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A NEW SESQUITERPENE FROM *LASERPITIUM LATIFOLIUM*

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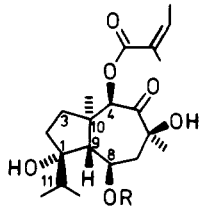
Except for *Laserpitium latifolium* L. (Apiaceae) and *Laserpitium halleri* Crantz subsp. *halleri* (1,2), all other *Laserpitium* species investigated so far have contained one or more different types of sesquiterpene lactones (3). Earlier investigations of *L. latifolium* (4-7) led to the isolation of a number of compounds of the daucane type but no sesquiterpene lactones. This chemotaxonomic irregularity prompted us to start a new investigation of plant materials collected in Austria, Sweden, and Finland. In the absence of any specific visualizing method for sesquiterpene lactones (8-10), we chose the rather cumbersome method of fractionating the plant extracts and screening the fractions for the characteristic γ-lactone band (1770-1750 cm^{-1}) (11) in the ir spectra. We found no sesquiterpene lactones but isolated a number of already known compounds and an as yet undescribed simple analog [**1**] of laserpitin [**2**]. The structure of **1**, including absolute configuration, was determined by means of ^1H nmr, ^{13}C nmr, cims, and by verifying that partial saponification of both **1** and **2** afforded **3**. The plant material from the three different locations showed no qualitative difference with respect to their constituents. The lack of sesquiterpene lactones in any detectable quantities together with the isolation of large amounts of daucane derivatives indicates that the biosynthesis of the sesquiterpene nucleus in *L. latifolium* is different from that of the other investigated species, including *L. halleri*. The daucane skeleton is believed to be formed at an early biosynthetic stage by cyclization of farnesyl pyrophosphate in contrast to the above-mentioned sesquiterpene lactones which are derived from the germacradiene skeleton (12).



1 R= 

2 R= 

3 R=H

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Optical rotations were measured with a Perkin-Elmer 241 polarimeter, and the ir spectra were measured on a Perkin-Elmer 781 Infared Spectrophotometer using KBr discs for crystalline compounds and 1.0 mm NaCl cuvettes for the collected fractions dissolved in $CHCl_3$. The ^1H-nmr and ^{13}C-nmr spectra were recorded on a Bruker HX 270 at 270 and 67.9 MHz, respectively, using $CDCl_3$ as solvent and TMS as internal standard. The cims spectrum was recorded on a VG 70-70 instrument using isobutane as reagent gas.

PLANT MATERIAL.—The underground parts of *L. latifolium* were collected by the authors near Graz, Austria, in July 1982 (no. 82-1), in Ahvenanmaa, Finland, in June 1985 (no. 85-1), and in Öland, Sweden in August 1985 (no. 85-2). Voucher specimens are deposited at the Department of Pharmacognosy, Royal Danish School of Pharmacy.

EXTRACTION AND FRACTIONATION.—The dried (50°), milled plant materials (250-500 g from each location) were extracted twice with EtOH, and the combined evaporated fractions were partitioned between H_2O and EtOAc. After filtration to remove crystallized laserpitin [**2**], the evaporated EtOAc phases were fractionated by

column chromatography on Si gel 60 (Merck) using EtOAc/toluene mixtures of increasing polarity as eluents, and ir spectra were recorded of representative fractions. Latifolon and β-sitosterol crystallized from two different fractions and were identified by ^{1}H-nmr and ir spectroscopy. From fractions following laserpitin [**2**], compound **1** was isolated, the ir spectrum of which showed pronounced resemblance with the ir spectrum of laserpitin. Compound **1** was further purified by hplc on a 8×250 mm, Lichrosorb RP18, 7 μm, with H_2O-MeOH (25:75)+1% HOAc (3 ml/min, refractive index and uv detection) Rt 11.5 min.

