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N-Methyl-DL-aspartic acid monohydrate

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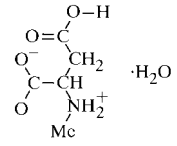
The title compound, $C_5H_9NO_4\cdot H_2O$, has been synthesized and crystallized. It crystallizes in *Cc* with one molecule in the asymmetric unit. The compound is found in its zwitterionic form. D and L forms of the compound are linked in the crystal *via* O—H···O and N—H···O hydrogen bonds, both directly between the aspartic acid-derivative entities and to the crystal water molecule. A weak intramolecular N—H···O interaction is found. The carbon skeleton is slightly twisted with C—C—C—C = 166.83 (11)°. A comparison with other derivatives of aspartic acid shows only two rotamers – one with a near planar carbon skeleton and one with a significantly twisted carbon skeleton.

Comment

Aspartic acid is one of the naturally formed amino acids and several substituted and unsubstituted structures have been published: L-aspartic acid (LASP; Derissen *et al.*, 1968), DL-aspartic acid hydrochloride (Dawson, 1977), DL-aspartic acid with X-rays (DLASP; Rao, 1973) and with neutrons (Sequeira *et al.*, 1989), *N*-methyl-D-aspartic acid monohydrate (NMDASP; Sawka-Dobrowolska *et al.*, 1990) and *N*-carbamyl-DL-aspartic acid (Zvargulis & Hambley, 1994). A charge-density study has recently been carried out on DL-aspartic acid (Flaig *et al.*, 1998). The values from the charge-density study will be used in the following comparison for DL-aspartic acid. Differences in the conformation of aspartic acid have been found between the present study of *N*-methyl-DL-aspartic acid monohydrate, (I), and the previous studies. The labelling scheme shown in Fig. 1 follows the standard used in other similar structures. A relabelling with C2 = C_α and C1 = C′ translates the present labelling scheme into that used in protein structures.

All of the bond distances in the present compound are, within the standard uncertainty, identical to those found in other aspartic acid structures, with C3—C4 [1.5145 (14) Å] (Table 1) significantly shorter than the other C—C bonds (Dawson, 1977; Derissen *et al.*, 1968; Rao, 1973; Sawka-Dobrowolska *et al.*, 1990; Zvargulis & Hambley, 1994; Flaig *et al.*, 1998).



(I)

Rao (1973) defined three four-atom planes to compare different conformations of aspartic acid: C1,C2,C3,C4 (*A*); O1,O2,C1,C2 (*B*); and O3,O4,C3,C4 (*C*). The r.m.s. deviations of the atoms from the least-squares planes are small: *A* = 0.082, *B* = 0.005 and *C* = 0.009 Å.

The dihedral angle between the β-carboxylic acid group (C4,O3,O4) with respect to the carbon skeleton (*A*,*C*) [15.70 (18)°] is between that found in DLASP and LASP, where the dihedral angles found were, respectively, 3.9 and 50.7°. The conformation around C1—C2 (corresponding to the torsion angle denoted ψ in protein crystallography) is significantly different from that found in LASP, DLASP and NMDASP, with ψ^1 = O1—C1—C2—N1 = 159.02 (12)° and ψ^2 = O2—C1—C2—N1 = −22.54 (17)°. In LASP, DLASP and the two conformers in NMDASP, ψ^1 = 172.2, 144.8 and 164.1/165.0°, and ψ^2 = −6.1, −37.8 and −17.7/−17.9°, respectively. Similarly, the orientation of the α-carboxylate group is somewhat distorted compared with the other structures, with *A*,*B* = 82.05 (5)° in (I), 64.2 in DLASP and 95.6° in LASP, respectively. The α-carboxylate group is oriented to facilitate a weak hydrogen bond, N1—H2···O2 (*cf.* Table 2). A similar weak N—H···O interaction is also found in NMDASP. The conformation around the C3—C4 bond is different from that found in LASP, with torsion angles C2—C3—C4—O3 = −11.94 (19)° and C2—C3—C4—O4 = 167.77 (12)° in (I), and corresponding values of 131.4 and −51.3° in LASP. In DLASP and the two conformers in NMDASP, the corresponding

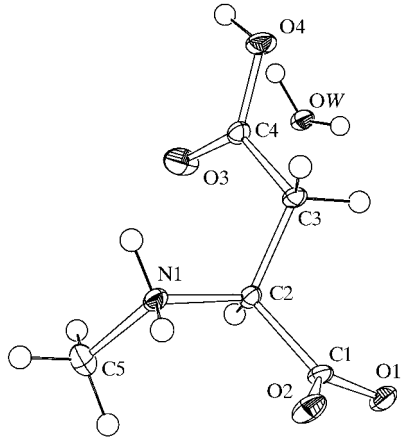


Figure 1
A molecular drawing of (I) showing the labelling scheme. The ellipsoids enclose 50% probability displacement.

