a glass tube oven at about 543 K under reduced pressure at 2 mmHg.

Crystal data

$C_{28}H_{16}N_2O_4$
M_r = 444.45
Monoclinic
$P2_1/c$
a = 8.3987 (15) Å
b = 6.890 (4) Å
c = 17.8585 (15) Å
β = 90.868 (11)°
V = 1033.3 (7) Å^3
Z = 2
D_x = 1.428 Mg m^{-3}
D_m = 1.425 Mg m^{-3}
D_m measured by flotation in aqueous KI
Mo $K\alpha$ radiation
λ = 0.7107 Å
Cell parameters from 25 reflections
θ = 21.9–24.8°
μ = 0.097 mm^{-1}
T = 296.2 K
Prismatic
0.60 × 0.40 × 0.30 mm
Colorless

Data collection

Rigaku AFC-5*R* diffractometer
ω–2θ scans
Absorption correction: none
3608 measured reflections
3273 independent reflections
1833 reflections with $I > 2\sigma(I)$
R_{int} = 0.016
θ_{max} = 30.0°
h = 0 → 11
k = 0 → 9
l = −24 → 24
3 standard reflections
every 100 reflections
intensity decay: 0.14%

Refinement

Refinement on F
R = 0.049
wR = 0.067
S = 1.145
1833 reflections
154 parameters
H-atom: see text
$w = 1/[\sigma^2(F_o) + 0.0009|F_o|^2]$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

O1—C7	1.196 (2)	C5—C6	1.385 (3)
O2—C14	1.205 (2)	C7—C8	1.480 (3)
N1—C4	1.434 (2)	C8—C9	1.377 (2)
N1—C7	1.409 (2)	C8—C13	1.384 (3)
N1—C14	1.396 (3)	C9—C10	1.384 (3)
C1—C2	1.369 (3)	C10—C11	1.401 (3)
C1—C6	1.378 (3)	C11—C11^i	1.488 (3)
C2—C3	1.382 (3)	C11—C12	1.405 (2)
C3—C4	1.376 (3)	C12—C13	1.371 (3)
C4—C5	1.383 (3)	C13—C14	1.486 (2)
C4—N1—C7	123.7 (2)	C7—C8—C13	108.7 (2)
C4—N1—C14	124.4 (2)	C9—C8—C13	120.6 (2)
C7—N1—C14	111.8 (1)	C8—C9—C10	117.4 (2)
C2—C1—C6	120.3 (2)	C9—C10—C11	123.0 (2)
C1—C2—C3	120.6 (2)	C10—C11—C11^i	120.9 (2)
C2—C3—C4	119.0 (2)	C10—C11—C12	118.3 (2)
N1—C4—C3	119.8 (2)	C11^i—C11—C12	120.9 (2)
N1—C4—C5	119.1 (2)	C11—C12—C13	118.3 (2)
C3—C4—C5	121.1 (2)	C8—C13—C12	122.5 (2)
C4—C5—C6	119.1 (2)	C8—C13—C14	108.3 (2)
C1—C6—C5	119.9 (2)	C12—C13—C14	129.2 (2)
O1—C7—N1	125.0 (2)	O2—C14—N1	125.5 (2)
O1—C7—C8	129.5 (2)	O2—C14—C13	128.7 (2)
N1—C7—C8	105.5 (2)	N1—C14—C13	105.8 (2)
C7—C8—C9	130.8 (2)		

Symmetry code: (i) 1 − x, −y, 1 − z.

H atoms were fixed geometrically and were not included in the refinement procedure.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1995). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

The authors thank Mr Masahiro Takekawa for his help in collecting the diffraction data.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: OA1075). Services for accessing these data are described at the back of the journal.

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Equilin

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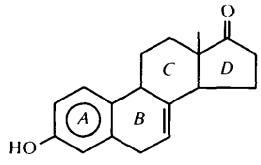
Abstract

3-Hydroxyestra-1,3,5(10),7-tetraen-17-one, $C_{18}H_{20}O_2$, crystallizes in space group $P2_12_12_1$ from ethyl acetate. The planarity of the *B* ring, and the difference in puckering of the *C* and *D* rings from that of estrone, are due to the presence of the C7=C8 double bond, which may explain its function as an inhibitor of human type 1 17β-hydroxysteroid dehydrogenase, instead of being its substrate.

