

# X-ray Crystal Structure Determination of C<sub>10</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>S

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## ABSTRACT

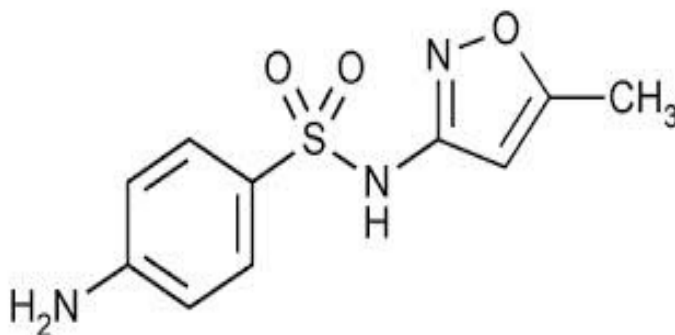
The crystal structure of C<sub>10</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>S was obtained by single crystal x-ray diffraction. Crystallization of C<sub>10</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>S occurs in the monoclinic space group C2/c with  $a = 16.0620(4) \text{ \AA}$ ,  $b = 5.47500(10) \text{ \AA}$ ,  $c = 25.7530(7) \text{ \AA}$ ,  $\beta = 96.1480(10) \text{ deg.}$ , Volume =  $2251.68(9) \text{ \AA}^3$ , Z=8 Calculated density =  $1.494 \text{ Mg/m}^3$ , MoK<sub>α</sub> radiation ( $\lambda=0.7107300 \text{ \AA}$ ), Crystal size =  $0.35 \times 0.35 \times 0.30 \text{ mm}$ . The crystal was solved by SHELX-97 program and the intensity data were collected by using the Bruker SMART CCD area detector Diffractometer with monochromatic MoK<sub>α</sub> radiation.

**Keywords:** single crystal, x-ray diffraction, crystallography etc.

## 1. INTRODUCTION

C<sub>10</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>S belongs to the family of Sulpha drug. Its IUPAC name is 4-amino-N-(5-methylisoxazole-3-yl)-benzene sulfanilamide. Sufamethoxazole is most often used these days as part of a synergistic combination with Trimethoprim in a 5:1 ratio. It is commonly used to treat urinary tract infections.

It can also be used to treat toxoplasmosis and is the drug of choice for *pneumocystis pneumonia* which affects primarily patients with HIV. Its chemical structure is shown in **Fig.1**.



**Fig.1 Chemical structure of title compound**

## 2. EXPERIMENTAL

Colorless well formed cube shaped crystals of the title compounds were obtained by slow evaporation from a solution of methyl alcohol. The density of the crystals was measured by flotation method using a mixture of benzene and carbon tetrachloride. The crystal was placed in RD bottle half filled with carbon tetrachloride. Benzene was slowly added to the RD bottle until the crystals floated in the middle of the mixture. Thus the crystal and solution were of same density. Then the density of solution was measured with pycnometer. The measured density is 1.491 mg/m<sup>3</sup> and calculated density is 1.494 mg/m<sup>3</sup>. The molecular weight of the sample is 253.28 g/mol and melting point is 169°C. The preliminary crystal data is given in **Table 1**.

**Table 1 Preliminary data**

Empirical formula	C <sub>10</sub> H <sub>11</sub> N <sub>3</sub> O <sub>3</sub> S
Formula weight	253.28
Temperature	293(2) K
Wavelength	0.71073 Å (MoK <sub>α</sub> )
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions	a=16.0620(4) Å, b = 5.47500(10)Å
c=25.7530(7) Å, β= 96.1480°(10)	
Volume	2251.68(9) Å <sup>3</sup>
Z, Calculated density	8, 1.494 Mg/m <sup>3</sup>
Absorption coefficient	0.288 mm <sup>-1</sup>
F(000)	1056
Crystal size	0.35 x 0.35 x 0.30 mm
Theta range for data collection	2.55 to 25.00 deg.
Limiting indices	-18<=h<=18, -6<=k<=6, -30<=l<=30
Reflections collected / unique	10028 / 1979 [R(int) = 0.0233]
Completeness to theta	25.00 99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9356 and 0.9021

