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cis-Dichlorobis(cyclohexylamine-*N*)platinum(II)–Bis(hexamethylphosphoramide)

BY C. J. L. LOCK, R. A. SPERANZINI AND M. ZVAGULIS

Institute for Materials Research, McMaster University, Hamilton, Ontario, Canada L8S 4M1

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Abstract

$[Pt(C_6H_{13}N)_2Cl_2].2C_6H_{18}N_3OP$, $C_{12}H_{26}Cl_2N_2Pt.2C_6H_{18}N_3OP$, triclinic, $P\bar{1}$, $Z = 2$, $a = 15{\cdot}728\ (3)$, $b = 12{\cdot}030\ (3)$, $c = 14{\cdot}312\ (3)$ Å, $\alpha = 123{\cdot}89\ (2)$, $\beta = 103{\cdot}24\ (2)$, $\gamma = 107{\cdot}62\ (2)°$ [this cell can be converted into the Delaunay reduced cell, $a = 12{\cdot}552$, $b = 12{\cdot}030$, $c = 13{\cdot}685$ Å, $\alpha = 92{\cdot}98$, $\beta = 106{\cdot}48$, $\gamma = 108{\cdot}82°$, by the matrix $(0,-1,-1/0,1,0/1,1,1)$], $V = 1852\ (1)$ Å^3, $D_c = 1{\cdot}48$ Mg m^{-3}. The structure was determined by heavy-atom methods and refined to $R_w = 0{\cdot}069$. The ligand atoms (2Cl, 2N) form a square plane about the Pt atom and interatomic distances and angles are normal. The crystal is composed of centrosymmetrically related hydrogen-bonded units of twice the molecular formula, with van der Waals forces between the units.

Introduction

The title compound was prepared by direct reaction of K_2PtCl_4 (1·6 g) and cyclohexylamine (0·792 g) in water (15 ml). The yellow crystalline precipitate was removed by filtration and washed sequentially with small amounts (2 × 10 ml) of water, methanol, ethanol and diethyl ether and dried *in vacuo*. Crystals suitable for X-ray diffraction were recrystallized from hexamethylphoshoramide (HMPA). Crystals were stored in a small amount of HMPA at 268 K. It proved impossible to obtain a satisfactory analysis as decomposition started immediately when the excess solvent was removed at room temperature. Analytical figures corresponded to ratios of HMPA:Pt complex of 2·7:1 for a sample removed directly from the solvent to 0·3:1 for a sample allowed to stand for two or three hours at room temperature.

A pale-yellow crystal, homogeneous under the polarizing microscope, was sealed to a fused quartz fibre and immediately cooled to 243 K, when the loss of HMPA is very slow. Photographs showed the crystal to be triclinic and the unit cell was determined by a least-squares fit of 15 well centred reflections ($19° < 2\theta < 26°$) at 243 K on a Syntex $P2_1$ diffractometer. The density could not be determined because of crystal decomposition. The intensities of 7277 independent reflections up to $2\theta = 55°$ were measured with Mo $K\alpha$ radiation at 243 K. The computer-controlled Syntex $P2_1$ diffractometer was operated in the 2θ(counter)–θ(crystal) scan mode with a crystal monochromator. After removal of reflections for which $I \leq \sigma(I)$ (1208, most occurring above $2\theta = 35°$), 4804 reflections were considered observed [$I > 3\sigma(I)$] and used for the structure determination; 1265 were considered unobserved [$3\sigma(I) > I > \sigma(I)$] and were given no weight in the structure determination unless $|F_c| > |F_o|$. The method of data treatment has been described previously (Hughes, Krishnamachari, Lock, Powell & Turner, 1977; Lippert, Lock, Rosenberg & Zvagulis, 1977). Corrections were made for absorption [crystal bounded by pairs of faces (100), ($\bar{1}$00); (001), (00$\bar{1}$); (010), (0$\bar{1}$0), at 0·065, 0·095 and 0·095 mm from the centre respectively, $\mu = 4{\cdot}25$ mm^{-1}; range of A^* 2·339 to 1·476] and extinction (Larson, 1967, $g = 6{\cdot}75 \times 10^{-8}$). The stability of the experimental system was monitored by measuring two standard reflections after every 48 reflections (22$\bar{3}$; 121). They showed e.s.d.'s of 2·8% and a slow decrease with time, indicating crystal decomposition. Corrections were applied to the intensity of each reflection to allow for this decomposition.

