

A Novel Type of '1-Methyluracil (Hmeu) Blue:' the Trinuclear, Mixed-metal Complex $cis-[(NH_3)_2Pt(meu)_2Pd(meu)_2Pt(NH_3)_2]^{3+}$

Wolfgang Micklitz,^a Gerhard Müller,^b Jürgen Riede,^b and Bernhard Lippert^{a*}

^a Institut für Anorganische und Analytische Chemie, Universität Freiburg, D-7800 Freiburg, Federal Republic of Germany

^b Anorganisch-chemisches Institut, Technische Universität München, D-8046 Garching, Federal Republic of Germany

The formation and crystal structure of a novel heteronuclear complex, containing two d⁸ (Pt^{II}) and one d⁷ (Pd^{III}) metals linked through four bridging 1-methyluracilato (meu) ligands is reported, and its relationship to the 'platinum pyrimidine blues' is briefly discussed.

'Platinum pyrimidine blues,' prepared by the reaction of aquated cisplatin, $cis-[(NH_3)_2Pt(OH_2)_2]^{2+}$, with pyrimidine bases such as uracil, thymine, or related ligands, have received considerable attention for their antitumour activity,¹ their property of staining nucleic acids,² and in particular for their challenging chemistry as oligomeric, mixed-valence-state compounds.³ To date, three well characterized 'platinum blues' are established, all having similar dimer-of-dimers structures [(I) in Figure 1] with bridging α -pyridonato,⁴ and 1-methyluracilato ligands,⁵ respectively, and a Pt(2.25) average oxidation state, resulting formally from the presence of three Pt^{II} and one Pt^{III}.

At least in the case of the '1-methyluracil blue,' the visible spectra clearly indicate that the Pt(2.25) species, which absorbs at 740 nm, is not responsible for the *blue* colour, but rather is a green component. With this in mind, and encouraged by our more recent findings on a rather facile substitution of NH₃ ligands in a diplatinum(III) complex,⁶ we

have attempted to synthesize, among others, a trinuclear, mixed-valence-state compound of type $cis-[(NH_3)_2Pt(meu)_2Pt(meu)_2Pt(NH_3)_2]^{3+}$ by the reaction of $cis-(NH_3)_2Pt(meu)_2$ and $[Pt(OH_2)_4]^{2+}$ under oxidizing conditions (Hmeu = 1-methyluracil). Although these attempts have been unsuccessful as yet, the heteronuclear Pt₂Pd analogue [(II) in Figure 1] could be isolated and characterized.

The title compound, $cis-[(NH_3)_2Pt(meu)_2Pd(meu)_2Pt(NH_3)_2]^{3+}$ (**3**), was obtained *via* three different routes (Scheme 1) in several modifications, depending on the conditions of crystallization (anions, pH, concentration). (a) HNO₃ oxidation of $cis-[(NH_3)_2Pt(meu)_2Pd(en)](NO_3)_2 \cdot 2H_2O$ (**1**) (en = ethylenediamine): a solution of (**1**)[†] (500 mg) in

[†] Complex (**1**) was obtained from $cis-(NH_3)_2Pt(meu)_2$ ⁷ and $[(en)Pd(OH_2)](NO_3)_2$ in analogy to related diplatinum(II) complexes with head-head arranged meu ligands.⁸ Orange-yellow crystals, characterized by elemental analysis and X-ray crystallography.

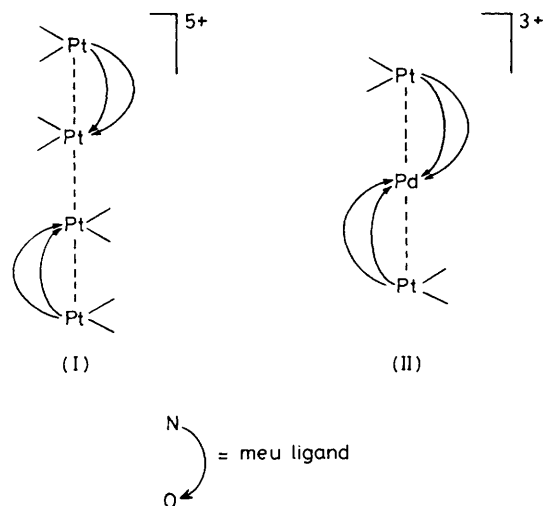


Figure 1. Comparison of $[Pt^{II}_3Pt^{III}]$ (I) and $[Pt^{II}_2Pd^{III}]$ (II) structures.

