Complete displacement of N,O bound amino acids (amacH) in *cis*-$[(NH_3)_2Pt(amac)]NO_3$ chelates by 9-methylguanine (9-MeGH) and 9-methyladenine (9-MeA). The crystal structure of *cis*-$[(NH_3)_2Pt(9\text{-}MeA\text{-}N^7)_2](NO_3)_2 \cdot 1.5H_2O$

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(Received February 13, 1990)

Abstract

The reactions of the complexes *cis*-$[(NH_3)_2Pt(amac)]NO_3$, where amac are glycine (gly), L-alanine (L-ala) and 2-aminobutyric acid (2-aba), chelated to Pt(II), with 9-methylguanine (9-MeGH) and 9-methyladenine (9-MeA) were studied in neutral and acidic aqueous solutions. Complete displacement of the amino acids resulted in the formation of the compounds *cis*-$[(NH_3)_2Pt(9\text{-}MeGH)_2](NO_3)_2$ in neutral and *cis*-$[(NH_3)_2Pt(9\text{-}MeA)_2](NO_3)_2$ in strongly acidic media. The latter compound contained two 9-MeA molecules, both coordinated through N(7). Its crystal structure was solved with X-ray diffraction techniques. Crystal data: space group $C2/c$, $a = 18.506(2)$, $b = 15.770(2)$, $c = 16.422(2)$ Å, $\beta = 108.38(2)°$, $V = 4548(2)$ Å^3, $Z = 8$, $R = 0.022$ for 4447 independent reflections. The results are compared with other analogous *cis*-$[(NH_3)_2Pt(\text{purine derivative})_2]^{2+}$ structures and discussed in terms of a possible cross-link between two N(7) sites of adjacent adenines in DNA.

Introduction

In an attempt to prepare and study ternary complexes of *cis*-$(NH_3)_2Pt(II)$ with amino acids and nucleobases, we have prepared the N,O amino acid chelates of the type *cis*-$[(NH_3)_2Pt(amac)]NO_3$ [1]** and allowed them to react with purine and pyrimidine nucleobases. In most cases the desired *cis*-$[(NH_3)_2Pt(amac)(nucleobase)]NO_3$ products, with the amino acids coordinated through their NH_2 groups only, were isolated [2, 3]. However, a number of byproducts, including the 1:2 complexes of the type *cis*-$(NH_3)_2Pt(nucleobase)_2](NO_3)_2$ were also formed during these reactions. Thus, a complete displacement of the N,O bound amino acid has taken place in these cases.

In that way and under the experimental conditions described below, the compounds *cis*-$[(NH_3)_2Pt(9\text{-}MeGH)_2](NO_3)_2$ and *cis*-$[(NH_3)_2Pt(9\text{-}MeA)_2](NO_3)_2$ were isolated and characterized. Both the 9-MeGH and 9-MeA ligands are coordinated through their N(7) atoms to *cis*-$(NH_3)_2Pt(II)$.

The structures of many compounds of composition *cis*-$[(NH_3)_2Pt(6\text{-oxopurine})_2]^{2+}$ with Pt coordination via N(7) are known [4–9]. On the other hand, no structures of analogous adenine derivatives have been reported as yet, although such compounds have been prepared [10, 11]. Moreover, there is a very detailed NMR solution study on $L_2Pt(5'\text{-AMP-}N^7)_2$ compounds available [12] and with the related 3-methyladenine ligand, the crystal structure of the bis(nuclobase) adduct of *cis*-$(NH_3)_2Pt(II)$ is known [13].

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**Abbreviations used: amacH = amino acid such as gly = glycine; ala = L-alanine; 2-aba = 2-aminobutyricacid; nucleobase: 9-MeA (9-methyladenine); 9-MeGH (9-methylguanine); 9-EtGH (9-ethylguanine); 3-MeA (3-methyladenine).

0020-1693/90/$3.50

N(9) substituted adenines are known to bind Pt(II) through N(1), N(7) and simultaneously through both sites. The respective preference of Pt(II) for N(1) and N(7) has been the subject of several studies [14–17]. It appears that, apart from pH, steric requirements of the Pt(II) entity markedly affect the binding site. Structural data is available for all three binding modes (N(1) [18]; N(7) [16, 19, 20]; N(1),N(7) [21]). In addition, a series of spectroscopic studies concerning the various binding patterns have been published, see for example refs. 22–25.

