

Structure of 4-Amino-*N*-(4,5-dimethyl-2-oxazolyl)benzenesulphonamide (Sulfamoxole), C₁₁H₁₃N₃O₃S

BY M. HARIDAS, R. K. TIWARI AND T. P. SINGH

Department of Physics, Sardar Patel University, Vallabh Vidyanagar 388 120, Gujarat, India

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Abstract. $M_r = 267.3$, monoclinic, $P2_1/c$, $a = 7.93$ (2), $b = 12.88$ (1), $c = 13.38$ (3) Å, $\beta = 106.5$ (5)°, $V = 1310$ (5) Å³, $Z = 4$, $D_m = 1.370$ (2), $D_x = 1.355$ (5) Mg m⁻³, $\lambda(\text{Cu } K\alpha) = 1.5418$ Å, $\mu(\text{Cu } K\alpha) = 1.97$ mm⁻¹, $F(000) = 560$, $T = 297$ K, photographic data, 1297 contributing reflections, $R = 0.071$, $R_w = 0.066$. The planes of the benzene and the oxazole rings are inclined with respect to each other at 76.7 (8)°. The torsion angle along the S–N bond is 33.3 (8)°. There is an N–H...O intermolecular hydrogen bond in the structure.

Introduction. 4-Amino-*N*-(4,5-dimethyl-2-oxazolyl)-benzenesulphonamide (sulfamoxole) is one of the most potent sulphonamides. It is particularly used for the treatment of respiratory- and urinary-tract infections. A study of the structure–activity relationship is essential in order to rationalize the chemical modifications of drugs to optimize the pharmacological properties. Therefore, we have been carrying out systematic studies on sulphonamides (Patel, Haridas & Singh, 1983). A preliminary account of this structure has been reported (Haridas, Tiwari & Singh, 1982). The structure of its isomer, sulfisoxazole, has been reported recently (Chatterjee, Dattagupta & Saha, 1982).

Experimental. Sulfamoxole samples synthesized by Nordmark Werke GMBH, Hamburg (Germany), and obtained directly on the open market in the form of tablets, crystallization by slow evaporation from a solution in acetone–ethanol. Rectangular yellow crystals; one, 0.80 × 0.31 × 0.30 mm, mounted along the needle axis a . Oscillation, precession and Weissenberg photographs: $2/m$ symmetry with systematic absences $0k0$ for k odd and $h0l$ for l odd. D_m by flotation in benzene–CCl₄. Intensity data from multiple-film equi-inclination Weissenberg photographs, nickel-filtered Cu $K\alpha$ radiation; 1297 reflections ($+h, +k, \pm l$), h 0–6, k 0–15, l –15–15 ($8.8 \leq 2\theta \leq 76.8^\circ$). Corrections for Lorentz and polarization effects and spot-shape distortions but not for absorption ($\mu_r = 0.591$). Layer and overall scale factors obtained from Wilson's (1942) statistics. Partial structure by *MULTAN* (Germain, Main & Woolfson, 1971), remaining non-H

atoms by subsequent difference Fourier maps. Non-H atoms refined anisotropically {individual anisotropic temperature factors of the form $\exp[-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + 2b_{12}hk + 2b_{23}kl + 2b_{13}hl)]$ } along with the isotropic H atoms (from difference maps); f values for non-H atoms from Cromer & Waber (1965) and for H atoms from Stewart, Davidson & Simpson (1965). $(\Delta/\sigma)_{\text{ave}} = 0.04$, $(\Delta/\sigma)_{\text{max}} = 0.16$ for non-H atoms and $(\Delta/\sigma)_{\text{ave}} = 0.15$, $(\Delta/\sigma)_{\text{max}} = 0.35$ for H atoms. $R = 0.071$, $R_w = 0.066$, subsequent $\Delta\rho$ excursions $0.25 \text{ e } \text{Å}^{-3}$. Weighting function $w = 1/(1 + 0.04 |F_o| + 0.005 |F_o|^2)$ (Cruickshank, 1961). $|F_o|$ used in the block-diagonal least-squares refinement [*SFLS*, originally written by Shiono (1968–1971) and modified by the authors]. All calculations on the MS University, Baroda, IBM 360/44 computer.

