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N-Acetyl-L-histidine-*N*-methylamide

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Abstract. $C_9H_{14}N_4O_2$, orthorhombic, $P2_12_12_1$; a = 13·951 (2), b = 15·705 (2), c = 4·898 (1) Å; Z = 4, D_x = 1·301 g cm^{-3}. The structure was solved by the direct method and refined to an R of 0·066. The molecular conformation of this simple peptide with two peptide linkages is $\varphi_{CN} = -72·2°$ and $\psi_{CC} = 156·3°$; this is consistent with the β structure of polypeptides.

Introduction. Prismatic crystals of *N*-acetyl-L-histidine-*N*-methylamide grown from 5% aqueous solution were supplied by Mr K. Harada. The intensity data were collected up to $2\theta = 156°$ on a Philips PW 1100 four-circle diffractometer with graphite-monochromated Cu $K\alpha$ radiation. The integrated intensities were measured by the θ–2θ scanning method with a scan speed of 4° min^{-1} in 2θ. The scans were repeated twice when the total number of counts during a single scan was less than 10^4. The background was measured at each end of the scan for half the total scan time. 1125 unique reflexions were measured as above the $2\sigma(I)$ level; this corresponds to 90% of the theoretically possible number of reflexions within the same angular range. Lorentz and polarization corrections were applied but no corrections were made for absorption or extinction. The structure was solved by the direct method with *MULTAN* (Main, Woolfson & Germain, 1971), based on 166 reflexions with $|E| > 1·5$. One of the phase sets having the highest figure of merit and the lowest R value gave the locations of all non-hydrogen atoms on the E map. The structure was refined by *ORFLS* (Busing, Martin & Levy, 1962). In the refinement process, the 11 strongest low-angle reflexions were excluded because of prominent disagreement between observed and calculated structure factors. At the final stage of refinement the following weighting system was introduced: $\sqrt{w} = \frac{1}{4}$ for $|F_o| \leq 10$; $\sqrt{w} = 1$ for $10 < |F_o| \leq 33·7$; $\sqrt{w} = 33·7/|F_o|$ for $33·7 < |F_o|$.

The atomic scattering factors for C, N and O atoms

Table 1. *The final atomic parameters* ($\times 10^4$, *for* H *atoms* $\times 10^3$) *with estimated standard deviations in parentheses*

The anisotropic temperature factor is of the form $T = \exp[-(\beta_{11}h^2 + \cdots + 2\beta_{23}kl)]$. The isotropic temperature factor is of the form $T = \exp(-B \sin^2\theta/\lambda^2)$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	−1499 (4)	5229 (4)	2714 (11)	54 (3)	48 (2)	310 (21)	−10 (2)	−23 (7)	1 (6)
C(2)	−950 (3)	5652 (2)	4970 (8)	51 (2)	25 (1)	199 (15)	−2 (2)	0 (6)	11 (4)
C(3)	556 (3)	5792 (2)	7371 (8)	45 (2)	27 (1)	172 (15)	0 (2)	1 (5)	−1 (4)
C(4)	879 (3)	6666 (3)	6417 (8)	54 (2)	28 (2)	177 (17)	5 (2)	6 (6)	20 (4)
C(5)	1514 (7)	8054 (4)	7822 (15)	105 (5)	38 (2)	411 (27)	−15 (3)	7 (12)	13 (7)
C(6)	1453 (4)	5251 (3)	7876 (12)	45 (2)	32 (2)	452 (26)	1 (2)	−1 (7)	25 (6)
C(7)	1254 (3)	4372 (2)	8873 (10)	46 (2)	31 (2)	252 (17)	−1 (2)	−8 (6)	10 (5)
C(8)	680 (4)	3384 (3)	11398 (11)	91 (4)	33 (2)	338 (23)	−5 (2)	10 (9)	16 (6)
C(9)	1538 (4)	3619 (3)	7807 (11)	63 (3)	33 (2)	341 (22)	4 (2)	8 (7)	5 (6)
O(1)	−1316 (2)	6227 (2)	6350 (7)	56 (2)	35 (1)	330 (14)	6 (1)	8 (5)	11 (4)
O(2)	940 (3)	6846 (2)	3937 (6)	101 (3)	38 (1)	135 (11)	−1 (2)	10 (5)	23 (4)
N(1)	−62 (3)	5384 (2)	5391 (7)	50 (2)	30 (1)	226 (15)	1 (1)	−3 (5)	−22 (4)
N(2)	1128 (3)	7210 (2)	8358 (7)	82 (3)	25 (1)	223 (16)	−5 (2)	11 (6)	−1 (4)
N(3)	716 (3)	4213 (2)	11179 (8)	87 (3)	34 (2)	294 (17)	−5 (2)	27 (7)	−6 (5)
N(4)	1174 (3)	2997 (2)	9468 (9)	82 (3)	25 (1)	368 (21)	−1 (2)	−4 (7)	−1 (4)

