lies 0·33 Å out of the plane of the acetyl group which is hydrogen bonded to it, and the angle H(11′)···O=C(20) is 122 ± 2°, indicating that the hydroxyl bond is probably directed toward one of the lone pair orbitals of O(20).

The authors wish to express their gratitude to Mr C.T.Lu for his patient and meticulous collection of the intensity data used in this investigation. They also wish to thank Dr K.Johnson, who supplied his program *ORTEP*, with which several of the Figures in this paper were produced, and Mrs K.DeVine and Mr A.Greaver for their assistance in preparing these Figures.

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The Crystal and Molecular Structure of 3β,17α-Dihydroxy-21-bromo-5α-pregnan-11,20-dione*

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The crystal structure of 3β,17α-dihydroxy-21-bromo-5α-pregnan-11,20-dione has been determined by three-dimensional X-ray analysis and refined to a final R value of 0·096. Unit cell constants are a = 12·039, b = 10·875, c = 7·605 Å, β = 97·55°, space group $P2_1$. Standard deviations for bond lengths and angles are in the ranges of 0·01–0·02 Å and 0·8–1·3°, respectively. Molecules related by unit-cell translations in the **a** direction are hydrogen bonded *via* the 3β-hydroxyl oxygen atom and the 17α-hydroxyl hydrogen atom. The 3β-hydroxyl hydrogen atoms hydrogen-bond to the 11-ketone oxygen atoms of molecules related by the screw axes.

Introduction

As a continuation of the studies on molecular stacking determinants and structural-functional relationships of steroids, as described in our earlier papers (Norton, 1965; Norton & Ohrt, 1966), the crystal structure of 3β,17α-dihydroxy-21-bromo-5α-pregnan-11,20-dione (Fig. 1) has been determined by X-ray analysis. The non-halogenated steroid, 3β,17α,21-trihydroxy-5α-pregnan-11,20-dione (Reichstein's substance D), is an intermediate metabolite in the enzymatic degradation of cortisone and has been isolated from the adrenal cortex and liver (Dorfman & Ungar, 1954; Fieser & Fieser, 1959).

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Experimental

The steroid, as supplied commercially, was in the form of regular parallelepipeds. One of these was ground into a spherical shape and was mounted on a General Electric single-crystal orienter. The unit cell was found to be monoclinic with space group $P2_1$ ($0k0$ absent for k odd) and density measurements indicated two molecules of steroid per unit cell. The crystal data are:

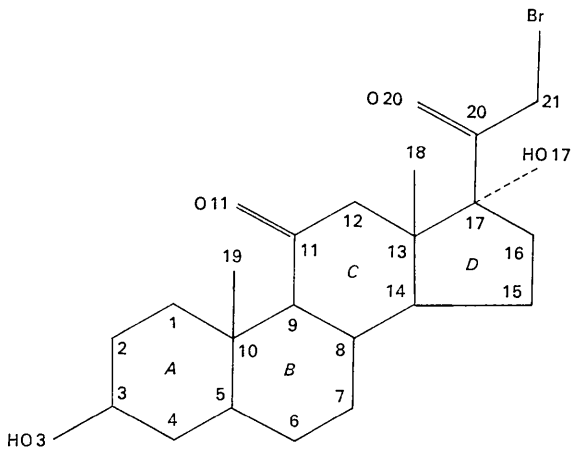


Fig. 1. 3β, 17α-Dihydroxy-21-bromo-5α-pregnan-11,20-dione. Schematic drawing showing the numbering scheme used in the discussion.

$C_{21}H_{31}O_4Br$, $M=427{\cdot}38$, $a=12{\cdot}039\pm0{\cdot}002$, $b=10{\cdot}875\pm0{\cdot}001$, $c=7{\cdot}605\pm0{\cdot}002$ Å, $\beta=97{\cdot}55\pm0{\cdot}01°$, λ(Cu $K\alpha$) = 1·5418 Å; $V_0=987{\cdot}07$ Å^3, $D_m=1{\cdot}40\pm0{\cdot}02$ (by flotation), $Z=2$, $D_c=1{\cdot}44$ g.cm^{-3}; $F(000)=448$. Space group $P2_1$ (C_2^2, no.4). Cu $K\alpha$ single-crystal diffractometry.

The intensities of 1846 independent X-ray spectra were measured on the single-crystal orienter by the stationary-crystal stationary-counter method using copper radiation and balanced nickel and cobalt filters. The intensities were counted for ten seconds with each filter, after which the usual corrections were applied for Lorentz and polarization effects. No corrections were applied for absorption of X-rays in the specimen or for the effects of extinction.

