

The Direct Determination of the Crystal Structure of the Anti-Radiation Compound, 2-Aminoethanethiosulfuric Acid*

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The structure has been determined by single-crystal X-ray diffraction film techniques using the symbolic addition procedure. The space group is $P\bar{1}$ with four molecules in the unit cell. For the cell as chosen the constants are: $a = 8.57 \pm 0.02$, $b = 7.39 \pm 0.02$, $c = 9.85 \pm 0.02$ Å, $\alpha = 80.5 \pm 1.4$, $\beta = 86.0 \pm 1.4$, $\gamma = 94.4 \pm 1.4^\circ$, and the measured density is 1.72 ± 0.02 g.cm⁻³. The final R index is 0.064. The molecules crystallize in zwitterion bonded dimers. These zwitterions are capable of capturing and holding a free radical, thus providing a likely explanation for the radiation protection afforded by this substance.

Introduction

The drug 2-aminoethanethiosulfuric acid (TATSA), $\text{NH}_2\text{C}_2\text{H}_4\text{S}_2\text{O}_3\text{H}$, is an anti-radiation drug whose ability to protect has been shown to be equal to that of the standard anti-radiation drug, cysteamine (Holmberg & Sorbo, 1959). Doherty, Burnett & Shapiro (1957) have proposed a theory for the action of anti-radiation drugs such as cysteamine based on their ability to capture the free radicals for a period of time by means of intermolecular resonance. This investigation was undertaken to explore the possibility of correlating the biological function of TATSA with its structure.

Experimental

The material used was kindly supplied by Dr A. S. Sabet of the Department of Chemistry of the University of Maryland. White needles with a mean diameter of 0.2 mm were crystallized from an aqueous solution at room temperature. Elongation was in the direction of the b axis.

The unit-cell dimensions for this compound were determined from rotation and Weissenberg photographs from crystals mounted about the a and b axes. Observation of the oscillation and Weissenberg photographs indicate that the crystal system is triclinic $P\bar{1}$ with unit-cell dimensions:

$$\begin{array}{ll} a = 8.57 \pm 0.02 \text{ \AA} & \alpha = 80.5 \pm 1.4^\circ \\ b = 7.39 \pm 0.02 & \beta = 86.0 \pm 1.4 \\ c = 9.85 \pm 0.02 & \gamma = 94.4 \pm 1.4 \\ V = 611.051 \pm 0.034 \text{ \AA}^3 & \text{M.W. } 157.196 \end{array}$$

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The density calculated on the basis of four molecules per unit cell is 1.709 ± 0.005 g.cm⁻³. The measured density is 1.721 ± 0.02 g.cm⁻³. Cu $K\alpha$ radiation was used throughout. Intensity data were obtained for $h0l$, $h1l$, $h2l$, and $h3l$ reflections from equi-inclination Weissenberg films integrated unidimensionally during the exposure. Of the 1645 possible reflections within the limits of observation with Cu $K\alpha$ radiation, 927 were observed. In order to integrate the reflections in a second direction and obtain an accurate measurement of the relative intensity of each reflection, an electronic integrating device was designed and constructed (Keefe, Williams, Ham & Stewart, 1968).

Interfilm ratios were calculated for each set of exposure. These ratios were then used to put each pack for each level on a common scale. Multiple measurements which lay within the linear response of the film were averaged in order to give the measured relative intensity of each reflection. All the intensities were scaled to a standard exposure interval and corrected for Lorentz and polarization effects. No corrections for extinction or absorption were applied. The resulting layer data were then scaled to a common basis by means of less extensive a -axis data.

All information including form factor tables was stored on a data tape using the DATRDN link of the X-ray 63 computing system (Stewart, 1964). E values for each reflection were calculated, arranged in descending order according to type of reflection. A comparison of theoretical and calculated expectation values of the E and $E^2 - 1$ values and a further comparison between the theoretical and calculated distribution of E values suggested that the space group was centrosymmetric.

Determination of the structure

If a crystal is centrosymmetric, the symbolic addition procedure (Karle & Karle, 1963) may be employed to solve the crystal structure. A slight variation in the

original procedure was devised by the authors. All reflections with a value of E greater than 1.5 were assigned letters and then a special program written by Dr Herman Ammon of the University of California for the X-ray 63 computing system was used to reduce, by means of the Σ_2 relation, the number of assigned letters to six. Three of these letters were then used to fix the origin and the other three were assigned signs of either plus or minus. This led to eight possible combinations of phases for these reflections. Eight E maps were calculated and a search of these led to only one that contained a recognizable structure. The peak positions in this map were selected as coordinates of the atoms in the asymmetric unit. Structure factors were then calculated using the coordinates taken from this map and an R value of 0.43 was obtained.