8-O-Desangeloyl-8-O-isobutanoyl-laserpitin [**1**].—Yield 0.05% (w/w) amorphous powder from dried plant material: $[\alpha]^{23}D=85°$ ($c=0.064$, EtOH); ir (KBr) ν max 3500, 2975, 2940, 2880, 1715, 1650, 1455, 1390, 1230, 1155 cm^{-1}; ^{1}H nmr δ 0.79, 0.90 (2×3H, each d, 6.8 Hz, 2×CH_3-C11), 1.18, 1.20 (2×3H, each d, 6.8 Hz, isobutanoyl), 1.40, 1.41 (2×3H, each s, CH_3-C6, CH_3-C10), 1.65 (5H, b, H11, 2×H2, 2×H3), 1.94 (3H, m, $J<1$ Hz, angeloyl), 2.00 (3H, dq, 7.3 Hz, angeloyl), 2.07 (1H, d, 11.1 Hz, H9), 2.27 (1H, d, 15.9 Hz, H7), 2.47 (1H, dd, 4, 15.9 Hz, H7′), 2.53 (1H, m, isobutanoyl), 5.26 (1H, s, H4), 5.36 (1H, dd, 4.9, 11.1 Hz, H8), 6.14 (1H, qm, 7.0 Hz, angeloyl); ^{13}C nmr δ 15.7 (angeloyl), 17.0, 17.9 (2×CH_3-C11), 18.2, 18.6 (isobutanoyl), 20.2 (angeloyl), 21.5, 28.7 (CH_3-C6, CH_3-C10), 31.2, 2×34.3, 39.7 (C2, C3, C7, isobutanoyl), 36.6 (C11), 45.7 (C10), 50.9 (C9), 69.0 (C8), 80.7 (C4), 76.2, 84.3 (C1, C6), 127.0 (angeloyl), 139.1 (angeloyl), 167.1 (angeloyl), 177.4 (isobutanoyl), 209.6 (C5); cims *m/z* 439 (M+1, 61%), 421 (14%), 391 (16%), 351 (3%), 333 (100%), 315 (30%), 233 (25%).

Laserpitin [**2**].—The ^{13}C-nmr data of laserpitin has not previously been published: δ 15.6, 15.7 (angeloyl), 17.1, 18.0 (2×CH_3-C11), 2×20.3 (angeloyl), 21.5, 28.9 (CH_3-C6, CH_3-C10), 31.2, 34.3, 39.9 (C2, C3, C7), 36.5 (C11), 45.9 (C10), 51.0 (C9), 68.4 (C8), 80.8 (C4), 76.2, 84.3 (C1, C6), 127.0, 127.3 (angeloyl), 139.2, 140.0 (angeloyl), 167.2, 168.3 (angeloyl), 209.7 (C5).

PARTIAL HYDROLYSIS OF 8-O-DESANGELOYL-8-O-ISOBUTANOYL-LASERPITIN [**1**].—Compound **1** (10 mg) in 300 μl MeOH was treated with 300 μl 2 M Na_2CO_3 for 20 h and extracted with Et_2O, and the formed **3** was purified by hplc on a 8×250 mm, Lichrosorb RP18, 7 μm, with H_2O-MeOH (25:75)+1% HOAc (3 ml/min, refractive and uv detection) Rt 6.5 min: $[\alpha]^{21}D=84.2°$ ($c=0.14$, EtOH) [lit. (6) $[\alpha]^{21}D=108.0°$]; ^{1}H nmr δ 0.75, 0.92 (2×3H, each d, 7 Hz, 2×CH_3-C11), 1.30, 1.41 (2×3H, each s, CH_3-C6, CH_3-C10), 1.65 (5H, b, H11, 2×H2, 2×H3), 1.92 (3H, s, angeloyl), 1.98 (3H, d, 7 Hz, angeloyl), 2.33 (1H, d, 16 Hz, H7), 2.51 (1H, dd, 5, 16 Hz, H7′), 4.15 (1H, b, H8), 5.31 (1H, s, H4), 6.16 (1H, q, 7 Hz, angeloyl).

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