Comment

The title compound, (I), a ring *B* unsaturated estrogen, is a component found in estrogen replacement therapy. It was initially isolated from the urine of a pregnant mare (Girard *et al.*, 1932), and was initially synthesized by Bagli *et al.* (1964) using the spores of *Nocardia restrictus*. It was later synthesized chemically by Stein *et al.* (1969). Recently, it has been shown to be an inhibitor of the conversion of 17β-estrone to 17β-estradiol by human type 1 17β-hydroxysteroid dehydrogenase (17β-HSD1), a key enzyme in the biosynthesis of 17β-estradiol from estrone in human breast tissues (Sawicki *et al.*, 1999). Inhibitors of 17β-HSD1, whose structure has been determined by X-ray crystallography (Ghosh *et al.*, 1995), may be important in regulating estradiol concentrations in breast tissues. This compound provides an excellent starting point from which other potential inhibitors of 17β-HSD1 may be synthesized.



(I)

In the crystal of (I), the *A* and *B* rings of the steroid are nearly coplanar, having a least-squares planarity of 0.102 (2) Å (using C1–C10) and a total puckering amplitude of 0.270 (2) Å (Cremer & Pople, 1975), which can be attributed to the presence of a double bond at C7=C8. This double bond rotates the *C* and *D* rings, which have a least-squares planarity of 0.268 (2) Å (C8, C9 and C11–C17) and a total puckering amplitude of 0.672 (2) Å, about the C7—C8—C9—C11 torsion, from the *anti*-periplanar angle of −179° seen in 17β-estrone (Busetta *et al.*, 1973) to an *anti*-clinal angle of 121°. This change causes a translation of atom O17 by 0.73 Å, with respect to the analogous O atom of 17β-estrone, upon superposition of the *A* rings, and may be responsible for the anti-17β-HSD1 inhibitory property of equilin. The only intermolecular hydrogen bond occurs between O3 and O17′($\frac{1}{2} - x$, $1 - y$, $\frac{1}{2} + z$), at a distance of 2.778 (2) Å.

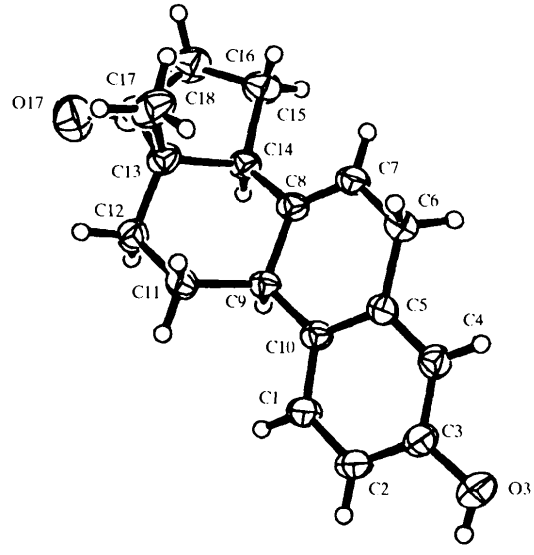


Fig. 1. The molecular structure of equilin. Probability ellipsoids are shown at the 50% level and H atoms are shown as circles of an arbitrary radius. The rotation of the *C* and *D* rings with respect to *A* and *B* due to C7=C8 is demonstrated.

Experimental

Commercially available samples of equilin were crystallized from ethyl acetate by evaporation at room temperature in a loosely closed vial, yielding crystals up to 1.0 mm in size.

Crystal data

$C_{18}H_{20}O_2$
M_r = 268.34
Orthorhombic
$P2_12_12_1$
a = 6.5429 (8) Å
b = 9.0345 (9) Å
c = 23.894 (4) Å
V = 1412.4 (3) Å^3
Z = 4
D_x = 1.262 Mg m^{-3}
D_m not measured
Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 25 reflections
θ = 7.1–13.7°
μ = 0.634 mm^{-1}
T = 293 (2) K
Plate
0.4 × 0.3 × 0.2 mm
Colorless

Data collection

CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
6070 measured reflections
2890 independent reflections
2782 reflections with $I > 2\sigma(I)$
R_{int} = 0.067
θ_{max} = 75.02°
$h = -2 \rightarrow 8$
$k = -2 \rightarrow 11$
$l = -29 \rightarrow 29$
5 standard reflections
every 300 reflections
frequency: 150 min
intensity decay: not significant

