

Two other minor ketones were separated by preparative glpc (column A at 175°). The ketone which formed 6% of the mixture was the isomeric ketone **32a**: ir (CCl₄) 1720 cm⁻¹; nmr 0.86 (s, 3 H) and 0.93 (s, 6 H). An exact mass determination gave *m/e* 206.1670 (calcd for C₁₄H₂₂O, 206.1670).

The least ketone was **27** as identified by glpc and ir.

Deuteration of 32b. A solution of **32b** (9 mg) in methanol-*d*₁ (0.5 ml) was added to a sodium methoxide solution prepared from sodium (10 mg) and methanol-*d*₁ (0.5 ml), and the mixture was refluxed for 1 hr under nitrogen. Deuterium oxide (3 drops) was added, and the solvent was evaporated *in vacuo*. The residue was dissolved in pentane and dried (MgSO₄). Removal of the solvent gave an oil, *m/e* 208 (M⁺).

2,6,6,9-Tetramethyltricyclo[5.4.0.0^{2,9}]undecan-*exo*-9-ol (35). A solution of **32b** (52 mg, 0.25 mmol) in dry ether (3 ml) was added to a methyl lithium solution, prepared from lithium (70 mg, 5 mmol) and methyl iodide (0.31 ml) in dry ether (4 ml), under nitrogen. The mixture was stirred for 5.5 hr at room temperature, and the reaction was then quenched with cold aqueous ammonium chloride. The organic layer was separated and washed with water and brine. Removal of the solvent left crystals, which were recrystallized from pentane at a Dry Ice-methanol temperature affording pure longipinanol (**35**) (44 mg, 80%): mp 98.0–98.5°; ir (KBr) 3370, 3025, 1109, 915, and 879 cm⁻¹; nmr 0.88 (s, 6 H), and 1.05 and 1.22 (s, 3 H each).³⁶

α- and β-Longipinenes (1a and 1b). Phosphorus oxychloride (0.16 ml) was added to a solution of **35** (42 mg, 0.19 mmol) in dry

pyridine (1 ml). The mixture was heated to 100° and kept at this temperature for 5 min. After cooling to room temperature, the mixture was poured into a stirred mixture of pentane (30 ml) and cold water (20 ml). Stirring was continued for further 20 min, and the organic layer was separated. The aqueous layer was extracted with two 30-ml portions of pentane. The combined organic layers were successively washed with water, dilute sodium carbonate, water, aqueous cupric sulfate, water, and brine, and dried (MgSO₄). The solvent was distilled off through a Vigreux column to leave an oil, whose pentane solution was passed through a column of neutral alumina (Woelm, activity II, 4 g). Removal of the solvent left a clear colorless oil. Glpc analysis (column B at 157°) indicated that the oil consisted of two main olefins (48 and 36%), along with two unidentified minor products (16%). The most abundant olefin was presumed to be α-longipinene by glpc. The products were separated by preparative glpc to give two main olefins. One of them was (±)-α-longipinene as identified by comparison of the ir and nmr spectra with those of (+)-α-longipinene: ir (film) 3030, 1656, and 786 cm⁻¹; nmr 0.82 (s, 6 H), 0.89 (s, 3 H), and 5.12 (m, 1 H).³⁶

The second olefin, (±)-β-longipinene, was identified by comparison of the ir and nmr spectra with those of (-)-β-longipinene: ir (film) 3070, 1642, and 973 cm⁻¹; nmr 0.68 (s, 3 H), 0.88 (s, 6 H), and 4.50 (m, 2 H, *W*_{1/2} = 6 Hz).³⁶

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Structure and Conformation of Amino Acids Containing Sulfur. II.^{1a} The Crystal Structure of *meso*-Lanthionine Dihydrochloride; a Short Intermolecular S···S Contact Distance

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Abstract: The crystal structure of *meso*-lanthionine dihydrochloride (C₆H₁₂N₂O₄S·2HCl) has a remarkably short S^γ···S^γ contact distance, 3.251 (2) Å, between two sulfide (C^β-S^γ-C^β) groups that are almost coplanar. A second sulfur contact, 3.515 (2) Å to Cl⁻, is also directed close to the plane through C^β-S^γ-C^β. Two intramolecular S^γ···H-N contacts, each 2.75 (8) Å long, are directed, in contrast, nearly normal to this plane. These results are interpreted in terms of the orbital geometry of S^γ's unshared pair of 3p electrons, and they suggest a smaller van der Waals radius for sulfur in the plane of the sulfide group. Both carboxyl carbon atoms are ± antiperiplanar to S^γ, an unusual conformation in structures of amino acids containing sulfur. Two carboxyl and one amino hydrogen atoms form short hydrogen bonds, 2.11 (7) Å long, to Cl⁻ ions. Each of five amino hydrogen atoms has two contacts with electronegative atoms, and lies in the plane through these atoms and its bonded nitrogen. The crystals have the space group *P*2₁/*a*. The cell constants [*T* = 22 ± 3°, λ(Cu Kα₁) 1.54051 Å] are *a* = 9.821 (1), *b* = 20.158 (1), and *c* = 5.706 (1) Å, β = 93.37 (1)°, *V*_c = 1127.7 Å³, and *Z* = 4; *d*_{obsd} is 1.67 (1) g/cm³ (floatation), *d*_{calcd} is 1.656 g/cm³, and μ is 68.4 cm⁻¹. Data were measured (Cu Kα, 2θ ≤ 160°) on a G. E. XRD-6 diffractometer, and were corrected for absorption. The structure, solved by the heavy atom method, was refined by least squares to an *R* of 0.056, using 1606 reflections.

