Table 7. *Asymmetry parameters and pseudorotation parameters*

	(I)	(II)
Ring *A*		
	$\Delta C_s^3 = 2 \cdot 39$	$\Delta C_s^3 = 2 \cdot 26$
	$\Delta C_2^{2,3} = 11 \cdot 75$	$\Delta C_2^{2,3} = 17 \cdot 21$
	$\Delta C_2^{1,2} = 28 \cdot 41$	$\Delta C_2^{1,2} = 38 \cdot 63$
Ring *B*		
	$\Delta C_s^5 = 1 \cdot 26$	$\Delta C_s^7 = 0 \cdot 56$
	$\Delta C_2^{5,6} = 1 \cdot 29$	$\Delta C_2^{5,10} = 1 \cdot 98$
	$\Delta C_2^{6,7} = 2 \cdot 48$	$\Delta C_2^{5,6} = 2 \cdot 31$
Ring *C*		
	$\Delta C_s^9 = 2 \cdot 48$	$\Delta C_s^{11} = 2 \cdot 37$
	$\Delta C_2^{9,11} = 3 \cdot 24$	$\Delta C_2^{9,11} = 3 \cdot 00$
	$\Delta C_2^{8,14} = 8 \cdot 01$	$\Delta C_2^{8,9} = 6 \cdot 87$
Ring *D*		
	$\Delta = 4 \cdot 71°$	$\Delta = 17 \cdot 75°$
	$\varphi_m = 47 \cdot 71°$	$\varphi_m = 50 \cdot 05°$

molecules per unit cell whereby the length lies parallel to a diagonal of the *ac* face. The width lies approximately in the (111) plane and the thickness in a plane perpendicular to this. There are no significant short intermolecular contacts.

We thank the University of Cape Town for research grants and the CSIR (Pretoria) for data collected on the diffractometer.

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Structure and Conformation of Amino Acids Containing Sulfur. V. *N*-Formyl-L-methionine

By Cheng-san Chen and R. Parthasarathy*

Center for Crystallographic Research, Roswell Park Memorial Institute, Buffalo, NY 14263, *USA*

(*Received* 6 *January* 1977; *accepted* 12 *April* 1977)

$C_6H_{11}NO_3S$ crystallizes in the orthorhombic space group $P2_12_12_1$ with cell parameters at 22 ±3°C: $a = 7 \cdot 507$ (2), $b = 14 \cdot 875$ (1), $c = 7 \cdot 561$ (1) Å, $Z = 4$, $D_o = 1 \cdot 39$, $D_c = 1 \cdot 394$ g cm^{-3}. With diffractometer data to a 2θ limit of 162° for Cu $K\alpha$, the structure was solved and refined by the least-squares method to an R of 0·053 for the correct absolute configuration. The planar carboxyl and acyl groups are inclined to each other at 18·2°. The methionine side chain has the transplanar zigzag extended conformation commonly found for other methionine side chains and aliphatic groups. Short hydrogen bonds (2·555 Å) from the OH of the carboxyl groups to the acyl O atom link the molecules in a head-to-tail fashion in infinite chains along the a axis. The conformations of the side chains of methionine residues are compared and it was found that some correlation exists between the values of χ^1 and χ^2. The preferred values are: $\chi^1 = \pm 60$, 180; $\chi^2 = 180$ and $\chi^3 = 180°$.

Introduction

The blocked amino acid *N*-formyl-L-methionine is the initiator amino acid in the synthesis of proteins in all bacterial systems (Lengyel & Söll, 1969). Protein synthesis in eucaryotic cells is initiated in a manner similar to that of bacteria, but the Met-tRNA initiator is not formylated. The growing polypeptide chain is rapidly deformylated (Adams, 1968) and before the nascent chain is 15 to 20 residues in length, the initiator methionine residue is removed (Wilson & Dintzis, 1970; Jackson & Hunter, 1970). Our interest was to investigate what selective advantage, if any, is conferred by methionine as the initiator amino acid to the protein-synthesizing systems over other amino acids.

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* To whom correspondence should be addressed.

