Contribution from the Institute of Materials Research, McMaster University, Hamilton, Ontraio, L8S 4M1, Canada, and the Anorganische-Chemisches Institut, Technische Universität München, 8046 Garching, Federal Republic of Germany

Bis(1-methylcytosine) Complexes of *cis*-Diammineplatinum(II) and the X-ray Structure of a Platinum Complex with Covalently Bonded and Hydrogen-Bonded 1-Methylcytosine, *cis*-Diamminebis(1-methylcytosine-N^3)platinum(II) Dinitrate–1-Methylcytosine, *cis*-$[Pt(NH_3)_2(C_5H_7N_3O)_2](NO_3)_2 \cdot C_5H_7N_3O$

R. FAGGIANI,[1a] B. LIPPERT,[1b] and C. J. L. LOCK*[1a]

Received February 9, 1981

Three bis(1-methylcytosine-N^3) complexes of *cis*-$Pt(NH_3)_2^{2+}$, *cis*-$[Pt(NH_3)_2(MeCyt)_2]X_2$ with X = Cl^- and NO_3^-, have been prepared, and the crystal structure of one of these has been determined. Bis(1-methylcytosine-N^3)-*cis*-diammineplatinum(II) dinitrate–1-methylcytosine, *cis*-$[Pt(NH_3)_2(C_5H_7N_3O)_2](NO_3)_2 \cdot C_5H_7N_3O$, crystallizes in space group $P\bar{1}$, with cell dimensions a = 14.020 (3) Å, b = 13.676 (3) Å, c = 7.031 (3) Å, α = 98.97 (3)°, β = 95.39 (3)°, γ = 110.16 (2)°, and two formula units in the cell. The structure was determined by standard methods and refined to R_1 = 0.0488 and R_2 = 0.0581 based on 5025 independent reflections. Data were collected by using Mo Kα radiation and a Syntex $P2_1$ diffractometer. The structure shows two 1-methylcytosine ligands coordinated to Pt through N(3) with normal Pt–N ligands of 2.032 (8) and 2.045 (6) Å and in addition a 1-methylcytosine molecule hydrogen bonded in the crystal lattice. The dihedral angles between the two bonded cytosine rings and between the rings and the ligand square plane are 102.0 (3), 78.7 (3), and 77.6 (3)°, respectively. The presence of both coordinated and "free" ligand in the compound permitted a detailed study of the effects of N(3) platination on the 1-methylcytosine ring. Though the X-ray results do not show significant perturbations of the cytosine ring upon N(3) platination, ^1H NMR, IR, and Raman spectroscopies do show distinct differences of the two species. Raman frequency shifts characteristic for N(3) platination both in solution and in the solid state are reported and supported by comparison with the spectra of *cis*-$[Pt(NH_3)_2(MeCyt)_2]X_2$ (X = Cl^-, NO_3^-), *trans*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$, and *cis*-$[PtCl(NH_3)_2(MeCyt)]X$ (X = Cl^-, NO_3^-).

Introduction

The reaction of the *cis*-diammineplatinum(II) moiety with 1-methylcytosine, MeCyt, as a possible model for a platinum–DNA interaction, as well as the multisite coordination properties of the cytosine ligand,[2] has been of interest to us for some time. Depending upon the degree of hydrolysis of the platinum starting material, *cis*-$Pt(NH_3)_2Cl_2$, and the ratio r between Pt and the 1-methylcytosine ligand, we have isolated different products. Although N(3) proved to be the preferred coordination site, additional binding through the deprotonated exocyclic amine group of cytosine and through the exocyclic keto group has been observed. For example, with *cis*-$PtCl_2(NH_3)_2$ and r = 1, *cis*-$[PtCl(NH_3)_2(MeCyt)]Cl$ is isolated as the major product,[3] with *cis*-$[PtCl(NH_3)_2(H_2O)]NO_3$ and r = 1, two crystallographically different *cis*-$[PtCl(NH_3)_2(MeCyt)]NO_3$ species are obtained in good yield.[4] With *cis*-$[Pt(NH_3)_2(H_2O)_2]^{2+}$ and r = 1, dimeric complexes with deprotonated 1-methylcytosine ligands are isolated from neutral or slightly acidic solution.[5] Di- and polymeric complexes with neutral 1-methylcytosine bridges (N(3), O(2)) are isolated from solvents having poor coordinating properties.[6] With r = 0.5, the diaquo species forms 1:2 complexes, *cis*-$[Pt(NH_3)_2(MeCyt)_2]^{2+}$; with further excess of ligand, a 1:3 compound is isolated. This compound, bis(1-methylcytosine-N^3)-*cis*-diammineplatinum(II) dinitrate-1-methylcytosine, contains two cytosine ligands coordinated to platinum through N(3) each and in addition a cytosine molecule hydrogen bonded in the crystal lattice. It represents an excellent example for the study of the effect of platinum coordination at N(3) of 1-methylcytosine since it contains the free ligand as an "internal" reference. The X-ray structure and ^1H NMR, IR, and Raman spectra are reported. The vibrational spectra are compared with the free ligand, MeCyt, with *cis*-$[Pt(NH_3)_2(MeCyt)_2]X_2 \cdot aq$ (X = Cl, NO_3) and *trans*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$. The X-ray structure of the latter has been reported by us before;[7] a structure determination of the corresponding cis compound was not possible because of rapid loss of water of crystallization which made the crystals unsuitable. However, it is felt that the principal properties of the 1:2 cis complex are similar to those reported here with the additional ligand in the crystal lattice.

Experimental Section

Preparation. *cis*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2 \cdot MeCyt$. *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$, obtained by reaction of *cis*-$Pt(NH_3)_2Cl_2$ with 2 mol of $AgNO_3$ in H_2O,[8] and 1-methylcytosine, MeCyt, were reacted in 1:3 ratio (0.022 M Pt, 40 h, 40 °C, stoppered flask); the solution (pH 5.85) was reduced in volume and crystallized at 22 °C; colorless cubes; yield 60–70%. Recrystallization from H_2O at 0 °C was accomplished with appreciable loss due to separation into *cis*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$ and MeCyt (Anal. Calcd: C, 24.72; H, 3.74; N, 25.0; O, 19.76; Pt, 26.77. Found: C, 24.26; H, 3.70; N, 25.02; O, 20.01; Pt, 27.07.) The compound was also obtained upon reaction of *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ and MeCyt in 1:2 ratio and subsequent slow crystallization; yield 20–25%. Coproducts in this reaction were bis(μ-(1-methylcytosinato-N^3,N^4))-bis(*cis*-diammineplatinum(II) dinitrate[5] (2% yield) and occasionally *trans*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$.[9] The main product of this reaction was *cis*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2 \cdot xH_2O$. Separation of the main product was achieved, due to its high and rapid solubility compared to the other products, by repeated recrystallization; yield 40–50%; colorless, transparent columns. The rapid loss of water of crystallization of the compound when exposed to air was accompanied by a loss of transparency. (Anal. Calcd for the dehydrated compound: C, 19.90; H, 3.25; N, 23.21; Pt, 32.21. Found: C, 19.78; H, 3.36; N, 23.25; Pt, 31.7.) In the laser beam (100 mW), the compound tended to decompose under prolonged exposure.

