C30	0.9249 (2)	0.3499 (2)	0.3365 (1)	6.49 (6)
C31	0.9700 (2)	0.4167 (2)	0.3153 (2)	7.13 (7)
C32	0.9332 (2)	0.4916 (2)	0.3268 (2)	7.26 (7)
C33	0.8473 (2)	0.4987 (1)	0.3587 (1)	5.38 (5)
C34	0.7563 (2)	0.9988 (1)	0.4792 (1)	3.67 (4)
C35	0.8410 (1)	1.0394 (1)	0.4471 (1)	3.95 (4)
C36	0.8992 (2)	0.9988 (2)	0.4037 (1)	5.05 (5)
C37	0.9753 (2)	1.0378 (2)	0.3756 (2)	6.29 (6)
C38	0.9934 (2)	1.1166 (2)	0.3907 (2)	6.13 (6)
C39	0.9364 (2)	1.1573 (2)	0.4359 (1)	5.62 (6)
C40	0.8614 (2)	1.1191 (1)	0.4642 (1)	4.64 (5)
C41	0.6683 (1)	1.0481 (1)	0.4686 (1)	3.83 (4)
C42	0.6607 (2)	1.1061 (1)	0.4172 (1)	4.44 (4)
C43	0.5790 (2)	1.1473 (1)	0.4060 (1)	5.56 (5)
C44	0.5031 (2)	1.1298 (2)	0.4455 (2)	6.18 (6)
C45	0.5075 (2)	1.0715 (2)	0.4954 (2)	6.12 (6)
C46	0.5903 (2)	1.0297 (1)	0.5069 (1)	5.09 (5)
C47	0.7782 (1)	0.9809 (1)	0.5555 (1)	3.97 (4)
C48	0.7538 (2)	1.0320 (1)	0.6087 (1)	5.39 (5)
C49	0.7758 (2)	1.0135 (2)	0.6764 (1)	6.62 (7)
C50	0.8219 (2)	0.9441 (2)	0.6919 (1)	6.95 (7)
C51	0.8489 (2)	0.8932 (2)	0.6395 (1)	6.71 (6)
C52	0.8266 (2)	0.9114 (2)	0.5719 (1)	5.46 (5)

Table 2. *Selected geometric parameters (Å, °)*

O1—C1	1.424 (2)	O8—C9	1.201 (3)
O1—C15	1.443 (2)	O9—C11	1.190 (3)
O2—C2	1.439 (2)	O10—C13	1.195 (3)
O2—C7	1.356 (3)	C1—C2	1.514 (3)
O3—C3	1.444 (2)	C2—C3	1.525 (3)
O3—C9	1.357 (2)	C3—C4	1.519 (3)
O4—C4	1.445 (2)	C4—C5	1.526 (3)
O4—C11	1.359 (3)	C5—C6	1.518 (3)
O5—C5	1.443 (2)	C7—C8	1.479 (4)
O5—C13	1.350 (2)	C9—C10	1.477 (3)
O6—C6	1.411 (2)	C11—C12	1.484 (4)
O7—C7	1.185 (3)	C13—C14	1.480 (4)
C1—O1—C15	117.0 (1)	O5—C5—C6	110.9 (2)
C2—O2—C7	116.7 (2)	C4—C5—C6	112.9 (2)
C3—O3—C9	118.2 (1)	O6—C6—C5	106.0 (1)
C4—O4—C11	118.3 (2)	O2—C7—O7	123.2 (2)
C5—O5—C13	116.9 (1)	O2—C7—C8	111.1 (2)
O1—C1—C2	107.6 (1)	O7—C7—C8	125.7 (2)
O2—C2—C1	111.1 (2)	O3—C9—O8	123.8 (2)
O2—C2—C3	104.9 (1)	O3—C9—C10	110.6 (2)
C1—C2—C3	112.7 (2)	O8—C9—C10	125.6 (2)
O3—C3—C2	105.3 (1)	O4—C11—O9	123.4 (2)
O3—C3—C4	109.5 (1)	O4—C11—C12	110.6 (2)
C2—C3—C4	113.9 (1)	O9—C11—C12	126.0 (3)
O4—C4—C3	109.4 (1)	O5—C13—O10	122.9 (2)
O4—C4—C5	106.2 (1)	O5—C13—C14	111.2 (2)
C3—C4—C5	113.0 (1)	O10—C13—C14	125.9 (2)
O5—C5—C4	104.5 (1)		
C15—O1—C1—C2	170.1 (2)	O3—C3—C4—O4	49.9 (2)
C34—O6—C6—C5	179.9 (2)	C2—C3—C4—C5	174.2 (2)
O1—C1—C2—O2	−69.8 (2)	O4—C4—C5—O5	−177.3 (2)
O1—C1—C2—C3	47.7 (2)	C3—C4—C5—C6	−178.0 (2)
O2—C2—C3—O3	178.5 (2)	O5—C5—C6—O6	−63.0 (2)
C1—C2—C3—C4	177.4 (2)	C4—C5—C6—O6	53.9 (2)

