Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1257). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O. & Taylor, R. (1983). *Acc. Chem. Res.* **16**, 146–153.
Alvarez-Larena, A., Piniella, J. F., Verdaguer, X., Moyano, A., Pericas, M. A. & Riera, A. (1993). *Z. Kristallogr.* **203**, 107–109.
Lautens, M., Ren, Y. & Delanghe, P. H. M. (1994). *J. Am. Chem. Soc.* **116**, 8821–8822.
Sheldrick, G. M. (1994). *SHELXTL/PC Users Manual.* Version 5.0. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Siemens (1994). *XSCANS. X-ray Single Crystal Analysis System.* Version 2.1. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Acta Cryst. (1997). C**53**, 938–940

3β,4β-Epoxy-5β-androstan-17-one

L. C. R. Andrade,[a] J. A. Paixão,[a] M. J. de Almeida,[a] E. J. Tavares da Silva,[b] M. L. Sá e Melo[c] and A. S. Campos Neves[b]

[a]*Departamento de Física, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, P-3000 Coimbra, Portugal,* [b]*Lab. Química Farmacêutica, Faculdade de Farmácia, Universidade de Coimbra, P-3000 Coimbra, Portugal, and* [c]*Centro de Estudos Farmacêuticos, Lab. Química Farmacêutica, Faculdade de Farmácia, Universidade de Coimbra, P-3000 Coimbra, Portugal. E-mail: jap@pollux.fis.uc.pt*

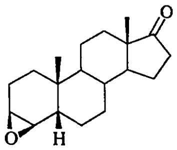
(*Received 10 December 1996; accepted 3 February 1997*)

Abstract

The title compound, $C_{19}H_{28}O_2$, has the configuration of a 5β epimer with an epoxy O atom at 3β,4β. The asymmetric unit contains two molecules with almost identical geometry. Cohesion of the crystal can be attributed to weak intermolecular C—H···O and van der Waals interactions.

Comment

As part of our study of steroids obtained as intermediate products during the synthesis of formestane (Tavares da Silva, Sá e Melo & Campos Neves, 1996), an irreversible aromatase inhibitor which has been shown to be very effective in the treatment of breast cancer, the crystal structure of 3β,4β-epoxy-5β-androstan-17-one, (I), was determined by X-ray diffraction analysis.



(I)

The unit cell contains two symmetry-independent molecules, *A* and *B*, with almost identical geometry, and one of these (molecule *A*) is illustrated in Fig. 1. The angle between the least-squares planes defined by rings *B*, *C* and *D* of the two molecules is 59.88 (6)°.

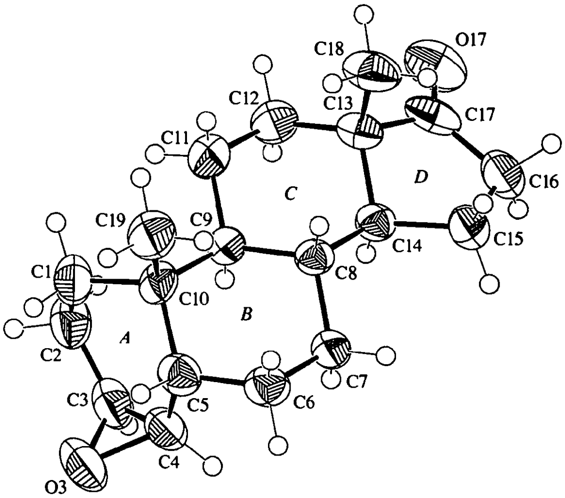


Fig. 1. *ORTEP*II (Johnson, 1976) plot of the title compound (molecule *A*). Displacement ellipsoids are drawn at the 50% probability level except for H atoms, which were given arbitrary radii.

Following Kálman, Argay, Scharfenberg-Pfeiffer, Höhne & Ribár (1991), who studied the isostructuralism of several structures, a test of similarity between the two non-symmetry-related molecules was performed through calculation of the factor

$$I_B^n = \{1 - [(\Sigma\Delta R_i/R)/n]^{0.5}\} \times 100$$

where the sum extends over the nR_i equivalent distances (or angles) of the two molecules. The values obtained are I_B^{25} (distances) = 99.4%, I_B^{23} (valency angles) = 99.5%.

