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The Crystal and Molecular Structure of a Novel Steroidal Rearrangement Product, $C_{19}H_{26}O_5 . H_2O$

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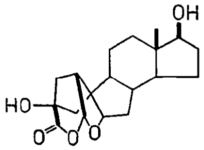
Crystals of the title compound are orthorhombic, $a=6{\cdot}623$ (1), $b=11{\cdot}963$ (2), $c=22{\cdot}403$ (4) Å, space group $P2_12_12_1$, $Z=4$. The structure was determined from diffractometer data by direct methods, and refined by full-matrix least-squares methods to R 0·042 for 1441 reflexions. The molecule consists of six fused rings of which the *B*, *C*, and *D* rings resemble those in any steroid molecule with the exception that ring *B* is five-membered instead of six-membered. The remaining rings consist of two five-membered rings and one six-membered ring, the latter containing a lactone group. All the five-membered rings have approximate envelope conformations, while ring *C* has a chair conformation and the δ-lactone ring has a distorted half-boat conformation. The molecules are linked by O–H$\cdots$O hydrogen bonds involving the water molecule.

Introduction

The preparation of an unusual steroidal rearrangement product of 6β,19-oxido-2,17-dihydroxyandrostan-1,4-diene-3-one and its characterization by ^{1}H n.m.r. chemical means have been reported (Chorvat, Bible & Swenton, 1974). A structure was proposed which was consistent with the physical and chemical data and was supported by a mechanism of formation. In view of the complexity of the proposed structure shown below, confirmation by X-ray crystallography was deemed necessary.



We report here the crystal structure of the hydrated form.

Experimental

Crystals of [3*S*-(3β,3aβ,5aα,5b*R*,5c*R*,7*R*,9a*R*,10aα,11aβ,11bα)]-tetradecahydro-3,7-dihydroxy-3a-methyl-1*H*-5b,7-methano-8*H*-*as*-indaceno[3′,2′:4,5]furo[2,3-*b*]-pyran-8-one in a hydrated form were kindly supplied by Dr R. J. Chorvat of G. D. Searle & Co. The space group and initial unit cell parameters were determined from oscillation, Weissenberg, and precession photographs. Accurate cell parameters were later obtained by a least-squares treatment of 19 $\sin^2\theta(hkl)$ values measured on a General Electric XRD 6 diffractometer with Cu $K\alpha$ radiation.

Crystal data

$C_{19}H_{26}O_5 . H_2O$, $M=352{\cdot}4$. Orthorhombic, $a=6{\cdot}623$ (1), $b=11{\cdot}963$ (2), $c=22{\cdot}403$ (4) Å, $U=1775$ Å^3, $D_m=1{\cdot}31$, $Z=4$, $D_c=1{\cdot}319$ g cm^{-3}, $F(000)=760$. Space group $P2_12_12_1$ (D_2^4, No. 19) from systematic absences. Cu $K\alpha$ radiation ($\lambda=1{\cdot}5418$ Å), $\mu=8{\cdot}11$ cm^{-1}.

Intensity data were collected on a Datex-automated General Electric XRD 6 diffractometer using the θ–2θ scan method at a rate of 2° min^{-1} in 2θ. The specimen used had approximate dimensions $0{\cdot}6\times0{\cdot}2\times0{\cdot}2$ mm and was mounted with the [201] vector parallel to the φ axis of the goniostat. A scintillation counter equipped with a nickel filter and pulse-height analyser ensured approximately monochromatic radiation. Of the 1663 independent reflexions measured with $2\theta\le125°$, 222 had $I<3\sigma(I)$ where $\sigma^2(I)=S+B+(0{\cdot}07S)^2$ and S is the scan count, and B the background count. The 1441 reflexions with $I>3\sigma(I)$ were used in structure solution and refinement. A standard reflexion was monitored at 90 min intervals and its intensity fluctuated by up to 7% throughout the data collection. The data were scaled accordingly and the structure amplitudes derived *via* Lorentz and polarization corrections. No absorption corrections were applied.

