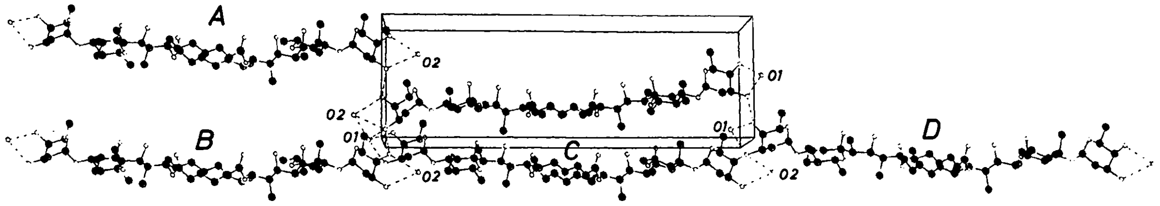

Fig. 3. The environment of one molecule, viewed parallel to a direction in the macrolidic ring.

O(18)···O(2^{i}) 3·04 Å], suggesting disordered or bifurcated hydrogen bonds involving the remaining hydroxyl protons. Each water molecule is then in a position to make two further hydrogen bonds [O(1^{i})···O(18) 2·81, O(1)···O(2) 3·08, O(2)···O(08) 3·15 Å].

Streptomyces albus ATCC 21838 is also able to generate polyether antibiotics of the salinomycin group (Miyazaki, Shibuya, Sugawara, Kawaguchi, Hirose, Nagatsu & Esumi, 1974). The structural formulae indicate that the biosynthesis of the two compounds follows similar paths. In the case of salbomycin the terminal saccharides are 2-deoxyfucose, a component of the antibiotic olivomycin (Berlin, Esipov, Kiseleva & Kolosov, 1967).

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Structure of a Favorskii Substitution Product, 3*β*-Acetoxy-17*β*-hydroxy-18-nor-5α,17α-pregnan-20-one,* $C_{22}H_{34}O_4$†

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(*Received* 19 *September* 1983; *accepted* 1 *December* 1983)

Abstract. $M_r = 362·5$, monoclinic, $C2$, $a = 14·746$ (4), $b = 7·483$ (4), $c = 36·916$ (20) Å, $\beta = 97·40$ (4)°, $V = 4039·5$ Å^3, $Z = 8$ (two molecules per asymmetric unit), $D_m = 1·188$ (4), $D_x = 1·192$ Mg m^{-3}, Cu $K\alpha_1$, $\lambda = 1·54056$ Å, $\mu = 0·60$ mm^{-1}, $F(000) = 1584$, $T = 293$ K, final $R = 0·049$ for 3704 observed reflections. The hydroxyl group at C(17) is *β*, *cis* to the C(19) methyl group. Rings *A*, *B* and *C* show essentially identical chair conformations in the two molecules, while ring *D*, here in the uncommon C(14)-envelope form, shows some small conformational differences, which may be related to the intermolecular hydrogen-bonding pattern.

Introduction. The title compound was obtained as a substitution product in a Favorskii rearrangement reaction of 3*β*-acetoxy-17-bromo-18-nor-5α-pregnan-20-one. Such substitution products from α-halogenated ketones are considered to be formed *via* epoxy ether intermediates, and subsequent hydrolysis of the epoxy ether (Engel, Lachance, Capitaine, Zee, Mukherjee & Mérand, 1983). The usual opening of the epoxy ring would result in an overall inversion of configuration at C(17), and the evidence suggested that it had done so in this case (Engel *et al.*, 1983), but a weakly positive Cotton effect of the title compound would have been compatible with a 17α-hydroxy configuration. The crystal structure was examined in order to establish the stereochemistry unambiguously, and confirmed that the hydroxyl group at C(17) was indeed in the expected *β* configuration.

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* IUPAC nomenclature: 20-oxo-18-nor-5α,17α-pregnane-3*β*,17*β*-diol 3-monoacetate.

† NRCC Publication No. 23033.

