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## The Constituents of *Glehnia littoralis* FR. SCHMIDT et MIQ. Structure of a New Coumarin Glycoside, Osthenol-7-O- $\beta$ -gentiobioside

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A new coumarin glycoside (**1**) was isolated from the root and rhizoma of *Glehnia littoralis* FR. SCHMIDT et MIQ. (Umbelliferae), together with fourteen known coumarins (**4**—**17**). The structure of **1** was elucidated as osthenol-7-O- $\beta$ -gentiobioside by chemical and spectral studies.

**Keywords**—*Glehnia littoralis*; Umbelliferae; simple coumarins; furanocoumarins; osthenol-7-O- $\beta$ -gentiobioside

*Glehnia littoralis* FR. SCHMIDT et MIQ. (syn, *Phellopterus littoralis* BENTH.) (Umbelliferae) is a perennial herb growing wild on the seashore in East Asia. The root and rhizoma of this plant are used as a diaphoretic, an antipyretic and an analgesic under the name of Běi Shā Shēn in China (Japanese name: Hamabōhu).<sup>2)</sup>

Earlier investigations of this plant, dealing with the isolation of several coumarins, were reported by Noguchi *et al.* (phellopterin)<sup>3)</sup> and by Yang *et al.* (bergapten and imperatorin).<sup>4)</sup> This paper deals with the isolation and the structure elucidation of a new coumarin glycoside, osthenol-7-O- $\beta$ -gentiobioside (**1**), as well as the isolation of fourteen known coumarins from the root and rhizoma of this plant.

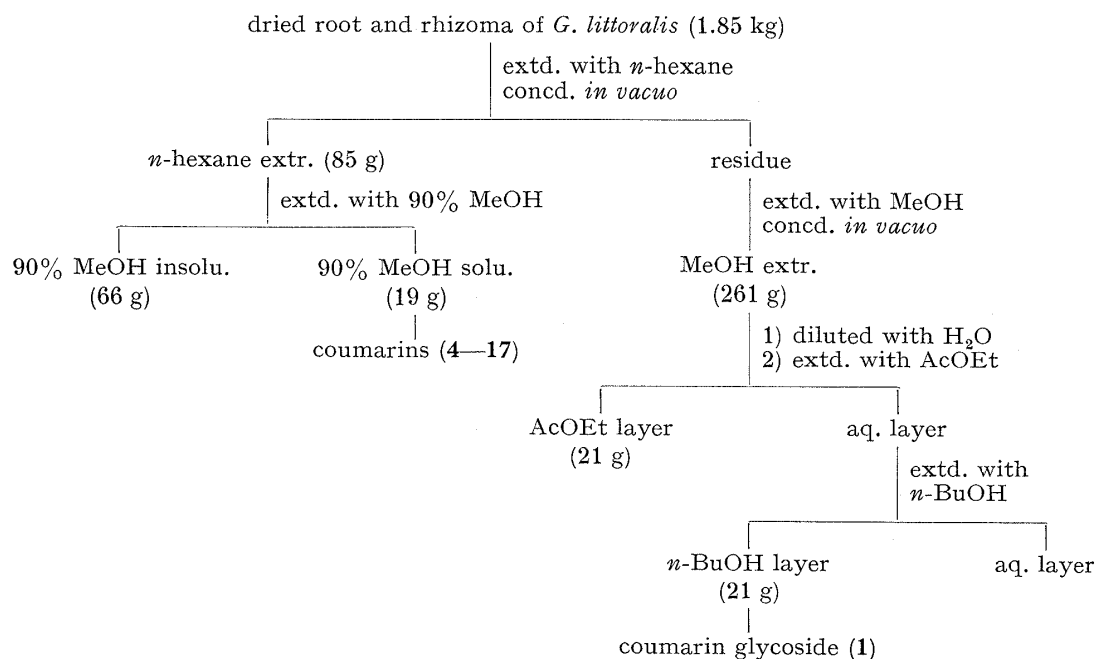


Chart 1. Isolation Procedure for Coumarins and Coumarin Glycoside

1) Location: Honcho 1-9-9, Izumi, Komae-shi, Tokyo 201, Japan.

2) "Zhong Yao Zhi (中藥誌)," Vol. I, ed. by The Pharmaceutical Institute, Chinese Academy of Medical Science, Peking, 1961, p. 191.

3) T. Noguchi and Kawakami, *Yakugaku Zasshi*, **60**, 57 (1940).

4) C.H. Yang and S.A. Brown, *Can. J. Chem.*, **40**, 383 (1962).

The *n*-hexane extract of the plant was concentrated and then extracted with 90% MeOH. The 90% MeOH-soluble part was repeatedly subjected to silica gel column chromatography to furnish psoralen (4), bergapten (5), xanthotoxin (6), isoimperatorin (7), imperatorin (8), bergapten (9), 8-geranyloxypsoralen (10), cnidilin (11), xanthotoxol (12), alloisoimperatorin (13), 8-(1,1-dimethylallyl)-5-hydroxypsoralen (14), marmesin (15), scopoletin (16) and 7-O-(3,3-dimethylallyl)scopoletin (17).

Crystalline compounds 4, 5, 6 and 8 were identified as psoralen, bergapten, xanthotoxin and imperatorin, respectively, on the basis of ultraviolet (UV), infrared (IR) and proton nuclear magnetic resonance ( $^1\text{H}$  NMR) spectral analysis as well as comparisons of physical constants with those reported in the literature.<sup>5)</sup>

8-Geranyloxypsoralen (10),<sup>6)</sup> alloisoimperatorin (13),<sup>7)</sup> marmesin (15),<sup>8)</sup> scopoletin (16)<sup>5)</sup> and 7-O-(3,3-dimethylallyl)scopoletin (17)<sup>9)</sup> were identified by direct comparison with the authentic compounds (mixed mp and IR). Compounds 7, 9, and 14 were identified as isoimperatorin,<sup>10)</sup> bergapten,<sup>11)</sup> and 8-(1,1-dimethylallyl)-5-hydroxypsoralen,<sup>12)</sup> respectively, by comparisons of spectral data with those of authentic materials.

