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'Platinum Phosphate Blues'. A Comparison with 'Amide Blues'

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There has been much interest in the blue solids and solutions which may be obtained by reactions in air of *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$ with organic molecules containing a $\overset{|}{N}-\overset{|}{C}=O$ grouping (*e.g.*, amides, uracil) [1]. Since the determination of the structure of the blue compound $[Pt_2(NH_3)_4(\alpha\text{-pyridone})_2]_2(NO_3)_5$ [2], it has been generally accepted that these compounds contain oligomeric chains with close Pt–Pt contacts, with at least some pairs of Pt atoms linked by Pt-N–C–O–Pt bridges, and with the average oxidation state of platinum between 2.0 and 2.5. Some of these compounds have impressive antitumour activity in many mammalian species, but proved unsuccessful in human clinical trials [3].

In 1972, Shooter *et al.* [4] reported, in a paper on the interaction of platinum complexes with bacteriophages, that solutions of *cis*-$Pt(NH_3)_2Cl_2$ or Pt(en)-Cl_2[†] in phosphate buffer solution at 37 °C slowly developed a blue colour. This report appears to have attracted little attention from chemists, and no further information is available in the literature on this system. We have investigated this system further, to attempt to determine the nature of the blue compounds formed, and to discover whether they are related to the 'amide blues'.

