Synthesis and crystal structure of a palladium(II) complex with the amino acid L-citrulline

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Synthesis and structural characterization of a novel palladium Pd(II) complex with the amino acid L-citrulline (Cit, $C_6H_{13}N_3O_3$) are presented in this paper. Elemental analysis indicates a 1:2 metal/ligand molar composition for the complex, with the molecular formula $PdC_{12}H_{24}N_6O_6$. The compound was also characterized by infrared (IR) spectroscopic measurements and the crystal structure has been solved by powder X-ray diffraction data with simulated annealing strategy in real space. The Pd(II) complex crystallizes in the triclinic system with space group P-1 and cell parameters $a = 4.6493(4)$ Å, $b = 5.222(4)$ Å, $c = 18.040(2)$ Å, $\alpha = 77.41(6)°$, $\beta = 94.72(7),°$ and $\gamma = 101.45(7)°$. The crystal structure confirms the presence of Pd(II) ions in a nearly square planar environment and the molecular formula with deprotonated citrulline as proposed by analytical and spectroscopic data. © *2015 International Centre for Diffraction Data*. [doi:10.1017/S0885715615000652]

Key words: X-ray, powder diffraction, amino acids, palladium complex

I. INTRODUCTION

Palladium (Pd) complexes have been extensively studied concerning its antitumoral, antifungal, and antibacterial properties (Garoufis *et al.*, 2009). In this context, our research group has contributed to the development of some biologically active Pd (II) complexes, mainly with amino acids and its derivatives. Carvalho *et al.* reported the synthesis of a Pd (II) complex with the amino acid L-tryptophan, $[Pd(trp)_2]$, which presents antibacterial activities against Gram-negative (*Escherichia coli and Pseudomonas aeruginosa*) and Gram-positive (*Staphylococcus aureus*) bacterial strains (Carvalho *et al.*, 2012). In addition, a novel water-soluble Pd (II) complex with L-alliin (S-allyl-L-cysteine sulfoxide), with the coordination formula $[Pd(alliin)_2]$, was prepared and evaluated about its antitumor activity over *HeLa* cells. The compound $[Pd(alliin)_2]$ was shown to be active over *HeLa* tumorigenic cells, with an IC_{50} close to cisplatin, which is used in cancer treatment. Such compound has also shown to have antimicrobial activities against Gram-positive and Gram-negative microorganisms in the range 125–500 μg mL^{-1} (Abbehausen *et al.*, 2013).

Bergamini *et al.* also reported the synthesis and characterization of a dimeric Pd (II) complex with 2-mercaptothiazoline (mtz), with the formula $[Pd_2(mtz)_4]$, where the ligand is coordinated to the metal by the sulfur and nitrogen atoms of the heterocyclic ring. However, this complex did not present antibacterial activities over the considered strains (Bergamini *et al.*, 2011).

L-Citrulline (2-amino-5-ureidopentanoic acid, $C_6H_{13}N_3O_3$, Cit) is an endogenous mammal's amino acid intermediate in the urea cycle (Kaore *et al.*, 2013). Although endogenous, L-citrulline is also found in foods such as watermelons, cucumbers, pumpkins, muskmelons, and bitter melons, and it is known to act on body process of ammonia detoxification through its conversion to urea. This amino acid may also act as a potent hydroxyl scavenger (Kaore *et al.*, 2013). Sketch of L-citrulline is shown in Chart 1.

In this paper the synthesis, structural characterization, and ancillary analytical and spectroscopic data of a novel Pd(II) complex with the amino acid L-citrulline, $[Pd(Cit)_2]$, are reported.

