L-Cysteine-I at 30 K

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Key indicators

The crystal structure of the orthorhombic phase I of L-cysteine, $C_3H_7NO_2S$, has been determined at 30 K. The molecule adopts a *gauche*$^+$ conformation and the structure consists of zwitterions connected into sinusoidal layers by N—H···O hydrogen bonds. Further N—H···O hydrogen bonds connect the structure into a three-dimensional array. Under ambient conditions, the thiol H atom is disordered in such a way as to form intermolecular S—H···S and S—H···O hydrogen bonds. At 30 K the structure is ordered with retention of the S—H···S contacts [S···S = 3.8489 (4) Å, S—H···S = 2.66 (3) Å and S—H···S = 150.8 (16)°].

Comment

The amino acid L-cysteine (Fig. 1) is known to crystallize in two polymorphic forms, *viz.* an orthorhombic phase ($P2_12_12_1$, $Z' = 1$) and a monoclinic phase ($P2_1$, $Z' = 2$). We refer to these as L-cysteine-I and L-cysteine-II, respectively. The crystal structure of L-cysteine-I was determined by Kerr & Ashmore (1973) by X-ray diffraction and then again by Kerr *et al.* (1975) by neutron diffraction. Both of these studies were at ambient temperature. L-Cysteine-II was characterized at ambient temperature by Harding & Long (1968) and later by Görbitz & Dalhus (1996) at 120 K; both of these determinations employed X-ray diffraction. Two new polymorphs (one orthorhombic and the other monoclinic) have recently been characterized by us at elevated pressure (Moggach *et al.*, 2005).

(I)
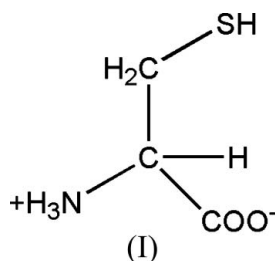
Both L-cysteine-I and L-cysteine-II crystallize with the molecule as its zwitterionic tautomer (Fig. 1). In principle, the N1—C2—C1—S1 torsion angle (χ_1) can adopt values of *ca* 60° (the *gauche+* conformer, g^+), −60° (g^-) and 180° (*trans* or *t*). In L-cysteine-I at 30 K, this parameter is 70.66 (9)°, which compares with a value of 65.3° as determined by X-ray diffraction at room temperature. This is consistent with the finding of Görbitz (1990) that in small molecules there is a strong preference for the g^+ conformation.

Intermolecular interactions in both forms of L-cysteine are dominated by N—H···O hydrogen bonds. In L-cysteine-I, the
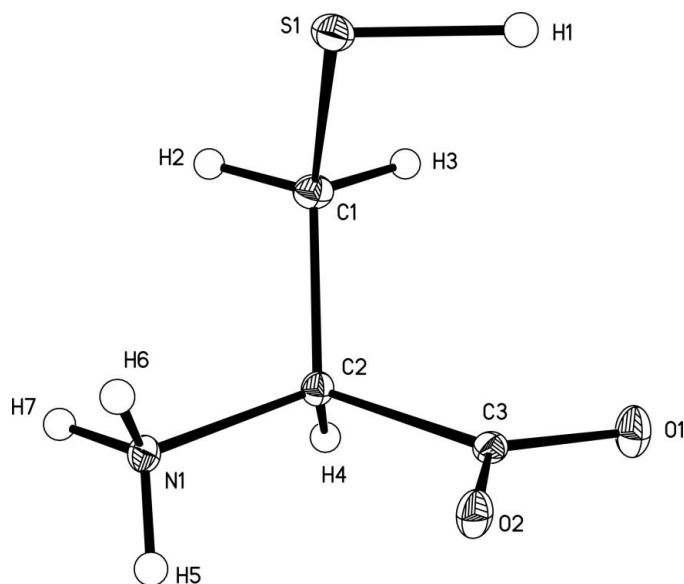
Figure 1
The molecular structure of L-cysteine as observed in the crystal structure of orthorhombic L-cysteine at 30 K and ambient pressure. The displacement ellipsoids are drawn at the 50% probability level, and the H atoms as circles of arbitrary radius.

Figure 2
Hydrogen-bonded layers in L-cysteine-I via N1—H7$\cdots$O2^{iv} and N1—H5$\cdots$O1^{ii} interactions. These build $R_4^4(16)$ rings. This view is along b. See Table 2 for symmetry codes.

