axes parallel to **b**. The arrangement is essentially the same as that found in crystals of cytosine, but more complicated due to the existence of two types of molecules *A* and *B*. The hierarchy of structure in crystals of thiocytosine is interesting: molecules–dimers–ribbons–bundles or ribbons, each step being associated with progressively weaker bonds.

The hydrogen bonds conform to the general stereochemistry of the molecule, being nearly linear, lying approximately in molecular planes, and forming angles of about 120° with adjacent C–N bonds. For example the angle between the two N–H$\cdots$S bonds of the amino group is 123·5° in molecule *A* and 124·3° in *B*. In general, the shortest hydrogen bonds are associated with the longest N–H distances, as is to be expected. The shortest intermolecular distance between hydrogen atoms is 2·46 Å (amino hydrogen atoms) and between nitrogen and sulfur atoms, 3·28 Å. The latter contact is, however, not a hydrogen bond, but rather a van der Waals contact, since there is no hydrogen atom between these two atoms.

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# The Crystal Structure of 2'-Hydroxymethanesulfonanilide

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The simple compound, 2'-hydroxymethanesulfonanilide (HMSA), HO–C$_6$H$_4$–NH–SO$_2$CH$_3$, is related to a series of new compounds possessing blood-pressure-control activity. This biological activity is possibly related to the hydrogen atom of the phenyl –N–H portion of these compounds. Furthermore, the infrared study of this compound had revealed an interesting hydrogen bonding pattern in the crystal. A detailed study of HMSA has been carried out to determine the stereochemistry around the nitrogen atom and to verify the hydrogen bonding. The crystals of HMSA are orthorhombic, space group $P2_12_12_1$, with $a=5·5913\pm0·004$, $b=10·8101\pm0·0009$, $c=13·6305\pm0·0012$ Å. The unit cell contains four molecules. The structure was solved using three-dimensional intensity data obtained with an automatic single-crystal diffractometer. Phasing was done by the Hall–Maslen method, and refinement was by least-squares methods with anisotropic temperature factors. The hydrogen atoms were revealed by a three-dimensional $\Delta F$ difference synthesis. HMSA molecules through hydrogen bonding form infinite chains parallel to the *a* axis. Each HMSA molecule also has an intramolecular hydrogen bond between the OH group and its nitrogen atom. The amine hydrogen atom sticks out alone on one side of the benzene ring while the whole methylsulfone group is on the opposite side. The thermal motions of the molecule have been analyzed.

## Introduction

The incorporation of the alkylsulfonamido group into the benzene ring of phenethanolamines unexpectedly leads to a series of compounds with interesting biological activity (Larsen & Lish, 1964). Many of these new compounds are strikingly similar in action to certain well-known phenolic phenethanolamines, *e.g.* phenylephrine and epinephrine. As an approach to an understanding of their biological activity a study of the crystal structure and stereochemistry of methanesulfonanilide (MSA), C$_6$H$_5$–NH–SO$_2$CH$_3$, was made (Klug, 1968). The related compound, 2'-hydroxymethanesulfonanilide (HMSA), HO–C$_6$H$_4$–NH–SO$_2$CH$_3$, also had

been prepared and investigated by infrared techniques. These studies (Larsen, 1968) led to the intriguing interpretation that the crystal contained hydrogen-bonded dimeric molecules in which each monomer unit further possessed an internal hydrogen bond, O–H$\cdots$N, involving the hydroxyl group hydrogen atom and the amido nitrogen atom. The structure of the dimer was depicted as the following:
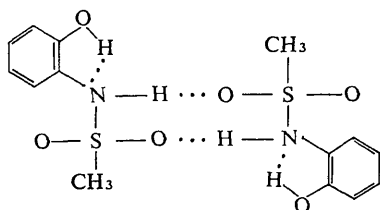
It thus seemed desirable to investigate HMSA by X-ray diffraction methods to verify these interesting bonding predictions and to study other aspects of the molecule's stereochemistry.

