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# 16-[4-(3-Chloropropoxy)-3-methoxybenzylidene]-4-androstene-3,17-dione

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**Key indicators**

Single-crystal X-ray study
*T* = 273 K
Mean σ(C–C) = 0.005 Å
Disorder in main residue
*R* factor = 0.056
*wR* factor = 0.153
Data-to-parameter ratio = 15.2

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



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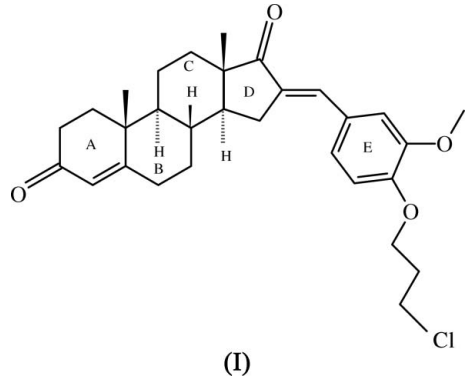
In the title compound, $C_{30}H_{37}ClO_4$, the cyclohexene ring *A* of the steroid nucleus has a 1α-sofa conformation. The cyclohexane rings adopt chair conformations. The cyclopentane ring adopts a 14β-envelope conformation. The benzylidene group has an *E* configuration with respect to the carbonyl group on the cyclopentane ring. The crystal packing is dictated by weak intermolecular C—H···O interactions.

## Comment

The present study is part of an ongoing investigation of the crystal structures of a series of androstene derivatives (Thamotharan *et al.*, 2002, and references therein; Thamotharan, Parthasarathi, Dubey *et al.*, 2004; Thamotharan, Parthasarathi, Gupta *et al.*, 2004; Hema *et al.*, 2003; Vasuki, Parthasarathi *et al.*, 2002; Vasuki, Thamotharan *et al.*, 2002). We are interested in the stereochemistry and the conformational flexibility of the steroid nucleus resulting from various substitutions at the C3, C16 and C17 positions, since it is well known that steroid receptors are able to modify the mode of binding at ring *D* to accommodate several different types of substitution at C17 (Duax & Norton, 1975). The X-ray crystal structure determination of the title compound, (I), has been undertaken in order to understand the influence of structural modifications on the overall molecular geometry and conformation, and the results are presented here.




(I)

The crystals of (I) are enantiomerically pure and the absolute configuration of the molecule has been confirmed independently by the X-ray diffraction experiment. Both methyl groups of the steroid nucleus adopt the expected staggered arrangements. The *A*/*B* ring junction is quasi-*trans* and the *B*/*C* and *C*/*D* ring junctions are all-*trans* (see scheme and Fig. 1). In the cyclohexene ring, *A*, the C4—C5 ($Csp^2$—$Csp^2$) distance of 1.327 (4) Å confirms the localization of a double bond at this position. This double bond imposes the

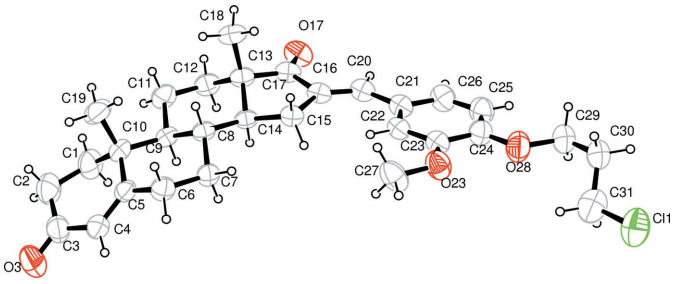



**Figure 1**
A view of the molecular structure of (I), with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as circles of arbitrary radii. The minor disorder component is not shown.

**Figure 2**
A superimposed fit of the non-H atoms of (I) (red) and corresponding atoms of (II) (green).

1$\alpha$-sofa conformation on ring *A*, with atom C1 at the flap position [puckering parameters (Cremer & Pople, 1975) $Q$ = 0.447 (5) Å, $q_2$ = 0.372 (4) Å, $q_3$ = 0.249 (4) Å, $\theta$ = 56.2 (5)° and $\varphi$ = 9.8 (7)° for the atom sequence C1—C2—C3—C4—C5—C10]. Rings *B* and *C* adopt chair conformations. The cyclopentane ring, *D*, having puckering parameters $Q$ = 0.387 (3) Å and $\varphi$ = 208.6 (5)°, adopts a 14$\beta$-envelope conformation, with a pseudo-rotation angle of 10.1 (3)° and a maximum torsion angle of 40.0 (2)° (Rao *et al.*, 1981) for the atom sequence C13—C14—C15—C16—C17. Atom C14 lies 0.587 (4) Å from the plane containing the four remaining atoms. In a related structure, in which atom C16 has no substitution, ring *D* has a 14$\alpha$-envelope conformation (Busetta *et al.*, 1972).

