CROMER, D. T. & WABER, J. T. (1965). *Acta Cryst.* **18**, 104.

DESIDERATO, R. & SASS, R. L. (1967). *Acta Cryst.* **23**, 430.

EVANS, H. T. (1961). *Acta Cryst.* **14**, 689.

JEFFREY, G. A. (1951). *Acta Cryst.* **14**, 58.

JOHNSON, C. K. (1965). *ORTEP, A Fortran Thermal Ellipsoid Plot Program For Crystal Structure Illustrations.* Oak Ridge National Laboratory, Oak Ridge, Tennessee.

LADELL, J. (1965). *Norelco Reporter,* **12**, 32.

LIPSON, H. & TAYLOR, C. A. (1958). *Fourier Transforms in X-ray Diffraction.* London: Bell.

PAULING, L. (1948). *The Nature of the Chemical Bond,* p. 187. Ithica, New York: Cornell Univ. Press.

SILVERTON, J. V., GIBSON, D. T. & ABRAHAMS, S. C. (1965). *Acta Cryst.* **19**, 651.

SIME, J. G. & ABRAHAMS, S. C. (1960). *Acta Cryst.* **13**, 1.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175.
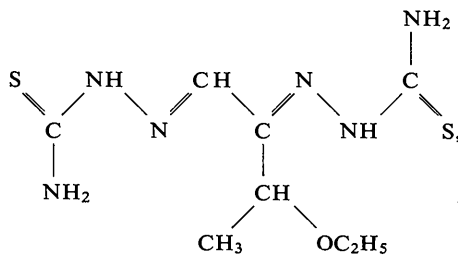
The Crystal Structure of 2-Keto-3-ethoxybutyraldehyde-bis(thiosemicarbazone)*

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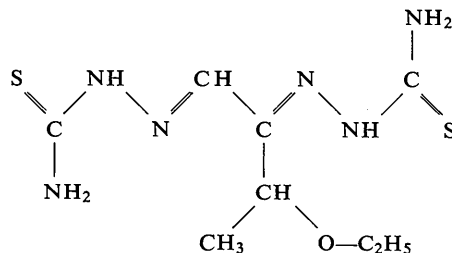
The structure of the compound 2-keto-3-ethoxybutyraldehyde-bis(thiosemicarbazone), commonly referred to as KTS and with formula

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 $a = 20{\cdot}846$, $b = 13{\cdot}809$, $c = 9{\cdot}557$ Å and $\beta = 95{\cdot}5°$. 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 $O\text{-}\text{-}\text{-}H\text{-}N$ hydrogen bond. The packing of the molecule seems dominated by the formation of $N\text{-}H\text{-}\text{-}\text{-}S$ hydrogen bonds. There is also one very short $C\text{-}H\text{-}\text{-}\text{-}S$ 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)

along with preliminary results on the free ligand; the structure of the latter is described in full in the present paper.

Experimental

Crystals of the free ligand, KTS, were supplied to us by Dr H.G.Petering, formerly of the Upjohn Company, Kalamazoo, Michigan. They were regular hexagonal prisms elongated in the **c** direction. A section of one of these prisms with dimensions $0.15 \times 0.17 \times 0.17$ mm was used for all measurements. The unit-cell dimensions are $a = 20.846$, $b = 13.809$, $c = 9.557$ Å and $\beta = 95.5°$ (standard deviations in length 0.13%, in angle 0.1°, $\lambda(Cu\ K\alpha_1) = 1.54050$ Å). The systematic absences in the diffraction pattern ($h0l$ with l odd; $0k0$ with k odd) showed that the space group is $P2_1/c$ and the density (observed 1.33 g.cm^{-3}, calculated 1.34 g.cm^{-3}) is consistent with the fact that there are two molecules of $C_8H_{16}N_6OS_2$ in the asymmetric unit.

The intensities of 6019 unique reflections with $2\theta \le 163°$ were measured on a General Electric XRD-5 diffractometer with nickel-filtered Cu radiation and the

Table 1. *Statistical data for the symbolic addition procedure*

(a) Statistical averages for normalized structure factors (E)

	$\langle |E| \rangle$	$\langle |E^2 - 1| \rangle$	$\langle |E|^2 \rangle$
Experimental for KTS	0.828	0.982	1.026
Theoretical: centrosymmetric	0.798	0.968	1.000
non-centrosymmetric	0.886	0.736	1.000

(b) Distribution of structure factors

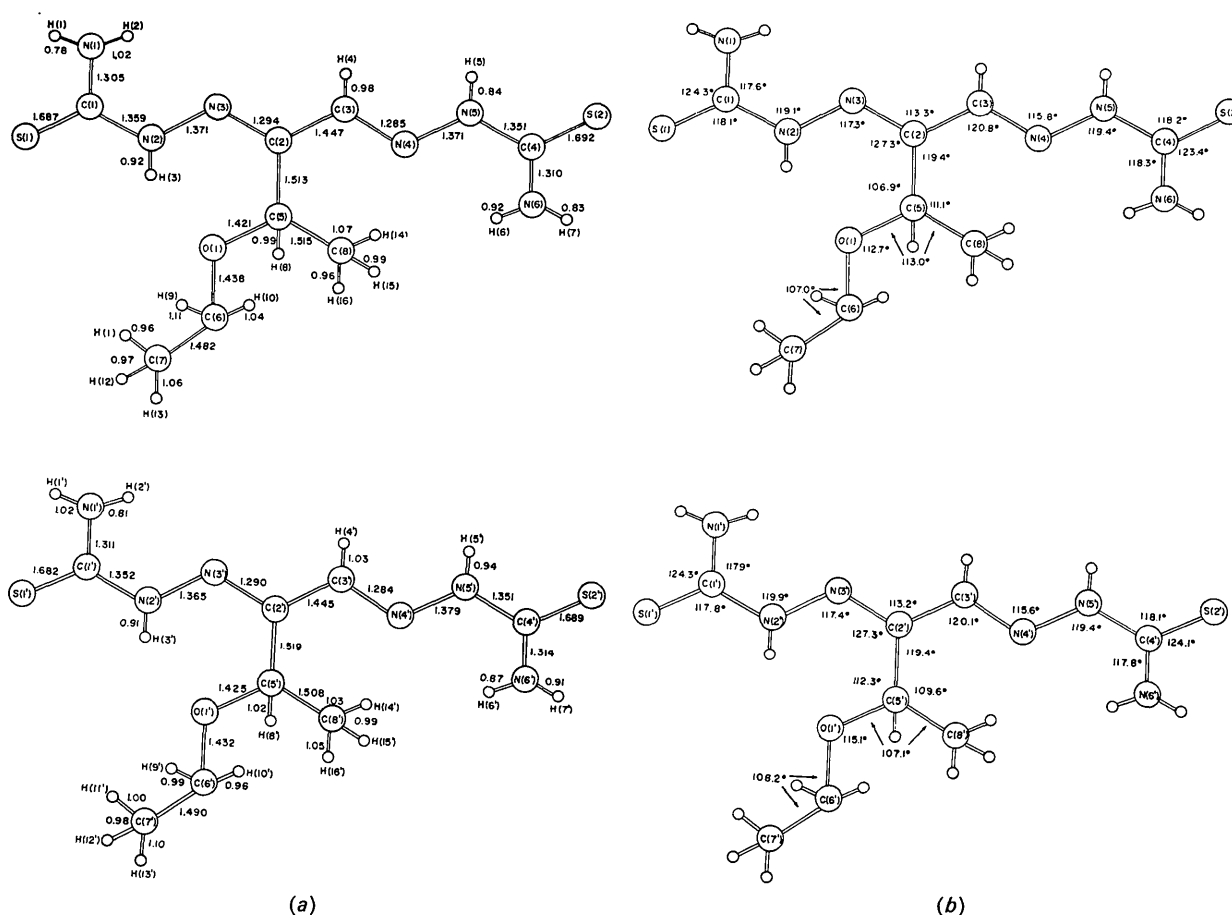|	Experimental	Theoretical (centrosymmetric)
$|E| > 3$	0.3%	0.3%
$|E| > 2$	4.7%	5.0%
$|E| > 1$	32.0%	32.0%

(a)

(b)

Fig. 1. (a) Interatomic distances in the two molecules (Å). (b) Interbond angles in the two molecules.