The positions of the bromine atoms in the unit cell were determined from the three-dimensional Patterson synthesis and the remainder of the atoms in the steroid molecules were located from successive three-dimensional Fourier syntheses, in which the phases of the coefficients were determined from the positions of those atoms which were already known. Positional and isotropic thermal parameters of all atoms, and the anisotropic thermal parameters of the bromine atoms, were refined by block-diagonal least-squares using weights inversely proportional to the variances of the derived structure amplitudes. [The quantity minimized was $\Sigma\, w(|F_o|-|F_c|)^2$]. The scattering factors used in

Table 1. *Positional and vibrational parameters of the atoms*

The standard deviations in the last two digits of each number are given in parenthesis.

	x/a	y/b	z/c	B(iso)
C(1)	0·4740 (8)	0·0447 (10)	0·0827 (13)	2·28 (16)
C(2)	0·6021 (9)	0·0187 (10)	0·1006 (14)	2·60 (17)
C(3)	0·6385 (8)	−0·0629 (10)	0·2612 (13)	2·25 (16)
C(4)	0·6127 (8)	0·0030 (9)	0·4286 (13)	2·11 (15)
C(5)	0·4828 (8)	0·0244 (9)	0·4126 (12)	1·84 (15)
C(6)	0·4451 (9)	0·0683 (10)	0·5841 (14)	2·56 (17)
C(7)	0·3156 (9)	0·0664 (10)	0·5676 (14)	2·67 (18)
C(8)	0·2598 (7)	0·1428 (9)	0·4090 (12)	1·90 (15)
C(9)	0·3103 (7)	0·1019 (9)	0·2384 (12)	1·78 (14)
C(10)	0·4413 (7)	0·1052 (9)	0·2506 (12)	1·83 (14)
C(11)	0·2443 (8)	0·1666 (10)	0·0766 (12)	2·12 (15)
C(12)	0·1222 (8)	0·1515 (10)	0·0534 (13)	2·53 (17)
C(13)	0·0758 (8)	0·1939 (10)	0·2189 (13)	2·33 (16)
C(14)	0·1358 (7)	0·1260 (9)	0·3823 (12)	1·96 (15)
C(15)	0·0649 (9)	0·1556 (11)	0·5292 (14)	2·82 (18)
C(16)	−0·0579 (10)	0·1751 (13)	0·4335 (17)	3·66 (22)
C(17)	−0·0478 (9)	0·1582 (11)	0·2334 (14)	2·74 (18)
C(18)	0·0911 (10)	0·3337 (12)	0·2361 (16)	3·34 (20)
C(19)	0·4859 (8)	0·2380 (12)	0·2741 (12)	2·72 (16)
C(20)	−0·1309 (9)	0·2328 (13)	0·1147 (14)	3·45 (20)
C(21)	−0·1508 (17)	0·1944 (20)	−0·0776 (26)	6·66 (41)
O(3)	0·7554 (6)	−0·0883 (7)	0·2779 (9)	2·44 (12)
O(11)	0·2918 (6)	0·2317 (8)	−0·0240 (9)	2·84 (13)
O(17)	−0·0635 (8)	0·0332 (9)	0·1815 (12)	3·95 (16)
O(20)	−0·1793 (11)	0·3179 (13)	0·1700 (16)	6·11 (25)
Br	−0·2780 (1)	0·2500 (3)	−0·2138 (2)	5·03 (−)*

* Equivalent B(iso). The anisotropic thermal parameters for the bromine atom in the form $\exp[-(b_{11}h^2+2b_{12}hk+\ldots)\times10^{-5}]$ are:

b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
875 (10)	1019 (12)	2075 (24)	220 (13)	−421 (13)	−7 (20)

the structure factor calculations were obtained from *International Tables for X-ray Crystallography* (1962) and the scattering factors of the bromine atoms were corrected for the real part of the anomalous dispersion correction ($\Delta f' = -0{\cdot}96$). Refinement of the parameters was ceased when no significant corrections to these parameters were obtained for two successive least-squares cycles and the final R index, defined as $\Sigma \, ||F_o| - |F_c|| / \Sigma \, |F_o|$, was 0·096. The final positional and thermal parameters for the atoms are given in Table 1.

