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# Novel platinum(II) complexes containing diaminocyclohexane and thiourea derivative ligands: Synthesis and X-ray crystal structure of (*trans*-1,2-diaminocyclohexane)dithioureaplatinum(II) nitrate monohydrate

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# 1. Introduction

The anticancer activity of the platinum-based first-generation drug cisplatin [cis-diamminedichloroplatinum(II)] was discovered in 1969 [1] and its clinical use was approved in 1978 [2]. Since then, thousands of new platinum complexes have been synthesized and evaluated for their anticancer activity [3,4]. The fact that cisplatin possesses considerable adverse side effects that limit its application has stimulated the extensive search for new platinum-based anticancer drugs. In an effort to overcome cisplatin's shortcomings, such as dose-limiting and acquired resistance, the second- and third-generation analogues carboplatin [cis-diammine(1,1-cyclobutanedicarboxylato)platinum(II)] and oxaliplatin [(1R,2R-diaminocyclohexane)oxalatoplatinum(II)] have been developed and also approved for clinical use. Studies show that these drugs can reduce renal toxicity in chemotherapy because they tend to react with the sulfur atoms in methionine and cysteine groups of proteins [5–7]. Strong affinity of platinum(II) towards sulfur-containing molecules has long been known. Thus, one modification to the platinum-based anticancer drugs is to use sulfur-containing molecules as carrier ligands along with the nitrogen-containing molecules because the platinum-sulfur interaction would prevent the side effects and

## ABSTRACT

Six novel platinum(II) complexes of the form [Pt(dach)L<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>, where dach = *trans*-1,2-diaminocyclohexane, L = thiourea (tu) or its derivatives, including 1-acetyl-2-thiourea, 1-ethyl-2-thiourea, 2-imidazolidinethione, 1,3-dimethyl-2-thiourea and 1,1,3,3-tetramethyl-2-thiourea, have been synthesized and characterized by elemental analysis, IR spectrometry, and NMR(<sup>1</sup>H and <sup>13</sup>C) spectroscopy. The general synthetic procedure involves the reaction of [Pt(dach)(H<sub>2</sub>O)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>, which is formed *in situ* by treating Pt(dach)I<sub>2</sub> with silver nitrate, and two equivalents of tu or its derivatives. All the complexes are ionic compounds with nitrate counter ions and thus water soluble. The crystal structure of [Pt(dach)(tu)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>·H<sub>2</sub>O is determined using a single crystal X-ray diffraction method. This compound crystallizes in the orthorhombic space group *Pnma* with centrosymmetry. © 2013 Elsevier B.V. All rights reserved.

improve the transport of the platinum drugs [5]. Commonly used sulfur-containing molecules include dithiocarbamates [8], thiosemicarbazones [9,10], xanthate [11], 2-imidazolidinethione [12], and 1,1,3,3-tetramethylthiourea [13]. In addition to being carrier ligand, some of these sulfur-containing molecules may also be used as protective and rescue agents in platinum-based chemotherapy [5]. Thiourea and its derivatives are of particular interest because of their unique anti-inflammatory, anticancer, and antiproliferative activities [5,14-19]. Both mono- and bi-functional thiourea derivatives have been used as alternative coordinating carrier groups in platinum(II) anticancer complexes [13]. These complexes consist of a cationic platinum(II) complex ion and a counter anion and therefore are soluble in water. Recently, Ma et al. reported that a thiourea derivative ligand, 1-(2-(acridin-9-ylamino)ethyl)-1,3dimethylthiourea, was released from the inner coordination sphere of ethylenediamineplatinum(II) cation, when this cation reacted with N-acetylcysteine, a derivative of cysteine [20]. Their findings suggested that the platinum-sulfur bond formed with thiourea was weakened when attacked by the cysteine sulfur. To further investigate the relative reactivity between platinum(II)-thiourea complexes and other sulfur-containing model molecules, we have selected trans-1,2-diaminocyclohexane (dach) as a carrier ligand because of its ability to form a chelate ring with platinum(II) and thus preventing its replacement by incoming sulfur-containing molecules. Furthermore, the chemistry between oxaliplatin and thiourea derivatives would be of special interest because both have