Structure analysis and refinement

The data were placed on an absolute scale (Wilson, 1942), and normalized structure amplitudes $|E_{hkl}|$ were derived. The structure was solved by direct methods using iterative application of the tangent formula (Karle & Hauptman, 1956; Karle & Karle, 1966). From a listing of the $\sum_2$ relationships between 81 $|E|$'s $\ge1{\cdot}8$, origin- and enantiomorph-defining reflexions were selected. Three further reflexions were assigned symbolic phases and included in the starting set of reflexions (Table 1). Manual expansion of these seven reflexions using the 81 reflexions with $|E|\ge1{\cdot}8$ gave no definite indications for the values of *a*, *b*, and *c*, so the seven starting reflexions were input to the tangent formula. Tangent refinement was applied by way of a modified version of Drew's program (Drew, Templeton & Zalkin, 1969). The symbols were allowed to assume the following values: $a\pm\pi/4$, $\pm3\pi/4$; $b\pm\pi/4$, $\pm3\pi/4$, and c 0 and π. 184 reflexions with $|E|\geq1\cdot5$ were input to the program and the first 100 $|E|$'s (in decreasing order of magnitude) were allowed to refine for six cycles, the first 150 for the next six cycles, and all 184 reflexions for a final eight cycles. In any cycle a phase assignment was rejected if the consistency index t was $<0\cdot25$, α was $<9\cdot0$, and the phase associated with a particular reflexion differed by more than 250 millicycles (1000 millicycles $=2\pi$) from its value in the previous cycle (Kennard *et al.*, 1971). The set for which symbol $a=3\pi/4$, $b=3\pi/4$, and $c=0$ assigned the largest number of phases, 180, had the lowest $R_{\rm Karle}$ value (Karle & Karle, 1966), 0·18, the highest consistency index, 0·61, and the highest α, 146. The remaining combinations of symbol phases produced $R_{\rm Karle}$ values ranging from 0·30 to 0·40.

Table 1. *Starting set of reflexions*

	h		$\|E(\mathbf{h})\|$	$\varphi(\mathbf{h})$	
0	7	16	2·652	$\pi/2$	Origin
5	0	3	2·942	$\pi/2$	
0	1	19	2·728	$\pi/2$	
3	4	0	2·164	$\pi/2$	Enantiomorph
6	3	7	2·623	a	
5	5	10	3·029	b	
0	2	21	2·217	c	

An E map was computed using the 180 phased $|E|$'s. From the E map all 24 non-hydrogen atoms in the steroid molecule were located. A difference Fourier synthesis revealed the oxygen atom of the water molecule. A structure-factor calculation based on all 25 non-hydrogen atoms gave R 0·21. Refinement was by least-squares methods in which the function minimized was $\sum w(F_o-F_c)^2$ with unit weights initially, and in the final stages of refinement, weights derived from counting statistics. Two cycles of full-matrix least-squares refinement on the positional and isotropic thermal parameters reduced R to 0·11. R fell to 0·086 upon the introduction of anisotropic temperature factors. All 28 hydrogen atoms were located in a difference Fourier synthesis and were included in the subsequent calculations with fixed positional and isotropic thermal parameters ($B=4\cdot0$ Å^2). A further refinement cycle gave R 0·052. Five reflexions (110, 020, 120, 111, and 021) were considered to suffer from extinction and were given zero weight. Two cycles of refinement brought convergence at R 0·042; no parameter shift was greater than $0\cdot38\sigma$. The weighted residual R_w (defined as $\sum w(F_o-F_c)^2/\sum wF_o^2$) was 0·054. For all 1663 data R was 0·054 and R_w 0·064. A final difference Fourier synthesis revealed no peaks higher than $\pm0\cdot22$ e Å^{-3}. Scattering factors for carbon and oxygen were taken from *International Tables for X-ray Crystallography* (1962), and those for hydrogen from Stewart, Davidson & Simpson (1965).* Final positional and thermal parameters are given in Tables 2 and 3.

Table 2. *Final positional (fractional* $\times10^4$*) parameters with estimated standard deviations in parentheses*

Hydrogen atoms are labelled with the number of the carbon atom followed by the letters *A*, *B*, and *C* where appropriate.

