Crystal Structures of Analogues of Purine-Nucleoside.
I. *cis*-1-(6-Acetoxymethyltetrahydro-2-pyranyl)-5,6-dichlorobenzotriazole (*cis*-ATD)

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cis-ATD was synthesized as a potential antimetabolite. 2997 independent reflexions were measured on an automatic diffractometer. The crystal structure was solved by the heavy-atom technique and refined by the least-squares method to $R=0.064$. The benzotriazole and the acetoxymethyl groups are planar-resonances and the tetrahydropyranyl group forms a regular chair. The torsion angles χ, ψ and φ in the acetoxymethyl group are indicative of the usual extended chain conformation for nucleosides but with the unusual *syn* orientation like that in the antibiotic formicin. $C-H \cdots N$ hydrogen bonds, which allow the molecules to pack into centrosymmetric dimers, are indicated. It is suggested that hydrogen bonding of this type could also occur in purine.

Introduction

The biological activity of the *cis*-ATD compound and other analogous derivatives is unknown. These compounds were synthesized by García Muñoz, Iglesias, Lora-Tamayo, Madroñero & Stud (1969) for the study of their activities as potential antimetabolites of purine-nucleosides. Analogous compounds, the D-ribofuranosides of 5,6-dichlorobenzotriazole (DRD), are antiviriasics (Tamm, Bablanian, Nemes, Shunk, Robinson & Kolkers, 1961). Fig. 1 illustrates the formula of a DRD(I) compound in comparison with that of *cis*-ATD(II) whose crystalline structure has been determined in the present work.

Although any type of structure-activity relationship is, in principle, rather difficult to ascertain, various attempts along these lines have already been reported (Ward, 1969). Some data derived from the present work may be relevant for the study of these relationships.

Experimental

Crystals of *cis*-ATD are transparent prisms, elongated along the *c* axis. The lattice constants were measured using nine separate reflexions at $\theta \simeq 30°$ (Cu $K\alpha$) on a four-circle diffractometer, and are shown in Table 1. The experimental density was measured by flotation in an aqueous potassium iodide solution.
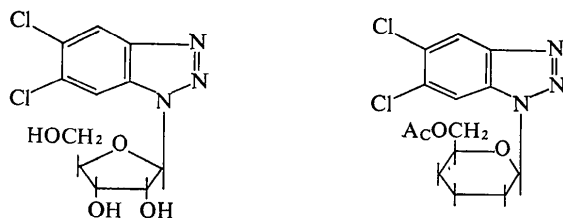

Fig. 1. DRD(I) and *cis*-ATD(II).

Table 1. *Crystal data for cis-ATD*

Standard deviations, given in parentheses, refer to the least significant digits.

Formula	$C_{14}H_{15}O_3N_3Cl_2$
Molecular weight	344·21
Wavelength (Cu $K\bar{\alpha}$)	1·5418 Å
a	12·178 (2) Å
b	11·680 (2)
c	5·686 (1)
α	93·2 (1)°
β	98·4 (1)
γ	95·1 (1)
V	794·6 (4) Å³
Z	2
D_{obs} (flotation)	1·40 g.cm⁻³
D_{cal}	1·43
μ (Cu $K\alpha$)	36·77 cm⁻¹
F(000)	356
Space group	$P\bar{1}$

The intensities were measured on an automatic Siemens four-circle diffractometer AED. A crystal with dimensions: $0.23 \times 0.10 \times 0.30$ mm was used for measuring 2997 independent reflexions at $5° < \theta < 70°$ using a coupled $\theta-2\theta$ scan, 188 of these reflexions having C_b (background counts) larger than C_p (peak counts). 951 reflexions were considered as unobserved according to the following criterion:

$$I < 2\sigma(I),$$

where

$$I = C_p - C_b$$

and

$$\sigma^2(I) = C_p + C_b + (0.005)^2 I^2;$$

I is the integrated intensity and $\sigma(I)$ is the estimated standard deviation of *I*. No correction was made for absorption. The total counting time, *Tm*, per reflexion was variable: $Tm = 4(100\Delta\theta)\delta T$, where $\Delta\theta$ is the variable amplitude scan and δT is the individual counting time for each θ step of 0·01°. The normal values for $\Delta\theta$, δT and *Tm* were 1°, 0·12 sec and 48 sec

respectively. The counting time per peak was twice the time for each background.

