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Mono-, di- and trinuclear Pt(II), mononuclear Pt(IV), mixed Pt(II),Pt(IV), mixed Pt(II),Ag(I) complexes of 9-methyladenine (9-MeA), and the X-ray structure of $[(dien)Pt(9\text{-}MeA\text{-}N^1)](NO_3)_2 \cdot H_2O$

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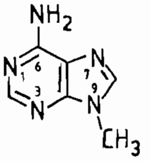
Abstract

Previously studied (^{1}H NMR) mono- and dinuclear complexes obtained by reactions of [(dien)Pt(II)] with 9-methyladenine (9-MeA) have been isolated and characterized: $[(dien)Pt(9\text{-}MeA\text{-}N^7)](NO_3)_2 \cdot H_2O$ (**1**), $[(dien)Pt(9\text{-}MeA\text{-}N^1)](NO_3)_2 \cdot H_2O$ (**2**) and $\{[(dien)Pt]_2(9\text{-}MeA\text{-}N^7,N^1)\}(NO_3)_4 \cdot 2H_2O$ (**3**). Complex **2**, which is only the third structurally characterized adenine complex having a metal exclusively bound through N(1), crystallizes in the space group $P\bar{1}$ with unit cell dimensions $a=8.797(2)$, $b=10.701(3)$, $c=12.156(3)$ Å, $\alpha=101.93(3)$, $\beta=118.18(3)$, $\gamma=101.11(3)°$, $V=929.4$ Å^3, Z=2. Trinuclear derivatives of **2**, $\{(NH_3)_2Pt[(N^7\text{-}9\text{-}MeA\text{-}N^1)Pt(dien)]_2\}(NO_2)_6 \cdot 6H_2O$, (**4**), (**5**) were prepared by reaction of **2** with *cis*- and *trans*-$(NH_3)_2Pt(II)$, respectively. Oxidation of **1** and **2** with H_2O_2 gave Pt(IV) compounds of composition *trans*-$[Pt(OH)_2(dien)(9\text{-}MeA\text{-}N^7)](ClO_4)_2 \cdot 2H_2O$ (**6**) and *trans*-$[Pt(OH)_2(dien)(9\text{-}MeA\text{-}N^1)]X_2 \cdot nH_2O$ ($X=ClO_4^-$, $n=2$ (**7a**); $X=NO_3^-$, $n=0$, (**7b**)). The mixed Pt(IV),Pt(II) complex *trans*-$[(OH)_2Pt(dien)(N^1\text{-}9\text{-}MeA\text{-}N^7)Pt(dien)](ClO_4)_4 \cdot 2H_2O$ (**8**) was obtained from **7** and (dien)Pt(II). The compounds prepared were characterized by elemental analysis and a variety of spectroscopic methods such at ^{1}H NMR, UV and Raman. Acid–base equilibria were determined for several of the compounds and the formations of heteronuclear complexes between Ag^+ and **1** and **2**, respectively, were followed by ^{1}H NMR.

Introduction

Metal binding patterns of adenosine, 5′-AMP, 5′-ATP and adenine model nucleobases such as 9-methyladenine (9-MeA) (Scheme 1) are extremely versatile [1]. Structurally characterized patterns include binding via N(7) [1, 2][†], N(1) [3], N(7),N(1) [4], N(1),N(6) (bridging) [5], N(1),N(6) (chelating) [6], phosphate oxygen [7], and the sugar entity [1a]. On the basis of NMR data, an additional binding mode – N(7),N(6) chelation [6] – has been anticipated. With unsubstituted adenine, the possibilities are even more numerous, reaching a record high of four CH_3Hg entities bound per base (N(3),N(6),N(6),N(9)) for example [8]. The involvement of N(9) in metal binding is biologically irrelevant, however.



Scheme 1.

As far as Pt(II) binding to adenine nucleobases is concerned, coordination at N(7) and N(1) as well as through both sites simultaneously has been observed in numerous model studies [2c, 9]. Two of the three patterns – N(7) binding and N(7),N(1) bridging – are realized when DNA is treated with higher concentrations of $[(dien)PtCl]^+$ [10]. X-ray structures exist of models of these two adducts [2b, 2c, 11; 4c]. Major points of interest in the coordination chemistry of Pt(II) electrophiles with adenine nucleobases have been the questions of N(1) versus

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[†] Compounds reported prior to *c*. 1979–1980 are not referred to individually (cf. reviews given in ref. 1), unless directly relevant to the subject of this paper.

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N(7) binding ratios [1c, 2c, 9k], acid–base equilibria of metallated adenine [2c, 9f, 9g], ligand rotation about the Pt–N(7) bond in *cis*-diamineplatinum(II) compounds [12], and conditions of formation of mixed adenine, guanine adducts of *cis*-$(NH_3)_2Pt(II)$ in DNA [13].

The present study had a further purpose. While previous work had focussed on N(7) as a potential metal binding sites in duplex DNA, the N(1) binding state, which is available in denaturated DNA, in single stranded DNA (cruciforms, slipped structures) and in RNA, has largely been ignored. Moreover, structural data on metal(adenine-N^1) complexes are rare, with only two examples — $[ZnCl_3(9\text{-MeA-}N^1)]^-$ [3a] and $[CH_3Hg(9\text{-MeA-}N^1)]^+$ [3b] — presently available. Finally, the existence of two donor sites of comparable strength in the adenine nucleobase initiated our attempt to prepare mixed metal and mixed valence (Pt(II)/Pt(IV) compounds which, to our knowledge, previously had not been synthesized.

