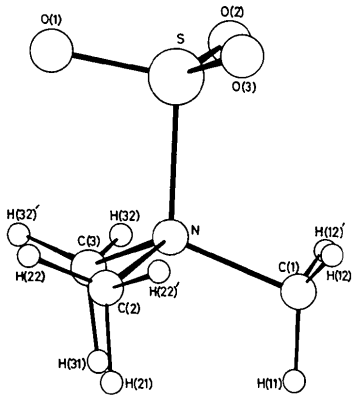


Fig. 1. Molecular stereochemistry and atom numbering. Atoms designated as (2) and (3) are related to (1) by crystallographic threefold rotational symmetry.

Table 1. *Atomic parameters of non-hydrogen atoms* ($\times 10^4$) *and hydrogen atoms* ($\times 10^3$) *(with estimated standard deviations in parentheses)*

U_{eq}(Å$^2 \times 10^4$) is defined as $(U_{11}U_{22}U_{33})^{1/3}$.

	x	y	z	Wyckoff notation	U_{eq}
S	0	0	0	*a*	333 (4)
N	2931 (7)	2931 (7)	2931 (7)	*a*	278 (12)
O	−1317 (5)	−1317 (5)	1263 (7)	*b*	692 (15)
C	4616 (8)	4616 (8)	1977 (9)	*b*	474 (18)
H(11)	617 (8)	617 (8)	357 (9)	*b*	
H(12)	328 (7)	502 (8)	87 (8)	*c*	

Table 2. *Interatomic distances* (Å) *and angles* (°) *with estimated standard deviations in parentheses*

	$(CH_3)_3N(SO_3)^a$	$H(CH_3)_2N(SO_3)^b$ (mean results)	$H_3N(SO_3)^c$ (mean results)
N–S	1·844 (2)	1·790 (6)	1·76 (2)
N–C	1·496 (2)	1·504 (10)	—
S–O	1·405 (2)	1·430 (5)	1·44 (2)
C–N–C	109·1 (1)	111·5 (7)	—
S–N–C	109·8 (1)	112·3 (5)	—
N–S–O	101·8 (1)	102·1 (3)	103·2 (9)
O–S–O	115·9 (1)	115·8 (4)	115·1 (9)

References: (*a*) this work; (*b*) Morris, Kennard, Hall & Smith (1982); (*c*) Sass (1960).

The authors wish to thank the Australian Research Grants Committee, the University of Queensland and the University of Western Australia for financial support. AJM wishes to thank the University of Queensland for a postgraduate scholarship and GS, the Queensland Institute of Technology for leave to work on this project.

References

CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.
MORRIS, A. J., KENNARD, C. H. L., HALL. J. R. & SMITH, G. (1982). *Inorg. Chim. Acta*, **62**, 247–252.
SASS, R. L. (1960). *Acta Cryst.* **13**, 320–324.
SHELDRICK, G. M. (1976). *SHELX* 76. Program for crystal structure determination. Univ. of Cambridge, England.
SHIMIZU, H. & MCLACHLAN, D. (1953). *J. Am. Chem. Soc.* **75**, 4352–4354.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Acta Cryst. (1983). C**39**, 82–87

Structure of the Tetrapeptide L-Methionyl-L-α-glutamyl-L-histidyl-L-phenylalanine Monohydrate, $C_{25}H_{34}N_6O_7S.H_2O$

BY G. ADMIRAAL AND AAFJE VOS

Department of Chemical Physics, University of Groningen, Nijenborgh 16, 9747 *AG Groningen, The Netherlands*

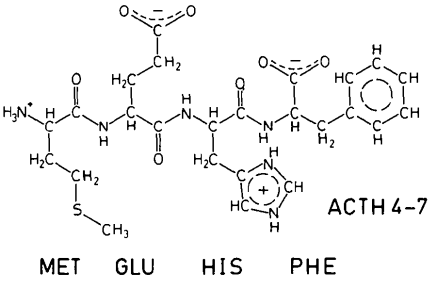
(*Received* 24 *March* 1982; *accepted* 3 *August* 1982)

Abstract. $M_r = 580{\cdot}68$, $C2$, $a = 23{\cdot}333$ (6), $b = 5{\cdot}4741$ (11), $c = 24{\cdot}783$ (5) Å, $\beta = 115{\cdot}03$ (2)°, $U = 2868$ (2) Å^3, $Z = 4$, $D_x = 1{\cdot}344$ Mg m^{-3}, λ(Mo $K\bar{\alpha}$) = 0·71069 Å, $\mu = 0{\cdot}169$ mm^{-1}, $F(000) = 1232$; 3494 independent reflections were measured at room temperature with Mo radiation on a diffractometer. The crystal structure was determined by a Patterson search based on dipeptide fragments with a large range of φ, ψ values. The conformation with the best 'measure of fit' was extended to an almost complete structure model by *DIRDIF*. Least-squares refinement gave $R = 0{\cdot}055$ for 3113 reflections with $w = 1$. The molecule is a double zwitterion with (terminal)NH_3^+, (terminal)CO_2^-, (Glu)CO_2^- and (imidazole)H^+ as charged groups. The backbone shows a helix-type bend at Glu and is almost fully extended at His with N–Cα(His)–C = 105·6 (4)°; NH and C=O of His are not involved in H bonding. The crystal contains regions with strong H

0108-2701/83/010082-06$01.50

bonding, and regions in which Phe and Met (disordered) are quite loosely packed by van der Waals interactions.

