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Biguanide

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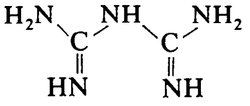
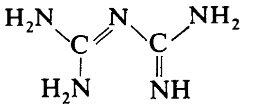
Abstract. $C_2H_7N_5$ (imidodicarbonimidic diamide; CAS [56-03-1])† monoclinic, $P2_1/c$, $a = 9{\cdot}5184\,(9)$, $b = 5{\cdot}0570\,(4)$, $c = 12{\cdot}1563\,(12)$ Å and $\beta = 126{\cdot}772\,(8)°$ (20 ± 1 °C), $D_m = 1{\cdot}43$, $D_x = 1{\cdot}43$ g cm^{-3} ($Z = 4$). The final residual index calculated for 1032 observed reflections was 0·059. The molecule was found to exist in an unsymmetrical tautomeric form.

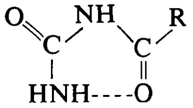
Introduction. Biguanide is generally written as the symmetrical structure (I), although the unsymmetrical form (II) has been postulated as the principal species in solution and many tautomers are at least conceptually possible (Kurzer & Pitchfork, 1968; Rây, 1961). Because of our interest in this class of compounds, we determined the structure of the parent molecule.



(I)



(II)



(III)

The space group was assigned on the basis of the extinct reflections: $h0l$, $l = 2n + 1$, and $0k0$, $k = 2n + 1$, observed on Weissenberg and precession photographs. An approximately spherical crystal (0·2 mm diameter) was used to obtain data on a Syntex $P\bar{1}$ four-circle autodiffractometer. The cell dimensions were refined from 25 reflections with 2θ in the range 34–44° (λMo $K\alpha = 0{\cdot}710730$ Å). Intensity data were collected in the θ–2θ scan mode with the variable scan rate adjusted between 1·0 and 12·0° min^{-1}. The upper and lower counting rate thresholds, for the selection of the scan rates, were chosen to give approximately 10000 counts for reflections within these thresholds. The X-ray tube was equipped with a graphite monochromator. Three control reflections were measured after every 50 data points to check for crystal deterioration. During the course of the data collection the intensities of the standard reflections decreased by about 2% and the rest of the data were scaled based on these standard reflections. In all, 1255 unique reflections were measured ($0 \le h \le 10, 0 \le k \le 5, -10 \le l \le 10$ and $0 \le 2\theta \le 80$) and of these, 105 were systematically extinct while 118 with $I_o \le 0$ were coded 'less-thans' in the refinement. The maximum error due to the absorption of X-rays by the sample was estimated to be less than 1% based on the spherical absorption factors tabulated by Weber (1969), and no absorption corrections were applied. Atomic scattering factors were taken from Table 3.3.1*A* of *International Tables for X-ray Crystallography* (1968).

The structure was solved by the symbolic addition method. Refinement of positional parameters and isotropic temperature factors gave a residual index $R = \Sigma\,||F_o| - |F_c||\,/\Sigma\,|F_o| = 0{\cdot}11$. A difference map revealed the positions of all seven H atoms, which were included in all further calculations with isotropic temperature factors equal to the temperature factors of the atom to which they were bonded. Further refinement of C and N positional and anisotropic temperature parameters decreased the residual index to 0·059 including only observed data. Computations were carried out using the X-RAY system of programs (Stewart,

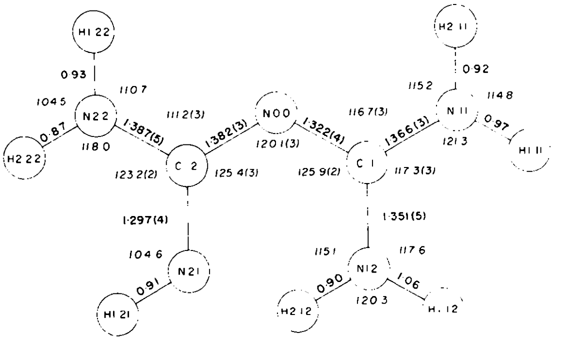


Fig. 1. Bond lengths (Å) and angles (°) with e.s.d.'s in parentheses. E.s.d.'s involving hydrogen atoms are not available.

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† *Chemical Abstracts* name with the registry number in square brackets.

Kundell & Baldwin, 1970) and the *ORTEP* program (Johnson, 1965) was used to prepare Fig. 2.

Discussion. The final parameters are given in Table 1 and bond lengths, bond angles and their associated e.s.d.'s are shown in Fig. 1.* Because the parameters of the H atoms were not refined, e.s.d.'s for these atoms are not available. A perspective drawing of the molecule is shown in Fig. 2 and Table 2 summarizes the proposed hydrogen-bonding scheme.

