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Synthetic Ways to Tris(nucleobase) Complexes Derived from *cis*-Diammineplatinum(II) and a Platinum(II) Complex Containing Four Different Ligands, Three of Which Are Nucleobases

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Reactions of *cis*-[PtCl(L-$\underline{\text{N7}}$)(NH$_3$)$_2$]Cl (L = 9-ethylguanine, 9-EtGH, or 9-methyladenine, 9-MeA) with excess KI leads in slightly acidic solution to *trans*-PtI$_2$(L)(NH$_3$). Partial or complete substitution of the iodo ligands by aqua, chloro, or nucleobase ligands can be achieved and gives a series of neutral or cationic complexes. Among others, tris(nucleobase) complexes containing three different nucleobases (9-EtGH, 9-MeA, and 1-methylcytosine, 1-MeC), [Pt(1-MeC)(9-EtGH)(9-MeA)(NH$_3$)]$^{2+}$ with SP-4-3 and SP-4-4 configuration numbers have been prepared and the deprotonated form SP-4-4-[Pt(1-MeC-$\underline{\text{N3}}$)(9-EtG-$\underline{\text{N7}}$)(9-MeA-$\underline{\text{N7}}$)(NH$_3$)]NO$_3$·2H$_2$O (**7b**) has been X-ray structurally characterized: monoclinic system, space group *C*2/*c*, $a = 23.817(5)$ Å, $b = 10.992(2)$ Å, $c = 21.647(4)$ Å, $\beta = 112.07(3)°$, $V = 5251.9$ Å^3, $Z = 8$. Moreover, the X-ray crystal structure analyses of *trans*-PtCl$_2$(9-EtGH-$\underline{\text{N7}}$)(NH$_3$)·0.5H$_2$O (**4**) and *trans*-[Pt(1-MeC-$\underline{\text{N3}}$)$_2$(9-EtG-$\underline{\text{N7}}$)(NH$_3$)]NO$_3$·3H$_2$O (**6b**) are reported. **4**: triclinic system, space group $P\bar{1}$ (No. 2), $a = 11.557(3)$ Å, $b = 12.742(2)$ Å, $c = 8.880(2)$ Å, $\alpha = 96.95(1)°$, $\beta = 94.91(2)°$, $\gamma = 88.32(2)°$, $V = 1293.1(5)$ Å^3, $Z = 4$. **6b**: triclinic system, space group $P\bar{1}$ (No. 2), $a = 10.957(2)$ Å, $b = 11.022(2)$ Å, $c = 12.916(2)$ Å, $\alpha = 81.18(3)°$, $\beta = 89.93(3)°$, $\gamma = 64.22(3)°$, $V = 1384.2(5)$ Å^3, $Z = 2$. Relative orientations of the nucleobases in these compounds appear to be dictated by intranucleobase H bond formation.

Introduction

We have previously described a synthetic route for the preparation of *trans*-PtCl$_2$(1-MeC)(NH$_3$) (1-MeC = 1-methylcytosine) starting out from *cis*-[PtCl(1-MeC)(NH$_3$)$_2$]Cl[2] and its subsequent conversion into bis-[3] and tris(nucleobase) complexes[4] as well as dinuclear, 1-methylcytosinato-bridged species.[5] As we have shown,[5] the use of KI and slightly acidic reaction conditions greatly increases the yield of the trans complex, thereby making this reaction useful for subsequent preparative work. Applying the same principle to the purine base complexes

$$cis\text{-[PtCl(1-MeC)(NH}_3)_2]\text{Cl} + \text{H}^+ \xrightarrow[-\,2\,\text{KCl}]{+\,2\,\text{KI}} trans\text{-PtI}_2\text{(1-MeC)(NH}_3) + \text{NH}_4^{\ +}$$

cis-[PtCl(9-EtGH)(NH$_3$)$_2$]Cl and *cis*-[PtCl(9-MeAH)(NH$_3$)$_2$](NO$_3$)$_2$ (9-EtGH = 9-ethylguanine; 9-MeAH = 9-methyladeninium), we have now obtained a series of new bis- and tris(nucleobase) complexes of Pt(II), including an example containing three different nucleobases bound simultaneously to Pt: 9-EtGH, 9-MeA, and 1-MeC. As we have previously hypothesized,[2,4] in theory, any of these compounds could be derived from an initial mono(nucleobase) adduct of the antitumor agent Cisplatin. Whether or not biologically relevant, it should be noted that *trans*-PtCl$_2$(NH$_3$)$_2$ is not expected to behave analogously. Rather a maximum of two nucleobases is expected to be bound under normal circumstances. As will be shown in this study, any combination of three nucleobases bound to Pt can be prepared provided the proper starting compound and reaction sequence are chosen.

Experimental Section

Preparations. 9-Ethylguanine (9-EtGH) was purchased from Chemogen (Konstanz, Germany), adenine was purchased from Fluka and was methylated at the N9 position according to the published route.[6] *cis*-[PtCl(9-EtGH)(NH$_3$)$_2$]Cl (**1**) was obtained from *cis*-PtCl$_2$(NH$_3$)$_2$[7] upon reaction with 9-EtGH as described.[8] SP-4-3-[PtI(1-MeC)(9-EtGH)(NH$_3$)]NO$_3$·3.5H$_2$O was prepared as described.[3]

***trans*-PtI$_2$(9-EtGH)(NH$_3$)** (**2**) was prepared as follows: **1** (0.3 mmol) and KI (1.2 mmol) were dissolved in water (150 mL). HNO$_3$ was added dropwise to reach pH 2.0, and then the mixture was kept on a water bath at 40 °C. After 4 days brown crystals of **2** were filtered off and washed with water. The product was dried in air, the yield being about 89%. Anal. Calcd for *trans*-PtI$_2$(9-EtGH)(NH$_3$) (C$_7$H$_{12}$N$_6$OPtI$_2$): C, 13.0; H, 1.9; N, 13.0. Found: C, 12.8; H, 1.8; N, 13.1. IR spectrum (KBr): 3490 (m), 3413 (m), 3361 (m), 3268 (s), 1701 (s), 1627 (s), 1574 (s), 1471 (m), 1422 (m), 1342 (m), 1313 (m), 1293 (m), 1211

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(w), 1176 (m), 1160 (m), 882 (w), 774 (m), 713 (w), 689 (w), 565 (w), 484 (w), 409 (m) cm^{-1} (s, strong; m, medium; w, weak).

***cis*-[PtCl(9-MeAH)(NH$_3$)$_2$](NO$_3$)$_2$** (**1′**) was obtained from reaction of *cis*-PtCl$_2$(NH$_3$)$_2$ (0.5 mmol) and 9-MeA (0.75 mmol). The components were combined in 75 mL of water, and HNO$_3$ was added dropwise to reach pH 1. AgNO$_3$ (0.5 mmol), dissolved in 5 mL of water, was added, and the mixture was stirred for 6 days at 35 °C with light excluded. The mixture was subsequently cooled in an ice bath for 2 h. Then the AgCl was removed by filtration leading to a clear, colorless solution containing **1′**. According to ^{1}H NMR spectroscopy, obtained from a D$_2$O sample obtained in the same way, only the N7 linkage isomer is formed (cf. Results and Discussion).

***trans*-PtI$_2$(9-MeA)(NH$_3$)·0.5DMF** (**2′**) was prepared from the solution of **1′** in the following way: KI (2.0 mmol) was added, and the mixture was kept at 40 °C for 5 days. A dark brown precipitate was filtered off and washed with water. The precipitate was recrystallized from DMF and washed with acetone to give **2′** as an orange powder in 58% yield based on *cis*-PtCl$_2$(NH$_3$)$_2$. **2′** contains half a molecule of DMF per Pt according to elemental analysis and ^{1}H NMR data (DMSO-d_6). N7 coordination of the nucleobase is assumed because it is certain for compound **9**, which was prepared from **2′** (see below). Anal. Calcd for *trans*-PtI$_2$(9-MeA)(NH$_3$)·0.5DMF (C$_{7.5}$H$_{13.5}$N$_{6.5}$O$_{0.5}$PtI$_2$): C, 13.8; H, 2.1; N, 14.0. Found: C, 14.1; H, 2.1; N, 14.0. IR (KBr): 3385 (s), 3291 (m), 3100 (s), 1652 (s), 1594 (s), 1584 (s), 1534 (w), 1491 (m), 1436 (m), 1335 (w), 1305 (s), 1236 (m), 1184 (w), 1070 (w), 965 (w), 932 (w), 790 (m), 717 (w), 634 (w), 611 (m), 544 (w), 475 (m) cm^{-1}. Raman (solid state): 1582 (m), 1538 (w), 1362 (m), 1336 (s), 1309 (w), 1235 (m), 778 (m), 717 (s), 541 (m), 529 (m), 377 (s), 368 (m) cm^{-1}.

