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THREE FLAVONOIDS FROM *AGERATUM TOMENTOSUM* VAR. *BRACTEATUM*

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Abstract—The three new compounds, 5,6,7,8,3′,4′,5′-heptamethoxyflavanone, 2′,4′-dihydroxy-5,6,7,8,5′-pentamethoxyflavone and 7-hydroxy-5,6,8,5′-tetramethoxy-3′,4′-methylenedioxyflavone were isolated from the aerial parts of *Ageratum tomentosum* var *bracteatum*, together with five known flavones and one known flavanone The structures of the new compounds were elucidated by spectral analysis

INTRODUCTION

Phytochemical studies of the genus *Ageratum* (tribe Eupatorieae, Compositae), which is placed in the Piqueria group [1] have shown the presence of chromenes, triterpenes and flavones [2, 3] Certain flavonoids seem to be characteristic of the genus *Ageratum* [3, 4, 5]. These have been found in the Mexican species *A houstonianum*, *A strictum* and *A corymbosum* In continuation of our systematic chemical study of these plants [6, 7], we now report on *A tomentosum* (Benth) Hemsel var. *bracteatum*, from which we isolated nine flavonoids Three of them are new natural products Their structures were established by spectroscopic means

RESULTS AND DISCUSSION

Extraction of the aerial parts of *A. tomentosum* var *bracteatum* afforded a mixture of nine flavonoids (**1–9**), which were separated by chromatographic methods. Six of them eupalestin (**1**) [8], gardenin A methyl ether (**6**) [8], agecorynin C (**7**) [4], agecorynin A (**5**) [4], linderoflavone B (**2**) [9] and agehoustin A (**8**) [10] have been isolated previously In addition, three new flavonoids 5,6,7,8,3′,4′,5′-heptamethoxyflavanone (**4**), 2′,4′-dihydroxy-5,6,7,8,5′-pentamethoxyflavone (**9**) and 7-hydroxy-5,6,8,5′-tetramethoxy-3′,4′-methylenedioxyflavone (**3**) were isolated

The known compounds were identified by comparison of their spectral data and physical constants with those reported in the literature. 5,6,7,8,3′,4′,5′-Heptamethoxyflavanone (**4**), $C_{22}H_{26}O_9$ (M^+ m/z 434), was isolated as a yellow gum Both the UV (276, 330 nm) and the IR (1680, 1590 cm^{-1}) absorptions are typical of a flavanone lacking free hydroxyl groups [11] The ^1H NMR spectrum (Table 1) is similar to that of **6** [8], but instead of a H-3 signal, compound **4** shows an ABX system at δ2 87, 3 02 and 5 38, due to the H-2 and H-3 protons which are indicative of a flavanone nucleus The MS of **4** further confirms the structure, since it shows fragments at m/z 240 ($C_{11}H_{12}O_6$) and 225 ($C_{10}H_9O_6$) that are derived from the A-ring, and fragments at m/z 194 ($C_{11}H_{14}O_3$) and 195 ($C_{10}H_{11}O_4$) derived from the B-ring [11]

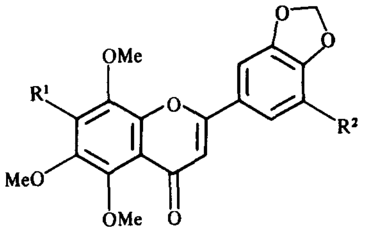
2′,4′-Dihydroxy-5,6,7,8,5′-pentamethoxyflavone (**9**), $C_{20}H_{20}O_9$ (M^+ at m/z 404), mp 239–241 was isolated as pale yellow crystals Both the IR (3420, 1650 cm^{-1}) and the UV (268, 370 nm) absorptions are typical of flavones [11] The ^1H NMR spectrum (Table 1) of **9** is similar to that of agecorynin D (**10**) [4], but lacks the C-5 hydrogen bonded hydroxyl group and shows an extra methoxyl signal, thus indicating that the four substituents of the A-ring in **9** are methoxyl groups The MS spectrum of **9** confirms the structure since it shows a peak at m/z 390 due to the loss of a methylene group from the molecular ion. The subsequent fragmentation is almost identical to that of **10** [4]

The third new compound 7-hydroxy-5,6,8,5′-tetramethoxy-3′,4′-methylenedioxyflavone (**3**) is a yellow crystalline substance, mp 188-190 , which was obtained from polar fractions The UV spectrum shows absorp-

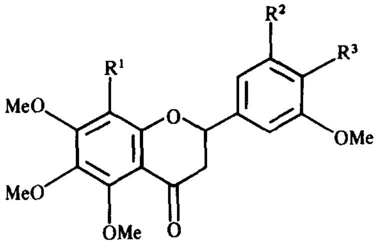
Table 1 ^1H NMR spectral data of compounds **3**, **4**, **9** and **10**

	3	**4***	**9**	**10** [8]
2 -H		5 38 *dd*		
3 -H	6 50 *s*	2 87 *dd*	6 64 *s*	6 59 *s*
3 -H		3 02 *dd*		
2′-H	7 20 *s*	6 68 *s*		
3′-H			7 25 *s*	7 15 *s*
6′-H	7 20 *s*	6 70 *s*	7 45 *s*	7 42 *s*
OMe	3 90 *s*	3 85 *s*	3 92 *s*	3 82 *s*
	3 95 *s*	3 86 *s*	3 95 *s* (6H)	3 84 *s*
	4 00 *s*	3 88 *s* (9H)	4 00 *s*	3 94 *s*
	4.05 *s*	3 90 *s*	4 10 *s*	4 03 *s*
		4 07 *s*		
OCH_2O	6 05 *s* (2H)			

