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Structure of *N*-Salicyloylglycine, $C_9H_9NO_4$

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Abstract. $M_r = 195{\cdot}18$, monoclinic, $P2_1/c$, $a = 13{\cdot}977\ (4)$, $b = 5{\cdot}064\ (2)$, $c = 13{\cdot}127\ (5)$ Å, $\beta = 105{\cdot}31\ (4)°$, $V = 896{\cdot}2\ (6)$ Å^3, $Z = 4$, $D_x = 1{\cdot}45$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}73$ cm^{-1}, $F(000) = 408$, $T = 293$ K, $R = 0{\cdot}045$ for 601 observed reflections. The non-H atoms of the molecule are moderately coplanar, the largest deviation from the least-squares plane amounts to 0·18 (1) Å. The peptide link has the *trans* configuration. The amide N–H group donates an intramolecular H bond to phenolic OH, which donates an intermolecular H bond to the oxo O atom of the peptide link. The carboxyl groups form dimer-type cyclic H bonds across centres of symmetry.

Introduction. In the human organism the well-known drug acetylsalicylic acid is hydrolysed and the toxic hydrolysis product, salicylic acid, is detoxicated by coupling with amino acids, particularly glycine, to form non-toxic peptide-like derivatives (Frömming & Vollenberg, 1966). The aim of this investigation is to determine the crystal structure of the title compound, which can be considered as the first member of the class of peptide-like amino-acid derivatives of salicylic acid.

Experimental. Crystals obtained from Dr Mukerjee, Pure Chemistry Department, Science College, University of Calcutta. Crystal 0·6 × 0·4 × 0·05 mm, Enraf–Nonius CAD-4F diffractometer, Zr-filtered Mo $K\alpha$ radiation, ω–2θ scan with $\omega = 0{\cdot}40° + 0{\cdot}35°\tan\theta$, lattice parameters from 17 reflections in the range $\theta = 5{\cdot}6$–$8{\cdot}0°$, 1771 intensities measured in the quadrant $0 \le h \le 15$, $0 \le k \le 5$, $-16 \le l \le 16$ with $2\theta_{max} = 50°$. Compound very sensitive to exposure of X-rays; 1 periodically measured standard reflection showed gradual decline of intensity of about 35%. Decay corrected for by polynomial fit, resulting in 601 reflections above $3{\cdot}5\sigma(I)$. level. Structure solved with *MULTAN* (Germain, Main & Woolfson, 1971), all H atoms located from difference maps and included in weighted anisotropic full-matrix refinement on F with isotropic thermal parameters, except carboxylic H, which was assigned thermal parameter equal to that of carrier atom. $R = 0{\cdot}045$, $wR(=\sum w^{1/2}\big||F_o| - |F_c|\big|/\sum w^{1/2}F_o) = 0{\cdot}046$, $w = [\sigma^2(F_o) + 0{\cdot}000928F_o^2]^{-1}$, $S = 1{\cdot}27$. Max. Δ/σ 0·014 and 0·024 for non-H and H parameters respectively. Final difference maps revealed electron densities between 0·30 and $-0{\cdot}18$ e Å^{-3}. Scattering factors from *International Tables for X-ray Crystallography* (1974). All calculations performed with *MULTAN*, *SHELX* (Sheldrick, 1976) and the *EUCLID* package (Spek, 1982) on the CDC Cyber-175 computer of the University of Utrecht.

Discussion. The atomic coordinates and equivalent isotropic temperature factors are listed in Table 1,* a view of the molecule with atomic numbering is shown in Fig. 1 and bond lengths, bond angles and torsion angles are presented in Table 2.

The non-H atoms of the molecule are moderately coplanar, the average deviation from the best plane amounts to 0·06 (5) Å.

