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New limonoids from *Harrisonia perforata* (Blanco) Merr.

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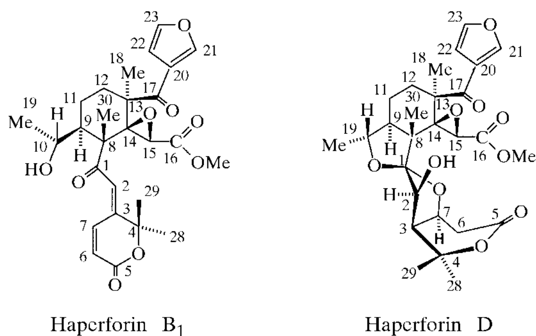
Two minor compounds were isolated from a sample of *Harrisonia perforata* leaves collected in central Vietnam, namely haperforin B_1, $C_{27}H_{32}O_9$, and haperforin D, $C_{27}H_{34}O_{10}$. Biogenetically, haperforin D and haperforin B_1 can be derived from each other by addition or elimination of water.

Comment

Harrisonia perforata (Blanco) Merr., a bush belonging to the Simaroubaceae, is common throughout Southeast Asia (Vietnam, Philippines, China). Chemical investigations performed by other groups (Byrne *et al.*, 1991; Wei *et al.*, 1985; TranVan *et al.*, 1995) and by ourselves (Khuong-Huu *et al.*, 2000) have shown the presence of limonoids belonging to the obacunol series (Taylor, 1984). From a sample of *Harrisonia perforata* leaves collected in central Vietnam, two minor compounds were isolated and named haperforin B_1 and haperforin D. Their complete structures were determined by X-ray crystallographic analyses.



The molecular structures of haperforin B_1 and haperforin D are depicted, respectively, in Figs. 1 and 2 with atomic labelling. The absolute configuration has been postulated as being similar to that of this series of limonoids. It appears that these two molecules are quite similar in the upper part (see Scheme and Figs. 1 and 2), while large differences occur in the lactonic part. In fact, biogenetically, they can be derived from each other by addition or elimination of water. The formation of haperforin D from haperforin B_1 requires the addition of water to the C2—C3 double bond and the formation of a hemiketal between the hydroxyl at C10 and the C1-ketone, followed by addition of hemiketalic hydroxyl to the C6—C7 double bond to afford the two tetrahydrofuran rings. In the structure of haperforin B_1, the ethylenic bond C2—C3 is partially conjugated with the carbonyl bond C1—O1 as illustrated by the torsion angles C3—C2—C1—O1 of −31.3 (5)° and C3—C2—C1—C8 of 153.1 (3)°. The packing of haperforin B_1 shows the existence of an intermolecular hydrogen bond

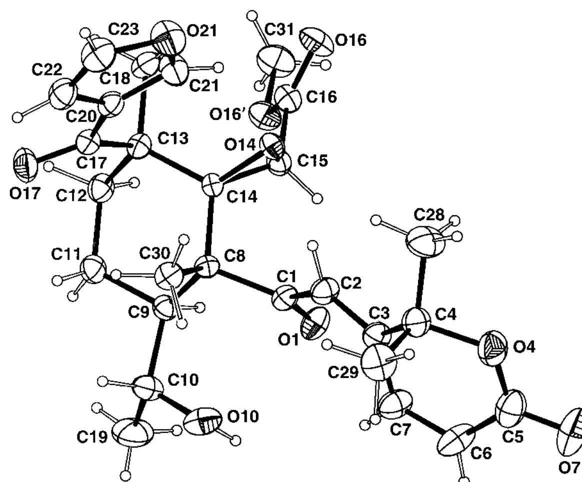


Figure 1
The molecular structure of haperforin B_1 showing 30% probability displacement ellipsoids.