Figure 3
The layers shown in Fig. 2 are connected by N1—H6$\cdots$O2^{iii} hydrogen bonds. The hydrogen bonds illustrated in Fig. 2 are shown in orange; the hydrogen bonds that connect the layers are shown in black. This view is along c.

shortest of these, N1—H7$\cdots$O2, lies along c to form a C(5) chain (Bernstein et al., 1995). The second shortest hydrogen bond, N1—H5$\cdots$O1, links molecules into C(5) chains, which run along a. The combination of these two C(5) chains yields a layer composed of $R_4^4(16)$ ring motifs (Fig. 2). The layer is parallel to the ac plane, though it is not planar, having a sinusoidal appearance when viewed in projection down c. The last of the N—H$\cdots$O interactions, N1—H6$\cdots$O2, acts to link the layers together along the b direction. Pairs of N1—H6$\cdots$O2 contacts form $R_3^2(9)$ ring motifs (Fig. 3).

Although the crystal structures of both polymorphs of L-cysteine are dominated by N—H$\cdots$O hydrogen bonding, the thiol group is also capable of forming hydrogen bonds. Hydrogen bonds where Csp^3—SH groups act as donors are very weak, leading to red shifts of only ca 20 cm^{-1} in vibrational spectra (Desiraju & Steiner, 1999). This weakness often results in disorder in the H-atom position, and thus geometric data for 'well behaved' S—H$\cdots$X interactions are rather sparse.

The structure of L-cysteine-II is unusual in thiol chemistry because it contains ordered thiol groups; intermolecular S—H$\cdots$S and S—H$\cdots$O hydrogen bonds are formed by the two molecules that make up the asymmetric unit. The H$\cdots$S and S$\cdots$S distances in L-cysteine-II are 2.78 (4) and 4.080 (1) Å, respectively (Görbitz & Dalhus, 1996). These are similar to other systems, e.g. hydrogen sulfide (2.68–2.74 and 3.985–4.027 Å; Cockcroft & Fitch, 1990) and hexa-kis(mercaptomethyl)benzene (ca 2.8 and 4.0 Å; Mallinson et al., 1997) quoted in a survey by Desiraju & Steiner (1999).

The thiol group is disordered in the crystal structure of L-cysteine-I at room temperature. Different components of the disorder lead to the formation of S—H$\cdots$O and S—H$\cdots$S hydrogen bonds, but the latter is marginally favoured. This result is consistent with t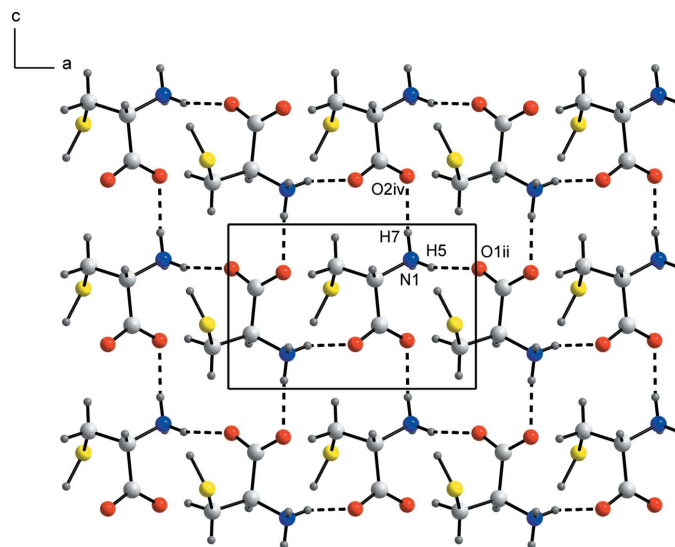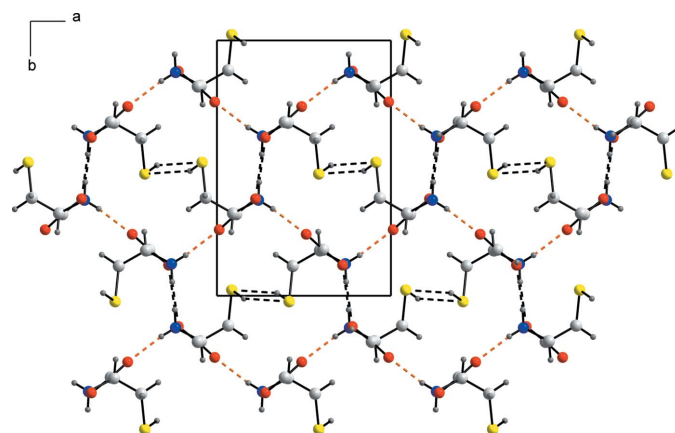he results of DFT calculations, which place the S—H$\cdots$S structure 4.11 kJ mol^{-1} lower in energy. This energy difference is small, and it suggests that the disorder may be frozen out at low enough temperatures.

