

Temperature Dependent ESR Studies on Platinum Pyrimidine "Blues": Evidence for a Structural Instability?

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Frozen samples of aqueous solutions of oxidized Pt 6-methyl-uracil "blue" were studied by ESR spectroscopy at temperatures T ranging between -196°C and -10°C . When T was raised a distinct change in the line pattern was observed at about -35°C . The resulting type of spectrum is very similar to the ESR spectrum of MAGNUS' Green Salt. The observed effect is suggested to be due to a change of the nature of the system's electronic states possibly indicating a structural rearrangement.

Introduction

The Pt pyrimidine "blues" have recently received considerable interest as a promising potent anti-tumor drug [1]. The "blues" are derived from *cis*-dichlorodiammineplatinum(II) (PDD) or from the hydrolysis product *cis*-diaquodiammineplatinum(II) (PDDa). Broad evidence of the tumor fighting activity of the compounds has been presented [1]. Their mode of action, however, is still open to question. The same holds true for their detailed molecular structure, as structure analysis is severely impeded by the fact that the compounds have never been obtained in the crystalline form. It is generally assumed, however, that the "blues" form oligomeric compounds as a result of partial oxidation and axial stacking of planar Pt monomers [2–12]. This assumption is consistent with X-ray diffraction studies of a crystalline PDDa- α -pyridone system [6].

The Pt pyrimidine "blues" exhibit paramagnetism [3, 7–11, 13] which can be detected by means of electron spin resonance (ESR) spectroscopy. The ESR results are consistent with the assumption that the unpaired electron spin is located in the $5d_{z^2}$ -orbital. They also support the concept of assuming the existence of oligomeric species. At least two basic types of ESR spectra exhibited by the "blues" have been obtained [10]. Studies are in progress to characterize the corresponding paramagnetic species in some more detail. In this report

we would like to describe some preliminary results concerning the effect of temperature changes on the ESR line pattern. Structural implications are briefly discussed.

Experimental

ESR spectra at varying temperatures were taken of an equimolar aqueous solution of PDDa-6-methyluracil which had been allowed to react at 70°C for about 4 h. The pH of the solution was 1.4. $300\ \mu\text{l}$ aliquots of the solution were treated with $20\ \mu\text{l}$ of 15% H_2O_2 . PDDa-6-methyluracil was chosen as a representative of a class of PDDa-uracil compounds since it had turned out to yield the highest spin concentration of all systems tested under a variety of experimental conditions. All spectra were recorded by means of a conventional X-band ESR spectrometer equipped with a variable temperature accessory.

Results and Discussion

The ESR spectrum of the PDDa-6-methyluracil solution after addition of the oxidizing agent (15% H_2O_2) is shown at the top of Figs. 1, 2. This type of spectrum, termed "type 0" [10], has been obtained previously, in a similar form, for a number of Pt "blues" compounds [3, 7, 11].

Frozen solution spectra of the type 0 species recorded at temperatures ranging from -196°C to approximately -13°C are shown in Fig. 1. Except for the expected decrease in intensity the type 0 spectrum remains unchanged for temperatures up to approximately -39°C . However, when T is raised to -34°C a significant and quite abrupt change in the line pattern occurs giving rise to a new type of spectrum "type X" at -34°C . The type X line pattern is essentially retained as T is lowered to values well below the region of the type 0 \rightarrow type X transition. This is illustrated by spectra 6 and 7 of Fig. 1. The type 0 pattern is readily regained, however, when the sample is melted and refrozen subsequently (Fig. 1, spectrum 8).

Fig. 2 clearly illustrates the characteristic differences in the distribution of relative line intensities in the g_{\perp} - and g_{\parallel} -regions of the type 0 and the type X spectra. In particular, the resolution in the g_{\parallel} -region of the type X spectrum is considerably reduced as compared to the type 0 pattern. Thus, the g_{\parallel} -line shape of the type X spectrum exhibits a striking similarity to the g_{\parallel} -signal of the 77 K ESR spectrum obtained from a powder sample of Magnus' Green Salt (MGS) (Fig. 2). In addition, the line intensity distribution in the g_{\perp} part also suggests the similarity of the two spectra.

The ESR spectrum of MGS has been analyzed in terms of localized $5d_{z^2}$ hole states. Thus, states extending over several, *i.e.* 7–9 coupled Pt centers have been assumed to account for the observed pattern [14]. The fact that the type X and MGS

