

C(11A)	0.7510 (4)	0.8070 (4)	1.0359 (3)	0.063 (1)
C(12A)	0.6960 (5)	0.8862 (3)	0.9975 (3)	0.069 (1)
C(13A)	0.5718 (4)	0.8860 (3)	0.9470 (3)	0.057 (1)
C(14A)	0.5180 (3)	0.6976 (2)	0.5832 (2)	0.039 (1)
C(15A)	0.5566 (5)	0.6054 (3)	0.5810 (3)	0.063 (1)
C(16A)	0.6883 (5)	0.5758 (4)	0.5410 (3)	0.078 (1)
C(17A)	0.7760 (4)	0.6388 (4)	0.5048 (3)	0.074 (1)
C(18A)	0.7367 (4)	0.7305 (4)	0.5058 (3)	0.068 (1)
C(19A)	0.6064 (4)	0.7612 (3)	0.5457 (3)	0.054 (1)
Se(1B)	0.3113 (1)	0.4731 (1)	0.1585 (1)	0.063 (1)
Se(2B)	0.2800 (1)	1.0140 (1)	0.3003 (1)	0.053 (1)
S(1B)	0.0761 (1)	0.7409 (1)	0.2516 (1)	0.035 (1)
N(1B)	0.1081 (3)	0.6151 (2)	0.2143 (2)	0.041 (1)
N(2B)	0.3290 (3)	0.6604 (2)	0.2179 (2)	0.036 (1)
N(3B)	0.3183 (3)	0.8221 (2)	0.2525 (2)	0.034 (1)
N(4B)	0.0938 (3)	0.8682 (2)	0.2823 (2)	0.037 (1)
C(1B)	0.2415 (3)	0.5869 (2)	0.1990 (2)	0.039 (1)
C(2B)	0.2580 (3)	0.7411 (2)	0.2402 (2)	0.033 (1)
C(3B)	0.2223 (3)	0.8975 (2)	0.2782 (2)	0.036 (1)
C(4B)	0.4847 (3)	0.6397 (2)	0.2276 (3)	0.048 (1)
C(5B)	0.5443 (4)	0.6893 (3)	0.3082 (3)	0.050 (1)
C(6B)	0.5730 (4)	0.7902 (2)	0.2866 (3)	0.050 (1)
C(7B)	0.4665 (3)	0.8360 (2)	0.2219 (2)	0.043 (1)
C(8B)	-0.0112 (3)	0.5595 (2)	0.2035 (3)	0.044 (1)
C(9B)	-0.0797 (4)	0.5259 (3)	0.2805 (3)	0.067 (1)
C(10B)	-0.1995 (5)	0.4770 (3)	0.2714 (5)	0.095 (2)
C(11B)	-0.2516 (5)	0.4608 (3)	0.1883 (6)	0.101 (2)
C(12B)	-0.1820 (6)	0.4946 (3)	0.1110 (5)	0.093 (2)
C(13B)	-0.0629 (4)	0.5446 (3)	0.1192 (3)	0.066 (1)
C(14B)	-0.0326 (3)	0.9229 (2)	0.3072 (2)	0.037 (1)
C(15B)	-0.0677 (4)	0.9386 (3)	0.3993 (3)	0.050 (1)
C(16B)	-0.1971 (5)	0.9857 (3)	0.4215 (3)	0.065 (1)
C(17B)	-0.2890 (4)	1.0136 (3)	0.3539 (4)	0.062 (1)
C(18B)	-0.2536 (4)	0.9965 (3)	0.2633 (3)	0.063 (1)
C(19B)	-0.1238 (4)	0.9515 (2)	0.2391 (3)	0.049 (1)

Table 2. Selected geometric parameters (\AA , $^\circ$)

