X-Ray Crystallographic Determination of the Structure of the *p*-Bromophenylboronate Ester of 17α,20β,21-Trihydroxypregn-4-en-3-one

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The *p*-bromophenylboronate ester formed by 17α,20β,21-trihydroxypregn-4-en-3-one has been shown by *X*-ray crystallography to have a six-membered ring structure involving the 17- and 21-hydroxy-groups. The dioxaborinane ring has an envelope-like conformation in which C(20) is the out-of-plane atom. The hydroxy-group at C(20) is not co-ordinated to boron, O · · · B being 3.05 Å. Crystals of 20β-hydroxy-3-oxopregn-4-ene-17α,21-diyl *p*-bromophenylboronate are orthorhombic, space group $P2_12_12_1$, with a = 16.85(3), b = 13.29(2), c = 11.08(1) Å, Z = 4. The structure was determined from diffractometer data by Patterson and tangent-formula procedures, and least-squares refinement converged at R 9.6% over 699 reflections.

THE biologically important corticosteroids can be stabilized for gas-chromatographic analysis by conversion to boronate esters.[1] Brooks has suggested that the steroidal 17,20,21-triols form six-membered cyclic esters involving the 17- and 21-hydroxy-groups with the oxygen atom at C(20) co-ordinated to the boron atom,[1] the latter feature being based on the structure suggested for glycerol phenylboronate.[2] In order to characterize the molecular geometry of a typical steroidal boronate ester we have elucidated the crystal structure of the *p*-bromophenylboronate ester formed by 17α,20β,21-trihydroxypregn-4-en-3-one

It was difficult to obtain a single crystal of the boronate suitable for *X*-ray study and it became apparent that an extensive range of *X*-ray intensities could not be obtained. Nevertheless, structural definition of the molecule was considered feasible with a restricted data set of limited quality. The atomic positions were deduced by Patterson and tangent-formula procedures and adjusted by least-squares calculations to R 9.6% over 699 independent reflections.

Atomic co-ordinates and thermal parameters are listed in Table 1, intramolecular distances in Table 2, valency angles in Table 3, torsion angles in Table 4, and displacements of atoms from various planes in Table 5. The high standard deviations are indicative of the poor quality of the crystal employed in the analysis.

The molecular structure is shown in Figure 1, and this demonstrates that the 17- and 21-hydroxy-groups of the steroid participate in the formation of a six-membered cyclic ester (1). The conformation of the dioxaborinane ring is shown in Figure 2 and is similar to that in *N*-(*p*-bromophenyl)-α-D-pyranosylamine 2,4-phenylboronate.[3] Atoms B, O(2), O(3), C(21), and C(17) are approximately coplanar (Table 5) while C(20) and O(4) are

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[1] G. M. Anthony, C. J. W. Brooks, I. MacLean, and I. Sangster, *J. Chromatog. Sci.*, 1969, **7**, 623; C. J. W. Brooks and D. J. Harvey, *J. Chromatog.*, 1971, **54**, 193.

[2] E. J. Bourne, E. M. Lees, and H. Wiegel, *J. Chem. Soc.*, 1965, 3798.

[3] H. Shimanouchi, N. Saito, and Y. Sasada, *Bull. Chem. Soc. Japan*, 1969, **42**, 1239.

displaced by 0.70 and 2.10 Å to one side of the mean plane. There is evidently no interaction between a lone pair of electrons on the oxygen atom at C(20) and the unfilled *p* orbital of the boron atom, since the O(4) · · · B separation is 3.05 Å while the sum of the appropriate

TABLE 1

Fractional atomic co-ordinates, with standard deviations in parentheses, and thermal parameters