II. EXPERIMENTAL

A. Materials and methods

L-Citrulline (98%), potassium hydroxide, and potassium tetrachloridopalladate(II) (98%) were purchased from

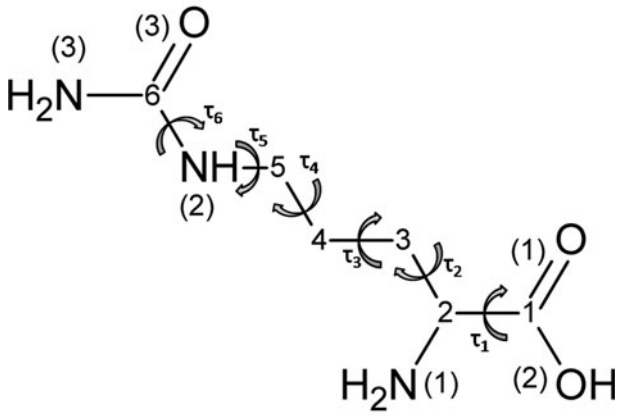

Chart 1. Sketch of citrulline where numbers replaced carbon atoms and the nitrogen and oxygen atoms were numbered in parenthesis. The τ_1 to τ_6 symbols illustrate the torsion angles defining the conformation of the salt of citrulline present in the $[Pd(Cit)_2]$ complex.

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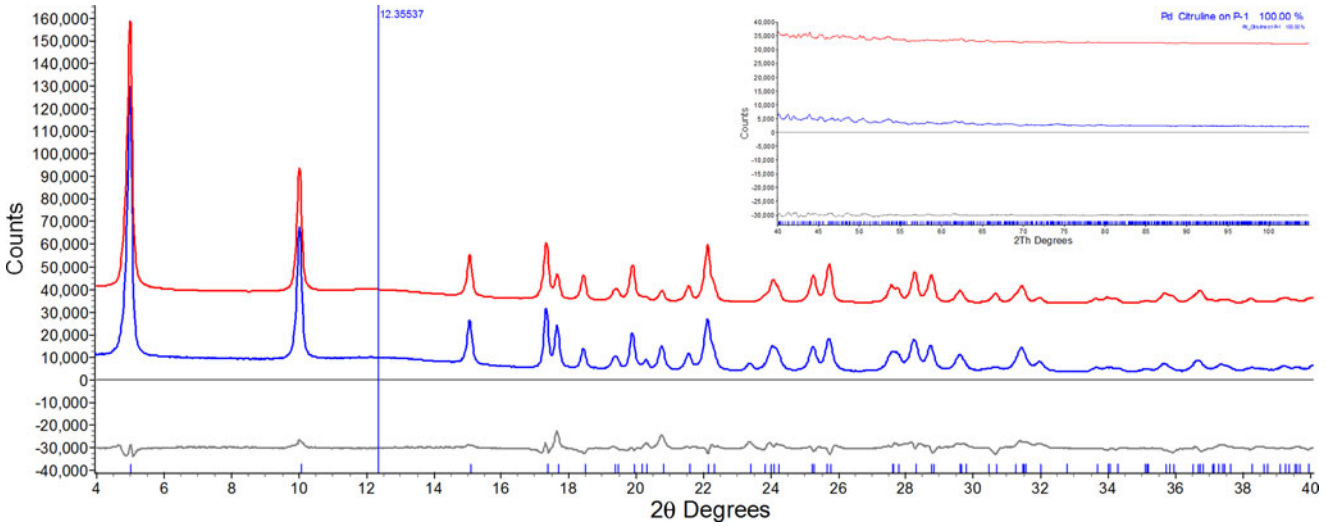

Figure 1. (Color online) Final Rietveld refinement plot in the range 4°–40° 2θ for [Pd(Cit)$_2$] with difference plot as grey line and peak markers at the bottom. The experimental data is present in blue line while calculated data is in red. Horizontal axis is 2θ(°) and vertical axis is counts. A very broad peak at 12.35° was inserted to describe the presence of a small amorphous portion. The inset shows the high-angle region.

Sigma-Aldrich Laboratories. Elemental analyses for carbon, hydrogen, and nitrogen were performed using a Perkin Elmer 2400 CHN Analyzer. IR spectra from 4000–400 cm^{-1} of citrulline and the Pd (II) complex were measured using a FT-IR spectrophotometer ABB Bomen MB Series; samples were prepared as KBr pellets.

