

# The Crystal and Molecular Structure of the Five-Membered-Ring Analogue of Vitamin-A Acid

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(Received 19 June 1970)

The crystal structure of the synthetically prepared five-membered-ring analogue of vitamin-A acid has been determined in order to establish the similarities with vitamin-A acid itself. The crystals of the analogue are monoclinic, space group  $P2_1/n$  with cell constants  $a=9.487$ ,  $b=8.260$ ,  $c=22.472$  Å,  $\beta=95.94^\circ$ ,  $Z=4$ . The structure has been solved with the help of a computerized version of the symbolic addition method. The final discrepancy index was 6.0%. The experimentally found planar conformation of the cyclopentene ring is probably not real but simulated by disorder. The planar conjugated system is in the all-*trans* configuration. The chain is curved in its plane. Owing to mutual steric interaction the carboxylic group and the methyl group C(19) are rotated by approximately  $15^\circ$  out of the normal conformations.

## Introduction

The five-membered-ring analogue of vitamin-A acid,  $C_{19}H_{26}O_2$ , also referred to as 5-vitacid, was synthesized by Huisman & Baas (1969). The molecular formula and the numbering of the atoms is given in Fig. 1.

The growth activity of the acetate of the five-membered-ring analogue of vitamin A is 50–60% compared with the activity of the acetate of vitamin A itself. The structural analysis of 5-vitacid was carried out in order to compare its molecular geometry with that of vitamin-A acid (Stam & MacGillivray, 1963).

## Experimental

The crystals of 5-vitacid are monoclinic. The unit cell was chosen such that the extinctions were  $h0l$  with

$h+k=\text{odd}$  and  $0k0$  with  $k=\text{odd}$  (space group  $P2_1/n$ ). The cell constants obtained by a least-squares method from Weissenberg diagrams calibrated with Al-powder lines are:

$$\begin{aligned} a &= 9.487 (2) \\ b &= 8.260 (1) \\ c &= 22.472 (2) \text{ \AA} \\ \beta &= 95.94 (2)^\circ. \end{aligned}$$

The experimental density measured by flotation was  $1.06 \text{ g.cm}^{-3}$ . For  $Z=4$  the calculated density is  $1.08 \text{ g.cm}^{-3}$ .

The intensities were collected by means of a Nonius automatic single-crystal diffractometer up to  $\theta=68.5^\circ$  with  $\theta-2\theta$  scanning. The background intensity was measured at both sides of the reflexion for half the scanning time. A reflexion was considered significant

Table 1. Final parameters and their *e.s.d.*'s

The positional parameters  $x, y, z$  values are given in fractions multiplied by  $10^4$ . The thermal parameters  $U_{ij}$  are given in  $\text{\AA}^2$  and multiplied by  $10^4$ .

	$x$	$\sigma(x)$	$y$	$\sigma(y)$	$z$	$\sigma(z)$	$U_{11}$	$U_{22}$	$U_{33}$	$2U_{12}$	$2U_{23}$	$2U_{31}$
C(1)	−0324	4	6085	5	2064	2	535	655	724	−006	075	268
C(2)	−1463	5	4970	6	2285	3	855	930	1804	−221	215	1351
C(3)	−1122	5	3254	6	2149	2	744	877	1125	−406	294	311
C(4)	0198	4	3347	5	1842	2	544	602	922	−095	274	078
C(5)	0667	4	4872	4	1793	2	498	496	791	−013	243	153
C(6)	1946	4	5271	4	1529	2	513	507	905	134	098	355
C(7)	2540	4	6721	4	1448	2	542	511	767	045	080	335
C(8)	3825	4	6995	4	1171	2	509	546	694	064	110	269
C(9)	4281	4	8530	4	1099	2	574	545	690	−042	043	334
C(10)	5516	4	9030	4	0820	2	534	576	632	028	122	284
C(11)	5905	4	0574	4	0764	2	589	579	693	012	091	391
C(12)	7123	4	1162	4	0483	2	586	559	595	041	095	346
C(13)	7355	4	2771	4	0489	2	685	504	848	067	075	681
C(14)	8506	4	3657	4	0251	2	701	503	718	023	012	512
C(15)	0818	5	1818	5	1632	3	792	518	1592	012	140	000
C(16)	0409	5	7028	7	2589	2	888	1347	725	−159	−330	273
C(17)	−0994	5	7261	6	1599	2	779	818	899	539	002	176
C(18)	4619	4	5549	5	0968	2	615	593	1399	184	165	808
C(19)	8023	4	9961	5	0196	2	703	549	965	044	010	712
O(1)	8274	3	5230	3	0225	1	795	455	1121	−022	050	773
O(2)	9593	3	3047	3	0101	1	718	552	1147	078	190	918