Refinement of the structure

The initial refinement of the trial coordinates obtained from the most promising E map was carried out by Fourier techniques. A careful study of a Fourier map calculated using the trial coordinates determined from the E map yielded the positions of several more atoms in the molecule. Structure factors were calculated and a R value of 0.316 obtained. Successive Fourier maps were calculated using trial coordinates selected from preceding Fourier maps. These continued to lower the R value and to make the structure more recognizable. At an R value of 0.22 isotropic Fourier refinement was terminated; the approximate positions of the hydrogen atoms bonded to the two carbon atoms were established, assuming the known tetrahedral configuration of the

Table 1. Fractional coordinates ($\times 10^4$) and anisotropic temperature parameters ($\times 10$) for the non-hydrogen atoms

Estimated standard deviations are in parentheses.

Molecule I	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C(11)	6435 (9)	2532 (18)	1635 (9)	35 (3)	64 (12)	59 (5)	12 (5)	-7 (3)	-25 (5)
C(12)	7294 (9)	954 (17)	1328 (9)	37 (4)	29 (11)	61 (5)	9 (5)	-7 (3)	-25 (5)
N(1)	8902 (7)	974 (12)	1835 (7)	36 (3)	28 (9)	48 (3)	9 (3)	-1 (2)	0.1 (4)
O(21)	9615 (6)	4510 (11)	2369 (7)	46 (3)	38 (6)	79 (4)	8 (3)	-23 (2)	-23 (3)
O(22)	7486 (6)	6195 (10)	2909 (6)	50 (3)	65 (6)	39 (3)	2 (3)	-2 (2)	-20 (3)
O(23)	9331 (7)	7571 (10)	912 (6)	61 (3)	23 (6)	53 (3)	1 (3)	11 (2)	-15 (3)
S(1)	7176 (3)	4794 (5)	510 (2)	54 (1)	57 (3)	39 (1)	8 (1)	-14 (1)	-19 (1)
S(1)	8561 (2)	5906 (5)	1838 (2)	36 (1)	40 (3)	32 (1)	2 (1)	-2 (1)	-12 (1)
Molecule II									
C(41)	3581 (9)	6693 (20)	2622 (9)	42 (4)	84 (13)	33 (4)	15 (5)	-8 (3)	-12 (5)
C(42)	3449 (8)	4617 (19)	3228 (9)	33 (3)	60 (11)	34 (4)	9 (4)	1 (3)	-11 (5)
N(4)	2041 (7)	4030 (13)	4256 (6)	39 (3)	58 (9)	32 (3)	2 (3)	3 (2)	23 (4)
O(31)	1998 (7)	10597 (11)	2730 (6)	62 (3)	55 (7)	52 (3)	11 (3)	-14 (3)	-13 (3)
O(32)	774 (6)	7679 (10)	4185 (6)	39 (2)	44 (7)	75 (4)	5 (3)	5 (2)	-3 (4)
O(33)	2177 (7)	9934 (11)	5197 (66)	63 (3)	62 (7)	47 (3)	13 (3)	-5 (2)	-23 (3)
S(3)	2016 (2)	9207 (5)	4007 (2)	31 (1)	40 (3)	40 (1)	3 (1)	-3 (1)	-17 (1)
S(4)	4108 (2)	8015 (4)	3902 (2)	32 (1)	40 (3)	47 (1)	7 (1)	-8 (1)	-22 (1)

Table 2. Fractional coordinates ($\times 10^4$) and isotropic temperature parameters ($\times 10$) for the hydrogen atoms

Estimated standard deviations are in parentheses

Molecule I	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
H(111)	6277 (65)	2612 (99)	2649 (59)	30	30	30	3	-3	-5
H(211)	5267 (70)	2556 (100)	1250 (60)	30	30	30	3	-3	-5
H(112)	6645 (70)	349 (100)	2015 (60)	30	30	30	3	-3	-5
H(212)	7363 (70)	1424 (100)	228 (60)	30	30	30	3	-3	-5
H(121)	9486 (70)	2371 (100)	1087 (60)	30	30	30	3	-3	-5
H(123)	9583 (70)	81 (100)	1833 (60)	30	30	30	3	-3	-5
H(133)	8627 (70)	400 (100)	2976 (60)	30	30	30	3	-3	-5
Molecule II									
H(141)	2892 (70)	7552 (100)	2161 (60)	30	30	30	3	-3	-5
H(241)	4527 (70)	7064 (100)	1831 (60)	30	30	30	3	-3	-5
H(142)	3419 (70)	3738 (100)	2350 (60)	30	30	30	3	-3	-5
H(242)	4380 (70)	4019 (100)	3759 (60)	30	30	30	3	-3	-5
H(432)	1136 (70)	4671 (100)	3645 (70)	30	30	30	3	-3	-5
H(422)	1872 (70)	3715 (100)	5138 (70)	30	30	30	3	-3	-5
H(431)	1483 (70)	2953 (100)	4074 (70)	30	30	30	3	-3	-5

