# XANTHONE CONSTITUENTS OF *HYPERICUM ANDROSAEMUM*

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Xanthone derivatives of various structural types have been isolated from several Hypericum species (1, 2, 3). An investigation of root material of *H. androsaemum* mainly showed the presence of hydroxy and methoxy substituted xanthones, two of which (**1** and **2**) represent oxygenation patterns hitherto not found in nature. A further new compound **3** may be the noncyclized precursor of toxyloxanthone B **4**. The xanthonolignan kielcorin, previously isolated from *Kielmeyera* species (4), was also present. Its structure was recently proved (5) to be represented by **5**, one of the alternatives originally proposed, and its enantiomer. The other xanthones isolated were known compounds.

## RESULTS AND DISCUSSION

In the ms of **1** fragmentation of $M^+$ (*m/e* 242$\sim C_{14}H_{10}O_4$) proceeds through loss of $\cdot CH_3$ followed by successive CO losses while peaks corresponding to $[M-\cdot CHO]^+$ or $[M-CH_2O]^+$ are not present. This is in accordance with the behaviour of 4-methoxyxanthone as contrasted with that of the 2-methoxy isomer (6).

The uv spectrum of **1** in MeOH shifts upon addition of NaOMe but not with NaOAc or $AlCl_3$ thus confining the position of the hydroxyl group to the 2- or equivalent 7-carbon.

A singlet at $\delta$ 10.02 in the pmr-spectrum of **1** in DMSO-$d_6$ confirms the above positioning of the hydroxyl group (7). On the basis of the pmr spectrum the choice between the alternatives: 2-hydroxy-4-methoxyxanthone and 2-hydroxy-5-methoxyxanthone can be made. For the former compound the signal corresponding to H–8 would be expected at $\delta$ 8.15, yet in the actual case it is at $\delta$ 7.72. The resonance of this and the remaining aromatic protons are in accordance with calculated values (8).

The fragmentation of $M^+$ (*m/e* 272 $\sim C_{15}H_{12}O_5$) in the ms of **2** resembles that of both 2-methoxy and 4-methoxy substituted xanthones (6), and the relevant three-proton signals are clearly seen in the pmr-spectrum. The remaining oxygen function is present in a hydroxyl group situated *para* to the carbonyl group as witnessed by a large K-band bathochromic shift (58 nm) and a hyperchromic shift upon addition of NaOAc to the uv test solution (9).

The pmr spectrum of **2** requires that one xanthone ring be substituted in the 2- and 3-position since two aromatic protons show up virtually as singlets at chemical shift values closely approaching those of the corresponding protons in 3-hydroxy-2-methoxyxanthone. This leaves the 5-position for the other methoxy group, a solution which is supported by the resonance of the remaining aromatic protons as in **1**.

Classification of **3** as a xanthone on the basis of its uv-spectrum implies that a $C_5$-unit and four oxygen functions be added to the nucleus to reach a MW of 328 ($M^+$, *m/e* 328$\sim C_{18}H_{16}O_6$). The uv spectrum *per se* resembles that of 1,3,6,7-tetrahydroxyxanthone (2). This is supported by bathochromic shifts upon addition of NaOAc, NaOAc/$H_3BO_3$, $AlCl_3$ and $AlCl_3$/HCl.

In the pmr-spectrum of **3** a low-field singlet represents the 1-hydroxyl group (7). The $C_5$-unit is a prenyl group showing two high-field three-proton signals and a vinylic proton signal at expected chemical shift values while the methylene group signal is at rather low field ($\delta$ 4.18). This indicates that it is situated at C-8 of the xanthone nucleus, *i.e.*, in the *peri* position and, thus, subject to an anisotropic effect from the carbonyl group. The solitary aromatic proton in this ring also resonates at a $\delta$-value in agreement with its positioning at C-5 rather than at C-8 (8).

## EXPERIMENTAL[1]

PLANT MATERIAL.—Roots of *Hypericum androsaemum* L. were collected from plants cultivated at The Botanical Gardens, Copenhagen, from seed obtained commercially. The water-washed roots were oven dried at 40–50° and ground to a coarse powder.

EXTRACTION AND FRACTIONATION.—Powdered roots (460 g) were defatted with petroleum ether, then extracted with chloroform and, later, methanol in a Sohxlet apparatus. The chloroform and methanol extracts were evaporated and subjected to column chromatography on Sephadex LH-20 (MeOH). Subsequent chromatography of the resulting fractions on silica gel 60 (Merck) columns eluted with benzene→ethyl acetate (gradient) yielded the following:

2-HYDROXY-5-METHOXYXANTHONE **1**.—Four mg; mp 257–259°; uv λ max (MeOH) nm 245 sh (log ε 4.37), 256 (4.43), 285 sh (3.20), 372 (3.55); λ max (MeOH+NaOMe) nm 255, 416; ir (KBr) $cm^{-1}$ 1640 sh, 1620, 1585, 1570, 1490, 1475, 1440, 1321, 1263, 1162, 1076, 764; ms *m/e* 242 (59%), 227 (60), 199 (19), 171 (100), 150 (6), 143 (14), 142 (21), 121 (35); pmr (DMSO-$d_6$, 270 MHz) $\delta$ 10.02 (s, OH), 7.72 (dd, *J* 8 and 1.5, H-8), 7.61 (d, *J* 9, H-4), 7.50 (dd, partly hidden, *J* (8) and 1.5, H-6), 7.48 (d, *J* 3, H-1), 7.38 (dd, *J* 8 and 8, H-7), 7.34 (dd, *J* 9 and 3, H-3), 3.99 (s, OMe).

