(Hamor & Hamor, 1978). The sums of bond angles in the dioxolane and tetrahydrofuran rings are 507·9 and 501·3°, respectively. The dioxolane and tetrahydrofuran rings adopt an envelope conformation with O(5) deviating 0·76 (1) and 0·815 (1) Å, respectively, from the planes containing the other four atoms in the rings. The dihedral angle between the two least-squares planes is 111·4 (1)°.

The dihedral angle between the plane defined by C(13), C(14), C(15) and C(16) and the epoxide plane is 90·5 (1)°. The rather short distance between C(13) and C(15) [2·132 (2) Å] and the small angle C(13)—O(5)—C(15) are also seen in norbornane skeletons. Two pairs of C—O bonds in the dioxolane ring reveal the asymmetry in the bond lengths. C(15)—O(5) and C(15)—O(4) are significantly shorter than C(13)—O(5) and C(12)—O(4), respectively. The two methyl ester groups linked to the phenyl ring take different conformations with respect to the phenyl ring. One is almost perpendicular and the other nearly parallel to the ring.

References

BIJVOET, J. M., PEERDEMAN, A. F. & VAN BOMMEL, A. J. (1951). *Nature (London)*, **168**, 271–272.

FRENZ, B. A. (1985). *Enraf–Nonius SDP-Plus Structure Determination Package*. Version 3.0. Enraf–Nonius, Delft, The Netherlands.

HAMOR, M. J. & HAMOR, T. A. (1978). *J. Chem. Soc. Perkin Trans.* 2, pp. 16–19.

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

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

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.

NORTH, A. C. T., PHILLIPS, D. C. & MATHEWS, F. S. (1968). *Acta Cryst.* A**24**, 351–360.

SHIRAHATA, K., IIDA, T. & HIRAYAMA, N. (1981). *24th Symposium on the Chemistry of Natural Products*, No. 26, Osaka.

TOMITA, F., TAMAOKI, T., MORIMOTO, M. & FUJIMOTO, K. (1981). *J. Antibiot.* **34**, 1519–1530.

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

Acta Cryst. (1989). C**45**, 634–638

Structure of the Linear Oligopeptide *tert*-Butyl 1-[1-(Benzyloxycarbonyl)amino-1-cyclohexanecarboxamido]-1-cyclohexanecarboxylate*

BY E. BENEDETTI, B. DI BLASIO, V. PAVONE, C. PEDONE AND A. SANTINI

Department of Chemistry, University of Naples, 80134 *Naples, Italy*

AND M. CRISMA AND C. TONIOLO

Biopolymer Research Centre, CNR, Department of Organic Chemistry, University of Padova, 35131 *Padova, Italy*

(*Received* 17 *June* 1988; *accepted* 19 *October* 1988)

Abstract. $C_{26}H_{38}N_2O_5$, $M_r = 458{\cdot}60$, triclinic, $P\bar{1}$, $a = 5{\cdot}971$ (5), $b = 14{\cdot}033$ (5), $c = 16{\cdot}011$ (11) Å, $\alpha = 103{\cdot}30$ (39), $\beta = 92{\cdot}97$ (65), $\gamma = 93{\cdot}25$ (44)°, $V = 1301$ (3) Å^3, $Z = 2$, $D_x = 1{\cdot}171$ g cm^{-3}, $D_m = 1{\cdot}16$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 6{\cdot}166$ cm^{-1}, $F(000) = 496$, $T = 295$ K. The final R value for 2298 observed [$I \geq 3\sigma(I)$] reflections is 0·068. The conformations of the urethane and peptide —CONH— groups is *trans*. The two Ac_6c residues show φ, ψ sets of torsion angles both falling in the region of the conformational energy map where α- and 3_{10}-helices are found, but their handedness is opposite. The two cyclohexyl rings adopt a slightly distorted chair conformation with the —NH group in the axial position.

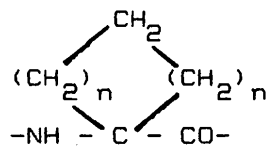
* Linear Oligopeptides. 197. Part 196: Moretto, Crisma, Bonora, Toniolo & Balaram (1988).

