

Synthesis and Spectroscopic Studies of some Diamine Platinum(II) Complexes of Diethyldithiocarbamate

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Abstract

The complexes of the type $[\text{Pt}(\text{LL})(\text{DDTC})\text{NO}_3]$ (where LL = en or pn) have been prepared and characterized by various physical methods. The conductivity data of the above complexes in conductivity water suggests they are 1:1 electrolytes. The electronic absorption spectra of these complexes can be interpreted in terms of their square planar geometry. The infrared (IR) spectra support the bonding of DDTC as bidentate complexes in these complexes. The ^1H nuclear magnetic resonance (NMR) spectra of these complexes in D_2O indicate that the two conformations of the ethylenediamine or propylenediamine chelate ring are rapidly exchanging. The ^1H NMR spectra further suggest that the $\text{C}\cdots\text{N}$ double bond character in bonded DDTC of the above complexes is increased as compared to free DDTC.

Introduction

The use of *cis*-diaminedichloroplatinum(II) (*cis*-platin) in cancer therapy has nephrotoxicity as a major side effect [1, 2]. Numerous strategies have been developed in an attempt to reduce this toxicity. One of them is using a variety of sulphur containing ligands such as cysteine, cystamine, pencillamine [3], methionine, thiourea [4], thiosulphate [5] and diethyldithiocarbamate (DDTC) [1, 6, 7], which inhibit the nephrotoxicity of cisplatin. The time of administration of these agents is critical and only thiourea at high dose and DDTC are effective when administered more than one hour after cisplatin. In addition, DDTC has the remarkable property of reversing platinum binding to the macromolecules responsible for host toxicity. However, it does not interfere with the tumoricidal platinum–DNA interaction in the tumor cell. Thus the protective action of DDTC against the toxicity of cisplatin seems to be the formation of stable platinum–DDTC complex. Here we report the synthesis and characterization of two stable diamine platinum(II) diethyldithiocarbamate complexes.

Experimental

$[\text{Pt}(\text{en})\text{Cl}_2]$ and $[\text{Pt}(\text{pn})\text{Cl}_2]$ (where en is ethylenediamine and pn is propylenediamine) were prepared by the literature method [8].

Preparation of Pt Complexes

$[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3 \cdot 2\text{H}_2\text{O}$

3.96 ml of AgNO_3 (0.1 M) was added to a solution of $[\text{Pt}(\text{en})\text{Cl}_2]$ (0.2 mmol) in distilled water, with stirring. The reaction mixture was further stirred for 6 h at 45–50 °C and for 16 h at room temperature (28 °C). The AgCl precipitate was removed by centrifugation. The clear yellow solution was mixed with solution of sodium diethyldithiocarbamate (DDTC is the abbreviation of the diethyldithiocarbamate anion) with stirring. This reaction mixture was stirred for 6 h at 40 °C and then centrifuged. The clear solution was concentrated in a vacuum desiccator over anhydrous calcium chloride to a small volume when yellow crystals were obtained. These crystals were filtered, washed with small quantity of chilled water, and dried in air. The crystals were finally dried in a vacuum desiccator over anhydrous calcium chloride. The yield was 80%. *Anal.* Found: C, 16.98; H, 3.63; N, 11.26. *Calc.* for $\text{C}_7\text{H}_{22}\text{N}_4\text{O}_5\text{S}_2\text{Pt}$: C, 16.76; H, 3.59; N, 11.17%.

$[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3 \cdot 2\text{H}_2\text{O}$

This compound was prepared by following the procedure of $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ except that $[\text{Pt}(\text{pn})\text{Cl}_2]$ was used in place of $[\text{Pt}(\text{en})\text{Cl}_2]$. The yield was <70%. *Anal.* Found: C, 18.49; H, 3.82; N, 11.09. *Calc.* for $\text{C}_8\text{H}_{24}\text{N}_4\text{O}_5\text{S}_2\text{Pt}$: C, 18.63; H, 3.88; N, 10.87%.

Physical Measurements

The molar conductances of the Pt(II) complexes in conductivity water was measured with a systronics conductivity bridge 305 using a conductivity cell having a cell constant of 0.59 cm^{-1} . The electronic absorption spectra of the Pt(II) complexes were recorded in distilled water using a Shimadzu UV-260

UV-Vis Recording Spectrophotometer. The infrared spectra of the ligands and their Pt(II) complexes were recorded on a Pye-Unicam SP-2000 Infrared Spectrophotometer in KBr pellets or Nujol mull in the range of 4000 to 200 cm^{-1} . The ^1H NMR spectra of the ligands and their Pt(II) complexes were recorded on a Varian XL-100 NMR Spectrometer in D_2O using DSS (sodium 2,2-dimethyl-2-silapentane-5-sulfonate). All ^1H NMR spectra were recorded in the range of 0 to 10 ppm.