From the X-ray analysis, a β configuration for this epimer was evident, with a *cis* junction between rings *A* and *B*. The values of the bowing angles are 81.53 (9)° (molecule *A*) and 81.97 (9)° (molecule *B*). The corresponding distances between terminal O atoms were found to be 8.929 (4) and 8.904 (4) Å and the values for the pseudo-torsion angles C19—C10—C13—C18 are 1.1 (3) and 2.7 (3)°, respectively. The bond lengths, bond angles and conformational details of these molecules are very similar to those found for the α epimer (Paixão *et al.*, 1997). Ring *A* is strongly distorted from the normal, slightly flattened, chair conformation of the cyclohexane rings of these steroids; short C2—C3 and C3—C4 distances are also observed [average values of all other C_{sp^3}—C_{sp^3} distances are 1.528 (9) Å for molecule *A* and 1.530 (10) Å for molecule *B*] as well as large values for the bond angles C2—C3—C4 and C3—C4—C5 [average values for all other internal hexane angles are 111 (2)° for both molecules *A* and *B*]. Ring *A* has a conformation intermediate between 1,10-half-chair and 10β-sofa as can be shown by the values of the asymmetry parameters defined by Duax & Norton (1975) [molecule *A* $\Delta C_2(3,4)$ = 5.3 (5), $\Delta C_s(3)$ = 18.8 (4), $\Delta C_2(1,2)$ = 49.5 (5)°; molecule *B* $\Delta C_2(3,4)$ = 5.6 (5), $\Delta C_s(3)$ = 18.8 (4), $\Delta C_2(1,2)$ = 50.2 (4)°]. Rings *B* and *C* have normal, slightly flattened, chair conformations [mean values of torsion angles are 55.5 (8) and 56 (3)°, respectively, for molecule *A*, and 54.7 (7) and 55 (2)° for molecule *B*]. The high values of the valency angles C12—C13—C17 and C8—C14—C15 for both molecules reflect the strain inherent in the *C*/*D* ring junctions. Ring *D* assumes a 14α-envelope conformation as can be seen by the asymmetry parameter ΔC_s (Duax & Norton, 1975) and pseudo-rotation parameters Δ and φ_m (Altona, Geize & Romers, 1968): molecule *A* $\Delta C_s(14)$ = 1.7 (4), φ_m = 45.1 (4), Δ = −32.8 (7)°; molecule *B* $\Delta C_s(14)$ = 3.3 (4), φ_m = 43.9 (3), Δ = −29.2 (7)°.

Cohesion of the crystal is due mainly to van der Waals interactions and weak C—H···O interactions. Details of the hydrogen bonds are given in Table 2. It should be noted that because none of the atoms is a strong enough anomalous scatterer at the Mo *Kα* wavelength, the absolute configuration could not be determined from the X-ray data. Fig. 1 shows the assumed absolute configuration.

Experimental

To prepare the title compound, a stirred solution of a mixture of 5β- and 5α-androst-3-en-17-one (67.5 mg, 0.25 mmol), easily obtained from the available androst-4-ene-3,17-dione in the presence of Zn/AcOH under ultrasonic irradiation (Salvador, Sá e Melo & Campos Neves, 1993), was treated in dichloromethane with 90% formic acid (0.05 cm³, 1.18 mmol) followed by 30% hydrogen peroxide (0.05 cm³, 0.44 mmol) at room temperature for 6 h (thin-layer chromatography). After pH neutralization, the solution was extracted with dichloromethane and the extract washed with aqueous $NaHCO_3$ and water, dried over magnesium sulfate and evaporated to dryness to give a mixture of 3β,4β-epoxy-5β-androstan-17-one and 3α,4α-epoxy-5α-androstan-17-one (69 mg, 96%). The title compound was isolated by slow crystallization, m.p. 408–410 K (from diethyl ether); ν_{max} (KBr)/cm^{-1} 1740; δ_H(500 MHz; $CDCl_3$; Me_4Si) 0.87 (3*H*, *s*, 18-H_3), 0.90 (3*H*, *s*, 19-H_3), 2.08 (1*H*, *ddd*, $J_{16\alpha,16\beta}$ = 19.0, $J_{16\alpha,15\beta}$ = 9.0, $J_{16\alpha,15\alpha}$ = 9.0, 16α-H), 2.46 (1*H*, *ddd*, $J_{16\beta,16\alpha}$ = 19.0, $J_{16\beta,15\beta}$ = 9.0, $J_{16\beta,15\alpha}$ = 1.0, 16β-H), 2.86 (1*H*, *d*, $J_{4\alpha,3\alpha}$ = 3.8, 4α-H), 3.23 (1*H*, *ddd*, $J_{3\alpha,4\alpha}$ = 3.8, $J_{3\alpha,2\alpha}$ = 1.8, $J_{3\alpha,2\beta}$ = 1.8, 3α-H); δ_C(50.3 MHz, $CDCl_3$; Me_4Si) 13.6 (C18), 22.2 (C19), 53.1 (C3), 56.2 (C4), 221.0 (C17); *m*/*z* (EI) 288.2 (M^+, 43.2%).