***trans*-[Pt(H$_2$O)$_2$(9-EtGH)(NH$_3$)](NO$_3$)$_2$** (**3**) was prepared by treatment of **2** (0.75 mmol) with AgNO$_3$ (1.5 mmol). The components were combined in 40 mL of water and were stirred for 24 h at room temperature with light excluded. The AgI was removed by filtration to give a clear, colorless solution of **3**.

***trans*-PtCl$_2$(9-EtGH)(NH$_3$)·0.5H$_2$O** (**4**) was obtained from **2** in the following way: To the solution of **3** was added a 5-fold excess of NaCl (3.75 mmol) and the colorless solution (pH 1.8) was stirred at 40 °C. After 3 days the solution was allowed to evaporate in air. Within 2 weeks yellow plates of **4** were obtained in 15% yield. Anal. Calcd for *trans*-PtCl$_2$(9-EtGH)(NH$_3$)·0.5H$_2$O (C$_7$H$_{13}$N$_6$O$_{1.5}$PtCl$_2$): C, 17.8; H, 2.8; N, 17.8. Found: C, 17.7; H, 2.7; N, 17.9. IR (KBr): 3428 (m), 3301 (s), 3200 (s), 3148 (m), 1682 (s), 1629 (s), 1600 (s), 1575 (s), 1545 (m), 1501 (m), 1425 (w), 1336 (m), 1257 (w), 1214 (w), 1182(m), 1092 (w), 1019 (w), 778 (m), 715 (m), 666 (w), 505 (m), 411 (w), 337 (m) cm^{-1}. Raman (solid state): 1684 (m), 1627 (w), 1599 (w), 1577 (s), 1502 (m), 1424 (w), 1399 (s), 1382 (m), 1355 (m), 1332 (s), 1184 (w), 1085 (m), 696 (m), 646 (s), 575 (w), 541 (m), 411 (m), 339 (m), 323 (s), 251 (w) cm^{-1}.

SP-4-2-[PtI(1-MeC)(9-EtGH)(NH$_3$)]NO$_3$·3H$_2$O (**5**) was prepared in the following way: To a solution of **2** (1 mmol) in 50 mL of DMF, AgNO$_3$ (0.99 mmol, dissolved in 40 mL of DMF) was added dropwise within 4 h. Then the mixture was stirred for another 20 h at room temperature with light excluded. The AgI was filtered off, and 1 mmol of 1-MeC was added to the filtrate. The clear yellow solution was stirred for 5 days at room temperature. The mixture was then concentrated by rotary evaporation to a minimum volume. After addition of 60 mL of CH$_2$Cl$_2$ a light yellow precipitate appeared immediately which was filtered off and dried in a vacuum. The precipitate, containing **5** and unreacted 1-MeC, was recrystallized from water, filtered off, and dried in air, the yield being 48%. Anal. Calcd for SP-4-2-[PtI(1-MeC)(9-EtGH)(NH$_3$)]NO$_3$·3H$_2$O (C$_{12}$H$_{25}$N$_{10}$O$_8$PtI): C, 19.0; H, 3.3; N, 18.4. Found: C, 18.7; H, 2.9; N, 18.4. IR (KBr): 3320 (s), 1685 (s), 1635 (s), 1594 (s), 1541 (m), 1498 (m), 1384 (s), 1339 (m), 1177 (w), 779 (w), 668 (w), 642 (w) cm^{-1}.

***trans*-[Pt(1-MeC)$_2$(9-EtGH)(NH$_3$)](NO$_3$)$_2$·1.5H$_2$O** (**6a**) was prepared as follows: **2** (0.5 mmol) and 1-MeC (1.0 mmol) were combined in 40 mL of water, and AgNO$_3$ (0.99 mmol) was added. The pH of the solution was adjusted to 6.4 by addition of 0.1 N NaOH. Then the mixture was stirred for 6 days at 40 °C in the dark. The AgI was filtered off, and the solution was concentrated to a volume of about 10 mL by rotary evaporation. Further evaporation in air gave **6a** as a colorless precipitate in 17% yield. Anal. Calcd for *trans*-[Pt(1-MeC)$_2$(9-EtGH)(NH$_3$)](NO$_3$)$_2$·1.5H$_2$O (C$_{17}$H$_{29}$N$_{14}$O$_{10.5}$Pt): C, 25.8; H, 3.7; N, 24.7. Found: C, 25.7; H, 3.6; N, 24.8. IR (KBr): 3316 (m), 1686 (s), 1667 (s), 1628 (s), 1536 (w), 1511 (m), 1428 (w), 1384 (s), 1338 (m), 1254 (w), 1177 (w), 828 (w), 772 (m), 686 (w), 643 (w), 454 (w), 419 (w), 362 (w) cm^{-1}. ^{1}H NMR (DMSO-d_6, ppm): NH$_3$, 4.34 (s). 1-MeC: CH$_3$, 3.31 (s); H5, 5.61/5.75, doublets each, $^3J = 7.2$ Hz; H6, 7.56/7.70, doublets each, $^3J = 7.2$ Hz; NH$_2$, 8.65 (s). 9-EtGH: CH$_3$, 1.26 (t), $^3J = 7.2$ Hz; CH$_2$, 4.06 (q), $^3J = 7.2$ Hz; NH$_2$, 6.92 (s); H8, 8.20 (s); NH(1), 11.57 (s).

***trans*-[Pt(1-MeC)$_2$(9-EtG)(NH$_3$)]NO$_3$·3H$_2$O** (**6b**) was obtained as follows: **6a** (0.1 mmol) was solved in the minimum amount of water, and 2 N NaOH was added dropwise to reach pH 12. Then the solution was cooled to 4 °C and allowed to evaporate. After several days colorless cubes of **6b** were isolated in 76% yield. Anal. Calcd for *trans*-[Pt(1-MeC)$_2$(9-EtG)(NH$_3$)]NO$_3$·3H$_2$O (C$_{17}$H$_{31}$N$_{13}$O$_9$Pt): C, 27.0; H, 4.1; N, 24.1. Found: C, 26.6; H, 4.2; N, 24.1. IR (KBr): 3132 (s), 1659 (s), 1595 (s), 1566 (m), 1539 (m), 1509 (m), 1458 (m), 1384 (s), 1332 (m), 1251 (w), 1196 (w), 797 (w), 771 (w), 643 (w), 425 (w) cm^{-1}.

SP-4-3-[Pt(1-MeC)(9-EtGH)(9-MeA)(NH$_3$)](NO$_3$)$_2$·H$_2$O (**7**) was prepared as follows: **5** (0.2 mmol) was suspended in 60 mL of water. AgNO$_3$ (0.2 mmol) and 9-MeA (0.2 mmol) were added, and the pH was adjusted to 2.5. The mixture was then stirred for 7 days at 40 °C with light excluded. The AgI was removed by filtration, and the resulting solution was concentrated to a volume of 10 mL by rotary evaporation. Further evaporation in air gave a colorless precipitate of **7** which was filtered of and washed with water. The yield was 33%. Anal. Calcd for SP-4-3-[Pt(1-MeC)(9-EtGH)(9-MeA)(NH$_3$)](NO$_3$)$_2$·H$_2$O (C$_{18}$H$_{28}$N$_{16}$O$_9$Pt): C, 26.8; H, 3.5; N, 27.8. Found: C, 26.9; H, 3.6; N, 27.8. IR (KBr): 3201 (m), 1685 (s), 1648 (s), 1585 (s), 1542 (m), 1514 (m), 1436 (m), 1384 (s), 1337 (m), 1305 (w), 1238 (w), 1194 (w), 781 (w), 719 (w) cm^{-1}.

