

A Steroid Crystal Structure without Hydrogen Bonds: Androstan-17-one

BY A. BANERJEE, B. N. DAS* AND W. SAENGER†

Abteilung Chemie, Max-Planck-Institut für experimentelle Medizin, Hermann-Rein-Strasse 3, 3400 Göttingen, Federal Republic of Germany

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Androstan-17-one ($C_{19}H_{30}O$) is an androstane derivative possessing a high androgenic potency of 1000 per IU. The compound crystallizes in space group $C2$ with cell dimensions $a = 12.636$, $b = 6.825$, $c = 18.962$ Å, $\beta = 101.76^\circ$. The structure was solved on the basis of X-ray counter data and refined to $R = 5.6\%$. The bond length C(2)–C(3) is slightly increased relative to 3-hydroxyl steroids but C(4)–C(3), 1.542 Å, is significantly longer.

Introduction

Following the elucidation of structures of natural androgens, numerous related compounds have been produced by partial synthesis from dehydroepiandrosterone or its reduction products. Androstan-17-one (I) is a monoketone androstane derivative having a high androgenic potency of 1000 per IU (Rodd, 1970; androgenic activity of 0.1 mg of androsterone = 1 IU). It is without the 3-hydroxyl group which is believed to cause neuromuscular blocking (Lewis, Martin-Smith, Muir & Ross, 1967) and, from a structural point of view, appears to be responsible for shortening of the C(2)–C(3) and C(4)–C(3) bonds from the average value of 1.533 Å. The present X-ray analysis of (I) was carried out in order to establish the influence of the 3-hydroxyl group on the geometry of the molecular and crystal structure.

Experimental

Androstan-17-one (I) crystallized from ethanol in the form of elongated prisms, data for which are summarized in Table 1. X-ray intensities were determined by means of an automated Stoe four-circle diffractometer equipped with a Cu tube (Ni filter) and operated in the $2\theta/\theta$ scan mode with stationary background counts on each side of the scan; reference reflections were monitored every two hours. Data were corrected for geometrical factors but not for absorption, since μ is small (Table 1). The structure was solved by direct methods using the program *MULTAN* (Germain, Main & Woolfson, 1971) and refined by full-matrix least-squares methods with H atoms located from difference Fourier syntheses. The final R factor is

* Present address: Department of Physics, Presidency College, Calcutta 9, India.

† To whom correspondence should be addressed.

Table 1. Crystal data

Androstan-17-one ($C_{19}H_{30}O$), $M_r = 274.0$, MV 400.3 Å ³ Monoclinic, $C2$ (systematic absences when $h + k$ odd in hkl)			
a	12.636 (3) Å	$F(000)$	608.0
b	6.825 (2)	Z	4
c	18.962 (4)	$\mu(\text{Cu } K\alpha)$	5.86 cm ⁻¹
β	101.76 (04)°	D_c	1.137 g cm ⁻³
V	1601 Å ³	D_o	1.142
m.p.	122°C		

5.8% for all the 1434 data. Refinement was considered terminated when the average shifts of non-hydrogen atom parameters were less than $\frac{1}{3}$ of the corresponding standard deviations.‡

Discussion

Refined positional parameters of the atoms in (I) are presented in Table 2, the atom-numbering scheme is in Fig. 1 and thermal vibrations are shown graphically in Fig. 2. The intramolecular geometry is expressed in Table 3 and compared with the data published for 3 β -hydroxy-5 α -androstan-17-one (epiandrosterone, Weeks, Cooper & Norton, 1971).

