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Structure of Agmatine Sulphate Dihydrate:* An Extensive Amine–Sulphate–Water Hydrogen-Bond Network

BY K. CHANDRASEKHAR,† VASANTHA PATTABHI AND S. RAGHUNATHAN‡

Department of Crystallography and Biophysics, University of Madras, Guindy Campus, Madras-600025, India

Abstract. $C_5H_{14}N_4.H_2SO_4.2H_2O$, $M_r = 264.3$, orthorhombic, *Pbca*, $a = 22.251$ (16), $b = 7.199$ (5), $c = 15.849$ (11) Å, $Z = 8$, $D_m = 1.390$, $D_c = 1.383$ (3) Mg m^{-3}. The structure was solved by heavy-atom and Fourier methods and refined to $R = 0.060$ for 1311 counter reflections. The agmatine chain is essentially planar, packing in layers parallel to *ac*. An elaborate network of N–H$\cdots$O and O–H$\cdots$O hydrogen bonds interlinks the amine, water and sulphate groups.

Introduction. Some of the amines produced from amino acids by bacteria have pharmacological activity in animals (Fruton & Simmonds, 1965). These oligoamines are low molecular weight, aliphatic, non-protein, nitrogenous bases and include the simple diamines putrescine and cadaverine, the aminopropyl derivatives spermidine and spermine, and the peculiar guanidine bases such as agmatine and octopine found in invertebrate tissues and microbes. Oligoamines stimulate chain elongation in systems containing DNA-dependent RNA-polymerase *in vitro* and also have follicle-stimulating hormone-releasing-factor activity.

Agmatine sulphate dihydrate (ASD) (Fig. 1) was crystallized from aqueous methanol. Preliminary cell parameters were obtained from Weissenberg photographs and accurate values by least-squares refinement (Main & Woolfson, 1963) of 17 diffractometer settings each measured at $\pm 2\theta$. Intensities were measured on a Picker four-circle diffractometer with

Fe-filtered Co $K\alpha$ radiation ($\lambda = 1.7903$ Å). A unique data set was collected out to $2\theta = 130°$ by the θ–2θ scan technique with a scan range of 2° and a scan rate of 2°min^{-1}. Stationary background measurements were made for 10s on either side of each scan. 1311 non-zero reflections were corrected for Lorentz, polarization and background effects as well as for absorption (North, Phillips & Mathews, 1966).

The position of S was determined from a three-dimensional Patterson synthesis ($R = 0.59$). A heavy-atom-phased Fourier map revealed only four peaks significantly above noise level and these were identified as the O atoms of the sulphate ($R = 0.56$). One cycle of full-matrix least-squares refinement (Gantzel, Sparks & Trueblood, 1961) of the parameters of the sulphate group reduced R to 0.50 and a Fourier calculation revealed the entire agmatine chain ($R = 0.44$). Refinement was continued and successive difference syntheses indicated the O atoms of two water molecules in the framework, and the H atoms close to their stereo-
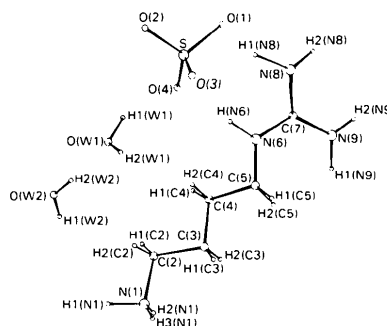
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* Agmatine is 1-(4-aminobutyl)guanidine.

† Present address: Laboratorium für chemische und mineralogische Kristallographie, Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland.

‡ Present address: Department of Biological Sciences, Purdue University, W. Lafayette, IN 47907, USA.

Fig. 1. Perspective view with atom-numbering scheme.

chemically expected positions ($R = 0.09$). Hydrogen-bonding considerations facilitated identification of the H atoms of the water molecules. Full-matrix refinement with anisotropic thermal parameters for the non-H atoms and unit weights for all atoms led to a final R of 0.060.* H-atom parameters were included in structure-factor calculations, but not refined. Scattering factors were taken from International Tables for X-ray Crystallography (1968).