Introduction. Fragments of the N-terminal part of the adrenocorticotropic hormone (ACTH) are involved in motivational, learning and memory processes in rats (de Wied, 1974, and references therein). The shortest fragment with behavioural activity in the pole-jumping test for rats is the title tetrapeptide ACTH 4–7.



Behavioural studies with ACTH 4–9 and ACTH 4–10, in which the amino acid residues at sites 4 and 7 or 8 were modified, have given rise to the hypothesis that the molecules have a loop or helix-like structure in which Met[4] comes close to Arg[8] and Phe[7] (Greven & de Wied, 1980). This hypothesis has been supported by circular-dichroism studies (Greff, Toma, Fermandjian, Löw & Kisfaludy, 1976). In crystals of ACTH 4–10 the molecules have the extended conformation and form an antiparallel β sheet (Admiraal, 1981; Admiraal & Vos, 1983). During the investigation of related compounds, ACTH 4–7 was the first to crystallize. Its crystal and molecular structure are reported in the present paper.

Experimental. A purified sample of ACTH 4–7 was kindly placed at our disposal by Drs H. M. Greven of the research laboratories of Organon, Int.B.V., Oss. Crystals obtained from a solution of ACTH 4–7 in a mixture of water and 2-propanol; a saturated solution at 338K was slowly cooled to room temperature with simultaneous addition of 2-propanol by liquid diffusion (Salemme, 1972); the largest crystals, 0·05 × 0·1 × 0·5 mm, were, although still small, of suitable quality for X-ray diffraction; crystals were mounted in thin-walled glass capillaries containing a drop of mother liquor, cell dimensions obtained from the θ, φ and χ values of 25 reflections optimized on a CAD-4F diffractometer, Zr-filtered Mo radiation; intensity-measurement crystal 0·5 × 0·05 × 0·05 mm, ω–2θ scan, scan angle $\omega_s = (1{\cdot}05 + 0{\cdot}525 \tan\theta)°$, slit width 1·0°, slit height 1·3°, θ(max.) 27·15°, reference reflections 400, 600 and 626 measured every 1·66 h, intensity variations ± 5%, total exposure time 169 h; corrections for average change in intensity of reference reflections, and for Lorentz and polarization effects, no correction for absorption; the reflection set of 3494 independent reflections contains 709 with $0 < I < 2\sigma(I)$ and 242 with $I < 0$.

No structure model could be obtained by application of direct methods with *MULTAN* (Germain, Main & Woolfson, 1971) of the XRAY system (1976), or *SIMPEL* (Schenk, 1980). Attempts to locate peaks corresponding to S···S distances failed for Harker sections of $|E|^2$ or partially sharpened Patterson syntheses. Later it appeared that the S atoms are disordered in the structure. A Patterson search with the program of Braun, Hornstra & Leenhouts (1969) failed if only single peptide units or His or Phe side groups were considered. For each case the number of solutions was high and in some cases groups were placed too close together. Good results were obtained for a search fragment consisting of two standard (Dickerson & Geis, 1969) peptide units; φ and ψ at the central Cα atom were varied in steps of 10°. Among the 190 conformations considered, one model ($\varphi = -90°$, $\psi = -30°$) gave by far the best fit to the Patterson synthesis. With this dipeptide chain as input, *DIRDIF* (Prick, 1979; Beurskens, Prick & Doesburg, 1979) generated the complete structure apart from Cε (1) (for numbering of atoms, see Fig. 1) and the H atoms. One water of crystallization molecule was found per molecule of ACTH 4–7.

The refinement was carried out with $w = 0$ for the reflections with $|F_o| < 2\sigma(|F_o|)$ for which $|F_c| < |F_o|$, and $w = 1$ for the remaining reflections. The H atoms of the Cε(1)H_3 group which were not observed in difference Fourier maps were not taken into account. The scattering factors of the non-hydrogen atoms were taken from Cromer & Mann (1968), for H the *f* curve of Stewart, Davidson & Simpson (1965) was applied. Anomalous dispersion for S was not taken into account. After a few cycles of isotropic refinement of the non-H atoms generated by *DIRDIF*, difference Fourier maps revealed positions for Cε(1) and for all H atoms except those of the Cε(1)H_3 group. The H