***cis*-$[Pt(NH_3)_2(MeCyt)_2]Cl_2 \cdot xH_2O$.** *cis*-$Pt(NH_3)_2Cl_2$ and MeCyt were reacted in H_2O in a 1:2 ratio (0.02 M Pt, 40 h, 40 °C, stoppered

(1) (a) McMaster University. (b) Technische Universität München.
(2) For reviews on this subject see, e.g.: (a) Marzilli, L. G. *Progr. Inorg. Chem.* **1979**, *23*, 255. (b) Gellert, R. W.; Bau, R. *Met. Ions Biol. Syst.* **1979**, *8*, 1. (c) Martin, R. B.; Mariam, Y. H. *Ibid.* **1979**, *8*, 57. (d) De Castro, B.; Kistenmacher, T. J.; Marzilli, L. G. *Agents Actions*, in press.
(3) Faggiani, R.; Lippert, B.; Lock, C. J. L., manuscript in preparation.
(4) Lippert, B.; Lock, C. J. L.; Speranzini, R. A. *Inorg. Chem.* **1981**, *20*, 335.
(5) Faggiani, R.; Lippert, B.; Lock, C. J. L.; Speranzini, R. A. *J. Am. Chem. Soc.* **1981**, *103*, 1111.
(6) Lippert, B., manuscript in preparation.
(7) Lippert, B.; Lock, C. J. L.; Speranzini, R. A. *Inorg. Chem.* **1981**, *20*, 808.
(8) Lippert, B.; Lock, C. J. L.; Rosenberg, B.; Zvagulis, M. *Inorg. Chem.* **1977**, *16*, 1525.
(9) Presumably caused by an impurity of trans Pt(II) in cis Pt(II). Cf. ref 7.

0020-1669/82/1321-3210$01.25/0

Table I

compd	$(C_5H_7N_3O)[Pt(C_5H_7N_3O)_2(NH_3)_2](NO_3)_2$, $C_{15}H_{27}N_{13}O_9Pt$
formula weight	728.55
cryst size, mm	cylinder, $r = 0.05$, $l = 0.30$
systematic absences	none
space group	$P\bar{1}$
unit cell	$a = 14.020$ (3) Å, $\alpha = 98.97$ (3)°, $b = 13.676$ (3) Å, $\beta = 95.39$ (3)°, $c = 7.031$ (3) Å, $\gamma = 110.16$ (2)
V, Å^3	1234.2 (7)
Z	2
d_{calcd}, g cm^{-3}	1.96
d_{obsd}, g cm^{-3}	1.97 (1)
linear abs coeff, cm^{-1}	60.6
abs cor factor limits	1.59
std reflctn (esd, %)	6,0,−1 (0.93), 4,4,−2 (1.78)
temp, °C	22
no. of independent reflctns	5025
no. with $I > 3\sigma(I)$	4032
$3\sigma(I) > I > 0$	785
$I < 0$	208
final R_1, R_2	0.0488, 0.0581
final shift/error max (av)	0.036, 0.002
g (secondary extinctn)	1.097×10^{-7}
final difference map	
highest peak, e/Å^3; location	2.1; 0.25, 0.10, 0.25
lowest valley, e/Å^3; location	1.2; 0.20, 0.15, 0.15
weighting scheme	$w = (\sigma^2 + (0.04F_o)^2)^{-1}$
error in an observation of unit weight	1.039

[a] $R_1 = (\Sigma||F_o| - |F_c||)/\Sigma|F_o|$. $R_2 = [(\Sigma w(|F_o| - |F_c|)^2)/\Sigma wF_o^2]^{1/2}$.

flask); the tan solution was concentrated by rotary evaporation and crystallized at 0 °C. After 4 days the formed precipitate was collected. It consisted of crystals of *cis*-$[Pt(NH_3)_2Cl(MeCyt)]Cl \cdot H_2O$[3] (30% yield) and *cis*-$[Pt(NH_3)_2(MeCyt)_2]Cl_2 \cdot xH_2O$ (7–10% yield). Separation of the compound was accomplished by repeated recrystallization. At a later stage of the crystallization process, mixtures of 1:1 and 1:2 complexes and unreacted starting materials were obtained. No attempts were made to separate these or to increase the yield of the 1:2 complex. Colorless columns rapidly lost water of crystallization when exposed to air. (Analysis depended upon time on air. E.g., Anal. Calcd for tetrahydrate: C, 19.27; H, 4.54; N, 17.99. Found: C, 19.42; H, 4.60; N, 17.64. Calcd for 1.5 hydrate: C, 20.78; H, 4.02; N, 19.39. Found: C, 20.85; H, 4.04; N, 19.05.) The tetrahydrate was obtained in good yield (65%) when *cis*-$[Pt(NH_3)_2Cl(MeCyt)]Cl \cdot H_2O$[3] and MeCyt were reacted in 1:1 ratio in H_2O (0.1 M Pt, 7 h, 80 °C, stoppered flask) and crystallized at room temperature. As a byproduct of this reaction, yellow crystals of *trans*-$Pt(NH_3)Cl_2(MeCyt) \cdot 0.5H_2O$ were obtained in low yield (5%), resulting from the interconversion *cis*-$[Pt(NH_3)_2Cl(MeCyt)]Cl \rightarrow$ *trans*-$Pt(NH_3)Cl_2(MeCyt) + NH_3$.[7] *trans*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$ was prepared according to ref 7 and *cis*-$[PtCl(NH_3)_2(MeCyt)]NO_3$ according to ref 4; the preparation of *cis*-$[PtCl(NH_3)_2(MeCyt)]Cl \cdot H_2O$ and its X-ray structure will be reported in detail shortly.[3]

Deuterated compounds were prepared by two to four recrystallizations from D_2O.

Apparatus. IR spectra were recorded on a Perkin-Elmer 580 grating spectrometer as Nujol mulls (CsI windows) and calibrated against polystyrene. The listed frequencies were taken from spectra recorded on an extended scale with a maximum resolution of 1.3 cm^{-1}.

Raman spectra were recorded on a Coderg PH 1 with krypton laser excitation (647.1 nm) and calibrated against indene. Spectral slit widths were as indicated. Reported intensities refer to signal heights.

^{1}H NMR spectra were recorded on a JEOL JNM-FX 60 Fourier transform spectrometer at 30 °C in D_2O. The internal reference was $[N(CH_3)_4]BF_4$; the chemical shifts (δ scale) were calculated relative to TSP (sodium 3-(trimethylsilyl)propane sulfonate. The shift of $[N(CH_3)_4]^+$ relative to TSP was taken as 3.19 ppm. pD measurements were performed with a glass electrode and 0.4 units were added to the obtained pH meter reading to give pD.[10]

(10) Lumry, R.; Smith, E. L.; Glantz, R. R. *J. Am. Chem. Soc.* **1951**, *73*, 4335.

