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## The Conformation of Non-Aromatic Ring Compounds. LXXXIII.\* The Crystal and Molecular Structure of 5 $\alpha$ ,17 $\alpha$ -Pregnane-3 $\beta$ ,20 $\alpha$ -diol at $-170^{\circ}\text{C}$

BY C. ROMERS, R. A. G. DE GRAAFF, F. J. M. HOOGENBOOM AND ELISABETH W. M. RUTTEN

*Gorlaeus Laboratoria, X-ray and Electron Diffraction Section, Rijksuniversiteit, Leiden, The Netherlands*

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Crystals of 5 $\alpha$ ,17 $\alpha$ -pregnane-3 $\beta$ ,20 $\alpha$ -diol are monoclinic. The space group is  $P2_1$ , with  $a=10.123$  (2),  $b=24.646$  (8),  $c=7.524$  (3) Å and  $\beta=91.78$  (3) $^{\circ}$  at  $-170^{\circ}\text{C}$ . The unit cell contains four steroid and two water molecules. Diffraction data were collected at  $-170^{\circ}\text{C}$  with a three-circle diffractometer using Mo  $K\alpha$  radiation. The solution was obtained by direct methods and the structure refined by the least-squares method resulting in unweighted and weighted indices  $R=0.075$  and  $R_w=0.057$ . With the exception of the conformations of rings  $C$  and  $D$  the geometry of the two non-equivalent molecules is the same on a 99% confidence level. The six-membered rings have chair conformations slightly distorted in  $B(\text{I})$ ,  $B(\text{II})$  and  $C(\text{I})$ . Ring  $D(\text{I})$  is a nearly ideal  $C(14\alpha)$  envelope, whereas ring  $D(\text{II})$  is a nearly ideal half-chair. The pattern of hydrogen bonds and the unexpectedly large thermal motions of several carbon atoms are discussed.

### Introduction

Natural 20-hydroxy-5 $\alpha$ ,17 $\beta$ -pregnanes are characterized by chirality  $S$  (Cahn, Ingold & Prelog, 1966) with respect to C(20). Their hydrogen atoms H(17 $\alpha$ ) and H(20 $\beta$ ) are in antiplanar *trans* configuration and the dihedral angle  $\varphi(13-17-20-21)$  amounts to  $\sim -57^{\circ}$  (Romers, Altona, Jacobs & de Graaff, 1974; Isaacs, Motherwell, Coppola & Kennard, 1972). According to chemical investigations (Glick & Hirschmann, 1962) and valence-force calculations (Altona & Hirschmann, 1970) this conformation [see Fig. 2(c)] is, indeed, the most stable one for the 20 $\alpha$  epimer with  $S$ -chirality, although other rotamers as well might contribute to the equilibrium in solution.

The occurrence of 17 $\alpha$ -substituted steroids is rare. Courcy (1962) isolated from the urine of a patient with adrenal hyperplasia the compound 3 $\alpha$ -hydroxy-5 $\beta$ ,17 $\alpha$ -pregnan-20-one. The title compound 5 $\alpha$ ,17 $\alpha$ -pregnane-3 $\beta$ ,20 $\alpha$ -diol (hereafter APD) was prepared by Glick & Hirschmann. The aim of the present study was to establish the side-chain conformation and the chirality

with respect to C(20). The numbering of atoms is indicated in Fig. 1(a).

### Experimental

The compound APD was recrystallized from acetone in the form of colourless monoclinic lath-shaped crystals with main faces {010} and elongated along [100]. The lattice constants at  $20^{\circ}\text{C}$  and at  $-170^{\circ}\text{C}$  (Table 1) were measured manually with a three-circle diffractometer using Cu  $K\alpha$  radiation ( $\lambda=1.54178$  Å). Systematic absences  $0k0$  for  $k$  odd point to the space group  $P2_1$ , the alternative group  $P2_1/m$  being excluded for optically active compounds. Because of the very small amount of APD (12 mg) the density was not measured. Taking into account the unit-cell dimensions we obtained the value  $d_x=1.1$  g cm $^{-3}$  for four molecules per cell.

Reflexion intensities were recorded at  $-170^{\circ}\text{C}$  with a three-circle diffractometer. The crystal was mounted with plane (100) perpendicular to the  $\varphi$  axis of the instrument. Mo  $K\alpha$  radiation was monochromated with graphite and the  $\omega$ -scan technique was employed in the range between  $\theta=4^{\circ}$  and  $\theta=27^{\circ}$ , which was dur-

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Table 1. *Crystal data of APD*

5 $\alpha$ ,17 $\alpha$ -Pregnane-3 $\beta$ ,20 $\alpha$ -diol sesquihydrate, C<sub>21</sub>H<sub>36</sub>O<sub>2</sub> · ½H<sub>2</sub>O,  
 M.W. 658.6, melting point 180–181°C,  $d_x = 1.143$  g cm<sup>-3</sup>  
 (20°C) space group *P*2<sub>1</sub>, *Z* = 4 molecules per unit cell, *F*(000)  
 = 732.