H atoms were visible in difference maps, but were placed in idealized positions with C—H = 0.95 Å and B_{iso} = 1.3B_{eq} of the bonded C atom, and were not refined.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *MolEN* (Fair, 1990). Structure solution: *RANTAN* (Yao, 1981). Structure refinement: *MolEN*. Molecular graphics: *ORTEP*II (Johnson, 1976). Preparation of material for publication: *MolEN*.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: PT1015). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1996). C**52**, 383–387

Cyclo(L-alanyl-L-seryl).H_2O and Cyclo-(glycyl-L-seryl)

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Abstract

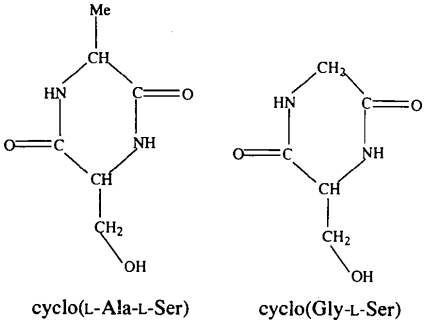
We have determined the crystal structures of two diketopiperazines, cyclo(L-alanyl-L-seryl).H_2O (*cis*-6-hydroxymethyl-3-methyl-2,5-piperazinedione hydrate, $C_6H_{10}N_2O_3.H_2O$) and cyclo(glycyl-L-seryl) (3-hydroxymethyl-2,5-piperazinedione, $C_5H_8N_2O_3$). The crystal structure of cyclo(L-alanyl-L-seryl).H_2O [cyclo(L-Ala-L-Ser)] consists of a peptide backbone that is hydrogen bonded to two adjacent diketopiperazine rings, forming extended chains through the crystal. The serine hydroxy group of cyclo(L-Ala-L-Ser) is hydrated by two adjacent water molecules in the crystal. In contrast, the crystal structure of cyclo(glycyl-L-seryl) [cyclo(Gly-L-Ser)] is

held together by a three-dimensional network of hydrogen bonds. The serine hydroxy group of cyclo(Gly-L-Ser) participates in two hydrogen bonds with the peptide backbone of neighboring molecules.

Comment

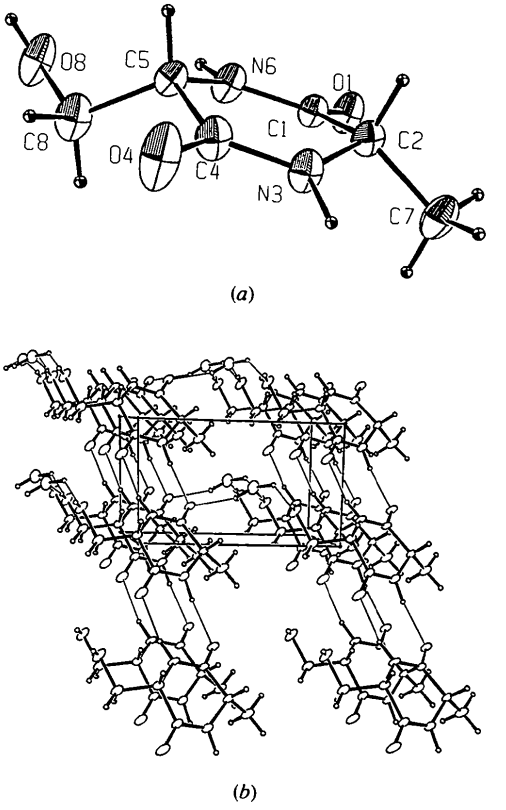
Cyclic dipeptides have been used as model systems for protein energetics (Gill, Hutson, Clopton & Downing, 1961; Murphy & Gill, 1989, 1990, 1991). We are currently studying cyclic dipeptides that contain serine side chains [specifically, cyclo(L-Ala-L-Ser), cyclo(L-Ser-L-Ser) and cyclo(Gly-L-Ser)] to investigate the effect of hydrogen bonding on structure and energetics. Comparison of the aqueous dissolution energetics of these compounds with those of other cyclic dipeptides containing non-hydrogen-bonding side chains allows an assessment of the contribution of hydrogen bonds to the thermodynamic values $\Delta G°$, $\Delta H°$, $\Delta S°$ and ΔC_p. The results of these thermodynamic studies will be reported elsewhere (Habermann & Murphy, in preparation).

