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Crystal Structure and Dynamic ^{1}H NMR of (1,2-Bis(pyridin-2-yl)ethane-N,N')bis(9-methylhypoxanthine-N^7)platinum(II) Dinitrate

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The synthesis, X-ray crystal structure, and dynamic ^{1}H NMR of (1,2-bis(pyridin-2-yl)ethane-N,N')bis(9-methylhypoxanthine-N^7)platinum(II) dinitrate, $[Pt(bpe)(9\text{-}MeHX)_2](NO_3)_2$, $C_{24}H_{24}N_{12}O_8Pt$, are described. NMR spectra of this and other Pt(II) compounds containing the bpe ligand show that this ligand forms a rigid seven-membered chelate. The solid-state structure of the title compound has been determined with the aid of single-crystal X-ray diffraction. Crystals are monoclinic, having space group $P2_1/c$ with cell dimensions $a = 8.891$ (3) Å, $b = 19.517$ (6) Å, $c = 16.314$ (7) Å, and $\beta = 91.06$ (3)°, and have four formula units in the unit cell. The structure has been solved by the heavy-atom method and refined by standard least-squares techniques to $R = 0.057$ and $R_w = 0.049$ for 3357 reflections with $I \geq 1.9\sigma(I)$. The compound consists of nitrate anions and $Pt(bpe)(9\text{-}MeHX)_2^{2+}$ cations. The cation is square-planar coordinated with a mean Pt–N distance of 2.013 (4) Å and N–Pt–N angles from 87.6 to 94.5°. The 9-MeHX ligands are roughly at right angles to the coordination plane (82.8 and 86.7°) and in a head-to-tail arrangement to each other. The pyridine rings of the bpe ligand have approximate angles of 65° to the coordination plane (62.5 and 69.4°). The solution behavior of the title compound has been studied by dynamic ^{1}H NMR. At low temperatures, rotation about the Pt–N(7) bond is slow, with the purines in a head-to-tail arrangement. This gives rise to two sets of resonances for the 9-MeHX ligands in the NMR spectra. Above the coalescence temperature (−32 °C) one "averaged" set of resonances is observed, indicating fast rotation of the 9-MeHX ligands about the Pt–N(7) bonds at these temperatures. $\Delta G^{\ddagger}$ for the interconversion of the rotamers is calculated to be about 50 kJ mol^{-1}.

Introduction

Antitumor-active platinum compounds like *cis*-$Pt(NH_3)_2Cl_2$ may form intrastrand cross-links in DNA.[2] This seems to be a key step in its mechanism of action.[3] Platinum is known to bind preferentially to the N(7) atoms of the guanosine bases as confirmed by both NMR[4] and crystallographic studies of platinum compounds containing two guanosines or other 6-oxopurines as ligands.[5] In the crystal structures reported so far, the purines were invariably found to be in a head-to-tail arrangement. However, this seems not to be the most likely arrangement when platinum forms a cross-link between two adjacent guanosines in DNA.

Recently, a NMR study of (N,N,N',N'-tetramethyl-1,2-diaminoethane)bis(guanosine)platinum(II) showed that in this compound rotation of the guanosines about the Pt–N(7) bonds is not fast on the NMR time scale.[6] However, the authors did not prove that fast rotation occurs in platinum compounds with amines that give less steric hindrance, because neither upon heating of the compound with methyl-substituted nitrogens nor upon cooling of a compound with no methyl groups on the nitrogens was a coalescence found. Furthermore, it was assumed, but not proven, that the guanosines in this compound are in a head-to-tail arrangement.

To obtain further information on the solution behavior of model compounds for Pt-DNA interactions, we are studying the rotational and conformational behavior in *cis*-bis(amine)bis(6-oxopurine)platinum(II) compounds. It occurred to us that a compound with an amine ligand that gives rise to different environments above and below the platinum coordination plane can give information about the conformation and rotational behavior of the two 6-oxopurine ligands. 1,2-Bis(pyridin-2-yl)ethane (bpe) was found to satisfy this purpose, giving a rigid seven-membered chelate ring with platinum. Because the chiral ribose of guanosine is not essential for this study, the simpler 6-oxopurine 9-methylhypoxanthine (9-MeHX) was used. The solid-state structure of the compound $[Pt(bpe)(9\text{-}MeHX)_2](NO_3)_2$ has been studied by a single-crystal structure determination and compared with the solution behavior as studied by ^{1}H NMR.

Experimental Section

Starting Materials. K_2PtCl_4 (Drijfhout, Amsterdam) and 1,2-bis(pyridin-2-yl)ethane (Alfred Bader Chemie) were commercially available. 2,2-Dimethyl-1,3-diaminopropane was a gift from BASF (Arnhem). 9-Methylhypoxanthine was prepared from 9-methyladenine[7] by treatment with $NaNO_2$.[8]

Syntheses. $Pt(bpe)I_2$. To a solution of 830 mg of K_2PtCl_4 (2 mmol) in 50 mL of water was added 8 g of KI. The resultant solution, containing PtI_4^{2-} ions, was mixed with a solution of the ligand (368 mg, 2 mmol) dissolved in 10 mL of ethanol. After the solution stood overnight, the formed precipitate was filtered. One gram of this precipitate was dissolved in 50 mL of N,N-dimethylformamide. To this solution was slowly added 20 mL of water. The yellow precipitate of $Pt(bpe)I_2$ was filtered, washed with water and ethanol, and dried in vacuo at 50 °C. Anal. Calcd: C, 22.76; H, 1.91; N, 4.42. Found: C, 22.88; H, 1.91; N, 4.26.