	x	y	z
O(1)	8907 (5)	3864 (2)	5423 (1)
O(2)	9436 (5)	2573 (2)	4748 (1)
O(3)	8122 (4)	1705 (2)	3909 (1)
O(4)	9862 (4)	5608 (2)	4698 (1)
O(5)	8167 (4)	3706 (3)	533 (1)
O(6)	1975 (5)	4647 (3)	407 (2)
C(1)	11319 (6)	4143 (3)	4042 (2)
C(2)	9614 (6)	4555 (3)	4431 (2)
C(3)	9265 (6)	3652 (4)	4911 (2)
C(4)	9841 (6)	2214 (3)	4130 (2)
C(5)	10272 (6)	3193 (3)	3716 (2)
C(6)	6754 (6)	2569 (3)	3708 (2)
C(7)	5789 (5)	2215 (3)	3117 (2)
C(8)	7192 (5)	2704 (3)	2646 (2)
C(9)	7675 (5)	3853 (3)	2909 (1)
C(10)	8089 (5)	3600 (3)	3576 (1)
C(11)	9222 (6)	4513 (3)	2549 (2)
C(12)	8563 (7)	4597 (3)	1890 (2)
C(13)	8060 (6)	3443 (3)	1626 (1)
C(14)	6440 (5)	2864 (3)	2013 (2)
C(15)	5746 (6)	1871 (3)	1642 (2)
C(16)	5874 (7)	2314 (4)	992 (2)
C(17)	6894 (6)	3465 (3)	1030 (2)
C(18)	9993 (6)	2744 (3)	1551 (2)
C(19)	7815 (6)	4598 (3)	4005 (2)
H(1*A*)	12539	3907	4215
H(1*B*)	12013	4583	3741
H(4)	10969	1616	4148
H(5)	11064	2738	3410
H(6)	5642	2779	4048
H(7*A*)	5631	1430	3073
H(7*B*)	4162	2515	3084
H(8)	8667	2212	2640
H(9)	6005	4263	2924
H(11*A*)	10545	4187	2526
H(11*B*)	9403	5255	2712
H(12*A*)	9522	5068	1601
H(12*B*)	7293	5057	1874
H(14)	5056	3324	2066
H(15*A*)	6826	1308	1710
H(15*B*)	4114	1769	1685
H(16*A*)	6632	1775	736
H(16*B*)	4497	2387	788
H(17)	5776	4138	1070
H(18*A*)	10588	2621	1907
H(18*B*)	9717	1969	1397
H(18*C*)	11214	3193	1342
H(19*A*)	7719	5258	3821
H(19*B*)	6301	4648	4189
H(O4)	11188	5618	4954
H(O5)	7340	3866	203
H(O6*A*)	574	4454	415
H(O6*B*)	1790	5249	564

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* A list of structure amplitudes has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30903 (16 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1 NZ, England.

Thermal motion analysis

Since the refinement resulted in quite an accurate structure analysis with no groups of atoms showing high thermal motion, it was felt that an analysis of the rigid-body thermal motion would be in order. The thermal motion has therefore been analysed in terms of the rigid-body modes of translation (T), libration (L), and screw (S) motion using the computer program *MGTLS* (Schomaker & Trueblood, 1968). The 24 non-hydrogen atoms comprising the rearrangement product were treated as a rigid body. Details of the rigid body are shown in Table 4. The r.m.s. standard deviation in the temperature factors U_{ij} is 0·0044 Å^2 while the r.m.s. difference between the observed and

Table 3. *Final thermal parameters* (Å × 10^2) *with standard deviations in parentheses*

The temperature factor expression is of the type:

$$\exp\left[-2\pi^2(U_{11}h^2a^{*2}+U_{22}k^2b^{*2}+U_{33}l^2c^{*2}+2U_{12}hka^*b^*+2U_{13}hla^*c^*+2U_{23}klb^*c^*)\right].$$