20°C	-170°C
<i>a</i> = 10.283 (1) Å	<i>a</i> = 10.123 (2) Å
<i>b</i> = 24.67 (1)	<i>b</i> = 24.646 (8)
<i>c</i> = 7.551 (1)	<i>c</i> = 7.524 (3)
$\beta$ = 91.99 (3)°	$\beta$ = 91.78 (3)°

Mo *K* $\alpha$  radiation,  $\lambda = 0.71069$  Å,  $\mu(\text{Mo } K\alpha) = 0.78$  cm<sup>-1</sup>

Observed reflexions	3964
Reflexions having counts < 2 $\sigma$	1548
Non-observed reflexions	68

ing a second run extended to  $\theta = 30^\circ$ . The measurements covered a total of 5600 symmetry-independent reciprocal-lattice points. 68 reflexions were not observed and 1548 had intensities less than twice the standard deviation calculated from counting statistics.

After each group of 19 reflexions one of the two reflexions 151 and 15 $\bar{1}$  was measured. Using these two reflexions a fifth-order polynomial function of the exposure time was determined in order to correct the intensities for loss in scattering power of the crystal. No absorption corrections were applied since the differences in transmission were less than 1.5%. The intensities were reduced to structure factors in the usual way. For each reflexion an e.s.d. was calculated ( $\sigma_F$ ) taking into account the counting statistics, errors in attenuation factors and errors due to the adjusted polynomial function. The reduction program also calculates a preliminary scale and overall isotropic temperature factor.

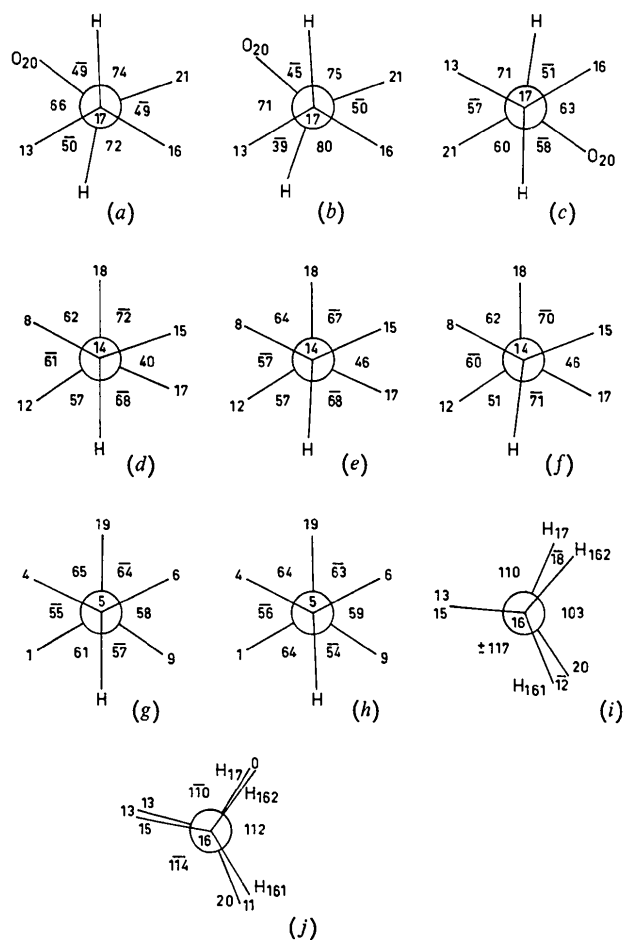


Fig. 2. Newman projections along 17–20, 14–13, 5–10 and 16–17. The projections (a), (d), (g) and (i) refer to molecule I, (b), (e), (h) and (j) refer to molecule II, (c) and (f) refer to 20 $\alpha$ -hydroxy-17 $\beta$ -pregn-4-en-3-one.

### Solution of the structure

It was decided to determine the structure by direct methods by applying a version described by Kennard, Isaacs, Motherwell, Coppola, Wampler, Larson & Watson (1971) and using the program published by Motherwell & Isaacs (1971). Taking the information of *all* measured reciprocal lattice points the scale and isotropic temperature factors were modified in such a way that the normalized structure factors *E* fulfilled as well as possible the statistical criteria listed in Table 2. The systematic error in *E* value caused by the non-accounting of the water molecule (see next section) did not hamper the analysis.

Notwithstanding the complexity of the structure containing 47 heavy atoms per asymmetric unit, its solution was quite straightforward. As starting set (Table 2) were chosen four strong reflexions: 210, 101, 1, 11, 0 and 2, 33, 1 which participate in several  $\Sigma_2$  relations between strong reflexions. The zero phase attributed to the first one fixes the origin in the direction

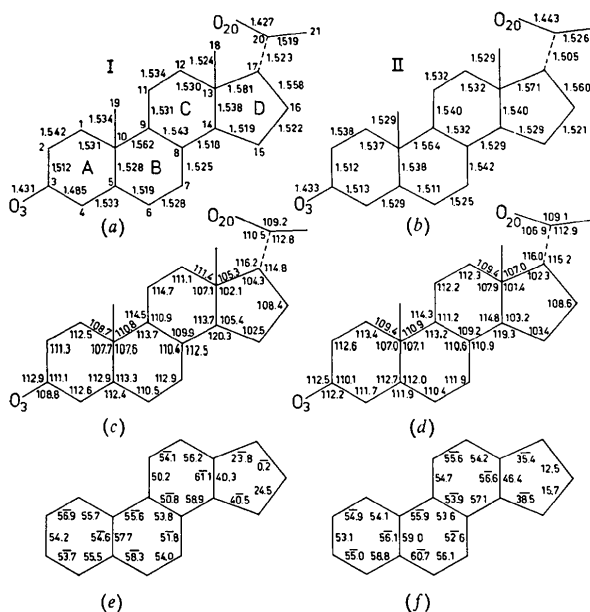


Fig. 1. Bond lengths [(a) and (b)], bond angles [(c) and (d)] and torsion angles [(e) and (f)] of APD. Molecule I is depicted in (a), (c) and (e), molecule II in (b), (d) and (f).

