Table 2. *Bond distances* (Å) *and angles* (°)

N(1)—N(2)	1·382 (5)	C(16)—C(44)	1·518 (9)
N(1)—C(5)	1·475 (6)	C(17)—C(34)	1·513 (7)
N(1)—C(21)	1·406 (6)	C(21)—C(22)	1·384 (7)
N(2)—C(3)	1·297 (6)	C(21)—C(26)	1·391 (8)
C(3)—C(4)	1·517 (7)	C(22)—C(23)	1·383 (8)
C(3)—C(31)	1·465 (7)	C(23)—C(24)	1·363 (9)
C(4)—C(5)	1·583 (7)	C(24)—C(25)	1·377 (8)
C(4)—C(41)	1·507 (7)	C(25)—C(26)	1·367 (8)
C(5)—C(6)	1·538 (7)	C(31)—C(32)	1·370 (8)
C(5)—C(14)	1·534 (7)	C(31)—C(36)	1·386 (8)
C(6)—C(7)	1·487 (8)	C(32)—C(33)	1·397 (7)
C(6)—O(61)	1·223 (6)	C(33)—C(34)	1·366 (8)
C(7)—C(8)	1·391 (8)	C(34)—C(35)	1·382 (8)
C(7)—C(12)	1·393 (7)	C(35)—C(36)	1·396 (7)
C(8)—C(9)	1·364 (8)	C(41)—C(42)	1·389 (8)
C(9)—C(10)	1·374 (9)	C(41)—C(46)	1·401 (7)
C(11)—C(12)	1·393 (8)	C(42)—C(43)	1·384 (8)
C(12)—C(13)	1·496 (8)	C(43)—C(44)	1·373 (9)
C(13)—C(14)	1·532 (8)	C(45)—C(46)	1·390 (8)
C(14)—C(15)	1·533 (8)		

N(2)—N(1)—C(5)	112·1 (4)	C(5)—C(14)—C(15)	114·8 (4)
N(2)—N(1)—C(21)	115·8 (4)	C(13)—C(14)—C(15)	111·5 (4)
C(5)—N(1)—C(21)	130·1 (4)	N(1)—C(21)—C(22)	122·8 (5)
N(1)—C(2)—C(3)	109·0 (4)	N(1)—C(21)—C(26)	118·2 (4)
N(2)—C(3)—C(4)	113·9 (4)	C(22)—C(21)—C(26)	118·9 (5)
N(2)—C(3)—C(31)	120·5 (4)	C(21)—C(22)—C(23)	119·2 (5)
C(4)—C(3)—C(31)	125·3 (4)	C(22)—C(23)—C(24)	122·6 (5)
C(3)—C(4)—C(5)	100·1 (4)	C(23)—C(24)—C(25)	117·5 (6)
C(3)—C(4)—C(41)	109·4 (4)	C(24)—C(25)—C(26)	121·9 (6)
C(5)—C(4)—C(41)	109·4 (4)	C(21)—C(26)—C(25)	120·0 (5)
N(1)—C(5)—C(4)	101·1 (4)	C(21)—C(26)—C(25)	120·0 (5)
N(1)—C(5)—C(6)	111·1 (4)	C(3)—C(31)—C(32)	122·0 (5)
N(1)—C(5)—C(14)	114·8 (4)	C(3)—C(31)—C(36)	119·7 (5)
C(4)—C(5)—C(6)	105·6 (4)	C(32)—C(31)—C(36)	118·3 (5)
C(4)—C(5)—C(14)	119·2 (4)	C(31)—C(32)—C(33)	121·1 (5)
C(6)—C(5)—C(14)	104·8 (4)	C(32)—C(33)—C(34)	121·0 (5)
C(5)—C(6)—C(7)	116·6 (4)	C(17)—C(34)—C(33)	122·6 (5)
C(5)—C(6)—O(61)	121·8 (5)	C(17)—C(34)—C(35)	119·1 (5)
C(7)—C(6)—O(61)	121·5 (5)	C(33)—C(34)—C(35)	118·2 (5)
C(6)—C(7)—C(8)	119·4 (5)	C(34)—C(35)—C(36)	121·1 (6)
C(6)—C(7)—C(12)	119·4 (5)	C(31)—C(36)—C(35)	120·2 (5)
C(8)—C(7)—C(12)	121·2 (5)	C(4)—C(41)—C(42)	120·7 (5)
C(7)—C(8)—C(9)	119·7 (5)	C(4)—C(41)—C(46)	119·9 (5)
C(8)—C(9)—C(10)	119·7 (6)	C(42)—C(41)—C(46)	119·3 (5)
C(9)—C(10)—C(11)	121·3 (6)	C(41)—C(42)—C(43)	120·6 (5)
C(10)—C(11)—C(12)	120·2 (5)	C(42)—C(43)—C(44)	121·3 (6)
C(7)—C(12)—C(11)	117·8 (5)	C(16)—C(44)—C(43)	121·4 (6)
C(7)—C(12)—C(13)	121·9 (5)	C(16)—C(44)—C(45)	121·0 (6)
C(11)—C(12)—C(13)	120·3 (5)	C(43)—C(44)—C(45)	117·6 (5)
C(12)—C(13)—C(14)	113·6 (4)	C(44)—C(45)—C(46)	123·1 (6)
C(5)—C(14)—C(13)	110·2 (4)	C(41)—C(46)—C(45)	118·0 (5)

