

## Structure and Conformation of Amino Acids Containing Sulfur.

### IV.\* The Crystal Structure of L-Cystine Dihydrobromide Dihydrate: a Novel Conformation

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L-Cystine dihydrobromide dihydrate ( $C_6H_{12}N_2O_4S_2 \cdot 2HBr \cdot 2H_2O$ ) crystallizes in the space group  $P2_1$ . The cell constants [ $\lambda(Cu K\alpha_1) = 1.54051 \text{ \AA}$ ,  $T = 22 \pm 3^\circ C$ ] are  $a = 9.512$  (1),  $b = 13.458$  (2), and  $c = 6.021$  (1)  $\text{\AA}$ ,  $\beta = 91.13$  (5)°,  $V_o = 770.7 \text{ \AA}^3$ , and  $Z = 2$ .  $D_{obs} = 1.87$  (1)  $\text{g cm}^{-3}$  (flotation),  $D_{calc} = 1.888 \text{ g cm}^{-3}$ , and  $\mu(Cu K\alpha) = 100.7 \text{ cm}^{-1}$ . Intensity data were measured ( $Cu K\alpha$ ,  $2\theta \leq 160^\circ$ ) on a G.E. XRD-490 automatic diffractometer, using the stationary-crystal stationary-counter technique with balanced Ni-Co filters, and were corrected for absorption (spherical crystal,  $\mu R = 1.7$ ). The structure, solved by the heavy-atom method, was refined by least-squares calculations to an  $R$  of 0.050 for 1691 reflections. The L-cystine cation in this structure does not possess twofold symmetry. The torsion angle about the disulfide bond is  $-80^\circ$ ; the S-S bond length is 2.044 (4)  $\text{\AA}$ . Both carboxyl carbon atoms are  $\pm$  anti-periplanar to the  $\gamma$ -sulfur atoms. The carboxyl groups form short hydrogen bonds to water and to bromide [ $O_1' \cdots O(\text{water})$  is 2.58 (1) and  $O_2'' \cdots Br^-$  is 3.09 (1)  $\text{\AA}$ ], and there is a short  $S \cdots Br^-$  distance of 3.551 (3)  $\text{\AA}$ .

#### Introduction

Monoclinic crystals of L-cystine dihydrobromide dihydrate were grown by Box, Freund, Lilga & Budzinski (1970). They were studied at our laboratory as part of a general structural comparison of amino acids containing sulfur (Rosenfeld, 1974).

#### Experimental

Clear, transparent, and well-formed crystals of L-cystine dihydrobromide dihydrate ( $C_6H_{12}N_2O_4S_2 \cdot 2HBr \cdot 2H_2O$ ), kindly provided by Box and Budzinski, have the space group  $P2_1$  ( $0k0$  reflections with  $k$  odd were absent). The cell parameters  $a = 9.512$  (1),  $b = 13.458$  (2), and  $c = 6.021$  (1)  $\text{\AA}$ ,  $\beta = 91.13$  (5)°, and  $V_o = 770.7 \text{ \AA}^3$  were obtained with  $Cu K\alpha$  radiation [ $\lambda(Cu K\alpha_1) = 1.54051 \text{ \AA}$ ], at room temperature ( $22 \pm 3^\circ C$ ), on a G. E. XRD-6 diffractometer, and were refined by the least-squares method from more than 40 measurements of  $2\theta$ . The crystals have an observed density,  $D_{obs}$ , of 1.87 (1)  $\text{g cm}^{-3}$  measured by flotation, and a calculated density,  $D_{calc}$ , of 1.888  $\text{g cm}^{-3}$ , with  $Z = 2$ .