SP-4-4-[Pt(1-MeC)(9-EtGH)(9-MeA)(NH$_3$)](NO$_3$)$_2$·3H$_2$O (**7a**) was prepared by reaction of SP-4-3-[PtI(1-MeC)(9-EtGH)(NH$_3$)]NO$_3$·3.5H$_2$O^3 (0.4 mmol, dissolved in 50 mL water) and AgNO$_3$ (0.4 mmol). The mixture was stirred at room temperature for 24 h with light excluded. AgI was then removed by filtration. 9-MeA (0.4 mmol) was added to the filtrate and the pH was adjusted to 3. The mixture was then stirred for 5 days at 40 °C. The solution was concentrated to 20 mL by rotary evaporation and subsequently allowed to evaporate in air. After several days, a colorless precipitate was filtered off and washed with small amounts of water. The product was dried in air, the yield being about 33%. Anal. Calcd for SP-4-4-[Pt(1-MeC)(9-EtGH)(9-MeA)(NH$_3$)](NO$_3$)$_2$·3H$_2$O (C$_{18}$H$_{32}$N$_{16}$O$_{11}$Pt): C, 25.6; H, 3.8; N, 26.6. Found: C, 25.6; H, 3.6; N, 26.6. IR (KBr): 3383 (s), 3127 (s), 1643 (s), 1584 (s), 1546 (m), 1503 (m), 1433 (m), 1384 (s), 1354 (s), 1256 (w), 1182 (m), 793 (w), 776 (w), 716 (w), 642 (w) cm^{-1}. Raman (solid state): 3110 (m), 2957 (m), 1706 (w), 1654 (w), 1585 (m), 1548 (w), 1506 (m), 1440 (w), 1384 (s), 1367 (m), 1339 (m), 1301 (w), 1263 (m), 1044 (s), 797 (m), 782 (w), 722 (m), 649 (w), 634 (m), 562 (w), 482 (w), 384 (w) cm^{-1}.

SP-4-4-[Pt(1-MeC)(9-EtG)(9-MeA)(NH$_3$)]NO$_3$·2H$_2$O (**7b**) was obtained as follows: **7a** (0.1 mmol) was dissolved in the minimum volume of water, and then 2 N NaOH was added to reach pH 12. The solution was cooled to 4 °C and allowed to evaporate. After 2 weeks **7b** was isolated as colorless sticks in 55% yield. Anal. Calcd for SP-4-4-[Pt(1-MeC)(9-EtG)(9-MeA)(NH$_3$)]NO$_3$·2H$_2$O (C$_{18}$H$_{29}$N$_{15}$O$_7$Pt): C, 28.3; H, 3.8; N, 27.5. Found: C, 28.1; H, 3.7; N, 27.1. IR (KBr): 3323 (s), 1643 (s), 1600 (s), 1562 (m), 1514 (w), 1481 (m), 1445 (m), 1410 (m), 1384 (s), 1333(m), 1195 (w), 795 (w), 773 (w), 716 (w), 644 (w) cm^{-1}.

[Pt(9-EtGH)$_3$(NH$_3$)](NO$_3$)$_2$·2.5H$_2$O (**8**) was prepared by reaction of **2** (0.15 mmol) and 9-EtGH (0.3 mmol) in 100 mL of water. AgNO$_3$ (0.3 mmol) was added, and the mixture was stirred for 7 days at room temperature in the dark. The AgI was filtered off, and the pale yellow solution was concentrated to 15 mL volume by rotary evaporation. Then the solution was kept on a water bath (40 °C) for further evaporation. After several days a white microcrystalline material was obtained in

Table 1. Crystallographic Data of Compounds **4**, **6b**, and **7b**

	4	**6b**	**7b**
empirical formula	$C_7H_{12}N_6O_{1.5}Cl_2Pt$	$C_{17}H_{31}N_{13}O_9Pt$	$C_{18}H_{29}N_{15}O_7Pt$
fw (g mol^{-1})	470.21	756.64	762.65
cryst color and habit	yellow plates	colorless cubes	colorless sticks
cryst dimens (mm)	0.20 × 0.12 × 0.42	0.30 × 0.26 × 0.25	0.625 × 0.113 × 0.025
cryst syst	triclinic	triclinic	monoclinic
space group	$P\bar{1}$ (No. 2)	$P\bar{1}$ (No. 2)	$C2/c$
a (Å)	11.557(3)	10.957(2)	23.817(5)
b (Å)	12.742(2)	11.022(2)	10.992(2)
c (Å)	8.880(2)	12.916(2)	21.647(4)
α (deg)	96.95(1)	81.18(3)	90.00
β (deg)	94.91(2)	89.93(3)	112.07(3)
γ (deg)	88.32(2)	64.22(3)	90.00
V (Å^3)	1293.1(5)	1384.2(5)	5251.9(18)
Z	4	2	8
ρ (calcd) (g cm^{-3})	2.42	1.815	1.929
radiation, λ (Å)	Mo Kα, 0.710 69	Mo Kα, 0.710 69	Mo Kα, 0.710 69
μ(cm^{-1})	112.20	51.38	54.15
absorption corrections	ψ scans (transm. factors 0.12−1.00)		
temperature (°C)	−100	20	20
$2\theta_{max}$ (deg)	50	51.3	51.4
no. of reflcns measured			
total	4820	36 652	75 887
unique	4570 ($R_{int} = 0.030$)	4699 ($R_{int} = 0.055$)	4842 ($R_{int} = 0.060$)
no. of reflections	3289 ($I > 3\sigma(I)$)	3490 ($F_o > 4\sigma(F_o)$)	3055 ($F_o > 4\sigma(F_o)$)
no. of variables	317	358	376
residuals	0.048; 0.061 (R; R_w)	0.038; 0.080 (R1; wR2)	0.038; 0.065 (R1; wR2)
goodness of fit	1.55	1.044	1.016
maximum peak in final difference map	2.47 e/Å^3 (close to Pt1)	0.808 e/Å^3	1.298 e/Å^3

33% yield and dried in air. Anal. Calcd for [Pt(9-EtGH)$_3$(NH$_3$)](NO$_3$)$_2$·2.5H$_2$O ($C_{21}H_{35}N_{18}O_{11.5}Pt$): C, 27.5; H, 3.8; N, 27.4. Found: C, 27.4; H, 3.6; N, 27.5. IR spectrum (KBr): 3414 (s), 1690 (s), 1636 (s), 1584 (s), 1549 (m), 1499 (m), 1384 (s), 1219 (w), 1179 (m), 1106 (w), 778 (w), 714 (w), 641 (w) cm^{-1}.

***trans*-[Pt(9-EtGH)$_2$(9-MeA)(NH$_3$)](NO$_3$)$_2$·1.5H$_2$O (9)** was prepared by reaction of **2′** (0.2 mmol) and 9-EtGH (0.4 mmol) in 100 mL of water. AgNO$_3$ (0.4 mmol) was added to the mixture, and then the resulting solution was stirred at room temperature for 7 days with light excluded (pH 4−5). The AgI was removed by filtration and the resulting solution was concentrated to a volume of 10 mL by rotary evaporation. Upon cooling to 4 °C, a small amount of unreacted 9-EtGH precipitated and was filtered off. Slow evaporation in air led to colorless needles of **9**, the yield being about 14%. Anal. Calcd for *trans*-[Pt(9-EtGH)$_2$(9-MeA)(NH$_3$)](NO$_3$)$_2$·1.5H$_2$O ($C_{20}H_{31}N_{18}O_{9.5}Pt$): C, 27.6; H, 3.6; N, 29.0. Found: C, 27.5; H, 3.5; N, 29.2. IR spectrum (KBr): 3399 (s), 1688 (s), 1631 (s), 1585 (s), 1498 (m), 1384 (s), 1183 (m), 1084 (w), 778 (w), 716 (w), 644 (w), 534 (w) cm^{-1}. Raman (solid state): 2946 (m), 1705 (m), 1638 (m), 1589 (s), 1505 (s), 1431 (m), 1386 (s), 1368 (s), 1342 (s), 1246 (m), 1087 (m), 1049 (s), 780 (m), 719 (s), 693 (m), 627 (s) 554 (m), 512 (w), 412 (w) 370 (w) cm^{-1}.

