

**Redox Properties
of Platinum Uracil "Blues":
A New Type
of Paramagnetic Species**

M. Seul, H. Neubacher*, and W. Lohmann

Institut für Biophysik, Strahlencentrum,
Justus-Liebig-Universität,
Leihgesterner Weg 217, D-6300 Gießen

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The observation of a new type of ESR spectrum in the course of redox experiments on a platinum uracil "blue" compound is reported. Some characteristic features of the ESR and optical absorption spectra are described. A tentative analysis of the ESR spectrum is presented, based on the assumption of localized states.

Introduction

Platinum pyrimidine "blues," a class of potent antitumor drugs [1] derived from *cis*-dichlorodiammineplatinum(II) (*cis*-PDD) or the corresponding hydrolysis product *cis*-diaquodiammineplatinum(II) (*cis*-PDDa), have lately been the subject of considerable research effort in order to elucidate their structure and mode of action.

The structure of platinum α -pyridone "blue," a Pt pyridine complex in some respects acting like the Pt pyrimidine "blues," has been determined by X-ray analysis since it can be obtained in the crystalline form [2]. As yet, all attempts to crystallize the Pt pyrimidine "blues" have been unsuccessful. The Pt pyrimidine "blues" are obtained in the course of the reaction of a square-planar Pt(II) complex with certain pyrimidine ligands. The Pt uracil "blues" under study here exhibit paramagnetism and blue or green colours. These phenomena are considered to be the result of an axial Pt-Pt stacking and an overlap of atomic wave functions of mainly $5d_{z^2}$ -character. The "blues" may be classified as Mixed Valence Compounds. We employed ESR spectroscopy and optical absorption spectroscopy to study the compounds' redox properties.

Experimental

Redox experiments were performed on a 0.1 M PDDa-6-methyluracil solution which had been allowed to react at 70 °C in the dark for some 4 h.

The ligand-to-PDDa concentration ratio was adjusted to unity. In most cases 0.1 M ascorbic acid and (diluted) perhydrole (15% H_2O_2) were employed as reducing and oxidizing agents, respectively. 20 μ l of these agents were added to identical 300 μ l aliquots of the Pt complex solution. X-band and Q-band low-temperature ESR spectra were taken on Varian E9 and E112 Q (century series) spectrometers, respectively. Second derivative recordings were obtained on the E9-spectrometer using low-frequency modulation of 1 KHz.

Results and Discussion

At 77 K, ESR spectra of considerable intensity and relatively high resolution (as compared to the spectra of various other PDDa-uracil "blues") were obtained from the frozen solutions (Fig. 1). The

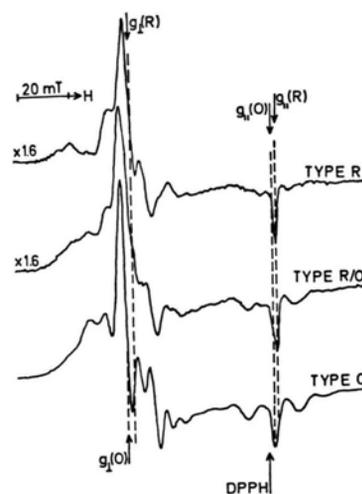


Fig. 1. Type R, type R/O and type O ESR spectra taken at 77 K of a 0,1 m PDDa-6-methyluracil aqueous solution which had been allowed to react at 70 °C for some 4h. Type R and type O spectra were obtained by treating 300 μ l aliquots of the solution with 20 μ l of 0.1 M ascorbic acid and 20 μ l of 15% H_2O_2 , respectively.

bottom spectrum (type 0") has been obtained previously, in a similar form, for a number of other "blue" compounds including PDDa- δ -valero-lactam, PDDa-uridine [3], PDDa- α -pyridone [4] and PDDa-5'-uridine monophosphate [5].

Addition of reducing agent to the above described solution of PDDa-6-methyluracil or to the solution exhibiting the type 0 spectrum resulted in a new type of ESR spectrum ("type R"). It is shown at the top of Fig. 1. Performing a redox titration, various intermediate types of spectra were obtained. The middle illustration (Fig. 1) gives a typical example of such a type R/type 0 intermediate ("type R/0") which is rather similar to the spectrum exhibited by the original PDDa-6-methyluracil

* Reprint requests to Dr. H. Neubacher.
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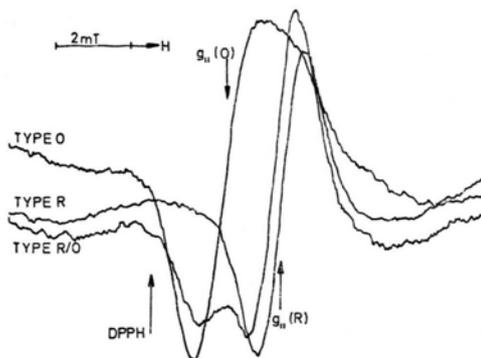


Fig. 2. Second derivative ESR spectra of type R, type R/O and type O $g_{||}$ -signals. The scan range was reduced by a factor of 10 as compared to Fig. 1.

solution. Close examination of the spectra revealed the $g_{||}$ -signal to be an appropriate measure of changes with respect to the type R/type 0 classification in the overall composition of the spectra. Second derivative tracings of the type R, type R/O and type 0 $g_{||}$ -signals are given in Fig. 2. Second derivative recordings proved to be a sensitive tool to detect type R and type 0 contributions to a given spectrum. Thus, it can be seen that the type R/O $g_{||}$ -line is, in fact, a superposition of both type R and type 0 contributions. The asymmetry of the type 0 $g_{||}$ -signal may be due to remaining traces of the type R signal.