One crystal was ground to a sphere of radius  $R = 0.167$  mm and mounted with the  $b^*$  axis parallel to the  $\phi$  axis of the goniostat. Intensity data were collected ( $Cu K\alpha$  radiation,  $2\theta \leq 160^\circ$ ) on an XRD-490 automatic diffractometer, using the stationary-crystal stationary-counter technique (Furnas & Harker, 1955)

with balanced Ni-Co Ross filters. Of the 1765 unique reflections measured, 1701 were selected for the refinement of the structure on the criterion that their intensity (Ni-filtered minus Co-filtered) at least equalled the average background (Co-filtered) value. Intensities of the remaining, 'weak' reflections were fixed at half the average background value. Lorentz, polarization, and  $\alpha_1$ - $\alpha_2$  splitting corrections were made. From the values of  $\mu_a$  (*International Tables for X-ray Crystallography* 1968), a linear absorption coefficient  $\mu$  of  $100.7 \text{ cm}^{-1}$  was calculated, and used ( $\mu R = 1.7$ ) in correcting for the absorption of a spherical crystal (*International Tables for X-ray Crystallography*, 1967).

#### Solution and refinement of the structure

The structure was solved by the heavy-atom method. Atomic parameters were refined by the method of block-diagonal least-squares, minimizing  $\sum_H w_H (|F_H|^{obs} - (1/k)|F_H|^{calc})^2$ , where  $w_H = (1/f_{oxy})$ . Scattering factor values for  $Br^-$ , S, O (all corrected for anomalous dispersion), N, and C were taken from *International Tables for X-ray Crystallography* (1968). With individual anisotropic thermal factors for all atoms, the structure was refined to a final  $R$  value of 0.050, for 1691 reflections ( $R$  is 0.057 over all 1765 reflections). During the final stages of the refinement, 10 reflections attenuated presumably by extinction effects ( $54 \leq |F_H|^{obs} \leq 103$ ,  $|F_H|^{obs} < |F_H|^{calc}$ ,  $\sin \theta/\lambda \leq 0.20$ ) were removed. An electron density difference synthesis revealed peaks that could be attributed to hydrogen atoms. Noise in the map, however, on the order of 0.1 to 0.3  $e \text{ \AA}^{-3}$ , made it impossible to accept any such peaks as evidence for the hydrogen positions. The final

\* Part III: Rosenfeld & Parthasarathy (1975).

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atomic parameters are listed in Table 1.\* In the final cycle of refinement, no atomic parameter shifted more than a tenth of its estimated standard deviation (e.s.d.), determined from the variance-covariance matrix.

\* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30755 (13 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

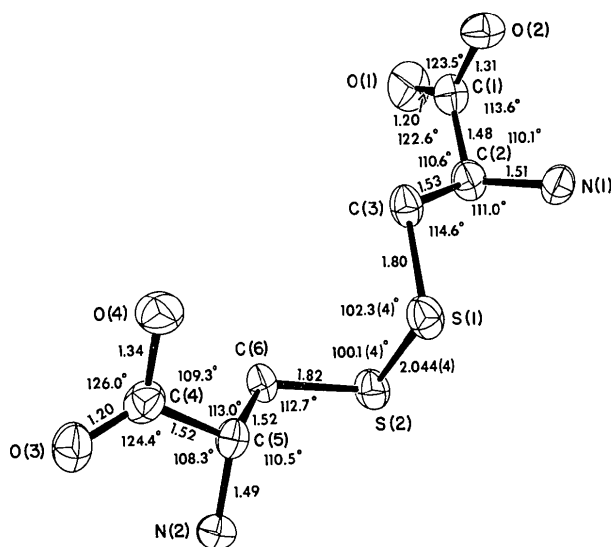


Fig. 1. Valence bond lengths (Å) and bond angles. E.s.d.'s not shown range from 0.010 to 0.017 Å and from 0.7 to 1.3°. Equivalent dimensions in the halves of the molecule-ion that show the largest differences are the angles S(2)-S(1)-C(3) and S(1)-S(2)-C(6), and C(2)-C(1)-O(2) and C(5)-C(4)-O(4). This drawing was made with the ORTEP program, using 50% probability ellipsoids.

## Bond lengths and angles

The valence bond lengths and bond angles of the divalent cation of L-cystine are shown in Fig. 1, and agree with those found in previously reported structures of L-cystine. Equivalent bond lengths and angles in the halves of the molecule differ by 1.6 e.s.d.'s on the average; however, two pairs of bond angles differ by 3 to 4 e.s.d.'s.

