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References

ACHESON, M. R., WALLIS, J. D. & WATKIN, D. J. (1980). *Acta Cryst.* B36, 3125–3127.
CHAKRABORTHY, D. K. & TALAPATRA, S. K. (1986). *Acta Cryst.* C42, 1435–1437.
CHANDRASHEKAR, K. & PATTABHI, V. (1980). *Acta Cryst.* B36, 1165–1169.
FALKENBERG, G. & CARLSTROM, D. (1971). *Acta Cryst.* B27, 411–418.
HARRIS, L. S. & UHLE, F. C. (1960). *J. Pharmacol. Exp. Ther.* 128, 358–362.
HO, C. Y., HAEGMAN, W. E. & PRISCO, F. (1986). *J. Med. Chem.* 29, 118–121.
HOULIHAH, W. J. (1973). *Chem. Abstr.* 79, 115651*m*.
HUGES, C. K., LIONS, F., MCKEAN, J. G., MURRY, A. J., CALLANAN, V., FREEMAN, D. H., RALPH, C. S., RASSACK, R., DORNBROSKI, J., FINCH, F., ANDREWS, R., BETTY, R. C., SCOTT, R. H., VERNON, C. W., FLACK, A. & LAWRENCE, C. H. (1938). *J. Proc. R. Soc. N.S.W.* 71, 458–461.
ISHIDA, T., INOUE, M. & TOMITA, K. (1979). *Acta Cryst.* B35, 1642–1648.
JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
REYNOLDS, B. & CARSON, J. (1970). *Chem. Abstr.* 72, 55528*v*.
SAKAKI, T., SOGO, A., WAKAHARA, A., KANAI, T., FUJIWARA, T. & TOMITA, K. (1976). *Acta Cryst.* B32, 3235–3242.
SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
SHOJA, M. (1988). *Acta Cryst.* C44, 2238–2239.
VIJAYALAKSHMI, B. K. & SRINIVASAN, R. (1975). *Acta Cryst.* B31, 999–1003.
WEI, P. H. L. & STANLEY, C. (1970). *Chem. Abstr.* 73, 66635*z*.
WHITE, A. C. & BLACK, R. M. (1986). *Chem. Abstr.* 85, 177505*z*.

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Structure of 5β-Dihydrotestosterone

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Abstract. 17β-Hydroxy-5β-androstan-3-one, $C_{19}H_{30}O_2$, $M_r = 290{\cdot}45$, orthorhombic, $P2_12_12_1$, $a = 11{\cdot}7821\ (6)$, $b = 21{\cdot}2184\ (8)$, $c = 6{\cdot}5322\ (2)$ Å, $V = 1633{\cdot}0\ (2)$ Å^3, $Z = 4$, $D_x = 1{\cdot}181$ Mg m^{-3}, λ(Cu $K\alpha$) $= 1{\cdot}54178$ Å, $\mu = 0{\cdot}58$ mm^{-1}, $F(000) = 640$, $T = 293$ K, $R = 0{\cdot}033$ for 1849 unique observed reflections. The molecular conformation of 5β-dihydrotestosterone shows the strong bending typical of 5β-steroids: the bowing angle of the *A* ring, relative to the remainder of the steroid, is 65·1°. Bowing shortens the distance between the terminal O atoms, O(3) and O(17), to 9·824 (2) Å which is *ca* 1 Å shorter than was observed in 5α-dihydrotestosterone and testosterone. The effects of both the bowing and the shorter separation between O(3) and O(17) may explain a difference in the affinity of 5β-dihydrotestosterone for the dexamethasone binding site on membranes compared to that of the other two compounds. A unique conformational feature of 5β-dihydrotestosterone is the flattening of the *A* ring on the side containing the C(3)—C(4) bond; this may be due to the combination of the 3-oxo substitution and the 5β-configuration.

