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6-Hydroxymexicanolide

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Key indicators

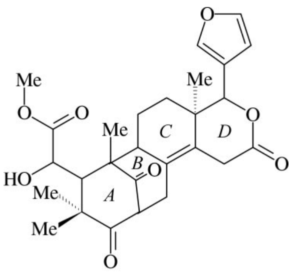
Single-crystal X-ray study
T = 293 K
Mean *σ*(C–C) = 0.005 Å
R factor = 0.050
wR factor = 0.134
Data-to-parameter ratio = 8.6

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

The title compound, 4-(3-furyl)-1,4,4a,5,6,6a,7,8*α*,9,10,11*α*,12-dodecahydro-4a,7,9,9-tetramethyl-2,10,13-trioxo-7,11-methano-2*H*-cycloocta[*f*][2]benzopyran-8-hydroxyacetic acid methyl ester ($C_{27}H_{32}O_8$), has for the first time been isolated from *Lansium domesticum*, Correa. The six-membered rings adopt boat, chair, distorted sofa and half-chair conformations. The furan ring is planar. The furan substituent and hydroxyacetate group are attached equatorially to the swietenine skeleton. The crystal structure is stabilized by C—H···O interactions.

Comment

Lansium domesticum, Correa is a genus of small trees from the family Meliaceae found wild and also cultivated in Thailand and the surrounding countries in South Asia. The seeds are traditionally known to be toxic to the malaria parasite (Leaman *et al.*, 1995). Preliminary testing of the dichloromethane extract of the seeds of *Lansium domesticum* was found to significantly inhibit *Plasmodium falciparum* with an IC_{50} (Inhibitory Concentration) of 9.9 µg ml^{-1}. The title compound, (I), was isolated as a major compound from the seeds of *Lansium domesticum.* As part of our research on bioactive constituents from Thai medicinal plants (Chantrapromma *et al.*, 1999, 2003; Chumkeaw *et al.*, 2003; Fun *et al.*, 2003), we have undertaken the X-ray crystal structure analysis of (I) in order to establish its molecular structure and relative stereochemistry. Although the title compound does not significantly inhibit *Plasmodium falciparum* (IC_{50} > 20 µg ml^{-1}), a modification of its molecular structure to enhance its anti-*Plasmodium falciparum* activity is now under investigation.



(I)

The structure of (I) contains a four-ring fused triterpenoid system, *A*/*B*/*C*/*D*, known as the swietenine skeleton (Fig. 1). The structure of (I) is similar to that of mexicanolide, in which an acetic acid methyl ester group is attached to C3. The structure and absolute configuration of mexicanolide has been reported (Sanni *et al.*, 1987*b*). Refinement of the Flack (1983) parameter failed to determine the absolute configuration of

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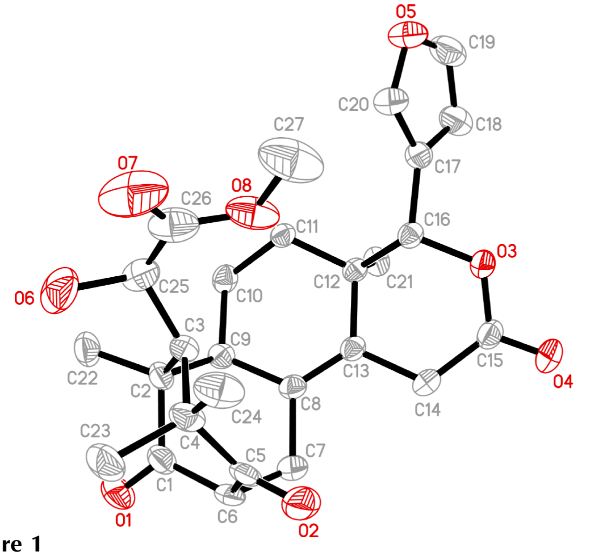

Figure 1
The structure of the title compound, showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms were omitted for clarify.

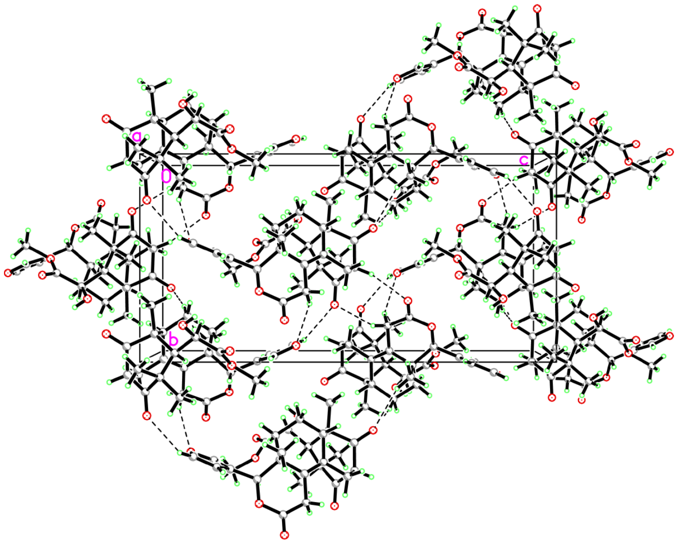

Figure 2
The molecular packing, viewed down the *a* axis.