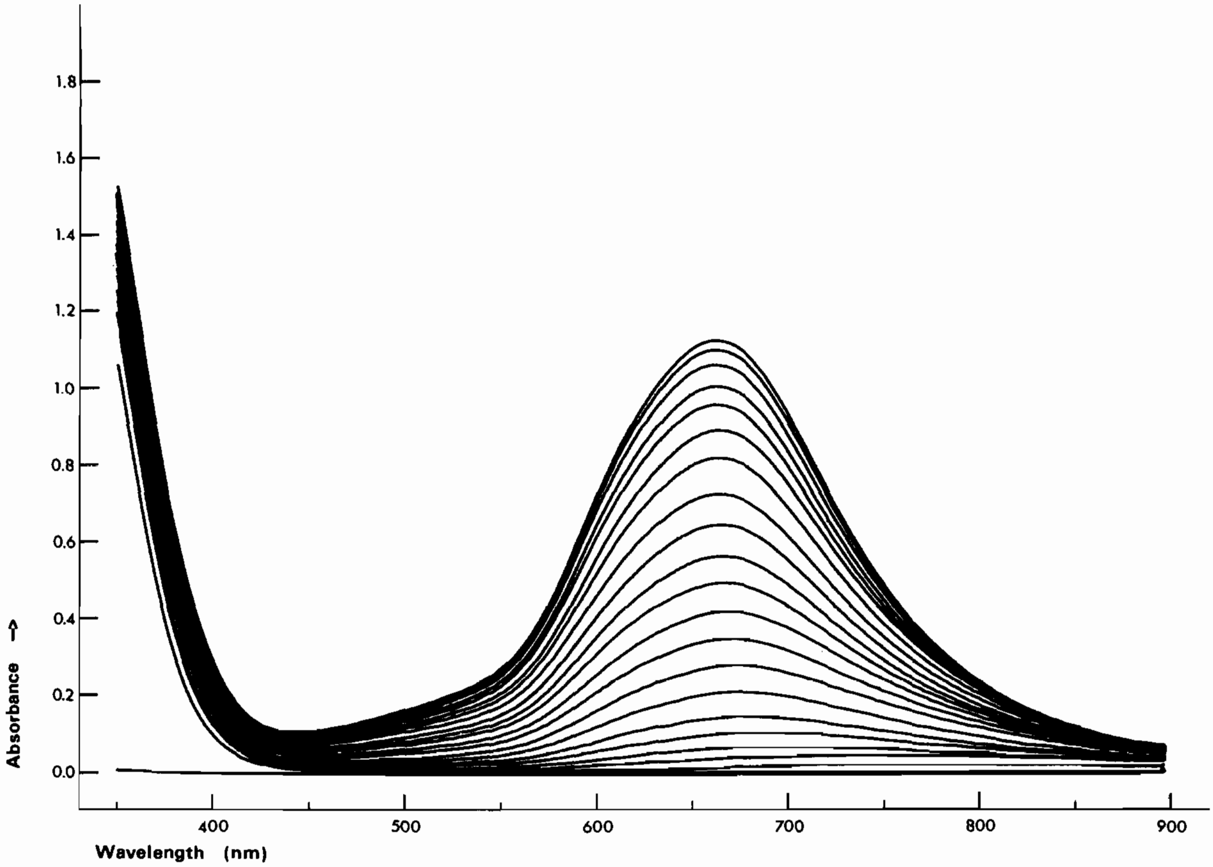

Fig. 1. Visible spectra at 20 minute intervals of a solution initially 0.44 *M* in each of *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ and KH_2PO_4, adjusted to pH 3.0 (small amounts of solid filtered off).

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*Author to whom correspondence should be addressed; no reprints available.

[†] Abbreviations: en 1,2-diaminoethane, $NH_2CH_2CH_2NH_2$; tn, 1,3-diaminopropane, $NH_2CH_2CH_2CH_2NH_2$.

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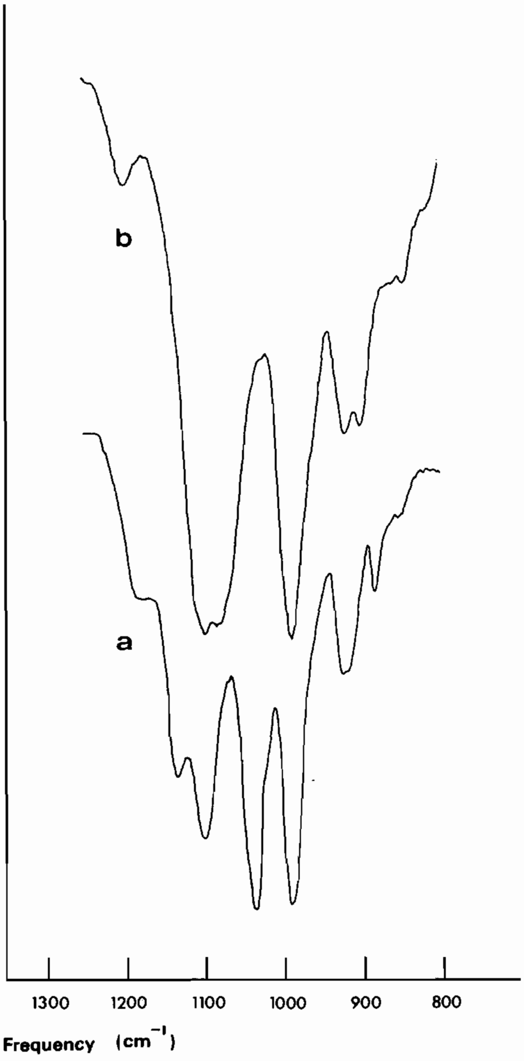


Fig. 2. IR spectra in ν_{P-O} region of (a) blue $H_n[Pt(NH_3)_2(PO_4)]\cdot\frac{1}{2}H_2O$, (b) white $H[Pt(NH_3)_2(PO_4)]\cdot\frac{1}{2}H_2O$.

We have found that a solution of *cis*-$Pt(NH_3)_2Cl_2$ (saturated) and KH_2PO_4 (0.44 *M*) in water at pH 4.5 at 40 °C, exposed to air, does develop a deep blue colour over several days. However, the reaction proceeds much more quickly, and a much more intense colour develops, if the aqua complex *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ is used, rather than *cis*-$Pt(NH_3)_2Cl_2$. Typically, when a solution 0.44 *M* in each of *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ and KH_2PO_4, with KOH solution added to adjust pH to 3, is allowed to stand at 30 °C in contact with air, the solution changes from pale yellow to pale green within 0.5 hour, and to a noticeably blue colour within an hour. The blue colour then increases in intensity over several hours (Fig. 1), while small quantities of very dark blue solid precipitate. The major peak in the visible spectrum occurs at 664 nm, with a shoulder near 624 nm.