The peptide-like linkage has the *trans* configuration, as follows from the values of the characteristic torsion angles ω[C(1)–C(7)–N–C(8)] and φ[C(7)–N–C(8)–C(9)], which are $-179{\cdot}3$ (6) and $-175{\cdot}5$ (5)°, respectively. The ranges of the bond lengths and angles of the benzene ring are rather wide, 1·363 (10)–1·408 (8) Å and 116·8 (5)–122·4 (6)°, respectively, but they compare well with those observed in the salicyloyl fragment of *N*-picolinylidene-*N'*-salicyloylhydrazine (Domiano, Musatti, Pelizzi & Predieri, 1974), where the bond lengths range from 1·377 (7) to 1·412 (7) Å and the angles from 117·8 (4) to 122·5 (4)°, with an average difference of corresponding distances and angles of 0·014 (7) Å and 1·1 (7)°, respectively.

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39837 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Atomic coordinates and equivalent isotropic thermal parameters* (Å² ×100) *with e.s.d.'s in parentheses*

$$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
O(1)	0·0166 (4)	0·8996 (11)	0·3691 (4)	5·7 (2)
O(2)	0·0713 (2)	0·7454 (8)	0·5329 (3)	4·8 (1)
O(3)	0·2654 (3)	0·1876 (9)	0·3699 (3)	6·1 (2)
O(4)	0·2188 (3)	0·1980 (9)	0·6688 (3)	4·8 (2)
N	0·1860 (3)	0·3864 (11)	0·4758 (4)	4·3 (2)
C(1)	0·3046 (4)	0·0428 (12)	0·5465 (4)	3·4 (2)
C(2)	0·2881 (4)	0·0329 (12)	0·6471 (4)	3·5 (2)
C(3)	0·3387 (4)	−0·1472 (14)	0·7200 (4)	4·7 (2)
C(4)	0·4083 (5)	−0·3154 (14)	0·6993 (5)	5·1 (3)
C(5)	0·4281 (5)	−0·3024 (15)	0·6015 (5)	5·5 (3)
C(6)	0·3771 (4)	−0·1293 (14)	0·5274 (5)	4·3 (2)
C(7)	0·2516 (4)	0·2126 (13)	0·4591 (4)	3·9 (2)
C(8)	0·1305 (5)	0·5572 (15)	0·3942 (5)	4·1 (2)
C(9)	0·0699 (4)	0·7419 (13)	0·4398 (4)	3·6 (2)

Table 2. *Interatomic distances* (Å), *bond angles* (°) *and torsion angles* (°)

O(1)–C(9)	1·300 (8)	C(1)–C(6)	1·408 (8)
O(2)–C(9)	1·217 (7)	C(2)–C(3)	1·375 (8)
O(3)–C(7)	1·242 (7)	C(3)–C(4)	1·373 (9)
O(4)–C(2)	1·365 (7)	C(4)–C(5)	1·385 (10)
N–C(8)	1·435 (9)	C(5)–C(6)	1·363 (10)
N–C(7)	1·330 (8)	C(8)–C(9)	1·489 (9)
C(1)–C(2)	1·400 (8)		
C(1)–C(7)	1·468 (8)		

C(7)–N–C(8)	122·4 (5)	C(4)–C(5)–C(6)	119·8 (6)
C(2)–C(1)–C(6)	116·8 (5)	C(1)–C(6)–C(5)	122·4 (6)
C(2)–C(1)–C(7)	125·7 (5)	O(3)–C(7)–N	120·5 (5)
C(6)–C(1)–C(7)	117·5 (5)	N–C(7)–C(1)	119·1 (5)
O(4)–C(2)–C(1)	118·5 (5)	O(3)–C(7)–C(1)	120·3 (5)
O(4)–C(2)–C(3)	121·6 (5)	N–C(8)–C(9)	109·4 (5)
C(1)–C(2)–C(3)	119·9 (5)	O(1)–C(9)–O(2)	124·2 (6)
C(2)–C(3)–C(4)	122·3 (5)	O(1)–C(9)–C(8)	112·2 (5)
C(3)–C(4)–C(5)	118·7 (6)	O(2)–C(9)–C(8)	123·5 (5)

