# The experimental library multipolar atom model refinement of L-aspartic acid

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Laboratoire de Cristallographie et Modélisation des Matériaux Minéraux et Biologiques (LCM³B), CNRS, UMR 7036, Université Henri Poincaré Nancy 1, Faculté des Sciences, BP 239, 54506 Vandoeuvre lès Nancy CEDEX, France
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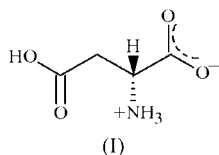The crystal structure of L-aspartic acid, $C_4H_7NO_4$, has been determined using two types of refinement, *viz.* the standard independent atom model (IAM) and the experimental library multipolar atom model (ELMAM). The ELMAM refinement shows a good improvement of the statistical indices compared with the IAM model, notably in terms of thermal displacement parameters and bond distances involving H atoms.

## Comment

Despite the importance of L-aspartic acid ($C_4H_7NO_4$), (I), only a few studies have been performed on the determination of its complexes. The X-ray crystal structure analysis of DL-aspartic acid was originally determined by Rao (1973) and a neutron structure analysis at room temperature has been reported by Sequeira *et al.* (1989). A topological analysis of the experimental charge density has been reported for DL-aspartic acid (Flaig *et al.*, 1998). The crystal structure of DL-aspartic acid nitrate monohydrate has also been characterized (Asath Bahadur & Rajaram, 1995), and more recently bis(DL-aspartic acid) sulfate (Srinivasan *et al.*, 2001) and L-aspartic acid nitrate L-aspartic acid (1/1) (Sridhar *et al.*, 2002) have also been reported. It is worth noting that the atomic coordinates reported for L-aspartic acid monohydrate by Umadevi *et al.* (2003) correspond to the D configuration.



(I)

The purpose of this study is the accurate low-temperature redetermination of the crystal structure of L-aspartic acid and the comparison of the refinements using the same intensity data set using the experimental library multipolar atom model refinement (ELMAM) (Zarychta *et al.*, 2007) and the standard independent atom model (IAM).

L-Aspartic acid, (I) (Fig. 1), was first prepared and its crystal and molecular structures characterized by Derissen *et al.* (1968) from single-crystal diffraction data at room temperature. However, a redetermination was considered worthwhile as, on the one hand, the atomic coordinates reported by Derissen *et al.* (1968) correspond to the D configuration, and on the other hand, fewer than 600 reflections were used to refine all structural parameters. The results reported here are based on data which are, to the best of our knowledge, the most extensive (sin $\theta/\lambda$ = 0.764 Å$^{-1}$), collected at 100 K with a conventional X-ray source (Mo $K\alpha$) and a two-dimensional CCD detector.

Compound (I) crystallizes as a zwitterion, like many other $\alpha$-amino acids. The deprotonated and protonated carboxyl groups can be clearly distinguished. In the deprotonated carboxyl group, the two $CT$—O bonds to the terminal O atoms ($OT1$ and $OT2$) are identical to within one s.u. [1.255 (2) and 1.254 (1) Å, respectively]. The protonated COOH group is, on the other hand, characterized by a double bond [$CG$—$OD1$ = 1.220 (2) Å] which is significantly shorter than the single bond involving the protonated O atom [$CG$—$OD2$ = 1.317 (3) Å] (Table 1). The C-atom skeleton is nearly fully extended, with a $CT$—$CA$—$CB$—$CG$ torsion angle of 179.6 (2)°. The $\alpha$-amino group is in a near perfect staggered conformation around the $CA$—$NT$ bond.

The crystal structure of (I) is made up of chains of aspartic acid molecules, linked by O—H···O hydrogen bonds, approximately parallel to the *c* axis (Fig. 2). The interchain interactions are provided mainly by three $NT$—H···O hydrogen bonds. Atom $OT2$ is involved twice in hydrogen bonding, while $OT1$ and $OD2$ are only involved in the O—H···O bond in the zigzag chain and $OD1$ in another O—H···$NT$ hydrogen bond, a total of four hydrogen bonds per molecule (Table 2). The O—H···O hydrogen bond between the two carboxyl groups is quite short and straight [$OD2$···$OT1$ = 2.567 (1) Å]. Such a short hydrogen bond is also seen in the crystal structures of other amino acids (Bendeif *et al.*, 2005). There is no intramolecular hydrogen bond.