## Crystal data

HMSA is a nicely crystalline, colorless solid, m.p. 112·5–115·0 °C (corrected). The material as supplied* yielded suitable crystals for study. The cell constants and their estimated standard deviations were calculated

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from single-crystal diffractometric measurements of 18 moderately high-angle reflections ($2\theta = 50 - 118°$) with Cu $K\alpha$ (1·54178 Å) radiation by a CDC 1604 program adapted from the University of Washington *Param* refinement program. Reflections of all types were observed except $h00$ with $h$ odd, $0k0$ with $k$ odd, and $00l$ with $l$ odd. The crystal data on HMSA are: $a = 5·5913 \pm 0·0004$, $b = 10·8101 \pm 0·0009$, $c = 13·6305 \pm 0·0012$ Å. $Z = 4$, M.W. 187·22, $D_x = 1·509$ g.cm$^{-3}$. Orthorhombic, space group $P2_12_12_1$; piezoelectric test positive. $F(000) = 392$. For Cu $K\alpha$ radiation $\mu R = 0·79$ for $R = 0·025$ cm.

## Determination of the structure

The structure has been determined with Cu $K\alpha$ intensity data obtained on a General Electric-Datex automatic single-crystal diffractometer by the moving-crystal, moving-counter technique ($\theta - 2\theta$ scan). The crystal used for the final intensity data measured approximately $0·27 \times 0·035 \times 0·27$ mm. All reflections in the copper sphere out to $\sin \theta/\lambda = 0·6191$ were measured. No correction was made for absorption, but in the course of the structure refinement it was found desirable to make an empirical extinction correction to 9 reflections that persistently calculated larger than observed. The procedure of Pinnock, Taylor & Lipson (1956) was used, and the overall improvement was dramatic for 8 of the 9 reflections. Other details of the data gathering and processing to observed structure factors, $F_o$ values, have been presented earlier (Klug, 1968). The total number of reflections measured (ex-
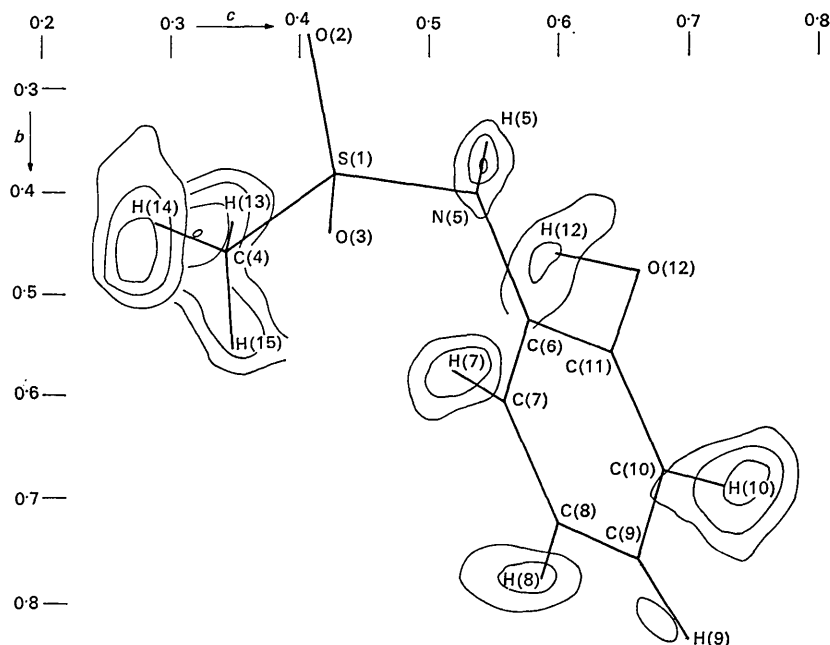


Fig. 1. Composite [100] projection of the hydrogen atoms of a molecule prepared from a three-dimensional $F_o$–$F_c$ synthesis. The contours are drawn at intervals of 0·1 e.Å$^{-3}$ beginning with 0·2 e.Å$^{-3}$. Values of $F_c$ used had the contributions of the hydrogen atoms omitted. The final positions of the hydrogen atoms and of the rest of the molecule are superposed.

cluding space group absences) was 978 of which 940 were listed as observed.

