Dimerization of *trans*-[Pt(NH$_3$)(1-MeC-*N3*)(H$_2$O)$_2$]$^{2+}$ and Oxidation to a Diplatinum(III) Species in the Presence of Glycine. Relevance for Platinum Cytosine Blue

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trans-Pt(NH$_3$)(1-MeC-*N3*)I$_2$ (**4**) with 1-MeC (1-methylcytosine) bound to Pt via N(3), obtained from *cis*-[Pt(NH$_3$)$_2$(1-MeC-*N3*)Cl]Cl, gives *trans*-[Pt(NH$_3$)(1-MeC-*N3*)(H$_2$O)$_2$]$^{2+}$ when treated with 2 equiv of AgNO$_3$. This diaqua species rapidly dimerizes in solution to give [Pt$_2$(NH$_3$)$_2$(1-MeC$^-$-*N3,N4*)$_2$(H$_2$O)$_2$]$^{2+}$ (**5**), a compound containing bridging 1-methylcytosinato ligands in a *head−tail* arrangement, as judged from ^{1}H NMR spectroscopy. In addition, an intensely purple, paramagnetic species **5′** forms, which is yet another representative of the class of "platinum pyrimidine blues". If dimerization to give **5** is carried out in the presence of the amino acid glycine, spontaneous oxidation to a yellow diplatinum(III) complex of composition [Pt$_2$(NH$_3$)$_2$(1-MeC$^-$-*N3,N4*)$_2$(gly-*N,O*)$_2$](NO$_3$)$_2$·3H$_2$O (**6**) takes place. The compound has been isolated and characterized by NMR spectroscopy (^{1}H, ^{195}Pt) and X-ray crystallography: triclinic system, space group $P\bar{1}$, a = 12.438(4) Å, b = 12.820(4) Å, c = 10.275(2) Å, α = 98.21(3)°, β = 112.84(2)°, γ = 62.24(2)°, V = 1335(2) Å^3, Z = 2. In **6**, the two methylcytosinato rings are oriented *head−tail*, and glycinate anions chelate Pt atoms via NH$_2$ (axial) and COO$^-$ (equatorial). The Pt−Pt bond length is 2.527(1) Å. When L-alanine is applied instead of glycine, a complex analogous to **6** is formed which occurs in solution in two diastereomeric forms, however, as evident from ^{1}H NMR spectroscopy. On the basis of **5**, an oligomerization process leading to "Pt cytosine blue" is proposed, according to which O(2) of 1-MeC$^-$ is involved in bridging dinuclear entities or dinuclear and mononuclear entities. The proposed oligomerization principle differs markedly from that observed in tetranuclear (Pt$^{2.25+}$)$_4$ complexes containing cyclic amidate ligands.

Introduction

Several years ago, we reported the displacement of an ammonia ligand from a *cis*-(NH$_3$)$_2$Pt^{II} complex of 1-methylcytosine, 1-MeC (eq 1).[2] Considering the long-postulated inertness

$$cis\text{-}[Pt(NH_3)_2(1\text{-}MeC)Cl]Cl \rightarrow trans\text{-}Pt(NH_3)(1\text{-}MeC)Cl_2 + NH_3 \quad (1)$$

of ammonia ligands in Cisplatin and its derivatives in nucleobase chemistry, this reaction was unusual and led us to speculate on its possible biological significance.[2] Subsequently we could show (eq 2) that eventually tris(nucleobase) complexes can be obtained from the *trans*-dichloro intermediate,[3,4] a feature not possible for *trans*-(NH$_3$)$_2$PtCl$_2$.[5]

$$trans\text{-}Pt(NH_3)(1\text{-}MeC)Cl_2 + 2L \xrightarrow[-2AgCl]{+2Ag^+} trans\text{-}[Pt(NH_3)(1\text{-}MeC)L_2]^{2+} \quad (2)$$

We now find that the diaqua species *trans*-[Pt(NH$_3$)(1-MeC)(H$_2$O)$_2$]$^{2+}$, which was prepared from the corresponding diiodo compound *trans*-Pt(NH$_3$)(1-MeC)I$_2$, spontaneously self-condenses with formation of 1-methylcytosinato-*N3,N4* bridges (1-MeC$^-$-*N3,N4*) and at the same time undergoes rapid air oxidation to an intensely colored blue-purple species. If amino acids are added at a later stage of this condensation reaction, a mixed 1-methylcytosinato−amino acid anion diplatinum(III) complex of composition [Pt$_2$(NH$_3$)$_2$(1-MeC$^-$-*N3,N4*)$_2$(amac$^-$-*N,O*)$_2$]$^{2+}$ (*head−tail*) forms, which for amac$^-$ = glycine anion (gly) has been structurally characterized by X-ray analysis. Our findings appear to be of considerable relevance to the chemistry of diplatinum(III) complexes in general and also to mixed-valence "platinum cytosine blues".

Experimental Section

Preparations. *cis*-[(NH$_3$)$_2$Pt(1-MeC-*N3*)Cl]Cl·H$_2$O (**1**) was obtained from *cis*-(NH$_3$)$_2$PtCl$_2$[6] and 1-MeC[7] as follows: *cis*-(NH$_3$)$_2$PtCl$_2$ (3 mmol, dissolved in 300 mL of H$_2$O) was combined with NaCl (6.3 mmol) and then 1-MeC (3 mmol, dissolved in 10 mL of H$_2$O), and the mixture was kept at 40 °C for 3 d with stirring in a stoppered flask. After filtration of some black precipitate, the filtrate (pH 1.65) was brought nearly to dryness, and a yellow precipitate, identified as unreacted *cis*-(NH$_3$)$_2$PtCl$_2$, was filtered off. The remaining pale yellow filtrate (60 mL) was allowed to evaporate on a water bath at 40 °C to a volume of 5 mL and was then left at room temperature for further evaporation. After 3 weeks, pale yellow crystals of **1** began to form. One week later the yield of **1** was 605 mg (45.5%). Upon prolonged standing, solutions from which **1** was isolated turned eventually purple. Anal. Calcd: C, 13.65; H, 3.41; N, 15.80. Found: C, 13.6; H, 3.4; N, 15.8. IR (cm^{-1}): 1660 (vs), 1605 (vs), 1575 (vs), 1535 (vs), 1510 (vs), 1440 (s), 1425 (vs), 1385 (vs), 1340 (vs), 1330 (vs), 800 (vs), 790 (vs), 770 (vs), 645 (vs), 545 (vs), 445 (vs), 420 (vs), 350 (vs).

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(5) It is noted, however, that *trans*-[a$_2$PtLCl]Cl (L = nucleobase) can react in an analogous way with ligand rearrangement according to 2 *trans*-[a$_2$PtLCl]Cl → *trans*-[a$_2$PtL$_2$]Cl$_2$ + *trans*-a$_2$PtCl$_2$. See, e.g.: (a) Krizanovic, O.; Pesch, F. J.; Lippert, B. *Inorg. Chim. Acta* **1989**, *165*, 145. (b) Pesch, F. J.; Wienken, M.; Preut, H.; Tenten, A.; Lippert, B. *Inorg. Chim. Acta* **1992**, *197*, 243.

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X-ray analyses of *cis*-$[(NH_3)_2Pt(1\text{-MeC-}N3)Cl]NO_3$[8] and *cis*-$[(NH_3)_2Pt(1\text{-MeC-}N3)Cl]_2[Pt(CN)_4]$[9] have been reported previously.

The iodo analogue of **1**, *cis*-$[(NH_3)_2Pt(1\text{-MeC-}N3)I]I\cdot H_2O$ (**2**), was obtained as colorless needles when an aqueous solution of **1** (0.5 mmol in 10 mL of H_2O) was mixed with excess KI (4 equiv) and the slightly orange solution (pH 7) kept at 6 °C overnight. A small amount of pure **2** (30 mg) was then recovered. At a later stage (sample kept at 22 °C), more **2** and in addition **4** (main product) were recovered. Recrystallization of **2** from water (3 mL, 2 min at 90 °C) resulted in appreciable decomposition of **2** and formation of yellow **4**. Anal. Calcd: C, 9.6; H, 2.4; N, 11.2. Found: C, 9.8; H, 2.7; N, 11.3. IR (cm^{-1}): 3355 (s), 3101 (vs), 1640 (vs), 1535 (vs), 1511 (vs), 1422 (s), 1380 (s), 1342 (s), 1255 (m), 1203 (m), 1163 (m), 992 (m), 793 (s), 763 (m), 647 (s), 564 (s), 450 (m), 423 (m), 413 (m).