Experimental

Preparations

[(dien)PtI]I [14], *cis*-$(NH_3)_2PtCl_2$ [15], *trans*-$(NH_3)_2PtCl_2$ [16] and 9-methyladenine (9-MeA) [17] were prepared as described. $[(dien)Pt(9\text{-MeA-}N^7)](NO_3)_2\cdot H_2O$ (**1**), $[(dien)Pt(9\text{-MeA-}N^1)](NO_3)_2\cdot H_2O$ (**2**) and $\{[(dien)Pt]_2(9\text{-MeA-}N^7,N^1)\}(NO_3)_4\cdot 2H_2O$ (**3** were prepared by reaction of $[(dien)Pt(H_2O)](NO_3)_2$, obtained from [(dien)PtI]I and $2AgNO_3$ in H_2O, and 9-MeA (1:4 ratio, 40 °C, 72 h), subsequent concentration to a small volume, fractional crystallization (**2** crystallizes first) and size exclusion chromatography (Sephadex G 10), respectively. Yields were *c.* 54% (**1**), 35% (**2**) and 5% (**3**) (NMR scale). The yield of **3** was increased substantially when **1** and **2** were reacted with $[(dien)PtH_2O]^{2+}$ (2 days, 40 °C, pH 6.4) and the mixture passed over Sephadex. *Anal.* Calc. for $C_{10}H_{22}N_{10}O_7Pt$ (**1**, **2**): C, 20.4; H, 3.8; N, 23.8. Found (**1**): C, 20.3; H, 3.7; N, 23.8. Found (**2**): 20.5; H, 3.5; N, 23.9%. From IR spectra and elemental analysis data it appears that **2** also exists as a di- and an anhydrate. *Anal.* Calc. for $C_{14}H_{37}N_{15}O_{14}Pt_2$ (**3**): C, 16.3; H, 3.6; N, 20.4. Found: C, 16.25; H, 3.85; N, 20.05%.

cis-$\{(NH_3)_2Pt[(N^7\text{-9-MeA-}N^1)Pt(dien)]_2\}(NO_3)_6\cdot 6H_2O$ (**4**) and *trans*-$\{(NH_3)_2Pt[(N^7\text{-9-MeA-}N^1)Pt(dien)]_2\}(NO_3)_6\cdot 6H_2O$ (**5**) were prepared by treating **2** with *cis*- and *trans*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ (2:1 ratio, 40 °C, H_2O, 12.5 days (*cis*) and 4.5 days (*trans*)), respectively, and evaporating the solutions. The solids were dissolved in a small amount of water (150 mg in 1 ml) and an excess of $NaNO_3$ (100 mg), and layered with a mixture of ether (2 ml) and methanol (2 ml). Storage of the stoppered flask at 4 °C gave **4** and **5** in *c.* 25% and 50% yield. *Anal.* Calc. for $C_{20}H_{58}N_{24}O_{24}Pt_3$ (**4**, **5**): C, 15.0; H, 3.7; N, 21.0. Found (**4**): C, 15.1; H, 3.5; N, 20.7. Found (**5**): C, 15.0; H, 3.3; N, 20.7%.

trans-$[Pt(OH)_2(dien)(9\text{-MeA-}N^7)](ClO_4)_2\cdot 2H_2O$ (**6**) and *trans*-$[Pt(OH)_2(dien)(9\text{-MeA-}N^1)]X_2\cdot nH_2O$ ($X=ClO_4$, $n=2$ (**7a**); $X=(NO_3)_2$, $n=0$ (**7b**)) were obtained by oxidation of **1** and **2** (ClO_4 and NO_3 salt, respectively) with an aqueous solution of 10% H_2O_2 (c_{Pt} 0.04 M; large excess H_2O_2, 40–50 °C, 20 h), evaporation to dryness and recrystallization from water. Slow evaporation at 4 °C gave crystals of **6** and **7a** and microcrystals of **7b**. Yields were 27% (**6**), 41% (**7a**) and 53% (**7b**). *Anal.* Calc. for $C_{10}H_{26}N_8O_{12}Cl_2Pt$ (**6**): C, 16.8; H, 3.7; N, 15.6. Found: C, 16.9; H, 3.6; N, 15.7%. *Anal.* Calc. for $C_{10}H_{26}N_8O_{12}Cl_2Pt$ (**7a**): C, 16.6; H, 3.8; N, 15.4. Found: C, 16.5; H, 3.9; N, 15.3%. *Anal.* Calc. for $C_{10}H_{22}N_{10}O_8Pt$ (**7b**): C, 19.8; H, 3.7; N, 23.1. Found: C, 19.8; H, 3.6; N, 23.1%.

trans-$[(OH)_2Pt(dien)(N^1\text{-9-MeA-}N^7)Pt(dien)](ClO_4)_4\cdot 2H_2O$ (**8**) was prepared by reacting **7** (aqueous solution, 0.4 mmol, c_{Pt} 0.03 M) with 1 equiv. of Pt(dien)I and 2 equiv. of $AgClO_4$ (50–60 °C, 5 days), filtration of AgI and evaporation of the resulting solution. The glassy, hygroscopic material was dissolved in a mixture of MeOH (25 ml) and H_2O (2.5 ml) and reprecipitated by addition of a small amount of ether. The yield of **8** was 20%. *Anal.* Calc. for $C_{14}H_{39}N_{11}O_{20}Cl_4Pt_2$ (**8**): C, 13.9; H, 3.2; N, 12.7. Found: C, 14.2; H, 3.3; N, 12.4%.