The observed structure factors were treated by direct phasing programs for noncentrosymmetric space groups (Hall & Ahmed, 1968; Oh & Maslen, 1968). These programs determine preliminary scale and temperature factors and reduce the structure factors

to normalized structure factors, $E$ values. Next, the programs use the $\sum_2$ relation and the tangent formula to calculate and refine a set of structure factor phases for all $|E|$ values above a specified minimum. This application provided 197 phases with $E \geq 1\cdot29$. The three-dimensional $E$ map from these phases should produce 12 major peaks in $\frac{1}{4}$ the cell volume. Actually, a series

## Table 1. Observed and calculated structure factors

The data are separated into groups having common $h$ and $k$ values. The three columns of each group list values of $l$, $10F_o$ and $10F_c$ in that order. An asterisk indicates an unobserved reflection.

of peaks was generated with a not too distinct break in the heights after the 13th highest. In a plot of these 13 peaks on a [100] projection the molecule was not immediately recognizable. By comparison with a three-dimensional Patterson synthesis it was verified that the strongest $E$ map peak was undoubtedly that due to the sulfur atom. At this point Karle's (1968) procedure was applied for phase determination when a portion of the structure is considered to be known. This application led to a set of phases identical to the original set. It was then concluded that the 12 strongest peaks of the $E$-map must be essentially correct and that, if so, they should refine to a recognizable and correct structure.

Table 2. *Fractional atomic coordinates* ($\times 10^4$) *and their estimated standard deviations,* $\sigma$

|  | $x$ | $y$ | $z$ |
|---|---|---|---|
| S(1) | 0140 (3) | 3821 (2) | 4259 (1) |
| O(2) | −0080 (11) | 2509 (4) | 4070 (4) |
| O(3) | 2464 (9) | 4384 (4) | 4231 (4) |
| O(12) | 2758 (10) | 4806 (5) | 6610 (4) |
| N(5) | −0884 (11) | 4033 (5) | 5356 (4) |
| C(4) | −1675 (15) | 4574 (6) | 3416 (5) |
| C(6) | −0902 (12) | 5272 (6) | 5766 (5) |
| C(7) | −2790 (13) | 6087 (7) | 5565 (5) |
| C(8) | −2722 (17) | 7272 (7) | 5969 (6) |
| C(9) | −0826 (16) | 7597 (7) | 6584 (6) |
| C(10) | 0978 (15) | 6786 (7) | 6783 (6) |
| C(11) | 0915 (14) | 5611 (6) | 6378 (5) |
| H(5) | −2036 | 3548 | 5421 |
| H(7) | −3649 | 5792 | 5146 |
| H(8) | −3979 | 7793 | 5855 |
| H(9) | −0684 | 8386 | 6974 |
| H(10) | 2134 | 6935 | 7247 |
| H(12) | 2526 | 4608 | 5978 |
| H(13) | −2977 | 4277 | 3469 |
| H(14) | −1266 | 4303 | 2866 |
| H(15) | −1828 | 5510 | 3457 |

Structure factors calculated with isotropic $B$ values, the original atomic coordinates and phases yielded an $R$ index of 0·414. After two cycles of least-squares refinement $R$ dropped to 0·305. At this point a [100] projection of the peaks of a three-dimensional Fourier synthesis disclosed all of the nonhydrogen atoms of the molecule except one carbon atom C(9) of the benzene ring. With the position of C(9) estimated, two more isotropic cycles of least-squares refinement reduced $R$ to 0·101. With the introduction of anisotropic $B_{ij}$'s, two additional cycles of least-squares refinement reduced $R$ to 0·088, a reduction rather less than expected. Examination of the $F_o$ and $F_c$ values revealed a serious discrepancy for reflection 521 whose $F_o$ proved to be in error. The need for an extinction correction was also revealed at the same time, and 9 reflections, 002, 004, 014, 021, 023, 103, 104, 111 and 112, were corrected as previously mentioned. The heavy atoms (nonhydrogen atoms) then refined in two further least-squares cycles to an $R$ of 0·071, with a final average shift/error for the 109 parameters refined of 0·099. In the last cycle the maximum change in any $x,y$, or $z$ was 0·0017, and the maximum change in a $B_{ij}$ was −0·22.

A three-dimensional difference Fourier synthesis with $F_c$ values calculated from the refined heavy-atom positions clearly indicated (Fig. 1) the 9 hydrogen atoms in their expected positions. The H(9) position comes out poorest and that of H(15) is not too well defined. The $\Delta F$ synthesis gives evidence of strong anisotropic motion of the hydrogen atoms, particularly of the methyl hydrogen atoms, in the $x$ direction. A few spurious peaks of equivalent height are observed, but in positions not chemically probable for hydrogen peaks. Attempts to refine the hydrogen positions by

Table 3. *Thermal parameters\* of the atoms and their estimated standard deviations,* $\sigma$

$B_{ij}$ values are in Å². Hydrogen atoms were treated as isotropic.

