XANTHONES FROM HYPERICUM SAMPSONII[1]

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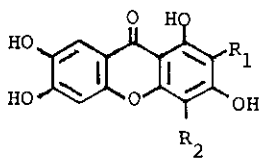
Abstract — Hypericum sampsonii Hance contains mangiferin, isomangiferin, 2-hydroxy-3,4-dimethoxyxanthone, toxyloxanthone B, and a new compound, hyperxanthone, which was identified as 5,9-dihydroxy-3,3-dimethylpyrano-[3,2-a]xanthen-12(3H)-one on the basis of spectroscopic evidences. Characteristic fragment ions in the mass spectrum of pyranoxanthone are discussed.

As a part of our chemical and biological studies on Formosan antitumor folk medicine, we have investigated the whole plant of Hypericum sampsonii Hance (Hypericaceae), known as one of the tumor inhibitory plants in Taiwan.[2] There is no report on the constituents of this plant, though several xanthone derivatives have been isolated from some Hypericum species.[3-10] We now report the isolation and characterization of five xanthone derivatives from this plant. Among the compounds isolated, 5,9-dihydroxy-3,3-dimethylpyrano[3,2-a]xanthen-12(3H)-one (V), named hyperxanthone, has not previously been reported from natural sources.

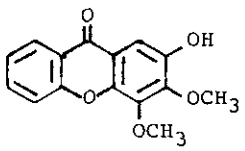
The ethanol extract of the plant material was fractionated on a charcoal column by elution with EtOH, EtOH/$CHCl_3$(7/3), and $CHCl_3$, respectively. The evaporated EtOH fraction was dissolved in least amount of water and was partitioned with EtOAc and n-BuOH, respectively. Two xanthone C-glucosides were isolated from the n-BuOH fraction by chromatography on polyamide and Sephadex LH-20 columns. Compounds I and II are isomers, mangiferin (I) and isomangiferin (II), and were identified on the basis of mass, ^{1}H-nmr, ^{13}C-nmr, and uv utilizing shift reagents.

Three xanthone derivatives, compounds III, IV, and V, were isolated from the EtOH/$CHCl_3$(7/3) fraction by repeated chromatography on silica gel. The least

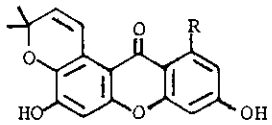


I. R_1 = glucosyl, R_2 = H

II. R_1 = H, R_2 = glucosyl



III.



IV. R = OH

V. R = H

polar compound III, 2-hydroxy-3,4-dimethoxyxanthone, was identified on the basis of mass, ^{1}H-nmr with decoupling at 8.23 ppm (8-H), and uv utilizing shift reagents. All these evidences were compatible with the structure.[11]

Compound IV, toxyloxanthone B, was eluted out next, and was identified on the basis of mass, ^{1}H-nmr, and uv utilizing shift reagents. They were all in accordance with the structure of 5,9,11-trihydroxy-3,3-dimethylpyrano[3,2-a]xanthen-12(3H)-one (IV), toxyloxanthone B.[12,13]

The new compound V, mp 285 °C (dec.), was eluted out last, with the molecular ion peak at m/z 310. The uv spectral pattern of V indicated that it was a xanthone. Inspection of the ^{1}H-nmr and mass spectra of V showed the similarity between the new compound and toxyloxanthone B. The presence of a 2,2-dimethyl-2H-pyran ring attached to the xanthone nucleus in an angular position was clearly shown by the low-field nmr signal at δ 8.17 for 1'-H of the 2H-pyran AB doublets with J=10.2 Hz, due to deshielding by the xanthone carbonyl group in V as well as in toxyloxanthone B.[12] In the mass spectrum of V, the base peak was observed at m/z 295 due to the loss of a methyl radical from the dimethylpyran ring to leave a resonance-stabilized pyrylium cation.[14] Further interpretation of the dominant fragment ions of dimethylpyranoxanthone couldn't be found in literature. Thus, a peak at m/z 267 due to the loss of elements of CO from $(M-CH_3)^+$ ion and a peak at m/z 269 due to the loss of an allyl radical from the molecular ion (Scheme 1), accompanied with their doubly-charged ions[15] (Table 1), were considered as the characteristic fragment ions of dimethylpyranoxanthone.

In comparison with toxyloxanthone B, the absence of an $AlCl_3$-induced shift[16] in

Scheme 1.

