degree of overlap between molecules in adjacent layers. The positively charged hypoxanthine ions are packed in a skewed 'stack' with virtually no overlap between neighboring molecules (Fig. 5). Such absence of overlap is also observed in adenine hydrochloride hemihydrate (Cochran, 1951) and in guanine hydrochloride monohydrate (Broomhead, 1951) and may reflect that repulsion between equally charged ions overrides the associative forces which are present in stacks of neutral purine moieties.

*Thermal motion*

The thermal motion of the atoms of this crystal is fairly low, and any correction in bond lengths because of rigid body motion would probably be negligible. The water oxygen and the chlorine ion show pronounced anisotropic thermal motion, while the thermal motion of the other atoms is approximately isotropic. The thermal ellipsoids at 50% probability are displayed in Fig. 1.
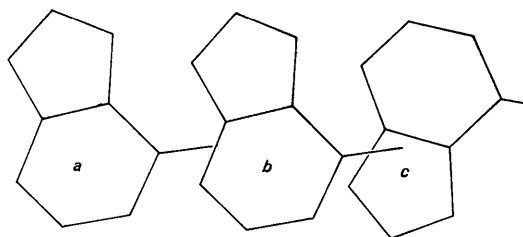
Fig. 5. Overlap between molecules in adjacent layers as viewed normal to the molecular plane. Molecules *a* and *c* are in a layer 3·18 Å below molecule *b*.

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# The Crystal Structure of 4-Methylthiomorpholine-1,1-dioxide

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The crystal structure of 4-methylthiomorpholine-1,1-dioxide has been determined by single-crystal X-ray diffraction techniques. The crystals are monoclinic, ($P2_1/c$), with $a = 11·439$ Å, $b = 5·88$ Å, $c = 11·090$ Å, $\beta = 98·56°$, $Z = 4$. A total of 814 reflections, measured above background, was collected by counter methods. The structure was refined by the method of full-matrix least-squares which led to a final weighted $R$ index of 4·1% ($R = 5·5\%$).

## Introduction

As part of a research program on the geometry of the sulfone group in ring systems, the structure of 4-methylthiomorpholine-1,1-dioxide has been determined by single-crystal X-ray diffraction techniques.

## Experimental

Crystals of 4-methylthiomorpholine-1,1-dioxide suitable for X-ray analysis were obtained from a commercial sample by slow evaporation of an anhydrous ether solution. The crystals were found to slowly sublime when exposed to the atmosphere and it was necessary to seal them in glass capillaries for all diffraction work. Crystals used in this study were prismatic in habit and averaged 0·15 mm in diameter.

On the basis of Weissenberg photographs, the systematic absences were:

$h0l$ absent for $l$ odd,
$0k0$ absent for $k$ odd.

These systematic absences uniquely determine the space group as $P2_1/c$.

The $a$ and $c$ cell constants and the $\beta$ angle were determined from measurements on a Phillips PAILRED diffractometer. The $b$ cell constant was determined from sodium-chloride-calibrated rotation photographs. The results of the measurements and their estimated standard deviations are (Cu $K\alpha_1 = 1\cdot54051$; Mo $K\alpha_1 = 0\cdot70926$ Å):

$$a = 11\cdot439\ (4)\ \text{Å},$$
$$b = 5\cdot88\ (1)\ \text{Å}\ [a_0(\text{NaCl}) = 5\cdot637\ \text{Å}],$$
$$c = 11\cdot090\ (3)\ \text{Å},$$
$$\beta = 98\cdot566\ (6)^\circ.$$

The calculated density assuming four molecules per unit cell was $1\cdot341$ g.cm$^{-3}$. The density measured by flotation methods was $1\cdot340$ g.cm$^{-3}$.

