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L-Alanyl-L-threonine

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Key indicators

Single-crystal X-ray study
T = 105 K
Mean σ(C–C) = 0.001 Å
R factor = 0.027
wR factor = 0.075
Data-to-parameter ratio = 15.3

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The crystal structure of the title compound, $C_7H_{14}N_2O_4$, contains an intramolecular hydrogen bond between the side-chain hydroxyl group and the main-chain carboxylate group. This is the first observation of such an interaction for a C-terminal L-Ser or L-Thr residue.

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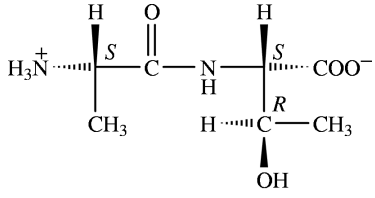
Comment

The crystal structures of only four dipeptides with one hydrophobic residue (Ala, Val, Leu, Ile, Phe and Met) and one small, polar residue (Asn, Gln, Ser, Thr and Cys) have been reported in the past: L-Ser–L-Ala (Görbitz, 2000), L-Ser–L-Leu (Słowikowska & Lipkowski, 2001), L-Ala–L-Ser (Jones *et al.*, 1978) and L-Val–L-Gln (Görbitz & Backe, 1996). We have now undertaken an investigation to determine the crystal structures of more compounds belonging to this group, with special focus on hydrogen-bonding preferences and aggregation patterns of hydrophobic groups. The structure of L-Ala–L-Thr, (I), is the first in this series.



(I)

The molecular structure of (I) is shown in Fig. 1. Bond lengths and angles are normal. The most interesting feature of the structure, the intramolecular hydrogen bond between the hydroxyl group of the Thr side chain and the C-terminal carboxylate group, is clearly seen. The N2—C4—C5—O2 torsion angle is *trans*, but is shifted away from the perfectly staggered orientation (180°), which would give a too short

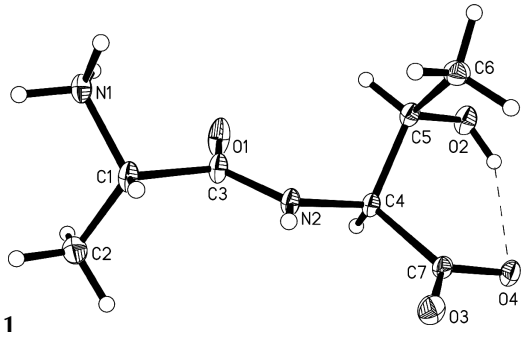


Figure 1
The molecular structure of L-Ala–L-Thr. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as spheres of arbitrary size. The intramolecular hydrogen bond between H5 and O4 is indicated by a dashed line.

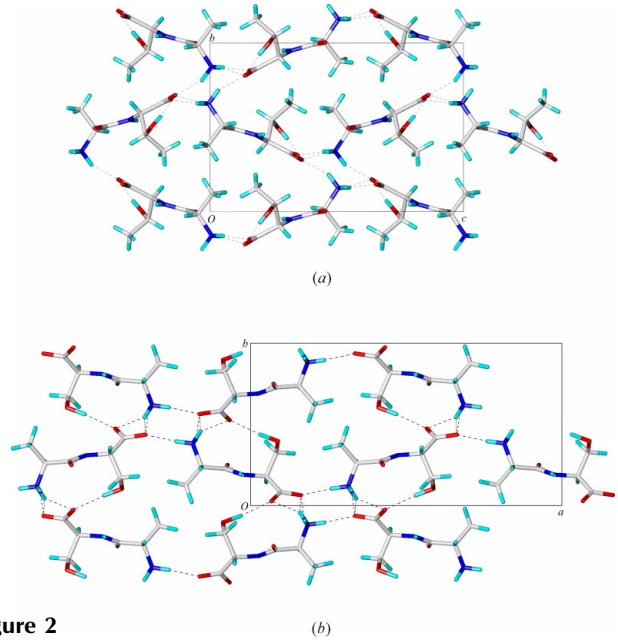


Figure 2
The molecular packing and unit cell of (*a*) L-Ala–L-Thr viewed along the *a* axis and (*b*) L-Ala–L-Ser (Jones *et al.*, 1978) viewed along the *c* axis.

O2···O4 distance of 2.565 Å. The observed value is 2.7756 (10) Å (Table 2), with N2—C4—C5—O2 = −164.34 (6)° (Table 1). The H atom of the hydroxyl group is in a *gauche*$^-$ position (C4—C5—O4—H5; Table 1). In this case, the rotation from −60.0° (ideal staggered) to −44.0 (11)° has the effect of reducing the H5···O4 distance from 2.130 to 2.065 (18) Å and increasing the O2—H5···O4 angle from 135.1 to 143.6 (18)° (Table 2).

