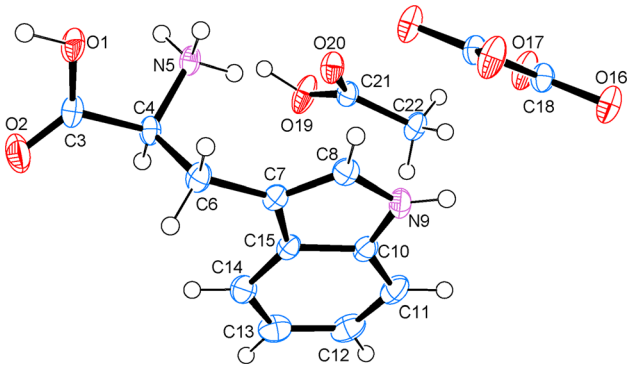
Amina Sayed and Ayesha Jacobs*

Crystal structure of bis(*DL*-1-carboxy-2-(1*H*-indol-3-yl)ethan-1-aminium) oxalate — acetic acid (1/2)



https://doi.org/10.1515/ncrs-2025-0091
Received February 24, 2025; accepted April 2, 2025;
published online April 23, 2025

Abstract

$C_{28}H_{34}N_4O_{12}$, triclinic, $P\bar{1}$ (no. 2), a = 8.5022(17) Å, b = 9.790(2) Å, c = 10.736(2) Å, α = 113.52(3)°, β = 91.93(3)°, γ = 115.68(3)°, V = 715.1(3) Å^3, Z = 2, $R_{gt}(F)$ = 0.0394, w$R_{ref}(F^2)$ = 0.1025, T = 173(2) K.

CCDC no.: 1407908

The molecular structure is shown in the figure. Table 1 contains the crystallographic data.

The list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

Table 1: Data collection and handling.

Crystal:	Colourless plate
Size:	0.32 × 0.28 × 0.11 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.11 mm^{-1}
Diffractometer, scan mode:	Bruker Apex II, ϕ and ω scans
θ_{max}, completeness:	28.4°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	6209, 3578, 0.019
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2,999
$N(param)_{refined}$:	224
Programs:	Bruker,[1,2] WinGX,[3] SHELX[4,5], XSeed[6]

1 Source of materials

DL-1-carboxy-2-(1*H*-indol-3-yl)ethan-1-amine, more commonly known as DL-tryptophan and oxalic acid were purchased from Sigma Aldrich. Acetic acid was obtained from Merck. *DL*-Tryptophan (0.148 mmol, 0.0302 g) and oxalic acid (0.143 mmol, 0.0129 g) were dissolved in 1 mL of acetic acid:water (1:1) with heating. The solution was allowed to cool to room temperature. Slow evaporation of the solution gave plate colourless crystals after 3 weeks.

2 Experimental details

The carboyxlic acid hydrogen atoms, indole hydrogen atom and the aminium hydrogen atoms were located in the difference electron density map and freely refined with isotropic temperature factors. The C–H atoms were geometrically constrained at 0.95 Å for aromatic, 0.98 Å for methyl H atoms and 0.99 Å for methylene H atoms. U_{iso}(H) = 1.2 for aromatic, methylene and tertiary H atoms with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms.

3 Comment

Tryptophan is an α amino acid and can occur in the L- or D-enantiomeric forms. L-tryptophan is an essential amino acid which is acquired through the diet or supplementation.[7] D-tryptophan is produced by probiotic bacteria.[8] Amino

Amina Sayed: Current address: Holistic Drug Discovery and Development Centre (H3D), University of Cape Town, Cape Town 7701, South Africa.

***Corresponding author: Ayesha Jacobs**, Chemistry Department, Faculty of Applied Sciences, Cape Peninsula University of Technology, PO Box 1906, Bellville 7535, South Africa, E-mail: jacobsa@cput.ac.za. https://orcid.org/0000-0002-5508-3291

Amina Sayed, Chemistry Department, Faculty of Applied Sciences, Cape Peninsula University of Technology, PO Box 1906, Bellville 7535, South Africa, E-mail: amina.sayed@uct.ac.za

acids are important biological molecules and thus have been a focus area for crystal engineering studies.[9–11] The crystal structure of *DL*-tryptophan revealed a zwitterion.[12] A multicomponent crystal of (*S*)-tryptophan, acetic acid and water also gave the zwitterionic form of tryptophan.[13] However the crystal structure of *D*-tryptophan with oxalic acid displayed the transfer of a proton from the oxalic acid to the amine nitrogen of tryptophan, forming a salt.[14] We have previously reported salts of tryptophan with *p*-toluenesulphonic and camphorsulphonic acids.[15]