$Pt(bpe)Cl_2$. To a suspension of the diiodo compound in water, containing 10% acetone, was added 1.95 equiv of $AgNO_3$ as a concentrated solution in water. The suspension was stirred for 3 h in the dark. The AgI precipitate was filtered off, and to the clear filtrate, supposed to contain the diaqua species, was added a large excess of NaCl. Slowly pale yellow crystals of $Pt(bpe)Cl_2$ formed. They were filtered, washed with water and ethanol, and dried in vacuo at 50 °C.

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(1) (a) State University Leiden. (b) Westfälischen Wilhelms-Universität.

(2) (a) Chottard, J. C.; Girault, J. P.; Chottard, G.; Lallemand, J. Y.; Mansuy, D. *J. Am. Chem. Soc.* **1980**, *102*, 5565. (b) Marcelis, A. T. M.; Canters, G. W.; Reedijk, J. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 391. (c) Tullius, T. D.; Lippard, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 4620.

(3) (a) Roberts, J. J.; Thomson, A. J. *Prog. Nucleic Acid Res. Mol. Biol.* **1972**, *22*, 71. (b) Rahn, R. O.; Johnson, N. P.; Hsie, A. W.; Lemont, J. F.; Masker, W. E.; Regan, J. D.; Dunn, W. C., Jr. In "The Scientific Basis of Toxicity Assessment"; Witschi, H., Ed.; Elsevier North-Holland: New York, 1980; p 153.

(4) (a) Kong, P. C.; Theophanides, T. *Inorg. Chem.* **1974**, *13*, 1167. (b) Chu, G. Y. H.; Mansy, S.; Duncan, R. E.; Tobias, R. S. *J. Am. Chem. Soc.* **1978**, *100*, 593. (c) Marcelis, A. T. M.; Van Kralingen, C. G.; Reedijk, J. *J. Inorg. Biochem.* **1980**, *13*, 213.

(5) (a) Marzilli, L. G.; Chalilpoyil, P.; Chiang, C. C.; Kistenmacher, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 2480. (b) Gellert, R. W.; Bau, R. *Ibid.* **1975**, *97*, 7379. (c) Bau, R.; Gellert, R. W. *Biochimie* **1978**, *60*, 1040. (d) Bau, R.; Gellert, R. W.; Lehovec, S. M.; Louie, S. *J. Clin. Hematol. Oncol.* **1977**, *7*, 51. (e) Kistenmacher, T. J.; Chiang, C. C.; Chalilpoyil, P.; Marzilli, L. G. *J. Am. Chem. Soc.* **1979**, *101*, 1143. (f) Kistenmacher, T. J.; Chiang, C. C.; Chalilpoyil, P.; Marzilli, L. G. *Biochem. Biophys. Res. Commun.* **1978**, *84*, 70. (b) Goodgame, D. M. L.; Jeeves, I.; Phillips, F. L.; Skapski, A. C. *Biochim. Biophys. Acta* **1975**, *378*, 153. (h) Cramer, R. E.; Dahlstrom, P. L.; Seu, M. J. T.; Norton, T.; Kashiwagi, M. *Inorg. Chem.* **1980**, *19*, 148.

(6) Cramer, R. E.; Dahlstrom, P. L. *J. Am. Chem. Soc.* **1979**, *101*, 3679.

(7) Krüger, G. *Z. Phys. Chem., Stoechiom., Verwandtschaftsl.* **1893**, *18*, 434.

(8) Elion, G. B. *J. Org. Chem.* **1962**, *27*, 2478.

Table I. Summary of Crystal Data and Intensity Collection

compd	$Pt(C_{12}H_{12}N_2)(C_6H_6N_4O)_2(NO_3)_2$
formula	$C_{24}H_{24}N_{12}O_8Pt$
fw	803.62
cryst dimens	needle, 0.24 × 0.10 × 0.08 mm
space group	monoclinic, $P2_1/c$
a	8.891 (3) Å
b	19.517 (6) Å
c	16.314 (7) Å
β	91.06°
V	2830.4 Å^3
Z	4
density(calcd)	1.886 g cm^{-3}
density(obsd)	1.87 g cm^{-3}
temp	20 °C
radiation	Mo Kα (λ(Mo K$\bar{\alpha}$) = 0.710 69 Å from graphite monochromator)
μ	52.9 cm^{-1}
no. of indep reflctns	5039
no. of reflctns with $I \geqslant 1.9\sigma(I)$	3357
2θ limit	54°
final no. of variables	386
R^a	0.057
$R_w{}^b$	0.049
weighting	$1/w = (\sigma(F_o))^2 + (0.01 \lvert F_o \rvert)^2$
min scan speed	4° min^{-1} (in 2θ)
max scan speed	30° min^{-1} (in 2θ)
bkgd counting	25% of counting time on each side

^{a} $R = \Sigma(\lvert\lvert F_o\rvert - \lvert F_c\rvert\rvert)/\Sigma\lvert F_o\rvert$. ^{b} $R_w = [\Sigma w(\lvert F_o\rvert - \lvert F_c\rvert)^2/\Sigma w F_o{}^2]^{1/2}$.

Anal. Calcd: C, 32.01; H, 2.69; N, 6.22. Found: C, 31.73; H, 2.79; N, 6.39. IR: ν(Pt–Cl) 336, 323 cm^{-1}.

