[Chem. Pharm. Bull 31(1) 64—69 (1983)]

Chemical Studies of *Coelopleurum gmelinii* (D.C.) LEDEB. I. Constituents of the Root[1)]

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(Received July 9, 1982)

Two new coumarins (**9** and **10**) and a new chromone (**14**), together with eight known coumarins (**1**—**8**) and three known chromones (**11**—**13**), which were identified by comparison with authentic samples, were isolated from the roots of *Coelopleurum gmelinii* (D.C.) LEDEB. (Umbelliferae). The structures of **9**, **10** and **14** were established as 6-[(1*R*,2*S*)-1,3-dihydroxy-2-isovaleryloxy-3-methylbutyl]-7-methoxycoumarin, 6-[(1*R*,2*S*)-2-angeloyloxy-3-β-D-glucosyloxy-1-hydroxy-3-methylbutyl]-7-methoxycoumarin (*tert-O*-glucosylangelol A) and (*S*)-7-β-D-glucosyloxymethyl-4-hydroxy-2-(1-hydroxy-1-methylethyl)-2,3-dihydro-5*H*-furo[3,2-*g*] [1] benzopyran-5-one (*prim-O*-glucosylangelicain), respectively.

Keywords——*Coelopleurum gmelinii*; Umbelliferae; coumarin; chromone; angelol; angelol I; angeloside A; *prim-O*-glucosylangelicain

Coelopleurum gmelinii (D.C.) LEDEB. (Japanese name; Ezonoshishiudo, Umbelliferae) is a stout perennial herb growing on the coast from Hokkaido to Okhotsk and Alaska. This plant had been classified into *Angelica sp.*, but at present is classified into *Coelopleurum sp.* by most taxonomists. As regards the constituents of this plant, Sano *et al.*[2)] reported the isolation of the three coumarins, isoimperatorin, prangolarin and oxypeucedanin, from the fruits. Recently, the authors reinvestigated this plant in order to study its coumarins and chromones, and were able to isolate ten coumarins (**1**—**10**) and four chromones (**11**—**14**). This paper describes in detail the identification and structure elucidation of these compounds.

The roots of *C. gmelinii* collected at the Hamatonbetsu coast of Hokkaido were treated as described in the experimental section. Seven coumarins (**1**—**7**) were identified as isoimperatorin (**1**), psoralen (**2**), imperatorin (**3**), bergapten (**4**), *tert-O*-methyloxypeucedanin hydrate (**5**), angelol A (**6**) and oxypeucedanin hydrate (**7**), and three chromones (**11**—**13**) were identified as hamaudol (**11**), 3'-*O*-acetylhamaudol (**12**) and visamminol (**13**) by comparison with authentic samples. A coumarin glycoside (**8**) was identified as eleutheroside B_1 on the basis of the finding that **8** gave 7-hydroxy-6,8-dimethoxycoumarin(isofraxidin) and glucose on treatment with β-glucosidase or on acid hydrolysis.

Compound **9**, mp 113—115°C, colorless needles, $C_{20}H_{26}O_7$. The optical rotatory dispersion (ORD) spectrum of **9** showed a negative plain curve. The ultraviolet (UV) spectrum of **9** showed absorption maxima at 222, 251, 300 and 324 nm. The infrared (IR) spectrum of **9** showed the presence of hydroxyl group, lactone and aromatic ring. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum (δ ppm, $CDCl_3$) of **9** exhibited signals due to protons of the C-4 and C-3 positions of the coumarin ring at 7.62 (1H, d, J=9.5 Hz) and 6.22 (1H, d, J=9.5 Hz), signals assignable to the protons of the C-5 and C-8 positions at 7.61 (1H, s) and 6.73 (1H, s), signals due to a methoxyl group at 3.92 (3H, s) and signals arising from a trihydroxyisopentyl group at 5.60(1H, br s), 5.09(1H, br s), 4.63(1H, br s), 2.87(1H, br s), 1.58 (3H, s) and 1.25(3H, s). Furthermore, the ^{1}H-NMR spectrum of **9** showed signals arising from an isovaleryl group at 2.00(2H, m), 1.80(1H, m), 0.74(3H, d, J=6.5 Hz) and 0.65(3H, d, J=6.5 Hz). These spectral data indicated that compound **9** was 7-methoxy-6-trihydroxyisopentylcoumarin, that is, an angelol-type coumarin, and that one of the hydroxyl groups on the isopentyl group was esterified with isovaleric acid.

