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COUMARINS FROM *METRODOREA FLAVIDA**

ANA CRISTINA S. BAETAS, MARA S. P. ARRUDA,† ADOLFO H. MÜLLER and ALBERTO C. ARRUDA

Departamento de Química, CCEN, Campus Universitário, Universidade Federal do Pará, 66075-900 Belém, PA, Brazil

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Key Word Index—*Metrodorea flavida*; Rutaceae; coumarin; furocoumarin; furofuran lignan.

Abstract—The leaves of *Metrodorea flavida* have afforded the new coumarin, 8-(2,3-dihydroxy-3-methylbutyll-oxy)-6,7-methylenedioxy-coumarin, in addition to several known furocoumarins, a furofuran lignan, sitosterol and lupeol. Their structures were elucidated on the basis of spectral data. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

The genus *Metrodorea* belongs to the family Rutaceae, sub-family Rutoideae, tribe Cusparieae [1]. From the *ca* eight species contained in the genus, all confined to Brazil [1, 2], only *Metrodorea nigra*, a species that grows in the Brazilian 'cerrado', was studied before [3]. It was reported to contain dihydrochalcones (fruits), coumarins, furoquinoline alkaloids, lignans and steroids (stems and leaves) [3].

The present work, part of our phytochemical and chemotaxonomic study on members of the Cusparieae of the Amazon region, describes the isolation and structural elucidation of sterol, triterpene, lignan and furocoumarin components from the leaves of *Metrodorea flavida*. During the present investigation a new coumarin (**1**) had been isolated.

RESULTS AND DISCUSSION

The leaves of *Metrodorea flavida* were percolated successively with hexane and dichloromethane. From the hexane and dichloromethane extracts we isolated the coumarins, bergapten (**2**) [4], xantotoxin (**3**) [4], heraclenol (**4**) [4] and 8-(2,3-dihydroxy-3-methyl-butylloxy)-6,7-methylenedioxy-coumarin (**1**), the furo-furan lignan eudesmine (**5**) [5, 6], lupeol [7] and sitosterol [8]. The known compounds were identified by comparison of their spectral data with those reported in the literature.

The novel coumarin (**1**) was identified and character-ized by spectroscopic methods. It was observed on TLC as a bluish-white fluorescent spot under UV light (366 nm) and showed UV absorption maxima at 321 and 231 nm, suggestive of a coumarin [9]. The molecu-

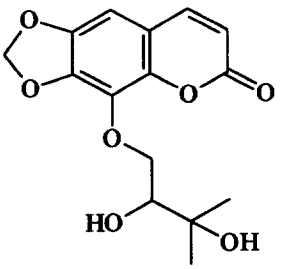
Table 1. ^{1}H NMR (300 MHz), HETCOR and COLOC data for compound **1**

H	**1**	Correlated carbon HETCOR	COLOC
3	6.28 *d* (J = 9.6 Hz)	114.0	C-2, C-4, C-10
4	7.55 *d* (J = 9.6 Hz)	143.6	C-2, C-5, C-9
5	6.60 *s*	100.0	C-4, C-6, C-7, C-9
MD	6.06 *s*	102.6	C-6, C-7
H-1′a	4.53 *dd* (J = 10.0; 2.4 Hz)	75.2	—
H-1′b	4.23 *dd* (J = 10.0; 7.9 Hz)	75.2	—
H-2′	3.78 *dd* (J = 7.9; 2.4 Hz)	76.0	—
Me	1.25 *s*	25.0	C-3′
Me	1.29 *s*	26.6	C-2′

Solution in $CDCl_3$ referenced to $CHCl_3$ at δ 7.26 (^{1}H) and δ 77.23 (^{13}C). Values in parentheses are coupling constants.

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

†Author to whom correspondence should be addressed.



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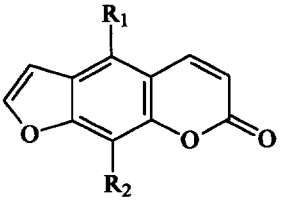
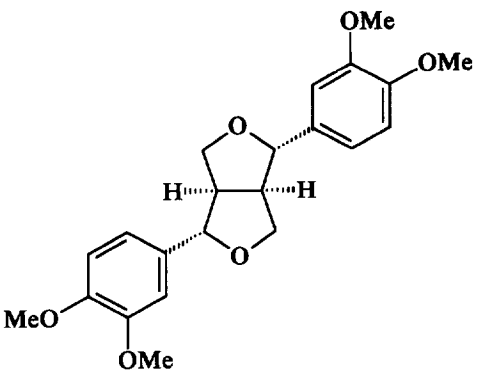