In the crystal structure of bis(*DL*-1-carboxy-2-(1*H*-indol-3-yl)ethan-1-aminium) oxalate acetic acid solvate more commonly named bis(*DL*-tryptophanium) oxalate acetic acid solvate, a proton is transferred from the oxalic acid to the amine nitrogen of tryptophan and the acetic acid remains neutral. The oxalate anion is situated on an inversion centre. The aminium moiety of the tryptophanium cation forms NH···O hydrogen bonds to two acetic acid molecules (N5···O20^a = 2.9719(14) Å; $a = x, y, z$; N5···O20^b = 2.827(2) Å; $b = -x, -y + 1, -z + 1$) and an oxalate anion (N5···O17^b = 2.8404(16) Å). The indole nitrogen forms an NH···O hydrogen bond with the carbonyl oxygen of another tryptophanium cation (N9···O2^c = 3.0209(16) Å; $c = x, y + 1, z$). The carboxylic acid group of the tryptophanium cation forms an OH···O hydrogen bond with the oxalate anion (O1···O17^d = 2.5582(13) Å; $d = x, y - 1, z$). The acetic acid is also hydrogen bonded to the oxalate anion (O19···O16^e = 2.5621(14) Å; $e = x - 1, y - 1, z$).

Two tryptophanium cations and two oxalate anions form $R_4^4(20)$ hydrogen bonded rings. Two tryptophanium cations and two acetic acid molecules form $R_4^2(8)$ rings. Tryptophanium cations and oxalate anions form $C_2^2(10)$ chains, resulting in hydrophilic and hydrophobic layers parallel to [100].

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interest: The authors declare no conflicts of interest regarding this article.

References

1. Bruker Apex2, Saint–Plus and Sadabs; Bruker AXS Inc.: Madison, Wisconsin, USA, 2009.
2. Bruker Xprep; Bruker AXS Inc.: Madison, Wisconsin, USA, 2004.
3. Farrugia, L. J. WinGX and Ortep for Windows: An Update. *J. Appl. Cryst.* **2012**, *45*, 849–854.
4. Sheldrick, G. M. A Short History of Shelx. *Acta Cryst.* **2008**, *A64*, 112–122.
5. Sheldrick, G. M. Crystal Structure Refinement with Shelxl. *Acta Cryst.* **2015**, *C71*, 3–8.
6. Barbour, L. J. *X–Seed*–A Software Tool for Supramolecular Crystallography. *Supramol. Chem.* **2001**, *1*, 189–191.
7. Wu, G. Amino Acids: Metabolism, Functions, and Nutrition. *Amino Acids* **2009**, *37*, 1–17.
8. Kepert, I.; Fonseca, J.; Müller, C.; Milger, K.; Hochwind, K.; Kostric, M.; Fedoseeva, M.; Ohnmacht, C.; Dehmel, S.; Nathan, P.; Bartel, S.; Eickelberg, O.; Schloter, M.; Hartmann, A.; Schmitt-Kopplin, P.; Krauss-Etschmann, S. D-Tryptophan from Probiotic Bacteria Influences the Gut Microbiome and Allergic Airway Disease. *J. Allergy Clin. Immunol.* **2017**, *139*, 1525–1535.
9. Tilborg, A.; Norberg, B.; Wouters, J. Pharmaceutical Salts and Cocrystals Involving Amino Acids: A Brief Structural Overview of the State-Of-Art. *Eur. J. Med. Chem.* **2014**, *74*, 411–426.
10. Görbitz, C. H. Crystal Structures of Amino Acids: From Bond Lengths in glycine to Metal Complexes and High-Pressure Polymorphs. *Crystallogr. Rev.* **2015**, *21*, 160–212.
11. Nugrahani, I.; Jessica, M. A. Amino Acids as the Potential Co-former for Co-crystal Development: A Review. *Molecules* **2021**, *26*, 3279.
12. Hübschle, C. B.; Messerschmidt, M.; Luger, P. Crystal Structure of DL–Tryptophan at 173K. *Cryst. Res. Technol.* **2004**, *39*, 274–278.
13. Li, J.; Liang, Z.-P.; Tai, X.-S. Crystal Structure of (*S*)-2-amino-3-(1*H*-indol-3-yl)propanoic acidate-acetic acid-water (1:1:1), $C_{11}H_{12}N_2O_2{\cdot}CH_3COOH{\cdot}H_2O$. *Z. Kristallogr. N. Cryst. Struct.* **2009**, *224*, 153–154.
14. Bakke, O.; Mostad, M.; Grynfarb, M.; Bartfai, T.; Enzell, C. R. The Structure and Conformation of Tryptophan in the Crystal of the Pure Racemic Compound and the Hydrogen Oxalate. *Acta Chem. Scand.* **1980**, *34*, 559.
15. Sayed, A.; Jacobs, A. Salts of Tryptophan with *p*-Toluenesulphonic Acid and Camphorsulphonic Acids. *J. Chem. Cryst.* **2016**, *46*, 57–66.