The bonds C(2)–C(3) and C(3)–C(4) in (I) are both longer than in epiandrosterone, with C(3)–C(4) increased by 0.038 Å. This effect can be attributed to the absence of the 3-hydroxyl group in (I). On the other hand, the difference in bond C(12)–C(13), 1.502 Å and 1.539 Å, could be due to packing forces because in this part the geometries of the two molecules are comparable. In the bond angles and torsion angles, no

‡ Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33080 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. Fractional atomic coordinates ($\times 10^4$) with standard deviations in parentheses

	x	y	z
C(1)	5484 (3)	-4554 (9)	3235 (2)
C(2)	5354 (3)	-5049 (10)	3999 (2)
C(3)	6159 (3)	-6597 (11)	4350 (2)
C(4)	7318 (3)	-5948 (10)	4322 (2)
C(5)	7435 (3)	-5449 (9)	3556 (2)
C(6)	8597 (3)	-4958 (10)	3519 (2)
C(7)	8726 (3)	-4622 (10)	2742 (2)
C(8)	7926 (3)	-3100 (9)	2352 (2)
C(9)	6757 (3)	-3678 (9)	2400 (2)
C(10)	6622 (3)	-3857 (9)	3197 (2)
C(11)	5894 (3)	-2351 (10)	1929 (2)
C(12)	6056 (3)	-2157 (10)	1151 (2)
C(13)	7183 (3)	-1466 (10)	1146 (2)
C(14)	8007 (3)	-2931 (9)	1565 (2)
C(15)	9084 (3)	-2355 (10)	1365 (2)
C(16)	8752 (3)	-1753 (11)	563 (2)
C(17)	7543 (3)	-1465 (10)	432 (2)
C(18)	7360 (4)	653 (10)	1429 (2)
C(19)	6831 (3)	-1875 (10)	3580 (2)
O(20)	6940 (2)	-1300 (10)	-164 (1)
H1(C1)	4639 (30)	4005 (70)	7072 (20)
H2(C1)	5099 (28)	6628 (70)	6992 (18)
H1(C2)	5436 (30)	4448 (70)	6013 (20)
H2(C2)	4579 (28)	6412 (70)	5716 (18)
H1(C3)	3991 (28)	2054 (70)	5901 (18)
H2(C3)	3952 (28)	3164 (70)	5144 (18)
H1(C4)	2177 (30)	2878 (70)	5499 (20)
H2(C4)	2487 (30)	5418 (70)	5385 (20)
H1(C5)	2758 (30)	3175 (70)	6726 (20)
H1(C6)	937 (30)	3939 (70)	6261 (20)
H2(C6)	1247 (30)	6337 (70)	6216 (20)
H1(C7)	1339 (30)	3849 (70)	7511 (20)
H2(C7)	544 (28)	5909 (70)	7295 (18)
H1(C8)	1881 (28)	8289 (70)	7425 (18)
H1(C9)	3406 (28)	4933 (70)	7816 (18)
H1(C11)	4810 (28)	7329 (70)	8065 (18)
H2(C11)	4172 (28)	9103 (70)	7896 (18)
H1(C12)	4511 (28)	8822 (70)	9116 (18)
H2(C12)	3996 (28)	6370 (70)	9034 (18)
H1(C14)	2212 (28)	5542 (70)	8626 (18)
H1(C15)	308 (28)	6493 (70)	8569 (18)
H2(C15)	608 (28)	8768 (70)	8339 (18)
H1(C16)	943 (28)	7153 (70)	9762 (18)
H2(C16)	950 (28)	9470 (70)	9563 (18)
H1(C18)	1914 (28)	11113 (70)	8629 (18)
H2(C18)	2728 (28)	10655 (70)	8094 (18)
H3(C18)	3100 (28)	11395 (70)	8762 (18)
H1(C19)	2441 (28)	8621 (70)	6488 (18)
H2(C19)	3109 (28)	7977 (70)	5920 (18)
H3(C19)	3756 (28)	9044 (70)	6537 (18)

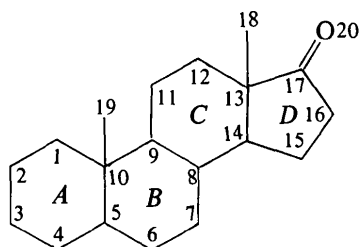


Fig. 1. A sketch of androstan-17-one, showing the atom designation.

