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17β-Hydroxy-4,14-androstadien-3-one*

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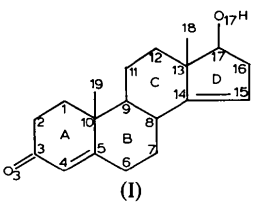
Abstract. $C_{19}H_{26}O_2$, $M_r = 286{\cdot}4$, monoclinic, $P2_1$, $a = 11{\cdot}817$ (2), $b = 6{\cdot}1492$ (5), $c = 11{\cdot}0639$ (5) Å, $\beta = 93{\cdot}739$ (5)° ($\lambda = 1{\cdot}5418$ Å, $t = 18$ °C), $V = 802{\cdot}2$ Å^3, $Z = 2$, $\rho_x = 1{\cdot}186$ g cm^{-3}. The conformation of ring *A* is a 1α-sofa and that of ring *D* is a 17α-envelope.

Introduction. The title molecule (I), whose trivial name is 14-dehydrotestosterone, is one of a series of steroid molecules investigated to evaluate conformational transmission effects and the dependence of function upon steroid conformation. It was synthesized in the hope that the resulting deformation of the *D* ring would enhance the androgenic potency. However, it was found that like 19-nortestosterone (Segaloff, 1963), 14-dehydrotestosterone has a decreased androgenic potency as compared with the natural steroid hormone testosterone when administered systematically (Segaloff & Gabbard, 1963), but both compounds have increased androgenic potency when assayed by topical application to the chick comb.



(I)

Crystallographic data were measured on a specimen crystal of dimensions 0·72 × 0·36 × 0·18 mm on an Enraf–Nonius CAD-4 automatic diffractometer using Ni-filtered Cu $K\alpha$ radiation. The condition $k = 2n$ limiting the $0k0$ reflections determined the space group to be $P2_1$. The lattice parameters were refined by a least-squares fit to measured 2θ values for 46 reflections in the interval $44° < 2\theta < 80°$. Integrated relative intensities for 1805 independent reflections accessible with $2\theta < 150°$ were measured as ω–2θ scans; 1650 of these reflections were measured to be observed above background ($I > 2\sigma_I$).

The intensities were reduced to structure factor amplitudes, and phase angles sufficient for location of the nonhydrogen atoms were derived using the direct-methods program *MULTAN* (Germain, Main & Woolfson, 1971) in conjunction with the negative-quartet figure of merit (De Titta, Edmonds, Langs & Hauptman, 1975). The H atoms were located on a difference electron density map prepared at an intermediate stage of least-squares refinement of structural parameters. In the final cycles of full-matrix least-squares refinement, positional parameters for all the atoms, anisotropic thermal vibration parameters for the nonhydrogen atoms and isotropic thermal vibration parameters for the H atoms were varied. The quantities $(1/\sigma_F^2)$, where σ_F was as defined by Stout & Jensen (1968, p. 457, equation *H*14) but with an instrumental instability factor of 0·06, were used to weight the least-squares differences for the observed data; differences for data determined to be unobserved were given zero weight. The final values of the residual ($R = \sum||F_o| - |F_c||/\sum|F_o|$) were 0·046 for the observed data and 0·051 for all the measured data. Final positional parameters are listed in Table 1.‡

Discussion. The crystallographically observed structure of the molecule is shown in Fig. 1. Fig. 2 shows the intramolecular dimensions involving the nonhydrogen atoms; the largest estimated standard deviation for the bond lengths is 0·004 Å, for the bond angles 0·2°, and for the torsion angles 0·4°. The molecule's 25 C—H bond distances range from 0·88 to 1·10 Å and average 1·01 Å. The O—H bond distance is 0·88 Å. All the bond lengths and angles in this structure are very similar to those observed in testosterone structures except the C(14)—C(15) bond which is shorter due to its double-bond character. The hydrogen-bond distance

* Conformational Analysis of Synthetic Androgens. I.

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‡ Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33606 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atomic coordinates of 17β-hydroxy-4,14-androstadien-3-one*

The *y* coordinate of C(5) was held fixed.