Fig. 2 shows the crystal packing arrangements of (I) and also of L-Ala–L-Ser, (II) (Jones *et al.*, 1978), which is related to (I). The peptide molecules have essentially the same backbone conformations, and both structures have three-dimensional hydrogen bond networks that include the maximum number of three interactions between charged amino groups and carboxylate groups. The small hydrophobic columns of (II) (Fig. 2*b*) encompass only the side-chain methyl groups of the Ala residues. When the *gauche*$^-$ H atoms of the Ser side chains are replaced by methyl groups to yield Thr residues, a rotation of the side chains is required for the new methyl groups to be integrated into the existing hydrophobic columns, thus producing the larger columns with highly elongated cross-sections seen in Fig. 2*a*. The N—C$^\alpha$—C$^\beta$—O$^\gamma$ torsion angles are then shifted from *gauche*$^+$ for (II) to *trans* for (I), whereupon the intermolecular hydrogen bond with the Ser-OH donor in (II) is broken and replaced by the intramolecular hydrogen bond in (I). Concomitant adaptations include a new acceptor for the amide >N—H donor, from peptide carbonyl for (II) to Ser-OH for (I) (Fig. 2 and Table 2). Accordingly, the peptide carbonyl groups accept no hydrogen bonds in (I); even the usually abundant C$^\alpha$—H···O=C contacts are missing.

The only other dipeptide with a Thr residue in the Cambridge Structural Database (Version 5.25, November 2003; Allen, 2002) is Gly–Thr, available as Gly–L-Thr dihydrate (Yadava & Padmanabhan, 1973, recent charge density studies by Benabicha *et al.*, 2000; Dittrich *et al.*, 2000) and Gly–D,L-Thr (Swaminathan, 1975). No intramolecular hydrogen bonds are present in either of these two structures or in five additional compounds with C-terminal Ser or Thr residues [Gly–L-Ser (Görbitz, 1999); L-Arg–L-Ser acetate monohydrate (Verdauger *et al.*, 1991); L-Lys–L-Tyr–L-Ser acetate (Verdaguer *et al.*, 1990); L-Arg–L-Ser Gly–L-Glu (1:1) (Suresh & Vijayan, 1985); L-Tyr–D-Thr–Gly–L-Phe–L-Leu–L-Thr hexahydrate (Flippen-Anderson *et al.*, 1994)], which all have the same *gauche*$^+$ rotamer for N—C$^\alpha$—C$^\beta$—O$^\gamma$ as (II) (Jones *et al.*, 1978).

Experimental

The title compound was obtained from Bachem. Crystals were prepared by slow evaporation of an aqueous solution of the peptide at ambient temperature.

Crystal data

$C_7H_{14}N_2O_4$
M_r = 190.20
Orthorhombic, $P2_12_12_1$
a = 6.03990 (10) Å
b = 9.7642 (2) Å
c = 14.6820 (4) Å
V = 865.87 (3) Å^3
Z = 4
D_x = 1.459 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 8870 reflections
θ = 2.5–35.0°
μ = 0.12 mm^{-1}
T = 105 (2) K
Block, colourless
0.45 × 0.18 × 0.14 mm

Data collection

Bruker SMART CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.929, T_{max} = 0.986
11596 measured reflections
2171 independent reflections
2087 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 35.0°
$h = -9 \rightarrow 9$
$k = -15 \rightarrow 15$
$l = -21 \rightarrow 23$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.075
S = 1.14
2171 reflections
142 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0486P)^2 + 0.0543P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

Table 1
Selected torsion angles (°).

N1—C1—C3—N2	136.81 (7)	N2—C4—C5—C6	71.62 (8)
C1—C3—N2—C4	173.74 (7)	N2—C4—C5—O2	−164.34 (6)
C3—N2—C4—C7	−166.22 (7)	C4—C5—O2—H5	−44.0 (11)
N2—C4—C7—O3	−3.67 (10)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O4^{i}	0.957 (16)	1.950 (16)	2.8160 (10)	149.5 (14)
N1—H2···O3^{ii}	0.937 (18)	1.842 (17)	2.7597 (9)	166.0 (15)
N1—H3···O4^{iii}	0.895 (18)	2.061 (17)	2.9137 (10)	158.9 (15)
N2—H4···O2^{iv}	0.860 (16)	2.067 (16)	2.9127 (9)	167.6 (13)
O2—H5···O4	0.828 (16)	2.065 (18)	2.7756 (10)	143.6 (18)

Symmetry codes: (i) $1-x, y-\frac{1}{2}, \frac{3}{2}-z$; (ii) $\frac{3}{2}-x, 1-y, z-\frac{1}{2}$; (iii) $\frac{1}{2}-x, 1-y, z-\frac{1}{2}$; (iv) $1+x, y, z$.

Positional parameters were refined for H atoms involved in hydrogen bonds; other H atoms were positioned geometrically and refined as riding, with C—H = 0.93 Å. U_{iso} values were $1.2U_{eq}$ of the carrier atom or $1.5U_{eq}$ for hydroxyl, amino and methyl groups.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT-Plus* (Bruker, 2001); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Bruker, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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