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FLAVONOL METHYL ETHERS FROM *CHRYSOTHAMNUS VISCIDIFLORUS*

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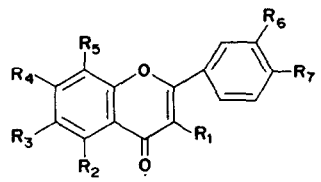
Key Word Index—*Chrysothamnus viscidiflorus*; Compositae; kaempferol and quercetin derivatives.

Abstract—Two new flavonols, 5,7,4′-trihydroxy-3,6,8,3′-tetramethoxyflavone and quercetagetin 3,5,6,3′-tetramethyl ether, were identified in leaves of *Chrysothamnus viscidiflorus*. Eight known methyl ethers based on kaempferol, quercetin or their 6-hydroxy derivatives were also detected.

RESULTS

Two new flavonol aglycones, 5,7,4′-trihydroxy-3,6,8,3′-tetramethoxyflavone (**1**) and quercetagetin 3,5,6,3′-tetramethyl ether (**2**), were characterized in connection with a biochemical systematic study of the genus *Chrysothamnus*. In addition, eight other aglycones were isolated: jaceidin (**3**), 6-hydroxy-kaempferol 3,6-dimethyl ether (**4**), quercetagetin 6,3′-dimethyl ether (**5**), quercetagetin 3,6-dimethyl ether (**6**), quercetin 3,3′-dimethyl ether (**7**), kaempferol 3-methyl ether (**8**), isorhamnetin (**9**), and quercetin 3-methyl ether (**10**).



(**1**) R_1, R_3, R_5, R_6 = OMe; R_2, R_4, R_7 = OH
(**2**) R_1, R_2, R_3, R_6 = OMe; R_4, R_7 = OH; R_5 = H
(**3**) R_1, R_3, R_6 = OMe; R_2, R_4, R_7 = OH; R_5 = H
(**4**) R_1, R_3 = OMe; R_2, R_4, R_7 = OH; R_5, R_6 = H
(**5**) R_3, R_6 = OMe; R_1, R_2, R_4, R_7 = OH; R_5 = H
(**6**) R_1, R_3 = OMe; R_2, R_4, R_6, R_7 = OH; R_5 = H
(**7**) R_1, R_6 = OMe; R_2, R_4, R_7 = OH; R_3, R_5 = H
(**8**) R_1 = OMe; R_2, R_4, R_7 = OH; R_3, R_5, R_6 = H
(**9**) R_6 = OMe; R_1, R_2, R_4, R_7 = OH; R_3, R_5 = H
(**10**) R_1 = OMe; R_2, R_4, R_7, R_6 = OH; R_3, R_5 = H

The mass spectrum of **1** exhibited a molecular ion at *m/e* 390 for $C_{19}H_{18}O_9$ in accord with a flavonol containing three hydroxyl and four methoxyl groups. The NMR spectrum confirmed the presence of these substituents: signals were observed for protons at C-2′, C-5′ and C-6′ (7·76, 6·85, 7·72, respectively* [1] and for the methoxyl groups (3·90, 3·89, 3·78, 3·76). The only question remaining concerned the position of the methoxyl groups. The presence of a hydroxyl group at the C-4′ is evident by the bathochromic shift (70 nm) and increase in intensity of Band I in the NaOMe spectrum relative to Band I of the MeOH spectrum [1]. Since the natural product appeared as a purple spot on paper when observed in UV light (366 nm), it must contain a hydroxyl group at C-5 and one of the methoxyl groups at C-3 [1]. The UV spectrum in $AlCl_3$–HCl confirmed the presence of a hydroxyl group at C-5 and oxygenation at C-6 (Band I at 368 nm relative to the MeOH spectrum Band I at 353 nm) [1,2]. The absence of a green precipitate when treated with Sr^{+2} indicated that a C-6 methoxyl group was present (the precipitate is observed for flavonoids containing a 5,6-dihydroxyl system) [3]. A methoxyl is assigned to C-3′ since a hypsochromic shift of only 9 nm was observed in Band I of the $AlCl_3$–HCl spectrum relative to Band I in $AlCl_3$ [1]. The remaining methoxyl group is assigned to C-8 rather than C-7 because the NaOMe UV spectrum exhibited a small peak at 346 nm characteristic for flavonoids containing a free 7-hydroxyl group; this assignment was further supported by comparison of the Band I's of the

* Values are given in ppm (δ scale) relative to TMS as internal standard.

