Molecular and Crystal Structure of Potassium-L-alaninato-dichloridoplatinate(II), $K[Pt(L\text{-}alaO)Cl_2]$

Stefan Schiesser, Peter Mayer, Thomas Carell, and Wolfgang Beck

Department Chemie, Ludwig-Maximilians-Universität München, Butenandtstr. 5–13, 81377 München, Germany

Reprint requests to Prof. Dr. W. Beck.
E-mail: wbe@cup.uni-muenchen.de

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Dedicated to Professor Gottfried Huttner on the occasion of his 75th birthday

The square-planar structure of the $[Cl_2Pt(alaninate)]^-$ anion was determined by X-ray crystallography. In the crystal structure the packing of the components is dominated by layers of potassium ions.

Key words: Platinum, Alaninate Chelate, *cis*-Dichlorido, X-Ray Crystallography

Introduction

Platinum complexes of amino acids and peptides [1 – 5] have found interest as potential antitumor drugs with the idea that the coordinated bioligands might favor the transport and/or the selective uptake of the cytotoxic platinum unit into tumor cells [6 – 8]. Complexes of the type $[Cl_2Pt(N,O\text{-amino acid anion})]^-$ are formed from $K_2[PtCl_4]$ and amino acids and have been reported as early as 1912 by Ley [9]. They have been characterized and used as starting compounds for other complexes by the pioneers in platinum/amino acid chemistry Volshtein and Slyudkin [1, 5, 10, 11]. Erickson and coworkers [12 – 17] could synthesize several complexes $[Cl_2Pt(\text{amino acid anion})]^-$ and have thoroughly studied their structure and chemistry by NMR spectroscopy. The complexes $K[Cl_2Pt(N\text{-}O)]$ (N-O = glycinate, alaninate) were reacted with nucleobases and nucleosides to give mixed-ligand compounds [18, 19]. Interestingly, the glycinate complex $[Cl_2Pt(glyO)]^-$ catalyzes the selective oxidation of sp^3 carbon-hydrogen bonds in water [20].

Lippard and coworkers [21, 22] screened complexes formed *in situ* from K_2PtCl_4 and combinations of α-amino acids regarding their ability to bind high mobility group protein **1** and to give DNA adducts. The lysinate complex $[Cl_2Pt(N,O\text{-}NH_2CH(CO_2)(CH_2)_4NH_3]$ which was first reported by Altman *et al.* [23, 24] could be identified as the best candidate with moderate cytotoxicity towards tumor cells [21, 22]. The latter effect was already reported for $K[Cl_2Pt(N\text{-}O)]$ (N-O = glycinate, serinate) [25]. And recently, moderate cytotoxic effects on human tumor cells were reported for the ornithinate complex $[Cl_2Pt(N,O\text{-}NH_2CH(CO_2)(CH_2)_3NH_3]$, and – notably – the complex with the D-enantiomer of ornithine showed a significantly higher cytotoxicity than that with the L-isomer [26]. In the following we report on the molecular and crystal structure of $K[Cl_2Pt(L\text{-alaninate})]$ (**1**).

Previously, crystallographic determinations of the structures of the dichlorido complexes $[Cl_2Pt(N\text{-}O)]$ (N-O = lysinate+H^+ [28], ornithinate+H^+ [27]) and $Cs[Cl_2Pt(N\text{-methyl-4-hydroxy-prolinate}]^-$ [29] and of the chloridoplatinate(IV) complexes *cis* and *trans*-$[Cl_2Pt(N\text{-}O)_2]$ (N-O = glycinate, alaninate) [30, 31], $[Cl_4Pt(glycinate)]^-$ [32] and $[Cl_3Pt(glycinate)(py)]$ [33] were carried out.

Results and Discussions

The molecular, square-planar structure of $K[Cl_2Pt(L\text{-}alaO)]$ is shown in Fig. 1, and the bond lengths and bond angles are given in Table 1. The

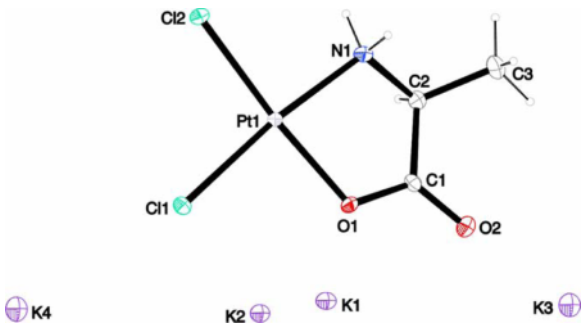

Fig. 1 (color online). Molecular structure of the anion and positions of some of the neighboring K^+ cations in the crystal structure of $K[Cl_2Pt(L\text{-}alaO)]$.