if the net count was greater than twice the standard deviation. In the observed part of the reciprocal space 1934 reflexions were significantly above zero. No absorption correction was applied.

### Solution and refinement

The carbon and oxygen atoms were located with the help of automatic computer programs (Schenk, 1969) based on the symbolic addition procedure (Karle & Karle, 1966). With 4 symbols and 3 origin defining reflexions as generators it was possible to give approximately 100 reflexions a symbolic sign with a probability of  $p > 0.99$ . A consistency analysis led to a classification of the  $2^4 = 16$  solutions in order of reliability. An  $E$  map of the most reliable solution, based on 250 signed reflexions, revealed all atoms of the molecule and showed no spurious peaks.

The refinement was carried out by means of a block-diagonal least-squares program using  $3 \times 3$  blocks for the positional parameters and  $6 \times 6$  blocks for anisotropic thermal parameters. The weights were calculated from  $w = 1/(2 + |F_o| + 0.03|F_o|^2)$  (Cruickshank, 1961). The form factors were those from *International Tables for X-ray Crystallography* (1962).

A difference synthesis revealed the hydrogen atoms, with peak heights between 0.3 and 0.5  $e.\text{\AA}^{-3}$ . However, the hydrogen atoms bonded to C(2) overlap, and their electron density has a more or less banana-form. The final least-squares cycles were carried out with anisotropic thermal parameters for the carbon and oxygen atoms and isotropic thermal parameters for the hydro-

gen atoms. The final  $R$  value was 6.0% for 1934 independent observed reflexions. The final parameters are given in the Tables 1 and 2. A Table of observed and calculated structure factors can be obtained from this laboratory.

Table 2. *Parameters of the hydrogen atoms with their e.s.d.'s (in brackets)*

The  $x, y, z$  values are given in fractions  $\times 10^3$ , and the  $B$  values in  $\text{\AA}^2$ .

	$x$	$\sigma(x)$	$y$	$\sigma(y)$	$z$	$\sigma(z)$	$B$
H(1)	751	7	920	9	003	3	9.5
H(2)	397	6	488	6	069	2	7.9
H(3)	842	10	-056	10	044	4	12.0
H(4)	542	5	583	6	076	2	5.5
H(5)	-236	8	536	9	201	3	13.0
H(6)	-200	6	530	6	258	2	9.5
H(7)	926	5	580	6	007	2	7.1
H(8)	083	6	616	7	291	2	8.9
H(9)	122	6	115	7	199	2	8.5
H(10)	013	7	130	8	129	3	10.1
H(11)	168	5	190	6	144	2	7.7
H(12)	-156	6	662	7	125	2	8.3
H(13)	-036	5	794	6	140	2	7.0
H(14)	-177	5	799	6	180	2	7.2
H(15)	116	5	769	6	247	2	7.0
H(16)	-033	5	766	6	286	2	7.8
H(17)	530	4	150	5	094	2	4.1
H(18)	-183	6	277	7	194	3	7.6
H(19)	-094	6	272	6	255	2	7.2
H(20)	209	3	773	4	158	1	1.7
H(21)	613	3	818	4	068	1	2.6
H(22)	669	4	352	5	065	2	4.2
H(23)	245	4	431	5	137	2	3.8
H(24)	867	4	044	5	-008	2	5.3
H(25)	363	3	945	4	125	2	2.6
H(26)	496	6	479	7	130	3	10.2

