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'Real' Model Compounds for Intrastrand Cross-Linking of Two Guanine Bases by Cisplatin:
Crystal Structures of *cis*-Diamminebis(9-ethylguanine-N^7)platinum(II) Dichloride Trihydrate, $[Pt(NH_3)_2(C_7H_9N_5O)_2]Cl_2 \cdot 3H_2O$, and *cis*-Diamminebis-(9-ethylguanine-N^7)platinum(II) Sesquichloride Hemibicarbonate Sesquihydrate, $[Pt(NH_3)_2(C_7H_9N_5O)_2]Cl_{1.5}(HCO_3)_{0.5} \cdot 1.5H_2O$

B. LIPPERT, GABRIELE RAUDASCHL

Anorganisch-Chemisches Institut, Technische Universität München, D-8046 Garching, F.R.G.

C. J. L. LOCK and P. PILON

Institute for Materials Research, McMaster University, Hamilton, Ontario L8S 4M1, Canada

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Abstract

The preparation, crystal structure and ^1H NMR spectrum of cis-diamminebis(9-ethylguanine-N^7)platinum(II) dichloride trihydrate, I and the crystal structure of cis-diamminebis(9-ethylguanine-N^7) platinum(II) sesquichloride hemibicarbonate sesquihydrate, II, are reported. Both complexes crystallize in the triclinic form, space group $P\bar{1}$ with very similar unit cell dimensions: $a = 12.238(3)$, $b = 10.787(2)$, $c = 12.883(4)$ Å, $\alpha = 92.18(2)$, $\beta = 123.32(2)$, $\gamma = 111.33(2)°$, $V = 1260.6(6)$ Å^3, $Z = 2$ for compound I, and $a = 12.378(3)$, $b = 10.748(3)$, $c = 12.664(4)$ Å, $\alpha = 92.23(2)$, $\beta = 123.40(2)$, $\gamma = 112.92(2)°$, $V = 1223.2(7)$ Å^3, $Z = 2$ for compound II. Data for both crystals were collected with Mo-Kα radiation at low temperature ($T = -71$ °C (I), $T = -48$ °C (II)) on a Syntex $P2_1$ diffractometer. The crystal structures were determined by standard methods and refined to $R = 0.0617$ on the basis of 3319 independent reflections (I) and $R = 0.0446$ on the basis of 3218 independent reflections (II). The structure and packing of the cations in both complexes are very similar. The dihedral angles between the purine bases are large (75.4(9)° for I, 74.4(9)° for II) and prevent any substantial intra-complex base-base interactions. In contrast to previously published models of bis(guanine) complexes of cis-Pt(II), the compounds described here contain the bases in a head–head arrangement, which makes them 'real' models of intrastrand cross-links between two adjacent guanines in DNA. The ^1H NMR spectrum of I in $Me_2SO\text{-}d_6$ shows substantially different chemical shifts of the guanine and NH_3 resonances as compared to the perchlorate salt in the same solvent. The differences are attributed to extensive hydrogen bonding between the chloride ions and NH_3, NH_2, NH and H(8) of cis-$[(NH_3)_2Pt(C_7H_9N_5O)_2]^{2+}$.

Introduction

A particularly attractive hypothesis concerning the mode of action of antitumor platinum drugs [1] involves binding of the *cis*-diamineplatinum(II) moiety to two adjacent guanine residues on the same strand of the DNA helix. Indirect evidence for the validity of this intrastrand cross-linking model [2] includes findings on the large buoyant density of platinated poly(dG)·poly(dC) [3], altered enzymatic digestion patterns of various DNAs after incubation with *cis*-Pt(II) [4, 5], CD enhancement induced in platinated DNA and bis(guanine) complexes [6], and the inhbition of intercalation of certain dyes in DNA [7, 8]. Because of the suspected biological significance of intrastrand guanine–guanine cross-linking, a number of model compounds containing Pt(II) and two oxopurines in *cis*-positions have been prepared and studied crystallographically [9–17]. Two noteworthy features evolved from these studies: First, all crystallographically studied examples of *cis*-bis(oxopurine) complexes of *cis*-Pt(II) have an approximate C_2 molecular symmetry, that is a head–tail arrangement of the bases relative to the Pt coordination plane. This also holds for other examples of *cis*-bis(nucleobase) complexes ' of *cis*-Pt(II) [18–20], but it is a rather unlikely arrangement of two bases cross-linked in native DNA. Only in solution has there been spectroscopic evidence for a head–head orientation of two guanines in a GpG complex of *cis*-Pt(II) [21]. Second, the extent of base–base interaction, though variable to some degree, may be divided into two categories: with large dihedral angles (>65°) between the nucleobase planes, substantial intercomplex base stacking is observed [9, 15, 17] whereas with small dihedral angles, *e.g.* 39.6° in a complex containing two phosphate methyl ester of GMP as ligands [14], only the

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intracomplex base–base interaction is significant.

