intense low-angle reflections, which should be most affected by absorption, the observed value of the reflection amplitude is greater than that of the calculated. The estimated intensities of the most intense spots had to be multiplied by large film factors to put them on the same basis as the weak ones. Since there is apt to be error in the determination of the film factor as well as in the estimated intensities, the largest errors are in the intense low-angle $|F_o|$ values. Therefore it is not surprising that the discrepancies for these low-angle reflections are as given in Table 1. The overall agreement between calculated and observed amplitudes confirms the correctness of the structure as reported.

Table 2. *Interatomic distances between nearest neighbors in* RhSi

Atom	Number of equivalent neighbors	Neighboring atom	Distance (Å)
Rh	1	Si	2·46±0·08
Rh	3	Si	2·44±0·05
Rh	3	Si	2·57±0·05
Rh	6	Rh	2·87±0·01
Si	6	Si	2·90±0·02

The important interatomic distances are given in Table 2.

This work has shown that there is a real difference between the rhodium parameter in RhSi and that of iron (0·1370±0.0020) in the FeSi structure (see Fig. 1).

We wish to thank J. Andrus for taking the powder diffraction photographs used in this study.

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The Crystal Structure of Creatine Monohydrate

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Creatine monohydrate crystallizes in the monoclinic system, space group $P2_1/c$, $a = 12{\cdot}50$, $b = 5{\cdot}01$, $c = 12{\cdot}16$ Å, $\beta = 109°$. The crystal structure was solved through the calculation of the Patterson projection along [010] and trial structure factors, and the atomic positions have been refined by Fourier series and least-squares calculations. The molecular structure found corresponds to that of a zwitter ion; the atoms of the substituted guanidine group lie nearly in one plane which is inclined at $84\frac{1}{2}°$ to a second plane containing the carboxyl group. The molecules are held in layers in the crystal by a very complete system of hydrogen bonds.

Introduction

Creatine plays an important role in the metabolism of proteins and is therefore of considerable biological interest. As there are no accurate data on the type of substituted guanidine group present in this molecule, we considered it worth while to study its structure in some detail.

Experimental

Creatine crystallizes as the monohydrate in well formed monoclinic prisms, elongated along [010] and showing {001}, {100} and {011} dominating. The crystals are described by Groth (1906–19), who gives references to measurements by several authors. Allowing for a change of nomenclature (a and c reversed), the quoted axial ratio, b:c, varying from 2·39 to 2·44, agrees well with the X-ray data; a:c generally differs widely but is based on doubtful measurements on small faces. The correct relation was derived by Fletcher (1887), who gives

$$a:b:c \text{ (goniometric)} = 2{\cdot}48:1:2{\cdot}40$$
$$(\text{cf. } a:b:c \text{ (X-ray data)} = 2{\cdot}49:1:2{\cdot}43)\,.$$

The preliminary crystallographic data are as follows:

$$a = 12{\cdot}50 \pm 0{\cdot}05,\quad b = 5{\cdot}01 \pm 0{\cdot}02,\quad c = 12{\cdot}16 \pm 0{\cdot}04 \text{ Å},$$
$$\beta = 109° \text{ (goniometric)};$$
$$\text{space group, } P2_1/c;\ n = 4;$$

$\varrho = 1{\cdot}369$ (measured by flotation), $\varrho = 1{\cdot}370$ calculated for $4(C_4N_3O_2H_9.H_2O)$ in the unit cell;

$$F_{000} = 320\,.$$

Optical measurements show that the plane of the optic axes is (010), with γ inclined at about 20° to a in the acute angle.

Oscillation photographs were taken of the crystal using Cu $K\alpha$ radiation and also a limited series of Weissenberg photographs, with b as rotation axis: k, 0–3; a and c as rotation axes: h and l, 0–6 respectively. The intensities of the reflexions were estimated visually by the multiple-film technique, corrected for the Lorentz and polarization factors, and placed on an approximately absolute scale using Wilson's method (Wilson, 1949, 1950).

It is perhaps amusing to note that both the crystals first measured here and those described by Fletcher were obtained from preparations labelled creatinine and were identified as creatine through the crystallographic investigations. They were presumably formed by transformation from creatinine during recrystallization.

Structure determination

(*a*) *Projection along* [010]

Since b is short, 5·01 Å, and some of the $h0l$ reflexions have high U values, an attempt was made first to solve the structure by direct methods. A number of sign relations were derived by Sayre's squaring method (Sayre, 1952), of which 19 out of 20 proved correct, and these were linked by a few signs derived by inequalities. Unfortunately one of these, that for $\bar{4},0,12$, was chosen incorrectly. It was based on an inequality given by Gillis (1948) which led to the relations

$$1{\cdot}14 \leq 1{\cdot}32\pm0{\cdot}16,\quad 0{\cdot}88 \leq 1{\cdot}06\pm0{\cdot}16\,.$$

The correct sign, negative, satisfies the relations by the narrow margin 0·02; the incorrect sign, which satisfies the relations by a much wider margin, was at first selected and led to a series of non-refinable Fourier projections.

