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Dimerization of metallated nucleobase pairs *via* hydrogen-bond formation: open metallated base quartets of mixed adenine-N^3, guanine-N^7 complexes of *trans*-$(H_3N)_2Pt^{II}$ with two different guanine–guanine pairing schemes

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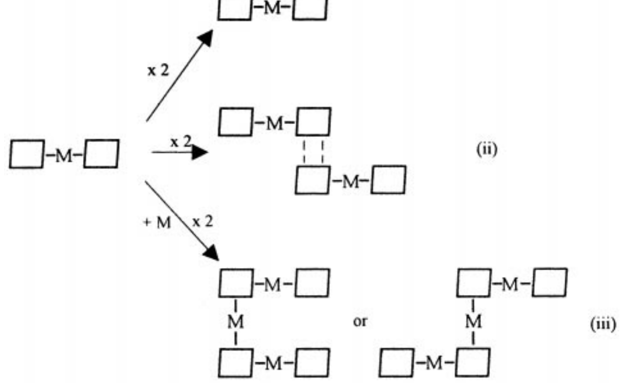
Reactions of *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)X]^{n+}$ (tmade = $N^{6'},N^{6'},N^9$-trimethyladenine, X = Cl, n = 1; X = H_2O, n = 2) with other nucleobases [9-ethylguanine (Hegua), 9-methyladenine (made) or 1-methylcytosine (mcyt)] have been studied in solution (D_2O) applying ^1H NMR spectroscopy. Mixed nucleobase complex formation has been observed in all cases. The complex *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(Hegua\text{-}N^7)][ClO_4]_2$ **1a** and its hemideprotonated form *trans*-$[\{Pt(NH_3)_2(tmade\text{-}N^3)(Hegua\text{-}N^7)\}\cdot\{Pt(NH_3)_2(tmade\text{-}N^3)(egua\text{-}N^7)\}][ClO_4]_2[NO_3]\cdot1.6H_2O$ **2** have been isolated in crystalline form and characterized by X-ray crystallography. In both cases mononuclear cations are associated *via* two (**1a**) and three (**2**) hydrogen bonds between the guanine nucleobases. In **1a** association is *via* N^3 and the amino group N^2, whereas in **2** a neutral Hegua and a deprotonated egua are joined *via* three hydrogen bonds involving O^6, N^1 and N^2 sites.

Substitution of hydrogen bonds between nucleobases by metal ions of suitable geometry leads to 'metal-modified' base pairs.[1,2] Additional aggregation of such modified pairs is feasible, either *via* hydrogen-bond formation[3] [Scheme 1, (i) and (ii)] or additional metal cross-linking [Scheme 1, (iii)].[4,5] As to type (ii), we have recently described a 'metal-modified' base quartet which involves two unexpected hydrogen bonds between an aromatic nucleobase proton (H5 of 1-methylcytosine) and a deprotonated ring nitrogen atom (N1 of 9-ethylguaninate), with the two bases cross-linked by a *trans*-$(H_3N)_2Pt^{II}$ entity.[3] Type (ii) hydrogen bonding is occasionally seen in the solid state, *e.g.* between pairs of N^3 and N^2 sites in adjacent N^7-platinated guanines,[6] but unlike (i) the latter pattern is usually not kept in polar, protic solvents.

In the course of our studies on platinum cross-linked nucleobase complexes, we have recently reported the synthesis of a mixed 9-ethylguanine (Hegua), $N^{6'},N^{6'},N^9$-trimethyladenine (tmade) complex,[7] *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(Hegua\text{-}N^7)]^{2+}$. This complex was unusual in that it represented a rare case[8] of metal binding to N^3 of a N^9-blocked adenine. We have now been able to obtain this compound as its ClO_4 salt in crystalline form, *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(Hegua\text{-}N^7)][ClO_4]_2$ **1a**, and likewise its hemideprotonated form, *trans*-$[\{Pt(NH_3)_2(tmade\text{-}N^3)(Hegua\text{-}N^7)\}\cdot\{Pt(NH_3)_2(tmade\text{-}N^3)(egua\text{-}N^7)\}][ClO_4]_2[NO_3]\cdot1.6H_2O$ **2**. In the case of **2** a hydrogen-bonding pattern of type (ii) with three bonds between a neutral and an anionic guanine nucleobase occurs, which is retained even in $(CD_3)_2SO$ solution.



