



FLAVONES AND ISOFLAVONES FROM *MILLETTIA ICHTHYOCHTONA*

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Key Word Index—*Millettia ichthyochtona*; Leguminosae; leaves; furanoflavone; pyrano-isoflavones.

Abstract—The leaves of *Millettia ichthyochtona* afforded, besides jamaicin, a new furanoflavone and a new pyranoisoflavone. Their structures were established by mass and NMR spectroscopy, especially NOE and HMBC experiments. © 1998 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

Millettia ichthyochtona is a tree, 5–10 m high, with pinnate leaves and white flowers, growing frequently in North and Middle Vietnam. The seeds serve as a fishpoison and insecticide [1]. *Millettia* species are known to contain flavones and isoflavones with annelated furan and pyran rings [2–4]. The constituents of *M. ichthyochtona* have not been investigated until now. In continuation of our studies on Vietnamese plants [5], we now report the isolation and structural elucidation of three flavones and isoflavones, respectively, from the leaves of this species.

RESULTS AND DISCUSSION

The *n*-hexane extract of the leaves afforded, upon repeated silica gel chromatography, three compounds belonging to the flavonoid and isoflavonoid class. Compound **1** (C₂₂H₁₈O₆, [M]⁺ *m/z* 378) was identified as the dimethylpyranoisoflavone, jamaicin, by comparison of its mass, ¹H and ¹³C NMR spectra with reference data. This compound is known from *M. ferruginea* [6].

Compound **2** showed a [M]⁺ at *m/z* 394 corresponding to the elemental composition C₂₃H₂₂O₆. In the NMR spectra (Tables 1 and 2), the significant oxygen-bearing methine group at δ_C 154.1 and δ_H 7.91 characterizes an isoflavone. The proton spectrum additionally exhibits a dimethylpyran ring with a 6H singlet at δ 1.49 and two olefinic doublets at δ 5.74 and 6.45 (*J* = 9.9 Hz). The placement of the three

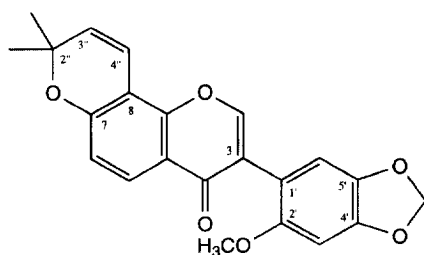
Table 1. ¹H spectral data of compounds **1–3** (CDCl₃, 300 MHz)

	1	2	3
2	7.91 <i>s</i>	7.91 <i>s</i>	—
5	8.05 <i>d</i> (8.6)	7.88 <i>s</i>	7.56 <i>s</i>
6	6.81 <i>d</i> (8.6)	—	—
8	—	6.79 <i>s</i>	—
2'	—	—	8.14 <i>dd</i> 7.9/1.2
3'	6.62 <i>s</i>	6.63 <i>s</i>	7.56*
4'	—	—	7.53*
5'	6.83 <i>s</i>	—	7.56*
6'	—	6.94 <i>s</i>	8.14 <i>dd</i> 7.9/1.2
2''	—	—	7.77 <i>d</i> 1.9
3''	5.72 <i>d</i> (9.8)	5.74 <i>d</i> (9.9)	7.18 <i>d</i> 1.9
4''	6.85 <i>d</i> (9.8)	6.45 <i>d</i> (9.9)	—
2''-Me ₂	1.50 <i>s</i>	1.49 <i>s</i>	—
3-OMe	—	—	3.93
6-OMe	—	—	4.11
2'-OMe	3.73 <i>s</i>	3.78 <i>s</i>	—
4'-OMe	—	3.93 <i>s</i>	—
5'-OMe	—	3.86 <i>s</i>	—
OCH ₂ O	5.96 <i>s</i>	—	—

* Overlapped.

methoxyl groups (three 3H singlets at δ 3.78, 3.86 and 3.93) at positions 2', 4' and 5' in ring B was established from the NOE difference spectra (Fig. 1). The residual aromatic protons of ring A appear as singlets, thus giving in contrast to structure **1**, a linear arrangement of the three annelated rings. Another compound exhibiting such a skeleton is auriculasin isolated from *M. auriculata* [3]. The structure of **2** with the new 2',4',5'-trimethoxy substitution pattern was confirmed by

