Studies on the Neutral Constituents of *Pachysandra terminalis* Sieb. et Zucc. Part IV.† *X*-Ray Structure of 3-*O*-Acetyl-16-*O*-*p*-bromobenzoylpachysandiol B: New Conformation of a Friedelin-type Triterpene

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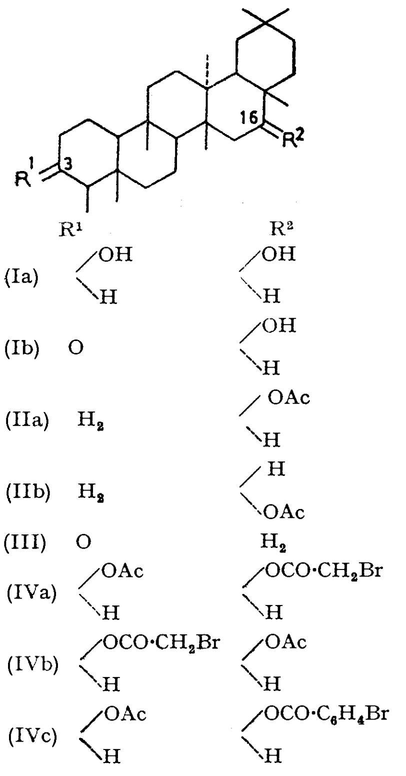
Crystals of the title compound (IVc) are orthorhombic, $a = 15{\cdot}58$, $b = 30{\cdot}88$, $c = 7{\cdot}40$ Å, space group $P2_12_12_1$, and $Z = 4$. The structure was solved from visually estimated three-dimensional *X*-ray data by the heavy-atom method, and refined by block-diagonal least-squares to *R* 14·3% (1722 independent reflections). A chair–chair–chair–boat–boat conformation of the five six-membered-ring skeleton was found, and it was confirmed that this and the *quasi*-all-chair are the stable conformations in friedelin-type triterpenes.

THE structures of pachysandiol B and pachysonol isolated from the neutral fraction of *Pachysandra terminalis* Sieb. et Zucc. (Buxaceae) were determined by chemical and spectroscopic methods to be (Ia) and (Ib),[1] except for the configuration of the asymmetric carbon atom C-16, and C-16 epimeric compounds were therefore prepared. The n.m.r. spectra of the epimeric 3-deoxoacetates (IIa and b) showed a triplet (τ 4·78, *J* 9 Hz) and a quartet (τ 4·81, *J* 7·5 and 8·5 Hz), indicating equatorial orientation of the 16-acetoxy-group in both. The configuration of C-16 could not therefore be uniquely determined by this method, and the existence of a conformation for the five rings different from the all-chair which had been suggested[2] for the friedelin molecule (III) was expected. The structure determination of a pachysandiol B derivative (IVc) by *X*-ray analysis was undertaken to determine this.



EXPERIMENTAL

Three heavy-atom derivatives (IV a—c) of pachysandiol B (Ia) were prepared, and after preliminary examination by oscillation, Weissenberg, and precession photography, those of 3-*O*-acetyl-16-*O*-*p*-bromobenzoylpachysandiol B (IVc) were chosen for further analysis.

Crystal Data.—$C_{39}H_{57}O_4Br$, $M = 669$. Orthorhombic, $a = 15{\cdot}58$, $b = 30{\cdot}88$, $c = 7{\cdot}40$ Å, $U = 3560$ Å^3, D_m (by flotation) $= 1{\cdot}210$, $Z = 4$, $D_c = 1{\cdot}236$. Space group $P2_12_12_1$. Cu-K_α radiation, $\lambda = 1{\cdot}5418$ Å; μ(Cu-K_α) $= 20{\cdot}27$ cm^{-1}, m.p. 264—266°.