Discussion. The final positional parameters for the non-H atoms are given in Table 1.* The interatomic distances and angles are listed in Table 2 and the numbering scheme is illustrated in Fig. 1. The average C–H and N–H distances in the structure are 1.0 (2) and 1.1 (2) Å respectively. The bond lengths and angles in the benzene ring have characteristic values. The S(8)–C(1) bond distance of 1.77 (1) Å is similar to those observed in other sulphonamides (Alléaume, Gulko, Herbstein, Kapon & Marsh, 1976). The S(8)–N(11) distance of 1.56 (1) Å is, however, slightly shorter than that observed in sulphonamide structures (Alléaume *et al.*, 1976; Chatterjee, Dattagupta & Saha, 1981, 1982). The S–N bond in sulphonic acid (Sass, 1960) is 1.764 (3) Å (by neutron diffraction) and thus the S(8)–N(11) distance in this structure must have a considerable amount of double-bond character. The S(8)–O(9) and S(8)–O(10) bond distances of 1.49 (1) and 1.46 (1) Å, respectively, are comparable to those

* Lists of structure factors, anisotropic thermal parameters, H-atom positions, bond lengths and angles involving H atoms, parameters of hydrogen bonds and equations of the least-squares planes have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39065 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Fractional atomic coordinates ($\times 10^4$) and isotropic thermal parameters ($\times 10^4$) with e.s.d.'s in parentheses

$$B_{eq} = (B_{11}B_{22}B_{33})^{1/3}$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq} (Å ²)
C(1)	20 (16)	8003 (8)	4146 (8)	76 (12)
C(2)	1018 (21)	8478 (10)	5074 (9)	106 (15)
C(3)	2009 (22)	9365 (12)	5047 (10)	121 (16)
C(4)	1995 (16)	8789 (9)	4089 (9)	84 (12)
C(5)	995 (15)	9311 (9)	3185 (8)	73 (11)
C(6)	0 (15)	8435 (9)	3198 (8)	75 (12)
N(7)	2948 (17)	10688 (9)	4066 (10)	134 (15)
S(8)	-1140 (5)	6833 (2)	4165 (3)	88 (3)
O(9)	164 (15)	6079 (7)	4779 (10)	155 (13)
O(10)	-2110 (18)	6558 (8)	3099 (8)	176 (15)
N(11)	-2492 (14)	7147 (7)	4764 (8)	91 (10)
C(12)	-2960 (15)	6452 (8)	5366 (9)	70 (11)
O(13)	-2418 (12)	5461 (7)	5648 (7)	108 (9)
C(14)	-3337 (15)	5114 (9)	6344 (9)	78 (12)
C(15)	-4370 (17)	5900 (9)	6452 (9)	93 (13)
N(16)	-4134 (11)	6752 (6)	5856 (7)	70 (8)
C(17)	-5559 (24)	6092 (13)	7093 (13)	168 (22)
C(18)	-3039 (21)	4048 (10)	6811 (12)	123 (16)

The phenyl and the isoxazole rings are essentially planar. In the molecule, the phenyl ring and the isoxazole ring are oriented with respect to each other at $76.7(8)^\circ$ [$111.9(5)^\circ$ in sulfisoxazole]. The torsion angle along the S(8)–N(11) bond is $33.3(8)^\circ$ [$-56.2(2)^\circ$ in sulfisoxazole]. C(18) and C(19) are displaced from the plane of the isoxazole ring by $-0.07(2)$ and $-0.02(2)$ Å respectively.

The packing of the molecules and the hydrogen bonding in the structure are shown in Fig. 2. The sulphonyl O atom O(10) is involved in a relatively weak hydrogen bond with N(7) of the amino group [N(7)⋯O(10) = $3.00(2)$ Å]. There is, however, one strong van der Waals interaction of $2.87(1)$ Å between the sulphonyl O atoms O(9) and O(9') [symmetry relation ($'$) $1+x, 1\frac{1}{2}-y, z-\frac{1}{2}$]. The packing appears to be compact and is evenly stabilized by the hydrogen-bonding scheme and the van der Waals forces.