The validity of the data is indicated by the values $\sum\sigma(F_o)/\sum F_o = 0.029$ for 3350 measurements and $\sum|\Delta F_o|/\sum F_o = 0.043$ for 343 $hk0 = \bar{h}\bar{k}0$ reflexions, where $\sigma(F_o)$ is the estimated standard deviation of the observed structure factor, and $\Delta F_o = F_{hk0} - F_{\bar{h}\bar{k}0}$.

The statistical distribution of the normalized structure factors, $E = 0.83$, $\bar{E}^2 = 0.982$ and $\langle E^2 - 1\rangle = 0.913$, in comparison with the theoretical values by Karle, Dragonette & Brenner (1965), suggests that the space group for cis-ATD is $P\bar{1}$; this was confirmed after the structure was solved.

Structure determination and refinement

The positional parameters for the two chlorine atoms were obtained from a three-dimensional Patterson map. All remaining non-hydrogen atoms were located on a three-dimensional electron density map. At this stage, refinement was started by the full-matrix least-squares method, where the function minimized was $\sum w(\Delta F)^2$. A Cruickshank weighting scheme was used to make $\langle w\Delta^2 F\rangle \sim 1$ when analysed against F_o. After the isotropic least-squares refinement, the R value was 0.212. A subsequent anisotropic refinement improved it to 0.087. In the calculation of the reliability index, $R = \sum|F_o - |F_c||/\sum F_o$, and in these refinements, the 951 non-observed reflexions were not included.

The positions of the 15 hydrogen atoms were determined from the usual $(F_o - F_c)$ synthesis, calculated with 1643 reflexions with $\sin\theta/\lambda < 0.5$ and $F_c > F_o \times 0.15$. The electron density of 11 hydrogen atoms was $0.48 \geq \varrho \geq 0.36$ e.Å^{-3}. The lower limit of 0.36 e.Å^{-3} corresponds to the 15th highest peak of the map. The electron density of the other four hydrogen atoms was

$0.32 > \varrho > 0.25$ e.Å^{-3}, see Table 3. The apparently toroidal electron cloud around the C(8') methyl group suggests the presence of disorder in the hydrogen atoms of this group. A new structure factor calculation, including the hydrogen atoms with isotropic temperature factors equal to those of the neighbouring carbon atoms, decreased the R index to 0.077. No extinction effects were observed.
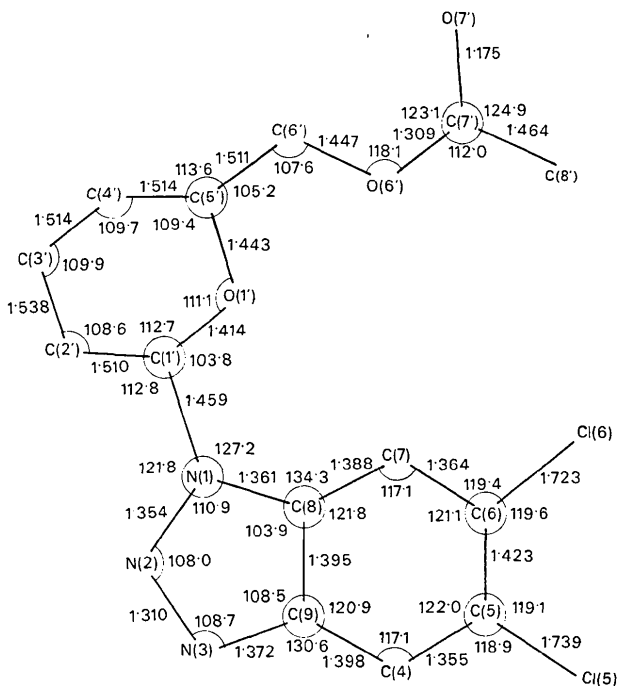

Fig. 2. Bond distances and angles between non-hydrogen atoms. Average standard deviations including Cl atoms: 0.0034 Å and 0.25°; including C(8'): 0.0071 Å and 0.43°; the rest with 0.0045 Å and 0.30°.