Discussion. Final atomic parameters are listed in Table 1 and interatomic distances and angles in Table 2. The imino and butylamino groups are protonated and the coordination of the sulphate ion is tetrahedral. The entire agmatine molecule is nearly planar, the equation to the least-squares plane being $0.4979X + 9.9792Y + 0.4099Z = 35.1103$. The atoms N(1) through N(8) are arranged in an all-trans configuration. The average bond lengths and angles in the butylamine segment [C–C 1.525 (6), C–N 1.491 (6) Å, ∠C–C–C 110.5 (5), ∠N–C–C 109.7 (5)°] compare well in general with those tabulated by Chandrasekhar & Pattabhi (1980) for other oligoamines. The guanidyl group is triangular planar and the three C–N lengths are equal within 2σ. The mean C–N length [1.333 (6) Å] and N–C–N angle [120.0 (5)°] are in accord with those in the guanidyl moieties of some other studies such as guanidinoacetic acid (Berthou, Laurent & Nakajima, 1976), β-guanidinopropionic acid

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* Lists of structure factors, anisotropic thermal parameters and coordinates of H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36889 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional positional* ($\times 10^4$) *and isotropic thermal parameters of the non-H atoms, with e.s.d.'s in parentheses*

	x	y	z	B_{eq}*(Å^2)
S	3596 (1)	6051 (2)	827 (1)	2.3
O(1)	4091 (2)	5576 (6)	263 (2)	5.4
O(2)	3030 (1)	6161 (6)	351 (2)	4.5
O(3)	3727 (2)	7808 (5)	1239 (2)	5.2
O(4)	3554 (2)	4571 (5)	1476 (2)	3.8
N(1)	3180 (2)	3894 (5)	5706 (2)	3.1
C(2)	3301 (2)	3847 (8)	4775 (3)	3.2
C(3)	3965 (2)	3988 (7)	4568 (3)	3.0
C(4)	4036 (2)	3852 (8)	3606 (3)	3.4
C(5)	4689 (2)	3961 (7)	3322 (3)	3.1
N(6)	4683 (2)	3953 (6)	2387 (2)	3.0
C(7)	5183 (2)	3895 (7)	1920 (3)	2.8
N(8)	5118 (2)	4065 (6)	1082 (2)	3.6
N(9)	5720 (2)	3702 (6)	2263 (2)	3.4
O($W1$)	2577 (2)	5714 (7)	2581 (3)	7.2
O($W2$)	1843 (2)	3631 (6)	3586 (2)	5.3

* $B_{eq} = \frac{4}{3}\sum_i\sum_j(\mathbf{a}_i\cdot\mathbf{a}_j)\beta_{ij}$ with $\sigma(B_{eq}) = \frac{4}{3}\sum_i\sum_j(\mathbf{a}_i\cdot\mathbf{a}_j)\sigma(\beta_{ij})$. $\sigma(B_{eq}) =$ 0.1 for S, 0.2 for other atoms.

Table 2. *Bond lengths* (Å) *and angles* (°) *involving non-*H *atoms, with e.s.d.'s in parentheses*

S–O(1)	1.459 (5)	C(3)–C(4)	1.536 (7)
S–O(2)	1.470 (3)	C(4)–C(5)	1.523 (6)
S–O(3)	1.453 (4)	C(5)–N(6)	1.482 (6)
S–O(4)	1.484 (4)	N(6)–C(7)	1.337 (6)
N(1)–C(2)	1.500 (6)	C(7)–N(8)	1.342 (6)
C(2)–C(3)	1.517 (6)	C(7)–N(9)	1.320 (6)
O(1)–S–O(2)	110.2 (2)	C(2)–C(3)–C(4)	108.1 (5)
O(1)–S–O(3)	109.1 (2)	C(3)–C(4)–C(5)	112.8 (5)
O(1)–S–O(4)	107.7 (2)	C(4)–C(5)–N(6)	106.7 (5)
O(2)–S–O(3)	110.8 (2)	C(5)–N(6)–C(7)	123.1 (5)
O(2)–S–O(4)	109.9 (2)	N(6)–C(7)–N(8)	117.1 (5)
O(3)–S–O(4)	109.0 (2)	N(6)–C(7)–N(9)	121.9 (5)
N(1)–C(2)–C(3)	112.7 (5)	N(8)–C(7)–N(9)	121.0 (5)

(Steward, Warner & Clarke, 1974) and γ-guanidinobutyric acid hydrochloride (Maeda, Fujiwara & Tomita, 1972).