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demonstrated anticancer activity. To our knowledge, there has been no report on platinum-dach compounds containing dithiourea ligands. Thus, our first goal of research is to synthesize and characterize the dach-platinum-thiourea type complexes. In this paper, we report the preparation and characterization of six novel platinum(II) complexes of the form [Pt(dach)L<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>, where L = thiourea (tu), 1-acetyl-2-thiourea (atu), 1-ethyl-2-thiourea (etu), 2-imidazolidinethione (imt), 1,3-dimethyl-2-thiourea (dmtu), and 1,1,3,3-tetramethyl-2-thiourea (tmtu). Each complex has been characterized by elemental analysis, IR spectrometry, and NMR (<sup>1</sup>H and <sup>13</sup>C) spectroscopy. All of the complexes are water soluble. The crystal structure of [Pt(dach)(tu)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>·H<sub>2</sub>O is determined using a single crystal X-ray diffraction method.

#### 2. Experimental

#### 2.1. Materials

Potassium tetrachloroplatinate ( $K_2$ PtCl<sub>4</sub>) was purchased from Johnson Matthey Electronics (Ward Hill, MA). Tu, atu, etu, imt, dmtu, tmtu, dach, and silver nitrate were purchased from Sigma– Aldrich Chemical Co. (St. Louis, MO). Potassium iodide was acquired from Fisher Scientific (Hanover Park, IL). All other chemicals and solvents were obtained from commercial suppliers and used without further purification. Deuterated dimethylsulfoxide (DMSO- $d_6$ ) was supplied by Cambridge Isotope Laboratories, Inc. (Andover, MA). 0.20-µm nylon acrodis syringe filters were purchased from Gelman Scientific (Ann Arbor, MI).

#### 2.2. Elemental analysis and spectroscopic measurements

Carbon, hydrogen and nitrogen analyses were carried out by Robertson Microlit Laboratories (Madison, NJ). FTIR spectra were recorded on a Nicolet 380 FTIR spectrometer. NMR spectra (<sup>1</sup>H and <sup>13</sup>C) were obtained on a JEOL 400 MHz spectrometer. The NMR experiments were conducted in DMSO- $d_6$  on which signals were locked. Chemical shifts for <sup>1</sup>H and <sup>13</sup>C NMR spectra were referenced to the instrument's locked values for the solvent DMSO- $d_6$ at 2.4662 and 40.0370 ppm, respectively.

### 2.3. Synthesis of complexes

All six platinum(II) complexes containing dach and tu or its derivatives were synthesized with a similar procedure. The synthesis started with reaction of  $Pt(dach)I_2$ , which was prepared by a method described by Dhara using the dach ligand instead of the ammine ligand [21], and two equivalents of silver nitrate followed by reacting the appropriate tu derivative. A typical synthetic approach of  $[Pt(dach)(tu)_2](NO_3)_2$  is given as an example. For the other five complexes, only their measured data are given.

