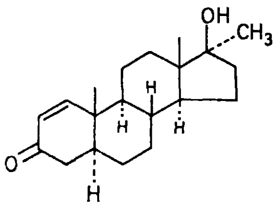
Crystal and Molecular Structure of 17β-Hydroxy-17α-methyl-5α-androst-1-en-3-one Hemihydrate

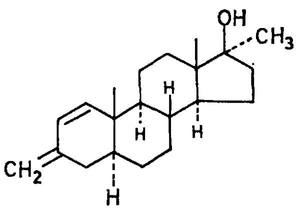
By **David F. Rendle** and **James Trotter,*** Department of Chemistry, University of British Columbia, Vancouver 8, British Columbia, Canada

Crystals of the title compound are orthorhombic, a = 10·464(1), b = 22·738(2), c = 7·463(1) Å, space group $P2_12_12$, $Z = 4$. The structure was determined from diffractometer data by direct methods, and refined by full-matrix least-squares methods to R 0·062 for 871 observed reflexions. Ring A is a distorted sofa, rings B and C have regular chair conformations, and ring D approximates to a C(13) envelope. The water molecule lies on the crystallographic two-fold axis and provides a hydrogen bond ' bridge ' between two steroid molecules with an O–H · · · O distance of 2·89 Å. Another O–H · · · O hydrogen bond (2·76 Å) provides the ' head-to-tail ' linkage between carbonyl oxygen and hydroxy-group of adjacent molecules, a common feature in many steroid structures.

THE ability of testosterone to cause nitrogen retention (anabolic effect) was first shown in 1935.[1] However, the potency of testosterone as an androgenic agent has prevented its widespread use as an anabolic agent, and as a result considerable effort has been made to synthesize anabolic agents possessing little or no androgenic activity. In 1961 Counsell *et al.*[2] reported the synthesis and anabolic–androgenic activity of a number of 5α-androst-1-enes, including 17β-hydroxy-17α-methyl-5α-androst-1-en-3-one (I). Further work[3] established that the 3-methylene derivative (II) possessed an even higher anabolic : androgenic activity ratio (therapeutic index). We have undertaken single crystal *X*-ray analyses of both compounds in an attempt to rationalize (from an electronic or steric point of view) the rise in therapeutic index upon substitution of the methylene group for the carbonyl oxygen. We now report the structure of (I).



(I)



(II)

EXPERIMENTAL

17β-Hydroxy-17α-methyl-5α-androst-1-en-3-one in the form of a powder was kindly supplied by Dr. K. Irmscher of E. Merck AG, Darmstadt, W. Germany. Crystals suitable for structural analysis were grown from acetone–water as colourless, thin rectangular plates elongated in the c direction. The crystal chosen for study had approximate dimensions of 0·7 × 0·1 × 0·4 mm^3, and was mounted with c parallel to the goniostat axis. The space group and

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[1] C. D. Kochakian and J. R. Murlin, *J. Nutrition*, 1935, **10**, 437.

[2] R. E. Counsell, P. D. Klimstra, and F. B. Colton, *J. Org. Chem.*, 1962, **27**, 248.

[3] K. Irmscher, H.-G. Kraft, and K. Brückner, *J. Medicin. Chem.*, 1964, **7**, 345.

initial unit cell parameters were determined from oscillation, Weissenberg, and precession photographs. Accurate unit cell parameters were later obtained by a least-squares treatment of 14 $\sin^2\theta(hkl)$ values measured on a General Electric XRD 6 diffractometer with Cu-K_α radiation.

Crystal Data.—$C_{20}H_{30}O_2,0{\cdot}5H_2O$, $M = 311{\cdot}5$. Orthorhombic, $a = 10{\cdot}464(1)$, $b = 22{\cdot}738(2)$, $c = 7{\cdot}463(1)$ Å, $U = 1775{\cdot}7$ Å^3, $D_m = 1{\cdot}15$ (aqueous KI), $Z = 4$, $D_c = 1{\cdot}165$, $F(000) = 684$. Cu-K_α radiation, $\lambda = 1{\cdot}5418$ Å; $\mu(\text{Cu-}K_\alpha) = 5{\cdot}9$ cm^{-1}. Space group $P2_12_12$ (D_2^3, No. 18) from systematic absences: $h00$, $h \neq 2n$, and $0k0$, $k \neq 2n$.