The structure exhibits a layerwise packing with the zigzag agmatine chains arranged in planes parallel to ac. S atoms also lie on these planes while the O atoms of water molecules form interleaving bands on either side. The infinite repeating unit along b thereby consists of layers of O($W1$), AS, O($W2$), AS, O($W1$) in that order.

The agmatine molecules are roughly equally inclined to both a and c. While adjacent molecules along b (related by a twofold screw axis) are similarly inclined but oppositely directed, adjacent molecules along a (related by a glide operation) are oppositely inclined and form a herring-bone-like pattern.

The structure, though well stabilized by hydrogen bonds, shows holes in unique positions especially as columns parallel to b. All the protons attached to the amino and guanidyl moieties form N–H$\cdots$O hydrogen bonds and the protons of the water molecules O–H$\cdots$O hydrogen bonds. There are twelve distinct hydrogen-bond linkages, eight of the N–H$\cdots$O type and four of the O–H$\cdots$O type. There are no other intermolecular short contacts. N(1) donates three hydrogen bonds, O($W1$), O($W2$), N(8) and N(9) two each and N(6) one. Hydrogen bonds about each of the atoms N(1), O(4) and O($W1$) are disposed in three of four tetrahedral directions while O($W2$) forms four hydrogen bonds which are in approximately tetrahedral coordination.

The O atoms of each sulphate ion form hydrogen bonds with six different agmatine molecules. Each sulphate ion is bonded to an adjoining agmatine through N(6)$\cdots$O(4) and N(8)$\cdots$O(1) interactions. Sulphate ions are joined together in linear chains along b by N(1)$\cdots$O(4) and N(1)$\cdots$O(3) hydrogen bonds. The N(8) atoms act as bridges between centrosymmetrically related sulphate ions through N(8)$\cdots$O(1) linkages. The O atoms of the water molecules form a continuous column of hydrogen bonds amongst themselves in the form of a distorted spiral with its axis along b.
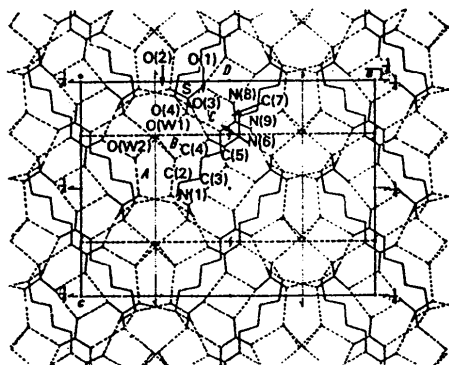
Fig. 2. Crystal structure projected down **b**. Hydrogen bonds are shown by broken lines.

Table 3. *Hydrogen-bond geometry*

Symmetry code: (a) x,y,z; (b) $\frac{1}{2} - x$, $1 - y$, $\frac{1}{2} + z$; (c) x, $\frac{3}{2} - y$, $\frac{1}{2} + z$; (d) x, $\frac{1}{2} - y$, $\frac{1}{2} + z$; (e) $1 - x$, $1 - y$, $-z$; (f) $1 - x$, $y - \frac{1}{2}$, $\frac{1}{2} - z$; (g) $\frac{1}{2} + x, y$, $\frac{1}{2} - z$; (h) $\frac{1}{2} - x$, $\frac{1}{2} + y, z$.

$D-H\cdots A$	$D\cdots A$ (Å)	$D-H$ (Å)	$H\cdots A$ (Å)	$\angle D-H\cdots A$ (°)
N(1)–H1(N1)–O(2^b)	2·751 (5)	1·15	1·65	156
N(1)–H2(N1)–O(3^c)	2·799 (5)	0·79	2·01	171
N(1)–H3(N1)–O(4^d)	2·899 (5)	0·94	1·96	176
N(6)–H(N6)–O(4^a)	2·931 (6)	1·04	1·89	179
N(8)–H1(N8)–O(1^a)	2·844 (6)	1·20	1·68	160
N(8)–H2(N8)–O(1^e)	2·777 (6)	0·83	1·96	164
N(9)–H1(N9)–O(3^f)	2·750 (5)	1·10	1·84	138
N(9)–H2(N9)–O($W2^g$)	2·839 (6)	0·83	2·02	168
O($W1$)–H1($W1$)–O(4^a)	2·910 (6)	1·19	1·99	130
O($W1$)–H2($W1$)–O($W2^h$)	2·935 (6)	0·68	2·28	165
O($W2$)–H1($W2$)–O(2^b)	2·816 (5)	0·81	2·05	157
O($W2$)–H2($W2$)–O($W1^a$)	2·730 (6)	0·84	1·92	161