Hydrogen atoms H(14) and H(13) are in a trans-pseudodiaxial disposition and situated on either side of Π(5): H(13)–Π(5) = 0·761, H(14)–Π(5) = −1·346 Å. The methyl group linked to C(14) is in a pseudoequatorial position as shown by the torsion angle H(13)—C(13)—C(14)—H(14) = 167·3°. Finally the distance H(4)—O(61) = 3·2 Å is rather large, much too large for a conformation of type (*B*), that would place atoms O(61) and H(4) close to each other, with a distance slightly larger than their van der Waals radii.

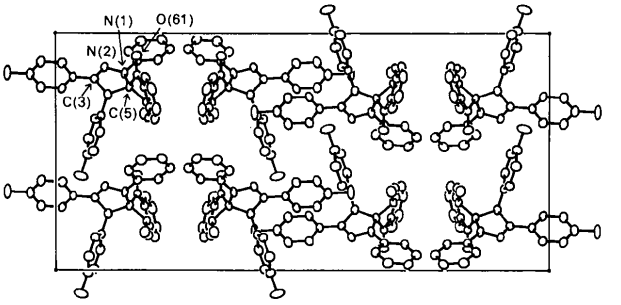

Fig. 2. View of the packing.

References

FRENZ, B. A. (1982). *SDP Structure Determination Package*. B. A. Frenz & Associates, College Station, Texas, USA, and Enraf–Nonius, Delft, The Netherlands.

International Tables for X-ray Crystallography (1974). Vol. IV, pp. 99 and 149. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

ITO, T. & SUGAWAKA, Y. (1983). *BEST PLANE Program*, 3rd ed. (*BP7C*). The Institute of Physical and Chemical Research, Wako-shi, Saitama 351, Japan.

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

KERBAL, A., TSHIAMALA, K., VEBREL, J. & LAUDE, B. (1988). *Bull. Soc. Chim. Belg.* **97**, 149–161.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1982). *MULTAN*11/82. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

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Chemotactic Peptide Analogs: Conformation of *N*-Formyl-L-methionyl-N^2-methyl-L-phenylalanine *tert*-Butyl Ester

BY DRAKE S. EGGLESTON

Department of Physical & Structural Chemistry, Smith Kline & French Laboratories, L-950, PO Box 1539, King of Prussia, PA 19406-0939, USA

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Abstract. $C_{20}H_{30}N_2O_4S$, $M_r = 394·54$, orthorhombic, $P2_12_12_1$, $a = 8·803$ (3), $b = 9·480$ (9), $c = 26·047$ (20) Å, $V = 2174$ (3) Å^3, $Z = 4$, $D_m = 1·21$ (2) (flotation in aqueous $ZnCl_2$), $D_x = 1·205$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, $\mu = 1·662$ cm^{-1}, $F(000) = 848$, $T = 253$ K, $R = 0·076$ for 1872 observations, $I \geq$