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. A scintillation counter equipped with a nickel filter and pulse height analyser ensured approximately monochromatic radiation. Of the 1864 independent reflexions ($2\theta \leqslant 135°$ for Cu radiation), 993 had intensities $<3\sigma(I)$ above background [$\sigma(I)$ is defined by $\sigma^2(I) = S + B + (0{\cdot}05S)^2$ where S = scan count and B = background count] and were classified as unobserved. A standard reflexion was monitored every 40 reflexions and its intensity fluctuated by up to 25% throughout the data collection. The data were accordingly scaled, Lorentz and polarization corrections applied, and the structure amplitudes derived. No absorption corrections were applied.

Structure Analysis and Refinement.—The data were placed on an absolute scale by the method of Wilson,[4] and normalized structure amplitudes $|E_{hkl}|$ were derived. A Σ_2 listing for the 56 reflexions with $|E| \geqslant 2{\cdot}00$ was obtained and the origin and enantiomorph were defined by fixing the phases of the 2 1 0, 0 10 1, 9 0 3, and 0 13 5 reflexions. Three further reflexions were assigned symbolic phases and these are included in the complete starting set listed in Table 1. These seven reflexions were expanded manually using the 56 reflexions with $|E| \geqslant 2{\cdot}00$. Symbols a and c are required by space group symmetry to be $\pm\pi/2$ and 0 or π respectively, but symbol b may assume any value between 0 and 2π. Manual determination gave no indication of the value of b and so the basic set of Table 1 was used directly as input to the tangent formula.[5,6] Tangent refinement was applied by way of a modified version of Drew's program.[7] The basic set of reflexions was split into 12 starting sets by allowing the symbols to assume the following values: $a \pm \pi/2$, b 200, 600, and 800 mcycles, and c 0 and π. A total of 197 reflexions with $|E| \geqslant 1{\cdot}50$ was input to the program and the first 60 were allowed to refine for 5 cycles, the first 140 for the next 5 cycles, and all the reflexions for a final 5 cycles. In any cycle a phase assignment was rejected if the consistency index, $t = \sqrt{A^2 + B^2}/\Sigma_K|E_K| \cdot |E_{H-K}|$ was $<0{\cdot}25$, $\alpha = |E_H| \cdot \sqrt{A^2 + B^2}$ was $<9{\cdot}0$, and the phase associated with a particular reflexion differed by more than 250 mcycles from its value in the previous cycle. The set for which $a = 250$, $b = 200$, and $c = 500$ mcycles assigned the greatest number of phases, 191, had the lowest R_{Karle} value,[6] 0·21, the highest consistency index, 0·62, and the highest α, 216. The remaining sets had R_{Karle} values ranging from 0·27 to 0·35. Using the same basic set, 222 reflexions with $|E| \geqslant 1{\cdot}45$ were input to the tangent refinement program with the symbol values set at the above values and the resulting 211 determined phases were used to generate an E-map.

TABLE 1

Starting set of reflexions

			$\|E(h)\|$	$\phi(h)$	
2	1	0	3·742	0	Origin
0	10	1	2·229	0	
9	0	3	2·171	$\frac{\pi}{2}$	
0	13	5	3·059	$\frac{\pi}{2}$	Enantiomorph
0	17	1	2·849	a	
1	17	2	4·087	b	
8	19	0	3·074	c	