Se(1A)—C(1A)	1.824 (3)	Se(1B)—C(1B)	1.826 (3)
Se(2A)—C(3A)	1.826 (3)	Se(2B)—C(3B)	1.825 (3)
S(1A)—C(2A)	1.719 (3)	S(1B)—C(2B)	1.712 (3)
S(1A)—N(1A)	1.899 (3)	S(1B)—N(1B)	1.901 (3)
S(1A)—N(4A)	1.910 (3)	S(1B)—N(4B)	1.907 (3)
N(1A)—C(1A)	1.304 (4)	N(1B)—C(1B)	1.309 (4)
N(2A)—C(2A)	1.348 (4)	N(2B)—C(2B)	1.344 (4)
N(2A)—C(1A)	1.419 (4)	N(2B)—C(1B)	1.411 (4)
N(3A)—C(2A)	1.344 (4)	N(3B)—C(2B)	1.340 (4)
N(3A)—C(3A)	1.425 (4)	N(3B)—C(3B)	1.418 (4)
N(4A)—C(3A)	1.302 (4)	N(4B)—C(3B)	1.300 (4)
C(2A)—S(1A)—N(1A)	83.1 (1)	C(2B)—S(1B)—N(1B)	82.9 (1)
C(2A)—S(1A)—N(4A)	83.0 (1)	C(2B)—S(1B)—N(4B)	82.8 (1)
N(1A)—S(1A)—N(4A)	166.1 (1)	N(1B)—S(1B)—N(4B)	165.6 (1)
C(1A)—N(1A)—S(1A)	116.0 (2)	C(1B)—N(1B)—S(1B)	115.9 (2)
C(2A)—N(2A)—C(1A)	114.5 (3)	C(2B)—N(2B)—C(1B)	114.7 (3)
C(2A)—N(3A)—C(3A)	114.8 (3)	C(2B)—N(3B)—C(3B)	115.0 (3)
C(3A)—N(4A)—S(1A)	116.0 (2)	C(3B)—N(4B)—S(1B)	116.1 (2)
C(14A)—N(4A)—S(1A)	117.1 (2)	N(1B)—C(1B)—N(2B)	108.8 (3)
N(1A)—C(1A)—N(2A)	109.0 (3)	N(1B)—C(1B)—Se(1B)	127.9 (2)
N(1A)—C(1A)—Se(1A)	127.3 (2)	N(2B)—C(1B)—Se(1B)	123.3 (2)
N(2A)—C(1A)—Se(1A)	123.7 (2)	N(3B)—C(2B)—N(2B)	125.0 (3)
N(3A)—C(2A)—N(2A)	125.4 (3)	N(3B)—C(2B)—S(1B)	117.4 (2)
N(3A)—C(2A)—S(1A)	117.2 (2)	N(2B)—C(2B)—S(1B)	117.5 (2)
N(2A)—C(2A)—S(1A)	117.3 (2)	N(4B)—C(3B)—N(3B)	108.6 (3)
N(4A)—C(3A)—N(3A)	108.7 (3)	N(4B)—C(3B)—Se(2B)	128.5 (2)
N(4A)—C(3A)—Se(2A)	128.3 (2)	N(3B)—C(3B)—Se(2B)	122.9 (2)
N(3A)—C(3A)—Se(2A)	122.9 (2)		

Data collection and data reduction were carried out using standard Enraf–Nonius routines. The structure was solved by direct methods using *SHELXS86* (Sheldrick, 1985) and refined using *SHELXL93* (Sheldrick, 1993). H atoms were placed in geometrically calculated positions and allowed to refine, riding on the atoms to which they are attached, with a common isotropic displacement parameter. The labelled structure diagram was produced using *ORTEPII* (Johnson, 1976).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: HR1038). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

- Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
- Billing, D. G., Boeyens, J. C. A., Denner, L., Hellyar, M. D., Lai, L.-L., Mathee, A. J. & Reid, D. H. (1992). *Acta Cryst. C47*, 2564–2567.
- Billing, D. G., Ferg, E. E., Lai, L.-L., Levendis, D. C. & Reid, D. H. (1993). *Acta Cryst. C49*, 917–921.
- Boessenkool, I. K. & Boeyens, J. C. A. (1980). *J. Cryst. Mol. Struct. 10*, 11–18.
- Evans, D. G. & Boeyens, J. C. A. (1989). *Acta Cryst. B45*, 581–590.
- Hall, S. R., Flack, H. D. & Stewart, J. M. (1992). Editors. *Xtal3.2 Reference Manual*. Universities of Western Australia, Australia, Geneva, Switzerland, and Maryland, USA.
- Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- Lai, L.-L. (1992). PhD thesis, University of the Witwatersrand, Johannesburg, South Africa.
- Sheldrick, G. M. (1985). *SHELXS86. Crystallographic Computing 3*, edited by G. M. Sheldrick, C. Krüger & R. Goddard, pp. 175–189. Oxford University Press.
- Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

Acta Cryst. (1996). **C52**, 973–978

Three Protected Tetrapeptides

EMMA FENUDE^a AND GIANLUIGI CASALONE^b

^aIstituto per l'Applicazione delle Tecniche Chimiche Avanzate ai Problemi Agrobiologici, CNR, 07100 Sassari, Italy, and ^bCentro del CNR per lo Studio delle Relazioni fra Struttura e Reattività Chimica, Via Golgi 19, 20133 Milano, Italy. E-mail: casalone@rs6.csrsrc.mi.cnr.it

(Received 30 June 1995; accepted 27 September 1995)

Abstract

The structures of three protected tetrapeptides, containing the Boc-Gly-Gly-Phe-X-OMe chain, *tert*-butoxycarbonyl-glycy-glycl-phenylalanine-leucine methyl ester dihydrate, Boc-Gly-Gly-L-Phe-D-Leu-OMe, C₂₅H₃₈N₄O₇·2H₂O, *tert*-butoxycarbonyl-glycy-glycl-phenylalanine-methionine methyl ester dihydrate, Boc-Gly-Gly-L-Phe-D-Met-OMe, C₂₄H₃₆N₄O₇S·2H₂O and *tert*-butoxycarbonyl-glycy-glycl-phenylalanine-norleucine methyl ester dihydrate, Boc-Gly-Gly-D-Phe-L-Nle-OMe, C₂₅H₃₈N₄O₇·2H₂O, are described. The three molecules have the same conformation of the tetrapeptide chain and display the same packing, consisting of couples