## Conformation of the molecule

The conformation angles of L-cystine are listed in Table 2. The torsion angle about the disulfide bond ( $\chi^3$ ) is  $-80^\circ$ , the same as that found in the previously reported structures of the L-cystine cation (Steinrauf, Peterson & Jensen, 1958; Peterson, Steinrauf & Jensen, 1960). The carboxyl carbon atoms are  $\pm$  anti-periplanar [using the nomenclature of Klyne & Prelog (1960)] to the  $\gamma$ -sulfur atoms, a conformation *not* found in any other reported structure of L-cystine. The molecule does not possess twofold symmetry; whereas, either *exact* or *approximate* twofold molecular symmetry is found in all other reported structures of L-cystine and its bis-derivatives.

## Hydrogen bonding

The interatomic contacts indicative of the hydrogen bonding with the carboxyl and amino groups are listed in Table 3 and illustrated in Fig. 2. These contacts indicate (1) that both carboxyl groups participate in strong hydrogen bonds, one to water and one to bromide, and (2) that seven hydrogen acceptors are available to participate in hydrogen bonding with the two amino groups.

Table 1. Final atomic fractional coordinates and thermal parameters

E.s.d.'s, given in parentheses, refer to the last digit. Anisotropic thermal factors are given by the expression  $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)]$ . Atoms are labeled according to the criteria of the IUPAC-IUB Commission on Biochemical Nomenclature (1970). After each cycle of refinement, the  $y$  coordinates of all atoms were shifted relative to the shift in the  $y$  coordinate of Br(1).

IUPAC name	$x$ ( $\times 10^4$ )	$y$ ( $\times 10^4$ )	$z$ ( $\times 10^3$ )	$\beta_{11}$ ( $\times 10^4$ )	$\beta_{22}$ ( $\times 10^4$ )	$\beta_{33}$ ( $\times 10^3$ )	$\beta_{12}$ ( $\times 10^3$ )	$\beta_{13}$ ( $\times 10^3$ )	$\beta_{23}$ ( $\times 10^3$ )	
Br(1)	8651 (1)	0 (1)	-6.3 (2)	95 (1)	35.6 (5)	16.3 (2)	1.3 (2)	3.8 (3)	-1.3 (2)	
Br(2)	5694 (1)	972 (1)	403.9 (2)	73 (1)	69.0 (8)	15.0 (2)	-2.8 (2)	-0.1 (3)	-0.8 (3)	
S(1)	S <sub>1</sub> <sup>7</sup>	3571 (3)	-1383 (3)	241.0 (5)	66 (3)	49 (2)	20.9 (7)	-2.0 (4)	-1.7 (7)	4.7 (6)
S(2)	S <sub>2</sub> <sup>7</sup>	2441 (3)	-2507 (2)	95.3 (4)	84 (3)	41 (1)	15.4 (6)	-0.2 (3)	5.7 (7)	0.8 (5)
O(1)	O <sub>1</sub> <sup>7</sup>	1872 (9)	857 (10)	-338 (2)	76 (9)	80 (8)	41 (4)	0 (2)	-22 (3)	7 (3)
O(2)	O <sub>1</sub> <sup>7</sup>	3489 (10)	1657 (7)	-139 (1)	104 (10)	33 (4)	23 (2)	1 (1)	-4 (2)	-1 (2)
O(3)	O <sub>2</sub> <sup>7</sup>	-837 (9)	-2698 (7)	759 (1)	85 (9)	58 (6)	17 (2)	1 (1)	5 (2)	1 (2)
O(4)	O <sub>2</sub> <sup>7</sup>	196 (11)	-1278 (7)	649 (2)	130 (12)	34 (5)	26 (3)	0 (1)	7 (3)	-4 (2)
O(W1)		3908 (12)	3110 (8)	260 (2)	134 (13)	54 (6)	26 (3)	-4 (2)	-4 (3)	0 (2)
O(W2)		2570 (12)	3261 (7)	674 (2)	135 (13)	40 (5)	31 (3)	3 (1)	2 (3)	1 (2)
N(1)	N <sub>1</sub>	5066 (9)	2 (10)	-106 (1)	68 (9)	45 (5)	20 (2)	2 (1)	2 (2)	2 (2)
N(2)	N <sub>2</sub>	844 (10)	-3840 (7)	510 (2)	84 (10)	32 (5)	19 (2)	0 (1)	3 (2)	1 (2)
C(1)	C <sub>1</sub>	2887 (11)	850 (10)	-216 (2)	75 (11)	44 (6)	16 (3)	-1 (2)	-1 (3)	-2 (2)
C(2)	C <sub>1</sub> <sup>7</sup>	3483 (10)	-76 (11)	-123 (2)	62 (10)	44 (6)	16 (2)	0 (2)	-1 (2)	6 (3)
C(3)	C <sub>2</sub> <sup>7</sup>	2858 (12)	-297 (9)	104 (2)	72 (11)	50 (7)	17 (3)	-2 (1)	3 (3)	1 (2)
C(4)	C <sub>2</sub> <sup>7</sup>	-35 (11)	-2256 (9)	645 (2)	61 (10)	39 (6)	16 (3)	1 (1)	-2 (3)	-3 (2)
C(5)	C <sub>3</sub> <sup>7</sup>	1006 (10)	-2747 (8)	491 (2)	52 (9)	33 (6)	13 (2)	0 (1)	0 (2)	-3 (2)
C(6)	C <sub>3</sub> <sup>7</sup>	821 (11)	-2418 (9)	250 (2)	57 (10)	43 (6)	15 (3)	-1 (1)	1 (3)	2 (2)

