The Crystal Structure of Methyl 2,3-Anhydro-4,6-benzylidene-α-D-mannopyranoside

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The crystal structure of methyl 2,3-anhydro-4,6-benzylidene-α-D-mannopyranoside, $C_{19}H_{16}O_5$, has been determined by a direct phase-determination method, and has been refined by least squares to a linear R value of 0·039 for 1283 observed independent reflexions measured by diffractometer. The space group is $P2_1$, with $Z=2$ and unit-cell dimensions $a=8·565$, $b=4·531$, $c=16·711$ Å and $\beta=90·42°$. The C(1)–O(1) bond in the pyranoside ring is 1·395 Å and the average value for C–O bonds in the structure is 1·424 Å. The C(2)–C(3) bond is 1·456 Å, significantly shorter than the average value of 1·512 Å for the other $C(sp^3)$–$C(sp^3)$ bonds, and atoms C(1), C(2), C(3) and C(4) are coplanar in the presence of the epoxide ring.

Introduction

The structural analysis of methyl 2,3-anhydro-4,6-benzylidene-α-D-mannopyranoside, $C_{19}H_{16}O_5$, was undertaken primarily to ascertain the effect of the epoxide ring on the conformation of the pyranoside ring and to contribute to data concerning those changes of the pyranoside ring in various sugars attributable to the nature and orientation of the substituents.

Experimental

Weissenberg and rotation photographs indicated monoclinic symmetry. The space group is uniquely determined as $P2_1$ by the optical activity of the compound and the systematic absences of $0k0$ reflexions with k odd. The unit-cell dimensions are summarized in Table 1. The X-ray intensities were obtained on an automatic Siemens diffractometer with monochromated Cu $K\alpha$ radiation. A crystal of dimensions $0·123 \times 0·617 \times 0·091$ mm (along the cell axes a, b and c) was mounted with the b axis along the diffractometer φ axis. Intensities for 1542 reflexions to 140° 2θ were measured by θ–2θ scans. The diffractometer automatically selects a measuring time up to a preset maximum, or inserts attenuators if appropriate, to achieve similar counting statistics for all but the weakest reflexions. Lorentz–polarization and absorption ($\mu=8·84$ cm^{-1}) corrections were applied. Preliminary scale and temperature factors were derived from a Wilson plot. The structure factors were then reduced to normalized structure factor magnitudes $|E(hkl)|$.

Table 1. *Crystal data*

Lattice constants	$a = 8·565$ (2) Å
	$b = 4·531$ (1)
	$c = 16·711$ (3)
	$\beta = 90·42$ (5)°
Cell volume	$V = 648·5$ Å^3
Density (X-ray)	$d = 1·659$ g.cm^{-3}
Molecules per unit cell	$Z = 2$
Space group	$P2_1$

Solution and refinement

The crystal structure was solved largely by the $\sum_2$ direct phase determination method (Karle & Karle, 1966). To define the origin three suitable linearly independent reflexions were chosen and arbitrarily given phase values zero. To choose between the two enantiomorphous solutions the sign of a seminvariant whose phase differs from zero or π must be specified (Hauptman & Karle, 1956). This was accomplished by successively giving the trial phase values $\frac{\pi}{4}, \frac{\pi}{2}, \frac{3\pi}{4}$ to a general reflexion. If none of these phases established an enantiomorph another reflexion was tried. Two additional starting phases were evaluated with the $\sum_1$ relation. The basic set, listed in Table 2, was extended and refined by use of a sum-of-angles formula, and a weighted-sum formula programmed for the IBM 1800 computer by Norrestam (1972),

$$\varphi_h \sim \langle \varphi_k + \varphi_{h-k} \rangle_{kr}$$

$$\varphi_h \sim \frac{\sum\limits_{kr} |E_k \cdot E_{h-k}|(\varphi_k + \varphi_{h-k})}{\sum\limits_{kr} |E_k E_{h-k}|}.$$

Table 2. *Phase assignments for specifying the origin and implementing the sum-of-angles formula*

h			φ_h	$|E_h|$	
3	0	10	0	3·24	origin
7	0	$\overline{11}$	0	2·97	
3	1	$\overline{12}$	0	2·67	
2	2	$\overline{11}$	$\pi/2$	3·05	enantiomorph
4	0	12	π	4·82	$\sum_1$
8	0	$\overline{2}$	0	3·31	

* The origin was shifted along the b axis after the structure had been determined.