trans-$Pt(NH_3)(1\text{-MeC-}N3)Cl_2\cdot 0.5H_2O$ (**3**) was prepared as described.[2] Its iodo analogue, *trans*-$Pt(NH_3)(1\text{-MeC-}N3)I_2$ (**4**), was prepared in the following way: **1** (2.5 mmol) was dissolved in H_2O (30 mL), and KI (5 mmol), dissolved in H_2O (10 mL), was added. To the colorless solution (pH 5.8) were added a few drops of 1 N $HClO_4$ to reach pH 1.9. Within 24 h at 40 °C, yellow needles formed, which were collected, washed with water, and dried in air. The pH of the remaining solution was readjusted from 3.3 to 1.9 with 1 N $HClO_4$ and kept for several days at 40 °C in an open beaker. Orange-yellow needles, which according to the IR spectra were identical with the first fraction, were recovered at intervals. Every filtration was followed by an adjustment of the pH value of the filtrate. The total yield of **4** was 1.41 g (94.4%). Anal. Calcd for $Pt(NH_3)(C_5H_7N_3O)I_2$: C, 10.16; H, 1.71; N, 9.48. Found: C, 10.2; H, 1.5; N, 9.5. IR (cm^{-1}): 3371 (vs), 3272 (s), 3180 (m), 3112 (m), 3061 (m), 1658 (vs), 1633 (vs), 1604 (vs), 1536 (s), 1491 (vs), 1420 (s) 1383 (s), 1337 (m), 1302 (s), 801 (m), 770 (m), 541 (m).

The "diaqua" species of **4** was obtained by treatment of **4** with $AgNO_3$ (typically 1 mmol in 30 mL of H_2O, 2 mmol of $AgNO_3$ added, stirring at 22 °C for several hours, repeated filtration of AgI). From ^1H NMR spectra recorded in parallel experiments, it was evident that dimerization of **4** to $[Pt_2(NH_3)_2(1\text{-MeC}^-\text{-}N3,N4)_2(H_2O)_2]^{2+}$ (**5**) was extensive at that point.

$[Pt_2(NH_3)_2(1\text{-MeC}^-\text{-}N3,N4)_2(\text{gly-}N,O)_2](NO_3)_2\cdot 3H_2O$ (**6**) was obtained as follows: *trans*-$Pt(NH_3)(1\text{-MeC})I_2$ (0.5 mmol) and $AgNO_3$ (1 mmol) were put into H_2O (20 mL), and the suspension was stirred for 2 h at 40 °C. After filtration of AgI, glycine, glyH (1.1 mmol), was added to the dark violet solution (pH 1.9). This solution (pH now 3.4) was stirred for 44 h at 40 °C and again filtered from AgI. Then the filtrate was concentrated to a small volume, and 4 weeks later yellow crystals of **6** were collected. The isolated yield of **6** was 30 mg (14.7%). According to ^1H NMR spectroscopy, at least 30−40% of the original monomer is converted to **6**, however. Anal. Calcd for $[Pt_2(NH_3)_2(C_5H_6N_3O)_2(C_2H_4NO_2)_2](NO_3)_2\cdot 3H_2O$: C, 16.87; H, 3.03; N, 16.86. Found: C, 16.7; H, 3.1; N, 16.9. IR (cm^{-1}): 3429 (m), 3264 (m), 3029 (s), 1637 (vs), 1560 (s), 1507 (m), 1384 (vs), 1311 (vs), 1100 (m), 1038 (m), 914 (m), 824 (m), 799 (m), 765 (s), 721 (m), 515 (s).

$[Pt_2(NH_3)_2(1\text{-MeC}^-\text{-}N3,N4)_2(\text{L-ala-}N,O)_2](NO_3)_2\cdot 5H_2O$ (**7**) was obtained in analogy to **6** as yellow cubes. **7** was prepared as follows: **4** (0.35 mmol) was mixed with $AgNO_3$ (0.7 mmol) and stirred in H_2O (6.5 mL) for about 90 min; then the mixture was filtered from yellow AgI (pH 2). L-Alanine (1.1 mmol) was added to the opaque solution, and the mixture was stirred for another 2 h at room temperature. The then light green solution (pH 3.2) was filtered again from AgI and kept at room temperature. After 2 days a small amount of a black precipitate was filtered off the solution. Color and pH remained constant. The solution was allowed to evaporate at room temperature; 2 weeks later, yellow needles appeared. Recrystallization from water gave yellow cubes. The isolated yield was 10.5 mg (5.6%). Anal. Calcd for $[Pt_2(NH_3)_2(1\text{-MeC}^-\text{-}N3,N4)_2(\text{L-ala-}N,O)_2](NO_3)_2\cdot 5H_2O$: C, 18.08; H, 3.79; N, 15.82. Found: C, 18.2; H, 3.8; N, 15.6. IR (cm^{-1}): 3076 (m), 1635 (vs), 1558 (s), 1384 (vs), 1314 (s), 1282 (s), 1039 (s), 508 (s), 416 (s).

Instrumentation. IR spectra (KBr) were recorded on Perkin-Elmer 580B and Bruker IFS 113v spectrometers; ^1H NMR (200.13 MHz, D_2O, TSP as internal reference) and ^{195}Pt NMR spectra (42.998 MHz, D_2O, referenced to Na_2PtCl_6) were obtained on a Bruker AC 200 instrument. The inverse mode of the instrument was applied in the 1D and 2D ^1H, ^{195}Pt HMQC experiments. There was no decoupling during acquisition.[10] Experimental parameters for Figure 3 were as follows: 256 t_1 increments of 1K data points, sweep width 2000 Hz (F2) and 8000 Hz (F1), 80 scans per F1 experiment, relaxation delay 2.5 s, window functions cos(F2) and sin(F1).

Reported pD values were determined with the use of a combination glass electrode at a Metrohm 6321 pH meter, with 0.4 unit added to the meter reading. The EPR spectrum of a dry, aged "diaqua" species **5** was recorded on a Varian E6 spectrometer at −85 °C. UV−vis spectra were obtained on a Perkin-Elmer Lambda 15 spectrophotometer at room temperature. Concentration of the solution was $\approx 10^{-5}$ M.

Table 1. Crystallographic Data and Details of the X-ray Structure Determination of **6**

A. Crystal Data	
empirical formula	$Pt_2O_{15}N_{12}C_{14}H_{32}$
formula weight	998.66
crystal color, habit	yellow, needle
crystal dimensions	0.340 × 0.140 × 0.080 mm
crystal system	triclinic
lattice parameters	$a = 12.438(4)$ Å
	$b = 12.820(4)$ Å
	$c = 10.275(2)$ Å
	$\alpha = 98.21(3)°$
	$\beta = 112.84(2)°$
	$\gamma = 62.24(2)°$
	$V = 1335(2)$ Å^3
space group	$P\bar{1}$ (No. 2)
z value	2
D_{calc}	2.485 g/cm^3
μ (Mo Kα)	106.69 cm^{-1}
B. Intensity Measurements	
diffractometer	Rigaku AFC6S
radiation	Mo Kα ($\lambda = 0.710\,69$ Å)
temperature	−120 °C
scan type	ω-2θ
$2\theta_{max}$	46.0°
no. of reflns measd	total: 3914
	unique: 3709 ($R_{int} = 0.029$)
corrections	Lorentz-polarization
	abs (transm factors: 0.64-1.00)
structure solution	direct methods
refinement	full-matrix least-squares
anomalous dispersion	all non-hydrogen atoms
no. of observns ($I > 3.00\sigma(I)$)	2619
no. of variables	383
reflection/parameter ratio	6.84
residuals: R, R_w	0.025, 0.032
goodness of fit indicator	1.20
max peak in final diff map	0.89 e/Å^3

X-ray Crystal Structure Determination of 6. All X-ray measurements were performed on a Rigaku AFC6S diffractometer using Mo Kα radiation ($\lambda = 0.710\,69$ Å) at −120 °C. Most of the crystals were twinned. After several trials, a small needlelike crystal of dimensions 0.34 × 0.14 × 0.08 mm was selected. The unit cell dimensions were determined by least-squares refinement of the setting angles of 25 high-angle reflections. The intensities of three standard reflections were monitored every 3 h of X-ray exposure, showing no significant changes. Empirical absorption corrections were applied with the transmission factors ranging 0.64− 1.00.