|  | $B_{11}$ | $B_{22}$ | $B_{33}$ | $B_{12}$ | $B_{13}$ | $B_{23}$ |
|---|---|---|---|---|---|---|
| S(1) | 2·08 (6) | 1·81 (6) | 2·43 (6) | 0·01 (7) | −0·08 (8) | −0·20 (6) |
| O(2) | 4·86 (28) | 1·18 (17) | 4·71 (26) | 0·10 (25) | −0·07 (32) | −0·80 (18) |
| O(3) | 1·83 (20) | 3·45 (24) | 4·06 (25) | −0·60 (20) | 0·40 (25) | −0·44 (24) |
| O(12) | 2·80 (24) | 2·86 (24) | 3·53 (25) | 0·03 (22) | −1·21 (22) | −0·12 (21) |
| N(5) | 3·66 (33) | 1·73 (25) | 2·78 (24) | −0·62 (23) | −0·25 (23) | 0·13 (21) |
| C(4) | 4·22 (42) | 2·75 (32) | 2·42 (31) | 0·22 (31) | −0·97 (31) | 0·04 (28) |
| C(6) | 3·14 (31) | 1·75 (25) | 2·31 (26) | −0·21 (25) | 0·45 (30) | 0·08 (27) |
| C(7) | 2·67 (31) | 2·99 (32) | 3·26 (34) | 0·28 (32) | 0·20 (27) | −0·33 (30) |
| C(8) | 4·46 (47) | 2·93 (35) | 3·80 (41) | 0·89 (35) | 0·95 (37) | −0·08 (31) |
| C(9) | 4·76 (48) | 2·06 (29) | 3·55 (36) | −0·23 (33) | 1·08 (34) | −0·38 (30) |
| C(10) | 3·35 (40) | 2·48 (31) | 3·36 (36) | −0·45 (32) | −0·19 (32) | −0·41 (31) |
| C(11) | 3·01 (36) | 2·02 (29) | 2·52 (30) | −0·25 (29) | 0·12 (27) | −0·15 (26) |
| H(5) | 8·00 |  |  |  |  |  |
| H(7) | 7·00 |  |  |  |  |  |
| H(8) | 7·00 |  |  |  |  |  |
| H(9) | 7·00 |  |  |  |  |  |
| H(10) | 7·00 |  |  |  |  |  |
| H(12) | 8·00 |  |  |  |  |  |
| H(13) | 8·00 |  |  |  |  |  |
| H(14) | 8·00 |  |  |  |  |  |
| H(15) | 8·00 |  |  |  |  |  |

\* For the heavy atoms the expression is: $\exp\left[-\tfrac{1}{4}(h^2a^{*2}B_{11} + \dots 2klb^*c^*B_{23})\right]$.

least-squares techniques were disappointing. Some of the hydrogen atoms invariably moved from what had been chemically acceptable positions to positions with too short or too long bond distances. Accordingly, the hydrogen positions have been manually adjusted by reference to the peaks of the difference synthesis, the accepted stereochemical concepts, and the observed change in the final $R$ value. The reported hydrogen atom positions are chemically reasonable and lead to a final $R$ of 0·062 for the structure. This procedure unfortunately does not provide a standard deviation for the hydrogen parameters and bond lengths. There can be little doubt, however, but that the hydrogen atoms are close to the reported positions. This type of hydrogen refinement problem may arise when the temperature motions are moderately strong or stronger. A solution would be to collect the intensity data with Mo $K\alpha$ radiation (to reduce absorption effects due to sulfur) and at low temperature (to reduce the thermal motion). The interest in this structure did not warrant the remeasurement of the data at low temperature.

In the refinement above the residual minimized was $\sum w(|F_o| - k|F_c|)^2$. The overall scale factor $k$ was refined at each cycle. The weight $w$ of each observation $F_o$ was taken as $w = 1/\sigma^2 (F_o)$ where $\sigma$ is the standard deviation $\sigma_F$ previously described (Klug, 1968). The calculations in this study were made on the IBM 7090 and CDC 1604 computers with the integrated systems of programs known as X-ray 63 and X-ray 67. All least-squares refinements were done with the full-matrix program. The scattering factors used were those applied in the study of MSA (Klug, 1968). The observed and calculated structure factors are listed in Table 1. The fractional atomic coordinates, the atomic thermal parameters, and the estimated standard deviations of each (for the non-hydrogen atoms only) are presented in Tables 2 and 3.