Phase determination was not immediately successful. Several determinations were started from different sets of initial phases. The origin-defining reflexions did not

Table 3. *Positional and anisotropic thermal parameters of the non-hydrogen atoms*

The β values refer to the temperature factor expression $\exp[-(h^2\beta_{11}+k^2\beta_{22}+l^2\beta_{33}+hk\beta_{12}+hl\beta_{13}+kl\beta_{23})]$.
Estimated standard deviations are given in parentheses. Values are $\times 10^4$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	3253 (3)	111 (7)	1079 (2)	126 (4)	378 (12)	28 (1)	81 (11)	8 (3)	−11 (6)
O(1)	4193 (2)	2439 (6)	826 (1)	136 (3)	527 (11)	39 (1)	−5 (9)	23 (2)	17 (5)
C(2)	1695 (3)	527 (8)	662 (2)	139 (4)	452 (12)	23 (1)	50 (12)	−6 (3)	−20 (5)
O(2)	592 (3)	−1819 (6)	781 (1)	166 (3)	530 (11)	37 (1)	−42 (10)	−14 (2)	−93 (5)
C(3)	282 (3)	1055 (7)	1120 (2)	110 (3)	463 (13)	28 (1)	40 (12)	−26 (3)	−19 (6)
C(4)	432 (3)	1208 (7)	2019 (2)	102 (3)	338 (10)	25 (1)	22 (10)	−7 (2)	−8 (5)
O(4)	−656 (2)	3265 (6)	2336 (1)	100 (2)	397 (8)	27 (1)	49 (7)	−10 (2)	−12 (4)
C(5)	2081 (3)	2171 (7)	2229 (2)	99 (3)	357 (11)	24 (1)	42 (10)	−8 (2)	−2 (5)
O(5)	3133 (2)	0	1926 (1)	115 (2)	439 (9)	26 (1)	119 (8)	−4 (2)	4 (4)
C(6)	2226 (3)	2394 (8)	3134 (2)	102 (3)	575 (15)	26 (1)	105 (12)	−18 (3)	−46 (6)
C(7)	−480 (3)	3372 (7)	3180 (2)	107 (3)	326 (10)	25 (1)	11 (10)	−6 (2)	21 (5)
C(8)	−1670 (3)	5446 (7)	3521 (2)	100 (3)	327 (10)	29 (1)	−29 (9)	9 (2)	14 (5)
C(9)	−1524 (3)	6399 (8)	4312 (2)	125 (3)	489 (13)	26 (1)	37 (12)	5 (3)	35 (6)
C(10)	−2631 (3)	8274 (9)	4637 (2)	163 (4)	562 (15)	29 (1)	49 (14)	33 (3)	−1 (7)
C(11)	−3898 (3)	9166 (9)	4188 (2)	139 (4)	556 (15)	40 (1)	132 (14)	33 (3)	−21 (7)
C(12)	−4054 (3)	8229 (10)	3407 (2)	125 (4)	687 (18)	45 (1)	186 (15)	−15 (3)	−19 (8)
C(13)	−2934 (3)	6386 (8)	3072 (2)	122 (3)	559 (14)	32 (1)	99 (13)	−17 (3)	−39 (7)
C(14)	5797 (4)	2061 (12)	1025 (3)	136 (4)	853 (25)	51 (2)	−67 (18)	16 (4)	−27 (11)

effectively define a primitive cell. In the E map which proved useful, two molecular fragments appeared stacked above each other along the b axis. Since many of the reflexions with large $|E|$ values have $k=2$ and enter into many sum-of-angles relations, the influence of the origin reflexion $3,1,\overline{12}$ (Table 2) was probably over-ridden.

