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The Crystal and Molecular Structure of 1-*p*-Chlorophenyl-4-(α -D-erythrofuranosyl)-4-imidazoline-2-thione

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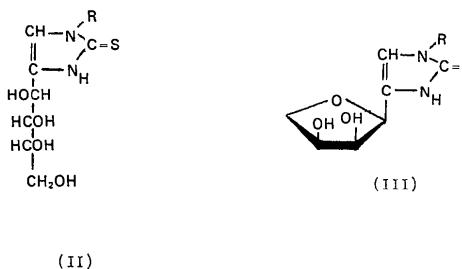
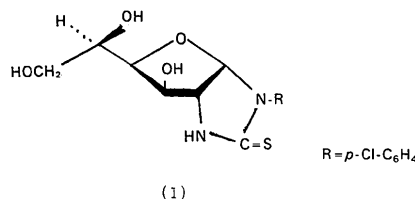
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The title compound, $\text{C}_{13}\text{H}_{13}\text{N}_2\text{O}_3\text{S}$, the definitive formula of which has been established by X-ray structural analysis, is orthorhombic, space group $P2_12_12_1$ with $a = 7.806$ (5), $b = 29.417$ (13) and $c = 5.921$ (5) Å, $Z = 4$. The structure has been solved by direct methods with *MULTAN* and refined anisotropically ($R = 0.073$) by a method of block-diagonal least-squares with 861 independent reflexions measured on a diffractometer (Cu $K\alpha$ radiation). The dihedral angle between the phenyl and imidazoline rings is 50° . The furanose ring is puckered so that C(10) deviates from the mean plane through the other sugar-ring atoms and the dihedral angle between the imidazoline and the furanose rings is 95° . The packing of the structure is effected by hydrogen bonds.

Introduction

The crystal structure of the title compound has been determined as part of a research programme on imidazole C-nucleosides and glucimidazole derivatives. Previous research has involved the X-ray structural determination of 4-(β -D-erythrofuranosyl)imidazoline-2-thione (Pérez-Garrido, López-Castro & Márquez, 1973).

Recently, in the Departamento de Química Orgánica of this University, a series of 1-aryl(alkyl)-4-(D-erythrofuranosyl)imidazoline-2-thione compounds have been prepared. In the preparation of the title compound, 1-chlorophenyl-4,5-(D-glucofurano)imidazolidine-2-thione (I) was refluxed in trifluoroacetic acid to give 1-chlorophenyl-4-D-arabino-tetrahydroxybutyl-imidazoline-2-thione (II). However, the chemical analysis of the product indicated the composition of the crystal to be $\text{C}_{13}\text{H}_{13}\text{N}_2\text{O}_3\text{S}$, which is consistent with 1-chlorophenyl-4-(D-erythrofuranosyl)imidazoline-2-thione (III) (García-González, Fernández-Bolaños & Fuentes-Mota, 1972; Fernández-Bolaños, Fuentes & Pradera de Fuentes, 1974). The dehydration of (II) in this process and the epimerization of the hydroxyl groups 1 and 4 of the polyolic chain are difficult to establish chemically and an X-ray analysis has consequently been undertaken to determine definitively the formula of the compound.



Experimental

Crystals of 1-*p*-chlorophenyl-4-(α -D-erythrofuranosyl)-4-imidazoline-2-thione were supplied by Professor J. Fernández-Bolaños of this University (Departamento de Química Orgánica). They are colourless needle-shaped prisms, elongated along *c*. Rotation and Weissenberg photographs were used to determine the space group and approximate unit-cell dimensions; more accurate values were calculated by a least-squares treatment of

(θ, χ, φ) angles of 15 reflexions measured on an automated diffractometer.

Crystal data

$a = 7.806(5) \text{ \AA}$	$V = 1358.86 \text{ \AA}^3$
$b = 29.417(13)$	$Z = 4$
$c = 5.921(5)$	$F(000) = 960$
$D_m = 1.53(2) \text{ g cm}^{-3}$	$\mu(\text{Cu } K\alpha) = 39.46 \text{ cm}^{-1}$
$D_x = 1.53 \text{ g cm}^{-3}$	

A crystal $0.05 \times 0.03 \times 0.021$ mm was chosen to collect intensities up to $\theta \leq 50^\circ$ on an automated on-line Siemens AED single-crystal diffractometer using Ni-filtered Cu $K\alpha$ radiation and the ω - 2θ scanning method. 861 independent reflexions were recorded, 293 of which, having $I < 2\sigma(I)$, were considered as unobserved. The intensity of a standard reflexion was measured periodically and subsequently used for scaling but no significant change was observed in its intensity during the data collection. The structure amplitudes were corrected for Lorentz and polarization effects, but no absorption corrections were applied.

