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L-Cysteinium semioxalate: a new monoclinic polymorph or a hydrate?

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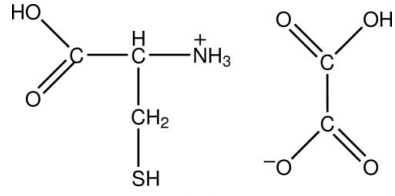
The title compound, $C_3H_8NO_2S^+\cdot C_2HO_4^-$, (I), crystallizes in the monoclinic *C*2 space group and is a new form (possibly a hydrate) of L-cysteinium semioxalate with a stoichiometric cation–anion ratio of 1:1. In contrast to the previously known orthorhombic form of L-cysteinium semioxalate, (I) has a layered structure resembling those of monoclinic L-cysteine, as well as of DL-cysteine and its oxalates. The conformations of the cysteinium cation and the oxalate anion in (I) differ substantially from those in the orthorhombic form. The structure of (I) has voids with a size sufficient to incorporate water molecules. The residual density, however, suggests that if water is in fact present in the voids, it is strongly disordered and its amount does not exceed 0.3 molecules per void. The difference in conformation of the cysteinium cations in (I) and in the orthorhombic form is similar to that in DL-cysteine under ambient conditions and in DL-cysteine under high pressure or at low temperature.

Comment

The sulfhydryl group plays an important role in biology (Jocelyn, 1972). In proteins, sulfhydryl-containing amino acids are involved in the formation of additional hydrogen bonds. In addition, the side chain of such an amino acid can easily be oxidized, giving rise to cystine with a disulfide bond. These interactions contribute to the stabilization of a protein active form. Therefore, investigation of the conformation of sulfhydryl-containing fragments and of their specific interactions is important. Cysteine is the simplest and most widespread sulfhydryl-containing amino acid and may be considered therefore as a model object. Notwithstanding its seeming simplicity, cysteine has already demonstrated a variety of different zwitterion conformations and hydrogen-bonding patterns even in the crystalline state. Under ambient conditions, there are two polymorphic modifications of L-cysteine, namely the monoclinic (Harding & Long, 1968; Görbitz & Dalhus, 1996) and orthorhombic (Kerr & Ashmore, 1973) forms, and one polymorph of DL-cysteine (Luger & Weber, 1999). On cooling, both DL-cysteine (Minkov, Tumanov *et al.*, 2009) and the orthorhombic polymorph of L-cysteine (Kolesov *et al.*, 2008) undergo polymorphic transformations, whereas only a subtle structural change has been reported for monoclinic L-cysteine (Bordallo *et al.*, 2010). With increasing pressure, a series of phase transitions occurs in DL-cysteine, as well as in the two polymorphs of L-cysteine (Moggach *et al.*, 2006; Minkov *et al.*, 2008; Minkov, Tumanov *et al.*, 2010; Minkov, Goryainov *et al.*, 2010). It is worth noting that all the polymorphs of L- and DL-cysteine, including those obtained and existing under non-ambient conditions only, differ substantially in their molecular conformation and intermolecular hydrogen bonds, especially in the hydrogen bonds formed by the side chain of the amino acid.



(I)

Another way to study the conformational lability of cysteine at ambient temperature and pressure is to investigate its salts and cocrystals. Several previously described cysteinium salts show the diversity of zwitterion conformations easily provoked by changing the crystalline environment (Shan & Huang, 1999; Fujii *et al.*, 2005; Drebushchak *et al.*, 2008; Minkov & Boldyreva, 2008; Minkov & Boldyreva, 2009). The present paper provides a new example of a cysteinium salt with interesting features in the crystal structure.