We now compare the two types of refinement models, *viz.* the usual independent atom model (IAM) and the experimental library multipolar atom model (ELMAM) (Zarychta *et al.*, 2007).

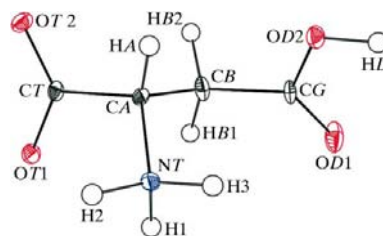In the IAM refinement, a conventional spherical neutral atom model was applied. Scale factor, atomic positions and



**Figure 1**
The L-aspartic acid molecule, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by spheres of arbitrary radii.

thermal displacement parameters for all atoms were refined using the *MOPRO* program (Guillot *et al.*, 2001; Jelsch *et al.*, 2005) until convergence. In the ELMAM refinements, the same parameters were varied, but a multipolar charged atom model was applied. The electron-density parameters were transferred from the library (Pichon-Pesme *et al.*, 1995, 2004) and subsequently kept fixed. The thermal riding restraints on H-atom *B* factors were applied similarly to the IAM refinement. Both refinements were carried out using the same intensity data and cut-off criterion [$I/\sigma(I) > 0$] and with no X—H distance restraint.

The ELMAM refinement shows a good improvement in statistical indexes compared with the IAM refinement: the $R(F)$ factor is reduced from 0.0553 to 0.0428, $wR(F)$ from 0.0255 to 0.0190 and the goodness-of-fit from 1.88 to 1.46. The improvement of X—H distances towards the values obtained from neutron diffraction data on DL-aspartic acid (Sequeira *et al.*, 1989) is clearly visible (Table 1 and Fig. 3). Indeed, the O—H and the tertiary CA—HA bond lengths from the ELMAM refinement agree very well with the neutron diffraction values. For the $CH_2$ group, the largest discrepancies are 0.011 and 0.041 Å with the ELMAM and IAM structure refinements, respectively. The N—H bond lengths in the ammonium ($-NH_3^+$) group obtained from the ELMAM refinement are slightly longer than those from the neutron diffraction experiment on DL-aspartic acid. The differences between the ELMAM and neutron diffraction values can be explained by the fact that the three H atoms are involved in different hydrogen-bond patterns in the L-aspartic and DL-aspartic crystal structures. The effect on other X—Y bonds (involving C, O and N atoms) is small.

We have also performed the rigid-bond test (Hirshfeld, 1976) for both refinements. In the ELMAM refinement, the
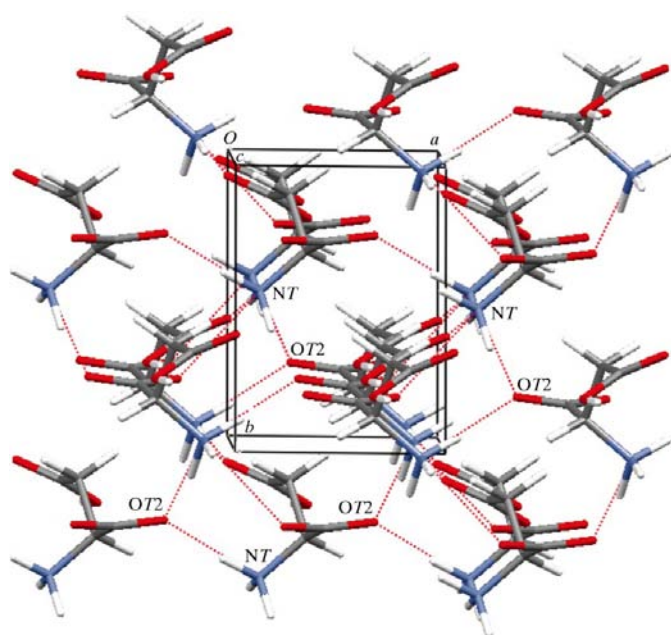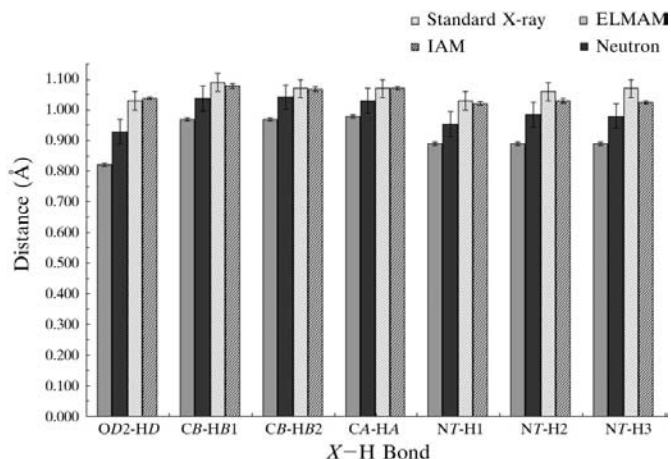