Compounds 11, mp 112–113°,  $\text{C}_{17}\text{H}_{16}\text{O}_5$ , was deduced to be a furocoumarin substituted with a methoxy group and a 3-methyl-2-butenyloxy group at the 5- and 8-positions of the coumarin nucleus on the basis of its UV and  $^1\text{H}$  NMR spectra (see experimental section), so it was considered that 11 might be phellopterin or cnidilin.<sup>13)</sup> Direct comparison (mixed mp and IR) of 11 with phellopterin showed that 11 was not phellopterin, so it was assumed to be cnidilin.

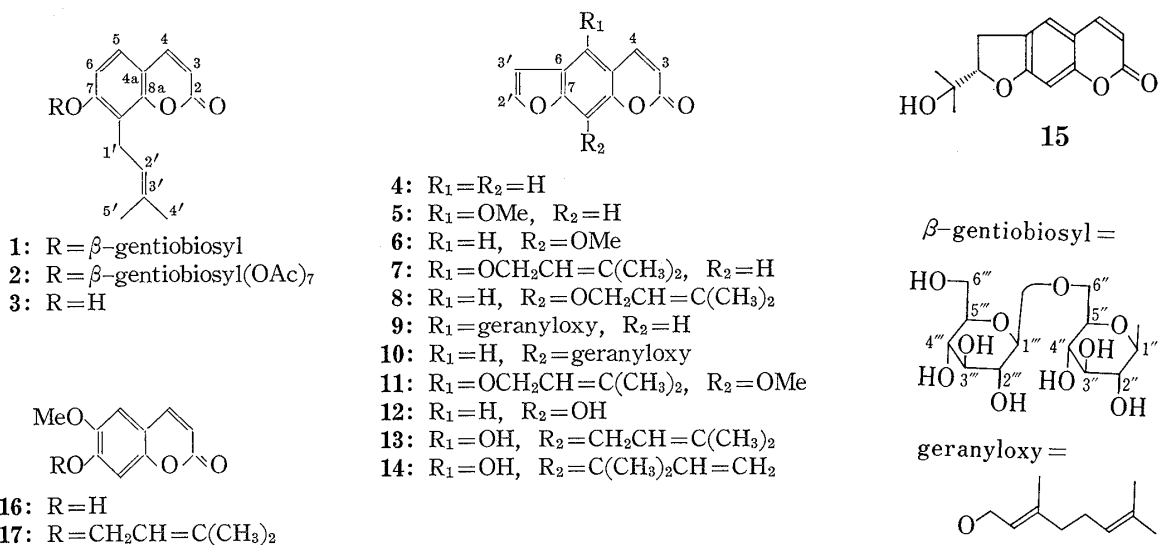


Chart 2

- 5) R.D.H. Murray, "Fortschritte der Chemie Organischer Naturstoffe," Vol. 35, ed. by W. Herz, H. Grisebach and G.W. Kirby, Springer Verlag, Vienna, 1978, p. 199; B.E. Nielsen, "The Biology and Chemistry of the Umbelliferae," ed. by V.H. Heywood, Academic Press, Inc., London, 1971, p. 325; A.I. Gray and P.G. Waterman, *Phytochemistry*, **17**, 845 (1978) and references cited therein.
- 6) R. Kumura, S.K. Banerjee, and K.L. Handa, *Planta Med.*, **30**, 291 (1976).
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- 11) F. Bohlmann, M. Grenz, and C. Zdero, *Chem. Ber.*, **108**, 2955 (1975).
- 12) A.G. Gonzalez, R.J. Cardona, H.L. Dorta, J.M. Medina, and F.R. Luis, *An. Quim.*, **72**, 588 (1976).
- 13) K.H. Lee and T.O. Soine, *J. Pharm. Sci.*, **58**, 675, 681 (1969). Further investigation of the structure of 11 was not done, since insufficient material was available.

Compound **12**, mp 244—245.5°,  $C_{11}H_6O_4$ , was methylated with  $CH_3N_2$  to give a mono-methyl ether, which was identified as xanthotoxin (**6**) by direct comparison (mixed mp and IR). Thus, **12** was confirmed to be xanthotoxin.<sup>5)</sup>

