Unusual Hydrogen Bonding Patterns of N^7 Metallated, N^1 Deprotonated Guanine Nucleobases: Acidity Constants of *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ and Crystal Structures of *cis*-$[Pt(NH_3)_2(egua)_2]\cdot 4H_2O$ and *cis*-$[Pt(NH_3)_2(egua)_2]\cdot$ Hegua$\cdot 7H_2O$ (Hegua = 9-ethylguanine)†

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Three closely related complexes of *cis*-$Pt^{II}(NH_3)_2$ with neutral 9-ethylguanine (Hegua) and anionic (N^1 deprotonated) 9-ethylguanine (egua), respectively, have been prepared and studied: *cis*-$[Pt(NH_3)_2(Hegua)(egua)]ClO_4\cdot 2H_2O$ **1**, *cis*-$[Pt(NH_3)_2(egua)_2]\cdot 4H_2O$ **2** and *cis*-$[Pt(NH_3)_2(egua)_2]\cdot$ Hegua$\cdot 7H_2O$ **3**. The crystal structures of complexes **2** and **3** have been determined. Platinum coordination in all cases is through N^7 of neutral (**1**) or anionic (**1**–**3**) guanine. The Pt^{II} electrophile coordinated at N^7 acidifies the N^1 proton of neutral 9-ethylguanine ($pK_a = 9.57 \pm 0.04$), giving $pK_{a1} = 8.02 \pm 0.01$ and $pK_{a2} = 8.67 \pm 0.01$ for the two Hegua ligands in *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$. All three compounds display interesting hydrogen-bonding patterns either in the solid state and/or in solution. According to ^1H NMR interaction shifts of guanine NH and NH_2 resonances of complex **1** in Me_2SO solution, this compound forms three intermolecular hydrogen bonds between neutral and deprotonated guanine ligands. For complex **2**, hydrogen bonding between two deprotonated guanines in the solid state is *via* N^1 and N^2H_2. In complex **3**, the neutral 9-ethylguanine is hydrogen bonded to one of the two anionic guanine ligands through three hydrogen bonds, involving N^1, N^2H_2 and O^6. This pattern represents a mismatch between two guanines, brought about by initial coordination of a Pt^{II} electrophile to N^7 and subsequent deprotonation of the N^1 position of the metallated nucleobase. The model character of these compounds with regard to metal-induced mutagenicity is briefly discussed.

Of all feasible and proposed cross-links of the antitumour agent cisplatin {*cis*-$[Pt(NH_3)_2Cl_2]$} with DNA nucleobases, the one involving the N^7 sites of two adjacent guanines in one strand (intrastrand egua–egua cross-link) is the most abundant one[1] and the one studied most intensively in model systems (model bases,[2,3] nucleosides,[4] nucleotides,[5] dinucleotides,[6,7] trinucleotides,[8] oligonucleotides[9,10]). On the basis of these studies, especially in cases where the two bases adopt the proper head-to-head orientation, the essential features of geometrical alterations of DNA structure (kinking and unwinding) have been rationalized.[11] The ultimate question of how these changes (or those of other cross-links) eventually lead to antitumour activity, has not been answered as yet.

Apart from stereochemical considerations the question concerning changes in electronic structure, as well as in acid–base and hydrogen-bonding properties of guanine (and nucleobases in general) as a consequence of metal binding appears to be of considerable significance, *e.g.* in the context of metal mutagenicity.[12] In the course of these studies it had been found that Pt binding to N^7 of guanine strongly affects the normal Watson-Crick base pairing with cytosine,[13] increases the acidity of the N^1 proton,[14] and causes unusual base pairing of the anionic guanine ligand.[14,15] In particular, a novel hydrogen-bonding scheme between anionic and neutral guanine had been observed in *cis*-$\{[Pt(NH_3)_2(Hmcyt)(Hegua)]$-$[(egua)(Hmcyt)Pt(NH_3)_2]\}[ClO_4]_3$ (with Hmcyt = 1-methylcytosine), involving N^1, N^2H_2 and O^6.[14,15]

This paper examines the question of base pairing patterns of N^7 platinated, N^1 deprotonated guanine ligands in more detail.

Experimental

Starting Materials.—The complexes *cis*-$[Pt(NH_3)_2Cl_2]$[16] and *cis*-$[Pt(NH_3)_2(Hegua)_2][ClO_4]_2\cdot H_2O$[2] were prepared as described and 9-ethylguanine (Hegua) was purchased from Chemogen, Konstanz, Germany.

Preparations.—*cis*-$[Pt(NH_3)_2(Hegua)(egua)]ClO_4\cdot 2H_2O$ **1**. The complex *cis*-$[Pt(NH_3)_2(Hegua)_2][ClO_4]_2\cdot H_2O$ (0.3 mmol) was suspended in H_2O (15 cm^3), 0.1 mol dm^{-3} NaOH (3.3 cm^3) was added, and the sample heated to 100 °C. After filtration from some undissolved material, the clear solution (pH 9.4) was slowly cooled, the precipitate filtered off and washed with a small amount of water. Colourless, transparent microcolumns were isolated in 70% yield (Found: C, 23.3; H, 3.7; N, 23.5. Calc. for $C_{14}H_{27}ClN_{12}O_8Pt$: C, 23.30; H, 3.80; N, 23.30%).

cis-$[Pt(NH_3)_2(egua)_2]\cdot 4H_2O$ **2**. The complex *cis*-$[Pt(NH_3)_2(Hegua)_2][ClO_4]_2\cdot H_2O$ (1 mmol) was heated to 90 °C in excess aqueous 0.1 mol dm^{-3} NaOH (40 cm^3), the solution filtered and slowly cooled in a stoppered flask. Colourless crystals of **2** were filtered off, washed with a small amount of

† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1995, Issue 1, pp. xxv–xxx.

water and briefly dried in air. The yield was 69% (Found: C, 25.8; H, 4.5; N, 25.9; Pt, 29.9. Calc. for $C_{14}H_{30}N_{12}O_6Pt$: C, 25.65; H, 4.60; N, 25.55; Pt, 29.65%).

cis-$[Pt(NH_3)_2(egua)_2]$·Hegua·$7H_2O$ **3**. Compound **2** was co-crystallized with 2 equivalents of Hegua from hot water (c_{Pt} = 7.5×10^{-3} mol dm^{-3}). A mixture of the starting material and of the adduct **3** (*ca.* 50% yield) was obtained and separated by hand under a microscope (Found: C, 28.3; H, 5.3; N, 26.5; Pt, 21.3. Calc. for $C_{21}H_{45}N_{17}O_{10}Pt$: C, 28.30; H, 5.10; N, 26.75; Pt, 21.90%).

Instrumentation.—The NMR spectra were recorded on JEOL JNM-FX60 and Bruker AC200 spectrometers. Proton NMR spectra were run in $(CD_3)_2SO$ using tetramethylsilane as internal reference. Infrared spectra of KBr pellets were recorded on Perkin-Elmer 580B and Bruker IFS 113v spectrometers, and Raman spectra of solid samples on a T64000 Instruments SA spectrometer using Ar^+ laser excitation (514.5 nm).

Potentiometric pH Titrations.—The equipment for the titrations regarding the determination of the acidity constants as well as the experimental procedures were the same as described recently.[17] It should be noted that the calculated acidity constants are so-called practical, mixed or Brønsted constants.[18] Their negative logarithms given for aqueous solutions at I = 0.1 mol dm^{-3} ($NaNO_3$) and 25 °C may be converted into the corresponding concentration constants by subtracting 0.02 from the listed pK_a values;[18] this conversion term contains both the junction potential of the glass electrode and the hydrogen ion activity.[18,19]

The aqueous stock solutions of Hegua and *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ were freshly prepared daily. All the other reagents used in the titration experiments were identical with those employed previously.[17] The solutions were prepared with distilled CO_2-free water.

