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The Crystal Structure of Creatinine

By Miss S. du Pré and H. Mendel

Laboratory of Crystal Chemistry, State University, Utrecht, The Netherlands

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Creatinine crystallizes in the monoclinic system, space group $P2_1/c$, with $a = 8{\cdot}06$, $b = 5{\cdot}97$, $c = 13{\cdot}34$ Å, $\beta = 121°$, and with 4 molecules per unit cell. The crystal structure was solved by inequalities and trial structure factors. The atomic positions have been refined by Fourier-series and least-squares calculations. The structure consists of strings of molecules, intimately hydrogen bonded, parallel to the c axis. Indications of a strongly asymmetric temperature factor have been found.

Introduction

Creatinine, as well as creatine, plays an important role in the metabolism of proteins and is for that reason of considerable biological interest. We also considered it worth while to study the structure of the guanidine group present in this molecule in some detail.

Experimental

The preliminary crystallographic data are:

$$a = 8{\cdot}06 \pm 0{\cdot}02,\ b = 5{\cdot}97 \pm 0{\cdot}01,\ c = 13{\cdot}34 \pm 0{\cdot}04\ \text{Å};\ \beta = 121°.$$

Space group: $P2_1/c$; $n = 4$.

$\varrho = 1{\cdot}38$ (measured by flotation).
$\varrho = 1{\cdot}37$ calculated for 4 $C_4H_7N_3O$ in the unit cell.
$F_{000} = 240$ e.

Oscillation photographs of the crystal were taken using Cu $K\alpha$ radiation, and also Weissenberg photographs with b and a as rotation axes. 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).

Structure determination

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

Since b is short, 5·97 Å, and some of the $h0l$ reflexions have high U values, it was thought to be promising to use inequalities on the $h0l$ projection.

Although it is possible to assign arbitrary signs to two reflexions (except h even and l even) no further relations could be deduced. It follows, however, from packing considerations that the sign of the 200 reflexion ($U = 0{\cdot}52$) must be negative, as otherwise severe overlapping would occur between atoms at the twofold screw axes and the centre of symmetry. It was now possible with the help of this reflexion to

Table 1

Chosen arbitrarily:

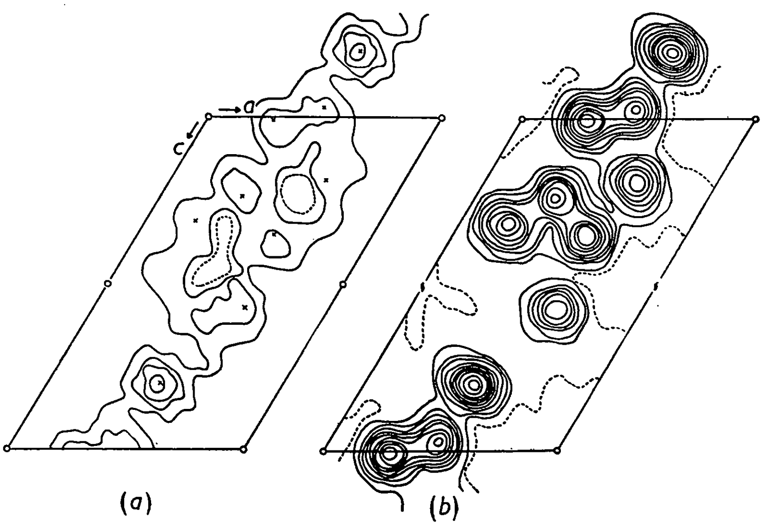
502 +
2,0,10 +

Assumed from packing considerations:

200 −

Deduced, the following groups:

