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N-Acetyl-L-tyrosine methyl ester monohydrate at 293 and 123 K

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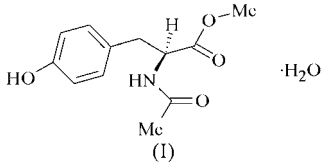
The crystal structure of a protected L-tyrosine, namely *N*-acetyl-L-tyrosine methyl ester monohydrate, $C_{12}H_{15}NO_4\cdot H_2O$, was determined at both 293 (2) and 123 (2) K. The structure exhibits a network of O—H···O and N—H···O hydrogen bonds, in which the water molecule plays a crucial role as an acceptor of one and a donor of two hydrogen bonds. Molecules of water and of the protected L-tyrosine form hydrogen-bonded layers perpendicular to [001]. C—H···π interactions are observed in the hydrophobic regions of the structure. The structure is similar to that of *N*-acetyl-L-tyrosine ethyl ester monohydrate [Soriano-García (1993). *Acta Cryst.* C**49**, 96–97].

Comment

The *N*-acetyl methyl ester of L-tyrosine was chosen from among amino acid residues that are responsible for binding the antiarrhythmics of classes I and III in sodium and potassium channels, respectively (Tseng, 2001), and was used in some experiments performed to reveal the mutual chemical recognition of antiarrhythmic agents by amino acids. The crystal structure of the title compound, L-AcYOMe·H_2O, (I), was determined to allow comparison with the structures of *N*-acetyl-L-tyrosine ethyl ester monohydrate (Pieret *et al.*, 1972; Soriano-García, 1993), L-tyrosine and L-tyrosine hydrochloride (Frey *et al.*, 1973). Charge density studies have also been performed on *N*-acetyl-L-tyrosine ethyl ester monohydrate (Dahaoui *et al.*, 1999).



(I)

Compound (I) crystallizes in the space group $P2_12_12_1$; the contents of the asymmetric unit at 123 (2) K are shown in Fig. 1. Selected geometric parameters at 293 (2) and 123 (2) K are given in Tables 1 and 3, respectively. In relation to L-tyrosine itself, the protected amino acid offers different possibilities of intermolecular interactions, which are closer to the specific interactions of small peptides. Owing to the inactivation of the amino and carboxyl groups, the water molecule can participate in a network of hydrogen bonds as an acceptor of one H atom and a donor of two. Water molecules and L-AcYOMe molecules form layers parallel to *ab* at $z = \frac{1}{2}$ (Fig. 2, and Tables 2 and 4). Each layer consists of alternating hydrophobic and hydrophilic areas. In the hydrophobic area, C—H···π interactions of type III in the classification of Malone *et al.* (1997) dominate [C5—H5···*Cg*1($x - \frac{1}{2}$, $-y + \frac{3}{2}$, $-z + 1$), where *Cg*1 is the centre of gravity of the C4–C9 benzene ring], whereas in the hydrophilic area, mainly O—H···O hydrogen bonds exist. There are weak C3—H3*A*···O10($x + 1$, y, z) interactions between hydrophobic and hydrophilic areas of the layers. The layers are linked by N—H···O hydrogen bonds, and between hydrophobic and hydrophilic areas of neighbouring layers there are weak C8—H8···O1($-x + 2$, $y + \frac{1}{2}$, $-z + \frac{3}{2}$) interactions (Fig. 3, and Tables 2 and 4). There is no obvious difference in molecular geometry between 293 and 123 K, except for the apparent elongation of bond lengths at the lower temperature due to a reduction in librational effects as the atomic displacements decrease.

Table 5 presents a comparison of the torsion angles that characterize the backbone conformation of (I), *N*-acetyl-L-tyrosine ethyl ester (Soriano-García, 1993) and *N*-acetyl-L-tyrosine ethyl ester at room- and low-temperature (Dahaoui *et al.*, 1999) with the conformation of the L-tyrosine residue in selected tripeptides and with the conformation of L-tyrosine itself and L-tyrosine hydrochloride (Frey *et al.*, 1973). The values of the torsion angles ω, φ, ψ_1, ψ_2, χ_1 and χ_2, which are defined in agreement with the IUPAC–IUB Commission on Biochemical Nomenclature (1970), are similar for protected L-tyrosine; the observed differences in torsion angles are in the range 0.7–5.2°. For tripeptides LYL and VYV (L, V, Y, A and G denote leucine, valine, tyrosine, alanine and glycine, respectively), the differences are of up to 25°, indicating that the conformation of the L-tyrosine residue is, in general, well preserved with small deviations caused by the N- and C-ends forming hydrogen bonds. However, in both LYL and VYV, the presence of relatively long hydrocarbon chains of L or V