Crystals of *N*-formyl-L-methionine (Sigma Chemical Co.) were grown by evaporation from supersaturated aqueous solutions. A crystal of dimensions 0·39 × 0·30 × 0·29 mm* was mounted with the *a* axis along the φ axis of a GE XRD-5 diffractometer equipped with a goniostat. Cell parameters (Table 1) were obtained by a least-squares refinement of 60 high-angle reflections for which the α_1,α_2 separation could be measured. The stationary-crystal stationary-counter technique (Furnas & Harker, 1955) with balanced Ni–Co Ross filters was used for measuring 1133 unique three-dimensional intensity data to a 2θ limit of 162° for Cu $K\alpha$ radiation (λ = 1·54051 Å); 34 reflections had intensities less than twice the average background intensity. The detailed absorption corrections (Coppens, 1970) (μ = 30·28 cm^{-1}) were carried out based on the crystal geometry.* Lorentz–polarization and $\alpha_1 - \alpha_2$ corrections were made in the usual way.

The structure was solved by the heavy-atom method. Block-diagonal least-squares (BDLS) refinement of all 11 non-hydrogen atoms with individual anisotropic thermal parameters led to an *R* ($R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$) value of 0·084. The 11 H atom positions were obtained from electron density difference maps at this stage. Continuation of structure refinement including all H atoms with individual isotropic thermal factors brought the *R* index down to 0·065. The absolute configuration of the molecule was determined by the *R* value technique (Hamilton, 1965). The ratio of the *R* values for the L and D isomers is 0·912, indicating that the coordinates in Table 2 correspond to the correct absolute configuration, namely L. The final *R* value for all observed reflections is 0·053. None of the shifts in the final cycle of refinement were greater than one-tenth of their estimated standard deviations for the non-hydrogen parameters and one-fifth the estimated standard deviations for the H parameters. The refinement was considered complete. The final positional and thermal parameters with e.s.d.'s are given in Table 2.* The refinement was carried out with the differential-synthesis weighting scheme of $1/f_C$ (f_C = scattering factor of carbon) and by minimizing $\{\Sigma w[|F_o| - (1/K)|F_c|]^2\}$. The 34 weak reflections were given zero weight during the refinement and for the *R* index calculations. Atomic scattering factors for S, O, N and C were those listed in *International Tables for X-ray Crystallography* (1968) and the anomalous dispersion corrections for S and O were those given by Cromer & Liberman (1970). For the H atoms, the scattering factors given by Stewart, Davidson & Simpson (1965) were used.

Table 1. *Crystal data*

Formula	$C_6H_{11}NO_3S$
M_r	177·22
Space group	$P2_12_12_1$
Z	4
a	7·507 (2) Å
b	14·875 (1)
c	7·561 (1)
D_c	1·394 g cm^{-3}
D_o (flotation)	1·39
λ(Cu $K\alpha_1$)	1·54051 Å
Temperature	22 ± 3°C
μ	30·28 cm^{-1}
m.p.	105°C
$[\alpha]_D^{25}$ (0·8, H_2O)	−10·0°

Table 2. *Positional parameters* (×10^4; ×10^3 *for* H *atoms*) *with e.s.d.'s in parentheses*

	x	*y*	*z*	*B* (Å^2) (×10)
S	−978 (2)	−7863 (1)	−623 (2)	
O(1)	−3467 (5)	−4967 (2)	−3444 (5)	
O(2)	−4097 (4)	−6063 (2)	−5336 (4)	
O(6)	2555 (4)	−5798 (2)	−5030 (5)	
N	77 (5)	−5224 (2)	−3812 (5)	
C(1)	−3007 (5)	−5581 (2)	−4356 (6)	
C(2)	−1098 (5)	−5910 (2)	−4505 (5)	
C(3)	−886 (6)	−6821 (2)	−3582 (5)	
C(4)	−1093 (7)	−6757 (2)	−1596 (6)	
C(5)	−999 (9)	−7542 (4)	1681 (7)	
C(6)	1808 (6)	−5211 (3)	−4128 (6)	
H(O2)	−549 (9)	−587 (4)	−504 (8)	58
H(N)	−26 (8)	−484 (4)	−314 (8)	53
H(C2)	−88 (8)	−599 (3)	−565 (8)	45
H(*A*C3)	−187 (7)	−730 (3)	−412 (7)	36
H(*B*C3)	7 (7)	−702 (3)	−380 (6)	33
H(*A*C4)	−227 (8)	−649 (4)	−125 (8)	54
H(*B*C4)	−18 (7)	−649 (3)	−114 (7)	39
H(*A*C5)	26 (9)	−742 (4)	195 (9)	56
H(*B*C5)	−124 (11)	−812 (5)	210 (11)	83
H(*C*C5)	−197 (8)	−70 (4)	212 (9)	56
H(C6)	246 (7)	−469 (3)	−366 (7)	39