The new glycoside (**1**) was obtained from the *n*-BuOH-soluble portion of the MeOH extract by column chromatography on charcoal and then on silica gel, as shown in Chart 1. Glycoside (**1**) was isolated as colorless needles (yield, 0.014%) of ill-defined mp,  $C_{26}H_{34}O_{13} \cdot H_2O$ ,  $[\alpha]_D \simeq 0^\circ$  ( $c=0.337$ , MeOH), the IR spectrum (KBr) of which showed absorption bands at 3400 (hydroxyls), 1720 (C=O), 1603 (C=C), 1560 and 1492 (aromatic ring)  $cm^{-1}$ . The UV spectrum (EtOH) of **1** exhibited absorption maxima at 246 (sh,  $\log \epsilon$ , 3.83), 256 (3.87) and 313 (4.24) nm, suggesting that **1** might be a 7-hydroxycoumarin derivative. The  $^1H$  NMR spectrum ( $CD_3OD$ ) of **1** showed two characteristic AB-type quartets, one of which at  $\delta$  6.27 and 7.83 (each 1H, d,  $J=9.5$  Hz) was assignable to  $C_{(3)}$ -H and  $C_{(4)}$ -H, respectively, while the other at  $\delta$  7.23 and  $\delta$  7.47 (each 1H, d,  $J=8.5$  Hz) was attributable to *ortho*-coupled aromatic protons. The observation that two methyl signals at  $\delta$  1.67 and  $\delta$  1.87 (each br s) were turned into sharp singlets by irradiation at  $\delta$  5.27 in a homonuclear decoupling experiment indicated that **1** is a simple coumarin having a prenyl side chain. The carbon ( $^{13}C$ ) NMR spectrum ( $DMSO-d_6$ ) of **1** showed nine carbon signals due to the coumarin nucleus, five signals due to a side chain and twelve signals due to sugar moieties (see experimental section). On acetylation with acetic anhydride and pyridine, **1** afforded a crystalline heptaacetate (**2**), mp 256.5—257.5°,  $C_{40}H_{48}O_{20}$ ,  $[\alpha]_D -27.6^\circ$  ( $c=0.283$ ,  $CHCl_3$ ). The mass spectrum of **2** showed a fragmentation pattern typical of an acetylated sugar at  $m/e$  619, 331, 169 and 109. On the basis of these data, **1** was assumed to be a disaccharide of a simple coumarin.

On enzymatic hydrolysis, **1** gave an aglycone (**3**) and glucose. Compound **3** was obtained as colorless needles, mp 131—132°,  $C_{14}H_{14}O_3$ , and gave a brown coloration with ferric chloride. The UV spectrum of **3** showed absorption maxima at 252 ( $\log \epsilon$ , 3.67), 260 (3.70) and 329 (4.21) nm, and the IR spectrum (KBr) exhibited absorption bands at 3340 (hydroxyl), 1705 (C=O), 1600 (C=C), 1570 and 1500 (aromatic ring)  $cm^{-1}$ . In the  $^1H$  NMR spectrum ( $CDCl_3$ ) of **3**, two AB-type quartets [ $\delta$  6.25 ( $J=9.5$  Hz, H-3) and 7.63 ( $J=9.5$  Hz, H-4);  $\delta$  6.83 ( $J=8.5$  Hz, H-6) and  $\delta$  7.22 ( $J=8.5$  Hz, H-5)] due to the coumarin nucleus were observed. Two methyl signals at  $\delta$  1.73 and 1.85 (each br s), a methylene signal at  $\delta$  3.60 (d,  $J=7.5$  Hz) and a methine signal at  $\delta$  5.30 (t,  $J=7.5$  Hz) revealed the presence of a 3-methyl-2-butenyl side chain on the aromatic ring. A broad singlet at  $\delta$  6.80, which disappeared on addition of  $D_2O$ , was assigned to a phenolic hydroxy group. These spectral data were reminiscent of osthenol.<sup>8)</sup> In fact, **3** was identified as osthenol by comparison of its IR and  $^1H$  NMR spectra with those of an authentic sample. All of the above results indicate that **1** is a diglycoside of osthenol.<sup>14)</sup>

To ascertain the structure of the sugar moiety, O-methylalditol acetates were prepared from **1** via permethylation by Hakomori's method<sup>15)</sup> and subsequent acid hydrolysis, reduction and acetylation.<sup>16)</sup> The presence of 1,5-di-O-acetyl-2,3,4,6-tetra-O-methyl glucitol and 1,5,6-tri-O-acetyl-2,3,4-tri-O-methyl glucitol was demonstrated by gas liquid chromatography (GLC), indicating a 1—6 linkage between the two glucose moieties. Lastly, the  $^1H$  NMR spectrum of **1** indicated the configuration of the glucose linkages to be  $\beta$  on the basis of the coupling constants of the anomeric proton signals ( $\delta$  4.40 and  $\delta$  5.07, each d,  $J=7.5$  Hz).

The structure of **1** was thus elucidated as osthenol-7-O- $\beta$ -gentiobioside.  $^{13}C$  NMR spectral data also support formula **1**.

14) Osthenol-7-O- $\beta$ -D-glucoside (vellein) was isolated by Bottomly *et al.* from *Velleia discophora* F. MUELL. (Goodeniaceae): W. Bottomly and D.E. White, *Aust. J. Sci. Res.*, **A4**, 112 (1951) [*C.A.*, **45**, 7127f (1951)].

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### Experimental

All melting points were determined on a Yanagimoto micromelting point apparatus (a hot stage type) and are uncorrected. The UV spectra were recorded with a Hitachi 624 digital spectrophotometer and the IR spectra with a Hitachi EPI-G2 unit. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were taken with Varian T-60 and FT-80A spectrometers, respectively, with tetramethylsilane as an internal standard. The mass spectra were recorded with a Hitachi double focusing mass spectrometer. The specific rotations were measured with a JASCO DIP-SL unit. GLC was run on a Hitachi 073 unit with a hydrogen flame ionization detector. Silica gel (Kieselgel 70—325 mesh, Merck) was used for column chromatography. Thin layer chromatography (TLC) was carried out on Merck plates precoated with Kieselgel 60 F<sub>254</sub>, and preparative layer chromatography (PLC) was carried out on plates (20×20 cm, 0.75 mm thick) coated with Kieselgel GF<sub>254</sub> (Merck).

**Isolation of 1**—The dried root and rhizoma of *Glehnia littoralis* (1.85 kg) was extracted with *n*-hexane (15 l×3) and then with MeOH (15 l×3) under reflux. The MeOH extract was concentrated *in vacuo* to give a brown mass (261 g), which was diluted with H<sub>2</sub>O (700 ml) and extracted with AcOEt (500 ml×3) then with *n*-BuOH (500 ml×3). The *n*-BuOH extract (21 g) was subjected to column chromatography on charcoal, developing with H<sub>2</sub>O and then MeOH. The MeOH eluate (4.9 g) was rechromatographed on silica gel, developing with a CHCl<sub>3</sub>–MeOH solvent system, and then purified by PLC[CHCl<sub>3</sub>–MeOH–H<sub>2</sub>O (35:15:3)] to afford **1** (260 mg, 0.014%).

