Guggulsterone E, a lipid-lowering agent from *Commiphora mukul*

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.011 Å
R factor = 0.063
wR factor = 0.237
Data-to-parameter ratio = 8.4

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

The crystal structure of the title compound [4,17(20)-(*cis*)-pregnadiene-3,16-dione, $C_{21}H_{28}O_2$] shows that the two molecules in the asymmetric unit have similar conformations. The fused-ring system contains one sofa, two chairs and one envelope. Weak intermolecular C—H···O hydrogen bonds, together with van der Waals interactions, stabilize the structure.

Comment

Guggulsterone E, an active constituent of an ayurvedic drug guggulip derived from *Commiphora mukul* (Verma *et al.*, 1998), possesses a significant cholesterol and lipid-lowering activity. It has been marketed in India as a hypolipidaemic drug. In view of its potential medicinal importance, the present study of the title compound, (I), was undertaken to determine the conformation of its steroid nucleus.

(I)
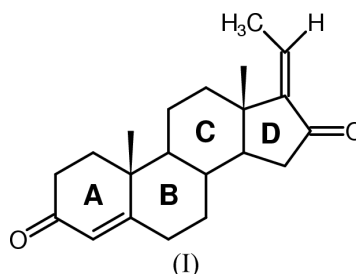
The X-ray diffraction study of (I) shows that the asymmetric unit contains two molecules of similar conformations and the structure of one molecule with the atomic numbering scheme is shown in Fig. 1. The molecule contains one fused-ring system (*A*/*B*/*C*/*D*) and five chiral centres. The torsion angles (Table 1) and least-squares-plane calculations indicate that, in both the molecules in the asymmetric unit, ring *A* is in a distorted sofa conformation, while rings *B* and *C* adopt a puckered and nearly a chair conformation, respectively. Ring *D* adopts an envelope conformation. The ring systems *B*/*C* and *C*/*D* are *trans*-fused with each other.

Based on literature precedence (Hill *et al.*, 1991), the pregnane steroids have C10-substituents in a β-orientation. Accordingly, the methyl groups at C10 and C13 have β-axial orientation in both the molecules in the asymmetric unit. The shorter bond lengths C3—C4/C33—C34 1.453 (12)/1.428 (11) Å and C16—C17/C46—C47 1.470 (11)/1.500 (12) Å are indicative of possible double-bond conjugation. The torsion angles C16—C17—C18—C19 −174.5 (7)° and C46—C47—C48—C49 −177.8 (7)° indicate that the title compound is the *E*-isomer of guggulsterone. The crystal structure analysis reveals the presence of weak intermolecular C—H···O

interactions (Table 2) which, along with the van der Waals forces, stabilize the solid-state structure.

Experimental

Guggulsterone E was isolated by column chromatography of the ethyl acetate extract from *Commiphora mukul* following the available protocol (Patil *et al.*, 1972). Diffraction-quality crystals were grown by slow evaporation of a methanol solution at room temperature.

Crystal data

$C_{21}H_{28}O_2$
$M_r = 312.44$
Monoclinic, $P2_1$
$a = 7.4634\,(11)$ Å
$b = 13.747\,(2)$ Å
$c = 17.352\,(3)$ Å
$\beta = 94.862\,(12)°$
$V = 1773.8\,(5)$ Å^3
$Z = 4$

$D_x = 1.170$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 50
  reflections
$\theta = 2.3–12.3°$
$\mu = 0.07$ mm^{-1}
$T = 293\,(2)$ K
Needle, colourless
$0.35 \times 0.25 \times 0.20$ mm

Data collection

Bruker $P4$ diffractometer
$\theta–2\theta$ scans
4388 measured reflections
3522 independent reflections
2257 reflections with $I > 2\sigma(I)$
$R_{int} = 0.031$
$\theta_{max} = 25.0°$

$h = -1 \rightarrow 8$
$k = -16 \rightarrow 1$
$l = -20 \rightarrow 20$
3 standard reflections
  every 97 reflections
  frequency: 60 min
  intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.063$
$wR(F^2) = 0.237$
$S = 0.92$
3522 reflections
421 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.1494P)^2 + 1.4424P]$
  where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}
Absolute structure: Flack (1983)
Flack parameter = −1 (4)

Table 1
Selected torsion angles (°).