Here we report the effects of the addition of a hydroxy group on the lattice interactions of diketopiperazines. The structure of cyclo(Gly-Gly) (Corey, 1938; Degeilh & Marsh, 1959) contains the same basic lattice interactions found in other *cis*-cyclic dipeptides that contain non-hydrogen-bonding side chains [specifically, cyclo(L-Ala-L-Ala) (Benedetti, Corradini & Pedone, 1969; Sletten, 1970), cyclo(Aib-Aib), cyclo(Aib-L-Ile) (Suguna, Ramakumar, Shamala, Venkataram Prasad & Balaram, 1982), cyclo-L-cystine (Varughese, Lu & Kartha, 1981) and cyclo(L-Phe-L-Phe) (Gdaniec & Liberek, 1986)] in that the peptide backbone is hydrogen bonded to two adjacent diketopiperazine rings forming long parallel chains with the side chains sequestered into channels.



cyclo(L-Ala-L-Ser) cyclo(Gly-L-Ser)

The addition of a single hydroxy group, comparing cyclo(L-Ala-L-Ser), with the above mentioned compounds, results in little change in the backbone interactions. The crystal structure determination of cyclo(L-Ala-L-Ser) shows that the peptide backbone is hydrogen bonded to adjacent diketopiperazine rings with the side chains sequestered into channels, as seen in Fig. 1. In order to satisfy the hydrogen bond of the serine hydroxy group there is a single water molecule per peptide molecule. The water molecule forms two hydrogen bonds by bridging serine hydroxy groups and forms a third hydrogen bond to a neighboring carbonyl. A similar crystal structure has been observed for cyclo(L-Leu-L-His) monohydrate (Tanaka, Iwata, Takahashi, Ashida & Tanihara, 1977), although the crystals are not isomorphous.



(*a*)

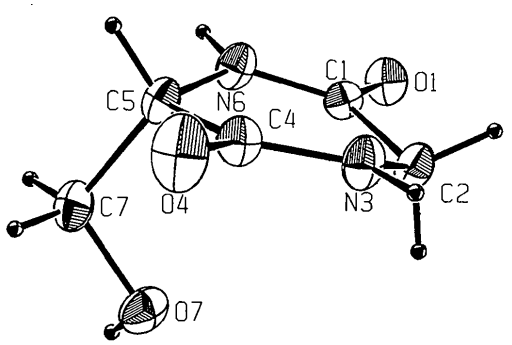
(*b*)

Fig. 1. (*a*) View and atomic numbering scheme of cyclo(L-Ala-L-Ser) and (*b*) the crystal structure. Thin lines indicate intermolecular hydrogen bonds. Note that the serine hydroxy groups are hydrogen bonded *via* bridging water molecules (*b* axis is horizontal, *a* axis is vertical).

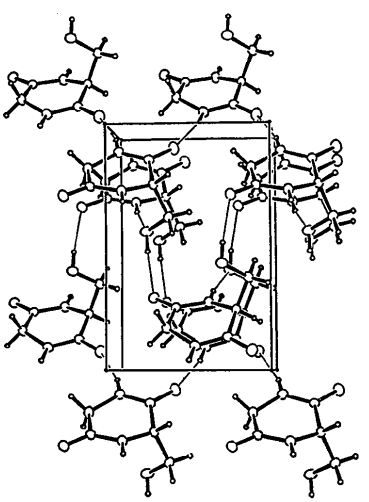
Interestingly, the presence of a second hydroxy group, comparing cyclo(L-Ala-L-Ser) to cyclo(L-Ser-L-Ser), greatly affects the crystal structure. The crystal structure of cyclo(L-Ser-L-Ser) has been determined previously by Fava, Belicchi, Marchelli & Dossena (1981). In this case, the serine hydroxy groups are hydrogen bonded to the peptide backbone of adjacent molecules while the peptide backbone is hydrogen bonded to adjacent serine hydroxy groups, connecting the diketopiperazine rings in parallel alternating chains. No water is incorporated in the lattice. Each cyclo(L-Ser-L-Ser) molecule, therefore, is involved in four hydrogen bonds, compared to two for the other cyclic dipeptides.

