Mono- and bis(9-ethylguanine) complexes of *trans*-$(CH_3NH_2)_2Pt^{II}$. X-ray structure of the 2:1 complex and redistribution of the 1:1 compound

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Abstract

trans-$[(CH_2NH_2)_2Pt(9\text{-EtGH})Cl]Cl$ (**1**) and *trans*-$[(CH_3NH_2)_2Pt(9\text{-EtGH})_2]Cl_2$ (**2**) with 9-EtGH = 9-ethylguanine have been prepared and studied. Pt binding in both compounds is through N7, as evident from ^{195}Pt–$^1H(8)$ coupling (**1**) and X-ray crystallography (**2**), respectively. The X-ray structure of **2** shows the cation to be centrosymmetric, with the two methylamine ligands disordered over two positions. In Me_2SO-d_6, the cation of **2** forms Watson–Crick hydrogen bonds with added 1-methylcytosine (1-MeC), as shown by concentration-dependent ^1H NMR spectroscopy. The solution behaviour (water) of **1** is remarkable in that it undergoes a partial redistribution according to $2(\mathbf{1}) \rightarrow (\mathbf{2}) + trans\text{-}(CH_3NH_2)_2PtCl_2$ in addition to N7,N1-bridge formation. If realized with DNA, this reaction could facilitate a migration of a monofunctionally bound *trans*-diamineplatinum(II) entity along DNA or its removal from DNA.

Introduction

Monofunctional adducts with coordination to guanine-N7 are the preferred first steps of both *cis* and *trans*-$(NH_3)_2PtCl_2$ reactions with DNA [1]. As a consequence of the inherent geometrical differences between the two isomers, the bis(nucleobase) adducts are different: While the *cis*-isomer forms 1.2 cross-links preferentially [1, 2], the *trans*-isomer forms 1.3 [3] and 1.4 adducts [4]**. The high affinity of *cis*-$(NH_3)_2Pt^{II}$ for adjacent guanines appears not to be retained in the case of the *trans*-isomer [5], as also demonstrated by the facile 1.3 → 1.4 cross-link switch [4].

As part of a systematic study on model nucleobase complexes of *cis*- and *trans*-diamineplatinum(II) species as well as monofunctional triamineplatinum(II) and various Pt(IV) compounds [6], we are also interested in intrinsic differences in the chemistry of the two diamineplatinum(II) isomers which, apart from steric aspects of DNA distortion, might possibly be relevant to biology as well. We have recently come across several differences in structure and reactivity patterns which, biologically relevant or not, are of interest from a purely chemical point of view. They include, for example (i) differences in the binding patterns of heteronuclear complexes derived from the bis(pyrimidine nucleobase) Pt^{II} compounds [7], (ii) the displacement of a nucleobase (1-methylcytosine, 1-MeC) from *trans*-$[(NH_3)_2Pt(1\text{-MeC})Cl]^+$ [8], or (iii) the basic differences in geometry of bis(nucleobase) complexes [9].

In continuation of this work we herewith report on mono- and bis-9-ethylguanine complexes of *trans*-$(CH_3NH_2)Pt^{II}$. Solution studies of *trans*-diammineplatinum(II) interactions with guanine nucleobases have been published before [10, 11], and there is a report on the X-ray structure of a tetrakis(9-methylguanine) complex of Pt(II) which contains two mutually *trans*-bis(guanine) entities [12].

Experimental

Preparation

trans-$(CH_3NH_2)_2PtCl_2$ [13] and 1-methylcytosine (1-MeC) [14] were prepared as previously described. 9-Ethylguanine (9-EtGH) was purchased from Chemogen (Konstanz, Germany). *trans*-$[(NH_2CH_3)_2Pt(9\text{-EtGH})Cl]Cl$ (**1**) and *trans*-$[(NH_2CH_3)_2Pt(9\text{-EtGH})_2]Cl_2$ (**2**) were prepared as follows. *trans*-$(NH_2CH_3)_2PtCl_2$ (2 mmol) and NaCl (6 mmol) were dissolved in water (400 ml, 40 °C) and 9-EtGH (2 mmol), dissolved in water (100 ml), was slowly added over a period of 2 h. After 72 h at 40 °C, the solution was concentrated

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**1.3 and 1.4 cross-links have 1 and 2 intervening bases, respectively.

