

Structure of 17 β -Hydroxy-7 α -methyl-4-androsten-3-one (7 α -Methyltestosterone)

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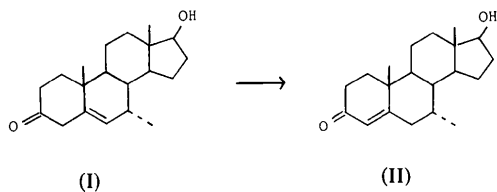
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Abstract. C₂₀H₃₀O₂, $M_r = 302.2$, $D_x = 1.18 \text{ Mg m}^{-3}$, monoclinic, $P2_1$, $Z = 2$, $a = 11.016 (5)$, $b = 6.156 (4)$, $c = 12.967 (4) \text{ \AA}$, $\beta = 104.49 (3)^\circ$, $U = 851.4 \text{ \AA}^3$, $\mu(\text{Mo } K\alpha) = 0.40 \text{ cm}^{-1}$. Final $R = 0.045$ for 1420 independent reflexions. Rings *B* and *C* are observed in chair conformations; ring *A* adopts a 1 α -sofa conformation and ring *D* a conformation midway between a C(13)-envelope and a half-chair. An O(2)—H \cdots O(1) hydrogen bond [2.832 (5) \AA] provides head-to-tail linkage between molecules in the crystal.

Introduction. Kendle (1979) has shown that 17 β -hydroxy-7 α -methyl-5-androsten-3-one, RMI 12,936 (I), inhibits progesterone biosynthesis by acting as a competitive substrate for Δ^5 -3-ketosteroid isomerase and is metabolized to its isomer 7 α -methyltestosterone (II) in the process. Suitable crystals of (II) were obtained after heating (I) under reflux with anhydrous oxalic acid in ethanol. We undertook an X-ray analysis of (II) as part of a programme to determine conformational parameters for steroids related to RMI 12,936. The crystallographic measurements were made on a CAD-4 automated diffractometer with monochromatized Mo $K\alpha$ radiation. The cell dimensions were derived by least-squares calculations from the angular settings of 25 reflexions measured at $\theta \text{ ca } 14^\circ$. Integrated relative intensities for 2032 independent reflexions with $\theta < 27^\circ$ were measured as 2θ - ω scans; 1420 reflexions had $I > 2.5\sigma(I)$.



Approximate coordinates of the C and O atoms were obtained with *MULTAN* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) and the H atoms were located in difference maps calculated at

intermediate states of refinement. In the final cycles of full-matrix least-squares calculations with *SHELX* (Sheldrick, 1976) the positional parameters for all atoms, anisotropic thermal parameters for the C and O atoms, and isotropic thermal parameters for H were varied. Convergence was reached at $R = 0.045$. The weighting scheme was $w = 1/\sigma^2(F_o)$. Atomic coordinates and the torsion angles are listed in Tables 1 and 2.*

Discussion. The molecular structure and the packing of the molecules in the unit cell are shown in Figs. 1 and 2.

* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36532 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

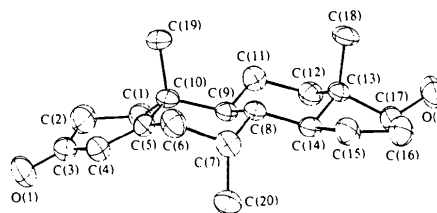


Fig. 1. The atomic arrangement in the molecule.

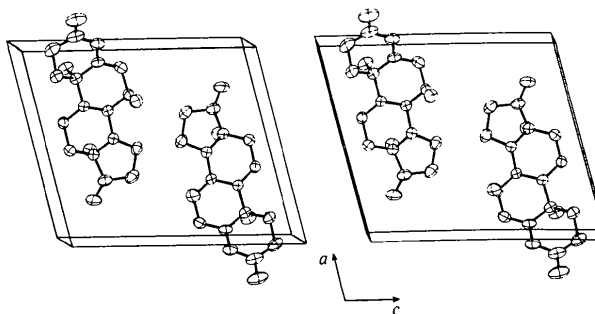


Fig. 2. A stereoscopic view of the molecular packing in the unit cell.

