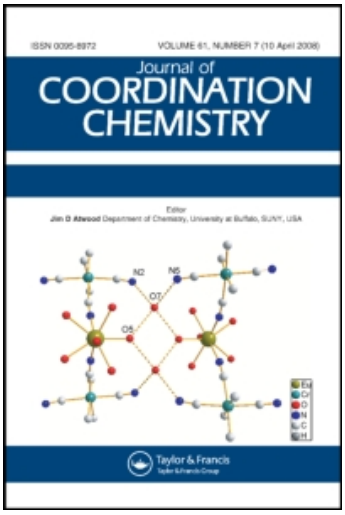

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Synthesis and crystal structure of a Pt(II) complex with 3-amino-5-methyl-5-phenylhydantoin

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The reaction of K_2PtCl_4 with 3-amino-5-methyl-5-phenylhydantoin (amphh, L) and KI in aqueous ethanol yields dark violet crystals of a binuclear platinum(II) complex. The molecular structure of the complex was determined by single-crystal X-ray diffraction methods. The complex crystallizes in the triclinic space group $P\bar{1}$ with $a = 8.458(3)$, $b = 11.016(2)$, $c = 16.249(3)$ (Å), $\alpha = 94.630(14)$, $\beta = 100.63(2)$, $\gamma = 108.55(4)^\circ$ and $Z = 2$. The structure consists of $[K_2L_4]^{2+}$ cations and $[Pt_2I_6]^{2-}$ anions bridged by K–I bonds to form *quasi*-one-dimensional chains along the *b* axis. Chains are linked by $K^+ \cdots \pi$(Ph) interactions and N–H $\cdots$ O hydrogen bonds. The complex is compared with data for related structures.

Keywords: Platinum(II); Hydantoin; Complex; Crystal structure

1. Introduction

Cis-diamminedichloroplatinum(II) (Cisplatin) was the first inorganic antineoplastic agent to find application in cancer chemotherapy [1, 2]. It is effective for the therapeutic management of various solid malignancies such as testicular teratoma, ovarian, cervical and bladder cancers, malignant melanoma, head and neck cancers, non-small cell lung cancer, endometrial cancer and others [3–5]. Unfortunately the clinical success of Cisplatin is limited by its severe side effects, which include nephrotoxicity, cumulative neurotoxicity, ototoxicity, and extreme emetogenic potential [4–6]. Another major factor compromising its clinical usefulness is the development of acquired or primary resistance of malignant cells [7–9]. Thus much attention has been focussed on designing Cisplatin analogues with reduced toxicity and a broader antitumor spectrum [9, 11]. In spite of the large number of compounds investigated, few have been used clinically [Carboplatin, Nedaplatin, Oxaliplatin [4, 8, 10, 11] and Heptaplatin [12]; Carboplatin = *cis*-diamminecyclobutan-1,1-dicarboxyplatinum(II),

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Nedaplatin = *cis*-diammineglycolatoplatinum(II), Oxaliplatin = *cis*-1*R*,2*R*-diaminocyclohexanediamineoxalatoplatinum(II), Heptaplatin = *cis*-malonato(4,5-*bis*(aminomethyl)-2-isopropyl-1,3-dioxolane)platinum(II)].

Polynuclear platinum complexes constitute one of the most important classes of platinum-based cytotoxic agents capable of binding to DNA in a manner distinct from that of Cisplatin. The compound BBR3464 ([(*trans*-$PtCl(NH_3)_2)_2$ μ-*trans*-$Pt(NH_3)_2(NH_2(CH_2)_6NH_2)_2)](NO_3)_4$) exerts profound cytotoxic effects in various *in vitro* and *in vivo* Cisplatin-resistant tumor models and has been the subject of clinical trials [13]. BBR3464 exhibits activity against malignant melanoma, colorectal, pancreatic and lung cancers and is characterized by a dose-limiting neutropenia and by lack of nephrotoxic and neurotoxic effects [13]. Currently BBR3464 is under phase II clinical trials [3, 13].

Other workers have adopted different approaches towards new Pt(II) complexes that may be biologically active. For example, a series of metal complexes with macrocyclic ligands has been characterized [15], notably a Pt(II) dibenzo-18-crown-6 (DB18C6) species. A structure analysis showed that it consists of two complex $K(DB18C6)^+$ cations and complex $Pt(SCN)_4^-$ anions bridged by $K^+ \cdots \pi$ interactions [16]. The present report concerns the synthesis and characterisation of a complex with similar structural features, *bis*(di-3-amino-5-methyl-5-phenylhydantoin)hexaiododiplatinate(II)).