NaOAc (378 nm) and NaOMe (423 nm) spectra (Band I in the NaOAc spectrum occurs at a shorter wavelength in flavonols having a free 7-hydroxyl group relative to Band I in the NaOMe spectrum). The NMR benzene-induced shifts observed for the methoxyl groups (+0·22, −0·03, +0·22, +0·42 Hz) are typical for methoxyls at the C-3, C-6, C-8 and C-3′, respectively [4]. The spectral findings establish that the new flavonol is 5,7,4′-trihydroxy-3,6,8,3′-tetramethoxyflavone.

The second new flavonol **2** also contains 4 methoxyls but only two hydroxyl groups (MS molecular ion at *m/e* 374). The NMR spectrum indicated the presence of aromatic protons (*δ* 7·78, 7·43, 6·74, 6·55) typical for those occurring at C-2′, C-3′, C-5′ and C-8 [1]. The presence of a hydroxyl group at the C-4′ is confirmed by the large bathochromic shift (55 nm) and increase in intensity of Band I in NaOMe relative to Band I in MeOH [1]. One of the methoxyls was assigned to C-5 since on paper in UV light the compound appeared blue changing to light yellow with fuming NH_3 vapours [1]. Since no hypsochromic shift of Band I in $AlCl_3$–HCl relative to Band I in $AlCl_3$ was observed, a methoxyl is assigned to C-3′. The benzene induced shifts (NMR), +0·13, +0·03, +0·38 Hz are typical for methoxyls at C-3, C-6, and C-3′, respectively [3]. Our data indicate that the methoxyl at C-5 shifts −0·07 Hz which is consistent with the shift previously observed for other flavonols methoxylated at C-5 and C-6 [5]. The remaining hydroxyl group must therefore be assigned to C-7. The structure for the new flavonol was confirmed by selectively demethylating the 5-position to give a compound identical (co-chromatography and UV spectra) with jaceidin.

Compounds **3–10** were also detected in *Chrysothamnus viscidiflorus*; these known compounds were identified in the usual way. Tables 1 and

Table 1. NMR spectra of *Chrysothamnus visicidiflorus* flavonol aglycones*

									OMe in CCl_4		
Compd	H-2′	H-6′	H-3′	H-5′	H-8	H-6	3-OMe	5-OMe	6-OMe	(Δ C_6D_6) 8-OMe	3′-OMe
1	7·76*d* (J = 2·5)	7·72*dd* (J = 2·0) (J = 5·0)	—	6·85*d* (J = 5·0)	—	—	3·90 (Δ + 0·22)	—	3·78 (Δ + 0·03)	3·76 (Δ + 0·22)	3·89 (Δ + 0·42)
2	7·58*d* (J = 2·0)	7·43*dd* (J = 1·5) (J = 8·0)	—	6·74*d* (J = 7·0)	6·55	—	3·91 (Δ + 0·13)	3·95 (Δ − 0·07)	3·80 (Δ + 0·03)	—	3·90 (Δ + 0·38)
3	7·62*d* (J = 2·0)	7·50*dd* (J = 1·5) (J = 7·0)	—	6·81*d* (J = 5·0)	6·48	—	3·89 (Δ + 0·07)	—	3·73 (Δ + 0·10)	—	3·88 (Δ + 0·36)
4	7·91*dd* (J = 1·5) (J = 5·0)	7·91*dd* (J = 1·5) (J = 5·0)	6·82*dd* (J = 1·5) (J = 6·0)	6·82*dd* (J = 1·5) (J = 6·0)	6·48	—	3·82 (Δ + 0·06)	—	3·71 (Δ + 0·10)	—	—
5	7·73*d* (J = 2·0)	7·56*dd* (J = 2·0) (J = 7·5)	—	6·82*d* (J = 5·0)	6·51	—	—	—	3·70 (Δ + 0·10)	—	3·85 (Δ + 0·30)
6	7·58*d* (J = 2·0)	7·51*dd* (J = 2·0) (J = 6·0)	—	6·83*d* (J = 4·0)	6·47	—	3·82 (Δ + 0·04)	—	3·67 (Δ + 0·09)	—	—
7	7·69*d* (J = 2·0)	7·58*dd* (J = 2·5) (J = 9·0)	—	6·89*d* (J = 8·5)	6·48*d* (J = 2·5)	6·19*d* (J = 2·5)	3·87 (Δ + 0·13)	—	—	—	3·84 (Δ + 0·49)
8	7·99*dd* (J = 2·0) (J = 8·5)	7·99*dd* (J = 2·0) (J = 8·5)	6·87*dd* (J = 2·0) (J = 8·5)	6·87*dd* (J = 2·0) (J = 8·5)	6·49*d* (J = 2·0)	6·17*d* (J = 2·0)	3·84 (Δ + 0·05)	—	—	—	—
9	7·73*d* (J = 2·0)	7·56*dd* (J = 2·5)	—	6·84*d* (J = 9·0)	6·55*d* (J = 2·0)	6·39*d* (J = 2·0)	—	—	—	—	3·87 (Δ + 1·31)
10	7·77*d* (J = 2·0)	7·58*dd* (J = 2·0) (J = 9·0)	—	6·38*d* (J = 9·0)	6·47*d* (J = 2·5)	6·16*d* (J = 2·5)	3·87 (Δ + 0·05)	—	—	—	—