Atom	x	y	z	B
Br	−0.1469(3)	0.3054(4)	0.4776(5)	*
O(1)	0.4029(16)	−0.3465(20)	0.1703(35)	*
O(2)	0.1921(17)	0.3373(22)	0.1116(28)	4.65 †
O(3)	0.1632(20)	0.5152(25)	0.1409(32)	*
O(4)	0.3236(13)	0.4718(18)	0.1844(21)	*
C(1)	0.4193(23)	−0.0721(32)	0.2239(39)	3.46
C(2)	0.4484(17)	−0.1840(24)	0.2339(28)	3.08
C(3)	0.4044(16)	−0.2571(22)	0.1423(29)	4.51
C(4)	0.3760(24)	−0.2081(28)	0.0391(33)	3.51
C(5)	0.3801(20)	−0.1077(28)	0.0045(33)	3.02
C(6)	0.3545(17)	−0.0770(19)	−0.1224(27)	4.74
C(7)	0.3006(17)	0.0224(26)	−0.1089(31)	4.22
C(8)	0.3424(23)	0.0997(28)	−0.0362(34)	2.03
C(9)	0.3546(20)	0.0585(29)	0.0978(31)	3.80
C(10)	0.4141(22)	−0.0348(32)	0.0992(37)	2.16
C(11)	0.3900(16)	0.1418(20)	0.1906(25)	3.14
C(12)	0.3311(21)	0.2361(26)	0.1860(31)	3.89
C(13)	0.3199(19)	0.2739(25)	0.0540(31)	1.62
C(14)	0.2874(23)	0.1951(25)	−0.0250(29)	4.06
C(15)	0.2635(19)	0.2491(22)	−0.1443(27)	4.83
C(16)	0.2393(20)	0.3557(26)	−0.0997(31)	3.71
C(17)	0.2595(18)	0.3616(27)	0.0337(27)	5.31
C(18)	0.4062(18)	0.3181(24)	0.0075(31)	4.12
C(19)	0.4989(18)	−0.0070(23)	0.0539(27)	2.86
C(20)	0.2891(26)	0.4710(34)	0.0625(42)	6.24
C(21)	0.2289(23)	0.5479(29)	0.0458(36)	5.38
C(22)	0.0742(17)	0.3847(24)	0.2348(26)	2.03
C(23)	0.0420(23)	0.2809(28)	0.2457(32)	4.54
C(24)	−0.0237(21)	0.2565(27)	0.3104(33)	3.94
C(25)	−0.0575(21)	0.3362(30)	0.3729(35)	4.92
C(26)	−0.0266(20)	0.4325(28)	0.3829(32)	3.79
C(27)	0.0356(22)	0.4564(27)	0.3110(33)	4.04
B	0.1493(33)	0.4121(38)	0.1674(43)	5.22

* For these atoms anisotropic temperature factors were employed in the form: $T = \exp[-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl)]$ with parameters ($b_{ij} \times 10^4$). † Mean standard deviation of isotropic temperature factors is 0.8 Å^2.

Atom	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
Br	75(3)	134(5)	155(6)	−92(6)	83(8)	−67(11)
O(1)	50(14)	36(19)	338(65)	−11(31)	6(50)	7(57)
O(3)	42(15)	100(26)	197(39)	1(32)	50(42)	−92(55)
O(4)	85(22)	119(33)	202(45)	−7(41)	102(53)	18(69)

TABLE 2

Bond lengths (Å), with standard deviations in parentheses

Br–C(25)	1.95(4)	C(9)–C(11)	1.62(5)
O(1)–C(3)	1.23(5)	C(10)–C(19)	1.56(4)
O(2)–C(17)	1.46(5)	C(11)–C(12)	1.60(5)
O(2)–B	1.38(6)	C(12)–C(13)	1.56(4)
O(3)–C(21)	1.59(5)	C(13)–C(14)	1.47(4)
O(3)–B	1.42(6)	C(13)–C(17)	1.56(5)
O(4)–C(20)	1.47(6)	C(13)–C(18)	1.65(4)
C(1)–C(2)	1.57(5)	C(14)–C(15)	1.56(5)
C(1)–C(10)	1.47(5)	C(15)–C(16)	1.56(5)
C(2)–C(3)	1.59(5)	C(16)–C(17)	1.52(5)
C(3)–C(4)	1.40(5)	C(17)–C(20)	1.57(6)
C(4)–C(5)	1.39(4)	C(20)–C(21)	1.45(6)
C(5)–C(6)	1.53(5)	C(22)–C(23)	1.49(5)
C(5)–C(10)	1.54(4)	C(22)–C(27)	1.43(5)
C(6)–C(7)	1.61(5)	C(22)–B	1.51(6)
C(7)–C(8)	1.48(5)	C(23)–C(24)	1.36(5)
C(8)–C(9)	1.60(4)	C(24)–C(25)	1.39(5)
C(8)–C(14)	1.58(4)	C(25)–C(26)	1.39(5)
C(9)–C(10)	1.60(5)	C(26)–C(27)	1.36(5)

