

of Pauling's covalent radii corrected for the electronegativities (Truter, 1962). The short and long C–C distances [average: 1.40 Å] alternating in the six-membered rings are rather interesting, but this phenomenon can hardly be regarded as significant owing to the large experimental errors. The C(1)–S–C(1'), O(1)–S–O(1') and O(1)–S–C(1) as well as the O(1)–S–C(1') bond angles are also comparable with the corresponding values in DDS. The dihedral angle between the best planes of the benzene rings of the symmetrical parts of the molecule is 106.7°. It is noteworthy that the crystal lattice (Fig. 4) contains enantiomeric pairs of molecules; this is in agreement with the chirality of the structure depicted in Fig. 3(a).

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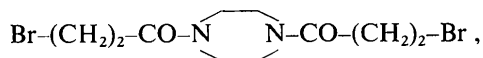
N,N'-Bis-(3-bromopropionyl)piperazine

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Abstract. Monoclinic, $P2_1/c$, $a = 10.58$ (1), $b = 5.81$ (1), $c = 10.83$ (5) Å; $\beta = 100.6$ (1)°; formula $C_{10}H_{16}N_2O_2Br_2$



$Z = 2$, $D_m = 1.81$, $D_x = 1.87$ g cm⁻³. The colorless crystals were recrystallized from water. The space group and cell content imply that the molecule is centrosymmetric. The structure, refined to $R = 0.079$, shows considerable steric strain, which may be connected with the oncolytic activity of the compound.

Introduction. All accessible intensity data from crystals mounted on axes a and c were collected using a Supper–Pace automated diffractometer with Cu $K\alpha$ radiation, Lorentz–polarization corrections applied, and the two axes correlated, giving a total of 1352 reflections. Elimination of reflections less than 4σ as unobserved left 754 unique reflections where σ is defined as

$$\sigma(I) = [(0.05I^2) + N_0 + K^2N_b]^{1/2}$$

[N_0 is gross count, N_b is background count and K is ratio of scan time to background time (Parker, Flynn & Boer, 1968)]. The systematic absences ($h0l$, l odd; $0k0$, k odd) uniquely determine the space group.

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A sharpened Patterson function was used to locate the bromine position. The remaining non-hydrogen atoms were located by electron-density synthesis and a minimum-function map which used the bromine positions as the points of superposition. Hydrogen atoms were located in a difference electron-density map ($F_o - F_c$ synthesis) and their positions optimized to give bond lengths of 1.0 Å. Full-matrix least-squares refinement

Table 1. *Final positions and anisotropic temperature factors*

	x/a	y/b	z/c
Br	0.8485 (1)	0.5633 (0)	0.1352 (2)
C(2)	0.8936 (9)	0.5555 (22)	0.3230 (13)
C(3)	0.7897 (8)	0.4554 (19)	0.3817 (13)
C(4)	0.6758 (7)	0.6164 (15)	0.3691 (11)
O	0.6833 (6)	0.8161 (12)	0.3392 (9)
N	0.5699 (7)	0.5228 (12)	0.4007 (10)
C(7)	0.4606 (8)	0.6742 (16)	0.4066 (12)
C(8)	0.5561 (8)	0.2996 (14)	0.4578 (12)
H(9)	0.633	0.206	0.456
H(10)	0.481	0.221	0.408
H(11)	0.476	0.829	0.372
H(12)	0.383	0.603	0.356
H(13)	0.822	0.424	0.475
H(14)	0.763	0.306	0.338
H(15)	0.911	0.716	0.356
H(16)	0.971	0.459	0.348

Table 1 (cont.)

	$10^4\beta_{11}$	$10^4\beta_{22}$	$10^4\beta_{33}$	$10^4\beta_{12}$	$10^4\beta_{13}$	$10^4\beta_{23}$
Br	123 (2)	406 (6)	151 (2)	-45 (4)	49 (2)	-14 (5)
C(2)	77 (8)	348 (34)	126 (15)	16 (30)	-18 (15)	8 (39)
C(3)	66 (7)	255 (30)	157 (17)	73 (27)	23 (15)	25 (37)
C(4)	54 (8)	193 (30)	134 (15)	52 (19)	-35 (15)	-52 (27)
O	86 (6)	179 (21)	174 (12)	45 (17)	42 (12)	49 (24)
N	78 (7)	127 (20)	126 (12)	91 (18)	28 (12)	33 (22)
C(7)	65 (7)	146 (23)	155 (16)	80 (23)	1 (14)	43 (31)
C(8)	79 (8)	109 (23)	149 (15)	56 (20)	31 (15)	-20 (27)

of the non-hydrogen positions and anisotropic temperature factors with all hydrogen parameters held constant resulted in the present R of 0.079 ($R = \sum ||F_o| - |F_c|| / \sum |F_o|$).

