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The Crystal Structure of *cis*-Diammine(orotinato)platinum(II)

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From the reaction of *cis*-$[Pt(NH_3)_2(H_2O)_2]$ with orotic acid, yellow needle crystals, green needle crystals, and dark-blue microcrystalline crystals were obtained. The results of elemental analyses, the IR absorption spectra, and X-ray Weissenberg photographs showed that the yellow and green needles are identical, whereas the dark-blue microcrystalline compound exhibits slight difference in the elemental analyses and IR spectra. Green needle crystals of *cis*-diammine(orotinato)platinum(II), *cis*-$[Pt(NH_3)_2(C_5H_2N_2O_4)]$, were subjected to X-ray single crystal analysis. The crystals belong to the monoclinic system, with the space group $P2_1/c$, and the cell dimensions are $a=7.468(5)$, $b=7.537(3)$, $c=15.618(9)$ Å, and $\beta=107.90(7)°$, with $Z=4$. The structure was solved by the heavy-atom method and refined to the final R value of 0.0567 for 1918 non-zero reflections. The complex is almost planar, and the platinum atom is coordinated by the orotic acid at N1 and carboxylic oxygen, forming a five-membered chelate ring. The structure of the pyrimidine ring of the orotic acid is compared with free and coordinated uracil and thymine. No definite explanation for the color difference was obtained.

Since the discovery of the antitumor activity of *cis*-diamminedichloroplatinum(II) by Rosenberg *et al.*,[1,2] considerable interest has been focused on this class of square-planar *cis*-diammineplatinum(II) complexes. The mechanism of the antitumor action has been supposed to be the complex formation between *cis*-diammineplatinum(II) compounds and purine or pyrimidine bases of DNA.[3] These bases have several possible coordinating sites, and many investigations have been carried out into the structures of the platinum complexes with purine or pyrimidine bases.[4–16] Among these complexes, the so-called "platinum-pyrimidine blues" are of special interest from the viewpoint of not only the mechanism of the complex formation between *cis*-diammineplatinum and pyrimidines, but also the anomalously deep blue color and the high antitumor activity of the complexes.[17] As for their structures in the solid and solution states, as well as their chemical properties, however, only a little knowledge has thus far been obtained. Although Lippard *et al.* reported the structure of platinum α-pyridon blue,[18,19] there are still a large number of other platinum pyrimidine blues whose formulas and structures are unknown. In the present paper, we wish to report on the crystal structure of the reaction product between *cis*-diammineplatinum and one of the uracil derivatives, orotic acid. We obtained three compounds, yellow needles, green needles and blue microcrystals, from the reaction solution. The green needle crystals were subjected to X-ray diffraction analysis in order to elucidate the structural relations among the three and to discuss whether there are structural changes in the pyrimidine ring of orotic acid due to coordination to a platinum atom.

Experimental

Preparation. The *cis*-diammineplatinum(II) hydrolysis product was prepared from 1 mmol of *cis*-$[Pt(NH_3)_2Cl_2]$ and 2 mmol of $AgNO_3$ in 10 ml of water in the dark. After removing the AgCl by centrifugation and filtration, an equivalent amount of orotic acid in a minimum amount hot water was added; this resulted in the decrease of the pH of the solution to 1—2. On standing at room temperature for 1 d, the solution yielded green needle crystals. If the solution was adjusted to pH 6—7 with NaOH and left to stand for 1 d, it yielded yellow needles. After the filtration of these green or yellow compounds, a small quantity of dark-blue microcrystals precipitated from the filtrate after 2—3 d. Found: Yellow needles; C, 15.35; H, 2.16; N, 14.48; Pt, 50.7%. Green needles; C, 15.38, H, 2.18; N, 14.70; Pt, 49.5%. Dark-blue microcrystals; C, 14.93; H, 2.21; N, 14.27; Pt, 53.0%. Calcd for $[Pt(NH_3)_2(C_5H_2N_2O_4)]$: C, 15.67; H, 2.10; N, 14.62; Pt, 50.91%. Although the results of elemental analyses for yellow and green needles are identical within the limits of experimental error, the platinum content of the dark-blue compound significantly differs from that of the yellow and green needles. Moreover, the IR spectra of the three compounds are very similar to one another; the yellow and green needles give the same spectra, whereas that of the dark-blue compounds shows only a slight difference. The latter has three more absorption peaks, at 545 (w), 660 (w), and 1100 (w) cm^{-1}, than those of yellow and green compounds. These findings suggest that the three compounds have very similar structures. In the present study, the crystal structure of the green compound was investigated by means of X-ray diffraction.