## Discussion of the molecular structure

Bond distances and angles in the HMSA molecule are presented in Fig. 2. The average standard deviation for bonds to the sulfur atom is ±0·006 Å, and for C–C, N–C, and C–O bonds it is ±0·010 Å. The angles at the sulfur atom have $\sigma = \pm 0·3°$; the inner angles of the benzene ring have an average $\sigma = \pm 0·7°$. No standard

Table 4. *Comparison of bonds to the tetrahedral sulfur atom*

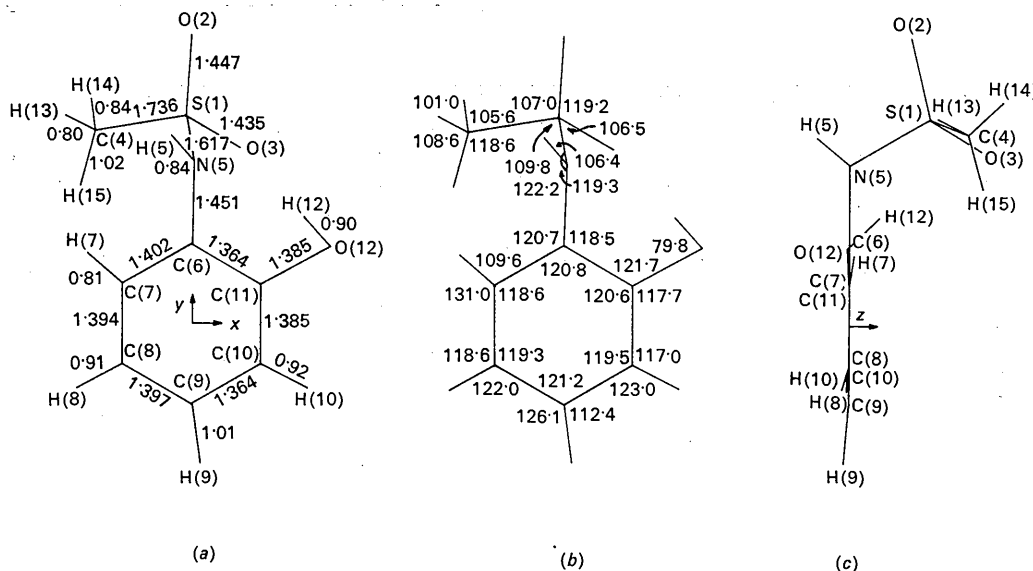| Bond | HMSA (This work) | MSA (Klug, 1968) | β-Sulfanilamide (O'Connell & Maslen, 1967) | γ-Sulfanilamide (Alléaume & Decap, 1965a,b) |
|------|------------------|------------------|--------------------------------------------|---------------------------------------------|
| S–O(2) | 1·447 ⎫ | 1·443 ⎫ | 1·454 ± 0·002 Å | 1·452 ± 0·014 Å |
| S–O(3) | 1·435 ⎪ ±0·006 Å | 1·425 ⎪ ±0·002 Å | 1·448 ± 0·001 | 1·438 ± 0·019 |
| S–N | 1·617 ⎪ | 1·633 ⎪ | 1·620 ± 0·002 | 1·666 ± 0·015 |
| S–C | 1·736 ⎭ | 1·746 ⎭ | 1·750 ± 0·002 | 1·739 ± 0·014 |



Fig. 2. Orthographic projection of the HMSA molecule onto the plane of the benzene ring. (*a*) Observed bond distances (Å), and molecular axial system chosen. Positive $Z$ is perpendicular to the plane of the ring and directed upward. (*b*) Observed bond angles (°). (*c*) Orthographic projection of the molecule edge-on to the plane of the benzene ring in the direction of positive $X$.

deviations can be given for bond distances and angles involving hydrogen atoms.

The HMSA molecule is presented in Fig. 2(a) and (b) as the orthographic projection on the least-squares plane of its benzene ring. The hexagonal benzene ring is only very slightly distorted. Ring C–C distances vary from 1·364 to 1·402 Å with the average 1·388 Å. Some of these differences in C–C distances could be significant. Recent studies of molecules containing a benzene ring with two or more different substituent groups reveal that such a spread is probably to be expected. The substituent groups apparently stabilize slightly different C–C distances around the ring. See, for instance, potassium p-nitrophenyldicyanomethide (Sass & Bugg, 1967), bis(N-isopropyl-3-methylsalicylaldiminato)palladium (Jain & Lingafelter, 1967), and tetryl, N-methyl-N,2,4,6-tetranitroaniline (Cady, 1967). With such deviations of the C–C bonds some deviations of the inner angles of the benzene ring from 120° are to be expected. Such deviations are evidently small, and the total spread in these angles is 2·58°, only slightly greater than $3\sigma = 2\cdot1°$.