Solution and refinement of the structure

Approximate absolute scale and temperature factors were obtained by Wilson's (1942) method. For the

Table 1. Reflexions used in the starting set, with phases in radians

h	k	l	φ
0	3	5	$\pi/2$
0	3	2	$\pi/2$
1	10	2	$\pi/4$
0	26	0	0
0	2	2	π
0	13	4	$\pi/2$
4	11	0	0 π
1	19	1	$\pm \pi/4, \pm 3\pi/4$

Table 3. Thermal parameters ($\times 10^2 \text{ \AA}^2$) with estimated standard deviations in parentheses

Anisotropic thermal parameters are in the form: $\exp[-\frac{1}{4}(B_{11}h^2a^{*2} + B_{22}k^2b^{*2} + B_{33}l^2c^{*2} + 2B_{12}hka^*b^* + 2B_{13}hla^*c^* + 2B_{23}klb^*c^*)]$.

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Cl	650 (26)	246 (16)	332 (20)	-90 (19)	-21 (27)	77 (18)
S	225 (18)	272 (17)	418 (22)	-3 (17)	-9 (25)	67 (20)
O(1)	427 (57)	191 (40)	220 (49)	-41 (43)	8 (50)	-74 (37)
O(2)	280 (53)	380 (50)	334 (55)	-79 (48)	-148 (51)	4 (48)
O(3)	493 (57)	200 (40)	340 (54)	59 (46)	-25 (62)	47 (42)
N(1)	221 (58)	109 (46)	335 (65)	-19 (44)	-86 (61)	28 (53)
N(2)	248 (59)	75 (46)	424 (71)	-40 (48)	74 (63)	-8 (49)
C(1)	362 (84)	308 (69)	183 (71)	-50 (66)	-83 (86)	25 (63)
C(2)	364 (91)	205 (64)	185 (74)	-50 (66)	-56 (73)	9 (60)
C(3)	333 (79)	201 (61)	300 (84)	-31 (65)	-102 (86)	75 (60)
C(4)	478 (83)	202 (62)	163 (69)	84 (66)	-73 (84)	113 (62)
C(5)	388 (86)	156 (58)	286 (79)	16 (65)	-17 (78)	-109 (58)
C(6)	410 (79)	200 (59)	145 (66)	-18 (67)	0 (80)	-81 (55)
C(7)	353 (79)	208 (60)	216 (74)	31 (66)	-35 (79)	-142 (60)
C(8)	426 (86)	310 (69)	87 (72)	-215 (77)	-61 (77)	-43 (56)
C(9)	315 (82)	252 (73)	280 (80)	-142 (67)	118 (83)	-62 (63)
C(10)	395 (78)	285 (68)	227 (73)	37 (64)	25 (89)	-119 (68)
C(11)	194 (69)	320 (68)	231 (76)	105 (63)	30 (69)	60 (62)
C(12)	395 (91)	221 (62)	205 (72)	-61 (68)	139 (81)	-8 (60)
C(13)	425 (90)	324 (73)	349 (91)	-235 (72)	144 (80)	-84 (68)

Table 2. Final atomic fractional coordinates ($\times 10^4$) with estimated standard deviations in parentheses

	x/a	y/b	z/c
Cl	4631 (6)	3007 (1)	-813 (8)
S	6838 (5)	1134 (1)	5821 (8)
O(1)	365 (14)	334 (3)	8303 (16)
O(2)	2665 (13)	577 (3)	12075 (18)
O(3)	269 (14)	47 (3)	13830 (18)
N(1)	3546 (14)	1484 (3)	5600 (23)
N(2)	3774 (15)	874 (3)	7665 (23)
C(1)	4324 (20)	2555 (5)	1098 (26)
C(2)	3543 (21)	2652 (4)	3141 (26)
C(3)	3293 (20)	2288 (4)	4725 (27)
C(4)	3928 (21)	1850 (4)	4016 (27)
C(5)	4694 (21)	1760 (5)	1873 (26)
C(6)	4990 (21)	2123 (4)	450 (24)
C(7)	4694 (20)	1171 (4)	6271 (25)
C(8)	1890 (21)	1405 (5)	6333 (24)
C(9)	2041 (20)	1024 (5)	7752 (26)
C(10)	691 (20)	805 (5)	9083 (27)
C(11)	955 (20)	738 (5)	11646 (25)
C(12)	-406 (21)	373 (5)	12217 (25)
C(13)	-800 (22)	141 (5)	9871 (28)

solution of the phase problem normalized structure factors $|E_{hkl}|$ were calculated. The values of the statistical averages $\langle |E| \rangle$ and $\langle |E^2 - 1| \rangle$ were 0.83 and 0.90 respectively.

