Crystal Structure of 2α,3α-Epithio-5α-androstan-17β-ol (*R*)-*S*-Oxide

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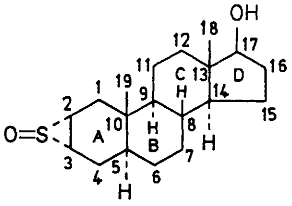
The crystal structure of the title compound (I) has been determined by three-dimensional *X*-ray analysis from diffractometer data. Crystals are othorhombic, $a = 22.806(5)$, $b = 6.276(2)$, $c = 11.978(3)$ Å, $Z = 4$, space group $P2_12_12_1$. The structure was solved by the heavy atom method and refined by full-matrix least-squares calculations to R of 0.057 for 2 065 independently observed reflections. Hydrogen atoms were located from a difference-Fourier synthesis. All the ring junctions are *trans,trans*. Rings B and C of the steroid skeleton have regular chair and rings A and D have distorted half-chair conformation.

As part of a continuing investigation into the structure–activity relationship in thiosteroid derivatives,[1,2] the synthesis and reactions of 2α,3α-epithio-5α-androstan-17β-ol (*R*)-*S*-oxide (1) were recently investigated.[3,4] We have previously determined the structures of 2α,3α-epithio-5α-androstan-17β-yl *p*-bromobenzoate [5] and 2α,3α-epithio-5α-androst-6-en-17β-yl *p*-bromobenzoate,[6] and found that introduction of the thiiran ring has some influence on the conformation of ring A. The present crystal structure determination was carried out in order to elucidate the detailed stereochemistry of (1), particularly the direction of the S–O bond at the sulphur atom in the thiiran ring.



(1)

EXPERIMENTAL

Crystals of (1) were prepared [7] and recrystallized from methanol as colourless prisms, m.p. 159—161 °C, elongated along the *b* axis. Preliminary space-group data were determined from Weissenberg and precession photographs by use of Cu-K_α ($\lambda = 1.5418$ Å) radiation, and accurate unit-cell dimensions were obtained by least-squares refinement of the setting angles of 20 reflections measured by automatic diffractometer.

Crystal Data.—$C_{19}H_{30}O_2S$, $M = 322.5$. Orthorhombic, $a = 22.806(5)$, $b = 6.276(2)$, $c = 11.978(3)$ Å, $U = 1\,714$ Å^3, $D_m = 1.244$ (by flotation), $Z = 4$, $D_c = 1.249$ g cm^{-3}, $F(000) = 704$. Space group $P2_12_12_1$ (D_2^4, No. 19), from systematic absences: $h00$ for h odd, $0k0$ for k odd, and $00l$ for l odd. Mo-K_α radiation, $\lambda = 0.710\,7$ Å; μ(Mo-K_α) $= 1.933$ cm^{-1}.

Three-dimensional intensity data were collected on a Hilger and Watts automatic four-circle Y 290 diffractometer controlled by a PDP 8 computer. Integrated

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[2] K. Takeda, T. Komeno, S. Hayashi, S. Ishihara, H. Itani, H. Iwakura, A. Tanaka, and T. Miyake, *Ann. Report Shionogi Research Laboratory*, 1969, **19**, 1.

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[4] M. Kishi, S. Ishihara, and T. Komeno, *Tetrahedron*, 1974, **30**, 2135.

[5] K. Utsumi-Oda and H. Koyama, *J.C.S. Perkin II*, 1973, 1866.

[6] K. Utsumi-Oda and H. Koyama, *J.C.S. Perkin II*, 1975, 993.

[7] S. Ishihara, ref. 5.

intensities were measured for $\theta < 27.5°$ by the θ—2θ scan technique with Mo-K_α radiation and a scintillation counter (with a Zirconium filter and pulse-height analyser). Each reflection was integrated in 80 steps of 0.01°, and a standard reflection monitored every 10 reflections. Scan counts (P) and background counts (B_1, B_2) were combined to yield the integrated intensities $I = P - 2(B_1 + B_2)$.

A total of 2 286 independent reflections were recorded, of which 2 065 having $I > 3\sigma(I)$ were considered observed. All intensities were corrected for Lorentz and polarization factors, and structure amplitudes were derived. No absorption corrections were applied since the specimen was considered to be sufficiently small (0.55 × 0.50 × 0.55 mm).

Structure Analysis.—The structure was solved by the SEARCHER programme for automatic heavy-atom analysis, written [8,9] for the CDC 3600 computer (later modified for CDC 6600 computer). Initial co-ordinates for the sulphur atom were easily derived from a three-dimensional Patterson synthesis. The atomic co-ordinates of 21 light atoms, which were treated as carbon atoms, were found from the first cycle of the SEARCHER programme (CDC 6600 computer).

