

Crystal Structure of 2-Chloro-1-(β -D-ribofuranosyl)benzimidazole. Hydrogen Bonding to the Furanose Ring Oxygen

BY S. SPRANG AND M. SUNDARALINGAM*

Department of Biochemistry, College of Agricultural and Life Sciences, University of Wisconsin, Madison,
Wisconsin 53706, U.S.A.

(Received 1 February 1973; accepted 23 April 1973)

The structure of 2-chloro-1-(β -D-ribofuranosyl)benzimidazole has been determined from 1058 reflections measured on a diffractometer. The compound crystallizes in the space group $P2_1$ with two molecules per unit cell of dimensions: $a=10.973$ (2), $b=9.257$ (2), $c=6.763$ (2) Å, and $\beta=115.33$ (2)°, $d_{\text{cal}}=1.521$ g cm⁻³, $d_{\text{obs}}=1.523$ g cm⁻³, $Z=2$. The complete structure was determined by tangent refinement of starting phases based on the coordinates of the benzimidazole fragment derived from a sharpened E^2-1 Patterson function. The final R value after least-squares refinement is 0.054. The molecule is in the *syn* conformation with respect to the glycosyl torsional angle; $\chi_{\text{CN}}=242.7^\circ$. The ribose assumes a $C(2)$ -*endo*- $C(1')$ -*exo* pucker (2T_1) and the conformation about $C(4')$ - $C(5')$ is *gauche-gauche*. Each molecule is involved in three hydrogen bonds to neighboring molecules, one of which is relatively uncommon in that the ribose ring oxygen acts as an acceptor. The chlorine atom is not involved in hydrogen bonding. The molecular packing consists of well defined hydrophilic and hydrophobic regions provided by the ribose and benzimidazole moieties respectively. Base stacking is very limited.

Introduction

The crystal structure of 2-chloro-1-(β -D-ribofuranosyl)benzimidazole (Fig. 1) has been determined as part of a continuing investigation of the conformational aspects of nucleoside analogs in this laboratory. This compound represents a new class of nucleoside analogs in which a benzimidazole ring replaces the base. Its natural counterpart is the α -D-5,6-dimethyl benzimidazole ribonucleoside moiety found in vitamin B₁₂. Previous investigation of C(8) bromo-substituted purine nucleoside analogs point to the tendency of these compounds to assume the *syn* conformation in the crystalline state (Tavale & Sobell, 1970). It is expected that a chloro substitution would produce the same effect. There is also much evidence to indicate that halogen substitution of the base increases the tendency towards vertical stacking both in solution (Ts'o, 1968) and in the solid state (Bugg, Thomas, Sundaralingam & Rao, 1971). Therefore, the effect of chloro substitution on the molecular packing of this benzimidazole ribonucleoside is of interest.

Experimental

A crystal measuring 0.08 × 0.15 × 0.46 mm was chosen from a sample supplied by Dr L. B. Townsend. Preliminary oscillation and Weissenberg photographs revealed systematic absences on $0k0$, where $k=2n+1$. The presence of asymmetric centers in the molecule constrains the space group to $P2_1$. The cell constants were determined from medium- and low-angle reflections on a Picker four-circle diffractometer with Ni-

filtered Cu $K\alpha$ radiation; they are: $a=10.973$ (2), $b=9.257$ (2), $c=6.763$ (2) Å, and $\beta=115.33$ (2)°. The density calculated for two molecules of C₁₂H₁₃N₂O₄Cl per unit cell is 1.521 g cm⁻³ which is consistent with a value of 1.523 g cm⁻³ obtained in a cyclohexane-chloroform mixture.

Three-dimensional intensity data were collected using the θ - 2θ scan mode at a rate of 2°/min with a scan range of 3.0° to a 2θ limit of 129°. Background counts of 10 s were taken on either side of each reflection maximum. Three standard reflections were checked at an interval of every 50 reflections and they showed fluctuations of $\pm 7.0\%$. After prolonged exposure to the X-ray beam, the crystal, originally achromic, acquired an amber coloration. 1058 unique reflections were collected, of which 1048 were considered observed using the criterion $I \geq 1.5\sigma$. The data were subjected to the usual Lorentz and polarization corrections, but no absorption corrections were made ($\mu=23.5$ cm⁻¹ for Cu $K\alpha$ radiation) because the main purpose of this study was to obtain information on the molecular conformation.

Structure determination

The positions of the chlorine and all atoms of the benzimidazole ring were derived from a sharpened three-dimensional E^2-1 Patterson synthesis. These atomic positions were then used as an initial phasing model to refine the phases of 185 normalized structure factors with $E > 1.3$ using the tangent formula (Karle & Hauptmann, 1956). A three-dimensional E map subsequently computed revealed all atomic positions in the molecule. A structure-factor calculation yielded an agreement index, $R = \sum ||F_o| - |F_c|| / \sum |F_o|$, of 0.24.

* To whom to address correspondence.