$\theta/2\theta$ scan technique. Of these reflections 3832 were of measurable intensity. The crystal was sufficiently regular for a spherical absorption correction to be applied and this was done with $\mu = 36.3$ cm^{-1} and a mean radius (for a sphere of volume equivalent to that of the crystal) of $R = 0.01$ cm. A correction was also applied for the

Table 2. *Final positional and temperature parameters*

Positional parameters are given as fractions of cell edges. Anisotropic temperature factors are expressed as

$$\exp\{-(h^2 b^{11} + k^2 b^{22} + l^2 b^{33} + 2hk b^{12} + 2hl b^{13} + 2kl b^{23})\}.$$

Isotropic temperature factors are of the form

$$\exp(-B \sin^2 \theta/\lambda^2)$$

and are given in Å^2. Standard deviations, determined from the inverted block diagonal matrices, are listed below the parameters with respect to the last decimal places given (except for isotropic B values).

Atom	x	y	z	b^{11}	b^{22}	b^{33}	b^{12}	b^{13}	b^{23}
S(1)	0.4043(1)	0.3579(1)	0.0123(1)	0.00195(3)	0.00414(8)	0.00996(15)	0.00107(5)	0.00116(6)	0.00056(10)
S(2)	0.7525(1)	-0.2235(1)	0.2787(1)	0.00171(3)	0.00392(15)	0.00983(4)	0.00090(15)	0.00105(7)	0.00120(10)
O(1)	0.6018(1)	0.2371(2)	-0.0578(1)	0.00195(9)	0.00331(20)	0.01099(45)	-0.00021(11)	0.00148(16)	0.00011(25)
N(1)	0.3972(2)	0.1928(3)	0.1515(4)	0.00194(11)	0.00440(27)	0.01228(59)	0.00088(14)	0.00236(21)	0.00145(33)
N(2)	0.4837(2)	0.2107(3)	0.0250(4)	0.00145(9)	0.00359(24)	0.00936(49)	0.00078(13)	0.00110(18)	0.00100(29)
N(3)	0.5094(2)	0.1276(3)	0.0855(4)	0.00138(9)	0.00333(23)	0.00803(44)	0.00035(12)	0.00048(17)	0.00046(28)
N(4)	0.6433(2)	-0.0232(3)	0.0941(4)	0.00132(9)	0.00303(23)	0.00734(44)	0.00041(12)	0.00038(16)	0.00044(26)
N(5)	0.6658(2)	-0.0975(3)	0.1804(4)	0.00142(9)	0.00357(24)	0.00872(48)	0.00076(12)	0.00134(17)	0.00142(28)
N(6)	0.7540(2)	-0.1089(3)	0.0566(4)	0.00144(10)	0.00566(29)	0.00960(51)	0.00071(14)	0.00150(18)	0.00218(33)
C(1)	0.4282(2)	0.2466(3)	0.0682(4)	0.00146(11)	0.00336(28)	0.00700(51)	0.00052(14)	0.00040(19)	-0.00083(30)
C(2)	0.5620(2)	0.0953(3)	0.0406(4)	0.00124(10)	0.00313(27)	0.00753(53)	0.00012(14)	0.00036(19)	-0.00023(31)
C(3)	0.5886(2)	0.0125(3)	0.1188(4)	0.00117(10)	0.00325(27)	0.00869(56)	0.00002(14)	0.00077(19)	0.00093(32)
C(4)	0.7237(2)	-0.1374(3)	0.1633(4)	0.00130(10)	0.00279(26)	0.00722(49)	0.00009(14)	0.00054(18)	-0.00006(31)
C(5)	0.5968(2)	0.1354(3)	-0.0786(4)	0.00137(11)	0.00292(27)	0.00881(55)	0.00027(14)	0.00094(20)	0.00010(32)
C(6)	0.6471(2)	0.2814(3)	-0.1423(5)	0.00231(15)	0.00481(35)	0.01128(69)	-0.00062(14)	0.00092(26)	0.00161(42)
C(7)	0.6594(3)	0.3806(4)	-0.0869(5)	0.00486(24)	0.00751(47)	0.01144(78)	-0.00038(37)	0.00119(35)	0.00044(52)
C(8)	0.5622(2)	0.1084(4)	-0.2199(5)	0.00228(14)	0.00585(37)	0.00877(61)	-0.00027(20)	0.00050(24)	0.00014(41)

Atom	x	y	z	b^{11}	b^{22}	b^{33}	b^{12}	b^{13}	b^{23}
S(1')	0.2671(1)	0.5305(1)	-0.2725(1)	0.00331(5)	0.00665(11)	0.00963(17)	-0.00004(6)	0.00316(7)	-0.00152(12)
S(2')	-0.0867(1)	0.5964(1)	0.5053(1)	0.00191(4)	0.01099(15)	0.01211(19)	0.00140(7)	0.00224(7)	0.00266(15)
O(1')	0.1218(1)	0.7317(2)	-0.1218(1)	0.00218(9)	0.00340(20)	0.00767(38)	-0.00022(12)	0.00028(15)	0.0002?(24)
N(1')	0.2408(2)	0.4255(3)	-0.0527(4)	0.00222(12)	0.00374(26)	0.01136(57)	0.00094(14)	0.00184(21)	0.00072(32)
N(2')	0.1771(2)	0.5574(3)	-0.1055(4)	0.00211(11)	0.00459(27)	0.00788(48)	0.00086(14)	0.00140(19)	0.00134(30)
N(3')	0.1474(2)	0.5419(3)	0.0138(4)	0.00154(10)	0.00392(25)	0.00829(48)	0.00022(13)	0.00121(17)	0.00097(28)
N(4')	0.0189(2)	0.6164(3)	0.1910(4)	0.00151(10)	0.00389(25)	0.00952(50)	0.00004(13)	0.00149(18)	-0.00017(30)
N(5')	-0.0040(2)	0.5907(3)	0.3165(4)	0.00140(9)	0.00494(28)	0.00912(51)	0.00032(14)	0.00104(18)	0.00030(30)
N(6')	-0.0090(2)	0.6751(3)	0.2503(4)	0.00149(10)	0.00678(33)	0.01239(59)	0.00082(15)	0.00120(20)	0.00189(37)
C(1')	0.2264(2)	0.4997(3)	-0.1354(4)	0.00183(12)	0.00379(29)	0.00722(53)	-0.00031(16)	0.00104(21)	-0.00123(33)
C(2')	0.1010(2)	0.5995(3)	0.0380(4)	0.00142(11)	0.00320(27)	0.00906(56)	0.00013(16)	0.00092(20)	0.00008(33)
C(3')	0.0720(2)	0.5760(3)	0.1652(5)	0.00141(11)	0.00406(30)	0.01024(63)	-0.00011(16)	0.00107(21)	0.00018(37)
C(4')	-0.0623(2)	0.6232(3)	0.3463(5)	0.00121(11)	0.00528(33)	0.01027(62)	-0.00015(16)	0.00092(21)	-0.00056(39)
C(5')	0.0734(2)	0.6819(3)	-0.0543(5)	0.00157(12)	0.00322(28)	0.01123(66)	0.00008(15)	0.00034(23)	0.00075(36)
C(6')	0.1633(2)	0.7924(3)	-0.0317(5)	0.00260(16)	0.00431(36)	0.01108(70)	-0.00007(19)	0.00010(27)	-0.00058(40)
C(7')	0.2152(3)	0.8297(4)	-0.1142(5)	0.00258(17)	0.00671(43)	0.01325(81)	-0.00132(29)	-0.00024(29)	0.00238(49)
C(8')	0.0256(3)	0.6423(4)	-0.1685(5)	0.00249(16)	0.00564(41)	0.01491(84)	-0.00039(21)	-0.00160(29)	0.00084(49)

