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The Crystal and Molecular Structure of Coformycin

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Coformycin, a unique nucleoside with strong inhibition activity against adenosine deaminase, crystallizes as the sesquihydrate in $P2_12_12$ with $a=11{\cdot}961$ (5), $b=23{\cdot}50$ (1), $c=4{\cdot}936$ (2) Å, $Z=4$. The structure was solved by the symbolic addition method and refined by the block-diagonal least-squares method to an R value of 0·057 including H atoms for 1021 observed structure factors. The structure was established as 3-(β-D-ribofuranosyl)-6,7,8-trihydroimidazo[4,5-*d*] [1,3]diazepin-8(*R*)-ol. The conformation about the glycosyl bond is *anti* and that of the ribose group is C1′-*exo*–C2′-*endo* and *gauche–gauche*.

Introduction

Coformycin was discovered in 1967 (Tsuruoka, Ezaki, Amano, Uchida & Niida) owing to its strong synergic activity with formycin which had been known as an antitumour antibiotic (Hori, Ito, Takita, Koyama, Takeuchi & Umezawa, 1964; Koyama & Umezawa, 1965). *Streptomyces* which produces formycin generally produces coformycin at the same time and the latter enhances the activity of the former in inhibiting bacterial and animal cells. Coformycin is the strongest inhibitor of adenosine deaminase ever known, and prevents inactivation of formycin by this enzyme in cells (Sawa, Fukagawa, Homma, Takeuchi & Umezawa, 1967).

Chemical elucidation of the structure was unsucessful but conclusive results on the coformycin structure have been obtained by X-ray analysis (Nakamura, Koyama, Iitaka, Ohno, Yagisawa, Kondo, Maeda & Umezawa, 1974) and stimulated the chemical synthesis of coformycin as described in a previous paper (Ohno, Yagisawa, Shibahara, Kondo, Maeda & Umezawa, 1974).

Experimental

The crystals were grown from an aqueous solution as colourless thin plates. Diffraction data were obtained from a crystal with approximate dimensions of $0{\cdot}13\times0{\cdot}025\times0{\cdot}9$ mm. The lattice constants were determined by the least-squares treatment of 8 reflexions measured on a Rigaku four-circle X-ray diffractometer using Ni-filtered Cu $K\alpha$ radiation. Crystal data are listed in Table 1.

Table 1. *Crystal data*

Coformycin sesquihydrate, $C_{11}H_{16}N_4O_5.1{\cdot}5H_2O$, F. W. 311·1, m.p. 182∼184°C
Orthorhombic, $P2_12_12$, $Z=4$, $D_x=1{\cdot}490$ g cm^{-3}. $a=11{\cdot}961$ (5), $b=23{\cdot}50$ (1), $c=4{\cdot}936$ (2) Å

Intensities were measured on the same diffractometer by the θ–2θ scanning method. The scan speed was 4° 2θ min^{-1} and the background was measured at both ends of the scan for 10 s. A total of 1438 independent reflexions were measured within $2\theta=130°$, in which 1021 reflexions with $F_o>2\sigma(F_o)$ were used for the subsequent analysis. The intensities were corrected with Lorentz and polarization factors but not absorption factors.

The structure was solved by the symbolic addition method (Karle & Karle, 1966). Starting with 7 reflexions including 3 unknown symbols, the phases of 182 reflexions with $E\geq1{\cdot}49$ were determined and refined by using the tangent formula. The resulting E map showed 17 non-hydrogen atoms. This structure was then refined by the least-squares method coupled with Fourier and difference Fourier syntheses. The locations of the remaining 5 atoms were found on the difference electron density maps along with those of 18 H atoms. The assignment of the atomic species was made during the refinement. The final refinement was carried out by the method of block-diagonal least squares using the *HBLS* program (Okaya & Ashida, 1967). Unit weight was applied to each reflexion. The R value was reduced to 0·057 for 1021 observed reflexions. The final difference electron density map showed no significant peaks even for the H atom to be bonded to the water O atom lying on the diad axis. The final atomic parameters are listed in Table 2.†

The atomic scattering factors for C, N and O atoms were those given in *International Tables for X-ray*

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† A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31368 (5 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