A set of $h0l$ intensity data was collected from Weissenberg photographs using Cu $K\alpha$ nickel-filtered radiation. This set of data was used to determine the $x$ and $z$ parameters of all non-hydrogen atoms. Three-dimensional data ($h, k = 0$–$4$, $l$) were collected on a Phillips PAILRED diffractometer employing equi-inclination geometry. One crystal, mounted along the $b$ axis, was used throughout the experiment. All data were collected with quartz-monochromatized molybdenum $K\alpha$ radiation. The fixed-counter moving-crystal method was used employing a $1\cdot5^\circ$ scan range and a $1^\circ$ per minute scan. Background was measured for a fixed time of $0\cdot4$ minutes at the beginning and end of each scan. The counting statistical error was calculated for every reflection (Ladell, 1965). All reflections for which the counting statistical error exceeded 40% of the measured intensity were rejected. All intensity data were corrected

Table 1. *Observed and calculated structure factors*

for Lorentz, polarization and Tunell factors (Bond, 1959). The maximum value of $\mu R$ was 0·036 and no absorption corrections were made.

## Structure determination

A Patterson projection, $P(uw)$, was synthesized using the $h0l$ visual reflection data. From the Patterson map a set of consistent peaks corresponding to sulfur interactions was located and the $x$ and $z$ coordinates of the sulfur atom were determined, ($x=0\cdot13$, $z=0\cdot16$). The remaining heavy atoms were located by synthesizing a fourfold sum function superposition of Patterson maps translated to the sulfur atom positions. This method involves the convolution of the Patterson function with a peak function which is zero everywhere but at the positions of the sulfur atoms (Lipson & Taylor, 1958).

This peak function may be represented by the electron density of point scatterers located at the sulfur atom positions. The transforms of the superposition are

$$S(h,k,l) = F(h,k,l)^2 . G(h,k,l) \ ,$$

where $F(h,k,l)$ is the observed structure factor and

$$G(h,k,l) = \exp\left[2\pi i(hx_s + ky_s + lz_s)\right]$$

($x_s, y_s, z_s$ are the sulfur atom coordinates).

The $x$ and $z$ coordinates for all heavy atoms were refined by full-matrix least-squares, by use of the program $ORFLS$ written by Busing, Martin & Levy (1962) to an $R$ index of 20%. Isotropic temperature factors of 3·0 were not refined. All structure factor calculations were made using the scattering factors of Cromer & Waber (1965).

Using the set of three-dimensional data, a three-dimensional Patterson function was synthesized. The sulfur–sulfur interactions were located and the $y$ coordinate of the sulfur atom was determined. A three-dimensional electron density, using phases determined by the position of the sulfur atom, was synthesized from which it was possible to determine the $y$ coordinates of the remaining atoms.

## Refinement

A total of 814 reflections was used in the three-dimensional full-matrix least-squares refinement. All calculations were performed on an IBM 7094 computer using the Busing, Martin & Levy least-squares program. The quantity minimized was $\Sigma w(|F_o| - S_q|F_c|)^2$, ($S_q$ being the scale factor for the $q$th layer.) The layer scale factor, $S_q$, was not refined, but rather was used to correct each layer for the effect of slow evaporation of the crystal by comparing periodically the values of the intensity of a reference reflection. After one cycle of refinement with all atoms assigned temperature factors of 3·0, the reliability index $\left(R = \dfrac{\Sigma \, ||F_o| - S_q|F_c||}{\Sigma \, |F_o|}\right)$ was calculated to be 18%. An additional cycle of refinement which included refinement of isotropic temperature factors reduced the $R$ to 14%. All reflections were now
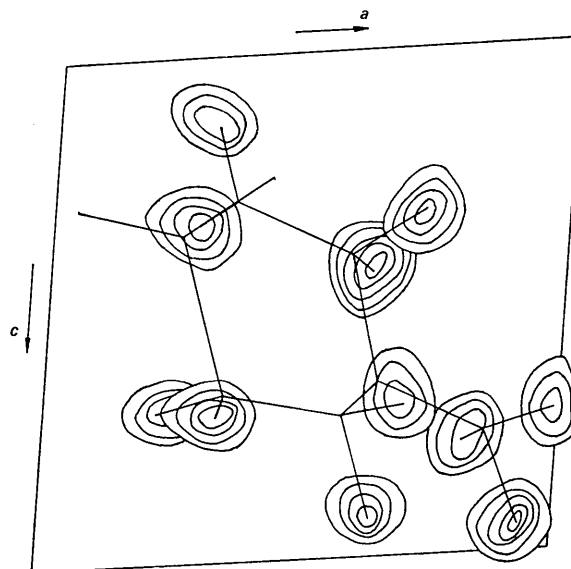


Fig. 1. A composite difference map showing observed hydrogen atom peaks. Contours are at intervals of 0·1 e.Å$^{-3}$, beginning with the 0·2 e.Å$^{-3}$ contour.