From the E-map 20 of the 23 non-hydrogen atoms were located and a structure factor calculation based on the E-map co-ordinates with $B = 3{\cdot}2$ Å^2 for all atoms, gave R 0·28. At this point it was realized that the wrong enantiomorph had initially been specified and this was corrected by substituting negative x co-ordinates for each of the atoms. A difference Fourier synthesis revealed the remainder of the atoms in the steroid skeleton and also the presence of the water molecule on the crystallographic twofold axis. A structure factor calculation based on all the non-hydrogen atoms gave R 0·24. Refinement was by least-squares methods in which the function minimized was $\Sigma w(F_o - F_c)^2$ with weights w derived from counting statistics. Two cycles of full-matrix, least-squares refinement on the positional and isotropic thermal parameters reduced R to 0·14. A difference Fourier synthesis at this point revealed all the hydrogen atoms in the steroid molecule, but those associated with the water molecule could not be located with any certainty. As a result of subsequent molecular geometry calculations (see Discussion section) the solvent molecule was found to participate in a hydrogen bonding scheme and so the unique water hydrogen atom was fixed at a distance of 0·85 Å from the water oxygen atom O(3) along the vector between O(3) and O(2). The methyl hydrogens associated with C(18) and C(19) had rather ill-defined geometry and it was decided to place them in calculated positions assuming C–H distances of 0·95 Å and ideal sp^3 geometry about the carbon atoms. R Fell to 0·11 upon the inclusion of the hydrogen atoms, each with $B = 4{\cdot}0$ Å^2. The non-hydrogen atoms were then refined with anisotropic temperature factors; the hydrogen atom contributions were included, but their positions and temperature factors were not refined. Scattering factors for carbon and oxygen were taken from ref. 8*a* and those for hydrogen from ref. 8*b*. Convergence was reached after three cycles of refinement with R at 0·062 for the 871 observed reflexions; no parameter shift was greater than 0·60. The weighted residual R_w [defined as $\Sigma w(F_o - F_c)^2/\Sigma w F_o^2$] stood at 0·071. A final difference Fourier synthesis showed no peak higher than 0·27 e Å^{-3}. Measured and calculated structure factors are listed in Supplementary Publication No. SUP 20975 (19 pp., 1 microfiche).*

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* For details see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1973, Index issue.

[4] A. J. C. Wilson, *Nature*, 1942, **150**, 151.

[5] J. Karle and H. Hauptman, *Acta Cryst.*, 1956, **9**, 635.

[6] J. Karle and I. L. Karle, *Acta Cryst.*, 1966, **21**, 849.

[7] See *e.g.* M. G. B. Drew, D. H. Templeton, and A. Zalkin, *Acta Cryst.*, 1969, **B25**, 261.

[8] (*a*) 'International Tables for *X*-Ray Crystallography,' Kynoch Press, Birmingham, 1962, vol. III, pp. 202—207; (*b*) R. F. Stewart, E. R. Davidson, and W. F. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.

Final positional and thermal parameters are given in Tables 2 and 3.

TABLE 2

Final positional (fractional × 10^4) parameters in 17β-hydroxy-17α-methyl-5α-androst-1-en-3-one hemihydrate with estimated standard deviations in parentheses *

	x	*y*	*z*
O(1)	8159(7)	−0675(2)	0544(9)
O(2)	5976(6)	4018(2)	2826(9)
O(3)	0	0	5134(14)
C(1)	7796(10)	0860(3)	−0090(12)
C(2)	8224(9)	0322(4)	−0331(14)
C(3)	7903(10)	−0167(4)	0913(13)
C(4)	7280(9)	−0002(4)	2593(12)
C(5)	7291(8)	0655(4)	3055(13)
C(6)	6563(9)	0794(3)	4720(13)
C(7)	6749(8)	1444(3)	5209(12)
C(8)	6449(8)	1860(3)	3679(12)
C(9)	7186(8)	1694(3)	1976(11)
C(10)	6960(8)	1041(3)	1430(12)
C(11)	6942(8)	2141(3)	0466(12)
C(12)	7200(9)	2774(3)	1047(11)
C(13)	6417(8)	2935(4)	2635(12)
C(14)	6716(8)	2503(3)	4139(12)
C(15)	6073(10)	2763(4)	5824(14)
C(16)	6189(12)	3433(4)	5511(15)
C(17)	6675(10)	3537(4)	3622(13)
C(18)	4987(9)	2921(4)	2157(13)
C(19)	5579(9)	0948(3)	0776(13)
C(20)	8062(10)	3705(4)	3554(16)
H(1)	8055	1118	−1043
H(2)	8952	0174	−0936
H(4A)	7749	−0205	3835
H(4B)	6458	−0044	2464
H(5)	8103	0714	3214
H(6A)	6924	0498	5967
H(6B)	5650	0714	4516
H(7A)	7622	1494	5522
H(7B)	6219	1532	6186
H(8)	5486	1771	3400
H(9)	8089	1723	2258
H(11A)	7554	2048	−0265
H(11B)	6250	2041	0086
H(12A)	8029	2761	1186
H(12B)	7106	3005	0249
H(14)	7630	2512	4464
H(15A)	6899	2654	6662
H(15B)	5181	2671	5724
H(16A)	6695	3632	6348
H(16B)	5288	3585	5506
H(18A)	4764	2535	1773
H(18B)	4499	3040	3123
H(18C)	4847	3186	1151
H(19A)	4984	1058	1718
H(19B)	5396	1171	−0249
H(19C)	5418	0537	0519
H(20A)	8148	4117	4399
H(20B)	8496	3399	3942
H(20C)	8573	3752	2462
HO(2)	6231	4171	1641
HO(3)	0304	0302	5762