carbon atom, and then anisotropic refinement was begun. The coordinates of the calculated hydrogen atoms, with overall isotropic temperature factors, were included in the anisotropic least-squares refinement but the coordinates of these atoms were not refined. The R value calculated at the end of this refinement was 0.07. Fourier and difference Fourier maps were calculated and searched for the hydrogen atoms bonded between the nitrogen and oxygen atoms. All were

located and complete hydrogen bonding established. The coordinates of the hydrogen atoms located between the nitrogen and oxygen atoms were included in the last least-squares refinement of the crystal structure. The final R value obtained for the observed reflections was 0.064.

The final atomic coordinates and their estimated standard deviations are shown in Tables 1 and 2. The final F_c and F_o values are listed in Table 3.

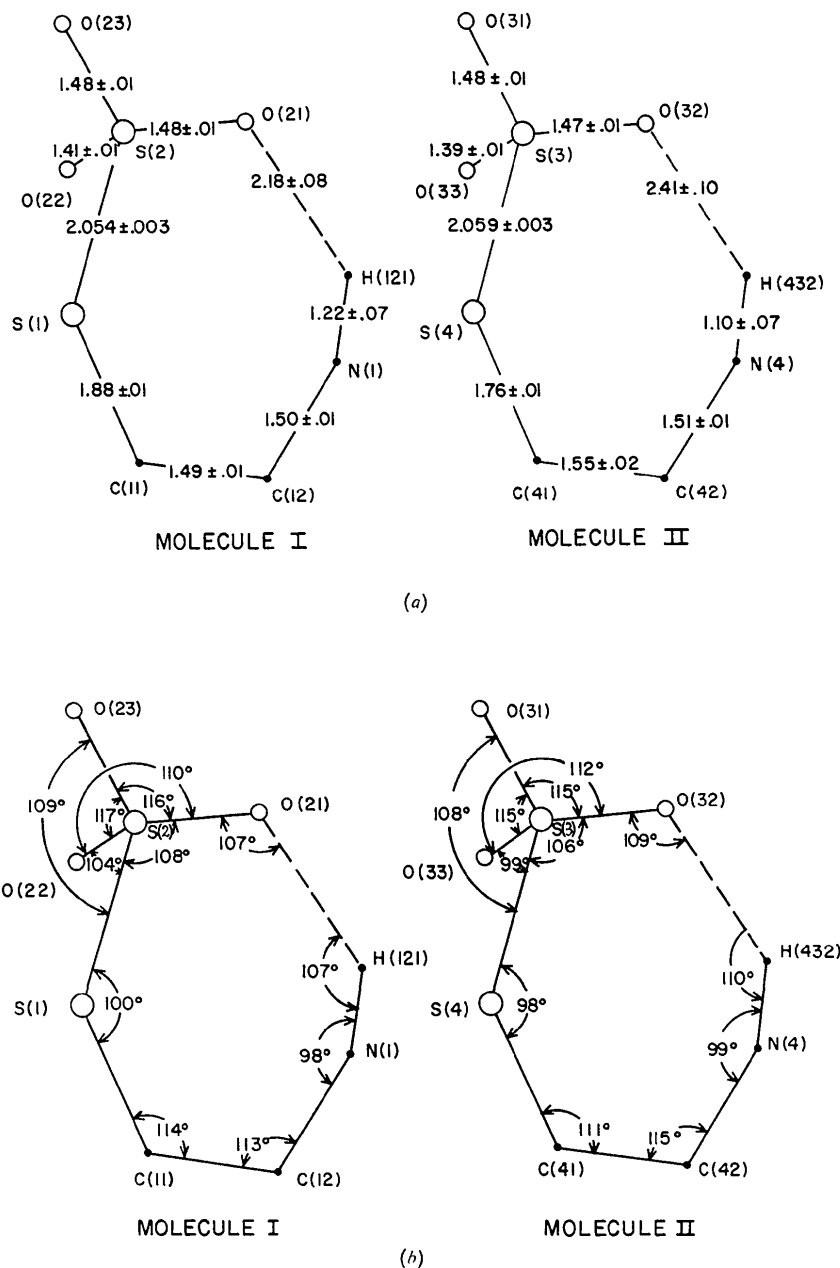


Fig. 1. (a) Bond distances in the 2-aminoethanethiosulfuric acid molecules (I & II). (b). Bond angles in the 2-aminoethanethiosulfuric acid molecules (I & II).

