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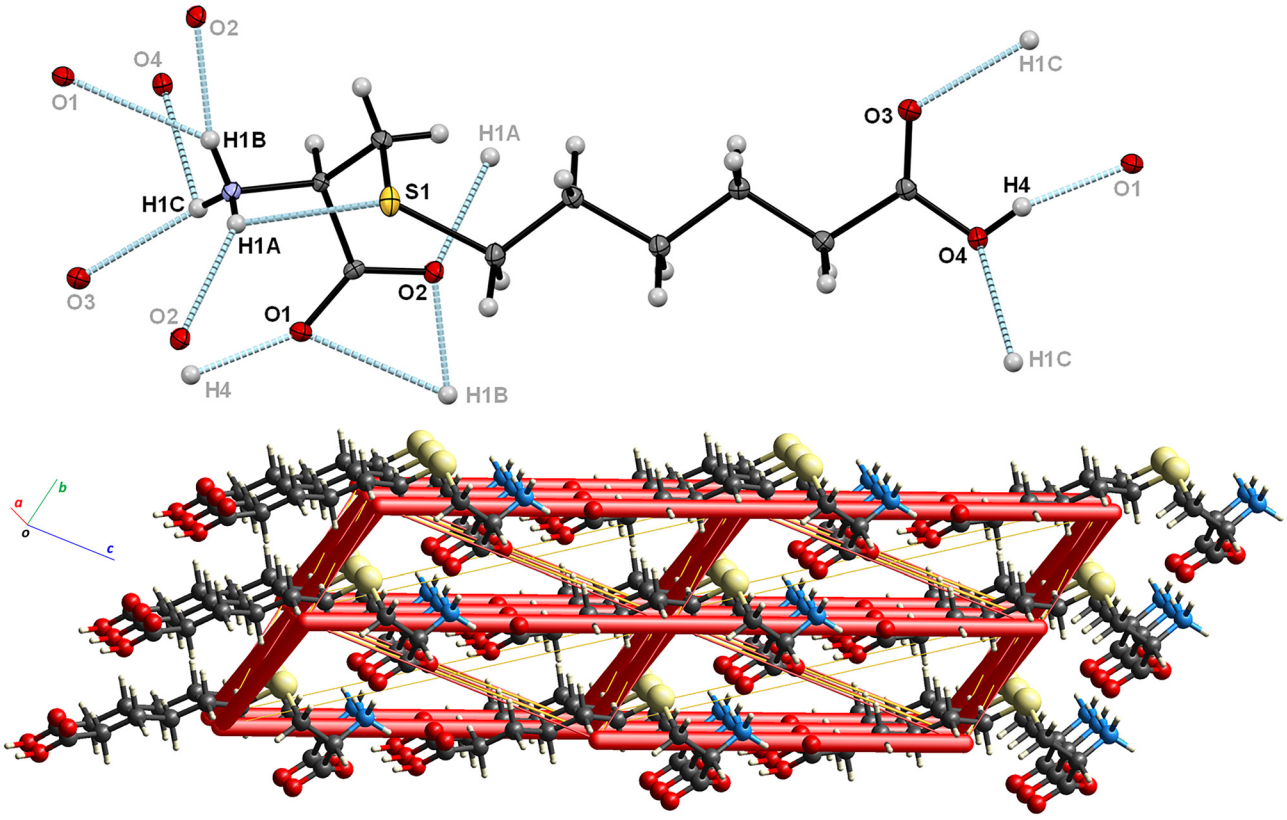
Crystal structure of (*R*)-2-ammonio-3-((5-carboxypentyl)thio)propanoate



https://doi.org/10.1515/ncrs-2025-0244
Received May 22, 2025; accepted June 23, 2025;
published online June 30, 2025

Abstract

$C_9H_{17}NO_4S$, triclinic, *P*1 (no. 1), a = 5.0048(2) Å, b = 5.1695(2) Å, c = 11.2674(6) Å, α = 77.311(2)°, β = 87.484(2)°, γ = 68.867(2)°, V = 265.07(2) Å^3, Z = 1, $R_{gt}(F)$ = 0.0259, w$R_{ref}(F^2)$ = 0.0663, T = 100 K.

CCDC no.: 2466334

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The molecular structure, hydrogen bonds, a part of the title crystal structure and the electrostatic energy framework are both 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:	Clear colourless needle
Size:	0.31 × 0.05 × 0.02 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.30 mm^{-1}
Diffractometer, scan mode:	Bruker APEX 2, φ and ω scans
θ_{max}, completeness:	32.1°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	11384, 3517, 0.019
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 3433
$N(param)_{refined}$:	187
Programs:	Bruker,[1] SHELX,[2,3] Olex2[4]

1 Source of materials

L-Cysteine (12.1 g, 0.1 mol) and 5-hexenoic acid (12.6 g, 0.11 mol) were dissolved in 500 ml of water containing 4.4 g (0.11 mol) of NaOH and left overnight at room temperature. The solution was acidified with 6.6 ml (0.11 mol) of glacial acetic acid and placed into a refrigerator for 2 days at 4 °C to form colourless needles. The crystalline mass of chromatographically pure CPnC was then filtered out, washed with cold 95 % ethanol, and used for analysis and subsequent diffraction studies. Elemental analysis. Calc. for $C_9H_{17}NO_4S$: N, 5.95 %. Found: N, 5.92 %. Exact mass of the $[M+H]^+$ ion in ESI mass-spectrum. Calc. for $C_9H_{18}NO_4S$: *m*/*z* 236.10. Found: *m*/*z* 236.09. Specific optical rotation $[\alpha]_D^{23} = -0.4°$ (c 1, 0.2 N HCl).