Table 2. *Atomic fractional coordinates and thermal parameters for non-hydrogen atoms*

Thermal factors are exp $(-2\pi^2\sum U_{ij}a_i^*a_j^*h_ih_j)$. Standard deviations, given in parentheses, refer to the least significant digits.

	10^4x	10^4y	10^4z	10^3U_{11}	10^3U_{22}	10^3U_{33}	10^3U_{12}	10^3U_{13}	10^3U_{23}
Cl(5)	1912 (1)	−2537 (1)	−949 (2)	116 (1)	51 (1)	86 (1)	10 (1)	21 (1)	−12 (1)
Cl(6)	2995 (1)	−1332 (1)	3978 (2)	120 (1)	80 (1)	63 (1)	41 (1)	2 (1)	9 (1)
N(1)	1229 (2)	2265 (2)	719 (4)	66 (1)	48 (1)	44 (1)	5 (1)	−15 (1)	−5 (1)
N(2)	643 (2)	2422 (2)	−1434 (5)	77 (2)	60 (2)	43 (1)	7 (1)	−15 (1)	−1 (1)
N(3)	537 (2)	1446 (2)	−2736 (5)	73 (2)	65 (2)	43 (1)	1 (1)	−11 (1)	−8 (1)
C(4)	1167 (3)	−515 (3)	−2001 (6)	73 (2)	57 (2)	47 (2)	−5 (1)	2 (1)	−12 (1)
C(5)	1743 (3)	−1095 (3)	−311 (6)	74 (2)	51 (2)	56 (2)	1 (1)	13 (1)	−9 (1)
C(6)	2237 (3)	−553 (3)	1945 (6)	67 (2)	58 (2)	48 (2)	9 (1)	7 (1)	0 (1)
C(7)	2110 (3)	570 (3)	2535 (5)	66 (2)	57 (2)	36 (2)	5 (1)	−6 (1)	−7 (1)
C(8)	1511 (2)	1165 (2)	818 (5)	59 (2)	45 (1)	42 (2)	−2 (1)	−5 (1)	−9 (1)
C(9)	1051 (2)	642 (3)	−1417 (5)	58 (2)	54 (2)	42 (2)	−2 (1)	−4 (1)	−6 (1)
C(1')	1441 (3)	3176 (3)	2637 (6)	65 (2)	51 (2)	49 (2)	2 (1)	−10 (1)	−9 (1)
C(2')	1124 (3)	4327 (3)	1821 (7)	81 (2)	55 (2)	69 (2)	10 (2)	−12 (2)	−4 (2)
C(3')	1508 (3)	5248 (3)	3886 (8)	86 (2)	54 (2)	86 (3)	14 (2)	−5 (2)	−14 (2)
C(4')	2733 (4)	5201 (3)	4803 (8)	90 (2)	47 (2)	86 (3)	4 (2)	−4 (2)	−21 (2)
C(5')	2934 (3)	3998 (3)	5510 (7)	87 (2)	49 (2)	64 (2)	1 (2)	−24 (2)	−19 (2)
O(1')	2594 (2)	3187 (2)	3469 (4)	67 (1)	44 (1)	56 (1)	4 (1)	−17 (1)	−14 (1)
C(6')	4147 (4)	3848 (3)	6320 (8)	99 (3)	49 (2)	84 (3)	−4 (2)	−36 (2)	−8 (2)
O(6')	4197 (3)	2738 (2)	7321 (5)	113 (2)	52 (1)	90 (2)	−1 (1)	−50 (2)	−7 (1)
C(7')	4783 (3)	2694 (3)	9430 (8)	77 (2)	69 (1)	80 (3)	10 (1)	−11 (2)	−4 (2)
O(7')	5298 (4)	3504 (3)	10504 (7)	182 (4)	81 (2)	115 (3)	3 (2)	−73 (3)	−15 (2)
C(8')	4732 (5)	1525 (5)	10238 (13)	98 (4)	99 (4)	128 (5)	17 (3)	−3 (3)	41 (3)