Structure refinement

The atomic parameters of all 19 non-hydrogen atoms were subjected to two cycles of isotropic full-matrix least-squares refinement using the program of Busing, Martin & Levy (1962). A Hughes (1941) type weighting scheme of the form

$$1/\sqrt{w} = 1 \text{ for } F_o \leq 40.48$$

$$1/\sqrt{w} = 40.48/F_o \text{ for } F_o > 40.48$$

was applied in the refinements. The nonhydrogen atoms were then subjected to two cycles of refinement

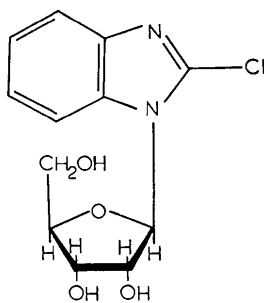


Fig. 1. Structural formula of 2-chloro-1-(β-D-ribofuranosyl)-benzimidazole.

with anisotropic temperature factors which reduced *R* to 0.059. A difference Fourier synthesis computed at this point revealed the positions of all 13 hydrogen atoms. Isotropic refinement of the hydrogen atoms followed by anisotropic refinement of the nonhydrogen atoms reduced *R* to 0.054 for the 1048 observed reflections. The final shift σ was less than 0.16 for all non-hydrogen atom parameters. A number of hydrogen atoms refined to positions that displayed abnormal C-H bond lengths. These hydrogen atoms were redetermined from a difference Fourier map and assigned the isotropic thermal parameters of the heavy atom to which they are attached. The peaks attributed to hydrogen atoms varied from less than one to two times the strongest background peak. The scattering factors for Cl, O, N, C used throughout the analysis were those of Cromer & Waber (1965), while that of H was from Stewart, Davidson & Simpson (1965).

Results

The observed and calculated structure factor amplitudes are given in Table 1. The final positional and thermal parameters for nonhydrogen atoms and hydrogen atoms are given in Table 2. An ORTEP drawing (Johnson, 1965) showing the thermal ellipsoids of

Table 1. Observed and calculated structure amplitudes

Columns 1, 2 and 3 represent *h*, $10|F_o|$ and $10|F_c|$ respectively. Reflections less than 1.5σ are marked with *U*, which were not included in the refinement.

