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# L-1-Methylproline Monohydrate

RUBÉN A. TOSCANO,[a] RAÚL G. ENRÍQUEZ,[a] WILLIAM F. REYNOLDS,[b] GIL A. MAGOS[c] AND DINO GNECCO[d]

[a]*Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Apartado Postal 70-213, México, DF, México,* [b]*Department of Chemistry, University of Toronto, Ontario, Canada M5S 1A1,* [c]*Departamento de Farmacología, Facultad de Medicina, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, México, DF, 04510 México, and* [d]*Centro de Química, ICUAP, Universidad Autónoma de Puebla, Apartado Postal J-29, Sn. Manuel, Puebla, 072570 México. E-mail: habib@servidor.unam.mx*

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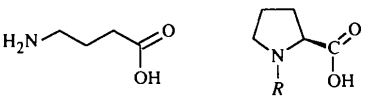
## Abstract

The title compound, $C_6H_{11}NO_2.H_2O$, crystallizes in the zwitterionic form with methyl and carboxyl substituents *anti* with respect to each other. The pyrrolidine ring displays an unusual half-chair conformation $C_2$–$C^\delta$-*endo* (N-*exo*). In the crystal, symmetry-related molecules form zigzag chains extending along the *a* axis. Water molecules connect pairs of these chains by forming two hydrogen bonds.

## Comment

*Casimiroa edulis* is a plant, whose aqueous infusion exhibits potent hypotensive properties, which has been the subject of numerous studies aimed at correlating the sustained hypotension with chemical structures (Lozoya & Enríquez, 1982). Among the secondary metabolites which have been reported in relation to such pharmacological attributes are Nα–Nα-dimethylhistamine, methylhistamine and histamine (Romero, Escobar, Lozoya & Enríquez, 1983). Nevertheless, the search for other constituents continues since a satisfactory understanding of the observed pharmacological properties is still lacking.

During the course of an investigation of the polar constituents of a seed extract, three free amino acids were found in a fraction with very similar chromatographic behaviour. Thus, γ-aminobutyric acid (GABA), (I), L-proline, (II), and L-1-methylproline (hygric acid), (III), were found as the main constituents of a homogeneous fraction exhibiting moderate hypotensive properties on animals. Proline analogues have also been found in other plants (Jones, Naidu, Paleg, Tiekink & Snow, 1987; Solomon, Beer, Waisel, Jones & Paleg, 1994; Jones *et al.*, 1995) and their presence correlated with the environmental stress of the plants.



(I) (II) $R = H$ (III) $R = CH_3$

It can be seen from Fig. 1 that the L-1-methylproline molecule is present in the zwitterionic form with methyl and carboxyl substituents *anti* with respect to each other [C6—N1—C2—C7 torsion angle: −76.3 (4)°]. The pyrrolidine ring adopts a half-chair conformation [Cremer & Pople (1975) parameters: $\varphi$ = 166 (1)° and $Q_T$ = 0.373 (6) Å], with a pseudo-$C_2$ axis passing through the C3 atom, and the atoms N1 and C5 displaced by 0.234 (3) and 0.219 (3) Å, respectively, in opposite directions from the mean plane of the five-membered ring. This half-chair conformation differs from the envelope conformation of the pyrrolidine ring observed in L-proline (Kayushina & Vainshtein, 1965), L-hydroxyproline (Donohue & Trueblood, 1952) and 3,4-dihydroxy-L-proline (Karle, 1970). Although half-chair conformations have been found in other methyl proline derivatives (Flippen-Anderson *et al.*, 1983) and the conformation of the pyrrolidine ring in prolyl residues has been found quite flexible (Karle, 1972), the $C_2$–$C^\delta$-*endo* (N-*exo*) conformation (after Ashida & Kakudo, 1974) observed in this work for the hygric acid is unusual. The dihedral angle $\chi_1$ (N1—C2—C3—C4) of −14.7 (5)° indicates that this amino acid belongs to conformation *B* (Balasubramanian *et al.*, 1971).

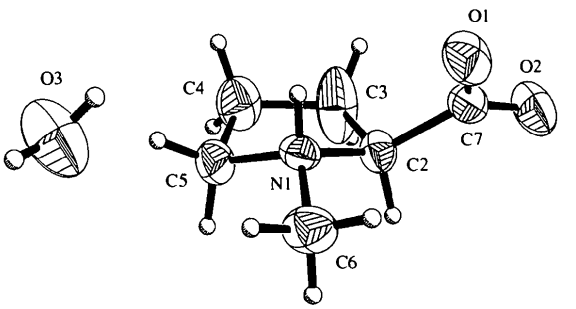



Fig. 1. The title compound showing the labelling of the non-H atoms. Displacement ellipsoids are shown at 50% probability levels.

Both C—O distances in the carboxyl group have the same value within experimental error as expected for the $-COO^-$ ion. This group makes a dihedral angle of 52.9 (2)° with the best mean plane of the pyrrolidine ring. The C3 atom has a larger vibrational amplitude than the rest of the atoms in the direction roughly perpendicular to the best plane of the pyrrolidine ring, probably due to some disorder.

