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Molecular Structure of 1-(2-Sulfoethyl)biguanide

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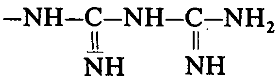
Abstract. $C_4H_{11}N_5O_3S.\frac{1}{2}H_2O$, $M_r = 209{\cdot}1$, monoclinic, $C2/c$, $a = 11{\cdot}498\,(10)$, $b = 18{\cdot}902\,(5)$, $c = 9{\cdot}329\,(12)$ Å, $\beta = 114{\cdot}52\,(4)°$, $V = 1845\,(5)$ Å^3, $Z = 8$, $D_x = 1{\cdot}505$ Mg m^{-3}, $F(000) = 880$, Mo $K\alpha$ ($\lambda = 0{\cdot}71069$ Å), μ(Mo $K\alpha$) = 0·287 mm^{-1}, $R = 0{\cdot}0553$ for 1150 observed reflections. The structure is characterized by linear molecules linked to surrounding molecules by two hydrogen bonds.

Introduction. Biguanides (imidodicarbonimidic diamides) are interesting chemicals and their importance is due to their pharmacological and industrial applications; they are also interesting as analytical reagents owing to their reactivity with metallic ions. Many papers have been published concerning biguanides, mostly dealing with the synthesis and pharmaceutical or industrial properties; however, very few articles have been published about their molecular structure (Brown, 1967; Handa & Saha, 1971; Ernst & Cagle, 1977; Ernst, 1977; Brown & Sengier, 1984; Hota, Saha & Pritzkow, 1984; Amigó, Martínez-Calatayud & Debaerdemaeker, 1985).

The general structure of the biguanide group (Slota & Tscheche, 1929; Ray & Saha, 1937) is



$$\begin{array}{c}-\mathrm{NH}-\underset{\underset{\mathrm{NH}}{\|}}{\mathrm{C}}-\mathrm{NH}-\underset{\underset{\mathrm{NH}}{\|}}{\mathrm{C}}-\mathrm{NH}_2\end{array}$$

This paper deals with the study of the molecular structure of 1-(2-sulfoethyl)biguanide. The authors only know of one published paper on such a biguanide and this deals with the synthesis and physical properties of the solid, the determination of pK_a values and the preparation and study of two complexes formed with Cu$^{\mathrm{II}}$ (Martínez-Calatayud, Campins-Falcó & Ibañez-Blasco, 1984).

Experimental. 1-(2-Sulfoethyl)biguanide was prepared from 1-cyanoguanidine and taurine in the presence of $CuSO_4.5H_2O$, according to the procedure previously published (Martínez-Calatayud, Campins-Falcó & Ibañez-Blasco, 1984). The biguanide is precipitated by adding ethanol and purified by double recrystallization in hot water. An analysis of the solid gives (%): C 22·01, H 5·22, N 32·06 and S 14·64. $C_4H_{11}N_5O_3S.\frac{1}{2}H_2O$ requires (%): C 22·01, H 5·54, N 32·08 and S 14·69. The amount of H_2O was calculated by means of thermogravimetric analysis; weight loss 4·15%, and calculated 4·12%.

Crystal 0·09 × 0·05 × 0·11 mm. 1760 independent reflections; Philips PW 1100 four-circle diffractometer; Mo $K\alpha$ radiation, graphite monochromator; ω–2θ scan, 1150 observed reflections with $F > 1{\cdot}5\sigma(F)$, $-12 \leq h \leq 12$, $0 \leq k \leq 22$, $0 \leq l \leq 11$, $2\theta_{\max} \leq 50°$. The intensities of three standards did not vary during the period of measurement. The cell parameters were obtained from the refinement of 25 reflections having $8 < \theta < 15°$. Structure solved by direct methods using the *XMY*84 program (Debaerdemaeker, 1984). The structure was refined by full-matrix least squares on F, first with isotropic and then with anisotropic temperature factors (Sheldrick, 1977), until the parameter shifts were less than the corresponding standard deviations. The H atoms were found from difference Fourier maps. The introduction and refinement of all H atoms with isotropic temperature factors led to an R value of 0·0553, $wR = 0{\cdot}0578$, $w = 1/[\sigma^2(F) + 0{\cdot}0050(F)^2]$, $(\Delta/\sigma)_{\max} = 0{\cdot}096$ [0·427 for O(4)], max. and min. peaks in final difference map 0·4 and $-0{\cdot}5$ e Å^{-3}. Atomic

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Table 1. *Atomic coordinates* (× 10⁴) *and temperature coefficients* (Å² × 10³)