h	$10 F_o $	$10 F_c $	h	$10 F_o $	$10 F_c $	h	$10 F_o $	$10 F_c $	h	$10 F_o $	$10 F_c $
0 166 165	-3.94 96	-5.129 125	10 166 165	-3.94 96	-5.129 125	20 166 165	-3.94 96	-5.129 125	30 166 165	-3.94 96	-5.129 125
1 107 83	1.466 88	-1.377 959	11 107 83	1.466 88	-1.377 959	21 107 83	1.466 88	-1.377 959	31 107 83	1.466 88	-1.377 959
2 186 230	1.251 184	0.203 251	12 186 230	1.251 184	0.203 251	22 186 230	1.251 184	0.203 251	32 186 230	1.251 184	0.203 251
3 252 150	0.818 150	1.190 180	13 252 150	0.818 150	1.190 180	23 252 150	0.818 150	1.190 180	33 252 150	0.818 150	1.190 180
4 56 64	0.533 152	1.167 210	14 56 64	0.533 152	1.167 210	24 56 64	0.533 152	1.167 210	34 56 64	0.533 152	1.167 210
5 225 94	0.298 159	0.278 289	15 225 94	0.298 159	0.278 289	25 225 94	0.298 159	0.278 289	35 225 94	0.298 159	0.278 289
6 235 131	1.71 72	0.538 129	16 235 131	1.71 72	0.538 129	26 235 131	1.71 72	0.538 129	36 235 131	1.71 72	0.538 129
7 36 55	0.466 158	0.166 251	17 36 55	0.466 158	0.166 251	27 36 55	0.466 158	0.166 251	37 36 55	0.466 158	0.166 251
8 220 122	0.56 57	0.166 251	18 220 122	0.56 57	0.166 251	28 220 122	0.56 57	0.166 251	38 220 122	0.56 57	0.166 251
9 251 280	0.87 78	0.166 251	19 251 280	0.87 78	0.166 251	29 251 280	0.87 78	0.166 251	39 251 280	0.87 78	0.166 251
10 48 53	0.114 112	0.166 251	20 48 53	0.114 112	0.166 251	30 48 53	0.114 112	0.166 251	40 48 53	0.114 112	0.166 251
11 60 54	0.166 251	0.166 251	21 60 54	0.166 251	0.166 251	31 60 54	0.166 251	0.166 251	41 60 54	0.166 251	0.166 251
12 108 101	-11.86 88	-11.86 88	22 108 101	-11.86 88	-11.86 88	32 108 101	-11.86 88	-11.86 88	42 108 101	-11.86 88	-11.86 88
13 290 424	5.93 89	-2.212 124	23 290 424	5.93 89	-2.212 124	33 290 424	5.93 89	-2.212 124	43 290 424	5.93 89	-2.212 124
14 126 104	0.201 121	-7.80 111	24 126 104	0.201 121	-7.80 111	34 126 104	0.201 121	-7.80 111	44 126 104	0.201 121	-7.80 111
15 242 174	0.166 251	-0.95 122	25 242 174	0.166 251	-0.95 122	35 242 174	0.166 251	-0.95 122	45 242 174	0.166 251	-0.95 122
16 216 216	0.82 69	-5.192 124	26 216 216	0.82 69	-5.192 124	36 216 216	0.82 69	-5.192 124	46 216 216	0.82 69	-5.192 124
17 65 62	0.166 251	-0.166 251	27 65 62	0.166 251	-0.166 251	37 65 62	0.166 251	-0.166 251	47 65 62	0.166 251	-0.166 251
18 64 73	0.166 251	-0.166 251	28 64 73	0.166 251	-0.166 251	38 64 73	0.166 251	-0.166 251	48 64 73	0.166 251	-0.166 251
19 95 95	0.166 251	-0.166 251	29 95 95	0.166 251	-0.166 251	39 95 95	0.166 251	-0.166 251	49 95 95	0.166 251	-0.166 251
20 156 100	2.156 146	-1.311 326	30 156 100	2.156 146	-1.311 326	40 156 100	2.156 146	-1.311 326	50 156 100	2.156 146	-1.311 326
21 116 100	0.166 251	-0.166 251	31 116 100	0.166 251	-0.166 251	41 116 100	0.166 251	-0.166 251	51 116 100	0.166 251	-0.166 251
22 116 84	0.166 251	-0.166 251	32 116 84	0.166 251	-0.166 251	42 116 84	0.166 251	-0.166 251	52 116 84	0.166 251	-0.166 251
23 125 119	2.191 711	2.116 107	33 125 119	2.191 711	2.116 107	43 125 119	2.191 711	2.116 107	53 125 119	2.191 711	2.116 107
24 125 119	2.191 711	2.116 107	34 125 119	2.191 711	2.116 107	44 125 119	2.191 711	2.116 107	54 125 119	2.191 711	2.116 107
25 125 119	2.191 711	2.116 107	35 125 119	2.191 711	2.116 107	45 125 119	2.191 711	2.116 107	55 125 119	2.191 711	2.116 107
26 125 119	2.191 711	2.116 107	36 125 119	2.191 711	2.116 107	46 125 119	2.191 711	2.116 107	56 125 119	2.191 711	2.116 107
27 125 119	2.191 711	2.116 107	37 125 119	2.191 711	2.116 107	47 125 119	2.191 711	2.116 107	57 125 119	2.191 711	2.116 107
28 125 119	2.191 711	2.116 107	38 125 119	2.191 711	2.116 107	48 125 119	2.191 711	2.116 107	58 125 119	2.191 711	2.116 107
29 125 119	2.191 711	2.116 107	39 125 119	2.191 711	2.116 107	49 125 119	2.191 711	2.116 107	59 125 119	2.191 711	2.116 107
30 125 119	2.191 711	2.116 107	40 125 119	2.191 711	2.116 107	50 125 119	2.191 711	2.116 107	60 125 119	2.191 711	2.116 107
31 125 119	2.191 711	2.116 107	41 125 119	2.191 711	2.116 107	51 125 119	2.191 711	2.116 107	61 125 119	2.191 711	2.116 107
32 125 119	2.191 711	2.116 107	42 125 119	2.191 711	2.116 107	52 125 119	2.191 711	2.116 107	62 125 119	2.191 711	2.116 107
33 125 119	2.191 711	2.116 107	43 125 119	2.191 711	2.116 107	53 125 119	2.191 711	2.116 107	63 125 119	2.191 711	2.116 107
34 125 119	2.191 711	2.116 107	44 125 119	2.191 711	2.116 107	54 125 119	2.191 711	2.116 107	64 125 119	2.191 711	2.116 107
35 125 119	2.191 711	2.116 107	45 125 119	2.191 711	2.116 107	55 125 119	2.191 711	2.116 107	65 125 119	2.191 711	2.116 107
36 125 119	2.191 711	2.116 107	46 125 119	2.191 711	2.116 107	56 125 119	2.191 711	2.116 107	66 125 119	2.191 711	2.116 107
37 125 119	2.191 711	2.116 107	47 125 119	2.191 711	2.116 107	57 125 119	2.191 711	2.116 107	67 125 119	2.191 711	2.116 107
38 125 119	2.191 711	2.116 107	48 125 119	2.191 711	2.116 107	58 125 119	2.191 711	2.116 107	68 125 119	2.191 711	2.116 107
39 125 119	2.191 711	2.116 107	49 125 119	2.191 711	2.116 107	59 125 119	2.191 711	2.116 107	69 125 119	2.191 711	2.116 107
40 125 119	2.191 711	2.116 107	50 125 119	2.191 711	2.116 107	60 125 119	2.191 711	2.116 107	70 125 119	2.191 711	2.116 107
41 125 119	2.191 711	2.116 107	51 125 119	2.191 711	2.116 107	61 125 119	2.191 711	2.116 107	71 125 119	2.191 711	2.116 107
42 125 119	2.191 711	2.116 107	52 125 119	2.191 711	2.116 107	62 125 119	2.191 711	2.116 107	72 125 119	2.191 711	2.116 107
43 125 119	2.191 711	2.116 107	53 125 119	2.191 711	2.116 107	63 125 119	2.191 711	2.116 107	73 125 119	2.191 711	2.116 107
44 125 119	2.191 711	2.116 107	54 125 119	2.191 711	2.116 107	64 125 119	2.191 711	2.116 107	74 125 119	2.191 711	2.116 107
45 125 119	2.191 711	2.116 107	55 125 119	2.191 711	2.116 107	65 125 119	2.191 711	2.116 107	75 125 119	2.191 711	2.116 107
46 125 119	2.191 711	2.116 107	56 125 119	2.191 711	2.116 107	66 125 119	2.191 711	2.116 107	76 125 119	2.191 711	2.116 107
47 125 119	2.191 711	2.116 107	57 125 119	2.191 711	2.116 107	67 125 119	2.191 711	2.116 107	77 125 119	2.191 711	2.116 107
48 125 119	2.191 711	2.116 107	58 125 119	2.191 711	2.116 107	68 125 119	2.191 711	2.116 107	78 125 119	2.191 711	2.116 107
49 125 119	2.191 711	2.116 107	59 125 119	2.191 711	2.116 107	69 125 119	2.191 711	2.116 107	79 125 119	2.191 711	2.116 107
50 125 119	2.191 711	2.116 107	60 125 119	2.191 711	2.116 107	70 125 119	2.191 711	2.116 107	80 125 119	2.191 711	2.116 107
51 125 119	2.191 711	2.116 107	61 125 119	2.191 711	2.116 107	71 125 119	2.191 711	2.116 107	81 125 119	2.191 711	2.116 107
52 125 119	2.191 711	2.116 107	62 125 119	2.191 711	2.116 107	72 125 119	2.191 711	2.116 107	82 125 119	2.191 711	2.116 107
53 125 119	2.191 711	2.116 107	63 125 119	2.191 711	2.116 107	73 125 119	2.191 711	2.116 107	83 125 119	2.191 711	2.116 107
54 125 119	2.191 711	2.116 107	64 125 119	2.191 711	2.116 107	74 125 119	2.191 711	2.116 107	84 125 119	2.191 711	2.116 107
55 125 119	2.191 711	2.116 107	65 125 119	2.191 711	2.116 107	75 125 119	2.191 711	2.116 107	85 125 119	2.191 711	2.116 107
56 125 119	2.191 711	2.116 107	66 125 119	2.191 711	2.116 107	76 125 119	2.191 711	2.116 107	86 125 119	2.191 711	2.116 107
57 125 119	2.191 711	2.116 107	67 125 119	2.191 711	2.116 107	77 125 119	2.191 711	2.116 107	87 125 119	2.191 711	2.116 107
58 125 119	2.191 711	2.116 107	68 125 119	2.191 711	2.116 107	78 12					