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3·0$\sigma(I)$. The peptide crystallizes with a *cis*-planar peptide bond, $\omega = -8{\cdot}1\ (5)°$; other principal backbone torsion angles are $\varphi_1 = -128{\cdot}6\ (6)$, $\psi_1 = 141{\cdot}2\ (6)$, $\varphi_2 = -103{\cdot}3\ (6)°$. The methionine side chain is disordered about the C^γ—S bond with one conformation (60% occupancy) described by the torsion angles $\chi_1^1 = -66{\cdot}0\ (7)$, $\chi_1^2 = -170\ (1)$, $\chi_1^3 = -168\ (1)°$ and the other (40% occupancy) with $\chi_1^2 = 164\ (1)$, $\chi_1^3 = 83\ (2)°$. The phenylalanine side chain adopts the g^- conformation with $\chi_2^1 = -54{\cdot}8\ (7)°$. The crystal conformation is in general agreement with one of two major conformers (*cis* and *trans*) deduced from solution NMR studies. The combination of *N*-methylation and C-terminal esterification appears to lock the phenylalanine side chain into the g^- conformation.

Introduction. As part of an investigation of the Freer model for *N*-formyl peptides at the rabbit neutrophil receptor (Freer *et al.*, 1982) the conformational propensities of a series of *N*-formyl peptides have been explored by solution NMR, theoretical calculations and crystal-structure analysis (Heald, 1982; Jeffs, Heald, Chodosh & Eggleston, 1984; Eggleston, 1988). Two of the principal interests of this study were the influence of *N*-methylation on the observed peptide conformations as compared to their non-methylated analogs, and the effect of C-terminal esterification on receptor binding and conformational preference.

As a continuation of these studies the crystal structure of *N*-formyl-L-methionyl-N^2-methyl-L-phenylalanine *tert*-butyl ester has been determined. This peptide displays very poor receptor affinity, failing to compete for binding sites with labeled For-Met-Leu-Phe on both polymorphonuclear leukocytes and rabbit alveolar macrophages and being able to ellicit a chemotactic response only at high concentrations in either system (Heald, 1982). In comparison, the unesterified *N*-methyl acid analogue has a measurable, but unspectacular binding affinity ($K_D = 30\ \mu M$)* while the parent, unmethylated acid has a significantly stronger affinity ($K_D = 300$ nM).

N-Methylation of peptide bonds may introduce a number of structural perturbations including suppression of hydrogen-bonding capabilities of the amide nitrogen, steric constraints and adoption of the *cis* geometry for the tertiary amide bond. While the *cis* conformation of *N*-methylated peptides has often been reported in solution studies there are very few examples of observations of this conformation in crystalline linear *N*-methylated peptides (Kojima, Kido, Itoh, Yamane & Ashida, 1980; Vitoux, Aubry, Cung, Boussard & Marraud, 1981); most known examples involve more constrained cyclic peptides (Iitaka, Nakamura, Takada & Takita, 1974; Springer *et al.*, 1984; Jain & Sobell, 1972; Petcher, Weber & Ruegger, 1976; Jolad *et al.*, 1977). The recent suggestion, through solution NMR studies, of a preferred *cis* geometry at the Met-Leu peptide bond in For-Met-Leu-Phe (Valensin *et al.*, 1986) lends even greater interest to the search for systems which might incorporate this feature.

NMR studies on *N*-For-L-Met-N^2-methyl-L-Phe-O'Bu indicated a significant population (21%) of the *cis* isomer in $CDCl_3$ solution, although interestingly the unesterified acid was shown to present a greater percentage (31%) of molecular population in the *cis* conformation (Heald, 1982). Subsequent crystallization of the ester thus far has led to isolation of only the *cis* isomer, as reported here, whereas crystallization of the corresponding acid led only to the *trans* isomer (Jeffs *et al.*, 1984).

Experimental. A colorless prism of approximate dimensions 0·15 × 0·15 × 0·30 mm, grown by evaporation from aqueous acetone, was mounted on a glass fiber in a cold stream at 253 (2) K. Cell dimensions were determined from the angular settings of 25 reflections with $30 \le 2\theta(\text{Mo}) \le 35°$ measured on an Enraf–Nonius CAD-4 diffractometer. Intensity data were collected with variable-speed ω–2θ scans using graphite-monochromated molybdenum radiation. Data were corrected for Lorentz–polarization effects, for an 11·5% decay in intensity over data-collection time (max. correction 1·141, min. correction 0·974) and for absorption using an empirical absorption correction based on ψ scans of nine reflections with $80 \le \chi \le 90°$ (min. transmission = 65·61%, max. transmission = 99·97%). A unique octant of data totaling 3118 reflections was collected, $2 \le 2\theta(\text{Mo}) \le 56°$, $0 \le h \le 11$, $0 \le k \le 12$, $0 \le l \le 34$, 1872 observed reflections with $I \ge 3{\cdot}0\sigma(I)$.

