NEW COUMARINS FROM CITRUS FUNADOKO[1]

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Abstract ——— From the roots of Citrus funadoko (Rutaceae), five new coumarins named funadonin (1), (Z)-suberenol (2), (Z)-methylsuberenol (3), (E)-methylsuberenol (4) and 6-hydroxymethylherniarin (5) were isolated and structures were elucidated on the basis of spectroscopic data.

On continuing our studies of the constituents of the genus Citrus plants,[2] we have so far isolated many kind of coumarins and acridone alkaloids. We now wish to describe the isolation and structure elucidation of five new coumarins, funadonin (1), (Z)-suberenol (2), (Z)-methylsuberenol (3), (E)-methylsuberenol (4) and 6-hydroxymethylherniarin (5) from the roots of Citrus funadoko Hort. ex. Y. Tanaka. Funadonin (1), oil, $[\alpha]_D$ + 9.43° ($CHCl_3$), $C_{14}H_{14}O_5$, showed typical uv absorption [λ_{max}^{EtOH} nm (log ε): 224 (4.14), 255 (sh, 3.55), 298 (3.78), 329 (4.03)] of 7-oxygenated coumarin.[3] The pmr spectrum showed characteristic doublets at δ 7.66 and 6.27 (each 1H, J= 9.52 Hz), two 1-H singlets at δ 7.61 and 6.80 attributable to the aromatic protons of 6-alkylated 7-oxycoumarin. Also observed, besides one methoxy signal at δ 3.90, were the ABX protons [δ 3.00 (dd, J= 17.82, 2.69 Hz), 2.68 (dd, J= 17.82, 9.28 Hz), 5.40 (br d, J= 9.28 Hz)], one hydroxyl [δ 3.64 (1H, br s)], and one acetyl [δ 2.21 (3H, s)] group. On the basis of these data, the alkyl side chain

at C_6 was presumed as $-CH_2-CH(OH)-COCH_3$ and further confirmed by cmr spectrum [δ 209.21 (s), 64.62 (d), 50.19 (t), 30.63 (q)]. From the above results, the structure of funadonin was established as 1 except for the absolute stereochemistry at C-2'.

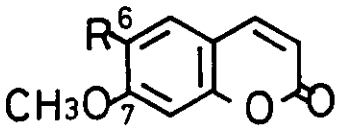
(Z)-Suberenol (2) was isolated as a colorless oil; $C_{15}H_{16}O_4$. The 7-methoxy-6-substituted coumarin skeleton of this compound was suspected by the uv spectrum [λ_{max}^{EtOH} nm (log ε): 225 (4.09), 253 (4.03), 299 (3.80), 334 (3.99)] and pmr spectrum [δ 7.63, 6.25 (each 1H, d, J= 9.28 Hz), 7.46, 6.79 (each 1H, s) and 3.91 (3H, s)]. Remaining pmr signals at δ 1.35 (6H, s), 1.60 (1H, s), 5.85 (1H, d, J= 12.69 Hz) and 6.30 (1H, d, J= 12.69 Hz) suggested the structure of a side chain at C_6 as [$(CH_3)_2C(OH)-CH=CH-$]. These data were very similar to those of suberenol[4] except for J values of olefinic protons and led us to conclude the cis-oriented structure 2.

(Z)-Methylsuberenol (3) was obtained as a colorless oil, $C_{16}H_{18}O_4$, and its uv spectrum [λ_{max}^{EtOH} nm (log ε): 225 (3.84), 257 (sh, 3.70), 299 (3.51), 334 (3.61)] showed a typical absorption due to 7-oxygenated coumarin.[3] The pmr spectrum showed two pairs of AB doublets [δ 7.65, 6.25 (each 1H, J= 9.28 Hz) and 6.48, 5.66 (each 1H, J= 12.69 Hz)] and five singlets [δ 7.60, 6.78 (each 1H), 3.90, 3.05 (each 3H) and 1.29 (6H)]. These data were very resembled to (Z)-suberenol except for the aliphatic methoxy signal at δ 3.05. We concluded the structure 3 for this compound.

(E)-Methylsuberenol (4) was also obtained as a colorless oil, $C_{16}H_{18}O_4$, and its spectral data (see Experimental) were similar to those of the above mentioned (Z)-methylsuberenol. Only the remarkable difference was the coupling constants of olefinic protons [δ 6.77 and 6.20 (each 1H, d, J= 16.6 Hz)] in the pmr spectrum suggesting the trans-orientation. From these results, the structure of (E)-methylsuberenol was confirmed as 4.

6-Hydroxymethylherniarin (5) was obtained as a colorless oil, $C_{11}H_{10}O_4$. This compound was also supposed to have 7-methoxy-6-substituted coumarin skeleton by the uv and pmr spectra [δ 7.64, 6.27 (each 1H, d, J= 9.52 Hz), 7.43, 6.82 (each 1H, s) and 3.93 (3H, s)]. The remaining signals at δ 4.72 (2H, s) and 2.20 (1H, br s) were assigned to a hydroxymethyl moiety. To confirm the structure of this compound, crenulatin (6)[5] was subjected to $NaBH_4$ reduction to give the compound 5 which was identical with the natural sample. From above data, the structure 5 was proposed to this coumarin.

We have the isolated many other new and known coumarins and acridone alkaloids from this plant and these results would be reported elsewhere.



