Chem. Pharm. Bull. 28(6)1847—1852(1980)

The Constituents of *Glehnia littoralis* Fr. Schmidt et Miq. Structure of a New Coumarin Glycoside, Osthenol-7-O-β-gentiobioside

Hiroshi Sasaki, Heihachiro Taguchi, Tohru Endo, and Itiro Yosioka

Tsumura Laboratory[1]

(Received January 10, 1980)

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-β-gentiobioside by chemical and spectral studies.

Keywords——*Glehnia littoralis*; Umbelliferae; simple coumarins; furanocoumarins; osthenol-7-O-β-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).[2]

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

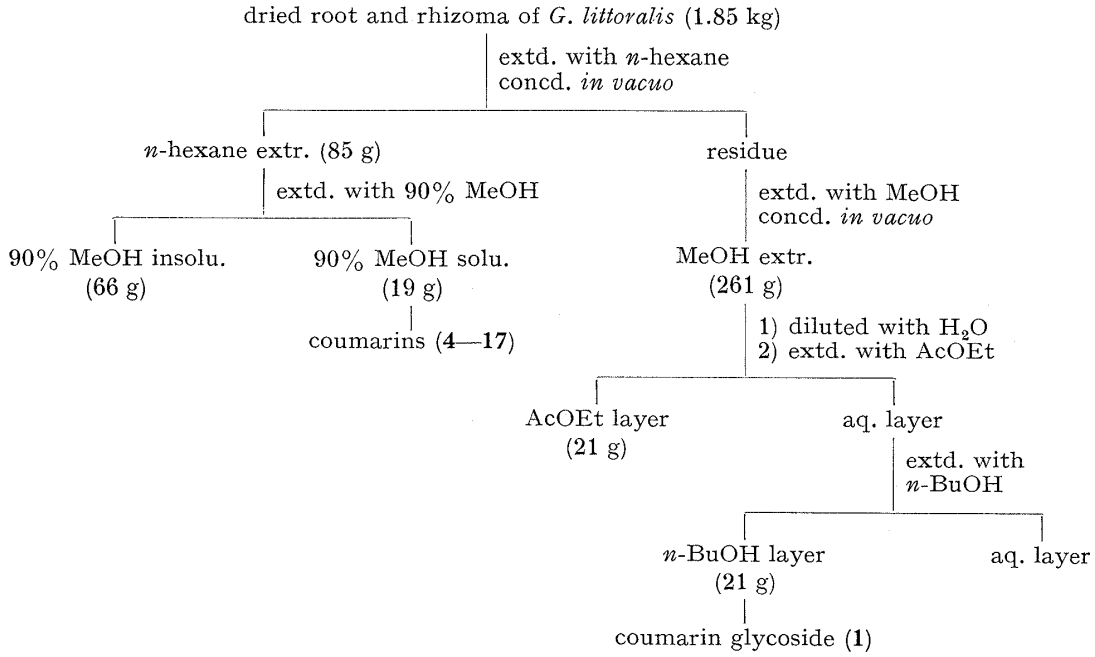


Chart 1. Isolation Procedure for Coumarins and Coumarin Glycoside

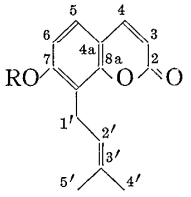
1) Location: *Honcho 1-9-9, Izumi, Komae-shi, Tokyo 201, Japan.*
2) "Zhong Yao Zhi (中葯誌)," Vol. I, ed. by The Pharmaceutical Institute, Chinese Academy of Medical Science, Peking. 1961, p. 191.
3) T. Noguchi and Kawakami, *Yakugaku Zasshi*, **60**, 57 (1940).
4) C.H. Yang and S.A. Brown, *Can. J. Chem.*, **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**), bergaptin (**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**).