Table 2. Torsion angles

	IUPAC (1970) designation	
$\tau(C_2^{\beta}-S_2^{\gamma}-S_1^{\gamma}-C_1^{\beta})$	$\chi^3$	$-80^\circ$
$\tau_2(S_1^{\gamma}-S_2^{\gamma}-C_1^{\beta}-C_2^{\beta})^*$	$(\chi_1^2, \chi_2^2)$	$(-82, -70)$
$\tau_2(S_1^{\gamma}-C_1^{\beta}-C_2^{\beta}-N_1)$	$(\chi_1^1, \chi_2^1)$	$(-55, -85)$
$\tau_2(S_1^{\gamma}-C_1^{\beta}-C_2^{\beta}-C_1)$		$(-177, 153)$
$\tau_2(N_1-C_1^{\beta}-C_2^{\beta}-O_1^{\beta})$	$(\psi_1^1, \psi_2^1)$	$(144, 0)$

\*  $\tau_2(S_1^{\gamma}-S_2^{\gamma}-C_1^{\beta}-C_2^{\beta})$  designates two equivalent torsion angles; hence, the subscript 2. For the first of these torsion angles,  $i=1$  and  $j=2$ , and for the second,  $i=2$  and  $j=1$ . Using the crystallographic nomenclature in Table 1, these torsion angles are, respectively,  $\tau[S(2)-S(1)-C(3)-C(2)]$  and  $\tau[S(1)-S(2)-C(6)-C(5)]$ .

Table 3. Hydrogen bonding with the carboxyl and amino groups

*D* is the donor and *A* is a possible acceptor atom. The following superscripts distinguish atoms related, by symmetry operations, to those in Table 1: none,  $x, y, z$ ; (i)  $x, y, -1+z$ ; (ii)  $-1+x, y, 1+z$ ; (iii)  $1-x, -\frac{1}{2}+y, -z$ ; (iv)  $-x, -\frac{1}{2}+y, -z$ ; (v)  $1-x, -\frac{1}{2}+y, 1-z$ ; (vi)  $1-x, \frac{1}{2}+y, -z$ ; (vii)  $x, y, 1+z$ ; (viii)  $1-x, \frac{1}{2}+y, 1-z$ ; (ix)  $-x, -\frac{1}{2}+y, 1-z$ .

