Structure of 3,6-Diethyl-1,4-dimethyl-3,6-epithio-2,5-piperazinedione

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Abstract. $C_{10}H_{16}N_2O_2S$, $M_r = 228 \cdot 31$, monoclinic, colourless prisms, $P2_1/c$, $a = 9 \cdot 268$ (1), $b = 12 \cdot 318$ (1), $c = 10 \cdot 691$ (1) Å, $\beta = 108 \cdot 50$ (1)°; $D_m = 1 \cdot 30$, $D_x = 1 \cdot 310$ Mg m^{-3} for $Z = 4$. Effects of the highly strained structure are manifested in longer distances and smaller angles of the endocyclic bonds, and shorter exocyclic bond lengths.

Introduction. In the course of a synthetic study of the 3,6-epidithio-2,5-piperazinedione skeleton, epithio derivatives were obtained as by-products (Yoshimura, Nakamura & Matsunari, 1975). The present work was undertaken in order to reveal the detailed molecular structure of this highly strained 2,5-piperazinedione system.

Intensity data were collected with graphite-mono-chromated Mo $K\alpha$ radiation on a Rigaku four-circle automatic diffractometer using a crystal of dimensions $0 \cdot 27 \times 0 \cdot 30 \times 0 \cdot 25$ mm. The θ–2θ scan was made for a range of $(1 \cdot 0 + 0 \cdot 35 \tan \theta)°$, the scan speed being $4°$ min^{-1} in 2θ. Three standard reflexions showed only statistical fluctuations throughout the data collection. The intensities were corrected for Lorentz–polarization effects, but not for absorption, μ(Mo $K\alpha$) $= 0 \cdot 259$ mm^{-1}. 2533 independent reflexions with $2\theta < 54 \cdot 0°$ were measured; 1876 with $|F_o| \geq 3\sigma(F_o)$ were taken as observed.

The structure was determined using *MULTAN* (Germain, Main & Woolfson, 1971). Block-diagonal-matrix least-squares refinement was followed by a difference Fourier synthesis in which all the H atoms were located. The final R was $0 \cdot 039$ for the observed reflexions and $0 \cdot 083$ for all reflexions. The weighting scheme used for minimizing $\sum w(|F_o| - |F_c|)^2$ was $w = 1/[\sigma^2(F_o) - 0 \cdot 01375|F_o| + 0 \cdot 00172|F_o|^2]$ for the observed reflexions. The atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). The atomic parameters obtained are given in Table 1.†

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† Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34842 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Final atomic coordinates* ($\times 10^5$ *for the non-hydrogen atoms,* $\times 10^4$ *for* H) *with their estimated standard deviations in parentheses*

	x	y	z
S	26088 (5)	15782 (4)	50576 (5)
O(1)	4810 (14)	35431 (10)	25291 (14)
O(2)	47369 (14)	11849 (11)	26535 (14)
N(1)	29914 (16)	31854 (12)	36402 (15)
N(2)	22380 (16)	11733 (12)	26053 (15)
C(1)	13398 (18)	17102 (14)	33504 (17)
C(2)	37199 (19)	14496 (14)	30873 (17)
C(3)	38837 (18)	22237 (15)	42614 (18)
C(4)	14995 (19)	29372 (14)	31148 (17)
C(5)	15854 (23)	5960 (18)	13678 (20)
C(6)	36078 (22)	42423 (17)	34997 (22)
C(7)	54934 (19)	24535 (16)	51377 (20)
C(8)	62538 (21)	14657 (20)	59214 (23)
C(9)	−2574 (20)	12898 (16)	30629 (21)
C(10)	−10614 (21)	17228 (21)	40012 (23)
H(71)	5462 (21)	3064 (16)	5748 (19)
H(72)	6057 (20)	2708 (16)	4537 (20)
H(91)	−188 (20)	468 (16)	3099 (18)
H(92)	−844 (19)	1510 (15)	2150 (19)
H(51)	2424 (22)	393 (19)	1019 (23)
H(52)	811 (23)	996 (20)	687 (23)
H(53)	1072 (21)	−62 (18)	1504 (22)
H(61)	3753 (24)	4656 (22)	4275 (25)
H(62)	2953 (25)	4626 (25)	2739 (26)
H(63)	4639 (26)	4238 (20)	3428 (26)
H(81)	7341 (20)	1657 (18)	6444 (21)
H(82)	6285 (20)	834 (18)	5301 (20)
H(83)	5733 (22)	1229 (18)	6527 (24)
H(101)	−2138 (22)	1478 (18)	3776 (22)
H(102)	−1158 (23)	2553 (20)	3932 (26)
H(103)	−545 (23)	1452 (18)	4892 (25)

Discussion. As shown in Figs. 1 and 2, the piperazine ring takes a deep-boat form with approximate C_2 symmetry. Table 2 gives the bond lengths and angles, and Table 3 the torsion angles and details of some least-squares planes in the molecule.