Table 2. Positional and thermal parameters of all atoms

Positional parameters of nonhydrogen atoms have been multiplied by 10^4 . Positional parameters of hydrogen atoms have been multiplied by 10^3 . Anisotropic thermal parameters have been multiplied by 10^4 . Anisotropic temperature factor is of the form $\exp[-(\beta_{11}h^2 + \dots + 2\beta_{12}hk + \dots)]$. Standard deviations in parentheses refer to the least significant digits. The standard deviations of the hydrogen positional parameters are 0.3 Å; for the hydrogen isotropic thermal parameters, 0.5 Å².

	<i>x</i>	<i>y</i>	<i>z</i>	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl	1715 (1)	5000 (0)	-5402 (2)	71 (2)	101 (2)	179 (3)	-5 (1)	47 (2)	-61 (2)
N(1)	1570 (5)	6573 (6)	-2061 (7)	73 (5)	75 (6)	206 (12)	-7 (4)	47 (7)	-12 (7)
C(2)	894 (6)	5766 (7)	-3903 (9)	73 (6)	83 (7)	180 (14)	-2 (5)	43 (7)	-27 (9)
N(3)	-374 (5)	5587 (6)	-4422 (8)	68 (5)	90 (6)	223 (13)	-6 (5)	35 (6)	-16 (8)
C(4)	-1760 (6)	6395 (7)	-2524 (11)	77 (7)	76 (7)	316 (19)	-12 (6)	44 (9)	-18 (10)
C(5)	-1727 (6)	7099 (9)	-711 (12)	75 (6)	115 (8)	363 (20)	-6 (6)	93 (10)	-15 (12)
C(6)	-499 (7)	7713 (9)	822 (13)	85 (7)	116 (9)	373 (23)	-22 (7)	112 (10)	-53 (13)
C(7)	688 (6)	7633 (8)	550 (10)	66 (6)	103 (7)	229 (15)	-8 (6)	53 (8)	-28 (10)
C(8)	602 (6)	6995 (7)	-1327 (10)	60 (6)	79 (7)	218 (15)	1 (5)	37 (8)	-2 (9)
C(9)	-578 (6)	6283 (7)	-2797 (10)	68 (8)	79 (6)	238 (16)	-6 (5)	34 (8)	9 (9)
C(1')	2948 (6)	7033 (7)	-1199 (9)	67 (6)	76 (7)	193 (14)	5 (5)	43 (8)	-2 (8)
O(1')	3703 (4)	6436 (5)	895 (7)	76 (4)	75 (5)	225 (10)	-4 (4)	40 (6)	10 (8)
C(2')	3171 (5)	8687 (6)	-855 (9)	65 (6)	56 (8)	216 (15)	3 (5)	59 (8)	6 (8)
O(2')	2897 (4)	3432 (6)	-2805 (6)	77 (4)	109 (5)	210 (10)	21 (4)	42 (5)	36 (7)
C(3')	4655 (6)	8718 (7)	681 (8)	81 (6)	66 (8)	198 (14)	5 (5)	53 (8)	-11 (8)
O(3')	5476 (4)	8549 (5)	-455 (7)	63 (4)	100 (6)	298 (12)	0 (4)	78 (6)	9 (7)
C(4')	4854 (5)	7390 (7)	2131 (9)	64 (6)	86 (7)	181 (14)	9 (5)	30 (7)	6 (8)
C(5')	4895 (6)	7687 (9)	4337 (9)	78 (6)	131 (9)	199 (16)	30 (7)	41 (9)	30 (10)
O(5')	3827 (5)	9633 (7)	4096 (7)	92 (5)	162 (8)	243 (12)	33 (6)	53 (6)	-16 (9)

Table 2 (cont.)

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i>
H(4)	-264	594	-371	3.1
H(5)	-260	721	-48	4.9
H(6)	-62	840	197	3.3
H(7)	157	810	167	3.3
H(1')	331	654	-225	2.7
H(2')	265	894	0	3.8
H(O2')	187	952	-360	2.9
H(3')	519	977	199	4.6
H(O3')	565	956	-108	4.9
H(4')	592	691	271	3.6
H(5')1	594	813	-487	4.4
H(5')2	505	664	-469	5.0
H(O5')	359	882	549	3.8

vibration with 50% probability surfaces for all nonhydrogen atoms and the atomic numbering are shown in Fig. 2. The bond distances and angles of the nonhydrogen atoms are shown in Fig. 3 and those involving the hydrogen atoms are in the normal range found in X-ray determinations and are not given.

