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Invariom-model refinement of L-valinol

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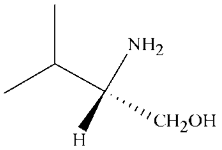
The structure of L-valinol [(*S*)-(+)-2-amino-3-methylbutan-1-ol or hydroxylated L-valine], $C_5H_{13}NO$, has been determined at 100 K by single-crystal X-ray diffraction. The independent atom model geometry, Flack parameter and figures of merit are compared with results from an invariom structure refinement. The latter provides H-atom positions free of independent atom model bias and therefore yields a more accurate hydrogen-bond pattern, and the geometry from invariom refinement shows an improved agreement with results from a quantum chemical geometry optimization.

Comment

L-Valinol, (I), the reduction product of L-valine, is not zwitterionic, as the carboxylate group is replaced by a CH_2OH group and the amino group is neutral. It occurs naturally, for example, in polypeptide peptaibol antibiotics (Chugh *et al.*, 2002).



(I)

The invariom concept (Dittrich *et al.*, 2004) provides a definition of a pseudoatom electron density employing the multipole formalism (Hansen & Coppens, 1978), where the pseudoatom is transferable from one molecule to another. In a conventional multipole refinement, the multipole model electron-density parameters are freely refined against the experimental data and stringent requirements apply for data quality. In invariom refinement, the multipole parameters are predicted by a procedure involving theoretical calculations and can be described as providing aspherical scattering factors. Hence, the number of parameters to be refined in the least-squares procedure does not increase when compared with a standard independent atom model (IAM) refinement. In this paper we compare a refinement of the same intensity data using the invariom model and the IAM.

It has been demonstrated that the accuracy of molecular geometry determination by conventional X-ray single-crystal diffraction experiments of organic molecules can be improved by invariom modelling, with bond lengths involving H atoms benefiting in particular (Dittrich *et al.*, 2005). When invariom-model aspherical scattering factors are employed to replace the spherical scattering factors of the conventional IAM, standard deviations and figures of merit also improve.

For both models, the same intensity data and cut off criteria were used. For invariom refinement of L-valinol, the *R* factor is reduced from 4.2 to 2.9%, the goodness of fit from 2.8 to 1.7 and the maximum residual density from 0.43 to 0.30 e Å^{-3} when compared with the IAM refinement. In the invariom refinement, the Hirshfeld (1976) test fails only for the C3—C5 bond and the average for all bonds is 5.7 × 10 $^{-4}$ Å^2; in the IAM, additionally the C1—C2 bond fails and the average is 7.2 × 10 $^{-4}$ Å^2. Therefore, the physical significance of the atomic displacement parameters improves with invariom scattering factors.

Table 2 compares the geometry from the invariom and IAM refinements, as well as a quantum chemical (QC) geometry optimization for an isolated molecule with *GAUSSIAN98* (Frisch *et al.*, 2002) employing the basis set D95++(3df,3pd). In order to show correctly the improvements of the geometry obtained from invariom refinement, ideally a comparison should be made with the results of a neutron experiment rather than with the geometry of an isolated molecule of different conformation. However, neutron data are not available for the title molecule. Still, a comparison of bond distances is revealing, and differences in conformation due to hydrogen bonding are discussed below. The most significant differences between IAM and invariom refinement occur for the C—O and the *X*—H bonds (*X* = C, N and O). The bond distances to H atoms from invariom refinement agree very well with results from the geometry optimization, whereas the IAM *X*—H bond distances are strongly affected by the well known systematic errors. We can conclude that *X*—H bonds can be observed free of promolecule bias with invarioms.

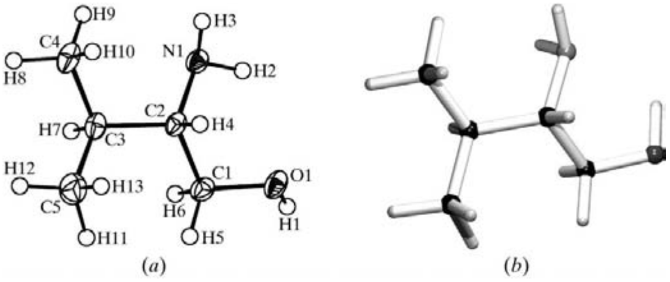


Figure 1
(*a*) An *ORTEPIII* (Burnett & Johnson, 1996) representation of the L-valinol molecular structure at 100 K after invariom refinement. Displacement ellipsoids are shown at the 50% probability level. (*b*) The conformation of the geometry-optimized isolated molecule.

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Fig. 1 compares an *ORTEPIII* (Burnett & Johnson, 1996) plot (Fig. 1*a*) of the molecular structure in the crystal with the conformation from the geometry optimization (Fig. 1*b*).