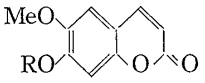
Crystalline compounds **4**, **5**, **6** and **8** were identified as psoralen, bergapten, xanthotoxin and imperatorin, respectively, on the basis of ultraviolet (UV), infrared (IR) and proton nuclear magnetic resonance (^{1}H NMR) spectral analysis as well as comparisons of physical constants with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

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

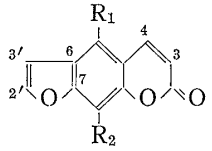
Compounds **11**, mp 112—113°, $C_{17}H_{16}O_5$, was deduced to be a furocoumarin substituted with a methoxy group and a 3-methyl-2-butenyloxy group at the 5- and 8-positions of the coumarin nucleus on the basis of its UV and ^{1}H NMR spectra (see experimental section), so it was considered that **11** might be phellopterin or cnidilin.[13] Direct comparison (mixed mp and IR) of **11** with phellopterin showed that **11** was not phellopterin, so it was assumed to be cnidilin.



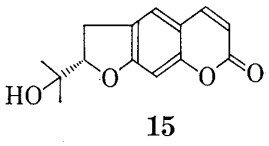
1: R=β-gentiobiosyl
2: R=β-gentiobiosyl(OAc)$_7$
3: R=H



16: R=H
17: R=$CH_2CH=C(CH_3)_2$

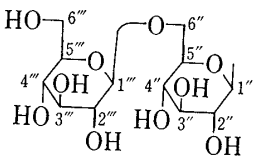


4: $R_1=R_2=H$
5: $R_1=OMe$, $R_2=H$
6: $R_1=H$, $R_2=OMe$
7: $R_1=OCH_2CH=C(CH_3)_2$, $R_2=H$
8: $R_1=H$, $R_2=OCH_2CH=C(CH_3)_2$
9: R_1=geranyloxy, $R_2=H$
10: $R_1=H$, R_2=geranyloxy
11: $R_1=OCH_2CH=C(CH_3)_2$, $R_2=OMe$
12: $R_1=H$, $R_2=OH$
13: $R_1=OH$, $R_2=CH_2CH=C(CH_3)_2$
14: $R_1=OH$, $R_2=C(CH_3)_2CH=CH_2$



15

β-gentiobiosyl=



geranyloxy=

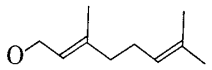


Chart 2

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).
7) Y. Saiki, K. Morinaga, O. Okegawa, S. Sakai, Y. Amaya, A. Ueno, and S. Fukushima, *Yakugaku Zasshi*, **91**, 1313 (1971).
8) H. Ishii, K. Hosoya, T. Ishikawa, and J. Haginiwa, *Yakugaku Zasshi*, **94**, 309 (1974).
9) M.M. Ballantyne, P.H. McCabe, and R.D.H. Murray, *Tetrahedron*, **27**, 871 (1971).
10) "Spectral Atlas of Terpenes and the Related Compounds," ed. by Y. Yukawa and S. Ito, Hirokawa Publishing Company, Inc., Tokyo, 1973, p. 94.
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_2N_2 to give a monomethyl ether, which was identified as xanthotoxin (**6**) by direct comparison (mixed mp and IR). Thus, **12** was confirmed to be xanthotoxol.[5]

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, $C_{26}H_{34}O_{13}\cdot H_2O$, $[\alpha]_D \simeq 0°$ (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 ε, 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 δ 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 δ 7.23 and δ 7.47 (each 1H, d, J=8.5 Hz) was attributable to *ortho*-coupled aromatic protons. The observation that two methyl signals at δ 1.67 and δ 1.87 (each br s) were turned into sharp singlets by irradiation at δ 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° (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 ε, 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 [δ 6.25 (J=9.5 Hz, H-3) and 7.63 (J=9.5 Hz, H-4); δ 6.83 (J=8.5 Hz, H-6) and δ 7.22 (J=8.5 Hz, H-5)] due to the coumarin nucleus were observed. Two methyl signals at δ 1.73 and 1.85 (each br s), a methylene signal at δ 3.60 (d, J=7.5 Hz) and a methine signal at δ 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 δ 6.80, which disappeared on addition of D_2O, was assigned to a phenolic hydroxy group. These spectral data were reminiscent of osthenol.[8] 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 diglucoside of osthenol.[14]

To ascertain the structure of the sugar moiety, O-methylalditol acetates were prepared from **1** *via* permethylation by Hakomori's method[15] and subsequent acid hydrolysis, reduction and acetylation.[16] 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 β on the basis of the coupling constants of the anomeric proton signals (δ 4.40 and δ 5.07, each d, J=7.5 Hz).