Finally, a refinement with anisotropic thermal motion for the heavy atoms and fixed isotropic thermal motion for the hydrogen atoms was carried out. The atomic scattering factor for the chlorine atom was corrected for anomalous dispersion. After three cycles, the (shift/σ) ratio was less than 0·2 for all heavy-atom parameters, and less than 0·7 for the hydrogen coordinates. The final R values were: $R_{obs}=0·064$, $R_{all}=0·087$, $R_1=0·99$, where $R_1=[\sum w(F_o-|F_c|)^2/(NO-NV]^{1/2}$, $NO=2436$ reflexions and $NV=245$ variables. (Because I_{unobs} was taken as $I+2\sigma(I)$, two scale factors, for F_{obs} and F_{unobs}, were used.)

The refined parameters are collected in Tables 2 and 3. A list of observed and calculated structure factors is available from the authors on request. The atomic scattering factors used are those of Hanson, Herman, Lea & Skillman (1964) for the heavy atoms, and those of Stewart, Davidson & Simpson (1965) for the hydrogen atoms.

Table 3. Atomic fractional coordinates and thermal parameters, $U=B/8\pi^2$, for hydrogen atoms

Standard deviations, given in parentheses, refer to the least significant digits.

	10^3x	10^3y	10^3z	10^3U	ϱ e.Å^{-3}
H(4)	81 (3)	−89 (3)	−347 (7)	57 (3)	0·44
H(7)	242 (3)	92 (3)	387 (6)	49 (3)	0·40
H(1′a)	94 (3)	295 (3)	399 (6)	51 (3)	0·45
H(2′a)	159 (3)	452 (3)	37 (7)	68 (4)	0·45
H(2′e)	30 (3)	431 (3)	136 (7)	68 (4)	0·46
H(3′a)	105 (3)	507 (3)	539 (8)	76 (4)	0·48
H(3′e)	128 (3)	601 (4)	328 (7)	76 (4)	0·32
H(4′a)	329 (3)	539 (3)	355 (7)	72 (4)	0·25
H(4′e)	290 (3)	581 (3)	624 (7)	72 (4)	0·38
H(5′a)	238 (3)	375 (3)	692 (6)	63 (3)	0·39
H(6′a)	456 (3)	385 (3)	479 (8)	73 (4)	0·36
H(6′e)	450 (3)	445 (3)	773 (7)	73 (4)	0·41
H(8′1)	516 (4)	146 (4)	1177 (9)	92 (5)	0·41
H(8′2)	407 (4)	124 (4)	1065 (9)	92 (5)	0·29
H(8′3)	516 (4)	109 (4)	953 (9)	92 (5)	0·26

Results and discussion

The bond lengths and angles involving the non-hydrogen atoms are shown in Fig. 2. Bond lengths and angles involving hydrogen atoms are listed in Table 4. The more significant intermolecular distances are given in Table 5 and those between heavy atoms are also shown in Fig. 3. Distances and angles are uncorrected for thermal motion.

A three-dimensional model of the cis-ATD molecule showing the torsional angles $\chi[C(8)N(1)C(1')O(1')]$, $\psi[C(4')C(5')C(6')O(6')]$, $\varphi[C(5')C(6')O(6')C(7')]$ and $\omega[C(6')O(6')C(7')C(8')]$ is illustrated in Fig. 4. In Fig. 5 the hydrogen atoms are shown.

The intramolecular distance C(7)–O(1′) of 3·063 (4) Å is a little shorter than the sum of the van der Waals radii, 3·16 Å. This is probably due to the syn conformation of the molecule. No other anomalous intramolecular distance was found. The intramolecular distance Cl(5)–Cl(6) is 3·119 (1) Å. The benzene

Table 4. Bond distances and angles involving hydrogen atoms

Average standard deviation 0·038 Å, 2·0° for CCH and 3·0° for HCH. For bonds involving C(8′) the standard deviations are 0·051 Å, 3·1 and 4·4° respectively.

