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Synthesis, structural characterization and DFT analysis of an unusual tryptophan copper(II) complex bound *via* carboxylate monodentate coordination: tetraaquabis(L-tryptophan) copper(II) picrate

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ABSTRACT

Herein, we report the synthesis, spectroscopy, crystal structure and theoretical studies of a new Cu(II) complex with formula [Cu(L-trp)₂(H₂O)₄](pic)₂·4H₂O (**1**), which exhibits an unusual tryptophan coordination to copper(II) *via* carboxylate monodentate binding. The complex has been prepared using the mixed ligand approach. Single crystal X-ray diffraction structural analysis of **1** revealed that, in the complex, the Cu(II) site shows a distorted octahedral geometry, and the tryptophan (trp) ligand is coordinated through the carboxylate group in a monodentate fashion. The picric acid (pic) co-ligand, which is present in the anionic form, resides outside the coordination sphere forming a charge-separated complex. Density Functional Theory (DFT; including time-dependent DFT) has been employed to calculate the equilibrium geometry of the complex as isolated species in dimethylsulfoxide (DMSO) solution, and also its electronic spectrum, which was used to understand details of the experimentally obtained ultraviolet-visible (UV-Vis) spectrum. The structural analysis was complemented by additional spectroscopic studies [infrared (IR) and electron paramagnetic resonance (EPR) spectroscopies], and the thermal stability of the complex evaluated by thermogravimetric analysis (TGA).

Keywords: Crystal structure, tryptophan, picric acid, TGA, UV-Visible, IR, EPR, DFT.

1. Introduction

Non-classical interactions, such as hydrogen bonds, π --- π stacking of aromatic rings, cation--- π interactions, and charge-transfer, play a crucial role in the structure and function of macromolecules [1-7]. Metal–(amino acid) complexes, in particular, have been extensively used to mimic non-classical interactions present in biological macromolecules [8].

Copper has been reported to be ubiquitous in redox-active metalloproteins [9]. The Cu(II) complexes of amino acids and their derivatives have attracted much attention as they are associated with proteasome inhibition [10], and show both DNA cleavage activity and cytotoxic effects toward various cell lines [11]. Tryptophan (trp), an α -amino acid having one amino, one indolic and one carboxylic group, has been shown to be a versatile ligand in coordination chemistry due to the electron donor capability of its amino acid and *N*-heterocyclic ring moieties [12,13]. The indole group of tryptophan has great potential for noncovalent interactions in mixed ligand complexes. There are several reports in the literature describing the structure of coordination compounds where either the amino groups or both amino and carboxylate groups of tryptophan act as coordination moieties [14,15]. However, according to the CSD 2017 database [16], there are no reports of complexes where tryptophan coordinates through the carboxylate oxygens in a monodentate way.

Herein, we report a tryptophan-based copper(II) complex, with formula [Cu(L-trp)₂(H₂O)₄](pic)₂·4H₂O (**1**), where the tryptophan carboxylate group is coordinated to the Cu(II) ion in a monodentate fashion, and the picrate anion acts as counter ion. Picric acid is known to act as an acceptor to form various π stacking complexes, and also as an acidic ligand through specific electrostatic or hydrogen bond interactions. We determined the molecular structure of **1** in crystalline phase, by single crystal X-ray diffraction, and interpreted it based also in calculations for the isolated Cu(II)-(L-trp)₂(H₂O)₄ nucleus performed using density functional theory (DFT). The structural analysis was complemented

by additional spectroscopic studies [infrared (IR), ultraviolet-visible (UV-Vis), electron paramagnetic resonance spectroscopy (EPR)], and the thermal stability of the complex probed by thermogravimetric analysis (TGA).