Table 2. *Direct-methods data of APD*

	Exp.	Theory				
$\langle  E^2 - 1  \rangle$	0.762	0.736	} non-centric distribution			
$\langle  E  \rangle$	0.888	0.886				
<i>hkl</i>	<i>E</i>	$\varphi$				
210	4.34	0	} origin-defining phases			
101	4.01	0				
1,11,0	3.41	$\pi/4$				
2,33,1	3.24	$\pi/4, 3\pi/4, 5\pi/4, 7\pi/4$				
Solution	$R_{\text{Karle}}$	$\alpha'$	<i>t</i>	$\langle \varphi \rangle$	$\langle  \varphi  \rangle$	Triplets
no. 1	23.9	302	0.76	$-0.008\pi$	$0.486\pi$	6479
no. 2	22.3	306	0.76	$0.026\pi$	$0.486\pi$	6514
no. 3	24.8	289	0.69	$0.014\pi$	$0.510\pi$	6477
no. 4	24.9	293	0.71	$-0.058\pi$	$0.448\pi$	6388

See Kennard *et al.* (1972) and Drew *et al.* (1969) for the meaning of  $R_{\text{Karle}}$ ,  $\alpha_{\text{Karle}}$  and  $t$ ;  $\alpha' = \alpha_{\text{Karle}} \sigma^{3/2} (2\sigma_3)^{-1}$ .

b. The third one has phases  $p, p + \pi, -p$  or  $-p + \pi$ . The choice  $\varphi(101) = 0$  and  $0 < \varphi(1,11,0) = p < \pi/2$  fixes both the enantiomorph and the origin on one of the screw axes. The trial value  $p = \pi/4$  allows a maximum error of  $\pi/4$  for  $\varphi(1,11,0)$ . The trial phases  $\pi/4, 3\pi/4, 5\pi/4$  and  $7\pi/4$  were assigned to the fourth reflexion.

According to criteria introduced by Karle & Karle (1966) and extended by Drew, Templeton & Zalkin (1969) and by van Ingen Schenau, Verschoor & Romers (1974), solution no. 2 (Table 2) was better than the other three solutions on all counts but one. Using the confidence level  $\alpha_{\text{min}} = 11.9$  we obtained the lowest  $R_{\text{Karle}}$  and highest values of  $\alpha'$  and  $t$  for the correct solution. In this solution was also used the largest number of triplet ( $\Sigma_2$ ) relations. If the structure is truly non-centric for any choice of origin, the average value

$\langle \varphi \rangle$  of the phase  $\varphi$  and the mean absolute value  $\langle |\varphi| \rangle$  should be zero and  $\pi/2$  respectively. It can be seen that solution no. 2 nearly satisfies these criteria.

It is interesting to note that the reflexion 2,33,1 scanned at  $\theta$  (Mo  $K\alpha$ ) =  $28.9^\circ$  lies outside the restricted scanning range ( $\theta_{\text{max}} = 27^\circ$ ) and outside the region of  $\theta$  values accessible for diffraction measurements with Cu  $K\alpha$  radiation. Attempts to find a solution with the restricted data set were unsuccessful.

### Refinement

A Fourier synthesis with  $E$  values as coefficients and phases obtained from solution no. 2 revealed the positions of 34 heavy atoms. Isotropic refinement of these atoms gave  $R = 0.40$ .

A second Fourier synthesis calculated with observed structure factors revealed 10 further heavy atoms; on subsequent refinement the  $R$  index dropped to 0.20. Scattering factors for carbon and oxygen were taken from *International Tables for X-ray Crystallography* (1962) and hydrogen scattering factors were taken from Stewart, Davidson & Simpson (1965). The function minimized during the refinement was  $\sum w(|F_o| - |F_c|)^2$ , where  $w = 1$  during the isotropic stages and  $w = \sigma_F^{-2}$  during the anisotropic cycles of the refinement. The conventional and weighted  $R$  indices are defined as  $R = \sum |F_o - F_c| / \sum |F_o|$  and  $R_w = \{ \sum w(F_o - F_c)^2 / \sum w F_o^2 \}^{1/2}$ .