**Figure 3**
Values of X—H distances in the structure of L-aspartic acid. The grey columns refer to the standard values used in X-ray diffraction. Values in the black columns were obtained from the IAM refinement and values in the light-grey dashed columns were obtained from the ELMAM refinement. Values in the dark-grey dashed columns were obtained from neutron diffraction data on DL-aspartic acid at room temperature (Sequeira *et al.*, 1989). Error bars are indicated for all values.

rigid bond test fails only for the CT—OT2, CB—CG and CA—CB bonds, and the average for all bonds is $\Delta = 1.1 \times 10^{-3}$ Å$^2$, whereas in the IAM refinement, all bonds fail except the CB—CG bond, and the average is $\Delta = 2.39 \times 10^{-3}$ Å$^2$. This analysis demonstrates that the atomic displacement parameters are more properly determined with the ELMAM refinement.

## Experimental

Crystals of L-aspartic acid were grown by slow evaporation of an aqueous solution when attempts were made to grow single crystals of a complex of L-aspartic acid with phosphoric acid. Crystals of (I) suitable for single-crystal X-ray diffraction were selected directly from the sample as prepared.

### Compound (I) in the ELMAM refinement

*Crystal data*

| | |
|---|---|
| $C_4H_7NO_4$ | $V = 263.48$ (3) Å$^3$ |
| $M_r = 133.11$ | $Z = 2$ |
| Monoclinic, $P2_1$ | Mo $K\alpha$ radiation |
| $a = 5.1135$ (2) Å | $\mu = 0.15$ mm$^{-1}$ |
| $b = 6.9059$ (3) Å | $T = 100$ (2) K |
| $c = 7.5925$ (3) Å | $0.2 \times 0.15 \times 0.1$ mm |
| $\beta = 100.662$ (4)° | |

*Data collection*

| | |
|---|---|
| Oxford Diffraction Xcalibur Sapphire2 diffractometer | 7129 measured reflections |
| | 995 independent reflections |
| Absorption correction: integration (*ABSORB*; DeTitta, 1985) | 968 reflections with $I > 0$ |
| $T_{min} = 0.971$, $T_{max} = 0.982$ | $R_{int} = 0.045$ |

*Refinement*

| | |
|---|---|
| $R[F > 2\sigma(F)] = 0.043$ | H atoms treated by a mixture of independent and constrained refinement |
| $wR(F) = 0.019$ | |
| $S = 1.47$ | |
| 968 reflections | $\Delta\rho_{max} = 0.30$ e Å$^{-3}$ |
| 110 parameters | $\Delta\rho_{min} = -0.20$ e Å$^{-3}$ |
| 7 restraints | |