Table 1. Fractional atomic coordinates ($\times 10^4$) and equivalent values of the anisotropic temperature factor coefficients ($\times 10^3$), with standard deviations in parentheses

$$U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33}).$$

| | x | y | z | U_{eq} (\AA^2) |
|--------|-----------|-----------|-----------|--------------------------------|
| O(1) | -1741 (3) | 9111 | 7584 (3) | 81 (2) |
| O(2) | 7688 (2) | 3075 (8) | 8467 (2) | 59 (2) |
| C(1) | 1213 (3) | 6605 (9) | 8878 (3) | 46 (2) |
| C(2) | -149 (4) | 7136 (10) | 8803 (4) | 60 (2) |
| C(3) | -825 (3) | 7907 (8) | 7730 (4) | 57 (2) |
| C(4) | -392 (3) | 7102 (9) | 6841 (3) | 50 (2) |
| C(5) | 598 (3) | 5777 (8) | 6933 (3) | 41 (2) |
| C(6) | 911 (3) | 4879 (9) | 5966 (3) | 48 (2) |
| C(7) | 2266 (3) | 5330 (9) | 5957 (3) | 42 (2) |
| C(8) | 3115 (3) | 4312 (8) | 6962 (3) | 32 (2) |
| C(9) | 2825 (3) | 5191 (8) | 7982 (3) | 33 (2) |
| C(10) | 1414 (3) | 5085 (7) | 7998 (3) | 35 (2) |
| C(11) | 3688 (3) | 4150 (9) | 8973 (3) | 41 (2) |
| C(12) | 5074 (3) | 4412 (9) | 9009 (3) | 40 (2) |
| C(13) | 5358 (3) | 3502 (7) | 8004 (3) | 35 (2) |
| C(14) | 4497 (3) | 4648 (8) | 7043 (3) | 34 (2) |
| C(15) | 5044 (4) | 4010 (10) | 6120 (3) | 51 (2) |
| C(16) | 6470 (4) | 3892 (10) | 6625 (3) | 59 (2) |
| C(17) | 6634 (3) | 4155 (9) | 7821 (3) | 46 (2) |
| C(18) | 5242 (4) | 1006 (8) | 7959 (3) | 45 (2) |
| C(19) | 1020 (3) | 2735 (8) | 8203 (3) | 50 (2) |
| C(20) | 2471 (4) | 7782 (9) | 5832 (3) | 55 (2) |
| HO(2) | 7884 (50) | 1747 (73) | 8127 (41) | |
| H(1A) | 1713 (31) | 7926 (50) | 8806 (27) | |
| H(1B) | 1590 (28) | 6050 (54) | 9606 (20) | |
| H(2A) | -235 (34) | 8073 (53) | 9402 (24) | |
| H(2B) | -620 (33) | 5798 (48) | 8906 (29) | |
| H(4) | -926 (27) | 7445 (69) | 6123 (19) | |
| H(6A) | 753 (35) | 3322 (42) | 5936 (30) | |
| H(6B) | 347 (34) | 5459 (62) | 5259 (24) | |
| H(7) | 2491 (30) | 4717 (65) | 5305 (22) | |
| H(8) | 2944 (30) | 2728 (43) | 6931 (27) | |
| H(9) | 3028 (25) | 6780 (40) | 8022 (21) | |
| H(11A) | 3516 (28) | 4713 (51) | 9626 (20) | |
| H(11B) | 3463 (33) | 2517 (41) | 8965 (28) | |
| H(12A) | 5588 (29) | 3761 (54) | 9696 (22) | |
| H(12B) | 5311 (28) | 5988 (38) | 9042 (24) | |
| H(14) | 4700 (30) | 6182 (42) | 7142 (25) | |
| H(15A) | 4696 (35) | 2584 (46) | 5816 (30) | |
| H(15B) | 4870 (37) | 5070 (54) | 5518 (25) | |
| H(16A) | 6925 (42) | 4947 (62) | 6264 (34) | |
| H(16B) | 6839 (44) | 2434 (49) | 6516 (40) | |
| H(17) | 6727 (29) | 5729 (43) | 7986 (25) | |
| H(18A) | 4400 (22) | 469 (74) | 7997 (26) | |
| H(18B) | 5887 (27) | 362 (80) | 8561 (23) | |
| H(18C) | 5407 (35) | 501 (95) | 7265 (21) | |
| H(19A) | 1480 (28) | 2376 (82) | 8941 (18) | |
| H(19B) | 1225 (32) | 1876 (74) | 7643 (23) | |
| H(19C) | 98 (20) | 2656 (81) | 8163 (25) | |
| H(20A) | 3356 (20) | 8112 (76) | 5825 (24) | |
| H(20B) | 2242 (34) | 8557 (85) | 6432 (23) | |
| H(20C) | 1905 (25) | 8160 (74) | 5129 (19) | |

The molecules are linked together by hydrogen bonding between hydroxy and carbonyl functions; the angle O(2)-H \cdots O(1)[x - 1, 1 + y, z] is 174 (5) $^\circ$ and the O-H and H \cdots O distances are 0.96 (5) and 1.87 (5) \AA .