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	4·87 (17)	6·51 (18)	3·62 (14)	−0·12 (15)	0·30 (13)	0·84 (13)
O(2)	5·33 (18)	4·38 (15)	4·19 (13)	0·35 (14)	−0·28 (13)	1·03 (12)
O(3)	4·02 (16)	3·86 (15)	5·89 (16)	0·35 (13)	−0·70 (14)	0·84 (12)
O(4)	4·50 (15)	4·73 (14)	4·07 (13)	−0·45 (14)	−0·34 (12)	−0·30 (11)
O(5)	4·46 (16)	7·93 (19)	3·39 (13)	0·09 (17)	0·06 (12)	0·64 (13)
O(6)	7·14 (23)	6·65 (20)	10·00 (26)	−2·44 (20)	4·21 (21)	−3·62 (19)
C(1)	2·39 (18)	5·41 (24)	4·45 (20)	−0·22 (18)	0·62 (16)	0·63 (17)
C(2)	3·13 (20)	4·11 (18)	3·72 (17)	−0·08 (18)	0·12 (16)	0·14 (15)
C(3)	2·33 (18)	5·85 (23)	3·87 (19)	0·40 (18)	−0·09 (16)	0·82 (17)
C(4)	3·70 (22)	4·55 (21)	4·96 (21)	1·14 (19)	−0·45 (18)	0·46 (17)
C(5)	2·64 (19)	4·87 (21)	3·95 (19)	0·78 (18)	0·42 (16)	−0·15 (17)
C(6)	2·82 (20)	4·10 (20)	4·17 (18)	0·36 (18)	0·48 (16)	0·98 (16)
C(7)	2·83 (20)	5·18 (22)	4·66 (20)	−1·14 (19)	0·09 (17)	0·45 (17)
C(8)	2·95 (18)	3·37 (17)	3·97 (18)	−0·25 (16)	−0·05 (16)	0·40 (15)
C(9)	2·86 (18)	3·79 (18)	3·44 (18)	0·16 (16)	0·06 (15)	0·06 (15)
C(10)	2·23 (17)	3·91 (19)	3·59 (18)	0·47 (17)	0·05 (15)	0·42 (14)
C(11)	5·11 (24)	3·77 (19)	4·11 (19)	−1·24 (20)	−0·46 (19)	0·06 (16)
C(12)	5·23 (24)	3·99 (19)	3·82 (19)	−0·31 (21)	−0·05 (18)	0·75 (15)
C(13)	2·99 (19)	4·07 (20)	3·51 (18)	0·42 (17)	−0·08 (16)	0·18 (15)
C(14)	2·68 (18)	4·06 (20)	4·00 (18)	0·11 (16)	−0·31 (16)	−0·35 (15)
C(15)	3·88 (22)	5·08 (21)	5·17 (22)	−0·57 (21)	−0·56 (19)	−0·72 (18)
C(16)	4·97 (26)	6·27 (26)	4·34 (21)	−0·07 (24)	−0·59 (20)	−0·72 (19)
C(17)	3·52 (21)	5·58 (24)	3·55 (18)	0·46 (20)	0·08 (17)	0·00 (16)
C(18)	3·18 (20)	5·64 (23)	4·96 (21)	0·54 (20)	−0·38 (18)	0·52 (19)
C(19)	3·42 (20)	3·86 (20)	3·89 (19)	0·91 (18)	−0·25 (16)	0·03 (15)

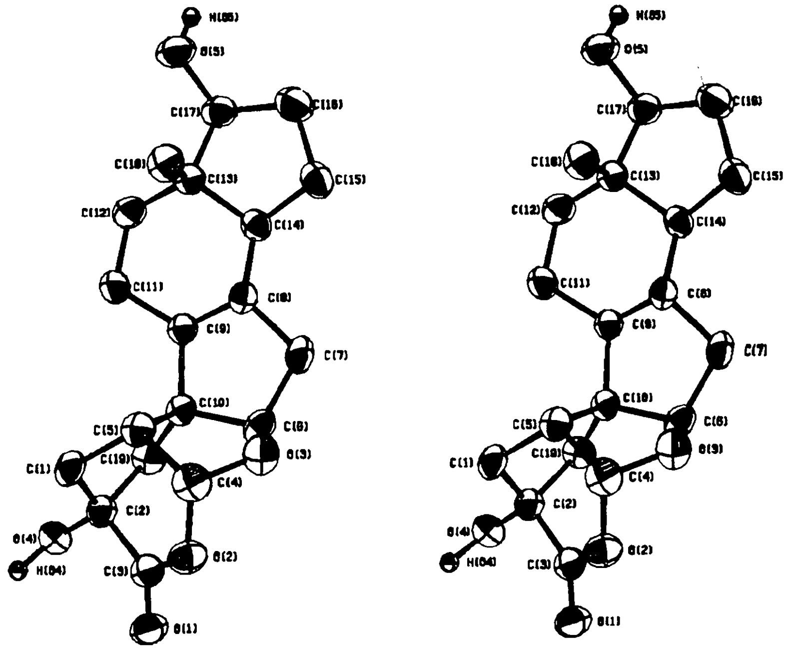


Fig. 1. Molecular structure of the rearrangement product, with crystallographic numbering scheme.

calculated U_{ij}'s (r.m.s. ΔU_{ij}) is 0·0041 Å^2, showing that the molecule as a whole is a good rigid body. The principal libration axis is essentially parallel to the direction of the **c** axis; this direction corresponds to the C(3)···C(17) vector. The other two libration axes are almost parallel to the *a* and *b* axes respectively, and their amplitude of libration is less than half that of the axis parallel to **c**. The effective screw motion is very small. Bond distances have been corrected for libration (Cruickshank, 1956, 1961) using shape parameters q^2 of 0·08 for all atoms. Riding motion corrections based on ΔU_{ij} (Busing & Levy, 1964) were applied, but as will be seen in the discussion the corrected bond lengths differ very little from those uncorrected.

