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NEW METHYLATED FLAVONES FROM *GOMPHRENA MARTIANA*

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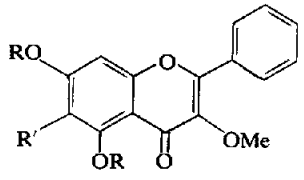
Key Word Index—*Gomphrena martiana*; Amaranthaceae; flavonoids; 3,5,6,7-tetramethoxyflavone; 3,6-dimethoxy-5,7-dihydroxyflavone; 3,5,7-trimethoxyflavone.

Abstract—Two new flavones, 3,5,6,7-tetramethoxyflavone and 3,6-dimethoxy-5,7-dihydroxyflavone together with 3,5,7-trimethoxyflavone have been identified from a whole plant extract of *Gomphrena martiana*.

We have previously reported [1] the isolation of 3,5-dimethoxy-6,7-methylenedioxyflavone (**1**), from *Gomphrena martiana* Moquin (Amaranthaceae). The present paper deals with the identification of two new naturally occurring flavones: 3,5,6,7-tetramethoxyflavone (**2**) and 3,6-dimethoxy-5,7-dihydroxyflavone (**3**), as well as the known 3,5,7-trimethoxyflavone (**4**) from the same plant.



2 R = Me, R' = OMe
3 R = H R' = OMe
4 R = Me, R' = H

The mother liquors from both precipitation and crystallization of 3,5-dimethoxy-6,7-methylenedioxyflavone (**1**) [1] were found to contain a mixture of three other flavonoids, which were separated chromatographically and characterized as follows. Compound **2**, $C_{19}H_{18}O_6$, mp 113–114° (MeOH—H_2O) was non-phenolic. A singlet at δ 6.77, typical for a proton in position 8, was observed in its ^{1}H NMR spectrum, as well as four singlets (δ 3.87, 3.92, 3.97 and 4.02, each 3H) indicating the presence of four OMe groups. Two multiplets at δ 7.50 and 8.08 integrating for two and three protons, respectively, were ascribed to an unsubstituted B ring. The signal of only one methoxyl was significantly shifted ($\simeq$0.7 ppm) in the ^{1}H NMR spectrum in benzene-d_6, whilst the other two were partially affected. Therefore, three OMe groups must be vicinal in ring A (5,6,7-trisubstitution); the fourth OMe was evidently attached to C-3, as was confirmed by the MS, which presented fragment A (*m/e* 210) in accordance with a ring A bearing three OMe groups and fragments corresponding to Ph (*m/e* 77) and PhCO (m/e 105) supporting the unsubstituted B ring. Fragment A-15 indicated the presence of one OMe either at position 6 or 8. The latter possibility was discarded because of the presence of an H-8 signal in the ^{1}H NMR spectrum. The structure of compound **2** is therefore 3,5,6,7-tetramethoxyflavone. This was confirmed by methylation of **3** to give a product identical with **2**. A synthesis of **2** has been previously reported [2].

Compound **3**, $C_{17}H_{14}O_6$, mp 175–176° (EtOH), was shown to be phenolic. Its UV spectrum indicated a free hydroxyl at position 5 since a bathochromic shift ($\Delta\lambda_I$ 19 nm) was observed in the presence of $AlCl_3$ and $AlCl_3$/HCl. Since on addition of NaOAc only a small bathochromic shift ($\Delta\lambda_{II}$ 1.5 nm) was observed, **3** was methylated to determine whether there was a free hydroxyl at C-7. The ^{1}H NMR spectrum of **2** showed the presence of four OMe groups, one of which was strongly shifted when recording the spectrum in benzene-d_6. This behaviour, typical for a methoxyl at C-7 [3], was not observed with **3**. The ^{1}H NMR spectrum of **3** showed the presence of two OMe groups (δ 3.87 and 4.05, each 3H singlet), one aromatic proton assigned to H-8 (6.58, one proton singlet) and an unsubstituted B ring (7.52 and 8.08, two complex multiplets integrating for 3 and 2H, respectively). The signal at δ 12.87 was ascribed to the 5-OH. The MS of **3** showed that one OMe group and two OH groups were located on ring A. The fragment at *m/e* 167 (A-15) accounted for one OMe located at either position 6 or 8. However, the presence of $M-H_2O$ and M − Me, the latter more important than M^+, supported a 6-methoxy-5,7-dihydroxyflavone structure [4]. The second OMe group must be attached at C-3. The presence of fragments at *m/e* 105 and 77 confirmed that ring B was unsubstituted. Thus, **3** must be 3,6-dimethoxy-5,7-dihydroxyflavone. This structure was confirmed by comparing the natural substance with a synthetic sample [5].