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Table 2. ^{13}C spectral data of compounds 1–3 in CDCl_3 (125 MHz)

	1	2*	3
2	153.8	154.1	154.6
3	121.9	121.5	141.5
4	175.7	175.7	174.8
5	126.7	123.6	99.8
6	115.0	119.7	144.1
7	152.9†	157.5†	148.1
8	109.2	104.0	118.7
9	157.1	157.9†	144.9
10	118.3	118.7	120.4
1'	112.8	112.4	131.0
2'	152.3†	151.9	128.3
3'	95.4	98.5	128.6
4'	141.1	149.8	130.5
5'	148.3	143.1	128.6
6'	111.2	115.4	128.3
2''	77.6	77.8	145.9
3''	115.0	131.6	104.7
4''	130.2	121.4	—
2''-Me ₂	28.1	28.4	—
3-OMe	—	—	60.2
6-OMe	—	—	56.5
2'-OMe	56.9	56.9	—
4'-OMe	—	56.2	—
5'-OMe	—	56.5	—
O—CH ₂ —O	101.4	—	—

* 75 MHz.

† Assignments interchangeable.

analysis of the CH-long-range correlations and NOE effects (Figs 1 and 2).

The HR mass spectrum of compound 3 gave the $[\text{M}]^+$ at m/z 322 with the molecular formula $\text{C}_{19}\text{H}_{14}\text{O}_5$. Analysis of the NMR spectra (Tables 1 and 2) reveals the presence of two methoxyl groups, an unsubstituted ring B and an anellated furan ring with the characteristic proton doublets at δ 7.77 and 7.18 ($J = 2$ Hz). The methoxyl group at δ 3.93 is located neighbouring the phenyl ring B, which follows from an NOE effect between this methoxyl group and H-2'/6' at δ 8.14. Additionally, these methoxyl protons give a $^3J_{\text{CH}}$ -correlation to the carbon at δ 141.5 (C-3), thus locating it in position 3 of a flavone and excluding a 2-methoxylated isoflavone, which would possess a higher carbon shift in the di-*O*-substituted position 2. The

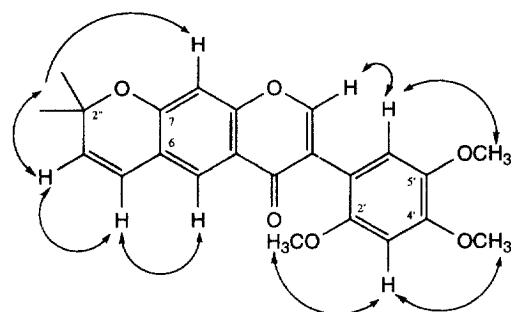


Fig. 1. NOE-effects observed in NOE difference spectra of compound 2.

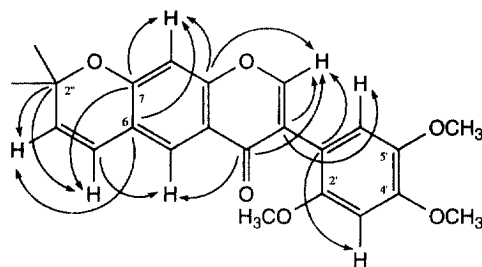


Fig. 2. Significant CH-long-range correlations observed in HMBC of compound 2.

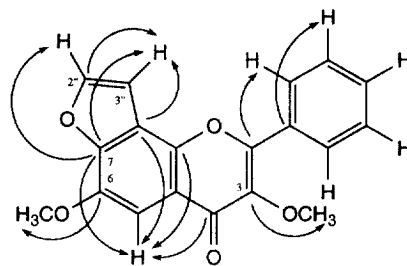


Fig. 3. Significant CH-long-range correlations observed in HMBC of compound 3.

second methoxyl group at δ 4.11 is located at C-6, because it gives an NOE effect to the aromatic singlet at δ 7.56, on account of its $^3J_{\text{CH}}$ -correlation to the carbonyl carbon C-4 located at position 5. Finally, the remaining positions 7 and 8 of ring A are occupied by the furan ring, resulting in the new structure 3,6-dimethoxyfuran[4'',5'': 8, 7] flavone, as confirmed by full analysis of the HMBC spectrum (Fig. 3). The 3,4'-dimethoxy isomer of 3 is known from *Derris mollis* [7].