	x	*y*	*z*
C(1)	0·8789 (2)	0·4953 (4)	0·6658 (2)
C(2)	0·8721 (2)	0·4302 (5)	0·5318 (2)
C(3)	0·7581 (2)	0·3514 (4)	0·4896 (2)
C(4)	0·6630 (2)	0·4403 (5)	0·5499 (2)
C(5)	0·6727 (2)	0·5835	0·6412 (2)
C(6)	0·5690 (2)	0·6860 (5)	0·6889 (2)
C(7)	0·5690 (2)	0·6649 (5)	0·8259 (2)
C(8)	0·6759 (1)	0·7687 (3)	0·8856 (2)
C(9)	0·7835 (1)	0·6656 (3)	0·8389 (1)
C(10)	0·7868 (2)	0·6579 (3)	0·6976 (1)
C(11)	0·8886 (2)	0·7790 (4)	0·9008 (2)
C(12)	0·8941 (2)	0·7480 (4)	1·0376 (2)
C(13)	0·7877 (2)	0·8330 (4)	1·0939 (2)
C(14)	0·6812 (1)	0·7552 (3)	1·0219 (2)
C(15)	0·6044 (2)	0·6838 (5)	1·0930 (2)
C(16)	0·6443 (2)	0·7028 (6)	1·2255 (2)
C(17)	0·7722 (2)	0·7248 (4)	1·2195 (2)
C(18)	0·7867 (2)	1·0827 (4)	1·1023 (2)
C(19)	0·8108 (2)	0·8836 (4)	0·6451 (2)
O(3)	0·7420 (2)	0·2258 (4)	0·4040 (1)
O(17)	0·8295 (2)	0·8255 (4)	1·3193 (1)
H(1*B*)	0·955 (2)	0·545 (5)	0·687 (2)
H(1*A*)	0·869 (3)	0·351 (9)	0·719 (3)
H(2*A*)	0·929 (2)	0·310 (7)	0·522 (2)
H(2*B*)	0·890 (2)	0·556 (8)	0·483 (3)
H(4)	0·592 (2)	0·408 (6)	0·518 (2)
H(6*A*)	0·503 (2)	0·623 (7)	0·644 (2)
H(6*B*)	0·569 (2)	0·839 (7)	0·660 (2)
H(7*A*)	0·571 (2)	0·498 (6)	0·848 (2)
H(7*B*)	0·496 (2)	0·746 (5)	0·855 (2)
H(8*B*)	0·673 (2)	0·915 (5)	0·859 (2)
H(9*A*)	0·786 (2)	0·504 (5)	0·866 (2)
H(11*B*)	0·880 (2)	0·942 (6)	0·878 (2)
H(11*A*)	0·960 (2)	0·725 (5)	0·873 (2)
H(12*B*)	0·964 (2)	0·806 (6)	1·072 (2)
H(12*A*)	0·893 (2)	0·575 (6)	1·056 (2)
H(15)	0·521 (2)	0·634 (8)	1·065 (3)
H(16*A*)	0·627 (3)	0·590 (11)	1·270 (3)
H(16*B*)	0·613 (3)	0·846 (9)	1·274 (3)
H(17*A*)	0·808 (2)	0·566 (7)	1·212 (2)
H(18*A*)	0·783 (3)	1·164 (8)	1·021 (3)
H(18*B*)	0·709 (2)	1·143 (5)	1·135 (2)
H(18*C*)	0·854 (2)	1·141 (6)	1·143 (2)
H(19*A*)	0·799 (3)	0·874 (8)	0·555 (3)
H(19*B*)	0·756 (2)	0·987 (7)	0·675 (2)
H(19*C*)	0·889 (2)	0·948 (6)	0·680 (2)
H(O17)	0·806 (2)	0·954 (7)	1·342 (2)

and other nonbonded contact distances less than 3·5 Å are listed in Table 2. The 17β-hydroxy group forms a hydrogen bond to O(3) of a translationally located molecule forming a linear chain of hydrogen-bonded molecules.

The conformation of the Δ^4-3-one *A* ring is a slightly distorted 1α-sofa very similar to the conformation of one of the two molecules in the structure of anhydrous testosterone (Roberts, Pettersen, Sheldrick, Isaacs & Kennard, 1973), as indicated by the ΔC_s(C1) and ΔC_2(C1–C2) asymmetry parameters (Duax, Weeks & Rohrer, 1976) of 7·9 and 17·1 compared with 7·9 and 18·2 respectively. The *D*-ring conformation of the 14-dehydrotestosterone molecule is a 17α-envelope. This conformation is a direct result of the C(14)–C(15) double bond and is characteristic of this type of

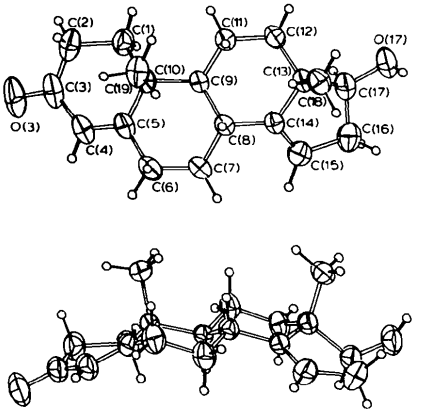

Fig. 1. *ORTEP* (Johnson, 1965) drawings of 14-dehydrotestosterone. Thermal ellipsoids for nonhydrogen atoms are scaled to 60% probability and H atoms are represented as spheres equivalent to $B = 1$ Å^2.