The Pt atom was found from a three-dimensional Patterson synthesis. Subsequent full-matrix least-squares refinement and three-dimensional electron density difference maps revealed all the remaining non-hydrogen atoms. At this stage the temperature factors for the Pt, Cl and P atoms were made anisotropic and further full-matrix least-squares refinement, minimizing $\sum w(|F_o| - |F_c|)^2$, was terminated at $R = 0{\cdot}055$ (0·061), $R_w = 0{\cdot}069$ (0·071) for the observed (all) reflections with a final maximum shift/error of 0·009. The weighting scheme applied was $1/w = \sigma_F^2 + (0{\cdot}03F_o)^2$;† the error in an observation of unit weight was 1·384. Scattering factors were taken from Cromer & Waber (1974) and correction for anomalous scattering was applied to Pt, Cl and P (Cromer, 1974). The final positional parameters are given in Table 1.‡

† The value 0·03 was chosen to make $\langle w(|F_o| - |F_c|)^2 \rangle$ locally independent of F_o and sin θ/λ.

‡ Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35233 (29 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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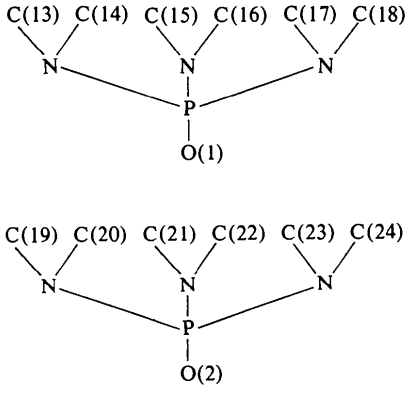
Table 1. *Final atomic positional parameters and temperature factors* (U_{eq} *or* U_{iso}, Å^2) ($\times 10^3$)

The hexamethylphosphoramide labelling is



	x	*y*	*z*	*U*
Pt	117·82 (3)	444·46 (5)	407·90 (4)	20·0 (2)*
Cl(1)	219·6 (3)	351·0 (4)	437·3 (4)	38 (3)*
Cl(2)	−28·9 (2)	227·6 (3)	333·9 (3)	27 (2)*
N(1)	38·9 (7)	549 (1)	395·4 (8)	39 (2)*
C(1)	−72·8 (9)	449 (1)	288 (1)	44 (3)*
C(2)	−111 (1)	559 (1)	305 (1)	53 (3)
C(3)	−221 (1)	459 (2)	193 (2)	80 (4)
C(4)	−228 (2)	360 (2)	67 (2)	108 (6)
C(5)	−195 (1)	252 (2)	48 (2)	94 (5)
C(6)	−80 (1)	347 (2)	155 (1)	59 (3)
N(2)	248·5 (7)	631 (1)	470 (1)	42 (2)
C(7)	329 (1)	747 (1)	614 (1)	50 (3)
C(8)	427 (1)	863 (2)	640 (1)	71 (4)
C(9)	507 (1)	979 (2)	786 (2)	95 (5)
C(10)	467 (1)	1068 (2)	870 (2)	103 (6)
C(11)	367 (1)	951 (2)	840 (2)	102 (6)
C(12)	286 (1)	832 (2)	692 (2)	84 (4)
P(1)	186·6 (2)	895·6 (4)	389·6 (3)	26 (2)*
O(1)	169·8 (6)	756 (1)	374 (1)	57 (2)
N(11)	83 (1)	847 (1)	278 (1)	63 (3)
C(13)	31 (1)	695 (2)	141 (2)	93 (5)
C(14)	49 (1)	957 (2)	294 (2)	85 (5)
N(12)	287 (1)	962 (1)	378 (1)	61 (3)
C(15)	307 (1)	1071 (2)	355 (2)	83 (4)
C(16)	360 (2)	907 (2)	375 (2)	114 (6)
N(13)	206 (1)	1044 (1)	528 (1)	63 (3)
C(17)	303 (2)	1189 (3)	630 (2)	149 (9)
C(18)	131 (2)	1022 (2)	572 (2)	111 (6)
P(2)	337·8 (3)	428·1 (4)	199·1 (3)	32 (2)*
O(2)	352 (1)	570 (1)	313 (1)	79 (3)
N(21)	425 (1)	393 (2)	234 (1)	82 (4)
C(19)	464 (2)	425 (3)	361 (2)	127 (7)
C(20)	492 (1)	368 (2)	182 (2)	101 (5)
N(22)	341 (1)	443 (2)	91 (1)	80 (3)
C(21)	416 (1)	594 (2)	137 (2)	102 (6)
C(22)	288 (2)	306 (2)	−49 (2)	108 (6)
N(23)	223 (1)	266 (2)	118 (1)	88 (4)
C(23)	214 (2)	121 (3)	77 (3)	160 (10)
C(24)	132 (2)	277 (3)	98 (2)	128 (7)