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

DISCUSSION

Figure 1 is a general view of the steroid molecule showing the atomic numbering scheme. For the sake of clarity the hydrogen atoms have not been labelled. Bond lengths and valency angles with their standard deviations are listed in Tables 4 and 5. The $C(sp^3)$–$C(sp^3)$ bond lengths show quite a scatter but nonetheless average to 1·53 Å. Of the remaining bonds, the C=C distance in ring A is 1·315(11) Å, the carbonyl distance is 1·216(9) Å, and the C(17)–O(2) distance is 1·443(9) Å. All these distances are in close agreement with those in similar steroid structures.[9-11] The valency angles about tetrahedral carbon atoms in the six-membered rings B and C fall into the three categories suggested by Geise *et al.*[12] The quaternary substituted carbon atoms C(10) and C(13) have valency angles which average to 109·5° (predicted: 109·5°), the tertiary substituted carbons C(5), C(8), C(9), and C(14) have angles which average to 112·4° (predicted: 110·5°), and the secondary substituted carbons C(6), C(7), C(11), and C(12) have angles which average to 111·7° (predicted: 111·5°). The valency angles in ring D show the characteristic departure from ' normal ' tetrahedral angles due to the fusion of five- and six-membered rings. Carbon–hydrogen bond distances range from 0·80 to 1·15 Å and tetrahedral angles involving hydrogen atoms from 92 to 140°. The O(2)–HO(2) distance is 0·99 Å and the C(17)–O(2)–HO(2) angle is 120°.

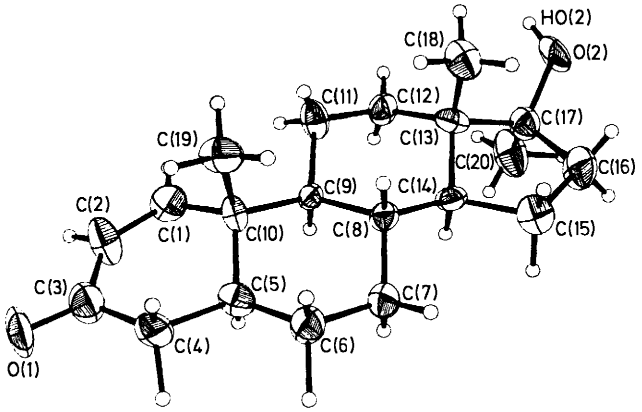

FIGURE 1 Molecular structure of 17β-hydroxy-17α-methyl-5α-androst-1-en-3-one

Bucourt and Hainaut [13] have studied the various conformations of cyclohexenes and noted that only the half-chair form corresponds to a true energy minimum. Providing one takes into account additional flattening of the cyclohexene ring upon substitution of another trigonal carbon atom (in the form of a carbonyl group), one may assume that the most stable conformations of cyclohexenones are analogous to those of the corresponding cyclohexene derivatives. However, when the cyclohexene ring is fused to another ring, two conformations corresponding to energy minima are found, the half-chair

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[9] N. W. Isaacs, W. D. S. Motherwell, J. C. Coppola, and O. Kennard, *J.C.S. Perkin II*, 1972, 2331.

[10] N. W. Isaacs, W. D. S. Motherwell, J. C. Coppola, and O. Kennard, *J.C.S. Perkin II*, 1972, 2335.

[11] P. J. Roberts, J. C. Coppola, N. W. Isaacs, and O. Kennard, *J.C.S. Perkin II*, 1973, 774.

[12] H. J. Geise, C. Altona, and C. Romers, *Tetrahedron*, 1967, **23**, 439.