#### 2.3.1. $[Pt(dach)(tu)_2](NO_3)_2 \cdot H_2O$

To a 30 mL suspension of  $Pt(dach)l_2$  (0.565 g, 1.0 mmol) was added 5 mL of AgNO<sub>3</sub> solution (0.330 g, 1.9 mmol). Then a small amount of acetone was added to the suspension. The mixture was stirred at room temperature in the dark for 24 h. Precipitated AgI was then filtered off, and to the filtrate was added 5 mL of tu (0.150 g, 1.9 mmol). Upon stirring at room temperature overnight, the solution was filtered again to remove any insoluble residue, and the solvent was evaporated at 45 °C under reduced pressure. When the volume was reduced to about 5 mL, an off-white precipitate appeared. After the volume was further reduced to about 1 mL, a small amount of acetone was added, resulting in the formation of more precipitate. The solid was then collected by vacuum filtration, washed with two portions of acetone and diethyl ether in sequence, and dried in vacuum oven at 30 °C. Yield, 73% (0.440 g). *Anal.* Calc. for  $C_8H_{24}N_8O_7S_2Pt$ : C, 15.92; H, 4.01; N, 18.57; S, 10.63. Found: C, 16.52; H, 3.71; N, 18.33; S, 10.39%. IR bands (cm<sup>-1</sup>): 3381-3131, 2937m, 2856w, 1633s, 1327s, 1169m, 1063s, 824s, 708w, 624w, 590w, 478s.

#### 2.3.2. $[Pt(dach)(atu)_2](NO_3)_2 H_2O$

Yield: 53%. Anal. Calc. for  $C_{12}H_{28}N_8O_9S_2Pt$ : C, 20.96; H, 4.10; N, 16.30; S, 9.33. Found: C, 21.10; H, 4.03; N, 15.17; S, 8.06%. IR bands (cm<sup>-1</sup>): 3500-3078, 2935w, 2864w, 1715s, 1622m, 1564m, 1373w, 1317m, 1294m, 1222s, 1162s, 1041s, 827w, 730br, 596m, 479s.

# 2.3.3. [Pt(dach)(etu)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>

Yield: 87%. Anal. Calc. for  $C_{12}H_{30}N_8O_6S_2Pt$ : C, 22.46; H, 4.71; N, 17.47; S, 10.00. Found: C, 22.60; H, 4.56; N, 17.28; S, 9.80%. IR bands (cm<sup>-1</sup>): 3397-3110, 2947w, 2860w, 1614vs, 1455s, 1322s, 1166s, 1065m, 1039w, 919m, 824s, 695s, 500m, 541s, 466m, 434m.

#### 2.3.4. [Pt(dach)(imt)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>·H<sub>2</sub>O

Yield: 75%. Anal. Calc. for  $C_{12}H_{28}N_8O_7S_2Pt(\%)$ : C, 21.98; H, 4.30; N, 17.10; S, 9.78. Found: C, 21.74; H, 4.14; N, 16.68; S, 9.82%. IR bands (cm<sup>-1</sup>): 3354-3131, 2930w, 2895w, 1520s, 1484m, 1311s, 1278s, 1192w, 1154m, 1064m, 1034s, 914m, 826m, 709s, 492m.

# 2.3.5. [Pt(dach)(dmtu)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>

Yield: 96%. Anal. Calc. for  $C_{12}H_{30}N_8O_6S_2Pt$ : C, 22.46; H, 4.71; N, 17.47; S, 10.00. Found: C, 22.58; H, 4.83; N, 17.31; S, 9.67%. IR bands (cm<sup>-1</sup>): 3289-3188, 2935m, 2864w, 1588s, 1506m, 1453w, 1372w, 1314s, 1171w, 1149m, 1036s, 826m, 725m, 611br.

#### 2.3.6. $[Pt(dach)(tmtu)_2](NO_3)_2$

Yield: 91%. Anal. Calc. for  $C_{16}H_{38}N_8O_6S_2Pt$ : C, 27.54; H, 5.49; N, 16.06; S, 9.19. Found: C, 27.54; H, 5.44; N, 15.36; S, 8.72%. IR bands (cm<sup>-1</sup>): 3423-3105, 2934m, 2861w, 1559s, 1498m, 1448m, 1319s, 1259m, 1157m, 1107m, 1059m, 1030w, 876m, 827m.

