Frenz, B. A. (1978). *The Enraf–Nonius CAD-4 SDP – a Real-Time System for Concurrent X-ray Data Collection and Crystal Structure Solution. Computing in Crystallography*, edited by H. Schenk, R. Olthof-Hazekamp, H. van Koningsveld & G. C. Bassi, pp. 64–71. Delft University Press.
Karthe, P., Gautham, N., Kumar, A. & Katti, S. B. (1997). *Nucleosides Nucleotides*, **11**, 1–10.
Lai, T. F. & Marsh, R. E. (1972). *Acta Cryst.* B**28**, 1982–1989.
Rainny, P. & Santi, D. V. (1983). *Proc. Natl Acad. Sci. USA*, **80**, 288–292.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.
Vicković, I. (1994). *J. Appl. Cryst.* **27**, 437.
Watson, D. G., Sutor, D. J. & Tollin, P. (1965). *Acta Cryst.* **19**, 111–124.

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Acetyl-ΔPhe-L-Ala-ΔPhe-D-Ala Methyl Ester

Angela Tuzi,[a] Adriano Fissi[b] and Osvaldo Pieroni[b,c]

[a]*Dipartimento di Chimica, Universitá di Napoli 'Federico II', Via Mezzocannone 4, 80134 Napoli, Italy,* [b]*CNR, Istituto di Biofisica, Via S. Lorenzo 26, 56100 Pisa, Italy, and* [c]*Dipartimento di Chimica e Chimica Industriale, Via Risorgimento 35, 56100 Pisa, Italy. E-mail: tuzi@chemna.dichi.unina.it*

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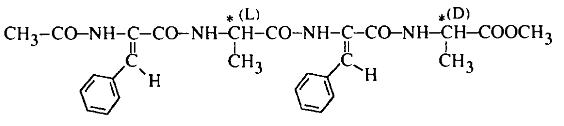
Abstract

The peptide chain of acetylphenylalanine-L-alanine-phenylalanine-D-alanine methyl ester, $C_{27}H_{30}N_4O_6$, adopts a 3_{10}-helical conformation having right-handed screw sense. The 3_{10}-helix is stabilized by intramolecular hydrogen bonds, between CO of the acetyl group and NH of ΔPhe^3, and between CO of ΔPhe^1 and NH of D-Ala^4. The hydrogen bonds form two consecutive ten-membered rings whose (φ, ψ) torsion angles are quite close to the standard values for type-III β-turns. In the crystal, the molecules are linked head-to-tail by intermolecular hydrogen bonds to form continuous helical columns. These are aligned along axes parallel to the *c* axis, with neighbouring columns running in opposite directions. There are no lateral hydrogen bonds between helical columns, but only hydrophobic interactions provided by the interdigitation of apolar side chains of the dehydro-phenylalanine residues, as well as of the C-terminal methyl ester groups.

Comment

Incorporation of α,β-unsaturated amino-acidic residues in a peptide sequence produces remarkable conformational consequences and can induce structural motifs which are not available when the same residues are saturated. Various types of helical structures have been found to occur depending on the specific sequence and positioning of dehydro residues (Rajashankar, Ramakumar, Jain & Chauhan, 1995; Tuzi *et al.*, 1996). 3_{10}-Helices have been observed for peptides containing two alternate dehydro-phenylalanine (ΔPhe) residues (Ciajolo, Tuzi, Pratesi, Fissi & Pieroni, 1991, 1992). Here we describe the crystal and molecular structure of the tetrapeptide Ac-ΔPhe^1-L-Ala^2-ΔPhe^3-D-Ala^4-OMe, (I).


(I)

In helix-forming peptides, the role of the chiral residues is known to be different depending on whether they are located at an internal position or at the C-terminal position; more specifically, if they are both of the L configuration, the alanine in position 2 would favour the right-handed screw sense whereas the alanine in position 4 would prefer the opposite left-handed sense (Pieroni, Fissi, Pratesi, Temussi & Ciardelli, 1993; Tuzi *et al.*, 1996). The presence of an alanine residue having D configuration at the C-terminal position, therefore, may be expected to produce a more marked propensity toward formation of a right-handed helix.