[Pt(bpe)(dmdap)]$(NO_3)_2$. To a solution of the diaquo compound, prepared as described for the dichloro compound, was added a small excess of 2,2-dimethyl-1,3-diaminopropane (dmdap). This mixture was allowed to react at 60 °C for 3 days. The resulting clear solution was concentrated to a few milliliters. Any precipitate formed at 5 °C was filtered off. To the filtrate was slowly added 30 mL of acetone. The white crystalline precipitate that formed was filtered, washed with acetone, and dried in vacuo at 50 °C.

[Pt(bpe)(9-MeHX)$_2$]$(NO_3)_2$. To a solution of the diaquo compound, prepared as described for the synthesis of the dichloro compound, was added 2 equiv of 9-MeHX. This mixture was allowed to react at 60 °C for 3 days. The clear solution was concentrated to 2 mL. Upon addition of 30 mL of a 1:1 mixture of acetone and diethyl ether, a white precipitate formed. Crystals suitable for X-ray analysis were obtained by allowing a solution of the compound in a 1:1 mixture of water and diethylene glycol dimethyl ether to evaporate slowly at room temperature.

NMR Spectra. Fourier-transform ^{1}H NMR spectra (100 MHz) were obtained on a JEOL PS-100 spectrometer. Spectra of the compounds Pt(bpe)X_2 (X = Cl and I) were obtained from solutions in $(CD_3)_2SO$ with Me_4Si (tetramethylsilane) as an internal reference. D_2O was used as the solvent for spectra of [Pt(bpe)(dmdap)]$(NO_3)_2$ and [Pt(bpe)(9-MeHX)$_2$]$(NO_3)_2$ at ambient or higher temperatures, with TSP (sodium salt of 2,2,3,3-tetradeuterio-3-(trimethylsilyl)-propionic acid) as internal reference. For the low-temperature spectra a solution of [Pt(bpe)(9-MeHX)$_2$]$(NO_3)_2$ in a 90% CD_3OD/10% D_2O mixture was used, with Me_4Si as internal reference. The temperature was determined from the chemical shift difference between the CH_3 and OH resonances from methanol in a separate sample.

X-ray Methods and Structure Determination. [Pt(bpe)(9-MeHX)$_2$]$(NO_3)_2$ crystallizes in the monoclinic space group $P2_1/c$ with four formula units in the unit cell. X-ray intensity data of 5039 unique reflections (a needle-shaped crystal measuring approximately 0.24 × 0.10 × 0.08 mm; calculated minimum and maximum absorption corrections are 0.37 and 0.67, respectively) were measured in the θ–2θ scan mode up to $(\sin\theta)/\lambda$ = 0.595 Å^{-1}, 3357 of which with $I \geq 1.9\sigma(I)$ were used for the structure determination. Crystal data and other numbers related to data collection are summarized in Table I. The density was obtained by flotation in a chloroform/dibromoethane mixture.

The intensity data were empirically corrected for absorption with ψ scans around the diffraction vector of 10 selected reflections. The intensity data were corrected for Lorentz and polarization effects. The structure was solved by means of a three-dimensional Patterson synthesis, using Pt as a heavy atom in the starting model, and a series of full-matrix least-squares refinements followed by block-diagonal-matrix least-squares refinements in the final cycles.

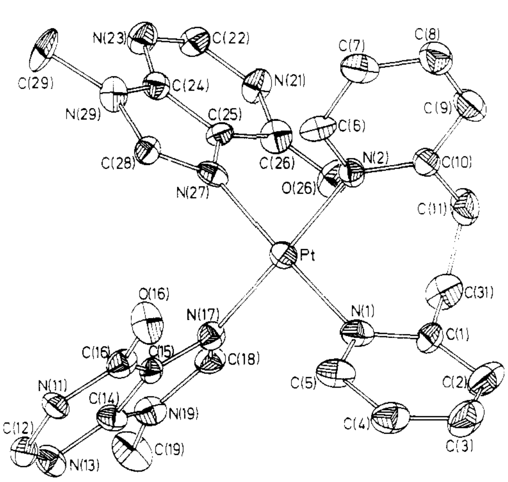

Figure 1. The cation (1,2-bis(pyridin-2-yl)ethane-*N*,*N'*)bis(9-methylhypoxanthine-*N*^{7})platinum(II) showing the atom numbering.

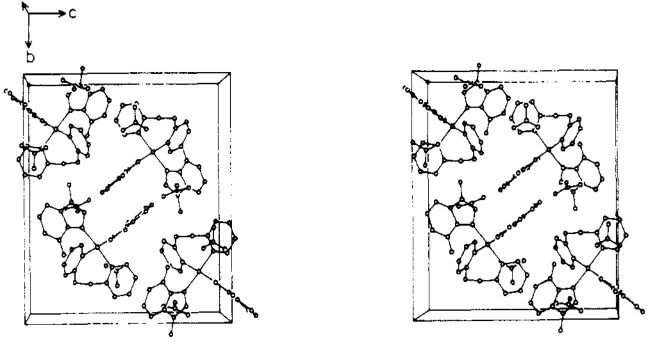

Figure 2. Stereoview of the packing of the Pt(bpe)(9-MeHX)$_2{}^{2+}$ cations within the unit cell.

All non-hydrogen atoms were refined with anisotropic temperature factors except O(2), O(4), O(5), and N(4). Because of considerably high temperature factors these atoms were refined only isotropically. The positions of the hydrogen atoms were either located in the final difference Fourier map (methyl groups) or calculated from the carbon atom coordinates to which they are attached. All hydrogen atoms were included in the structure factor calculations (with assumption of C–H distances of 0.95 Å, N–H distances of 0.87 Å, and B values of 4.0 Å^2) but were not refined.