Discussion

The interatomic distances and the bond angles of *N*-formyl-L-methionine are illustrated in Figs. 1 and 2. There is good agreement between the bond distances and angles of this molecule and the values available in the literature for the various groups, such as sulfides (Pauling, 1960; Sutton, 1965), amides and peptides (Marsh & Donohue, 1967), *N*-acyl amino acids (Chen & Parthasarathy, 1977), and the methionine side chains (see Table 3). In the only other *N*-formyl amino acid whose structure has been studied (Ohki, Takenaka,

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* A diagram showing the shape and dimensions of the crystals has been deposited. See following footnote.

* Lists of structure factors and anisotropic thermal parameters, and a diagram have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32667 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Shimanouchi & Sasada, 1975), the N–C(6)–O(6) angle of 122·2° is significantly smaller than in *N*-formyl-L-methionine.

Three conformational features of this molecule are noteworthy. The *N*-acyl group is in the *trans*-planar conformation [O(6)–C(6)–N–C(2) torsion angle is −0·9°] and is inclined at 18·2° to the plane of the carboxyl group. This feature agrees with the observations (Marsh & Glusker, 1961; Freeman, Robinson & Schoone, 1964) that the carboxyl groups are nearly parallel or perpendicular to the adjacent peptide plane in dipeptides. The torsion angles of −163·6° for φ [C(6)–N–C(2)–C(1)] and −164·5° for ψ_T^1 [N–C(2)–C(1)–O(2)] (IUPAC–IUB Commission on Biochemical Nomenclature, 1970) show that the backbone of the molecule is nearly in the fully extended conformation. The methionine side chain is in the zigzag *trans*-planar fully extended conformation. The conformational angles χ^1, χ^2 and χ^3 (Lakshminarayanan, Sasisekharan & Ramachandran, 1967) are respectively 54·3, 176·1 and 173·6°. When χ^1 is 60°, the conformation with S (±)*gauche* to C(2) (*i.e.* $\chi^2 = 60$ or $-60°$) is unfavorable because of ensuing short contacts between S and the carboxyl or amide groups. The conformation with $\chi^1 = 60°$ and S *trans* to C(2) (*i.e.* $\chi^2 = 180°$) is favorable and this conformation

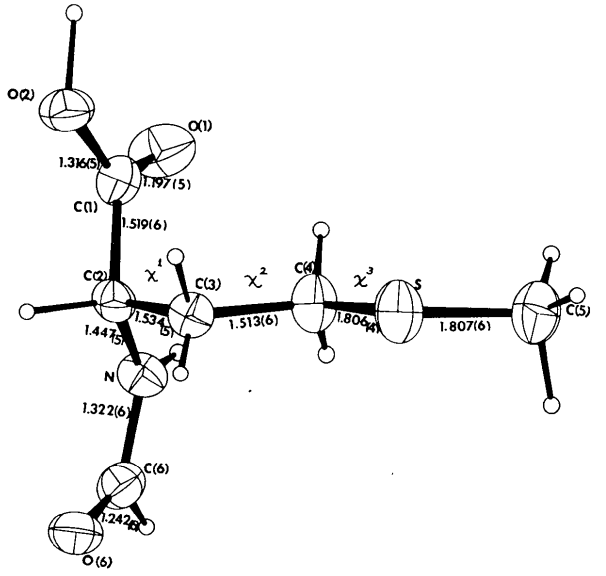

Fig. 1. Covalent bond distances (Å) of *N*-formyl-L-methionine. χ^1, χ^2 and χ^3 denote conformation angles about the bonds C(2)–C(3), C(3)–C(4) and C(4)–S.