The title compound, (I), consisting of L-cysteinium cations with neutral carboxyl groups and partially deprotonated semioxalate anions may be classified as a salt. As in the case of the orthorhombic form of L-cysteinium semioxalate, (II), the H atom of the carboxyl group in (I) is in a *trans* position with respect to the ammonium group (Fig. 1). Depending on the orientation of the $-CH_2-SH$ side chain, cysteinium cations are prone to adopt *gauche*+ or *gauche*− conformations with positive or negative values of the S—C—C—N torsion angle of *ca* +60 and −60°, respectively. There is only one exception, namely the monoclinic polymorph of L-cysteine (Harding & Long, 1968), in which one of the two molecules in the asym-

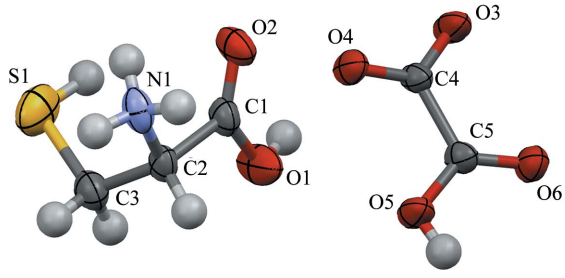


Figure 1
The asymmetric unit of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as spheres of arbitrary radii.

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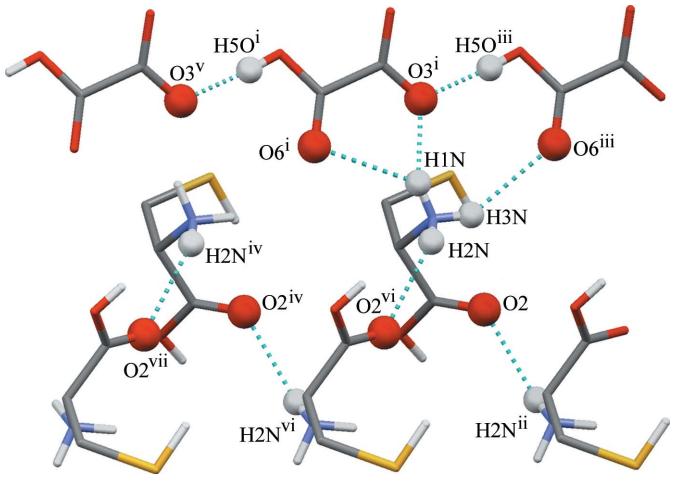

Figure 2
Hydrogen bonding (dashed lines) between semioxalate anions and L-cysteinium cations in (I). [Symmetry codes: (i) $x-\frac{1}{2}, y-\frac{1}{2}, z-1$; (ii) $-x+\frac{1}{2}, y+\frac{1}{2}, -z+1$; (iii) $x-\frac{1}{2}, y+\frac{1}{2}, z-1$; (iv) $x, y-1, z$; (v) $x-\frac{1}{2}, y-\frac{3}{2}, z-1$; (vi) $-x+\frac{1}{2}, y-\frac{1}{2}, -z+1$; (vii) $-x+\frac{1}{2}, y-\frac{3}{2}, -z+1$.]

metric unit has an orientation of the side chain corresponding to a *trans* conformation (with S—C—C—N torsion angles of *ca* 180°) and the other molecule to a *gauche*+ conformation. In (I), the conformation of the cysteinium cation is *gauche*+ (Table 1), similar to that in the orthorhombic polymorph of L-cysteine (Kerr & Ashmore, 1973) and DL-cysteinium semioxalate (Minkov & Boldyreva, 2009). In all the L-cysteinium salts known up to now the orientation of the $-CH_2-SH$ residue corresponds to a *gauche*− conformation (Shan & Huang, 1999; Fujii *et al.*, 2005; Minkov & Boldyreva, 2008). The same holds for the high-pressure polymorphs of L-cysteine (Moggach *et al.*, 2006). Such a large variation in the amino acid side chain orientations in cysteinium salts (the difference in the torsion angles N—C—C—S is about 120°) is comparable with the difference in the values of the N—C—C—S torsion angle in the ambient-temperature (*gauche*− conformation) and the low-temperature or high-pressure (*gauche*+ conformation) polymorphs of racemic DL-cysteine (Minkov, Tumanov *et al.*, 2009). The semioxalate anion is somewhat twisted, the value of an angle between the carboxyl and carboxylate planes being 13.9 (3)°, which is significantly smaller than in (II) [38.6 (3)°] and larger than in DL-cysteinium oxalates [0 and 7.1 (3)°].