Table II. Atomic Positional Parameters $\times 10^4$

	x	y	z
Pt	2240.3 (2)	1568.1 (3)	2697.3 (4)
N(11)	896 (6)	368 (6)	2858 (11)
N(12)	3009 (7)	550 (6)	2923 (12)
N(1)	240 (6)	2915 (6)	251 (10)
C(2)	852 (7)	2326 (7)	524 (11)
N(3)	1417 (5)	2512 (5)	2346 (9)
C(4)	1366 (7)	3255 (7)	3834 (10)
C(5)	702 (8)	3828 (8)	3536 (15)
C(6)	164 (8)	3656 (8)	1736 (14)
C(1)	−371 (9)	2712 (9)	−1689 (17)
O(2)	873 (5)	1649 (5)	−826 (9)
N(4)	1934 (7)	3416 (7)	5557 (12)
N(1A)	5274 (6)	3866 (6)	4105 (10)
C(2A)	4288 (6)	3228 (6)	4256 (11)
N(3A)	3593 (5)	2738 (5)	2532 (9)
C(4A)	3868 (6)	2924 (6)	783 (11)
C(5A)	4869 (7)	3645 (7)	675 (13)
C(6A)	5556 (7)	4079 (7)	2340 (13)
C(1A)	6033 (7)	4302 (7)	5930 (13)
O(2A)	4035 (5)	3107 (5)	5844 (9)
N(4A)	3179 (6)	2422 (6)	−828 (11)
N(1B)	6783 (6)	2126 (6)	2752 (12)
C(2B)	5760 (7)	1630 (7)	2900 (13)
N(3B)	5031 (6)	1246 (6)	1264 (11)
C(4B)	5322 (7)	1343 (7)	−485 (12)
C(5B)	6387 (8)	1872 (8)	−662 (14)
C(6B)	7075 (9)	2235 (8)	959 (11)
C(1B)	7573 (9)	2508 (9)	4495 (16)
O(2B)	5508 (6)	1560 (6)	4545 (11)
N(4B)	4588 (7)	975 (7)	−2073 (12)
N(5)	1576 (7)	−579 (6)	7378 (12)
O(51)	1450 (9)	−784 (9)	8954 (16)
O(52)	819 (8)	−956 (8)	6012 (14)
O(53)	2376 (10)	−29 (9)	6932 (17)
N(6)	7989 (7)	4775 (7)	285 (12)
O(61)	8148 (7)	4219 (7)	−1105 (13)
O(62)	8411 (7)	4815 (7)	1972 (13)
O(63)	7484 (7)	5292 (7)	63 (12)

Collection of the Crystal Data. A colorless crystal, chosen after examination under a polarizing microscope for homogeneity, was ground to a cylinder and used for data collection. Precession photographs of the crystal showed it was triclinic, and a Delaunay test showed no hidden symmetry. Unit cell parameters were obtained from least-squares fit of χ, ϕ, and 2θ for 15 reflections for the compound in the range $20° < 2\theta < 28°$ recorded on a Syntex $P2_1$ diffractometer using graphite-monochromated Mo Kα radiation (λ 0.71069 Å). Crystal data and other numbers related to data collection are summarized in Table I. The density was obtained by flotation in a bromoform–chloroform mixture. Intensities were also recorded on the Syntex $P2_1$ diffractometer with a coupled θ(crystal)–2θ(counter) scan. The methods of selection of scan rates and initial data treatment have been described.[11,12] Corrections were made for Lorentz–polarization effects and absorption.

Solution of the Structure. The coordinates of the platinum atom were found from a three-dimensional Patterson synthesis and a series of full-matrix least-squares refinements followed by three-dimensional electron density difference syntheses revealed all the nonhydrogen atoms. After refinement, the temperature factor of the platinum atom, which was previously isotropic, was made anisotropic. Further refinement with full-matrix least squares minimizing $\sum w(|F_o| - |F_c|)^2$ was terminated when the maximum shift/error was about 0.04. No attempt was made to locate the hydrogen atoms. Corrections were made for secondary extinction with use of the method of Larson.[13] Throughout the refinement, the scattering curves were taken from ref 14, and anomalous dispersion corrections from ref 15 were applied

(11) Hughes, R. P.; Krishnamachari, N.; Lock, C. J. L.; Powell, J.; Turner, G. *Inorg. Chem.* **1977**, *16*, 314.
(12) Lippert, B.; Lock, C. J. L.; Rosenberg, B.; Zvagulis, M. *Inorg. Chem.* **1977**, *16*, 1525.
(13) Larson, A. C. *Acta Crystallogr.* **1965**, *18*, 502.
(14) 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 ff.

Table III. Selected Interatomic Distances (Å) and Angles (Deg)[a]

		Nonhydrogen Bonds			
N(1)-C(1)	1.47 (1)	N(1)-C(2)	1.38 (1)	C(2)-N(3)	1.38 (1)
N(1A)-C(1A)	1.48 (1)	N(1A)-C(2A)	1.38 (1)	C(2A)-N(3A)	1.39 (1)
N(1B)-C(1B)	1.47 (1)	N(1B)-C(2B)	1.38 (1)	C(2B)-N(3B)	1.37 (1)
N(3)-C(4)	1.37 (1)	C(4)-C(5)	1.43 (2)	C(5)-C(6)	1.35 (1)
N(3A)-C(4A)	1.36 (1)	C(4A)-C(5A)	1.43 (1)	C(5A)-C(6A)	1.35 (1)
N(3B)-C(4B)	1.34 (1)	C(4B)-C(5B)	1.44 (1)	C(5B)-C(6B)	1.33 (1)
C(6)-N(1)	1.38 (1)	C(2)-O(2)	1.23 (1)	C(4)-N(4)	1.33 (1)
C(6A)-N(1A)	1.38 (1)	C(2A)-O(2A)	1.22 (1)	C(4A)-N(4A)	1.335 (9)
C(6B)-N(1B)	1.38 (1)	C(2B)-O(2B)	1.25 (1)	C(4B)-N(4B)	1.34 (1)
N(5)-O(51)	1.20 (2)	N(5)-O(52)	1.26 (1)	N(5)-O(53)	1.22 (2)
N(6)-O(61)	1.23 (1)	N(6)-O(62)	1.26 (1)	N(6)-O(63)	1.24 (2)
Pt-N(11)	2.056 (7)	Pt-N(12)	2.05 (1)	Pt-N(3)	2.032 (8)
Pt-N(3A)	2.045 (6)				
		Possible Hydrogen Bonds			
N(11)-O(2)[a]	3.03 (1)	N(11)-O(52)[b]	2.93 (1)	N(11)-O(52)	3.06 (1)
N(12)-O(53)	3.17 (1)	N(4)-O(62)[c]	2.96 (1)	N(4)-O(2A)	3.11 (1)
N(4)-O(63)[c]	3.18 (1)	N(4A)-O(2)	3.04 (1)	N(4A)-O(2A)[d]	2.87 (1)
N(4B)-O(53)[d]	2.89 (1)	N(4B)-O(2B)[d]	2.91 (1)		
		Interatomic Angles			
C(6)-N(1)-C(2)	122.3 (8)	N(1)-C(2)-N(3)	118.2 (8)	C(2)-N(3)-C(4)	120.5 (8)
C(6A)-N(1A)-C(2A)	122.1 (7)	N(1A)-C(2A)-N(3A)	117.5 (7)	C(2A)-N(3A)-C(4A)	120.9 (6)
C(6B)-N(1B)-C(2B)	120.3 (8)	N(1B)-C(2B)-N(3B)	120.1 (9)	C(2B)-N(3B)-C(4B)	119.3 (8)
N(3)-C(4)-C(5)	120.4 (8)	C(4)-C(5)-C(6)	119 (1)	C(5)-C(6)-N(1)	120 (1)
N(3A)-C(4A)-C(5A)	120.6 (7)	C(4A)-C(5A)-C(6A)	118.3 (8)	C(5A)-C(6A)-N(1A)	120.5 (8)
N(3B)-C(4B)-C(5B)	121.2 (8)	C(4B)-C(5B)-C(6B)	118 (1)	C(5B)-C(6B)-N(1B)	121 (1)
C(1)-N(1)-C(2)	118.3 (8)	C(1)-N(1)-C(6)	119 (1)	O(2)-C(2)-N(1)	120.2 (8)
C(1A)-N(1A)-C(2A)	117.0 (7)	C(1A)-N(1A)-C(6A)	120.9 (7)	O(2A)-C(2A)-N(1A)	121.1 (7)
C(1B)-N(1B)-C(2B)	120.4 (9)	C(1B)-N(1B)-C(6B)	119.3 (9)	O(2B)-C(2B)-N(1A)	119.3 (8)
O(2)-C(2)-N(3)	121.6 (9)	N(4)-C(4)-N(3)	118 (1)	N(4)-C(4)-C(5)	121.4 (9)
O(2A)-C(2A)-N(3A)	121.5 (7)	N(4A)-C(4A)-N(3A)	118.5 (7)	N(4A)-C(4A)-C(5A)	120.9 (8)
O(2B)-C(2B)-N(3B)	120.6 (9)	N(4B)-C(4B)-N(3B)	118.1 (8)	N(4B)-C(4B)-C(5B)	120.6 (9)
O(51)-N(5)-O(52)	118.6 (9)	O(51)-N(5)-O(53)	126 (1)	O(52)-N(5)-O(53)	115 (1)
O(61)-N(6)-O(62)	119 (1)	O(61)-N(6)-O(63)	121.7 (9)	O(62)-N(6)-O(63)	120 (1)
Pt-N(3)-C(4)	123.0 (6)	Pt-N(3)-C(2)	116.4 (6)	N(11)-Pt-N(3)	88.7 (3)
Pt-N(3A)-C(4A)	121.2 (4)	Pt-N(3A)-C(2A)	117.3 (5)	N(12)-Pt-N(3A)	89.6 (3)
N(11)-Pt-N(3A)	178.7 (4)	N(11)-Pt-N(12)	89.2 (4)	N(3)-Pt-N(3A)	92.6 (3)
N(12)-Pt-N(3)	176.6 (3)				