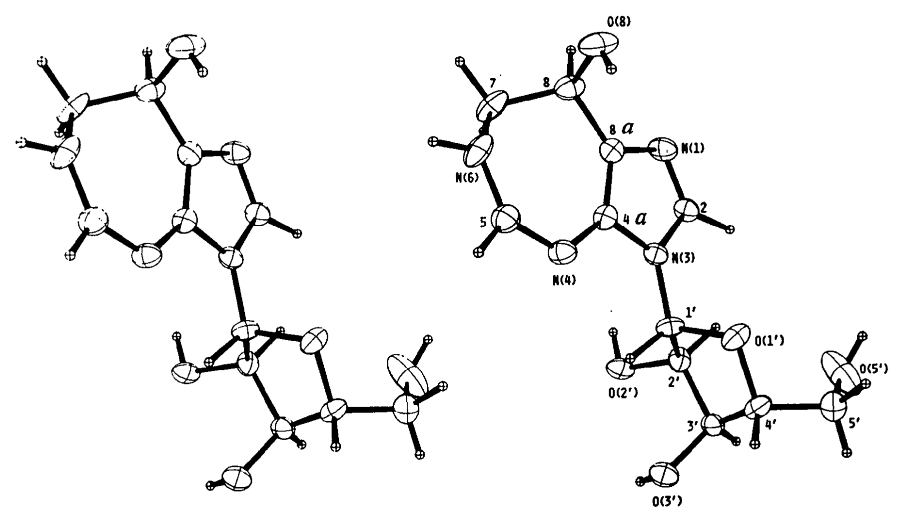

Fig. 1. A stereoscopic view of the coformycin molecule drawn by *ORTEP* (Johnson, 1965). Thermal vibration ellipsoids are scaled to 50% probability. H atoms are drawn as spheres on an arbitrary scale.

Crystallography (1962) as SX-6, 7 and 8, respectively and those for the H atom were from Stewart, Davidson & Simpson (1965).

The absolute configuration was deduced from the known configuration of the D-ribofuranose moiety which had been chemically determined.

Discussion

The structure of coformycin is illustrated in Fig. 1 by an *ORTEP* stereoscopic drawing (Johnson, 1965) which also clearly shows the conformation of the molecule.

The chemical structure of coformycin has now been established as 3-(β-D-ribofuranosyl)-6,7,8-trihydroimidazo[4,5-*d*] [1,3]diazepin-8(*R*)-ol (Fig. 2) and accounts for the results of chemical and biological studies which had suggested a purine nucleoside structure. The structure of the base is not that of a usual purine base but is a derivative of imidazodiazepin having a hydroxyl group attached to the seven-membered ring. This ring is hydrogenated at C(7) and C(8) and protonated at N(6). As a result of the hydrogenation, the conjugated system in the diazepin ring is interrupted and the ring takes a puckered form. The strong inhibitory activity against adenosine

Table 2. *Atomic parameters with estimated standard deviations in parentheses*

The parameters for non-hydrogen atoms are × 10^4 and the coordinates and temperature factors for H atoms are × 10^3 and × 1, respectively. The temperature factors for non-hydrogen atoms are of the form: $T=\exp\,[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)]$ and those for H atoms: $T=\exp\,[-\beta_{11}\,(\sin\theta/\lambda)^2]$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	3998 (4)	3857 (2)	1890 (12)	30 (4)	13 (1)	210 (25)	2 (2)	−21 (10)	8 (6)
C(2)	5010 (6)	4047 (3)	1457 (13)	31 (5)	10 (1)	146 (28)	2 (2)	−13 (11)	6 (5)
N(3)	5751 (4)	3802 (2)	3214 (11)	26 (4)	8 (1)	160 (23)	2 (2)	20 (9)	−5 (5)
C(4*a*)	5168 (5)	3420 (3)	4840 (13)	34 (5)	8 (1)	121 (26)	−1 (2)	12 (11)	2 (6)
N(4)	5724 (4)	3122 (2)	6829 (12)	28 (4)	11 (1)	175 (24)	−1 (2)	−4 (10)	8 (5)
C(5)	5223 (6)	2731 (3)	8235 (16)	37 (5)	11 (1)	214 (31)	0 (2)	8 (12)	3 (6)
N(6)	4192 (5)	2520 (2)	8097 (13)	53 (4)	11 (1)	201 (25)	−10 (2)	38 (11)	6 (5)
C(7)	3412 (6)	2544 (3)	5808 (15)	47 (6)	14 (1)	260 (34)	−15 (3)	−12 (13)	−2 (7)
C(8)	3096 (5)	3147 (3)	5050 (15)	33 (5)	12 (1)	199 (32)	−3 (2)	14 (12)	−12 (6)
C(8*a*)	4082 (5)	3464 (3)	4028 (14)	32 (5)	8 (1)	229 (32)	0 (2)	−3 (11)	2 (6)
O(8)	2565 (4)	3434 (2)	7295 (10)	31 (3)	19 (1)	298 (25)	−5 (2)	27 (9)	−22 (5)
C(1′)	6941 (5)	3916 (3)	3381 (13)	22 (4)	11 (1)	137 (29)	−2 (2)	−1 (10)	−5 (6)
C(2′)	7551 (6)	3958 (3)	653 (14)	38 (5)	7 (1)	188 (30)	0 (2)	26 (12)	−4 (6)
C(3′)	8632 (5)	4247 (3)	1623 (15)	27 (5)	8 (1)	252 (34)	1 (2)	−2 (12)	18 (6)
C(4′)	8242 (6)	4632 (3)	3969 (15)	30 (5)	10 (1)	244 (36)	−6 (2)	−2 (12)	3 (6)
O(1′)	7092 (4)	4461 (2)	4584 (10)	35 (3)	11 (1)	173 (21)	−7 (1)	32 (8)	−17 (4)
O(2′)	7736 (4)	3421 (2)	−528 (9)	31 (3)	13 (1)	171 (20)	2 (2)	−18 (7)	−8 (4)
O(3′)	9409 (4)	3840 (2)	2661 (10)	35 (3)	12 (1)	194 (21)	3 (2)	−14 (8)	3 (4)
C(5′)	8259 (6)	5250 (3)	3365 (20)	49 (6)	10 (1)	583 (53)	0 (3)	15 (17)	−6 (8)
O(5′)	7794 (5)	5352 (2)	750 (14)	114 (6)	23 (1)	509 (37)	29 (3)	98 (14)	46 (6)
O(*W*1)	5264 (4)	1583 (2)	2161 (11)	34 (4)	22 (1)	296 (25)	−3 (2)	−21 (8)	10 (5)
O(*W*2)	0 (0)	0 (0)	3249 (18)	123 (9)	15 (2)	315 (39)	−12 (3)	0 (0)	0 (0)

