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The Crystal and Molecular Structure of 1-Methyl-4,5-(D-glucofurano)imidazolidine-2-thione

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The crystal structure has been determined from three-dimensional X-ray data. The space group is $P2_12_12_1$ with four molecules in a unit cell of dimensions $a=21{\cdot}466$ (6), $b=8{\cdot}804$ (4) and $c=5{\cdot}819$ (2) Å. The structure was solved by direct methods and refined with anisotropic temperature factors by full-matrix least-squares procedures. The final R value for 1154 independent reflexions is 0·074. The molecules related by the twofold screw axis are linked by N–H···S hydrogen bonds to form a helicoidal packing arrangement. Other hydrogen bonds are present.

Introduction

The structure of 1-methyl-4,5-(D-glucofurano)imidazolidine-2-thione is reported. This work is part of a research programme on the structure of the compounds obtained by reaction of 2-amino-2-desoxy-D-glucose with alkyl (aryl) isothiocyanates. In earlier reports the structures of 1-alkyl(aryl)-4,5-(D-glucopyrano)imidazolidine-2-thione were proposed (García-González, Fernández-Bolaños & Ruiz-Cruz, 1951; Fernández-Bolaños, García-González, Gasch & Menéndez, 1963; Morel, 1961; Krüger & Rudy, 1963). Subsequently, a furanoid structure for the sugar moiety of these compounds (aryl derivatives) was established by spectroscopy, periodate degradation (Fritz, Morel & Wacker, 1968) and oxidative estimation of a terminal glycol group with periodate and lead tetraacetate (García-González, Fernández-Bolaños & Pradera-Adrian, 1973).

The principal aim of this investigation is to obtain more detailed information about the structure of these compounds. The structural interest has centred on the parameters of the glucofurano and imidazolidine heterocycles. In addition, these compounds have chemical and pharmacological applications.

Experimental

Crystals of 1-methyl-4,5-(D-glucofurano)imidazolidine-2-thione were obtained by Professor J. Fernández-Bolaños of this University. They are colourless needle-shaped prisms, elongated along **c**. Oscillation and Weissenberg photographs taken about the three crystallographic axes showed the space group to be $P2_12_12_1$.

Unit-cell dimensions were calculated by a least-squares procedure from 25 accurate spot positions measured on an automatic diffractometer. The density of the crystal was determined by flotation.

Crystal data

a	$=21{\cdot}466$ (6) Å	D_x	$=1{\cdot}41$ g cm^{-3}
b	$=8{\cdot}804$ (4)	D_m	$=1{\cdot}40$ (2) g cm^{-3}
c	$=5{\cdot}819$ (2)	μ(Mo $K\alpha$)	$=2{\cdot}66$ cm^{-1}
Z	$=4$	$F(000)$	$=496$.

The ω–2θ scan mode of the Philips PW 1100 diffractometer, monochromated with a graphite crystal, was used for recording the intensity data. Three reflexions were monitored every 47 measurements and showed good stability, as indicated by a root-mean-square deviation of less than 1% in intensity and a maximum deviation of 3%. 1154 independent reflexions were collected in the range $3° < \theta < 25°$. Of this total, 944 were directly observed and 210 were considered as unobserved according to the criterion $I < 2\sigma(I)$, were $I = C_p - C_{b_1} - C_{b_2}$ and $\sigma^2(I) = C_p + C_{b_1} + C_{b_2} + (0{\cdot}04I^2)$, I being the integrated intensity and $\sigma(I)$ its estimated standard deviation.

The structure amplitudes were obtained after the usual Lorentz and polarization reduction. No correction for absorption was applied ($\mu R = 0{\cdot}064$).

Structural analysis

The structure was solved by direct methods. The observed structure factors were converted into nor-

Table 1. *Intensity distribution statistics*

The overall temperature factor of 3·80 Å^2, obtained by linear isotropic least-squares fit to a Wilson plot, was used in the calculation of normalized structure factors.

	Theoretical		
	Centric	Acentric	Experimental
$\langle\|E\|\rangle$	0·798	0·886	0·882
$\langle E^2\rangle$	1·000	1·000	1·000
$\langle\|E^2-1\|\rangle$	0·968	0·736	0·864
$\|E\|>3$	0·3%	0·01%	0·0%
$\|E\|>2$	1·0%	1·8%	3·0%
$\|E\|>1$	32·0%	36·8%	35·0%

malized structure amplitudes, $|E|$, by using the scale factor and the overall temperature factor obtained from Wilson's statistics. The E statistics, as shown in Table 1, indicated an acentric structure consistent with the space group determined from the systematic absences.