Scheme 1

Experimental

Starting materials

The model nucleobases tmade and Hegua were obtained from Chemogen, Konstanz (Germany) and the other nucleobases 9-methyladenine (made)[9] and 1-methylcytosine (mcyt)[10] were synthesized as reported in the literature, as were *trans*-$[Pt(NH_3)_2Cl_2]$,[11] *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)Cl]ClO_4$[7] and *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(Hegua\text{-}N^7)][ClO_4][NO_3]$ **1**.[7]

Syntheses

***trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(Hegua\text{-}N^7)][ClO_4]_2$ 1a.** The compound was obtained upon recrystallization of the previously[7] described mixed nitrate–perchlorate salt from water at 40 °C and slow evaporation. From the IR spectrum it was evident that the compound no longer contained NO_3^- but only ClO_4^-. This conclusion was confirmed by X-ray analysis.

***trans*-$[\{Pt(NH_3)_2(tmade\text{-}N^3)(Hegua\text{-}N^7)\}\cdot\{Pt(NH_3)_2(tmade\text{-}N^3)(egua\text{-}N^7)\}][ClO_4]_2[NO_3]\cdot1.6H_2O$ 2.** The complex *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)Cl]ClO_4$ (0.185 mmol) and $AgNO_3$ (0.185 mmol) were suspended in water (20 cm^3) and stirred at 60 °C for 3 h with light excluded. After filtration of AgCl, the filtrate was brought to pH 5 (1 mol dm^{-3} NaOH) and the solution treated with Hegua (0.185 mmol) for 4 d at 40 °C. Then the clear solution (pH 5.9) was concentrated to 10 cm^3 in a stream of N_2 and left at room temperature for 2 d in a vial capped with pierced Parafilm. Yellowish crystals that had formed by then and were floating on top of the solution were used for the X-ray study. A second batch, removed after 2 weeks, and of different crystal shape proved unsuitable for X-ray crystallography. Elemental analysis data of this second batch (yield 23%) suggested a higher water content (Found: C, 24.0; H, 3.8; N, 22.6. Calc. for 5.5 hydrate, $C_{30}H_{62}Cl_2N_{25}O_{18.5}Pt_2$: C, 23.6; H, 4.1; N, 22.9%). The ^1H NMR spectrum (H^8 resonance of Hegua/egua) of this second species was clearly consistent with its anticipated composition (*cf.* Results and Discussion section).

***trans*-[Pt(NH_3)$_2$(tmade-N^3)(egua-N^7)]ClO_4 3.** This complex was obtained in 80% yield as a colourless precipitate upon dissolving **1** (0.065 mmol) in NaOH (0.1 mol dm^{-3}, 4 cm^3) at 70 °C (stoppered flask) and cooling to room temperature. The IR spectrum indicated the presence of ClO_4^- as anion and the absence of NO_3^-. The complex was characterized by ^{1}H NMR spectroscopy [$(CD_3)_2SO$] only.

Spectroscopy

Proton NMR spectra were recorded on Bruker AC 200 and DRX 400 FT spectrometers in D_2O solutions and in $(CD_3)_2SO$ containing sodium 3-trimethylsilylpropanesulfonate as internal reference. The pD values of D_2O solutions were determined by use of a glass electrode and addition of 0.4 units to the pH-meter reading.[12] The pK_a values were determined graphically from plots of chemical shifts of protons against pH* (uncorrected);[13] the pH* values were adjusted by means of DNO_3 and NaOD. Infrared spectra (KBr) were obtained on a Bruker IFS 28 instrument.

X-Ray crystallography

Intensity data for complexes **1a** and **2** were collected at 293(2) K on an Enraf-Nonius-KappaCCD diffractometer[14] with graphite-monochromated Mo-Kα radiation (λ = 0.710 69 Å). The whole sphere of reciprocal space was covered by measurement of 360 frames rotating about ω in steps of 1° with 35 s/4 s scan time per frame for **1a**/**2**. Unit-cell parameters were obtained from the peaks of the first ten frames, respectively, and refined using the whole data set. Data reduction and cell refinement were carried out using the programs DENZO and SCALEPACK.[15] Reflections, which were partly measured on previous and following frames, were used to scale these frames on each other. This procedure in part eliminates absorption effects and also takes account of crystal decay if present.

The structures were solved by standard Patterson methods[16] and refined with Fourier-difference syntheses, using SHELXTL PLUS[17] and SHELXL 93 programs.[18] The scattering factors for the atoms were those given in the SHELXTL PLUS program. Hydrogen atoms were placed in geometrical calculated positions and refined with a common isotropic thermal parameter, except for H(1) in **2** which was found by Fourier-difference synthesis to be on an inversion center. All non-hydrogen atoms were refined anisotropically with the following exceptions: C(92) and C(92a) of the disordered ethyl group (occupancy factors 0.51/0.49 **1a** and 0.4/0.6 **2**), the disordered perchlorate oxygens O(22), O(22a), O(23), O(23a), O(24) and O(24a) in **1a** and O(11a), O(12a), O(13a) and O(14a) in **2** and the atoms of the nitrate anion of the same structure, which are on an inversion center.

