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Carnosine (β-Alanyl-L-histidine)

BY H. ITOH, T. YAMANE AND T. ASHIDA

Department of Applied Chemistry, Nagoya University, Chikusa-ku, Nagoya 464, *Japan*

AND M. KAKUDO

Institute for Protein Research, Osaka University, Suita, Osaka 565, *Japan*

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Abstract. $C_9H_{14}N_4O_3$, $M_r = 226{\cdot}23$, monoclinic, $C2$, $a = 24{\cdot}740\ (10)$, $b = 5{\cdot}428\ (10)$, $c = 7{\cdot}992\ (10)$ Å, $\beta = 100{\cdot}12\ (10)°$, $Z = 4$, $D_m = 1{\cdot}43$, $D_x = 1{\cdot}423$ g cm^{-3}, $\mu = 8{\cdot}75$ cm^{-1} (for Cu $K\alpha$). $R = 0{\cdot}036$ for the 824 reflexions. The carnosine molecule has an extended conformation, which is very similar to that of methyl L-pyroglutamyl-L-histidinate.

Introduction. Carnosine (β-alanyl-L-histidine) is found in various organ tissues of vertebrates, though its biological function has not yet been elucidated. The X-ray analysis of the copper–carnosine complex has been carried out by Freeman & Szymanski (1967). The disorder in the crystal, however, reduces the precision of the determination of the molecular structure. The present study was undertaken to obtain a more detailed knowledge of the molecular structure.

The crystals were supplied by Professor A. Musashi of Kobe Women's College of Pharmacy. The intensity data were collected on a Rigaku automatic four-circle diffractometer (AFC-II, at the Institute for Protein Research, Osaka University) with Ni-filtered Cu $K\alpha$ radiation. 824 independent reflexions with $\sin\theta/\lambda \leq 0{\cdot}56$ were obtained by the ω–2θ scan method. The scan range was $(1{\cdot}10 + 0{\cdot}15\tan\theta)°$ (ω), and the speed was 2° min^{-1} (ω). The intensity data were corrected for Lorentz and polarization effects.

The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971). The refinement was first carried out by the block-diagonal least-squares method with *HBLS* (Ashida, 1973*a*). For the non-hydrogen atoms anisotropic temperature factors and for the H atoms isotropic temperature factors were applied. The final refinement was carried out by the full-matrix least-squares method with *FMLS* (Ashida, 1973*b*). The final R was 0·036 for all reflexions (0·035 for 808 non-zero reflexions). The weighting scheme was: $\omega = \frac{1}{2}$ for $|F_o| = 0$, $\omega = 1$ for $|F_o| \leq 25$ and $\omega = (25/|F_o|)^2$ for $|F_o| > 25$. The atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). All the calculations were carried out on a FACOM 230-60 of Nagoya University. The final atomic parameters are listed in Tables 1 and 2.*

Table 1. *Positional parameters* ($\times 10^4$) *with their standard deviations in parentheses*

	x	y	z
C(1)	5714 (2)	5311*	3623 (6)
C(2)	5235 (2)	4946 (13)	2231 (5)
C(3)	4898 (2)	2724 (12)	2484 (5)
C(4)	3971 (2)	965 (12)	2062 (5)
C(5)	3847 (2)	−292 (12)	316 (5)
C(6)	3443 (2)	2042 (12)	2540 (5)
C(7)	3012 (2)	178 (13)	2659 (5)
C(8)	2629 (2)	−2990 (13)	3565 (5)
C(9)	2497 (2)	30 (13)	1741 (6)
N(1)	6016 (2)	7580 (12)	3352 (5)
N(2)	4356 (2)	2984 (12)	2033 (4)
N(3)	3094 (2)	−1721 (12)	3830 (4)
N(4)	2259 (2)	−2009 (12)	2336 (5)
O(1)	5115 (1)	789 (11)	3065 (5)
O(2)	3880 (2)	−2598 (11)	240 (4)
O(3)	3725 (1)	1087 (11)	−946 (4)

* The y coordinate of C(1) was held fixed to prevent a singular matrix.

* Lists of structure factors and temperature factors have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32724 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. *Positional parameters* ($\times 10^3$) *of hydrogen atoms*

Standard deviations are given in parentheses.