The structure was solved using *MULTAN*80 (Main *et al.*, 1980), revealing a starting fragment which was subsequently expanded by difference Fourier syntheses and least-squares refinements (on *F*). The function minimized was $\sum w(|F_o| - |F_c|)^2$ where the weights, $w = 4F_o^2/s^2(I)$ with $s(I)$ defined as $[\sigma(I)^2 + (0{\cdot}05F_o)^2]^{1/2}$. Non-H atoms were refined with anisotropic vibrational amplitudes. The methionine side chain is disordered beyond C1*G* with two distinct sites apparent for both the S atom and C1*E*. There was no evidence for disorder extending further back along the side chain. At the isotropic stage, the occupancy factors of each site were set to be equivalent and were refined to a 60:40 distribution for (S,C1*E*) and (S′,C1*E*′), respectively. Subsequently,

* A typographical error in the original manuscript lists this value as 30 nM rather than 30 μM.

occupancies were held fixed at the 60:40 ratio while refinement of anisotropic displacement parameters was completed.

Many H-atom positions could be assigned from a difference Fourier map; however, in the final refinement cycles hydrogen positions were held fixed at positions calculated initially to be 1 Å from the atom to which they were attached and the atoms were assigned fixed isotropic temperature factors. In the later stages an extinction coefficient of the type defined by Zachariasen (1963) was refined to 7·43 (1) $\times 10^{-8}$. The full-matrix refinement converged (max. $\Delta/\sigma = 0{\cdot}05$) to the standard agreement factors $R = 0{\cdot}076$, $wR = 0{\cdot}092$, 263 variables. A final difference Fourier map showed a maximum residual electron density of 0·916 e Å^{-3}, near the disordered S atom. Refinement using 2663 observations for which $I \geq 0{\cdot}01\sigma(I)$ gave residuals of $R = 0{\cdot}100$, $wR = 0{\cdot}094$, $S = 2{\cdot}03$. All programs were from the *SDP* system (Frenz, 1987). Neutral-atom scattering factors were from *International Tables for X-ray Crystallography* (1974); H-atom scattering factors were those of Stewart, Davidson & Simpson (1965).

Table 1. *Positional parameters for N-For-L-Met-N-Me-L-Phe-O'Bu*

$B_{eq} = (4/3)\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}(Å^2)
S	0·4571 (4)	0·3091 (2)	0·55215 (9)	4·69 (6)
S′	0·4691 (8)	0·2531 (4)	0·5783 (2)	8·3 (1)
O′	0·1533 (4)	−0·1723 (3)	0·4930 (1)	3·30 (7)
O1′	0·6197 (4)	−0·1000 (4)	0·4074 (1)	3·27 (7)
O2″	0·1683 (5)	−0·0100 (4)	0·2745 (1)	4·79 (9)
O2′	0·1672 (4)	−0·1330 (3)	0·3484 (1)	2·94 (6)
N1	0·4081 (4)	−0·1489 (4)	0·4808 (1)	2·33 (7)
N2	0·4522 (4)	0·0165 (4)	0·3582 (1)	2·24 (7)
C′	0·2848 (6)	−0·2142 (5)	0·4977 (2)	2·57 (9)
C1*B*	0·4701 (7)	0·1056 (5)	0·4822 (2)	3·6 (1)
C1	0·0781 (6)	−0·2543 (5)	0·3279 (2)	3·0 (1)
C1*A*	0·4026 (5)	−0·0186 (5)	0·4514 (2)	2·39 (9)
C1′	0·4960 (5)	−0·0375 (5)	0·4039 (2)	2·23 (9)
C1*E*	0·359 (1)	0·310 (1)	0·6137 (3)	4·6 (2)
C1*G*	0·3784 (8)	0·1434 (6)	0·5288 (2)	4·4 (2)
C1*E*′	0·432 (2)	0·409 (2)	0·5466 (8)	7·6 (6)
C2*A*	0·3041 (6)	0·0819 (5)	0·3481 (2)	2·37 (9)
C2*G*	0·4159 (6)	0·3287 (5)	0·3422 (2)	2·9 (1)
C2*Z*	0·6016 (8)	0·5415 (6)	0·3819 (2)	4·8 (1)
C2′	0·2035 (5)	−0·0239 (5)	0·3179 (2)	2·50 (1)
C2Me	0·5501 (6)	−0·0133 (6)	0·3143 (2)	3·7 (1)
C2	0·0606 (8)	−0·3449 (6)	0·3755 (2)	4·9 (1)
C2*B*	0·3140 (6)	0·2209 (5)	0·3180 (2)	3·2 (1)
C3	0·1656 (8)	−0·3279 (7)	0·2874 (2)	5·6 (1)
C4	−0·0772 (7)	−0·2042 (7)	0·3101 (3)	5·2 (1)
C2*D*1	0·5447 (7)	0·3732 (6)	0·3165 (2)	4·0 (1)
C2*E*1	0·6361 (8)	0·4796 (6)	0·3364 (2)	5·2 (1)
C2*D*2	0·3792 (7)	0·3907 (6)	0·3878 (2)	4·2 (1)
C2*E*2	0·4760 (8)	0·4984 (6)	0·4087 (2)	5·2 (1)