Atom	x	y	z	B
H(1)	0.3629(17)	0.2063(27)	0.1715(38)	4.3 (1.1)
H(2)	0.4172(20)	0.1288(31)	0.1855(42)	6.7 (1.3)
H(3)	0.5133(19)	0.2421(30)	-0.0246(43)	6.0 (1.3)
H(4)	0.5654(16)	-0.0150(26)	0.1940(36)	3.1 (1.0)
H(5)	0.6428(19)	-0.1071(29)	0.2467(41)	5.5 (1.2)
H(6)	0.7366(18)	-0.0640(27)	-0.0069(39)	4.5 (1.1)
H(7)	0.7928(18)	-0.1236(29)	0.0566(38)	4.9 (1.1)
H(8)	0.6399(17)	0.1057(26)	-0.0779(36)	3.4 (1.0)
H(9)	0.6929(21)	0.2403(33)	-0.1292(46)	7.2 (1.4)
H(10)	0.6208(21)	0.2921(33)	-0.2389(47)	7.7 (1.5)
H(11)	0.6919(21)	0.4109(32)	-0.1359(46)	7.9 (1.5)
H(12)	0.6753(24)	0.3744(38)	0.0111(51)	10.2 (1.7)
H(13)	0.6142(21)	0.4147(30)	-0.0833(45)	6.9 (1.4)
H(14)	0.5552(19)	0.0316(30)	-0.2258(41)	5.8 (1.2)
H(15)	0.5887(20)	0.1303(31)	-0.2948(43)	6.3 (1.3)
H(16)	0.5196(18)	0.1345(29)	-0.2248(39)	4.8 (1.1)

Atom	x	y	z	B
H(1')	0.2132(20)	0.4111(30)	0.0274(44)	6.6 (1.4)
H(2')	0.2707(19)	0.3890(29)	-0.0611(41)	5.6 (1.2)
H(3')	0.1663(20)	0.6118(30)	-0.1560(41)	6.1 (1.3)
H(4')	0.0963(17)	0.5256(28)	0.2292(38)	4.2 (1.1)
H(5')	0.0201(18)	0.5473(27)	0.3768(39)	4.4 (1.1)
H(6')	-0.1328(19)	0.6999(30)	0.2679(42)	5.7 (1.2)
H(7')	-0.0776(20)	0.6960(31)	0.1733(44)	6.8 (1.4)
H(8')	0.0505(17)	0.7272(27)	0.0085(38)	4.0 (1.1)
H(9')	0.1356(19)	0.8433(30)	0.0033(42)	6.0 (1.3)
H(10')	0.1781(18)	0.7504(29)	0.0447(40)	4.8 (1.1)
H(11')	0.1975(20)	0.8711(31)	-0.1948(43)	6.6 (1.3)
H(12')	0.2463(21)	0.8695(34)	-0.0568(45)	7.7 (1.4)
H(13')	0.2437(21)	0.7704(32)	-0.1526(45)	7.1 (1.4)
H(14')	0.0083(21)	0.6967(31)	-0.2348(45)	6.4 (1.3)
H(15')	-0.0007(20)	0.6129(30)	-0.1167(43)	6.5 (1.3)
H(16')	0.0462(20)	0.5975(30)	-0.2228(42)	6.3 (1.3)

Table 3. *Observed and calculated structure factors*

Each entry lists, in order, h, $|F_o|$, F_c, w (where w is the weight, used in the least-squares calculations, multiplied by 10^-). There are 2187 unobserved reflections which are omitted from the Table. Threshhold values varied from 3·9 to 9·7. Of these 251 reflections had values of $|F_c|$ greater than the threshhold value of $|F_o|$, and 4 reflections had values of $|F_c|$ greater than twice the threshhold value of $|F_o|$.

Table 3 (cont.)

slight variation of the standard count. The weights to be used for least-squares calculations were assigned on a statistical basis (Gabe, Glusker, Minkin & Patterson, 1967).

Structure determination

The structure was solved by the symbolic addition procedure (Karle & Karle, 1963). The statistical totals

are listed in Table 1. Only the 278 terms with $|E| \geq 2 \cdot 0$ were used to prepare the first Σ_2 listing. The signs of the terms 3, 3, 1 $(E=3 \cdot 74)$; $\bar{9}$, 6, 7 $(E=3 \cdot 25)$; $\bar{13}$, 1, 4 $(E=2 \cdot 92)$ were arbitrarily fixed as $+$ and that of 6, 4, 2 as a. These terms were chosen after two or three attempts with other sets of terms, to give the best access to a large range of indices. (Although the term $\bar{15}$, 2, 5 $(E=3 \cdot 93)$ is stronger than 3, 3, 1, the large number of combinations for the latter made it more suitable as a starting reflection.) The listing gave 58 pairs for 3, 3, 1, 22 pairs for $\bar{9}$, 6, 7 and 40 pairs for $\bar{13}$, 1, 4. The signs of 274 additional terms were then fixed and it soon became obvious that $a=+$. A special program was written to search the Σ_2 listings for the next 594 terms $(2 \cdot 00 > |E| \geq 1 \cdot 50)$ and to fix the signs. Only 36 out of the total of 872 terms studied gave uncertain signs and were not used in the E map. It was later found from the final parameters that the signs of all the other 836 terms had been determined correctly.