In the crystal structure of (I), semioxalate anions are linked to each other *via* O5—H5O···O3^{iv} hydrogen bonds, forming infinite *C*(5) chains extending along the crystallographic *b* axis (Fig. 2; all symmetry codes in this discussion are as in Table 2). The distance between atoms O3^{iv} and O5 in this strongest hydrogen bond is slightly shorter than that in (II) [2.5346 (18) Å; Table 2]. At the same time, a slightly longer O1—H1O···O4 hydrogen bond connecting the carboxyl group of the cysteinium cation with the semioxalate anion is also present in the structure of (I), similar to (II). The carboxyl group of the cysteinium cation forms an $R_2^2(6)$ motif with neighbouring ammonium and carboxylate groups. Each H atom of the amino group in the cysteinium cation participates in the formation of four different hydrogen bonds with neighbouring semioxalate anions, and one with another cation. The N1—H2N···O2^{ii} hydrogen bond links cations into infinite chains along a 2_1 screw axis and the crystallographic *b* axis. The same H atom, H2N, also participates in the formation of an N1—H2N···O4^{ii} hydrogen bond with a semioxalate anion. As in all the previously investigated cysteinium oxalates, in (I) there is a common $R_1^2(5)$ ring motif formed by an N—H···O bifurcated hydrogen bond between the N1—H1N group and atoms O3 and O6 of the semioxalate anion as acceptors. Although in (II) this motif includes the protonated O atom from the semioxalate carboxyl group, this is not the case for (I). Interestingly enough, in spite of the significant difference in the electronegativity between the protonated (O5) and nonprotonated (O4) O atoms of the carboxyl group in the structure of (II), the difference in the two N—O distances [2.912 (2) and 3.041 (2) Å] in this bifurcated bond is smaller than that in (I). In addition to the N1—H1N···O6^{i} hydrogen bond, there is a very long N1—H3N···O6^{iii} hydrogen bond. Moreover, atom H3N participates in the formation of this long hydrogen bond only.

We could not see any strong directional hydrogen bonds formed by the SH groups in the structure of (I). The shortest S···S distance in the structure is 4.201 (1) Å, *i.e.* much longer than required to form an S—H···S hydrogen bond. For a comparison, the S···S distance in a very weak S—H···S hydrogen bond in the structure of the monoclinic polymorph of L-cysteine is 4.080 (1) Å. At the same time, there are some short contacts [S···O3^{viii}, S···O4^{viii} and S···O5^{viii}; symmetry code: (viii) $-x+1, y, -z+1$] of the SH group with a neighbouring semioxalate anion [with S···H distances of 3.649 (3), 3.720 (2) and 3.716 (3) Å, respectively]. This would suggest that the sulfhydryl group interacts simultaneously with several O atoms of the same semioxalate anion. The SH groups could also weakly interact with potential host water molecules in the crystal voids. Anyhow, if the SH group is involved in attractive S—H···O interactions, these interactions should be very weak.