* $U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33} + 2U_{12}\cos\gamma + 2U_{13}\cos\beta + 2U_{23}\cos\alpha)$.

All calculations were carried out on CDC 6400 or Cyber 170/730 computers.*

Discussion

Since the initial discovery of the anti-cancer activity of *cis*-$[PtCl_2(NH_3)_2]$ (Rosenberg, VanCamp, Trosko & Mansour, 1969) much work has been carried out on the anti-cancer activity of other complexes of Pt. In particular, it was shown that against the tumour system ADJ/PC6A in mice, complexes of the type *cis*-$[Pt(RNH_2)_2Cl_2]$, where R is a saturated cyclic hydrocarbon group, could have significantly better therapeutic indices than *cis*-$[Pt(NH_3)_2Cl_2]$. Much of this improvement lay, not in the ability to attack the cancer, but in the lower toxicity. The reason for this improvement was postulated to be structural (Braddock, Connors, Jones, Khokhar, Melzack & Tobe, 1975; Connors, Jones, Ross, Braddock, Kokhar & Tobe, 1972). The drug with the best therapeutic index was *cis*-$[Pt(C_6H_{11}NH_2)_2Cl_2]$ and previous studies have suggested that unlike other Pt^{II} complexes this compound does not have a planar arrangement of ligands about the Pt atom (Faggiani, Lock, Speranzini & Turner, 1976; Iball & Scrimgeour, 1977).

This distortion does not exist, however, in the title compound, as can be seen from Fig. 1, the selected interatomic distances and angles in Table 2 and the planes data in Table 3. The molecule is essentially planar and has very similar structural parameters about the Pt atom to those found in *cis*-$[PtCl_2(NH_3)_2]$ (Milburn & Truter, 1966), *cis*-$[Pt(C_3H_5NH_2)_2Cl_2]$, *cis*-$[Pt(C_4H_7NH_2)_2Cl_2]$ (Lock & Zvagulis, 1980*b*), *cis*-$[Pt\{NH_2(CH_2)_2NH_2\}Cl_2]$ (Iball, MacDougall & Scrimgeour, 1975), *cis*-$[Pt\{(CH_2)_2NH\}_2Cl_2]$ (Barnes, Iball & Weakley, 1975) and the three independent

* Most programs used for initial data treatment were from the XRAY package (Stewart, 1976). The structure was solved using the internally written Fourier and full-matrix least-squares programs *SYMFOU* and *CUDLS* written by J. S. Rutherford and J. S. Stephens, respectively. The least-squares planes were calculated using *PALS* (P. G. Ashmore). The diagrams were prepared using *ORTEP* II (Johnson, 1976).

