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Lupeol

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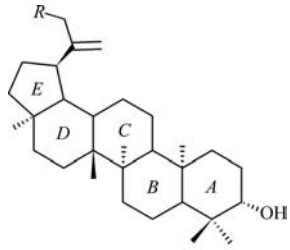
The title compound [systematic name: 3β-lup-20(29)-en-3-ol], $C_{30}H_{50}O$, was isolated from the leaves of *Garcinia brasiliensis* (common name: bacupari; a member of the Guttiferae family) and has been shown to have many useful medicinal and biological properties. The lupeol molecule consists of four six-membered rings (adopting chair conformations) and one five-membered ring (with an envelope conformation), all fused in *trans* fashion. Lupeol is isomorphic with the pentacyclic triterpene 3β,30-dihydroxylup-20(29)-ene, which differs from lupeol due to the presence of an additional hydroxy group. The crystal packing is stabilized by van der Waals interactions and intermolecular O—H$\cdots$O hydrogen bonds, giving rise to an infinite helical chain along the *c* axis.

Comment

As part of our ongoing studies on the chemical constituents of Brazilian medicinal plants (Da Cruz *et al.*, 2008; Derogis *et al.*, 2008; Martins *et al.*, 2007; Doriguetto *et al.*, 2006, 2001; Soares *et al.*, 2006; Lemos *et al.*, 2006), we have studied lupeol, (I), a natural pentacyclic triterpene isolated from the leaves of *Garcinia brasiliensis*, known popularly as bacupari (Corrêa, 1978). From *Garcinia* genus (Guttiferae family), biflavonoids, xanthones, proanthocyanins, poliprenilated benzophenones, sesquiterpenes and pentacyclic triterpenes (PCTT) have been isolated (Derogis *et al.*, 2008; Dos Santos *et al.*, 2007; Delle Monache *et al.*, 1983). In particular, (I) has shown many interesting biological properties, such as inhibition of cardiotoxicity induced by cyclosphosphamide (Sudharsan *et al.*, 2006), and hepatoprotective (Sahdeo *et al.*, 2007), anticancer (Laszczyk *et al.*, 2006) and cytotoxic activities (Gauthier *et al.*, 2006). Previous studies have also shown that (I) is a potential anti-inflammatory agent, preventing the production of some pro-inflammatory mediators (Fernández *et al.*, 2001). Other biological targets of (I) are microorganisms such as bacteria and fungi (Shai *et al.*, 2008).

In spite of its biological importance, up until now, (I) has been characterized only by spectroscopic and spectrometric analysis (Śliwowski & Kasprzyk, 1974; Shamma *et al.*, 1962). Therefore, in the present paper, we report for the first time the crystal structure of (I) (Fig. 1). The anomalous scattering was not large enough to permit the determination of the enantiomer present and therefore distinguish between the enantiomorphous space groups $P4_1$ and $P4_3$ (Flack, 2003).



(I) R = H
(II) R = OH

However, $P4_3$ was chosen because this space group is consistent with the stereochemistry specified by biosynthesis (Śliwowski & Kasprzyk, 1974). Thus, the chiral atoms present the following configurations: C3(*S*), C5(*R*), C8(*R*), C9(*S*), C10(*R*), C13(*R*), C14(*R*), C17(*R*), C19(*R*). Interestingly, another PCTT recently determined by us, namely 3β,30-dihydroxylup-20(29)-ene, (II) (Pimenta *et al.*, 2006), which differs chemically from (I) due to the hydroxy group present at C30, was reported in the enantiomorphous $P4_1$ (or $P4_3$) space group [a = 19.038 (1) Å and c = 7.2290 (4) Å]. It is also important to mention that space groups $P4_3$ and $P4_1$ are rare for organic and organometallic compounds. Currently, in the Cambridge Structural Database (Version 5.29, updated in August 2008; Allen, 2002), there are only 341 and 454 structures deposited with space groups $P4_3$ and $P4_1$, respectively. Indeed, (I) is the first PCTT determined in $P4_3$ on the basis of X-ray diffraction analysis and biosynthesis arguments (Śliwowski & Kasprzyk, 1974).

