mission to use the EDSAC. One of us (G. K.) thanks the Nuffield Foundation for the award of an Indian Travelling Fellowship in Natural Sciences.

References

Brinkman, J. A. (1954). *J. Appl. Phys.* **25**, 961.
Cochran, W. (1956). *Acta Cryst.* **9**, 259.
Cochran, W. & Kartha, G. (1956). *Acta Cryst.* **9**, 941.
Cooper, H. G., Koehler, J. S. & Marx, J. W. (1954). *Phys. Rev.* **94**, 496.
Eshelby, J. D. (1954). *J. Appl. Phys.* **25**, 255.
Huang, K. (1947). *Proc. Roy. Soc.* A, **190**, 102.
Huntingdon, H. B. (1953). *Phys. Rev.* **91**, 1092.
James, R. W. (1948). *The Optical Principles of the Diffraction of X-rays*. London: Bell.
Kinchin, G. H. & Pease, R. S. (1955). *Rep. Progr. Phys.* **18**, 1.
Seitz, F. (1949). *Disc. Faraday Soc.* **5**, 271.
Tucker, C. W. & Sampson, J. B. (1954). *Acta Metallurg.* **2**, 433.
Tucker, C. W. & Senio, P. (1955*a*). *Acta Cryst.* **8**, 371.
Tucker, C. W. & Senio, P. (1955*b*). *Phys. Rev.* **99**, 1777.

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The Crystal Structure of Cycloserine Hydrochloride*

By J. W. Turley and R. Pepinsky

X-Ray and Crystal Analysis Laboratory, Department of Physics, The Pennsylvania State University, State College, Pennsylvania, U.S.A.

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The hydrochloride of cycloserine, 4-amino-3-isoxazolidone, is orthorhombic, $P2_12_12_1$, with four molecules in a unit cell of dimensions $a = 9{\cdot}72$, $b = 10{\cdot}34$, $c = 5{\cdot}73$ Å. A successful X-ray analysis was accomplished by means of ($hk0$) and ($h0l$) projections, and three-dimensional syntheses were used to refine atomic coordinates. Bond distances are normal, with the five-membered ring appearing nearly planar. Each chlorine atom forms three weak hydrogen bonds with amino nitrogens, and the ring nitrogen and oxygen have a close approach to the slightly enolized ketone oxygen.

Introduction

Cycloserine is a new broad-spectrum antibiotic produced by *Streptomyces orchidaceus*. The compound was discovered by R. Harned and E. Kropp, and isolated and crystallized by a research team of the Commercial Solvents Corporation (Welch, Putnam & Randall, 1955; Harned, Hidy & Kropp la Baw, 1955). Subsequent chemical and clinical studies on the material have been carried out jointly by groups at the Commercial Solvents Corporation and Eli Lilly and Company. (The name for the compound used by the latter group is Seromycin.)

Cycloserine is an unusual antibiotic, dissimilar in chemical structure with any previously identified, and the culture which produces it is different from any previously known. It is active against both gram-positive and gram-negative bacteria, and seems to differ in its mode of action from other antibiotics presently known. Contrary to *in vitro* results, it has a high degree of *in vivo* efficacy, and is equally effective by oral and subcutaneous routes (Cuckler, Frost, McClelland & Solotorovsky, 1955).

The investigation of the crystal structure of this compound was suggested by Dr Jerome Martin of the Commercial Solvents Corporation, and crystalline material was furnished by him and by Dr Harry Rose of Eli Lilly and Company.

The X-ray analysis completely confirms the chemical elucidation of the antibiotic structure, and provides accurate measurements of bond lengths and angles.

Experimental

Weissenberg photographs of cycloserine reveal the space group as $P2_12_12_1$, with cell constants

$$a = 9{\cdot}72,\ b = 10{\cdot}34,\ c = 5{\cdot}73\ \text{Å}\ .$$

The crystal density, measured by the displacement method using cyclohexane, is 1·598 g.cm.$^{-3}$, from which calculation shows four molecules per unit cell.