$C-D \cdots A$	$D \cdots A$	$\angle C-D \cdots A$
$C(1)-O(2) \cdots O(W2^i)$	2.58 (1) Å	113.3 (7)°
$C(4)-O(4) \cdots Br(1^{iii})$	3.09 (1)	118.8 (7)
$C(2)-N(1) \cdots O(W1^{iii})$	2.89 (2)	105.1 (8)
$C(2)-N(1) \cdots Br(2^i)$	3.293 (9)	99.6 (6)
$C(2)-N(1) \cdots Br(2)$	3.379 (9)	104.2 (6)
$C(5)-N(2) \cdots O(1^{iv})$	2.79 (1)	102.3 (6)
$C(5)-N(2) \cdots Br(2^v)$	3.33 (1)	89.1 (5)
$C(5)-N(2) \cdots Br(1^v)$	3.40 (1)	120.6 (6)
$C(5)-N(2) \cdots Br(1^{iii})$	3.45 (1)	111.4 (6)

Three interatomic distances involving the water oxygens indicate hydrogen bonding, and are illustrated in Fig. 2:  $O(W1) \cdots N(1^{vi})$  and  $O(W2) \cdots O(2^{viii})$  in Table 3, and  $O(W2) \cdots Br(1^{iii})$ , 3.31 (1) Å.  $O(W1)$  and  $O(W2)$  lie 2.83 (2) Å from each other, just beyond the accepted van der Waals contact distance of 2.8 Å (Pauling, 1960).

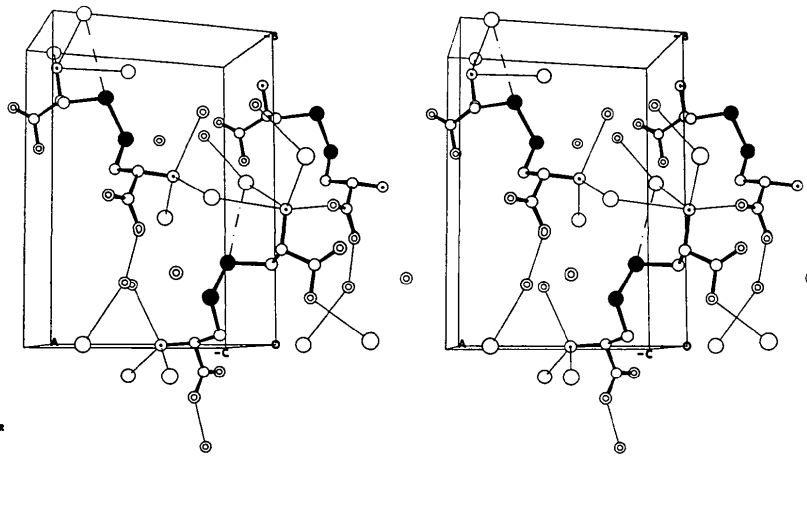


Fig. 2. Packing diagram; a stereo pair. Contacts indicative of hydrogen bonding (see Table 3 and the text) are shown by thin lines. The short  $S(2) \cdots Br(1^{iii})$  distance (described in the text) is shown by a broken line.

## Packing

The packing is illustrated in Fig. 2. The contact between  $S(2)$  and  $Br(1^{iii})$  in the figure has a distance of 3.551 (3) Å, which is 0.25 Å shorter than the accepted van der Waals contact distance (Pauling, 1960). The  $S(1)-S(2) \cdots Br(1^{iii})$  contact angle is  $156.1 (1)^\circ$  and the  $S(2) \cdots Br(1^{iii})$  direction is  $66.3^\circ$  from the normal to the plane through the sulfide group  $S(1)-S(2)-C(6)$ . This finding agrees with evidence presented earlier by us (Rosenfield & Parthasarathy, 1974, 1975) suggesting that the van der Waals radius of  $S^{\gamma}$  or  $S_i^{\gamma}$  ( $i=1$  or  $2$ ) is about 0.2 Å smaller in the vicinity of the plane through the atoms  $C_1^{\beta}-S^{\gamma}-C_2^{\beta}$  or  $S_j^{\gamma}-S_i^{\gamma}-C_i^{\beta}$  ( $j=1$  or  $2, j \neq i$ ) than in the direction normal to each of these planes.