The acidity constant K^H_{Hegua} of Hegua was determined by titrating 25 cm^3 of aqueous 1.2×10^{-4} mol dm^{-3} HNO_3 and $NaNO_3$ (I = 0.1 mol dm^{-3}; 25 °C) in the presence and absence of 7×10^{-4} mol dm^{-3} Hegua under N_2 with 1 cm^3 of 3×10^{-3} mol dm^{-3} NaOH. A further set of independent pairs of titrations was carried out by employing 25 cm^3 of aqueous 5×10^{-3} mol dm^{-3} HNO_3 and 10^{-3} mol dm^{-3} Hegua using 3 cm^3 of 6×10^{-2} mol dm^{-3} NaOH; in this way the acidity constant $K^H_{H_2egua}$ of N^7-protonated $[H_2egua]^+$ could be obtained. The constants were calculated with a curve-fit procedure and a desk-top computer[17] within the pH range corresponding to about 2% (pH 7.9) to 87% (pH 10.4) of neutralization for the equilibrium Hegua–$[egua]^-$ or within the pH range corresponding to about 15% (pH 2.5) neutralization for $[H_2egua]^+$–Hegua and 94% (pH 10.8) for Hegua–$[egua]^-$. Under both conditions, the self-association of 9-ethylguanine is clearly negligible as follows from the self-association tendency of related guanine derivatives;[20,21] hence, certainly the acid–base properties of the monomeric species were measured.

The acidity constants, $K^H_{Pt(Hegua)_2}$ and $K^H_{Pt(egua)(Hegua)}$, of *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ were determined by titrating 25 cm^3 of aqueous 1.2×10^{-4} mol dm^{-3} HNO_3 and $NaNO_3$ (I = 0.1 mol dm^{-3}; 25 °C) in the presence and absence of 3.5×10^{-4} mol dm^{-3} $[Pt(Hegua)_2]^{2+}$ under N_2 with 1 cm^3 of 3×10^{-2} mol dm^{-3} NaOH. The constants were calculated[17] as given above within the pH range corresponding to about 4% (pH 6.6) neutralization for the equilibrium $[Pt(Hegua)_2]^{2+}$–$[Pt(Hegua)(egua)]^+$ and 98% (pH 10.4) for $[Pt(Hegua)(egua)]^+$–$[Pt(egua)_2]$.

The final results are the averages of eight or five independent pairs of titrations for Hegua or $[Pt(Hegua)_2]^{2+}$], respectively.

Crystal Structure Analysis.—All X-ray measurements were performed on a Rigaku AFC6S diffractometer at −100 °C (**2**) and −120 °C (**3**) using Mo-Kα radiation (λ = 0.710 69 Å). Pertinent crystallographic data are described in Table 1. Unit-cell dimensions were determined using the setting angles of 25 high-angle reflections. Intensities of three standard reflections were monitored throughout the data collection, showing no

Table 1 Crystallographic data and details of refinement for complexes **2** and **3**

	2	**3**
Formula	$C_{14}H_{30}N_{12}O_6Pt$	$C_{21}H_{45}N_{17}O_{10}Pt$
M	657.56	882.72
Crystal colour, habit	Colourless, needle	Yellow, prism
Crystal dimensions/mm	0.46 × 0.26 × 0.24	0.42 × 0.30 × 0.21
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$ (no. 2)	$P2_1/n$ (no. 14)
a/Å	11.872(3)	11.425(3)
b/Å	12.059(3)	25.976(5)
c/Å	9.460(3)	11.639(1)
α/°	112.68(2)	
β/°	109.60(3)	101.59(1)
γ/°	73.90(2)	
U/Å^3	1160(1)	3383(1)
Z	2	4
D_c/g cm^{-3}	1.882	1.748
μ(Mo-Kα)/cm^{-1}	61.64	42.61
T/°C	−100	−120
F(000)	648	1792
Scan type	ω–2θ	ω
No. measured reflections	4297	6433
No. unique reflections (R_{int})	4066 (0.019)	6115 (0.032)
Structure solution	Patterson method	Direct methods (SIR88)
No. observations [$I > 3.00\sigma(I)$]	3542	3916
No. variables	298	421
Reflection/parameter ratio	11.89	9.30
R, R'	0.027, 0.036	0.044, 0.059
Goodness of fit	1.32	1.48
Maximum peak/e Å^{-3}	1.36	1.69

Details in common: Mo-Kα radiation (λ = 0.710 69 Å), Rigaku AFC6S diffractometer, $2\theta_{max}$ = 50°, full-matrix least-squares refinement, all non-hydrogen atoms anomalously dispersed. Function minimized in refinement: $\Sigma w(|F_o| - |F_c|)^2$ with $w^{-1} = \sigma^2(F_o)$.

Table 2 Atomic positional parameters with estimated standard deviations (e.s.d.s) in parentheses for compound **2**

Atom	*x*	*y*	*z*
Pt	0.340 69(2)	0.084 85(2)	0.263 37(2)
O(1W)	0.329 9(4)	−0.204 3(3)	−0.384 2(5)
O(2W)	−0.196 2(5)	−0.189 6(5)	−0.591 4(6)
O(3W)	0.427 4(6)	0.124 4(5)	0.953 4(7)
O(6A)	0.441 3(4)	0.217 1(3)	0.673 1(5)
O(6B)	0.246 4(4)	−0.042 2(4)	−0.140 0(5)
O(4W1)	0.243(1)	0.330(1)	0.902(1)
O(4W2)	0.162(2)	0.296(2)	0.890(3)
N(1A)	0.450 4(4)	0.420 5(4)	0.785 8(5)
N(1B)	0.054 3(4)	0.013 5(4)	−0.279 9(6)
N(3A)	0.392 4(4)	0.557 2(4)	0.630 7(5)
N(3B)	−0.101 8(4)	0.147 4(4)	−0.153 1(6)
N(4A)	0.465 6(6)	0.624 2(4)	0.902 0(6)
N(4B)	−0.138 8(5)	0.065 2(5)	−0.425 4(6)
N(7A)	0.343 8(4)	0.265 3(4)	0.353 8(5)
N(7B)	0.163 5(4)	0.121 9(4)	0.160 2(5)
N(9A)	0.319 5(5)	0.453 2(4)	0.348 7(5)
N(9B)	−0.027 5(4)	0.216 3(4)	0.135 0(6)
N(11)	0.521 2(5)	0.054 0(5)	0.372 2(6)
N(12)	0.338 3(4)	−0.097 0(4)	0.156 5(5)
C(2A)	0.434 1(5)	0.529 7(5)	0.765 7(7)
C(2B)	−0.058 2(5)	0.077 3(5)	−0.278 4(7)
C(4A)	0.367 6(5)	0.457 9(5)	0.505 3(7)
C(4B)	−0.015 4(5)	0.151 2(5)	−0.016 7(6)
C(5A)	0.381 9(5)	0.341 5(5)	0.508 2(6)
C(5B)	0.103 1(5)	0.092 7(5)	−0.001 5(6)
C(6A)	0.426 9(5)	0.320 3(5)	0.657 7(7)
C(6B)	0.140 4(5)	0.017 1(5)	−0.141 3(7)
C(8A)	0.307 1(6)	0.335 5(5)	0.263 3(7)
C(8B)	0.082 2(5)	0.195 1(5)	0.236 4(6)
C(9A1)	0.275 1(6)	0.555 2(5)	0.285 3(7)
C(9B1)	−0.135 3(6)	0.298 6(6)	0.182 0(8)
C(9A2)	0.142 9(8)	0.596 4(8)	0.267(1)
C(9B2)	−0.114 8(8)	0.426 4(8)	0.263(1)