Table 3 provides the results of an analysis of the hydrogen-bond pattern. Both the amine N and the hydroxyl O atoms act as donors and acceptors simultaneously. An intramolecular N—H···O hydrogen bond, as well as intermolecular N—H···O and O—H···N hydrogen bonds, form one-dimensional zigzag chains, which are further extended into a two-dimensional network structure of sheets perpendicular to the *c* axis, as depicted in Fig. 2. A classification of the hydrogen bonds in terms of graph-set notation (Etter *et al.*, 1990) reveals a first-level graph set $N_1 = C_1^1(5)S_1^1(5)C_1^1(5)$ and a second-level graph set $N_2 = C_2^2(4)$, a product of the two $C(5)$ chain motifs. Graph-set assignments were confirmed using the GSET routine in *RPLUTO* (Motherwell *et al.*, 1999).

The conformation of the CNO skeleton of the molecule as defined by the torsion angles, *e.g.* N1—C2—C3—C4, is similar in the observed X-ray and optimized geometry. The largest discrepancy is found for the C1—C2—C3—C5 torsion angle, which is 62.2 (1)° in the experiment and 55.0° in the calculation. Changes associated with the intra- or intermolecular hydrogen bonds affect the H1—O1—C1—C2, H2—N1—C2—C1 and H3—N1—C2—C1 torsion angles, as listed in Table 1. Values for the other torsion angles involving the hydrogen-bonded H atoms can be found in the supplementary information.

The fact that the aspherical electron density is available from invariom modelling allows calculation of the dipole moment of 1.9 Debye (with individual components $x = -0.3$, $y = 1.9$, $z = 0.1$) for the geometry found in the crystal. The result from a single point energy calculation of 1.1 Debye ($x = -0.4$, $y = 0.6$, $z = -0.8$) using *GAUSSIAN98* (Frisch *et al.*, 2002) and the experimental geometry agrees reasonably well with this value.

The Flack (1983) parameter obtained from the IAM refinement, 0.1 (10), has a high standard deviation of 1. Flack & Bernardinelli (2000) have pointed out that this is the physical range of the parameter. The value of the parameter is improved to 0.0 (6) when invariom scattering factors are used (Dittrich *et al.*, 2006). This means that a definite conclusion on absolute structure and chirality of the molecule cannot be drawn, a result that is not surprising, considering that there is only one O atom in the structure and that Mo *Kα* radiation was used. For the inverted structure, the IAM value was 0.9 (10) and the invariom value 1.0 (6). The chirality of the sample was known from the chemical synthesis.

It is common practice to merge Friedel pairs as recommended by IUCr journals. However, this and our recent study (Dittrich *et al.*, 2006) show that extra information due to anomalous dispersion can be extracted for light-atom structures that contain O and F, even when Mo *Kα* radiation is used. In our opinion, even when the standard deviation of the Flack parameter is higher than the significance limit of 0.12 (Flack & Bernardinelli, 2000), invariom refinement including high-order data often gives a reliable indication of whether or not the absolute structure is correct (Dittrich *et al.*, 2006) (although this hypothesis is not supported by the data reported in this paper). We therefore recommend keeping Friedel pairs unmerged for high-resolution light-atom structures containing oxygen or slightly heavier elements.

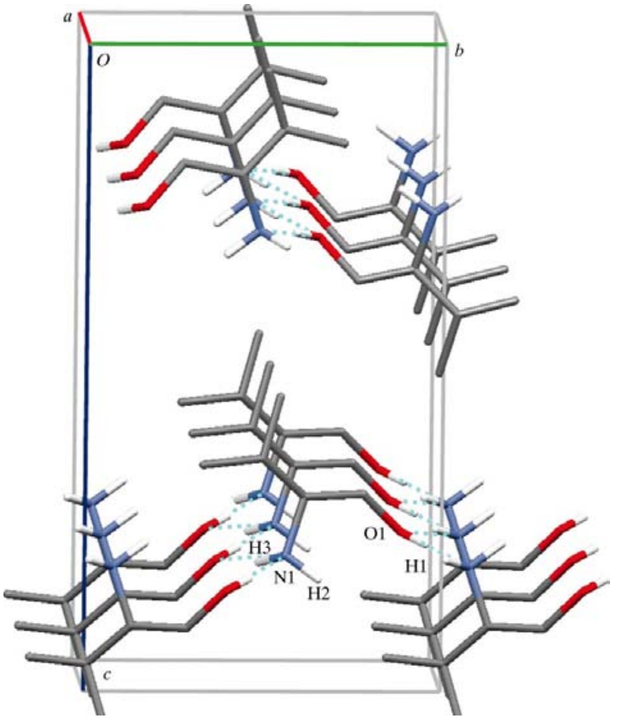

Figure 2
The hydrogen-bond pattern in L-valinol, generated with *MERCURY* (Macrae *et al.*, 2006).

Experimental

A crystal of (I) was grown by slow cooling of the pure liquid. Owing to the low melting point, a spherical crystal formed while mounting the crystal, which was ice-cooled before the experiment.