A difference map displayed one large peak ( $5 \text{ e } \text{\AA}^{-3}$ ) which could be identified as an oxygen atom of a water molecule donating one and accepting one hydrogen bond (see Fig. 3). Apparently the solvent used (acetone) contained a small amount of water favourable to the

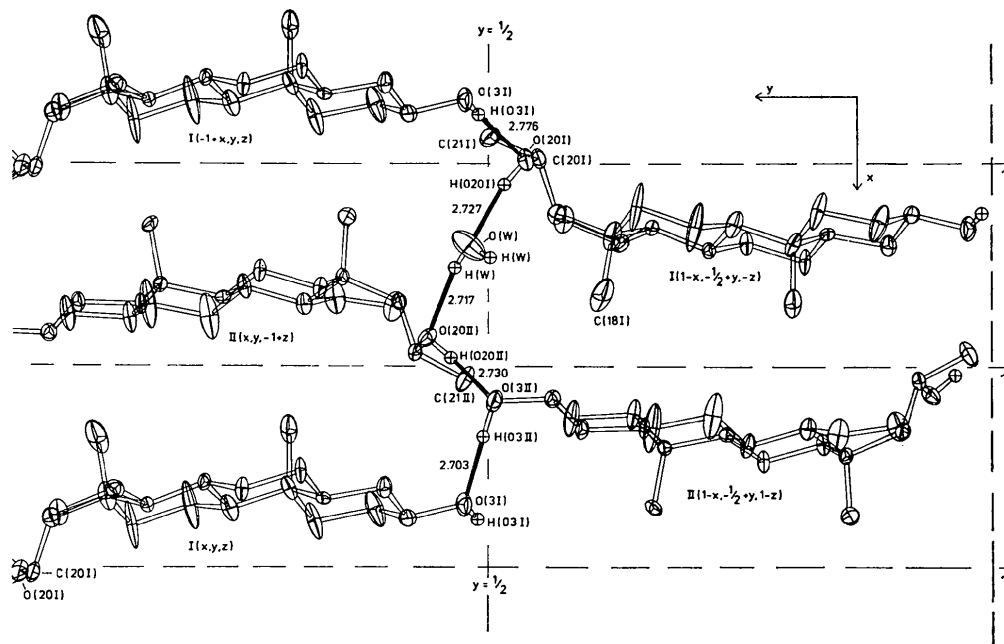


Fig. 3. ORTEP projection along [001] of a part of the structure. The thermal ellipsoids of the non-hydrogen atoms are scaled to enclose a 40% probability. The hydrogen bonds are indicated by thick lines, the numbers ( $\text{\AA}$ ) refer to their lengths.





Table 4 (cont.)

Molecule II	x	y	z
C(1)	3480 (4)	8505 (2)	9692 (5)
C(2)	3441 (4)	9126 (2)	9903 (5)
C(3)	4198 (4)	9417 (2)	8488 (5)
C(4)	3729 (6)	9230 (2)	6661 (5)
C(5)	3818 (5)	8613 (2)	6471 (5)
C(6)	3498 (8)	8430 (2)	4593 (7)
C(7)	3785 (7)	7827 (2)	4388 (7)
C(8)	3047 (5)	7480 (2)	5744 (5)
C(9)	3310 (4)	7691 (2)	7636 (5)
C(10)	3001 (4)	8310 (2)	7843 (5)
C(11)	2655 (4)	7326 (2)	9015 (5)
C(12)	3073 (4)	6731 (2)	8847 (5)
C(13)	2802 (4)	6507 (2)	6972 (5)
C(14)	3473 (4)	6886 (2)	5646 (5)
C(15)	3315 (6)	6581 (2)	3882 (5)
C(16)	3528 (5)	5992 (2)	4412 (5)
C(17)	3409 (4)	5943 (2)	6469 (5)
C(18)	1310 (4)	6467 (2)	6615 (8)
C(19)	1518 (5)	8418 (2)	7608 (8)
C(20)	4660 (4)	5784 (2)	7469 (5)
C(21)	5325 (5)	5287 (2)	6680 (7)
O(3)	4141 (3)	9995 (1)	8669 (4)
O(20)	4302 (3)	5664 (1)	9269 (4)

	x	y	z	B(iso)
H(11)	306 (3)	832 (1)	1066 (4)	16 (8)
H(12)	434 (3)	837 (1)	988 (4)	0 (6)
H(21)	387 (3)	920 (1)	1109 (4)	8 (7)
H(22)	245 (4)	923 (2)	993 (6)	48 (12)
H(31)	502 (3)	933 (1)	868 (4)	11 (7)
H(41)	282 (5)	936 (2)	661 (7)	78 (15)
H(42)	398 (4)	948 (2)	581 (5)	41 (11)
H(51)	484 (4)	848 (2)	670 (6)	44 (11)
H(61)	253 (3)	849 (1)	439 (4)	14 (7)
H(62)	399 (4)	858 (2)	382 (5)	38 (10)
H(71)	443 (6)	778 (3)	457 (9)	111 (20)
H(72)	230 (3)	749 (1)	545 (4)	9 (7)
H(81)	348 (5)	766 (2)	308 (7)	65 (13)
H(91)	410 (3)	762 (1)	789 (5)	17 (8)
H(111)	166 (3)	739 (1)	881 (5)	18 (8)
H(112)	282 (3)	741 (1)	1023 (4)	7 (7)
H(121)	282 (4)	646 (2)	978 (5)	24 (8)
H(122)	391 (4)	675 (1)	912 (5)	23 (9)
H(141)	440 (3)	687 (1)	608 (4)	3 (6)
H(151)	258 (4)	664 (2)	320 (5)	42 (11)
H(152)	382 (6)	679 (2)	280 (8)	81 (16)
H(161)	287 (4)	575 (2)	377 (5)	34 (10)
H(162)	439 (3)	584 (1)	401 (4)	12 (7)
H(171)	265 (3)	567 (2)	675 (4)	15 (7)
H(181)	87 (4)	620 (2)	757 (5)	24 (9)
H(182)	84 (4)	681 (2)	668 (6)	42 (11)
H(183)	127 (3)	634 (1)	517 (5)	18 (8)
H(191)	104 (5)	821 (2)	656 (7)	63 (14)
H(192)	129 (5)	878 (2)	771 (6)	58 (13)
H(193)	126 (5)	817 (2)	857 (7)	80 (16)
H(201)	516 (4)	615 (2)	754 (5)	28 (9)
H(211)	475 (4)	500 (2)	647 (5)	29 (9)
H(212)	578 (5)	538 (2)	558 (7)	71 (14)
H(213)	592 (4)	516 (2)	750 (5)	25 (9)
H(O3)	326 (7)	1100 (3)	852 (8)	109 (20)
H(O20)	479 (4)	542 (2)	969 (6)	49 (11)