With pH initially adjusted to 4, much higher yields of the dark blue solid are obtained, with a corresponding decrease in the intensity of the colour of the supernatant solution. If pH is lower than 1.5, or higher than 4.5, no blue colour appears under these conditions. At lower concentration of the reactants, pH 3, the blue colour develops only very slowly, and even after several weeks is much weaker than would be anticipated on the basis of Beer's Law. No blue colour develops if air is excluded. The colour does develop in solutions kept in the dark. The 'amide blues' show an analogous sensitivity to pH and concentration [5].

The blue colour of a solution is discharged by addition of dilute KOH solution, dilute HNO_3, dilute HCl (*cis*-$Pt(NH_3)_2Cl_2$ precipitates), the reducing agent ascorbic acid, or the oxidizing agent hydrogen peroxide (with warming), again in parallel with the behaviour of 'amide blues' [5, 6].

If concentrated solutions of *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ and KH_2PO_4 are mixed (to give a solution 0.5 *M* in each) and pH is adjusted to 1 with HNO_3, no blue product is obtained, but a *white* solid slowly deposits which analyses for $H[Pt(NH_3)_2(PO_4)]\cdot\frac{1}{2}H_2O$. Mixing concentrated solutions at pH 3–4 also gives this solid, but it is then difficult to prevent its contamination with blue compounds. The dark blue solids which precipitate from blue solutions give similar analyses to the white solid, and are formulated as $H_n[Pt(NH_3)_2(PO_4)]\cdot\frac{1}{2}H_2O$, where $n < 1$, corresponding to an average oxidation state of $Pt > 2$. The IR spectra of the blue and white solids are quite different. A comparison of the spectra in the P–O stretching region is given in Fig. 2.

The white solid is diamagnetic and gives no ESR signals. The blue solids are weakly paramagnetic, with an average magnetic moment per Pt atom of 0.5 ± 0.2 Bohr Magnetons. Blue solids give a complex ESR spectrum. An example is shown in Fig. 3, together with a spectrum of the 'insoluble' fraction prepared by us using a standard uracil blue preparation [7], for comparison. No detailed analysis has been attempted. The major peaks in the phosphate blue spectrum, as for the uracil blue, occur in the g-value range 1.9–2.4 as reported for 'blues' in the literature [2, 6, 8]. However, the phosphate blue gives a significant peak as well at $g = 4.29$. For the uracil blue, we observed a weak peak near $g = 4$ and a stronger one near $g = 6$ (Fig. 3). Previous workers may not have run spectra over this range. The spectrum of a blue solution frozen at −196 °C is also shown in Fig. 3.

There are three isomeric structures possible for $H[Pt(NH_3)_2(PO_4)]$; a simple chelate (I), a dimeric pair (II), or an oligomeric chain (III). Structure (II) is similar to that reported for $[Pt(NH_3)_2]_2(P_2O_7)$ (IV) [9]. This is a platinum(II) complex, and is not