**Figure 2**
The crystal packing of L-aspartic acid. Dotted lines represent hydrogen bonds.

**Table 1**
Selected geometric parameters (Å, °) for (I) in the ELMAM refinement.

| | | | |
|---|---|---|---|
| NT—H1 | 1.04 (4) | CT—OT2 | 1.254 (1) |
| NT—H2 | 1.07 (3) | CB—CG | 1.510 (2) |
| NT—H3 | 1.08 (3) | CB—HB1 | 1.09 (3) |
| NT—CA | 1.492 (3) | CB—HB2 | 1.07 (2) |
| CA—CT | 1.535 (2) | CG—OD1 | 1.220 (3) |
| CA—CB | 1.532 (3) | CG—OD2 | 1.317 (3) |
| CA—HA | 1.07 (3) | OD2—HD | 1.03 (2) |
| CT—OT1 | 1.255 (2) | | |
| | | | |
| NT—CA—CT | 109.7 (3) | CA—CB—HB2 | 104. (2) |
| NT—CA—CB | 110.7 (4) | CT—CA—CB | 108.0 (4) |
| NT—CA—HA | 108. (2) | CT—CA—HA | 110. (3) |
| H1—NT—H2 | 109. (5) | CB—CA—HA | 111. (3) |
| H1—NT—H3 | 108. (5) | CB—CG—OD1 | 121.8 (5) |
| H1—NT—CA | 109. (2) | CB—CG—OD2 | 113.9 (4) |
| H2—NT—H3 | 111. (5) | CG—CB—HB1 | 109. (3) |
| H2—NT—CA | 109. (2) | CG—CB—HB2 | 108. (2) |
| H3—NT—CA | 111. (2) | CG—OD2—HD | 110. (3) |
| CA—CT—OT1 | 116.5 (3) | OT1—CT—OT2 | 126.5 (4) |
| CA—CT—OT2 | 116.9 (3) | OD1—CG—OD2 | 124.2 (5) |
| CA—CB—CG | 114.6 (4) | HB1—CB—HB2 | 111. (4) |
| CA—CB—HB1 | 110. (3) | | |
| | | | |
| CT—CA—CB—CG | 179.6 (2) | | |

**Table 3**
Selected geometric parameters (Å, °) for (I) in the IAM refinement.

| | | | |
|---|---|---|---|
| NT—H1 | 0.95 (4) | CT—OT2 | 1.254 (3) |
| NT—H2 | 0.98 (4) | CB—CG | 1.510 (3) |
| NT—H3 | 0.98 (4) | CB—HB1 | 1.04 (3) |
| NT—CA | 1.493 (2) | CB—HB2 | 1.04 (2) |
| CA—CT | 1.530 (2) | CG—OD1 | 1.214 (3) |
| CA—CB | 1.524 (4) | CG—OD2 | 1.315 (4) |
| CA—HA | 1.03 (4) | OD2—HD | 0.93 (1) |
| CT—OT1 | 1.257 (2) | | |
| | | | |
| NT—CA—CT | 109.7 (5) | CA—CB—HB2 | 100. (9) |
| NT—CA—CB | 110.7 (5) | CT—CA—CB | 108.5 (5) |
| NT—CA—HA | 107.1 (3) | CT—CA—HA | 108. (8) |
| H1—NT—H2 | 108. (6) | CB—CA—HA | 112. (1) |
| H1—NT—H3 | 109. (2) | CB—CG—OD1 | 122.0 (7) |
| H1—NT—CA | 109. (2) | CB—CG—OD2 | 113.6 (5) |
| H2—NT—H3 | 108. (2) | CG—CB—HB1 | 110. (7) |
| H2—NT—CA | 109. (3) | CG—CB—HB2 | 111. (5) |
| H3—NT—CA | 112. (3) | CG—OD2—HD | 113. (2) |
| CA—CT—OT1 | 116.5 (4) | OT1—CT—OT2 | 126.3 (5) |
| CA—CT—OT2 | 117.2 (5) | OD1—CG—OD2 | 124.4 (7) |
| CA—CB—CG | 114.9 (6) | HB1—CB—HB2 | 111. (8) |
| CA—CB—HB1 | 108. (7) | | |
| | | | |
| CT—CA—CB—CG | 179.6 (3) | | |