The crystal structures of the compounds described here have been undertaken with regard to these two aspects: the arrangement of the two purine bases in the *cis*-$[(NH_3)_2Pt(9\text{-}EtG)_2]^{2+}$ cation, and the extent of purine–purine interaction which is a measure for a local distortion of DNA in a guanine, guanine intrastrand cross-link.

Experimental

Preparation

cis-$[(NH_3)_2Pt(9\text{-}EtG)_2]Cl_2 \cdot 3H_2O$, **I**, has been prepared as follows: 0.5 mmol *cis*-$(NH_3)_2PtCl_2$ [22] and 1.5 mmol 9-ethylguanine (9-EtG) were suspended in 15 ml H_2O and kept at 40 °C for 4 d. A white precipitate (110 mg) of unreacted 9-EtG and *cis*-$[(NH_3)_2Pt(9\text{-}EtG)Cl]Cl \cdot 0.5H_2O$ [23] was removed by filtration and the colorless filtrate (pH 4) was allowed to evaporate at 40 °C to 5 ml volume, filtered again and crystallized slowly (7 d) at 22 °C in air. Several fractions of **I** were obtained and briefly air-dried (180 mg colorless, transparent cubes). *Anal.* Calcd. for $[(NH_3)_2Pt(C_7H_9N_5O)_2]Cl_2 \cdot 3H_2O$: C, 23.60; H, 4.25; N, 23.59; Cl, 9.95. Found: C, 23.46; H, 4.01; N, 23.97; Cl, 9.33.

cis-$[(NH_3)_2Pt(9\text{-}EtG)_2]Cl_{1.5}(HCO_3)_{0.5} \cdot 1.5H_2O$, **II**, was isolated from a preparation carried out analogously to that described above, but with Pt:(9-EtG) = 1 and a longer time of crystallization (15 d). The first four fractions of precipitate consisted of *cis*-$[(NH_3)_2Pt(9\text{-}EtG)Cl]Cl \cdot 0.5H_2O$ [23] (yield 35%) before the bis(9-EtG) complex precipitated (yield 30%). Elemental analysis of this product was identical with that of **I** within experimental error. Neither the ^1H NMR nor the IR spectrum of it revealed any difference as compared to **I**. In particular, the IR spectrum of the product did not show bands caused by HCO_3^-. It is suspected that only a small fraction of the bulk material contained HCO_3^- and that the crystals selected for X-ray measurements happened to be those of the mixed Cl, HCO_3 compound. We assume that during the long crystallization process in air some CO_2 had been taken up from the air.

Spectra

IR spectra were recorded as KBr pellets and Nujol mulls on a Perkin Elmer 580 grating spectrometer. ^1H NMR spectra were taken on a Jeol JNM-FX 60 Fourier-transform spectrometer at 30 °C, with D_2O (internal $[N(CH_3)_4]BF_4$ reference) and $Me_2SO\text{-}d_6$ (TMS as internal reference) as solvents.

