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A NEW MINOR BUTENOLIDE FROM *Machilus odoratissima*

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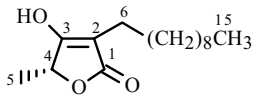
*A new butenolide, designated odoratinolide (**1**), was isolated from the bark of the Vietnamese medicinal plant* Machilus odoratissima. *Its structure was determined by spectroscopic analyses.*

Keywords: *Machilus odoratissima*, Lauraceae, butenolide.

In our previous papers [1, 2] the chemical profile of the *n*-hexane-soluble fraction of the MeOH extract of the bark of *Machilus odoratissima* Nees (Lauraceae) was found. Gradient chromatographic separation of this soluble fraction on silica gel gave mono- and sesquiterpenoids, β-sitosterol and stigmasterol [1], and lignans and neolignans [1, 2] in the order of increasing polarity. In the framework of our continuing study of the CH_2Cl_2-soluble fraction of the same MeOH extract, a new minor 3-hydroxybutenolide **1** was isolated. This paper discussed the isolation and structure elucidation of this compound.

Extraction and liquid-liquid fractionation of the MeOH extract of the dried bark of *M. odoratissima* gave the *n*-hexane, CH_2Cl_2, EtOAc, and 1-BuOH-soluble fractions. A procedure was established for the isolation of the minor butenolide **1**, including successive gradient column chromatography (CC) on silica gel and ODS (octadecyl silica gel) and ODS HPLC purification.

Compound **1** was obtained as an amorphous powder. The molecular formula of **1** was determined to be $C_{15}H_{26}O_3$ by positive-ion HR-FAB-MS *m/z*: 255.1960 $[M + H]^+$. The IR spectrum of **1** showed absorption bands of hydroxyl groups (3382 cm^{-1}) and a double bond (1643 cm^{-1}). The ^1H NMR spectrum of **1** established the presence of a long alkyl chain [δ 0.79 (3H, t, J = 6.8 Hz), 1.17 (14H, br.s), 1.34 (2H, br.s), and 1.98 (2H, t, J = 7.8 Hz)] and a secondary methyl group [δ 1.29 (3H, d, J = 6.6 Hz, H_3-5)] which was bonded to an isolated oxymethine [δ 4.39 (1H, q, J = 6.6 Hz)]. The methylene group at δ 1.98 (2H, t) was clearly attached to a double bond. Analysis of the ^{13}C NMR spectrum of **1** showed the signals of a lactone ring (δ 178.9), a double bond (δ 131.9 and 147.2), and an oxymethine group (δ 75.7). The other carbon 13 signals were attributed to two methyl groups and the aliphatic methylenes of the long alkyl chain. On the basis of the spectroscopic data, three double-bond equivalents calculated from the molecular formula of **1** can be accounted for by an α,β-unsaturated γ-lactone. Comparison of the NMR data ravealed the related structure of **1** to the synthetic (+)-(5*S*)-3-dodecyl-5-methylfuran-2(5*H*)-one [3] except for an additional hydroxyl group at C-3 leading to the existence of an isolated oxymethine group in **1**. The butenolide core skeleton of **1** was also supported by the structures of the butenolides isolated from *Hortonia* species [4]. The stereochemistry at C-4 was assigned to the *R*-configuration by comparison of its $[\alpha]$ with those of similar compounds [4, 5]. Thus, the absolute structure of **1**, which was designated odoratinolide, was determined as shown.



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EXPERIMENTAL

General Experimemtal Procedures. Optical rotation was measured on a JASCO P-1030 digital polarimeter. FT-IR spectrum was recorded on a Horiba FT-710 spectrophotometer. ^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a JEOL JNM-α 400 NMR spectrometer with tetramethylsilane as an internal standard. Positive-ion HR-FAB-MS spectra were measured on a JEOL SX-102 mass spectrometer with PEG-400 as a calibration matrix. HPLC was performed with a JASCO PU-1580 pump and an UV-2075 Plus detector (set at 210 nm) using YMC ODS analytical (150 × 4.6 mm i.d.) and preparative (150 × 20 mm i.d.) columns at the corresponding flow rates of 0.5 and 5 mL/min. TLC glass plates (Merck, silica gel 60 F_{254}) were used for analysis. Silica gel 60 (0.063–0.200 mm, Merck, Germany), and reversed-phase ODS (YMC, Japan) were used for CC.

Plant Material. The bark of *M. odoratissima* (voucher specimen No. HCTN 2000-6) was collected and identified by Dr. Nguyen Hoanh Coi (Military Center for Drug Control and Research, Hanoi, Vietnam) in June 2000 in Thai Nguyen Province, Northern Vietnam.

Extraction and Isolation. The air-dried bark of *M. odoratissima* (2.0 kg) was powdered and then extracted three times (each time for 3 days) with MeOH at room temperature. The MeOH extract was partitioned between H_2O and *n*-hexane, CH_2Cl_2, EtOAc, and 1-BuOH, successively, to afford the corresponding soluble fractions [2]. The CH_2Cl_2-soluble fraction (17.8 g) was chromatographed on a gradient silica gel column using $CHCl_3$–MeOH, 15:1, 10:1, 6:1, and 3:1 as solvent systems to afford four main fractions on the basis of their TLC pattern. Fraction 1 (1.8 g) was subjected to gradient column chromatography on ODS eluting with MeOH–H_2O, 3:2, 3:1, and 4:1, and subfraction 1 was purified by using preparative ODS HPLC (MeOH–H_2O, 3:1) to yield **1** (1.6 mg).

Odoratinolide (1). White amorphous powder, $[\alpha]_D^{25}$ –1.75° (*c* 0.16, MeOH). IR (film, ν_{max}, cm^{-1}): 3382, 1707, 1643, 1566, 1454, 1261, 1076. Positive-ion HR-FAB-MS *m/z*: 255.1960 $[M + H]^+$ (calcd for $C_{15}H_{27}O_3$: 255.1961). ^1H NMR ($CDCl_3$, δ, ppm, J/Hz): 0.79 (3H, t, J = 6.8, 3H-15), 1.17 (14H, br.s, 2H-8 – 2H-14), 1.29 (3H, d, J = 6.6, 3H-5), 1.34 (2H, br.s, 2H-7), 1.98 (2H, t, J = 7.8, 2H-6), 3.28 (1H, br.s, 3-OH), 4.39 (1H, q, J = 6.6, H-4). ^{13}C NMR ($CDCl_3$, δ, ppm): 13.6, 17.5, 20.9, 22.4, 28.4, 28.9, 29.3, 29.4, 29.5 (C-5, C-7, C-8, C-9, C-10, C-11, C-12, C-13, C-14, C-15), 31.6 (C-6), 75.7 (C-4), 131.9 (C-2), 147.2 (C-3), 178.9 (C-1).

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