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Article

Coumarins and Alkaloids from the Stems of *Metrodorea Flavida*

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Uma nova cumarina , a 5,6-metilenodioxi-7,8-dimetoxicumarina, foi isolada a partir dos galhos de *Metrodorea flavida*, juntamente com outras cumarinas e alcalóides conhecidos. As estruturas das substâncias isoladas foram definidas por análises de seus dados espectrais , bem como por comparação com dados da literatura.

A new coumarin, 5,6-methylenedioxy-7,8-dimethoxycoumarin has been isolated from the stems of *Metrodorea flavida*, as well as known coumarins and alkaloids. The structures of the new and the known compounds were established by spectral data and by comparison with the literature data.

Keywords: Metrodorea flavida, *Rutaceae, coumarins, alkaloids*

Introduction

In a previous paper, we reported the characterization of a new coumarin, 8-(2,3-dihydroxy-3-methylbutyloxy)-6,7-methylenedioxycoumarin, together with known furocoumarins and a furofuran lignan, which were isolated from the leaves of *Metrodorea flavida*[1]. In continuation of our phytochemical studies on the constituents of this species, we report from the stem the isolation and structural elucidation of a new coumarin 5,6-methylenedioxy-7,8-dimethoxycoumarin (**1**), in addition to the known compounds: scoparone (**2**)[2]; 6,7-methylenedioxy-8-methoxycoumarin (**3**)[3]; xanthotoxin (**4**)[4]; isopimpinellin (**5**)[4]; imperatorin (**6**)[4]; braylin (**7**)[5]; γ-fagarine (**8**)[6]; kokusaginine (**9**)[7] ; maculin (**10**)[8]; syringic aldehyde (**11**)[9]; rutaecarpine (**12**)[10]; sitosterol and lupeol.

All the compounds were isolated by chromatographic techniques. The structural elucidation of these compounds were based on spectrometric data, especially IR, ^{1}H NMR and ^{13}C NMR, involving comparison with the literature data.

Experimental

Equipment

Mps uncorr. IR were recorded in KBr discs. ^{1}H and ^{13}C-NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ on a Varian GEMINI 300 instrument and at 400 and 100 MHz, in DMSO, on a Brucker ARX 400 instrument. EIMS were obtained by direct probe insertion at 70 eV.

Plant material

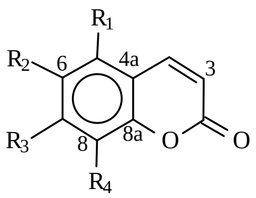
Metrodorea flavida was collected in Paragominas, State of Pará, Brazil, in December 1991. A voucher specimen is deposited at the Herbarium of the CPATU-EMBRAPA, Belém, Brazil.

Extraction and isolation

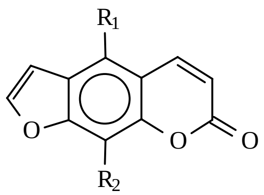
After drying, stems (231 g) were ground and percolated with hexane and CH_2Cl_2, successively. The concd. hexane extract (3.5 g) was submitted to CC using silica gel 60 Merck (particula size 0.063-0.200 mm) packed in hexane. Elution was performed with a gradient of hexane, Me_2CO and MeOH, affording 22 frs. The frs 3 and 7 after prep. TLC (silica gel and hexane- CH_2Cl_2- MeOH/10:10:0.1) yielded lupeol and sitosterol, respectively.

Fr. 12 was rechromatographed on silica gel using gradients of hexane, CH_2Cl_2 and MeOH. Those frs. containing homogeneous components, as judged by TLC, were combined and the solvent removed. Frs. 12/9-12 and 12/14-17 subjected to prep. TLC on silica gel (hexane-Me_2CO/75:25) afforded **6** (31.4 mg) and **12** (7.5 mg) , respectively. Fr.17 was subjected to CC on silica gel eluting with gradients of hexane, CH_2Cl_2, Me_2CO and MeOH affording **9** (3.1 mg).