Final values of the position and temperature parameters are listed in Table 1. Bond lengths and angles are given in Table 2. The molecular structure is shown in Fig. 1. A list of observed and calculated structure factors is given in Table 3.

Table 2. Bond lengths and angles for non-hydrogen atoms with standard deviations

Br—C(2)	2.002 (13) Å	Br—C(2)—C(3)	112.8 (7)°
C(2)—C(3)	1.485 (17)	C(2)—C(3)—C(4)	111.1 (9)
C(3)—C(4)	1.511 (13)	C(3)—C(4)—O	121.8 (8)
C(4)—O	1.211 (12)	C(3)—C(4)—N	114.5 (8)
C(4)—N	1.345 (12)	O—C(4)—N	123.6 (8)
N—C(7)	1.464 (12)	C(4)—N—C(7)	118.0 (7)
N—C(8)	1.456 (12)	C(4)—N—C(8)	128.4 (7)
C(7)—C(8)	1.519 (18)	C(7)—N—C(8)	112.0 (8)
		N—C(7)—C(8)	109.6 (8)
		N—C(8)—C(7)	111.1 (8)

Discussion. The substance has oncolytic activity against certain leukemias, lymphomas and solid tumors (Stein, Carben, Langden & Richards, 1960; Bond, Rohn, Hodes & Yardley, 1962; McNair *et al.*, 1963). Its mechanism of action is not known. Two possibilities are alkylation (Emmelot, 1964) involving the CH_2 -Br bond and acylation (Moncrief & Heller, 1967) involving the amide group.

If a planar amide with the generally accepted bond lengths and angles (Corey & Pauling, 1953) is assumed the hydrogen atoms attached to the ring carbon C(8)

and those attached to C(3) are potentially sterically crowded. If C(2) is also assumed to be coplanar with the amide, the two hydrogens on C(3) would each be 2.0 Å from one of the hydrogens on C(8), considerably less than the accepted van der Waals distance of 2.4 Å. The oxygen would in this case be 2.45 Å from one of the hydrogen atoms on C(7) and, if the bromine is also assumed to be in the plane of the amide, 2.5 Å from the hydrogens on C(2). A diffraction study was undertaken to ascertain the manner in which the molecule relieves this strain and to attempt to obtain molecular parameters which could contribute to the understanding of the mechanism of oncolytic activity of this molecule.

An examination of the bond distances and angles in Table 2 will indicate several significant departures from the usual amide values. Most important in relieving the strain of the steric interaction is the increase of the C(4)—N—C(8) angle to 128.4° and the decrease of the C(4)—N—C(7) angle to 118.0°. The C(4)—O distance is shorter while the C(4)—N bond is somewhat longer than usual indicating some decrease in conjugation. From Table 4, it is evident that the amide groups of the determined structure are essentially planar with only small deviations from a planar configuration. The angle between the plane determined by C(3), C(4), N, and O and the plane of C(4), N, C(7), and C(8) is 2° 12.5'.

The net result is that the hydrogens on C(3) are 2.3 and 2.1 Å from the nearest hydrogen on C(8) while O is 2.3 Å from the nearest C(7) hydrogen and 2.5 Å from the nearest C(2) hydrogen.

In amides in which a hydrogen and one larger atom are bonded to an amide nitrogen and a bulky group is bonded to the carbonyl, the hydrogen on the nitrogen is generally found *trans* to the oxygen unless there is some constraint which forbids this. In diketopiperazine the ring structure requires the hydrogen to be *cis* and the C—N—C angle is observed to be 126.0° (Degeilh & Marsh, 1959). In the tripeptide leucyl-propyl-glycine the C—N—C angle involving the carbon bound to N *trans* to the oxygen of the amide carbonyl was found to be 126.1° while the C—N—C angle containing the carbon *cis* to the oxygen was 121.4° (Leung & Marsh, 1958). These deviations from the usual amide values while smaller in magnitude do agree with those found in the present study.