## Table 2. Final positional and thermal parameters for non-hydrogen atoms and their estimated standard deviations

The values in the table have been multiplied by $10^4$. The temperature factors are of the form:

$$T = \exp\left(-\beta_{11}h^2 - \beta_{22}k^2 - \beta_{33}l^2 - 2\beta_{12}hk - 2\beta_{13}hl - 2\beta_{23}kl\right) .$$

|  | $X$ | $Y$ | $Z$ | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ | $\beta_{12}$ | $\beta_{13}$ | $\beta_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| S | 1282 (1) | 1099 (2) | 1689 (1) | 75 (1) | 168 (1) | 40 (1) | 19 (2) | 10 (1) | −1 (1) |
| N | 3134 (3) | −1862 (6) | 3309 (3) | 49 (3) | 224 (17) | 80 (3) | 16 (5) | 13 (2) | 9 (5) |
| O(1) | 0024 (3) | 1388 (6) | 1387 (2) | 91 (3) | 405 (15) | 82 (3) | 77 (5) | −12 (2) | −21 (5) |
| O(2) | 2034 (3) | 2600 (5) | 1106 (3) | 166 (4) | 159 (13) | 78 (3) | −40 (5) | 37 (3) | 24 (4) |
| C(1) | 1670 (4) | −1744 (8) | 1438 (4) | 72 (4) | 186 (19) | 65 (4) | −2 (6) | −1 (3) | −11 (6) |
| C(2) | 2943 (4) | −2197 (8) | 2002 (4) | 65 (4) | 184 (19) | 86 (4) | 6 (6) | 16 (3) | −35 (6) |
| C(3) | 2981 (4) | 0530 (8) | 3628 (3) | 63 (4) | 298 (23) | 54 (4) | 6 (6) | 16 (3) | −22 (7) |
| C(4) | 1716 (4) | 1294 (8) | 3272 (3) | 76 (4) | 232 (18) | 52 (3) | 22 (7) | 17 (3) | −8 (6) |
| C(5) | 4297 (4) | −2664 (9) | 3854 (4) | 77 (5) | 409 (25) | 106 (5) | 32 (8) | 8 (4) | −2 (8) |

assigned weights according to the weighting scheme of Evans (1961), where $\sigma = \frac{1}{2}[A(1+b)/(1-b)]|^{1/2}$. In this equation, $A$ is the geometric factor applied to the measured intensities and $b$ equals the total background divided by the total number of counts.

Additional refinement of coordinates and anisotropic temperature factors reduced the conventional $R$ index to 8%. All eleven hydrogen atoms were then



Fig. 2. Bond lengths and angle in the molecule.

located in a three-dimensional difference synthesis. Isotropic temperature factors for the hydrogen atoms ranging from 4·0 to 6·0 were assigned by examination of the peaks in the difference map. A composite of the three-dimensional difference map, viewed down the $b$ axis, is shown in Fig. 1.

The final cycles of refinement were carried out by alternately varying the heavy atom positional and anisotropic temperature factors as a block and then varying the hydrogen positional parameters as a block. The maximum value of the final parameter shifts divided by the estimated standard deviations was 0·020 for the non-hydrogen atoms and 0·021 for the hydrogen atoms. The hydrogen atom scattering factors used were those of Stewart, Davidson & Simpson (1965). An attempt was made to refine on the hydrogen atom temperature factors without success. The final weighted $R'$ $\{R' = [\Sigma \ w(F_o - S_q F_c)^2]^{1/2}/(\ \Sigma \ w F_o^2)^{1/2}\}$ using of all 814 reflections was 4·1% while the conventional $R$ was reduced to 5·5%.