Three reflexions were selected to establish the origin and enantiomorph: 17,2,1, $\varphi=\pm\pi/4$; 730, $\varphi=\pi/2$ and 463, $\varphi=\pi/4$. From these reflexions (17,2,1 with two phase angles) the phase angles of 13 restricted-phase reflexions including $4\times4\times2$ structure invariant reflexions were generated.

This information was used as input to *FASTAN* to compute the absolute figure of merit (ABS FOM) and the residual (RES). The set of largest ABS FOM and least RES was taken. The phase angles of the 180 reflexions with E greater than 1·4 were generated and refined by application of the weighted tangent formula (Germain, Main & Woolfson, 1971). An E map based on the phases derived for the 180 reflexions revealed all the atomic positions except one, which corresponded to the carbon atom of a CH_2OH group. The structure (excluding H atoms) was completed from a three-dimensional electron-density synthesis in which the phase angles were determined solely from known atomic positions. A structure-factor calculation with the set of coordinates obtained gave an R index of 0·24. After two cycles of Fourier syntheses and structure-factor calculation the R value dropped to 0·13 for all observed reflexions. Isotropic temperature factors, $\exp(-B\sin^2\theta/\lambda^2)$, were used in the calculations.

Table 2. *Final atomic parameters with estimated standard deviations*

(*a*) Fractional coordinates

	x/a	y/b	z/c
S	0·30912 (4)	0·34928 (3)	0·02031 (20)
O(1)	0·01803 (10)	0·30779 (27)	0·04801 (45)
O(2)	0·11525 (10)	0·12091 (28)	0·24039 (43)
O(3)	0·02951 (11)	0·01007 (27)	−0·27269 (47)
O(4)	0·02274 (11)	−0·26378 (26)	0·01221 (54)
N(1)	0·18613 (13)	0·39828 (35)	−0·02493 (56)
N(2)	0·21190 (12)	0·25288 (33)	0·27407 (51)
C(1)	0·23334 (16)	0·33242 (41)	0·09439 (63)
C(2)	0·24876 (18)	0·16295 (59)	0·43407 (73)
C(3)	0·12632 (16)	0·37464 (43)	0·10123 (63)
C(4)	0·14414 (15)	0·26622 (40)	0·29323 (73)
C(5)	0·07910 (14)	0·28726 (36)	−0·04902 (67)
C(6)	0·09988 (15)	0·11948 (37)	0·00254 (72)
C(7)	0·04900 (14)	0·00029 (42)	−0·03724 (70)
C(8)	0·074130 (15)	−0·15782 (35)	0·00539 (76)

Six cycles of least-squares refinement, the final three with anisotropic thermal factors, reduced the discrepancy index to 0·074. The full-matrix program *ORFLS* (Busing, Martin & Levy, 1962) was used. In the final structure-factor calculation the weighting scheme was $W_{hkl}=[\sigma^2(F_{hkl})]^{-1}$. The atomic parameters from the final least-squares cycle are given in Table 2 and the observed and calculated structure factors in Table 3.

Description of the structure and discussion

Intramolecular bond lengths and angles with their associated e.s.d.'s from the least-squares refinement are given in Table 4 and Fig. 1. Bond lengths and angles are uncorrected for thermal motion. The equation for the least-squares plane calculated for the imidazolidine ring is:

$$0·1330X+0·8051Y+0·5780Z+3·3147=0.$$

The deviations of the atoms from this plane are given in Table 5. The S and C(2) atoms (not included in the calculation of the plane) lie almost on the imidazolidine plane but are displaced on opposite sides. The S atom is 0·112 Å above the plane and the C(2) atom 0·011 Å below. The torsion angles S–C(1)–N(1)–N(2) and C(2)–N(2)–C(1)–C(4) are 3·5° and 1·2° respectively.