Prisms elongated along the *c* axis, were grown from dichloromethane–methanol solution by slow evaporation. The specimens used for the equi-inclination Weissenberg data were 1·54 × 0·12 × 0·07 (*hk*0 and *hk*1), 2·86 × 0·17 × 0·10 (*hk*2—6) *c* axis, and 0·11 × 0·07 × 0·08 mm (0—6*kl*) *a* axis. Visually estimated intensities, corrected for spot-shape and Lorentz and polarization factors, yielded 1772 independent reflections, corresponding to 35% of the total number of independent reflections within the copper.

The position of the bromine atom in the asymmetric unit was obtained from three-dimensional Patterson maps. Calculation of structure factors with the contribution from the bromine atoms alone gave *R* 52·8%. The remaining atoms in the asymmetric unit were located by three successive Fourier structure-factor calculations (*R* 27·8%). The structure was refined by least-squares methods using 4 × 4 matrix blocks for the positional and isotropic thermal parameters of the carbon atoms and 9 × 9 matrix blocks for the positional and anisotropic thermal parameters of the bromine and oxygen atoms. Atomic scattering factors given in ref. 3 were employed throughout. The weights used in the last stage of the refinement were $w = (4F_{\text{min.}}/F_o)^2$ when $F_o > 4F_{\text{min.}}$ and $w = 1$ when $F_o \leqslant 4F_{\text{min.}}$. The quantity minimized was $\Sigma w(|F_o| - |F_c|)^2$. Refinement was terminated for reasons of economy when the speed of

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† Preliminary report: T. Kikuchi, M. Niwa, and N. Masaki, *Tetrahedron Letters*, 1972, 5249. Part III, T. Kikuchi and T. Toyoda, *Chem. and Pharm Bull.* (*Japan*), 1971, **19**, 753.

[1] T. Kikuchi, M. Takayama, T. Toyoda, M. Arimoto, and M. Niwa, *Tetrahedron Letters*, 1971, 1535.

[2] E. J. Corey and J. J. Ursprung, *J. Amer. Chem. Soc.*, 1956, 78, 5041.

[3] 'International Tables for *X*-ray Crystallography,' vol. 3, Kynoch Press, Birmingham, 1962.

Table 1

Final atomic (fractional co-ordinates × 10^4) and thermal parameters, with standard deviations in parentheses

Atom	x/a	y/b	z/c	$B/\text{Å}^2$
Br	1631(2)	1407(1)	2202(5)	*
O(1)	3448(12)	2929(5)	5382(27)	*
O(2)	3405(17)	2423(7)	7445(41)	*
O(3)	3810(9)	875(4)	4650(23)	*
O(4)	2737(11)	393(6)	4292(28)	*
C(1)	3516(16)	3863(7)	6644(31)	3·4(5)
C(2)	3948(17)	3439(8)	7512(37)	4·3(6)
C(3)	4222(17)	3107(9)	6129(36)	4·2(6)
C(4)	4741(17)	3317(8)	4630(37)	4·3(6)
C(5)	4326(15)	3702(8)	3715(32)	3·4(5)
C(6)	5026(15)	3893(7)	2343(34)	3·1(5)
C(7)	4721(15)	4376(8)	1670(32)	3·5(5)
C(8)	4627(14)	4680(7)	3304(29)	2·7(4)
C(9)	3875(14)	4512(7)	4563(28)	2·2(4)
C(10)	4148(14)	4037(7)	5319(30)	2·7(4)
C(11)	3839(16)	4803(8)	6227(34)	3·7(5)
C(12)	1205(14)	4688(7)	704(28)	2·4(4)
C(13)	413(15)	4552(7)	9589(31)	2·9(5)
C(14)	420(14)	4840(7)	7783(31)	2·9(4)
C(15)	4582(14)	282(7)	3299(29)	2·6(4)
C(16)	4217(14)	741(7)	2925(32)	2·9(5)
C(17)	4874(13)	1073(7)	2437(29)	2·1(4)
C(18)	567(15)	4057(7)	8944(30)	3·0(5)
C(19)	608(17)	3761(8)	665(34)	4·0(6)
C(20)	705(17)	3288(8)	135(36)	4·0(6)
C(21)	4953(17)	1846(8)	1171(35)	4·0(6)
C(22)	4346(15)	1478(8)	1731(32)	3·7(5)
C(23)	39(19)	2047(9)	6769(39)	5·3(7)
C(24)	3505(16)	3572(8)	2548(35)	4·7(6)
C(25)	2950(16)	4508(8)	3703(33)	3·5(5)
C(26)	1226(15)	4746(7)	6552(32)	3·4(5)
C(27)	4588(15)	382(7)	9290(30)	3·1(5)
C(28)	319(16)	3763(8)	5748(32)	3·6(5)
C(29)	1567(20)	3198(9)	9374(39)	5·4(7)
C(30)	549(21)	3015(10)	1969(46)	6·6(8)
C(1′)	3140(21)	2566(10)	5923(43)	6·5(8)
C(2′)	2962(22)	2405(11)	5044(52)	7·3(9)
C(3′)	3063(17)	701(8)	5198(37)	4·4(6)
C(4′)	2755(15)	881(7)	6862(32)	3·3(5)
C(5′)	2293(15)	584(8)	8115(33)	3·5(5)
C(6′)	2010(17)	736(8)	9681(37)	4·2(6)
C(7′)	2124(19)	1163(9)	9929(39)	5·2(7)
C(8′)	2500(16)	1478(9)	8833(36)	4·4(6)
C(9′)	2818(15)	1315(8)	7210(34)	4·0(5)