and high-angle reflexions no correlation could be found between this effect and the vibrational parameters. Moreover, separate refinement of the structure with low- and high-angle reflexions resulted in essentially the same odd  $U_{ij}$  values.

## Molecular geometry

The molecular geometry of molecules I and II is depicted in Fig. 1. A number of relevant geometrical data not indicated in Fig. 1 are listed in Table 6.

The program-computed positional standard errors are about 0.037, 0.0047, 0.003 and 0.0043 Å for hydrogen, carbon, oxygen and O(water). In view of the block-diagonal refinement and the large vibrational parameters for a number of atoms (see above and below) the standard deviations of bond lengths, bond angles and torsion angles involving the heavy atoms are at best 0.01 Å, 0.5° and 0.8°, respectively. Never-

Table 5. Heavy-atom vibrational parameters

Estimated standard deviations in the least significant digits are given in parentheses.

Molecule I	U(11)	U(22)	U(33)	2U(21)	2U(23)	2U(31)
C(1)	112 (5)	22 (2)	33 (2)	-61 (5)	-16 (4)	43 (6)
C(2)	106 (4)	31 (2)	31 (2)	-60 (6)	-24 (4)	53 (5)
C(3)	25 (2)	22 (2)	54 (3)	-2 (3)	-28 (4)	0 (4)
C(4)	37 (2)	19 (2)	26 (2)	1 (3)	10 (3)	-4 (3)
C(5)	13 (2)	17 (2)	29 (2)	-2 (3)	3 (3)	-10 (3)
C(6)	53 (3)	9 (1)	28 (2)	-4 (4)	3 (3)	22 (4)
C(7)	46 (2)	13 (1)	21 (2)	2 (4)	3 (3)	13 (4)
C(8)	22 (2)	13 (1)	21 (2)	3 (3)	6 (3)	-5 (3)
C(9)	57 (3)	25 (2)	15 (2)	-27 (4)	-4 (3)	-11 (4)
C(10)	44 (2)	20 (2)	17 (2)	-29 (4)	1 (3)	-5 (3)
C(11)	194 (7)	23 (2)	20 (2)	-82 (7)	-8 (4)	-9 (7)
C(12)	191 (7)	14 (2)	24 (2)	-68 (6)	-3 (4)	16 (7)
C(13)	68 (3)	26 (2)	24 (2)	-24 (4)	6 (4)	-45 (4)
C(14)	20 (2)	15 (1)	14 (1)	-2 (3)	3 (3)	-6 (3)
C(15)	26 (2)	25 (2)	29 (2)	-7 (3)	0 (3)	10 (3)
C(16)	60 (3)	30 (2)	21 (2)	-8 (4)	0 (4)	-23 (4)
C(17)	33 (2)	24 (2)	25 (2)	-4 (4)	6 (3)	-17 (3)
C(18)	89 (4)	42 (3)	138 (6)	-53 (7)	66 (7)	-183 (9)
C(19)	68 (3)	22 (2)	62 (3)	-4 (5)	0 (4)	-94 (6)
C(20)	31 (2)	16 (2)	37 (2)	12 (3)	-3 (3)	-16 (4)
C(21)	32 (2)	33 (2)	42 (2)	-15 (4)	-16 (4)	11 (4)
O(3)	47 (2)	18 (1)	42 (1)	0 (3)	-17 (2)	15 (3)
O(20)	39 (1)	22 (1)	33 (1)	9 (2)	4 (2)	11 (2)
O(W)	75 (2)	91 (3)	39 (2)	-90 (5)	-20 (4)	11 (3)