TABLE 3

Valency angles (°), with standard deviations in parentheses

O(3)–B–O(2)	121(2)	C(17)–C(13)–C(14)	102(2)
C(22)–B–O(2)	119(2)	C(18)–C(13)–C(14)	113(2)
C(22)–B–O(3)	118(3)	C(18)–C(13)–C(17)	105(2)
C(10)–C(1)–C(2)	114(2)	C(13)–C(14)–C(8)	114(2)
C(3)–C(2)–C(1)	113(2)	C(15)–C(14)–C(8)	117(2)
C(4)–C(3)–C(2)	113(2)	C(15)–C(14)–C(13)	106(2)
C(2)–C(3)–O(1)	116(3)	C(16)–C(15)–C(14)	103(2)
C(4)–C(3)–O(1)	130(3)	C(17)–C(16)–C(15)	107(3)
C(5)–C(4)–C(3)	130(2)	C(20)–C(17)–C(16)	108(3)
C(6)–C(5)–C(4)	120(2)	C(16)–C(17)–C(13)	104(3)
C(10)–C(5)–C(4)	116(2)	C(20)–C(17)–C(13)	117(2)
C(10)–C(5)–C(6)	124(2)	C(13)–C(17)–O(2)	105(2)
C(7)–C(6)–C(5)	107(2)	C(16)–C(17)–O(2)	113(2)
C(8)–C(7)–C(6)	111(2)	C(20)–C(17)–O(2)	109(3)
C(9)–C(8)–C(7)	109(2)	C(21)–C(20)–C(17)	114(3)
C(14)–C(8)–C(7)	109(2)	C(17)–C(20)–O(4)	109(3)
C(14)–C(8)–C(9)	106(2)	C(21)–C(20)–O(4)	113(3)
C(10)–C(9)–C(8)	111(2)	C(20)–C(21)–O(3)	102(2)
C(11)–C(9)–C(8)	114(2)	C(27)–C(22)–C(23)	114(2)
C(11)–C(9)–C(10)	107(2)	B–C(22)–C(23)	125(3)
C(19)–C(10)–C(1)	109(2)	B–C(22)–C(27)	121(3)
C(9)–C(10)–C(1)	108(2)	C(24)–C(23)–C(22)	124(2)
C(5)–C(10)–C(1)	117(2)	C(25)–C(24)–C(23)	115(3)
C(19)–C(10)–C(9)	113(2)	C(26)–C(25)–C(24)	126(2)
C(9)–C(10)–C(5)	104(2)	C(24)–C(25)–Br	117(2)
C(19)–C(10)–C(5)	106(2)	C(26)–C(25)–Br	116(2)
C(12)–C(11)–C(9)	107(2)	C(27)–C(26)–C(25)	117(2)
C(13)–C(12)–C(11)	111(2)	C(26)–C(27)–C(22)	123(2)
C(14)–C(13)–C(12)	112(2)	B–O(2)–C(17)	121(3)
C(17)–C(13)–C(12)	117(2)	B–O(3)–C(21)	121(3)
C(18)–C(13)–C(12)	107(2)		