Throughout the refinement scattering curves were taken from ref 9. Atomic coordinates of the non-hydrogen atoms are given in Table II, together with the calculated isotropic thermal parameters. The anisotropic thermal parameters are available as supplementary material, as well as the parameters of the hydrogen atoms.[10] A listing of observed and calculated structure factors is also available.[10]

Results and Discussion

Description of the Structure. Figure 1 shows the Pt(bpe)(9-MeHX)$_2{}^{2+}$ cation, whereas the molecular packing of the complex is shown in Figure 2. The numbering scheme in the 9-MeHX ligands is such that the last digit corresponds with the IUPAC–IUB nomenclature for purines. Bond lengths and bond angles are given in Tables III and IV, respectively. The two 9-MeHX ligands are bound through N(7) to platinum. The coordinating nitrogen atoms are arranged roughly square planar around the platinum atom. Pt–N distances

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(9) Cromer, D. T.; Waber, J. T. "International Tables for X-ray Crystallography"; Ibers, J. A., Hamilton, W. C., Eds.; Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.2A, p 72.

(10) Supplementary material.

Table II. Coordinates of the Non-Hydrogen Atoms of $[Pt(bpe)(9\text{-}MeHX)_2](NO_3)_2$ with Standard Deviations in Parentheses

atom	*x*	*y*	*z*	B_{eq}[a]
Pt	0.22163 (5)	0.19875 (3)	0.14656 (3)	2.99
N(1)	0.2547 (10)	0.2807 (5)	0.0744 (6)	3.94
C(1)	0.2235 (14)	0.3445 (6)	0.1028 (7)	3.77
C(2)	0.2738 (16)	0.4015 (7)	0.0618 (8)	5.45
C(3)	0.3491 (17)	0.3953 (8)	−0.0098 (9)	6.51
C(4)	0.3756 (16)	0.3305 (8)	−0.0416 (8)	5.37
C(5)	0.3312 (13)	0.2739 (7)	0.0018 (7)	3.87
N(2)	0.3858 (10)	0.2356 (5)	0.2213 (5)	3.07
C(6)	0.5092 (13)	0.1959 (7)	0.2280 (6)	3.76
C(7)	0.6324 (13)	0.2164 (7)	0.2770 (7)	4.65
C(8)	0.6302 (16)	0.2766 (7)	0.3170 (8)	5.40
C(9)	0.5011 (17)	0.3174 (7)	0.3088 (7)	5.36
C(10)	0.3815 (13)	0.2961 (7)	0.2596 (6)	3.55
C(11)	0.2438 (16)	0.3410 (7)	0.2585 (8)	4.97
C(31)	0.1437 (15)	0.3467 (7)	0.1820 (8)	4.79
N(11)	0.1756 (10)	0.0421 (5)	−0.0908 (5)	3.34
C(12)	0.0323 (14)	0.0277 (6)	−0.1159 (7)	3.76
N(13)	−0.0896 (10)	0.0526 (5)	−0.0860 (6)	3.87
C(14)	−0.0588 (12)	0.0944 (6)	−0.0228 (7)	3.30
C(15)	0.0787 (12)	0.1147 (6)	0.0079 (6)	2.84
C(16)	0.2094 (13)	0.0875 (6)	−0.0283 (7)	3.64
O(16)	0.3430 (9)	0.0980 (5)	−0.0086 (6)	5.06
N(17)	0.0617 (10)	0.1578 (5)	0.0733 (6)	3.32
C(18)	−0.0864 (12)	0.1636 (6)	0.0823 (7)	3.35
N(19)	−0.1619 (10)	0.1260 (5)	0.0262 (6)	3.68
C(19)	−0.3280 (13)	0.1208 (8)	0.0168 (8)	5.19
N(21)	−0.0422 (11)	0.1348 (5)	0.4000 (6)	3.90
C(22)	−0.0227 (14)	0.0702 (7)	0.4246 (7)	4.21
N(23)	0.0578 (12)	0.0237 (5)	0.3898 (6)	4.22
C(24)	0.1237 (12)	0.0485 (6)	0.3236 (7)	3.14
C(25)	0.1123 (12)	0.1139 (6)	0.2924 (6)	3.04
C(26)	0.0227 (13)	0.1640 (7)	0.3313 (8)	4.01
O(26)	−0.0014 (10)	0.2235 (4)	0.3100 (5)	4.80
N(27)	0.1974 (9)	0.1176 (5)	0.2215 (5)	3.02
C(28)	0.2576 (12)	0.0562 (6)	0.2106 (7)	3.12
N(29)	0.2179 (10)	0.0134 (5)	0.2733 (6)	3.67
C(29)	0.2664 (17)	−0.0578 (7)	0.2847 (9)	5.72
N(3)	0.3519 (13)	0.5318 (6)	0.2489 (8)	6.26
O(1)	0.4074 (10)	0.5067 (6)	0.3139 (6)	6.41
O(2)	0.2218 (16)	0.5502 (8)	0.2546 (9)	10.9 (4)[b]
O(3)	0.4227 (13)	0.5433 (6)	0.1867 (6)	8.26
N(4)	0.7377 (14)	0.3089 (7)	0.0460 (7)	7.2 (3)[b]
O(4)	0.7416 (23)	0.3709 (11)	0.0457 (12)	18.2 (7)[b]
O(5)	0.6547 (13)	0.2854 (6)	0.1023 (7)	8.8 (3)[b]
O(6)	0.7652 (16)	0.2791 (6)	−0.0145 (7)	9.18

[a] The equivalent isotropic thermal parameters B_{eq} ($Å^2$) are calculated as one-third of the orthogonalized B_{ij} tensor: $B_{eq} = {}^1/_3\Sigma_i\Sigma_jB_{ij}a_i^*a_j^*a_ia_j$. [b] These atoms were refined with isotropic temperature factors only.