#### 2.4. X-ray crystallography

Suitable crystals of [Pt(dach)(tu)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>·H<sub>2</sub>O were grown by slow evaporation of an aqueous solution at room temperature. All measurements were made with a Bruker DUO platform diffractometer equipped with a 4 K CCD APEX II detector and an Incoatec 30 Watt Cu microsource with compact multilayer optics. A hemisphere of data (2713 frames at 4 cm detector distance) was collected using a narrow-frame algorithm with scan widths of 0.50 deg in omega and an exposure time of 20 s/frame. The data were integrated using the Bruker-Nonius SAINT program, with the intensities corrected for Lorentz factor, polarization, air absorption, and absorption due to variation in the path length through the detector faceplate. A  $\psi$  scan absorption correction was applied based on the entire data set. Redundant reflections were averaged. Final cell constants were refined using 8167 reflections having  $I > 10\sigma(I)$ , and these, along with other information pertinent to data collection and refinement, are listed in Table 1. The Laue symmetry was determined to be mmm, and from the systematic absences noted the space group was shown to be either Pna2(1) or Pnma. The asymmetric unit consists of one-half cation situated on a mirror plane, one nitrate anion, and one-half molecule of solvate water also on the mirror plane. The dach ligand is disordered across the mirror, yielding a 50:50 mix of the two different chiralities of this moiety. This is consistent with the racemic mix of dach used in the reaction. Refinement in the non-centrosymmetric space group Pna2(1) resulted in a 50:50 merohedral twin indication, again showing a mix of dach chiralities. Laser measurements showed no second harmonic generation, indicating that the true Table 1

Crystallographic data and structure refinement for [Pt(dach)(tu)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>·H<sub>2</sub>O.

Empirical formula	$C_8H_{24}N_8O_7S_2Pt$
Formula weight	603.56
Temperature (K)	100(2)
Wavelength (Å)	1.54178
Crystal color and shape	pale yellow block
Crystal dimensions (mm)	$0.35\times0.30\times0.20$
Crystal system	orthorhombic
Space group	Pnma
Unit cell dimensions	
a (Å)	14.2412(4)
b (Å)	14.3464(4)
<i>c</i> (Å)	9.4739(2)
α (°)	90
β (°),	90
γ (°)	90
$V(Å^3)$	1935.61(9)
Ζ	4
$D_{\text{calc}}$ (g cm <sup>-3</sup> )	2.071
F(000)	1176
$\mu$ (Cu K $lpha$ , cm $^{-1}$ )	160.34
$\theta$ Range for data collection (°)	5.60-66.61
Limiting indices	$0 \leqslant h \leqslant 16, 0 \leqslant k \leqslant 17, 0 \leqslant l \leqslant 11$
Reflections collected/unique	12725/1966 [R <sub>int</sub> = 0.0584]
Maximum and minimum transmission	7528, 0.4877
Refinement method	full-matrix least-squares on F <sup>2</sup>
Data/restraints/parameters	1758/42/164
Goodness-of-fit (GOF) on $F^2$	1.161
Final <i>R</i> indices $[I > 4\sigma(I)]^a$	$R_1 = 0.0217$ , $wR_2 = 0.0544$
R indices (all data)	$R_1 = 0.0219, wR_2 = 0.0548$
Largest difference peak and hole (e $Å^{-3}$ )	0.871 and -1.234
<sup>a</sup> $R_1 = \sum   F_0  -  F_c   / \sum  F_0 , wR_2 = \sum (w(F_0^2 - F_0)) wR_2$	$(-F_c^2)^2)/\sum w(F_o^2)^2$ .

space group is centrosymmetric. Therefore final refinement was carried out in *Pnma*.

