Pergamon

Phytochemistry, Vol. 45, No. 8, pp. 1697–1699, 1997

0031-9422/97 $17.00+0.00

PII: S0031-9422(96)00729-7

METHOXYFLAVONES FROM *FICUS MAXIMA**

GASPAR DIAZ M., ALBERTO C. ARRUDA,† MARA S. P. ARRUDA and ADOLFO H. MÜLLER

Laboratório de Química-Pesquisa, Universidade Federal do Pará, P.O. Box 8600, 66075-970, Belém, PA, Brazil

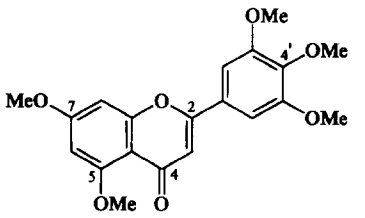
(*Received* 10 *September* 1996)

Key Word Index—*Ficus maxima*; Moraceae; leaves; new methoxyflavone

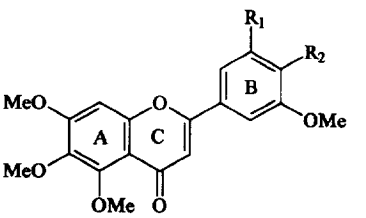
Abstract—Four methoxyflavones were obtained from the leaves of *Ficus maxima*, one of which is the novel 5,6,7,3′,5′-pentamethoxy-4′-prenyloxyflavone. Their structures were determined on the basis of spectral data.

INTRODUCTION

The genus *Ficus* (Moraceae) is predominantly distributed in the tropics and sub-tropics. *Ficus maxima*, popular name caxinguba, is a native plant of Brazilian's Amazonian rain forest. It has been used in the folk medicine as an anthelmintic and anti-rheumatic agent, and like *F. insipida* as anti-anaemic and anti-pyretic [1]. There are no reports of any phytochemical studies on this species. In this paper we report the isolation and structural elucidation of a novel methoxyflavone, with a prenyloxy substituent, from the leaves of *F. maxima*. Compounds of this type have not previously been recorded in the Moraceae.



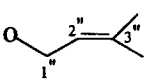
1



2 $R_1 + R_2 = OCH_2O$

3 $R_1 = R_2 = OMe$

4 $R_1 = OMe$, R_2 =



RESULTS AND DISCUSSION

Four compounds were obtained from the leaves by the initial extraction into hexane and subsequent filtration into ethyl acetate followed by column chromatography. The known compounds, 5,7,3′,4′,5′-pentamethoxyflavone (**1**), 5,6,7,5′-tetramethoxy-3′,4′-methylenedioxyflavone (**2**), 5,6,7,3′,4′,5′-hexamethoxyflavone (**3**) were identified by their mp, UV, IR, ^{1}H NMR, ^{13}C NMR and mass spectral data which were in good agreement with those reported in the literature [2–4].

The flavone **4** showed IR absorption bands at 1636, 1600, 1505 cm^{-1} typical of a non-phenolic flavone [5]. The UV spectrum was consistent with a flavonoid exhibiting two absorptions at 275 and 317 nm, assigned to bands II and I respectively [6]. The ^{1}H NMR spectrum of **4**, showed signals for five aromatic methoxy groups, a singlet at δ 7.06 assigned to two equivalent protons (H-2′ and H-6′) and two sharp singlets at δ 6.79 and 6.61 assigned to H-8 and H-3, respectively. The remaining signals at δ 4.58 (2H, *d*, J = 7.1 Hz), 5.56 (1H, *t*, J = 7.1 Hz), 1.75 (3H, *s*) and 1.68 (3H, *s*) were attributed to a prenyloxy substituent. The most obvious feature on the ^{1}H NMR spectrum was the coincidence of the H-2′ and H-6′ resonances. As a consequence, ring B must be symmetrically substituted and two of the methoxy groups should be placed at C-3′ and C-5′. One of the three remaining methoxy groups was located at C-5, as no aromatic

*Based in part on M.Sc. dissertation that will be presented by G.D.M. to the Universidade Federal do Pará, Belém-PA, Brazil.

†Author to whom correspondence should be addressed.

Table 1. ^{13}C NMR spectral data of flavone **4**

C	δ_C
2	161.12
3	108.18
4	177.12
5	154.50
6	140.03
7	157.77
8	96.28
9	152.62
10	112.92
1′	126.75
2′	103.59
3′	154.05
4′	140.47
5′	154.05
6′	103.59
1″	69.65
2″	120.36
3″	138.61
2 Me	25.78
OMe	62.16
OMe	61.49
2 OMe	56.41
OMe	56.32

Solution in $CDCl_3$ referenced to $CHCl_3$, 77.23 ppm.

protons were observed around δ 8.0 a chemical shift characteristic of an H-5 adjacent to a carbonyl [7].

The EI-mass spectrum showed a molecular ion peak at *m/z* 456 (3) according to the $C_{25}H_{28}O_8$ molecular formula. The base peak at *m/z* 373 $[M-83]^+$, reflected the facile loss of the prenyl $[C_5H_8]$ followed by the loss of a radical $[CH_3]$ [8] (Scheme 1). The *O*-prenyl group could not be located at C-6 due to the absence of the *m/z* 387 and 192 fragments, the former appearing as the base peak, that could be attributed to the stable quinonoid ion formation and the latter by the retro-Diels–Alder reaction. The *O*-prenyl group on ring-**B** at C-4′ was confirmed on base to the observation of the *m/z* 178 (9), 181 (9) and 195 (10) fragments, which would be expected for this type of compound [8] (Scheme 1).

