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L-Methioninium chloride and L-selenomethioninium chloride at 103 K

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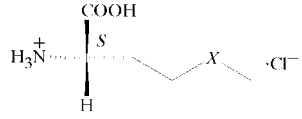
The crystal structures of the title compounds, (*S*)-1-carboxy-3-(methylsulfanyl)propanaminium chloride, $C_5H_{12}NO_2S^+\cdot Cl^-$, and (*S*)-1-carboxy-3-(methylselanyl)propanaminium chloride, $C_5H_{12}NO_2Se^+\cdot Cl^-$, are isomorphous. The protonated L-methionine and L-selenomethionine molecules have almost identical conformations and create very similar contacts with the Cl^- anions in the crystal structures of both compounds. The amino acid cations and the Cl^- anions are linked *via* $N-H\cdots Cl^-$ and $O-H\cdots Cl^-$ hydrogen bonds.

Comment

L-Methionine (Met) is an essential amino acid and in humans and animals it is involved in many very important processes, such as the initiation of translation of messenger RNA, the transfer of methyl groups and sulfur metabolism. A naturally occurring selenium analogue of methionine is L-selenomethionine (SeMet). Although SeMet is toxic, it is also one of the most important nutritional sources of selenium. L-Selenomethionine is extensively used in protein crystallography for solving the phase problem: incorporation of SeMet into proteins allows the use of single- or multi-wavelength anomalous dispersion methods (Hendrickson, 1991; Hendrickson & Ogata, 1997), since, usually, substitution of Met by SeMet does not change the three-dimensional structure of a protein and such labelling is more effective than other methods of protein derivatization.

In this study, the structures of L-methioninium chloride, (I), and L-selenomethioninium chloride, (II), at 103 K are reported (Fig. 1), this being a similar temperature to that used during X-ray data collection on protein crystals. The geometrical data thus obtained for SeMet may be applied to refinement and/or comparison with the geometry of SeMet incorporated into proteins. The crystal structure of L-methioninium chloride has previously been determined at 295 K (di Blasio *et al.*, 1977), but the structure of L-selenomethioninium chloride has not been reported to date. The structure of DL-selenomethionine is known (Rajeswaran & Parthasarathy, 1984) and is the only selenium analogue of Met reported in the Cambridge Structural Database (CSD, November 2003 version; Allen, 2002; Bruno *et al.*, 2002).



(I) X = S
(II) X = Se

The crystal structures of (I) at 103 K (this work) and 295 K (di Blasio *et al.*, 1977), and the structure of (II) at 103 K (this work) are isomorphous. Both (I) and (II) crystallize in space group $P2_12_12_1$, with very similar unit-cell parameters. For the low-temperature structures, the *c* parameter is slightly different, at 24.2330 (7) and 25.0978 (12) Å for (I) and (II), respectively. Equivalent bonds in both structures have very similar lengths; only the C—Se distances (C4—Se and C5—Se) are longer than the C—S distances (Tables 1 and 3).

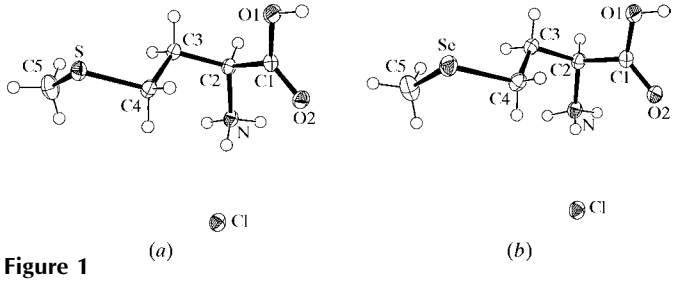


Figure 1
The molecular structures of (*a*) (I) and (*b*) (II), with the atom-numbering schemes. Displacement ellipsoids are drawn at the 50% probability level and H atoms are drawn as small spheres of arbitrary radii.

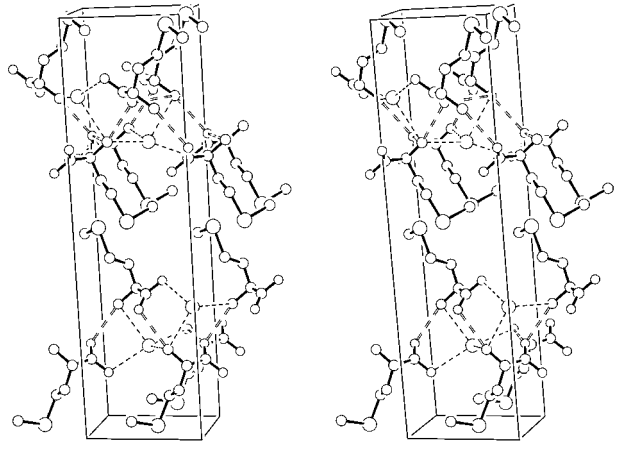


Figure 2
A stereoview of the crystal packing of (II). Cl^- ions and Se atoms are shown as the largest spheres. H atoms have been omitted. Hydrogen bonds are indicated by single dashed lines, and short contacts between atom O2 and the N atoms are indicated by double dashed lines. The *b* axis is horizontal and the *c* axis is vertical.

