

**S-Carboxymethyl-L-cysteine Sulfone**

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**Abstract.** C<sub>5</sub>H<sub>9</sub>SO<sub>6</sub>N, orthorhombic,  $P2_12_12_1$ ;  $a=9.205$  (4),  $b=5.223$  (2),  $c=15.891$  (7) Å;  $Z=4$ ,  $D_x=1.836$ ,  $D_m=1.86$  (2) g cm<sup>-3</sup> (floatation, 21 °C). The structure has been determined by direct methods and refined to an  $R=0.045$  for 944 independent reflections. The title compound exists as a zwitterion. Two carboxyl groups in adjacent molecules [O...O, 2.504 (5) Å] are involved in a strong hydrogen bond. The hydrogen atom was found to be covalently bonded to the carboxyl group in the carboxymethyl moiety.

**Introduction.** The title compound (SCMC-sulfone) was prepared by oxidation of *S*-carboxymethyl-L-cysteine. A colorless crystal (0.03 × 0.06 × 0.35 mm) was selected for film and diffractometer work. Precession photographs showed *mmm* symmetry. Systematic absences ( $h00$ ,  $h=2n+1$ ;  $0k0$ ,  $k=2n+1$ ;  $00l$ ,  $l=2n+1$ ) observed on the films and verified on the diffractometer indicated the space group to be  $P2_12_12_1$ . 944 reflections were measured (649 were measured a second time) on a diffractometer out to  $\theta=75^\circ$  using Cu  $K\alpha$  X-radiation ( $\lambda=1.54188$  Å).† A Si(Li) solid state detector was used to monochromate the diffracted beam (Hubbard, 1973). The  $\theta-2\theta$  scan technique was used with the scan

range of  $(2.2 + \tan \theta)^\circ$  and with a scan speed of 4° min<sup>-1</sup>. Three standard reflections, measured at regular intervals, showed no significant decrease in intensity during the course of data collection. 68 reflections were considered to be 'less than' according to the criterion  $I < 2\sigma(I)$ , where  $\sigma(I)=[\sqrt{S+(t_s/t_b)}/B+0.005S]$ ,  $S$ =scan count (time  $t_s$ ), and  $B$ =background count (time  $t_b$ ). The 'less than' reflections were excluded from refinement. The intensities were corrected for Lorentz and polarization effects but not for absorption ( $\mu=38.3$  cm<sup>-1</sup>). For the final data set, the 649 duplicate intensities were averaged ( $R=0.02$ ).

A trial model was obtained with *MULTAN* (Germain, Main & Woolfson, 1971). After preliminary refinement, a difference map was calculated and all hydrogen atoms in the molecule were located. In the final model positional parameters for the three hydrogen atoms attached to the nitrogen and the hydrogen atom attached to O(4) were allowed to refine. The five hydrogen atoms attached to C(2), C(3) and C(4) were assigned calculated positions based on the tetrahedral-chain approximation with  $d(\text{C-H})=1.0$  Å. A thermal parameter of  $U=0.033$  was assigned to each hydrogen atom and held fixed. An extinction parameter was not included. The scattering factors for S, O, N and C atoms were from Cromer & Mann (1968). The scattering factors for the hydrogen atom were from Stewart Davidson & Simpson (1965). Anomalous dispersion factors  $Af'$  and  $Af''$  for S, O, N, C atoms were from

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† This weighted average wavelength is on the Deslattes & Henins (1973) scale where  $\lambda(\text{Cu } K\alpha_1)=1.5405981$  Å.

Table 1. Positional ( $\times 10^4$ ) and thermal parameters ( $\text{\AA}^2 \times 10^3$ ) of the non-hydrogen atoms with their standard deviations in parentheses

Thermal parameters are in the form  $T = \exp[-2\pi^2(a^*h^2U_{11} + b^*k^2U_{22} + c^*l^2U_{33} + 2a^*b^*hkU_{12} + 2a^*c^*hlU_{13} + 2b^*c^*klU_{23})]$ .

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{11}$	$U_{22}$	$U_{33}$	$U_{12}$	$U_{13}$	$U_{23}$
N	4725 (5)	9139 (9)	10395 (3)	28 (2)	25 (2)	28 (2)	2 (2)	0 (2)	-1 (2)
S	3606 (1)	7309 (2)	8550 (1)	27 (1)	26 (1)	25 (1)	-2 (1)	-2 (1)	-1 (1)
C(1)	6151 (4)	12646 (10)	9745 (2)	22 (2)	27 (2)	30 (2)	1 (3)	-4 (2)	2 (2)
C(2)	5401 (5)	10002 (9)	9595 (3)	28 (2)	25 (3)	24 (2)	2 (2)	-1 (2)	-1 (2)
C(3)	4290 (5)	10316 (10)	8885 (3)	27 (2)	21 (2)	29 (2)	-6 (2)	-6 (2)	-2 (2)
C(4)	2218 (5)	8129 (10)	7808 (3)	31 (2)	35 (3)	28 (2)	4 (2)	1 (2)	3 (2)
C(5)	1502 (5)	5663 (10)	7517 (3)	26 (2)	36 (3)	26 (2)	1 (3)	-7 (2)	2 (2)
O(1)	5736 (4)	13928 (7)	10339 (2)	43 (2)	29 (2)	36 (2)	-1 (2)	2 (2)	-4 (2)
O(2)	7141 (3)	13200 (8)	9220 (2)	33 (2)	43 (2)	30 (1)	-10 (2)	2 (1)	-2 (2)
O(3)	798 (3)	4327 (8)	7996 (2)	41 (2)	41 (2)	34 (2)	-10 (2)	3 (2)	0 (2)
O(4)	1724 (4)	4944 (7)	6733 (2)	49 (2)	41 (2)	30 (2)	-12 (2)	1 (2)	-5 (2)
O(5)	4721 (3)	5962 (8)	8099 (2)	39 (2)	36 (2)	39 (2)	8 (2)	-4 (2)	-7 (2)
O(6)	2954 (3)	6045 (7)	9261 (2)	38 (2)	33 (2)	28 (1)	-5 (2)	-3 (1)	1 (2)

