

D,L- α -Methylglutamic Acid Hemihydrate

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Abstract. $C_6H_{11}NO_4 \cdot \frac{1}{2}H_2O$, $M_r = 170.2$, monoclinic, $C2/c$, $a = 21.466$ (5), $b = 8.233$ (2), $c = 10.573$ (3) Å, $\beta = 119.81$ (1)°, $U = 1621$ Å³, D_m (floatation) = 1.39 (1), $D_x = 1.39$ Mg m⁻³, $Z = 8$, melting point 429 (2) K. Final $R = 0.046$ for 1870 unique reflexions. The compound exists as a zwitterion in the crystal. The side chain adopts a *trans* conformation in contrast to the *gauche* conformation of the parent L-glutamic acid. The water molecule is located in a special position on a twofold axis and forms four hydrogen bonds within the structure.

Introduction. The structure determination of the title compound was undertaken to investigate a possible conformational explanation for its activity at glutamate receptors in the vertebrate central nervous system (Haldeman, Huffman, Marshall & McLennan, 1972; Curtis, Duggan, Felix, Johnston, Tebécis & Watkins, 1972).

Transparent, tapered-acicular crystals were grown from water and a crystal ca $0.4 \times 0.45 \times 0.45$ mm was selected for intensity measurements. Data were collected on a Philips PW 1100 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0.71069$ Å). All unique reflexions were measured in the range $6.0 \leq 2\theta \leq 60.0^\circ$ with an ω - 2θ scan, a constant scan speed of 0.05° s⁻¹ and an ω scan range of $(1.0 + 0.05 \tan \theta)^\circ$. Cell dimensions were calculated from the diffractometer settings of 22 high-angle reflexions. Lp corrections but no absorption correction [$\mu(\text{Mo } K\alpha) = 0.072$ mm⁻¹] were applied and 1870 unique reflexions with $I \geq 3\sigma(I)$ were used in the refinement.

The systematic absences hkl , $h + k = 2n + 1$ and $h0l$, $l = 2n + 1$ indicated possible space groups $C2/c$ and Cc ; the centrosymmetric space group was suggested by the E statistics ($\langle |E^2 - 1| \rangle = 0.95$) and confirmed by the structure solution and satisfactory refinement.

The structure was solved by direct methods (SHELX 76). An E map calculated from 253 reflexions with $E \geq 1.5$ showed all the non-hydrogen atoms;

the O atom of the water molecule [O(5)] is located on a twofold axis. Isotropic full-matrix least-squares refinement ($R = 0.27$) followed by a difference synthesis revealed five H atoms: the remaining H atoms were located after further anisotropic refinement. H atoms bonded to C were included in calculated positions (C–H 1.08 Å, H–C–H 109.5°) and refined with a riding model in which C–H vectors were constant in magnitude and direction but not position. The N–H and O–H lengths were tied (± 0.02 Å) to two free variables which refined to 0.92 and 0.89 Å respectively. A common isotropic temperature factor [0.047 (2) Å²] was refined for all H atoms. The thermal parameters of O(4) are high suggesting that there may be some disorder in this portion of the molecule. Thirteen strong reflexions exhibiting extinction effects were omitted from the final refinement which converged

Table 1. Fractional atomic coordinates ($\times 10^4$)

	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	3747 (1)	3815 (2)	541 (1)
C(2)	3600 (1)	4340 (2)	1765 (1)
C(3)	3483 (1)	2851 (2)	2502 (2)
C(4)	4090 (1)	1585 (2)	3035 (2)
C(5)	3960 (1)	255 (2)	3848 (2)
C(6)	2940 (1)	5459 (2)	1131 (2)
N	4236 (1)	5277 (2)	2880 (1)
O(1)	3270 (1)	2986 (1)	-453 (1)
O(2)	4321 (1)	4267 (2)	606 (1)
O(3)	3542 (1)	-909 (2)	3036 (1)
O(4)	4210 (1)	248 (2)	5143 (2)
H(1)*	2473 (1)	4869 (2)	266 (2)
H(2)*	3064 (1)	6531 (2)	709 (2)
H(3)*	2833 (1)	5803 (2)	1990 (2)
H(4)	4317 (10)	6283 (22)	2578 (21)
H(5)	4201 (10)	5463 (25)	3696 (19)
H(6)	4655 (9)	4720 (23)	3231 (23)
H(7)*	3441 (1)	3262 (2)	3427 (2)
H(8)*	2988 (1)	2270 (2)	1725 (2)
H(9)*	4596 (1)	2165 (2)	3754 (2)
H(10)*	4107 (1)	1076 (2)	2111 (2)
H(11)	3439 (11)	-1643 (24)	3513 (22)
O(5)	5000	2142 (2)	7500
H(12)	4775 (10)	1477 (24)	6737 (20)

* Atoms in calculated positions.