Table 2 (*cont.*)

	x	y	z	β_{11}
H(C2)	533 (5)	441 (3)	4 (16)	3 (2)
H(C5)	573 (6)	258 (3)	968 (18)	3 (2)
H(N6)	408 (5)	221 (2)	896 (14)	3 (2)
H(C7)	374 (5)	240 (3)	419 (15)	3 (2)
H′(C7)	274 (5)	232 (2)	656 (13)	2 (1)
H(C8)	240 (6)	312 (3)	344 (17)	6 (2)
H(O8)	301 (6)	356 (3)	838 (17)	6 (2)
H(C1′)	741 (5)	360 (2)	465 (13)	1 (1)
H(C2′)	703 (7)	427 (3)	−83 (19)	6 (2)
H(C3′)	900 (5)	444 (3)	−17 (16)	3 (2)
H(C4′)	874 (4)	460 (2)	588 (12)	1 (1)
H(O2′)	711 (6)	334 (3)	−132 (16)	4 (2)
H(O3′)	959 (6)	362 (3)	160 (17)	5 (2)
H(C5′)	899 (6)	535 (3)	380 (15)	4 (2)
H′(C5′)	782 (5)	548 (3)	538 (15)	3 (2)
H(O5′)	717 (8)	554 (4)	78 (21)	10 (3)
H(O*W*1)	591 (5)	157 (2)	242 (14)	3 (2)
H′(O*W*1)	500 (7)	128 (3)	351 (18)	8 (2)

deaminase may be explained in terms of its structural similarity to a hypothetical reactive substrate intermediate, proposed for the enzymatic deamination of adenosine (Woo, Dion, Lange, Dahl & Durham, 1974). The potent synergic activity of coformycin with formycin may then be explained by its inhibitory activity against adenosine deaminase, because formycin itself easily undergoes deamination by the enzyme and loses its activity.

Bond lengths and angles are listed and compared with those of inosine in its free and hydrated crystals in Tables 3 and 4. The effect of increasing the six-membered ring of the purine nucleus by an atom is clearly seen in the endocyclic bond angles. The angles subtended at C(8*a*), C(4*a*), N(4), C(5) and N(6), all of which are involved in the conjugated system, are several degrees greater than the corresponding angles in inosine, whereas those at C(7) and C(8) are not far from the usual tetrahedral bond angles. The planarity of the base is shown in Table 5. The imidazole ring and the three atoms directly bonded to the ring, N(4), C(8) and C(1′), lie nearly in a plane, while C(5), N(6) and C(7) of the trihydrodiazepin ring, especially C(7), deviate from the plane in the opposite direction to O(8). The equation of the plane is $-0{\cdot}1650X+0{\cdot}7333Y+0{\cdot}6596Z=6{\cdot}465$, where X, Y and Z are measured in Å along the crystallographic a, b and c axes, respectively. The puckering of the ring may be

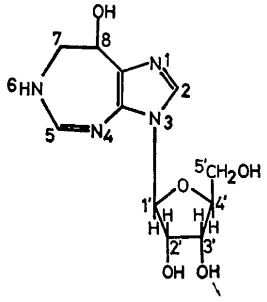

Fig. 2. Chemical structure of coformycin. Numbering of the atoms is also shown.