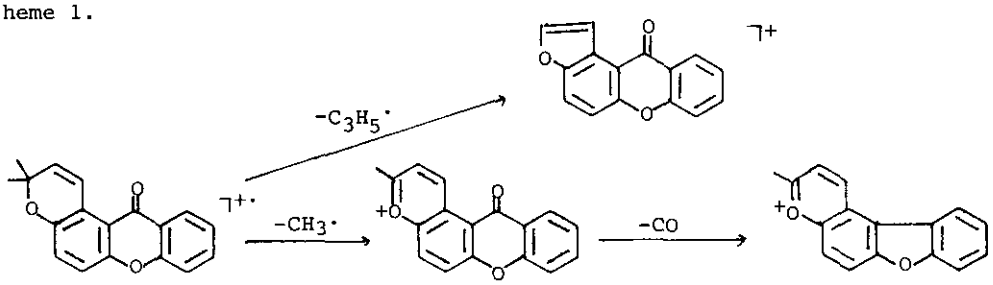


Table 1. Characteristic fragment ions of pyranoxanthone, m/z(%)

Compound	M^+ M^{++}	$(M-CH_3)^+$ $(M-CH_3)^{++}$	$(M-CH_3CO)^+$ $(M-CH_3CO)^{++}$	$(M-C_3H_5)^+$ $(M-C_3H_5)^{++}$
IV	326(42.1)	311 (100.0)	283 (2.2)	285 (8.3)
	163(2.2)	155.5(11.6)	141.5(1.7)	142.5(0.6)
V	310(40.4)	295 (100.0)	267 (2.4)	269 (10.6)
	155(4.3)	147.5(9.5)	133.5(3.1)	134.5(1.2)

the uv spectra of V and the absence of the 1-OH low-field signal in the ^{1}H-nmr spectrum of V indicated the absence of a chelated hydroxyl group. Together with the presence of a low-field aromatic proton resonance at δ 8.06 (d, J=8.8 Hz), assigned to 1-H, due to deshielding by the xanthone carbonyl group[17], 5,9-dihydroxy-3,3-dimethylpyrano[3,2-a]xanthen-12(3H)-one (V), named hyperxanthone, was the structure of the new compound. The resonance of the aromatic protons were in agreement with the calculated values.[18]

It is of interest to note that hyperxanthone (V) is reported for the first time from nature. This is the first report of 2-hydroxy-3,4-dimethoxyxanthone and isomangiferin from Hypericum species. Together with mangiferin and toxyloxanthone B, they are of significance in chemotaxonomy. Besides, the characteristic fragment ions of dimethylpyranoxanthone in the mass spectrum are of considerable analytical interest.

EXPERIMENTAL

Melting points were determined with Yazawa BY-2 and are uncorrected. Ir and uv

spectra were measured on Perkin Elmer 710B spectrophotometer and Hitachi 200 Double Beam UV spectrophotometer respectively. Mass spectra were recorded on JEOL JMS-D100 spectrometer. ^{1}H- and ^{13}C-nmr spectra were reocrded on JEOL JNM-FX100 spectrometer using tetramethylsilane as an internal standard.

Isolation

The dried whole herbs of Hypericum sampsonii Hance (Hypericaceae) (2.5 Kg) collected from herbal store were powdered and extracted repeatedly with hot ethanol. The combined extracts were subjected to charcoal column eluting succesively with EtOH, EtOH/$CHCl_3$(7/3), and $CHCl_3$. The EtOH fraction was evaporated under reduced pressure, and partitioned between water and EtOAc, n-BuOH respectively. The n-BuOH fraction (12 g) was chromatographed on polyamide (H_2O-EtOH) resulting in the isolation of mangiferin (90 mg) from the 10% EtOH eluent. The 20% EtOH eluent was subjected to gel filtration on a Sephadex LH-20 column eluting with 10% EtOH afforded isomangiferin (30 mg). Repeated column chromatography on silica gel of the EtOH/$CHCl_3$(7/3) fraction (25 g) resulted in the isolation of 2-hydroxy-3,4-dimethoxyxanthone (2 mg), toxyloxanthone B (3 mg) and hyperxanthone (2 mg).

Mangiferin (I)

Pale yellow needles (75% EtOH), mp 270°C (dec.); uv λ_{max} nm (log ε): (MeOH) 241 (4.26), 257(4.29), 315(3.98), 365(3.93); (MeOH+NaOMe) 247, 271, 389; (MeOH+NaOAc) 238, 259, 375; (MeOH+$AlCl_3$) 234, 267, 351, 416; (MeOH+$AlCl_3$+HCl) 231, 265, 337, 404; ms m/z(rel. int.): 404(11), 386(14), 368(100), 350(36), 326(10), 300(29), 285(10), 284(14), 273(32); ^{1}H-nmr (DMSO-d_6): δ 13.73(s, 1-OH), 7.36(s, 8-H), 6.85 (s, 4-H), 4.59(d, J=9.9 Jz, 1'-H); ^{13}C-nmr (DMSO-d_6): δ 179.3, 163.9, 161.6, 156.6, 154,0, 151,1, 143.8, 112.1, 108.4, 107.7, 102.9, 101.7, 93.7, 81.8, 79.2, 73.5, 70.9, 70.6, 61.8. The final identification was confirmed by comparison with authentic sample.

