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Chemical Studies on the Constituents of the Chinese Crude Drug "Quiang Huo"[1)]

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The Chinese crude drug "Quiang Huo" (Umbelliferae) afforded three new coumarins, notopterol (**7**), notoptol (**8**) and anhydronotoptol (**9**) together with isoimperatorin (**1**), bergapten (**2**), bergaptol (**3**), nodakenin (**4**), osthenol (**5**), demethylfuropinnarin (**6**), *p*-hydroxyphenethyl anisate (**10**), phenethyl ferulate (**11**) and farcarindiol (**12**). The structures of **7**—**9** were established as *dl*-5[(2*E*)-5-hydroxy-3,7-dimethyl-2,6-octadienyloxy]psoralen, 5-[(2*E*,5*E*)-7-hydroxy-3,7-dimethyl-2,5-octadienyloxy]psoralen and 5-[(2*E*,5*E*)-3,7-dimethyl-2,5,7-octatrienyloxy]psoralen, respectively.

Keywords——*Notopterygium* sp.; coumarin; notopterol; notoptol; anhydronotoptol; farcarindiol; phenethyl ferulate; *p*-hydroxyphenethyl anisate

The Chinese crude drug "Quiang Huo" (Japanese name; Tou-Kyoukatsu) (Umbelliferae) has been used as a diaphoretic, an antifebrile and an anodyne; the plants of origin are *Notopterygium incisum* TING., *N. forbesii* BOISS and *N. franchetii* BOISS in China.[2)] As regards the constituents of this drug, Kohda *et al.* have reported the isolation of *p*-hydroxyphenethyl anisate and the presence of furocoumarins.[3)]

In the course of our studies on the constituents of Umbelliferous plants, the authors investigated this drug (purchased in Osaka market). Tou-Kyoukatsu was treated as described in the experimental section, and six coumarins (**1**—**6**), two aromatic esters (**10**, **11**) and a polyacetylene compound (**12**) as well as three new coumarins, notopterol (**7**), notoptol (**8**) and anhydronotoptol (**9**), were isolated. Of these compounds, **1**—**4** were identified as isoimperatorin (**1**), bergapten (**2**), bergaptol (**3**) and nodakenin (**4**) by direct comparison with authentic samples.

Compound **5** was identified as osthenol on the basis of ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectral analysis and the formation of osthol on methylation. Compound **6** was identified as demethylfuropinnarin on the basis of ultraviolet (UV) and ^{1}H-NMR spectral analysis and the formation of furopinnarin[4)] on methylation. Compounds **10** and **11** were identified as *p*-hydroxyphenethyl anisate and phenethyl ferulate,[5)] respectively, by analysis of ^{1}H-NMR spectra and from the facts that on alkaline hydrolysis the former gave *p*-hydroxyphenethyl alcohol and anisic acid, and the latter gave phenethyl alcohol and ferulic acid. Compound **12** was characterized as farcarindiol by analysis of the UV, ^{1}H-NMR and ^{13}C-NMR spectra of **12** and **12**-diacetate.[6)]

Compound **7**, colorless needles, mp 90—92 °C, $C_{21}H_{22}O_5$. The infrared (IR) spectrum of **7** indicated the presence of a hydroxyl group, a furan ring and a coumarin ring. The UV spectrum of **7** showed absorption maxima at 223.0, 250.5, 259.0, 268.0 and 309.5 nm. The ^{1}H-NMR spectrum of **7** exhibited signals arising from α and β protons of the furan ring at δ 7.59 (1H, d, J=2.5 Hz) and 6.96 (1H, dd, J=2.5 and 1.0 Hz), a signal assignable to an aromatic proton at δ 7.14 (1H, m), and signals due to the protons of the 3 and 4 positions of the couma-