Spectroscopy. ^{1}H NMR spectra (200.13 MHz, TSP as internal reference for D$_2$O solutions; TMS for DMSO-d_6) and ^{195}Pt NMR spectra (42.998 MHz, Na$_2$PtCl$_6$ as external reference) were recorded on a Bruker AC 200 FT NMR spectrometer. pD values of D$_2$O solutions were determined by use of a glass electrode on a Metrohm 6321 pH meter, with addition of 0.4 unit to the meter reading. IR spectra (KBr) were taken on a Perkin-Elmer 580 B FT spectrometer. Raman spectra (solid state) were recorded on a Coderg T800 spectrometer with argon (514.5 nm) or krypton laser (647.1 nm) exitation.

X-ray Crystallography. X-ray measurements for **4** were carried out on a Rigaku AFC6S diffractometer using Mo Kα radiation (γ = 0.710 69 Å). Calculations were performed on a VAX station 3520 computer by using the TEXSAN 5.0 software[9] and in the later stages on a Silicon Graphics Indigo 2 Extreme computer with the TEXSAN 1.7 package.[10] Unit cell dimensions were determined by applying the setting angles of 25 high-angle reflections. Three standard reflections were monitored during the data collection showing no significant variance. The intensities were corrected for absorption by applying ψ scans of several reflections with the transmission factors within the range 0.12−1.00.

The structure was solved by direct methods in SIR88.[11] Two independent molecules of the compound were found in the unit cell. Full-matrix least-squares refinement with anisotropic thermal displacement parameters for all non-hydrogen atoms yielded the final R of 0.048 (R_w = 0.061). The hydrogen atoms were found in difference Fourier maps and included in the calculation without further refinement. The final electrone density map showed a peak 2.47 e/Å^3 high in the vicinity of the Pt1 atom.

Data collection of **6b** and **7b** was performed on an Enraf-Nonius KappaCCD diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.710 69 Å).[12] It covered the whole sphere of reciprocal space by measurement of 360 frames rotating about ω in steps of 1° with a scan time of 30/60 s for each frame. The detector was positioned at a distance of 26.77/26.84 mm to the crystal. Unit cell parameters were obtained from the peaks of the first 10 frames with the resolution limits 4.5 and 0.82 Å and refined using the whole data set. Data reduction and cell refinement was carried out using the programs DENZO and SCALEPACK.[13] Reflections, which were partly measured on previous and following frames, were used to scale these frames on each other. This procedure in part eliminates absorption effects and also considers any crystal decay.

The structure was solved by standard Patterson methods[14] and refined with difference Fourier syntheses, using the SHELXTL-PLUS[15] and SHELXL-93 programs.[16] The scattering factors for the atoms were those given in the SHELXTL-PLUS program. The hydrogen atoms were placed in geometrically calculated positions and refined with a common isotropic temperature factor, except those for the disordered

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(9) *TEXSAN 5.0: Single-Crystal Structure Analysis Software*; Molecular Structure Corp.: The Woodlands, TX 77381, 1989.

(10) *TEXSAN 1.7: Single-Crystal Structure Analysis Software*; Molecular Structure Corp.: The Woodlands, TX 77381, 1995.

(11) Burla, M. C.; Camalli, M.; Cascarone, G.; Giacovazzo, C.; Polidori, G.; Spagna, R.; Viterbo, D. *J. Appl. Crystallogr.* **1989**, *22*, 389.

(12) *KappaCCD package*; Nonius BV: Röntgenweg 1, P.O. Box 811, 2600 AV Delft, The Netherlands.

(13) Otwinowsky, Z.; Minor, W. DENZO and SCALEPACK. *Methods Enzymol.* **1997**, *276*, 307.

(14) Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467.

(15) Sheldrick, G. M. *SHELXTL-PLUS (VMS)*; Siemens Analytical X-ray Instruments, Inc.: Madison, WI, 1990.

(16) Sheldrick, G. M. *SHELXL-93: Program for crystal structure refinement*; University of Göttingen: Germany, 1993.

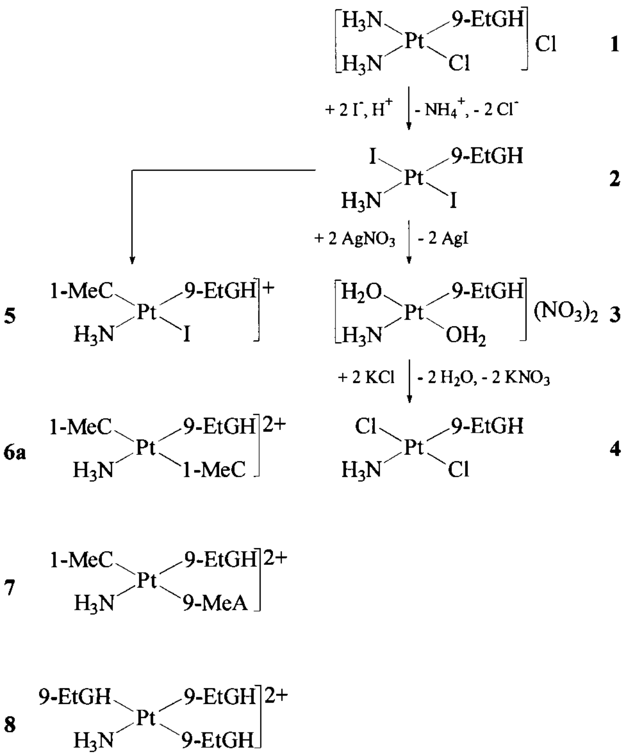

Figure 1. Synthesis route for the compounds derived from *cis*-[PtCl(9-EtGH-$\underline{N7}$)$(NH_3)_2$)]Cl (**1**).

ethyl group in **6b**. The nitrate anion in **6b** is disordered over two positions, each half occupied. Relevant crystallographic data are listed in Table 1.

Results and Discussion

Synthetic Procedure and Aqua Species. The general pathway for the synthesis of all compounds derived from *cis*-[PtCl(9-EtGH-$\underline{N7}$)$(NH_3)_2$]Cl (**1**) is outlined in Figure 1. A similar procedure was applied to the 9-MeAH$^+$ analogue of **1**, *cis*-[PtCl(9-MeAH-$\underline{N7}$)$(NH_3)_2$]$(NO_3)_2$ (**1′**), with this compound not isolated, however. **1′** was observed in the ^{1}H NMR spectrum (pD 1.0) and displayed chemical shifts (H8, 8.90 (s); H2, 8.58 (s); CH_3, 3.99 (s) ppm) that are consistent with the N1 position being protonated in this pH range.[17] *trans*-PtI_2(9-MeA-$\underline{N7}$)-(NH_3)·0.5DMF (**2′**) and the tris(nucleobase) complex *trans*-[Pt-(9-EtGH-$\underline{N7}$)$_2$(9-MeA-$\underline{N7}$)(NH_3)]$^{2+}$ (**9**) were prepared in a similar way as the analogous 9-ethylguanine compounds.

***cis*-[PtCl(9-EtGH)(NH$_3$)$_2$]Cl** (**1**) was obtained as previously reported and was converted practically quantitatively into *trans*-PtI_2(9-EtGH)(NH_3) (**2**). When dissolved in DMSO-d_6, **2** is readily converted into the bis(solvent) species with replacement of the iodo ligands as evident from the fact that subsequent addition of Ag$^+$ and precipitation of I$^-$ as AgI has no effect on the ^{1}H NMR resonances. 9-EtGH resonances of this complex occur downfield from those of the free nucleobase but are not shifted to the same extent as for the protonated nucleobase 9-EtGH$_2^+$. Chemical shifts [δ, ppm] of *trans*-[Pt(DMSO)$_2$(9-EtGH-$\underline{N7}$)(NH_3)]$^{2+}$ in DMSO-d_6 are as follows: CH_3, 1.38 (t); CH_2, 4.08 (q); NH_2(2), 6.89 (s); H8, 8.60 (s); NH(1), 11.23 (s); NH_3, 4.61 (s).

