

Cyclic Hemiacetals with Seven-Membered Rings from an Undescribed *Salacia* Species from Monteverde, Costa Rica

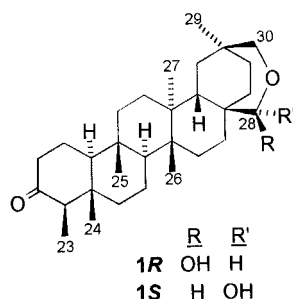
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Received August 7, 1998

The two cyclic hemiacetals of 30-hydroxyfriedelan-3-on-28-al (**1R** and **1S**) were found in an undescribed *Salacia* species from Costa Rica and characterized by spectral methods.

The cytotoxicity of an undescribed *Salacia* species (Hippocrateaceae), a canopy liana from Monteverde, Costa Rica, is apparently due to the presence of large amounts of tingenone, a highly oxidized friedelin derivative.¹ Extracts from this plant were also found to contain smaller amounts of friedelin and friedelin derivatives friedelan-3-on-29-al, canophyllol, and 29-hydroxyfriedelan-3-one.¹ We now report the isolation and characterization of two new friedelin derivatives, 30-hydroxyfriedelan-3-on-28-al 28*R*-hemiacetal (**1R**) and 30-hydroxyfriedelan-3-on-28-al 28*S*-hemiacetal (**1S**), from this plant.



These new compounds occurred together in a silica gel chromatography fraction that was separable from the above compounds. A high-resolution EI mass spectrum showed a molecular ion at m/z 456.3618, consistent with molecular formula $C_{30}H_{48}O_3$, and fragmentation peaks for the loss of a methyl group, water, and a methyl group and water. An IR spectrum showed a carbonyl peak at 1710 cm^{-1} and a hydroxyl peak at 3430 cm^{-1} . ^1H NMR, HMQC, and HMBC spectra showed the sample to be an equimolar mixture of **1R** and **1S**, the two tautomeric hemiacetals of 30-hydroxyfriedelan-3-on-28-al. The chemical shift assignments and coupling constants are listed in Table 1. Most A- and B-ring atom shifts were the same in both stereoisomers.

It was readily established which peaks corresponded to **1R** and which to **1S** using the strong HMBC peaks that accompany 180° H–C–C–C dihedral angles. The anomeric effect makes the hydroxyl groups in both epimers axial, since both H-28's have strong HMBC peaks with C-30. The H-28 that has a strong HMBC peak with C-18 must be in **1R**, where this angle is close to 180° . This assignment is supported by the downfield shifts of H-16 β , H-18, and H-26 in **1R**, in which these protons are close to the hydroxyl

Table 1. Chemical Shifts (δ , CDCl_3) and Coupling Constants (Hz, in Parentheses) for **1R** and **1S**

position	1R		1S	
	δ_C	δ_H^a	δ_C	δ_H^a
1	22.1	2.00, 1.71	22.1	2.00, 1.71
2	41.4	2.30, 2.40	41.4	2.30, 2.40
3	213.5		213.5	
4	58.1	2.25 q (6.5)	58.1	2.25 q (6.5)
5	41.7		41.7	
6	41.0	1.27, 1.75	41.0	1.27, 1.75
7	18.0	1.49, 1.33	18.0	1.49, 1.33
8	50.5	1.38	50.3	1.42
9	37.4		37.4	
10	59.5	1.56	59.5	1.56
11	34.8	1.35, 1.46	34.8	1.35, 1.46
12	28.3	1.24, 1.49	27.8	1.27, 1.44
13	39.4		39.1	
14	38.4		38.9	
15	28.0	1.30, 1.30	27.3	1.32, 1.32
16	31.5	1.05, 1.82	32.3	1.30, 1.57
17	38.9		38.4	
18	32.5	2.51 dd (10.1, 6.7)	38.9	2.00
19	37.6	1.23, 1.48	33.2	1.13, 1.70
20	34.3		35.2	
21	31.0	1.27, 1.62	34.2	1.27, 1.39
22	31.5	1.27, 1.48	25.2	1.53, 2.17
23	6.8	0.881 d (6.5)	6.8	0.881 d (6.5)
24	14.5	0.722	14.5	0.722
25	18.9	0.917	18.9	0.905
26	14.6	0.971	15.2	0.845
27	15.1	1.09	14.8	1.07
28	103.5	4.44 d (3.1)	104.4	4.73 d (2.9)
29	28.6	0.803	28.7	0.827
30	72.9	3.22 d (11.6, eq), 3.78 d (11.6, ax)	72.4	3.76 d (11.6, ax), 3.21 d (11.6, eq)
OH		2.43 d (3.1) ^b		2.35 d (2.9) ^b