All calculations were carried out on a VAXstation 3520 computer by using the TEXSAN 5.0 crystallographic software package.[11] The structure was solved by direct methods (SIR 88).[12] Full-matrix least-squares refinement with anisotropic thermal displacement parameters for all non-hydrogen atoms gave a final R of 0.025 ($R_w = 0.032$). The

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Table 2. Atomic Positional Parameters and B(eq) Values for **6**

atom	x	y	z	B(eq), Å^2
Pt(1)	0.39042(3)	0.27462(3)	0.90406(4)	1.27(3)
Pt(2)	0.63613(3)	0.19173(3)	0.99382(3)	1.22(3)
O(1W)	0.9481(7)	0.2156(7)	0.5128(7)	3.6(5)
O(1A)	0.3581(6)	0.4290(6)	1.0022(6)	1.7(4)
O(1B)	0.6637(6)	0.0576(5)	1.1086(6)	1.5(4)
O(2W)	0.1299(7)	0.6652(7)	0.7392(7)	3.3(5)
O(2A)	0.2038(7)	0.3474(6)	0.5838(7)	2.4(5)
O(2B)	0.8046(6)	0.0775(5)	0.7996(6)	1.7(4)
O(3W)	0.8023(7)	0.2719(6)	0.6864(7)	2.8(5)
O(3A)	0.2158(7)	0.5817(6)	1.0703(8)	3.0(5)
O(3B)	0.8025(6)	−0.0815(6)	1.2777(6)	1.8(4)
O(11)	0.6525(8)	0.1883(7)	0.4018(8)	3.3(5)
O(12)	0.5377(7)	0.2203(6)	0.5307(6)	2.3(5)
O(13)	0.4519(8)	0.3241(6)	0.3346(7)	2.7(5)
O(21)	1.1620(7)	0.1846(7)	0.9975(8)	3.5(5)
O(22)	1.0855(7)	0.2881(6)	1.1561(7)	3.3(5)
O(23)	1.0173(7)	0.1630(6)	1.0378(8)	3.2(5)
N(1O)	0.549(1)	0.2436(8)	0.4248(9)	2.4(6)
N(1A)	0.2784(8)	0.4571(7)	0.5238(8)	2.0(5)
N(1B)	0.7192(7)	−0.0410(6)	0.6697(7)	1.5(5)
N(2O)	1.0830(8)	0.2164(7)	1.0526(9)	1.8(5)
N(2A)	0.1810(7)	0.3494(7)	0.8398(8)	2.1(5)
N(2B)	0.8493(8)	0.1005(7)	1.0901(8)	1.8(5)
N(3A)	0.3895(7)	0.3510(7)	0.7422(7)	1.6(5)
N(3B)	0.6237(7)	0.0904(7)	0.8224(7)	1.5(5)
N(4A)	0.5988(8)	0.3254(6)	0.8794(8)	1.5(5)
N(4B)	0.4217(7)	0.1252(7)	0.8098(8)	1.4(5)
N(5A)	0.4030(7)	0.2005(7)	1.0760(7)	1.6(5)
N(5B)	0.6386(8)	0.2963(8)	1.1627(8)	2.1(5)
C(1A)	0.247(1)	0.4880(8)	1.007(1)	2.1(7)
C(1B)	0.780(1)	−0.0043(9)	1.200(1)	1.6(6)
C(2A)	0.286(1)	0.3825(9)	0.617(1)	2.0(6)
C(2B)	0.720(1)	0.0466(8)	0.766(1)	1.4(6)
C(3A)	0.143(1)	0.445(1)	0.936(1)	2.4(6)
C(3B)	0.886(1)	0.030(1)	1.214(1)	2.1(6)
C(4A)	0.489(1)	0.3767(8)	0.768(1)	1.6(6)
C(4B)	0.5209(8)	0.0632(8)	0.7694(9)	1.0(5)
C(5A)	0.475(1)	0.4609(8)	0.677(1)	1.6(6)
C(5B)	0.529(1)	−0.0322(8)	0.6782(9)	1.3(6)
C(6A)	0.369(1)	0.4973(8)	0.557(1)	1.8(6)
C(6B)	0.6279(9)	−0.0822(8)	0.6309(9)	1.4(6)
C(7A)	0.170(1)	0.488(1)	0.388(1)	3.0(7)
C(7B)	0.816(1)	−0.0856(9)	0.601(1)	2.0(6)

hydrogen atoms including those of the solvent water molecules were located from difference Fourier maps and included in calculations without refinement. The final difference map was featureless, the highest peak being 0.89 e/Å^3.

Experimental details of the X-ray data collection, the structure solution, and refinement as well as crystal data for **6** are compiled in Table 1. Final atomic coordinates and equivalent isotropic temperature factors are given in Table 2. The anisotropic thermal parameters are included in the supplementary material.

Results and Discussion

Precursor *trans*-Pt(NH$_3$)(1-MeC)I$_2$ (4). The original preparation of *trans*-Pt(NH$_3$)(1-MeC)Cl$_2$·0.5H$_2$O (**3**) proceeded in low or moderate yields only.[2] By taking advantage of the higher kinetic *trans* effect of I$^-$ over Cl$^-$, reaction of *cis*-[(NH$_3$)$_2$Pt(1-MeC)Cl]Cl (**1**) with excess I$^-$ and in the presence of H$^+$ (to avoid back-reaction of NH$_3$) gave the iodo analogue of **3**, *trans*-Pt(NH$_3$)(1-MeC)I$_2$, **4**, in good yield (eq 3).

$$cis\text{-}[(NH_3)_2Pt(1\text{-}MeC)Cl]Cl + H^+ \xrightarrow[-2KCl]{+2KI} trans\text{-}Pt(NH_3)(1\text{-}MeCl)I_2 + NH_4^+ \quad (3)$$

In the absence of H$^+$ and at room temperature, simple halogen exchange (Cl$^-$ vs I$^-$) takes place with formation of *cis*-[(NH$_3$)$_2$Pt(1-MeC)I]I·H$_2$O (**2**). **4** was isolated as orange-yellow needles and characterized by elemental analysis and IR spectroscopy. With the exception of the 3600−3500 cm^{-1} region (ν_{OH} of **3**) and the region below 350 cm^{-1} (bands at 340 and 315 cm^{-1} for **3**; absence of these bands in the spectrum of **4**), the IR spectra of **3** and **4** are largely superimposable.

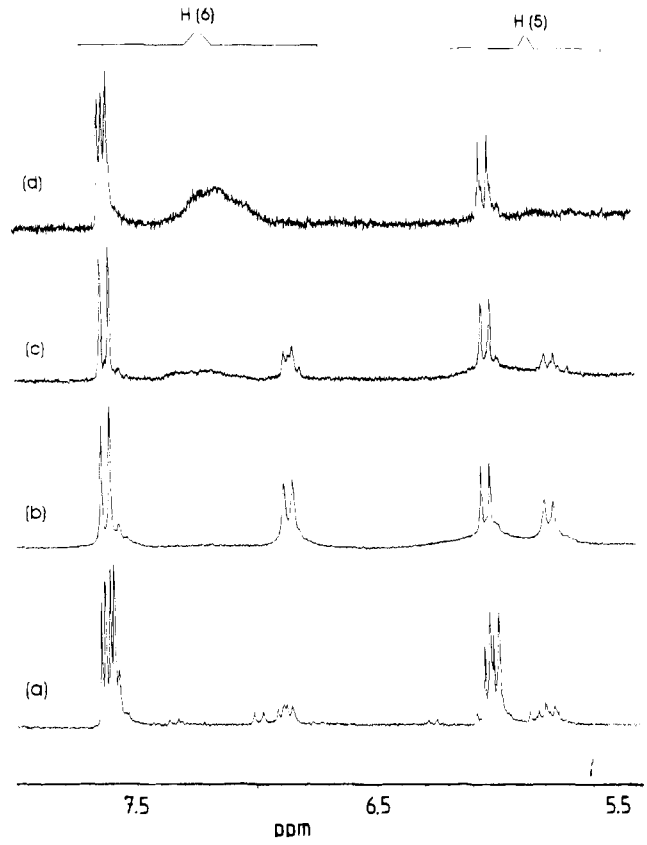
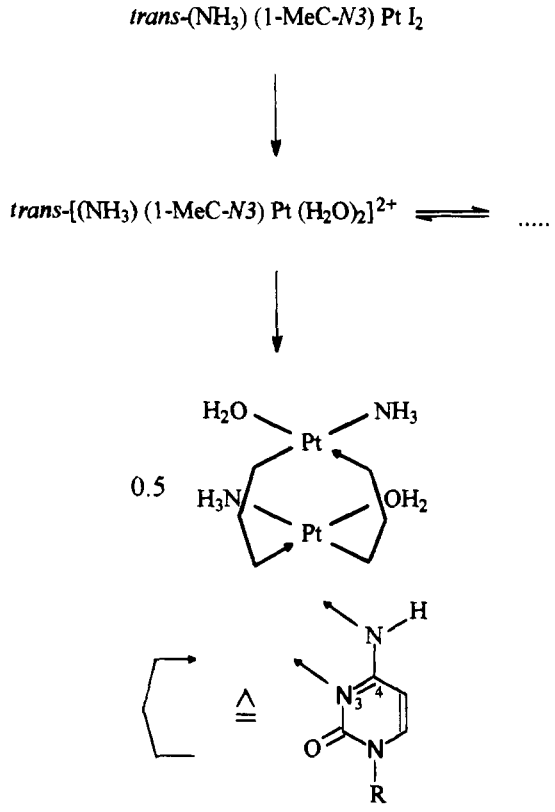


Figure 1. Sections of ^{1}H NMR spectra (D$_2$O): (a) "diaqua" species of **4**, pD 2.5, after addition of AgNO$_3$, 22 °C, light excluded, I$^-$ abstraction not complete yet, yellow solution; (b) "diaqua" species of **4**, 21 h after spectrum a, pD 2.4 (sample dark purple; more AgI removed by centrifugation); (c) aged "diaqua" species of **4**, 8 d after spectrum b, pD 2.3; (d) aged "diaqua" species of **4**, 8 d after spectrum c. There is partial isotopic exchange at C(5), leading to a third H(6) singlet in the center of the sharp H(6) doublet. The broad H(6) resonance centered at ca. 7.2 ppm (spectra c and d) is assigned to oligomeric species (cf Figures 6 and 7).