Discussion. The positional parameters, along with their standard deviations as estimated from the inverse matrix, are listed in Table 1.* Principal bond lengths and angles are presented in Table 2. The *N*-For-L-Met-*N*^{2}-methyl-L-Phe-O'Bu molecule crystallized in a somewhat coiled conformation; the central peptide bond is *cis*-planar with $\omega = 8{\cdot}1\ (5)°$, as illustrated in Fig. 1. Principal backbone torsion angles are $\varphi_1 = -128{\cdot}6\ (6)$, $\psi_1 = 141{\cdot}2\ (6)$ and $\varphi_2 = -103{\cdot}3\ (6)°$, in the range of accepted values for extended structures. Measurements by ^{1}H and ^{13}C NMR in $CDCl_3$ are in agreement with such an extended form as a principal conformation in solution (Heald, 1982). Solution studies also display resonances attributable to both the *cis* and the *trans* peptide conformation, with the *cis* isomer present at only the 20% level at ambient temperature.

The formyl group is planar [O′—C′—N1—C1*A* = −4·2 (6)°] with the formyl oxygen *syn* to C1*A* as in other formyl-Met peptides (Eggleston, 1988). The esterified carboxylate group sits nearly perpendicular to the peptide backbone as illustrated by the torsion angles of 68·4 (8)° (N2—C2*A*—C2′—O2′) and −110·2 (8)° (N2—C2*A*—C2′—O2″). This orientation contrasts dramatically to those observed in the non-*N*-methylated analog *N*-For-L-Met-D-Phe-O'Bu (Eggleston, 1988) and places the carbonyl oxygen, O2″, nearly synplanar with C2*B* [C2*B*—C2*A*—C2′—O2″ = 16·0 (8)°] and staggered between the two C*B* protons. Such a staggered orientation for the terminal ester may be dictated by steric requirements of the *N*-methyl group which preclude adoption of a more commonly observed conformation in which one or the other carboxyl O atoms is synplanar with respect to the preceding nitrogen.

The Met and Phe side chains are disposed on the same side of the peptide backbone due to the *cis* geometry of the peptide bond. The methionine side chain is disordered beyond C1*G*. This disorder has been modeled by a two-site occupancy with occupancies of 60% and 40% for (S, C1*E*) and S′, C1*E*′), respectively. Thus the disorder observed here differs from that reported in the structure of *N*-For-Met-Leu-D-Phe (Morffew & Tickle, 1981). The resulting side-chain torsion angles are $\chi_1^1 = -66{\cdot}0\ (7)$, $\chi_1^2 = -170\ (1)$, $\chi_1^3 = -168\ (1)$, $\chi_1^{2'} = 164\ (1)$, $\chi_1^3 = 83\ (2)°$. The side-chain rotamer with χ_1^1 near −60° was calculated to be the principal populant in solution studies as well.