Table 4. *Parameters for the* 24-*atom rigid body*

Axes of reference are orthogonal ångstrom axes parallel to the crystal axes. E.s.d.'s of components of **L** are given in parentheses in units of the last place shown.

Libration tensor, $\mathbf{L} \times 10(°)^2$

$$\begin{bmatrix} 40\,(3) & 2\,(3) & 21\,(16) \\ & 21\,(3) & 24\,(5) \\ & & 156\,(16) \end{bmatrix}$$

Principal axis representations

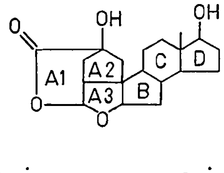
	r.m.s. amplitude	Direction cosines (×10^3)		
L	4·1°	170	165	972
	1·9	982	−109	−153
	1·3	078	981	−180
Reduced **T**	0·20 Å	104	523	846
	0·18	−220	−817	532
	0·15	970	−244	031

Displacement of libration axes from intersecting (Å)

Parallel to $\mathbf{L}_1$	−0·21
Parallel to $\mathbf{L}_2$	0·09
Parallel to $\mathbf{L}_3$	−0·97

Discussion

Fig. 1 is a stereo view of the molecule showing the atomic numbering scheme. The majority of hydrogen atoms have been omitted for the sake of clarity. The molecule may be said to consist of six fused rings, for convenience labelled thus:



The *C* and *D* rings are recognizable as a steroid fragment while *B* has been reduced from a six- to a five-membered ring. The *A*1/*A*3, *A*1/*A*2, *A*2/*A*3, and *A*3/*B* ring junctions are all *cis* and the *B*/*C* and *C*/*D* junctions are *trans*. The 'cage'-like structure consisting of rings *A*1, *A*2, and *A*3 is extremely rigid, and, as has already been mentioned, the whole molecule may be treated as a rigid body. Thermal motion of the atoms is low, shown by the small thermal ellipsoids in the diagram. Bond distances and valency angles, uncorrected for thermal libration are given in Tables 5 and 6. The C–H distances range from 0·89 to 1·21 Å and the O–H distances from 0·81 to 1·05 Å.

Table 5. *Bond lengths* (Å) *with estimated standard deviations in parentheses*

O(1)–C(3)	1·198 (4)	C(7)—C(8)	1·522 (5)
O(2)–C(3)	1·346 (5)	C(8)—C(9)	1·530 (5)
O(2)–C(4)	1·476 (5)	C(8)—C(14)	1·515 (5)
O(3)–C(4)	1·383 (5)	C(9)—C(10)	1·547 (5)
O(3)–C(6)	1·446 (4)	C(9)—C(11)	1·524 (5)
O(4)–C(2)	1·404 (4)	C(10)–C(19)	1·543 (5)
O(5)–C(17)	1·426 (4)	C(11)–C(12)	1·544 (5)
C(1)–C(2)	1·509 (5)	C(12)–C(13)	1·538 (5)
C(1)–C(5)	1·518 (6)	C(13)–C(14)	1·544 (5)
C(2)–C(3)	1·541 (5)	C(13)–C(17)	1·543 (5)
C(2)–C(19)	1·528 (5)	C(13)–C(18)	1·538 (5)
C(4)–C(5)	1·520 (5)	C(14)–C(15)	1·521 (5)
C(5)–C(10)	1·558 (5)	C(15)–C(16)	1·552 (5)
C(6)–C(7)	1·530 (5)	C(16)–C(17)	1·536 (6)
C(6)–C(10)	1·546 (5)		

Table 6. *Valency angles* (°)

