

## The Structure of 19*R*-Methoxy-5,19-methyleneoxido-17 $\beta$ -acetoxy-5 $\beta$ -androstan-3-one

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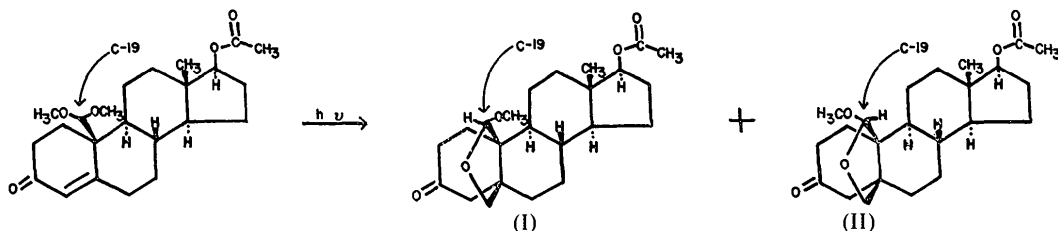
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$C_{23}O_5H_{34}$ , monoclinic,  $P2_1$ ,  $a = 10.098$  (4),  $b = 7.394$  (2),  $c = 15.916$  (7) Å,  $\beta = 116.60$  (5)°,  $Z = 2$ ,  $\rho_{calc} = 1.221$  g cm<sup>-3</sup>. The compound was the major product from the ultraviolet irradiation of 19,19-dimethoxy-17 $\beta$ -acetoxy-4-androsten-3-one. Upon irradiation, ring closure occurred between one of the methoxy groups and C(5) with the consequence that the *A/B* ring junction is *cis*. In the major product the other methoxy group on C(19) has the *R* stereoconfiguration, *i.e.* it is directed over ring *B*. The crystals studied were twinned unequally, so that the observed data were easily corrected for intensity contributions from the minor twin.

### Introduction

The ultraviolet irradiation of 19,19-dimethoxy-17 $\beta$ -acetoxy-4-androsten-3-one gave a major and a minor product, which were thought to be epimers differing only in the configuration at carbon C(19) (Jeger & Wehrli, 1972). The reaction is shown below.



An X-ray investigation of the major photoproduct was undertaken in order to determine the stereoconfiguration and confirm the proposed structure. The crystals studied were obtained from Drs Oskar Jeger and H. Wehrli of the ETH of Zürich, Switzerland, and Dr Bernhard Witkop of the National Institutes of Health. Precession and Weissenberg photographs showed  $2/m$  reciprocal lattice symmetry and the systematic absences ( $0k0$  missing with  $k$  odd) of space group  $P2_1$  or  $P2_1/m$ . The photographs also revealed the presence of a minor twin. The statistical distribution of  $|E|$  values and the value  $Z = 2$  suggested by a density calculation indicated the space group  $P2_1$ , and the structure determination and refinement were successfully carried out in this space group.

The setting angles of 12 general reflections were determined on an automatic four-circle diffractometer, and the lattice parameters were determined from a least-squares fit to these setting angles. The data were collected using Cu  $K\alpha$  radiation ( $\lambda_{avg} = 1.5418$  Å) and the  $\theta$ - $2\theta$  scan technique. A total of 1852 reflections were measured in the range  $0 < 2\theta \leq 125^\circ$ ; all reflections were retained in the least-squares refinement.

