

ESR Study on Complexes Formed on Reaction of *cis*-Dichlorodiammineplatinum(II) with Cytosine and Cytidine

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The ESR spectra of novel paramagnetic complexes between *cis*-dichlorodiammineplatinum(II) and cytosine or cytidine in aqueous solution are presented and discussed. The results imply a complex containing a binuclear metal-metal bonded platinum moiety with an unpaired electron spin delocalized over the d_{z^2} -orbitals.

Introduction

cis-Dichlorodiammineplatinum(II) (PDD) is known as a potent anti-tumor compound [1, 2]. Therefore its interaction with DNA and its constituents has frequently been studied [3]. Concerning its interaction with cytosine and cytidine it is known that bis complexes are formed in the pH range 3–5.5 whereas mono complexes occur in the pH range 5.5–8.5. The binding site is the N(3) nitrogen [4]. These results have been obtained with solutions containing 25 mM of *cis*-diaquodiammineplatinum(II), an hydrolysis product of *cis*-PDD, and 50 mM of cytidine reacting at 25 °C. Under different experimental conditions, *e.g.* higher reaction temperature and/or higher concentrations of PDD and cytosine or cytidine dark blue solutions occur after relatively long reaction times. These solutions contain several platinum complexes, including paramagnetic species [5, 6].

If the preparation procedure is changed only slightly, new types of paramagnetic platinum complexes are formed giving some insight into their molecular structure by means of electron spin resonance (ESR) spectroscopy. The presented results may be a useful contribution to the relatively complicated chemistry of the formation of platinum pyrimidine blue complexes which have also been shown to possess antitumor potency [7].

Experimental

The paramagnetic solutions were prepared in the following way. *cis*-Dichlorodiammineplatinum(II)

(0.04 M) and cytosine (0.08 M) reacted in aqueous solution for 10 d at 90 °C (pH 5) to give a pale yellow solution containing the paramagnetic species. Using the same molar ratio of the constituents, but higher concentrations (0.1 M PDD and 0.2 M cytosine), the solution became colored and exhibited another type of ESR spectrum, which will be discussed elsewhere.

The paramagnetic PDD-cytidine complex was obtained by the reaction of 0.2 M PDD with 0.2 M cytidine in aqueous solution after 4 d at 90 °C (pH 3.5). The solution becomes dark blue. After subsequent addition of cytidine to such a solution (*e.g.* 0.8 M of cytidine) and after reaction times longer than 4 d (pH 4), the new paramagnetic species are predominant.

ESR measurements have been performed at 77 K by a conventional X-band spectrometer using 100 kHz modulation with a modulation amplitude of 0.5 mT and 1 mW microwave power.

cis-Dichlorodiammineplatinum(II) and cytidine were purchased from SERVA, Heidelberg, and cytosine from MERCK, Darmstadt, and were of reagent grade quality.

Results and Discussion

The ESR spectra of aqueous solutions of PDD and cytosine or cytidine prepared in the above mentioned way are shown in Fig. 1. Both spectra can be discussed together. The differences between the two spectra A and B depend on the preparation conditions of the solutions. The different intensities are due to the actual platinum content. The additional lines in the ESR spectrum of the platinum-cytidine solution are residues of a spectrum which can be obtained when PDD and cytidine are present in equimolar ratio and the solution has become blue. The discussion of the spectra will be done in analogy to that used by Krigas and Rogers [8] on the interpretation of radical spectra induced by gamma-irradiation of single crystals of K_2PtCl_4 .

The spectra are due to axially symmetrical complexes with the g -values $g_{\perp} > 2 > g_{\parallel}$. Using the assumption of low spin d^7 Pt(III) with the unpaired electron occupying a d_{z^2} -orbital the following g -values have been derived for second order spin-orbit coupling correction [8, 9].

$$g_{\parallel} = 2.002 - 3 (\xi_{\text{eff}}/\Delta E_{xz,yz \rightarrow z^2})^2$$

$$g_{\perp} = 2.002 + 6 (\xi_{\text{eff}}/\Delta E_{xz,yz \rightarrow z^2})^2 - 6 (\xi_{\text{eff}}/\Delta E_{xz,yz \rightarrow z^2})^2$$

where ξ_{eff} has been used to take into account the influence of the covalency on the spin-orbit interaction parameter ξ .

There are six hyperfine lines in the g_{\perp} -range of the spectrum. The line pattern is due to a paramagnetic complex with an unpaired electron delocalized over two platinum centers stacked in z -direction. The complexes contain ^{195}Pt in 33.7% natural abundance which has a nuclear spin $I = 1/2$.