The C17—C16—C20—C21 torsion angle of 177.4 (3)° indicates that the benzylidene ring has an *E* configuration with respect to the carbonyl group at position C17. The C3···C16 distance, 8.84 (1) Å, which is a measure of the length of the steroid nucleus, indicates that the steroid nucleus is in a completely extended form (Karle, 1970). The distance between terminal atoms O3 and Cl1 is 17.72 (1) Å. The C19—C10···C13—C18 pseudo-torsion angle, which gives a measure of the molecular twist, is 5.2 (3)°. The C15—C16—C20 exocyclic angle [131.7 (3)°] is slightly larger than the normal value, possibly as a consequence of steric repulsion between atoms H15*B* and H22 (H···H = 2.15 Å). A superimposed fit of the non-H atoms of (I), without the substituents at the benzylidene ring, and the corresponding atoms in a related structure, 16-(4-isopropylbenzylidene)androst-4-ene-3,17-dione (Thamotharan, Parthasarathi, Dubey *et al.*, 2004), (II), gives an r.m.s. deviation of 0.885 Å. This indicates that the conformation of the steroid skeleton is not very much altered by replacing the isopropyl group attached to the benzylidene ring by the chloropropoxy group and adding a methoxy group to the benzylidene ring at the 3-position.

The crystal packing is dictated by weak intermolecular C—H···O interactions. The C14—H14···O17$^{i}$ interaction links the molecules into a *C*(5) chain (Bernstein *et al.*, 1995) that runs parallel to the *a* axis (refer to Table 1 for symmetry codes). The C27—H27*B*···O17$^{ii}$ and the C30—H30*A*···O3$^{iii}$ interactions form *C*(10) and *C*(19) chains, which run along the *a* and *c* axes, respectively.

## Experimental

16-[4-(3-Chloropropoxy)-3-methoxybenzylidene]-17-oxo-5-androsten-3$\beta$-ol (1 g, 2 mmol) was dissolved in a mixture of cyclohexanone (10 ml) and dry toluene (150 ml). Traces of moisture were removed by azeotropic distillation. The distillation was continued at a slow rate while adding a solution of aluminium isopropoxide (1 g) in dry toluene (15 ml) dropwise. The reaction mixture was refluxed for 5 h and then allowed to stand overnight at room temperature. The slurry was filtered and the residue was washed thoroughly with dry toluene. The combined filtrate and the washings were steam distilled until the removal of organic solvents was effected. The solid obtained was filtered off, washed with water, dried and crystallized from diethyl ether and *n*-hexane (9:1) to afford (I) (yield 0.7 g, 70.28%; m.p. 438–440 K).

*Crystal data*

$C_{30}H_{37}ClO_4$
$M_r$ = 497.05
Orthorhombic, $P2_12_12_1$
$a$ = 8.0046 (4) Å
$b$ = 17.4763 (9) Å
$c$ = 19.6133 (10) Å
$V$ = 2743.7 (2) Å$^3$
$Z$ = 4
$D_x$ = 1.203 Mg m$^{-3}$
Mo $K\alpha$ radiation
$\mu$ = 0.17 mm$^{-1}$
$T$ = 273 (2) K
Plate, yellow
0.10 × 0.08 × 0.04 mm

*Data collection*

Bruker SMART APEX CCD area detector diffractometer
$\omega$ scans
Absorption correction: none
20024 measured reflections
4850 independent reflections
3335 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.030
$\theta_{max}$ = 25.0°

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.153
$S$ = 1.00
4850 reflections
320 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0799P)^2 + 0.3313P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.29 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.16 e Å$^{-3}$
Absolute structure: Flack (1983), 2083 Friedel pairs
Flack parameter: 0.00 (13)

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| C14—H14···O17$^{i}$ | 0.98 | 2.51 | 3.430 (3) | 156 |
| C27—H27*B*···O17$^{ii}$ | 0.96 | 2.43 | 3.306 (5) | 151 |
| C30—H30*A*···O3$^{iii}$ | 0.97 | 2.56 | 3.390 (6) | 144 |

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

Atoms C30 and Cl1 of the chloropropoxy group are disordered over two sites with a site-occupation factor of 0.856 (2) for the major conformation. Two sets of positions were refined by applying constraints. The same anisotropic displacement parameters were used for atoms Cl1 and Cl1*A*, and atoms C29, C30 and C30*A*. Similarity restraints were applied to the disordered atoms, so as to maintain similar geometry about the chemically equivalent atoms. Methyl H atoms were constrained to an ideal geometry (C—H = 0.96 Å), with $U_{iso}$(H) values of $1.5U_{eq}$(C), but were allowed to rotate freely about the C—C bonds. All remaining H atoms were placed in idealized positions (C—H = 0.93–0.98 Å) and were constrained to ride on their parent atoms, with $U_{iso}$(H) values of $1.2U_{iso}$(C).

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997), *PLATON* (Spek, 2003) and *Qmol* (Gans & Shalloway, 2001); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1995).

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