2. Experimental and Computational Methods

2.1. Materials and instrumentation

All chemicals (including solvents) used in this study were of high purity. L-Tryptophan was supplied by Loba Chemie and used without purification. Pieric acid was used after recrystallization. The IR spectrum was recorded with a Perkin–Elmer FTIR 2000 spectrometer with 4 cm⁻¹ resolution and 64 accumulations, for the compound in a KBr pellet. The thermogravimetric analysis (TGA) measurements were performed on an SDT Q600 (V20.9 Build 20) instrument (Artisan Technology Group, Champaign, IL), under N₂ atmosphere, with a heating rate of 10 °C min⁻¹. UV-Visible absorbance spectra were recorded on a Shimadzu UV-1800 spectrophotometer. Powder X-ray diffraction (PXRD) measurements were performed on a Bruker AXS D8 Advance X-ray (Cu-K α_1 radiation, $\lambda = 1.5406$ Å) diffractometer in the 5–35° 2 θ range using a 0.02° s⁻¹ step size. The sample was prepared by making a thin film from the finely powdered sample (~30 mg) over a glass slide. EPR measurements were carried out in a BRUKER Xenon EMX-ER073 spectrometer. Elemental analyses for C, H, and N were undertaken using a FLASH Ea1112 SERIES CHNS analyser.

2.2. Single crystal X-ray diffraction analysis

Single crystal X-ray diffraction data collection was carried out on a Bruker SMART APEX II CCD diffractometer, using graphite monochromated Mo-K α ($\lambda = 0.71073$ Å) radiation. The frames were collected at T = 298 K. Data reduction and unit cell refinement for 1 was performed using SAINT-Plus [17]. The SHELXL-2014/7 [18,19] software was used to

solve the structure of **1** by the direct method, the refinement procedure being done by fullmatrix least-squares, based on F^2 values against all reflections. Hydrogen atoms were fixed at the calculated positions with isotropic thermal parameters. The hydrogen atoms of the lattice water molecules could not be located from the difference Fourier map; however their contributions were included in the empirical formula. Details of the crystallographic data collection are given in Table 1. CCDC number 1558367 contains the supplementary crystallographic data for this paper. This data can be obtained free of charge via www. ccdc.cam.ac.uk/data request/cif [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk].

Compound	[Cu(L-trp) ₂ (H ₂ O) ₄](pic) ₂ ·4H ₂ O
Empirical formula	$C_{34}H_{44}CuN_{10}O_{26}$
Formula weight	1072.32
Crystal system	monoclinic
Crystal size	0.32 imes 0.20 imes 0.12
Space group	<i>C</i> 2
Unit cell dimensions	$a = 34.88(2)$ $\alpha = 90$
(Å), (°)	$b = 7.542(5)$ $\beta = 94.877(8)$
	$c = 9.030(6)$ $\gamma = 90$
Volume ($Å^3$), Z	2367(3), 2
$\rho_{\rm calc} ({\rm g cm}^{-3})$	1.488
$\mu (\mathrm{cm}^{-1})$	0.560
<i>F</i> (000)	1086
Range of data collection	2.264 - 25.800
Limiting frequency	$-42 \le h \le 41, -9 \le k \le 9, -10 \le l \le 10$
Total reflections	13114
Independent reflections	4371 [$R_{\text{int}} = 0.0877$]
Completeness to theta $= 25.00$	99.7 %
Refinement method	Full matrix least squares on F^2
Data / restraints / parameters	4371 / 88 / 323
Goodness of fit on F^2	0.948
Final <i>R</i> indices $[I > 2(I)]$	$R_1 = 0.0807, wR_2 = 0.2053$
R indices (all data)	$R_1 = 0.1365, wR_2 = 0.2319$
Largest diff. peak & hole ($e \text{ Å}^3$)	0.88 and -0.46

Table 1. Crystallographic data for complex [Cu(L-trp)₂(H₂O)₄](pic)₂·4H₂O.