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Not only is the intramolecular geometry of the methioninium and selenomethioninium cations similar, but the contacts between the cations and Cl^- anions present in both structures are also identical. The Cl^- ions are acceptors in N—H···Cl^- and O—H···Cl^- hydrogen bonds, which are the most important interactions for structure stability. H atoms from four different amino acid residues surround every Cl^- ion. The distances between N atoms and Cl^- ions are around 3.2 Å (Tables 2 and 4), and the distances between Cl^- and O1 are shorter [3.0239 (10) Å in (I) and 3.0309 (16) Å in (II)]. The arrangement of donors around the Cl^- ion may be described as highly distorted from tetrahedral, with the angles in (II), defined by the donors and the Cl^- ion, being N···Cl···$O1^i$ = 89.09 (4), N···Cl···N^{ii} = 96.80 (3), N···Cl···N^{iii} = 108.28 (5), N^{ii}···Cl···N^{iii} = 105.52 (3), N^{ii}···Cl···$O1^i$ = 84.85 (4) and N^{iii}···Cl···$O1^i$ = 158.12 (5)° [symmetry codes: (i) x, $y-1$, z; (ii) $1-x$, $y-\frac{1}{2}$, $\frac{1}{2}-z$; (iii) $x-1$, y, z]. The coordination of the Cl^- anion in (I) is very similar and the N^{iii}···Cl···$O1^i$ angle is also strongly distorted [158.61 (3)°].

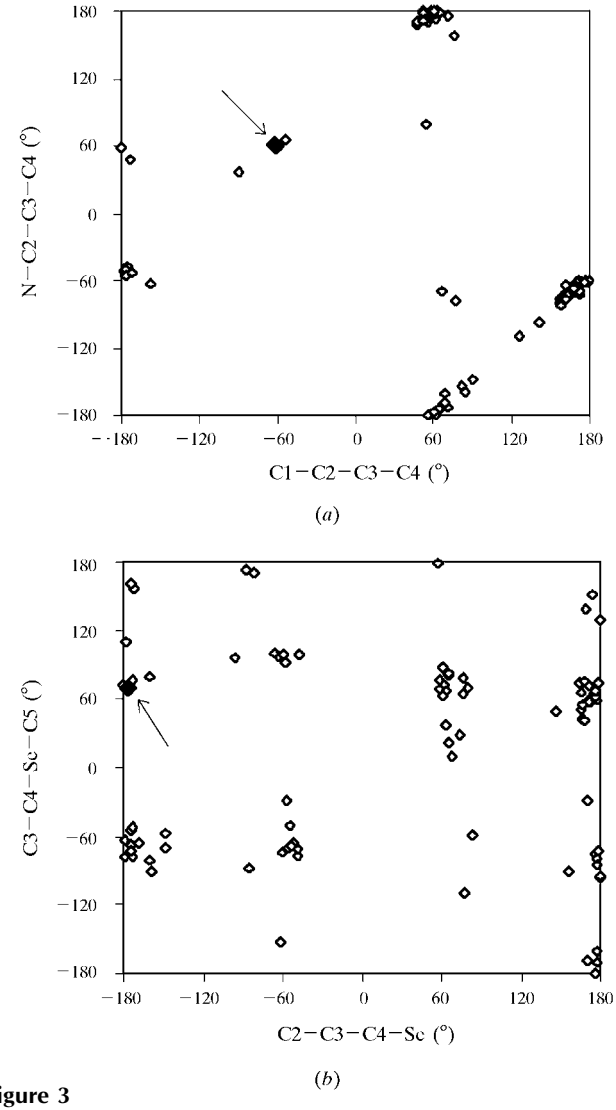

Figure 3
The SeMet torsion angles reported in a subset of the PDB, showing (*a*) C1—C2—C3—C4 *versus* N—C2—C3—C4 and (*b*) C2—C3—C4—Se *versus* C3—C4—Se—C5. Angles derived from protein structures are marked as open diamonds. The solid diamond represents the dihedral angles describing the conformation of selenomethionine in (II).

In the structures of (I) and (II) reported here, both hydrophobic and hydrophilic layers are present (Fig. 2). The hydrophobic layers consist of the methionine or selenomethionine side chains, while the hydrophilic layers contain the Cl^- ions, and the amino and carboxylic acid groups.