[13] R. Bucourt and D. Hainaut, *Bull. Soc. chim. France*, 1965, 1366.

TABLE 3

Final thermal parameters * (Å² × 10²) with standard deviations in parentheses

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(I)	14·55(72)	1·97(33)	5·88(49)	0·70(41)	1·76(58)	−0·97(34)
O(2)	8·56(50)	2·20(35)	5·70(50)	2·68(33)	0·55(45)	0·51(36)
O(3)	9·56(83)	7·11(64)	8·23(87)	−1·89(62)	0	0
C(1)	7·11(77)	2·98(52)	3·90(63)	−1·59(50)	0·21(67)	0·85(48)
C(2)	5·80(68)	3·51(53)	7·21(76)	0·49(52)	2·31(71)	−0·72(58)
C(3)	7·55(78)	3·56(61)	4·36(67)	0·37(51)	1·09(69)	0·05(53)
C(4)	6·17(66)	2·43(45)	4·79(63)	−0·72(46)	−0·72(64)	0·82(56)
C(5)	3·59(56)	2·76(49)	4·31(66)	−0·73(45)	0·05(60)	0·61(48)
C(6)	6·42(73)	3·04(48)	3·54(61)	−0·20(48)	0·28(63)	0·04(51)
C(7)	5·08(62)	3·81(50)	3·22(54)	0·82(47)	0·56(58)	−0·14(49)
C(8)	4·17(61)	2·30(46)	2·62(54)	−0·21(41)	−0·62(53)	−0·13(44)
C(9)	3·65(55)	2·02(44)	1·84(54)	−0·09(37)	−0·14(51)	−0·01(41)
C(10)	3·11(58)	2·18(44)	3·82(59)	0·10(39)	0·78(53)	−0·62(43)
C(11)	4·75(58)	2·30(39)	4·52(62)	−0·39(39)	1·45(57)	−0·17(46)
C(12)	5·57(66)	3·44(51)	2·47(53)	0·33(48)	0·89(57)	0·27(46)
C(13)	2·47(54)	3·67(54)	3·44(65)	0·61(44)	0·05(52)	1·15(52)
C(14)	3·70(55)	2·90(45)	2·59(57)	0·01(43)	−1·19(54)	0·12(46)
C(15)	5·01(68)	4·82(62)	5·11(71)	0·56(55)	0·24(65)	−0·38(57)
C(16)	9·14(92)	3·03(49)	5·44(74)	0·05(56)	−0·52(79)	−1·57(55)
C(17)	5·45(73)	2·83(48)	3·92(65)	0·30(49)	0·29(64)	−0·11(48)
C(18)	5·14(58)	4·03(52)	5·78(75)	0·45(46)	0·17(68)	−0·37(59)
C(19)	5·25(64)	2·90(46)	5·79(67)	−1·36(43)	−1·82(57)	0·87(51)
C(20)	6·60(72)	3·95(54)	9·38(94)	−0·40(51)	0·75(75)	−2·10(61)

* The temperature factor expression is of the type: $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$.

and the sofa (1,2 diplanar) conformations. By definition, the half-chair form consists of atoms C(1)—C(3) and C(10) coplanar [14] while C(4) and C(5) alternate above and below this plane. Also by definition, the sofa conformation requires five consecutive coplanar atoms [*e.g.* C(1)—C(4) and C(10), or C(1)—C(3), C(5), and C(10)] with the remaining atom [C(5) or C(4)] above or below the plane. In the case of 17β-hydroxy-17α-methyl-5α-androst-1-en-3-one ring A appears to have a conformation closest to that of a sofa with C(5) out of the plane formed by C(1)—C(4) and C(10). Admittedly atoms C(1)—C(3) and C(10) form a much better plane than do atoms C(1)—C(4) and C(10), but a half-chair conformation must be ruled out because atoms C(4) and C(5) both lie on the same side of the four-atom plane (see Table 7). Furthermore, the dihedral angles (Table 6)