Experimental. Colourless plate-shaped crystals supplied by Professor Ch. R. Engel, specimen 0·50 × 0·40 × 0·14 mm cut from a larger piece, D_m by flotation in aqueous KI solution, Ni-filtered Cu $K\alpha$, Enraf–Nonius CAD-4F diffractometer, cell parameters from least squares applied to 18 reflections with $30 < \theta < 42°$, 4498 unique reflections (*hkl* and $\bar{h}kl$), 3704 considered observed at the $2\sigma(I)$ level, $\theta < 75°$, ω–2θ scans, $\Delta\omega = 1{\cdot}5(1{\cdot}0 + 0{\cdot}14\tan\theta)°$, 3 standard reflections monitored after every 3000 s of exposure, intensity variation ±1·7% from mean, Lp correction, absorption ignored; data with $\theta < 20°$ remeasured during the refinement stage with crystal 0·37 × 0·13 × 0·07 mm and structure-factor agreement significantly improved for 17 *h*0*l* reflections; systematic absences consistent with *C*2, *Cm*, *C*2/*m* but short *b* axis precluded equivalent positions of *Cm* or *C*2/*m*; structure solved stepwise using *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), all permutations being characterized by very poor figures of merit. An *E* map obtained using 350 reflections, 3500 relationships and 75 ψ_0 reflections, corresponding to fifth-highest combined figure of merit (RESID = 33%), showed a 15-atom fragment.This was recycled as an oriented group, and a further *E* map (third-highest CFOM, RESID = 34%) using the same conditions showed 23- + 5-atom fragments, which were developed *via* weighted Fourier maps to 49 atoms. The last three non-H atoms were shown on a weighted Fourier map only after two cycles of isotropic least squares (they did not appear on the corresponding difference map). Block-diagonal (9 × 9) least-squares refinement minimizing $\sum w(F_o - F_c)^2$ with anisotropic thermal parameters for C and O, the two hydroxyl H atoms included as fixed contributions at their difference-map locations, other H-atom positions calculated but not refined, scattering factors for C and O from *International Tables for X-ray Crystallography* (1974) and for H from Stewart, Davidson & Simpson (1965), weighting scheme chosen to give uniform values of $\langle w(|F_o| - |F_c|)^2\rangle$ over ranges of $|F_o|$ and $\sin^2\theta$, $w^{-1} = 1 + [(|F_o| - 10)/30]^2$. Final $R = 0{\cdot}049$, $R_w =$

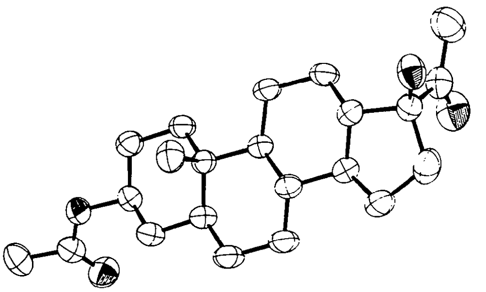

Fig. 1. A view of molecule (II). Thermal ellipsoids are shown at 50% probability, and those of oxygen atoms are shown with one shaded octant.

Table 1. *Fractional coordinates* (×10⁴) *and equivalent isotropic thermal parameters for the non-hydrogen atoms*