Crystal data and data collection parameters are summarized in Table 1. Structure-factor tables are available from the authors.

CCDC reference number 186/978.

See http://www.rsc.org/suppdata/dt/1998/2059/ for crystallographic files in .cif format.

Results and Discussion

Guanine-containing complexes

The synthesis and NMR (^{1}H, ^{195}Pt) spectroscopic features of *trans*-[Pt(NH_3)$_2$(tmade-N^3)(Hegua-N^7)][ClO_4][NO_3] **1** have been reported before.[7] Recrystallization of **1** now yielded crystals of this compound as its perchlorate salt **1a** which proved suitable for X-ray crystallography. Selected bond lengths and angles are given in Table 2, and the cation of **1a** is depicted in

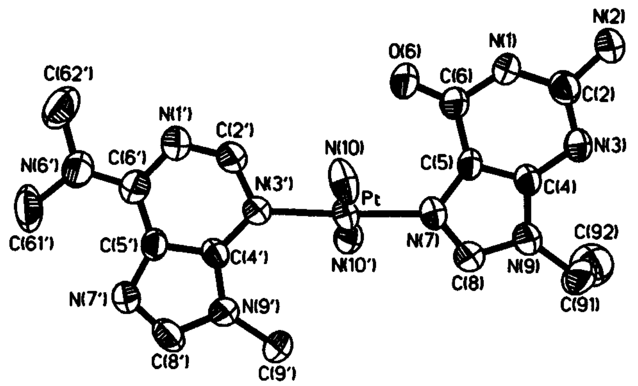


Fig. 1 View of the cation of complex **1a** with the atom numbering scheme. 50% Probability ellipsoids are shown

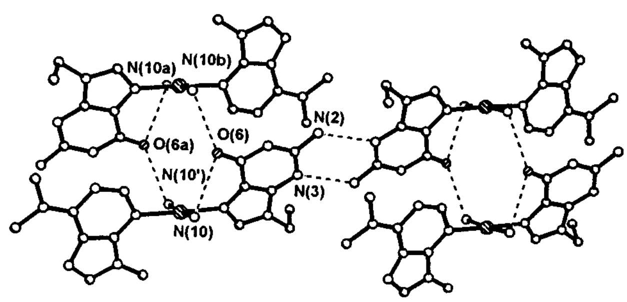
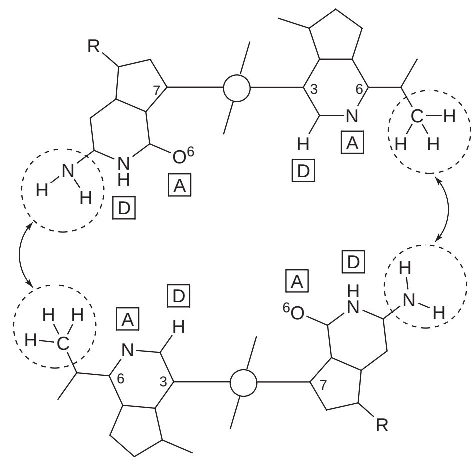


Fig. 2 Section of the packing pattern of cations of complex **1a**. Cation interactions include hydrogen bonding between NH_3 groups and O^6 sites of the Hegua ligands, partial stacking between Hegua and tmade, as well as hydrogen bonding between adjacent Hegua ligands *via* N^2 and N^3 positions

Fig. 1. The *trans*-$(H_3N)_2Pt^{II}$ binding is through N^3 of the tmade nucleobase and N^7 of Hegua. The two purine bases are oriented such that the exocyclic $C^{9'}$ methyl group of tmade and O^6 of Hegua are at opposite sides of the platinum plane, a situation postulated from ^{1}H NMR chemical shifts to occur in aqueous solution.[7] The two purine bases are not coplanar but form a moderate dihedral angle of 13°. The co-ordination of Pt displays some slight, although not unusual deviations from ideal square planarity. Angles between the PtN_4 plane and the two purine bases are 61.8(2) (Hegua) and 71.9(2)° (tmade). The $Pt\cdots C^{9'}$ separation is 3.44(1) Å, very similar to values observed for [Pt(dien)(tmade-N^3)][ClO_4]$_2$ and *trans*-[Pt(NH_3)$_2$(tmade-N^3)Cl]ClO_4.[7] The separation between O^6 of Hegua and $C^{2'}$ of tmade [4.28(1) Å] is too long to imply any significant hydrogen-bonding interaction. We raise this point since interbase hydrogen bonding is a recurring feature of bis(nucleobase) complexes of *trans*-diam(m)ineplatinum(II),[1–6] also contributing to coplanarity of the two nucleobases, and because $CH\cdots O$ hydrogen bonding is an emerging phenomenon in nucleic acids chemistry.[19]