Introduction. Dexamethasone binding sites have been identified on both nuclear envelopes and plasma membranes (Howell & Lefebvre, 1989; Howell, Po & Lefebvre, 1989) and are postulated to be important in the transport of hormones. Our study of the activity profile of steroids that interact with the dexamethasone binding sites has shown that steroid affinity for these sites is strongly correlated to the distance between the terminal O atoms of the steroid (Roszak, Codding & Lefebvre, 1990). Analysis of the crystal structures of pregnanes showed that the distance between the O atoms, O(3) and O(20), is consistently in the range 11·2–11·9 Å whereas, for testosterone, the distances between the terminal O atoms, O(3) and O(17β), are 10·94 and 10·93 Å in the two independent molecules of testosterone

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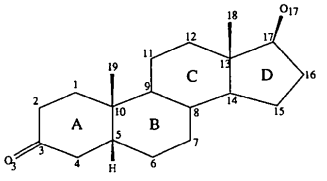
(Roberts, Pettersen, Sheldrick, Isaacs & Kennard, 1973), and 10·83 and 10·86 Å in the two polymorphs of testosterone monohydrate (Busetta, Courseille, Leroy & Hospital, 1972; Precigoux, Hospital & Van den Bosche, 1973). The corresponding distances in the structure of 5α-dihydrotestosterone (17β-hydroxy-5α-androstan-3-one, 5α-DHT) are 10·77 and 10·66 Å in the two independent molecules (Courseille, Precigoux, Leroy & Busetta, 1973) and 10·84 Å in the structure of 5α-dihydrotestosterone monohydrate (Busetta, Courseille, Fornies-Marquina & Hospital, 1972). The pregnanes exhibited highly competitive binding at the dexamethasone site; in contrast, testosterone and 5α-dihydrotestosterone displayed a similar, moderate affinity which may be related to the similarity in the distance between the terminal O atoms in these compounds and to the fact that this separation is shorter than that found in the pregnanes. Of the testosterones, 5β-dihydrotestosterone (5β-DHT) was unique and displayed low affinity. The crystal structure of 5β-DHT and thus the separation between terminal O atoms was not available; therefore its molecular structure was determined to test the hypothesized correlation of affinity and interatomic distances.

Experimental. Title compound from Steraloids Inc. (Wilton, New Hampshire, USA), colorless crystals grown from ethyl acetate by slow evaporation, crystal specimen: 0·33 × 0·32 × 0·12 mm, Enraf–



5β-DHT

Nonius CAD-4F diffractometer, Cu radiation with Ni filter, ω–2θ scan mode; accurate cell parameters from least-squares refinement for 25 reflections with $30 < \theta < 49°$; three standards [$\bar{4}$,$\bar{1}$5,0: 1196 (12); 922: 281 (4); 2,10,4: 299 (5)]; two octants collected, h −14/0, k −26/0, l 0/8 and h 0/14, k 0/26, l 0/8; maximum $(\sin\theta/\lambda) = 0{\cdot}6258$ Å^{-1}; 4212 reflections measured, 1952 unique reflections ($R_{int} = 0{\cdot}06$), 103 unobserved reflections [$I < 2{\cdot}5\sigma(I)$]; no absorption correction.

Structure solved by direct methods with *SHELXS*86 (Sheldrick, 1985); blocked least-squares refinement on F's with *XRAY*76 (Stewart, 1976); all H atoms located in a difference Fourier synthesis and refined with isotropic thermal parameters; anisotropic thermal parameters for non-H atoms; 311 parameters refined.

Final $R = 0{\cdot}033$, $wR = 0{\cdot}037$ [$w^{-1} = \sigma^2(F) + 0{\cdot}00002|F|^2$] and $S = 1{\cdot}13$ for 1849 observed reflections; empirical isotropic extinction parameter (g) converged at 1·87 (8) × 10^{-3} (Larson, 1967); maximum $(\Delta/\sigma) = 0{\cdot}04$ in final cycle; maximum $(\Delta\rho) = 0{\cdot}21$, minimum $(\Delta\rho) = -0{\cdot}12$ e Å^{-3} in final ΔF synthesis. Scattering factors from Cromer & Mann (1968) except those for H atoms from Stewart, Davidson & Simpson (1965). Other computer programs used: *ORTEP*II (Johnson, 1976), *PROFIT* (Smith, 1983) and *MMS* (Dempsey, 1986).