Molecule II	U(11)	U(22)	U(33)	2U(21)	2U(23)	2U(31)
C(1)	35 (2)	8 (1)	25 (2)	-2 (3)	6 (3)	-22 (3)
C(2)	32 (2)	14 (1)	26 (2)	-3 (3)	-5 (3)	-15 (3)
C(3)	25 (2)	19 (2)	35 (2)	0 (3)	-1 (3)	-18 (3)
C(4)	102 (4)	17 (2)	22 (2)	-29 (5)	9 (3)	-2 (5)
C(5)	75 (3)	14 (2)	19 (2)	-20 (4)	1 (3)	9 (4)
C(6)	199 (7)	22 (2)	24 (2)	-50 (7)	9 (4)	2 (7)
C(7)	176 (6)	29 (2)	16 (2)	-52 (7)	0 (4)	20 (6)
C(8)	48 (2)	16 (2)	21 (2)	-15 (4)	5 (3)	-25 (4)
C(9)	16 (2)	21 (2)	15 (1)	1 (3)	1 (3)	-3 (3)
C(10)	18 (2)	15 (1)	23 (2)	2 (3)	-2 (3)	-13 (3)
C(11)	42 (2)	11 (1)	24 (2)	3 (3)	2 (3)	17 (4)
C(12)	37 (2)	15 (2)	22 (2)	6 (3)	3 (3)	10 (3)
C(13)	23 (2)	14 (1)	20 (2)	0 (3)	-8 (3)	-9 (3)
C(14)	39 (2)	20 (2)	15 (2)	-4 (3)	-6 (3)	-3 (3)
C(15)	86 (4)	34 (2)	16 (2)	-14 (5)	-4 (4)	8 (5)
C(16)	70 (3)	38 (2)	24 (2)	22 (5)	-9 (4)	1 (4)
C(17)	23 (2)	18 (2)	24 (2)	-2 (3)	-2 (3)	-1 (3)
C(18)	26 (2)	25 (2)	84 (4)	1 (4)	-17 (5)	-32 (5)
C(19)	21 (2)	21 (2)	119 (5)	13 (4)	-17 (5)	-45 (5)
C(20)	25 (2)	14 (1)	31 (2)	5 (3)	8 (3)	4 (3)
C(21)	50 (3)	25 (2)	49 (3)	37 (4)	20 (4)	38 (5)
O(3)	39 (1)	18 (1)	41 (1)	-15 (2)	0 (2)	-18 (3)
O(20)	28 (1)	27 (1)	31 (1)	21 (2)	15 (2)	2 (2)

Table 6. Molecular data of APD not given in Fig. 1

Bond angle (°)	I	II	
1-10-9	110.2	109.7	
5-10-19	112.6	112.6	
12-13-17	118.1	118.7	
14-13-18	112.7	112.1	
Intramolecular distance (1...4 type) (Å)			
	I	II	
O(20)····C(12)	2.960	2.922	
O(20)····C(18)	3.961	4.038	
O(20)····C(13)	3.112	3.073	
C(21)····C(16)	3.009	3.008	
O(3)····O(20)	10.52	10.70	
O(3)····C(21)	11.96	11.74	
H(162)··H(17)	2.29	2.28	
H(161)··C(20)	2.60	2.61	
Average distances (Å)			
	I	II	I, II
⟨C-C⟩	1.531	1.533	1.532
⟨C-H⟩	0.97	0.99	0.98
⟨Δ(C-C)⟩			-0.001
⟨ Δ(C-C) ⟩			0.007
Discrepancy of bond angle (°)			
⟨Δ(C-C-C)⟩	0.25		
⟨ Δ(C-C-C) ⟩	0.9		

theless, the agreement between the corresponding entities in molecules I and II is surprisingly good. The average absolute errors in bond lengths and bond angles are only 0.007 Å and 0.9°. The mean C(sp<sup>3</sup>)-C(sp<sup>3</sup>) bond length is 1.532 Å, in good agreement with the commonly observed value of 1.533 Å (Sutton, 1965). The C-H bond lengths range from 0.81 to 1.11 Å with a mean value of 0.98 Å. The C(3)-C(4) distance and the endocyclic torsion angles in rings C and D are unusual. The difference in length (0.028 Å) observed for C(3)-C(4) is probably significant on a 95% confidence level and needs no further comment. On the other hand the observed differences in torsion angles of rings C and D are highly significant and will be discussed below. Ignoring these exceptions the geometry of the two non-equivalent molecules is the same on a 99% confidence level. The two longest carbon-carbon bonds are C(9)-C(10) and C(13)-C(17), having mean lengths of 1.563 (7) and 1.576 (7) Å. The average weighted (standard) values for these sp<sup>3</sup>-sp<sup>3</sup> distances calculated from 17 steroids with 5α-configuration and containing no substituents in the 17α-position (Romers *et al.*, 1974) are 1.553 (1) and 1.553 (1) Å, respectively. In comparison with the standard value the bond C(13)-C(17) can therefore be considered to be significantly long on a 99% significance level. It is interesting to note that the force-field calculation of APD (Altona, unpublished data) results in the value 1.565 Å for the length of bond C(13)-C(17).

The bent shape of the molecules is illustrated in Fig. 3. Note the elongated vibrational ellipsoids of a number of atoms, *e.g.* C(1), C(2), C(11) and C(12) of molecule I and C(6), C(7) and C(19) of molecule II. The

bowing of the carbon skeleton of saturated 5α-steroids towards the α-side is a well-known phenomenon and has been reported earlier (Geise, Altona & Romers, 1967).