Lanthionine (3,3'-thiodialanine) is a rare, naturally occurring amino acid, the sulfide analog of cystine. It was isolated originally from wool, chicken feathers, lactalbumin, and human hair, after treatment with dilute alkali;² and it has also been found in the peptide

(1) (a) For Part I, see S. Narasinga Rao, R. Parthasarathy, and F. E. Cole, *Acta Crystallogr., Sect. B.*, **29**, 2373 (1973); (b) Center for Crystallographic Research; (c) State University of New York at Buffalo.
(2) M. J. Horn, D. B. Jones, and S. J. Ringel, *J. Biol. Chem.*, **138**, 141 (1941); **144**, 87 (1942).

antibiotics subtilin^{3a} and nisin.^{3b} du Vigneaud and Brown were the first to synthesize the D, L, and *meso* forms.⁴ We decided to study lanthionine's crystal structure in order to compare it with the several structures already reported for L-cystine, L-cysteine, and

(3) (a) J. C. Lewis and N. S. Snell, *J. Amer. Chem. Soc.*, **73**, 4812 (1951); (b) E. Gross and J. L. Morell, *J. Amer. Chem. Soc.*, **93**, 4634 (1971).

(4) V. du Vigneaud and G. B. Brown, *J. Biol. Chem.*, **138**, 151 (1941); G. B. Brown and V. du Vigneaud, *ibid.*, **140**, 767 (1941).

Table I. Crystal Structures of L-Cystine, L-Cysteine, and Their Derivatives

Compound	Ref
L-Cystine	
L-Cystine dihydrochloride	a
L-Cystine	b
L-Cystine dihydrobromide	c
L-Cystine derivatives	
N,N'-Diglycyl-L-cystine dihydrate	d
L-Cystinediamide dihydrochloride	e
L-Cysteine	
L-Cysteine	f
L-Cysteine hydrochloride hydrate	g
L-Cysteine derivatives	
Cysteinylglycine-0.5NaI	h
S-Methyl-L-cysteine sulfoxide	i
L-Cysteine ethyl ester hydrochloride urea	j
L-Cystic acid	k
Glutathione	l

^a L. K. Steinrauf, J. Peterson, and L. H. Jensen, *J. Amer. Chem. Soc.*, **80**, 3835 (1958). ^b B. M. Oughton and P. M. Harrison, *Acta Crystallogr.*, **12**, 396 (1959); *Struct. Rep.*, **23**, 593 (1959). ^c J. Peterson, L. K. Steinrauf, and L. H. Jensen, *Acta Crystallogr.*, **13**, 104 (1960). ^d H. L. Yakel, Jr., and E. W. Hughes, *ibid.*, **7**, 291 (1954). ^e M. O. Chaney and L. K. Steinrauf, *Acta Crystallogr.*, *Sect. B*, **24**, 1564 (1968). ^f M. M. Harding and H. A. Long, *ibid.*, **24**, 1096 (1968). ^g R. Ramachandra Ayyar, *Z. Kristallogr. Kristallgeometrie, Kristalphys., Kristallchem.*, **126**, 227 (1968). ^h H. B. Dyer, *Acta Crystallogr.*, **4**, 42 (1951). ⁱ R. Hine, *ibid.*, **15**, 635 (1962). ^j D. J. Haas, *ibid.*, **19**, 860 (1965). ^k H. Konishi, T. Ashida, and M. Kakudo, *Bull. Chem. Soc. Jap.*, **41**, 2305 (1968). ^l F. E. Cole, *Acta Crystallogr.*, in press.

their derivatives (Table I), as well as with the structures of L-cystine dihydrobromide dihydrate,⁵ 3,3-dimethyl-L-cysteine hydrochloride hydrate,⁶ and 3,3,3',3'-tetramethyl-D-cystine dihydrochloride⁷ being studied in our laboratory.

Experimental Section

DL-Lanthionine and a mixture of L- and *meso*-lanthionine were purchased from Mann Research Laboratories, New York, N. Y. Aqueous solutions were prepared by dissolving each powder with normal or concentrated HCl, and were allowed to evaporate slowly at room temperature ($22 \pm 3^\circ$). After many unsuccessful attempts, colorless, transparent, and well-formed crystals of *meso*-lanthionine dihydrochloride ($C_6H_{12}N_2O_4S \cdot 2HCl$), shaped like flat needles, were grown. They were monoclinic, with the unique *b* axis normal to the large face and with the *c* axis parallel to the needle direction. The crystal used for this study, referred to as crystal I, was cut with a fresh razor blade nearly perpendicular to the *c* axis, and was mounted with the *c** axis parallel to the ϕ axis of the goniostat. It measured $0.15 \times 0.057 \times 0.13$ mm along *a*, *b*, and *c*, respectively, and displayed a hexagonal cross section bounded by faces (010), (0 $\bar{1}$ 0), (120), ($\bar{1}$ $\bar{2}$ 0), ($\bar{1}$ 20), and ($\bar{1}$ 20).

Reflections were systematically absent for *h*0*l*, *h* odd, and *0k*0, *k* odd, suggesting uniquely the space group $P2_1/a$. The following unit cell parameters were obtained with copper radiation [$\lambda(Cu K\alpha_1)$ 1.54051 Å] on a G.E. XRD-5 diffractometer at room temperature ($22 \pm 3^\circ$): *a* = 9.821 (1), *b* = 20.158 (1), and *c* = 5.706 (1) Å, β = 93.37 (1)°, V_c = 1127.7 Å³. These dimensions were refined (and their standard deviations estimated), by the least-squares method, from 40 independent measurements of reasonably intense reflections at large 2θ angles, where the peaks from Cu $K\alpha_1$ and Cu $K\alpha_2$ could be distinguished. The buoyant density observed for the crystal, d_{obsd} = 1.67 (1) g/cm³, was measured from a mixture of benzene and 1,2-dibromoethane; the density calculated from the cell parameters, d_{calcd} , is 1.656 g/cm³, taking Z = 4.