Solution studies also showed an extremely strong preference for χ_2^1 near −60° with no population of the +60° rotamer. In agreement with solution results, the observed χ_2^1 is −54·8 (7)°. The aromatic ring is twisted away from its normal perpendicular disposition toward the nitrogen with $\chi_2^{2,1} = 116{\cdot}5\ (9)°$ and $\chi_2^{2,2} = -67{\cdot}6\ (9)°$. Taken together with observa-

* Lists of structure factors, anisotropic thermal parameters, H-atom positions and distances involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52734 (19 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Principal bond distances* (Å) *and angles* (°)

S—C1*E*	1·821 (7)	S—C1*G*	1·821 (5)
S′—C1*E*′	1·72 (2)	S′—C1*G*	1·838 (5)
O′—C′	1·230 (4)	C2′—C2*A*	1·552 (5)
O1′—C1′	1·244 (4)	C2*A*—C2*B*	1·535 (5)
O2″—C2′	1·180 (4)	C2*B*—C2*G*	1·498 (5)
O2′—C1	1·490 (4)	C2*G*—C2*D*1	1·382 (6)
O2′—C2′	1·342 (4)	C2*G*—C2*D*2	1·365 (5)
N1—C′	1·325 (4)	C2*Z*—C2*E*1	1·356 (6)
N1—C1*A*	1·455 (4)	C2*Z*—C2*E*2	1·370 (7)
N2—C1′	1·351 (4)	C2*D*1—C2*E*1	1·391 (6)
N2—C2*A*	1·467 (4)	C2*D*2—C2*E*2	1·437 (6)
N2—C2Me	1·460 (5)	C1—C2	1·516 (5)
C1*A*—C1′	1·496 (5)	C1—C3	1·482 (6)
C1*A*—C1*B*	1·545 (5)	C1—C4	1·502 (6)
C1*B*—C1*G*	1·501 (6)		

C1*E*—S—C1*G*	96·8 (3)	N1—C1*A*—C1*B*	111·1 (3)
C1*E*′—S′—C1*G*	93·8 (6)	N1—C1*A*—C1′	108·4 (3)
C′—N1—C1*A*	122·9 (3)	C1*B*—C1*A*—C1′	108·1 (3)
C1—O2′—C2′	120·6 (3)	O1′—C1′—N2	119·7 (3)
C1′—N2—C2*A*	124·8 (3)	O1′—C1′—C1*A*	118·5 (3)
C1′—N2—C2Me	116·6 (3)	N2—C1′—C1*A*	121·8 (3)
C2*A*—N2—C2Me	117·8 (3)	S—C1*G*—C1*B*	105·7 (3)
O′—C′—N1	126·0 (3)	S′—C1*G*—C1*B*	117·9 (4)
C1*A*—C1*B*—C1*G*	113·3 (3)	N2—C2*A*—C2′	108·9 (3)
O2′—C1—C2	101·5 (3)	N2—C2*A*—C2*B*	113·8 (3)
O2′—C1—C3	110·1 (3)	C2′—C2*A*—C2*B*	109·2 (3)
O2′—C1—C4	110·0 (3)	C2*B*—C2*G*—C2*D*1	119·7 (3)
C2—C1—C3	111·6 (4)	C2*B*—C2*G*—C2*D*2	121·1 (4)
C2—C1—C4	109·6 (4)	C2*D*1—C2*G*—C2*D*2	119·0 (4)
C3—C1—C4	113·3 (4)	C2*E*1—C2*Z*—C2*E*2	119·8 (4)
O2″—C2′—O2′	126·2 (3)	C2*A*—C2*B*—C2*G*	113·9 (3)
O2″—C2′—C2*A*	124·2 (3)	C2*G*—C2*D*1—C2*E*1	121·0 (4)
O2′—C2′—C2*A*	109·6 (3)	C2*Z*—C2*E*1—C2*D*1	120·7 (5)
C2*G*—C2*D*2—C2*E*2	119·7 (4)	C2*Z*—C2*E*2—C2*D*2	119·8 (4)

tions on Phe residue conformational preferences in general (Benedetti, Morelli, Nemethy & Scheraga, 1983) and on other formylmethionyl peptides, these side-chain dispositions suggest that the combination of *N*-methylation and C-terminal esterification effectively locks the intervening side-chain χ^1 into a single, sterically most favorable conformation.

Packing arrangements in this structure involve two possible hydrogen-bonding interactions. The acylated nitrogen, N1, acts as a donor to the acyl oxygen, O′, of an adjacent molecule; the acyl carbon, C′, also may act as a donor to the peptide carbonyl oxygen, O1′, of a second adjacent molecule. The metrical details are N1···O′ = 2·828 (4), HN1···O′ = 1·96 Å with an angle at hydrogen of 161° (symmetry operation 3; 0, $\bar{1}$, 1); C′···O1′ = 3·37, HC′···O1′ = 2·60 Å with an angle at hydrogen of 138° (symmetry operation 3; $\bar{1}$, $\bar{1}$, 1). Such C—H···O interactions involving the formyl proton are common in *N*-formylmethionyl peptides (Eggleston, 1988).