0108-2701/89/040634-05$03.00

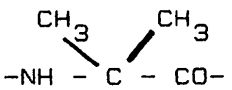
Introduction. Our conformational energy computations on Ac-Ac_6c-NHMe (Ac acetyl, Ac_6c 1-aminocyclohexane-1-carboxylic acid and NHMe methylamino) (Paul, Sukumar, Bardi, Piazzesi, Valle, Toniolo & Balaram, 1986; Pavone, Benedetti, Barone, Di Blasio, Lelj, Pedone, Santini, Crisma, Bonora & Toniolo, 1988) indicated that this $C^{\alpha,\alpha}$-dialkylated, cyclic α-amino acid residue is conformationally restricted and that its minimum energy conformation falls in the $\alpha/3_{10}$-helical region, irrespective of the position (either axial or equatorial) of the α-amino group. The results of the theoretical analysis were corroborated by crystal-state investigations (Bardi, Piazzesi, Toniolo, Sukumar, Raj & Balaram, 1985; Paul, Sukumar, Bardi, Piazzesi, Valle, Toniolo & Balaram, 1986; Pavone, Benedetti, Barone, Di Blasio, Lelj, Pedone, Santini, Crisma, Bonora & Toniolo, 1988) of Ac_6c-rich tri- and

© 1989 International Union of Crystallography

tetrapeptides that provided experimental evidence for the onset of the 3_{10}-helical conformation. Taken together, these findings strongly support the view that the conformational preferences of the Ac_6c residue closely parallel those of Aib (α-aminoisobutyric acid), the prototype of $C^{\alpha,\alpha}$-dialkylated α-amino acids (Toniolo, Bonora, Bavoso, Benedetti, Di Blasio, Pavone & Pedone, 1983; Toniolo, Benedetti & Pedone, 1986).



n=2: Ac_6c



Aib

In an attempt to gain a better understanding of the geometry and conformation of the Ac_6c residue without the influence of the constraints produced by intramolecular hydrogen bonds, we have recently focused our attention on Ac_6c derivatives and dipeptides too short to form (incipient) 3_{10} or α-helices (Valle, Crisma, Toniolo, Sen, Sukumar & Balaram, 1988). In this paper we present the results of an X-ray diffraction study of the terminally-protected homo-dipeptide Z-Ac_6c-Ac_6c-O^{t}Bu (Z benzyloxycarbonyl and O^{t}Bu *tert*-butyloxy).

Experimental. Colourless crystals (0·3 × 0·3 × 0·6 mm) of Z-Ac_6c-Ac_6c-O^{t}Bu (Crisma, Bonora, Toniolo, Bavoso, Benedetti, Di Blasio, Pavone & Pedone, 1988) were obtained from an ethyl acetate solution by slow evaporation. Density measured by flotation.

Preliminary oscillation and Weissenberg photographs were taken to establish the crystal symmetry and the space group. Determination of the cell constants and collection of the X-ray intensity data were performed on a CAD-4 Enraf–Nonius diffractometer of the Centro Interdipartimentale di Metodologie Chimico-Fisiche at the University of Naples, equipped with PDP8/E and PDP11/34 digital computers. For the structure determination and refinement, the *SDP* package (Enraf–Nonius, 1979) was used. Unit-cell parameters were obtained by a least-squares procedure on the angular parameters of 25 reflections in the θ range 17–22°. The analysis of the peak profiles suggested an ω–2θ scan mode with a scan angle equal to $(1{\cdot}0 + 0{\cdot}15\tan\theta)°$; background counts were taken in an additional area of $\Delta\omega/4$ on both sides of the main scan with the same scan speed for each reflection. A crystal-to-counter distance of 368 mm was used with counter entrance aperture of 4 mm. The tube placed between the goniometer head and the detector was evacuated. Prescan runs were made at a speed of 3·5° min^{-1}. Reflections with a net intensity $I < 0{\cdot}5\sigma(I)$ were flagged as 'weak'; those having $I \geq 0{\cdot}5\sigma(I)$ were measured at lower speed (1·0–3·5° min^{-1}) depending on the value of $\sigma(I)/I$. Two intensity control reflections were measured every 60 min of X-ray exposure time in order to monitor the crystal and the electronic stability; no significant change in intensity was observed during data collection. Orientation matrix checks were made with respect to the scattering vectors of four well-centred reflections every 200 reflections measured; reorientation was made by using 25 high-angle reflections, if the displacements of the measured scattering vector exceeded the calculated value by 0·15°. The total number of independent reflections collected (θ range being 0–70°) were 4840 and those used in the refinement [$I \geq 3\sigma(I)$] 2298, h, k, l range being −7→7, −17→17, 0→19, respectively. All reflections were corrected for Lorentz and polarization effects.