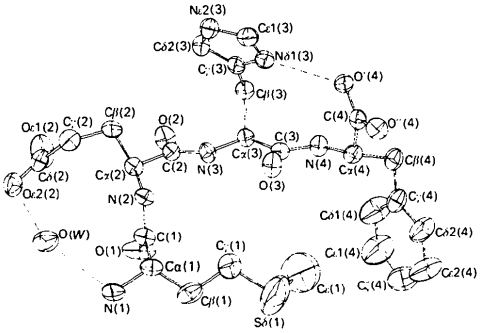


Fig. 1. Molecule with numbering scheme and 50% probability plots for thermal ellipsoids.

positions found indicated clearly that the terminal NH_2 and the imidazole (Im) group are protonated. In the final refinement cycles the H atoms were treated as follows: (*a*) no constraints for H linked to N in ImH^+ as these atoms are involved in short H bonds, which makes an *a priori* constraint of their positions impossible; (*b*) further H atoms of side groups were placed at geometrically reasonable positions with C—H = 1·08 Å; (*c*) all backbone and H_2O H atoms were constrained along the (C, N or O)—H directions found in previous anisotropic refinement cycles, with O—H = 0·954, N—H = 1·00 and C—H = 1·08 Å (van der Wal, 1979; Momany, McGuire, Burgess & Scheraga, 1975). Anisotropic temperature factors were considered for non-hydrogen atoms and isotropic temperature factors for H. With the constraints discussed above the index *wR* decreased to 0·060 and the goodness of fit *S* to 0·54. Phe has a strong libration around Cβ(4)—Cγ(4). Apart from Cβ(1) the Met group is disordered. Partial atoms were used to make the difference map flat in the Met region. The average structure for Met is given in Table 1. Introduction of the disorder decreased *wR* to 0·052 for the 3113 reflections with $w = 1$, $S = 0{\cdot}48$. With the exception of the Met group, the final parameters are listed in Table 2.* The highest peak of 0·23 e Å^{-3} = 4σ in the final difference map lies in the Met region and is smaller than the peaks observed for H atoms, 0·35 e Å^{-3}. It was therefore concluded that, apart from the water molecule mentioned above, the structure does not contain solvent molecules.

Discussion. Fig. 1 shows ACTH 4–7 and the water molecule, with the numbering scheme and 50% probability plots for the thermal ellipsoids. The molecule is a double zwitterion with as charged groups: (terminal)NH_3^+, (imidazole)H^+ (ImH^+), (terminal)CO_2^- and (Glu)CO_2^-. All charged H-bonding (HB) groups lie at one side of the backbone, whereas the non-H-bonding (NHB) groups are located at the other side. As in crystal structures of many other oligopeptides (Admiraal, 1981) the ACTH 4–7 and water molecules are packed such that the crystal contains HB regions with a network of H bonds and NHB regions in which the molecules are held together by van der Waals interactions. In Fig. 2, which gives the projection of the structure along the *b* axis, the HB region lies around $(x,y,0)$ and the NHB region around $(x,y,\frac{1}{2})$.

The H bonding is depicted in Figs. 2 and 3. A string *A*(I,II) of H bonds connects the NH_3^+ heads of molecules (II) with the CO_2^- tails of neighbouring molecules (I) (Fig. 2). The string is strengthened by H bonds of type N(4)—H···O''(4;*y*−1). Another string, *B*, connects successive (Glu)CO_2^- groups along *y via* water molecules *W*. The Glu residues are further involved in bonds of type O(2)···H—N(2;*y*−1) between successive backbones along *y*. String *A*(I,II) is linked to *B* by

Table 2. *Fractional coordinates* (×10⁴) *and* U_{eq} *or U values* (10⁻³Å²)

Hydrogen atoms were constrained to their respective heavy atoms, except for Hδ1 (3) and Hε2 (3). For numbering of atoms see Fig. 1.