The nature of the twinning is shown in Fig. 1. Exact coincidence of reciprocal lattice points from the major and minor twins occurs for all  $hk0$  reflections, but corrections can be made directly, because the coincident reflections have the same indices in the reciprocal lattices of both twins. Measurements of the intensities of 37 reflections from the minor twin showed that those

intensities were 4.5% of the intensities of the corresponding reflections from the major twin. The  $hk7$  and  $hk14$  reflections of the major twin are in near-coincidence with minor-twin reflections of differing indices. The following equations give the corrections for these reflections, assuming exact coincidence,

$$I_{hk7} = \frac{I_{hk7}^o - KI_{(h+4)k7}^o}{1 - K^2}$$

$$I_{(h+4)k7} = I_{(h+4)k7}^o - KI_{hk7}$$

and similarly for the  $hk14$  reflections.  $K$  is the factor 0.045,  $I$  is a true intensity, and  $I^o$  is an observed intensity, where all indices refer to the reciprocal lattice of the major twin. Corrections thus calculated were of consequence only for reflections of low intensity. Since such corrections were only approximate in the actual case of near-coincidence, it was thought best to neglect the corrections for  $hk7$  and  $hk14$ .

Lorentz and polarization corrections were applied to the measured intensities, which were approximately scaled to an absolute level by means of a  $K$ -curve. Normalized structure factor magnitudes,  $|E|$ , were then derived for use in the phase determination. Values for the phases of a basic set of 83 reflections were obtained by the symbolic addition procedure for noncentro-

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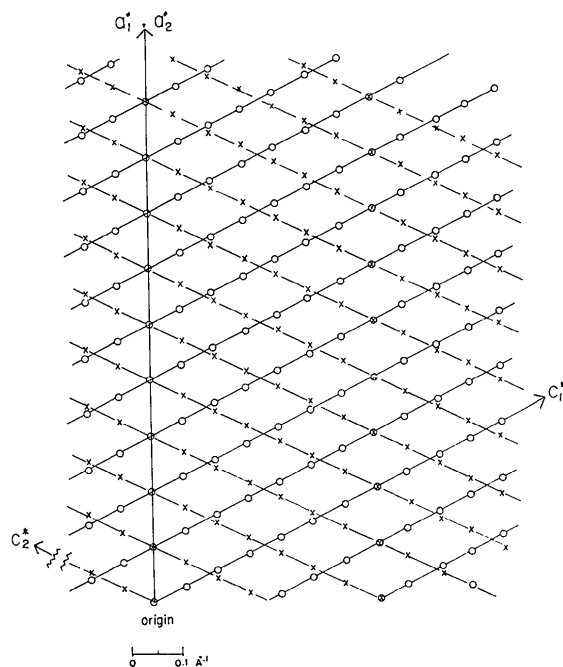


Fig. 1. The  $h0l$  net of the reciprocal lattices of the major and minor twins. Major twin lattice points are shown as circles and minor twin points as crosses. This diagram is representative of all nets perpendicular to the  $b$  direction.

symmetric crystals (Karle & Karle, 1966). The initial assignment of four phases and three symbols is given in Table 1, along with the phases given the symbols in the tangent refinement which led to the correct structure. This refinement assigned phases to 616 reflections of  $|E|$  value greater than 1.0. Table 1 also shows the final values of the phases as given by the least-squares refinement.

Table 1. Phases used to initiate the symbolic addition procedure

			Initial assignment	Least-squares value	$ E $	
5	0	9	} Origin	0.0°	3.68	
2	0	-1		0.0	2.77	
1	-1	-1		180.0	2.68	
5	-5	-6	(Enantiomorph)	90.0	89.8	2.73
8	0	5	} (A)	180.0	3.11	
2	0	-2		180.0	2.39	
1	-2	-12		-135.0	2.55	

Two cycles of full-matrix isotropic least-squares refinement followed by three cycles of anisotropic refinement led to difference maps which revealed the positions of 26 hydrogen atoms. Atomic scattering factors were taken from *International Tables for X-ray Cryst-*

Table 2. Fractional coordinates and thermal parameters with standard deviations

The thermal parameters are of the form  $T = \exp[-\frac{1}{4}(B_{11}h^2a^{*2} + B_{22}k^2b^{*2} + B_{33}l^2c^{*2} + 2B_{12}hka^*b^* + 2B_{13}hla^*c^* + 2B_{23}klb^*c^*)]$ .