Relevant bond lengths, angles and torsion angles are reported in Table 1. They are in good agreement with corresponding values usually observed in peptides, including those containing dehydro-phenylalanine residues (Singh, Narula & Patel, 1990). The C═C double bonds show a *trans* configuration of the phenyl ring with respect to the C═O group. As already observed in analogous compounds (Ciajolo *et al.*, 1991, 1992), the slight shortening of N—C$^\alpha$ and C$^\alpha$—CO bonds in ΔPhe^1 and ΔPhe^3 seems to indicate partial conjugation of the styryl side chains with the peptide chain. Complete conjugation, however, is hindered for steric reasons. In fact, for Phe^1, the plane of the C═C double bond (including atoms C1*A*, C1*B*, C1C, N1 and C1′) forms a skew angle of 132.7 (2)° with the plane of the preceding peptide bond (including atoms N1, C2, O1 and C1*A*) and an angle of 30.8 (2)° with the plane of the next peptide bond (involving atoms N2, C1′, O1′ and C1*A*). For Phe^3, the values of the corresponding angles are 61.6 (1) and 150.7 (2)°. The styryl groups themselves are not planar; in ΔPhe^1, the planes of the phenyl ring and the C═C double-bond plane form an angle of 34.4 (2)°, while in ΔPhe^3, they deviate from planarity to a minor extent [6.0 (9)°].

The molecular conformation of the peptide is shown in Fig. 1. It is characterized by the presence of two intramolecular hydrogen bonds (C═O of the acetyl group with NH of ΔPhe^3, and C=O of ΔPhe^1 with NH of D-Ala^4) that stabilize two consecutive β-turns. As a consequence, the molecule adopts a 3_{10}-helical structure, only slightly distorted. The values of (φ, ψ) torsion angles around the NH—C$^\alpha$ and C$^\alpha$—CO bonds for ΔPhe^1, Ala^2 and ΔPhe^3 are, in fact, quite close to those for type-III β-turns ($\varphi = -60°$, $\psi = -30°$). Since ΔPhe^1 and ΔPhe^3 are achiral residues, the right-handed sense of the 3_{10}-helix is determined by the chirality of the internal L-alanine. The terminal D-Ala residue, in fact, collocates outside the spiralized part of the molecule, and its (φ, ψ) torsion angles [48.0 (3), 40.0 (4)°] are of opposite sign with respect to the preceding ones. Therefore, the Ala residue having D configuration seems to make no contribution to the propensity of the molecule to adopt a right-handed helical conformation.

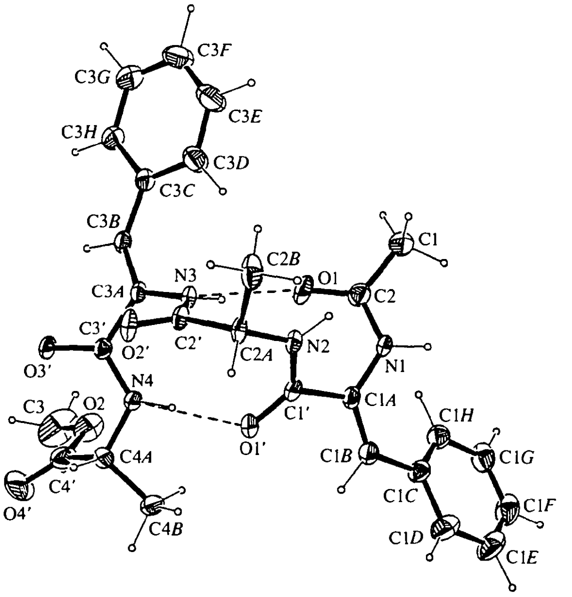


Fig. 1. *ORTEP*II (Johnson, 1976) view of Ac-ΔPhe^1-L-Ala^2-ΔPhe^3-D-Ala^4-OMe. Displacement ellipsoids are shown at the 30% probability level; H atoms are drawn as small circles of arbitrary radii. Dashed lines indicate intramolecular hydrogen bonds.

Crystal packing is shown in Fig. 2. It is characterized by the formation of columns of helical molecules, with a hydrogen-bonding pattern similar to that of a long 3_{10}-helical chain, as already observed for other short dehydro-peptides (Ciajolo *et al.*, 1992). In fact, NH and CO groups not involved in intramolecular hydrogen bonds are positioned at opposite ends of the 3_{10}-helix in a way that allows formation of head-to-tail hydrogen bonds between adjacent molecules. Since D-Ala^4 residues are located outside the spiralized part of the molecules they are not involved in the formation of the helical columns. Distances and angles of various hydrogen bonds are reported in Table 2. Each column of molecules, whose axis is parallel to the **c** direction, is faced with another column related by a twofold screw axis and forms a sort of double helical column. This double column is surrounded by other double columns whose axes run in a direction antiparallel to **c**. There are no lateral hydrogen bonds between columns of helices, but only hydrophobic interactions provided by the interdigitation of apolar side chains of dehydro-Phe residues, as well as of the C-terminal methyl ester groups.

