

Cinnamolid-3 β -ol hemihydrate and 3 β -hydroxycinnamolide acetate, two drimanolide-class sesquiterpene lactones from *Warburgia ugandensis*

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Received 23 February 2006

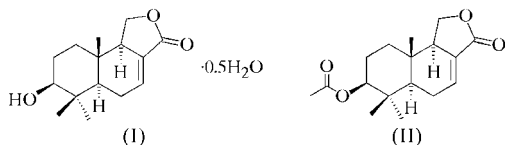
Accepted 27 February 2006

Online 18 March 2006

3 β -Hydroxy-7-drimen-12,11-olide hemihydrate, C₁₅H₂₂O₃·0.5H₂O, (I), has two sesquiterpene molecules and one water molecule in the asymmetric unit. The OH groups of both molecules and both H atoms of the water molecule are involved in near-linear intermolecular hydrogen bonds, having O···O distances in the range 2.632 (3)–2.791 (2) Å. 3 β -Acetoxy-7-drimen-12,11-olide, C₁₇H₂₄O₄, (II), has its ring system in very nearly the same conformation as the two molecules of (I).

Comment

Plants of the genus *Warburgia* are of interest because of their use by herbalists in Kenya for the treatment of a number of parasitic diseases (Kokwaro, 1976). Isolation of drimanolide-class sesquiterpenes (I) and (II) (see scheme) from the stem bark of *Warburgia ugandensis* Sprague (Canellaceae) has been described by Kioy *et al.* (1990). The molecular structures of 3 β -hydroxy-7-drimen-12,11-olide hemihydrate, (I), and 3 β -acetoxy-7-drimen-12,11-olide, (II), were determined in order to ascertain unambiguously the relative stereochemistry of the 3-OH and 3-OAc groups, respectively, as well as to confirm the relative configurations of the other asymmetric centers.



One of the two independent molecules of (I) is shown in Fig. 1. The OH group at C3 is seen to be β -oriented and the configurations at the other chiral centers are confirmed to be those reported by Kioy *et al.* (1990). The conformations of the two independent molecules are nearly identical, with a maximum deviation in an endocyclic torsion angle of 2.5 (6) $^\circ$ about the double bond C7=C8. The OH-carrying A ring has a

chair conformation, the central B ring a half-chair conformation, and the lactone ring a C₂ half-chair conformation, with the axis passing through C12 and bisecting C9–C11. The most notable difference in the conformations of the two molecules involves the OH group, in which the O–H bond is roughly parallel to C10–C15 in the A molecule and roughly anti-parallel in the B molecule, in accordance with the hydrogen-bonding scheme. The OH group of the A molecule donates a hydrogen bond to the water molecule, while the OH of the B molecule instead donates to the OH group of the A molecule. The lactone carbonyl atom O2 of the A molecule accepts a hydrogen bond (from water), but that of the B molecule is not involved in hydrogen bonding. The acceptor for the second hydrogen bond donated by water is the OH group of the B molecule.

Compound (II) is shown in Fig. 2, and the configurations at all the chiral centers are seen to be the same as those of (I). The conformation of the ring system also agrees well with that of (I); the largest individual difference between an endocyclic torsion angle in (II) and the corresponding average value in (I) is 4.1 (5) $^\circ$ for C7–C8–C9–C10. The conformations of the ring system in both title compounds agree fairly well with those of two molecules also having the drimanolide skeleton,

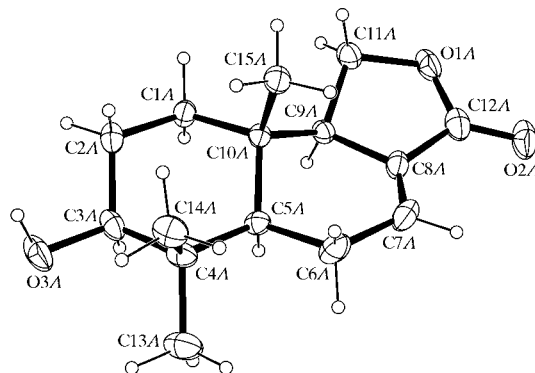


Figure 1

One of the two independent molecules (molecule A) in (I), showing the atom-numbering scheme and with displacement ellipsoids drawn at the 50% probability level.