$$B_{\rm eq} = \tfrac{8}{3}\pi^2\textstyle\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	*y*	*z*	$B_{\rm eq}$(Å²)
Molecule (I)				
O(1)	−6405 (2)	−5466 (3)	−338 (1)	4·4
O(2)	−6493 (2)	−8235 (5)	−562 (1)	7·6
O(3)	−2210 (2)	2974 (5)	−1884 (1)	6·0
O(4)	−3562 (2)	560 (6)	−2571 (1)	8·1
C(1)	−5843 (2)	−1962	−1000 (1)	4·5
C(2)	−6268 (2)	−2848 (5)	−691 (1)	4·7
C(3)	−6049 (2)	−4818 (5)	−665 (1)	4·1
C(4)	−5036 (2)	−5174 (5)	−643 (1)	4·5
C(5)	−4638 (2)	−4291 (5)	−960 (1)	3·9
C(6)	−3634 (2)	−4764 (6)	−967 (1)	5·1
C(7)	−3278 (2)	−4017 (6)	−1299 (1)	5·3
C(8)	−3432 (2)	−2004 (5)	−1341 (1)	3·9
C(9)	−4446 (2)	−1514 (5)	−1326 (1)	3·9
C(10)	−4804 (2)	−2240 (5)	−977 (1)	3·6
C(11)	−4609 (2)	490 (6)	−1386 (1)	5·1
C(12)	−4257 (3)	1220 (6)	−1726 (1)	5·5
C(13)	−3247 (2)	743 (6)	−1717 (1)	4·5
C(14)	−3124 (2)	−1287 (6)	−1693 (1)	4·2
C(15)	−2132 (3)	−1535 (7)	−1751 (1)	5·5
C(16)	−2013 (3)	−169 (9)	−2059 (1)	6·6
C(17)	−2681 (2)	1384 (6)	−2020 (1)	4·9
C(19)	−4330 (3)	−1287 (6)	−635 (1)	5·0
C(20)	−3304 (3)	1805 (7)	−2362 (1)	5·7
C(21)	−3623 (3)	3655 (9)	−2436 (1)	7·6
C(22)	−6585 (2)	−7222 (6)	−319 (1)	4·9
C(23)	−6931 (3)	−7692 (7)	27 (1)	6·0
Molecule (II)				
O(1)	−1765 (1)	−2451 (4)	−4647 (1)	4·4
O(2)	−2821 (2)	−1137 (5)	−4355 (1)	5·8
O(3)	5067 (2)	−118 (4)	−3162 (1)	5·0
O(4)	3627 (2)	−676 (5)	−2484 (1)	6·6
C(1)	469 (2)	−3412 (4)	−4061 (1)	4·0
C(2)	−347 (2)	−3617 (5)	−4366 (1)	4·5
C(3)	−1085 (2)	−2267 (5)	−4324 (1)	3·8
C(4)	−720 (2)	−378 (5)	−4296 (1)	4·0
C(5)	80 (2)	−223 (4)	−3991 (1)	3·7
C(6)	395 (2)	1709 (5)	−3931 (1)	4·5
C(7)	1131 (2)	1869 (5)	−3607 (1)	4·6
C(8)	1930 (2)	617 (4)	−3634 (1)	3·5
C(9)	1609 (2)	−1333 (4)	−3702 (1)	3·4
C(10)	871 (2)	−1516 (4)	−4041 (1)	3·3
C(11)	2430 (2)	−2587 (5)	−3714 (1)	4·6
C(12)	3146 (2)	−2427 (5)	−3376 (1)	4·8
C(13)	3454 (2)	−495 (5)	−3332 (1)	3·9
C(14)	2647 (2)	727 (5)	−3297 (1)	3·6
C(15)	3101 (2)	2546 (5)	−3209 (1)	4·6
C(16)	3985 (3)	2087 (6)	−2962 (1)	5·4
C(17)	4209 (2)	110 (5)	−3026 (1)	4·0
C(19)	1291 (2)	−1119 (6)	−4393 (1)	4·8
C(20)	4175 (2)	−1043 (6)	−2692 (1)	4·7
C(21)	4775 (3)	−2623 (7)	−2633 (1)	6·7
C(22)	−2602 (2)	−1798 (5)	−4625 (1)	4·3
C(23)	−3214 (3)	−2000 (7)	−4976 (1)	5·7

Table 2. *Torsional angles* (°) *for ring D*

	(I)	(II)
C(13)–C(14)–C(15)–C(16)	−40·7 (4)	−36·9 (3)
C(14)–C(15)–C(16)–C(17)	29·6 (4)	20·8 (4)
C(15)–C(16)–C(17)–C(13)	−6·5 (4)	3·1 (4)
C(16)–C(17)–C(13)–C(14)	−18·9 (4)	−26·2 (4)
C(17)–C(13)–C(14)–C(15)	37·6 (4)	39·4 (3)
C(15)–C(16)–C(17)–C(20)	−126·6 (4)	−115·6 (3)
C(15)–C(16)–C(17)–O(3)	108·1 (4)	118·8 (3)
C(13)–C(17)–O(3)–H(O)	176	−164
C(16)–C(17)–O(3)–H(O)	63	82
C(20)–C(17)–O(3)–H(O)	−65	−46