The observed and final calculated structure factors are shown in Table 1. The final coordinates and anisotropic temperature factors along with estimated standard deviations for all non-hydrogen atoms are shown in Table 2. Final coordinates and isotropic temperature factors for the hydrogen atoms are shown in Table 3.

Table 3. *Final positional and thermal parameters for hydrogen atoms*

The values for the coordinates have been multiplied by $10^4$.

|        | X          | Y           | Z          | B   |
|--------|------------|-------------|------------|-----|
| H(1)   | 1503 (38)  | −2148 (81)  | 0635 (43)  | 6·0 |
| H(2)   | 1210 (36)  | −2867 (83)  | 1804 (38)  | 4·5 |
| H(3)   | 3439 (39)  | −1063 (80)  | 1694 (34)  | 4·5 |
| H(4)   | 3151 (29)  | −3845 (81)  | 1883 (28)  | 4·0 |
| H(5)   | 1199 (32)  | 0287 (69)   | 3544 (29)  | 5·0 |
| H(6)   | 1626 (29)  | 2941 (75)   | 3407 (28)  | 4·5 |
| H(7)   | 3209 (32)  | 0650 (66)   | 4570 (34)  | 4·5 |
| H(8)   | 3508 (36)  | 1648 (78)   | 3179 (35)  | 5·5 |
| H(9)   | 4468 (36)  | −2366 (83)  | 4750 (48)  | 4·0 |
| H(10)  | 4402 (51)  | −4136 (134) | 3566 (53)  | 5·5 |
| H(11)  | 4922 (69)  | −1731 (145) | 3499 (67)  | 5·5 |



4-METHYLTHIOMORPHOLINE-1,1-DIOXIDE          4-METHYLTHIOMORPHOLINE-1,1-DIOXIDE

Fig. 3. Stereogram showing the 4-methylthiomorpholine-1,1-dioxide molecule with thermal ellipsoids for non-hydrogen atoms scaled to enclose 50% probability.

Table 4. *Bond distances and angles and their estimated standard deviations*

| S —O(1) | 1·438 (3) Å | | C(1)-H(2) | 0·971 (5) Å |
|---|---|---|---|---|
| S —O(2) | 1·451 (3) | | C(2)-H(3) | 0·970 (5) |
| S —C(1) | 1·763 (5) | | C(2)-H(4) | 1·011 (5) |
| S —C(4) | 1·756 (4) | | C(3)-H(5) | 1·041 (4) |
| C(1)-C(2) | 1·521 (5) | | C(3)-H(6) | 1·065 (4) |
| C(2)-N | 1·448 (5) | | C(4)-H(7) | 0·919 (4) |
| C(3)-C(4) | 1·511 (5) | | C(4)-H(8) | 0·988 (5) |
| C(3)-N | 1·467 (5) | | C(5)-H(9) | 1·000 (5) |
| C(5)-N | 1·456 (5) | | C(5)-H(10) | 0·936 (5) |
| C(1)-H(1) | 0·914 (4) | | C(5)-H(11) | 1·025 (5) |