Since we considered the isolated bis(9-methyladenine) complex of *cis*-$(NH_3)_2Pt(II)$ a possible model of a hypothetical cross-link between the two N(7) positions of two adjacent adenines in DNA, we decided to study this compound by X-ray diffraction.

Experimental

Preparation

Reaction of cis-[$(NH_3)_2Pt$(amac)]NO_3 (amac = L-ala, 2-aba) with 9-MeGH

A suspension of 0.7 mmol of 9-MeGH in 60 ml of H_2O (pH adjusted to 5.0 ± 0.5 with dilute HNO_3) was heated to 60 °C until a clear solution was obtained. *cis*-[$(NH_3)_2$Pt(amac)]NO_3(0.5 mmol), prepared as described in [1], was then added to the above solution (platinum:nucleobase ratio = 1:1.4). The mixture was kept at 60 °C and a pH of 5.0 ± 0.5 (addition of dilute HNO_3) for 2 days, then cooled in an ice bath and filtered from precipitated 9-MeGH. The filtrate was evaporated to dryness and the ^{1}H NMR spectrum of the solid was recorded. This solid was further loaded on a Sephadex G-10 column and eluted with H_2O. Two ml fractions were collected. The order of elution was: amino acid, *cis*-[$(NH_3)_2$)Pt(amac)(9-MeGH)]NO_3 and *cis*-[$(NH_3)_2$Pt(9-MeGH)$_2$]$(NO_3)_2$, all identified by means of IR and/or ^{1}H NMR spectroscopy.

Preparation of cis-[$(NH_3)_2Pt$(9-MeGH)$_2$]$(NO_3)_2$

This complex was prepared for comparison purposes in a similar way to *cis*-[$(NH_3)_2$Pt(9-EtGH)$_2$]$(NO_3)_2 \cdot 2H_2O$, described in ref. 5.

Preparation of cis-[$(NH_3)_2Pt$(9-MeA)$_2$] $(NO_3)_2 \cdot 1.5H_2O$

One mmol of *cis*-[$(NH_3)_2$Pt(gly)]$(NO_3) \cdot 2H_2O$ [1] was dissolved in 15 ml of 0.1 N HNO_3 and 1.8 mmol of 9-MeA were added. The pH of the resulting solution was 1.2. This solution was heated in a stoppered flask for 2 days at 45 °C. The solution (pH = 1.6) was then refrigerated overnight, whereupon protonated ligand (9-MeAH$^+$) was removed. After 2 more days of refrigeration another small amount of protonated ligand was removed. Finally, after 3 more days, the title compound had crystallized as white transparent cubes. A total of 125 mg of product was collected after one recrystallization from H_2O. *Anal.* Calc. for $C_{12}H_{23}N_{14}O_{7.5}Pt$: C, 21.2; H, 3.4; N, 28.9; Pt, 28.8. Found: C, 20.8; H, 3.6; N, 29.2; Pt, 28.5%.

Spectra

IR spectra were recorded as KBr pellets on a Perkin-Elmer 580 grating spectrometer covering the region 4000–200 cm^{-1}. ^{1}H NMR spectra were recorded on an AM-300 Bruker spectrometer (0.2 M in D_2O, $[(CH_3)_4N]BF_4$ as internal standard). Chemical shifts are given in ppm, relative to sodium 3-(trimethylsilyl)propanesulfonate 3.187 ppm upfield from the internal standard.

X-ray structure analysis

A colorless parallelepipedic crystal ($0.300 \times 0.175 \times 0.125$ mm) was sealed on a glass fiber and transferred to a CAD4 Enraf-Nonius diffractometer equipped with a graphite monochromator. Crystallographic data are summarized in Table 1. The unit cell was obtained by using 25 reflections in the θ range of 13–21.3°. A total of 4603 intensity data was collected in the $\theta/2\theta$ scan mode (scan width: $0.70° + 0.35 \tan\theta$, scan speed: 1.1–8.2° min^{-1}) up to $2\theta = 52°$. A set of three standard reflections was measured every 2 h of exposure time, with no noticeable change in intensity observed during the collection. Lorentz-polarization and empirical absorption [25] corrections were made with SDP [26]. There were 4447 independent reflections after merging $hk0$ and $\bar{h}k0$ reflections ($R_{av} = 0.017$).

