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Hydroxyguanidinium Sulphate Monohydrate

BY INGRID KJØLLER LARSEN

Chemical Laboratory C, The Royal Danish School of Pharmacy, DK-2100 Copenhagen Ø, Denmark

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$2[CH_6N_3O]^+[SO_4]^{2-}.H_2O$, $M=266·24$, monoclinic, $P2_1/c$, $a=6·284$ (2), $b=12·042$ (2), $c=14·94$ (2) Å, $\beta=110·38$ (4)°, $Z=4$, D_m(flotation) = 1·66, $D_x=1·67$ g cm^{-3}. The dimensions of the two crystallographically non-equivalent hydroxyguanidium ions are almost identical. The ions are not quite planar and are linked to the sulphate ions and the water molecules by a network of hydrogen bonds.

X-ray intensities were collected on a Nonius three-circle automatic diffractometer by the moving-crystal stationary-detector technique, with graphite-monochromatized Mo $K\alpha$ radiation ($\lambda=0·71069$ Å), scan range 1·2°, and scan speed 1·2° min^{-1} in the θ range 2·5–25°. Single crystals of hydroxyguanidium sulphate monohydrate (Eastman) were obtained by recrystallization from aqueous ethanol. The crystal chosen for data collection (0·2 × 0·3 × 0·4 mm) was mounted in a glass capillary and oriented with **c** parallel to the φ axis of the goniostat. 1873 independent reflexions were measured; 1530 with $I>2·5\sigma(I)$ were used in the analysis. μ(Mo $K\alpha$) is 3·5 cm^{-1} and no absorption correction was applied.

The structure was solved by the heavy-atom method. Full-matrix least-squares refinement of the parameters of the non-hydrogen atoms resulted in $R=0·057$, and a subsequent difference map revealed the 14 H atoms. Further least-squares refinement of positional parameters for all atoms and anisotropic temperature parameters for the non-hydrogen atoms led to a final R of 0·035. The quantity minimized was $\sum w(|F_o|-|F_c|)^2$ with the weighting scheme $w=1·0/\{1+[(F_o-B)/A]^2\}$, where $A=13·0$ and $B=15·0$. Scattering factors were taken from *International Tables for X-ray Crystallography* (1962). The final values of atomic positions and temperature parameters are listed in Table 1.* The programs used in the refinement were the X-RAY System (Stewart, Kundell & Baldwin, 1972) and the figures were drawn with *ORTEP* (Johnson, 1965).

Discussion

Hydroxyguanidine, $H_2NC{:}NHNHOH$, was found to be an inhibitor of DNA synthesis (HeLa cells) of the same inhibitory potency as that of hydroxyurea and some other hydroxamic acid derivatives (Young, Schochetman, Hodas & Balis, 1967). Hill & Gordon (1968) pointed out the possible importance of the pK_a values for the inhibitory action of such compounds. Recently hydroxyguanidine was reported to be an antitumour drug because of antiviral as well as cytotoxic effects (Adamson, 1972). A structure determination of the compound, as the sulphate monohydrate, was undertaken as part of a series of structure determinations of this type of inhibitor (Larsen, 1974). It is the

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* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30894 (30 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

first compound in the series which is not a hydroxamic acid.

Bond lengths and angles of the ions and the water molecule are given in Table 2. The only apparently significant difference in the dimensions of the two crystallographically non-equivalent hydroxyguanidinium ions is the length of one of the C–N bonds, *viz* C(12)–N(13) and C(22)–N(23) (the notation of the atoms is given in Fig. 1). In ion 1 this bond, involving the hydroxylated N atom, is significantly longer than the other two C–N bonds, but this is not the case in ion 2. The other two C–N bonds are significantly different in each of the ions, but corresponding bonds of the two ions are of equal lengths. The variations of the C–N lengths are too small, however, to merit any explanation. The three C–N bonds of the guanidinium ions are of equal lengths in the structures of zinc guanidinium sulphate (Morimoto & Lingafelter, 1970) and guanidinium chloride (Haas, Harris & Mills, 1965), but not in the structure of guanidinium carbonate (Adams & Small, 1974).