* Anisotropic thermal parameters (× 10^4), with their estimated standard deviations in parentheses, in the form: $T = \exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

Atom	β_{11}	β_{22}	β_{33}	$2\beta_{12}$	$2\beta_{13}$	$2\beta_{23}$
Br	59(2)	30(1)	278(8)	−0(2)	77(7)	−0·0066(4)
O(1)	43(9)	5(2)	390(52)	−27(7)	−45(43)	0·0040(18)
O(2)	115(17)	18(3)	621(90)	−74(14)	−94(89)	0·0074(34)
O(3)	23(7)	5(2)	262(41)	−14(6)	34(30)	−0·0026(15)
O(4)	32(9)	12(2)	376(57)	−4(8)	108(40)	−0·0040(21)

convergence became sufficiently slow.† R was 14·3% for all observed reflections. To determine the absolute configuration of the molecule, two sets of structure factors were calculated, with $f''_{\text{Br}} \pm 1{\cdot}46$. The unique solution was obtained by consideration of the significant differences of Bijvoet pairs for 19 reflections. Observed and calculated structure factors are listed in Supplementary Publication No. SUP 21230 (3 pp., 1 microfiche).‡ Final atomic co-ordinates and thermal parameters are given in Table 1. Co-ordinates of the hydrogen atoms, except for those of the methyl groups, were calculated assuming C–H 1·00 Å, and tetrahedral or trihedral geometry. Most of these positions corresponded to peaks of residual electron density on a three-dimensional difference map, but their contributions were not included in the final structure-factor calculations.

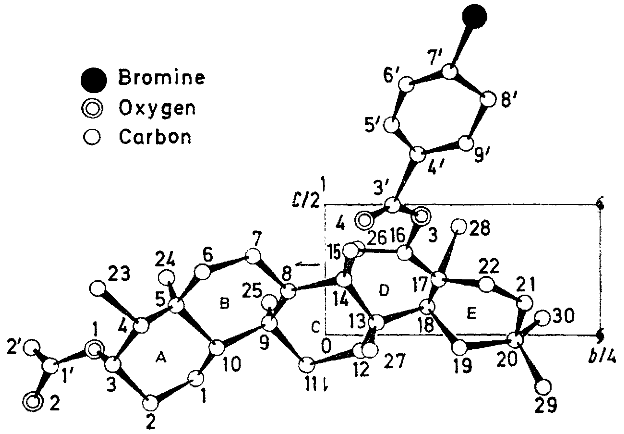

Figure 1 A perspective view of the molecule along the a axis, showing the atom numbering system used in the analysis