In the previous paper[3)] we had reported that angelol-type coumarins could be classified into four groups, 6-[(1*R*,2*S*)-2-acyloxy-1,3-dihydroxy-3-methylbutyl]-7-methoxycoumarins

(I), 6-[(1*R*,2*S*)-1-acyloxy-2,3-dihydroxy-3-methylbutyl]-7-methoxycoumarins (II), 6-[(1*R*,2*R*)-2-acyloxy-1,3-dihydroxy-3-methylbutyl]-7-methoxycoumarins (III) and 6-[(1*R*,2*R*)-1-acyloxy-2,3-dihydroxy-3-methylbutyl]-7-methoxycoumarins (IV) depending on the signal patterns of the two methine protons and *gem*-dimethyl protons in the hydroxyisopentyl group linked to the 6-position of these compounds in the ^{1}H-NMR spectrum.

In the ^{1}H-NMR spectrum of **9**, the signals arising from the two methine protons of the C-11 and C-12 positions were observed at 5.60 and 5.09, and *gem*-dimethyl protons were observed at 1.58 and 1.25. From this data and the ORD curve, it became clear that **9** belonged to group I of angelols. On alkaline hydrolysis, **9** gave isovaleric acid, which was identified by derivation to the *p*-phenyl phenacyl ester. Thus, the structure of **9** was established as 6-[(1*R*,2*S*)-1, 3-dihydroxy-2-isovaleryloxy-3-methylbutyl]-7-methoxycoumarin. This compound was named angelol I.

Compound **10**, colorless viscid substance, $C_{26}H_{34}O_{12}$. The UV spectrum of **10** showed absorption maxima at 220, 252, 302 and 328 nm. The ^{1}H-NMR spectrum (δ ppm, acetone-d_6) of **10** exhibited signals due to protons of the C-4 and C-3 positions of the coumarin ring at 7.82(1H, d, J=9.5 Hz) and 6.15(1H, d, J=9.5 Hz), signals assignable to the protons of the C-5 and C-8 positions at 7.60(1H, s) and 6.84(1H, s), signals assignable to a trihydroxyisopentyl group at 5.52(1H, m), 5.24(1H, d, J=1.5 Hz), 4.66(1H, d, J=4.0 Hz), 1.57(3H, s), 1.41(3H, s) and signals arising from the angeloyl group at 5.86(1H, m), 1.76(3H, m), 1.64(3H, m). These signal patterns were similar to those of angelol A (group I). Furthermore, the ^{1}H-NMR spectrum of **10** showed signals due to a glycosyl moiety. Therefore, **10** was presumed to be a glycoside of angelol A. On being treated 5% H_2S0_4, **10** gave angelol B(**15**) and angelol D(**16**) as aglycones in addition to glucose. However, it was unreactive upon hydrolysis with β-glucosidase.

From the above results and the observations that a hydroxyl group proton at 4.66(1H, d, J=4.0 Hz) was coupled to a methine proton of the C-11 position at 5.52(1H, m), and that the coupling constant of the anomeric proton was 7.5 Hz, **10** was confirmed to be a β-monoglucoside whose glucosyl group is linked at the tertiary hydroxyl group at the C-13 position of the aglycone. Though in this reaction **10** gave angelol B (**15**) having tiglic acid as the ester moiety at the C-12 position and angelol D (**16**) having the same ester moiety at the C-11 position, it is clear that the acid forming the ester at C-12 in **10** is angelic acid from the ^{1}H-NMR and ^{13}C-NMR spectra of **10** (Table I), so it appears that in this reaction the angeloyl group was isomerized to a tigloyl group, and then partial acyl migration occurred. The occurrence isomerization followed by acyl migration was confirmed by the fact that **6** afforded **15** and **16** under the same conditions.

From the above evidence, the structure of **10** was established as 6-[(1*R*,2*S*)-2-angeloyloxy-3-β-D-glucosyloxy-1-hydroxy-3-methylbutyl]-7-methoxycoumarin (*tert-O*-glucosyl-angelol A). This compound was named angeloside A.