		R_1	R_2
Bergapten	2	OMe	H
Xantotoxin	3	H	OMe
Heraclenol	4	H	$OCH_2CH(OH)C(CH_3)_2OH$



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lar formula was found to be $C_{15}H_{16}O_7$ from EI-mass spectral data. The IR spectrum indicated the presence of a lactone carbonyl typical of coumarin (1710 cm^{-1}) [9]. The ^1H NMR spectrum (Table 1) revealed the typical H-3/H-4 protons of the coumarin nucleus. The chemical shift for H-4 (δ 7.55) indicated the absence of any oxygenation at C-5 [9]. Two more signals indicated an aromatic proton (δ 6.60) and methylenedioxy group (δ 6.06). The remaining signals at δ 4.53 (1H, *dd*, J = 10.0; 2.4 Hz), 4.23 (1H, *dd*, J = 10.0; 7.9 Hz), 3.78 (1H, *dd*, J = 7.9; 2.4 Hz), 1.29 (3H, *s*) and 1.25 (3H, *s*) were attributed to a 2,3-dihydroxy-3-methylbutylloxy substituent, which could be placed at C-8. As there was no oxygenation at C-5, the aromatic singlet must be assigned to H-5 and this was confirmed by a NOE difference experiment, where irradiation of the signal at δ 6.60 enhanced only the signal of the H-4 proton and not the signal of H-1′ which would be expected if the prenyloxy group was at position C-6, confirming the linear orientation of the methylenedioxy. The ^{13}C NMR spectrum was assigned by DEPT pulse sequence (Table

Table 2. ^{13}C NMR (75 MHz) spectral data of compound **1**

C	1	DEPT
2	160.2	C
3	114.0	CH
4	143.6	CH
5	100.0	CH
6	145.6*	C
7	141.3*	C
8	130.7	C
9	143.7	C
10	113.3	C
1′	75.2	CH_2
2′	76.0	CH
3′	71.4	C
Me	25.0	CH_3
Me	26.6	CH_3
MD	102.2	CH_2

Solution in $CDCl_3$ referenced to $CHCl_3$ at δ 77.23.

*Interchangeable signals.

2) and HETCOR spectrum (Table 1). The remaining problem of assigning the quaternary carbon atoms was addressed by a heteronuclear multiple bond correlation (COLOC) experiment (Table 1) optimized for $^{2}J_{(CH)}$ and $^{3}J_{(CH)}$ coupling.

The classes of compounds we have isolated from *Metrodorea flavida* reinforces its position as a member of the Rutaceae [10].

EXPERIMENTAL

General. 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. 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, leaves (391 g) were ground and percolated with hexane and CH_2Cl_2, successively. The concd hexane extract (9.3 g) was subjected to CC on silica gel using hexane, EtOAc and MeOH at different ratios of increasing polarity furnishing 36 frs. Frs 19–25 afforded a mixt of sitosterol and lupeol (27 mg). Fr. 28 afforded bergapten (44 mg) after recrystn with MeOH. Fr. 31 was subjected to rechromatography on silica gel using hexane, EtOAc and MeOH at different ratios of increasing polarity to yield 33 mg of xantotoxin. The CH_2Cl_2 extract (5.7 g) was suspended in 50% aq. MeOH and partitioned with hexane, CH_2Cl_2 and MeOH, respectively. Part of the hexane–soluble fr. (100 mg) after recrystn with MeOH yielded bergapten (7.4 mg). The CH_2Cl_2-sol fr. (1.2 g) was submitted to CC on silica gel using hexane, CH_2Cl_2 and MeOH at different ratios of increasing polarity to give 27 frs. Fr. 5 afforded lupeol (5 mg). Fr. 8 afforded sitosterol (6.2 mg). Fr. 22 after repeated CC and prep. TLC on silica gel afforded heraclenol (7.8 mg) and **1** (3.4 mg). The EtOAc-soluble fr. (730 mg) was subjected to CC on silica gel using hexane, EtOAc and MeOH as eluent. Fr. 12 afforded the furofuran lignan eudesmine (3.0 mg).

8-(2,3-*Dihydroxy*-3-*methylbutylloxy*)-6,7-*methylenedioxy-coumarin* (**1**). Amorphous solid. $[\alpha]_D$ +13.6° ($CHCl_3$; *c* 0.5). IR ν_{max} cm^{-1}: 3420, 2920, 1710, 1586, 1434. ^{1}H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z* (rel. int.): 308 $[M]^+$ (4), 206 $[M - C_5H_{10}O_2]^+$ (100), 178 $[206 - CO]^+$ (44), 59 $[C_3H_7O]^+$ (15).

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