Table 3 Atomic positional parameters with e.s.d.s in parentheses for compound **3**

Atom	*x*	*y*	*z*
Pt	0.086 07(3)	0.058 08(1)	0.110 94(3)
O(1W)	0.731 8(8)	0.075 0(4)	0.946 0(8)
O(2W)	0.744(1)	0.066 7(4)	0.580(1)
O(3W)	0.550(1)	0.134 7(4)	0.508(1)
O(4WA)*	0.960(1)	0.110 6(7)	0.643(1)
O(4WB)*	0.998(1)	0.088 8(6)	0.587(1)
O(5WA)*	0.363(1)	0.077 5(5)	0.408(1)
O(5WB)*	0.340(1)	0.032 9(6)	0.449(1)
O(6WA)*	0.094(1)	0.052 6(6)	0.401(1)
O(6WB)*	0.038(1)	0.073 8(5)	0.443(1)
O(7W)*	0.240(1)	0.024 4(5)	0.556(1)
O(8W)*	0.819(1)	0.031 7(6)	0.376(1)
O(61)	0.118 5(6)	0.059 0(3)	−0.186 5(5)
O(62)	0.177 8(6)	0.141 8(2)	0.320 2(5)
O(63)	0.258 7(7)	0.325 7(3)	0.513 2(6)
N(1)	−0.078 1(9)	0.059 8(3)	0.158 3(8)
N(2)	0.109 3(7)	−0.015 4(3)	0.171 6(7)
N(11)	0.302 4(8)	0.061 5(3)	−0.233 3(9)
N(12)	0.166 1(7)	0.228 2(3)	0.292 9(6)
N(13)	0.263 2(7)	0.239 1(3)	0.547 6(7)
N(21)	0.486(1)	0.062 3(4)	−0.287(1)
N(22)	0.158 0(8)	0.316 7(3)	0.266 6(7)
N(23)	0.256 9(9)	0.151 1(4)	0.569 5(8)
N(31)	0.485 7(8)	0.063 1(4)	−0.085(1)
N(32)	0.081 1(7)	0.267 5(3)	0.103 6(6)
N(33)	0.336 4(7)	0.198 9(4)	0.731 3(7)
N(71)	0.250 6(7)	0.058 8(3)	0.073 9(7)
N(72)	0.063 3(7)	0.130 7(3)	0.058 1(7)
N(73)	0.374 5(8)	0.335 8(4)	0.778 2(8)
N(91)	0.447 8(8)	0.062 3(4)	0.111(1)
N(92)	0.015 5(7)	0.203 3(3)	−0.045 9(6)
N(93)	0.409 5(8)	0.261 5(5)	0.880 8(7)
C(21)	0.423(1)	0.063 2(4)	−0.195(2)
C(22)	0.134 7(8)	0.269 5(3)	0.220 2(8)
C(23)	0.287 1(8)	0.196 8(5)	0.617 6(8)
C(41)	0.412 7(8)	0.061 7(4)	−0.006(1)
C(42)	0.065 3(8)	0.218 6(4)	0.066 5(8)
C(43)	0.358 6(9)	0.248 8(5)	0.768 0(8)
C(51)	0.288 7(8)	0.060 0(4)	−0.035(1)
C(52)	0.096 7(8)	0.174 7(4)	0.131 9(7)
C(53)	0.337 3(8)	0.292 5(4)	0.705 7(8)
C(61)	0.229 0(8)	0.060 4(4)	−0.153(1)
C(62)	0.147 4(7)	0.180 1(3)	0.252 6(7)
C(63)	0.286(1)	0.290 3(4)	0.584 4(9)
C(81)	0.348(1)	0.060 3(5)	0.159(1)
C(82)	0.018(1)	0.150 7(4)	−0.0453(9)
C(83)	0.418(1)	0.314 5(6)	0.882(1)
C(91A)*	0.560(2)	0.062 3(8)	0.204(2)
C(91B)*	0.586(2)	0.068 2(8)	0.149(2)
C(92)	−0.029(1)	0.236 3(4)	−0.147 3(8)
C(93)	0.454(1)	0.225 8(7)	0.978(1)
C(101A)*	0.607(2)	0.119 1(7)	0.217(2)
C(101B)*	0.605(2)	0.077 8(9)	0.275(2)
C(102)	0.075(1)	0.255 1(6)	−0.199(1)
C(103)	0.353(1)	0.205 3(6)	1.031(1)

* Occupancy 50%.

significant decay or instrument instability. Reflections having $I > 3\sigma(I)$ were corrected for Lorentz-polarization factors. The intensities were corrected for absorption using ψ scans of several reflections with the χ angle close to 90°. The transmission factors ranged from 0.61–1.00 (**2**) and 0.88–1.00 (**3**). All calculations were carried out on a VAXstation 3520 computer using the TEXSAN 5.0 crystallographic software package.[22] The structures were solved by Patterson and Fourier techniques (**2**) and by direct methods (**3**), respectively.[23] For complex **2**, the H atoms including those of the solvent water molecules except for the water (W4) were located from Fourier-difference maps and included in calculations without refinement. The water molecule (W4) was found to be disordered between two sites. The oxygen atoms of this water molecule [O(4W)] representing the two sites were refined with isotropic thermal displacement parameters and the population parameters of 0.7 and 0.3, respectively. The final difference map showed the highest peak of 1.36 e Å^{-3} in the vicinity of the Pt atom. For complex **3**, the positions of eight molecules of water of crystallization were located in the unit cell. Some of these water molecules were disordered between two sites. The oxygen atoms were refined with isotropic thermal displacement parameters. The population factors for water molecules O(4W)–O(8W) were assumed to be 0.5. The ethyl group of guanine 1 was found to be disordered between two locations refined with an occupancy of 0.5 and isotropic thermal factors. The largest peak in the final Fourier-difference map, about 1.7 e Å^{-3} high, was located in the vicinity of the Pt atom. Final positional parameters for complexes **2** and **3** are listed in Tables 2 and 3.

Additional material available from the Cambridge Crystallographic Data Centre comprises thermal parameters (**2**,**3**), H-atom coordinates (**2**) and intermolecular bond lengths and angles (**2**,**3**).