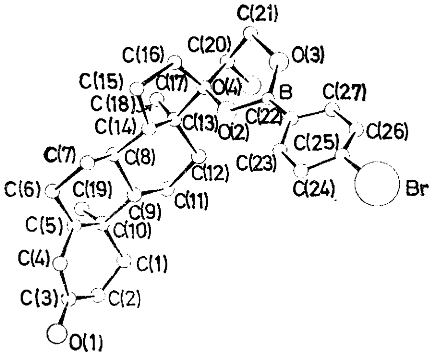
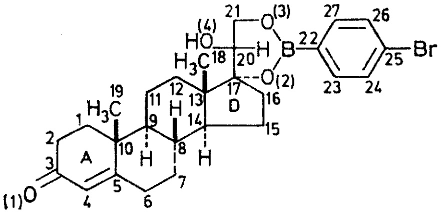


FIGURE 1 A general view of the molecular structure



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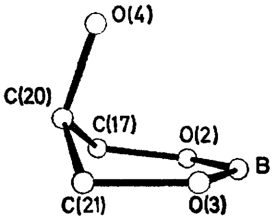

FIGURE 2 The conformation of the dioxaborinane ring

TABLE 4

Torsion angles (°) *

B–O(2)–C(17)–C(13)	146
B–O(2)–C(17)–C(16)	−102
B–O(2)–C(17)–C(20)	19
C(17)–O(2)–B–O(3)	7
C(17)–O(2)–B–C(22)	173
B–O(3)–C(21)–C(20)	−34
C(21)–O(3)–B–O(2)	0
C(21)–O(3)–B–C(22)	−166
C(10)–C(1)–C(2)–C(3)	−47
C(2)–C(1)–C(10)–C(5)	41
C(2)–C(1)–C(10)–C(9)	158
C(2)–C(1)–C(10)–C(18)	−79
C(1)–C(2)–C(3)–O(1)	−156
C(1)–C(2)–C(3)–C(4)	26
O(1)–C(3)–C(4)–C(5)	−177
C(2)–C(3)–C(4)–C(5)	0
C(3)–C(4)–C(5)–C(6)	171
C(3)–C(4)–C(5)–C(10)	−7
C(4)–C(5)–C(6)–C(7)	135
C(10)–C(5)–C(6)–C(7)	−47
C(4)–C(5)–C(10)–C(1)	−15
C(4)–C(5)–C(10)–C(9)	−134
C(4)–C(5)–C(10)–C(19)	106
C(6)–C(5)–C(10)–C(1)	167
C(6)–C(5)–C(10)–C(9)	48
C(6)–C(5)–C(10)–C(19)	−71
C(5)–C(6)–C(7)–C(8)	52
C(6)–C(7)–C(8)–C(9)	−64
C(6)–C(7)–C(8)–C(14)	−180
C(7)–C(8)–C(9)–C(10)	66
C(7)–C(8)–C(9)–C(11)	−173
C(14)–C(8)–C(9)–C(10)	−176
C(14)–C(8)–C(9)–C(11)	−56
C(7)–C(8)–C(14)–C(13)	175
C(7)–C(8)–C(14)–C(15)	−61
C(9)–C(8)–C(14)–C(13)	58
C(9)–C(8)–C(14)–C(15)	−178
C(8)–C(9)–C(10)–C(1)	−177
C(8)–C(9)–C(10)–C(5)	−52
C(8)–C(9)–C(10)–C(19)	62
C(11)–C(9)–C(10)–C(1)	58
C(11)–C(9)–C(10)–C(5)	−177
C(11)–C(9)–C(10)–C(19)	−62
C(8)–C(9)–C(11)–C(12)	56
C(10)–C(9)–C(11)–C(12)	179
C(9)–C(11)–C(12)–C(13)	−54
C(11)–C(12)–C(13)–C(14)	59
C(11)–C(12)–C(13)–C(17)	176
C(11)–C(12)–C(13)–C(18)	−66
C(12)–C(13)–C(14)–C(8)	−61
C(12)–C(13)–C(14)–C(15)	169
C(17)–C(13)–C(14)–C(8)	173
C(17)–C(13)–C(14)–C(15)	43
C(18)–C(13)–C(14)–C(8)	60
C(18)–C(13)–C(14)–C(15)	−70
C(12)–C(13)–C(17)–O(2)	−41
C(12)–C(13)–C(17)–C(16)	−160
C(12)–C(13)–C(17)–C(20)	80
C(14)–C(13)–C(17)–O(2)	81
C(14)–C(13)–C(17)–C(16)	−38
C(14)–C(13)–C(17)–C(20)	−158
C(18)–C(13)–C(17)–O(2)	−161
C(18)–C(13)–C(17)–C(16)	81
C(18)–C(13)–C(17)–C(20)	−39
C(8)–C(14)–C(15)–C(16)	−159
C(13)–C(14)–C(15)–C(16)	−32
C(14)–C(15)–C(16)–C(17)	7
C(15)–C(16)–C(17)–O(2)	−95
C(15)–C(16)–C(17)–C(13)	18
C(15)–C(16)–C(17)–C(20)	144
O(2)–C(17)–C(20)–O(4)	68
O(2)–C(17)–C(20)–C(21)	−59
C(13)–C(17)–C(20)–O(4)	−51
C(13)–C(17)–C(20)–C(21)	−178
C(16)–C(17)–C(20)–O(4)	−169
C(16)–C(17)–C(20)–C(21)	64
O(4)–C(20)–C(21)–O(3)	−63
C(17)–C(20)–C(21)–O(3)	62
C(27)–C(22)–C(23)–C(24)	7
B–C(22)–C(23)–C(24)	177
C(23)–C(22)–C(27)–C(26)	−2
B–C(22)–C(27)–C(26)	−173
C(23)–C(22)–B–O(2)	0
C(23)–C(22)–B–O(3)	166
C(27)–C(22)–B–O(2)	169
C(27)–C(22)–B–O(3)	−25
C(22)–C(23)–C(24)–C(25)	−3
C(23)–C(24)–C(25)–Br	−175
C(23)–C(24)–C(25)–C(26)	−6
Br–C(25)–C(26)–C(27)	−180
C(24)–C(25)–C(26)–C(27)	11
C(25)–C(26)–C(27)–C(22)	−6