Refinement of the structure

In the refinement of the structure only the observed data were used. The R value for parameters determined from the E map was $0 \cdot 27$. This was reduced to $0 \cdot 15$ by three cycles of differential synthesis and then to $0 \cdot 076$ with four cycles of block-diagonal least-squares calculations with anisotropic temperature factors. At this stage all the hydrogen atoms were located on a
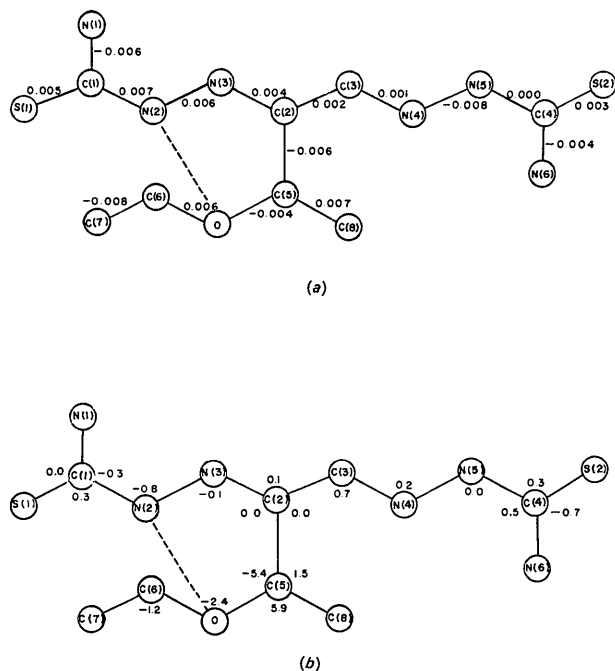

(a)

(a)

Fig. 2. Differences in the dimensions of the two molecules. Differences are expressed as (molecule 1)—(molecule 2). (a) Differences in bond lengths (Å). (b) Differences in interbond angles (degrees).
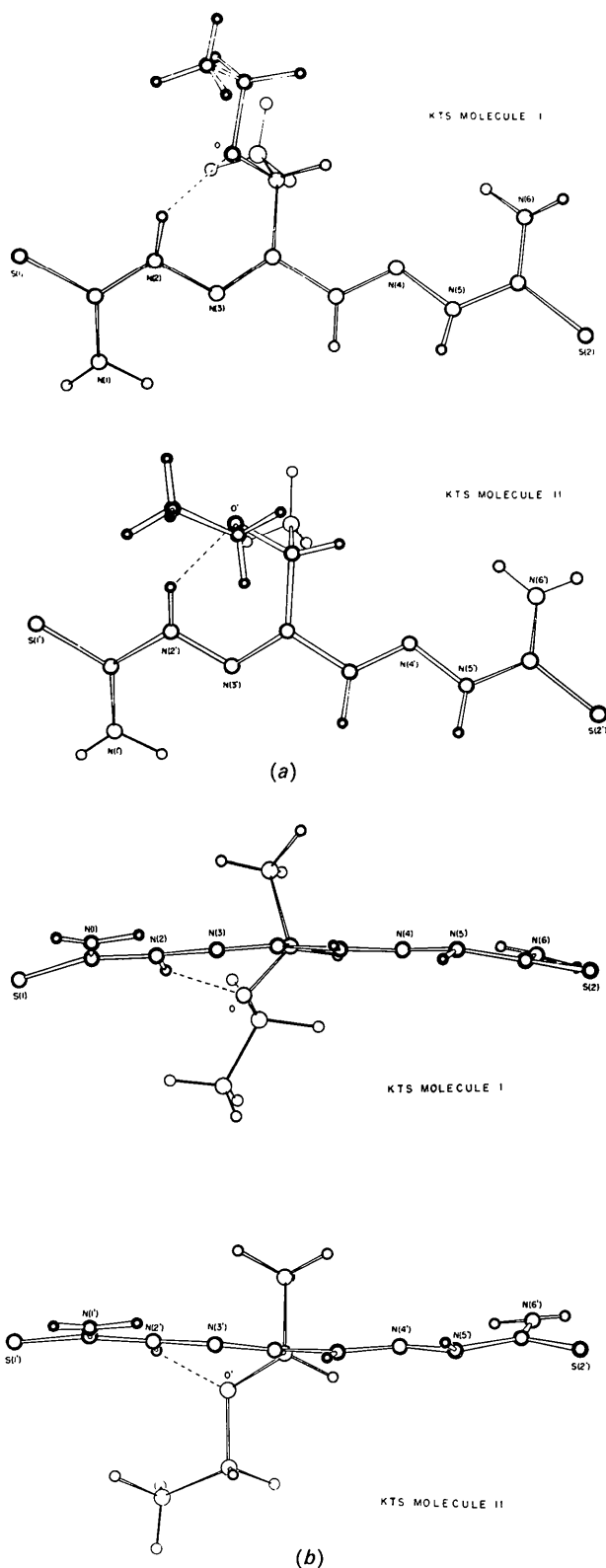

(b)

Fig. 3. (a) View of molecules perpendicular to the plane of the main part of the molecule. (b) View of molecules along the plane of the main part of the molecule.

difference map. A further five cycles of least-squares calculations, including two in which only the hydrogen atom parameters were refined isotropically, reduced the R value to 0·050.

Computations

Most of the calculations were carried out on a 20K IBM 1620 computer with programs listed by Johnson (1965) and Gabe, Glusker, Minkin & Patterson (1967). In addition an *Isotropic Structure Factor Program* (ICR No.17) and a *Differential Synthesis Routine* (ICR No.18) were written by Gabe. Several routines written especially for this structure were necessary, notably a structure factor and least-squares program, in order to accommodate the large computations in the limited memory space available. The final least-squares cycle and agreement analysis were computed on an IBM 360 model 65 with the programs *NRC*-10 and *NRC*-14 (Ahmed, Hall, Pippy & Saunderson, 1967).

In all the calculations the scattering factor curves given in *International Tables for X-ray Crystallography* (1962) were used except for hydrogen atoms for which the curve of Stewart, Davidson & Simpson (1965) was used. In the least-squares calculations the quantity $\Sigma\,w(k|F_o|-|F_c|)^2$ was minimized.

Discussion of the structure

The final parameters are given in Table 2. A list of the observed and calculated structure factors and the weights used is given, for observed data only, in Table 3.

The interatomic distances and angles in the two molecules, shown in Fig.1, are remarkably similar, except for the angles in the region of the side chain, as illustrated in Fig.2 (which shows the differences in dimensions). The standard deviations of the differences between the molecules, excluding the differences in side chains, are 0·005 Å for distances and 0·4° for angles not involving hydrogen atoms. The maximum differences here (excluding the side chains) are 0·008 Å and 0·8° which are probably not significant. On the other hand, the bond angles around C(5) differ considerably between the two molecules, as shown. The standard deviations of results, estimated from the inverted block-diagonal matrices, are given in Table 4. A comparison of the results of this structure determination with those of the cupric complex will be discussed when the latter structure is published.

Table 4. *Standard deviations of results*

(a) Standard deviations of positional coordinates:

S	0·0014 Å
O	0·0029
N	0·0035
C	0·0045
H	0·041

(b) Standard deviations of bond lengths:

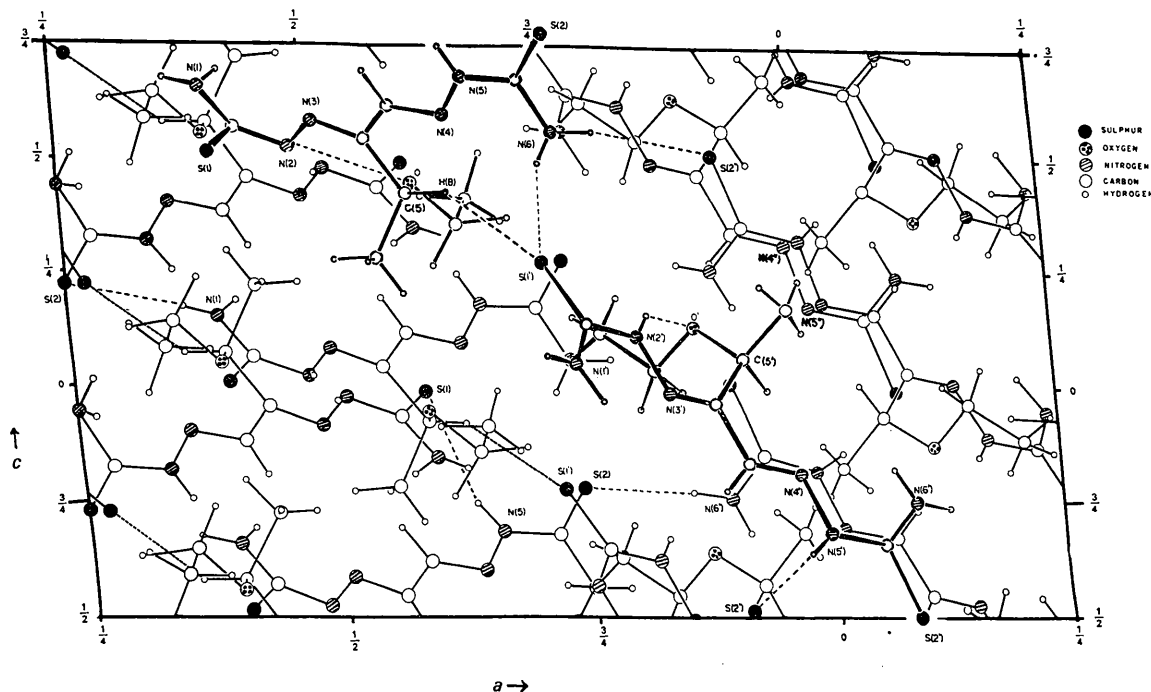|	
N–S	0·004 Å
N–C	0·006
S–C	0·004
C–O	0·005
N–H	0·04
C–H	0·04

Fig. 4. Packing of the molecules showing the hydrogen bond system. Two molecules related by a short C–H---S packing distance are indicated by heavier lines.

Table 4 (cont.)

(c) Standard deviations of interbond angles involving:

S, O, C, N only 0·3°
One H   2°
Two H   4°

(d) Standard deviations of temperature factors:

S   0·07 Å²
O, N, C 0·2
H   1·3

The principal axes of the thermal ellipsoids are listed in Table 5. It can be seen that the thermal motions of the sulphur atoms in molecule 2 are greater than those for the sulphur atoms in molecule 1. No explanation for this, based on different hydrogen-bonding (see Fig. 6) or packing can be offered.

There is a hydrogen atom attached to N(2) which, from a consideration of possible resonance structures derived from measured bond distances, must be highly acidic. This is the hydrogen atom which is ionized when the compound forms a complex in the presence

Table 5. *Principal axes of thermal ellipsoids*

Values of the temperature factors $(B_i$ in Å²) and the root mean square displacement $(U_i$ in Å) along the major, intermediate and minor axes of the thermal ellipsoids are given together with the direction cosines of these axes $(l_1, l_2$ and $l_3)$ with respect to the three axes $(E_1, E_2$ and $E_3)$ of the orthonormal E system (Patterson, 1952) defined by the γ matrix below $(E_2$ coincides with **b**, E_1 and E_3 lie in the plane containing **a** and **c**).

$$\begin{bmatrix} 20\cdot837 & 0 & -0\cdot629 \\ 0 & 13\cdot809 & 0 \\ -0\cdot629 & 0 & 9\cdot536 \end{bmatrix}$$

Atom	B_i	U_i	l_1	l_2	l_3
S(1)	4.75	0.245	0.667	0.582	0.465
	3.28	0.204	-0.230	-0.432	0.872
	1.97	0.158	0.708	-0.689	-0.154
S(2)	4.54	0.240	0.535	0.581	0.614
	2.92	0.192	-0.445	-0.424	0.789
	1.94	0.157	0.718	-0.695	0.032
O(1)	4.47	0.238	0.558	-0.043	0.829
	2.87	0.191	0.671	-0.564	-0.481
	2.36	0.173	0.488	0.825	-0.286
N(1)	5.89	0.273	-0.543	-0.417	-0.729
	2.98	0.194	0.091	0.834	-0.545
	1.98	0.158	0.835	-0.362	-0.414
N(2)	4.16	0.230	0.492	0.538	0.684
	2.66	0.184	-0.366	-0.585	0.724
	1.69	0.146	0.790	-0.606	-0.091
N(3)	3.13	0.199	-0.387	-0.544	0.684
	2.62	0.182	0.510	0.547	-0.664
	2.06	0.161	0.769	0.636	0.066
N(4)	2.91	0.192	0.486	0.604	0.632
	2.51	0.178	-0.525	-0.376	0.764
	1.82	0.151	0.698	-0.703	0.135
N(5)	4.31	0.234	0.498	0.560	0.662
	2.21	0.167	-0.229	-0.651	0.723
	1.66	0.145	0.836	-0.512	-0.196
N(6)	5.48	0.263	0.339	0.756	0.559
	2.77	0.187	0.316	-0.652	0.689
	1.85	0.153	0.886	-0.057	-0.460
C(1)	3.28	0.204	0.556	0.734	-0.390
	2.59	0.181	0.587	-0.015	0.810
	1.73	0.148	0.588	-0.679	-0.439
C(2)	2.77	0.187	0.012	0.319	-0.948
	2.42	0.175	0.456	0.842	0.289
	2.05	0.161	0.890	-0.435	-0.135
C(3)	3.45	0.209	-0.200	-0.439	-0.876
	2.29	0.170	-0.387	0.856	-0.341
	1.83	0.152	0.900	0.271	-0.341
C(4)	2.68	0.184	0.378	0.014	0.926
	2.24	0.168	0.663	0.694	-0.281
	2.02	0.160	-0.646	0.720	0.253
C(5)	3.39	0.207	-0.422	-0.145	-0.895
	2.42	0.175	0.523	0.768	-0.371
	1.88	0.154	0.741	-0.624	-0.248
C(6)	4.84	0.248	-0.357	0.697	0.623
	4.32	0.234	0.789	0.132	0.600
	2.50	0.178	0.500	0.705	-0.503
C(7)	10.81	0.370	0.821	-0.571	0.022
	4.35	0.235	0.226	0.361	0.905
	3.01	0.195	0.525	-0.737	0.425
C(8)	4.61	0.242	0.414	-0.910	-0.033
	3.79	0.219	0.901	0.405	0.153
	3.15	0.200	-0.126	-0.093	0.988