Table 2. Torsion angles ($^\circ$)

| | | | |
|-------------------------|------------|-------------------------|------------|
| C(10)-C(1)-C(2)-C(3) | -51.1 (5) | C(2)-C(1)-C(10)-C(5) | 44.2 (5) |
| C(2)-C(1)-C(10)-C(9) | 164.6 (4) | C(2)-C(1)-C(10)-C(19) | -73.5 (4) |
| C(1)-C(2)-C(3)-O(1) | -153.4 (4) | C(1)-C(2)-C(3)-C(4) | 29.2 (6) |
| O(1)-C(3)-C(4)-C(5) | -179.8 (4) | C(2)-C(3)-C(4)-C(5) | -2.4 (7) |
| C(3)-C(4)-C(5)-C(6) | 174.8 (4) | C(3)-C(4)-C(5)-C(10) | -3.5 (7) |
| C(4)-C(5)-C(6)-C(7) | 126.5 (4) | C(10)-C(5)-C(6)-C(7) | -55.1 (5) |
| C(4)-C(5)-C(10)-C(1) | -17.5 (5) | C(4)-C(5)-C(10)-C(9) | -136.9 (4) |
| C(4)-C(5)-C(10)-C(19) | 102.1 (5) | C(6)-C(5)-C(10)-C(1) | 164.1 (4) |
| C(6)-C(5)-C(10)-C(9) | 44.7 (5) | C(6)-C(5)-C(10)-C(19) | -76.3 (4) |
| C(5)-C(6)-C(7)-C(8) | 58.6 (5) | C(5)-C(6)-C(7)-C(20) | -67.3 (5) |
| C(6)-C(7)-C(8)-C(9) | -57.5 (4) | C(6)-C(7)-C(8)-C(14) | 179.8 (3) |
| C(20)-C(7)-C(8)-C(9) | 66.1 (4) | C(20)-C(7)-C(8)-C(14) | -56.6 (5) |
| C(7)-C(8)-C(9)-C(10) | 51.4 (4) | C(7)-C(8)-C(9)-C(11) | -179.9 (3) |
| C(14)-C(8)-C(9)-C(10) | 176.7 (3) | C(14)-C(8)-C(9)-C(11) | -54.6 (4) |
| C(7)-C(8)-C(14)-C(13) | -176.0 (3) | C(7)-C(8)-C(14)-C(15) | -52.8 (5) |
| C(9)-C(8)-C(14)-C(13) | 59.3 (4) | C(9)-C(8)-C(14)-C(15) | -177.5 (3) |
| C(8)-C(9)-C(10)-C(1) | -163.0 (3) | C(8)-C(9)-C(10)-C(5) | -42.5 (4) |
| C(8)-C(9)-C(10)-C(19) | 75.9 (4) | C(11)-C(9)-C(10)-C(1) | 69.1 (4) |
| C(11)-C(9)-C(10)-C(5) | -170.4 (3) | C(11)-C(9)-C(10)-C(19) | -52.0 (4) |
| C(8)-C(9)-C(11)-C(12) | 54.8 (4) | C(10)-C(9)-C(11)-C(12) | -175.2 (3) |
| C(9)-C(11)-C(12)-C(13) | -55.9 (5) | C(11)-C(12)-C(13)-C(14) | 56.1 (4) |
| C(11)-C(12)-C(13)-C(17) | 165.8 (3) | C(11)-C(12)-C(13)-C(18) | -69.2 (4) |
| C(12)-C(13)-C(14)-C(8) | -60.3 (4) | C(12)-C(13)-C(14)-C(15) | 168.0 (3) |
| C(17)-C(13)-C(14)-C(8) | 179.2 (3) | C(17)-C(13)-C(14)-C(15) | 47.5 (4) |
| C(18)-C(13)-C(14)-C(8) | 63.8 (4) | C(18)-C(13)-C(14)-C(15) | -67.9 (4) |
| C(12)-C(13)-C(17)-O(2) | 75.4 (5) | C(12)-C(13)-C(17)-C(16) | -157.2 (4) |
| C(14)-C(13)-C(17)-O(2) | -169.7 (3) | C(14)-C(13)-C(17)-C(16) | -42.3 (4) |
| C(18)-C(13)-C(17)-O(2) | -50.9 (5) | C(18)-C(13)-C(17)-C(16) | 76.5 (4) |
| C(8)-C(14)-C(15)-C(16) | -162.4 (4) | C(13)-C(14)-C(15)-C(16) | -34.5 (4) |
| C(14)-C(15)-C(16)-C(17) | 7.6 (5) | C(15)-C(16)-C(17)-O(2) | 149.8 (4) |
| C(15)-C(16)-C(17)-C(13) | 22.0 (5) | | |