[a] Key: (a) $-x, -y, -z$; (b) $-x, -y, 1-z$; (c) $1-x, 1-y, 1-z$; (d) $x, y, z-1$.

to the curve for platinum. The atom parameters for nonhydrogen atoms are listed in Table II.[16]

Results and Discussion

The molecular cation is shown in Figure 1a, the neutral 1-methylcytosine molecule is given in Figure 1b, and selected interatomic distances and angles are given in Table III. The platinum has square-planar coordination, and Pt–N distances are normal.[17] This is in contrast to the $[Pt(NH_3)_2(3\text{-}CMP)_2]^{4-}$ anion,[18] where the Pt–N(3) distance was 2.16 (3) Å. It was postulated that the long distance might be caused by cytosine–cytosine interactions, although it was noted the errors were large. The second reason appears to be the correct one since, with an almost identical arrangement of cytosine rings, the Pt–N(3) distances (N(3) = 2.032 (8), N(3A) = 2.045 (6) Å) are not anomalously large. The two bound rings are at the normal substantial dihedral angle to each other (102.0 (3)°) and to the ligand square plane (78.7 (3), 77.6 (3)°) (c.f. ref 18, 85.6 and 68.1°) (Table IV). The rings are oriented head-to-tail such that O(2) and O(2A) can hydrogen bond intramolecularly to N(4A) and N(4), as was observed in ref 18, and the distances (N(4)–O(2A) = 3.11 (1), N(4A)–O(2) = 3.04 (1) Å) are comparable to those given in ref 18 (3.11

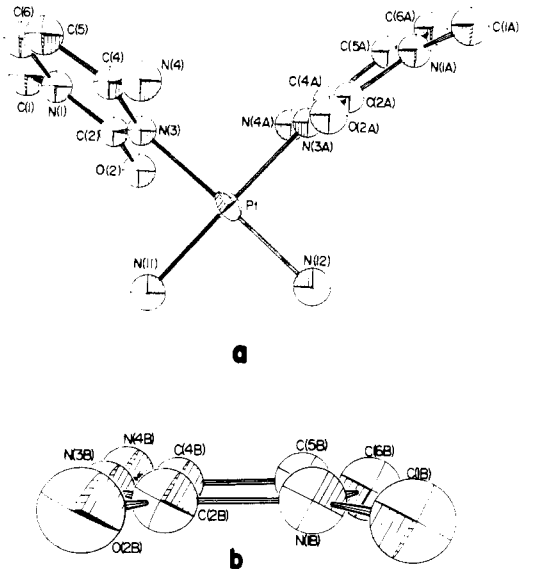

Figure 1. (a) Molecular cation $Pt(NH_3)_2(C_5H_7N_3O)_2^{2+}$. (b) Neutral molecule $C_5H_7N_3O$. Both show the numbering from Table II.

(15) Cromer, D. T. Reference 14, Table 2.3.1, pp 149–150.
(16) All computations were carried out on CDC 6400 or CYBER 170/730 computers. Programs used for initial data treatment were from the XRAY 76 package (Stewart, J. M. Technical Report TR-446; University of Maryland: College Park, MD, 1976). The structure was solved with SHELX (Sheldrick, G. M. Cambridge University: Cambridge, England, 1976). Final refinements and difference synthesis used the internally written programs CUDLS and SYMFOU (J. S. Stephens and J. S. Rutherford, respectively). Planes were calculated using NRC-22 (Ahmed, F. R.; Pippy, M. E. National Research Council of Canada: Ottawa, Canada, 1978). Diagrams were prepared from ORTEP II (Johnson, C. K. Report ORNL-5138; Oak Ridge National Laboratory: Oak Ridge, TN, 1976).
(17) Lock, C. J. L.; Speranzini, R. A.; Zvagulis, M. *Acta Crystallogr., Sect. B* **1980**, *B36*, 1789.
(18) Wu, S. M.; Bau, R. *Biochem. Biophys. Res. Commun.* **1979**, *88*, 1435.
(19) Roberts, J. J. *Recent Results Cancer Res.* **1974**, *79*, 48.
(20) Lock, C. J. L.; Bradford, J.; Faggiani, R.; Speranzini, R. A.; Turner, G.; Zvagulis, M. *J. Clin. Hematol. Oncol.* **1977**, *7*, 63.

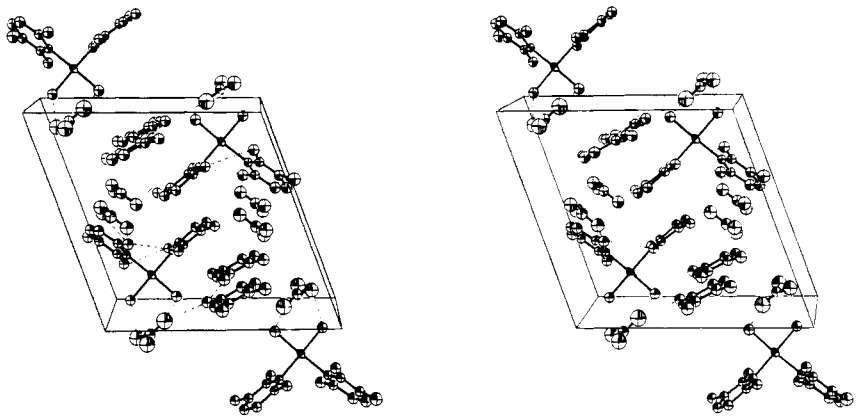

Figure 2. Packing of the molecules and ions in the unit cell. a and $(a \times b) \times a$ are parallel to the bottom and side of the page, respectively, and the view is down c^*.

