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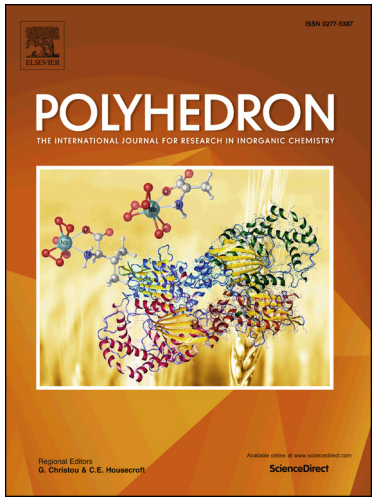

In vitro kinetic based adduct formation mechanism of a cytotoxic Pt(II) complex with sulfur containing bio-relevant molecules and a theoretical approach

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In vitro kinetic based adduct formation mechanism of a cytotoxic Pt(II) complex with sulfur containing bio-relevant molecules and a theoretical approach

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Abstract

An exploration of the mechanism of the interaction of cytotoxic Pt(II) complexes with sulfur containing biomolecules is relevant from a biological aspect in order to understand their drug-reservoir activity. In this context two thiol substituted platinum complexes, [Pt(MAMP)(GSH)] (**3**) and [Pt(MAMP)(TGA)] (**4**) (where MAMP = 2(methylamino)methylpyridine, GSH = glutathione and TGA = thioglycolic acid), were synthesised and characterised spectroscopically. The mechanism of the interaction of the cis-diaqua platinum complex $[Pt(MAMP)(H_2O)_2](ClO_4)_2$ (**2**), obtained from the hydrolysis of the complex $[Pt(MAMP)Cl_2]$ (**1**) with two important biomolecules, GSH and TGA, have been investigated spectrophotometrically in aqueous medium. At pH 4.0, both reactions were found to take place in two distinct consecutive steps. The equilibrium constant (K_E) for the outer sphere association of the ligands and the rate constants for both anation steps have been evaluated. The activation parameters ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) were calculated using the Eyring equation and on the basis of the kinetic investigations and activation parameters an associative mechanism is proposed for both reactions. A computational study using Density Functional Theory (DFT) was incorporated in this present study to investigate the electronic structures of the proposed complexes. Time dependent-density functional theory (TD-DFT) was performed in order to understand the nature of the electronic transitions in the product complexes. Furthermore, to predict the reactivity of complexes **3** and **4** toward Pt(II)-DNA adduct formation, reactivity parameters like chemical hardness (η), ionisation

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