2 Experimental details

Crystal data, data collection and structure refinement details are summarized in Table 1. The Flack absolute structure parameter determined (–0.01(2) for 166 quotients[5]) is consistent with the (2*R*) configuration, which was assigned for this molecule on the basis of the known configuration for the starting material L-cysteine. The hydroxyl and ammonium hydrogen atoms were located in difference Fourier maps and were allowed to refine freely. The remaining H-atoms were placed at calculated positions and included in the refinement using a riding model. All hydrogen atom thermal parameters were constrained to ride on the carrier atoms (U_{iso}(methine H) = 1.2U_{eq} and U_{iso}(methyl H) = 1.5U_{eq}).

3 Comment

Thioether-containing amino acids are an important and interesting class of biologically significant molecules, which are represented by the essential for all life forms methionine, lanthionine-based antibiotics,[6] or a natural insecticide *S*-(2-carboxyethyl)-L-cysteine (*β*-CEC).[7] *In cellula*, we demonstrated that *β*-CEC, along with a homologous mucolytic drug *S*-carboxymethyl-L-cysteine (carbocisteine, CMC[8]) possess the anti-inflammatory and antioxidant potential, the ability to mitigate cytotoxicity of heavy metals and organic pollutants.[9,10] In continuation of these studies, we have synthesized the title compound, *S*-(5-carboxypentyl)-L-cysteine (CPnC), and report its molecular and crystal structure.

CPnC crystallizes in the acentric, triclinic *P*1 space group, with a single molecule per unit cell. The molecular structure with the atomic numbering and displacement ellipsoids at the 50 % probability level is shown in the figure generated by Mercury.[11] The valence bond lengths and angles of this dicarboxylic amino acid are in the expected ranges. The molecule exists as a zwitterion, with positively charged protonated *α*-amino group and negatively charged deprotonated *α*-carboxylic group. The carboxypentylthio portion of the molecule is essentially flat, with all non-hydrogen atoms located within 0.1 Å from the mean plane involving the O3, O4, C3, C4, C5, C6, C7, C8, and S1 atoms. There is a weak intramolecular hydrogen bond between the ammonium donor and thioether acceptor heteroatoms (N1···S1 = 3.1223(15) Å, H1*A*···S1 = 2.71(3) Å, N1–H1*C*···S1 = 113(3)°). The conventional hydrogen bonding in crystal structure of CPnC involves all heteroatoms, and forms network layers propagating in parallel to (001). Each layer is formed by a system of intercrossing chains. In the [010] direction, the hetero-atomic chain ···H1*C*–N1–H1*B*···O1···H4–O4···H1*C*–N1–H1*B*··· incorporates the shortest hetero atom contact formed between the *α*- and *θ*-carboxylic groups (O4···O1′ = 2.610(2) Å, H4···O1′ = 1.80(3) Å, O4–H4···O1′ = 166(3)°, ′ = *x*, –1 + *y*, –1 + *z*). In the [100] direction, the antidromic chain ···H1*C*···O3–C8–O4···H1*C*··· and the antidromic chain ···H1*A*–N1–H1*B*···O2···H1*A*–N1–H1*B*···O2··· feature bifurcated H-bonds at the H1*C* and the O2 atoms, respectively. The network is reinforced by the short C1–H1···O1 and C7–H7*A*···O3 contacts contributing to the polar interactions in the crystal structure, as well. Both the molecular and crystal structure of CPnC bear a significant degree of similarity to the homologous *S*-(carboxyalkyl)-L-cysteines.[10,12]

To account for all interactions contributing to the crystal structure, we have performed DFT calculations, at the B3LYP/6-31 G(d,p) theory level,[13,14] of the electrostatic, dispersion, polarization, and repulsion energies in the crystal structure. According to the calculations, the interactions between pairs of molecules linked *via* the three-centered O1″···H1*B*···O2″ hydrogen bond (″ = –1 + *x*, 1 + *y*, *z*) provided the largest contribution, about 42 %, to the lattice energy, with the electrostatic interactions contributing the most for the attractive forces between neighbouring CPnC molecules (*i.e.* E_{elstat} = –121.2 kJ/mol, $E_{polarization}$ = –32.2 kJ/mol for 2 – *x*, –1/2 + *y*, 1/2 – *z*). The spatial distribution of the energetically most significant interactions is illustrated in the figure, showing the electrostatic energy framework as red cylinders penetrating the crystal lattice of CPnC. The cylinders connect centroids of the interacting molecules, and their diameters are proportional to the total energies of the interactions, with the 5 kJ/mol cut-off, for clarity. To estimate the total structural energy, all energies of unique pairwise interactions between molecules were integrated, thus yielding E_{total} = –312.3 kJ/mol for the CPnC crystal.

Research funding: We gratefully acknowledge financial support by the University of Missouri Agriculture Experiment Station Chemical Laboratories and by the USDA National Institute of Food and Agriculture (Hatch project 1023929).

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