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New Glycosides and Furocoumarin from the *Glehnia littoralis* Root and Rhizoma

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A new hemiterpenoid glycoside, phenylpropanoid glycoside, and furocoumarin were isolated from the methanolic extract of the root and rhizoma of *Glehnia littoralis* FR. SCHMIDT ex MIQ. (Umbelliferae, "Hamabōfu" in Japanese). Their structures were determined by the spectral investigations.

Key words *Glehnia littoralis*; hemiterpenoid glycoside; phenylpropanoid glycoside; furocoumarin; Umbelliferae

In previous papers,[1] we reported the isolation of twelve coumarin glycosides and seven monoterpenoid glycosides from the methanol extract of the root and rhizoma of *Glehnia* (*G.*) *littoralis* FR. SCHMIDT ex MIQ (Umbelliferae, "Hamabōfu" in Japanese). Further examination of the same extract has now resulted in the isolation of two new glucosides (**1** and **2**) and cnidioside A (**3**)[2] from the water-soluble portion, and imperatorin, isoimperatorin, 8-geranyloxypsoralen (**5**), bergaptin, 8-[(2*E*,5*E*)-7-hydroxy-3,7-dimethylocta-2,5-dienyloxy]psoralen (**6**)[3] and a new furocoumarin (**4**) from the ether-soluble portion. In this paper, we discuss the glycosides, **1** and **2**, and furocoumarin **4**.

Glycoside **1** ($C_{16}H_{28}O_{10}$, an amorphous powder, $[\alpha]_D^{22}$ $-84°$) showed $[M+K]^+$, $[M+Na]^+$ and $[M+H]^+$ ion peaks at *m/z* 419, 403 and 381 in the positive FAB-MS. The ^1H-, ^{13}C- and ^{13}C–^1H correlation spectroscopy (COSY) NMR spectral data of **1** (*vide* Experimental) showed the presence of one β-apiofuranosyl-(1→6)-β-glucopyranosyl,[1] two *tert*-methyls, one terminal-monosubstituted double bond, and one oxygenated quaternary carbon. Thus, **1** was characterized as 2-methyl-3-buten-2-ol β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside.

Glycoside **2** ($C_{16}H_{22}O_8$, mp 149—151 °C, $[\alpha]_D^{22}$ $-66°$) showed $[M+Na]^+$ and $[M+H]^+$ ion peaks at *m/z* 365 and 343 in the positive FAB-MS. The ^1H-, ^{13}C- and ^{13}C–^1H COSY NMR spectral data of **2** (*vide* Experimental) showed the presence of one β-glucopyranosyl, 1,2,4-trisubstituted benzene, one methoxyl, one *prim*-methyl and one methylene group, and one carbonyl carbon. Thus, **2** was suggested to be a glucoside of phenylpropanoid having methoxyl and carbonyl groups. As the nuclear Overhauser and exchange spectroscopy (NOESY) spectrum showed nuclear Overhauser effect (NOE) interactions between the methoxyl proton and H-3, H-2′a and H-3, H-2′b and H-5, and between the glucosyl anomeric proton and H-6 (Fig. 1), the location of the glycosyl, methoxyl and propionyl units were revealed to be at C-1, C-2 and C-4 of benzene ring, respectively. Therefore, **2** was characterized as 2-methoxy-4-(1-propionyl)phenyl β-D-glucopyranoside.

Furocoumarin **4** ($C_{21}H_{22}O_5$, a colorless gum, $[\alpha]_D^{22}$ $-23°$) showed $[M+H]^+$, $[M-(C_{10}H_{16}O$, oxygeranyl skeleton$)+H]^+$ and $[M-(C_{11}H_6O_4$, furocoumaryl skeleton$)+H]^+$ ion peaks at *m/z* 355, 203 and 153 in the positive FAB-MS. The ^1H- and ^{13}C-NMR spectrum of **4** (*vide* Experimental) showed the presence of an additional carbonyl group, and were similar to those of **5** except for the proton and carbon signals of 4″ to 9″ belonging to the oxygeranyl skeleton. So, **4** was considered to be the oxo derivative of 8-(6″,7″-dihydrogeranyloxy)psoralen. From results of the heteronuclear multiple-bond correlation (HMBC) experiment, the partial structure described in **4** (Fig. 1, shown in heavy lines) was assigned, and the position of the carbonyl group was suggested to be C-6″. The observed NOE interactions between H-1″ and H_3-10″, and between H-2″ and H-4″ in its NOESY spectrum indicated that the double bond at C-2″ was *E*. From these facts, **4** was characterized as 8-[(2*E*)-6-oxo-3,7-dimethyloct-2-enyloxy]psoralen.

