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A Platinum(II) Dimer with Bridging 1-Methylthyminato Ligands in Head-to-Head Arrangement

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Introduction

With the structure of blue platinum antitumor agents containing pyrimidine-2.4 diones as ligands [1] not yet solved, structural details of related compounds and precursors are of great interest. Recently the structure of a yellow platinum dimer containing two bridging 1-methylthymine anions in head to tail arrangement has been reported [2]. We herewith report on the preparation and the structure of the corresponding head to head dimer, bis-(μ-1-methylthyminato-N3,O4)bis-(*cis*-diammineplatinum(II)) dinitrate. This geometry, expected from the way of preparation, has been verified by X-ray analysis. The compound is compared with the head-to-tail dimer and the recently described 'α-pyridone blue' [3]. Its relationship with 'platinum 1-methylthymine blues' is briefly discussed.

Experimental

The title compound was obtained in two ways:

(1) *Cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ [4] and 4 equivalents of 1-methylthymine were brought to pH 7 in an aqueous solution and reacted at 90 °C for 3 h. Upon filtration of unreacted ligand from the concentrated solution and cooling to 3 °C for 3 days a precipitate was obtained that consisted of at least three different kinds of crystals. Repeated treatment of the precipitate with small amounts of H_2O left the title compound in 2–5% yield as yellow, transparent crystals. C 16.83, H 3.14, N 16.11, Pt 46.0; theory for $(NH_3)_2Pt(C_6H_7N_2O_2)(NO_3)_2$: C 16.75, H 3.05, N 16.28, Pt 45.33. Further concentration of the solution yielded, among others, colorless crystals of composition $(NH_3)_2Pt(C_6H_7N_2O_2)_2X2.5\ H_2O$: C 26.12, H 4.71, N 15.21; theory C 26.08, H 4.57, N 15.21.

An X-ray structure of a derivative of this compound is being performed. It shows the two 1-methylthymine anions to be coordinated in a monodentate fashion via N(3) [5].

(2) Starting with the 2:1 complex, *cis*-$(NH_3)_2Pt(C_6H_7N_2O_2)_2$, and reacting it with 1 equivalent of *cis*-$[(NH_3)_2Pt(H_2O)_2](NO_3)_2$ at room temperature for several days (pH 3), the title compound was obtained in 60–70% yield. Greenish-yellow crystals, bright yellow after recrystallization from H_2O. As a coproduct of this reaction an amorphous blue material of very good water solubility was obtained upon addition of excess ethanol to the concentrated blue reaction mixture.

Slight warming (40 °C) of the title compound in an aqueous $NaNO_3$ solution ($c_{\text{Pt compound}} = 0.004\ M$, $c_{NaNO_3} = 0.04\ M$, pH = 4.3, open flask) over a period of 9 days lead to a colour change from pale yellow via green and purple to blue. From the concentrated solution 40% of the Pt dimer was recovered. Upon slow evaporation at room temperature a new type of yellow crystals and a blue material were obtained.

The crystal data are: $a = 8.36(2)$, $b = 17.55(3)$, $c = 18.40(3)$ Å, $\beta = 121.15(8)°$, V = 2310.4 Å^3, $P2_1/c$, $Z = 4$, mol. wt. 860.7, $D_c = 2.47$ g cm^{-3}, $D_m = 2.45$ g cm^{-3}, $\mu = 128.0$ cm^{-1}. 4042 independent reflections were measured on a Syntex $P2_1$ diffractometer (Mo-Kα, λ = 0.71069 Å, graphite monochromator). Using the Syntex-XTL program the structure was solved by the heavy atom method without absorption corrections. Full matrix least squares refinement gave a final R value of 0.094 for 2038 relections with $F_0 \geqslant 6.5\ \sigma_{F_0}$.

Results

The dimer cation is shown in Fig. 1. Pt(1) is coordinated by two NH_3 groups *cis* to each other and two N(3) atoms of the 1-methylthymine rings. Pt(2) is coordinated by two NH_3 groups in *cis* position and two oxygen atoms of the exocyclic keto groups of the thymine rings. Thus the 1-methylthyminato ligands are arranged in head-to-head fashion. There is some uncertainty concerning the numbering of the coordinating keto groups. N(1) and C(5) could possibly be interchanged, thus leading to N(3), O(2) bridging instead of the N(3), O(4) binding indicated in Fig. 1. For the second heterocycle N(3A), O(4A) coordination appears to be certain, judging from the thermal parameters of N(1A) and C(5A). It is pointed out that, despite this obvious ambiguity, our conclusions concerning the possible importance of head to head complexation in platinum blues (*cf.* Discussion) are not invalidated. The Pt–Pt distance within the dimer (2.909(3) Å) is somewhat shorter than in the corresponding head-to-tail dimer (2.974(1) Å). It is, however, clearly longer than in the partially oxidized α-pyridone dimer unit (2.7745(4) Å). The distance

