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FLAVONOIDS AND XANTHONOLIGNOIDS OF *HYPERICUM ERICOIDES*

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Key Word Index—*Hypericum ericoides*; Guttiferae; quercetin; hyperin; 6-*C*-methyl-7-*O*-methylapigenin; xanthonolignoid; kielcorin.

Abstract—*Hypericum ericoides* contains quercetin, hyperin, kielcorin and a new flavone, identified as 5,4'-dihydroxy-7-methoxy-6-methylflavone or 6-*C*-methyl-7-*O*-methylapigenin.

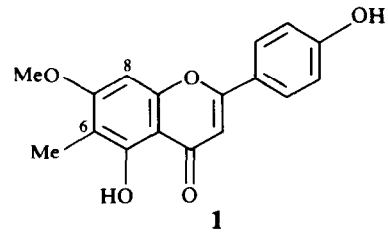
INTRODUCTION

Hypericum ericoides is a small shrub which grows exclusively in the east and south-east of Spain and in North Africa [1–3] and is used in folk medicine [1, 2]. Several flavonoids have been found in different species of *Hypericum* [4–6]; the xanthonolignoid kielcorin was recently isolated from *H. maculatum*, *H. calycinum* and *H. perforatum* [7]. We have also isolated four xanthones from *H. ericoides* [8]. As a continuation of this study, we report here on four more components of *H. ericoides*.

RESULTS AND DISCUSSION

Structure of 6-C-*methyl*-7-O-*methylapigenin* (*see Experimental*)

Compound **1** was identified as 6-*C*-methyl-7-*O*-methylapigenin by spectroscopic evidence. Isotopic molecular ions afforded the molecular formula $C_{17}H_{14}O_5$. Of the five oxygens, one is a methoxyl group as shown by a singlet at δ 3.89 for 3H in the ^{1}H NMR spectrum. Two oxygens belong to the flavone skeleton, one as a carbonyl group (IR ν_{max} 1655 cm^{-1}), another as an ether group (IR ν_{max} 1250 and 1140 cm^{-1}). The two remaining oxygens are phenolic groups, one located at C-5 (ring A), another at C-4' (ring B). The hydroxyl group located at C-5 is required by its usual singlet at δ 13.09 in the ^{1}H NMR spectrum, as shown by UV spectroscopy. **1** showed a band II at 275 nm, characteristic of a benzoyl moiety (ring A) in methanol, and it underwent a bathochromic shift with aluminium chloride, this spectrum being unchanged on adding hydrochloric acid, which indicates a 5-hydroxyl group [9]. The absence of a shift of band II either with sodium acetate or NaOAc–H_3BO_3 precludes the presence of a 7-hydroxyl group. The other phenolic hydroxyl group must be located at the 4'-position of ring B. Band I, characteristic of a cinnamoyl moiety, appeared at 331 nm and underwent a bathochromic shift with sodium methoxide without a decrease in intensity, which is characteristic of the presence of a 4-hydroxyl group [9]. This hydroxyl location was confirmed by the signals of H-2', H-6' and H-3', H-5' which appeared as doublets at δ 7.97 and 6.94 with splitting J = 8.75 Hz. The appearance of the fragment



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at *m/z* 121 (29.27%) confirmed monohydroxylation of ring B [10, 15]. The locations of the methyl (signal at δ 2.0, 3H, *s*) and methoxyl groups (signal at δ 3.89, 3H, *s*) should be such that the two remaining aromatic protons appear as singlets. Moreover, the methoxyl group may be placed at the 7-position on biogenetic grounds. There are only two possible structures consistent with these results, and they are with the methyl at the 6- or 8-position. However, the positive Gibbs reaction requires a phenol unsubstituted in the *p*-position and thus supports 6-substitution. This result was confirmed by ^{1}H NMR spectrum of the silyl derivative. The signal of proton 6 is the same in the 4'-silyl ether and 5,4'-silyl ether, but signals of protons 3 and 8 are different in these spectra [9]. Therefore, the spectrum of a mixture of 4'-silyl and 5,4'-silyl ethers of the 6-methyl isomer should give four singlets for H-3 and H-8 and the same spectrum of the 8-methyl isomer should give three singlets. In fact, there was a section of four singlets at δ 6.63, 6.59, 6.53 and 6.49.

Taxonomic interest and biogenetic role

C-Methylflavones are relatively rare, being found only in Pinaceae [11–13] of the Gymnospermae and in Didieriaceae [14–16] and Myrtaceae [17–18] of the Angiospermae. This is the fifth *C*-methylflavone mentioned in the literature [12] and is the first to be found in the Guttiferae.