Measurements

^1H NMR spectra (D_2O) were recorded on Bruker AC 200 and AM 300 spectrometers using TSP as an internal reference. Reported pD values were obtained by adding 0.4 to the pH meter reading. For the determination of pK_a values by ^1H NMR spectroscopy, the uncorrected pD* values were taken. IR spectra were recorded on Perkin-Elmer 580 B and Bruker IFS 113 spectrometers, Raman spectra on a Coderg T 800 with Ar (514.8 nm) and Kr (647.1 nm) laser excitation and UV spectra on a Perkin-Elmer Lamda 15. pK_a values for **1** (protonation at N(1)), **2** (protonation at N(7), deprotonation of exocyclic amino group $N(6)H_2$) and **3** (deprotonation of exocyclic amino group $N(6)H_2$) were determined by ^1H NMR (**1**, **2**), UV (**1**, **2**) [18] and potentiometry (**3**). The values obtained were: **1**, 1.9 (^1H NMR), 1.5 (UV); **2**, 0.7 (^1H NMR), 0.3 (UV), 13–14 (^1H NMR); **3**, 10.5. Formation constants of heteronuclear Pt, Ag complexes were determined according to ref. 19 using ^1H NMR spectroscopy [20].

Crystallography

The X-ray measurements of **2** were carried out on a Philips-PW 1100 single crystal diffractometer using graphite monochromated Mo Kα radiation ($\lambda = 0.71069$ Å) at room temperature. Details relevant to data collection and refinement are given in Table 1; atomic coordinates and isotropic temperature factors in Table 2. Intensity data were corrected for Lorentz and polarization effects and, at a later stage, for absorption by using a method of Walker and Stuart [21]. The coordinates of the Pt atom were found in a three-dimensional Patterson map. The other non-hydrogen atoms were determined by subsequent ΔF syntheses; H atoms were ignored. Complex scattering factors for neutral atoms were taken from refs. 22 and 23. The SHELX program package was used for the calculations [24].

Results and discussion

Mono- and dinuclear Pt(II) complexes

[(dien)Pt(9-MeA-N^7)]$(NO_3)_2 \cdot H_2O$ (**1**), [(dien)Pt(9-MeA-N^1)]$(NO_3)_2 \cdot H_2O$ (**2**) and {[(dien)Pt]$_2$(9-MeA-N^7,N^1)}$(NO_3)_4 \cdot 2H_2O$ (**3**) have been isolated and characterized. All three compounds have previously been separated by den Hartog *et al.* [9g] as the chloride salts using cation exchange chromatography. ^{1}H NMR chemical shifts as well as relevant pK_a values were reported. Our NMR and pK_a data, as determined by pH-dependent ^{1}H NMR and UV spectroscopy, agree generally well with theirs (see 'Experimental'), but we note that we observe three overlapping, relatively broad resonances of the aromatic protons of **3** in the ^{1}H NMR spectrum (*c.* 8.70, 8.75, 8.82 ppm) instead of two as reported (8.75, 8.87 ppm). We assume that slow rotation of the rigid (dien)Pt moiety about one of the two Pt–N bonds in **3** is responsible for this phenomenon, although in the spectra of both **1** and **2** single resonances for H(8) and H(2) are observed only. Prolonged heating of aqueous solutions of either **1** or **2** yielded mixtures of **1**, **2**, **3** and free 9-MeA, as found by ^{1}H NMR spectroscopy. However, after 3 days at 70 °C, in both cases the starting compound dominated in the mixture by 70–75%.

TABLE 1. Crystallographic data for [(dien)Pt(9-MeA-N^1)]$(NO_3)_2 \cdot H_2O$ (**2**)

Formula weight	589.44
Space group	$P\bar{1}$
a(Å)	8.797(2)
b (Å)	10.701(3)
c (Å)	12.156(3)
α (°)	101.93(3)
β (°)	118.18(3)
γ (°)	101.11(3)
V (Å^3)	929.4
Z	2
D_{calc} (g cm^{-3})	2.107
D_{meas} (g cm^{-3})	2.109
Crystal size (mm)	0.3, 0.3, 0.3
μ (cm^{-1})	72.9
θ range (°)	2–28
No. unique reflections	4500
No. reflections used in calculations	3890 ($F_o > 5\sigma F_o$)
No. parameters	253
R	0.075
$R_w(F)$	0.064 ($w^{-1} = \sigma^2(F) + 0.00006F^2$)

TABLE 2. Atomic coordinates and equivalent isotropic temperature factors (Å^2) for **2**