As can be seen in Fig. 2, the type R and type 0 $g_{||}$ -values differ significantly. $g_{||}(0) = 1.991$, $g_{||}(R) = 1.983$, and so $g_{||}(0) - g_{||}(R) = 0.008$ corresponding to a shift in resonance field values of about 1.5 mT.

While details concerning the type 0 spectrum shall be given elsewhere [6] here we briefly outline some of the features of the type R spectrum.

I) Recordings in the Q-band at about 130 K of both type R and type 0 systems reveal their spectra to be due to different paramagnetic species. In particular, different relaxation mechanisms seem to be in effect for the two species. Thus, while for the type R species the X-band line pattern is essentially retained at Q-band frequencies, the type 0 species merely yields a single anisotropic line of larger line width ($\Delta H_{pp} = 30$ mT).

II) In the type R X-band spectrum the distribution of line intensities appears to be roughly symmetrical with respect to the central g_1 -line. These lines seem to be grouped into 3 triples. The spectra obtained in the Q-band appear to confirm the notion that the 9 line pattern is due to hf coupling. The intensity distribution in the g_1 -region changed considerably when the ligand-to-PDDa concentration ratio ($=r$) was increased (leaving [PDDa]-constant). The major intensity shifted towards the line adjacent to the central g_1 -peak of the type R spectrum at lower field.

III) The linewidth of the rather narrow $g_{||}$ -line is determined from the 2nd derivative tracing

(Fig. 2) to be approximately 1.4 mT. No indications of any other than type R contributions to the $g_{||}$ -signal can be detected from the 2nd derivative recordings. For instance, such indications are present in the case of the type 0 signal, as can be seen from its asymmetric lineshape (see Fig. 2). A computer analysis, fitting a superposition of Lorentzian and Gaussian lines to the type R $g_{||}$ -signal, yielded best fits with the two shape functions typically contributing 30% and 70%, respectively.

IV) As compared to the type 0 species the amount of paramagnetism present in the type R reaction mixture is reduced by a factor of about 2.

V) The optical absorption spectra of solutions exhibiting the type R, type R/O and type 0 ESR spectra are shown in Fig. 3. The spectra reveal a reduction of both the λ_{max} -value by about 100 nm and of the overall optical density of the type R with respect to the type 0 solution.

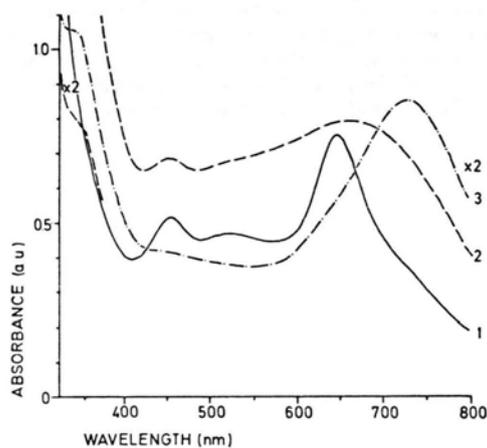


Fig. 3. Optical spectra of type R (1), type R/O (2) and type 0 solutions (3) taken at RT. Sensitivity was reduced by a factor of 2 where indicated.

Further investigations of the type 0 and type R species including room temperature ESR spectroscopy, vapor pressure osmometry, and thin layer chromatography are currently in progress. For Magnus' Green Salt [7] and PDDa- α -pyridone "blue" [4] an extension of the electronic states along many Pt-stacks in a chainlike structure has been proposed. However, for the type R system the concept of electronic states localized to approximately a single Pt-site appears to best account for the spectra recorded.

This is consistent with the fact that in a chainlike structure inequivalent Pt-sites (in the sense of [8]) will essentially act as impurities. As the number of inequivalent sites or the extent of inequivalency between adjacent Pt centers (as characterized by the delocalization coefficient defined in [8]), increases, localized electronic states are energetically

avored. In the case of the type R species inequivalent Pt sites may be caused by different local pyrimidine-ligand-to-Pt stoichiometries which may vary from 0 to 2 for each square planar unit. The observation that the g_1 -line intensities change with varying r could also be related to this variation.

^{195}Pt with $I=1/2$ is 33.7% abundant while all other Pt isotopes possess $I=0$. Therefore hf coupling of the electronic spin to one Pt nuclear spin results in a triple of lines of relative intensities 1:4:1. The hf coupling constant can be expected to be large for 3rd row elements [9] and is taken from the g_1 -line pattern to be about $A=11$ mT. A 9 line pattern may be due to a ligand hf (lhf) type coupling of the electronic spin localized on one Pt atom to the nuclear spin of an adjacent Pt center. The corresponding coupling constant will be smaller than the hf coupling constant. The lhf coupling is accordingly associated with the 5–6 mT splittings within the g_1 -line triples.

To account for the variations of the intensity distribution occurring upon varying r , the presence of another species in addition to the type R species may be assumed. In fact, this species has to be very similar to the type R species itself as no significant

changes of the g_{\parallel} -value are observed (see III). The species may evolve from the type R system, due to minor distortions in the plane of the Pt units, as more ligands are bound to the complex. As a consequence of this assumption the 5 line pattern in the g_{\parallel} -region is readily explained as are some details of the g_1 -intensity distribution.

In addition, rhombic distortions of the axial symmetry assumed in the analysis may also be present.

The observation of the type R spectrum has turned out to be of help in the understanding of some other ESR experiments performed on the "blues." It offers an explanation of the intermediate type spectra which represent the type of spectrum obtained under most experimental conditions.

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