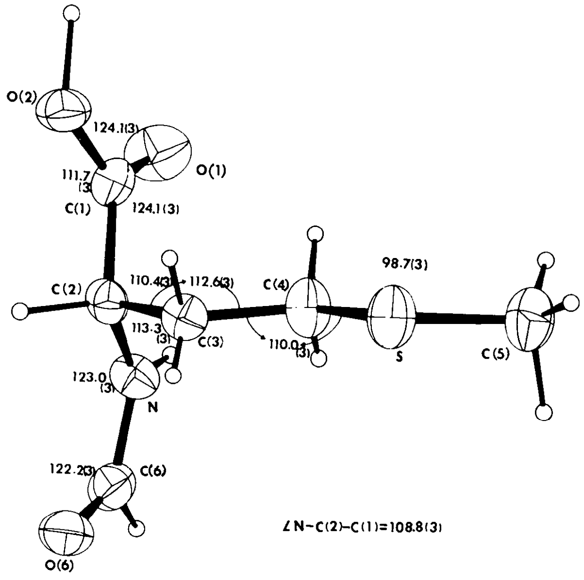

Fig. 2. Covalent bond angles (°) of *N*-formyl-L-methionine.

Table 3. *Comparison of bond lengths and angles about methionine side chain with the published structures*

Standard deviations are given in parentheses.

Code	Compound	C(2)–C(3)	C(3)–C(4)	C(4)–S	S–C(5)	∠C(2)C(3)C(4)	∠C(3)C(4)S	∠C(4)SC(5)	References
*M*1	DL-Methionine (α-form)	1·55 Å	1·51 Å	1·79 Å	1·77 Å	111·0°	111·7°	99·1°	Mathieson (1952)
*M*2	DL-Methionine (β-form)	1·60	1·52	1·80	1·78	112·3	107·4	100·3	Mathieson (1952)
*M*3	*N*-Acetylmethionyl-dimethylamide	1·568 (2)	1·550 (2)	1·823 (1)	1·826 (1)	108·6 (1·0)	108·3 (9)	98·5 (6)	Aubry, Marraud, Protas & Néel (1971)
*M*4	L-Methionine (molecule *A*)	1·52 (2)	1·51 (2)	1·83 (3)	1·80 (9)	111·0 (1·2)	107·3 (1·1)	99·8 (1·0)	Torii & Iitaka (1973)
*M*5	L-Methionine (molecule *B*)	1·53 (4)	1·51 (4)	1·79 (4)	1·71 (5)	117·9 (1·7)	113·3 (1·4)	101·8 (1·5)	Torii & Iitaka (1973)
*M*6	DL-Alanyl-L-methionine	1·527 (5)	1·508 (6)	1·811 (4)	1·792 (7)	113·9 (3)	110·0 (3)	99·1 (3)	Stenkamp & Jensen (1974)
*M*7	*N*-Acetylmethionine methyl ester	1·538 (6)	1·516 (6)	1·800 (5)	1·760 (7)	113·0 (3)	109·8 (3)	102·0 (3)	Geddes, Hamodrakas & Sheldrick (1974)
*M*8	L-Methionyl-L-methionine (1st residue)	1·531 (4)	1·515 (5)	1·816 (3)	1·803 (5)	112·7 (3)	108·7 (2)	99·8 (2)	Stenkamp & Jensen (1975)
*M*9	L-Methionyl-L-methionine (2nd residue)	1·543 (4)	1·523 (4)	1·813 (3)	1·794 (6)	112·2 (2)	113·4 (2)	99·9 (2)	Stenkamp & Jensen (1975)
*M*10	*N*-Formyl-L-methionine	1·534 (5)	1·513 (6)	1·806 (4)	1·807 (6)	112·6 (3)	110·0 (3)	98·7 (3)	
	Average*	1·536 (5)	1·518 (5)	1·811 (4)	1·787 (13)	112·7 (1·0)	110·1 (8)	100·0 (4)	

* *M*1 and *M*2 are excluded for this average.

