

A Tetrasulphide Derivative of Hyalodendrin*

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Abstract. $C_{14}H_{16}O_3N_2S_4$, monoclinic, $P2_1/c$, $a = 9.995$ (3), $b = 10.344$ (2), $c = 17.385$ (3) Å, $\beta = 109.06$ (2)°, $U = 1698.91$ Å³, $Z = 4$, $D_m = 1.514$, $D_c = 1.519$ g cm⁻³, $F(000) = 808$. The structure was solved by direct methods, and refined by block-diagonal least squares to $R = 0.040$ with 2441 observed reflexions. The tetrasulphide bridge across the piperazinedione ring is twisted so that its first and last S atoms are close to the carbonyl O atoms, and its central S atoms are close to the N atoms of the ring. Each pair of centrosymmetrically related molecules are interlinked by two hydrogen bonds $O-H \cdots O$ to form a dimer, but the dimers are not interconnected.

Introduction. Structural studies of compounds containing an epidithiodiketopiperazine moiety have shown that the disulphide bridge adopts a preferred conformation with each S atom situated closer to the adjacent carbonyl C than to the adjacent N atom (Michel, Chaney, Jones, Hoehn & Nagarajan, 1974, and references therein). However, in the two crystal structures containing an epitetrathiodiketopiperazine moiety (Davis & Bernal, 1973; Przybylska & Gopalakrishna, 1974), the tetrasulphide bridge is found to be twisted so that its two central S atoms are in close contact with the N atoms. Since the molecular orbital calculations carried out on two conformers of 3,6-epitetrathio-*N,N'*-dimethyl-2,5-diketopiperazine (Gregory & Przybylska, 1976) did not indicate a strong conformation preference for the tetrasulphide bridge, it was of interest to determine the stereochemistry of the bridge in the present derivative. The crystals were obtained from Dr G. M. Strunz who prepared them from the fungitoxic metabolic product hyalodendrin (Strunz, Kakushima & Stillwell, 1975).

The space group was uniquely determined from the systematic absences on precession photographs. The cell parameters and intensities were measured on a four-circle diffractometer with Ni-filtered Cu radiation, $\lambda(K\alpha_1) = 1.54050$, $\lambda(K\alpha_2) = 1.54434$ Å. All 2886 reflexions within $\sin \theta/\lambda = 0.59$ were scanned by the $\theta-2\theta$ method, but only 2443 (84.0%) were observed above threshold. The intensities were corrected for

Lorentz and polarization effects. No absorption correction was applied since the crystal was a small fragment in the shape of a flattened sphere, 0.20 mm thick and 0.23 mm in diameter. For $\mu(Cu K\alpha) = 50.7$ cm⁻¹, the absorption correction is estimated to be 1.0 to 1.16, but < 1.08 for the large majority of the reflexions (*International Tables for X-ray Crystallography*, 1959).

The structure was solved by direct methods (Karle & Karle, 1963) with 453 reflexions with $|E| > 1.4$ for the E map. After partial refinement, $R = 0.06$, the H atoms were located from a difference map and included in the block-diagonal least-squares refinement. The quantity minimized was $\sum w(|F_o| - |F_c|)^2$, where $w = 1/\{1 + [(|F_o| - 30)/25]^4\}$ and $2.2 \leq |F_o| \leq 166.9$. The refinement was carried out with the observed reflexions only, excluding 634 and 700 which appeared to be erroneous. In the final cycle, $R = 0.040$, $R_w = 0.044$, $[\sum w\Delta^2/(m-n)]^{1/2} = 0.90$ for the 2441 observed reflexions included in the refinement,† average (Δ /e.s.d.) = 0.1 and maximum (Δ /e.s.d.) = 0.55. There were no bad discrepancies among the unobserved reflexions. The residual electron densities in the final difference map were in the range -0.51 to 0.33 e Å⁻³ in the neighbourhood of the S atoms, and within ± 0.2 e Å⁻³ elsewhere. The scattering factors were those of Hanson, Herman, Lea & Skillman (1964) for C, N, O, S, and of Stewart, Davidson & Simpson (1965) for H. The programs by Ahmed, Hall, Pippy & Huber (1973) were employed for all the calculations.