Discussion. The fractional coordinates and B_{eq} values for the non-H atoms of 5β-DHT are given in Table 1.* The molecular conformation and atomic labeling scheme are shown in Fig. 1. Bond lengths and angles and endocyclic torsion angles are listed in Table 2. The C—H bond distances range from 0·94 to 1·04 Å with an average of 0·99 Å (with σ of sample of 0·02 Å). The O(17)—H(O17) bond length is 0·81 (3) Å.

The major conformational feature of the 5β-DHT molecule, in comparison to molecules of 5α-DHT and testosterone, is the 5β-configuration of the steroid backbone. A 5β-configuration produces a *cis* junction between rings *A* and *B*; 5α-DHT and testosterone have a 5α-configuration and a *trans* junction between rings *A* and *B*. The 5β-configuration and the *cis A*/*B* junction results in a strong bending of the steroid nucleus along the line through atoms C(6) and C(10). The bowing of the *A* ring relative to the remainder of the steroid, defined by the dihedral angle between the least-squares plane of atoms C(1) to C(5) and C(10), and the least-squares plane through atoms C(5) to C(17), is 68·8° in 5β-DHT. Similar bowing, by 65·1°, was observed in the structure of the closely related compound, 5β-androstane-3α,17β-diol (Weeks, Cooper, Norton, Hauptman & Fisher, 1971), and in several naturally occurring

* Lists of anisotropic thermal parameters for non-H atoms, coordinates, isotropic thermal parameters, bond distances and bond angles for the H atoms, and structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52925 (14 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

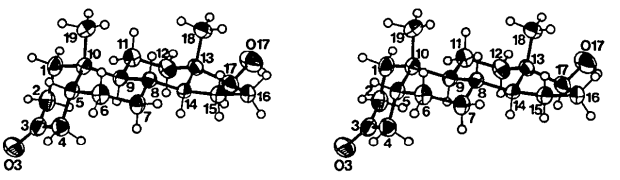


Fig. 1. Stereoview of the title molecule showing the labeling of the non-H atoms, with thermal ellipsoids drawn at the 50% probability level (*ORTEP*II, Johnson, 1976).

Table 1. *Fractional coordinates* ($\times 10^5$) *and* B_{eq} *values* ($Å^2 \times 10^2$) *for the non-H atoms (e.s.d.'s in parentheses)*

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

	x	y	z	B_{eq}
C(1)	37574 (16)	3627 (8)	11183 (34)	380 (8)
C(2)	46358 (19)	1451 (9)	−4417 (33)	424 (9)
C(3)	57381 (17)	−278 (8)	5646 (30)	374 (8)
C(4)	61528 (16)	4069 (8)	22145 (32)	372 (8)
C(5)	52376 (16)	6715 (7)	36618 (29)	309 (7)
C(6)	57438 (17)	11861 (8)	50317 (29)	361 (8)
C(7)	59595 (16)	17988 (8)	38770 (30)	342 (7)
C(8)	49030 (15)	20353 (7)	27536 (27)	270 (6)
C(9)	44346 (14)	15151 (7)	13224 (27)	269 (6)
C(10)	41591 (15)	9010 (7)	25281 (29)	299 (7)
C(11)	34471 (16)	17429 (8)	−295 (30)	359 (8)
C(12)	37168 (17)	23606 (9)	−11583 (32)	378 (8)
C(13)	40884 (15)	28703 (8)	3434 (28)	317 (7)
C(14)	51354 (15)	26295 (7)	15066 (28)	293 (7)
C(15)	56007 (17)	32219 (8)	25668 (35)	402 (9)
C(16)	53452 (19)	37519 (8)	10182 (42)	477 (10)
C(17)	45780 (19)	34662 (9)	−6535 (36)	439 (9)
C(18)	31094 (16)	30628 (9)	17693 (33)	394 (8)
C(19)	31950 (18)	10106 (9)	40936 (36)	433 (9)
O(3)	62726 (13)	−4948 (7)	712 (25)	542 (8)
O(17)	37112 (15)	38911 (7)	−13044 (29)	670 (9)