rin ring at δ 6.26 (1H, d, J=9.5 Hz) and 8.15 (1H, dd, J=9.5 and 0.7 Hz). Furthermore, the ^{1}H-NMR spectrum showed a signal due to a hydroxyl group at δ 1.52 (1H, br s), signals arising from the protons of three olefinic methyl groups at δ 1.76 (3H, d, J=1.3 Hz), 1.73 (3H, d, J=1.3 Hz) and 1.69 (3H, d, J=1.3 Hz), signals assignable to O–CH_2–CH=C– at δ 4.98 (2H, d, J=7.0 Hz), 5.64 (1H, m, J=7.0 and 1.3 Hz) and signals due to =C–CH_2–CH(O)–CH=C– at δ 5.18 (1H, m, J=8.5 and 1.3 Hz), 4.52 (1H, m, J=8.5, 8.0 and 5.5 Hz), 2.32 (1H, dd, J=14.0 and 8.0 Hz), 2.21 (1H, dd, J=14.0 and 5.5 Hz). These spectral data indicated that **7** is mono-substituted furocoumarin of linear type, and it was considered that the side chain was linked by an ether bond to the C-5 position of the coumarin ring from the observations that in the ^{1}H-NMR spectrum of **7** the signal arising from the proton of the C-4 position of the coumarin ring was shifted to lower field. Catalystic hydrogenation of **7** with Adams catalyst in ethyl alcohol readily gave bergaptol (**3**). The methylation of **7** with CH_3I and Ag_2O gave a monomethyl ether (**13**), and the acetylation of **7** with acetic anhydride and pyridine gave a monoacetate (**14**). The ^{1}H-NMR spectrum of **14** exhibited a signal due to a methine proton at δ 5.67 (1H, m, J=9.0, 8.0 and 6.0 Hz), which was shifted to lower field, in contrast to that of **7** at δ 4.52 (1H, m, J=8.5, 8.0 and 5.5 Hz). On oxidation with CrO_3-pyridine complex, **7** gave a ketone (**15**), mp 94.5 °C, $C_{21}H_{20}O_5$. The ^{1}H-NMR spectrum of **15** showed signals arising from =C–CH_2–CO–CH=C=$(CH_3)_2$ at δ 6.06 (1H, m, J=1.3 Hz), 3.16 (2H, s), 2.15 (3H, d, J=1.3 Hz), 1.88 (3H, d, J=1.3 Hz), in addition to signals due to the 5-alkoxyfurocoumarin ring and signals arising from O–CH_2–CH=C–CH_3. From the above results, compound **7** was indicated to be a linear-type furocoumarin bearing a 5-hydroxy-3,7-dimethyl-2,6-octadienoxyl group at the C-5 position. Determination of the geometric configuration on the side chain of **7** was accomplished on the basis of ^{13}C-NMR spectral analysis, that is, three methyl carbons were observed at δ 25.49 (q), 18.00 (q) and 16.86 (q), and it appeared that two of them were shifted to higher field by γ-effect. Consequently, the geometric configuration at the side chain of **7** was concluded to be *E*. In addition, compound **7** was optically inactive. From the above evidence, the structure of **7** was established as *dl*-5[(2*E*)-5-hydroxy-3,7-dimethyl-2,6-octadienyloxy]psoralen.

Compound **8**, colorless needles, mp 73 °C, $C_{21}H_{22}O_5$. The IR spectrum of **8** showed the presence of a hydroxyl group, a furan ring and a coumarin ring. The UV spectrum of **8** showed absorption maxima at 221.5, 250.5, 259.0, 268.0 and 309.5 nm. These spectral data indicated that **8** was also a linear-type furocoumarin. The ^{1}H-NMR spectrum of **8** exhibited signals assignable to protons of the α and β positions of the furan ring at δ 7.59 (1H, d, J=2.5 Hz) and 6.94 (1H, dd, J=2.5 and 1.0 Hz), a signal due to a benzene proton at δ 7.14 (1H, m), signals due to protons of the C-3 and C-4 positions of the coumarin ring at δ 6.27 (1H, d, J=9.5 Hz) and 8.14 (1H, dd, J=9.5 and 0.7 Hz), a signal assignable to a hydroxyl group at δ 1.47 (1H, s) and signals due to olefinic methyl protons at δ 1.67 (3H, s) and gem-dimethyl protons at δ 1.32 (6H, s). Further, signals arising from O–CH_2–CH=C– at δ 4.94 (2H, d, J=7.0 Hz), 5.56 (1H, m, J=7.0 and 1.3 Hz) and signals assignable to =C–CH_2–CH=CH–C– at δ 2.76 (2H, d, J=6.0 Hz), 5.65 (1H, d, J=16.0 Hz), 5.58 (1H, m, J=16.0 and 6.0 Hz) were observed. Catalytic hydrogenation of **8** gave bergaptol as in the case of **7**. The methylation of **8** with CH_3I and Ag_2O afforded a monomethyl ether (**16**). On acetylation with acetic anhydride and pyridine, **8** did not give an acetate corresponding to that of **7**, but on acetylation with acetic anhydride and sodium acetate under reflux, **8** gave **14** (a monoacetate of **7**) with difficulty. Thus, it was considered that during the latter acetylation **8** isomerized to **7**, and was then acetylated. In the above reaction, **8** also gave a dehydrated compound which was identical with **9** directly obtained from the same crude drug. The ^{1}H-NMR spectrum of **9** exhibited signals due to O–CH_2–CH=C– at δ 4.96 (2H, d, J=7.5 Hz) and 5.60 (1H, br t, J=7.5 Hz) and signals assignable to =C–CH_2–CH=CH–C(CH_3)=CH_2 at δ 2.88 (2H, br d, J=