The seven C–H distances in the molecule vary from 0·80 to 1·02 Å with the average 0·90 Å, a value a bit on the short side (see Klug, 1968; Reeke & Marsh, 1966; and High & Kraut, 1966). The single N–H distance is 0·84 Å, again a little shorter than the average value 0·895 Å found in 5-ethyl-6-methyluracil (Reeke & Marsh, 1966). The O–H distance is 0·90 Å, the same as the average O–H distance observed in tetrahydroxy-p-benzoquinone (Klug, 1965). The C–N distance in the anilide group is 1·451 ± 0·010 Å, to be compared with 1·438 ± 0·003 Å found in MSA (Klug, 1968) and 1·43 ±

0·01 Å reported for acetanilide (Sutton, 1965). This C–N bond is essentially a pure single bond. Its LCAO–MO double bond order p is only 0·08 as calculated by the method of Coulson (1939) as modified by Liquori & Vaciago (1956). Bonding around the sulfur atom is distorted somewhat from regular tetrahedral [Fig. 2(b)]. The various observed bond distances are compared with those reported in MSA and β- and γ-sulfanilamide (Table 4).

The equation for the least-squares best plane passing through the six carbon atoms of the benzene ring is:

$$-0\cdot50895\ X - 0\cdot33775\ Y + 0\cdot79175\ Z = 4\cdot5661\ .$$

Here X, Y and Z are the atomic coordinates in Å units referred to the crystallographic axes, and 4·5661 is the distance from the plane to the origin in Å units. The standard deviation of the atoms defining the plane from the plane is $\sigma = 0\cdot0084$ Å. The perpendicular distances of the various atoms from this plane are as follows:

| C(6) | 0·012 Å | H(5) | −0·568 Å |
|---|---|---|---|
| C(7) | −0·011 | H(7) | 0·089 |
| C(8) | 0·005 | H(8) | −0·040 |
| C(9) | −0·001 | H(9) | −0·093 |
| C(10) | 0·002 | H(10) | −0·116 |
| C(11) | −0·008 | H(12) | 0·516 |
| N(5) | 0·007 | | |
| O(12) | −0·028 | | |

The excellent planarity of the benzene ring is very evident. Also the N(5) and O(12) atoms are essentially in the plane of the ring. Since the hydrogen atom positions are not accurately determined, the deviations of the ring hydrogen atoms from the ring plane have very

Table 5. *Intermolecular distances in the structure*

| Atoms defining distance | Observed distance | Type of contact | Expected value or limit |
|---|---|---|---|
| I O(2) ····II N(5) | 2·983 Å | Hydrogen bond | > ~3·00 Å |
| I O(2) ····II O(12) | 2·930 | O ····O | > ~2·8* |
| II O(12)···III C(9) | 3·596 | O ····CH | > ~3·1* |
| I C(4) ····III C(10) | 4·154 | CH₃···CH | > ~3·7* |
| I C(4) ····III C(11) | 4·258 | CH₃···C | > ~3·7* |
| I C(4) ····III O(12) | 3·362 | CH₃···O | > ~3·4* |
| I C(4) ····II C(9) | 3·839 | CH₃···CH | > ~3·7* |
| I O(3) ····II C(8) | 3·627 | O ····CH | > ~3·1* |
| I C(7) ····II C(8) | 3·943 | CH ···CH | > ~3·4* |
| I C(7) ····II C(7) | 4·417 | CH ···CH | > ~3·4* |
| I C(8) ····II C(8) | 3·877 | CH ···CH | > ~3·4* |
| I C(8) ····II C(7) | 3·888 | CH ···CH | > ~3·4* |

\* Pauling (1960).