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

14) Osthenol-7-O-β-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**, 7127*f* (1951)].
15) S. Hakomori, *J. Biochem.* (Tokyo), **55**, 205 (1964).
16) J.S. Sawardeker, J.H. Sloneker, and A.J. Jeanes, *Anal. Chem.*, **37**, 1602 (1965); H. Björndal, B. Lindberg, and S. Svensson, *Acta Chem. Scand.*, **21**, 1801 (1967).

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 ^1H and ^{13}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_{254}, and preparative layer chromatography (PLC) was carried out on plates (20×20 cm, 0.75 mm thick) coated with Kieselgel GF_{254} (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_2O (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_2O and then MeOH. The MeOH eluate (4.9 g) was rechromatographed on silica gel, developing with a $CHCl_3$–MeOH solvent system, and then purified by PLC[$CHCl_3$–MeOH–H_2O (35:15:3)] to afford **1** (260 mg, 0.014%).

Osthenol-7-O-β-gentiobioside (1)——Colorless needles from H_2O, ill-defined mp, $[\alpha]_D^{26} \simeq 0°$ ($c=0.337$, MeOH). UV λ_{max}^{EtOH} nm (log ε): 246 (sh 3.83), 256 (3.87), 313 (4.24). IR ν_{max}^{KBr} cm^{-1}: 3400, 1720, 1603, 1560, 1492. *Anal.* Calcd for $C_{26}H_{34}O_{13}\cdot H_2O$: C, 54.54; H, 6.34. Found: C, 54.53; H, 6.29. ^1H NMR (δ in CD_3OD): 1.67, 1.87 (each 3H, br s, $(C\underline{H}_3)_2C=CH-$), 4.40 (1H, d, $J=7.5$ Hz, H-1″), 5.07 (1H, d, $J=7.5$ Hz, H-1‴), 5.27 (1H, m, $-CH_2-C\underline{H}=\overset{|}{C}-$), 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}C-NMR (δ in DMSO-d_6):[17] 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:[18] 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_2O 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_2SO_4, 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°, $[\alpha]_D^{28}$ −27.7° ($c=0.283$, $CHCl_3$). UV $\lambda_{max}^{dioxane}$ nm (log ε): 243 (3.97), 253 (3.96), 298 (4.18), 320 (sh 4.08). IR ν_{max}^{KBr} cm^{-1}: 1755, 1735, 1608, 1570, 1493. *Anal.* Calcd for $C_{40}H_{48}O_{20}$: 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). ^1H-NMR (δ in $CDCl_3$): 1.67, 1.87 (each 3H, br s, $(C\underline{H}_3)_2C=CH-$), 1.90, 2.03, 2.05, 2.08 (each 3H, s, 4×$COCH_3$), 2.10 (9H, s, 3×$COCH_3$), 3.50 (2H, d-like, $J=7.5$ Hz, Ar-$C\underline{H}_2$-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——β-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_2O–EtOH, 11 mg), mp 131—132°. $FeCl_3$ in $CHCl_3$–pyridine: brown. UV λ_{max}^{EtOH} nm (log ε): 252 (sh 3.67), 260 (3.70), 329 (4.21). IR ν_{max}^{KBr} cm^{-1}: 3340, 1705, 1600, 1570, 1500. *Anal.* Calcd for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 73.16; H, 6.18. ^1H-NMR (δ in $CDCl_3$): 1.73, 1.85 (each 3H, br s, $(C\underline{H}_3)_2C=CH-$), 3.60 (2H, d, $J=7.5$ Hz, Ar-$C\underline{H}_2$-CH=), 5.30 (1H, t, $J=7.5$ Hz, $-CH_2-C\underline{H}=\overset{|}{C}-$), 6.25 (1H, d, $J=9.5$ Hz, H-3), 6.80 (1H, br s, quenched with D_2O), 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 ^1H 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_2; 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_2 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_2 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_2SO_4 (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 $BaCO_3$ and passed through an Amberlite IR-120 (H^+) column. The eluate was concentrated to give a brown residue, which was reduced with $NaBH_4$ (20 mg) in H_2O (3 ml) at room temperature for 16 hr. The reaction mixture was passed through an Amberlite IR-120 (H^+) column and concentrated to dryness. The residue was acetylated with Ac_2O and pyridine (each 0.5 ml) at 100° for 1 hr. Alditol acetates were identified by comparison with authentic materials on GLC. Conditions: column, 3% ECNSS-M on Gaschrom Q, 3 mm×2 m; oven temperature, 180°; injection temperature, 250°; carrier gas, 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×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**)[5]——Colorless needles from *n*-hexane–AcOEt, mp 163—164°. UV λ_{max}^{EtOH} nm (log ε): 242 (sh 4.38), 247 (4.40), 291 (4.03), 330 (3.80). IR ν_{max}^{KBr} cm^{-1}: 1720, 1710, 1630, 1575. *Anal.* Calcd for $C_{11}H_6O_3$: C, 70.97; H, 3.25. Found: C, 71.17; H, 3.33. ^{1}H-NMR (δ in $CDCl_3$): 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**)[5]——Colorless needles from EtOH, mp 188—190°. UV λ_{max}^{EtOH} nm (log ε): 223 (4.35), 243 (sh 4.18), 250 (4.23), 260 (4.18), 269 (4.22), 311 (4.14). IR ν_{max}^{KBr} cm^{-1}: 1730, 1620, 1600, 1580. *Anal.* Calcd for $C_{12}H_8O_4$: C, 66.67; H, 3.73. Found: C, 66.75; H, 3.79. ^{1}H-NMR (δ in $CDCl_3$): 4.27 (3H, s, OCH_3), 6.23 (1H, d, J=9.5 Hz, H-3), 6.98 (1H, d, 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**)[5]——Colorless needles from EtOH, mp 148—149.5°. UV λ_{max}^{EtOH} nm (log ε): 219 (4.38), 245 (sh 4.34), 250 (4.37), 264 (sh 4.13), 300 (4.07). IR ν_{max}^{KBr} cm^{-1}: 1720, 1710, 1620, 1582, 1545. *Anal.* Calcd for $C_{12}H_8O_4$: C, 66.67; H, 3.73. Found: C, 66.89; H, 3.87. ^{1}H-NMR (δ in $CDCl_3$): 4.30 (3H, s, 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**)[10]——Colorless prisms from EtOH, mp 109.5—110.5°. UV λ_{max}^{EtOH} nm (log ε): 223 (4.25), 244 (sh 4.07), 251 (4.13), 260 (4.08), 269 (4.07), 310 (4.02). IR ν_{max}^{KBr} cm^{-1}: 1730, 1620, 1605, 1580, 1545. *Anal.* Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.87; H, 5.18. ^{1}H-NMR (δ in $CDCl_3$): 1.72, 1.80 (each 3H, br s, $(C\underline{H}_3)_2C$=CH–), 4.85 (2H, d, J=7.5 Hz, –$OC\underline{H}_2$CH–), 5.55 (1H, t-like, J=7.5 Hz, –CH_2–C$\underline{H}$=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}H-NMR spectra with those of an authentic sample.