Atom	x	y	z	U
Pt1	0.1440(1)	0.2841(1)	0.2757(1)	0.027(1)
N10	−0.0061(19)	0.4070(13)	0.2791(12)	0.037(6)
C10	−0.1427(25)	0.3410(18)	0.3148(18)	0.044(9)
C11	−0.0508(24)	0.2653(17)	0.4099(17)	0.039(9)
N11	0.0105(21)	0.1724(12)	0.3388(15)	0.040(8)
C12	0.1211(29)	0.0966(17)	0.4069(22)	0.052(12)
C13	0.1907(26)	0.0365(16)	0.3238(19)	0.043(9)
N12	0.2844(21)	0.1515(13)	0.2987(13)	0.039(7)
N1	0.2866(21)	0.4015(12)	0.2196(14)	0.036(8)
C2	0.4739(23)	0.4684(16)	0.3181(16)	0.036(8)
N3	0.5876(20)	0.5588(13)	0.3065(15)	0.043(8)
C4	0.5056(23)	0.5785(15)	0.1888(16)	0.032(8)
C5	0.3200(22)	0.5144(15)	0.0819(16)	0.031(7)
C6	0.2116(23)	0.4142(15)	0.0999(17)	0.034(7)
N6′	0.0351(20)	0.3389(14)	0.0053(14)	0.042(7)
N7	0.2896(20)	0.5612(13)	−0.0207(14)	0.039(7)
C8	0.4467(23)	0.6519(16)	0.0215(16)	0.036(8)
N9	0.5828(20)	0.6648(12)	0.1466(15)	0.039(7)
C9′	0.7753(26)	0.7506(19)	0.2200(19)	0.051(10)
N20	0.2994(19)	0.7177(13)	0.3837(14)	0.036(7)
O20	0.1469(22)	0.6793(16)	0.2720(16)	0.076(9)
O21	0.4284(20)	0.8057(15)	0.4051(18)	0.079(10)
O22	0.3075(20)	0.6646(12)	0.4664(13)	0.056(7)
N30	0.3087(20)	0.0213(14)	0.0160(12)	0.037(7)
O30	0.3021(22)	0.0153(16)	−0.0912(15)	0.075(9)
O31	0.3894(29)	0.1361(18)	0.1007(19)	0.099(13)
O32	0.2472(25)	−0.0720(18)	0.0350(16)	0.098(10)
O40	0.3895(24)	0.0200(17)	0.6791(18)	0.081(11)

The use of specific Raman marker bands as a means of establishing the Pt binding pattern at 9-MeA [25] is verified in the present study. The characteristic ring-breathing mode [26] of 9-MeA is at 715 cm^{-1} in the case of **1** and at 724 cm^{-1} with **2**, while a second mode, which involves a motion of the CH_3 group, is observed at 777 (**1**) and 755 (**2**) cm^{-1} in the solid state spectra. For **3**, these modes are at 725 and 795 cm^{-1}.

The X-ray structure of **2** was determined since no crystallographic data exists for a Pt complex with adenine binding through N(1). Figure 1 gives a view of the cation of [(dien)Pt(9-MeA-N^1)]$(NO_3)_2 \cdot H_2O$

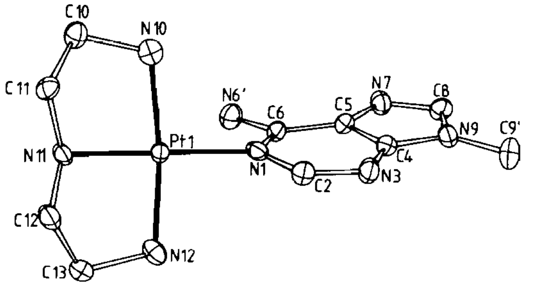


Fig. 1. View of the cation of [(dien)Pt(9-MeA-N^1)]$(NO_3)_2 \cdot H_2O$ (**2**) with atom numbering.

TABLE 3. Interatomic distances (Å) and selected angles (°)

Pt1–N10	2.04(2)	N10–Pt1–N11	85.7(6)
Pt1–N11	2.02(1)	N10–Pt–N12	168.8(5)
Pt1–N12	2.03(2)	N10–Pt1–N1	94.2(5)
Pt1–N1	2.04(1)	N11–Pt1–N12	84.1(6)
N10–C10	1.56(2)	N11–Pt1–N1	177.7(7)
C10–C11	1.55(2)	N12–Pt1–N1	95.8(5)
C11–N11	1.52(2)		
N11–C12	1.45(2)		
C12–C13	1.51(3)		
C13–N12	1.51(2)		
N1–C2	1.41(2)		
C2–N3	1.33(2)		
N3–C4	1.35(2)		
C4–C5	1.42(2)		
C5–C6	1.42(2)		
C6–N6'	1.35(2)		
C6–N1	1.33(2)		
C5–N7	1.37(2)		
N7–C8	1.31(2)		
C8–N9	1.38(2)		
N9–C9'	1.46(2)		
N9–C4	1.36(2)		

(**2**). Interatomic distances and selected angles are listed in Table 3. The geometry of the (dien)Pt(II) entity is not unusual and compares well with published data [27, 28], including the deviation of angles at the Pt from 90°. Of the four CH_2 groups of the dien ligand, the two central ones C(11) and C(12) are pointing on the same side of the PtN_3 plane, deviations from the PtN_4 plane being 0.66 and 0.50 Å. The e.s.d.s of the bond lengths and angles do not justify a detailed comparison of bond distances of the 9-MeA ligand with the free 9-MeA [29] and N(7) platinated one [2b, 2c].

The 9-MeA plane forms an angle of 65.2° with the PtN_4 plane, which is close to that observed in $[(NH_3)_3Pt(9\text{-MeA-}N^7)]^{2+}$ (69.9°) [2b]. The arrangement of [(dien)Pt(9-MeA-N^1)]$^{2+}$ cations in the crystal of **2** is such that pairs of centrosymmetrically related cations stack via their imidazole rings, leading to a head–tail orientation of two adenines (Fig. 2). The distance between the two planes is 3.2 Å. It is unclear whether this stacking interaction is maintained in aqueous solution. ^1H NMR spectra of **2** in D_2O (pD 6.6±0.3; no acid base equilibrium) displayed smooth downfield shifts of CH protons of both dien and 9-MeA ligands with increasing concentrations. These were 14.1 (dien-CH_2 centre), 9.5 (H(2)), 4.7 (CH_3) and 2.7 (H(8)) Hz in the concentration range 9–150 mmol l^{-1}. Base stacking of the adenine rings, on the other hand, should cause upfield shifts of 9-MeA resonances with increasing concentrations. While hydrogen bonding between two adenines via the N(7),N(6') position is possible, we doubt that it would affect H(2), CH_3 and CH_2(dien) resonances to the extent observed. We hesitate to postulate any H bonding patterns that involve C–H protons, although we note that in the solid state C–H...N interactions are documented [30] and that 9-MeA displays a remarkably short (2.524(2) Å) contact between N(3) and C(9) [29c]. In contrast, hydrogen bonding distances and angles in **2** are not remarkable (Table 4).