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torsion angles are 2.4 and 7.2/19.1°, and −176.9 and −172.5/−162.9°, respectively.

In all the derivatives of aspartic acid found in the literature, the hydrogen-bond pattern varies significantly. Aspartic acid has, furthermore, been crystallized both in the optically active form with only one handedness of the molecule in the crystal structure as well as in the optically inactive form with both hands present in the crystal structure. Most are found in the zwitterionic form, except *N*-carbamyl-DL-aspartic acid. The aspartic acid side chain has, however, only been found in basically two rotamers – one with a near planar carbon skeleton (C1,C2,C3,C4) and one with a carbon skeleton twisted about 60° (*e.g.* as found in *N*-methyl-D-aspartic acid monohydrate). The ideal rotamers are slightly distorted to facilitate the maximum number of hydrogen bonds [about 13° in (I) with C1—C2—C3—C4 = 166.83 (11)°]. The β-carboxylic acid group is, however, rather flexible to form the maximum number of hydrogen bonds, as demonstrated by the high variation in the angle (*A*,*C*) between the previously defined planes.

The findings show that the rotamers used in protein crystallography structure determination are very persistent even in the case of substituted amino acids in the zwitterionic form.

Experimental

The compound was synthesized by dissolving maleic acid in ethanol and subsequent slow addition of an equimolar amount of methylamine. The solution was heated to about 343 K for 3–4 h. Cooling the solution slowly to room temperature gave crystals suited for X-ray diffraction almost immediately. The crystals were very unstable in air. They were therefore produced immediately before the data collection to give the best possible crystal quality.

Crystal data

$C_5H_9NO_4\cdot H_2O$
M_r = 165.15
Monoclinic, *Cc*
a = 9.282 Å
b = 10.803 Å
c = 7.887 Å
β = 111.45°
V = 736.1 Å^3
Z = 4
D_x = 1.490 Mg m^{-3}
Synchrotron radiation
Cell parameters from 6678 reflections
θ = 2.97–28.03°
μ = 0.134 mm^{-1}
T = 122 (2) K
Multi-faceted, colourless
0.2 × 0.15 × 0.15 mm

Data collection

MAR Image Plate diffractometer
φ scans
6678 measured reflections
893 independent reflections
891 reflections with $I > 2\sigma(I)$
R_{int} = 0.029
θ_{max} = 28.03°
$h = -12 \rightarrow 11$
$k = -14 \rightarrow 14$
$l = -9 \rightarrow 9$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.074
S = 1.312
893 reflections
145 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0480P)^2 + 0.1021P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.042
$\Delta\rho_{max}$ = 0.39 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.048 (9)

Table 1
Selected geometric parameters (Å, °).

C1—C2	1.535 (2)	C3—C4	1.5145 (14)
C2—C3	1.5268 (19)		
O1—C1—C2—N1	159.02 (12)	N1—C2—C3—C4	−71.80 (14)
O2—C1—C2—N1	−22.54 (17)	C1—C2—C3—C4	166.83 (11)
O1—C1—C2—C3	−78.94 (15)	C2—C3—C4—O3	−11.94 (19)
O2—C1—C2—C3	99.49 (15)	C2—C3—C4—O4	167.77 (12)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O*W*—H1*W*···O1^{i}	0.87 (4)	1.87 (5)	2.7337 (15)	169 (4)
O*W*—H2*W*···O1^{ii}	0.83 (3)	1.92 (3)	2.7472 (17)	175 (3)
O4—H9···O2^{i}	0.82 (4)	1.77 (4)	2.5761 (18)	171 (3)
N1—H2···O2	0.89 (3)	2.18 (3)	2.6658 (18)	114 (2)
N1—H2···O*W*^{iii}	0.89 (3)	2.18 (3)	2.9596 (18)	146 (2)
N1—H3···O*W*^{iv}	0.84 (3)	2.00 (2)	2.7931 (17)	158 (2)

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

The data were collected at the Swiss–Norwegian beamline at the European Synchrotron Radiation Facility.

Data collection: *MAR* software; cell refinement: *DENZO* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *CCP*4 (Evans, 1994); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV1045). Services for accessing these data are described at the back of the journal.

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