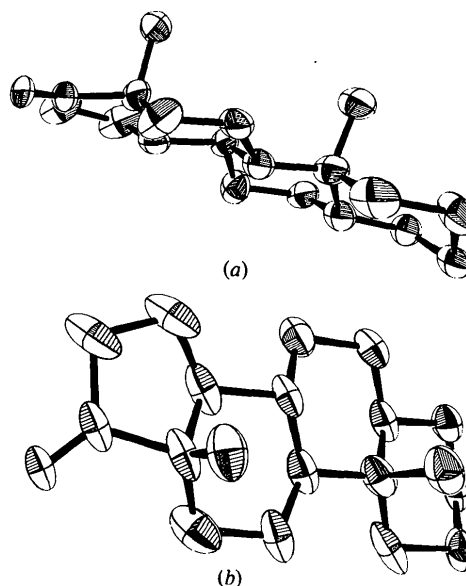


Fig. 2. Views of an individual androstan-17-one molecule with 50% thermal ellipsoids (Johnson, 1965): (a) along a, (b) along b.

discrepancies occur between the two structures and the peculiarities of ring *D* as discussed by Weeks *et al.* (1971) are similar.

The melting point of (I) is lower (122°C) than that of epiandrosterone (185°C) and of androsterone (175°C) which are both able to form hydrogen bonds. Hydrogen bonding in the last two compounds does not appear to assist in reducing the molecular volume, since the molecular volumes of (I) (400 Å³) and 5β-androstane-3,17-dione (414.6 Å³) (Norton, Lu & Campbell, 1962), in which there are no possibilities for intermolecular hydrogen bonding, are the same as or smaller than those of epiandrosterone (422.7 Å³) (Weeks *et al.*, 1971), androsterone (414.5 Å³) (High & Kraut, 1966) and 5β-androstane-3α,17β-diol (423 Å³) (Weeks *et al.*, 1971). It appears that hydrogen bonding influences the molecular packing but not the molecular volume. The crystal packing of (I) is shown in Fig. 3. It is quite different from that observed for epiandrosterone and for androsterone. Seemingly, having no hydrogen bonding, the molecules try to pack in an antiparallel arrangement about the symmetry axes. They are held together by van der Waals forces and by weak interactions between O(17) of the molecule at (*x*, *y*, *z*) and C(16) and C(17) of related molecules at ($\frac{1}{2} - x$, $\frac{1}{2} + y$, $-z$) at distances 3.27 and 3.42 Å apart.

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Table 3. *Intramolecular geometry of androstan-17-one (I) and epiandrosterone (II) (Weeks et al., 1971)*

The numbers in parentheses are standard deviations of the last figures.

(a) Interatomic distances (Å)

	(I)	(II)
C(1)—C(2)	1.530 (6)	1.530 (6)
C(1)—C(10)	1.530 (6)	1.537 (6)
C(2)—C(3)	1.523 (5)	1.512 (7)
C(3)—C(4)	1.542 (6)	1.504 (6)
C(3)—O(3)	—	1.430 (5)
C(4)—C(5)	1.528 (5)	1.539 (6)
C(5)—C(6)	1.522 (6)	1.525 (6)
C(5)—C(10)	1.553 (6)	1.545 (5)
C(6)—C(7)	1.532 (7)	1.526 (6)
C(7)—C(8)	1.531 (6)	1.521 (6)
C(8)—C(9)	1.550 (5)	1.551 (5)
C(8)—C(14)	1.522 (5)	1.524 (6)
C(9)—C(10)	1.560 (5)	1.564 (5)
C(9)—C(11)	1.553 (5)	1.552 (6)
C(10)—C(19)	1.532 (5)	1.541 (6)
C(11)—C(12)	1.536 (5)	1.537 (6)
C(12)—C(13)	1.502 (7)	1.539 (6)
C(13)—C(14)	1.542 (6)	1.530 (6)
C(13)—C(17)	1.514 (5)	1.521 (6)
C(13)—C(18)	1.542 (7)	1.537 (7)
C(14)—C(15)	1.536 (6)	1.543 (6)
C(15)—C(16)	1.549 (5)	1.551 (7)
C(16)—C(17)	1.510 (5)	1.496 (7)
C(17)—O(20)	1.232 (6)	1.211 (6)

