

Photophysics and photochemistry of diazide Pt^{IV} complexes prospective for anti-cancer photodynamic therapy

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Pt^{IV} complexes are tested as prodrugs for anticancer photodynamic therapy, which can be provided in the absence of dissolved oxygen. Mechanism of action is based on photoreduction of Pt^{IV} to Pt^{II} complexes inhibiting DNA transcription and replication similar to cisplatin. The therapeutic effect of diazide Pt^{IV} complexes **1** and **2** (Fig. 1) is close to that of cisplatin [1].

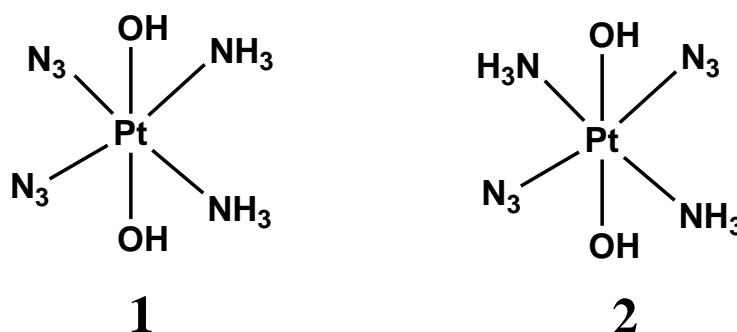
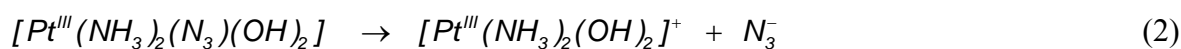
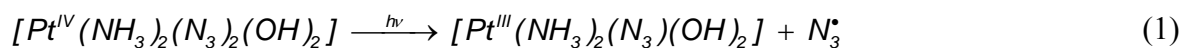


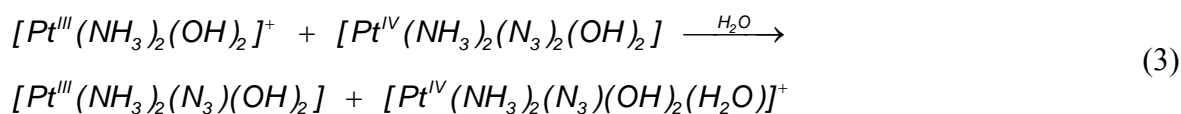
Figure 1. *cis,trans,cis*-[Pt^{IV}(N₃)₂(OH)₂(NH₃)₂] (**1**) and *trans,trans,trans*-[Pt^{IV}(N₃)₂(OH)₂(NH₃)₂] (**2**)

In this work primary photochemical processes were studied for aqueous solutions of **1** and **2** by means of steady-state photolysis, nanosecond laser flash photolysis and ultrafast kinetic spectroscopy (time resolution ~ 100 fs). The process is shown to be multistage. The first stage is the photosubstitution of an azide ligand to a water molecule. This process was shown to be a chain reaction with the concentration-dependent quantum yield.

In the laser flash photolysis experiments the formation of two sequentially occurring Pt^{III} intermediates were recorded. Disproportionation of Pt^{III} intermediates leads to the formation of final Pt^{II} products, providing the therapeutic effect of the initial compounds. The reaction mechanism represented by equations (1-7) is proposed.

Chain initiation



Chain propagation*Chain termination*

The typical results of the ultrafast kinetic spectroscopy experiments (kinetic curves and Species Associated Differential Spectra (SADS)) are shown in Fig. 2. The kinetic curves were globally fitted by the three-exponential functions with the characteristic lifetimes of ca. 1.5 and 20 ps, and infinity. The observed processes were interpreted as the successive transitions of the Frank-Condon excited states to the lowest electronic excited states and to the reaction products (SADS S_A , S_B and S_C in Fig. 2b). The spectrum S_C is similar to the spectrum of the $[Pt^{III}(NH_3)_2(N_3)(OH)_2]$ intermediate observed in the nanosecond time scale.

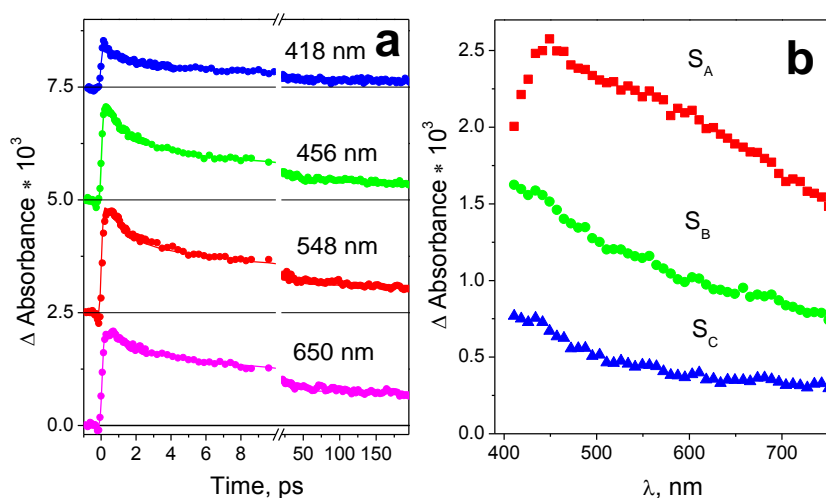


Figure 2. Results of ultrafast kinetic spectroscopy experiments ($\lambda_{\text{pump}} = 320$ nm) with complex **1** (2.5×10^{-3} M in water, pH 7.4, 1 mm cell). **a** – experimental kinetic curves (dots) and three-exponential fits (solid lines); **b** – SADS obtained from the three-exponential global fit with characteristic lifetimes 1.5 ps, 18 ps and infinity.

Finally, photochemistry of complexes **1** and **2** was studied in time scale from absorption of light quanta to the formation of final reaction products.

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References:

- [1] P.J. Bednarski, F.S. Mackay, P.J. Sadler, *Anti-Cancer Agents Med. Chem.*, **2007**, *7*, 75.