Table 1. Bond lengths (Å) and angles (deg) of K[Cl_2Pt(L-alaO)].

Pt1–Cl1	2.3218(8)	Cl1–Pt1–Cl2	93.36(3)
Pt1–Cl2	2.2866(8)	Cl1–Pt1–O1	91.25(6)
Pt1–O1	2.028(2)	Cl1–Pt1–N1	173.75(8)
Pt1–N1	2.015(3)	Cl2–Pt1–O1	175.28(6)
O1–C1	1.304(3)	Cl2–Pt1–N1	92.89(8)
O2–C1	1.223(3)	O1–Pt1–N1	82.50(9)
N1–C2	1.480(5)	Pt1–N1–C2	109.8(2)
C1–C2	1.528(5)	O1–C1–O2	122.1(3)
C2–C3	1.504(5)	O1–C1–C2	116.6(3)
		O2–C1–C2	121.3(3)
		N1–C2–C3	112.4(3)
		C1–C2–C3	114.1(3)
		N1–C2–C1	109.0(3)
K1–Cl1	3.243(1)		
K1–O1	2.747(3)		
K2–Cl1	3.246(1)		
K2–O1	2.782(3)		

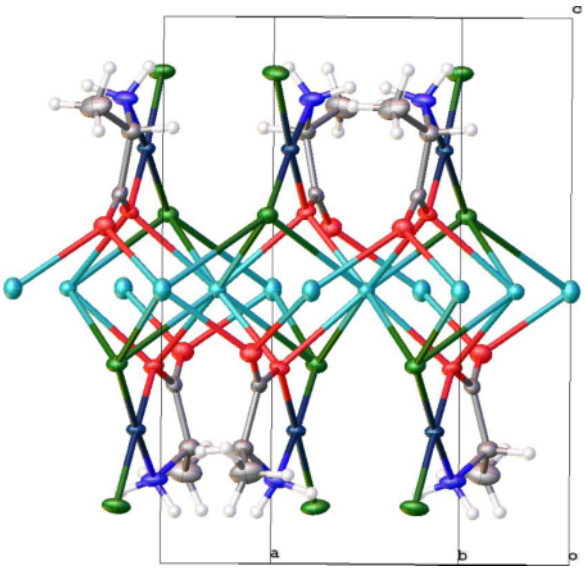

Fig. 2 (color online). Packing of the components in the crystal structure of K[Cl_2Pt(L-alaO)] (color code: K turquoise, Pt dark blue, Cl green, O red, N blue). Each of the K^+ cations is located on a special position with 1/4 occupancy.

five-membered chelate ring Pt1–O1–C1–C2–N1 is puckered and adopts a ${}^{C2}T_{N1}$ twist conformation which is slightly distorted towards an E_{N1} *envelope* conformation [34]. C2 and N1 deviate from the least-squares plane through the chelate ring by 0.185(4) and –0.177(6) Å, respectively. The "coordination bite" [N(amino)–Pt–O(carboxyl)] of 83.5° agrees perfectly with those of other platinum(II) α-aminocarboxylates (Table 2). Freeman [35, 36] has observed a linear relationship between the metal–N/O bond lengths and the N–metal–O angle of amino acid metal complexes, which is true also for K[Cl_2Pt(L-alaO)] with an angle of 83.5° and a mean Pt–donor atom bond length of 2.0 Å. In Table 2 the Pt–N and Pt–O bond lengths of comparable platinum complexes are listed. The Pt–Cl bond lengths are slightly different, which might be due to the stronger *trans*-influence of the *trans*-amino group in comparison to that of the carboxylate-O atom. The same observation was made for other chloro-aminocarboxylato-Pt complexes (Table 2) [27, 28, 30].

In the crystal (Fig. 2) the packing of the title compound is dominated by layers parallel to the *ab* plane. Each layer consists of a central layer of potassium ions (turquoise in the packing diagram; color online). On both sides of this potassium layer, the platinum complexes are arranged with their molecular planes approximately parallel to the *bc* plane and, hence, almost perpendicular to the layers of the potassium ions. The

Table 2. Bond lengths (Å) and coordination bite angles (deg) of aminocarboxylato platinum chelates.