The structure was solved by means of direct methods, using *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). The analysis of the E map of the set of phases with the best combined figure of merit revealed the positions of most of the non-hydrogen atoms. The positions of the remaining atoms were derived from subsequent difference Fourier maps. The refinement used a full-matrix least-squares procedure, minimizing the quantity $\sum w(F_o - F_c)^2$ with weights w equal to $1/\sigma(F_o^2)$. All C, N and O atoms were refined with anisotropic temperature factors. Hydrogen atoms were introduced in their stereochemically expected positions with isotropic temperature factors equal to the equivalent B factor of the atom to which each of them was linked.

Refinements were ended when the shifts in the atomic coordinates and anisotropic temperature factors for the C, N and O atoms were less than $\frac{1}{5}$ and $\frac{1}{3}$ of the corresponding standard deviations, respectively. The atomic scattering factors, with the real and imaginary dispersion corrections, for all atomic species were calculated according to Cromer & Waber (1974). The final R values were $R = 0{\cdot}068$ and $wR = 0{\cdot}065$; $S = 0{\cdot}98$. $(\Delta/\sigma)_{max}$ in the final refinement cycle for non-hydrogen atoms 0·01. Max. and min. heights in final ΔF synthesis +0·168 and −0·200 e Å^{-3}. Table 1 gives the final atomic coordinates and equivalent isotropic thermal parameters for all non-hydrogen atoms.*

Discussion. The molecular structure of Z-Ac_6c-Ac_6c-O^{t}Bu with the numbering of atoms is illustrated in Fig. 1. Selected bond lengths and bond angles with their estimated standard deviations are listed in Table 2. Since the molecule is achiral, it crystallizes in a

* Lists of structure factors, anisotropic thermal parameters and hydrogen-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51528 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atomic coordinates and equivalent isotropic thermal parameters* (Å²) *for the non-hydrogen atoms of* Z-Ac$_6$c-Ac$_6$c-O^{t}Bu (*with e.s.d.'s in parentheses*)

$B_{eq} = \frac{4}{3}[a^2\beta_{11} + b^2\beta_{22} + c^2\beta_{33} + ab\beta_{12}\cos\gamma + ac\beta_{13}\cos\beta + bc\beta_{23}\cos\alpha]$.

	x	y	z	B_{eq}
O(1)	0·9646 (6)	0·3971 (2)	0·2716 (2)	5·73 (16)
O(2)	0·5889 (6)	0·4172 (2)	0·2724 (2)	6·12 (17)
O1	0·1506 (5)	0·1774 (5)	0·2260 (2)	5·39 (16)
O2	−0·0631 (6)	0·0939 (3)	0·3770 (3)	7·34 (20)
O2*	0·2522 (6)	0·0211 (2)	0·3312 (2)	5·87 (17)
N1	0·7285 (6)	0·2678 (3)	0·2234 (2)	4·56 (17)
N2	0·4355 (6)	0·2049 (3)	0·3284 (2)	4·98 (18)
C(1)	1·0008 (9)	0·5509 (4)	0·2264 (4)	5·64 (26)
C(6)	1·1736 (11)	0·5413 (4)	0·1708 (4)	7·70 (33)
C(5)	1·1578 (12)	0·5833 (5)	0·1001 (4)	9·39 (38)
C(4)	0·9735 (13)	0·6345 (5)	0·0869 (4)	8·99 (37)
C(3)	0·8058 (11)	0·6458 (5)	0·1426 (4)	8·47 (35)
C(2)	0·8180 (10)	0·6023 (4)	0·2125 (4)	6·87 (29)
C(7)	1·0124 (10)	0·5017 (4)	0·3013 (4)	6·54 (29)
C(8)	0·7418 (9)	0·3646 (4)	0·2566 (3)	5·23 (23)
C^{α}_1	0·5213 (8)	0·2115 (3)	0·1818 (3)	4·71 (21)
$C^{\beta 1}_1$	0·4065 (10)	0·2622 (4)	0·1164 (3)	6·45 (26)
$C^{\beta 1}_2$	0·5829 (9)	0·1090 (4)	0·1374 (3)	5·53 (26)
$C^{\gamma 1}_1$	0·5625 (11)	0·2645 (5)	0·0429 (4)	8·81 (33)
$C^{\gamma 1}_2$	0·7284 (11)	0·1095 (5)	0·0610 (4)	7·60 (35)
C^{δ}_1	0·6192 (12)	0·1629 (6)	−0·0018 (4)	9·01 (42)
C'_1	0·3496 (8)	0·1979 (3)	0·2479 (3)	4·99 (22)
C^{α}_2	0·2909 (8)	0·1915 (4)	0·3977 (3)	5·22 (23)
$C^{\beta 2}_1$	0·1486 (9)	0·2786 (4)	0·4253 (3)	5·74 (25)
$C^{\beta 2}_2$	0·4489 (9)	0·1794 (4)	0·4745 (3)	6·03 (25)
$C^{\gamma 2}_1$	0·2877 (10)	0·3725 (4)	0·4679 (4)	6·80 (29)
$C^{\gamma 2}_2$	0·5817 (10)	0·2746 (4)	0·5184 (4)	6·40 (28)
C^{δ}_2	0·4301 (10)	0·3586 (5)	0·5456 (4)	6·84 (31)
C'_2	0·1355 (10)	0·0972 (4)	0·3663 (3)	6·02 (26)
C(9)	0·1403 (10)	−0·0772 (4)	0·2960 (4)	6·59 (29)
C(10)	−0·0236 (11)	−0·0736 (5)	0·2206 (4)	7·86 (35)
C(11)	0·3363 (11)	−0·1389 (4)	0·2664 (5)	7·91 (35)
C(12)	0·0229 (12)	−0·1141 (4)	0·3671 (4)	8·71 (34)