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and passed over a cation exchange column. On elution with 0.1 molar NaCl solution, compound **1** was obtained, and **2** eluted with 0.2 molar NaCl solution. The solutions were concentrated to small volumes and then allowed to evaporate at 22 °C in air. **1** was isolated as thin, colourless needles, while **2** crystallized as monoclinic, colourless crystals. Yields were 24% (**1**) and 12% (**2**). *Anal.* Calc. for $C_9H_{19}N_7OCl_2Pt$ (**1**): C, 21.3; H, 3.8; N, 19.3. Found: C, 21.5; H, 4.1; N, 19.1%. Calc. for $C_{16}H_{28}N_{12}O_2Cl_2Pt$ (**2**): C, 28.0; H, 4.1; N, 24.5. Found: C, 27.9; H, 4.0; N, 24.6%. The ClO_4-salt analogue of **2**, **2a**, was obtained as a microcrystalline material in 95% yield on addition of $LiClO_4$ to a solution of **2**. Elemental analysis data for C, H, N and Cl were consistent with the formulation $[(NH_2CH_3)_2Pt(9\text{-}EtGH)_2](ClO_4)_2$ (**2a**).

trans-$[(NH_2CH_3)_2Pt(9\text{-}EtGH)_2](ClO_4)_2 \cdot 2(1\text{-}MeC)$ (**3**) was obtained as a microcrystalline material in 90% yield upon addition of 1-MeC (2 equiv.) to an aqueous solution of **2a** at 25 °C. *Anal.* Calc. for $C_{26}H_{42}N_{18}O_{12}Cl_2Pt$ (**3**): C, 29.3; H, 4.0; N, 23.7. Found: C, 29.4; H, 3.5; N, 23.6%.

TABLE 1. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2 \times 10^4$)[a]

	x	*y*	*z*	U_{eq}
Pt(1)	0.25	0.25	0.0	484
Cl(1)	0.2180(2)	0.12056(9)	0.5829(4)	627
N(5)	0.351(1)	0.2799(5)	0.232(2)	337
C(51)	0.453(1)	0.3099(7)	0.226(3)	528
N(5″)	0.210(1)	0.2368(5)	−0.276(2)	387
C(51″)	0.293(3)	0.2552(8)	−0.367(5)	894
N(1)	−0.0460(6)	0.3697(2)	0.0182(9)	423
C(2)	−0.0214(7)	0.4199(3)	0.009(1)	379
N(2)	−0.0952(6)	0.4517(3)	0.038(1)	575
N(3)	0.0660(5)	0.4358(2)	−0.028(1)	378
C(4)	0.1334(6)	0.3977(3)	−0.047(1)	382
C(5)	0.1178(6)	0.3476(3)	−0.034(1)	376
C(6)	0.0211(7)	0.3300(3)	−0.002(1)	383
O(6)	−0.0101(5)	0.2866(2)	0.008(1)	589
N(7)	0.2055(6)	0.3221(3)	−0.062(1)	507
C(8)	0.2688(8)	0.3569(4)	−0.093(2)	691
N(9)	0.2273(6)	0.4031(3)	−0.091(1)	574
C(91)	0.2843(9)	0.4508(4)	−0.108(2)	756
C(92)	0.361(2)	0.4660(7)	0.055(2)	1282

The positions N(5), C(51), N(5″), C(51″) belong to disordered positions (occupancy 0.5). [a] $U_{eq} = (1/3\ \Sigma_i \Sigma_j U_{ij} a^*_i a^*_j \mathbf{a}_i \cdot \mathbf{a}_j$.

Instruments

^1H NMR spectra were recorded on Bruker AC 200 and AM 300 spectrometers in D_2O (TSP as internal reference) and $Me_2SO\text{-}d_6$ (TMS as internal reference). pD values of D_2O solutions were obtained by using a glass electrode and adding 0.4 to the pH meter reading. IR spectra (KBr pellets) were measured on Perkin-Elmer 580B and Bruker IFS 113v spectrometers.

X-ray analysis

The crystal structure of *trans*-$[(NH_2CH_3)_2Pt(9\text{-}EtGH)_2]Cl_2$ (**2**) was determined on a Nicolet R 3m/V diffractometer with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). Crystallographic data are as follows: $C_{16}H_{28}N_{12}O_2Cl_2Pt$, $M_r = 686.47$, monoclinic system, space group $C2/c$, $a = 12.786(5)$, $b = 26.648(8)$, $c = 7.773(3)$ Å, $\beta = 107.78(3)°$, $V = 2522(2)$ Å^3, $Z = 4$, $D_{calc} = 1.808$ (g cm^{-1}), $F(000) = 1344$, $\mu = 5.87$ mm^{-1}, $T = 291(1)$ K, final $R = 0.044$ for 1829 unique observed ($F > 4.0\sigma(F)$) diffractometer data. The correctness of the space group was checked by using MISSYM [15].