* Spectra for compounds **1–6** were recorded on a Varian EM 360 while spectra for compounds **7–10** were recorded on a Varian A-60 spectrometer. All spectra were recorded in CCl_4 and C_6D_6 (only OMe signals are given for the latter solvent). Values are given in ppm (δ-scale) relative to TMS as an internal standard. Numbers in parentheses denote coupling constants in Hz. Signals are singlets unless otherwise noted: *d* (doublet), *dd* (double doublet).

Table 2. UV spectra (λ_{max} nm) of several *Chrysothamnus viscidiflorus* flavonol aglycones

Compd	Methanol	+ NaOMe	+ $AlCl_3$	+ $AlCl_3$–HCl	+ NaOAc	+ NaOAc–H_3BO_3
1	353 277 257	423 346 282	(420)* 377 (306) 286 265	(422) 368 287 264	378 280	
2	343 (264)	398 334 (269) 255	341 (264) (252)	343 (264) (249)	395 333 (268) (255)	344 (263)
4	341 270	401 327 275	(401) 365 306 278	(400) 365 304 276	396 330 274	347 271
5	370 (273) 255	404 334 dec. 265	431 (370) (304) 267	431 373 (303) 263	412 328 dec. 270	373 (366) 254
6	358 (266) 257	404 336 269	436 338 (306) 275	(401) 371 (300) (277) 265	386 (336) 266	380 (271) 263

* Numbers in parentheses denote shoulders.

Table 3. MS data for several flavonol aglycones of *Chrysothamnus viscidiflorus*

Compd	M+	M–H (M–1)	M–Me (M–15)	Other major fragments		
1	390* (100)†	389 (3)	375 (57·6)	376 (12·1)	247 (3)	197 (3) 141 (6)
2	374 (74·9)	373 (32·7)	359 (100)	360 (20·6)	355 (7·7)	343 (6·8) 316 (24·1) 173 (4·3)
4	330 (100)	329 (23·5)	305 (41·1)	287 (29·4)	165 (35·2)	149 (52·9)
5	346 (100)	345 (4)	331 (10·4)	328 (33·8)	317 (6·4)	304 (14) 303 (75·8) 151 (10·8)

* Numbers denote observed *m/e* values for fragment ions.
† Numbers in parentheses denote relative intensity of observed ion.

2 contain NMR and UV data for compounds not previously recorded with our standard procedures [1] and Table 3 presents MS data for several of them.

EXPERIMENTAL

A voucher specimen (Urbatsch *et al.*, 1470) is deposited in the University of Texas Herbarium (TEX). Air dried leaves, 200 g, (collected from U.S.A.: Arizona; Coconino Co.) of *Chrysothamnus viscidiflorus* were extracted at room temperature 1 × $CHCl_3$ for 24 hr and 1 × $CHCl_3$: EtOAc (3:1) for 24 hr. The combined extracts were chromatographed over a polyamide column (25 × 10 cm). Elution began with 30% EtOAc in $CHCl_3$ and continued until the bands ceased movement. Remaining compounds were eluted with $CHCl_3$–MeOH–MeCOEt (12:3:1). 8 fractions contained flavonoids. These fractions were appropriately rechromatographed using PC, Whatman 3 mm, (1 D 50% aq. HOAc or 15% aq. HOAc) or smaller polyamide columns (12 × 4 cm) with MeOH as the eluent until the flavonoids were isolated and sufficiently purified for the analyses. The compounds were eluted from the column in the same order as numbered in this paper. The UV and NMR procedures were those outlined in Mabry *et al.* [1].

Selective demethylation was accomplished by adding compound **2** (4·6 mg) to a soln of anhydrous $AlCl_3$ (0·10 g) in Et_2O (2 ml) and allowing this mixture to stand at room temp for 3 hr. The solvent was removed and the residue was treated with 2·5 ml cold 18% aq. HCl. The reaction mixture was warmed on a steam bath for 5 min, cooled, and extracted with $CHCl_3$. The residue for the $CHCl_3$ extract was purified using silica gel TLC. The purple (under 366 nm UV light) flavonoid was eluted from the silica gel; it was found by co-chromatography and UV spectral analysis to correspond to jaceidin.

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