The mean absolute values of endocyclic torsion angles of rings A, B and C (average values of both molecules) are 55.2, 55.6 and 55.2°, in good agreement with the standard values (55.0, 55.9, 55.4°) determined by Romers *et al.* and theoretical values (54.7, 56.3 and 55.9°) calculated by Altona & Faber (1974) using the force-field proposed by Warshel & Lifson (1970). Conformational differences between the two molecules are, indeed, observed in rings C and D and to lesser extent in ring B. The phase angle and the maximum puckering angle (Altona, Geise & Romers, 1968) are Δ = -37.1° and φ<sub>m</sub> = 42.1° for molecule I and Δ = -4.6° and φ<sub>m</sub> = 46.1 for molecule II. Ring D of molecule I is an ideal C<sub>s</sub>(14α) envelope, while the five-membered ring of molecule II is a nearly ideal C<sub>2</sub>(16) half-chair. At first glance the large negative Δ value of I disagrees with the positive Δ values (≈ 10°) observed by Romers *et al.* for 5α,17β pregnane-like steroids. Force-field calculations of APD result, however, in the value Δ = -29.6°: therefore the envelope conformation of I is the rule rather than the half-chair conformation of II.

According to Geise *et al.* the sum of the torsion angles |φ(12-13-14-8)| and |φ(17-13-14-15)| amounts to 109 ± 3° for *trans* C/D junctions. The observed values are 101.4 and 103.0° for I and II. The 'sum rule' demands a much larger value of |φ(12-13-14-8)| in molecule I than in II. The observed value in molecule II (-56.6°) nearly equals the mean value of endocyclic torsion angles in ring C (55.2°). Consequently the chair conformation of ring C in molecule II is quite regular. On the other hand the rather high value of φ(12-13-14-8) in molecule I (-61.1°) causes a significant distortion of its ring C. In accordance with the prediction of Bucourt & Hainaut (1965) the opposing torsion angles φ(8-9-11-12), φ(14-8-9-11) and to a less degree φ(9-11-12-13) are reduced to the values 50.2, -50.7 and -54.1°, respectively.

The rings B of the two molecules are similarly distorted. The dihedral angles φ(7-6-5-10) and φ(6-5-10-9) with mean values of -59.5 and 58.4° are significantly larger than the dihedral angles φ(6-7-8-9) and φ(7-8-9-10) with mean values of -52.2 and 53.7°. Since the geometry of rings B is about the same we might say that the transmission effect is limited to rings C and D. The chair conformation of ring A(I) is quite regular, while its counterpart A(II) is somewhat distorted. The differences between A(I), A(II) and their average structure are, however, not significant on a 99% confidence level.

A number of Newman projections along the bonds 17-20, 14-13, 5-10 and 16-17 are collected in Fig. 2. The diagrams (a), (d), (g) and (i) refer to molecule I, (b), (e), (h) and (j) to molecule II, while (c) and (f) are Newman projections of 20α-hydroxy-17β-pregn-4-en-3-one (Isaacs *et al.*, 1972). Comparison of the projec-

tions (a), (b) and (c) shows that both 17 $\alpha$ - and 17 $\beta$ -pregnanes contain the 17 $\alpha$ - and 20 $\beta$ -hydrogen atoms in antiplanar *trans* configuration. The antiplanar configuration is, however, not perfect: the H-17-20-H dihedral angle amounts to  $-160^\circ$  for APD (average value) and to  $-208^\circ$  for the 17 $\beta$ -pregnene compound. From spin-spin coupling constants observed in n.m.r. experiments Kirk & Mudd (1970) calculated the value  $-145^\circ$  using the Karplus (1959) equation. Taking into account the large positional errors for hydrogen atoms resulting from X-ray diffraction experiments as well as the allowance for errors of about  $3^\circ$  in the use of the Karplus equation the agreement is satisfactory and an indication that the distortion of the antiplanar configuration is correct. The probable reasons for the distortion are the interactions of O(20) with C(12) and C(13) (see Table 6) and hydrogen atoms bonded to C(12). The torsion angle 13-17-20-O(20) adopts the rather large values of 66 and  $71^\circ$  in molecules I and II. The diagrams (d), (e), (g) and (h) demonstrate that such an effect is absent about the bonds 13-14 and 5-10: within errors of observation the configurations of H(14) and C(18) and that of H(5) and C(19) are ideally antiplanar.

According to the Cahn-Prelog-Ingold rule (Cahn, Ingold & Prelog, 1966) the chirality about C(20) [see Fig. 3(a), (b) and (c)] is *S* in APD as well as in 20 $\alpha$ -hydroxy-17 $\beta$ -pregn-4-en-3-one.

The zero endocyclic torsion angle about bond 16-17 in I suggest an eclipse of hydrogen atoms H(161) and H(162) with C(20) and H(17), respectively. Contrary to this expectation the projections 3(i) and 3(j) show that the eclipse occurs in molecule II and not in I. It can be seen in Table 6 that the intramolecular contacts H(162)-H(17) and H(161)-C(20) are equal for both molecules but their lengths are fairly short in view of the van der Waals radii of hydrogen and carbon.

#### Packing

Fig. 3 shows the molecules I( $x, y, z$ ), I( $-1+x, y, z$ ), I( $1-x, -\frac{1}{2}+y, -z$ ), II( $x, y, -1+z$ ) and II( $1-x, -\frac{1}{2}+y, 1-z$ ) in a projection along *c*. Note that I and II are arranged in opposite directions, while C(18) and C(19) of both molecules point in the *a* direction. The stacking is parallel to *b* and perpendicular to *a* in such a way that the planes (010) are pseudo-centred.