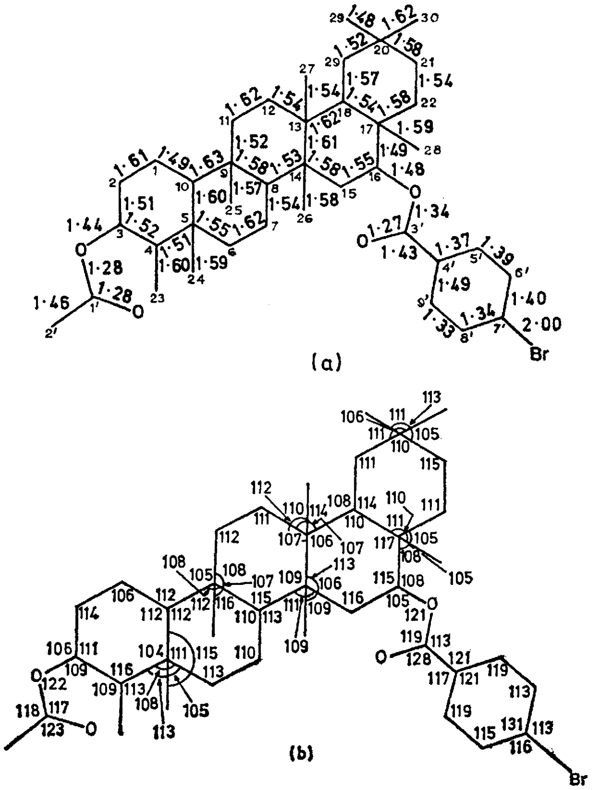

Figure 2 (a) Bond lengths (Å) and (b) bond angles (deg.)

RESULTS AND DISCUSSION

A perspective view of the molecule of (IVc) along the a axis is shown in Figure 1. Bond lengths and valency

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† Two further cycles of least-squares refinement were later carried out. The mean value of the shift-to-σ ratio for a co-ordinate was reduced from 0·13 to 0·03 for bromine, and from 0·17 to 0·05 for oxygen and carbon. R was reduced from 14·3 to 14·1%, but no significant changes were observed in atom co-ordinates.

‡ See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1974, Index issue.

angles calculated from the final co-ordinates are shown in Figure 2. Standard deviations are in the range 0·03—0·05 Å for bond lengths and 1·6—2·9° for valency angles.

The molecules are composed of five six-membered rings A—E with a bromobenzoyl, an acetyl, and eight methyl groups. Rings A—C are in the chair and rings D and E in the boat conformation. As a whole, the molecule is in an extended form. Two planar groups, comprising the trigonally hybridized carbonyl carbon atoms and their three bonded neighbours, are attached to rings A and D with torsion angles of C(4)–C(3)–O(1)–C(1′) 142 and C(17)–C(16)–O(3)–C(3′) 146°. The plane of the *O*-benzoyl group makes an angle of 36° with that of the benzene ring. Details of planes are given in Table 2.

TABLE 2

(*a*) Equations of least-squares planes through the molecule, in the form $lx + my + nz = d$, where the directions of x, y, and z are referred to the crystallographic axes a, b, and c

Plane	Atoms	l	m	n	d
(1)	Ring A	−0·8526	−0·2957	0·4307	−3·5993
(2)	Ring B	−0·8614	−0·0843	0·5007	0·8887
(3)	Ring C	−0·8461	0·1591	0·5087	5.0182
(4)	Ring D	0·6883	−0·1225	−0·7150	−5·8504
(5)	Ring E	−0·6919	0·2176	0·6884	6·8604
(6)	Rings A, B, C	−0·8934	−0·0673	0·4442	0·9751
(7)	Benzene	−0·8786	−0·1792	0·4426	1·8478
(8)	*O*-Benzoyl	−0·5162	−0·6753	0·5267	−5·5556
(9)	*O*-Acetyl	−0·6175	0·5624	−0·5499	6·5929

(*b*) Interplanar angles (deg.)