The three above-mentioned guanidinium ions were all found to be planar within the accuracy of the analyses. In the hydroxyguanidinium ions of this structure, the C and N atoms were also found to be nearly coplanar (Table 3), whereas the N–O bonds are twisted 7–8° about the respective C–N bonds. Several of the H atoms are also out of the least-squares planes through

Table 1. *Fractional atomic coordinates and thermal parameters for hydroxyguanidinium sulphate monohydrate*

The form of the anisotropic thermal ellipsoid is exp $\{-2\pi^2(U_{11}h^2a^{*2}+\ldots+2U_{23}klb^*c^*)\}$. The thermal parameters are ×10².

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
S	0·74231 (9)	0·19803 (5)	0·11701 (4)	1·77 (3)	3·12 (3)	2·25 (3)	−0·03 (2)	0·48 (2)	0·13 (2)
O(5)	0·6702 (3)	0·3127 (1)	0·1288 (1)	3·41 (9)	3·50 (11)	3·97 (10)	0·75 (8)	0·29 (8)	−0·03 (8)
O(6)	0·9770 (3)	0·2021 (2)	0·1166 (1)	2·20 (8)	5·00 (11)	3·20 (9)	−0·23 (8)	1·03 (7)	0·41 (8)
O(7)	0·5915 (3)	0·1509 (2)	0·0283 (1)	2·92 (9)	5·69 (12)	3·35 (10)	−0·94 (9)	0·44 (8)	−1·17 (9)
O(8)	0·7414 (3)	0·1310 (2)	0·1992 (1)	3·47 (10)	4·33 (11)	3·54 (10)	0·36 (8)	1·84 (8)	0·91 (8)
O(9)	0·2226 (4)	0·3761 (2)	0·0779 (2)	3·28 (10)	4·43 (12)	4·96 (12)	−0·49 (9)	1·56 (9)	0·56 (9)
N(11)	0·8367 (4)	0·6321 (2)	0·1276 (2)	2·61 (11)	5·12 (15)	3·13 (12)	−0·37 (10)	1·11 (9)	0·06 (11)
C(12)	0·6435 (4)	0·6196 (2)	0·1436 (2)	2·52 (12)	2·50 (12)	2·84 (12)	0·12 (9)	0·89 (9)	0·19 (10)
N(12)	0·6353 (4)	0·6233 (2)	0·2298 (2)	2·44 (11)	5·84 (16)	2·66 (12)	−0·04 (10)	0·84 (9)	−0·28 (10)
N(13)	0·4554 (3)	0·5963 (2)	0·0689 (2)	2·36 (10)	4·37 (13)	2·76 (11)	−0·16 (9)	0·74 (9)	−0·04 (10)
O(14)	0·2521 (3)	0·5957 (2)	0·0872 (1)	2·25 (9)	4·98 (12)	4·32 (11)	0·18 (8)	1·18 (8)	−0·37 (9)
N(21)	0·7258 (4)	0·3692 (2)	0·3613 (2)	2·80 (13)	6·25 (17)	4·37 (14)	−0·44 (11)	0·93 (11)	0·77 (13)
C(22)	0·9436 (4)	0·3866 (2)	0·3745 (2)	2·98 (13)	2·51 (12)	3·17 (13)	0·22 (10)	0·90 (10)	−0·02 (10)
N(22)	1·0968 (4)	0·3899 (2)	0·4605 (2)	2·94 (11)	5·30 (15)	2·99 (12)	0·31 (10)	1·12 (10)	−0·11 (10)
N(23)	1·0001 (4)	0·4056 (2)	0·2982 (2)	3·18 (11)	4·38 (14)	3·02 (12)	−0·37 (10)	0·96 (9)	−0·12 (10)
O(24)	1·2311 (3)	0·4096 (2)	0·3125 (1)	3·64 (10)	4·44 (12)	4·68 (12)	0·19 (9)	2·11 (9)	0·00 (9)

	x	y	z	U		x	y	z	U
H(111)	0·957 (7)	0·641 (3)	0·180 (3)	4·31	H(211)	0·675 (8)	0·363 (4)	0·410 (3)	5·32
H(112)	0·824 (7)	0·629 (3)	0·067 (3)	4·31	H(212)	0·636 (8)	0·367 (4)	0·308 (3)	5·32
H(121)	0·746 (8)	0·642 (4)	0·274 (3)	4·43	H(221)	1·052 (7)	0·372 (3)	0·508 (3)	4·56
H(122)	0·500 (7)	0·622 (3)	0·240 (3)	4·43	H(222)	1·232 (8)	0·393 (3)	0·467 (3)	4·56
H(13)	0·436 (7)	0·623 (3)	0·012 (3)	3·80	H(23)	0·908 (7)	0·380 (3)	0·238 (3)	4·05
H(14)	0·228 (6)	0·517 (4)	0·089 (3)	4·43	H(24)	1·257 (7)	0·485 (4)	0·310 (3)	4·81
H(91)	0·136 (8)	0·335 (4)	0·093 (3)	5·19	H(92)	0·360 (8)	0·352 (4)	0·110 (3)	5·19