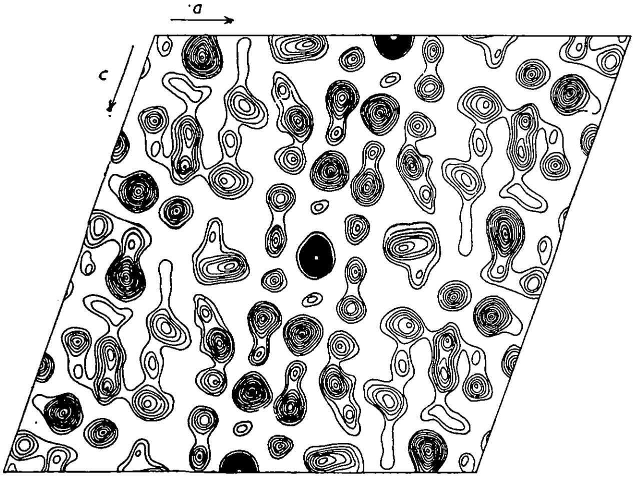


Fig. 1. Patterson projection, $P(x, z)$, for creatine monohydrate.

Direct methods were therefore abandoned and the structure analysis was approached by the calculation of the half sharpened Patterson [010] projection. The configuration of the molecule was derived from a consideration of the peaks directly surrounding the origin (Fig. 1) and the relative positions of the molecules in the cell were limited to two possibilities by examination of the Patterson peak pattern as a whole. For both of these possibilities water molecules were fitted in positions suggested by three strong, high-order reflexions. Structure-factor calculations then eliminated one of the two possibilities and the b-axis electron-density projection was calculated and refined normally (Fig. 2). The structure-factor calculations, based on Hartree f values for carbon, nitrogen and oxygen, indicated a small modification of the absolute scale and a value for the temperature factor B of $2{\cdot}8\times10^{-16}$ cm.^{2}. This was used to refine the parameters by the method of least squares.

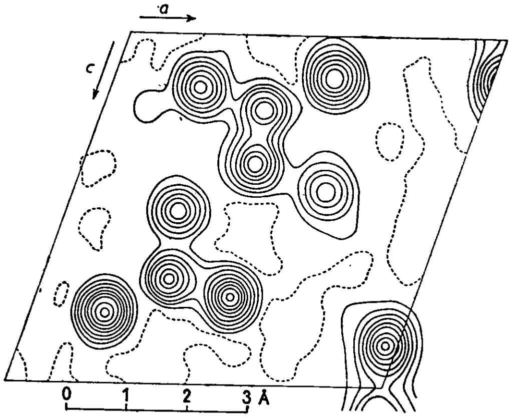
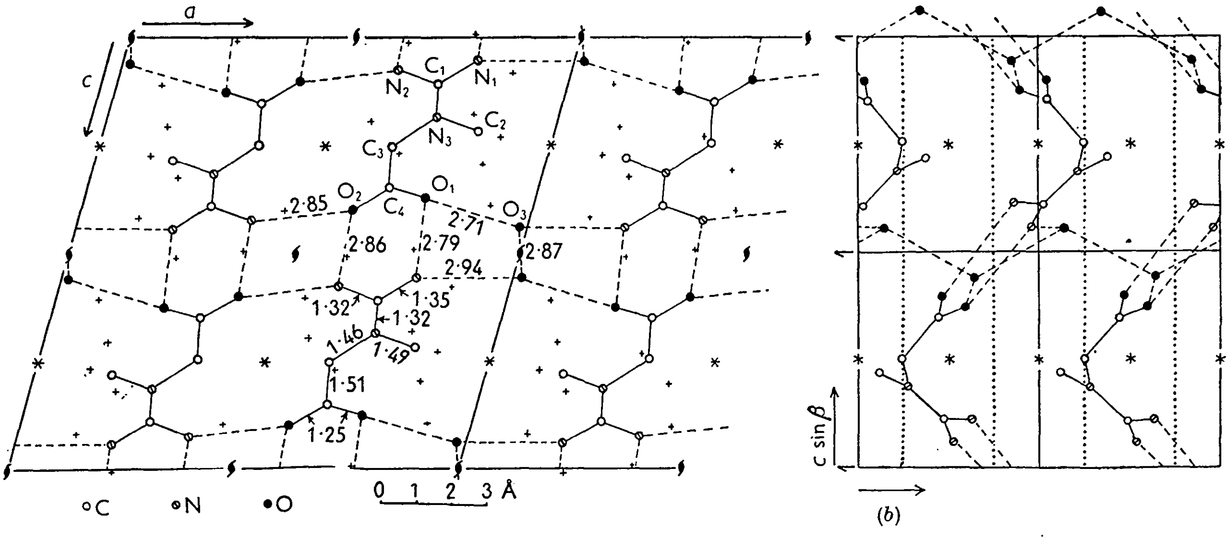