Results and Discussion

Crystal Structures of Complexes **2** *and* **3**.—Drawings of the molecules of **2** and **3** are given in Figs. 1 and 2, and selected bond distances and angles in Tables 4 and 5. In both compounds Pt co-ordination is through the N^7 sites of two 9-ethylguaninate ligands, which are arranged *cis* to each other and which adopt a head-to-tail orientation. The latter feature distinguishes complexes **2** and **3** from their cationic precursor *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ in which the bases are arranged

Table 4 Bond distances (Å) and angles (°) for complex **2**

Pt–N(7A)	2.014(5)	N(7A)–C(5A)	1.391(7)	N(1B)–C(2B)	1.346(8)	N(9B)–C(8B)	1.359(7)
Pt–N(7B)	2.004(5)	N(7A)–C(8A)	1.321(7)	N(1B)–C(6B)	1.359(7)	N(9B)–C(9B1)	1.469(7)
Pt–N(11)	2.040(5)	N(7B)–C(5B)	1.403(7)	N(3A)–C(2A)	1.340(8)	C(4A)–C(5A)	1.376(8)
Pt–N(12)	2.034(4)	N(7B)–C(8B)	1.317(7)	N(3A)–C(4A)	1.339(7)	C(4B)–C(5B)	1.375(8)
O(6A)–C(6A)	1.266(7)	N(9A)–C(4A)	1.382(7)	N(3B)–C(2B)	1.336(7)	C(5A)–C(6A)	1.431(8)
O(6B)–C(6B)	1.263(7)	N(9A)–C(8A)	1.356(7)	N(3B)–C(4B)	1.346(7)	C(5B)–C(6B)	1.419(8)
N(1A)–C(2A)	1.354(7)	N(9A)–C(9A1)	1.466(7)	N(4A)–C(2A)	1.372(7)	C(9A1)–C(9A2)	1.48(1)
N(1A)–C(6A)	1.355(7)	N(9B)–C(4B)	1.380(7)	N(4B)–C(2B)	1.379(7)	C(9B1)–C(9B2)	1.48(1)
N(7A)–Pt–N(7B)	88.9(2)	N(1B)–C(2B)–N(3B)	128.2(5)	Pt–N(7B)–C(5B)	129.2(4)	N(7B)–C(5B)–C(6B)	133.0(5)
N(7A)–Pt–N(11)	89.0(2)	N(1B)–C(2B)–N(4B)	115.2(5)	Pt–N(7B)–C(8B)	124.3(4)	C(4B)–C(5B)–C(6B)	118.4(5)
N(7A)–Pt–N(12)	175.7(2)	N(3B)–C(2B)–N(4B)	116.5(5)	C(5B)–N(7B)–C(8B)	105.9(4)	O(6A)–C(6A)–N(1A)	121.2(5)
N(7B)–Pt–N(11)	177.9(2)	N(3A)–C(4A)–N(9A)	126.7(5)	C(4A)–N(9A)–C(8A)	106.5(4)	O(6A)–C(6A)–C(5A)	123.7(5)
N(7B)–Pt–N(12)	90.4(2)	N(3A)–C(4A)–C(5A)	126.5(5)	C(4A)–N(9A)–C(9A1)	127.9(5)	N(1A)–C(6A)–C(5A)	115.1(5)
N(11)–Pt–N(12)	91.7(2)	N(9A)–C(4A)–C(5A)	106.8(5)	C(8A)–N(9A)–C(9A1)	125.1(5)	O(6B)–C(6B)–N(1B)	121.1(5)
C(2A)–N(1A)–C(6A)	119.9(5)	N(3B)–C(4B)–N(9B)	126.9(5)	C(4B)–N(9B)–C(8B)	107.2(5)	O(6B)–C(6B)–C(5B)	123.3(5)
C(2B)–N(1B)–C(6B)	120.1(5)	N(3B)–C(4B)–C(5B)	126.6(5)	C(4B)–N(9B)–C(9B1)	127.6(5)	N(1B)–C(6B)–C(5B)	115.6(5)
C(2A)–N(3A)–C(4A)	110.9(5)	N(9B)–C(4B)–C(5B)	106.5(5)	C(8B)–N(9B)–C(9B1)	125.1(5)	N(7A)–C(8A)–N(9A)	112.1(5)
C(2B)–N(3B)–C(4B)	111.0(5)	N(7A)–C(5A)–C(4A)	108.7(5)	N(1A)–C(2A)–N(3A)	128.7(5)	N(7B)–C(8B)–N(9B)	111.7(5)
Pt–N(7A)–C(5A)	131.9(4)	N(7A)–C(5A)–C(6A)	132.4(5)	N(1A)–C(2A)–N(4A)	115.3(5)	N(9A)–C(9A1)–C(9A2)	111.3(5)
Pt–N(7A)–C(8A)	122.2(4)	C(4A)–C(5A)–C(6A)	118.9(5)	N(3A)–C(2A)–N(4A)	116.0(5)	N(9B)–C(9B1)–C(9B2)	112.0(5)
C(5A)–N(7A)–C(8A)	105.9(5)	N(7B)–C(5B)–C(4B)	108.7(5)				

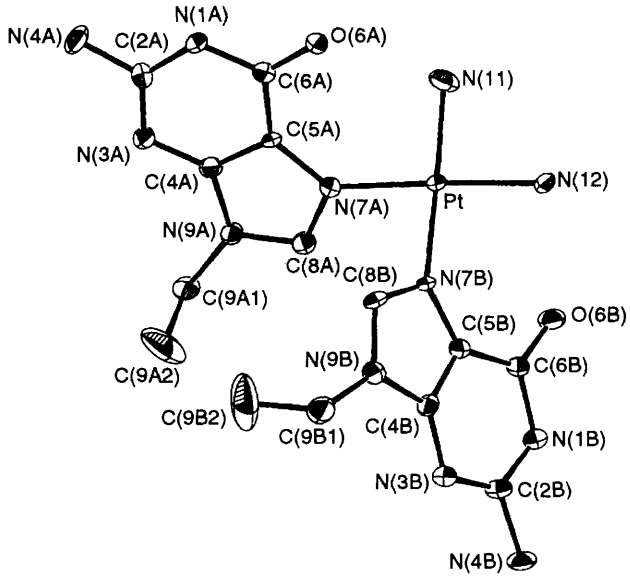

Fig. 1 View of *cis*-$[Pt(NH_3)_2(egua)_2]$ **2** with the atom numbering scheme. The exocyclic amino groups at the 2 position of the guanine rings are labelled as N(4A) (ring A) and N(4B) (ring B), respectively

head-to-head.[2] Platinum co-ordination geometries in both compounds are normal, with Pt–N(guaninate) bonds being somewhat shorter than Pt–N(ammonia) bonds. Bond lengths and angles of the 9-ethylguaninate anions do not differ much from those found in N^7-platinated neutral 9-ethylguanine ligands[2,14] except for the internal ring angles at N^1. Expectedly,[24] they are smaller in both **2** and **3** as compared to the neutral ligands and a consequence of deprotonation. The geometry of the neutral 9-ethylguanine molecule in **3** is normal.[25]

All purine rings are essentially planar as evident from the small (1–3°) dihedral angles between the pyrimidine and imidazole entities. However, as with the four X-ray structurally characterized *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ compounds,[2] deviations of Pt from the guanine anion planes are variable and occasionally substantial: for example, Pt in **2** is out of the plane of ring B by 0.26 Å, whereas it is almost coplanar with ring A (deviation 0.04 Å). In **3**, Pt deviations are relatively small, 0.04 Å (ligand 1) and 0.02 Å (ligand 2).

