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Lignans from Leaves of *Laurus nobilis* L.

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Three lignan glycosides, (+)-secoisolariciresinol 9-*O*-β-D-xylopyranoside, (+)-5′-methoxyisolariciresinol 9′-*O*-β-D-xylopyranoside and schizandraside, along with *Z*-3-hexenyl-*O*-β-D-glucopyranoside were isolated from the leaves of *Laurus nobilis* L. (Lauraceae).

Keywords——*Laurus nobilis*; Lauraceae; lignan glycoside; (+)-secoisolariciresinol 9-*O*-xyloside; (+)-5′-methoxyisolariciresinol 9′-*O*-xyloside; schizandraside; *Z*-3-hexenyl-*O*-glucoside

In the course of our chemical studies on the constituents of lauraceous plants, we found the occurrence of a variety of diterpenoids in the bark of *Cinnamomum genus*.[1] In connection with this study, we investigated the ingredients of other species of the same family, *Laurus nobilis* L. (Lauraceae), widely distributed in China and Europe, and has been used as an antiscabietic and a spice. This paper deals with isolation and structure elucidation of four glycosides obtained from the plant.

A methanolic extract of fresh leaves of this plant was partitioned between EtOAc and water. The aqueous extract was chromatographed by using a combination of silica gel, Sephadex LH-20, Bondapak C_{18} and MCI gel CHP-20P to give four glycosides (**1**, **2**, **3** and **4**).

Compound **1**, $[\alpha]_D$ +0.4°, showed a molecular ion peak at *m/z* 494 in the fast atom bombardment mass spectrum (FAB-MS). The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **1** showed β-xylopyranosyl signals and the eighteen carbon signals and two methoxyl signals of a diarylbutan-type aglycone. Comparison of the ^{13}C-NMR spectrum of the aglycone part of **1** with that of secoisolariciresinol[2] disclosed that both were almost the same, except for the C-9 and C-8 carbon signals. The glycosylation shifts[3] in the ^{13}C-NMR spectrum of **1** were +8.4 and −4.0 ppm at C-9 (δ 68.9) and C-8 (δ 39.7), respectively, thus suggesting that β-xylopyranose was attached to C-9 of the aglycone. As regards the configurations at C-8 and C-8′, the circular dichroism (CD) spectrum of **1** gave positive Cotton effects at 227 and 290 nm, indicating both *R* configurations. Consequently, the structure of **1** was determined to be (+)-secoisolariciresinol 9-*O*-β-D-xylopyranoside, which has not been described in the literature before.

Compound **2**, $[\alpha]_D$ +29.2°, showed a molecular ion peak at *m/z* 522 in the positive FAB-MS. Acid hydrolysis of **2** gave xylose and (+)-5′-methoxyisolariciresinol. The ^{13}C-NMR spectrum, showing β-xylopyranosyl carbons signals, was almost identical to that of (+)-5′-methoxyisolariciresinol except for the signal due to C-9′ at δ 67.1 in the aglycone. Therefore, the structure of **2** was identified as (+)-5′-methoxyisolariciresinol 9′-*O*-β-D-xylopyranoside.[4]

Compound **3**, $[\alpha]_D$ +39.8°, showed a molecular ion peak at *m/z* 492 in the positive FAB-MS. Acid hydrolysis of **3** gave xylose and (+)-isolariciresinol. The structure of **3** was shown to be identical to schizandriside[5] by comparing the reported ^{13}C-NMR and CD data.

Compound **4**, $[\alpha]_D$ −21.7°, showed signals due to two olefinic protons at δ 5.33 (2H, m), a terminal methyl group at δ 0.92 (t, J=7 Hz) and an anomeric proton at δ 4.13 (d, J=7 Hz) in the proton (^{1}H)-NMR spectrum. Acid hydrolysis of **4** gave glucose. The ^{13}C-NMR spectrum of **4** showed signals due to a β-glucopyranosyl moiety and Δ^3 (*Z*)-hexenol at δ 14.0 (q), 20.1 (t), 27.3 (t), 68.4 (t), 124.9 (d) and 133.2 (d). Consequently, the structure of **4** was identified as *Z*-3-hexenyl-*O*-β-D-glucopyranoside,[6] isolated from the leaves of *Pertya scandens* SCH. BIP. (Compositae).