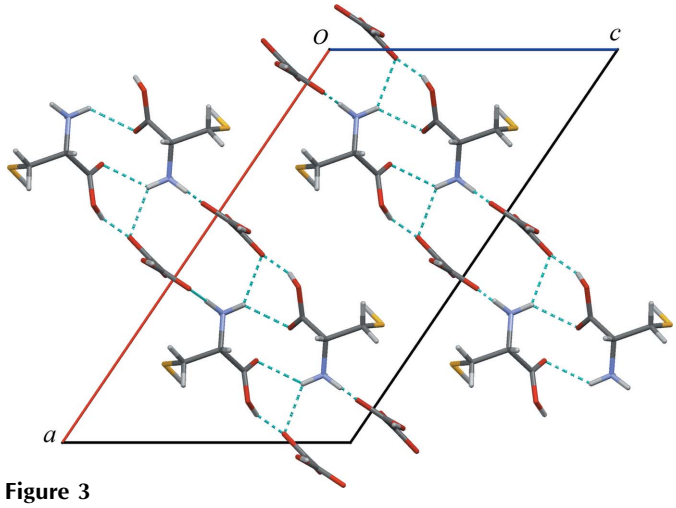

Figure 3
A fragment of the crystal structure of (I) projected on the *ac* plane. Hydrogen bonds are shown as dashed lines.

The crystal packing in (I) and (II) is significantly different. In (II), as well as in the orthorhombic polymorph of L-cysteine, the crystal structure is built as a three-dimensional framework with infinite channels, with the $-CH_2-SH$ side chains inside these channels. Moreover, these channels are preserved on cooling and with increasing pressure, even after the phase transitions (Moggach *et al.*, 2006). In contrast, the crystal structure of (I) is layered, as in the case of the monoclinic polymorph of L-cysteine or of DL-cysteine (Fig. 3). The layers are parallel to the $(20\overline{1})$ crystallographic plane and are formed by infinite chains of cations and anions stretched along the crystallographic *b* axis. The distance between layers in (I) [8.863 (3) Å] is longer than in DL-cysteinium semioxalate [8.197 (3) Å], but is significantly shorter than the interlayer distance in the monoclinic polymorph of L-cysteine [10.719 (3) Å; Görbitz & Dalhus, 1996]. The layers are not bound together by any hydrogen bonds.

Several structures with no hydrogen bonds between the layers have been described earlier for the 'cysteine-family' [DL-cysteine-II (Minkov *et al.*, 2009), monoclinic L-cysteine (Görbitz & Dalhus, 1996), and DL-cysteinium oxalate (Drebushchak *et al.*, 2008) and semioxalate (Minkov & Boldyreva, 2009)]. In most of these structures, the SH groups were involved in hydrogen bonds within the layers. At the same time, in DL-cysteinium semioxalate, the SH groups form no significant hydrogen bonds, although they are involved in many short contacts with O atoms, and this is confirmed also by Raman spectra (Minkov & Boldyreva, 2009), which are very sensitive to the interactions of SH groups with the environment. Unfortunately, we could not study the interactions of the SH group in the crystal structure of (I) by Raman spectroscopy, since the few crystals available were used for the single-crystal diffraction study and a new attempt at crystallization was not successful (see *Experimental*).

The major difference between the crystal packing in the two salts of L-cysteine is that in (I) the infinite chains formed by the semioxalate anions and those formed by the cysteinium cations are both extended along the same crystallographic *b* axis, whereas in (II) these chains extend along orthogonal directions. Interestingly, the crystal packing in (I) is similar to that in DL-cysteinium semioxalate. In the latter, cations form dimers, not infinite chains as in (I), but these dimers are further stacked into stacks and are linked also with each other *via* oxalate anions. These stacks and infinite chains of semioxalate anions are directed along the same crystallographic axis.

Experimental

Colorless prismatic crystals of (I) were obtained by slow diffusion of acetonitrile into a saturated aqueous solution of L-cysteine and oxalic acid in an equimolar ratio. The crystals were not stable on storage. After being taken out of the mother solution and kept in air for a few days they were found to be cracked, which may indicate that the new form is a solvate (a hydrate?) and loses crystal water. Unfortunately, we could not analyze the phase after cracking due to the small amount of sample available. Additional tests using complementary techniques [thermogravimetric, differential scanning calorimetry (DSC) and IR spectroscopy] would be necessary to distinguish between a true new polymorph and a new 'crystal form' which is actually a hydrate. However, we could not grow any more crystals of (I) to either carry out these tests or redo the single-crystal diffraction experiment using protective oil from the beginning.