The observed value of 1·689 Å for the bond length S–C(1) is intermediate between the sum of the covalent bond radii (1·81 Å) and the double-bond value (1·59 Å), and the C(1)–N distances of mean value 1·35 Å indicate the effect of the thiourea resonance system. The same considerations apply to trimethylenethiourea (Dias & Truter, 1964), to tetramethylenethiourea (Mammi,

Table 2 (*cont.*)

(*b*) Anisotropic temperature coefficients in the expression $f=\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^3+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)]$

	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
S	0·00170 (2)	0·0148 (2)	0·0330 (2)	−0·00122 (5)	0·00097 (8)	−0·0020 (3)
O(1)	0·00144 (5)	0·0102 (3)	0·0275 (9)	0·0004 (5)	0·0008 (2)	0·0026 (5)
O(2)	0·00206 (6)	0·0094 (4)	0·0265 (9)	−0·0016 (1)	−0·0022 (2)	0·0049 (6)
O(3)	0·00297 (5)	0·0062 (3)	0·031 (1)	−0·0001 (1)	−0·0024 (2)	−0·0041 (6)
O(4)	0·00275 (6)	0·0073 (3)	0·0292 (9)	−0·0022 (1)	0·0006 (2)	−0·0008 (6)
N(1)	0·00173 (7)	0·0098 (4)	0·028 (1)	−0·0009 (1)	−0·0009 (3)	0·0002 (7)
N(2)	0·00179 (7)	0·0096 (4)	0·019 (1)	−0·0008 (1)	−0·0003 (2)	0·0011 (7)
C(1)	0·00188 (8)	0·0070 (9)	0·025 (1)	−0·0009 (2)	0·0033 (3)	−0·0024 (9)
C(2)	0·00256 (2)	0·0202 (5)	0·031 (1)	−0·0000 (2)	−0·0030 (2)	0·0076 (7)
C(3)	0·00181 (8)	0·0090 (5)	0·022 (1)	−0·0003 (2)	−0·0003 (3)	0·0028 (7)
C(4)	0·00148 (8)	0·0089 (5)	0·031 (1)	−0·0013 (2)	−0·0003 (3)	0·0004 (8)
C(5)	0·00153 (7)	0·0066 (4)	0·026 (1)	−0·0002 (2)	+0·0007 (3)	−0·0001 (7)
C(6)	0·00166 (8)	0·0056 (4)	0·027 (1)	−0·0006 (1)	−0·0008 (3)	0·0028 (8)
C(7)	0·00148 (7)	0·0077 (5)	0·029 (1)	−0·0001 (1)	+0·0001 (3)	−0·0010 (8)
C(8)	0·00192 (8)	0·0046 (4)	0·039 (1)	−0·0007 (1)	−0·0001 (3)	0·0026 (9)

Table 3. *Observed and calculated structure factors*

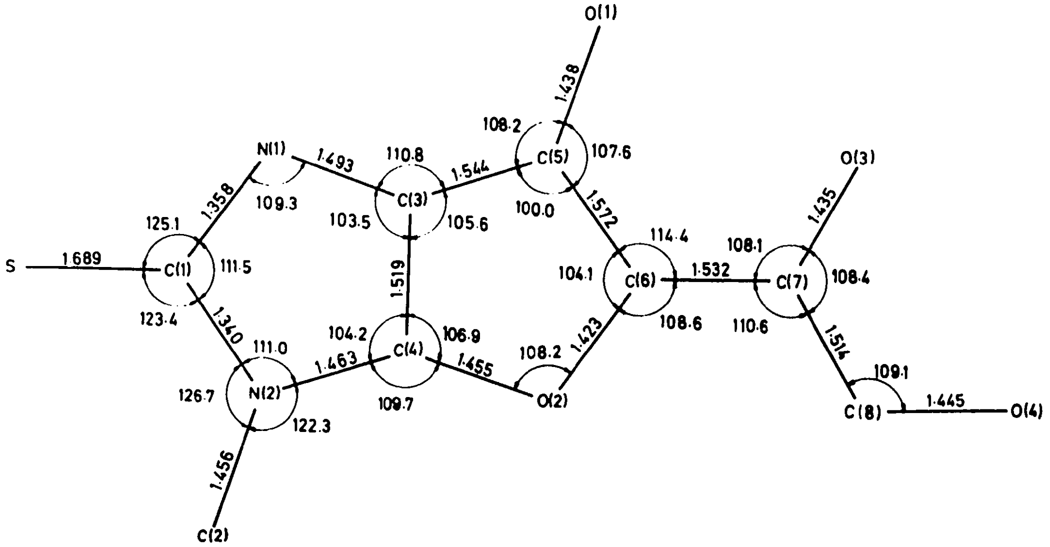

Fig. 1. Schematic representation of the molecule showing the bond distances (Å) and the bond angles (°).