Table 3. *Bond lengths*

The corresponding bond lengths in coformycin and inosine molecules are compared.

	Coformycin·1.5H_2O	Inosine (1)	Inosine.2H_2O (2) *A* molecule	 *B* molecule
Imidazole group				
N(1)—C(2)	1·308 (9) Å	1·307 (4) Å	1·311 Å	1·301 Å
N(1)—C(8*a*)	1·405 (9)	1·371 (4)	1·371	1·379
C(2)—N(3)	1·368 (8)	1·372 (4)	1·359	1·369
N(3)—C(4*a*)	1·391 (8)	1·372 (4)	1·372	1·370
C(4*a*)–C(8*a*)	1·364 (9)	1·374 (4)	1·382	1·367
N(3)—C(1′)	1·450 (8)	1·477 (4)	1·460	1·452
Trihydrodiazepin group or pyrimidine group				
C(4*a*)–N(4)	1·376 (8)	1·365 (4)	1·362	1·364
N(4)—C(5)	1·300 (9)	1·308 (5)	1·307	1·308
C(5)—N(6)	1·330 (9)	1·355 (5)	1·360	1·351
N(6)—C(7)	1·466 (10)	1·397 (4)	1·401	1·390
C(7)—C(8)	1·515 (10)	—	—	—
C(8)—C(8*a*)	1·483 (9)	1·433 (5)	1·429	1·436
C(8)—O(8)	1·444 (9)	1·233 (4)	1·221	1·235
Ribofuranose group				
C(1′)-C(2′)	1·535 (9)	1·530 (4)	1·525	1·516
C(1′)-O(1′)	1·425 (8)	1·417 (4)	1·416	1·410
C(2)′-C(3′)	1·536 (9)	1·525 (4)	1·517	1·529
C(2′)-O(2′)	1·408 (8)	1·420 (4)	1·417	1·407
C(3′)-C(4′)	1·542 (10)	1·522 (4)	1·526	1·525
C(3′)-O(3′)	1·429 (8)	1·413 (4)	1·418	1·412
C(4′)-O(1′)	1·464 (8)	1·459 (4)	1·452	1·450
C(4′)-C(5′)	1·483 (10)	1·506 (4)	1·513	1·503
C(5′)-O(5′)	1·425 (12)	1·428 (4)	1·437	1·418
		Average e.s.d.	0·004	0·004

(1) Munns & Tollin (1970). (2) Thewalt, Bugg & Marsh (1970).

Table 4. *Bond angles*

The corresponding bond angles in coformycin and inosine molecules are compared.