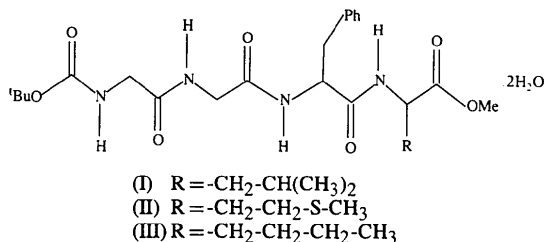
of molecules linked head-to-tail by two hydrogen (N—H···O) bonds; other hydrogen bonds, also involving two water molecules of crystallization, link these couples together and give rise to a planar structure.

Comment

Endogenous enkephalin, a linear pentapeptide functioning as a natural analgesic with opiate-like activity, occurs in the brain as H-Tyr-Gly-Gly-Phe-Leu-OH (leucine-enkephalin) and H-Tyr-Gly-Gly-Phe-Met-OH (methionine-enkephalin) in varying proportions, depending upon the species (Hughes, Smith, Kosterlitz, Fothergill, Morgan & Morris, 1975).

From the pharmacological viewpoint, endogenous enkephalin is very similar to morphine. The enkephalin molecule is flexible and capable of adopting various folded or extended conformations; this could explain why it is recognized by both μ - and δ -receptor sites (Schiller, 1984). Some μ - or δ -specific analogues of leucine-enkephalin have been obtained by introduction of conformational constraints (Hansen & Morgan, 1984), but attempts to correlate closely any one of the possible conformations of leucine-enkephalin with that of the rigid morphine molecule have failed hitherto. Different crystal structures have been reported for leucine-enkephalin (Smith & Griffin, 1978; Aubry, Birlirakis, Sakarellos-Daitsiotis, Sakarellos & Marraud, 1988) and for its fragments (Prangé & Pascard, 1979).

This work is part of a more general study on the crystalline conformations of enkephalin, its analogues, fragments and related compounds; here we present the crystal structures of Boc-Gly-Gly-L-Phe-D-Leu-OMe, (I), Boc-Gly-Gly-L-Phe-D-Met-OMe, (II), and Boc-Gly-Gly-D-Phe-L-Nle-OMe, (III). We would have preferred to study compounds of the same chiral series, but the preparation of crystals of these substances suitable for X-ray analysis is not easy, so we were satisfied with the first crystals we obtained. The chiral structure of (II) was confirmed by refining the Flack (1983) parameter, while for (I) and (III) this kind of refinement was not significant and the structure was assigned on the basis of chemical synthesis.



All three compounds have similar structures, with the same space group and cell parameters differing by less than 2%. Fig. 1 shows the three molecules with their atomic numbering schemes. Table 4 reports selected

bond lengths, bond angles and torsion angles. As can be seen, ignoring the sign of the torsion angles and depending on the different chiral series, the equivalent geometrical parameters of the three chains are very close to one another (see Table 4). The tetrapeptide chain presents a conformation all *trans* from N₄ to C₂₂ (glycine-glycine group), while the conformation around N₂—C₂₂, C₂₂—C₂₁ and N₁—C₁₂ is *gauche*, in such a way that the two hydrophobic groups, the benzyl group of phenylalanine and the aliphatic chain of the residue, are nearly coplanar and face each other. Fig. 2 emphasizes the similarities of the conformations of the three molecules. The packing of all these compounds comprises layers of molecules, perpendicular to the *c* axis; while these layers are linked to each other only by residual forces, the molecules within the layer are bonded by a network of hydrogen bonds, involving the iminic H atoms and those of the two co-crystallized water molecules (see Fig. 3). Table 5 reports the X···O distances of the hydrogen bonds.

