

The Crystal and Molecular Structure of 3-[(5*S*)-5-Carboxy-2-oxotetrahydrofuran-5-yl]- (2*S*)-alanine (Lycoperdic Acid)

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The crystal structure of a new dicarboxylic amino acid, isolated from the mushroom *Lycoperdon perlatum*, has been solved by direct methods and refined by full-matrix least squares to $R = 0.059$ for 930 independent reflexions measured on a diffractometer. Crystals of $C_8H_{11}NO_6$ are orthorhombic, space group $P2_12_12_1$, with $a = 6.411$ (2), $b = 22.889$ (5), $c = 6.270$ (2) Å, $Z = 4$. The folded conformation of the molecule is presumably related to the presence of an intramolecular N—H...O bond. Molecular packing is determined by a system of two N—H...O and one O—H...O intermolecular bonds.

Introduction

The title compound was isolated from the mushroom *Lycoperdon perlatum* in the course of research on the distribution of various amino acids and peptides in Basidiomycetes. It was identified by chemical methods as a new dicarboxylic amino acid (lycoperdic acid) with the formula depicted in Fig. 1(a).

The *S* configuration at C(2) was determined by chemical methods (Rhugenda-Banga, Welter, Jadot & Casimir, 1978).

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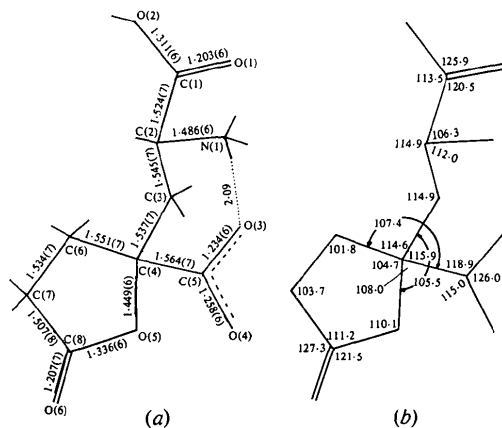


Fig. 1. Lycoperdic acid: (a) atom labelling and bond lengths (Å); (b) bond angles (°).

This investigation was carried out to determine the molecular structure of the new compound, particularly the configuration at C(4).

Experimental

Crystals of the title compound were obtained by slow evaporation from a water–ethanol solution. Weissenberg photographs indicated the orthorhombic space group $P2_12_12_1$. The unit-cell dimensions, together with other crystal data, are given in Table 1. Measurements of the intensities of 983 independent reflexions were performed on a Hilger & Watts four-circle diffractometer with Cu $K\alpha$ radiation (up to $2\theta = 140^\circ$) using a crystal $0.50 \times 0.33 \times 0.25$ mm.

From the collected data, 35 reflexions with $I < 2\sigma(I)$ were treated as unobserved.

Determination and refinement of the structure

The structure was solved by direct methods using the *MULTAN 77* system of programs (Main, Lessinger,

Table 1. Crystal data

$C_8H_{11}NO_6$	Z	4
Orthorhombic, $P2_12_12_1$	D_x	1.567 g cm ⁻³
a 6.411 (2) Å	FW	217.18
b 22.889 (5)	$F(000)$	456
c 6.270 (2)	$\lambda(\text{Cu } K\alpha)$	1.5418 Å
V 920.07 Å ³	$\mu(\text{Cu } K\alpha)$	11.952 cm ⁻¹

Woolfson, Germain & Declercq, 1977). From 200 reflexions with $|E| > 1.28$, 24 sets of phases were obtained using the 'magic-integer' phase permutation. The E map corresponding to a phase set with the highest combined figure of merit (2.91) revealed the positions of all non-hydrogen atoms. The value of R at this stage was 0.36.

Two cycles of block-diagonal least-squares refinement of positions and isotropic temperature factors gave $R = 0.146$. This was reduced to 0.090 after four subsequent cycles of anisotropic refinement.

At this stage the positions of H atoms bonded to C were calculated from geometrical considerations. With these positions fixed, and constant B values of 2.0 \AA^2 , two cycles of refinement yielded $R = 0.077$. The difference Fourier synthesis then revealed four peaks, three close to N(1) and one close to O(2). However, these peaks showed bond lengths and angles highly distorted from the expected geometry and also from the directions of intermolecular $\text{N} \cdots \text{O}$ hydrogen bonding. Therefore, the positions of the H atoms were calculated with the assumption of tetrahedral geometry at N(1) and the existence of intermolecular hydrogen bonds between O(2) and O(4).