Isomangiferin (II)

Pale yellow needles (50% EtOH), mp 258°C (dec.); uv λ_{max} nm (log ε): (MeOH) 241 (4.02), 256(4.15), 312(3.85), 363(3.70); (MeOH+NaOMe) 248, 271, 387; (MeOH+NaOAc) 238, 259, 375; (MeOH+$AlCl_3$) 233, 266, 350, 416; (MeOH+$AlCl_3$+HCl) 230, 264, 336, 406; ms m/z(rel. int.): 404(100), 386(43), 368(75), 350(33), 326(17), 300(28),

285(10), 284(25), 273(54); ^{1}H-nmr (DMSO-d_6); δ 13.32(s, 1-OH), 7.38(s, 8-H), 6.87 (s, 5-H), 6.25(s, 2-H), 4.73(d, J=9.2 Hz, 1'-H); ^{13}C-nmr (DMSO-d_6): δ 179.4, 163.5, 161.5, 156.2, 154.1, 151.1, 143.9, 111.9, 108.1, 104.3, 103.1, 102.1, 99.1, 81.6, 78.9, 73.7, 71.2, 71.2, 61.9.

2-Hydroxy-3,4-dimethoxyxanthone (III)

Pale yellow needles (n-hexane-EtOAc), mp 186-189°C; uv λ_{max} nm (log ε); (MeOH) 236(4.12), 256(4.23), 290(3.66), 307(3.68), 353(3.42); (MeOH+NaOMe) 236, 273, 295, 330, 395; ms m/z(rel. int.): 272(M^+, 100), 257(36), 229(21), 214(23), 186(9); ^{1}H-nmr (acetone-d_6): δ 8.90(s, 2-OH), 8.23(dd, J=8 and 2 Hz, 8-H), 7.81(3d, J=8, 8, and 2 Hz, 6-H), 7.60(dd, J=8 and 2 Hz, 5-H), 7.44(3d, J=8, 8, and 2 Hz, 7-H), 7.24(s, 1-H), 3.97(s, 3H, OCH_3), 3.95(s, 3H, OCH_3).

Toxyloxanthone B (IV)

Yellow needles (n-hexane-EtOAc), mp 305°C (dec.); uv λ_{max} nm (log ε): (MeOH) 243 (4.56), 261(4.54), 323(4.03), 331(4.46), 377(3.94); (MeOH+NaOMe) 261, 268, 355, 393, (MeOH+NaOAc) 244, 261, 335, 350, 385; (MeOH+$AlCl_3$) 246, 270, 355, 420; (MeOH +$AlCl_3$+HCl) 245, 269, 353, 420; ms m/z(rel. int.): 326(M^+, 41), 325(12), 311(100), 285(8), 283(3), 163(3), 155.5(12), 142.5(0.6), 141.5(2); ^{1}H-nmr (acetone-d_6): δ 13.32(s, 1-OH), 9.86 and 9.25(each s, OH) 8.01(d, J=12 Hz, 1'-H), 6.80(s, 5-H), 6.31(d, J=2 Hz, 4-H), 6.18(d, J=2 Hz, 2-H), 5.92(d, J=12 Hz, 2'-H), 1.47(s, 6H, CH_3).

Hyperxanthone (V)

Yellow needles ($CHCl_3$-MeOH), mp 285°C (dec.); uv λ_{max} nm(log ε): (MeOH) 243(4.08), 253(4.06), 322(4.00), 364(3.48); (MeOH+$AlCl_3$) no change; (MeOH+NaOMe) 247, 360, 382; (MeOH+NaOAc) 243, 330, 355; ms m/z(rel. int.): 310(M^+, 40), 309(17), 295(100), 269(11), 267(2), 155(4), 147.5(10), 134.5(1), 133.5(3); ^{1}H-nmr (acetone-d_6): δ 8.17 (d, J=10.2 Hz, 1'-H), 8.06(d, J=8.8 Hz, 1-H), 8.01(s, OH), 6.89(dd, J=8.8 and 2.2 Hz, 2-H), 6.83(s, 5-H), 6.82(d, J=2.2 Hz, 4-H), 5.90(d, J=10.2 Hz, 2'-H), 1.46(s, 6H, CH_3).

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