This proves to be the case, and at 30 K the thiol H atom in L-cysteine-I is ordered (Fig. 4), forming an S—H$\cdots$S hydrogen bond, with parameters given in Table 2. The geometrical parameters of this interaction are S$\cdots$S = 3.8489 (4) Å, H$\cdots$S = 2.66 (3) Å and S—H$\cdots$S = 150.8 (16)°. This bond is shorter than that in L-cysteine-II and the other systems cited above. The S—H$\cdots$S interactions form an infinite hydrogen-bonded chain which zigzags along c. These interactions support the $R_3^2(9)$ ring motifs in connecting the sinusoidal layers formed by $R_4^4(16)$ ring motifs (Fig. 3).

At 0.06 Å^2, the isotropic displacement parameter of the thiol H atom is high relative to those of the other atoms in the

system ($0.008 - 0.017$ Å^2). This suggests that the thiol H atom is still quite mobile at 30 K, and its behaviour at still lower temperatures would be of considerable interest.

Experimental

Crystals of orthorhombic L-cysteine-I were obtained from Sigma (99%, catalogue number G, 1002) and used as received.

Crystal data

$C_3H_7NO_2S$	Mo $K\alpha$ radiation
$M_r = 121.16$	Cell parameters from 4210
Orthorhombic, $P2_12_12_1$	reflections
$a = 8.1435$ (4) Å	$\theta = 3.0$–$31.0°$
$b = 11.9365$ (5) Å	$\mu = 0.50$ mm^{-1}
$c = 5.4158$ (3) Å	$T = 30$ K
$V = 526.44$ (4) Å^3	Block, colourless
$Z = 4$	$0.40 \times 0.20 \times 0.17$ mm
$D_x = 1.529$ Mg m^{-3}	

Data collection

Bruker–Nonius APEX CCD area-detector diffractometer	1516 independent reflections
	1474 reflections with $I > 2\sigma(I)$
ω scans	$R_{int} = 0.021$
Absorption correction: multi-scan	$\theta_{max} = 30.8°$
($SADABS$; Sheldrick, 2004)	$h = -11 \rightarrow 9$
$T_{min} = 0.775$, $T_{max} = 0.920$	$k = -17 \rightarrow 17$
4686 measured reflections	$l = -6 \rightarrow 7$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F^2) + (0.02P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.017$	$+ 0.04P]$
$wR(F^2) = 0.047$	where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$S = 1.03$	$(\Delta/\sigma)_{max} = 0.001$
1514 reflections	$\Delta\rho_{max} = 0.27$ e Å^{-3}
93 parameters	$\Delta\rho_{min} = -0.18$ e Å^{-3}
All H-atom parameters refined	Absolute structure: Flack (1983), 592 Friedel pairs
	Flack parameter: -0.02 (5)

Table 1
Selected geometric parameters (Å, °).

S1—C1	1.8237 (10)	C2—N1	1.4843 (12)
S1—H1	1.31 (3)	C3—O1	1.2444 (12)
C1—C2	1.5223 (13)	C3—O2	1.2623 (11)
C2—C3	1.5359 (13)		
S1—C1—C2	113.91 (6)	C2—C3—O1	116.98 (8)
C1—C2—C3	111.11 (8)	C2—C3—O2	116.87 (8)
C1—C2—N1	110.73 (7)	O1—C3—O2	126.14 (10)
C3—C2—N1	110.96 (8)		