Refinement method	Full-matrix least-squares on $F^2$
Data / restraints / parameters	1979 / 4 / 166
Goodness-of-fit on $F^2$	1.088
Final R indices [ $I > 2\sigma(I)$ ]	$R_1 = 0.0348$ , $wR_2 = 0.0967$
R indices (all data)	$R_1 = 0.0400$ , $wR_2 = 0.1019$
Largest diff. peak and hole	0.313 and $-0.271 \text{ e.}\text{\AA}^{-3}$

### 3. DATA COLLECTION AND STRUCTURE SOLUTION

The complete three dimensional intensity data collection was done at SAIF, IIT Chennai on a computerized automatic Bruker Kappa apex 2 CCD diffractometer. The temperature of crystal during data collection was 293k. All the data were corrected for Lorentz and polarization effects and absorption corrections because the coefficient of absorption was  $0.288 \text{ mm}^{-1}$ . The data collection was done by a  $\theta$  range of  $2.38$  to  $31.26^\circ$ . The entire data were collected where  $h$  varies from  $-18$  to  $18$ ,  $k$  from  $-6$  to  $6$  and  $l$  from  $-30$  to  $30$ . The total number of reflection measured was  $10028$  out of which only  $1979$  were unique. the structure was solved using **SHELXS-97**.<sup>1</sup>

### 4. REFINEMENT

The positional coordinates of non-hydrogen atoms were obtained from **SHELXS-97** and their isotropic temperature factors were subjected to refinement by **SHELXL-97** refinement program. The refinement was carried out using Full matrix block diagonal least square refinement. During refinement, calculated weighting scheme was employed. The Refinement of  $F^2$  against all reflections. The weighted R-factor  $wR$  and goodness of fit  $s$  are based on  $F^2$ , conventional R-factors  $R$  are based on  $F$ , with  $F$  set to zero for negative  $F^2$ . The threshold expression of  $F^2 > 2\sigma(F^2)$  is used only for calculating R-factors (gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on  $F^2$  are statistically about twice as large as those as based on  $F$ , and R-factors based on all data will be even larger.

After a few initial cycles of refinement the overall R-factor dropped to  $0.0736$ . Further refinement of the structure was carried out with individual anisotropic temperature factor of the form:

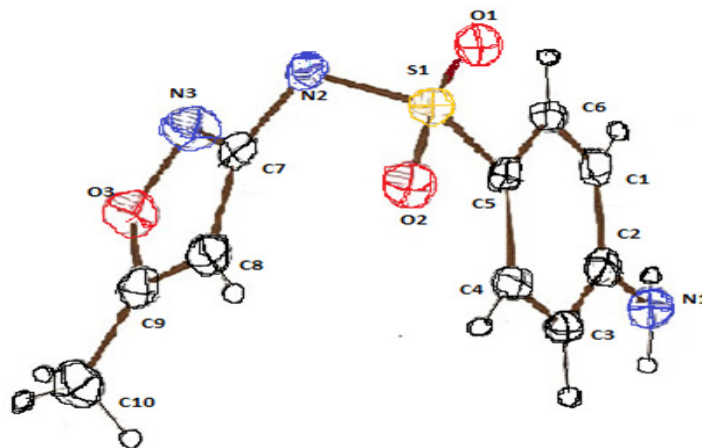
$$\text{Exp. } [-(U_{11}h^2 + U_{22}k^2 + U_{33}l^2 + 2U_{12}hk + 2U_{23}kl + 2U_{13}hl)]$$

Refinement of the structure was terminated after three more cycles of refinement when all the shifts in the parameters became much smaller than the corresponding e.s.d's. The final R-value was