1. Synthesis of [Pd(Cit)$_2$]

The Pd (II) complex with citrulline was synthesized by the reaction of 5.0 ml of an aqueous solution of potassium tetrachloridopalladate(II), $K_2[PdCl_4]$ (5.0×10^{-4} mol), with 10.0 ml of a freshly prepared aqueous solution of the alkaline salt of L-citrulline containing 1.0×10^{-3} mol of the ligand. The $K_2[PdCl_4]$ aqueous solution was added dropwise to the alkaline solution of citrulline under magnetic stirring and at room temperature. After 2 h of constant stirring, the yellow solid obtained was vacuum-filtered, washed with cold water, and dried in a desiccator over P_4O_{10}. The [Pd(Cit)$_2$] complex is insoluble in water and in common organic solvents such as methanol, ethanol, acetonitrile, dimethylsulfoxide, chloroform, and dichloromethane. Elemental analysis led to a 1:2 metal: ligand composition for the complex. Anal. Calcd. For $PdC_{12}H_{24}N_6O_6$ (%): C, 31.7; H, 5.32; N, 18.5. Found (%): C, 30.7; H, 5.56; N, 17.6; IR bands: ν_{asym} (–(CO)$\underline{NH_2}$) 3446 cm^{-1}, ν_{sym} (–(CO)$\underline{NH_2}$) 3344 cm^{-1}, ν_{asym} (–NH$_2$) 3217 cm^{-1}, ν_{sym} (–NH$_2$) 3130 cm^{-1}, ν_{asym} (–COO$^-$) 1639 cm^{-1}, ν_{sym} (–COO$^-$) 1364 cm^{-1}. The IR spectrum and additional discussions about the IR data are provided as supplementary material 1.

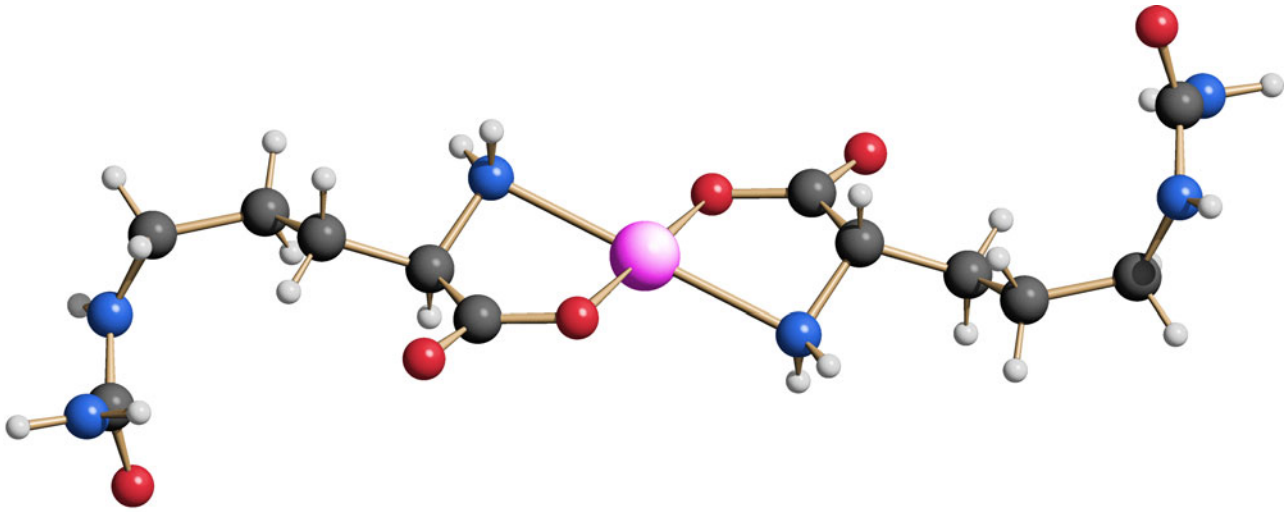

Figure 2. (Color online) Crystal structure of [Pd(Cit)$_2$] drawn using SCHAKAL (Keller, 1986). Color codes: Pd(II): pink; carbon: grey; hydrogen: white; nitrogen: blue and oxygen: red. The Pd(II) ion is lying on inversion center as pivot for citrullinate ligand.