Collection of X-ray Data

The crystals of the two compounds were sealed in Lindemann capillaries to stop decomposition caused by the loss of water from the lattice. Both crystals were plate-like and colourless (0.32 mm × 0.23 mm × 0.10 mm (**I**) and 0.40 mm × 0.40 mm × 0.15 mm (**II**)). Precession photographs of **II** suggested a triclinic cell and a Delaunay reduction showed no hidden symmetry. The cell for crystal **I** was found on the basis of the cell for **II**. The unit cell parameters were obtained from a least squares fit of χ, ϕ and 2θ for 15 reflections in the range $17.1° < 2\theta < 25.7°$ for **I** and $17.6° < 2\theta < 29.1°$ for **II**. The crystal data were: **I**, $a = 12.238(3)$ Å, $b = 10.787(2)$ Å, $c = 12.883(4)$ Å, $\alpha = 92.18(2)°$, $\beta = 123.32(2)°$, $\gamma = 111.33(2)°$, $V = 1260.6(6)$ Å^3, $Z = 2$, $\rho_{calc} = 1.88$ g cm^{-3}, $\rho_{obs} = 1.88(1)$ g cm^{-3}, $\mu = 61.2$ cm^{-1}; **II**, $a = 12.378(3)$ Å, $b = 10.748(3)$ Å, $c = 12.664(4)$ Å, $\alpha = 92.23(2)°$, $\beta = 123.40(2)°$, $\gamma = 112.92(2)°$, $V = 1223.2(7)$ Å^3, $Z = 2$, $\rho_{calc} = 1.90$ g cm^{-3}, $\rho_{obs} = 1.92(1)$ g cm^{-3}, $\mu = 62.33$ cm^{-1}. Reflections were collected up to a maximum 2θ value of 45° for both crystals, consisting of h, ±k, ±l. The number of reflections measured was 3656 for **I** and 3542 for **II**, of which 3319 and 3218 were independent, respectively. R_{int} for **I** is 0.0186, for **II**, 0.0181. The stability of the crystals was monitored by measuring the intensity of two standards every 48 reflections. The same standards were used for both crystals: −2, 4, −1 (e.s.d. = 2.09% (**I**), 1.10% (**II**)) and 2, 0, 2 (e.s.d. = 1.62% (**I**), 2.23% (**II**)). Two types of absorption corrections were made on the crystals: an empirical absorption correction by the ψ scan method using 11 reflections, range $4.25° < 2\theta < 42.88°$ (**I**), range $6.49° < 2\theta < 40.39°$ (**II**) to correct for the crystal shape, and a 2θ absorption correction using the average radius of the crystals to calculate R (0.52 for **I** and 1.1 for **II**) and the appropriate A* values for a cylindrical absorption correction (**I**) or a spherical absorption correction (**II**). Corrections were made for Lorentz-polarization effects.

Solution of the Structure

The position of the platinum atom in complex **II** was found from a three-dimensional Patterson synthesis. A series of full-matrix least squares refinements, minimizing $\Sigma w(|F_o| - |F_c|)^2$, followed by three-dimensional difference syntheses revealed the remaining atoms. No attempts were made to find the hydrogen atoms. The atomic positions for **I** were found on the basis of the known positions in **II**. In complex, **I**, 183 parameters were refined using 3162 non-zero reflections to a final $R = 0.0617$, $wR = 0.0618$ and 169 parameters were refined, using 3124 non-zero reflections in **II** to a final $R = 0.0446$ and $wR = 0.0511$. The weighting scheme used was $w = (\sigma^2 + gF^2)^{-1}$ where $g = 0.0001$ for structure **I** and 0.0003 for structure **II**.

Refinement was terminated when the maximum shift/error (average shift/error) was 0.089 (0.009) for **I** and 0.128 (0.015) for **II**. The highest peak in the

TABLE I. Atomic Parameters and Isotropic or Equivalent Temperature Factors ($\times 10^3$) for [*cis*-$(NH_3)_2(9\text{-Et-G})_2Pt]Cl_2\cdot 3H_2O$ (**I**) and [*cis*-$(NH_3)_2(9\text{-Et-G})_2Pt]Cl_{1.5}(HCO_3)_{0.5}\cdot 1.5H_2O$ (**II**).