	Coformycin·1.5H$_2$O	Inosine (1)	Inosine.2H$_2$O (2) *A* molecule	*B* molecule
Imidazole group				
C(2)—N(1)—C(8*a*)	106·3 (5)°	103·8 (3)°	104·3°	103·4°
N(3)—C(2)—N(1)	110·6 (6)	113·6 (3)	113·5	113·8
C(4*a*)-N(3)—C(2)	108·2 (5)	105·7 (3)	106·0	105·8
C(4*a*)-N(3)—C(1′)	125·3 (5)	126·0 (3)	125·1	128·3
C(2)—N(3)—C(1′)	126·5 (5)	128·1 (3)	128·9	125·9
N(3)—C(4*a*)-C(8*a*)	105·0 (5)	105·4 (3)	105·6	105·3
N(1)—C(8*a*)-C(4*a*)	109·8 (6)	111·6 (3)	110·6	111·6
Trihydrodiazepin group or pyrimidine group				
N(1)—C(8*a*)-C(8)	121·9 (6)	130·1 (3)	129·7	128·8
C(4*a*)-C(8*a*)-C(8)	128·2 (6)	118·3 (3)	119·7	119·5
N(4)—C(4*a*)-N(3)	119·8 (5)	126·1 (3)	126·7	126·7
N(4)—C(4*a*)-C(8*a*)	135·1 (6)	128·5 (3)	127·7	128·0
C(5)—N(4)—C(4*a*)	121·2 (6)	111·9 (3)	111·2	110·7
N(6)—C(5)—N(4)	131·6 (7)	124·6 (3)	126·2	126·7
C(7)—N(6)—C(5)	127·9 (6)	125·4 (3)	124·5	124·4
C(8)—C(7)—N(6)	112·6 (6)	—	—	—
C(8*a*)-C(8)—C(7)	110·9 (6)	111·0 (3)	110·6	110·7
C(8*a*)-C(8)—O(8)	112·1 (5)	128·4 (3)	128·1	128·6
C(7)—C(8)—O(8)	111·0 (6)	120·6 (3)	121·2	120·6
Ribofuranose group				
C(1′)-O(1′)-C(4′)	106·3 (5)	109·6 (2)	109·9	108·1
C(2′)-C(1′)-N(3)	115·4 (5)	111·5 (2)	113·4	114·4
C(2′)-C(1′)-O(1′)	104·3 (5)	106·8 (2)	105·1	105·1
N(3)-C(1′)-O(1′)	108·3 (5)	108·4 (2)	107·6	107·3
C(3′)-C(2′)-C(1′)	98·9 (5)	100·6 (2)	101·4	100·6
C(3′)-C(2′)-O(2′)	113·2 (5)	107·5 (2)	115·6	112·2
C(1′)-C(2′)-O(2′)	112·3 (5)	109·6 (2)	113·9	114·4
C(4′)-C(3′)-C(2′)	103·9 (5)	101·5 (2)	102·7	102·5
C(4′)-C(3′)-O(3′)	108·7 (5)	114·2 (2)	107·8	109·1
C(2′)-C(3′)-O(3′)	111·3 (5)	115·9 (2)	112·0	111·2
O(1′)-C(4)′-C(3′)	106·1 (5)	104·0 (2)	105·8	106·9
O(1′)-C(4′)-C(5′)	108·9 (6)	110·0 (3)	107·8	108·8
C(3′)-C(4′)-C(5′)	114·8 (6)	114·1 (3)	117·4	115·8
O(5′)-C(5′)-C(4′)	110·0 (6)	112·0 (3)	111·2	112·5
		Average e.s.d.	0·5	0·5

(1) Munns & Tollin (1970). (2) Thewalt, Bugg & Marsh (1970).

Table 5. *Planarity of the base*

Plane-forming atom	Deviation	Deviation of atom from the plane	
N(1)	0·008 Å	C(1′)	0·014 Å
C(2)	−0·004	C(5)	−0·109
N(3)	−0·002	N(6)	−0·314
C(4*a*)	−0·015	C(7)	−0·864
C(8*a*)	0·011	O(8)	1·322
N(4)	0·010		
C(8)	−0·008		

caused by the strain in this seven-membered ring and by the steric repulsions between the atoms bonded to C(7) and C(8).

In bond distances, a slight but probably significant lengthening of the bonds C(8*a*)–C(8), C(8*a*)–N(1) and C(4*a*)–N(3) and a shortening of the bonds C(5)–N(6) and C(4*a*)–C(8*a*) are observed in coformycin as compared to inosine. The lengths of the bonds N(6)–C(7), C(7)–C(8) and C(8)–O(8) are acceptable as single-bond distances. In the ribose moiety, no anomalous features are observed.

The conformation angle about the glycosyl bond χ (73·3°) lies in the range of usual *anti* conformation contrary to the *syn* conformation found in the formycin molecules in the crystals of hydrobromide and monohydrate ($\chi = -149{\cdot}3$ and 109·8°, respectively). The torsion angles and the conformation of the ribose moiety are listed in Table 6 and compared with those found in inosine. Although the angles do not differ so much from the corresponding angles in the inosine dihydrate, the conformation of the furanose ring in coformycin may be described as C1′-*exo*–C2′-*endo* rather than C2′-*endo*. This is more clearly shown by the displacements of the ring C atoms from the least-squares plane as seen in Table 6. The equation of the plane through C(3′), C(4′) and O(1′) is $0{\cdot}3412X - 0{\cdot}6688Y + 0{\cdot}6605Z = -2{\cdot}623$, where X, Y and Z are measured in Å along the *a*, *b* and *c* axes respectively. The orientation of the C(5′)–O(5′) bond with respect to the furanose ring, defined by φ_{OO} and φ_{OC} is *gauche-gauche* which is the most common conformation found in nucleosides and nucleotides.