Atom	B_i	U_i	l_1	l_2	l_3
S(1')	7.36	0.305	0.746	-0.460	0.482
	4.47	0.238	0.424	0.886	0.190
	2.03	0.160	-0.514	0.062	0.855
S(2')	9.41	0.345	-0.289	0.897	0.335
	4.12	0.231	0.412	-0.432	0.802
	2.14	0.165	0.864	-0.094	-0.494
O(1')	3.84	0.221	0.971	-0.218	-0.101
	2.83	0.189	0.181	0.388	0.904
	2.47	0.177	-0.158	-0.895	0.416
N(1')	5.34	0.260	0.661	0.372	0.652
	3.18	0.201	-0.410	-0.549	0.729
	2.06	0.162	0.629	-0.749	-0.210
N(2')	4.97	0.251	0.662	0.619	0.438
	2.59	0.181	-0.587	0.778	-0.225
	2.27	0.170	-0.480	-0.110	0.870
N(3')	3.82	0.220	-0.471	-0.545	-0.693
	2.66	0.184	-0.461	0.823	-0.333
	2.03	0.160	0.752	0.162	-0.639
N(4')	3.93	0.223	-0.516	0.053	-0.855
	2.97	0.194	0.103	0.995	0.010
	1.94	0.157	0.850	-0.089	-0.519
N(5')	3.98	0.225	0.323	0.848	0.421
	3.35	0.206	0.257	-0.506	0.823
	2.06	0.161	0.911	-0.157	-0.382
N(6')	6.15	0.279	0.276	0.791	0.546
	3.78	0.219	-0.003	-0.565	0.825
	2.18	0.166	0.961	-0.235	-0.145
C(1')	3.86	0.221	0.619	-0.561	0.549
	2.68	0.184	0.732	0.666	-0.145
	2.01	0.160	-0.285	0.491	0.823
C(2')	3.45	0.209	-0.392	-0.092	-0.915
	2.48	0.177	0.326	0.917	-0.232
	2.15	0.165	0.860	-0.389	-0.330
C(3')	3.87	0.221	-0.326	-0.065	-0.943
	3.12	0.199	-0.175	0.985	-0.007
	2.14	0.165	0.929	0.163	-0.332
C(4')	4.21	0.231	0.026	0.853	0.522
	3.66	0.215	0.272	-0.508	0.817
	1.89	0.155	0.962	0.121	-0.246
C(5')	4.16	0.230	-0.044	0.222	0.974
	2.72	0.186	0.974	0.228	-0.005
	2.35	0.173	-0.224	0.948	-0.226
C(6')	4.95	0.250	0.897	-0.398	-0.193
	4.12	0.228	0.043	-0.356	0.934
	2.77	0.187	-0.441	-0.846	-0.302
C(7')	7.28	0.304	-0.520	0.690	0.504
	4.11	0.228	0.545	-0.186	0.817
	3.09	0.198	0.657	0.700	-0.279
C(8')	7.00	0.298	0.592	-0.235	-0.771
	4.15	0.229	0.058	-0.966	-0.250
	3.17	0.200	0.804	0.103	0.586

Table 6. *Hydrogen bonds and close contacts*

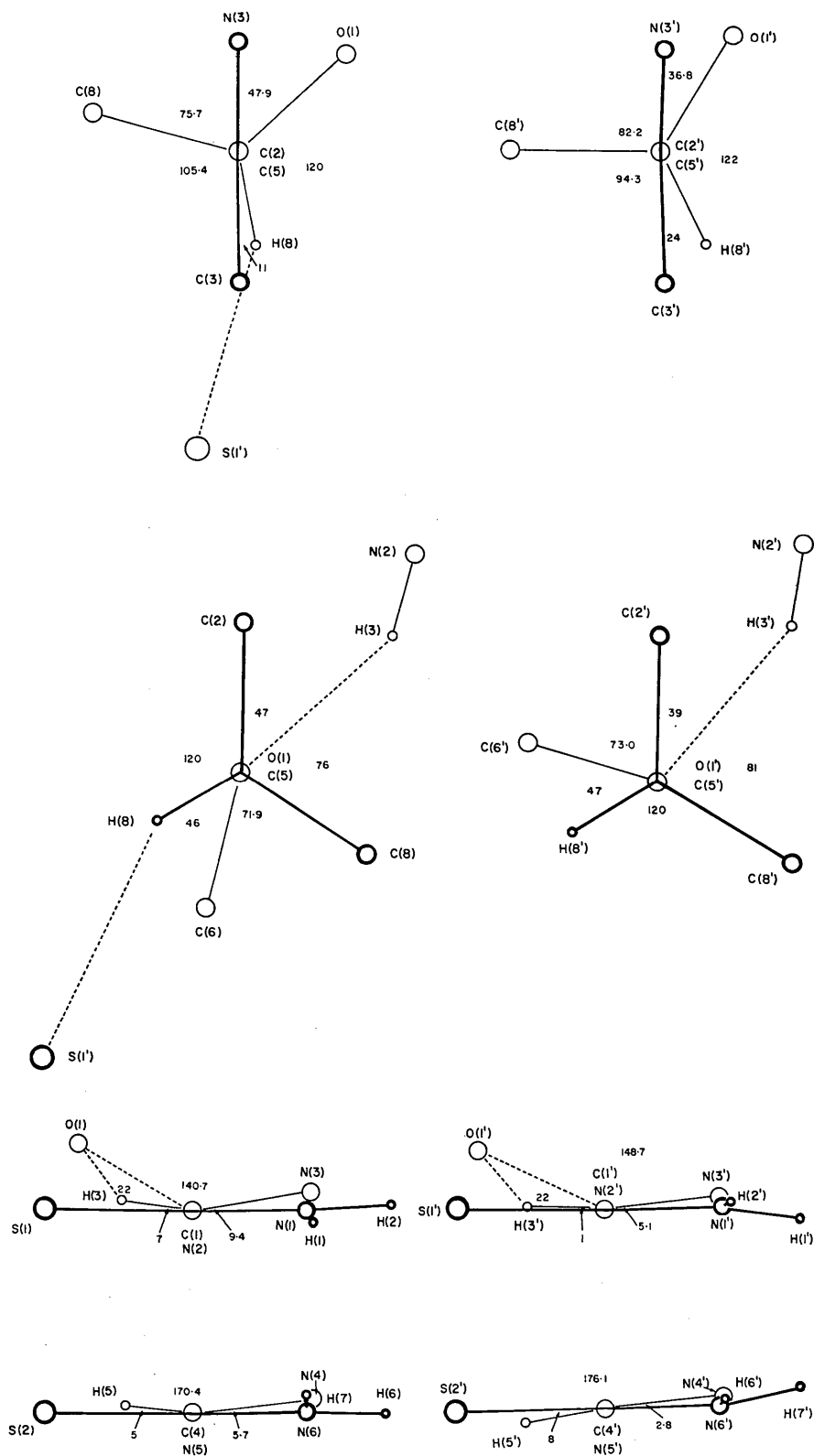| D (Donor at x,y,z)	H (Hydrogen)	A (Acceptor)	Acceptor A at	D---H (Å)	H---A (Å)	D---A (Å)	$\angle D$-H---A (°)	$\angle H$-D---A (°)	$\angle HDC$ (°)
(a) Hydrogen bonds									
N(1)–H(1)		S(2)	$1-x, y+\frac{1}{2}, -z$	0.78	2.68	3.45	172	6	122
N(5)–H(5)		S(1)	$1-x, y-\frac{1}{2}, -z$	0.84	2.63	3.46	167	10	113,127
N(6)–H(7)		S(2')	$1+x, y-\frac{1}{2}, z$	0.83	2.63	3.41	155	19	118
N(5')–H(5')		S(2')	$1-x, 1-y, -z$	0.94	2.62	3.54	167	9	121,119
N(6')–H(6')		S(2)	$1-x, y+\frac{1}{2}, -z$	0.87	2.63	3.49	171	7	120
N(6)–H(6)		S(1')	$1-x, y-\frac{1}{2}, -z$	0.92	2.47	3.32	153	19	122
N(2)–H(3)		O(1)	x, y, z	0.92	1.90	2.68	141	27	128,111
N(2')–H(3')		O(1')	x, y, z	0.91	1.94	2.67	136	31	122,118
(b) Close contacts									
N(1')–H(1')		S(2)	$1-x, \frac{1}{2}+y, -z$	1.02	2.67	3.32	122	43	119
N(1')–H(2')		S(1)	x, y, z	0.81	2.84	3.53	145	28	124
C(5)–H(8)		S(1')	$1-x, y-\frac{1}{2}, -z$	0.99	2.72	3.60	148	24	110,107,111

