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(8*R*,9*S*,13*S*,14*S*)-17-Butyl-3-methoxy-17-aza-*D*-homoestra-1,3,5(10)-triene-16,17a-dione

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Key indicators

Single-crystal X-ray study
T = 160 K
Mean σ(C–C) = 0.002 Å
R factor = 0.043
wR factor = 0.109
Data-to-parameter ratio = 13.5

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

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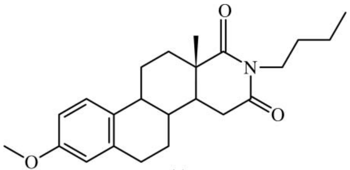
In the title compound, $C_{23}H_{31}NO_3$, a modified synthetic D-homo steroid derivative, the cyclohexene ring adjacent to the aromatic ring adopts a half-chair conformation, while the cyclohexane ring has an ideal chair conformation. The heterocyclic ring adopts a 14α-sofa conformation. The butyl substituent is nearly planar, this plane lying almost perpendicular to the least-squares plane of the heterocyclic ring. The structure displays some weak intermolecular C—H···O interactions.

Comment

Structural changes in one part of a steroid alters the rate of reaction at a distant point, a phenomenon known as conformational transmission. The activities of certain estrogenic and androgenic steroids are significantly altered by methylation of the C3 hydroxy group (Duax *et al.*, 1979). As a continuation of our previous studies on *D*-homoestra-1,3,5(10)-triene derivatives (Hema *et al.*, 2004, 2005*a*,*b*), the X-ray crystal structure determination of the title compound, (I), has been undertaken in order to better understand the influence of structural modifications upon overall molecular geometry and conformation. Compound (I) possesses a bulky substituent at the N atom of the heterocyclic ring, and has a methoxy substituent at C3 of the aromatic ring. The structure of the analogous 17-butyl-16,17*a*-dioxo-17-aza-*D*-homoestra-1,3,5(10)-trien-3-ol, (II), was presented in the preceding paper (Hema *et al.*, 2005*b*).



(I)

A view of the molecule of (I) with the atom-labelling scheme is shown in Fig. 1. The bond lengths and bond angles in (I) are comparable with those in the structures of (II) and the related 17-butyl- and 17-allyl-16,17a-dioxo-17-aza-*D*-homoestra-1,3,5(10)-trien-3-yl acetate derivatives, (III) and (IV), respectively (Hema *et al.*, 2004, 2005*a*). In (I), the cyclohexene ring, *B*, adjacent to the aromatic ring adopts a 7α,8β-half-chair conformation [puckering parameters (Cremer & Pople, 1975) Q = 0.4825 (18) Å, θ = 44.6 (2)°, φ = 145.5 (3)°] as a result of the fusion with the planar aromatic ring *A*. The cyclohexane ring, *C*, has an ideal chair conformation [Q = 0.5903 (18) Å, θ = 5.97 (17)°, φ = 39.1 (18)°].

The butyl substituent at N17 is nearly planar, this plane lying almost perpendicular to the least-squares plane of the heterocyclic ring, *D*. The r.m.s. deviation of the butyl group

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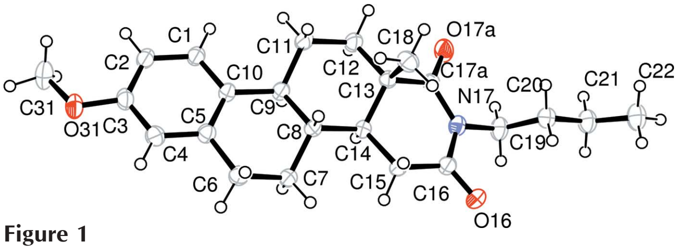

Figure 1
View of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids for non-H atoms are drawn at the 50% probability level.

atoms N17, C19, C20, C21 and C22 from their mean plane is 0.044 Å, and the dihedral angle between the plane of the butyl group and the least-squares plane through ring *D* is 82.52 (10)°. The corresponding values observed in (II), (III) and (IV) are 89.91 (16), 82.1 (2) and 84.5 (5)°, respectively (Hema *et al.*, 2004, 2005*a*,*b*). Ring *D* in (I) adopts a flattened 14α-sofa conformation [Q = 0.5189 (18) Å, θ = 61.1 (2)°, φ = 199.8 (2)°] and the flattening of the ring is indicated by the torsion angles C13—C17*a*—N17—C16 [−1.1 (2)°] and C17*a*—N17—C16—C15 [14.4 (2)°]. The flattening is associated with the constraints to the ring conformation introduced by the normal planar arrangement about the amide N—C bond (sum of the angles at N17 = 359.9°). The *B*/*C* and *C*/*D* rings are *trans* fused. In (I), the plane of the methoxy group attached to atom C3 is oriented at an angle of 33.33 (17)° to the plane of aromatic ring *A*. The corresponding dihedral angle for the acetate substituent at C3 in (III) and (IV) are 50.84 (18) and 44.78 (9)°, respectively.