(I) owing to the absence of heavy atoms. The enantiomer has been assigned by reference to mexicanolide. The bond lengths and angles in the title compound are comparable with the corresponding values in mexicanolide (Sanni *et al.*, 1987*b*) and angolensate (Sanni *et al.*, 1987*a*).

In the swietenine skeleton, the cyclohexane ring *A* adopts a boat conformation, ring *B* has an approximate chair conformation and ring *D* adopts a half-chair conformation (Cremer & Pople, 1975). The presence of a double bond between C8 and C13 forces ring *C* to adopt a distorted sofa conformation. The furan ring is planar within 0.008 (5) Å. The hydroxyacetate group and the furan substituent are attached equatorially to rings *A* and *D*, respectively. The conformation of the methoxycarbonyl group is (+)-synperiplanar, the O7—C26—O8—C27 torsion angle being 2.3 (7)°. The O6—C25—C26—O7 torsion angle of −8.0 (7)° characterizes the (−)-synperiplanar conformation of the O6 and O7 atoms.

The crystal structure is stabilized by C—H···O interactions (Table 2), linking the molecules together to form a molecular network (Fig. 2).

Experimental

Air-dried and powdered seeds of *Lansium domesticum* (2.0 kg) were extracted with dichloromethane at room temperature. The dichloromethane extract was dried under reduced pressure to yield a crude extract (90.15 g). The crude extract was separated by quick column chromatography on silica gel and eluted initially with hexane enriched with dichloromethane, then ethyl acetate, followed by an increasing amount of methanol in ethyl acetate and finally with methanol. Each fraction was monitored by TLC; fractions that appeared similar on TLC were combined to yield 21 major fractions, F1–F21. Fraction F7 (4.65 g) was rechromatographed on a silica gel flash column, followed by preparative TLC with 20% ethyl acetate/dichloromethane to give (I) (2.90 g, R_f 0.54). Compound (I) was recrystallized from chloroform/methanol, yielding colorless single crystals, m.p. 537–538 K.

Crystal data

$C_{27}H_{32}O_8$
$M_r = 484.53$
Orthorhombic, $P2_12_12_1$
$a = 10.6293$ (6) Å
$b = 10.7405$ (6) Å
$c = 21.4937$ (13) Å
$V = 2453.8$ (2) Å^3
$Z = 4$
$D_x = 1.312$ Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 5306 reflections
$\theta = 2.7$–$26.0°$
$\mu = 0.10$ mm^{-1}
$T = 293$ (2) K
Block, colorless
0.30 × 0.28 × 0.22 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{\min} = 0.972$, $T_{\max} = 0.979$
13401 measured reflections
2744 independent reflections
2249 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.029$
$\theta_{\max} = 26.0°$
$h = -12 \rightarrow 13$
$k = -13 \rightarrow 11$
$l = -19 \rightarrow 26$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.050$
$wR(F^2) = 0.135$
$S = 1.11$
2744 reflections
320 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0595P)^2 + 0.8864P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.22$ e Å^{-3}
$\Delta\rho_{\min} = -0.18$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C13—C8	1.341 (5)	C20—O5	1.356 (5)
C14—C15	1.484 (5)	C25—O6	1.428 (5)
C15—O4	1.204 (4)	C25—C26	1.480 (7)
C15—O3	1.338 (4)	C26—O7	1.197 (6)
C16—O3	1.457 (4)	C26—O8	1.342 (7)
C16—C17	1.497 (5)	C27—O8	1.462 (6)
C17—C20	1.332 (6)	O1—C1	1.203 (4)
C17—C18	1.417 (6)	O2—C5	1.197 (5)
C18—C19	1.330 (6)	C1—C6	1.487 (6)
C19—O5	1.347 (7)		
O7—C26—O8	122.9 (6)	O8—C26—C25	113.1 (4)
O7—C26—C25	124.0 (6)	C26—O8—C27	113.6 (5)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C3—H3*A*···O8	0.98	2.51	2.911 (4)	104
C6—H6*A*···O4^{i}	0.98	2.43	3.387 (5)	166
C10—H10*B*···O1^{ii}	0.97	2.54	3.503 (5)	172
C14—H14*A*···O5^{iii}	0.97	2.56	3.402 (6)	146
C14—H14*B*···O2^{iv}	0.97	2.49	3.362 (5)	149
C19—H19*A*···O2^{v}	0.93	2.49	3.208 (6)	135
C21—H21*A*···O1^{ii}	0.96	2.56	3.478 (5)	161
C22—H22*A*···O6	0.96	2.53	2.891 (6)	103
C23—H23*C*···O6	0.96	2.47	3.039 (6)	118

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

H atoms were placed in calculated positions, with an O—H distance of 0.82 Å and C—H distances in the range 0.93–0.98 Å. The $U_{\rm iso}$ values were constrained to be $1.5U_{\rm eq}$ of the carrier atom for hydroxyl and methyl H atoms and $1.2U_{\rm eq}$ for the remaining H atoms. The Friedel reflections were merged before the final refinement because of the absence of significant anomalous scattering effects.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL, PARST* (Nardelli, 1995) and *PLATON* (Spek, 1990).

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