Compound **14**, mp 130—132°C, colorless needles, $C_{21}H_{26}O_{11}$. This compound gave a dark blue coloration with Gibbs reagent and ammonia aq. and it gave a positive (dark violet coloration) ferric chloride reaction. The UV spectrum of **14** showed absorption maxima at 215, 232.5, 251.5, 256 and 298 nm, which were shifted to longer wavelengths by aluminum chloride. The IR spectrum of **14** showed the presence of hydroxyl group, carbonyl group and aromatic ring. The ^{1}H-NMR spectrum (δ ppm, DMSO-d_6) of **14** showed signals due to an olefinic proton and a benzene proton at 6.52(1H, s) and 6.45(1H, s), a hydroxyl proton at 12.96(1H, s) and *gem*-dimethyl protons at 1.17(6H, s) as well as signals suggesting the presence of a sugar moiety at 5.40—2.70 [anomeric H (4.35, d, J=7.5 Hz)]. The ^{13}C-NMR spectrum (DMSO-d_6) of **14** exhibited signals arising from a β-D-glucosyl group (Table II). Upon hydrolysis with 5% H_2SO_4 or β-glucosidase, **14** gave angelicain (**18**) and glucose. The treatment of **14** with acetic anhydride and sodium acetate afforded a hexaacetate (**17**). Compound **14** was methylated by the Kuhn method to give a hexamethyl ether (**19**), which afforded

angelicain dimethyl ether (**20**) upon hydrolysis with 1 N MeOH–HCl. The ^{1}H-NMR spectrum (δ ppm, DMSO-d_6) of **20** showed signals due to a hydroxymethyl group at 5.66 (1H, t, J=6.0 Hz) and 4.32 (2H, d, J=6.0 Hz, +D_2O d→s). Accordingly, **14** was confirmed to be a β-monoglucoside whose glucosyl group was linked at the secondary alcoholic hydroxyl group of **18**.