**Osthenol-7-O- $\beta$ -gentiobioside (1)**—Colorless needles from H<sub>2</sub>O, ill-defined mp,  $[\alpha]_D^{25} \approx 0^\circ$  ( $c=0.337$ , MeOH). UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 246 (sh 3.83), 256 (3.87), 313 (4.24). IR  $\nu_{\text{max}}^{\text{KBr}}$  cm<sup>-1</sup>: 3400, 1720, 1603, 1560, 1492. Anal. Calcd for C<sub>26</sub>H<sub>34</sub>O<sub>13</sub>·H<sub>2</sub>O: C, 54.54; H, 6.34. Found: C, 54.53; H, 6.29.  $^1\text{H}$  NMR ( $\delta$  in CD<sub>3</sub>OD): 1.67, 1.87 (each 3H, br s, (CH<sub>3</sub>)<sub>2</sub>C=CH–), 4.40 (1H, d,  $J=7.5$  Hz, H-1''), 5.07 (1H, d,  $J=7.5$  Hz, H-1'), 5.27 (1H, m, –CH<sub>2</sub>–CH=C–), 6.27 (1H, d,  $J=9.5$  Hz, H-3), 7.23 (1H, d,  $J=8.5$  Hz, H-6), 7.47 (1H, d,  $J=8.5$  Hz, H-5), 7.83 (1H, d,  $J=9.5$  Hz, H-4).  $^{13}\text{C}$ -NMR ( $\delta$  in DMSO-*d*<sub>6</sub>):<sup>17</sup> 160.2 (C-2), 112.9 (C-3), 144.5 (C-4), 117.6 (C-4a), 127.1 (C-5), 112.3 (C-6), 158.0 (C-7), 113.6 (C-8), 152.3 (C-8a), 21.8 (C-1'), 121.6 (C-2'), 131.5 (C-3'), 25.4 (C-4'), 17.8 (C-5'); sugar moieties:<sup>18</sup> 101.1 (C-1''), 103.5 (C-1''), 73.5, 73.7 (C-2'', C-2''), 76.8 (2×C, C-3'', C-3''), 70.0, 70.4 (C-4'', C-4''), 76.2, 76.8 (C-5'', C-5''), 68.8 (C-6''), 61.3 (C-6'').

**Acetylation of 1**—A solution of **1** (16 mg) in Ac<sub>2</sub>O and pyridine (each 0.5 ml) was allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water and extracted with AcOEt. The AcOEt extract was dried over Na<sub>2</sub>SO<sub>4</sub>, concentrated *in vacuo* and then purified by PLC (ether) to give the heptaacetate (**2**) as colorless needles (from acetone, 12 mg), mp 256.5–257.5°,  $[\alpha]_D^{25} -27.7^\circ$  ( $c=0.283$ , CHCl<sub>3</sub>). UV  $\lambda_{\text{max}}^{\text{dioxane}}$  nm (log  $\epsilon$ ): 243 (3.97), 253 (3.96), 298 (4.18), 320 (sh 4.08). IR  $\nu_{\text{max}}^{\text{KBr}}$  cm<sup>-1</sup>: 1755, 1735, 1608, 1570, 1493. Anal. Calcd for C<sub>40</sub>H<sub>48</sub>O<sub>20</sub>: C, 56.60; H, 5.70. Found: C, 56.54; H, 5.64. MS  $m/e$  (%): 619 (5), 331 (69), 230 (6), 229 (10), 187 (9), 175 (12), 169 (100), 109 (39).  $^1\text{H}$ -NMR ( $\delta$  in CDCl<sub>3</sub>): 1.67, 1.87 (each 3H, br s, (CH<sub>3</sub>)<sub>2</sub>C=CH–), 1.90, 2.03, 2.05, 2.08 (each 3H, s, 4×COCH<sub>3</sub>), 2.10 (9H, s, 3×COCH<sub>3</sub>), 3.50 (2H, d-like,  $J=7.5$  Hz, Ar–CH<sub>2</sub>–CH=), 6.33 (1H, d,  $J=9.5$  Hz, H-3), 7.03 (1H, d,  $J=8.5$  Hz, H-6), 7.48 (1H, d,  $J=8.5$  Hz, H-5), 7.72 (1H, d,  $J=9.5$  Hz, H-4).

**Enzymatic Hydrolysis of 1**— $\beta$ -Glucosidase (Miles Laboratories (PTY) Ltd., 5 mg) was added to a solution of **1** (34 mg) in 0.1 M acetate buffer solution (pH 5, 10 ml). The mixture was allowed to stand overnight at 38° and then extracted with AcOEt. The AcOEt extract was concentrated *in vacuo* and the residue was purified by PLC (ether) to give **3** as colorless needles (from H<sub>2</sub>O–EtOH, 11 mg), mp 131–132°. FeCl<sub>3</sub> in CHCl<sub>3</sub>–pyridine: brown. UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 252 (sh 3.67), 260 (3.70), 329 (4.21). IR  $\nu_{\text{max}}^{\text{KBr}}$  cm<sup>-1</sup>: 3340, 1705, 1600, 1570, 1500. Anal. Calcd for C<sub>14</sub>H<sub>14</sub>O<sub>3</sub>: C, 73.02; H, 6.13. Found: C, 73.16; H, 6.18.  $^1\text{H}$ -NMR ( $\delta$  in CDCl<sub>3</sub>): 1.73, 1.85 (each 3H, br s, (CH<sub>3</sub>)<sub>2</sub>C=CH–), 3.60 (2H, d,  $J=7.5$  Hz, Ar–CH<sub>2</sub>–CH=), 5.30 (1H, t,  $J=7.5$  Hz, –CH<sub>2</sub>–CH=C–), 6.25 (1H, d,  $J=9.5$  Hz, H-3), 6.80 (1H, br s, quenched with D<sub>2</sub>O), 6.83 (1H, d,  $J=8.5$  Hz, H-6), 7.22 (1H, d,  $J=8.5$  Hz, H-5), 7.63 (1H, d,  $J=9.5$  Hz, H-4). The IR and  $^1\text{H}$  NMR spectra of **3** were superimposable upon those of osthenol. The aqueous layer was concentrated to dryness and the residue was trimethylsilylated by a usual method. The presence of glucose was demonstrated by GLC. Conditions: column, 2% OV-17 on Uniport Q, 3 mm×2 m; oven temperature, 170°; injection temperature, 220°; carrier gas, N<sub>2</sub>; flow, 40 ml/min.  $t_R$ (min): 8.3 and 12.2.