Ten atoms belonging to one of the molecular fragments were selected and refined by the least-squares method. The rest of the non-hydrogen atoms were obtained by a combination of least-squares refinements and difference Fourier syntheses. Anisotropic thermal parameters were then assigned to all non-hydrogen atoms and after three cycles of full-matrix least-squares refinement the value of R had fallen to 0·075 for 1288 observed independent reflexions. At this stage a difference synthesis revealed all hydrogen atoms at reasonable positions. After introduction of the hydrogen atoms into the least-squares analysis with isotropic temperature factors the residual was reduced to 0·043.

The observed values of the five strongest structure factors were much smaller than the calculated ones, perhaps because of extinction. When these reflexions were excluded the R value dropped to 0·039. The observed and calculated structure factors for these reflexions are included, however, in Table 5 and marked with asterisks.

The full-matrix least-squares refinements were performed by the program $LALS$ (Gantzel, Sparks & True-blood, 1966). Hughes's weighting scheme was applied with $F_{o,\min}=0·95$ and $h=4·0$. The atomic scattering factor curves for oxygen, nitrogen and carbon were taken from Freeman (1959) and that for hydrogen from Stewart, Davidson & Simpson (1965).

The positional and thermal parameters of the non-hydrogen atoms are listed in Table 3 with calculated estimated standard deviations, those for the hydrogen atoms in Table 4. The observed and calculated structure factors are given in Table 5.

Table 4 *Positional and isotropic thermal parameters of the hydrogen atoms, with estimated standard deviations in parentheses*

	$x \times 10^3$	$y \times 10^3$	$z \times 10^3$	B
H(C1)	365 (4)	−165 (9)	93 (2)	3·7 (6) Å^2
H(C2)	175 (3)	100 (7)	14 (2)	2·8 (5)
H(C3)	−50 (3)	212 (8)	88 (2)	3·3 (6)
H(C4)	20 (4)	−78 (9)	227 (2)	4·2 (6)
H(C5)	222 (3)	404 (7)	199 (2)	2·5 (5)
H1(C6)	318 (3)	317 (7)	331 (2)	3·2 (5)
H2(C6)	197 (4)	32 (10)	342 (2)	5·2 (7)
H(C7)	−56 (4)	153 (9)	337 (2)	3·6 (6)
H(C9)	−64 (4)	572 (8)	461 (2)	4·1 (6)
H(C10)	−255 (4)	892 (12)	516 (3)	6·9 (9)
H(C11)	−464 (4)	1036 (10)	439 (2)	5·5 (8)
H(C12)	−494 (4)	869 (9)	303 (2)	5·5 (8)
H(C13)	−297 (4)	580 (9)	257 (2)	5·0 (8)
H1(C14)	592 (4)	135 (11)	154 (3)	6·0 (9)
H2(C14)	622 (5)	81 (11)	69 (3)	6·3 (10)
H3(C14)	628 (6)	399 (14)	100 (3)	9·0 (14)

Results and discussion

Atoms belonging to different asymmetric units are labelled as follows.

Superscript	Coordinates	Superscript	Coordinates
None	$x, \quad y, z$	iv	$-x, y+\frac{1}{2}, \quad -z$
i	$x, y-1, z$	v	$-x, y-\frac{1}{2}, 1-z$
ii	$x+1, y-1, z$	vi	$1-x, y+\frac{1}{2}, \quad -z$
iii	$x+1, \quad y, z$		

A perspective view of the molecule showing the atom numbering is given in Fig. 1. The bond distances and bond angles involving non-hydrogen atoms are given in Tables 6 and 7. No attempt has been made to correct bond lengths for the effect of thermal motion The average estimated standard deviations in the bond distances and angles involving non-hydrogen atoms are 0·004 Å and 0·3°.