Discussion

The configuration of the atoms and the stereochemistry of the molecule are shown in Fig. 3. Interatomic distances and angles and the least-squares planes through relevant portions of the steroid nucleus are given in Fig. 2 and Table 2, respectively. Apart from the bromine–carbon bond, which is about 0·1 Å shorter than expected, none of the bond distances or angles differs significantly from those found in other steroids (Norton, 1965; Norton & Ohrt, 1966).

Table 2(*c*). *Interplanar angles*

Plane 1	Plane 2	Angle
*A*1	*A*2	124°
*A*3*B*1	*A*2	131
*A*3*B*1	*B*2	121
*B*3*C*1	*B*2	137
*B*3*C*1	*C*2	131
*C*3*D*1	*C*2	136
*C*3*D*1	*D*2	138
*C*3*D*1	*D*3	150
A	*B*	168
B	*C*	173
C	*D*	175
C(1)–C(17)	(100)	105
C(1)–C(17)	(010)	164
C(1)–C(17)	(001)	96

In other steroids whose structures have been solved in this laboratory, the Br–C bond distances have been found to be in the range 1·93–2·00 Å. Inclusion of the imaginary part of the anomalous dispersion correction to the bromine scattering factors did not have the effect of changing this bond distance (*cf.* Ueki, Zalkin &

Table 2(*a*). *Least-squares planes through the atoms*

The planes are in the form $lx+my+nz=p$, where x, y, z and p are in Å and x, y and z are referred to an orthogonal coordinate system with $x \| \mathbf{a}$, $y \| \mathbf{c} \times \mathbf{a}$ and $z \| \mathbf{a} \times (\mathbf{c} \times \mathbf{a})$.

Plane	Atoms	*l*	*m*	*n*	*p*
*A*1	C(2), C(3), C(4)	0·9013	0·4209	0·1023	6·606
*A*2	C(1), C(2), C(4), C(5)	0·1574	0·9833	0·0911	1·407
*A*3*B*1	C(1), C(5), C(6), C(10)	0·8378	0·5243	0·1520	5·097
*B*2	C(6), C(7), C(9), C(10)	−0·0287	0·9879	0·1523	1·270
*B*3*C*1	C(7), C(8), C(9), C(11)	0.6650	0·7318	0·1493	3·361
*C*2	C(8), C(11), C(12), C(14)	−0·1302	0·9866	0·0979	1·475
*C*3*D*1	C(12), C(13), C(14), C(15)	0·5939	0·7832	0·1841	2·283
*D*2	C(13), C(15), C(16), C(17)	−0·0764	0·9942	0·0761	2·068
*D*3	C(14), C(15), C(16), C(17)	0·2058	0·9750	−0·0842	1·357
A	C(1), C(2), C(3), C(4), C(5), C(10)	0·4640	0·8791	0·1087	3·330
B	C(5), C(6), C(7), C(8), C(9), C(10)	0·2731	0·9447	0·1816	2·557
C	C(8), C(9), C(11), C(12), C(13), C(14)	0·1858	0·9760	0·1134	2·143
D	C(13), C(14), C(15), C(16), C(17)	0·1037	0·9888	0·1076	2·036
C(1)–C(17)		0·2552	0·9608	0·1082	2·106

Table 2(*b*). *Distances from the least-squares planes* (Å)

	A	*B*	*C*	*D*	*A*2	*A*3*B*1	*B*2	*B*3*C*1	*C*2	*C*3*D*1	*D*2	*D*3	C(1)–C(17)
C(1)	−0·23				0·01	−0·03							−0·14
C(2)	0·25				−0·01								−0·00
C(3)	−0·27				−0·73								−0·66
C(4)	0·27				0·01								0·05
C(5)	−0·25	−0·27			−0·01	0·04	−0·69						−0·14
C(6)		0·25				−0·04	−0·00						0·30
C(7)		−0·21					0·00	−0·04					−0·12
C(8)		0·21	0·23				0·66	0·04	0·00				0·41
C(9)		−0·23	−0·21				−0·00	0·04	−0·66				0·04
C(10)	0·23	0·25	0·22		0·69	0·03	−0·00						0·49
C(11)			−0·23					−0·04	−0·00				0·43
C(12)			0·23						0·00	−0·08			−0·12
C(13)			−0·25	0·30					0·68	0·08	0·10	0·70	0·28
C(14)				−0·24					−0·00	0·07	−0·58	−0·01	−0·16
C(15)				0·09						−0·07	−0·10	0·01	0·02
C(16)				0·08							0·16	−0·01	−0·21
C(17)				−0·23							−0·16	0·01	−0·47