#### 3. Results and discussion

#### 3.1. Synthesis of complexes

The steps involved in the synthesis of the six platinum(II) complexes containing dach and tu or its derivatives are outlined in Scheme 1. Reaction of  $[Pt(dach)(H_2O)_2](NO_3)_2$ , which was formed *in situ* by treating  $Pt(dach)I_2$  with AgNO<sub>3</sub> in the absence of light, with two equivalents of tu or its derivatives, produced the desired complexes, in which the coordinated atoms are sulfur atoms as evidenced by spectroscopic measurements. Although sulfur-containing ligands exert stronger *trans*-labilizing effect than nitrogen-containing ligands, only the *cis* complexes were obtained because of the pre-existence of the chelate ring formed by dach and platinum atom. The nitrate counter ions make all the complexes soluble in polar solvents such as water and acetone. Three of the complexes contain one water molecule in their formula.

#### 3.2. IR and NMR spectroscopy

All the complexes show broad or unresolved bands in the region of 3500-3078 cm<sup>-1</sup>, which are assignable to either OH or NH stretching vibrations due to the hydrated water and the coordinated ligands. Since both dach and tu or its derivatives, except for the tmtu ligand, contain NH or NH<sub>2</sub> groups, distinguishing between the two sources is difficult in their IR spectra. The characteristic nitrate bands are observed for all the complexes in two general regions from 1311 to  $1327 \text{ cm}^{-1}$  and from 827 to 824 cm<sup>-1</sup>, respectively [22]. As pointed out by Bellamy, the thiocarbonyl C=S vibrations can occur in several regions due to the strong coupling in all the compounds when the carbon atom is bonded directly to nitrogen [23]. It is this coupling that leads to the C=S vibration in thioamides as a mixed vibration [23,24].

The <sup>1</sup>H and <sup>13</sup>C NMR spectra of all the complexes are well-defined and their signals can be easily assigned according to their structures. Table 2 summarizes the NMR data for these complexes. The dach ligand in all six complexes show similar chemical shifts for protons and carbon-13 atoms. In an attempt to differentiate the NH or NH<sub>2</sub> signals of tu or its derivatives from the dach ligand, the <sup>1</sup>H and <sup>13</sup>C NMR spectra of the pure [Pt(dach)(H<sub>2</sub>O)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub> complex and the free dach ligand were also recorded in addition to the thiourea ligands. [Pt(dach)(H<sub>2</sub>O)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub> exhibited a doublet at 6.57 ppm and a triplet at 6.17 ppm, which are attributed to the two nonequivalent NH<sub>2</sub> groups of the coordinated dach ligand, while the free dach did not show the NH<sub>2</sub> signals in the <sup>1</sup>H NMR spectra. Upon reacting [Pt(dach)(H<sub>2</sub>O)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub> with tu or its derivatives the two amino signals with the same pattern were shifted upfield with a larger separation ( $\sim$ 1 ppm), indicating the dach ligand remained coordinated. The proton signals on the cyclohexane ring in all the complexes showed the same pattern with similar chemical shifts, ranging between 1.01 and 3.34 ppm. The recorded <sup>1</sup>H and <sup>13</sup>C signals for the coordinated dach ligand are consistent with those reported for other Pt-dach complexes [25,26]. Downfield shifts are observed for the NH or NH<sub>2</sub> protons in all the coordinated tu or its derivatives with respect to their free ligands (see Fig. 1). The proton signals of the alkyl groups on the nitrogen of the tu derivatives are also shifted downfield but to a lesser extent. Unlike the other derivatives, atu contains an additional deshielding carbonyl group. As a consequence, the NH proton in the coordinated atu ligand shows the largest chemical shift of 11.96 ppm because this proton is deshielded by the two double bonds (C=S and C=O). The carbonyl group also exerts some deshielding effect on the NH<sub>2</sub> group, which shows two singlets at 10.21 and 10.14 ppm, respectively. Contrary to the downfield shifts in the <sup>1</sup>H NMR spectra upon complexation, the <sup>13</sup>C NMR signals of the C=S group in the tu or its derivatives are all shifted upfield to a maximum of 10 ppm, indicating the formation of platinum-sulfur bonds. Results from the NMR data suggest that the bond order of the C=S is lowered somewhat while the bond order of the C-N is increased upon coordination, leading to the chemical shifts in opposite direction in the <sup>1</sup>H and <sup>13</sup>C NMR signals [13,27]. Similar shifts for metal complexes with tu or its derivatives have been observed [13,27]. Large deshielding of the NH protons is attributed to the increase in  $\pi$  electron density in the C–N bond upon coordination. In most cases, except for the imt ligand, two closely spaced but well-resolved singlets for the protons of the NH<sub>2</sub> or NH groups are observed in their <sup>1</sup>H NMR spectra (see Fig. 1). This observation suggests that the two NH<sub>2</sub> or NH groups of tu or its derivatives are nonequivalent because the free rotation around the C-N bond is restricted owing to the resonance interaction between the unshared pair of electrons on nitrogen and the thiocarbonyl group [28].