(3) Å). Like Bau, we do not feel that the Pt···O(2) and Pt···O(2A) distances (3.027 (8) and 3.083 (8) Å) represent any bonding interactions. Calculations based on the Pt–N(3) lengths and the ring geometries show that if O(2), O(2A), N(4), and N(4A) attempt to get as far from platinum as possible, with Pt···O(2) being equal to Pt–N(4), the Pt···O(N) distances will be 3.08 Å. We assume the small deviations from this value are caused by the weak intramolecular hydrogen bonding. Bond lengths and angles within the 1-methylcytosine rings do not differ significantly for both the bound and free species, and they agree well with values found previously.[7,21,22] The changes in the observed internal angles going from unbound to bound cytosine at C(2), N(3), and C(4) (namely, decrease, increase, and decrease) are in the direction noted by Singh[23] for addition of an atom at N(3) and N(3A), but they lie within the errors, so clearly any effect is not as great as that caused by protonation.[24] The rings are essentially planar as are the nitrate ions although certain bonded exocyclic atoms lie significantly out of the planes of the rings (Pt –0.126 (1) Å, O(2) –0.044 (7) Å, and N(4) 0.035 (10) Å from cytosine N(1) to C(6); Pt 0.320 (1) Å, C(1A) 0.114 (10) Å, O(2A) –0.101 (7) Å, and N(4A) 0.067 (8) Å from cytosine N(1A) to C(6A); C(1B) 0.053 (12) Å from cytosine N(1B) to C(6B)). We have observed deviations of this magnitude before, and we assume these are caused by the exigencies of crystal packing.

The packing within the unit cell is shown in Figure 2. The free 1-methylcytosine, the N(5) nitrate, and the N(1A) 1-methylcytosine group are stacked along the b direction roughly parallel to each other and to the $1\bar{2}0$ plane. This will maximize π–π interactions. The other bound cytosine ring (N(1)) and the N(6) nitrate group to which it is bonded through the bifurcated hydrogen bond N(4)–O(62)^c, O(63)^c, and the corresponding groups related by the inversion center at 0, $^1/_2$, $^1/_2$ (or 1, $^1/_2$, $^1/_2$) comprise a rough plane roughly parallel to $33\bar{1}$, again maximizing π–π interactions. These planes are stacked up the c direction at $x = 0$ and $y = {}^1/_2$.

Hydrogen bonding plays an important part in holding the structure together. Thus close to the 010 face there is an extensive network involving the N(6) nitrate group which is bound to N(4B) of the free 1-methylcytosine, to N(11) and N(12) of the cation, and to N(12) of another centrosymmetrically related to the first. N(11) is also bound to O(2) of a centrosymmetrically related cation. In addition, in the c direction, there are hydrogen bonds between the N(4) and O(2) atoms on molecules related by the c translation for both the free 1-methylcytosine and the bound N(1A) 1-methylcytosine.

Table IV. Raman Frequencies of cis-[Pt(NH3)2(MeCyt)2](NO3)2·MeCyt in H2O (C = 0.25 M (Pt), pH 6.8, f = 4–6 cm^{-1})

free ligand		complex	shift[a]	assignt
269 (0.1)[b]		258 (0.1)	+11	
		324 (0.2)		
354 (0.1)				
387 (0.1)		425 (1.0)		
422 (0.3)		452 (0.2)		
	479 (4.2)			
		524 (1.0) dp[c]		ν(Pt–NH$_3$)
		536 (1.7)		
577 (0.4)		583 (1.2)	+6	
623 (0.7)		645 (2.4)	+22	
		718 (0.3) dp		ν_4(NO$_3$)
776 (6.0)		794 (10.0)	+18	
789[d]		832 (1.8)	+43	
	969 (0.3)			
980 (0.3)		1005 (0.5)	+25	
		1046 (8.2)		ν_1(NO$_3$)
		1131 (0.1)		
	1164 (1.3)			
	1208 (0.8)			
1276 (4.0)		1263 (8.7)	–13	
		1340 (0.6)		
1383 (0.3)		1392 (0.9)	+9	
	1435 (0.6)			
	1444 (0.3) dp			
1482 (0.1)		1475 (0.6)	–7	
1532 (0.5)		1543 (1.5)	+11	
	1612 (0.6)			
	1435 (0.6)			
	1444 (0.3) dp			
1482 (0.1)		1475 (0.6)	–7	
1532 (0.5)		1543 (1.5)	+11	
	1612 (9.6)			
		1642 (0.8)		
1657 (0.6)		1677 (1.3)	+20	

[a] Shift difference = (complex – free ligand) in cm^{-1}. [b] Intensities relative to strongest band with intensity 10. [c] dp = depolarized. [d] Band not resolved, but cf. Figure 3a.

Spectroscopy. Raman Solution Spectra. In Table IV Raman frequencies of cis-[Pt(NH3)2(MeCyt)2](NO3)2·MeCyt in H_2O between 250 and 1700 cm^{-1} are listed and assigned to the two types of 1-methylcytosine present. This was possible because the spectrum represented a clean superposition of the individual spectra of MeCyt and cis-[Pt(NH3)2(MeCyt)2](NO3)2 in water. Spectra of all three compounds were recorded. The spectrum of 1-methylcytosine in H_2O has been reported before by Lord and Thomas.[25] Our data agree well

(21) Voet, D.; Rich, A. *Prog. Nucleic Acid Res. Mol. Biol.* **1970**, *10*, 183.
(22) Lock, C. J. L.; Speranzini, R. A.; Powell, J. *Can. J. Chem.* **1976**, *54*, 53.
(23) Singh, C. *Acta Crystallogr.* **1965**, *19*, 861.
(24) Lock, C. J. L.; Pilon, P.; Lippert, B. *Acta Crystallogr., Sect. B* **1979**, *B35*, 2533.

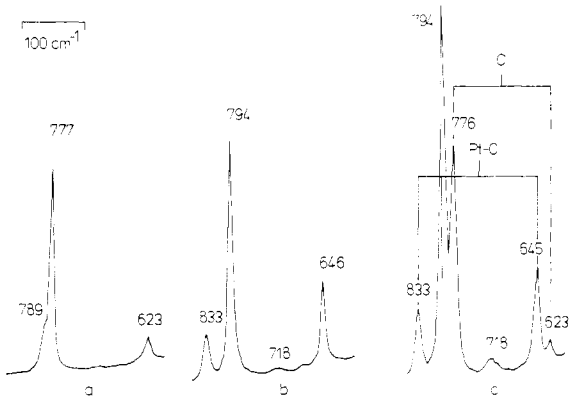

Figure 3. Raman solution spectra (H_2O) between 600 and 850 cm^{-1} (f = 4 cm^{-1}, MeCyt = free cytosine ligand; Pt–MeCyt = cytosine ligand bound to platinum): (a) MeCyt (pH 6.0); (b) *cis*-[Pt(NH_3)$_2$(MeCyt)](NO_3)$_2$ (pH 7.0); (c) *cis*-[Pt(NH_3)$_2$(MeCyt)$_2$](NO_3)$_2$·MeCyt (pH 6.8).

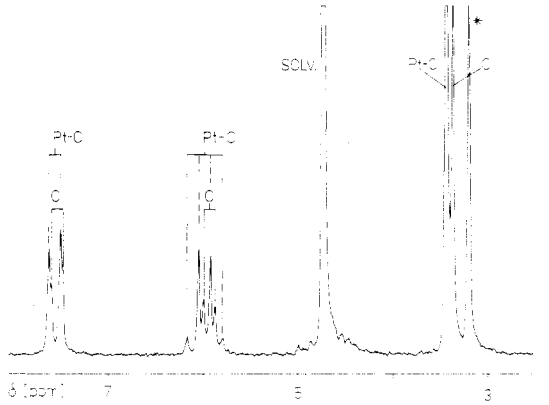

Figure 4. ^1H NMR spectrum (D_2O) of *cis*-[Pt(NH_3)$_2$(MeCyt)$_2$](NO_3)$_2$·MeCyt (C = 0.1 M (Pt), pD 6.8, * = $[(CH_3)_4N]BF_4$ reference, MeCyt = free cytosine ligand, and Pt–MeCyt = cytosine ligand bound to platinum).

with theirs with the exception of a few additional weak bands which we observed.