Treatment of an aqueous solution of **2** with 2 equiv of $AgNO_3$ and filtration of AgI yields a solution containing *trans*-[Pt$(H_2O)_2$-(9-EtGH-$\underline{N7}$)(NH_3)]$^{2+}$ (**3**), in equilibrium with hydroxo species. A remarkable drop in pH is observed over the first hours following addition of Ag$^+$, presumably caused by the acidity of the diaqua species and/or as a consequence of subsequent condensation reactions leading to μ-OH and/or μ-9-EtG species. In the following days the pH continues to drop, although slightly only (ca. 0.3 unit within 24 days). This process is accompanied by the appearance of several new signals in the ^{1}H NMR spectrum of **3**. For example, new guanine H8 resonances occur upfield from the 8.29 ppm resonance, which is assigned to monomeric **3**, between 8.24 and 7.98 ppm. In very dilute solution (0.005 M), these new resonances are not detectable, but their formation is favored in more concentrated solution (0.02−0.04 M). This behavior is reminiscent of the behavior of *cis*-[Pt(H_2O)(9-EtGH)$(NH_3)_2$]$^{2+}$ [18] and *trans*-[Pt(H_2O)(9-EtGH)$(CH_3NH_2)_2$]$^{2+}$ [19] for which we have postulated condensation reactions leading to N1,N7-bridged species.

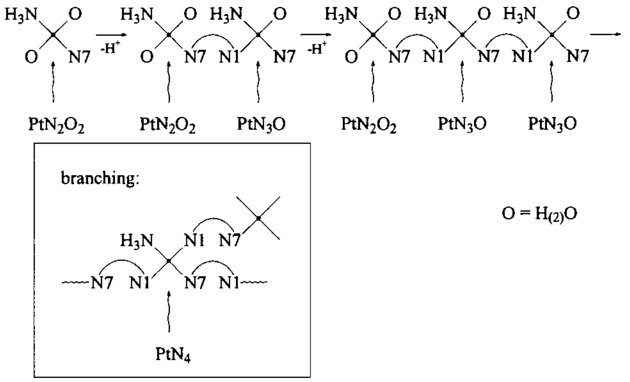

Figure 2. Possible condensation reactions of **3** giving rise to oligomers with bridging 9-EtG and terminal 9-EtGH groups. There is no indication from ^{195}Pt NMR spectroscopy for any branching since a ^{195}Pt resonance consistent with a PtN_4 coordination sphere is not observed.

Within several days a very fine brown-red precipitate forms. In the ^{195}Pt spectrum of an aged sample (4 days at room temperature, 0.02 M, pD 1.6) three distinct signals are observed at 212, −1339, and −2020 ppm with relative intensities 1:3:6. Chemical shifts[20] of −1339 and −2020 ppm are consistent with Pt(II) species having N_2O_2 and N_3O coordination spheres, respectively. For the simplest condensation product of **3**, containing a single 9-EtG bridge, PtN_3O and PtN_2O_2 coordination spheres should be formed in a 1:1 ratio. As the condensation proceeds, the signal due to PtN_3O is expected to increase relative to that of PtN_2O_2 (Figure 2). This is indeed what is observed. Apparently branching does not take place to a measurable extent, since a signal due to a PtN_4 environment, expected around −2400 ppm, is not observed.

The third signal at 212 ppm is in the range typical of a [Pt(III)]$_2$ species.[21] The fact that a singlet is observed for this compound is consistent with a dimeric species bridged by two nucleobases in a head−tail fashion, leading to two chemically equivalent Pt centers (assuming they have the same axial ligands) at short distance (2.5−2.6 Å). A head−tail arrangement with either N7 and O6 or N1 and O6 positions of 9-EtG(H)

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(17) (a) den Hartog, J. H. J.; van den Elst, H.; Reedijk, J. *J. Inorg. Biochem.* **1984**, *21*, 83. (b) Schwarz, F.; Lippert, B.; Schöllhorn, H.; Thewalt, U. *Inorg. Chim. Acta* **1990**, *176*, 113.

(18) Raudaschl-Sieber, G.; Marzilli, L. G.; Lippert, B.; Shinozuka, K. *Inorg. Chem.* **1985**, *24*, 989.

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(21) O'Halloran, T. V.; Roberts, M. M.; Lippard, S. J. *Inorg. Chem.* **1986**, *25*, 957.

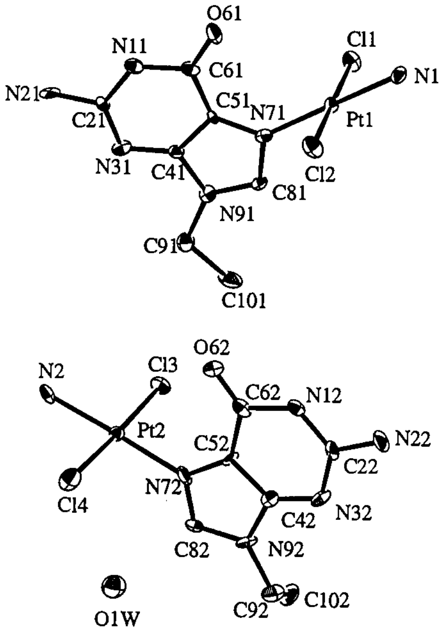

Figure 3. View of the two crystallographic independent molecules of *trans*-$PtCl_2$(9-EtGH-$\underline{N7}$)(NH_3)·0.5H_2O (**4**). Thermal ellipsoids are drawn at the 50% probability level.

Scheme 1

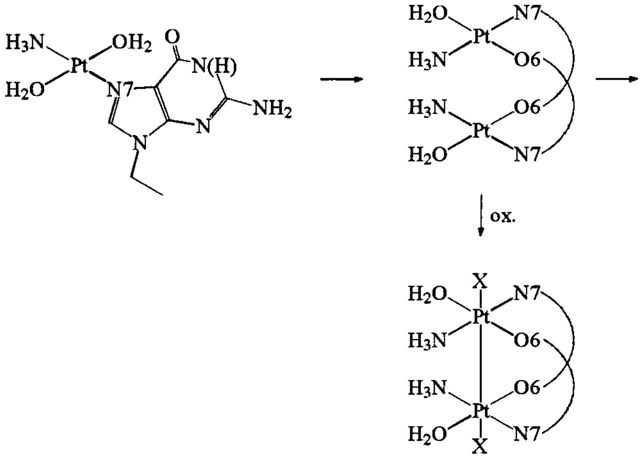

Table 2. Selected Bond Distances (Å) and Bond Angles (deg) for **4**

Pt(1)−Cl(1)	2.306(3)
Pt(1)−Cl(2)	2.292(4)
Pt(1)−N(1)	2.03(1)
Pt(1)−N(71)	2.01(1)
Pt(2)−Cl(3)	2.307(4)
Pt(2)−Cl(4)	2.283(4)
Pt(2)−N(2)	2.03(1)
Pt(2)−N(72)	2.02(1)
Cl(1)−Pt(1)−Cl(2)	178.6(1)
Cl(1)−Pt(1)−N(1)	90.1(3)
Cl(1)−Pt(1)−N(71)	91.9(3)
Cl(2)−Pt(1)−N(1)	88.6(3)
Cl(2)−Pt(1)−N(71)	89.4(3)
N(1)−Pt(1)−N(71)	178.0(4)

involved in metal coordination would satisfy this requirement. N7,O6 bridging has been reported for the dimeric Rh(II) species $[Rh_2(O_2CCF_3)_2(9\text{-EtGH})_2((CH_3)_2CO)_2]^{2+}$ and $Rh_2(O_2CCH_3)_2$(9-EtG)$_2$(CH_3OH)$_2$.[22] The metal−metal distances in these two compounds are 2.52 and 2.48 Å, confirming a short N7,O6 bite distance. We note that with the related complex *trans*-[Pt(H_2O)$_2$(1-MeC-$\underline{N3}$)(NH_3)]$^{2+}$ we have shown that head−tail dimerization, albeit via N3 and N4, occurs readily, followed by binding of a chelating ligand (glycine) and oxidation to the diplatinum(III) species in air.[5] We therefore propose a similar reaction scheme in the present case and tentatively favor N7,-O6 bridging (Scheme 1).