A			*B*			*C* ($\bar{7}04 \equiv +$)			*D* ($\bar{7}04 \equiv -$)		
		U			*U*			*U*			*U*
200	−	0·52	$\bar{7}04$	≡ +	0·45	$\bar{5}$,0,12	≡ +	0·65	$\bar{5}$,0,12	≡ +	0·65
502	+	0·53									
2,0,10	+	0·74									
302	−	0·50	$\bar{8}$,0,12	−	0·74	$\bar{7}$,0,12	−	0·67	$\bar{7}$,0,12	−	0·67
$\bar{1}08$	−	0·44	$\bar{5}04$	−	0·28	$\overline{10}$,0,10	+	0·47	$\overline{10}$,0,10	+	0·47
$\bar{3}08$	+	0·44	$\bar{6}$,0,12	+	0·56	300	−	0·13	300	+	0·13
$\bar{5}08$	−	0·43	$\bar{3}$,0,14	−	0·27	202	−	0·19	202	+	0·19
4,0,10	−	0·41	$\bar{9}$,0,10	−	0·22						
2,0,10	+	0·74	$\bar{5}$,0,14	−	0·35						
0,0,10	−	0·59									
$\bar{2}$,0,10	+	0·29									



(a) (b)

Fig. 1. (a) Fourier obtained from inequalities. Crosses indicate atomic positions. (b) Electron distribution for creatinine projected along [010]. Contours at intervals of 1 e.Å^{-2} with the 1-electron contour broken.

deduce the signs in column A, Table 1 by means of the Kasper–Harker (1948) inequality

$$(U_H \pm U_{H'})^2 \leqslant (1 \pm U_{H+H'})(1 \pm U_{H-H'}) \,.$$

In using this inequality we assumed an error of 10% in all U values and considered a sign to be certain only when the same sign was given by applying the error margin in the most unfavourable way. By assuming the sign of the $\bar{7}04$ reflexion, column B Table 1 could be deduced, and in exactly the same way columns C and D were deduced by assuming the $\bar{5}$,0,12 reflexion.

It is easily seen that the following combinations are possible:

$$A+B+C$$
$$A+B-C$$
$$A-B+D$$
$$A-B-D$$

Fouriers from all four combinations were calculated and the one shown in Fig. 1 was chosen (combination $A-B+D$). The interpretation of this Fourier was not straightforward, as there were difficulties in assigning the positions of atoms C_2 and N_2 (see Fig. 3). Only after having determined these positions by means of structure-factor graphs was it possible to refine the structure normally by means of Fourier projections. 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 $2{\cdot}4\times10^{-16}$ cm.^{2}. The final disagreement factor proved to be 16%.

(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. Trial structure-factor calculations of the $0kl$ reflexions with $(k+l)$ even fixed the origin in a centre of symmetry; calculations on the $01l$ and $02l$ reflexions with $k+l$ odd determined the y parameter of the arbitrarily chosen origin. These approximate y parameters were refined by means of Fourier projections along [100]. Finally the y parameters of the two overlapping atoms O and C_2 were refined by least-square calculations, using y_1 and y_3 as the only variables.

The final disagreement factor for this projection (Fig. 2), after having introduced as value for the temperature factor $B = 1{\cdot}3\times10^{-16}$ cm.^{2}, proved to be 18%.

Final coordinates are shown in Table 2.

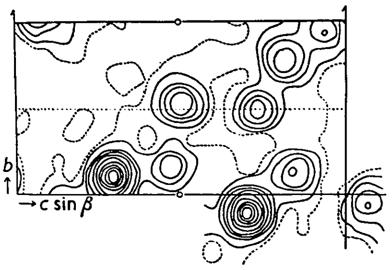


Fig. 2. Electron distribution for creatinine projected along [100]. Contours at intervals of 2 e.Å^{-2} with the 2-electron contour broken.

Table 2. *Atomic coordinates*

	x	y	z
C_1	0·232	0·585	−0·012
C_2	0·325	0·456	0·096
C_3	0·310	0·478	0·284
C_4	0·175	0·742	0·118
N_1	0·283	0·562	0·174
N_2	0·100	0·886	0·157
N_3	0·143	0·763	0·005
O	0·233	0·549	−0·102