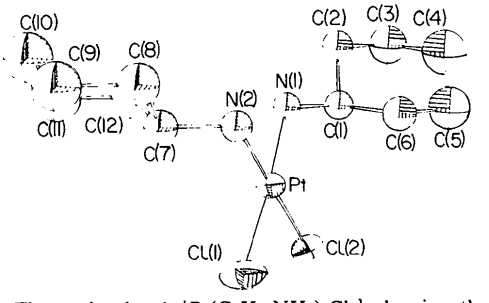


Fig. 1. The molecule *cis*-$[Pt(C_6H_{11}NH_2)_2Cl_2]$ showing the atom numbering.

Table 2. *Interatomic distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

Pt–Cl(1)	2·305 (5)	Pt–N(1)	2·07 (1)	N(1)–C(1)	1·52 (1)
Pt–Cl(2)	2·325 (3)	Pt–N(2)	2·05 (1)	N(2)–C(7)	1·52 (1)
C(1)–C(2)	1·54 (3)	C(2)–C(3)	1·52 (2)	C(3)–C(4)	1·46 (3)
C(7)–C(8)	1·53 (2)	C(8)–C(9)	1·55 (2)	C(9)–C(10)	1·52 (3)
C(4)–C(5)	1·44 (4)	C(5)–C(6)	1·57 (2)	C(6)–C(1)	1·54 (2)
C(10)–C(11)	1·52 (3)	C(11)–C(12)	1·56 (2)	C(12)–C(7)	1·49 (3)
P(1)–O(1)	1·49 (1)	P(1)–N(11)	1·65 (2)	P(1)–N(12)	1·63 (2)
P(2)–O(2)	1·45 (1)	P(2)–N(21)	1·61 (2)	P(2)–N(22)	1·66 (2)
P(1)–N(13)	1·63 (1)	N(11)–C(13)	1·49 (2)	N(11)–C(14)	1·49 (3)
P(2)–N(23)	1·67 (1)	N(21)–C(19)	1·54 (4)	N(21)–C(20)	1·43 (3)
N(12)–C(15)	1·49 (3)	N(12)–C(16)	1·49 (3)	N(13)–C(17)	1·43 (2)
N(22)–C(21)	1·46 (3)	N(22)–C(22)	1·47 (2)	N(23)–C(23)	1·44 (5)
N(13)–C(18)	1·48 (3)	N(23)–C(24)	1·46 (4)		
Possible hydrogen bonds					
Cl(2)–N(1)	3·34 (1)	O(1)–N(1)	2·93 (2)	O(1)–N(2)	2·89 (2)
O(2)–N(2)	2·97 (2)				
Cl(1)–Pt–Cl(2)	91·8 (2)	Cl(1)–Pt–N(1)	174·6 (2)	Cl(1)–Pt–N(2)	86·9 (4)
Cl(2)–Pt–N(1)	93·0 (3)	Cl(2)–Pt–N(2)	178·3 (4)	N(1)–Pt–N(2)	88·3 (5)
Pt–N(1)–C(1)	120·4 (8)	N(1)–C(1)–C(2)	108·7 (9)	N(1)–C(1)–C(6)	109 (1)
Pt–N(2)–C(7)	115 (1)	N(2)–C(7)–C(8)	109 (1)	N(2)–C(7)–C(12)	109 (1)
C(6)–C(1)–C(2)	111 (1)	C(1)–C(2)–C(3)	109 (1)	C(2)–C(3)–C(4)	112 (2)
C(12)–C(7)–C(8)	111 (1)	C(7)–C(8)–C(9)	108 (2)	C(8)–C(9)–C(10)	111 (2)
C(3)–C(4)–C(5)	114 (3)	C(4)–C(5)–C(6)	110 (1)	C(5)–C(6)–C(1)	107 (1)
C(9)–C(10)–C(11)	110 (2)	C(10)–C(11)–C(12)	110 (2)	C(11)–C(12)–C(7)	110 (2)
O(1)–P(1)–N(11)	110·2 (6)	O(1)–P(1)–N(12)	110·2 (8)	O(1)–P(1)–N(13)	114·3 (8)
O(2)–P(2)–N(21)	112·5 (7)	O(2)–P(2)–N(22)	111·3 (9)	O(2)–P(2)–N(23)	113·1 (8)
P(1)–N(11)–C(13)	119 (1)	P(1)–N(11)–C(14)	125·2 (7)	C(13)–N(11)–C(14)	114 (2)
P(1)–N(12)–C(15)	123 (1)	P(1)–N(12)–C(16)	124 (2)	C(15)–N(12)–C(16)	113 (2)
P(1)–N(13)–C(17)	124 (2)	P(1)–N(13)–C(18)	120·9 (9)	C(17)–N(13)–C(18)	113 (2)
P(2)–N(21)–C(19)	119 (2)	P(2)–N(21)–C(20)	129 (2)	C(19)–N(21)–C(20)	110 (2)
P(2)–N(22)–C(21)	119 (1)	P(2)–N(22)–C(22)	123 (2)	C(21)–N(22)–C(22)	116 (2)
P(2)–N(23)–C(23)	122 (2)	P(2)–N(23)–C(24)	119 (2)	C(23)–N(23)–C(24)	120 (2)