2.3. Theoretical calculations

The geometry of the open shell d^9 (doublet state) Cu(II) complex 1 was optimized at the unrestricted DFT/CAM-B3LYP [20] level of theory, with the LANL2DZ (Los Alamos National Laboratory 2 double- ζ) [21–23] valence and effective core potential (ECP) functions for copper and the standard double- ζ plus polarization 6-31G(d,p) basis set for the remaining atoms. The X-ray determined structure was used as input for geometry optimization, and a C_2 symmetry constrain was imposed, in accordance with the solid state symmetry of the complex. The bulk solvent effects of dimethyl sulfoxide (DMSO) were considered through the polarizable continuum model (PCM) using the integral equation formalism variant (IEFPCM) [24, 25]. Calculation of the vibrational frequencies was carried out for the optimized geometry to certify that the stationary point found was a true minimum (*i.e.*, with no imaginary frequencies). Time-dependent DFT (TD-DFT) calculations were carried out for the optimized geometry using the CAM-B3LYP functional to obtain the vertical excitation energies for the lowest 30 excited states (up to 5.3 eV). The bulk solvent effects of DMSO were considered by using the IEFPCM [24, 25] solvent model. To assess the occurrence of spin-contamination in the U-DFT calculations, the value obtained for $\langle S^2 \rangle$ was compared with the expected S(S + 1) for the spin state (doublet state). In all the calculations spincontamination was found to be smaller than 3 %, and therefore, negligible. DFT and TD-DFT calculations for the picrate anion were also carried out using the same functional, basis set (6-31G(d,p)) and solvent model. The DFT calculations were performed using Gaussian 09 program and Gauss View was used for visualization of the structure, simulated UV/Vis spectra and molecular orbitals [26].

2.4. Synthesis of $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O(1)$

Copper picrate was synthesised by a modified literature procedure [27]. Picric acid (2 mmol; 458 mg) was added to a 1 mmol basic copper carbonate (221 mg) solution in distilled

water. The solution was stirred for an hour and heated at 50 °C, with evolution of CO₂. The obtained green coloured solution was filtered and left for slow evaporation. Green coloured crystals of copper picrate were formed after 1 week. An aqueous solution of copper picrate 0.5 mmol (114.55 mg) was then added to a clear solution of 1 mmol of tryptophan (204.22 mg) in 6–8 mL of distilled water, giving rise to a solution of yellowish green colour. This solution was stirred overnight at room temperature. A red coloured complex was afforded, which was collected by filtration and dried in desiccator. Yield: 0.804 g (75%). Anal. Calcd. for $C_{34}H_{44}CuN_{10}O_{26}$: C, 38.08; H, 4.14; N, 13.06. Found: C, 38.42; H, 3.12; N, 13.15. IR spectrum (KBr disk, selected peaks; $\bar{\nu}$): 3403, 3154, 1625, 1598, 1565, 1533, 1416, 1327, 1294, 1165, 1080, 917, 743, 705, 509 cm⁻¹ (see Figures S1 and S2, Supporting Information).

3. Results and Discussion

3.1. Synthesis and crystal structure description of $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O(1)$.

The copper picrate was synthesised using copper carbonate and picric acid in water, as described in Section 2.5. The reaction between copper picrate and tryptophan afforded a highly crystalline product of formula of $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ (1) (see Scheme 1). The complex 1 was first characterized by elemental analysis and infrared spectroscopy (see above), Single crystal X-ray diffraction analysis showed that 1 crystallizes in a monoclinic unit cell, space group *C*₂, exhibiting an asymmetric unit that consists of half of Cu(II), located at the inversion centre, one molecule of tryptophan, one picrate anion, two coordinated *aqua* ligands and two lattice occluded water molecules (Scheme 1 and Figure 1). The overall charge of the complex nucleus is balanced by the lattice picrate anions. Complex 1 contains a distinctive structural motif containing a unique Cu(II) ion in a distorted octahedral coordination *yia* the carboxylate group.



Scheme 1. Synthesis of the complex $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$.

The ORTEP diagram of the complex is shown in Figure 1. Selected bond lengths and bond angles are listed in Table 2. As shown in Figure 1, the octahedral geometry at the Cu(II) center is satisfied with two carboxylate oxygen atoms belonging to two different tryptophan molecules, in a monodentate coordination mode and in *trans*-fashion, and by four water molecules. The two carboxylate groups of the coordinated tryptophan molecules are nearly perpendicular to each other, as shown by the torsion angle $(73.37\pm0.10^{\circ})$ between the planes of the two carboxylate groups determined experimentally. The tryptophan molecule exhibits a staggered conformation with respect to indole ring, and *gauche* relatively to the amino group [28].