Trinuclear Pt(II) compounds

Reactions of **1** and **2** with *cis*$[(NH_3)_2Pt(H_2O)_2]^{2+}$ and *trans*-$[(NH_3)_2Pt(H_2O)_2]^{2+}$ were studied by means of ^1H NMR spectroscopy. In the case of **2**, the products *cis*-$\{(NH_3)_2Pt[(N^7\text{-9-MeA-}N^1)Pt(dien)]_2\}(NO_3)_6 \cdot 6H_2O$ (**4**) and *trans*-$\{(NH_3)_2Pt[(N^7\text{-9-MeA-}N^1)Pt(dien)]_2\}(NO_3)_6 \cdot 6H_2O$ (**5**) were also isolated. In accordance with expectations (intracomplex base stacking in **4**), 9-MeA resonances in **4** (8.80; 8.74; 3.84 ppm) are upfield from those of **5** (9.17; 9.05; 8.92; 8.85; 4.03 ppm). The simplicity of the spectrum of **4** is consistent with the presence of a single rotamer in solution which, according to suggestions of Reily and Marzilli [12], most likely is the head–tail isomer. In contrast, **5** exhibits at least four resonances due to aromatic protons, which are of different intensities, however. This finding suggests that rotation either around Pt–N(7) *or* Pt–N(1) is slow on the NMR time scale, resulting in at least two different species in solution. The reaction of **1** with *cis*- and *trans*-$[(NH_3)_2Pt(D_2O)_2]^{2+}$ in a 2:1 ratio yields a mixture of di- and trinuclear species with at least five to six new aromatic 9-MeA resonances in the 8.61–9.06 (*cis*-Pt(II)) and 8.76–9.18 (*trans*-Pt(II)) ppm range, respectively. The insensitivity of these resonances towards H^+ in the pD range 1–3 is a clear indication of N(7),N(1) bridging. However, the products were not separated and isolated.

Raman spectra (solid state) of **4** and **5** are very similar as far as 9-MeA modes are concerned. The characteristic ring modes referred to above are at 728 and 800 cm^{-1} (**4**) and 732 and 800 cm^{-1} (**5**).

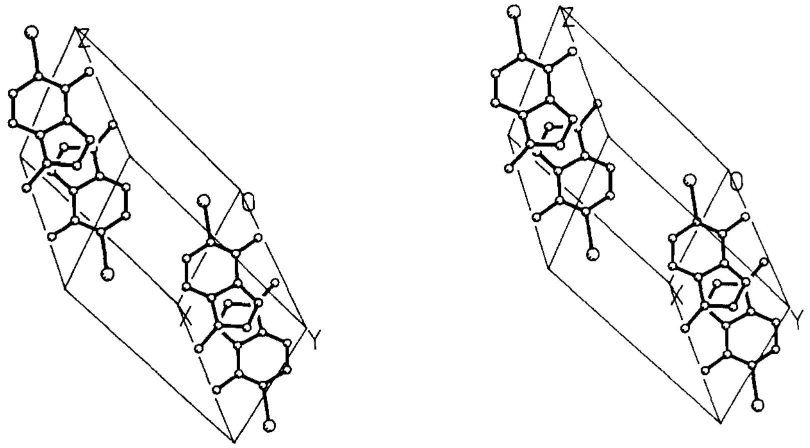
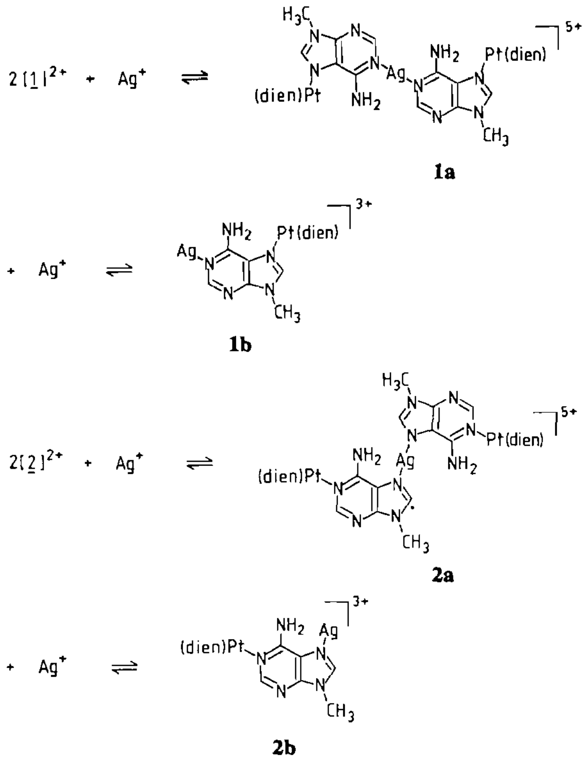


Fig. 2. Stereoscopic view along *c*-axis of packing of adenine rings in **2**. Dien ligands, NO_3^- anions and H_2O are omitted for clarity.