The mean C–C bond distance, 1·384 Å, in the benzene ring is compatible with the expected value 1·394 (5) Å (Sutton, 1965). The $C(sp^3)$–$C(sp^3)$ bond lengths, excluding C(2)–C(3), have a mean value of 1·512 Å, in agreement with values observed in other carbohydrates (Berman, Chu & Jeffrey, 1967). The bond length C(2)–C(3), 1·456 Å, is shorter than this mean value by $\sim 19\sigma$ in the presence of the epoxide ring. The mean C–O bond length is 1·424 Å, in good agreement with the values in many previous investigations of mono- and disaccharides (Berman, Chu & Jeffrey, 1967). The axial anomeric C(1)–O(1) bond distance, 1·395 Å, is shorter than this mean value by $\sim 7\sigma$. The magnitude of this shortening is in the range observed for unsubstituted pyranose sugars (Berman & Kim, 1968). The C–H bond distances range from 0·88 to 1·08 Å, mean value 0·94 Å, in good agreement with values found in some precisely determined X-ray structures (Stewart, Davidson & Simpson, 1965). Least-squares planes through portions of the molecule are given in Table 8. The pyranoside ring has been flattened, relative to the ordinary chair form, in the presence of the epoxide ring. Atoms C(1), C(2), C(3) and C(4) are coplanar within

Table 5. *Observed and calculated structure amplitudes*

The columns use the running index k, $10|F_o|$ and $10|F_c|$ respectively.
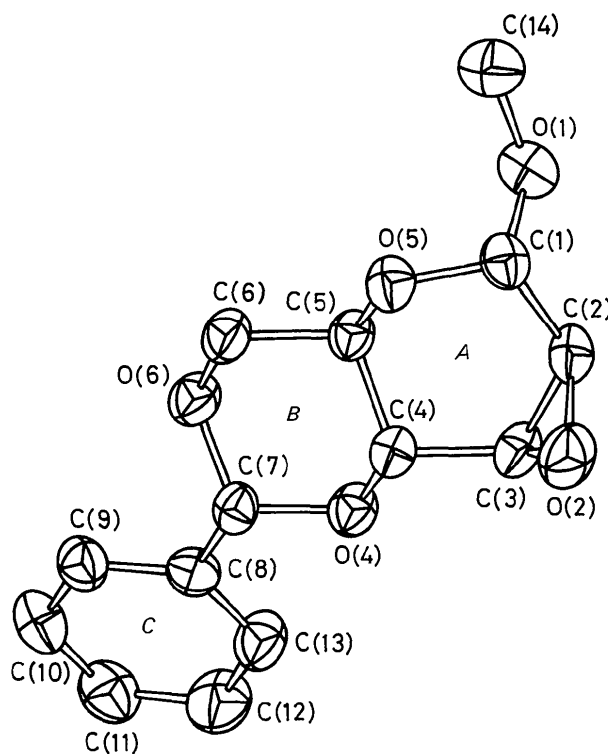
Table 5 *(cont.)*

Fig. 1. A perspective view of the molecule.

Table 6. Bond distances between non-hydrogens atoms with estimated standard deviations in parentheses

C(1)—O(1)	1·395 (4) Å
C(1)—C(2)	1·513 (3)
C(1)—O(5)	1·420 (3)
O(1)—C(14)	1·422 (4)
C(2)—O(2)	1·437 (4)
C(2)—C(3)	1·456 (3)
C(3)—O(2)	1·446 (4)
C(3)—C(4)	1·509 (3)
C(4)—O(4)	1·423 (3)
C(4)—C(5)	1·517 (3)
O(4)—C(7)	1·417 (2)
C(5)—O(5)	1·429 (3)
C(5)—C(6)	1·521 (3)
C(6)—O(6)	1·435 (3)
O(6)—C(7)	1·413 (3)
C(7)—C(8)	1·502 (3)
C(8)—C(9)	1·395 (3)
C(8)—C(13)	1·380 (3)
C(9)—C(10)	1·387 (4)
C(10)-C(11)	1·375 (4)
C(11)-C(12)	1·378 (4)
C(12)-C(13)	1·392 (4)