Diaqua Species of 4. Iodide abstraction from **4** by means of AgNO$_3$ initially gives the diaqua species *trans*-[Pt(NH$_3$)(1-MeC)(H$_2$O)$_2$]$^{2+}$, in equilibrium with possible OH and μ-OH species. Neither of these species has been isolated. According to ^{1}H NMR spectroscopy, new doublets of the H(5) and H(6) protons of cytosine ligands appear upfield, at 5.76 and 6.85 ppm, respectively (Figure 1). This shift is characteristic of a deprotonated 1-methylcytosine (1-MeC$^-$) with metals coordinated at both N(3) and the monodeprotonated N(4) positions.[13,14] Unambiguous proof, e.g. by ^{195}Pt coupling,[13] was not obtained due to use of a 200 MHz NMR spectrometer, which did not allow the ^{195}Pt satellites to be detected. At a concentration applied in the NMR experiment (ca. 0.05 mol/L), ca. 40% of the monomer have dimerized within 1 d at room temperature. The pH of a freshly prepared diaqua solution is fairly low, pH ca. 2 (pD 2.4). Since no 1-MeC resonances are observed that could be assigned to a species having *one* bridging 1-MeC$^-$ and *one* terminal 1-MeC ligand, it is concluded that a dinuclear compound having two 1-MeC$^-$ ligands has formed. In agreement with the structure of the mixed glycine, 1-MeC$^-$ compound

(13) Lippert, B. *Gazz. Chim. Ital.* **1988**, *118*, 153.
(14) (a) Krumm, M.; Zangrando, E.; Randaccio, L.; Menzer, S.; Lippert, B. *Inorg. Chem.* **1993**, *32*, 700. (b) Krumm, M.; Zangrando, E.; Randaccio, L.; Menzer, S.; Danzmann, A.; Holthenrich, D.; Lippert, B. *Inorg. Chem.* **1993**, *32*, 2183.

Scheme 1



6 (*vide infra*), the following condensation reaction takes place:

$$2\ trans\text{-}[Pt(NH_3)(1\text{-}MeC)(H_2O)_2]^{2+} \rightarrow [Pt_2(NH_3)_2(1\text{-}MeC^-)_2(H_2O)_2]^{2+} + 2H_3O^+ \quad (4)$$

The dinuclear complex **5** has the two 1-methylcytosinato ligands in a *cis*-arrangement with mutual *head–tail* orientation (Scheme 1).

Parallel to formation of **5** or following it, an intensely colored purple (λ_{max} 516 nm; ca. 630 nm) species **5′** develops which, as evident from its EPR spectrum ($g_\perp$, 2.38; $g_\parallel$, 1.98), is paramagnetic (supplementary material). The purple species forms in a matter of hours.

Reaction of Diaqua Species with Glycine. Addition of the amino acid glycine (gly) to the diaqua species of **4** (*trans*-[Pt(NH$_3$)(1-MeC-*N3*)(H$_2$O)$_2$]$^{2+}$) leads to products that differ depending on the experimental procedure. (i) If gly is added in excess to **4** prior to iodide abstraction by Ag^+, neither formation of a condensation product is seen in the ^{1}H NMR, nor is there any development of color. This clearly tells that glycine displaces the aqua ligands, forming the mononuclear mixed glycine–cytosine complex *trans*-(gly)$_2$Pt(1-MeC-*N3*)(NH$_3$). The stoichiometry (two gly vs one 1-MeC) is evident from relative ^{1}H NMR intensities and NH_2 coordination of gly from ^{195}Pt coupling ($^3J \cong 35$ Hz) with gly-CH_2. Moreover, the pH dependence of this resonance (protonation with $pK_a \cong 2.8$) is consistent with NH_2 binding.[15] (ii) If glycine (2–3 equiv per Pt) is added during the condensation reaction (Figure 2), the following features are seen in the ^{1}H NMR spectra: First, H(5) and H(6) resonances of the (presumably monomeric) aqua species become more complex, suggesting coordination of gly. Second, resonances due to the *head–tail* Pt(II) dimer **5** (Scheme 1) gradually diminish. Third, as the Pt(II) dimer resonances diminish, resonances due to the diplatinum(III) complex **6** appear

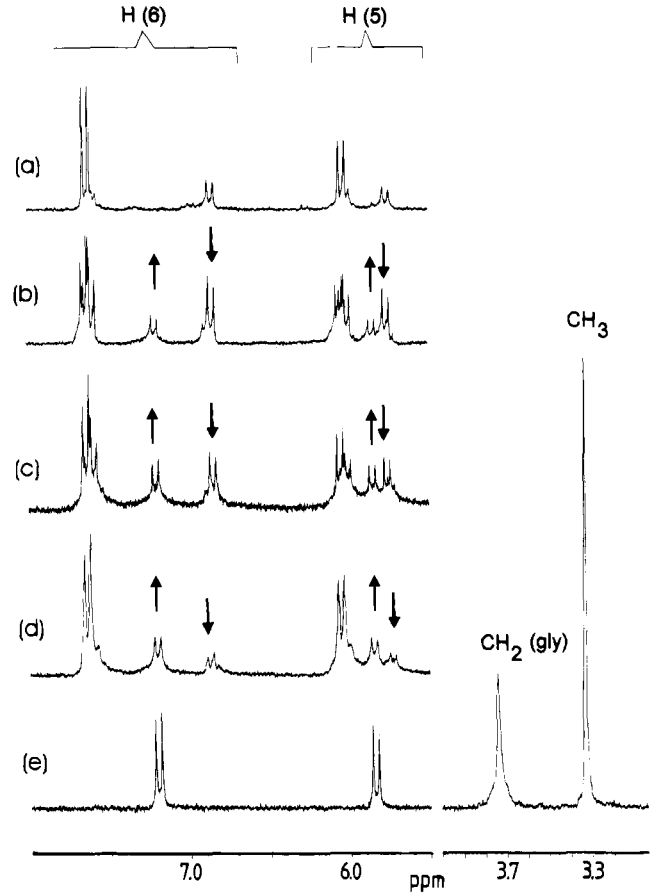


Figure 2. Sections of ^{1}H NMR spectra (D_2O): (a) mixture of species of **4** and dinuclear **5**, pD 2.0; (b) mixture a after addition of excess gly, 1 d, 22 °C, pD 3.7; (c) mixture b after 2 d, pD 3.6; (d) mixture b after 6 d at 22 °C and 17 h at 40 °C; (e) isolated **6**, pD 7.4. The appearance (↑) of 1-MeC$^-$ resonances of the diplatinum(III) complex **6** at the expense of **5** (↓) is indicated.

downfield from the former. Conversion of the diplatinum(II) species to the diplatinum(III) complex, which is accompanied by a slight drop in pH (from ca. 3.5 to ca. 3), is complete within 7–8 d at room temperature. No oxidant had been added, but O_2 was not rigorously excluded either (stoppered NMR tube and evaporation in air, respectively). Depending on the time of addition of glycine to the aged "diaqua" species **4** (still yellow or already purple), the solution from which **6** (and likewise **7**) is isolated stays either (greenish-)yellow or faint purple. In any case, the typical intense purple color of an aged "diaqua" species **4** is not reached in the presence of excess amino acid.