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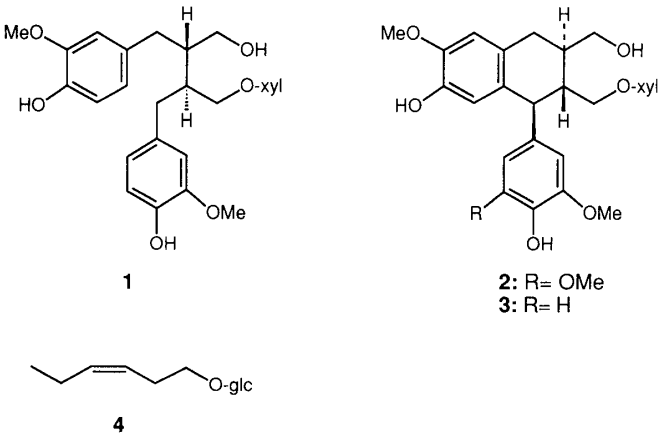

Formulae

In this work, we isolated three lignan glycosides and *Z*-3-hexenyl-*O*-*β*-D-glucopyranoside, from *L. nobilis*. Cinnamom iditerpenoids, however, have been not isolated from or detected in the title plant before.

Experimental

All melting points were determined on a Yanagimoto micro-melting point apparatus (hot-stage type) and are uncorrected. The optical rotations were measured with a JASCO DIP 360 digital polarimeter. The MS were measured with a JEOL JMS-DX 303HF (FAB ion source, Xe atom beam; accelating voltage, 3 kV; matrix, MeOH/glycerin). The NMR spectra were recorded with a JEOL JNM-GX-270 (^{13}C) and FX-100 (^{1}H) spectrometers; chemical shifts are given on a δ (ppm) scale with tetramethylsilane as an internal standard. Column chromatography was carried out with MCI-gel CHP-20P (75–150 μ, Mitsubishi Chemical Industries Co., Ltd), Kieselgel 60 (70–230 mesh, Merck), Bondapak C_{18} (Waters Associates) and Sephadex LH-20 (25–100 μ, Pharmacia Co., Ltd.). TLC was performed on precoated Kieselgel 60 F_{254} plates (0.2 mm, Merck) using a $CHCl_3$-MeOH-H_2O system as the developing solvent for the free compounds and detection was achieved by spraying 20% H_2SO_4 reagent followed by heating.

Extraction and separation——Fresh leaves of *Laurus nobilis* (2.0 kg) were extracted two times with MeOH. The MeOH extract was partitioned between EtOAc and water. The aqueous extract (350 g) was chromatographed on MCI gel CHP 20P (H_2O-40%-60%-100% MeOH, gradiently), and then the 40% MeOH eluate fraction (25 g) was subjected to a combination of column chromatographies by using Sephadex LH-20 (MeOH), silica gel ($CHCl_3$-MeOH-H_2O=80:10:0.5) and Bondapak C_{18} (30–40% MeOH) to furnish **1** (30 mg), **2** (16 mg), **3** (48 mg) and **4** (32 mg).

Compound 1——White powder, $[\alpha]^{22}_D$ +0.4° (c=0.27, MeOH), positive FAB-MS m/z 494 $[M]^+$, CD (c=9.01×10^{-5}, EtOH) [θ] (nm): +2800 (227), +990 (290). ^{1}H-NMR (CD_3OD) δ: 1.80–2.30 (2H, m, H-8, 8′), 2.40–2.76 (4H, m, H_2-7, 7′), 3.6–4.5 (m, sugar), 3.77 (6H, s, OMe), 6.66 (6H, m, Ar-H). ^{13}C-NMR (DMSO-d_6) δ: 33.5×2 (C-7, 7′), 39.7 (C-8), 42.2 (C-8′), 55.3×2 (OMe), 60.3 (C-9′), 65.7 (xyl C-5), 68.9 (C-9), 69.6 (xyl C-4), 73.3 (xyl C-2), 76.6 (xyl C-3), 103.8 (xyl C-1), 112.9 ×2 (C-2, 2′), 115.0 ×2 (C-5, 5′), 121.1 ×2 (C-6, 6′), 131.7* (C-1), 132.2* (C-1′), 144.2 (C-4, 4′), 147.2 (C-3, 3′). * Assignments may be interchangeable.

Acid hydrolysis of 1——A solution of **1** (10 mg) in 1 N HCl-50% MeOH (3 ml) was heated at 80°C for 1 h. Usual work-up gave the aglycone (5 mg), identical with (+)-secoisolariciresinol, $[\alpha]^{24}_D$+29.0° (c=0.27, MeOH), ^{1}H-NMR (CD_3OD) δ: 2.06 (2H, m), 3.68 (6H, m), 6.60 (6H, m), and xylose which was detected by TLC ($CHCl_3$–MeOH–H_2O=7:3:0.5).