**Table 2**
Hydrogen-bond geometry (Å, °) for (I) in the ELMAM refinement.

| $D$—H$\cdots A$ | $D$—H | H$\cdots A$ | $D\cdots A$ | $D$—H$\cdots A$ |
|---|---|---|---|---|
| OD2—HD$\cdots$OT1[i] | 1.03 | 1.55 | 2.567 (1) | 171 |
| NT—H2$\cdots$OT2[ii] | 1.07 | 1.74 | 2.792 (2) | 169 |
| NT—H3$\cdots$OD1[iii] | 1.08 | 1.73 | 2.806 (2) | 175 |
| NT—H1$\cdots$OT2[iv] | 1.04 | 1.81 | 2.838 (3) | 170 |

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

**Table 4**
Hydrogen-bond geometry (Å, °) for (I) in the IAM refinement.

| $D$—H$\cdots A$ | $D$—H | H$\cdots A$ | $D\cdots A$ | $D$—H$\cdots A$ |
|---|---|---|---|---|
| OD2—HD$\cdots$OT1[i] | 0.93 | 1.64 | 2.571 (3) | 179 |
| NT—H2$\cdots$OT2[ii] | 0.98 | 1.82 | 2.792 (3) | 169 |
| NT—H3$\cdots$OD1[iii] | 0.98 | 1.83 | 2.808 (3) | 173 |
| NT—H1$\cdots$OT2[iv] | 0.95 | 1.90 | 2.839 (4) | 170 |

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

## Compound (I) in the IAM refinement

*Crystal data*

| | |
|---|---|
| $C_4H_7NO_4$ | $V = 263.48$ (3) Å$^3$ |
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| $a = 5.1135$ (2) Å | $\mu = 0.15$ mm$^{-1}$ |
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| | |
|---|---|
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| Absorption correction: integration ($ABSORB$; DeTitta, 1985) | 995 independent reflections |
| | 968 reflections with $I > 0$ |
| $T_{min} = 0.971$, $T_{max} = 0.982$ | $R_{int} = 0.045$ |

*Refinement*

| | |
|---|---|
| $R[F > 2\sigma(F)] = 0.055$ | H atoms treated by a mixture of independent and constrained refinement |
| $wR(F) = 0.026$ | |
| $S = 1.88$ | $\Delta\rho_{max} = 0.43$ e Å$^{-3}$ |
| 968 reflections | $\Delta\rho_{min} = -0.26$ e Å$^{-3}$ |
| 110 parameters | |
| 7 restraints | |

The crystal structure of L-aspartic acid (Fig. 1) was solved in the noncentrosymmetric space group $P2_1$ by direct methods using the program *SHELXS97* (Sheldrick, 1997). Least-squares refinement, based on $|F|$, was carried out using the program *MOPRO* (Guillot *et al.*, 2001; Jelsch *et al.*, 2005) using the conventional spherical neutral-atom model. The reflection weights were set equal at $1/\sigma^2(F_o)$. All H atoms were located in difference Fourier maps. Their $U_{iso}$(H) values were restrained to be $1.2U_{eq}$ of the attached atom with a standard deviation of 0.01 Å. Observations with significantly large $\Delta F$ values (>10) were carefully excluded at every stage in order to avoid their undue influence on the course of refinement. In the absence of suitable anomalous scattering, refinement of the Flack (1983) parameter led to inconclusive values, so a definite conclusion on the absolute structure and chirality of the molecule cannot be drawn (Flack & Bernardinelli, 2000). Therefore, Friedel equivalents were merged prior to the final refinements, and the absolute structure was set by reference to the known chirality of the enantiopure acid used in the crystallization experiment.

For both refinements, data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *MOPRO6* (Jelsch *et al.*, 2005). Molecular graphics: *ORTEPIII* (Burnett & Johnson, 1996) for (I) in the ELMAM refinement; *PLATON* (Spek, 2003) for (I) in the IAM refinement. For both refinements; software used to prepare material for publication: *enCIFer* (Allen *et al.*, 2004).

# organic compounds

Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV3087). Services for accessing these data are described at the back of the journal.

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