**Permethylation of 1, followed by Acid Hydrolysis to give Alditol Acetates**—According to Hakomori's method, NaH (500 mg) was stirred with dimethylsulfoxide (DMSO, 5 ml) at 50–60° for 1 hr under N<sub>2</sub> gas flow. Compound **1** (11 mg) in DMSO (3 ml) was added to this reagent and the mixture was kept at room temperature for 2 hr with stirring under N<sub>2</sub> gas flow. Methyl iodide (1 ml) was added and the whole was stirred at room temperature for 2 hr. After dilution with ice-water, the mixture was extracted with AcOEt and the organic layer was washed with water, dried and concentrated. A portion of the residue (1 mg) was dissolved in 85% HCOOH (1 ml), heated in a boiling water bath for 2 hr and then concentrated *in vacuo*. The residue obtained here was further heated with 0.5 N H<sub>2</sub>SO<sub>4</sub> (1 ml) in a boiling water bath for 3 hr. After

17) Measured at 60°. "Topics in Carbon-13 NMR Spectroscopy," Vol. 2, ed. by G.C. Levy, John Wiley, and Sons, Inc., New York, 1976, p. 111.

18) T. Usui, N. Yamaoka, K. Matsuda, and K. Tuzimura, *J. Chem. Soc. Perkin I*, 1973, 2425.

cooling, the reaction mixture was neutralized with  $\text{BaCO}_3$  and passed through an Amberlite IR-120 ( $\text{H}^+$ ) column. The eluate was concentrated to give a brown residue, which was reduced with  $\text{NaBH}_4$  (20 mg) in  $\text{H}_2\text{O}$  (3 ml) at room temperature for 16 hr. The reaction mixture was passed through an Amberlite IR-120 ( $\text{H}^+$ ) column and concentrated to dryness. The residue was acetylated with  $\text{Ac}_2\text{O}$  and pyridine (each 0.5 ml) at  $100^\circ$  for 1 hr. Alditol acetates were identified by comparison with authentic materials on GLC. Conditions: column, 3% ECNSS-M on Gaschrom Q, 3 mm  $\times$  2 m; oven temperature,  $180^\circ$ ; injection temperature,  $250^\circ$ ; carrier gas,  $\text{N}_2$ ; flow, 40 ml/min;  $t_R$ (min): 9.7 (1,5-di-O-acetyl-2,3,4,6-tetra-O-methyl glucitol), 23.6 (1,5,6-tri-O-acetyl-2,3,4-tri-O-methyl glucitol).

**Isolation of 4–17**—*n*-Hexane extracts were concentrated to ca 250 ml and extracted with 90% MeOH (300 ml  $\times$  3). The 90% MeOH solution was concentrated to dryness *in vacuo* and the residue (19 g) was chromatographed on silica gel, developing with an *n*-hexane–AcOEt solvent system, to give five main fractions A, B [each eluted with *n*-hexane–AcOEt (4: 1)], C [eluted with *n*-hexane–AcOEt (3: 1)], D and E [each eluted with *n*-hexane–AtOEt (2: 1)].

Fraction A (8.4 g) was rechromatographed on silica gel, developing with a benzene–ether solvent system, to furnish isoimperatorin (7) (yield 120 mg, 0.006%) and bergaptin (9) (300 mg, 0.016%).

Fraction B (3.2 g) was rechromatographed on silica gel, developing with an *n*-hexane–ether solvent system, to furnish 8-geranyloxypsoralen (10) (100 mg, 0.005%) and cnidilin (11) (15 mg, 0.0008%).

Fraction C (2.5 g) was rechromatographed on silica gel, developing with a benzene–ether solvent system, to furnish psoralen (4) (500 mg, 0.027%), bergapten (5) (300 mg, 0.016%) and imperatorin (8) (770 mg, 0.042%).

Fraction D (1.0 g) was purified by PLC to furnish xanthotoxin (6) (230 mg, 0.012%), xanthotoxol (12) (150 mg, 0.008%), alloisoimperatorin (13) (30 mg, 0.002%) and 7-O-(3,3-dimethylallyl)scopoletin (17) (20 mg, 0.001%).

Fraction E (1.6 g) was rechromatographed on silica gel, developing with an *n*-hexane–AcOEt solvent system, to furnish 8-(1,1-dimethylallyl)-5-hydroxypsoralen (14) (10 mg, 0.0005%), marmesin (15) (10 mg, 0.0005%) and scopoletin (16) (20 mg, 0.001%).

