electronic reprint

Acta Crystallographica Section E
Structure Reports
Online
ISSN 1600-5368
Editors: **W. Clegg and D. G. Watson**

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Key indicators

Single-crystal X-ray study
T = 160 K
Mean σ(C–C) = 0.005 Å
R factor = 0.046
wR factor = 0.124
Data-to-parameter ratio = 8.1

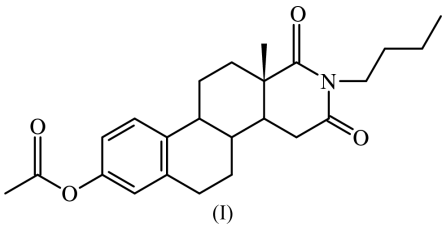
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 4 October 2004
Accepted 6 October 2004
Online 16 October 2004

In the title compound, a modified synthetic D-homo steroid, $C_{24}H_{31}NO_4$, the cyclohexene ring adjacent to the aromatic ring adopts a half-chair conformation, while the cyclohexane ring has an ideal chair conformation and the heterocyclic ring has a sofa conformation. The butyl substituent is nearly planar, with this plane lying almost perpendicular to the least-squares plane of the heterocyclic ring. The crystal structure contains a series of weak C—H···O intermolecular interactions.

Comment

Modified steroids containing alkylating or other reactive functional groups that are capable of bonding covalently to the active sites of their receptor proteins, or to those of enzymes that use them as substrates, are of biological and medicinal interest (Dence, 1980). Because of the common phenolic ring, *A*, estradiol structures analogous to the title compound, (I), are expected to bind to the oestrogen receptor (Roszak *et al.*, 1991). The title compound, however, does not possess a 17β-hydroxy function, which is important for high affinity binding. When the 17β-hydroxy substituent is replaced with a 17-carbonyl group as, for example, in estrone, the binding affinity may be decreased (for example, see Roszak *et al.*, 1991). It has also been suggested that the absence of an oxygen substituent, comparable with the estradiol 17-O atom, accounts for the inactivity or antagonistic properties observed for some ligands (Duax *et al.*, 1985). Thus, the title 17-butyl-estrone derivative may be an agonist at the estrogen receptor. The X-ray crystal structure determination of (I) has been undertaken to investigate the stereochemistry of the molecule and the conformational changes resulting from the presence of carbonyl groups at positions 16 and 17a and a butyl group at N17.



(I)

A view of the molecule of (I) with the atomic labelling scheme is shown in Fig. 1. In (I), cyclohexene ring *B*, adjacent to the aromatic ring, has a 7α,8β-half-chair conformation [puckering parameters (Cremer & Pople, 1975): *Q* = 0.530 (3) Å, θ = 48.7 (3)° and φ = 155.7 (5)°] as a result of the fusion with the planar aromatic ring, *A*. Cyclohexane ring *C*

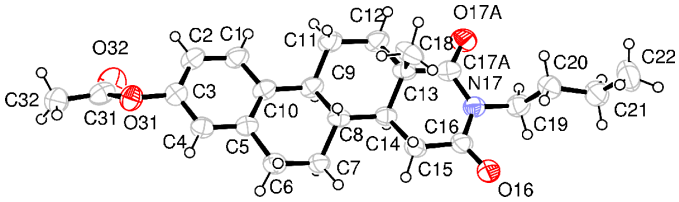


Figure 1
View of the molecule of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary radii.

has an ideal chair conformation [Q = 0.575 (4) Å, θ = 0.9 (3)° and φ = 319 (32)°]. With the substitution by the relatively planar butyl group at N17, heterocyclic ring *D* adopts a 14α-sofa conformation [Q = 0.509 (3) Å, θ = 59.0 (3)° and φ = 195.3 (4)°]. The torsion angle C19—C20—C21—C22 [−177.8 (3)°] shows that the backbone of the butyl group is planar. The dihedral angle between the plane of the butyl group and the least-squares plane of ring *D* is 82.1 (3)°. Ring *D* is flattened, as indicated by the torsion angles C13—C17A—N17—C16 [-0.9 (4)°] and C17A—N17—C16—C15 [11.0 (5)°]. This is associated with the constraints on the ring conformation introduced by the normal planar arrangement about the two amide N—C bonds (sum of angles at N17 = 359.7°). The *B*/*C* and *C*/*D* rings are *trans*-fused. The plane of the acetate group attached to atom C3 is oriented at an angle of 50.84 (18)° to the plane of aromatic ring *A*.