TABLE 4. Close contacts <3.4 Å

N10–O20	3.00	Pt1–N10–O20	113
N10–O22	2.99	Pt1–N10–O22	98
N12–O31	2.94	Pt1–N12–O31	105
O30–O40^1	3.24	N30–O30–O40^1	166
N11–O30^2	2.83	Pt1–N11–O30^2	101
N6'–O32^2	3.17	C6–N6'–O32^2	134
N10–N7^3	3.10	Pt1–N10–N7^3	121
N6'–N7^3	3.31	C6–N6'–N7^3	118
N6'–O20^3	2.91	C6–N6'–O20^3	125
O32–O40^4	3.25	N30–O32–O40^4	96
N12–O21^5	3.13	Pt1–N12–O21^5	115
N12–O22^5	3.16	Pt1–N12–O22^5	104
O21–O40^5	2.89	N20–O21–O40^5	152

Symmetry operations: ^{1}: $x, y, -1+z$; ^{2}: $-x, -y, -z$; ^{3}: $-x, 1-y, -z$; ^{4}: $1-x, -y, 1-z$; ^{5}: $1-x, 1-y, 1-z$.



Scheme 2.

Heteronuclear Pt(II),Ag(I) complexes

Crystal structures of *catena*-μ(9-methyladenine) metal compounds with N(7),N(1) bridged arrangements have been reported for Ag^+ [4b] and Zn^{2+} [4d]. Addition of increasing amounts of $AgNO_3$ to solutions of **1** and **2**, respectively, in D_2O causes downfield NMR shifts of 9-MeA resonances which are interpreted in terms of Ag(I) coordination at N(1) (compound **1**) and N(7) (compound **2**). In the case of **1**, H(2) is shifted more than H(8) and CH_3, while the reverse is true for **2**. We disregard Ag(I) binding to the N(3) site of **2** on the basis of all presently available evidence of metal binding to *neutral* adenines. Only with anionic adenines (unsubstituted adenines, N(9) deprotonated [31]; adenines metallated at exocyclic amino group [8] does the N(3) site appear to be available for metal coordination. We propose the species shown in Scheme 2 to be present in solution. An analysis of the downfield shifts of 9-MeA resonances according to the method of Kan and Li [19b] gives, under conditions of excess Ag^+ (1:1 complex formation), consistent *K* values of *c*. 17 l mol^{-1} for H(2) and H(8) for the equilibrium

$$\mathbf{1} + Ag^+ \rightleftharpoons \mathbf{1b}$$

With compound **2**, a similar analysis yielded *K* values that differed by a factor of 10 for the two signals (H(8), 65.3; H(2), 6.7). This finding is suggestive of either no simple equilibria as with **1** or complications due to base stacking (viz. destacking as a consequence of Ag^+ binding) or the phenomenon of concentration dependent chemical shifts mentioned above.

Mononuclear Pt(IV) complexes

Oxidation of **1** and **2** with H_2O_2 gave *trans*-$[Pt(OH)_2(dien)(9\text{-}MeA\text{-}N^7)](ClO_4)_2 \cdot 2H_2O$ (**6**) and *trans*-$[Pt(OH)_2(dien)(9\text{-}MeA\text{-}N^1)](ClO_4)_2 \cdot 2H_2O$ (**7**), respectively. The assignment of the +4 oxidation state in both compounds is straightforward by use of ^1H NMR spectroscopy: in both cases one of the aromatic protons (H(8) in **6**, H(2) in **7**) displays $^{195}Pt\text{–}^1H$ coupling of 11.2 and 10.9 Hz, respectively. The magnitude of coupling is in agreement with predictions [32] and agrees well with that of the previously reported $[Pt(OH)_2(NH_3)_3(9\text{-}MeA\text{-}N^7)]^{2+}$ [2b]. The fact that under high field conditions (300 MHz) $^{195}Pt\text{–}^1H$ coupling is usually lost with Pt(II), yet not with Pt(IV), has been observed before [33] (Fig. 3). Another characteristic difference between the Pt(II) compounds **1** and **2** and their respective Pt(IV) oxidation products refers to the dien resonances (Fig. 4). The eight carbon protons of the dien ligands are grouped in signal sets of relative intensities 2:4:2 in both Pt(II) and Pt(IV) species, but chemical shifts are different for the two oxidation states. Only the two less intense sets display ^{195}Pt satellites, which are, however, severely broadened in the case of Pt(II) species (**1**, **2**). The coupling constants, which are *c*. 71 Hz for Pt(II) (**1**, **2**) and *c*. 46 and 50 Hz for **6** and **7**, respectively, show the expected dependence on the metal oxidation state. We tentatively assign the two resonances with ^{195}Pt satellites to the protons adjacent to the central NH group (a, b, of abcd spin system).

pH variable NMR spectra of **6** and **7** (Fig. 5 for **7**) in the range 0–13 reveal the following acid–base equilibria

$$[(dien)Pt(OH)_2(9\text{-}MeAH\text{-}N^1)]^{3+} \overset{pK_1}{\rightleftharpoons} [(dien)Pt(OH)_2(9\text{-}MeA\text{-}N^1)]^{2+} + H^+$$

$$[(dien)Pt(OH)_2(9\text{-}MeA\text{-}N^1)]^{2+} \overset{pK_2}{\rightleftharpoons} [(dien^-)Pt(OH)_2(9\text{-}MeA\text{-}N^1)]^{+} + H^+$$

$$[(dien^-)Pt(OH)_2(9\text{-}MeA\text{-}N^1)]^{+} \overset{pK_3}{\rightleftharpoons} [(dien^-)Pt(OH)_2(9\text{-}MeA^-\text{-}N^1)] + H^+$$

