

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 13 α -envelope to a distorted 13 α ,14 β -half chair.

This work was supported in part by Grant No. CA-10906 from the National Cancer Institute, DHEW, and in part by a group from Pensacola, Florida, who have been patients of the Ochsner Medical Institutions.

Acta Cryst. (1978). **B34**, 2915–2917

17 β -Hydroxy-4,14-estradien-3-one*

BY DOUGLAS C. ROHRER† AND WILLIAM L. DUAX

Medical Foundation of Buffalo, Inc., 73 High Street, Buffalo, New York 14203, USA

AND ALBERT SEGALOFF

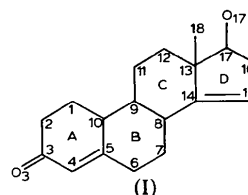
Alton Ochsner Medical Foundation, New Orleans, Louisiana 70121, USA

(Received 17 January 1978; accepted 9 May 1978)

Abstract. C₁₈H₂₄O₂, *M_r* = 272.4, orthorhombic, *P*2₁2₁, *a* = 9.7757 (4), *b* = 25.519 (1), *c* = 6.1158 (4) Å (λ = 1.5418 Å, *t* = 18°C), *V* = 1525.7 Å³, *Z* = 4, ρ_x = 1.186 g cm⁻³. The conformation of ring *A* is a 1 α ,2 β -half chair and that of ring *D* is a 17 α -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).



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 *K* α radiation. The conditions *h* = 2*n*, *k* = 2*n*, and *l* = 2*n* limiting, respectively, the *h*00, 0*k*0, and 00*l* reflections determined the space group to be *P*2₁2₁. Lattice parameters were refined

* Conformational Analysis of Synthetic Androgens. II.

† To whom correspondence should be addressed.

References

- DE TITTA, G. T., EDMONDS, J. W., LANGS, D. A. & HAUPTMAN, H. (1975). *Acta Cryst.* **A31**, 472–479.
- DUAX, W. L., WEEKS, C. M. & ROHRER, D. C. (1976). *Topics in Stereochemistry*, Vol. 9, edited by E. L. ELIEL & N. ALLINGER, pp. 271–383. New York: John Wiley.
- GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* **A27**, 368–376.
- JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
- ROBERTS, P. J., PETTERSEN, R. C., SHELDRIK, G. M., ISAACS, N. W. & KENNARD, O. (1973). *J. Chem. Soc. Perkin Trans. 2*, pp. 1978–1984.
- SEGALOFF, A. (1963). *Steroids*, **1**, 299–315.
- SEGALOFF, A. & GABBARD, R. B. (1963). *Steroids*, **1**, 77–89.
- STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination*. New York: Macmillan.

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

	x	y	z
C(1)	0.6289 (6)	0.7920 (2)	0.3146 (13)
C(2)	0.4890 (6)	0.7834 (2)	0.4023 (11)
C(3)	0.4571 (5)	0.8210 (2)	0.5814 (9)
C(4)	0.5049 (4)	0.8751 (1)	0.5490 (8)
C(5)	0.5879 (4)	0.8888 (1)	0.3890 (6)
C(6)	0.6200 (4)	0.9453 (2)	0.3434 (8)
C(7)	0.7741 (4)	0.9549 (1)	0.3449 (7)
C(8)	0.8468 (4)	0.9178 (1)	0.1832 (6)
C(9)	0.8137 (4)	0.8597 (1)	0.2328 (7)
C(10)	0.6567 (4)	0.8495 (2)	0.2396 (7)
C(11)	0.8865 (4)	0.8250 (1)	0.0660 (8)
C(12)	1.0425 (4)	0.8312 (1)	0.0854 (7)
C(13)	1.0880 (4)	0.8884 (1)	0.0497 (6)
C(14)	1.0002 (4)	0.9249 (1)	0.1839 (6)
C(15)	1.0753 (4)	0.9601 (1)	0.2898 (6)
C(16)	1.2265 (4)	0.9531 (2)	0.2486 (7)
C(17)	1.2334 (4)	0.8981 (2)	0.1486 (7)
C(18)	1.0821 (5)	0.9034 (2)	-0.1925 (7)
O(3)	0.3842 (5)	0.8081 (1)	0.7333 (7)
O(17)	1.3451 (3)	0.8962 (1)	0.0025 (5)
H(1A)	0.703 (5)	0.782 (2)	0.429 (10)
H(1B)	0.639 (7)	0.768 (3)	0.167 (14)
H(2B)	0.412 (6)	0.786 (2)	0.278 (9)
H(2A)	0.485 (5)	0.744 (2)	0.471 (12)
H(4)	0.451 (4)	0.905 (1)	0.629 (6)
H(6B)	0.571 (4)	0.960 (1)	0.189 (7)
H(6A)	0.581 (4)	0.970 (1)	0.470 (7)
H(7B)	0.802 (4)	0.993 (1)	0.299 (7)
H(7A)	0.798 (4)	0.943 (2)	0.494 (7)
H(8B)	0.810 (3)	0.927 (1)	0.022 (6)
H(9A)	0.849 (3)	0.851 (1)	0.384 (6)
H(10B)	0.617 (4)	0.859 (1)	0.102 (6)
H(11A)	0.858 (4)	0.793 (2)	0.089 (7)
H(11B)	0.856 (5)	0.836 (2)	-0.096 (9)
H(12A)	1.071 (4)	0.817 (1)	0.241 (6)
H(12B)	1.091 (5)	0.805 (2)	-0.031 (9)
H(15)	1.026 (5)	0.986 (2)	0.356 (8)
H(16B)	1.265 (5)	0.984 (2)	0.164 (7)
H(16A)	1.290 (7)	0.967 (2)	0.363 (15)
H(17A)	1.249 (4)	0.870 (1)	0.272 (5)
H(18C)	1.157 (5)	0.879 (2)	-0.269 (8)
H(18B)	1.096 (6)	0.944 (2)	-0.212 (9)
H(18A)	0.980 (5)	0.891 (2)	-0.253 (8)
H(O17)	1.340 (5)	0.865 (2)	-0.059 (8)