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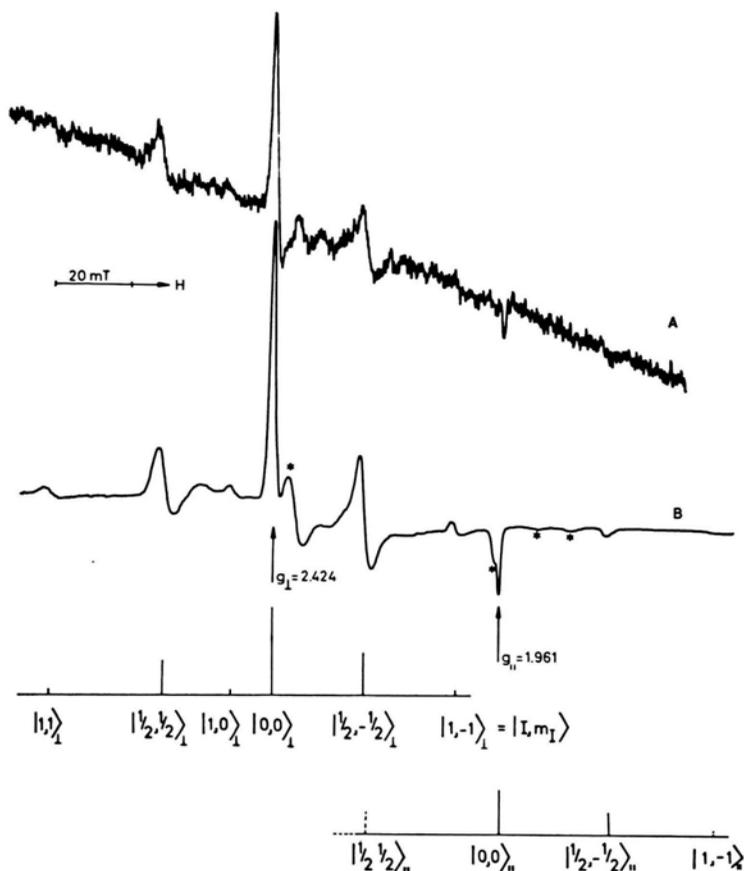


Fig. 1. ESR spectra of frozen aqueous solutions (77 K) of PDD and cytosine (A) or cytosine (B) (preparation see text). The total nuclear moment and its components assumed to be attributable to the ESR lines are also shown. The lines in spectrum B indicated by * are residues of paramagnetic species contained in the platinum cytosine blue solution.

All the other isotopes of platinum have $I = 0$. The unpaired electron, therefore, interacts with the total nuclear spin $I = I^{(1)} + I^{(2)}$ of the two equivalent platinum nuclei, which can be $I = 0$, $I = 1/2$, or $I = 1$. Each of these cases can be described by the following Hamiltonian

$$H = \beta \cdot g_{\parallel} H_z S_z + \beta \cdot g_{\perp} (H_x S_x + H_y S_y) + A_{\parallel} S_z (I_z^{(1)} + I_z^{(2)}) + A_{\perp} (S_x (I_x^{(1)} + I_x^{(2)}) + S_y (I_y^{(1)} + I_y^{(2)}))$$

Theoretically, a triplet, a doublet, and a singlet line with the relative line intensities 1, 7.9, and 16.5 are expected. Taking into account the different line-widths, these line intensities can approximately be observed in Fig. 1.

In the g_{\parallel} -part of the spectrum, only two lines ($|0, 0\rangle_{\parallel}$ and $|1/2, -1/2\rangle_{\parallel}$) can be detected unambiguously. Q-band investigations show that the other doublet line ($|1/2, 1/2\rangle_{\parallel}$) is camouflaged by the $|1/2, -1/2\rangle_{\perp}$ line. The triplet should have rather low intensity.

This interpretation requires a binuclear metal-metal bonded platinum unit in the paramagnetic complex. It is interesting to compare this spectrum with the ESR spectra of platinum pyrimidine blue

solutions. In the latter case, there is one type of ESR spectrum belonging to a complex with an optical absorption band at about 700 nm and it can also be explained by an electron spin delocalized over two platinum centers [10]. Due to an additional platinum center bound in axial position to the two equivalent ones, however, an additional hyperfine splitting can be observed. Because of the fact that no other hf structure can be detected on the 6 lines of the spectrum shown in Fig. 1, it is very unlikely that other platinum ions are bound in axial position. The optical absorption bands of this complex occur at wavelengths shorter than 380 nm.

Speculations can be made as to the structure of this paramagnetic complex, which is present in the solution probably concomitantly with further diamagnetic species. The ESR spectrum, which is due to a spin $S = 1/2$ system, suggests that the paramagnetic complex consists of two magnetically equivalent platinum centers. This fact is formally equivalent to a dimer containing of Pt(II)-Pt(III) or Pt(III)-Pt(IV) units. The experiments do not allow to decide between the two possibilities. It is likely that both platinum atoms are bound to the same types of ligands through N(3) of cytosine and

cytidine, resp., although no nitrogen hf coupling can be resolved. The complexes are formed at a pH value, where usually bis-complexes are found after short reaction times [4]. Therefore, the ESR spectrum shown in Fig. 1 might be attributed tentatively

to a binuclear platinum complex, with each of the platinum centers bound to two cytosine or cytidine molecules.

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