X-ray Structure Analysis of 4. Figure 3 gives a view of the two crystallographically independent molecules of *trans*-$PtCl_2$(9-EtGH-$\underline{N7}$)(NH_3)·0.5H_2O (**4**). Selected interatomic distances and angles are given in Table 2. Pt binding is via the N7 position of the purine nucleobase. Two trans positioned chloro ligands as well as an ammine ligand trans to guanine complete the coordination geometry of the Pt. There are no unusual distances and angles, neither in the Pt coordination sphere, nor in the guanine heterocycle. The dihedral angles between the Pt and the guanine planes are 96.1 and 105.0° for the two molecules.

Intermolecular H bonding in **4** is found between the exocyclic oxygen atom O(61) and the ammine ligand N(2) (2.90(2) Å) and between O(62) and N(21) (2.87(1) Å), respectively, each of the cation at $-x + 1$, $-y$, $-z + 2$. Short contacts also are found between the water molecule O(1W) and N(22) (2.91(2) Å) of the cation at $-x + 2$, $-y + 1$, $-z + 1$ and N(2) (2.94(2) Å) of the cation at x, y, $z - 1$, respectively. In addition, there is a longer contact between the water molecule and C82 (3.36(2) Å), strongly suggesting a weak H bonding interaction between these sites (N72−C82−O1W, 128.4°; N92−C82−O1W, 116.9°).

Characterization of Mixed Guanine, Cytosine Complexes 5 and 6a. The syntheses of [PtI(1-MeC)(9-EtGH)(NH_3)]NO_3·3H_2O (**5**) and *trans*-[Pt(1-MeC)$_2$(9-EtGH)(NH_3)](NO_3)$_2$·1.5H_2O (**6a**) from **2** is straightforward. **5** is yet another example[3] of a square planar Pt(II) complex having four different ligands. The configuration number[23] of the isomer expected for **5** is SP-4-2. Of the four ligands, iodide is trans to 1-MeC and therefore the arrangement is different from the previously[3] reported SP-4-3 isomer having the same cation composition.

The ^1H NMR spectrum of **5** (pD 5.3) displays a single set of signals for each nucleobase with shifts characteristic of N3 coordinated 1-MeC (H6, 7.56; H5, 5.94, doublets each, ^3J = 7.4 Hz; CH_3, 3.42 (s) ppm) and N7 coordinated 9-EtGH (CH_3, 1.38 (t), ^3J = 7.4 Hz; CH_2, 4.07 (q), ^3J = 7.4 Hz; H8, 8.08 (s) ppm), respectively. Integration of the resonances is consistent with a 1:1 ratio of the bases. Surprisingly, there are no significant differences between the ^1H NMR spectra of **5** and the previously reported SP-4-3 isomer. Differences between the two isomers are expected for the ^3J (^{195}Pt−N−C−$^1H8$) coupling constant, which should decrease with increasing trans influence of the ligand trans positioned to 9-EtGH.[8] However, Pt coupling with H8 is not detected due to the use of a 200 MHz NMR spectrometer.[24]

The ^1H NMR spectrum of a freshly prepared solution of **6a** (pD 6.1) displays two sets of resonances for the two types of nucleobases, consistent with two different rotational isomers being present. The chemical shifts of resonances of **6a** are very similar to those found for **5**, only the H8 resonances of the

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(24) Lallemand, J.-Y.; Soulie, J.; Chottard, J.-C. *J. Chem. Soc., Chem. Commun.* **1980**, 436.

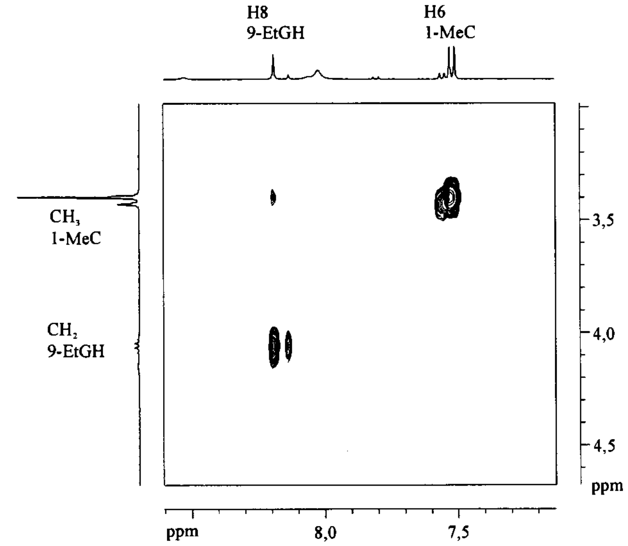
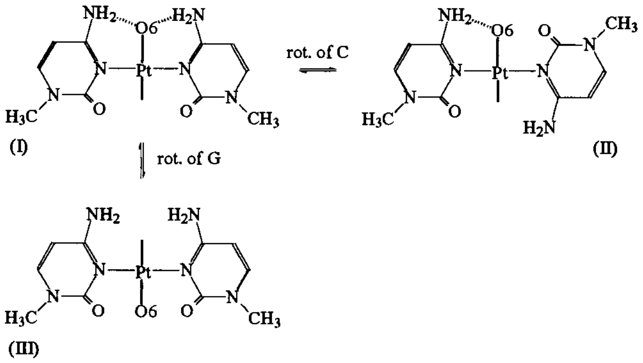


Figure 4. Section of the NOESY spectrum of **6a** with cross-peaks between H8 and CH_2 (of 9-EtGH each), H6 and CH_3 (of 1-MeC each), as well as H8 (9-EtGH) and CH_3 (1-MeC).

Scheme 2



guanine ligand (8.20 and 8.14 ppm) display a marked downfield shift. Integration of the H8 resonances of 9-EtGH and the CH_3 resonances of 1-MeC reveals a 4:1 ratio of the two species; all other signals are superimposed and cannot be integrated separately. There are two possible explanations for the two rotamers: First, the trans positioned cytosine ligands adopt a head−head or a head−tail orientation with respect to each other with the guanine ligand fixed (Scheme 2, I and II). Isomers of this form have been intensively studied for bis(1-methylcytosine) complexes, e.g. *trans*-[Pt(1-MeC-$\underline{N3}$)$_2$(NH_2CH_3)$_2$]$^{2+}$.[25] The head−head orientation (I) as found in the solid-state structure of **6b**, permits intramolecular hydrogen bond formation between N4 of both cytosine ligands and O6 of guanine, whereas the head−tail orientation (II) allows a single intracomplex H bond only. Second, the 9-EtGH ligand adopts two different orientations with respect to two head−head arranged cytosine rings (Scheme 2, I and III). In that case either two H bonds are possible (I) or none at all (III). Simultaneous rotations of the three ligands do not lead to any additional possible species. Attempts to follow equilibration of the rotamers by recording time-dependent spectra after dissolving a sample, were unsuccessful in that either equilibration is fast (reached within minutes) or both rotamers coexist in the solid state, either as a mixture or within single crystals.

To clarify the question concerning the mutual ligand orientation in solution at least for the preferred species, a NOESY spectrum of **6a** (Figure 4) was recorded (90% H_2O, 10% D_2O). A NOESY cross-peak between H8 of 9-EtGH and CH_3 of 1-MeC was observed, but no cross-peak between H8 of 9-EtGH and NH_2 of 1-MeC was detected. This strongly supports the structure I as that of the major rotamer. It is the only conformation with H8 of 9-EtGH lying on the same side of the Pt coordination plane with both the methyl groups of 1-MeC, whereas the NH_2 groups of the 1-MeC ligands are on opposite sides of the square plane.