Discussion

Molecular conformation

The glycosyl bond

The glycosyl torsional angle, χ_{CN} , defined as O(1')-C(1')-N(1)-C(2) (Sundaralingam, 1969) is 242.7°, thus placing it in the *syn* range. Although purine nucleosides with C(2')-*endo* puckering (discussed below) appear to show about equal preference for both *syn* and *anti* conformations (Sundaralingam, 1972), the presence of a chlorine substituent at C(2) sterically constrains χ_{CN} to the *syn* range, as found in the C(8) bromine substituted purine nucleosides (Tavale & Sobell, 1970). Some pertinent torsion angles in 2-chloro-(1- β -D-ribofuranosyl)benzimidazole are given in Table 3.

Sugar puckering

The ribose assumes the C(2')-*endo* mode of puckering and is in the twist conformation 2T_1 (for details of the abbreviated nomenclature see Sundaralingam, 1972) in which C(2') and C(1') are displaced 0.249 and 0.221 Å, respectively, on opposite sides of the furanose five-atom least-squares plane. In terms of the pseudorotation model (Altona & Sundaralingam, 1972), the maximum amplitude of puckering, τ_m , is 41.42° and the phase angle of pseudorotation, *P*, is 154.23°.

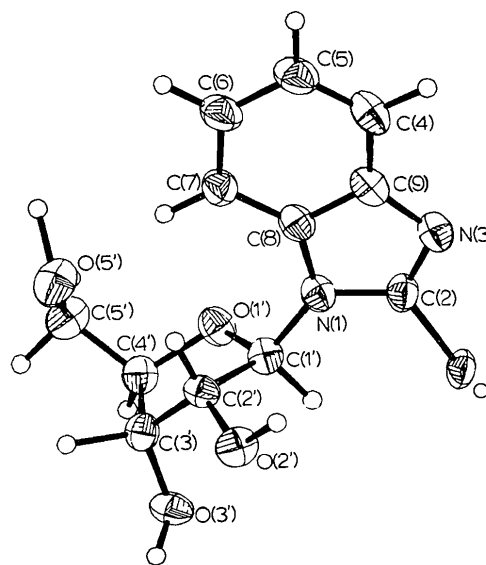


Fig. 2. The thermal ellipsoid plot (Johnson, 1965) showing the anisotropic vibration of the nonhydrogen atoms.

Table 3. Torsion angles of 2-chloro-1-(β -D-ribofuranosyl)benzimidazole

			Conformation
χ^*	O(1')-C(1')-N(1)-C(2)†	242.7 (6)°	<i>syn</i>
τ_n	C(4')-O(1')-C(1')-C(2')	-29.2 (6)	2T_1
τ_1	O(1')-C(1')-C(2')-C(3')	40.7 (6)	
τ_2	C(1')-C(2')-C(3')-C(4')	-36.4 (6)	
τ_3	C(2')-C(3')-C(4')-O(1')	20.6 (6)	
τ_4	C(3')-C(4')-O(1')-C(1')	5.7 (6)	
ψ	C(3')-C(4')-C(5')-O(5')	45.8 (7)	<i>gauche-gauche</i>

* The nomenclature used here is identical to that used earlier (Sundaralingam, 1969). It may be noted that the torsion angles χ and ψ are designated as positive angles (0 to 360°), while the ring torsion angles (τ 's) are positive (0 to 180°) or negative (180 to 360°). The right hand convention for the torsion angles is used throughout.

† N(1) and C(2) are labeled N(9) and C(8) respectively in the purine convention.

A survey of ring conformations for the *syn* nucleosides indicates that, in all cases, the sugar pucker lies between $P=145$ and 181° , i.e. between 2T_1 and 2T_3 . It is particularly noteworthy that the C(2) [or C(8)] substituted benzimidazole (or purine) nucleosides occupy the region between 2E and 2T_1 (Fig. 4).

The conformation about the C(4')-C(5') bond is *gauche-gauche*, as is also the case with the 8-bromo substituted adenosine and guanosine. In the benzimidazole base a carbon atom in the seven position substitutes for the ring nitrogen N(3) of the purine base.

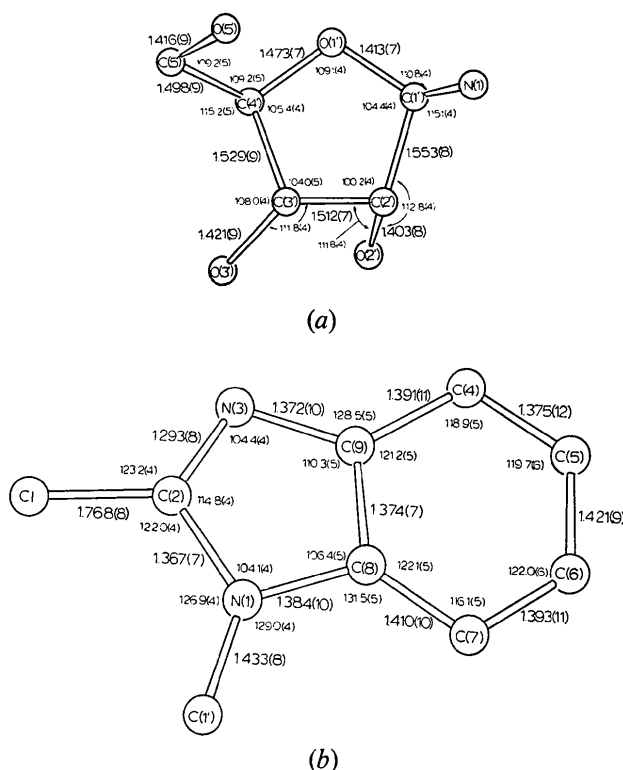


Fig. 3. The bond lengths and valence bond angles for the non-hydrogen atoms of the ribosyl (a) and the benzimidazole (b) portions of the molecule.