Fig. 2. Electron distribution for creatine monohydrate projected along [010]. Contours at intervals of 1 e.Å^{-2} with the 1-electron contour broken.

(*b*) *Determination of the y parameters*

With x and z found for each atom, and approximate interatomic distances known, it was possible to assign rough y parameters, relative to an arbitrary origin. In the $h0l$ projection (Fig. 3(*a*)) the distance C_3–N_3 is 1·46 Å, the length of a single bond, and these two atoms must have nearly the same y parameters. Two possible configurations of the molecule, which may be described as having C_1–N_3 and C_3–C_4 '*cis*' and '*trans*' respectively, were considered. Trial structure-factor calculations on the hll reflexions showed that the '*cis*' configuration was correct, with N_3 and C_3 at $y \sim \frac{1}{4}$ and the water molecules roughly $\frac{1}{2}b$ from the methyl groups. The approximate y parameters were refined, first by calculation of the generalized projection, using hll amplitudes only, then by a series of



(*a*) (*b*)

Fig. 3. Atomic positions in creatine monohydrate projected along (*a*) [010], (*b*) [100]. Crosses indicate probable hydrogen atom positions.

least-squares calculations, using finally *x*, *y* and *z* as variables. The atomic coordinates derived are given in Table 1. The disagreement factor calculated for these coordinates on 1200 *hkl* reflexions* was $R = 15\%$; on the *h0l* reflexions alone it was $16\frac{1}{2}\%$. The coordinates differ a little from the best coordinates derived from the [010] projection, and the introduction of hydrogen-atom contributions might be expected to introduce further small variations.

Table 1. *Atomic coordinates*

	x	*z*	*y*
N_1	0·289	0·306	0·472
N_2	0·119	0·329	0·370
N_3	0·224	0·434	0·715
C_1	0·211	0·358	0·520
C_2	0·331	0·472	0·874
C_3	0·148	0·502	0·744
C_4	0·170	0·600	0·542
O_1	0·256	0·625	0·397
O_2	0·098	0·651	0·529
O_3	0·484	0·689	0·356

(*c*) *Hydrogen atoms*

The appearance of the [010] projection suggested that positions could be assigned to many of the hydrogen atoms in the structure. Structure-factor calculations were therefore carried out for the *h0l* reflexions including hydrogen atom contributions. These showed improvement in agreement for the low-order reflexions but deterioration for the higher-order terms unless f_H was modified by a temperature factor with *B* approximately twice the value given above. While these calculations confirm the probable positions of most of the hydrogen atoms present, it is clear that the present data are insufficiently accurate to warrant assigning precise coordinates.

Description of the structure

As might be expected, the structure of creatine found in the crystal corresponds with that of a zwitter ion. The three C–N bonds within the guanidine group (Table 2) may be taken as equal within the limits of error; their average value is 1·33 Å, a little smaller than 1·36 Å, the average value found for the C–N bonds in the guanidine group of dicyandiamide (Hughes, 1940), and close to 1·335 Å, the C–N distance in urea (Vaughan & Donohue, 1952). The atoms,

Table 2. *Interatomic distances and bond angles*

		δl			δl
N_1–C_1	1·35 Å	0·011 Å	N_3–C_3	1·46 Å	0·011 Å
N_2–C_1	1·32	0·011	C_3–C_4	1·51	0·012
N_3–C_1	1·32	0·011	C_4–O_1	1·25	0·010
N_3–C_2	1·49	0·011	C_4–O_2	1·25	0·010
O_1–N_1'	2·79	0·009	O_3–O_3'	2·87	0·011
O_2–N_2'	2·86	0·009	O_2–N_2'	2·85	0·009
O_1–O_3	2·71	0·008	N_1'–O_3'	2·94	0·009

$N_1C_1N_2$	118°	$C_1N_3C_2$	121°	$C_3C_4O_1$	121°
$N_1C_1N_3$	121	$C_1N_3C_3$	119	$C_3C_4O_2$	118
$N_2C_1N_3$	121	$C_2N_3C_3$	117	$O_1C_4O_2$	123
$N_3C_3C_4$	113				
$C_4O_2N_2'$	123	$C_4O_1N_1'$	121	$O_1O_3O_3'$	120
$O_2N_2'C_1'$	189	$O_1N_1C_1'$	123	$O_3O_3'O_3''$	108
$N_2''O_2N_2'$	86	$N_1'O_1O_3$	81	$N_1'O_3'O_3$	76
$O_2N_2'O_2''$	107	$O_1N_1'O_3'$	106		

Accuracy of bond angles: 4°.