Atom	I				II			
	x	y	z	U_{iso} or U_{eq}^{a}	x	y	z	U_{iso} or U_{eq}^{a}
Pt	34.23(6)	479.26(6)	208.21(5)	30.0(9)^a	43.98(4)	483.66(4)	217.09(4)	18.6(6)^a
N(12)	17(1)	661(1)	202(1)	60(3)	37(1)	669.8(9)	219.6(9)	46(2)
N(11)	236(1)	575.6(9)	247.1(9)	42(2)	248.3(9)	584.0(8)	258.4(8)	35(2)
N(1A)	−207(1)	11(1)	−95(1)	47(3)	−214.5(9)	1.6(8)	−104.6(8)	38(2)
C(2A)	−182(1)	−93(1)	−41(1)	42(3)	−189(1)	−100(1)	−51(1)	36(2)
N(2A)	−251(1)	−219(1)	−123(1)	49(3)	−262.4(9)	−231.1(9)	−137.9(9)	45(2)
N(3A)	−91(1)	−71(1)	88(1)	43(2)	−95.0(8)	−74.6(8)	79.7(8)	33(2)
C(4A)	−26(1)	65(1)	156(1)	38(3)	−28(1)	62.9(9)	152.4(9)	30(2)
C(5A)	−45(1)	177(1)	112(1)	40(3)	−50(1)	170.6(9)	106.0(9)	31(2)
C(6A)	−144(1)	147(1)	−27(1)	49(3)	−147(1)	145(1)	−31.5(9)	34(2)
O(6A)	−171(1)	235.1(9)	−84.8(9)	63(2)	−176.7(8)	228.5(8)	−90.1(8)	51(2)
N(7A)	43(1)	295.2(9)	213.8(9)	38(2)	44.9(8)	296.4(8)	216.6(8)	34(2)
C(8A)	115(1)	260(1)	321(1)	43(3)	118(1)	261(1)	324(1)	36(2)
N(9A)	74(1)	120(1)	288.2(9)	43(2)	77.3(8)	120.1(8)	288.9(8)	35(2)
C(9A)	127(1)	37(1)	377(1)	56(3)	130(1)	36(1)	378(1)	56(3)
C(10A)	242(2)	130(2)	520(2)	89(5)	247(2)	129(1)	525(1)	70(4)
N(1B)	−499(1)	391.9(9)	−104.8(9)	44(2)	−486.8(9)	394.3(8)	−99.6(8)	39(2)
C(2B)	−592(1)	303(1)	−84(1)	44(3)	−583(1)	305(1)	−79(1)	40(2)
N(2B)	−736(1)	273(1)	−166(1)	55(3)	−726(1)	276.0(9)	−160.6(9)	50(2)
N(3B)	−550(1)	246.0(9)	13.4(9)	41(2)	−540.6(9)	249.9(8)	20.9(8)	41(2)
C(4B)	−403(1)	287(1)	88(1)	40(3)	−396(1)	289(1)	94(1)	36(2)
C(5B)	−305(1)	371(1)	71(1)	35(3)	−294(1)	375(1)	79(1)	35(2)
C(6B)	−347(1)	436(1)	−30(1)	43(3)	−334(1)	439(1)	−22(1)	34(2)
O(6B)	−270.3(9)	518.4(8)	−53.3(8)	49(2)	−257.9(7)	521.0(7)	−48.4(7)	40(2)
N(7B)	−165(1)	382(1)	171(1)	45(2)	−157.3(9)	383.4(8)	177.0(8)	38(2)
C(8B)	−190(1)	299(1)	239(1)	46(3)	−182(1)	303(1)	247(1)	46(3)
N(9B)	−332.7(9)	241.0(9)	191.3(9)	35(2)	−326.2(9)	244.3(9)	200.6(9)	43(2)
C(9B)	−397(1)	146(1)	245(1)	46(3)	−391(1)	151(1)	256(1)	54(3)
C(10B)	−469(2)	−3(2)	168(2)	65(4)	−472(2)	−6(1)	171(2)	72(4)
Cl(1)^b	22.9(9)	283(1)	550.1(9)	32(11)^a	23.6(4)	288.1(4)	562.7(3)	43(5)^a
Cl(11)^b	29(1)	731(1)	441.6(9)	39(13)^a	–	–	–	–
Cl(2)^b	484.4(7)	445.2(7)	451.5(7)	40(10)^a	495.3(6)	450.6(7)	464.8(6)	37(8)^a
Cl(3)^b	390.6(7)	948.5(6)	380.3(6)	33(9)^a	–	–	–	–
OH(1)^b	350(2)	486(2)	694(2)	39(5)	364(2)	488(1)	691(1)	37(3)
OH(11)^b	605(3)	501(2)	315(2)	75(8)	426(2)	503(2)	677(2)	63(4)
OH(2)^b	−152(2)	473(2)	462(2)	85(6)	193(3)	548(2)	543(2)	102(7)
OH(3)^b	569(2)	860(2)	623(2)	59(5)	–	–	–	–
OH(4)^b	312(2)	790(2)	442(2)	72(5)	–	–	–	–
OH(5)^b	499(3)	677(3)	608(3)	102(7)	–	–	–	–
O(3)^b	–	–	–	–	441(2)	153(2)	390(2)	51(4)
O(4)^b	–	–	–	–	596(2)	31(2)	610(2)	86(6)
O(5)^b	–	–	–	–	395(2)	−115(2)	436(2)	81(5)
CO^b	–	–	–	–	481(3)	92(3)	443(3)	59(6)

$^a U_{eq} = 1/3[U_{11} + U_{12} + U_{13} + 2(U_{23}\cos\alpha + U_{13}\cos\beta + U_{12}\cos\gamma)]$. ^{b}These atoms were given a site occupancy of one-half.

final difference map was 1.86 e$Å^{-3}$ for **I** and 1.42 e$Å^{-3}$ in **II** and the lowest valley was −2.52 e$Å^{-3}$ in **I** and −0.73 e$Å^{-3}$ in **II**. A secondary extinction correction was applied using the method listed in SHELX (X = 0.0008 in **I** and X = −0.0004 in **II**. Scattering factors were from Cromer and Waber [24a] and the corrections for anomalous dispersion applied were from Cromer [24b].