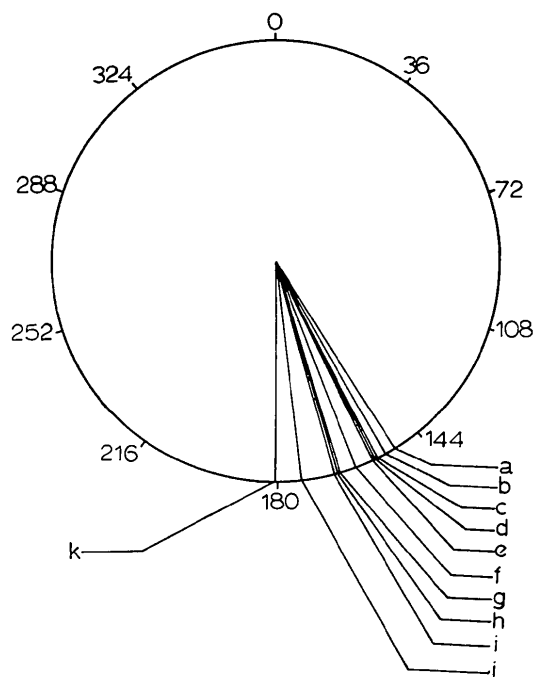


Fig. 4. A pseudorotation diagram (Altona & Sundaralingam, 1972) showing the pseudorotation phase angles for *syn* β -purine nucleosides. Phase angles for ideal C(2')-*endo*-C(3')-*exo*, C(2')-*endo*-C(1')-*exo* conformations are 180, 162 and 144° respectively. The glycosyl torsion angles followed by the phase angle of pseudorotation, P , of the above compounds are given in parentheses. (a) Formycin monohydrate (109.8, 148.3) (Prusiner *et al.*, 1973); (b) 2-thio-1-(β -D-ribofuranosyl)-3*H*-benzimidazole (250, 152.1) (Prusiner & Sundaralingam, 1973); (c) 8-bromoguanosine (230, 153.8) (Bugg & Thewalt, 1969); (d) 2-chloro-1-(β -D-ribofuranosyl)benzimidazole (242.7, 154.2); (e) 3'-*O*-acetyladenosine (227, 154.5) (Rao & Sundaralingam, 1970); (f) 6-thioinosine, molecule 2 (216, 159.6) (Shefter, 1968); (g) 8-bromoadenosine (240, 163.8) (Tavale & Sobell 1970); (h) 6-thioinosine, molecule 1 (215, 163.6) (Shefter, 1968); (i) deoxyguanosine (211, 165.1) (Haschemeyer & Sobell, 1965); (j) N^2 -dimethylguanosine (256, 173.7) (Brennan *et al.*, 1972); (k) 5'-methylammonium-5'-deoxyadenosine (209, 180.8) (Saenger, 1971). The crystal structure of a *syn* conformer of inosine has recently been determined (Subramanian, Madden & Bugg, 1973). χ_{CN} is 283.1° and the ribose conformation is C(2')-*endo*. Pseudorotation values are not available.

It would appear that contacts between the hydrogen atom attached to C(7) and O(5') of the ribose would affect the stability of the *gauche-gauche* conformation about C(4')-C(5'). However, it turns out that this conformation is allowed. The distance between C(7) and O(5') is 3.78 Å, and between C(7) and O(1') is 3.401 Å while that between H(7) and O(5') is 2.37 Å. The latter distance is slightly less than the van der Waals contact distance (Pauling, 1960) for the respective atoms, and may represent a weak attractive C-H...O interaction.

The benzimidazole ring

The benzimidazole ring is planar with a r.m.s. deviation of the fitted atoms from the plane of 0.048 Å. The Cl and C(1') atoms deviate 0.099 (6) and 0.071 (6)

Å respectively, on opposite sides of the benzimidazole plane. The dihedral angle between the least-squares plane of the base and that of the ribose is 89° .

Hydrogen bonding and molecular packing

The intermolecular hydrogen-bonding scheme is shown by broken or dotted lines in Figs. 5 and 6 and by solid single lines in the stereoscopic packing diagram, Fig. 7. Each molecule of 2-chloro-1-(β -D-ribofuranosyl)benzimidazole is involved in three hydrogen bonds to neighboring molecules. The only hydrogen bond to the base is $O(2')-H(O2') \cdots N(3)$ and those to the ribose are $O(3')-H(O3') \cdots O(1')$ and $O(5')-H(O5') \cdots O(2')$. The hydrogen-bonding scheme is summarized in Table 5.

One of the more interesting aspects of this structure is the involvement of the ribose ring $O(1')$ as an acceptor in the moderately strong hydrogen bond to $H(O3')$. Participation of $O(1')$ in hydrogen bonding is relatively uncommon, and is known to be generally weak in the several cases in which it occurs (Table 4). The strong hydrogen-bonded interactions of $O(1')$ with $N(3)$ in 6-azauridine (Schwalbe & Saenger, 1971) and with $O(3)$ in ethyl-1-thio- β -D-glucopyranoside (Parthasarathy & Davis, 1967) (the latter is not a nucleoside) are exceptional. The occurrence of $O(1')$ interactions does not appear to depend on the glycosyl torsion angle, χ_{CN} , or the nature of the base. The same inference may be made of correlation with the mode of sugar puckering. Of the cases listed in Table 4, two lie in the higher *anti* region, e.g. virazole I (Prusiner & Sundaralingam, 1973a) and formycin (Prusiner, Brennan & Sundaralingam, 1973) and the other in the low *anti*, e.g. azauridine (Schwalbe & Saenger, 1971). Only

the 2-chloro benzimidazole furanoside is *syn*. From these observations it appears that $O(1')$ can participate in hydrogen-bonded interaction in the nucleic acids.