Table 2. List of programs used

Operation	Name	Origin
Data reduction	<i>DATRED</i>	Adapted from Main (1970)
Direct methods	<i>MULTAN 77</i>	Main <i>et al.</i> (1977)
Refinement (block-diagonal)	<i>NRC-10</i>	Ahmed, Hall, Pippy & Saunderson (1967)
Calculation of H-positions	<i>HFINDR</i>	Zalkin & Ward (1974)
Bond lengths and valency angles	<i>NRC-12</i>	Ahmed <i>et al.</i> (1967)
Mean planes	<i>NRC-22</i>	Ahmed <i>et al.</i> (1967)
Torsional angles	<i>TORS</i>	Local program (Dupont)
Representations of the molecule and the structure	<i>ORTEP II</i>	Johnson (1971)

Table 3. The final fractional positional coordinates ($\times 10^4$) with their *e.s.d.*'s in parentheses

	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	-1214 (8)	4199 (2)	11163 (8)
C(2)	254 (7)	4085 (2)	9297 (8)
C(3)	2522 (8)	3936 (2)	9931 (7)
C(4)	3831 (8)	3854 (2)	8156 (8)
C(5)	4776 (8)	4082 (2)	6471 (8)
C(6)	2704 (9)	3160 (2)	6914 (9)
C(7)	4497 (9)	2731 (2)	6490 (10)
C(8)	6077 (9)	2880 (2)	8185 (10)
N(1)	140 (7)	4613 (2)	7921 (7)
O(1)	-2560 (6)	4564 (2)	11029 (7)
O(2)	-916 (6)	3846 (2)	12780 (6)
O(3)	3661 (6)	4471 (2)	5726 (6)
O(4)	6640 (5)	3981 (2)	5963 (6)
O(5)	5540 (5)	3364 (1)	9237 (6)
O(6)	7634 (7)	2610 (2)	8635 (7)

The positions of all the H atoms and their isotropic temperature factors taken as $B = 2.0 \text{ \AA}^2$ were then included in the structure factor calculations but not refined. Convergence was obtained after two cycles at $R_1 = 0.059$ (if 18 reflexions with $\Delta F > 0.5F_o$ were excluded) and at $R_2 = 0.069$ (for the whole set of 948 observed reflexions).

The weight of an individual reflexion was $w = 1$ throughout, as this weighting function proved to give the best distribution of $w(\Delta F)^2$ values.

The atomic scattering factors were those given by Hanson, Herman, Lea & Skillman (1964). All calculations were carried out on a IBM 370/158 computer in the Computing Centre of the University of Liège. The programs used are listed in Table 2. The final atomic positions are given in Table 3.*

Discussion

Molecular geometry

A stereoscopic view of the molecule is depicted in Fig. 2.

The bond lengths and angles shown in Fig. 1(a) and (b), respectively, are consistent with literature data for similar amino acids, and for compounds containing a lactone system. One comparatively long distance, C(4)–C(5), should be noted.

Since the *S* configuration at C(2) agrees with that revealed by chemical methods (Rhugenda-Banga *et al.*, 1978), the enantiomorph described here can be accepted as correct: the configuration at C(4) in the enantiomorph is *S*.

The carbonyl C–O distances suggest the presence of an H atom at O(2) in the α group C(1)–O(2)–O(1) and deprotonation of the δ group C(5)–O(3)–O(4).

* Lists of structure factors, anisotropic thermal parameters, and calculated positional coordinates for H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33813 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

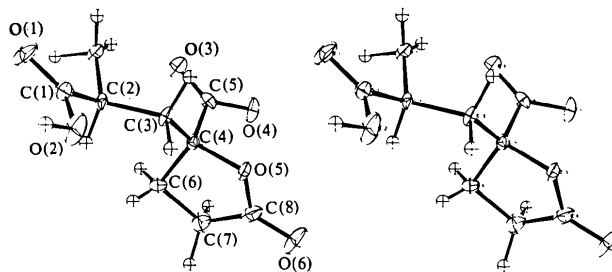


Fig. 2. A stereoscopic view of the molecule.

This is rather unexpected, since in most dicarboxylic amino acids deprotonation takes place first at the α carboxyl group (for example, Dupont, Dideberg & Welter, 1975; Lehmann, Koetzle & Hamilton, 1972; Derissen, Endeman & Peerdeman, 1968).