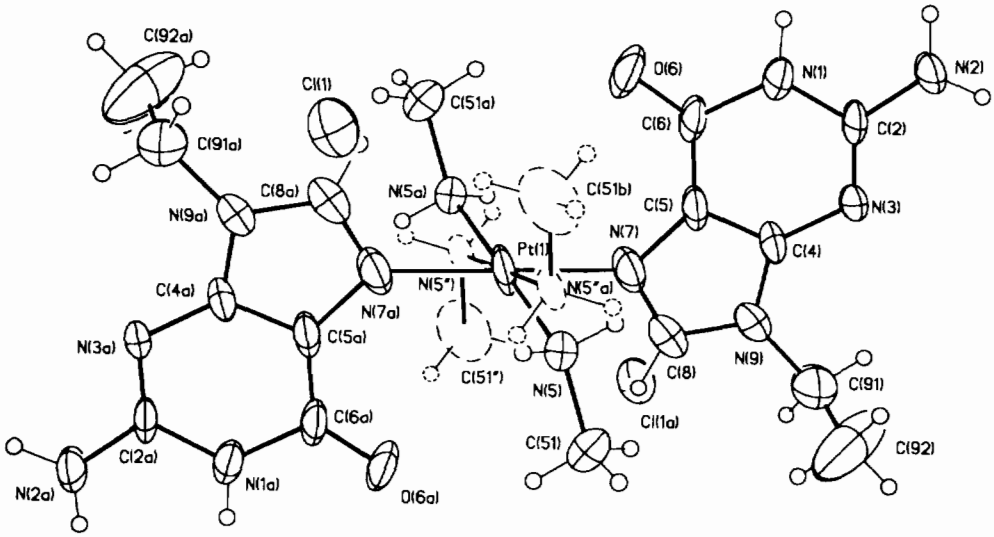


Fig. 1. View (SHELXTL Plus) of *trans*-$[(CH_3NH_2)_2Pt(9\text{-}EtGH)_2]Cl_2$ (**2**) with atom numbering scheme. Anisotropic ellipsoids represent 50% probability boundaries. H atoms are represented as spheres of arbitrary radii. The CH_3NH_2 groups are disordered (occupancy factor 0.5).

TABLE 2. Selected bond distances (Å) and bond angles (°) in **2**

Pt(1)–N(5)	2.03(1)[a]
Pt(1)–N(5″)	2.08(2)[a]
Pt(1)–N(7)	2.020(7)
N(5)–C(51)	1.54(2)[a]
N(5″)–C(51″)	1.53(4)[a]
N(1)–C(2)	1.380(9)
N(1)–C(6)	1.40(1)
C(2)–N(2)	1.34(1)
C(2)–N(3)	1.31(1)
N(3)–C(4)	1.37(1)
C(4)–C(5)	1.36(1)
C(4)–N(9)	1.35(1)
C(5)–C(6)	1.42(1)
C(5)–N(7)	1.38(1)
C(6)–O(6)	1.232(9)
N(7)–C(8)	1.30(1)
C(8)–N(9)	1.34(1)
N(9)–C(91)	1.49(1)
C(91)–C(92)	1.40(2)
N(5″)–Pt(1)–N(7)	87.3(5)[a]
N(5)–Pt(1)–N(7)	83.9(4)[a]
Pt(1)–N(5)–C(51)	119(1)[a]
Pt(1)–N(5″)–C(51″)	116(1)[a]
C(2)–N(1)–C(6)	124.8(7)
N(1)–C(2)–N(3)	123.3(7)
N(1)–C(2)–N(2)	115.1(7)
N(2)–C(2)–N(3)	121.6(7)
C(2)–N(3)–C(4)	113.1(6)
N(3)–C(4)–N(9)	125.9(7)
N(3)–C(4)–C(5)	127.6(8)
C(5)–C(4)–N(9)	106.5(7)
C(4)–C(5)–N(7)	109.1(7)
C(4)–C(5)–C(6)	119.6(7)
C(6)–C(5)–N(7)	131.3(7)
N(1)–C(6)–C(5)	111.6(6)
C(5)–C(6)–O(6)	129.5(8)
N(1)–C(6)–O(6)	118.9(8)
Pt(1)–N(7)–C(5)	127.8(6)
C(5)–N(7)–C(8)	105.0(8)
Pt(1)–N(7)–C(8)	125.2(7)
N(7)–C(8)–N(9)	112.4(9)
C(4)–N(9)–C(8)	106.9(8)
C(8)–N(9)–C(91)	125.1(9)
C(4)–N(9)–C(91)	127.4(8)
N(9)–C(91)–C(92)	113(1)

[a]Bond distances and bond angles belong to disordered positions.

The largest peaks in the final $\Delta\rho$ map were $\pm 2.1(2)$ e Å^{-3}. Atomic scattering factors for neutral atoms and real and imaginary dispersion terms were taken from the International Tables for X-ray Crystallography [16]. The programs used were PARST [17], SHELXTL PLUS [18], SADIAN [19], MISSYM [15] and SCHAKAL [20]. Positional parameters and the equivalent values of the anisotropic displacement parameters for the non-H atoms are given in Table 1. See also 'Supplementary material'.