The standard deviations are those calculated by the least-squares program.

	$x$	$y$	$z$	$B_{11}$	$B_{22}$	$B_{33}$	$B_{12}$	$B_{13}$	$B_{23}$
C(1)	0.3164 (7)	0.4820 (9)	0.1596 (4)	5.4 (3)	3.6 (3)	3.4 (3)	-0.0 (3)	1.1 (2)	0.0 (2)
C(2)	0.1675 (6)	0.5576 (10)	0.1531 (4)	3.6 (3)	6.2 (4)	4.9 (3)	-0.4 (3)	0.8 (2)	1.2 (3)
C(3)	0.1205 (7)	0.7111 (11)	0.0840 (5)	4.2 (3)	6.4 (4)	4.4 (3)	0.6 (3)	0.7 (2)	-1.0 (3)
C(4)	0.2312 (7)	0.8541 (9)	0.0986 (4)	4.4 (3)	3.9 (3)	3.4 (3)	0.6 (3)	0.4 (2)	-0.2 (3)
C(5)	0.3862 (6)	0.7863 (8)	0.1191 (4)	4.5 (3)	3.6 (3)	2.6 (2)	0.1 (2)	1.1 (2)	0.5 (2)
C(6)	0.4949 (7)	0.9456 (8)	0.1547 (4)	5.8 (3)	2.5 (3)	3.2 (3)	-0.1 (2)	2.1 (2)	0.5 (2)
C(7)	0.5362 (6)	1.0003 (8)	0.2555 (4)	4.5 (3)	2.9 (3)	3.4 (2)	0.2 (2)	1.3 (2)	0.4 (2)
C(8)	0.6048 (6)	0.8429 (8)	0.3205 (4)	3.9 (3)	3.0 (3)	2.8 (2)	0.1 (2)	1.4 (2)	0.1 (2)
C(9)	0.5051 (6)	0.6766 (0)	0.2925 (4)	3.7 (3)	2.4 (3)	2.7 (3)	0.2 (3)	1.5 (3)	0.1 (3)
C(10)	0.4418 (6)	0.6213 (8)	0.1878 (4)	4.5 (3)	3.0 (3)	2.8 (2)	0.5 (2)	1.3 (2)	0.1 (2)
C(11)	0.5790 (6)	0.5135 (9)	0.3592 (4)	5.4 (3)	4.1 (3)	2.5 (2)	-1.0 (3)	0.9 (2)	0.2 (2)
C(12)	0.6327 (6)	0.5652 (8)	0.4643 (4)	5.1 (3)	4.1 (3)	2.8 (2)	-0.9 (3)	1.6 (2)	0.2 (3)
C(13)	0.7334 (6)	0.7288 (7)	0.4911 (4)	3.6 (3)	2.7 (3)	3.2 (2)	0.1 (2)	1.8 (2)	0.2 (2)
C(14)	0.6451 (5)	0.8863 (8)	0.4232 (3)	2.7 (3)	3.0 (3)	2.6 (3)	-0.1 (3)	1.1 (3)	-0.1 (3)
C(15)	0.7362 (7)	1.0555 (8)	0.4684 (4)	5.0 (3)	3.6 (3)	3.5 (3)	-0.7 (3)	0.6 (2)	-0.4 (3)
C(16)	0.7974 (7)	1.0224 (10)	0.5767 (4)	5.0 (3)	5.4 (4)	3.0 (3)	-0.3 (3)	-0.2 (2)	-0.2 (3)
C(17)	0.7647 (7)	0.8180 (9)	0.5861 (4)	4.3 (3)	4.8 (4)	2.4 (2)	-0.2 (3)	0.5 (2)	0.0 (3)
C(18)	0.8771 (6)	0.6851 (9)	0.4870 (4)	3.5 (3)	4.8 (4)	6.1 (3)	0.7 (3)	2.1 (2)	1.2 (3)
C(19)	0.5560 (7)	0.5340 (9)	0.1594 (4)	4.9 (3)	5.1 (4)	2.8 (2)	0.9 (3)	1.5 (2)	-0.0 (3)
C(20)	0.3863 (7)	0.7036 (10)	0.0309 (4)	6.5 (3)	5.0 (4)	2.8 (3)	1.3 (3)	1.6 (2)	0.0 (3)
C(21)	0.8025 (8)	0.5188 (14)	0.1816 (5)	5.2 (4)	13.7 (8)	7.5 (5)	1.3 (5)	2.7 (3)	-4.1 (5)
C(22)	0.8764 (9)	0.5986 (12)	0.7083 (4)	7.2 (4)	6.6 (5)	3.3 (3)	-2.0 (4)	1.3 (3)	0.8 (3)
C(23)	1.0235 (8)	0.5395 (13)	0.7880 (5)	6.3 (4)	9.0 (7)	7.0 (4)	-0.2 (4)	-1.1 (3)	3.8 (5)
O(1)	-0.0078 (6)	0.7185 (8)	0.0217 (4)	5.2 (2)	8.4 (4)	7.7 (3)	-0.3 (3)	-1.2 (2)	0.3 (3)
O(2)	0.4949 (5)	0.5614 (7)	0.0611 (2)	6.4 (2)	6.3 (3)	2.8 (2)	1.8 (2)	1.9 (2)	-0.5 (2)
O(3)	0.6979 (4)	0.6096 (7)	0.2066 (3)	4.4 (2)	5.7 (2)	3.9 (2)	0.7 (2)	2.1 (2)	-1.0 (2)
O(4)	0.8928 (4)	0.7475 (6)	0.6659 (3)	4.4 (2)	5.0 (2)	3.1 (2)	-0.7 (2)	0.5 (2)	0.5 (2)
O(5)	0.7603 (6)	0.5260 (9)	0.6853 (4)	7.6 (3)	10.8 (5)	6.1 (3)	-4.0 (3)	1.6 (2)	2.2 (3)