Sasaki *et al.* reported osthenol 7-*O*-β-gentiobioside (**7**) as the major glycoside of the root and rhizoma of *G. littoralis*.[4] However, this compound was not found in the present investigation of the sample collected in Niigata prefecture.[5]

Experimental

The instruments used and the experimental conditions for obtaining spectral data and for chromatography were the same as in the preceding paper.[1]

Extraction and Isolation *G. littoralis* FR. SCHMIDT ex MIQ. was collected at Kakizaki, Niigata prefecture, Japan, in October 1994. The methanol extract (76.2 g) of the fresh root and rhizoma (6.0 kg) was treated

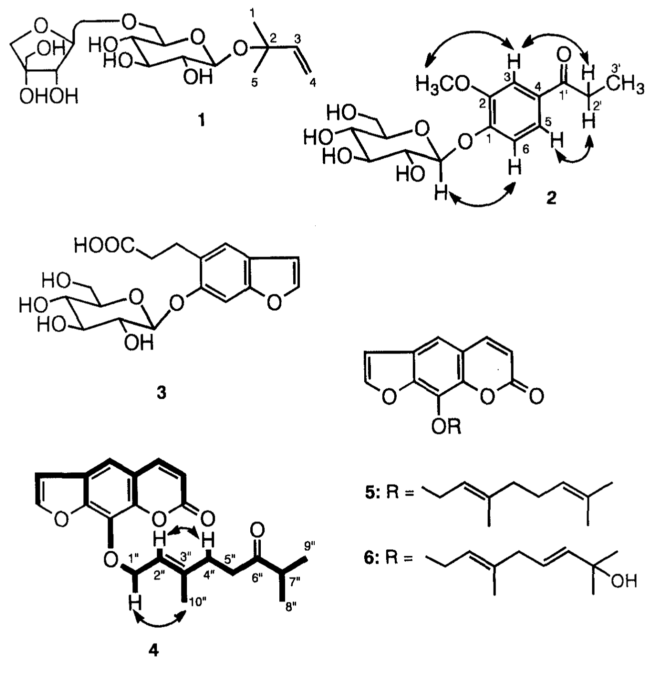

Fig. 1. Partial Structure of **4** solved by HMBC Spectrum (Heavy Lines), NOE Interactions Observed in NOESY Spectra of **2** and **4**, and Structures of **1** to **6**

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as described in the previous paper,[1] and frs. 1 to 7 were obtained from the water-soluble portion by Amberlite XAD-II and Sephadex LH-20 chromatography. Fraction 3 (13.8 g) was chromatographed over silica gel [$CHCl_3$–MeOH–H_2O (4 : 1 : 0.1→7 : 3 : 0.5)→MeOH] to give sixteen fractions (frs. 3-1—3-16). Fraction 3-2 (216 mg) was subjected to a Lobar RP-8 column [MeOH–H_2O (3 : 7)] and HPLC [octadecyl silica (ODS), MeOH–H_2O (3 : 7)] to give **2** (5 mg). Fraction 3-7 (1.92 g) was chromatographd over a Lobar RP-8 column [MeOH–H_2O (1 : 4)] to give sixteen fractions (frs. 3-7-1—3-7-16), and from fr. 3-7-3, **3** (24 mg) was isolated by silica gel [$CHCl_3$–MeOH–H_2O (4 : 1 : 0.1)], Sephadex LH-20 (MeOH) chromatography and HPLC [ODS, MeOH–H_2O (3 : 22)]. From fr. 3-7-6, **1** (3 mg) was isolated by silica gel [$CHCl_3$–MeOH–H_2O (4 : 1 : 0.1)] chromatography and HPLC [ODS, MeOH–H_2O (2 : 8)]. The ether-soluble portion (9.1 g) was chromatographed over silica gel [hexane–EtOAc (4 : 1→3 : 1→2 : 1→1 : 1)→EtOAc→MeOH] to give seven fractions (frs. 1′—7′). From the fr. 2′ (0.96 g), bergaptin (10 mg) was isolated by repeated chromatography over silica gel [hexane–EtOAc (4 : 1, 17 : 3)] and Sephadex LH-20 (MeOH). Fraction 3′ (2.37 g) was subjected to repeated chromatography over silica gel [hexane–EtOAc (4 : 1→7 : 3→3 : 2)] and Sephadex LH-20 (MeOH) to give isoimperatorin (482 mg), **4** (6 mg) and **6** (6 mg). From the fr. 4′ (2.31 g), imperatorin (960 mg) and 8-geranyloxypsoralen (**5**, 16 mg) were isolated by repeated silica gel [hexane–EtOAc (7 : 3, 3 : 2)] chromatography.