The structure was solved by multiresolution tangent-formula refinement (Germain, Main & Woolfson, 1971) of 170 reflexions with $E \geq 1.30$. Some difficulty was experienced in obtaining a direct solution from the 128 original sets in which 20 different sets with the same ABS FOM were encountered.

A successful starting set was obtained. The first three reflexions in Table 1 were used to fix the origin and the enantiomorph. The 0,26,0 and 022 reflexions had a probability $P \geq 0.9$ and, therefore, were considered as known phases. From these and two appropriate symbolic phases, eight phase sets were generated. Four had an ABS FOM of 1.22. The E map based on 170

reflexions calculated for these sets corresponded to the same structure with origin translation. The *E* map gave directly the positions of the whole structure (excluding the hydrogen atoms) as well as several

spurious peaks resulting from the propagation of parallel interatomic vectors.

Seven cycles of least-squares block-diagonal refinement with isotropic thermal parameters improved the conventional *R* index from 24 to 9.7%. This value dropped to 0.073 after four cycles with anisotropic thermal parameters. The shifts in the last cycle of refinement were less than 0.3σ for all parameters. The quantity minimized was $\sum w|AF|^2$ and unit weights were used.

Table 4. Observed and calculated structure factors

The columns are in the order *h, k, l, F_o* and *F_c*.

<i>h</i>	<i>k</i>	<i>l</i>	<i>F_o</i>	<i>F_c</i>
0	0	0	100	100
0	0	1	100	100
0	0	2	100	100
0	0	3	100	100
0	0	4	100	100
0	0	5	100	100
0	0	6	100	100
0	0	7	100	100
0	0	8	100	100
0	0	9	100	100
0	0	10	100	100
0	0	11	100	100
0	0	12	100	100
0	0	13	100	100
0	0	14	100	100
0	0	15	100	100
0	0	16	100	100
0	0	17	100	100
0	0	18	100	100
0	0	19	100	100
0	0	20	100	100
0	0	21	100	100
0	0	22	100	100
0	0	23	100	100
0	0	24	100	100
0	0	25	100	100
0	0	26	100	100
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0	0	84	100	100
0	0	85	100	100
0	0	86	100	100
0	0	87	100	100
0	0	88	100	100
0	0	89	100	100
0	0	90	100	100
0	0	91	100	100
0	0	92	100	100
0	0	93	100	100
0	0	94	100	100
0	0	95	100	100
0	0	96	100	100
0	0	97	100	100
0	0	98	100	100
0	0	99	100	100
0	0	100	100	100

Atomic scattering factors of Cromer & Mann (1968) were used in the calculations. Positional and thermal parameters are quoted in Tables 2 and 3. The observed and calculated structure factors are given in Table 4.

Results and discussion

This structure analysis was undertaken primarily to determine the ring conformation of the molecule in the solid state to assist in understanding the reaction mechanism involved in formation of the compound and to ascertain the compound's definitive formula.

(i) Planarity in the molecule

The atoms of best fit for the rings in the molecule and their atomic displacements are listed in Table 5.

Table 5. Least-squares planes through various rings and deviations of the atoms from the planes

(a) Equations of planes

Each plane is represented by $AX+BY+CZ=D$, where *X, Y, Z* are the coordinates in Å referred to the crystal axes.

	<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>
I Phenyl ring	0.8883	0.1976	0.4145	4.7702
II Imidazoline ring	0.2010	0.5760	0.7923	5.6740
III Glucosufurane ring	0.7048	-0.6744	0.2199	0.5976

(b) Distances in Å of the atoms from the plane

Atoms excluded from the calculation of the least-squares planes are denoted by an asterisk.

Plane I	Plane II	Plane III
Atom Deviation	Atom Deviation	Atom Deviation
C(1) -0.017	N(1) 0.024	C(11) -0.020
C(2) -0.001	N(2) -0.005	C(12) 0.030
C(3) 0.002	C(7) -0.025	C(13) -0.032
C(4) 0.014	C(8) -0.012	O(1) 0.022
C(5) -0.033	C(9) 0.018	C(9)* -0.497
C(6) 0.034	S* 0.051	C(10)* -0.632
Cl* -0.011	C(10)* 0.060	O(2)* 1.296
N(1)* -0.074		O(3)* 1.258

Both the phenyl and the imidazoline rings are planar with mean atomic displacements of 0.02 and 0.01 Å respectively. The dihedral angle between the phenyl and imidazoline rings ($\approx 50^\circ$), according to the theory of Kitaigorodskii (1965), indicates that the most important term in the conformational energy is the potential energy. The molecular stability of the organic crystals is reached when the free vibrational energy, as a sum

of intra- and intermolecular energies, corresponds to a minimum. In substances such as these the energies involved are the potential energy, the resonance energy and the lattice energy. The first term reaches a minimum when the phenyl ring is perpendicular to the imidazoline ring, while the other two terms attain minima when the two rings are coplanar.