All calculations were carried out on a CYBER 170/730 computer. The programs DATCOS, ABSORB AND DATRDN from the XRAY 76 program [25] were used for preliminary data treatment. The structure was solved with SHELX [26]. Plane and dihedral angle calculations were made with NRC-22 [27]. Diagrams were prepared with the program ORTEP II [28].

TABLE II. Bond Lengths (Å) and Angles (°) for [*cis*-$(NH_3)_2Pt(9\text{-}Et\text{-}G)_2]Cl_2 \cdot 3H_2O$ (I) and [*cis*-$(NH_3)_2Pt(9\text{-}Et\text{-}G)_2]Cl_{1.5}(HCO_3)_{0.5} \cdot 1.5H_2O$ (II).

	I		II	
	A	B	A	B
Atoms	Distance			
Pt–N(11)	2.04(1)	–	2.05(1)	–
Pt–N(12)	2.05(1)	–	2.04(1)	–
Pt–N(7)	2.03(1)	2.03(1)	2.018(9)	2.03(1)
N(1)–C(2)	1.38(2)	1.36(2)	1.36(2)	1.37(2)
C(2)–N(2)	1.33(2)	1.36(2)	1.35(1)	1.35(2)
C(2)–N(3)	1.34(2)	1.34(2)	1.32(1)	1.34(2)
N(3)–C(4)	1.36(2)	1.36(2)	1.35(1)	1.34(2)
C(4)–C(5)	1.40(2)	1.35(2)	1.37(2)	1.37(2)
C(5)–C(6)	1.44(2)	1.43(2)	1.40(1)	1.41(2)
C(6)–O(6)	1.26(2)	1.22(2)	1.23(1)	1.22(2)
C(6)–N(1)	1.36(2)	1.40(2)	1.40(1)	1.41(1)
C(5)–N(7)	1.36(1)	1.42(2)	1.41(1)	1.40(1)
N(7)–C(8)	1.33(2)	1.34(2)	1.33(1)	1.33(2)
C(8)–N(9)	1.37(2)	1.34(2)	1.36(1)	1.37(2)
C(4)–N(9)	1.36(1)	1.37(2)	1.37(1)	1.37(1)
N(9)–C(9)	1.49(2)	1.49(2)	1.49(2)	1.48(2)
C(9)–C(10)	1.54(2)	1.50(2)	1.53(2)	1.54(2)
CO–O(3)	–	–	1.02(4)	–
CO–O(4)	–	–	1.16(3)	–
CO–O(5)	–	–	1.37(3)	–
	Angles			
N(11)–Pt–N(12)	91.1(5)	–	90.6(4)	–
N(11)–Pt–N(7)	91.5(5)	179.1(4)	91.7(4)	179.5(4)
N(12)–Pt–N(7)	177.5(6)	89.7(5)	177.6(5)	89.9(4)
N(7A)–Pt–N(7B)	87.8(5)	–	87.9(4)	–
C(6)–N(1)–C(2)	125(1)	125(1)	125.0(8)	125.5(9)
N(1)–C(2)–N(2)	117(1)	117(1)	116.2(9)	118(1)
N(1)–C(2)–N(3)	123(1)	125(1)	123.8(9)	123(1)
N(2)–C(2)–N(3)	120(1)	118(1)	120(1)	119(1)
C(2)–N(3)–C(4)	112(1)	111(1)	112.4(9)	112(1)
N(3)–C(4)–C(5)	130(1)	128(1)	127.5(8)	128(1)
N(3)–C(4)–N(9)	125(1)	123(1)	125.1(9)	124(1)
C(5)–C(4)–N(9)	105(1)	109(1)	107.4(8)	108(1)
C(4)–C(5)–C(6)	116(1)	121(1)	120.1(9)	121(1)
C(4)–C(5)–N(7)	110(1)	108(1)	107.9(8)	108(1)
C(6)–C(5)–N(7)	134(1)	131(1)	132(1)	131(1)
C(5)–C(6)–O(6)	125(1)	129(1)	128.8(9)	130(1)
N(1)–C(6)–O(6)	121(1)	122(1)	120.0(8)	120(1)
N(1)–C(6)–C(5)	114(1)	110(1)	111.2(9)	110(1)
C(5)–N(7)–Pt	126.1(8)	132(1)	126.7(7)	132.2(9)
C(5)–N(7)–C(8)	107(1)	105(1)	106.4(8)	106(1)
C(8)–N(7)–Pt	126.3(9)	122.8(9)	126.0(7)	121.9(8)
N(7)–C(8)–N(9)	110.3(9)	112(1)	110.8(8)	112(1)
C(8)–N(9)–C(4)	108(1)	107(1)	107.4(9)	106(1)
C(4)–N(9)–C(9)	124(1)	128(1)	124.1(8)	128(1)
C(8)–N(9)–C(9)	127.9(9)	125(1)	128.5(8)	126(1)
N(9)–C(9)–C(10)	111(1)	110(2)	112(1)	109(1)
O(3)–CO–O(4)	–	–	116(2)	–
O(3)–CO–O(5)	–	–	137(2)	–
O(4)–CO–O(5)	–	–	108(3)	–