Table III. Bond Distances (Å) of $[Pt(bpe)(9\text{-}MeHX)_2](NO_3)_2$

	Platinum		
Pt–N(1)	2.012 (10)	Pt–N(17)	2.006 (9)
Pt–N(2)	2.017 (9)	Pt–N(27)	2.015 (9)
	Hypoxanthine 1		
N(11)–C(16)	1.38 (2)	C(16)–O(16)	1.24 (1)
N(11)–C(12)	1.36 (2)	N(17)–C(15)	1.37 (1)
C(12)–N(13)	1.29 (2)	N(17)–C(18)	1.33 (1)
N(13)–C(14)	1.34 (2)	C(18)–N(19)	1.34 (2)
C(14)–C(15)	1.37 (2)	N(19)–C(14)	1.37 (1)
C(15)–C(16)	1.42 (2)	N(19)–C(19)	1.48 (1)
	Hypoxanthine 2		
N(21)–C(26)	1.39 (2)	C(26)–O(26)	1.23 (2)
N(21)–C(22)	1.33 (2)	N(27)–C(25)	1.40 (1)
C(22)–N(23)	1.29 (2)	N(27)–C(28)	1.33 (2)
N(23)–C(24)	1.33 (2)	C(28)–N(29)	1.37 (2)
C(24)–C(25)	1.38 (2)	N(29)–C(24)	1.37 (1)
C(25)–C(26)	1.42 (2)	N(29)–C(29)	1.47 (3)
	Pyridine 1		
N(1)–C(1)	1.36 (2)	C(2)–C(3)	1.36 (2)
N(1)–C(5)	1.38 (1)	C(3)–C(4)	1.39 (2)
C(1)–C(31)	1.49 (2)	C(4)–C(5)	1.38 (2)
C(1)–C(2)	1.38 (2)	C(31)–C(11)	1.52 (2)
	Pyridine 2		
N(2)–C(6)	1.35 (2)	C(8)–C(9)	1.40 (2)
N(2)–C(10)	1.34 (2)	C(9)–C(10)	1.38 (2)
C(6)–C(7)	1.40 (2)	C(10)–C(11)	1.51 (2)
C(7)–C(8)	1.35 (2)		
	Nitrate N(3)		
N(3)–O(1)	1.26 (2)	N(3)–O(3)	1.23 (2)
N(3)–O(2)	1.22 (2)		
	Nitrate N(4)		
N(4)–O(4)	1.21 (3)	N(4)–O(6)	1.17 (2)
N(4)–O(5)	1.28 (2)		

range from 2.006 (9) to 2.017 (9) Å and are normal for Pt compounds with coordinating purines,[5] imidazoles,[11] or pyridines.[12] Planes through the purines are approximately perpendicular to the square coordination plane (82.8 and 86.7°). The two 6-oxopurines point in opposite directions (head-to-tail arrangement). The bond lengths and the bond angles within the purine rings are normal and do not deviate much from the values observed in other compounds with metal atoms coordinated to N(7) of 9-MeHX.[13] The interior angles about N(11) (123.1 (10)°), N(21) (125.1 (10)°), N(13) (111.1 (10)°), and N(23) (110.9 (10)°) indicate that both 9-MeHX ligands are protonated at the expected N(1) position.[14]

The bpe ligand forms a seven-membered chelate ring by coordination through its nitrogen atoms N(1) and N(2). The two pyridine moieties of this ligand are twisted from the square plane with angles of 62.5 and 69.4°. The ethylene bridge is located above the platinum coordination plane. The conformation of the seven-membered chelate can be described as boatlike. In six-membered chelates of 1,3-propanediamines with platinum chair-type conformations are more common.[15] Relevant interatomic distances are found between the nitrate O(6) and N(21) (2.79 Å) and between O(1) and N(11) (2.77 Å), indicating two relatively strong hydrogen bridges with angles of 175° (N(21)–HN(21)–O(6)) and 167° (N(11)–H-N(11)–O(1)).

The N(27)–Pt–O(26) (64.4°) and N(17)–Pt–O(16) (63.5°) angles suggest that free rotation of the purines about the Pt–N(7) bonds may be hindered, when a bulky ligand is present in a cis position. As seen from Figure 2, the planes of the 9-methylhypoxanthine ligands in different cations are almost parallel. However, these bases lie opposite to each other with O(16)–O(16) contacts of 4.74 Å, connected through a center of symmetry, and do not stack. On the other hand, there is a weak stacking interaction between part of one of the pyridine rings (C(2), C(3), and C(4)) and the six-membered ring of one 9-MeHX ligand. Some short contacts are (in Å) C(2)···C(22) = 3.47, C(3)···C(22) = 3.52, C(3)···C(24) = 3.52, C(3)···N(23) = 3.43, C(2)···N(23) = 3.67, and C(4)···C(25) = 3.71. All other intermolecular contacts can be considered to be normal.