#### 3.3. X-ray crystal structure

The structure of the complex  $[Pt(dach)(tu)_2](NO_3)_2 \cdot H_2O$  with the atom labeling scheme adopted and the hydrogen bonding network between the cation, anions, and solvent are presented in Figs. 2 and 3, respectively. The crystal structure shows that this complex is monomeric and four-coordinated with one bidentate

$$K_2 PtCl_2 \xrightarrow{1. Kl} Pt(dach)I_2 \xrightarrow{3. AgNO_3} [Pt(dach)(tu)_2](NO_3)_2$$

Scheme 1. Synthesis of the complexes.

Table 2
$^{1}$ H and $^{13}$ C chemical shifts for the complexes of [Pt(dach)(L) <sub>2</sub> ](NO <sub>3</sub> ) <sub>2</sub> . <sup>a</sup>

L	Tu derivative				Dach ligand			
	<sup>1</sup> H shift (ppm)		<sup>13</sup> C shift (ppm)		<sup>1</sup> H shift (ppm)		<sup>13</sup> C shift (ppm)	
	NH	СН	C=S	СН	NH <sub>2</sub>	CH or CH <sub>2</sub>	CH or CH <sub>2</sub>	
None					6.57, 6.17	2.44, 1.97, 1.54, 1.31, 1.07	61.5, 32.6, 24.2	
Tu	8.30(s), 7.90(s)		175.7		5.84, 4.89	2.27, 1.94, 1.50, 1.22, 1.01	61.9, 32.8, 24.7	
Atu	11.96(s), 10.21(s), 10.14(s)	2.13	175.4, 172.7	24.3	6.10, 5.14	2.31, 1.95, 1.52, 1.25, 1.04	62.1, 32.7, 24.6	
Etu	8.68(s), 8.13(t)	3.18, 1.05	171.3	38.9, 14.0	5.89, 4.94	2.29, 1.96, 1.50, 1.22, 1.05	61.8, 32.7, 24.7	
Imt	9.06(s)	3.71	174.8	45.5	5.86, 4.98	2.29, 1.96, 1.52, 1.26, 1.02	62.2, 32.7, 24.7	
Dmtu	8.60(s), 8.27(s)	2.92	172.6	32.2	5.88, 4.99	2.34, 1.94, 1.51, 1.23, 1.01	61.9, 32.7, 24.7	
Tmtu		3.18	182.0	44.3	5.81, 5.06	2.27, 1.93, 1.52, 1.30, 1.03	62.0, 32.5, 24.6	

<sup>a</sup> The chemical shifts were referenced to the residual proton resonance of deuterated DMSO-*d*<sub>6</sub> at 2.4662 ppm in <sup>1</sup>H NMR and the carbon of DMSO-*d*<sub>6</sub> at 40.0370 ppm in <sup>13</sup>C NMR.



Fig. 1. <sup>1</sup>H NMR spectra of (a) tu, (b) [Pt(dach)(H<sub>2</sub>O)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>, and (c) [Pt(dach)(tu)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub> in DMSO-d<sub>6</sub>.