^a α signal listed first. ^b May be reversed.

group. The large 180° H–C–C–C HMBC peaks also permitted the assignments of protons within methylene groups as given in Table 1.

The finding of stable seven-membered cyclic hemiacetals is unusual but not unprecedented. Cyclamigenins A¹ and C are β -amyrin derivatives with the same ring system as **1R** and **1S**² but are acetals rather than hemiacetals, have C-30 rather than C-28 in the higher oxidation state, and are believed to be artifacts of the isolation procedure, and the open form (cyclamiretin D)³ is more stable than the hemiacetal forms in this system. **1R** and **1S** appear to be the first isolated seven-membered cyclic hemiacetals in the triterpene series, but there are examples among terpene derivatives⁴ and in very simple systems.⁵ **1R** and **1S** are presumably more stable than 30-hydroxyfriedelin-3-on-28-al (the open form) because besides replacing a π bond by a

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σ bond, they provide some relief of the strains generally present in the D and E rings of friedelins.

Canophyllol and/or 29-hydroxyfriedelan-3-one¹ are likely biological intermediates between friedelin and hemiacetals **1R** and **1S**.

Experimental Section

General Experimental Procedures. MS were obtained using direct inlet on a Hewlett-Packard GC/MS system. NMR spectra were run at 500 MHz on a Bruker AM-500 spectrometer with TMS as internal standard and CDCl₃ as solvent.

Plant Material. *Salacia* sp. (Hippocrateaceae), an undescribed liana in Monteverde, Costa Rica, with stems 15–30 m long, 2–3 cm in diameter when mature, usually reaching the subcanopy and often the canopy, with stem nodes often conspicuously thicker than internodes; leaves simple, opposite, with petioles 2–2.5 cm, blades from 6 × 15 cm to 11 × 26 cm, glabrous, thick and leathery, elliptic, margin entire, apex abruptly acuminate, base obtuse to rounded, midvein expressed above and below, the lateral veins 5–8 per side, flat above and expressed below; small, red flowers densely clustered on 3–8 cm, much-branched, axillary inflorescences; fruit a globose berry, 6–9 cm in diameter, with tough leathery skin, containing 2–6 seeds. *S. petenensis*, the only congener of this liana species in the Monteverde region, differs in growing as a free-standing tree reaching 15–25 m tall and 30 cm dbh, with leaves about half as large (to 6.5 × 14 cm), on windswept ridges in cloud forest at 1500–1700 m elevation (lower montane wet forest life zone). *S.* sp. grows in sheltered forest

on the Pacific slope just below the level of the cloud forest at 1200–1500 m elevation (premontane wet forest life zone). Flowers and fruits of the two species are very similar and will require detailed comparison to determine key character differences. Voucher specimens deposited with the Missouri Botanical Garden and the Museo Nacional de Costa Rica; collection no. Haber and Bello 8297.

Extraction and Isolation. The stem bark (2.50 kg) was collected and extracted with chloroform (4 h) to give 42.7 g extract, of which 25 g was subjected to flash chromatography on silica gel.¹ The fraction containing **1R** and **1S** (94 mg; equimolar mixture) came between those for canophyllol and 29-hydroxyfriedelan-3-one.¹

Compounds 1R and 1S: colorless needles; mp 243–249 °C; IR spectral data, see text; NMR spectral data, see Table 1; MS data, see text.

References and Notes

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NP980345J