Acta Chemica Scandinavica A 34 (1980) 593–595

The Structure of a Second Crystallographic Modification of Cyclo-D-alanyl-L-alanyl

JORUNN SLETTEN

Department of Chemistry, University of Bergen, N-5014 Bergen-Univ., Norway

The structure of cyclo-D-alanyl-L-alanyl, (*trans*-3,6-dimethylpiperazine-2,5-dione), $C_6H_{10}N_2O_2$, has been determined by X-ray crystallographic methods. The crystals are monolinic, space group $P2_1/c$, $a = 8.498(2)$, $b = 6.148(1)$, $c = 7.209(2)$ Å, $\beta = 111.08(2)°$. 840 independent reflections were recorded on a diffractometer using the θ-2θ scan technique and monochromatized Mo$K\alpha$ radiation. The structure was solved by direct methods and refined by least-squares to an R of 0.034. The molecular dimensions of the present and the previously investigated modification are identical within the limits of error, except for the bond angles at N. The six-membered ring shows a slight deviation from planarity, adopting a chair conformation with the methyl groups in quasi-equatorial positions, as opposed to axial positions in the other modification. The arrangement of hydrogen bonds is quite different in the two crystalline forms; in the present structure the molecules are linked together in ribbons, while in the previous investigation hydrogen bonded layers of molecules were found.

The crystal and molecular structure of cyclo-D-alanyl-L-alanyl has been determined earlier by two independent investigations.[1,2] Recently we discovered that the compound also crystallizes in another modification. The present investigation was undertaken primarily to study any differences in molecular conformation and packing arrangement in the two forms.

CRYSTAL DATA

Present investigation
(later referred to as modification II)

$P2_1/c$
$a = 8.498(2)$ Å
$b = 6.148(1)$ Å
$c = 7.209(2)$ Å
$\beta = 111.08(2)°$
$V = 351.4(4)$ Å^3
$Z = 2$
$D_x = 1.344$ g cm^{-3}
$\mu_{\mathrm{Mo}K\alpha} = 1.10$ cm^{-1}

Previous investigation[2]
(later referred to as modification I)

	$P2_1/n$	$P2_1/c$
a	$= 6.3497(3)$ Å	6.3497 Å
b	$= 6.2203(4)$ Å	6.2203 Å
c	$= 9.0438(5)$ Å	10.5107 Å
β	$= 95.814(9)°$	121.13°
V	$= 355.37$ Å^3	
Z	$= 2$	
D_x	$= 1.329$ g cm^{-3}	

EXPERIMENTAL

Modification II crystallizes from methanol by slow evaporation at approximately 5 °C. In the earlier investigations, methanol at room temperature[2] and water[1] were used as solvents. The crystal used for data collection had dimensions 0.36 × 0.56 × 0.59 mm. A total of 840 independent reflections were recorded ($0° < 2\theta < 56°$) on an Enraf-Nonius CAD-4 diffractometer using the θ-2θ scan technique and monochromatized Mo$K\alpha$ radiation. 79 of the reflections had intensities less than $2\sigma_c$ (σ_c = estimated error due to counting statistics) and were later given zero weight in the refinement. Fluctuations in the intensities of the three reference reflections, remeasured eighteen times at regular intervals during data collection,

0302-4377/80/080593-03\$02.50

Table 1. The final atomic parameters. (a) Non-hydrogen atoms. Standard deviations are in parentheses. Anisotropic temperature factor $\exp[-\frac{1}{4}(B_{11}h^2a^{*2}+\ldots+2B_{23}klb^*c^*)]$.

Atom	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
O	−0.17826(9)	−0.3585(1)	0.029(1)	4.15(3)	1.65(2)	5.75(3)	−0.35(2)	2.23(2)	−0.04(2)
N	−0.0594(1)	0.2060(1)	0.0054(1)	3.42(3)	1.25(2)	3.81(3)	0.18(2)	1.27(2)	0.02(2)
C1	−0.0941(1)	−0.1940(1)	0.0018(1)	3.42(3)	1.51(3)	2.80(3)	−0.02(2)	1.01(2)	0.03(2)
C2	−0.1674(1)	0.0267(1)	0.0160(1)	3.43(3)	1.58(3)	3.10(3)	0.01(2)	1.42(2)	−0.06(2)
C3	−0.3419(1)	0.0523(2)	−0.1417(2)	3.15(3)	3.06(4)	5.81(5)	0.33(3)	1.18(3)	−0.16(4)

(b) Hydrogen atoms. Isotropic temperature factor $\exp[-B\sin^2\theta)/\lambda^2]$.

Atom	x	y	z	B
H1	−0.093(2)	0.327(2)	0.011(2)	3.7(3)
H21	−0.176(1)	0.027(2)	0.150(2)	3.0(2)
H31	−0.335(2)	0.038(2)	−0.273(2)	5.2(3)
H32	−0.389(2)	0.196(3)	−0.128(2)	6.2(4)
H33	−0.412(2)	−0.056(3)	−0.121(2)	6.4(4)

were within ±3 %. The error in the intensity of any one reflection is estimated as $\sigma_I=[\sigma_c^2+(0.01N_{net})^2]^{\frac{1}{2}}$, where N_{net} is the net count of the reflection. Absorption correction was carried out, the maximum and minimum transmission factors being 0.96 and 0.91, respectively.

The structure was solved by direct methods and refined to an R of 0.034 using anisotropic thermal parameters on non-hydrogen atoms. The extinction coefficient was also included in the refinement. This gave an excessive extinction correction for the major part of the data due to exceptionally large differences between F_o and F_c in the three reflections 002, $10\bar{2}$ and 100. These three reflections were subsequently given zero weight in the refinement. The extinction coefficient, g, (defined by the equation $|F_{ccor}|=|F_c|(1+gI_c)^{-1})$ then arrived at for the remaining data is 1.030×10^{-5}.