Results and discussion

Characterization of trans-[(ma)$_2$Pt(9-EtGH)Cl]Cl and trans-[(ma)$_2$Pt(9-EtGH)$_2$]Cl$_2$

trans-[(ma)$_2$Pt(9-EtGH)Cl]Cl (**1**) and *trans*-[(ma)$_2$-Pt(9-EtGH)$_2$]Cl$_2$ (**2**) were prepared by reaction of *trans*-(ma)$_2$PtCl$_2$ and 9-EtGH in water, and isolated after chromatographic separation and crystallization. Both compounds were isolated in crystalline form, but only crystals of **2** proved suitable for X-ray analysis. Composition of **1** was straightforward on the basis of elemental analysis and its IR spectrum with ν(Pt–Cl) at 347 cm^{-1}. As with the analogous NH_3 compounds, H8 of the guanine ring occurs for **1** upfield (8.50 ppm, pD 6.8) from that of **2** (8.64 ppm, pD 3–7) in the ^{1}H NMR spectrum [21]. The methylamine resonances display the behaviour previously observed for *trans*-[(CH$_3$NH$_2$)$_2$Pt(1-MeC)Cl]$^+$, namely triplet structure immediately after dissolving in water and simplification to a singlet with $^3J(^{195}\text{Pt}-^1\text{H})$ of 37.1 (**1**) and 35.2 (**2**) Hz after some time [22]. Prior to completion of isotopic exchange, the NH_2 resonances of the amine ligands are observed around 4.3–4.5 ppm as broad signals.

Figure 1 gives a view of *trans*-[(CH$_3$NH$_2$)$_2$Pt(9-EtGH)$_2$]Cl$_2$ (**2**) and Table 2 lists interatomic distances and angles of **2**. Pt is on a center of symmetry and therefore the two guanines, which are coordinated through N7, are oriented head-to-tail. Unlike the respectively *trans*-positioned guanines in [Pt(9-MeGH-*N*7)$_4$]$^{2+}$ [12], which are propeller-twisted, the guanines in **2** are coplanar. The two methylamine groups at Pt are disordered over two positions, with occupancy factors of 0.5 each. Superficially, **2** can be considered a metal analogue of a hemiprotonated guanine [23], in which a single proton resides between the N7 positions of two guanine rings. The N7....N7a distance (4.04 Å in **2**) is longer than in the case of (GH$_2$)$^+$(GH) (2.637(3) Å), of course. There are no unusual structural features with the two guanine rings when compared with guanine complexes of other Pt amine complexes [24]. The two halves of the purine ring form a slight angle of 2.1(3)°. The dihedral angle of each nucleobase with the Pt coordination plane is 75.7(3)°. Pt is not coplanar with guanine but rather deviates substantially ($-0.492(1)$ Å) from the best plane. This value compares with a maximum of 0.36 Å from six guanine rings in three crystal structure analyses of compounds of *cis*-[(NH$_3$)$_2$Pt(9-EtGH)$_2$]$^{2+}$ [24b]. Deviations of the exocyclic atoms of the guanines are not unusual and are as follows: O6, 0.070(7); N2, $-0.064(9)$; C91, $-0.014(14)$; C92, $-1.324(16)$ Å.

A stereo view of the unit cell of **2** is given in Fig. 2. The cations are oriented in such a way, that the guanine planes are aligned roughly along the *z* axis. There are several, albeit not unusual intermolecular H

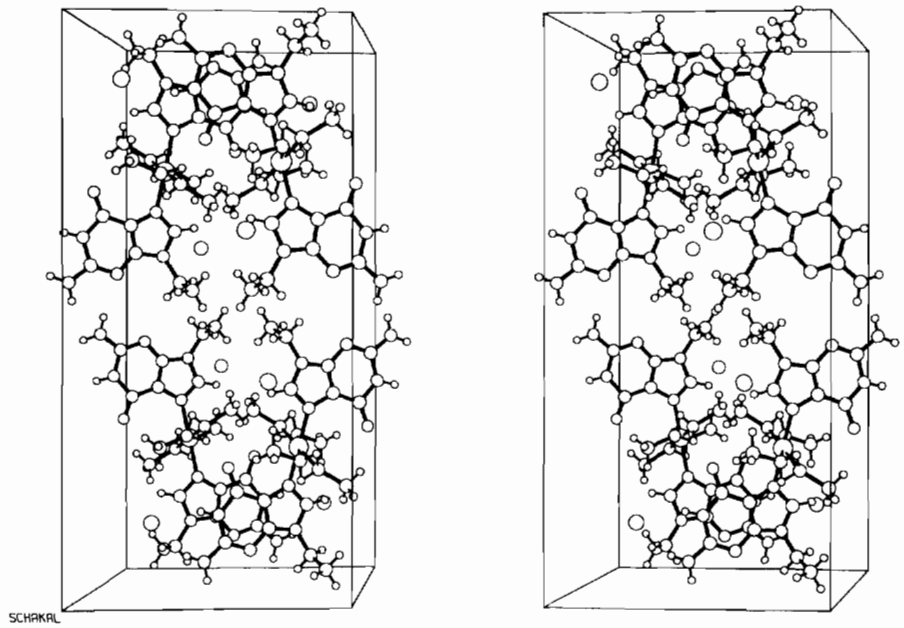


Fig. 2. Packing diagram (SCHAKAL) of **2**. Both possible orientations of the methylamine ligands are shown.

bonds (2.93(1)–3.27(1) Å), that can be classified according to the sites involved: (i) between $N(5)H_2$ and O6, (ii) simultaneous H bonding of Cl^- to both N(1)H and $N(2)H_2$, (iii) between $N(5)H_2$ and Cl^-, and (iv) between N(2) and N(3). See also 'Supplementary material'.