C(4)–H(4)	0·95 Å	C(9)—C(4)–H(4)	121°
		C(5)—C(4)–H(4)	122
C(7)–H(7)	0·86	C(8)—C(7)–H(7)	121
		C(6)—C(7)–H(7)	122
C(1′)–H(1′a)	1·08	O(1′)—C(1′)–H(1′a)	112
		N(1)—C(1′)–H(1′a)	109
		C(2′)—C(1′)–H(1′a)	107
C(2′)–H(2′a)	1·09	C(1′)—C(2′)–H(2′a)	106
		C(3′)—C(2′)–H(2′a)	108
		H(2′e)–C(2′)–H(2′a)	114
C(2′)–H(2′e)	1·00	C(1′)—C(2′)–H(2′e)	111
		C(3′)—C(2′)–H(2′e)	109
C(3′)–H(3′a)	1·11	C(2′)—C(3′)–H(3′a)	110
		C(4′)—C(3′)–H(3′a)	107
C(3′)–H(3′e)	1·02	C(2′)—C(3′)–H(3′e)	107
		C(4′)—C(3′)–H(3′e)	116
		H(3′a)-C(3′)–H(3′e)	107
C(4′)–H(4′a)	1·08	C(3′)—C(4′)–H(4′a)	116
		C(5′)—C(4′)–H(4′a)	105
		H(4′e)-C(4′)–H(4′a)	110
C(4′)–H(4′e)	1·04	C(3′)—C(4′)–H(4′e)	104
		C(5′)—C(4′)–H(4′e)	113
C(5′)–H(5′a)	1·16	C(4′)—C(5′)–H(5′a)	109
		O(1′)—C(5′)–H(5′a)	107
		C(6′)—C(5′)–H(5′a)	112
C(6′)–H(6′a)	1·07	C(5′)—C(6′)–H(6′a)	108
		O(6′)—C(6′)–H(6′a)	109
		H(6′e)-C(6′)–H(6′a)	115
C(6′)–H(6′e)	1·05	C(5′)—C(6′)–H(6′e)	111
		O(6′)—C(6′)–H(6′e)	105
C(8′)–H(8′1)	0·96	C(7′)—C(8′)–H(8′1)	114
C(8′)–H(8′2)	0·91	C(7′)—C(8′)–H(8′2)	116
C(8′)–H(8′3)	0·88	C(7′)—C(8′)–H(8′3)	112
		H(8′1)-C(8′)–H(8′2)	95
		H(8′1)-C(8′)–H(8′3)	92
		H(8′2)-C(8′)–H(8′3)	122

Table 5. The shorter intermolecular distances

Less than 3·5 Å for non-hydrogen to non-hydrogen distances (e.s.d. = 0·0046 Å). Less than 3,0 Å for non-hydrogen to hydrogen distances (e.s.d. = 0·038 Å). Less than 2·75 Å for hydrogen to hydrogen distances (e.s.d. = 0·055 Å).

		Second atom in position		
C(4)—N(3)	3·446 Å	−x	−y	−1−z
C(8)—C(4)	3·454	−x	−y	−z
C(6′)—O(7′)	3·456	x	y	−1+z
C(5)—N(2)	3·472	−x	−y	−z
C(5)—N(3)	3·487	−x	−y	−z
C(4′)—O(7′)	3·494	x	y	−1+z
O(7′)—H(6′e)	2·52	1−x	1−y	2−z
N(3)—H(4)	2·53	−x	−y	−1−z
O(7′)—H(4′e)	2·68	1−x	1−y	2−z
N(3)—H(1′a)	2·70	x	y	−1+z
O(7′)—H(6′a)	2·74	x	y	1+z
N(2)—H(1′a)	2·78	x	y	−1+z
N(2)—H(5′a)	2·81	x	y	−1+z
C(7)—H(8′2)	2·83	x	y	−1+z
Cl(5)—H(4′e)	2·89	x	−1+y	−1+z
C(2′)—H(2′e)	2·95	−x	1−y	−z
H(2′e)–H(2′e)	2·38	−x	1−y	−z
H(2′a)–H(5′a)	2·46	x	y	−1+z
H(3′a)–H(3′a)	2·52	−x	1−y	1−z
H(8′3)–H(8′3)	2·63	x	−y	2−z
H(4′a)–H(6′a)	2·70	1−x	1−y	1−z
H(2′e)–H(3′a)	2·75	−x	1−y	1−z

ring is slightly elongated along the C(4)–C(7) direction.