The C–S bonds are longer than those in L-cystine dihydrochloride (Jones, Bernal, Frey & Koetzle, 1974) and L-cysteine (Kerr, Ashmore & Koetzle, 1975). It can be seen that all the intraring bond distances are longer than the corresponding ones found in unbridged boat-shaped piperazinediones (Benedetti, Marsh & Goodman, 1976). The endocyclic bond angles are
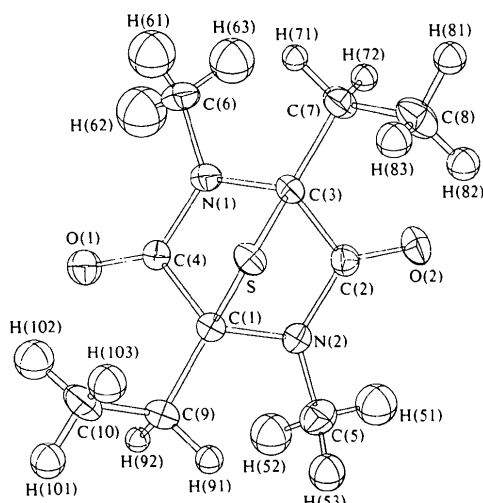
Fig. 1. Molecular structure and the atomic numbering. Thermal ellipsoids are drawn at the 30% probability level.
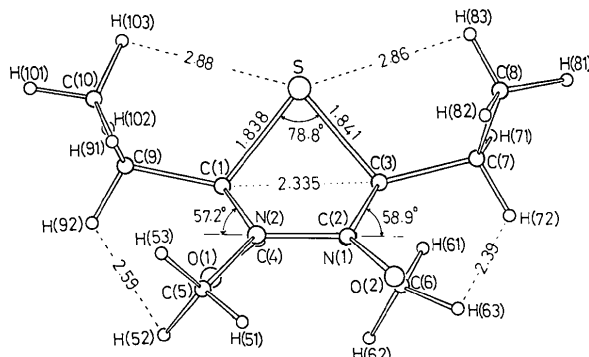

Fig. 2. Side view of the molecule (distances are in Å).

Table 2. *Interatomic distances* (Å) *and angles* (°)

S—C(1)	1·838 (2)	N(2)—C(2)	1·348 (2)
S—C(3)	1·842 (2)	N(2)—C(5)	1·453 (3)
O(1)—C(4)	1·211 (2)	C(1)—C(4)	1·547 (3)
O(2)—C(2)	1·220 (2)	C(1)—C(9)	1·505 (3)
N(1)—C(3)	1·477 (3)	C(2)—C(3)	1·545 (3)
N(1)—C(4)	1·352 (2)	C(3)—C(7)	1·515 (3)
N(1)—C(6)	1·448 (3)	C(7)—C(8)	1·518 (3)
N(2)—C(1)	1·479 (2)	C(9)—C(10)	1·523 (3)
C(5)—H(51)	1·00 (3)	C(8)—H(81)	1·01 (2)
C(5)—H(52)	0·98 (2)	C(8)—H(82)	1·03 (2)
C(5)—H(53)	0·97 (2)	C(8)—H(83)	0·97 (3)
C(6)—H(61)	0·95 (3)	C(9)—H(91)	1·01 (2)
C(6)—H(82)	0·97 (3)	C(9)—H(92)	0·99 (2)
C(6)—H(63)	0·98 (3)	C(10)—H(101)	1·00 (2)
C(7)—H(71)	1·00 (2)	C(10)—H(102)	1·03 (3)
C(7)—H(72)	1·00 (2)	C(10)—H(103)	0·98 (3)
S···C(2)	2·627 (3)	S···C(4)	2·611 (3)
S···N(1)	2·585 (2)	S···N(2)	2·582 (2)
C(1)···C(3)	2·335 (4)		