2-Methyl-3-buten-2-ol *β*-D-Apiofuranosyl-(1→6)-*β*-D-glucopyranoside (1) An amorphous powder, $[\alpha]_D^{22}$ −84° (c=0.2, MeOH). Positive FAB-MS *m/z*: 419.1373 $[M+K]^+$ (base, Calcd for $C_{16}H_{28}O_{10}K$: 419.1230), 403.1619 $[M+Na]^+$ (Calcd for $C_{16}H_{28}O_{10}Na$: 403.1580), 381.1767 $[M+H]^+$ (Calcd for $C_{16}H_{29}O_{10}$: 381.1760). ^{1}H-NMR (pyridine-d_5) δ: 1.42 (3H, s, H_3-1), 1.55 (3H, s, H_3-5), 5.16 (1H, dd, J=1.0, 11.0 Hz, H-4a), 5.30 (1H, dd, J=1.0, 17.5 Hz, H-4b), 6.34 (1H, dd, J=11.0, 17.5 Hz, H-3), 4.90 (1H, d, J=7.5 Hz, glucosyl H-1), 5.80 (1H, d, J=2.0 Hz, apiosyl H-1). ^{13}C-NMR (pyridine-d_5) δ: 28.09 (C-1), 77.96 (C-2), 145.24 (C-3), 113.61 (C-4), 26.65 (C-5), glucosyl [99.73 (C-1), 75.07 (C-2), 78.78 (C-3), 72.05 (C-4), 76.86 (C-5), 69.15 (C-6)], apiosyl [111.17 (C-1), 77.74 (C-2), 80.54 (C-3), 75.24 (C-4), 65.71 (C-5)].

2-Methoxy-4-(1-propionyl)phenyl *β*-D-Glucopyranoside (2) Colorless needles (MeOH), mp 149—151 °C, $[\alpha]_D^{22}$ −66° (c=0.3, MeOH). Positive FAB-MS *m/z*: 365.1192 $[M+Na]^+$ (base, Calcd for $C_{16}H_{22}O_8Na$: 365.1213), 343.1371 $[M+H]^+$ (Calcd for $C_{16}H_{23}O_8$: 343.1393). ^{1}H-NMR (pyridine-d_5) δ: 1.19 (3H, t, J=7.5 Hz, H_3-3′), 2.91 (2H, br q, J=7.5 Hz, H_2-2′), 3.76 (3H, s, OCH_3), 7.61 (1H, d, J=8.5 Hz, H-6), 7.64 (1H, dd, J=2.0, 8.5 Hz, H-5), 7.77 (1H, d, J=2.0 Hz, H-3), 5.80 (1H, d, J=7.5 Hz, glucosyl H-1). ^{13}C-NMR (pyridine-d_5) δ: 151.77 (C-1, C-2), 111.44 (C-3), 131.49 (C-4), 122.95 (C-5), 114.91 (C-6), 199.33 (C-1′), 31.54 (C-2′), 8.74 (C-3′), 55.79 (OCH_3), glucosyl [101.62 (C-1), 74.71 (C-2), 78.46 (C-3), 71.26 (C-4), 79.09 (C-5), 62.39 (C-6)].

