

## The Crystal and Molecular Structure of the Alkaloid Gerrardine

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The structure of one enantiomorph of the alkaloid gerrardine ( $C_{11}H_{19}O_2S_4N$ ) has been determined from diffractometer data. The final  $R$  value is 0.066 after full-matrix least-squares refinement excluding hydrogen atoms. The molecule is found to be 1-methyl-2,5-bis-(4-hydroxy-1,2-dithiolan-3-yl)pyrrolidine and possesses a strong intramolecular O-H...N hydrogen bond. One dithiolan ring is essentially planar with the central pyrrolidine ring and the other is at right angles to it. Intermolecular O-H...O hydrogen bonds join molecules to form sheets normal to the  $a$  axis.

### Introduction

The alkaloid gerrardine ( $C_{11}H_{19}NO_2S_4$ ) was isolated, crystallized and submitted for structure analysis by Professor F. L. Warren and Dr W. G. Wright of the University of Natal, Pietermaritzburg, who have explained its chemical behaviour, mass- and infrared spectra in terms of its structure as determined here (Wright & Warren, 1967). This is the second alkaloid from species of the genus *Cassipourea* which contains four sulphur atoms per molecule. The other is cassipourine (Cooks, Warren & Williams, 1967; Gafner & Admiraal, 1969). Structural similarities were expected for these two alkaloids but not found. No information on the possible structure of gerrardine was available when submitted for analysis other than its elemental analysis and formula weight.

### Experimental

The original structure analysis was carried out on visually estimated photographic intensity data. This analysis, although basically correct in the structure it gave, was considered too inaccurate for publication as  $R$  was 0.17 and differences of up to 0.2 Å were found between equivalent bonds. Intensities were thus measured diffractometrically when the necessary instrumentation became available. This redetermination of the structure is described here.

All X-ray measurements were made on a crystal which was cut to a cube of 0.5 mm edge from a needle-shaped crystal. Preliminary cell constants, which were obtained using photographic methods, were refined using least-squares procedures on diffractometrically measured spot positions (Busing & Levy, 1967).

The cell data are as follows:

$$a = 17.614 \pm 0.002, b = 12.212 \pm 0.002, (\text{needle axis}) c = 6.79 \pm 0.01 \text{ \AA}.$$

Space group:  $P2_12_12_1$  (absences  $h00$ ,  $0k0$  and  $00l$  for  $h$ ,  $k$  and  $l$  odd respectively).

$$Z = 4, \rho_m = 1.49, \rho_c = 1.48 \text{ g.cm}^{-3},$$

$$\text{formula weight} = 325.5.$$

Densities were measured in  $K_2HgI_4/H_2O$  and bromoform/methanol solutions using flotation methods.

Data were collected using the  $\omega$  scan method on a Hilger & Watts automatic single-crystal diffractometer. Zr-filtered Mo radiation was used ( $\lambda = 0.70926 \text{ \AA}$ ). Background was measured as a function of  $\theta$  by counting at closely spaced points next to a central lattice row. The results obtained were found to agree satisfactorily with measurements made at the positions of the systematic absences. The 832 intensities in one octant with  $\theta \leq 20^\circ$  were measured and, of these, 135 fell below the 'observed' criterion which was taken as three times the background count. These reflexions are marked with asterisks in the  $F_o$  column of Table 2.

Lorentz and polarization corrections were applied to the measured intensities. Absorption corrections were obviated by the low  $\mu R$  value of 0.14 which makes the absorption correction < 1% when intensities are measured at  $\theta$  angles below  $20^\circ$ .

### Structure determination and refinement

The trial structure, excluding hydrogen atoms, was built up from four Fourier syntheses, the first of which was phased on the positions of the four sulphur atoms as established from a Patterson synthesis.