The glucofuran ring is not planar, as expected. The C(10) atom is 0.63 Å out of the least-squares plane through the other sugar ring atoms whose mean deviation from the plane is 0.03 Å. The dihedral angle between the imidazoline and sugar rings ($\approx 95^\circ$) shows also that the potential energy terms predominate largely.

The C(9), O(2) and O(3) atoms bonded to the glucofuran ring deviate to the same side of the mean plane through the ring; therefore, this corresponds to an α -configuration of the group.

(ii) Molecular dimensions

Bond lengths and angles in the molecule with estimated standard deviations are listed in Table 6. Fig. 1

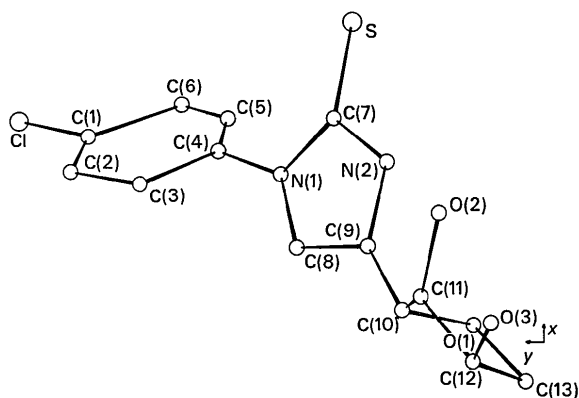


Fig. 1. Molecular conformation.

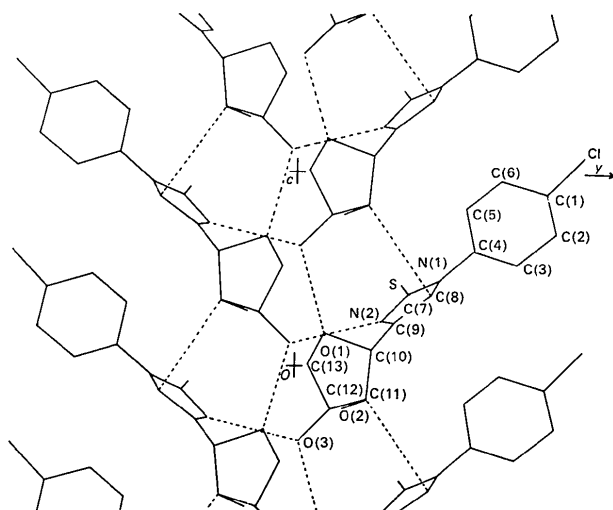


Fig. 2. Packing of the structure viewed down *c*.

shows a labelled perspective drawing of the origin molecule in the cell.

Table 6. Bond lengths (Å) and angles ($^\circ$) with estimated standard deviations