Fig. 5. Some torsion angles in the two molecules(°).

of cupric ions (Taylor, 1967). In the free ligand this hydrogen atom is involved in a hydrogen bond to the ether oxygen atom O(1). This is a short N–H---O hydrogen bond in both molecules and the lengths are 2·682 and 2·667 Å. The H---O distances are 1·90 and 1·94 Å and the N–H---O angles are 141 and 136° as there are geometrical constraints on the hydrogen atom. The distances and angles involved in close packing and hydrogen bondings are given in Table 6. The bond lengths measured for the molecule of KTS are consis-

Table 7. *Equations of some planes and perpendicular deviations of atoms from these planes*

The equations are expressed in the form

$$lX + mY + nZ = D$$

where distances are expressed in Å and X, Y, Z are coordinates in the E system (see Table 5).

(a) Equations of planes

Designation of plane	Atoms in plane	l	m	n	D
(1)	S(1), S(2), N(1), N(2), N(3), N(4), N(5), N(6), C(1), C(2), C(3), C(4)	0·4473	0·5592	0·6640	6·222
(1')	S(1'), S(2'), N(1'), N(2'), N(3'), N(4'), N(5'), N(6'), C(1'), C(2'), C(3') C(4')	0·5450	0·6885	0·4784	6·779
(2)	N(3), N(4), C(2), C(3)	0·4631	0·6177	0·6356	6·268
(2')	N(3'), N(4'), C(2'), C(3')	0·5620	0·6586	0·5004	6·723
(3)	S(2), N(6), C(4), N(5)	0·4222	0·7095	0·5643	5·592
(3')	S(2'), N(6'), C(4'), N(5')	0·4067	0·8359	0·3687	7·815
(4)	N(2), N(3), C(2), C(5)	0·5173	0·5610	0·6463	6·787
(4')	N(2'), N(3'), C(2'), C(5')	0·6162	0·6284	0·4748	6·617
(5)	S(1), C(1), N(1), N(2)	0·4704	0·4083	0·7823	5·869
(5')	S(1'), C(1'), N(1'), N(2')	0·5879	0·5648	0·5791	5·904

(b) Deviations, Δ (in Å), from these planes (atoms used in the calculation of the plane are indicated by an asterisk)

Atoms (molecule) 1 or 2	Δ(1)	Δ(1')	Δ(2)	Δ(2')	Δ(3)	Δ(3')	Δ(4)	Δ(4')	Δ(5)	Δ(5')
S(1)	0·413*	0·068	0·596	−0·059					0·001*	0·004
N(1)	−0·174*	−0·294	−0·075	−0·342					0·001*	0·005
C(1)	0·043*	−0·097	0·190	−0·197			−0·038	−0·002	−0·004*	−0·013
N(2)	−0·021*	0·033	0·148	−0·102			0·008*	0·004	0·001*	0·005
N(3)	−0·114*	0·061	0·026*	−0·054			−0·016*	−0·009	0·205	0·145
C(2)	−0·184*	0·197	−0·022*	0·048			0·017*	0·009		
C(3)	−0·159*	0·190	−0·031*	0·065			0·108	−0·032		
N(4)	−0·117*	0·096	0·028*	−0·058	0·094	0·078				
N(5)	−0·009*	0·128	0·100	0·002	−0·003*	0·002				
C(4)	0·073*	−0·082	0·197	−0·236	0·008*	−0·006				
S(2)	0·315*	0·065	0·394	−0·055	−0·002*	0·002				
N(6)	−0·067*	−0·366	0·104	−0·572	−0·003*	0·002				
H(1)	−0·25	−0·40	−0·16	−0·43					−0·10	−0·02
H(2)	−0·32	−0·35	−0·24	−0·37					0·07	0·03
H(3)	0·20	0·22	0·40	0·05					0·10	0·04
H(4)	−0·14	0·25	−0·05	0·16						
H(5)	0·11	0·24	0·19	0·15	0·05	−0·10				
H(6)	−0·23	−0·46	−0·04	−0·69	−0·04	0·04				
H(7)	0·16	−0·29	0·34	−0·51	0·18	0·14				
C(5)	−0·264	0·287	−0·046	0·075			−0·008*	−0·004		
C(8)	−1·650	−1·100	−1·412	−1·335			−1·401	−1·420		
O(1)	0·748	1·010	0·988	0·781			0·954	0·756		
H(8)	−0·12	0·73	0·10	0·50			0·214	0·362		

(c) Angles between these planes (in degrees)

Planes	Angle (molecule 1)	Angle (molecule 2)
1–2	2·2	2·3
1–3	8·6	13·2
1–4	4·7	5·3
1–5	13·0	9·5
2–3	7·1	15·5
2–4	4·5	3·8
2–5	14·7	7·2
3–4	11·2	18·0
3–5	21·6	22·4
4–5	12·0	7·2

tent with a set of resonance forms indicating that N(2) and N(1) probably have some residual positive charge and the sulphur atom a negative charge. The short internal hydrogen bond may imply a residual negative charge on the ether oxygen atom. The differences in the distances C(5)---O(1) and C(6)---O(1) are consistent with the fact that there is a planar carbon atom, C(2) adjacent to C(5) (Sundaralingam, 1968), although the differences are only 3σ for molecule 1 and 1.5σ for molecule 2.