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TABLE I. Crystallographic data of $[Pd(Cit)_2]$.

Empirical formula	$C_{12}H_{24}N_6O_6Pd$
Formula weight	454.77
T(K)	298
λ(Cu$K\alpha$) (Å)	1.5418
Crystal system	Triclinic
Space group	P-1
a (Å)	4.6493(4)
b (Å)	5.222(4)
c (Å)	18.040(2)
α (°)	77.41(6)°
β(°)	94.72(7)°
γ (°)	101.45(7)°
V (Å^3)	418.56(6)
Z	1
d_{calc} (g cm^{-3})	1.8042(2)
μ (mm^{-1})	93.73(1)
F (000)	430
Number of Parameters	39
R_{Bragg},R_{wp}	0.055/0.084

The alkaline salt of citrulline used in the synthesis of the Pd(II) complex was prepared by the reaction of equimolar quantities of the amino acid and potassium hydroxide under stirring and at room temperature.

B. X-ray powder diffraction data collection and structure determination

To perform the powder diffraction analysis, the polycrystalline $[Pd(Cit)_2]$ was gently grounded in an agate mortar and it was deposited in hollow of PMMA sample-holder plate. The diffraction data were collected by overnight scans in the 2θ range of 4°–105° with steps of 0.02° using a *Bruker AXS D8 da Vinci* diffractometer, equipped with Ni-filtered Cu$K\alpha$ radiation ($\lambda = 1.5418$ Å), a Lynxeye linear position-sensitive detector and the following optics: primary beam Soller slits (2.94°), fixed divergence slit (0.3°) and receiving slit (8.73 mm). The generator was set at 40 kV and 40 mA. Approximate unit cell parameters were determined using 22 first standard peaks, followed by indexing through the single-value decomposition approach (Coelho, 2003) implemented in TOPAS (TOPAS, 2009), the Goodness-on-Fit value equal 53.13 (Wolff, 1968) was afforded for indexing stage. In the present case, space group P-1 was chosen and the cell parameters were refined using 4–55 2θ range by Pawley method (Pawley, 1981), giving a good $R_{wp} = 5.950$. Then, the structure solution process was performed by the simulated annealing technique (Coelho, 2000) also implemented in TOPAS. No higher symmetric system was suggested by PLATON (Spek, 2009). Since the P-1 space group has $Z = 2$ and density considerations suggested $Z = 1$ the Pd(II) ion was placed in

TABLE II. List of the 50 first observed and calculated peaks for $[Pd(Cit)_2]$.

$2\theta_{obs}$(°)	d_{obs} (Å)	I/Io	h	k	l	$2\theta_{calc}$(°)	d_{calc}(Å)	$2\theta_{obs}$–$2\theta_{calc}$(°)
5.03	17.565	100.0	0	0	1	5.02	17.591	0.01
10.07	8.776	53.2	0	0	2	10.05	8.796	0.02
15.12	5.855	18.1	0	0	3	15.10	5.864	0.02
17.40	5.093	23.9	0	1	1	17.37	5.101	0.03
17.70	5.007	16.3	0	1	0	17.70	5.007	0.00
18.50	4.792	7.6	0	1	2	18.48	4.798	0.02
19.45	4.560	4.9	1	0	0	19.48	4.553	−0.03
19.95	4.447	14.6	1	0	−1	19.93	4.452	0.02
20.30	4.372	2.5	1	0	1	20.33	4.365	−0.04
20.82	4.264	9.6	0	1	3	20.80	4.268	0.02
21.63	4.106	6.3	1	0	−2	21.59	4.113	0.03
22.20	4.002	19.9	0	−1	2	22.15	4.010	0.05
23.44	3.792	2.8	1	−1	−1	23.41	3.797	0.03
24.10	3.690	9.5	1	−1	−2	24.08	3.692	0.02
25.31	3.516	9.7	0	0	5	25.29	3.518	0.02
25.78	3.453	12.9	1	−1	−3	25.77	3.454	0.01
27.76	3.214	7.6	0	1	5	27.80	3.207	−0.04
28.31	3.150	12.5	1	−1	−4	28.30	3.151	0.01
28.79	3.099	10.0	1	0	4	28.77	3.101	0.02
29.67	3.009	6.2	0	−1	4	29.65	3.011	0.02
30.72	2.908	1.3	1	−1	3	30.69	2.911	0.03
31.49	2.839	9.4	1	−1	−5	31.49	2.839	0.00
33.70	2.658	1.5	1	1	4	33.68	2.659	0.02
34.03	2.632	1.6	1	1	−3	34.05	2.631	−0.02
35.74	2.510	2.9	1	0	−6	35.71	2.512	0.03
36.73	2.445	4.2	1	−2	−2	36.73	2.445	0.00
37.45	2.399	2.4	0	2	4	37.45	2.399	0.00
38.28	2.349	1.0	1	−1	5	38.28	2.349	0.01
39.30	2.291	1.4	1	−1	−7	39.26	2.293	0.04
39.62	2.273	1.0	0	2	5	39.61	2.274	0.01
40.21	2.241	2.1	1	0	−7	40.24	2.239	−0.03
41.30	2.185	1.7	0	1	8	41.26	2.186	0.04
42.02	2.149	1.2	0	−2	3	42.03	2.148	−0.01
43.29	2.085	0.5	1	−2	−6	43.28	2.089	0.02
43.94	2.059	2.1	1	−2	3	43.90	2.061	0.04