by a least-squares fit to measured 2θ values for 38 reflections in the interval $41^\circ < 2\theta < 79^\circ$. Integrated relative intensities for 1838 independent reflections accessible with $2\theta < 150^\circ$ were measured as ω - 2θ scans; 1252 of these reflections were measured to be observed above background ($I > 2\sigma_I$).

The structure solution and refinement to R values of 0.065 for the observed data and 0.107 for all data was the same as that described in the previous paper. Table 1 contains the positional parameters.*

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33607 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

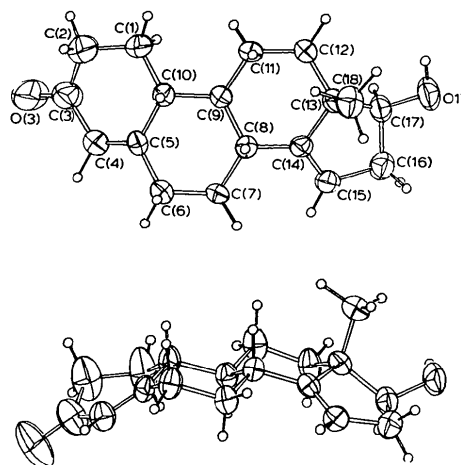


Fig. 1. ORTEP (Johnson, 1965) drawings of 14-dehydro-19-nortestosterone. Thermal ellipsoids for nonhydrogen atoms are scaled to 60% probability and the H atoms are represented as spheres equivalent to $B = 1 \text{ \AA}^2$.

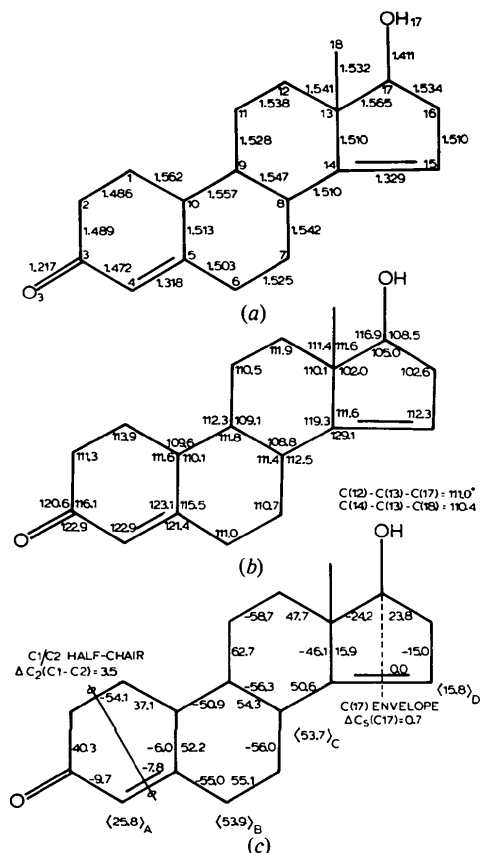


Fig. 2. Intramolecular dimensions of 14-dehydro-19-nortestosterone. (a) Bond distances (Å). (b) Bond angles (°). (c) Endocyclic torsion angles (°). Values in angle brackets are the average ring dihedral angles (°). A torsion angle α - β - γ - δ is positive if, when viewed down the β - γ bond, the α - β bond will eclipse the γ - δ bond when rotated less than 180° in a clockwise direction.