The superposition of the non-H atoms of all four six-membered rings of the title compound with the corresponding atoms of the related structures *N*-chloro-3-methoxy-17-aza-D-homoestra-1,3,5(10)-trien-16-one and *N*-chloro-3-methoxy-17-aza-D-homoestra-1,3,5(10)-trien-17a-one (Roszak *et al.*, 1991) gives r.m.s. deviations of 0.37 and 0.40 Å, respectively, which shows that the structures have nearly the same conformation.

Atom C4 acts as a donor for a weak C—H···O intermolecular interaction (*via* H4) with carbonyl atom O17*A* of a symmetry-related molecule. This interaction links the molecules into chains which run in the [010] direction and can be described by graph-set motif *C*(10) (Bernstein *et al.*, 1995; Table 1). Atom C8 is involved in a weak C—H···O interaction with carbonyl atom O16 of another adjacent molecule and thereby produces a continuous chain which runs in the [100] direction and has a *C*(6) graph-set motif. Atom C9 interacts *via* H9 with O17*A* in yet another neighbouring molecule to give chains which run in the [010] direction and have a *C*(7) graph-set motif. Finally, atom C15 has a C—H···O interaction with the carbonyl O atom in the ester substituent of an adjacent molecule. This interaction generates chains which run in the [010] direction and have a *C*(12) graph-set motif.

Experimental

A mixture of 16,17*a*-dioxo-17-aza-D-homooestra-1,3,5(10)-trien-3-yl acetate (0.2 g, 0.585 mmol), dry ethyl methyl ketone (50 ml) and anhydrous potassium carbonate (0.5 g) was refluxed with stirring for 10 min. *n*-Butyl iodide (2 ml) was added to the stirred solution and the mixture was refluxed for 5 h. The solid obtained after removing the solvent was washed with water and crystallized from methanol to afford crystals of (I) (yield: 0.15 g, 65.2%; m.p. 447–451 K).

Crystal data

$C_{24}H_{31}NO_4$
M_r = 397.51
Orthorhombic, $P2_12_12_1$
a = 9.7793 (4) Å
b = 11.3997 (4) Å
c = 19.1470 (7) Å
V = 2134.53 (14) Å^3
Z = 4
D_x = 1.237 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2182 reflections
θ = 2.0–25.0°
μ = 0.08 mm^{-1}
T = 160 (1) K
Plate, colourless
0.25 × 0.13 × 0.05 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans with κ offsets
Absorption correction: none
22 788 measured reflections
2164 independent reflections
1675 reflections with $I > 2\,s(I)$
R_{int} = 0.074
θ_{max} = 25.1°
$h = -11 \rightarrow 11$
$k = -12 \rightarrow 13$
$l = -22 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.124
S = 1.04
2159 reflections
266 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0768P)^2 + 0.0087P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.014 (3)

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C4—H4···O17A^{i}	0.95	2.41	3.315 (4)	160
C8—H8···O16^{ii}	1.00	2.47	3.454 (4)	169
C9—H9···O17A^{iii}	1.00	2.59	3.476 (4)	148
C15—H152···O32^{iv}	0.99	2.46	3.223 (4)	133

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

The methyl H atoms were constrained to an ideal geometry (C—H = 0.98 Å) with U_{iso}(H) = 1.5U_{eq}(C), but were allowed to rotate freely about the C—C bonds. All remaining H atoms were placed in geometrically idealized positions (C—H = 0.95–1.00 Å) and constrained to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(C). Due to the absence of any significant anomalous scatterers in the molecule, attempts to confirm the absolute configuration by refinement of the Flack (1983) parameter in the presence of 1601 Friedel pairs led to an inconclusive value (Flack & Bernardinelli, 2000) of −0.8 (15). Therefore, the Friedel pairs were merged before the final refinement and the absolute configuration was assigned to correspond with that of the known chiral centres in a precursor molecule, which remained unchanged during the synthesis of the title compound. Five low-angle reflections partially obscured by the beam stop were omitted.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *DENZO-SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN* and *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to

prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2003).

RH thanks the UGC, India, for the award of a minor research project, and RG thanks the late Professor D. P. Jindal for his guidance and help rendered in the synthesis of the title compound.

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