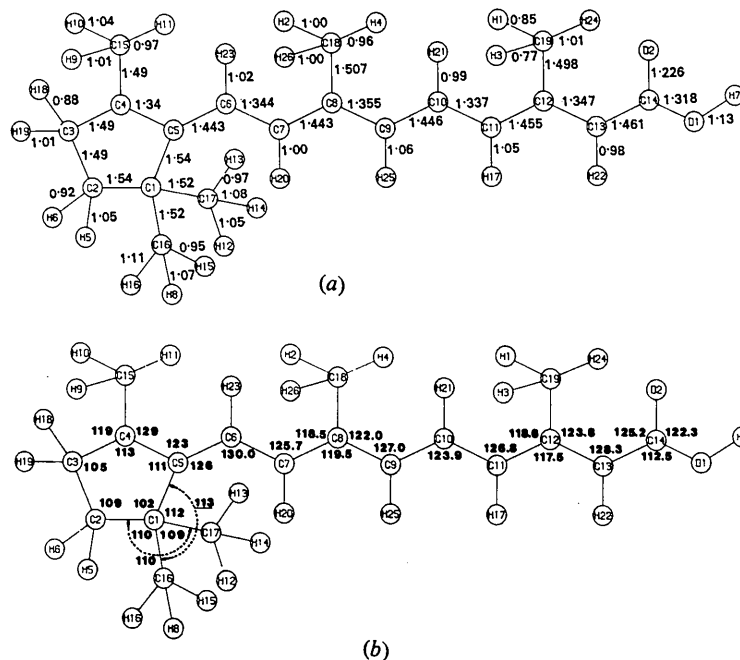


Fig. 1. (a) Bond lengths and (b) bond angles. The values given for the ring lengths and angles should be regarded with caution, because of possible disorder in this part of the molecule (see *Discussion*). For the other angles and lengths the e.s.d.'s are: 0.005 (C-C and C-O); 0.08 Å (C-H, O-H) and 0.35° (heavy atom angles).

## Discussion

## Disorder

The most striking features of the structure are the planarity of the cyclopentene ring (see Fig. 2), the small bond length C(2)–C(3) (1.49 Å, see Fig. 1) and the very high thermal parameters of some atoms (see Table 3), but we question the significance of these features.

The principal axes of largest root-mean-square amplitude (see Table 3) are all approximately in the direction of the normal to the plane of the molecule, which makes angles of 64.93 and 26° with the standard orthogonal axes (*y* parallel to **b**; *z* parallel to **c**\*). Some thermal parameters of the ring atoms C(2), C(3), C(4) and the ring-methyl groups C(15), C(16) and C(17) are abnormally large compared with those of the chain atoms. It is not very probable that this is a real effect because, if anything, one expects the cyclopentene ring

to have smaller thermal parameters than the chain, because the ring is more rigid.

A more plausible interpretation would be that the cyclopentene ring occurs in two different conformations as a result of disorder. In the related compounds canthaxanthin, 15-15'-dehydrocanthaxanthin (Bart & MacGillavry, 1968*a, b*) and retro-vitamin-A acid (Schenk, 1969) conformational disorder was found. In these cases only one atom in a substituted cyclohexene ring is out of the plane of the ring. The distance of this atom from the ring plane is more than 0.5 Å and therefore the disorder was found by the appearance of extra peaks in the electron density maps.

We investigated the disorder by means of models of 1,1,4-trimethylcyclopentene-5-carboxylic acid (Schenk, 1969) and its mirror image. In this molecule the pentene ring is in an envelope conformation with C(2) only 0.3 Å out of the ring plane. If we make the atoms C(1), C(5) and C(6) of the mirror images approximately coin-

Table 3. Root-mean-square amplitudes of the vibration ellipsoids of the heavy atoms with the angles *a*, *b* and *c* relative to the standard orthogonal axes *x*, *y* and *z*