Additionally, the triterpene, taraxerone, was isolated from the leaves and identified by comparison of its mass and NMR spectra with reference data [8].

EXPERIMENTAL

EI-MS: 70 eV. CC: silica gel 60, 230–400 mesh ASTM.

Plant material

Leaves and branches of *M. ichthyochtona* Drake were collected in the National Park Cuc phuong, Province Ninh binh, North Vietnam, in October 1994 and identified by Dr Tran Dinh Dai. A voucher specimen is deposited at the Institute of Ecology of the National Centre for Scientific Research and Technology, Hanoi, Vietnam.

Extraction and isolation

Dried and powdered leaves (47 g) were extracted with *n*-hexane at room temp. and the solvent removed under red. pres. The residue obtained (1.3 g) was chromatographed on silica gel (35 g) using *n*-hexane–EtOAc mixt. of increasing polarity. The frs eluting with 15% EtOAc were recrystallized from EtOAc to yield 18 mg of 3.

Dried and powdered leaves and branches (1.64 kg) were extracted 3 × with 95% aq. MeOH. The aq. soln, which remained after evapn of the organic solvent under red. pres., was extracted 3 × with *n*-hexane and 3 × with CHCl₃ to yield 33 g *n*-hexane extract and 19.5 g CHCl₃ extract. The *n*-hexane extract (13 g) was separated on silica gel (150 g) with *n*-hexane–EtOAc mixt. of increasing polarity. From the frs eluting with 5% EtOAc, 20 mg taraxerone were obtained after recrystallization from 5% EtOAc in *n*-hexane (mp 167–168°). The CHCl₃ extract (19.5 g) was chromatographed on silica gel (200 g) with a gradient of 20–40% EtOAc in *n*-hexane (60 frs of 50 ml). Frs 17–24, eluted with 30% EtOAc, gave 10 mg of 1. Frs 36–43, eluted with 35% EtOAc, yielded 64 mg of 2.

Jamaicin (1). Amorphous. MS *m/z* (rel. int.): 378 [M]⁺ (100), 363 [M – Me]⁺ (67), 347 [M – OMe]⁺ (53), 187 (13). ¹H NMR: Table 1. ¹³C NMR: Table 2.

2',4',5'-Trimethoxy-2'',2''-dimethylpyrano[5'',6'':6,7]isoflavone (2). Needles from EtOAc, mp 181–183°. UV λ_{max}^{MeOH} nm (log ε): 260 (4.48), 229 (4.59). IR ν_{max}^{KBr} (cm⁻¹): 3091, 2963, 2926, 2830, 1646, 1615, 1520, 1477, 1280, 1204, 1138, 1108, 1032, 899, 843, 816, 793.

MS *m/z* (rel. int.): 394 [M]⁺ (100), 379 [M – Me]⁺ (62), 363 [M – OMe]⁺ (22), 349 (14), 321 (4), 203 (5), 189 (11), 168 (7); HRMS 394.1407 [M]⁺ (C₂₃H₂₂O₆ requires 394.1416). ¹H NMR: Table 1. ¹³C NMR: Table 2.

3,6-Dimethoxyfurano[4'',5'':8,7]flavone (3). Rhombic crystals from EtOAc, mp 188–190°. UV λ_{max}^{EtOH} nm (log ε): 308 (4.96), 260 (5.06), 220 (5.27). IR ν_{max}^{CHCl₃} (cm⁻¹): 2939, 2844, 1613, 1590, 1570, 1484, 1445, 1381, 1350, 1310, 1175, 1142, 1068, 1052, 961, 924, 883. MS *m/z* (rel. int.): 322 [M]⁺ (58), 321 [M – H]⁺ (100), 303 [M – H – H₂O]⁺ (13), 261 (7), 191 (7), 190 [RDA-product]⁺ (17), 162 (12), 149 (9), 147 (8), 119 (9), 105 (7); HRMS 322.0834 [M]⁺ (C₁₉H₁₄O₅ requires 322.0841). ¹H NMR: Table 1. ¹³C NMR: Table 2.

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