7.5 Hz), 6.19 (1H, br d, $J=15.0$ Hz), 5.60 (1H, dt, $J=15.0$ and 7.5 Hz), 4.93 (2H, br s), and 1.87 (3H, br s). From these spectral data, it was considered that the dehydration occurred at the terminal point of the side chain. Consequently, it became clear that compound **8** is a furocoumarin bearing a 7-hydroxy-3,7-dimethyl-2,5-octadienoxyl group at the C-5 position of the coumarin ring. On the other hand, compound **9** is a furocoumarin bearing a 3,7-dimethyl-2,5,7-octatrienoxyl group at the C-5 position.

The geometric configurations at the side chain of **8** and **9** were concluded to be 2*E* and 5*E* since in the ^{1}H-NMR spectra of **8** and **9** the coupling constant between the olefinic protons at the **5** and **6** positions of the side chain was 15.0 Hz, while in the ^{13}C-NMR spectrum of **8** a signal due to olefinic methyl carbon was observed at δ 16.70 (q).

From the above evidence, the structures of **8** and **9** were established as 5-[(2*E*,5*E*)-7-hydroxy-3,7-dimethyl-2,5-octadienyloxy]psoralen and 5-[(2*E*,5*E*)-3,7-dimethyl-2,5,7-octatrienyloxy]psoralen, respectively.