Data were collected to the limit $2\theta = 160^\circ$ (Cu $K\alpha$ radiation) on an XRD-6 diffractometer using the stationary crystal-stationary

(5) R. E. Rosenfield, Jr., and R. Parthasarathy, submitted for publication in *Acta Crystallogr.*

(6) See ref 1a.

(7) R. E. Rosenfield, Jr., and R. Parthasarathy, *Acta Crystallogr.*, submitted for publication.

counter technique⁸ with balanced Ni-Co Ross filters. Of the 2484 unique reflections measured, 1606 were considered as observed, on the criterion that their intensities were at least twice the average background intensity. Lorentz, polarization, and α_1 - α_2 splitting corrections were made. A detailed correction for absorption⁹ was applied, based on the geometry of the crystal and on the linear absorption coefficient, $\mu = 68.4$ cm⁻¹, calculated from ref 10. The transmission coefficients varied from 0.44 to 0.71.

No decay had been observed in the intensities of the reflections used as standards during the collection of the data. However, the crystal started becoming cloudy 2 months later. One other single crystal, II, of *meso*-lanthionine dihydrochloride was found in another solution.¹¹ It was elongated in the *c* direction and had a triangular cross section bounded by faces (010), ($\bar{1}$ $\bar{1}$ 0), and ($\bar{1}$ $\bar{1}$ 0), each about 0.2 mm wide. After being cut nearly perpendicular to the *c* axis to a length of 0.2 mm, and mounted with *c** parallel to the ϕ axis, the crystal was used to refine the cell parameters. We began collecting new data, but several reflections used as standards showed more than a 10% loss in intensity after only one-third of the way through. A comparison with the data from the original crystal left no doubt that both crystals had the same structure; but, thereafter, these new data were abandoned.

Results

Solution and Refinement of the Structure. The structure was solved by the heavy atom method. From a sharpened Patterson synthesis all vectors from the three heavy atoms were located, using the Harker section (*u*, $1/2$, *w*) and Harker line ($1/2$, *v*, 0). A Fourier synthesis, with phases determined from the heavy atoms, yielded the structure.

Atomic parameters were refined by the method of least squares with block-diagonal approximation, each block containing the parameters of one atom. The quantity minimized was

$$\sum_H w_H \left(|F_H^o| - \frac{1}{k} |F_H^c| \right)^2$$

where $w_H = (1/f_{oxy})$. Scattering factor values for Cl⁻, S, O, N, and C were obtained from ref 10 and for H from Stewart, Davidson, and Simpson.¹² With individual anisotropic thermal factors for all the non-hydrogen atoms, the structure was refined to an *R* of 0.072. An electron density difference synthesis showed the positions of all the hydrogen atoms at peak heights from 0.4 to 0.7 eÅ⁻³, and the succeeding structure refinement included the hydrogens with individual isotropic thermal factors.

Real and imaginary parts of the anomalous dispersion corrections¹⁰ were applied to the scattering factors of Cl⁻, S, and O. The final *R* value was 0.056 for all observed reflections. In the last cycle of refinement, all the non-hydrogen parameters shifted by less than a tenth of their estimated standard deviations (esd), and the hydrogen parameters by no more than a third.¹³

Bond Lengths and Angles. The refined atomic

(8) T. F. Furnas, Jr., and D. Harker, *Rev. Sci. Instrum.*, **26**, 449 (1955).

(9) P. Coppens in "Crystallographic Computing," F. R. Ahmed, Ed., Munksgaard Publishers, Copenhagen, 1970, pp 255-270.

(10) "International Tables for X-ray Crystallography," Vol. III, 2nd ed, Kynoch Press, Birmingham, England, 1968, pp 166, 202-207, 214.

(11) It is noteworthy that crystal I of *meso*-lanthionine dihydrochloride came from a solution of DL-lanthionine and crystal II from a solution of L- and *meso*-lanthionine. Gross and Morell (see ref 3) have observed that L-lanthionine transforms to *meso*- and DL-lanthionine at a ratio of 0.43:0.57 "when exposed to the conditions of standard acid hydrolysis."

(12) R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, **42**, 3175 (1965).

(13) See paragraph at end of paper regarding supplementary material.

