

FLAVONOID AGLYCONES FROM SOME CANARY ISLANDS SPECIES OF *SIDERITIS*

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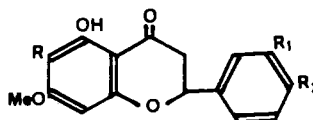
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Diterpenes, triterpenes, and flavones have been isolated from the genus *Sideritis* (Lamiaceae). In previous work, we have studied the flavones of some species endemic to the Canary Islands (1,2). The present work describes the isolation of several flavones and flavanones of other species of Canarian *Sideritis* that grow in La Gomera, Tenerife, and Gran Canaria, three of the seven islands of this archipelago.

5-Hydroxy-3,7,4'-trimethoxyflavone (3,7,4'-tri-*O*-methylkaempferol) (3) was obtained from *Sideritis lotsy* (Pit.) Ceb. et Ort., *Sideritis marmorea* Bolle, and *Sideritis nutans* Svent. These three species are endemic to the island of La Gomera. From the two latter species, 5-hydroxy-7,4'-dimethoxyflavone (7,4'-di-*O*-methylapigenin) (4) was also isolated. *S. nutans* also contained 5-hydroxy-3,6,7,4'-tetramethoxyflavone (3,4'-di-*O*-methyl-eupalitin) (5,6), 5-hydroxy-6,7,4'-trimethoxyflavone (salvigenin) (7), 5-hydroxy-6,7,3',4'-tetramethoxyflavone (3'-*O*-methyleupatorin) (8), and 5,3'-dihydroxy-6,7,4'-trimethoxyflavone (eupatorin) (9). *Sideritis cystosiphon* Svent., a plant endemic to Tenerife, afforded 5-hydroxy-3,7,4'-trimethoxyflavone (3), 5-hydroxy-6,7,3',4'-tetramethoxyflavone (8), and 5-hydroxy-6,7,3',4'-tetramethoxyflavanone [1]. *Sideritis infernalis* Bolle, also endemic to Tenerife, contained the flavanones 5-hydroxy-7,4'-dimethoxyflavanone (7,4'-di-*O*-methylapigenin) [2] (10,11) and 5-hydroxy-7,3',4'-trimethoxyflavanone (7,3',4'-tri-*O*-methyleuriodictyol) [3] (12). Cirsimaritin (13) and 5,4'-dihydroxy-6,7-dimethoxyflavanone [5] (12)



- 1 R = R₁ = R₂ = OMe
- 2 R = R₁ = H, R₂ = OMe
- 3 R = H, R₁ = R₂ = OMe
- 4 R = R₂ = OMe, R₁ = H
- 5 R = OMe, R₁ = H, R₂ = OH

were isolated from *Sideritis sventenii* (Kunk) Mend-Heu., a species endemic to Gran Canaria. The flavanone 5-hydroxy-6,7,4'-trimethoxyflavanone [4] (12) was obtained from *Sideritis gomerae* Bolle with other previously reported flavones (2).

5-Hydroxy-6,7,3',4'-tetramethoxyflavanone, the only flavanone isolated from *S. cystosiphon*, is a new natural product. Its structure was determined as 1 in accordance with the following considerations: The high resolution mass spectrum indicated a molecular formula of C₁₉H₂₀O₇, corresponding to a flavanone with one hydroxyl and four methoxyl groups. The former must be situated at C-5 because a hydrogen associated with the carbonyl groups of the pyran ring appears as a singlet at δ 11.87 in the ¹H-nmr spectrum. Two of the methoxyls were at C-3' and C-4' because the characteristic proton resonances of this substitution of the B ring, the H-5 (6.89 δ , d, J = 8 Hz) and the H-2' and H-6' (6.97 δ , m, 2H), also appear in this spectrum. The other two methoxyls must be at C-6, C-7 or at C-7, C-8. As the spectroscopic data were not sufficient to distinguish between these two alternatives, we obtained, by treatment of 1 with DDQ, the corresponding flavone

(8), which has also been isolated from the same species. We propose the name cystosiphonin for this new flavanone. Its methyl ether has been obtained from *Chromolaena heteroclina* (14).