In contrast to the comparison of cyclo(L-Ala-L-Ser) with cyclo(L-Ala-L-Ala), the single hydroxy group

in cyclo(Gly-L-Ser) results in a significantly different crystal structure from those of the compounds containing non-hydrogen-bonded side chains (Fig. 2). In this case the crystal structure is held together by a three-dimensional network of hydrogen bonds. Each cyclo(Gly-L-Ser) molecule is involved in three hydrogen bonds. The serine hydroxy group forms one hydrogen bond to a neighboring carbonyl and a second to a neighboring amino group in a separate molecule. A third hydrogen bond is formed between the peptide backbone and the backbone of adjacent molecules.



(*a*)



(*b*)

Fig. 2. (*a*) View and atomic numbering scheme of cyclo(Gly-L-Ser) and (*b*) the crystal structure. Thin lines indicate intermolecular hydrogen bonds (*b* axis is horizontal, *c* axis is vertical).

In conclusion, previously published structures of diketopiperazines with non-hydrogen-bonding side chains show little variation in backbone interactions as functional groups are added. The addition of a hydroxy group presents a much more complex situation in which the lattice can respond by incorporation of solvent or by rearrangement of the backbone interactions.

Experimental

The cyclic dipeptides cyclo(L-Ala-L-Ser) and cyclo(Gly-L-Ser) were obtained from Bachem Bioscience (Philadelphia, PA). Both compounds were crystallized by heating a saturated solution of the cyclic dipeptide in water followed by slow cooling to obtain colorless needle-shaped crystals.

Cyclo(L-Ala-L-Ser)

Crystal data

$C_6H_{10}N_2O_3.H_2O$
$M_r = 176.18$
Triclinic
$P1$
$a = 5.222\ (2)$ Å
$b = 8.389\ (2)$ Å
$c = 4.7590\ (10)$ Å
$\alpha = 93.04\ (3)°$
$\beta = 102.59\ (2)°$
$\gamma = 92.57\ (2)°$
$V = 202.84\ (10)$ Å^3
$Z = 1$
$D_x = 1.442$ Mg m^{-3}
Mo $K\alpha$ radiation
$\lambda = 0.71070$ Å
Cell parameters from 45 reflections
$\theta = 7–19°$
$\mu = 0.121$ mm^{-1}
$T = 291\ (2)$ K
Needle
0.43 × 0.21 × 0.12 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\theta–2\theta$ scans
Absorption correction: none
1653 measured reflections
913 independent reflections
588 observed reflections $[I > 2\sigma(I)]$
$R_{int} = 0.032$
$\theta_{max} = 27.5°$
$h = -6 \rightarrow 6$
$k = -10 \rightarrow 10$
$l = -6 \rightarrow 5$
4 standard reflections
frequency: 480 min
intensity decay: 0.98%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0463$
$wR(F^2) = 0.1346$
$S = 1.168$
913 reflections
130 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.0348P)^2 + 0.0710P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.336$
$\Delta\rho_{max} = 0.260$ e Å^{-3}
$\Delta\rho_{min} = -0.210$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.2105 (387)
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 isotropic or equivalent isotropic displacement parameters (Å^2) for cyclo(L-Ala-L-Ser)*

U_{iso} for H atoms; $U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$ for all others.