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$

	x	*y*	*z*	U_{eq}
S	6973 (1)	3717 (1)	10321 (1)	25 (5)
O(1)	6083 (3)	4294 (2)	9645 (5)	43 (3)
O(2)	7343 (3)	3381 (2)	9171 (4)	35 (3)
O(3)	8068 (3)	3922 (2)	11733 (4)	39 (5)
N(1)	4109 (4)	2393 (2)	−173 (5)	27 (14)
N(2)	4964 (4)	1281 (3)	509 (5)	30 (9)
N(3)	3029 (4)	1596 (2)	630 (5)	29 (10)
N(4)	2449 (5)	526 (3)	−762 (5)	39 (10)
N(5)	1863 (5)	777 (3)	1257 (7)	38 (7)
C(1′)	5116 (5)	2708 (3)	−524 (6)	27 (6)
C(2′)	6134 (5)	3071 (3)	912 (6)	25 (3)
C(3)	4048 (4)	1743 (2)	303 (5)	22 (4)
C(4)	2475 (4)	957 (2)	367 (6)	23 (7)
O(4)	5000	9 (3)	2500	37 (14)

Table 2. *Bond lengths* (Å), *bond angles* (°) *and possible intermolecular contacts* (Å)

O(1)–S	1·449 (3)	O(2)–S–O(1)	112·2 (2)
O(2)–S	1·454 (3)	O(3)–S–O(1)	112·6 (2)
O(3)–S	1·448 (3)	O(3)–S–O(2)	112·2 (2)
C(2′)–S	1·779 (0)	O(1)–S–C(2′)	94·2 (2)
C(3)–N(3)	1·357 (5)	O(2)–S–C(2′)	106·9 (3)
C(4)–N(3)	1·340 (5)	O(3)–S–C(2′)	106·3 (2)
C(2)–N(2)	1·318 (6)	S–C(2′)–C(1′)	110·7 (4)
C(2′)–C(1′)	1·527 (7)	C(4)–N(3)–C(3)	122·2 (4)
N(1)–C(1′)	1·457 (6)	N(1)–C(1′)–C(2′)	112·2 (4)
N(3)–C(3)	1·357 (5)	N(2)–C(3)–N(3)	123·0 (4)
N(2)–C(3)	1·318 (6)	N(1)–C(3)–N(3)	116·0 (4)
N(1)–C(3)	1·318 (6)	N(1)–C(3)–N(2)	121·0 (4)
N(3)–C(4)	1·340 (5)	N(5)–C(4)–N(3)	116·6 (5)
N(5)–C(4)	1·336 (6)	N(4)–C(4)–N(3)	123·5 (4)
N(4)–C(4)	1·321 (6)	N(4)–C(4)–N(5)	119·7 (5)
		C(3)–N(1)–C(1′)	128·0 (4)
N(2)···O(4)	3·03	H(4*w*)···O(3)	2·06
O(3)···O(4)	2·89	H(2*b*)···O(4)	2·20

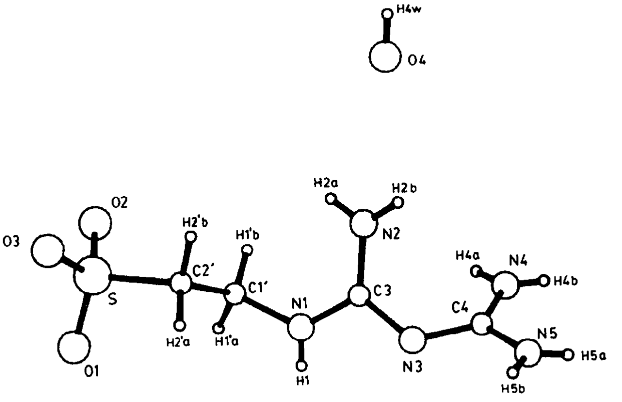
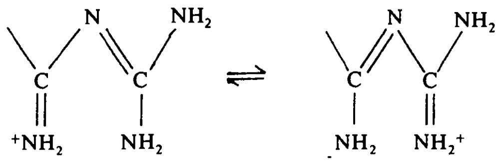


Fig. 1. The molecular structure of the title compound (Motherwell & Clegg, 1978).

scattering factors from *International Tables for X-ray Crystallography* (1974).

Discussion. Final atomic coordinates and equivalent isotropic thermal parameters are given in Table 1,* main interatomic distances and angles in Table 2. A drawing of the molecule with the atomic numbering is shown in Fig. 1 and a perspective drawing of the packing is shown in Fig. 2.