Crystal data

$C_5H_{13}NO$
$M_r = 103.17$
Orthorhombic, $P2_12_12_1$
$a = 4.8154$ (9) Å
$b = 8.518$ (5) Å
$c = 15.624$ (5) Å
$V = 640.9$ (5) Å^3

$Z = 4$
$D_x = 1.065$ Mg m^{-3}
Mo *Kα* radiation
$\mu = 0.07$ mm^{-1}
$T = 100$ K
Spherical, colourless
0.59 × 0.59 × 0.59 mm

Data collection

Oxford Diffraction Xcalibur-S diffractometer
ω scans
Absorption correction: multi-scan (Blessing, 1995)
$T_{\min} = 0.911$, $T_{\max} = 0.960$

37777 measured reflections
4056 independent reflections
3015 reflections with $F > 2\sigma(F)$
$R_{\rm int} = 0.030$
$\theta_{\max} = 40.1°$

Refinement

Refinement on F
$R[F^2 > 2\sigma(F)] = 0.028$
$wR(F) = 0.018$
$S = 1.71$
3015 reflections
117 parameters
All H-atom parameters refined

$w1 = 1/[\sigma^2(F_o)]$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.30$ e Å^{-3}
$\Delta\rho_{\min} = -0.13$ e Å^{-3}
Absolute structure: Dittrich *et al.* (2006)
Flack parameter: −0.0 (6)

Table 1

Selected torsion angles (°) for invariom refinement and the quantum chemical geometry optimization.

	Invariom	Quantum chemistry
N1—C2—C1—O1	54.9 (1)	51.17
N1—C2—C3—C4	−54.4 (1)	−58.92
N1—C2—C3—C5	−176.9 (1)	−177.30
H1—O1—C1—C2	−148.9 (9)	−37.81
H2—N1—C2—C1	−35.0 (6)	−159.04
H3—N1—C2—C1	−153.1 (6)	80.30

Table 2

Bond distances (Å) for invariom and promolecule models compared with quantum chemical geometry optimization for L-valinol.

Atom *A*	Atom *B*	Invariom	IAM	Quantum chemistry
O1	C1	1.4146 (6)	1.4203 (11)	1.415
O1	H1	0.875 (9)	0.721 (13)	0.969
N1	C2	1.4747 (7)	1.4728 (11)	1.473
N1	H2	0.961 (7)	0.721 (13)	1.011
N1	H3	0.961 (9)	0.850 (11)	1.014
C2	C1	1.5244 (7)	1.5202 (11)	1.535
C2	C3	1.5382 (7)	1.5381 (11)	1.545
C2	H4	1.101 (8)	1.022 (10)	1.096
C1	H5	1.078 (7)	1.000 (9)	1.101
C1	H6	1.072 (9)	0.947 (11)	1.089
C3	C4	1.5309 (8)	1.5279 (14)	1.533
C3	C5	1.5327 (8)	1.5301 (13)	1.535
C3	H7	1.128 (8)	0.984 (11)	1.098
C4	H8	1.056 (8)	0.928 (10)	1.091
C4	H9	1.032 (8)	0.917 (10)	1.091
C4	H10	1.095 (11)	0.978 (14)	1.094
C5	H11	1.035 (9)	0.908 (12)	1.089
C5	H12	1.034 (10)	0.935 (13)	1.094
C5	H13	1.136 (12)	0.984 (16)	1.091

Table 3

Hydrogen-bonding scheme (Å, °) in L-valinol.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···N1^{i}	0.874 (9)	1.899 (9)	2.7607 (6)	168.2 (8)
N1—H2···O1	0.960 (7)	2.265 (7)	2.7800 (3)	112.6 (2)
N1—H3···O1^{ii}	0.963 (9)	2.115 (9)	3.0502 (6)	163.5 (6)

Symmetry code: (i) $-x, y+\frac{1}{2}, -z+\frac{3}{2}$; (ii)$-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$.

The 13 H atoms were found as the 13 highest peaks in the difference Fourier map. An IAM refinement with *SHELXL97* (Sheldrick, 1997) provided starting values for IAM and aspherical atom refinements, both performed with *XDLSM* of the *XD* package (Koritsánszky *et al.*, 2003), which included reflections with $F_o > 2\sigma(F_o)$. *XD* input files were prepared with the program *INVARIOMTOOL* (Hübschle & Dittrich, 2004). Aspherical valence scattering contributions for C, N and O atoms were obtained from theoretical calculations on model compounds that included nearest neighbours, whereas H-atom model compounds involved next-nearest neighbours. The basis set D95++(3df,3pd) was used to optimize the geometry of these model compounds. The deviation from electroneutrality was 0.17 electrons out of 44 valence electrons and electroneutrality was achieved by scaling H-atom monopoles only. Full details of the general modelling procedure will be published elsewhere (Hübschle *et al.*, 2006). The relatively high goodness-of-fit of 1.71 is due to the weighting scheme ($1/\sigma^2$) employed.

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: *XD* (Koritsánszky *et al.*, 2003); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *enCIFer* (Allen *et al.*, 2004) and *publCIF* (Westrip, 2006).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ3028). Services for accessing these data are described at the back of the journal.

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