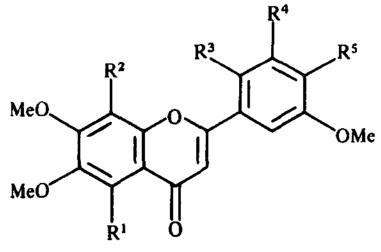
*Coupling constants are $J_{2,3}=5$, $J_{2,3}=11$, $J_{3,3}=16$ Hz



1 $R^1 = R^2 = OMe$
2 $R^1 = OMe$, $R^2 = H$
3 $R^1 = OH$, $R^2 = OMe$



4 $R^1 = R^2 = R^3 = OMe$
5 $R^1 = H$, $R^2 = R^3 = OCH_2O$



6 $R^1 = R^2 = R^4 = R^5 = OMe$, $R^3 = H$
7 $R^1 = R^2 = R^3 = R^5 = OMe$, $R^4 = H$
8 $R^1 = R^4 = R^5 = OMe$, $R^2 = R^3 = H$
9 $R^1 = R^2 = OMe$, $R^3 = R^5 = OH$, $R^4 = H$
10 $R^1 = R^3 = R^5 = OH$, $R^2 = OMe$, $R^4 = H$

tions at 246, 275, 330 nm and the IR shows bands at 1630, 1566, 1520 cm^{-1} which are typical of flavones [11] The ^1H NMR spectrum clearly indicates that **3** is a heptasubstituted flavone, since it shows two singlets at 6.50 (1H) and 7.20 (2H) ppm The one-proton singlet is due to H-3 [12] and the two-proton singlet to H-2′ and H-6′ The ^1H NMR spectrum also shows the presence of four methoxy groups, a two proton singlet of a methylenedioxy group and a broad one-proton singlet at 2.90 ppm which is exchangeable with D_2O. The intense (100%) $[M - 15]^+$ peak at m/z 387 in the MS indicates that the substituents at C-6 or C-8 or both are methoxy groups [13]. The other significant fragmentations are in full agreement with the structure. The molecular ion is at m/z 402 ($C_{20}H_{18}O_9$) and the fragments due to the A-ring appear at m/z 211 ($C_9H_7O_6$) and 183 ($C_8H_7O_5$), while those due to the B-ring appear at m/z 179 ($C_9H_7O_4$) and 176 ($C_{10}H_8O_3$). The position of the hydroxyl group at C-7 is confirmed by the bathochromic effect of the II-band (275–286 nm) in the UV spectrum of **3** when measured in the presence of sodium acetate [11].

EXPERIMENTAL

Ageratum tomentosum (Benth) Hemsel var *bracteatum* M. F. Johnson was collected near Telixtlahuaca, Oax México in September 1986 A specimen is deposited at the Herbarium of the Instituto de Biología UNAM México Voucher (MEXU 432418)

Dried leaves and flowers (150 g) were successively extracted with hexane and EtOAC and the extracts concd *in vacuo* Addition of a small amount of EtOAc to the hexane extract afforded an amorphus solid, which after purification by CC (hexane-EtOAc, 3 2) yielded 10 mg of **1** [8] Chromatography of the remaining hexane extracts (4 5 g) on silica gel (150 g) using hexane with increasing proportions of EtOAc gave (4 1) 9.8 mg of **4**, (1 1) 8 3 mg of **6** [8] and (3 7) 6 mg of **7** [4] Chromatography of the EtOAc extracts (6 01 g)on silica gel (210 g) using C_6H_6 with increasing proportions of EtOAc and MeOH gave (C_6H_6) 5 mg of **5** [4], C_6H_6-EtOAc, 4 1) 4 8 mg of **2** [9], (EtOAc) 4 mg of **8** [10], (EtOAc–MeOH 4 1) 10 mg of **9** and (EtOAc-MeOH, 1 1) 4 mg of **3**

5,6,7,8,3′,4′5′-Heptamethoxyflavanone (**4**). Gum UV λ_{max}^{MeOH} nm (ε) 276 (13 500), 330 (6000) IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1680, 1590, 1510, 832. EIMS 70 eV, m/z (rel int) 434 M^+ (41), 240 (90), 225 (100), 197 (45), 195 (20), 194 (20)

2′,4′-Dihydroxy-5,6,7,8,5′-pentamethoxyflavone (**9**) mp 239–241°, UV λ_{max}^{MeOH} nm (ε) 268 (10 600), 370 (10 500). IR ν_{max}^{KBr} cm^{-1} 3420, 1650, 1594, 1428. EIMS 70 eV, m/z (rel. int) 404 M^+ (8.5), 390 (75.4), 375 (100), 211 (18.2), 183 (16).

7-Hydroxy-5,6,8,5′-tetramethoxy-3′,4′-methylenedioxyflavone (**3**) UV λ_{max}^{MeOH} nm (ε) 246 (10 400), 275 (6100), 330 (10 500). IR ν_{max}^{nujol} cm^{-1} 3120, 1630, 1566 EIMS 70 eV m/z (rel int) 402 M^+ (29), 387 (100), 344 (26), 211 (8), 183 (10), 179 (16), 176 (15)

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