Solution behaviour of 1

According to ^1H NMR spectroscopy, **1** is unstable in aqueous solution (pD 6.8), as evident from the appearance of both new 9-ethylguanine and methylamine resonances and the simultaneous drop in pD by *c.* 4 log units. Immediately after dissolving **1** in D_2O, a single guanine H8 resonance (8.50 ppm) with ill-resolved ^{195}Pt satellites ($^3J \approx 27$ Hz) is observed. With time (7 days, 40 °C, pD dropped from 6.8 to 3.6), at least three additional guanine-H8 resonances (8.63, 8.53, 8.38 ppm) are detected. Within 2 more weeks (40 °C, pD 3.2 then), a number of additional resonances appear which, due to their low intensities, will not be further discussed, however. Nevertheless, their formation is confirmed by the simultaneous appearance of an array of new CH_3ND_2 resonances (Fig. 3). Of the three more intense, new guanine H8 resonance, the one furthest downfield (8.63 ppm) can be assigned to the bis(9-ethylguanine) complex *trans*-$[(CH_3NH_2)_2(9\text{-EtGH-}N7)_2]^{2+}$ (**2**).

Like **1**, the aqua species of **1**, *trans*-$[(CH_3NH_2)_2Pt(9\text{-EtGH-}N7)(D_2O)]^{2+}$, obtained upon treatment with 2 equiv. of $AgNO_3$ and filtration of AgCl, undergoes changes in D_2O, albeit at a faster rate. Within 24 h at 22 °C (Fig. 4), new guanine H8 resonances are detected around 8.52 and 8.38 ppm, and the pD has dramatically dropped to 2. A major difference to **1** is the absence of the 8.63 ppm resonance.

The observed drop in pD in both systems indicates reactions that involve liberation of H^+. At least three possible ways can be anticipated:

(i) μ-OH complex formation according to

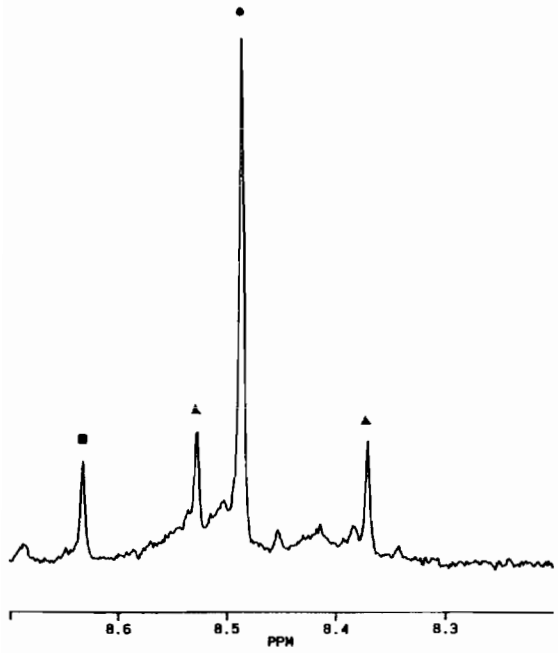
$$2[a_2(\text{GH-}N7)Pt(H_2O)]^{2+} \rightleftharpoons [a_2(\text{GH-}N7)Pt(OH)Pt(\text{GH-}N7)a_2]^{3+} + H_3O^+$$

(ii) N7,N1 bridge formation according to

$$2[a_2(\text{GH-}N7)Pt(H_2O)]^{2+} \rightleftharpoons [a_2(\text{GH-}N7)Pt(\text{G-}N1,N7)Pta_2(H_2O)]^{3+} + H_3O^+$$

(iii) a combination of (i) and (ii) with (at least) tetranuclear species formed, containing both μ-OH and μ-(9-EtG-*N1,N7*) bridges.

Since (i) is not expected to lead to two distinctly different guanine H8 resonances (even if hindered rotation about the Pt–OH–Pt bonds is assumed), only (ii) and (iii) are realistic models to account for the observed features. In either case it is believed that two different 9-ethylguanine entities (9-EtGH-*N7* at lower field, 9-EtG-*N1,N7* at higher field) are present and responsible for the major newly formed species. Hindered rotation about the Pt–N1(guanine) bond could be responsible for a doubling of resonances. This interpretation is supported by findings in the *cis*-$(NH_3)_2Pt$/guanine system [25–27] and in addition by the fact that the H8 resonance attributed to G-*N1,N7* is pH independent in its chemical shift, unlike H8 of the GH-*N7* ligand.