Imperatorin (**8**)[5]——Colorless prisms from EtOH, mp 101—102°. UV λ_{max}^{EtOH} nm (log ε): 220 (4.41), 245 (sh 4.35), 250 (4.37), 264 (sh 4.13), 301 (4.08). IR ν_{max}^{KBr} cm^{-1}: 1720, 1710, 1620, 1585. *Anal.* Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.96; H, 5.06. ^{1}H-NMR (δ in $CDCl_3$): 1.73 (6H, br s, $(C\underline{H}_3)_2C$=CH–), 5.02 (2H, d, J=7.5 Hz, $OC\underline{H}_2$CH–), 5.63 (1H, t-like, J=7.5 Hz, –$CH_2C\underline{H}$=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**)[11]——Colorless needles from *n*-hexane–ether, mp 55—56°. UV λ_{max}^{EtOH} nm (log ε): 222 (4.39), 244 (sh 4.20), 251 (4.25), 260 (4.20), 269 (4.19), 310 (4.14). IR ν_{max}^{KBr} cm^{-1}: 1725, 1620, 1600, 1580, 1540. *Anal.* Calcd for $C_{21}H_{22}O_4$: C, 74.53; H, 6.55. Found: C, 74.63; H, 6.58. ^{1}H NMR (δ in $CDCl_3$): 1.62 (3H, br s, $C\underline{H}_3$–C–CH–), 1.70 (6H, br s, $(C\underline{H}_3)_2C$=CH–), 2.08, 2.13 (each 2H, =C–$C\underline{H}_2C\underline{H}_2$–CH=), 4.95 (2H, d, J=7.5 Hz, $OC\underline{H}_2$–CH=), 5.05 (1H, m, –CH_2–C$\underline{H}$=C–), 5.57 (1H, t-like, J=7.5 Hz, –CH_2–C$\underline{H}$=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}H-NMR spectrum with that of an authentic sample.