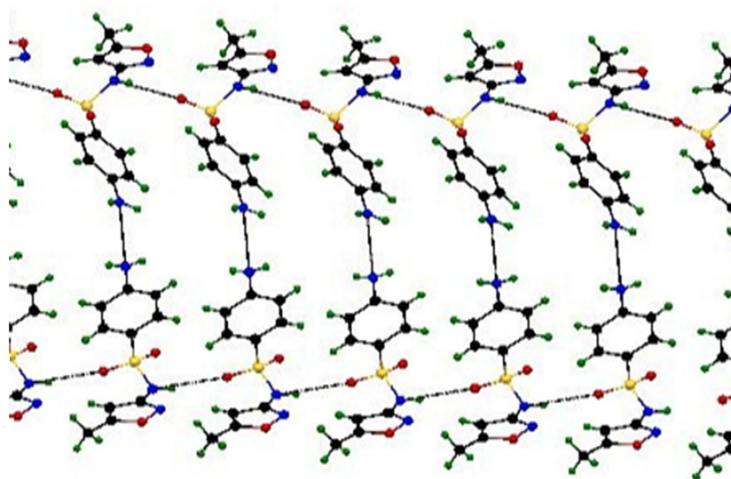
0.0348 for all the 1979 observed unique reflections. The final positional parameters are shown in **Table 2**.

## 5. RESULTS AND DISCUSSION

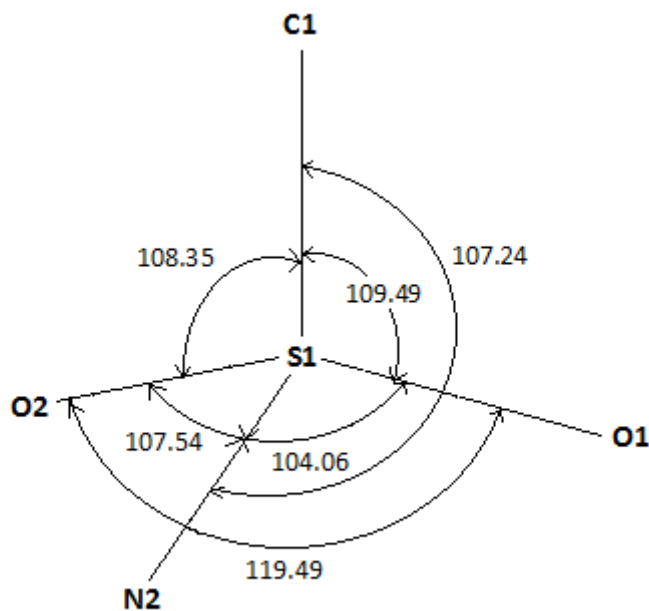
The ORTEP<sup>2</sup> view of the molecule the numbering scheme is shown in **Fig. 2**. The packing diagram seen down *c*-axis is shown in **Fig. 3**. The bond lengths and bond angles are given in **Tables 3 and 4** respectively. The C(1)-N(1) distance of 1.378(3)Å is a characteristic bond length as in other sulfonamide structures<sup>3-24</sup>. The bond lengths and angles in the benzene ring have characteristic values. The S(1)-C(1) bond distance of 1.746(2)Å is similar to those observed in other sulfonamides<sup>3-24</sup>. In all these comparable structures, the S-C distance is considerably shorter than 1.82Å, which is the sum of Pauling's covalent radii<sup>25</sup> of carbon and sulfur atoms except in sulfamethoxypyridazine<sup>26</sup>. Abrahams<sup>27</sup> has calculated the S-C single bond distance to be 1.82Å. So in all these structures there is a considerable amount of double bond nature in the S-C bond. The S(1)-N(2) distance 1.645(2)Å is however, slightly shorter than those observed in similar structures<sup>3-24</sup>. Sass<sup>28</sup> has estimated the S-N bond distance by 1.764(3) Å. So, the S-N distance in this structure is having a considerable amount of double bond character. The S(1)-O(1) and S(1)-O(2) distances of 1.434(2) and 1.429(2)Å respectively are comparable to those observed in analogue structures. The tetrahedral geometry around the Sulfur S(1) is shown in **Fig. 4**. The tetrahedral geometry around sulfur is slightly distorted from the ideal tetrahedral geometry. The largest deviations are in the angles O(1)-S(1)-O(2) 119.43°(10), and O(1)-S(1)-N(2) 104.06°(10) conforms to the altered-tetrahedral arrangement commonly observed in sulfonamides.