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Table 2. Bond lengths (Å) and angles ($^\circ$)

C(1)–C(2)	1.41 (2)	S(8)–N(11)	1.56 (1)
C(1)–C(6)	1.38 (2)	N(11)–C(12)	1.32 (2)
C(2)–C(3)	1.39 (2)	C(12)–O(13)	1.37 (1)
C(3)–C(4)	1.39 (2)	O(13)–C(14)	1.40 (2)
C(4)–C(5)	1.39 (1)	C(14)–C(15)	1.33 (2)
C(5)–C(6)	1.38 (2)	C(15)–N(16)	1.40 (2)
N(7)–C(4)	1.39 (2)	N(16)–C(12)	1.34 (2)
S(8)–C(1)	1.77 (1)	C(17)–C(15)	1.46 (3)
S(8)–O(9)	1.49 (1)	C(18)–C(14)	1.50 (2)
S(8)–O(10)	1.46 (1)		
C(2)–C(1)–C(6)	119.7 (10)	N(11)–C(8)–O(10)	108.2 (6)
C(2)–C(1)–S(8)	121.5 (9)	O(9)–S(8)–O(10)	118.6 (7)
C(6)–C(1)–S(8)	118.8 (9)	S(8)–N(11)–C(12)	119.0 (9)
C(1)–C(2)–C(3)	120.9 (13)	N(11)–C(12)–O(13)	133.2 (10)
C(2)–C(3)–C(4)	119.1 (13)	N(11)–C(12)–N(16)	116.9 (10)
C(3)–C(4)–C(5)	118.9 (11)	N(16)–C(12)–O(13)	109.8 (9)
C(3)–C(4)–N(7)	118.9 (11)	C(12)–O(13)–C(14)	107.8 (9)
C(5)–C(4)–N(7)	122.1 (11)	O(13)–C(14)–C(18)	121.2 (10)
C(4)–C(5)–C(6)	122.7 (10)	O(13)–C(14)–C(15)	105.9 (10)
C(5)–C(6)–C(1)	118.6 (10)	C(15)–C(14)–C(18)	132.9 (12)
C(1)–S(8)–O(9)	106.2 (6)	C(14)–C(15)–N(16)	110.5 (11)
C(1)–S(8)–O(10)	109.1 (6)	C(14)–C(15)–C(17)	134.9 (13)
C(1)–S(8)–N(11)	102.9 (6)	N(16)–C(15)–C(17)	114.4 (11)
N(11)–S(8)–O(9)	110.9 (6)	C(15)–N(16)–C(12)	105.9 (9)

observed in analogous structures. The distances around the S atom in the sulfamoxole molecule (Table 2) agree well with the corresponding distances in other sulphonamides. The geometry around S is slightly distorted from ideal tetrahedral. The largest deviation is in the angle O(9)–S(8)–O(10), $118.6(7)^\circ$, but it conforms to the non-tetrahedral arrangement commonly observed in sulphonamides (Tiwari, 1983). The dimensions of the oxazole ring show good agreement with those observed in the isomer sulfisoxazole (Chatterjee, Dattagupta & Saha, 1982) and 3,4'-biisoxazole (Biagini, Cannas & Marongiu, 1969).

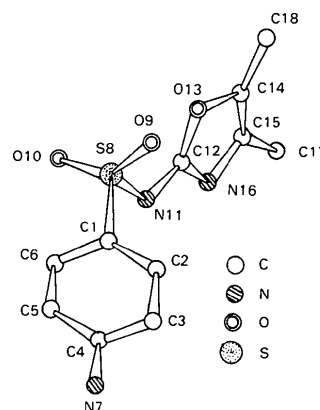


Fig. 1. The perspective view of the molecule viewed along *a* and the numbering scheme.