2. Experimental

The ligand 3-amino-5-methyl-5-phenylhydantoin was synthesized by R. Buyukliev using a previously described method [16]. All other chemicals were of analytical grade. IR spectra were recorded on a Shimadzu FTIR-8101M spectrophotometer in the range 4500–400 cm^{-1} (nujol).

2.1. *Synthesis*

The complex was prepared according to a reported procedure [17]; 0.400 g of $K_2[PtCl_4]$ (0.965 mmol) was added to a saturated aqueous solution of potassium iodide (6.622 g) and heated on a water bath for 5 min, when $K_2[PtCl_4]$ was quantitatively converted to $K_2[PtJ_4]$. To this was added 0.405 g (1.977 mmol) of 3-amino-5-methyl-5-phenylhydantoin (L). The solution was heated to 50°C with constant stirring for 1 h and then cooled to 0°C. The dark violet crystals formed were filtered off and purified via repeated recrystallization from H_2O/C_2H_5OH. Yield: 80.4%, m.p. > 200°C (dec.). The complex is soluble in DMSO. Anal. Calcd for $C_{20}H_{22}I_3KN_{16}O_4Pt$ (%): Pt, 19.02; C, 23.41; H, 2.15; N. 8.12; K, 3.81. Found: Pt, 20.93; C, 22.82; H, 1.63; N, 7.93; K, 3.55. IR (nujol, cm^{-1}): ν(C=O) 1717s, 1771s, $\nu(NH_2)$ 3301 m, ν(NH) 3357 m, $\nu(NH_2)$ 1601 w, amide II 1590 m.

2.2. *Crystallography*

X-ray data collection was carried out at 290 K on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Mo-Kα radiation ($\alpha = 0.71073$ Å).

Unit cell parameters were determined by least-squares refinement of 22 reflections with $18 < \theta < 20^\circ$. The $\omega/2\theta$ technique was used for data collection using Nonius software [18]. Lorentz and polarization corrections were applied using WinGX [19]. The structure was solved by direct methods using SHELXS-97 [20] and refined by full-matrix least-squares procedures on F^2 with SHELXL-97 [21]. H atoms were placed in ideal positions ($C–H_{aromartic} = 0.93$, $C–H_{methyl} = 0.96$, $N–H_{amino} = 0.86$, $N–H = 0.96$ Å) and were constrained to ride on their parent atoms with $U_{iso}(H) = 1.2U_{eq}$ (C or N). Data for publication were prepared with SHELXL, WinGX and Mercury [22]. Crystallographic data (excluding structure factors) for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication. CCDC 288656.

3. Results and discussion

The structure of the complex is illustrated in figure 1 and experimental conditions summarized in table 1. Selected bond distances and bond angles are listed in table 2. Hydrogen bonds geometry is presented in table 3. An ORTEP diagram of the structure (50% probability ellipsoids) and the atom numbering scheme is shown in figure 2. The structure analysis shows that the complex consists of $[Pt_2I_6]^{2-}$ anions and $[K_2L_4]^{2+}$ cations, bridged by K–I bonds to form *quasi*-one-dimensional chains along the *b* axis (figure 3). Chains are linked by $K^+ \cdots \pi$(Ph) interactions and $N–H \cdots O$ hydrogen bonds.

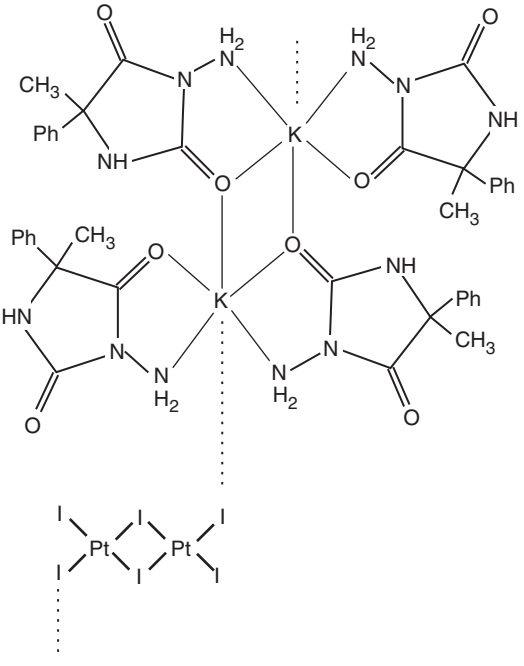


Figure 1. Graphical representation of the complex salt.