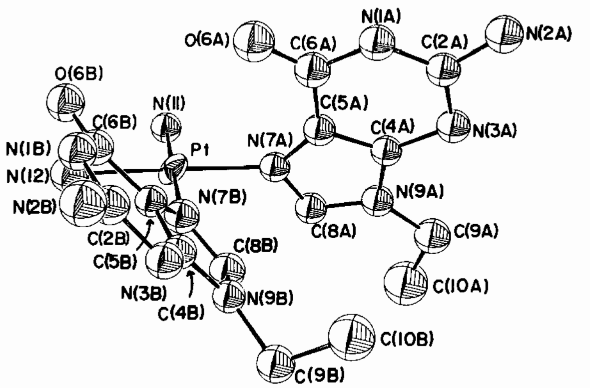

Fig. 1. The cation $[Pt(NH_3)_2\text{-}(9\text{-}EtG)_2]^{2+}$ in $[Pt(NH_3)_2(9\text{-}EtG)_2]Cl_2 \cdot 3H_2O$, I, showing the atom numbering.

Discussion

The atomic parameters and temperature factors are listed in Table I for both complexes. The bond lengths and angles are listed in Table II and the molecular structure and labelling of the atoms of the cation in I are shown in Fig. 1. The two complexes are very similar and differ only in the anions and the number of water molecules present in the lattice.

The binding of the platinum atom to the 9-ethylguanine ligand occurs through N7 as seen in all complexes of platinum with N9-blocked guanine residues studied so far [9, 11, 14, 15, 17, 29–32]. There is no indication in **I** and **II** of an interaction between O6 on any of the ligands and the central platinum atom, the shortest distance being Pt–O(6A) = 3.392(9) Å in complex **I** and 3.430(7) Å in complex **II**.

The geometry around the platinum atom is square planar and the Pt–N bond distances, ranging from 2.018(9) Å to 2.05(1) Å are normal for these types of complexes.

The bond lengths and angles within the purine rings are in agreement with the average values calculated from a number of structures of nucleosides and nucleotides [33] particularly with those of 9-ethylguanine [34]. The purine rings are almost planar as indicated by the dihedral angles between the pyrimidine and the imidazole ring (range = 1(1)° to 2(1)°). The two rings in the cations differ in the amount to which the ethyl groups extend away from the purine plane. In the ring labelled with the a atoms (Ring A), C10 is 0.07(2) Å out of the plane in **I** (0.04(2) Å in **II**). In ring B however the distance is 1.33(2) Å in **I** and 1.40(2) Å in **II**. This leads to 3 different types of base-base stacking in the unit cells (see below).

Both structures show large dihedral angles between the purine ligand, A, and the platinum coordination plane, ($A\text{–}PtN_4$ = 75.4(9)° (**I**) and 74.4(9)°(**II**)). The B ring makes a smaller angle with the platinum plane (49.2(9)° (**I**), 50.6(9)° (**II**)) and this is indicative of an internal hydrogen bond between O6 and one of the ammine ligands on the platinum atom [17, 30]. These bonds are O(6B)···N(12) = 2.92(1) Å (**I**), and O(6B)···N(12) = 2.965(8) Å (**II**). The dihedral angles between the purine ligands are large (68(1)° (**I**), 70(1)° (**II**)) and indicate that there is little or no intracomplex base–base interaction. There is, however, substantial intercomplex base stacking between A rings and between B rings of symmetry related cations in the unit cell (see below).