	r.m.s.a.	<i>a</i>	<i>b</i>	<i>c</i>		r.m.s.a.	<i>a</i>	<i>b</i>	<i>c</i>		r.m.s.a.	<i>a</i>	<i>b</i>	<i>c</i>
C(1)	+0.2243 Å	163°	97°	74°	C(8)	+0.2707 Å	74°	72°	24°	C(15)	+0.4038 Å	101°	86°	12°
	+0.2743	77	70	24		+0.2299	85	21	110		+0.2801	168	93	101
	+0.2539	101	21	107		+0.2177	163	80	77		+0.2267	88	176	86
C(2)	+0.4472	69	87	21	C(9)	+0.2721	63	87	27	C(16)	+0.3741	82	163	76
	+0.3134	71	160	94		+0.2369	64	152	100		+0.2960	164	101	101
	+0.2227	151	110	69		+0.2208	141	118	65		+0.2595	103	78	18
C(3)	+0.2341	140	127	78	C(10)	+0.2644	68	64	35	C(17)	+0.2296	43	133	89
	+0.3469	99	60	31		+0.2352	114	29	106		+0.3272	133	137	89
	+0.3137	128	51	118		+0.2177	147	103	60		+0.2999	90	91	179
C(4)	+0.3140	100	69	23	C(11)	+0.2787	60	79	32	C(18)	+0.3854	74	83	17
	+0.2417	130	48	112		+0.2401	108	18	93		+0.2465	69	25	102
	+0.2252	139	131	83		+0.2193	145	104	58		+0.2127	153	66	78
C(5)	+0.2892	92	70	20	C(12)	+0.2660	53	72	43	C(19)	+0.3331	61	88	29
	+0.2239	161	73	98		+0.2344	111	22	95		+0.2353	75	18	100
	+0.2115	109	153	72		+0.2147	135	102	48		+0.2232	147	72	63
C(6)	+0.3050	78	82	15	C(13)	+0.3195	57	85	34	O(1)	+0.3553	63	89	27
	+0.2323	54	39	104		+0.2237	88	8	98		+0.2447	29	99	117
	+0.2084	142	52	86		+0.2151	147	84	57		+0.2125	98	170	85
C(7)	+0.2833	72	81	20	C(14)	+0.2960	49	88	41	O(2)	+0.3651	64	83	28
	+0.2252	77	23	104		+0.2256	53	54	123		+0.2331	104	14	91
	+0.2216	154	69	76		+0.2235	117	36	69		+0.2159	149	102	62

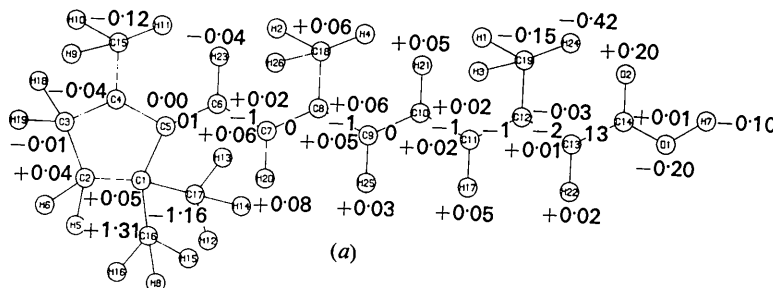


Fig. 2. The planarity of the molecule. The overall plane of the molecule was calculated with the method of Schomaker, Waser, Marsh & Bergman (1959) through all heavy atoms of the molecule except C(16) and C(17). The expression is  $0.4425X - 0.0485Y + 0.8954Z - 3.490 = 0$  in which *X*, *Y* and *Z* are the orthogonal coordinates. In the Figure the deviations of many of the atoms from this plane are given together with the torsional angles around the bonds.

cide and the alternative C(2)–C(3) bonds cross (see Fig. 3), then the distances between corresponding atoms in the two models vary between 0 and 0.3 Å. For each atom this distance is approximately equal to twice the excess of its largest r.m.s. amplitude over that of the chain atoms.

Thus it appears to be quite satisfactory to ascribe the high r.m.s. amplitudes of the ring atoms and their methyl groups to positional disorder. From the fact that the average pentene ring is planar one can then infer that both conformations occur on a 50–50 basis.

The disorder leads to the following conclusions:

(1) the planar conformation of the pentene ring (see Fig. 2) is not real;

(2) the bond lengths and angles involving the atoms C(1), C(2), C(3), C(4), C(5), C(15), C(16) and C(17) are unreliable;

(3) the 'thermal' parameters of these atoms cannot be used in a thermal analysis.