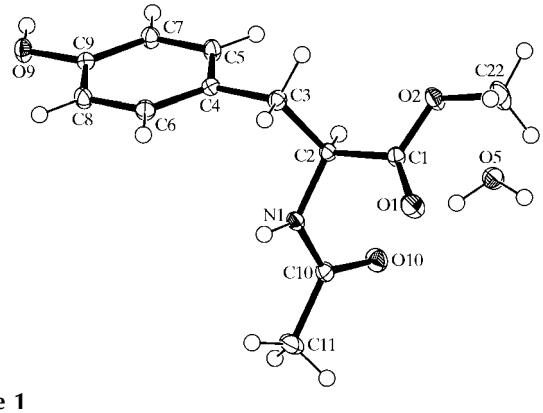


Figure 1
The asymmetric unit of *N*-acetyl-L-tyrosine methyl ester monohydrate at 123 K, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

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residues provides steric hindrance for such intermolecular interactions. In GYA, owing to a lack of hydrocarbon chains, the N- and C-ends are free to form hydrogen bonds. The moderate N—H···O hydrogen bonds could change the torsion angles of the L-tyrosine residue by 50°. In the cases of L-tyrosine and its hydrochloride, the most pronounced conformational differences arise because of specific patterns of hydrogen bonding.

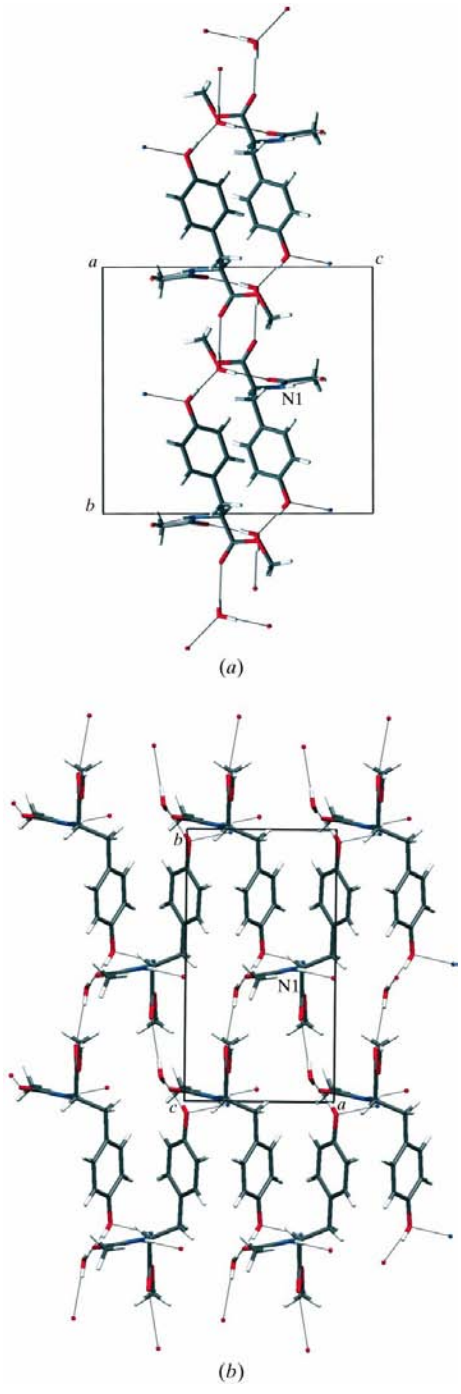

Figure 2
(*a*) The role of hydrogen bonds formed by water molecules in joining molecules of *N*-acetyl-L-tyrosine ethyl ester into layers, and (*b*) a projection on to the $(x, y, \frac{1}{2})$ layer, showing hydrophobic and hydrophilic areas alternating along [010].

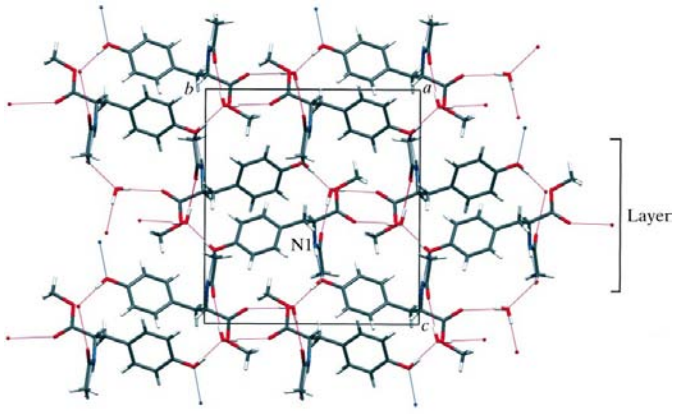

Figure 3
The arrangement of layers in projection along [100].