EXPERIMENTAL

Plant material. Stems, leaves and flowers of *H. ericoides* were collected in Valencia (Spain) during July 1977 and classified by Professor Mansanet, Department of Botany, University of Valencia.

Extraction and fractionation. Powdered and dried stems, leaves and flowers of *H. ericoides* (5 g) were extracted successively with petrol (bp 40–60°), Et_2O and 96% EtOH. The Et_2O extract (35 g) was fractionated by K_2CO_3 and NaOH (5%) into neutral (15.7 g), phenolic (11.3 g) and acidic (1 g) fractions. The phenolic fraction was chromatographed over Si gel and gave on elution with C_6H_6–Et_2O (20:1) and (4:1), two crystalline products **1** (7 mg) and kiolcorin (30 mg). The alcoholic extract (350 g) was dissolved in cold H_2O and filtered. This aq. soln was extracted continuously and successively with Et_2O and isoamyl alcohol. The Et_2O extract was concd to *ca* 50 ml and on standing gave quercetin (1 g). The isoamyl extract was concd to dryness and redissolved in EtOH. EtOH concn gave on standing quercetin 3-galactoside (0.5 g).

The four known compounds were identified by mp and spectral (UV, IR, MS, ^{1}H NMR) comparison with lit. data. Quercetin 3-galactoside (hyperin) was further identified by acid hydrolysis to quercetin and galactose, the latter identified by PC and GC.

6-C-*Methyl*-7-O-*methylapigenin* (**1**). Yellow needles from MeOH, mp 284–286°. UV λ_{max}^{MeOH} 230 sh 275, 331 nm (log ϵ 4.06, 4.16), λ_{max}^{NaOMe} 241 sh, 275, 305 sh, 387 nm, λ_{max}^{NaOAc} 274, 300 sh, 386 nm, $\lambda_{max}^{NaOAc-H_3BO_3}$ 276, 336 nm, $\lambda_{max}^{AlCl_3}$ 264 sh, 288, 303, 354, 400 sh, $\lambda_{max}^{AlCl_3-HCl}$ 264 sh, 288, 302, 360 nm, Gibbs' test λ_{max} 690 nm. IR ν_{max}^{KBr} cm^{-1}: 3380, 3150, 2950, 1655, 1605, 1490, 1450, 1355, 1250, 1175, 1140, 830. MS 70 eV *m/z* (rel. int.) 298 $[M]^+$ (100), 297 $(M-1]^+$ (23.2), 283 $[M-15]^+$ (12.6), 280 $[M-18]^+$ (15.8), 269 $[M-CHO]^+$ (45.2), 268 $[M-CH_2O]^+$, (28.7), 255 $[M-CH_2-CO]^+$ (7.8), 239 $[M-CO-OMe]^+$ (6.5), 151 (10.3), 137 (12.6), 121 (29.27), 109 (13.8). ^{1}H NMR (90 MHz, DMSO-d_6): δ 13.12 (*s*, 5-OH), 7.97 (2H, *d*, J = 8.75 Hz, H-2′ and H-6′), 6.94 (2H, *d*, J = 8.75 Hz, H-3′ and H-5′), 6.87 (1H, *s*, H-8), 6.84 (1H, *s*, H-3), 3.89 (3H, *s*, OMe), 2.0 (3H, *s*, Me).

Mixture of 4′-silyl and 5,4′-silyl ethers of **1**. ^{1}H NMR (90 MHz, $CDCl_3$): δ 12.87 (*s*, 5-OH), 7.81 (2H, *d*, J = 8.75 Hz, H-2′ and H-6′), 6.96 (2H, *d*, J = 8.75 Hz, H-3′ and H-5′), 6.63 (*s*, H-8), 6.59 (*s*, H-3), 6.53 (*s*, H-3), 6.49 (*s*, H-8), 3.93 (3H, *s*, OMe), 2.11 (3H, *s*, Me). 4′-Silyl ether of **1** was prepared by exposing the above mixture to the atmosphere for 5 hr in the same measuring tube [9]. ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.81 (2H, *d*, J = 8.75 Hz, H-2′ and H-6′), 6.96 (2H, *d*, J = 8.75 Hz, H-3′ and H-5′), 6.60 (1H, *s*, H-3), 6.49 (1H, *s*, H-8), 3.93 (3H, *s*, OMe), 2.11 (3H, *s*, Me). The absence of the 5-OH signal is due to the interchange with deuterium.

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