The bond distances and angles and their estimated deviations calculated from Tables 1 and 2 are shown in Fig. 1.

Discussion of the structure

The molecule 2-aminoethanethiosulfuric acid is a zwitterion and, in the crystalline state, forms an intramolecular hydrogen-bonded seven membered ring. Also, dimerization takes place in the crystalline state: the two molecules in the asymmetric unit are held in position by two equivalent hydrogen bonds. Each molecule has additional intermolecular hydrogen bonds to non-dimer neighbors. Fig. 2 shows this bonding. The hydrogen bond lengths are listed in Table 4.

Fig. 1(a) and (b) are schematic representations of the two molecules that make up the asymmetric unit of TATSA. Fig. 1(a) gives a visual comparison of the similarities and differences in the bond lengths of the two molecules, and Fig. 1(b) gives a visual comparison of the bond angles in the two molecules. The short sulfur to oxygen bond, S(2)–O(22), 1.41 ± 0.01 Å, in molecule I has its equivalent in the S(3)–O(33) bond 1.39 ± 0.01 Å, in molecule II. The only hydrogen bonds in which the oxygen atoms, O(22) and O(33), participate are those involved in the formation of the dimer. The remainder of the oxygen atoms in the molecules participate in at least two hydrogen bonds (Table 4). The other S–O bond distances in the two molecules are longer, *i.e.* 1.48 ± 0.01 Å. The average value for the S–O bond length as determined from a list compiled by one of the authors from the first nineteen volumes of *Acta Crystallographica* for molecules containing SO_4^{2-} groups is 1.48 ± 0.04 Å. Usually, resonance exists in SO_3^- groups and the three S–O bonds in each molecule of TATSA should have the same length. It is postu-

lated that the hydrogen bonding found in these molecules leads to stabilization of the molecule and prevents resonance. This same effect was noted by Donohue in his determination of the crystal structure of alanine (Donohue, 1950a).

The asymmetrical bifurcated hydrogen bonds [H(422)–O(32) and H(422)–O(22); H(432)–O(32) and H(432)–O(21)] as found in TATSA have been shown to be present in glycine (Albrecht & Corey, 1939) and in nitramide (Beevers & Trotman-Dickenson, 1957) and are discussed in some detail by Donohue (1968).

The shortening of one of the S–O bonds in the molecules also leads to a decrease in the S–S–O angle associated with the short bond. The short S–O bond apparently allows the oxygen to approach closer to the straight line joining the two sulfur atoms. The greater repulsion between the two oxygen atoms in comparison to the repulsion between an oxygen atom and a sulfur atom is shown by the larger magnitude in general of the O–S–O angles over those of the S–S–O angles. This is due to the greater electronegativity of oxygen (3.5) in comparison with that of sulfur (2.5) (Pauling, 1960).

The only difference between the two molecules of TATSA concerns the long C–S bond in molecule I of 1.88 ± 0.01 Å. This bond appears to be too long when compared with the average values given by Sutton (1965), 1.78 ± 0.05 Å, and with the average of 1.81 ± 0.04 Å as determined by one of the authors from six compounds similar to TATSA. However, Okaya (1965) reports a value of 1.84 Å for 2-aminobutylthiosulfuric acid, Donohue (1950b) reported 1.86 Å for this bond in 2,2'-diiododiethyl trisulfide, Yakel & Hughes (1954) obtained a value of 1.87 Å for this bond in *N,N'*-diglycyl-L-cystine dihydrate, and Peterson, Steinauf & Jensen (1960) reported a value of 1.862 Å for cystine.

Results

The structural determination of TATSA shows it to be a zwitterion capable of forming a seven membered hydrogen-bonded ring. Thus, it would be possible for TATSA to capture an electron from a free radical and through resonance retain the electron for a period of time in the same manner as proposed by Doherty for cysteamine.