Cnidioside A (3) An amorphous powder, $[\alpha]_D^{22}$ −43° (c=2.0, MeOH), [lit.,[2] $[\alpha]_D^{27}$ −42.1° (c=0.59, H_2O)].

8-[(2*E*)-6-Oxo-3,7-dimethyloct-2-enyloxy]psoralen (4) A colorless gum, $[\alpha]_D^{22}$ −23° (c=0.5, $CHCl_3$). Positive FAB-MS *m/z*: 355.1568 $[M+H]^+$ (Calcd for $C_{21}H_{23}O_5$: 355.1546), 203 $[M-C_{10}H_{16}O+H]^+$ (base), 153 $[M-C_{11}H_6O_4+H]^+$. ^{1}H-NMR ($CDCl_3$) δ: 1.08 (6H, d, J=7.0 Hz, H_3-8″, H_3-9″), 1.71 (3H, s, H_3-10″), 2.27 (2H, t, J=7.5 Hz, H_2-4″), 2.53 (2H, t, J=7.5 Hz, H_2-5″), 2.58 (1H, qq, J=7.0, 7.0 Hz, H-7″), 5.01 (2H, d, J=7.0 Hz, H_2-1″), 5.60 (1H, t, J=7.0 Hz, H-2″), 6.37 (1H, d, J=9.5 Hz, H-3), 6.81 (1H, d, J=2.5 Hz, H-3′), 7.37 (1H, s, H-5), 7.69 (1H, d, J=2.5 Hz, H-2′), 7.77 (1H, d, J=9.5 Hz, H-4). ^{13}C-NMR ($CDCl_3$) δ: 160.50 (C-2), 114.73 (C-3), 144.37 (C-4), 113.35 (C-5), 125.88 (C-6), 148.69 (C-7), 131.54 (C-8), 143.92 (C-9), 116.49 (C-10), 146.65 (C-2′), 106.77 (C-3′), 69.98 (C-1″), 119.72 (C-2″), 141.98 (C-3″), 33.08 (C-4″), 38.45 (C-5″), 213.97 (C-6″), 40.92 (C-7″), 18.25 (C-8″, C-9″), 16.80 (C-10″). 8-Geranyloxypsoralen (**5**): ^{1}H-NMR ($CDCl_3$) δ: 1.57, 1.64 (each 3H, s, H_3-8″, H_3-9″), 1.69 (3H, s, H_3-10″), 2.01 (4H, br d, J=3.0 Hz, H_2-4″, H_2-5″), 5.03 (2H, d, J=7.0 Hz, H_2-1″), 5.03 (1H, m, H-6″), 5.60 (1H, t, J=7.0 Hz, H-2″), 6.37 (1H, d, J=9.5 Hz, H-3), 6.81 (1H, d, J=2.5 Hz, H-3′), 7.36 (1H, s, H-5), 7.69 (1H, d, J=2.5 Hz, H-2′), 7.77 (1H, d, J=9.5 Hz, H-4). ^{13}C-NMR ($CDCl_3$) δ: 160.42 (C-2), 114.61 (C-3), 144.29 (C-4), 113.15 (C-5), 125.77 (C-6), 148.67 (C-7), 131.62 (C-8), 143.85 (C-9), 116.37 (C-10), 146.53 (C-2′), 106.67 (C-3′), 70.62 (C-1″), 119.34 (C-2″), 143.07(C-3″), 39.52 (C-4″), 26.31 (C-5″), 123.68 (C-6″), 131.47 (C-7″), 17.64, 25.64 (C-8″, C-9″), 16.52 (C-10″).

8-[(2*E*,5*E*)-7-Hydroxy-3,7-dimethylocta-2,5-dienyloxy]psoralen (6) A colorless gum, $[\alpha]_D^{22}$ −12° (c=0.5, $CHCl_3$).

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Referances and Notes

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5) Recently, we isolated **7** from the fresh fruit of the examined plant.