Acta Cryst. (1988). C**44**, 148–150

Structure of *cyclo*(Tri-D-azetidine-2-carboxylic acid)

BY JINDŘICH SYMERSKÝ AND KAREL BLÁHA

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 *Praha* 6, *Czechoslovakia*

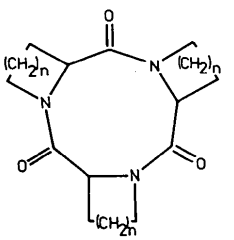
AND JIŘÍ JEČNÝ

Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences, 162 02 *Praha* 6, *Czechoslovakia*

(*Received* 28 *April* 1987; *accepted* 14 *September* 1987)

Abstract. $C_{12}H_{15}N_3O_3$, $M_r = 249{\cdot}27$, monoclinic, $P2_1$, $a = 5{\cdot}231$ (2), $b = 8{\cdot}547$ (3), $c = 13{\cdot}646$ (6) Å, $\beta = 99{\cdot}03$ (3)°, $V = 602{\cdot}5$ (4) Å^3, $Z = 2$, $D_x = 1{\cdot}37$ (1) Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}094$ mm^{-1}, $F(000) = 264$, $T = 295$ K, final $R = 0{\cdot}043$ for 1680 observed reflections. The nearly C_3 symmetry of the molecule is violated by the torsion around one of the peptide bonds and by the extremely high non-planar bond arrangement at the N atom of this peptide bond.

Introduction. The synthesis and spectral properties (excluding NMR) of the title compound, *cyclo*(-D-Aze-)$_3$, were described in detail by Vičar, Maloň, Trka, Smoliková, Frič & Bláha (1977) along with *cyclo*(-L-Pro-)$_3$. A single conformation was predicted for the first cyclotripeptide in the crystalline state. Mutual spatial interaction of the three amide groups is thought to be the reason for the CD spectral pattern of the two compounds. The crystal structure of the *cyclo*(-L-Pro-)$_3$ was determined earlier (Druyan, Coulter, Walter, Kartha & Ambady, 1976) and shows considerable conformational variation, suggesting less rigidity than anticipated for the prolyl rings. Neither of the independent *cyclo*(-L-Pro-)$_3$ molecules in the crystal has threefold symmetry. The crystal structure of the enantiomeric *cyclo*(-L-Aze-)$_3$ was also mentioned (Coulter, 1978) but coordinates were not published. This molecule is more constrained due to four-membered side rings.



Aze: $n = 2$, Pro: $n = 3$

Experimental. A small sample of the title compound was recrystallized by slow evaporation from a solution in propanol. A colorless long prismatic single-crystal block was cut. The larger part was used for preliminary measurement of cell dimensions and for space-group determination using oscillation and Weissenberg photographs with Cu $K\alpha$ radiation. Density measurement could not be performed because there were insufficient crystals. Intensity data were collected on a Syntex $P2_1$ diffractometer with graphite monochromator. Mo $K\alpha$ radiation, $[(\sin\theta)/\lambda]_{max} = 0{\cdot}7042$ Å^{-1}, the crystal used measured 0·2 × 0·4 × 0·55 mm. Final cell dimensions were refined on 25 diffractometer reflections with $5{\cdot}5 < 2\theta < 24{\cdot}5°$, θ–2θ scan, $0 \le h \le 7$, $0 \le k \le 12$, $-19 \le l \le 19$, in a range up to $2\theta = 60°$. 2054 reflections measured, 374 considered unobserved with $I < 1{\cdot}96\sigma_I$. Standard reflections 100, 020 and 002 did not show a decrease in intensity or instability over 144 measurements. Scale corrections (Langer, 1973) were applied and corrections for Lorentz and polarization factors, but not for absorption. Net intensities were calculated using the classic BPB method. The structural model was derived by using direct methods. *MULTAN*80 (Main *et al.*, 1980) failed. The correct set was revealed by *YZARC*80 (Declercq, Germain, Wright & Woolfson, 1980). *E*-map interpretation showed all non-H atoms of the molecule. Refinement was performed on $|F|$ by the full-matrix LS method with the program *SHELX*76 (Sheldrick, 1976). Almost none of the H atoms were revealed on $\Delta\rho$ map. H-atom position parameters were calculated and then successfully refined along with isotropic thermal parameters. No unusual geometrical features were found in bond lengths and angles. An empirical correction for secondary extinction was included as $F_c^{corr} = F_c(1-gF_c^2/\sin\theta)$, $g = 0{\cdot}9(3) \times 10^{-6}$. 223 parameters refined, $(\Delta/\sigma)_{max} = 0{\cdot}016$, final $R = 0{\cdot}0429$, $wR = 0{\cdot}0455$, $w = 0{\cdot}7942/(\sigma_F^2 + 0{\cdot}0009F^2)$, σ_F was taken from counting statistics, instability factor was derived from analysis of variance, 1680 observed reflections. Corresponding values for all reflections:

0108-2701/88/010148-03$03.00

$R = 0.0562$, $wR = 0.0508$, $w = 1/(\sigma_F^2 + 0.0009F^2)$; residuals on final $\Delta\rho$ map 0·239 and −0·261 e Å^{-3}. Atomic scattering factors were taken from the *International Tables for X-ray Crystallography* (1974). The final geometrical calculations were performed with *PARST*83 (Nardelli, 1983). The enantiomorph change had no influence on the final R value.

Discussion. The molecule with atom labelling is shown in Fig. 1. Fractional atomic coordinates and B_{eq} values are given in Table 1, selected bond lengths and angles in Table 2. The crystal packing is shown in Fig. 2. The molecules are fixed by the weak C—H···O contacts.*

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and thermal parameters and weak hydrogen contacts have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44369 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

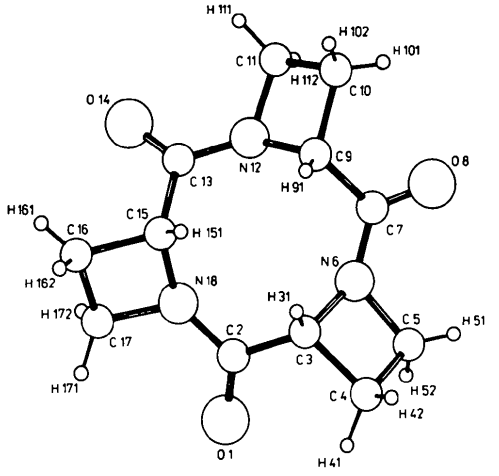


Fig. 1. The minimum overlap view of the molecule.

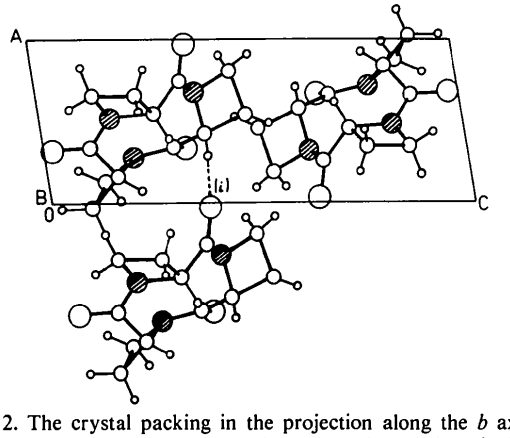


Fig. 2. The crystal packing in the projection along the b axis. N atoms are shaded. The dashed line shows the significant C—H···O contact. Symmetry code: (i) $x+1, y, z$.

Table 1. *Fractional atomic coordinates* (× 10^4) *and* B_{eq} *values* (Å^2) *with e.s.d.'s in parentheses*

	x	y	z	B_{eq}*
O1	−6777 (5)	−4544 (4)	−9770 (1)	5·60 (6)
C13	−2553 (4)	−3946 (4)	−6565 (1)	2·74 (5)
O8	−6630 (5)	−8721	−6643 (1)	5·71 (6)
N6	−7185 (4)	−6975 (4)	−7875 (1)	3·64 (5)
C9	−5768 (4)	−6054 (4)	−6160 (2)	2·94 (5)
C11	−1916 (5)	−6151 (5)	−5340 (2)	4·09 (6)
N12	−3219 (3)	−5343 (3)	−6244 (1)	3·09 (4)
N18	−4816 (4)	−3652 (4)	−8308 (1)	3·71 (5)
C5	−8743 (7)	−7990 (5)	−8632 (2)	5·06 (9)
O14	−353 (3)	−3433 (3)	−6319 (1)	3·80 (5)
C15	−4552 (5)	−3036 (4)	−7277 (2)	3·04 (5)
C3	−8390 (5)	−5508 (4)	−8329 (2)	3·65 (6)
C7	−6576 (5)	−7366 (4)	−6908 (2)	3·45 (6)
C16	−3465 (8)	−1497 (4)	−7645 (2)	4·79 (8)
C17	−3467 (7)	−2290 (5)	−8658 (2)	4·98 (8)
C2	−6600 (6)	−4540 (4)	−8861 (2)	3·73 (6)
C4	−10292 (7)	−6545 (5)	−9031 (2)	5·11 (8)
C10	−4562 (5)	−6679 (5)	−5130 (2)	3·82 (6)