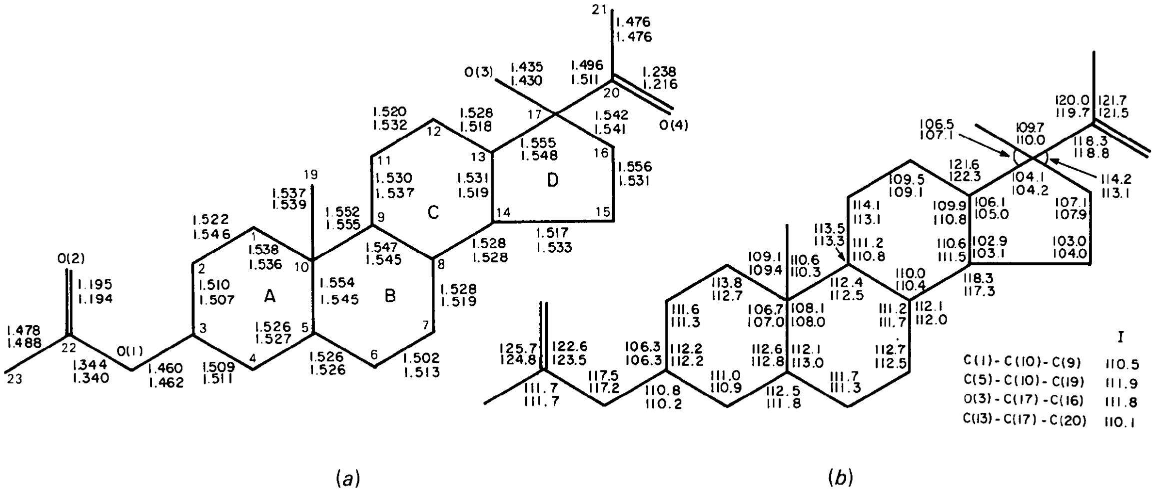

Fig. 2. (*a*) Atom numbering and bond distances (Å). Values for molecule (I) are given above, those for molecule (II) below. E.s.d.'s are in the range 0·004–0·008 Å. (*b*) Bond angles (°). The top value of each pair is for molecule (I), and the bottom value is for molecule (II). E.s.d.'s are in the range 0·2–0·4°.

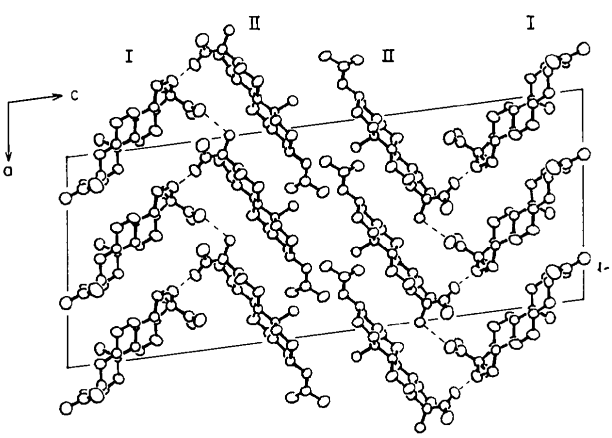

Fig. 3. The crystal structure viewed along the *b* axis. Hydrogen-bonded chains near $z = \frac{1}{4}$ rise one cell unit vertically as x increases from 0 to 1. Near $z = \frac{3}{4}$, the chain direction is opposite, dropping one cell length vertically as x increases 0→1. Atom O(3) is obscured behind ring *D* in type (I) molecules.

0·060, $S = 1{\cdot}004$ for all observed reflections;* 4 very strong reflections apparently affected by secondary extinction were excluded from refinement, mean and max. final Δ/σ were 0·03 and 0·19, max. and min. final $\Delta\rho$ excursions were 0·22 and −0·21 e Å^{-3}. Computer programs of Ahmed, Hall, Pippy & Huber (1973) as well as *MULTAN*78 and *ORTEP* II (Johnson, 1971) were used.

Discussion. The atomic parameters are given in Table 1, and a view of one of the molecules is shown in Fig. 1. Bond lengths and angles are given in Fig. 2. There is good general agreement between corresponding values in the two molecules. The analysis establishes that the hydroxyl group at C(17) is *β*, *cis* to the C(19) methyl group. Rings *A*, *B* and *C* are all chair shaped, and the ring junctions *A*/*B*, *B*/*C* and *C*/*D* are *trans*. Unlike most pregnane structures, where ring *D* generally is in a C(13)-envelope or a half-chair conformation, ring *D* is here in the C(14)-envelope conformation. Pertinent torsional angles are listed in Table 2, and show minor conformational differences in ring *D* for the two molecules. In the relatively few other cases of C(14)-envelope conformation in the pregnane series, this form is forced on ring *D* by C(16)–C(17) double bonds or small rings fused at that position in all but four structures (refcodes DXTMPO,* KCANRO,† OHPRGB‡ and PREGDO§ in the Cambridge Crystallographic Database). The search yielding this information was based on the January 1983 release. Substantial differences (~19°) in the torsional angles involving H(O) in the two molecules accompany the differences in the endocyclic torsional angles, suggesting that the hydroxyl group may be pulling ring *D* into conformations favourable for the intermolecular hydrogen bonds.

The packing arrangement is shown in Fig. 3. An array of type I molecules faces a similar array of type II molecules in a herringbone pattern, with intermolecular hydrogen bonds connecting O(3) of a molecule (I) to

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* Lists of structure factors, H-atom parameters, anisotropic thermal parameters, details of hydrogen bonding and supplementary torsional angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39079 (26 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

* Enslin, Coetzer & Kruger (1977).