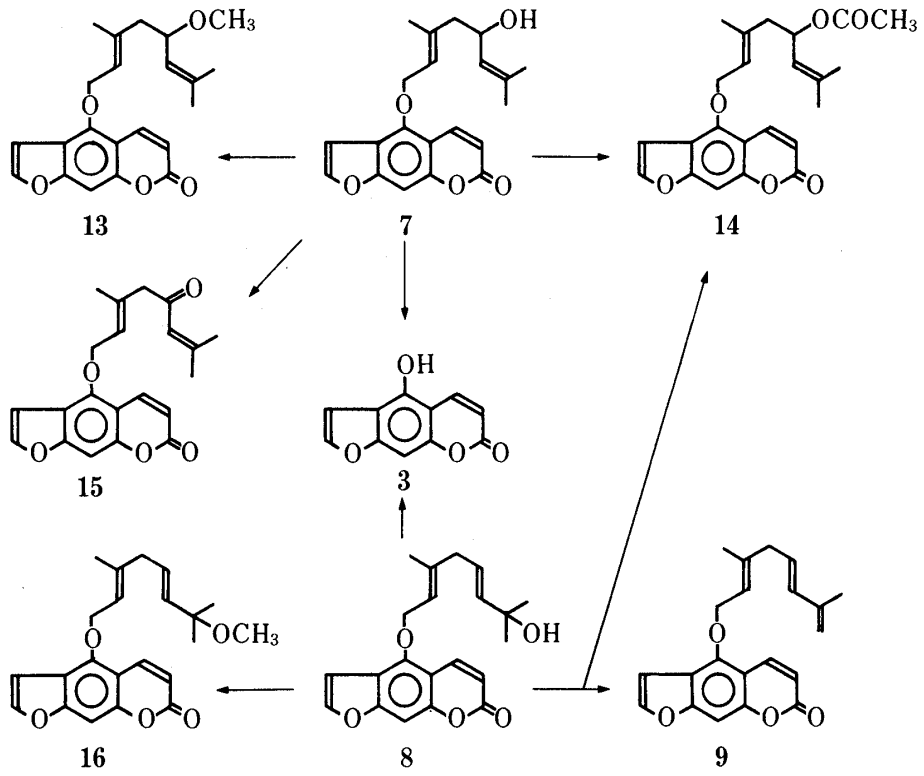

Chart 1

Experimental

All melting points were measured on a Büchi melting point apparatus and are uncorrected. The UV spectra were recorded with a Shimadzu UV-200S spectrometer, IR spectra with a Hitachi EPI-G2 spectrometer, and optical rotatory dispersion (ORD) spectra with a JASCO ORD/UV-5 spectrometer. The ^{1}H-NMR spectra were taken with Hitachi R-40 (90 MHz) and Nihondenshi JEOL FX-200 (200 MHz) spectrometers with tetramethylsilane as an internal standard, and ^{13}C-NMR spectra with a Nihondenshi JEOL FX-100 (25 MHz) spectrometer. For column chromatography on silica gel, we used Merck silica gel 60 (70—230 mesh). For thin-layer chromatography (TLC) and preparative TLC, Merck plate Silica gel 60 F_{254} (0.25 mm) and Merck plate Silica gel 60 F_{254S} (concentrating zone, 2 mm) were employed and the developed spots were detected under a UV lamp (253.7 and 365 nm).

Isolation of the Compounds——The dried and crushed crude drug (9 kg), Tou-kyoukatsu, obtained from Osaka market was extracted 3 times by refluxing with hexane (20 l) and with ethyl acetate (20 l) for 5 h (for each extraction). Each solution was concentrated under reduced pressure to give the corresponding extract: hexane extract (849 g) and ethyl acetate extract (818 g). The hexane extract was further treated with petr. ether at room temperature and divided into soluble (598 g) and insoluble (220 g) portions. The insoluble portion (220 g) was chromatographed on silica gel

(2.1 kg) with a hexane–EtOAc solvent system [hexane→hexane–EtOAc (1 : 4)] to afford isoimperatorin (**1**) (9.93 g), bergaptol (**3**) (790 mg), demethylfuropinnarin (**6**) (1.91 g), notopterol (**7**) (1.95 g), notoptol (**8**) (2.96 g), *p*-hydroxyphenethyl anisate (**10**) (715 mg), phenethyl ferulate (**11**) (3.65 g) and farcarindiol (**12**) (25.5 g). The ethyl acetate extract (818 g) was chromatographed on silica gel (5.5 kg) with a hexane–EtOAc solvent system [hexane–EtOAc (20 : 1→1 : 4)] to give **1** (5.24 g), bergapten (**2**) (70 mg), **3** (70 mg), nodakenin (**4**) (5.13 g), osthenol (**5**) (94 mg), **6** (78 mg), **7** (6.1 g), **8** (9.1 g), anhydronotoptol (**9**) (164 mg), **10** (6.2 g), **11** (7.5 g) and **12** (7.5 g).

Osthenol (5)——Recrystallized from hexane–EtOAc to give colorless needles, mp 130—130.5 °C. IR ν_{max}^{Nujol} cm^{-1}: 3360 (OH), 1705 (CO), 1605, 1575, 1560 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 7.65 (1H, d, J=9.5 Hz), 7.29 (1H, s), 7.20 (1H, d, J=8.5 Hz), 6.86 (1H, d, J=8.5 Hz), 6.22 (1H, d, J=9.5 Hz), 5.27 (1H, t, J=8.0 Hz), 3.60 (2H, d, J=8.0 Hz), 1.87, 1.73 (each 3H, s). *Anal.* Calcd for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 72.78; H, 6.14.

Methylation of 5——**5** (40 mg) was methylated with CH_2N_2–Et_2O in the usual way. The reaction product was subjected to TLC on silica gel with hexane–EtOAc (3 : 1), and a spot corresponding to osthol was detected under the UV lamp (Rf=0.19).

