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The Chemical Components of *Artemisia apiacea* HANCE. II.[1] More Coumarins from the Flower Heads

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A new coumarin, 7-isopentenyloxy-8-methoxycoumarin, was isolated together with 7-hydroxy-8-methoxycoumarin and daphnetin from the flower heads of *Artemisia apiacea* HANCE.

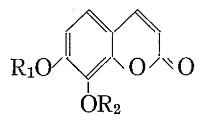
Keywords——*Artemisia apiacea* HANCE; Compositae; coumarins; daphnetin; 7-hydroxy-8-methoxycoumarin; 7-isopentenyloxy-8-methoxycoumarin

Artemisia apiacea HANCE (Compositae) is a winter annual plant growing on waste land or river banks. It is considered that the plant was introduced into Japan from China as a medicinal plant.[3] The volatile constituents, *i.e.* α-pinene, artemisia ketone and others, have been isolated from the roots of the plant by Yano.[4]

We attempted to isolate active substance from *A. apiacea*, because the ethanol extract from the aerial part of the plant showed inhibitory effects on the growth of shoots of *Brassica rapa* L. var. *pervidis* BAILLEY (Japanese name: Komatsuna). In the preceding paper, we reported the isolation of three coumarins, 7,8-dimethoxycoumarin, 7,8-methylendioxycoumarin and 7-methoxycoumarin, as well as phytosterols, from the flower heads.[1] We now report the isolation of three more coumarins (I—III) from the same source.

The concentrated ethanol extract of the flower heads of *A. apiacea* was extracted with *n*-hexane, ether and ethyl acetate successively. Three coumarins (I—III) were obtained from the ethyl acetate extract in addition to the three previously reported coumarins by column chromatography.

I, mp 152°, was obtained as colorless needles, and was found to correspond to $C_{10}H_8O_4$ by elemental analysis (EA) and mass spectroscopy (MS). The ultraviolet (UV) spectrum showed maxima at 258 and 326 nm. The nuclear magnetic resonance (NMR) spectrum taken in chloroform-d_1 showed a methoxy group at δ 4.12, a *cis*-alkene at 6.24 and 7.64, and two adjacent aromatic protons at 6.88 and 7.12 ppm. In benzene-d_6, the resonance of the methoxy proton moved to δ 3.48.[5] These data suggest that I is 7-hydroxy-8-methoxycoumarin. The identity of I was established by direct comparison with an authentic sample.[6]



I: $R_1=H$, $R_2=CH_3$
II: $R_1=(CH_3)_2C=CHCH_2$
$R_2=CH_3$
III: $R_1=R_2=H$

Chart 1

II, mp 101°, was obtained as colorless needles, and was assigned the formula $C_{15}H_{16}O_4$ by EA and MS. The UV spectrum showed maxima at 258 and 322 nm, values similar to those of daphnetin. The NMR spectrum showed signals at δ 3.98 ($-O-C\underline{H}_3$), 1.78 and 1.80

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[2] Location: *1432-1, Horinouchi, Hachioji, Tokyo 192-03, Japan.*

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[4] K. Yano, 13th Symposium on the Chemistry of Terpenes, Essential Oils and Aromatics, Japan, 1969, p. 4.

[5] F.M. Dean, A.M.B.S.R.C.S. Costa, J.B. Harborne, and D.M. Smith, *Phytochemistry*, **17**, 505 (1978).

[6] S.K. Talapatra, S.K. Mukhopadhyay, and B. Talapatra, *Phytochemistry*, **12**, 2312 (1973).

($(C\underline{H}_3)_2C=$), 4.65 ($-O-C\underline{H}_2-CH=$) and 5.48 ($-O-CH_2-C\underline{H}=$), suggesting the presence of a γ,γ-dimethylallyl group and a methoxy group. Based on these data and direct comparison with a synthesized authentic sample, II was identified as 7-isopentenyloxy-8-methoxycoumarin.

III, mp 253°, was obtained as pale tan needles, and was assigned the formula $C_9H_6O_4$ by EA and MS. III was identified as daphnetin by direct comparison with an authentic sample.[7)]

Compound II has not previously been reported as a naturally occurring coumarin, and I and III have been isolated from *A. apiacea* for the first time. Examination of the plant growth inhibitory effects of these three coumarins is in progress.

Experimental

All melting points are uncorrected. NMR spectra were recorded at 100 MHz with TMS as an internal standard. TLC was performed on Kieselgel 60 (Merck) using toluene–ethyl formate–formic acid (5: 4: 1), and *Rf* values in this system were 0.28 (I), 0.4 (II) and 0.23 (III).