The packing scheme may be described as follows: a series of molecules related by $2_1$ screw-axis symmetry form a zigzag chain extending along the *a* axis, connected by a hydrogen bond [H1···O1$^{i}$ 1.96 (5), N1···O1$^{i}$ 2.761 (4) Å and N1—H1···O1$^{i}$ 151 (4)°; symmetry code: (i) $\frac{1}{2}+x$, $\frac{1}{2}-y$, $-z$]. Water molecules connect pairs of these chains by forming two hydrogen bonds [H3*C*···O2$^{ii}$ 1.97 (6), O3···O2$^{ii}$ 2.819 (5) Å and O3—H3*C*···O2$^{ii}$ 173 (6)°; H3*D*···O2$^{i}$ 2.24 (7), O3···O2$^{i}$ 2.987 (4) Å and H3*D*—O3···O2$^{i}$ 172 (7)°; symmetry code: (ii) $\frac{1}{2}-x$, $-y$, $-\frac{1}{2}+z$] (Fig. 2).

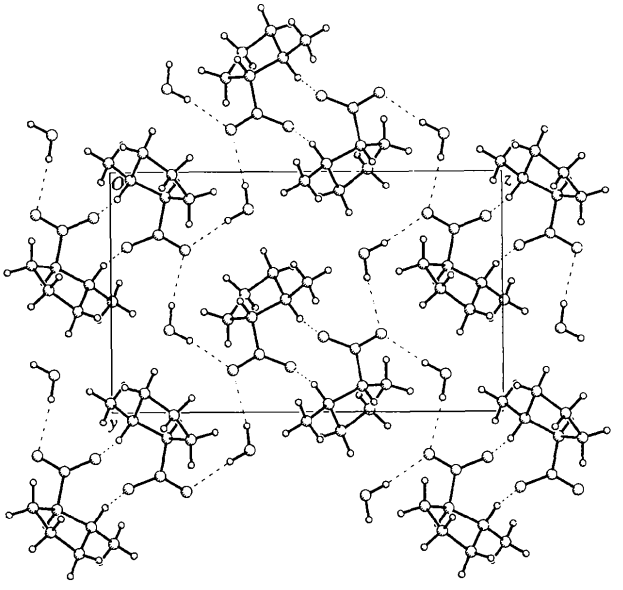


Fig. 2. Crystal packing of L-1-methylproline viewed along the *a* axis.

## Experimental

Finely ground seeds of *Casimiroa edulis* were extracted with hexane and methylene chloride to fractionate its constituents according to increasing polarity. The extraction, carried out with $CH_2Cl_2$/MeOH (70/30), afforded a viscous residue that was submitted to column $SiO_2$ chromatography using a mixture of chloroform, propanol and aqueous ammonia (10%) in a 50:40:10 ratio, respectively. The title compound co-elutes with (I) and (II), with an $R_f$ of ~0.5 as a single spot as seen in $SiO_2$–TLC developed with iodine. This fraction was re-chromatographed and from the mixture, L-1-methylproline crystallized out; uncorrected m.p. 397–398 K, $[\alpha]_D = -72.1°$ ($c$ = 1.4 mg ml$^{-1}$, $l$ = 1 dm in methanol).

*Crystal data*

$C_6H_{11}NO_2.H_2O$
$M_r$ = 147.17
Orthorhombic
$P2_12_12_1$
$a$ = 5.995 (1) Å
$b$ = 8.726 (1) Å
$c$ = 14.535 (2) Å
$V$ = 760.4 (2) Å$^3$
$Z$ = 4
$D_x$ = 1.286 Mg m$^{-3}$
$D_m$ not measured
Mo $K\alpha$ radiation
$\lambda$ = 0.71073 Å
Cell parameters from 38 reflections
$\theta$ = 5.0–12.5°
$\mu$ = 0.102 mm$^{-1}$
$T$ = 293 (2) K
Block
0.36 × 0.24 × 0.22 mm
Colourless

*Data collection*

Siemens *P4/PC* diffractometer
$\omega$ scans
Absorption correction: none
809 measured reflections
809 independent reflections
631 reflections with $I > 2\sigma(I)$
$\theta_{max}$ = 25°
$h = 0 \rightarrow 7$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 18$
3 standard reflections every 97 reflections
intensity decay: 3%

*Refinement*

Refinement on $F^2$
$R(F)$ = 0.048
$wR(F^2)$ = 0.108
$S$ = 1.10
807 reflections
101 parameters
H atoms not refined
$w = 1/[\sigma^2(F_o^2) + (0.0524P)^2 + 0.1226P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.003$
$\Delta\rho_{max}$ = 0.20 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.18 e Å$^{-3}$
Extinction correction: *SHELXL93* (Sheldrick, 1993)
Extinction coefficient: 0.13 (2)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute configuration: assigned to agree with the known chirality at C2 arising from its precursor L-1-methylproline