	x	y	z	U_{eq}/U_{iso}
O1	0.3165 (7)	0.2433 (5)	0.9458 (8)	0.0390 (10)
O4	−0.2802 (8)	−0.0775 (5)	0.0144 (10)	0.063 (2)
O10	0.4703 (10)	0.5698 (6)	0.0819 (9)	0.0568 (13)
H10A	0.37 (2)	0.452 (16)	0.02 (3)	0.14 (4)
H10B	0.53 (2)	0.647 (15)	−0.04 (3)	0.15 (5)
O8	0.3174 (8)	−0.3029 (5)	0.5454 (10)	0.0530 (13)
H8	0.357 (16)	−0.355 (12)	0.39 (2)	0.08 (3)
N3	−0.1878 (9)	0.1462 (6)	0.3103 (10)	0.0391 (12)

H3	−0.339 (14)	0.180 (9)	0.208 (18)	0.07 (2)
N6	0.2517 (8)	0.0289 (5)	0.6275 (8)	0.0345 (12)
H6	0.382 (13)	−0.001 (7)	0.720 (14)	0.041
C1	0.1993 (9)	0.1736 (6)	0.7122 (11)	0.0310 (13)
C2	−0.0052 (10)	0.2606 (7)	0.5051 (12)	0.0372 (13)
H2	0.0868 (10)	0.3258 (7)	0.3888 (12)	0.045
C4	−0.1332 (10)	0.0023 (6)	0.2124 (11)	0.0377 (15)
C5	0.1221 (10)	−0.0638 (6)	0.3634 (11)	0.0335 (13)
H5	0.2416 (10)	−0.0627 (6)	0.2307 (11)	0.040
C7	−0.1571 (12)	0.3700 (7)	0.6618 (13)	0.048 (2)
H7*A*	−0.0375 (14)	0.447 (3)	0.786 (7)	0.071
H7*B*	−0.251 (7)	0.3082 (10)	0.775 (7)	0.071
H7*C*	−0.280 (6)	0.424 (4)	0.5240 (13)	0.071
C8	0.0726 (11)	−0.2355 (7)	0.4281 (12)	0.0434 (15)
H8*A*	−0.0400 (11)	−0.2399 (7)	0.5652 (12)	0.052
H8*B*	−0.0159 (11)	−0.2967 (7)	0.2525 (12)	0.052

Table 2. *Selected geometric parameters (Å, °) for cyclo(L-Ala-L-Ser)*

O1—C1	1.247 (6)	N6—C5	1.456 (6)
O4—C4	1.224 (6)	C1—C2	1.527 (7)
O8—C8	1.433 (6)	C2—C7	1.510 (8)
N3—C4	1.336 (7)	C4—C5	1.514 (7)
N3—C2	1.459 (7)	C5—C8	1.511 (8)
N3—H3	0.9 (1)	C5—H5	0.98
N6—C1	1.318 (7)		
H10*A*—O10—H10*B*	130 (10)	N6—C1—C2	117.6 (4)
C8—O8—H8	103 (6)	N3—C2—C7	109.4 (5)
C4—N3—C2	126.4 (5)	N3—C2—C1	110.5 (4)
C4—N3—H3	113 (5)	C7—C2—C1	112.3 (4)
C2—N3—H3	119 (5)	O4—C4—N3	123.3 (5)
C1—N6—C5	127.0 (4)	O4—C4—C5	119.7 (5)
C1—N6—H6	113 (5)	N3—C4—C5	117.0 (4)
C5—N6—H6	119 (5)	N6—C5—C8	109.8 (4)
O1—C1—N6	122.9 (4)	N6—C5—C4	113.5 (4)
O1—C1—C2	119.4 (5)	C8—C5—C4	109.7 (4)

Table 3. *Hydrogen-bonding geometry (Å, °) for cyclo(L-Ala-L-Ser)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O8—H8···O10^{i}	0.92 (10)	1.78 (10)	2.690 (7)	171 (8)
N3—H3···O1^{ii}	0.90 (7)	2.06 (7)	2.959 (5)	175 (7)
N6—H6···O4^{iii}	0.78 (7)	2.15 (7)	2.927 (6)	173 (6)
O10—H10*A*···O1^{iv}	1.11 (14)	1.76 (14)	2.820 (6)	159 (10)
O10—H10*B*···O8^{v}	0.98 (14)	2.10 (14)	2.788 (7)	125 (6)

Symmetry codes: (i) $x, y-1, z$; (ii) $x-1, y, z-1$; (iii) $1+x, y, 1+z$; (iv) $x, y, z-1$; (v) $x, 1+y, z-1$.