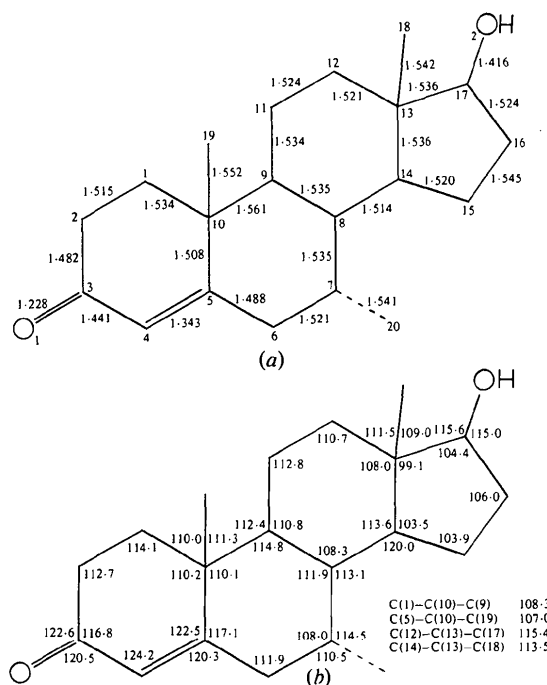


Fig. 3. (a) Bond lengths (\AA) and (b) bond angles ($^\circ$).

Fig. 3 shows the bond lengths and angles involving the C and O atoms; e.s.d.'s range from 0.005 to 0.008 \AA for the bond distances and from 0.3 to 0.4 $^\circ$ for the angles. The conformational asymmetry parameters, $\Delta C_s(1)$ 8.6 $^\circ$, $\Delta C_s(5)$ 2.6 $^\circ$, and $\Delta C_s(9)$ 3.1 $^\circ$, are very similar to those found for 7 α -methyl-4-androstene-3,17-dione (Cowe, Cox & Sim, 1982). The D-ring parameters (Δ 17.3 $^\circ$, φ_m 48.0 $^\circ$) are similar

to the values (Δ 22.7°, φ_m 46.8°) found for RMI 12,936 (Cox, Mkandawire & Mallinson, 1981). Both *A* and *D* rings are known to be somewhat flexible in steroids related to testosterone (Roberts, Pettersen, Sheldrick, Isaacs & Kennard, 1973). The intramolecular distance between O(1) and O(2) is 10.819 (4) Å [*cf.* 10.902 (3) Å in RMI 12,936].

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17 β -Hydroxy-19-nor-5 α ,17 α -pregn-20-yn-3-one

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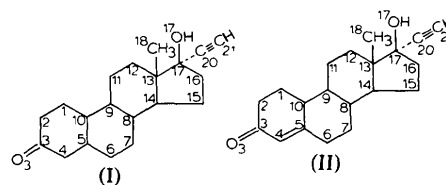
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Abstract. C₂₀H₂₈O₂, $M_r = 300.4$, $\rho_x = 1.159$ Mg m⁻³, orthorhombic, $P2_12_12_1$, $Z = 4$, $a = 12.391$ (3), $b = 21.066$ (5), $c = 6.597$ (1) Å, $V = 1722.0$ Å³. Final $R = 0.063$ for 1477 independent reflections with $I \geq 2\sigma(I)$. The C(5)–C(6) bond in the *A* ring of this molecule (I) is saturated making ring *A* conformationally rigid and the C(3) carbonyl substituent unconjugated. The parent molecule, 19-norethindrone (II), has an *A* ring containing a 4-en-3-one conjugated grouping. The result of saturating the *A* ring is to flatten the steroid backbone and reduce the progestational activity of the molecule. The position of O(3) is shifted 0.53 Å in the β -face direction compared to the position of O(3) in the 19-norethindrone structure [Mornon, Lepicard & Delettré (1976). *C.R. Acad. Sci. Sér. C*, 282, 387–390].

Introduction. The structure determination of the title compound (I), also known as 5 α -dihydro-19-norethindrone, was undertaken as part of a study of synthetic progestational agents directed toward identifying the structural features important for activity. Earlier papers (Rohrer, Duax & Zeelen, 1976, 1978) showed that the overall shape of the steroid backbone had a direct relationship to the relative progestational activity of the molecule. In this compound the usual

4-en-3-one *A*-ring conjugated system has been removed by saturating the C(4)–C(5) bond while retaining the C(3) carbonyl substituent.



Crystal data were measured on a crystal of dimensions 0.08 × 0.40 × 0.76 mm with a Syntex P_3f automatic diffractometer with Nb-filtered Mo $K\alpha$ radiation. The crystals are orthorhombic and the space group is $P2_12_12_1$. The lattice dimensions were refined by a least-squares fit to a set of measured 2θ values [$\lambda(\text{Mo } K\alpha) = 0.7107$ Å] for 25 reflections in the interval $25^\circ < 2\theta < 30^\circ$. Integrated relative intensities for 1813 independent reflections with $2\theta < 50^\circ$ were measured by ω - 2θ scans; 1477 of these reflections were determined to be observed above background ($I > 2\sigma_I$).

The intensities were reduced to structure factor amplitudes and phase angles sufficient to locate the