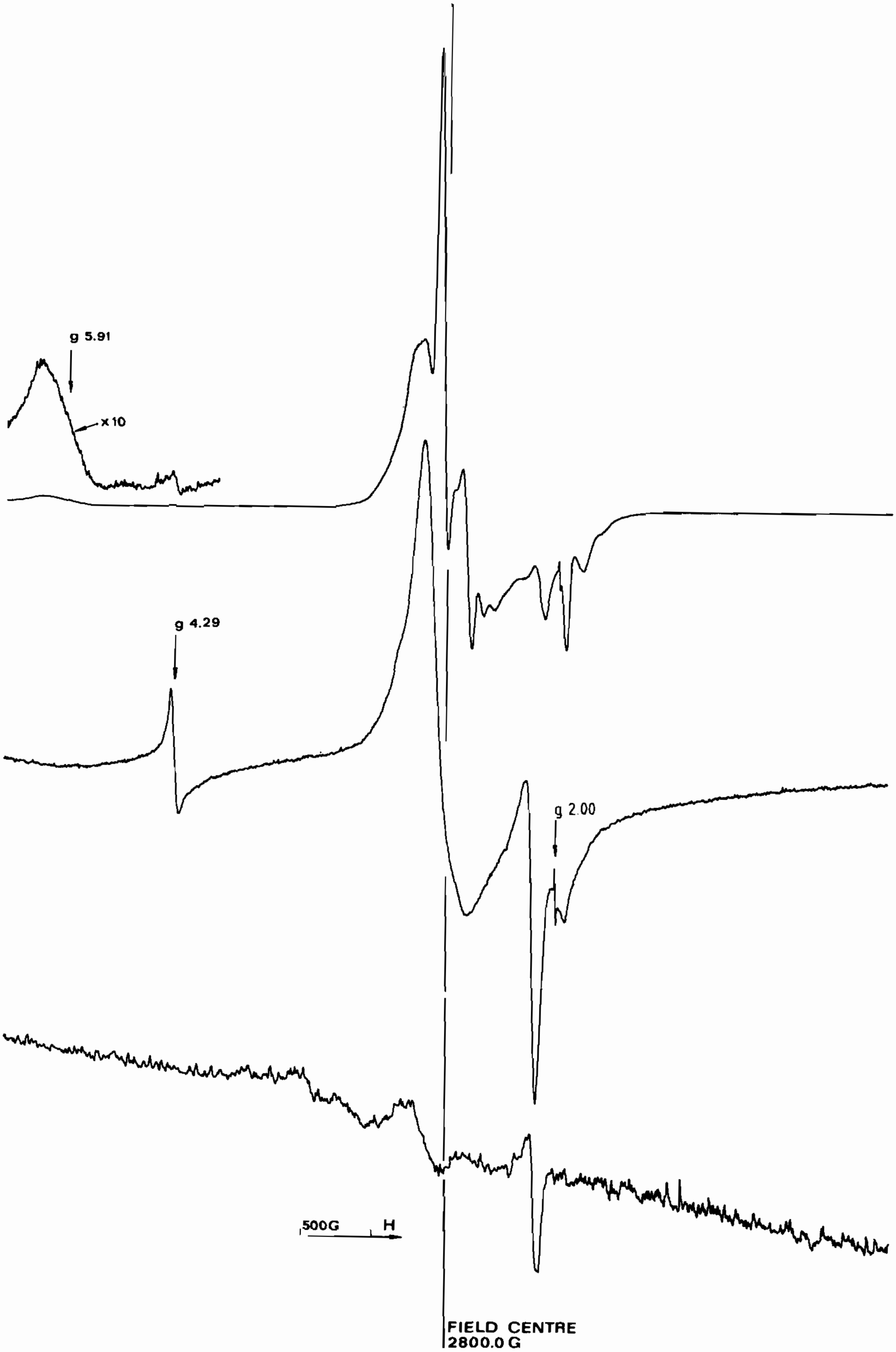
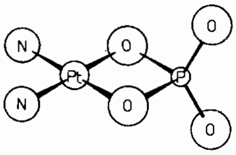


Fig. 3. ESR spectra (−196 °C): (a) uracil blue preparation (see text), (b) blue solid $H_n[Pt(NH_3)_2(PO_4)]\cdot\frac{1}{2}H_2O$, (c) blue solution from $[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ and KH_2PO_4 (pH 1). (All spectra run on a Bruker ER 200D instrument, under similar conditions except for instrument gain. Gain for (b) and (c) respectively 6 and 20 times that for (a)).