Compound **4**, $C_{18}H_{16}O_5$, mp 201–203° (MeOH), was non-phenolic. Its ^{1}H NMR spectrum suggested a

5,7-disubstituted A ring because of the appearance of two doublets at δ 6.33 and 6.50 showing *meta*-coupling ($J = 2$ Hz), each integrating for one proton. Signals at δ 3.88 and 3.96 (6 and 3H singlet, respectively) were attributable to three OMe groups. Since ring B was shown to be unsubstituted (δ 7.46, 3H multiplet and 8.02, 2H multiplet) and two OMe groups should be located at C-5 and C-7, the third OMe had to be at C-3. The MS confirmed the presence of two methoxyl groups in ring A(*m/e* 180) and an unsubstituted B ring (*m/e* 105 and 77). All these data were in agreement with the identity of **4** as 3,5,7-trimethoxyflavone. This structure was also confirmed by comparison with a synthetic sample prepared in our laboratory.

Compounds **2** and **3** are new naturally occurring substances, whilst **4** has been found only once before, in *Aniba riparia* (Lauraceae) [6]. A few chemical studies on the genus *Gomphrena* are known [7–9]. A recent report [9] deals with the isolation of 3,5,4′-trihydroxy-6,7-methylenedioxyflavone (gomphrenol) from *Gomphrena globosa*. This structure is closely related to that of 3,5-dimethoxy-6,7-methylenedioxyflavone **1** which we described from *G. martiana* [1]. Although flavonoids with a methylenedioxy group attached at the 6 and 7 positions are not common in nature, three compounds of this type have been isolated from the Amaranthaceae [1, 9, 10]. So it is of interest that flavones with this structure are present in two species of the genus *Gomphrena*. The occurrence of an unsubstituted B ring in all the flavones we have until now isolated from *G. martiana* is also noteworthy.

EXPERIMENTAL

General details have been previously described [1].

Isolation and identification of flavones. Dried and ground whole plant (2.2 kg) was extracted with petrol and concd to give a yellow ppt. which was removed by filtration. (Impure **2** was obtained from the filtrate by Si gel chromatography and purified by liquid chromatography.) The ppt. was succesively cryst. from EtOH yielding **1**; the residue (500 mg) obtained after evapn of mother liquors was chromatographed on a Si gel column using Cl_2CH_2 and Cl_2CH_2—EtOAc (19:1) as solvents. Three main fractions were collected. The first fraction was a mixture (320 mg) of two phenolic compounds, which were separated by liquid chromatography on a Si gel column using C_6H_6—Me_2CO (49:1) as eluent yielding **3** (90 mg) and another compound which has not been completely characterized. The second fraction (100 mg) was mainly impure **1**; the third was purified by PLC (C_6H_6—Me_2CO, 4:1) and the principal band rechromatographed on a dry Si gel column to give 10 mg of **4**.

3,5,6,7-*Tetramethoxyflavone* (**2**). Mp 113–114° (MeOH—H_2O). UV λ_{max}^{MeOH} nm: 241, 261 and 312. No changes were observed when $AlCl_3$, $AlCl_3$—HCl, NaOMe, NaOAc and NaOAc—H_3BO_3 were added. ^{1}H NMR ($CDCl_3$, 60 MHz): δ 3.87 (3 H, *s*, OMe), 3.92 (3H, *s*, OMe), 3.97 (3H, *s*, OMe), 4.02 (3H, *s*, OMe), 6.77 (1H, *s*, H-8), 7.50 (3H, *m*, H-3′, 4′ and 5′), 8.08 (2H, *m*, H-2′ and 6′); (C_6D_6): δ 3.27 (3H, *s*, OMe), 3.78 (3H, *s*, OMe), 3.83 (3H, *s*, OMe), 4.07 (3H, *s*, OMe). MS *m/e* (%): 344 (M+2, 1.80); 343 (M+1, 11.30); 342 (M, 56.70); 341 (M−1, 46.10); 328 (M−14, 20.47); 327 (M−15, 100); 324 (M−18, 3.50); 323 (M−19, 14.80); 284 (19.30); 283 (12.20); 211 (A+H, 3.30); 210 (A, 4.70); 195 (A−15, 11.90); 167 (A−15−28, 18.60); 105 (PhCO, 21.00); 77 (Ph, 12.80).