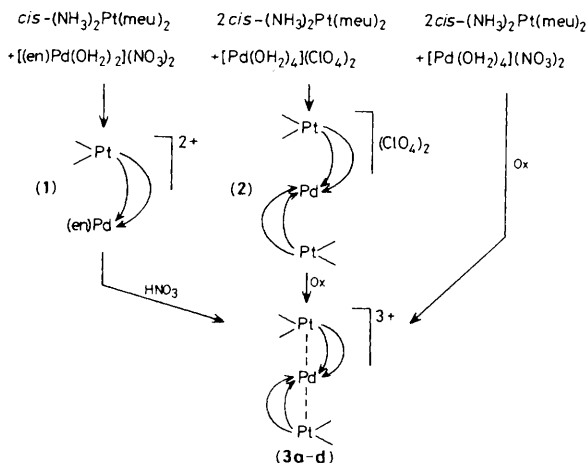
conc. HNO_3 (2 ml) was kept at room temperature for 24 h. The deep blue solution was then diluted with H_2O to 20 ml and allowed to evaporate slowly at $3^\circ C$. The yield after 2 days was 75 mg of $(3)(NO_3)_3 \cdot HNO_3 \cdot 5H_2O$, (**3a**).^{‡§} In one instance, a second modification, $(3)(NO_3)_3 \cdot 11H_2O$, (**3b**),[§] was obtained in low yield. (b) To a solution of $cis-(NH_3)_2Pt(meau)_2$ (240 mg) in H_2O (20 ml) at $40^\circ C$ an aqueous solution (5 ml) of $[Pd(OH_2)_4](NO_3)_2$ ¹⁰ (ca. 20 mmol l^{-1} in 1.3 M HNO_3) was slowly added. After an initial colour change to red, the solution eventually became intensely blue. After removal by filtration of a small amount of a red precipitate, the solution was allowed to evaporate at $3^\circ C$. After 6 days, 130 mg of $(3)(NO_3)_3 \cdot 5H_2O$, (**3c**)[‡] was filtered off and briefly dried in air. (c) To a solution of $cis-[(NH_3)_2Pt(meau)_2Pd(meau)_2Pt(NH_3)_2](ClO_4)_2 \cdot 2H_2O$ (**2**)[¶] (195 mg) in H_2O (20 ml) at $60^\circ C$, $NaClO_4$ (50 mg) and finally freshly prepared Cl_2 -water (2 ml) were

[‡] Satisfactory elemental analyses (C, H, N, O) [and Cl for (**3d**)] were obtained.

[§] *Crystal data* for (**3a**): $C_{20}H_{43}N_{16}O_{25}PdPt_2$, $M = 1403.88$, triclinic, space group $P\bar{1}$, $a = 10.032(2)$, $b = 10.160(2)$, $c = 11.666(2)$ Å, $\alpha = 103.33(1)$, $\beta = 106.29(1)$, $\gamma = 96.03(1)^\circ$, $U = 1092.1$ Å³, $D_m = 2.135$, $D_c = 2.134$ g cm^{-3} , $Z = 1$, $\mu(Mo-K\alpha) = 69.6$ cm^{-1} , $F(000) = 677$, $T = -35^\circ C$. 4748 Unique reflections, 4448 'observed' with $I \geq 2.0 \sigma(I)$, Lorentz-polarisation and empirical absorption correction [ω scans, $\Delta\omega = 0.8^\circ$, $(\sin \theta/\lambda)_{max} = 0.639$, $+h, \pm k, \pm l$, $Mo-K\alpha$ radiation, $\lambda = 0.71069$ Å, graphite monochromator, Syntex P2₁]. Solution by Patterson methods; $R = 0.042$, $R_w = 0.057$, $w = 1/\sigma^2(F_o)$ for 324 refined parameters (SHELX 76), $\Delta\rho_{fin.} = +1.75/-1.23$ e Å⁻³.