Results and Discussion

$[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ and $[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3$ were prepared and characterized by chemical analysis, conductance measurement, ultraviolet-visible, infrared and ^1H NMR spectroscopic methods. The conductance measurements of $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ and $[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3$ complexes (10^{-3} M) in conductivity water show the molar conductance values of 114.4 and 110.8 $\text{cm ohm}^{-1} \text{mol}^{-1}$, respectively. These values suggest that these complexes are 1:1 electrolytes [9].

The electronic absorption spectra of the $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ in distilled water show absorption maxima at 207 (extinction coefficient, $\epsilon = 3.64 \times 10^4$), 235 shoulder ($\epsilon = 1.40 \times 10^4$), 265 ($\epsilon = 0.70 \times 10^4$) and 297 ($\epsilon = 1.20 \times 10^4$) nm. The first band is an intraligand $\pi \rightarrow \pi^*$ transition located on the $\text{N} \cdots \text{C} \cdots \text{S}$ group of diethyldithiocarbamate. The second band is a shoulder which is attributed to a $\pi \rightarrow \pi^*$ transition of the $\text{S} \cdots \text{C} \cdots \text{S}$ group of diethyldithiocarbamate. The third band is $n \rightarrow \pi^*$ electronic transition located on the sulphur atom. The fourth band is due to charge transfer (CT) transition of type $\text{M} \rightarrow \text{L}$. $[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3$ shows also four absorption maxima at 209 ($\epsilon = 3.46 \times 10^4$), 235 shoulder ($\epsilon = 0.90 \times 10^4$), 265 ($\epsilon = 0.40 \times 10^4$) and 300 ($\epsilon = 1.04 \times 10^4$) nm. These bands are assigned similar to assignments of bands for $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ and suggest the square planar configuration of these complexes [10].

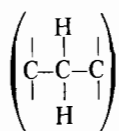
The IR spectra of $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ and $[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3$ show a strong $\nu(\text{C} \cdots \text{N})$ band at 1541 and 1534 cm^{-1} , respectively. These complexes show a medium $\nu(\text{C} \cdots \text{S})$ band at 1054 and 1086 cm^{-1} , respectively. The positions of the above bands in these complexes suggest that DDTC is bound to platinum as a bidentate ligand. The $\nu(\text{Pt}-\text{S})$ band at 388 and 386 cm^{-1} in $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ and $[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3$ respectively, suggests further that DDTC is acting as bidentate ligand [11]. The $\nu(\text{Pt}-\text{N})$ bands in $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ are at 534 and 486 cm^{-1} [11] and in $[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3$ are at 467 and 511 cm^{-1} [12].

The ^1H NMR spectrum of ethylenediamine in $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$ complex shows a sharp peak

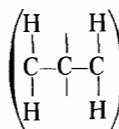


Fig. 1. The 100 MHz ^1H NMR spectra of (a) $[\text{Pt}(\text{en})(\text{DDTC})]\text{NO}_3$, and (b) $[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3$, in D_2O .

at 2.27 ppm with two ^{195}Pt satellites ($^3J(\text{Pt}-\text{H}) = 42$ Hz, Fig. 1). The methylene protons



of propylenediamine in $[\text{Pt}(\text{pn})(\text{DDTC})]\text{NO}_3$ show a multiplet at 1.86 ppm and other protons



show a triplet at 2.92 ppm with two ^{195}Pt triplet satellites ($^3J(\text{Pt}-\text{H}) = 42.7$ Hz). These observations are consistent with rapid conformational equilibrium of the ethylenediamine and propylenediamine chelate rings, respectively [13-16]. The methyl protons at 1.26 ppm of DDTC in the ethylenediamine and propylenediamine complexes, respectively, show a very small downfield shift as compared to the free DDTC (1.24 ppm). However, the methylene protons of DDTC at 3.62 and 3.63 ppm in the ethylenediamine and propylenediamine complexes, respectively, have large upfield shift as compared to the free DDTC (4.04 ppm). This can be explained in terms of an increase in the $\text{C} \cdots \text{N}$ double bond character in complexed DDTC as compared to free DDTC, which

is due to an increase in the nitrogen electronegativity in going from the sp^3 hybrid to the sp^2 hybrid [17, 18].

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