TABLE 4

Bond lengths (Å) with estimated standard deviations in parentheses

O(1)–C(3)	1·216(9)	C(9)–C(10)	1·558(10)
O(2)–C(17)	1·443(9)	C(10)–C(19)	1·540(11)
C(1)–C(2)	1·315(11)	C(11)–C(12)	1·528(11)
C(1)–C(10)	1·491(12)	C(12)–C(13)	1·486(11)
C(2)–C(3)	1·490(12)	C(13)–C(14)	1·525(11)
C(3)–C(4)	1·462(12)	C(13)–C(18)	1·539(12)
C(4)–C(5)	1·537(11)	C(13)–C(17)	1·578(12)
C(5)–C(6)	1·491(12)	C(14)–C(15)	1·544(11)
C(5)–C(10)	1·536(11)	C(15)–C(16)	1·546(12)
C(6)–C(7)	1·536(10)	C(16)–C(17)	1·517(13)
C(7)–C(8)	1·514(11)	C(17)–C(20)	1·502(13)
C(8)–C(14)	1·527(10)		
C(8)–C(9)	1·533(11)		
C(9)–C(11)	1·540(10)		

TABLE 5

Valency angles (degrees) with estimated standard deviations in parentheses

C(2)–C(1)–C(10)	124·1(8)	C(16)–C(17)–C(13)	103·9(7)
C(1)–C(2)–C(3)	122·3(9)	C(16)–C(17)–C(20)	113·2(9)
C(2)–C(3)–O(1)	121·3(9)	C(16)–C(17)–O(2)	109·3(8)
C(2)–C(3)–C(4)	116·4(8)	C(13)–C(17)–O(2)	112·3(7)
C(4)–C(3)–O(1)	122·4(8)	C(13)–C(17)–C(20)	111·7(8)
C(3)–C(4)–C(5)	116·0(8)	O(2)–C(17)–C(20)	106·5(7)
C(4)–C(5)–C(6)	112·9(8)	C(8)–C(9)–C(11)	111·1(6)
C(4)–C(5)–C(10)	112·2(8)	C(10)–C(9)–C(11)	114·4(7)
C(6)–C(5)–C(10)	115·0(7)	C(9)–C(10)–C(1)	111·9(7)
C(5)–C(6)–C(7)	109·7(7)	C(9)–C(10)–C(5)	107·6(7)
C(6)–C(7)–C(8)	113·3(7)	C(9)–C(10)–C(19)	110·8(7)
C(7)–C(8)–C(9)	111·5(6)	C(5)–C(10)–C(19)	112·6(7)
C(7)–C(8)–C(14)	112·9(7)	C(1)–C(10)–C(19)	105·8(7)
C(9)–C(8)–C(14)	109·3(7)	C(1)–C(10)–C(5)	108·2(7)
C(8)–C(9)–C(10)	112·0(7)	C(9)–C(11)–C(12)	112·7(7)
C(17)–C(13)–C(18)	107·1(7)	C(11)–C(12)–C(13)	111·1(7)
C(13)–C(14)–C(15)	105·2(6)	C(12)–C(13)–C(14)	108·4(6)
C(13)–C(14)–C(8)	114·5(7)	C(12)–C(13)–C(17)	119·4(7)
C(8)–C(14)–C(15)	118·1(8)	C(14)–C(13)–C(17)	100·4(7)
C(14)–C(15)–C(16)	102·8(8)	C(12)–C(13)–C(18)	110·2(8)
C(15)–C(16)–C(17)	108·7(8)	C(14)–C(13)–C(18)	110·9(7)

TABLE 6

Torsional angles compared with ' standard ' values *

Ring A			Ring B		
Bond	Obs.	Standard	Bond	Obs.	Standard
1–2	0·3 (1·1)	0	9–10	−54·4 (0·7)	−56·9
2–3	−10·7 (1·1)	0	10–5	57·0 (0·8)	58·0
3–4	−12·7 (0·9)	−28	5–6	−56·1 (0·8)	−57·2
4–5	44·3 (0·9)	56	6–7	52·7 (0·8)	53·4
5–10	−51·1 (0·8)	−54	7–8	−52·9 (0·8)	−51·9
10–1	31·0 (1·0)	27	8–9	54·3 (0·7)	54·6
Ring C			Ring D		
Bond	Obs.	Standard	Bond	Obs.	Standard
11–12	−57·0 (0·8)	−55·0	13–14	43·7 (0·7)	43·8
11–9	53·1 (0·7)	53·7	14–15	−33·1 (0·8)	−33·3
9–8	−50·8 (0·7)	−52·8	15–16	8·6 (0·8)	10·0
8–14	55·6 (0·7)	56·7	16–17	17·8 (0·9)	17·2
14–13	−59·0 (0·7)	−59·2	17–13	−37·3 (0·8)	−37·7
13–12	57·4 (0·8)	55·6			

* See text for references.