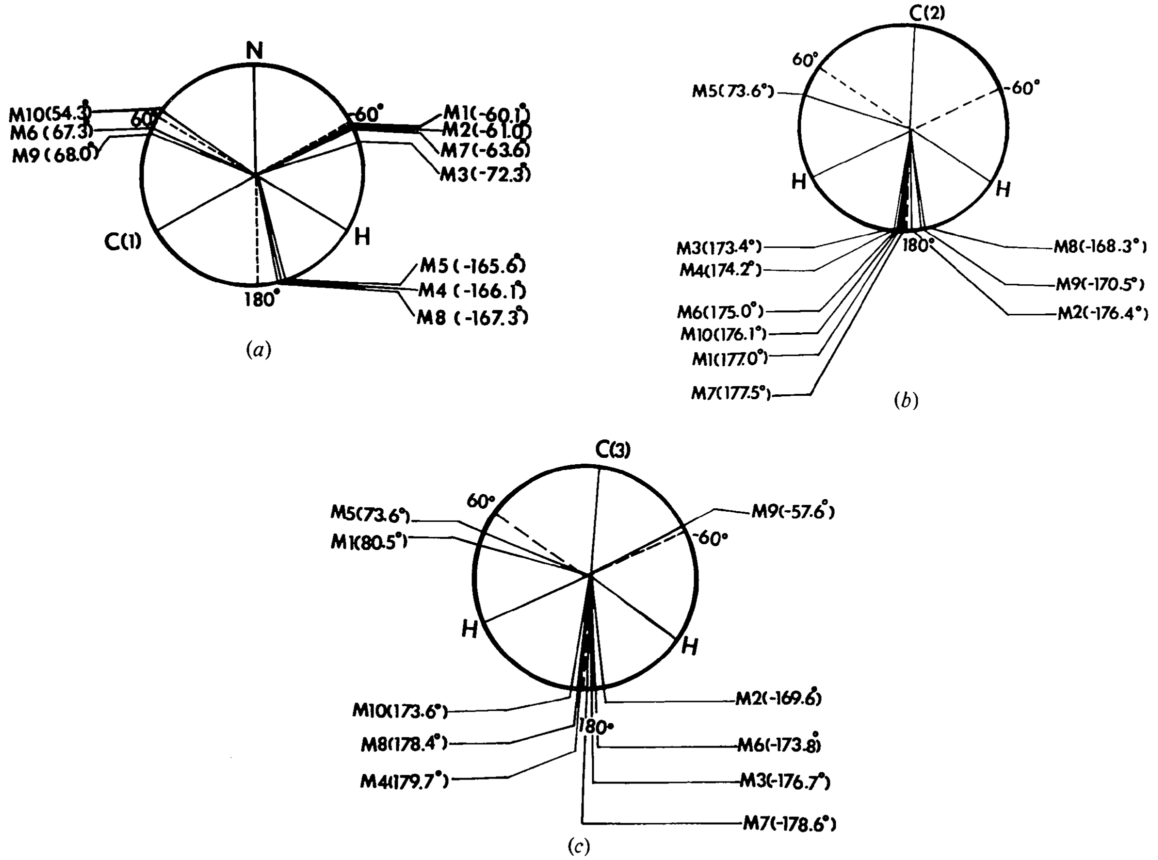

Fig. 3. The distribution of the conformation angles χ^1, χ^2 and χ^3 of methionine side chains. (*a*) $\chi^1 = \tau[\mathrm{N-C(2)-C(3)-C(4)}]$: orientation of C(4) with respect to N, viewed along C(3)–C(2). (*b*) $\chi^2 = \tau[\mathrm{C(2)-C(3)-C(4)-S}]$: orientation of S with respect to C(2), viewed along C(4)–C(3). (*c*) $\chi^3 = \tau[\mathrm{C(3)-C(4)-S-C(5)}]$: orientation of C(5) with respect to C(3), viewed along S–C(4).