Other short interatomic distances between non-bonded atoms are listed in Table 4.

Table 4. Additional short distances between non-bonded atoms

Intermolecular		Intramolecular	
$N(1) \cdots Br(1)$	3.452 (9) Å	$N(1) \cdots O(2)$	2.69 (1) Å
$S(2) \cdots C(4^i)$	3.57 (1)	$N(1) \cdots S(1)$	3.16 (1)
$C(1) \cdots Br(2^i)$	3.55 (1)	$N(2) \cdots O(3)$	2.70 (1)
$C(4) \cdots O(W2^{ix})$	3.13 (2)		

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## Optical Induction in Chiral Crystals. II.\* The Crystal and Molecular Structures of 1-(2,6-Dichlorophenyl)-4-phenyl-*trans,trans*-1,3-butadiene

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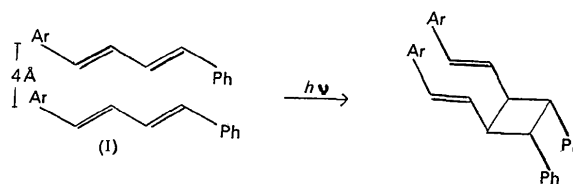
The title compound ( $C_{16}H_{12}Cl_2$ ) crystallizes in space group  $P2_12_12_1$  with  $a=9.3881$  (2),  $b=4.0286$  (1) and  $c=35.3073$  (3) Å,  $Z=4$ . The structure has been determined by direct methods from three-dimensional diffractometer data collected with Cu  $K\alpha$  radiation, and refined to  $R=0.04$ . The absolute configuration of the molecules in the analysed crystal was determined by the anomalous scattering of the chlorine atoms. The rotations of the phenyl and the dichlorophenyl groups from the butadiene plane are  $15^\circ$  and  $40^\circ$  respectively. The molecular conformation is believed to control the exclusive photoreactivity of the double bond adjacent to the phenyl ring and the formation of an optically active heterodimer in a mixed single crystal of the title compound with its thiophene analogue.

### Introduction

Two of the necessary conditions for optical synthesis discussed in part I (Rabinovich & Shakked, 1974), chiral space group and *prochiral* conformation, were observed in the designing of another asymmetric synthesis experiment, namely, the photodimerization of parallel C=C double bonds stacked along a short (*ca* 4 Å) axis. Irradiation of such a system yields a cyclobutane possessing a mirror plane (Schmidt, 1967). However, as was suggested by Lahav (1968), the irradiation of a chiral single crystal containing a guest molecular species may lead to the formation of unequal amounts of enantiomeric heterodimers if the molecules are heavily distorted from planarity.

The present analysis deals with the crystal and molecular structures of 1-(2,6-dichlorophenyl)-4-phenyl-*trans,trans*-1,3-butadiene (I) which crystallizes in a chiral space group ( $P2_12_12_1$ ) with a short (4.03 Å) axis and is expected to possess a pronounced *prochiral* con-

formation due to the two *ortho*-substituted chlorines. This compound yields under irradiation a single cyclobutane resulting from exclusive dimerization at the double bond adjacent to the phenyl ring (Cohen, Elgavi, Green, Ludmer & Schmidt, 1972).



Ph = phenyl, Ar = 2,6-dichlorophenyl

(I) and its thiophene analogue [1-(2,6-dichlorophenyl)-4-thienyl-*trans,trans*-1,3-butadiene, (II)] are isomorphous and show extensive solid solubility. Irradiation of a mixed single crystal of (I) and (II) (approximate ratio 4:1) in the thienyl absorbing wavelength range yields one of the two enantiomeric heterodimers in excess (Elgavi, 1973; Elgavi, Green & Schmidt, 1973).

\* Part I: Rabinovich & Shakked (1974).