Table 2. *Selected bond lengths* (Å) *and angles* (°) *for* Z-Ac$_6$c-Ac$_6$c-O^{t}Bu (*with e.s.d.'s in parentheses*)

N_1–C^{α}_1	1·470 (6)	N_2–C^{α}_2	1·479 (5)
C^{α}_1–C'_1	1·546 (6)	C^{α}_2–C'_2	1·539 (7)
C'_1=O_1	1·220 (6)	C'_2=O2	1·206 (7)
C'_1–N_2	1·343 (5)	C'_2–O2*	1·338 (6)
C^{α}_1–$C^{\beta 1}_1$	1·548 (6)	C^{α}_2–$C^{\beta 2}_1$	1·523 (7)
C^{α}_1–$C^{\beta 1}_2$	1·525 (7)	C^{α}_2–$C^{\beta 2}_2$	1·557 (6)
$C^{\beta 1}_1$–$C^{\gamma 1}_1$	1·543 (7)	$C^{\beta 2}_1$–$C^{\gamma 2}_1$	1·515 (7)
$C^{\beta 1}_2$–$C^{\gamma 1}_2$	1·537 (7)	$C^{\beta 2}_2$–$C^{\gamma 2}_2$	1·516 (8)
$C^{\gamma 1}_1$–C^{δ}_1	1·506 (10)	$C^{\gamma 2}_1$–C^{δ}_2	1·527 (7)
$C^{\gamma 2}_2$–C^{δ}_1	1·529 (8)	$C^{\gamma 2}_2$–C^{δ}_2	1·525 (8)
N1–C^{α}_1–C'_1	111·9 (6)	N2–C^{α}_2–C'_2	109·6 (6)
N1–C^{α}_1–$C^{\beta 1}_1$	111·5 (6)	N2–C^{α}_2–$C^{\beta 2}_1$	111·3 (6)
N1–C^{α}_1–$C^{\beta 1}_2$	107·9 (6)	N2–C^{α}_2–$C^{\beta 2}_2$	106·7 (6)
$C^{\beta 1}_1$–C^{α}_1–C'_1	108·1 (6)	$C^{\beta 2}_1$–C^{α}_2–C'_2	109·3 (6)
$C^{\beta 1}_2$–C^{α}_1–C'_1	106·6 (6)	$C^{\beta 2}_2$–C^{α}_2–C'_2	108·8 (6)
C^{α}_1–$C^{\beta 1}_1$–$C^{\gamma 1}_1$	109·3 (7)	C^{α}_2–$C^{\beta 2}_1$–$C^{\gamma 2}_1$	112·9 (7)
$C^{\beta 1}_1$–$C^{\gamma 1}_1$–C^{δ}_1	111·8 (8)	$C^{\beta 2}_1$–$C^{\gamma 2}_1$–C^{δ}_2	110·6 (7)
$C^{\gamma 1}_1$–C^{δ}_1–$C^{\gamma 1}_2$	111·7 (9)	$C^{\gamma 2}_1$–C^{δ}_2–$C^{\gamma 2}_2$	110·2 (8)
C^{δ}_1–$C^{\gamma 1}_2$–$C^{\beta 1}_2$	111·2 (8)	C^{δ}_2–$C^{\gamma 2}_2$–$C^{\beta 2}_2$	112·1 (7)
$C^{\gamma 1}_2$–$C^{\beta 1}_2$–C^{α}_1	112·6 (7)	$C^{\gamma 2}_2$–$C^{\beta 2}_2$–C^{α}_2	112·1 (7)
$C^{\beta 1}_1$–C^{α}_1–$C^{\beta 1}_2$	110·8 (6)	$C^{\beta 2}_1$–C^{α}_2–$C^{\beta 2}_2$	110·6 (6)
C^{α}_1–C'_1–O1	121·1 (7)	C^{α}_2–C'_2–O2	122·9 (7)
C^{α}_1–C'_1–N2	115·9 (6)	C^{α}_2–C'_2–O2*	111·1 (7)
O1–C'_1–N2	122·9 (6)	O2–C'_2–O2*	125·9 (8)
C(8)–N1–C^{α}_1	123·5 (6)	C'_1–N_2–C^{α}_2	121·6 (6)