Table 1. Crystal data and structure solution methods and refinement results for $[K(amphh)_2]_2[Pt_2J_6]$.

Empirical formula	$C_{20}H_{22}I_3KN_6O_4Pt$
Formula weight	1025.32
Temperature (K)	290(2)
Wavelength (Å)	0.71073
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions (Å, °)	
a	8.458(3)
b	11.016(2)
c	16.249(3)
α	94.630(14)
β	100.63(2)
γ	108.55(4)
Volume (Å^3)	1394.8(7)
Z, calculated density (mg m^{-3})	2, 2.441
Absorption coefficient (mm^{-1})	8.535
$F(000)$	944
Crystal size (mm^3)	$0.25 \times 0.23 \times 0.23$
Crystal colour/shape	Violet/prismatic
θ range for data collection (°)	1.29–25.97
Index ranges	$-10 \le h \le 10$, $-13 \le k \le 13$, $-20 \le l \le 20$
Reflections collected/unique [R_{int}]	10933/5468[0.0262]
Completeness (%)	100 (to 25.97°)
Observed reflections [$I > 2\sigma(I)$]	4180
Refinement method	Full-matrix least-squares on F^2
Weight, w	$1/[\sigma^2(F_o^2) + (0.0720P)^2 + 0.7043P]$ where $P = (F_o^2 + 2F_c^2)/3$
Data/restraints/parameters	5468/0/317
Goodness of fit on F^2	1.069
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0446$, $wR_2 = 0.1129$
R indices (all data)	$R_1 = 0.0622$, $wR_2 = 0.1225$
Extinction coefficient	0.0022(2)
Largest peak and hole (e Å^{-3})	2.302 and −2.870

Table 2. Bond lengths (Å) and angles (°) around Pt and K atoms in $[K(amphh)_2]_2[Pt_2J_6]$.

I(1)–Pt(1)	2.5970(8)	N(24)–K(1)	2.948(7)
I(2)–Pt(1)	2.5898(13)	O(12)–K(1)	2.656(5)
I(2)–Pt(1)^{i}	2.5938(8)	O(12)–K(1)^{ii}	2.746(5)
I(3)–Pt(1)	2.5918(14)	O(24)–K(1)	2.828(5)
I(3)–K(1)	3.782(2)	N(14)–K(1)	2.956(6)
I(3)–Pt(1)–I(2)^{i}	90.85(3)	O(12)–K(1)–O(12)^{ii}	73.37(16)
I(3)–Pt(1)–I(1)	92.01(3)	O(12)^{ii}–K(1)–O(24)	79.80(14)
I(2)–Pt(1)–I(2)^{i}	84.79(3)	O(24)–K(1)–N(24)	59.06(15)
I(2)–Pt(1)–I(1)	92.31(3)	O(12)–K(1)–N(14)	60.33(14)
Pt(1)–I(2)–Pt(1)^{i}	95.21(3)	N(24)–K(1)–N(14)	77.60(17)
I(3)–Pt(1)–K(1)	76.57(4)		

Symmetry codes are (i): $1-x, 2-y, 1-z$; (ii): $1-x, 1-y, 1-z$.

The complex anion is typically planar units with deviations from the coordination plane being of 0.02 to 0.04 Å. Centrosymmetrically equivalent pairs of $[PtI_3]$-fragments form edge-sharing dimers. Pt–I distances are in good agreement with those previously reported (table 2). The $[K_2L_4]^{2+}$ cation is built up by four organic molecules and two

Table 3. Hydrogen bonds details for $[K(amphh)_2]_2[Pt_2J_6]$ (Å and °).

D–H···A	D(D–H)	d(H···A)	d(D···A)	∠(DHA)
N(14)–H(14B)···O(14)^{i}	0.90	2.60	3.125(7)	117.7
N(24)–H(24B)···O(14)^{i}	0.90	2.40	3.000(8)	124.4
N(21)–H(21)···O(22)^{ii}	0.86	2.04	2.866(7)	159.5
N(11)–H(11)···O(24)^{iii}	0.86	2.10	2.930(7)	161.3

Symmetry codes are (i): $-x+2$, $-y+2$, $-z+1$; (ii): $-x+2$, $-y+2$,$-z+2$; (iii): $-x+1$, $-y+1$, $-z+1$.