Crystal data

$C_{19}H_{28}O_2$
M_r = 228.42
Monoclinic
$P2_1$
a = 12.041 (2) Å
b = 10.731 (2) Å
c = 13.011 (2) Å
β = 106.49 (2)°
V = 1611.9 (5) Å^3
Z = 4
D_x = 1.188 Mg m^{-3}
D_m not measured

Mo *Kα* radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 8–15°
μ = 0.075 mm^{-1}
T = 293 (2) K
Parallelepiped
0.56 × 0.37 × 0.12 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
Profile data from ω–2θ scans
Absorption correction: none
4537 measured reflections
3132 independent reflections
2415 reflections with $I > 2\sigma(I)$

R_{int} = 0.0482
θ_{max} = 25.0°
$h = -14 \rightarrow 13$
$k = -12 \rightarrow 12$
$l = -15 \rightarrow 15$
3 standard reflections every 120 reflections intensity decay: 1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.096
S = 1.027
3132 reflections
383 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.053P)^2 + 0.1879P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.107 e Å^{-3}
$\Delta\rho_{min}$ = −0.103 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute configuration: Flack (1983)
Flack parameter = 0.5 (19)

Table 1. *Selected geometric parameters (Å, °)*

C1—C2	1.519 (6)	C13—C17	1.519 (6)
C2—C3	1.484 (5)	C13—C14	1.530 (4)
C3—O3	1.440 (4)	C14—C15	1.533 (5)
C3—C4	1.457 (5)	C15—C16	1.530 (5)
C4—O3	1.459 (4)	C16—C17	1.513 (6)
C4—C5	1.507 (5)	C17—O17	1.209 (4)
C5—C10	1.543 (5)		
C4—C3—C2	120.7 (4)	C8—C14—C15	120.4 (3)
C3—C4—O3	59.2 (2)	O17—C17—C16	124.7 (4)
C3—C4—C5	122.6 (3)	O17—C17—C13	126.4 (4)
C1—C10—C5	107.4 (3)	C16—C17—C13	108.9 (3)
C12—C13—C17	117.0 (3)	C3—O3—C4	60.3 (2)
C10—C1—C2—C3	46.1 (5)	C3—C4—C5—C10	−20.3 (5)
C1—C2—C3—C4	−13.4 (5)	C2—C1—C10—C5	−64.7 (4)
C2—C3—C4—C5	1.4 (6)	C4—C5—C10—C1	49.0 (4)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C6—H6*A*···O3^{i}	0.97	2.554 (5)	3.499 (5)	164.7 (3)
C6′—H6*B*′···O3′^{ii}	0.97	2.564 (4)	3.511 (4)	165.3 (4)
C11′—H11*B*′···O17′^{iii}	0.97	2.572 (6)	3.373 (6)	139.9 (4)

Symmetry codes: (i) $1 - x, y - \frac{1}{2}, 2 - z$; (ii) $1 - x, \frac{1}{2} + y, 1 - z$; (iii) $-x, y - \frac{1}{2}, 1 - z$.

The structure was solved by direct methods. The H atoms were placed at calculated positions and refined as riding using the *SHELXL*93 defaults: O—H = 0.82, C—H = 0.93 Å, U(H) = $1.5U_{\rm iso}$(parent atom). Examination of the crystal structure with *PLATON* (Spek, 1995) showed that there is one small (14 Å^3) solvent-accessible void in the asymmetric unit cell located at (0.425, 0.175, 0.735). However, the very small residual density at the void position excludes the possibility of occupation by a water molecule. All calculations were performed on a Pentium 150 MHz PC running LINUX.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: Enraf–Nonius *SDP-Plus* (Frenz, 1985). Program(s) used to solve structure: *MULTAN*11/82 (Main *et al.*, 1982). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

We are indebted to the Cultural Service of the German Federal Republic Embassy, the Deutscher Akademischer Austauschdienst (DAAD) and the German Agency for Technical Cooperation (GTZ) for the offer of a CAD-4 automatic diffractometer which enabled the experimental work to be carried out. This work was supported by JNICT and the CIÊNCIA program.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1084). Services for accessing these data are described at the back of the journal.