Table 2. *Bond distances* (Å) *and angles* (°) *for hydroxyguanidinium sulphate monohydrate*

Cation (1)		Cation (2)	
N(11)–C(12)	1·326 (4)	N(21)–C(22)	1·330 (4)
C(12)–N(12)	1·306 (4)	C(22)–N(22)	1·311 (3)
C(12)–N(13)	1·343 (3)	C(22)–N(23)	1·326 (4)
N(13)–O(14)	1·397 (3)	N(23)–O(24)	1·393 (3)
N(11)–H(111)	0·89 (4)	N(21)–H(211)	0·89 (6)
N(11)–H(112)	0·87 (5)	N(21)–H(212)	0·80 (4)
N(12)–H(121)	0·81 (4)	N(22)–H(221)	0·87 (5)
N(12)–H(122)	0·91 (5)	N(22)–H(222)	0·82 (5)
N(13)–H(13)	0·87 (4)	N(23)–H(23)	0·94 (4)
O(14)–H(14)	0·96 (4)	O(24)–H(24)	0·93 (5)

Sulphate ion		Water molecule	
S–O(5)	1·484 (2)		
S–O(6)	1·478 (2)	O(9)–H(91)	0·83 (5)
S–O(7)	1·450 (2)	O(9)–H(92)	0·89 (4)
S–O(8)	1·471 (2)		

O···O distances within the sulphate tetrahedron			
O(5)···O(6)	2·403 (3)	O(6)···O(7)	2·400 (3)
O(5)···O(7)	2·405 (3)	O(6)···O(8)	2·392 (3)
O(5)···O(8)	2·402 (3)	O(7)···O(8)	2·406 (4)

Cation (1)		Cation (2)	
N(11)—C(12)–N(12)	121·8 (2)	N(21)—C(22)–N(22)	121·1 (3)
N(11)—C(12)–N(13)	118·0 (3)	N(21)—C(22)–N(23)	118·0 (2)
N(12)—C(12)–N(13)	120·1 (3)	N(22)—C(22)–N(23)	120·9 (3)
C(12)—N(13)–O(14)	116·0 (2)	C(22)—N(23)–O(24)	116·8 (2)
H(111)–N(11)–H(112)	131 (4)	H(211)–N(21)–H(212)	119 (5)
H(111)–N(11)–C(12)	114 (3)	H(211)–N(21)–C(22)	122 (3)
H(112)–N(11)–C(12)	115 (3)	H(212)–N(21)–C(22)	119 (4)
H(121)–N(12)–H(122)	117 (5)	H(221)–N(22)–H(222)	122 (4)
H(121)–N(12)–C(12)	120 (4)	H(221)–N(22)–C(22)	117 (2)
H(122)–N(12)–C(12)	121 (2)	H(222)–N(22)–C(22)	119 (3)
H(13)—N(13)–C(12)	121 (3)	H(23)—N(23)–C(22)	121 (3)
H(13)—N(13)–O(14)	111 (3)	H(23)—N(23)–O(24)	115 (3)
H(14)—O(14)–N(13)	100 (3)	H(24)—O(24)–N(23)	103 (3)

Sulphate ion		Water molecule	
O(5)–S–O(6)	108·5 (1)	H(91)—O(9)—H(92)	105 (4)
O(5)–S–O(7)	110·1 (1)		
O(5)–S–O(8)	108·7 (1)		
O(6)–S–O(7)	110·1 (1)		
O(6)–S–O(8)	108·4 (1)		
O(7)–S–O(8)	110·9 (1)		

the C and N atoms, especially those of the hydroxyl groups, H(14) and H(24). The O–H bonds of both ions are twisted about 76° about the N–O bonds and directed toward the acceptors of the respective hydrogen bonds (Fig. 2 and Table 4).

