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XANTHONE CONSTITUENTS OF *HYPERICUM CANARIENSIS*

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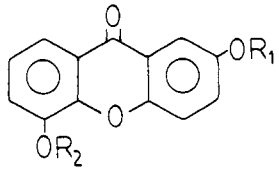
As part of our continuing study of the genus *Hypericum* (1,2), we have examined *Hypericum canariensis* L., which grows in the Canary Islands (Spain). No previous phytochemical work has been reported on this species. We now wish to report the isolation and structure elucidation of four xanthones from aerial parts of this plant. Among the compounds isolated, 2,5-dihydroxyxanthone has not previously been reported from natural sources and 2-hydroxy-5-methoxyxanthone has been reported only once from *Hypericum androsaemum* (3). Both compounds have oxygenation patterns that are infrequent in nature.

RESULTS AND DISCUSSION

A $CHCl_3$ extract of the plant material was chromatographed on a silica gel column, affording four crystalline compounds. The first two eluted products were identified as euxanthone (1,7-dihydroxyxanthone) and 2-hydroxyxanthone on the basis of spectroscopic properties and by comparison with an authentic sample (1).

The third-eluted product (**1**) was classified as a xanthone on the basis of its ir and uv spectra. The mass spectrum of **1** showed a molecular ion peak at *m/z* 242 ($C_{14}H_{10}O_4$) consistent with a hydroxymethoxyxanthone. The hydroxyl group in this xanthone is placed at C-2 on the following basis: The uv spectrum in MeOH shifts upon addition of NaOMe but not with NaOAc or $AlCl_3$ (4), the nmr spectrum on DMSO-d_6 showed a singlet at δ 9.99 (5), and the Gibbs' test was negative (4). The methoxyl group is situated at C-4 (or its equivalent C-5) in accordance with the fragmentation of M^+ which underwent loss of CH_3 followed by successive CO losses in the mass spectrum (6). The ^{1}H-nmr spectrum showed, besides the singlets of hydroxyl and methoxyl (3.96 δ) groups, a complex group of signals between 7.25 and 7.75 δ corresponding to six aromatic protons. The assignment of these signals (see Table 1) follow from spin decoupling experiments, and the chemical shifts of the signals corresponding to H-8 (7.69 δ) enabled us to place the two substituent groups in different rings. Consequently, the structure of 2-hydroxy-5-methoxyxanthone was assigned to compound **1**.



1 R_1=H; R_2=CH_3
2 R_1=R_2=H
3 R_1=R_2=CH_3

A new natural product (**2**) was eluted last from the column. By spectroscopic analysis, the structure of 2,5-dihydroxyxanthone was assigned to it. The uv spectrum is characteristic of the xanthone skeleton. The mass spectrum showed a molecular ion peak at *m/z* 228 ($C_{13}H_8O_4$) consistent with a dihydroxyxanthone. The location of these hydroxyl groups was made on the following grounds. Its uv spectra in MeOH and in MeOH+$AlCl_3$ are superimposable; therefore, the hydroxyls are not at C-1 or C-8. Positions C-3 (or C-6) can also be excluded because the uv spectrum did not undergo a large k-band bathochromic shift upon addition of NaOAc to the uv test solution. Thus, the two hydroxyl groups must be situated at the C-2 (or C-7) and C-4 (or C-5). This assignment also agrees with the values of

TABLE 1. ^{1}H-nmr (250 MHz)[a] Chemical Shifts of Compounds **1**, **2**, and **3** in DMSO-d_6[b]

	Compounds		
	1	**2**	**3**
H-1	7.45 (d, J=3.0 Hz	7.45 (d, J=3.0 Hz)	7.55 (dd, J=3.1 and 0.4 Hz)
H-3	7.30 (dd, J=9.0 and 3.0 Hz)	7.31 (dd, J=9.0 and 3.0 Hz)	7.47 (dd, J=9.1 and 3.1 Hz)
H-4	7.58 (d, J=9.0 Hz)	7.55 (d, J=9.0 Hz)	7.69 (dd, J=9.1 and 0.4 Hz)
H-6	7.47 (dd, J=7.9 and 1.7 Hz)	7.29 (dd, J=7.7 and 1.8 Hz)	7.50 (dd, J=8.0 and 1.7 Hz)
H-7	7.35 (t, J=7.9 Hz)	7.21 (t, J=7.7 Hz)	7.38 (t, J=8.0 Hz)
H-8	7.69 (dd, J=7.9 and 1.7 Hz)	7.57 (dd, J=7.7 and 1.8 Hz	7.73 (dd, J=8.0 and 1.7 Hz)
Other Signals	9.99 (OH) and 3.96 (OCH_3)	9.96 and 10.39 (OH)	3.98 and 3.87 (OCH_3)

[a]The spectrum of **3** has been measured at 200 MHz.