Features of the packing pattern of the cations of complex **1a** are given in Fig. 2. Pairs of cations (symmetry transformation $-x + 1, -y + 2, -z + 1$) are partially stacked (average distance 3.2 Å) and are held together by four hydrogen bonds between NH_3 groups and O^6 sites of two Hegua ligands. The NH_3–Pt–NH_3 entities within a pair are almost parallel and intra- [$N^{10}\cdots O^6$ 2.99(1) Å] and inter-molecular [$O^6\cdots N^{10b}$ 2.97(1) Å] hydrogen bonds are identical within experimental error. In addition, centrosymmetric pairs of Hegua ligands interact *via* hydrogen bonds through the N^3 and the N^2 amino groups [3.06(1) Å, symmetry operation $-x + 1, -y + 3, -z + 2$]. This situation is reminiscent of that in various N^7-platinated guanine residues[6,20] as well as guaninium salts,[21] for example. Applying the 'base pair' notion, two cations of **1a** joined in this way thus represent an open metallated base quartet structure as schematically depicted in (ii) of Scheme 1.



Scheme 2

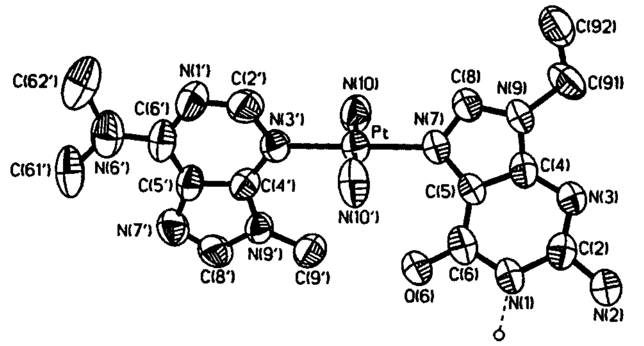


Fig. 3 View of the cation of complex **2**. 50% Probability ellipsoids are shown

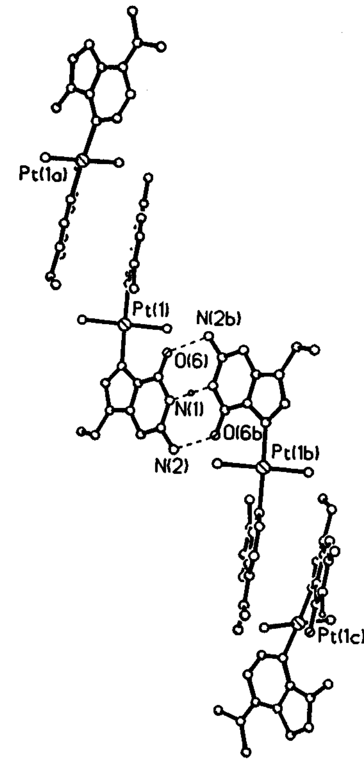


Fig. 4 Representation of the large dihedral angle between the two purine bases in complex **2**: while tmade is roughly perpendicular to the PtN_4 co-ordination plane, the guanine is markedly twisted, making a short contact through O^6 with a NH_3 group at Pt [2.98(1) Å]. Intermolecular stacking (3.4 Å) between tmade and (H)egua is essentially restricted to the two N-methyl groups of tmade and the pyrimidine part of (H)egua

There is no evidence from ^1H NMR spectroscopy (concentration dependency) that this hydrogen bonding pattern is retained in solution, nor for the existence of a closed quartet [Scheme 1, (i)]. Although the donor (D), acceptor (A) sequence of cation **1a**, in principle, should permit formation of a closed structure, the steric bulk of the methyl group at $N^{6'}$ of tmade pointing toward NH_2 of Hegua (Scheme 2) disfavours such an interaction by keeping the cations at too large a distance for hydrogen bonding.

Other hydrogen bonds exist between cations and oxygen atoms of the anions. Among these, that between N^1 of Hegua and O^{12} is reasonably short [2.89(1) Å].

