XANTHONE CONSTITUENTS OF *HYPERICUM INODORUM*

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Abstract - The isolation and identification of six xanthones from the aerial parts of *Hypericum inodorum* are reported. One of these compounds , 5-hydroxy-2-methoxyxanthone, is described for the first time.

In connection with our phytochemical work on the genus *Hypericum*,[1-4] we undertook investigation of *Hypericum inodorum* Mill, which grows in the Canary Islands (Spain). There is no report on the constituents of this plant, though several xanthone derivatives have been isolated from some *Hypericum* species.[1-6] We now wish to report the isolation and structure elucidation of six xanthones from aerial parts of this plant, including a new natural product 5-hydroxy-2-methoxyxanthone.

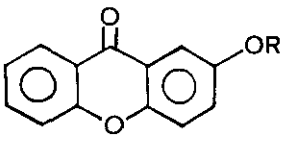
The chloroform extract of the plant material was fractionated on a silica gel column, affording four groups of eluates, which in turn yielded six different xanthones (**1-6**) after chromatographic purification.

The first three products were identified as 2-methoxyxanthone (**1**), euxanthone (1,7-dihydroxyxanthone) (**2**) and 2-hydroxyxanthone (**3**) on the basis of spectroscopic properties and by comparison with authentic samples.[1-2,7-8]

The compound (**4**) was classed as xanthone on the basis of its uv spectrum (267, 401 nm).[9] Its molecular weight, determined by ms (M^+ 258), was consistent with a dihydroxymethoxyxanthone. The hydroxyl groups were placed at C-1 and C-7, as the uv maxima in MeOH show a bathochromic shift upon addition of NaOMe and $AlCl_3$, but not in the presence of NaOAc or H_3BO_3.[9] This assignment also agrees with the values of chemical shifts (DMSO-d_6) of the signals corresponding to hydroxyl groups (δ 11.98 for HO- at C-1 and δ 10.10 for HO- at C-7).[10] The methoxyl group was situated at C-4 (or its equivalent C-5) in accordance with the fragmentation of M^+ which underwent a loss of CH_3 followed by successive CO losses in the mass spectrum.[11] The ^{1}H-nmr spectrum showed, besides the singlets of hydroxyl and methoxyl (δ 3.88) groups, signals of an AB system for two *ortho*-coupled protons (δ 7.45 and 6.70, J = 8.9 Hz) and typical signals[12] of three protons on a 2- or 7-substituded ring: at δ 7.44 a doublet (J = 3.0 Hz) of H-8, at δ 7.35 a double doublet (J = 9.0 and 3.0 Hz) of H-6 and at δ 7.59 a doublet (J = 8.9 Hz) of H-5. Consequently, the structure of 1,7-dihydroxy-4-methoxyxanthone

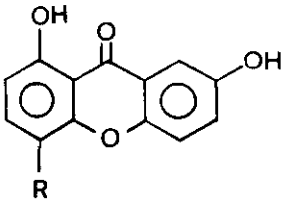
was assigned to compound (**4**). This compound has been reported only once[8] from *Vismia guaramirangae*, which belongs to the family Guttiferae and subfamily Hypericoideae, as *Hypericum* genus.[13]

Compounds (**5**) and (**6**) were also classed as xanthones in view of their uv spectra.[9] Their molecular weights, determined by mass spectrometry (M^+ 242), were consistent with those of a hydroxymethoxyxanthone. The compound (**6**) was easily identified as 2-hydroxy-5-methoxyxanthone, previously isolated by us[12] from *Hypericum canariensis* and by Nielsen and Arends[14] from *Hypericum androsaemum*.



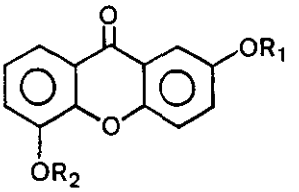
1 R = CH_3

3 R = H



2 R = H

4 R = OCH_3



5 $R_1 = CH_3$; R_2 = H

6 R_1 = H ; $R_2 = CH_3$

7 $R_1 = R_2 = CH_3$

The ^{1}H-nmr spectrum of compound (**5**) showed the same substitution pattern that **6**, i.e. typical signals of three protons on a 2-substituted[12] ring: at δ 7.68 a doublet (J = 2.1 Hz) of H-1, at δ 7.49 a double doublet (J = 8.7 and 2.9 Hz) of H-3 and at δ 7.65 a doublet (J = 8.8 Hz) of H-4, as well as signals of three vicinal protons on a 4-substituted ring (or its equivalent 5-substituted): at δ 7.30 a double doublet (J = 7.8 and 1.9 Hz) of H-6, at δ7.24 a triplet (J = 7.8 Hz) of H-7 and at δ 7.57 a double doublet (J = 7.8 and 1.9 Hz) of H-8. Consequently, the structure of 5-hydroxy-2-methoxyxanthone was assigned to compound (**5**). This is the first report on this xanthone.Both compounds (**5**) and (**6**) were transformed with ethereal solution of diazomethane in an identical dimethoxyxanthone, with physical and spectroscopic properties in agreement with those reported in the literature[12,15] for the 2,5-dimethoxyxanthone (**7**).

EXPERIMENTAL

Spectra were recorded with the following instruments: ms, Varian 160; nmr, Bruker AC-200 (200.1 MHz) and uv, Perkin-Elmer Lambda 2.

Isolation.