C(1)—S—C(3)	78·7 (1)	O(2)—C(2)—C(3)	125·8 (2)
C(3)—N(1)—C(4)	111·0 (2)	N(2)—C(2)—C(3)	109·9 (2)
C(3)—N(1)—C(6)	125·8 (2)	S—C(3)—N(1)	101·8 (1)
C(4)—N(1)—C(6)	123·0 (2)	S—C(3)—C(2)	101·4 (1)
C(1)—N(2)—C(2)	111·2 (2)	S—C(3)—C(7)	116·4 (1)
C(1)—N(2)—C(5)	124·5 (2)	N(1)—C(3)—C(2)	103·5 (1)
C(2)—N(2)—C(5)	123·4 (2)	N(1)—C(3)—C(7)	115·4 (2)
S—C(1)—N(2)	101·7 (1)	C(2)—C(3)—C(7)	116·1 (2)
S—C(1)—C(4)	100·6 (1)	O(1)—C(4)—N(1)	127·0 (2)
S—C(1)—C(9)	116·7 (1)	O(1)—C(4)—C(1)	126·0 (2)
N(2)—C(1)—C(4)	104·5 (1)	N(1)—C(4)—C(1)	106·9 (2)
N(2)—C(1)—C(9)	115·0 (2)	C(3)—C(7)—C(8)	112·7 (2)
C(4)—C(1)—C(9)	116·2 (2)	C(1)—C(9)—C(10)	113·6 (2)
O(2)—C(2)—N(2)	127·1 (2)	C(7)—C(8)—H(81)	109 (1)
N(2)—C(5)—H(51)	108 (1)	C(7)—C(8)—H(82)	111 (1)
N(2)—C(5)—H(52)	115 (1)	C(7)—C(8)—H(83)	112 (1)
N(2)—C(5)—H(53)	111 (1)	H(81)—C(8)—H(82)	108 (2)
H(51)—C(5)—H(52)	109 (2)	H(81)—C(8)—H(83)	109 (2)
H(51)—C(5)—H(53)	109 (2)	H(82)—C(8)—H(83)	109 (2)
H(52)—C(5)—H(53)	105 (2)	C(1)—C(9)—H(91)	107 (1)
N(1)—C(6)—H(61)	110 (2)	C(1)—C(9)—H(92)	108 (1)
N(1)—C(6)—H(62)	111 (2)	C(10)—C(9)—H(91)	111 (1)
N(1)—C(6)—H(63)	115 (2)	C(10)—C(9)—H(92)	109 (1)
H(61)—C(6)—H(62)	110 (2)	H(91)—C(9)—H(92)	109 (2)
H(61)—C(6)—H(63)	102 (2)	C(9)—C(10)—H(101)	113 (1)
H(62)—C(6)—H(63)	108 (2)	C(9)—C(10)—H(102)	111 (2)
C(3)—C(7)—H(71)	108 (1)	C(9)—C(10)—H(103)	109 (2)
C(3)—C(7)—H(72)	106 (1)	H(101)—C(10)—H(102)	103 (2)
C(8)—C(7)—H(71)	110 (1)	H(101)—C(10)—H(103)	106 (2)
C(8)—C(7)—H(72)	111 (1)	H(102)—C(10)—H(103)	114 (2)
H(71)—C(7)—H(72)	108 (2)		

significantly smaller than normal. These features can be attributed to the steric repulsion between S and N or carbonyl C atoms. Concomitantly, all the exocyclic bonds are significantly shorter than those in related compounds (Benedetti *et al.*, 1976), suggesting rehybridization of the orbitals of the ring atoms.

Intramolecular repulsion between the O atom and the ethyl group causes remarkable elongation of the C(1)—C(4) and C(2)—C(3) bonds, expansion of the C(1)—C(4)—O(1) and C(3)—C(2)—O(2) angles and deviation of the O(1) (−0·040 Å) and O(2) (−0·051 Å) atoms from the C(4), C(1), N(1) and C(2), C(3), N(2) planes, respectively, compared with the corresponding values in related molecules (Benedetti *et al.*, 1976). The repulsion between *N*-methyl and ethyl groups is mainly demonstrated by larger out-of-plane deviations: −0·230 Å for C(5) and −0·096 Å for C(6) from the N(2), C(1), C(2) and N(1), C(3), C(4) planes, respectively. There are no abnormally short intermolecular contacts.

In connexion with the higher chemical shift of the *N*-methyl protons in the NMR spectra of the present compound ($\delta = 2·77$ p.p.m.) than those of the epidithio compound (3·05 p.p.m.), Yoshimura *et al.* (1975) argued that the relative orientation of the *N*-methyl group with respect to the carbonyl group on the opposite side of the molecule is changed to a large extent by conformational constraint. In Fig. 3 the dispositions of *N*-methyl groups with respect to the opposite amide plane in the present compound are compared with those of gliotoxin (molecule *A*) whose

Table 3. *Deviations (Å) of atoms from the least-squares planes and torsion angles (°)*

An asterisk denotes atoms used to calculate the plane.