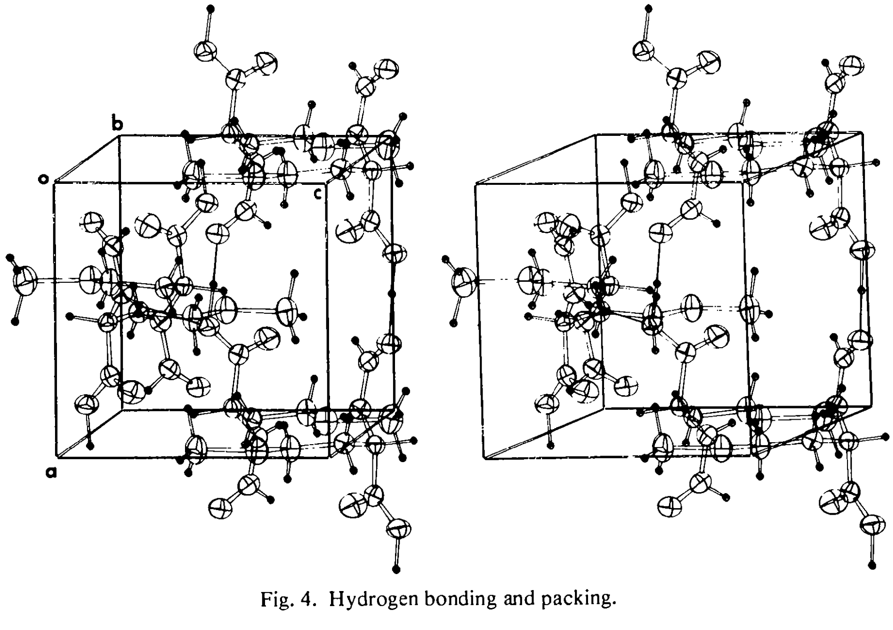

Fig. 4. Hydrogen bonding and packing.

is found for three molecules (Fig. 3). If χ^1 is 180°, the conformation with S (−)*gauche* to C(2) (*i.e.* $\chi^2 = -60°$) is unfavorable because of short contacts to the carboxyl group. Consequently, χ^2 can take up either +60° or 180°; of the molecules for which $\chi^1 = 180°$, only one has χ^2 60°; the rest have $\chi^2 = 180°$. If χ^1 is −60°, $\chi^2 = -60°$ is unfavorable. Of the two possibilities $\chi^2 = 180$ or −60°, only $\chi^2 = 180°$ is preferred by all the molecules. These results indicate some correlation between χ^1 and χ^2, and also that $\chi^2 = 180°$ is preferred, since in this conformation S is far away from the amide or carboxyl groups. For χ^3, the value of 180° is preferred though three molecules exhibit different conformations. Stenkamp & Jensen (1975) have recently discussed the conformation of the methionine side chains and have pointed out that the torsion angles observed in the crystal structures differ from the minimum-energy conformation of methionine side chains calculated by Ralston & DeCoen (1974).

The two polar hydrogens H(O2) and H(N) take part in hydrogen bonding (Fig. 4). The hydrogen bond from the carboxyl OH to the formyl O is quite short and presumably strong. This mode of hydrogen bonding from the carboxyl to the acyl group is exhibited in almost all *N*-acyl amino acids and peptides (Chen & Parthasarathy, 1977). Similarly, several *N*-acyl amino acids and peptides show N—H···O(carboxyl) contacts which may be interpreted as weak hydrogen bonds. The present structure also follows this pattern. The atom O(1) is not involved in any hydrogen bonding.

The molecules are oriented so that the extended 'backbone' is approximately along the *a* axis. These molecules are hydrogen bonded head-to-tail and form infinite chains along the *a* axis. The zigzag planar side chains are parallel to the *bc* plane but do not come close to each other (Fig. 4). The shortest contact to S is 2·97 Å, from H(C6) of a neighboring molecule; all other contacts are longer than the sum of the van der Waals radii of contacting atoms.

We are grateful to Dr D. Harker for his keen interest and valuable comments. This project was supported in part by grant No. CA16844 from the National Institutes of Health. The use of the following programs is acknowledged: *ORTEP* for plotting, a general Fourier summation program and torsion-angle program by Dr S. T. Rao.

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