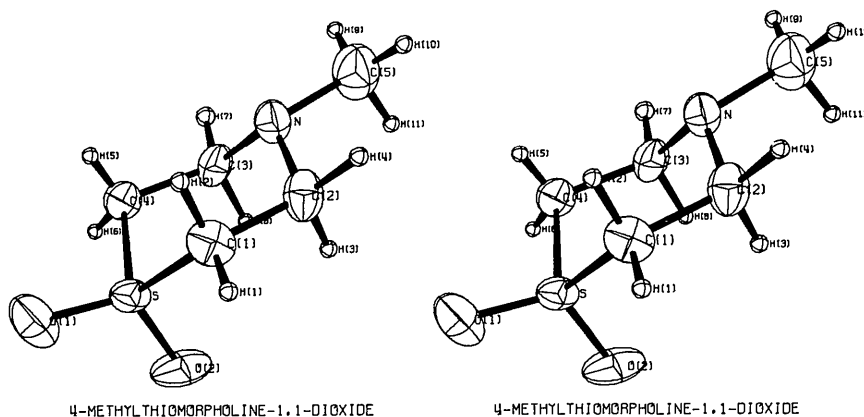| O(1)-S —O(2) | 117·6° (2) | | C(2)—N—C(3) | 111·5° (3) |
|---|---|---|---|---|
| O(1)-S —C(4) | 110·5 (2) | | C(2)—N—C(5) | 111·4 (3) |
| O(1)-S —C(1) | 109·9 (2) | | C(3)—N—C(5) | 110·2 (3) |
| O(2)-S —C(4) | 107·9 (2) | | H(1)—C(1)-H(2) | 100·5 (3) |
| O(2)-S —C(1) | 109·0 (2) | | H(3)—C(2)-H(4) | 116·8 (3) |
| C(1)-S —C(4) | 100·4 (2) | | H(5)—C(3)-H(6) | 110·7 (3) |
| S —C(1)-C(2) | 110·4 (3) | | H(7)—C(4)-H(8) | 119·7 (4) |
| S —C(4)-C(3) | 111·0 (3) | | H(9)—C(5)-H(10) | 110·0 (4) |
| C(1)-C(2)-N | 112·4 (3) | | H(10)-C(5)-H(11) | 104·1 (4) |
| C(4)-C(3)-N | 111·5 (3) | | H(9)—C(5)-H(11) | 103·5 (4) |

## Discussion

The crystal structure determination shows the ring to be in the expected chair conformation. The bond distances and angles for all non-hydrogen atoms are shown in Fig.2. All bond distances and angles are given in Table 4. Thermal ellipsoids for all heavy atoms were calculated and are described in Table 5. All bond distances and angles, and thermal ellipsoid calculations were made on a 7094 computer using the program *ORFFE*, written by Busing, Martin & Levy (1964). A stereoscopic drawing of the molecule with 50% probability ellipsoids for the non-hydrogen atoms and spheres of constant radius 0·1 Å representing the hydrogen atoms is shown in Fig.3. Fig.3 was drawn with the use of the program *ORTEP*, written by Johnson (1965).

Table 5. *R.m.s. displacements* ( × 10⁴) *along the principal axes of the thermal ellipsoids and the angles between these axes and the a, b, and c\* axes*

| | | *a* | *b* | *c\** |
|---|---|---|---|---|
| S | 1534 (15) Å | 80° | 75° | 161° |
| | 1670 (22) | 104 | 157 | 108 |
| | 2259 (15) | 162 | 73 | 96 |
| N | 1692 (61) | 155 | 115 | 91 |
| | 2008 (62) | 66 | 148 | 110 |
| | 2233 (49) | 97 | 72 | 160 |
| O(1) | 1889 (44) | 136 | 116 | 122 |
| | 2224 (46) | 104 | 124 | 38 |
| | 3154 (45) | 131 | 46 | 73 |
| O(2) | 1430 (70) | 103 | 27 | 66 |
| | 2205 (43) | 98 | 116 | 27 |
| | 3322 (41) | 164 | 99 | 103 |
| C(1) | 1748 (80) | 96 | 11 | 98 |
| | 1942 (59) | 63 | 79 | 29 |
| | 2295 (64) | 152 | 91 | 62 |
| C(2) | 1595 (87) | 73 | 30 | 114 |
| | 2056 (68) | 17 | 107 | 86 |
| | 2385 (59) | 93 | 114 | 155 |

Table 5 (*cont.*)

| | | *a* | *b* | *c\** |
|---|---|---|---|---|
| C(3) | 1657 (68) | 62 | 73 | 146 |
| | 2055 (60) | 29 | 94 | 62 |
| | 2343 (84) | 95 | 18 | 73 |
| C(4) | 1666 (68) | 66 | 66 | 145 |
| | 1982 (69) | 71 | 39 | 57 |
| | 2319 (62) | 149 | 61 | 101 |
| C(5) | 2142 (75) | 155 | 112 | 102 |
| | 2551 (63) | 96 | 105 | 16 |
| | 2769 (77) | 114 | 27 | 79 |