TABLE 1. Crystallographic data of [$(NH_3)_2$Pt(9-MeA)$_2$]-$(NO_3)_2 \cdot 1.5H_2O$

Chemical formula	$C_{12}H_{23}N_{14}O_{7.5}Pt$
Formula weight	678.5
Space group	monoclinic *C2/c* (No. 15)
a (Å)	18.506(2)
b (Å)	15.770(2)
c (Å)	16.422(2)
β (°)	108.38(2)
V (Å^3)	4548(2)
Z	8
Temperature (°C)	20
λ (Å)	0.71073
ρ_{calc} (g/cm^3)	1.98
μ (cm^{-1})	62.9
Transmission coefficient	0.79–1.00
$R(F_o)$	0.022
R_w	0.027

The structure was solved by a Patterson map calculation and the refinement and ΔF process with SHELX 76 [27] using 2802 reflections, having $F_o^2 > 3\sigma(F_o^2)$. The atomic scattering factors are those of ref. 28 for heavy atoms, including anomalous dispersion effects, and those of ref. 29 for hydrogens. Three water molecules were found in special positions. All non-hydrogen atoms were refined anisotropically using full-matrix least-squares techniques. All hydrogen atoms except those of water molecules, were observed and introduced into calculations in constrained geometry (C–H = N–H = 0.97 Å) with an isotropic temperature factor $U = 0.05$ Å^2. The refinement converged with a mean shift/e.s.d. of 0.025 on the final cycle. The weighting scheme used was: $w = [\sigma^2(F_o) + 0.001\ F_o^2]^{-1}$ and gave satisfactory results. Goodness of fit was 1.1 with 313 variable parameters. The maximum residual peak was 0.9 e/Å^3. All calculations were performed on a Vax 11/730 DEC computer. Final fractional atomic coordinates are given in Table 2.

TABLE 2. Fractional atomic coordinates with e.s.d.s in parentheses

Atom	x/a	y/b	z/c
Pt	0.22961(1)	0.15118(1)	0.23774(1)
N(1a)	0.0691(2)	0.3127(3)	−0.0172(3)
C(2a)	0.1088(3)	0.3679(4)	−0.0489(4)
N(3a)	0.1828(2)	0.3841(3)	−0.0200(3)
C(4a)	0.2175(3)	0.3373(2)	0.0492(3)
C(5a)	0.1837(2)	0.2775(2)	0.0866(2)
C(6a)	0.1049(2)	0.2662(3)	0.0522(3)
N(6a)	0.0645(2)	0.2107(3)	0.0822(3)
N(7a)	0.2403(2)	0.2428(2)	0.1570(2)
C(8a)	0.3045(2)	0.2822(3)	0.1600(3)
N(9a)	0.2935(2)	0.3400(2)	0.0963(2)
C(9a)	0.3523(3)	0.3946(3)	0.0813(3)
N(1b)	0.3993(2)	0.3047(2)	0.4917(3)
C(2b)	0.3637(3)	0.3604(3)	0.5259(3)
N(3b)	0.2893(2)	0.3795(2)	0.5009(2)
C(4b)	0.2515(3)	0.3336(2)	0.4320(3)
C(5b)	0.2807(2)	0.2740(2)	0.3892(2)
C(6b)	0.3603(2)	0.2588(3)	0.4227(2)
N(6b)	0.3979(2)	0.2025(3)	0.3911(3)
N(7b)	0.2221(2)	0.2409(2)	0.3227(2)
C(8b)	0.1600(2)	0.2794(3)	0.3245(3)
N(9b)	0.1749(2)	0.3353(2)	0.3895(3)
C(9b)	0.1178(3)	0.3936(4)	0.4101(4)
N(10	0.2182(2)	0.0575(2)	0.3187(2)
N(11)	0.2366(2)	0.0588(2)	0.1527(2)
N(12)	0.0766(3)	−0.0599(2)	0.1314(4)
O(1)	0.0791(3)	0.0023(3)	0.0804(4)
O(2)	0.0171(2)	−0.1013(3)	0.1185(3)
O(3)	0.1355(3)	−0.0773(3)	0.1933(4)
N(13)	0.3854(3)	−0.0408(4)	0.3086(4)
O(4)	0.3185(3)	−0.0700(3)	0.2850(4)
O(5)	0.4404(3)	−0.0846(5)	0.3027(5)
O(6)	0.3977(4)	0.0327(4)	0.3377(5)
Ow(1)	1/2	0.3941(5)	3/4
Ow(2)	1/2	0.2805(5)	1/4
Ow(3)	1/2	0.1007(5)	1/4