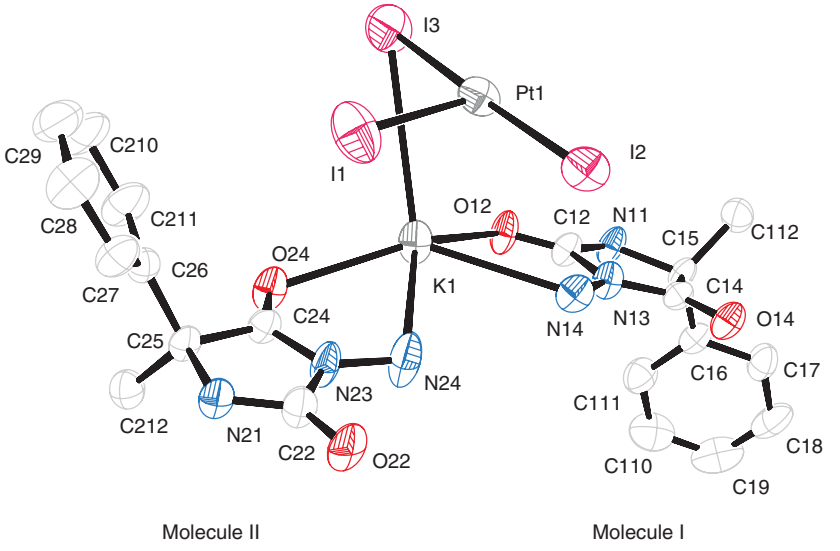
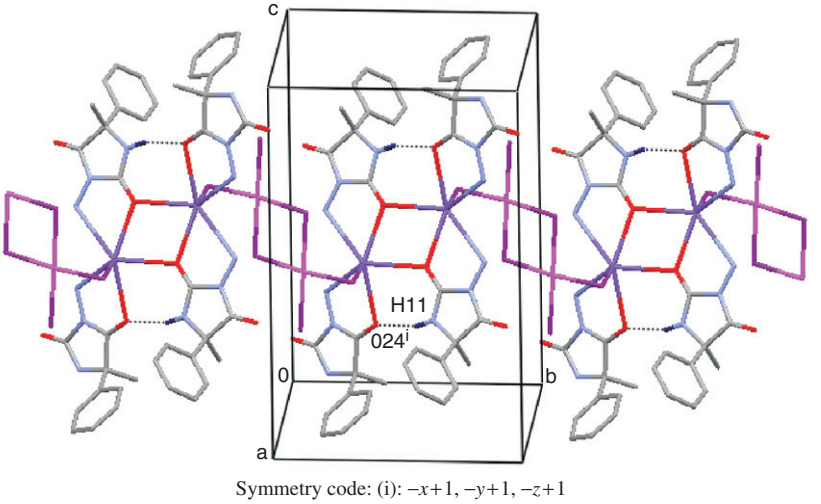


Figure 2. An ORTEP diagram of the structure (50% probability ellipsoids) showing the atom numbering scheme.



Symmetry code: (i): $-x+1$, $-y+1$, $-z+1$

Figure 3. $[Pt_2I_6]^{2-}$ anions and $[K_2L_4]^{2+}$ cations bridged by K–I bonds to form *quasi*-one-dimensional chains along the *b* axis.

potassium ions, arranged in a centrosymmetric oxo-bridged complex. Within the complex the potassium atoms are penta-coordinated by two nitrogen and three oxygen atoms in an almost planar manner; the deviation of K ion from the coordination plane is 0.65 Å. The coordination sphere of the potassium atom is completed by the I3 atom to form a distorted pentagonal pyramid. The K–I distance of 3.781 Å is comparable to that found in K_2PtI_5 and K_2PtI_6 [23, 24]. The I3 atom is common to both anion and cation, connecting them into an infinite chain parallel to the *b* axis. 3D packing unit is stabilized by four hydrogen bonds and a very weak $K^+ \cdots \pi$(Ph) interaction where $K \cdots C110_{Ph}$ $(2-x, 1-y, 1-z)$ is 4.50 Å. This distance is significantly different to those (~3.28 Å) found in the Pt(II) dibenzo-18-crown-6 complex [16]. The orientation of the $K^+ \cdots \pi$(Ph) contact with respect to the Ph plane is described by the two angles $K \ldots H110–C110$ $(2-x, 1-y, 1-z) = 149.8^\circ$ and $K \cdots C110 \cdots Cg$ (centre of Ph ring) $= 156.6^\circ$.