(1) R= $-CH_2-\overset{OH}{CH}-COCH_3$ (1' 2')

(2) R= $-CH=C(H)-C(CH_3)_2-OH$

(3) R= $-CH=C(H)-C(CH_3)_2-OCH_3$

(4) R= $-CH=C(H)-C(CH_3)_2-OCH_3$

(5) R= $-CH_2OH$

(6) R= $-CHO$

EXPERIMENTAL

Extraction and Isolation ——— The roots (1 kg) of Citrus funadoko cultivated at Okitsu Branch, Fruit Tree Research Station, Ministry of Agriculture Foresty and Fisheries, Shimizu, Shizuoka was extracted with acetone. The acetone extract was evaporated under reduced pressure and the residue (104.6 g) was chromatographed over silica gel and eluted with benzene, CH_2Cl_2, benzene-EtOAc, EtOAc, acetone, and MeOH successively. Repeated PTLC using solvent systems acetone:hexane (1:4), acetone:$CHCl_3$ (1:9), and isopropyl ether afforded funadonin (1) (4.6 mg) from EtOAc fraction, (Z)-suberenol (2) (13.0 mg), (Z)-methylsuberenol (3) (4.7 mg), (E)-methylsuberenol (4) (8.1 mg) and 6-hydroxymethylherniarin (5) (17.8 mg) from acetone, MeOH fraction.

Funadonin (1) ——— colorless oil, $[\alpha]_D$ + 9.43° (c= 0.00297, $CHCl_3$), $C_{14}H_{14}O_5$, ms m/z: 262 (M^+), 244, 213, 206, 205 (base peak), 204, 203, 177, 176, 175, ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1720, 1715, 1620, uv λ_{max}^{EtOH} nm (log ε): 224 (4.14), 255 (sh, 3.55), 298 (3.78), 329 (4.03), ^{1}H-nmr ($CDCl_3$) δ: 7.66 (1H, d, J= 9.52 Hz), 7.61 (1H, s), 6.80 (1H, s), 6.27 (1H, d, J= 9.52 Hz), 5.40 (1H, br d, J= 9.28 Hz), 3.90 (3H, s), 3.64 (3H, s), 3.00 (1H, dd, J= 17.82, 2.69 Hz), 2.68 (1H, dd, J= 17.82, 9.28 Hz), 2.21 (3H, s), ^{13}C-nmr ($CDCl_3$) δ: 209.21 (s), 161.06 (s), 158.87 (s), 155.25 (s), 143.54 (d), 128.62 (s), 125.64 (d), 113.50 (d), 112.39 (s), 98.90 (d), 64.62 (d), 56.03 (q), 50.19 (t), 30.63 (q).

(Z)-Suberenol (2) ——— colorless oil, $C_{15}H_{16}O_4$, ms m/z: 260 (M^+), 246, 245, 203, 190, 189 (base peak), 159, 131, ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3570, 1720, 1615, uv λ_{max}^{EtOH} nm (log ε): 225 (4.09), 253 (4.03), 299 (3.80), 334 (3.99), ^{1}H-nmr ($CDCl_3$) δ: 7.63 (1H, d, J= 9.28 Hz), 7.46 (1H, s), 6.79 (1H, s), 6.30 (1H, d, J= 12.69 Hz), 6.25 (1H, d, J= 9.28 Hz), 5.85 (1H, d, J= 12.69 Hz), 3.91 (3H, s), 1.60 (br s, OH), 1.35 (6H, s).

(Z)-Methylsuberenol (3) ——— colorless oil, $C_{16}H_{18}O_4$, ms m/z: 274 (M^+), 260, 259 (base peak), 243, 227, 189, ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720, 1620, uv λ_{max}^{EtOH} nm (log ε): 225 (3.84), 257 (sh, 3.70), 299 (3.51), 334 (3.61), ^{1}H-nmr ($CDCl_3$) δ: 7.65 (1H, d, J= 9.28 Hz), 7.60 (1H, s), 6.78 (1H, s), 6.48 (1H, d, J= 12.69 Hz), 6.25 (1H, d, J= 9.28 Hz),

5.66 (1H, d, J= 12.69 Hz), 3.90 (3H, s), 3.05 (3H, s), 1.29 (6H, s).

(E)-Methylsuberenol (4) ——— colorless oil, $C_{16}H_{18}O_4$, ms m/z: 274 (M^+), 260, 259 (base peak), 243, 227, 189, ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720, 1620, uv λ_{max}^{EtOH} nm (log ε): 258 (4.19), 299 (3.74), 309 (3.74), 342 (3.90), ^{1}H-nmr ($CDCl_3$) δ: 7.64 (1H, d, J= 9.27 Hz), 7.51 (1H, s), 6.80 (1H, s), 6.77 (1H, d, J= 16.6 Hz), 6.27 (1H, d, J= 9.27 Hz), 6.20 (1H, d, J= 16.6 Hz), 3.90 (3H, s), 3.23 (3H, s), 1.39 (6H, s).

6-Hydroxymethylherniarin (5) ——— colorless oil, $C_{11}H_{10}O_4$, ms m/z: 206 (M^+, base peak), 205, 189, 177, ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3420, 1720, 1620, uv λ_{max}^{EtOH} nm (log ε): 224 (4.13), 255 (sh, 3.50), 298 (3.78), 330 (4.05), ^{1}H-nmr ($CDCl_3$) δ: 7.64 (1H, d, J= 9.52 Hz), 7.43 (1H, s), 6.82 (1H, s), 6.27 (1H, d, J= 9.52 Hz), 4.72 (2H, s), 3.93 (3H, s), 2.20 (1H, br s). Crenulatin (6) (5.2 mg) was dissolved in MeOH (10 ml) and treated with $NaBH_4$ (15 mg). The usual work up afforded authentic samples of 5 (yield 4.6 mg) which was identical to the natural sample in ir, ^{1}H-nmr spectra and co-TLC.

REFERENCES AND NOTES

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