Results and discussion

The major product in the reaction of *cis*-$[(NH_3)_2Pt(amac)]NO_3$ with 9-MeGH was *cis*-$[(NH_3)_2Pt(amac)(9\text{-MeGH})]NO_3$ (eqn. (1)), while *cis*-$[(NH_3)_2Pt(9\text{-MeGH})_2](NO_3)_2$ was formed as a byproduct according to eqn. (2).

$$cis\text{-}[(NH_3)_2Pt(amac)]NO_3 + 9\text{-MeGH} \xrightarrow[60\ °C]{pH\sim 5} cis\text{-}[(NH_3)_2Pt(amac)(9\text{-MeGH})]NO_3 \quad (1)$$

$$cis\text{-}[(NH_3)_2Pt(amac)]NO_3 + 2(9\text{-MeGH}) \xrightarrow[60\ °C]{pH\sim 5} cis\text{-}[(NH_3)_2Pt(9\text{-MeGH})_2](NO_3)_2 + amacH \quad (2)$$

In the case of 9-MeA, however, only *cis*-$[(NH_3)_2Pt(9\text{-MeA})_2](NO_3)_2$ could be isolated from the reaction mixture in strongly acidic aqueous solutions.

$$cis\text{-}[(NH_3)_2Pt(amac)]NO_3 + 2(9\text{-MeA}) \xrightarrow{pH\sim 1} cis\text{-}[(NH_3)_2Pt(9\text{-MeA})_2](NO_3)_2 + amacH \quad (3)$$

Spectroscopy

In the 300 MHz ^{1}H NMR spectrum of the reaction mixture of *cis*-$[(NH_3)_2Pt(amac)]NO_3$ with 9-MeGH (pD 5), the presence of *cis*-$[(NH_3)_2Pt(9\text{-MeGH-}N^7)_2]^{2+}$ was detected and the signals identified by comparison with the compound prepared in an alternative way (H(8) 8.01, CH_3 3.63 ppm). Under the conditions of the experiment the distribution of the main product *cis*-$[(NH_3)_2Pt(9\text{-MeGH})_2](NO_3)_2$ and *cis*-$[(NH_3)_2Pt(amac)(9\text{-MeGH})]NO_3$ was approximately 1.16:1 with ala or 1:3 with 2-aba (based on Pt).

The ^{1}H NMR spectrum of *cis*-$[(NH_3)_2Pt(9\text{-MeA-}N^7)_2](NO_3)_2$ (D_2O, pD 3, 0.02 M), which was isolated according to reaction (3), showed three singlets at 8.63, 8.33 and 3.81 ppm, which are assigned to H(8), H(2) and CH_3, respectively [23]. These values compare with 8.19, 8.06 and 3.79 ppm for the free ligand (D_2O, pD 6, 0.02 M). Compared to $[(NH_3)_3Pt(9\text{-MeA-}N^7)]^{2+}$ [20], the 9-MeA resonances in the bis(nucleobase) complex are shifted somewhat upfield, most likely a consequence of intra-molecular base stacking.

The IR spectra of the complex *cis*-$[(NH_3)_2Pt(9\text{-MeA})_2](NO_3)_2$ show bands at 1696(s), and 1640(s) cm^{-1} due to $\delta NH_2 + \nu$(pyrimidine), at 1549(m) cm^{-1} due to ν(imidazole), while the other NH_2 deformation motions are found at 1302(m), 1192(m) and 533(m

br) cm^{-1}. The NO_3^-frequencies are at 1388(vs), 1043(s) and 828(s) cm^{-1}. The bands at 783(m), 774(s) and 719(s) cm^{-1} are assigned to ring motions. These assignments were based on ref. 30.

Crystal structure

The cation *cis*-$[(NH_3)_2Pt(9\text{-MeA})_2]^{2+}$ is depicted in Fig. 1 and selected bond lengths and angles are given in Table 3.

Both 9-MeA bases are coordinated to Pt(II) through their N(7) nitrogen atoms and are oriented in a head-to-tail fashion. The distance between the two N(7) sites is 2.846 Å.