Table 2. *Bond lengths* (Å), *bond angles and endocyclic torsion angles* (°) *for the non-H atoms (e.s.d.'s in parentheses)*

C(1)—C(2)	1·524 (3)	C(2)—C(1)—C(10)	114·5 (2)
C(1)—C(10)	1·542 (3)	C(1)—C(2)—C(3)	111·6 (2)
C(2)—C(3)	1·501 (3)	C(2)—C(3)—C(4)	116·5 (2)
C(3)—C(4)	1·500 (3)	C(2)—C(3)—O(3)	122·0 (2)
C(3)—O(3)	1·218 (2)	C(4)—C(3)—O(3)	121·5 (2)
C(4)—C(5)	1·540 (3)	C(3)—C(4)—C(5)	115·9 (2)
C(5)—C(6)	1·533 (3)	C(4)—C(5)—C(6)	110·2 (1)
C(5)—C(10)	1·549 (3)	C(4)—C(5)—C(10)	113·3 (2)
C(6)—C(7)	1·524 (2)	C(6)—C(5)—C(10)	112·0 (1)
C(7)—C(8)	1·530 (3)	C(5)—C(6)—C(7)	112·6 (2)
C(8)—C(9)	1·548 (2)	C(6)—C(7)—C(8)	112·4 (1)
C(8)—C(14)	1·526 (2)	C(7)—C(8)—C(9)	110·2 (1)
C(9)—C(10)	1·557 (2)	C(7)—C(8)—C(14)	112·4 (1)
C(9)—C(11)	1·539 (3)	C(9)—C(8)—C(14)	109·3 (1)
C(10)—C(19)	1·546 (3)	C(8)—C(9)—C(10)	111·4 (1)
C(11)—C(12)	1·537 (3)	C(8)—C(9)—C(11)	113·1 (1)
C(12)—C(13)	1·524 (3)	C(10)—C(9)—C(11)	113·3 (1)
C(13)—C(14)	1·536 (3)	C(1)—C(10)—C(5)	107·7 (1)
C(13)—C(17)	1·535 (3)	C(1)—C(10)—C(9)	112·5 (2)
C(13)—C(18)	1·538 (3)	C(1)—C(10)—C(19)	106·3 (1)
C(14)—C(15)	1·536 (2)	C(5)—C(10)—C(9)	109·5 (1)
C(15)—C(16)	1·542 (3)	C(5)—C(10)—C(19)	109·5 (2)
C(16)—C(17)	1·542 (3)	C(9)—C(10)—C(19)	111·2 (1)
C(17)—O(17)	1·427 (3)	C(9)—C(11)—C(12)	112·8 (1)
		C(11)—C(12)—C(13)	110·8 (2)
		C(12)—C(13)—C(14)	108·2 (1)
		C(12)—C(13)—C(17)	114·8 (2)
		C(12)—C(13)—C(18)	111·3 (2)
		C(14)—C(13)—C(17)	100·5 (1)
		C(14)—C(13)—C(18)	113·0 (2)
		C(17)—C(13)—C(18)	108·7 (1)
		C(8)—C(14)—C(13)	113·2 (1)
		C(8)—C(14)—C(15)	120·0 (2)
		C(13)—C(14)—C(15)	103·7 (1)
		C(14)—C(15)—C(16)	103·4 (2)
		C(15)—C(16)—C(17)	107·0 (1)
		C(13)—C(17)—C(16)	104·1 (2)
		C(13)—C(17)—O(17)	112·2 (2)
		C(16)—C(17)—O(17)	112·5 (2)
C(10)—C(1)—C(2)—C(3)	53·8 (2)	C(14)—C(8)—C(9)—C(11)	−49·8 (2)
C(1)—C(2)—C(3)—C(4)	−42·9 (2)	C(8)—C(9)—C(11)—C(12)	50·1 (2)
C(2)—C(3)—C(4)—C(5)	39·5 (2)	C(9)—C(11)—C(12)—C(13)	−54·4 (2)
C(3)—C(4)—C(5)—C(10)	−44·4 (2)	C(11)—C(12)—C(13)—C(14)	58·3 (2)
C(4)—C(5)—C(10)—C(1)	51·7 (2)	C(12)—C(13)—C(14)—C(8)	−61·4 (2)
C(5)—C(10)—C(1)—C(2)	−58·0 (2)	C(13)—C(14)—C(8)—C(9)	56·5 (2)
C(10)—C(5)—C(6)—C(7)	−53·3 (2)	C(17)—C(13)—C(14)—C(15)	46·3 (2)
C(5)—C(6)—C(7)—C(8)	53·4 (2)	C(13)—C(14)—C(15)—C(16)	−34·5 (2)
C(6)—C(7)—C(8)—C(9)	−54·7 (2)	C(14)—C(15)—C(16)—C(17)	9·4 (2)
C(7)—C(8)—C(9)—C(10)	57·1 (2)	C(15)—C(16)—C(17)—C(13)	19·0 (2)
C(8)—C(9)—C(10)—C(5)	−56·9 (2)	C(16)—C(17)—C(13)—C(14)	−39·6 (2)
C(9)—C(10)—C(5)—C(6)	54·5 (2)		