The molecule is only very roughly planar (Fig. 3), being constrained in this conformation by a relatively strong intramolecular hydrogen bond between N(12) (donor) and N(21) (acceptor). A similar situation can be noted in the analogous compounds biuret hydrate† (III, R = $-NH_2$) (Hughes, Yakel & Freeman, 1961; Craven, 1973) and carbromal‡ [III, R = $-CBr-(C_2H_5)_2$] (Craven & Lesser, 1974) in which intramolecular hydrogen bonds occur between amine donor and carbonyl acceptor groups. A three-dimensional hydrogen-bond network apparently accounts for the rather high melting point of the compound (135 °C). The molecules are linked in chains parallel to (001) by hydrogen bonding between N(22)···H–N(12), the molecules being related by the *c* glide. Each N(00) atom is weakly hydrogen bonded to an N(11) and to an N(22), the donor molecule being related to the acceptors by the twofold screw axis.

The C–N bonds involving C(1) are all of intermediate length between single and double-bond values. Our values in unprotonated biguanide [1·322 Å ≤ C(1)–N ≤ 1·366 Å] may be compared with the

Table 2. *Distances* (Å) *and angles* (°) *for the proposed hydrogen bonds*

The superscripts refer to atoms generated by the application of the following symmetry operations to the positions listed in Table 1: (I) x,y,z; (II) $x, \frac{1}{2}-y, \frac{1}{2}+z$; (III) $1-x, 1-y, 1-z$; (IV) $1-x, -y, 1-z$.

Acceptor	Donor	N···H	N···N	Angle N–H–N
N(21)$^{\mathrm{I}}$···	H(2)–N(12)$^{\mathrm{I}}$	1·98	2·64	128·5
N(22)$^{\mathrm{I}}$···	H(1)–N(12)$^{\mathrm{II}}$	2·01	3·06	173·7
N(00)$^{\mathrm{I}}$···	H(1)–N(22)$^{\mathrm{III}}$	2·21	3·13	169·9
N(00)$^{\mathrm{I}}$···	H(2)–N(11)$^{\mathrm{IV}}$	2·29	3·20	171·5

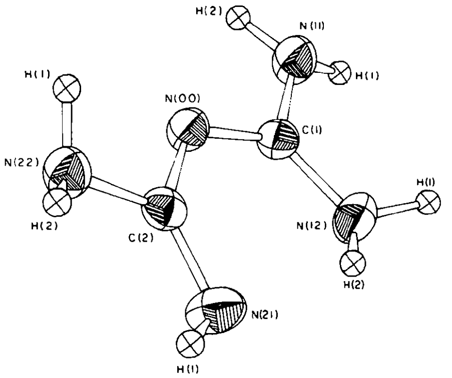

Fig. 2. Perspective drawing of biguanide viewed along the *b* axis. Nonhydrogen atoms are represented by 50% probability thermal ellipsoids.

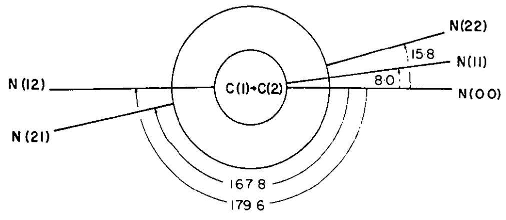

Fig. 3. Dihedral angles projected on a plane perpendicular to the C(1)–C(2) vector.

Table 1. *Final atomic parameters and their e.s.d.'s*

Fractional coordinates (×10^4); anisotropic temperature factors (×10^4) defined by $\exp[-(h^2\beta_{11}+k^2\beta_{22}+l^2\beta_{33}+2hk\beta_{12}+2hl\beta_{13}+2kl\beta_{23})]$, and hydrogen isotropic temperature factors defined by $\exp(-B\sin^2\theta/\lambda^2)$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(00)	6698 (2)	2616 (4)	5336 (2)	99 (3)	234 (9)	65 (2)	−31 (4)	52 (2)	−11 (4)
C(1)	6861 (3)	1223 (5)	4498 (2)	88 (3)	240 (10)	58 (3)	17 (5)	41 (2)	12 (4)
C(2)	7881 (3)	4610 (5)	6126 (2)	92 (3)	214 (10)	53 (3)	15 (4)	36 (2)	18 (4)
N(11)	5570 (3)	−574 (5)	3676 (2)	134 (4)	300 (11)	80 (3)	38 (5)	68 (3)	39 (4)
N(12)	8127 (3)	1533 (5)	4323 (3)	144 (4)	419 (13)	91 (3)	−18 (6)	86 (3)	−22 (5)
N(21)	9381 (3)	4952 (5)	6350 (2)	104 (3)	327 (11)	104 (3)	−31 (5)	61 (3)	36 (5)
N(22)	7312 (3)	6136 (5)	6738 (2)	125 (4)	251 (10)	70 (3)	−14 (5)	59 (2)	−20 (4)