**Fig. 2.** View of the cation showing the atom numbering scheme. Thermal ellipsoids are 50% equiprobability envelopes, with hydrogens as spheres of arbitrary diameter. Only one orientation of the disordered dach ligand is shown.

dach and two monodentate tu, which form bonds with the platinum via the sulfur atoms. The complex has an orthorhombic space group *Pnma* with centrosymmetry. Selected bond lengths, bond angles, and torsion angles are given in Table 3. The two nitrogen and two sulfur donor atom array form a near square-planar geometry about the platinum atom that is disposed slightly (0.0905 Å)



Fig. 3. View of a portion of the hydrogen bonding network between the cation, anions, and solvent.

out of the plane of donor atoms. The Pt–S bond distance of 2.288 Å is slightly shorter than the reported value for similar complexes containing tu derivatives such as  $[Pt(tu)_4]Cl_2$  (2.313 Å) [29] and  $[Pt(imt)_4]I_2$  (2.328 Å) [12]. The Pt–N bond distance, 2.070 Å, is similar to those found in other platinum-dach complexes [26,30–33] but significantly shorter than the Pt–S bond length. The

Table 3	
Selected bond length (Å), bond angles (°), and torsion angles (°).	

Bond lengths Pt-N(1) Pt-S(1) N(1)-C(1)	2.070(3) 2.2880(10) 1.474(8)	$Pt-N(1)^{a}$ $Pt-S(2)^{a}$ S(1)-C(7)	2.070(3) 2.2881(10) 1.716(4)
Bond angles N(1)-Pt-N(1) <sup>a</sup> N(1)-Pt-S(1) N(1) <sup>a</sup> -Pt-S(1) Pt-N(1)-C(1) Pt-S(1)-C(7) N(2)-C(7)-N(3) N(3)-C(7)-S(1)	82.79(17) 93.24(9) 173.92(9) 110.6(4) 108.55(13) 119.3(3) 117.6(3)	$\begin{array}{l} N(1) - Pt - S(1)^{a} \\ N(1)^{a} - Pt - S(1)^{a} \\ S(1)^{a} - Pt - S(1) \\ Pt - N(1)^{a} - C(6) \\ Pt - S(1)^{a} - C(7)^{a} \\ N(2) - C(7) - S(1) \end{array}$	173.92(9) 93.24(9) 90.33(6) 105.8(3) 108.55(13) 123.0(3)
Torsion angles N(1)-Pt-S(1)-C(7) N(1) <sup>a</sup> -Pt-N(1)-C(1) N(1)-Pt-N(1) <sup>a</sup> -C(6) Pt-S(1)-C(7)-N(2)	-92.83(17) -11.6(5) 18.9(5) 13.9(4)	$S(1)^{a}$ -Pt-S(1)-C(7) S(1)-Pt-N(1)-C(1) $S(1)$ -Pt-N(1)^{a}-C(6) Pt-S(1)-C(7)-N(3)	92.09(14) 173.0(4) -156.5(5) -167.6(3)

<sup>a</sup> Symmetry transformations used to generate equivalent atoms:  $x_1 - y + 3/2$ , z.

**Table 4** Hydrogen bonds for  $[Pt(dach)(tu)_2](NO_3)_2 \cdot H_2O$  (Å and °).<sup>a</sup>

D–H…A	<i>d</i> (D–H)	<i>d</i> (H…A)	<i>d</i> (D…A)	<(DHA)
N(1)-H(1NA)O(2) <sup>i</sup>	0.92	2.39	3.277(4)	161.7
N(1)–H(1NA)…O(3) <sup>i</sup>	0.92	2.20	2.987(5)	142.4
N(1)-H(1NB)O(3)	0.92	2.07	2.978(4)	169.7
N(2)-H(2NA)…O(2) <sup>ii</sup>	0.850(10)	2.054(12)	2.903(4)	177(5)
N(2)-H(2NB)…O(4)	0.851(10)	2.32(2)	3.100(5)	153(4)
N(3)–H(3NA)…O(1) <sup>ii</sup>	0.848(10)	2.065(13)	2.908(5)	173(5)
N(3)-H(3NB)…O(1) <sup>iii</sup>	0.850(10)	2.44(2)	3.239(5)	157(4)
N(3)-H(3NB)…O(3) <sup>iii</sup>	0.850(10)	2.40(3)	3.172(5)	151(4)
O(4)-H(4C)O(1)	0.956(10)	2.464(14)	3.275(3)	143(2)