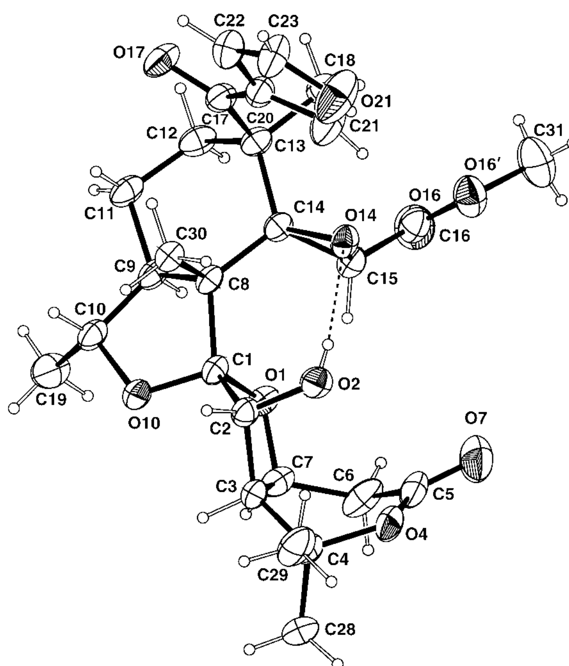


Figure 2
The molecular structure of haperforin D showing 30% probability displacement ellipsoids.

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between the hydroxyl group O10—H and the carbonyl-O atom O16 of a neighbouring molecule. In haperforin D, an intramolecular hydrogen bond bridges the hydroxyl group O2—H to the epoxide O atom O14. The methoxycarbonyl group at C15 is rotated by 180° in haperforin D with respect to that of haperforin B_1. In both molecules, the six-membered rings C8–C14 adopt a chair conformation. If we superimpose these two molecules on these six-membered rings (*BMFIT*; Nyburg, 1974), we observe a perfect superimposition for the furan and epoxide substituents (except the C15—C16 rotation of the methoxycarbonyl group). Due to the *cis* junction of the five- (C1–O1) and six-membered (C3–C7) rings, the lactone ring is orientated in different directions (the O7 atoms are 5.1 Å apart). It is interesting to note that in haperforin B_1, a biogenetic precursor of haperforin D, the hydroxyl O10 atom is near the C1 atom of the carbonyl group [intramolecular distance O10···C1 of 2.719 (4) Å] and so the conformation adopted by the chain at C8 corresponds to a pro-*R* cyclization at C1 of the hydroxyl O10 (C1 being *R* in haperforin D).

Experimental

The limonoids were extracted according to the procedure described by Polonsky (1959) with slight modifications. The complex mixture obtained was separated by successive column and preparative thin-layer chromatography. Haperforin B_1 has the following characteristics: m.p. 473 K (MeOH), $[\alpha]_D = -72.8$ ($CHCl_3$, $c = 1.02$); HRCIMS: MH^+ 501.2116 (calculated 501.2124 for $C_{27}H_{33}O_9$); UV: λ_{max} (EtOH): 272.6 nm ($\varepsilon = 13750$); IR (film, ν, cm^{-1}): 3437 (OH), 1757, 1728, 1714, 1651 (C═O), 1302, 1124 (C—O); ^{1}H NMR (δ, p.p.m., $CDCl_3$, 400 MHz): 0.96 (3H, *s*, CH_3), 1.19 (3H, *s*, CH_3), 1.24 (3H, *d*, $J = 6$ Hz, CH_3), 1.34 (1H, *d*, $J = 7$ Hz, H-12*b*), 1.50 (3H, *s*, CH_3), 1.57 (3H, *s*, CH_3), 1.66 (2H, *m*, CH_2-11), 2.47 (1H, *dd*, $J = 7$, $J' = 3$ Hz, H-12*a*), 2.56 (1H, *t*, $J = 8$ Hz, H-9), 3.30 (1H, *m*, H-10), 3.49 (1H, *s*, H-15), 3.79 (3H, *s*, CO_2CH_3), 5.25 (1H, *s*, OH), 6.06 (1H, *dd*, $J = 10$, $J' = 2$ Hz, H-6), 6.32 (1H, *s*, H-2), 7.01 (1H, *s*, H-22), 7.46 (1H, *s*, H-23), 7.68 (1H, *d*, $J =$ 10 Hz, H-7), 8.53 (1H, *s*, H-21); ^{13}C NMR (δ, p.p.m.): 15.39 (CH_3), 22.77 (CH_2-11), 23.33 (CH_3-19), 24.39 (CH_3), 29.14 (CH_3), 29.72 (CH_3), 34.93 (CH_2-12), 49.69 (CH-9), 51.65 (C-13), 52.72 (OCH_3), 56.07 (C-8), 58.74 (CH-15), 69.87 (CH-10), 70.44 (C-14), 83.45 (C-4), 110.34 (CH-22), 122.63 (CH-6), 126.55 (C-20), 127.42 (CH-2), 138.16 (CH-7), 143.60 (CH-23), 145.88 (C-3), 149.21 (CH-21), 163.80 (C═O ester C-16), 166.27 (C═O lactone C-5), 196.0 (C═O C-17), 204.85 (C═O C-1).