Fig. 1 shows that (I) contains five rings, all *trans*-fused, where all of the six-membered rings (*A*, *B*, *C* and *D*) adopt chair conformations, while the five-membered ring (*E*) adopts an envelope conformation with atom C17 in the flap position.

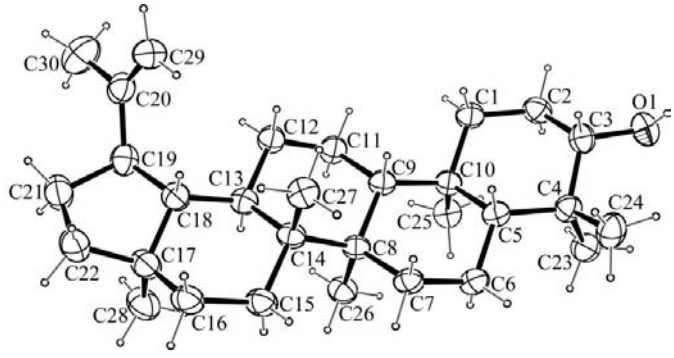


Figure 1
The structure of lupeol, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

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The hydroxy group is linked at atom C3 in an equatorial position. The intramolecular geometric parameters were analyzed by a *Mogul* check (Bruno *et al.*, 2004). All geometrical values agree with those of other reported PCTT structures (*e.g.* Pimenta *et al.*, 2006; Madureira *et al.*, 2004; Silva *et al.*, 2002; Nakai *et al.*, 1985).

Compound (I) contains an intermolecular O—H···O hydrogen bond (Fig. 2 and Table 1). This interaction stabilizes the packing and gives rise to an infinite helical chain along the *c* axis. The molecules are related by 4_3 improper symmetry. Additionally, parallel chains are linked together to form a 'cogwheel' structure, connected *via* van der Waals interactions (Fig. 2). These interactions are probably the driving force for the growth of (I) as single crystals with a needle habit.

Comparison of (I) with (II) (Pimenta *et al.*, 2006) by the Kabsch (1976) method showed them to be very similar in terms of intramolecular geometry, with an r.m.s. deviation between homologous atoms of 0.024 (17) Å. The largest deviation between the analogues takes place at atom C30 [the displacement is 0.09 (2) Å]. However the most surprising result highlighted by the X-ray diffraction analysis is that (I) and (II) (Pimenta *et al.*, 2006) are isomorphs: they crystallize in an enantiomorphous space group with almost identical cell parameters and supramolecular structures. Thus, the hydroxy group linked to atom C3 in both molecules is more important in terms of the packing than the hydroxy group linked to atom C30 in (II) (Pimenta *et al.*, 2006). Although a similar supramolecular structure is observed, the forces that stabilize the crystal packing are slightly different in (I) and (II). In Fig. 2, which gives the crystal structure of (I) projected on to the *ab* plane, we observe the hydrophilic head hydrogen bonded along the [001] direction through the unit-cell center, whereas the hydrophobic tails, linked by weak van der Waals forces, are stacked along the [001] direction through unit-cell corners. These characteristics could explain the difficulty in obtaining single crystals of lupeol and their fragility. In (II) (Pimenta *et al.*, 2006), there are additionally intermolecular hydrogen bonds at the unit-cell corners, which give rise to more mechanical stability in (II) than in (I).

