Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.047$
$wR(F^2) = 0.152$
$S = 1.064$
3845 reflections
297 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0841P)^2 + 0.132P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.27$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O1	0.95 (2)	1.86 (2)	2.785 (2)	165 (2)
N1—H1B···O2^i	0.91 (2)	1.90 (2)	2.794 (2)	169 (2)

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

The H atoms were refined as riding with $U(H) = 1.5U_{eq}(C)$. The ammonium-H atoms were located and refined. The CF$_3$ group is freely rotating in the structure, and this behaviour was initially modelled as three CF$_3$ groups sharing a common C atom, subject to C—F = 1.29±0.01 Å and F···F = 2.11±0.02 Å. The C—F distance of 1.29 Å is the mean from a number of measurements of trifluoroacetates (Gleghorn & Small, 1995). For a free CF$_3$CO$_2^-$ anion, a sixfold barrier to rotation about the C—C bond is expected. As the barrier is low, of the order of 10–20 J mol^{-1}, the most appropriate model would be one involving a continuous, uniform distribution of the F electrons. As an alternative, the electrons were modelled as six sets of F atoms. Each set was given the same displacement parameters by an EADP instruction, and the 18 F atoms were restrained into an approximate circle by a 'FLAT $F' instruction. For this model, one of the sets had an unacceptably large displacement parameter, and the anion was modelled instead over five sets of F atoms. All F atoms were refined anisotropically, but an 'ISOR $F 0.01' restraint had to be used.

Data collection: *SMART* (Siemens, 1996a). Cell refinement: *SAINT* (Siemens, 1996b). Data reduction: *SAINT*. Program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997a). Program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997b). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1050). Services for accessing these data are described at the back of the journal.

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1,4-Bis(2-hydroxy-5-methylbenzyl)-piperazine

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Abstract

The title compound, C$_{20}$H$_{26}$N$_2$O$_2$, lies across a crystallographic inversion centre. The piperazine ring adopts a chair conformation. The molecules are stabilized by intramolecular O—H···N-type hydrogen bonds in addition to van der Waals forces.

Comment

Piperazine salts are very active against roundworm and pinworm infections in both humans and animals. These drugs are absorbed from the gastrointestinal

tract and have adverse side-effects involving both the gastrointestinal system and the central nervous system, including nausea and vomiting, headache, muscle weakness and convulsions (Roche & Kier, 1981). To provide structural data to assist in the understanding of the mechanism of these side-effects, an X-ray crystal structure determination of the title compound, (I), has been carried out.

(I)
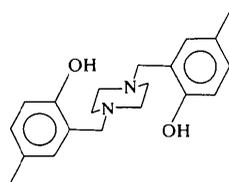
A *ZORTEP* (Zsolnai, 1997) plot of the molecule is shown in Fig. 1. There is only one half molecule present in the asymmetric unit and the unit cell contains two molecules. One half of the molecule is related to the other by a centre of inversion. Atoms C9 and C10 are connected to C10' and C9' of the second half and *vice versa*.
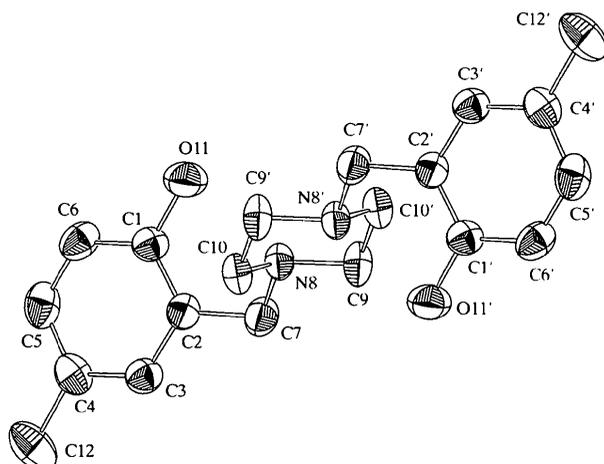
Fig. 1 The molecular structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms have been omitted for clarity.

Atom N8 is in a pyramidal configuration (Perales *et al.*, 1977). The bond lengths and angles observed in the molecule are normal (Allen *et al.*, 1987). The piperazine ring adopts a chair conformation with atoms N8 and N8' deviating equally by 0.676 (1) Å on either side from the best least-squares plane through atoms C9, C10, C9' and C10'. This is also confirmed by the Cremer & Pople (1975) puckering parameters $q_2 = 0.566\,(2)$ Å, $q_3 = -0.347\,(2)$ Å, $\varphi_2 = 150.0\,(2)^\circ$, $Q_T = 0.664\,(2)$ Å and $\theta_2 = 121.5\,(2)^\circ$. The p-cresol group is planar, with a maximum deviation of $-0.018\,(3)$ Å for atom C12. The angle between the best planes of the piperazine ring and the phenolic ring is $63.03\,(5)^\circ$.

Interestingly, an intramolecular O—H$\cdots$N hydrogen bond is observed between atoms O11 and N8 [O11$\cdots$N8 = 2.711 (1) and O11—H11 = 0.90 (2) Å, and O11—H11$\cdots$N8 = 154 (2)°].

Experimental

The title compound was prepared by the modified procedure suggested by Hodgkin (1984), by mixing p-cresol in ethanol with piperazine in the presence of formaldehyde. Single crystals of (I) were grown by slow evaporation of a methanol–benzene mixture.