Table 4. *Geometry of the N(1) environment*

Symmetry code			
(i)	$-x + 0.5,$	$-y + 1,$	$z + 0.5$
(ii)	$-x - 0.5,$	$-y + 1,$	$z - 0.5$
N(1)···O(3)	2.66 Å	C(2)–N(1)–O(3)	99.2°
N(1)···O(3 ^b)	2.84	C(2)–N(1)–O(3 ^b)	103.1
N(1)···O(1 ⁱⁱ)	2.77	C(2)–N(1)–O(1 ⁱⁱ)	146.1
		O(3)–N(1)–O(3 ^b)	100.4
		O(3)–N(1)–O(1 ⁱⁱ)	111.5

Table 5. *Torsion angles (°)*

Amino acid moiety	Biochemical nomenclature		
		(a)	(b)
N(1)C(2)C(1)O(1)	$\psi^1 \text{NC}^\alpha \text{CO}^1$	19.6	12
N(1)C(2)C(1)O(2)	$\psi^2 \text{NC}^\alpha \text{CO}^2$	–164.0	–168
C(3)C(2)C(1)O(1)		143.9	
C(3)C(2)C(1)O(2)		–39.7	
C(1)C(2)C(3)C(4)		163.3	
N(1)C(2)C(3)C(4)	$\chi^1 \text{NC}^\alpha \text{C}^\beta \text{C}^\gamma$	–75.6	71
C(2)C(3)C(4)C(6)		–45.2	
C(2)C(3)C(4)O(5)		–159.8	
C(2)C(3)C(4)C(5)	$\chi^2 \text{C}^\alpha \text{C}^\beta \text{C}^\gamma \text{C}^\delta$	80.7	–92
C(3)C(4)C(5)O(3)	$\chi^{3,1} \text{C}^\beta \text{C}^\gamma \text{C}^\delta \text{O}^\epsilon$	–44.9	55
C(3)C(4)C(5)O(4)	$\chi^{3,2} \text{C}^\beta \text{C}^\gamma \text{C}^\delta \text{O}^\epsilon$	136.8	–123
C(6)C(4)C(5)O(4)		–93.6	
O(5)C(4)C(5)O(4)		18.8	
O(6)C(4)C(5)O(3)		84.6	
O(5)C(4)C(5)O(3)		–162.9	

Lactone moiety

	(a)	(c)	(d)	(e)				(f)
				(R = R' = H)	(R = CH ₃ , R' = H; Z)	(R = CH ₃ , R' = H; E)	R = R' = CH ₃	
C(3)C(4)O(5)C(8)	146.7							
C(6)C(4)O(5)C(8)	25.4			–21.0	16.2	–15.3	–17.2	–25.1
C(5)C(4)O(5)C(8)	–88.8							
C(4)O(5)C(8)O(6)	170.2							
C(4)O(5)C(8)C(7)	–10.8	4; 5	–3.0	4.5	2.1	–5.1	–0.9	7.9
O(5)C(8)C(7)C(6)	–8.5	16	–17.7	14.3	–19.6	23.7	18.4	13.0
O(6)C(8)C(7)C(6)	170.4							
C(8)C(7)C(6)C(4)	22.3	–28; 29	29.9	–25.9	28.3	–31.4	–27.6	–27.1
C(7)C(6)C(4)O(5)	–28.8	31	–31.2	28.4	–27.6	29.1	28.0	31.5
C(7)C(6)C(4)C(3)	–143.9							
C(7)C(6)C(4)C(5)	85.9							
Deviation (Å) of C(6) from the least-squares plane C(4)O(5)C(8)C(7)	0.43		0.52	0.361	–	0.570		

(a) This work. (b) Glutamato bis(ethylenediamine)cobalt(III) (Gillard, Payne & Robertson, 1970). (c) 6,7-Dihydrocanrenone (Surcouf, 1977, 1978). (d) Dendrosterone (Berg, Karlsson, Pilotti & Söderholm, 1977). (e) 2,2-*R,R'*-4-Benzyl-4-phenylbutanoic 1,4-lactones (Harlow & Simonsen, 1976). (f) Canrenone (Weeks, Hazel & Duax, 1976).

The N atom is protonated and involved in three hydrogen bonds; the environment of N(1) is described in Table 4. The occurrence of the intramolecular bond N(1)···O(3) is most probably responsible for the conformation corresponding to the idealized values $-60, 60^\circ$ of the torsion angles χ^1, χ^2 (Table 4) (IUPAC–IUB Commission on Biochemical Nomenclature, 1970).