The ^{13}C NMR spectrum (Table 1) of **4** was in total agreement with the 5,6,7-trimethoxy substitution in the ring A, suggested for the MS, appearing two signals down-field, δ 62.16 and 61.49, chemicals shift characteristic of methoxy groups di-*ortho* substituted [9]. With this substitution pattern in the ring A, obviously the remaining prenyloxy substituent was confirmed on ring B at C-4′. On the basis of these observations along with the characteristic mass spectral fragmentation [8], **4** was assigned to be the structure 5,6,7,3′,5′-pentamethoxy-4′-prenyloxyflavone.

EXPERIMENTAL

General. Mps uncorr. IR and UV were recorded in $CHCl_3$ and MeOH, respectively. ^1H and ^{13}C NMR spectra were recorded at 300 and 75.4 MHz, respectively, in $CDCl_3$. EIMS were obtained by direct probe insertion at 70 eV. Silica gel 60 GF_{254} (Merck 7730) was used for TLC, silica gel 60 PF_{254} (Merck 7747) for PTLC and silica gel 60 (Merck 7734) for CC.

Plant material. Ficus maxima was collected at São Miguel do Guamá county, State of Pará, Brazil and identified by Dr. Maria Elisabeth van den Berg in Botanic Department of Museu Paraense Emílio Goeldi, Belém, Pará.

Extraction and isolation of flavonoids. The ground dried leaves (1.9 kg) were extracted to drain with hexane, CH_2Cl_2, and MeOH, successively. The hexane extract (42.7 g) was submitted to filtration over silica gel using CH_2Cl_2, EtOAc and MeOH as eluent. Fr. EtOAc after CC over silica gel eluting with hexane–EtOAc mixts of increasing polarity afforded 12 frs. Fr. 6 eluted with hexane–EtOAc (20%) contained the flavone **1**, while fr. 7 eluted with hexane–EtOAc (30%) contained the flavones **2–4**. Frs 6 and 7 were purified by repeated CC on silica gel with mixts of 2–40% EtOAc in hexane followed by PTLC (silica gel; hexane–EtOAc, 1:1, several runs) to give **1** (12 mg), **3** (33 mg), **4** (18 mg) and **2** (25 mg).

5,6,7,3′,5′-*Pentamethoxy-4′-(prenyloxy)flavone* (**4**). Needles, mp 137–138 (MeOH). UV λ_{max}^{MeOH} nm: 275 and 317. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2925, 2875, 1636, 1600, 1419, 1351, 1249, 1121. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.68 (3H, *s*, H-4″), 1.75 (3H, *s*, H-5″), 3.91 (3H, *s*, OMe), 3.93 (6H, *s*, 2 OMe), 3.98 (6H, *s*, 2 OMe), 4.58 (2H, *d*, J = 7.1 Hz, H-1″), 5.56 (1H, *t*, J = 7.1 Hz, H-2″), 6.61 (1H, *s*, H-3), 6.79 (1H, *s*, H-8), 7.06 (2H, *s*, H-2′ and H-6′). ^{13}C NMR: see Table 1. EIMS *m/z* (rel. int.): 456 $[M]^+$ (2), 388 (52), 373 (100), 357 (36), 342 (30), 329 (14), 195 (10), 181 (9), 178 (9), 167 (30), 139 (7).

Acknowledgements—The authors are grateful to Financiadora de Estudos e Projetos (FINEP) and Coordenação de Aperfeiçoamento de Ensino Superior (CAPES) for financial support. NMR studies were performed in the Universidade Federal do Pará, NMR laboratory. We also thank to LEMAR (Laboratório de Massa de Alta Resolução)–LNP–PADETEC, Universidade Federal do Ceará, for mass spectra.

REFERENCES

1. Berg, M. E. van den., *Etnobotânica de Magnoliopsida na Amazônia* (unpublished) Botanic Department of Museu Paraense Emilio Goeldi-Belém-PA, Brazil.
2. Fraser, A. W. and Lewis, J. R., *Phytochemistry*, 1974, **13**, 1564.
3. Chen, C. C., Chen, Y. P., Hsu, H. Y. and Chen, Y. L., *Chemical and Pharmaceutical Bulletin*, 1984, **32**, 166.

4. Gonzales, A. G., Aguiar, Z. E., Grillo, T. A., Luis, J. G., Rivera, A. and Calle, J. M., *Phytochemistry*, 1991, **30**, 1269.
5. Mabry, T. J., Markham, K. R. and Thomas, M. B., *The Systematic Identification of Flavonoids*. Springer, New York, 1970.
6. Markhan, K. R., *Techniques of Flavonoid Identification*. Academic Press, London, 1982.
7. Markham, K. R. and Mabry, T. J., in *The Flavonoids*, eds J. B. Harborne, T. J. Mabry and H. H. Mabry. Academic Press, New York, 1975, pp. 63–64.
8. Mabry, T. J. and Markham, K. R., in *The Flavonoids*, eds J. B. Harborne, T. J. Mabry and H. H. Mabry. Academic Press, New York, 1975, pp. 82–90.
9. Iinuma, M., Matsuura, S. and Kusuda, K., *Chemical and Pharmaceutical Bulletin*, 1980. **28**, 708.