All bond lengths and valency angles associated with the sulfur atom are compared with corresponding values observed for some related compounds in Table 6. The sulfur–carbon bond distances found in the literature vary considerably. Abrahams (1956) reports a mean value of 1·82 Å based on six compounds. The values reported in this paper of 1·756 (4) Å and 1·763
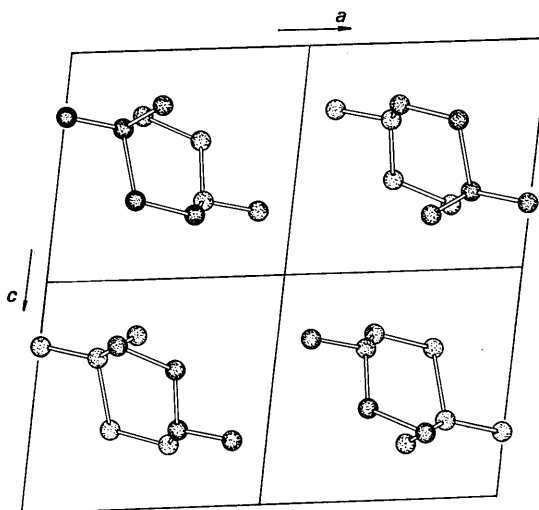


Fig.4. An (010) projection of the structure.

Table 6. *Sulfur valency angles and bond distances in* 4-*methylthiomorpholine*-1,1-*dioxide compared with values in related compounds*

| | | |
|---|---|---|
| O–S–O | 117·6 (0·2)° | $CH_3NC_4H_8SO_2$ (This paper) |
| | 119·3 (0·9) | $(CH_3SO_2)_3CH$ (Silverton, Gibson & Abrahams, 1965) |
| | 120·4 (0·4) | $(p–ClC_6H_4)_2SO_2$ (Sime & Abrahams, 1960) |
| | 120·4 (0·7) | $(CH_3)_2C_2H_2SO_2$ (Desiderato & Sass, 1967) |
| O–S–C | 110·5 (0·2) | $CH_3NC_4H_8SO_2$ |
| | 109·9 (0·2) | |
| | 107·9 (0·2) | |
| | 109·0 (0·2) | |
| | 107 (1)° | $(CH_3SO_2)_3CH$ |
| | 106 (1) | |
| | 107 (1) | |
| | 111 (1) | |
| | 107·3 (0·3)° | $(p–ClC_6H_4)_2SO_2$ |
| | 108·0 (0·3) | |
| | 109 (5)° | $(p–BrC_6H_4)_2SO_2$ (Abrahams, 1956) |
| | 105 (3)° | $(CH_3)_2SO_2$ (Abrahams, 1956) |
| C–S–C | 100·4 (0·2)° | $CH_3NC_4H_8SO_2$ |
| | 105 (1) | $(CH_3SO_2)_3CH$ |
| | 100 (5) | $(p–BrC_6H_4)_2SO_2$ |
| | 99·6 (2) | $\beta–CH_3C_4H_5SO_2$ (Jeffrey, 1953) |
| S–O | 1·438 (3) Å | $CH_3NC_4H_8SO_2$ |
| | 1·451 (3) | |
| | 1·435 (10) | $(CH_3SO_2)_3CH$ |
| | 1·436 (17) | $\beta–CH_3C_4H_5SO_2$ |
| | 1·43 (2) | $(CH_3)_2SO_2$ |
| S–C | 1·763 (5) Å | $CH_3NC_4H_8SO_2$ |
| | 1·756 (4) | |
| | 1·83 (1) Å | $(CH_3SO_2)_3CH$ |
| | 1·73 (2) | |
| | 1·75 (2) Å | $\beta–CH_3C_4H_5SO_2$ |
| | 1·80 (2) | $(CH_3)_2SO_2$ |
| | 1·73 Å | $(CH_3)_2C_2H_2SO_2$ |

(5) Å are somewhat shorter than this mean value, but in good agreement with the value of 1·75 (2) Å reported by Jeffrey (1951) for β-isoprene sulfone. All other bond distances and angles in 4-methylthiomorpholine-1,1-dioxide were found to be quite normal.