The benzotriazole group has a resonance structure with some double-bond character for the C(4)–C(5), C(6)–C(7), C(8)–C(9) and N(2)–N(3) bonds.

The C–N bond distances are normal for compounds of this type, such as purine (Watson, Sweet & Marsh, 1965). The N–N bond distances are in resonance between a double bond, 1·26 Å, and a single bond 1·46 Å (Sabesan & Venkatesan, 1971).

Equations of the more important least-squares planes through various groups of atoms in the molecule and the deviations of the atoms from these planes are presented in Table 6. The dihedral angles between these planes are also given.

The atoms Cl(5), Cl(6), C(1′), H(4) and H(7) are out of the C plane by −0·01, 0·07, −0·09, −0·08 and 0·05 Å respectively.

The acetoxymethyl group lies in the B plane and its bond lengths indicate the resonance present. In the normally disordered methyl group, the best localized hydrogen atom H(8′1) is at 0·01 (5) Å from the B plane.

In Table 6, the data for the D plane indicate that the pyranyl group has a regular chair form. The distances of the axial and the equatorial hydrogen atoms from the D plane are 1·31 to 1·40 Å, and 0·09 to 0·19 Å respectively.

The crystalline structure of the cis-ATD as illustrated in Fig. 3 is of laminar type with a distance between layers about 3·0 Å. Equation A of Table 6 indicates the degree of planarity of the molecule.

Hydrogen bonds

There are various factors that point to the existence of weak hydrogen bonds C–H···N between cis-ATD molecules. These are:

(a) The distances and angles shown in Fig. 6

The N(3)–H(4) distance of 2·53 (3) Å is less than the sum of the van der Waals radii 1·57 + 1·17 = 2·74 Å (Kitaigorodsky, 1961).

The deviation [0·08 (3) Å] of the atom H(4) from the benzotriazole plane in the direction of its acceptor, N(3), could also be significant.

Fig. 3. View of the cis-ATD structure along the b axis. The shorter van der Waals contacts, including the probable H-bonds of 3·446 (4) Å, are indicated.

(b) The probable donor character of the aromatic C(4) in the benzotriazole group

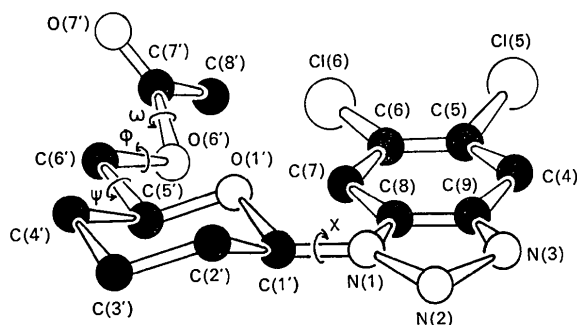Allerhand & Schleger (1963) investigated by infrared spectroscopy the ability of the C–H bond to be

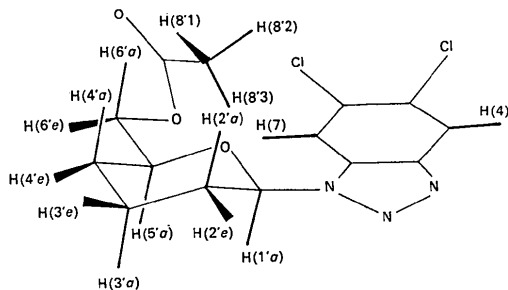Fig. 4. A view of the cis-ATD molecule conformation, showing the torsional angles $\chi = -38\cdot8°$, $\psi = -170\cdot3°$, $\varphi = 129\cdot8°$ and $\omega = -178\cdot4°$.

Fig. 5. As Fig. 4, showing the location of hydrogen atoms.
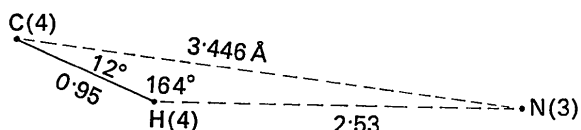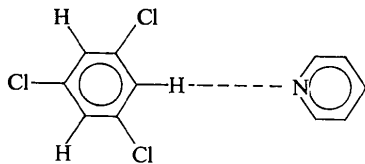

Fig. 6. Probable H-bond in cis-ATD structure.