The coordinated *aqua* molecules are H-bonded to the phenolic oxygen atom and nitro functionality of the picrate anion (see Figure 2 and Table S1 in Supporting Information). The protonated amino group of the tryptophan ligands is also H-bonded, with all the three H atoms being involved in the H-bond network and being connected to oxygen atoms belonging to the carboxylate group of a neighboring tryptophan molecule, the phenolate moiety of the picrate anion, or a water molecule. The carbonyl oxygen atom of the tryptophan ligand forms

a four membered ring with graph set $R_2^2(4)$, defined by two tryptophan neighboring molecules and involving also the NH₃⁺ moieties of the same two molecules (see Figure 2). The pyrrolyl hydrogen atom is also H-bonded to an oxygen atom of a nitro group of picrate anion, connecting two adjacent molecules. The nitro groups of the picrate moiety are twisted out of the benzene ring plane by 5–19°. Noteworthy, the 2D structure of **1** shows only 2.8% solvent accessible voids (SAVs) per unit volume, as calculated using PLATON [29], demonstrating the dense packing of the molecules in the crystal. Crystal packing shows the indole and picrate rings aligned parallel to each other, indicating aromatic ring stacking interaction between them, as displayed in Figure 3. Although these interactions, as measured by the distances between the interacting rings (4.208-4.916 Å) are week, they certainly play a relevant role in the stabilization of the three dimensional network of the crystal.



Fig. 1. ORTEP drawing of complex **1** depicting 30% thermal ellipsoid probability, with atom labeling scheme. H-atoms have been omitted for clarity. Symmetry transformations used to generate equivalent atoms are: (i) -x, y, -z.



Fig. 2. H-bond interactions (N–H---O and O–H---O) in the crystal of 1, viewed along the *b*-axis.



Fig. 3. Display of $\pi^{-}\pi$ stacking interactions between the indole and picrate rings, which align parallel to each other.

Table 2. Selected geometric parameters obtained for the crystal of $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ (1) by X-ray diffraction and calculated at the unrestricted CAM-B3LYP/LanL2DZ level for the $[Cu(L-trp)_2(H_2O)_4]^{2+}$ complex in DMSO solvent.

Bond distances (Å)	Experimental	CAM-B3LYP (in DMSO)	Deviation ^{<i>a</i>}
$Cu(1)-O(2)^{i}$	1.911(6)	1.943	0.032
Cu(1)-O(2)	1.911(6)	1.943	0.032
$Cu(1)-O(1W)^{i}$	2.097(11)	2.185	0.088
Cu(1)-O(1W)	2.097(11)	2.185	0.088
Cu(1)-O(2W)	2.098(16)	2.158	0.060
$Cu(1)-O(2W)^{i}$	2.098(16)	2.158	0.060
Bond Angles (°)			
$O(2)^{i}$ -Cu(1)-O(2)	177.1(8)	170.6	-6.5
$O(2)^{i}$ -Cu(1)-O(1W)^{i}	86.1(4)	82.4	-3.7
$O(2)-Cu(1)-O(1W)^{i}$	92.0(4)	90.9	-1.1
$O(2)^{i}$ -Cu(1)-O(1W)	92.0(4)	90.9	-1.1
O(2)-Cu(1)-O(1W)	86.1(4)	82.4	-3.7
O(1W)i-Cu(1)-O(1W)	99.4(7)	89.1	-10.3
O(2)i-Cu(1)-O(2W)	83.5(5)	91.3	7.8
O(2)-Cu(1)-O(2W)	98.7(5)	95.6	-3.1
$O(1W)^{i}-Cu(1)-O(2W)$	89.4(5)	92.4	3.0
O(1W)-Cu(1)-O(2W)	169.8(6)	177.4	7.6
$O(2)^{i}-Cu(1)-O(2W)^{i}$	98.7(5)	95.6	-3.1
$O(2)-Cu(1)-O(2W)^{i}$	83.5(5)	91.3	7.8
$O(1W)^{i}$ -Cu(1)-O(2W)^{i}	169.8(6)	177.4	7.6
$O(1W)-Cu(1)-O(2W)^{i}$	89.4(5)	92.4	3.0
$O(2W)-Cu(1)-O(2W)^{i}$	82.3(10)	86.0	3.7

^{*a*} Mean absolute deviation between the theoretical and experimental structures is 0.06 Å for bond lengths and 4.9° for bond angles. See Figure 1 for atom numbering.