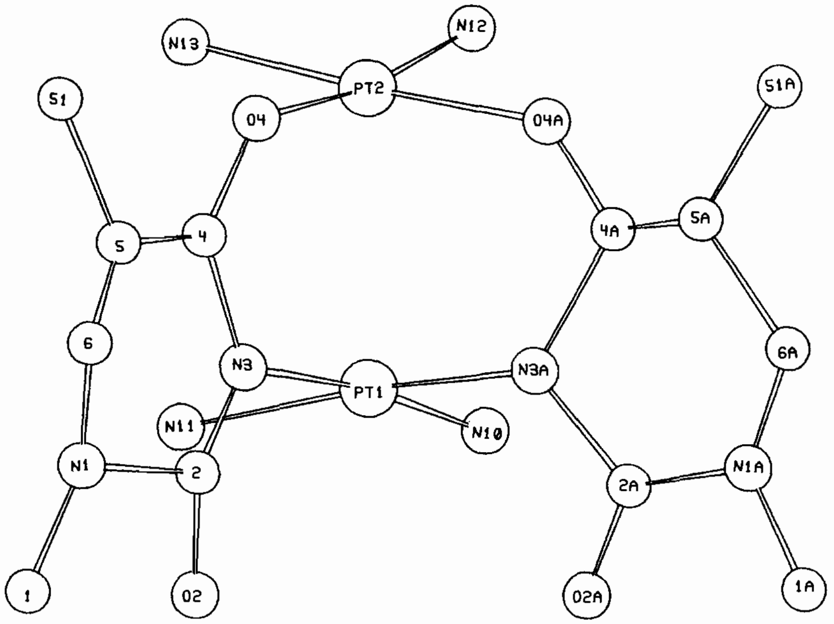

Fig. 1. The molecular cation $[(NH_3)_2Pt(C_6H_7N_2O_2)]_2^{2+}$. If not otherwise indicated (N, O, Pt), the atoms represent C atoms. *E. g.*, 5A means C(5) of ring with A notation.

between the nearest Pt atoms of two dimer units (5.615(3) Å) is very similar to that found in the head-to-tail dimer (5.92 Å), but considerably longer than in the α-pyridone structure (2.8770(5) Å). Each of the two Pt atoms in the title compound is displaced by approximately 0.1 Å from the best plane put through the four coordinating atoms in such a way that the Pt atoms get closer to each other. There is a similar tilting of the two Pt coordination planes in this compound (29.5°) as in the α-pyridone structure (27.4°) and the head-to-tail 1-methylthymine dimer (36.1°). In contrast to these two structures the twisting of the Pt coordination planes about the Pt–Pt axis (22° in the α-pyridone structure and approximately 14° in the head-to-tail 1-methylthymine dimer) is not observed in the here described compound. There the coordinating NH_3 groups lie practically above each other (torsional angle N(12)–Pt(2)–Pt(1)–N(10) = 0.4°, N(13)–Pt(2)–Pt(1)–N(11) = 1.7°). This can be seen clearly when viewed along the Pt–Pt vector (Fig. 2).

Discussion

The compound described here bears close resemblance to one half of the '*cis*-diammineplatinum α-pyridone blue'. In this compound two Pt dimers with head-to-head arranged α-pyridonato ligands are linked through a Pt–Pt bond and intramolecular hydrogen bonds between the NH_3 protons and the platinated oxygen atoms of the two binuclear units. As a consequence of this arrangement, platinum is stabilized in the unusual oxidation state of +2.25. A corresponding structure cannot be formed in the 1-methylthymine system if the ligands are head-to-tail within each dimer [2]. Such a geometry prevents any close contact between two dimer units due to the steric hindrance of the exocyclic keto groups not coordinated to platinum. In contrast, head-to-head arrangement of the 1-methylthymine ligands should enable tetramer formation via the Pt(2) coordination plane and, upon partial oxidation, lead to a '1-methylthymine blue' analogous to the 'α-pyridone blue'. Indeed, the title compound forms a 'blue' when kept in an aqueous solution on air (*cf.* Experimental). However, since we have not been able so far to crystallize the blue product we cannot be sure whether it actually is the 'α-pyridone blue' analogue.