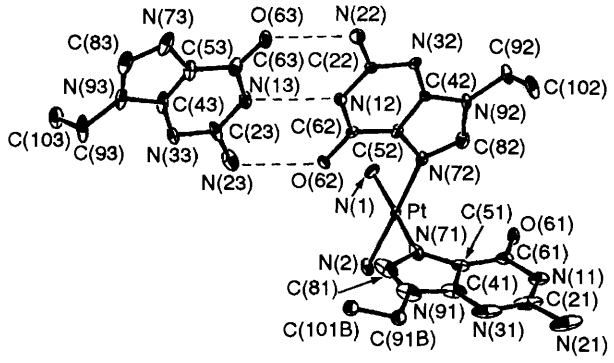

Fig. 2 View of *cis*-$[Pt(NH_3)_2(egua)_2]$·Hegua **3** with the atom numbering scheme

The dihedral angles, as defined by the convention of Kistenmacher and Marzilli,[26] between the Pt co-ordination planes and the two guaninate rings in **2** and **3** as well as the base–base angles are listed in Table 6. When compared with the corresponding data of the parent complexes containing neutral guanine ligands,[2] it is evident that similar variations exist in **2** and **3** as observed with *cis*-$[Pt(NH_3)_2(Hegua)_2]X_2$ containing different anions X {X = Cl, $X_2 = SO_4$ or $[Pt(CN)_4]$}. Included in Table 6 are also additional relationships[27] between the Pt co-ordination planes and the guanine planes, namely the torsional angles β [C(8)–N(7)–Pt–NH_3(*cis*)], the α out-of-plane bending angle (formed by the Pt–N bond and the guanine plane), and the rocking angle Δ, which represents the difference between the two bond bending angles [C(5)–N(7)–Pt and C(8)–N(7)–Pt]. Comparison[27] with a large crystallographic data base of compounds of composition *cis*-$[Pt(am)_2(Hegua)_2]^{2+}$ (am = NH_3 or amine), containing both head-to-head and head-to-tail arranged neutral guanine bases, confirms that ring 2 in compound **3** shows a rare case of a negative rocking angle (−6.5°), meaning that the C(8)–N(7)–Pt angle is larger than the C(5)–N(7)–Pt angle by this value. For the second ring, this Δ angle is 9.9° and in the positive range observed in most cases. The difference in Pt ··· O(6) distances [3.28 Å for O(62) ··· Pt, 3.56 Å for O(61) ··· Pt] reflects this situation.

Intermolecular hydrogen bonding in both complexes **2** and **3** is extensive. Specifically, in **3** almost all possible sites on the Pt complex and the free 9-ethylguanine are involved in hydrogen

Table 5 Bond distances (Å) and angles (°) for complex **3**

Pt–N(1)	2.059(9)	N(72)–C(52)	1.43(1)	N(13)–C(63)	1.40(1)	N(93)–C(83)	1.38(2)
Pt–N(2)	2.034(8)	N(72)–C(82)	1.32(1)	N(21)–C(21)	1.41(2)	N(93)–C(93)	1.47(2)
Pt–N(71)	2.012(8)	N(73)–C(53)	1.42(1)	N(22)–C(22)	1.35(1)	C(41)–C(51)	1.39(1)
Pt–N(72)	1.985(8)	N(73)–C(83)	1.33(2)	N(23)–C(23)	1.33(1)	C(42)–C(52)	1.38(1)
O(61)–C(61)	1.24(1)	N(91)–C(41)	1.34(2)	N(31)–C(21)	1.33(2)	C(43)–C(53)	1.34(2)
O(62)–C(62)	1.27(1)	N(91)–C(81)	1.36(2)	N(31)–C(41)	1.36(2)	C(51)–C(61)	1.40(1)
O(63)–C(63)	1.24(1)	N(91)–C(91A)	1.51(2)	N(32)–C(22)	1.37(1)	C(52)–C(62)	1.41(1)
N(11)–C(21)	1.36(2)	N(91)–C(91B)	1.56(2)	N(32)–C(42)	1.34(1)	C(53)–C(63)	1.42(1)
N(11)–C(61)	1.38(1)	N(92)–C(42)	1.38(1)	N(33)–C(23)	1.33(1)	C(91A)–C(101A)	1.57(3)
N(12)–C(22)	1.37(1)	N(92)–C(82)	1.37(1)	N(33)–C(43)	1.37(1)	C(91B)–C(101B)	1.46(3)
N(12)–C(62)	1.34(1)	N(92)–C(92)	1.46(1)	N(71)–C(51)	1.42(1)	C(92)–C(102)	1.51(1)
N(13)–C(23)	1.36(1)	N(93)–C(43)	1.36(1)	N(71)–C(81)	1.34(1)	C(93)–C(103)	1.51(2)
N(1)–Pt–N(2)	89.4(3)	C(41)–N(91)–C(81)	108.3(9)	N(13)–C(23)–N(23)	117.7(9)	C(43)–C(53)–C(63)	120(1)
N(1)–Pt–N(71)	176.5(3)	C(41)–N(91)–C(91A)	141(1)	N(13)–C(23)–N(33)	124(1)	O(61)–C(61)–N(11)	120(1)
N(1)–Pt–N(72)	89.6(3)	C(41)–N(91)–C(91B)	112(1)	N(23)–C(23)–N(33)	119(1)	O(61)–C(61)–C(51)	124.8(8)
N(2)–Pt–N(71)	91.2(3)	C(81)–N(91)–C(91A)	111(1)	N(31)–C(41)–N(91)	126(1)	N(11)–C(61)–C(51)	114.9(9)
N(2)–Pt–N(72)	177.7(3)	C(81)–N(91)–C(91B)	140(1)	N(31)–C(41)–C(51)	125(1)	O(62)–C(62)–N(12)	120.6(8)
N(71)–Pt–N(72)	89.7(3)	C(42)–N(92)–C(82)	106.2(8)	N(91)–C(41)–C(51)	109(1)	O(62)–C(62)–C(52)	122.9(8)
C(21)–N(11)–C(61)	120(1)	C(42)–N(92)–C(92)	127.4(8)	N(32)–C(42)–N(92)	125.6(8)	N(12)–C(62)–C(52)	116.5(8)
C(22)–N(12)–C(62)	120.8(8)	N(72)–C(52)–C(62)	132.8(8)	N(32)–C(42)–C(52)	127.0(8)	O(63)–C(63)–N(13)	120(1)
C(23)–N(13)–C(63)	125.4(9)	C(42)–C(52)–C(62)	118.5(8)	N(92)–C(42)–C(52)	107.4(8)	O(63)–C(63)–C(53)	130(1)
C(21)–N(31)–C(41)	111(1)	C(82)–N(92)–C(92)	126.3(8)	N(33)–C(43)–N(93)	123(1)	N(13)–C(63)–C(53)	111(1)
C(22)–N(32)–C(42)	111.0(8)	C(43)–N(93)–C(83)	105(1)	N(33)–C(43)–C(53)	128.9(9)	N(71)–C(81)–N(91)	110(1)
C(23)–N(33)–C(43)	111.4(9)	C(43)–N(93)–C(93)	127(1)	N(93)–C(43)–C(53)	108(1)	N(72)–C(82)–N(92)	113.7(9)
Pt–N(71)–C(51)	131.2(6)	C(83)–N(93)–C(93)	128(1)	N(71)–C(51)–C(41)	106(1)	N(73)–C(83)–N(93)	113(1)
Pt–N(71)–C(81)	121.3(9)	N(11)–C(21)–N(21)	113(2)	N(71)–C(51)–C(61)	134.1(8)	N(91)–C(91A)–C(101A)	107(1)
C(51)–N(71)–C(81)	107(1)	N(11)–C(21)–N(31)	129(1)	C(41)–C(51)–C(61)	120(1)	N(91)–C(91B)–C(101B)	104(2)
Pt–N(72)–C(52)	124.8(6)	N(21)–C(21)–N(31)	118(1)	N(72)–C(52)–C(42)	108.7(7)	N(92)–C(92)–C(102)	109.8(9)
Pt–N(72)–C(82)	131.3(7)	N(12)–C(22)–N(22)	117.4(8)	N(73)–C(53)–C(43)	110.4(9)	N(93)–C(93)–C(103)	111(1)
C(52)–N(72)–C(82)	104.0(8)	N(12)–C(22)–N(32)	126.2(8)	N(73)–C(53)–C(63)	130(1)		
C(53)–N(73)–C(83)	103(1)	N(22)–C(22)–N(32)	116.3(8)				