	Bonded to	x	y	z
H(1)	C(1)	563 (2)	530 (14)	474 (7)
H(2)	C(1)	597 (3)	365 (13)	372 (8)
H(3)	C(2)	501 (2)	633 (11)	205 (6)
H(4)	C(2)	538 (2)	480 (11)	122 (7)
H(5)	C(4)	416 (2)	−19 (10)	294 (5)
H(6)	C(6)	330 (2)	330 (13)	169 (6)
H(7)	C(6)	354 (2)	320 (11)	372 (6)
H(8)	C(8)	256 (2)	−439 (13)	416 (6)
H(9)	C(9)	228 (2)	107 (13)	81 (6)
H(10)	N(1)	576 (3)	890 (15)	342 (9)
H(11)	N(1)	612 (2)	757 (12)	227 (7)
H(12)	N(1)	631 (2)	779 (12)	425 (6)
H(13)	N(2)	422 (2)	431 (12)	156 (6)
H(14)	N(4)	192 (3)	−247 (15)	188 (7)

Discussion. The bond distances and angles concerning the non-hydrogen atoms are shown in Fig. 1, together with the numbering of atoms in the molecule. The e.s.d.'s of the bond distances and angles are 0·008–0·010 Å and 0·5–0·7°, respectively. An *ORTEP* (Johnson, 1965) drawing of the molecule is shown in Fig. 2. The carnosine molecule is made up of four planes: the β-alanyl residue [N(1),C(1),C(2),C(3)], the peptide group, the carboxyl group and the imidazole group. The equations of their best planes, the dihedral angles and the displacements of atoms from the planes are listed in Table 3.

The torsion angles are given in Table 4; the definition of the torsion angles given by the IUPAC–IUB Commission on Biochemical Nomenclature (1970) is adopted. The molecule is in a highly extended conformation. In the chain of N(1)–C(1)–C(2)–C(3)–N(2)–C(4)–C(6)–C(7), all the bonds are *trans*, or very close to *trans*; the torsion angles N(1)–C(1)–C(2)–C(3) and C(3)–N(2)–C(4)–C(6) are −177·4 and 146·3°, respectively.

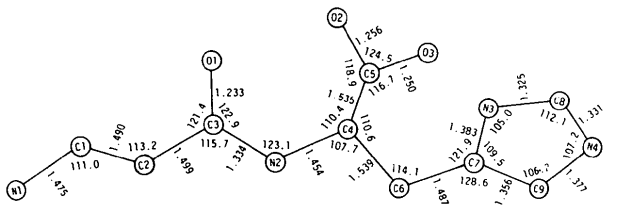

Fig. 1. Bond distances (Å) and angles (°).

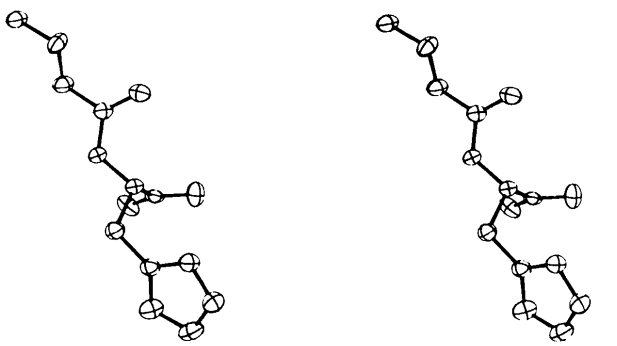

Fig. 2. A stereoscopic view, showing vibration ellipsoids at 50% probability.

Table 3. *Best planes*

(*a*) Equations of the best planes

$X = ax + cz\cos\beta$, $Y = by$, $Z = cz\sin\beta$

I $-0.6703X + 0.5403Y + 0.5087Z + 6.1122 = 0$ β-Alanine

II $-0.2546X + 0.3028Y + 0.9184Z + 0.7615 = 0$ Peptide group

III $-0.9944X - 0.0724Y + 0.0772Z + 9.3936 = 0$ Carboxyl group

IV $-0.4708X + 0.5720Y + 0.6717Z + 1.8667 = 0$ Imidazole group

(*b*) Dihedral angles (°) between the planes

	I	II	III
II	36·7		
III	48·2	72·4	
IV	14·9	24·5	61·4

(*c*) Displacements (× 10³ Å) of atoms from the planes

I		II		III		IV	
C(1)	−16	C(2)	−31	C(4)	−1	C(6)	0
C(2)	−16	C(3)	9	C(5)	4	C(7)	−5
C(3)	16	C(4)	−18	O(2)	−2	C(8)	−5
N(1)	16	N(2)	51	O(3)	−2	C(9)	3
N(2)*	769	O(1)	−6	C(6)*	1351	N(3)	6
O(1)*	−625	H(13)*	−9	N(2)*	−1032	N(4)	1
		C(1)*	783			H(8)*	−4
		C(5)*	−1470			H(9)*	34
		C(6)*	855			H(14)*	−23
						C(4)*	−1234

* Atom not included in the calculation of the plane.

The torsion angles in methyl L-pyroglutamyl-L-histidinate (Cotrait & Allard, 1973), L-*N*-acetylhistidine (Kistenmacher, Hunt & Marsh, 1972), and carnosine in its Cu complex (Freeman & Szymanski, 1967) are also shown in Table 4 for comparison. It is worthwhile to mention that the conformation of the present peptide is very similar to that of methyl L-pyroglutamyl-L-histidinate (Cotrait & Allard, 1973).