The crystal structure projected down **b** is illustrated in Fig. 2 and the hydrogen-bond geometry listed in Table 3. The disposition of the elaborate hydrogen-bonding network can best be described by considering four regions A, B, C and D indicated in the figure.

Region A depicts hydrogen bonding between N(1), O(2), O($W1$) and O($W2$). The sequence of hydrogen bonds N(1)$\cdots$O(2), O(2)$\cdots$O($W2$), O($W2$)$\cdots$O($W1$), O($W1$)$\cdots$O($W2$), O($W2$)$\cdots$O(2), O(2)$\cdots$N(1) may be visualized as a spiral with its axis along **b**. The b glide causes this pattern of linkages to be repeated as an infinite chain of alternately left- and right-handed spirals. Region B encompasses a continuous sequence of hydrogen bonds N(1)$\cdots$O(4), O(4)$\cdots$O($W1$), O($W1$)$\cdots$O($W2$), O($W2$)$\cdots$N(9), N(9)$\cdots$O(3), O(3)$\cdots$N(1) spiralling along **b** in a right-handed sense. The bonding scheme N(6)$\cdots$O(4), N(8)$\cdots$O(1) between an agmatine chain and O atoms of the same sulphate ion can be seen in region C, while region D illustrates the approximately rhomboidal arrangement of hydrogen bonds N(8)$\cdots$O(1) across centres of inversion.

The configurational similarity of phosphate and sulphate moieties and the observed extended confor-

Table 4. *Some inter-sulphate distances (Å) with e.s.d.'s in parentheses*

Symmetry code: (a) x, y, z; (b) x, $1 + y$, z; (c) $\frac{1}{2} + x$, y, $\frac{1}{2} - z$; (d) $\frac{1}{2} + x$, $\frac{3}{2} - y$, $-z$; (e) x, $\frac{1}{2} - y$, $\frac{1}{2} + z$; (f) x, $\frac{3}{2} - y$, $\frac{1}{2} + z$; (g) $1 - x$, $\frac{1}{2} + y$, $\frac{1}{2} - z$; (h) $1 - x$, $1 - y$, $-z$; (i) $1 - x$, $2 - y$, $-z$.

$S^a\cdots S^b$	7·199 (5)	$S^a\cdots S^f$	8·195 (6)
$S^a\cdots S^c$	12·325 (9)	$S^a\cdots S^g$	8·951 (6)
$S^a\cdots S^d$	11·619 (8)	$S^a\cdots S^h$	6·943 (5)
$S^a\cdots S^e$	9·431 (7)	$S^a\cdots S^i$	8·845 (6)

mation for agmatine in the present study suggest interesting possibilities for binding of agmatine with nucleic acids. Some inter-sulphate distances of relevance in this context are listed in Table 4.

The distance between successive phosphate groups along the helix in polynucleotides is 7·3 Å (Langridge, Marvin, Seeds, Wilson, Cooper, Wilkins & Hamilton, 1960) which may be compared to that of 7·2 Å between successive sulphate ions along **b** in ASD crystals. Further, in ASD the separation of closest sulphate ions within the same sheet is 12·3 Å and the distance between sulphate ions forming hydrogen bonds with the two termini of the same agmatine molecule is 11·6 Å, both of which are comparable to the perpendicular distance of about 13 Å (Tsuboi, 1964) between the two polynucleotide chains across the shallow groove in Li–DNA. Perhaps agmatine could therefore combine with and stabilize the structure of double-helical DNA by forming an oblique bridge between the two helices.

Aspects of agmatine–nucleic acid binding are being investigated in detail and will be published elsewhere.

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