Table 6. *Principal values of the* **T** *and* ω *tensors for the* HMSA *molecule relative to the orthogonal molecular axes* **X, Y, Z**

| R.m.s. amplitude of translation | Direction angles with respect to X,Y,Z | | | R.m.s. amplitude of oscillation | Direction angles with respect to X,Y,Z | | |
|---|---|---|---|---|---|---|---|
| 0·126 (10) Å | 105·5° | 47·5° | 46·5° | 2·74 (30)° | 152·4° | 95·2° | 63·0° |
| 0·171 (7) | 68·8 | 126·3 | 43·9 | 5·38 (8) | 106·8 | 29·1 | 113·0 |
| 0·143 (17) | 153·3 | 116·2 | 85·0 | 3·06 (37) | 68·8 | 61·4 | 36·9 |

Error of fit is 1·85.

little significance. These features are depicted in an orthographic projection [Fig. 2(c)] of the HMSA molecule as viewed edge-on to the plane of the benzene ring. The distribution of all atoms of the molecule relative to the least-squares plane is strikingly shown, and is very similar to that found in MSA (Klug, 1968). In both HMSA and MSA the amine hydrogen atom H(5) in HMSA, clearly sticks out alone on the opposite side of the benzene plane from the methyl sulfone group.

## Hydrogen bonding

Hydrogen bonding is very important in HMSA, as postulated from the infrared studies (Larsen, 1968). Instead of the suggested centrosymmetric dimers, hydrogen bonding between the N–H of one molecule and the O(2) of a neighboring molecule leads to infinite chains along the $a$ axis. In Fig. 3 the distance, II N(5)$\cdots$I O(2), in these N–H$\cdots$O bonds is 2·98 Å. It compares well with the corresponding hydrogen bond distance, 3·03 Å, in the centrosymmetric dimer of MSA (Klug, 1968) and with a similar bond, 3·02 Å, in sulfamide (Trueblood & Mayer, 1956).

The intramolecular hydrogen bond

$$O(12)–H(12)\cdots N(5),$$
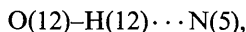
also predicted from the infrared studies, is less satisfactorily established (Fig. 1). The distance O(12)$\cdots$N(5) is 2·79 Å, a typical O–H$\cdots$N hydrogen bond distance. For example, Fuller (1959) reports 2·81 Å for such bonds in both $NaCN.2H_2O$ and formamidoxime. This represents a rather strong intramolecular O–H$\cdots$N bond, and, the infrared investigator suggests, is favored by the increased electron density of the N(5) atom as a result of the formation of the N–H$\cdots$O bonds in the chain. Indeed, the O–H$\cdots$N and N–H$\cdots$O bonds mutually reinforce each other. This may account for the angle C(11)–O(12)–H(12) being strongly distorted from an expected value of $\sim 105°$ to only $\sim 80°$.*

The environment of the amine hydrogen atom H(5), is believed to be of prime importance in the biological activity of the compound. According to the infrared results (Larsen, 1968), in a highly polar aqueous medium at physiological $pH$ the HMSA would no longer be present as a chain, but as the monomer with a free NH group and with no intramolecular OH$\cdots$N bond.

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* One reviewer proposed a possible alternative hydrogen bond, I O(12)–I H(12)$\cdots$II O(2). The distance involved, 2·93 Å, is, however, a bit on the long side for an O–H$\cdots$O bond. There is also no evidence for such a bond in the difference Fourier synthesis. The somewhat inconclusive bond to the nitrogen atom is the only possible hydrogen bond involving the OH group for which the data provide any support.