centrosymmetric space group and in the crystal molecules of both screw senses are present.

The bond lengths and bond angles observed for this dipeptide agree well with those previously reported for the geometry of the *N*-terminal benzyloxycarbonyl group (Benedetti, Pedone, Toniolo, Dudek, Nèmethy & Scheraga, 1983), the *C*-terminal *tert*-butyl ester group (Schweizer & Dunitz, 1982), the peptide moiety (Benedetti, 1982) and the cyclohexyl ring (Pavone, Benedetti, Barone, Di Blasio, Lelj, Pedone, Santini, Crisma, Bonora & Toniolo, 1988). In particular, the bond angles of the two Ac$_6$c residues indicate an asymmetric geometry for the C^{α} atom.

Both Ac$_6$c residues adopt a conformation in the helical region of the φ, ψ map, but their handedness is opposite. The pertinent values are: φ_1 [C(8)–N_1–C^{α}_1–C'_1] = −73·9 (7)°, ψ_1 [N_1–C^{α}_1–C'_1–N_2] = −23·3 (6)°; φ_2 [C'_1–N_2–C^{α}_2–C'_2] = +48·8 (6)°, ψ_2 [N_2–C^{α}_2–C'_2–O2*] = +49·7 (6)° (IUPAC–IUB Commission on Biochemical Nomenclature, 1970). These values differ by less than 20° from those pertaining to the ideal 3_{10}-helix (±60, ±30°) or α-helix (±55, ±45°).

The C(8)–O(1)–C(7)–C(1) and O(1)–C(7)–C(1)–C(6) torsion angles, giving the orientation of the phenyl ring relative to the urethane moiety, have values of ∓81·2 (7)° and ∓74·0 (8)°. The urethane linkage is found in the usual *trans* conformation, the ω_0 [C^{α}_1–N_1–C(8)–O(1)] value being +165·9 (7)°. This structural property and the *trans* arrangement of the N(1)–C(8)–O(1)–C(7) angle, ±175·3 (8)°, allows us to classify this Z-urethane moiety as the common type *b* (Benedetti, Ciajolo, Di Blasio, Pavone, Pedone, Toniolo & Bonora, 1979; Benedetti, Pedone, Toniolo, Dudek, Nèmethy & Scheraga, 1983).

The torsion angles of the *tert*-butyl ester group show the characteristic staggering of the three methyls with respect to the C'_2–O2* bond. The ester moiety adopts a disposition close to the anticlinal conformation, the value of the N_2–C^{α}_2–C'_2–O_2 torsion angle being ±133·8 (9)° (Dunitz & Strickler, 1968). In addition the

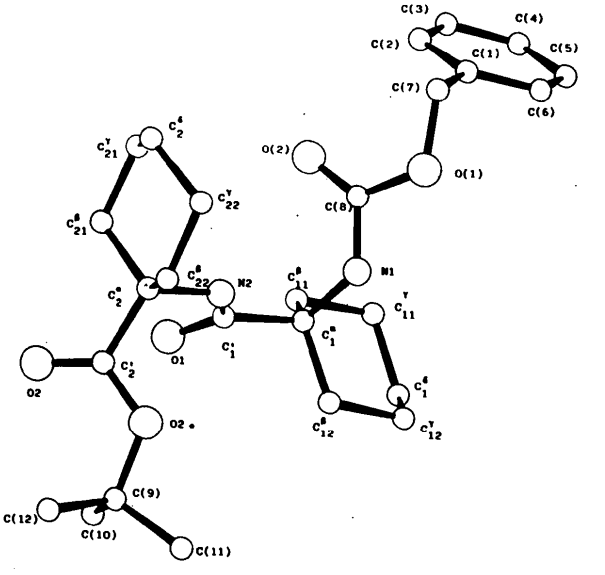


Fig. 1. Molecular structure of Z-Ac$_6$c-Ac$_6$c-O^{t}Bu with the numbering of atoms.