Continued

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TABLE II. Continued

$2\theta_{obs}$(°)	d_{obs} (Å)	*I*/*Io*	*h*	*k*	*l*	$2\theta_{calc}$(°)	d_{calc}(Å)	$2\theta_{obs}$–$2\theta_{calc}$(°)
44.59	2.031	0.5	1	1	−6	44.61	2.030	−0.02
45.30	2.000	1.2	2	−1	3	45.26	2.002	0.04
45.52	1.991	1.2	0	2	7	45.52	1.991	0.00
46.75	1.942	1.1	2	1	0	46.76	1.941	−0.02
47.45	1.914	0.8	2	1	2	47.47	1.914	−0.02
48.03	1.893	1.0	1	2	5	48.05	1.892	−0.02
48.46	1.877	1.2	2	0	5	48.47	1.877	−0.01
48.69	1.869	1.4	2	1	3	48.70	1.868	−0.02
50.16	1.817	0.9	2	1	−3	50.13	1.818	0.04
50.49	1.806	1.4	2	1	4	50.49	1.806	0.00

fixed position at 0.0, 0.0, and 0.0. In addition, the citrullinate rigid body model, based on single-crystal data (Sridhar *et al.*, 2002) was built using *Z* matrix formalism, with free rotations and translations as well torsion angles as described in Chart 1.

In the simulated annealing step only torsion angles, rotation, and translation parameters concerning the ligand were used. In the refinement stage, carried out by the Rietveld method (Young, 1981), 38 parameters were refined including 10 parameters for background modeled by a Chebyshev polynomial function and broad peak at 12.3° (2θ) was inserted to describe the presence of a small amorphous portion. The rigid body description introduced at the solution stage was maintained in the final refinement. An isotropic thermal parameter set up at 3.0 (0.2) Å^2 was assigned to all atoms.

The final Rietveld refinement plot, the sketch of the crystal, and the molecular structure for [Pd(Cit)$_2$] are shown in Fig. 1, Chart 1, and Fig. 2, respectively. Table I contains the relevant crystal data for [Pd(Cit)$_2$] while Tables II and III contain relevant powder diffraction features and final fractional atomic coordinates for [Pd(Cit)$_2$], respectively.

TABLE III. Fractional atomic coordinates for [Pd(Cit)$_2$].