	x	y	z	B ($\times 10$ Å^2)		x	y	z	B ($\times 10$ Å^2)
H(C1)	−213 (4)	514 (3)	313 (12)	48 (13)	H(C6)	188 (4)	525 (4)	652 (15)	58 (15)
H′(C1)	−173 (6)	577 (5)	91 (20)	103 (22)	H′(C6)	188 (4)	566 (3)	944 (12)	52 (12)
H″(C1)	−113 (4)	477 (4)	212 (14)	61 (15)	H(C8)	22 (4)	309 (4)	1263 (16)	65 (16)
H(C3)	9 (3)	596 (3)	876 (12)	41 (10)	H(C9)	199 (5)	352 (4)	629 (18)	80 (19)
H(C5)	198 (5)	820 (4)	912 (15)	69 (16)	H(N1)	24 (3)	499 (3)	447 (11)	38 (11)
H′(C5)	200 (9)	788 (7)	706 (32)	159 (42)	H(N2)	104 (4)	705 (4)	1031 (13)	50 (13)
H″(C5)	106 (6)	846 (5)	749 (21)	93 (24)	H(N4)	120 (4)	245 (4)	939 (14)	68 (14)

were those given in *International Tables for X-ray Crystallography* (1962) as SX-6, 7 and 8 respectively, and for H those given by Stewart, Davidson & Simpson (1965). The final R value was 0·066 for 1114 reflexions. The atomic parameters are listed in Table 1.*

Discussion. The bond lengths and angles are listed in Table 2. They are in good agreement with the standard values proposed for peptides (Pauling & Corey, 1953). All the bond lengths, except C(1)–C(2) (1·501 Å) which involves a terminal C atom, coincide with the standard values (within experimental error). The short C(1)–C(2) distance may be attributed to the librational thermal motions of the terminal atom, as has been observed in *N*-acetyl-DL-phenylalanine-*N*-methylamide (Harada & Iitaka, 1974*a*). The conformation of the molecule can be seen in Fig. 1. The molecule consists of four planar groups, two peptide groups, an imidazole ring and an aliphatic chain. The planarities of these groups are shown in Table 3. The r.m.s. deviations of atoms forming the least-squares planes are 0·025, 0·022, 0·008 and 0·006 Å respectively, indicating that the peptide groups are somewhat deformed. The extent of the deformation can also be seen in the ω angles which show that the deviations from the exact *cis* conformation are 4·8 and 4·2° for the two peptide groups. This sort of deformation is often observed in related compounds and the peptide groups in proteins (Ramachandran & Sasisekharan, 1968).

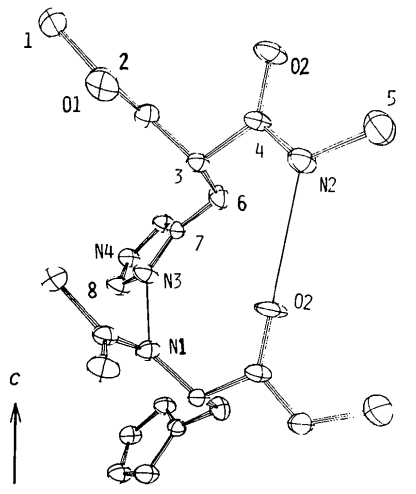

Fig. 1. A perspective view of *N*-acetyl-L-histidine-*N*-methylamide drawn by *ORTEP* (Johnson, 1965). Two types of hydrogen bond link the molecules translated along **c**.