The co-ordinates of the 22 atoms from the first SEARCHER cycle were refined [10] by full-matrix least-squares calculations. After three cycles, with isotropic temperature factors, R was 0.093. At this stage, a three-dimensional difference-Fourier synthesis was calculated and the positions of the 30 hydrogen atoms were found. The final five cycles of full-matrix least-squares refinement, which were carried out with anisotropic temperature factors, decreased R to 0.057 for the 2 084 observed reflections. In this refinement the function minimized was $\Sigma w(F_o - F_c)^2$ with unit weights; hydrogen atoms were included in the least-squares calculations with isotropic temperature factors (B fixed at 1.948 Å^2).

TABLE 1

Final fractional atomic co-ordinates (× 10^4), with estimated standard deviations in parentheses

Atom	x	y	z
S	4 546(0)	−546(2)	6 583(1)
O(1)	5 165(1)	−1 098(6)	6 258(3)
O(2)	73(1)	−848(6)	5 409(3)
C(1)	3 451(1)	−528(8)	5 387(4)
C(2)	4 104(1)	24(7)	5 335(3)
C(3)	4 324(1)	1 953(8)	5 915(4)
C(4)	3 913(1)	3 451(8)	6 489(5)
C(5)	3 297(1)	2 528(7)	6 688(3)
C(6)	2 893(2)	4 242(8)	7 123(4)
C(7)	2 275(1)	3 448(8)	7 350(4)
C(8)	2 012(1)	2 366(6)	6 336(3)
C(9)	2 424(1)	557(7)	5 928(3)
C(10)	3 051(1)	1 387(6)	5 639(3)
C(11)	2 143(1)	−797(8)	5 001(4)
C(12)	1 522(1)	−1 566(8)	5 267(4)
C(13)	1 130(1)	277(7)	5 594(3)
C(14)	1 410(1)	1 414(6)	6 598(3)
C(15)	922(2)	2 845(8)	7 058(4)
C(16)	364(1)	1 550(9)	6 862(4)
C(17)	538(1)	−388(8)	6 143(4)
C(18)	1 014(2)	1 743(10)	4 613(4)
C(19)	3 044(2)	2 842(9)	4 623(4)

Observed and calculated structure amplitudes and anisotropic thermal parameters are listed in Supplementary Publication No. SUP 21926 (7 pp., 1 microfiche).* Atomic scattering factors used in all calculations were taken from ref. 11 for non-hydrogen and from ref. 12 for hydrogen atoms. Final positional parameters, with their estimated standard deviations, are given in Tables 1 and 2.

TABLE 2

Fractional atomic co-ordinates (× 10^3) for the hydrogen atoms, labelled according to the atom to which they are bonded

Atom	x	y	z
H(1a)	336	−109	465
H(1b)	339	−155	581
H(2)	433	−30	464
H(3)	463	265	562
H(4a)	389	477	600
H(4b)	406	385	707
H(5)	330	145	724
H(6a)	303	491	769
H(6b)	291	528	662
H(7a)	206	445	747
H(7b)	225	227	800
H(8)	200	351	573
H(9)	246	−39	652
H(11a)	217	16	425
H(11b)	235	−183	482
H(12a)	140	−246	460
H(12b)	151	−266	583
H(14)	147	37	718
H(15a)	91	431	665
H(15b)	97	333	775
H(16a)	7	252	646
H(16b)	15	119	761
H(17)	59	−166	664
H(18a)	81	109	400
H(18b)	84	300	474
H(18c)	132	266	434
H(19a)	289	202	396
H(19b)	285	408	473
H(19c)	337	347	444
H[O(2)]	12	−167	493

DISCUSSION

The configuration of the molecule is illustrated [13] in Figure 1. The steroid skeleton consists of the thiiran ring and the basic 5α-androstane moiety with rings A—D *trans*-connected. Atoms C(18), C(19), and O(2) are

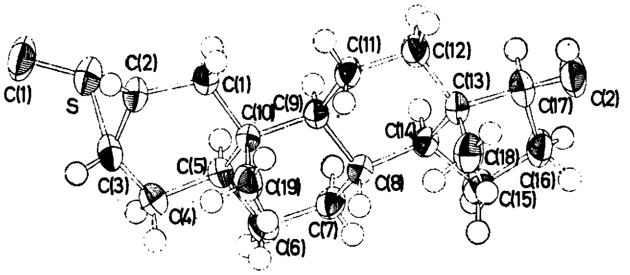

FIGURE 1 An ORTEP drawing of the molecule, showing the atom numbering system used

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1976, Index issue.