Atom O2, in both structures, is involved in short contacts. Firstly, it is an acceptor for a hydrogen bond in which a H atom is donated by atom C2. Secondly, it participates in an interesting short contact with an N atom, with an O2···N($1-x$, $y+\frac{1}{2}$, $\frac{1}{2}-z$) distance of 2.9554 (12) Å in (I) and 2.972 (2) Å in (II). In this type of contact, atom O2 points to the middle of a triangle, the corners of which are defined by amino H atoms, with O2···H distances in the range 2.6–3.0 Å and O2···H—N angles in the range 85–105°. An interaction of this type is not very common: in the CSD (November 2003 version), only ten crystal structures have contacts between an O atom and protonated amino groups with geometries similar to those reported here for (I) and (II).

Rajeswaran & Parthasarathy (1984) noticed that the conformations of methionine and selenomethionine are almost identical and thus there should be no conformational reason for selecting SeMet over Met in proteins. The conformations of protonated SeMet and Met molecules in the reported structures of (I) and (II) are also very similar (Tables 1 and 3). From the point of view of conformational flexibility, SeMet incorporated into a protein should behave similarly to Met. The larger size of Se compared with S is probably the most important factor that may influence the interactions and conformations of amino acids in a labelled protein. In order to compare the conformation of the selenomethionine side chain in (II) with the conformations of SeMet in protein molecules, the Protein Data Bank (PDB, August 2004 version; Berman *et al.*, 2000) was searched. Only SeMet residues having one well defined conformation and derived from structures refined with resolution higher than 1.4 Å were taken into account. Overall, 89 residues were analyzed. The results are presented in Fig. 3. Surprisingly, torsion angles similar to those reported in Table 3 are rarely (three of 89) observed in protein structures. This may be related to the packing observed in the present structure. Also, in proteins, the conformation of a residue is restrained by covalent bonds in the polypeptide chain. For the C1—C2—C3—C4 and N—C2—C3—C4 angles, values close to 60 and 180°, or 180 and −60°, respectively, are mostly observed. In the case of the angles C2—C3—C4—Se and C3—C4—Se—C5, the conformational flexibility is higher, but combinations of values close to −60, 60 and 180° occur most often.

Experimental

L-Selenomethionine hydrochloride, (II), was crystallized at room temperature by slow evaporation of an aqueous solution of L-selenomethionine (25 mg ml^{-1}) and 0.1 *M* HCl in a 1:1 ratio. An

analogous procedure was used to crystallize L-methionine hydrochloride, (I), but the concentration of L-Met was 50 mg ml^{-1}. Both L-Met and L-SeMet were purchased from Sigma. Crystals were needle-shaped and were cut for data collection.

Compound (I)

Crystal data

$C_5H_{12}NO_2S^+\cdot Cl^-$
M_r = 185.67
Orthorhombic, $P2_12_12_1$
a = 5.2740 (1) Å
b = 7.0220 (2) Å
c = 24.2330 (7) Å
V = 897.45 (4) Å^3
Z = 4
D_x = 1.374 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 9199 reflections
θ = 3.0–27.5°
μ = 0.61 mm^{-1}
T = 103 (2) K
Prism, colourless
0.20 × 0.05 × 0.05 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans with χ offsets
Absorption correction: multi-scan (Otwinowski *et al.*, 2003)
T_{min} = 0.932, T_{max} = 0.970
9199 measured reflections
2058 independent reflections
2009 reflections with $I > -3\sigma(I)$
R_{int} = 0.029
θ_{max} = 27.5°
$h = -6 \rightarrow 6$
$k = -8 \rightarrow 9$
$l = -26 \rightarrow 31$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.019
$wR(F^2)$ = 0.050
S = 1.07
2058 reflections
140 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0266P)^2 + 0.0878P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Absolute structure: Flack (1983), with 814 Friedel pairs
Flack parameter = −0.01 (5)

Table 1
Selected geometric parameters (Å, °) for (I).

S—C5	1.8013 (14)	N—C2	1.4922 (14)
S—C4	1.8078 (11)	C1—C2	1.5147 (16)
O1—C1	1.3228 (14)	C2—C3	1.5338 (14)
O2—C1	1.2084 (14)	C3—C4	1.5217 (17)
C5—S—C4	100.79 (6)	N—C2—C3	112.02 (9)
O2—C1—O1	125.03 (11)	C1—C2—C3	114.41 (9)
O2—C1—C2	123.22 (10)	C4—C3—C2	113.56 (9)
O1—C1—C2	111.72 (9)	C3—C4—S	113.68 (8)
N—C2—C1	107.59 (9)		
O2—C1—C2—N	1.99 (15)	N—C2—C3—C4	58.93 (13)
O1—C1—C2—N	−179.94 (9)	C1—C2—C3—C4	−63.86 (12)
O2—C1—C2—C3	127.14 (12)	C2—C3—C4—S	−179.73 (8)
O1—C1—C2—C3	−54.78 (13)	C5—S—C4—C3	70.14 (10)