The Br—C(2) distance in this molecule is 2.00 Å,

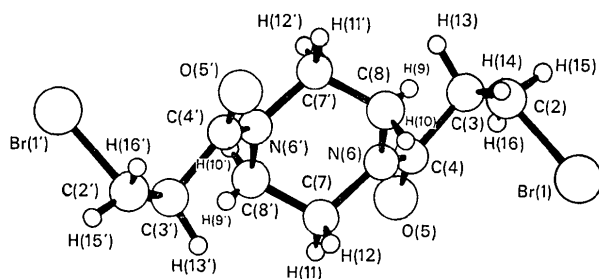


Fig. 1. The molecular structure of *N,N'*-bis-(3-bromopropionyl)piperazine.

Table 3. Observed and calculated structure factors

h	k	l	F _o	F _c	h	k	l	F _o	F _c	h	k	l	F _o	F _c	h	k	l	F _o	F _c		
-1	1	1	1461	1459	-1	2	1	1571	1570	-1	3	1	1	1681	1680	-1	4	1	1	1791	1790
-1	2	1	1220	1219	-1	3	2	1330	1329	-1	4	2	1	1440	1439	-1	5	2	1	1550	1549
-1	3	1	1079	1078	-1	4	3	1189	1188	-1	5	3	1	1299	1298	-1	6	3	1	1409	1408
-1	4	1	938	937	-1	5	4	1048	1047	-1	6	4	1	1158	1157	-1	7	4	1	1268	1267
-1	5	1	797	796	-1	6	5	907	906	-1	7	5	1	1017	1016	-1	8	5	1	1127	1126
-1	6	1	656	655	-1	7	6	766	765	-1	8	6	1	876	875	-1	9	6	1	986	985
-1	7	1	515	514	-1	8	7	625	624	-1	9	7	1	735	734	-1	10	7	1	845	844
-1	8	1	374	373	-1	9	8	484	483	-1	10	8	1	594	593	-1	11	8	1	704	703
-1	9	1	233	232	-1	10	9	343	342	-1	11	9	1	453	452	-1	12	9	1	563	562
-1	10	1	92	91	-1	11	10	202	201	-1	12	10	1	312	311	-1	13	10	1	422	421
1	1	1	1461	1459	1	2	1	1571	1570	1	3	1	1	1681	1680	1	4	1	1	1791	1790
1	2	1	1220	1219	1	3	2	1330	1329	1	4	2	1	1440	1439	1	5	2	1	1550	1549
1	3	1	1079	1078	1	4	3	1189	1188	1	5	3	1	1299	1298	1	6	3	1	1409	1408
1	4	1	938	937	1	5	4	1048	1047	1	6	4	1	1158	1157	1	7	4	1	1268	1267
1	5	1	797	796	1	6	5	907	906	1	7	5	1	1017	1016	1	8	5	1	1127	1126
1	6	1	656	655	1	7	6	766	765	1	8	6	1	876	875	1	9	6	1	986	985
1	7	1	515	514	1	8	7	625	624	1	9	7	1	735	734	1	10	7	1	845	844
1	8	1	374	373	1	9	8	484	483	1	10	8	1	594	593	1	11	8	1	704	703
1	9	1	233	232	1	10	9	343	342	1	11	9	1	453	452	1	12	9	1	563	562
1	10	1	92	91	1	11	10	202	201	1	12	10	1	312	311	1	13	10	1	422	421

Table 4. Displacements from least-squares plane through atoms C(3), C(4), O, N, C(7) and C(8) (Å)

(Equation of plane: 0.1750X + 0.2997Y + 0.9379Z = 5.9164)

Br(1)	2.062
C(2)	0.183
C(3)	-0.016
C(4)	0.036
O(5)	-0.038
N(5)	0.091
C(7)	-0.027
C(8)	-0.045
C(7')	-1.367
C(8')	-1.349

somewhat longer than the usual value, 1.94 Å (Sutton, 1958), but in agreement with some other studies (Craven, 1962; Mathieson & Taylor, 1963; Craven, 1964; Mackay & Mathieson, 1965). The C(2)-C(3) distance of 1.49 Å is shorter than expected but is not inconsistent with similar values found by Craven (1962, 1964) and by Mackay & Mathieson (1965). This somewhat long

C-Br bond distance and the short C(2)-C(3) distance indicate more than usual ionic character in the carbon-bromine bond and support possible C-Br involvement in physiological alkylation.