The disordered methionine side chain lies within a large cavity in the cell which is bordered by the phenyl rings of two screw-related molecules, as may be appreciated from Fig. 2. The motional freedom displayed by this moiety thus appears attributable to loose crystal molecular packing. Dynamics calculations on the molecule using periodic boundary conditions to simulate the crystal environment show that the two conformers are very close in energy (9·7 kJ mol^{-1}) and that the predominant conformational isomer observed in the crystal is of lower energy (Kitson, Aubelj, Eggleston & Hagler, 1986).

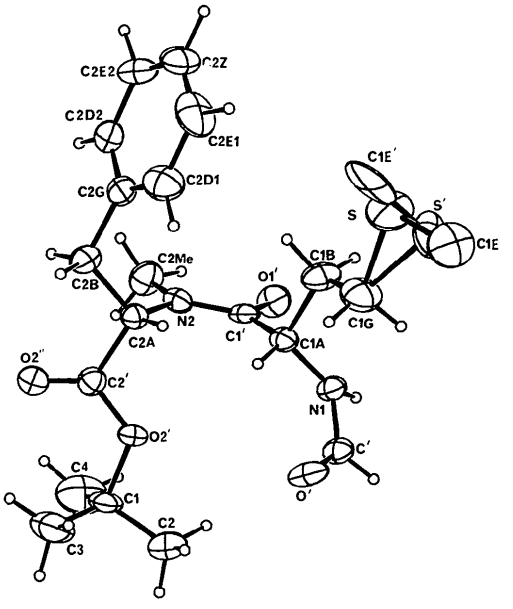

Fig. 1. *ORTEP* (Johnson, 1976) drawing of *N*-For-L-Met-N^2-Me-L-Phe-O′Bu. Non-H atoms are drawn as principal ellipses at the 50% probability level. H atoms are illustrated as spheres of arbitrary size.

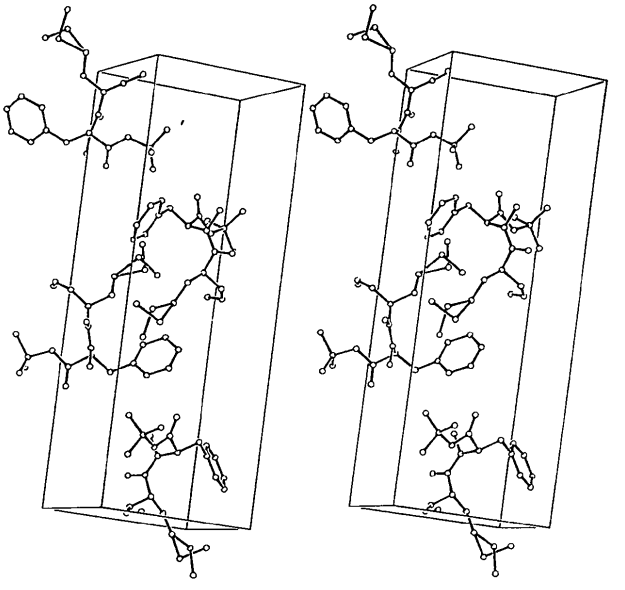

Fig. 2. A stereoview of the molecular packing for a crystal of *N*-For-L-Met-N^2-Me-L-Phe-O′Bu. The *c* axis is approximately vertical. The methionine side chain displays a two-site disorder.

The barrier to interconversion between the two rotamers also is extremely low (2·5 kJ mol^{-1}).

These results confirm the presence of a *cis* peptide bond geometry for the *N*-methyl peptide as suggested from solution studies. Furthermore, our observations suggest that intramolecular interactions arising from the *N*-methyl group and C-terminal esterification determine the conformational features of this blocked dipeptide. The lack of biological activity evident for this molecule, combined with the structural information, suggests that *cis* peptide bond geometry at the *N*-For-Met-*X* juncture may be unfavorable for stimulation of chemotactic responses in general. The general effect of C-terminal esterification on biological activity in these chemotactic peptides may also warrant further investigation.