<sup>a</sup> Symmetry transformations used to generate equivalent atoms: i, -x + 1, -y + 1, -z + 1; ii, -x + 1, -y + 1, -z; iii, x - 1/2, y, -z + 1/2.

average C–S and C–N bond lengths in the coordinated tu ligand are 1.716 and 1.324 Å, respectively, being essentially the same as those reported for the free tu ligand (1.71 and 1.33 Å, respectively) [28]. This result demonstrates that the bonding has limited effect on the double-bond character of C=S bond in terms of bond lengths. The S–C–N bond angles are 123.0° and 122.2° for the coordinated and free tu ligands, respectively. However the strained N–C–N bond angle in the free tu (115.6°) is released to the carbon's sp<sup>2</sup> geometry in the coordinated tu (119.3°). The cyclohexane ring takes the chair conformation as illustrated in Fig. 3. An interesting feature is the orientation of the amino groups of tu in the structure. Both tu's NH<sub>2</sub> groups are bent over toward the same side of the molecular plane (see Fig. 3), being due to the formation of hydrogen bonds.

In the present structure there was a strong network of hydrogen bonding involving the solvated water molecule, the counter nitrate ions and the amino groups of dach. Hydrogens attached to either nitrogen or oxygen atoms form hydrogen bonds, stabilizing the structure. All hydrogen bonding are intermolecular and no intramolecular hydrogen bonding is observed (see Table 4). The strongest interactions occur between N1–H and O3 (nitrate, H…O, 2.07 Å; N–H…O, 169.7°), between N2–H and O2 (nitrate, H…O, 2.054 Å; N–H…O, 177°), and between N3–H and O1 (nitrate, H…O, 2.065 Å; N–H…O, 173°). In contrast, the interaction between O–H (water) and O (nitrate) is weak with a bond distance of 2.464 Å (H…O) and bond angle of 143° (O–H…O).

### 4. Conclusion

Oxaliplatin is a platinum-based third-generation anticancer drug and contains a carrier dach ligand and leaving oxalate ligand. Modifications to this compound such as varying the leaving ligand have been extensively carried out. We report here a novel class of water-soluble platinum(II) complexes that contain dach and two tu or two tu derivative ligands. The general synthetic procedure involves the reaction of  $[Pt(dach)(H_2O)_2](NO_3)_2$ , which is formed *in situ* by treating Pt(dach)I<sub>2</sub> with silver nitrate, and two equivalents of tu or its derivatives. All the complexes have been characterized by elemental analysis, IR spectrometry, and NMR (<sup>1</sup>H and <sup>13</sup>C) spectroscopy. Spectroscopic measurements indicate that there are a decrease in C=S bond order and an increase in C-N bond order for all the tu ligands upon complexation. The crystal structure of  $[Pt(dach)(tu)_2](NO_3)_2 \cdot H_2O$  is determined using a single crystal X-ray diffraction method. This compound crystallized in the orthorhombic space group *Pnma* with centrosymmetry.

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#### **Appendix A. Supplementary material**

Crystallographic data has been deposited with the Cambridge Crystallographic Data Center. CCDC No. 963642. Copies of the data can be obtained, free of charge, on application to The Director, CCDC, Union Road 12, Cambridge CB2 1EZ, UK (fax: +44 1223/ 336 033 or e-mail: deposite@ccdc.cam.ac.uk).

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