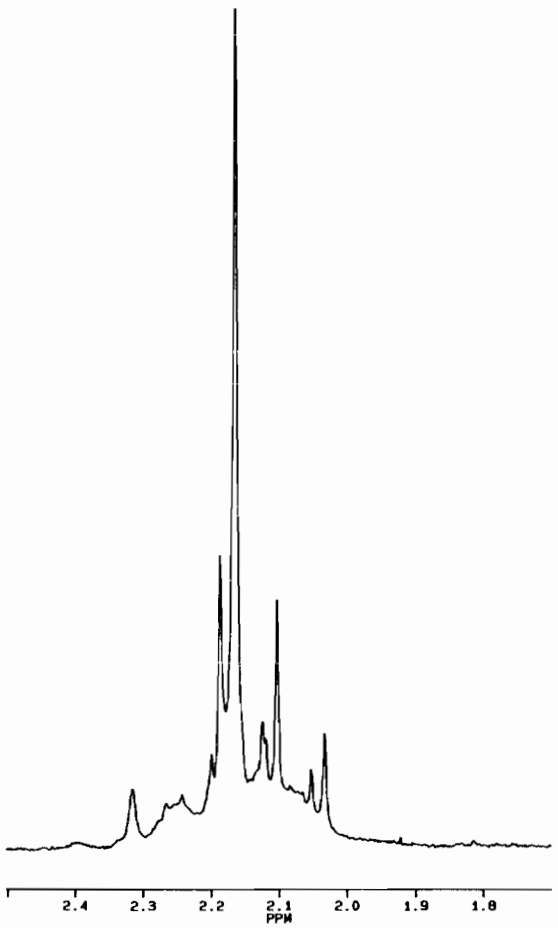


Fig. 3. Sections (guanine-H8 and CH_3ND_2) of ^1H NMR spectrum of an aged sample of **1** in D_2O (3 weeks at 22 °C, pD dropped from originally 6.8 to 3.2). The more intense guanine-H8 signals are assigned as follows: ●, **1**; ■, *trans*-$[a_2Pt(9\text{-EtGH-}N7)_2]^{2+}$; ▲, *trans*-$[a_2(9\text{-EtGH-}N7)Pt(9\text{-EtG-}N1,N7)Pta_2(X)]^{n+}$ ($X=Cl^-, n=2$; $X=H_2O$, $n=3$).

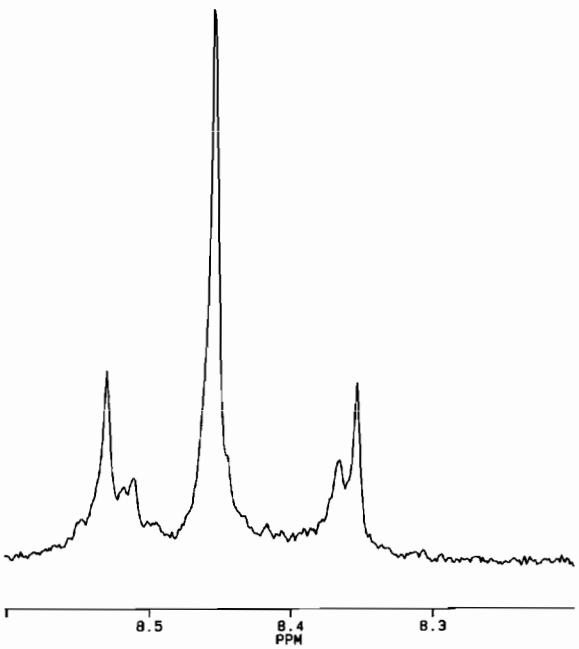


Fig. 4. Section (guanine-H8) of ^1H NMR spectrum of an aged solution of *trans*-$[(CH_3NH_2)_2Pt(9\text{-EtGH-}N7)(D_2O)]^{2+}$ (1 day at 22 °C, pD dropped to 2.0).

Formation of **2** from **1** deserves some further comment. Since this reaction is observed only with the Cl complex **1**, yet not with its aqua derivative, we conclude that it is a consequence of the *trans*-effect of Cl^-, which removes neutral 9-ethylguanine from **1** and, in a parallel reaction, leads to **2**.

$$trans\text{-}[a_2Pt(GH)Cl]Cl \xrightarrow{slow} trans\text{-}a_2PtCl_2 + GH$$

$$trans\text{-}[a_2Pt(GH)X]^{n+} + GH \xrightarrow{fast} trans\text{-}[a_2Pt(GH)_2]^{2+} + X^{-2+n}$$

$X=Cl$, $n=1$; $X=H_2O$, $n=2$

The overall redistribution reaction is then

$$2trans\text{-}[a_2Pt(GH)Cl]Cl \longrightarrow trans\text{-}a_2PtCl_2 + trans\text{-}[a_2Pt(GH)_2]Cl_2$$

This interpretation gets support from similar findings with *trans*-$[a_2Pt(1\text{-MeC})Cl]Cl$ [8] and from a mass spectroscopic study, in which guanine *trans* to Cl^- has been found to be displaced [28].