Data Collection. A crystal of 0.15 mm × 0.05 mm × 0.25 mm was used for intensity measurements; the cell dimensions were obtained from twelve 2θ values measured on a diffractometer. The crystal data for *cis*-$[Pt(NH_3)_2(C_5H_2N_2O_4)]$ are: monoclinic $P2_1/c$, $a=7.468$ (5), $b=7.537$ (3), $c=15.618$ (9) Å, $\beta=107.90$ (7)°, $M.W.=383.2$, $Z=4$, $D_x=3.04$ g cm^{-3}, $\mu=176.4$ cm^{-1} for Mo $K\alpha$. The intensity measurements were performed on a Philips four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation. The ω-2θ scan mode was employed at the scan rate of 1° min^{-1} in 2θ, and the reflections were measured up to 60° in 2θ. Three reference reflections monitored periodically showed no significant intensity loss during the course of the data collection. The data were corrected for Lorentz and polarization effects, and a total of 1918 reflections with $|F_o|\geqq 3\sigma(|F_o|)$ were used for structural analysis.

Solution and Refinement of the Structure. The structure was solved by the heavy-atom method. The platinum atom was located from a three-dimensional Patterson map, while all the remaining non-hydrogen atoms were located from the successive Fourier sytheses. Although a difference synthesis was calculated at the final stage of the analysis, the hydrogen atoms were not located. The positional and anisotropic temperature factors were refined by the blockdiagonal least-squares method to the final R factor of 0.0567. All the atomic

Table 1. Final positional parameters ($\times 10^4$) and isotropic temperature factors($\times 10^2$), with their estimated standard deviations in parentheses

	x	y	z	$B_{eq}/\text{Å}^2$
Pt	2987(1)	1995(1)	4065(1)	168(2)
C2	1544(24)	−1693(22)	4266(10)	191(25)
C4	1503(23)	−2926(25)	5731(10)	197(23)
C5	2394(24)	−1310(24)	6120(11)	214(27)
C6	2783(23)	−57(22)	5586(10)	172(23)
C7	3704(24)	1661(22)	5964(10)	181(25)
N1	2310(18)	−184(19)	4647(8)	167(20)
N3	1085(21)	−3012(22)	4791(9)	206(21)
N4	2102(22)	1064(22)	2774(8)	200(22)
N5	3693(20)	4320(18)	3588(9)	197(22)
O2	1161(20)	−2030(20)	3442(8)	247(20)
O4	1059(20)	−4178(18)	6123(8)	237(20)
O5	3924(18)	2857(18)	5380(7)	206(18)
O6	4308(20)	1934(20)	6777(7)	234(19)

scattering factors used were taken from Ref. 20, while the correction of the effect of the anomalous dispersion for platinum was based on Ref. 21. The final atomic coordinates and thermal parameters are given in Table 1.

Results and Discussion

The bond lengths and angles within the molecule are listed in Table 2, while the molecular structure and the numbering scheme are depicted in Fig. 1. Orotic acid coordinates to the platinum atom by chelating with deprotonated N1 and carboxylic O5 atoms to form a five-membered ring. It is of interest where, in uracil or its derivatives, is the coordinating site to platinum atoms and how much the bond lengths and angles within the pyrimidine ring are changed by coordination. Although uracil or thymine deprotonates first at the N3 site, and although the pK_a value is 9.5 for both uracil and thymine,[22] most of the platinum complexes so far investigated by X-ray diffraction or NMR show that coordination takes place at N1.[4] One exception is the triammineplatinum uracil complex, $[Pt(NH_3)_3(C_4H_3N_2O_2)]NO_3$, where the platinum atom is considered, on the basis of the NMR spectra, to be coordinated by uracil at N3.[5] In the present complex, the coordination at N1 is much more favored due to the chelate formation.