Fig. 7. H-bond between 1,3,5-trichlorobenzene and pyridine-d_5.

involved in hydrogen bonding. They concluded that some C(sp^2)–H compounds give evidence of proton-donating ability in hydrogen bonding, e.g. polysubstituted benzene derivatives with at least three strongly electron-withdrawing substituents. These authors found that while 1,3,5-trichlorobenzene (Fig. 7) and 3,5-dinitro-2,4,6-trichlorobenzene form hydrogen bonds with strong proton acceptors (pyridine-d_5), in m-dichlorobenzene the existence of hydrogen bonds represents a borderline case.

In a similar way the C(4) (sp^2) of the cis-ATD molecule could act as a proton donor.* This fact could partially explain the abnormal distance of the three bonds to C(5) (Fig. 2). The larger double bond character of the C(4)–C(5) bond results in a lengthening of the C(5)–C(6) and C(5)–Cl(5) bonds compared with the expected values of 1·395 for C–C aromatics and 1·709 Å for C(aromatic)–Cl (Rudman, 1971).

(c) The probable acceptor character of the aromatic N(3) in the benzotriazole group

It is well known that a nitrogen atom in an unsaturated ring can be an excellent hydrogen-bond donor or an equally good acceptor (Marsh, 1967).

Thus, the donor character of C(4) and acceptor character of N(3) could lead to the zwitterion of Fig. 8.

Assuming the existence of weak hydrogen bonds, the cis-ATD molecules would then form dimers lying across symmetry centres (Fig. 3). The distance between the two benzotriazole planes forming each dimer is 0·56 Å.

As far as we know, no references to hydrogen bonds of the type C–H···N in crystal structure determinations are available. In the crystal structure of purine (Watson et al., 1965), however, there are two groups C–H···N around helicoidal axes, Fig. 9, that could similarly be considered to be weak hydrogen bonds. In this case, structures of the purine types (e) and (f) (Fig. 10) (Marsh, 1967) ought to be taken into account.

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* The existence of a hydrogen bond, C–H···N, was tested using the infrared spectra in solid and solution samples of the substance. The spectrum of cis-ATD in CCl₄ solution shows an absorption band at 3102 cm⁻¹ that may be assigned to the C–H stretching vibration of the aromatic ring. In the solid state (KBr pellet), four absorption bands are observed between 3000 and 3100 cm⁻¹ at 3020, 3040, 3067 and 3092 cm⁻¹. Nevertheless, the interpretation of the spectrum in the solid state is not easy and precludes the reaching of any conclusion about the formation of a hydrogen bond in the cis-ATD crystals.

Table 6. Some least-squares planes in the molecule (minus hydrogen atoms) and their dihedral angles

The normalized equations $lx + my + nz = d$ are referred to triclinic axes.

Plane	Group	l	m	n	d	$|\delta|$	$|\delta_{max}|$	$|\delta_{min}|$
A	Molecule (22 atoms)	−0·8002	−0·1632	0·6774	−1·520	0·28 Å	0·82 Å	
B	Acetoxymethyl (5 atoms)	−0·8857	0·2228	0·5528	−1·497	0·008	0·016	
C	Benzotriazole (9 atoms)	0·8877	0·2159	−0·4987	1·706	0·008	0·021	
D	Pyranyl (6 atoms)	−0·6199	−0·2233	0·8333	−0·897	0·237	0·250	0·217 Å

$AB = 23\cdot3$, $AC = 12\cdot8$, $AD = 14\cdot8$, $BC = 25\cdot9$, $BD = 33\cdot7$, $CD = 26\cdot7°$.

Conformation

It does not seem probable that a *cis* analogue of purine nucleoside could be inserted in a DNA or RNA molecule.

The torsion angles χ, ψ, φ and ω indicated in Fig. 4 and defined by Sundaralingam (1969) have been calculated for the *cis*-ATD. These values are $\chi = -38{\cdot}8$, $\psi = -170{\cdot}3$, $\varphi = 129{\cdot}8$ and $\omega = -178{\cdot}4°$ (or the set of angles of the opposite sign for the enantiomorphic molecule).