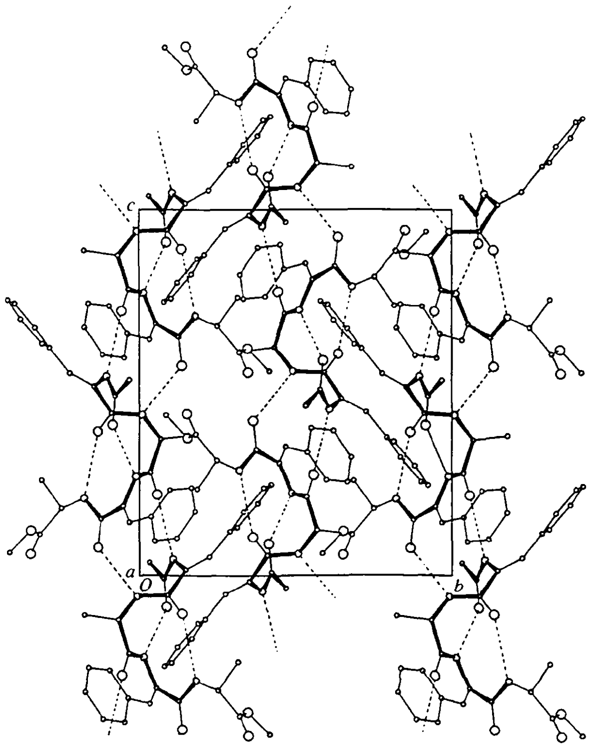


Fig. 2. Crystal packing as viewed along the *a* axis. Dashed lines indicate intermolecular and intramolecular hydrogen bonds.

Experimental

The title compound was synthesized according to Pieroni *et al.* (1993). Crystals suitable for X-ray analysis were obtained by slow evaporation of 1:1 methanol–water solution.

Crystal data

$C_{27}H_{30}N_4O_6$
$M_r = 506.56$
Orthorhombic
$P2_12_12_1$
$a = 13.303$ (1) Å
$b = 13.365$ (1) Å
$c = 15.493$ (1) Å
$V = 2755$ (1) Å^3
$Z = 4$
$D_x = 1.221$ Mg m^{-3}
D_m not measured

Cu *K*α radiation
$\lambda = 1.5418$ Å
Cell parameters from 25 reflections
$\theta = 16$–$24°$
$\mu = 0.685$ mm^{-1}
$T = 295$ K
Platelet
0.53 × 0.20 × 0.08 mm
Colourless

Data collection

Enraf–Nonius CAD-4 single-crystal diffractometer
ω/θ scans
Absorption correction: none
2928 measured reflections
2928 independent reflections
2647 reflections with $I > 3\sigma(I)$
$\theta_{max} = 70°$
$h = 0 \rightarrow 16$
$k = 0 \rightarrow 16$
$l = 0 \rightarrow 18$
1 standard reflection
frequency: 120 min
intensity decay: 1%

Refinement

Refinement on F
$R = 0.046$
$wR = 0.063$
$S = 1.870$
2647 reflections
307 parameters
H atoms not refined
$w = 4F_o^2/[\sigma^2(F_o^2) + (0.04F_o^2)^2]$
$(\Delta/\sigma)_{max} = 0.03$
$\Delta\rho_{max} = 0.29$ e Å^{-3}
$\Delta\rho_{min} = 0.22$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