**Fig. 2** ORTEP view of the molecule



**Fig. 3** Packing seen down c-axis



**Fig. 4** Tetrahedral geometry around Sulfur atom

The dimensions of the Oxazole ring show good agreement with those observed in its isomer, Sulfoxazole and 3-4-biisoxazole and they have characteristic values. The variations in bond

lengths of these molecules are in the same range (sulfamoxole-1.33(2) to 1.40(2) Å, Sulfisoxazole-1.307(3) to 1.414(4) Å, 3-4 biisoxazole-1.322(3) to 1.428(4) Å, but the range of variation of bond angles is small. The phenyl and isoxazole rings are essentially planar and oriented with respect to each other at an angle of 76.7°. The torsional angle along the S(1)-N(2) bond is 56.89°(18). C(10) atom is displaced from the plane of isoxazole ring by -0.07(2) Å. Some important dihedral angles are shown in **Table 5**.

## 6. HYDROGEN BONDING AND MOLECULAR PACKING

The hydrogen bonds in the structure are given in **Table 6**. The amide nitrogen N(1) is involved in two hydrogen bonds with symmetry related oxygen atoms (3.324(3) and 3.281(3) Å respectively. Similarly the amino nitrogen N(2) is involved in hydrogen bonding with oxygen of another symmetry related oxygen atom (3.240(2) Å). The symmetry relations are ( $x+1/2, y+1/2, z$ ;  $x+1/2, y-1/2, z$ ;  $x, y+1, z$ ). The density of the crystals being higher in comparison to reported sulfonamides indicates that the intermolecular forces are acting very strongly to bring the molecules closer to have a compact arrangement.

**Table 2 Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic temperature parameters ( $\text{Å}^2 \times 10^3$ ) for non-hydrogen. U (eq) is defined as one third of the trace of the orthogonalized Uij tensor. Corresponding e.s.d's are given in paranthesis.**

Atom	X	Y	Z	U(eq)
C(1)	1597(1)	1351(3)	6601(1)	34(1)
C(2)	2159(1)	-425(4)	6477(1)	39(1)
C(3)	2997(1)	-178(4)	6649(1)	42(1)
C(4)	3287(1)	1846(4)	6939(1)	38(1)
C(5)	2717(1)	3625(4)	7054(1)	41(1)
C(6)	1877(1)	3393(4)	6888(1)	38(1)
C(7)	795(1)	2687(4)	5440(1)	37(1)
C(8)	1028(1)	561(4)	5192(1)	42(1)
C(9)	1407(1)	1360(4)	4785(1)	44(1)
C(10)	1788(1)	137(5)	4361(1)	61(1)
N(1)	4119(1)	2043(5)	7131(1)	57(1)
N(2)	347(1)	2930(3)	5877(1)	42(1)
N(3)	1017(2)	4652(4)	5213(1)	63(1)
O(1)	46(1)	2090(3)	6764(1)	54(1)
O(2)	378(1)	-1347(3)	6198(1)	47(1)

**Table 3 Bond lengths [Å] of non-hydrogen atoms. Corresponding e.s.d's are given in paranthesis.**

C(1)-C(2)	1.387(3)
C(1)-C(6)	1.388(3)
C(1)-S(1)	1.746(2)
C(2)-C(3)	1.378(2)
C(3)-C(4)	1.388(3)
C(4)-N(1)	1.378(3)
C(4)-C(5)	1.390(3)
C(5)-C(6)	1.377(3)
C(7)-N(3)	1.293(3)
C(7)-C(8)	1.397(3)
C(7)-N(2)	1.404(3)
C(8)-C(9)	1.343(3)
C(9)-O(3)	1.345(3)
C(9)-C(10)	1.468(3)
N(2)-S(1)	1.6450(19)
N(3)-O(3)	1.408(3)
O(1)-S(1)	1.4343(15)
O(2)-S(1)	1.4286(15)

