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Stigmasterol hemihydrate

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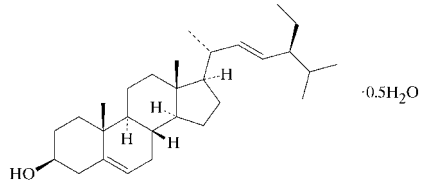
The title compound, stigmasta-5,22-dien-3β-ol hemihydrate, $C_{29}H_{48}O{\cdot}0.5H_2O$, previously thought to be the monohydrate, has two sterol molecules and one water molecule in the asymmetric unit. In both sterol molecules, the methyl group of the ethyl substituent at the end of the hydrocarbon chain is disordered over two sites. The OH group of molecule *A* donates a hydrogen bond to a water molecule and accepts a hydrogen bond from the OH group of molecule *B*. The OH group of molecule *B* accepts two hydrogen bonds from water molecules.

Comment

Stigmasterol is a ubiquitous phytosterol, occurring naturally in a wide variety of plants. In each of the past 25 years, it has been mentioned in 100–200 publications in the chemical literature. It is thus somewhat surprising that, despite the fact that the cell dimensions of a material said to be stigmasterol monohydrate were reported over 60 years ago (Bernal *et al.*, 1940), no crystal structure of stigmasterol or of any solvate has yet been reported. We have encountered crystals of stigmasterol hemihydrate on a number of occasions during our phytochemical studies over the last two decades. Such crystals are frequently of poor quality. Room-temperature diffraction data from the better crystals has led to models in which the hydrocarbon chain at C17 is particularly poorly defined. We have now obtained fairly high-quality crystals of the title compound, (I), from *Parthenium hysterophorus*, and diffraction data at 120 K have yielded a model for which the hydrocarbon chain is reasonably well defined, except for a slight disorder of the ethyl group.

The asymmetric unit of (I) consists of two sterol molecules, one of which is illustrated in Fig. 1, and one water molecule. In the *A* molecule, the terminal methyl group of the disordered ethyl substituent occupies two sites with an occupancy ratio of about 70:30. In the *B* molecule, the occupancy ratio is about 60:40. The water molecule forms hydrogen bonds with the OH groups of both *A* and *B* molecules, but in different fashions. Both water H atoms donate to OH groups on *B* molecules, and the water molecule also accepts a hydrogen bond from the OH group of the *A* molecule (Table 2). Additionally, the OH group of the *B* molecule donates a hydrogen bond to the OH group of the *A* molecule. Molecules are arranged in the cell (Fig. 2) in a bilayer structure, with all the hydrogen bonding occurring near $z = \frac{1}{2}$, and the hydrocarbon ends of the molecules near $z = 0$.



(I)

Neither sterol molecule exhibits significant out-of-plane bending of the skeleton. For the *A* molecule, the 21-atom O1/C1–C17/C20–C22 group exhibits a maximum deviation of 0.472 (5) Å from coplanarity. The planarity of the *B* molecule is similar, with a maximum deviation of 0.490 (5) Å.

The close match of the room-temperature cell dimensions of stigmasterol hemihydrate [a = 9.523 (2), b = 7.5789 (7), c = 36.980 (3) Å, β = 94.213 (10)°, V = 2661.8 (8) Å^3 at 299 K] to those of the 'monohydrate' reported by Bernal *et al.* (1940) make it nearly certain that the previously studied compound was also the hemihydrate. One of the aims of that study was molecular-weight determination of steroids by measurement of densities and unit-cell volumes, a process complicated by the uncertainty in the degree of hydration. A derived molecular weight of 406±7 amu (atomic mass units) was reported, which differs from the calculated value (412.67) by about half the mass of a water molecule, but within experimental error. Although the hemihydrate fit their data better, Bernal *et al.* (1940) considered the monohydrate to be the best interpretation, by analogy to ergosterol, which was well known at the time to crystallize as the monohydrate. Hull & Woolfson (1976) later confirmed the structure of ergosterol monohydrate, which also suffers from a poorly defined hydrocarbon chain at room temperature.

The structure of stigmasta-5-en-3β-ol, differing from the title sterol only in having the C22—C23 bond saturated

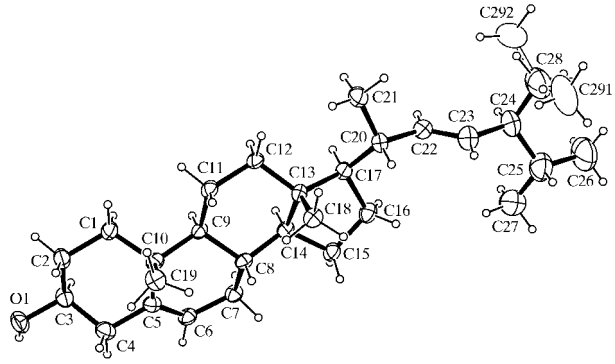


Figure 1
The atom-numbering scheme and ellipsoids at the 40% probability level for molecule *A* of the title compound. Partially occupied methyl sites have been shown with boundary ellipses only.