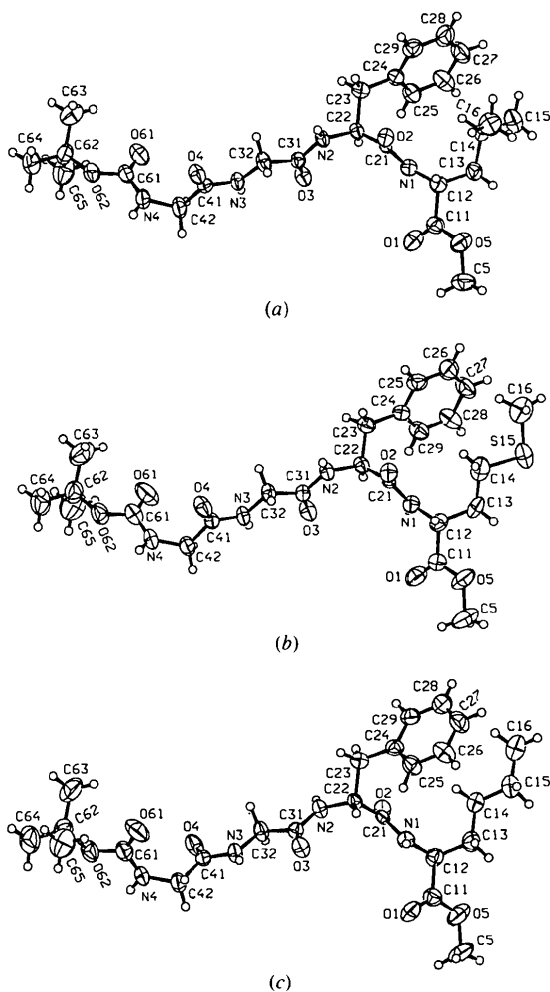


Fig. 1. ORTEP plots of (a) (I), (b) (II) and (c) (III). Ellipsoids are drawn at the 50% probability level and H atoms are not to scale.

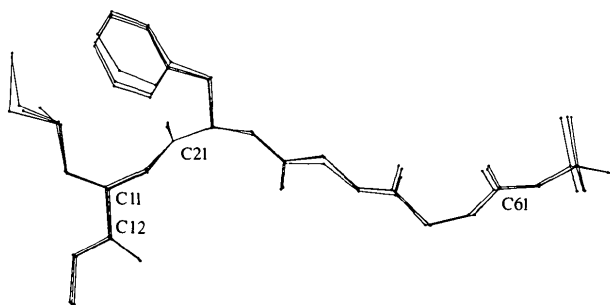


Fig. 2. Schematic projection of the three molecules on the common plane of C11, C12 and C61 with the origin at C21.

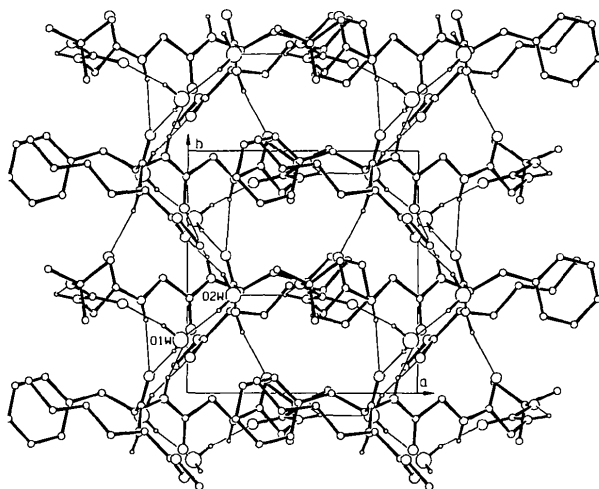


Fig. 3. A layer (1/2 of c axis) of hydrogen-bonded molecules of compound (III). Only H atoms involved in hydrogen bonds (thin lines) are shown. The hydrogen-bonding networks of (I) and (II) are very similar.

Experimental

The synthesis of the tetrapeptides was carried out by conventional methods (Vaughan & Osato, 1952) and the crystals were obtained in all cases from aqueous methanol solutions. The crystals of all three compounds contain two water molecules of crystallization in the asymmetric unit and are stable for a long time at room temperature.

Compound (I)

Crystal data

$C_{25}H_{38}N_4O_7 \cdot 2H_2O$

$M_r = 542.63$

Orthorhombic

$P2_12_12_1$

$a = 8.826(1) \text{ \AA}$

$b = 9.464(1) \text{ \AA}$

$c = 35.020(4) \text{ \AA}$

$V = 2925.2(6) \text{ \AA}^3$

$Z = 4$

$D_x = 1.232 \text{ Mg m}^{-3}$

D_m not measured

Mo $K\alpha$ radiation

$\lambda = 0.71073 \text{ \AA}$

Cell parameters from 36 reflections

$\theta = 2.82\text{--}11.85^\circ$

$\mu = 0.094 \text{ mm}^{-1}$

$T = 293(2) \text{ K}$

Tablet

$0.34 \times 0.30 \times 0.10 \text{ mm}$

Colourless

Data collection

Siemens P4 diffractometer

ω scans

Absorption correction:

none

7424 measured reflections

5163 independent reflections

3643 observed reflections

$[I > 2\sigma(I)]$

$R_{int} = 0.0237$

$\theta_{max} = 25^\circ$

$h = -1 \rightarrow 10$

$k = -11 \rightarrow 11$

$l = -41 \rightarrow 41$

3 standard reflections

monitored every 50

reflections

intensity decay: 7.45%

Refinement

Refinement on F^2

$R[F^2 > 2\sigma(F^2)] = 0.0477$

$wR(F^2) = 0.1071$

$S = 1.055$

5163 reflections

491 parameters

$w = 1/[\sigma^2(F_o^2) + (0.0395P)^2 + 0.2133P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.036$

$\Delta\rho_{max} = 0.200 \text{ e \AA}^{-3}$

$\Delta\rho_{min} = -0.187 \text{ e \AA}^{-3}$

Extinction correction:

SHELXL93 (Sheldrick, 1993)

Extinction coefficient:

0.0039 (6)