The shapes of the molecules are indicated in Fig. 3 in which the differences in the orientations of the side chains are shown. The equations of certain planes in the molecules and angles between these planes are given in Table 7. In Fig. 3(b), which is a view down the C(2)---C(5) bond, the staggered conformation of C(8), H(8) and O(2) is shown for molecule 2 whereas for molecule 1 H(8) is nearly in the plane of the main part of the molecule (see Table 7 for distances). In Fig. 4 the packing of the molecules in the cell is illustrated. In molecule 1, atom C(5) packs very close to S(1') of molecule 2 at a distance of 3·60 Å with H(8) pointing in the general direction of the sulphur atom (see Figs. 4 and 5). The C–H---S angle is 148°. The surroundings of C(5') in molecule 2 are quite different with N(4") at 3·69 Å and N(5") at 3·81 Å. If there is
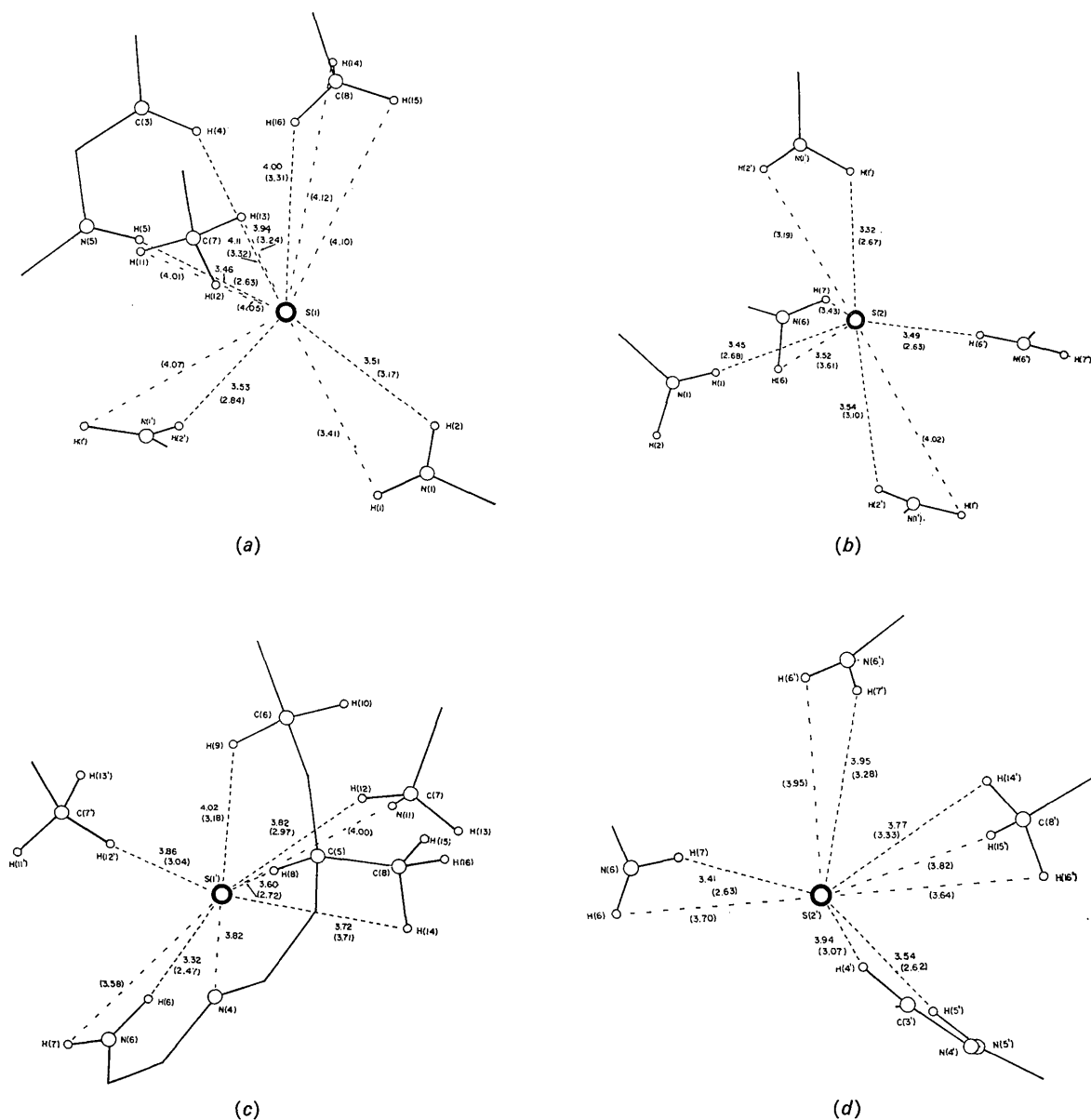

(a)

(b)

(c)

(d)

Fig. 6. The surroundings of each sulphur atom. Values in parentheses refer to distances from the hydrogen atom. (a) Surroundings of S(1). (b) Surroundings of S(2). (c) Surroundings of S(1'). (d) Surroundings of S(2'). (View down the C–S bond.)

a real attraction between H(8) and S(1') (which lie almost in the plane of the backbone of molecule 1), it would explain why the side chain in molecule 1 is not in the expected staggered configuration but twisted about the C(2) − C(5) bond.

The hydrogen bonds are listed in Table 6 and the surroundings of each sulphur atom are shown in Fig. 6. It seems that the packing of the molecule is dominated by the tendency to form N–H---S hydrogen bonds. As seen, the H---S distances are 2·47–2·68 Å in an N–H---S hydrogen bond. These values could possibly be shortened by about 0·15 Å if it is assumed that the N–H distance should be nearly 1·00 Å and that the N---S distance has been accurately measured. The H---S distance of C(5)–H(8)---S(1') is only 2·72 Å. One hesitates to postulate a hydrogen bond from a carbon atom, especially to a sulphur atom, but some electrostatic interaction with a slight positive charge on the hydrogen atom seems to be consistent with our results.

This tendency to association, between two molecules of opposite absolute configuration (but not across a center of symmetry), may explain why there are two molecules in the asymmetric unit. It involves molecule 1 (at x,y,z as listed in Table 2), which is associated with molecule 2 (at $-x, y-\frac{1}{2}, -\frac{1}{2}-z$ with respect to parameters for the second molecule listed in Table 2) through the contact C(5)–H(8)---S(1') and through the hydrogen bond N(6)–H(6)---S(1') to form a ten-membered ring (including hydrogen atoms).

References

AHMED, F. R., HALL, S. R., PIPPY, M. E. & SAUNDERSON, C. P. (1967). NRC Crystallographic Programs for the IBM/360 System, NRC Ottawa.

BOOTH, B. A., JOHNS, D. G., BERTINO, J. R. & SARTORELLI, A. C. (1968). Nature, Lond. 217, 250.

CRIM, J. A. & PETERING, H. G. (1967). Cancer Res. 27, 1278.

GABE, E. J., GLUSKER, J. P., MINKIN, J. A. & PATTERSON, A. L. (1967). Acta Cryst. 22, 366.

International Tables for X-ray Crystallography (1962). Vol. III, p. 202. Birmingham: Kynoch Press.

JOHNSON, C. K. (1965). Acta Cryst. 18, 1004.

KARLE, I. L. & KARLE, J. (1963). Acta Cryst. 16, 969.

PATTERSON, A. L. (1952). Acta Cryst. 5, 829.

PETERING, H. G., BUSKIRK, H. H. & CRIM, J. A. (1967). Cancer Res. 27, 1115.

PETERING, H. G., BUSKIRK, H. H. & UNDERWOOD, G. E. (1964). Cancer Res. 24, 367.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). J. Chem. Phys. 42, 3175.

SUNDARALINGAM, M. (1968). Biopolymers, 6, 189.

TAYLOR, M. R. (1967). Unpublished work.

TAYLOR, M. R., GABE, E. J., GLUSKER, J. P., MINKIN, J. A. & PATTERSON, A. L. (1966). J. Amer. Chem. Soc. 88, 1845.

The Crystal Structure of the β-Form of 2,4,6-Trimethyl-1,3,5-Trithiane, 'Trithioacetaldehyde'*

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The crystal structure of the β-form of 2,4,6-trimethyl-1,3,5-trithiane, *i.e.* trithioacetaldehyde, m.p. 126°C, has been determined by X-ray photographic three-dimensional data and refined by full-matrix least-squares ($R = 0.078$). The crystals are orthorhombic, space group $P2_12_12_1$, $a = 14.668$, $b = 13.438$, $c = 4.751$ Å, $Z = 4$. The molecule is a six-membered ring in the chair conformation, with three methyl groups in the equatorial positions and with C–S = 1·80 Å, C–S–C = 98·4°, S–C–S = 115·3°.

Introduction

Two isomeric 2,4,6-trimethyl derivatives of 1,3,5-trithiane are described in the literature (Klinger, 1878;

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* Work carried out with CNR aid.

Wörner, 1896): an α form, with melting point 101°C, and a β form, with melting point 126°C. They are reported to differ from each other in having a chair ring with two and three methyl groups respectively in equatorial positions, as indicated by chemical evidence (Chattaway & Kellett, 1930), by electron-diffraction