	x	y	z	B (Å^2)		x	y	z	B (Å^2)
H(1 11)	5750	−2000	3240	3·04	H(1 21)	9760	6550	6770	3·20
H(2 11)	4860	−990	3930	3·04	H(1 22)	6100	6310	6160	2·67
H(1 12)	7900	720	3430	3·42	H(2 22)	7700	7750	6970	2·67
H(2 12)	8790	3000	4710	3·42					

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* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32027 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

† Biuret: imidodicarbonic diamide, CAS [108-19-0].

‡ Carbomal: *N*-(aminocarbonyl)-2-bromo-2-ethyl-butanamide, CAS [77-65-6].

C—N bond lengths reported for the protonated biguanide derivatives paludrin* ($1{\cdot}307$ Å ≤ C—N ≤ $1{\cdot}345$ Å (Brown, 1967) and morpholine biguanide† ($1{\cdot}311$ Å ≤ C—N ≤ $1{\cdot}376$ Å) (Handa & Saha, 1973).

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* Paludrin: *N*-(4-chlorophenyl-*N'*-(1-methylethyl)-imidodicarbonimidic diamide monohydrochloride, CAS [637-32-1].

† Morpholine biguanide hydrobromide: *N*-(aminoiminomethyl)-4-morpholinecarboximidamide monohydrobromide, CAS [41305-70-8].

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Biguanide Hydrochloride

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Abstract. $C_2H_8N_7Cl$, monoclinic, $P2_1/n$, $a = 4{\cdot}384$ (1), $b = 17{\cdot}549$ (2), $c = 8{\cdot}363$ (1) Å, $\beta = 101{\cdot}76$ (1)° (23 ± 3 °C), $D_m = 1{\cdot}46$, $D_x = 1{\cdot}45$ g cm^{-3}, $Z = 4$. The final residual calculated for 1020 observed reflections was 0·045. The molecule exists in a tautomeric form with all C—N bond lengths approximately equal.

Introduction. The compound (BgHCl) was prepared by adding a stoichiometric amount of $BaCl_2$ to an aqueous solution of biguanide sulfate and removing the $BaSO_4$ by filtration. Needle-like crystals elongated along [100] were grown from a slowly evaporating aqueous solution and generally showed the forms {100}, {010}, and {011}. The space group was assigned uniquely from the extinct reflections: $h0l$, $h + l = 2n + 1$; and $0k0$, $k = 2n + 1$, observed on Weissenberg and precession photographs. A small crystal, 0·22 × 0·22 × 0·15 mm, was cleaved from a longer crystal and mounted on a quartz fiber with [100] aligned with the φ axis for data collection on a Nonius CAD-4 autodiffractometer equipped with a Cu X-ray tube and graphite monochromator ($\lambda_{\mathrm{Cu}K\alpha} = 1{\cdot}5418$ Å). Lattice parameters were obtained by a least-squares procedure using 18 reflections centred at + and -2θ.

Intensities were measured using the θ–2θ scan technique with the variable scan rate adjusted to obtain 2500 counts. The scan range was calculated as $\Delta\theta = 0{\cdot}5 + 0{\cdot}4 \tan\theta$ and this range was extended 25% on either side to measure background intensities. The intensities and corresponding standard deviations were calculated according to the formulae: $I = [\mathrm{Scan} - (\mathrm{Bkg1} + \mathrm{Bkg2}) \times 2] \times (\mathrm{Scan\ Rate})$; $\sigma(I) = [\mathrm{Scan} + (\mathrm{Bkg1} + \mathrm{Bkg2}) \times 4]^{1/2} \times (\mathrm{Scan\ Rate})$, where Scan is the count obtained during the θ–2θ scan, Bkg1 and Bkg2 are the counts obtained from the background scans and Scan Rate is the scan rate in deg min^{-1}. 15 standard reflections were measured after each 100 data points as a check for crystal deterioration and to monitor instrumental variations. The scaling ratios derived from the standard reflections varied by about ±5% and the data were adjusted accordingly. Within the sphere $2\theta < 150°$, 1308 unique reflections were measured. The 288 reflections with intensities $< 3\sigma(I)$ were defined

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