To observe the homogeneity and crystallinity of the bulk material, the powder X-ray diffraction (PXRD) pattern of the sample was also recorded, which fits nicely the simulated

pattern generated from the obtained single-crystal X-ray data and, thus, confirmed the homogeneity and purity of the crystalline phase (Figure 4).



Fig. 4. The powder X-ray pattern of 1: simulated from the single crystal X-ray structure using the Mercury 3.9 software (lower, blue trace) and the as-synthesized sample (upper, black trace).

3.2. DFT studies

To gain insight into the geometry and electronic structure of complex **1**, DFT calculations were performed at the CAM-B3LYP/6-31G(d,p)+LanL2DZ level of theory using the geometric parameters obtained from X-ray analysis as starting structure. The structural parameters calculated for the isolated complex considering the bulk solvents effects of DMSO are shown in Table 2, where they can be compared with the experimental X-ray structure. The mean absolute deviation between the theoretical and experimental structures is 0.06 Å for bond lengths and 4.9° for bond angles. These differences are small and involve, to a major extent, the coordination of the four inner sphere water molecules. Taking into account that the picrate anions in the crystal are involved in H-bonding with the coordinated water ligands, and also that these counter ions were not included in the geometry optimization, these structural differences are expected. The interactions arising from the packing in the crystal are also absent in the theoretical calculations and may also contribute to the differences found. The geometry around the metal center in the calculated structure (Figure 5a) is distorted octahedral, as found experimentally for the complex (Figure 5b).

Similarly to what was found for the solid state structure, intramolecular H-bonds between the protonated amino groups and the oxygen atoms of the carbonyl groups of tryptophan are observed in the calculated structure.



Fig. 5. (a) Unrestricted CAM-B3LYP optimized molecular structure of the $[Cu(L-trp)_2(H_2O)_4]^{2+}$ complex. (b) ORTEP drawing showing the distorted octahedral geometry of complex **1** as determined experimentally. Symmetry transformations used to generate equivalent atoms are: (i) –x, y, –z.

3.3. Hirshfeld surface analysis

The Hirshfeld surface analysis [30] was performed, using Crystal Explorer 3.1 [31,32], to access details of the intermolecular interactions in the crystal. The Hirshfeld surfaces of complex **1** are illustrated in Figure 6. The surfaces have been mapped over d_{norm} and 2D fingerprint plots (plot of d_i versus d_e), allowing identification of different types of intermolecular interactions. In the figure, the d_{norm} Hirshfeld surfaces are displayed using a red–white–blue colour scheme, where red highlights shorter contacts, white is used for contacts around the r^{vdW} separation, and blue is for longer contacts. As it can be seen from the figure, the O····H interactions are dominant, covering ~33% of the total Hirshfeld surface, with two distinct spikes in the 2D fingerprint plots (see Figure 6b,c), and that can be viewed as dark red spots on the d_{norm} surface (Figure 6a). The C····H and O···O interactions have also a significant contribution to the total Hirshfeld surfaces, as displayed in Figure S3 (Supporting Information).



Fig. 6. (a) Hirshfeld surfaces representation for **1** mapped with d_{norm} with all types of intermolecular interactions considered. (b, c) Fingerprint plots of **1**: (b) all contacts accounted for, and (c) resolved into O⁻⁻H interactions, showing the percentages of contacts contributing to the total Hirshfeld surface area.

3.4. Electronic spectroscopy and results of TD-DFT calculations

The electronic absorption spectrum of $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ (1) was recorded in DMSO (5.12 × 10⁻⁵ M) at room temperature (Figure 7a). The complex exhibits an intense absorption band with a maximum at 370 nm. Interestingly, the tryptophan-picrate complex shows a charge-transfer band at 380 nm, due to the stacking between the indole and the picrate rings, as shown in Figures S4 and S5. For $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ this band is blue shifted to 370 nm, indicating the transfer of some electron density to the metal orbitals, thus suggesting ligand to metal charge-transfer that is coupled with the charge-transfer between the indole and the picrate rings. A weak broad band is also observed at 747 nm, ascribable to a Cu(II) *d*–*d* transition.