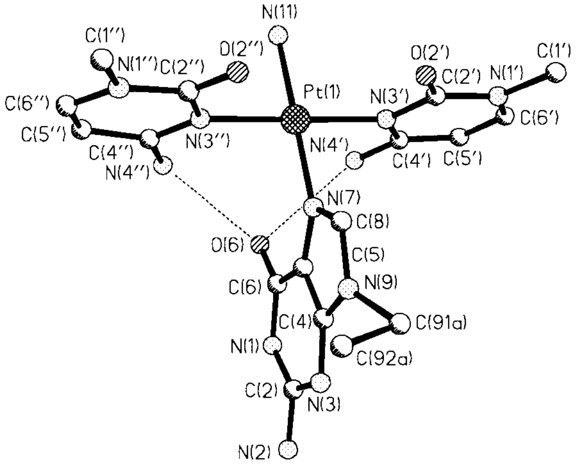


Figure 5. View of the cation of *trans*-[Pt(1-MeC)$_2$(9-EtG)(NH_3)]NO_3·$3H_2O$ (**6b**) with atom numbering scheme.

Table 3. Selected Bond Distances (Å) and Bond Angles (deg) for **6b**

Pt(1)−N(7)	2.012(6)
Pt(1)−N(11)	2.026(5)
Pt(1)−N(3′)	2.027(5)
Pt(1)−N(3″)	2.046(5)
N(7)−Pt(1)−N(3′)	88.8(2)
N(7)−Pt(1)−N(11)	178.7(2)
N(3′)−Pt(1)−N(11)	90.4(2)
N(7)−Pt(1)−N(3″)	90.9(2)
N(3′)−Pt(1)−N(3″)	178.5(2)
N(11)−Pt(1)−N(3″)	89.8(2)

X-ray Structure Analysis of 6b. Figure 5 provides a view of the cation of *trans*-[Pt(1-MeC)$_2$(9-EtG)(NH_3)]NO_3·$3H_2O$ (**6b**), selected bond lengths and angles are given in Table 3. Pt coordination is through the N7 site of 9-EtG and the N3 sites of the 1-MeC ligands, respectively. The two cytosine bases are trans to each other adopting a head−head orientation. The square planar coordination sphere of the metal is completed by an ammine ligand. The guanine ligand is deprotonated at the N1 position, leading to a significant decrease of the C2−N1−C6 angle (118.0(6)°) of the guanine base as compared to N7 coordinated neutral 9-EtGH, e.g. 125(1) and 126(1)°, found for the two crystallographically independent molecules of **4**.

The planes of the cytosine rings are roughly coplanar (dihedral angle 3.9(4)°) and close to perpendicular to the Pt coordination plane (dihedral angles 83.8(2) and 83.2(2)°) and also to the guanine ligand with dihedral angles of 88.9(2) and 85.1(2)°. Intramolecular hydrogen bonding is found between the amino groups of both 1-MeC ligands and guanine O6 (N4′···O6, 2.917(8) Å; N4″···O6, 2.792(9) Å). These H bonds appear to stabilize the observed head−head arrangement of the two cytosine nucleobases.

The guanine base is approximately perpendicular to the Pt coordination plane with a dihedral angle of 87.3(1)°. Each 9-EtG anion of a given molecule is hydrogen bonded through a pair of N1···N(2)H_2 bonds (3.001(11) Å) to the 9-EtG base

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(25) Holthenrich, D.; Sóvágó, I.; Fusch, G.; Erxleben, A.; Fusch, E. C.; Rombeck, I.; Lippert, B. *Z. Naturforsch., Teil B* **1995**, *50*, 1767.

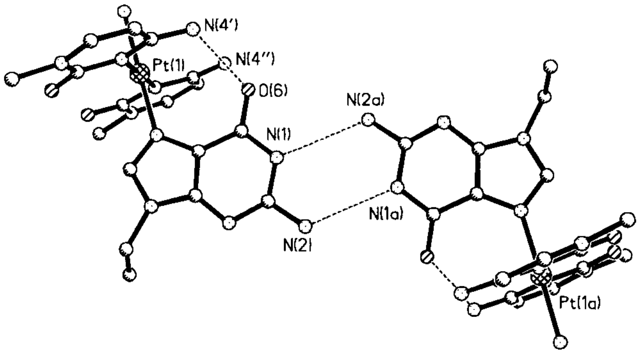

Figure 6. Base pairing between N1 deprotonated 9-ethylguanine ligands in **6b**.

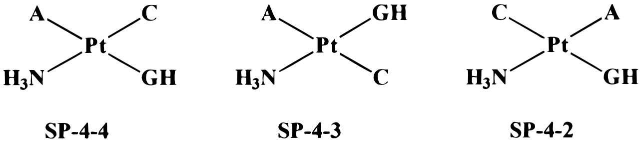

Figure 7. Configuration numbers of the three isomers of the square planar complex [Pt(1-MeC)(9-EtGH)(9-MeA)(NH_3)]$^{2+}$. The ligands arranged by decreasing priority are as follows: (C = 1-MeC) > (GH = 9-EtGH) > (A = 9-MeA) > NH_3.

of the cation at $-x + 1$, $-y$, $-z$. This base pairing pattern requires N1 deprotonation and was first established for the complex *cis*-Pt(9-EtG)$_2$(NH_3)$_2$ as a novel homoguanine H bonding pattern.[26] The base pairing of the guanine bases of **6b** is illustrated in Figure 6. Short intermolecular H bond contacts are also found between N4′and the water molecule O4W (2.916(10) Å, symmetry operation *x*, *y*, *z*) and N2 and O2WB (2.925(7) Å, symmetry operation $-x + 1$, $-y$, $-z$).

Tris(nucleobase) Complex Containing Three Different Nucleobases (7). The three possible isomers of the tris(nucleobase) complex [Pt(1-MeC)(9-EtGH)(9-MeA)(NH_3)]$^{2+}$ are illustrated in Figure 7. The expected configuration number[23] of compound **7**, based on the way of its preparation and considering the relative inertness of Pt(II) complexes to isomerization, is SP-4-3. The iodo ligand in **5** is replaced by 9-MeA positioned trans to 1-MeC. The ^{1}H NMR spectrum of **7** (D_2O, pD 6.5) is consistent with its composition. The chemical shifts [δ, ppm] of the individual resonances are as follows. 9-MeA: H8, 8.49 (s); H2, 8.30 (s); CH_3, 3.82 (s). 9-EtGH: H8, 8.13 (s); CH_2, 3.97 (q), ^3J = 7.4 Hz; CH_3, 1.24 (t), ^3J = 7.4 Hz. 1-MeC: H6, 7.59; H5, 5.97, doublets each, ^3J = 7.4 Hz; CH_3, 3.48 (s). The ^{195}Pt spectrum displays a single signal at −2456 ppm, which is in agreement with expectations for a Pt(II) species with a N_4 coordination sphere.[20]

Assuming that the three bases are approximately perpendicular to the platinum coordination plane, three different arrangements of the bases, each leading to two intramolecular hydrogen bonds, are feasible. These involve the carbonyl oxygens O6 of 9-EtGH and O2 of 1-MeC and the amino groups of 9-MeA and 1-MeC, respectively. The different conformations are provided in the Supporting Information. Hydrogen bonding could occur, in principle, between the bases in cis position relative to each other, as well as between the 1-MeC and 9-MeA ligands in trans position via N6 and O2, as seen in *trans*-[Pt(1-MeC)(9-MeA)(NH_3)$_2$]$^{2+}$.[27] The fact that no splitting of the NMR resonances in **7** is observed either reflects the fact that one of these conformations is strongly favored over the others or, alternatively, that there is fast rotation of the ligands on the NMR time scale.