C^{α}_2–C'_2–O2*–C(9) torsion angle (ω_2) is in the usual *trans* conformation [$\mp$179·7 (8)°]. The secondary peptide group adopts the common *trans* arrangement (Benedetti, 1982; Ashida, Tsunogae, Tanaka & Yamane, 1987), the value of the C^{α}_1–C'_1–N_2–C^{α}_2 torsion angle (ω_1) being $\pm$178·8 (8)°. In both Ac_6c residues the two torsion angles N–C^{α}–$C^{\beta 1}$–$C^{\gamma 1}$ ($\chi^{1,1}$) and N–C^{α}–$C^{\beta 2}$–$C^{\gamma 2}$ ($\chi^{1,2}$), relating the peptide chains to the cyclohexyl ring, show a (g^+, g^-) conformation, with values close to those predicted (+60°, −60°). These are $\pm$64·0 (7), $\mp$67·5 (7)° for residue 1 and $\mp$66·1 (7), $\pm$70·7 (7)° for residue 2. In this conformation the N–H and C=O groups of each residue are accommodated in the axial and equatorial positions respectively. This feature was also observed in the structures of most of the Ac_6c-containing peptides studied previously (Bardi, Piazzesi, Toniolo, Sukumar, Raj & Balaram, 1985; Paul, Sukumar, Bardi, Piazzesi, Valle, Toniolo & Balaram, 1986; Pavone, Benedetti, Barone, Di Blasio, Lelj, Pedone, Santini, Crisma, Bonora & Toniolo, 1988; Valle, Crisma, Toniolo, Sen, Sukumar & Balaram, 1988). The axial orientation of the amino group was indeed anticipated in the early work of Kenner, Preston & Sheppard (1965). Interestingly, in the zwitterionic Ac_6c amino acid the ammonium function is equatorial (Varughese, Chacko & Zand, 1975); in contrast, the structure of the Ac_6c amino acid hydrochloride shows the ammonium group in the axial position (Chacko, Srinivasan & Zand, 1971).

The endocyclic torsion angles indicate a slightly distorted chair conformation for the cyclohexyl ring (Cremer & Pople, 1975) of both Ac_6c residues, with a mean absolute value of 55·1°. This should be compared with the expected mean torsion angle for a free cyclohexane (54·7°) with a C–C–C bond angle of 111·5° (Bixon & Lifson, 1967). This result is similar to those already described for the structures of the Ac_6c-containing compounds solved so far (Chacko, Srinivasan & Zand, 1971; Varughese, Chacko & Zand, 1975; Bardi, Piazzesi, Toniolo, Sukumar, Raj & Balaram, 1985; Paul, Sukumar, Bardi, Piazzesi, Valle, Toniolo & Balaram, 1986; Pavone, Benedetti, Barone, Di Blasio, Lelj, Pedone, Santini, Crisma, Bonora & Toniolo, 1988; Valle, Crisma, Toniolo, Sen, Sukumar & Balaram, 1988).

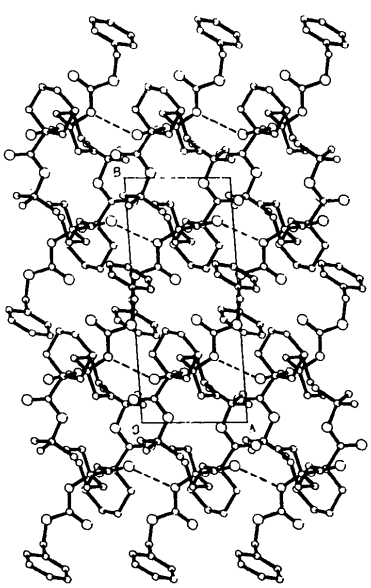


Fig. 2. Mode of packing of the Z-Ac_6c-Ac_6c-O'Bu molecules viewed down the *c* axis. The intermolecular hydrogen bond is indicated as a dashed line.

Table 3. *Backbone torsion angles* (°) *for* N^{α}*-blocked* Ac_6c *and* Aib *homo-dipeptides*

Only the sets of torsion angles having a negative φ_1 value have been reported.

Compound	φ_1	ψ_1	φ_2	ψ_2	Ref.
Z-Ac_6c-Ac_6c-O'Bu	−73·9	−23·3	48·8	49·7	This work
Boc-Ac_6c-Ac_6c-OH*	−57·6	−46·1	49·3	38·1	(*a*)
Z-Aib-Aib-OH	−65·9	−26·2	49·4	45·5	(*b*)
Tfa-Aib-Aib-O'Bu†	−68·1	137·4	51·4	45·6	(*c*)
Boc-Aib-Aib-OBzl‡	−59·7	−51·9	51·4	−138·4	(*d*)

(*a*) Valle, Crisma, Toniolo, Sen, Sukumar & Balaram (1988). (*b*) Valle, Formaggio, Crisma, Bonora, Toniolo, Bavoso, Benedetti, Di Blasio, Pavone & Pedone (1986). (*c*) Valle, Toniolo & Jung (1987). (*d*) Van Roey, Smith, Balasubramanian & Marshall (1983).