By means of the screw-axis operation hydrogen bonds O(3I)···O(20I) and O(20II)···O(3II) are responsible for a head-tail packing parallel to [010]. The water molecule participates in two hydrogen bonds, *viz.* one with I and one with II, thereby donating a hydrogen atom to O(20II) and accepting a hydrogen atom from O(20I). The second hydrogen atom of the water molecule is, however, 'free'. A fifth hydrogen bond connects I and II *via* O(3II)···O(3I). The result is an infinite pseudo-helical array of hydrogen bonds

Table 7. Intermolecular contacts between molecules I( $x, y, z$ ), II( $x, y, z$ ) and neighbouring molecules I, II and H<sub>2</sub>O. Taken into consideration are hydrophobic (*o*) H···H interactions between 2.2 and 3.0 Å and hydrophilic (*y*) O···O contacts.

Molecule	Operation	Number	Average value	Minimum	Character
Molecule I	I $x, y, 1+z$	8	2.76	2.58	<i>o</i>
	I $x, y, -1+z$	8	2.76	2.58	<i>o</i>
	II $x, y, z$	12	2.76	2.47	<i>o</i>
	II $x, y, -1+z$	8	2.80	2.46	<i>o</i>
	II $1+x, y, -1+z$	3	2.67	2.22	<i>o</i>
	II $1+x, y, z$	8	2.72	2.41	<i>o</i>
	I $2-x, \frac{1}{2}+y, -z$	2	2.78	2.63	<i>o</i>
	I $2-x, \frac{1}{2}+y, 1-z$	3	2.65	2.51	<i>o</i>
	I $2-x, -\frac{1}{2}+y, -z$	2	2.78	2.63	<i>o</i>
	I $2-x, -\frac{1}{2}+y, 1-z$	3	2.65	2.51	<i>o</i>
	II $2-x, \frac{1}{2}+y, 1-z$	1	2.81	2.81	<i>o</i>
	H <sub>2</sub> O $1-x, \frac{1}{2}+y, -z$	1	2.73	2.73	<i>y</i>
	I $2-x, \frac{1}{2}+y, -z$	1	2.77	2.77	<i>y</i>
	I $2-x, -\frac{1}{2}+y, -z$	1	2.77	2.77	<i>y</i>
	II $1-x, -\frac{1}{2}+y, 1-z$	1	2.70	2.70	<i>y</i>
	Molecule II	II $x, y, 1+z$	9	2.68	2.31
II $x, y, -1+z$		9	2.68	2.31	<i>o</i>
I $x, y, 1+z$		8	2.80	2.46	<i>o</i>
I $x, y, z$		12	2.76	2.47	<i>o</i>
I $-1+x, y, 1+z$		3	2.67	2.22	<i>o</i>
I $-1+x, y, z$		8	2.72	2.41	<i>o</i>
II $1-x, -\frac{1}{2}+y, 2-z$		2	2.80	2.59	<i>o</i>
II $1-x, \frac{1}{2}+y, 2-z$		2	2.80	2.59	<i>o</i>
I $1-x, -\frac{1}{2}+y, 1-z$		5	2.81	2.60	<i>o</i>
II $1-x, -\frac{1}{2}+y, 1-z$		4	2.70	2.46	<i>o</i>
II $1-x, \frac{1}{2}+y, 1-z$		4	2.70	2.46	<i>o</i>
H <sub>2</sub> O $x, y, 1+z$		1	2.72	2.72	<i>y</i>
II $1-x, -\frac{1}{2}+y, 2-z$		1	2.70	2.73	<i>y</i>
II $1-x, \frac{1}{2}+y, 2-z$		1	2.73	2.73	<i>y</i>
I $-1+x, y, 1+z$		1	2.70	2.70	<i>y</i>



parallel to [100] at positions  $y \approx 0$  and  $y \approx \frac{1}{2}$  according to the scheme  $\cdots O(3I)-H \cdots O(20I)H \cdots O(W)-H \cdots O(20II)-H \cdots O(3II)-H \cdots O(3I)-H \cdots$ . They form the hydrophilic part of the structure. Their lengths, indicated in Fig. 3, vary between 2.703 and 2.776 Å.

In Table 7 are listed intermolecular contacts between molecules I and II and neighbouring molecules. Only hydrophobic  $H \cdots H$  interactions  $< 3.0$  Å and hydrophilic  $O \cdots O$  hydrogen bonds were taken into account. In view of considerations by Kitaigorodsky (1961) the overall structure is close-packed, since molecules I and II are both surrounded by 15 neighbours. However, by subtracting the single hydrophilic contacts a less dense packing with 11 neighbours for both molecules is left. For this reason the density has the quite normal value of  $1.14 \text{ g cm}^{-3}$ . Nevertheless, if we neglect the hydrogen bonds and contacts established by means of screw-axis operations, we note a fairly loose packing with six neighbours in which most interactions occur by intervention of the protruding methyl groups C(18) and C(19). Although we cannot offer an adequate explanation for the observed large thermal motions of many skeleton carbon atoms we suggest that the loose packing is somehow correlated with the unusual thermal behaviour of these atoms.

All calculations were performed on an I.B.M. 360/65 computer of the University of Leiden. The authors are indebted to Dr G. C. Verschoor for his critical survey of the data set and for his comments concerning the refinement of the structure.

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