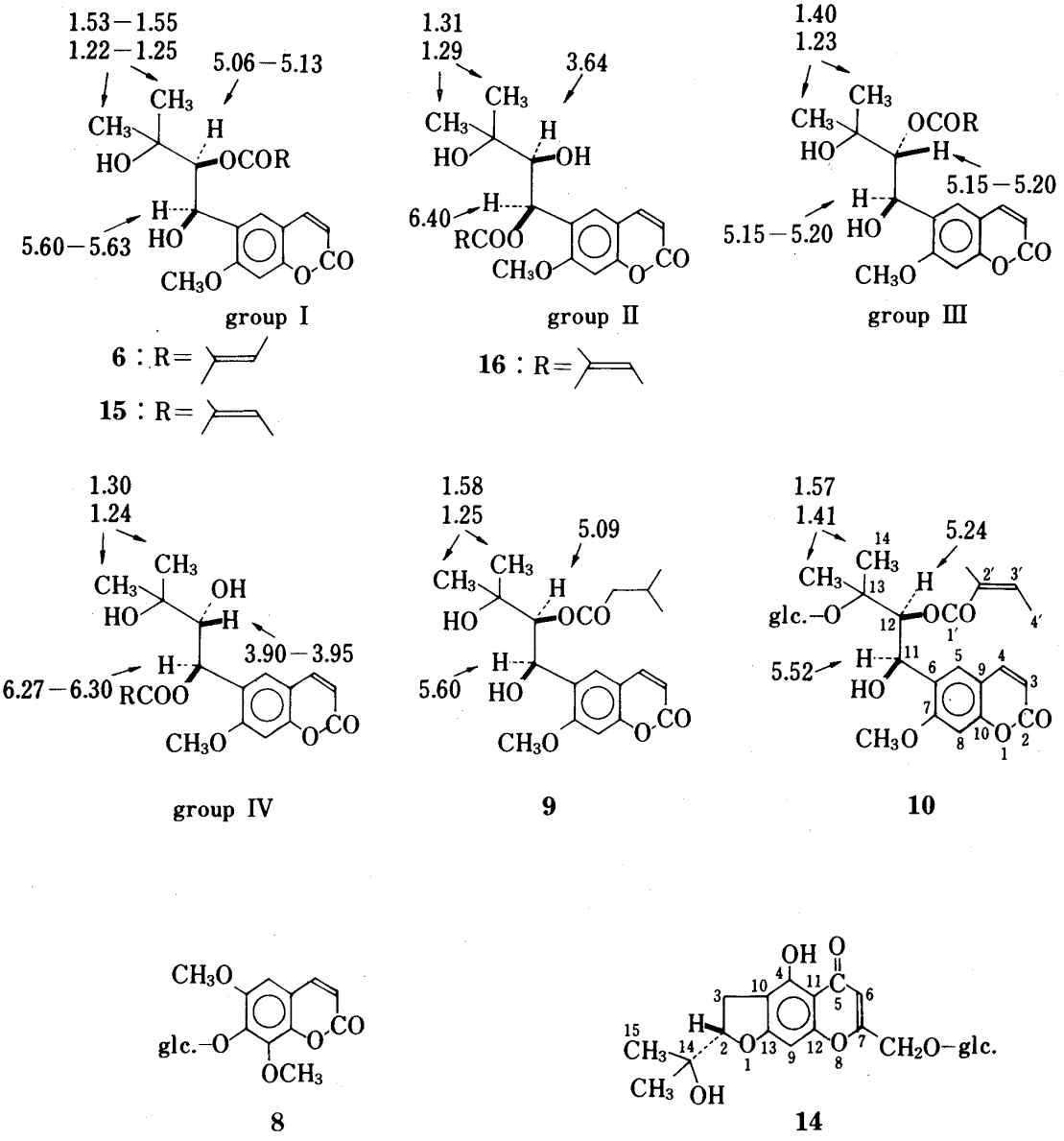

Chart 1

TABLE I. ^{13}C-NMR Spectral Data for Angeloside A (**10**) (δ ppm, acetone-d_6)

C_2	160.18(s)	C_{11}	77.22(d)*	$C_{4'}$	14.65(q)
C_3	112.41(d)	C_{12}	65.93(d)	$C_{2'}$-CH_3	19.77(q)
C_4	143.92(d)	C_{13}	79.77(s)	Glucosyl	
C_5	126.57(d)	C_{14}	23.17(q)**	C_1	97.35(d)
C_6	128.03(s)	C_{13}-CH_3	24.34(q)**	C_2	74.03(d)
C_7	159.27(s)	OCH_3	55.81(q)	C_3	76.64(d)*
C_8	98.20(d)	$C_{1'}$	166.53(s)	C_4	70.85(d)
C_9	111.65(s)	$C_{2'}$	128.03(s)	C_5	77.43(d)*
C_{10}	155.15(s)	$C_{3'}$	136.02(d)	C_6	62.13(t)

Values with single asterisk and double asterisk may be exchanged, respectively.

TABLE II. ^{13}C-NMR Spectral Data for *prim-O*-Glucosylangelicain (**14**) (δ ppm, DMSO-d_6)

C_2	88.82(d)	C_{11}	109.24(s)	Glucosyl	
C_3	25.90(t)	C_{12}	157.44(s)*	C_1	102.48(d)
C_4	166.48(s)*	C_{13}	166.28(s)*	C_2	73.37(d)
C_5	181.95(s)	C_{14}	70.04(s)	C_3	76.53(d)***
C_6	107.04(d)	C_{15}	24.82(q)**	C_4	70.04(d)
C_7	104.88(s)	C_7-CH_2O	65.33(t)	C_5	77.03(d)***
C_9	91.57(d)	C_{14}-CH_3	25.72(q)**	C_6	61.12(t)
C_{10}	155.69(s)				

Values with single asterisk, double asterisk and triple asterisk may be exchanged, respectively.

From the results described above, the structure of **14** was established as (*S*)-7-β-D-glucosyloxymethyl-4-hydroxy-2-(1-hydroxy-1-methylethyl)-2,3-dihydro-5*H*-furo[3,2-*g*][1]benzopyran-5-one (*prim-O*-glucosylangelicain).