X-ray intensity data for the ($hk0$) projection, the ($h0l$) projection, and five layers along the c axis, were obtained from Weissenberg moving-film photographs taken with Cu $K\alpha$ radiation; 616 symmetry-unrelated reflections were recorded with the multiple-film technique, and intensities were estimated visually by comparison with a scale made from a reflection from the same crystal. The c-axis layers were scaled to each other using ($h0l$) data. Lorentz and polariza-

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* Taken from work submitted by J. W. Turley in partial fulfillment of requirements for the degree of Ph.D.

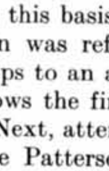
tion factors were applied, and the data were placed on an absolute scale at a later stage of the analysis by comparison with calculated values. All structure-factor calculations were made using McWeeny scattering-factor data (McWeeny, 1953).

Determination of the structure

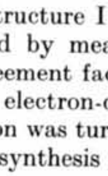
The ($hk0$) projection (114 reflections) was examined first. A Patterson synthesis suggested a position for the chlorine atom, but a Fourier synthesis based on the signs of this atom did not show well-defined peaks, and left considerable doubt about the position of the molecule. Because of uncertainty in choice of this chlorine position from the Patterson map, Sayre's method (Sayre, 1952) was applied in an effort to determine enough signs to confirm or reject these coordinates. Unitary structure factors were calculated using the Wilson curve correction, and all $U_{hk0} \geq 0{\cdot}28$ were tested. Out of 29 U_{hk0}, 20 signs were determined. Adding 14 reflections of amplitudes $0{\cdot}25 \leq U_{hk0} < 0{\cdot}28$, the signs of all 43 reflections were determined. These were used for a Fourier map, which clearly showed seven resolved peaks for the molecule, and confirmed the previously-chosen chlorine position.

At this time, although there was evidence for the presence of a carbonyl oxygen, an amino nitrogen and a five-membered ring, the chemical structure of the compound was unknown. Therefore, the first structure-factor calculations were made by assigning a nitrogen weight to all atoms, with the hope that in an $F_o - F_c$ Fourier synthesis errors due to wrong weight assignment would be large enough to show carbon atoms in holes and oxygens on peaks. Carbon atom positions were chosen in this way; but nothing definite could be said about the other positions. This left four possible structures, and a structure-factor calculation was done for each. These structures are shown below, together with the resulting agreement factors $R_1 = \Sigma||F_o|-|F_c|| \div \Sigma|F_o|$ and $R_2 = \Sigma(|F_o|-|F_c|)^2 \div \Sigma|F_o|^2$ (Booth, 1948).

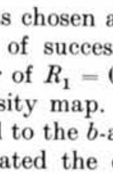
I



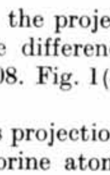
II



III



IV



	I	II	III	IV
R_1	$0{\cdot}137$	$0{\cdot}157$	$0{\cdot}138$	$0{\cdot}156$
R_2	$0{\cdot}0199$	$0{\cdot}0268$	$0{\cdot}0223$	$0{\cdot}0278$

On this basis, structure I was chosen and the projection was refined by means of successive difference maps to an agreement factor of $R_1 = 0{\cdot}108$. Fig. 1(a) shows the final electron-density map.

Next, attention was turned to the b-axis projection. The Patterson synthesis located the chlorine atom;