The most prominent spectral changes upon N(3)-platinum binding occurred in the 770–840-cm^{-1} range with the higher wave number shifts of the intense ring-breathing mode[25,26] and of a second, weaker ring mode. This is shown in Figure 3. A comparison of the two bands at 776 cm^{-1} (MeCyt) and 794 cm^{-1} (Pt complex) revealed that the ring-breathing mode decreased in intensity by 15–20% upon N(3) platination. On the contrary, the 623-cm^{-1} band of free 1-methylcytosine was shifted to 645 cm^{-1} on platination and more than doubled its intensity (Figure 3). Other changes in cytosine modes are shown in Table IV. Bands at 1046 and 718 cm^{-1} were assigned to NO_3^- vibrations and the superimposed bands at 536 and 524 cm^{-1} to the Pt–NH_3 stretching modes (ν_s and ν_{as}, respectively). The Raman spectra of aqueous solution of *cis*-[PtCl(NH_3)$_2$(MeCyt)]X (X = Cl^-, NO_3^-) showed very similar band positions ($\leq$2 cm^{-1}) for the cytosine ligand modes and only few more pronounced changes ($\sim$5 cm^{-1}) of the bands around 580, 990–1000, and 1670 cm^{-1}. The same applied to related complexes of composition *cis*-[Pt(NH_3)$_2$(MeCyt)(T-H)]ClO_4, where T-H is a thymine monoanion bound to platinum through N(1) and MeCyt is 1-methylcytosine bound through N(3).[27]

The observed Raman spectral changes when going from free 1-methylcytosine to a N(3)-platinated one resemble those observed by Tobias and co-workers for the interaction between cytidine and Pt and Hg electrophiles using Raman difference spectroscopy.[28,29] In addition to their findings, some other spectral changes were noticed in our system, but the large shift of the cytidine-stretching mode upon Pt binding (52 cm^{-1}) for Pt with r = 1 was less pronounced in our compound and appears not to be of any strong diagnostic value.

^1H NMR Spectrum. In Figure 4 the ^1H NMR spectrum of *cis*-[Pt(NH_3)$_2$(MeCyt)$_2$](NO_3)$_2$·MeCyt in D_2O is shown. Signals caused by the free ligand and the Pt bound ligand were identified by their relative intensities. The H(5) signal of the platinated cytosine showed sidebands caused by coupling to the ^{195}Pt isotope of spin $^1/_2$. The coupling constant was 15.0 Hz, in agreement with earlier findings.[4,27] All signals of the platinated ligands were shifted downfield relative to the free ligand: H(5) (0.05 ppm) slightly more than H(6) (0.02 ppm) and, somewhat surprisingly, the N–CH_3 signal even more than the two others (0.07 ppm). The coupling constant between H(5) and H(6) was unaffected by platinum binding (7.3 Hz).

Table V. Characteristic Raman Frequency Shifts of 1-Methylcytosine Modes upon N(3)-Platinum Binding, Taken from Solid-State Spectra

1-MeCyt	Pt(1-MeCyt-N^3)	1-MeCyt	Pt(1-MeCyt-N^3)
ca. 625 s[a]	ca. 640–650 s	1150 m	1160–1180 m s
770 vs	790–795 vs	1215 s	1200–1207 m w
780 m	830 s	1525 s	1535–1540 s

[a] Frequencies given in cm^{-1}. Intensities: w = weak, m = medium, s = strong, vs = very strong.

Solid-State Vibrational Spectra. Cytosine Modes. Since intermolecular coupling and intercomplex hydrogen bonding are absent in solution or at least very much reduced, Raman data obtained from solution spectra gave a more reliable information on the effects of metal coordination than do solid-state spectra. On the other hand, low solubility of compounds sometimes preclude solution studies, and strong Rayleigh scattering usually prevents detection of low-frequency bands in solution. In general, the solid-state spectrum of the title compound agreed well with the solution spectrum, and for most of the ligand modes similar shifts were observed upon complexation as in H_2O. This also applied to the modes of "free" MeCyt despite different bonding patterns in crystalline MeCyt[30] and the present complex *cis*-[Pt(NH_3)$_2$(MeCyt)$_2$](NO_3)$_2$·MeCyt. Differences in corresponding band positions did not exceed 10–12 cm^{-1} and were thus in the range usually found in heterocyclic systems with differing hydrogen-bonding schemes.[31]

In Table V, frequency shifts of selected Raman-active MeCyt vibrations are listed, which appear to be characteristic for N(3)-platinum binding. They have been taken from solid-state spectra of MeCyt *cis*-[Pt(NH_3)$_2$(MeCyt)$_2$]X_2 (X = Cl^-, NO_3^-), *trans*-[Pt(NH_3)$_2$(MeCyt)$_2$](NO_3)$_2$, *cis*-[Pt(NH_3)$_2$(MeCyt)$_2$](NO_3)$_2$, and *cis*-[Pt(NH_3)$_2$(MeCyt)$_2$](NO_3)$_2$·MeCyt (cf. supplementary material) as well as several other related complexes.[3,4,27] Because of their high intensities and large shifts upon platination, the two MeCyt modes around 770 cm^{-1} appear to be particularly suitable for a "first look"

(25) Lord, R. C.; Thomas, G. J., Jr. *Spectrochim. Acta, Part A* **1967**, *23A*, 2551.
(26) In unsubstituted cytosine the most intense mode at 790 cm^{-1} is assigned to an in-plane fundamental involving both angle deformation and bond-stretching motions of the skeleton. C.f.: Susi, H.; Ard, J. S.; Purcell, J. M. *Spectrochim. Acta, Part A* **1973**, *29A*, 725.
(27) Faggiani, R.; Lippert, B.; Lock, C. J. L.; Pfab, R. *Inorg. Chem.* **1981**, *20*, 2381.
(28) Chu, G. Y. H.; Duncan, R. E.; Tobias, R. S. *Inorg. Chem.* **1977**, *10*, 2625.
(29) Mansy, S.; Wood, T. E.; Sprowles, J. C.; Tobias, R. S. *J. Am. Chem. Soc.* **1974**, *96*, 1762.
(30) Mathews, F. S.; Rich, A. *Nature (London)* **1964**, *201*, 179.
(31) Lippert, B. *J. Raman Spectrosc.* **1980**, *9*, 324.

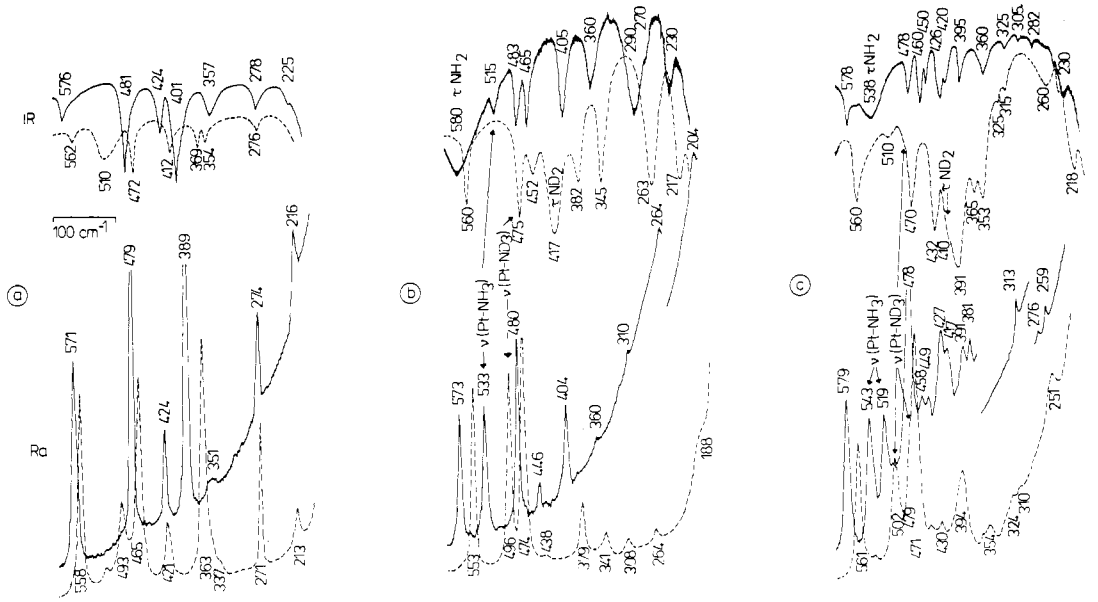

Figure 5. Infrared and Raman spectra between 600 and 200 cm^{-1} (H form (solid line) and D form (broken line); f = 2–4 cm^{-1}): (a) MeCyt; (b) *trans*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$; (c) *cis*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_3 \cdot MeCyt$.