**Table 4 Bond angles [°] of non-hydrogen atoms. Corresponding e.s.d's are given in paranthesis.**

C(2)-C(1)-C(6)	120.37(19)
C(2)-C(1)-S(1)	120.40(15)
C(6)-C(1)-S(1)	119.20(15)
C(3)-C(2)-C(1)	119.59(19)
C(2)-C(3)-C(4)	120.78(19)
N(1)-C(4)-C(3)	120.8(2)
N(1)-C(4)-C(5)	120.3(2)
C(3)-C(4)-C(5)	118.89(19)
C(6)-C(5)-C(4)	121.00(19)
C(5)-C(6)-C(1)	119.35(18)
N(3)-C(7)-C(8)	112.7(2)

N(3)-C(7)-N(2)	118.24(19)
C(8)-C(7)-N(2)	129.02(19)
C(9)-C(8)-C(7)	104.60(19)
C(8)-C(9)-O(3)	109.2(2)
C(8)-C(9)-C(10)	133.9(2)
O(3)-C(9)-C(10)	116.9(2)
O(2)-S(1)-O(1)	119.49(10)
O(2)-S(1)-N(2)	107.54(10)
O(1)-S(1)-N(2)	104.06(10)
O(2)-S(1)-C(1)	108.35(9)
O(1)-S(1)-C(1)	109.49(9)
N(2)-S(1)-C(1)	107.24(9)
C(7)-N(2)-S(1)	120.54(14)
C(7)-N(3)-O(3)	104.71(18)
C(9)-O(3)-N(3)	108.72(17)

**Table 5 Torsion angles [deg]. Corresponding e.s.d's are given in paranthesis.**

C(6)-C(1)-C(2)-C(3)	1.4(3)
S(1)-C(1)-C(2)-C(3)	179.36(15)
C(1)-C(2)-C(3)-C(4)	-1.1(3)
C(2)-C(3)-C(4)-N(1)	177.2(2)
C(2)-C(3)-C(4)-C(5)	0.2(3)
N(1)-C(4)-C(5)-C(6)	- 176.61(19)
C(3)-C(4)-C(5)-C(6)	0.4(3)
C(4)-C(5)-C(6)-C(1)	-0.1(3)
C(2)-C(1)-C(6)-C(5)	-0.8(3)
S(1)-C(1)-C(6)-C(5)	-178.82(15)
N(3)-C(7)-C(8)-C(9)	-0.8(3)
N(2)-C(7)-N(3)-O(3)	-177.03(17)
C(8)-C(9)-O(3)-N(3)	0.7(3)
C(10)-C(9)-O(3)-N(3)	179.8(2)
C(7)-N(3)-O(3)-C(9)	-1.2(3)
C(7)-N(2)-S(1)-O(2)	-59.45(18)
C(7)-N(2)-S(1)-O(1)	172.86(16)



C(7)-N(2)-S(1)-C(1)	56.89(18)
C(2)-C(1)-S(1)-O(2)	14.21(19)
C(6)-C(1)-S(1)-O(2)	-167.77(15)
C(2)-C(2)-S(1)-O(1)	146.09(17)
C(6)-C(1)-S(1)-O(1)	-35.89(18)
C(2)-C(1)-S(1)-N(2)	-101.60(17)
C(6)-C(1)-S(1)-N(2)	76.42(17)

**Table 6 Hydrogen bonds [Å and deg.]. Corresponding e.s.d's are given in paranthesis.**

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1A)...O(1)#1	0.828(16)	2.64(2)	3.324(3)	141(2)
N(1)-H(1B)...O(1)#2	0.819(16)	2.493(17)	3.281(3)	162(3)
N(2)-H(2A)...O(2)#3	0.818(17)	2.458(18)	3.240(2)	160(2)

Symmetry transformations used to generate equivalent atoms:

#1  $x+1/2, y+1/2, z$  #2  $x+1/2, y-1/2, z$  #3  $x, y+1$

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