The two independent organic molecules present in the unit cell have geometrical parameters within the expected ranges [25]. Although both molecules are coordinated through one amino and one oxygen atom, they employ different oxygen atoms in the coordination process and thus play different structural roles. The O12 atom is connected to two symmetrically equivalent potassium ions and determines the bridging character of molecule I, while the O24 atom in molecule II is coordinated to only one potassium ion. The molecules participate with almost similar hydrogen bonding style in the three-dimensional packing arrangement (table 3). Both contribute to the $N11 \cdots O24$ $(1-x, 1-y, 1-z)$ hydrogen bond which stabilizes the $[K_2L_4]^{2+}$ cation. In addition there are two hydrogen bonds, $N14 \cdots O14$ and $N21 \cdots O22$, which connect molecules of the some type to form bimolecular ring motifs. We note that the arrangement of the hydantoin moieties around the potassium ion leads to an almost in-plane coordination mode similar to that in the Pt(II) dibenzo-18-crown-6 complex [15].

References

[1] B. Rosenberg, L.V. Camp, J.E. Trosko, V.H. Mansour. *Nature*, **222**, 385 (1969).
[2] B. Rosenberg, L.V. Camp. *Cancer Res.*, **30**, 1799 (1970).
[3] P.R. Canal. Platinum compounds. In *A Clinician's Guide to Chemotherapy Pharmacokinetics and Pharmacodynamics*, L.G. Grochow, M.M. Ames (Eds), p. 345, Williams and Willkins, Baltimore (1998).
[4] D. Michael-Colvin. In *Cancer Medicine*, J.F. Holland, E. Frei III, R.C. Bast (Eds), 4th Edn, p. 648, Williams and Wilkins, Baltimore (1998).
[5] B. Desoize, C. Medoulet. *Crit. Rev. Oncol.*, **42**, 317 (2002).
[6] M.H. Hanigan, P. Devarajan. *Cancer Therapy*, **1**, 47 (2003).
[7] C. Bokemeyer, H. Sauer, H.-J. Schmoll. In *Kompendium Internistische Onkologie*, H.-J. Schmoll, K. Höffken, K. Possinger (Eds), Teil 1, p. 1131, Springer-Verlag, Berlin (1996).
[8] T. Boulikas, M. Vougiouka. *Oncol. Rep.*, **10**, 1663 (2003).
[9] S.-I. Akiyama, Z.-S. Chen, T. Sumizawa, T. Furukawa. *Anti-cancer Drug Design*, **14**, 143 (1999).
[10] C. Xin Zhang, S.J. Lippard. *Curr. Opinion Chem. Biol.*, **7**, 481 (2003).
[11] J. Reedijk. *Curr. Opinion Chem. Biol.*, **3**, 236 (1999).
[12] M. Galanski, M.A. Jakupec, B.K. Keppler. *Curr. Med. Chem.*, **12**, 2075 (2005).
[13] L.R. Kelland. *J. Inorg. Biochem.*, **77**, 121 (1999).
[14] J.-H. Wu, M. Wang, P.-J. Zheng, J.-Z. Zhang, Z. Chen, J.-M. Sheng, Y.-H. Yang. *J. Clin. Struct. Chem.*, **10**, 67 (1991).
[15] Li Xue, Jian-Min Dou, Ying Liu, Lan-Ying Zhi, Pei-Ju Zheng. *Acta Cryst.*, **C56**, 1185 (2000).
[16] R. Wildonger, M. Winstead. *J. Med. Chem.*, **10**, 981 (1967).
[17] S. Dhara. *Indian J. Chem.*, **8**, 193 (1970).

[18] *Enraf-Nonius Diffractometer Control Software, Release 5.1*, Enraf-Nonius, Delft, The Netherlands (1993).
[19] L.J. Farrugia. *J. Appl. Cryst.*, **32**, 837 (1999).
[20] G.M. Sheldrick. *SHELXS-97. Program for the Solution of Crystal Structures*, University of Göttingen, Germany (1990).
[21] G.M. Sheldrick. *SHELXL-97. Program for Crystal Structure Determination*, University of Göttingen, Germany (1997).
[22] I.J. Bruno, J.C. Cole, P.R. Edgington, M. Kessler, C.F. Macrae, P. McCabe, J. Pearson, R. Taylor. *Acta Cryst.*, **B58**, 389 (2002).
[23] G. Thiele, C. Mrozek, K. Wittmann, H. Wirkner. *Naturwissenschaften*, **65**, 206 (1978).
[24] G. Thiele, C. Mrozek, D. Kammerer, K. Wittmann. *Zeits. Naturforsch., B, Anorg. Chem., Org. Chem.*, **38**, 905 (1983).
[25] B. Shivachev, R. Petrova, E. Naydenova. *Acta Cryst.*, **C61**, 524 (2005).