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20(29)-Lupene-3β,28β-diacetate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.042
wR factor = 0.118
Data-to-parameter ratio = 8.8

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

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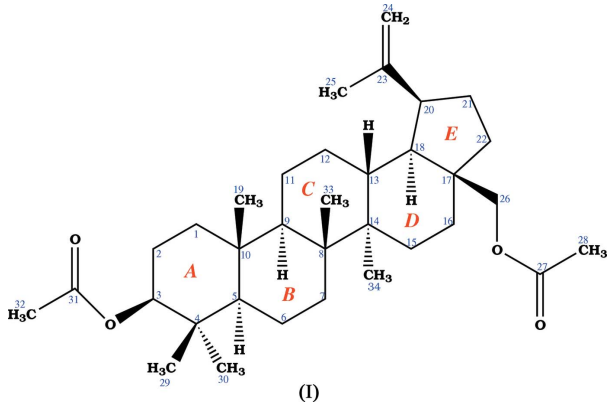
The triterpene 20(29)-lupene-3β,28β-diacetate, $C_{34}H_{54}O_4$, was obtained by acetylation of naturally occurring betulin. The cyclopentane ring adopts a twisted envelope conformation and the cyclohexane rings are all in chair conformations. The molecular structure is stabilized only by weak intramolecular C—H···O hydrogen bonds.

Comment

Diospyros mespiliformis (Hochst. ex A.DC), an important member of the Ebenaceae family, is a tropical shrub which occurs widely in Sudan throughout the high rainfall savannahs in the Red Sea Hills (Erkowit), Blue Nile, Kassala, Kordofan, Darfur along Bahr el Ghazal and Equatoria (El Amin, 1990). The genus *Diospyros* and the whole Ebenaceae family are known to produce dimeric naphthoquinones and triterpenoids of the lupane series (Zhong *et al.*, 1984). Several ethnopharmacological uses have been reported in respect of *D. mespiliformis*; for example, as an unusual remedy for fever, whooping cough and wounds. Barks and roots are used against serious infections, malaria, pneumonia, syphilis, leprosy and dermatomycoses; it facilitates child birth and it is also used as an antihelmintic drug (Watt & Brandwijk, 1962).



(I)

Betulin is a pentacylic triterpene isolated from *Diospyros mespiliformis*; it has a wide spectrum of biological activities. Many derivatives of betulin have been reported in the literature in respect of their anti-inflammatory and antitumor activities (Zdzisinska *et al.* 2003; Kim *et al.*, 1998). Betulin has been shown to be a potent phospholipase A2 inhibitor (Bernard *et al.*, 2001). Moreover, it also inhibits leukocyte elastase or serine proteases such as trypsin and chymotrypsin (Rajic *et al.*, 2001; Ying *et al.*, 1991). With this background, we thought it very important to determine the stereochemistry of this compound. The X-ray crystal structure analysis of (I) is

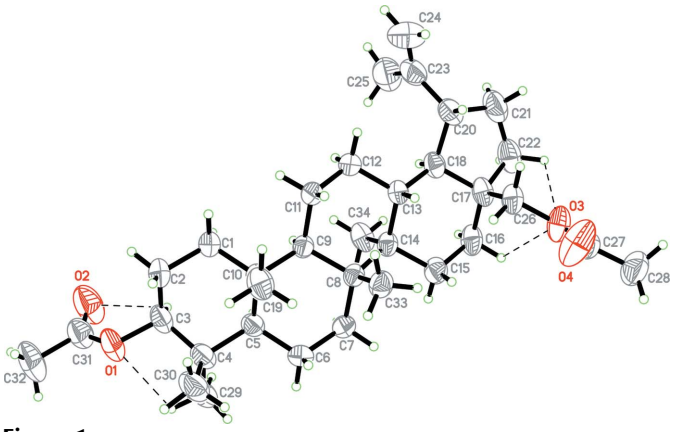


Figure 1
The structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. The dashed lines indicate intramolecular hydrogen bonds.