Discussion. The tetrathiopiperazinedione, in this structure, is found to exhibit the same main features as in the previous X-ray studies of: (I) *N,N'*-dimethyl-3,6-epitetrathio-2,5-piperazinedione (Davis & Bernal, 1973), and (II) sporidesmin G etherate (Przybylska & Gopalakrishna, 1974). In these three structures, the two middle S atoms of the tetrasulphide bridge are attracted towards the N atoms of the piperazinedione ring, and this pattern is therefore expected to be maintained in

† A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32002 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

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other compounds. A projection of the molecule on to the mean plane of the piperazinedione ring, showing this predominant feature, is presented in Fig. 1.

The bond lengths and angles for the refined parameters in Table 1, and their estimated standard deviations, are given in Fig. 2. No significant differences are observed in the lengths of equivalent bonds, and the mean of each equivalent pair agrees well with the corresponding values of I and II, except the C-S length which has mean values 1.866 (2) in I, 1.875 (7) in II, and 1.897 (2) Å in the present structure, III. Equivalent valency angles in III show small but significant differences; the largest is 1.9° between S(1)-S(2)-S(3) and S(2)-S(3)-S(4). Such differences do not occur in I since the molecule lies on a crystallographic twofold axis, but similar small differences are observed in II. In these three compounds the mean S-C-N angle is always considerably larger than the mean S-C-C(ring). They are 113.9 and 108.6 (1)° in I,

112.7 and 105.2° in II, and 112.1 and 103.2° in III respectively.

In III, the piperazinedione ring has a slightly twisted boat conformation with both C(1) and C(4) projecting on the same side of the ring as the tetrasulphide chain. As shown in Fig. 1, the deviations of the ring atoms

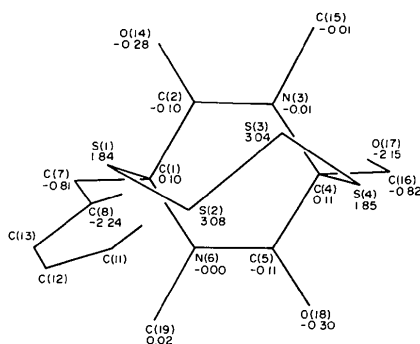


Fig. 1. A projection of the molecule on to the mean plane of the piperazinedione ring, showing the molecular conformation, and the deviations (Å) of the atoms from the mean plane. C(9) and C(10) have been excluded for clarity.

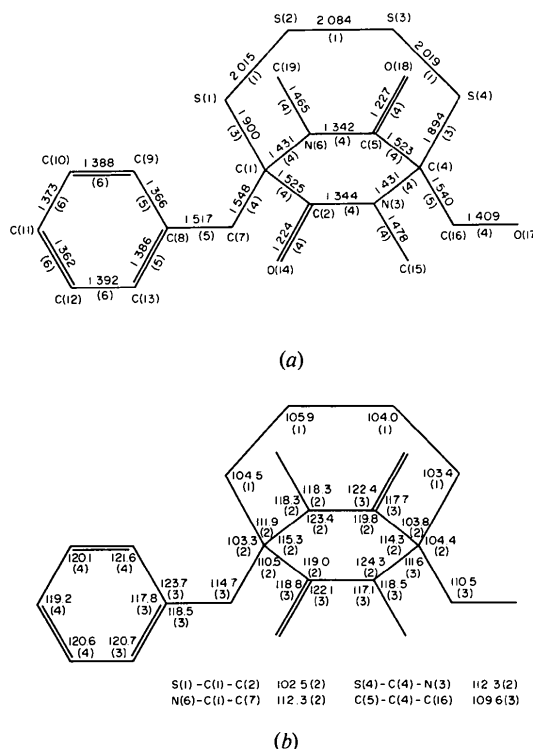


Fig. 2. (a) Bond lengths (Å) and (b) valency angles (°), and their estimated standard deviations in parentheses.