*tallography* (1969). The weighting scheme is described elsewhere in detail (Gilardi, 1973; Jones & Karle, 1974). The hydrogen atoms were then held in fixed positions and assigned the thermal parameters of the atoms to which they were bonded. Two more cycles of anisotropic refinement, including an isotropic correction for secondary extinction, were carried out, leading to an *R* value of 0.075.

Up to this point, the origin along the **b** direction of the unit cell had been specified by fixing the *y* coordinate of one atom in the molecule. The final values of the estimated standard deviations in the *y* coordinates of the atoms not fixed were found to average 0.008 Å, while the average deviations for the *x* and *z* coordinates were 0.006 Å. In addition, the *y* coordinates of all the atoms were strongly correlated, with correlation coefficients ranging between 0.3 and 0.5. This apparent ill behavior among the *y* coordinates is not a reflection of errors in the data, but is an indication that the origin along **b** is not adequately specified by fixing the *y* coordinate of just one atom in an equal-atom structure of this size. A more successful origin designation can be obtained by fixing the *y* coordinate of the centroid of the entire molecule. This was effectively accomplished by constraining the sum of *y* coordinates to have a constant value equal to the value of this sum at the conclusion of the previous refinement cycle. A repeat of the final cycle of refinement, with this constraint added, then gave the same estimated standard deviations for *x*, *y* and *z* coordinates, 0.006 Å. Correlation among the *y* coordinates was greatly reduced with all correlation coefficients less than 0.3. The final *R* index was unchanged. The final positions and thermal

parameters of the heavy atoms as determined by the constrained refinement are given in Table 2.