NMR Spectra of Isolated 6. The proton-decoupled ^{195}Pt NMR spectrum (D_2O, pD 6.8) consists of a single resonance at −506 ppm. The position of this resonance is roughly in a shift range intermediate between typical complexes of Pt(IV) and Pt(II),[16] thereby supporting the +III oxidation state of platinum. The ^{1}H NMR spectrum of **6** in D_2O (pD 7.45) is very simple (Figure 2e): H(5) and H(6) doublets of the 1-MeC$^-$ ligands are observed at 7.20 and 5.84 ppm, respectively, with ^3J being 7.6 Hz. The CH_3 singlet is at 3.33 ppm and CH_2 of gly at 3.83 ppm. The latter displays unresolved ^{195}Pt satellites of ca. 17 Hz. While ^{195}Pt coupling of the aromatic cytosine protons is not seen in the ^{1}H NMR spectrum recorded at 200 MHz,[17] a

(15) Schwarz, F.; Lippert, B.; Iakovidis, A.; Hadjiliadis, N. *Inorg. Chim. Acta* **1990**, *168*, 275.

(16) (a) Pregosin, P. S. *Annu. Rep. NMR Spectrosc.* **1986**, *17*, 285. (b) Ismail, I. M.; Sadler, P. J. In *Platinum, Gold, and Other Metal Chemotherapeutic Agents*; Lippard, S. J., Ed.; ACS Symposium Series 209; American Chemical Society: Washington, DC, 1983; pp 171–190.

(17) Lallemand, J.-Y.; Soulie, J.; Chottard, J.-C. *J. Chem. Soc., Chem. Commun.* **1980**, 438.

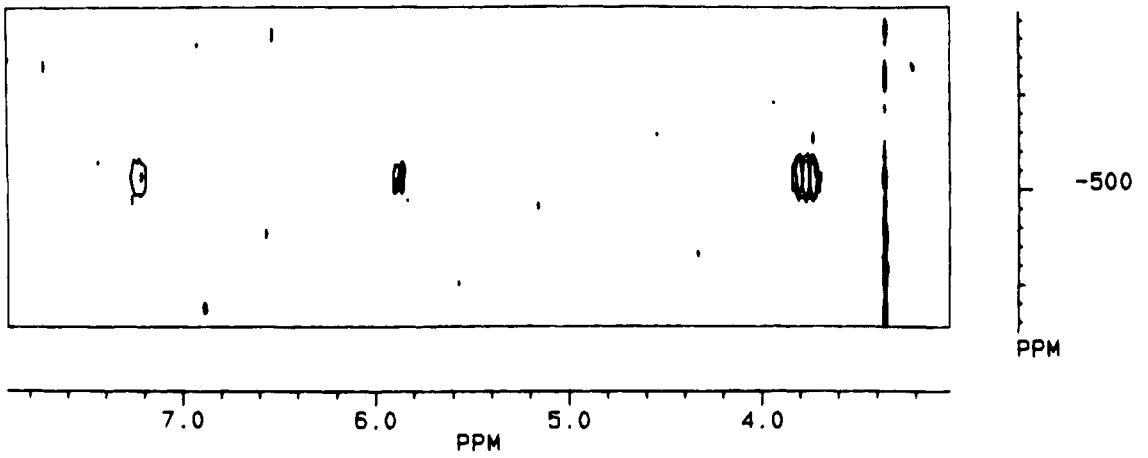


Figure 3. ^{1}H, ^{195}Pt HMQC spectrum of **6** in D_2O, indicating ^{195}Pt coupling with cytosine H(5), H(6) and glycine CH_2.

^{195}Pt−^{1}H correlation clearly establishes coupling of ^{195}Pt to *both* H(5) and H(6) in addition to CH_2 of gly (Figure 3). Coupling to both cytosine protons unambiguously verifies a dinuclear structure with cytosinate binding to Pt via N(3) and N(4) also in solution.[13] With N(3) coordination, *only* coupling to H(5) is observed[2,8,18] whereas, with N(4) coordination, *only* coupling to H(6) is observed.[19] The magnitude of the coupling constants of **6** (^4J(^{195}Pt−H(5)), 5.5 Hz; ^5J(^{195}Pt−H(6)), 5.7 Hz), as determined in a HMQC experiment, is clearly smaller than in the case of the related diplatinum(II) *head−tail* complex *cis*-$[NH_3)_2Pt(1\text{-}MeC^-)_2Pt(NH_3)_2]^{2+}$,[13] consistent with a higher Pt oxidation state in **6**.[20] Similarly, coupling of gly-CH_2 with the ^{195}Pt isotope in **6** is clearly reduced (17 Hz) as compared to typical Pt(II) gly compounds (see preceding paragraph).

Solution Behavior of 6. The aqueous solution chemistry of diplatinum(III) species derived from *cis*-(amine)$_2$Pt^{II} and cyclic amides (1-methyluracil,[21] α-pyridone,[22,23] α-pyrrolidone[24]) is dominated by fast ligand exchange reactions, involving primarily the axial ligands, but occasionally even equatorial ammine ligands,[21b] as well as rapid reduction unless the pH is kept very low. In this respect, **6** is unique in that pH-dependent ^{1}H NMR spectra in the range 3 < pD < 9 do not indicate any (fast) decomposition reaction. As a matter of fact, **6** remains unchanged at pH 9 at room temperature for at least 8 d (experiment stopped then). We tentatively assign this feature to the fact that the chelating amino acid makes the diplatinum(III) compound much more inert toward axial substitution reactions and effectively reduces the redox potential to an extent where water oxidation and concomitant reduction to mixed-valence and eventually diplatinum(II) species is prevented. The ease of formation of **6** at pH 3−4 clearly supports this view and contrasts the rather harsh conditions (strongly acidic pH; fairly strong oxidizing agents such as concentrated HNO_3, Ce(IV)/H_2SO_4, Cl_2, etc.) usually necessary to prepare diplatinum(III) compounds. We propose that the chelating function of the amino acid accounts for this fact: Initial O binding of gly via H_2O substitution at the diplatinum(II) precursor facilitates subsequent N-binding via the axial position, thereby "forcing" Pt(II) to adopt a higher coordination number and to lower the redox potential. There was no particular reason to use amino acids in our experiments, except that we were interested in ternary metal/nucleobase/amino acid complexes. Work is underway to determine whether chelating ligands in general show this effect.

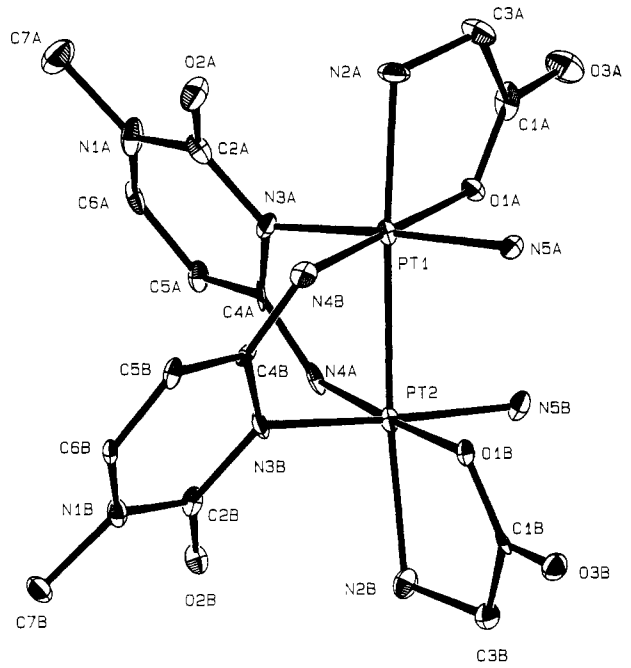


Figure 4. View and atom-numbering scheme of the cation of $[Pt_2(NH_3)_2(1\text{-}MeC^-N3,N4)_2(gly\text{-}N,O)_2](NO_3)_2{\cdot}3H_2O$ (*head−tail*) (**6**).