3,6-*Dimethoxy*-5,7-*dihydroxyflavone* (**3**). Mp 175–176° (EtOH). UV λ_{max}^{MeOH} nm: 270.5, 323; $AlCl_3$: 281.5, 342; $AlCl_3$+HCl: 281.5, 342; NaOMe: 270.5, 360; NaOAc: 270.5, 360; NaOAc—H_3BO_3 270.5, 323. ^{1}H NMR ($CDCl_3$, 60 MHz): δ 3.87 (3H, *s*, OMe C-3), 4.05 (3H, *s*, OMe C-6), 6.58 (1H, *s*, H-8), 7.52 (3H, *m*, H-3′,4′ and 5′), 8.08 (2H, *m*, H-2′ and 6′), 12.87 (1H, *s*, 5-OH); (C_6D_6): δ 3.65; 3.67 (6H, each *s*, 2 OMe). MS *m/e* (%): 316 (M+2, 2,50); 315 (M+1), 18.80); 314 (M, 100); 313 (M−1, 43.10); 299 (M−15, 41.70); 296 (M−18, 28.10); 295 (M−19, 17.10); 271 (M−43, 40.90); 253 (12.30); 228 (11.20); 167 ($C_8H_6O_5$−15, 6.10); 105 (PhCO, 20.90); 77 (C_6H_5, 13.40).

3,5,7-*Trimethoxyflavone* (**4**). Mp 201–203° (MeOH). UV λ_{max}^{MeOH} nm: 241, 262, 297.5, 323.5. No shifts were observed with the usual UV reagents. ^{1}H NMR ($CDCl_3$): δ 3.88 (6H, *s*, 2 OMe), 3.96 (3H, *s*, 1 OMe), 6.33 (1H, *d*, $J = 2$ Hz, H-6), 6.50 (1H, *d*, $J = 2$ Hz, H-8), 7.46 (3H, *m*, H-3′,4′ and 5′), 8.04 (2H, *m*, H-2′ and 6′). MS *m/e* (%): 314 (M+2, 1.20); 313 (M+1, 10.90); 312 (M, 85.30); 311 (M−1, 100); 297 (M−15, 6.70); 294 (M−18, 8.30); 293 (M−19, 37); 181 (A+H, 7.70); 180 (A, 5.10); 105 (PhCO, 26.10); 77 (Ph, 26.90).

Methylation of **3**. This was performed with Me_2SO_4—KOH in the usual manner yielding **2**.

Synthesis of **4**. This was accomplished from 2,4,6-trihydroxy-*w*-methoxyacetophenone [11] and benzoic anhydride/sodium benzoate by a literature method [12].

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REFERENCES

1. Buschi, C. A., Pomilio, A. B. and Gros. E. G. (1979) *Phytochemistry* **18,** 1249.
2. Asakawa, Y., Genjida, F. and Suga, T. (1971) *Bull. Chem. Soc. Jpn* **44,** 297.
3. Wilson, R. G. (1968) *Tetrahedron* **24,** 1407.
4. Goudard, M., Favre-Bonvin, J., Lebreton, P. and Chopin, J. (1978) *Phytochemistry* **17,** 145.
5. Goudard, M. and Chopin, J. (1976) *C. R.* **282,** 683.
6. Franca, N. C., Gottlieb, O. R., Magalhães, M. T., Mendes, P. H., Maia, J. G. S., Da Silva, M. L. and Gottlieb, H. E. (1976) *Phytochemistry* **15,** 572.
7. Minale, L., Piatelli, M. and De Stefano, S. (1967) *Phytochemistry* **6,** 703.
8. Piatelli, M. and Minale, L. (1964) *Phytochemistry* **3,** 547.
9. Bouillant, M. L., Redolfi, P., Cantisani, A. and Chopin, J. (1978) *Phytochemistry* **17,** 2138.
10. Crabbe, P. and Djerassi, C. (1958). *J. Am. Chem. Soc.* **80,** 5258.
11. Slater, W. K. and Stephen, H. (1920) *J. Chem. Soc.* **117,** 309.
12. Robinson, R. and Venkataraman, K. (1929) *J. Chem. Soc.* **126,** 61.