	x	*y*	*z*	U_{eq} or *U*
N(1)	2001 (2)	4132 (8)	2303 (2)	44 (1)
Cα(1)	2678 (2)	4112 (9)	2411 (2)	39 (1)
C(1)	2785 (2)	1648 (9)	2176 (2)	39 (1)
O(1)	2698 (2)	−237 (7)	2385 (2)	63 (2)
N(2)	2954 (2)	1751 (7)	1724 (2)	32 (1)
Cα(2)	3004 (2)	−497 (8)	1432 (2)	32 (1)
Cβ(2)	2829 (2)	−56 (9)	771 (2)	40 (1)
Cγ(2)	2139 (2)	663 (8)	421 (2)	46 (2)
Cδ(2)	1665 (2)	−1147 (10)	459 (2)	46 (1)
Oε1 (2)	1803 (2)	−3348 (8)	523 (2)	76 (1)
Oε2 (2)	1134 (2)	−318 (8)	394 (2)	58 (1)
C(2)	3652 (2)	−1713 (9)	1723 (2)	34 (1)
O(2)	3690 (2)	−3942 (6)	1662 (2)	48 (1)
N(3)	4141 (2)	−260 (7)	2006 (2)	37 (1)
Cα(3)	4793 (2)	−1079 (8)	2283 (2)	33 (1)
Cβ(3)	5016 (2)	−2001 (7)	1817 (2)	36 (1)
Cγ(3)	4943 (2)	−194 (9)	1343 (2)	36 (1)
Nδ1 (3)	5328 (2)	1809 (8)	1439 (2)	38 (1)
Cδ2 (3)	4509 (2)	−31 (11)	767 (2)	47 (1)
Cε1 (3)	5145 (2)	3116 (11)	937 (2)	47 (2)
Nε2 (3)	4646 (2)	2028 (10)	524 (2)	51 (1)
C(3)	5178 (2)	1132 (8)	2632 (2)	32 (1)
O(3)	4938 (2)	3142*	2568 (2)	47 (1)
N(4)	5783 (2)	711 (7)	2990 (2)	37 (1)
Cα(4)	6196 (2)	2761 (8)	3296 (2)	36 (1)
Cβ(4)	6795 (2)	1819 (9)	3822 (2)	44 (1)
Cγ(4)	6671 (2)	1150 (10)	4353 (2)	49 (2)
Cδ1 (4)	6373 (4)	−976 (14)	4379 (3)	85 (3)
Cδ2 (4)	6871 (3)	2648 (13)	4835 (2)	71 (3)
Cε1 (4)	6252 (4)	−1496 (16)	4877 (3)	97 (3)
Cε2 (4)	6766 (4)	2121 (18)	5336 (3)	96 (3)
Cζ(4)	6448 (3)	40 (17)	5344 (3)	86 (3)
C(4)	6374 (2)	4255 (8)	2865 (2)	35 (1)
O'(4)	6351 (1)	3286 (6)	2400 (1)	40 (1)
O''(4)	6547 (2)	6425 (6)	3018 (2)	45 (1)
O(*W*)	1251 (2)	3723 (8)	1088 (2)	60 (1)

* Kept constant during refinement.

* Lists of structure factors, anisotropic thermal parameters, coordinates of H atoms, the description of Met by split atoms and Table 6 have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38100 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Average structure for Met*

Coordinates are multiplied by 10^4 and U_{eq} (Å²) values by 10^3. $U_{eq} = \frac{1}{3}\sum_i U_{ii}$ after diagonalization of the **U** tensor.

	x	*y*	*z*	U_{eq}
Cβ(1)	3116 (3)	4439 (11)	3069 (2)	58 (4)
Cγ(1)	3808 (3)	4861 (17)	3160 (3)	116 (8)
Sδ(1)	4335 (2)	5445 (9)	3886 (2)	170 (3)
Cε(1)	4873 (6)	3122 (45)	4044 (6)	250 (20)

Bond lengths (Å) and angles (°)

Cα(1)—Cβ(1)	1·526 (7)	Cα(1)—Cβ(1)—Cγ(1)	111
Cβ(1)—Cγ(1)	1·54	Cβ(1)—Cγ(1)—Sδ(1)	115
Cγ(1)—Sδ(1)	1·73	Sγ(1)—Sδ(1)—Cε(1)	104
Sδ(1)—Cε(1)	1·71		

$\chi^1 = -170$, $\chi^2 = 176$, $\chi^3 = 120$; literature C—S: 1·817 (5) Å (Sutton, 1965).

(N^+H_2)–H···O(*W*) bonds, whereas *B* is connected *via* the ImH^+ group to string *A'*(I,II) related to *A*(I,II) by the twofold axis $[\frac{1}{2},y,0]$. There are two such connections between *A*(I,II) and *A'*(I,II) which are related by the twofold axis $[\frac{1}{2},y,0]$ (Fig. 2).

Details of the H bonds are listed in Table 3. The regularities observed for the categories 1 to 4 and the deviations from linearity can be compared with those observed in other compounds (Olovsson & Jönsson, 1976; Koetzle & Lehmann, 1976; Marsh & Donohue, 1967; Donohue, Lavine & Rollett, 1956; Bennett, Davidson, Harding & Morelle, 1970). The strong C–H···O interactions given in category 5 of Table 3 do not fall in the category of H bonds according to the classification of Olovsson & Jönssen (1976), which requires O···H < 2·4 Å for H bonding. The electronegative groups linked to the C–H groups involved withdraw electrons from C–H which makes the close O···H approach possible. The network of H bonds makes the packing of the backbones rigid. Consequently, the thermal motion for the backbone atoms, including Cβ, is relatively small, $\langle U_{eq}\rangle = 0{\cdot}04$ Å^2.