Cl—C(1)	1.762 (16)	N(2)—C(9)	1.424 (19)
C(1)—C(2)	1.384 (22)	C(9)—C(8)	1.406 (21)
C(2)—C(3)	1.437 (19)	C(8)—N(1)	1.383 (20)
C(3)—C(4)	1.443 (18)	C(9)—C(10)	1.465 (22)
C(4)—C(5)	1.427 (22)	C(10)—C(11)	1.544 (22)
C(5)—C(6)	1.378 (20)	C(11)—C(12)	1.548 (22)
C(6)—C(1)	1.426 (20)	C(12)—C(13)	1.578 (22)
C(4)—N(1)	1.459 (18)	C(13)—O(1)	1.418 (19)
N(1)—C(7)	1.345 (17)	C(10)—O(1)	1.482 (17)
C(7)—S	1.698 (16)	C(11)—O(2)	1.439 (18)
C(7)—N(2)	1.400 (18)	C(12)—O(3)	1.452 (18)
Cl—C(1)—C(2)	117.7 (20)	C(9)—C(8)—N(1)	104.1 (20)
C(1)—C(2)—C(3)	118.5 (26)	C(8)—N(1)—C(7)	114.5 (24)
C(2)—C(3)—C(4)	115.4 (21)	C(8)—N(1)—C(4)	121.1 (26)
C(3)—C(4)—C(5)	124.6 (28)	C(8)—C(9)—C(10)	127.7 (31)
C(4)—C(5)—C(6)	118.0 (26)	N(2)—C(9)—C(10)	124.5 (28)
C(5)—C(6)—C(1)	117.7 (25)	C(9)—C(10)—C(11)	119.3 (26)
C(6)—C(1)—Cl	116.8 (17)	C(10)—C(11)—C(12)	102.2 (19)
C(6)—C(1)—C(2)	125.4 (29)	C(10)—C(11)—O(2)	109.8 (20)
C(3)—C(4)—N(1)	113.7 (19)	O(2)—C(11)—C(12)	111.7 (21)
C(5)—C(4)—N(1)	121.4 (26)	C(11)—C(12)—C(13)	104.0 (20)
C(4)—N(1)—C(7)	124.0 (25)	C(11)—C(12)—O(3)	110.7 (20)
N(1)—C(7)—N(2)	105.0 (17)	O(3)—C(12)—C(13)	111.4 (21)
N(1)—C(7)—S	130.9 (22)	C(12)—C(13)—O(1)	106.2 (19)
S—C(7)—N(2)	123.9 (20)	C(13)—O(1)—C(10)	106.3 (20)
C(7)—N(2)—C(9)	108.4 (21)	O(1)—C(10)—C(11)	102.1 (17)
N(2)—C(9)—C(8)	107.8 (20)	O(1)—C(10)—C(9)	111.5 (20)

The average bond length and angle in the phenyl ring, 1.42(2) Å and $119(3)^\circ$ respectively, are within the expected ranges. The Cl atom is in the plane of the phenyl ring and the Cl—C(1) distance of 1.762(16) agrees well with the Cl—C(ring) length in phenyl monochloro derivatives. The inter-ring distance C(4)—N(1) of 1.459(18) Å agrees with a single bond N—C distance and the N(1) atom lies in the phenyl mean plane.

The observed value 1.698(16) Å for the bond length S—C(7) is intermediate between the S—C single-bond distance of 1.81 Å and double-bond value of 1.59 Å. This partial double-bond character is in agreement with the canonical resonance forms of the thiourea system and is a normal feature of these compounds (Valle, Cojazzi, Busetti & Mammi, 1970; Pérez-Garrido, López-Castro & Márquez, 1973; Jiménez-Garay, López-Castro & Márquez, 1974). The bond distances and angles in the imidazoline ring are in agreement with the values reported in the literature. The rather longer value of 1.400(18) Å for the C(7)—N(2) bond is worth noting. Therefore, there is an intramolecular contact N(2)—O(2) of 2.886(17) Å.

In the sugar ring the values of the bond lengths are normal. As in other structures, O(1)—C(10) is slightly longer than O(1)—C(13). The values of the C—C—C, C—C—O and C—O—C angles in the furanose ring agree with those found in analogous compounds.

The intramolecular contacts listed in Table 7 may indicate the presence of some intramolecular packing.

Table 7. *Interatomic contacts less than the sum of the van der Waals radii*

(a) Intramolecular		
O(1)···C(9)		2·437 (18) Å
O(2)···O(3)		2·647 (14)
O(2)···N(2)		2·886 (17)
O(2)···C(9)		2·919 (19)
C(3)···C(8)		2·975 (20)
(b) Intermolecular		
O(1)···O(3) (i)		2·781 (14) Å
N(2)···O(3) (ii)		2·894 (13)
C(8)···C(11) (i)		3·476 (21)
Symmetry code:		
(i)	$x, y, -1+z$	
(ii)	$\frac{1}{2}-x, \bar{y}, -\frac{1}{2}+z$	

(iii) *Molecular packing*

Significant non-bonded interactions, less than the sum of the van der Waals radii (Pauling, 1960), are given in Table 7. Fig. 2 illustrates the packing of the molecules down *c*.

The O(1)···O(3) distance of 2·781(14) Å is in the range of O—H···O distances found in the literature and it seems reasonable to classify this contact as a hydrogen bond. The two contacts C(8)···C(1) of 3·476(21) Å and N(2)···O(3) of 2·894(13) Å show significant shortening with respect to the sum of the corresponding van der Waals radii and must be classified as definite hydrogen bonds. There are no other non-bonded distances less than the sum of the van der Waals radii in the structure.

The molecules are stacked in rows, parallel to *c*, related by a N···O hydrogen bond. Within each row,

adjacent molecules are linked by O···O and C···O hydrogen bonds.

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