*International Tables for X-ray Crystallography* (1974). (Both the D and L configurations for the cysteine moiety were refined isotropically. As expected, the model with the L configuration refined to a significantly lower *R* value.)

The model was refined by full-matrix least-squares analysis to a conventional *R*, based on *F*, of 0.045 (0.048 including 'less than' reflections) and  $R_w = [\sum w(|F_o| - |F_c|)^2 / \sum w(F_o)^2]^{1/2} = 0.050$ ,\* function minimized:  $\sum w(|F_o| - |F_c|)^2$  with  $w = [\sigma(F_o)]^{-2}$ . The average and the maximum shift/error for the parameters were

\* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31818 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. Positional ( $\times 10^3$ ) parameters of the hydrogen atoms

The standard deviations for the refined hydrogen atoms are given in parentheses.

	<i>x</i>	<i>y</i>	<i>z</i>
H1(N)	488 (5)	762 (11)	1046 (3)
H2(N)	533 (4)	997 (10)	1098 (3)
H3(N)	383 (5)	1000 (10)	1043 (3)
H(O4)	220 (5)	613 (10)	636 (3)
H(C2)	615	871	943
H1(C3)	477	1119	840
H2(C3)	346	1140	909
H1(C4)	148	928	808
H2(C4)	266	905	732

0.05 and 0.40 respectively. A final difference electron density map showed no peak greater than  $0.2 \text{ e } \text{\AA}^{-3}$ , except a peak of  $0.4 \text{ e } \text{\AA}^{-3}$  near the sulfur position. Tables 1 and 2 list the atomic parameters. Computer programs used in the refinement were from X-RAY 72 (Stewart, Kruger, Ammon, Dickinson & Hall, 1972).

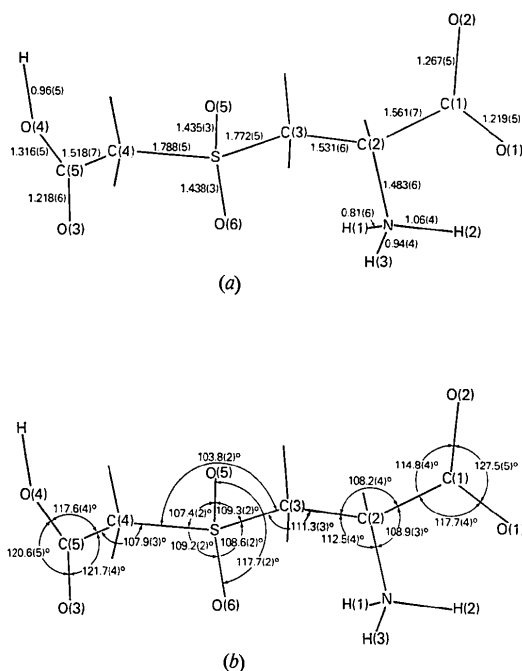


Fig. 1. (a) Bond lengths and (b) bond angles of SCMC-sulfone.

Table 3. Hydrogen-bond distances and angles

<i>A</i> —H $\cdots$ <i>B</i> — <i>C</i>	$d_{A-H}$	$d_{H\cdots B}$	$d_{A\cdots B}$	$\angle A-H\cdots B$	$\angle H\cdots B-C$
O(4)—H $\cdots$ O(2) <sup>i</sup> —C(1) <sup>i</sup>	0.96 (5) Å	1.54 (5) Å	2.504 (5) Å	175 (5)°	121 (2)°
N—H(1) $\cdots$ O(1) <sup>ii</sup> —C(1) <sup>ii</sup>	0.81 (6)	2.09 (6)	2.875 (6)	163 (5)	134 (1)
N—H(2) $\cdots$ O(3) <sup>iii</sup> —C(5) <sup>iii</sup>	1.06 (4)	1.85 (4)	2.854 (5)	157 (4)	127 (2)
N—H(3) $\cdots$ O(2) <sup>iv</sup> —C(1) <sup>iv</sup>	0.94 (4)	1.90 (4)	2.820 (6)	165 (4)	120 (1)