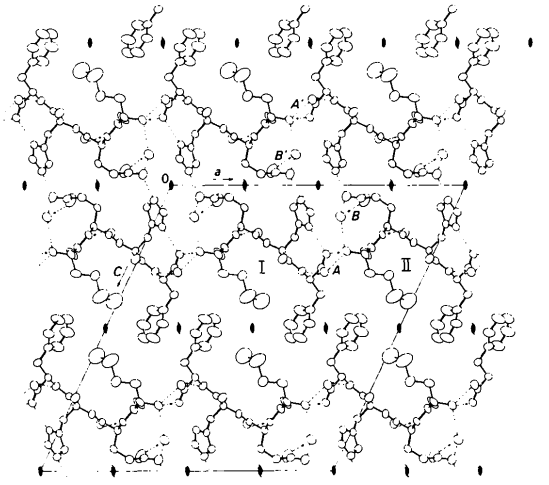


Fig. 2. Projection of the structure along **b** onto the (010) plane. Regions of H bonding are indicated by *A*, *B*, *A'*, *B'*. Molecule (II) = I($x+\frac{1}{2}$, $y+\frac{1}{2}$, z). --- H bonds; ---→ H bonds to atoms with $y-1$.

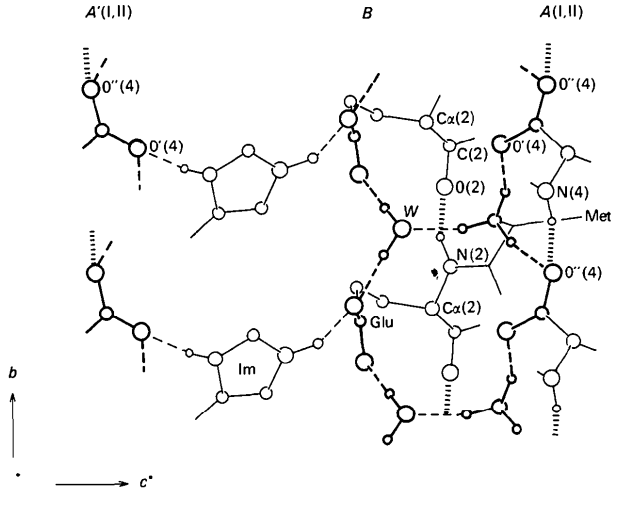


Fig. 3. Projection along **a** of the H bonds. The region around *A*···*B*···*A'* in Fig. 2 is given. Bold: strings *A*(I,II), *B* and (part of) *A'*(I,II). --- H bonds connecting NH_3^+(*A*) with H_2O(*B*), or (Glu)CO_2(*B*) *via* ImH^+ with (terminal)CO_2^-(*A'*). ||||| H bonds involving backbone N–H groups.

Table 3. *Hydrogen bonds*

D = donor, *A* = acceptor, lengths in Å, angles in °.

	Symmetry	*D*···*A*	*D*–H	H···*A*	*D*–H···*A*
Type 1: N⁺(Im)–H···O					
Nε2 (3)–H···Oε2 (2)	*d*	2·663 (5)	1·06 (6)	1·68 (7)	151 (7)
Nδ1 (3)–H···O' (4)		2·686 (4)	0·92 (4)	1·77 (4)	174 (5)
Type 2: H_2N^+–H···O					
N(1)–H···O' (4)	*b*	2·800 (6)	1·00*	1·90	148
N(1)–H···O'' (4)	*a*	2·837 (6)	1·00*	1·86	165
N(1)–H···O(*W*)		2·779 (5)	1·00*	1·79	171
Type 3: N–H···O					
N(4)–H···O'' (4)	*e*	2·929 (5)	1·00*	1·97	159
N(2)–H···O(2)	*c*	2·958 (5)	1·00*	2·06	149
Type 4: O(*W*)–H···O					
O(*W*)–H···Oε2 (2)		2·745 (6)	0·954*	1·79	178
O(*W*)–H···Oε1 (2)	*c*	2·779 (7)	0·954*	1·84	169
Type 5: special cases					
Cα(1)–H···O(1)	*c*	3·095 (6)	1·08*	2·43	119
Cα(3)–H···O(3)	*e*	3·228 (5)	1·08*	2·40	132

Symmetry code
(*a*) $x-\frac{1}{2}, y-\frac{1}{2}, z$ (*d*) $-x+\frac{1}{2}, y+\frac{1}{2}, -z$
(*b*) $x-\frac{1}{2}, y+\frac{1}{2}, z$ (*e*) $x, y-1, z$
(*c*) $x, y+1, z$

* H atoms constrained.

Around $(x,y,\frac{1}{2})$ the molecules are kept together by van der Waals interactions. Only the intramolecular distances Cγ(4)···N(4) = 3·13 (1), Cδ1(4)···Cα(4) = 3·26 (1) and Hδ1(4)···H(4) = 2·30 (3) Å are shorter, approximately 0·1 Å, than the sum of the relevant van der Waals radii [*r*(S) = 1·85, *r*(C) = 1·7, *r*(N) = 1·5, *r*(O) = 1·4, *r*(H) = 1·2 Å (Pauling 1960; Robertson, 1953)]. The packing of Phe groups around the twofold screw axes at $z=\frac{1}{2}$ is by no means intimate, the intermolecular H···H distances starting at 2·50 Å, C···H at 2·81 Å and C···C at 3·53 Å. Only the distance Hδ2(4)···Cδ2(4;$-x+\frac{3}{2}$, $y+\frac{1}{2}$, $-z+1$) = 2·81 (2) Å is significantly shorter than the sum of the van der Waals radii.