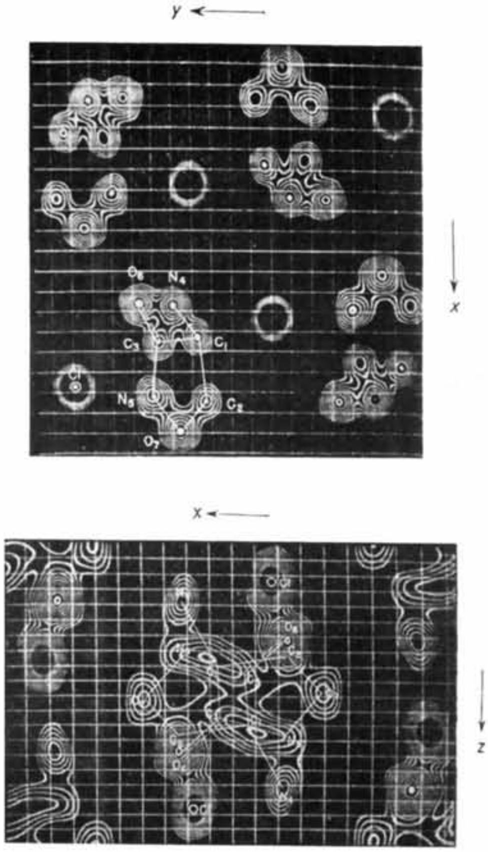


Fig. 1. Cycloserine hydrochloride: final X-RAC electron-density map (a) of the (001) projection with one molecule drawn, (b) of the (010) projection with two molecules drawn to show overlap.

but, again, the Fourier synthesis based on the chlorine atom was of no help. In addition to difficulties arising from wrong phases, two molecules overlap in this projection. However, the chemical structure was now known and the problem reduced to that of finding the z coordinates of the atoms. A one-dimensional application of Fourier-transform principles led to a solution, which was refined to an agreement factor of $R_1 = 0{\cdot}162$. The final electron-density map is shown in Fig. 1(b).

Two three-dimensional structure-factor calculations were done using the IBM 604 calculating punch, and two three-dimensional Fourier syntheses were done on X-RAC (Pepinsky, 1952). Both the F_c and F_o syntheses were done for sections along the x and z axes. The final agreement factor in three dimensions is $R_1 = 0{\cdot}159$.

Results of the analysis

Atomic coordinates corrected for series-termination and phase-lag errors are listed in Table 1, bond lengths and angles in Table 2, and some short intermolecular distances in Table 3. The standard deviations of the

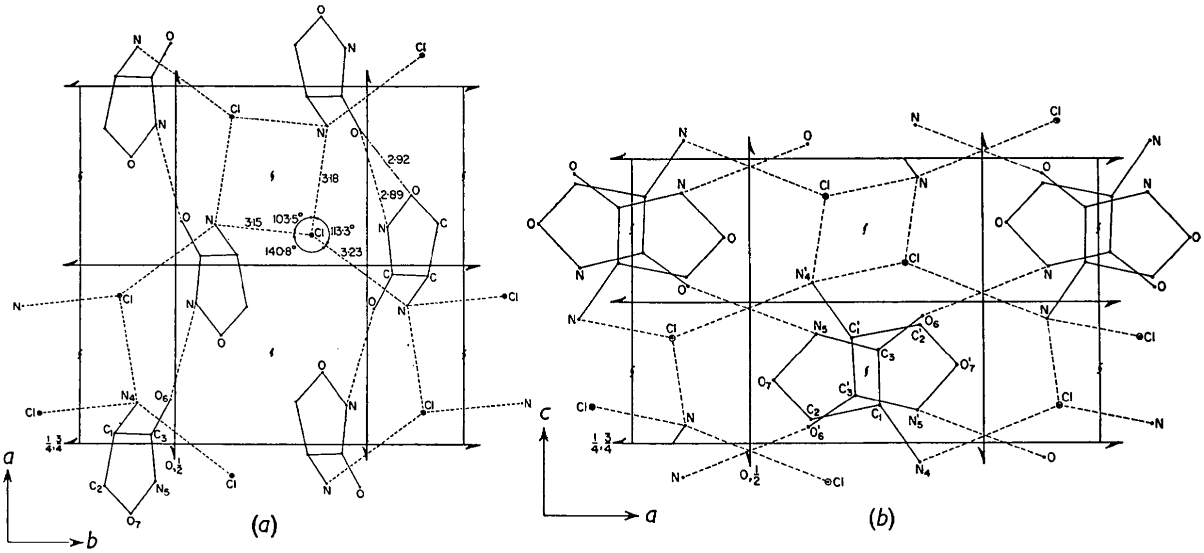


Fig. 2. Cycloserine hydrochloride: schematic projection (*a*) on (001), (*b*) on (010).