Table 6 Dihedral angles,[a] torsional angles β,[b] out-of-plane angles α[b] and rocking angles Δ[b] (°) in complexes **2** and **3**

	2	**3**
Pt co-ordination plane/egua plane	123.9 (base A)	81.0 (base 1)
	122.9 (base B)	89.6 (base 2)
egua plane/egua plane	112.7 (A/B)	88.4 (1/2)
egua plane 1/Hegua plane 3	—	3.7
β[C(8)–N(7)–Pt–NH_3(*cis*)]	124.7 (base A)	71.0 (base 1)
	129.6 (base B)	92.2 (base 2)
α	1.1 (base A)	1.1 (base 1)
	7.5 (base B)	0.6 (base 2)
Δ	9.7 (base A)	9.9 (base 1)
	4.9 (base B)	−6.5 (base 2)

[a] Definition according to ref. 26. [b] Definition according to ref. 27.

bonds to water molecules. Two of the hydrogen-bonding interactions, between guaninate ligands in **2** and between a guaninate ligand and neutral guanine in **3**, are of particular significance. In **2**, each guaninate anion on a given molecule is hydrogen bonded through a pair of $N^1 \cdots H_2N^2$ hydrogen bonds [2.994(7) Å for ring A and 2.997(7) Å for ring B] to its centrosymmetrically related anion on another molecule [Fig. 3(*a*)]. This base pairing pattern, which is possible after N^1 deprotonation only, has not been reported before. It is clearly different from any other intermolecular H-bonding patterns between guanines predicted,[28,29] calculated,[30] and experimentally observed. Established homoguanine H-bonding patterns are (*i*) pairwise between N^3 and N^2H_2 sites [d(CpG)[31] (where C = cytosine base, G = guanine base and CpG = dinucleotide containing C and G) or N^7 platinated guanines[6,8]], (*ii*) between N^1 and N^2H_2 of one guanine and O^6 and N^7 of a second guanine [G(*syn*)·G(*anti*) pairs,[30] C(*anti*)·G(*anti*)·G(*syn*) triples in tRNA[31,32], quartets[33]] or (*iii*) a combination of (*i*) and (*ii*) [G triplets[34]]. There appears to be also the case that there is no hydrogen bonding (or a 'weak' one only) between guanines in a double-stranded oligonucleotide if both egua

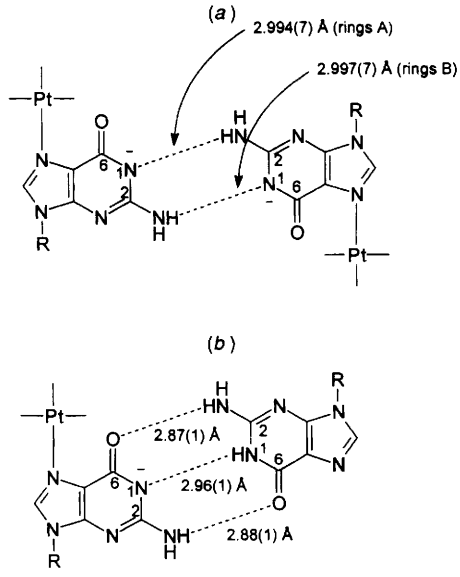

Fig. 3 Schematic representations of interguanine hydrogen bonds observed in complexes **2** (*a*) and **3** (*b*) with hydrogen bond lengths as observed in the solid state

ligands in the mismatch adopt an *anti* conformation.[35] The most significant feature of compound **3** is the three hydrogen bonds between a N^7 platinated, N^1 deprotonated guanine ligand and a neutral guanine [Fig. 3(*b*)]. The two bases involved in hydrogen bonding are close to coplanar (dihedral angle 3.7°) and hydrogen bonds are 2.88(1) Å [N(22) · · · O(63)], 2.87(1) Å [N(23) · · · O(62)], and 2.96(1) Å [N(12) · · · N(13)]. A similar pattern, albeit between a platinated neutral and a platinated anionic guanine, has been reported by us before in the case of *cis*- {[$Pt(NH_3)_2$(Hmcyt)(Hegua)][(egua)(Hmcyt)-

Table 7 Negative logarithms of the acidity constants of protonated guanine and two of its derivatives as determined by potentiometric pH titrations in aqueous solution at 25 °C and I = 0.1 mol dm^{-3} ($NaNO_3$)

	$H^+(N^7)$ site	$H(N^1)$ site		
	$pK^H_{H_2egua}$ [equation (1)]	pK^H_{Hegua} [equation (2)] or $pK^H_{Pt(Hegua)_2}$ [equation (3)]	$pK^H_{Pt(egua)(Hegua)}$ [equation (4)]	Ref.
$(H_2gua)^+$	3.3[a]	9.4[a]		36
$(H_2egua)^+$	3.27 ± 0.04	9.57 ± 0.04		*b*
cis-$[Pt(NH_3)_2(Hegua)_2]^{2+}$		8.02 ± 0.01	8.67 ± 0.01	*b*

[a] These values are 'near 25 °C and 0.1 mol dm^{-3} ionic strength' (ref. 36); they are defined in analogy to equations (1) and (2). Similar values from the literature are $pK^H_{H_2gua}$ = 3.3 (25 °C, I undefined, ref. 38; as well as T and I undefined, ref. 39) and pK^H_{Hgua} = 9.42 (25 °C, I = 0.1 mol dm^{-3}, ref. 40). [b] This work. The error limits correspond to three times the standard error of the mean value or the sum of the probable systematic errors, whichever is larger.

$Pt(NH_3)_2]^{3+}$}.[14,15] Differences in hydrogen-bond lengths in the two compounds can be traced back to differences in dihedral angles between the guanines involved in hydrogen bonding. Unlike in complex **3**, where platinated guaninate ligand and free guanine are almost coplanar, the platinated guanine (guaninate) ligands in the other case are strongly propeller-twisted (angle 39°).

Acidity Constants of $[H_2egua]^+$ *and cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$.—9-Ethylguanine (Hegua) is used below for comparisons. This guanine derivative may accept a proton at N^7 and release one from the HN^1 site;[36,37] hence, the equilibria (1) and (2) have to be considered.

$$[H_2egua]^+ \rightleftharpoons H^+ + Hegua \quad (1a)$$

$$K^H_{H_2egua} = [H^+][Hegua]/[(H_2egua)^+] \quad (1b)$$

$$[Hegua] \rightleftharpoons H^+ + [egua]^- \quad (2a)$$

$$K^H_{Hegua} = [H^+][(egua)^-]/[(Hegua)] \quad (2b)$$

In *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ Hegua is co-ordinated to Pt^{II} *via* N^7;[2] hence, this site is no longer accessible for a proton. However, both N^7 co-ordinated 9-ethylguanines may release a proton, one each from their HN^1 site; this is expressed in equilibria (3) and (4).

$$[Pt(Hegua)_2]^{2+} \rightleftharpoons H^+ + [Pt(Hegua)(egua)]^+ \quad (3a)$$

$$K^H_{Pt(Hegua)_2} = [H^+][Pt(Hegua)(egua)^+]/[Pt(Hegua)_2{}^{2+}] \quad (3b)$$

$$[Pt(Hegua)(egua)]^+ \rightleftharpoons H^+ + [Pt(egua)_2] \quad (4a)$$

$$K^H_{Pt(egua)(Hegua)} = [H^+][Pt(egua)_2]/[Pt(egua)(Hegua)^+] \quad (4b)$$

The results obtained *via* potentiometric pH titrations for the various acidity constants of equilibria (1)–(4) are listed in Table 7, together with the corresponding constants [equations (1) and (2)] for N^7-monoprotonated guanine, ($[H_2gua]^+$), taken from the literature.[36,38–40] The acidity constant of equilibrium (2a) had previously been determined[14] at the same ionic strength (I = 0.1 mol dm^{-3}, $NaClO_4$) but at a slightly lower temperature (20 °C); this earlier value, pK^H_{Hegua} = 9.75 ± 0.1, is in fair agreement with the present result.