Cyclo(Gly-L-Ser)

Crystal data

$C_5H_8N_2O_3$
$M_r = 144.14$
Monoclinic
$P2_1$
$a = 4.896$ (2) Å
$b = 6.550$ (3) Å
$c = 9.737$ (4) Å
$\beta = 90.80$ (4)°
$V = 312.2$ (2) Å^3
$Z = 2$
$D_x = 1.534$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71070$ Å
Cell parameters from 25 reflections
$\theta = 12$–19°
$\mu = 0.128$ mm^{-1}
$T = 291$ (2) K
Plate
0.30 × 0.29 × 0.16 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
θ–2θ scans
Absorption correction: none
2234 measured reflections
976 independent reflections
854 observed reflections $[I > 2\sigma(I)]$
4 standard reflections
frequency: 480 min
intensity decay: 1.10%

$R_{int} = 0.019$
$\theta_{max} = 30.0°$
$h = -6 \rightarrow 6$
$k = -9 \rightarrow 1$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0300$
$wR(F^2) = 0.0877$
$S = 1.093$
976 reflections
123 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0598P)^2 + 0.0055P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.028$
$\Delta\rho_{max} = 0.219$ e Å^{-3}
$\Delta\rho_{min} = -0.224$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 4. *Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2) for cyclo(Gly-L-Ser)*

U_{iso} for H atoms; $U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$ for all others.

	x	*y*	*z*	U_{eq}/U_{iso}
C1	0.0943 (3)	0.5818 (2)	0.2574 (1)	0.0271 (3)
C2	−0.1592 (3)	0.6214 (3)	0.1725 (2)	0.0326 (3)
N3	−0.2616 (3)	0.4441 (2)	0.0991 (1)	0.0332 (3)
C4	−0.2143 (3)	0.2520 (3)	0.1341 (1)	0.0297 (3)
C5	−0.0044 (3)	0.2107 (2)	0.2473 (1)	0.0280 (3)
N6	0.1626 (3)	0.3879 (2)	0.2808 (1)	0.0313 (3)
C7	−0.1484 (4)	0.1286 (3)	0.3743 (2)	0.0354 (3)
O1	0.2285 (3)	0.7290 (2)	0.3011 (1)	0.0369 (3)
O4	−0.3296 (3)	0.1044 (2)	0.0800 (2)	0.0492 (4)
O7	−0.3321 (2)	0.2795 (2)	0.4247 (1)	0.0395 (3)
H3	−0.388 (5)	0.466 (5)	0.039 (3)	0.051 (7)
H6	0.305 (4)	0.374 (4)	0.330 (2)	0.033 (5)
H7	−0.316 (5)	0.27 (5)	0.509 (3)	0.050 (6)
H2*A*	−0.131 (6)	0.726 (5)	0.105 (3)	0.052 (7)
H2*B*	−0.292 (5)	0.666 (4)	0.234 (2)	0.042 (6)
H5	0.120 (4)	0.108 (4)	0.221 (2)	0.030 (5)
H7*A*	−0.002 (5)	0.105 (4)	0.440 (2)	0.044 (6)
H7*B*	−0.237 (5)	0.003 (5)	0.350 (3)	0.049 (6)

Table 5. *Selected geometric parameters (Å, °) for cyclo(Gly-L-Ser)*

C1—O1	1.239 (2)	C4—C5	1.521 (2)
C1—N6	1.332 (2)	C5—N6	1.455 (2)
C1—C2	1.504 (2)	C5—C7	1.530 (2)
C2—N3	1.450 (2)	C5—H5	0.94 (2)
C2—H2*A*	0.96 (3)	C7—O7	1.429 (2)
C2—H2*B*	0.93 (2)	C7—H7*A*	0.97 (2)
N3—C4	1.323 (2)	C7—H7*B*	0.96 (3)
C4—O4	1.234 (2)		
O1—C1—N6	123.53 (13)	N6—C5—C7	111.28 (13)
O1—C1—C2	118.95 (14)	C4—C5—C7	109.53 (12)
N6—C1—C2	117.51 (13)	N6—C5—H5	105 (1)
N3—C2—C1	114.21 (14)	C4—C5—H5	111 (1)
N3—C2—H2*A*	106.5 (16)	C7—C5—H5	106 (1)
C1—C2—H2*A*	111.9 (16)	C1—N6—C5	125.68 (12)
N3—C2—H2*B*	108.9 (15)	C1—N6—H6	114 (2)
C1—C2—H2*B*	106.3 (13)	C5—N6—H6	120 (2)
H2*A*—C2—H2*B*	109 (2)	O7—C7—C5	109.51 (14)
C4—N3—C2	125.21 (13)	O7—C7—H7*A*	110 (2)
C4—N3—H3	117 (2)	C5—C7—H7*A*	104 (1)
C2—N3—H3	116 (2)	O7—C7—H7*B*	113 (2)
O4—C4—N3	123.91 (14)	C5—C7—H7*B*	108 (2)
O4—C4—C5	118.1 (2)	H7*A*—C7—H7*B*	111 (2)
N3—C4—C5	118.03 (14)	C7—O7—H7	104 (2)
N6—C5—C4	113.13 (13)		