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on the β side of the steroid skeleton, while the sulphur atom is on the α side.

Intramolecular bond distances and angles are given in Table **3**, together with their estimated standard deviations computed from the least-squares residuals.

TABLE 3

Interatomic distances (Å) and angles (°), with standard deviations in parentheses

(*a*) Bond distances

S–O(1)	1.503(3)	C(8)–C(14)	1.529(5)
S–C(2)	1.839(4)	C(9)–C(10)	1.561(5)
S–C(3)	1.832(5)	C(9)–C(11)	1.537(6)
O(2)–C(17)	1.407(5)	C(10)–C(19)	1.522(6)
C(1)–C(2)	1.530(5)	C(11)–C(12)	1.528(5)
C(1)–C(10)	1.538(6)	C(12)–C(13)	1.514(6)
C(2)–C(3)	1.483(7)	C(13)–C(14)	1.537(6)
C(3)–C(4)	1.495(7)	C(13)–C(17)	1.559(5)
C(4)–C(5)	1.538(5)	C(13)–C(18)	1.515(7)
C(5)–C(6)	1.509(6)	C(14)–C(15)	1.534(6)
C(5)–C(10)	1.550(6)	C(15)–C(16)	1.527(6)
C(6)–C(7)	1.518(6)	C(16)–C(17)	1.542(7)
C(7)–C(8)	1.515(6)		
C(8)–C(9)	1.551(5)		

(*b*) Valency angles

O(1)–S–C(2)	110.4(2)	C(1)–C(10)–C(9)	109.0(3)
O(1)–S–C(3)	110.0(2)	C(1)–C(10)–C(19)	108.6(3)
C(2)–S–C(3)	47.6(2)	C(5)–C(10)–C(9)	107.7(3)
C(2)–C(1)–C(10)	114.0(3)	C(5)–C(10)–C(19)	112.0(3)
S–C(2)–C(1)	117.1(3)	C(9)–C(10)–C(19)	111.4(3)
S–C(2)–C(3)	65.9(2)	C(9)–C(11)–C(12)	114.2(3)
C(1)–C(2)–C(3)	119.7(3)	C(11)–C(12)–C(13)	111.0(3)
S–C(3)–C(2)	66.4(2)	C(12)–C(13)–C(14)	108.1(3)
S–C(3)–C(4)	120.7(3)	C(12)–C(13)–C(17)	114.5(3)
C(2)–C(3)–C(4)	121.0(3)	C(12)–C(13)–C(18)	111.4(3)
C(3)–C(4)–C(5)	114.0(4)	C(14)–C(13)–C(17)	98.8(3)
C(4)–C(5)–C(6)	110.0(3)	C(14)–C(13)–C(18)	113.4(4)
C(4)–C(5)–C(10)	112.2(3)	C(17)–C(13)–C(18)	109.7(3)
C(6)–C(5)–C(10)	112.8(3)	C(8)–C(14)–C(13)	113.1(3)
C(5)–C(6)–C(7)	113.2(4)	C(8)–C(14)–C(15)	119.8(3)
C(6)–C(7)–C(8)	111.7(3)	C(13)–C(14)–C(15)	104.5(3)
C(7)–C(8)–C(9)	109.9(3)	C(14)–C(15)–C(16)	103.7(4)
C(7)–C(8)–C(14)	111.4(3)	C(15)–C(16)–C(17)	106.9(3)
C(9)–C(8)–C(14)	108.7(3)	O(2)–C(17)–C(13)	116.3(4)
C(8)–C(9)–C(10)	112.3(3)	O(2)–C(17)–C(16)	108.4(3)
C(8)–C(9)–C(11)	112.3(3)	C(13)–C(17)–C(16)	104.3(3)
C(10)–C(9)–C(11)	113.9(3)		
C(1)–C(10)–C(5)	107.8(3)		