(1)–(2)	13	(8)–(4)	50
(2)–(3)	14	(7)–(4)	26
(3)–(4)	15	(9)–(1)	83
(4)–(5)	5	(1)–(5)	35
(7)–(8)	36	(1)–(3)	27

(*c*) Deviations (Å) of relevant atoms from the planes

Plane (1): C(1) −0·27, C(2) 0·20, C(3) −0·18, C(4) 0·22, C(5) −0·27, C(10) 0·31

Plane (2): C(5) −0·21, C(6) 0·21, C(7) −0·26, C(8) 0·30, C(9) −0·29, C(10) 0·24

Plane (3): C(8) 0·23, C(9) −0·21, C(11) 0·23, C(12) −0·27, C(13) 0·28, C(14) −0·26

Plane (4): C(13) −0·50, C(14) 0·35, C(15) 0·07, C(16) −0·34, C(17) 0·23, C(18) 0·19

Plane (5): C(17) −0·23, C(18) −0·19, C(19) 0·44, C(20) −0·25, C(21) −0·19, C(22) 0·42

Plane (6): C(1) −0·49, C(2) 0·31, C(3) 0·17, C(4) 0·44, C(5) −0·37, C(6) 0·13, C(7) −0·34, C(8) 0·13, C(9) −0·54, C(10) −0·01, C(11) 0·02, C(12) −0·11, C(13) 0·66, C(14) −0·01, C(15) 0·83, C(16) 1·56, C(17) 0·87, C(18) 0·33, C(19) 0·90, C(20) 0·69, C(21) 1·34, C(22) 1·92

Plane (7): Br 0·05, C(3′) 0, C(4′) −0·03, C(5′) 0·01, C(6′) 0·01, C(7′) −0·01, C(8′) −0·01, C(9′) 0·03

Plane (8): C(3′) 0·02, C(4′) −0·01, O(3) −0·01, O(4) −0·01

Plane (9): C(1′) 0·09, C(2′) −0·03, O(1) −0·03, O(2) −0·03

The carbon atoms of three methyl groups, C(24)—(26), and an oxygen atom of the acetyl group, O(1), are on the β-side of the molecule and make three pairs of 1,3-diaxial systems in the six-membered rings. Tetrahedra of the angular carbon atoms linking the pertinent methyl groups are compared in Figure 3(a) where the deviations (Δ) are given of the methyl groups from the central carbon atoms in the projection on the plane of the other three carbon atoms. On the whole, the systematic deformation of the tetrahedra, caused by steric hindrance of the methyl groups cannot be detected, although differences in individual valency angles and bond lengths are significant. The apparent effects of overcrowding are shown in Figure 3(b) where the three 1,3-diaxial pairs consisting of the methyl groups and the oxygen atom are depicted, together with the differences (δ) between the interatomic distances of the pair atoms and those of the linking carbon atoms. The deviation of each atom from the least-squares plane of the other four atoms is also given. As expected, from Figure 3(b), co-operative deformation of the ring system occurs.