Table 6. *Hydrogen-bonding geometry (Å, °) for cyclo(Gly-L-Ser)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3···O4^{i}	0.86 (2)	2.01 (3)	2.837 (2)	163 (3)
N6—H6···O7^{ii}	0.85 (2)	2.08 (2)	2.914 (2)	167 (3)
O7—H7···O1^{iii}	0.83 (3)	1.91 (3)	2.731 (2)	172 (3)

Symmetry codes: (i) $-1-x, \frac{1}{2}+y, -z$; (ii) $1+x, y, z$; (iii) $-x, y-\frac{1}{2}, 1-z$.

For cyclo(L-Ala-L-Ser), H3, H6, H8, H10*A* and H10*B* were refined; U_{iso}(H6) = $1.2U_{eq}$(N6); H2, H5, H7*A*, H7*B*, H7*C*, H8*A* and H8*B* were refined using a riding model with U_{iso} = $1.2U_{iso}$(C).

For both compounds, data collection: *CAD*-4 *Software* (Enraf–Nonius, 1977); cell refinement: *CAD*-4 *Software*; data reduction: *MolEN* (Fair, 1990); program(s) used to solve structures: *MULTAN*80 (Main *et al.*, 1980); program(s) used to refine structures: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*93.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: SX1004). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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The Ribonucleotide Reductase R1 Inhibitor *N*-Acetyl-*N*,*O*-di(propylcarbamoyl)hydroxylamine, an Analogue of Caracemide

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Abstract

The molecular structure of the caracemide analogue *N*-acetyl-*N*,*O*-di(propylcarbamoyl)hydroxylamine (*Chemical Abstracts* nomenclature: *N*-[(propylamino)carbonyl]-*N*-{[(propylamino)carbonyl]oxy}acetamide), $C_{10}H_{19}N_3O_4$, is comparable to the structure of the parent compound *N*-acetyl-*N*,*O*-di(methylcarbamoyl)hydroxylamine. The caracemide moiety of the compound consists of two nearly planar moieties, which are almost perpendicular to each other as in the crystal structure of caracemide itself. The two propyl groups in each of the two molecules (*A* and *B*) in the asymmetric unit have different conformations. One of these groups adopts the *gauche* conformation, with torsion angles of 49.1 (6) and −61.3 (4)° for molecules *A* and *B*, respectively, while the other adopts a fully extended conformation, with respective torsion angles of 179.2 (3) and 176.5 (3)°. The main differences in bond lengths, angles and torsion angles between molecules *A* and *B* are found in one of the propyl groups.

Comment

The enzyme ribonucleotide reductase (RNR) catalyzes the reduction of ribonucleotides to deoxyribonucleotides. Being an indispensable enzyme in the *de novo* synthesis of DNA precursors, RNR is a potential target for antibacterial, antiviral or antineoplastic agents. A number of RNR inhibitors have been described (Lammers & Follmann, 1983; Larsen, 1990*a*; Stubbe, 1990).

The anticancer drug caracemide [*N*-acetyl-*N*,*O*-di(methylcarbamoyl)hydroxylamine, CAR] inhibits the enzyme RNR (Moore & Loo, 1984; Newman *et al.*, 1986). CAR was originally tested on partially purified RNR of Novikoff ascites tumor cells. Using highly purified RNR of *E. coli*, it has recently been shown that CAR inhibits RNR by specific irreversible inactivation of the larger R1 subunit of the enzyme (Larsen, Cornett, Karlsson, Sahlin & Sjöberg, 1992). The substrates