(*c*) Bond distances (Å) associated with hydrogen positions

C(1)–H(1a)	0.97	C(12)–H(12a)	1.00
C(1)–H(1b)	0.83	C(12)–H(12b)	0.97
C(2)–H(2)	1.00	C(14)–H(14)	0.97
C(3)–H(3)	0.89	C(15)–H(15a)	1.04
C(4)–H(4a)	1.01	C(15)–H(15b)	0.89
C(4)–H(4b)	0.82	C(16)–H(16a)	1.01
C(5)–H(5)	0.95	C(16)–H(16b)	1.04
C(6)–H(6a)	0.86	C(17)–H(17)	1.00
C(6)–H(6b)	0.89	C(18)–H(18a)	0.94
C(7)–H(7a)	0.81	C(18)–H(18b)	0.89
C(7)–H(7b)	1.08	C(18)–H(18c)	0.96
C(8)–H(8)	1.01	C(19)–H(19a)	1.00
C(9)–H(9)	0.93	C(19)–H(19b)	0.89
C(11)–H(11a)	1.07	C(19)–H(19c)	0.87
C(11)–H(11b)	0.84	O(2)–H[O(2)]	0.78

Mean estimated standard deviations are *ca.* 0.006 Å and 0.3°. Most observed bond distances and angles are comparable to those found in other 5α-androstane type steroids.[14-21] Two or three differences which appear to be significant in terms of the estimated standard deviations are more likely to indicate a slight underestimation of errors.

TABLE 4

Equations of planes and in square brackets displacements (Å) of the atoms from the mean planes: *X*, *Y*, and *Z* are orthogonal co-ordinates (Å)

Plane (I): S, C(2), C(3)

$$-0.8264X + 0.0200Y + 0.5626Z = -4.1399$$

[O(1) −1.39, H(C2) −0.90, H(C3) −0.76]

Plane (II): C(1)—(4)

$$-0.1369X + 0.5126Y - 0.8475Z = -6.7092$$

[C(1) −0.00, C(2) 0.01, C(3) −0.01, C(4) 0.00, C(5) −0.29, C(10) 0.47]

Plane (III): C(6), C(7), C(9), C(10)

$$-0.3710X + 0.6066Y - 0.7030Z = -6.8168$$

[C(5) −0.64, C(6) −0.01, C(7) 0.01, C(8) 0.67, C(9) −0.01, C(10) 0.01]

Plane (IV): C(8), C(11), C(12), C(14)

$$-0.3824X + 0.5558Y - 0.7380Z = -6.5506$$

[C(8) 0.01, C(9) −0.60, C(11) −0.01, C(12) 0.01, C(13) 0.71, C(14) −0.01]

Plane (V): C(15)—(17)

$$-0.1836X + 0.5271Y - 0.8296Z = -6.4596$$

[C(13) 0.51, C(14) −0.22]

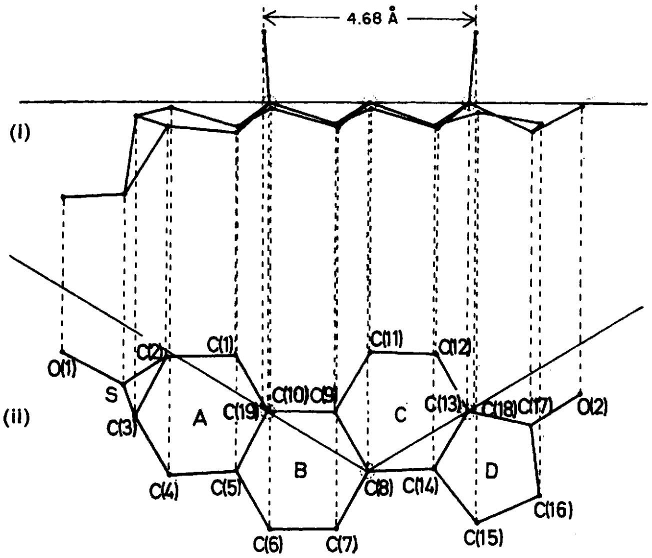

FIGURE 2 Projection of the molecule (i) and parallel to and (ii) in the plane of C(8), C(10), and C(13)

The mean C–C single-bond distance in the steroid skeleton is 1.530 Å. The C–S bonds (1.839 and 1.832 Å) in the thiiran ring are significantly longer than the similar distances (1.775 and 1.778 Å) found in 2α,3α-epithio-5α-androstan-17β-yl *p*-bromobenzoate.[5] The C–H distances range from 0.81 to 1.08 Å, the mean

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(0.95 Å) being shorter than the internuclear separations (1.08 Å) obtained spectroscopically.[22]

The bond angles in the thiiran ring are close to their expected value. The mean interbond angle in rings A—C is 111.4°, except for the angles at atoms C(2) and C(3), which are slightly, but not significantly, greater than the normal tetrahedral angle of 109.4°. The angles in the five-membered ring D are very similar to the corresponding angles in other steroids. Maximum distortion of bond angles occurs at C(13) in ring D. The angle C(14)–C(13)–C(17) of 98.8° is an indication of strain imposed at the C–D junction.