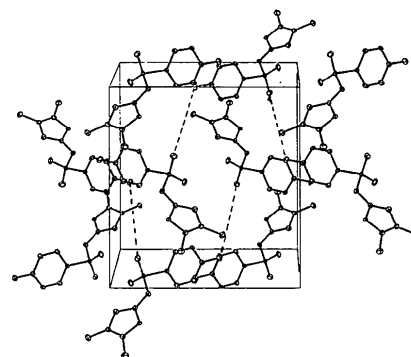


Fig. 2. The molecular packing as seen down *a*. Dashed lines represent hydrogen bonds.

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Radioprotectant Bis(2-guanidinoethyl) Disulfide Dihydrobromide, $C_6H_{18}N_6S_2^{2+} \cdot 2Br^-$

BY TOSHIMASA ISHIDA* AND MASATOSHI INOUE

Osaka College of Pharmacy, 2-10-65 Kawai, Matsubara, Osaka 580, Japan

KUNIHIRO KITAMURA,* AKIO WAKAHARA AND KEN-ICHI TOMITA

Faculty of Pharmaceutical Sciences, Osaka University, Yamadaoka, Suita, Osaka 565, Japan

AND MASATO SHINODA

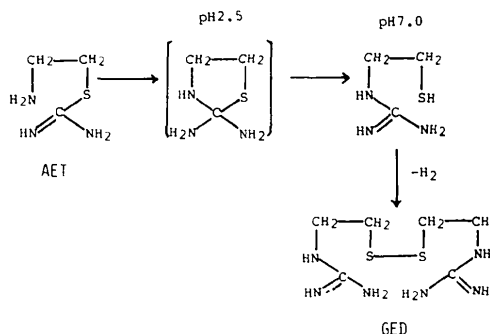
Hoshi College of Pharmacy, 2-4-41 Ebara, Shinagawa-ku, Tokyo 142, Japan

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Abstract. $M_r = 398.18$, orthorhombic, $Pca2_1$, $a = 24.159(4)$, $b = 4.904(2)$, $c = 12.451(3)$ Å, $V = 1475.0(7)$ Å³, $Z = 4$, $D_m = 1.791(6)$, $D_x = 1.793$ Mg m⁻³, $\lambda(\text{Mo } K\alpha) = 0.7107$ Å, $\mu(\text{Mo } K\alpha) = 6.076$ mm⁻¹, $F(000) = 800$, $T = 293$ K, final $R = 0.087$ for 861 independent reflections with $F_o \geq 3\sigma(F_o)$. The molecule takes an extended conformation with no indication of an intramolecular N...S interaction. The crystal structure is stabilized by the formation of intermolecular NH...Br and NH...S hydrogen bonds and by many short contacts.

Introduction. S-containing compounds such as cysteine, cysteamine and 2-(2-aminoethyl)thiouonium (AET) are well known as prominent radioprotective agents (Patt, Tyree, Straube & Smith, 1949; Herve & Bacq, 1952; Langendorff, Koch & Hagen, 1954; Doherty & Burnett, 1955; Crough & Overman, 1957; Doherty, Burnett & Shapira, 1957).

Bis(2-guanidinoethyl) disulfide (GED) synthesized by the transguanylation of AET has been shown to be a radioprotectant to an extent similar to that of AET (Hino, Tanaami, Yamada & Akaboshi, 1966*a,b*).



Several theories on chemical radioprotection have been proposed (for example, Hanaki & Akaboshi, 1966). Among them, the interaction of the radioprotectants with biological macromolecules such as nucleic acids is of particular importance. Thus, the elucidation of the detailed molecular geometry of these compounds is relevant to the development of these theories. As part of the structural studies on radioprotectants (Inoue, Sakaki, Wakahara & Tomita, 1978; Ishida, Shimizu, Inoue, Kitamura, Wakahara, Tomita & Shinoda, 1981), the X-ray analysis of GED dihydrobromide has been carried out.

* To whom correspondence should be addressed.