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32136 (5 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. *Bond lengths, bond angles and torsion angles*

C(1)–C(2)	1·501 (7) Å	O(1)–C(2)–C(1)	120·9 (4)°
C(2)–O(1)	1·238 (5)	O(1)–C(2)–N(1)	122·2 (4)
C(2)–N(1)	1·323 (6)	C(1)–C(2)–N(1)	116·9 (4)
C(3)–C(4)	1·519 (6)	C(4)–C(3)–C(6)	108·0 (4)
C(3)–C(6)	1·531 (6)	C(4)–C(3)–N(1)	111·7 (3)
C(3)–N(1)	1·447 (5)	C(6)–C(3)–N(1)	110·5 (4)
C(4)–O(2)	1·250 (5)	O(2)–C(4)–C(3)	121·6 (4)
C(4)–N(2)	1·325 (5)	O(2)–C(4)–N(2)	122·3 (4)
C(5)–N(2)	1·455 (8)	C(3)–C(4)–N(2)	116·1 (4)
C(6)–C(7)	1·491 (6)	C(7)–C(6)–C(3)	114·4 (4)
C(7)–C(9)	1·353 (6)	C(9)–C(7)–C(6)	129·0 (4)
C(7)–N(3)	1·377 (6)	C(9)–C(7)–N(3)	108·5 (4)
C(8)–N(3)	1·307 (6)	C(6)–C(7)–N(3)	122·5 (4)
C(8)–N(4)	1·316 (7)	N(3)–C(8)–N(4)	112·3 (5)
C(9)–N(4)	1·374 (6)	N(4)–C(9)–C(7)	106·6 (4)
		C(2)–N(1)–C(3)	121·4 (3)
		C(4)–N(2)–C(5)	123·7 (5)
		C(8)–N(4)–C(9)	106·9 (4)
		C(7)–N(3)–C(8)	105·6 (4)

φ	τ[C(4)–C(3)–N(1)–C(2)]	−71·6°
ψ	τ[N(2)–C(4)–C(3)–N(1)]	155·7
ω_1	τ[C(3)–N(1)–C(2)–C(1)]	175·2
ω_2	τ[C(3)–C(4)–N(2)–C(5)]	175·8
χ^{21}	τ[C(7)–C(6)–C(3)–N(1)]	−58·5
χ^{21}	τ[C(9)–C(7)–C(6)–C(3)]	124·6
χ^{22}	τ[N(3)–C(7)–C(6)–C(3)]	−55·5

Table 3. *Deviations* (Å) *of atoms from the least-squares planes*

X, Y and Z are the orthogonal coordinates measured in Å along $X \| a^*$, $Y \| b$ and $Z \| c$.

(1) Peptide group I (acetyl side)

$$-0{\cdot}3181X - 0{\cdot}6799Y + 0{\cdot}6608Z = -4{\cdot}015$$

C(1)	−0·024	O(1)	0·005
C(2)	0·010	N(1)	0·038
C(3)	−0·030		

(2) Peptide group II (methylamide side)

$$0{\cdot}9359X - 0{\cdot}3505Y - 0{\cdot}0340Z = -2{\cdot}608$$

C(3)	0·023	O(2)	0·001
C(4)	−0·022	N(2)	−0·027
C(5)	0·024		

(3) Aliphatic group

$$0{\cdot}0280X + 0{\cdot}3206Y + 0{\cdot}9468Z = 6{\cdot}361$$

C(4)	0·005	C(6)	−0·007
C(3)	−0·005	C(7)	0·006

(4) Imidazole ring

$$0{\cdot}8248X + 0{\cdot}0274Y + 0{\cdot}5648Z = 4{\cdot}089$$

C(7)	−0·003	N(3)	0·007
C(8)	−0·009	N(4)	0·007
C(9)	−0·002	C(6)†	−0·012

Dihedral angle between two planes

(1) and (2)	94·7°	(1) and (3)	33·4°
(2) and (3)	96·8	(3) and (4)	55·5

† Not included in the least-squares calculation.