Demethylfuropinnarin (6)——Recrystallized from EtOAc to give pale yellow needles, mp 231 °C. UV λ_{max}^{MeOH} nm (log ε): 224.5 (4.43), 246.0 (4.11), 251.5 (4.13), 273.5 (4.31), 314.5 (4.09). IR ν_{max}^{Nujol} cm^{-1}: 3150 (OH), 1690 (CO), 1615, 1580 (arom.). ^{1}H-NMR ($CDCl_3$ + DMSO-d_6) δ: 10.00 (1H, br s), 8.27 (1H, d, J=9.5 Hz), 7.52 (1H, d, J=2.5 Hz), 7.16 (1H, d, J=2.5 Hz), 6.39 (1H, dd, J=18.0 and 10.5 Hz), 6.16 (1H, d, J=9.5 Hz), 4.98 (1H, d, J=18.0 Hz), 4.94 (1H, d, J=10.5 Hz), 1.78 (6H, s). *Anal.* Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.05; H, 5.09.

Methylation of 6——A solution of **6** (220 mg) in MeOH (2 ml) was added to CH_2N_2–Et_2O and the mixture was treated in the usual way. The reaction mixture was evaporated to dryness and the residue was recrystallized from hexane–EtOAc to afford a monomethyl ether (50 mg), mp 131—132 °C, whose spectral data coincided with those of an authentic sample of furopinnarin.

***p*-Hydroxyphenethyl Anisate (10)**——Recrystallized from hexane–EtOAc to give colorless needles, mp 129—129.5 °C. UV λ_{max}^{MeOH} nm (log ε): 204.5 (4.35), 208.0 (4.35), 224.5 (4.04), 256.5 (4.33). IR ν_{max}^{Nujol} cm^{-1}: 3435 (OH), 1680 (CO), 1600, 1505 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 7.92 (2H, d, J=8.5 Hz), 7.12 (2H, d, J=8.5 Hz), 6.89 (2H, d, J=8.5 Hz), 6.79 (2H, d, J=8.5 Hz), 5.85 (1H, br s), 4.46 (2H, t, J=7.0 Hz), 3.84 (3H, s), 3.00 (2H, t, J=7.0 Hz). *Anal.* Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.41; H, 6.05.

Alkaline Hydrolysis of 10——A solution of **10** (2 g) in 5% EtOH–NaOH (50 ml) was heated on a boiling water bath for 10 min. The mixture was cooled, diluted with water (50 ml) and then acidified with 20% H_2SO_4. The solution was extracted with Et_2O. The extract was separated into neutral and acidic portions in the usual way. The neutral portion was purified by chromatography on silica gel with hexane–EtOAc (3 : 1) to give colorless needles (670 mg), mp 91 °C, whose spectral data coincided with those of an authentic sample of *p*-hydroxyphenethyl alcohol. The acidic portion was purified by chromatography on silica gel with hexane–EtOAc (3 : 1) to afford colorless needles (716 mg), mp 183 °C, whose spectral data coincided with those of an authentic sample of anisic acid.

Phenethyl Ferulate (11)——Colorless viscid oil. UV λ_{max}^{MeOH} nm (log ε): 210.5 (4.14), 235.5 (3.98), 296.5 (4.04), 325.5 (4.20). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3545 (OH), 1710 (CO), 1635 (C=C), 1610, 1605, 1520 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 7.62 (1H, d, J=16.0 Hz), 7.27 (5H, br s), 7.04 (1H, dd, J=8.5 and 2.5 Hz), 7.01 (1H, d, J=2.5 Hz), 6.90 (1H, d, J=8.5 Hz), 6.31 (1H, s), 6.28 (1H, d, J=16.0 Hz), 4.43 (2H, t, J=7.0 Hz), 3.85 (3H, s), 3.02 (2H, t, J=7.0 Hz). *Anal.* Calcd for $C_{18}H_{18}O_4$: C, 72.46; H, 6.08. Found: C, 72.55; H, 6.11.

Alkaline Hydrolysis of 11——A solution of **11** (2 g) in 5% EtOH–NaOH (50 ml) was heated on a boiling water bath for 10 min. The mixture was diluted with water (50 ml) and then acidified with 20% H_2SO_4. The solution was extracted with Et_2O. The extract was separated into the neutral and acidic portions in the usual way. The neutral portion was purified by chromatography on silica gel with hexane–EtOAc (3 : 1) to afford a colorless viscid oil (530 mg), whose spectral data coincided with those of an authentic sample of phenethyl alcohol. The acidic portion was recrystallized from hexane–EtOAc to give colorless needles (488 mg), mp 168—170 °C, which were identical with an authentic sample of ferulic acid.