Aerial parts of *H. inodorum* were collected at Las Mercedes-Moquinal, Anaga, Tenerife, Canary Islands (Spain) and authenticated by Prof. Pérez de Paz (Botany Department of the Faculty of Biological Sciences, University of La Laguna, Tenerife). A voucher specimen was deposited in the herbarium of the same department.

The plant material (3.0 Kg) was extracted exhaustively in a Soxhlet apparatus, first with hexane and then with $CHCl_3$ (20 l for 40 h , each solvent). The $CHCl_3$ extract (82 g) was chromatographed on a silica gel column (80 cm x 9 cm I.D.) using hexane-ether mixtures as eluents. Four main groups of eluates were obtained: A (65:35), B (60:40), C (55:45) and D (40:60). Repeated application of the chromatographic procedure yielded compounds as follows: **1** (8 mg) from A; **2** (20 mg) from B; **3** (8 mg), **4** (23 mg) and **5** (5 mg) from C and **6** (35 mg) from D.

1,7-dihydroxy-4-methoxyxanthone 4.

mp 235-237°C (dichloromethane); ms *m/z* (rel. int.) 258 (M^+, 33), 243 (M-CH_3, 100), 215 (M-CH_3-CO, 8), 187 (M-CH_3-2CO, 3); uv λ_{max} nm: (MeOH) 237, 267, 328, 401; (MeOH + NaOMe) 256, 275, 433; (MeOH + NaOAc): no change; MeOH + NaOAc + H_3BO_3): no change; (MeOH + $AlCl_3$) 239, 287, 353, 477; (MeOH + $AlCl_3$ + HCl) 239, 287, 353, 477. ^{1}H-Nmr (DMSO-d_6): δ 11.98 (s, HO-1), 10.10 (s, HO-7), 7.59 (d, J = 8.9 Hz, H-5), 7.45 (d, J = 8.9 Hz, H-3), 7.44 (d, J = 3.0 Hz, H-8), 7.35 (dd, J = 9.0 and 3.0 Hz, H-6), 6.70 (d, J = 8.9 Hz, H-2) and 3.88 (s, CH_3O-).

5-Hydroxy-2-methoxyxanthone 5.

Non-crystalline; ms *m/z* (rel. int.) 242 (M^+, 49), 227 (M-CH_3, 16), 213 (13), 212 (M-CH_2O, 15), 199 (M-CH_3-CO, 9), 171 (M-CH_3-2CO, 34), 167 (32), 149 (100); uv λ_{max} nm: (MeOH) 238, 257, 272, 368; (MeOH + NaOMe) 241, 274, 401; (MeOH + NaOAc): no change; (MeOH + NaOAc + H_3BO_3): no change; (MeOH + $AlCl_3$): no change; (MeOH + $AlCl_3$ + HCl): no change. ^{1}H-Nmr (DMSO-d_6): δ 10.46 (s, HO-5), 7.68 (d, J = 2.1 Hz, H-1), 7.65 (d, J = 8.8 Hz, H-4), 7.57 (dd, J = 7.8 and 1.9 Hz, H-8), 7.49 (dd, J = 8.7 and 2.9 Hz, H-3), 7.30 (dd, J = 7.8 and 1.9 Hz, H-6), 7.24 (t, J = 7.8 Hz, H-7) and 3.88 (s, CH_3O-).

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REFERENCES

1. M. L. Cardona and E. Seoane, *J. Nat. Prod.*, 1982, **45**, 134.
2. M. L. Cardona, M. I. Fernández, J. R. Pedro, E. Seoane, and R.Vidal, *J. Nat. Prod.*, 1986, **49**, 95.
3. M. L. Cardona, I. Fernández, J. R. Pedro, and A. Serrano, *Heterocycles*, 1989, **29**, 2297.
4. M. L. Cardona, I. Fernández, J. R. Pedro, and A. Serrano, *Phytochemistry*, 1990, **29**, 3003.
5. M. V. S. Sultanbawa, *Tetrahedron*, 1980, **36**, 1465.
6. G. J. Bennett and H. H. Lee, *Phytochemistry*, 1989, **28**, 967.
7. S. P. Gunasekera, S. Ramachandran, S. Selliah, and M. U. S. Sultanbawa, *J. Chem. Soc. ,Perkin Trans. I*, 1975, 2447.
8. F. Delle Monache, M. Marquina Mac-Quhae, G. Delle Monache, G. B. Marini Bettolo, and R. Alves de Lima, *Phytochemistry,* 1983, **22**, 227.
9. A. A. L. Mesquita, D. B. Correa, O. R. Gottlieb, and M. T. Magalhaes, *Anal. Chim. Acta*, 1968, **42**, 311.
10. P. Arends and P. Helboe, *Acta Chem. Scand.*, 1972, **26**, 4180.
11. P. Arends, P. Helboe, and J. Moller, *Org. Mass. Spectrom.*, 1973, **7**, 667.
12. M. L. Cardona, J. R. Pedro, E. Seoane, and R. Vidal, *J. Nat. Prod.*, 1985, **48**, 467.
13. M. Melchoir, *A Engler's Syllabus der Pflanzenfamilien*, 12th ed., Vol. 2, Gebrüder Bornträger, Berlin, 1964, p. 444.
14. H. Nielsen and P. Arends, *J. Nat. Prod.*, 1979, **42**, 303.
15. R. A. Finnegan and K. E. Merkel, *J. Org. Chem.*, 1972, **37**, 2986.

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