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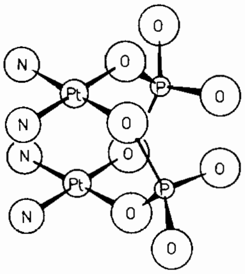

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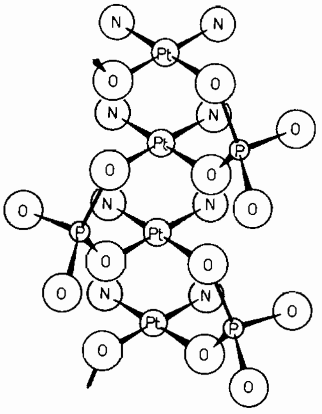

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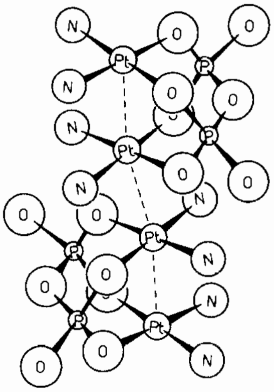

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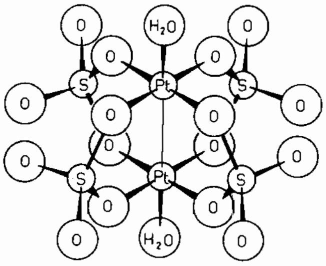

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blue, but it is of interest to note that the intermolecular Pt–Pt distance (3.11 Å) is even shorter than the intramolecular Pt–Pt distance (3.22 Å). We propose that the phosphate blues consist primarily of oligomeric chains, with strong interactions between adjacent Pt atoms, with at least some of the Pt atoms bridged by phosphate, as in (III), or possibly (II). Some of the phosphate ions will be fully deprotonated. The difference between the IR spectra of the blue and white compounds may be due in part to this deprotonation of the phosphate group.

The 'phosphate blues' thus appear to be closely analogous to the 'amide blues', with Pt–O–P–O–Pt bridging replacing Pt–N–C–O–Pt bridging.

Shooter *et al.* [4] claimed that sedimentation measurements indicated a molecular weight near 1000 for their aggregates. It is difficult to see how a meaningful result can be obtained for these systems by this technique, because the aggregates are not simply inert molecules in a phosphate 'buffer' medium, but react with phosphate to an extent determined by concentration. Increasing phosphate concentration of a blue solution causes a rapid increase in intensity of the blue colour, while diluting the solution causes a slow decrease in the colour intensity.

'Amide blues' are obtainable only from ammine complexes [5], but coloured phosphate compounds are formed with a wider range of amines. Depending on conditions, phosphate with $Pt(en)(H_2O)_2^{2+}$ gives blue of purple solutions, with *cis*-$Pt(NH_2Me)_2(H_2O)_2^{2+}$, solutions from yellow to green or blue, and with $Pt(tn)(H_2O)_2^{2+}$, solutions ranging from blue-green to purplish-brown. These differences presumably reflect steric effects on degree of oligomerization, and closeness of Pt–Pt approach in oligomers. No blue colour develops with *trans*-$Pt(NH_3)_2(H_2O)_2^{2+}$ under conditions where solutions of the *cis*-isomer become intensely coloured.

Blue solids, once precipitated, are almost insoluble in water. They dissolve readily in alkali, but with loss of the blue colour.

Solutions of *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$ with sulfate or perchlorate as counter-ions do not form blues under comparable conditions. However, we have found that concentration of a solution of *cis*-$[Pt(NH_3)_2(H_2O)_2]SO_4$ and dilute H_2SO_4 to near dryness by heating in air gives dark blue material mixed with $Pt(NH_3)_2SO_4$. Addition of water gives a blue solution whose colour quickly fades. This behaviour may be related to the production of a dark blue solid from *cis*-$Pt(NH_3)_2Cl_2$ and conc. H_2SO_4 [10–12]. Preparation of a blue solid $Pt_3(NH_3)_4(OH)_6SO_4$ by UV irradiation of a solution of *cis*-$[Pt(NH_3)_2(H_2O)_2]SO_4$ has been recently reported [13]. The yellow platinum(III) compound $K_2[Pt_2(SO_4)_4(H_2O)_2]$ has structure (V), with Pt–O–S–O–Pt bridges [14].

It has also been reported that solutions of $[Pt(NH_3)_2(OH)]_2CO_3$ allowed to stand in alkaline solution in air, then neutralized, turn blue [15]. Further investigation may reveal many other oligomeric mixed oxidation state complexes incorporating bridging anions.

Acknowledgements

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