molecules in $[Pt\{C_6H_{10}(NH_2)_2\}Cl_2]_3.H_2O$ (Lock & Pilon, 1980): Pt–Cl [2·305 (5), 2·325 (3) Å *vs* (range) 2·273 (4)–2·333 (9) Å] and Pt–N [2·07 (1), 2·05 (1) Å *vs* (range) 1·85 (6)–2·08 (3) Å] distances are normal as are the Cl–Pt–Cl [91·8 (2)° *vs* (range) 90·2 (4)–96·4 (6)°] and N–Pt–N [88·3 (5)° *vs* (range) 73 (2)–91·4 (5)°] angles. The dihedral angle of 2·8° between the $PtCl_2$ and PtN_2 planes is small and in the range (0–3°) normally observed for these structures.

A reason for the low toxicity of the cyclic amine complexes has been suggested by Rosenberg (1976). He suggested that the flexibility of the larger rings would allow orientation of the rings so that they protect the axial positions above and below the square planes, thus preventing coordination to the S atoms in the kidney tubules (the latter being the postulated mechanism for kidney toxicity) (Slater, Ahmed & Ibrahim, 1977). It can be seen clearly in this structure that the rings are oriented so that the H atoms attached to C(1), C(6) and C(7), C(12) will be in a position to block the axial sites. The fact that this arrangement occurs in the solid state does not prove that a similar arrangement exists in solution, but the arrangement is clearly possible. The rings exist in the chair form and the ring

Table 3. *A least-squares plane and torsional angles in cis-*$[Pt(C_6H_{11}NH_2)_2Cl_2]$

Plane	Distances from plane ($\sigma \leq 0·01$) (Å)
Cl(1)Cl(2)N(1)N(2)Pt*	Cl(1), 0·03; Cl(2), −0·03; N(1), 0·04; N(2), −0·04; Pt, −0·01

Torsion angles ($\sigma \leq 1·0$) (°)†

PtN(1)C(1)C(2)	179·2	PtN(2)C(7)C(8)	171·4
PtN(1)C(1)C(6)	−58·9	PtN(2)C(7)C(12)	−68·2
N(1)C(1)C(2)C(3)	176·3	N(2)C(7)C(8)C(9)	180·0
C(1)C(2)C(3)C(4)	−54·6	C(7)C(8)C(9)C(10)	−59·2
C(2)C(3)C(4)C(5)	58·4	C(8)C(9)C(10)C(11)	58·1
C(3)C(4)C(5)C(6)	−59·1	C(9)C(10)C(11)C(12)	−56·5
C(4)C(5)C(6)C(1)	57·1	C(10)C(11)C(12)C(7)	58·5
C(5)C(6)C(1)C(2)	−56·6	C(11)C(12)C(7)C(8)	−61·2
C(6)C(1)C(2)C(3)	55·9	C(12)C(7)C(8)C(9)	61·1
N(1)C(1)C(6)C(5)	−176·6	N(2)C(7)C(12)C(11)	179·9

Dihedral angle

PtCl(1)Cl(2)–PtN(1)N(2) 2·8°

* Pt was given no weight in calculating the plane; other atoms were given unit weights.