Experimental

All melting points were measured on a Büchi melting point apparatus and are uncorrected. The IR spectra were recorded with a Hitachi EPI-G2 spectrometer, and the UV and ORD spectra with a JASCO ORD/UV-5 spectrometer. The ^{1}H-NMR spectra were taken with a Hitachi R-40(90MHz) spectrometer and a Nihondenshi JEOL FX-100(100 MHz) spectrometer with tetramethylsilane as an internal standard, and ^{13}C-NMR spectra were obtained with a Nihondenshi JEOL FX-100 (25 MHz) spectrometer. For column chromatography on silica gel, we used Merck silica gel 60 (70—230 mesh).

Isolation of the Compounds——The fresh roots (3 kg) of *Coeloplurum gmelinii* (D.C.) LEDEB. (Japanese name; Ezonoshishiudo, Umbelliferae) collected at the Hamatonbetsu coast of Hokkaido were sliced and extracted 3 times with 10 l of MeOH for a week (for each extraction). The MeOH extract was suspended in water and extracted with ether to give an ether extract (120 g) and an aqueous layer. The aqueous layer was extracted with *n*-butanol to give a *n*-butanol extract (131 g) and an aqueous layer. The ether extract (120 g) was chromatographed on silica gel (1 kg) with mixtures of hexane and ethyl acetate as eluents, and the eluate was collected in fractions (300 ml/fraction): F 1—15 (10:1), F 16—31 (5:1), F 32—123 (4:1), F 124—199 (3:1), F 200—344 (2:1) and F 345—450 (1:1) (figures in parentheses show the ratio of the solvents in v/v). F 23—34 gave isoimperatorin (**1**) (450 mg), F 40—69 (12.7 g) was rechromatographed on silica gel (100 g) with $CHCl_3$ to give psoralen (**2**) (390 mg), imperatorin (**3**) (120 mg), bergapten (**4**) (51 mg) and 3′-*O*-acetylhamaudol (**12**) (161 mg). F 70—104 gave hamaudol (**11**) (420 mg). F 105—144 (1.24 g) was rechromatographed on silica gel (50 g) with hexane–EtOAc (2:1) to give visamminol (**13**) (154 mg). F 145—175 and F 207—261 gave *tert-O*-methyloxypeucedanin hydrate (**5**) (230 mg) and angelol A (**6**) (5.0 g). F 262—366 (5.2 g) was rechromatographed on silica gel (100 g) with hexane–EtOAc (3:1) to afford angelol I (**9**) (2.49 g). F 381-396 gave oxypeucedanin hydrate (**7**) (234 mg). The *n*-butanol extract (131 g) was chromatographed on silica gel (1.7 kg) with mixtures of $CHCl_3$ and MeOH as eluents, and the eluate was divided into fractions (400 ml/fractions); F 1—35 (5:1) and F 35—130 (4:1). The pale brown viscid oil(2.88 g) obtained from F 37 was rechromatographed on silica gel (100 g) with $CHCl_3$–MeOH (5:1) to give a colorless viscid oil (2.48 g), which was further subjected to droplet countercurrent (DCC) chromatography with the solvent system $CHCl_3$–MeOH–H_2O (7:3:1) (descending method) to give angeloside A (**10**) from F 21—24 (8 ml/fraction). The pale brown oil (12.53 g) from F 38—45 was subjected to DCC chromatography with the same solvent system as described above to give eleutheroside B_1 (**8**) and *prim-O*-glucosylangelicain (**14**) from F 63—70 and F 78—80 (8 ml/fraction), respectively.

Eleutheroside B_1 (8)——Recrystallized from MeOH to give colorless needles, mp 204—205°C. UV λ_{max}^{MeOH} nm (log ϵ): 209 (4.55), 229.5 (4.32), 290.5 (4.07), 339 (3.86). IR ν_{max}^{Nujol} cm^{-1}: 3450, 3410(OH) 1710(CO) 1605, 1570, 1485(arom.). ORD (c=0.19, MeOH) [α]^{16} (nm): +82.1°(589), +112.8°(550), +153.9°(500), +235.9°(450), +430.8°(400). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.93 (1H, d, J=9.5 Hz), 7.09 (1H, s), 6.36 (1H, d, J=9.5 Hz), 3.00—5.30 (11H), 3.92 (3H s) 3.83 (3H, s). ^{13}C-NMR (DMSO-d_6) δ ppm: 159.72(s), 149.37(s), 144.31(d), 142.32(s), 141.65(s), 140.18(s), 114.65(d), 114.44(s), 105.46(d), 102.10(d), 77.44(d), 76.48(d), 74.08(d), 69.83(d), 61.23(q), 60.74(t), 56.55(q). *Anal.* Calcd for $C_{17}H_{20}O_{10}\cdot 1/2H_2O$: C, 51.91; H, 5.34. Found: C, 51.80; H, 5.27.