Certainly the most interesting feature of the compounds described here is the head–head arrangement of the two 9-EtG ligands which is in contrast to all previously reported structures of *cis*-bis(nucleobase)complexes of *cis*-Pt(II), and which makes them 'real' models for intrastrand guanine, guanine cross-links.

As mentioned earlier, there are three types of intercomplex ring-ring interactions in the cells, as illustrated in Figs. 2 and 3. The first interaction involves the stacking of the A rings. These stack at a distance of 3.36(2) Å and 3.38(2) Å along the *a* direction in complexes **I** and **II** respectively and are related by the centre of symmetry at the origin. In addition, adjacent molecules along *a*, related by the inversion centre at ½, 0, 0 are hydrogen bonded together. The A ring of one molecule is bonded to the B ring of the other (N(3A)···N(2B) = 3.07(2) Å.

The B rings are stacked along the *b* direction at x = ½, z = 0 and there are two types of ring–ring

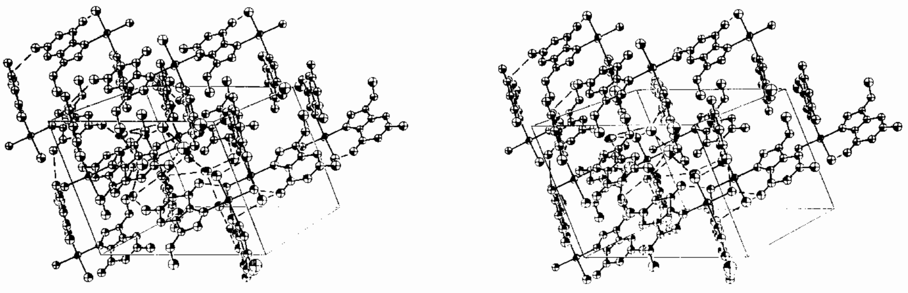

Fig. 2. The packing of $[Pt(NH_3)_2(9\text{-}EtG)_2]Cl_2 \cdot 3H_2O$, **I**. *a* and $c^* \times a$ are parallel to the bottom and sides of the page respectively and the view is down c^*.

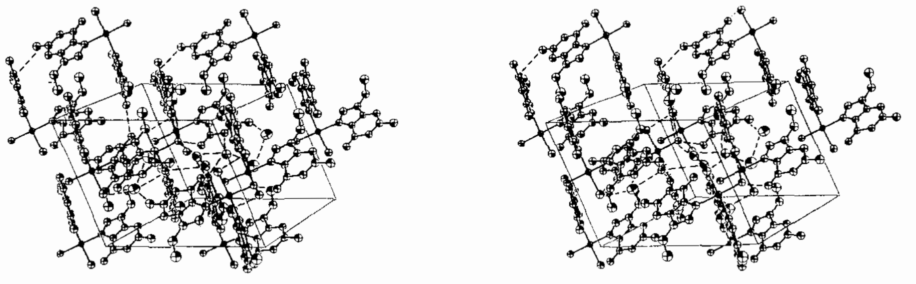

Fig. 3. The packing of $[Pt(NH_3)_2(9\text{-}EtG)_2]Cl_{1.5}(HCO_3)_{0.5}\cdot 1.5H_2O$, **II**. *a* and *c** × *a* are parallel to the bottom and sides of the page respectively and the view is down *c**.

interaction, caused by the orientation of the ethyl groups. At y = ½. the bases are costacked to maximize π–π interactions and the rings are 3.37(2) Å (**I**) and 3.33(2) Å (**II**) apart. Because the ethyl groups are roughly normal to the purine (B) plane, the rings of adjacent molecules along *b* related by the ½, 0, 0, inversion centre cannot pack in this manner and the ring-ring distances are long (4.86(2) Å (**I**) and 4.87(2) Å (**II**), the contacts being between the terminal methyl group and the purine plane. In addition, molecules in the *b* direction are bound by hydrogen bonding between O(6B) of one molecule and N(2A) of a translationally equivalent molecule (O(6B)··· N(2A) = 2.97(2) Å (**I**) and 2.94(1) Å (**II**)).