Atomic scattering factors

from *International Tables for Crystallography* (1992,

Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2) for (I)

$$U_{eq} = (1/3) \sum_i \sum_j U_{ij} a_i^* a_j^* \cdot a_i \cdot a_j$$

	x	y	z	U_{eq}
O1	0.0161 (3)	0.3749 (3)	0.12823 (7)	0.0705 (7)
O2	0.1701 (2)	-0.0423 (2)	0.16706 (5)	0.0431 (5)
O3	0.0191 (3)	0.2580 (2)	0.26569 (6)	0.0473 (6)
O4	-0.3525 (2)	-0.0393 (2)	0.32782 (6)	0.0494 (6)
O5	0.0547 (3)	0.3003 (2)	0.06870 (6)	0.0626 (7)
O61	-0.2682 (3)	0.1442 (3)	0.42710 (7)	0.0691 (7)
O62	-0.4941 (3)	0.0543 (2)	0.44758 (5)	0.0520 (5)
N1	0.2203 (3)	0.1897 (3)	0.15750 (7)	0.0376 (6)
N2	0.0980 (3)	0.0476 (2)	0.24269 (7)	0.0351 (6)
N3	-0.2019 (3)	0.1386 (3)	0.30921 (7)	0.0387 (6)
N4	-0.4704 (4)	0.1249 (3)	0.38805 (8)	0.0478 (7)
C11	0.0803 (4)	0.2991 (3)	0.10608 (9)	0.0462 (8)
C12	0.2026 (4)	0.1929 (3)	0.11621 (8)	0.0405 (7)
C13	0.3519 (4)	0.2306 (4)	0.09645 (10)	0.0485 (9)
C14	0.4790 (4)	0.1248 (4)	0.10107 (9)	0.0470 (8)
C15	0.6291 (5)	0.1933 (5)	0.08895 (12)	0.0704 (11)
C16	0.4508 (5)	-0.0091 (4)	0.07891 (13)	0.0728 (12)
C21	0.2039 (3)	0.0762 (3)	0.17937 (8)	0.0308 (6)
C22	0.2288 (3)	0.0990 (3)	0.22181 (8)	0.0330 (7)
C23	0.3708 (4)	0.0207 (3)	0.23589 (9)	0.0420 (7)
C24	0.5176 (3)	0.0570 (3)	0.21599 (8)	0.0393 (7)
C29	0.5597 (4)	0.1962 (4)	0.20944 (9)	0.0478 (8)
C28	0.6953 (5)	0.2289 (5)	0.19174 (11)	0.0637 (10)
C27	0.7894 (5)	0.1229 (6)	0.18014 (11)	0.0701 (11)
C26	0.7517 (4)	-0.0150 (6)	0.18642 (11)	0.0696 (12)
C25	0.6145 (4)	-0.0491 (4)	0.20421 (10)	0.0530 (9)
C31	0.0051 (3)	0.1288 (3)	0.26318 (7)	0.0325 (6)
C32	-0.1174 (4)	0.0489 (3)	0.28389 (9)	0.0428 (8)
C41	-0.3146 (3)	0.0848 (3)	0.33000 (8)	0.0363 (7)
C42	-0.4001 (5)	0.1871 (4)	0.35529 (10)	0.0524 (9)
C5	-0.0476 (5)	0.4068 (5)	0.05437 (13)	0.0739 (12)
C61	-0.3997 (4)	0.1115 (3)	0.42139 (9)	0.0459 (8)
C62	-0.4599 (4)	0.0606 (4)	0.48867 (8)	0.0528 (9)
C63	-0.3202 (6)	-0.0241 (6)	0.49801 (12)	0.0863 (14)
C64	-0.6004 (5)	-0.0054 (5)	0.50578 (11)	0.0738 (12)
C65	-0.4458 (7)	0.2134 (5)	0.50056 (13)	0.0887 (15)
O1W	-0.0189 (4)	0.3083 (4)	0.39413 (9)	0.1062 (11)
O2W	0.2071 (4)	0.1115 (4)	0.36497 (14)	0.1184 (13)