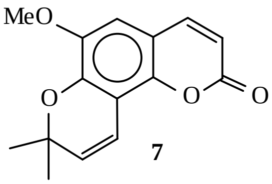
The CH_2Cl_2 extract (4.2 g) was subjected to chromatographic treatments similar to those used for the hexane



1 R_1–R_2 = OCH_2O,
R_3 = R_4 = OCH_3
1a R_1 = R_4 = OCH_3,
R_2–R_3 = OCH_2O
1b R_1 = R_2 = OCH_3,
R_3–R_4 = OCH_2O
2 R_1 = R_4 = H,
R_2 = R_3 = OCH_3
3 R_1 = H,
R_2–R_3 = OCH_2O,
R_4 = OMe



4 R_1 = H, R_2 = OCH_3
5 R_1 = R_2 = OCH_3
6 R_1 = H,
R_2 = $OCH_2CH{=}C(CH_3)_2$



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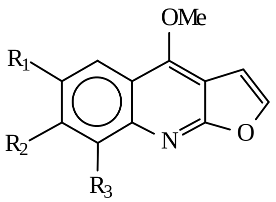
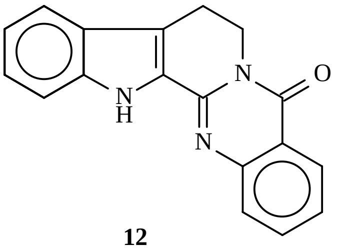


8 R_1 = R_2 = H, R_3 = OMe
9 R_1 = R_2 = OMe, R_3 = H
10 R_1–R_2 = OCH_2O, R_3 = H



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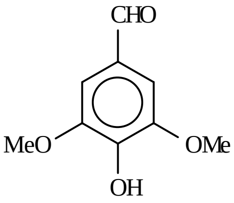

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extract. Frs. 4-5 afforded a mixture (6.3 mg) of lupeol and sitosterol. The Fr. 7 afforded **6** (4.8 mg). Fr. 8 was rechromatographed on silica gel using gradients of hexane, Me_2CO and MeOH yielding **4** (3.7 mg), **6** (8.1 mg), **7** (5.2 mg) and **12** (1.3 mg). Fr. 9 was subjected to CC on silica gel using hexane, Me_2CO and MeOH at different ratios of increasing polarity to give 7.0 mg of the new coumarin **1**, **2** (2.7 mg), **3** (0.5 mg), **4** (6.3 mg), **5** (4.3 mg), **8** (2.3 mg), **10** (3.2 mg), **11** (2.4 mg) and **12** (1.4 mg).

5,6-*Methylenedioxy*-7,8-*dimetoxycoumarin* (**1**). Amorphous solid. ^1H and ^{13}C-NMR: see Table 1.

Results and Discussion

The new coumarin **1** was obtained from the dichloromethane extract of *M. flavida* and showed as a blue color on TLC under UV light 336 nm. Its ^1H NMR spectrum exhibited resonances typical of H-3 and H-4 (δ 6.20 and 7.91) of the coumarin nucleus in which C-5 was oxygenated[11]. The presence of a methylenedioxy group was indicated from the methylene hydrogens signal at δ 6.01 (*s*) and two methoxy groups from the signals at δ 4.04 and 3.99 (*s*, 3H each one). These groups were located at the positions 5, 6, 7 and 8 suggesting one of the possible structures **1**, **1a** or **1b**. Further information concerning the actual positions of the methoxy groups was obtained by analysis of the 1D-NOE difference spectrum. Irradiation of the signal at δ 7.91 (*d*, H-4) didn't enhance the signals at δ 4.04 and 3.99 (2x OMe), which confirmed the placement of the methylenedioxy group at C-5/C-6. This result is consistent with the structure **1**. The assignments of the signals of carbons 3,4 and –OCH_2O- moiety in the ^{13}C-NMR spectrum were established by HETCOR (^{13}C, ^1H-COSY-$^1J_{CH}$) spectrum and the attribution of the quaternary carbons was made by COLOC (^{13}C, ^1H-COSY-$^nJ_{CH}$, n = 2 and 3) experiment (Table 1).

Table 1. NMR data for compound 1 ($CDCl_3$, *J* values, in Hz, are given in parentheses).

Position	^{13}C	^1H	COLOC
2	160.5		H-4
3	112.0	6.20, *d* (9.7)	
4	138.8	7.91, *d* (9.7)	
4a	107.0		H-3
5	142.9		OCH_2O
6	132.8		OCH_2O
7	133.4		MeO-7
8	126.9		MeO-8
8a	143.7		H-4
7-OMe	61.1	4.04, *s*	
8-OMe	61.1	3.99, *s*	
OCH_2O	102.1	6.01, *s*	

Hydrogens correlating with carbon resonance.

This is the first report of the occurrence of one indolopiridoquinazoline alkaloid (rutaecarpine) from the genus *Metrodorea*. This fact reinforces the taxonomic position of the *Metrodorea flavida* into the Cusparieae tribe, due to the occurrence of this type of alkaloid in the tribes Cusparieae and Xanthoxyleae.

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