Crystal data

$C_3H_8NO_2S^+\cdot C_2HO_4^-$
M_r = 211.20
Monoclinic, *C*2
a = 18.604 (4) Å
b = 5.5723 (6) Å
c = 11.270 (2) Å
β = 124.192 (13)°
V = 966.4 (3) Å^3
Z = 4
Mo *Kα* radiation
μ = 0.34 mm^{-1}
T = 293 K
0.41 × 0.34 × 0.14 mm

Data collection

Stoe IPDS 2 diffractometer
Absorption correction: numerical (*X-SHAPE*; Stoe & Cie, 2003)
T_{min} = 0.657, T_{max} = 0.885
4404 measured reflections
2112 independent reflections
1500 reflections with $I > 2\sigma(I)$
R_{int} = 0.045

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.093
S = 0.99
2112 reflections
122 parameters
2 restraints
H atoms treated by a mixture of independent and constrained refinement
Δρ$_{max}$ = 0.45 e Å^{-3}
Δρ$_{min}$ = −0.19 e Å^{-3}
Absolute structure: Flack (1983), 788 Friedel pairs
Flack parameter: −0.08 (11)

Table 1
Selected torsion angles (°).

O2—C1—C2—N1	−12.6 (3)	C1—C2—C3—S1	−58.3 (3)
O1—C1—C2—N1	168.5 (2)	O4—C4—C5—O6	−165.1 (2)
O2—C1—C2—C3	110.7 (3)	O3—C4—C5—O6	14.1 (3)
O1—C1—C2—C3	−68.3 (3)	O4—C4—C5—O5	13.7 (3)
N1—C2—C3—S1	62.4 (2)	O3—C4—C5—O5	−167.1 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1N···O3^{i}	0.89	1.89	2.715 (2)	153
N1—H1N···O6^{i}	0.89	2.56	3.242 (3)	134
N1—H2N···O4^{ii}	0.89	2.29	2.992 (3)	136
N1—H2N···O2^{ii}	0.89	2.35	3.021 (3)	133
N1—H3N···O6^{iii}	0.89	2.47	3.243 (3)	145
O1—H1O···O4	0.82	1.81	2.611 (3)	164
O5—H5O···O3^{iv}	0.82	1.71	2.523 (3)	171

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

Methine, methylene and hydroxy H atoms were placed in geometrically calculated positions and constrained to ride on their parent atoms, with *X*—H distances of 0.98, 0.97 and 0.82 Å, respectively. The H atoms of the ammonium group were also constrained to an ideal geometry, with N—H distances of 0.89 Å, but were allowed to rotate freely about the N—C bond. The position of the sulfhydryl H atom was found from a difference Fourier map and refined with a restraint on the S—H distance of 1.20 (2) Å. In order to check the localization of the sulfhydryl H atom, a dummy SH_3 group was

introduced. The occupancies of several possible H-atom positions were refined and eventually estimated as 0.54 for the relevant H atom and less than 0.15 for the other two H atoms. The positions for the H atoms found from the difference Fourier map and from the introduced dummy SH_3 group are coincident. For all H atoms, U_{iso}(H) values were set at $1.2U_{eq}$(parent atom). In the current structural model, a residual electron-density peak of 0.45 e still remained. A search for solvent-accessible voids in the structure showed the presence of two voids of 34 Å^3 (grid = 0.2 Å and probe radius = 1.2 Å) and an electron count of 3 (cutoff level = 0.5 e Å^{-3}). Both voids are located between layers exactly in (0.000, 0.405, 0.500) and (0.500, −0.095, 0.500). The total positive electron count in the voids per unit cell is 6. Although the volume of a void is somewhat smaller than is typically required to host a water molecule (40 Å^3), one can suppose that the structure can in fact be a hydrate, with highly disordered guest molecules and an average void occupancy not exceeding 0.3 molecules per void. Crystal cracking on storage in air can be a consequence of dehydration. However, the potential water guest molecules, if present, could not be refined in a structural model of a hydrate, probably because of low occupancy and strong disorder.