* Boc *tert*-butyloxycarbonyl.
† Tfa trifluoroacetyl.
‡ OBzl benzyloxy.

The crystal structure of Z-Ac_6c-Ac_6c-O'Bu (Fig. 2) is characterized by a single intermolecular N–H···O=C hydrogen bond between the urethane N_1–H and the peptide O_1=C'_1 of a symmetry related molecule ($x+1,y,z$). The N···O distance, 2·89 (2) Å, indicates the formation of a strong hydrogen bond (Ramakrishnan & Prasad, 1971; Taylor, Kennard & Versichel, 1984). The peptide N_2H group is involved in intramolecular interaction with the N_1 atom: the N_2···N_1 distance is 2·74 (1) Å, the N_2–H···N_1 angle is 108°. Packing is obtained through van der Waals interactions between methyls and phenyls of the C- and N-terminal protecting groups, respectively.

It may be concluded that the crystal-state conformation exhibited by this dipeptide is similar to that shown by Boc-Ac_6c-Ac_6c-OH (Table 3), the only other Ac_6c homo-dipeptide studied so far by X-ray diffraction. In these two peptides all four Ac_6c residues are helical, but the last residue in each peptide chain shows a handedness opposite to that observed in the preceding one. If we compare the structures of the Ac_6c homo-dipeptides with those of the homo-dipeptides from Aib, the prototype of $C^{\alpha,\alpha}$-dialkylated α-amino acids, it turns out that this feature is present also in Z-Aib-Aib-OH (Table 3). However, a greater conformational versatility appears to characterize the Aib short peptides where the intramolecular hydrogen bonds typical of the (incipient) 3_{10}/α-helices are not possible.

References

ASHIDA, T., TSUNOGAE, Y., TANAKA, I. & YAMANE, T. (1987). *Acta Cryst.* B43, 212–218.

BARDI, R., PIAZZESI, A. M., TONIOLO, C., SUKUMAR, M., RAJ, P. A. & BALARAM, P. (1985). *Int. J. Pept. Protein Res.* 25, 628–639.

BENEDETTI, E. (1982). *Chemistry and Biochemistry of Amino Acids, Peptides and Proteins*, edited by B. WEINSTEIN, Vol. 6, pp. 105–184. New York: Dekker.

BENEDETTI, E., CIAJOLO, A., DI BLASIO, B., PAVONE, V., PEDONE, C., TONIOLO, C. & BONORA, G. M. (1979). *Int. J. Pept. Protein Res.* 14, 130–142.

BENEDETTI, E., PEDONE, C., TONIOLO, C., DUDEK, M., NÈMETHY, G. & SCHERAGA, H. A. (1983). *Int. J. Pept. Protein Res.* 21, 163–181.

BIXON, M. & LIFSON, S. (1967). *Tetrahedron*, 23, 769–784.

CHACKO, K. K., SRINIVASAN, R. & ZAND, R. (1971). *J. Cryst. Mol. Struct.* 1, 261–269.

CREMER, D. & POPLE, J. A. (1975). *J. Am. Chem. Soc.* 97, 1354–1358.

CRISMA, M., BONORA, G. M., TONIOLO, C., BAVOSO, A., BENEDETTI, E., DI BLASIO, B., PAVONE, V. & PEDONE, C. (1988). *Macromolecules*, 21, 2071–2074.

CROMER, D. T. & WABER, J. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, 2nd edition, Table 2.2B. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

DUNITZ, J. D. & STRICKLER, P. (1968). *Structural Chemistry and Molecular Biology*, edited by A. RICH & N. DAVIDSON, pp. 595–602. San Francisco: Dekker.

Enraf–Nonius (1979). *Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.

IUPAC–IUB COMMISSION ON BIOCHEMICAL NOMENCLATURE (1970). *J. Mol. Biol.* 52, 1–17.

KENNER, G. W., PRESTON, J. & SHEPPARD, R. C. (1965). *J. Chem. Soc.* pp. 6239–6244.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

MORETTO, V., CRISMA, M., BONORA, G. M., TONIOLO, C. & BALARAM, P. (1988). *Macromolecules*. In the press.