A clue as to how N(1) substituted pyrimidine-2.4 diones could possibly be arranged in 'blues' other than the dimer of dimer type structure, is the reaction of bis-(1-methylthyminato-N3) *cis*-diammineplatinum (II) with the *cis*-diaquodiammineplatinum(II) cation. This reaction not only leads to the head-to-head dimer but also to a substantial amount of a blue product. Formation of at least two types of products could be rationalized if it is assumed that the 1-methylthymine ligands in bis-(1-methylthyminato-N3) *cis*-diammineplatinum(II) can rotate around the Pt–N(3) bond. As indicated in Fig. 3, two kinds of reaction products could be formed: A dimer, identi-

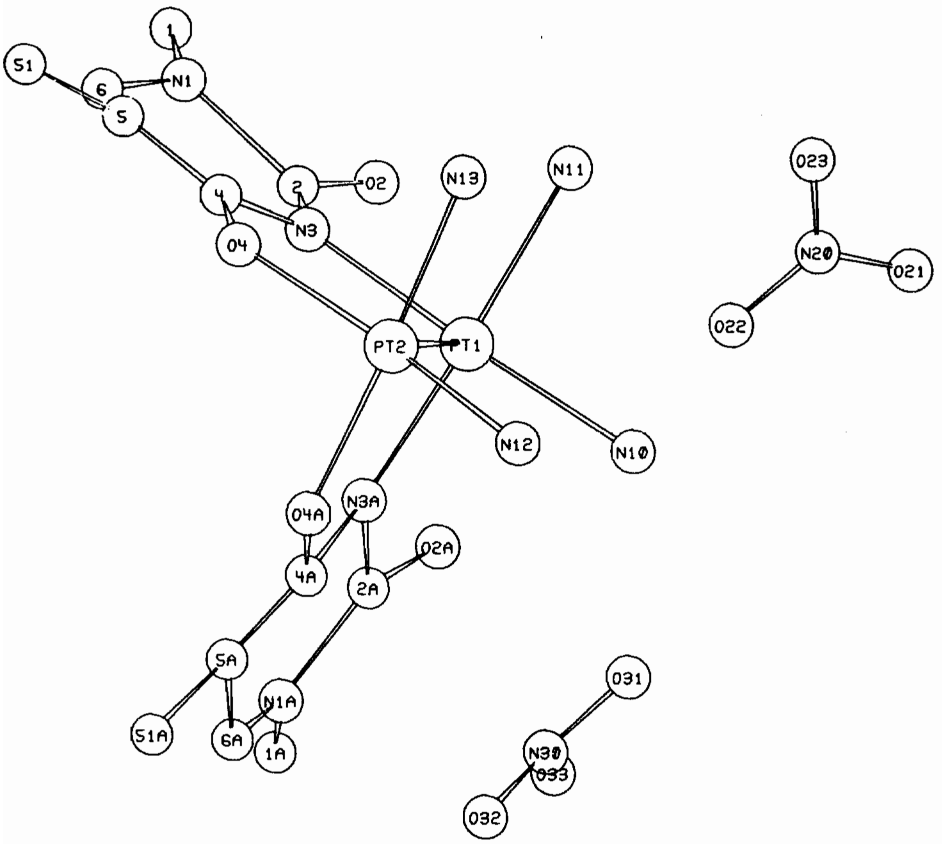

Fig. 2. The molecule viewed down the Pt(2)–Pt(1) axis.

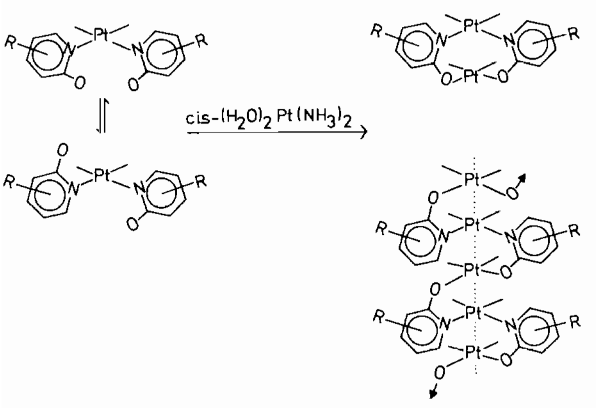

Fig. 3. Possible products from reaction of bis(1-methylthyminato-N3)*cis*-diammineplatinum(II) with *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$. The methylthymine rings are simplified in a way that only N(3) and an adjacent coordinating keto oxygen, most likely O(4), are shown.

cal with the title compound, and a chain with *alternating* PtN_4 and PtN_2O_2 units. In both cases the thymine ligands are bridging in head-to-head fashion. The chain (or ring, if cyclic) could vary in its length, thus leading to a mixture of oligomers. The Pt–Pt distances within the chain (or ring) would be sufficiently short to accomplish metal–metal interaction and, upon oxidation, stabilize Pt in a mixed valence oxidation state. Therefore this model would be in agreement with all the characteristics of 'platinum pyrimidine blues' we presently know of [6].

It is noted, however, that there appears to be no convincing argument why head-to-tail binding of pyrimidine-2.4 diones with *successive* PtN_3O units should, apart from forming the head to tail dimer, not lead to a similar polymeric structure. If such a structure is formed, one might also expect oligomerization and Pt–Pt interactions to occur. Work is in progress to clarify this question and to find out whether head to head complexation is a necessary condition for the formation of 'platinum pyrimidine blues'.

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