Our previous potentiometric titration experiments[7] had revealed that the Hegua ligand in complex **1** deprotonates at N^1 with a pK_a of *ca.* 8 in water. We had therefore expected that we might be able to obtain the hemideprotonated complex *trans*-$[\{Pt(NH_3)_2(tmade)(Hegua)\}\cdot\{Pt(NH_3)_2(tmade)(egua)\}]^{3+}$ **2** from an aqueous solution of pH = $pK_a \approx 8$. To our surprise, this compound was obtained even at considerably lower pH (5.9). It was isolated as a mixed nitrate–perchlorate salt, $[ClO_4]_2[NO_3]$, with $1.6H_2O$ per dimeric unit. The cation is shown in Fig. 3. As compared to **1a**, the two purine bases adopt a different orientation with respect to each other, with O^6 of egua and the methyl group $C^{9'}$ of tmade now facing each other. There are no significant differences in bond lengths and angles in the platinum co-ordination spheres of **1a** and **2** (Table 2). Although deprotonation of Hegua is expected to lead to a lengthening of the C^6–O^6 bond this effect is not significant (2σ). On the other hand the expected decrease in the internal ring angle at N^1 of guanine as a consequence of (hemi) deprotonation is clearly seen, 120.1(8)° in **2** *vs.* 128.2(7)° in **1a** (8σ). There is also a reversal in relative sizes of the two external angles about the platinum binding sites at the nucleobases in **1a** and **2**, but only in the case of the tmade ligand are these significant [C(2′)–N(3′)–Pt, Δ 4.5° (5σ); C(4′)–N(3′)–Pt, Δ 5.1° (6σ)]. As a consequence of the orientation of the two bases, the protons of the 9-methyl group of tmade are within the reach [3.36(2) Å] of O^6 of the guanine ligand, making possible a weak hydrogen-bonding interaction. The deviation of $C^{9'}$ from the plane of tmade [0.19(1) Å] in the direction of O^6 adds further support to this interpretation. At the same time the ammine ligand $N^{10'}$ forms a shorter hydrogen bond [2.98(1) Å] with O^6. The most dramatic difference between **1a** and **2** is the large dihedral angle between the two purine bases of 42.7(2)° in **2**, which is a consequence of the rather small angle [52.6(2)°] formed between the guanine and the platinum co-ordination plane (Fig. 4). Complex **2** is only the second example of a large series of bis(nucleobase) complexes of *trans*-$(am)_2Pt^{II}$[1–6,22] displaying such a large angle, topped only by *trans*-$[Pt(MeNH_2)_2(mcyt)_2][PF_6]_2$ [56(1)°].[23] In all other cases the bases are reasonably coplanar.

The most remarkable feature about complex **2** certainly is its interguanine hydrogen-bonding pattern. The two halves of **2** are linked by three hydrogen bonds with lengths of 2.83(1) ($N^2\cdots O^{6a}$) and 2.90(1) Å ($N^1\cdots N^{1a}$). These distances compare with 2.99(1) and 2.73(1) Å, respectively, in *cis*-$[\{Pt(NH_3)_2(mcyt)(Hegua)\}\cdot\{Pt(NH_3)_2(mcyt)(egua)\}]^{3+}$,[24] the only other X-ray structurally characterized example of this type. The main difference between **2** and the previously reported $[Pt(NH_3)_2Cl_2]$-derived complex lies in the high propeller twist (39°) between the guanine nucleobases in the latter case as compared to the coplanarity of the guanine bases in **2**. It also explains the differences in hydrogen-bond lengths in the two compounds. There are two other structural studies relevant to this hydrogen-bonding pattern: that observed in *cis*-$[Pt(NH_3)_2(egua\text{-}N^7)_2]\cdot$Hegua[25] and one seen with hemiprotonated 7-methylguanosine (mguo)[26a] (Table 3). The position of the proton shared between the two guanines in **2**, symmetrical according to X-ray crystallography, is believed to be disordered over two positions, hence it should be described as a 1 : 1 mixture of $N^1H\cdots N^{1a}$ and $N^1\cdots HN^{1a}$. In hemiprotonated 7,9-dimethylguanine[26b] a