The structure of the crystal is shown in Figs. 3 and 4. All the atoms which are considered to have the ability to form hydrogen bonds are actually involved in hydrogen bonds. In addition to the seven such hydrogen bonds involving imino and hydroxyl groups, the C(2)H group in the imidazole ring forms a C–H···O hydrogen bond to the water O atom O(*W*2). These hydrogen bonds are shown in the figures by

Table 6. *Torsional angles and displacement of atoms from the furanose ring*

Torsion angles	Coformycin.1·5H_2O	Inosine (1)	Inosine.2H_2O (2) *A* molecule	Inosine.2H_2O (2) *B* molecule
χ[C(2)-N(3)-C(1′)-O(1′)]	73·3°	12·4°	120·1°	49·0°
τ_0[O(1′)-C(1′)]	−39·7	7·8	−22·5	−31·2
τ_1[C(1′)-C(2′)]	45·3	−30·6	36·9	41·2
τ_2[C(2′)-C(3′)]	−33·3	40·6	−36·6	−34·7
τ_3[C(3′)-C(4′)]	11·7	−37·1	24·4	17·8
τ_4[C(4′)-O(1′)]	17·2	18·6	−1·3	8·0
Puckering	C1′-*exo*-C2′-*endo*	C3′-*endo*	C2′-*endo*	C2′-*endo*
φ_{OO}[O(1′)-C(4′)-C(5′)-O(5′)]	−74·2	74·7	−55·3	−73·4
φ_{OC}[C(3′)-C(4′)-C(5′)-O(5′)]	44·6	−169·0	64·0	47·0
Conformation about C(4′)-C(5′)	*gg*	*gt*	*gg*	*gg*
Displacement of atoms from the least-squares plane				
C(1′)	0·404* Å	0·042 Å	−0·004 Å	0·028 Å
C(2′)	−0·303*	−0·025	−0·589*	−0·605*
C(3′)	0	0·626*	0·004	−0·026
C(4′)	0	0·026	−0·007	0·043
O(1′)	0	−0·043	0·007	0·045

* Not included in the least-squares calculation.

(1) Munns & Tollin (1970). (2) Thewalt, Bugg & Marsh (1970).

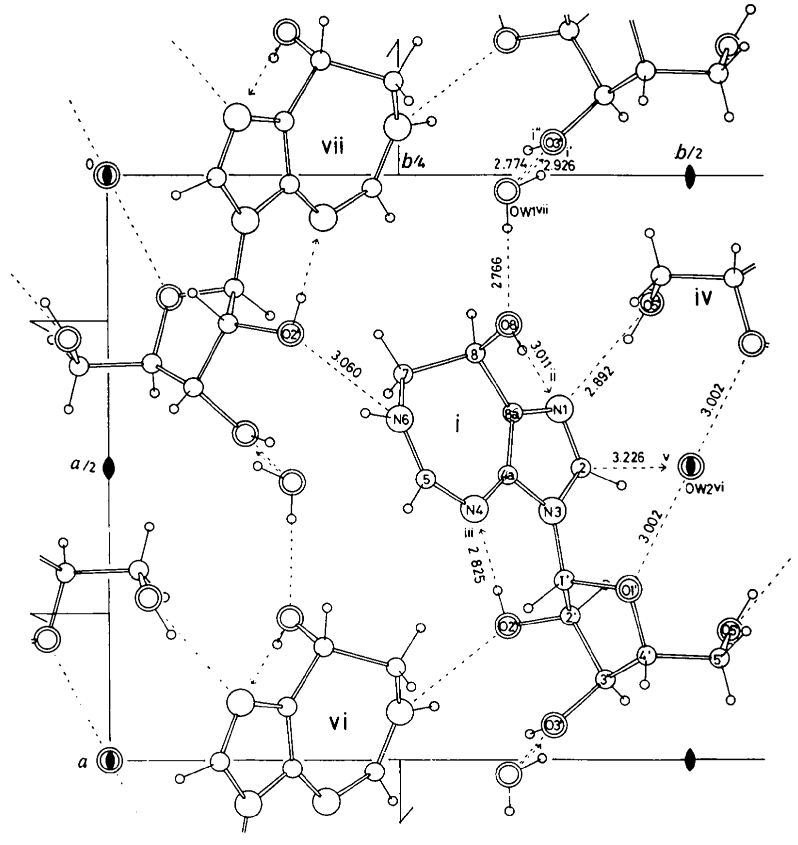

Fig. 3. Projection of the crystal structure along the *c* axis. Hydrogen bonds are shown by broken lines. Symmetry operations are given in Table 7. Those denoted by i′ and i″ represent $-1+x,y,z$ and $-1+x,y,1+z$, respectively.