Table 1. *Final atomic coordinates for cycloserine*.HCl

	x	y	z
C_1	0·535	0·410	0·130
C_2	0·381	0·440	0·082
C_3	0·525	0·311	0·331
N_4	0·612	0·350	0·934
N_5	0·390	0·304	0·382
O_6	0·622	0·266	0·445
O_7	0·304	0·367	0·231
Cl	0·415	0·104	0·869

Table 2. *Bond lengths and angles in cycloserine*.HCl

C_1–C_3–N_5	105·0°	C_1–C_2	1·55 Å
C_1–C_3–O_6	126·6	C_2–O_7	1·36
O_6–C_3–N_5	127·4	O_7–N_5	1·37
C_3–C_1–C_2	101·8	N_5–C_3	1·35
C_3–C_1–N_4	108·7	C_3–C_1	1·54
C_2–C_1–N_4	115·8	C_3–O_6	1·24
C_1–C_2–O_7	107·9	C_1–N_4	1·48
C_2–O_7–N_5	109·0		
O_7–N_5–C_3	115·6		
N_4'–Cl–N_4	140·6		
N_4–Cl–N_4'	104·0		
N_4'–Cl–N_4''	113·1		

Table 3. *Short intermolecular distances in cycloserine*.HCl

N_4–Cl	3·15 Å
N_4'–Cl	3·18
N_4''–Cl	3·23
O_7–N_5	2·89
O_6–O_7	2·92

Table 4. *Standard deviations of coordinates in cycloserine*.HCl

	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
C_1	0·014 Å	0·013 Å	0·022 Å
C_2	0·021	0·014	0·021
C_3	0·016	0·013	0·019
N_4	0·008	0·008	0·014
N_5	0·011	0·010	0·013
O_6	0·010	0·010	0·011
O_7	0·010	0·010	0·013
Cl	0·003	0·003	0·005

Table 5. *Probable errors in angles and bond lengths in cycloserine*.HCl

C_1–C_3–N_5	±2·2°	C_1–C_2	±0·026 Å
C_1–C_3–O_6	±3·4	C_2–O_7	±0·022
O_6–C_3–N_5	±2·9	O_7–N_5	±0·016
C_3–C_1–C_2	±2·2	N_5–C_3	±0·019
C_3–C_1–N_4	±3·3	C_3–C_1	±0·026
C_2–C_1–N_4	±2·6	C_3–O_6	±0·019
C_1–C_2–O_7	±2·2	C_1–N_4	±0·022
C_2–O_7–N_5	±2·3		
O_7–N_5–C_3	±2·3		

coordinates were estimated using the expression (Cruickshank, 1949)

$$\sigma(x_{rj}) = \frac{1}{V}\frac{2\pi}{a_j}\left\{\sum_3 h_j \Delta F^2\right\}^{\frac{1}{2}} \Big/ \frac{\partial^2\varrho}{\partial x_j^2}\ ,$$

where x_{rj} is the jth coordinate of the rth atom, a_j is the cell side, h_j are plane indices, $\Delta F = |F_o|-|F_c|$, $\partial^2\varrho/\partial x_j^2$ is the curvature of the peak in the x_j direction, and $\sum_3$ indicates summation over all planes included in the series. Since this expression is derived for centrosymmetric structures, and $P2_12_12_1$ is non-centrosymmetric but contains some zones which are centrosymmetric, values obtained from the above expression are multiplied by a factor of 1·6, rather than the factor of 2 which has been shown to apply to completely non-centrosymmetric structures (Cruickshank, 1950). Table 4 lists these results. Using the general error formula

$$E_f^2 = (\partial f/\partial a)^2E_a^2 + (\partial f/\partial b)^2E_b^2 + (\partial f/\partial c)^2E_c^2 + \dots\ ,$$

where $f(a, b, c, \ldots)$ is the function, E_f is the probable error in the function, and E_a etc. are the probable errors of the independently measured quantities, the probable errors in the bond lengths and angles have been calculated and are listed in Table 5. Finally, Table 6 shows the comparison of some 630 calculated and observed structure factors for the final three-dimensional IBM calculation.*