Table II. Final Atomic Fractional Coordinates and Thermal Parameters^a

Atom	x	y	z	b ₁₁	b ₂₂	b ₃₃	b ₁₂	b ₁₃	b ₂₃
Cl(1)	0.0258 (2)	-0.34386 (7)	-0.2673 (3)	0.0104 (2)	0.00160 (3)	0.0294 (5)	-0.0002 (1)	0.0066 (4)	0.0017 (2)
Cl(2)	0.4143 (2)	0.37819 (6)	0.0214 (3)	0.0088 (1)	0.00145 (3)	0.0261 (4)	-0.0007 (1)	-0.0042 (4)	0.0004 (2)
S	0.3958 (1)	-0.43922 (6)	-0.5648 (3)	0.0079 (1)	0.00085 (2)	0.0245 (4)	0.00022 (9)	0.0022 (4)	0.0005 (2)
O(1)	0.0719 (5)	-0.5956 (2)	-0.1710 (8)	0.0105 (5)	0.0020 (1)	0.024 (1)	-0.0035 (4)	0.006 (1)	-0.0011 (6)
O(2)	0.1491 (4)	-0.5091 (2)	0.0462 (7)	0.0086 (5)	0.0019 (1)	0.022 (1)	0.0002 (3)	0.003 (1)	-0.0005 (6)
O(3)	0.2550 (5)	-0.2410 (2)	-0.9087 (8)	0.0136 (6)	0.0016 (1)	0.030 (2)	0.0043 (4)	-0.001 (2)	0.0026 (7)
O(4)	0.1991 (5)	-0.2126 (2)	-0.5484 (8)	0.0124 (6)	0.0015 (1)	0.028 (2)	0.0024 (4)	0.000 (1)	0.0013 (6)
N(1)	0.2405 (5)	-0.5727 (2)	-0.5041 (9)	0.0100 (6)	0.0011 (1)	0.023 (2)	-0.0013 (4)	0.006 (1)	-0.0010 (6)
N(2)	0.3727 (6)	-0.2964 (2)	-0.3411 (10)	0.0142 (7)	0.0011 (1)	0.029 (2)	0.0013 (5)	-0.013 (2)	-0.0002 (7)
C(1)	0.3140 (6)	-0.4673 (2)	-0.3059 (10)	0.0080 (6)	0.0010 (1)	0.024 (2)	-0.0002 (4)	0.000 (2)	0.0004 (7)
C(2)	0.1982 (6)	-0.5151 (2)	-0.3611 (10)	0.0080 (6)	0.0011 (1)	0.022 (2)	-0.0004 (4)	0.001 (2)	0.0003 (7)
C(3)	0.1379 (6)	-0.5392 (3)	-0.1359 (10)	0.0076 (6)	0.0015 (1)	0.020 (2)	-0.0010 (4)	-0.002 (2)	0.0008 (7)
C(4)	0.2901 (6)	-0.3705 (3)	-0.6698 (10)	0.0082 (6)	0.0011 (1)	0.021 (2)	-0.0001 (4)	0.000 (2)	0.0006 (7)
C(5)	0.3513 (6)	-0.3030 (3)	-0.5961 (11)	0.0084 (6)	0.0010 (1)	0.030 (2)	0.0010 (4)	-0.006 (2)	0.0009 (7)
C(6)	0.2606 (6)	-0.2470 (3)	-0.6810 (11)	0.0091 (6)	0.0011 (1)	0.026 (2)	0.0007 (4)	-0.006 (2)	-0.0006 (7)

Atom	x	y	z	B, ^b Å ²	Atom	x	y	z	B, Å ²
H(1)	0.378 (5)	-0.487 (3)	-0.209 (9)	1.5	H(8)	0.219 (6)	-0.374 (3)	-0.594 (10)	2.2
H(2)	0.286 (7)	-0.431 (3)	-0.215 (12)	3.1	H(9)	0.291 (6)	-0.371 (3)	-0.833 (10)	1.8
H(3)	0.121 (6)	-0.490 (3)	-0.477 (11)	2.5	H(10)	0.451 (7)	-0.298 (4)	-0.621 (13)	4.3
H(4)	0.287 (8)	-0.564 (4)	-0.650 (14)	4.5	H(11)	0.285 (10)	-0.297 (5)	-0.246 (17)	7.0
H(5)	0.164 (7)	-0.596 (4)	-0.538 (13)	3.9	H(12)	0.396 (8)	-0.250 (4)	-0.294 (14)	4.5
H(6)	0.286 (9)	-0.598 (5)	-0.410 (17)	6.7	H(13)	0.442 (8)	-0.334 (4)	-0.265 (14)	5.0
H(7)	0.042 (6)	-0.611 (3)	-0.036 (12)	3.0	H(14)	0.202 (7)	-0.208 (4)	-0.953 (13)	4.1

^a The thermal factor for atoms having anisotropic parameters is given by the expression $\exp\{-b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl\}$. Estimated standard deviations, obtained from the least-squares matrix, are indicated in parentheses. ^b The average esd for B is 1.6 Å².

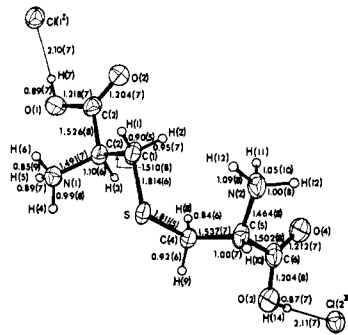


Figure 1. Valence bond lengths (in Å). Esd's are given in parentheses. This drawing and those in Figures 2, 3, and 4 were made with the ORTEP program, using 50% probability ellipsoids for the non-hydrogen atoms and 0.08-Å radii for the hydrogens.

parameters listed in Table II were used to calculate the bond lengths and angles (Figures 1 and 2, respectively) of *meso*-lanthionine dihydrochloride. The distances and angles not involving hydrogen atoms are commensurate with the corresponding ones observed in previously reported structures of amino acids containing sulfur (Table I), as well as with the corresponding average values (about C^α) reported by Marsh and Donohue.¹⁴ In general, there is reasonable agreement between the halves of the molecule, with equivalent bond lengths and angles differing by 1.6 esd's on the average. However, larger differences are present, up to 5 esd's, which have no apparent simple explanation. The covalent bond lengths from hydrogen to carbon, nitrogen, and oxygen average about 0.1 Å shorter than comparable lengths observed in neutron diffraction studies, as is usually found.¹⁵

Conformation of the Molecule. The torsion angles

(14) R. E. Marsh and J. Donohue, *Advan. Protein Chem.*, **22**, 235 (1967).

(15) W. C. Hamilton and J. A. Ibers, "Hydrogen Bonding in Solids," W. A. Benjamin, New York, N. Y., 1968, pp 52, 63-66.

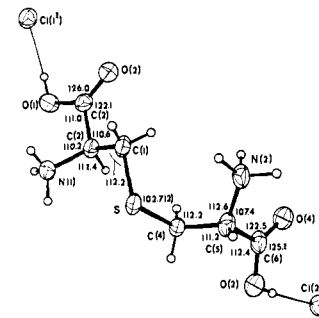


Figure 2. Valence bond angles, excluding those involving hydrogen atoms (in deg). Esd's are 0.4-0.6°. The largest difference between equivalent bonds and angles is between the angles N-C^α-C.