The molecular packing is such that there are well defined hydrophobic and hydrophilic regions in the cell, consisting of a linear array of benzimidazole and ribose moieties aligned parallel to the *b* axis (Fig. 5). This requires a head-to-tail packing of screw-related benzimidazole bases, thereby allowing the Cl substituents to direct themselves toward the ribose of the adjacent screw-related molecules. The plane of the benzimidazole ring is tilted approximately 30° from the *h0l* plane (Figs. 6 and 7). There is little base stacking evident between screw-related benzimidazole rings, the dihedral angle between them being 64° . The closest contact between screw-related benzimidazole moieties is that between $C(6)$ and $N(3)$ of 3.45 \AA . The benzimidazole ring planes of molecules in adjacent unit cells are separated by a perpendicular distance of about 3.1 \AA .

It has been observed that halogen substitution markedly increases the tendency towards vertical stacking of the base moieties (Bugg *et al.*, 1971; Ts'o, 1968; Ts'o & Chan, 1964). In the case of the two 8-bromo substituted purine nucleosides (Bugg & Thewalt, 1969; Tavale & Sobell, 1970), the bromine is positioned over the $N(7)$ of the adjacent purine. This type of interaction is not found in the present structure, and the chlorine is involved in only one contact within van der Waals limits, *viz.* to the $C(7)$ (3.47 \AA) of the molecule related by a translation along *c* (shown with dashed lines in Fig. 6). It is possible that the proximity of the $Cl \cdots C(7)$ contact between *c*-translation related bases prevents direct vertical interactions.

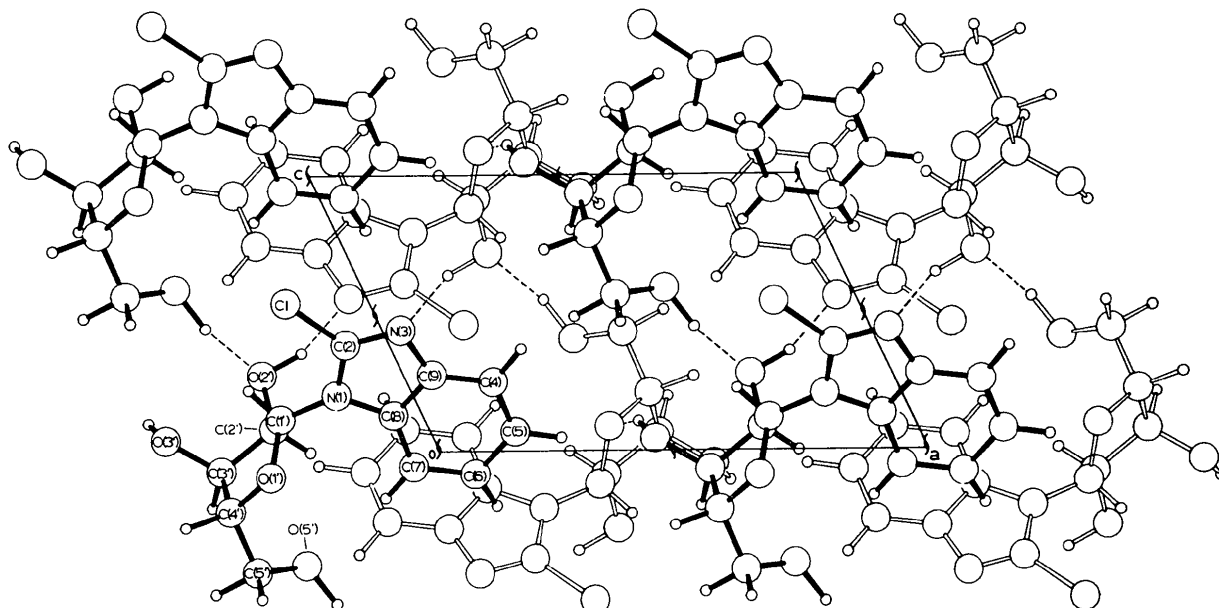


Fig. 5. A projection along the *b* axis. Hydrogen-bonded contacts are shown by broken lines.

Table 4. O(1') hydrogen bonding in nucleosides and related compounds

Correlation with selected conformational parameters.

Compound	Donor atom	Angle at hydrogen (°)	Donor-acceptor distance (Å)	Ribose conformation	χ_{C-N} (°)
6-Azauridine, molecule B ^a	N(3)	164	2.837	³ T ₂	82.7
Virazole ^b	C(8)	176	3.28	₂ T ¹	110.0
Formycin ^c	N(6)	131	2.99	² T ₁	109.5
α -D-2'-Amino-2'-deoxyadenosine monohydrate ^d	O(water)	131	3.044	³ T ₂	298
Ethyl-1-thio- α -D-glucufuranoside ^e	O(3')	165	2.77	—	—

(a) Data for molecule A, which also exhibits N(3)-H(3)···O(1') hydrogen bonding, are not given because of an apparent error in the positional parameter C(4'), Schwalbe & Saenger (1971); (b) Prusiner & Sundaralingam (1973a); (c) Prusiner *et al.* (1973); (d) Rohrer & Sundaralingam (1970); (e) Parthasarthy & Davis (1967).