O4	-0.3456 (2)	0.5628 (2)	0.32850 (6)	0.0534 (5)	O3—C31—C32	122.4 (3)	122.6 (3)	122.6 (2)
O5	-0.0475 (3)	0.2200 (3)	0.07182 (6)	0.0762 (7)	N2—C31—C32	114.3 (2)	113.6 (2)	113.8 (2)
O61	-0.2850 (3)	0.3673 (3)	0.42093 (7)	0.0895 (9)	N3—C32—C31	111.9 (2)	111.8 (2)	112.1 (2)
O62	-0.5114 (2)	0.4508 (2)	0.44125 (5)	0.0614 (6)	O4—C41—N3	122.4 (3)	122.0 (3)	122.3 (2)
N1	0.2100 (3)	0.3342 (2)	0.15882 (6)	0.0396 (5)	O4—C41—C42	120.9 (3)	121.3 (3)	121.1 (2)
N2	0.1015 (3)	0.4741 (2)	0.24430 (6)	0.0388 (6)	N3—C41—C42	116.6 (3)	116.6 (3)	116.6 (2)
N3	-0.2021 (3)	0.3825 (2)	0.30830 (6)	0.0407 (6)	N4—C42—C41	115.0 (3)	113.8 (3)	114.0 (2)
N4	-0.4838 (3)	0.3875 (3)	0.38219 (7)	0.0473 (6)	O61—C61—N4	124.6 (3)	124.6 (4)	124.5 (3)
C11	0.0719 (4)	0.2233 (3)	0.10838 (9)	0.0508 (8)	O61—C61—O62	125.3 (3)	124.5 (4)	124.9 (3)
C12	0.1857 (3)	0.3371 (3)	0.11859 (7)	0.0461 (7)	N4—C61—O62	110.2 (3)	110.9 (3)	110.6 (3)
C13	0.3333 (4)	0.3210 (4)	0.09667 (10)	0.0592 (9)	N3—C41—C42—N4	-154.1 (3)	-155.2 (3)	155.4 (3)
C14	0.4416 (4)	0.4448 (4)	0.10234 (10)	0.0636 (9)	C42—C41—N3—C32	-178.7 (3)	-178.2 (3)	178.0 (3)
C15	0.5886 (5)	0.4252 (6)	0.08242 (13)	0.0936 (15)	C41—N3—C32—C31	-179.7 (3)	177.0 (3)	-177.7 (2)
C16	0.6959 (6)	0.5488 (6)	0.08709 (12)	0.108 (2)	N3—C32—C31—N2	172.6 (3)	177.8 (3)	-176.8 (2)
C21	0.1997 (3)	0.4471 (3)	0.18126 (7)	0.0335 (6)	C32—C31—N2—C22	-176.8 (3)	-176.1 (3)	176.2 (2)
C22	0.2293 (3)	0.4214 (3)	0.22274 (7)	0.0346 (6)	C31—N2—C22—C21	-115.3 (3)	-112.8 (3)	113.6 (3)
C23	0.3718 (3)	0.4976 (3)	0.23614 (9)	0.0443 (7)	N2—C22—C21—N1	126.5 (3)	125.6 (3)	-125.9 (2)
C24	0.5163 (3)	0.4584 (3)	0.21640 (7)	0.0419 (7)	C22—C21—N1—C12	179.8 (3)	-179.7 (3)	180.0 (2)
C29	0.6223 (3)	0.5633 (4)	0.20830 (8)	0.0525 (8)	C21—N1—C12—C11	121.8 (3)	129.7 (3)	-127.5 (3)
C28	0.7573 (4)	0.5296 (5)	0.19112 (10)	0.0685 (10)				
C27	0.7881 (4)	0.3897 (5)	0.18165 (10)	0.0738 (11)				
C26	0.6859 (4)	0.2845 (4)	0.18924 (10)	0.0651 (9)				
C25	0.5512 (3)	0.3179 (3)	0.20681 (9)	0.0515 (8)				
C31	0.0081 (3)	0.3920 (3)	0.26399 (7)	0.0334 (6)				
C32	-0.1081 (3)	0.4747 (3)	0.28569 (8)	0.0424 (7)				
C41	-0.3144 (3)	0.4352 (3)	0.32843 (7)	0.0360 (6)				
C42	-0.4090 (4)	0.3280 (3)	0.35007 (9)	0.0489 (8)				
C5	-0.0539 (6)	0.1101 (6)	0.05798 (12)	0.0932 (14)				
C61	-0.4158 (4)	0.3982 (3)	0.41520 (9)	0.0545 (8)				
C62	-0.4717 (4)	0.4498 (4)	0.48142 (8)	0.0639 (9)				
C63	-0.3366 (6)	0.5465 (6)	0.48848 (11)	0.0963 (14)				
C64	-0.6122 (5)	0.5104 (6)	0.49943 (11)	0.095 (2)				
C65	-0.4465 (6)	0.2984 (5)	0.49415 (14)	0.1004 (15)				
O1W	-0.0294 (3)	0.2183 (3)	0.39247 (9)	0.0946 (9)				
O2W	0.1985 (3)	0.4040 (3)	0.36100 (10)	0.0967 (9)				

Table 4. Selected geometric parameters (\AA , $^\circ$)