The *x* and *z* coordinates shown are essentially unchanged from the results of the unconstrained refinement. The *y* coordinates, however, show a systematic change: with one exception, all are shifted by  $-0.0002$  to  $-0.0005$  fractional units. The exception is C(8), the atom whose *y* coordinate was fixed to specify the origin in the previous refinement cycle. Its shift was  $+0.0004$  units. Bond lengths and angles are shown in Fig. 2. The only significant changes over the results of the un-

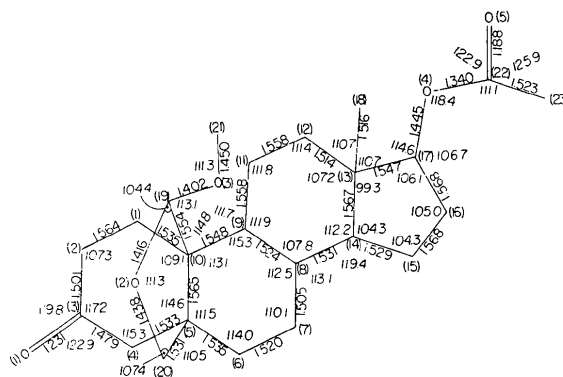


Fig. 2. Bond lengths and angles. Ten angles not shown in the diagram are: C(10)–C(1)–C(2), 115.0°; C(20)–C(5)–C(4), 110.8°; C(20)–C(5)–C(10), 100.5°; C(4)–C(5)–C(6), 108.7°; C(1)–C(10)–C(9), 112.4°; C(1)–C(10)–C(19), 105.0°; C(19)–C(10)–C(5), 101.6°; C(12)–C(13)–C(17), 115.7°; C(18)–C(13)–C(14), 112.9°; and O(3)–C(19)–O(2), 111.7°. Standard deviations in the bond lengths range from 0.006 to 0.009 Å, and deviations in the angles range from 0.3 to 0.7°.

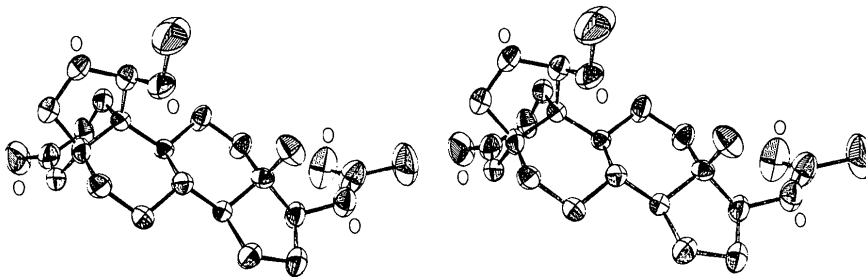


Fig. 3. A stereoisometric representation of the molecule. Figs. 3 and 4 were drawn with the aid of the *ORTEP* computing program (Johnson, 1965).

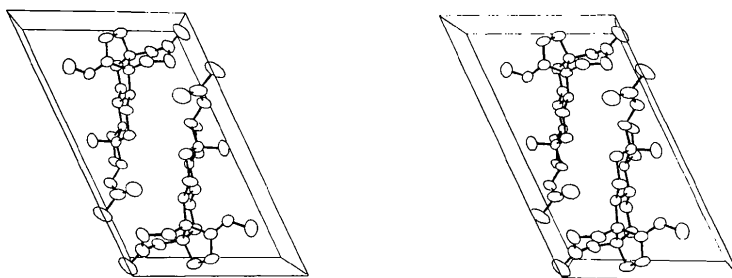


Fig. 4. A stereoisometric representation of the molecular packing. The axial directions are **a** →, **c** ↖, and **b** points away from the viewer.

constrained refinement are in the neighborhood of C(8), where bond lengths changed by as much as 0.004 Å and angles changed by as much as 0.3°. While these changes are not large as compared to the estimated standard deviations, they are an indication of errors which may be encountered if the origin is not well specified.\*