TD-DFT calculations were carried out to obtain further information on the nature of the excited states and help interpret the UV-Vis absorption spectrum. The absorption spectrum in

DMSO solution was calculated for both the $[Cu(L-trp)_2(H_2O)_4]^{2+}$ complex and the picrate anion by TD-DFT with the long-range corrected CAM-B3LYP functional, which has been found to give improved results for charge-transfer excitations compared with the B3LYP functional [20]. The simulated absorption spectra are shown in Figure 7b, in comparison with the experimental spectrum for the complex with the picrate anions.



Fig. 7. (a) UV-Visible spectrum of $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ (1) in DMSO; (b) Simulated TD-DFT/CAM-B3LYP absorption spectra for the $[Cu(L-trp)_2(H_2O)_4]^{2+}$ complex (red line) and the picrate anion (black line) in DMSO. Note that the higher energy band seen in the theoretical spectrum of the complex is outside the region studied experimentally.

The comparison of the absorption spectra calculated for the $[Cu(L-trp)_2(H_2O)_4]^{2+}$ complex and for the picrate anions separately (Figure 7b) with the experimental spectrum obtained for the $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ system (Figure 6a), suggests that, in the experimentally observed spectrum, there is a superposition of the absorptions from the two species, and that the picrate anions have a very significant contribution to the total spectrum. Studies undertaken in similar compounds, specifically Cu(glycine)picrate, Cu(phenylalanine)picrate, and tryptophan-picrate confirm the dominance of the picrate bands also in the UV-Vis spectra of these compounds (Figure S5). In fact, since the concentration of picrate anions in solution is twice the concentration of $[Cu(L-trp)_2(H_2O)_4]^{2+}$, the picrate

contribution to the experimental UV-Vis spectrum of the studied compound shall be even larger than it is suggested by Figure 7b. In here, one will first analyze the theoretical spectrum calculated for the core structure of the complex (without taking into account the picrate counterions). The corresponding absorption spectrum was calculated for energies up to 5.3 eV and the vertical excitation energies, oscillator strengths and main contributions to the excited states of $[Cu(L-trp)_2(H_2O)_4]^{2+}$ are summarized in Table 3.

Table 3. TD-DFT/CAM-B3LYP calculated vertical excitation energies (eV), wavelengths (λ / nm), oscillator strengths (*f*) and main contributions to the excited states (only the contributions ≥ 10 % are given) for the [Cu(L-trp)₂(H₂O)₄]²⁺ complex in DMSO.

Energy (eV)	λ (nm)	f^{a}	Main contributions (%)
1.80	689	0.0006	$\text{H-28} \rightarrow \text{L}\beta \ (55\%) + \text{H-27} \rightarrow \text{L}\beta \ (15\%) + \text{H-34} \rightarrow \text{L}\beta \ (11\%)$
3.76	330	0.018	$H \rightarrow L\beta (98\%)$
4.20	295	0.225	$\text{H-10} \rightarrow \text{L}\beta \text{ (56\%)} + \text{H-11} \rightarrow \text{L}\beta \text{ (35\%)}$
4.43	280	0.030	$\text{H-11} \rightarrow \text{L}\beta \text{ (51\%)} + \text{H-10} \rightarrow \text{L}\beta \text{ (23\%)} + \text{H-7} \rightarrow \text{L}\beta \text{ (18\%)}$
4.99	249	0.018	$\text{H-14} \rightarrow \text{L}\beta \text{ (49\%)} + \text{H-12} \rightarrow \text{L}\beta \text{ (34\%)} + \text{H-8} \rightarrow \text{L}\beta \text{ (10\%)}$
5.13	242	0.158	$\mathrm{H} \rightarrow \mathrm{L+2\beta} \ (12\%) + \mathrm{H} \rightarrow \mathrm{L+1\alpha} \ (12\%) + \mathrm{H-2} \rightarrow \mathrm{L+2\beta} \ (10\%) +$
			$H-3 \rightarrow L+1\alpha (10\%)$
5.22	238	0.197	$\text{H-1} \rightarrow \text{L+1}\alpha (12\%) + \text{H-1} \rightarrow \text{L+2}\beta (12\%)$

^{*a*} Results are listed for excited states with oscillator strength ≥ 0.018 and also for the *d*-*d* transition at 689 nm.