The average estimated standard deviation is 0·3°

C(3)—O(2)—C(4)	123·2	O(2)—C(4)—C(5)	112·5
C(4)—O(3)—C(6)	108·2	O(3)—C(4)—C(5)	106·0
C(2)—C(1)—C(5)	100·4	C(1)—C(5)—C(4)	111·7
O(4)—C(2)—C(1)	116·8	C(1)—C(5)—C(10)	106·7
O(4)—C(2)—C(3)	110·5	C(4)—C(5)—C(10)	100·9
O(4)—C(2)—C(19)	109·1	O(3)—C(6)—C(7)	109·4
C(1)—C(2)—C(3)	106·6	C(6)—C(7)—C(8)	103·7
C(1)—C(2)—C(19)	103·5	C(7)—C(8)—C(9)	101·9
C(3)—C(2)—C(19)	110·0	C(7)—C(8)—C(14)	119·8
O(1)—C(3)—O(2)	118·6	C(9)—C(8)—C(14)	108·4
O(1)—C(3)—C(2)	123·3	C(8)—C(9)—C(10)	103·5
O(2)—C(3)—C(2)	118·1	C(8)—C(9)—C(11)	113·7
O(2)—C(4)—O(3)	108·3	C(10)–C(9)—C(11)	119·5
C(5)—C(10)–C(9)	114·9	C(17)–C(13)–C(18)	109·4
C(5)—C(10)–C(19)	103·0	C(8)—C(14)–C(13)	110·7
C(9)—C(10)–C(19)	115·4	C(8)—C(14)–C(15)	120·8
C(9)—C(11)–C(12)	110·5	C(13)–C(14)–C(15)	104·7
C(11)–C(12)–C(13)	111·8	C(14)–C(15)–C(16)	103·2
C(12)–C(13)–C(14)	109·7	C(15)–C(16)–C(17)	106·2
C(12)–C(13)–C(17)	115·2	O(5)—C(17)–C(13)	112·5
C(12)–C(13)–C(18)	110·5	O(5)—C(17)–C(16)	113·5
C(14)–C(13)–C(17)	98·4	C(13)–C(17)–C(16)	104·6
C(14)–C(13)–C(18)	113·3	C(2)—C(19)–C(10)	105·8

The C(sp^3)–C(sp^3) bond distances average 1·534 Å in the molecule, close to the accepted value, and need no further mention. However, the C(sp^3)–C(sp^2) distance of 1·542 Å for C(2)–C(3) is abnormally long when compared with corresponding distances in (for example) 20(*S*)-hydroxyprogesterone (Isaacs, Motherwell, Coppola & Kennard, 1972*a*) (1·448 (6) Å), epitestosterone (Isaacs, Motherwell, Coppola & Kennard, 1972*b*) (1·504 (6) Å), and 17*β*-hydroxy-17*α*-methyl-5*α*-androst-1-en-3-one (Rendle & Trotter, 1974*a*) (1·462 (12) Å). This may well compensate for the rather short bonds associated with atom C(2), *viz*. C(2)–O(4) at 1·403 Å and C(2)–C(1) at 1·510 Å. The usual C–O single bond length as quoted by Sutton

(1965) is 1·426 (5) Å, precisely that found in the C(17)–O(5) bond. Even allowing for rigid-body motion followed by riding-motion corrections, the length of C(2)–O(4) only increases to 1·406 Å. Other 'corrected' distances show similarly small and insignificant differences from the uncorrected distances.

The unit consisting of rings *A*1 and *A*2 appears to be quite strained, as evidenced by the smaller-than-tetrahedral angles around sp^3 hybridized carbon atoms, *e.g.* C(2)–C(1)–C(5) 100·4°. This is probably to be expected with the *cis*-fusion of five- and six-membered rings. The presence of the δ-lactone grouping also contributes to the strain in that ring system, as such a grouping tends to be planar. Indeed, atoms C(2), C(3), O(1), O(2), and C(4) do form a plane (Table 7) with atoms C(1) and C(5) displaced 0·93 and 0·09 Å to the same side of the plane. Cheung, Overton & Sim (1965) have suggested that δ-lactones normally adopt the half-chair conformation if free to do so [in our case C(1) and C(5) would have had to have been on *opposite* sides of the lactone plane], but may adopt the half-boat conformation [as is the case with our compound] as a result of special circumstances, *e.g.* the *cis*-fusion of a six-membered ring to a five-membered ring. Many examples of δ-lactones with half-boat conformations are quoted in this reference and most of them form more regular half-boats, with the two atoms displaced from the lactone plane by almost equal distances. In the present case, C(1) is much farther from the plane than C(5). In fact C(5) is almost in the plane, and one might say ring *A*1 has a sofa conformation. However, a distorted half-boat conformation seems appropriate.

Table 7. *Equations of planes in the form* $lX+mY+nZ=p$ *where X, Y, Z are orthogonal coordinates in* Å

Deviations (Å) of atoms from the planes are given in square brackets, the average e.s.d. being 0·004 Å.