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

D—H$\cdots$$A$	D—H	H$\cdots$$A$	$D$$\cdots$$A$	D—H$\cdots$$A$
S1—H1$\cdots$S1^i	1.30 (3)	2.66 (3)	3.8489 (4)	151 (2)
N1—H5$\cdots$O1^{ii}	0.83 (2)	1.97 (2)	2.7694 (11)	162 (2)
N1—H6$\cdots$O2^{iii}	0.87 (1)	2.12 (1)	2.9451 (11)	159 (2)
N1—H7$\cdots$O2^{iv}	0.89 (2)	1.87 (2)	2.7546 (11)	170 (1)
C1—H2$\cdots$O1^{iv}	0.96 (2)	2.56 (2)	3.2748 (13)	132 (1)
C2—H4$\cdots$S1^v	0.93 (1)	2.85 (1)	3.7770 (9)	175 (1)

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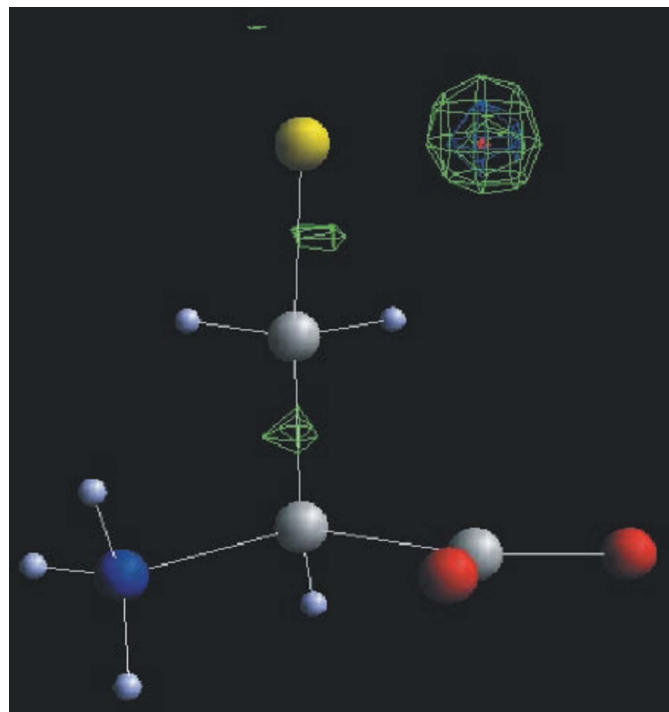

Figure 4
Difference map showing location of the thiol H atom. Contours are drawn at 0.4 (green), 0.6 (blue) and 0.8 eÅ^{-3} (red).

H atoms were located in a difference map. The aim of this structure determination was to determine the position of the H atom attached to S1, and therefore all H atoms were refined independently with isotropic displacement parameters. Two reflections were omitted, one as an outlier, the other because it was obscured by the beam stop.

The *ab initio* calculations were performed with the plane-wave pseudopotential implementation of density functional theory (DFT) using the *CASTEP* code (Segall *et al.*, 2002). Plane-wave basis sets have many benefits compared with conventionally used quantum chemistry basis sets; in particular, there exists a simple parameter, the cutoff energy, to determine the completeness of the basis. This gives us confidence that the wavefunction can describe any properties without bias towards any other particular result (Clark *et al.*, 1998). In our calculations, the many-body exchange and correlation inter-actions are described using the generalized gradient approximation (Perdew & Wang, 1992). Such calculations are capable of giving accurate and reliable structural and electronic information. Ultrasoft pseudopotentials (Vanderbilt, 1990) are used to describe the electron-ion interactions. A cut-off energy of 380 eV is used, which converged the total energy of the system to 1.0 meV atom^{-1}. The Monkhorst–Pack k-point sampling scheme (Monkhorst & Pack, 1976) was used to perform the integrations in k-space over the first Brillouin zone with the grids for each cell chosen to be dense enough to also converge the total energy to 1.0 meV atom^{-1}. For each structure considered, the geometry (atomic positions and unit-cell parameters) was optimized using a conjugate gradient algorithm. The tolerances used give energy differences between structures accurate to better than 1.0 meV.

Data collection: *APEX* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *CAMERON* (Watkin *et al.*, 1996), *DIAMOND* (Crystal Impact,

2004), *MERCURY* (Bruno *et al.*, 2002; Taylor & Macrae, 2001), *MCE Fourier Map Viewer* (Hušák & Kratochvila, 2003) and *SHELXTL* (Sheldrick, 2001); software used to prepare material for publication: *CRYSTALS*, and *PLATON* (Spek, 2003) as incorporated into *WinGX* (Farrugia, 1999).

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