

3-Benzyloxy-16-[(*N*-methyl-*N*-phenylamino)methylidene]estra-1,3,5(10)-trien-17-one

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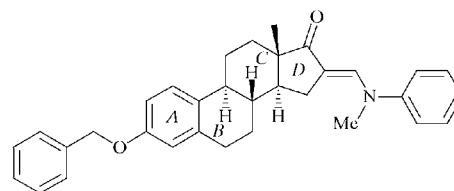
In the title compound, C₃₃H₃₅NO₂, the five-membered ring adopts a half-chair conformation. The *N*-methyl-*N*-phenyl-substituted keto–enamine moiety shows a comparatively long *Csp*²–N bond.

Comment

Recently, there has been interest in the annelation of five- and six-membered nitrogen-containing heteroaromatic rings to the *D* ring of estrane derivatives. The title compound, (I), is an excellent starting material for such pyrimidino- and pyrazolo-annelated systems. In order to optimize the reaction conditions for the transformation of (I), a good understanding of the stereoelectronic prerequisites of (I) is important. For this reason, an X-ray crystal structure analysis of (I) was carried out and the results are presented here.

There is one independent molecule of (I) per asymmetric unit cell (Fig. 1). Ring *A* shows little distortion from planarity, as is evident in other estrones and estradiols for which X-ray

crystal structure analyses have been carried out. Ring *C*, with *trans* fusion to rings *B* and *D*, has a chair conformation. As a cyclohexene, ring *B* in estranes is usually conformationally more flexible (Bucourt & Hainault, 1967; Matsumoto *et al.*, 2004; Yamamoto *et al.*, 2004). In (I), ring *B* has a half-chair conformation, as evaluated with the Cremer & Pople (1975) puckering parameters $Q = 0.494$ (3) Å, $\theta = 46.0$ (2)° and $\varphi = 160.8$ (3)° [for a perfect half-chair conformation, $\theta = 50.8$ ° and $\varphi = k \times 60 + 30$ °; for a perfect chair conformation (the next closest conformation), $\theta = 0$ ° (Boeyens, 1978)]. This configuration is also in accordance with the relative signs of the endocyclic torsion angles within ring *B* (see Boeyens, 1978).



(I)

Ring *D* has a half-chair conformation [$Q = 0.415$ (3) Å and $\varphi = 204.7$ (3)°], with a pseudorotation angle $\Delta = 6.2$ (2)°, and a maximum torsion angle $\varphi_m = 42.3$ (1)° (Rao *et al.*, 1981) for the atom sequence C13–C14. The important keto–enamine moiety O2–C17–C16–C26–N1 has an *E*-configured C16–C26 olefinic bond, with the keto and amino functionalities on opposing sides (Table 1). This mirrors the results of X-ray structure analyses of other keto–enamines (Skinnemoen & Ottersen, 1980; Groselj *et al.*, 2002; Larsen, 1981) and can be explained by electronic repulsion of the keto O atom and amine N atom. The C16–C17 bond [1.481 (3) Å] is significantly longer than in other non-annelated aminomethylidene-cyclopentanones (Groselj *et al.*, 2002; Larsen, 1981). Previously, we have observed longer bond lengths for C16–C17 in other estrane derivatives compared with analogously substituted but non-annelated cyclopentanes (Matsumoto *et al.*, 2004). The other bond lengths involving atoms that define the keto–enamine moiety of (I), C16–C26 [1.346 (3) Å] and C26–N1 [1.369 (3) Å], cannot be compared directly with results from the literature, as X-ray crystal structures of other keto–enamines with a phenyl and an alkyl substituent on the

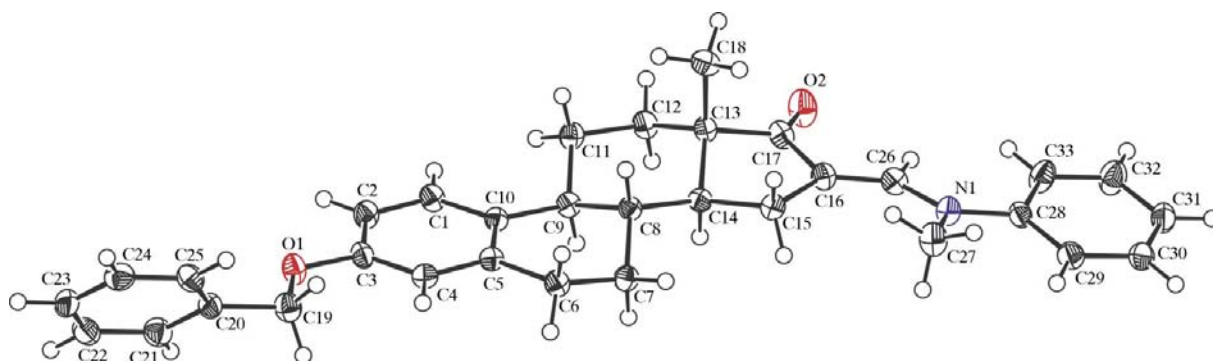


Figure 1

A view of the molecule of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

N atom have not been published to date. A phenyl substituent on the N atom (Skinnemoen & Ottersen, 1980), however, increases the N—C(enamine) bond length compared with an alkyl substituent in mono-*N*-substituted ketoenamides (Larsen, 1981). In (I), the methyldene C16—C26 and keto C17—O2 bonds show some deviation from synplanarity, with a C26—C16—C17—O2 torsion angle of 6.1 (4)°