steroids with a 5β- configuration: cholanic acids isolated from bile acids (*e.g.* 3α,6α-dihydroxy-5β-cholan-24-oic acid; Hall, Maslen & Cooper, 1974), 5β-cholestane alcohols isolated from bile alcohols [*e.g.* 3β,16β,23(*R*),26-tetrahydroxy-5β-cholestane; Einck & Pettit, 1980], cardenolides isolated from digitalis (*e.g.* digitoxigenin; Karle & Karle, 1969), and bufadienolides (*e.g.* bufalin; Rohrer, Fullerton, Kitatsuji, Nambara & Yoshii, 1982). Such a bowing of the *A* ring causes atom O(3) to be far from the average molecular plane through the rings *B*, *C* and *D*. In 5β-DHT, O(3) is 3·262 Å from the plane of the *B*, *C* and *D* rings. In 5β-androstane-3α,17β-diol this distance is even larger, 3·66 Å, because atom O(3) is not a carbonyl but a hydroxyl O atom and is α-oriented.

Importantly, because of the bowed structure, the separation between the terminal O atoms in 5β-DHT is only 9·824 (2) Å. A similar shortened distance of 9·58 Å is found in 5β-androstane-3α,17β-diol. In contrast, in the 5α-DHT and testosterone structures the bowing of the *A* ring is between 6·5 and 23·4° (Duax & Norton, 1975) which displaces atom O(3) from the *B–C–D* plane by 1·44 to 1·96 Å and produces a separation between O(3)···O(17) of 10·66–10·94 Å. It seems to be clear, therefore, that the larger overall bending of the 5β-DHT molecule (by about 45°) and the significantly shorter O(3)··· O(17) separation (by about 1 Å) are the reasons that 5β-DHT has lower affinity for the dexamethasone binding sites than has either 5α-DHT or testosterone (Howell & Lefebvre, 1989; Howell, Po & Lefebvre, 1989). Our correlation between terminal O-atom separation and affinity predicts that affinity of 5β-androstane-3α,17β-diol would also be low; measurement of the affinity is under investigation.