Hydrogen bonding of 2a with 1-MeC

Mixing of aqueous solution of **2a** and 1-methylcytosine (1-MeC) resulted in precipitation of a compound that analyzed as *trans*-$[(CH_3NH_2)_2Pt(9\text{-EtGH})_2](ClO_4)_2 \cdot 2(1\text{-MeC})$ (**3**). A comparison of the IR spectra of isolated **3** and an admixture of **2a** and two equivalents of 1-MeC showed clear differences, which were particularly evident in the 3400–2800 and 1700–1600 cm^{-1} ranges.

Following arguments outlined elsewhere [29], it was tentatively concluded, that **2a** and 1-MeC form hydrogen bonds, most likely according to Watson–Crick. This assumption was supported by ^{1}H NMR spectra (Me_2SO-d_6) of *trans*-$[(CH_3NH_2)_2Pt(9\text{-EtGH})_2]$ $(ClO_4)_2$ (**2a**) in the presence of 1-MeC. Two sets of experiments were carried out. (i) A mixture of **2a** (0.15 M l^{-1}) and 1-MeC (0.30 M l^{-1}) in Me_2SO-d_6 was successively diluted to lower concentrations and the chemical shifts of all protons were compared to resonances at identical concentrations, in the absence of the respective partner. $\Delta\delta$ values of guanine-N(1)H, guanine-N(2)H_2 and cytosine-N(4)H_2 followed the pattern characteristic of Watson–Crick base pairing [30], with guanine-N(1)H shifted approximately twice as much as the NH_2 resonances of guanine and cytosine. Absolute shifts of these resonances (*c.* 0.8 ppm for N(1)H, *c.* 0.4 ppm for both NH_2 resonances at the highest concentration applied) are smaller than those observed in *cis*-$(NH_3)_2Pt^{II}$ complexes of 9-EtGH [31], but this is probably a consequence of the differences in stacking effects of nucleobases in the two isomers of bis(nucleobase) compounds. (ii) To a sample of **2a** (0.15 M l^{-1}) in Me_2SO-d_6 was added increasing amounts of 1-MeC, and the shifts of all resonances recorded. Again, guanine N(1)H and guanine N(2)H_2 resonances displayed strong downfield shifts on addition of increasing amounts of 1-MeC, with that of guanine-N(1)H being almost twice as large as that of guanine-N(2)H_2. Other resonances of the guanine compound **2a** were affected only slightly.

Considering this data, and also results from crystal structure determinations of a Pt^{IV} [32] as well as Pt^{II} complex of N9-substituted guanines with cocrystallized cytosine [9], it is indeed reasonable to interpret the IR spectra of **3** in terms of H bonding between N7 platinated guanine and free cytosine according to the Watson–Crick manner.

Conclusions

The X-ray structure determination of *trans*-$[(CH_3NH_2)_2Pt(9\text{-EtGH-}N7)_2]Cl_2$ (**2**) shows no unusual features. Hydrogen bonding with 1-methylcytosine is retained in Me_2SO solution. The precursor of **2**, *trans*-$[(CH_3NH_2)_2Pt(9\text{-EtGH-}N7)Cl]^+$ (**1**), rearranges in aqueous solution to give both **2** and free *trans*-$(CH_3NH_2)_2PtCl_2$. Possible biological consequences are the same as for the corresponding 1-MeC complex [8], namely ease of migration along DNA or ease of removal from DNA, but more relevant in the present case, considering the preferential monofunctional binding of *trans*-$(NH_3)_2PtCl_2$ to N7 of guanine in DNA. In a parallel reaction, **1** undergoes condensation reactions to 9-ethylguaninato (9-EtG) species with Pt binding to both N7 and N1. In this respect **1** behaves similar to *cis*-$[(NH_3)_2Pt(9\text{-EtGH-}N7)H_2O]^{2+}$.

Supplementary material

Positional parameters and anisotropic temperature factors of **2**, short contacts, a listing of observed and calculated structure factors and experimental details of the structure determination can be obtained from the Fachinformationszentrum Karlsruhe, D-7514 Eggenstein-Leopoldhafen 2 under CSD 56313 on request. Requests should be accompanied by the complete literature citation.