Protonation of **7** occurs with a pK_1 of 0 which expectedly is somewhat lower than for the Pt(II) complex **2** and probably comparable with the step leading to twofold protonation of the free ligand. The dien ligand deprotonates in weakly alkaline solution ($pK_2 \sim 8$). Its acidity is in the range found for $Pt(IV)NH_3$ species [34]. This deprotonation process is accompanied by formation of an intense yellow

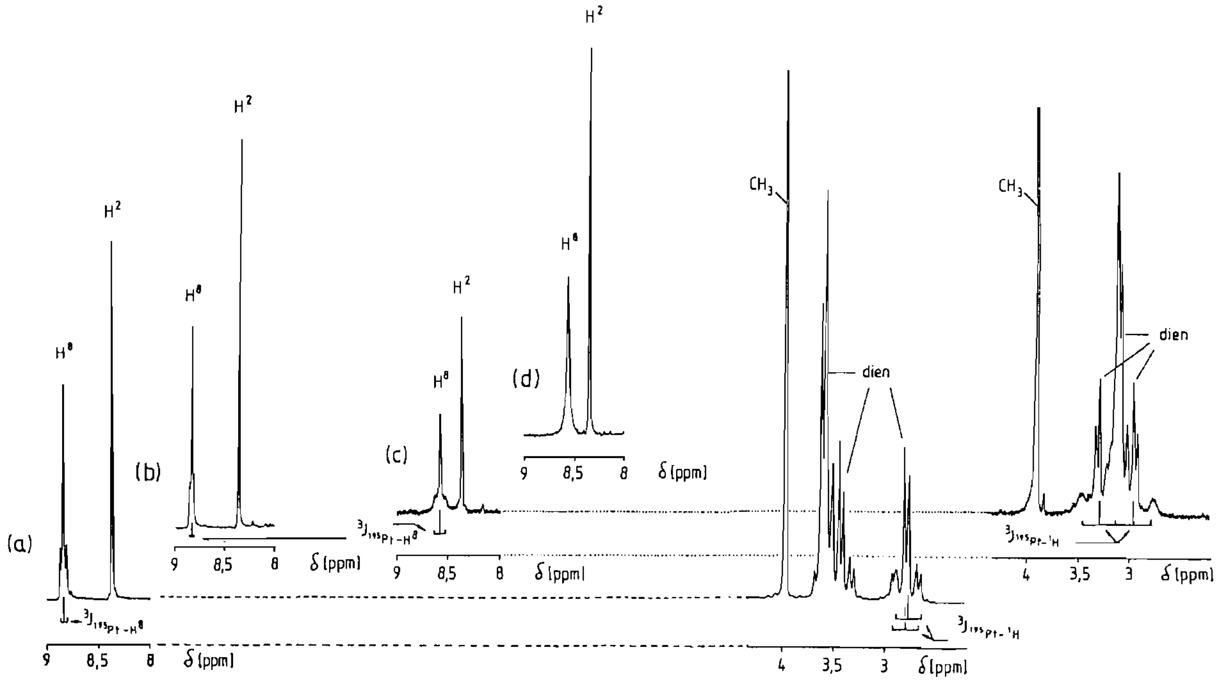


Fig. 3. Sections of ^1H NMR spectra of: (a) **6** in D_2O, pD 4.7, 200 MHz; (b) **6** in D_2O, pD 5.4, 300 MHz; (c) **1** in D_2O, pD 8.2, 200 MHz; (d) spectrum (c) recorded at 300 MHz.

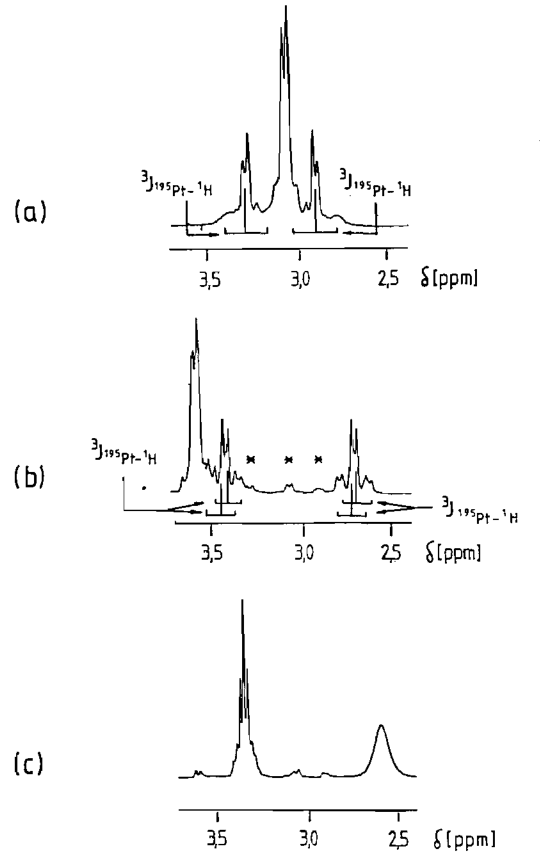


Fig. 4. ^{1}H NMR resonances (D_2O) of dien ligands in: (a) **2**, pD 2.4; (b) **7b**, pD 2.2; (c) **7b**, pD 9.45. Resonances indicated by asterisks in (b) are due to impurities of Pt(II) (dien) or **2**.