*$B_{eq} = \frac{8}{3}\pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \mathbf{a}_j$.

Table 2. *Bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

O1—C2	1·229 (3)	C11—N12	1·483 (4)
C13—N12	1·337 (4)	C11—C10	1·525 (4)
C13—O14	1·228 (3)	N18—C15	1·488 (3)
C13—C15	1·524 (4)	N18—C17	1·479 (5)
O8—C7	1·215 (4)	N18—C2	1·340 (4)
N6—C5	1·490 (4)	C5—C4	1·530 (6)
N6—C3	1·494 (4)	C15—C16	1·548 (5)
N6—C7	1·350 (3)	C3—C2	1·517 (4)
C9—N12	1·486 (3)	C3—C4	1·547 (4)
C9—C7	1·531 (4)	C16—C17	1·539 (4)
C9—C10	1·543 (4)		

O14—C13—C15	120·8 (3)	C13—C15—N18	112·0 (2)
N12—C13—C15	118·5 (2)	N18—C15—C16	88·8 (2)
N12—C13—O14	120·7 (2)	C13—C15—C16	113·0 (2)
C3—N6—C7	129·2 (3)	N6—C3—C4	88·0 (2)
C5—N6—C7	123·6 (3)	N6—C3—C2	113·8 (2)
C5—N6—C3	93·0 (2)	C2—C3—C4	113·7 (2)
C7—C9—C10	112·6 (3)	N6—C7—C9	117·9 (3)
N12—C9—C10	88·2 (2)	O8—C7—C9	121·1 (3)
N12—C9—C7	113·9 (2)	O8—C7—N6	120·9 (3)
N12—C11—C10	89·0 (2)	C15—C16—C17	88·2 (2)
C9—N12—C11	92·6 (2)	N18—C17—C16	89·4 (2)
C13—N12—C11	125·4 (2)	N18—C2—C3	117·8 (2)
C13—N12—C9	132·4 (2)	O1—C2—C3	121·8 (3)
C17—N18—C2	126·1 (2)	O1—C2—N18	120·4 (3)
C15—N18—C2	133·3 (2)	C5—C4—C3	89·4 (3)
C15—N18—C17	92·8 (2)	C9—C10—C11	88·8 (2)
N6—C5—C4	88·8 (2)		

The central nine-membered ring has a crown conformation, C_α atoms being above the LS weighted plane through the ring and O atoms being below the plane. The four-membered-ring LS-weighted planes are tilted about 36 (1)° relative to the central-ring plane creating a propeller conformation. The torsional angles C_α—C_β—C_γ—N are about 7·5 (1)°. In Table 3 the conformational parameters of the amide groups (Warshel, Levitt & Lifson, 1970; Winkler & Dunitz, 1971) are

Table 3. *Twist and out-of-plane bending parameters* (°) *describing the amide groups* (*Warshel, Levitt & Lifson,* 1970; *Winkler & Dunitz,* 1971)

Amide group	τ'	χ_C	χ_N
C2–N18	0·1 (5)	0·9 (5)	39·6 (5)
C13–N12	−0·1 (4)	−2·5 (4)	43·6 (4)
C7–N6	−11·2 (5)	−1·1 (4)	51·5 (5)

given. The non-planar bond arrangement at N (χ_N) is common for the three amide groups as well as the nearly planar arrangement at carbonyl C (χ_C). The torsion (τ') around the CO–N peptide bond is significant for the third amide group which also has a pronouncedly higher pyramidicity at N. The significant difference of this amide group is also visible in bond lengths and angles. A superposition of the Aze residues, excluding H atoms, also shows that only two of the residues are comparable. The angles between LS-weighted planes of the amide groups 1, 2, 3 are 1–2: 125 (1)°; 1–3: 133 (1)°; and 2–3: 126 (1)°. The shorter C7–O8 carbonyl bond length and the longer C7–N6 peptide bond length are probably correlated with extremely high non-planarity at N6 (χ_N).