The coordination geometry of Pt is normal with slight deviations from ideal square-planarity only (e.g. N(10)–Pt–N(11), 88.3(1)°). Pt–N(adenine) and Pt–NH_3 distances are not significantly different and compare well with data from related adenine and/or NH_3 compounds [13, 16, 19–21]. Likewise, the geometry of the two adenine rings is not unusual. While Pt is virtually coplanar with the adenine ring b, it is slightly (0.06 Å) out of the plane of ring a (Table 4). Both adenine rings are at approximately right angle to each other (90.7°) (Fig. 2), virtually identical with the situation in *cis*-$[(NH_3)_2Pt(3\text{-MeA}$-

TABLE 3. Selected bond lengths (Å) and angles (°) of $[(NH_3)_2Pt(9\text{-MeA})_2](NO_3)_2 \cdot 1.5H_2O$

(a) Primary coordination sphere about the Pt atom			
Bond lengths (Å)			
Pt–N(7a)	2.013(4)	Pt–N(7b)	2.022(3)
Pt–N(10)	2.043(4)	Pt–N(11)	2.050(4)
Bond angles (°)			
N(7a)–Pt–N(7b)	89.7(1)	N(7b)–Pt–N(10)	90.7(1)
N(7a)–Pt–N(10)	179.4(1)	N(7b)–Pt–N(11)	179.0(2)
N(7a)–Pt–N(11)	91.2(1)	N(10)–Pt–N(11)	88.3(1)
(b) 9-Methyladenine bases			
Bond lengths (Å)			
N(1a)–C(2a)	1.345(8)	N(1b)–C(26)	1.324(7)
C(2a)–N(3a)	1.325(7)	C(2b)–N(3b)	1.342(6)
N(3a)–C(4a)	1.337(6)	N(3b)–C(4b)	1.340(5)
C(4a)–C(5a)	1.378(6)	C(4b)–C(5b)	1.383(6)
C(5a)–C(6a)	1.400(5)	C(5b)–C(6b)	1.421(5)
C(6a)–N(6a)	1.342(7)	C(6b)–N(6b)	1.330(6)
C(5a)–N(7a)	1.403(4)	C(5b)–N(7b)	1.377(4)
N(7a)–C(8a)	1.329(6)	N(7b)–C(8b)	1.309(6)
C(8a)–N(9a)	1.352(6)	C(8b)–N(9b)	1.345(6)
N(9a)–C(4a)	1.376(5)	N(9b)–C(4b)	1.369(5)
N(9a)–C(9a)	1.468(7)	N(9b)–C(9b)	1.517(7)
Bond angles (°)			
C(6a)–N(1a)–C(2a)	120.0(4)	C(6b)–N(1b)–C(2b)	120.4(4)
N(1a)–C(2a)–N(3a)	127.9(5)	N(1b)–C(2b)–N(3b)	128.3(4)
C(2a)–N(3a)–C(4a)	111.3(5)	C(2b)–N(3b)–C(4b)	110.5(4)
N(3a)–C(4a)–C(5a)	126.3(4)	N(3b)–C(4b)–C(5b)	127.8(4)
N(3a)–C(4a)–N(9a)	126.4(4)	N(3b)–C(4b)–N(9b)	127.0(4)
C(5a)–C(4a)–N(9a)	107.3(3)	C(5b)–C(4b)–N(9b)	105.2(3)
C(4a)–C(5a)–C(6a)	118.0(3)	C(4b)–C(5b)–C(6b)	116.3(3)
C(4a)–C(5a)–N(7a)	108.0(3)	C(4b)–C(5b)–N(7b)	108.9(3)
C(6a)–C(5a)–N(7a)	134.0(4)	C(6b)–C(5b)–N(7b)	134.8(4)
C(5a)–C(6a)–N(1a)	116.4(4)	C(5b)–C(6b)–N(1b)	116.8(4)
C(5a)–C(6a)–N(6a)	124.4(4)	C(5b)–C(6b)–N(6b)	124.6(3)
N(1a)–C(6a)–N(6a)	119.1(4)	N(1b)–C(6b)–N(6b)	118.7(4)
Pt–N(7a)–C(5a)	128.4(3)	Pt–N(7b)–C(5b)	127.2(3)
Pt–N(7a)–C(8a)	125.7(2)	Pt–N(7b)–C(8b)	126.3(3)
C(5a)–N(7a)–C(8a)	105.9(3)	C(5b)–N(7b)–C(8b)	106.5(3)
N(7a)–C(8a)–N(9a)	111.8(3)	N(7b)–C(8b)–N(9b)	111.1(3)
C(8a)–N(9a)–C(4a)	107.0(4)	C(8b)–N(9b)–C(4b)	108.2(4)
C(8a)–N(9a)–C(9a)	125.9(3)	C(8b)–N(9b)–C(9b)	126.3(4)
C(4a)–N(9a)–C(9a)	127.1(4)	C(4b)–N(9b)–C(9b)	125.5(4)

