Structural precursor of the hemideprotonated guanine pair

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A pairing scheme (GG7) between two neutral guanine nucleobases taking place *via* the Watson–Crick faces and involving two bridging water molecules is presented, which upon removal of a $H_5O_2^+$ entity could convert into the hemideprotonated guanine pair (GG5).

Self-pairing between N(9) substituted guanine nucleobases (G), as observed in their solid state structures as well as in nucleic acids, occurs in a number of variations. In Fig. 1 the four most common self-pairing patterns GG1–GG4 are listed. They are observed in ribbon-like assemblies of G molecules (GG1 + GG4; GG3) [1,2] or as part of the cyclic G quartet (GG2).[3] In antiparallel B-DNA only GG2 can be realized, as it is the only self-pair with a *cis* orientation of the glycosidic bonds, with one sugar adopting an *anti* configuration, and the second one being *syn*.[4] GG3 can also be part of a CG·G triplet (C = cytosine).[5] In RNA structures additional variants are found, among others one with a water molecule inserted between N(3) of one G and N(1)H of the other.[6]

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We are interested in effects of metal ion coordination on hydrogen bonding properties of nucleobases,[7] and have observed in addition to GG1[8] and GG4 [9] patterns of N(7) platinated G bases also pairing schemes between neutral and N(1)-deprotonated guanine bases (GG5).[10,11] This "hemideprotonated guanine pair" gives rise to three hydrogen bonds and exceeds the GC Watson–Crick pair in strength by far.[12] In a way GG5 resembles GG6, the hemiprotonated pair of 7-methylguanine bases,[13,14] which likewise has three H bonds.

Here we report on a self-pair between two N(7) platinated neutral guanine bases, GG7, which involves two water molecules between the Watson–Crick faces. Inclusion of water in base pairing schemes has occasionally been reported, both in mismatches (*e.g.* U·C, T·G or C·A with U = uracil and A = adenine)[15] and in metal complexes of nucleobases.[10e] We consider GG7 a structural precursor of hemideprotonated GG5 because all it requires to convert GG7 into GG5 is the removal of a $H_5O_2^+$ from GG7 and a small slide toward each other to produce this pair: $GG7 \rightarrow [GG5]^- + H_5O_2^+$. Moreover, $H_5O_2^+$ has recently been shown to be crucial in the transport of protons in aqueous solution.[16]
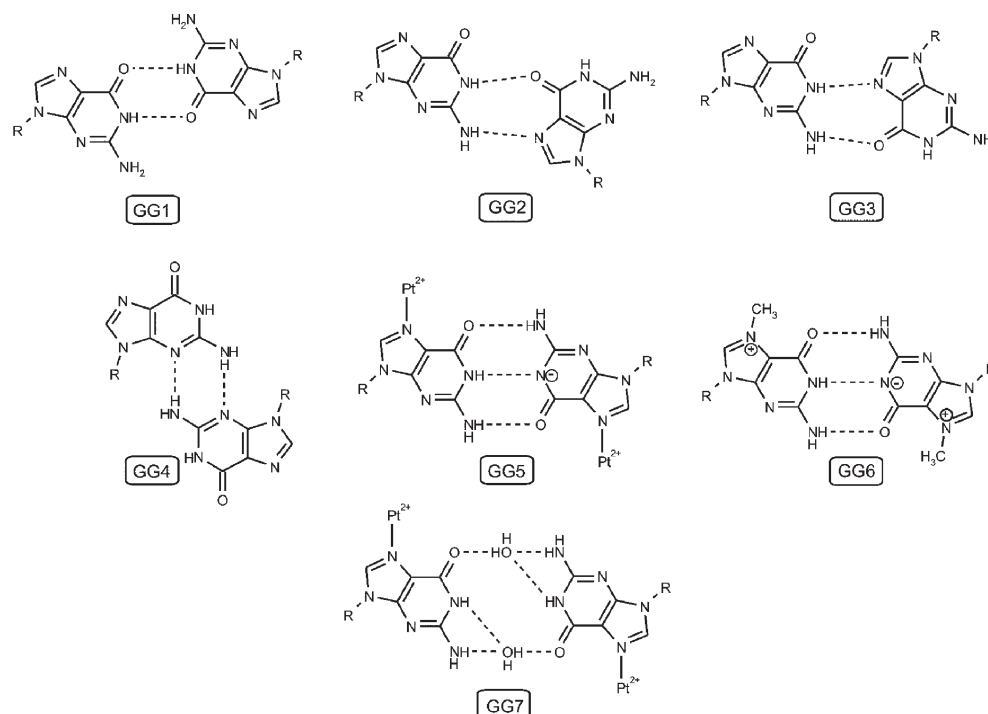