In the *c* direction, there is hydrogen bonding between pairs of molecules related by the center of symmetry at 0, ½, 0 from O(6A) to N(11)′ and N(12)′. The anions and lattice water molecules form a hydrogen bonded chain which runs through the middle of the unit cell at ½, *b*, ½. In complex **I**, there are two chloride ions Cl(2) and Cl(3), which are disordered about the centers of symmetry at ½, ½, ½ and ½, 0, ½ respectively. The disordered positions were chosen because the temperature factors were more reasonable than they were with the ion on the special position. In addition, this allowed the choice of reasonable hydrogen bond distances to half of the disordered water molecules. The half occupancy of two hydrogen bonded chains, running through the crystal, results in the observed disorder. For clarity, only one of the chains is shown in Figs. 2, 3 and 4. One chain (see Fig. 4) consists of the following atoms:Cl(3)′, O(H3)′, Cl(2), O(H4), O(H5), Cl(3)′. Joining the chain are O(H1), which cross-links O(H5) to Cl(1), and O(H11′), which links Cl(2) to O(H2) and thus to Cl(1) and Cl(11′). The presence of O(H2) suggested further disorder since both Cl(1′) and O(H1′) are too close to the O(H2) position. Thus both these atoms were given half-occupancy, as were the related disordered atoms Cl(11) and O(H11), O(H1) and O(H11)′ form strong hydrogen bonds to N(1B) (2.73(2) Å, 2.79(3) Å, respectively). There is a strong interaction between Cl(2) and O(H11′). The Cl(2)···O(H11′) distance (2.82(4) Å) is short for normal O···Cl distances but the error involved is large. Similar Cl···O contacts have been seen previously ranging between 2.68 Å and 2.90(2) Å [35–37].

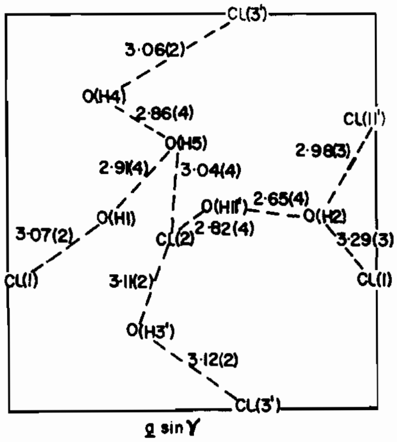

Fig. 4. A schematic diagram of part of the hydrogen bonding network between lattice water molecules and chloride ions in $[cis\text{-}Pt(NH_3)_2(9\text{-}Et\text{-}G)_2]Cl_2\cdot 3H_2O$.

In complex **II**, the chain along the *b* axis consists of two disordered anions: a chloride ion near ½, ½, ½ and a bicarbonate ion near ½, 0, ½. There is a strong interaction between Cl(2) and O(3) of the bicarbonate ion (3.00(2) Å) presumably caused by a hydrogen bond. O(H1) is disordered, as it was in complex **I**, because of contact with O(H2), but Cl(1) is not.

Since we have no analytical evidence for the bicarbonate ion and since the geometry is not particularly good, we considered the possibility of other anions such as nitrate or acetate, even though neither of these anions had been used in the preparation of complex **II**. The acetate group can be ruled out from ^1H NMR studies; no CH_3 resonance consistent with an acetate ion, was observed. The nitrate ion was discarded because it gave no advantage over the bicarbonate ion; the geometric anomalies would apply to it as well. We finally chose the bicarbonate because the unexpected incorporation of bicarbonate ions into a crystal from water and carbon dioxide in the air is well established [38, 40] and an anomalous geometry has been observed previously [38].

Comparison of the ^{1}H NMR spectra (Me_2SO-d_6) of the *cis*-diamminebis(9-ethylguanine)platinum(II) dichloride described here with the related, though structurally undetermined perchlorate salt [17, 41], reveals substantial differences in chemical shifts: guanine and NH_3 shifts of the chloride salt in general occur downfield from those of the perchlorate salt. At a concentration of Pt = 0.1 *M*, for example, shift differences are *ca.* 0.22 ppm for N(1)H, 0.11 ppm for H(8), 0.35 ppm for NH_2, and 0.26 ppm for NH_3, whereas CH_2 and CH_3 of the ethyl groups are unaffected. With no other cations than $[(NH_3)_2Pt(9\text{-}EtG)_2]^{2+}$ present, the observed differences must be attributed to anion effects, specifically to hydrogen bonding interactions between Cl^- and the respective protons. Marzilli *et al.* in earlier reports [42, 43] demonstrated that chloride and bromide, unlike nitrate and perchlorate, interact with guanosine through hydrogen bond formation in Me_2SO solution. Taking the fact into consideration that NH_2 and NH_3 signals correspond to two and six protons, respectively, the order of Cl···H interactions in Me_2SO is $NH_3 \gg NH_2 > N(1)H > H(18)$.

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