Formation of Platinum Blues by Pyrimidine Nucleotides

David M. L. Goodgame and Ian Jeeves

Chemistry Department, Imperial College of Science and Technology, London, S W 7 2AY, U. K.

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The formation is reported of platinum blues by 5′-CMP and by 5′-UMP.

There has recently been interest in the deep blue (or purple) products obtained by reacting certain platinum (II) species such as *cis*-$[Pt(NH_3)_2(H_2O)_2]^{2+}$ with amides or pyrimidines, notably uracil and thymine. Some of these substances have been reported to have anti-tumor activity [1 – 4] and they have also been used as cytologic stains for electron microscopy [5].

Because of the difficulties in obtaining the blues in pure form, their exact nature is still poorly understood, though the X-ray studies of Barton, et al. [6] on a blue formed by α-pyridone support the general assumption that these unusual compounds probably contain chains of closely interacting platinum atoms.

Most studies of the platinum blues involving species which are components of nucleic acids have hitherto concerned the pyrimidine bases or, more recently, uridine [7, 8]. During our work [9] on the interactions of *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$ with nucleotides we have obtained blues with 5′-CMP and 5′-UMP. Although attempts to obtained crystals suitable for X-ray studies have been unsuccessful, we summarize here the synthetic details as the formation of platinum blues by nucleotides has not apparently been reported hitherto.

The 5′-CMP and 5′-UMP platinum blues were obtained by the following procedure. An aqueous solution of equimolar amounts of the disodium salt of the nucleotide and *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ at pH 4.0 was allowed to evaporate at room temperature. When the volume had been reduced to approx.

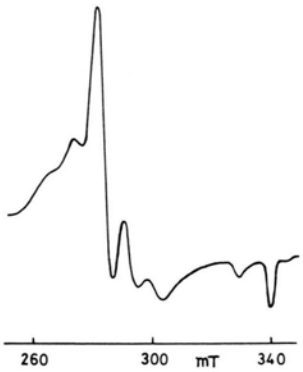

Fig. 1. X-Band (9.534 GHz) e. p. r. spectrum of a Pt(5′-UMP) blue.

⅕ methanol was added to the blue solution, whereupon a dark blue solid precipitated. This was collected by centrifuging, washed with methanol and dried in vacuo over P_2O_5.

The compounds are hygroscopic and, in common with other platinum blues, it was difficult to obtain completely reproducible analyses. However, it appears that the 5′-UMP blue contains the nucleotide in base-deprotonated form (= 5′-UMP^{3-}) (Found: C, 16.62; H, 2.95%. Calc. for $[Pt_3(NH_3)_6(5'\text{-}UMP^{3-})_2]$ C, 16.66; H, 3.03%) whereas in the 5′-CMP blue the nucleotide is present as coordinated 5′-CMP^{2-} (Found: C, 17.37; H, 4.21% Calc. for $Pt(NH_3)_2$(5′-CMP) · 4 H_2O; C, 17.34; H, 3.94%).

Blues were not formed by 5′-GMP or 5′-IMP under these conditions, nor did $[Pten(H_2O)_2](NO_3)_2$ or *trans*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ yield blues with 5′-CMP or 5′-UMP.

The X-band e. p. r. spectrum of the blue formed by 5′-UMP (Fig. 1) is very similar to that reported by Lippert for a uracil blue [7].

The observation that *cis*-$[Pt(NH_3)_2(OH_2)_2]^{2+}$ forms blues with pyrimidine nucleotides provides further support for the view [6, 9, 10] that both ring nitrogen and exocyclic oxygen atoms of the heterocyclic bases may be the binding sites in DNA for the anti-tumor active aquation product of *cis*-$Pt(NH_3)_2Cl_2$.

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