Table 4. *Bond lengths and angles with their associated e.s.d.'s*

(*a*) Bond lengths (Å)

S——C(1)	1·689 (4)	C(5)–C(6)	1·572 (5)
C(1)–N(1)	1·358 (5)	C(4)–O(2)	1·455 (4)
C(1)–N(2)	1·340 (5)	O(2)–C(6)	1·423 (5)
N(1)–C(3)	1·493 (5)	C(5)–O(1)	1·438 (4)
N(2)–C(4)	1·463 (4)	C(6)–C(7)	1·532 (5)
C(3)–C(4)	1·519 (5)	C(7)–C(8)	1·514 (5)
N(2)–C(2)	1·456 (5)	C(7)–O(3)	1·435 (5)
C(3)–C(5)	1·544 (5)	C(8)–O(4)	1·445 (4)

(*b*) Angles (°)

S——C(1)–N(2)	125·1 (3)	C(4)–O(2)–C(6)	108·2 (3)
S——C(1)–N(1)	123·4 (3)	O(2)–C(6)–C(5)	104·1 (3)
C(1)–N(2)–C(2)	126·7 (3)	C(3)–C(5)–C(6)	100·0 (3)
C(1)–N(2)–C(4)	111·0 (3)	C(4)–C(3)–C(5)	105·6 (3)
C(2)–N(2)–C(4)	122·3 (3)	C(3)–C(5)–O(1)	108·3 (3)
N(1)–C(1)–N(2)	111·5 (3)	O(1)–C(5)–C(6)	107·6 (3)
C(1)–N(1)–C(3)	109·3 (3)	C(5)–C(6)–C(7)	114·4 (3)
N(1)–C(3)–C(4)	103·5 (3)	O(2)–C(6)–C(7)	108·6 (3)
C(3)–C(4)–N(2)	104·2 (3)	C(6)–C(7)–C(8)	110·6 (3)
N(1)–C(3)–C(5)	110·8 (3)	C(6)–C(7)–O(3)	108·1 (3)
N(2)–C(4)–O(2)	109·7 (3)	O(3)–C(7)–C(8)	108·4 (3)
C(3)–C(4)–O(2)	106·9 (3)	C(7)–C(8)–O(4)	109·1 (3)

Table 5. *Deviations* (Å) *of the atoms from the imidazolidine* (I) *and the sugar* (II) *planes*

	I	II
S	0·112*	
O(1)		1·971*
O(2)		0·106
N(1)	−0·044	
N(2)	0·004	
C(1)	0·026	
C(2)	0·011*	
C(3)	0·042	0·060
C(4)	−0·029	−0·101
C(5)		0·539*
C(6)		−0·065

* Not included in the calculation of the planes.

Del Pra & Di Bello, 1967) and to 1-thiocarbamoylimidazoline-2-thione (Valle, Cojazzi, Busetti & Mammi, 1970). The N(2)–C(2) bond of 1·456 Å is slightly but not significantly shorter than the accepted N–C single-bond distance of 1·47 Å, although it is comparable with the N–C (1·458 Å) distance given by Singh & Vijayan (1973). The rather small value (1·519 Å) of the C(3)–C(4) bond length is also worth noting. It is comparable with those found in trimethylenethiourea (1·518 Å), tetramethylenethiourea (1·51 Å) and 1-thiocarbamoylimidazolidine-2-thione (1·507 Å).

The difference between the C(2)–N(2)–C(1) and the C(2)–N(2)–C(4) angles, 126·7° (3) and 122·3° (3) respectively, is assumed to be due to distortion in the bicyclic configuration.

The sugar ring is puckered so that C(5) is lying out of the mean plane through the other sugar ring atoms on the same side of the plane as O(3). The displacement of C(5) is 0·54 Å. The equation of the least-squares plane through C(3), C(4), O(2) and C(6) is $-0{\cdot}9185X+0{\cdot}2007Y+0{\cdot}3408Z-1{\cdot}6869=0$, the displacement of O(1) from the sugar ring plane is 1·971 Å (Table 5).