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å$^2$)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

| | $x$ | $y$ | $z$ | $U_{eq}$ |
|---|---|---|---|---|
| O1 | 0.1203 (6) | 0.3118 (3) | 0.0423 (2) | 0.0512 (9) |
| O2 | 0.0168 (6) | 0.3237 (3) | 0.1897 (2) | 0.0568 (9) |
| O3 | 0.5662 (9) | −0.1571 (4) | −0.1477 (2) | 0.0744 (14) |
| N1 | 0.2957 (5) | 0.0312 (3) | 0.0540 (2) | 0.0326 (7) |
| C2 | 0.2156 (7) | 0.1055 (4) | 0.1409 (2) | 0.0349 (9) |
| C3 | 0.4238 (9) | 0.1144 (7) | 0.2014 (3) | 0.075 (2) |
| C4 | 0.5935 (9) | 0.0095 (6) | 0.1581 (3) | 0.0563 (12) |
| C5 | 0.4738 (7) | −0.0785 (4) | 0.0845 (3) | 0.0429 (10) |
| C6 | 0.1173 (8) | −0.0378 (5) | −0.0026 (3) | 0.0483 (11) |
| C7 | 0.1067 (7) | 0.2608 (4) | 0.1219 (3) | 0.0365 (9) |

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

| | | | |
|---|---|---|---|
| O1—C7 | 1.241 (5) | N1—C5 | 1.501 (5) |
| O2—C7 | 1.251 (5) | N1—H1 | 0.88 (4) |
| O3—H3*C* | 0.85 (6) | C2—C3 | 1.529 (6) |
| O3—H3*D* | 0.76 (6) | C2—C7 | 1.529 (5) |
| N1—C6 | 1.478 (5) | C3—C4 | 1.506 (6) |
| N1—C2 | 1.499 (4) | C4—C5 | 1.500 (6) |

| | | | |
|---|---|---|---|
| C6—N1—C2 | 114.4 (3) | C4—C3—C2 | 106.3 (3) |
| C6—N1—C5 | 114.8 (3) | C5—C4—C3 | 106.6 (4) |
| C2—N1—C5 | 104.8 (3) | C4—C5—N1 | 103.0 (3) |
| N1—C2—C3 | 104.2 (3) | O1—C7—O2 | 127.2 (4) |
| N1—C2—C7 | 111.6 (3) | O1—C7—C2 | 117.3 (4) |
| C3—C2—C7 | 114.1 (3) | O2—C7—C2 | 115.5 (3) |

H atoms attached to N and O were located on a difference electron-density map and their coordinates refined with $U_{iso}$ = $1.3U_{eq}$ of parent atom.

Data collection: *XSCANS* (Siemens, 1993). Cell refinement: *XSCANS*. Data reduction: *XSCANS*. Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *SHELXTL/PC* (Sheldrick, 1990). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BK1308). Services for accessing these data are described at the back of the journal.

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# *n*-Butyl α-Cyano-4-[2-(4-pyridyl)ethenyl]-cinnamate†

TAKASHI OHHARA,[a] HIDEHIRO UEKUSA,[a] YUJI OHASHI,[a] SHIGEHITO KONDO[b] AND MASAKI HASEGAWA[b]

[a]*Department of Chemistry, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152, Japan, and* [b]*Department of Materials Science and Technology, Toin University of Yokohama, Kurogane-cho, Aoba-ku, Yokohama 225, Japan. E-mail: yohashi@chem.titech.ac.jp*

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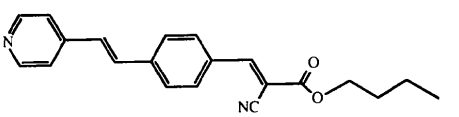
## Abstract

The crystal structure of the title compound, $C_{21}H_{20}N_2O_2$, is compared with related compounds. There are two crystallographically independent molecules, which form two respective stacking columns along the *a* axis. Neither stacking modes are favorable for a [2+2] photopolymerization reaction.

## Comment

The crystal structures of a number of alkyl esters of α-cyano-4-[2-(4-pyridyl)ethenyl]cinnamates have been analyzed in order to correlate their structures with their photoreactivity. For the methyl ester, photodimerization occurred between pyridyl-side olefinic groups of neighboring molecules. Oligomerization was observed on further photo-irradiation. For the ethyl and *n*-propyl homologs, however, dimerization occurred between the ester-side olefinic groups. Although the reaction terminated at the dimer formation for the *n*-propyl ester, the dimer of the ethyl ester gave a polymer on further irradiation (Maekawa, Kato, Saigo, Hasegawa & Ohashi, 1991; Hasegawa & Hashimoto, 1992; Hasegawa, 1995). This paper reports the structure of the *n*-butyl ester, (I). Recently, preliminary experiments on polymer formation have been performed and a variety of oligomeric compounds obtained. Although the products were investigated thoroughly, no high polymeric compounds were obtained.




(I)

There are two crystallographically independent molecules, *A* and *B*, both of which form infinite columns, *A* and *B*, along the *a* axis. The molecular structures

† Alternative name: *n*-butyl 2-cyano-3-{4-[2-(4-pyridyl)ethenyl]phenyl}propenoate.