### Results and discussion

The stereodiagram of Fig. 3 shows the molecular configuration of the major product, with the methoxy group attached to C(19) pointing towards C(18), *i.e.* the *R* stereoconfiguration (photoproduct (I) in the reaction shown above). The *A/B* ring junction is necessarily *cis*, while the *trans* junction predominates among the saturated androstanes whose crystal structures have thus far been reported (see *e.g.* Duax, 1972). The *B/C* and *C/D* ring junctions are both *trans*. Other than requiring a *cis A/B* junction, the addition of the five-membered ring (ring *AB*) between C(5) and C(10) flattens rings *A* and *B* near their junction. The torsional angles, given in Table 3, are 5 to 10° smaller than normal in this region. In ring *C*, the torsional angles at C(8)–C(14) and C(14)–C(13) show increased puckering in the ring. This phenomenon may be occasioned by some repulsion between O(3) and H(8). The O(3)···H(8) separation is 2.21 Å.

For ring *D*, the value of the pseudorotational angle  $\Delta$  is +5.8° (Altona, Geise & Romers, 1968). The conformation of ring *D* is closer therefore to a half-chair ( $\Delta=0^\circ$ ) than to a  $\beta$ -envelope ( $\Delta=+36^\circ$ ). The heterocyclic ring *AB* has a value of +23.0° for  $\Delta$ , thus it is closer to an envelope conformation with atom C(5) out of the plane of the other four atoms.

The methyl group in the methoxy moiety on C(19) is *trans* with respect to C(10). The torsional angle C(10)C(19)O(3)C(21) is +177°.

A stereoisomer of the molecular packing is given in Fig. 4. No unusual contacts were found, the shortest contact distance being a C···O distance of 3.49 Å.

\* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30266 (10 pp.). Copies may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. Torsion angles around the rings of the steroid nucleus

The angle ABCD is positive if, when looking from B to C, a clockwise rotation of A superimposes it on D.

Ring A	{	C(10)–C(1)–C(2)–C(3)	57.1 (6)°
		C(1)–C(2)–C(3)–C(4)	–51.6 (8)
		C(2)–C(3)–C(4)–C(5)	46.3 (8)
		C(3)–C(4)–C(5)–C(10)	–41.5 (7)
		C(4)–C(5)–C(10)–C(1)	44.9 (6)
Ring B	{	C(5)–C(10)–C(1)–C(2)	–54.6 (6)
		C(10)–C(5)–C(6)–C(7)	–52.2 (6)
		C(5)–C(6)–C(7)–C(8)	58.7 (6)
		C(6)–C(7)–C(8)–C(9)	–55.8 (6)
		C(7)–C(8)–C(9)–C(10)	49.7 (6)
Ring C	{	C(8)–C(9)–C(10)–C(5)	–43.0 (6)
		C(9)–C(10)–C(5)–C(6)	43.0 (6)
		C(11)–C(9)–C(8)–C(14)	–55.8 (5)
		C(12)–C(11)–C(9)–C(8)	53.1 (6)
		C(13)–C(12)–C(11)–C(9)	–54.2 (6)
Ring D	{	C(14)–C(13)–C(12)–C(11)	57.1 (6)
		C(8)–C(14)–C(13)–C(12)	–62.9 (5)
		C(9)–C(8)–C(14)–C(13)	61.9 (5)
		C(17)–C(13)–C(14)–C(15)	45.9 (5)
		C(13)–C(14)–C(15)–C(16)	–36.2 (6)
Ring AB	{	C(14)–C(15)–C(16)–C(17)	11.8 (7)
		C(15)–C(16)–C(17)–C(13)	17.1 (7)
		C(16)–C(17)–C(13)–C(14)	–38.0 (5)
		C(19)–C(10)–C(5)–C(20)	36.6 (5)
		C(10)–C(5)–C(20)–O(2)	–26.6 (6)
Ring AB	{	C(5)–C(20)–O(2)–C(19)	5.0 (7)
		C(20)–O(2)–C(19)–C(10)	19.4 (7)
		O(2)–C(19)–C(10)–C(5)	–35.1 (6)

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