Table 7. *Hydrogen-bond lengths and angles*

Symmetry operations are: i at x,y,z; ii at $x,y,1+z$; iii at $x,y,-1+z$; iv at $1-x,1-y,z$; v at $\frac{1}{2}+x,\frac{1}{2}-y,-z$; vi at $\frac{1}{2}+x,\frac{1}{2}-y,1-z$; vii at $-\frac{1}{2}+x,\frac{1}{2}-y,1-z$.

Atom 1	Atom 2	Atom 3	Distance 1–3	Distance 2–3	Angle 3–1–2
N(6)——	H(N6)······	O(2'$^{\mathrm{vii}}$)	3·060 (7) Å	2·32 (6) Å	26 (5)°
O(8)——	H(O8)······	N(1$^{\mathrm{ii}}$)	3·011 (8)	2·21 (8)	7
O(2')——	H(O2')·····	N(4$^{\mathrm{iii}}$)	2·825 (7)	1·96 (7)	2
O(3')——	H(O3')·····	O(*W*1$^{\mathrm{v}}$)	2·774 (7)	2·08 (8)	22
O(5')——	H(O5')·····	N(1$^{\mathrm{iv}}$)	2·892 (8)	2·07 (9)	15
O(*W*1)–	H'(O*W*1)···	O(3'$^{\mathrm{vii}}$)	2·926 (7)	2·04 (9)	24
O(*W*1)–	H(O*W*1)····	O(8$^{\mathrm{vi}}$)	2·766 (6)	1·99 (6)	4
O(*W*2)–	H*··········	O(1'$^{\mathrm{vii}}$)	3·002 (5)	—	—
C(2)——	H(C2)······	O(*W*2$^{\mathrm{v}}$)	3·226 (9)	2·17 (7)	21

* This atom was not located.

Table 8. *Intermolecular distances less than* 3·5 Å

H atoms are not included.

From atom 1 at i	To atom 2	Distance
C(3')	O(*W*1$^{\mathrm{v}}$)	3·331 (8) Å
O(2')	O(*W*1$^{\mathrm{v}}$)	3·129 (6)
C(2)	O(*W*2$^{\mathrm{vi}}$)	3·441 (9)
N(3)	O(*W*2$^{\mathrm{vi}}$)	3·433 (7)
O(2')	C(7$^{\mathrm{vi}}$)	3·349 (9)
O(3')	N(6$^{\mathrm{vi}}$)	3·228 (7)
N(1)	C(5'$^{\mathrm{iv}}$)	3·469 (9)
N(4)	C(2$^{\mathrm{ii}}$)	3·266 (9)
N(4)	C(2'$^{\mathrm{ii}}$)	3·492 (8)
C(5)	C(2$^{\mathrm{ii}}$)	3·488 (9)
C(5)	O(2'$^{\mathrm{ii}}$)	3·470 (8)
C(5)	O(*W*1$^{\mathrm{ii}}$)	3·322 (9)
N(6)	O(*W*1$^{\mathrm{ii}}$)	3·243 (8)
C(1')	O(2'$^{\mathrm{ii}}$)	3·360 (8)
O(1')	C(2'$^{\mathrm{ii}}$)	3·266 (8)

Symmetry operations are listed in Table 7.

chain lines and their bond lengths and angles are listed in Table 7.

The two molecules related by a diad axis are bound together by the O(5')–H...N(1) hydrogen bonds. The water molecule O(*W*2) lying on the diad axis also binds these two molecules with the weak O(1')···H–O(*W*2) hydrogen bonds.

As shown in Table 8 and Fig. 4, most of the closest molecular approaches are seen between those molecules translated along the *c* axis. On account of the large angle of tilt (48·7°) of the imidazole ring to the *c* axis, the perpendicular distance between the successive base planes becomes short (3·256 Å). The bases on these planes are partly overlapped and some short distances, N(4)···C(2) 3·266, C(5)···C(2) 3·488 Å, are observed between the bases in addition to the hydrogen bonds O(8)–H···N(1).