The authors are indebted to Dr Karel Huml for useful consultations.

References

COULTER, C. L. (1978). *Am. Crystallogr. Assoc. Ser.* 2, **6**, 22.

DECLERCQ, J.-P., GERMAIN, G., WRIGHT, H. & WOOLFSON, M. M. (1980). *YZARC*80. *A Random Approach to Crystal Structure Determination.* Univs. of Louvain, Belgium, and York, England.

DRUYAN, M. E., COULTER, C. L., WALTER, R., KARTHA, G. & AMBADY, G. K. (1976). *J. Am. Chem. Soc.* **98**, 5496–5502.

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

LANGER, V. (1973). *INTER.* ÚMCH-111. Institute of Macromolecular Chemistry, Prague, Czechoslovakia.

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.

NARDELLI, M. (1983). *PARST*83. *A System of Computer Routines for Calculating Molecular Parameters from the Results of Crystal Structure Analysis.* Univ. of Parma, Italy.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

VIČAR, J., MALOŇ, P., TRKA, A., SMOLÍKOVÁ, J., FRIČ, I. & BLÁHA, K. (1977). *Collect. Czech. Chem. Commun.* **42**, 2701–2717.

WARSHEL, A., LEVITT, M. & LIFSON, S. (1970). *J. Mol. Spectrosc.* **33**, 84–89.

WINKLER, F. K. & DUNITZ, J. D. (1971). *J. Mol. Biol.* **59**, 169–182.

Acta Cryst. (1988). C**44**, 150–154

Structure and Conformation of 3′-*O*-Acetyl-2′-deoxy-5-methoxymethyluridine

BY J. WILSON QUAIL,* GUY TOURIGNY,* LOUIS T. J. DELBAERE,† OSSAMA A. L. EL-KABBANI,† ALLAN L. STUART‡ AND SAGAR V. GUPTA‡

Departments of Chemistry, Biochemistry and Veterinary Physiological Sciences, University of Saskatchewan, Saskatoon, Canada S7N 0W0

(*Received* 9 *July* 1987; *accepted* 7 *September* 1987)

Abstract. $C_{13}H_{18}N_2O_7$, $M_r = 314{\cdot}297$, triclinic, $P1$, $a = 6{\cdot}0321$ (4), $b = 6{\cdot}775$ (5), $c = 9{\cdot}6699$ (7) Å, $\alpha = 76{\cdot}917$ (6), $\beta = 78{\cdot}871$ (6), $\gamma = 75{\cdot}344$ (6)°, $V = 368{\cdot}54$ Å^3, $Z = 1$, $D_m = 1{\cdot}43$, $D_x = 1{\cdot}416$ g cm^{-3}, Cu $K\alpha$ radiation (Ni filtered), $\lambda = 1{\cdot}5418$ Å, $F(000) = 166$, $T = 287$ K, final conventional R factor = 0·034, $wR = 0{\cdot}044$ for 1359 reflections and 268 variables. The structure was solved using the *XTAL* system. The conformation of the furanose ring is best described as intermediate between ^2E and ^2_1T; the pseudorotational parameters are $P = 148{\cdot}9°$ and $\tau_m = 33{\cdot}4°$. The CH_2OH, C(5′), side chain has the g^+ conformation, the carbonyl bond of the 3′-acetoxy group is *syn* to the C(3′)–O(3′,1) bond on the sugar ring and the glycosidic bond conformation is *anti* [$\chi = -137{\cdot}6$ (3)°]. The methoxy group of the 5-methoxymethyl substituent is on the same side of the pyrimidine plane as O(4′) of the furanose ring. Comparison with 2′-deoxy-5-methoxymethyluridine shows that intermolecular attractions have little effect on the internal conformations of the molecule in the solid state.

Introduction. The marginal efficacy of antiviral drugs in topical treatment of herpes simplex virus infections is due to poor penetration into the cells of the epidermis where virus replication is occurring (Richards, Kern, Overall & Glasgow, 1982). This limitation can be overcome by utilizing pro-drug derivatives with greater

* Department of Chemistry.
† Department of Biochemistry.
‡ Department of Veterinary Physiological Sciences.

0108-2701/88/010150-05$03.00