**Psoralen (4)**<sup>5)</sup>—Colorless needles from *n*-hexane–AcOEt, mp  $163\text{--}164^\circ$ . UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 242 (sh 4.38), 247 (4.40), 291 (4.03), 330 (3.80). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1720, 1710, 1630, 1575. Anal. Calcd for  $\text{C}_{11}\text{H}_8\text{O}_3$ : C, 70.97; H, 3.25. Found: C, 71.17; H, 3.33.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 6.37 (1H, d,  $J=10$  Hz, H-3), 6.83 (1H, d,  $J=2$  Hz, H-3'), 7.47 (1H, br s, H-8), 7.67 (1H, s, H-5), 7.68 (1H, d,  $J=2$  Hz, H-2'), 7.78 (1H, d,  $J=10$  Hz, H-4).

**Bergapten (5)**<sup>5)</sup>—Colorless needles from EtOH, mp  $188\text{--}190^\circ$ . UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 223 (4.35), 243 (sh 4.18), 250 (4.23), 260 (4.18), 269 (4.22), 311 (4.14). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1730, 1620, 1600, 1580. Anal. Calcd for  $\text{C}_{12}\text{H}_8\text{O}_4$ : C, 66.67; H, 3.73. Found: C, 66.75; H, 3.79.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 4.27 (3H, s,  $\text{OCH}_3$ ), 6.23 (1H, d,  $J=9.5$  Hz, H-3), 6.98 (1H, d,  $J=2.5/1$  Hz, H-3'), 7.08 (1H, d,  $J=1$  Hz, H-8), 7.55 (1H, d,  $J=2.5$  Hz, H-2'), 8.10 (1H, d,  $J=9.5$  Hz, H-4).

**Xanthotoxin (6)**<sup>5)</sup>—Colorless needles from EtOH, mp  $148\text{--}149.5^\circ$ . UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 219 (4.38), 245 (sh 4.34), 250 (4.37), 264 (sh 4.13), 300 (4.07). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1720, 1710, 1620, 1582, 1545. Anal. Calcd for  $\text{C}_{12}\text{H}_8\text{O}_4$ : C, 66.67; H, 3.73. Found: C, 66.89; H, 3.87.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 4.30 (3H, s,  $\text{OCH}_3$ ), 6.35 (1H, d,  $J=9.5$  Hz, H-3), 6.82 (1H, d,  $J=2.5$  Hz, H-3'), 7.33 (1H, s, H-5), 7.68 (1H, d,  $J=2.5$  Hz, H-2'), 7.75 (1H, d,  $J=9.5$  Hz, H-4).

**Isoimperatorin (7)**<sup>10)</sup>—Colorless prisms from EtOH, mp  $109.5\text{--}110.5^\circ$ . UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 223 (4.25), 244 (sh 4.07), 251 (4.13), 260 (4.08), 269 (4.07), 310 (4.02). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1730, 1620, 1605, 1580, 1545. Anal. Calcd for  $\text{C}_{16}\text{H}_{14}\text{O}_4$ : C, 71.10; H, 5.22. Found: C, 70.87; H, 5.18.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 1.72, 1.80 (each 3H, br s,  $(\text{CH}_3)_2\text{C}=\text{CH}-$ ), 4.85 (2H, d,  $J=7.5$  Hz,  $-\text{OCH}_2\text{CH}-$ ), 5.55 (1H, t-like,  $J=7.5$  Hz,  $-\text{CH}_2-\text{CH}=\text{C}-$ ), 6.25 (1H, d,  $J=10$  Hz, H-3), 6.93 (1H, d,  $J=2.5$  Hz, H-3'), 7.12 (1H, br s, H-8), 7.58 (1H, d,  $J=2.5$  Hz, H-2'), 8.12 (1H, d,  $J=10$  Hz, H-4). This compound was identified as isoimperatorin by comparison of the IR and  $^1\text{H-NMR}$  spectra with those of an authentic sample.

**Imperatorin (8)**<sup>5)</sup>—Colorless prisms from EtOH, mp  $101\text{--}102^\circ$ . UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 220 (4.41), 245 (sh 4.35), 250 (4.37), 264 (sh 4.13), 301 (4.08). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1720, 1710, 1620, 1585. Anal. Calcd for  $\text{C}_{16}\text{H}_{14}\text{O}_4$ : C, 71.10; H, 5.22. Found: C, 70.96; H, 5.06.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 1.73 (6H, br s,  $(\text{CH}_3)_2\text{C}=\text{CH}-$ ), 5.02 (2H, d,  $J=7.5$  Hz,  $\text{OCH}_2\text{CH}-$ ), 5.63 (1H, t-like,  $J=7.5$  Hz,  $-\text{CH}_2\text{CH}=\text{C}-$ ), 6.37 (1H, d,  $J=9.5$  Hz, H-3), 6.82 (1H, d,  $J=2.5$  Hz, H-3'), 7.37 (1H, s, H-5), 7.72 (1H, d,  $J=2.5$  Hz, H-2'), 7.75 (1H, d,  $J=9.5$  Hz, H-4).