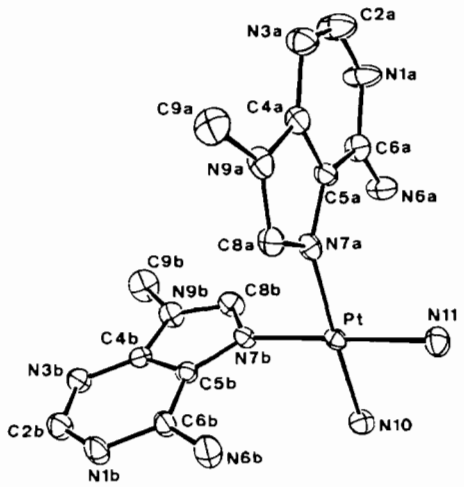


Fig. 1. ORTEP plot of the *cis*-$[(NH_3)_2Pt(9\text{-}MeA)_2]^{2+}$ cation.

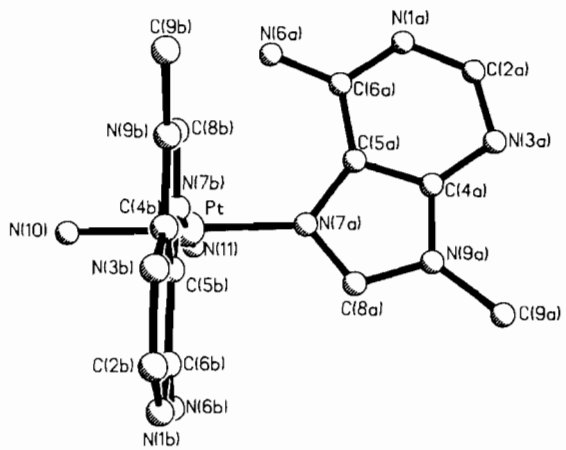


Fig. 2. Conformational drawing of *cis*-$[(NH_3)_2Pt(9\text{-}MeA)_2]^{2+}$ depicting the virtually perpendicular orientation of the two bases.

TABLE 4. Least-squares planes equations and deviations (Å) therefrom[a]

(a) Plane 1: $(-0.90723)X+(0.02469)Y+(-0.41990)Z-(-4.22995)=0$

(Primary coordination sphere)

Pt	−0.0050(2)*	N(10)	0.001(4)
N(7a)	0.001(3)	N(11)	−0.001(4)
N(7b)	−0.001(3)		

(b) Plane 2: $(0.37243)X+(-0.71301)Y+(-0.59406)Z-(-2.844117)=0$

(9-Methyladenine ligand A)

N(1a)	−0.006(5)	C(6a)	−0.013(4)
C(2a)	0.001(6)	N(6a)	−0.003(4)
N(3a)	0.006(4)	N(7a)	0.011(3)
C(4a)	−0.003(4)	C(8a)	−0.023(4)
C(5a)	0.019(4)	Pt	0.0643(2)*

(c) Plane 3: $(0.36499)X+(0.70909)Y+(-0.60330)Z-(0.54933)=0$

(9-Methyladenine ligand B)

N(1b)	0.003(4)	C(6b)	0.005(4)
C(2b)	−0.001(5)	N(6b)	−0.014(4)
N(3b)	−0.007(4)	N(7b)	0.000(3)
C(4b)	0.002(4)	C(8b)	−0.009(5)
C(5b)	0.016(4)	Pt	−0.0076(2)*

[a]Starred atoms are not included in planes calculations.