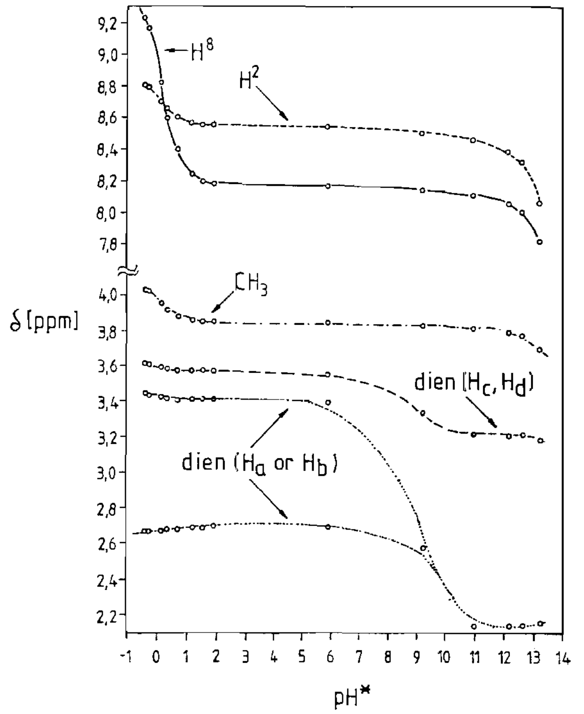


Fig. 5. pH* dependence of ^{1}H chemical shifts of resonances of **7**.

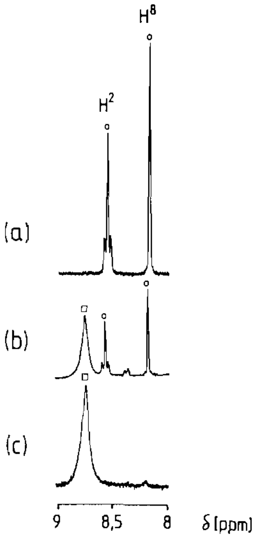
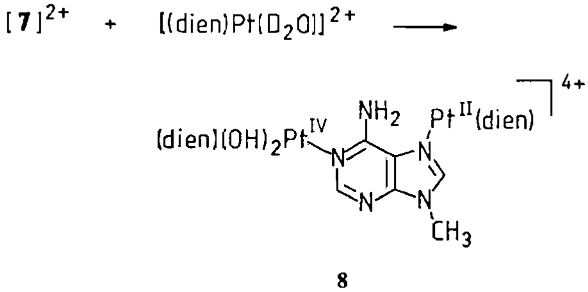


Fig. 6. Low field portions of ^{1}H NMR spectra of: (a) **7**, pD 6.5; (b) **7** after addition of $[(dien)Pt(H_2O)]^{2+}$ (1:1), pD 3.3; (c) **8**, pD 4.8. ○ and □ refer to **7** and **8**, respectively.

color (λ ~ 320 nm). Deprotonation of the 9-MeA ring at the exocyclic amino group $NH_2(6)$ starts at pD 10 with an estimated pK_a of *c*. 13–14. As in related *trans*-dihydroxo complexes of Pt(IV), protonation of the OH groups is not occurring above pH 0 [2b, 35]. The pK_a values for the respective equilibria of **6** are 2.1 (pK_1), ~ 8.3 (pK_2) and ~ 13–14 (pK_3). On heating, the NMR spectra of **6** and **7** become extremely complex. We have not been able as yet to identify any of the products formed. In principle, a chemistry similar to that of Pt(IV) complexes of 1-methylcytosine [35, 36] is feasible, namely N(1),N(6) and/or N(7),N(6) chelation and migration to N(6). Chelate formation has already been shown to occur with $(Cp)_2Mo(Cl_2)$ [6].

Mixed Pt(IV),Pt(II) complex

As evident from ^{1}H NMR spectroscopy (Fig. 6), $[(dien)Pt(D_2O)]^{2+}$ reacts with **7** to give a mixed-valence compound **8** (Scheme 3). H(2) and H(8) resonances of the 9-MeA ligand overlap in **8** and are close to the position of the diplatinum(II) complex **3**, but the two sets of dien resonances quite clearly show the presence of both Pt(II) and Pt(IV). Among others, we have been interested in **8** in order to find out if any metal-to-metal charge transfer (MMCT) from the Pt(II) to the Pt(IV) entity via the nucleobase skeleton might be detected in the electronic absorption spectrum. Low-energy MMCT transitions are frequently observed in mixed-valence



8

Scheme 3.

state Pt(II),Pt(IV) compounds with direct metal–metal contact or via halogen bridges [37]. On the other hand, there are also examples where no such interactions are found and transitions occur at quite high energies, for example at 295 nm between $[Pt(NH_3)_5Cl]^{3+}$ and $[Pt(CN)_4]^{2-}$ [38]. In the case of **8**, UV–Vis spectra of **8** as well as a superposition of spectra of $[(dien)Pt(H_2O)]^{2+}$ and **7** or difference spectra of **8** and **7** provide no indication of a band that may be attributed to a charge transfer between the two metal centers.

Conclusions

Of all naturally occurring nucleobases, adenine is the only one having two donor sites (N(1) and N(7)) almost equally significant for metal binding at physiological pH. This fact not only allows formation of isomer complexes but also favors formation of N(1), N(7) bridged species. While di- and polynuclear adenine complexes containing a single metal in a fixed oxidation state have been reported previously, this work extends the list to dinuclear, mixed Pt(II),Pt(IV) species, to discrete trinuclear Pt(II) as well as heteronuclear Pt,Ag compounds.

Supplementary material

Observed and calculated structure factors as well as anisotropic thermal factors can be obtained from the authors on request.

Acknowledgement

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