**Bergaptin (9)**<sup>11)</sup>—Colorless needles from *n*-hexane–ether, mp  $55\text{--}56^\circ$ . UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 222 (4.39), 244 (sh 4.20), 251 (4.25), 260 (4.20), 269 (4.19), 310 (4.14). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1725, 1620, 1600, 1580, 1540. Anal. Calcd for  $\text{C}_{21}\text{H}_{22}\text{O}_4$ : C, 74.53; H, 6.55. Found: C, 74.63; H, 6.58.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 1.62 (3H, br s,  $\text{CH}_3=\text{C}-\text{CH}-$ ), 1.70 (6H, br s,  $(\text{CH}_3)_2\text{C}=\text{CH}-$ ), 2.08, 2.13 (each 2H,  $=\text{C}-\text{CH}_2\text{CH}_2-\text{CH}=\text{C}-$ ), 4.95 (2H, d,  $J=7.5$  Hz,  $\text{OCH}_2-\text{CH}=\text{C}-$ ), 5.05 (1H, m,  $-\text{CH}_2-\text{CH}=\text{C}-$ ), 5.57 (1H, t-like,  $J=7.5$  Hz,  $-\text{CH}_2-\text{CH}=\text{C}-$ ), 6.28 (1H, d,  $J=9.5$  Hz, H-3), 6.97 (1H, d,  $J=2.5$  Hz, H-3'), 7.13 (1H, br s, H-8), 7.60 (1H, d,  $J=2.5$  Hz, H-2'), 8.15 (1H, d,  $J=9.5$  Hz, H-4). This compound was identified as bergaptin by comparison of the  $^1\text{H-NMR}$  spectrum with that of an authentic sample.

**8-Geranyloxypsoralen (10)**<sup>6)</sup>—Colorless needles from *n*-hexane–ether, mp  $59\text{--}60^\circ$ . UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 218 (4.48), 245 (sh 4.38), 250 (4.40), 265 (sh 4.17), 301 (4.11). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1720, 1710, 1625, 1590. Anal. Calcd for  $\text{C}_{21}\text{H}_{22}\text{O}_4$ : C, 74.53; H, 6.55. Found: C, 74.67; H, 6.36.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 1.55, 1.63,

1.68 (each 3H, br s,  $(\text{CH}_3)_2\text{C}=\text{CH}-$ ,  $\text{CH}_3-\text{C}=\text{CH}-$ ), 1.98, 2.03 (each 2H,  $-\dot{\text{C}}=\text{CH}_2\text{CH}_2\text{CH}=\text{C}-$ ), 5.05 (1H, m,  $-\text{CH}_2\text{CH}=\text{C}-$ ), 5.05 (2H, d,  $J=7.5$  Hz,  $\text{OCH}_2-\text{CH}=\text{C}-$ ), 5.63 (1H, t-like,  $J=7.5$  Hz,  $-\text{CH}_2-\text{CH}=\dot{\text{C}}-$ ), 6.37 (1H, d,  $J=9.5$  Hz, H-3), 6.82 (1H, d,  $J=2.5$  Hz, H-3'), 7.37 (1H, s, H-5), 7.70 (1H, d,  $J=2.5$  Hz, H-2'), 7.75 (1H, d,  $J=9.5$  Hz, H-4). This compound was identified as 8-geranyloxypsoralen by direct comparison with an authentic sample (mixed mp and IR).

**Cnidilin (11)<sup>13)</sup>**—Colorless needles from EtOH, mp 112–113°. UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 224 (4.41), 243 (4.16), 251 (4.18), 270 (4.27), 313 (4.09). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1720, 1600, 1590. Anal. Calcd for  $\text{C}_{17}\text{H}_{16}\text{O}_5$ : C, 67.99; H, 5.37. Found: C, 67.71; H, 5.32.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 1.65, 1.77 (each 3H, br s,  $(\text{CH}_3)_2\text{C}=\text{CH}-$ ), 4.17 (3H, s,  $\text{OCH}_3$ ), 4.78 (2H, d,  $J=7$  Hz,  $-\text{OCH}_2-\text{CH}=\text{C}-$ ), 5.53 (1H, t,  $J=7$  Hz,  $-\text{CH}_2-\text{CH}=\dot{\text{C}}-$ ), 6.27 (1H, d,  $J=10$  Hz, H-3), 6.93 (1H, d,  $J=2.5$  Hz, H-3'), 7.60 (1H, d,  $J=2.5$  Hz, H-2'), 8.08 (1H, d,  $J=10$  Hz, H-4). Direct comparison (mixed mp, IR and TLC) of 11 with phellopterin showed that 11 was not phellopterin.

**Xanthotoxol (12)<sup>9)</sup>**—Slightly yellow needles from EtOH, mp 244–245.5°. UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 220 (4.49), 244 (sh 4.28), 251 (4.33), 263 (4.27), 269 (4.28), 309 (4.14). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3275, 1700, 1590. Anal. Calcd for  $\text{C}_{11}\text{H}_6\text{O}_4$ : C, 65.35; H, 2.99. Found: C, 65.56; H, 3.20.  $^1\text{H-NMR}$  ( $\delta$  in acetone- $d_6$ ): 6.33 (1H, d,  $J=10$  Hz, H-3), 6.97 (1H, d,  $J=2.5$  Hz, H-3'), 7.42 (1H, s, H-5), 7.90 (1H, d,  $J=2.5$  Hz, H-2'), 7.98 (1H, d,  $J=10$  Hz, H-4). Compound 12 (23 mg) was methylated with  $\text{CH}_3\text{N}_2$  in a mixture of ether and acetone at room temperature for 3 hr. The reaction mixture was concentrated and purified by PLC [benzene–ether (5:1)] to afford 6 as colorless needles (from EtOH, 10 mg); this material was identified as xanthotoxin (6) by direct comparison with an authentic sample (mixed mp and IR).

**Alloisioimperatorin (13)<sup>7)</sup>**—Slightly yellow needles from EtOH, mp 234–235.5° (dec.). UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 224 (4.46), 245 (4.14), 253 (4.21), 268 (4.27), 274 (4.27), 317 (4.08). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3320, 1720, 1593. Anal. Calcd for  $\text{C}_{16}\text{H}_{14}\text{O}_4$ : C, 71.10; H, 5.22. Found: C, 70.81; H, 5.21.  $^1\text{H-NMR}$  ( $\delta$  in acetone- $d_6$ ): 1.67, 1.87 (each 3H, br s,  $(\text{CH}_3)_2\text{C}=\text{CH}-$ ), 3.78 (2H, d,  $J=7$  Hz,  $\text{ArCH}_2-\text{CH}=\text{C}-$ ), 5.20 (1H, t-like,  $J=7$  Hz,  $-\text{CH}_2-\text{CH}=\dot{\text{C}}-$ ), 6.32 (1H, d,  $J=10$  Hz, H-3), 7.05 (1H, d,  $J=2$  Hz, H-3'), 7.88 (1H, d,  $J=2$  Hz, H-2'), 8.17 (1H, d,  $J=10$  Hz, H-4). This compound was identified as alloisioimperatorin by direct comparison with an authentic sample (mixed mp and IR).