|			
C10—C1—C2—C3	−52.0 (8)	C32—C33—C34—C35	−4.6 (12)
C1—C2—C3—C4	29.3 (10)	C33—C34—C35—C40	−4.7 (12)
C2—C3—C4—C5	−1.3 (13)	C40—C35—C36—C37	−54.2 (9)
C3—C4—C5—C10	−4.6 (13)	C35—C36—C37—C38	54.4 (9)
C10—C5—C6—C7	−48.0 (10)	C36—C37—C38—C39	−54.9 (8)
C5—C6—C7—C8	52.5 (9)	C37—C38—C39—C40	56.8 (8)
C6—C7—C8—C9	−56.8 (8)	C32—C31—C40—C50	−75.4 (8)
C7—C8—C9—C10	58.3 (7)	C32—C31—C40—C35	45.4 (8)
C2—C1—C10—C5	45.3 (8)	C34—C35—C40—C31	−15.8 (10)
C2—C1—C10—C20	−72.9 (8)	C36—C35—C40—C39	50.9 (8)
C4—C5—C10—C1	−17.5 (10)	C38—C39—C40—C35	−52.0 (7)
C6—C5—C10—C9	45.3 (8)	C41—C42—C43—C51	−68.0 (8)
C8—C9—C10—C5	−50.8 (7)	C47—C43—C44—C45	38.1 (7)
C11—C12—C13—C21	−67.0 (8)	C43—C44—C45—C46	−38.0 (8)
C17—C13—C14—C15	40.0 (6)	C44—C45—C46—C47	22.2 (8)
C13—C14—C15—C16	−36.8 (7)	C45—C46—C47—C43	1.2 (8)
C14—C15—C16—C17	19.7 (8)	C44—C43—C47—C46	−23.5 (7)
C15—C16—C17—C13	5.6 (8)	C46—C47—C48—C49	−177.8 (7)
C14—C13—C17—C16	−27.8 (6)	H9—C9—C8—H8	−178
C16—C17—C18—C19	−174.5 (7)	H39—C39—C38—H38	−179
C40—C31—C32—C33	−54.8 (9)	C21—C13—C14—H14	176
C31—C32—C33—C34	33.3 (10)	C51—C43—C44—H44	176
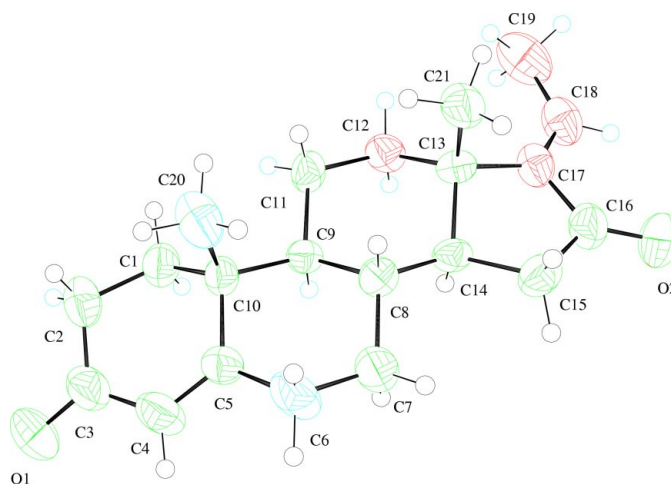
Figure 1
The molecular structure of (I) with labelling of the non-H atoms and displacement ellipsoids at the 50% probability level.

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

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
C21—H21$C\cdots$O2^{i}	0.96	2.745	3.625 (10)	153
C21—H21$B\cdots$O31^{i}	0.96	2.813	3.723 (10)	159
C32—H32$B\cdots$O2^{ii}	0.97	2.453	3.237 (10)	138
C45—H45$A\cdots$O1^{iii}	0.97	2.425	3.274 (11)	146
C50—H50$B\cdots$O32^{iii}	0.96	2.759	3.641 (10)	153
C51—H51$B\cdots$O1^{iii}	0.96	2.725	3.678 (12)	172

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

All H atoms were placed in idealized positions geometrically and allowed to ride on their parent atoms. The present study does not establish the absolute configuration of the title molecule, and it is not known from other work. There are only 281 Friedel pairs, and the anomalous scattering effects are negligible.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL-NT* (Bruker, 1997); program(s) used to refine structure: *SHELXTL-NT*; molecular graphics: *NRCVAX* (Gabe *et al.*, 1989) and *ORTEP* (Johnson, 1965); software used to prepare material for publication: *SHELXTL-NT*.

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