Table 2. Bond lengths and angles within the molecule, with their estimated standard deviations in parentheses

	l/Å		l/Å
Pt-N1	2.012(28)	C5-C6	1.349(28)
N4	2.039(31)	C6-N1	1.402(21)
N5	2.049(16)	C2-O2	1.255(20)
O5	2.055(14)	C4-O4	1.226(27)
N1-C2	1.329(27)	C6-C7	1.499(30)
C2-N3	1.397(27)	C7-O5	1.328(24)
N3-C4	1.405(21)	C7-O6	1.228(19)
C4-C5	1.430(31)		
	ϕ/°		ϕ/°
N4-Pt-N5	88.4(5)	C6-N1-C2	117.5(14)
N5-Pt-N1	96.5(5)	N1-C2-O2	124.3(16)
N1-Pt-O5	82.3(5)	O2-C2-N3	116.0(15)
O5-Pt-N4	92.8(5)	N3-C4-O4	118.6(15)
Pt-N1-C2	129.1(11)	O4-C4-C5	127.2(15)
Pt-N1-C6	113.3(10)	C5-C6-C7	121.4(15)
N1-C2-N3	119.7(14)	N1-C6-C7	114.1(14)
C2-N3-C4	124.4(14)	C6-C7-O6	122.1(15)
N3-C4-C5	114.1(15)	C6-C7-O5	117.0(13)
C4-C5-C6	119.6(16)	C7-O5-Pt	113.2(10)
C5-C6-N1	124.4(15)	O5-C7-O6	120.9(15)

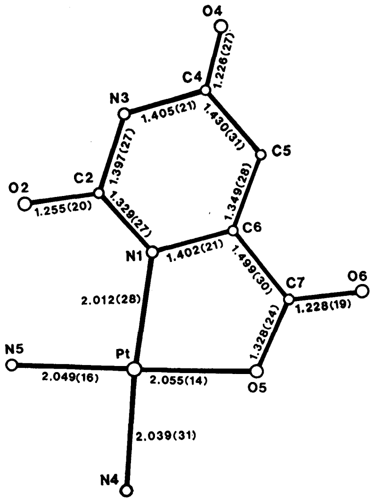

Fig. 1. The molecular structure and the numbering scheme for *cis*-$[Pt(NH_3)_2(C_5H_2N_2O_4)]$.

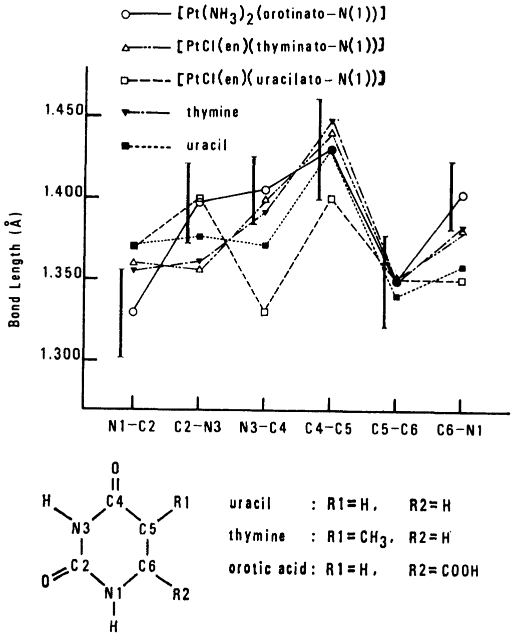

Fig. 2. Comparison of C–C and C–N bond lengths in pyrimidine rings of $[Pt(NH_3)_2(\text{orotinato-N(1)})]$, $[PtCl(en)(\text{thyminato-N(1)})]$, $[PtCl(en)(\text{uracilato-N(1)})]$, thymine and uracil. Standard deviations in $[Pt(NH_3)_2(\text{orotinato-N(1)})]$ are shown with error bars and those of other complexes are in the range one tenth to half of those in $[Pt(NH_3)_2(\text{orotinato-N(1)})]$.