Table 1. Fractional coordinates ($\times 10^4$ for C, N, O, S and $\times 10^3$ for H), anisotropic thermal parameters ($\times 10^4$) for the expression $T = \exp[-2\pi^2(U_{11}a^{*2}h^2 + \dots + 2U_{23}b^*c^*kl + \dots)]$, and B(H) in Å²

	x	y	z	U ₁₁	U ₂₂	U ₃₃	2U ₂₃	2U ₁₃	2U ₁₂
S (1)	10721 (1)	1661 (1)	1874 (1)	236 (3)	531 (5)	425 (4)	-89 (8)	281 (6)	-24 (7)
S (2)	10873 (1)	1322 (1)	764 (1)	417 (5)	615 (5)	573 (5)	-175 (9)	679 (9)	128 (8)
S (3)	9964 (1)	2919 (1)	54 (1)	603 (5)	593 (5)	56E (5)	62 (9)	810 (9)	-213 (9)
S (4)	8042 (1)	2282 (1)	-644 (1)	644 (5)	564 (5)	346 (4)	108 (8)	572 (8)	-15 (9)
C (1)	8760 (3)	1492 (3)	1724 (2)	280 (14)	366 (16)	291 (14)	-112 (25)	254 (23)	10 (24)
C (2)	8214 (3)	2865 (3)	1504 (2)	282 (14)	364 (16)	381 (15)	-105 (26)	365 (24)	-27 (24)
N (3)	7467 (2)	3140 (2)	727 (1)	391 (13)	289 (12)	407 (14)	20 (22)	338 (22)	40 (21)
C (3)	7007 (3)	2197 (3)	93 (2)	414 (16)	347 (16)	373 (15)	13 (27)	334 (27)	12 (27)
C (4)	7196 (3)	802 (3)	390 (2)	309 (14)	366 (16)	308 (14)	-93 (25)	334 (24)	-25 (25)
N (6)	8102 (2)	527 (2)	1132 (1)	317 (12)	289 (12)	329 (12)	-16 (20)	291 (20)	42 (20)
C (7)	8737 (3)	1130 (3)	2584 (2)	371 (16)	483 (18)	317 (15)	-41 (28)	279 (26)	34 (28)
C (8)	7306 (3)	699 (3)	2617 (2)	438 (17)	402 (17)	374 (16)	-92 (28)	467 (28)	-8 (28)
C (9)	6051 (3)	1227 (4)	2149 (2)	393 (18)	737 (25)	638 (22)	520 (40)	532 (34)	110 (35)
C (10)	4767 (4)	814 (5)	2209 (3)	418 (20)	1027 (34)	836 (29)	477 (52)	607 (41)	2 (43)
C (11)	4737 (4)	-133 (4)	2756 (3)	609 (24)	834 (30)	842 (29)	10 (47)	870 (44)	-368 (44)
C (12)	5979 (5)	-655 (4)	3239 (3)	923 (30)	508 (22)	758 (26)	29 (40)	1027 (47)	-366 (43)
C (13)	7263 (4)	-253 (3)	3169 (2)	633 (22)	419 (20)	562 (21)	-117 (32)	558 (36)	25 (34)
C (14)	8514 (2)	3692 (2)	2037 (1)	547 (14)	414 (12)	514 (14)	-332 (22)	325 (22)	11 (21)
C (15)	7147 (4)	4516 (3)	517 (2)	668 (24)	334 (18)	650 (23)	125 (34)	414 (38)	156 (34)
C (16)	5458 (4)	2421 (3)	-441 (2)	472 (19)	502 (21)	466 (19)	37 (32)	152 (31)	86 (32)
O (17)	4568 (2)	2453 (2)	43 (2)	415 (13)	458 (14)	819 (16)	-103 (25)	439 (24)	29 (21)
C (18)	6559 (2)	-41 (2)	85 (1)	509 (13)	404 (12)	413 (12)	-162 (20)	256 (20)	-116 (20)
C (19)	8447 (3)	-832 (3)	1343 (2)	510 (19)	330 (17)	457 (18)	-1 (28)	293 (31)	142 (30)
	x	y	z	B	x	y	z	B	
H (7, 1)	946 (3)	44 (3)	282 (2)	3.8 (0.7)	H (15, 2)	781 (4)	503 (4)	93 (2)	7.3 (1.1)
H (7, 2)	906 (3)	194 (3)	295 (2)	4.0 (0.7)	H (15, 3)	721 (5)	465 (4)	-4 (3)	8.2 (1.2)
H (9)	599 (4)	185 (4)	172 (2)	5.2 (0.9)	H (16, 1)	537 (4)	328 (3)	-78 (2)	5.0 (0.8)
H (10)	386 (4)	99 (4)	177 (2)	6.6 (1.0)	H (18, 2)	519 (3)	176 (3)	-87 (2)	3.3 (0.7)
H (11)	380 (4)	-85 (4)	277 (2)	5.3 (0.9)	H (17)	418 (4)	156 (4)	8 (3)	7.2 (1.1)
C (12)	602 (5)	-130 (4)	364 (3)	7.1 (1.1)	H (19, 1)	833 (4)	85 (2)	5.6 (0.9)	
H (13)	814 (3)	-61 (3)	351 (2)	4.0 (0.8)	H (19, 2)	780 (4)	-126 (4)	159 (2)	7.0 (1.1)
H (15, 1)	621 (4)	475 (4)	45 (3)	7.5 (1.1)	H (19, 3)	940 (3)	-86 (3)	174 (2)	4.7 (0.8)