Haperforin D has the following characteristics: m.p. 512 K (EtOH), $[\alpha]_D = -98$ ($CHCl_3$, $c = 0.98$); HRCIMS: MH^+ 519.2244 (calculated 519.2230 for $C_{27}H_{35}O_{10}$), 501.2099 (calculated 501.2124 for $C_{27}H_{33}O_9$, MH^+–H_2O); IR ($CHCl_3$, ν, cm^{-1}): 1762, 1725, 1662 (C═O); ^{1}H NMR (δ, p.p.m., $CDCl_3$, 400 MHz): 1.0 (3H, *s*, CH_3), 1.06 (3H, *s*, CH_3), 1.24 (3H, *d*, $J = 6$ Hz, CH_3), 1.32 (3H, *s*, CH_3), 1.40 (1H, *m*, CH_2-12*a*), 1.48 (3H, *s*, CH_3), 1.80 (2H, *m*, CH_2-11), 2.42 (1H, *m*, H-9), 2.58 (2H, *m*, H-3, H-12*b*), 2.80 (2H, *ABX*, $J = 18$, $J' = 8$ Hz, H-6), 3.55 (1H, *s*, OH), 3.66 (1H, *dd*, $J = 10$, $J' = 6$ Hz, H-10), 3.82 (3H, *s*, CO_2CH_3), 3.98 (1H, *d*, $J = 4$ Hz, H-2), 4.72 (1H, *td*, $J = 8$, $J' = 1$ Hz, H-7), 5.08 (1H, *s*, H-15), 6.92 (1H, *s*, H-22), 7.38 (1H, *s*, H-23), 8.35 (1H, *s*, H-21); ^{13}C NMR (δ, p.p.m.): 14.35 (CH_3), 19.08 (CH_2-11), 20.67 (CH_3-19), 23.93 (CH_3), 27.23 (CH_3), 28.73 (CH_3), 34.72 (CH_2-6), 37.11 (CH_2-12), 46.15 (CH-3), 51.69 (C-13), 52.15 (CH-9), 52.45 (OCH_3), 52.80 (C-8), 59.04 (CH-15), 69.88 (C-4), 71.98 (CH-7), 72.63 (CH-2), 75.66 (CH-10), 79.43 (C-14), 110.59 (CH-22), 117.30 (C-1), 125.59 (C-20), 142.61 (CH-23), 149.34 (CH-21), 167.83 (C═O), 169.51 (C═O), 196.46 (C═O C-17).

Haperforin B_1

Crystal data

$C_{27}H_{32}O_9$
$M_r = 500.53$
Orthorhombic, $P2_12_12_1$
$a = 12.216$ (4) Å
$b = 12.463$ (5) Å
$c = 16.781$ (7) Å
$V = 2554.9$ (17) Å^3
$Z = 4$
$D_x = 1.301$ Mg m^{-3}

Cu $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 14.0$–22.1°
$\mu = 0.812$ mm^{-1}
$T = 293$ (2) K
Prism, colourless
0.53 × 0.26 × 0.20 mm

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
3271 measured reflections
2327 independent reflections
2192 reflections with $I < 2\sigma(I)$
$R_{int} = 0.026$
$\theta_{max} = 66.85°$

$h = -10 \rightarrow 14$
$k = 0 \rightarrow 14$
$l = 0 \rightarrow 19$
3 standard reflections
frequency: 120 min
intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.049$
$wR(F^2) = 0.128$
$S = 1.087$
2327 reflections
325 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0859P)^2 + 0.5597P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.004$
$\Delta\rho_{max} = 0.24$ e Å^{-3}
$\Delta\rho_{min} = -0.26$ e Å^{-3}

Table 1
Selected torsion angles (°) for haperforin B_1.