Experimental

The protected amino acid was purchased from Bachem Chemical Company. Crystals suitable for X-ray structure determination were obtained by vapour diffusion at room temperature between heptane and an acetone solution containing *N*-acetyl-L-tyrosine ethyl ester and lidocaine in a 1:1 molar ratio. Lidocaine, which was used to provide the correct ionic strength of the solutions, was purchased from Sigma Chemical Company. The diffraction intensity measurements at 293 (2) and 123 (2) K were performed on two different crystals.

Compound (I), at 293 K

Crystal data

$C_{12}H_{15}NO_4\cdot H_2O$
$M_r = 255.27$
Orthorhombic, $P2_12_12_1$
$a = 7.2117$ (1) Å
$b = 12.9868$ (3) Å
$c = 14.2470$ (4) Å
$V = 1334.33$ (5) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.10$ mm^{-1}
$T = 293$ (2) K
0.52 × 0.52 × 0.37 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*DENZO* and *SCALEPACK*; Otwinowski & Minor, 1997)
$T_{min} = 0.950$, $T_{max} = 0.964$
8443 measured reflections
2223 independent reflections
1847 reflections with $I > 2\sigma(I)$
$R_{int} = 0.020$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.101$
$S = 1.01$
2223 reflections
181 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.16$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °) for (I) at 293 K.

N1—C10	1.344 (3)	C2—C3	1.538 (3)
N1—C2	1.447 (2)	O2—C12	1.444 (2)
C1—O1	1.198 (2)	C10—O10	1.228 (2)
C1—C2	1.522 (2)		
N1—C2—C1	110.4 (2)	C1—C2—C3	109.1 (2)
N1—C2—C3	110.7 (2)	C1—O2—C12	117.3 (2)
O1—C1—C2—N1	−18.5 (3)	O1—C1—C2—C3	103.3 (2)
O2—C1—C2—N1	162.6 (2)	O2—C1—C2—C3	−75.6 (2)

Table 2
Hydrogen-bond geometry (Å, °) for (I) at 293 K.

*Cg*1 is the centre of gravity of the C4–C9 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O9—H9···O5^{i}	0.89 (3)	1.82 (3)	2.707 (2)	173 (3)
N1—H1···O9^{ii}	0.88 (3)	2.12 (3)	3.004 (2)	177 (2)
O5—H5*A*···O1^{iii}	0.75 (4)	2.14 (4)	2.880 (2)	170 (4)
O5—H5*B*···O10	0.99 (4)	1.76 (4)	2.740 (2)	174 (3)
C3—H3*A*···O10^{iv}	0.97	2.63	3.417 (3)	138
C8—H8···O1^{v}	0.93	2.62	3.503 (2)	160
C5—H5···*Cg*1^{vi}	0.93	2.94	3.73 (5)	144

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

Compound (I), at 123 K

Crystal data

$C_{12}H_{15}NO_4\cdot H_2O$
M_r = 255.27
Orthorhombic, $P2_12_12_1$
a = 7.1118 (2) Å
b = 12.9364 (3) Å
c = 14.1538 (4) Å
V = 1302.17 (6) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 123 (2) K
0.40 × 0.37 × 0.25 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*DENZO* and *SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.961, T_{max} = 0.975
10167 measured reflections
2790 independent reflections
2605 reflections with $I > 2\sigma(I)$
R_{int} = 0.020

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.032
$wR(F^2)$ = 0.084
S = 1.00
2790 reflections
184 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

Owing to the absence of significant anomalous scattering, Friedel pairs were merged. The absolute configuration of the purchased materials was known. H atoms bonded to N and O atoms were located in difference Fourier maps and included in the refinement without constraints. For the sp^2-bound methyl group (C11), the procedure for finding the H atom relied on locating the maximum electron density around the circle representing the locus of possible H-atom positions (Sheldrick, 1997). For this methyl group, C—H distances and C—C—H angles were kept fixed, while the torsion angles were allowed to refine, with the U_{iso}(H) values set at 1.2U_{eq}(C11). H atoms attached to other C atoms were included with appropriate geometrical constraints and were treated as riding, with U_{iso}(H) values of 1.2U_{eq} of the parent atoms.

Table 3
Selected geometric parameters (Å, °) for (I) at 123 K.