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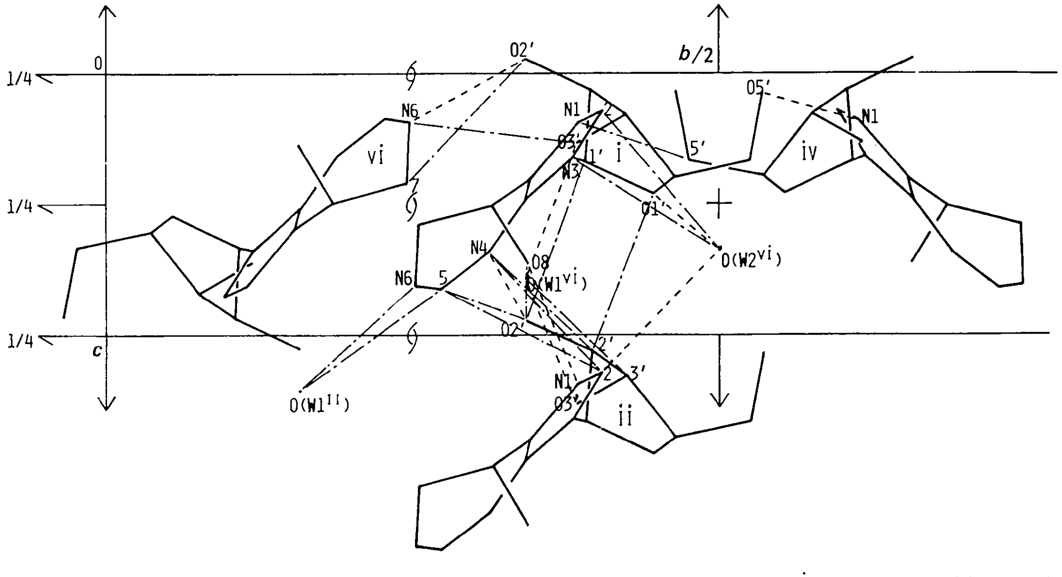

Fig. 4. Projection of the crystal structure along the *a* axis. Hydrogen bonds are shown by broken lines and intermolecular short contacts listed in Table 8 are shown by chain lines.

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The Crystal and Molecular Structure of 2,3,4,5-Tetrachlorotricyclo[4,2,2,$0^{2,5}$]deca-3,7-diene ($C_{10}H_8Cl_4$)

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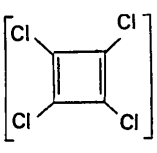
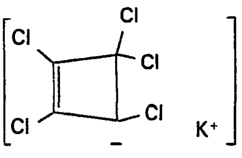
The title compound crystallizes in space group $P2_1/c$ with $a=7{\cdot}556$ (1), $b=18{\cdot}545$ (2), $c=8{\cdot}496$ (1) Å, $\beta=113{\cdot}73$ (1)°, and $Z=4$. The structure was determined by direct methods from data collected on a fully automated X-ray diffractometer. Full-matrix least-squares refinement of 128 parameters based on 3362 independent reflections [$\sin\theta/\lambda(\text{Mo } K\alpha)\le 0{\cdot}725$] yielded a final $R=0{\cdot}045$. An unusually long C–C single bond (1·591 Å) is observed in the highly strained junction between the cyclobutene ring and the bicyclohexene ring system.

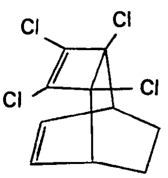
Introduction

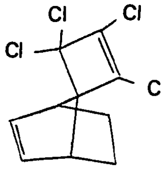
The reaction of 3*H*-pentachlorocyclobutene with potassium bases apparently (Scherer & Meyers, 1968, 1969) generates the unstable molecule tetrachlorocyclobutadiene (1) by β elimination of chloride ion from intermediate (2). Empirical evidence suggests that both (1) and (2) can be intermediates in subsequent reactions (Willcott & Cargle, 1967; Scherer & Meyers, 1969; Semmelhack & DeFranco, 1972).


(1)


(2)

If (1) is the important intermediate, the product of the reaction between basic 3*H*-pentachlorocyclobutene and 1,3-cyclohexadiene would be (3) [2,3,4,5-tetrachlorotricyclo[4,2,2,$0^{2,5}$]deca-3,7-diene (TCTCDD)]; if intermediate (2) predominates, (4) would be the principal product.


(3)


(4)

The present analysis proves that (3) is the principal product of this reaction. A complete summary of additional evidence pertaining to the possible intermediates (1) and (2) in this and related systems is given by Semmelhack & DeFranco (1972).

Experimental

Colorless crystals, which proved to be TCTCDD, were supplied by Drs M. F. Semmelhack and R. J. DeFranco of the Cornell University Department of Chemistry. The crystals turned yellow when exposed to X-rays in the open atmosphere; this effect was eliminated by sealing a crystal ($0{\cdot}7\times0{\cdot}5\times0{\cdot}5$ mm, $D_m=1{\cdot}646$ g cm^{-3})

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