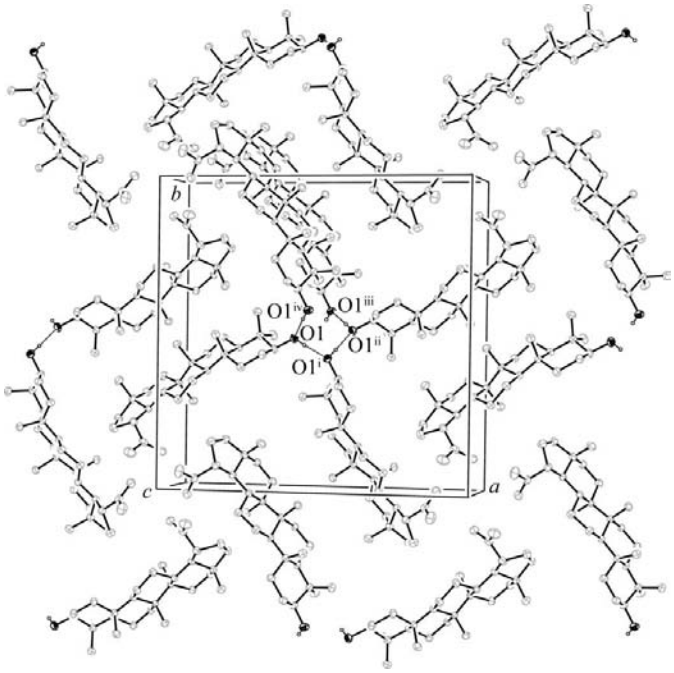

Figure 2
The crystal packing of (I) projected on to the *ab* plane, showing the hydrophilic head (center) and the hydrophobic tail (corner). Hydrogen bonds linking the molecules of (I) form a helix along the *c* axis. [Symmetry codes: (i) $-y+1, x, z-\frac{1}{4}$; (ii) $-x+1, -y+1, z-\frac{1}{2}$; (iii) $y, -x+1, z-\frac{3}{4}$; (iv) $y, -x+1, z+\frac{1}{4}$.]

Experimental

The leaves of *G. brasiliensis* were collected in Viçosa, Minas Gerais state, Brazil, in 2006. A voucher specimen (VIC26240) is deposited at the herbarium of Universidade Federal de Viçosa. The leaves were dried and submitted to a dichloromethane extraction. The solvent was removed in vacuum and the dichloromethane extract (10 g) was submitted to column chromatography using silica gel. This extract was eluted with increasing amounts of hexane, hexane/ethyl acetate, ethyl acetate and ethyl acetate/ethanol, obtaining 95 fractions. From fraction 26 (hexane/ethyl acetate 9:1 *v*/*v*), a white solid was obtained by recrystallization from methanol, yielding lupeol (525 mg). Single crystals were obtained after one week by slow evaporation from a chloroform and methanol (2:1 *v*/*v*) solution at 283 K.

Crystal data

$C_{30}H_{50}O$
M_r = 426.7
Tetragonal, $P4_3$
a = 19.1006 (14) Å
c = 7.2128 (4) Å
V = 2631.5 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.06 mm^{-1}
T = 298 K
0.40 × 0.06 × 0.04 mm

Data collection

Nonius KappaCCD diffractometer
7896 measured reflections
2655 independent reflections
1943 reflections with $I > 2\sigma(I)$
R_{int} = 0.080

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.113
S = 1.03
2655 reflections
284 parameters
1 restraint
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.1 e Å^{-3}
$\Delta\rho_{min}$ = −0.10 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O1^{i}	0.82 (4)	1.94 (4)	2.756 (3)	171 (4)

Symmetry code: (i) $-y+1, x, z-\frac{1}{4}$.

H atoms bound to C atoms were located from an electron-density difference synthesis and refined as riding on their parent atoms, with U_{iso}(H) values of 1.5U_{eq}(C) for methyl H atoms or 1.2U_{eq}(C) for the remaining H atoms. The hydroxy H atom was located by difference Fourier synthesis and was refined isotropically. In the absence of significant anomalous scattering, the Friedel pair reflections were merged before the final refinement.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: EM3022). Services for accessing these data are described at the back of the journal.

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