Description of Crystal Structure of 6. The dinuclear cation of $[Pt_2(NH_3)_2(1\text{-}MeC^-\text{-}N3,N4)_2(gly\text{-}N,O)_2](NO_3)_2{\cdot}3H_2O$ (**6**) is depicted in Figure 4. Selected interatomic distances and angles are given in Table 3. The two Pt ions are bridged by two 1-methylcytosinato ligands (1-MeC$^-$) in a *head−tail* fashion via N(3) and N(4) sites. The coordination sphere of each Pt is completed by an equatorial ammine ligand as well as a chelating glycinate ion which binds equatorially via a carboxylate oxygen and axially via the amino group. There is a short Pt−Pt bond of 2.527(1) Å. This bond is shorter than in a structurally related

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(19) (19) Lippert, B.; Schöllhorn, H.; Thewalt, U. *J. Am. Chem. Soc.* **1986**, *108*, 6616.
(20) Pregosin, P. S.; Omura, H.; Venanzi, L. M. *J. Am. Chem. Soc.* **1973**, *95*, 2047.
(21) (a) Lippert, B.; Schöllhorn, H.; Thewalt, U. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1983**, *38B*, 1441. (b) Lippert, B.; Schöllhorn, H.; Thewalt, U. *Inorg. Chem.* **1986**, *25*, 407. (c) Lippert, B.; Schöllhorn, H.; Thewalt, U. *J. Am. Chem. Soc.* **1986**, *108*, 525. (d) Schöllhorn, H.; Eisenmann, P.; Thewalt U.; Lippert, B. *Inorg. Chem.* **1986**, *25*, 3384. (e) Lippert, B. *New. J. Chem.* **1988**, *12*, 715. (f) Trötscher, G.; Micklitz, W.; Schöllhorn, H.; Thewalt, U.; Lippert, B. *Inorg. Chem.* **1990**, *29*, 2541.
(22) (a) Hollis, L. S.; Lippard, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 6761. (b) Hollis, L. S.; Lippard, S. J. *Inorg. Chem.* **1982**, *21*, 2116. (c) O'Halloran, T. V.; Roberts, M. M.; Lippard, S. J. *Inorg. Chem.* **1986**, *25*, 957.
(23) Matsumoto, K. Personal communication.
(24) (a) Matsumoto, K.; Watanabe, T. *J. Am. Chem. Soc.* **1986**, *108*, 1308. (b) Abe, T.; Moriyama, H.; Matsumoto, K. *Inorg. Chem.* **1991**, *30*, 4198. (c) Matsumoto, K.; Harashima, K. *Inorg. Chem.* **1991**, *30*, 3032.

Table 3. Selected Bond Lengths (Å) and Angles (deg) in **6**

Pt(1)−Pt(2)	2.527(1)	O(23)−N(20)	1.25(1)
Pt(1)−O(1A)	2.025(6)	N(1A)−C(2A)	1.40(1)
Pt(1)−N(2A)	2.159(8)	N(1A)−C(6A)	1.36(1)
Pt(1)−N(3A)	2.040(8)	N(1A)−C(7A)	1.46(1)
Pt(1)−N(4B)	1.956(7)	N(1B)−C(2B)	1.39(1)
Pt(1)−N(5A)	2.044(8)	N(1B)−C(6B)	1.37(1)
Pt(2)−O(1B)	2.045(6)	N(1B)−C(7B)	1.48(1)
Pt(2)−N(2B)	2.187(8)	N(2A)−C(3A)	1.48(1)
Pt(2)−N(3B)	2.034(7)	N(2B)−C(3B)	1.46(1)
Pt(2)−N(4A)	1.986(8)	N(3A)−C(2A)	1.36(1)
Pt(2)−N(5B)	2.035(8)	N(3A)−C(4A)	1.35(1)
O(1A)−C(1A)	1.25(1)	N(3B)−C(2B)	1.38(1)
O(1B)−C(1B)	1.30(1)	N(3B)−C(4B)	1.37(1)
O(2A)−C(2A)	1.21(1)	N(4A)−C(4A)	1.33(1)
O(2B)−C(2B)	1.21(1)	N(4B)−C(4B)	1.31(1)
O(3A)−C(1A)	1.24(1)	C(1A)−C(3A)	1.53(1)
O(3B)−C(1B)	1.22(1)	C(1B)−C(3B)	1.53(1)
O(11)−N(10)	1.25(1)	C(4A)−C(5A)	1.43(1)
O(12)−N(10)	1.24(1)	C(4B)−C(5B)	1.42(1)
O(13)−N(10)	1.28(1)	C(5A)−C(6A)	1.34(1)
O(21)−N(20)	1.20(1)	C(5B)−C(6B)	1.34(1)
O(22)−N(20)	1.30(1)		

Pt(2)−Pt(1)−O(1A)	96.1(2)	C(2B)−N(1B)−C(6B)	122.3(8)
Pt(2)−Pt(1)−N(2A)	176.6(2)	C(2B)−N(1B)−C(7B)	118.4(8)
Pt(2)−Pt(1)−N(3A)	85.7(2)	C(6B)−N(1B)−C(7B)	119.2(7)
Pt(2)−Pt(1)−N(4B)	83.9(2)	O(21)−N(20)−O(22)	120.5(9)
Pt(2)−Pt(1)−N(5A)	90.8(2)	O(21)−N(20)−O(23)	121.4(9)
O(1A)−Pt(1)−N(2A)	81.3(3)	O(22)−N(20)−O(23)	116.0(7)
O(1A)−Pt(1)−N(3A)	88.0(3)	Pt(1)−N(2A)−C(3A)	106.8(6)
O(1A)−Pt(1)−N(4B)	179.8(3)	Pt(2)−N(2B)−C(3B)	108.6(6)
O(1A)−Pt(1)−N(5A)	89.8(3)	Pt(1)−N(3A)−C(2A)	120.2(6)
N(2A)−Pt(1)−N(3A)	96.4(3)	Pt(1)−N(3A)−C(4A)	117.6(6)
N(2A)−Pt(1)−N(4B)	98.7(3)	C(2A)−N(3A)−C(4A)	122.0(8)
N(2A)−Pt(1)−N(5A)	87.0(3)	Pt(2)−N(3B)−C(2B)	120.3(6)
N(3A)−Pt(1)−N(4B)	92.2(3)	Pt(2)−N(3B)−C(4B)	118.1(6)
N(3A)−Pt(1)−N(5A)	175.7(3)	C(2B)−N(3B)−C(4B)	121.5(8)
N(4B)−Pt(1)−N(5A)	90.0(3)	Pt(1)−N(4B)−C(4B)	124.8(6)
Pt(1)−Pt(2)−O(1B)	92.5(2)	O(1A)−C(1A)−O(3A)	123(1)
Pt(1)−Pt(2)−N(2B)	171.3(2)	O(1A)−C(1A)−C(3A)	119.9(8)
Pt(1)−Pt(2)−N(3B)	85.1(2)	O(3A)−C(1A)−C(3A)	117(1)
Pt(1)−Pt(2)−N(4A)	84.3(2)	O(1B)−C(1B)−O(3B)	122.5(9)
Pt(1)−Pt(2)−N(5B)	92.0(2)	O(1B)−C(1B)−C(3B)	116.8(9)
O(1B)−Pt(2)−N(2B)	78.8(3)	O(3B)−C(1B)−C(3B)	120.6(8)
O(1B)−Pt(2)−N(3B)	88.5(3)	O(2A)−C(2A)−N(1A)	120(1)
O(1B)−Pt(2)−N(4A)	176.8(3)	O(2A)−C(2A)−N(3A)	123(1)
O(1B)−Pt(2)−N(5B)	91.4(3)	N(1A)−C(2A)−N(3A)	117(1)
N(2B)−Pt(2)−N(3B)	95.0(3)	O(2B)−C(2B)−N(1B)	119.6(8)
N(2B)−Pt(2)−N(4A)	104.4(3)	O(2B)−C(2B)−N(3B)	123.7(9)
Pt(2)−N(4A)−C(4A)	123.0(6)	N(1B)−C(2B)−N(3B)	116.7(9)
N(2B)−Pt(2)−N(5B)	87.8(3)	N(2A)−C(3A)−C(1A)	111.6(8)
N(3B)−Pt(2)−N(4A)	91.4(3)	N(2B)−C(3B)−C(1B)	111.4(8)
N(3B)−Pt(2)−N(5B)	177.1(3)	N(3A)−C(4A)−N(4A)	119.6(8)
N(4A)−Pt(2)−N(5B)	88.5(3)	N(3A)−C(4A)−C(5A)	119.5(8)
Pt(1)−O(1A)−C(1A)	116.2(6)	N(4A)−C(4A)−C(5A)	120.9(9)
Pt(2)−O(1B)−C(1B)	118.5(6)	N(3B)−C(4B)−N(4B)	117.5(8)
O(11)−N(10)−O(12)	121.8(9)	N(3B)−C(4B)−C(5B)	118.7(8)
O(11)−N(10)−O(13)	118.5(8)	N(4B)−C(4B)−C(5B)	123.7(8)
O(12)−N(10)−O(13)	119.7(9)	C(4A)−C(5A)−C(6A)	117.6(9)
C(2A)−N(1A)−C(6A)	121.8(8)	C(4B)−C(5B)−C(6B)	119.2(8)
C(2A)−N(1A)−C(7A)	116.9(9)	N(1)A)−C(6A)−C(5A)	121.2(9)
C(6A)−N(1A)−C(7A)	121.3(8)	N(1B)−C(6B)−C(5B)	120.2(8)

diplatinum(III) compound containing two bridging 1-MeC$^-$ entities, $[(NO_2)Pt(NH_3)_2(1\text{-}MeC^-)_2Pt(NH_3)_2(NO_2)](NO_3)_2{\cdot}2H_2O$ (2.584(1) Å),[25] and the shortest one of all X-ray structurally characterized diplatinum(III) complexes containing bridging 1-methyluracilato bases.[18] In fact, it appears to be the shortest one reported for any diplatinum(III) complex containing a bridging amidate ligand.[22,24,26] The shortness of this bond is, partially or fully, due to the weak *trans*-influence of the axial NH_2−R ligands. Pt(1)−N(2A) (2.159(8) Å) and Pt(2)−N(2B) (2.187(8) Å) bond lengths are significantly longer as compared to those found in glycine complexes of Pt(II)[27] and also substantially longer than the equatorial Pt−N bonds, which are normal. Angles about the Pt centers deviate in most cases from ideal 90°. Deviation is largest for the chelate bite angle of gly which is 81.3(3)° for Pt(1) and 78.8(3)° for Pt(2). However, a similar situation is seen in gly chelates of Pt(II).[28]