Table 1 Crystallographic data for compounds **1a** and **2**

	1a	**2**
Chemical formula	$C_{15}H_{26}Cl_2N_{12}O_9Pt$	$C_{15}H_{27.1}ClN_{12.5}O_{7.3}Pt$
M	784.47	729.93
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/c$
a/Å	8.966(2)	9.131(2)
b/Å	12.343(2)	17.354(3)
c/Å	13.684(3)	17.113(3)
α/°	114.89(3)	
β/°	96.06(3)	98.04(3)
γ/°	100.51(3)	
U/Å^3	1322.1(5)	2685.1(9)
Z	2	4
μ(Mo-Kα)/mm^{-1}	5.578	5.385
2θ Range/°	9.5–51.3	9.6–51.4
No. reflections collected	32 337	70 210
No. independent reflections [$I > 2\sigma(I)$]	4070	4603
R_{int}	0.038	0.059
$R1$ (observed data)	0.0418	0.0407
$wR2$ (observed data)	0.0933	0.0821

$R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{\frac{1}{2}}$.

Table 2 Selected distances (Å) and angles (°) of complexes **1a** and **2**

	1a	**2**
Pt–N(7)	1.989(7)	2.008(7)
Pt–N(3′)	2.023(6)	2.010(7)
Pt–N(10)	2.040(7)	2.025(7)
Pt–N(10′)	2.053(7)	2.038(8)
C(6)–O(6)	1.225(9)	1.254(9)
N(7)–Pt–N(3′)	176.6(3)	177.4(3)
N(7)–Pt–N(10)	89.5(3)	91.9(3)
N(3′)–Pt–N(10)	88.3(3)	90.4(3)
N(7)–Pt–N(10′)	89.7(3)	89.2(3)
N(3′)–Pt–N(10′)	92.4(3)	88.4(4)
N(10)–Pt–N(10′)	175.5(3)	178.8(3)
C(8)–N(7)–Pt	128.5(6)	125.9(7)
C(5)–N(7)–Pt	126.4(5)	128.9(5)
C(8)–N(7)–C(5)	105.0(7)	105.0(7)
C(2′)–N(3′)–Pt	117.2(5)	121.7(7)
C(4′)–N(3′)–Pt	131.4(5)	126.3(7)
C(2′)–N(3′)–C(4′)	111.1(7)	111.7(8)
C(6)–N(1)–C(2)	128.2(7)	120.1(8)
PtN(4)/Hegua	61.8(2)	52.6(2)
PtN(4)/tmade	71.9(2)	86.3(2)
tmade/Hegua	12.6(3)	42.7(2)

similar situation is realized although not proven by X-ray analysis.

Fig. 5 reveals that the interguanine hydrogen-bonding pattern leads to a characteristic Z shape as far as the Pt(1)(Hegua)·(egua)Pt(1a) entity is concerned, with an angle of 79.4(3)° between the bars of the Z. In the case of the twofold binding (N^7 and N^1) of Pt^{II} to adenine nucleobases,[4,5,27,28] we have frequently seen that the two Pt^{II}–N vectors are close to 90°, a feature that had led us to pursue the synthesis of 'molecular squares' and 'rectangles'.[5,28] Comparison with N^7,N^1-diplatinated guanine ligands is restricted to two examples: in $[\{Pt(dien)\}_2(mgua)][ClO_4]_3$ (Hmgua = 9-methylguanine) the angle between Pt–N^7 and Pt–N^1 vectors is 87.4(4)°, whereas it is 83.9(3)° in *cis*-$[(H_3N)_2Pt(mura\text{-}N^3)(mgua)Pt(dien)][ClO_4]_2$ (mura = 1-methyluracilate).[29] Inspection of the X-ray data of these two compounds strongly suggests that this difference essentially is a consequence of differences in the external ring angles at N^7, whereas there is little flexibility of the external ring angles at N^1. In fact the Pt–N^1–C^2 and likewise Pt–N^1–C^6 angles do not differ significantly in the two compounds. In

Table 3 Comparison of interguanine hydrogen bonding in complex **2**, *cis*-$[\{Pt(NH_3)_2(mcyt)(Hegua)\}\cdot\{Pt(NH_3)_2(mcyt)(egua)\}]^{3+}$ **A**, *cis*-$[Pt(NH_3)_2(egua)_2]$·Hegua **B** and $[mguo\cdot Hmguo]^+$ **C**

	2	**A**[a]	**B**[b]	**C**[c]
$N^1\cdots N^1$/Å	2.90(1)	2.73(1)	2.96(1)	2.90(2)
$N^2\cdots O^6$/Å	2.83(1)	2.99(1)	2.87(1)	2.78(2)
			2.88(1)	2.89(2)
egua/Hegua/°	0	39(1)	3.7	1.8
Pt–N^7/$N^1\cdots N^1$/°	79.4(3)	73.6(5)	77.4(3)	

[a] Ref. 24. [b] Ref. 25. [c] Ref. 26(*a*).