The TD-DFT calculations indicate that the absorption spectrum of the complex has three dominant bands in the region studied theoretically, with maxima at 295 nm, 242 nm and 238 nm. The band at 295 nm corresponds to a β -spin HOMO-10 (highest occupied molecular orbital-10) to LUMO (lowest unoccupied molecular orbital) transition (56%), together with a β -spin HOMO-11 \rightarrow LUMO transition (35%). The electronic density distribution in the orbitals involved in these transitions (Figure 8) indicates that this excitation has a dominant ligand to metal charge transfer character (LMCT). The two bands at 242 and 238 nm are very close and are observed in the simulated spectrum (see Figure 7b) as a single band. These bands involve contributions from HOMO β , HOMO-1 β , HOMO-2 β to LUMO+2 β and from HOMO α , HOMO-1 α and HOMO-3 α to LUMO+1 α , and are ligand based transitions with a

dominant $\pi \to \pi^*$ character. The weak band predicted at 689 nm corresponds to the experimental band observed at 747 nm and involves contributions from β -spin HOMO-28 (55%), β -spin HOMO-27 (15%) and β -spin HOMO-34 (11%) to β -spin LUMO. The orbital LUMO β is essentially localized on the metal and to a small extent on the water ligands and on the carboxylic groups. This orbital involves a combination of metal *d* orbitals, with a large contribution from the $d_{x^2-y^2}$ orbital. The orbitals HOMO-28 β , HOMO-27 β and HOMO-34 β are delocalized over the whole molecule, and include significant charge on the metal *d* orbitals. Therefore, the band at 689 nm can be considered to have *d*-*d*, together with LMCT, characters. The remaining excitations listed on Table 3, with absorptions at 330, 280 and 248 nm, are weaker and involve transitions from HOMO β , HOMO-7 β , HOMO-8 β , HOMO-10 β , HOMO-11 β , HOMO-12 β and HOMO-14 β to LUMO β . These are essentially LMCT transitions.

If we consider now the absorption spectrum calculated for the picrate anion, this spectrum reproduces the shape of the experimental UV-Vis spectrum obtained for the [Cu(L-trp)₂(H₂O)₄](pic)₂·4H₂O system in DMSO. The bands are, however, shifted to higher energies by *ca*. 60 nm, which is within the expected error for TD-DFT/CAMB3LYP calculations. Table 4 summarizes the results for the calculated vertical excitation energies, oscillator strengths and main contributions to the excited states of the picrate anion in DMSO solution. The calculated absorption spectrum of the picrate anion has a dominant band with a maximum at 307 nm (experimental maximum at 370 nm), which corresponds to a HOMO \rightarrow LUMO+1 (82%), together with a HOMO-1 \rightarrow LUMO+2 (13%) excitation. A second strong band has its maximum at 367 nm (observed experimentally as a shoulder around 420 nm) and corresponds to a HOMO \rightarrow LUMO (100%) transition. Additional weaker bands have calculated absorption maxima at 222, 193 and 187 nm. Figure 9 shows the molecular orbitals of picrate involved in the main contributions to the excitations at 307 and 367 nm and the

molecular orbitals involved in the weaker excitations at 222, 193 and 187 nm can be seen in the supplementary material (Figure S6).



Fig. 8. Schematic representation of the main contributions to the TD-DFT/CAM-B3LYP calculated excitations for the $[Cu(L-trp)_2(H_2O)_4]^{2+}$ complex.

Table 4. TD-DFT/CAM-B3LYP calculated vertical excitation energies (eV), wavelengths (λ / nm), oscillator strengths (*f*) and main contributions to the excited states (only the contributions > 15 % are given) for the picrate anion in DMSO.

Energy (eV)	λ (nm)	f^a	Main contributions (%)
3.38	367	0.206	$H \rightarrow L (100\%)$
4.04	307	0.328	$H \rightarrow L+1 (82\%) + H-1 \rightarrow L+2 (13\%)$
5.59	222	0.183	$\text{H-2} \rightarrow \text{L} (60\%) + \text{H-5} \rightarrow \text{L} (25\%)$
6.41	193	0.157	H-7 → L (79%)
6.64	187	0.115	$H-8 \to L+1 (72\%)$

^{*a*} Results are listed for excited states with oscillator strength ≥ 0.100 .