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Table 2. Torsion angles ($^{\circ}$) involving non-hydrogen atoms

Sign convention as defined by Klyne & Prelog (1960).

C(1)–C(2)–C(3)–C(4)	52.9 (2)
C(2)–C(3)–C(4)–C(5)	175.2 (1)
C(4)–C(3)–C(2)–C(6)	174.4 (1)
C(4)–C(3)–C(2)–N	–66.5 (2)
C(3)–C(2)–C(1)–O(1)	58.6 (2)
C(3)–C(2)–C(1)–O(2)	–122.5 (2)
C(6)–C(2)–C(1)–O(1)	–63.6 (2)
C(6)–C(2)–C(1)–O(2)	115.3 (2)
N–C(2)–C(1)–O(1)	178.3 (1)
N–C(2)–C(1)–O(2)	–2.8 (2)
C(3)–C(4)–C(5)–O(3)	85.6 (2)
C(3)–C(4)–C(5)–O(4)	–94.0 (2)

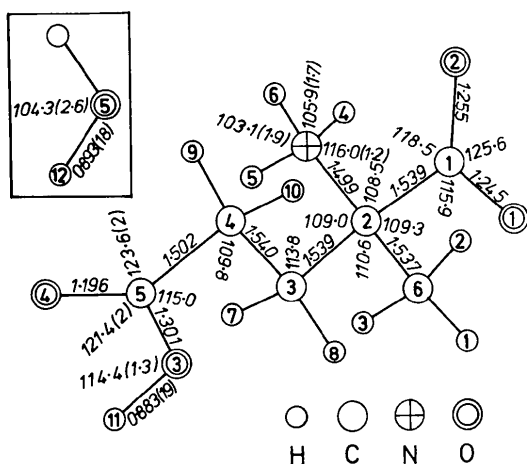


Fig. 1. Atomic numbering scheme, bond lengths (\AA) and angles ($^{\circ}$) for D,L- α -methylglutamic acid. E.s.d.'s are 0.002 \AA for bonds and 0.1 $^{\circ}$ for angles except where indicated otherwise. Bond lengths and angles not included on the figure are given below. Bond lengths (\AA): N–H(4) 0.935 (16), N–H(5) 0.915 (16), N–H(6) 0.907 (16). Bond angles ($^{\circ}$): C(2)–N–H(5) 111.0 (1.2), C(2)–N–H(6) 113.0 (1.3), H(4)–N–H(5) 106.8 (1.8), C(1)–C(2)–C(3) 110.8 (1), C(6)–C(2)–N 108.4 (1).

to $R = 0.046$, $R' = 0.053$ ($R' = \sum w^{1/2} \Delta / \sum w^{1/2} |F_o|$) for 126 parameters: reflexions were weighted as $w = 1/\sigma^2(F_o)$.

Final atomic coordinates are given in Table 1 and the torsion angles involving non-hydrogen atoms in Table 2. The molecular geometry is illustrated in Fig. 1.*

Discussion. In common with L-glutamic acid (Hirokawa, 1955; Lehmann, Koetzle & Hamilton, 1972), D,L- α -methylglutamic acid exists as a zwitterion

in the crystal. The carboxyl group at C(1) is deprotonated [C(1)–O(1) 1.245 (2), C(1)–O(2) 1.255 (2) \AA] whereas that at C(5) is protonated [C(5)–O(3) 1.301 (2), C(5)–O(4) 1.196 (2) \AA]. The H atoms of the protonated amino group adopt a staggered conformation [H(6)–N–C(2)–C(1) –55.2 $^{\circ}$].

The chain C(2), C(3), C(4), C(5) adopts a *trans* conformation in contrast to L-glutamic acid (Lehmann, Koetzle & Hamilton, 1972) and L-glutamic acid in a mixed crystal with L-pyroglutamic acid (Taira & Watson, 1977) in which the chains adopt a *gauche* conformation (Table 3). However, comparison with similar diacidic α -amino acids indicates that the two latter structures are atypical, the *trans* conformation being adopted in all other cases (Table 3).

The geometry of the non-hydrogen atoms is in good agreement with that found for L-glutamic acid (Lehmann, Koetzle & Hamilton, 1972) and also L-glutamic acid in a mixed crystal with L-pyroglutamic acid (Taira & Watson, 1977).