Crystal data

$C_{20}H_{26}N_2O_2$	Mo $K\alpha$ radiation
$M_r = 326.43$	$\lambda = 0.71073$ Å
Monoclinic	Cell parameters from 42
$P2_1/c$	reflections
$a = 5.894\,(1)$ Å	$\theta = 6.22\text{--}13.51^\circ$
$b = 8.806\,(1)$ Å	$\mu = 0.079$ mm^{-1}
$c = 17.176\,(1)$ Å	$T = 293\,(2)$ K
$\beta = 92.92\,(1)^\circ$	Needle
$V = 890.3\,(2)$ Å^3	$0.40 \times 0.35 \times 0.27$ mm
$Z = 2$	Colourless
$D_x = 1.218$ Mg m^{-3}	
D_m not measured	

Data collection

Siemens *P4* diffractometer	$\theta_{max} = 27.5^\circ$
$\theta/2\theta$ scans	$h = -1 \rightarrow 7$
Absorption correction: none	$k = -1 \rightarrow 11$
2946 measured reflections	$l = -22 \rightarrow 22$
2036 independent reflections	3 standard reflections
1342 reflections with	every 97 reflections
$I > 2\sigma(I)$	intensity decay: <1%
$R_{int} = 0.033$	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0961P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.044$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.134$	$(\Delta/\sigma)_{max} = 0.01$
$S = 0.868$	$\Delta\rho_{max} = 0.15$ e Å^{-3}
2036 reflections	$\Delta\rho_{min} = -0.19$ e Å^{-3}
161 parameters	Extinction correction: none
All H-atom parameters	Scattering factors from
refined	*International Tables for*
	Crystallography (Vol. C)

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

C1—O11	1.374 (2)	N8—C10	1.466 (2)
C2—C7	1.511 (2)	N8—C9	1.472 (2)
C4—C12	1.509 (2)	C9—C10'	1.505 (2)
C7—N8	1.474 (2)	C10—C9'	1.505 (2)
N8—C7—C2	113.06 (11)	C7—N8—C9	109.95 (11)
C10—N8—C7	111.74 (12)	N8—C9—C10'	111.16 (12)
C10—N8—C9	108.75 (11)	N8—C10—C9'	110.66 (12)

Symmetry code: (i) $-x, 1-y, 1-z$.

All H atoms were located from a difference Fourier map and refined isotropically. The C—H distances vary from 0.92 (2) to 1.02 (2) Å, with the bond angles supportive of the refined positions of the H atoms.

Data collection: *XSCANS* (Siemens, 1994). Cell refinement: *XSCANS*. Data reduction: *XSCANS*. Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *ZORTEP* (Zsolnai, 1997). Software used to prepare material for publication: *PARST* (Nardelli, 1983, 1995).

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3α-Hydroxy-5α-androstane-4,17-dione

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Abstract

The asymmetric unit of the title compound, $C_{19}H_{28}O_3$, contains two independent molecules with almost identical geometry. The molecules have a planar 5α config-

uration as a result of a *trans-A/B* junction of the rings. The compound crystallizes in a triclinic cell, which is unusual for steroids. The molecules are linked head-to-tail *via* hydrogen bonds between the ring *A* hydroxyl group and the ketone group of ring *D*, forming two independent chains running along the *c* axis.

Comment

Our interest in preparing steroid aromatase inhibitors (Campos Neves *et al.*, 1999; Tavares da Silva *et al.*, 1996, 1997), clinically used as antitumor agents especially in the treatment of estrogen-positive breast cancers, led us to the title compound, 3α-hydroxy-5α-androstane-4,17-dione, (I). 3α,4β-Dihydroxy-5α-androstan-17-one, a key intermediate in the aforementioned synthesis, was selectively oxidized at C_4 with oxone, a mixed persulfate reagent, to give (I). The best conditions to perform this reaction (Tavares da Silva, 1997) use the oxidant in the presence of hydrated alumina (Hirano *et al.*, 1991) under ultrasonic irradiation. Furthermore, an efficient and environmentally friendly chemical process has been achieved for this particular transformation, using the combination of a solid supported reagent and sonochemistry.
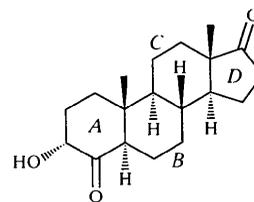
(I)

The unit cell contains two crystallographically independent molecules (1 and 2) with almost identical geometry. An *ORTEP*II (Johnson, 1976) view of the two molecules with the atom-numbering scheme is shown in Fig. 1. The internal degree of isostructurality between the two molecules as defined by Kálman *et al.* (1991) is given by I_D^{25} (distances) = 99.5% and I_D^{23} (valency angles) = 99.5%. The *trans-A/B* ring junctions produce almost planar molecules [bowing angle 6.43 (10)° for molecule 1 and 7.8 (2)° for molecule 2], with an angle of 19.02 (6)° between the average least-squares planes of molecules 1 and 2. The distances between terminal O atoms were found to be 9.707 (6) and 9.657 (6) Å, and the values of the pseudo-torsion angles C19—C10—C13—C18 are 3.1 (2) and 1.7 (2)°, respectively, for molecules 1 and 2, indicating that molecule 1 is slightly more twisted than molecule 2. Rings *A*, *B* and *C* have slightly flattened chair conformations evidenced by the mean values of their torsion angles being less than 60% [57 (2), 56.0 (6) and 55 (5)° for molecule 1, and 57 (2), 56.0 (8) and 55 (5)° for molecule 2]. Ring *D* adopts a less common 13β,14α-half-chair conformation distorted towards a 14α-envelope, as can be seen from