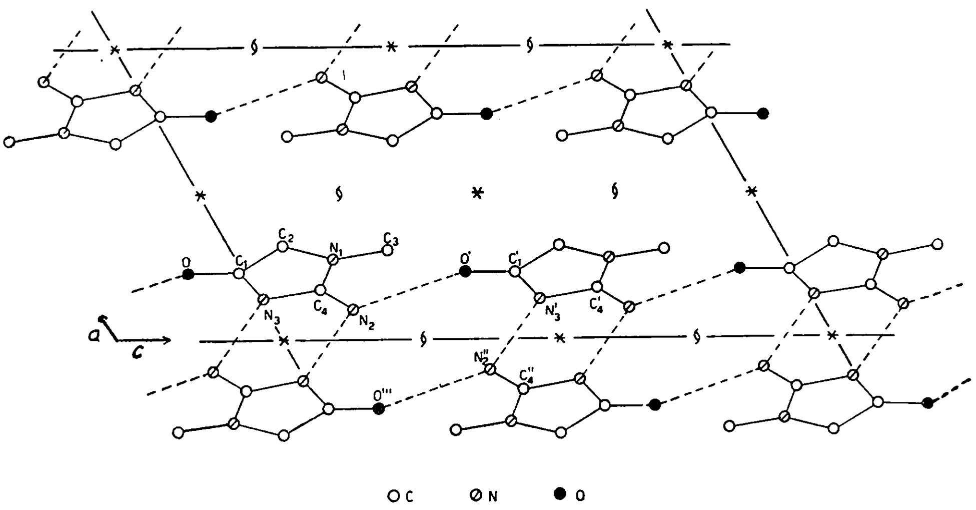


Fig. 3. Atomic positions in creatinine projected along [010].

Table 3. *Bond distances and angles*

(See also Fig. 3)

C_1–O	1·22 Å	N_1–C_3	1·46 Å	C_4–N_3	1·40 Å
C_1–C_2	1·47	N_1–C_4	1·34	C_1–N_3	1·37
C_2–N_1	1·40	C_4–N_2	1·30		

$\angle$ O_1–C_1–C_2	127°	$\angle$ C_1–C_2–N_1	107°
$\angle$ O_1–C_1–N_3	124	$\angle$ C_1–N_3–C_4	107
$\angle$ C_2–C_1–N_3	107		
$\angle$ C_2–N_1–C_3	129°	$\angle$ N_1–C_4–N_2	127°
$\angle$ C_2–N_1–C_4	107	$\angle$ N_1–C_4–N_3	112
$\angle$ C_3–N_1–C_4	123	$\angle$ N_2–C_4–N_3	120

The accuracy of the bond distances is estimated to be of the order of 0·03 Å.

The accuracy of the bond angles is estimated to be of the order of 4–5°.

The angle between the plane of the molecule and the *a–c* plane is 70°.

Discussion of the structure

The bond distances in the molecule (Table 3) show a nearly complete system of resonance with the exception of the bond N_1–C_3. This explains very well the planarity of the molecule; the greatest deviation from the plane is 0·02 Å, with the bond N_1–C_3 0·25 Å out of this plane. This means that N_1 is an asymmetric atom, so that the molecule is optically active; therefore the crystal contains the *l* and *d* forms joined by the centres of symmetry.

The structure can be best described as two strings of molecules, parallel to *c*, intimately bound by hydrogen bridges; in the *b* direction and between the strings only van der Waals forces are acting. For this structure an asymmetric temperature factor is to be expected, as was observed (see above). As the intensities are, however, estimated visually and no absorption correction was applied it is intended to make a more accurate study of the asymmetric temperature movement by using Geiger-counter measurements and applying also absorption corrections.

The hydrogen bridges N_2–O′ and N_2''–N_3' lie well within known limits and appear in directions consistent with Donohue's (1952) conclusion (see Table 4).

Table 4. *Hydrogen bridges*

(See also Fig. 3)

N_2–O′	2·85 Å	$\angle$ C_4–N_2–O′	124°
N_3'–N_2''	2·92	$\angle$ N_2–O′–C_1'	154
$\angle$ C_1'–N_3'–N_2''	130°	$\angle$ O‴–N_2''–N_3'	118°
$\angle$ C_4'–N_3'–N_2''	123	$\angle$ N_3'–N_2''–C_4''	117

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