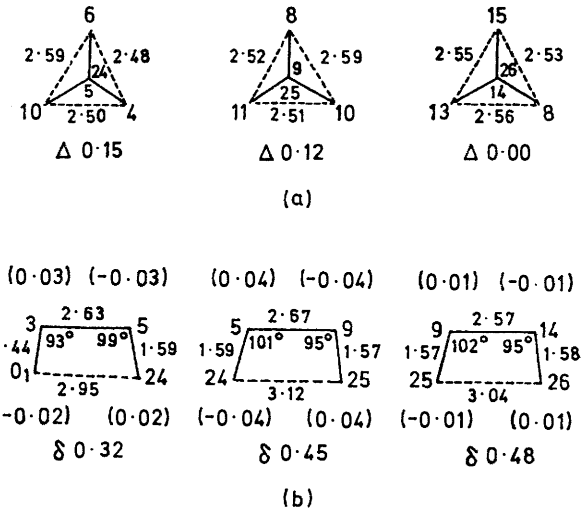

FIGURE 3 Steric strain of the methyl groups

The internal torsion angles of the five rings are shown in Figure 4. Mean torsion angles of 57 for rings A—C and 37° for rings D and E compare well with the ideal values of 60 and 40° for the chair and boat conformations, and with the calculated values (55·8 and 36°) for cyclohexane[4] under minimum-energy conditions.

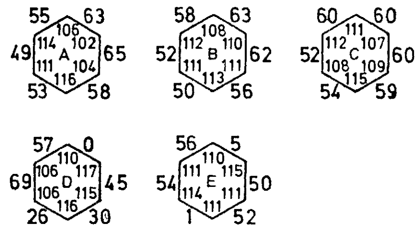

FIGURE 4 Torsion angles (deg.) in rings A—E

The agreement between solid-state torsion angles and

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

those calculated by empirical equation[5] from n.m.r. results indicates that the boat conformation of ring D persists in solution.

The structure of (IVc) has a new conformation for elucidating the D-ring conformation only. As seen in Table 4, ten compounds derived from pachysandiol B (Ia) are classified into two groups having S or F conformation by n.m.r. spectroscopy. The oxygen atom attached to C(16) behaves as a key function in selection of the conformation in those pachysandiol derivatives.

TABLE 3

Probable conformations and steric hindrances of D and E rings in friedelin-type triterpenes

Ring	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
D	Chair	Chair	Chair	Boat 16-bow	Boat 16-bow	Boat 17-bow	Boat 17-bow	Boat 17-bow
E	Chair	Boat 21-bow	Boat 20-bow	Boat 22-bow (20*β*-*ax*, 21*β*-*ax*)	Boat 22-bow (20*β*-*eq*, 21*β*-*eq*)	Chair	Boat 20-bow	Boat 21-bow
Steric hindrance	C(27) ↔ C(29)	C(21) ↔ C(27) Δ release C(27) ↔ C(29)	C(28) ↔ C(30)	O	C(27) ↔ C(29)	C(26) ↔ C(28)	C(26) ↔ C(28) C(16) ↔ C(29)	C(26) ↔ C(28)

five-ring systems deduced to be chair–chair–chair–boat–boat, and this differs from that shown in the two-dimensional *X*-ray analysis of friedelan-3α-ol chloroacetate.[2] To a first approximation, the conformations of six-membered rings were considered to be either chair or boat. A Dreiding model shows that only eight conformations (Table 3) are possible in the D/E *cis*-fused five six-membered-ring (friedelin-type) skeleton if rings A—C are to be kept in the chair form. When the five methyl groups corresponding to C(26)—(30) of Figure 1 are attached to each model, two of them (indicated in Table 3) are as close as the C–C bond distances in a cyclohexane ring in all conformations except (4). Conformations (3), (6), (7), and (8) are in the most extreme condition where two methyl groups are occupying axial positions at the bow and stern of a boat; (2) is in the second most extreme, and (1) and (5) the third. The severe steric interference of methyl groups C(27) and C(29) in (1) is removed in (3) and lessened a little in (2). The skeleton of friedelan-3α-ol chloroacetate[2] appears to be in a conformation intermediate between (1) and (3). One stable *quasi*-all-chair conformation can therefore be produced from (1)—(3). Conformation (4), which gives fewest methyl–methyl interactions is therefore the one found for (IVc), although a methyl group C(27) shares the axial position at the bow and stern of the boat with a hydrogen atom attached to C(16). It may be concluded that two types of conformation, S and F (Figure 5), are possible for friedelin-type triterpenes.