TABLE 5. Hydrogen bond lengths (Å) and angles (°) with e.s.d.s in parentheses; D and A are the donor and acceptor atoms, respectively; hydrogen atoms of water molecules are not found

D	A	D...A	H...A	D-H...A	H
N(6a)	O(1)	3.299(7)	2.35	166	H1(N6a)
N(6b)	O(6)	2.817(8)	2.02	138	H2(N6b)
N(10)	N(3bi)	3.168(5)	2.21	170	H2(N10)
	O(4)	2.906(7)	2.07	143	H2(N10)
	O(6)	3.261(8)	2.48	138	H2(N10)
	O(3)	3.019(6)	2.21	140	H3(N10)
N(11)	O(1)	2.919(6)	2.01	156	H2(N11)
	O(3)	3.056(7)	2.26	139	H2(N11)
	O(4)	3.011(6)	2.21	139	H3(N11)
Ow(2)	O(2ii)	2.944(7)			
	O(2iii)	2.944(7)			
Ow(2)	Ow(3)	2.835(11)			
Ow(3)	Ow(2)	2.835(11)			
Ow(3)	O(6)	2.921(8)			
Ow(3)	O(6iv)	2.921(8)			

Symmetry operations: (i) $\frac{1}{2}-x, \frac{1}{2}-y, 1-z$; (ii) $\frac{1}{2}+x, \frac{1}{2}+y, z$; (iii) $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$; (iv) $1-x, y, \frac{1}{2}-z$; (v) $-x, y, \frac{1}{2}-z$; (vi) $\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}+z$; (vii) $-x, -y, -z$.

$N^7)_2](NO_3)_2$ [13]. Relevant angles between the Pt coordination plane and the 9-MeA planes, as determined by the convention introduced by Orbell *et al.* [31] are 96.1° (PtN_4/ring A) and 93.5° (PtN_4/ring B).

A network of hydrogen bonds, which involves the NH_3 ligands, water molecules, nitrate oxygens as well as N(6) and N(3) positions of the 9-MeA ligands, is formed in the crystal lattice (Table 5 and Fig. 3).

Surprisingly, the N(1) positions of the two 9-MeA rings do not participate in hydrogen bonding. This is so despite their basicity, which is, however, somewhat reduced by N(7) bound Pt.

Intermolecular base stacking of pairs of adenine rings is very efficient, as seen from Fig. 3 (rings b) and in particular from Fig. 4 (rings a).

Formation

The similar affinities of *cis*-$(NH_3)_2Pt(II)$ for N(1) and N(7) sites at the adenine [12, 14, 15, 17] and the marked tendency to form N(1),N(7) bridged

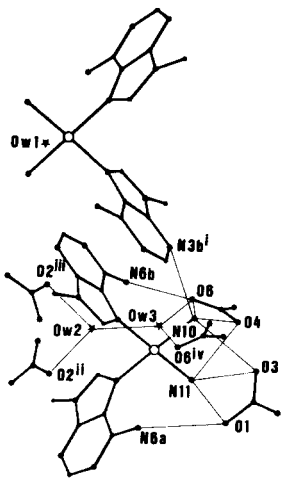


Fig. 3. Schematic representation of hydrogen bonds (dotted lines). Symmetry operations are the following: (i) $\frac{1}{2}-x$, $\frac{1}{2}-y$, $1-z$; (ii) $\frac{1}{2}+x$, $\frac{1}{2}+y$, z; (iii) $\frac{1}{2}-x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$; (iv) $1-x$, y, $\frac{1}{2}-z$. Values from 2.817 to 3.299 Å, the only intercomplex hydrogen bond being N(10)...N(3b)^{i}: 3.168 Å.

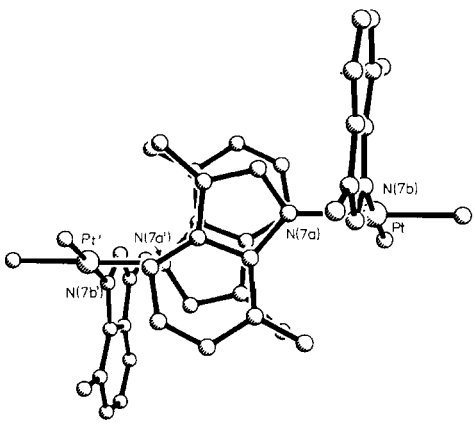
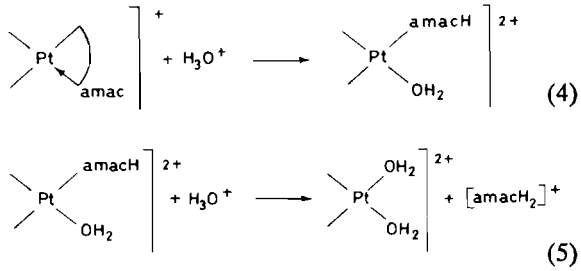
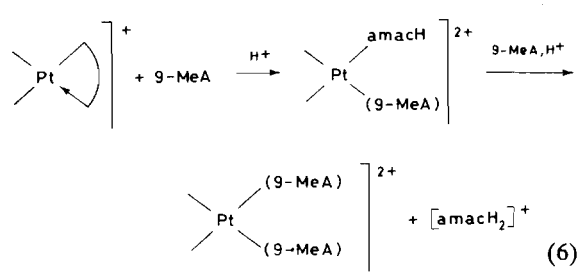