The torsion angle of the glycoside bond χ shows a *syn* conformation. Ward (1969) has suggested that though the nucleoside conformation in the double chains is *anti*, a *syn-anti* interconversion would not be difficult in purine nucleosides. Thus it is found that the antibiotic formicin, a highly cytotoxic compound analogous to adenosine, preserves the *syn* conformation in crystals, the mixed conformation in single stranded molecules and the *anti* conformation in ordered Watson–Crick type double stranded helices (Ward, 1969). In addition, the same author has pointed out that if a significant proportion of H-bonded nucleoside units adopt any conformation other than *anti* there will be a tendency to reduce the stability of the helical structures.

The values of ψ and φ are in the permitted region of the (ψ, φ) plane, Sundaralingam (1969). The value $\psi \simeq 180°$ corresponds to the more populated conformation (of less energy) detected in the liquid state by n.m.r. (M. Rico, unpublished results). The sign of φ is such that $O(7')$ tends to be in the mean plane of the molecule *i.e.* in the equatorial direction. Similar values for (ψ, φ) have been found in the nucleotide adenosine 3'-phosphate dihydrate, Sundaralingam (1969).
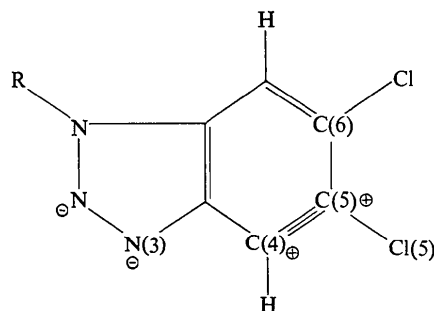
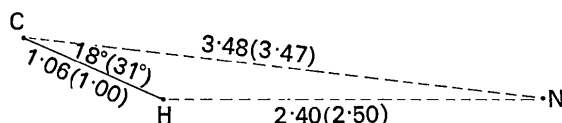Fig. 8. Possible zwitterion for the *cis*-ATD structure.

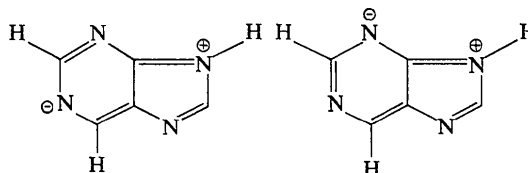Fig. 9. The two suspected H-bonds in the purine structure.

Fig. 10. Other zwitterions suggested for the purine structure.

References

ALLERHAND, A. & SCHLEYER, P. VON R. (1963). *J. Amer. Chem. Soc.* **85**, 1715.

GARCÍA-MUÑOZ, G., IGLESIAS, J., LORA-TAMAYO, M., MADROÑERO, R. & STUD, M. (1969). *J. Heterocyclic Chem.* **6**, 5.

HANSON, H. P., HERMAN, F., LEA, I. D. & SKILLMAN, S. (1964). *Acta Cryst.* **17**, 1040.

KARLE, I. L., DRAGONETTE, K. S. & BRENNER, S. A. (1965). *Acta Cryst.* **19**, 713.

KITAIGORODSKY, A. I. (1961). *Organic Chemical Crystallography.* New York: Consultants Bureau.

MARSH, R. E. (1967). *Structural Chemistry and Molecular Biology,* p. 484. San Francisco: Freeman.

RUDMAN, R. (1971). *Acta Cryst.* **B27**, 262.

SABESAN, M. N. & VENKATESAN, K. (1971). *Acta Cryst.* **B27**, 990.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175.

SUNDARALINGAM, M. (1969). *Biopolymers,* **7**, 821.

TAMM, I., BABLANIAN, R., NEMES, M. M., SHUNK, C. H., ROBINSON, F. M. & KOLKERS, K. A. (1961). *J. Exp. Med.* **113**, 625.

WARD, D. C. (1969). *Annual Reports in Medicinal Chemistry,* p. 272. New York: Cain.

WATSON, D. G., SWEET, R. M. & MARSH, R. E. (1965). *Acta Cryst.* **19**, 573.