* Standard deviation of torsion angle *ca.* 4°.

TABLE 5

Displacements (Å) of atoms from various planes. Atoms not included in the derivation of a plane are italicized

Plane (*a*): B −0.01, O(2) 0.05, O(3) −0.03, C(21) 0.03, C(17) −0.04, *C(20) −0.70, O(4) −2.10*

Plane (*b*): C(2) 0.00, C(3) 0.00, C(4) 0.00, C(5) 0.00, *C(1) −0.64, C(10) −0.16*

Plane (*c*): C(6) −0.01, C(7) 0.01, C(9) −0.01, C(10) 0.01, (*C5*) *−0.51, C(8) 0.76*

Plane (*d*): C(8) 0.00, C(11) 0.00, C(12) 0.00, C(14) 0.00, (*C9*) *−0.70, C(13) 0.68*

Plane (*e*): C(14) −0.03, C(15) 0.04, C(16) −0.04, C(17) 0.03, *C(13) 0.62*

van der Waals radii is 3.07 Å.[4] In order to achieve a shorter separation between these atoms the ring would require to adopt a boat conformation.

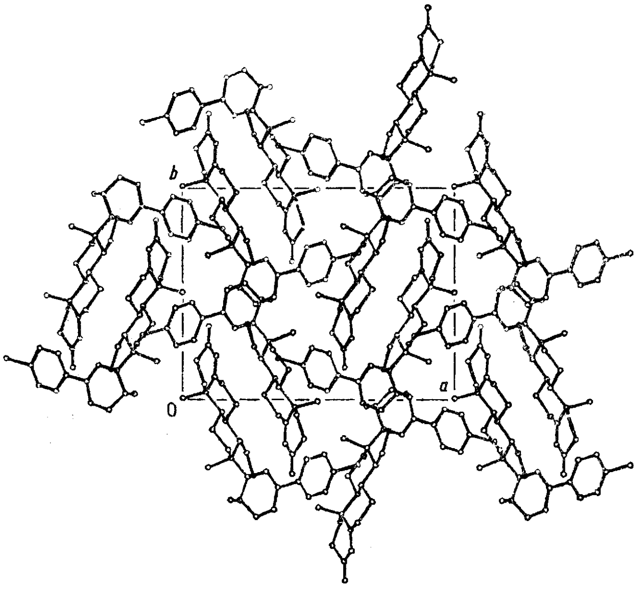

FIGURE 3 The crystal structure, viewed in projection along the *c* axis

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A preliminary report of an X-ray study of a five-membered cyclic boronate ester, the *p*-bromophenylboronate derivative of the antiobiotic streptovaricin C, has been published.[5]