from their mean plane are within ± 0.11 Å. The four S atoms of the bridge are oriented so that each S is involved in one short intramolecular contact (Table 2). Thus, S(1) and S(4) are only 3.126 and 3.140 Å from the carbonyl O atoms, while S(2) and S(3) are 3.148 and 3.092 Å from the N atoms. The corresponding van der Waals contacts are 3.25 for S...O and 3.35 Å for S...N (Pauling, 1960). The shortest intramolecular S...H contacts are in the range 2.70–2.90 Å. The mean plane of the piperazinedione ring makes an angle of 88.8° with the mean plane of the C(1)–S(1)–S(2)–S(3)–S(4)–C(4) bridge. The con-

formation angles of the piperazinedione and the epitetrasulphide are listed in Table 3.

Each pair of centrosymmetrically related molecules forms a dimer through two hydrogen bonds O(17)–H(17)...O(18') and O(17')–H(17')...O(18), where the nonprimed atoms are at (x, y, z) and the primed atoms at $(1-x, -y, -z)$. The dimensions of the hydrogen bonds are O(17)–H(17) = 1.10, H(17)...O(18') = 1.74, O(17)...O(18') = 2.749 Å, and O(17)–H(17)...O(18') = 176.8° . No short intermolecular contacts are present between the different dimers.

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Table 2. Some intramolecular distances (Å) involving the S atoms

The e.s.d.'s are about 0.003 Å. Distances considered significantly shorter than van der Waals distances are marked with an asterisk.

S(1)...O(14)	3.126*	S(4)...O(18)	3.140*
S(1)...C(19)	3.361	S(4)...C(15)	3.377
S(2)...N(6)	3.148*	S(3)...N(3)	3.092*
S(2)...C(5)	3.558	S(3)...C(2)	3.507
S(2)...C(19)	3.667	S(3)...C(15)	3.576
S(2)...C(2)	3.674	S(3)...C(5)	3.721

Table 3. Conformation angles ($^\circ$) of the piperazinedione ring and epitetrasulphide bridge

Piperazinedione

N(6)–C(1)–C(2)–N(3)	–16.7
C(1)–C(2)–N(3)–C(4)	7.0
C(2)–N(3)–C(4)–C(5)	10.5
N(3)–C(4)–C(5)–N(6)	–19.4
C(4)–C(5)–N(6)–C(1)	10.0
C(5)–N(6)–C(1)–C(2)	7.9

Epitetrasulphide

C(4)...C(1)–S(1)–S(2)	–29.9
C(1)–S(1)–S(2)–S(3)	70.7
S(1)–S(2)–S(3)–S(4)	–103.1
S(2)–S(3)–S(4)–C(4)	73.7
S(3)–S(4)–C(4)...C(1)	–33.6
S(4)–C(4)...C(1)–S(1)	15.3

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