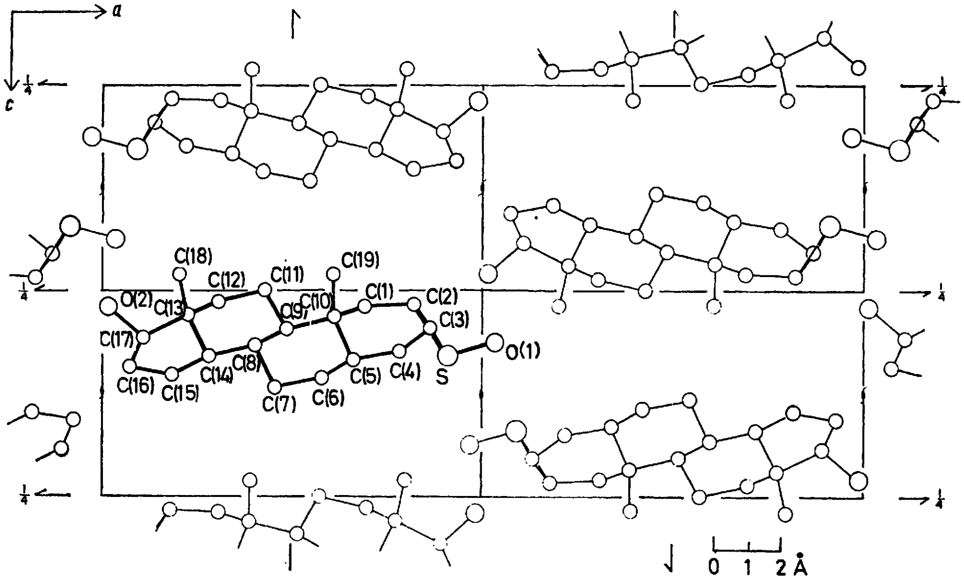

FIGURE 3 Packing of the structure viewed down the *b* axis

The displacements of atoms from some least-squares mean planes are listed in Table 4. Ring A of the steroid skeleton has a distorted half-chair conformation. Atoms C(1)—(4) are planar and atoms C(5) and C(10) are displaced by −0.29 and 0.47 Å to opposite sides to this plane. Rings B and C are in the normal chair form, while ring D has a conformation somewhere between a half-chair and a β envelope.

In order to obtain detailed information on the molecular shape and the conformational features we have calculated the displacements from the planes through C(8), C(10), and C(13) in the steroid skeleton (Figure 2). The geometry of molecule (1) is somewhat different from that of the previously reported 2α,3α-epithio-5α-androstan-17β-yl *p*-bromobenzoate. The largest differences occur in the C–S bond length, and are due to the presence of the S–O bond in (1). The distance (4.680 Å) between the C(18) and C(19) axial methyl groups is comparable to that found in other steroids. The width of the steroid skeleton, calculated as the distance between C(3) and O(2), is 9.872 Å. The dihedral angle between the thiiran ring and the least-squares plane through atoms C(1)—(4) is *ca.* 110.7°. The torsion angle H(2)–C(2)–C(3)–H(3) is *ca.* −0.1°.

The packing of molecules in the unit-cell is illustrated in Figure 3. The average plane of the steroid skeleton is nearly parallel to the *ac* plane of the cell. The two molecules are linked by the intermolecular hydrogen bond, O(1) · · · H–O(2^{I}) (2.775 Å). All intermolecular distances were calculated, and the most significant contacts (<3.60 Å) are given in Table 5. The molecular packing is efficient with several contacts approaching the sum of the van der Waals radii; the shortest non-hydrogen contact is C(3) · · · O(2^{III}) 3.378 Å.

TABLE 5

Intermolecular distances (<3.600 Å)

S · · · O(2^{I})	3.501	O(1) · · · C(18^{III})	3.508
O(1) · · · O(2^{I})	2.775	C(2) · · · O(2^{I})	3.542
O(1) · · · C(4^{II})	3.432	C(3) · · · O(2^{III})	3.378

Roman numerals as superscripts refer to the following equivalent positions relative to the reference molecule at x, y, z:

I $\frac{1}{2} + x, -\frac{1}{2} - y, 1 - z$
II $1 - x, -\frac{1}{2} + y, \frac{3}{2} - z$
III $\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$

We thank Dr. T. Komeno for suggesting this investigation, and S. Ishihara for the preparation of suitable crystals.

[6/1390 *Received*, 16*th July*, 1976]

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