The structures of the other flavanones also deserve special mention. Compound **3** was obtained previously from the fern *Notholaena limitana* var. *mexicana* (12). The flavanones **4** and **5** have been isolated only once before, as minor constituents from the fern *Cheilanthes argentea* (12). These authors gave the structures of compounds **4** and **5** with "a small uncertainty as to the exact substitution of ring A." Now, in this work, we confirm the structures given to these flavanones, relating **4** with the corresponding flavone, salvigenin (7), by dehydrogenation with DDQ. Salvigenin was also isolated from *S. gomerae* (2). On the other hand, in the flavanone **5** the non-associated hydroxyl group was assigned to C-4', in accordance with fragment B (*m/z* 120) formed by cleavage of ring C and by the bathochromic shift observed in the uv on the addition of NaOMe. Methylation of this compound with ethereal CH₂N₂ afforded **4**.

The flavones contained in this genus are interesting from the phytochemical point of view. *S. nutans* has similar flavones to *S. gomerae* (2), confirming other phytochemical results based on their diterpenic content (1) and the morphological botanical classification of these two species in the same section (15).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Nmr spectra were determined in CDCl₃, ir in CHCl₃, and uv in EtOH. Ms were obtained at 70 eV in the electron impact mode.

COLLECTION OF PLANT MATERIAL.—*S. gomerae* (2.0 kg), *S. lotoy* (1.9 kg), *S. marmorea* (0.5 kg), and *S. nutans* (0.7 kg) were collected in La Gomera (island) on the north road (km 4), El Paso (near Alajeró), Roque de Aluce, and El Santo (near Arure), respectively. *S. cystosiphon* (1.1 kg) and *S. infernalis* (1.6 kg) were collected in Tenerife at Roques de Tamaimo, beside the north road at km 94, and Barranco del Infierno, respec-

tively. *S. sventenii* (1.0 kg) was collected on the island of Gran Canaria at Presa de la Gambuesa. Voucher specimens have been deposited in the Herbarium of the Instituto Canario de Investigaciones Agrarias (Tenerife).

ISOLATION OF FLAVONOID COMPOUNDS.—The flavonoids were isolated as reported previously (2). *S. gomerae* yielded 5-hydroxy-6,7,4'-trimethoxyflavanone [**4**] (45 mg). *S. lotoy* yielded 3,7,4'-tri-*O*-methylkaempferol (30 mg). *S. marmorea* yielded 3,7,4'-tri-*O*-methylkaempferol (150 mg) and 5-hydroxy-7,4'-di-*O*-methylapigenin (30 mg). *S. nutans* yielded 3,7,4'-tri-*O*-methylkaempferol (100 mg), 7,4'-di-*O*-methylapigenin (25 mg), 3,4'-di-*O*-methylpupatin (55 mg), salvigenin (110 mg), 3-*O*-methylpupatorin (300 mg), and eupatorin (40 mg). *S. cystosiphon* yielded 3,7,4'-tri-*O*-methylkaempferol (20 mg), 5-hydroxy-6,7,3',4'-tetramethoxyflavone (45 mg), cystosiphonin [**1**] (90 mg). *S. infernalis* yielded 5-hydroxy-7,4'-dimethoxyflavanone (35 mg) and 5-hydroxy-7,3',4'-trimethoxyflavanone [**3**] (20 mg). *S. sventenii* yielded cirsimaritin (45 mg) and 5,4'-dihydroxy-6,7-dimethoxyflavanone (30 mg).