3-HYDROXY-2,5-DIMETHOXYXANTHONE **2**.—Four mg; mp 215–218°; uv λ max (MeOH) nm 249 (log ε 4.32), 272 sh (3.80), 285 sh (3.62), 315 (3.58), 362 (3.74); λ max (MeOH+NaOMe) nm 245, 272 sh, 285 sh, 373 (log ε 3.96); λ max (MeOH+NaOAc) nm 245, 272 sh, 285 sh, 373 (log ε 4.10); ir (KBr) $cm^{-1}$ 1640, 1612, 1592, 1574, 1492, 1475, 1440, 1351, 1319, 1300, 1272, 1217, 1139, 1075, 754; ms m/e 272 (100%), 257 (41), 243 (6), 242 (13), 229 (6), 201 (3), 136 (2); pmr (DMSO-$d_6$, 270 MHz) $\delta$ 7.73 (dd, *J* 8 and 2, H-8), 7.51 (s, H-1), 7.47 (dd, *J* 8 and 2, H-6), 7.36 (dd, *J* 8 and 8, H-7), 6.98 (s, H-4), 3.97 and 3.90 (2 s, 2 OMe).

1,3,6,7-TETRAHYDROXY-8-PRENYLXANTHONE **3**.—Twenty mg; mp 194.5–195.5°; uv λ max (MeOH) nm 241 (log ε 4.29), 256 (4.36), 313 (4.11), 364 (3.77); λ max (MeOH+NaOMe) nm 267, 378; λ max (MeOH+NaOAc) nm 241, 259, 374; λ max (MeOH+NaOAc/$H_3BO_3$) nm 262, 318, 361; λ max (MeOH+$AlCl_3$) nm 237, 270, 358, 426; λ max (MeOH+$AlCl_3$/HCl) nm 237, 266, 338, 410; ir (KBr) $cm^{-1}$ 1640, 1605, 1565, 1500, 1478, 1465, 1355, 1300, 1285, 1169, 1118, 1032, 832, 807, 760; ms m/e 328 (53%), 313 (8), 285 (100), 273 (21), 272 (25), 164 (1), 142.5 (2.5); pmr ($(CD_3)_2CO$, 90 MHz) $\delta$ 13.52 (s, OH), 6.82, (s, H-5), 6.29 (d, *J* 2, H-4), 6.18 (d, *J* 2, H-2), 5.31 (t, *J* 6, =CH-), 4.18 (d, *J* 6, $-CH_2-$), 1.84 and 1.64 (2 s, 2 $CH_3$).

3-HYDROXY-2-METHOXYXANTHONE.—A quantity of 2.5 mg was isolated. The compound was identified by comparison with synthetic material (10).

1,5,6-TRIHYDROXY-3-METHOXYXANTHONE.—A quantity of 6.3 mg was isolated. The structure was confirmed by comparison with data given for the compound isolated from *Canscora decussata* Schult (11).

1,3,5,6-TETRAHYDROXYXANTHONE.—A quantity of 13 mg was isolated. The compound was identified by comparison with synthetic material (12).

1,3,6,7-TETRAHYDROXYXANTHONE.—A quantity of 8.5 mg was isolated. The compound was identified by comparison with synthetic material (13).

TOXYLOXANTHONE B 4.—A quantity of 33 mg was isolated. The compound was identical to that obtained from *Toxylon pomiferum* Rafin (14).

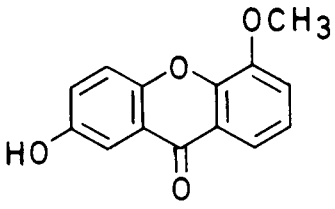
KIELCORIN **5**.—A quantity of 15 mg was isolated. The identity was confirmed by comparison with kielcorin isolated from *Kielmeyera coriacea* (4).

[1]The melting points were determined on a Leitz Mikroscope-Heiztich 350 and are corrected. The ultraviolet spectra were determined in MeOH on a Perkin-Elmer Ultraviolet-Visible Spectrophotometer, model 402.

The infrared spectra were taken on a Perkin-Elmer Grating Infrared Spectrophotometer, model 457.

Mass spectra were obtained on AEI MS-902 or Finnigan 3100 D instruments by direct inlet at 70 eV.

Nuclear magnetic resonance spectra were determined in the stated solvents on a Bruker HFX-90 or Bruker HX-270 instrument with tetramethylsilane as internal standard and chemical shifts reported in ppm ($\delta$).

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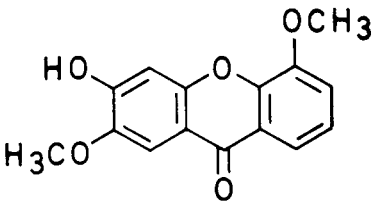


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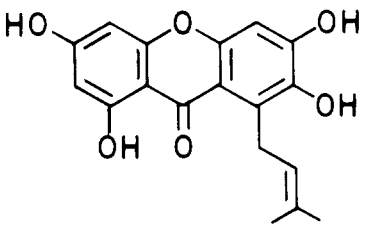


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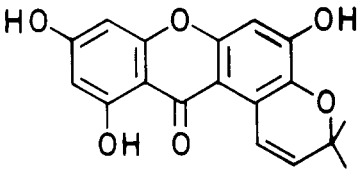


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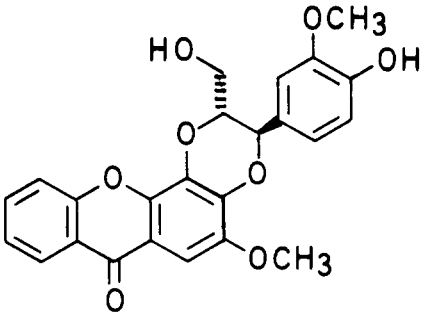


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