8-Geranyloxypsoralen (**10**)[6]——Colorless needles from *n*-hexane–ether, mp 59—60°. UV λ_{max}^{EtOH} nm (log ε): 218 (4.48), 245 (sh 4.38), 250 (4.40), 265 (sh 4.17), 301 (4.11). IR ν_{max}^{KBr} cm^{-1}: 1720, 1710, 1625, 1590. *Anal.* Calcd for $C_{21}H_{22}O_4$: C, 74.53; H, 6.55. Found: C, 74.67; H, 6.36. ^{1}H-NMR (δ in $CDCl_3$): 1.55, 1.63,

1.68 (each 3H, br s, $(C\underline{H}_3)_2C=CH-$, $C\underline{H}_3-C=CH-$), 1.98, 2.03 (each 2H, $-\dot{C}=C\underline{H}_2C\underline{H}_2CH=$), 5.05 (1H, m, $-CH_2C\underline{H}=C-$), 5.05 (2H, d, $J=7.5$ Hz, $OC\underline{H}_2-CH=C-$), 5.63 (1H, t-like, $J=7.5$ Hz, $-CH_2-C\underline{H}=\dot{C}-$), 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)[13]——Colorless needles from EtOH, mp 112—113°. UV λ_{max}^{EtOH} nm (log ε): 224 (4.41), 243 (4.16), 251 (4.18), 270 (4.27), 313 (4.09). IR ν_{max}^{KBr} cm^{-1}: 1720, 1600, 1590. *Anal.* Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 67.71; H, 5.32. ^{1}H-NMR (δ in $CDCl_3$): 1.65, 1.77 (each 3H, br s, $(C\underline{H}_3)_2C=CH-$), 4.17 (3H, s, OCH_3), 4.78 (2H, d, $J=7$ Hz, $-OC\underline{H}_2-CH=$), 5.53 (1H, t, $J=7$ Hz, $-CH_2-C\underline{H}=\dot{C}-$), 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)[5]——Slightly yellow needles from EtOH, mp 244—245.5°. UV λ_{max}^{EtOH} nm (log ε): 220 (4.49), 244 (sh 4.28), 251 (4.33), 263 (4.27), 269 (4.28), 309 (4.14). IR ν_{max}^{KBr} cm^{-1}: 3275, 1700, 1590. *Anal.* Calcd for $C_{11}H_6O_4$: 65.35; H, 2.99. Found: C, 65.56; H, 3.20. ^{1}H-NMR (δ 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 CH_2N_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)] tc 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).

Alloisoimperatorin (13)[7]——Slightly yellow needles from EtOH, mp 234—235.5° (dec.). UV λ_{max}^{EtOH} nm (log ε): 224 (4.46), 245 (4.14), 253 (4.21), 268 (4.27), 274 (4.27), 317 (4.08). IR ν_{max}^{KBr} cm^{-1}: 3320, 1720, 1593. *Anal.* Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.81; H, 5.21. ^{1}H-NMR (δ in acetone-d_6): 1.67, 1.87 (each 3H, br s, $(C\underline{H}_3)_2C=CH-$), 3.78 (2H, d, $J=7$ Hz, $ArC\underline{H}_2-CH=$), 5.20 (1H, t-like, $J=7$ Hz, $-CH_2-C\underline{H}=\dot{C}-$), 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 alloisoimperatorin by direct comparison with an authentic sample (mixed mp and IR).