The superposition of the non-H atoms common to the structures of (I) and (II) gives an r.m.s. deviation of 0.57 Å, with the main differences resulting from variations in the conformation of ring *D*. For comparison, the matrix of corresponding r.m.s. deviations for the superposition of the non-H atoms common to the structures of (I)–(IV), *N*-chloro-3-methoxy-17-aza-D-homoestra-1,3,5(10)-trien-16-one, (V), and *N*-chloro-3-methoxy-17-aza-D-homoestra-1,3,5(10)-trien-17a-one, (VI) (Roszak *et al.*, 1991), are listed in Table 2. The table shows that the most profound effect on the conformation of the backbone of D-homoestra-1,3,5(10)-trien derivatives is observed when a methoxy substituent is present at C3.

In (I), atom C12 acts as a donor for a weak intermolecular C—H···O interaction (*via* H121) with the carbonyl atom O16 of a symmetry-related molecule, thereby forming extended chains, which run parallel to the [010] direction and can be described by a *C*(7) graph-set motif (Bernstein *et al.*, 1995; Table 1). Atom C31 is similarly involved in a weak intermolecular C—H···O interaction with the carbonyl atom O16 of another adjacent molecule and thereby links the molecules into continuous chains, which run in the [001] direction and can be described by the graph-set motif *C*(13).

Experimental

n-Butyl iodide (2 ml) was added to a solution of 3-methoxy-17-aza-*D*-homoestra-1,3,5(10)-triene-16,17a-dione (0.1 g, 0.32 mmol) in dry ethyl methyl ketone (50 ml). Anhydrous potassium carbonate (0.5 g) was added to the hot solution with stirring. The reaction mixture was refluxed for 5 h with constant stirring. The slurry obtained was filtered and the solvent was removed under reduced pressure. The residue obtained was washed with water and crystallized from *n*-hexane to afford crystals of (I) (yield 0.075 g, 63.69%; m.p. 356–359 K).

Crystal data

$C_{23}H_{31}NO_3$
M_r = 369.49
Orthorhombic, $P2_12_12_1$
a = 5.9243 (1) Å
b = 11.0968 (3) Å
c = 30.2328 (7) Å
V = 1987.53 (8) Å^3
Z = 4
D_x = 1.235 Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 3360 reflections
θ = 2.0–30.0°
μ = 0.08 mm^{-1}
T = 160 (2) K
Prism, colourless
0.30 × 0.18 × 0.18 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans with κ offsets
Absorption correction: none
34883 measured reflections
3343 independent reflections

2699 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.059
$\theta_{\rm max}$ = 30.0°
$h = -8 \rightarrow 8$
$k = -15 \rightarrow 15$
$l = -42 \rightarrow 42$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.110
S = 1.03
3339 reflections
247 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0577P)^2 + 0.1792P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max}$ = 0.001
$\Delta\rho_{\rm max}$ = 0.21 e Å^{-3}
$\Delta\rho_{\rm min}$ = −0.20 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
C12—H121···O16$^{\rm i}$	0.99	2.59	3.504 (2)	154
C31—H312···O16$^{\rm ii}$	0.98	2.37	3.347 (2)	174

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

Table 2
Matrix of r.m.s. deviations (Å) for the superposition of the non-H atoms common to the structures of (I)–(VI)..

Compound	(I)	(II)	(III)	(IV)	(V)
(II)	0.57	–	–	–	–
(III)	0.25	0.32	–	–	–
(IV)	0.24	0.23	0.06	–	–
(V)	0.13	0.19	0.37	0.09	–
(VI)	0.21	0.21	0.40	0.18	0.16

The methyl H atoms were constrained to an ideal geometry (C—H = 0.98 Å) with $U_{\rm iso}$(H) = 1.5$U_{\rm eq}$(C), but were allowed to rotate freely about the C—C bonds. All other H atoms in the structures were placed in geometrically idealized positions (C—H = 0.95–1.00 Å) and constrained to ride on their parent atoms with $U_{\rm iso}$(H) = 1.2$U_{\rm eq}$(C). Owing to the absence of any significant anomalous scatterers in the molecule, attempts to confirm the absolute structure by refinement of the Flack (1983) parameter in the presence of 2473 sets of Friedel pairs led to an inconclusive value (Flack & Bernardinelli, 2000) of −0.4 (9). Therefore, the Friedel pairs were merged before the final refinement and the absolute configuration was assigned to correspond to that of the known chiral centres in a precursor molecule, which remained unchanged during the synthesis of the title compound. Four low-angle reflections (012, 013, 021 and 101) were partially obscured by the beam stop and 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: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1999); software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2003).

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