References

Altona, C., Geize, H. J. & Romers, C. (1968). *Tetrahedron*, **24**, 13–32.

Duax, W. L. & Norton, D. A. (1975). In *Atlas of Steroid Structure*, Vol. 1. New York: Plenum.

Enraf–Nonius (1989). *CAD*-4 *Software*. Version 5. Enraf–Nonius, Delft, The Netherlands.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Frenz, B. A. (1985). *Enraf–Nonius SDP-Plus Structure Determination Package*. Version 3.0. Enraf–Nonius, Delft, The Netherlands.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Kálman, A., Argay, G., Scharfenberg-Pfeiffer, D., Höhne, E. & Ribár, B. (1991). *Acta Cryst.* B**47**, 68–77.

Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1982). *MULTAN*11/82. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Universities of York, England, and Louvain, Belgium.

Paixão, J. A., Ramos Silva, M., de Almeida, M. J. M., Tavares da Silva, E. J., Sá e Melo, M. L. & Campos Neves, A. S. (1997). *Acta Cryst.* C**53**, 347–349.

Salvador, J. A. R., Sá e Melo, M. L. & Campos Neves, A. S. (1993). *Tetrahedron Lett.* **34**, 357–360.

Sheldrick, G. M. (1993). *SHELXL*93. *Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

Spek, A. L. (1995). *PLATON. Molecular Geometry Program*. Version of July 1995. University of Utrecht, Utrecht, The Netherlands.

Tavares da Silva, E. J., Sá e Melo, M. L. & Campos Neves, A. S. (1996). *J. Chem. Soc. Perkin Trans.* 1, pp. 1649–1650.

Acta Cryst. (1997). C**53**, 940–942

A Cyclic Monomer of Tetraethyleneglycol Succinate

Leroy Cronin, Madeleine H. Moore, J. Anthony Semlyen and Barry R. Wood

Department of Chemistry, University of York, Heslington, York YO1 5DD, England. E-mail: jas3@york.ac.uk

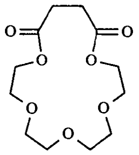
(*Received 10 December 1996; accepted 18 February 1997*)

Abstract

The title compound, 1,4,7,10,13-pentaoxacycloheptadecane-14,17-dione, $C_{12}H_{20}O_7$, was prepared in a mixture of large ether–ester rings and isolated by preparative gel-permeation chromatography. The maximum internal diameter of its cavity was found to be 7.5 Å.

Comment

As part of a general study into large-ring molecules and cyclic polymers (Semlyen, 1986; Clarson & Semlyen, 1993; Semlyen, 1996), we have been developing a method of forming large cyclic esters and ether–esters (Wood, Semlyen & Hodge, 1997; Hamilton & Semlyen, 1997). The synthetic route involves producing a linear polymer from suitable monomers in a polyesterification reaction, then equilibrating the polymer in dilute solution to yield a range of cyclic compounds. These are then separated into a series of either individual compounds or narrow molar mass fractions by preparative gel-permeation chromatography (GPC). A monomeric ether–ester cyclic compound, (I), was recovered from a mixture of $[O(CH_2CH_2O)_4CO(CH_2)_2CO]_x$, where $x = 1$.



(I)

The structure (Fig. 1) indeed demonstrates that the polymer is cyclic with a maximum internal diameter (C3···C8) of 7.55 (1) Å. The ester unit is planar with O4—C7 and O5—C7 bond lengths of 1.350 (8) and 1.199 (9) Å, respectively. The ester O4—C7—O5 angle is 121.4 (7)°. The ether linkages O2—C2 and O2—C3 are 1.431 (10) and 1.390 (9) Å, respectively, with a C2—O2—C3 bond angle of 114.6 (6)°.

The ring contains two planar ester units and two ether units, which are not crystallographically equivalent. The two ether units connected *via* O2 are buckled in the same manner, with O2—C2—C1—O1 and O2—