8-(1,1-Dimethylallyl)-5-hydroxypsoralen (14)[12]——Yellow prisms from EtOH, mp 239—241° (dec.). UV λ_{max}^{EtOH} nm (log ε): 225 (4.43), 244 (sh 4.16), 252 (4.16), 266 (sh 4.22), 274 (4.30), 296 (4.06), 316 (4.11). IR ν_{max}^{KBr} cm^{-1}: 3110, 1685, 1608, 1575. MS *m/e* (%): 270 (M^+, 78), 255 (100), 242 (15), 227 (45), 199 (27), 171 (16), 128 (13), 115 (15), 92 (15), 77 (13). ^{1}H-NMR (δ in acetone-d_6): 1.77 (6H, s, $(C\underline{H}_3)_2C=CH-$), 4.93 (1H, d, d, $J=10/2$ Hz), 4.98 (1H, d,d, $J=18/2$ Hz) ($-CH=C\underline{H}_2$), 6.22 (1H, d, $J=10$ Hz, H-3), 6.40 (1H, d,d, $J=18/10$ Hz, $-C\underline{H}=CH_2$), 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}H-NMR).

Marmesin (15)[8]——Colorless prisms from AcOEt, mp 191—192°. $[\alpha]_D^{22}$ +26.6° ($c=0.263$, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 226 (3.88), 250 (3.45), 260 (3.38), 300 (sh 3.63), 337 (4.08). IR ν_{max}^{KBr} cm^{-1}: 3440, 1700, 1625, 1565. *Anal.* Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.03; H, 5.68. ^{1}H-NMR (δ in $CDCl_3$): 1.27, 1.37 (each 3H, s, $(CH_3)_2-\dot{C}-OH$), 2.00 (1H, br s, OH, quenched with D_2O), 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)[5]——Colorless needles from *n*-hexane–AcOEt, mp 205.5—208°. UV λ_{max}^{EtOH} nm (log ε): 230 (4.16), 254 (3.71), 263 (sh 3.66), 300 (3.73), 347 (4.11). IR ν_{max}^{KBr} cm^{-1}: 3320, 1700, 1622, 1603, 1563, 1505. *Anal.* Calcd for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.79; H, 4.32. ^{1}H-NMR (δ in acetone-d_6): 3.90 (3H, s, 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)[9]——Colorless needles from ether–pet.ether, mp 179—180.5°. UV λ_{max}^{EtOH} nm (log ε): 231 (4.26), 253 (3.81), 263 (sh 3.69), 288 (sh 3.72), 297 (3.78), 346 (4.10). IR ν_{max}^{KBr} cm^{-1}: 1720, 1713, 1610, 1561, 1511. *Anal.* Calcd for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 69.45; H, 6.26. ^{1}H-NMR (δ in $CDCl_3$): 1.78 (6H, br s, $(C\underline{H}_3)_2C=CH-$), 3.90 (3H, s, OCH_3), 4.68 (2H, d, $J=7$ Hz, $OC\underline{H}_2-CH=$), 5.52 (1H, t-like, $J=7$ Hz, $-CH_2-C\underline{H}=\dot{C}-$), 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).

Acknowledgement The authors wish to express their gratitude to the following researchers for providing authentic specimens: Prof. R.D.H. Murray, University of Glasgow[7-O-(3,3-dimethylallyl)scopoletin], Dr. S.K. Banerjee, Regional Research Laboratory in India (8-geranyloxypsoralen), Prof. Y. Saiki, Kobe Gakuin University (alloisoimperatorin and phellopterin), Prof. K. Hata, Osaka College of Pharmacy (marmesin), Assoc. Prof. H. Ishii, Chiba University (marmesin and spectral charts of osthenol) and Assoc. Prof. Y. Kano, Hokkaido Institute of Pharmaceutical Sciences (scopoletin). They are also grateful for the provision of spectral charts by Prof. F. Bohlmann, Technischen Universität Berlin (bergaptin) and Prof. A.G. Gonzalez, University of La Laguna [8-(1,1-dimethylallyl)-5-hydroxypsoralen]. Thanks are due to Mr. Y. Shida, Tokyo College of Pharmacy, for measurements of mass spectra.