† Rohrer, Weeks & Duax (1976).

‡ Beloeil, Bertranne, Fétizon & Prangé (1981).

§ Romers, de Graaff, Hoogenboom & Rutten (1974).

O(4) of molecule (II) $[\mathrm{H(O)_{I}\cdots O(4)_{II}} = 1{\cdot}87\ \text{Å}]$ and O(3) of molecule (II) to O(4) of another molecule (I) $[\mathrm{H(O)_{II}\cdots O(4)_{I}} = 1{\cdot}86\ \text{Å}]$, related to the first by the lattice centring. The zigzag chains near $z = \frac{1}{4}$ extend parallel to one *ab* cell diagonal, and near $z = \frac{3}{4}$ they are parallel to the other *ab* diagonal. There are no other intermolecular contacts shorter than the corresponding van der Waals distances.

We thank Professor Ch. R. Engel of Université Laval for suggesting the problem and supplying the crystals, and Mrs M. E. Pippy for assistance with the computations.

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Structure of 2-(2-Hydroxy-3-{[2-(1*H*-indol-3-yl)-1,1-dimethylethyl]amino}propoxy)benzonitrile: MJ-13,105-1 (Bucindolol), $C_{22}H_{25}N_3O_2$

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(*Received* 28 *June* 1983; *accepted* 12 *December* 1983)

Abstract. $\beta_1 + \beta_2$-adrenoceptor blocking agent. Antihypertensive. $M_r = 363{\cdot}4$, triclinic, $P\bar{1}$, $a = 8{\cdot}801$ (1), $b = 8{\cdot}883$ (2), $c = 13{\cdot}662$ (1) Å, $\alpha = 99{\cdot}79$ (1), $\beta = 92{\cdot}22$ (1), $\gamma = 105{\cdot}43$ (1)°, $V = 1010{\cdot}6$ (4) Å^3, $Z = 2$, $D_x = 1{\cdot}19$ g cm^{-3}, $\lambda(\mathrm{Cu}\ K\bar{\alpha}) = 1{\cdot}54178$ Å, $\mu = 12{\cdot}6$ cm^{-1}, $F(000) = 388$, room temperature. Final $R = 0{\cdot}035$ for 1938 reflections. The conformation is compared with a previous model of aryloxypropanolamine β-blockers and with some pentacyclic alkaloids of the yohimbine series. N—H···O and O—H···N hydrogen bonds contribute to the crystalline cohesion.

Introduction. In the course of determining structure–activity relationships in antihypertensive drugs, bucindolol has attracted our attention. This drug belongs to a series of antihypertensive indole derivatives of phenoxypropanolamines with β-adrenergic receptor antagonism and vasodilating activity (Kreighbaum, Matier, Dennis, Minielli, Deitchman, Perhach & Comer, 1980). In anaesthetized dogs, bucindolol antagonizes β_1 and β_2 adrenoceptors approximately equally and with a potency similar to that of propranolol (Deitchman, Perhach & Snyder, 1980). Part, but not all, of the vasodilator effect of bucindolol is due to α_1-adrenoceptor blockade (Deitchman *et al.*, 1980).

Experimental. White elongated prisms (from ethanol), $0{\cdot}42 \times 0{\cdot}17 \times 0{\cdot}17$ mm, Enraf–Nonius CAD-4 diffractometer with graphite monochromator, Cu $K\bar{\alpha}$, 25 reflections ($5 < \theta < 40°$) used to refine orientation matrix, no systematic absences, 2541 ($\pm h$, $\pm k$, l) independent reflections with $\theta < 55°$, h from −9 to +9, k from −9 to +9, l from 0 to +15, 1938 with $I \geq 3\sigma(I)$, Lp correction, absorption ignored; two check reflections ($1\bar{2}0$, 300) every 3600 s showed no unusual variation (all within $\pm 3\sigma$); direct methods [*MULTAN* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978)], anisotropic diagonal matrix, refinement on F using observed reflections and weight w with $w = 1$ if $|F_o| < P$, $P = (F_o{}^2{}_{\max}/10)^{1/2}$, $w = (P/F_o)^2$ if $|F_o| > P$, H from ΔF synthesis, isotropic, $R = 0{\cdot}035$, $wR = 0{\cdot}029$, $S = 0{\cdot}612$ (1938 reflections, 344 parameters), maximum peak $\pm 0{\cdot}3$ e Å^{-3} in final ΔF

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