Templeton, 1966). An approximate correction of 0·04 Å, however, may be obtained to compensate for the thermal motion of the bromine atom (Busing & Levy, 1964), this motion being almost perpendicular to the C(12)–Br bond. The observed distance of 1·84 ± 0·02 Å is then only just significantly short. The bond angles in the steroid nucleus are somewhat larger than normal tetrahedral angles; this enlargement may be related to the flattening of the ring system. Rings *A*, *B* and *C* are chair-shaped, ring *D* is a *β*-envelope (torsional angle C(14)–C(15)–C(16)–C(17) = +1·5°) and all rings are *trans*-fused. The least-squares planes through rings *A*, *B*, *C* and *D* are almost parallel [Table 2(*c*)] and the r.m.s. deviation of the atoms of the steroid nucleus from the least-squares plane through the four rings is 0·30 Å. The steroid nucleus lies almost perpendicular to the *c* face of the crystal.

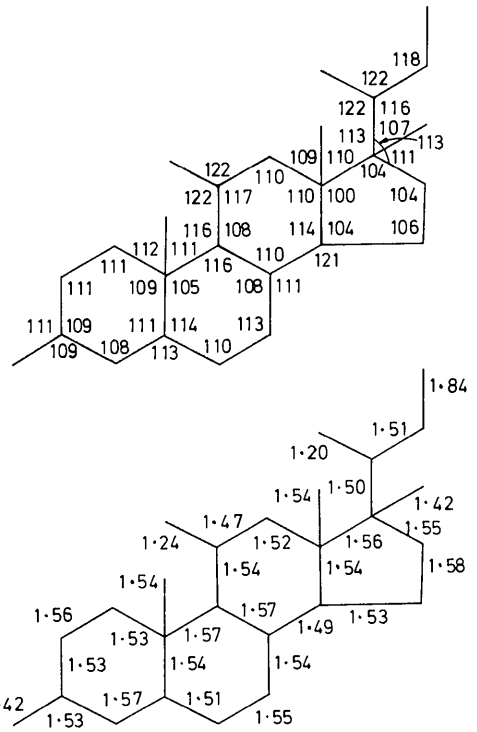


Fig. 2. Interatomic angles and distances. Standard deviations are in the ranges 0·8–1·3° and 0·01–0·02 Å, respectively.

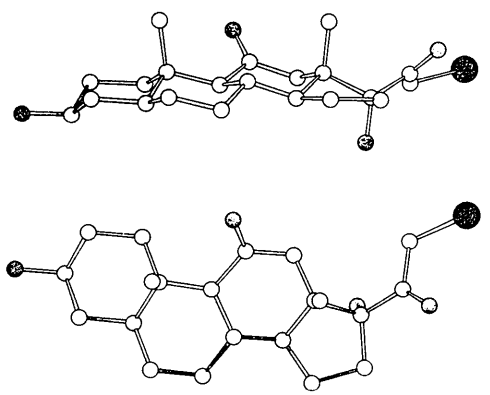


Fig. 3. Perspective views of the molecule. The top view shows the *trans* fusion of rings *A*, *B*, *C* and *D*. Large shaded circles: Br; small shaded circles :O; small open circles: C.

The packing of the molecules is influenced mainly by the formation of hydrogen bonds from the hydroxyl group at C(3) to the ketone oxygen atom O(11), and from the hydroxyl group at C(17) to the hydroxyl group at C(3), the oxygen–oxygen distance being 2·74 Å in each case. These bonds may be seen in the axial projections given in Fig. 4. There are twenty-four intermolecular distances less than 4·0 Å, of which ten are associated with the hydrogen-bonded atoms or those atoms in their immediate vicinity. Of the remainder of the shorter intermolecular contacts (Table 3), three involve the bromine atom in the side chain and three involve the remainder of the side chain. There are four contacts with the axial methyl groups, C(18) and C(19).

Table 3. *Intermolecular distances less than* 4·0 Å

The hydrogen bonded groups are marked by an asterisk. Equivalent position nomenclature: O(20)–C(7) 2/1̄00 is taken to mean atom O(20) to (atom C(7) at equivalent position 2, translated 1 unit cell in the $\bar{x}$ direction). Equivalent position 1 is *xyz*; equivalent position 2 is $1-x, \frac{1}{2}+y, 1-z$.