concerning the way of binding. If Pt coordination occurs in a different way, for example, through N(3) and N(4),[5] the 770-cm^{-1} mode is shifted to 817 cm^{-1}, whereas the 625-cm^{-1} cytosine mode is only shifted to 633 cm^{-1} compared to (average) 645 cm^{-1} with N(3) platination. In all cases the very intense cytosine stretching mode around 1270 cm^{-1} appears to be too insensitive to be of any usefulness as diagnostic means for the site of metal coordination.

IR and Raman frequencies of platinated 1-methylcytosine in general were similar in cis and trans complexes. In the spectra of the *cis*-diammineplatinum(II) compounds, however, bands are sometimes split, and the cytosine mode at 405 cm^{-1} in the trans complex appears in all cis complexes, including the 1:1 complexes, at 415–425 cm^{-1}.

Solid State. (A) Skeletal Modes. In Figure 5 the 600–200-cm^{-1} IR and Raman range of C_1 *cis*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$ and *trans*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$ (H and D form) are shown. As far as the donor atoms of the $[Pt(NH_3)_2]^{2+}$ skeleton are concerned, C_{2v} symmetry for the cis complexes and D_{2h} symmetry for the trans complex can be assumed, which is reduced to C_1 site symmetry for *cis*-$[Pt(NH_3)_2(MeCyt)_2]_2(NO_3)_2 \cdot MeCyt$ and to C_i for *trans*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$ in the respective crystalline states. The distribution of the nine skeletal modes (Ra = Raman) is as follows:[32]

$$\text{cis complex } \Gamma_{skel} = 2A\ (IR, Ra) + 2B\ (IR, Ra) + 3A\ (IR, Ra) + 2B\ (IR, Ra)$$

$$\text{trans complex } \Gamma_{skel} = 2A_g\ (Ra) + 2A_1\ (IR) + A_g\ (Ra) + 4A_u\ (IR)$$

stretching modes

The Pt–NH_3 stretching modes were readily identified on the basis of their positions[33] and their deuteration shifts, which were close to values expected when the simple point mass model was used. As to the position of the Pt–Cyt stretching modes, a comparison of the spectra of 1-methylcytosine and the trans complex did not give any indication of a band above 315 cm^{-1} that could be assigned to such a mode. With the exception of the Pt–NH_3 modes, all bands could be related to cytosine modes and generally had deuteration shifts too high for a Pt–cytosine mode. With regard to the bands below 315 cm^{-1} (cf. supplementary material), only the weak Raman band at 310 cm^{-1} had no counterpart in the spectrum of the free ligand and was insensitive toward deuteration (308 cm^{-1}). Therefore, the band at 310 cm^{-1} is tentatively assigned to the Raman-active Pt–Cyt stretching mode. The corresponding IR active Pt–Cyt stretching mode could not be identified.

The identification of the Pt–Cyt stretching modes in the spectra of the cis complexes presented a similar problem. As with the trans complex, all of the cis complexes described here exhibited a weak band around 320 cm^{-1} with no corresponding band in the free ligand. In all spectra this band was almost insensitive toward deuteration. However, only the *cis*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2 \cdot MeCyt$ compound had a weak Raman band in this range which did not exhibit the coincidence with its IR counterpart expected for a Pt–Cyt mode under C_1 symmetry. Interestingly, the IR and Raman intensities of this band as well as that of the Pt–Cl stretching mode of the *cis*-$[PtCl(NH_3)_2(MeCyt)]^+$ complexes are subject to considerable changes (NO_3^- salts, $C2/c$, 341 s and 320 m s (IR), 334 s and 314 m (Ra); $P2_1/c$, 336 m s and 321 s (IR), 331 m and 314 s (Ra); Cl salt, $P1$, 332 w and 313 s (IR), 325 s and 312 s (Ra)). In the corresponding *trans*-$[PtCl(NH_3)_2(MeCyt)]Cl$ compound, only one strong IR band, the Pt–Cl stretching mode, was observed.[34] Even though we cannot assign the Pt–Cyt stretching modes with certainty at present, the following two conclusions can be drawn: First, these modes must be relatively weak in both the Raman and the IR, and second, their upper limit should be around 320 cm^{-1} or below.[35]

(B) Nitrate Vibrations. The nitrate vibrations in *cis*- and *trans*-$[Pt(NH_3)_2(MeCyt)_2](NO_3)_2$ are observed at values close to those found in other nitrate salts.[36] There was a curious doubling of the intense symmetric NO_3 stretching mode in the Raman spectrum (1038 (5), 1050 (5.8) cm^{-1}) of *cis*-[Pt-

(32) The notation used refers to the proper site symmetries of the compounds in the crystal lattice.

(33) For ν(Pt–NH_3) modes of related compounds see, e.g.: (a) Faggiani, R.; Lippert, B.; Lock, C. J. L.; Rosenberg, B. *J. Am. Chem. Soc.* **1977**, *99*, 777. (b) Reference 4.

(34) Preparation of *trans*-$[PtCl(NH_3)_2(MeCyt)]Cl$ by reaction of *trans*-$PtCl_2(NH_3)_2$ with MeCyt in H_2O; colorless crystals. Satisfactory analysis for C, H, N, and Pt.

(35) In *cis*-$[Pt(NH_3)_2(MeCyt)Cl]NO_3$[4] we have tentatively assigned the 260-cm^{-1} Raman band to a Pt–Cyt stretching mode for these reasons: (1) its considerable intensity compared to the MeCyt mode expected in this range, (2) its insensitivity on deuteration, (3) the fact that *cis*-$[Pt(NH_3)_2(MeCyt)Cl]$ had two bands in this range.

(36) See, e.g.: (a) Addison, C. C.; Sutton, D. *Prog. Inorg. Chem.* **1967**, *8*, 195. (b) Gatehouse, B. M.; Livingstone, S. E.; Nyholm, R. S. *J. Chem. Soc.* **1957**, 4222.

$(NH_3)_2(MeCyt)_2](NO_3)_2 \cdot MeCyt$ which was observed in the spectrum of the deuterated compound as well (1037 (7), 1060 (8) cm^{-1}). The two bands may arise from the two different nitrate ions, but it is also possible that the splitting arose from Fermi resonance between the weak 1-methylcytosine mode at 1052 cm^{-1} and the intense NO_3 vibration usually observed around 1045 cm^{-1} in nitrate salts.

Acknowledgment. We thank the National Cancer Institute of Canada, the Natural Sciences and Engineering Research Council of Canada, McMaster University Science and Engineering Research Board, Johnson, Matthey, Mallory, Ltd., the Deutsche Forschungsgemeinschaft, and the Technische Universität München for financial support of this work.