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(11) (a) Graves, B. J.; Hodgson, D. J.; Van Kralingen, C. G.; Reedijk, J. *Inorg. Chem.* **1978**, *17*, 3007. (b) Cingi, M. B.; Lanfredi, A. M. M.; Tiripichio, A.; Van Kralingen, C. G.; Reedijk, J. *Inorg. Chim. Acta* **1980**, *39*, 265. (c) Korte, H.-J.; Krebs, B.; Van Kralingen, C. G.; Marcelis, A. T. M.; Reedijk, J. *Ibid.* **1981**, *52*, 61.

(12) (a) Melanson, R.; Rochon, F. D. *Can. J. Chem.* **1976**, *54*, 1002. (b) Thiele, G.; Wagner, D. *Chem. Ber.* **1978**, *111*, 3162. (c) Colamarino, P.; Orioli, P. L. *J. Chem. Soc., Dalton Trans.* **1975**, 1656.

(13) (a) Sletten, E. *Acta Crystallogr., Sect. B* **1974**, *B30*, 1961. (b) Bélanger-Gariépy, F.; Beauchamp, A. L. *J. Am. Chem. Soc.* **1980**, *102*, 3461. (c) Sletten, E.; Kaale, R. *Acta Crystallogr., Sect. B* **1977**, *B33*, 158.

(14) Singh, C. *Acta Crystallogr.* **1965**, *19*, 861.

(15) (a) Van Kralingen, C. G.; Reedijk, J.; Spek, A. L. *Inorg. Chem.* **1980**, *19*, 1481. (b) Nakayama, Y.; Ooi, S.; Kuroya, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 914.

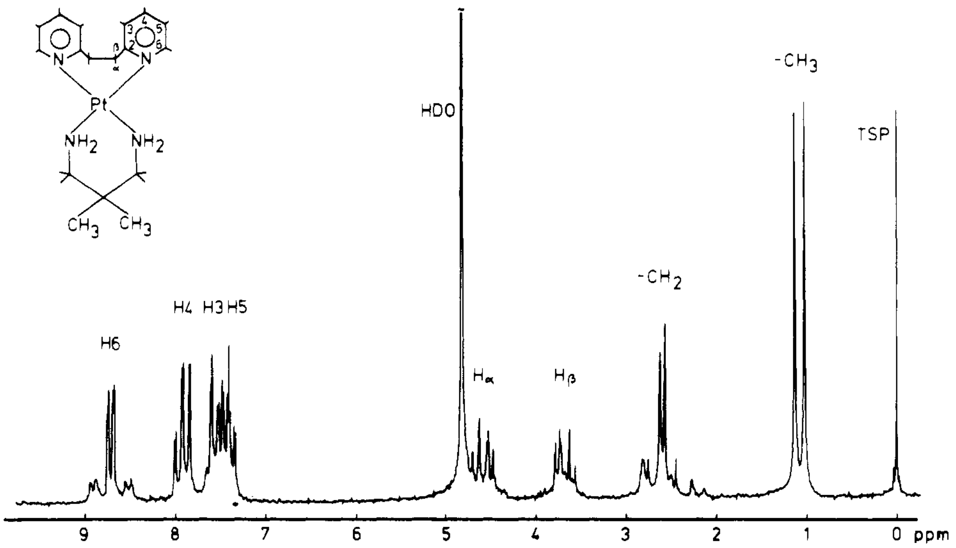

Figure 3. ^{1}H NMR spectrum of [Pt(bpe)(dmdap)]$(NO_3)_2$ at room temperature (100 MHz, D_2O).