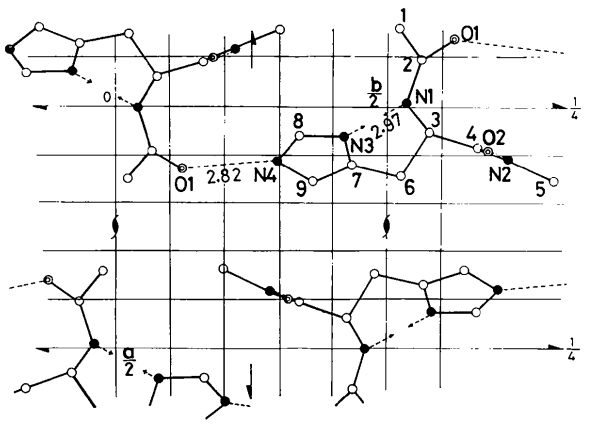

Fig. 2. The projection of the crystal structure along **c**.

Various torsion angles are listed in Table 2. If the φ_{CN} and ψ_{CC} angles defining the conformation of the main chain are plotted on the Ramachandran map (IUPAC-IUB Commission on Biochemical Nomenclature, 1970), the (φ,ψ) values of the present compound fall nearly at the small-angle limit of φ in the allowed region for the β structure. This is also reflected in a large dihedral angle between the two peptide groups. This angle is 94·7°, significantly larger than those found in other related compounds [usually it is about 70° in the β structure, and 62·2° in the parallel-chain pleated-sheet model of Pauling & Corey (1953)], indicating that the main chain is more folded or twisted. The twisting of the main chain may result from the formation of lateral hydrogen bonds as shown in Fig. 2. It should be noted that the φ,ψ values of the present compound are rather close to those of the proposed models of polyglycine II (Crick & Rich, 1955) and collagen (Ramachandran & Kartha, 1955; Rich & Crick, 1955; Ramachandran, Sasisekharan & Thathachari, 1960) and also very close to those found in *N*-acetylalanine-*N*-methylamide (Harada & Iitaka, 1974*b*) and *N*-acetylglycine-*N*-methylamide (Iwasaki, 1974).

The structure of the crystal is illustrated in Fig. 2. The main chains of the molecules lie nearly perpendicular to the *c* axis as shown in Fig. 1. These chains are arranged in parallel, separated by a repeat distance of *c* (4·898 Å) and bound together through the N(2)—H···O(2) hydrogen bond. A similar type of main-chain arrangement is often found in the related compounds in which a sheet structure resembling that of the parallel-chain pleated sheet is formed. Thus, for example, in *N*-acetyl-DL-alanine-*N*-methylamide (Harada & Iitaka, 1974*b*), and *N*-acetyl-DL-phenylalanine-*N*-methylamide and *N*-acetyl-L-phenylalanine-*N*-methylamide (Harada & Iitaka, 1974*a*, 1977), the main chains are bound by the two kinds of N—H···O hydrogen bonds utilizing the two imino N atoms and the two carbonyl O atoms. In the present structure, one of the hydrogen bonds, N(1)—H···O(1), is broken and each of the N(1) and O(1) atoms forms another hydrogen bond: N(1)—H···N(3) and O(1)···H—N(4) respectively. These hydrogen bonds connect the side chains to the main chain as illustrated in Fig. 2. The interatomic distances and angles associated with the hydrogen bonds are listed in Table 4.

Table 4. *Interatomic distances and angles associated with hydrogen bonds*

Symmetry code: (i) $-x, -\frac{1}{2}+y, \frac{3}{2}-z$; (ii) $x, y, 1+z$.

	N(4)···O(1^{i})	N(2)···O(2^{ii})	N(1^{ii})···N(3)
	2·814 (5) Å	2·803 (5) Å	2·972 (5) Å
∠(O=C···N)	36·9 (2)°	1·3 (2)°	–
∠(C=O···N)	128·7 (3)	178·1 (3)	–

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