Table 7. Interatomic angles with estimated standard deviations

C(1)—O(1)—C(14)	113·3°	0·3°
O(1)—C(1)—C(2)	106·0	0·3
O(1)—C(1)—O(5)	112·0	0·2
C(1)—C(2)—C(3)	120·8	0·2
C(1)—C(2)—O(2)	115·0	0·3
C(2)—O(2) C(3)	60·7	0·2
C(2)—C(3)—C(4)	117·8	0·2
O(2)—C(3)—C(2)	59·4	0·2
O(2)—C(3)—C(4)	114·6	0·3
C(3)—C(2)—O(2)	60·0	0·2
C(3)—C(4)—C(5)	108·4	0·2
C(3)—C(4)—O(4)	110·5	0·2
C(4)—O(4)—C(7)	109·1	0·2
C(4)—C(5)—O(5)	108·0	0·2
C(4)—C(5)—C(6)	108·6	0·2
O(4)—C(4)—C(5)	109·6	0·2
O(4)—C(7)—O(6)	111·2	0·2
O(4)—C(7)—C(8)	109·4	0·2
C(5)—O(5)—C(1)	112·2	0·2
C(5)—C(6)—O(6)	107·2	0·2
O(5)—C(1)—C(2)	113·2	0·2
O(5)—C(5)—C(6)	110·5	0·2
C(6)—O(6)—C(7)	112·0	0·3
O(6)—C(7)—C(8)	108·8	0·3
C(7)—C(8)—C(9)	119·8	0·2
C(7)—C(8)—C(13)	121·2	0·2
C(8)—C(9)—C(10)	120·2	0·3
C(9)—C(8)—C(13)	119·0	0·3
C(9)—C(10)-C(11)	120·4	0·3
C(10)-C(11)-C(12)	119·8	0·3
C(11)-C(12)-C(13)	120·2	0·3
C(12)-C(13)-C(8)	120·4	0·3

Table 8. Least-squares planes

The planes are described in terms of a vector basis m∥a*, n∥b and p∥c

Plane A: 0·1644 m + 0·9848 n − 0·0561 p = 0·4092
Plane B: −0·4075 m − 0·7326 n + 0·5452 p = 1·2812
Plane C: −0·5191 m − 0·7958 n + 0·3117 p = 0·6138

Plane A		Plane B		Plane C	
C(1)	−0·002 Å	C(4)	0·005 Å	C(8)	0·002 Å
C(2)	0·003	O(4)	−0·005	C(9)	0·005
C(3)	−0·003	C(5)*	−0·705	C(10)	−0·007
C(4)	0·002	C(6)	−0·005	C(11)	0·003
C(5)*	0·645	O(6)	0·005	C(12)	0·004
O(5)*	−0·147	C(7)*	0·666	C(13)	−0·006

* These atoms are not included in the least-squares planes.

The intermolecular packing arrangement is projected normal to the b axis in Fig. 2. The intermolecular distances, given in Table 9, are normal except for the distances O(2)-C(3^i), 3·289 Å, and C(2)-O(2^{iv}), 3·321 Å, both significantly shorter than the normal van der Waals separation, 3·40 Å, between methyl carbon and oxygen (Pauling, 1960).

0·003 Å. O(5) and C(5), however, deviate by −0·147 and 0·645 Å from this plane. Ring B has a slightly distorted chair conformation. The four atoms C(6), O(6), C(4) and O(4) of ring B are coplanar while atoms C(7) and C(5) lie 0·705 Å below and 0·666 Å above this plane respectively.
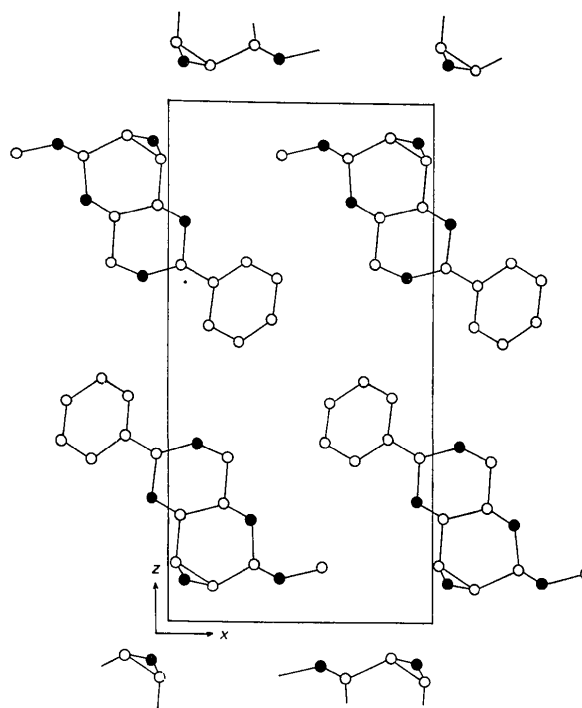