† The angle is between the planes defined by *ABC* and *BCD* in the atomic series *ABCD*.

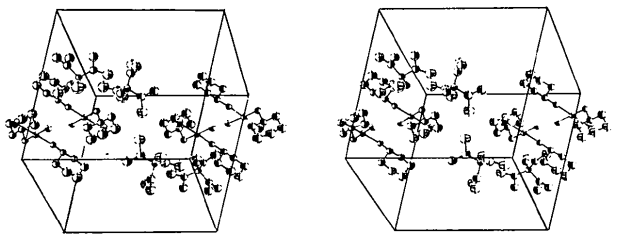


Fig. 2. The packing of *cis*-$[Pt(C_6H_{11}NH_2)_2Cl_2].2C_6H_{18}N_3OP$ in the unit cell. **a** and **a** × (**c** × **a**) are parallel to the bottom and side of the page and the view is down **b***.

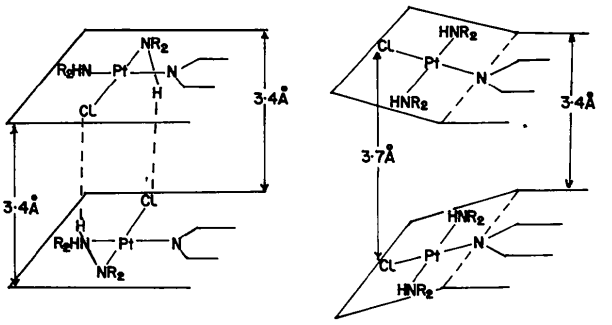


Fig. 3. Pairs of *cis*- and *trans*-$[Pt(NHR_2)_2Cl_2]$ molecules attached to adjacent bases on a DNA chain. The dotted lines represent hydrogen bonds. (Distances are in Å.)

bond lengths and angles (Table 2) and torsion angles (Table 3) are very similar to those obtained previously from *trans*-$[Pt(C_6H_{11}NH_2)_2Cl_2]$ (Zanotti, Del Pra, Bombieri & Tamburro, 1978), *trans*-$[Pt(C_6H_{11}NH_2)_2Br_2]$ (Lock & Zvagulis, 1980*a*) and *cis*-$[Pt(C_6H_{11}NH_2)_2Cl_2]$ (Iball & Scrimgeour, 1977).

The packing of the molecules in the crystal is shown in Fig. 2. The Pt-containing molecules are arranged so that they are hydrogen bonded into pairs related by the inversion centre at $0,\frac{1}{2},\frac{1}{2}$ through N(1)—H···Cl(2). The remaining H atoms on the amine groups are involved in bonding to the hexamethylphosphoramide groups through N(1)—H···O(1), N(2)—H···O(1) and N(2)—H···O(2). Thus we have a six-molecule group (two Pt complexes, four HMPA) hydrogen bonded together, with the molecules so oriented that the H atoms of the hydrocarbon units and the two Cl atoms cover the outside of the six-molecule group. The interactions between these groups are van der Waals.

The hydrogen-bonded molecular-pair arrangement mentioned above, with about 3·4 Å between the square planes, is very common in *cis*-diaminedichloroplatinum(II) complexes (Milburn & Truter, 1966; Lock & Zvagulis, 1980; Iball *et al.*, 1975; Lock & Pilon, 1980) but has not been found in the corresponding *trans* complexes (Zanotti *et al.*, 1978; Milburn & Truter, 1966). Srivastava, Froehlich & Eichhorn (1978) have suggested this as the basis for a model of the primary lesion in the anti-cancer activity of the Pt drugs. They suggested mono-functional coordination of each of a pair of Pt-containing molecules to adjacent bases on a DNA strand so that the Pt complexes and bases are 'co-stacked'. It is easy to see why stacking of this type could occur for these *cis* complexes, but not the *trans* complexes. As shown in Fig. 3, amine—Cl hydrogen bonding can occur easily for the *cis* complex but not for the *trans*. It is interesting to note that *cis* complexes do not show activity if there is not at least one H atom on the amine group.