After preliminary refinement with isotropic temperature factors ( $R = 0.12$ ), three cycles of full-matrix least-squares refinement using anisotropic temperature factors and equal weighting resulted in no further significant shifts and gave a final  $R$  value of 0.066. The program used was *ORFLS* of Busing, Martin & Levy (1962), which minimizes  $\sum \omega(|F_o| - |F_c|)^2$ , on an IBM 360/65 computer. The atomic scattering factors used were those of Hanson, Herman, Lea & Skillman (1964).

Table 1. Atomic parameters and their e.s.d.'s

	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>	<i>U<sub>11</sub></i>	<i>U<sub>22</sub></i>	<i>U<sub>33</sub></i>	<i>U<sub>12</sub></i>	<i>U<sub>13</sub></i>	<i>U<sub>23</sub></i>
S(1)	0.2008 (2)	0.0466 (4)	0.0044 (9)	0.0047 (2)	0.0108 (4)	0.0636 (20)	0.0026 (2)	0.0035 (5)	0.0068 (8)
S(2)	0.1371 (2)	0.1342 (3)	0.2046 (6)	0.0040 (1)	0.0081 (3)	0.0345 (12)	0.0000 (2)	0.0022 (4)	0.0059 (6)
S(3)	0.1575 (2)	0.1637 (3)	0.1643 (6)	0.0038 (1)	0.0087 (3)	0.0280 (10)	0.0005 (2)	0.0013 (4)	0.0022 (6)
S(4)	0.2369 (2)	0.0955 (3)	0.3545 (7)	0.0036 (1)	0.0114 (4)	0.0424 (14)	0.0019 (2)	0.0010 (4)	0.0036 (7)
C(1)	0.1670 (8)	0.1133 (12)	0.2180 (23)	0.0044 (6)	0.0112 (14)	0.0366 (48)	0.0035 (8)	0.0002 (15)	0.0016 (24)
C(2)	0.1078 (6)	0.2021 (11)	0.1651 (23)	0.0021 (5)	0.0107 (13)	0.0354 (45)	0.0005 (7)	0.0004 (11)	0.0017 (23)
C(3)	0.1264 (6)	0.2506 (10)	0.0326 (20)	0.0028 (5)	0.0075 (10)	0.0237 (38)	0.0002 (6)	0.0014 (13)	0.0008 (22)
C(4)	0.0704 (7)	0.3412 (11)	0.1044 (22)	0.0031 (5)	0.0076 (11)	0.0347 (45)	0.0012 (7)	0.0014 (13)	0.0004 (27)
C(5)	0.0861 (8)	0.3756 (12)	0.3291 (24)	0.0052 (7)	0.0116 (15)	0.0341 (45)	0.0032 (9)	0.0014 (13)	0.0008 (22)
C(6)	0.0089 (7)	0.3558 (11)	0.4319 (21)	0.0032 (5)	0.0085 (12)	0.0352 (44)	0.0019 (7)	0.0012 (14)	0.0030 (22)
C(7)	0.0276 (7)	0.2685 (10)	0.3032 (20)	0.0027 (5)	0.0072 (11)	0.0269 (39)	0.0012 (6)	0.0017 (12)	0.0011 (20)
C(8)	0.1139 (6)	0.2535 (9)	0.3512 (19)	0.0029 (5)	0.0069 (10)	0.0220 (35)	0.0017 (7)	0.0014 (11)	0.0027 (18)
C(9)	0.1238 (7)	0.1987 (10)	0.5535 (20)	0.0032 (5)	0.0075 (11)	0.0242 (38)	0.0017 (7)	0.0008 (12)	0.0026 (18)
C(10)	0.2086 (7)	0.1695 (11)	0.5744 (22)	0.0036 (5)	0.0075 (11)	0.0330 (42)	0.0016 (7)	0.0006 (13)	0.0006 (22)
C(11)	0.0595 (7)	0.3924 (10)	0.0205 (21)	0.0040 (5)	0.0097 (12)	0.0304 (40)	0.0029 (6)	0.0005 (14)	0.0032 (20)
O(1)	0.0328 (4)	0.1550 (7)	0.1612 (14)	0.0033 (3)	0.0107 (8)	0.0316 (25)	0.0000 (4)	0.0043 (8)	0.0027 (15)
O(2)	0.0779 (4)	0.1037 (7)	0.5696 (13)	0.0041 (3)	0.0077 (7)	0.0268 (26)	0.0004 (4)	0.0007 (8)	0.0009 (12)
N	0.0109 (6)	0.3002 (8)	0.0937 (16)	0.0036 (4)	0.0060 (8)	0.0286 (32)	0.0002 (5)	0.0003 (11)	0.0000 (15)