In the crystal structure, molecules of (I) pack in four distinct columns arranged in a stepwise fashion. Interactions between molecules are mostly of a dispersive nature, but there are also a number of weak C—H··· π interactions (Table 2), the contact distances being in the typical range for reported C—H··· π interactions (Nishio & Hirota, 1989; Nishio *et al.*, 1998), where the H atoms are directed towards the π system. Other close contacts that may play a role in the crystal packing are C15—H15···O2($x - 1, y, z$) (2.70 Å) and C23—H24···O2($-\frac{1}{2} - x, -y, \frac{1}{2} + z$) (2.61 Å).

Experimental

Compound (I) was prepared by the reaction of 3-benzyloxy-16-(hydroxymethylidene)estra-1,3,5(10)-trien-17-one with *N*-methyl-*N*-phenylammonium trifluoroacetate, according to the literature method of Matsumoto *et al.* (2003). The crystal used for X-ray structure analysis was obtained by recrystallization of (I) from chloroform–ether–hexane (1:1:1).

Crystal data

C ₃₃ H ₃₅ NO ₂	Mo K α radiation
$M_r = 477.65$	Cell parameters from 5574 reflections
Orthorhombic, $P2_12_12_1$	$\theta = 3.3\text{--}27.5^\circ$
$a = 6.1333$ (2) Å	$\mu = 0.08$ mm ⁻¹
$b = 11.4780$ (5) Å	$T = 123.1$ K
$c = 35.447$ (2) Å	Needle, colourless
$V = 2495.4$ (2) Å ³	$0.13 \times 0.08 \times 0.06$ mm
$Z = 4$	
$D_x = 1.271$ Mg m ⁻³	

Data collection

Rigaku Saturn70 CCD area-detector diffractometer	3276 independent reflections
ω scans	2156 reflections with $F^2 > 2\sigma(F^2)$
Absorption correction: multi-scan (Jacobson, 1998)	$R_{\text{int}} = 0.056$
$T_{\text{min}} = 0.908, T_{\text{max}} = 0.995$	$\theta_{\text{max}} = 27.5^\circ$
25 566 measured reflections	$h = -7 \rightarrow 7$
	$k = -14 \rightarrow 14$
	$l = -46 \rightarrow 45$

Refinement

Refinement on F^2	$w = 1/[0.578\sigma(F_o^2)]/(4F_o^2)$
$R(F) = 0.034$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$wR(F^2) = 0.062$	$\Delta\rho_{\text{max}} = 0.25$ e Å ⁻³
$S = 1.00$	$\Delta\rho_{\text{min}} = -0.21$ e Å ⁻³
3276 reflections	Extinction correction: Larson (1970), equation 22
361 parameters	Extinction coefficient: 42.1 (40)
H atoms treated by a mixture of independent and constrained refinement	

Table 1

Selected geometric parameters (Å, °).

O2—C17	1.229 (3)	C16—C17	1.481 (3)
N1—C26	1.369 (3)	C16—C26	1.346 (3)
C26—C16—C17—O2	6.1 (4)		

Table 2

Short-contact geometry (Å, °).

Cg1 denotes the centre of the C28—C33 ring, Cg2 the centre of the C1—C5/C10 ring and Cg3 the centre of the C20—C25 ring.

$D\text{—}H\cdots A$	$D\text{—}H$	$H\cdots A$	$D\cdots A$	$D\text{—}H\cdots A$
C15—H15···O2 ⁱ	0.95	2.70	3.607 (3)	161
C23—H24···O2 ⁱⁱ	0.95	2.61	3.395 (3)	141
C1—H1···Cg1 ⁱⁱⁱ	0.95	2.99	3.685 (3)	131
C29—H31···Cg2 ^{iv}	0.95	2.97	3.694 (3)	134
C32—H34···Cg3 ^v	0.95	2.56	3.456 (3)	158
C33—H35···Cg3 ^v	0.95	2.73	3.582 (3)	149

Symmetry codes: (i) $x - 1, y, z$; (ii) $\frac{1}{2} - x, -y, \frac{1}{2} + z$; (iii) $1 - x, y - \frac{1}{2}, \frac{3}{2} - z$; (iv) $-x, \frac{1}{2} + y, \frac{3}{2} - z$; (v) $\frac{1}{2} - x, -y, z - \frac{1}{2}$.

All H atoms were refined as riding on their parent atoms, with C—H = 0.95 Å and all $U_{\text{iso}}(\text{H})$ values were set at $1.2U_{\text{eq}}(\text{C})$. The absolute configuration could not be determined from the X-ray data but was known from the synthetic route.

Data collection: *CrystalClear* (Rigaku, 1999); cell refinement: *CrystalClear*; data reduction: *CrystalStructure* (Rigaku/MS, 2004); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997) and *CRYSTALS* (Watkin *et al.*, 1996); molecular graphics: *PLATON* (Spek, 2003) and *MERCURY* (Bruno *et al.*, 2002); software used to prepare material for publication: *CrystalStructure*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GA1072). Services for accessing these data are described at the back of the journal.

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