Fig. 2. The structure as seen in projection down the b axis.
○ Carbon   ● Oxygen

Table 9. *Intermolecular distances less than* 3·8 Å

C(1)—O(1ⁱ)	3·594 Å
O(1)—C(14ᵛⁱ)	3·736
C(2)—O(2ⁱᵛ)	3·321
O(2)—O(2ⁱᵛ)	3·597
O(2)—C(2ⁱ)	3·600
O(2)—C(3ⁱ)	3·289
O(2)—C(4ⁱ)	3·780
O(2)—O(4ⁱ)	3·592
C(3)—O(2ⁱᵛ)	3·397
C(4)—O(4ⁱ)	3·756
O(5)—C(5ⁱ)	3·696
O(5)—C(12ⁱⁱ)	3·534
C(6)—C(12ⁱⁱ)	3·728
C(6)—C(10ᵛ)	3·759
O(6)—C(10ᵛ)	3·582
C(7)—C(8ⁱ)	3·777
C(7)—C(9ⁱ)	3·793
C(8)—C(11ⁱ)	3·608
C(14)-O(4ⁱⁱⁱ)	3·772

used in the work, for valuable discussions and assistance with the collection of the data. The authors also wish to thank Dr Rolf Norrestam for helpful discussions and Dr Don Koenig for correcting the English of this paper.

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Structure and Absolute Configuration of the Alkaloid Clivorine*

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Clivorine hydrate, $C_{21}H_{27}NO_7.H_2O$, m.p. 147–149°C, crystallizes in the orthorhombic space group $P2_12_12_1$ with four molecules in a unit cell of dimensions $a = 12.765$ (1), $b = 14.772$ (1), $c = 11.145$ (1) Å (at −160°C). The densities are: $D_x = 1.34$ g.cm⁻³ (at −160°C), $D_m = 1.28$ g.cm⁻³ (at room temperature). The structure was determined by the symbolic-addition method from data collected at −160°C on a four-circle diffractometer using the $\theta/2\theta$ scan technique. It was refined by the block-diagonal least-squares method to $R = 0.0388$ for 2506 observed reflexions. There is a trans-annular interaction between the nitrogen atom and the carbonyl carbon atom across the eight-membered ring: the N···C(8) distance is 1.993 (3) Å and the C(8)==O(6) bond is 1.258 (3) Å. Molecules of clivorine are hydrogen bonded via the water molecules and form spirals extended in the direction of the c axis.

Introduction

The alkaloid clivorine was isolated from *Ligularia clivorum* Maxim. by Klásek, Vrublovský & Šantavý (1967). On the basis of chemical evidence and p.m.r. spectral data the structure (I), which has the empirical formula $C_{21}H_{29}NO_8$, was ascribed to it (Klásek, Sedmera & Šantavý, 1970). In order to determine the configuration at C(3), C(4) and C(5) it was decided to carry out an X-ray analysis. The result, reported in a preliminary communication (Birnbaum, Klásek, Sedmera,

Snatzke, Johnson & Šantavý, 1971), showed the structure to be the hydrate of (II) with the empirical formula $C_{21}H_{27}NO_7.H_2O$.

(I)   (II)

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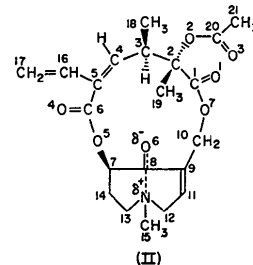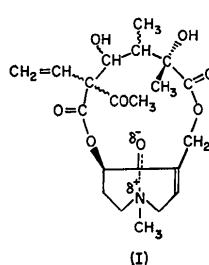
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