Compound 2——Colorless needles, mp 233–235°C (from dil. MeOH), $[\alpha]^{22}_D$ +29.2° (c=0.30, MeOH), positive FAB-MS m/z 522 $[M]^+$, CD (c=1.91×10^{-4}, EtOH) [θ] (nm): +6200 (241), +7300 (272), −11000 (288). ^{13}C-NMR (DMSO-d_6) δ: 32.5 (C-7), 37.4 (C-8), 43.8 (C 8′), 46.1 (C-7′), 55.5 (OMe), 55.9 ×2 (OMe), 62.6 (C-9), 65.6 (xyl C-5), 67.1 (C-9′), 69.5 (xyl C-4), 73.2 (xyl C-2), 76.5 (xyl C-3), 104.5 (xyl C-1), 106.2 ×2 (C-2′, 6′), 111.7 (C-2), 116.1 (C-5), 126.9 (C-1), 132.5 (C-6), 133.6 (C-4′), 135.7 (C-1′), 144.0 (C-4), 145.4 (C-3), 147.7 ×2 (C-3′, 5′).

Acid hydrolysis of 2——A solution of **2** (10 mg) in 1 N HCl-50% MeOH (3 ml) was heated at 80°C for 1 h. An usual work-up gave algycone (4 mg), (+)-5′-methoxyisolariciresinol: white powder, $[\alpha]^{24}_D$+51.1° (c=0.25, MeOH), EI-MS m/z 390 $[M]^+$, ^{1}H-NMR (acetone-d_6) δ: 1.80–2.05 (2H, m, H-8, 8′), 2.79–3.00 (2H, m, H_2-7), 3.78, 3.79, 3.82 (each 3H, s, OMe), 6.26 (1H, s, H-2), 6.50 (2H, s, H-2′, 6′), 6.69 (1H, s, H-5), 7.08, 7.17 (each 1H, br s, Ar-

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OH), and xylose.

Compound 3——White powder, $[\alpha]_D^{22}$ +39.8° (c=0.20, MeOH), positive FAB-MS m/z 492 $[M]^+$, CD (c=4.09×10^{-5}, EtOH) $[\theta]$ (nm): +12000 (240), +9200 (277), −13700 (292). ^{13}C-NMR (DMSO-d_6) δ: 32.5 (C-7), 37.6 (C-8), 44.0 (C-8′), 45.6 (C-7′), 55.5, 55.6 (OMe), 62.6 (C-9), 65.6 (xyl C-5), 67.3 (C-9′), 69.5 (xyl C-4), 73.3 (xyl C-2), 76.5 (xyl C-3), 104.4 (xyl C-1), 111.8 (C-2), 113.9 (C-2′), 115.4* (C-5), 116.2* (C-5′), 121.0 (C-6′), 127.0 (C-1), 132.6 (C-6), 136.8 (C-1′), 144.0* (C-4), 144.4* (C-4′), 145.5* (C-3), 147.1* (C-3′). * Assignments may be interchangeable.

Acid hydrolysis of 3——A solution of **3** (10 mg) in 2 N HCl-50% MeOH (10 ml) was heated for 1 h. An usual work-up gave aglycone (3 mg), (+)-isolariciresinol, white powder, $[\alpha]_D^{24}$ +39.0° (c=0.26, MeOH), EI-MS m/z 360 $[M]^+$. ^{1}H-NMR (acetone-d_6) δ: 2.00 (2H, m, H-8, 8′), 2.85 (2H, m, H_2-7), 3.78, 3.79 (each 3H, s, OMe), 6.19 (1H, d, J=2 Hz), 6.61 (1H, dd, J=2, 8 Hz), 6.66 (1H, s), 6.74 (1H, s), 6.78 (1H, d, J=8 Hz), and xylose.

Compound 4——White powder, $[\alpha]_D^{22}$ −21.7° (c=0.30, MeOH). ^{1}H-NMR (DMSO-d_6) δ: 0.92 (3H, t, J=7 Hz, H_3-6), 1.70–2.55 (4H, m, H_2-2, 5), 4.13 (1H, d, J=7 Hz, glc H-1), 5.33 (2H, m, H-3, 4). ^{13}C-NMR (DMSO-d_6) δ: 14.0 (C-6), 20.1 (C-5), 27.3 (C-2), 60.6 (glc C-6), 68.4 (C-1), 69.8 (glc C-4), 73.2 (glc C-2), 76.2 (glc C-5), 76.3 (glc C-3), 102.4 (glc C-1), 124.9 (C-4), 133.2 (C-3).

Acid hydrolysis of 4——A solution of **4** (5 mg) in 1 N HCl-50% MeOH (3 ml) was heated at 80°C for 1 h. An usual work-up gave glucose detected by TLC ($CHCl_3$–MeOH–acetone–H_2O=3:3:3:1).

References and Notes

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