Table 2. *Hydrogen-bond and nonbonded intermolecular distances (<3.5 Å between nonhydrogen atoms, <2.8 Å between a nonhydrogen atom and a hydrogen atom, and <2.4 Å between hydrogen atoms)*

Donor <i>D</i>	Acceptor <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> -H	H... <i>A</i>	$\angle D-H...A$	Symmetry operator for second atom
O(17)	O(3)	2.812 Å	0.89 Å	1.97 Å	157.5°	-1 + <i>x</i> , <i>y</i> , 1 + <i>z</i>
C(3)	O(17)	3.393				-1 + <i>x</i> , <i>y</i> , 1 + <i>z</i>
C(4)	O(17)	3.228				-1 + <i>x</i> , <i>y</i> , 1 + <i>z</i>
C(5)	O(17)	3.355				-1 + <i>x</i> , <i>y</i> , <i>z</i>
C(15)	C(18)	3.482				<i>x</i> , <i>y</i> , 1 + <i>z</i>
C(3)	H(O17)	2.72				-1 + <i>x</i> , <i>y</i> , 1 + <i>z</i>
O(17)	H(4)	2.52				1 + <i>x</i> , <i>y</i> , -1 + <i>z</i>
H(1 <i>B</i>)	H(12 <i>B</i>)	2.11				$-\frac{1}{2} + x$, $\frac{3}{2} - y$, - <i>z</i>
H(16 <i>B</i>)	H(16 <i>A</i>)	2.28				$\frac{3}{2} - x$, 2 - <i>y</i> , $-\frac{1}{2} + z$

Discussion. The conformation of the molecule observed in the crystalline state is illustrated in Fig. 1, and Fig. 2 shows the atom numbering and the intramolecular dimensions involving the nonhydrogen atoms. In Fig. 2, estimated standard deviations range from 0.005 to 0.008 Å for the bond distances, from 0.3 to 0.4° for the bond angles, and from 0.3 to 0.7° for the torsion angles. The 23 C-H bond distances in the molecule range from 0.87 to 1.12 Å with estimated standard deviations that range from 0.03 to 0.08 Å; the average of the C-H bond distances is 1.04 ± 0.06 Å. In the 17 β -hydroxy group the O-H bond distance is 0.89 (5) Å and the C(17)-O-H bond angle is 104 (2)°. The shortness of the C(14)-C(15), O(3)-C(3), and C(4)-C(5) bonds reflects their double-bond character, and, the latter two bonds being conjugate to one another, the intervening C(3)-C(4) bond is somewhat shorter than the other C-C single bonds in the molecule. The C(1)-C(2) and C(2)-C(3) bonds are also somewhat shorter than the other C-C single bonds in the molecule, but part of this shortening may be due to the thermal vibrations of C(1), C(2), and C(3), which have considerably larger amplitudes than for any of the other atoms in the steroid nucleus (see Fig. 1). Hydrogen-bond and other nonbonded distances are given in Table 2.

The conformation of the Δ^4 -3-one *A* ring is a 1 α ,2 β -half chair [$\Delta C_2(C1-C2) = 3.5$; $\Delta C_2(C1-C2)$ as defined by Duax, Weeks & Rohrer (1976)] very similar to one of the three conformers of 19-nortestosterone [$\Delta C_2(C1-C2) = 3.5$] (Precigoux, Busetta, Courseille & Hospital, 1975) but unlike the *A*-ring conformation in 14-dehydrotestosterone (a slightly distorted 1 α -sofa conformation) or any testosterone structure. This indicates that removal of the angular methyl substituent

on C(10) allows the molecule more conformational flexibility in the *A* ring, as seen in the three structures of 19-nortestosterone and now 14-dehydro-19-nortestosterone.

The partially unsaturated *D* ring has a 17 α -envelope conformation. This is the third steroid crystal structure reported with a 14-dehydro *D* ring and a C(13) β -methyl substituent. In all three structures [14-dehydrotestosterone, 14-dehydroestradiol 3-methyl ether (Rohrer, Blessing, Duax & Segaloff, 1978) and the title compound], the conformation is a 17 α -envelope with C(17) displaced away from the C(13) β -methyl substituent.

This work was supported in part by Grant No. CA-10906 from the National Cancer Institute, DHEW, and in part by a group from Pensacola, Florida, who have been patients of the Ochsner Medical Institutions.

References

- DUAX, W. L., WEEKS, C. M. & ROHRER, D. C. (1976). *Topics in Stereochemistry*, Vol. 9, edited by E. L. ELIEL & N. ALLINGER, pp. 271-383. New York: John Wiley.
- JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
- PRECIGOUX, G., BUSETTA, B., COURSEILLE, C. & HOSPITAL, M. (1975). *Acta Cryst.* B31, 1527-1532.
- ROBEL, P. (1974). Personal communication to A. SEGALOFF.
- ROHRER, D. C., BLESSING, R. H., DUAX, W. L. & SEGALOFF, A. (1978). *Acta Cryst.* Submitted.
- ROHRER, D. C., STRONG, P. D., DUAX, W. L. & SEGALOFF, A. (1978). *Acta Cryst.* B34, 2913-2915.
- SEGALOFF, A. & GABBARD, R. B. (1973). *Steroids*, 22, 99-105.
- SHAIN, S. A. & BOESEL, R. W. (1975). *J. Steroid Biochem.* 6, 43-50.