The final atomic parameters and their estimated standard deviations are given in Table 1 with the  $U_{ij}$  values from the expression

$$\exp[-2\pi^2(h^2a^*U_{11} + k^2b^*U_{22} + l^2c^*U_{33} + 2hka^*b^*U_{12} + 2klb^*c^*U_{23} + 2hla^*c^*U_{13})].$$

The inclusion of hydrogen atoms at their expected positions gave no significant reduction of  $R$  before anisotropic refinement and their contribution is thus excluded from Table 2 which lists final calculated and observed structure factors after anisotropic refinement.

### Molecular geometry

This analysis indicated that the alkaloid is 1-methyl-2,5-bis-(4-hydroxy-1,2-dithiolan-3-yl)pyrrolidine. In contrast to cassipourine, in which the four sulphur atoms are contained in a 1,2,5,6-tetrathiacyclo-octane ring, the sulphur atoms in gerrardine are in pairs in two dithioanyl rings. These dithioanyl rings are *trans* to one another. Atomic nomenclature, bond lengths and angles and deviations from the best plane containing the pyrrolidine ring and the S(3), S(4) dithioanyl ring are given in Fig. 1. The equation to this plane is:

$$-0.5101x + 0.8486y - 0.1403z = 2.9445$$

with respect to the crystallographic axes. The deviations from this plane indicate coplanarity of these two

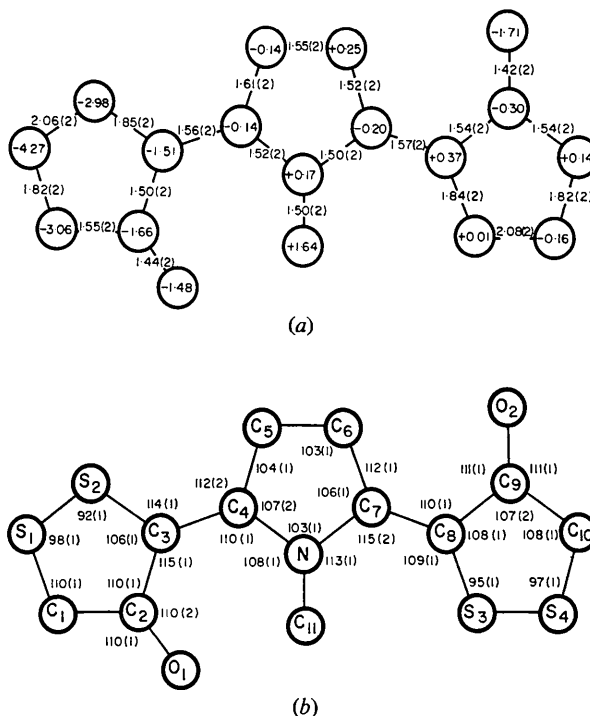


Fig. 1. (a) Bond lengths in Å and their standard deviations with reference to the last significant figure. Deviations from the plane through the central and right-hand side rings are given in the circles in Å. (b) Atomic nomenclature, bond angles and their standard deviations in degrees.



of such bonds on crystallization is the more probable cause of the insolubility of crystals in the chloroform in which they grew from gerrardine generated from its salt. This is in contrast to the proposal of Wright & Warren (1967) that this is due to zwitterion formation. No hydrogen bonds exist between planes of stacks.