C(8)–N–C(7)–O(3)	−1·8 (9)
C(8)–N–C(7)–C(1)	−179·3 (5)
C(7)–N–C(8)–C(9)	−175·5 (5)
C(6)–C(1)–C(2)–O(4)	179·6 (5)
C(6)–C(1)–C(2)–C(3)	−2·7 (8)
C(7)–C(1)–C(2)–O(4)	−1·7 (9)
C(7)–C(1)–C(2)–C(3)	176·0 (6)
C(2)–C(1)–C(6)–C(5)	1·3 (9)
C(7)–C(1)–C(6)–C(5)	−177·5 (6)
C(2)–C(1)–C(7)–N	4·5 (9)
C(2)–C(1)–C(7)–O(3)	−173·0 (6)
C(6)–C(1)–C(7)–N	−176·8 (5)
C(6)–C(1)–C(7)–O(3)	5·6 (8)
O(4)–C(2)–C(3)–C(4)	179·7 (6)
C(1)–C(2)–C(3)–C(4)	2·1 (9)
C(2)–C(3)–C(4)–C(5)	0·1 (10)
C(3)–C(4)–C(5)–C(6)	−1·5 (10)
C(4)–C(5)–C(6)–C(1)	0·8 (10)
N–C(8)–C(9)–O(1)	−179·0 (5)
N–C(8)–C(9)–O(2)	1·7 (9)

Table 3. *Hydrogen-bond distances* (Å) *and angles* (°)

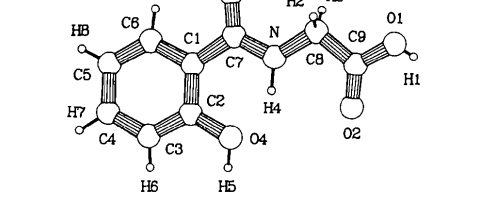
D–H···*A*	*D*···*A*	*D*–H	H···*A*	*D*–H···*A*	Symmetry operation*
O(1)–H(1)···O(2)	2·689 (7)	0·67 (7)	2·03 (7)	168 (8)	3576
N–H(4)···O(4)	2·632 (7)	0·96 (5)	1·80 (5)	143 (5)	1555
O(4)–H(5)···O(3)	2·612 (6)	0·96 (7)	1·65 (7)	177 (7)	4555

* The symmetry operation is performed on the acceptor O atoms. The first digit indicates one of the following symmetry operations: (1) x, y, z; (2) $-x, \frac{1}{2}+y, \frac{1}{2}-z$; (3) $-x, -y, -z$; (4) $x, \frac{1}{2}-y, \frac{1}{2}+z$. The other digits indicate the lattice translations, *e.g.* 3467 is $-a, +b, +2c$ from 3555.

The geometry of the peptide link is normal and in agreement with that found in *trans* peptides (Marsh & Donohue, 1967; Benedetti, 1982).

In the crystal structure there are three H bonds (Table 3); one is intramolecular, connecting the N–H donor to the phenolic O(4) acceptor, and two are intermolecular, involving phenolic O(4)–H as a donor and oxo O(3) as an acceptor, and two centrosymmetrically related carboxyl groups respectively. The O(4)–H···O(3) bonds form infinite chains in the **c** direction, propagated by the *c* glide plane (Fig. 2). The molecules in this chain are side-ways connected to two similar chains by centrosymmetric carboxylic-acid dimer-type H bonds. Because of the skew orientation of the carboxyl group with respect to the glide plane, the separation between these two chains is three translations along **b**.

This H-bond pattern can be schematically represented by the coded sequence



in which single arrows denote the H bonds generated by the glide plane, the double arrows relate to the

Fig. 1. A view of the *N*-salicyloylglycine molecule with atom numbering.