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

D—H···A	D—H	H···A	D···A	D—H···A
N—H1N···Cl	0.924 (18)	2.383 (19)	3.3054 (10)	176.7 (15)
N—H2N···Cl^{i}	0.890 (16)	2.286 (16)	3.1683 (10)	171.1 (13)
N—H3N···Cl^{ii}	0.932 (14)	2.273 (15)	3.1709 (10)	161.5 (13)
O1—H1···Cl^{iii}	0.81 (2)	2.24 (2)	3.0239 (10)	164 (2)
C2—H1C2···O2^{i}	0.965 (14)	2.410 (14)	3.2627 (14)	147.1 (10)

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

Compound (II)

Crystal data

$C_5H_{12}NO_2Se^+\cdot Cl^-$
M_r = 232.57
Orthorhombic, $P2_12_12_1$
a = 5.2370 (5) Å
b = 7.0660 (3) Å
c = 25.0960 (12) Å
V = 928.67 (11) Å^3
Z = 4
D_x = 1.663 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 18 743 reflections
θ = 3.0–31.5°
μ = 4.28 mm^{-1}
T = 103 (2) K
Prism, colourless
0.40 × 0.10 × 0.10 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω with χ offset scans
Absorption correction: multi-scan (Otwinowski *et al.*, 2003)
T_{min} = 0.592, T_{max} = 0.652
18 743 measured reflections
3082 independent reflections
2934 reflections with $I > -3\sigma(I)$
R_{int} = 0.060
θ_{max} = 31.5°
$h = -7 \rightarrow 7$
$k = -9 \rightarrow 10$
$l = -36 \rightarrow 36$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.026
$wR(F^2)$ = 0.069
S = 1.05
3082 reflections
125 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0322P)^2 + 0.0408P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.89 e Å^{-3}
$\Delta\rho_{min}$ = −0.87 e Å^{-3}
Absolute structure: Flack (1983), with 1248 Friedel pairs
Flack parameter = 0.000 (7)

Table 3
Selected geometric parameters (Å, °) for (II).

Se—C4	1.9467 (18)	N—C2	1.484 (2)
Se—C5	1.950 (2)	C1—C2	1.518 (2)
O1—C1	1.319 (2)	C2—C3	1.530 (2)
O2—C1	1.214 (2)	C3—C4	1.520 (3)
C4—Se—C5	97.24 (9)	N—C2—C3	112.01 (15)
O2—C1—O1	125.20 (17)	C1—C2—C3	114.23 (14)
O2—C1—C2	122.94 (17)	C4—C3—C2	113.45 (14)
O1—C1—C2	111.84 (15)	C3—C4—Se	113.47 (12)
N—C2—C1	107.88 (13)		
O2—C1—C2—N	0.7 (2)	N—C2—C3—C4	61.1 (2)
O1—C1—C2—N	179.19 (16)	C1—C2—C3—C4	−61.9 (2)
O2—C1—C2—C3	125.94 (19)	C2—C3—C4—Se	−175.86 (13)
O1—C1—C2—C3	−55.6 (2)	C5—Se—C4—C3	70.09 (16)

Table 4
Hydrogen-bonding geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
N—H1N···Cl	0.79 (3)	2.53 (3)	3.2974 (17)	166 (3)
N—H2N···Cl^{i}	0.92 (3)	2.26 (3)	3.1638 (16)	166 (2)
N—H3N···Cl^{ii}	0.98 (3)	2.22 (3)	3.1681 (17)	161 (3)
O1—H1···Cl^{iii}	0.82	2.25	3.0309 (16)	160
C2—H1C2···O2^{i}	1.03 (3)	2.32 (3)	3.244 (2)	149 (2)

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

The absolute structures of both compounds were determined unambiguously by successful refinement of the Flack parameter (Flack, 1983) and the subsequent observation that the error in the

Flack parameter was small, specifically 0.05 in the case of (I) and 0.007 in the case of (II). All H atoms in (I) and most of those in (II) were located in difference Fourier maps and refined freely. The methyl and carboxylic acid H atoms of (II) were placed in geometric positions and treated as riding, with C—H = 0.96 Å and O—H = 0.82 Å, and $U_{iso}(H) = 1.5U_{eq}(C,O)$.

For both compounds, data collection: *HKL*2000 (Otwinowski & Minor, 1997); cell refinement: *HKL*2000; data reduction: *HKL*2000; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997) and *HKL*2000; molecular graphics: *ORTEP*III (Burnett & Johnson, 1996), *ORTEP*-3 (Farrugia, 1997) and *HKL*2000; software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1150). Services for accessing these data are described at the back of the journal.

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