A comparison of the structures of free and coordinating orotic acid would give valuable information on the change in the electronic structure due to the coordination. However, as no X-ray investigation of free orotic acid has thus far been reported, a comparison with thymine and uracil was carried out. The C–C and C–N bond lengths in thymine,[23)] uracil,[24)] the platinum thymine complex,[4)] the platinum uracil complex,[4)] and orotic acid in the present compound are compared in Fig. 2. The corresponding C–C and C–N bond lengths are significantly different from uracil to thymine; these differences were satisfactorily explained by Gerdil[23)] in terms of the canonical structures. The C–C and C–N bond lengths of free and coordinating thymine are considered to be identical with each other, whereas the C2–N3, N3–C4, and C4–C5 bond lengths of uracil are slightly different from those of the coordinating uracil. The bond lengths of coordinating orotic acid are different from both uracil and thymine; the N1–C2 distance of orotic acid is significantly shorter than that of uracil or thymine, whereas the C6–N1 distance of orotic acid is longer than that of uracil or thymine. This is explained by the electron flow from the C2–O2 to the N1–C2 bond and from the C6–N1 to the C6–C7 bond, a flow which is aroused by the electrophilic carboxyl group substituted at C6. The comparison of the C=O distances shows that most differences are within the standard deviations and that, therefore, no significant differences are observed. As for the bond angles of the ring nitrogens, C6–N1–C2 (117.5(14)°) is significantly smaller than C2–N3–C4 (124.4(14)°). This fact is consistent with Singh's report[25)] that the nitrogen valence angle with an extraannular hydrogen atom is 125±3°, whereas that without any attachment is 116±3°. The coordination of the N1 to the platinum atom does not seem to affect the nitrogen valence angle, since C6–N1–C2 is essentially the same as the valence angle for the nitrogen without any hydrogen attachment. Similarly the two kinds of nitrogen valence angles are also observed in the platinum–uracil complex, (H_5O_2)-$[PtCl(en)(C_4H_3N_2O_2)]Cl$, and the platinum–thymine complex, $[PtCl(en)(C_5H_5N_2O_2)]$.[4)]

TABLE 3. THE BEST LEAST-SQUARES PLANES AND THE DEVIATIONS OF EACH ATOM (Å)

Best plane calcd from all the atoms
$-0.91149X+0.39487Y-0.11516Z+0.40060=0.0$
Pt, 0.045(18); N1, 0.011(22); N3, 0.042(24);
N4, 0.128(23); N5, 0.026(24); O2, −0.076(23);
O4, 0.068(23); O5, 0.013(22); O6, −0.151(23);
C2, −0.018(25); C4, 0.033(25); C5, 0.011(25);
C6, −0.023(25); C7, −0.038(25).

Best plane calcd from pyrimidine ring
$-0.90314X+0.41168Y-0.12188Z+0.47151=0.0$
N1, 0.029(15); N3, 0.015(17); C2, −0.019(19);
C4, −0.004(19); C5, −0.005(19); C6, −0.013(18).

Best plane calcd from Pt, N1, N4, N5, O5
$-0.92308X+0.36910Y-0.10814Z+0.35706=0.0$
Pt, 0.002 (12); N1, 0.025(18); N4, 0.026(19);
N5, −0.012 (20); O5, −0.034(18).

The coordinate system is:
$X(\text{Å})=ax+cz(\cos\beta)$
$Y=by$
$Z=cz(\sin\beta)$

All the atoms in the molecule are almost coplanar, and the dihedral angle between the best least-squares plane of Pt, N1, N4, N5, and O5, and that of the

TABLE 4. POSSIBLE HYDROGEN BOND DISTANCES AND ANGLES IN $[Pt(NH_3)_2(C_5H_2N_2O_4)]$, WITH THEIR ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

	l/Å
$N3\cdots O4^{i}$	2.771(37)
$N4\cdots O5^{ii}$	2.921(36)
$O6^{iii}$	3.145(24)
$N5\cdots O2$	2.733(42)
$O2^{iv}$	2.960(38)
$O6^{iii}$	2.999(35)

	ϕ/°		ϕ/°
$C4–N3–O4^{i}$	118.8(11)	N5–O2–C2	102.4(11)
$C2–N3–O4^{i}$	116.7(10)	$N5–O2–N5^{v}$	115.3(6)
$Pt–N4–O5^{ii}$	127.2(6)	$C2–O2–N5^{v}$	129.8(11)
$Pt–N4–O6^{iii}$	101.5(6)	$C4–O4–N3^{i}$	122.2(12)
$O5^{ii}–N4–O6^{iii}$	118.9(6)	$Pt–O5–N4^{ii}$	138.0(7)
Pt–N5–O2	87.6(6)	Pt–O5–C7	113.2(10)
$Pt–N5–O2^{iv}$	114.8(7)	$C7–O5–N4^{ii}$	107.4(10)
$Pt–N5–O6^{iii}$	106.1(7)	$C7–O6–N5^{vi}$	122.4(12)
$O2–N5–O2^{iv}$	113.7(7)	$C7–O6–N4^{vi}$	140.4(12)
$O2–N5–O6^{iii}$	151.0(8)	$N4^{vi}–O6–N5^{vi}$	55.2(5)*
$O2^{iv}–N5–O6^{iii}$	84.1(5)		