	Pt–Cl	Pt–N	Pt–O	N–Pt–O	Ref.
[Cl_2Pt(L-alaO)]$^-$	2.29/2.32	2.015(3)	2.028(2)	82.5(1)	this work
[Cl_2Pt(*N*-methyl-hydroxyprolinate)]$^-$	2.26/2.38	1.97(1)	2.06(1)	85.5	[29, 41]
[Cl_2Pt(lysinate+H^+)]	2.28/2.32	2.03(2)	2.01(1)	83.0(6)	[28]
[Cl_2Pt(ornithinate+H^+)]	2.29/2.32	2.06(1)	2.036(9)	83.1(3)	[27]
Cl_2Pt(diaminopropionate+H^+)]	2.28/2.31	2.01(2)	2.01(1)	82.7(4)	[28]
trans-[Pt(glyO)$_2$]	–	2.037(4)	2.002(4)	82.5(2)	[36]
cis-[Pt(glyO)$_2$]	–	2.013	2.015	83.0	[37]
[(H_3N)$_2$Pt(alaO)]$^+$	–	2.08(2)	2.05(2)	83.2(8)	[38]
[(phen)Pt(alaO)]$^+$	–	2.031(6)	1.991(3)	82.8(1)	[39]
[(bmp)Pt(alaO]$^+$	–	2.009(8)	1.994(7)	82.0(3)	[40]
cis-[Cl_2Pt(glyO)$_2$]	2.29/2.31	2.034(6)	2.010(6)	84.4(2)	[30]
		2.040(6)	2.019(5)	83.5(3)	

Table 3. Crystallographic data of K[Cl_2Pt(L-alaO)].

Formula	$C_3H_6Cl_2KNO_2Pt$
M_r	393.167
Crystal size, mm^3	$0.21 \times 0.06 \times 0.05$
T, K	173(2)
Crystal system	orthorhombic
Space group	$P222$
a, Å	7.17910(10)
b, Å	9.0902(2)
c, Å	12.8246(2)
V, $Å^3$	836.93(3)
Z	4
Calcd. density, g cm^{-3}	3.12
μ(MoK_α), mm^{-1}	17.8
Absorption correction	multi-scan
Transmission factor range	0.1306 – 0.2780
θ range, deg	3.18 – 27.57
Refls. measured / unique / R_{int}	21579 / 1948 / 0.0405
Mean $\sigma(I)/I$	0.0188
Refls. with $I > 2\,\sigma(I)$	1911
Refls. used in refinement	1948
Refined parameters	95
$R(F)$ ($I > 2\,\sigma(I)$) / wR $(F^2)^{a,b}$ (all data)	0.0167 / 0.0411
$(\text{shift/error})_{max}$	0.001
x/y (weighting scheme)^b	0.0187 / 1.0754
S^c	1.124
Flack parameter	−0.020(11)
Res. electron density (max / min), e $Å^{-3}$	0.57 / −1.93

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; [b] $wR = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$, $w = [\sigma^2(F_o^2) + (xP)^2 + yP]^{-1}$, where $P = (\text{Max}(F_o^2, 0) + 2F_c^2)/3$; [c] $S = \text{GoF} = [\Sigma w(F_o^2 - F_c^2)^2/(n_{obs} - n_{param})]^{1/2}$.

potassium ions are coordinated by the oxygen atoms of the carboxylate group of the alanine and one of the two chloride ions (Cl1). The other chloride ion (Cl2) as well as the NH_2 group of the alanine are not involved in potassium coordination, but link the layers along the c axis by hydrogen bonds of the type N–H···Cl.

Experimental

Potassium dichlorido-(L-alaninato)-platinate(II)

To a solution of potassium tetrachloroplatinate(II) (122 mg, 0.29 mmol, 1.5 eq.) in D_2O (1.3 mL) was added L-alanine (18 mg, 0.20 mmol, 1.0 eq.). The resulting red solution was stirred at 120 °C for 3 h and then cooled to 4 °C to obtain colorless crystals. – ^{1}H NMR (400 MHz, D_2O): δ (ppm) = 4.11 (q, ^3J = 7.2 Hz, 1H, CH), 1.57 (d, ^3J = 7.2 Hz, 3H, CH_3). – ^{13}C NMR (101 MHz, D_2O): δ (ppm) = 191.0 (CO), 55.1 (CH), 18.4 (CH_3).

X-Ray structure determination

Diffraction data were collected at 173 K with MoK_α radiation (λ = 0.71073 Å) with a Nonius KappaCCD diffractometer equipped with a rotating anode. The structure was solved with Direct Methods [42] and refined with SHELXL-97 by full-matrix least-squares on F^2 [43]. The K^+ counterions are located on special positions with 1/4 occupancy (numbered K1 to K4). All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were calculated in ideal geometry and treated as riding on their parent atoms in the final refinement. The crystallographic data of **1** are listed in Table 3.

CCDC 881403 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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