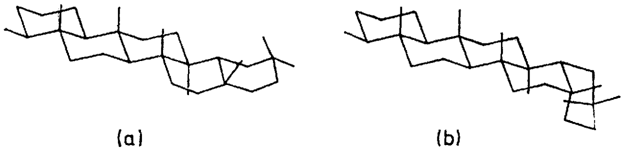
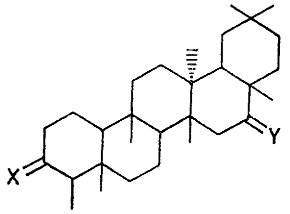

(a) (b)

FIGURE 5 The two possible conformations for friedelin-type triterpenes (a) S (stretched) and (b) F (folded) forms

As S and F have boat and chair conformations of ring D respectively, they can be distinguished by

TABLE 4

N.m.r. data for pachysandiol B derivatives



X	Y	τ[C(16)*H*·OR]	Multiplicity	*J*/Hz	Class
OAc H	OAc H	4·80	t	9·0	S
OH H	OAc H	4·80	t	9·0	S
O	OAc H	4·80	t	9·0	S
H_2	OAc H	4·78	t	9·0	S
OAc H	OH H	6·00	t	9·0	S
OAc H	OBrac * H	4·74	t	9·0	S
OBrac * H	OAc H	4·82	t	9·0	S
OAc H	OBrBz * H	4·56	t	9·0	S
H_2	H OAc	4·81	q	7·5, 8·5	F
OAc H	H OAc	4·82	q	7·5, 8·5	F

* Brac = $CO{\cdot}CH_2Br$, BrBz = $CO{\cdot}C_6H_4Br$-*p*

It is clear that the 16α-oxygen atom cannot remain in an axial position; it therefore changes the conformation

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[5] R. J. Abraham and J. S. E. Holker, *J. Chem. Soc.*, 1963, 806.

to F because the methyl group at C(27) and the oxygen atom occupy the axial positions in the bow and stern of the boat. However the reason why the oxygen atom cannot remain in a 16β axial position is not so clear. Steric interaction of the oxygen atom in a 16β axial position with the methyl group at C(26) (1,3-diaxial) is probably stronger than that of O(1) with C(24) in the actual structure, because another methyl group C(25) lines up with C(26) and the oxygen atom and these three methyl groups share all the two pairs of 1,3-diaxial positions. On the basis of discussion related to Figure 3, the overcrowding effect seems to be the main reason why the 16β axial oxygen atom makes the conformation S.

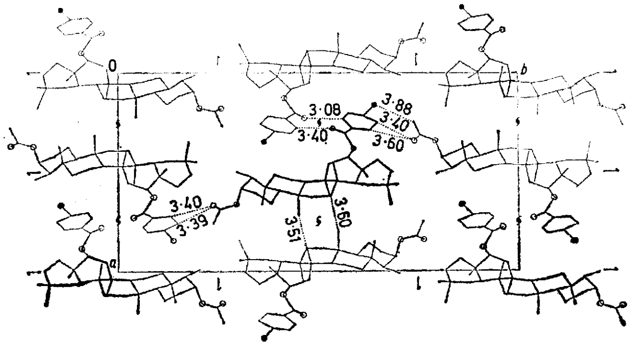

FIGURE 6 The crystal structure viewed along the *c* axis

Figure 6 shows molecular packing and short intermolecular distances. Two carbonyl oxygen atoms [O(4) and O(2)] make contacts (3·08 and 3·40 Å) with the carbon atoms in the benzene ring. The former is likely to be a hydrogen bond since the calculated angle C–H · · · O is 131°. Other distances are the normal sums of van der Waals radii. On the whole, molecular packing effects do not seem to be a cause of distortion in the molecule.

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