#### Configurational and conformational aspects

The configuration of the conjugated system is all-*trans*, which has been found only in *trans*- $\beta$ -ionylidene-crotonic acid (Eichhorn & MacGillavry, 1959). Other related structures have approximately 5-*cis*-conformations for the bonds connecting ring and chain (see compilation in Bart & MacGillavry, 1968*b*).

The methyl groups C(16) and C(17) form parts of staggered conformations [see Fig. 4(c) and (d)]. The methyl groups C(15) and C(18) have a conformation in which one of the hydrogen atoms eclipses the double bond of the chain [Fig. 4(b) and 4(e)], as normally found for methyl groups connected to double-bond systems (Herschbach & Krisher, 1958).

With exclusion of the COOH group the conjugated system is almost planar as shown in Fig. 2. The COOH group is rotated by approximately 13° out of this plane

[Fig. 4(a)]. This is caused by the steric interaction between H(24) and O(2). This interaction affects also the conformation of methyl group C(19), which is rotated by approximately 15° out of the normal eclipsed conformation [Fig. 4(b)]. In spite of the two rotations the distance between H(24) and O(2) is only 2.3 Å whereas the accepted van der Waals distances for O and H are 1.5 and 1.2 Å respectively.

#### Bond lengths and angles

The bond lengths in the side chain are normal and there are no significant differences between similar bonds. The bonds C(18)–C(8) and C(19)–C(12) are approximately 1.50 Å as normally found for  $sp^2$ – $sp^3$  bonds.

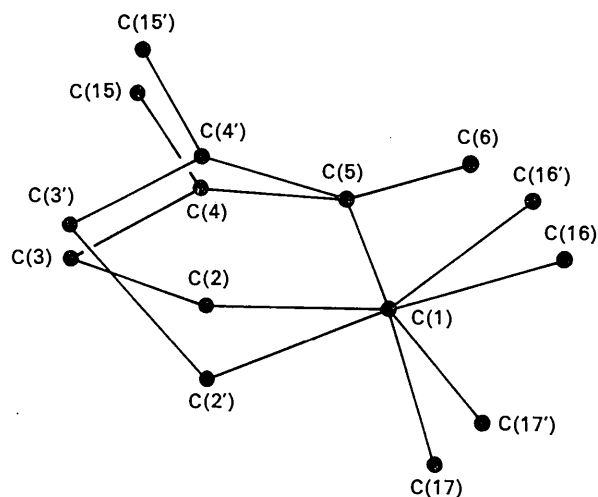


Fig. 3. Perspective view of a model of 1,1,4-trimethylcyclopentene-5-carboxylic acid and its mirror image, in which the atoms C(1), C(5) and C(6) coincide; see also the discussion of the disorder.

Table 4. Bond angles involving hydrogen atoms

		E.s.d.'s vary between 3 and 5°.			
C(1)–C(2)–H(5)	100°	C(9)–C(10)–H(21)	118°	C(1)–C(17)–H(12)	110°
C(1)–C(2)–H(6)	121	C(11)–C(10)–H(21)	118	C(1)–C(17)–H(13)	117
C(3)–C(2)–H(5)	110			C(1)–C(17)–H(14)	109
C(3)–C(2)–H(6)	125	C(10)–C(11)–H(17)	119	H(12)–C(17)–H(13)	104
H(5)–C(2)–H(6)	82	C(12)–C(11)–H(17)	114	H(12)–C(17)–H(14)	106
				H(13)–C(17)–H(14)	111
C(2)–C(3)–H(18)	112	C(12)–C(13)–H(22)	121	C(8)–C(18)–H(2)	109
C(2)–C(3)–H(19)	104	C(14)–C(13)–H(22)	111	C(8)–C(18)–H(4)	113
C(4)–C(3)–H(18)	114			C(8)–C(18)–H(26)	114
C(4)–C(3)–H(19)	111	C(4)–C(15)–H(9)	110	H(2)–C(18)–H(4)	107
H(18)–C(3)–H(19)	109	C(4)–C(15)–H(10)	110	H(2)–C(18)–H(26)	105
		C(4)–C(15)–H(11)	118	H(4)–C(18)–H(26)	108
C(5)–C(6)–H(23)	115	H(9)–C(15)–H(10)	120		
C(7)–C(6)–H(23)	115	H(9)–C(15)–H(11)	97		
		H(10)–C(15)–H(11)	101		
C(6)–C(7)–H(20)	120			C(12)–C(19)–H(1)	110
C(8)–C(7)–H(20)	114	C(1)–C(16)–H(8)	107	C(12)–C(19)–H(3)	108
		C(1)–C(16)–H(15)	112	C(12)–C(19)–H(24)	115
C(8)–C(9)–H(25)	115	C(1)–C(16)–H(16)	114	H(1)–C(19)–H(3)	97
C(10)–C(9)–H(25)	118	H(8)–C(16)–H(15)	109	H(1)–C(19)–H(24)	112
		H(8)–C(16)–H(16)	100	H(3)–C(19)–H(24)	113
		H(15)–C(16)–H(16)	114		