Fig. 2 compares the steroid backbone conformations and the positions of atom O(3) for 5β-DHT (thin line) and for all examples of 5α-DHT and testosterone (thick lines). The superposition shown was obtained by a least-squares fit (*PROFIT*; Smith, 1983) of atoms C(5) to C(18) in all three structures. After the least-squares fit, the average separation

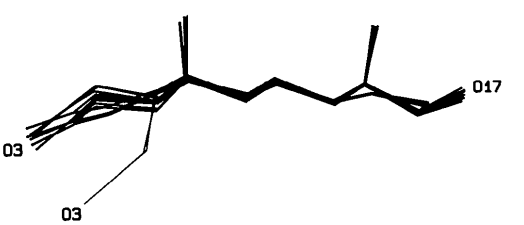


Fig. 2. Least-squares fit of 5β-DHT (thin line) with molecules of 5α-DHT (Courseille *et al.*, 1973; Busetta, Courseille, Fornies-Marquina & Hospital, 1972) and testosterone (Roberts *et al.*, 1973; Busetta, Courseille, Leroy & Hospital, 1972; Precigoux *et al.*, 1973) drawn with thick lines.

between matched atoms was less than 0·096 Å. The minimum distance between O(3) atoms of 5β-DHT and the other molecules is 1·866 Å (maximum 2·446 Å).

The bond lengths and angles in 5β-DHT are all close to the expected values. In the *A* ring, the lengths of the bonds C(2)—C(3) and C(3)—C(4) are in good agreement with the value of 1·505 Å predicted for an sp^3–sp^2 C—C bond (Bartell & Bonham, 1960). A similar shortening of the C(2)—C(3) and C(3)—C(4) bonds was observed in the structure of 7α-methyldihydrotestosterone acetate (MeDHT hereafter; Hazel, Rohrer, Duax & Wolff, 1976) and in the structures of 5α-DHT. Also, the C(2)—C(3)—C(4) angle is enlarged to 116·2 (2)° in 5β-DHT and to 115·1° in MeDHT. The C(2)—C(3) and C(3)—C(4) bonds in the saturated, unsubstituted *A* ring of androstan-17-one (Banerjee, Das & Saenger, 1978) are 1·523 (5) and 1·542 (6) Å and the angle C(2)—C(3)—C(4) is 109·9 (3)°; thus the effect of the 3-carbonyl substituent on the geometry of ring *A* is clear. Junctions between rings *B* and *C*, as well as between *C* and *D*, are *trans* in all these structures.

In 5β-DHT, the angle C(3)—C(4)—C(5) is 115·9 (2)° which is significantly larger than the corresponding angle found in 5α-DHT, MeDHT and androstan-17-one, which vary from 108 to 112°. This larger angle is correlated to the 3-oxo-5β-configuration of 5β-DHT; the other 3-oxo-5β-steroid, 17β-acetoxy-5-methyl-5β-estran-3-one (Boeyens, Bull & van Rooyen, 1980), shows a similar effect: the C(3)—C(4)—C(5) angle is 115·4 (8)°. In both compounds, this effect is accompanied by an extensive flattening of the *A* ring which is expressed by diminished torsion angles along the bonds C(2)—C(3), C(3)—C(4) and C(4)—C(5). These angles are −42·9 (2), 39·5 (2) and −44·4 (2)° in 5β-DHT and are −47·6 (13), 46·2 (12) and −49·0 (11)° in 5β-estran-3-one. This flattening may be due to the close approach of the H atoms on C(4), C(7), C(2) and C(9).

Nevertheless, the overall shape of the *A* ring is still approximately the chair conformation typical for totally saturated *A* rings. Distortions from that ideal form can be expressed by the loss of mirror symmetry through atoms C(2) and C(5) [$\Delta C_s(2) = 13{\cdot}1$; definition of asymmetry parameters from Duax & Norton (1975)] with a retention of perpendicular rotational symmetry [$\Delta C_s(1,10) = 1{\cdot}8$]. Ring *B* has a highly symmetrical chair conformation with all asymmetry parameters below 3·7. Ring *C*, because of strain at the junction with the five-membered *D* ring [C(2)—C(13)—C(14)—C(8) torsion angle over 60°], has a distorted chair form [$\Delta C_s(9) = 2{\cdot}2$, $\Delta C_2(8,14) = 10{\cdot}0$]. Chair conformations of rings *B* and *C* were observed for all 5α-DHT and testosterone molecules, as can be seen in Fig. 2.