The bond lengths and angles (Table 4) of the sugar ring are in good agreement with accepted values. As in other structures, the O(2)–C(4) bond is slightly longer than the O(2)–C(6) bond. The three types of angle within the furanose ring, C–C–C, C–C–O, C–O–C, have average values of 102·8°, 105·5° and 108·2° respectively, and agree well with those found in the deoxyuridine (Rahman & Wilson, 1972).

It is worth noting some short intramolecular distances. The N(1)–C(5) bond of 2·36 Å, and the N(1)–C(6) bond of 2·50 Å indicate a strong interaction between the two heterocycles. The dihedral angle between the imidazoline and the sugar rings is 103·7°. Other contacts, listed in Table 6, may indicate the presence of intramolecular packing.

Table 6. *Significant interatomic contacts*

Intermolecular		Intramolecular	
S——N(1) (i)	3·46 Å	O(1)–C(7)	2·83 Å
O(1)–O(3) (iii)	2·60	O(2)–C(2)	3·10
O(1)–O(4) (iii)	2·77	O(2)–C(8)	2·94
O(3)–O(4) (iii)	2·68	O(4)–C(7)	2·41
		N(1)–C(5)	2·36
		N(1)–C(6)	2·50

Key to symmetry operations

(i)	$\frac{1}{2}-x$	$1-y$	$\frac{1}{2}+z$
(ii)	$-1-x$	$\frac{1}{2}+y$	$-\frac{1}{2}-z$
(iii)	$-1-x$	$\frac{1}{2}+y$	$\frac{1}{2}-z$

Molecular packing

Two projections of the structure along the *b* and *c*

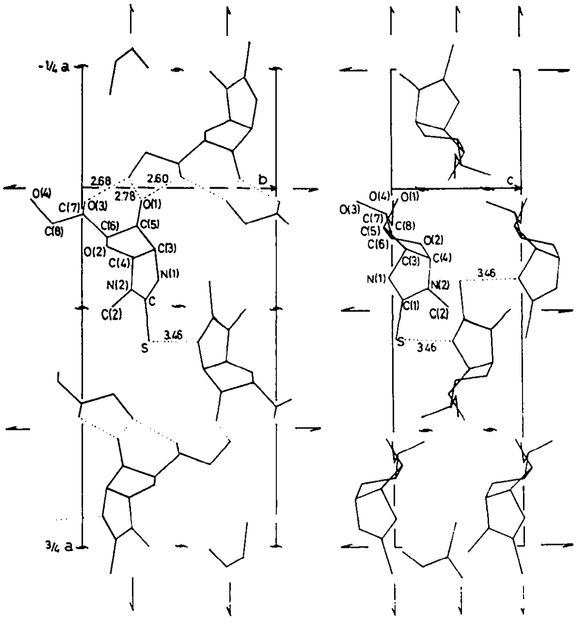

Fig. 2. Two projections of the structure along the *b* and *c* axes.

axes are shown in Fig. 2. The more significant interatomic contacts are given in Table 6.

The molecules related by the 2_1 screw axis are linked by N–H···S hydrogen bonds. Each sulphur atom is linked by an N–H···S hydrogen bond to N(1) of the nearest neighbour molecule related by the twofold screw axis to form a helicoidal packing arrangement. The N–H···S distance of 3·46 Å observed in the hydrogen bridges is longer than the sum of the van der Waals radii reported by Pauling (1948) (N, 1·50; S, 1·85 Å). Such examples of A–H···B bonding with $d_{AB} > r_A + r_B$ are often thought to provide little evidence for the presence of hydrogen bonding (Wheatley, 1953; Kunchur & Truter, 1958; Pimentel & McClellan, 1960). It must be pointed out, however, that there is some uncertainty in the values of the van der Waals radii as is reported by Valle *et al.* (1970). Furthermore, it should be noted that almost all the N–H···S distances observed in crystal structures with geometries compatible with hydrogen bonding range from 3·3 to 3·5 Å (Wheatley, 1953; Kunchur & Truter, 1958; Truter, 1960; Dias & Truter, 1964; Braibanti, Manotti Lanfredi, Tiripicchio & Logiudice, 1969; Domiano, Fava Gasparri, Nardelli & Sgarabotto, 1969).

Apart from these weak hydrogen bonds, the molecules are involved in O···O contacts (Fig. 2) in the range usually found for O–H···O hydrogen bonds (James & Matsushima, 1973; Sherfinski & Marsh, 1973).

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