Symmetry code

i	$-x$,	$-1.0-y$,	$1.0-z$
ii	$1.0-x$,	$1.0-y$,	$1.0-z$
iii	x,	$0.5-y$,	$-0.5+z$
iv	$-x$,	$0.5+y$,	$0.5-z$
v	$-x$,	$-0.5+y$,	$0.5-z$
vi	x,	$0.5-y$,	$0.5+z$

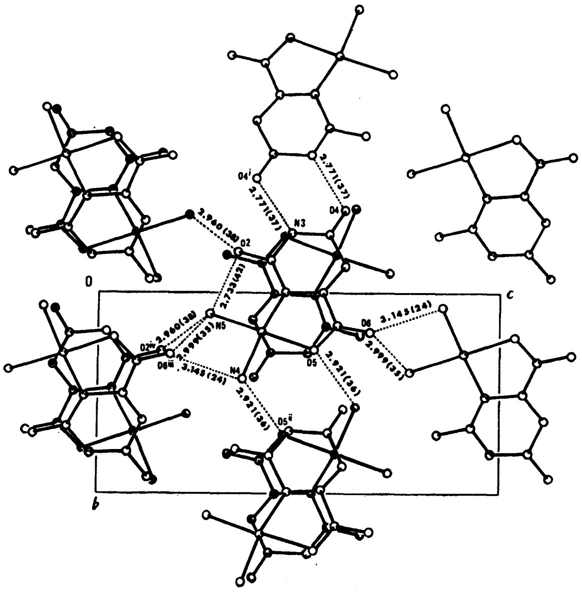

Fig. 3. Projection of the structure of *cis*-$[Pt(NH_3)_2(C_5H_2N_2O_4)]$ down the a axis showing part of the hydrogen bonding scheme and their lengths.

pyrimidine ring is 2.81°. The best least-squares planes calculated from all the atoms, the pyrimidine ring and Pt, N1, N4, N5, and O5, are shown in Table 3.

The molecules are hydrogen-bonded to each other; the possible hydrogen bond distances and angles are listed in Table 4 and are shown in Fig. 3. Using the expected coordinates for hydrogen atoms, the donor-hydrogen atom-acceptor angles were calculated. They are between 145.6° and 172.7°, satisfactory for hydrogen-bondings. The only angle which is marked with an asterisk is small; in this case, the hydrogen atom may shift greatly from the donor-acceptor line.

Although the present work has been undertaken in order to elucidate the structural relations among the three complexes, yellow needles, green needles, and dark-blue microcrystals, preliminary Weissenberg photographs show that the yellow and green needles are structurally identical. Since the dark-blue microcrystals are too small for X-ray single-crystal analysis, only the green needle crystals were subjected to X-ray intensity measurement. There is no definite explanation for the color difference at present, but after the X-ray diffraction analysis had been completed, a close microscopic examination of the crystals showed that the yellow and green needles seem to differ only in their habit of crystal growth; that is, they are identical complexes actually, but seem slightly different in color because of the difference in crystal growth. Otherwise, although the results of ESCA showed no difference, a slight difference in the oxidation states of the platinum atoms, which cannot be detected with ESCA, might exist between the yellow and green needles. It has been reported that platinum α-pyridon blue contains platinum atoms of the formal oxidation state, 2.25.[19] The shortest platinum-platinum distance in the present complex is 4.601(1) Å. A comparison of the platinum-platinum distances with those of other complexes, *cis*-diammineplatinum α-pyridon blue: 2.7745(4) and 2.8770(5) Å,[19] and Magnus' green salts: 3.25—3.46 Å,[26] shows that the platinum-platinum distance of the present complex is much longer, and there seems to be no interaction between adjacent platinum atoms.

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