The torsion angles (φ) around the N–C$^{\alpha}$ bonds of various His residues may be classified into two groups of about −80° and −150°, as shown in Table 4. The torsion angle in the present molecule belongs to the former, while that in the carnosine–Cu complex

Table 4. *Torsion angles* (°)

	Reference	ψ_1	ω_1	φ_2	ψ_2	χ^1_2	$\chi^{2,1}_2$
Carnosine	1	141·4	174·8	−92·9	130·5	−178·7	56·7
Methyl L-pyroglutamyl-L-histidinate	2	154·7	173·3	−80·6	138·7	−177·9	62·2
L-*N*-Acetylhistidine (*A*)	3	–	172·2	−152·0	165·0	79·6	−75·6
L-*N*-Acetylhistidine (*B*)	3	–	−174·8	−80·2	167·9	−62·6	−82·9
Cu(β-Ala-L-His)	4	6·0	−169·3	−152·6	174·2	53·1	−115·3

References: (1) This study. (2) Cotrait & Allard (1973). (3) Kistenmacher, Hunt & Marsh (1972). (4) Freeman & Szymanski (1967).

Table 5. *Hydrogen bonds D–H···A*

D	H	*A*	*D*···*A*	H···*A*	∠*D*–H···*A*
N(1)	H(10)	O(1^{i})	2·806 Å	1·88 Å	161°
N(1)	H(11)	O(2^{ii})	2·929	2·01	164
		O(3^{ii})	2·858	2·25	121
N(1)	H(12)	N(3^{iii})	2·886	1·96	178
N(2)	H(13)	O(2^{i})	2·932	2·08	176
N(4)	H(14)	O(3^{iv})	2·696	1·82	171

Symmetry code
(i) $x, 1+y, z$; (ii) $1-x, 1+y, -z$; (iii) $1-x, 1+y, 1-z$; (iv) $\frac{1}{2}-x, -\frac{1}{2}+y, -z$.

(Freeman & Szymanski, 1967) belongs to the latter. The difference in the conformations may be attributed to the carnosine–Cu interaction. The χ_2^1 of His in the present peptide is −178·7° and that in methyl L-pyroglutamyl-L-histidinate (Cotrait & Allard, 1973) is −177·9°. The conformations of His in these peptides are, therefore, different from either the open or closed forms which are proposed by Kistenmacher, Hunt & Marsh (1972), χ_2^1 of the open and closed forms being very roughly −60 and +60° respectively. On the other hand, the conformation in the Cu complex is of the closed form ($\chi_2^1 = 53·1°$).

The hydrogen-bond scheme is summarized in Table 5.

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Caesium Enneabromodibismuthate(III)

BY F. LAZARINI

Department of Chemistry, Faculty of Natural Sciences and Technology, University of Ljubljana, Murnikova 6, 61000 *Ljubljana, Yugoslavia*

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Abstract. $Cs_3Bi_2Br_9$; trigonal, $P\bar{3}m1$; hexagonal axes; $a = 7·972$ (2), $c = 9·867$ (5) Å; $D_o = 4·65$ (2) g cm^{-3}, $Z = 1$, $D_c = 4·694$ g cm^{-3}; $R = 0·058$ for 424 reflexions [$I > 3\sigma(I)$]. Cs and Br are in a cubic close-packed structure, with Bi in $\frac{1}{6}$ of the octahedral holes. The $BiBr_6$ octahedra share three *cis*-vertices with three other octahedra forming corrugated layers.

Introduction. This investigation is a part of a systematic study of bromo- and iodobismuthates(III) (Lazarini, 1977*a*,*b*). It is typical for $A_3B_2X_9$ structures (Wells, 1975) that A and X atoms are in either cubic or hexagonal closest packing with B atoms occupying $\frac{2}{3}$ of the X_6 holes, *i.e.* $\frac{1}{6}$ of the total number of octahedral holes. Two different groups of structures are possible. In the first group of $A_3B_2X_9$ structures, with A and X atoms in hexagonal closest packing, complex $B_2X_9^{3-}$ ions are present, consisting of two BX_6 octahedra sharing a face. The representative examples of this group are: $K_3W_2Cl_9$ (Watson & Waser, 1958), with a strong bond between W atoms shifted to the bridging Cl atoms, a more symmetrical variant, $Cs_3Cr_2Cl_9$ (Wessel & IJdo, 1957), $Cs_3Bi_2I_9$ (Lindqvist, 1968) with the same structure, and $Cs_3Tl_2Cl_9$ (Hoard & Goldstein, 1935*a*; Powell & Wells, 1935) with a more uniform spatial distribution of the complex anions. In the second