An alternative reason for the lower toxicity of *cis*-$[Pt(C_6H_{11}NH_2)_2Cl_2]$ might lie in the apparent distortion of the structure observed by Faggiani *et al.* (1976) and Iball & Scrimgeour (1977), but detailed examination does not show this to be the case.

Faggiani *et al.* (1976) obtained an initial solution of the structure of *cis*-$[Pt(C_6H_{11}NH_2)_2Cl_2].2(C_2H_5)_2O$ in $P\bar{1}$, showing a Pt-containing molecule which appeared to be half square planar [Cl—Pt—Cl, 88·2 (5)°] and half tetrahedral [N—Pt—N, 108 (2)°] with a $PtCl_2$—PtN_2 dihedral angle of 35°. A Delaunay test showed, however, that the true cell was *C*-centred (*C*2, *Cm* or *C*2/*m*) but attempts at refinement including the disordered ether molecule were unsatisfactory. We have not yet solved this structure and have yet to be convinced that the distortion is not an artifact of a space-group error.

The distortion found in *cis*-$[Pt(C_6H_{11}NH_2)_2Cl_2]$ (Iball & Scrimgeour, 1977) is even greater. Both Cl—Pt—Cl and N—Pt—N angles are 151° and the $PtCl_2$—PtN_2 dihedral angle is 45°. Since the Cl—Pt—N angle is 97°, the compound is better considered a distorted form of *trans*-$[Pt(C_6H_{11}NH_2)_2Cl_2]$. Indeed, a detailed comparison of the structures of the *cis* and *trans* compounds (Iball & Scrimgeour, 1977; Zanotti *et al.*, 1978) shows that the space groups and cell parameters are the same and the atom parameters of the *cis* form can be converted roughly into those of the *trans* form by $x,y,z \rightarrow x, -y, \frac{1}{4}+z$, and if the C atoms are renumbered C(6) → C(1), C(5) → C(2), C(4) → C(3), C(1) → C(4), C(2) → C(5), C(3) → C(6). Thus, the structure of the '*cis*' form is probably an incorrect solution of the structure of the *trans* form caused by an incorrect choice of the Pt position on the twofold axis (necessary for the *cis* form) rather than at the inversion centre.

This error has wide implications since Professor Tobe, who supplied the crystals of the *cis* form for the structural analysis also supplied the material for the animal tests (Braddock *et al.*, 1975; Connors *et al.*, 1972). These tests showed clearly that the *cis* form was active whereas the *trans* form was not, but since the *trans* crystal came from a sample of supposedly *cis* compound, the question still remains as to whether this *cis* compound was really a mixture of *cis* and *trans*, in which case the *cis* form might be much more active

than indicated, or whether the process of recrystallization converts the *cis* form to the *trans* form.

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References

BARNES, J. C., IBALL, J. & WEAKLEY, T. J. R. (1975). *Acta Cryst.* B**31**, 1435–1437.

BRADDOCK, P. D., CONNORS, T. A., JONES, M., KHOKHAR, A. R., MELZACK, D. H. & TOBE, M. L. (1975). *Chem.-Biol. Interact.* **11**, 145–161.

CONNORS, T. A., JONES, M., ROSS, W. C. J., BRADDOCK, P. D., KHOKHAR, A. R. & TOBE, M. L. (1972). *Chem.-Biol. Interact.* **5**, 415–424.

CROMER, D. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, Table 2.3.1, pp. 149–150. Birmingham: Kynoch Press.

CROMER, D. T. & WABER, J. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, Table 2.2A, pp. 72ff. Birmingham: Kynoch Press.