	Plane				
	1	2	3	4	5
S	1·181	1·190	2·212	1·744	1·742
O(1)	−2·266	−0·010	−0·583	−0·888	1·441
O(2)	−0·064	−2·284	−0·611	1·390	−0·916
N(1)	−1·293	−0·009*	0·013*	1·150	0·000*
N(2)	0·004*	−1·291	0·013*	0·000*	1·168
C(1)	−0·002*	−0·005*	0·779	0·000*	1·987
C(2)	−0·003*	−1·341	−0·013*	1·119	0·000*
C(3)	0·002*	0·005*	0·801	1·974	0·000*
C(4)	−1·341	0·009*	−0·013*	0·000*	1·143
C(5)	−0·215	−2·446	−0·816	−1·151	1·453
C(6)	−2·422	−0·133	−0·734	1·449	−1·102
C(7)	0·289	0·296	1·156	3·405	−1·078
C(8)	1·718	0·526	2·154	4·257	−0·882
C(9)	0·273	0·257	1·091	−1·068	3·409
C(10)	0·489	1·675	2·069	−0·901	4·287

Equations of the planes $AX + BY + CZ + D = 0$ in which X, Y and Z are Cartesian coordinates in Å referred to a, b and c^*, respectively

Plane	A	B	C	D
1	−0·0375 (15)	−0·7815 (11)	0·6228 (13)	−0·467 (6)
2	−0·4517 (12)	0·2138 (17)	0·8662 (8)	−3·350 (5)
3	−0·2883 (17)	−0·3387 (10)	0·8956 (7)	−1·520 (6)
4	0·5869 (24)	0·0393 (20)	0·8087 (18)	−2·892 (4)
5	−0·9065 (9)	−0·4007 (14)	0·1333 (33)	2·474 (13)

Interplanar angles (°)

Plane	2	3	4	5
1	67·1 (2)	33·6 (1)	63·2 (2)	64·5 (2)
2		33·5 (1)	63·7 (2)	64·0 (2)
3			57·2 (2)	58·9 (2)
4				116·1 (3)

Torsion angles

φ	C(4)—C(1)—N(2)—C(2)	62·8 (3)
ψ	N(2)—C(1)—C(4)—N(1)	−62·7 (3)
ω	C(3)—N(1)—C(4)—C(1)	−1·6 (3)
	C(9)—C(1)—N(2)—C(5)	22·4 (4)
	C(9)—C(1)—C(4)—O(1)	−12·8 (4)
	C(2)—C(3)—N(1)—C(4)	65·0 (3)
	N(1)—C(3)—C(2)—N(2)	−64·9 (3)
	C(1)—N(2)—C(2)—C(3)	0·7 (3)
	C(7)—C(3)—N(1)—C(6)	17·7 (4)
	C(7)—C(3)—C(2)—O(2)	−15·4 (4)

coordinates are taken from Fridrichsons & Mathieson (1967). The deviations of atoms from the corresponding projected planes are: C(6), 2·42 Å, in the present molecule and C(13), 1·72 Å, in gliotoxin.
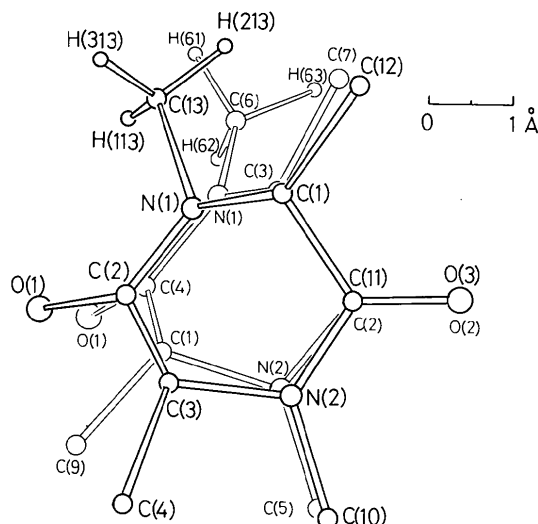

Fig. 3. Comparison of the dispositions of N-methyl groups. Gliotoxin, drawn with thick lines, is projected on the C(1), C(11), N(2), C(3) plane and the present molecule is on the C(3), C(2), N(2), C(1) plane.

Judging from these geometries, the diamagnetic anisotropy of the sp^2-hybridized N atom (Jackman & Sternhell, 1969), in addition to that of carbonyl group, should be taken into account in the interpretation of the rather large change of chemical shift mentioned above.

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