N1—C10	1.349 (2)	C2—C3	1.541 (2)
N1—C2	1.449 (2)	O2—C12	1.449 (1)
C1—O1	1.209 (1)	C10—O10	1.234 (2)
C1—C2	1.526 (1)		
N1—C2—C1	110.4 (1)	C1—C2—C3	108.8 (1)
N1—C2—C3	110.3 (1)	C1—O2—C12	116.4 (1)
O1—C1—C2—N1	−16.5 (2)	O1—C1—C2—C3	104.7 (1)
O2—C1—C2—N1	164.8 (1)	O2—C1—C2—C3	−74.1 (1)

Table 4
Hydrogen-bond geometry (Å, °) for (I) at 123 K.

*Cg*1 is the centre of gravity of the C4–C9 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O9—H9···O5^{i}	0.86 (3)	1.83 (3)	2.693 (1)	173 (3)
N1—H1···O9^{ii}	0.88 (2)	2.09 (2)	2.968 (1)	174 (2)
O5—H5*A*···O1^{iii}	0.79 (3)	2.07 (3)	2.853 (1)	173 (3)
O5—H5*B*···O10	0.88 (3)	1.85 (3)	2.729 (1)	176 (2)
C3—H3*A*···O10^{iv}	0.99	2.54	3.356 (2)	140
C8—H8···O1^{v}	0.95	2.55	3.462 (2)	160
C5—H5···*Cg*1^{vi}	0.95	2.84	3.65 (4)	144

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

For both compounds, data collection: *COLLECT* (Nonius, 1997); cell refinement: *DENZO-SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003), *ORTEP-3 for Windows* (Farrugia, 1997) and *Mercury* (Version 1.4; Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM3032). Services for accessing these data are described at the back of the journal.

Table 5
A comparison of torsion angles (°) describing the conformation of backbones in L-tyrosine derivatives.

φ, ψ, χ and ω are defined in agreement with the IUPAC–IUB Commission on Biochemical Nomenclature (1970).

Torsion angle	Symbol	AcYOMe, 293 K	AcYOMe, 123 K	AcYOEt[a]	AcYOEt[b]	AcYOEt[c]	GYA[d]	LYL(*b*)[e]	VYV[f]	Y[g]	Y·HCl[h]
C2—N1—C10—C11	ω	172.8 (2)	172.9 (1)	174.6 (4)	−174.3	−174.7	172.8	175.3	−172.0	–	–
C1—C2—N1—C10	φ	−71.3 (2)	−70.3 (1)	−74.8 (5)	75.1	74.2	−119.0	−82.8	−83.4	–	–
O1—C1—C2—N1	ψ1	−18.5 (3)	−16.5 (2)	−17.2 (5)	16.4	13.3	−61.6	−46.3	−37.3	−14.2	−31.8
O2—C1—C2—N1*	ψ2	162.6 (2)	164.8 (1)	164.0 (4)	−164.0	−167.0	120.0	137.3	145.7	166.3	151.1
N1—C2—C3—C4	χ1	−63.5 (2)	−64.0 (1)	−61.7 (5)	62.3	63.0	−86.4	−76.8	−64.3	69.1	−178.1
C1—C2—C3—C4	χ2	175.0 (1)	174.8 (1)	175.5 (4)	−175.3	−174.8	154.3	162.8	172.9	−53.1	62.8
C2—C3—C4—C5	—	−67.5 (2)	−67.7 (1)	−63.2 (5)	62.9	64.6	−112.9	−71.2	−66.1	−86.0	−113.7

Notes: (*) equivalent to N2—C1—C2—N1 in tripepetides. References: (*a*) *N*-acetyl-L-tyrosine ethyl ester (Soriano-García, 1993); *N*-acetyl-L-tyrosine ethyl ester (*b*) at room temperature and (*c*) at 110 K (Dahaoui *et al.*, 1999) [notice the opposite sequence of torsion angle signs, which indicates the opposite configuration at C_α; in fact, the deposited data for *N*-acetyl-D-tyrosine ethyl ester [Cambridge Structural Database (Allen, 2002; Version 5.28) refcodes ATYREE02 and ATYREE03] concern the *N*-acetyl-D-tyrosine ethyl ester structural model]; (*d*) glycyl-L-tyrosyl-L-alanine dihydrate (Eggleston & Baures, 1992); (*e*) L-leucyl-L-tyrosyl-L-leucine monohydrate (Wu *et al.*, 1987); (*f*) D-valyl-L-tyrosyl-L-valine dihydrate (Mishnev *et al.*, 1978); (*g*) L-tyrosine; (*h*) L-tyrosine hydrochloride (Frey *et al.*, 1973).

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