O1—C1—C2—C3	−31.3 (5)	O4—C5—C6—C7	12.6 (7)
C8—C1—C2—C3	153.1 (3)	C5—C6—C7—C3	−8.2 (7)
C1—C2—C3—C7	−9.7 (6)	C6—C7—C3—C4	−18.2 (6)
C1—C2—C3—C4	177.4 (3)	C8—C9—C10—O10	−33.8 (4)
C7—C3—C4—O4	37.8 (4)	C13—C14—C15—C16	6.8 (4)
C3—C4—O4—C5	−35.9 (5)	C14—C15—C16—O16	99.9 (4)
C4—O4—C5—C6	11.6 (6)		

Table 2
Hydrogen-bonding geometry (Å, °) for haperforin B_1.

D—H···A	D—H	H···A	D···A	D—H···A
O10—HO10···O16^i	0.82	2.25	2.933 (4)	141

Symmetry code: (i) $-x, y - \frac{1}{2}, \frac{1}{2} - z$.

Haperforin D

Crystal data

$C_{27}H_{34}O_{10}$
$M_r = 518.54$
Monoclinic, $P2_1$
$a = 10.148$ (5) Å
$b = 11.225$ (7) Å
$c = 11.356$ (8) Å
$\beta = 99.44$ (2)°
$V = 1276.1$ (14) Å^3
$Z = 2$

$D_x = 1.350$ Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 15.2$–21.0°
$\mu = 0.860$ mm^{-1}
$T = 293$ (2) K
Prism, colourless
0.35 × 0.35 × 0.20 mm

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
3411 measured reflections
2389 independent reflections
2368 reflections with $I > 2\sigma(I)$
$R_{int} = 0.061$
$\theta_{max} = 66.89°$
$h = -11 \rightarrow 11$
$k = 0 \rightarrow 13$
$l = 0 \rightarrow 13$
3 standard reflections
frequency: 120 min
intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.066$
$wR(F^2) = 0.155$
$S = 1.089$
2385 reflections
334 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1223P)^2 + 0.1273P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.023$
$\Delta\rho_{max} = 0.37$ e Å^{-3}
$\Delta\rho_{min} = -0.40$ e Å^{-3}

Table 3
Selected torsion angles (°) for haperforin D.

O1—C1—C2—C3	−43.0 (3)	C5—O4—C4—C3	−32.7 (5)
C1—C2—C3—C7	33.4 (3)	O4—C4—C3—C7	52.3 (4)
C2—C3—C7—O1	−13.2 (3)	O10—C1—C8—C9	−42.2 (3)
C3—C7—O1—C1	−14.6 (3)	C1—C8—C9—C10	45.1 (3)
C7—O1—C1—C2	36.3 (3)	C8—C9—C10—O10	−32.9 (3)
C4—C3—C7—C6	−23.0 (5)	C9—C10—O10—C1	5.5 (3)
C3—C7—C6—C5	−24.5 (5)	C10—O10—C1—C8	23.9 (3)
C7—C6—C5—O4	47.5 (5)	C13—C14—C15—C16	0.7 (5)
C6—C5—O4—C4	−17.0 (6)	C14—C15—C16—O16	−92.8 (5)

Table 4
Hydrogen-bonding geometry (Å, °) for haperforin D.

D—H···A	D—H	H···A	D···A	D—H···A
O2—HO2···O14	0.82	1.94	2.738 (3)	165

For both compounds, data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *NONIUS* (Riche, 1989); program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *R3M* (Riche, 1983) and *ORTEP* (Johnson, 1965).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GS1076). Services for accessing these data are described at the back of the journal.

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