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[14] E. Toromanoff, *Topics Stereochem.*, 1967, **2**, 162.

TABLE 7

Equations of planes in the form $lX + mY + nZ = p$ where X, Y, Z are orthogonal co-ordinates in Å. Deviations (Å) of atoms from the planes are given in square brackets

Plane (1): C(1)—C(4), C(10)

$$-0{\cdot}8405X - 0{\cdot}2493Y - 0{\cdot}4811Z = -7{\cdot}2696$$

[C(1) −0·041(10), C(2) −0·027(10), C(3) 0·087(10), C(4) −0·062(9), C(10) 0·045(9), C(5) −0·611(9)]

Plane (2): C(1)—C(3), C(10)

$$-0{\cdot}8092X - 0{\cdot}2141Y - 0{\cdot}5472Z = -6{\cdot}9834$$

[C(1) 0·001(10), C(2) −0·001(10), C(3) 0·001(10), C(10) −0·001(9), C(4) −0·238(9), C(5) −0·756(9)]

Plane (3): C(14)—C(17)

$$-0{\cdot}9133X - 0{\cdot}0607Y - 0{\cdot}4028Z = -7{\cdot}9850$$

[C(14) −0·023(9), C(15) 0·049(10), C(16) −0·060(12), C(17) 0·029(10), C(13) 0·655(9)]

Plane (4): C(5)—C(17)

$$-0{\cdot}9773X - 0{\cdot}0703Y - 0{\cdot}1996Z = -7{\cdot}7156$$

observed in ring A compare well with the 'standard' values calculated for a sofa conformation in ref. 13.

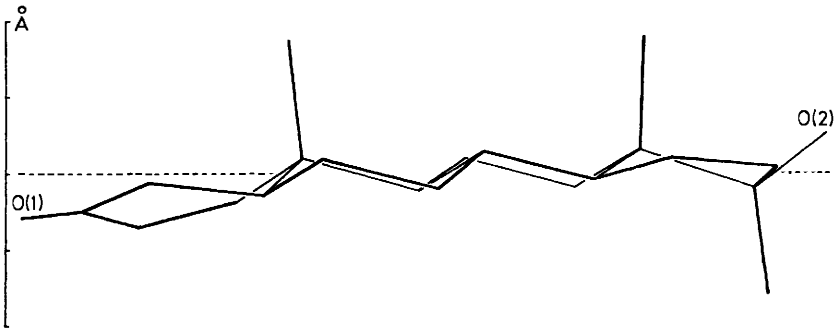

FIGURE 2 Steroid skeleton viewed parallel to the best plane through atoms C(5)—C(17)

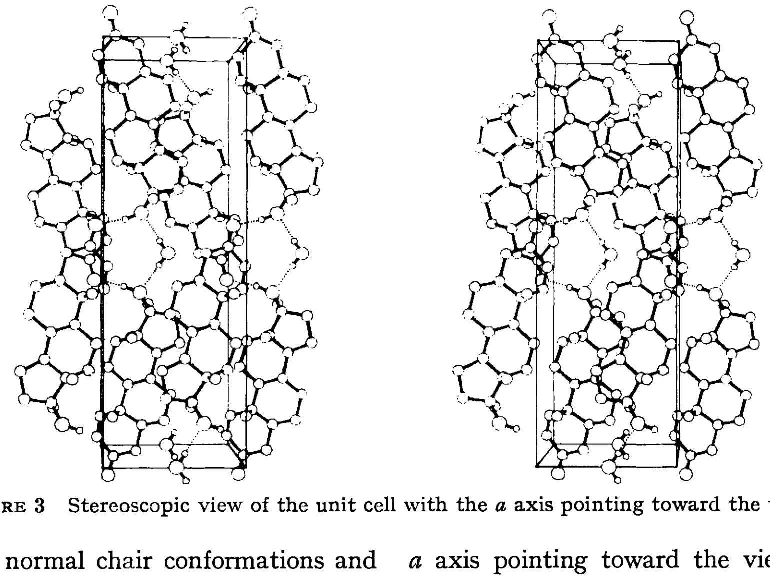

FIGURE 3 Stereoscopic view of the unit cell with the *a* axis pointing toward the viewer