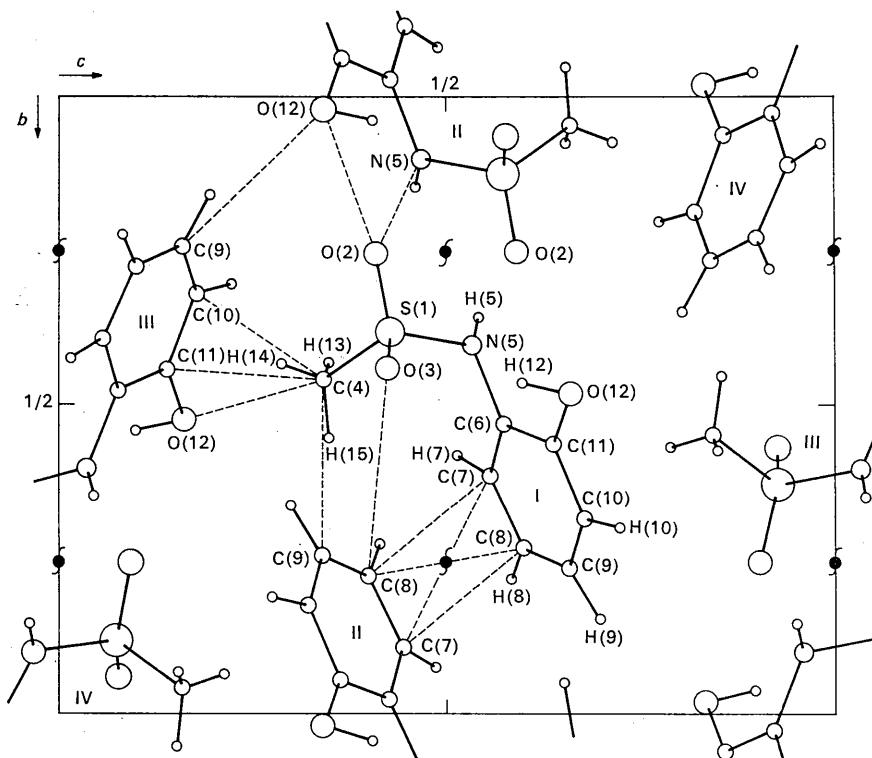Fig. 3. Projection of the structure onto the (100) plane. Positive $a$ is vertical and upward. The screw axes parallel to [100] have been indicated. Atoms of the asymmetric unit (molecule I) have been identified by chemical symbol and number. Selected atoms in other molecules are given their corresponding symbol and number as an aid in identifying the intermolecular distances (dashed lines in the Figure) listed in Table 5.

Thus, the exposed position of H(5), Fig. 2(c), on the opposite side of the benzene ring plane from the methyl sulfone group should make it readily available for reaction with a biological receptor molecule.

## Molecular packing

The molecular packing in the crystal cell is depicted in Fig. 3. HMSA molecules, through

II N(5)–II H(5)$\cdots$I O(2)
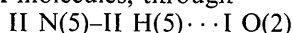
hydrogen bonds, form infinite chains along the screw axis at $y=0{\cdot}25$, $z=0{\cdot}50$ and the equivalent screw axis at $y=0{\cdot}75$, $z=0$. All other contacts between molecules are of the van der Waals type, and are always in the expected range. Some of these contacts are marked on Fig. 3 and listed in Table 5.

## Analyses of thermal motion

The thermal motions of the heavy atoms in the HMSA molecule have been analyzed in terms of possible rigid-body motions by the method of Cruickshank (1956a). The calculations were done with a program *DIAGUS* for the IBM 7090 computer written by Stewart (1966). The application of *DIAGUS* has been briefly described in connection with MSA (Klug, 1968).

Molecular axes of reference [Fig. 2(a) and (c)] for HMSA were defined in the following manner. Positive Z was taken as the direction of the unit normal to the least-squares plane of the benzene ring. The direction C(9) to C(6) was used to define a vector $\mathbf{Y}'$. The description and definition of the axial system is then completed by the vector relations $\mathbf{X}=\mathbf{Y}'\times\mathbf{Z}$ and $\mathbf{Y}=\mathbf{Z}\times\mathbf{X}$. The HMSA molecule does indeed vibrate as a unit. Table 6 presents the root-mean-square amplitudes of the translational motion and angular libration corresponding to the three principal axes of the T and $\omega$ ellipsoids respectively, and the orientation of these axes relative to the molecular axes, X,Y,Z. The molecule's translational motions are only slightly anisotropic, and its librations are somewhat more anisotropic. The maximum librational motion of the molecule is approximately a 5° oscillation about the $\omega_2$ axis of the $\omega$ tensor. This axis lies close to the YZ plane and makes an angle of $\sim29°$ with positive Y. This motion, essentially a torsional wobble of the molecule about a direction close to the Y axis, appears from Fig. 3 to be in complete harmony with the hydrogen bonding scheme.

The observed mean-square amplitudes of vibration, $U_{ij}$ values, of the atoms when compared with the values

calculated from the rigid-body model showed completely satisfactory agreement. The r.m.s. $\Delta U=0{\cdot}0061$ Å$^2$, and the corresponding $\sigma(U_{ij})=0{\cdot}0067$. The Cruickshank (1956b) corrections to bond lengths due to rotational oscillations of the molecule were not calculated. These corrections in a molecule such as HMSA would be expected to increase the bond lengths of Fig. 2(a) by approximately 0·005–0·008 Å.

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