A (010) projection of the structure indicating the crystal packing is shown in Fig.4. All intermolecular distances less than 4·0 Å were calculated and are shown in Table 7. There were no contacts shorter than the accepted van der Waals contact (Pauling, 1948).

Table 7. *Non-hydrogen atom intermolecular contacts less than* 4·0 Å

| | |
|---|---|
| S —O(1) (a) | 3·809 (3) Å |
| O(1)–O(1) (a) | 3·477 (4) |
| O(1)–C(1) (a) | 3·438 (4) |
| C(3)–O(2) (b) | 3·291 (5) |
| C(4)–O(2) (b) | 3·180 (4) |
| O(1)–S (c) | 3·926 (3) |
| O(1)–N (c) | 3·820 (4) |
| O(1)–O(1) (c) | 3·856 (4) |
| O(1)–C(1) (d) | 3·491 (5) |
| O(1)–C(4) (d) | 3·557 (5) |
| C(1)–O(2) (d) | 3·378 (5) |
| C(2)–O(2) (d) | 3·335 (5) |

Table 7 (*cont.*)

Letters in parenthesis refer to the following positions

(a)  $\bar{x}$,      $\bar{y}$,      $z$
(b)  $x$, $\frac{1}{2}-y$, $\frac{1}{2}+z$
(c)  $\bar{x}$, $\frac{1}{2}+y$, $\frac{1}{2}-z$
(d)  $x$, $y-1$,      $z$

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# The Crystal Structure of 2-Keto-3-ethoxybutyraldehyde-bis(thiosemicarbazone)*

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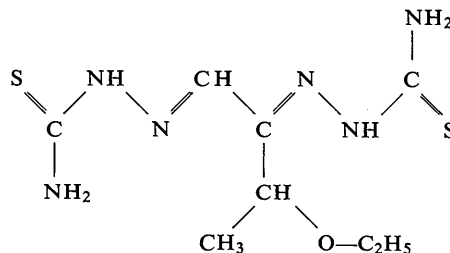
The structure of the compound 2-keto-3-ethoxybutyraldehyde-bis(thiosemicarbazone), commonly referred to as KTS and with formula
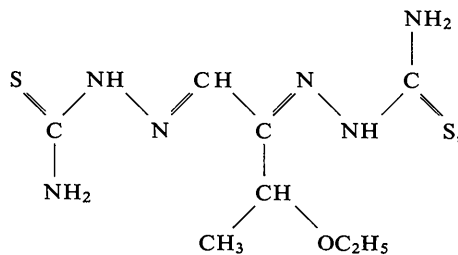


has been determined. KTS is an effective antitumor agent in certain animals in the presence of cupric ions. It crystallizes in the space group $P2_1/c$ and the unit-cell dimensions are $a = 20.846$, $b = 13.809$, $c = 9.557$ Å and $\beta = 95.5°$. There are two molecules of $C_8H_{16}N_6OS_2$ per asymmetric unit. The structure was solved by an application of the symbolic addition procedure. The molecule is fully extended from one sulphur atom to the other and is approximately planar except for the side chain. The bond distances and angles are very similar in the two molecules. There is an internal O---H–N hydrogen bond. The packing of the molecule seems dominated by the formation of N–H---S hydrogen bonds. There is also one very short C–H---S packing distance between the two molecules in the asymmetric unit which appears to involve an interaction strong enough to cause some distortion in one of the molecules. This tendency to association, occurring between molecules which are unrelated crystallographically and which have opposite absolute configurations, may explain why there are two molecules in the asymmetric unit.

## Introduction

The compound 2-keto-3-ethoxybutyraldehyde-bis(thiosemicarbazone),



KTS, has been shown to be a very effective antitumor agent in animals, especially in the presence of cupric ions (Petering, Buskirk & Underwood, 1964; Petering, Buskirk & Crim, 1967; Crim & Petering, 1967; Booth, Johns, Bertino & Sartorelli, 1968). The structure of the cupric complex has already been reported briefly (Taylor, Gabe, Glusker, Minkin & Patterson, 1966)