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References

1 (a) A. M. J. Fichtinger-Schepman, J. L. van der Veer, J. H. J. den Hartog, P. H. M. Lohman and J. Reedijk, *Biochemistry, 24* (1985) 707; (b) R. B. Ciccarelli, M. J. Solomon, A. Vashavsky and S. J. Lippard, *Biochemistry, 24* (1985) 7533; (c) J.-L. Butour and N. P. Johnson, *Biochemistry, 25* (1986) 4534; (d) A. Eastman, *Pharmacol. Ther., 34* (1987) 155. (e) D. P. Bancroft, C. A. Lepre and S. J. Lippard, *J. Am. Chem. Soc., 112* (1990) 6860.
2 (a) S. E. Sherman and S. J. Lippard, *Chem. Rev., 87* (1987) 1153; (b) J. Reedijk, A. M. J. Fichtinger-Schepman, A. T. van Oosterom and P. van de Putte, *Struct. Bonding (Berlin), 67* (1987) 53.
3 (a) C. A. Lepre, L. Chassot, C. E. Costello and S. J. Lippard, *Biochemistry, 29* (1990) 811; (b) D. Gibson and S. J. Lippard, *Inorg. Chem., 26* (1987) 2275.
4 K. M. Comess, C. E. Costello and S. J. Lippard, *Biochemistry, 29* (1990) 2102.
5 (a) A. Eastman, M. M. Jennerwein and D. L. Nagel, *Chem.-Biol. Interact., 67* (1988) 71; (b) A. L. Pinto and S. J. Lippard, *Proc. Natl. Acad. Sci. U.S.A., 82* (1985) 4616.
6 B. Lippert, *Prog. Inorg. Chem., 37* (1989) 1.
7 M. Krumm, B. Lippert, L. Randaccio and E. Zangrando, *J. Am. Chem. Soc., 113* (1991) 5129.
8 O. Krizanovic, F. J. Pesch and B. Lippert, *Inorg. Chim. Acta, 165* (1989) 145.
9 I. Dieter-Wurm, M. Sabat and B. Lippert, *J. Am. Chem. Soc., 114* (1992) 357.
10 G. Y. H. Chu, S. Mansy, R. E. Duncan and R. S. Tobias, *J. Am. Chem. Soc., 100* (1978) 593.
11 A. T. M. Marcelis, C. G. van Kralingen and J. Reedijk, *J. Inorg. Biochem., 13* (1980) 213.
12 H.-J. Korte and R. Bau, *Inorg. Chim. Acta, 79* (1983) 251.
13 J. Arpalahti, B. Lippert, H. Schlöllhorn and U. Thewalt, *Inorg. Chim. Acta, 153* (1988) 45.

14 T. J. Kistenmacher, M. Rossi, J. P. Caradonna and L. G. Marzilli, *Adv. Mol. Relaxation Interact. Processes, 15* (1979) 119.
15 Y. Le Page, *J. Appl. Crystallogr., 20* (1987) 264.
16 *International Tables for X-ray Crystallography* Vol. IV, Kynoch, Birmingham, UK, 1974.
17 M. Nardelli, *Comput. Chem., 7* (1983) 95.
18 G. M. Sheldrick, *SHELXTL PLUS* (Release 3.4), for Nicolet R3m/V crystallographic systems, University of Göttingen, Göttingen, Germany, 1987.
19 W. H. Baur and G. Wenninger, *SADIAN*, program for calculation of atomic distances and angles in crystal structures, University of Illinois, Chicago, IL, 1969.
20 E. Keller, *SCHAKAL*, a Fortran program for the graphic representation of molecular and crystallographic models, University of Freiburg, Freiburg, Germany, 1986.
21 G. Raudaschl and B. Lippert, *Inorg. Chim. Acta, 80* (1983) L49.
22 F. J. Pesch, H. Preut and B. Lippert, *Inorg. Chim. Acta, 169* (1990) 195.
23 G. S. Mandel and R. E. Marsh, *Acta Crystallogr., Sect. B, 31* (1975) 2862.
24 (a) B. Lippert, G. Raudaschl-Siebert, C. J. L. Lock and P. Pilon, *Inorg. Chim. Acta, 93* (1984) 43; (b) H. Schöllhorn, G. Raudaschl-Sieber, G. Müller, U. Thewalt and B. Lippert, *J. Am. Chem. Soc., 107* (1985) 5932; (c) L. Sindellari, H. Schöllhorn, U. Thewalt, G. Raudaschl-Sieber and B. Lippert, *Inorg. Chim. Acta, 168* (1990) 27.
25 G. Raudaschl-Sieber, L. G. Marzilli, B. Lippert and K. Shinozuka, *Inorg. Chem., 24* (1985) 989.
26 J. L. van der Veer, H. van den Elst and J. Reedijk, *Inorg. Chem., 26* (1987) 1536.
27 G. Frommer, I. Mutikainen, F. J. Pesch, E. C. Hillgeris, H. Preut and B. Lippert, *Inorg. Chem., 31* (1992) 2429.
28 I. A. G. Roos, A. J. Thomson and J. Eagles, *Chem.-Biol. Interact., 8* (1974) 421.
29 Y. Kyogoku, S. Higuchi and M. Tsuboi, *Spectrochim. Acta, Part A, 23* (1967) 969.
30 (a) R. R. Shoup, H. T. Miles and E. D. Becker, *Biochem. Biophys. Res. Commun., 23* (1966) 194; (b) R. A. Newmark and C. R. Cantor, *J. Am. Chem. Soc., 90* (1968) 5010.
31 B. Lippert, *J. Am. Chem. Soc., 103* (1981) 5691.
32 H.-K. Choi, S. K. S. Huang and R. Bau, *Biochem. Biophys. Res. Commun., 156* (1988) 1125.