Table IV. Bond Angles (Deg) of [Pt(bpe)(9-MeHX)$_2$]$(NO_3)_2$

	Platinum		
N(1)-Pt-N(2)	87.6 (4)	N(2)-Pt-N(27)	89.9 (4)
N(17)-Pt-N(27)	88.0 (4)	N(2)-Pt-N(17)	177.4 (4)
N(1)-Pt-N(17)	94.5 (4)	N(1)-Pt-N(27)	177.4 (4)
	Hypoxanthine 1		
C(16)-N(11)-C(12)	123 (1)	N(11)-C(16)-O(16)	120 (1)
N(11)-C(12)-N(13)	127 (1)	O(16)-C(16)-C(15)	128 (1)
C(12)-N(13)-C(14)	111 (1)	C(18)-N(17)-C(15)	105.2 (9)
N(13)-C(14)-C(15)	129 (1)	Pt-N(17)-C(15)	128.5 (7)
N(13)-C(14)-N(19)	126 (1)	Pt-N(17)-C(18)	126.3 (8)
C(15)-C(14)-N(19)	105 (1)	N(19)-C(18)-N(17)	111 (1)
C(14)-C(15)-C(16)	118 (1)	C(18)-N(19)-C(19)	126 (1)
C(14)-C(15)-N(17)	111 (1)	C(18)-N(19)-C(14)	108.1 (9)
C(16)-C(15)-N(17)	131 (1)	C(14)-N(19)-C(19)	126 (1)
N(11)-C(16)-C(15)	112 (1)		
	Hypoxanthine 2		
C(26)-N(21)-C(22)	125 (1)	N(21)-C(26)-O(26)	123 (1)
N(21)-C(22)-N(23)	127 (1)	O(26)-C(26)-C(25)	128 (1)
C(22)-N(23)-C(24)	111 (1)	C(28)-N(27)-C(25)	106.9 (9)
N(23)-C(24)-C(25)	127 (1)	Pt-N(27)-C(25)	127.5 (7)
N(23)-C(24)-N(29)	126 (1)	Pt-N(27)-C(28)	125.6 (7)
C(25)-C(24)-N(29)	106 (1)	N(29)-C(28)-N(27)	109.9 (9)
C(24)-C(25)-C(26)	121 (1)	C(28)-N(29)-C(29)	126 (1)
C(24)-C(25)-N(27)	109 (1)	C(28)-N(29)-C(24)	108.3 (9)
C(26)-C(25)-N(27)	131 (1)	C(24)-N(29)-C(29)	125 (1)
N(21)-C(26)-C(25)	109 (1)		
	Pyridine 1		
C(1)-N(1)-C(5)	119 (1)	C(2)-C(1)-C(31)	124 (1)
Pt-N(1)-C(1)	119.7 (8)	C(1)-C(2)-C(3)	121 (1)
Pt-N(1)-C(5)	120.2 (8)	C(2)-C(3)-C(4)	119 (1)
N(1)-C(1)-C(31)	115 (1)	C(3)-C(4)-C(5)	119 (1)
N(1)-C(1)-C(2)	120 (1)	N(1)-C(5)-C(4)	121 (1)
	Pyridine 2		
C(6)-N(2)-C(10)	120 (1)	C(8)-C(9)-C(10)	120 (1)
Pt-N(2)-C(6)	115.1 (7)	N(2)-C(10)-C(9)	121 (1)
Pt-N(2)-C(10)	124.8 (8)	N(2)-C(10)-C(11)	123 (1)
N(2)-C(6)-C(7)	121 (1)	C(9)-C(10)-C(11)	117 (1)
C(6)-C(7)-C(8)	121 (1)	C(10)-C(11)-C(31)	121 (1)
C(7)-C(8)-C(9)	118 (1)	C(11)-C(31)-C(1)	115 (1)
	Nitrate N(3)		
O(1)-N(3)-O(2)	114 (1)	O(2)-N(3)-O(3)	121 (1)
O(1)-N(3)-O(3)	125 (1)		
	Nitrate N(4)		
O(4)-N(4)-O(5)	112 (2)	O(5)-N(4)-O(6)	124 (1)
O(4)-N(4)-O(6)	119 (2)		

NMR Spectroscopy. The presence of a bifunctional chelating ligand in a square-planar platinum(II) bis(6-oxopurine) compound, which introduces an asymmetric environment with respect to the coordination plane, allows one to obtain information about the rotational behavior of the two purine ligands. If in the NMR spectrum two sets of resonances for these ligands are found, they must have a hindered rotation about the platinum–purine N(7) bond, with the ligands in a head-to-tail arrangement. If only one set of resonances is found, there are two possibilities. First, there may be a hindered rotation with the ligands in a head-to-head arrangement. Secondly, rotation may be fast on the NMR time scale, giving rise to averaged signals in the NMR spectrum. The coordination of 1,2-bis(pyridin-2-yl)ethane results in a rigid seven-membered chelate ring with platinum, as is seen from the NMR spectra of its platinum compounds. This is in sharp contrast with the five- and six-membered chelate rings of 1,2-diaminoethane and 1,3-diaminopropane with platinum, which remain flexible down to −50 °C, giving rapid interconversions between various chair and boat conformations.[16] The chemical shifts of the platinum compounds containing the bpe ligand are listed in Table V.

Two distinct chemical shifts are observed for the ethylene bridge protons, indicating the rigidness of the chelate ring. When the compound is heated to 50 °C, no coalescence is found. However, at this temperature the halide compounds rapidly decompose, probably by reaction with the solvent.[17] To obtain a water-soluble compound, and to see how this ligand influences other ligands, we synthesized a compound containing both a bpe and a dmdap ligand. The NMR spectrum of this compound (Figure 3) shows the presence of both ligands. The platinum satellites and the integration confirm the proposed composition. Due to the rigid conformation of the platinum–bpe chelate the methyl groups of the dmdap ligand are inequivalent. Even the protons within the CH_2 groups are inequivalent and give rise to an AB pattern. When this compound is heated to 85 °C, all resonances remain sharp, and no evidence for decomposition or broadening due to the onset of coalescence is found.

The NMR spectrum of [Pt(bpe)(9-MeHX)$_2$]$(NO_3)_2$ at room temperature shows the presence of both ligands. The resonances for the protons of the 9-MeHX ligand are found at 8.87 (H(8)), 8.23 (H(2)), and 3.88 (CH_3) ppm. Weak ^{195}Pt–^{1}H satellites are found on the bpe H(6) resonances (J_{Pt-H} = 39 Hz), and on the 9-MeHX H(8) resonances (J_{Pt-H} = 22 Hz). Together with the value of the integrated signals, this

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(16) Appleton, T. G.; Hall, J. R. *Inorg. Chem.* **1970**, *9*, 1807.

(17) Kerrison, S. J. S.; Sadler, P. J. *J. Chem. Soc., Chem. Commun.* **1977**, 861.

Table V. ^1H NMR Chemical Shifts and Pt-H Coupling Constants of Platinum-bpe Compounds[a]

compd	$H(6)(J_{Pt-H})$	H(5)	H(4)	H(3)	$-CH-H_\alpha$	$-CH-H_\beta$
$Pt(bpe)Cl_2$	9.05 (45)	7.47	8.03	7.66	4.64	3.58
$Pt(bpe)I_2$	9.08 (45)	7.44	7.98	7.63	4.43	3.57
$[Pt(bpe)(dmdap)](NO_3)_2$	8.69 (39)	7.40	7.91	7.55	4.58	3.68
$[Pt(bpe)(9\text{-}MeHX)_2](NO_3)_2$	8.92 (39)	7.36	7.89	7.61	5.26	3.86

[a] Chemical shifts are in ppm; coupling constants J_{Pt-H} (in Hz) are given in parentheses. Solvents and references are given in the Experimental Section. Spectra were recorded at room temperature.