The crystal packing is illustrated in Fig. 2 and the geometry of the intermolecular hydrogen-bonding is given in Table 4. O(3)–H(11) \cdots O(1) bonds link the molecules to form zigzag chains which are linked by N–H(5) \cdots O(2) and N–H(6) \cdots O(2) hydrogen bonds. Interstitial water molecules act as further hydrogen-bond bridges across the zigzag structure. The water molecule is unusual in that it furnishes four H bonds as in ordinary ice (Pauling, 1960); hydrogen-bonded arrays involving a maximum of three hydrogen bonds to water are more commonly found in hydrated crystal structures.

It has been suggested that *trans*-L-glutamic acid is the active conformer at the glutamate receptor (Johnston, Curtis, Davies & McCulloch, 1974). D,L- α -Methylglutamic acid, which exhibits weak antagonistic activity (Haldeman, Huffman, Marshall & McLennan,

Table 3. Torsion angles ($^{\circ}$) corresponding to C(2)–C(3)–C(4)–C(5) of D,L- α -methylglutamic acid

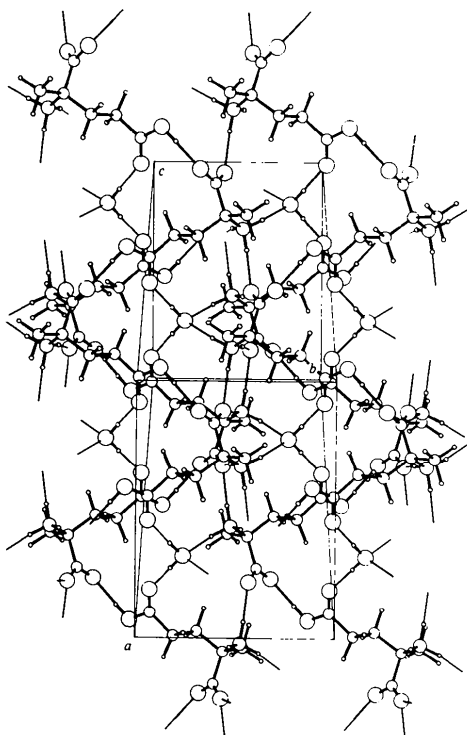
	Reference	
D,L- α -Methylglutamic acid	This work	175.2 (1)
L-Glutamic acid	I	–73.1 (2)
L-Glutamic acid (in a mixed crystal with pyroglutamic acid)	II	–65.2 (8)
Ca L-glutamate. 3H ₂ O	III	174.6
Ca L-glutamate chloride. H ₂ O	IV	170.2 (2)
Cu glutamate. 2H ₂ O	V	182.9 (6)
Zn glutamate. 2H ₂ O	VI	183.4 (6)
L-Glutamic acid. HCl	VII	–173.1 (5)
DL-O-Serine phosphate. H ₂ O	VIII	–168.1
DL-Homocysteine acid	IX	165

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34393 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

I, Lehmann *et al.* (1972). II, Taira & Watson (1977). III, Einspahr & Bugg (1974). IV, Einspahr, Gartland & Bugg (1977). V, Gramaccioli & Marsh (1966). VI, Gramaccioli (1966). VII, Sequeira, Rajagopal & Chidambaram (1972). VIII, Putkey & Sundaralingam (1970). IX, Clarke & Steward (1977).

Table 4. *Geometry of intermolecular hydrogen-bonding*

$A-H \cdots B$	Symmetry of acceptor	$A-H$ (Å)	$H \cdots B$ (Å)	$A \cdots B$ (Å)	$\angle A-H \cdots B$ (°)
O(5)-H(12) \cdots O(4)	x, y, z	0.89 (2)	1.82 (2)	2.705 (2)	173 (2)
O(3)-H(11) \cdots O(1)	$x, -y, \frac{1}{2} + z$	0.88 (2)	1.72 (2)	2.597 (2)	174 (2)
N-H(4) \cdots O(5)	$1 - x, 1 - y, 1 - z$	0.94 (2)	1.99 (2)	2.832 (2)	148 (2)
N-H(5) \cdots O(2)	$x, 1 - y, \frac{1}{2} + z$	0.94 (2)	1.92 (2)	2.821 (2)	160 (2)
N-H(6) \cdots O(2)	$1 - x, y, \frac{1}{2} - z$	0.91 (2)	1.95 (2)	2.814 (2)	158 (2)

Fig. 2. Crystal packing diagram projected along a^* .

1972) or inactivity (Curtis *et al.*, 1972), has been found in this study also to exist in the *trans* conformation. The implications of this will be discussed elsewhere.

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