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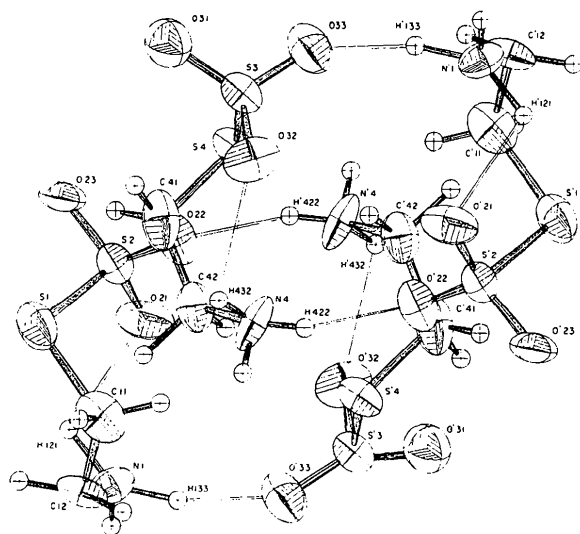


Fig. 2. Molecules I and II of 2-aminoethanethiosulfuric acid viewed approximately along the *a* axis to show the hydrogen-bonded seven-membered ring structure and the hydrogen-bonded dimerization of the two molecules.

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The Crystal Structures of Free Radical Salts and Complexes. III. (*N,N'*-Dibenzyl-4,4'-bipyridylum)²⁺-(7,7,8,8-Tetracyanoquinodimethane)₄²⁻

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The 4:1 complex formed between tetracyanoquinodimethane (TCNQ) and dibenzylbipyridylum (DBBP) crystallizes in the triclinic system with the space group $P\bar{1}$ and lattice constants $a=7.15$, $b=16.82$, $c=12.10$ Å, $\alpha=99.5^\circ$, $\beta=83.8^\circ$, $\gamma=91.8^\circ$ and having $Z=1$. The structure was solved by Patterson methods and refined by block-diagonal least squares using 1936 reflexions measured on a linear diffractometer. The four TCNQs are packed plane-to-plane to form a column along the b axis. The characteristic overlap and short interplanar spacings indicate charge transfer interaction between the four TCNQ moieties stacked as tetramers.

Introduction

Molecular complexes containing TCNQ ions and molecules include some of the best electrically conducting organic compounds known. TCNQ is a powerful electron acceptor and forms TCNQ⁻ by accepting an additional electron. The TCNQ⁻ forms simple salts with cations of many types and complexes containing neutral TCNQ in addition to TCNQ⁻. These complexes of the type M⁺TCNQ⁻TCNQ have been found to exhibit higher electrical conductivity than most simple salts M⁺TCNQ⁻. In most crystal structure determinations of this type of complex the TCNQs have been found to be indistinguishable moieties with a formal charge $\frac{1}{2}-$. The 4:1 TCNQ DBBP complex salt is a member of the same series of complexes since it has equal numbers of TCNQ⁰ and TCNQ⁻. Its structure determination was undertaken to see how it is related structurally to M⁺TCNQ⁻TCNQ⁰ complexes and in general to provide data for relating structures to conductivity.

Experimental

Crystal data

(C₂₄H₂₂N₂)(C₁₂H₄N₄)₄, M.W. 1155.2.

Triclinic,

$a=7.15 \pm 0.03$, $b=16.82 \pm 0.04$, $c=12.10 \pm 0.04$ Å,

$\alpha=99.5 \pm 0.1^\circ$, $\beta=83.8 \pm 0.1^\circ$, $\gamma=91.8 \pm 0.5^\circ$;

$U=1422.8$ Å³;

$D_m=1.341$ g.cm⁻³, $Z=1$, $D_c=1.348$ g.cm⁻³,
 $F(000)=596$.

Mo $K\alpha$ ($\lambda=0.7107$ Å), $\mu=0.91$ cm⁻¹.

Space group $P\bar{1}$ (assumed).

Black plate-like crystals of the complex were deposited when equimolar solutions of Li⁺TCNQ⁻ and TCNQ were dissolved in a minimum quantity of hot acetonitrile, and added to a concentrated solution of DBBP Cl₂ in water, the mixture being allowed to cool very slowly. The space group and the cell constants were obtained initially from oscillation and Weissenberg photographs taken with the crystals rotating about all the three crystallographic axes using Cu $K\alpha$ radiation and were subsequently refined on a Hilger and Watts linear diffractometer. Intensity data for the layers $0kl$ to $7kl$ were collected with the crystal rotating about the a axis on the diffractometer using a scintillation counter and molybdenum $K\alpha$ radiation with balanced filters. Out of the 4750 reflexions measured, significant counts were recorded for 1936. No absorption corrections were made because of the small size of the crystal, ($1 \times 0.5 \times 0.1$ mm). The intensities were corrected for Lorentz and polarization factors.

Structure determination

If the space group is $P\bar{1}$, the single DBBP ion in the cell must occupy a centre of symmetry, while the four TCNQ moieties may lie in general positions as two