Plane 1: O(1), O(2), C(2), C(3), C(4)
$-0{\cdot}9786X-0{\cdot}0109Y-0{\cdot}2057Z=-8{\cdot}3255$
[O(1) 0·004, O(2) −0·012, C(1) −0·928, C(2) −0·007, C(3) 0·010, C(4) 0·016, C(5) −0·086]

Plane 2: O(2), C(2), C(3), C(4), C(5)
$-0{\cdot}9733X-0{\cdot}0082Y-0{\cdot}2294Z=-8{\cdot}5336$
[O(2) −0·015, C(1) −0·882, C(2) 0·014, C(3) 0·002, C(4) 0·046, C(5) −0·029]

Plane 3: C(2), C(5), C(10), C(19)
$0{\cdot}4277X+0{\cdot}6638Y-0{\cdot}6136Z=0{\cdot}2923$
[C(1) 0·648, C(2) −0·042, C(5) 0·045, C(10) −0·057, C(19) 0·068]

Plane 4: O(3), C(5), C(6), C(10)
$0{\cdot}1063X-0{\cdot}3107Y-0{\cdot}9445Z=-8{\cdot}3308$
[O(3) −0·002, C(4) −0·538, C(5) 0·004, C(6) 0·006, C(10) −0·005]

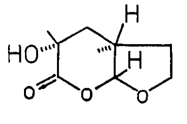
Plane 5: C(6), C(7), C(9), C(10)
$0{\cdot}7850X-0{\cdot}5741Y-0{\cdot}232Z=-0{\cdot}1572$
[C(6) −0·029, C(7) 0·020, C(8) 0·660, C(9) −0·016, C(10) 0·025]

Plane 6: C(8), C(11), C(12), C(14)
$0{\cdot}7809X-0{\cdot}5421Y-0{\cdot}3104Z=0{\cdot}0996$
[C(8) 0·026, C(9) −0·653, C(11) −0·030, C(12) 0·033, C(13) 0·705, C(14) −0·027]

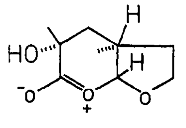
Plane 7: C(14), C(15), C(16), C(17)
$0{\cdot}9192X-0{\cdot}3931Y-0{\cdot}0244Z=2{\cdot}4848$
[C(13) 0·714, C(14) −0·022, C(15) 0·044, C(16) −0·051, C(17) 0·026]

The conformations of the five-membered rings in the compound may conveniently be described as envelopes showing varying degrees of distortion. A series of mean-plane calculations through sets of four atoms was calculated for each ring, and the results are shown in Table 7. In ring *A*2, C(1) is displaced 0·648 Å from the plane C(2)–C(5)–C(10)–C(19); in *A*3, C(4) is displaced 0·538 Å from the plane O(3)–C(6)–C(10)–C(5); in *B*, C(8) is displaced 0·660 Å from the plane C(6)–C(7)–C(9)–C(10). Ring *D* has a C(13) envelope conformation with C(13) 0·714 Å from the plane C(14)–C(15)–C(16)–C(17). The maximum torsion angle φ_m, and the phase angle of pseudorotation Δ, two parameters usually quoted when describing ring *D* in a steroid molecule (Altona, Geise & Romers, 1968) are 48·0° and 17·2° respectively. Ring *C* has a relatively undistorted chair conformation with atoms C(9) and C(13) 0·653 and 0·705 Å on either side of the plane through atoms C(8), C(11), C(12), and C(14).

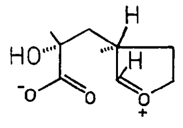
The distribution of endocyclic C–O bond lengths in ring *A*1 and ring *A*3 is rather interesting. C(3)–O(2) is 1·346 Å, O(2)–C(4) is 1·476 Å, C(4)–O(3) is 1·383 Å, and O(3)–C(6) is 1·446 Å. The planarity of the lactone group (I) is due to contributions from structure (II), but it would appear from the distribution of the C–O bond lengths that a further structure (III) may also contribute.



(I)



(II)



(III)

The C(3)–O(2) bond undoubtedly has some double bond character. It is shorter than the C(sp^3)–O distance of 1·37 Å in withaferin A acetate *p*-bromobenzoate,

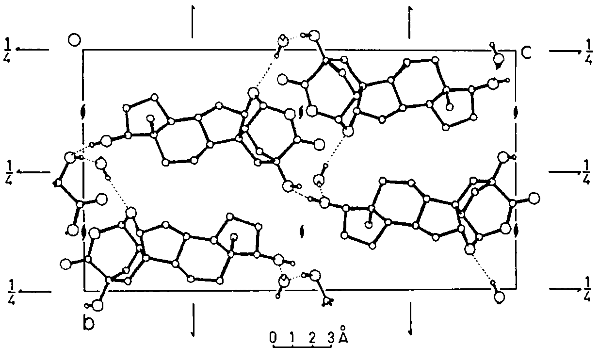


Fig. 2. Projection of the unit cell with the *a* axis pointing toward the viewer.