Hydrolysis of 8——A solution of **8** (162 mg) in 5% H_2SO_4 (30 ml) was heated on a boiling water bath for 1 h. The reaction mixture was diluted with water(50 ml) and extracted with EtOAc. The EtOAc solution was washed with water, dried and evaporated to dryness. The residue was recrystallized from hexane–EtOAc to give colorless needles (60 mg), mp 143—144°C whose spectral data and chemical properties coincided with those of an authentic sample of 7-hydroxy-6,8-dimethoxycoumarin (isofraxidin). The aqueous layer was neutralized with $BaCO_3$, then filtered. The filtrate was concentrated to a syrup, and this was subjected to thin

layer chromatography (TLC) on silica gel (Merck, HPTLC plates si 50000 F_{254}) with *n*-propanol–H_2O–NH_4OH (80:20:1); a spot corresponding to glucose was detected at Rf=0.34.

Hydrolysis of 8 with β-Glucosidase———β-Glucosidase (10 mg) (Toyobo, act. 11.1 u/mg) was added to a solution of **8** (20 mg) in AcOH–AcONa buffer (pH 5.0, 10 ml) and the whole was incubated at 37°C over night. The mixture was extracted with EtOAc, and the EtOAc extract was subjected to TLC on silica gel (Merck plates Silica gel 60 F_{254}) with hexane–EtOAc (1:1). A spot coinciding with that of authentic isofraxidin was obtained. The aqueous layer was treated in the same way as described before and glucose was detected.

Angelol I (9)———Recrystallized from Et_2O to give colorless needles, mp 113—115°C. UV λ_{max}^{MeOH} nm (log ϵ): 222(4.36), 251(3.84), 300(3.94), 324(4.11). IR ν_{max}^{Nujol} cm^{-1}: 3350(OH), 1730, 1705(CO), 1620, 1560 (arom.). ORD (c=0.47, EtOH) $[\alpha]^{20}$ (nm): −127.6°(589), −153.2°(550), −212.8°(500), −310.6°(450), −578.4°(400), −748.9°(385). ^{1}H-NMR ($CDCl_3$) δ ppm: 7.62 (1H, d, J=9.5 Hz), 7.61 (1H, s), 6.73 (1H, s), 6.22 (1H, d, J=9.5 Hz), 5.60 (1H, br s), 5.09 (1H, br s), 4.63 (1H, br s), 3.92 (3H, s), 2.87 (1H, br s), 2.00 (2H, m), 1.80 (1H, m), 1.58 (3H, s), 1.25 (3H, s), 0.74 (3H, d, J=6.5 Hz), 0.65 (3H, d, J=6.5 Hz).

Hydrolysis of 9———A 5% NaOH solution (20 ml) was added dropwise to a solution of **9** (500 mg) in pyridine (10 ml) and the mixture was stirred in a stream of N_2 at room temperature. After being stirred for 30 min, the mixture was cooled and diluted with water (50 ml) then acidified with 20% H_2SO_4. The solution was extracted with Et_2O, and the Et_2O extract was separated into neutral and acidic portions in the usual way. The acidic portion was led to the *p*-phenylphenacyl ester in the usual way. The product was purified by chromatography on silica gel with hexane–EtOAc (10:1) and recrystallized from hexane to give colorless plates (13 mg), mp 78°C, which were identical with an authentic sample of *p*-phenylphenacyl isovalerate.