All intermolecular approaches of less than 4 Å are listed in Table 3. None of these, excluding the O(1)···H-O(2) hydrogen bond, is shorter than the expected van der Waals separation. The only atoms not participating in such approaches are C(3), C(7), C(8) and N which are all sited towards the centre of the molecule and are thus shielded.

Table 3. Intermolecular contacts shorter than 4 Å

Atom in parent molecule	Atom in symmetry related molecule	Symmetry operator	Interatomic distance
S(1)	C(1)	I	3.58 Å
S(1)	S(1)	I	3.98
S(2)	C(11)	II	3.76
S(2)	C(10)	III	3.92
S(2)	C(1)	IV	3.96
S(3)	C(5)	II	3.74
S(4)	C(5)	V	3.80
S(4)	C(10)	VI	3.88
S(4)	C(2)	VII	3.91
S(4)	C(5)	II	3.98
C(1)	C(11)	VIII	3.88
C(2)	C(6)	IX	3.75
C(2)	O(2)	IX	3.92
C(4)	O(2)	X	3.42
C(5)	C(10)	III	3.72
C(5)	O(2)	X	3.89
C(6)	O(1)	IV	3.72
C(9)	O(1)	IV	3.41
C(11)	O(2)	X	3.59
O(1)	O(2)	IX	2.75

Symmetry operator	Translation elements		
I	$\frac{1}{2}-x$	$-y$	$\frac{1}{2}+z$
II	$-x$	$y-\frac{1}{2}$	$\frac{1}{2}-z$
III	$\frac{1}{2}+x$	$\frac{1}{2}-y$	$1-z$
IV	$x$	$y$	$1+z$
V	$x-\frac{1}{2}$	$\frac{1}{2}-y$	$1-z$
VI	$-x-\frac{1}{2}$	$-y$	$z-\frac{1}{2}$
VII	$x-\frac{1}{2}$	$\frac{1}{2}-y$	$-z$
VIII	$-x$	$y-\frac{1}{2}$	$-z-\frac{1}{2}$
IX	$x$	$y$	$z-1$
X	$-x$	$\frac{1}{2}+y$	$\frac{1}{2}-z$

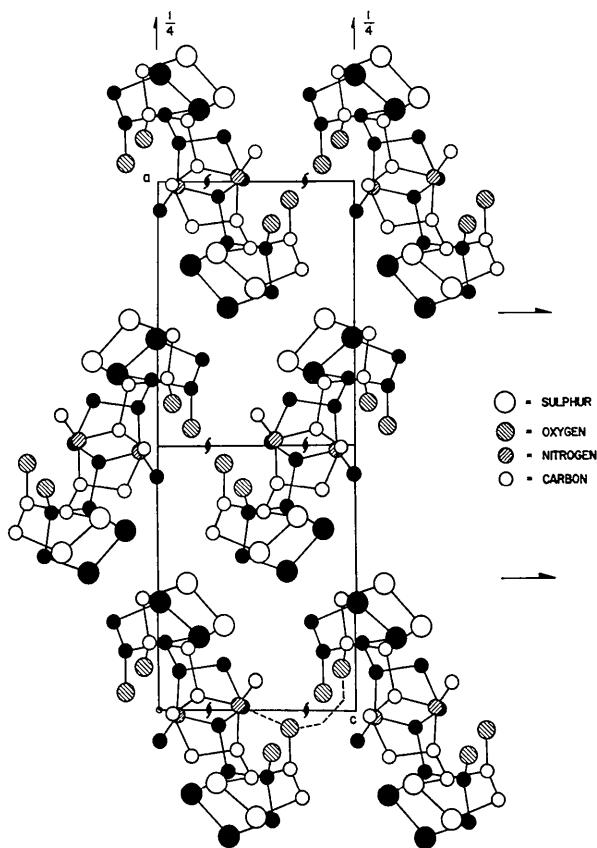


Fig. 2. Projection of the structure down [010].

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