Data collection: *X-AREA* (Stoe & Cie, 2007); cell refinement: *X-AREA*; data reduction: *X-RED* (Stoe & Cie, 2007); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *Mercury* (Version 1.4.2; Macrae *et al.*, 2008); software used to prepare material for publication: *publCIF* (Westrip, 2010).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: KU3041). Services for accessing these data are described at the back of the journal.

References

Bordallo, H. N., Boldyreva, E. V., Fischer, J., Koza, M. M., Seydel, T., Minkov, V. S., Drebyshchak, V. A. & Kyriakopoulos, A. (2010). *Biophys. Chem.* **148**, 34–41.
Drebushchak, T. N., Bizyaev, S. N. & Boldyreva, E. V. (2008). *Acta Cryst.* C**64**, o313–o315.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Fujii, I., Baba, H. & Takahashi, Y. (2005). *X-ray Struct. Anal. Online*, **21**, x175–x176.
Görbitz, C. H. & Dalhus, B. (1996). *Acta Cryst.* C**52**, 1756–1759.
Harding, M. M. & Long, H. A. (1968). *Acta Cryst.* B**24**, 1096–1102.
Jocelyn, P. C. (1972). *The Biochemistry of the SH Group*, p. 404. London: Academic Press.
Kerr, K. A. & Ashmore, J. P. (1973). *Acta Cryst.* B**29**, 2124–2127.
Kolesov, B. A., Minkov, V. S., Boldyreva, E. V. & Drebushchak, T. N. (2008). *J. Phys. Chem. B*, **112**, 12827–12839.
Luger, P. & Weber, M. (1999). *Acta Cryst.* C**55**, 1882–1885.
Macrae, C. F., Bruno, I. J., Chisholm, J. A., Edgington, P. R., McCabe, P., Pidcock, E., Rodriguez-Monge, L., Taylor, R., van de Streek, J. & Wood, P. A. (2008). *J. Appl. Cryst.* **41**, 466–470.
Minkov, V. S. & Boldyreva, E. V. (2008). *Acta Cryst.* C**64**, o344–o348.
Minkov, V. S. & Boldyreva, E. V. (2009). *Acta Cryst.* C**65**, o245–o247.
Minkov, V. S., Goryainov, S. V., Boldyreva, E. V. & Görbitz, C. H. (2010). *J. Raman Spectrosc.* **41**, 1748–1758.
Minkov, V. S., Krylov, A. S., Boldyreva, E. V., Goryainov, S. V., Bizyaev, S. N. & Vtyurin, A. N. (2008). *J. Phys. Chem. B*, **112**, 8851–8854.
Minkov, V. S., Tumanov, N. A., Boldyreva, E. V. & Cabrera, R. Q. (2010). *CrystEngComm*, **12**, 2551–2560.
Minkov, V. S., Tumanov, N. A., Kolesov, B. A., Boldyreva, E. V. & Bizyaev, S. N. (2009). *J. Phys. Chem. B*, **113**, 5262–5272.
Moggach, S. A., Allan, D. R., Clark, S. J., Gutmann, M. J., Parsons, S., Pulham, C. R. & Sawyer, L. (2006). *Acta Cryst.* B**62**, 296–309.
Shan, Y. & Huang, S. D. (1999). *Z. Kristallogr. New Cryst. Struct.* **214**, 41–42.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Stoe & Cie (2003). *X-SHAPE*. Stoe & Cie, Darmstadt, Germany.
Stoe & Cie (2007). *X-AREA* and *X-RED*. Stoe & Cie, Darmstadt, Germany.
Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.