Extraction and Isolation——The flower heads of *A. apiacea* were collected at Noda, Chiba Prefecture, in August, 1976. The extraction procedures were described in the preceding paper.[1)] The AcOEt extract was chromatographed on silica gel with the *n*-hexane–AcOEt system, and three coumarins (I—III) were isolated in addition to the coumarins described in the previous paper.[1)]

7-Hydroxy-8-methoxycoumarin (I)——Colorless needles, mp 152° (benzene), *Anal.* Calcd for $C_{10}H_8O_4$: C, 62.20; H, 4.20. Found: C, 62.24; H, 4.17. MS *m/e*: 192 (M^+), 177, 164, 149, 121. UV $\lambda_{max}^{95\%EtOH}$ nm: 250 (s), 258, 326. NMR ($CDCl_3$) δ: 4.12 (3H, s, $OC\underline{H}_3$), 6.24 and 7.64 (each 1H, d, $J=10$ Hz, 3-H and 4-H), 6.88 and 7.12 (each 1H, d, $J=8$ Hz, 5-H and 6-H). The resonance at 4.12 moved to 3.48 in benzene-d_6. The melting point was not depressed on admixture with authentic 7-hydroxy-8-methoxycoumarin samples obtained from *Boeninghausenia albiflora* and by synthesis. The TLC and NMR data were consistent with this structure.

Synthesis of I——Daphnin (100 mg) isolated from the cortex of *Daphne odora* Thunb. was methylated with CH_2N_2, and the methylated daphnin was refluxed in 5% H_2SO_4–MeOH (20 ml) for 2 hr. After removal of MeOH, the reaction mixture was diluted with H_2O (20 ml) and extracted with ether (4 × 30 ml). The ether layer was washed with H_2O, and dried, and the solvent was removed. On recrystallization of the residue from benzene, a coumarin, mp 152° (*ca.* 10 mg), was obtained as needles. Its melting point and NMR, IR and MS spectral data were consistent with the structure 7-hydroxy-8-methoxycoumarin.

7-Isopentenyloxy-8-methoxycoumarin (II)——Colorless needles, mp 101° (EtOH), *Anal.* Calcd for $C_{15}H_{16}O_4$; C, 69.22; H, 6.20. Found: C, 69.22; H, 6.08. MS *m/e*: 260 (M^+), 192 (base peak), 177, 164, 149, 146, 121, 120, 105. UV$\lambda_{max}^{95\%EtOH}$nm: 250 (s), 258, 322. NMR ($CDCl_3$) δ: 1.78 and 1.80 (each 3H, s, $(C\underline{H}_3)_2C=$), 3.98 (3H, s, $C\underline{H}_3O-$), 4.65 (2H, d, $J=6$ Hz, $=CH-C\underline{H}_2-O-$), 5.48 (1H, t, $J=6$ Hz, $=C\underline{H}-CH_2-O-$), 6.22 and 7.58 (each 1H, d, $J=9$ Hz, 3-H and 4-H), 6.82 and 7.12 (each 1H, d, $J=8$ Hz, 5-H and 6-H). The melting point was not depressed on admixture with a synthesized authentic sample, and the TLC and spectral data were identical.

Synthesis of II——I (90 mg), 1-bromo-3-methyl-2-butene (0.1 ml) and K_2CO_3 were dissolved in acetone, (3 ml) and refluxed at 70° for 1 hr. After removal of acetone, the reaction mixture was diluted with H_2O (10 ml), and extracted with ether (7 × 10 ml). The ether layer was washed with H_2O, dried, and the solvent was removed. The residue was crystallized from EtOH (*ca.* 30 mg), mp 101°. *Anal.* Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 69.06; H, 6.15.

Daphnetin (III)——Pale tan needles, mp 253° (dil. EtOH). *Anal.* Calcd for $C_9H_6O_4$: C, 60.68; H, 3.40. Found: C, 60.46; H, 3.54. MS *m/e*: 178 (M^+), 152, 122, 94, 76, 66. UV $\lambda_{max}^{95\%EtOH}$ nm: 265, 330. NMR (CD_3OD) δ: 6.16 and 7.82 (each 1H, d, $J=9$ Hz, 3-H and 4-H), 6.78 and 6.98 (each 1H, d, $J=8$ Hz, 5-H and 6-H). The material was identical with daphnetin on the basis of the mixed fusion test and comparison of the spectral data and TLC with those of synthesized daphnetin.

Synthesis of III[7)]——Pyrogallol (6.5 g) and malic acid (5.3 g) were stirred in H_2SO_4 (12 ml) at 120—130° for 1.5 hr. The mixture was allowed to cool and, after addition of H_2O (40 ml), was extracted with ether (7 × 100 ml). The ether layer was washed with H_2O, dried, and the solvent was removed, leaving a pink solid (*ca.* 3.5 g). Recrystallization from dil. EtOH yielded pale tan needles, mp 254°. *Anal.* Calcd for $C_9H_6O_4$: C, 60.68; H, 3.40. Found: C, 60.46; H, 3.54.

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