Farcarindiol (12)——Colorless viscid oil. UV λ_{max}^{MeOH} nm (log ε): 232.0 (3.24), 245.0 (3.22), 257.5 (3.08), 266.0 (2.89). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3595, 3365 (OH), 2250, 2150 (C≡C), 1650 (C=C). ^{1}H-NMR ($CDCl_3$) δ: 5.93 (1H, m, J=17.0, 10.0 and 5.5 Hz), 5.60 (1H, m, J=11.0 and 7.5 Hz), 5.50 (1H, dd, J=11.0 and 7.5 Hz), 5.45 (1H, d, J=17.0 Hz), 5.23 (1H, d, J=10.0 Hz), 5.19 (1H, d, J=7.5 Hz), 4.92 (1H, d, J=5.5 Hz), 3.00 (2H, br s), 2.11 (2H, m, J=7.5 Hz), 1.29 (10H, br s), 0.88 (3H, t, J=6.5 Hz). ^{13}C-NMR ($CDCl_3$) δ: 135.94 (d), 134.51 (d), 127.79 (d), 117.24 (t), 79.97 (s), 78.44 (s), 70.29 (s), 68.76 (s), 63.41 (d), 58.57 (d), 31.83 (t), 29.35 (t), 29.20 (t), 29.16 (t), 27.72 (t), 22.66 (t), 14.10 (q).

Acetylation of 12——A solution of **12** (1 g) in a mixture of Ac_2O (5 ml) and pyridine (5 ml) was allowed to stand at room temperature for 36 h. The reaction mixture was treated in the usual way, the product was extracted with ether, and the extract was washed with water, dried and concentrated to dryness. The residue was purified by chromatography on silica gel with hexane–EtOAc (5 : 1) to give the diacetate (892 mg), colorless viscid oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2160 (C≡C), 1740 (CO), 1645 (C=C). *Anal.* Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found: C, 73.14; H, 8.04.

Notopterol (7)——Recrystallized from hexane–EtOAc to give colorless needles, mp 90—92 °C. UV λ_{max}^{MeOH} nm (log ε): 223.0 (4.36), 250.5 (4.22), 259.0 (4.17), 268.0 (4.17), 309.5 (4.12). IR ν_{max}^{Nujol} cm^{-1}: 3540 (OH), 3140 (furan), 1725

(CO), 1625, 1605, 1580, 1550 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 8.15 (1H, dd, J=9.5 and 0.7 Hz), 7.59 (1H, d, J=2.5 Hz), 7.14 (1H, m), 6.96 (1H, dd, J=2.5 and 1.0 Hz), 6.26 (1H, d, J=9.5 Hz), 5.64 (1H, m, J=7.0 and 1.3 Hz), 5.18 (1H, m, J=8.5 and 1.3 Hz), 4.98 (2H, d, J=7.0 Hz), 4.52 (1H, m, J=8.5, 8.0 and 5.5 Hz), 2.32 (1H, dd, J=14.0 and 8.0 Hz), 2.21 (1H, dd, J=14.0 and 5.5 Hz), 1.76 (3H, d, J=1.3 Hz), 1.73 (3H, d, J=1.3 Hz), 1.69 (3H, d, J=1.3 Hz), 1.52 (1H, br s). ^{13}C-NMR ($CDCl_3$) δ: 160.98 (s), 157.85 (s), 152.32 (s), 148.58 (s), 144.72 (d), 139.28 (s), 139.28 (d), 134.89 (s), 127.34 (d), 121.73 (d), 113.65 (s), 112.16 (d), 106.95 (s), 104.82 (d), 93.76 (d), 69.22 (t), 66.24 (d), 47.49 (t), 25.49 (q), 18.00 (q), 16.86 (q). *Anal.* Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.15; H, 6.19.

Catalytic Hydrogenation of 7——A solution of **7** (200 mg) in EtOH (10 ml) was added to prereduced Adams catalyst (PtO_2: 100 mg) in EtOH (50 ml), and the mixture was stirred in the presence of hydrogen until consumption of hydrogen ceased (26 ml). The catalyst was filtered off and the filtrate was evaporated to dryness. The residue was purified by chromatography on silica gel with $CHCl_3$–MeOH (50 : 1) to give a colorless crystalline powder (51.8 mg), mp 275—279 °C, which was identical with an authentic sample fo bergaptol (**3**).