5-HYDROXY-6,7,3',4'-TETRAMETHOXYFLAVANONE (CYSTOSIPHONIN) [1**].**—Mp 151–153°; [M]⁺ at 360.1219, C₁₉H₂₀O₇ requires 360.1207; uv λ max 296 and 346 nm; ¹H nmr (200 MHz) δ 2.78 (1H, dd, *J* = 3 and 17 Hz, H-3), 3.11 (1H, d, *J* = 13 and 17 Hz, H-3), 3.83, 3.87, 3.90 and 3.92 (each 3H, s), 5.35 (1H, dd, *J* = 3 and 13 Hz, H-2), 6.11 (1H, s, H-8), 6.89 (1H, d, *J* = 8 Hz, H-5'), 6.97 (2H, m, H-2' and H-6'), 11.87 (1H, s, H-5); ms *m/z* [M]⁺ 360 (100), 345 (9), 196 (83), 181 (63), 164 (53).

5-HYDROXY-7,3',4'-TRIMETHOXYFLAVANONE [3**].**—Mp 156–157° [lit. (12) 156°]; [M]⁺ at 330.1086, C₁₈H₁₈O₆ requires 330.1102; uv λ max 287 and 336 nm; ¹H nmr (200 MHz) δ 2.79 (1H, dd, *J* = 3 and 17 Hz, H-3), 3.11 (1H, dd, *J* = 13 and 17 Hz, 3.80, 3.90, and 3.91 (each 3H, s), 5.36 (1H, dd, *J* = 3 and 13 Hz, H-2), 6.05 and 6.07 (each 1H, d, *J* = 2 Hz, H-6 and H-8), 6.88 (1H, d, *J* = 9 Hz, H-5'), 6.97 (2H, m, H-2' and H-6'), 12.02 (1H, s, H-5); ms *m/z* [M]⁺ 330 (76), 313 (6), 298 (6), 287 (4), 193 (18), 192 (5), 167 (9), 164 (100), 151 (98), 149 (28).

5-HYDROXY-6,7,4'-TRIMETHOXYFLAVANONE [4**].**—Mp 148–150° [lit. (12) 146–147°]; [M]⁺ at 330.1097, C₁₈H₁₈O₆ requires 330.1091; ir ν max 2960, 1630, 1570, 1505; uv λ max 289 and 343; ¹H nmr (200 MHz) δ 2.78 (1H, dd, *J* = 3 and 17 Hz, H-3), 3.10 (1H, dd, *J* = 13 and 17 Hz, H-3), 3.83 and 3.92 (each 3H, s), 5.36 (1H, dd, *J* = 3 and 13 Hz, H-2), 6.10 (1H, s, H-8), 6.95 and 7.38 (each 2H, d, *J* = 8 Hz, H-3', H-5' and H-2', H-6'), 11.87 (1H, s,

H-5); ms m/z $[M]^+$ 330 (72), 315 (8), 196 (83), 181 (100), 168 (15), 153 (39), 134 (23), 119 (19).

5,4'-DIHYDROXY-6,7-DIMETHOXYFLAVANONE [5].—Mp 180–181° [lit. (12) 181°]; uv λ max 288 and 340 nm, (EtOH + NaOMe) 238, 287, and 384 nm; nmr (200 MHz) δ 2.78 (1H, dd, $J = 3$ and 17 Hz, H-3), 3.10 (1H, dd, $J = 13$ and 17 Hz, H-3), 3.84 and 3.86 (each 3H, s), 5.35 (1H, dd, $J = 3$ and 13 Hz, H-2), 6.10 (1H, s, H-8), 6.89 and 7.32 (each 2H, d, $J = 8$ Hz, H-3', H-5' and H-2', H-6'), 11.87 (1H, s, H-5); ms m/z $[M]^+$ 346 (3), 316 (86), 301 (8), 196 (81), 181 (100), 168 (18), 152 (46), 120 (19).

DEHYDROGENATION OF 1 OR 4.—The flavanone 1 (9 mg) in dry dioxane (6 ml) was treated with DDQ (9 mg) at reflux under N_2 for 8 h. The reaction mixture was concentrated in vacuo, chromatographed on Si gel, and eluted with petroleum ether-EtOAc (3:2) to afford a flavone, identical with one also isolated from *S. cystosiphon*. The same reaction on 4 afforded a flavone identical with salvigenin, also obtained from *S. gomerae* (2).

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