References

BENEDETTI, E., MORELLI, G., NEMETHY, G. & SCHERAGA, H. A. (1983). *Int. J. Pept. Protein Res.* **22**, 1–15.

EGGLESTON, D. S. (1988). *Int. J. Pept. Protein Res.* **31**, 164–172.

FREER, R. J., DAY, A. R., MUTHUKUMARASWAMY, N., PINON, D., WU, A., SHOWELL, H. J. & BECKER, E. L. (1982). *Biochemistry*, **21**, 257–263.

FRENZ, B. (1987). *Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.

HEALD, S. L. (1982). PhD Dissertation. Duke Univ., Durham, NC, USA.

IITAKA, Y., NAKAMURA, H., TAKADA, K. & TAKITA, T. (1974). *Acta Cryst.* B**30**, 2817–2825.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

JAIN, S. C. & SOBELL, H. M. (1972). *J. Mol. Biol.* **68**, 1–20.

JEFFS, P. W., HEALD, S. L., CHODOSH, D. F. & EGGLESTON, D. S. (1984). *Int. J. Pept. Protein Res.* **24**, 442–446.

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

JOLAD, S. D., HOFFMAN, J. J., TORRANCE, S. J., WIEDHOPF, R. M., COLE, J. R., ARORA, S. K., BATES, R. B., GARGUILO, R. L. & KRIEK, G. R. (1977). *J. Am. Chem. Soc.* **99**, 8040–8044.

KITSON, D. H., AUBELJ, F., EGGLESTON, D. S. & HAGLER, A. T. (1986). *Ann. NY Acad. Sci.* pp. 145–162.

KOJIMA, T., KIDO, T., ITOH, H., YAMANE, T. & ASHIDA, T. (1980). *Acta Cryst.* B**36**, 326–331.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *MULTAN*80. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

MORFFEW, A. J. & TICKLE, I. (1981). *Cryst. Struct. Commun.* **10**, 781–783.

PETCHER, T. J., WEBER, H. P. & RUEGGER, A. (1976). *Helv. Chim. Acta*, **59**, 1480–1488.

SPRINGER, J. P., COLE, R. J., DORNER, J. W., COX, R. H., RICHARD, J. L., BARNES, C. L. & VAN DER HELM, D. (1984). *J. Am. Chem. Soc.* **106**, 2388–2392.

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

VALENSIN, G., LEPRI, A., PASINI, F. L., ORRICO, A., CECCATELLI, L., CAPECCHI, P. L. & DIPERRI, T. (1986). *Int. J. Pept. Protein Res.* **28**, 334–341.

VITOUX, B., AUBRY, A., CUNG, M. T., BOUSSARD, G. & MARRAUD, M. (1981). *Int. J. Pept. Protein Res.* **17**, 469–479.

ZACHARIASEN, W. H. (1963). *Acta Cryst.* **16**, 1139–1144.

Acta Cryst. (1990). C**46**, 1318–1324

Structures of Two Products of Arynic Condensation of Ketone Enolates

BY S. IANELLI AND M. NARDELLI*

Istituto di Chimica Generale, Università degli Studi di Parma, Centro di Studio CNR per la Strutturistica Diffrattometrica, Viale delle Scienze, I-43100 Parma, Italy

D. BELLETTI

Istituto di Strutturistica Chimica, Università degli Studi di Parma, Centro di Studio CNR per la Strutturistica Diffrattometrica, Viale delle Scienze, I-43100 Parma, Italy

AND P. GEOFFROY, M. C. CARRÉ, A. MOUADDIB AND P. CAUBÈRE

Laboratoire de Chimie Organique I, *UA CNRS n°* 457, *Université de Nancy* I, *BP* 239, 54506 *Vandoeuvre-Les-Nancy CEDEX, France*

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Abstract. 2,3,3a,4,5,9b-Hexahydro-1*H*-benz[*e*]indene-3-spiro-2′-(1,3-dioxolan)-5-one (1), $C_{15}H_{16}O_3$, M_r = 244·3, monoclinic, $P2_1/a$, a = 11·023 (2), b = 12·020 (1), c = 9·419 (1) Å, β = 100·74 (1)°, V = 1226·1 (3) Å^3, Z = 4, D_x = 1·323 Mg m^{-3}, λ(Cu $K\alpha$) = 1·540562 Å, μ = 0·702 mm^{-1}, $F(000)$ = 520, T =

* To whom correspondence should be addressed.

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