	Position	Distance
Br———C(2)	1/1̄00	3·88
Br———C(4)	1/1̄0$\bar{1}$	3·93
Br———C(9)	2/1̄0$\bar{1}$	3·85
HO(3)—O(17)	1/100	2·74*
HO(3)—C(16)	1/100	3·74
HO(3)—C(17)	1/100	3·62
HO(3)—O(11)	2/0$\bar{1}$1	2·74*
HO(3)—C(8)	2/0$\bar{1}$0	3·79
HO(3)—C(11)	2/0$\bar{1}\bar{1}$	3·79
HO(3)—C(15)	2/0$\bar{1}$0	3·70
O(11)—C(7)	1/00$\bar{1}$	3·63
O(11)—C(2)	2/00$\bar{1}$	3·45
O(11)—C(3)	2/00$\bar{1}$	3·06
HO(17)–C(2)	1/1̄00	4·00
HO(17)–C(3)	1/1̄00	3·86
HO(17)–C(18)	2/1̄1̄1	3·83
O(20)—C(7)	2/1̄00	3·85
C(1)—C(6)	1/00$\bar{1}$	3·77
C(2)—C(20)	1/100	3·96
C(2)—C(21)	1/100	3·92
C(4)—C(19)	2/0$\bar{1}$0	3·94
C(5)—C(19)	2/0$\bar{1}$0	3·91
C(6)—C(19)	2/0$\bar{1}$0	3·81
C(12)—C(15)	1/00$\bar{1}$	3·96

The authors are grateful to Mr C. T. Lu and Mrs C. DeVine who were responsible for the collection and initial preparation of the intensity data and to Dr C. Johnson who supplied his computer program *ORTEP* with which Fig. 3 was prepared. Computations were carried out on an IBM 7040 computer at this laboratory.