Crystal data for (**3b**): $C_{20}H_{54}N_{15}O_{28}PdPt_2$, $M = 1448.96$, triclinic, space group $P\bar{1}$, $a = 11.611(4)$, $b = 10.083(2)$, $c = 12.121(4)$ Å, $\alpha = 109.19(2)$, $\beta = 106.29(2)$, $\gamma = 99.73(2)^\circ$, $U = 1231.8$ Å³, $D_c = 1.953$ g cm^{-3} , $Z = 1$, $\mu(Mo-K\alpha) = 61.7$ cm^{-1} , $F(000) = 705$, $T = -40^\circ C$. 4846 Unique reflections with 4240 'observed' [ω scans, $\Delta\omega = 1^\circ$, $(\sin \theta/\lambda)_{max} = 0.617$]. Patterson methods, $R = 0.045$, $R_w = 0.052$, $w = 1/\sigma^2(F_o)$ for 275 refined parameters, $\Delta\rho_{fin.} = +2.93/-1.17$ e Å⁻³. Additional, partial occupancy by water molecules of sites in the unit cell cannot be excluded on the basis of the last difference map. Atomic co-ordinates, bond lengths and angles, and thermal parameters for (**3a**) and (**3b**) have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

[¶] Complex (**2**) was prepared from $cis-(NH_3)_2Pt(meau)_2$ ⁷ and $[Pd(OH_2)_4](ClO_4)_2$ ¹⁰ in 90% yield. Golden-brownish crystals, characterized by elemental analyses (C, H, N, O, Cl), u.v.-visible spectroscopy, and X-ray analysis.⁹



Scheme 1. Methods of preparation of (**3**) from the dinuclear complex (**1**) and the trinuclear precursor complex (**2**).

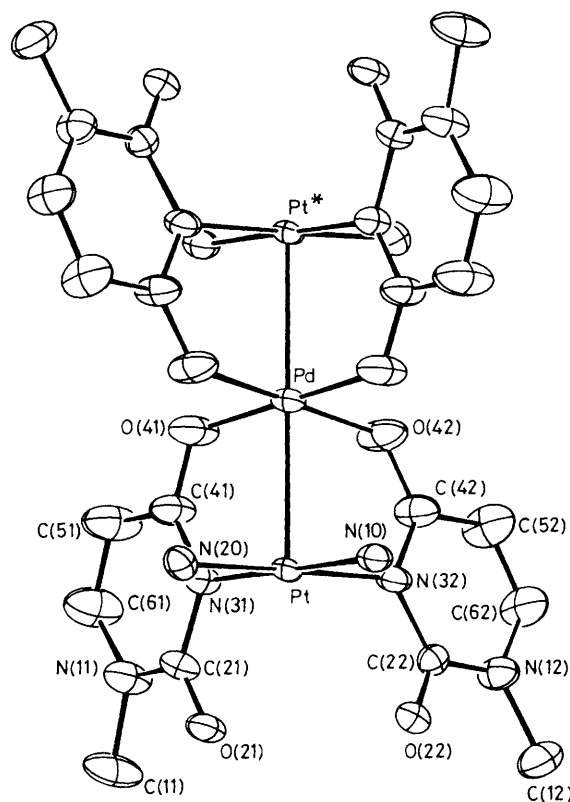


Figure 2. Molecular structure of the cation $[(NH_3)_2Pt(meau)_2Pd(meau)_2Pt(NH_3)_2]^{3+}$ (**3a**) with atom numbering (ORTEP, 50% thermal ellipsoids). Principal distances (Å) and angles ($^\circ$) for (**3a**) [(**3b**): Pt-Pd, 2.634(1) [2.641(1)]; Pt-N(31), 2.034(7) [2.038(8)]; Pt-N(32), 2.025(7) [2.027(7)]; Pt-N(10), 2.049(7) [2.050(7)]; Pt-N(20), 2.043(7) [2.052(8)]; Pd-O(41), 1.963(7) [1.987(6)]; Pd-O(42), 1.998(7) [1.998(7)]; N(31)-Pt-N(10), 178.9(3) [179.0(3)]; N(32)-Pt-N(20), 178.9(3) [177.7(3)]; Pd-Pt-N(31), 83.2(2) [82.8(2)]; Pd-Pt-N(32), 83.9(2) [83.2(2)]; Pt-Pd-O(41), 86.6(2) [87.1(2)]; Pt-Pd-O(42), 86.1(2) [85.6(2)].

added. The then deep-blue solution (pH 2.2) was brought to room temperature and then kept in an open beaker at $3^\circ C$. Complex (**3**)(ClO_4)₃·6H₂O, (**3d**)[‡] (100 mg) was filtered off after 24 h and, on addition of another 30 mg $NaClO_4$ and 0.5 ml of Cl_2 -water, 30 mg of (**3d**) after a further 2 h.