Fig. 2 shows the general features of the packing. The three N–Cl distances indicate weak hydrogen bonds, and the calculations of N–Cl–N angles show that the four atoms lie nearly in a plane. An interesting point in this structure is the close approach of both the ring oxygen and the ring nitrogen to the carbonyl oxygen of the next molecule. It seems at least possible that a bifurcated hydrogen bond exists here. The plane of atoms 1, 3, 5, and 6 was calculated and found to be

$$0{\cdot}009075x+0{\cdot}1987y+0{\cdot}1577z-1 = 0\,.$$

Of the ring atoms, the oxygen was found to lie furthest from this plane, at a distance of 0·06 Å. Thus the ring is very nearly planar.

This analysis was accomplished under Grant No. A-228 from the National Institutes of Health, and computations on X-RAC were supported by Contract No. N6onr-26916, T.O. 16, with the Office of Naval Research. We are extremely grateful for the assistance of Dr P. F. Eiland at various stages of the analysis.

References

Booth, A. D. (1948). *Fourier Technique in X-ray Organic Structure Analysis*, p. 103. Cambridge: University Press.

Cruickshank, D. W. J. (1949). *Acta Cryst.* **2**, 65.

Cruickshank, D. W. J. (1950). *Acta Cryst.* **3**, 72.

Cuckler, A. C., Frost, B. M., McClelland, L. & Solotorovsky, M. (1955). *Antibiotics and Chemotherapy*, **5**, 191.

Harned, R. L., Hidy, P. H. & Kropp la Baw, E. (1955). *Antibiotics and Chemotherapy*, **4**, 204.

McWeeny, R. (1953). *Acta Cryst.* **6**, 631.

Pepinsky, R. (1952). *Computing Methods and the Phase Problem in X-Ray Crystal Analysis.* (Edited by R. Pepinsky.) The Pennsylvania State College: X-Ray and Crystal Analysis Laboratory.

Sayre, D. (1952). *Acta Cryst.* **5**, 60.

Welch, H., Putnam, L. E. & Randall, W. A. (1955). *Antibiotic Medicine*, **1**, 72.

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* Table 6 has been deposited as Document No. 4852 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D.C., U.S.A. A copy may be secured by citing the Document number and by remitting $2·50 for photoprints, or $1·75 for 35 mm. microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.

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A Method for Converting Experimental X-ray Intensities to an Absolute Scale

By Jan Krogh-Moe*

Department of Physics, University of Missouri, Columbia, Mo., U.S.A.

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A relationship between the density of a sample and an integral over the scattered X-ray intensity is derived. The relationship is shown to be useful in adjusting experimental X-ray intensities to an absolute scale.

In nearly all X-ray work the scattered intensity is observed on an arbitrary relative scale. It is often desirable to obtain the intensities on an absolute scale. In the case of an X-ray amorphous scatterer, this has usually been done by assuming that the observed intensity converges at large scattering angles to the sum of the squares of the atomic form factors and incoherent scattering. This procedure is not quite satisfactory, as it requires accurate measurements of the low intensity scattered at large angles. In addition, the observed intensity will still have appreciable undulations in this region, making a curve-fitting procedure somewhat ambiguous. The purpose of this paper is to develop an analytical method, primarily intended for liquid scattering, but which may also be adapted for crystalline powder patterns. The equations are derived for a system containing one kind of atoms, but the generalization to complex systems is straightforward.

A pair distribution function $\sigma(r)$ is defined by

$$\sigma(r) = \int_V \int_f \varrho(\mathbf{p})\varrho(\mathbf{p}+\mathbf{r})\,df\,dV\,, \qquad (1)$$

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* Present address: Department of Ceramics, The Pennsylvania State University, University Park, Pa., U.S.A.