h)–Pt(1)–N(7a)	178.8(4)
Pt(1)–N(7a)	1.998(8)		
Ag(1)–N(1a)	2.173(8)	N(1h)*–Ag(1)–N(1a)	173.9(3)
Ag(1)–N(1h)*	2.149(8)	N(3h)–Ag(2)–O(1w)	74.9(5)
Ag(2)–N(3h)	2.312(9)	N(3h)–Ag(2)–O(7n)	87.6(6)
Ag(2)–O(1w)	2.92(2)	O(7n)–Ag(2)–O(1w)†	167.1(7)
Ag(2)–O(7n)	2.58(2)		
Ag(1)–Ag(1)*	7.404(3)		
Pt(1)–Pt(1)*	10.703(3)		
		Pt(1)–N(7h)/Ag(1)*–N(1h)	86.0(5)
N(6a)···O(6h)	3.036(12)	Pt(1)–N(7a)/Ag(1)–N(1a)	88.1(5)
N(1)···O(6n)	2.981(18)	base a/base h	9.4(3)
N(1)···O(2n)‡	2.878(13)		
N(2)···O(4n)¶	2.973(16)		
C(8a)···O(3n)‡	2.967(16)		
N(1)···O(2w)	3.176(12)		
N(6a)···O(3w)§	2.845(12)		
O(6h)···O(3w)‖	2.713(12)		
O(2w)···O(3w)	2.725(12)	O(2w)–O(3w)–O(4w)‖	107.2(4)
O(2w)···O(4w)	2.835(13)	O(3w)‖–O(4w)–O(2w)	95.7(4)
O(3w)···O(4w)‖	2.747(13)	O(4w)–O(3w)–O(3w)	106.8(4)

* $2-x, 2-y, 1-z$. † $2-x, 3-y, 2-z$. ‡ $-x, 1-y, 1-z$. ¶ $1-x, 2-y, 2-z$. § $1+x, y, z$. ‖ $1-x, 2-y, 1-z$.

near the value obtained, not even when metal binding is through deprotonated N(1) [35–37]. Finally, the thermal ellipsoids of the two exocyclic groups seemed odd in the sense that the one of the NH_2 group was small and that of the oxygen considerably larger. Subsequently a model was tested, in which the purine bases were inverted. The refinement was not fully satisfactory either: although the thermal ellipsoids of $N(6)H_2$ and O(6) increased and decreased, respectively, the bond lengths to the exocyclic groups became identical within the error limits, 1.29(1) Å for C(6)–O(6) and 1.30(1) Å for C(6)–N(6). Both models gave almost identical *R* values. Attempts to apply disorder models with the two purine bases interchanged in different ratios were fully unsatisfactory in that they led to higher *R* values. In the absence of any other hard evidence, we presently favor the second model (used in Fig. 5), primarily because the first one appears less likely for the reasons given above. Also it should be noted, that 3-fold metalation of another 6-oxopurine base, of 9-ethyl-guanine, via N(1), N(3),