Table 1. *Selected geometric parameters (Å, °)*

N1—C1*A*	1.412 (4)	O3′—C3′	1.240 (3)
N2—C1′	1.345 (4)	O4′—C4′	1.197 (5)
N2—C2*A*	1.453 (3)	C1′—C1*A*	1.504 (4)
N3—C2′	1.342 (3)	C2′—C2*A*	1.522 (4)
N3—C3*A*	1.427 (3)	C3′—C3*A*	1.498 (4)
N4—C3′	1.334 (3)	C4′—C4*A*	1.515 (4)
N4—C4*A*	1.450 (4)	C1*A*—C1*B*	1.334 (4)
O1′—C1′	1.234 (3)	C3*A*—C3*B*	1.331 (4)
O2′—C2′	1.227 (3)		
C1′—N2—C2*A*	120.2 (2)	N2—C2*A*—C2′	112.4 (2)
C2′—N3—C3*A*	118.9 (2)	N2—C2*A*—C2*B*	109.7 (2)
C3′—N4—C4*A*	122.1 (2)	N3—C3*A*—C3′	115.5 (2)
N2—C1′—C1*A*	116.1 (2)	N3—C3*A*—C3*B*	124.9 (2)
O1′—C1′—C1*A*	121.6 (3)	N4—C4*A*—C4′	113.1 (3)
O2′—C2′—C2*A*	119.2 (2)	N4—C4*A*—C4*B*	107.9 (2)
N4—C3′—C3*A*	116.5 (2)	C1*A*—C1*B*—C1*C*	128.6 (3)
O3′—C3′—C3*A*	121.8 (2)	C3*A*—C3*B*—C3*C*	132.2 (2)
N1—C1*A*—C1′	117.3 (2)	C1*B*—C1*C*—C1*D*	117.8 (3)
N1—C1*A*—C1*B*	124.0 (3)	C3*B*—C3*C*—C3*D*	125.2 (3)
C2—N1—C1*A*—C1′	−49.2 (4)	C4*A*—N4—C3′—C3*A*	179.4 (2)
C1′—N2—C2*A*—C2′	−60.8 (3)	N2—C1′—C1*A*—N1	−28.0 (3)
C2′—N3—C3*A*—C3′	−56.5 (3)	O1′—C1′—C1*A*—C1*B*	−34.2 (4)
C3′—N4—C4*A*—C4′	48.0 (3)	N3—C2′—C2*A*—N2	−24.1 (4)
C2*A*—N2—C1′—C1*A*	179.5 (2)	N4—C3′—C3*A*—N3	−30.6 (3)
C3*A*—N3—C2′—C2*A*	173.9 (2)	O2—C4′—C4*A*—N4	40.0 (4)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—HN1···O2′^{i}	0.96	1.950 (2)	2.867 (3)	160.1 (1)
N2—HN2···O3′^{i}	0.92	1.986 (2)	2.856 (3)	156.7 (1)
N3—HN3···O1	0.86	2.087 (2)	2.932 (3)	169.1 (2)
N4—HN4···O1′	0.97	1.976 (2)	2.949 (3)	175.7 (1)

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

H atoms attached to C atoms were placed at idealized positions, while those bonded to N atoms were located from difference Fourier maps. During refinement, all H atoms were allowed to ride with isotropic displacement parameters set at U_{eq} of the carrier atom.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *SDP* (Enraf–Nonius, 1985). Data reduction: *SDP*. Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1993) (direct methods). Program(s) used to refine structure: *SDP*. Molecular graphics: *ORTEP*II (Johnson, 1976) and *PLUTO* (Motherwell & Clegg, 1978).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1026). Services for accessing these data are described at the back of the journal.

References

Altomare, A., Cascarano, G., Giacovazzo, C. & Guagliardi, A. (1993). *J. Appl. Cryst.* **26**, 343–350.

Ciajolo, M. R., Tuzi, A., Pratesi, C. R., Fissi, A. & Pieroni, O. (1991). *Int. J. Peptide Protein Res.* **38**, 539–544.

Ciajolo, M. R., Tuzi, A., Pratesi, C. R., Fissi, A. & Pieroni, O. (1992). *Biopolymers*, **32**, 717–724.

Enraf–Nonius (1985). *Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.

Enraf–Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.

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

Motherwell, W. D. S. & Clegg, W. (1978). *PLUTO. Program for Plotting Molecular and Crystal Structures*. University of Cambridge, England.

Pieroni, O., Fissi, A., Pratesi, C. R., Temussi, P. A. & Ciardelli, F. (1993). *Biopolymers*, **33**, 1–10.

Rajashankar, K. R., Ramakumar, S., Jain, R. M. & Chauhan, V. S. (1995). *J. Am. Chem. Soc.* **117**, 11773–11779.

Singh, T. P., Narula, P. & Patel, H. C. (1990). *Acta Cryst.* B**46**, 539–543.

Tuzi, A., Ciajolo, M. R., Picone, D., Crescenzi, O., Temussi, P. A., Fissi, A. & Pieroni, O. (1996). *J. Peptide Sci.* **2**, 47–58.

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Diastereoselectivity in the Transannular Diels–Alder Reaction of a *trans-trans-trans* 14-Membered Macrocycle Leading to Steroids

Marc Drouin,[a] Michel Couturier[b] and Pierre Deslongchamps[b]

[a]*Laboratoire de diffraction des rayons-X, Département de chimie, Faculté des Sciences, Université de Sherbrooke, Sherbrooke, Québec, Canada J1K 2R1, and* [b]*Laboratoire de synthèse organique, Département de chimie, Faculté des Sciences, Université de Sherbrooke, Sherbrooke, Québec, Canada J1K 2R1. E-mail: mdrouin@courrier.usherb.ca*

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Abstract

A novel 14-membered macrocyclic ring with *trans-trans-trans* triene geometry, trimethyl (4*E*,10*E*,12*E*)-(1*R**,14*S**)-5-methyl-17-oxobicyclo[12.3.0]heptadeca-