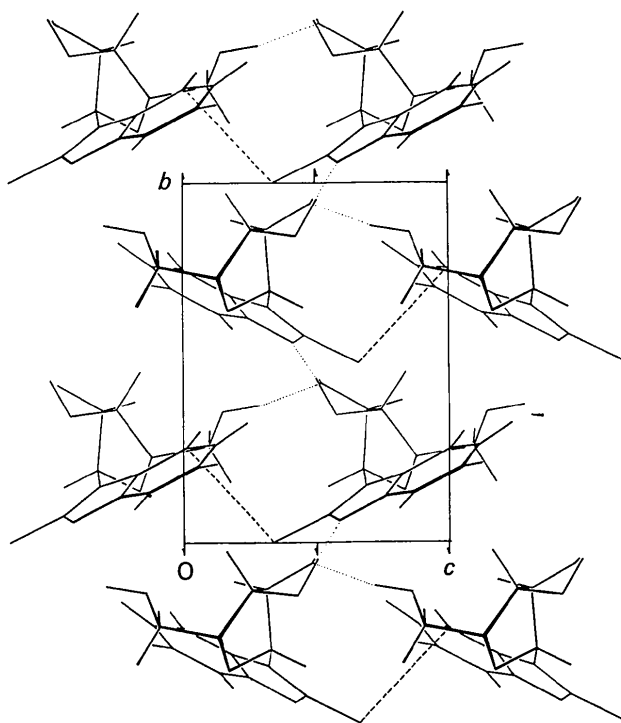


Fig. 6. A projection down the *a* axis. Hydrogen-bonded contacts are shown with dotted lines and the 3.47 Å van der Waals contact between C1 and C7 with broken lines. The O(3')···O(1') hydrogen bond is not shown here (see Fig. 5).

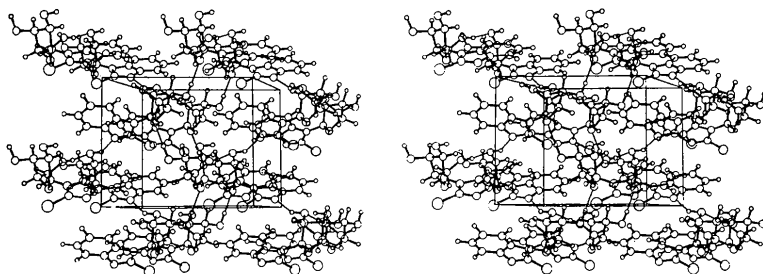


Fig. 7. Stereoscopic view of the crystal structure along the *c* direction, with the *a* axis horizontal. Hydrogen-bonded contacts are shown by single lines.

Conclusion

2-Chloro-1-(β -D-ribofuranosyl)benzimidazole conforms with the general trend towards the *syn* conformation and C(2')-*endo* ribose puckering displayed by C(8) substituted purine nucleosides. It is exceptional, however, in that it exhibits hydrogen-bonded interactions to the ribose ring O(1') and it lacks pronounced base stacking in the lattice.

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Table 5. *Hydrogen-bond distances and angles*

Atom A	Atom B	Symmetry code	Distance (Å)	Bond	Angle (°)
O(3')	O(1')	i	2.88	O(3')-H(O3') \cdots O(1')	148
O(5')	O(2')	ii	2.79	O(4')-H(O5') \cdots O(2')	164
O(2')	N(3)	iii	2.81	O(2')-H(O2') \cdots N(3)	151
Symmetry code		i $1 + \bar{x}, y + \frac{1}{2}, \bar{z}$;	ii $x, y, z + 1$;	iii $\bar{x}, y + \frac{1}{2}, \bar{z} - 1$.	

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The Crystal and Molecular Structure of 1,2,3-Benzotriazin-4(3H)-one

BY JOHAN HJORTÅS

Institutt for røntgenteknikk, Universitetet i Trondheim-NTH, N-7034 Trondheim-NTH, Norway

(Received 26 March 1973; accepted 27 March 1973)

The title compound crystallizes in space group $P2_12_12_1$ with $a = 3.802$ (2), $b = 7.712$ (3), $c = 22.213$ (8) Å, $Z = 4$. Data were collected on an automatic diffractometer with Cu $K\alpha$ radiation. The structure was solved by the symbolic addition procedure in the $0kl$ projection. Refinement was by full-matrix least-squares methods to an R of 0.036 based on 654 observed reflexions corrected for secondary extinction. The molecules show only small deviations from planarity. The triazine ring has an N(1)-N(2) double bond of 1.274 (3) Å and the hydrogen atom is bonded to N(3). The molecules are bonded together by almost linear N-H \cdots O hydrogen bonds into polymers around screw axes in the x direction. The N \cdots O distance is 2.828 (3) Å and the H \cdots O distance is 1.86 (3) Å.

Introduction

Derivatives of the three possible ring systems 1,3,5-triazine (or *s*-triazine), 1,2,4-triazine and 1,2,3-triazine (or *v*-triazine) are known. 1,3,5-Triazine has been extensively studied by both X-ray diffraction (Wheatley, 1955; Coppens, 1967) and neutron diffraction (Coppens, 1967). The parent 1,2,4- and 1,2,3-triazines have never been prepared but 1,2,3-benzotriazine can readily be

obtained as first described by Weddige & Finger (1887). Numerous derivatives of this bicyclic system are known [see reviews by Erickson (1956) or Modest (1961)]. Substituted 1,2,3-benzotriazin-4-ones have potential pharmacological applications (Zaika & Joullié, 1966). The structure of 1,2,3-benzotriazin-4-one is usually drawn as in Fig. 1, but it has a tautomer with the hydrogen atom at N(1) instead of N(3). It was one of the purposes of this investigation to locate this hydrogen. The struc-