The weight assigned to each reflection in the refinement was $w=1/\sigma_F^2$, where $\sigma_F=\sigma_I(I\cdot Lp)^{-\frac{1}{2}}$. Atomic scattering factors used were for oxygen, nitrogen and carbon those of Cromer and Waber,[3] and for hydrogen those of Stewart *et al.*[4] All calculations were carried out on a PDP 11/55 computer using the Enraf-Nonius structure determination program (SDP).[5]

Lists of structure factors may be obtained from the author.

RESULTS AND DISCUSSION

Atomic parameters are listed in Table 1a, b. Bond distances and angles are shown in Fig. 1.

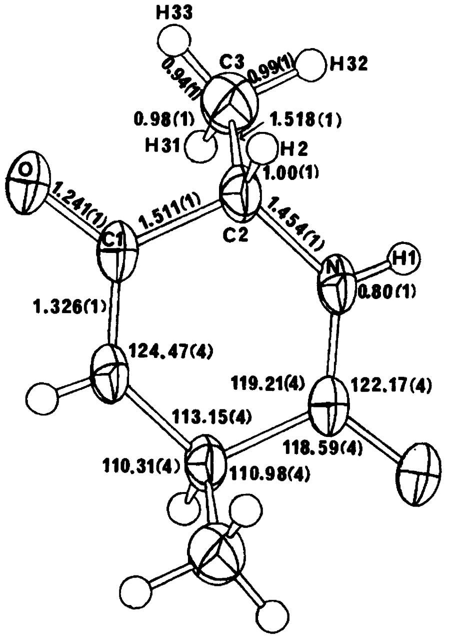

Fig. 1. Bond distances and angles. Numbers in parentheses are standard deviations as obtained from the least-squares inverse matrix. Thermal ellipsoids are plotted at the 50 % probability level.

They closely resemble those found in modification I.[1,2] The one significant difference in molecular dimensions is in the bond angles at the nitrogen atom. The internal angle at N is approximately 3.5° smaller in modification II, and the direction of the N – H bond differs somewhat in the two structures.

The six-membered ring is almost planar, but slightly more puckered than in I. Deviations from the best least-squares plane through the six ring atoms (N,C1,C2 and their centrosymmetrically related atoms) are as follows: N +0.017 Å, C1

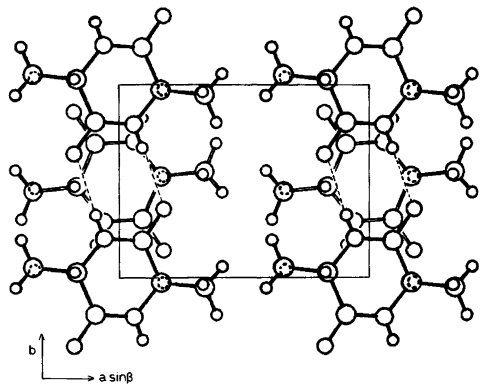

Fig. 2. Crystal packing and hydrogen bonding.

+0.016 Å, C2 − 0.015 Å, O + 0.035 Å, C3 + 1.112 Å. The torsional angles usually quoted for peptide structures[6] are as follows: ϕ_{N-C_α} $(=\phi_{N-C2})$ $=175.3°$, $\psi_{C_\alpha-C'}$ $(=\psi_{C2-C1})=184.2°$ and $\omega_{C'-N_{+1}})$ $=\omega_{C1-N_{+1}})=175.1°$; all angles being referred to the L-amino acid residue. The corresponding values found in I are 183.1°, 177.2° and 183.2°, respectively. These differences in torsional angles imply that while in I the methyl groups were found to be axial, they are quasi-equatorial in II. One may easily envisage a transformation between the two forms; which in solution exist in a dynamic equilibrium.

The differences in molecular conformation may be related to the hydrogen bonding pattern in the two modifications. As Benedetti *et al.*[1] have pointed out, two different schemes of hydrogen bonds in the crystal may easily be envisaged, one giving hydrogen bonded layers of molecules, the other one giving rise to hydrogen bonded chains of molecules. The former type exists in I; while in the present structure hydrogen bonded chains of molecules related by centers of symmetry and running along the *b*-axis are found. In this context it may be noted that also in the crystal structure of the L,L-form (cyclo-L-alanyl-L-alanyl) hydrogen bonded rows of molecules are found,[2,7] running along a repeat distance of 6.08 Å. The crystal packing and hydrogen bonding are illustrated in Fig. 2. The relevant hydrogen bond dimensions are: $N\cdots O=2.859(1)$ Å, $\angle C1-O\cdots H=124.5°$, $\angle N-H\cdots O=175.8°$; as compared to corresponding values of 2.886 Å, 149.9° and 158.8° in I.[2]

REFERENCES

1. Benedetti, E., Corradini, P. and Pedone, C. *J. Phys. Chem. 73* (1969) 2891.
2. Sletten, E. *J. Am. Chem. Soc. 92* (1970) 172.
3. Cromer, D. T. and Waber, J. T. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1974, Vol. IV, p. 99.
4. Stewart, R. F., Davidson, E. R. and Simpson, W. T. *J. Chem. Phys. 42* (1965) 3175.
5. Frez, B. *The SDP User's Guide*, Enraf-Nonius, Delft (Holland) 1979.
6. Edsall, J. T., Flory, P. J., Kendrew, J. C., Liquori, A. M., Némethy, G., Ramachandran, G. N. and Scheraga, H. A. *J. Biol. Chem. 241* (1966) 1004.
7. Benedetti, E., Corradini, P. and Pedone, C. *Biopolymers 7* (1969) 751.

Received April 22, 1980.