Atom	*x*/*a*	*y*/*b*	*z*/*c*
Pd	0	0	0
C1	0.4846	0.1244	0.0999
C2	0.3106	−0.1384	0.1415
C3	0.5110	−0.2754	0.2014
C4	0.3246	−0.4989	0.2556
C5	0.4815	−0.5374	0.3335
C6	0.4606	−0.2150	0.4024
N1	0.1972	−0.3108	0.08577
N2	0.3763	−0.4648	0.3912
N6	0.7443	−0.0976	0.3982
O1	0.7018	0.2363	0.1308
O2	0.3937	0.2235	0.0308
O3	0.2702	−0.0883	0.4170
H2	0.1513	−0.1029	0.1650
H11	0.08840	−0.4750	0.1117
H12	0.3585	−0.3430	0.0623
H31	0.6197	−0.1482	0.2284
H32	0.6411	−0.3466	0.1770
H41	0.2976	−0.6586	0.2367
H42	0.1398	−0.4516	0.2590
H21	0.2420	−0.5905	0.4241
H51	0.6762	−0.4381	0.3291
H52	0.4855	−0.7219	0.3513
H61	0.8191	0.0025	0.3510
H62	0.8705	−0.1146	0.4424

Isotropic thermal parameter was assigned to all atoms as 3.0(0.2) Å^2.

TABLE IV. Main bond lengths (Å) and angles (°) of [Pd(Cit)$_2$].

Distance/Å		Angle/°	
Pd–N1	2.27(3)	N1–Pd–O2	78.4(6)
Pd–O2	2.07(1)	N1–Pd–O2^i	101.6(6)

i code: 1 − *x*, 1 − *y*, 1 − *z*.

III. DISCUSSION

In the [Pd(Cit)$_2$] complex the Pd(II) ions were fixed at special position 0.0, 0.0, and 0.0 (see Table III). Since Pd (II) ions lie on inversion centers they act as pivot for the citrullinate ions where, as expected, the Pd(II) ions were surrounded by two ligands. Each ligand bonds to Pd(II) ions by one oxygen (O2) from the carboxylate group and by the nitrogen from alfa-amino group (N1) forming a square planar geometry around the metal center. The main distances and angles of [Pd(Cit)$_2$] are listed on Table IV. The angle between N–Pd–O of [Pd(Cit)$_2$] is 78.4(6)° and it falls in the range found in a complete Cambridge Structural Database (CSD) search, 82 ± 6° for 134 hits. The distance between O and Pd which is 2.07(1) Å is in good agreement than the average (2.05 ± 0.1 Å) found in the CSD database for Pd(II) complexes with N– and –O donor ligands. However, the Pd–N bond lengths 2.27(3) Å of [Pd(cit)$_2$] is little longer compared with the CSD Pd–N average, 2.04 ± 0.16 Å. The intermolecular hydrogen-bond interactions are present between H atoms of N6 with O3 and H atoms of N1 with O1 and O2 (carboxylate group).

IV. CONCLUSION

A Pd(II) complex with citrulline was obtained and the molecular formula $PdC_{12}H_{24}N_6O_6$ was confirmed by elemental analysis. The IR data support that citrulline salt bonds to Pd (II) ions by oxygen and nitrogen atoms. In the absence of crystals of suitable size and quality amenable to conventional single-crystal characterization, the structure of the new Pd (II) complex was determined by standard laboratory X-ray powder diffraction techniques. The diffraction pattern of [Pd (Cit)$_2$] was successfully indexed and the crystal structure was derived therefrom using *state-of-the-art real-space structure solution* methods: The [Pd(Cit)$_2$] complex belongs to triclinic system (P-1) with cell parameters a = 4.6493(4) Å, b = 5.222(4) Å, c = 18.040(2) Å, α = 77.41(6)°, β = 94.72(7)°, and γ = 101.45(7)°. Its crystal structure consists in Pd(II) ions surrounded by N and O atoms from 2-citrulline ligands (as an ionic ligand) in a closed square-planar geometry. Once

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again, it has been shown that powder diffraction methods can supply relevant (otherwise inaccessible) structural information, though of lower quality than that can be obtained from single crystal analyses (Masciocchi and Sironi 1997; Silva, *et al.*, 2014). Further studies about the antibacterial and antitumor activities of the complex are envisaged.

SUPPLEMENTARY MATERIAL

For supplementary material for this article, please visit http://dx.doi.org/10.1017/S0885715615000652

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