	(I)	(II)	(III)
O1—C11	1.199 (4)	1.194 (4)	1.194 (4)
O2—C21	1.237 (3)	1.236 (3)	1.239 (3)
O3—C31	1.231 (3)	1.228 (3)	1.225 (3)
O4—C41	1.224 (3)	1.226 (3)	1.224 (3)
O5—C11	1.329 (4)	1.317 (4)	1.322 (4)
O61—C61	1.218 (4)	1.218 (5)	1.214 (4)
O62—C61	1.352 (4)	1.340 (4)	1.351 (4)
N1—C12	1.454 (4)	1.447 (4)	1.452 (3)
N1—C21	1.328 (3)	1.325 (4)	1.327 (3)
N2—C22	1.450 (4)	1.456 (4)	1.457 (3)
N2—C31	1.333 (3)	1.336 (4)	1.330 (3)
N3—C32	1.436 (4)	1.436 (4)	1.445 (3)
N3—C41	1.333 (4)	1.329 (4)	1.324 (3)
N4—C42	1.431 (4)	1.431 (4)	1.436 (4)
N4—C61	1.330 (4)	1.324 (5)	1.327 (4)
C11—C12	1.516 (5)	1.506 (5)	1.511 (4)
C12—C13	1.531 (4)	1.555 (6)	1.533 (4)
C21—C22	1.518 (4)	1.527 (4)	1.522 (4)
C22—C23	1.537 (4)	1.532 (5)	1.528 (4)
C31—C32	1.506 (4)	1.509 (4)	1.504 (4)
C41—C42	1.513 (4)	1.521 (5)	1.518 (4)
C21—N1—C12	125.3 (3)	124.2 (3)	124.9 (2)
C31—N2—C22	124.6 (2)	124.0 (2)	124.7 (2)
C41—N3—C32	120.0 (3)	120.8 (3)	121.0 (2)
C61—N4—C42	122.7 (3)	121.5 (3)	121.8 (3)
O1—C11—O5	123.4 (3)	124.1 (3)	123.6 (3)
O1—C11—C12	125.6 (3)	124.8 (3)	125.1 (3)
O5—C11—C12	111.0 (3)	111.1 (3)	111.3 (3)
N1—C12—C11	108.8 (3)	109.4 (3)	108.9 (2)
N1—C12—C13	111.2 (3)	111.4 (3)	112.1 (3)
C11—C12—C13	110.6 (2)	110.8 (3)	112.3 (2)
O2—C21—N1	124.0 (3)	124.1 (3)	123.5 (2)
O2—C21—C22	120.3 (2)	119.7 (3)	119.8 (2)
N1—C21—C22	115.7 (2)	116.2 (3)	116.7 (2)
N2—C22—C21	109.3 (2)	108.3 (3)	109.0 (2)
N2—C22—C23	109.0 (2)	108.3 (2)	108.8 (2)
C21—C22—C23	111.3 (2)	111.8 (3)	112.0 (2)
O3—C31—N2	123.3 (3)	123.8 (3)	123.6 (2)

Table 5. Hydrogen-bond distances (\AA)*

	(I)	(II)	(III)
N1...O4 ⁱ	2.864 (3)	2.839 (4)	2.843 (3)
N3...O2 ⁱ	3.145 (3)	3.046 (3)	3.051 (3)
N2...O3 ⁱⁱ	2.945 (3)	2.907 (3)	2.902 (3)
N4...O2W ⁱⁱⁱ	2.962 (5)	2.927 (5)	2.925 (4)
O1W...O61	2.931 (4)	2.859 (4)	2.850 (4)
O2W...O1W	2.914 (5)	2.883 (5)	2.893 (5)
O1W...O2 ⁱ	2.894 (4)	2.887 (4)	2.900 (3)
O2W...O1 ⁱⁱ	2.992 (4)	2.921 (4)	2.940 (4)

Symmetry codes for (I) and (II): (i) $-x, \frac{1}{2} + y, \frac{1}{2} - z$; (ii) $-x, -\frac{1}{2} + y, \frac{1}{2} - z$; (iii) $x - 1, y, z$. Symmetry codes for (III): (i) $-x, -\frac{1}{2} + y, \frac{1}{2} - z$; (ii) $-x, \frac{1}{2} + y, \frac{1}{2} - z$; (iii) $x - 1, y, z$. * X—H...O angles are larger than 147° for (I), 150° for (II) and 159° for (III).

For (I) and (III), H atoms were refined with the geometry restrained (*DFIX* in *SHELXL93*; Sheldrick, 1993). For (II), the H atoms bonded to C13 and C14 were constrained to ride on their bonded atoms. The other H atoms were refined with restraints (*DFIX* in *SHELXL93*). For all compounds, isotropic *B*'s of methyl groups were constrained to have the same value.

For all compounds, data collection: *XSCANS* (Siemens, 1994); cell refinement: *XSCANS*; data reduction: *XSCANS*. Program(s) used to solve structures: *SIR92* (Altomare *et al.*, 1994) for (I); *SHELXS86* (Sheldrick, 1990) for (II) and (III). For all compounds, program(s) used to refine structures: *SHELXL93* (Sheldrick, 1993); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL93*.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: AS1206). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

- Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435–436.
- Aubry, A., Birlirakis, N., Sakarellos-Daitsiotis, M., Sakarellos, C. & Marraud, M. (1988). *J. Chem. Soc. Chem. Commun.* pp. 963–964.
- Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
- Hansen, P. E. & Morgan, B. A. (1984). In *The Peptides. Analysis, Synthesis, Biology*, Vol. 6, edited by S. Udenfriend & J. Meienhofer. London: Academic Press.