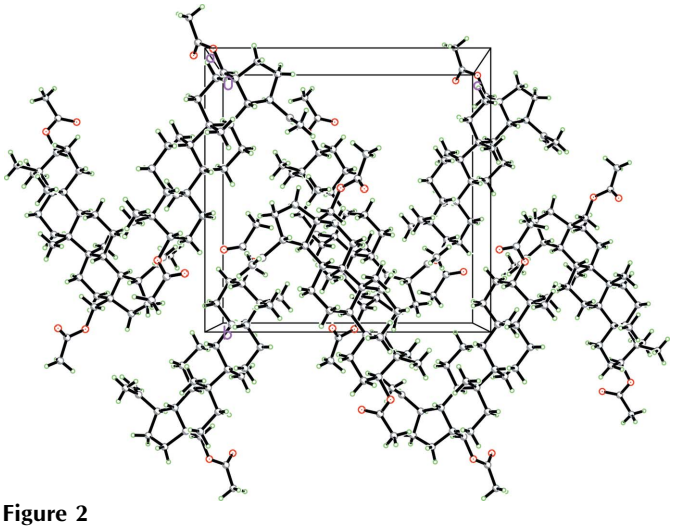


Figure 2
The molecular packing in (I), viewed down the *a* axis.

part of our ongoing study of the molecular structures and relative stereochemistry of biologically active natural products (Awan *et al.*, 2005; Choudhary *et al.*, 2006; Anjum *et al.*, 2005).

The crystal structure of (I) has been reported previously by Das *et al.* (1983) [Cambridge Structural Database, Version 5.27 (CSD; Allen, 2002), refcode CUBYAZ] with an *R* value of 0.055. However, the earlier paper did not discuss the molecular or crystal structure. Our work is of higher precision and reports structural details.

The bond lengths in (I) show normal values (Allen *et al.*, 1987). All ring junctions in the lupane nucleus are *trans*-fused. The cyclopentane ring adopts a twisted envelope conformation at C17—C18. The six-membered rings adopt normal chair conformations (Cremer & Pople, 1975).

An *O*-acetyl group is attached to atom C3 of ring *A* in an equatorial orientation; the torsion angle C31—O1—C3—C2 is 94.0 (3)°. The isopropyl group is equatorially attached to atom C20 of cyclopentane ring *E*; the torsion angle C21—C20—C23—C24 is −107.1 (4)°.

Molecules are packed along the *a* axis, in a zigzag fashion, parallel to the *bc* plane (Fig. 2). No classical hydrogen bonding is observed. However, the molecular structure is stabilized by weak intramolecular C—H···O interactions. *S*5 graph-set motifs are formed by H16*A*···O3—C26—C17—C16—, H22*A*···O3—C26—C17—C22—, C3—H3*A*···O2—C31—O1— and C30—H30*A*···O1—C3—C4— (Bernstein *et al.*, 1995).

Experimental

Purified betulin (15.0 mg, 0.032 mmol) was dissolved in pyridine (1 ml), followed by the addition of acetic anhydride (2 ml, 21.2 mmol). The reaction mixture was stirred overnight at room temperature. The resulting mixture was poured into ice water and extracted with ethyl acetate. This extract was concentrated under vacuum and purified by flash chromatography using a silica column to yield compound (I) (10 mg, 0.019 mmol, 59.5% yield).

Crystal data

$C_{34}H_{54}O_4$
M_r = 526.77
Orthorhombic, $P2_12_12_1$
a = 12.5710 (13) Å
b = 15.6745 (16) Å
c = 15.7618 (16) Å
V = 3105.8 (6) Å^3
Z = 4
D_x = 1.127 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 7765 reflections
θ = 1.8–25.0°
μ = 0.07 mm^{-1}
T = 293 (2) K
Block, colorless
0.36 × 0.34 × 0.15 mm

Data collection

Siemens SMART CCD area detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.867, T_{max} = 0.990
15663 measured reflections
3072 independent reflections
2868 reflections with $I > 2\sigma(I)$
R_{int} = 0.016
θ_{max} = 25.0°
h = −14 → 14
k = −18 → 17
l = −18 → 16

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.118
S = 1.04
3072 reflections
350 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0708P)^2 + 0.5698P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C3—H3*A*···O2	0.98	2.32	2.702 (4)	102
C16—H16*A*···O3	0.97	2.49	2.876 (3)	104
C22—H22*A*···O3	0.97	2.52	2.929 (4)	106
C30—H30*A*···O1	0.96	2.54	2.914 (4)	106

H atoms were placed in calculated positions with C—H distances in the range 0.93–0.98 Å. The U_{iso}(H) values were constrained to be 1.5U_{eq} of the carrier atom for methyl H atoms and 1.2U_{eq} for the other H atoms. In the absence of significant anomalous dispersion effects, Friedel pairs were averaged.

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, 2003).

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