tene analogue. This is reflected in the physiological activities of the various analogues; the pentene analogue has a growth activity which is 50–60% of that of vitamin A, but the other analogues do not show any appreciable activity (Huisman & Baas, 1969; Skolnik, 1969).

Thanks are due to Professor C. H. MacGillavry and Dr C. H. Stam for their interest in the investigation and their critical reading of the manuscript, to Mr A. Kreuger for his participation in the experimental work and to Professor Dr H. O. Huisman and Dr J. L. Baas for providing the sample.

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## The Crystal Structure of Zinc Diborate, $ZnB_4O_7$

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(Received 20 July 1970)

Zinc diborate crystallizes in the orthorhombic system, space group *Pbca*, with eight formula units in a cell of dimensions  $a = 13.714 \pm 0.005$ ,  $b = 8.091 \pm 0.005$  and  $c = 8.631 \pm 0.005$  Å. The calculated density is  $3.07 \text{ g.cm}^{-3}$ , and all atoms are in general positions. The structure of  $ZnB_4O_7$  has been solved by three-dimensional Fourier syntheses. The positional and isotropic thermal parameters were refined by the least-squares method based on 530 observed reflexions. The final conventional *R* index is 0.067. The structure consists of  $BO_3$  triangles and  $BO_4$  tetrahedra sharing a common vertex. Each zinc atom is surrounded by four close oxygen atoms, arranged in an irregular tetrahedron.

#### Introduction

The binary system  $ZnO-B_2O_3$  has been studied by several workers (Harrison & Hummel, 1956; Bauer, 1963; Weir & Schroeder, 1964). Fayos, Garcia-Blanco & Rivoir (1966) investigated the system using calcined samples. Three compounds were reported:  $Zn_3(BO_3)_2$  (Garcia-Blanco & Fayos, 1968),  $Zn_4O(BO_2)_6$  (Smith, Garcia-Blanco & Rivoir, 1964), and a third compound having approximate composition  $ZnO \cdot 2B_2O_3$ . The purpose of the present paper is to report on the crystal structure of the last compound.

The structures of several compounds with a metal oxide to boron oxide ratio of 1 to 2 are known. The mineral borax,  $Na_2O \cdot 2B_2O_3 \cdot 10H_2O$  (Morimoto, 1956), contains a double ring polyion as an isolated unit. In anhydrous lithium diborate,  $Li_2B_4O_7$  (Krogh-Moe,

1968), and in cadmium diborate,  $CdB_4O_7$  (Ihara & Krogh-Moe, 1966), however, these double ring polyions are condensed into three-dimensional networks where half the boron atoms are fourfold coordinated. On the other hand, the structure of the isomorphous compounds  $SrB_4O_7$  and  $PbB_4O_7$  (Perloff & Block, 1966), contains a completely different type of network, having all the boron atoms in fourfold coordination. The unusual feature is the occurrence of an oxygen atom common to three  $BO_4$  tetrahedra. In the barium compound  $BaB_4O_7$  (Block & Perloff, 1965), the borate network can be described as a three-dimensional linkage of both six-membered and double rings. The former contain two tetrahedral boron atoms and one triangular boron atom, and the latter contain two tetrahedral boron atoms and three triangular boron atoms. Since structural data about other diborates are