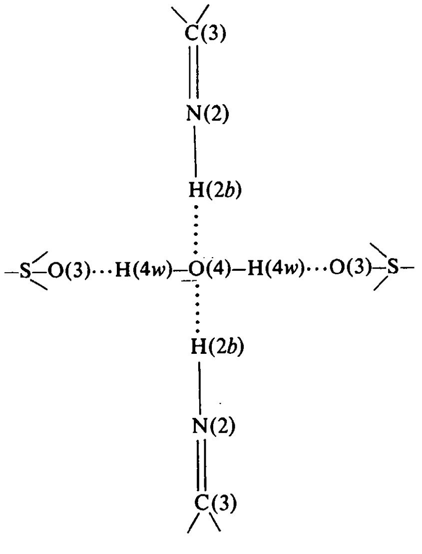
The average C—N bond length in the biguanide group is about 1·32 Å; there is no formal distinction between double and single bonds. This may be compared with the C—N bond reported elsewhere (Brown, 1967; Ernst & Cagle, 1977; Ernst, 1977; Brown & Sengier, 1984; Amigó, Martínez-Calatayud & Debaerdemaeker, 1985). A reasonable model for the bonding in the biguanide group is that the formal positive charge is delocalized according to the equivalent mesomeric forms



The biguanide group in this molecule is not planar and can be seen as consisting of the two planes N(3)—N(2)—C(3)—N(1) and N(3)—C(4)—N(5)—N(4) inclined to each other at an angle of 55·5°.

The bond length of S—O has an average value of about 1·45 Å; such a distance may be compared with the reported values of the S—O bond in the SO_3 group.

Inspection of Fig. 1 suggests that the H_2O molecule is the link between four biguanide molecules by means of H bonds, as can be seen in Fig. 2 and as shown below:



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* Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44909 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

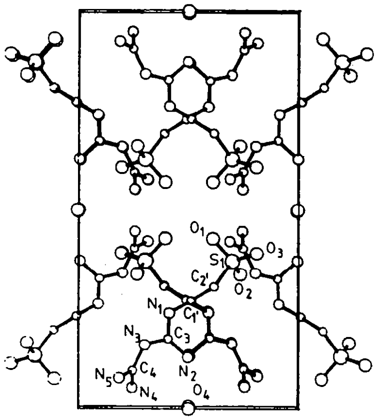

Fig. 2. The unit cell, showing the packing of the molecules.

Table 2 shows that the intermolecular contacts N(2)—O(4) and O(3)—O(4) are similar to the corresponding H-bond values. On the other hand, the distances N(2)—H(2*b*) (2·20 Å) [calculated from N(2)—O(4) minus O(4)···H(3); and close to the N—H values reported by Ernst & Cagle (1977) and Ernst (1977)] and O(4)—H(4*w*) (0·83 Å) suggest that H atoms from the water bridge with the SO_3 group and that the H from N(2) links with the biguanide.

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Structure of N^4-Aminocytidine Hemihydrate

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Abstract. $C_9H_{14}N_4O_5.0{\cdot}5H_2O$, $M_r = 267{\cdot}24$, orthorhombic, $P2_12_12_1$, $a = 14{\cdot}573$ (3), $b = 17{\cdot}894$ (3), $c = 8{\cdot}722$ (2) Å, $V = 2274{\cdot}4$ (8) Å^3, $Z = 8$, $D_m = 1{\cdot}509$ (2), $D_x = 1{\cdot}561$ Mg m^{-3}, $\lambda(\text{Cu } K\alpha) = 1{\cdot}5418$ Å, $\mu = 1{\cdot}07$ mm^{-1}, m.p. = 411–413 K, $F(000) = 1128$, $T = 295$ K, final $R = 0{\cdot}041$ for 2082 unique reflections. The structure of N^4-aminocytidine, a nucleoside analog having a potent mutagenicity, has been determined. In two independent molecules the conformations around the C(1′)—N(1) and C(4′)—C(5′) bonds are *anti* and *gauche–gauche*, respectively, and the sugar puckerings are C(2′)-*endo* (^2E) type. The two independent cytosine bases are overlapped in nearly parallel to form a pair of molecules. The molecules are held together by 11 kinds of hydrogen bonds to form a three-dimensional network.

Introduction. N^4-Aminocytidine is a compound of biological interest because it is a potent mutagen in phages and bacteria (Negishi, Harada, Ohara, Oohara, Nitta & Hayatsu, 1983), in cultured mammalian cells (Nomura, Negishi, Hayatsu & Kuroda, 1987; Takahashi, Nishizawa, Negishi, Hanaoka, Yamada & Hayatsu, 1988), and in *Drosophila* (Negishi, Negishi, Ryo, Kondo & Hayatsu, 1988). The synthesis of the compound as a crystalline hemihydrate has recently been reported (Negishi, Kawakami, Kayasuga, Odo & Hayatsu, 1987). In the present article the precise molecular conformations in the crystals, as determined by X-ray diffraction analysis, are reported.

Experimental. Crystals were prepared by slow recrystallization from an aqueous–ethanol solution (*ca*

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