The endocyclic torsion angles for ring A represent a conformation intermediate between a C_2 form, in which the 'symmetry' axis passes through C(1), and a C_s form, in which the 'symmetry' plane passes through the midpoint of the bond C(1)–C(2); the deviations from the ideal conformations are $\Delta(C_2)$ 30° and $\Delta(C_s)$ 24°, similar to values for other 4-en-3-one steroids (*cf.* Table 3 in chap. 4, Part III, of ref. 6). Rings B and C have chair conformations and ring D is intermediate between C(13)-envelope (C_s) and half-chair (C_2) forms, the pseudorotational parameters being Δ 13° and ϕ_m 43°.[7]

There is an intermolecular hydrogen bond O(1) $\cdots$ $O(4)^{I}$ of length 2.77 Å. Figure 3 shows the packing of the molecules in the unit cell.

EXPERIMENTAL

Crystal Data.—$C_{27}H_{34}BBrO_4$, $M = 513.3$. Orthorhombic, $a = 16.85(3)$, $b = 13.29(2)$, $c = 11.08(1)$ Å, $U = 2\,482$ Å^3, $Z = 4$, $D_c = 1.37$, $F(000) = 1\,072$. Mo-K_α radiation, $\lambda = 0.7107$ Å, μ(Mo-K_α) = 17.90 cm^{-1}. Space group $P2_12_12_1$ (D_2^4).

Crystallographic Measurements.—Cell dimensions were adjusted by least-squares analysis of the angular settings of 12 reflections measured on a Hilger and Watts computer-controlled four-circle diffractometer at θ(Mo-K_α) *ca.* 16°. The octant *hkl* was measured in the range $\theta \leqslant 27°$ by the θ—ω step-scan method with background counts at each end of the scan range. In all, the intensities of 1 382 independent reflections were obtained, of which 776 having $I > 2.5\sigma(I)$ were considered observed. No absorption correction was applied.

Structure Analysis.—The co-ordinates of the bromine atom were determined by a sharpened Patterson synthesis; structure factors were calculated on the basis of this position, but a resulting Fourier synthesis failed to reveal the positions of the remaining atoms unambiguously. The initial phases of the structure factors were therefore used in tangent-formula calculations with the 274 reflections for which $|E| > 1.0$ and the revised phases yielded an E map from which a further seven atoms were located. A structure-factor calculation based on the eight atoms gave R 37.5% and a Fourier synthesis revealed the remaining non-hydrogen atom positions.

Least-squares calculations with isotropic thermal parameters lowered R to 13.6%. The bromine and three of the oxygen atoms which had high thermal motion were assigned anisotropic thermal parameters and this led to R 9.6% for 699 reflections; hydrogen atoms were not included and unit weights ($w = 1$) were used throughout the least-squares calculations, $< w\Delta^2 >$ being approximately constant over different ranges of $|F_o|$ and $\sin\theta$. The mean and largest shift-to-error ratio in the final cycle of calculations were 0.010 and 0.044, respectively. Calculations were performed with a modified version of the Gantzel, Sparks, and Trueblood full-matrix programme, and scattering factors were taken from ref. 8. The absolute configuration of the molecule could not be determined by the anomalous-dispersion method, so the normal absolute configuration of a steroid molecule was assumed. Observed and calculated structure amplitudes, together with a Table of intermolecular separations are listed in Supplementary Publication No. SUP 21521 (6 pp.).*

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* See Notice to Authors No. 7, in *J.C.S. Perkin II*, 1975, Index issue.

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