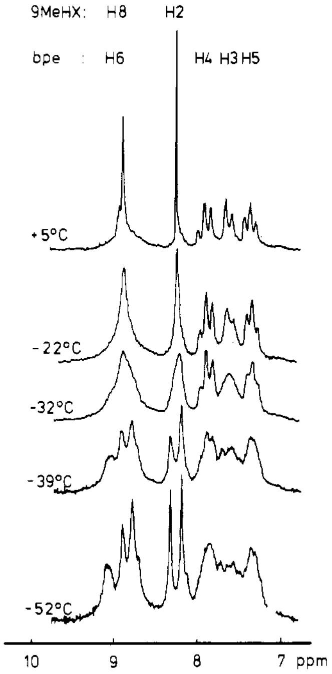

Figure 4. Aromatic region of the ^1H NMR spectra of $[Pt(bpe)(9\text{-}MeHX)_2](NO_3)_2$ at various temperatures (100 MHz, 10% D_2O/90% CD_3OD, Me_4Si).

confirms the proposed composition. As is seen from Table V, the $CH-H_\alpha$ resonance is shifted considerably downfield as compared to the resonance in the other Pt-bpe compounds. This downfield shift is most likely due to the deshielding by the O(6) of the 9-MeHX ligand, which can be quite close to these protons, as is seen from the X-ray study (2.57 and 2.73 Å). This observation also allows one to assign the $CH-H_\alpha$ resonance to the protons in the ethylene bridge that are closest to the Pt atom. At room temperature and above only one set of resonances is found for the 9-MeHX protons. When the temperature is lowered, the resonances first broaden, and coalescence is found at −32 °C. Below this temperature two sets of resonances are found for the 9-MeHX H(8) and H(2) protons (Figure 4). These results prove that at low temperatures the 9-MeHX ligands are in a head-to-tail arrangement, just as found in the single-crystal structure (vide supra) and that rotation about the Pt–N(7) bonds is slow on the NMR time scale. At low temperatures the apparent mirror symmetry in the compound, due to fast rotation of the purines about the Pt–N(7) bonds, is broken. All protons of the bpe ligand now should give rise to different signals. The splitting is most evident for the H(6) resonances, although one of the resonances partially overlaps with one of the H(8) resonances of 9-MeHX (see Figure 4). The other pyridine resonances cannot be observed separately due to extensive overlap and small differences in chemical shifts, as is also seen from Figure 4. The protons of the ethylene bridge cannot be observed because they disappear under the residual solvent and CH_3 (9-MeHX) resonances.

So at these low temperatures rotation of the 9-MeHX ligands about the Pt–N(7) bonds is slow on the NMR time scale. When the compound is heated, rotation becomes faster, resulting first in coalescence and finally in one averaged set of signals.

From the coalescence temperature and the line width at half-height at this temperature the free activation energy $\Delta G^\ddagger$ for the interconversion between the rotamers can be calculated[18] to be about 50 kJ mol^{-1}.

Concluding Remarks

The ligand bpe was found to be very suitable for the study of the conformation and rotational behavior of *cis*-platinum bis(6-oxopurine) compounds. There have been only very few reports of coordination compounds with the bpe ligand.[19] To our knowledge no coordination compound with this ligand has been structurally investigated before. Also its ability to form a rigid chelate has never been exploited. Although this ligand gives different environments above and below the platinum coordination plane, it does not influence the 9-MeHX ligands enough to force them in a head-to-head arrangement. This is clearly seen in both the X-ray structure and the low-temperature NMR spectra. Because the ethylene bridge of bpe forces the pyridine rings to form angles of approximately 65° with the square plane, the pyridines interfere to some extent with the rotation of the 9-MeHX ligands about the Pt–N(7) bonds. So when the temperature is changed, both slow and fast rotation on the NMR time scale can be observed. We have shown that in *cis*-platinum bis(6-oxopurine) compounds the purines rotate rapidly on the NMR time scale, provided that the other ligands do not give much steric hindrance, and that the preferred conformation both in solution and in the solid state is a head-to-tail arrangement for the two 6-oxopurines.

This study also provides profound evidence for the assumptions made by Cramer and Dahlstrom[6] and reconfirms their conclusions. Rotation about a Pt–purine or Pt–pyrimidine bond may be important for intrastrand cross-linking of Pt compounds in DNA. Cross-linking will be easier if—after an initial monofunctional binding—the Pt adduct can rotate to accommodate a second base, to which it is able to bind.

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Registry No. $[Pt(bpe)(9\text{-}MeHX)_2](NO_3)_2$, 82823-19-6; $Pt(bpe)Cl_2$, 82823-20-7; $Pt(bpe)I_2$, 82823-21-0; $[Pt(bpe)(dmdap)](NO_3)_2$, 82823-23-2; K_2PtCl_4, 10025-99-7.

Supplementary Material Available: Tables of anisotropic thermal parameters, hydrogen atomic positions, observed and calculated structure factors, and least-squares planes (18 pages). Ordering information is given on any current masthead page.

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(18) Gutowski, H. S.; Cheng, H. N. *J. Chem. Phys.* **1975**, *63*, 2439.

(19) Keeton, M.; Lever, A. B. P. *Inorg. Chem.* **1971**, *10*, 47.