The conformation of the *D* ring in 5β-DHT is intermediate between 13β,14α-half chair [$\Delta C_2(13,14) = 7{\cdot}7$] and 13$\beta$-envelope [$\Delta C_s(13) = 11{\cdot}9$] with pseudorotation parameters (Altona, Geise & Romers, 1968) $\Delta = 11{\cdot}8$ and $\varphi_m = 46{\cdot}5$. The deviation from the half-chair conformation is evident from the unequal distances of C(13) and C(14) from the plane through C(15), C(16) and C(17); C(13) is 0·485 Å over this plane (on the β-side of steriod) and C(14) is 0·245 Å below this plane. This conformation of the *D* ring is within the range of observed conformations for this relatively flexible ring; the range for *D* rings consisting of five sp^3 C atoms is between 13β-envelope and 13β,14α-half chair (*i.e.* with positive pseudoparameter Δ).

In the crystal, molecules of 5β-DHT are linked head-to-tail by hydrogen bonds between the hydroxyl and carbonyl O atoms. The geometry of the hydrogen bond is O(17)···O(3) = 2·784 (2), H(O17)···O(3) = 2·02 (3) Å and ∠[O(17)—H···O(3)] = 156 (3)°. Chains of hydrogen-bonded molecules are parallel to the *b* axis, about the twofold screw axis at $\frac{1}{2}$, *y*, $-\frac{1}{4}$. The adjacent chains are packed with van der Waals contacts.

In summary, the bowed structure of the 5β-skeleton and concomitant short distance between the O atoms appears to be the reason for the low affinity of 5β-DHT for the sites on nuclear envelopes and plasma membranes. Thus, the crystal structure of 5β-DHT supports our hypothesis (Roszak *et al.*, 1990) regarding the correlation between the binding affinity for dexamethasone sites and the separation of terminal O atoms on the steroids.

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References

ALTONA, C., GEISE, H. J. & ROMERS, C. (1968). *Tetrahedron*, **24**, 13–32.

BANERJEE, A., DAS, B. N. & SAENGER, W. (1978). *Acta Cryst.* B**34**, 1141–1144.

BARTELL, L. S. & BONHAM, R. A. J. (1960). *J. Chem. Phys.* **32**, 824–826.

BOEYENS, J. C. A., BULL, J. R. & VAN ROOYEN, P. H. (1980). *S. Afr. J. Chem.* **33**, 45–50.

BUSETTA, B., COURSEILLE, C., FORNIES-MARQUINA, J. M. & HOSPITAL, M. (1972). *Cryst. Struct. Commun.* **1**, 43–46.

BUSETTA, B., COURSEILLE, C., LEROY, F. & HOSPITAL, M. (1972). *Acta Cryst.* B**28**, 3293–3299.