Comparison of the acidity constants for $[H_2gua]^+$ (Hgua = guanine) and $[H_2egua]^+$ in Table 7 shows that replacement of the hydrogen atom at N^9 by an ethyl residue hardly affects the acid–base properties of the H^+N^7 and HN^1 sites. This agrees with the similar electronegativities of the H and CH_2CH_3 units and it indicates further that the solvation properties of the purine system are hardly altered by this N^9 substitution. This is quite different if the hydrogen at N^9 is substituted by a ribose residue which gives the nucleoside guanosine (Hguo): $pK^H_{H_2guo}$ = 2.11 ± 0.04 [analogous to equation (1)] and pK^H_{Hguo} = 9.22 ± 0.01 [analogous to equation (2)] (25 °C; I = 0.1 mol dm^{-3}, $NaNO_3$).[41] Now especially the acid–base property of N^7 is strongly affected; *i.e.*, the acidity of the H^+N^7 site is increased by about 1.2 pK_a units due to the sugar residue.

Deprotonation of the two HN^1 sites in the $[Pt(Hegua)_2]^{2+}$ complex occurs with $pK^H_{Pt(Hegua)_2}$ = 8.02 ± 0.01 and $pK^H_{Pt(egua)(Hegua)}$ = 8.67 ± 0.01 (Table 7) according to equilibria (3) and (4). Their difference, ΔpK_a = 0.65 ± 0.02, is very close to the statistically expected value of 0.6,[17] indicating that the two HN^1 sites hardly influence each other. This result is somewhat surprising as one might have expected that the first HN^1 deprotonation could affect the π interaction between the purine system and Pt^{II} and that this then influences the deprotonation of the second HN^1 site.

For the comparisons below the microacidity constants of the two symmetric HN^1 sites in *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ are needed. It is evident that the acidity of both sites has to be identical; *i.e.*, the corresponding microacidity constant must be the average of the two macroconstants: pK^H_{Pt/HN^1} = 8.35 ± 0.02 [=(8.02 + 8.67)/2].

This microconstant is 1.22 (±0.04) pK_a units below pK^H_{Hegua} (=9.57; Table 7) indicating a significant acidifying effect of Pt^{2+} co-ordinated at the N^7 sites in the imidazole rings of the purine systems on the two HN^1 sites in the pyrimidine rings. Indeed, the twofold positive charge of Pt^{2+} is expected to exercise such a repulsive effect on the proton in the HN^1 unit. Similar acidifications of N^7-co-ordinated metal ions on HN^1 sites have been observed before; in the following examples the ΔpK_a value [$=pK^H_{HN^1(ligand)} - pK^H_{HN^1(complex)}$] is given in parentheses after the chemical formula of the complex that is deprotonated at its HN^1 site: $[Ru(NH_3)_5(Hguo)]^{2+}$ (0.8),[42] $[Ru(NH_3)_5(Hguo)]^{3+}$ (2.2),[42] $[Cu(Hguo)]^{2+}$ (2.2) [calculated[43] from the data in ref. 44], [Pt(dien)(GMP)] (1.1)[45] (dien = diethylenetriamine = 1,4,7-triazaheptane; GMP^{2-} = guanosine 5′-monophosphate), [Ni(GMP)] (ca. 2.4),[41] and $[Ni(GTP)]^{2-}$ (1.0)[20] (GTP^{4-} = guanosine 5′-triphosphate).

The extent of the acidifying effect of Pt^{2+} on HN^1 in *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ fits into the general picture but for the identification of clear systematic trends regarding this effect more work is needed. However, in the context of the present study it is of utmost interest to note that the acidifying effect of ΔpK_a = 1.2 in $[Pt(Hegua)_2]^{2+}$ means that the HN^1 site is transformed into an even better H donor suitable for hydrogen bonding than is the case in the uncomplexed guanine residue and this fact is meaningful for the various hydrogen-bonded

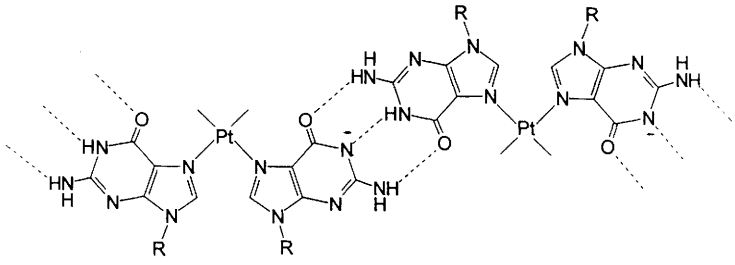

Fig. 4 Proposed hydrogen-bonding scheme of *cis*-$[Pt(NH_3)_2(Hegua)(egua)]^+$ **1** in Me_2SO solution

structures discussed in this study, especially for *cis*-$[Pt(NH_3)_2(egua)(Hegua)]^+$ **1** (Fig. 4).

^1H NMR Spectra.—The ^1H NMR spectrum of the precursor of complexes **2** and **3**, *cis*-$[Pt(NH_3)_2(Hegua)_2][ClO_4]_2 \cdot H_2O$, and its hydrogen-bonding behaviour towards free guanine, cytosine and thymine model bases has been reported.[13] There is virtually no self-association of this cation in Me_2SO, as is evident from the insensitivity of chemical shifts of the individual resonances on changes in complex concentration. With water present in $(CD_3)_2SO$, some association between the Pt complex and water is observed.

The very low solubility of complex **2** in $(CD_3)_2SO$ does not permit a study on the self-association of this compound in solution and hence no evaluation of the relevance of the H bonds between two guaninate ligands (as observed in the solid state) in solution. At the highest concentration obtainable (*ca.* 0.003 mol dm^{-3} Pt), the following shifts (ppm) are observed: H^8, 7.40; NH_3, 5.43; N^2H_2, 4.9 (br); CH_2, 4.00; CH_3, 1.21.