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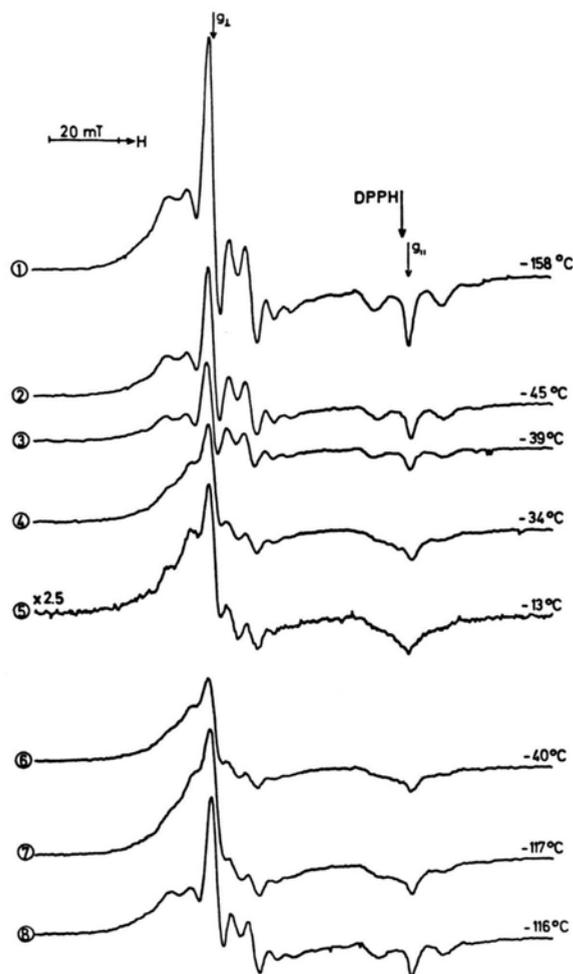


Fig. 1. ESR spectra of 0.1 M PDDa-6-methyluracil solution ($\rho = (6\text{-methylura})/(\text{PDDa}) = 1$; 4 h at 70 °C) after addition of oxidizing agent (15% H_2O_2) taken at varying temperatures. The T values are given at the right hand side of each spectrum. Except for the bottom spectrum all spectra were obtained from one frozen sample. Spectrum 8 was recorded after melting the sample at RT and subsequent refreezing to the temperature indicated.

Table I. g-Values of the ESR spectra.

Pt complex	$g_{\perp} (\pm 0.005)$	$g_{\parallel} (\pm 0.005)$
PDDa-6-methyluracil:		
type O	2.394	1.991
type X	2.405	1.998
Magnus' Green Salt	2.497	1.948

line patterns are practically identical concerning the hyperfine structure strongly suggests that states of this type may also be responsible for the type X

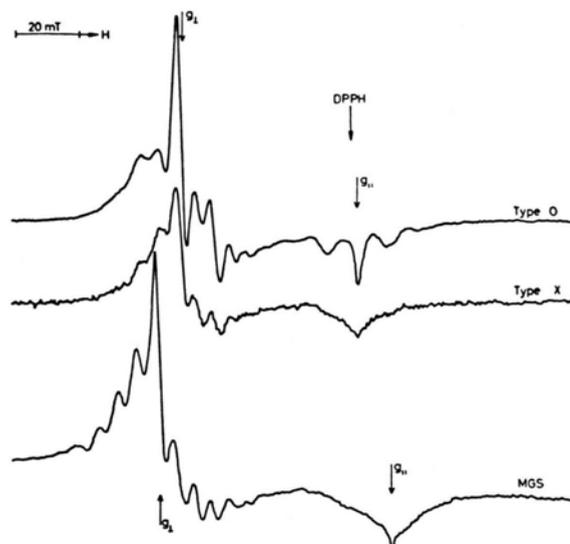


Fig. 2. The type O and type X spectra were obtained from a 0.1 M PDDa-6-methyluracil solution ($\rho = 1$; 4 h at 70 °C) after treatment with H_2O_2 , measured at 77 K (type O) and at -34 °C (type X).

The MGS spectrum was obtained from a powder sample at 77 K.

spectrum obtained from the type 0 species after raising the temperature. The type 0 spectrum has been explained by assuming the interaction of an electron spin with three or four Pt centers [13]. The g-values of the ESR spectra are summarized in Table I.

The "blues" are generally assumed to form one-dimensional (1D) oligomers. In terms of an idealized model it appears plausible to envisage those oligomers as a disordered 1D system. The disorder, as described by a random potential V_R , may arise from variations of the local ligand-to-Pt stoichiometries and from distortions of the ideal 1D geometry found for instance in the case of PDDa- α -pyrimidine from X-ray analysis [6, 7]. These effects can be expected to be especially pronounced after short reaction times. They presumably result in ligand fields of varying strength and symmetry acting on different Pt centers in the stack. Furthermore, "surface" effects due to the chain ends have to be taken into account especially for short oligomers. Assuming V_R (root mean square) to be of the same order of magnitude as the "bandwidth" of the unperturbed system, the electronic states of the disordered system will be localized to approximately a single lattice site [15–18].

It is suggested that, as the temperature is raised, the disorder may eventually become ineffective due to the dynamics of the 1D "lattice". Consequently, extended rather than strongly localized electronic states may be expected. The fact that the observed

type 0 \rightarrow type X transition is irreversible as long as the sample remains frozen suggests a permanent structural rearrangement involving the surrounding solvent molecules. Further investigations have to elucidate the possible relation between the observed

transition and structural instabilities such as the PEIERLS-FROEHLICH instability or the KOHN anomaly which are characteristic for 1D systems [19] and are known to exist for a number of quasi-metallic mixed valence complexes of Pt [20-21].

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