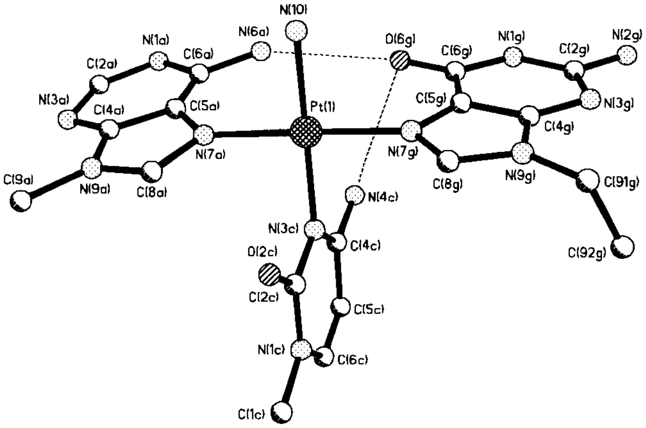

Figure 8. View of the cation of SP-4-4-[Pt(1-MeC)(9-EtG)(9-MeA)(NH_3)]NO_3·$2H_2O$ (7**b**) with atom numbering scheme.

Table 4. Selected Bond Distances (Å) and Bond Angles (deg) for **7b**

Pt(1)−N(7G)	2.004(5)
Pt(1)−N(7A)	2.012(5)
Pt(1)−N(10)	2.024(5)
Pt(1)−N(3C)	2.024(5)
N(7G)−Pt(1)−N(7A)	178.3(2)
N(7G)−Pt(1)−N(10)	90.0(2)
N(7A)−Pt(1)−N(10)	91.6(2)
N(7G)−Pt(1)−N(3C)	89.7(2)
N(7A)−Pt(1)−N(3C)	88.8(2)
N(10)−Pt(1)−N(3C)	176.5(2)

Tris(nucleobase) Complexes Containing Three Different Nucleobases (7a and 7b). Starting out from the previously[3] reported isomer SP-4-3-[PtI(1-MeC)(9-EtGH)(NH_3)]$^+$ and replacing the iodo ligand by 9-MeA gave SP-4-4-[Pt(1-MeC)(9-EtGH)(9-MeA)(NH_3)](NO_3)$_2$·$3H_2O$ (**7a**). The configuration number[23] is now SP-4-4 since the ligand 1-MeC is now the one with the highest priority number and trans to NH_3. The ^{1}H NMR spectrum of **7a** in D_2O (pD 5.0) displays two sets of resonances (approximate ratio 1:1.5), consistent with two rotational isomers being present. In this aspect **7a** differs markedly from its configurational isomer **7**. Analogous to compound **7** three possible arrangements (Supporting Information) of the base planes are each stabilized by two intramolecular hydrogen bonds between the exocyclic groups of the bases (O6 of 9-EtGH, O2 of 1-MeC, and the NH_2 groups of 9-MeA and 1-MeC). However, it is uncertain which of these species are detected in the NMR spectrum. The chemical shifts are in the expected range for nucleobases with the observed coordination pattern. Heating of the sample to 55 °C causes the two signal sets to coincide as a consequence of fast rotation of the rings on the NMR time scale. These changes seem to be fully reversible. In the ^{195}Pt spectrum of **7a** at room-temperature two signals for the two rotamers are detected at −2417 (minor rotamer) and −2428 ppm (major rotamer).

The SP-4-4 isomer was eventually structurally characterized in the deprotonated form [Pt(1-MeC)(9-EtG)(9-MeA)(NH_3)]NO_3·$2H_2O$ (**7b**). Figure 8 gives a view of the cation of **7b** with the atom numbering scheme. Selected bond distances and angles are presented in Table 4. The Pt atom is coordinated to the nucleobases via the N7 positions of 9-EtG and 9-MeA and the N3 position of 1-MeC, respectively. The square planar coordination sphere is completed by an ammine ligand. There

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are neither unusual bond lengths or angles in the metal coordination sphere nor in the heterocycles. The C2−N1−C6 angle of 118.6(6)° of the guanine ligand confirms N1 deprotonation of this base.[28]

The heterocycles are approximately perpendicular to the Pt coordination plane, with dihedral angles of 82.2(1) (9-EtG), 77.6(2) (9-MeA), and 81.7(2)° (1-MeC). The 9-EtG and 9-MeA ligands are positioned trans to each other with a dihedral angle of 11.8(2)°. The angles with respect to 1-MeC are 85.2(1) (9-EtG) and 84.8(2)° (9-MeA). The base planes are oriented in a way that allows H bonding between guanine O6 with the amino groups of the two remaining rings (N6A···O6G, 2.912(6) Å; N4C···O6G, 2.958(8) Å).

Tris(9-ethylguanine) Complex 8. $[Pt(9\text{-}EtGH)_3(NH_3)](NO_3)_2 \cdot 2.5H_2O$ (**8**) is the guanine analogue of the previously reported tris(1-methylcytosine) Pt complex $[Pt(1\text{-}MeC)_3(NH_3)]^{2+}$.[4] The latter was prepared from *trans*-$PtCl_2(1\text{-}MeC)(NH_3)$ and 1-MeC.

The ^1H NMR spectrum of **8** in D_2O (pD 5.6) displays two sets of resonances in a 2:1 ratio for the two mutually trans positioned 9-EtGH ligands (CH_3, 1.46 (t), $^3J = 7.4$ Hz; CH_2, 4.12 (q), $^3J = 7.4$ Hz; H8, 8.29 (s) ppm) and for the 9-EtGH ligand trans to NH_3 (CH_3, 1.42 (t), $^3J = 7.4$ Hz; CH_2, 4.14 (q), $^3J = 7.4$ Hz; H8, 8.24 (s) ppm), respectively. The spectrum is either consistent with a head−head orientation of the mutually trans positioned nucleobases or, alternatively, with fast rotation of these ligands, with the third nucleobase fixed. ^{195}Pt NMR spectroscopy reveals a signal at −2353 ppm, which is characteristic of a Pt(II) species coordinated to four nitrogen donors.[20]

***trans*-$[Pt(9\text{-}EtGH\text{-}\underline{N7})_2(9\text{-}MeA\text{-}\underline{N7})(NH_3)](NO_3)_2 \cdot 1.5H_2O$ (9).** The ^1H NMR spectrum of **9** in D_2O agrees with its composition. The two 9-EtGH ligands are chemically equivalent, suggesting that the two bases are oriented head−head or, alternatively, that their rotation is fast, with 9-MeA fixed. A head−head orientation of all three nucleobases would permit internal H bonding between one of the two NH_2 protons of 9-MeA (NH_2 group coplanar with heterocycle) and two O6 oxygen atoms of the two guanine ligands.

The pH dependence of the aromatic nucleobase protons in the range 1−12 confirms that all three bases are bound via the N7 positions: The 9-EtGH ligands undergo deprotonation at N1 with a pK_a of 8.5,[29] while the two 9-MeA resonances are shifted upfield at acidic pH ($pK_a \approx 2.5$), as expected for protonation at N1.[17,30]

Summary

The work described here was performed in order to assess the synthetic potential of complexes of type *cis*-$[PtCl(L)(NH_3)_2]^{n+}$ (with L being a model nucleobase) as precursors of tris(nucleobase) complexes containing two or three different nucleobases. At the same time we were interested in the role of intracomplex hydrogen bond formation in determining the relative orientation of the nucleobases in such complexes. Both aspects are potentially relevant to reactions of tri- and tetrafunctional Pt(II) species such as $[PtCl_3(NH_3)]^-$ and $[PtCl_4]^{2-}$, respectively, with DNA and models thereof as well as to reactions of *cis*-$PtCl_2(NH_3)_2$ with DNA that occur with partial loss of NH_3. While tris-[4] and even tetrakis[31,32] nucleobase complexes have been characterized before, these examples contain a single type of nucleobase bound to Pt only, unlike the compounds reported here.

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Supporting Information Available: Tables of crystallographic data, positional parameters, anisotropic thermal displacement parameters, bond distances and angles, interatomic contacts, stereoviews of the unit cells of **4**, **6b**, and **7b**, and views of possible conformations of cations **7** and **7a** (32 pages). Ordering information is given on any current masthead page.

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