A characteristic feature of the structure is the large space available for the Met side groups around the twofold axes at $z=\frac{1}{2}$ (Fig. 2). The translation period along **b** (5·47 Å) is 0·4 Å longer than the translation period of 5·07 Å between the Met groups in L-methionyl-L-methionine (Stenkamp & Jensen, 1975).

According to the shortest distances in the Met region [$C\gamma(1)\cdots C(1) = 3{\cdot}13$ (1), $C\beta(1)\cdots O(1) = 3{\cdot}00$ (1), $C\beta(1)\cdots O(1;y+1) = 3{\cdot}30$ (1), $H\gamma2(1)\cdots C(1) = 2{\cdot}79$ (3) Å] only $C\beta(1)$ is rather rigidly fixed between O(1) and O(1, $y+1$); the remaining Met side-chain atoms are disordered.

Bond lengths and angles are given in Fig. 4 and torsion angles are listed in Table 4. The Phe and His side groups are planar within experimental error. For the peptide units the deviations from the respective planes are $\lesssim 0{\cdot}04$ Å.

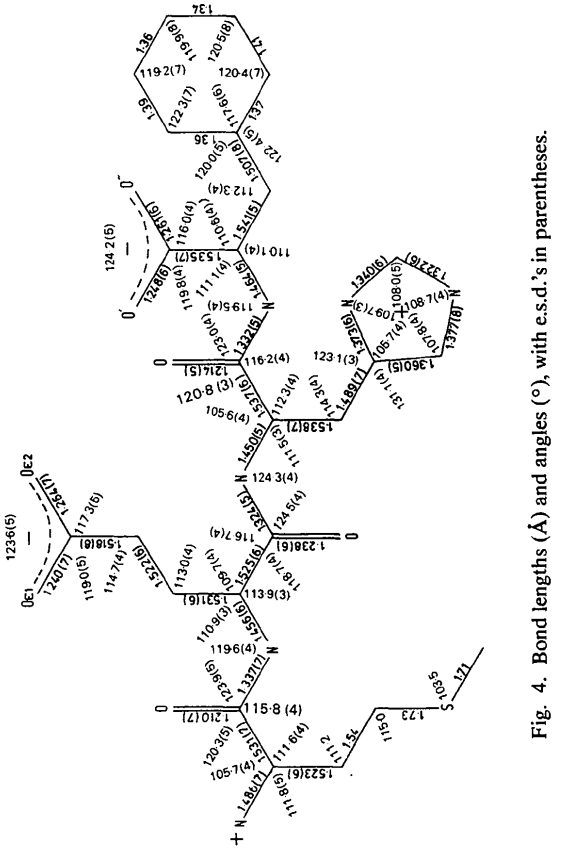


Fig. 4. Bond lengths (Å) and angles (°), with e.s.d.'s in parentheses.

The backbone has α-helix-type bends at Cα(2) and Cα(4). Between Cα(2) and Cα(4) the chain is almost fully extended. The torsion angles at the Cα atoms for Glu and His do not lie in the fully allowed region of the Ramachandran plot (Ramachandran, Ramakrishnan & Sasisekharan, 1963), implying that the backbone exhibits considerable strain. At Cα(3) the angle between successive peptide planes is only 8·3°. The bond angle N(3)–Cα(3)–C(3) = 105·6 (4)° and the distance N(3)···O(3) = 2·584 (4) Å are remarkably small. Both the N(3)–H and the C(3)–O(3) group are excluded from inter- and intramolecular H bonding. The conformation at His lies close to the planar *C5* conformation. Theoretical PCILO (Perturbative Configuration Interaction using Localized Orbitals) calculations have shown that this conformation corresponds to a local energy minimum in conformational space (Maigret & Pullman, 1974). In dilute CCl_4 solutions of the 'dipeptide' CH_3CO–Phe–$NHCH_3$ this conformation has been observed for 55% of the molecules (IR experiments; Cung, Marraud & Néel, 1973). In crystal structures it does not always occur, however, at residues for which both NH and C=O are excluded from H bonding (Table 5). Further theoretical calculations are necessary to understand the differences between the conformations of the molecules given in Table 5 and to explain why N···O and N–Cα–C are smallest at His in ACTH 4–7.H_2O.

The conformation of Met (Table 1), which is not well defined because of the disorder, may be compared with the various conformations of Met groups found in different crystal structures (Stenkamp & Jensen, 1975; Table 5). The Im ring is folded back over the backbone with the trace of the $C\beta(3)$–$C\gamma(3)$ bond approximately bisecting the N(3)–Cα(3)–C(3) angle. A similar situation occurs in *cyclo*(-L-histidyl-L-aspartyl-) trihydrate (Ramani, Venkatesan & Marsh, 1978). As noted by Lin & Webb (1973) the torsion angle χ^2 must be close to 90° to prevent interference between Im and the backbone. The present (absolute) value of 73·8 (7)° may be compared with the value of 71° in *cyclo*(-L-histidyl-L-aspartyl-) trihydrate. In the latter peptide the backbone angle N–Cα(His)–C = 113·4°. This implies that the present small value for

Table 4. *Torsion angles* (°)

Apart from Met, standard deviations are 0·5 – 0·8°. Torsion angles for an idealized α bend are $\varphi = -67°$, $\psi = -44°$, and for the idealized antiparallel β-sheet $\varphi = -140°$, $\psi = 135°$ (Dickerson & Geis, 1969).