COURSEILLE, C., PRECIGOUX, G., LEROY, F. & BUSETTA, B. (1973). *Cryst. Struct. Commun.* **2**, 441–446.
CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.
DEMPSEY, S. (1986). *MMS. The UCSD Molecular Modeling System*. Version 1.3. Univ. of California, San Diego, La Jolla, USA.
DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steriod Structure*, Vol. 1. New York: Plenum.
EINCK, J. J. & PETTIT, G. R. (1980). *Acta Cryst.* B**36**, 1398–1402.
HALL, S. R., MASLEN, E. N. & COOPER, A. (1974). *Acta Cryst.* B**30**, 1441–1447.
HAZEL, J. P., ROHRER, D. C., DUAX, W. L. & WOLFF, M. E. (1976). *Cryst. Struct. Commun.* **5**, 121–124.
HOWELL, G. M. & LEFEBVRE, Y. A. (1989). *J. Steroid Biochem.* **33**, 997–986.
HOWELL, G. M., PO, C. & LEFEBVRE, Y. A. (1989). *Biochem. J.* **260**, 435–441.
JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
KARLE, I. L. & KARLE, J. (1969). *Acta Cryst.* B**25**, 434–442.
LARSON, A. C. (1967). *Acta Cryst.* **23**, 664–665.
PRECIGOUX, G., HOSPITAL, M. & VAN DEN BOSCHE, G. (1973). *Cryst. Struct. Commun.* **2**, 435–439.
ROBERTS, P. J., PETTERSEN, R. C., SHELDRICK, G. M., ISAACS, N. W. & KENNARD, O. (1973). *J. Chem. Soc. Perkin Trans.* 2, 1978–1984.
ROHRER, D. C., FULLERTON, D. S., KITATSUJI, E., NAMBARA, T. & YOSHII, E. (1982). *Acta Cryst.* B**38**, 1865–1868.
ROSZAK, A. W., CODDING, P. W. & LEFEBVRE, Y. A. (1990). *J. Steriod Biochem. Mol. Biol.* **37**. In the press.
SHELDRICK, G. M. (1985). *SHELXS*86. In *Crystallographic Computing* 3, edited by G. M. SHELDRICK, C. KRÜGER & R. GODDARD, pp. 175–189. Oxford Univ. Press.
SMITH, G. D. (1983). *PROFIT*. A molecular fitting program. Medical Foundation of Buffalo, Buffalo, New York, USA.
STEWART, J. M. (1976). The *XRAY*76 system. Computer Science Center, Univ. of Maryland, College Park, Maryland, USA.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
WEEKS, C. M., COOPER, A., NORTON, D. A., HAUPTMAN, H. & FISHER, J. (1971). *Acta Cryst.* B**27**, 1562–1572.

Acta Cryst. (1990). C**46**, 1704–1707

Structure of Delvestine: a Norditerpenoid Alkaloid from *Delphinium vestitum* Wall

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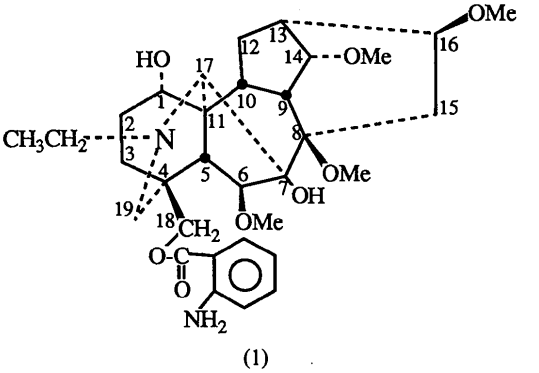
Abstract. $C_{32}H_{46}N_2O_8$, $M_r = 586{\cdot}73$, m.p. 458–460 K, monoclinic, $P2_1$, $a = 9{\cdot}187$ (2), $b = 14{\cdot}979$ (3), $c = 11{\cdot}474$ (2) Å, $\beta = 104{\cdot}09$ (2)°, $V = 1531{\cdot}5$ (9) Å^3, $Z = 2$, $D_x = 1{\cdot}27$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 7{\cdot}1$ cm^{-1}, $F(000) = 632$, room temperature, $R = 0{\cdot}039$, $wR = 0{\cdot}053$ for 3077 observed reflections [$I > 3\sigma(I)$]. The aminoethyl C(21) atom is disordered. There is an intramolecular hydrogen bond between O(1)—H(O1) and N(1) atoms, and between O(3)—H(O3) and O(4), stabilizing the boat conformations adopted by the rings *A* and *D*.

Introduction. The polyoxygenated norditerpenoid alkaloids of *Aconitum* and *Delphinium* species have been recognized since antiquity as poisonous towards animals and as possessing medicinal properties (Benn & Jacyno, 1983). In an earlier investigation, we have reported the isolation and structure determination of delvestine (1) from *Delphinium vestitum* Wall (Desai, Joshi & Pelletier, 1985). We report here the X-ray crystallographic studies of delvestine to confirm the structure and stereochemistry of this norditerpenoid alkaloid as 4-{[(2-aminobenzoyl)oxy]methyl}-20-ethyl-6β,8,16β-tetramethoxyaconitane-1α,7-diol.



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