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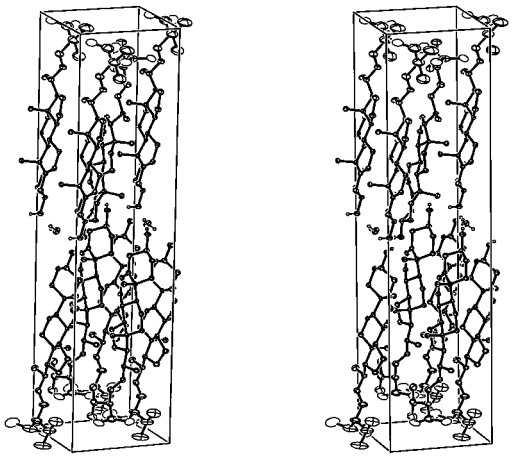

Figure 2
Stereoview of the unit cell. The origin is in the lower left foreground, the *a* axis is horizontal, and the *c* axis is vertical. Only H atoms on O atoms are shown.

(Argay *et al.*, 1996), has also been reported as the monohydrate, and has cell dimensions a = 10.399 (2), b = 7.5888 (10), c = 35.369 (4) Å and β = 94.51 (2)° at 295 K, also quite similar to the cell dimensions of stigmasterol hemihydrate. While that structure is not isostructural with the title compound, it also has $Z' = 2$, with a similar bilayer packing. Its water molecules are reported to be disordered, as is the C1–C5/C10 ring and the OH groups.

Experimental

The crude dichloromethane extract of the aerial parts of *Parthenium hysterophorus* was chromatographed by standard vacuum liquid chromatography procedures (Cantrell *et al.*, 1996) using silica gel with solvent mixtures of increasing polarity. Stigmasterol hemihydrate was isolated from non-polar fractions. Crystals were obtained from dichloromethane.

Crystal data

$C_{29}H_{48}O{\cdot}0.5H_2O$
M_r = 421.68
Monoclinic, $P2_1$
a = 9.367 (2) Å
b = 7.5127 (15) Å
c = 36.857 (7) Å
β = 93.184 (9)°
V = 2589.7 (10) Å^3
Z = 4
D_x = 1.082 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3373 reflections
θ = 2.5–27.4°
μ = 0.06 mm^{-1}
T = 120 K
Prism, colorless
0.47 × 0.18 × 0.10 mm

Data collection

KappaCCD diffractometer (with an Oxford Cryosystems Cryostream cooler)
ω scans with κ offsets
10 659 measured reflections
6072 independent reflections
4631 reflections with $I > 2\sigma(I)$
R_{int} = 0.038
θ_{max} = 27.4°
$h = -12 \rightarrow 12$
$k = -9 \rightarrow 5$
$l = -47 \rightarrow 47$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.059
$wR(F^2)$ = 0.156
S = 1.05
6072 reflections
582 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.0705P)^2 + 0.6772P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.007
$\Delta\rho_{max}$ = 0.30 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}

Table 1
Selected interatomic distances (Å).

O1*A*—C3*A*	1.435 (4)	O1*B*—C3*B*	1.430 (4)
C5*A*—C6*A*	1.327 (5)	C5*B*—C6*B*	1.329 (5)
C22*A*—C23*A*	1.336 (5)	C22*B*—C23*B*	1.334 (6)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*A*—H1*A*···O1*W*^{i}	0.84	2.10	2.894 (4)	158
O1*B*—H1*B*···O1*A*^{i}	0.84	1.95	2.787 (4)	172
O1*W*—H1*W*···O1*B*	0.85 (6)	2.37 (6)	3.212 (4)	171 (5)
O1*W*—H2*W*···O1*B*^{ii}	0.85 (5)	2.00 (5)	2.834 (4)	168 (5)

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

The ethyl CH_3 group (C29) is disordered over two positions in the *A* and *B* molecules. Population parameters were initially refined, then fixed at 70:30 in the *A* molecule and at 60:40 in the *B* molecule for the final structure refinement. The absolute structure was not determined, but was chosen to agree with the accepted configuration of steroids (Fieser & Fieser, 1959). The water H-atom positions were refined isotropically, with $U_{iso} = 1.5U_{eq}$(O). Other H atoms were placed in calculated positions, with C—H bond distances of 0.98 (CH), 0.97 (CH_2) and 0.96 Å (CH_3), and $U_{iso} = 1.2U_{eq}$ of the attached C atom (1.5 for methyl), and thereafter treated as riding. A torsional parameter was refined for each OH group and for methyl groups C18, C19, and C21. The remaining methyl groups were modeled as staggered.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK*; program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996)

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BK1624). Services for accessing these data are described at the back of the journal.

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