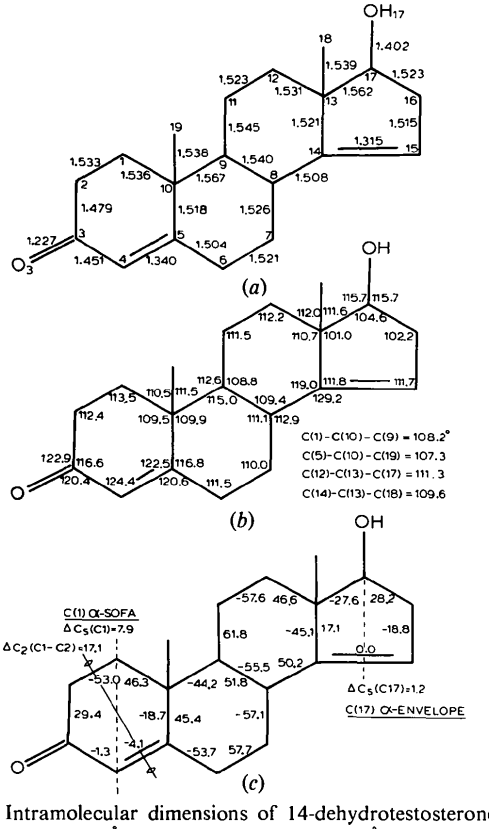

Fig. 2. Intramolecular dimensions of 14-dehydrotestosterone. (*a*) Bond distances (Å); σ range = 0·002–0·004 Å. (*b*) Bond angles (°); σ range = 0·1–0·2°. (*c*) Endocyclic torsion angles (°). A torsion angle α–β–γ–δ is positive if, when viewed down the β–γ bond, the α–β bond will eclipse the γ–δ bond when rotated less than 180° in a clockwise direction.

Table 2. *Hydrogen-bond and nonbonded intermolecular contact distances* <3·5 Å

		Symmetry operator
O(17)—H···O(3)	2·852 Å	$x, -1+y, -1+z$
C(2)···O(17)	3·396	$x, y, -1+z$
C(3)···C(19)	3·389	$x, -1+y, z$
C(19)···O(3)	3·453	$x, 1+y, z$

unsaturated *D* ring even though this would not have been predicted from Dreiding models. The *D*-ring conformation in testosterone varies from a distorted 13α-envelope to a distorted 13α,14β-half chair.

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17β-Hydroxy-4,14-estradien-3-one*

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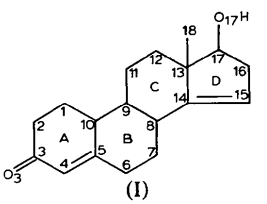
Abstract. $C_{18}H_{24}O_2$, $M_r = 272{\cdot}4$, orthorhombic, $P2_12_12_1$, $a = 9{\cdot}7757\,(4)$, $b = 25{\cdot}519\,(1)$, $c = 6{\cdot}1158\,(4)$ Å ($\lambda = 1{\cdot}5418$ Å, $t = 18$°C), $V = 1525{\cdot}7$ Å^3, $Z = 4$, $\rho_x = 1{\cdot}186$ g cm^{-3}. The conformation of ring *A* is a 1α,2β-half chair and that of ring *D* is a 17α-envelope.

Introduction. Part I of the present series described the conformation of 14-dehydrotestosterone (Rohrer, Strong, Duax & Segaloff, 1978). The title molecule (I), whose trivial name is 14-dehydro-19-nortestosterone, is the second in this series of androgenic steroids which was investigated to evaluate conformational transmission effects and the dependence of function upon steroid conformation. This compound has been shown (Segaloff & Gabbard, 1973) to be a very potent androgen whose activity relative to the natural steroid hormone, testosterone, is enhanced by removal of the 19-methyl group and by introduction of the C(14)—C(15) double bond. The title molecule may well be the intracellular one since it binds more tightly to the cytoplasmic androgenic receptor (Shain & Boesel, 1975) and is the most effective androgen in stimulating growth of prostate in tissue culture (Robel, 1974).



(I)

Crystallographic diffraction data were measured on a specimen crystal of dimensions 0·04 × 0·40 × 0·62 mm on an Enraf–Nonius CAD-4 automated diffractometer using Ni-filtered Cu *Kα* radiation. The conditions $h = 2n$, $k = 2n$, and $l = 2n$ limiting, respectively, the *h*00, 0*k*0, and 00*l* reflections determined the space group to be $P2_12_12_1$. Lattice parameters were refined

* Conformational Analysis of Synthetic Androgens. II.

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