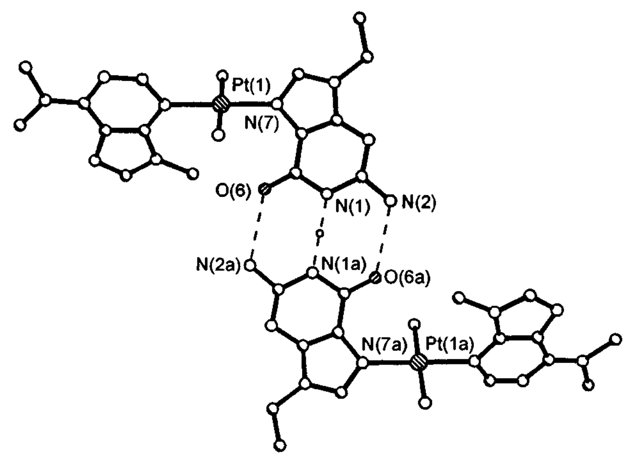


Fig. 5 The *Z*-shaped hydrogen-bond interaction between Hegua and egua in complex **2**. The angle between the Pt–N^7 and N^{1a}–N^1 vectors is 79.4(3)°

contrast, the Pt–N^7–C^5 and Pt–N^7–C^8 angles differ strongly. For example, in $[\{Pt(dien)\}_2(mgua)]^{3+}$ the Pt–N^7–C^5 angle is larger by 5.6° (4.3 σ) compared to that of the mixed mura–mgua complex and it correlates with the larger angle between the two Pt–N vectors.

Similar arguments appear to be valid also for complex **2** when compared with *cis*-$[\{Pt(NH_3)_2(mcyt)(Hegua)\}\cdot\{Pt(NH_3)_2(mcyt)(egua)\}]^{3+}$.[24] Again, the larger angle between the two vectors Pt–N^7 and N^1–N^{1a} in **2** [79.4(3)°] as compared to the *cis*-$(H_3N)_2Pt^{II}$ compound [73.6(5)°] correlates with a larger Pt–N^7–C^5 angle [128.9(5)° in **2** *vs.* 122.6(9)°, 6 σ]. In *cis*-$[Pt(NH_3)_2(egua)_2]$·Hegua[25] the Pt–N^7–C^5 angle is intermediate between the ones discussed [124.8(6)°] and so is the angle between the Pt–N^7 and N^1–N^{1a} vectors [77.4(3)°]. In summary, these data suggest that factors influencing the size of the external ring angle Pt–N^7–C^5, such as intracomplex hydrogen bonding with a second nucleobase or repulsion between exocyclic groups of nucleobases, essentially determine how strongly the angle between Pt–N^7 and Pt–N^1 (N^1–N^{1a}) vectors deviates from 90°.

As expected, in solution $[(CD_3)_2SO]$ the neutral and the anionic guanine ligands in complex **2** cannot be differentiated due to rapid proton exchange. If proton chemical shifts of **2** are compared with those of **1** and the fully deprotonated species *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(egua\text{-}N^7)]^+$ **3** (Table 4), it is evident that the tmade resonances are virtually unaffected and that the H^8 resonance of guanine in **2** represents the arithmetical mean of those of **1** and **3**, as expected. In contrast, the NH_2 resonance of the guanine in **2** is shifted downfield by 0.21 ppm relative to the mean, which would be 6.21 ppm. Since a single, averaged resonance for the two amino protons is observed, rotation about the C^2–N^2 bond is rapid on the NMR time-scale, the large effect on a single NH proton (2 × 0.21 ppm downfield at $c_2 \approx 9 \times 10^{-3}$ mol dm^{-3}) on this resonance reflects a high association constant.

Table 4 Selected ^1H NMR chemical shifts (δ) of complexes **1**, **2** and **3** in $(CD_3)_2SO$ *

	tmade			(H)egua		
Complex	H^8	H^2	N^9CH_3	H^8	NH_2	NH
1	8.31	8.57	4.82	8.49	6.92	11.28
2	8.30	8.56	4.81	8.33	6.42	n.o.
3	8.31	8.57	4.81	8.18	5.49	

* n.o. = not observed. $c(\mathbf{1}) = c(\mathbf{2}) = 19 \times 10^{-3}$, $c(\mathbf{3}) = 9 \times 10^{-3}$ mol dm^{-3} (dimer).