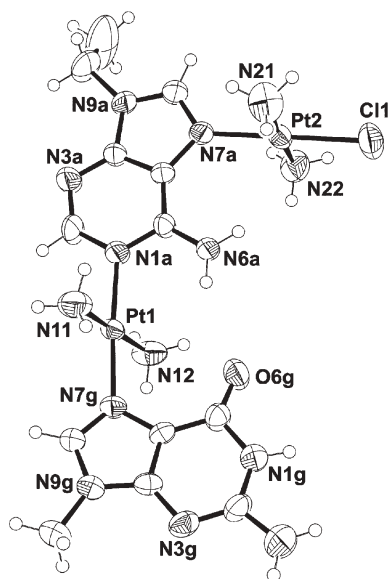**Fig. 1** Common guanine-guanine self-pairing patterns (GG1–GG4), as well as schemes of the hemi-deprotonated GH-G-pair (GG5), the hemiprotonated 7-methylguanine pair (GG6) and a new pairing pattern involving two water molecules between the Watson–Crick faces (GG7).

Fig. 2 Cation of **1**.

GG7 is realized in *trans,trans*-[(9mguaH-*N7*)(NH$_3$)$_2$Pt(μ-*N1*-9eade-*N7*)Pt(NH$_3$)$_2$Cl] (ClO$_4$)$_3$·3H$_2$O (**1**) (with 9meguaH = 9-methylguanine, 9eade = 9-ethyladenine). **1** was prepared from *trans*-[Pt(NH$_3$)$_2$(9mguaH-*N7*)(9eade-*N1*)]$^{2+}$ [17] and subsequent reaction with *trans*-Pt(NH$_3$)$_2$Cl$_2$ in an attempt to obtain a precursor for a cyclic, *trans*-(NH$_3$)$_2$Pt^{II} cross-linked mixed AG quartet (Scheme 1).† The cation of **1** is depicted in Fig. 2. The two nucleobases are not exactly co-planar, but form a dihedral angle of 17.1(3)°. They are connected by *trans*-(NH$_3$)$_2$Pt^{II} *via* N(1) of 9eda and N(7) of 9mguaH and in addition by a weak hydrogen bond between the exocyclic groups of A and G (3.204(9) Å). The N(1)a–Pt1–N(7)g angle deviates from linearity (175.4(3)°). The second Pt entity, *trans*-(NH$_3$)$_2$ClPt^{II} is bonded *via* N(7) of the A base, with its Pt(2)–N(7) vector almost perpendicular to the Pt(1)–N(1) vector (84.9°). Otherwise there are no unusual structural features within the cation of **1**. The most interesting aspect of this compound is its dimerization pattern (Fig. 3) which takes place *via* two water molecules (O(1w) and O(1wa)). Selected distances (Å) are as follows: N(1g)···O(1wa), 2.83(2); N(2g)···O(1wa), 3.05(2);
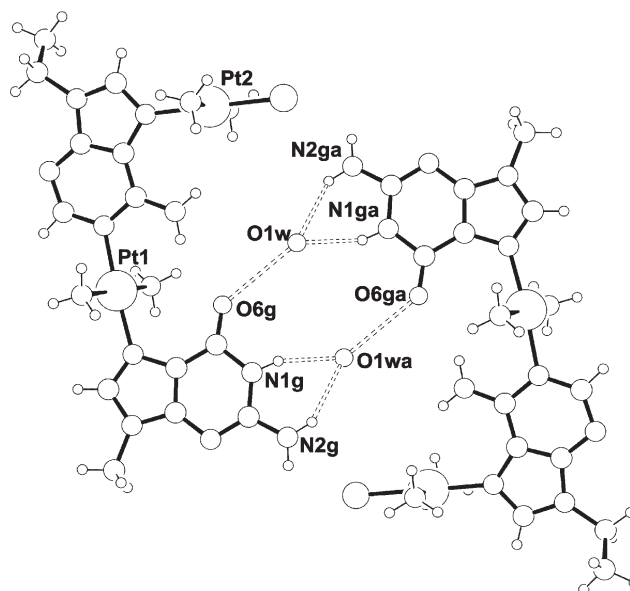