Code	Definition	Met i=1	Glu i=2	His i=3	Phe i=4
φ_i	C($i-1$)–N(i)–Cα(i)–C(i)		−87·8	−171·7	−74·9
ψ_i	N(i)–Cα(i)–C(i)–N($i+1$)/O′(i)	117·4	−28·0	171·2	−23·2
ω_i	Cα(i)–C(i)–N($i+1$)–Cα($i+1$)	−173·9	−176·8	174·3	
χ^1_i	N(i)–Cα(i)–Cβ(i)–Cγ(i)	−170*	−65·1	55·9	−77·2
χ^2_i	Cα(i)–Cβ(i)–Cγ(i)–S/CNδ1(i)	176*	−56·5	73·8	77·0
χ^3_i	Cβ(i)–Cγ(i)–Cδ(i)–C/Oε1(i)	120*	−30·7		

* Calculated for average atomic positions.

Table 5. *Comparison of conformations of residues with non-H-bonded* NH *and* C=O *groups*

Compound	Residue	φ	ψ	N···O (Å)	N–Cα–C (°)	Reference
(ACTH 4–7)·H_2O	His	−172	171	2·58	105·6	1
Boc-Gly-Pro	Gly	172	177	2·59	108	2
Pro-Tyr-Ile-Leu	Ile	−127	134	2·76	107·4	3
Cys-Pro-Leu-Gly(NH_2)	Leu	−106	10	3·58	111	4

References: (1) present paper; (2) Benedetti, Palumbo, Bonora & Toniolo (1976); (3) Cotrait, Geoffre, Hospital & Precigoux (1979); (4) Rudko & Low (1975).

N(3)–Cα(3)–C(3) = 105·6 (4)° discussed above is not required to accommodate the Im group. For Phe $\chi^1 = -77{\cdot}2$ (5)° is comparable with the values −59·7° in glycyl-DL-phenylalanine (Marsh, Ramakumar & Venkatesan, 1976) and −71·1 (4)° in Gly-Gly-Phe-Leu (Prangé & Pascard, 1979).

In ACTH 4–7 bond angles of a certain type show quite strong variations. The difference of 8·0 (6)° between the two exocyclic angles at Cγ(3) of Im is mainly due to the difference of approximately 0·2 Å between the van der Waals radii of C and N. In *cyclo*(-L-histidyl-L-aspartyl-) trihydrate the corresponding difference is 8·5 (4)° (Ramani, Venkatesan & Marsh, 1978). Apart from the C=O bonds, the bonds of the backbone are equal within $1{\cdot}5\sigma$ to the respective average values: Cα–C = 1·532, C–N = 1·331, N–Cα = 1·457, Cα–Cβ = 1·533 Å. Significant deviations from the standard values (Momany, McGuire, Burgess & Scheraga, 1975) occur for C(1)–O(1) and C(3)–O(3) which are relatively short, presumably because they are not involved in C–O···H–N bonding. The bond angles for the imidazole group (compare with Ramani, Venkatesan & Marsh, 1978; Table 6)*, and the lengths of the Cα–N(terminal), (Glu)CO_2 and (terminal)CO_2 bonds support the presence of ImH^+, (terminal)NH_3^+ and of charged CO_2^- groups, deduced from the positions of the H atoms in the Fourier synthesis. For the CO_2^- groups, C–O does not vary significantly due to the variations in the H bonding of the O atoms. The lengths of the C–C single bonds agree with those accepted for C(sp^2)–C(sp^3) (Ruysink & Vos, 1974), or for C(sp^3)–C(sp^3) bonds (Kuchitsu, 1968).

We thank Drs H. M. Greven (Oss) and Dr W. G. J. Hol for valuable discussions, and Mr W. Janssen (Oss) and Mr A. B. Verweij for help with chemical problems and crystallization experiments. Facilities for the Mo measurements were provided by Professor P. T. Beurskens and Dr J. H. Noordik (Nijmegen) and for the Cu measurements by Professor J. Drenth and Mr K. H. Kalk. The computations were carried out at the Computing Centre of the University of Groningen.

* See deposition footnote.

References

ADMIRAAL, G. (1981). Thesis, Univ. of Groningen.

ADMIRAAL, G. & VOS, A. (1983). To be published.

BENEDETTI, E., PALUMBO, M., BONORA, G. M. & TONIOLO, C. (1976). *Macromolecules*, **9**, 417–420.

BENNETT, I., DAVIDSON, A. G. H., HARDING, M. M. & MORELLE, I. (1970). *Acta Cryst.* B**26**, 1722–1729.