Supplementary Material Available: Tables of temperature factors, least-squares planes and dihedral angles, Raman frequencies, and the moduli of observed and calculated structure factors and Figures A, Raman spectra in the ring-breathing mode region, and B, low-frequency Raman spectra (29 pages). Ordering information is given on any current masthead page.

Contribution from the Institute for Materials Research, McMaster University, Hamilton, Ontario L8S 4M1, Canada, and the Anorganisch-Chemisches Institut, Technische Universität München, 8046 Garching, Federal Republic of Germany

Model Complexes of Possible Cross-Linking Products of *cis*-$Pt(NH_3)_2^{2+}$ with Cytosine and Guanine Bases of DNA: X-ray Structures of Three Mixed-Ligand Complexes of *cis*-Diammineplatinum(II) with 1-Methylcytosine and Neutral and Anionic 9-Ethylguanine

R. FAGGIANI,[1a] B. LIPPERT,[1b] C. J. L. LOCK,*[1a] and R. A. SPERANZINI[1a]

Received June 25, 1981

Three different mixed-ligand complexes of *cis*-$Pt(NH_3)_2^{2+}$ with 1-methylcytosine, C, and 9-ethylguanine, G, have been synthesized and studied by X-ray crystallography. *cis*-$[Pt(NH_3)_2GC](ClO_4)_2$ (I) has the space group $P2_1/n$ with a = 20.117 (7) Å, b = 27.017 (5) Å, c = 8.727 (2) Å, and β = 105.13 (2)° and has eight formula units in the unit cell. *cis*-$[Pt(NH_3)_2(G\text{-}H)C]ClO_4 \cdot 4H_2O$ (II) has the space group $P2_1/c$ with a = 12.344 (4) Å, b = 16.103 (5) Å, c = 12.517 (4) Å, and β = 90.36 (3)° and has four formula units in the unit cell. *cis*-$[Pt(NH_3)_2GC][Pt(NH_3)_2(G\text{-}H)C](ClO_4)_3$ (III) has the space group $C2/c$ with a = 23.467 (16) Å, b = 11.960 (3) Å, c = 16.093 (4) Å, and β = 106.56 (4)° and has four formula units in the unit cell. Data for all three compounds were collected with use of Mo Kα radiation and a Syntex $P2_1$ diffractometer. The crystal structures were determined by standard methods and refined to R_1 = 0.0552 (I), 0.0473 (II), and 0.0484 (III) and R_2 = 0.0662 (I), 0.0668 (II), and 0.0667 (III), on the basis of 3875 (I), 3749 (II), and 3279 (III) independent reflections. III crystallizes in a structure containing a novel hydrogen-bonding scheme between a neutral and an anionic guanine ligand which involves $N(2)H_2$, N(1), and O(6) of both G ligands. The acidity of the 9-ethylguanine ligand in I has been found to increase by 1.6 pK units as a consequence of platinum binding to the N1 position. This means that at a pH corresponding to the physiological pH, I and II are distributed approximately 85:15. Infrared and Raman spectra of the three compounds are presented. The effect of guanine deprotonation on the vibrational modes is studied. The conclusions on the nature of the short hydrogen bond between the N1 positions in III, drawn from IR and Raman spectra, are critically examined.

Introduction

There is substantial evidence pointing to DNA as the principal target of platinum antitumor drugs,[2] and to their ability to block DNA replication.[3] A preferential binding of platinum to DNA rich in guanine and cytosine content has been observed,[4] and several hypotheses have been forwarded to explain these findings. The two most popular theories presently discussed are those of intrastrand cross-linking of two guanine bases[5] and N7, O6 chelation of guanine by *cis*-diammineplatinum(II) complexes.[6] Though both models might explain the activity of cis complexes compared to that of the respective trans complexes, there are serious arguments against the N7, O6 proposal on stereochemical grounds.[7] In any case, strong binding of platinum to guanine is generally assumed. It is not certain whether the effect is kinetic in origin[8] or whether it is thermodynamically controlled,[9a] since the claim that equilibrium constants for 1:1 complexes of cis Pt(II) with guanosine, adenosine, and cytidine are nearly identical has been disputed.[9b] The consensus is that the effect is kinetic.[9b] Interestingly, results on the reaction of cis Pt(II) with G, C dinucleosides are controversial, supporting both preferential binding to G[10] and to C.[11]

We have recently started to systematically synthesize nucleobase model complexes of cis Pt(II) containing a single base,[12] two identical bases,[13] and two different bases. As a

(1) (a) McMaster University. (b) Technische Universität München.
(2) See, e.g.: Rosenberg, B. *Biochimie* **1978**, *60*, 859.
(3) Roberts, J. J.; Thomason, A. J. *Progr. Nucleic Acid Res. Mol. Biol.* **1979**, *22*, 71.
(4) (a) Mansy, S. Ph.D. Thesis, Michigan State University, East Lansing, MI, 1972. (b) Stone, P. J.; Kelman, A. D.; Sinex, F. M. *Nature (London)* **1974**, *251*, 736. Stone, P. J.; Kelman, A. D.; Sinex, F. M.; Bhargava, M. M.; Halvorson, H. O. *J. Mol. Biol.* **1976**, *104*, 793. (c) Munchausen, L. L.; Rahn, R. O. *Cancer Chemother. Rep., Part 1* **1975**, *59*, 643; *Biochim. Biophys. Acta* **1975**, *414*, 242.
(5) (a) Kelman, A. D.; Peresie, H. J. *Cancer Treat. Rep.* **1979**, *63*, 1445. Kelman, A. D.; Buchbinder, M. *Biochimie* **1978**, *60*, 893. (b) Cohen, G. L.; Ledner, J. A.; Bauer, W. R.; Ushay, H. M.; Caravana, C.; Lippard, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 2487.
(6) (a) Millard, M. M.; Macquet, J. P.; Theophanides, T. *Biochim. Biophys. Acta* **1975**, *402*, 166. Macquet, J. P.; Theophanides, T. *Bioinorg. Chem.* **1975**, *5*, 59. (b) Goodgame, D. M. L.; Jeeves, I.; Phillips, F. L.; Skapski, A. C. *Biochim. Biophys. Acta* **1975**, *378*, 153. (c) Dehand, J.; Jordanov, J. *J. Chem. Soc., Chem. Commun.* **1976**, 598.
(7) Chu, G. Y. H.; Mansy, S.; Duncan, R. E.; Tobias, R. S. *J. Am. Chem. Soc.* **1978**, *100*, 593.
(8) Mansy, S.; Chu, G. Y. H.; Duncan, R. E.; Tobias, R. S. *J. Am. Chem. Soc.* **1978**, *100*, 607.
(9) (a) Scovell, W. M.; O'Connor, T. *J. Am. Chem. Soc.* **1977**, *99*, 120. (b) Vestues, P. I.; Martin, R. B. *Ibid.* **1981**, *103*, 806.
(10) Inagaki, K.; Kidani, Y. *J. Inorg. Biochem.* **1979**, *11*, 39.
(11) (a) Jordanov, J.; Williams, R. J. P. *Bioinorg. Chem.* **1978**, *8*, 77. (b) Chottard, J. C.; Girault, J. P.; Chottard, G.; Lallemand, S. Y.; Mansuy, D. *Proc. Int. Conf. Coord. Chem., 21st* **1980**, 427.
(12) (a) Faggiani, R.; Lippert, B.; Lock, C. J. L.; Speranzini, R. A. *J. Am. Chem. Soc.* **1981**, *103*, 111. (b) Lippert, B.; Lock, C. J. L.; Speranzini, R. A. *Inorg. Chem.* **1981**, *20*, 808.

0020-1669/82/1321-3216$01.25/0