Fig. 3 Guanine moieties of two cations of **1** forming a pairing pattern which involves two water molecules between the Watson–Crick faces. O1w and O1wa are symmetry related (1−*x*, −*y*, 1−*z*).

O(6ga)···O(1wa), 2.94(2); O(1w)···O(1wa), 3.80(3)). The two guanine bases and the water molecules are planar. Guanine ligands of **1** are stacked in head–tail fashion (3.47 Å) to produce pairs of cations, which are separated by perchlorate anions.

As indicated in Scheme 1, our attempts to dimerize **1** upon removal of 2 equiv. of HCl failed, according to ^{1}H NMR spectroscopy. Addition of AgNO$_3$ to abstract the Cl ligand from Pt^{II} likewise did not lead to the desired cyclic complex, and neither did addition of base (pH 9). A possible explanation is that formation of the hemideprotonated derivative of **1** is a competitive process.

p*D* dependent ^{1}H NMR spectroscopy was applied to determine the p*K*$_a$ values of 9mguaH and 9eade ligands in **1**.[18] p*K*$_a$ values, converted to H$_2$O,[19] are 7.9 ± 0.1 for deprotonation of the guanine ligand at N(1), and 10.9 ± 0.1 for deprotonation of the exocyclic amino group of the adenine nucleobase. These findings are consistent with expectations.[7] With regard to formation to
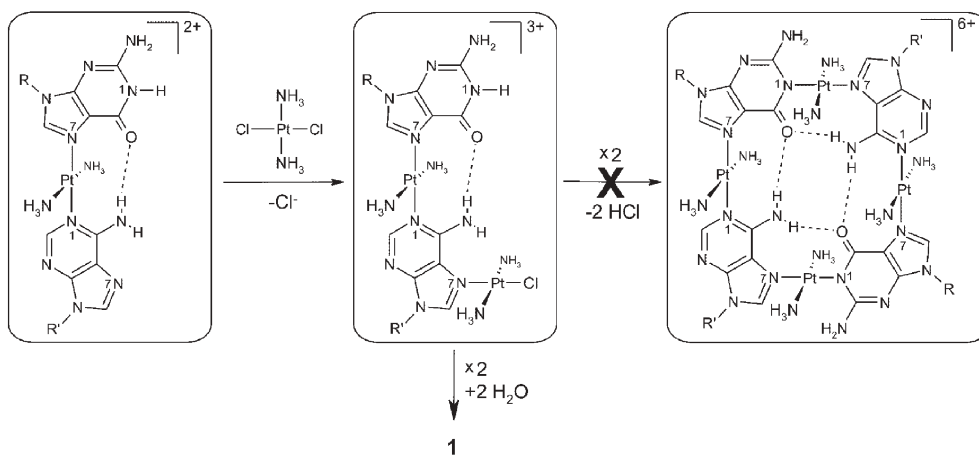
Scheme 1

GG5 from GG7, the pK_a of the guanine base implies that it starts below pH 7. Although we have not been able as yet to isolate GG5 derived from the herein described compound, previous experience with Pt compounds displaying the GG5 pattern[10,11] also makes its existence in this case very likely.

The association pattern between two neutral, N(7) platinated guanine bases seen in **1** appears not to be an isolated case. Going back to two related compounds reported by us several years ago,[20] we now realize that there rather similar H bonding patterns between G bases are realized which had escaped our attention.

In summary, the function of the two water molecules in **1** primarily and foremost appears to screen electrostatic repulsion between the two N(1)H protons of the two guanine ligands. This feature lends support to the idea that the second function of the two water molecules could be to remove the origin of this repulsion, a single H$^+$, and to convert GG7 into a highly attractive pair containing a neutral and an anionic guanine base (GG5).‡

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