Compounds (**3a**)—(**3d**) exhibit the same appearance, having a metallic blue–purple lustre. When crushed, the compounds look deep blue. According to i.r. and u.v.–visible spectra, the cations in (**3a**)—(**3d**) are identical. The u.v.–visible spectrum (0.1 M HNO₃ or 0.1 M HClO₄) shows three absorptions at 608 ($\epsilon \sim 9800 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$), 546 (~ 3800), and 354 nm (~ 3100). As judged from ¹H n.m.r. spectra, solutions of (**3**) in D₂O or DNO₃ are paramagnetic, giving a magnetic moment of 1.9 μ_B .¹¹ E.s.r. spectra of polycrystalline (**3**) are qualitatively similar to those of platinum blues,⁵ with somewhat different *g* values of 2.167(\perp) and 1.986(\parallel) and no fine structure at room or liquid nitrogen temperatures.

Figure 2 depicts the cation of (**3a**). The cation of (**3b**) is virtually identical. Two *cis*-(NH₃)₂Pt(meu-N³)₂ units are linked *via* four exocyclic O(4) oxygen atoms to palladium to give a centrosymmetric, trinuclear complex. The three metals have square-planar co-ordination spheres with two adjacent planes tilted by 14.5°. Angles about the metals are close to 90°, and Pt–N [2.025(7)—2.049(7) Å] and Pd–O distances [1.963(7), 1.998(7) Å] are normal. Certainly the most significant feature of cation (**3a**) is its very short Pt–Pd separation of 2.634(1) Å [2.641(1) Å in (**3b**)], which is a consequence of metal–metal bonding within the Pt,Pd,Pt chain. This intermetallic distance compares with 2.927(1) Å in the dinuclear (Pt^{II},Pd^{II}) complex (**1**) and 2.839(1) Å in the trinuclear (Pt^{II},Pd^{II},Pt^{II}) complex (**2**).⁹ For an unambiguous assessment of the charge of the cations in (**3a**) and (**3b**) the number of anions becomes crucial. Regardless of appreciable disorder of some of the NO₃[−] ions in the structures of (**3a**) and (**3b**), the existence of more than three counter-ions can be definitely excluded for (**3b**). In (**3a**), two disordered NO₃[−] ions form dimers not unlike the known hydrogen bonded [H(NO₃)₂][−] species¹² thereby corroborating further the presence of HNO₃ in the crystal lattice.

Finally, we note that we have isolated the complete series of complexes (**1**)—(**3**) with (en)Pt substituting the *cis*-(NH₃)₂Pt moieties.

We thank the Deutsche Forschungsgemeinschaft and Degussa (loan of K₂PtCl₄) for their support. W. M. thanks the Technische Universität München for a fellowship.

Received, 23rd July 1986; Com. 1042

References

- 1 J. P. Davidson, P. J. Faber, R. G. Fischer, S. Mansy, H. J. Peresie, B. Rosenberg, and L. VanCamp, *Cancer Chemother. Rep., Part 1*, 1975, **59**, 287; R. J. Speer, H. Ridgway, L. M. Hall, D. P. Stewart, K. E. Howe, D. Z. Lieberman, A. D. Newman, and J. M. Hill, *ibid.*, 1975, **59**, 629.
- 2 S. K. Aggarwal, G. A. Ofosu, and Y. Waku, *J. Clin. Hematol. Oncol.*, 1977, **7**, 547.
- 3 S. J. Lippard, *Science*, 1982, **218**, 1075; B. Lippert, *Inorg. Chem.*, 1981, **20**, 4326.
- 4 J. K. Barton, D. J. Szalda, H. N. Rabinowitz, J. W. Waszczak, and S. J. Lippard, *J. Am. Chem. Soc.*, 1979, **101**, 1434; T. V. O'Halloran, M. M. Roberts, and S. J. Lippard, *ibid.*, 1984, **106**, 6427.
- 5 P. K. Mascharak, I. D. Williams, and S. J. Lippard, *J. Am. Chem. Soc.*, 1984, **106**, 6428.
- 6 B. Lippert, H. Schöllhorn, and U. Thewalt, *Inorg. Chem.*, 1986, **25**, 407.
- 7 D. Neugebauer and B. Lippert, *J. Am. Chem. Soc.*, 1982, **104**, 6596.
- 8 B. Lippert, D. Neugebauer, and G. Raudaschl, *Inorg. Chim. Acta.*, 1983, **78**, 161.
- 9 W. Micklitz, G. Müller, B. Huber, J. Riede, and B. Lippert, to be published.
- 10 L. I. Elding, *Inorg. Chim. Acta*, 1972, **6**, 647.
- 11 D. F. Evans, *J. Chem. Soc.*, 1959, 2003.
- 12 J. Emsley, *Chem. Soc. Rev.*, 1980, **9**, 91.