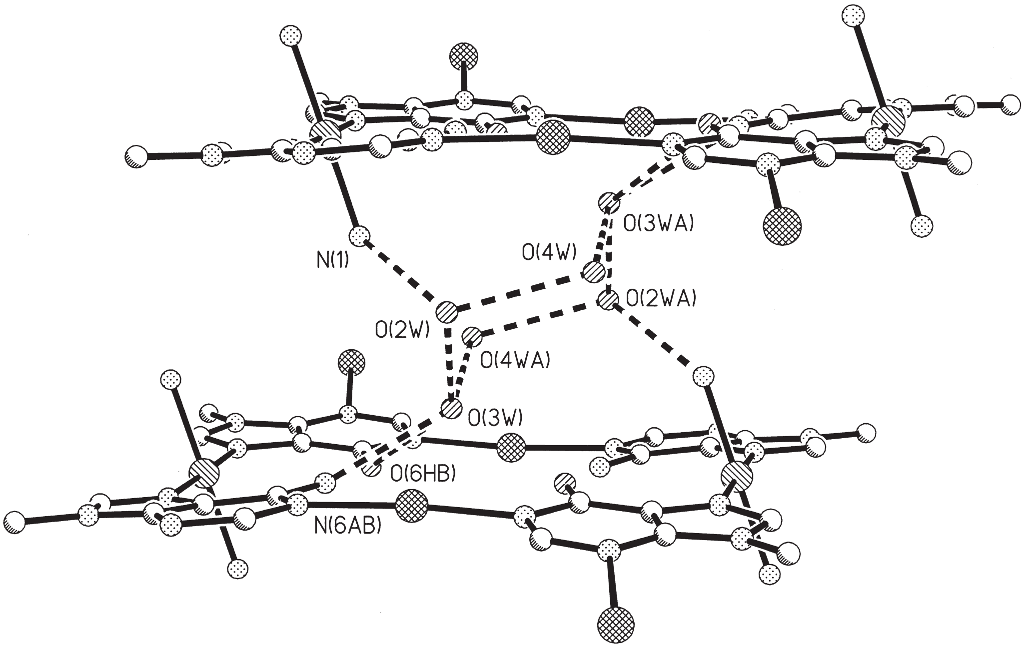

FIGURE 7 Section of stack of cations of **4**, viewed from the side. The distance between adjacent purine quartets is ca. 7.0 Å. This space hosts a hydrogen bonded water hexamer (O(3W), O(2W), O(4W), O3(WA), O2(WA), O4(WA)) which adopts a chair conformation.

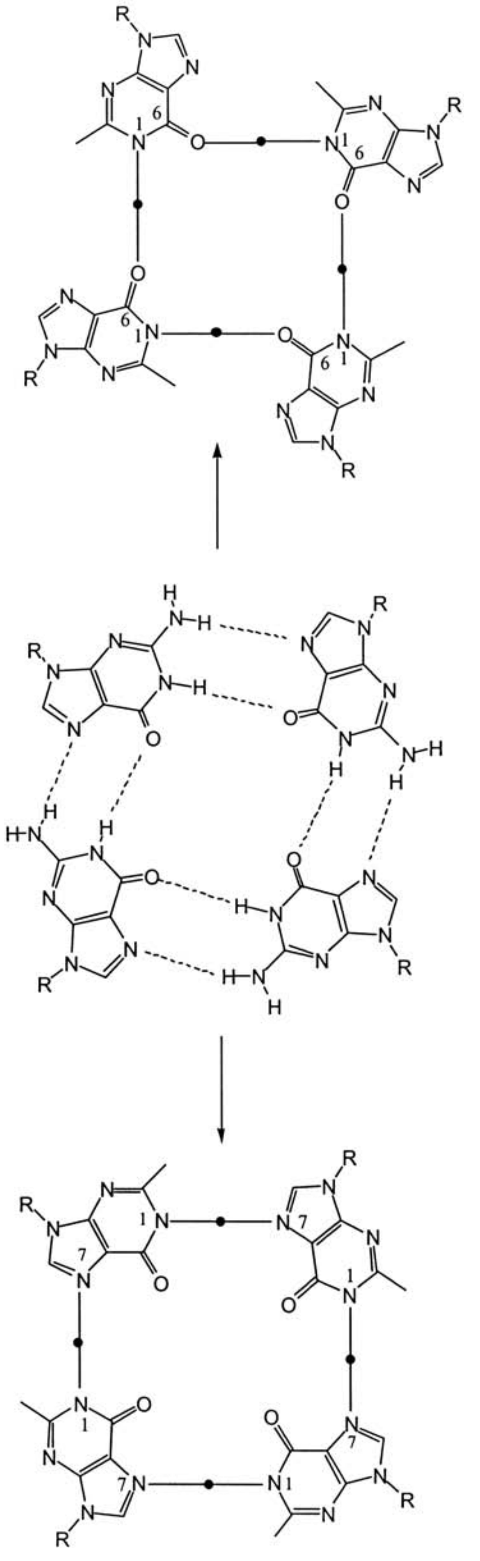

FIGURE 8 Relationship between natural G_4 base quartet (middle), and metalated forms: Shin/Eichhorn model with metal cross-linking the deprotonated N(1) position and O(6) (top), and model with N(1), N(7) metal cross-linking (bottom). Substituents at the 2-positions of the metalated quartets have been omitted. It needs to be emphasized that the quartet at the bottom may also contain pairs of different purine bases, e.g. adenine and guanine or adenine and hypoxanthine.

and N(7) has been previously observed by us [38]. We are aware that the use of different 9-substituents of the two purine bases could have solved the question unambiguously. Unfortunately, our attempts have been unsuccessful as yet to obtain single crystals of a similar compound with 9-ethyladenine substituting for 9-methyladenine.