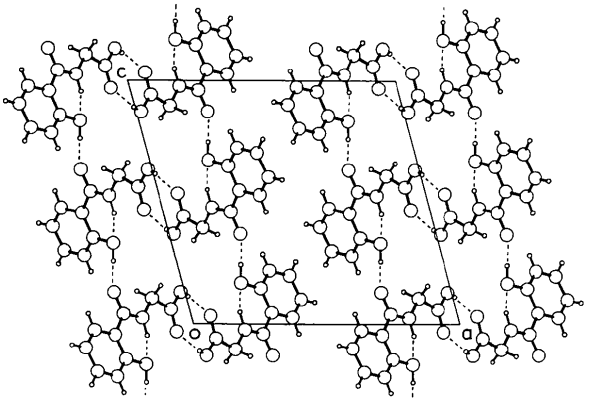


Fig. 2. Projection of the crystal structure along **b**. H bonds are denoted by dashed lines.

acid-dimer H bonds and the symmetry code is that given in Table 3. In this way these H bonds constitute a closely packed interwoven structure parallel to the *bc* plane, whereas the interactions in the **a** direction only involve the peripheral non-polar part of the molecule. Here, only one short intermolecular contact, of 2·76 (5) Å, between C(4) of the benzene ring and H(7) at $1-x, \frac{1}{2}+y, \frac{3}{2}-z$ is worth mentioning.

All C···C contacts are larger than 3·40 Å.

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Structure of 5-β-D-Galactopyranosyl-1,3-dimethylbarbituric Acid Monohydrate,* $C_{12}H_{18}N_2O_8.H_2O$

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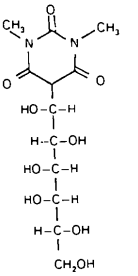
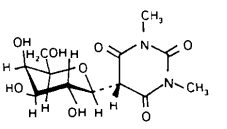
Abstract. $M_r = 336{\cdot}30$, orthorhombic, $P2_12_12_1$, $a = 9{\cdot}147$ (1), $b = 23{\cdot}054$ (2), $c = 6{\cdot}921$ (1) Å, $V = 1459{\cdot}5$ (3) Å^3, $Z = 4$, $D_m = 1{\cdot}53$ (1), $D_x = 1{\cdot}531$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}7107$ Å, $\mu = 0{\cdot}12$ mm^{-1}, $F(000) = 712$, $T = 300$ K, $R = 0{\cdot}055$ for 1623 observed independent reflexions. The galactopyranose ring adopts a $^4C_1$ conformation and the dihedral angle between the two rings in the molecule is 89·1 (1)°. The molecules are linked by an extensive three-dimensional hydrogen-bond network involving the water hydration molecule which stabilizes the crystal structure.

Introduction. The structure determination of the title compound was undertaken as part of a continuing project on conformational details of *C*-nucleosides in the solid state. In this connexion some imidazole *C*-nucleosides have been studied (Criado, Conde & Márquez, 1983, 1984, for example). The discovery of *C*-nucleosides and their pharmacological properties has directed considerable attention to the development of synthetic routes to this class of compounds. Many ways to prepare them are known, but they are generally very laborious and require the convenient protection and functionalization of the sugar precursor. Recently, an easy synthesis of *C*-nucleoside derivatives of barbituric acids by reaction of aldoses with the barbituric acid (or its 1,3-dimethyl derivative) has been reported (Avalos González, 1981; Galbis Pérez, Avalos González, Jiménez Requejo & Palacios Albarrán, 1983). In this way, the reaction of 1,3-dimethylbarbituric acid with D-galactose yields the acyclic *C*-glycoside (I) or its cyclic analogue (II) by dehydration of the sugar side chain. After acetylation, the cyclic form was established for the tetra-*O*-acetyl derivative from spectral data (UV, IR and ^{1}H NMR). For the non-acetylated compound the acyclic form was initially proposed and an X-ray analysis was suggested to elucidate the molecular form and, finally, the cyclic *C*-nucleoside structure was established.



(I)



(II)

* Barbituric acid is 2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione.

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