Table III. Torsion Angles

Torsion angle description	IUPAC-IUB designation ^b	Torsion angle value, deg
$\tau_2(\text{C}^{\beta'}-\text{S}^{\gamma}-\text{C}^{\beta}-\text{C}^{\alpha})^a$	(χ_1^2, χ_2^2)	$\pm (85, 100)$
$\tau_2(\text{S}^{\gamma}-\text{C}^{\beta}-\text{C}^{\alpha}-\text{N})$	(χ_1^1, χ_2^1)	$\pm (54, -58)$
$\tau_2(\text{S}^{\gamma}-\text{C}^{\beta}-\text{C}^{\alpha}-\text{C})$		$\pm (178, -179)$
$\tau_2(\text{N}-\text{C}^{\alpha}-\text{C}=\text{O}')$	(ψ_1^1, ψ_2^1)	$\pm (147, -13)$

^a $\tau_2(\text{C}^{\beta'}-\text{S}^{\gamma}-\text{C}^{\beta}-\text{C}^{\alpha})$ designates the two equivalent torsion angles $\tau[\text{C}(4)-\text{S}-\text{C}(1)-\text{C}(2)]$ and $\tau[\text{C}(1)-\text{S}-\text{C}(4)-\text{C}(5)]$, in that order; hence, the subscript "2". The sign " \pm " refers to the two enantiomorphs in the structure, with the upper sign designating the conformation of the molecule in Table II. ^b IUPAC-IUB Commission on Biochemical Nomenclature, *J. Mol. Biol.*, **52**, 1 (1970).

found in *meso*-lanthionine are listed in Table III. It is most interesting that the sulfur atom is \pm synclinal¹⁶ to the nitrogen atoms and \pm antiperiplanar¹⁶ to the carboxyl carbon atoms. Although similar conformations have been found in related structures studied in our laboratory (see the first paragraph of this paper), the previously reported structures in Table

(16) W. Klyne and V. Prelog, *Experientia*, **16**, 521 (1960).

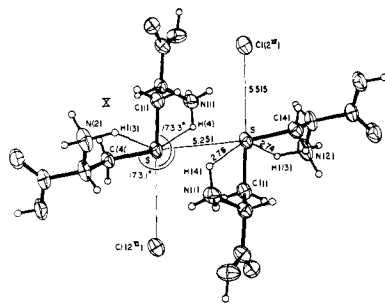


Figure 3. The environment of sulfur (distances in Å). Atoms C(1), S, C(4), and Cl(2^{X1}), and atoms C(1^X), S^X, C(4^X), and Cl(2^{V1}) related by a center of inversion are nearly in a plane. The S...H contacts are directed away from this plane on either side. This environment suggests that S^γ's electronic repulsion is somewhat weaker in the plane through C^{β'}-S^γ-C^β than in the direction normal to it.

I most commonly have shown S^γ + synclinal to N and - synclinal to C.¹⁷ An extensive comparison of all the conformation angles found in the structures of L-cystine, L-cysteine, and their derivatives is in preparation.

Hydrogen Bonding. Both hydrogen atoms of the carboxyl groups form nearly linear and relatively strong hydrogen bonds to the chloride ions (Table IV), whereas

Table IV. Hydrogen Bonds Involving the Carboxyl Groups

D-H...A ^a	Distance (esd), Å		Angle (esd), deg
	H...A	D...A	D-H...A
O(1)-H(7)...Cl(1 ^b)	2.10 (7)	2.992 (5)	175 (6)
O(3)-H(14)...Cl(2 ¹¹)	2.11 (7)	2.970 (5)	172 (7)

^a D is the donor and A is the acceptor atom. ^b The following superscripts distinguish atoms related, by symmetry operations, to those in Table II: none, *x, y, z*; I, $-x, -1 - y, -z$; II, $1/2 - x, -1/2 + y, -1 - z$; III, $x, -1 + y, -1 + z$; IV, $x, y, -1 + z$; V, $-x, -1 - y, -1 - z$; VI, $x, -1 + y, z$; VII, $x, y, 1 + z$; VIII, $1/2 + x, -1/2 - y, z$; IX, $1 - x, -y, -z$; X, $1 - x, -1 - y, -1 - z$; XI, $1 - x, -y, -1 - z$; XII, $x, 1 + y, z$; XIII, $-1/2 + x, -1/2 - y, z$.

Table V. Hydrogen Bonds and Weaker Hydrogen Interactions Involving the Amino Groups

D-H...A ^a	Distance (esd), Å		Angle (esd), deg	
	H...A ₁	D...A ₁	H...A ₁	A ₁ ...D...A ₂
D-H...A ₂	H...A ₂	D...A ₂	H...A ₂	(sum) ^b
N(1)-H(4)...Cl(2 ¹¹)	2.60 (8)	3.431 (5)	142 (6)	110 (3)
N(1)-H(4)...S	2.76 (8)	3.122 (5)	102 (5)	(354)
N(1)-H(5)...Cl(1 ^V)	2.44 (7) ^c	3.313 (5)	165 (6)	95 (3)
N(1)-H(5)...O(1)	2.33 (7)	2.634 (7)	100 (5)	(360)
N(1)-H(6)...O(4 ¹¹)	2.32 (10)	2.895 (6)	125 (8)	84 (3)
N(1)-H(6)...Cl(2 ^{V1})	2.74 (10)	3.505 (5)	150 (8)	(359)
N(2)-H(11)...O(3 ^{V11})	2.27 (10)	3.002 (7)	126 (7)	93 (3)
N(2)-H(11)...Cl(1)	2.71 (10)	3.588 (6)	141 (7)	(360)
N(2)-H(12)...Cl(1 ^{V111})	2.27 (8) ^c	3.219 (5)	157 (6)	
N(2)-H(13)...Cl(2 ^{1X})	2.12 (8) ^c	3.159 (6)	158 (6)	100 (3)
N(2)-H(13)...S	2.74 (8)	3.163 (5)	102 (5)	(360)

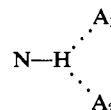
^a D is the donor and A is a possible acceptor atom. ^b Sum = $\langle (D-H...A_1 + D-H...A_2 + A_1...H...A_2) \rangle$. ^c Considered as a hydrogen bond.