Only a single set of proton resonances for the guanine ligands of *cis*-$[Pt(NH_3)_2(Hegua)(egua)]ClO_4 \cdot 2H_2O$ **1** is observed in $(CD_3)_2SO$.[46] This indicates exchange of HN^1 between Hegua and egua. Coupling of H^8 with ^{195}Pt and of NH_3 with ^{195}Pt cannot be detected, not even at 60 MHz. The H^8 and N^2H_2 resonances show a concentration dependency in their chemical shifts over the concentration range studied: H^8, 7.95 (0.1 mol dm^{-3} Pt); 7.939 (0.025); N^2H_2, 7.318 (0.1); 7.26 (0.025). The HN^1 resonance is easily observed with a sample of $c_{Pt} = 0.1$ mol dm^{-3}, but even then it is very broad (half width 1.3 ppm). Its position at δ 14.2 indicates a tremendous downfield shift as compared to the parent compound *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$ (δ 11.47), and is a consequence of extremely strong hydrogen bonding. This downfield shift can be followed if NaOD (plus molecular sieves to remove water) is added to a solution of the parent compound in $(CD_3)_2SO$ or if **1** is added to the parent compound. Owing to the difficulty of determining accurately the amount of dissolved NaOD in Me_2SO, the second possibility was chosen to quantitatively follow the shifts of individual resonances (for an illustration, *cf.* ref. 46). While H^8 is shifted upfield as expected for averaging between neutral and anionic guanine ligands, the NH_2 resonance is shifted in the opposite direction, thus indicating that H bonding is exceeding the upfield shift expected for signal averaging of Hegua and egua. The HN^1 resonance is strongly shifted downfield and broadened. The magnitudes of HN^1 and N^2H_2 downfield shifts are unusually high. The HN^1 shift of 2.7 ppm at a concentration of 0.1:0.1 mol dm^{-3} egua–Hegua compares with *ca.* 0.75 ppm for the guanine–cytosine Watson-Crick base pair at the same concentration in the same solvent.[13] The N^2H_2 downfield shift at $c_{Pt} = 0.1$ mol dm^{-3} calculates as $\Delta NH_2 = \delta_{obsd} - 0.5(\delta_1 + \delta_2) = 7.32 - 0.5(6.95 + 4.9) = 1.39$ ppm and compares with *ca.* 0.35 ppm in the Watson-Crick pair between neutral guanine and cytosine {δ_1 = shift for *cis*-$[Pt(NH_3)_2(Hegua)_2]^{2+}$; δ_2 = shift for complex **2**}. The shift of NH_2 ($\Delta NH_2 \approx 0.5\Delta NH$) is close to the expected value if a hydrogen-bonding scheme for **1** is assumed that involves two of the four NH_2 protons as well as the N^1 proton (Fig. 4).

Vibrational Spectra.—Indication for a specific hydrogen-bonding interaction between platinated guaninate and neutral guanine in solid **3** originally came from IR spectroscopy. The comparison of IR spectra of the individual components **2** and 9-ethylguanine, or of a mechanical 1:1 mixture of both, with that of the adduct **3** revealed considerable differences in particular in the NH, OH stretching region and in the double-bond stretching region of the spectra. Likewise, a comparison of the solid-state Raman spectra of **2**, **3** and Hegua clearly revealed that **3** does not represent a mere superposition of the spectra of **2** and Hegua. In fact, some of the most intense in-plane modes of the Hegua nucleobase,[47] *e.g.* those at 1581, 1485, 1360 and 634 cm^{-1} are shifted by 5–15 cm^{-1} in **3** and are superimposed with egua modes of **2**. These findings tentatively ruled against a situation as observed for the adduct *cis*-$[Pt(NH_3)_2(Hmyct)_2][NO_3]_2 \cdot$Hmcyt, where the unco-ordinated cytosine nucleobase stacks on top of a platinated cytosine ligand without hydrogen bonding to it.[48] Moreover, the fact that the highest-frequency IR band in the double-bond stretching region occurred at 1675 cm^{-1} in **3** [as compared to 1710(sh) cm^{-1} in free 9-ethylguanine], pointed towards an involvement in hydrogen bonding of at least this group. The detailed picture of the hydrogen-bonding pattern was obtained from the X-ray structure analysis only, however.

A second feature worth mentioning with regard to speculations[49] on the possible existence of an N^7, O^6 chelate of *cis*-$Pt^{II}(NH_3)_2$ with either neutral or anionic guanine, relates to the position of the highest frequency IR mode in the 1800–1600 cm^{-1} range, usually attributed to ν(CO) of guanine. This mode, around 1700–1715 cm^{-1} in *cis*-$[Pt(NH_3)_2(Hegua\text{-}N^7)_2]X_2$ compounds (solid state), is shifted by 70 cm^{-1} to 1645 cm^{-1} in **2** as a consequence of N^1 deprotonation. Shifts of that order have been suggested to be indicative of N^7, O^6 chelation, but as has been pointed out by us before,[50] changes in this spectral region may also originate from other Pt binding patterns as well.

Relevance of Interguanine Hydrogen Bonding.—Internucleobase hydrogen bonding between identical bases (homo base pairing) and formation of ordered oligonucleotide structures has been demonstrated in a number of cases, *e.g.* with hemiprotonated cytosine (duplex,[51] double duplex[52]), protonated adenine (duplex[53]), neutral guanine (tetraplex[32]) and in parallel-stranded, low pH DNA containing suitable sequences.[54] Likewise, dinucleotides such as $[d(CpG)]_2$[31] and $[CpA]_2$ (A = adenine base)[55] can be crystallized at low pH in a parallel-stranded fashion containing hemiprotonated cytosine pairs, in addition to G_2 and A_2 pairs, respectively. Non-Watson-Crick G–G pairs appear to be also of considerable importance in the RNA tertiary structure of a particular HIV domain.[56] In principle, it should be possible to construct parallel-stranded oligonucleotides, containing deprotonated guanines (with hydrogen bonds *via* N^1 and N^2H_2) or hemideprotonated guanines (with hydrogen bonds *via* N^1, N^2H_2 and O^6), respectively. However, unlike protonation of a nucleobase, deprotonation of the negatively charged nucleotides makes such a possibility certainly less favourable, although not impossible. Misinsertion of 5-bromo- and 5-fluoro-uracil

during DNA synthesis has recently been correlated with base ionization rather than base tautomerization.[57] Moreover, initial nucleobase metallation (*e.g.* at guanine N^7) by a positively charged metal entity, can compensate for this charge effect and at the same time does diminish the pH necessary to accomplish nucleobase deprotonation. The nucleobase acidification is, of course, largely independent of the co-ordination geometry of the metal ion in that *trans*-$Pt^{II}(am)_2$, monofunctional Pt^{II} as well as other divalent cations should not differ greatly in this respect.

The question remains whether the hydrogen-bonding patterns seen in our compounds, are relevant with regard to metal binding to nucleic acids. There is probably no chance of formation of a guanine pair in DNA as seen in complex **2**, both from a statistical point of view (necessary to have independently metallated guanines in close proximity) and the requirement for parallel polynucleotide strands in a duplex DNA (*trans*-oriented glycosidic bonds). This second argument applies, in principle, also to the interguanine hydrogen-bonding pattern seen in complex **3**. However, in a hypothetical purine–purine–pyrimidine triple, the two purines (neutral guanine and metallated, deprotonated guanine) would be in a relative orientation suitable for triple hydrogen-bond formation with each other. Purine–purine–pyrimidine triplex structures are in fact a newly emerging feature in nucleic acid chemistry,[58] and in some cases metal ions seem to be necessary for their stabilization[59] (even though no nucleobase deprotonation has been invoked).

Finally the guanine–guanine pairing pattern observed in complex **3** represents a model for a nucleobase mispair, formed as a consequence of an initial metal co-ordination to one base. For this very reason it is of interest with regard to mechanisms of metal-induced mispairing steps leading to a mutagenic event. To the best of our knowledge, it is the only X-ray structurally characterized metal complex relevant to this aspect as yet.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft (DFG), the Fonds der Chemischen Industrie (FCI), the Swiss National Science Foundation and the Human Capital and Mobility Programme (for B. L. *via* the Commission of the European Communities in Brussels and for H. S. *via* the Swiss Federal Office for Education and Science). This research is also part of the COST D1 programme. B. S. is grateful for a leave of absence from the ZhongShan (Sun Yatsen) University in GuangZhou, PRC.

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Received 5*th June* 1995; *Paper* 5/03575I