**8-(1,1-Dimethylallyl)-5-hydroxypsoralen (14)<sup>12)</sup>**—Yellow prisms from EtOH, mp 239–241° (dec.). UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 225 (4.43), 244 (sh 4.16), 252 (4.16), 266 (sh 4.22), 274 (4.30), 296 (4.06), 316 (4.11). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3110, 1685, 1608, 1575. MS  $m/e$  (%): 270 ( $\text{M}^+$ , 78), 255 (100), 242 (15), 227 (45), 199 (27), 171 (16), 128 (13), 115 (15), 92 (15), 77 (13).  $^1\text{H-NMR}$  ( $\delta$  in acetone- $d_6$ ): 1.77 (6H, s,  $(\text{CH}_3)_2\text{C}=\text{CH}-$ ), 4.93 (1H, d,  $J=10/2$  Hz), 4.98 (1H, d,  $J=18/2$  Hz) ( $-\text{CH}=\text{CH}_2$ ), 6.22 (1H, d,  $J=10$  Hz, H-3), 6.40 (1H, d,  $J=18/10$  Hz,  $-\text{CH}=\text{CH}_2$ ), 7.15 (1H, d,  $J=2.5$  Hz, H-3'), 7.78 (1H, d,  $J=2.5$  Hz, H-2'), 8.27 (1H, d,  $J=10$  Hz, H-4). The spectra of 14 were superimposable upon those of an authentic sample (UV, IR, MS and  $^1\text{H-NMR}$ ).

**Marmesin (15)<sup>8)</sup>**—Colorless prisms from AcOEt, mp 191–192°.  $[\alpha]_D^{25} + 26.6^\circ$  ( $c=0.263$ ,  $\text{CHCl}_3$ ). UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 226 (3.88), 250 (3.45), 260 (3.38), 300 (sh 3.63), 337 (4.08). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3440, 1700, 1625, 1565. Anal. Calcd for  $\text{C}_{14}\text{H}_{14}\text{O}_4$ : C, 68.28; H, 5.73. Found: C, 68.03; H, 5.68.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 1.27, 1.37 (each 3H, s,  $(\text{CH}_3)_2-\dot{\text{C}}-\text{OH}$ ), 2.00 (1H, br s, OH, quenched with  $\text{D}_2\text{O}$ ), 3.22 (2H, d,  $J=9$  Hz, H-3'), 4.73 (1H, t,  $J=9$  Hz, H-2'), 6.17 (1H, d,  $J=9.5$  Hz, H-3), 6.68 (1H, s, H-5), 7.20 (1H, br s, H-8), 7.53 (1H, d,  $J=9.5$  Hz, H-4). This compound was identified as marmesin by direct comparison with an authentic sample (mixed mp and IR).

**Scopoletin (16)<sup>5)</sup>**—Colorless needles from *n*-hexane–AcOEt, mp 205.5–208°. UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 230 (4.16), 254 (3.71), 263 (sh 3.66), 300 (3.73), 347 (4.11). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3320, 1700, 1622, 1603, 1563, 1505. Anal. Calcd for  $\text{C}_{10}\text{H}_8\text{O}_4$ : C, 62.50; H, 4.20. Found: C, 62.79; H, 4.32.  $^1\text{H-NMR}$  ( $\delta$  in acetone- $d_6$ ): 3.90 (3H, s,  $\text{OCH}_3$ ), 6.40 (1H, d,  $J=10$  Hz, H-3), 6.83 (1H, s, H-5), 7.23 (1H, s, H-8), 7.83 (1H, d,  $J=10$  Hz, H-4). This compound was identified as scopoletin by direct comparison with an authentic sample (mixed mp and IR).

**7-O-(3,3-Dimethylallyl)scopoletin (17)<sup>9)</sup>**—Colorless needles from ether–pet.ether, mp 179–180.5°. UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 231 (4.26), 253 (3.81), 263 (sh 3.69), 288 (sh 3.72), 297 (3.78), 346 (4.10). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1720, 1713, 1610, 1561, 1511. Anal. Calcd for  $\text{C}_{15}\text{H}_{16}\text{O}_4$ : C, 69.21; H, 6.20. Found: C, 69.45; H, 6.26.  $^1\text{H-NMR}$  ( $\delta$  in  $\text{CDCl}_3$ ): 1.78 (6H, br s,  $(\text{CH}_3)_2\text{C}=\text{CH}-$ ), 3.90 (3H, s,  $\text{OCH}_3$ ), 4.68 (2H, d,  $J=7$  Hz,  $\text{OCH}_2-\text{CH}=\text{C}-$ ), 5.52 (1H, t-like,  $J=7$  Hz,  $-\text{CH}_2-\text{CH}=\dot{\text{C}}-$ ), 6.28 (1H, d,  $J=9.5$  Hz, H-3), 6.83 (1H, s, H-5), 6.87 (1H, s, H-8), 7.60 (1H, d,  $J=9.5$  Hz, H-4). This compound was identified as 7-O-(3,3-dimethylallyl)scopoletin by direct comparison with an authentic sample (mixed mp and IR).

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