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.134
S = 1.071
2890 reflections
184 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.0926P)^2 + 0.1263P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.345 e Å^{-3}
$\Delta\rho_{min}$ = −0.235 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.0107 (13)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = −0.2 (3)

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

O3—C3	1.364 (2)	C8—C14	1.494 (2)
O17—C17	1.216 (3)	C8—C9	1.5140 (19)
C5—C6	1.509 (2)	C9—C10	1.5122 (19)
C6—C7	1.496 (2)	C9—C11	1.546 (2)
C7—C8	1.324 (2)		
O3—C3—C4	117.94 (16)	C17—C13—C14	99.20 (13)
O3—C3—C2	122.73 (15)	C12—C13—C14	110.53 (12)
C4—C3—C2	119.33 (15)	C18—C13—C14	112.26 (14)
C8—C7—C6	124.03 (14)	C8—C14—C15	122.46 (15)
C7—C8—C14	125.80 (14)	C8—C14—C13	110.61 (12)
C7—C8—C9	122.88 (14)	C15—C14—C13	104.39 (13)
C14—C8—C9	111.27 (13)	C14—C15—C16	101.82 (15)
C13—C12—C11	110.18 (14)	C17—C16—C15	106.09 (15)
C17—C13—C12	117.01 (15)	O17—C17—C13	126.02 (18)
C17—C13—C18	106.44 (13)	O17—C17—C16	125.57 (18)
C12—C13—C18	110.91 (14)	C13—C17—C16	108.37 (16)

Structure solution was conducted by direct methods using *SHELXS*96 (Sheldrick, 1996) and the structure was refined using *SHELXL*97 (Sheldrick, 1997). H atoms were generated and refined as riding groups, except for H3 (bound to O3), which was located from a difference Fourier map.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1995). Molecular graphics: *CHAIN* (Sack, 1988). Software used to prepare material for publication: *ORTEP*III (Burnett & Johnson, 1996).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1048). Services for accessing these data are described at the back of the journal.

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N,*N*-Dimethyl-5-methoxymethyl-2′-deoxycytidine

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Abstract

In the title compound, $C_{13}H_{21}N_3O_5$, the pyrimidine ring adopts the antiperiplanar (*−ap*) conformation [χ = 193.54 (19)°]. The deoxyribose sugar ring has the C2′-*exo*–C3′-*endo* ($_2T^3$) twist conformation. The pseudorotational parameters of the deoxyribose sugar ring are P = 6.83 (2)° and τ_m = 38.27 (2)°. The exocyclic side chain at C5′ has the g^+ conformation [γ = 47.7 (3)°]. The 5-methoxymethyl group is distal to the deoxyribose sugar ring, with a C6—C5—C52—O52 torsion angle of −91.9 (3)°.

Comment

Our studies on 2′-deoxycytidine nucleoside analogues with selectivity against the *Herpes simplex* virus (HSV) have shown that substituents at the C5 position of the pyrimidine ring play an important role in biological activity (Gupta *et al.*, 1991, 1993; Stuart *et al.*, 1997). When deamination is prevented, 5-methoxymethyl-2′-deoxycytidine (MMdCyd) and (*E*)-5-(2-bromovinyl)-2′-deoxycytidine (BrVdCyd) are potent and selective anti-herpes agents (Aduma, Gupta, Stuart & Tourigny, 1990; Aduma, Gupta & De Clercq, 1990; Jia *et al.*, 1990*a*; Gupta *et al.*, 1991, 1993). Systematic investigations on the modification of the cytosine (N^4) moiety have indicated that substituents on the N^4 position have profound influence on biological activity (Zoghaib, Kamaly, Kumar *et al.*, 1996; Zoghaib, Kamaly, De Clercq *et al.*, 1996; Gupta, unpublished results). As part of this research programme, our studies have shown that loss of bio-activity is due to the conformation of the molecule (Jia *et al.*, 1990*b*; Gupta *et al.*, 1992; Audette *et al.*, 1997; Audette *et al.*, 1998).

N,*N*-Dimethyl-5-methoxymethyl-2′-deoxycytidine [*N*,*N*-dimethyl-MMdCyd], (I), was prepared in order to

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