(17) A. V. Lakshminarayanan, V. Sasisekharan, and G. N. Ramachandran in "Conformation of Biopolymers," Vol. I, G. N. Ramachandran, Ed., Academic Press, New York, N. Y., 1967, pp 61-82.

the amino hydrogens show multiple, bent contacts with electronegative atoms (Table V). Each of five of the amino hydrogens lies in the plane through two contacting atoms and the bonded nitrogen, as seen by the sum of the angles about the hydrogen atom.

All the contact distances with the amino hydrogen atoms are less than the sum of the H and A van der Waals radii, using Pauling's values¹⁸ for S (1.85 Å), Cl⁻ (1.8 Å), and O (1.4 Å) and Baur's value¹⁹ for H (1.0 Å). An additional contact, at the limit of the van der Waals contact distance, exists between H(4) and O(2^{1V}); the distances and angle, H...A, N...A, and N-H...A are respectively 2.40 (8) Å, 2.961 (6) Å, and 115 (5)°.

Three contacts in Table V are considered as hydrogen bonds, while the rest are considered as hydrogen interactions.^{20,21} The planar configuration



has been observed in other structures (see ref 20), including that of 3,3,3',3'-tetramethyl-D-cystine dihydrochloride,⁷ and can be understood in terms of electrostatic forces between the electropositive hydrogen atom and the two electronegative acceptors.

Sulfur Environment. The sulfur atom has four non-bonded atomic contacts (Figure 3, Table VI). An

Table VI. Contacts with Sulfur

S...X	Distance (esd), Å	Directed distance (Å) of X from the C(1)-S-C(4) plane
	S...X	
S...H(4)-N(1)	2.76 (8)	2.41
S...H(13)-N(2)	2.74 (8)	-2.48
S...S ^X	3.251 (2)	0.058
S...Cl(2 ^{X1})	3.515 (2)	-0.386

unusually short S...S^X contact distance, 3.251 (2) Å, exists between two sulfide (C^{β'}-S^γ-C^β) groups that are almost coplanar across the center of inversion at $(1/2, -1/2, -1/2)$; this distance is 0.45 Å shorter than the accepted van der Waals contact distance.¹⁸ A second sulfur contact, with Cl⁻, is also directed close to the plane through the sulfide group (Table VI). The remaining two contacts with sulfur, the intramolecular S...H-N contacts (Table V), are, in contrast, directed less than 30° from the normal to either side of the plane through C(4)-S-C(1).

Assuming sulfur's 3p orbitals to be unhybridized, that orbital containing an unshared pair of electrons should extend from S normal to the plane through C(4)-S-C(1),²² with its maximal electron density on either side of this plane 0.81 Å from the sulfur atom.²³ The plane itself is a nodal surface for *this* 3p orbital,²²

(18) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, p 260.

(19) W. H. Baur, *Acta Crystallogr., Sect. B*, **28**, 1456 (1972).

(20) R. Parthasarathy, *Acta Crystallogr., Sect. B*, **25**, 509 (1969).

(21) T. F. Koetzle, W. C. Hamilton, and R. Parthasarathy, *Acta Crystallogr., Sect. B*, **28**, 2083 (1972).

(22) C. C. Price and S. Oae, "Sulfur Bonding," Ronald Press, New York, N. Y., 1962, pp 1-7.

(23) J. C. Slater, "Quantum Theory of Molecules and Solids," Vol. 2, McGraw-Hill, New York, N. Y., 1965, p 103.

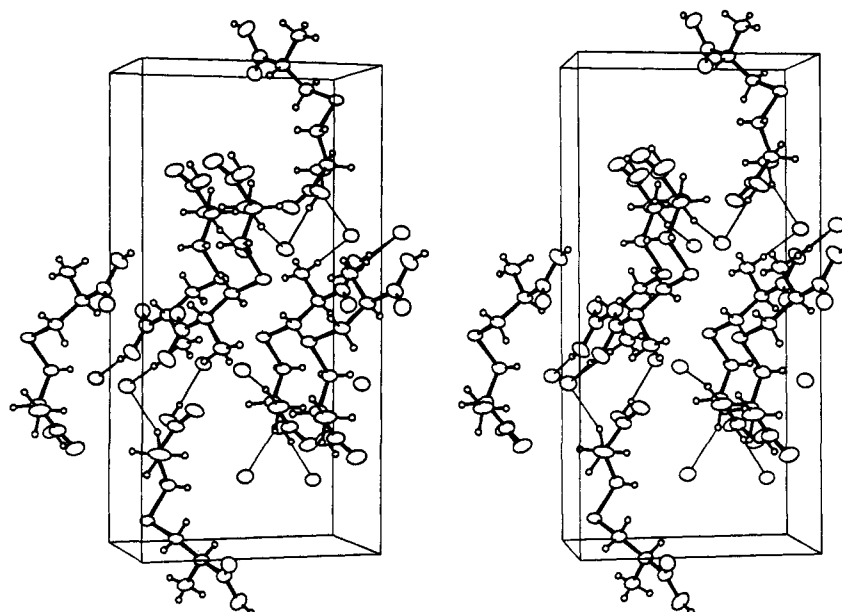


Figure 4. The packing of *meso*-lanthionine dihydrochloride; a stereo pair. The positive *a* direction points left. The five hydrogen bonds (Tables IV and V) are shown, but not the weaker hydrogen interactions. The chloride ions lie between wavy layers of *meso*-lanthionine cations.

so that near the plane the electron density of the unshared pair of 3p electrons should be quite small.