(McPhail & Sim, 1968) but is also longer than the corresponding distances observed in 6α-bromo-17β-hydroxy-17α-methyl-4-oxa-5α-androstan-3-one (McKechnie, Kubina & Paul, 1970) (1·28 Å), and 17β-hydroxy-17α-methyl-2-oxa-5α-androstan-3-one (Rendle & Trotter, 1974*b*) (1·331 Å). The C(sp^3)–O distance of 1·476 Å in the δ-lactone ring is much longer than the values 1·45, 1·45, and 1·469 Å quoted by McPhail & Sim (1968), McKechnie, Kubina & Paul (1970), and Rendle & Trotter (1974*b*). This would support the inclusion of structure (III), a structure with no bond between O(2) and C(4) although the contribution from (III) would likely be much less than that from (I) and (II). Another factor supporting the inclusion of (III) is the significant difference between the bonds C(4)–O(3) and O(3)–C(6). The degree of symmetry in the lactone ring and also the planarity of the lactone groups are illustrated by the torsion angles in Table 8.

Table 8. *Observed torsional angles* (°) (*average e.s.d. is* 0·3°)

Ring *A*1		Ring *A*2		Ring *A*3	
Bond	Obs.	Bond	Obs.	Bond	Obs.
1– 2	70·8	1– 2	−45·2	4– 5	38·3
2– 3	−37·9	2–19	35·3	5–10	−21·8
3–O(2)	−3·1	19–10	−10·6	10– 6	0·8
O(2)– 4	6·5	10– 5	−17·6	6–O(3)	23·4
4– 5	32·0	5– 1	39·0	O(3)– 4	−39·1
5– 1	−70·4				

Ring *B*		Ring *C*		Ring *D*	
Bond	Obs.	Bond	Obs.	Bond	Obs.
6– 7	22·5	8– 9	−57·6	13–14	47·5
7– 8	−40·9	9–11	54·6	14–15	−34·5
8– 9	44·1	11–12	−52·0	15–16	7·4
9–10	−29·9	12–13	55·6	16–17	22·2
10– 6	4·6	13–14	−60·4	17–13	−41·8
		14– 8	60·0		

Intermolecular contacts less than 3·4 Å are few, and the majority of these are between oxygen atoms and involve hydrogen bonds. Table 9 is a list of intermolecular contacts less than 3·4 Å. Fig. 2 is a molecular packing diagram in the form of a projection with the *a* axis pointing towards the viewer. Intermolecular hydrogen bonds are signified by broken lines. The water molecule is securely bound, being involved in no less than three hydrogen bonds, the strongest with O(4) and the weakest with O(3). Table 10 gives details of the hydrogen bond geometries.

Table 9. *Intermolecular distances* < 3·4 Å ((*average e.s.d. is* 0·005 Å)

$O(1)\cdots C(4^{i})$	3·150	$O(4)\cdots O(6^{iii})$	2·647
$O(1)\cdots C(6^{ii})$	3·208	$O(4)\cdots O(5^{iii})$	2·864
$O(1)\cdots O(5^{iii})$	3·224	$O(4)\cdots C(17^{iii})$	3·389
$O(1)\cdots O(3^{ii})$	3·240	$O(5)\cdots O(6^{v})$	2·776
$O(1)\cdots O(6^{iii})$	3·258	$O(6)\cdots C(2^{vi})$	3·285
$O(3)\cdots O(6^{iv})$	2·901		

Roman numeral superscripts refer to the following equivalent positions:

i	$-\frac{1}{2}+x,$	$\frac{1}{2}-y,$	$1-z$	iv	$1-x,$	$-\frac{1}{2}+y,$	$\frac{1}{2}-z$
ii	$\frac{1}{2}+x,$	$\frac{1}{2}-y,$	$1-z$	v	$1+x,$	$y,$	z
iii	$\frac{3}{2}-x,$	$1-y,$	$\frac{1}{2}+z$	vi	$\frac{3}{2}-x,$	$1-y,$	$-\frac{1}{2}+z$

Table 10. *Details of hydrogen-bond geometry with estimated standard deviations in parentheses*

	$O\cdots O$	O–H	$H\cdots O$	$O–H\cdots O$
$O(6)–H(O6A)\cdots O(5)$	2·776 (5) Å	0·96 Å	1·85 Å	163°
$O(6)–H(O6B)\cdots O(3)$	2·901 (4)	0·81	2·11	167
$O(5)–H(O5)\cdots O(4)$	2·864 (4)	0·94	1·95	163
$O(4)–H(O4)\cdots O(6)$	2·647 (4)	1·05	1·62	166

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