Fig. 9. CAM-B3LYP optimized molecular structure of the picrate anion and schematic representation of the main contributions to the TD-DFT/CAM-B3LYP excitations at 307 and 367 nm.

3.5. Thermal analysis

The termal stability of any compoud is the prime feature to use it as functional material. Thereby, thermogravimetric analysis (TGA) measurements were performed for complex **1** under nitrogen atmosphere (Figure **S**7). The first weight loss ~15.75% was observed in the temperature range 25–120 °C which corresponds to loss of nine water molecules. However, there are only eight water molecules present in the crystal lattice. This inconsistancy for one water molecule may be related to the the existance of moisture content in the crystaline sample used for the TGA measurements. The complex **1** is further decomposed in subsequent steps in the range of 190–500 °C, which correspond to the progressive destruction of organic framework.

3.6. EPR spectroscopy studies

The polycrystalline powder EPR spectrum of $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ (1) at room temperature (Figure 10) is characteristic of a typical for axial-type Cu(II) complex with g_{\parallel} $(2.530) > g_{\perp}$ (2.109) > 2.03, suggesting a $d_{x^2-y^2}$ ground state consistent with a distorted octahedral geometry [33]. The $g_{\parallel} > 2.3$ indicates a considerable covalent character [34,35], and the broadening of the spectrum is probably due to spin relaxation. The calculated G

value, $[(g_{\parallel}-2.0023)/(g_{\perp}-2.0023)] > 4$, indicates that the spin exchange interaction between Cu(II) centers in the solid state is negligible [36].



Fig. 10. X-band EPR spectrum of $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ (1).

4. Conclusion

The copper(II)-tryptophan amino acid complex $[Cu(L-trp)_2(H_2O)_4](pic)_2 \cdot 4H_2O$ (1) was prepared and structurally characterized. The metal complex exhibits distorted octahedral geometry (Jahn-Teller distortion), and an unusual tryptophan coordination to copper(II) *via* carboxylate monodentate binding. The picric acid (pic) co-ligand, which is present in the anionic form, resides outside the coordination sphere forming a charge-separated complex.

Comparison between the experimental and theoretical structural results indicates that the structure optimized at the unrestricted DFT/CAM-B3LYP level of theory, with the LANL2DZ (Los Alamos National Laboratory 2 double- ζ) valence and effective core potential (ECP) functions for copper and the standard double- ζ plus polarization 6-31G(d,p) basis set for the remaining atoms, reproduces well that observed in the crystalline phase, with the major differences in the two sets of structural parameters occurring for the parameters associated with the coordination of the four inner sphere water molecules. These differences might be ascribed to the larger uncertainties in the experimental determination of the

parameters of these water molecules and also to the fact that picrate counterions, with which the water ligands are involved in H-bond type interactions, were not included in the calculations.

The electronic structure of the complex was also evaluated theoretically and the UV-Vis spectrum predicted through TD-DFT calculations, the calculated spectrum matching well that obtained experimentally. The calculations also reveal that the electronic spectrum of the compound in solution has a dominant contribution from the picrate ions. In addition, the theoretical results indicate that the LUMO β orbital has a significant contribution from the metal $d_{x^2-y^2}$ orbital, in accordance with the EPR experimental results, and that the main transitions contributing to the observed spectrum involve charge transfer from the ligand to the metal.

The thermal stability of the complex evaluated by TGA. The first weight loss was observed in the temperature range 25–120 °C, and corresponds to loss of water molecules. Subsequent weight losses take place in the 190–500 °C range, and correspond to the progressive destruction of organic framework.

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Highlights

The reaction between $Cu(pic)_2 \cdot 6H_2O$ (pic = picrate anion) and tryptophan (trp) in aqueous solution resulted in a mononuclear Cu(II) complex Cu(L-trp)₂(H₂O)₄](pic)₂·4H₂O, which exhibits an unusual tryptophan coordination to Cu(II) via carboxylate monodentate binding in trans-fashion.