(b) Valency angles (°)

C(2)—C(1)—C(10)	113.3 (4)	112.8 (3)
C(1)—C(2)—C(3)	112.2 (4)	111.4 (3)
C(2)—C(3)—C(4)	109.9 (3)	111.0 (3)
C(2)—C(3)—O(3)	—	110.8 (4)
C(4)—C(3)—O(3)	—	109.2 (3)
C(3)—C(4)—C(5)	112.0 (3)	111.3 (4)
C(4)—C(5)—C(6)	112.0 (3)	112.0 (3)
C(4)—C(5)—C(10)	112.9 (4)	112.9 (2)
C(6)—C(5)—C(10)	112.6 (3)	112.0 (4)
C(5)—C(6)—C(7)	111.7 (4)	111.2 (3)
C(6)—C(7)—C(8)	112.1 (3)	112.9 (2)
C(7)—C(8)—C(9)	110.1 (3)	110.6 (3)
C(7)—C(8)—C(14)	110.9 (4)	111.9 (3)
C(9)—C(8)—C(14)	109.4 (3)	107.5 (3)
C(8)—C(9)—C(10)	111.8 (4)	111.9 (2)
C(8)—C(9)—C(11)	112.6 (3)	112.0 (4)
C(10)—C(9)—C(11)	113.7 (3)	113.5 (3)
C(1)—C(10)—C(5)	107.8 (3)	106.7 (3)
C(1)—C(10)—C(9)	111.0 (3)	109.8 (3)
C(1)—C(10)—C(19)	109.0 (3)	109.3 (3)
C(5)—C(10)—C(9)	106.6 (4)	106.7 (3)

Table 3 (cont.)

C(5)—C(10)—C(19)	112.1 (3)	113.2 (3)
C(9)—C(10)—C(19)	110.3 (3)	111.0 (4)
C(9)—C(11)—C(12)	112.9 (4)	112.8 (3)
C(11)—C(12)—C(13)	110.2 (4)	109.3 (3)
C(12)—C(13)—C(14)	109.6 (3)	108.6 (3)
C(12)—C(13)—C(17)	117.6 (4)	115.9 (3)
C(12)—C(13)—C(18)	111.3 (3)	112.4 (3)
C(14)—C(13)—C(17)	99.6 (4)	99.8 (3)
C(14)—C(13)—C(18)	113.2 (3)	114.6 (3)
C(17)—C(13)—C(18)	105.2 (3)	105.1 (3)
C(8)—C(14)—C(13)	112.4 (3)	114.1 (3)
C(8)—C(14)—C(15)	120.1 (3)	119.9 (3)
C(13)—C(14)—C(15)	104.3 (4)	103.5 (3)
C(14)—C(15)—C(16)	103.5 (3)	102.4 (3)
C(15)—C(16)—C(17)	105.0 (3)	105.7 (3)
C(13)—C(17)—C(16)	109.3 (3)	108.5 (3)
C(13)—C(17)—O(17)	125.2 (4)	125.6 (5)
C(16)—C(17)—O(17)	125.4 (3)	125.8 (3)

(c) Torsion angles (°) in the rings

$\psi(A-B)$ is the torsion angle about the $A-B$ bond, in which the other two atoms required to define the angle are those attached to either end of the bond, and are in the ring in question. The sign convention for the direction of the torsion angle is that of Klyne & Prelog (1960).