Methylation of 7——A solution of **7** (103 mg) in $CHCl_3$ (1 ml) was added to a mixture of Ag_2O (4 g) and CH_3I (4 ml). The mixture was refluxed on a boiling water bath for 1 h, and Ag_2O was removed by filtration. The filtrate was concentrated to dryness and the residue was purified by chromatography on silica gel with $CHCl_3$ to afford a monomethyl ether (**13**) (74 mg), colorless crystalline powder, mp 50—51 °C. UV λ_{max}^{MeOH} nm (log ε): 222.0 (4.25), 250.5 (4.12), 258.0 (4.07), 267.5 (4.06), 310.0 (4.02). IR ν_{max}^{Nujol} cm^{-1}: 3110 (furan), 1720 (CO), 1620, 1605, 1575 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 8.16 (1H, d, J=9.5 Hz), 7.60 (1H, d, J=2.5 Hz), 7.13 (1H, s), 6.97 (1H, d, J=2.5 Hz), 6.25 (1H, d, J=9.5 Hz), 5.59 (1H, t, J=6.0 Hz), 5.03 (1H, d, J=7.5 Hz), 4.96 (2H, d, J=6.0 Hz), 4.04 (1H, m), 3.23 (3H, s), 2.41 (1H, dd, J=14.0 and 7.0 Hz), 2.16 (1H, dd, J=14.0 and 7.0 Hz), 1.76 (6H, s), 1.70 (3H, s).

Acetylation of 7——A solution of **7** (200 mg) in a mixture of Ac_2O (5 ml) and pyridine (5 ml) was allowed to stand at room temperature overnight. The reaction mixture was treated in the usual way, and the product was recrystallized from hexane–EtOAc to give a monoacetate (**14**) (162 mg), colorless needles, mp 113—114 °C. ^{1}H-NMR ($CDCl_3$) δ: 8.16 (1H, d, J=9.5 Hz), 7.59 (1H, d, J=2.5 Hz), 7.14 (1H, s), 6.93 (1H, dd, J=2.5 and 1.0 Hz), 6.26 (1H, d, J=9.5 Hz), 5.67 (1H, m, J=9.0, 8.0 and 6.0 Hz), 5.57 (1H, m, J=7.0 and 1.0 Hz), 5.10 (1H, m, J=9.0 Hz), 4.93 (2H, d, J=7.0 Hz), 2.42 (1H, dd, J=13.5 and 8.0 Hz), 2.22 (1H, dd, J=13.5 and 6.0 Hz), 1.99 (3H, s), 1.75 (3H, s), 1.72 (6H, d, J=1.3 Hz).

Oxidation of 7 with CrO_3–Pyridine Complex——A solution of **7** (200 mg) in dry pyridine (2.5 ml) was added dropwise with stirring to CrO_3–pyridine complex which had been prepared from dry pyridine (3 ml) and CrO_3 (300 mg) under ice cooling. The mixture was allowed to stand at room temperature for 2.5 h, then diluted with ice water (250 ml), acidified with 15% H_2SO_4 and extracted with Et_2O. The extract was dried and evaporated to dryness. The residue was recrystallized from hexane–EtOAc to afford **15** (89 mg), colorless needles, mp 94.5 °C. IR ν_{max}^{Nujol} cm^{-1}: 3080 (furan), 1730, 1690 (CO), 1625, 1610, 1580 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 8.15 (1H, d, J=9.5 Hz), 7.59 (1H, d, J=2.5 Hz), 7.14 (1H, m), 6.94 (1H, dd, J=2.5 and 1.0 Hz), 6.26 (1H, d, J=9.5 Hz), 6.06 (1H, m, J=1.3 Hz), 5.62 (1H, m, J=7.0 and 1.3 Hz), 4.99 (2H, d, J=7.0 Hz), 3.16 (2H, s), 2.15 (3H, d, J=1.3 Hz), 1.88 (3H, d, J=1.3 Hz), 1.74 (3H, m).