PAUL, P. K. C., SUKUMAR, M., BARDI, R., PIAZZESI, A. M., VALLE, G., TONIOLO, C. & BALARAM, P. (1986). *J. Am. Chem. Soc.* 108, 6363–6370.

PAVONE, V., BENEDETTI, E., BARONE, V., DI BLASIO, B., LELJ, F., PEDONE, C., SANTINI, A., CRISMA, M., BONORA, G. M. & TONIOLO, C. (1988). *Macromolecules*. In the press.

RAMAKRISHNAN, C. & PRASAD, N. (1971). *Int. J. Protein Res.* 3, 209–231.

SCHWEIZER, W. B. & DUNITZ, J. D. (1982). *Helv. Chim. Acta*, 65, 1547–1554.

TAYLOR, R., KENNARD, O. & VERSICHEL, W. (1984). *Acta Cryst.* B40, 280–288.

TONIOLO, C., BENEDETTI, E. & PEDONE, C. (1986). *Gazz. Chim. Ital.* 116, 355–359.

TONIOLO, C., BONORA, G. M., BAVOSO, A., BENEDETTI, E., DI BLASIO, B., PAVONE, V. & PEDONE, C. (1983). *Biopolymers*, 22, 205–215.

VALLE, G., CRISMA, M., TONIOLO, C., SEN, N., SUKUMAR, M. & BALARAM, P. (1988). *J. Chem. Soc. Perkin Trans.* 2. In the press.

VALLE, G., FORMAGGIO, F., CRISMA, M., BONORA, G. M., TONIOLO, C., BAVOSO, A., BENEDETTI, E., DI BLASIO, B., PAVONE, V. & PEDONE, C. (1986). *J. Chem. Soc. Perkin Trans.* 2, pp. 1371–1376.

VALLE, G., TONIOLO, C. & JUNG, G. (1987). *Gazz. Chim. Ital.* 117, 549–553.

VAN ROEY, P., SMITH, G. D., BALASUBRAMANIAN, T. M. & MARSHALL, G. (1983). *Acta Cryst.* C39, 894–896.

VARUGHESE, K. I., CHACKO, K. K. & ZAND, R. (1975). *Acta Cryst.* B31, 866–868.

Acta Cryst. (1989). C45, 638–642

Structure of Quinine Monohydrate Toluene Solvate

BY BARBARA PNIEWSKA AND ALINA SUSZKO-PURZYCKA

Department of Chemistry, Agricultural and Teachers University in Siedlce, ul. 3 Maja 54, 08-110 *Siedlce, Poland*

(*Received* 16 *August* 1988; *accepted* 2 *November* 1988)

Abstract. $C_{20}H_{24}N_2O_2.H_2O.\frac{1}{2}C_7H_8$, $M_r = 388{\cdot}5$, orthorhombic, $C222_1$, $a = 10{\cdot}376\ (1)$, $b = 16{\cdot}726\ (1)$, $c = 25{\cdot}255\ (9)$ Å, $V = 4383$ Å^3, $Z = 8$, $D_m = 1{\cdot}17$, $D_x = 1{\cdot}177$ g cm^{-3}, Cu $K\alpha = 1{\cdot}5418$ Å, $\mu = 6{\cdot}28$ cm^{-1}, $F(000) = 1672$, $T = 295$ K, $R = 0{\cdot}040$, $wR = 0{\cdot}036$ for 2564 observed reflections. The asymmetry of the C–N bonds of the quinuclidine N atom [1·471 (4), 1·494 (4) Å], the short C–C bond of 1·356 (4) Å in the quinoline ring and the short intermolecular C···C distance between the overlapping quinoline planes [3·273 (4) Å] differentiate quinine from its derivatives and other *Cinchona* alkaloids. The water molecule, as a donor and an acceptor, connects three molecules of quinine by hydrogen bonds [O(12)···N(1) 2·867 (3), O(12)···N(2) 2·876 (2) and O(12)···O(1) 2·722 (3) Å]. The toluene and quinoline planes make a dihedral angle of 83·1 (1)° with a minimum intermolecular C···C distance of 3·648 (4) Å.

Introduction. Quinine, the best-known and perhaps the most important alkaloid of the *Cinchona* group, has several interesting pharmacological properties as an antimalarial, antibacterial and cardioactive agent. The results of the crystal structure analysis of two derivatives of quinine have been previously reported (Suszko-Purzycka, Lipińska, Piotrowska & Oleksyn, 1985;

0108-2701/89/040638-05$03.00

© 1989 International Union of Crystallography