Other bis(base) complexes

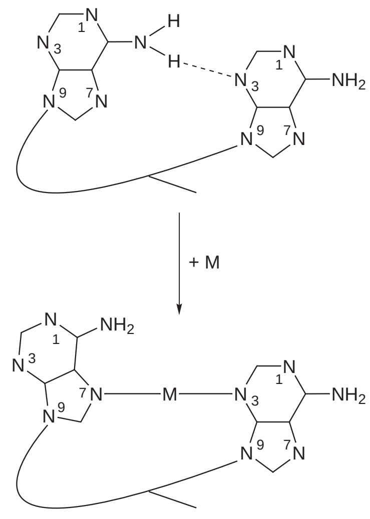
Reactions of *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(H_2O)]^{2+}$, obtained from the starting compound *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)Cl]$-$ClO_4$ upon $AgNO_3$ treatment, with an excess of tmade as well as made and mcyt were carried out on an NMR scale. Surprisingly, reaction with an excess of tmade (fivefold, pD 4.2) did not readily give the expected bis(tmade) complex *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)_2]^{2+}$. A new set of H^8 and H^2 resonances at δ 8.15 and 8.70, slightly downfield from that of the starting compound (Cl species) and of low intensity, *ca*. 5–10% of the former after 24 h at 40 °C, is tentatively assigned to the bis(tmade) complex. Considering the ready formation of mixed nucleobase complexes with purine (N^7) and pyrimidine nucleobases (N^3) this behavior is noteworthy.

Reaction of *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(D_2O)]^{2+}$ with made was carried out at acidic pH in order to block the N^1 position of made by protonation and to direct Pt to N^7. Formation of *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(Hmade\text{-}N^7)]^{3+}$ [^1H NMR, D_2O, pH* 1.2: Hmade, δ 9.17 (H^8), 8.60 (H^2), 4.16 (CH_3); tmade, 9.04 (H^2), 8.33 (H^8), 5.11 (N^9–CH_3), 3.55 and 3.90 (N^6–CH_3)] was unambiguously confirmed by pH*-dependent ^1H NMR spectroscopy. Deprotonation of the Hmade ligand occurs with a pK_a of 2.3, only consistent with a N^7-platinated species.[30] In more strongly acidic pH the tmade ligand is protonated ($pK_a = 0.8$), as expected.[7]

Reaction of the tmade aqua complex with mcyt, carried out at pD 6.4 (D_2O; 1 equivalent mcyt per Pt, 40 °C) leads to 50% complex formation within a day. Resonances of the mixed nucleobase complex *trans*-$[Pt(NH_3)_2(tmade\text{-}N^3)(mcyt\text{-}N^3)]^{2+}$ occur slightly downfield from those of the starting materials [^1H NMR, D_2O: mcyt, δ 7.67 (d, ^3J 7.4 Hz, H^6), 6.08 (d, H^5), 3.47 (CH_3); tmade, δ 8.76 (H^2), 8.11 (H^8), 4.92 (N^9–CH_3), *ca*. 3.4 and 3.7 (N^6–CH_3)]. The pH*-dependent spectra confirm N^3 binding of Pt to mcyt (no effect on resonances of mcyt in 8.4 < pH* < 0.9).

Conclusion

Apart from substantiating a rare metal binding pattern, N^3 of adenine, and an interesting hydrogen-bonding scheme, guanine, guaninate, as well as providing examples of metallated nucleobase quartets in general in this work, the question remains whether cross-linking of adenine-N^3 and purine-N^7 or pyrimidine-N^3 by *any* metal ion is potentially relevant to nucleic acid chemistry. Clearly, realization of these cross-linking schemes requires at first an appropriate mutual orientation of the donor sites. With adenine-N^3 located in the minor groove of DNA and the other sites either in the major groove or in the center of DNA, they appear to be unrealistic in regular, double-stranded DNA. With RNA and its enormous structural diversity, such possibilities are more likely. For example, metal modification of the recently discovered 'adenine platform motif',[31] in which two adenines are oriented side by side in the loop region of an RNA strand (P4-P6 domain of *Tetrahymena thermophila* self-splicing intron), *via* N^3 and N^7 would be in perfect agreement with such a possibility (Scheme 3).



Scheme 3

Finally, crystal packing patterns of helical DNA fragments reveal the possibility of close interhelical hydrogen-bonding contacts which usually involve hydrogen-bonding sites of the minor groove of the two helices.[32] Tetraplex structures as proposed precursors during strand exchange processes are believed to follow similar rules.[33] Provided a close approach between two duplex helices *via* major and minor grooves is possible, N^3–M–N^7 cross-linking between purines may indeed be a possibility.

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