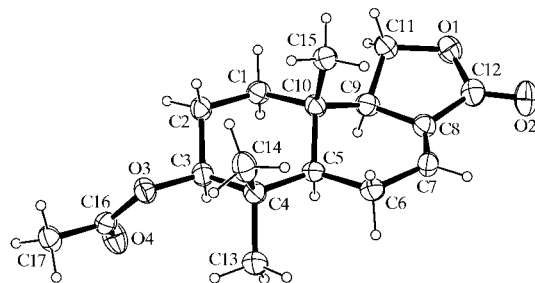


Figure 2

A view of the acetate, (II), showing the atom-numbering scheme and with displacement ellipsoids drawn at the 50% probability level.

viz. insulicolide A (Rahbaek *et al.*, 1997) and iresin dibromobenzoate (Rossman & Lipscomb, 1958). The cell dimensions of (II) at room temperature (299 K), measured on a Nonius CAD-4 diffractometer using Cu K α radiation, are $a = 6.8885$ (6) Å, $b = 7.9753$ (8) Å and $c = 14.411$ (2) Å, and $\beta = 101.613$ (7)°.

Experimental

Compounds (I) and (II) were isolated from the stem bark of *Warburgia ugandensis* Sprague (Canellaceae) collected in Eldoret, Uasin Gishu District, Kenya, as described by Kioy *et al.* (1990). Crystals were grown from a solution in acetone–hexane (1:1 *v/v*).

Drimanolide (I)

Crystal data

C₁₅H₂₂O₃·0.5H₂O
M_r = 259.33
 Monoclinic, *P*₂₁
 $a = 12.875$ (3) Å
 $b = 6.153$ (2) Å
 $c = 18.268$ (4) Å
 $\beta = 106.031$ (16)°
 $V = 1390.9$ (6) Å³
 $Z = 4$

$D_x = 1.238$ Mg m⁻³
 Mo K α radiation
 Cell parameters from 4619 reflections
 $\theta = 2.5$ –32.0°
 $\mu = 0.09$ mm⁻¹
 $T = 120$ K
 Prism, colorless
 0.42 × 0.35 × 0.20 mm

Data collection

Nonius KappaCCD area-detector diffractometer (with an Oxford Cryosystems Cryostream cooler)
 ω scans with κ offsets
 17077 measured reflections
 5214 independent reflections

3773 reflections with $I > 2\sigma(I)$
 $R_{int} = 0.040$
 $\theta_{max} = 32.0^\circ$
 $h = -19 \rightarrow 19$
 $k = -8 \rightarrow 9$
 $l = -27 \rightarrow 26$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.049$
 $wR(F^2) = 0.112$
 $S = 1.03$
 5214 reflections
 353 parameters
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0505P)^2 + 0.0592P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} = 0.003$
 $\Delta\rho_{max} = 0.38$ e Å⁻³
 $\Delta\rho_{min} = -0.23$ e Å⁻³
 Extinction correction: *SHELXL97* (Sheldrick, 1997)
 Extinction coefficient: 0.007 (2)

Table 1

Selected geometric parameters (Å, °) for (I).

O1A–C12A	1.342 (3)	O2B–C12B	1.203 (2)
O2A–C12A	1.220 (2)	O3B–C3B	1.437 (2)
C7A–C8A	1.314 (3)	C7B–C8B	1.322 (3)
C10A–C1A–C2A–C3A	–58.2 (2)	C10B–C1B–C2B–C3B	–57.0 (2)
C1A–C2A–C3A–C4A	61.9 (2)	C1B–C2B–C3B–C4B	59.2 (3)
C2A–C3A–C4A–C5A	–55.2 (2)	C2B–C3B–C4B–C5B	–53.4 (2)
C3A–C4A–C5A–C10A	48.4 (2)	C3B–C4B–C5B–C10B	49.0 (2)
C10A–C5A–C6A–C7A	–42.8 (3)	C10B–C5B–C6B–C7B	–42.0 (3)
C5A–C6A–C7A–C8A	7.3 (3)	C5B–C6B–C7B–C8B	8.2 (3)
C6A–C7A–C8A–C9A	3.0 (4)	C6B–C7B–C8B–C9B	0.5 (4)
C12A–C8A–C9A–C11A	–21.9 (2)	C12B–C8B–C9B–C11B	–20.3 (2)
C7A–C8A–C9A–C10A	22.6 (3)	C7B–C8B–C9B–C10B	24.9 (3)
C2A–C1A–C10A–C5A	49.5 (2)	C2B–C1B–C10B–C5B	50.3 (2)
C8A–C9A–C10A–C5A	–53.8 (2)	C8B–C9B–C10B–C5B	–54.40 (19)
C4A–C5A–C10A–C1A	–46.5 (2)	C4B–C5B–C10B–C1B	–48.1 (2)
C6A–C5A–C10A–C9A	65.3 (2)	C6B–C5B–C10B–C9B	64.1 (2)
C12A–O1A–C11A–C9A	–19.5 (2)	C12B–O1B–C11B–C9B	–20.1 (2)
C8A–C9A–C11A–O1A	24.7 (2)	C8B–C9B–C11B–O1B	23.8 (2)
C11A–O1A–C12A–C8A	5.3 (2)	C11B–O1B–C12B–C8B	7.1 (3)
C9A–C8A–C12A–O1A	11.4 (2)	C9B–C8B–C12B–O1B	9.3 (2)

Table 2

Hydrogen-bond geometry (Å, °) for (I).