This combination was described as energetically unfavourable by Ponnuswamy & Sasisekharan (1971) in their theoretical study of conformations of amino acids with δ atoms. However, they did not take into account the possibility of hydrogen-bond formation between the N atom and one of the side-chain atoms. The conformation of lycoperdic acid can be classified as folded, by analogy with the conformations of glutamic acid, which correspond to χ^1, χ^2 combinations of $(-60, -60^\circ)$ and $(60, -60^\circ)$ (Bhat & Vijayan, 1977). The last case is that of glutamatobis(ethylenediamine)cobalt(III) perchlorate (Gillard, Payne & Robertson, 1970) where an intramolecular hydrogen bond between the N atom and an O atom of the δ carboxyl group was also found.

As can be seen from Table 6 [and from the torsion angles about C(2)–C(1) (Table 5)], O(1), O(2), C(1), C(2) and N(1) are almost coplanar, the deviation from planarity being comparable to that found in the glutamic acid chelate mentioned above.

Some other relevant planes, together with the dihedral angles between them, are listed in Table 6.

The conformation of the lactone ring is an envelope, with C(6) deviating by 0.43 Å from the mean plane through C(4), C(7), C(8) and O(5) (Table 6). Very similar geometry for this moiety was observed in

various compounds containing a lactone ring, as shown by a comparison of torsion angles (Table 5).

Molecular packing

As shown in Figs. 3 and 4, the structure can be formally described as consisting of molecular layers parallel to the (010) plane. The layers are formed by

chains along the *a* direction interlinked *via* hydrogen bonds N(1)···O(3^I) and N(1)···O(1^{II}).

The molecules in the chains interact through short O(4)–O(2) hydrogen bonds, very similar to those described by Lehmann, Koetzle & Hamilton (1972). Adjacent layers seem to cohere only *via* van der Waals forces. The following distances correspond to the inter-layer contacts shorter than 3.5 Å: C(8)···O(6) 3.18, O(5)···O(6) 3.20 Å, the coordinates of O(6) being (*x* – 0.5, –*y* + 0.5, –*z* + 2).

Table 6. Distances (Å × 10⁴) of atoms from the least-squares planes

E.s.d.'s are in parentheses.

	1	2	3	4	5
C(1)			8 (5)		
C(2)			158 (5)*		
C(3)			–715 (9)		
C(4)	31 (5)*	0.0*		–2 (5)*	40 (5)*
C(5)				–9 (5)*	
C(6)	–433 (5)	0.0*			–597 (5)
C(7)	30 (6)*	0.0*			282 (6)
C(8)	55 (6)*				–63 (6)*
N(1)			–129 (4)*		
O(1)			60 (4)*		
O(2)			–98 (4)*		
O(3)				3 (4)*	
O(4)				3 (4)*	
O(5)	56 (3)*				–29 (3)*
O(6)	185 (4)				53 (4)*

Dihedral angles (°) between the planes

1–2	26.5	3–4	22.9	1–5	6.9
1–4	89.9	1–3	110.5		

* Atoms used to define the planes.

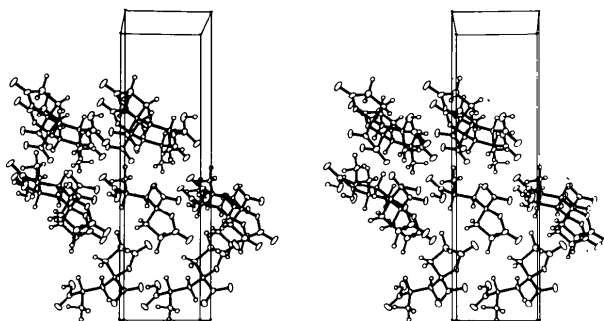


Fig. 3. A stereoscopic view of the structure.

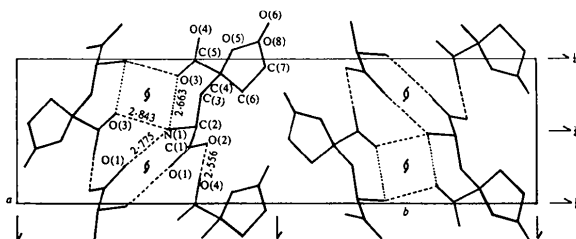


Fig. 4. The structure projected along *c*.

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