Angeloside A (10)———Colorless viscid oil. UV λ_{max}^{MeOH} nm (log ϵ): 220(4.30), 252(3.57), 302(3.75), 328(4.03). ORD (c=0.545, EtOH) $[\alpha]^{24}$ (nm): −91.7°(589), −113.8°(550), −168.8°(500), −242.2°(450), −447.7°(400), −660.6°(380). ^{1}H-NMR (acetone-d_6) δ ppm: 7.82 (1H, d, J=9.5 Hz), 6.15 (1H, d, J=9.5 Hz), 7.60 (1H, s), 6.84 (1H, s), 5.86 (1H, m), 5.52 (1H, m), 5.24 (1H, d, J=1.5 Hz), 4.66 (1H, d, J=4.0 Hz), 4.00 (3H, s), 4.50-2.60 [11 H (anomeric H: 4.68, d, J=7.5 Hz)], 1.76 (3H, m), 1.64 (3H, m), 1.57 (3H, s), 1.41 (3H, s). The ^{13}C-NMR data are summarized in Table I. *Anal.* Calcd for $C_{26}H_{34}O_{12}$: C, 57.98; H, 6.36. Found: C, 57.86; H, 6.36.

Hydrolysis of 10———A solution of **10** (100 mg) in 5% H_2SO_4 (15 ml) was heated on a boiling water bath for 20 min. The reaction mixture was diluted with water (20 ml) and extracted with Et_2O. The Et_2O solution was washed with water, dried and evaporated to dryness. The residue was subjected to preparative TLC (Merck PLC plates silica gel 60 F_{254}) with hexane–EtOAc (2:1) to give **15** (25 mg) and **16** (10 mg), whose IR, ORD and ^{1}H-NMR spectral data were identical with those of authentic samples of angelol B and angelol D, respectively. On the other hand, the aqueous layer was neutralized with $BaCO_3$, then filtered. The filtrate was concentrated to a syrup, which was subjected to TLC on silica gel (Merck HPTLC plates si 50000 F_{254}) with *n*-propanol–H_2O–NH_4OH (80:20:1); a spot corresponding to glucose was detected.

Treatment of Angelol A (6) with 5% H_2SO_4———A solution of angelol A (50 mg) in a mixture of 5% H_2SO_4 (10 ml) and AcOH (5 ml) was heated on a boiling water bath for 20 min. The whole was extracted with Et_2O. After being washed with $NaHCO_3$ solution then water, the ether solution was dried and evaporated to dryness. The residue was subjected to TLC on silica gel with hexane–EtOAc (1:2). The positions of the spots were measured with a TLC scanner (Hg lamp, exciting wavelength of 313 nm) and two spots corresponding to **15** and **16** were detected. The ratio of the formation of **15** to **16** was 2.8 to 1.

***prim-O*-Glucosylangelicain (14)**———Recrystallized from EtOH to give colorless needles, mp 130—132°C. This product gave a dark blue coloration with Gibbs reagent and ammonia aq. and gave a positive (dark violet coloration) ferric chloride reaction. UV λ_{max}^{MeOH} nm (log ϵ): 215(4.43), 232.5(4.22), 251.5(4.14), 256(4.13), 298(4.03). UV $\lambda_{max}^{MeOH+AlCl_3}$ nm: 216.5, 236, 266, 317.5, 350, 370. IR ν_{max}^{Nujol} cm^{-1}: 3350(OH), 1665(CO), 1635, 1585(arom). ORD (c=0.580, EtOH) $[\alpha]^{22}$ (nm): +13.7°(589), +20.6°(550), +27.4°(500), +37.7°(450), +58.3°(400). ^{1}H-NMR (DMSO-d_6) δ ppm: 12.96 (1H, s), 6.52 (1H, s), 6.45 (1H, s), 5.40—2.70 [16H (anomeric H: 4.35, d, J=7.5 Hz)], 1.17 (6H, s). ^{13}C-NMR are summarized in Table II. *Anal.* Calcd for $C_{21}H_{26}O_{11}\cdot 1/2H_2O$: C, 54.43; H, 5.83. Found: C, 54.41; H, 5.83.