Table 3. *Deviations of atoms from the least-squares planes through the hydroxyguanidinium ions*

The equations of the planes are in direct space, and the planes are defined by the C and N atoms only.

Ion (1) $-0{\cdot}972x+11{\cdot}807y-0{\cdot}899z=6{\cdot}542$
Ion (2) $-1{\cdot}145x+11{\cdot}816y+1{\cdot}827z=4{\cdot}187$

Ion (1)	Å	Ion (2)	Å
N(11)	−0·006	N(21)	0·005
C(12)	0·019	C(22)	−0·015
N(12)	−0·007	N(22)	0·005
N(13)	−0·006	N(23)	0·005
O(14)	0·168	O(24)	−0·185
H(111)	−0·07	H(211)	0·08
H(112)	0·02	H(212)	−0·01
H(121)	0·06	H(221)	−0·07
H(122)	0·10	H(222)	−0·11
H(13)	0·38	H(23)	−0·30
H(14)	−0.74	H(24)	0.67

The angle between the normals to the planes is 10·7°.

The sulphate ion (Table 2) is a rather regular tetrahedron, but one of the S–O bonds, S–O(7), is found to be significantly shorter than the others. As shown in Table 4 and Fig. 3, O(7) is acceptor for two hydrogen bonds, whereas O(5), O(6) and O(8) are each acceptors for three hydrogen bonds, and the longer S–O bonds in these cases may be attributed to less double-bond character due to the hydrogen bonding. A similar but larger effect was observed in the structure of zinc guanidinium sulphate due to Zn–O interaction.

The most interesting feature of the structure is the very high degree of hydrogen bonding. The O atoms of the sulphate ion are involved in 11 hydrogen bonds (Table 4, Fig. 3). Nine of these link the ion to seven hydroxyguanidinium ions, and the remaining two to two water molecules. In addition the O atom of the water molecule is acceptor for two hydrogen bonds, and only one of the 14 H atoms of the structure, H(212), is not involved in hydrogen bonding. The geometry of the hydrogen bonds is given in Table 4, and it should be noticed that two N···O distances are considered non-bonded in spite of the fact that these distances are of lengths which are quite normal for NH···O hydrogen bonds. The reason for this is that the H···O distances for the H atoms bonded to each of the appropriate N atoms, N(11) and N(21), are too long (*i.e.* >2·5 Å), and, in addition, the N–H···O angles are all unfavourable for hydrogen bonding (*i.e.*

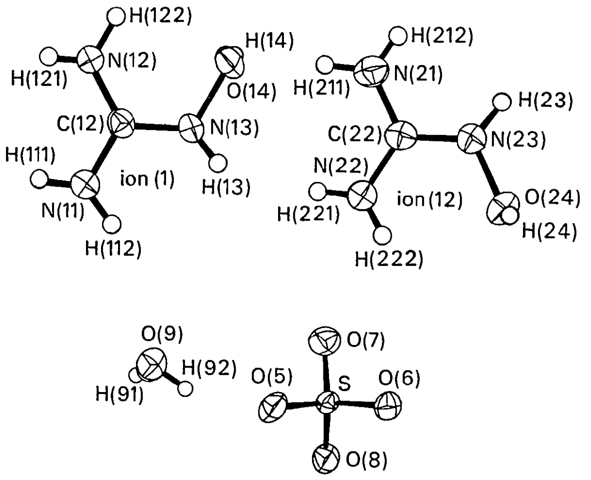

Fig. 1. Notation of atoms, thermal vibration ellipsoids (scaled to 50% probability), and conformations of each of the ions and the water molecule of hydroxyguanidinium sulphate monohydrate.