Both Pt atoms are essentially within the equatorial coordination planes defined by N(3), N(4), N(5), and O(1), deviations being −0.03 Å (Pt(1)) and +0.05 Å (Pt(2)). These planes are tilted only slightly (10.8°), but the twist angle about the Pt−Pt vector is substantial, −66.5(3)° for N(5A)−Pt(1)−Pt(2)−N(5B). Dihedral angles between the equatorial Pt coordination planes and the N(3)-bound 1-MeC$^-$ ligands are 69.02° (Pt(1)) and 66.48° (Pt(2)), and that between the two cytosinato rings is 79.4°. While deviations of N(4)-bound Pt atoms from the 1-MeC$^-$ planes are not unexpected, deviations of the N(3)-bound Pt's are also substantial; e.g., Pt(1) is out of ring A by −0.51 Å and Pt(2) is out of ring B by 0.47 Å.

Within the crystal lattice, dinuclear cations are well separated from each other (supplementary material). Unusually short H bonds are not observed. The shortest H bonds (2.79(1) and 2.81(1) Å) exist between water molecules or between water molecules and atoms of the diplatinum(III) complex; e.g. O(2B)···O(3W) = 2.88(1) Å.

Reaction of Diaqua Species with Alanine. Reaction of an aged solution of the diaqua species of **4** (with condensation to diplatinum(II) species having occurred) with L-alanine is qualitatively similar to that of the glycine (supplementary material). There is, however, an important difference: All ^{1}H NMR resonances of the diplatinum(III) complex $[Pt_2(NH_3)_2(1\text{-}MeC^-\text{-}N3,N4)_2(L\text{-}ala\text{-}N,O)_2](NO_3)_2{\cdot}5H_2O$ (**7**) are doubled (Figure 5). This feature is due to the fact that the *head−tail* arrangement of the two nucleobases, which makes the diplatinum complex chiral, when reacted with a chiral amino acid such as L-alanine, leads to formation of a pair of diastereomers. Although we have not been able as yet to obtain crystals suitable for X-ray crystallography, models of the two diastereomers clearly confirm this view.

Relevance of 5 to Oligomerization and Formation of "Platinum Cytosine Blue". As demonstrated in this work, monomeric *trans*-$[Pt(NH_3)(1\text{-}MeC)(H_2O)_2]^{2+}$ spontaneously dimerizes with deprotonation of the exocyclic amino group of cytosine (eq 4) and formation of a bis(μ-1-methylcytosinato-*N3,N4*)-bridged species **5**. While the postulated dinuclear *head−tail* complex **5** has not been isolated, its existence is reasonable considering the composition of the amino acid derivatives **6** and **7**. Formation of **5** is accompanied by formation of an intensely colored species **5′**, which is paramagnetic according to EPR spectroscopy and therefore displays features typical of "platinum pyrimidine blues".[29,30] The only X-ray structurally characterized Pt blue containing a pyrimidine

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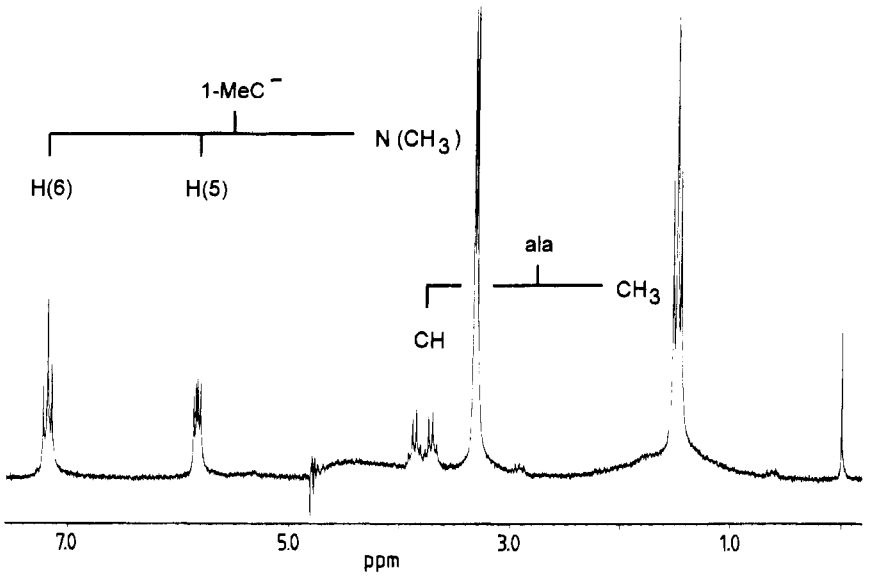

Figure 5. ^{1}H NMR spectrum (D_2O, pD 8.6) of $[Pt_2(NH_3)_2(1\text{-}MeC^-\text{-}N3,N4)_2(\text{L-ala-}N,O)_2]^{2+}$ (**7**). All resonances are doubled as a consequence of the existence of **7** as a pair of diastereomers. The water resonance has been suppressed.

nucleobase is that of 1-methyluracil,[31] which is of a composition similar to that of blues containing other cyclic amidates L,[32-34] viz. those consisting of a pair of *head–head* dimers of composition *cis*-$[(NH_3)_2PtL_2Pt(NH_3)_2]_2^{5+}$. Variations of this theme are feasible when halogen bridging is allowed.[35] A *head–tail* orientation of the two ligands L in a dinuclear complex derived from *cis*-(amine)$_2$Pt a priori excludes an analogous structure since it does not permit the close approach of two dimers necessary for partial metal oxidation.

Formation of tetra- or oligomeric species with strongly interacting Pt centers from **5** can be envisaged for (at least) the following conditions.

(i) Isomerization of the *Head–Tail* Dimer 5 to *Head–Head* and Subsequent Dimer-of-Dimer Stacking as in the Case of $[Pt^{2.25+}]_4$.[31-34] While such isomerization reactions have been observed in a few cases for *cis*-a_2Pt^{II} complexes containing cyclic amide ligands,[36,37] a similar reaction has never been observed by us with the *head–tail* dimer *cis*-$[(NH_3)_2Pt(1\text{-}MeC^-\text{-}N3,N4)_2Pt(NH_3)_2]^{2+}$.[38] For this reason, we consider such a possibility in the case of **5** less likely.

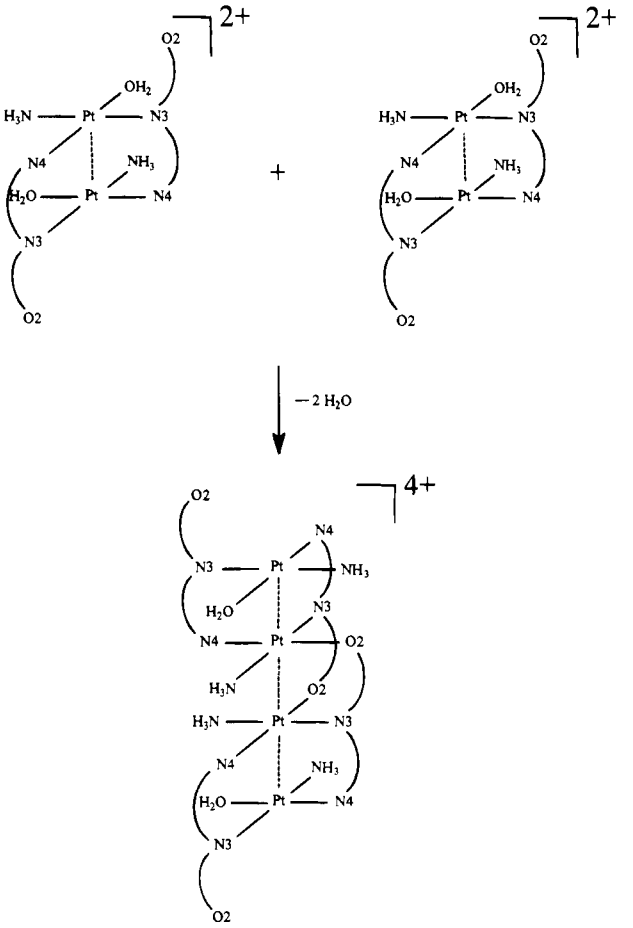

Figure 6. Hypothetical condensation of two dinuclear species **5** with H_2O molecules replaced by O(2) oxygens of 1-MeC$^-$ ligands. Condensation beyond the tetramer level (oligomerization) is possible. Subsequent partial oxidation could lead to paramagnetism and color formation (CT). The condensation principle requires *identical* enantiomers to combine. It is not possible to combine one enantiomer with its mirror image in the same fashion.