	(I)	(II)
Ring A	$\psi(A-B)$	$\psi(A-B)$
C(1)—C(2)	-56.9	-57.7
C(2)—C(3)	54.1	55.1
C(3)—C(4)	-54.0	-54.5
C(4)—C(5)	56.1	56.7
C(5)—C(10)	-54.8	-55.7
C(1)—C(10)	55.0	56.2
Ring B		
C(5)—C(6)	-56.2	-57.8
C(6)—C(7)	53.1	53.3
C(7)—C(8)	-53.8	-52.3
C(8)—C(9)	58.0	56.0
C(9)—C(10)	-59.2	-58.6
C(5)—C(10)	58.0	59.4
Ring C		
C(8)—C(9)	-50.2	-52.7
C(9)—C(11)	50.4	54.1
C(11)—C(12)	-54.5	-55.6
C(12)—C(13)	58.8	57.4
C(13)—C(14)	-61.8	-62.0
C(8)—C(14)	56.3	58.4
Ring D		
C(13)—C(14)	42.5	44.4
C(14)—C(15)	-36.8	-39.2
C(15)—C(16)	15.7	17.9
C(16)—C(17)	11.3	9.9
C(13)—C(17)	-33.2	-33.6

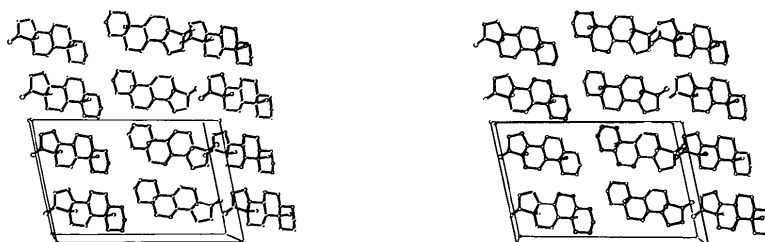


Fig. 3. A stereoview of the crystal packing down b .

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The Crystal and Molecular Structure of (2*R*,5*R*,8*R*,11*R*)-2,5,8,11-Tetraethyl-1,4,7,10-tetraazacyclododecane

BY TOSIO SAKURAI, KIMIKO KOBAYASHI, KAORU TSUBOYAMA AND SEI TSUBOYAMA

The Institute of Physical and Chemical Research (Rikagaku Kenkyusho), Wako-shi, Saitama 351, Japan

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$C_{16}N_4H_{36}$, orthorhombic, $P2_12_12_1$, $a = 9.392(2)$, $b = 9.422(2)$, $c = 43.162(10)$ Å, $U = 3819(2)$ Å³, $D_m = 1.00$, $D_c = 0.99$ g cm⁻³, $Z = 8$. The structure is pseudo tetragonal, and was solved by a trial and error method. The azacyclododecane ring forms a square conformation, typical of the 12-membered cycloalkanes.

Introduction

Several cyclic tetramers of chiral aziridines have been synthesized in our Institute (Tsuboyama, Tsuboyama, Higashi & Yanagita, 1970). These tetramers have four different geometrical isomers depending on the chirality of the original aziridine, as shown in Fig. 1.

Corresponding to these geometrical differences, many crystal forms were obtained, and the lattice parameters and the space groups were reported

(Tsuboyama, Tsuboyama, Uzawa & Higashi, 1974). Also, some derivatives of these tetramers form interesting clathrate-type compounds with several aromatic molecules. However, none of the structures has yet been solved. Therefore, in order to establish the fundamental geometry of these tetramers using a simple form of this series, the title compound was synthesized and the X-ray diffraction study was performed.

Experimental

Single crystals were obtained by recrystallization from benzene–acetonitrile solution. The crystal consists of transparent square plates which pile up to form a square pyramid. For the X-ray diffraction work, a plate was stripped off from the pile and cut to a narrow plate with dimensions 0.5 × 0.2 × 0.1 mm. X-ray diffraction data were measured on a Rigaku automated four-circle diffractometer with graphite-monochromatized Cu $K\alpha$ radiation. Within the range of $2\theta \leq 140^\circ$, 998 independent reflections were observed. The crystal at first appeared to be tetragonal $P4_12_12$ (or $P4_32_12$) with $a = 9.4$ and $c = 43.2$ Å. However, careful examination of the lattice parameters and the intensity distribution revealed that the crystal belongs to the orthorhombic system $P2_12_12_1$.