<i>D</i> –H... <i>A</i>	<i>D</i> –H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> –H... <i>A</i>
O3A–H3OA...O1W ⁱ	0.86 (3)	1.79 (3)	2.632 (3)	164 (3)
O3B–H3OB...O3A ⁱⁱ	0.82 (3)	1.83 (4)	2.641 (2)	168 (3)
O1W–H1W...O2A	0.90 (3)	1.90 (3)	2.791 (2)	169 (3)
O1W–H2W...O3B ⁱⁱⁱ	0.88 (4)	1.83 (4)	2.694 (3)	166 (3)

Symmetry codes: (i) $x + 1, y, z$; (ii) $x - 1, y, z$; (iii) $x, y + 1, z$.

Drimanolide (II)

Crystal data

C₁₇H₂₄O₄
M_r = 292.36
 Monoclinic, *P*₂₁
 $a = 6.802$ (3) Å
 $b = 7.918$ (4) Å
 $c = 14.302$ (8) Å
 $\beta = 101.22$ (2)°
 $V = 755.6$ (7) Å³
 $Z = 2$

$D_x = 1.285$ Mg m⁻³
 Mo K α radiation
 Cell parameters from 2218 reflections
 $\theta = 2.5$ –30.0°
 $\mu = 0.09$ mm⁻¹
 $T = 120$ K
 Prism, colorless
 0.33 × 0.18 × 0.15 mm

Data collection

Nonius KappaCCD area-detector diffractometer (with an Oxford Cryosystems Cryostream cooler)
 ω scans with κ offsets
 8695 measured reflections
 2353 independent reflections

1456 reflections with $I > 2\sigma(I)$
 $R_{int} = 0.057$
 $\theta_{max} = 30.0^\circ$
 $h = -9 \rightarrow 9$
 $k = -11 \rightarrow 11$
 $l = -20 \rightarrow 20$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.051$
 $wR(F^2) = 0.108$
 $S = 0.98$
 2353 reflections
 195 parameters
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0473P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} < 0.001$
 $\Delta\rho_{max} = 0.22$ e Å⁻³
 $\Delta\rho_{min} = -0.20$ e Å⁻³
 Extinction correction: *SHELXL97* (Sheldrick, 1997)
 Extinction coefficient: 0.012 (3)

Table 3

Selected geometric parameters (Å, °) for (II).

O2–C12	1.207 (3)	C7–C8	1.326 (4)
O4–C16	1.201 (3)		
C10–C1–C2–C3	–56.9 (3)	C2–C1–C10–C5	50.6 (3)
C1–C2–C3–C4	61.2 (3)	C8–C9–C10–C5	–55.4 (3)
C2–C3–C4–C5	–56.6 (3)	C4–C5–C10–C1	–49.4 (3)
C3–C4–C5–C10	50.9 (3)	C6–C5–C10–C9	62.9 (3)
C10–C5–C6–C7	–39.4 (3)	C12–O1–C11–C9	–17.0 (3)
C5–C6–C7–C8	7.1 (4)	C8–C9–C11–O1	20.2 (3)
C6–C7–C8–C9	–1.6 (4)	C11–O1–C12–C8	6.0 (3)
C12–C8–C9–C11	–17.1 (3)	C9–C8–C12–O1	7.6 (3)
C7–C8–C9–C10	27.8 (4)		

H atoms were placed in calculated positions, guided by difference maps, with C–H bond distances in the range 0.95–1.00 Å and with $U_{iso}(H) = 1.2U_{eq}(C)$ or $1.5U_{eq}(\text{methyl } C)$, and thereafter treated as riding. The coordinates for OH H atoms were refined. A torsional parameter was refined for each methyl group. The absolute configuration could not be established from the X-ray data, but was assigned based on the configuration of insulicolide A (Rahbaek *et al.*, 1997). Friedel pairs were averaged.

For both compounds, data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*;

program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

The purchase of the diffractometer was made possible by grant No. LEQSF(1999–2000)-ESH-TR-13, administered by the Louisiana Board of Regents.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ3003). Services for accessing these data are described at the back of the journal.

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