No intermolecular contacts significantly shorter than expected van der Waals distances were found in the structure.

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Lithium Sulphate – a Redetermination

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Abstract. Li_2SO_4 , monoclinic, $P2_1/c$, $a=8.45$ (1), $b=4.95$ (1), $c=8.21$ (1) Å, $\beta=107.5$ (2)°, $Z=4$, $D_x=2.23$ g cm⁻³. Crystals were grown from a melt of Li_2SO_4 . The redetermination confirms the work of Albright [*Z. Kristallogr.* (1932). **84**, 150–158]. The lithium atom is tetrahedrally coordinated with a Li–O distance of 1.96 Å (mean) and there is a S–O distance of 1.472 Å (mean) in the SO_4^{2-} tetrahedra.

Introduction. The crystals were grown by heating $\text{Li}_2\text{SO}_4 \cdot \text{H}_2\text{O}$ in a platinum crucible to remove water and then to fusion. The crystals obtained on cooling are hygroscopic and were protected by a coating of shellac; they are generally of poor quality.

The intensities and cell dimensions were obtained with a Stoe–Weissenberg diffractometer (graphite monochromator, ω -scan, no attenuators, Mo $K\alpha$, $\lambda=0.7107$ Å; data collected for layers $h0l$ to $h5l$ to a maximum 2θ value of 90°). Because of difficulty of finding suitable crystals, no crossing data were collected and, consequently, the anisotropic temperature factors are not known absolutely. Corrections for Lorentz and polarization factors were applied, but none were made for absorption. 1319 reflexions were considered to be observed with $I/\sigma(I) > 3.0$.

Systematic absences $h0l$, $l \neq 2n$ and $0k0$, $k \neq 2n$ confirm space group $P2_1/c$. [The a and c axes of Albright (1932) have been exchanged to give the standard space-group setting.] Unit-cell constants were obtained from the reflecting position of high-angle reflexions on the diffractometer and their errors estimated from the accuracy of measurement.

Trial refinement of the S and O positions of Albright gave an R index of 0.17 and a difference Fourier synthesis showed the lithium atoms, also fairly close to Albright's positions. Final least-squares refinement gave $R=0.081$, with a weighting scheme of the form:

$$\sigma^2(F) = (6200 + F + 0.0011F^2)/40$$

to compensate for the slight F and F^2 dependence of the average Δ^2 versus F curve. Atomic coordinates and temperature factors are given in Table 1 together with those of Albright (1932), and bond lengths and angles are in Table 2. A list of structure factors is obtainable as Supplementary Publication No. SUP 30026 (7 pp).*

Discussion. This structure determination was undertaken as part of a study of lattice energies of sulphate crystals (e.g. Jenkins, 1972), in which anomalous results were found for Li_2SO_4 that might have been due to incorrect atomic positions. The structure was originally determined (Albright, 1932) by trial-and-error methods without refinement, but this work shows that the positions were broadly correct. The unit-cell lengths agree well with those reported by Swanson, McMurdie, Morris & Evans (1968), namely $a=8.474$ (1), $b=4.9533$ (3), $c=8.2414$ (4) Å and $\beta=107.98$ (5)°. In the present determination S–O is 1.472 Å (mean) and Li–O is 1.96 Å (mean) which may be compared with the corresponding S–O distances 1.402 Å (Na_2SO_4), 1.491 Å (K_2SO_4), 1.502 Å (Rb_2SO_4) and 1.493 Å (Cs_2SO_4), and corresponding M–O distances 2.32 Å ($M=\text{Na}$), 2.66 Å ($M=\text{K}$), 2.88 Å ($M=\text{Rb}$) and 3.04 Å ($M=\text{Cs}$) in other sulphates (data from Wyckoff, 1966). The latter figures suggest an 'ionic' radius for the oxygen of a sulphate group of 1.34 Å (mean), by subtracting standard ionic radii (Shannon & Prewitt, 1969) for the alkali metals from these S–O distances. This is al-

* This table has been deposited with the National Lending Library, England. Copies may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.