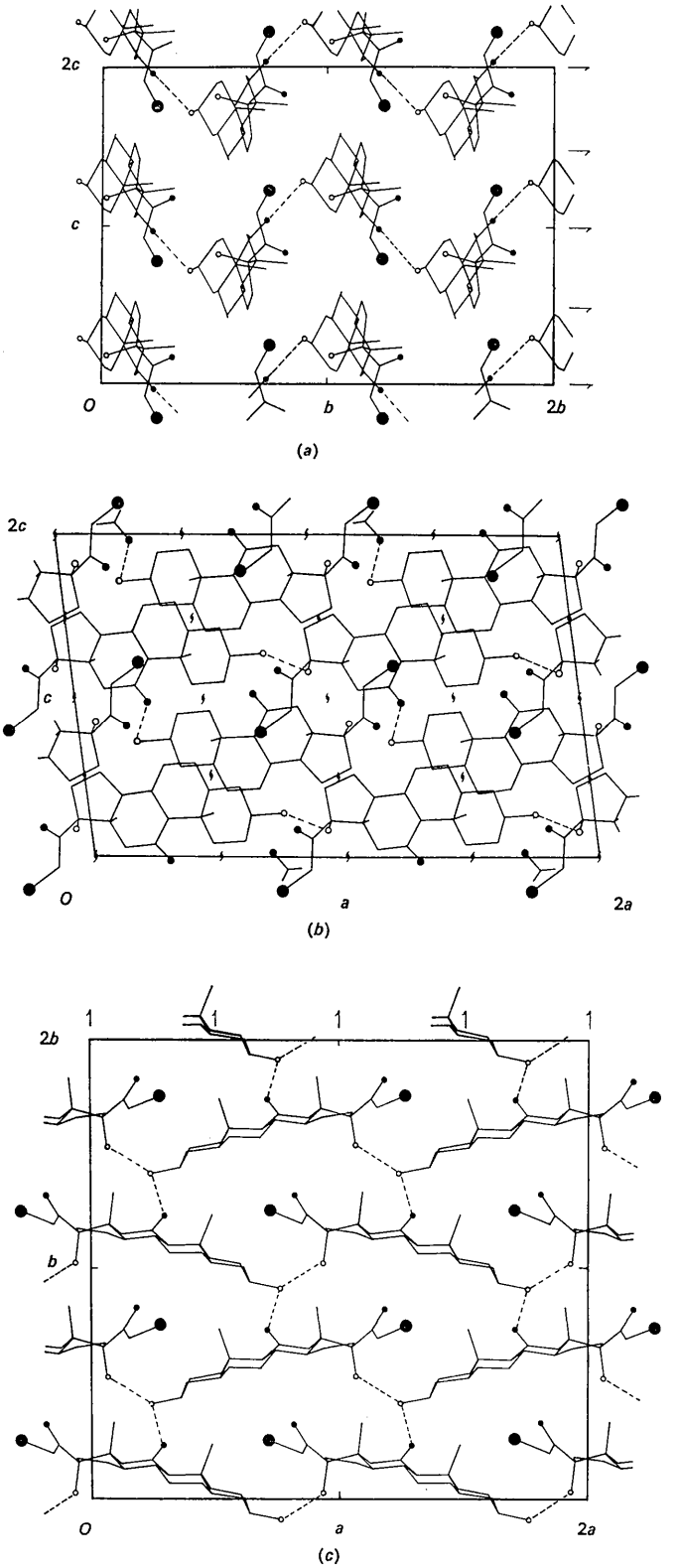
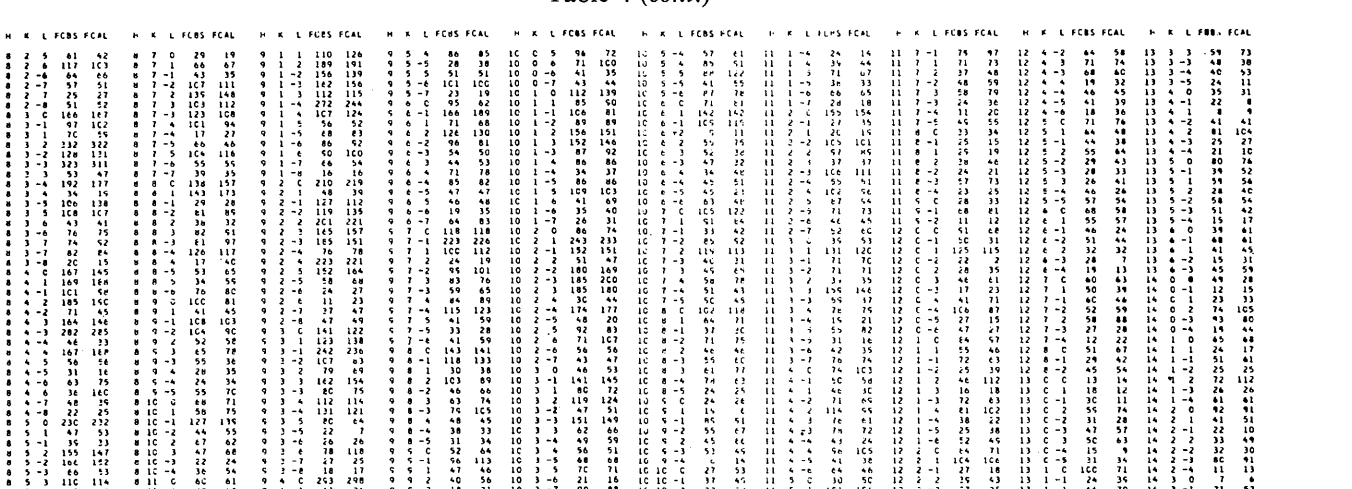


Fig. 4. Projections of four unit cells onto the planes (*a*) (100), (*b*) (010) and (*c*) (001). The hydrogen bonding between 3β- and 17α-hydroxyl groups and the 11-keto group is shown by the broken lines. Large shaded circles: bromine; small shaded circles: ketone oxygen; small open circles: hydroxyl oxygen.

Table 4. *Comparison between the values of $|F_o|$ and $|F_c|$ calculated for the refined atomic parameters*

$|F_o|$ and $|F_c|$ are given on ten times absolute scale.

Table 4 (*cont.*)



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The Refinement of the Crystal Structures of β-D-Glucose and Cellobiose

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The structures of β-D-glucose and cellobiose have been refined anisotropically from new data obtained at room temperature with Cu $K\alpha$ radiation on an automatic diffractometer. The earlier results are confirmed except for small changes in bond distances and bond angles. In both structures, the equatorial glycosidic C(1)–O(1) bonds are significantly short.

The crystal structure of β-D-glucose was determined by Ferrier (1963) and that of cellobiose by Jacobson, Wunderlich & Lipscomb (1961) and by Brown (1966). These structures have now been refined from new experimental data obtained on a Picker four-angle automatic diffractometer. The primary purpose of this refinement was to obtain bond distances with an accuracy comparable to those from other recent structure determinations of pyranose sugars (Berman, Chu & Jeffrey, 1967). The cell parameters, remeasured on the