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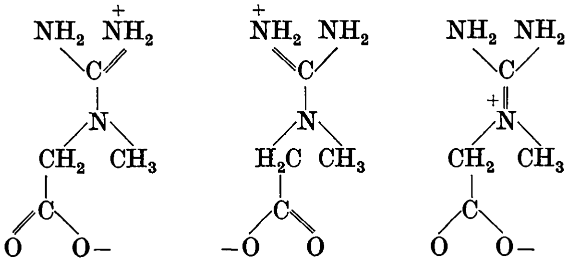
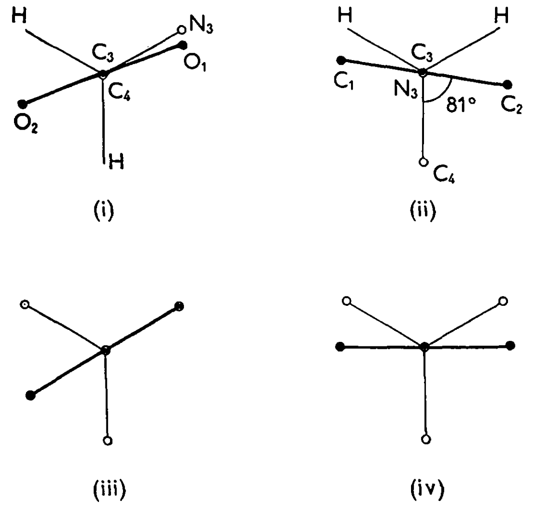
* For the observed and calculated *F* values see Mendel (1954).

N_1, C_1, N_2 and N_3 all lie in one plane, and the methyl group carbon atom, C_2, is also only 0·1 Å from this plane. As a whole, the character of the guanidine group can be accounted for in terms of the resonating bond arrangements:



The atoms of the carboxyl group, C_3, C_4, O_1 and O_2 lie in a second plane, which makes an angle with the first of 84½°, giving the molecule as a whole a bent appearance.

The stereochemical conditions which lead to the adoption of this bent configuration are illustrated by the diagrams in Fig. 4. This shows views of the atomic positions in creatine projected down the bonds C_4–C_3 and N_3–C_3, C_3 being the one carbon atom with tetrahedral character. From Fig. 4(i) it is clear that the carboxyl group plane lies only 10° from the plane of the C_3–N_3 bond, i.e. very near the arrangement which Pauling & Corey (1951) have shown to be preferred in many amino acid structures. Here, as in the amino acids, the small formal positive charge on the nitrogen encourages this particular bond orientation within the general type of configuration shown (Fig. 4(iii)). The arrangement in the molecule relative to the atoms attached to C_3 of the second planar or near-planar group, (Fig. 4(ii)), is, however, not of this preferred type, but corresponds more nearly to the alternative (Fig. 4(iv)) mentioned by Pauling & Corey. Here this may represent an approach to a normal staggered arrangement. It results in reasonable distances between non-bonded atoms within the molecule and is favourable for the formation of intermolecular hydrogen bonds.



(i) (ii)

(iii) (iv)

Fig. 4. Diagram to illustrate the packing of non-bonded atoms within the molecule of creatine. In (i) and (ii) the atoms are seen viewed along the bonds C_4–C_3 and N_3–C_3. Atoms shown as blocked circles project above those shown as open circles.

In the crystal structure the molecules are held together in layers by the interionic attraction between the carboxyl and guanidine groups of neighbouring molecules and by a very complete system of hydrogen bonds (Fig. 3). The water of crystallization forms a zigzag around the twofold axis, each water molecule being linked within the zigzag to those above and below it, and also to one carboxyl oxygen and one NH_2 group of different creatine molecules. This links the molecules together both within and between the layers. All the hydrogen bonds appear to form in directions consistent with Donohue's conclusions—the greatest angular deviation observed between the line joining two hydrogen bonded atoms and the probable direction of the NH or OH bonds is about 14°. The complete structure accounts well for such macroscopic features of the crystals, as the crystal habit and the cleavages along both (100) and (010).

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