[b]All chemical shift values are given in δ (ppm) relative to TMS. Coupling constants are given in Hz. The separation of signal was perfect in the expanded spectrum and with gaussian multiplication.

chemical shifts of the signals corresponding to hydroxyl groups (9.96 for hydroxyl group at C-2 and 10.39 δ for hydroxyl group at C-4 or C-5) (5). Of the two possible structures: 2,4-dihydroxyxanthone and 2,5-dihydroxyxanthone, we have chosen the second. For the former compound, the signal corresponding to H-8 would be expected at δ>8, (7); however, in our case it is at 7.57. The assignment of the signal of remaining aromatic protons (see Table 1) from spin decoupling experiments agrees with the proposed structure. By comparison of ^{1}H-nmr spectra data of **1** and **2**, a slight diamagnetic shift of the proton signal only at C-6, C-7, and C-8 was observed (7). The physical and spectroscopic properties of compound **2** agree well with those reported in the literature for the synthetic 2,5-dihydroxyxanthone (8).

As a final proof of the structures of compounds **1** and **2**, both were subjected to methylation with CH_2N_2 to give an identical dimethoxyxanthone (mp, mmp, glc, ir, uv) with physical and spectroscopic properties in agreement with those reported in the literature for the 2,5-dimethoxyxanthone **3** (8).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The melting points were determined on a Büchi apparatus and are uncorrected. The uv spectra were measured on a Perkin-Elmer uv-visible spectrophotometer, model 575. The ir spectra were recorded in KBr pellets on a Perkin-Elmer 281 spectrophotometer. ^{1}H-nmr spectra were recorded on a Bruker WM (250 MHz) instrument or a Varian XL-200 (200 MHz) instrument. Mass spectra were taken with a Varian-160 spectrometer at 70 ev.

EXTRACTION AND FRACTIONATION.—The plant material was collected in La Palma (Canary Islands, Spain) and classified by Dr. Pérez de Paz, Professor of Botany at the University of La Laguna (Tenerife). A voucher specimen was deposited in the herbarium TFC of the Botany Department, Faculty of Biological Sciences, University of La Laguna. Powdered and dried stems, leaves, and flowers of *H. canariensis* (3.5 kg) were extracted successively with hexane, $CHCl_3$, and EtOH. The $CHCl_3$ extract (25 g) was chromatographed on silica gel (310 g) from which hexane-EtOAc eluted successively four yellow crystalline products.

1,7-DIHYDROXYXANTHONE.—A quantity of 138 mg was eluted with hexane-EtOAc (85:15); mp 236-238° (from hexane-EtOAc). The compound was identified by comparison with 1,7-dihydroxyxanthone isolated from *Hypericum ericoides* [lit (1), mp 237-238°].

2-HYDROXYXANTHONE.—A quantity of 77 mg was eluted with hexane-EtOAc (8:2); mp 238-239° (from hexane-EtOAc). The compound was identical to that obtained from *H. ericoides* [lit (1), mp 238-239°].

2-HYDROXY-5-METHOXYXANTHONE (**1**).—Twenty five mg; eluent hexane-EtOAc (8:2); mp 280-282° (from $CHCl_3$-EtOAc); [lit (3), mp 257-259°]; uv λ max (MeOH) nm 238 (log ε 4.40), 253sh (4.28), 370 (3.17); λ max (MeOH+NaOMe) nm 247 285sh, 413; ir (KBr) cm^{-1} 3350-3050, 2845, 1620, 1590, 1570,

1500, 1475, 1440, 1340, 1265, 1220, 1210, 1187, 1170, 1155, 1080, 870, 817, 785, 758; ms *m/z* (rel. int.) 242 (100, M^+), 227 (77.7, M-CH_3), 199 (12.5, M-CH_3-CO), 171 (24.5, M-CH_3-2CO).

2,5-DIHYDROXYXANTHONE (**2**).—Six mg; eluent hexane-EtOAc (75:25) mp 288-290° (from hexane-EtOAc) [lit (8), mp 303-305°]; uv λ max (MeOH) nm 240sh (log ε 4.32), 245sh (4.37), 256 (4.45), 291sh (3.34), 373 (3.58); λ max (MeOH+NaOMe) nm 254sh, 265sh, 276, 301sh, 425, λ max (MeOH+NaOAc) nm 240, 265, 271sh, 399; Gibbs' test λ max 734 nm; ir (KBr) cm^{-1} 3500-3000, 1635, 1595, 1490, 1470, 1455, 1345, 1310, 1245, 1215, 1172, 1155, 1060, 875, 835, 790, 760; ms *m/z* (rel. int.) 228 (100, M^+), 200 (10.9, M-CO), 172 (3.1, M-2CO), 171 (8.2, M-CO-CHO), 144 (5.5, M-3CO).

2,5-DIMETHOXYXANTHONE (**3**).—Compound **1**, 2-hydroxy-5-methoxyxanthone (3 mg) or compound **2**, 2,5-dihydroxyxanthone (0.6 mg) dissolved in Et_2O-EtOH was treated with an ethereal solution of CH_2N_2 (excess). The reaction product worked up was 2,5-dimethoxyxanthone, mp 168-169° (from hexane-Et_2O) [lit (8), mp 176-177°]; uv λ max (MeOH) nm 237sh (log ε 4.16), 245sh (4.21), 255 (4.35), 285sh (3.14), 364 (3.42); ir (KBr) cm^{-1} 2840, 1660, 1620, 1600, 1580, 1490, 1440, 1370, 1315, 1270, 1225, 1190, 1155, 1080, 1030, 995, 870, 825, 780, 755.

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