Notoptol (8)——Recrystallized from hexane–EtOAc to give colorless needles, mp 73 °C. UV λ_{max}^{MeOH} nm (log ε): 221.5 (4.42), 250.5 (4.30), 259.0 (4.24), 268.0 (4.22), 309.5 (4.18). IR ν_{max}^{Nujol} cm^{-1}: 3480 (OH), 3125 (furan), 1720 (CO), 1620, 1605, 1580, 1540 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 8.14 (1H, dd, J=9.5 and 0.7 Hz), 7.59 (1H, d, J=2.5 Hz), 7.14 (1H, m), 6.94 (1H, dd, J=2.5 and 1.0 Hz), 6.27 (1H, d, J=9.5 Hz), 5.65 (1H, d, J=16.0 Hz), 5.58 (1H, m, J=16.0 and 6.0 Hz), 5.56 (1H, m, J=7.0 and 1.3 Hz), 4.94 (2H, d, J=7.0 Hz), 2.76 (2H, d, J=6.0 Hz), 1.67 (3H, s), 1.47 (1H, s), 1.32 (6H, s). ^{13}C-NMR ($CDCl_3$) δ: 161.12 (s), 158.08 (s), 152.65 (s), 148.91 (s), 144.94 (d), 141.67 (s), 140.68 (d), 139.45 (d), 123.63 (d), 119.72 (d), 114.28 (s), 112.59 (d), 107.57 (s), 105.00 (d), 94.20 (d), 70.54 (s), 69.79 (t), 42.10 (t), 29.90 (q), 29.90 (q), 16.70 (q). *Anal.* Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.06; H, 6.48.

Catalytic Hydrogenation of 8——A solution of **8** (200 mg) in EtOH (10 ml) was added to prereduced Adams catalyst (PtO_2: 100 mg) in EtOH (50 ml), and the mixture was treated in the same way as described for **7**. The product was purified by chromatography on silica gel with $CHCl_3$–MeOH (50 : 1) to give **3** (57.0 mg).

Methylation of 8——A solution of **8** (100 mg) in $CHCl_3$ (1 ml) was added to a mixture of Ag_2O (4 g) and CH_3I (3 ml). The mixture was refluxed on a boiling water bath for 1 h, and Ag_2O was removed by filtration. The filtrate was concentrated to dryness and the residue was purified by chromatography on silica gel with $CHCl_3$ to afford a monomethyl ether (**16**) (67 mg), colorless viscid oil. UV λ_{max}^{MeOH} nm (log ε): 207.0 (4.43), 222.0 (4.43), 250.5 (4.30), 259.0 (4.24), 267.0 (4.22), 309.0 (4.17). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (CO), 1625, 1610, 1575 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 8.13 (1H, d, J=9.5 Hz), 7.59 (1H, d, J=2.5 Hz), 7.13 (1H, s), 6.95 (1H, d, J=2.5 Hz), 6.25 (1H, d, J=9.5 Hz), 5.55 (3H, m), 4.96 (2H, d, J=6.5 Hz), 3.16 (3H, s), 2.83 (2H, d, J=3.0 Hz), 1.71 (3H, s), 1.27 (6H, s).

Acetylation of 8——A solution of **8** (100 mg) in a mixture of Ac_2O (10 ml) and NaOAc (200 mg) was refluxed for 1 h. The mixture was treated in the usual way, and the product was purified by chromatography on silica gel with hexane–EtOAc (4 : 1) to give two compounds **9** (17 mg) and **14** (35 mg).

Anhydronotoptol (9)——Colorless viscid oil. UV λ_{max}^{MeOH} nm (log ε): 225.0 (4.74), 248.0 (4.41), 258.0 (4.32), 268.0 (4.29), 307.5 (4.25). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO), 1625, 1610, 1580 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 8.17 (1H, d, J=9.5 Hz), 7.61 (1H, d, J=2.5 Hz), 7.16 (1H, s), 6.96 (1H, d, J=2.5 Hz), 6.27 (1H, d, J=9.5 Hz), 6.19 (1H, br d, J=

15.0 Hz), 5.60 (1H, dt, $J=15.0$ and 7.5 Hz), 5.60 (1H, br t, $J=7.5$ Hz), 4.96 (2H, d, $J=7.5$ Hz), 4.93 (2H, br s), 2.88 (2H, br d, $J=7.5$ Hz), 1.87 (3H, br s), 1.73 (3H, s).

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References and Notes

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