

**XANTHONE CONSTITUENTS OF *HYPERICUM INODORUM***

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**Abstract** - The isolation and identification of six xanthenes 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*,<sup>1-4</sup> 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.<sup>1-6</sup> We now wish to report the isolation and structure elucidation of six xanthenes from aerial parts of this plant, including a new natural product 5-hydroxy-2-methoxyxanthone.

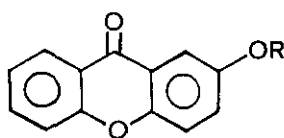
The chloroform extract of the plant material was fractionated on a silica gel column, affording four groups of eluates, which in turn yielded six different xanthenes (1-6) after chromatographic purification.

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.<sup>1-2,7-8</sup>

The compound (4) was classed as xanthone on the basis of its uv spectrum (267, 401 nm).<sup>9</sup> 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<sub>3</sub>, but not in the presence of NaOAc or H<sub>3</sub>BO<sub>3</sub>.<sup>9</sup> This assignment also agrees with the values of chemical shifts (DMSO-d<sub>6</sub>) of the signals corresponding to hydroxyl groups ( $\delta$  11.98 for HO- at C-1 and  $\delta$  10.10 for HO- at C-7).<sup>10</sup> 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<sub>3</sub> followed by successive CO losses in the mass spectrum.<sup>11</sup> The <sup>1</sup>H-nmr spectrum showed, besides the singlets of hydroxyl and methoxyl ( $\delta$  3.88) groups, signals of an AB system for two *ortho*-coupled protons ( $\delta$  7.45 and 6.70,  $J = 8.9$  Hz) and typical signals<sup>12</sup> of three protons on a 2- or 7-substituted ring: at  $\delta$  7.44 a doublet ( $J = 3.0$  Hz) of H-8, at  $\delta$  7.35 a double doublet ( $J = 9.0$  and 3.0 Hz) of H-6 and at  $\delta$  7.59 a doublet ( $J = 8.9$  Hz) of H-5. Consequently, the structure of 1,7-dihydroxy-4-methoxyxanthone

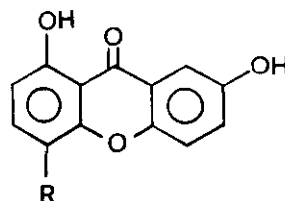
was assigned to compound (4). This compound has been reported only once<sup>8</sup> from *Vismia guaramirangae*, which belongs to the family Guttiferae and subfamily Hypericoideae, as *Hypericum* genus.<sup>13</sup>

Compounds (5) and (6) were also classed as xanthenes in view of their uv spectra.<sup>9</sup> 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<sup>12</sup> from *Hypericum canariensis* and by Nielsen and Arends<sup>14</sup> from *Hypericum androsaemum*.



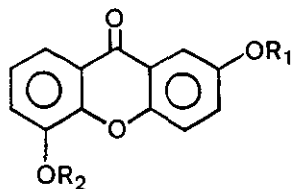
1 R = CH<sub>3</sub>

3 R = H



2 R = H

4 R = OCH<sub>3</sub>



5 R<sub>1</sub> = CH<sub>3</sub> ; R<sub>2</sub> = H

6 R<sub>1</sub> = H ; R<sub>2</sub> = CH<sub>3</sub>

7 R<sub>1</sub> = R<sub>2</sub> = CH<sub>3</sub>

The <sup>1</sup>H-nmr spectrum of compound (5) showed the same substitution pattern that 6, i.e. typical signals of three protons on a 2-substituted<sup>12</sup> ring: at  $\delta$  7.68 a doublet ( $J = 2.1$  Hz) of H-1, at  $\delta$  7.49 a double doublet ( $J = 8.7$  and 2.9 Hz) of H-3 and at  $\delta$  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  $\delta$  7.30 a double doublet ( $J = 7.8$  and 1.9 Hz) of H-6, at  $\delta$  7.24 a triplet ( $J = 7.8$  Hz) of H-7 and at  $\delta$  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<sup>12,15</sup> 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  $\text{CHCl}_3$  (20 l for 40 h, each solvent). The  $\text{CHCl}_3$  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 ( $\text{M}^+$ , 33), 243 (M- $\text{CH}_3$ , 100), 215 (M- $\text{CH}_3$ -CO, 8), 187 (M- $\text{CH}_3$ -2CO, 3); uv  $\lambda_{\text{max}}$  nm: (MeOH) 237, 267, 328, 401; (MeOH + NaOMe) 256, 275, 433; (MeOH + NaOAc): no change; MeOH + NaOAc +  $\text{H}_3\text{BO}_3$ : no change; (MeOH +  $\text{AlCl}_3$ ) 239, 287, 353, 477; (MeOH +  $\text{AlCl}_3$  + HCl) 239, 287, 353, 477.  $^1\text{H-Nmr}$  (DMSO- $d_6$ ):  $\delta$  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,  $\text{CH}_3\text{O}$ -).

### 5-Hydroxy-2-methoxyxanthone 5.

Non-crystalline; ms  $m/z$  (rel. int.) 242 ( $\text{M}^+$ , 49), 227 (M- $\text{CH}_3$ , 16), 213 (13), 212 (M- $\text{CH}_2\text{O}$ , 15), 199 (M- $\text{CH}_3$ -CO, 9), 171 (M- $\text{CH}_3$ -2CO, 34), 167 (32), 149 (100); uv  $\lambda_{\text{max}}$  nm: (MeOH) 238, 257, 272, 368; (MeOH + NaOMe) 241, 274, 401; (MeOH + NaOAc): no change; (MeOH + NaOAc +  $\text{H}_3\text{BO}_3$ ): no change; (MeOH +  $\text{AlCl}_3$ ): no change; (MeOH +  $\text{AlCl}_3$  + HCl): no change.  $^1\text{H-Nmr}$  (DMSO- $d_6$ ):  $\delta$  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,  $\text{CH}_3\text{O}$ -).

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