The $S \cdots S^X$ and $S \cdots Cl(2^{X1})$ contacts lie nearly in this nodal plane. Since there is no theoretical justification to infer a $S \cdots S^X$ attraction, nor the presence of strong forces in the crystal that could squeeze the sulfur atoms close together, the orientation of this short contact distance suggests for sulfur a somewhat weaker electronic repulsion (or a smaller van der Waals radius, 1.625 Å) in the plane through $C^{\beta'}-S^{\gamma}-C^{\beta}$ than in the direction normal to this plane. The disposition of the $S \cdots H(4)$ and $S \cdots H(13)$ contacts nearly normal to the sulfide plane, on the other hand, permits weak hydrogen interactions with sulfur's unshared pair of 3p electrons. It should be noted that the conformation angles $\tau_2(C^{\beta'}-S^{\gamma}-C^{\beta}-C^{\alpha})$ of $\pm (85^\circ, 100^\circ)$ facilitate $S \cdots H$ directions favorable for these interactions.

The environment of the sulfur atom cannot be so readily interpreted electronically if complete sp^3 hybridization is assumed for sulfur. Although the $S \cdots S^X$ contact will lie in a "nodal" plane between the hybridized orbitals containing sulfur's two unshared pairs of electrons, the $S \cdots H-N$ contacts will be directed $40-60^\circ$ from these orbitals. Additional evidence, found by us in the structure of 3,3,3',3'-tetramethyl-D-cystine dihydrochloride⁷ and elsewhere,^{24,25} tends to support a model for the electronic distribution about S^{γ} based on pure p sulfur bonding, and will be discussed in a later paper.

Packing. The molecule of *meso*-lanthionine extends itself about 10 Å mainly along the *b* axis. Wavy layers, composed of molecules related by the twofold screw axis along *b* and the translation along *c*, are stacked normal to the a^* axis and are spaced $(2a^*)^{-1} = 4.90$ Å apart (Figure 4). Adjacent molecular layers have opposite chirality, and the chloride ions lie between them.

(24) J. L. Flippen and I. L. Karle, *J. Phys. Chem.*, **74**, 769 (1970).

(25) Short contacts with sulfur near the plane through $S^{\gamma'}-S^{\gamma}-C^{\beta}$ are found in the structures of L-cystine, L-cystine dihydrochloride, L-cystine dihydrobromide, L-cystinediamide dihydrochloride (all in Table I), and L-cystine dihydrobromide dihydrate.⁸

Table VII. Additional Interatomic Distances

X...Y	Distance (esd), Å		
	X...Y	X...Y	
Cl(1)...H(8)	2.81 (6)	O(1)...H(6)	2.57 (9)
Cl(1)...H(2)	3.10 (6)	O(2)...H(2)	2.59 (7)
Cl(2)...C(3 ^{X11})	3.265 (6)	O(2)...C(3 ^I)	3.054 (7)
Cl(2)...H(1 ^{X11})	3.04 (5)	O(4)...H(10 ^{X111})	2.46 (7)
S...H(1 ^X)	3.03 (5)	O(4)...H(12)	2.47 (8)
		O(4)...H(11)	2.53 (10)

The position of Cl(1) is stabilized by three hydrogen bonds and one weaker $N-H \cdots Cl^-$ interaction; that of Cl(2) is stabilized by two hydrogen bonds and two weaker $N-H \cdots Cl^-$ interactions (see Tables IV and V). Additional contacts with the chloride ions are given in Tables VI and VII. The $Cl(2) \cdots C(3^{X11})$ contact (Table VII) is directed 2° from the normal to the plane through the carboxyl group at $C(3^{X11})$.

The strongest contacts between the lanthionine molecules appear to be the hydrogen interactions $N(1)-H(6) \cdots O(4^{11})$ and $N(2)-H(11) \cdots O(3^{VI1})$ (Table V), occurring within each molecular layer. Between adjacent layers, the most important packing distance is between S and S^X (Table VI). Additional short interatomic distances are listed in Table VII.

Acknowledgment. It has been our pleasure to have had many interesting discussions of this work with Dr. D. Harker, whose advice and encouragement have been invaluable. We are grateful also to Drs. J. Edmonds and P. Coppens for making available to us their program for absorption correction. We thank Dr. G. Tsoucaris for bringing the lanthionine compound to our attention, Mrs. C.-L. Rosenfield for her excellent assistance with the drawings, and our referee for his helpful criticisms. The following programs were used in the course of the analysis: BDL-6 (a modified version of the Gaentzel, Sparks, and Trueblood ACA Old Program #317), a general program for Fourier summation by S. T. Rao, and ORTEP by C. K. Johnson. We

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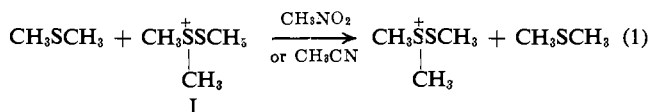
Supplementary Material Available. A list of $|F_o|$ and $|F_c|$ and a diagram of the geometry of crystal I will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JACS-74-1925.

Communications to the Editor

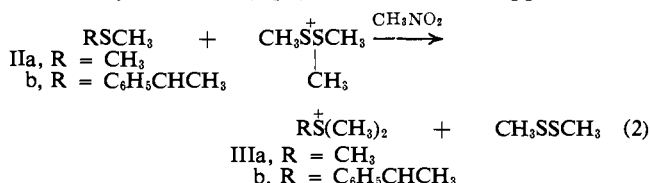
Alkylated Disulfides. A Degenerate Rearrangement

Sir:

Alkylated disulfide salts of the type $R_2S^+SR^-$ are often encountered as intermediates in cleavage reactions of S-S bonds assisted by electrophiles.^{1,2} Although they are not generally isolable, dimethylmethylthio-sulfonium fluoroborate (I) is relatively stable and can be prepared by the methylation of methyl disulfide with trimethyloxonium fluoroborate.³ The ease with which the S-S bond of I is cleaved is evident in the rapid exchange reaction it undergoes with methyl sulfide (eq 1).⁴⁻⁶ We find, however, that an irreversible reaction



intervenes on prolonged standing or heating of these reagents which leads to trimethylsulfonium fluoroborate and methyl disulfide (eq 2). This reaction appears to be



a straightforward displacement at methyl carbon of I by methyl sulfide. 1-Phenylethyl methyl sulfide (IIb) also reacts with I in nitromethane to give the sulfonium salt IIIb, but, in contrast to IIa, we find this reaction is not a simple SN2 displacement and involves an alkylated disulfide intermediate that rapidly undergoes a degenerate carbon-to-sulfur rearrangement. The evidence for this follows. (1) Using RSCD_3 where $\text{R} = 1$ -phenylethyl, the deuterium label was found in the disulfide and *not* in the salt IIIb.⁷⁻⁹ This means that the

reaction of eq 2 is not in this case a simple methyl transfer from I to IIb but involves C-S cleavage of the sulfide. (2) The disulfide obtained from RSCD_3 and I was found by mass spectral analysis to be a mixture of CH_3SSCH_3 , CH_3SSCD_3 , and CD_3SSCD_3 .¹⁰ Furthermore, unreacted sulfide recovered from the reaction of a twofold excess of RSCD_3 with I showed that extensive methyl exchange had occurred. The ratio of RSCH_3 to RSCD_3 was determined by nmr as 1:2. (3) The (-)-enantiomer of RSCH_3 , IIb,¹¹ gave *racemic* salt IIIb on reaction with I. Control reactions showed that IIIb was configurationally stable under the reaction conditions¹² and that IIb was likewise stable except in the presence of I. (4) Nmr spectra and optical rotations recorded as frequently as possible after mixing the reagents showed that reaction was substantially complete within 15 min at room temperature. Resonances due to products were immediately apparent;⁹ some methyl sulfide was also evident but disappeared as the reaction proceeded. (5) Most significantly, the sulfide is evidently racemized during reaction since nitromethane solutions of a 2:1 mole ratio of (-)-IIb to I lost almost 80% of its activity within minutes of mixing and thereafter slowly decayed to zero (see Figure 1); since the product salt is racemic, the residual activity of the sulfide would be 50% of its initial value had no racemization occurred.

The foregoing results can be explained by the mechanistic sequence of Scheme I. Rapid S-S cleavage of I is shown to occur *reversibly* in the *first step* by nucleophilic attack of II at dicoordinate sulfur to give the

(7) RSCD_3 was prepared from the sodium salt of 1-phenylethanethiol⁹ and CD_3I .

(8) S. Siegel and A. F. Graefe, *J. Amer. Chem. Soc.*, **75**, 4521 (1953).

(9) The salt IIIb isolated from reaction 2 was identical with that prepared from the methylation of IIb with trimethyloxonium fluoroborate; nmr in CH_3NO_2 δ 2.65 and 2.91 (s, 3, CH_3S), 1.92 (d, 3, $J = 7$ Hz, $\text{CH}_3\text{-CH}$), 4.82 (quart, 1, $J = 7$ Hz, CH_3CH), and 7.56 (m, 5, C_6H_5).

(10) Using a slight excess of RSCD_3 over I, the relative intensity of the M^+ peaks 94, 97, and 100 of methyl disulfide was 10:28:20.

(11) (-)-IIb, prepared from sodium methylthiolate and 1-phenylethyl chloride $[\alpha]^{25\text{D}} + 76.5^\circ$ in ethanol, had $[\alpha]^{25\text{D}} - 112.9^\circ$; the chloride was obtained from 1-phenylethanol $[\alpha]^{25\text{D}} - 42.6^\circ$ and phosphorus oxychloride and pyridine in carbon disulfide (R. L. Burwell, A. D. Shields, and H. Hart, *J. Amer. Chem. Soc.*, **76**, 908 (1954); W. J. Chambers, W. R. Brasen, and C. R. Hauser, *ibid.*, **79**, 879 (1957)); 1-phenylethanol was resolved by way of the brucine salt of the acid phthalate as described in A. J. H. Houssa and J. Kenyon, *J. Chem. Soc.*, 2260 (1930); J. Kenyon, "Organic Syntheses," Coll. Vol. I, Wiley, New York, N. Y., 1941, p 418; E. D. Hughes, C. K. Ingold, and A. D. Scott, *J. Chem. Soc.*, 1202 (1937).

(12) (-)-IIIb $[\alpha]^{25\text{D}} - 20.9^\circ$ (CH_3NO_2) was prepared as the fluoroborate salt by the methylation of IIb $[\alpha]^{25\text{D}} - 29.95^\circ$ (CH_3NO_2).

(1) J. L. Kice, *Accounts Chem. Res.*, **1**, 58 (1968); J. L. Kice and J. P. Cleveland, *J. Amer. Chem. Soc.*, **95**, 104 (1973).

(2) B. Miller and C. H. Han, *Chem. Commun.*, 623 (1970); *J. Org. Chem.* **36**, 1513 (1971).

(3) (a) G. K. Helmkamp, H. N. Cassey, B. A. Olsen, and D. J. Pettitt, *J. Org. Chem.*, **30**, 933 (1965); (b) H. Meerwein, K. F. Zenner, and R. Gipp, *Justus Liebigs Ann. Chem.*, **688**, 67 (1965).

(4) J. L. Kice and N. A. Favstritsky, *J. Amer. Chem. Soc.*, **91**, 1751 (1969).

(5) S. H. Smallcombe and M. C. Caserio, *J. Amer. Chem. Soc.*, **93**, 5826 (1971).

(6) The specific rate k for the reaction of eq 1 in nitromethane at 40° has been determined by nmr methods as $4.5 \times 10^5 \text{ M}^{-1} \text{ sec}^{-1}$ (ref 4 and 5).