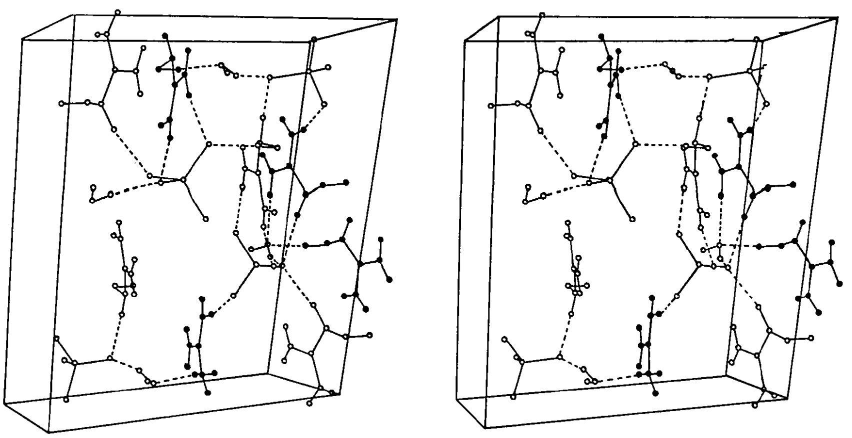

Fig. 2. Stereo diagram showing the content of the unit cell of hydroxyguanidinium sulphate monohydrate. The atoms of the two crystallographically non-equivalent hydroxyguanidinium ions are indicated by filled and empty circles for ion (1) and ion (2), respectively.

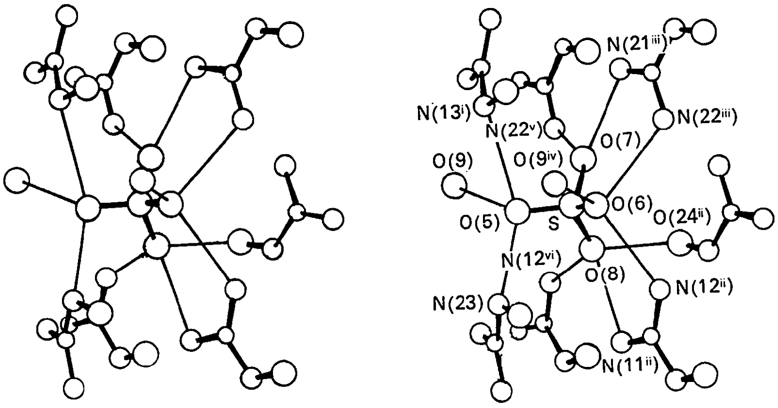

Fig. 3. Stereo diagram showing the coordination of the sulphate ion in the crystal structure of hydroxyguanidinium sulphate monohydrate.

Table 4. *Distances and angles concerning the hydrogen-bonding system*

Symmetry code

i	$1-x$,	$1-y$,	$-z$
ii	$2-x$,	$-\frac{1}{2}+y$,	$\frac{1}{2}-z$
iii	x,	$\frac{1}{2}-y$,	$-\frac{1}{2}+z$
iv	$1+x$,	y,	z
v	$-1+x$,	$\frac{1}{2}-y$,	$-\frac{1}{2}+z$
vi	$1-x$,	$-\frac{1}{2}+y$,	$\frac{1}{2}-z$
vii	$-1+x$,	y,	z

	Distances (Å)		Angle (°)
O···H–X	O···X	O···H	O···H–X
O(5)···H(23)—N(23)	2·880 (3)	1·96 (4)	166 (4)
O(5)···H(13)—N(13^{i})	2·988 (4)	2·12 (4)	170 (4)
O(5)···H(92)—O(9)	2·753 (3)	1·93 (5)	156 (5)
O(6)···H(121)–N(12^{ii})	2·866 (3)	2·06 (4)	175 (4)
O(6)···H(221)–N(22^{iii})	2·908 (4)	2·05 (5)	168 (4)
O(6)···H(91)—O(9^{iv})	2·780 (3)	1·98 (5)	163 (5)
O(7)···H(211)–N(21^{iii})	2·909 (5)	2·02 (5)	174 (4)
O(7)···H(222)–N(22^{v})	2·956 (3)	2·18 (4)	156 (4)
O(8)···H(111)–N(11^{ii})	2·991 (3)	2·12 (4)	169 (4)
O(8)···H(122)–N(12^{vi})	2·913 (4)	2·03 (5)	164 (3)
O(8)···H(24)—O(24^{ii})	2·681 (3)	1·76 (5)	170 (4)
O(9)···H(14)—O(14)	2·651 (3)	1·70 (4)	167 (4)
O(9)···H(112)–N(11^{i})	2·962 (5)	2·09 (5)	177 (4)
Non-bonded short distances			
O(14)···H(112)–N(11^{vii})	2·909 (4)	2·63 (5)	100 (4)
O(24)···H(212)–N(21^{iv})	2·976 (3)	2·62 (5)	109 (5)

< 110°) (Kvick, 1974). No hydrogen bonds connect the hydroxyguanidinium ions of the structure, but the ions are packed very closely.

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