Hughes, J., Smith, T. W., Kosterlitz, H. W., Fothergill, L. A., Morgan, B. A. & Morris, H. R. (1975). *Nature (London)*, **258**, 577–579.
 Johnson, C. K. (1976). *ORTEPII*. Report ORNI-5138. Oak Ridge National Laboratory, Tennessee, USA.
 Prangé, P. T. & Pascard, C. (1979). *Acta Cryst.* **B35**, 1812–1819.
 Schiller, P. W. (1984). In *The Peptides, Analysis, Synthesis, Biology*. Vol. 6, edited by S. Udenfriend & J. Meienhofer. London: Academic Press.
 Sheldrick, G. M. (1990). *SHELXTL/PC User's Manual*. Version 4.1. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
 Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
 Siemens (1994). *XSCANS. X-ray Single Crystal Analysis System*. Version 2.1. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
 Smith, G. D. & Griffin, J. F. (1978). *Science*, **199**, 1214–1216.
 Vaughan, J. R. Jr & Osato, R. L. (1952). *J. Am. Chem. Soc.* **74**, 676–678.

Acta Cryst. (1996). **C52**, 978–980

4-*tert*-Butyloxycarbonyl-6(*S*)-(hydroxymethyl)-3(*S*)-(1-methylethyl)piperazin-2-one

THOMAS KOLTER,^a FRANK RÜBSAM,^a ATHANASSIOS GIANNIS^a AND MARTIN NIEGER^b

^a*Institut für Organische Chemie und Biochemie der Universität, Gerhard-Domagk-Str. 1, 53121 Bonn, Germany,* and ^b*Institut für Anorganische Chemie der Universität, Gerhard-Domagk-Str. 1, 53121 Bonn, Germany. E-mail: giannis@uni-bonn.de*

(Received 21 June 1995; accepted 25 September 1995)

Abstract

The six-membered ring of the title ester [IUPAC name: *tert*-butyl 5-(hydroxymethyl)-2-(1-methylethyl)-3-oxo-piperazine-1-carboxylate], $C_{13}H_{24}N_2O_4$, adopts a distorted half-chair configuration with C5 lying out of plane. Hydrogen bonds are formed between the OH group and the protecting carbonyl group, and between NH and the piperazine oxo group.

Comment

Substituted piperazinones are of interest in the development of peptidomimetics, *i.e.* low-molecular weight compounds that can replace peptides in their interaction with receptors (Giannis & Kolter, 1993). The piperazinone ring can serve as a rigid template exposing substituents in a conformation resembling the side chains of a parent peptide in its receptor-bound conformation (Giannis & Kolter, 1993). Little is known about

the three-dimensional structures of these compounds (Michel, Evrard & Norberg, 1987). We report here the structure of the title compound, (I).

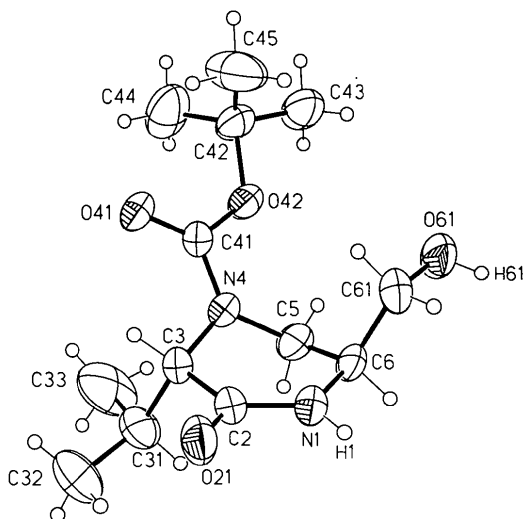
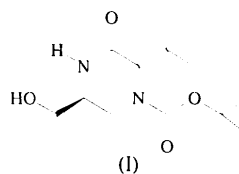


Fig. 1. Perspective drawing of (I) showing the crystallographic numbering scheme. Non-H atoms are shown with 30% probability ellipsoids.

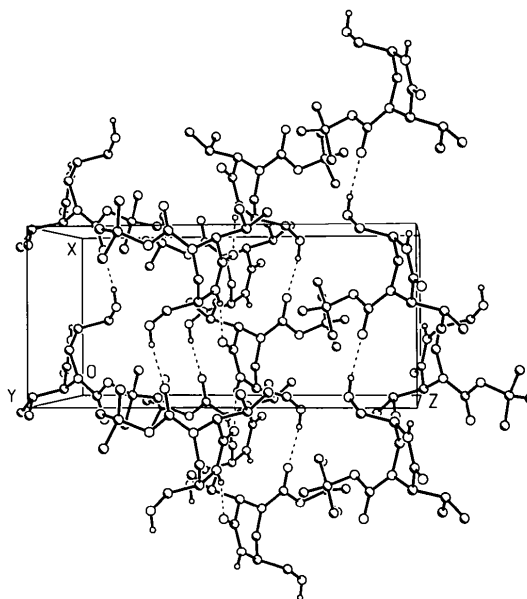


Fig. 2. A view of the unit cell showing intermolecular hydrogen bonding.