Hexaacetate of 14 (17)———A solution of **14** (200 mg) in a mixture of Ac_2O (10 ml) and AcONa (500 mg) was heated for 1 h. After the reaction mixture had been treated in the usual way, the product was purified by column chromatography on silica gel with hexane–EtOAc (1:1) to afford a colorless viscid oil (**17**) (185 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1745, 1665(CO), 1620, 1470(arom.). ^{1}H-NMR ($CDCl_3$) δ ppm: 6.65 (1H, s), 6.14 (1H, s), 5.40—3.00 (12H), 2.44, 2.11, 2.07, 2.03 (each 3H, s), 2.05 (6H, s), 1.57, 1.54 (each 3H, s).

Hydrolysis of 14———**14** (700 mg) was dissolved in 5% H_2SO_4 (50 ml) and the whole was extracted with EtOAc. The EtOAc solution was washed with water, dried, and evaporated to dryness. The product was purified by chromatography on silica gel with $CHCl_3$–MeOH (30:1) to give colorless needles (**18**) (450 mg), mp 192—194°C, which was identified as angelicain by comparison with an authentic sample. The aqueous layer was neutralized with $BaCO_3$, then filtered. The filtrate was concentrated to a syrup, which was subjected to TLC on silica gel (Merck HPTLC plates si 50000 F_{254}) with *n*-propanol–H_2O–NH_4OH (80:20:1) as a developing solvent; a spot corresponding to glucose was observed at Rf 0.34.

Hydrolysis of 14 with β-Glucosidase———β-Glucosidase (10 mg) was added to a solution of **14** (20 mg) in

AcOH–AcONa buffer (pH 5.0, 10 ml) and the whole was incubated at 37°C overnight. The mixture was extracted with EtOAc. The EtOAc extract was subjected to TLC on silica gel (Merck plates silica gel 60 F_{254}) with $CHCl_3$–MeOH (10:1) and gave a spot identical with that of angelicain (**18**). The aqueous layer was treated in the same way as described before, and glucose was detected.

Hexamethyl Ether of 14 (19)——**14** (1 g) in DMF (40 ml) was methylated with CH_3I (12 ml) and Ag_2O (12 g) in the usual way (Kuhn method). The reaction mixture was diluted with water (100 ml) and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried and evaporated to dryness. The residue was subjected to DCC chromatography with the solvent system $CHCl_3$–MeOH–H_2O (7:3:1) (descending method) to give a colorless viscid oil (**19**) (600 mg). ORD (c=0.350, EtOH) $[\alpha]^{24}$ (nm): +33.9°(589), +39.6°(550), +42.4°(500), +45.2°(450), +56.6°(400). ^{1}H-NMR ($CDCl_3$) δ ppm: 6.53 (1H, s), 6.27 (1H, s), 4.79 (1H, t, J=8.5 Hz), 4.37 (1H, d, J=7.5 Hz), 4.5—2.7 (6H), 3.97, 3.64, 3.62, 3.55, 3.41, 3.31 (each 3H, s), 3.17 (2H, d, J=8.5 Hz), 1.27 (3H, s), 1.24 (3H, s).

Hydrolysis of 19——A solution of **19** (560 mg) in 1 N MeOH–HCl (20 ml) was heated on a boiling water bath. The reaction mixture was diluted with H_2O (50 ml) and extracted with EtOAc. The EtOAc solution was washed, dried and evaporated to dryness. The residue was purified by chromatography on silica gel with EtOAc to afford angelicain dimethyl ether (**20**) (21 mg) as colorless needles, mp 152—153°C. IR ν_{max}^{Nujol} cm^{-1}: 3310(OH), 1650(CO), 1600, 1570(arom.). ^{1}H-NMR (DMSO-d_6) δ ppm: 6.64 (1H, s), 6.07 (1H, s), 5.66 (1H, t, J=6.0 Hz), 4.86 (1H, t, J=8.5 Hz), 4.32 (2H, d, J=6.0 Hz), 3.84 (3H, s), 3.35 (2H, d, J=8.5 Hz), 3.20 (3H, s), 1.18 (6H, s).

Acknowlegement We are greatly indebted to Dr. Kyosuke Nomoto of Suntory Institute for Bioorganic Research for measurements of ^{1}H-NMR and ^{13}C-NMR spectra. We also thank Prof. Atsushi Numata and Mrs. Yoshiko Tsukamoto of this college for measurements of ^{1}H-NMR spectra and elementary analysis, respectively.

References and Notes

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