Fig. 4. Stacking interaction between adenine rings *a* of two cations. The view is perpendicular to ring *a* of the upper cation.

species probably explain why *cis*-$[(NH_3)_2Pt(adenine\text{-}N^7)_2]^{2+}$ species have only rarely [10–12] been described. As has previously been demonstrated [19, 23], reaction in acidic medium, which causes protonation at N(1) of adenine ($pK_a \sim 3.5$), can lead to selective platination at N(7). We assume that the acidic reaction conditions used in the preparation of *cis*-$[(NH_3)_2Pt(9\text{-MeA-}N^7)_2](NO_3)_2$ also added to the formation of a single product with two nucleobases coordinated via N(7). Another reason for its formation could have been due to the role of the chelated amino acid: in acidic medium, decomposition according to eqns. (4) and (5) takes place [32].



In the presence of 9-MeA (9-MeAH$^+$), the ^{1}H NMR spectra indicate formation of an intermediate ternary complex according to eqn. (6).



It is feasible, that a reduced reactivity of the ternary complex also supports formation of the bis(nucleobase) complex with two identical donor sites.

Relevance as a model

There is presently no evidence that *cis*-$(NH_3)_2PtCl_2$ forms a bis(adenine) cross-link to any appreciable extent when reacted with DNA. With guanine-N(7) being the kinetically favored binding site, mixed guanine,adenine adducts have, however, been identified among the known cross-links [33]. Nevertheless, cross-linking of two adjacent adenines should be possible in principle.

While *cis*-$[(NH_3)_2Pt(9\text{-MeA-}N^7)_2]^{2+}$ represents a better model for a hypothetical cross-link of *cis*-$(NH_3)_2Pt(II)$ with two adenines in duplex DNA than the 3-MeA-N^7 analogue [13] as far as the nucleobase is concerned, the head–tail arrangement of the two bases in both compounds clearly limits the model character. In duplex DNA a head–tail arrangement of two adjacent bases would require a complete rotation of one of the two bases about the glycosidic bond, a situation that may be difficult to accomplish in intact double stranded DNA. In denaturated DNA such a possibility certainly is more likely. As far as the expected distortion of duplex DNA by an adenine,adenine cross-link with head–head arranged bases is concerned, a base/base angle close to 90°, as observed in the model compounds with head–tail arranged 9-MeA and 3-MeA ligands, appears to be possible only if the base/PtN_4 angles deviate markedly

from 90°. Otherwise the exocyclic amino groups in the 6-positions would clash severely.

The base/base angle of 90.7° in the title compound is markedly larger than in any of the known bis(guanine nucleobase) complexes of *cis*-(diamine)Pt(II), regardless of whether the two bases adopt a head–head [4, 5] or a head–tail [6–9] arrangement. Considering the generally higher tendency of adenine as compared to guanine bases for stacking, this situation may be considered strange. However, as with the 3-MeA complex [13], it appears that this is a consequence of strong intercomplex base stacking which overrules the intracomplex stacking forces.

In DNA the question of base/base angle and hence distortion may thus be determined by the nature of the bases flanking the binding site. It is likely that a bis(adenine) cross-link of the type discussed here would distort DNA at least to the extent a bis(guanine) cross-link does, but probably even more so.

Supplementary material

Atomic coordinates, thermal parameters, bond lengths and angles, least-squares planes equations (7 pages) and tables of observed and calculated structure factors (14 pages) are available from J.-P.L. on request.

Acknowledgements

This work was supported by joint project of the ministries of research and technology of Greece and the F.R.G. We thank Iris Dieter for preparing Figs. 2 and 4.

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