Irrespective of the crystallographic question of properly differentiating the two purines in **4**, the metal binding pattern within the rectangle is not in question: Pt^{II} cross-links the N(1) position of adenine with the deprotonated N(1) site of hypoxanthine. The Ag(1)–N(1) distances to the two bases are rather similar in both models, and do not differ greatly (c.f. Table II). It is noted that the adenine-N(1)–Ag(1) distance is dramatically shorter in **4** (2.173(8) Å) as compared to the helical compound **3** (2.321(4) Å). Unlike Ag(2), which is strictly linear, the coordination geometry of Ag(1) deviates from linearity (173.9(3)°) and there are two longer contacts to oxygen atoms of H_2O (3.030(9) Å) and NO_3^- (2.957(11) Å).

As evident from a side view (Fig. 7), molecular rectangles of **4** are roughly parallel (distance ca. 7.0 Å), but slightly shifted, resulting in intermolecular Pt···Pt distances for 7.520(2) Å. The space between stacked base quartets is occupied by six water molecules, which adopt a chair conformation and display hydrogen bonds between 2.725(12) and 2.835(13) Å (Table II). These distances compare well with findings in a similar water hexamer hosted by an organic lattice [39] as well as related water clusters [21,40]. The water chair is anchored via six additional hydrogen bonds, which extend from $N(6)H_2$ of adenine, O(6) of hypoxanthinate, as well as NH_3 ligands (Fig. 7 and Table II).

SUMMARY

The X-ray crystal structure of **4** lends credit to a suggestion made by Bélanger-Gariépy and Beauchamp [41], who on the basis of a bis(9-methylhypoxanthine) complexes of Ag^+ have proposed that an alternative to the Shin/Eichhorn model (Fig. 1) exists in which the metal ions bind exclusively to the N(1) and N(7) sites of 9-MeHx rather than to N(1) and O(6). Irrespective of the use of two different purine bases in **4**, which results in the formation of two intramolecular hydrogen bonds, and the use of two different metal entities, structural aspects of **4** support this view. As we have pointed out before [17,20,42] metal binding to N(1) and N(7) sides makes purine bases building blocks with 90° angles. The metal binding patterns realized in **4**—pair wise N(7), N(7) and N(1), N(1) coordination—leads to a rectangular structure. It needs to be pointed out that a linkage isomer involving mixed N(1), N(7) metal coordination is also feasible which would generate a square of ca. $12 \times 12\,\text{Å}^2$. There is a close structural relationship between the prototype of a purine quartet, the G_4 quartet on one hand, and the Ag-hypoxanthine quartet as postulated by Shin and Eichhorn, as well as the hypothetical linkage isomer of **4** on the other. Thus, replacement of the intermolecular H bonds between O(6) and N(1)H by a linear metal entity (and concomitant loss of the H bonds between N(2)H_2 and N(7)) leads to the Shin/Eichhorn model, while replacement of the H bonds and N(1), N(7) metal bridging produces the linkage isomer of **4** (Fig. 8). It may depend on the nature of the linear metal ion, which metal modification is realized. Whether or not metalated purine quartets play any physiological role, e.g. in nucleic acid condensation brought about by metal ions, is unclear. However, studying the interaction of cationic, artificial metal containing nucleobase quartets with natural ones should be an interesting and challenging task. After all, it has been shown [43,44] that telomerase inhibition can be brought about by planar, cationic species, possibly though stabilization of G_4 structures in the telomeres.

Finally, it should be mentioned that Houlton *et al.* [45,46] recently described yet two other types of artificial, metal containing guanine quartets in which neither (N1) nor O(6) sites are occupied by metal ions.

Formation of **4** poses yet another interesting question: How is Ag^+ binding to N(1) of 9-MeHx brought about in moderately acidic medium? This position has to be deprotonated, but Pt^{II} binding to N(7) of 9-methylhypoxanthine acidifies this proton only moderately, by ca. 1.5 log units ($pK_a \cong 7.7$) [47]. An attractive hypothesis is that Ag^+ binding to N(3) assists deprotonation of this site by further acidifying the N(1) proton. If true, this possibility could further support the assignment of the two purine bases in **4**.

X-RAY DATA DEPOSITION

X-ray data of **2** and **4** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-172243 and 172244.

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