Rings B and C have normal chair conformations and their dihedral angles are compared with 'standard' values[12] in Table 6. In the notation of Altona *et al.*[15] ring D has a maximum angle of torsion (ϕ_m) of 43·9° and a phase angle of pseudo-rotation (Δ) of 11·4°. In more qualitative terms ring D has a conformation which is closest to a C(13) envelope. Least-squares plane calculations through sets of four atoms in ring D revealed that atoms C(14)—C(17) form the best plane. In Table 6 the dihedral angles observed in ring D are compared with a set of angles predicted for one of a number of conformational energy minima.[16]

Figure 2 shows the steroid skeleton viewed parallel to the best plane through atoms C(5)—C(17). The molecule is slightly convex towards the β-side presumably as a consequence of the interaction of the C(18) and C(19) methyl hydrogens with the axial hydrogens at C(8) and C(11). The absence of bulky groups on the α-face of the molecule would certainly permit this bending.

The molecules are linked in the solid state by a system of hydrogen bonds which involves the water molecule on the crystallographic two-fold axis. Figure 3 is a stereo-view of the unit cell and its contents with the *a* axis pointing toward the viewer, and Figure 4 is a projection of the unit cell viewed down *c*. Hydrogen

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[15] C. Altona, H. J. Geise, and C. Romers, *Tetrahedron*, 1968, **24**, 13.

[16] J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1961, **83**, 4537; 1963, **85**, 4059.

bonds are represented by dotted lines. Each water molecule is involved in a hydrogen-bonding 'bridge' between steroid molecules which are related by the *two-fold axis*. The unique O(2) ··· O(3) distance is 2·89 Å. The usual 'head-to-tail' linkage is provided by a hydrogen bond between the carbonyl oxygen O(1) and the hydroxy-oxygen O(2) of adjacent molecules. The O(1) ··· O(2) distance is 2·76 Å and the angle O(2)–HO(2) ··· O(1) is 169·7°. These distances are in good agreement with other quoted values.[17] Angles C(3)–O(1) ··· HO(2) and O(3) ··· O(2)–HO(2) are 118·1 and 107·2° respectively, very close to the theoretical values of 120 and 109·5° one would expect upon consideration of the direction of the lone pair orbitals on the carbonyl oxygen and the hydroxy oxygen atom. There are no other intermolecular contacts of $<3·4$ Å.

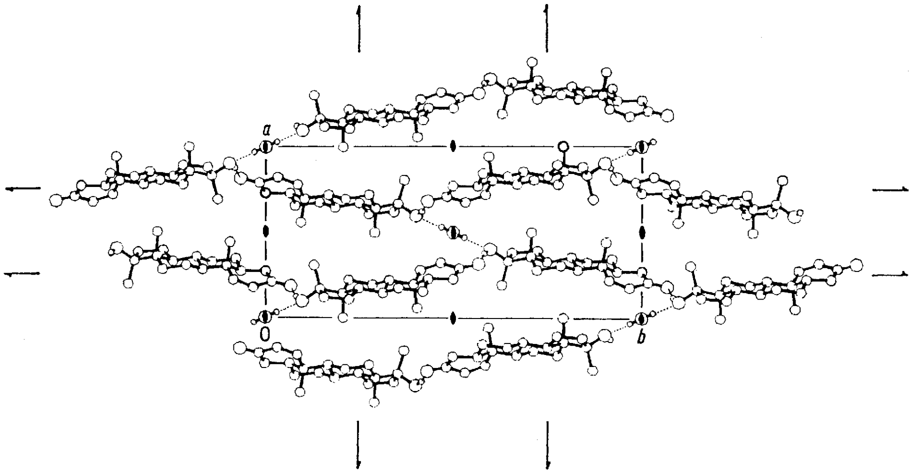

FIGURE 4 Projection of the unit cell viewed down *c*

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[4/025 *Received, 7th January,* 1974]

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[17] W. C. Hamilton and J. A. Ibers, 'Hydrogen Bonding in Solids,' Benjamin, New York, 1968, p. 260.