BEURSKENS, P. T., PRICK, P. A. J. & DOESBURG, H. M. (1979). *Acta Cryst.* A**35**, 765–772.

BRAUN, P. B., HORNSTRA, J. & LEENHOUTS, J. I. (1969). *Philips Res. Rep.* **24**, 85–118.

COTRAIT, M., GEOFFRE, S., HOSPITAL, M. & PRECIGOUX, G. (1979). *Acta Cryst.* B**35**, 114–118.

CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.

CUNG, M. T., MARRAUD, M. & NÉEL, J. (1973). *Conformation of Biological Molecules and Polymers*, edited by E. D. BERGMANN & B. PULLMAN, pp. 69–83. Jerusalem Academic Press.

DICKERSON, R. E. & GEIS, I. (1969). *The Structure and Action of Proteins*, pp. 13–25. New York: Harper & Row.

DONOHUE, J., LAVINE, L. R. & ROLLETT, J. S. (1956). *Acta Cryst.* **9**, 655–662.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

GREFF, D., TOMA, F., FERMANDJIAN, S., LÖW, M. & KISFALUDY, L. (1976). *Biochim. Biophys. Acta*, **439**, 219–231.

GREVEN, H. M. & DE WIED, D. (1980). *Hormones and the Brain*, edited by D. DE WIED & P. A. VAN KEEP. Falcon House: MTP.

KOETZLE, TH.F. & LEHMANN, M. S. (1976). *The Hydrogen Bond*, Vol. II, edited by P. SCHUSTER, G. ZUNDEL, & C. SANDORFY, pp. 457–469. Amsterdam: North-Holland.

KUCHITSU, K. (1968). *J. Chem. Phys.* **49**, 4456–4462.

LIN, C. F. & WEBB, L. E. (1973). *J. Am. Chem. Soc.* **95**, 6803–6811.

MAIGRET, B. & PULLMAN, B. (1974). *Theor. Chim. Acta*, **35**, 113–128.

MARSH, R. E. & DONOHUE, J. (1967). *Advances in Protein Chemistry*, Vol. 22, edited by C. B. ANFINSEN JR, M. L. ANSON, J. T. EDSALL & F. M. RICHARDS, pp. 235–256. London: Academic Press.

MARSH, R. E., RAMAKUMAR, S. & VENKATESAN, K. (1976). *Acta Cryst.* B**32**, 66–70.

MOMANY, F. A., MCGUIRE, R. F., BURGESS, A. W. & SCHERAGA, H. A. (1975). *J. Phys. Chem.* **79**, 2361–2381.

OLOVSSON, I. & JÖNSSON, P. G. (1976). *The Hydrogen Bond*, Vol. II, edited by P. SCHUSTER, G. ZUNDEL & C. SANDORFY, pp. 393–456. Amsterdam: North-Holland.

PAULING, L. (1960). *The Nature of the Chemical Bond*, 3rd ed., p. 260. Ithaca: Cornell Univ. Press.

PRANGÉ, T. & PASCARD, C. (1979). *Acta Cryst.* B**35**, 1812–1819.

PRICK, P. A. J. (1979). PhD Thesis, Univ. of Nijmegen.

RAMACHANDRAN, G. N., RAMAKRISHNAN, C. & SASISEKHARAN, V. (1963). *J. Mol. Biol.* **7**, 95–99.

RAMANI. R., VENKATESAN, K. & MARSH, R. E. (1978). *J. Am. Chem. Soc.* **100**, 949–953.

ROBERTSON, M. J. (1953). *Organic Crystals and Molecules*, p. 227. Ithaca: Cornell Univ. Press.

RUDKO, A. D. & LOW, B. W. (1975). *Acta Cryst.* B**31**, 713–725.

RUYSINK, A. F. J. & VOS, A. (1974). *Acta Cryst.* B**30**, 1997–2002.

SALEMME, F. R. (1972). *Arch. Biochem. Biophys.* **151**, 533–539.

SCHENK, H. (1980). *Computing in Crystallography*, edited by R. DIAMOND, S. RAMASESHAN & K. VENKATESAN, pp. 7.01–7.22, 10.01–10.18. Bangalore: The Indian Academy of Sciences.

STENKAMP, R. E. & JENSEN, L. H. (1975). *Acta Cryst.* B**31**, 857–861.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

SUTTON, L. E. (1965). *Tables of Interatomic Distances and Configuration in Molecules and Ions*, Suppl. 1956–1959. London: The Chemical Society.

WAL, H. R. VAN DER (1979). PhD Thesis, p. 39. Univ. of Groningen.

WIED, D. DE (1974). *The Neurosciences, Third Study Program*, edited by O. F. SCHMIDT & F. C. WORDEN, pp. 653–666. Cambridge: MIT Press.

XRAY system (1976). Dutch version of the XRAY system. Tech. Rep. TR-192. Computer Science Center, Univ. of Maryland, College Park, Maryland.