FAGGIANI, R., LOCK, C. J. L., SPERANZINI, R. A. & TURNER, G. (1976). Abstr. Chem. Inst. Canada Annu. Conf., London, Ontario, June 1976, p. 25.

HUGHES, R. P., KRISHNAMACHARI, N., LOCK, C. J. L., POWELL, J. & TURNER, G. (1977). *Inorg. Chem.* **16**, 314–319.

IBALL, J., MACDOUGALL, M. & SCRIMGEOUR, S. N. (1975). *Acta Cryst.* B**31**, 1672–1674.

IBALL, J. & SCRIMGEOUR, S. N. (1977). *Acta Cryst.* B**33**, 1194–1196.

JOHNSON, C. K. (1976). *ORTEP* II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee.

LARSON, A. C. (1967). *Acta Cryst.* **23**, 664–665.

LIPPERT, B., LOCK, C. J. L., ROSENBERG, B. & ZVAGULIS, M. (1977). *Inorg. Chem.* **16**, 1525–1529.

LOCK, C. J. L. & PILON, P. (1980). *Acta Cryst.* In the press.

LOCK, C. J. L. & ZVAGULIS, M. (1980*a*). *Acta Cryst.* In the press.

LOCK, C. J. L. & ZVAGULIS, M. (1980*b*). In preparation.

MILBURN, G. H. W. & TRUTER, M. R. (1966). *J. Chem. Soc. A*, pp. 1609–1616.

ROSENBERG, B. (1976). Private communication.

ROSENBERG, B., VANCAMP, L., TROSKO, J. E. & MANSOUR, V. H. (1969). *Nature (London)*, **222**, 385–386.

SLATER, T. F., AHMED, M. & IBRAHIM, S. A. (1977). *J. Clin. Hemat. Oncol.* **7**, 534–546.

SRIVASTAVA, R. C., FROEHLICH, J. & EICHHORN, G. L. (1978). *Biochimie*, **60**, 879–891.

STEWART, J. M. (1976). The XRAY 76 system. Tech. Rep. TR-446. Computer Science Center, Univ. of Maryland, College Park, Maryland.

ZANOTTI, G., DEL PRA, A., BOMBIERI, G. & TAMBURRO, A. M. (1978). *Acta Cryst.* B**34**, 2138–2141.

Acta Cryst. (1980). B**36**, 1793–1797

The Structure of the Cytosine–Calcium Chloride (1 : 1) Complex. The First Evidence for Direct Binding of Calcium to Cytosine Base

BY KEIZO OGAWA, MIYOKO KUMIHASHI AND KEN-ICHI TOMITA

Faculty of Pharmaceutical Sciences, Osaka University, Yamada-kami, Suita, Osaka 565, *Japan*

AND SYOICHI SHIROTAKE

Faculty of Pharmaceutical Sciences, Chiba University, Yayoicho, Chiba, Chiba 260, *Japan*

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Abstract

The crystal structure of $[Ca(C_4H_5N_3O)Cl_2].H_2O$ was determined by X-ray diffraction. The complex crystallizes in the monoclinic space group $P2_1/c$ with a = 7·410 (1), b = 16·152 (2), c = 8·351 (1) Å, β = 107·60 (2)° and Z = 4. The final R value is 0·070. The Ca^{2+} cation is in a pentagonal-bipyramidal environment and is coordinated in the basal plane by two Cl atoms, the N(3) and O(2) atoms of a cytosine base, and the O(2) atom of an adjacent cytosine base. The axial sites are occupied by a Cl atom and an H_2O molecule. A one-dimensional polymer parallel to the c axis is generated by cross-linking through Ca—Cl—Ca and Ca—O(2)—Ca bridges and two hydrogen bonds, N(4)—H···Cl and N(1)—H···Cl, together with direct coordination between Ca and the cytosine bases on the basal plane. The molecular packing is stabilized by base stacking and two O(W)—H···Cl hydrogen bonds between adjacent one-dimensional polymeric units.

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