(ii) Involvement of O(2) of 1-MeC$^-$ in Pt Binding. The availability of two additional binding sites in **5** (two H_2O ligands) permits, in principle, easy stacking of *head–tail* dimers with the assumption that H_2O ligands are substituted by O(2) sites of 1-MeC$^-$ ligands (Figure 6); hence 1-MeC$^-$ can act as

(30) While most work on "Pt pyrimidine blues" has focused on uracil and thymine "blues" (or "greens" or "purples"), some limited work has been reported on "cytosine blues", e.g.: (a) Goodgame, D. M. L.; Jeeves, I. *Z. Naturforsch., C* **1979**, *34C*, 1287. (b) Ettore, R. *Inorg. Chim. Acta* **1980**, *46*, L27. (c) Zaplatynski, R.; Neubacher, H.; Lohmann, W. *Z. Naturforsch., B* **1979**, *34B*, 1466.

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(33) Matsumoto, K.; Takahashi, H.; Fuwa, K. *J. Am. Chem. Soc.* **1984**, *106*, 2049.

(34) With open amides, higher-nuclearity clusters have been prepared: (a) Sakai, K.; Matsumoto, K. *J. Am. Chem. Soc.* **1989**, *111*, 3074. (b) Sakai, K.; Matsumoto, K.; Nishio, K. *Chem. Lett.* **1991**, 1081. (c) Matsumoto, K.; Sakai, K.; Nishio, K.; Tokisue, Y.; Ito, R.; Nishide, T.; Shichi, Y. *J. Am. Chem. Soc.* **1992**, *114*, 8110.

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(36) O'Halloran, T. V.; Lippard, S. J. *Inorg. Chem.* **1989**, *28*, 1289.

(37) Matsumoto, K.; Miyamae, H.; Moriyama, H. *Inorg. Chem.* **1989**, *28*, 2959.

(38) The existence of a *head–head* dimer derived from enPd^{II} has been reported, however: Häring, U. K.; Martin, R. B. *Inorg. Chim. Acta* **1983**, *78*, 259.

a tridentate ligand. We consider this possibility realistic in that we have now, in a related system, found 1-MeC$^-$ to bind simultaneously three metal ions via N(3), the deprotonated N(4), and O(2).[39] Moreover, with the 1-methyluracilato anion, 1-MeU$^-$, which is isoelectronic with 1-MeC$^-$, we have previously shown that all three sites—N(3), O(4), O(2)—can be used simultaneously for metal binding.[40] If dinuclear entities **5** are combined accordingly, the coordination spheres of Pt atoms in a hypothetical oligomer are N(3), N(4), NH_3, and O(2) within the stack and N(3), N(4), NH_3, and H_2O at the ends. There are two (within stack) or one (end) additional Pt in the axial positions of each Pt. An important consequence of interlocking the chiral[41] dinuclear species **5** according to this fashion is that *only identical enantiomers* can combine, whereas different enantiomers *cannot*. Thus oligomerization of dinuclear **5** would produce two types of oligomers in 1:1 ratio which differ in the helix sense only.

There are several additional structural permutations to this theme feasible, all of which imply the use of O(2) of **5** as a third Pt binding site at 1-MeC$^-$. For example, dinuclear **5** can condense with its mononuclear precursor *trans*-[$(H_2O)_2$Pt(NH_3)-(1-MeC)]$^{2+}$ (**4**) at either side, leading to tri, tetra-, or higher oligomeric structures (Figure 7). The incoming mononuclear species could conceivably bind with deprotonation of its amino group (4) or even (without deprotonation) via O(2). Simultaneous N(3) and O(2) metal binding to neutral 1-MeC has been verified before.[42] Finally, if within an oligomeric structure built up of dinuclear **5**, ligand rotation about Pt—N(3) is allowed, and hence O(2) and N(4) become interchanged, variants of the oligomer can be constructed which differ in the orientations of the N(1)—CH_3 groups.

Summary

Loss of NH_3 from the Cisplatin—nucleobase adduct *cis*-[$(NH_3)_2$Pt(1-MeC-*N3*)Cl]$^+$ and subsequent halogen solvolysis give *trans*-[(NH_3)Pt(1-MeC-*N3*)]$(H_2O)_2]^{2+}$, a species that readily dimerizes to give [$(NH_3)(H_2O)$Pt(1-MeC$^-$-*N3,N4*)$_2$Pt(H_2O)-$(NH_3)]^{2+}$ (**5**). At the same time, a purple, presumably oligomeric mixed-valence Pt species forms. In the presence of amino acids (gly, L-ala), **5** spontaneously is converted into a mixed nucleobase—amino acid diplatinum(III) complex which, for glycine (**6**), has been isolated.

On the basis of the dinuclear complex **5**, a possible oligomerization process is proposed which, in the simplest case, consists of stacking of dinuclear entities **5** with H_2O molecules replaced by O(2) oxygens of 1-MeC$^-$ ligands. If realized, it would differ markedly from the well-established dimer-of-dimer pattern of blue tetranuclear $Pt^{2.25+}$ amidate complexes in the following points: First, a *head—tail* orientation of nucleobases within the dinuclear precursor is allowed rather than the *head—head* orientation required by the known $[Pt^{2.25+}]_4$ compounds. Second, loss of an ammonia ligand (*cis* to nucleobase) from Pt is necessary: Third, the resulting structure would be truly oligomeric and not limited to a tetranuclear structure as in the case of $[Pt^{2.25+}]_4$. These points apply, of course, also to uracil and thymine "blues" (involvement of N(3), O(4), and O(2)). We and others, in various instances,[2,21b,43,44] have observed amine loss from *cis*-(amine)$_2$Pt compounds. Specifically, we have detected NH_4^+ in typical preparations[29a] leading to Pt blues.[45]

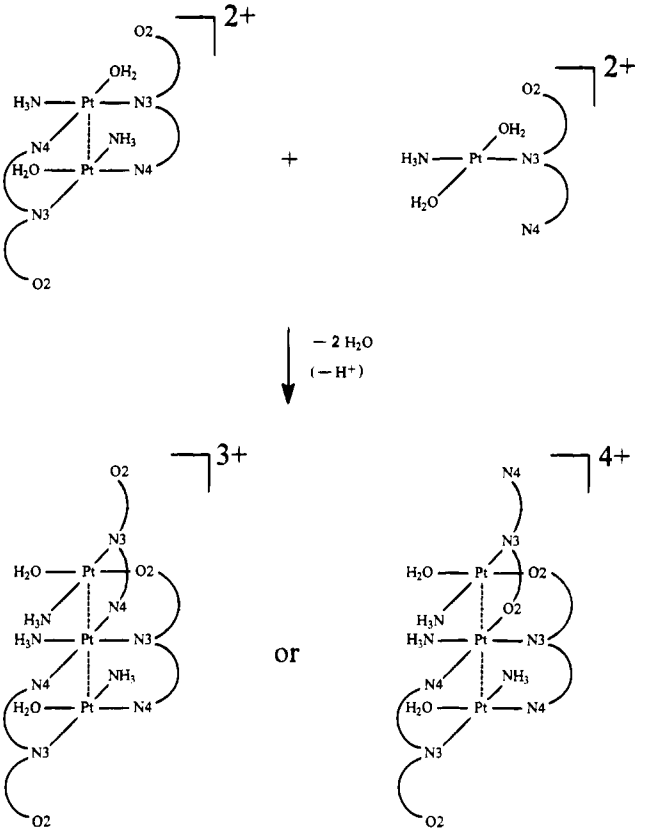

Figure 7. Hypothetical condensation of a dinuclear species **5** with a monomeric *trans*-[(NH_3)Pt(1-MeC-*N3*)$(H_2O)_2]^{2+}$ (**4**) species. The incoming monomer could replace the H_2O molecules of **5** by N(4) groups (deprotonated) or O(2) sites. Additional condensation reactions can take place at either end of the trinuclear species.

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Supplementary Material Available: Tables of anisotropic thermal displacement parameters, intermolecular distances, torsion and conformation angles, positional parameters for H atoms, and least-squares planes, a packing diagram of **6**, visible and EPR spectra for **5′**, and a figure showing the formation of **7** by ^{1}H NMR (15 pages). Ordering information is given on any current masthead page.

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