Symmetry code

(i)	$1-x$	$-\frac{1}{2}+y$	$\frac{3}{2}-z$	(iii)	$\frac{1}{2}+x$	$\frac{3}{2}-y$	$2-z$
(ii)	$x$	$-1+y$	$z$	(iv)	$-\frac{1}{2}+x$	$\frac{5}{2}-y$	$2-z$

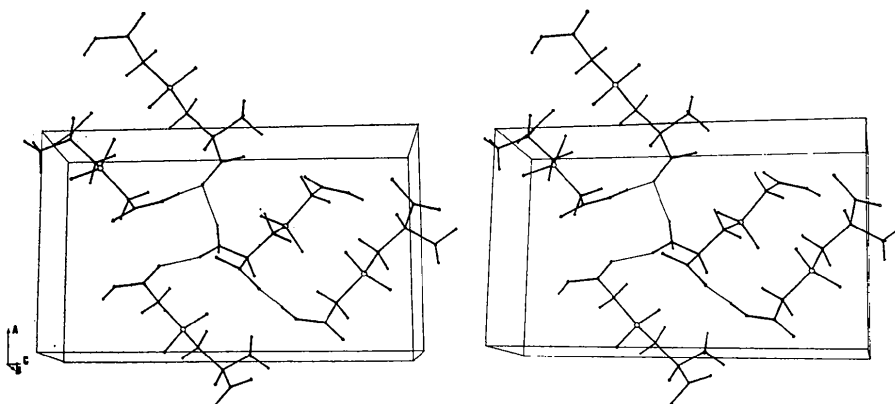


Fig. 2. Stereoscopic view of the packing along *b* (ORTEP: Johnson, 1965).

**Discussion.** Carboxymethylation of sulfhydryl ( $-SH$ ) groups of proteins is used in studies concerning protein structure, and enzyme structure and function (Bradbury & Smyth, 1973). The *S*-carboxymethyl-cysteine residues that result from carboxymethylation procedures are subject to facile oxidation to the corresponding sulfoxides and sulfone. To understand the chemistry of these compounds better the two epimeric SCMC-sulfoxides and the SCMC-sulfone were prepared by oxidation of *S*-carboxymethyl-L-cysteine. The structures of one of the epimeric sulfoxides (Zervos, Staffa, Mighell & Hubbard, 1977) and the title compound have been determined to ascertain the conformation of these molecules and to allow one to correlate structure with the chemistry of the compounds.

The distances and angles for the SCMC-sulfone molecule are given in Fig. 1. The molecule is in the zwitterion form as are other neutral amino acids whose hydrogen atom positions were well located. The C(5) carboxyl group is protonated [the H(O4) was located in the difference map and refined] and the C(1) carboxyl group is unprotonated. The neutron diffraction study of the similar glutamic acid (a neutral, dicarboxylic amino acid) (Lehmann, Koetzle & Hamilton, 1972) revealed the same zwitterion-protonated C(5) carboxyl pattern.

In SCMC-sulfone, as in glutamic acid, the differences between the two carboxyl groups are also reflected in the interatomic distances. For the C(5) carboxyl group of SCMC-sulfone, the C(5)–O(3) distance of 1.218 (6) Å corresponds to a double bond (C=O), and the C(5)–O(4) distance of 1.316 (5) Å corresponds to a single bond (C–OH). These two bond lengths are nearly identical to the related pair in glutamic acid [1.219 (2) and 1.312 (2) Å].

For the C(1) carboxyl group of SCMC-sulfone, the difference,  $\Delta$ , (0.048 Å) between the C(1)–O(2) bond of 1.267 (5) Å and the C(1)–O(1) bond of 1.219 (5) Å appears to be unusually large when compared to the  $\Delta$  (0.001 Å) of the L-glycine zwitterion (Jönsson & Kvick, 1972). The larger  $\Delta$  observed in SCMC-sulfone can be attributed to the unequal hydrogen bonding to these two oxygen atoms (Table 3). O(2) is involved in a very short hydrogen bond to the hydrogen attached to O(4) and also in a weaker hydrogen bond

to H(3) from an ammonium group. O(1) is involved in only one weak hydrogen bond to H(1) of an ammonium group. A similar but smaller difference was observed in glutamic acid ( $\Delta=0.020$  Å). Presumably in glutamic acid  $\Delta$  is smaller because O(1) is involved in two weak hydrogen bonds (instead of one) and O(2) is involved in only the strong hydrogen bond (no N–H $\cdots$ O bond). Thus the distances in the carboxyl groups appear to be sensitive to the overall hydrogen-bonding scheme.

The packing is shown in Fig. 2. Each SCMC-sulfone molecule is hydrogen-bonded [via O(2) $\cdots$ H–O(4)] to two symmetry-related molecules to form chains parallel to the *b* axis. These chains are interlinked by three (N–H $\cdots$ O) hydrogen bonds between the ammonium and the carboxyl groups. The N–H $\cdots$ O distances and angles (Table 3) indicate that these hydrogen bonds are important in the three-dimensional packing.

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